Macromolecules
ARTICLE

Macromolecules **2009**, *42*, 9435–9442 **9435**
DOI: 10.1021/ma901713p

Synthesis of Poly(*n*-butyl acrylate)-*b*-poly(ε-caprolactone) through Combination of SG1 Nitroxide-Mediated Polymerization and $Sn(Oct)_2$-Catalyzed Ring-Opening Polymerization: Study of Sequential and One-Step Approaches from a Dual Initiator

Nelly Chagneux,[†] Thomas Trimaille,*[,†] Marion Rollet,[†] Emmanuel Beaudoin,[†] Pierre Gérard,[‡] Denis Bertin,[†] and Didier Gigmes[†]

[†]*Laboratoire Chimie Provence (LCP), UMR 6264, Universités d'Aix-Marseille I, II et III-CNRS, Equipe Chimie Radicalaire Organique et Polymères de Spécialité, Case 542, Av. Escadrille Normandie-Niemen, 13397 Marseille Cedex 20, France and* [‡]*ARKEMA, Groupement de Recherches de Lacq, BP 64, 64170 Lacq, France*

Received July 31, 2009; Revised Manuscript Received October 24, 2009

ABSTRACT: A hydroxyl-functionalized alkoxyamine derived from the SG1 nitroxide was used as a dual initiator for ring-opening polymerization (ROP) of ε-caprolactone (CL) and nitroxide-mediated polymerization (NMP) of *n*-butyl acrylate (BA) to obtain the corresponding block copolymer. Both sequential and *one-step* strategies were investigated, using the tin(II) 2-ethylhexanoate ($Sn(Oct)_2$) ROP catalyst. The *NMP first* sequential approach (consisting of performing the NMP before the ROP) successfully provided the diblock copolymer through well-controlled NMP and ROP processes. This copolymer was fully characterized by size exclusion chromatography (SEC), liquid chromatography at the critical conditions (LC-CC) of PBA and PCL, and gradient polymer elution chromatography (GPEC). Conversely, the *ROP first* strategy led to badly defined PCL (bimodal distribution) in the first ROP step. This was attributed to a side reaction of $Sn(Oct)_2$ with the SG1 nitroxide arising from the alkoxyamine dissociation at the ROP temperature. This strategy was consequently not suitable for obtaining the diblock copolymers. Finally, PBA-*b*-PCL copolymers were successfully prepared from the dual initiator through a NMP/ROP *one-step* process in toluene, as shown by ^{1}H NMR spectroscopy, SEC, and GPEC. The success of this *one-step* approach was explained by a much faster consumption of the BA by NMP than that of the CL by ROP, making the process looking like a *NMP first* in a one pot experiment.

Introduction

Block copolymers containing a biodegradable aliphatic polyester block (like polycaprolactone (PCL) or polylactide (PLA)) have been receiving increasing attention over the past decade due to their potential in bio-related applications,[1] as compatibilizing agents for polymer blends,[2] or for the fabrication of nanoporous materials.[3] These block copolymers can be now easily obtained through the combination of ring-opening polymerization (ROP) and controlled radical polymerization (CRP), such as atom transfer radical polymerization (ATRP), reversible addition−fragmentation chain transfer (RAFT), and nitroxide-mediated polymerization (NMP). Several strategies can be envisioned to achieve such block copolymers: (i) macromolecular coupling between two homopolymers bearing complementary reactive functions, for example through the use of click chemistry,[4] (ii) end-chain functionalization of the first block with the suitable moiety to initiate the second polymerization type (macro-initiator approach),[5] or (iii) the use of heterobifunctional initiator able to initiate both polymerizations.[6−8] These different ROP/CRP combination pathways have been recently reviewed by Dove.[9] Among these three methods, the latter "dual initiator" strategy is particularly attractive due to the limited number of steps to afford the block copolymer and the possibility of a *one-step* process. Regarding this approach, ROP/ATRP combination[10] has been extensively used compared to ROP/RAFT and ROP/NMP, mainly because of the easy preparation of the difunctional initiators, particularly through the use of commercially available halogenoalkyl halide reactants (such as bromoisobutyryl bromide). Up to now, the approaches to combine ROP and NMP from a difunctional initiator have been principally based on 2,2,6,6-tetramethylpiperidinoxyl (TEMPO)[7,11] and 2,2,5-trimethyl-4-phenyl-3-azahexane-3-oxy (TIPNO)[12] nitroxides and often required a multistep synthesis for preparation of the initiator. In a recent paper,[13] we described the potential of an easily accessible hydroxyl-functionalized alkoxyamine derived from the *N*-*tert*-butyl-*N*-1-diethylphosphono-(2,2-dimethylpropyl) (SG1) nitroxide as a dual initiator for ROP and NMP. This alkoxyamine was obtained from simple reaction of the *N*-hydroxysuccinimide (NHS) ester activated MAMA-SG1[14] (BlocBuilder, from Arkema Co.) with ethanolamine and successfully used to prepare polystyrene-*b*-poly(DL-lactide) (PS-*b*-PLA) block copolymers by combining the NMP and ROP techniques. In the present paper we aimed at focusing on the combination of tin(II) 2-ethylhexanoate ($Sn(Oct)_2$)-catalyzed ROP and NMP from this difunctional initiator to prepare block copolymers. $Sn(Oct)_2$ is one of the most used catalysts for ROP, since it presents numerous advantages such as solubility in many organic solvents, stability on storage, and FDA approval, making it attractive for biomedical and food packaging applications. Additionally, this catalyst is typically used at ROP

*To whom correspondence should be addressed. E-mail: thomas.trimaille@univ-provence.fr.

Published on Web 11/17/2009

temperatures of 90−130 °C, corresponding roughly to the temperature range used in SG1-NMP, which allows to envision ROP/NMP combination upon *one-pot* or *one-step* processes. We particularly focused on poly(*n*-butyl acrylate)-*b*-poly(ε-caprolactone) (PBA-*b*-PCL) block copolymers which are promising precursors of impact modifiers of amorphous matrices.[15] In this study, both sequential and *one-step* type processes for ROP/NMP combination were investigated to achieve the diblock copolymers.

Experimental Section

Materials. BlocBuilder (MAMA-SG1, >99%) was kindly provided by Arkema (France). *n*-Butyl acrylate (BA, 99%), pivalic acid (99%), *N*-hydroxysuccinimide (NHS, 98%), *N*,*N*′-dicyclohexylcarbodiimide (DCC, 99%), ethanolamine (99%), and tin(II) 2-ethylhexanoate ($Sn(Oct)_2$, 95%) were purchased from Aldrich and used as received. ε-Caprolactone (CL, 99%) was purchased from Aldrich and distilled over calcium hydride. Toluene was distilled over sodium/benzophenone, and other solvents were used as received.

Synthesis of Initiators. The dual-headed initiator was synthesized and characterized as previously described.[13] The model initiator *N*-(2-hydroxyethyl)pivalamide) was obtained through activation of the pivalic acid with *N*-hydroxysuccinimide (NHS), followed by reaction with ethanolamine: DCC (11.1 g, 53,8 mmol) in tetrahydrofuran (THF, 5 mL) was dropwise added to a mixture of pivalic acid (5 g, 48.9 mmol) and NHS (6.76 g, 58.7 mmol) in THF (45 mL). After filtration of the white precipitate of dicyclohexylurea (DCU), the THF was distilled off and the resulting white gum was dissolved in ethyl acetate. The obtained solution was placed at −20 °C overnight to precipitate the residual DCU. After filtration, ethyl acetate was distilled off, leading to the NHS ester of pivalic acid, as a white powder (yield: 61%, 6.74 g). ^{1}H NMR (ppm, D_2O): 2.83 (s, 4H, $-CH_2-CH_2-$), 1.39 (s, 9H, $C(CH_3)_3$). Ethanolamine (1.6 mL, 26.5 mmol) was dropwise added to the NHS ester derivative (3.5 g, 17.6 mmol) in acetonitrile (150 mL), and a white precipitate corresponding to the expected *N*-(2-hydroxyethyl)pivalamide) rapidly appeared. The mixture was further stirred for 1 h. The product was filtered, washed with acetonitrile, and further dried under vacuum (yield: 93%, 2.4 g). ^{1}H NMR (ppm, D_2O): 3.78 (t, 2H, $-CH_2-OH$), 2.61 (t, 2H, $-CH_2-NH-CO-$), 2.62 (s, 9H, $-C(CH_3)_3$), ESI MS: $[M + H]^+ = 146$.

Polymerizations. *NMP of BA*. Typically, BA (70 g, 0.546 mol), dual initiator (0.99 g, 2.3 mmol, for a targeted M_n of 30 000 g mol^{-1}), and free SG1 (7 mg, 0.023 mmol) were introduced in a 250 mL two-neck round-bottom flask, fitted with septum and condenser, and degassed for 20 min by argon bubbling. The mixture was then heated to 115 °C (25 min ramp temperature: 20−115 °C) under argon with vigorous stirring. After polymerization, the mixture was cooled by immersing the flask in iced water, and the residual BA was removed under vacuum at 60 °C.

ROP of CL. ROP experiments were run either in bulk or toluene from dual initiator or PBA−OH at different temperatures (80−120 °C) with $Sn(Oct)_2$ as catalyst. Typically, the dual initiator (0.848 g, 2 mmol) and $Sn(Oct)_2$ (0.405 g, 1 mmol) were placed in a Schlenk, submitted to vacuum/argon cycles. CL (20 g, 0.175 mol, for a targeted M_n of 10 000 g mol^{-1}) and toluene (when needed) were then added through the septum under argon atmosphere in the Schlenk, which was finally immersed into an oil bath previously heated to the desired temperature. After polymerization, the mixture was quenched with nondistilled THF. The polymer was precipitated in cold methanol and dried at 30 °C under vacuum. For the *one-step* experiments, a similar procedure was followed, except that BA was introduced in the Schlenk with CL.

Analytical Techniques. ^{1}H NMR (300 MHz) analysis was performed on a Bruker Avance 300 spectrometer in $CDCl_3$, D_2O, or DMSO-d_6.

Size Exclusion Chromatography (SEC). The determinations of polymer molecular weights and molecular weight distribution were performed on a system composed of a Waters 515 HPLC pump equipped with a precolumn Macherey Nagel Nucleogel (50 × 7.7 mm), two Nucleogel columns (Macherey Nagel) used in series 104-5 (300 × 7.7 mm, separation between 5000 and 500 000 g mol^{-1}) and 103-5 (300 × 7.7 mm, separation between 500 and 60000 g mol^{-1}), and placed in an oven at 30 °C, and two detectors: UV/vis (Waters 486) and RI (Waters 2414) A third column, 100-5 (300 × 7.7 mm, separation until 4000 g mol^{-1}) was used in some cases. THF was the mobile phase, with a flow rate of 1 mL min^{-1}. Calibration was based on polystyrene standards. PBA molecular weights were determined using the Mark−Houwink parameters in THF at 30 °C ($K_{PS} = 11.4 \times 10^{-3}$ mg L^{-1}, $\alpha_{PS} = 0.716$; $K_{PBA} = 12.2 \times 10^{-3}$ mg L^{-1}, $\alpha_{PBA} = 0.700$).[16] PCL molecular weights were determined by applying a correction factor of 0.56 to the M_n obtained from PS calibration.[17]

Liquid Chromatography at Critical Conditions (LC-CC). The analysis was carried out with a system consisting of an Waters Alliance 2695 module, a column oven at 30 °C, and an evaporative light scattering detector PL-ELS 2100 (Polymer Laboratories) and a RI detector in some cases. A flow rate of 0.7 mL min^{-1} was used. The injected volume was 20 μL. Critical conditions for PBA were obtained in reverse phase with two C18 Nucleosil columns in series (250 mm × 4.6 mm; 5 μm particle size, 300 and 120 Å pore size respectively) from Macherey-Nagel for a THF/acetonitrile 50/50 (w/w) eluent mixture. The H-PBA-H standards of different molecular weights (6000 to 45000 g mol^{-1}) used for searching the CC were prepared by NMP initiated by the SG1-$C(H)MeC(O)_2Bu$ alkoxyamine, followed by treatment of the SG1 moiety with thiophenol (10 equiv) in *tert*-butylbenzene at 130 °C. Critical conditions for PCL were obtained in normal phase with two Nucleosil columns in series (250 mm × 4.6 mm; 7 μm particle size, 300 and 100 Å pore size, respectively) from Macherey-Nagel, for an acetone/hexane 55.6/44.4 (w/w) eluent mixture.[18] Polymer sample solutions were prepared in the corresponding eluent mixture at 0.5 wt %. The PCL standards (5000−20 000 g mol^{-1}) used for determining the CC were prepared by ROP of CL with $Sn(Oct)_2$ as catalyst (bulk at 110 °C).

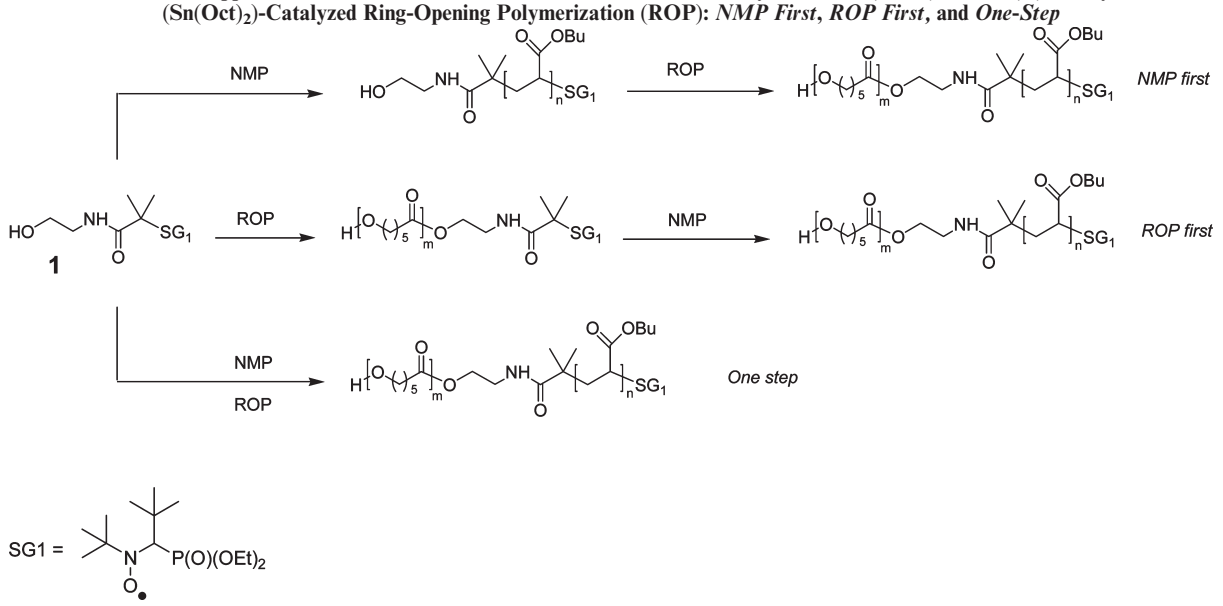
Normal Phase Gradient Polymer Elution Chromatography (NP-GPEC). The measurements were carried out with a system consisting in an Waters Alliance 2695 module, a column oven, and an evaporative light scattering detector PL-ELS 2100 (Polymer Laboratories). A Nucleosil column (250 mm × 4.6 mm; 7 μm particle size, 100 Å pore size) from Macherey-Nagel was used at 30 °C. Dilute polymer solutions were made in THF (2.5 mg/mL). The injected volume was 20 μL. At a constant flow rate of 0.8 mL min^{-1}, a linear binary gradient in heptane/THF (nonsolvent/solvent for the polymers used in the analysis, respectively) starting from 100:0 at $t = 0$ min to 0:100 at $t = 20$ min was used, followed by constant flow of THF during 10 min, and finally a reverse gradient from 0:100 to 100:0 (heptane/THF) in 15 min for the subsequent analysis.

Matrix-Assisted Laser Desorption-Ionization Time-of-Flight (MALDI TOF) Mass Spectrometry. The analysis was performed using a Autoflex mass spectrometer (Bruker) equipped with a MALDI ionization source (laser power ($\lambda = 337$ nm): 42%). A solution of PCL at 1.3 g L^{-1} in THF (5 μL) was mixed with 40 μL of 2,5-dihydroxybenzoic acid at 20 g L^{-1} in THF and 2 μL of sodium iodine solution at 5.4 g L^{-1} in THF. This mixture (1 μL) was placed on the target for analysis.

Results and Discussion

Our methodology to prepare the PBA-*b*-PCL copolymers is based on the combination of ROP and NMP from a hydroxyl-functionalized alkoxyamine derived from SG1. This alkoxyamine was obtained in two steps, as previously described,[13] through

Scheme 1. Different Approaches Envisioned To Combine Nitroxide-Mediated Polymerization (NMP) and Tin(II) 2-Ethylhexanoate ($Sn(Oct)_2$)-Catalyzed Ring-Opening Polymerization (ROP): *NMP First*, *ROP First*, and *One-Step*



(i) activation of the carboxylic function of the MAMA-SG1 alkoxyamine (also referred as BlocBuilder) with *N*-hydroxysuccinimide and (ii) reaction with the amino group of ethanolamine. The obtained compound **1** presents both SG1 and hydroxyl moieties that can initiate NMP and ROP processes, respectively (Scheme 1). The dissociation rate constant of this alkoxyamine (k_{d1}) was measured by electron paramagnetic resonance (EPR) following a previously described procedure[19] in *tert*-butylbenzene at 120 °C, and the activation energy E_a was estimated using the average frequency factor 2.4×10^{14} s^{-1}.[19,20] The k_{d1} value was found to be of 5.8×10^{-3} s^{-1} (E_a = 125 kJ mol^{-1}), much lower than the k_{d1} measured for MAMA-SG1 and NHS-activated MAMA-SG1 under the same experimental conditions (k_{d1} = 0.32 s^{-1}, E_a = 112 kJ mol^{-1} and k_{d1} = 5 s^{-1}, E_a = 103 kJ mol^{-1}, respectively).[13] This value was rather unexpected for a tertiary alkoxyamine. The secondary amide function is strongly suspected to be involved in the stabilization of this alkoxyamine, through hydrogen bonding.[21] This initiator was further exploited for combining ROP of CL and NMP of BA, first following a sequential approach (*NMP first*, consisting in performing the NMP step before the ROP one, or *ROP first*) and then a *one-step* strategy (Scheme 1).

***NMP First* Approach.** The *NMP first* approach was first envisioned from this dual initiator, which consists of initiating NMP step before the ROP. Considering the low dissociation constant of the dual initiator **1**, free SG1 had to be added in the medium for the NMP of the BA monomer, which presents high propagation rate constant (k_p), to help the persistent radical effect to take place.[22] The NMP was performed at 115 °C, with 1 mol % free SG1 compared to initiator, targeting a M_n of 30 000 g mol^{-1}. The evolution of the $\ln([M]_0/[M])$ vs time (Figure 1a) appeared to be a smooth upward-curving function rather than a strictly linear one. Yet, a linear evolution of the M_n (determined from SEC in THF by universal calibration using the Mark−Houwink coefficients) with conversion was observed, very close to the theoretical curve, and polydispersities remained quite narrow (PDI ∼ 1.3), showing the controlled character of the polymerization (Figure 1b).

The obtained OH-functionalized PBA polymer (at 45% conversion, M_n = 15 000 g·mol^{-1}, PDI = 1.25) was further used, after BA removal, as macroinitiator for $Sn(Oct)_2$-catalyzed ROP of CL. The ROP was performed in bulk at

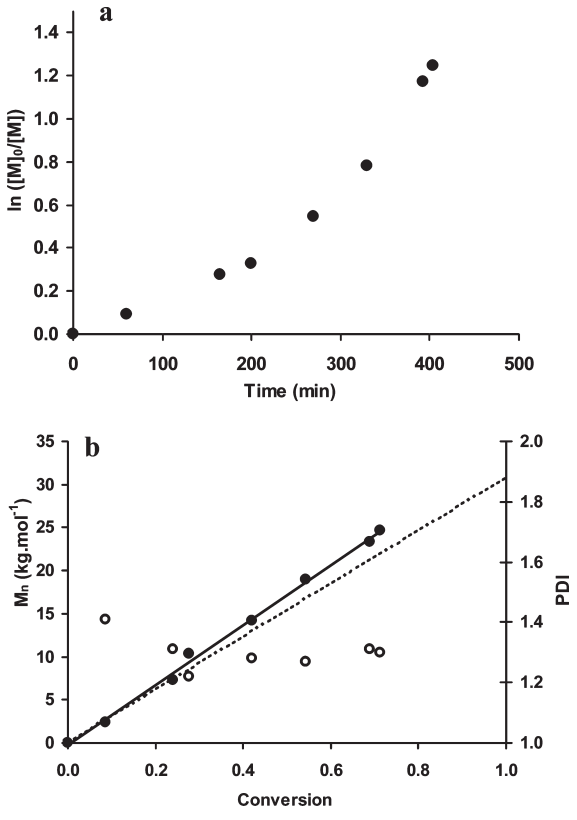


Figure 1. (a) Plots of $\ln([M]_0/[M])$ vs time and (b) number-average molecular weight (M_n, ●) and polydispersity index (PDI, ○) vs conversion curves for the nitroxide-mediated polymerization of *n*-butyl acrylate (BA) in bulk at 115 °C, with 1 mol % of free SG1 compared to initiator (dotted line is the theoretical curve). Molecular weights were obtained from universal calibration.

120 °C, using a catalyst-to-macroinitiator molar ratio of 0.5 and targeting a PCL molecular weight of 10 000 g mol^{-1}. The polymerization appeared to be well controlled, as shown in Figure 2a,b, from the linear evolution of both the $\ln([M]_0/[M])$ as a function of time and the M_n as a function of conversion, respectively, together with acceptable polydispersity values (PDI ∼ 1.5). The SEC trace of the final

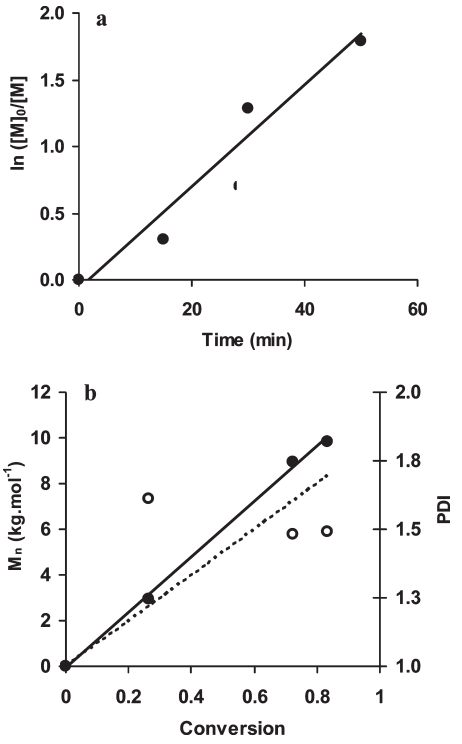


Figure 2. (a) Plot of $\ln([M]_0/[M])$ vs time and (b) number-average molecular weight (M_n, ●) and polydispersity index (PDI, ○) vs conversion curves for the ring-opening polymerization of ε-caprolactone (CL) from hydroxyl-terminated poly(*n*-butyl acrylate) (PBA−OH) in bulk at 120 °C with a $Sn(Oct)_2$ to PBA−OH ratio of 0.5 (dotted line is the theoretical curve).

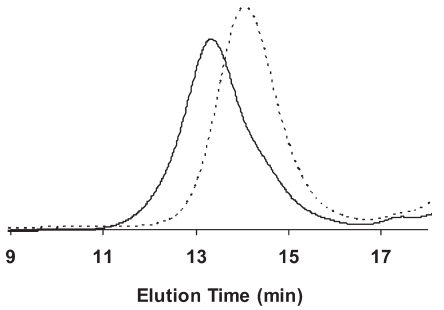


Figure 3. Size exclusion chromatography analysis of the final poly(*n*-butyl acrylate)-*b*-poly(ε-caprolactone) (PBA-*b*-PCL) copolymer (continuous line) and hydroxyl-terminated PBA (PBA−OH) precursor (dotted line).

copolymer was clearly shifted to higher molecular weights, comparing to the PBA−OH precursor (Figure 3). A slight shoulder toward low molecular weight was however observed (explaining the PDI value of about 1.5, Figure 2b). Liquid chromatography at critical conditions (LC-CC)[23] was then used to further characterize the copolymers and particularly to detect the presence of eventual homopolymers in the copolymer sample. At critical conditions of a given polymer species, obtained at the transition point between exclusion and adsorption modes, the retention of this polymer becomes independent of the hydrodynamic volume (i.e., molecular weight) and is only dictated by the chemical structure, i.e., end groups (functionality or second block for a copolymer) or architecture. Applied to block copolymers, it means that at the CC of PBA, for example, PBA homopolymers can be separated from PBA-*b*-PCL copolymers, whose elution volume is dictated by the PCL

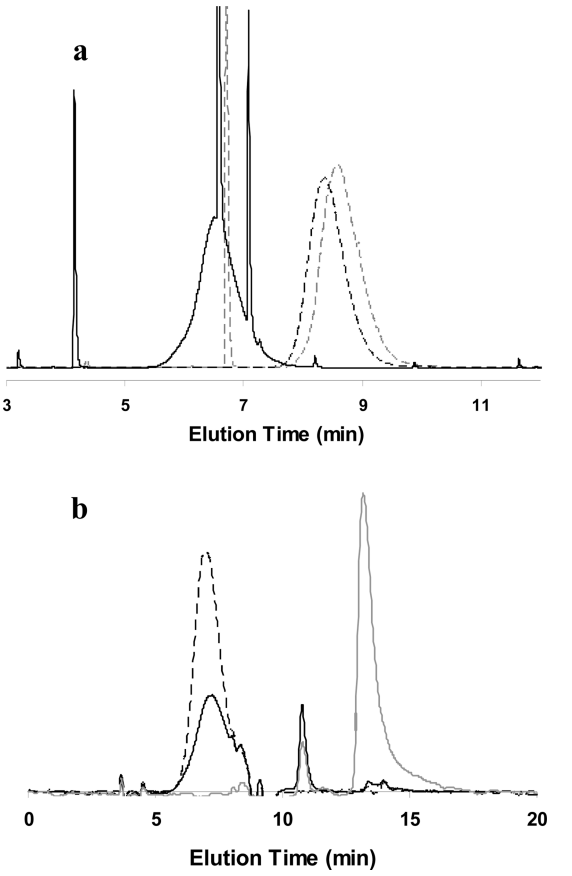


Figure 4. Liquid chromatography at critical conditions (LC-CC) analysis of the poly(*n*-butyl acrylate)-*b*-poly(ε-caprolactone) (PBA-*b*-PCL) copolymer (continuous black line) and hydroxyl-terminated PBA (PBA−OH) precursor (dotted black line): (a) at the critical conditions of PBA (in dotted gray line, chromatogram of a PBA standard polymer used for searching the PBA CC); (b) at the critical conditions of PCL (in gray line, chromatogram of a PCL standard polymer used for searching the PCL CC).

block (PBA is "chromatographically" invisible). The reverse is true at the critical conditions of PCL. Typically, to find the critical conditions of a given polymer, standard samples of different molecular weights were prepared, and the composition of adsorli/desorli eluent mixture was varied until that the elution time was independent of the polymer molecular weight. Critical conditions for PBA were obtained in reverse phase with a THF/acetonitrile 50/50 (w/w) eluent mixture (Figure S1, Supporting Information) for PBA standards ranging from 6000 to 45 000 g/mol. Critical conditions for PCL were obtained in normal phase with an acetone/hexane 55.6/44.4 (w/w) mixture[18] for PCL standards ranging from 5000 to 20 000 g/mol (Figure S2a). For both PBA and PCL critical conditions, we checked that the other homopolymer was eluted in exclusion (Figures S1 and S2b). In Figure 4a are presented the chromatograms of the PBA−OH homopolymer precursor and the block copolymer sample at the critical conditions of PBA. Despite some electric artifacts during the ELS detection, the analysis of the copolymer sample clearly showed the absence of residual PBA−OH precursor, indicating a very good initiation efficiency of the ROP from this macroinitiator. This shows that the slight shouldering toward low molecular weights observed on the SEC chromatogram (Figure 3) does not correspond to residual PBA−OH precursor, as it could be suspected at first sight. The copolymer sample was then further analyzed at the critical conditions of the PCL (Figure 4b). Interestingly, the

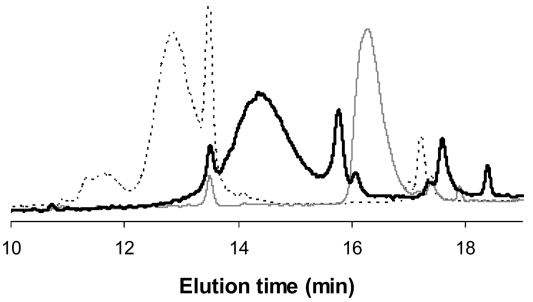


Figure 5. Normal phase gradient polymer elution chromatography (NP-GPEC) analysis of the poly(*n*-butyl acrylate)-*b*-poly(ε-caprolactone) (PBA-*b*-PCL) copolymer (continuous black line) compared to that of the hydroxyl-terminated PBA (PBA−OH) precursor (dotted black line). Commercial PCL of 10 000 g mol^{-1} (continuous gray trace) is also shown as a reference.

analysis showed, beside the expected diblock PBA-*b*-PCL (peak at 7.1 min), the presence of a few amount of PCL homopolymer species at 10.3 and 12.9 min, by comparing with the PCL standard showed as reference (see also Figure S2a). These side PCL species are most probably due to side ROP initiation of CL from water traces in the medium (Figure S3). Finally, it has to pointed out here that negative solvent peak was observed after the copolymer peak in RI detection. This may indicate a preferential solvation of the copolymer in one of the two solvents of the binary mixture (common phenomenon in LC−CC). Negative values of intensity were truncated in Figure 4b for sake of clarity.

Finally, the copolymer sample was analyzed by normal phase gradient polymer elution chromatography (NP-GPEC),[24] which consists of eluting the copolymer from an apolar solvent (heptane, 100% at $t = 0$ min) to a more polar one (THF, 100% at $t = 20$ min), performing a linear binary solvent gradient. The PBA−OH precursor and a PCL homopolymer ($M_n \sim 10\,000$ g·mol^{-1}) were injected as controls. Being less polar, the PBA−OH was eluted before the PCL ($t \sim 12.9$ min for PBA, $t \sim 16.3$ min for PCL), as shown in Figure 5. As expected, the PBA-*b*-PCL copolymer sample was eluted between the homopolymers ($t \sim 14.4$ min), demonstrating the block architecture. Despite the presence of a side peak due to an impurity in the system (13.5 min) and some minor side peaks arising from the sample, the analysis also confirmed the absence of residual PBA−OH precursor, corroborating the LC-CC analysis. The presence of PCL homopolymer side product in the copolymer sample could be strongly hypothesized as well, from peaks around 16 min, even if their position is slightly before the peak position of the reference PCL of 10 000 g/mol. Indeed, even if GPEC separation is mainly based on the difference in polarity between the different samples, a slight deviation between different molecular weight of the same sample is possible.

***ROP First* Approach.** The *ROP first* approach consisted of initiating the ROP of the CL before the NMP step was also investigated. The ROP of the CL from the dual initiator **1** was performed either in bulk or toluene. Surprisingly, whatever the conditions (bulk or toluene, temperatures ranging from 80 to 120 °C, catalyst/initiator molar ratio from 0.05 to 0.5), no optimal control could be obtained, since a bimodal distribution was observed by SEC, as shown in Figure 6a (for the ROP of CL at 120 °C in bulk with a catalyst/initiator ratio of 0.5), even if the M_n vs conversion curve was quite linear and fitted with the theoretical one (Figure 6b). To investigate the potential implication of the SG1 fragment in this lack of ROP control, a model initiator bearing a methyl group instead of the

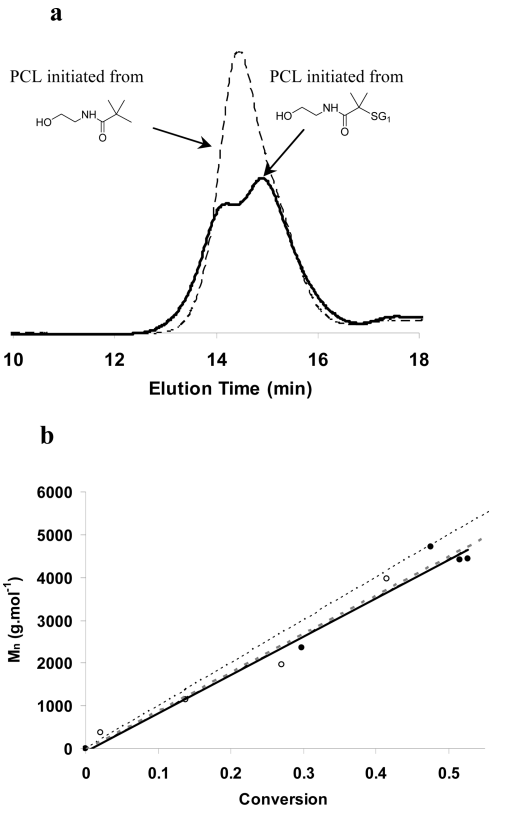


Figure 6. (a) Size exclusion chromatography (SEC) analysis (at 65 min polymerization) and (b) number-average molecular weight (M_n) vs conversion curves of poly(ε-caprolactone) (PCL) obtained from the dual initiator **1** (continuous trace) or from the model initiator (dotted trace) by ring-opening polymerization in bulk at 120 °C (catalyst/initiator molar ratio of 0.5). Theoretical curve for (b) is the thin dotted trace.

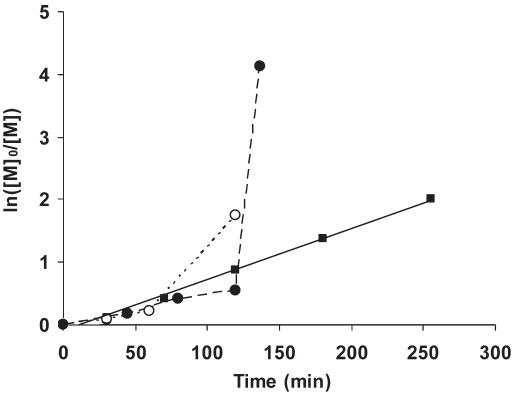


Figure 7. Effect of $Sn(Oct)_2$ catalyst onto the kinetics of nitroxide-mediated polymerization (NMP) of *n*-butyl acrylate initiated with the MAMA-SG1 alkoxyamine (in presence of free SG1): (■) reference NMP; (○) $Sn(Oct)_2$ addition after 65 min polymerization; (●) $Sn(Oct)_2$ addition after 125 min polymerization.

SG1, namely *N*-(2-hydroxyethyl)pivalamide, was prepared. In strictly same conditions, a monomodal and symmetric distribution (as well as a good ROP control) was obtained from this model initiator (Figure 6a,b), indicating that the SG1 moiety was involved in the perturbation of the ROP process.

Further experiments consisting in adding $Sn(Oct)_2$ in the NMP medium of *n*-butyl acrylate initiated with the MAMA-SG1 alkoxyamine (which is known to be well controlled[22]) showed a runaway of the polymerization just after the adding

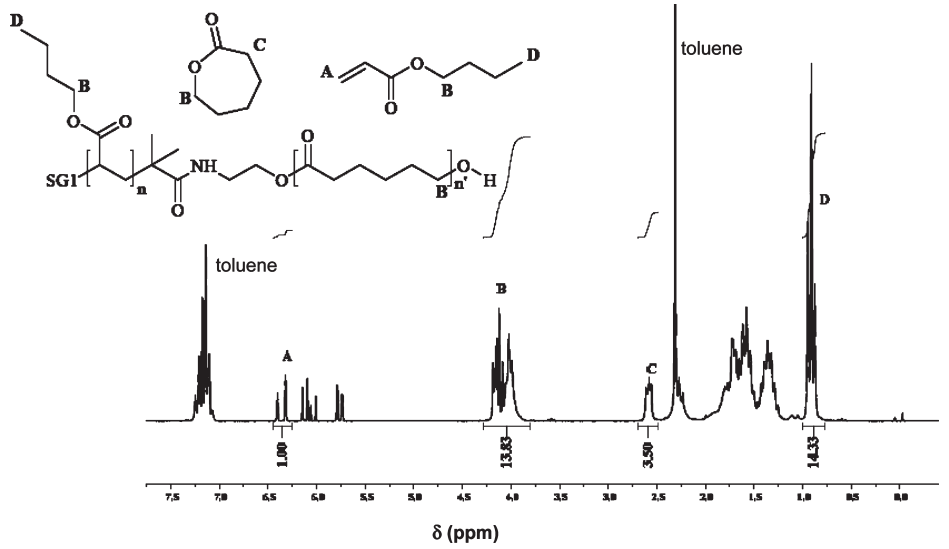
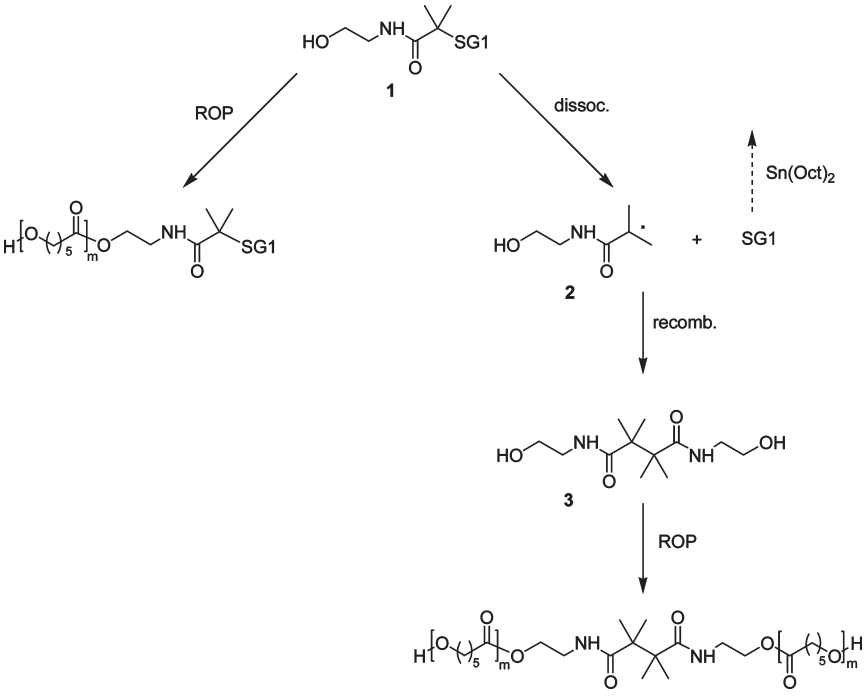


Figure 8. ^{1}H NMR ($CDCl_3$) spectrum of the crude mixture (withdrawn at 200 min) of the *one-step* synthesis of poly(*n*-butyl acrylate)-*b*-poly(ε-caprolactone).

Scheme 2. Probable Reaction Pathway Explaining the Bimodal Distribution of the Poly(ε-caprolactone) Obtained by Ring-Opening Polymerization from the Dual Initiator 1



(Figure 7). This strongly suggests a consumption of the SG1 nitroxide by the $Sn(Oct)_2$, preventing the recombination of PBA macro-radicals with the SG1 into dormant species and thus leading to uncontrolled propagation. A control experiment consisting in heating of a mixture of SG1 nitroxide and excess of $Sn(Oct)_2$ at 80 °C indeed led to colorless solutions, indicating the disappearance of the SG1. Further EPR studies on these mixtures in *tert*-butylbenzene revealed a decrease of the SG1 signal to less than 10% of the initial amount. Previous studies reported in the same way the occurrence of rapid addition reactions of TEMPO nitroxides onto divalent tin-based compounds,[25] similar to $Sn(Oct)_2$.

Considering these results, a quite plausible explanation for the bimodal distribution obtained for the ROP of CL from the dual initiator was formulated in the Scheme 2. During ROP, the free SG1 nitroxide formed from the initiator is consumed by the $Sn(Oct)_2$. This prevents the occurrence of the persistent radical effect, namely the excess of SG1 nitroxide compared to the terminating transitory radicals **2**, which normally favors the displacement of the equilibrium toward alkoxyamine initiator **1**. As a result, the significant formation of some dihydroxylated species (3) by self-termination of the radical fragments **2** is observed, and these species **3** yield over polymerization to PCL chains that are of double molecular weight compared to those initiated with the intact dual initiator **1**, explaining the bimodal distribution.

This hypothesis was confirmed by performing a deconvolution of the SEC chromatogram of the PCL obtained from the dual initiator **1** (Figure 6a), which revealed a ratio of about 2 between the both deconvoluated peak molecular weights (about 5000 and 12 000 g mol^{-1}). Finally, MALDI TOF analysis also supported our assumption since,

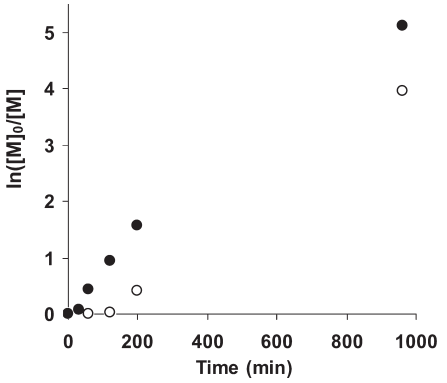


Figure 9. Plot of $\ln([M]_0/[M])$ vs time for the *one-step* nitroxide-mediated polymerization of *n*-butyl acrylate (filled circles) and ring-opening polymerization of ε-caprolactone (empty circles) in toluene at 110 °C ($Sn(Oct)_2$ to initiator molar ratio of 0.5, 1 mol % free SG1 compared to initiator, 50 wt % monomer in toluene).

besides the expected species, it was detected the presence of PCL chains arising from the dihydroxyl initiator **3** and terminated at both chain ends by an octanoate ester instead of a hydroxyl group. The latter termination is due to the esterification of the hydroxyl end groups of the PCL chains with octanoate, which was previously reported to occur, particularly at such high $Sn(Oct)_2$ concentrations ($Sn(Oct)_2$/initiator molar ratio of 0.5).[26]

The *ROP first* approach was then not applicable for the block copolymer formation due to the interaction between the $Sn(Oct)_2$ and SG1 species. Regarding these results, one can reasonably wonder why the ROP of the CL from the previously obtained HO-PBA-SG1 by NMP (*NMP first* approach) is relatively well controlled and does not lead to such bimodal distributions. Indeed, the same mechanism of formation of dihydroxyl species could be expected upon dissociation of the PBA macro-alkoxyamine. However, here the termination between two HO-PBA macroradicals, which is known to be controlled by diffusion, is expected to be limited considering the macromolecular nature of the species concerned and the viscosity of the medium.

***One Step* Approach.** The *one-step* NMP/ROP approach was finally tested from the heterobifunctional initiator **1**, in bulk or toluene solution at 110 °C, with $Sn(Oct)_2$ to initiator molar ratio of 0.5 and 1 mol % free SG1 compared to initiator and targeting molecular weights of 30 000 and 10 000 g mol^{-1} for the PBA and PCL blocks, respectively. The conversions in each monomer could be calculated from ^{1}H NMR of the crude mixtures (Figure 8) as follows, by calibrating the integral of one BA vinyl proton (6.4 ppm) at 1 ($A = 1$):

$$c_{BA} = (D-3)/D \qquad c_{CL} = (B-(2/3)D-C)/(B-(2/3)D)$$

where D is the integral of the signal at 0.91 ppm corresponding to the CH_3 protons of the PBA polymer and BA monomer, B is the integral of the broad signal at 4.1 ppm relative to the $CH_2OC(O)$ protons of the PBA and PCL polymers and BA and CL monomers, and C is the integral of the signal at 2.58 ppm relative to the $CH_2C(O)O$ protons of the CL monomer.

The bulk polymerization experiment revealed rapid conversion in BA (90% in ~200 min), while almost no conversion in CL was observed. This could be due to the high viscosity taking place in the medium as a result of fast BA polymerization, making probably difficult the initiation of the ROP. The same *one-step* polymerization was then performed in toluene solution (50 wt % in monomer). As a result, the NMP of BA was slightly slowed down, with 80% conversion in 200 min, and the conversion in CL reached 34% for this time (Figure 9). The polymerization was continued up to 16 h to reach 100% conversion in both monomers.

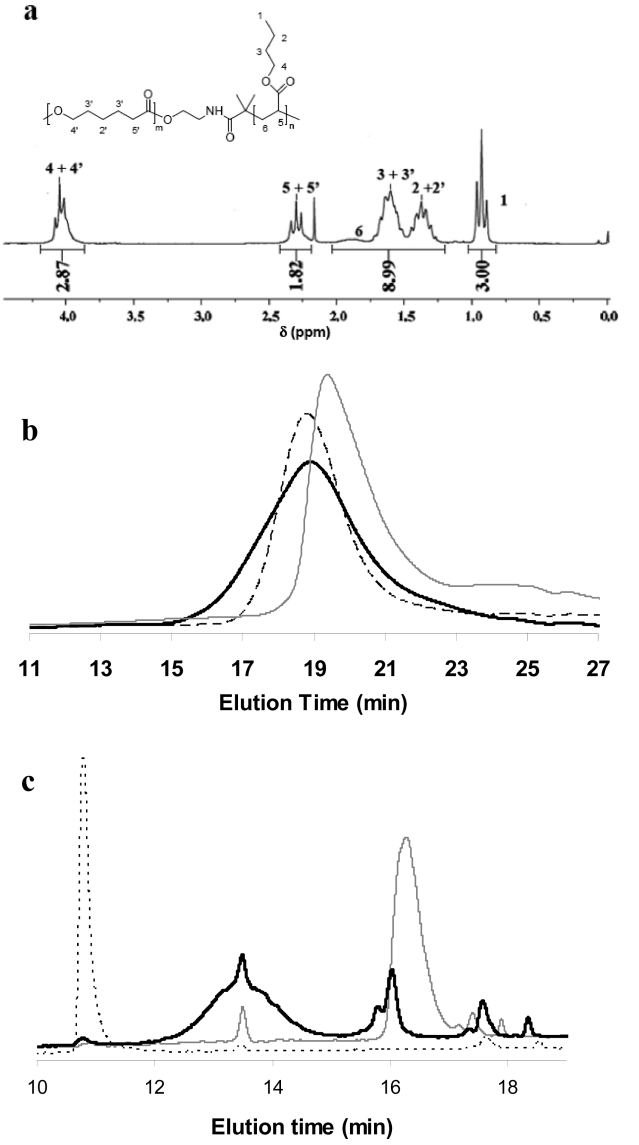


Figure 10. ^{1}H NMR spectrum in $CDCl_3$ (a), size exclusion chromatography analysis (b) and normal phase gradient polymer elution chromatography analysis (c) of the poly(*n*-butyl acrylate)-*b*-poly(ε-caprolactone) (PBA-*b*-PCL) copolymer (continuous black line) obtained by the *one-step* process after purification by precipitation in methanol; PCL of 10 000 g mol^{-1} (continuous gray trace) and PBA of 30 000 g mol^{-1} (dotted black trace) are shown as controls for SEC and NP-GPEC .

The ^{1}H NMR spectrum of the copolymer after precipitation in methanol (Figure 10a) showed, by integration, a copolymer weight composition PCL/PBA of 29/71, close to that expected (25/75). The SEC chromatogram of the copolymer (Figure 10b) revealed a quite symmetric distribution. As the expected molecular weights in PCL and PBA blocks at 100% conversion were 10 000 and 30 000 g mol^{-1}, respectively, the SEC chromatogram of the copolymer was compared with chromatograms of reference PCL and PBA polymers of 10 000 and 30 000 g mol^{-1} (Figure 10b). The results strongly suggest the formation of the diblock

PBA-*b*-PCL copolymer rather than a mixture of two homopolymers. The distribution was however relatively broad (PDI = 1.91), probably due to occurrence of side transesterification reactions (ROP) and radical transfer to PBA block (NMP), considering the rather long polymerization time. Finally, the block copolymer formation was clearly evidenced by NP-GPEC (Figure 10c), despite once again the presence of side minor peak (impurity in the system at 13.5 min). The copolymer sample was indeed eluted between the PCL and PBA homopolymer controls. PCL homopolymer seemed to be detected in the sample (~16 min), while no PBA homopolymer was observed, similar to that observed in the *NMP first* process.

It is here interesting to mention that the NMP of BA in the *one-step* process is faster than that performed in the *NMP first* one, for similar conditions used (targeted M_n of 30 000 g mol^{-1}, 1% free SG1 compared to initiator). Indeed, about 80 or 90% conversion (in toluene or bulk conditions at 110 °C, respectively) was obtained in 200 min in the *one-step* experiment whereas only 40% conversion was obtained for this polymerization time in the *NMP first* strategy for a slightly higher temperature of 115 °C (Figure 1a). This faster conversion for the *one-step* process is due to the presence of the $Sn(Oct)_2$ in the medium, which can trap some free SG1, displacing the active-dormant equilibrium toward the active species. Therefore, in the first part of the process the growing of the PBA chains through NMP is predominant. In a second part, the ROP of CL can proceed from the PBA−OH growing chains with the $Sn(Oct)_2$ catalyst still present in the medium. This *one-step* experiment can be thus viewed as a "*NMP first one-pot*" process.

Conclusion

We showed in this study that $Sn(Oct)_2$-catalyzed ROP and NMP could be efficiently combined using an easily accessible dual initiator (from MAMA-SG1), to achieve PBA-*b*-PCL block copolymers. The sequential *NMP first* approach was successful to provide well-defined block copolymers, whereas the *ROP first* approach led, in the ROP step, to bimodal PCL distribution, consequently not further exploitable for NMP process. This was attributed to side reaction between the $Sn(Oct)_2$ catalyst and the SG1 arising from the dual initiator dissociation. The potential of this dual initiator was further evidenced through the successful preparation of the block copolymer by a straightforward *one-step* process. Finally, liquid chromatography techniques (LC-CC and NP-GPEC) appeared to be efficient to characterize the species present in the copolymer sample (namely, the diblock copolymer, and some homo-PCL). Such combination of ROP and NMP techniques through the successful *NMP first* and *one-step* strategies is currently applied to the preparation of enlarged library of block copolymers.

Acknowledgment. The authors are grateful to Arkema for financial support of PhD student N.C. and to Valerie Monnier and Laurence Charles (Spectropole, Marseille) for the MALDI TOF characterization.

Supporting Information Available: Chromatograms of PBA and PCL standards (Figures S1 and S2) and MALDI TOF mass spectrometry of the PCL standard of 5000 g·mol^{-1} (Figure S3). This material is available free of charge via the Internet at http://pubs.acs.org.

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