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Establishing $\alpha$-bromo-$\gamma$-butyrolactone as a platform for synthesis of functional aliphatic polyesters – bridging the gap between ROP and SET-LRP†

Peter Olsén, Jenny Undin, Karin Odelius and Ann-Christine Albertsson*

Utilizing $\alpha$-bromo-$\gamma$-butyrolactone ($\alpha$BryBL) as a comonomer with $\varepsilon$-caprolactone ($\varepsilon$-CL) or 1-lactide (LLA) produces copolymers with active and available grafting sites, e.g., for SET-LRP, where the choice of the grafting monomers is limited only by one’s imagination. This was deduced by utilizing a wide range of different acrylates of varying polarities and was realized with the aid of a fluorinated alcohol, 2,2,2-trifluoroethanol, which acts as a universal solvent for both the hydrophobic macrorinitiators and the grafting monomers. Using $\alpha$BryBL successfully provides a simple route to merge the two polymerization methodologies, ROP and SET-LRP. $\alpha$BryBL inherently meets all of the prerequisites to act as a platform monomer for the synthesis of functional aliphatic polyesters, i.e., it is inexpensive, available, and able to form isolated grafting sites along the polymer chain. The copolymerization of $\alpha$BryBL together with two of the most commonly used cyclic ester monomers, $\varepsilon$-CL and LLA, proceeds with a high degree of control and a linear relationship between the feed ratio of $\alpha$BryBL and its composition in the copolymer. The formation of isolated units of $\alpha$BryBL in the copolymer is visualized by the reactivity ratios of the copolymerization reactions and confirmed by $^{13}$C-NMR spectroscopy. The incorporation of isolated $\alpha$BryBL is the feature that makes this class of copolymers unique, and it can be considered to provide a route to the “perfect graft copolymer” with a degradable backbone.

Introduction

In the early era of polymer science, great emphasis was placed on the mere ability to create polymers, whereas today, functionality is the key. Functional polymers open up applications with endless possibilities, where properties can be tailored, altered, and/or maintained over the complete lifetime of the material. In light of this, the focus today is on conferring function to the main chain of the polymer. One class of polymers that is inherently of great value for many applications is aliphatic polyesters; because of their ester functionality, they most often degrade within a reasonable time frame. Unfortunately, many of these monomers lack sites that allow alterations and modifications of the polymer backbone.

Therefore, a major scientific focus has been on imparting different functionalities to aliphatic polyesters. The routes pursued range from copolymerization with functional monomers and post-polymerization modifications to functional initiators, to name a few. They all have their pros and cons, yet copolymerization with functional monomers offers a high degree of functionality, most often with the retention of a high degree of control. Important aspects to consider when copolymerizing a functional monomer are its reactivity, maintenance of its function, and how the functionality is spread throughout the polymeric chain. The routes for the synthesis of functional monomers appropriate for ring-opening polymerization are, in theory, infinite. In the literature, there exist descriptions of numerous elegant monomers that yield the desired polymeric properties, but they are often hindered by lengthy synthetic routes resulting in low yields at high cost, thereby limiting their applicability to a large scale.

Hence, we felt inspired to find an inexpensive and straightforward monomer that can bestow the desired functionality on commonly used aliphatic polyesters. We therefore turned our attention towards a relatively unexploited family of lactones: the $\gamma$-lactones. $\gamma$-Lactones are a class of monomers with a complicated past; unsubstituted $\gamma$-butyrolactone was identified as being unable to polymerize as early as 1932 by Carothers et al. Subsequently, there have been numerous attempts and even quantum mechanical calculations reconfirming this statement. Not considering polymers synthesized under extreme pressure and high temperature or the formation of oligomers, this statement still holds true.

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† Electronic supplementary information (ESI) available: Equations used for calculation of conversions and compositions, $^1$H-NMR spectra of $n$BuAc grafted poly($\varepsilon$-CL-$\alpha$BryBL), and conversion against time from the SET-LRP grafting experiments. See DOI: 10.1039/c4py00148f

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Many monomers that are unable to homopolymerize, however, can be copolymerized, as shown with γ-butyrolactone, 1,3-dioxane, 1,4-dioxane, etc. In 1964, Tada et al. performed the first copolymerization of γ-butyrolactone together with the more ring-strained monomer, β-propiolactone. γ-Butyrolactone's ability to act as a comonomer was further explored in terms of its thermodynamic and kinetic behavior, and the altered properties of the synthesized copolymers have been documented. The main objective for forming these copolymers includes the use of an inexpensive, flexible, and degradable monomer that, together with β-butyrolactone, resembles polymers produced by bacterial fermentation, i.e., polyhydroxybutyrate. Recently, γ-butyrolactone's ability to form isolated units along the polymer chain at moderate conversion during copolymerization has been highlighted.

Combining ring-opening polymerization with controlled radical graft polymerization offers the ability to specify the graft copolymer for a specific task. Therefore, much effort has been concentrated on developing monomers with these characteristics, starting in 1999, when ε-caprolactone with an attached ATRP initiator at the γ-position was synthesized. Others have realized this feature by synthesizing α-substituted ε-caprolactones with chlorine and bromine thus successfully producing radical graft copolymers with degradable backbones. However, factors that are often overlooked include how the monomers with radical initiating sites are dispersed throughout the polymer chain and what the useable grafting monomers are.

To overcome these shortcomings, we turned our attention towards a scarcely used building block, α-bromo-γ-butyrolactone. We believe that this monomer inherently has desirable properties such as being inexpensive and having functionality and low homo-reactivity, together with being two-sided, i.e., both having the ability to be ring-opened while at the same time functioning as a SET-LRP initiator. Its anticipated inability to form a homopolymer should result in isolated sites that are susceptible to SET-LRP, thus providing “the perfect graft copolymer”. The hypothesis is that this building block will provide an easy way to merge SET-LRP with controlled ROMP. Our aim is to establish α-bromo-γ-butyrolactone as a platform monomer for the synthesis of functional aliphatic polysters. This will be achieved by copolymerizing α-bromo-γ-butyrolactone with γ-lactide or ε-caprolactone, followed by a sequential grafting of acrylates of varying polarities: n-butyl acrylate, methyl methacrylate, and 2-hydroxyethyl methacrylate, under SET-LRP conditions with the aid of the universal solvent, 2,2,2-trifluoroethanol.

### Experimental

#### Materials

e-Caprolactone (εCL) (Aldrich) was dried over calcium hydride for at least 24 h and subsequently distilled at reduced pressure under an inert atmosphere prior to use. γ-Lactide (LA) (≥99%, Boehringer Ingelheim) was recrystallized twice from toluene (HPLC grade, Fisher Scientific, Germany) and once from toluene (99.8%, Sigma-Aldrich, Sweden) and was dried in vacuo for at least 48 h prior to use. α-Bromo-γ-butyrolactone (αBrγBL) (97%, Sigma-Aldrich, Sweden) was dried over molecular sieves (3 Å) and stored under an inert atmosphere prior to use.

Stannous octoate (SnOct2) (Sigma-Aldrich, Sweden) was dried over molecular sieves (3 Å) before use. n-Butyl acrylate (nBuAc) (Alfa Aesar, Germany), methyl methacrylate (MMA) (Merck, Germany), and 2-hydroxyethyl methacrylate (HEMA) (Aldrich, Germany) were purified by passing through aluminum oxide (Merck Chemicals, Germany) prior to use. Tris(2(dimethylamino)ethyl)amine (Me2TREN) (Sigma-Aldrich, Sweden) and Cu(n)Br2 (Sigma-Aldrich, Sweden) were stored under a nitrogen atmosphere prior to use. Benzyl alcohol (≥99%, Sigma-Aldrich, Sweden), chloroform (HPLC grade, Fisher Scientific, Germany), methanol (general purpose grade, Fisher Scientific, Germany), 2,2,2-trifluoroethanol (TFE) (Sigma-Aldrich, Sweden), and chloroform (d99.8%, with silver foil, Cambridge Isotope Laboratories) were used as received.

#### Polymerization reactions

ROP copolymerization of αBrγBL with LLA and εCL. All reaction vessels were dried in an oven at 150 °C for 48 h before use. Firstly, the desired amounts of benzyl alcohol and SnOct2, were added to the flask followed by addition of the monomers LLA or εCL together with αBrγBL. The amounts of main monomer (εCL, LLA), initiator, and SnOct2, [M]/[SnOct2] ≈ 200; [Me2Cl]/[I] ≈ 400; [MεL]/[I] ≈ 200) were held constant, whereas the added amount of αBrγBL varied (αBrγBL/[εCL]/εCL = 0.35 → 0.03). All reactions were performed in the bulk under an inert N2(g) atmosphere at 110 °C. All of the reactants were weighed into a two-neck round-bottom flask (25 mL) under a nitrogen atmosphere in a glovebox (Mbraun MB 150-GI). Each flask was equipped with a magnetic stirring bar and sealed with a two-way valve and a septum. All reactants were stirred at a constant temperature that was maintained (±2 °C) using an ILAMAG® RCT basic safety control magnetic stirrer.

After 20 h, the reaction mixture was cooled to room temperature, and the copolymers were dissolved in chloroform and precipitated three consecutive times in methanol. The precipitates were dried under reduced pressure for 4 days.

Grafting via SET-LRP. All the SET-LRP reactions were carried out in 25 mL double-necked round-bottom flasks equipped with three-way valves and septa under a nitrogen atmosphere. In a typical SET-LRP reaction, the catalyst, Cu(n)Br2, the ligand, tris(2(dimethylamino)ethyl)amine (Me2TREN), and the monomers, methyl methacrylate (MMA), butyl acrylate (nBuAc), or 2-hydroxyethyl methacrylate (HEMA), were solvated in 2,2,2-trifluoroethanol (TFE) with an initiator: catalyst: ligand: monomer ratio of 1:1:2:50. In other 25 mL double-necked round-bottom flasks equipped with three-way valves and septa, the different initiator polymers, poly(εCL-r-αBrγBL) or poly(εLLA-r-αBrγBL), that were chosen based on the highest amount of incorporated αBrγBL, were dissolved in TFE. Both systems were cooled in dry ice, and the air was removed by three freeze–vacuum–nitrogen–thaw cycles. The initiator polymers were subsequently transferred into the first round-bottom flask under an inert atmosphere. A 10 cm length of copper wire...
(Cu(0)) with a diameter of 20 gauge was then added to the flask. The flask was immersed in a thermostatted oil bath at 25 °C. Samples were withdrawn at specific time intervals under a nitrogen atmosphere, and the conversion and molecular weights were determined by 1H-NMR and GPC. The reaction was ended after 15 h. The resulting polymer was dissolved in chloroform and precipitated in cold methanol and then dried at room temperature until all the solvent had evaporated.

**Instruments**

Nuclear Magnetic Resonance (NMR). 1H-NMR (400.13 MHz) and 13C-NMR (100.62 MHz) spectra were recorded with a Bruker Avance 400 spectrometer at 298 K. For measurements, either ~10 mg (1H-NMR) or ~100 mg (13C-NMR) of the polymer was dissolved in 0.8 mL CDCl3 in a 5 mm diameter sample tube. The spectra were calibrated using the residual solvent signals, 7.26 ppm (1H-NMR) and 77.0 ppm (13C-NMR), for CHCl3. The copolymer compositions and monomer conversion were determined from the 1H-NMR spectra by comparing the relative intensities of the peaks originating from the monomers with the resonance peaks from the polymers (δH (LLA) = 5.01 ppm, δH (PLLA) = 5.17 ppm, δC (CL) = 4.22 ppm, δC (PCL) = 4.05 ppm, δC (BRy) = 4.55 ppm, δC (xBrY) = 4.34 ppm, and δC (xBrY = LLA) = 4.43 ppm). The 13C-NMR spectrum was used to qualitatively determine the macromolecular architecture. For the equations used to calculate the composition and conversion of the different monomers, see ESI.

**Gel Permeation Chromatography (GPC).** GPC was used to determine the number-average molecular weights (Mn) and dispersity indices (DIs) of the polymers during and after polymerization using a Verotech PL-GPC 50 Plus equipped with a PL-RI detector and two PLgel 5 μm MIXED-D columns, 300 × 7.5 mm (Varian, Santa Clara). Samples were injected with a PLAS RT autosampler (Polymer Laboratories), and chloroform was used as the mobile phase at a flow rate of 1 mL min⁻¹ at 30 °C with toluene as an internal standard. The calibration was set using polystyrene standards with a narrow molecular weight distribution ranging from 160–371 000 g mol⁻¹.

**Results and discussion**

Our aim was to establish 2-bromo-γ-butyrolactone (zBrYBL) as a platform monomer for the synthesis of functional aliphatic polyesters. The hypothesis was that zBrYBL, an easily accessible monomer, will inherently act as a bridge between ring-opening polymerization (ROP) and grafting by single electron transfer living radical polymerization (SET-LRP) (Scheme 1). It was also anticipated that zBrYBL, when copolymerized by ring-opening polymerization, would form isolated sites along the copolymer chain. Although zBrYBL was shown to possess all of these features, it has, to our knowledge, previously been neglected in this context, and it has been shown that the unopened zBrYBL by itself can act as a radical initiator for ATRP. To fully elucidate the properties of zBrYBL, we concentrated on two different questions: how does zBrYBL copolymerize with commonly used lactones or lactides focusing on the kinetics and the formed macromolecular architecture, and how does it behave during a grafting step via SET-LRP.

**Grafting of acrylates from the aliphatic polyester main chain**

There is a great focus in polymer science on joining controlled radical polymerization with controlled ring-opening polymerization. More specifically, we are interested in forming radical graft copolymers using acrylic monomers on a degradable backbone composed of aliphatic polyesters.1,2,3,31-33-35

One method that holds vast potential for grafting from aliphatic polyesters is SET-LRP. SET-LRP was originally developed by Perek et al. for the synthesis of polyvinyl chloride and later for polyacrylates and provides a polymerization method with excellent control and high chain end vitality.36-38 Our group has previously grafted various acrylates via SET-LRP from a hydrophilic hemi-cellulose backbone, where the required polarity of the solvents is more a necessity rather than a drawback.39-42 But the polarity of these solvent restricts the use of aliphatic polyesters such as poly(c-caprolactone) (PCL) as a polymeric grafting initiator due to its hydrophobicity. However, recently, the same group together with Haddleton et al. resolved this issue by introducing a new class of solvents for SET-LRP, fluorinated alcohols.43-45 These solvents have been coined “universal solvents” for SET-LRP, as they open the possibility of using hydrophobic monomers, and in our case, open the possibility of using a hydrophobic pre-polymer as an initiator.

The copolymerization of z-bromo-γ-butyrolactone (zBrYBL) with εCL or LLA yielded a macrominitiator with active and available grafting sites for SET-LRP. The grafting of the different acrylic monomers, methyl methacrylate (MMA), 2-hydroxyethyl methacrylate (HEMA), and butyl acrylate (nBuAc) from poly(εCL-γ-zBrYBL), proceeded in a controlled manner with a linear relationship between the conversion and the molecular weight (Fig. 1). However, when using poly(εLLA-γ-zBrYBL) as a macrominitiator, the grafting of MMA was accompanied by severe degradation of the main chain (Fig. 1). The exact nature of this degradation behavior is still under investigation. Most likely it is due to the fact that Me₆-TREN can act as a transesterification catalyst during grafting, which is further supported by the disperity evolution of poly(εCL-γ-zBrYBL) grafted with both MMA and HEMA. All selected monomers were successfully grafted onto the polymer backbone, thereby highlighting the versatility and ability of zBrYBL to act as a bridge between SET-LRP and ROP, for a wide range of monomers.

**Elucidating the copolymerization behavior of zBrYBL with εCL or LLA**

In the 1930s, Carothers et al. stated that “the γ-lactones and other five-membered cyclic esters show no tendency to polymerize, and no corresponding polymers are known”. This was concluded after γBL had been heated both in the presence and absence of catalyst for one year.18 Later, in the end of the 1990s, γBL was polymerized using Al(OiPr)₃ as a catalyst, forming short oligomers.17,18 Although oligomers were formed, the original statement is still valid to a large extent, and hence similar behavior is to be expected for zBrYBL. This was also verified in this work when no homopolymerization of zBrYBL was observed after 20 h with Sn(Oct)₄ as a catalyst at 110 °C.
The chemical structure of α-BrγBL suggests that the most suitable ROP catalyst would be a coordination-insertion catalyst. This is based on the notion that any catalyst with a slightly basic character, such as 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and 4-(dimethylamino)pyridine (DMAP), could lead to an elimination of the

Scheme 1 Synthetic outline for the formation of aliphatic polyester graft copolymers. First, ring-opening polymerization of α-bromo-γ-butyrolactone with ε-caprolactone or L-lactide forms the macroinitiator, followed by the grafting of different acrylates via SET-LRP.

Fig. 1 The relationship of the monomer consumption with the molecular weight obtained from GPC of the SET-LRP grafted copolymers of poly(LLA-r-αBrγBL) and poly(cCL-r-αBrγBL). The polymerization reactions were conducted with a Me6-TREN/αBrγBL ratio of 2 and 10 cm of copper wire.
bromine moiety at the α-position, hence removing the monomer’s ability to further act as an initiator for SET-LRP. Therefore, Sn(Oct)_2 was chosen as a catalyst for the copolymerization of zBrγBL with εCL or LLA.

The change in the chemical shift of the α-proton for zBrγBL of the precipitated copolymers of zBrγBL and either εCL or LLA revealed that the monomer had been incorporated into the polymer chain (Fig. 2a and b). The difference in the shift of the α-proton upon copolymerization of zBrγBL depends on which comonomer was used, i.e., εCL or LLA, and the chemical shifts of the α-proton of the zBrγBL unit were δ_p(zBrγBL-γ-εCL) = 4.34 ppm and δ_p(zBrγBL-γ-LLA) = 4.43 ppm when polymerized with εCL and LLA, respectively. This also indicates that there is an absence of homosequences of zBrγBL along the polymer chain, which would lead to the appearance of a peak at the same chemical shift in both copolymers.

**Kinetic features of the copolymerization of zBrγBL with εCL or LLA**

The kinetic features of the copolymerization of zBrγBL with either εCL or LLA were examined using two main experiments: the amount of monomer incorporation with a varying feed ratio of zBrγBL and the monomer consumption at prolonged reaction times. Although the five-membered lactone ring is considered easy to open, it is also easy to close. Therefore, the intuitive trend would be that the lower the ratio of zBrγBL to the comonomer, the higher the conversion of zBrγBL would be. In other words, the incorporation of the monomer is a matter of statistics. If there exist more reactive monomers in the vicinity of the newly ring-opened zBrγBL that can react with the active chain end, the probability of zBrγBL to be “locked-in” the polymerizing chain is increased.

To visualize how the conversion of zBrγBL is affected by the initial feed ratio, several reactions were conducted at a constant monomer-to-initiator ratio of the more reactive monomer, εCL and LLA, [M]/[I] = 400 or 200, where only the ratio of zBrγBL was varied. The notion of a “locking-in” methodology during copolymerization was based on the idea that the most probable addition of zBrγBL occurs at the chain end during the propagation of the chain and not through trans-esterification-basedROP.

The incorporated amount and conversion of zBrγBL during copolymerization with both εCL and LLA follow the expected trends. That is, the higher the feed ratio of zBrγBL to the comonomer, the more units are incorporated into the main chain, and the lower is the monomer’s total conversion (Fig. 3a and b). The amount of zBrγBL was determined by 1H-NMR spectroscopy and calculated using the difference in the chemical shifts of the α-proton of the monomer and the formed polymer (Table 1). Composition of the copolymers of zBrγBL and εCL or LLA as a function of varying feed ratios and monomer-to-initiator ratios.

It is possible to incorporate quite a high amount of zBrγBL into the copolymers (up to 12 mol%) (Table 1). This is, however, connected to a low total conversion of zBrγBL during copolymerization (Fig. 3a). The low conversion of zBrγBL would be considered a major drawback if it simply acted as a property-altering monomer, but because its main purpose is to act as an initiator for SET-LRP, the incorporated amount is more than enough. The limited degree of incorporation could even be considered an advantage, i.e., if the conversion of zBrγBL is high, the formation of homosequences is more likely. It has been shown that during the copolymerization of γ-butyrolactone (γBL) and εCL when the conversion exceeds 12%, the block sequences of γBL were formed.13 This result was in contrast to what had previously been shown, that is, the formation of isolated monomers even at conversions as high as 22%.14 Although there is some discrepancy in the numbers, it should be safe to conclude that if the conversion is below 12%, copolymers with isolated γBL units are formed. Hence, the polymerization behavior of γBL is used as a template for the anticipated polymerization behavior of zBrγBL.

During controlled polymerization, control over the dispersity of the formed polymers is of immense importance. For the performed copolymerization reactions, it is evident that when εCL was used as a comonomer, higher dispersities (1.6–1.7) were attained, in contrast to the results for LLA (1.2–1.3). Possible explanations could be either that the aggregation state during bulk polymerization at 110 °C is vital, PCL has a T_m ~ 60 °C, PLLA has a T_m ~ 160 °C, or that the difference in reactivity of εCL and LLA results in a different dispersity (Table 1). To elucidate the mechanism of zBrγBL addition, we conducted kinetic experiments where the dependence of M_n, D, monomer consumption, and the composition of zBrγBL and εCL on time were determined (Fig. 4). The reaction conditions chosen were 110 °C, 1 mol% Sn(Oct)_2, [MCL]/[I] = 400, and [M_CL]/[M_brγBL] = 2.

The number average molecular weight and dispersity of the zBrγBL and εCL copolymers show a clear dependence on the
A good way to describe copolymerization behavior is to use the system-specific reactivity ratios during copolymerization. To calculate these ratios, it is vital to keep the conversion low (often below 35%) in order to obtain accurate values. The restricted ability of zBrγBL to homopolymerize will render a relatively true value of the reactivity ratios even at maximum conversions of the most reactive monomer (i.e., εCL or LLA). Even so, all calculations were performed at a conversion below 20%.

The reactivity ratios were calculated using the Fineman and Ross method, where the reactivity ratios, \( r_1 = k_{11}/k_{12} \) and \( r_2 = k_{23}/k_{21} \), are given as the ratios of the rate constants between the different possible copolymerization reactions. The \( r_1 \) reactivity ratios of the copolymerization of zBrγBL with εCL and LLA were determined to be 4.4 and 18.5, respectively, whereas the \( r_2 \) ratios were close to zero for both (Fig. 5a). This can mean two things: the non-existence of the zBrγBL chain-end addition to the monomeric form of zBrγBL, or the reactivity for the addition to εCL is many times higher. If zBrγBL was able to

### Table 1: Composition of the copolymers of zBrγBL and εCL or LLA as a function of varying feed ratios and monomer-to-initiator ratios

<table>
<thead>
<tr>
<th>Polymer</th>
<th>M_1</th>
<th>M_2</th>
<th>F(zBrγBL)</th>
<th>[I] : [M_1] : [M_2]</th>
<th>F(zBrγBL)</th>
<th>M_n (GPC)</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>P[εCL-εzBrγBL]</td>
<td>εCL</td>
<td>zBrγBL</td>
<td>0.03</td>
<td>1 : 400 : 8</td>
<td>0.02</td>
<td>54 800</td>
<td>1.61</td>
</tr>
<tr>
<td>P[εCL-εzBrγBL]</td>
<td>εCL</td>
<td>zBrγBL</td>
<td>0.07</td>
<td>1 : 400 : 30</td>
<td>0.04</td>
<td>52 700</td>
<td>1.57</td>
</tr>
<tr>
<td>P[εCL-εzBrγBL]</td>
<td>εCL</td>
<td>zBrγBL</td>
<td>0.11</td>
<td>1 : 400 : 44</td>
<td>0.05</td>
<td>46 000</td>
<td>1.71</td>
</tr>
<tr>
<td>P[εCL-εzBrγBL]</td>
<td>εCL</td>
<td>zBrγBL</td>
<td>0.18</td>
<td>1 : 400 : 72</td>
<td>0.08</td>
<td>48 100</td>
<td>1.69</td>
</tr>
<tr>
<td>P[εCL-εzBrγBL]</td>
<td>εCL</td>
<td>zBrγBL</td>
<td>0.28</td>
<td>1 : 400 : 116</td>
<td>0.12</td>
<td>35 600</td>
<td>1.68</td>
</tr>
<tr>
<td>P[LLA-εzBrγBL]</td>
<td>LLA</td>
<td>zBrγBL</td>
<td>0.06</td>
<td>1 : 200 : 12</td>
<td>0.02</td>
<td>17 300</td>
<td>1.28</td>
</tr>
<tr>
<td>P[LLA-εzBrγBL]</td>
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<td>zBrγBL</td>
<td>0.09</td>
<td>1 : 200 : 18</td>
<td>0.03</td>
<td>22 600</td>
<td>1.20</td>
</tr>
<tr>
<td>P[LLA-εzBrγBL]</td>
<td>LLA</td>
<td>zBrγBL</td>
<td>0.14</td>
<td>1 : 200 : 28</td>
<td>0.04</td>
<td>17 000</td>
<td>1.15</td>
</tr>
<tr>
<td>P[LLA-εzBrγBL]</td>
<td>LLA</td>
<td>zBrγBL</td>
<td>0.19</td>
<td>1 : 200 : 38</td>
<td>0.04</td>
<td>18 900</td>
<td>1.18</td>
</tr>
<tr>
<td>P[LLA-εzBrγBL]</td>
<td>LLA</td>
<td>zBrγBL</td>
<td>0.33</td>
<td>1 : 200 : 70</td>
<td>0.07</td>
<td>20 100</td>
<td>1.17</td>
</tr>
</tbody>
</table>

*a* Feed ratio [M_2]/[M_1] mol%. *b* Polymer composition ratio [M_2]/[M_1].

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### Architectural features of the copolymerization of zBrγBL with εCL and LLA

A good way to describe copolymerization behavior is to use the system-specific reactivity ratios during copolymerization. To calculate these ratios, it is vital to keep the conversion low (often below 35%) in order to obtain accurate values.

![Fig. 4](image1.png)

**Fig. 4** (a and b) Conversion in the copolymerization of zBrγBL and εCL as a function of time (a) and the effects on the number molecular weight (M_n) and dispersity of the copolymer (b).

During the initial stage of the copolymerization, the addition of zBrγBL shows a linear relationship to the conversion of εCL. Hence, the addition of zBrγBL is dependent on having a more reactive monomer, in this case εCL, acting as an end-capping monomer. If there is no more reactive monomer available in the reaction, after the addition of zBrγBL to the propagating chain end, it will ring-close again and resume its monomeric form. When the more reactive monomer is fully consumed, the addition of zBrγBL stops, and the molecular weight decreases rapidly, together with an increase of the dispersity (Fig. 4a and b). The molecular weight behavior of the copolymers is consistent with what has been observed during the copolymerization of γBL and LLA, which was attributed to the occurrence of transesterification reactions. In contrast to what was found here, they did not observe any reduction in the amount of γBL in the copolymers with time. The reduction observed here is believed to be a consequence of zBrγBL being more easily transesterified than εCL, resulting in chain ends of zBrγBL that, for thermodynamic reasons, ring-closes to produce the monomeric unit, thus reducing the amount of zBrγBL in the copolymer.

![Fig. 5](image2.png)

**Fig. 5** (a and b) The Fineman and Ross method was used to calculate the reactivity ratios as shown by the linear fit (a). The ^13^C-NMR spectrum shows the isolated units of z-bromo-γ-butyrolactone (zBrγBL) along the polymer chain during copolymerization with ε-caprolactone (εCL) (b).
homopolymerize, the latter explanation would result in the formation of “diblock-like” copolymers. However, zBrγBL’s inability to homopolymerize yields a solid conclusion of the macromolecular architecture based on the reactivity ratio $r_3$, that is, isolated zBrγBL units are formed throughout the polymer main chain. Although the $r_3$ value for the copolymerization of zBrγBL and LLA does not rule out the formation of homo-sequences of zBrγBL, the deviation from zero is interpreted as a function of the line regression rather than the system itself.

The existence of isolated units of zBrγBL along the main chain of the copolymers was further verified by $^{13}$C-NMR spectroscopy. The carbonyl group is very sensitive to its neighboring units; this makes it a valuable tool to verify the architectural features of copolymers. Isolated zBrγBL along the main chain of the $\varepsilon$CL copolymer was found as three distinct peaks of equal intensity (Fig. 4b). For copolymers with $\varepsilon$CL, there is often assumed triplet behavior, meaning that each carbonyl group is affected by its two neighboring units. In summarization, the copolymers synthesized are shown to be isolated zBrγBL units along the chain, providing excellent sites for subsequent SET-LRP.

## Conclusions

z-Bromo-$\gamma$-butyrolactone (zBrγBL) as a comonomer with $\varepsilon$-caprolactone ($\varepsilon$CL) or $\varepsilon$-lactide (LLA) produces copolymers (poly($\varepsilon$CL-$r$-zBrγBL) or poly($\varepsilon$CL-$r$-zBrγBL), respectively) with active and available grafting sites for SET-LRP. The different grafted acrylates range from hydrophobic $n$-butyl acrylate and methyl methacrylate to hydrophilic 2-hydroxyethyl methacrylate. These copolymerization reactions were accomplished with the aid of a fluorinated alcohol, 2,2,2-trifluoroethanol, which acts as a universal solvent for both the hydrophobic macrorinitiator and the grafting monomers. The grafting via SET-LRP from poly($\varepsilon$CL-$r$-zBrγBL) for all acrylates proceeded in a controlled manner with a linear relationship between the conversion and the molecular weight. This successfully shows that zBrγBL provides a versatile and simple route to merge the two polymerization methodologies, ROP and SET-LRP.

The copolymerization of zBrγBL together with two of the most commonly used cyclic ester monomers, $\varepsilon$-CL, and LLA, proceeds with high control, and a linear relationship between the feed ratio of zBrγBL and its composition in the copolymer is observed. During the copolymerization, the consumption of $\varepsilon$CL and zBrγBL is linearly related to each other, although the rate is lower for zBrγBL. When the most active comonomer, $\varepsilon$CL, is fully consumed, the conversion of zBrγBL stops. We can therefore conclude that the addition of zBrγBL occurs mainly at the active chain end rather than as an effect of transesterification. Its inherent inability to form homo-sequences under ordinary polymerization conditions was observed both in the $^{13}$C-NMR spectra, which only displayed peaks originating from isolated zBrγBL units along the polymer chain, and from the calculated reactivity ratios.

We believe that zBrγBL inherently holds all the prerequisites to act as a platform monomer for the synthesis of functional aliphatic polyesters, i.e., it is inexpensive, available, and able to form isolated grafting sites along the polymer chain. The incorporation of isolated zBrγBL is a feature that makes this class of copolymers unique and is considered to provide a route to the “perfect graft copolymer” with a degradable backbone.

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## Notes and references
