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Valentin Puchelle, Yannick Latreyte, Mélanie Girardot, Laura Garnotel, Léa Levesque, et al.. Functional Poly(ester- alt -sulfide)s Synthesized by Organo-Catalyzed Anionic Ring-Opening Alternating Copolymerization of Oxiranes and γ -Thiobutyrolactones. *Macromolecules*, 2020, 53 (13), pp.5188-5198. 10.1021/acs.macromol.0c00261 . hal-03158438

HAL Id: hal-03158438

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Submitted on 3 Mar 2021

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Functional poly(ester-*alt*-sulfide)s synthesized by organo-catalyzed anionic ring-opening alternating copolymerization of oxiranes and γ -thiobutyrolactone

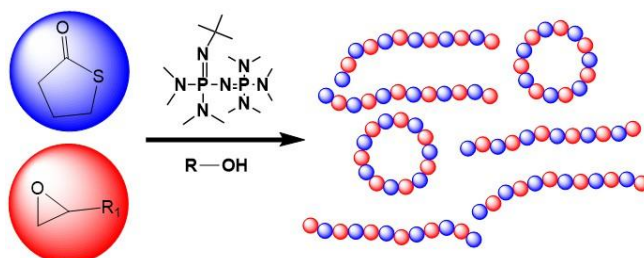
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KEYWORDS: alternating copolymerization, anionic ring-opening polymerization, γ -thiobutyrolactone, epoxides, polysulfide.

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ABSTRACT.

The copolymerization of *tert*-butyl glycidyl ether (*t*BuGE), allyl glycidyl ether (AGE), ethoxyethyl glycidyl ether (EEGE) and 1,2-epoxybutane (BO) with γ -thiobutyrolactone was investigated using benzyl alcohol-phosphazene bases as initiating systems. The prepared copolymers display perfect (poly(ester-*alt*-sulfide)) alternating structures for all epoxide monomers as evidenced by ^1H , ^{13}C , 2D NMR and MALDI-TOF mass spectrometry. A marked influence of the reaction temperature on the occurrence of transesterification side reactions has been evidenced. In particular, at elevated temperature, transesterification reactions led to the formation of alternating macrocycles. The choice of the phosphazene base (*t*BuP₄, *t*BuP₂ or *t*BuP₁) has a strong impact on the system reactivity and on the control of the polymerization. The use of *t*BuP₁ led to very slow polymerization rates. The polymerization is much faster in the presence of *t*BuP₂ even at low temperature. The use of *t*BuP₄ shows an intermediate polymerization rate and enabled a good polymerization control at moderate temperatures. Finally, the synthesis of well-defined polyether-block-poly(ester-*alt*-sulfide) and the polymerization of a challenging substituted γ -thiolactone were proven to be feasible.

INTRODUCTION

The ring-opening polymerization (ROP) of cyclic esters has been widely studied over the last decades.¹⁻⁶ It is noteworthy that several papers have reported the (co)polymerization of γ -butyrolactone despite the low strain energy of its five-membered ring.⁷⁻⁹ On the contrary, the polymerization of cyclic thioesters has been the subject of little investigation due to their low polymerizability. The polymerizations of 4-, 6- and 7-membered thiolactones (respectively, β -propiothiolactone,¹⁰ δ -thiovalerolactone,¹¹ and ϵ -thiocaprolactone^{11, 12}) have been sporadically reported since the sixties.¹³ Recently, Suzuki and coll.¹⁴ performed the controlled ring-opening polymerization of β -thiolactone derived from cysteine. 4-Hydroxyproline-derived

recyclable polythioesters and DNA-mimicking polythioesters were prepared by controlled ROP of δ -thiolactones,^{15, 16} and well-defined poly(ϵ -thiocaprolactone) were achieved by organocatalytic ROP in the presence of thiourea¹⁷ and by lipase-catalyzed ROP.^{18, 19} However, to the best of our knowledge, the ring-opening homopolymerization of γ -thiobutyrolactone has never been reported. In 2011, Du Prez and coll. demonstrated that γ -thiolactones bearing allyl groups can be ring-opened by primary amines releasing a thiol-containing AB monomer, that can be subsequently polymerized by radical (photo) polymerization in a stepwise fashion.²⁰ And recently, the ring-opening copolymerization of substituted γ -thiolactones with trimethylene carbonate was reported.²¹

Alternating copolymers have attracted meaningful attention from both academia and industry due to their unique properties compare to random copolymers. Alternating polymerization do open up opportunities for controlling the chain microstructure and the macroscopic properties of polymer materials. Indeed, copolymer properties are dominated not only by comonomer composition but also their sequence distribution. Perfectly alternating structure can magnify the properties of the copolymer, e.g. as separation membranes²² or solubilities and thermal properties,²³ or biodegradability.²⁴ In 1998, Nishikubo and coll. reported the alternating copolymerization of γ -thiobutyrolactone with oxiranes catalyzed by quaternary onium salts, affording poly(thioether-*alt*-ester)s with high dispersities (\bar{M}_w/\bar{M}_n) and low molar-mass control.²⁵ However, despite the fact that poly(thioether-*alt*-ester)s are very promising materials due to the presence of repeating units of both biodegradable ester groups and oxydable thioether groups in the main backbone,²⁶ no further investigation have been conducted using γ -thiobutyrolactone since this pioneering paper. At the same time, large libraries of functional epoxides²⁷ and functional γ -thiolactones^{28, 29} have been developed, urging the need for controlled copolymerization of such monomers and opening the way to multiple promising combinations. Very recently, phosphazene base-containing initiating

systems have been shown to efficiently catalyze the alternating copolymerizations of epoxides with either 3,4-dihydrocoumarin^{30,31} or nonstrained γ -selenobutyrolactone.³²

In this paper, the efficiency of alcohol-phosphazene bases as initiating systems³³⁻³⁶ for the anionic ring-opening alternating polymerization of γ -thiobutyrolactone with different oxiranes is evaluated (Figure 1). Particular attention is given to the control of molar mass, dispersity and the nature of the chain ends. The influence of the strength of the phosphazene base on the occurrence of side reactions is assessed. The possibility to extend the scope of this method to block copolymer synthesis or to substituted γ -thiolactones is presented. The resulting polymers have been fully characterized and their structure fully elucidated by NMR, SEC, and MALDI-ToF MS.

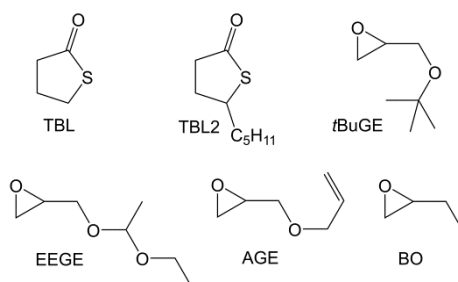


Figure 1. γ -thiobutyrolactones and oxiranes used as monomers for the alternating copolymerization.

EXPERIMENTAL SECTION

Materials. Phosphazene base *t*BuP₄ solution (0.8 mol.L⁻¹ in hexane, Sigma-Aldrich), phosphazene base *t*BuP₂ solution (2.0 mol.L⁻¹ in THF, Sigma-Aldrich), phosphazene base EtP₂ (>98%, Sigma-Aldrich), phosphazene base *t*BuP₁ (>97%, Sigma-Aldrich), CaH₂ (93%, 0-2 mm grain size, Acros Organics), benzyl alcohol (99.8% anhydrous, Sigma-Aldrich), activated aluminum oxide (neutral, Brockmann I) and acetic acid (99%, Aldrich) were used as received. 1,2-epoxybutane (BO) (>99%, Sigma-Aldrich), *tert*-butyl glycidyl ether (*t*BuGE)

(99%, Sigma Aldrich), allyl glycidyl ether (AGE) (>99%, Sigma-Aldrich) and γ -thiobutyrolactone (TBL) (98%, Sigma-Aldrich) were distilled over CaH_2 twice prior use. Pentyl-substituted γ -thiobutyrolactone was synthesized following the reported procedure²⁸ and dried over molecular sieves (3 Å). Poly(ethylene glycol) methyl ether (PEG750) ($M_n = 750 \text{ g mol}^{-1}$, Aldrich) was dried by azeotropic distillation of toluene. Ethoxyethyl glycidyl ether (EEGE) was synthesized according to Zhang et al.³⁷ and was distilled over CaH_2 twice prior to use. Toluene and THF were dried with an MBRAUN MB SPS-800 solvent purification system under nitrogen.

Instruments. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 or CD_3COCD_3 using a Bruker 400 MHz NMR spectrometer. Size Exclusion Chromatography Experiment (SEC) were carried out on three PL gel Mixed-C $5\mu\text{m}$ columns ($7,5 \times 300 \text{ mm}$; separation limits: 0,2 to $2000 \text{ kg}\cdot\text{mol}^{-1}$) maintained at 40°C and sample Viscotek GPCmax delivery module and 2 modular detectors: a Viscotek 3580 differential refractive index (RI) detector and a Shimadzu SPD20-AV diode array UV detector. THF was used as the mobile phase at a flow rate of $1 \text{ mL}\cdot\text{min}^{-1}$, toluene was used as a flow rate marker. All polymers were injected ($50 \mu\text{L}$) at a concentration of $5 \text{ mg}\cdot\text{mL}^{-1}$ after filtration through a $0.45 \mu\text{m}$ pore-size membrane. The OmniSEC 4.6.2 software was used for data acquisition and analysis. Number-average molar masses (M_n), weight-average molar masses (M_w) and dispersities ($D = M_w/M_n$) were determined by SEC with a calibration curve based on poly(methyl methacrylate) (PMMA) standards (from Polymer Standard Services), using the RI detector. *Matrix-Assisted Laser Desorption and Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)*. Mass spectra were recorded by MALDI -TOF MS using dithranol as a matrix and NaI as cationizing agent using a Bruker Autoflex III smartbeam mass spectrometer, equipped with a laser that produces pulses at 337 nm or using an Applied Biosystems 4700 Proteomics Analyzer instrument. Spectra were recorded in reflector or in linear mode at an accelerating

potential of 20 kV. Samples were prepared by dissolving the polymer in THF at a concentration of 2 mg.mL⁻¹. A 10 μL aliquot of this solution was mixed with 20 μL of matrix solution and 10 μL of NaI solution (both at 20 mg.mL⁻¹ in THF). Poly(ethylene oxide) standards (Polymer Standards Service) of known structures, $M_n = 1120, 3500$ and 5500 g.mol^{-1} were used to calibrate the mass scale. In all cases, to determine m/z , the molar mass of the sodium cation was added. The *thermal decomposition* of a poly(TBL-*alt*-*t*BuGE) was evaluated by thermogravimetric analysis (TGA) using a TA Q50 apparatus. Data were collected using a 20 °C/min ramp to 600 °C. The experiment was run under a stream of nitrogen. DSC measurements were carried out using a TA DSC Q2000 calibrated with indium standard. Sample (ca 15 mg) was placed in an aluminum cell and initially cooled at -70°C. Two heating (10 K min⁻¹) - cooling (10 K min⁻¹) cycles were then applied in the -70 to 200 °C temperature range.

General copolymerization procedure. The (co)polymerization was carried out according to the following typical procedure. In a glove-box, 1.0 mL of toluene, 20 μL of benzyl alcohol (0.1933 mmol), 0.685 mL of tert-butyl glycidyl ether (4.8252 mmol), and 0.420 mL of γ -thiobutyrolactone (4.8517 mmol) were introduced under nitrogen into a polymerization tube fitted with a Rotaflo[®]. Then, 240 μL of *t*BuP₄ solution (0.1920 mmol) was added using a microsyringe. After closure of the reaction flask, the reaction mixture was stirred at 50 °C and left to react for the required period of time. The progress of the reaction was monitored by removing samples from the polymerization reactor through a septum at various reaction times for ¹H NMR analyses. The conversion of *t*BuGE was calculated by comparing the signals corresponding to the -C(CH₃)₃ of both monomer and polymer and the CH group of the oxirane group (Figure S2). The conversion of TBL was calculated by comparing the signals of the -CH₂-CH₂-CH₂- of the monomer to the one of its ring-opened counterpart (Figure S2).

The reaction was quenched by addition with 0.2 mL of 1 mol.L⁻¹ acetic acid (2.0 mmol). After removing residual monomers and solvent by rotary evaporation, the polymer was dissolved in ethyl acetate, stirred for 30 min in the presence of neutralized aluminum oxide and purified by passing through neutralized aluminum oxide. After removing the solvent under vacuum at 50 °C a colorless viscous liquid was obtained. Yield: 88 %. Deviations from this general procedure are summarized in Tables 1 and 2. The polymers were fully characterized by ¹H and ¹³C NMR spectrometry and MALDI TOF mass spectrometry. Molar masses were determined by SEC using PMMA standards and by ¹H NMR (end-group analysis) using the aromatic protons of the initiator and the CH₃ in each repeating unit. ¹H NMR (CDCl₃): 7.34 (m, 4 H, aromatic), 5.11 (s, 2 H, Ar-CH₂-OCO-), 4.98 (quint, 13.34 H, -CHR-O- polymer backbone), 3.79 (m, 13.34 H, -CHR-OH), 3.49 (d+m, 31.81, -CH₂-O-*t*Bu), 2.56-2.83 (m, 62.78, -S-CH₂-CHR-O, -CH₂-CH₂-S-), 2.44 (t, 29.68 H, -OCO-CH₂-), 1.91 (quint, 29.68, -CH₂-CH₂-CH₂-S-), 1.16 (m, 139.58 H, -C(CH₃)₃). ¹³C NMR (CDCl₃): 172.54 (-OCO-), 128.64, 128.29, 128.27 (Ar-), 73.34 (-O-C(CH₃)₃), 72.65 (-CHR-O-), 69.88 (-CHR-OH), 66.33 (Ar-CH₂-O-), 64.47 (-CH₂-O-*t*Bu terminal unit), 61.73 (-CH₂-O-*t*Bu), 35.71 (-S-CH₂-CHR-OH), 33.20 (-CH₂-CH₂-CH₂-S-), 32.48 (-S-CH₂-CHR-O-), 31.92 (-CH₂-CH₂-CH₂-S-), 27.58 (-C(CH₃)₃), 24.81 (-CH₂-CH₂-CH₂-S-).

Table 1. Experimental conditions and molecular characteristics of poly(TBL-*alt*-*t*BuGE) samples synthesized in toluene using benzyl alcohol and different phosphazene bases as initiating systems.

Run	Base	[<i>t</i> BuGE] ₀ /[TBL] ₀ /[ROH] ₀ /[Base]	T (°C)	Time (h)	C _{V<i>t</i>BuGE} (%)	C _{V_{TBL}} (%)	<i>M</i> _{<i>n,th</i>} (g mol ⁻¹) 1)	<i>M</i> _{<i>n,NMR</i>} ^a (g mol ⁻¹)	<i>M</i> _{<i>n,SEC</i>} ^b (g mol ⁻¹) 1)	<i>D</i> ^b
1	<i>t</i> BuP ₄	50/0/1/1	25	18	40	-	2600	2650	2500	1.09
2	<i>t</i> BuP ₄	0/50/1/1	90	48	-	4	-	-	-	-
3	<i>t</i> BuP ₄	25/25/1/1	90	22	100	100	5900	4150	2100	2.73
4	<i>t</i> BuP ₄	25/25/1/1	50	18	69	69	4000	3750	3700	1.21
5	<i>t</i> BuP ₄	25/25/1/1	50	19	73	72	4350	4000	3900	1.22
6	<i>t</i> BuP ₄	25/25/1/0.5	50	19	35	36	2050	1950	2350	1.36
7	<i>t</i> BuP ₄	50/50/1/1	50	168	96	96	11100	10600	6900	1.41
8	<i>t</i> BuP ₄	25/25/1/1	40	162	99.7	97	5800	5000	4200	1.34
9	<i>t</i> BuP ₄	25/25/1/1	35	18	37	38	2200	1950	2000	1.18
10	<i>t</i> BuP ₄	25/25/1/1	35	116	91	90	5300	4200	3900	1.24
11	<i>t</i> BuP ₄	25/25/1/1	25	94	44	45	2600	2300	1750	1.29
12	<i>t</i> BuP ₄	25/25/1 ^c /1	25	25	35	37	2900	3050	3200	1.28
13	<i>t</i> BuP ₁	25/25/1/1	90	23	25	23				
				144	99	99	5900	3900	4600	1.62
14	<i>t</i> BuP ₂	25/25/1/1	50	18	100	100	5900	4900	3250	2.32
15	<i>t</i> BuP ₂	25/25/1/1	35	18	100	100	5900	5800	3250	2.55
16	<i>t</i> BuP ₂	25/25/1/1	25	5	99	99	5900	5800	5050	1.38
17	<i>t</i> BuP ₂ ^d	25/25/1/1	25	1	93	96	5700	6100	4600	1.37
18	EtP ₂	25/25/1/1	25	1	88	86	5100	4400	4300	1.26
19	<i>t</i> BuP ₂	100/100/1/2	25	192	60	60	14000	10500	9000	1.31

20	<i>t</i> BuP ₂	25/25/1/1	-20	2.5	61	61				
				18	100	100	5900	5750	6600	1.29
21	<i>t</i> BuP ₂	12/12 ^c /1/1	90	26	99	99	3700	2900	1000	1.75
22	<i>t</i> BuP ₂	12/12 ^c /1/1	30	4	64	64	2200	2050	1600	1.51

^a Determined by ¹H NMR in CDCl₃.

^b Determined by SEC (THF, 40 °C, PMMA standards).

^c PEG750 was used instead of benzyl alcohol.

^d *t*BuP₂ was introduced first in the polymerization tube and THF was subsequently evaporated using high vacuum from a vacuum line ($\approx 10^{-6}$ hPa) before introducing the solvent and all the other reactants.

^e The pentyl-substituted γ -thiobutyrolactone (TBL2) was used instead of TBL.

RESULTS AND DISCUSSION

In the first part of the work, homopolymerizations (Table 1, runs 1 and 2) and copolymerization (Table 1, runs 3 to 11) of *t*BuGE and TBL were performed in toluene using benzyl alcohol-*t*BuP₄ (1-1 or 1-0.5) as initiating system at different temperatures. Targeted degrees of polymerization (assuming quantitative initiation) were deliberately set at moderate values ($X_n=50-100$) so that chain ends could be easily evidenced by ¹H NMR and MALDI TOF MS.

As previously reported with *t*BuP₄ and benzyl alcohol,³⁸ the homopolymerization of *t*BuGE is controlled at 25°C (Table 1, run 1). On the contrary after 48 h, no homopolymerization of TBL has occurred at 90°C (Table 1, run 2). TBL conversion was determined by ¹H NMR analysis of the reaction mixture after solvent evaporation (Figure S1) and is equal to 4% demonstrating the ring-opening of TBL, possibly followed by one additional monomer unit. Several reaction temperatures were investigated for the copolymerization (Table 1 runs 3-11). The obtained polymers display spectroscopic data consistent with the ring-opened alternating

structure, whatever the polymerization conditions. An assignment of all the signals observed in ^1H , ^{13}C and COSY NMR could be made and is available directly on the spectra (Figure 2 and Figure S3). In the case of the *t*BuGE homopolymerization (Table 1 run 1), the $-\text{CH}_2-$ of the initiator is in alpha position of an ether group and its ^1H NMR singlet is located at 4.52 ppm (Figure S4). For the copolymerization reactions, no ^1H NMR signal is visible around 4.6 ppm and the singlet corresponding to the initiator $-\text{CH}_2-$ is shifted at 5.11 ppm. This value is in agreement with a CH_2 attached to an ester group. From these observations, it can be concluded that after deprotonation by the phosphazene base, the benzyl alcoholate predominantly attacked the thioester and ring-opened the TBL (Scheme 1). The first monomer unit of a polymer chain is therefore a ring-opened TBL.

The chemical shift of the ^1H NMR quintet corresponding to the $-\text{CHR}-$ group of the oxirane monomer at 4.98 ppm and the absence of signals corresponding to polyether blocks between 3.6 and 3.8 ppm are in favor of a strictly alternating structure of the chains (Figure 2). The low intensity signal at 3.79 ppm can be attributed to the $-\text{CHR}-$ group of the last oxirane monomer unit. In addition, from the intensity ratio of protons of the oxirane $-\text{CHR}-$ group at 4.98 and 3.79 ppm (h and h' in Figure 2) vs TBL $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ at 1.91 ppm (e in Figure 2), the *t*BuGE/TBL ratio was found to be 1/1 for each run of Table 1 having total monomer conversion ranging between 35 and 100 %. Interestingly, Nishikubo et al. prepared alternating copolymers using initiating systems for which the homopolymerization of both monomers was not possible under the same conditions.²⁵ Here, using benzyl alcohol - *t*BuP₄ as initiating system, NMR spectra confirmed that all the copolymers were obtained by the perfect ring-opening alternating copolymerization of *t*BuGE and TBL as shown in Scheme 1 even if the homopolymerization of *t*BuGE is possible under the same conditions.

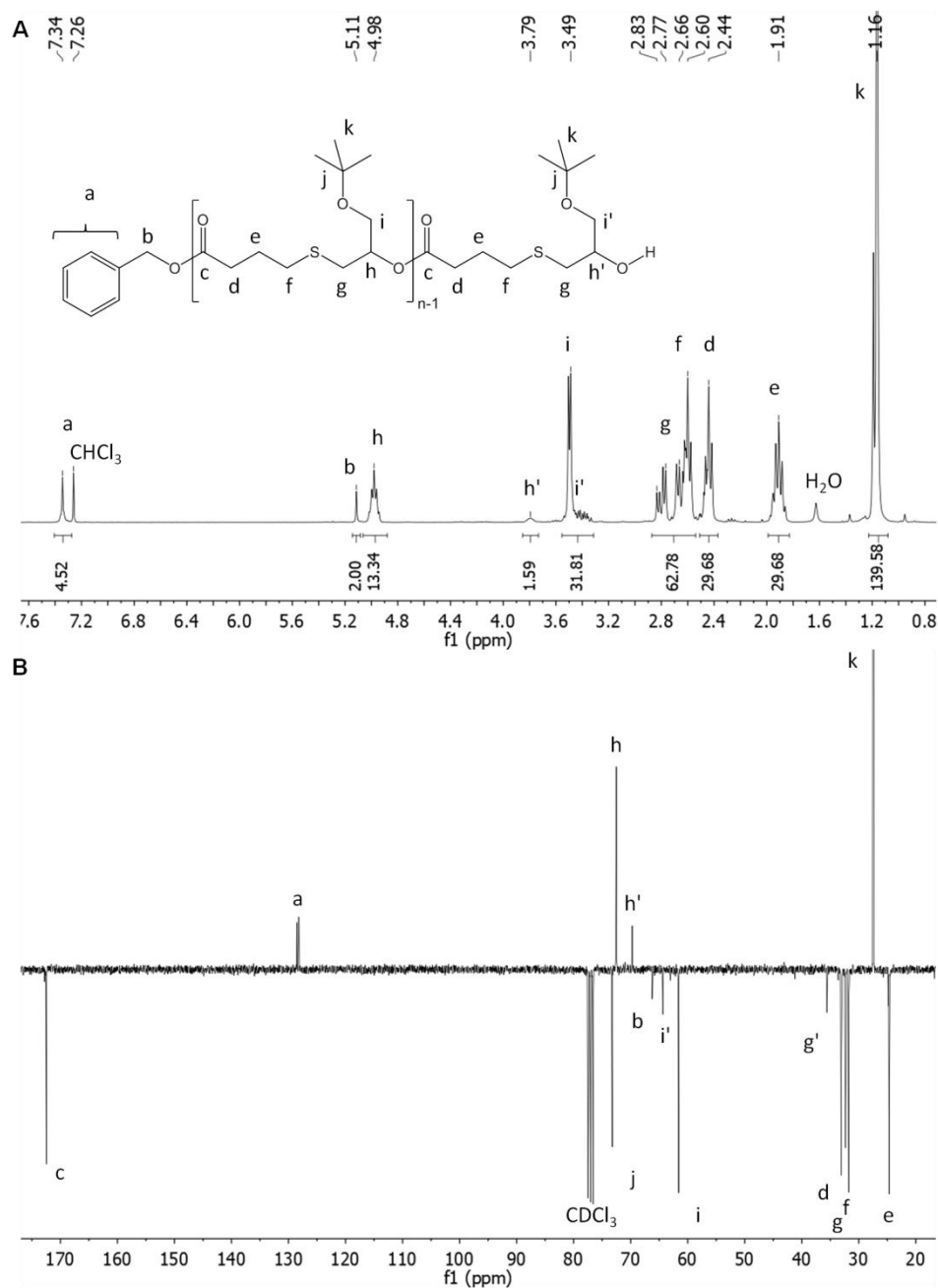
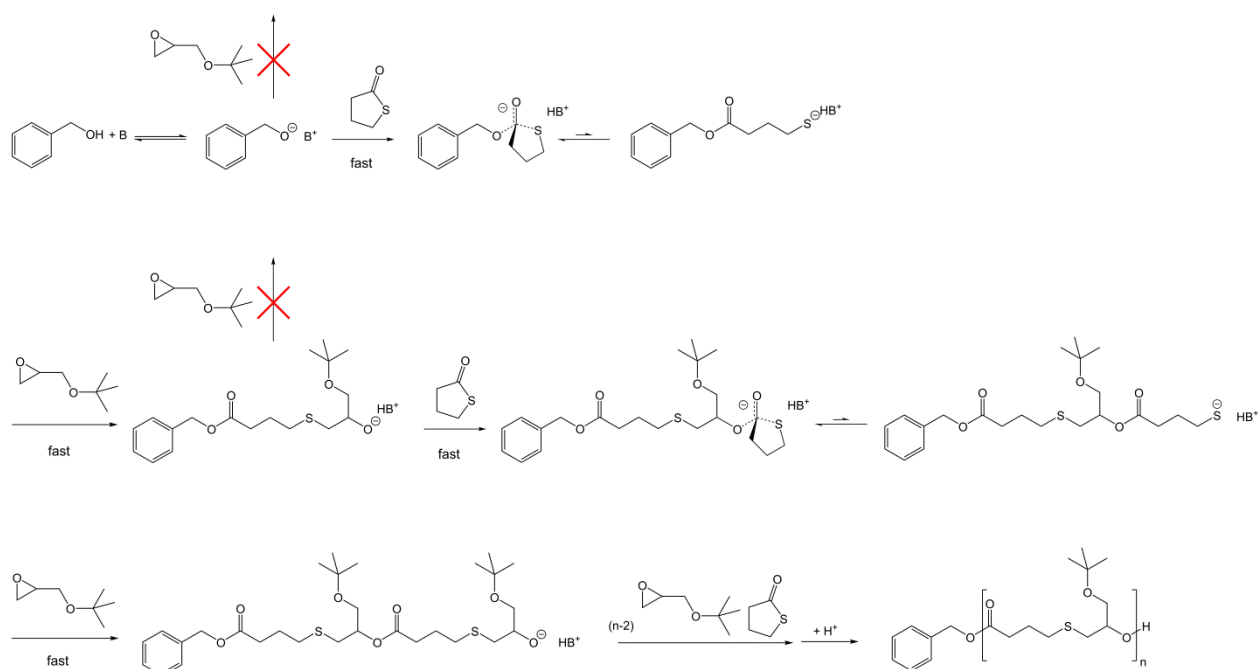


Figure 2. (a) ^1H NMR and (b) ^{13}C NMR spectra of poly(TBL-*alt*-*t*BuGE) in CDCl_3 at 25°C (Table 1, run 4).



Scheme 1. Postulated mechanism for the alternating ROP of γ -thiobutyrolactone and tert-butylglycidylether using benzyl alcohol-phosphazene base $t\text{BuP}_4$ as initiating system.

The effect of the reaction temperature was examined. A first copolymerization was performed at 90°C (Table 1, run 3), which is the temperature predominantly used by Nishikubo *et al.* with quaternary ammonium salts or crown ether complexes as initiating systems.²⁵ After 22 h reaction time, full conversions of both monomers were obtained. No polyether fragments are detectable by MALDI ToF, ^1H and ^{13}C NMR analyses (Figure 4 and S5). The experimental molar mass determined by SEC (Figure 3A) was lower than the theoretical one. A part of this difference could be due to difference in the hydrodynamic volume of the PMMA standards used for SEC calibration with that of the poly(ester-alt-sulfide). However, the extent of this difference and a broad dispersity (Figure 3A) strongly suggest the occurrence of transfer reactions. This observation is in contrast to the results obtained by Nishikubo *et al.* who observed at the same temperature the formation of higher molar masses than the theoretical ones due to a step-growth polymerization mechanism.²⁵ The MALDI TOF spectrum (Figure 4, Table 1 run 3) displays 4 distributions, for which it is worth noting that the molar mass difference between two peaks is strictly equal to the molar mass of

one alternating repeat unit (232.11 mass unit). The four populations have been identified as follows in order of importance. The main distribution corresponds to the expected alternating polymer cationized by a sodium ion and end-terminated by a benzyloxy group at one end and by a hydroxy group at the other end. The second most important distribution can be attributed to perfectly alternating macrocycles cationized by sodium ion. It can be noted, that the presence of polymer chains initiated by enolate anions has been ruled out due to the absence of the corresponding double bond signals on the ^1H and ^{13}C NMR spectra (Figure S5). The macrocyclization can be explained by an intramolecular transesterification reaction occurring during the polymerization process as shown in Scheme S1. Similarly, intermolecular transesterification reactions must occur but they cannot be detected by mass spectrometry because they do not generate structural differences. The large distribution and the gap observed between theoretical and experimental molar masses measured by SEC in this reaction might be partly explained by these intermolecular transesterification reactions. The third distribution is due to alternating macrocycles containing one additional oxirane unit. We assume that the additional unit might be due to the introduction of a slight initial excess of oxirane and is occurring after the full BTL conversion. Surprisingly, the linear counterpart, namely the expected alternating structure containing one additional oxirane unit, is barely visible on the MALDI TOF spectrum, suggesting their high cyclization tendency. The last minor population corresponds to alternating polymer chains containing one additional oxirane unit, cationized by a sodium ion and end-terminated by a hydroxy group at both ends. This chain structure could be explained by the presence of moisture traces in BTL and water initiation according to Scheme S2.

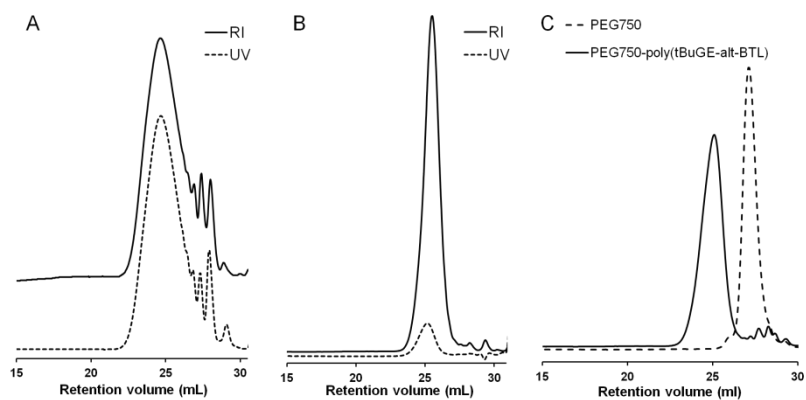


Figure 3. A. SEC traces of poly(TBL-*alt*-*t*BuGE) initiated by benzyl alcohol in the presence of *t*BuP₄ synthesized at 90°C (Table 1, run 3) and B. at 50°C (Table 1, run 4); C. SEC traces of PEG750 (dashed line) and of PEG750-*block*-poly(TBL-*alt*-*t*BuGE) initiated by PEG750 in the presence of *t*BuP₄ synthesized at 25°C (Table 1, run 12).

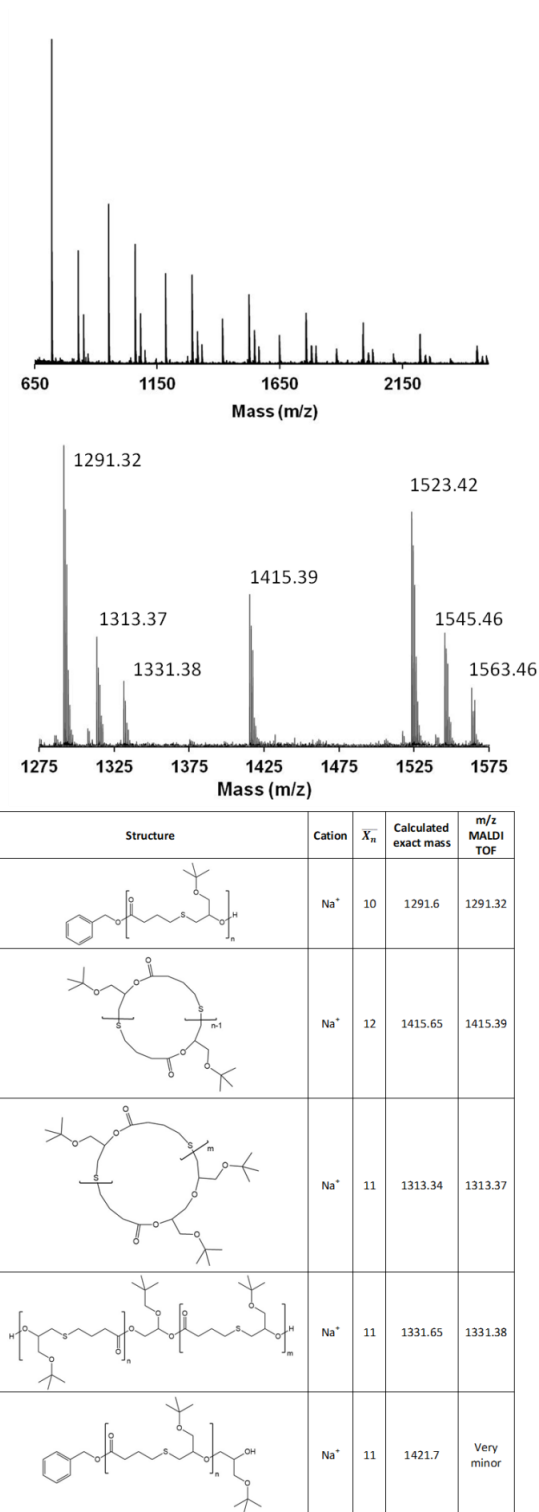


Figure 4. MALDI TOF spectra (reflectron mode) of a poly(TBL-*alt*-*t*BuGE) synthesized using benzyl alcohol-phosphazene base *t*BuP₄ as initiating system at 90°C (Table 1, run 3).

The reaction temperature was decreased to 50°C (Table 1, run 4). For this run, the M_n determined by ¹H NMR and SEC is in very good agreement with the theoretical one. In

addition, the resulting polymer exhibits a lower molar mass distribution ($D = 1.21$) with significantly less low-molar-mass tailing compared to the polymer prepared at 90°C suggesting a strong decrease of the transesterification reactions (Figure 3). Under the same conditions, M_n increased linearly with conversion and low dispersities (<1.22) are observed (Figure S7). These results support the control of M_n at 50°C. This result is confirmed by MALDI TOF MS analysis, which displays a very major distribution corresponding to the expecting alternating structure initiated by benzyl alcoholate and a minor distribution due to moisture initiation (Figure 5). However, residual alternating macrocycles are still detectable in the low molar mass region. A detailed kinetics experiment was carried out at 40°C. As shown in Figure S8, conversions of both monomers TBL and *t*BuGE increased equally with time as expected for an alternating copolymerization. The fast increase of the conversions at the beginning of the polymerization is due to the heat release observed during phosphazene base addition. SEC traces gradually shift toward higher molar masses (Figure S9). However, the M_n versus conversion plot shows an increasing discrepancy between theoretical and experimental molar masses with increasing conversion (Figure S10). A further temperature decrease to 35°C fully suppressed the cyclization reaction according to the MALDI TOF spectrum (Figure S11). The regioregularity of the ring-opening reactions of epoxides during the polymerization was calculated using ^1H NMR spectra. The β -cleavage of the epoxy ring of *t*BuGE was found to be higher than 98% at 90°C (Figure S6) and 100% for lower temperatures.

In addition, a copolymerization was performed at 25°C using *t*BuP₄ to deprotonate a PEG750 macroinitiator (Table 1, run 12). SEC traces of the PEG750 macroinitiator and of the resulting copolymer are shown in Figure 3C. No remaining homopolymer is visible on the chromatogram, demonstrating a 100% macroinitiator efficiency. A well-defined block copolymer with an alternating segment, PEG750-*block*-poly(TBL-*alt*-*t*BuGE), is obtained.

Interestingly, at a temperature of 50°C or lower, only perfectly alternating structures are detected by MALDI TOF MS without any defect. Moreover, for all the tested conditions and for partial monomer conversions, all the linear polymer chains are terminated by a hydroxy group. Taking into account the absence of thiol-terminated polymer chains, the perfectly alternating structure, the absence of *t*BuGE homopolymerization and the fact that the copolymerization is slower than the epoxide homopolymerization, we postulate that a fast complexation takes place between the generated phosphazanium alcoholates and a thiolactone (Scheme 1) preventing *t*BuGE homopolymerization. The generated complex is in equilibrium with the thiolate-terminated polymer chain. In the next step, the ring-opening of the thiolactone is immediately followed by a fast nucleophilic addition between the highly nucleophilic thiolate anion³⁹ and an oxirane ring. In this mechanism, the equilibrium is the rate-determining step, which is supported by the linear increase of monomer conversions with time (Figure S8), demonstrating a zero-order kinetics independent of monomer concentration.

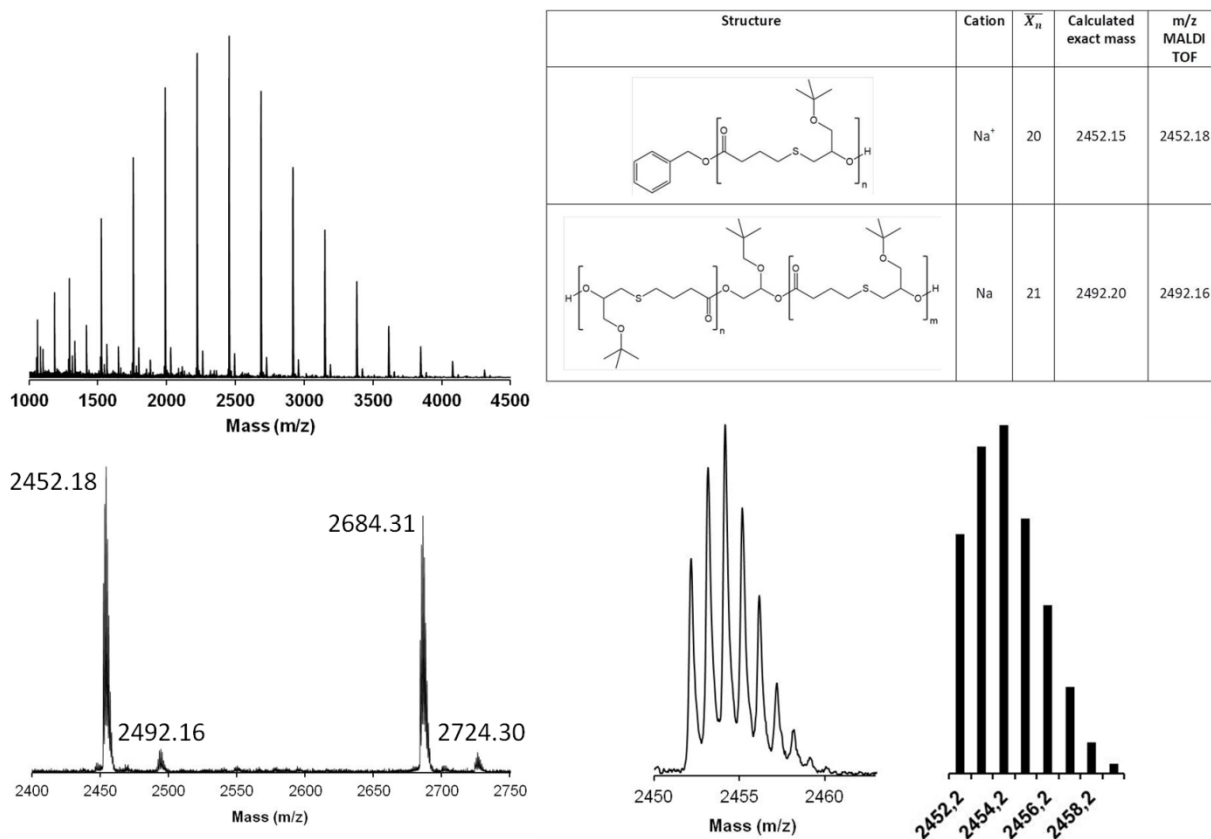


Figure 5. MALDI TOF spectra (reflectron mode) of a poly(TBL-*alt*-*t*BuGE) synthesized using benzyl alcohol-phosphazene base *t*BuP₄ as initiating system at 50°C (Table 1, run 4).

Tetrameric *t*BuP₄H⁺ phosphazanium alcoholates are highly reactive and have a tendency to attack ester groups.⁴⁰ Alcoholates of monomeric and dimeric phosphazanium salts are expected to be less reactive with ester groups due to a reduced charge delocalization of their cations. The results obtained with monomeric (*t*BuP₁, pK_a, ACN = 26.9) and dimeric (*t*BuP₂, pK_a, ACN = 33.5; EtP₂, pK_a, ACN = 32.9)⁴¹ phosphazene bases are summarized in Table 1. The use of *t*BuP₁ led to a strong decrease of the polymerization kinetics at 90°C (Table 1, run 13). This decrease of the reactivity was expected considering the less bulky *Ht*BuP₁⁺ cation and shorter interionic distances with the propagating centers.⁴¹ The reactivity decrease simultaneously led to the reduction of the transfer reactions and to higher M_n compared to *t*BuP₄ at 90°C.

In the presence of the dimeric phosphazene base $t\text{BuP}_2$ (Table 1, runs 14-20), an intermediate behavior between $t\text{BuP}_1$ and $t\text{BuP}_4$ was expected. However, the propagating species are far more reactive in the presence of $\text{H}t\text{BuP}_2^+$ than $\text{H}t\text{BuP}_4^+$ cations: 99% monomer conversion after 5 h at 25°C with $t\text{BuP}_2$ (Table 1, run 16) compared to only 45% conversion after 96 h with $t\text{BuP}_4$ (Table 1, run 11). A polymerization was carried out at -20°C for which full monomer conversions were reached after 18h (Table 1, run 14). Commercially-available $t\text{BuP}_2$ is diluted in THF and added as-is in the polymerization tube. But, it is known that the addition of a small amount of Lewis bases, such as ethers, has a tremendous effect on the kinetics of the propagation in apolar solvent with higher propagation rates than the original ones.⁴² Therefore, a reaction was performed at 25°C by adding first $t\text{BuP}_2$ and by evaporating out the THF prior to the addition of the solvent and the other reactants (Table 1 run 17). In addition, an identical reaction was carried out with pure EtP_2 (Table 1 run 18). Kinetics remained much faster with dimeric phosphazene bases than with $t\text{BuP}_4$ even in the absence of THF. In order to explain the rate difference, we assume that the basicity of the phosphazene base has an impact on the equilibrium between the alcoholate-thiolactone complex and the thiolate-terminated polymer chain: the higher basicity of $t\text{BuP}_4$ being more favorable to an intramolecular backbiting attack of the thiolate regenerating the γ -thiolactone. The polymerization performed with $t\text{BuP}_2$ at -20°C or 25°C reached full conversions while maintaining a good control of the number-average molar masses (Table 1, runs 16-18 and 20). The dispersity decreased with the reaction temperature, even though a high-molar-mass shoulder is visible on the size exclusion chromatogram for the reaction at -20°C (Figure S12). As previously, a temperature increase led to more transfer reactions and a discrepancy between experimental and theoretical number-average molar masses is observed for polymerization performed at temperature higher than 35°C (Table 1, runs 14-15).

Reaction conditions have been identified allowing the synthesis of well-defined poly(TBL-*alt-t*BuGE) with limited degrees of polymerization ($X_n < 50$). In order to increase the polymer number-average molar masses, two reactions were carried out by increasing the $([t\text{BuGE}]_0 + [\text{TBL}]_0)/[\text{ROH}]_0$ ratio. X_n values of 100 and 200 were targeted in the presence of $t\text{BuP}_4$ at 50°C (Table 1, run 7) and in the presence of $t\text{BuP}_2$ at 25°C (Table 1, run 19), respectively. In both cases however, the increase of the reaction time favored the generation of macrocycles and thus, the obtained number-average molar masses ($M_n = 6900$ and $9000 \text{ g}\cdot\text{mol}^{-1}$) are lower than the theoretical ones ($M_{n,th} = 11100$ and $14000 \text{ g}\cdot\text{mol}^{-1}$, respectively). A similar limitation of the M_n due to intramolecular transesterification (backbiting) has already been reported for the alternating copolymerization of epoxides and dihydrocoumarin catalyzed by phosphazene bases.⁴³

Table 2. Experimental conditions and molecular characteristics of poly(TBL-*alt-M*₁) samples synthesized in the bulk using benzyl alcohol and $t\text{BuP}_4$ as initiating system.

Run	M ₁	[M ₁] ₀ /[TBL] ₀ /[ROH] ₀ /[$t\text{BuP}_4$]	T (°C)	Time (h)	Conv _{M1} (%)	Conv _{TBL} (%)	M _{n,th} (g mol ⁻¹)	M _{n,NMR} ^a (g mol ⁻¹)	M _{n,SEC} ^b (g mol ⁻¹)	D ^b
1	<i>t</i> BuGE	25/25/1/1	90	18	99	99	5850	4200	3050	1.87
2	<i>t</i> BuGE	12.5/12.5/1/1	60	18	98	98	2900	2100	2250	1.44
3	<i>t</i> BuGE	25/25/1/1	40	24	81	83	4800	4100	4050	1.22
4	AGE	25/25/1/1	40	4.5	79	82	4450	4200	3900	1.28
5	AGE	25/25/1/1	25	22	93	93	5100	4800	4200	1.27
6	EEGE	25/25/1/1	50	48	99	99	6250	4100	3000	2.41
7	EEGE	25/25/1/1	25	96	99	99	6250	6050	6200	1.35
8	BO	25/25/1/1	60	19	81 ^c	62	2800	2100	1500	1.32

9	BO	25/25/1/1	40	119	81 ^c	68	3050	3000	2050	1.59
10	BO	25/25/1/1	25	113	45 ^c	41	2000	1800	1175	1.38

^a Determined by ¹H NMR in CDCl₃. ^b Determined by SEC (THF, 40 °C, PMMA standards). ^c

BO boiling point is 63°C, part of the monomer evaporated and penetrated the rubber stopper.

In order to develop a family of poly(ester-*alt*-thioether) with various pendant groups, we decided to extend the scope of used monomers. To determine if the alternating copolymerization can be extended to substituted γ -thiobutyrolactone, preliminary experiments have been carried out with a pentyl-substituted γ -thiobutyrolactone (BTL2, Figure 1). As the copolymerization is expected to be more challenging due to the steric hindrance introduced by the pentyl group in alpha position of the sulfur atom, a first polymerization was performed at 90°C in the presence of previously determined very efficient *t*BuP₂ (Table 1, run 21). After 26 h, full monomer conversions were achieved. The ¹H NMR spectrum of the obtained polymer is compatible with a fully alternating polymer structure (Figure S14). The MALDI TOF spectrum is shown in Supporting Information (Figure S15). The 5 major and 3 minor populations correspond to the expected alternating repeating unit confirming the ¹H NMR result. 4 of the 5 major populations could be identified (Table S1). The main population corresponds to the expected structure. As previously at high temperature, two types of macrocycles are present in the final polymer: perfectly alternating macrocycles and alternating macrocycles with one additional oxirane unit. Thus, MALDI TOF spectrum demonstrates the presence of non-negligible transesterification reactions, which explains the low number-average molar mass determined by SEC. In a second experiment, the reaction temperature was decreased to 30°C (Table 1, run 22). Compared to the previous reaction, a higher M_n and a lower dispersity were obtained, suggesting a decrease of the transesterification reactions.

In the last part of this work, the polymerization reactions were performed in the bulk with γ -thiobutyrolactone and four different oxirane monomers: *t*BuGE, AGE, EEGE and BO. Regardless of the oxirane nature, ^1H NMR spectra are in excellent agreement with alternating copolymerization mechanisms (Figure 6, Figures S16-17): -CHR- attached to an ester group and no signals corresponding to polyether blocks. For the monomers having an electronegative oxygen in beta position of the oxirane rings (*t*BuGE, AGE and EEGE), reaction conditions have been identified that allow the control of the number-average molar mass and the preparation of monomodal polymers with dispersities around 1.2-1.3. In the case of 1,2-epoxybutane, only low molar-mass polymers have been synthesized due to difficulties in the control of the copolymerization with slower kinetics and transfer reactions even at 25°C. The β -cleavage occurred with 100% selectivity in the case of the copolymerization of BTL with EEGE and AGE. However, the weak signals from 4.0 to 4.3 ppm in the ^1H NMR spectrum (Figure S17) imply that the ring-opening of BO also occurs in a α -scission manner when attacked by the thiolate at 60°C, however to a much lesser extent (<4%) than for the more sterically favored β -scission.

The thermal behavior of a poly(TBL-*alt-t*BuGE) was determined using DSC and TGA. A TGA trace for a poly(TBL-*alt-t*BuGE) (Table 1 run 4) is presented in Figure S18. The decomposition temperature after 20% weight loss occurred around 330°C and the decomposition temperature at maximum degradation rate (derivative thermogravimetry) was 350°C. DSC curves corresponding to a poly(TBL-*alt-t*BuGE) (Table 1 run 4) revealed a glass transition temperature at -32°C (Figure S19).

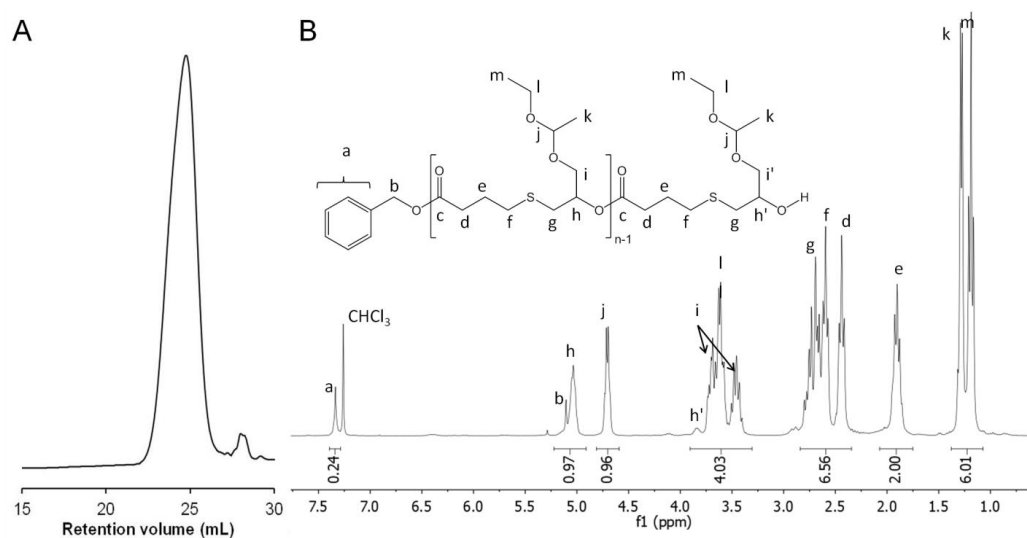


Figure 6. SEC trace (left) and ^1H NMR spectrum (right) of poly(TBL-*alt*-EEGE) in CDCl_3 (Table 2, run 7).

CONCLUSION

Benzyl alcohol - phosphazene bases are effective initiating systems for the alternating copolymerization of epoxides and γ -thiobutyrolactone. Perfectly alternating sequences were achieved and proved by ^1H , ^{13}C NMR and for the first time by MALDI TOF mass spectrometry. Optimized polymerization conditions were determined to allow the synthesis of well-defined poly(ester-*alt*-sulfide) with controlled chain ends. However, molar mass of the alternating copolymer is still limited. Indeed, reaction temperature or time increase led to the apparition of transesterification reactions resulting in macrocycle formation, molar mass limitation and higher dispersities. Different phosphazene bases were evaluated: $t\text{BuP}_1$ is not sufficiently active to ensure high monomer conversion in a reasonable amount of time, $t\text{BuP}_4$ is more active but $t\text{BuP}_2$ displayed the highest reactivity with very fast conversion at room temperature while maintaining well-defined copolymer structures. Different epoxide monomers were copolymerized with γ -thiobutyrolactone leading to original poly(ester-*alt*-

sulfide)s. The possibility to synthesize well-defined polyether-block-poly(ester-*alt*-sulfide) was also demonstrated. In addition, the polymerizability of γ -substituted thiobutyrolactone was shown by preliminary experiments, which paves the way to a multitude of combinations between epoxides and γ -thiobutyrolactones considering the rich chemistry of both families of monomers.^{28, 44} The properties of this attractive class of functional, (bio)degradable and ROS-sensitive²⁴ alternating copolymers are currently under investigation.

ASSOCIATED CONTENT

Supporting Information.

The Supporting Information is available free of charge on the ACS publication website at DOI: ¹H and ¹³C NMR spectra of a TBL homopolymerization reaction mixture (Table 1, run 2) of a *t*BuGE homopolymerization reaction mixture (Table 1, run 1), of a copolymerization between *t*BuGE and TBL (Table 1, run 3 and 9), of a poly(TBL-*alt*-BO) in CDCl₃ (Table 2, run 8), of a poly(TBL2-*alt*-*t*BuGE) (Table 1, run 21) and of a poly(TBL-*alt*-AGE) in CDCl₃ (Table 2, run 5). 2D COSY-NMR spectrum of a poly(TBL-*alt*-*t*BuGE) (Table 1, run 4). Relationship observed between number-average molar mass and monomer conversion for a copolymerization at 40°C and at 50°C (Table 1, runs 5 and 8). MALDI TOF spectra of a poly(TBL-*alt*-*t*BuGE) (Table 1, run 9) and of a poly(TBL2-*alt*-*t*BuGE) (Table 1, run 21). SEC traces of poly(TBL-*alt*-*t*BuGE) (Table 1, run 8 and 19-20), of poly(TBL2-*alt*-*t*BuGE) (Table 1, run 21) and of poly(TBL-*alt*-AGE) (Table 2, run 5). Mechanisms for the intramolecular transesterification explaining the formation of macrocycles and for the alternating ROP of γ -thiobutyrolactone and *tert*-butyl glycidylether initiated by moisture traces. TGA trace and DSC curve of a poly(TBL-*alt*-*t*BuGE) (Table 1, run 4).

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest

ACKNOWLEDGMENT

The authors would like to acknowledge Gilles Clodic and Dr Lucrèce Matheron-Duprez (Mass Spectrometry facility, Institut de Biologie Paris Seine) for their help and the constructive discussions on MS analysis.

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