Bio-based ABA triblock copolymers with central degradable moieties.

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ABSTRACT

A set of (poly-α-methylene-γ-butyrolactone)-*co*-(poly-δ-decalactone)-*co*-(poly-α-methylene-γ-butyrolactone) (PMBL-*co*-PDL-*co*-PMBL) ABA block copolymers containing different stimuli cleavable groups at the central point of the δ-polydecalactone (PDL) block were synthesized by a combination of Ring Opening Transesterification Polymerization (ROTEP) of DL, diol end group functionalization as α-bromoester and Atom Transfer Radical Polymerization (ATRP) of α-methylene-γ-butyrolactone (MBL). Diols containing acetal, spiroacetal, thioacetal and disulphide units were used as initiators for the bulk room temperature controlled polymerization of δ-decalactone (DL) using 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) as catalyst. PDL diols were functionalized in a one-pot two-steps procedure using N-(2-bromoisobutyryl)imidazole (BiB-Im). The resulting macroinitiators were chain extended by atom transfer radical polymerization (ATRP) in DMF at 50 °C using MBL as methacrylic-like monomer and the conventional CuCl/$CuCl_2$/2,2'-bipyridine catalyst system. The cleavage behaviour of the copolymers under reductive, acidic and photooxidative conditions has been studied and the resulting AB block copolymers structurally characterized.

1 - INTRODUCTION

During recent years, environmental concerns have led to a growing interest towards sustainable polymers in which material renewability and degradability are key issues. [1, 2, 3] In this way, a plethora of monomers derived from agricultural feedstocks by direct extraction or by chemical or microorganism transformation, have been provided for both academia and industry. [4,5,6]

In parallel, significant progress have been made in the development of polymerization techniques, especially in controlled radical polymerization (CRP) allowing the precise tuning of compositions, architectures and functionalities. [7,8,9,10] ABA block copolymers are one of the most successful and simpler architectures due to their remarkable ability to assemble on the nanoscale level, giving rise to materials with a variety of properties and applications such as pressure sensitive adhesives (PSA), [11] drug nanocarriers, [12] or simply as components for industrial, aircraft and household appliances.

Thermoplastic elastomers (TPEs) are one of the most outstanding type of ABA block copolymers, combining a soft central rubbery block with glassy end blocks. Former styrene-butadiene or styrene-isoprene ABA copolymers lack ambient resistance, exhibit relatively low service temperature and are virtually non-recyclable. Consequently, many efforts have been made to improve their performance for example by combining different acrylate and methacrylate monomers by anionic or controlled radical polymerization techniques.[13] However, radical chemistry is unable to produce degradable polymers unless coupled with other polymerization techniques such as Ring Opening Transesterification Polymerization (ROTEP) following either a two or three-step pathway. [14]

ROTEP is the most efficient method for the synthesis of polyesters. Renewable cyclic esters (lactones) can be polymerized using metal-free organocatalysts to produce polyesters with moderate energy input, solvent-free conditions and with a controlled molecular weight. [15, 16, 17] By selecting the appropriate nature, ring size and substituents, lactones can give rise to both hard highly crystalline blocks (e.g. L-lactide) and very soft ones (e.g δ-decalactone, ε-decalactone or menthide). In fact, ABA block copolymers prepared by combining two-step sequential ROTEP of different cyclic esters have been described. [18,19,20] Moreover, telechelic soft polyester blocks can be extended by Controlled Radical Polymerization (CRP) methods such as Atom Transfer Radical Polymerization (ATRP), using methyl methacrylate [21] or their natural cyclic counterparts α-methylene-γ-butyrolactone (MBL or tulipalin A) and γ–methyl-α-methylene-γ-butyrolactone (MMBL). In this approach, the soft polyester must be appropriately functionalized before being used as macroinitiator for ATRP following a three-step route. This three-step methodology has been elegantly proved by Hillmyer et al. providing fully renewable TPEs. [22,23] Achieving the goals of renewability and superior performance is highly desired for both large commodity and specialty materials but, keeping life cycle assessment in mind, degradability or recoverability became also relevant issues. Removing industrial TPEs is still a challenging issue and efforts must be done to promote a fast break down of copolymer blocks under certain conditions during paper recovery and recycling. [24]

Soft aliphatic polyester chains exhibit inherent long-term degradation producing different biocompatible products. Conversely, hard acrylic-like blocks do not degrade easily so a convenient way to facilitate recovery and recycling is triggering significant changes on the TPEs properties in response to external stimuli, i.e. cleaving the ABA block copolymer into AB copolymers with lower molecular weight. With this target in mind, ABA block copolymers must be designed containing at least one cleavable group which, in an appropriate media, sparks cleavage when their useful life has ended. Important research endeavour has been done in designing materials prone to respond to specific environment changes (temperature, light, pH, redox, etc.) mainly focused to therapeutic applications. [25,26] When TPEs are targeted, the triggering stimuli should match with the redox and pH conditions used in paper and carboard recycling (bleach, sulphites, acidic conditions, etc.).

In this work, we explore the preparation of detachable ABA block copolymers based on δ-decalactone (DL) [27,28] and α-methylene-γ-butyrolactone (MBL) [29][30][31] starting from stimuli cleavable diols by combining the ROTEP/functionalization/ATRP three step approach. The controlled bulk, room temperature ROTEP of DL initiated by selected diols using 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) [32,33] as catalyst is used to provide a set of alkyl-branched polyester diols that would constitute the central soft segment in resemblance to some described block-copolymers based on DL [34,35]. After convenient functionalization as bis-α-bromoisobutyrates (BiB), polyester macroinitiators were chain extended with MBL using conventional ATRP to provide the end hard blocks. The structural features of MBL led to high Tg rigid hard blocks when polymerized by controlled radical polymerization [36,37] thus leading to fully renewable stimuli responsive ABA block copolymers.

2- EXPERIMENTAL PART

2.1 – Synthesis of I_n-PDL-Br macroinitiators. (Figures SI.23 to SI.30)

Step 1- ROTEP of DL. [DL]:[I] = 150:1, [TBD]:[I] = 0.8:1, 25°C, in bulk for 12h.

Using conventional inert atmosphere handling techniques about 0.20 mmol of diol initiator (I_0 = 29.2 mg; I_1 = 30.9 mg; I_2 = 59.7 mg; I_3 = 73.5 mg; I_4 = 33.7 mg and I_5 = 54.9 mg) were dissolved in 5.4 mL (5.10 g, 30.0 mmol) of δ-decalactone into a cylindrical 25 mL Schlenk flask to prepare a solution with lactone/initiator molar ratio about 150:1 (determined by ^{1}H NMR). Once homogenized, the solution was transferred via cannula under positive argon pressure to another Schlenk flask containing 22.3 mg (0.160 mmol) of TBD under argon atmosphere ([TBD]:[I] = 0.8:1, [TBD] = 30 mM). The mixture was gently stirred to dissolve TBD and put in a water bath (25±2°C) to allow the polymerization to proceed until the desired conversion. Samples for ^{1}H-NMR analysis were withdrawn under argon flow and dissolved in a 0.03 M solution of benzoic acid (PhCOOH) in $CDCl_3$. Samples for I_n-PDL-OH structural characterization was also taken.

Step 2- I_n-PDL-OH modification with BiB-Im. [BiB-Im]:[OH] = 4:1; 55 °C, in bulk for 24h.

To the polymerization mixture under argon flow, 346 mg (1.60 mmol) of BriB-Im (4 Eq. with respect to OH) were added and the temperature was increased up to 55 °C and let react overnight. Samples were taken for NMR analysis to confirm the complete esterification. Next, the crude reaction mixture was brought to room temperature and 5 mL of 0.5 M solution of PhCOOH in DCM was added and stirred for 20 min. to neutralize the TBD and the imidazole formed. Finally, the mixture was diluted with additional 10 mL of DCM and was precipitated twice into 800 mL of cold acetonitrile. The pure polymer was dried under vacuum at 50 °C for 48 hours.

2.2 – Synthesis of I_n-PDL-PMBL block copolymers. [MBL]:[I_n-PDL-Br]:[CuCl]:[$CuCl_2$]:[bpy]; 125:1:2.2:0.2:4.8, 50 °C, DMF (55 % v/v). (Figures SI.36 to SI.42)

In a typical experiment, (data given for I_0-PDL-Br; 18900 g/mol), 0.852 g (0.045 mmols) of macroinitiator were transferred to a 25 mL cylindrical Schlenk flask equipped with a Teflon coated magnetic stir bar. Then, 1.23 mg (0.009 mmols) of $CuCl_2$, 2.83 mg (0.018 mmols) of bipyridine, 490 μL (5.62 mmol) of MBL and 850 μL of DMF were added in this order. The reaction mixture was introduced into a preheated bath at 50 °C until complete homogenization. Once the macroinitiator was completely solubilized, the mixture was degassed through 4 freeze-pump-thaw cycles. After the deoxygenation process, the reaction mixture was returned to the bath at 50 °C for 10-15 minutes until complete homogenization. Separately, a CuCl/bpy stock solution containing 79.6 mg (0.80 mmols) of CuCl, 254 mg (1.60 mmols) of bpy and 4.0 mL of deoxygenated DMF was prepared. Finally, 500 μL of the CuCl/bpy stock solution (0.10 mmols of CuCl and 0.20 mmols of bipyridine; total amount of bypyridine 0.218 mmol) was added dropwise within a period of 5 minutes. The reaction was stopped after 120 min at 41% of conversion by diluting with 0.5 mL of DMF and bubbling air through the mixture. The crude of the reaction was diluted with 8 mL of DCM and passed through a short basic alumina column to remove the catalyst. Finally, the polymer was isolated by precipitation in cold methanol and dried under vacuum.

2.3 – Cleavage of I_n-PDL-PMBL block copolymers

2.3.1 - Reductive cleavage of I_1-PDL-PMBL (Scheme SI.14 and Figure SI.46)

In a 50 ml Schlenk flask with a Teflon coated stirring bar and sealed with a rubber septum, 220 mg of I_1-PDL-PMBL (Mn_{SEC} 20100 g/mol) were dissolved in 20.0 mL of THF. Then, 320 μL of Bu_3P were introduced using a syringe ($[Bu_3P]$ = 0.078M; 150 eq.). The mixture was stirred at room temperature and samples were withdrawn at pre-set times and analysed by SEC and ^{1}H NMR.

2.3.2.-Acid cleavage of I_2-PDL-PMBL (Scheme SI.15 and Figure SI.47)

Two tests using 0.01M and 0.5M solutions of TFA were carried out.

In a 100 ml Schlenk flask with a Teflon coated stirring bar and sealed with a rubber septum, 250 mg ($1.2x10^{-5}$ mol) of I_2-PDL-PMBL (Mn_{SEC} 20600 g/mol) was stirred in 30 mL of THF containing 150μL (0.5 % w/w) of water until complete solution. Then 25 μL (0.01M) or 1200 μL (0.5M) of TFA was introduced using a syringe. The mixture was stirred at room temperature and samples were withdrawn at pre-set times for analysis.

2.3.3.-Acid cleavage of I_3-PDL-PMBL (Figure SI.48)

In a 100 ml Schlenk flask with a Teflon coated stirring bar and sealed with a rubber septum, 400 mg of I_3-PDL-PMBL (Mn_{SEC} 22900 g/mol) was dissolved in 50 mL of THF containing 250μL (0.5 % w/w) of water until complete solution. Then 2.0 mL of TFA was introduced using a syringe ([TFA] = 0.5M). The mixture was heated at 40 °C and samples were withdrawn at pre-set times for analysis by SEC and ^{1}H NMR.

2.3.4 – Homogeneous photolysis of I_4-PDL-PMBL and I_5-PDL-PMBL in acetone solution with TPP/O_2 under UV irradiation. (Figure SI.53)

Tests were carried out in DURAN® cylindrical Schlenk flasks refrigerated with water and irradiated with a 400 W high pressure sodium lamp (Philips HPI-T Plus 400W 645 E40).

About 100 mg of the thioacetal containing block copolymer (Mn_{SEC} = 20.000 g/mol (Đ = 1.18) and Mn_{SEC} = 19.000 g/mol (Đ = 1.15) for I_4 and I_5 block copolymers respectively) was placed in a 50 mL cylindrical flask equipped with a Teflon-coated magnetic stirrer. Then, 20 mL of a 10^{-5} M solution of *meso*-tetraphenylporphyrin (TPP) in acetone was added. Once the polymer was completely solubilized, a gentle oxygen stream was bubbled throughout the reaction mixture while irradiated. Samples were withdrawn at pre-set times and analysed by SEC. After 48 h a new amount of TPP was added and the irradiation and monitoring were continued.

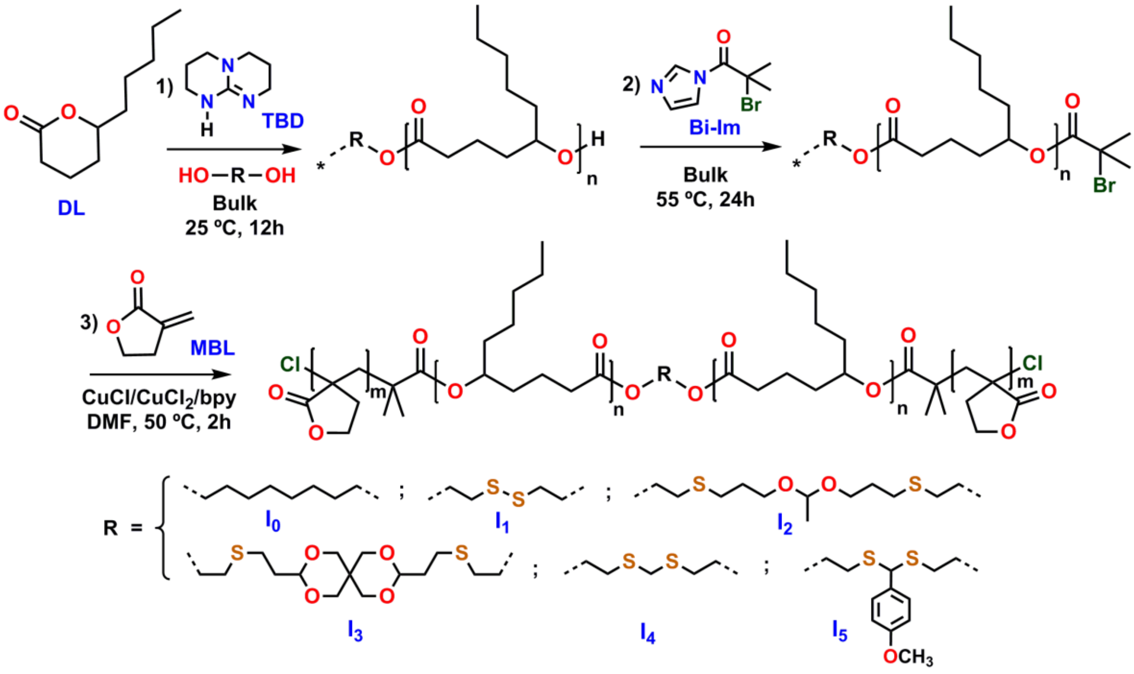
2.3.5 – Photolysis of I_4-PDL-PMBL and I_5-PDL-PMBL with TPP/H_2O_2 under UV irradiation. (Figures SI.55 and SI.56)

About 150 mg of the thioacetal containing block copolymer (Mn_{SEC} = 20.000 g/mol (Đ = 1.18) and Mn_{SEC} = 19.000 g/mol (Đ = 1.16) for I_4-PDL-PMBL and I_5-PDL-PMBL block copolymers respectively) was solubilized in 30 mL of a 10^{-5} M solution of TPP in acetone. The polymer solution was split into three 25 mL cylindrical flask and the solvent evaporated under vacuum to form thin films. Then, 15 mL of a 15% hydrogen peroxide in phosphate buffer solution (pH 7.4) was added to each flask which were irradiated. After pre-set times (3h and 6h) the aqueous phase was removed, and the polymer analysed by SEC and ^{1}H NMR.

In all cases the withdrawn samples were conveniently neutralized with solid $NaHCO_3$ (when necessary), dried with anhydrous $MgSO_4$ and concentrated to dryness. Once the degradation was complete, the remaining solutions were concentrated under vacuum and precipitated twice over cold methanol and the polymer isolated by centrifugation, dried under vacuum for 24 h.

3. RESULTS AND DISCUSSION

The synthetic route to (poly-α-methylene-γ-butyrolactone)-*co*-(poly-δ-decalactone)-*co*-(poly-α-methylene-γ-butyrolactone) (I_n-PDL-PMBL) ABA block copolymers followed in this work is depicted in Scheme 1.



Scheme 1. Synthesis of PMBL-co-PDL-co-PMDL (I_n-PDL-PMBL) triblock copolymers by one-pot two-steps ROTEP of DL with initiators I_0 to I_5, BiB-Im modification, and ulterior ATRP chain extension with MBL.

3.1- Synthesis of α,ω-poly(δ-decalactone)diols (I_n-PDL-OH) (Step 1 in Scheme 1)

In order to prepare poly(δ-decalactone)diols with a cleavable sensitive moiety, different diols (**I_1** to **I_5**) which have disulphide, acetal or thioacetal groups were chosen. 1,8-octanediol (**I_0**) was also used as “non-cleavable” reference and model for the different functionalization and chain extension steps. (Scheme 1)

Non-commercial diols (**I_2** to **I_5**) were synthesized following different reported methods selected by considering their ease to be scaled and the purification procedure (SI.1.3) Acetals **I_2** and **I_3** were obtained by photo initiated thiol-ene addition of 2-mercaptoethanol to acetaldehyde diallylacetal and commercial 3,9-divinyl-2,4,8,10-tetraoxaspiro[5,5]undecane respectively [38]. Thioacetals **I_4** and **I_5** were synthesized by reaction of 2-mercaptoethanol with methylene dibromide in basic media (NaOH) [39] and with anisaldehyde catalysed by $NiCl_2 \cdot 6H_2O$ [40] respectively.

Polymerization of δ-decalactone (DL) with 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) has been extensively studied by Martello et al. [33] Following the reported procedure, ROTEP of DL using 1,8-octanediol (**I_0**) as initiator [DL]:[1,8-Oct] = 150:1 and TBD as catalyst [TBD]:[1,8-Oct] = 0.8:1 ([TBD]:[-OH] = 0.4:1) was carried out in bulk at 25 °C . According to ^{1}H NMR and SEC measurements (SI.1.6.1), the polymerization proceeds with fair molecular weight control (Đ = 1.2-1.5) up to 70-80% conversion which corresponds to the maximum thermodynamic conversion of δ-DL at 25 °C. Previous ROTEP tests using methanol to isolate the polymer, indicated an overestimation of the CHOH end group ^{1}H NMR signal in the resulting samples due to TBD induced methanolysis of unreacted DL during the work up. This fact, that was confirmed by the presence of methyl 5-hydroxydecanoate in the volatile fraction collected under vacuum, has been previously described in ROTEP of lactones [41]. To suppress this undesired reaction, acetonitrile was tested as precipitating media. Results (Table SI.1 and Figure SI.11) indicate the convenience of this solvent giving similar polymer recoveries and preventing the formation of undesired hydroxyl impurities.

3.2- Synthesis of α,ω-poly(δ–decalactone)diol bis-α-bromoisobutyrylesters (I_n-PDL-Br) (Step 2 in Scheme 1)

Commonly, the activation of polyesterdiols as α-bromoisobutyrates is performed in a multistep sequence that involves the isolation and purification of the polyester, the reaction with α-bromoisobutyryl bromide (BiB-Br) in presence of organic bases (Et_3N, DMPA) and finally the isolation and purification of the resulting modified ester. [21, 42, 43] This latter step implies removing insoluble amine salts, aqueous work-up and very often an ulterior polymer purification to remove the brown impurities that usually accompanied this protocol. We sought for a more straightforward route to prepare these macroinitiators by direct functionalization of the hydroxyl end groups in the polymerization mixture once the theoretical maximum conversion was reached.

Acylimidazoles have been described as effective acylating agents and can be conveniently synthesized from the corresponding acyl halide and imidazole or the parent carboxylic acid and carbonyldiimidazol. [44] Acylimidazoles give imidazole as the only by-product, which is easily removable and do not produce strong pH changes in the medium, thus contributing to negligible chain degradation. Accordingly, these acylating agents have been previously used to activate hydroxyl groups to perform ATRP [45] or SET-LRP. [46,47] Moreover, N-(α-bromoisobutyryl)imidazole (BiB-Im) is an easy to handle stable reagent that can be easily synthesized in large quantities [45].

Reaction of I_0-PDL-OH with BiB-Im (4 eq) in THF at 60 °C did not afford appreciable acylation. On the contrary, after the addition of DBU or TBD (ca. 5%) the reaction proceeds smoothly, and complete esterification took place after few hours. This result prompted us to use BiB-Im directly into the bulk ROTEP medium once the ceiling conversion has been reached. Thus, addition of BiB-Im (4 eq) to the polymerization mixture gave the desired I_o-PDL-Br after rising the temperature to 55 °C for 24h.

To assess the method effectiveness, I_0-PDL-OH esterification assays were carried out following three different strategies by comparing the resulting BiB esters in terms of degree of modification, molecular weight and ease of isolation and purification. (SI.1.6.3) First approach involved two separate steps, i) ROTEP of DL and isolation of the resulting I_0-PDL-OH and ii) conventional modification with BiB-Br in DCM/TEA. In the second, the two steps were carried out consecutively in one pot after diluting with DCM. The third, involved the same two steps-one pot procedure but using BiB-Im instead of BiB-Br. Similar molecular weights (Table SI.2) and complete esterification degree were obtained in all cases, but polyesters obtained with BiB-Br have a slightly higher polydispersity index and a marked brown colour which needed for further purification. Thus, the use of BiB-Im, allow us to perform the DL polymerization and I_0-PDL-OH activation following two sequential steps in one pot reaction (Step 2 in scheme 1). Precipitation in acetonitrile was found to effectively eliminate not only unreacted DL and TBD but also the excess of BiB-Im, imidazole and the traces of N-(α-bromoisobutyryl)-1,5,7-triazabicyclo[4.4.0]dec-5-ene formed in small quantities during the modification step (Figure SI.12). The fidelity of end group modification with BiB-Im was also assessed by MALDI-TOF (Figure 1).

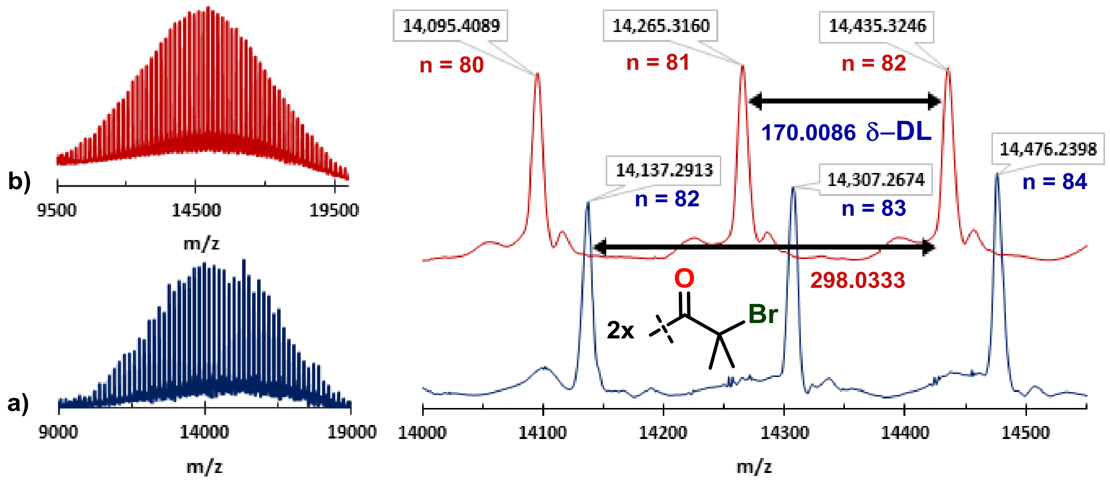


Figure 1.- MALDI-TOF spectra of a) I_0-PDL-OH and b) I_0-PDL-Br obtained by one-pot two-steps modification with BiB-Im. Samples prepared using trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) as matrix and potassium trifluoroacetate (KTFA) as cationization agent (recorded in reflector mode).

The two-step procedure was applied to initiators $\mathbf{I_0}$ to $\mathbf{I_5}$ using the same polymerization conditions: [DL]:[I_n] = 150:1; [TBD]:[I_n] = 0.8:1 ([TBD]:[-OH] = 0.4:1); bulk at 25 °C with targeted Mn around 20x10^3 g/mol. Polymerizations were stopped at around 75% monomer conversion (10h). The exact conversions and molecular weights determined by ^{1}H NMR and SEC for each initiator are indicated in Table 1. In all cases, small samples of the polymerization mixture were withdrawn to have also the corresponding I_n-PDL-OH for characterization purposes. Following, addition of BiB-Im (4 eq) and rising the temperature up to 55 °C was carried out for the modification step. I_n-PDL-Br macroinitiators were isolated by precipitation in cold acetonitrile with yields ranging 60-70 %, after drying, as colourless transparent viscous liquids.

The different polyesters (I_n-PDL-OH and I_nPDL-Br) were characterized by SEC in THF, ^{1}H NMR and ^{13}C NMR spectroscopy and by MALDI-TOF when samples were stable enough under MALDI conditions. (Figures SI.15 to SI.30). Polymer conversions, yields and molecular weight characteristics are collected in table 1.

Table 1- Conversion and molecular weight characteristics of the macroinitiators obtained by polymerization of DL with TBD initiated with initiators I_0 to I_5 and ulterior modification

with Bib-Im. Polymerization conditions [DL]:[I] = 150:1, [TBD]:[OH] = 0.4:1 in bulk at 25 °C for 10h; Modification conditions [BIB-Im]:[OH] = 4:1 at 55 °C for 12h.

I	Conv.[a] (%)	Yield[b] (%)	$Mn_{Theor.}$[c] (g/mol) ($x10^{-3}$)	Mn_{NMR}[d] (g/mol) ($x10^{-3}$)	$Mn_{NMR,}$[e] (g/mol) ($x10^{-3}$)	Mn_{SEC}[f] (g/mol) ($x10^{-3}$)	Đ[f]
I_0	77	68	20.0	18.9	18.1	23.5 (5.8)	1.16 (1.15)
I_1	80	71	20.7	21.7	20.4	24.8 (5.9)	1.29 (1.23)
I_2	79	66	20.5	20.1	19.6	22.4 (5.0)	1.16 (1.11)
I_3	82	75	21.3	22.5	22.4	24.3 (6.0)	1.17 (1.11)
I_4	78	65	20.2	20.1	19.2	23.3 (5.6)	1.18 (1.20)
I_5	78	62	20.2	19.9	19.3	22.9 (5.4)	1.16 (1.18)

[a] Determined by ^{1}H-NMR spectroscopy by comparing the intensity of the signals of the polymer backbone (4.88 ppm) and the unreacted monomer (4.28 ppm). [b] Polymer recovery after precipitation in cold acetonitrile. [c] Determined from targeted DP and the obtained conversion. [d] Determined by ^{1}H-NMR spectroscopy by comparing the intensity of the signals of the polymer backbone ($C\underline{H}$-OOC) at 4.88 ppm and the initiator ($C\underline{H}_2O$): I_0 = 4.05 ppm, I_1 = 4.33 ppm, I_2 = 4.21 ppm, I_3 = 4.21 ppm, I_4 = 4.25 ppm and I_5 = 4.17 ppm. [e] Determined by ^{1}H-NMR spectroscopy by comparing the intensity of the signals of the polymer backbone ($C\underline{H}$-OOC) at 4.88 ppm and the methyl BiB groups at 1.93 ppm. [f] Plain values determined using SEC in THF, relative to polystyrene standards; values between brackets, determined using SEC in DMF (0.05% LiBr) relative to PMMA standards.

As can be seen, molecular weights determined by ^{1}HNMR spectroscopy from both the initiator ($C\underline{H}_2$-OOC) and the BiB groups ($OOCC(C\underline{H}_3)_2Br$) (Figure SI.13) match reasonably well with those of the theoretical ones calculated from the conversion degree, indicating an adequate control of the molecular weight and a negligible hydrolysis during the modification and work up steps. Molecular weights determined by SEC vary depending on the solvent polarity due to changes in hydrodynamic volume. In THF using PS standards, they are slightly higher than the calculated by ^{1}H NMR (in the range of 22-25x10^3 g/mol) whereas in DMF fall to 5.0-6.0x10^3 g/mol. In both cases monomodal distributions with Đ values between 1.16-1.18 (in THF) were observed except for I_1-PDL-OH obtained with the commercial disulphide-diol. Repeated attempts to obtain a narrower polymer with this initiator were unsuccessful, which could be related with some TBD mediated disulphide exchange with trace amounts of thiol impurities during the polymerization process. [48] Similar polydispersity values have been reported in the TBD catalysed ROTEP of disulphide monomers. [49]

The ROTEP and modification steps could be followed by ^{1}H NMR by the changes in the chemical shifts of the pristine initiator I_n, the I_n-PDL-OH polyester and the I_n-PDL-Br macroinitiator. In figure 2 a, b and c, the ^{1}H NMR spectra of I_3, I_3-PDL-OH and I_3-PDL-Br are shown with the most relevant assignments as a representative example.

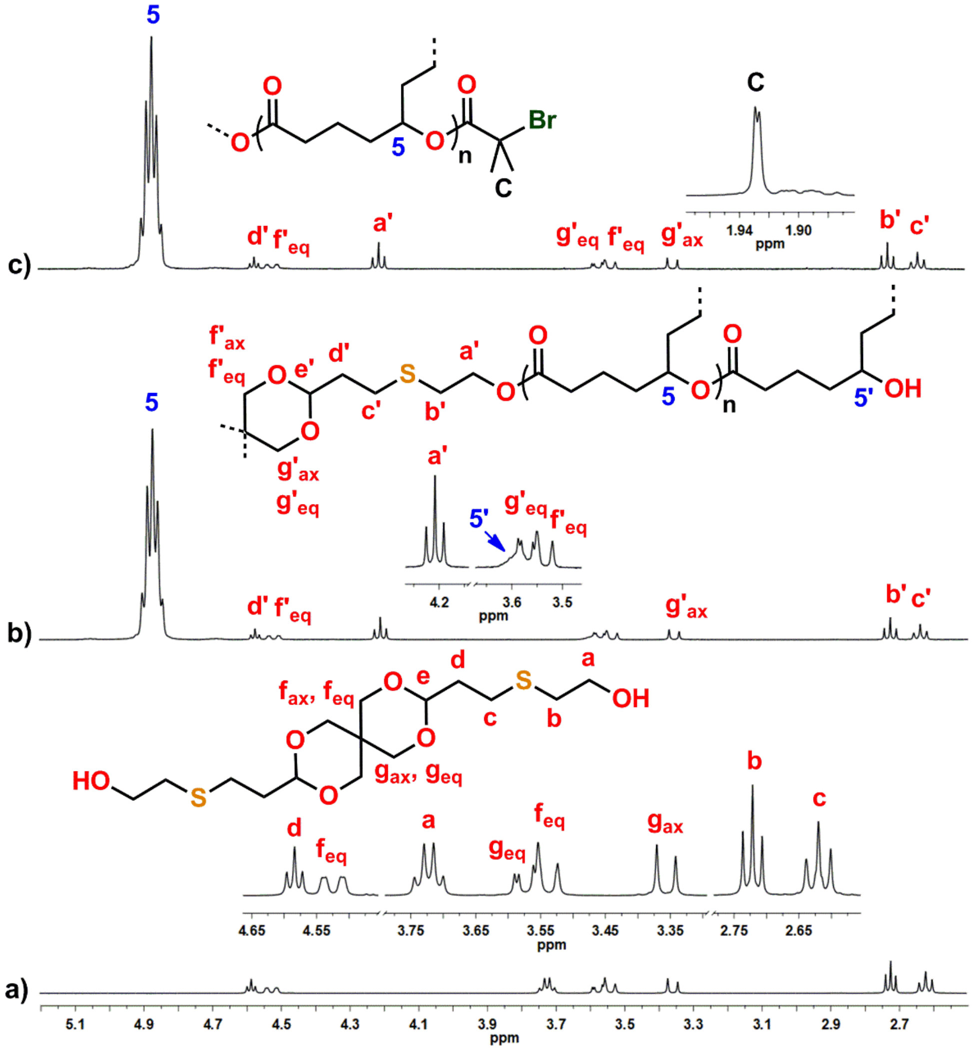


Figure 2.- Region between 5.2 and 2.5 ppm of the ^{1}H NMR spectra of a) initiator I_3 ; b) I_3-PDL-OH and c) I_3-PDL-Br recorded in $CDCl_3$.

As can be seen, the multiplet signal at 3.73 ppm (**a**) corresponding to the $-CH_2OH$ group in the initiator (figure 2a), shifts to 4.20 ppm (**a'**) in I_3-PDL-OH (figure 2b). Moreover, the multiplet of the final CH-OH end-groups at 3.58 ppm (**5'**) can be observed. No signals of the starting diols were detected in the isolated polyesters. After BIB esterification, the

CHOH signal at 3.58 ppm disappear and the new CH-O-BiB signal shifts to 4.8 ppm overlapping with that of the PDL main chain (**5**). Moreover, new signals corresponding to the methyl's in the BiB ester group at 1.93 ppm (**C**) are observed (Figure 2c).

^{13}C NMR spectra also confirmed the structures, being the most remarkable trend the up shielding of the methine end group from 71.4 ppm to 75.7 ppm upon esterification. Noticeably, in ^{13}C NMR spectra of I_n-PDL-OH (figure 3), signals of the methine (**5'**) and the carbonyl (**1'** and **1''**) of the two last repetitive units appear split independently of the sample molecular weight. gHSQC correlation experiments (Figure SI.14) indicate that both ^{13}C NMR $\underline{C}$H-OH signals correlate with the same ^{1}H signal at 3.58 ppm. Moreover, the ^{1}HNMR splitting disappears after trifluoroacetilation leading a single signal at -76.2 ppm in ^{19}F-NMR thus confirming the existence of a single type of hydroxyl end-group. These facts seem to indicate that splitting is due to sequence sensitivity probably favoured by intramolecular hydrogen bonding in the ultimate units.

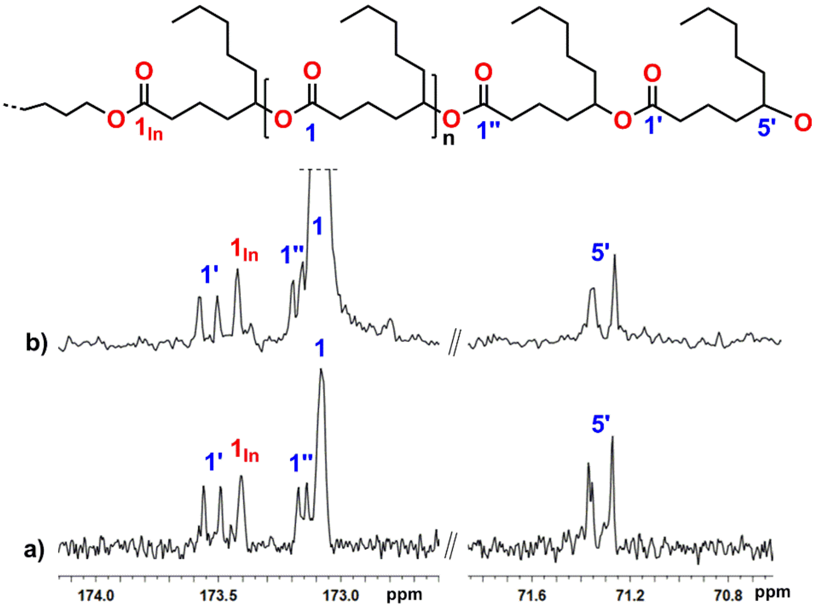


Figure 3.- Regions between 174 and 172 ppm and betewen 71.7 and 70.7 ppm of the ^{13}C NMR spectra of a) I_0-PDL-OH of Mn_{MNR} 1520 g/mol; b)) I_0-PDL-OH of Mn_{NMR} 18.900 g/mol, recorded in $CDCl_3$.

MALDI-TOF spectra of both I_n-PDL-OH and I_n-PDL-Br (Figure SI.15 and SI.23) resulted challenging and high energy pulses had to be used in most cases. Consequently, some low molecular scission products were observed in polymers containing acetal linkages and in minor extent polymers containing thioacetal linkages. Despite this, clear pattens with peaks differing 170.13 mass units were observed. In the case of I_1-PDL-OH and I_1-PDL-Br only low molecular weight fragmentation products were observed according to the reported ease of scission and oxidation of disulphides under MALDI sample preparation. [50] In all cases no peaks of remaining I_n-PDL-OH could be detected.

3.3- ATRP chain extension with MBL. Synthesis of I_n-PDL-PMBL (Step 3 in Scheme 1)

After preparing the different I_n-PDL-Br soft segment macroinitiators with a DP around 120 (20000 g/mol), chain extension with MBL was faced (step 3 in Scheme 1). According to previous works [22, 23, 37] phase segregation is reached when 15-20% (w/w) of the hard block is incorporated. Accordingly, a final DP of the PMBL block of 40 (4000 g/mol) was targeted. A specific DP can be achieved by tuning several parameters, [51] for instance, targeting a high final DP and limiting the conversion degree or targeting the desired DP and extending the conversion upon completion. Considering sustainability issues, the ideal situation would be that most of the monomer became incorporated in the final polymer. However, the combination of low targeted DP and moderate-high conversions could involve an increase of dead chain fraction (DCF). Moreover, the limited solubility of PMBL requires using polar solvents such as DMF which influence the initiation efficiency [52] and reduces $[MBL]_0$ which in turn also increases DCF. Consistently, in order to establish a proper balance between monomer conversion and chain extension fidelity, MBL polymerization using 1,4-phenylene-bis(methylene)bis(2-bromoisobutyrate) (I_{Ph}-Br) as model difunctional ATRP initiator was carried out. Since BiB groups possess limited initiation efficiency for MMA like monomers [53] and MBL has higher reactivity than MMA, the halogen exchange approach was used. [54]

Thus polymerization using the conditions $[MBL]:[I_{Ph}\text{-}Br]:[CuCl]:[CuCl_2]:[bpy] = 125:1:2.2:0.2:4.8$ in DMF (55% v/v) at 50 °C was followed up to 85% conversion. (SI.1.7). Molecular weight increased linearly and polydispersities decreased with conversion up to Đ = 1.07 (Figures SI.32 and SI.33). Molecular weights determined by ^{1}H NMR spectroscopy and by SEC were slightly higher than the theoretical ones as expected by limited initiator efficiency. Structural analysis (figure SI.31 and SI.34) showed the presence of about 5-7% of α-chloroisobutyryl groups in the final polymers. These groups, which are much less effective for initiation, could most likely be produced by halogen exchange with the initiator during the initiation (Figure 4c). This feature is supported by presence of some low molecular tails in the SEC chromatogram corresponding to monoinitiated polymers (Figure SI.32).

This assay showed that, with the tested conditions, high monomer incorporation ratios can be achieved (40-50%) with reasonably good fidelity and high initiation efficiency (~ 90%) Accordingly, the same ATRP conditions were applied for macroinitiators I_n-PDL-Br.

Polymerizations procced smoothly with a notable viscosity increase and after 60-90 min, 38-45% conversions determined by ^{1}H NMR spectroscopy were reached (Figure SI.35). I_n-PDL-PMBL copolymers were isolated as white rubbery filamentous flakes which were characterized by ^{1}H and ^{13}C NMR spectroscopy and SEC. Result are collected in Table 2.

Table 2 - Conversion and molecular weight characteristics in the polymerization of MBL with macroinitiators I_n-PDL-Br. Polymerization conditions [MBL]:[I_n-PDL-Br]:[CuCl]:[$CuCl_2$]:[bpy]; 125:1:2.2:0.2:4.8, 50 °C, in DMF (55 % v/v).

I_n-PDL-PMBL	Conv.[a] (%)	Mn_{SEC}[b] (g/mol) ($x10^{-3}$)	Đ[b]	Mn_{NMR} (g/mol) ($x10^{-3}$)[c]		% (wt) of PMBL
				Poly(DL)	Poly(MBL)	
I_0-PDL-PMBL	41	18.9	1.17	19.2	3.8	16.5
I_1-PDL-PMBL	39	20.1	1.27	20.2	3.6	17.8
I_2-PDL-PMBL	44	20.6	1.17	19.5	4.1	17.4
I_3-PDL-PMBL	45	22.9	1.17	21.1	4.0	16.6
I_4-PDL-PMBL	42	20.0	1.18	19.0	3.9	17.0
I_5-PDL-PMBL	38	19.0	1.16	20.1	3.7	15.5

[a]Determined by ^{1}H-NMR spectroscopy from the crude reaction mixture using the signals of monomer (5.68 ppm) and polymer backbone (4.38 ppm). [b]Determined by SEC using DMF (0.05% (w/w) LiBr) as eluent and PMMA standards. [c] Determined by ^{1}H-NMR spectroscopy from the isolated polymer using the signal of the initiator (I_0 = 4.05 ppm, I_1 = 2.91 ppm, I_2 = 2.65 ppm, I_3 = 2.64 ppm, I_4 = 2.87 ppm, I_5 = 3.81 ppm) and the PDL backbone signal (4.87 ppm) and PMBL backbone signal (4.38 ppm) respectively.

SEC measurements in DMF (Figure SI.36) show monomodal distributions with a clear increase on the molecular weight indicating that chain extension occurs in all cases. Polydispersity values of the final copolymers slightly increase due to the presence of the above mentioned low molecular monoininitiated species (Figure 4a).

^{1}H-NMR analysis of I$_n$-PDL-PMBL block copolymers could be conducted CDCl$_3$ (Figure 4b and SI.37-42). The incorporation of 15-17 % of PMBL could be determined from the relative intensity of the signals at 4.87 ppm (CH-O in PDL backbone) and 4.38 ppm (CH$_2$O in PMBL ring). Moreover, molecular weight of both segments could be estimated from the signals of the initiator. Initiation efficiency could not be calculated since the methyl signals of the chain extended isobutyryl units appear overlapped with the broad signal of methylenes **7**, **8** and **9** of the PDL moiety (Figure 4b). In most cases, small methyl peaks at c.a. 1.77 ppm associated to the formation of chloroisobutyryl groups were detected indicating the presence of small percentages of monoinitiated species which correlate with the tails in the SEC traces (Figure 4a).

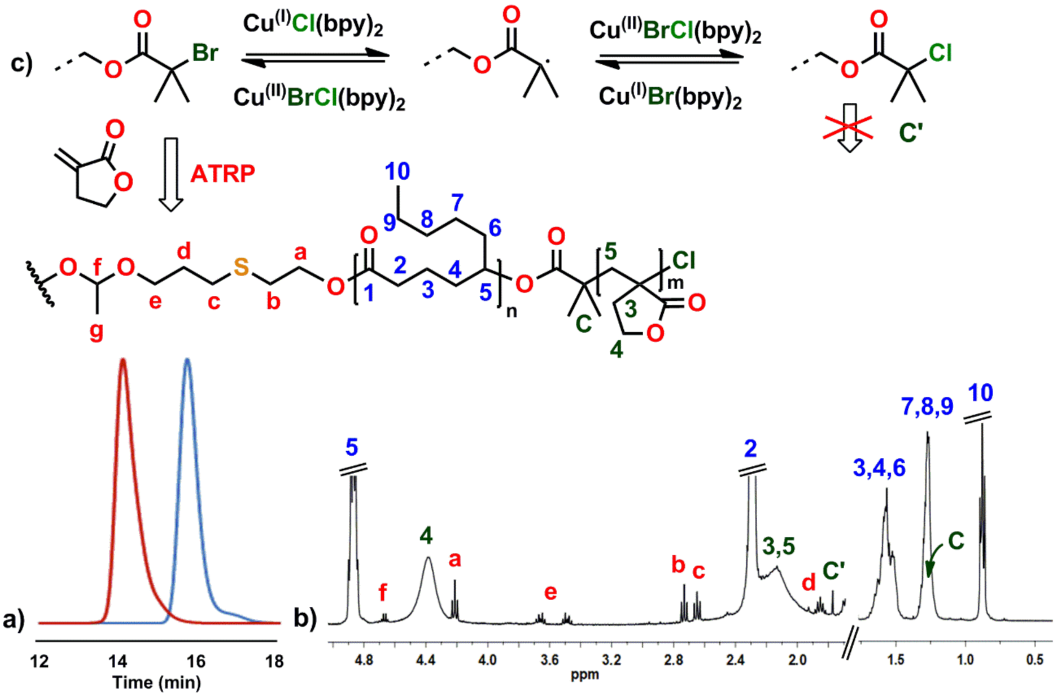


Figure 4.- a) SEC chromatograms in the MBL chain extension of I$_2$-PDL-Br (red trace) to I$_2$-PDL-PMBL (blue trace); b) region between 4.9 and 0.5 ppm of the ^{1}H NMR spectrum of I$_2$-PDL-PMBL with the corresponding assignments; c) proposed mechanism for the halogen-exchange deactivation of α-bromoisobutyryl groups in ATRP.

^{13}C NMR spectra also confirm the extensive chain extension and support the calculated ratios between the soft and hard segments by comparing the intensities of the carbonyl (C=O), methylene (CH$_2$OOC) and methine (CHOOC) carbons of both repeating units (**1**, **4** and **5** in figures SI. 37b to 42b). Signals of methylenes **5** and **3** in the MBL repeating unit appear as broad signals at about 42 and 30 ppm respectively.

3.4- Thermal properties of I_n-PDL-PMBL

Although a detailed characterization of the thermo-mechanical properties of these materials was not within the scope of this work, the representative thermal and thermo-mechanical behaviour of I_0-PDL-PMBL copolymer was analysed by TGA, DSC and DMTA. All synthesized ABA copolymers possess similar molecular weights and comparable structure and consequently must present similar thermal and mechanical properties.

Thermal behaviour of I_0-PDL-PMBL was compared with that of I_0-PDL-OH and I_{Ph}-PMBL as representatives of the soft and hard blocks. Weight loss profiles (Figure SI.43) of PDL indicate higher resistance to degradation than the reported in the literature [34] in both the homopolymer and the copolymer soft segment ($T_{5\%}$ 300 °C and T_{max} 349 °C for I_0-PDL-OH) which can be associated to the effective removal of trace impurities that catalyse depolymerisation processes. In the case of I_{Ph}-PMBL, a single degradation step correlating with the data reported in the literature was observed ($T_{5\%}$ 317 °C and T_{max} 349 °C).[55] Accordingly, I_0-PDL-PMBL shows a two-step degradation with maximums at 351 and 413 °C.

Analysis by DSC of I_0-PDL-OH and I_{Ph}-PMBL (Figure SI.44) also agree with the reported literature values (Tg = − 53 °C for I_0-PDL-OH and Tg = 181 °C for I_{Ph}-PMBL). [33, 55] In the case of I_0-PDL-PMBL block copolymer, a first glass transition corresponding to the PDL soft block is clearly observed at − 52 °C. The second transition corresponding to the PMBL hard block can be perceived around 170 °C suggesting the occurrence of phase-separation. This second transition is about 25 °C lower than the reported for other MBL copolymers (~ 195 °C) [36] which has to be related with the plasticizing effect of a small fraction of AB block copolymer due to incomplete initiation as above mentioned.

The thermomechanical properties of I_0-PDL-PMBL block copolymer were analysed in a in a three-point bending configuration monitoring the modulus as function of temperature from − 80 to 220 °C (Figure SI.45). Tan δ plot showed a first peak at − 36 °C corresponding to the glass transition of the soft PDL block. Below this temperature the material showed a storage modulus (E’) of 1674 MPa, indicating that is hard and brittle. After the first glass transition the storage modulus (E’) lowered until 11.9 MPa and showed a plateau which dominates over the viscous response (E’ > E’’, and tan (δ) tending to zero) correlating with the region of elastomeric behaviour. A second glass transition, corresponding to the PMBL hard block, was observed as a second tan δ peak at 164 °C. An additional smooth transition at c.a. 10 °C was detected in the storage modulus (E') and Tan δ plots. This transition could be attributed to the I_0PDL-PMBL AB block fractions which could also be the cause of the lower softening temperature of the hard block (164 °C) compared to similar copolymers (~ 195°C). [36] In this way, mono-initiated chains seems to act as plasticizer rarefying the mechanical response and reducing the elastomeric temperature range from − 36 to 164 °C.

3.5- Cleavage of I_n-PDL-PMBL

As last step, we faced the cleavage tests using the stimuli and reaction conditions reported in the literature. Reductive scission of disulphide linkages it is commonly carried out by thiol-disulphide exchange or using phosphines as reducing agents. [56,57,58] Bu_3P/H_2O in THF at room temperature ($[Bu_3P]$ = 0.078M; 150 eq.) (SI.1.9.1) effectively cleaved the copolymer after 30 min. SEC chromatograms showed than molecular weight of the resulting AB copolymer (Mn_{SEC} 9900 g/mol; Đ = 1.20) was about half the starting ABA copolymer (Mn_{SEC} 20.100 g/mol; Đ = 1.27) after 30 min (Figure 5a).

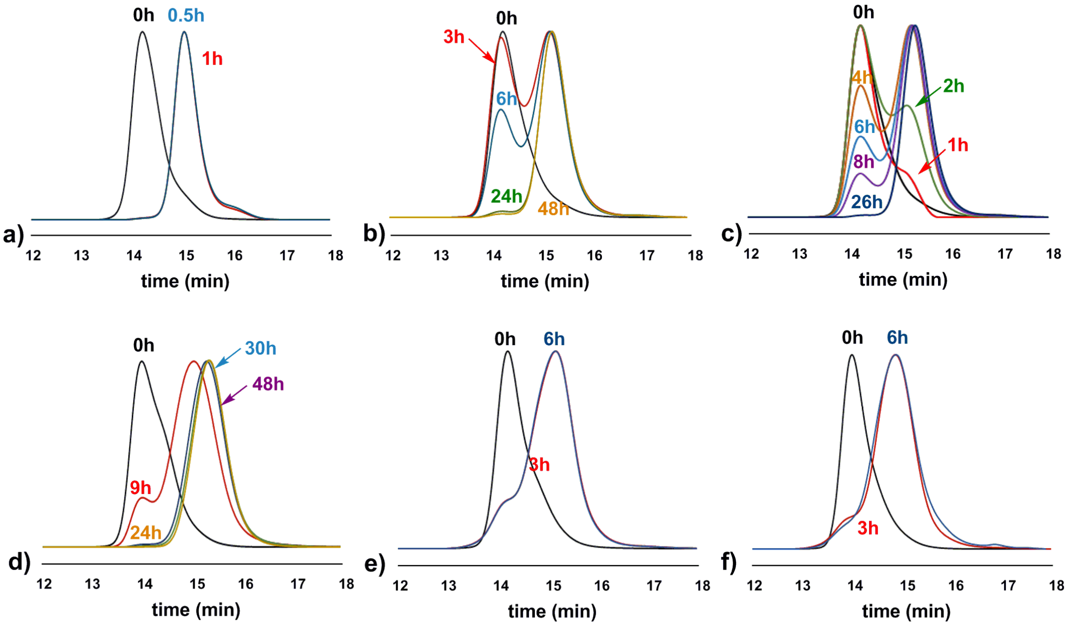
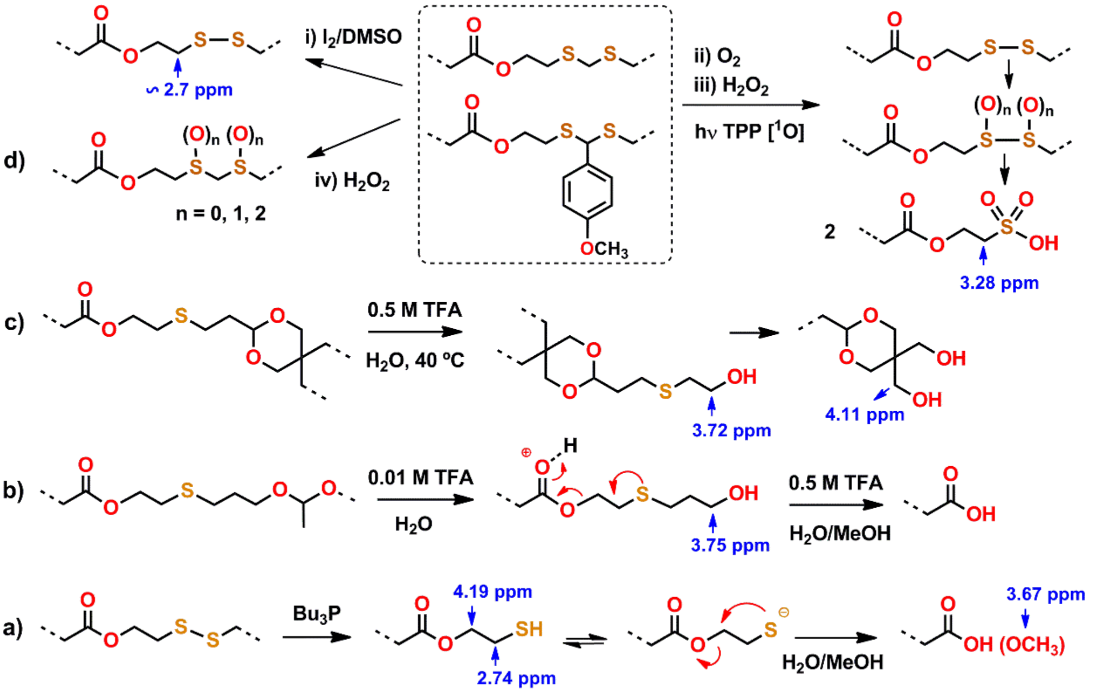


Figure 5.- SEC chromatograms of the I_n-PDL-PMBL cleavage experiments versus time: a) I_1-PDL-PMBL in THF using Bu_3P/H_2O at room temperature ; b) I_2-PDL-PMBL in THF/H_2O using TFA (0.01M) at room temperature; c) I_2-PDL-PMBL in THF/H_2O using TFA (0.5M) at room temperature; d) I_3-PDL-PMBL in THF/H_2O using TFA (0.5M) at 40 °C; e) I_4-PDL-PMBL and f) I_5-PDL-PMBL using H_2O_2/TPP/hν without solvent.

The cleaved polymer showed a low molecular weight tail most likely arising from the monoinitiated chains present in the starting sample. In fact, I_1-PDL-PMBL possessed the widest Đ value and the higher amount of chloroisobutyryl free groups.

^{1}H NMR spectra of the obtained AB copolymer (Figure SI.46 and Scheme SI.14) showed the signals of both PDL and PMBL segments and the complete disappearance of the signal at 2.92 ppm corresponding to the disulphide moiety $-CH_2-S-S-CH_2-$. Moreover, two new signals at 4.19 and 2.74 ppm attributable to the $–COOCH_2CH_2SH$ end-group were observed. The relatively low intensity of these signals and the presence of a methyl ester signal at 3.67 ppm, seems to indicate that some intramolecular S_N2 displacement of the intermediate thiolate groups and ulterior esterification during the methanolic work-up may also occur. (Scheme 2a) [56,59]



Scheme 2. Cleavage experiments displaying the different detected species, the proposed cleavage mechanisms and some of the characteristic ^{1}H NMR signals chemical shifts. a) cleavage of I_1-PDL-PMBL in THF using Bu_3P/H_2O; b) cleavage of I_2-PDL-PMBL in THF/H_2O using 0.01M and 0.5M TFA; c) cleavage of I_3-PDL-PMBL in THF/H_2O using 0.5M TFA at 40 °C; d) cleavage of thioacetal derivatives: i) cleavage of I_4-M and I_5-M in $DMSO_{d6}/I_2$ at 90 °C; ii) cleavage of I_5-M, I_4-PDL-PMBL and I_5-PDL-PMBL using O_2/TPP/hν in acetone; iii) cleavage of I_4-PDL-PMBL and I_5-PDL-PMBL using H_2O_2/TPP/hν without solvent; iv) oxidation of I_4-M with 50% H_2O_2.

Acetals and related groups (orthoesters) are one of the most studied functionalities for producing acid cleavable polymers [60] with the ability to fine tune the hydrolysis pH by selecting the appropriate substituents [61]. The acid triggered cleavage response of I_2-PDL-PMBL and I_3-PDL-PMBL was studied using TFA in THF solution containing 0.5% of water (Figure SI.47and Scheme SI.15). In the case of I_2-PDL-PMBL, 0.01M and 0.5M TFA solutions were tested at room temperature. SEC chromatograms show that complete degradation takes place after about 24h in both cases. The initial ABA copolymer with Mn_{SEC} = 20.600 g/mol and Đ = 1.17 lead to AB block copolymers with similar narrow distributions and Mn_{SEC} = 10.400 g/mol (Đ = 1.10) and Mn_{SEC} 10000 g/mol (Đ = 1.10) respectively (Figure 5b and 5c). ^1H NMR analysis of the recovered polymers confirmed the complete disappearance of the acetalic group signals but revealed differences in the structure of the end-groups (Figure SI.47). In 0.01M TFA solution, the signals of the expected (3-hydroxypropyl)thioethyl ester end-grups ($HOCH_2CH_2CH_2SCH_2CH_2OOC$-) were clearly observed at 4.38, 3.75, 2.75 and 2.69 ppm indicating the hydrolysis of the acetal group as the only process (Scheme 2b). On the contrary, in 0.5M TFA solution these signals are absent suggesting the sulphur-assisted selective hydrolysis of the terminal ester linkage promoted under strong acidic conditions, (Scheme 2b). Similarly, β-thiopropionate esters are well known as acid labile groups and have been extensively used in acid-sensitive polymeric devices [62, 63, 64].

According to literature, tetraoxospiroacetals show a significant resistance to acid hydrolysis. [38, 65] Our preliminary tests with I_3-PDL-PMBL (Mn_{SEC} 22.900 g/mol; Đ = 1.17) evidenced no significant hydrolysis after 24h at room temperature, thus degradation was performed at 40 °C in 0.5M TFA/H_2O in THF. Under these conditions, SEC traces (Figure 5d) showed a progressive cleavage which was almost complete after 24 h leading to a monomodal polymer distribution of approximately half the molecular weight of the starting copolymer (Mn_{SEC} 11.500 g/mol; Đ = 1.11) which remain unaltered after 48h indicating no noticeable hydrolysis of the polyester main chain under these conditions. Even though, cleavage is evident from SEC traces, the ^1H NMR spectrum of the recovered polymer (Figure SI.48) showed the persistence of most signals of the tetraoxospiroacetal moiety. In addition, two new signals at 3.72 and 4.11 ppm could be observed. The triplet signal at 3.72 ppm can be assigned to hydroxyethylthio end-groups

(HOC$\underline{H}_2$CH$_2$-S-) arising from sulphur assisted hydrolysis of the β-thioethyl ester units in a similar way as observed for the hydrolysis of I$_2$-PDL-PMBL under strong acidic conditions (Scheme SI.15). The singlet at 4.11 ppm can be assigned to the C(CH$_2$OH)$_2$ groups resulting from the subsequent progressive hydrolysis of the acetal units. [66] Thus, even though cleavage of I$_3$-PDL-PMBL can be triggered under strong acidic conditions, it mainly proceeds by β-thioethyl ester hydrolysis leading to tetraoxospiroacetal units that are hydrolysed at slower rates (Scheme 2c).

Chemoselective cleavage of thioacetals under mild conditions is still a challenging process. Unless acetal groups, thioacetals are resistant to conventional acid and basic hydrolysis requiring quite harsh conditions. As a key step in synthesis, a plethora of cleavage methods have been developed which generally require heavy metal derivatives and other environmentally hazardous reagents. [67] A common approach involves the transformation of thioethers into better leaving sulfonium groups by using different halogen sources. Interestingly, catalytic amounts of iodine proved to be effective in thioacetal deprotection when DMSO is used as oxygen source. [68, 69] Moreover, the cleavage by iodonium ions would give access to a more general procedure using chloronium ions in bleach, a common chemical used in paper processing.

This procedure was first tested on two thioacetal model compounds I$_4$-M and I$_5$-M obtained by esterification of diols I$_4$ and I$_5$ with dodecanoyl chloride (SI.1.9.4.2). I$_4$-M and I$_5$-M were dissolved in DMSO-d6 containing 1% of I$_2$ at 90 °C and the reaction monitored by ^{1}H NMR spectroscopy. In both cases the characteristic thioacetal signal at 3.72 and 5.02 ppm respectively disappeared. In the case of I$_5$-M, deprotection was complete after only 30 min but 12h were required for I$_4$-M in accordance to the lower stability of the intermediate cationic species in methylene thioacetals (Scheme SI.18). However, according to the ^{1}H NMR spectra (Figure SI.51b and c) the cleavage produces a mixture of aldehyde and the disulphide derivative, what supposes an effective deprotection of the carbonyl group but not a real cleavage of the polymer chains (Scheme 2d, i)). Recent studies confirm the formation of disulphides in the H$_2$O$_2$ oxidative [70] and the iodine activated photooxidative [71] deprotection of thioacetals.

Precisely, photooxidative cleavage is another common approach which has recently experienced an increasing interest when applied to the production of ROS-responsive polymeric drug carriers. [72,73] Photooxidative deprotection of cyclic and acyclic thioacetals has been described to proceed under mild conditions with light irradiation. [71,74,75] Singlet oxygen ($^1O_2$) has been proposed as reactive species in the S-C bond cleavage leading to different products depending on the nature of the substituents and the redox potential of the sensitizer used. [75]

Initial tests were carried out using UV irradiation in a saturated oxygen atmosphere and *meso*-tetraphenylphorphin (TPP) as sensitizer. Photolysis of thioacetal I_5-M in acetone solution was monitored by ^{1}H NMR spectroscopy (Figure SI.52). Rapid deprotection leading to anisaldehyde and the corresponding disulfide was observed at the beginning (2h). After complete consumption of the thioacetal, spectra became more complex indicating the formation of different oxidized species which, according to the literature, [76] could be attributed to a mixture of sulfinothioate (R-S-SO-S) and sulfonothioate (R-S-SO_2-R) an some thioacetal oxidation compounds formed following stablished mechanisms (Scheme SI.19). Delightfully, after 12h a simpler spectrum showed the formation of a main product whose ^{1}H NMR signals suggest the formation of the carbonyloxyethanesulfonic derivative (-$COOCH_2CH_2SO_3H$) together with some remaining disulfide (Scheme 2d, ii)) and Figure SI.52d).[77] With these results, the same methodology was applied to I_4-PDL-PMBL (Mn_{SEC} 20.000 g/mol; Đ = 1.18) and I_5-PDL-PMBL (Mn_{SEC} 19.000 g/mol; Đ = 1.16) copolymers (Scheme 2d, ii)). In both cases, SEC traces (Figure S.I.53 a and b) indicate a progressive slow cleavage leading to polymers with about half the initial molecular weight. However, the process seems to be incomplete and some high molecular weight fractions remain after 24-48h especially in the case of I_4-PDL-PMBL. Prolonging irradiation after a new TPP addition seems not increase substantially the cleavage extend.

Hydrogen peroxide, a common paper processing chemical, has also been described as an effective source of ROS in the photolysis of thioacetals in aqueous media. [78,79] With the aim to improve the extend of cleavage we tested heterogeneous-phase photolysis using H_2O_2 as oxygen source. Accordingly, thin films of I_4-PDL-PMBL and I_5-PDL-PMBL containing catalytic amounts of TPP were irradiated in presence of a 15 % H_2O_2 in a phosphate buffer solution (pH 7.4). As can be seen in Figure 5e and f, SEC traces show fast degradation which is almost complete for I_5-PDL-PMBL in 3h. The effective oxidative cleavage must be related to photoactivation processes since oxidation of I_4-M with 50% H_2O_2 in absence of irradiation and photosensitizer was proved to give only the corresponding sulfoxide-sulfone thioacetal derivatives (Scheme 2d, iv) and Figure SI.54). ^{1}H NMR spectra of the resulting polymers (Figure SI.55 and SI.56) showed the complete disappearance of thioacetal signals. In the case I_4-PDL-PMBL, small intensity signals attributable to the sulfonic end groups are mainly detected together with some signals attributable to disulphide oxidized compounds related to the remaining high molecular weight fractions (Scheme 2d, iii)). In the case I_5-PDL-PMBL, no significant end-group signals are observed. In both cases, the small intensity of the end-group signals and the presence of a singlet at ca. 3.67 ppm (-$COOCH_3$) seem to indicate extensive end-group hydrolysis/methanolysis during the photolysis and methanolic work up.

CONCLUSIONS

ABA triblock copolymers containing different central stimuli cleavable groups have been prepared from bio-based δ-decalactone (DL) and α-methylene-γ-butyrolactone (MBL). Polyester soft block macroinitiators have been prepared by ROTEP of DL with TBD as catalyst, followed by esterification of the hydroxyl end-groups with BiB-Im in a one-pot two-steps procedure. This protocol proved to give the corresponding macroinitiators with good control of the molecular weight and high end-group fidelity skipping intermediate isolation and purification steps. ATRP chain extension with MBL was carried out targeting relatively high MBL conversions in order to maximize monomer usage. Under the tested conditions, good molecular weight control and reasonably high initiation efficiencies were achieved in all cases. Microstructural characterization revealed that halogen exchange during the initial steps forming 2-chloroisobutiryl groups is responsible for the incomplete initiation and the presence of some low molecular weight tails in SEC traces. The cleavage of all block copolymers under the appropriate stimuli produced the expected AB copolymers. Reductive and acidic cleavage of disulphide and acetal groups proceeds nicely under mild conditions. On the contrary, cleavage of the tetraoxospiro group requires stronger acidic conditions and occurs mainly by hydrolysis of the β-thioethyl ester linking groups. The cleavage of the thioacetal groups have been studied with the aid of model compounds. Photooxidative conditions in presence of TPP as sensitizer using either O_2 or H_2O_2 as oxygen source, lead to almost complete cleavage in the case of aromatic thioacetal. The concomitant formation of intermediate disulphide compounds and their oxidized derivatives seem to prevent the complete cleavage in the case of the methylene thioacetal.

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Data Availability

The raw/processed data required to reproduce these findings cannot be shared at this time due to technical or time limitations.

Declaration of Competing interest

There are no conflicts to declare

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