

Mastering Macromolecular Architecture by Controlling Backbiting Kinetics during Anionic Ring-Opening Polymerization

Vincent Nieboer, Noé Fanjul-Mosteirín, Peter Olsén,* and Karin Odelius*



Cite This: *Macromolecules* 2024, 57, 3397–3406



Read Online

ACCESS |



Metrics & More

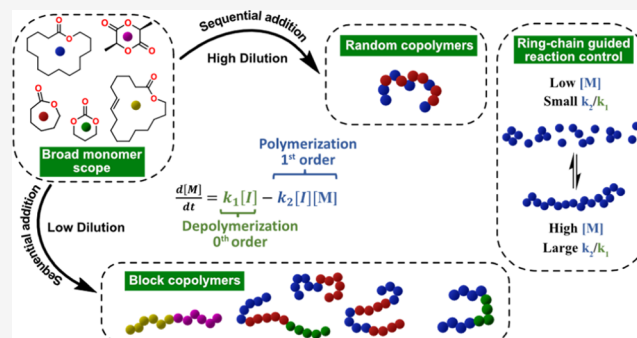


Article Recommendations



Supporting Information

ABSTRACT: Defined macromolecular architecture using anionic ring-opening copolymerization (ROcP) of lactones and cyclic carbonates offers facile routes toward copolymers with unique material properties, ranging from thermoplastic to elastomeric. However, monomers with a slow ROP rate are hampered by competing backbiting reactions, scrambling the macromolecular sequence, and, thereby, a loss of material properties occurs. We here solve this issue by controlling the rate of backbiting. Through our approach, we show how block structures previously inaccessible can be synthesized from monomers with vastly different ROP rates, covering small lactones and even including macrolactones. This control can also be extended beyond block structures to include random and gradient architectures by tuning monomer concentration to the relative ROP and backbiting rate.



1. INTRODUCTION

Block copolymers can combine vastly different polymeric behaviors in the same chain.^{1–7} Toward this, the synthesis of block copolymers through ring-opening copolymerization (ROcP) is interesting as it opens up for the use of biobased cyclic monomers to synthesize polymers with material properties similar to many of the commodity-plastics while simultaneously offering chemical recyclability to the polymeric material. During ROcP, the polymerization behavior is closely connected to the ring size of the monomer. Therefore, combining monomers with high and low ring strain is challenging, where the least reactive monomer, the monomer with the lowest ring strain, will dictate the required catalytic system. Thus, we must resort to highly reactive polymerization systems to have generality in the monomer scope. One of the most reactive catalytic systems for the polymerization of lactones is anionic ring-opening polymerization (AROP). AROP dates back to 1961 with the polymerization of β -propiolactone⁸ and has since been used to polymerize a variety of different small-sized enthalpy-driven cyclic ester monomers such as lactides,^{9–19} ϵ -caprolactone (ϵ CL),^{15,19–22} δ -valerolactone (δ VL),^{17,18} β -butyrolactone(s) (β BL),^{18,23–25} pivalolactone,^{26,27} undecanolide and dodecanolide,²⁸ and even the entropy driven and strainless macrocyclic ω -pentadecalactone (PDL).²⁹ Well-defined architectures such as block copolymers based on small-ring-sized lactones such as ϵ CL, δ VL, and β BL have also been reported.^{15,17,19,30–32}

Still, the high reactivity of the propagating chain-end during AROP of lactones leads to extensive amounts of side reactions, in particular, backbiting transesterification (which commonly is

not seen for less reactive systems), generating fractions of macrocyclic oligomers in addition to the main linear polymer, and thereby increasing dispersity of the polymers with reaction time.^{9,10,16,21,22,28,33–42} Thus, AROP must be terminated before significant macrocycle formation occurs to yield, *e.g.*, P(ϵ CL) and P(δ VL) with low \bar{D} values (~ 1.1).⁴³ This in turn means that the reactivity of the catalytic system can be used to mediate macrocycle formation,^{15,17,20} However, this approach only works for monomers with fast ring-opening kinetics (*i.e.*, monomers with small-sized rings driven by enthalpy through the release of ring strain) and advanced polymer architectures that include monomers with slow ring-opening kinetics (*i.e.*, monomers with large-sized rings driven by entropy through increasing their conformations in linear form) remain unachievable. The issue originates from the low reactivity for larger ring sizes due to the lack of strain, where entropy is the main driving force. This results in the need of nondiscriminating catalytic systems for the monomer and macrocycle, where backbiting is promoted over interchain transesterification.⁴⁴ Interchain transesterification is problematic as it leads to sequence randomization regardless of a clean block transition from a monomer conversion perspective.

Received: November 30, 2023

Revised: January 29, 2024

Accepted: March 1, 2024

Published: March 20, 2024



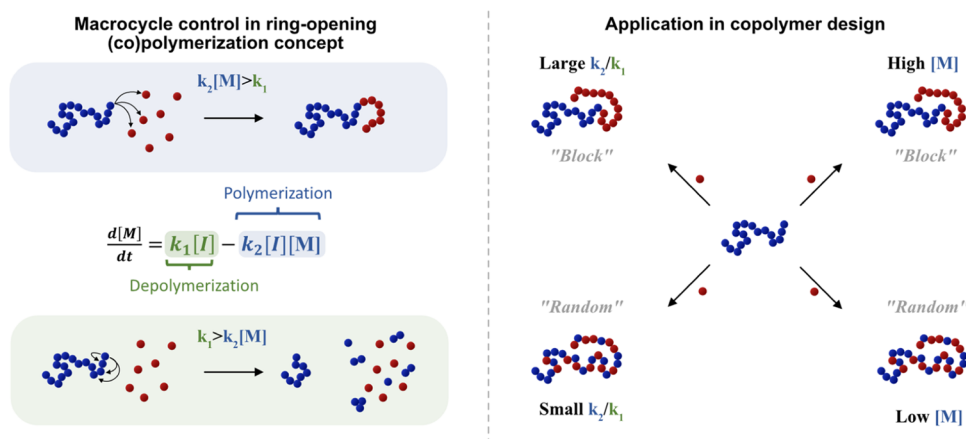


Figure 1. Overview of macrocycle control in ring-opening polymerization and its application in copolymer design and synthesis.

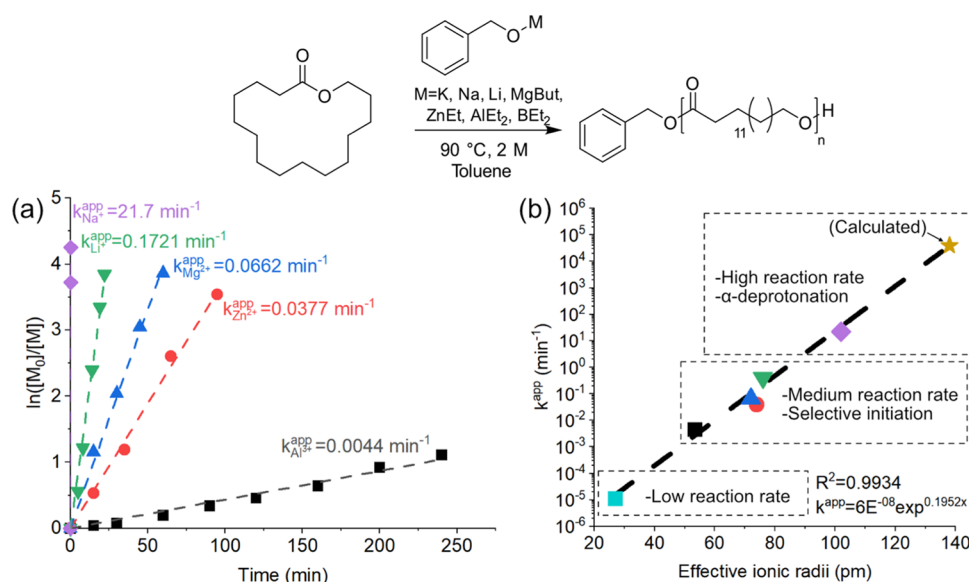


Figure 2. (a) Polymerization of $[PDL] = 2\text{ M}$ in toluene using different metal alkoxides $[PDL]/([BnOM] \text{ or } [{}^t\text{BuOM}])/[BnOH] = 50/1/1$. (b) k^{app} of **1a** versus ionic radii. Counterions studied were (cyan box solid) B^{3+} , (black box solid) Al^{3+} , (red circle solid) Zn^{2+} , (blue triangle up solid) Mg^{2+} , (green triangle down solid) Li^+ , (purple solid tilted square solid) Na^+ , (yellow star solid) K^+ . The values for the effective radii were taken from the literature.⁴⁷

Hence, in order to achieve clean block transitions, we considered the ring–chain equilibria during polymerization of macrolactones to control backbiting, not catalytically through selective catalysis, but kinetically through the control of macrocycle formation and polymerization. The ring chain equilibria and rate of macrocycle formation are described through the Jacobson–Stockmayer theory,⁴⁵ which states that the probability for a polymer chain to fold decreases proportionally to the ring size to the power of $-5/2$. Hence, smaller ring sizes are formed faster and in higher quantities in comparison to larger ring sizes. Important to note, this does not only relate to macrolactones but, as ROP is an equilibrium reaction, also to the homopolymerization of δVL or ϵCL initiated by K^+ , Na^+ , or Li^+ anionic initiators yields rings of varying size.^{34,40,42,46}

Our hypothesis is that during AROP, manipulating the rate-of-polymerization relative to the rate-of-macrocycle formation should yield copolymers spanning architectures from defined block structures to random copolymers. Based on this knowledge, we aim to develop synthetic concepts that allow the formation of defined block copolymers based on monomers

with different ring sizes (Figure 1). Toward this, we will first explore different anionic polymerization systems; second, we will elucidate how we can promote polymerization over macrocycle formation and finally apply this in the synthesis of block copolymers from small and large ring-sized monomers.

2. RESULTS AND DISCUSSION

2.1. AROP Kinetics of PDL: Effect of Counterion. The first step to defined block copolymers based on enthalpy (small ring size) and entropy-driven (larger ring size) monomers was to elucidate the effect of the counterion during AROP. Therefore, a series of metallic benzyloxides with different effective ionic radii were evaluated for AROP with PDL as a model monomer. Alkoxides were generated in situ through deprotonation of the BnOH by the basic alkyl ligands for BEt_3 , AlEt_3 , ZnEt_2 , and MgBu_2 , or added directly in the form of *tert*-butoxide groups ${}^t\text{BuOLi}$, ${}^t\text{BuONa}$, or ${}^t\text{BuOK}$. For all counterions, except for B^{3+} , PDL was efficiently polymerized to high conversions and we found an exponential relationship between the rate and the counterion size, by means of effective ionic radii data taken from Shannon,⁴⁷ (Figure 2). The cationic-size-dependent reactivity is

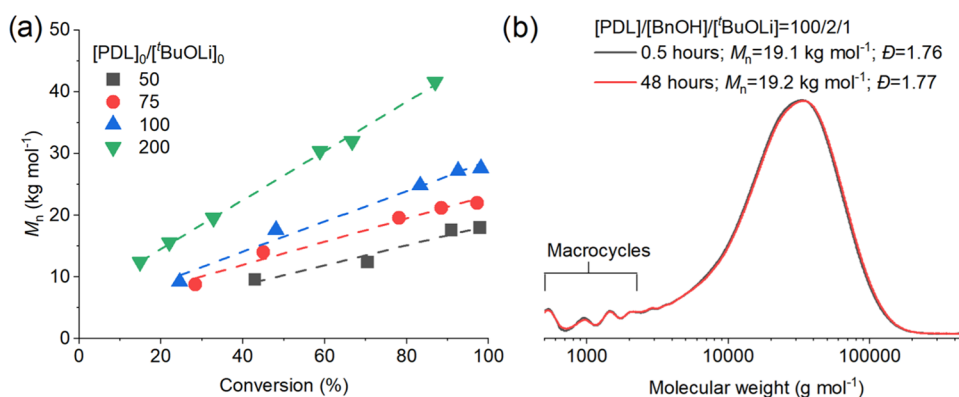


Figure 3. (a) SEC-derived M_n versus conversion for reactions initiated with different $t\text{BuOLi}$ concentrations. (b) SEC elugrams of the polymerization of $[\text{PDL}]_0 = 2 \text{ M}$ in toluene after 0.5 and 48 h left at 90°C .

in good agreement with the literature on anionic polymerization of anions and cations of different hardness for cyclic monomers such as lactones, ethers, and siloxanes, among others (ion pair tightness: $\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Cs}^+$).^{48–56} AROP of PDL with K^+ and Na^+ reached full conversion of PDL within seconds (Table S1, entries 2 and 3). These speeds are remarkable compared to previous results where, for example, a highly active yttrium phosphasalen catalyst required 4 h to polymerize PDL under similar conditions at room temperature.⁵⁷ The drawback of the high reactivity was that AROP with soft and large-sized counterions, K^+ or Na^+ , leads to a competitive initiation reaction through α -deprotonation, as observed by ^1H NMR spectroscopy (Figure S1) and MALDI TOF analysis (Figure S2 and Scheme S1).⁵⁸ Based on this, the counterions were divided into three groups: large cations that led to high reaction rates, but simultaneously also to side reactions; medium-sized cations with medium reaction rates and no side reactions and finally small cations with low reaction rates leading to low PDL conversion (<10%) within the measured time frame (Table S1, entry 1). In summary, a favorable combination of high reaction rate and no competing side reactions was found for $t\text{BuOLi}$, which was chosen as the primary initiator from here on (Figure S1).

2.1.1. AROP Kinetics of Macrolactones: Effect of Initiator Concentration. The second step toward defined block copolymers is elucidating how the alcohol initiator concentration affects the polymerization, which is central during the later two-step chain extension reactions to yield block copolymers. Therefore, different BnOH concentrations compared to the Lewis acids Li^+ , Zn^{2+} , and Al^{3+} were evaluated. An increase in the amount of BnOH led to a decrease in molecular weight with both ZnEt_2 and $t\text{BuOLi}$ as initiators, revealing that all BnOH and $t\text{BuOLi}$ groups initiate polymer chains (Figure S3) and that the rate of chain transfer exchange is many times more rapid than AROP (Scheme S2). Also, due to the strong coordinative nature of ZnEt_2 and AlEt_3 , the polymerization rate was found dependent on BnOH concentration (Figure S4), which is attributed to BnOH-induced deaggregation of the catalyst.^{38,59}

2.2. AROP Kinetics of Macrolactones: Transesterification and Reaction Control. With the knowledge surrounding counterion effects and the effect of initiator concentration, we could test our central hypothesis that tuning the rate of polymerization to the rate of macrocycle formation should yield copolymers with different architectures. Our initial assumption was that transesterification mainly occurs intrachain through a backbiting mechanism. To test this hypothesis, we performed

AROP of $[\text{PDL}]_0 = 2 \text{ M}$ in toluene initiated by $t\text{BuOLi}$ at 90°C and studied the polymers via size exclusion chromatography (SEC) (Figure 3). High control over molecular weight and moderate \bar{D} via pseudo-first-order polymerization kinetics (Figure S5) and a linear correlation between M_n and conversion were found (Figure 3a). Chain extension was possible, as shown by allowing a polymerization of PDL to react for 2 h to full conversion, followed by an equimolar second addition of PDL in toluene, which again achieved complete PDL conversion, creating a polymer with a similar \bar{D} and a M_n increase matching the added PDL concentration (Figure S6). The occurrence of intermolecular transesterification reactions and alterations with time was studied by leaving the reaction for 48 h after complete conversion at 90°C . No SEC trace-broadening was detected; and the same was true for several of the evaluated Lewis acids (Figures 3b and S7) and also for an enthalpy-driven monomer, ϵCL (Figure S8). These results suggest that interpolymer transesterification is suppressed as the \bar{D} is not widening. Backbiting or intramolecular transesterification is commonly observed for AROP of small lactones, leading to macrocyclic oligomer formation.^{9,10,16,21,22,28,33–41} The same observation was found here, with low molecular weight macrocyclic oligomer traces around $500\text{--}2000 \text{ g mol}^{-1}$ observed in the SEC elugrams (Figure 3b). It should be pointed out that the M_n derived from SEC is about ~ 3 times higher than the theoretical and ^1H NMR-derived values (Figure S7), due to the differences in the hydrodynamic volume of PPDL compared to polystyrene.⁶⁰ Although the \bar{D} is high for the formed PPDL ($\bar{D} \sim 1.60\text{--}1.80$), it is still comparable to most other metal and organic catalysts,^{61–63} yet, compared to the AROP of ϵCL , the \bar{D} is much higher.^{64,65} In similar anionic polymerization systems, adding a strong and bulky Lewis acid cocatalyst⁶⁶ or utilization of very short reaction times⁴³ can lead to narrow disperse PCL (down to $\bar{D} = 1.15$). However, for PDL, the low reactivity of the monomer means that significant cycle formation will occur before all of the PDL is consumed. It is also important to stress that we were not aiming for low \bar{D} , but rather an understanding of how to achieve a clean transition between blocks in block copolymers.

2.3. Ring–Chain Equilibria during PDL-CL Copolymerization. The ring–chain equilibria are central for achieving defined copolymers of monomers with different ring size, in other words, thermodynamic driving forces, enthalpic (small-sized rings), or entropic (large-sized rings). To study this, PDL and ϵCL were copolymerized using $t\text{BuOLi}$ under simultaneous and sequential monomer addition at two different monomer

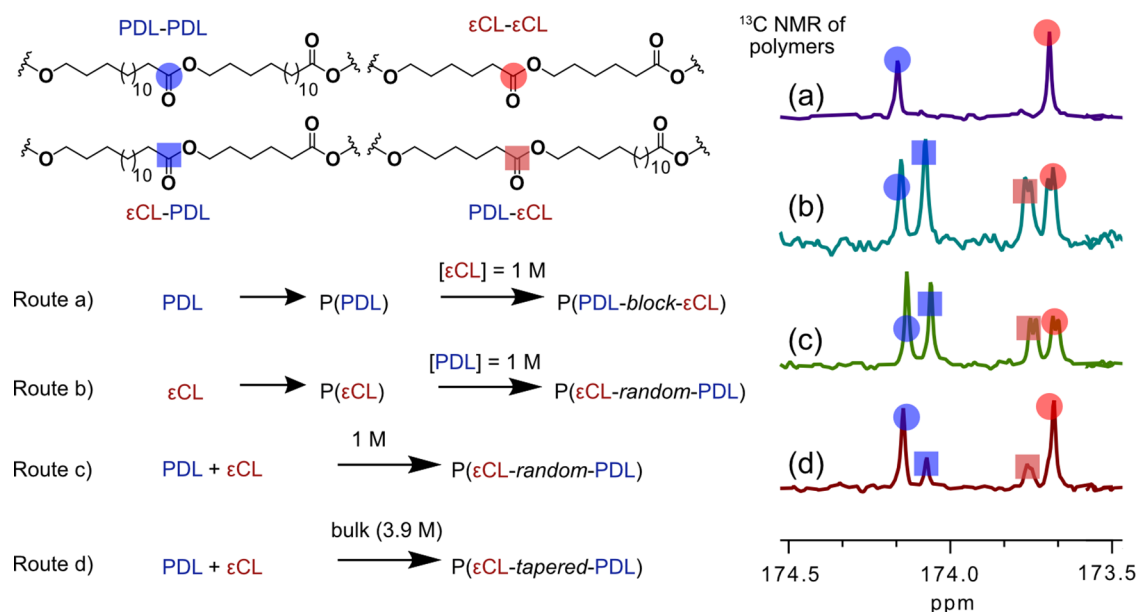


Figure 4. Polymerizations and copolymerizations were performed at 90 °C using 1 mol % ^tBuOLi catalyst and, if applicable, in toluene solvent for 2 h. Schematic representation of different approaches to PDL-CL copolymer synthesis with the resulting ¹³C NMR spectra (298 K, CDCl₃). Reaction details can be found in Table S1, entries 4–7 for runs a–d, respectively.

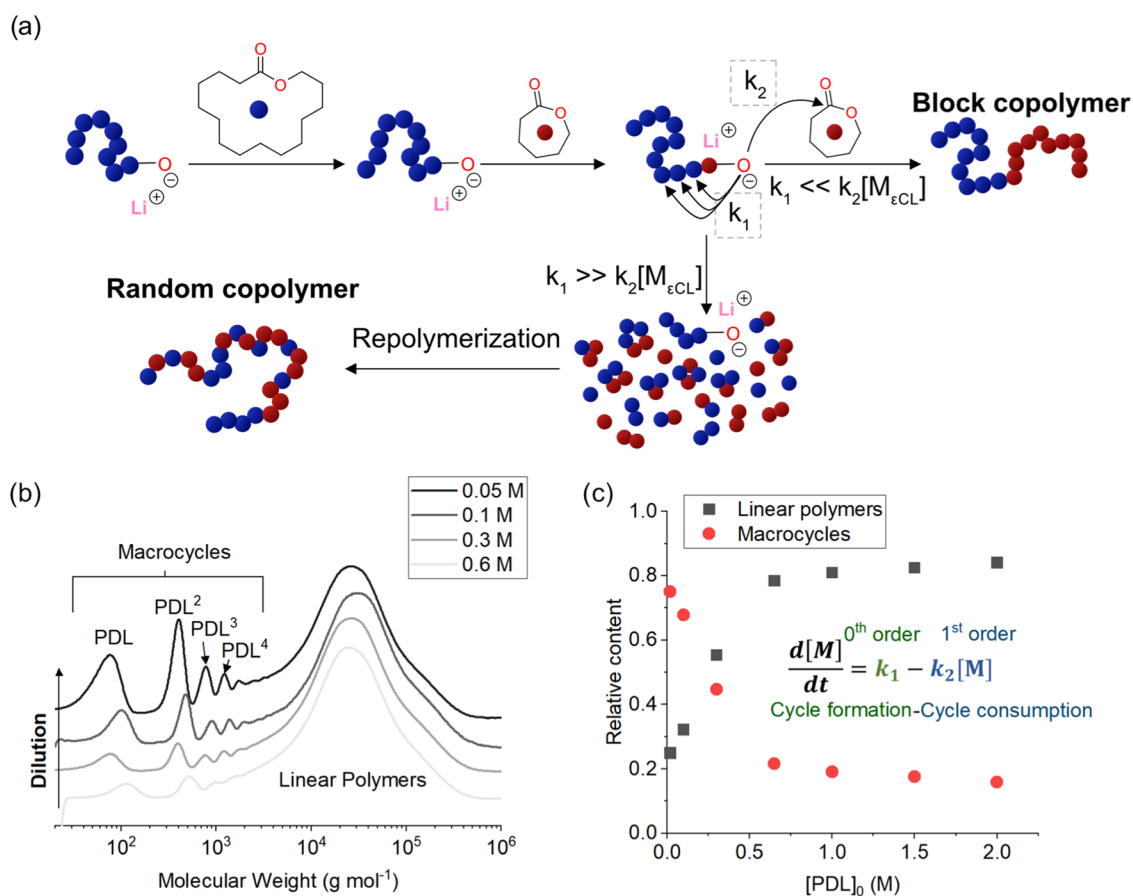


Figure 5. (a) Conditions for block and random copolymerization and hypothesized mechanism for the formation of random copolymers by sequential addition. (b) SEC (CHCl₃, 0.5 mL min⁻¹) elugrams for the polymerization equilibria achieved with PDL polymerized by 1 mol % ^tBuOK at 90 °C. (c) Relative concentration of macrocycles and linear polymers for elugrams shown in Figure 4b.

concentrations. It was clear that the copolymer architecture depended on the order of monomer addition and the reaction system concentration. For runs at 1 M monomer concentration,

block copolymers through sequential monomer addition with PDL (entropy driven) as the first block followed by the addition ϵ CL (enthalpy driven) could be synthesized with high definition

and no hetero dyads observable in the carbonyl region of ^{13}C NMR (Figure 4). Even when the system is left for an additional 13 h after full conversion at $90\text{ }^\circ\text{C}$, no hetero dyads were observed. These results suggest that intermolecular transesterification is suppressed and that randomization during copolymerization is related to backbiting and repolymerization rather than interchain transesterification. However, when the experiment was repeated with the AROP of ϵCL first, followed by the sequential addition of PDL, entirely random copolymers were formed (Figure 4). These observations are coherent with previous work on block copolymers containing PDL blocks, where the small-ring-sized monomer of enthalpic driving force, such as lactide,^{63,67} ϵCL ,⁶³ or 2,2-dimethyltrimethylene carbonate,⁶⁸ for sequential monomer addition is exclusively used as a second block. In contrast, as far as we know, there are no examples of well-defined block copolymers with PDL as the second block, except reports of simultaneous addition to yield tapered block copolymers.⁶⁹ The prospect of macrocycles contaminating the ^{13}C carbonyl signals is disregarded, as the copolymers are obtained by precipitation in methanol from chloroform, which isolates the linear polymers from the much smaller macrocycle byproducts.

$$\frac{d[M]}{dt} = \underbrace{k_1[I]}_{\text{Depolymerization}} - \underbrace{k_2[I][M]}_{\text{Polymerization}}$$

Kinetics relating to the change in monomer concentration.

The copolymerization between PDL and ϵCL shows that the concentration affects the block structure, which is inherent in the difference in kinetic dependence between polymerization and depolymerization. To elaborate, the rate equation for the polymerization of lactones is summarized as eq 1, where $d[M]/dt$ represents the change in cycle (monomer + macrocycles) concentration with time, $[I]$ the concentration of the initiator, $[M]$ the concentration of cycles, k_1 the rate constant for cyclo-depolymerization, and k_2 the rate constant for polymerization. If k_1 exceeds $k_2[M]$, then depolymerization occurs. Even during polymerization, cyclo-depolymerization occurs, although at a much lower rate than the polymerization rate. Suppose the overall cyclo-depolymerization rate (k_1) is competitive with the polymerization rate ($k_2[M]$); in that case, macrocycles are formed faster than they are consumed, resulting in the formation of larger cycles consisting of mixtures of monomer, which subsequently are repolymerized to form random copolymers (Figure 5a). The k_2 variable is influenced by the ring-opening thermodynamic driving force of the monomer, while k_1 , forming strainless macrocycles, is expected to be dependent only on the macrocycle size. Hence, the k_2/k_1 ratio is small for monomers with entropy-driven thermodynamics. SEC traces of systems at equilibrium for the homopolymerization of PDL in toluene at $90\text{ }^\circ\text{C}$ at various monomer concentrations (Figure 5b) reveal that with an increasing monomer concentration, the relative concentration of macrocycles decreases, as the macrocycle polymerization is first-order-dependent, while macrocycle formation has zero-order-dependent (Figure 5c). This can cause a polymer to lose a significant amount of its molecular weight simply by dilution, yielding macrocycles that can subsequently be repolymerized and cause chain scrambling (Figure S9). It should be pointed out that it takes a long time to

reach equilibrium for large PDL multimer cycles ($>\text{PDL}^4$) when $^t\text{BuOLi}$ is used. For this reason, Figure 5b,5c was obtained by using the much faster $^t\text{BuOK}$ initiator.

The predictive power of eq 1 was tested under two different concentrations, 1 M and bulk, during the simultaneous addition of PDL and ϵCL (Figure 4c,d). Due to the much higher polymerization rate of ϵCL (enthalpy driven) than PDL (entropy driven),⁷⁰ most of ϵCL is converted before PDL is, which should lead to a block copolymer if no/little backbiting occurs. Indeed, the ^{13}C NMR spectra show a clear difference in the randomness for the two copolymers, depending on their initial monomer concentrations, as observed by the intensity of carbonyl (~ 174.0 ppm) and methylene positions (~ 64.4 ppm) related to the dyads of $\epsilon\text{CL}-\epsilon\text{CL}$ and PDL-PDL (Figure 4 routes (c) and (d)). Thermal stability and temperature-dependent phase transitions, determined by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC), support the formation of block-like structures in bulk and more random structures at 1 M (Figure S10). The polymer architecture is, therefore, dependent on two factors, the monomer concentration and the AROP reaction rate of the second block, and their effect can be understood from eq 1 as only transesterification via backbiting reactions occurs. To clarify with ϵCL as an example, the reaction forming a linear polymer is faster than the rate at which cyclic oligomers are formed from the linear polymer.^{34,42} It is thus no surprise that PDL, which homopolymerizes much more slowly where backbiting is comparable in rate, is more prone to generate random copolymers if polymerized as the second monomer. Still, a sequential copolymerization of PDL followed by ϵCL at a low concentration of 0.5 M also yields a random copolymer, indicating that the fast polymerization kinetics of ϵCL is suppressed enough due to the low monomer concentration to allow depolymerization to macrocycles via backbiting transesterification, which subsequently are polymerized, leading to a random copolymer (Figure S11).

2.4. Ring Chain Equilibrium—Theoretical Context. We now know that the concentration of the macrocycles formed via backbiting reactions will govern the block structure during copolymerization. By applying the Jacobson–Stockmayer theory, we plotted the ring size to the power of $-5/2$ against the size of each possible ring when combining PDL- ϵCL in their copolymerization system (Figure S12a). Synthetically, it is known that the ϵCL monomer does not form during depolymerization in solution.^{34,40,42} A careful comparison of the theoretically predicted macrocycle concentration and the SEC results (Figure S12b) reveals a strong disagreement about the type and concentration of macrocycles formed. The Jacobson and Stockmayer theory assumes identical reactivity of each cycle;⁴⁵ consequently, the theory does not hold for copolymers. Instead, the equilibrium concentration should be corrected for the number of ester groups in the ring, as these dictate the reactivity of each ring (Figure S12c) (eq 2).

$$\text{corr. concentration} = \frac{n^{-2.5} \times s}{s_0} \quad (2)$$

Relative concentration correction of the Jacobson–Stockmayer theory for macrocycles consisting of more than one monomer. Where n represents the number of atoms in the cycle, s the number of atoms in the cycle per ester group, and s_0 the number of atoms in the ring of the smallest monomer.

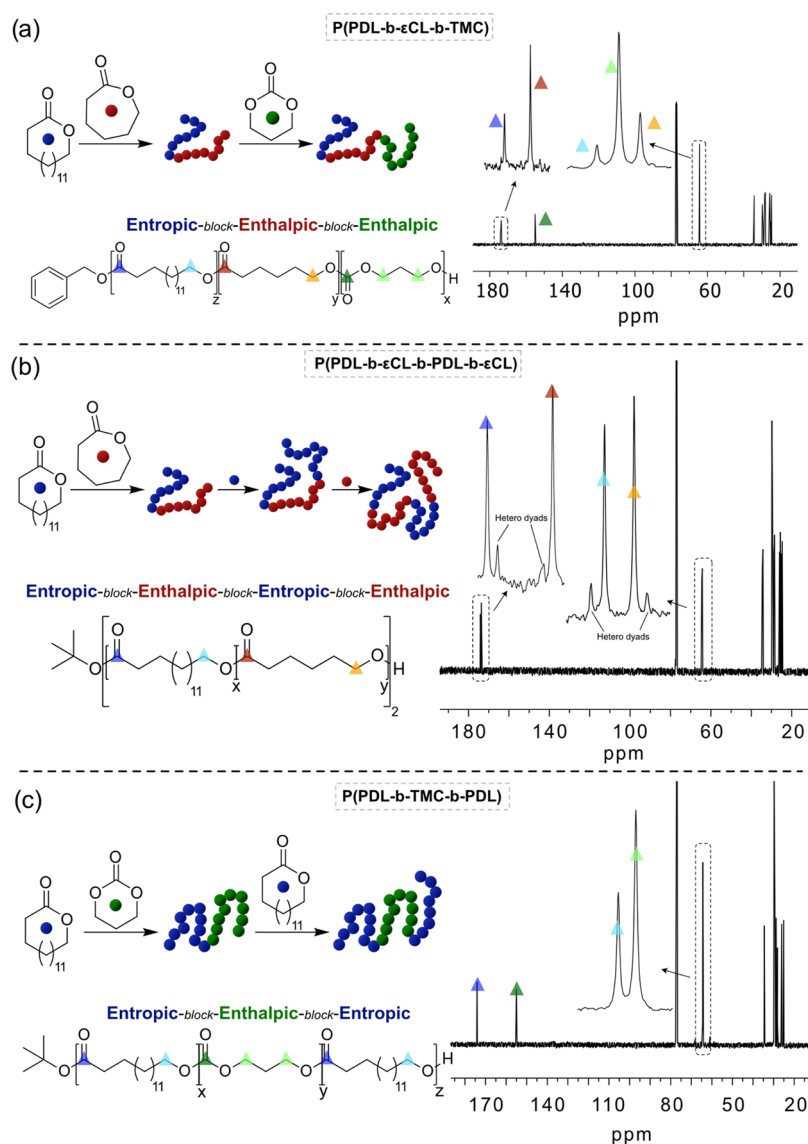


Figure 6. Synthesis pathways and ^{13}C NMR (298 K, CDCl_3) spectra of (a) P(PDL-*b*- ϵ CL-*b*-TMC), (b) P(PDL- ϵ CL)₂, and (c) P(PDL-*b*-TMC-*b*-PDL) copolymers.

This correction enabled a better agreement between SEC data and theoretically predicted values (Figure S12d) and suggests that mixed cycles are less reactive than ϵ CL cycles of similar size. Thus, much of the homo ϵ CL will be converted to mixed cycles, leading to random copolymers upon subsequent ring-opening. Scrambling of macrocycles could be observed by consecutive SEC analysis during the sequential addition copolymerization of ϵ CL followed by $[\text{PDL}]_0 = 0.5 \text{ M}$ at 90°C initiated by $^t\text{BuOLi}$ (Figure S12e). Before the addition of PDL, the oligomers of ϵ CL are visible in the SEC traces. However, after the addition of PDL, new macrocycles form at different retention volumes, which do not correspond to ϵ CL or PDL homomacrocycles. Still, polymerization to form a linear copolymer continues, as is evident by the increase in molecular weight of the linear fraction, demonstrating that cycle formation occurs constantly throughout the polymerization. The backbiting transesterification reaction leading to macrocyclic formation is limited in size to approximately ten monomeric units, as is expected from the decreasing probability of their theoretical formation. By SEC, macrocycle traces are visible with $200\text{--}5000 \text{ g mol}^{-1}$ molecular

weights, and linear polymers have molecular weights over 7000 g mol^{-1} (Figure S11b,e). If the polymerization can incorporate ten monomeric units faster than that backbiting transesterification occur, only homomacrocycles are formed, which subsequently will not affect the block transition, and clean block copolymers can be formed. Therefore, the dependency on the homopolymer polymerization rate and the reaction concentration allows for incredible control over the polymerization and polymer architecture by using the same catalytic system. Due to the abundance of transesterification using transesterification catalysts, several studies have reported the synthesis of random copolymers of PDL.^{62,69,71–73} With the simple anionic systems studied here, randomness or block structures can be triggered simply by varying reaction concentrations.

The origin of the suppression of interpolymer transesterification observed in AROP was investigated using the atomic scale information provided by molecular dynamics (MD) simulations (see Supporting Information (SI) section "Molecular Dynamics"). It was found that intramolecular coordination of ester units to the counterion pulls all ester

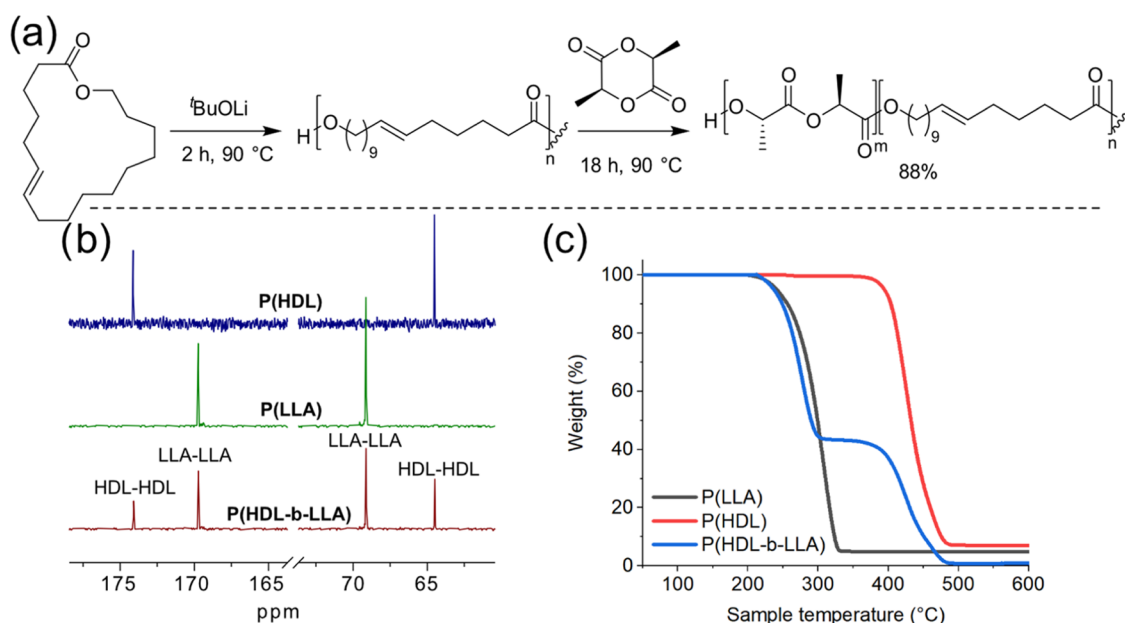


Figure 7. (a) Synthesis of P(HDL-*b*-LLA) copolymer and its analysis (b) ^{13}C NMR (CDCl_3 , 298 K), and (c) TGA (10 K min^{-1} , N_2).

units closer to the propagating chain-end. Such behavior yields large steric bulk, which likely hinders the propagating chain-end from reacting intermolecularly with other polymer chains.

2.5. Well-Defined Copolymers of Monomers with Different Thermodynamic Driving Forces. The acquired detailed understanding of the ring–chain equilibria and kinetic profiles of the different monomers was successfully applied to synthesize (multi)block copolymers. To exemplify, we demonstrate the previously unachievable block copolymer based on the sequential addition of first an enthalpically driven monomer (ϵCL or trimethylene carbonate (TMC)) followed by an entropically driven monomer (PDL). Specifically, three (multi)-block copolymers were synthesized and characterized (^1H NMR, ^{13}C NMR, SEC, TGA, DSC, and diffusion-ordered spectroscopy (DOSY)):

- (1) P(PDL-*b*- ϵCL -*b*-TMC) (Figures 5a and S16–S20).
- (2) P(PDL-*b*- ϵCL -*b*-PDL-*b*-CL) (Figures 5b and S21–S24).
- (3) P(PDL-*b*-TMC-*b*-PDL) (Figures 5c and S25–S28).

We selected ϵCL and TMC as comonomers based on their inherent fast homopolymerization rate. In these cases, macrocycle formation occurs only after complete conversion (large k_2/k_1 ratio (eq 1)). To demonstrate the versatility in the synthesis and handling, a P(PDL-*b*-TMC-*b*-PDL) copolymer was also made through a two-step synthesis pathway using ZnEt_2 to generate the alkoxide in situ to perform a chain extension reaction on an isolated polymer (Figure S29). Additionally, to demonstrate that copolymers can be synthesized in a one-pot fashion using initiators other than BuOLi , P(PDL-*b*- ϵCL -*b*-TMC) and P(PDL-*b*-TMC-*b*-PDL) were also prepared using a BnOH-ZnEt_2 initiating system (Figures S30 and S31). Highly defined block copolymers were obtained, and only homo dyads were present in the carbonyl region in ^{13}C NMR (Figure 6a,6c). P(PDL-*b*- ϵCL -*b*-PDL-*b*- ϵCL) (Figure 6b) was an exception, portraying low-intensity hetero linkages, which is expected when PDL is not added as the first block due to its polymerization behavior (low k_2/k_1 ratio), as discussed prior (see eq 1 and Figures 4 and 5). Hence, these polymerizations were performed at high concentrations, limiting the macrocycle formation (eq 1). In addition, we demonstrated block copolymer formation via

AROP based on ω -6-hexadecenlactone (HDL) and L-lactide (LLA) to further expand the scope. HDL is known to have low polymerization rates, much like PDL, as the ratio of k_2/k_1 (eq 1) is small for HDL. Hence, LLA is an excellent candidate as a second block monomer as this enthalpy-driven monomer is polymerized rapidly and showed no formation of macrocycles during homopolymerization. Indeed, only homo dyads are visible by ^{13}C NMR (Figure 7b), and TGA analysis displays a two-step degradation for the isolated copolymer (Figure 7c). A more detailed discussion for P(HDL-*b*-LLA) including ^1H , ^{13}C , and DOSY NMR, SEC, and DSC data, is presented in the Supporting Information (see SI section P(HDL-*b*-LLA) and Figures S32–S37).

The benefits of controlled AROP for block copolymer synthesis are certainly not limited to lactones; other cyclic monomers such as cyclic ethers, sulfides, carbonates, amides, phosphates, siloxanes, imines, and ureas are all established to be polymerizable by anionic mechanisms.^{74–76} The combined understanding of interpolymer transesterification and macrocycle formation generated in this work may open up an array of new defined copolymers without limitations to the different block compositions.

3. CONCLUSIONS

In this work, we have presented the concept of relative polymerization/backbiting reaction kinetics for different monomers that enabled the facile synthesis of block copolymers consisting of entropy-driven strainless macrocyclic lactones (PDL or HDL) and enthalpy-driven strained small-ring-sized lactones and cyclic carbonates (ϵCL , TMC, LLA). AROP exhibits a high polymerization rate and a low degree of interpolymer transesterification reactions that enable clean block transitions during a one-pot chain extension. Thus, this allows us to predict and understand the copolymerization architectural outcomes. Strainless entropy-driven lactones require high concentrations to achieve block transitions, whereas strained enthalpy-driven lactones lead to clean block transitions at much lower concentrations. In a larger context, this work focuses on the polymerization of cyclic esters and cyclic

carbonates. However, we believe this knowledge might be instrumental in designing block copolymers of other cyclic monomers with vastly different polymerization behaviors toward tailored applications.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.macromol.3c02477>.

Procedures, reagents, polymer characterization, additional experiments and discussion (PDF)

AUTHOR INFORMATION

Corresponding Authors

Peter Olsén – Department of Fibre and Polymer Technology, KTH Royal Institute of Technology, SE-100 44 Stockholm, Sweden; orcid.org/0000-0002-5081-1835; Email: polsen@kth.se

Karin Odélius – Department of Fibre and Polymer Technology, KTH Royal Institute of Technology, SE-100 44 Stockholm, Sweden; orcid.org/0000-0002-5850-8873; Email: hoem@kth.se

Authors

Vincent Nieboer – Department of Fibre and Polymer Technology, KTH Royal Institute of Technology, SE-100 44 Stockholm, Sweden; orcid.org/0000-0002-3644-0839

Noé Fanjul-Mosteirín – Department of Fibre and Polymer Technology, KTH Royal Institute of Technology, SE-100 44 Stockholm, Sweden; orcid.org/0000-0003-3850-5373

Complete contact information is available at: <https://pubs.acs.org/doi/10.1021/acs.macromol.3c02477>

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors acknowledge funding from the Swedish Research Council (Grant Number 2020-03455).

REFERENCES

- (1) Wang, Z.; Chan, C. L. C.; Zhao, T. H.; Parker, R. M.; Vignolini, S. Recent Advances in Block Copolymer Self-Assembly for the Fabrication of Photonic Films and Pigments. *Adv. Opt. Mater.* **2021**, *9* (21), No. 2100519.
- (2) Kadota, S.; Aoki, K.; Nagano, S.; Seki, T. Photocontrolled Microphase Separation of Block Copolymers in Two Dimensions. *J. Am. Chem. Soc.* **2005**, *127* (23), 8266–8267.
- (3) Lohse, D. J.; Hadjichristidis, N. Microphase Separation in Block Copolymers. *Curr. Opin. Colloid Interface Sci.* **1997**, *2* (2), 171–176.
- (4) Sinturel, C.; Bates, F. S.; Hillmyer, M. A. High χ –Low N Block Polymers: How Far Can We Go? *ACS Macro Lett.* **2015**, *4* (9), 1044–1050.
- (5) Dau, H.; Jones, G. R.; Tsogtgerel, E.; Nguyen, D.; Keyes, A.; Liu, Y.-S.; Rauf, H.; Ordóñez, E.; Puchelle, V.; Basbug Alhan, H.; Zhao, C.; Harth, E. Linear Block Copolymer Synthesis. *Chem. Rev.* **2022**, *122* (18), 14471–14553.
- (6) Feng, H.; Lu, X.; Wang, W.; Kang, N.-G.; Mays, J. W. Block Copolymers: Synthesis, Self-Assembly, and Applications. *Polymers* **2017**, *9* (10), No. 494, DOI: [10.3390/polym9100494](https://doi.org/10.3390/polym9100494).
- (7) Xie, X.; Huo, Z.; Jang, E.; Tong, R. Recent Advances in Enantioselective Ring-Opening Polymerization and Copolymerization. *Commun. Chem.* **2023**, *6* (1), No. 202, DOI: [10.1038/s42004-023-01007-z](https://doi.org/10.1038/s42004-023-01007-z).
- (8) Inoue, S.; Tomoi, Y.; Tsuruta, T.; Furukawa, J. Organometallic-Catalyzed Polymerization of Propiolactone. *Makromol. Chem.* **1961**, *48* (1), 229–233.
- (9) Kricheldorf, H. R.; Kreiser-Saunders, I. Poly lactones, 19. Anionic Polymerization of L-Lactide in Solution. *Makromol. Chem.* **1990**, *191* (5), 1057–1066.
- (10) Kricheldorf, H. R.; Boettcher, C. Poly lactones 27. Anionic Polymerization of L-Lactide. Variation of Endgroups and Synthesis of Block Copolymers with Poly(Ethylene Oxide). *Makromol. Chem., Macromol. Symp.* **1993**, *73* (1), 47–64.
- (11) Kricheldorf, H. R.; Boettcher, C. Poly lactones 26. Lithium Alkoxide-Initiated Polymerizations of L-Lactide. *Makromol. Chem.* **1993**, *194* (6), 1665–1669.
- (12) Kricheldorf, H. R.; Boettcher, C. Poly lactones, 24. Polymerizations of Racemic and Meso-D,L-Lactide with Al–O Initiators. Analyses of Stereosequences. *Makromol. Chem.* **1993**, *194* (6), 1653–1664.
- (13) Kricheldorf, H. R.; Kreiser-Saunders, I. Poly lactones: 30. Vitamins, Hormones and Drugs as Co-Initiators of AlEt₃-Initiated Polymerizations of Lactide. *Polymer* **1994**, *35* (19), 4175–4180.
- (14) Kasperczyk, J. E. Microstructure Analysis of Poly(Lactic Acid) Obtained by Lithium Tert-Butoxide as Initiator. *Macromolecules* **1995**, *28* (11), 3937–3939.
- (15) Bero, M.; Adamus, G.; Kasperczyk, J.; Janeczek, H. Synthesis of Block Copolymers of ϵ -Caprolactone and Lactide in the Presence of Lithium t-Butoxide. *Polym. Bull.* **1993**, *31* (1), 9–14.
- (16) Bero, M.; et al. Synthesis of disyndiotactic polylactide. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 4038–4042, DOI: [10.1002/\(SICI\)1099-0518\(19991115\)37:223.O.CO;2-F](https://doi.org/10.1002/(SICI)1099-0518(19991115)37:223.O.CO;2-F).
- (17) Kurcok, P.; Penczek, J.; Franek, J.; Jedlinski, Z. Anionic Polymerization of Lactones. 14. Anionic Block Copolymerization of δ -Valerolactone and L-Lactide Initiated with Potassium Methoxide. *Macromolecules* **1992**, *25* (9), 2285–2289.
- (18) Jedliński, Z.; Kurcok, P.; Lenz, R. W. Synthesis of Potentially Biodegradable Polymers. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **1995**, *32* (4), 797–810.
- (19) Jacobs, C.; Dubois, P.; Jerome, R.; Teyssie, P. Macromolecular Engineering of Poly lactones and Poly lactides. 5. Synthesis and Characterization of Diblock Copolymers Based on Poly- ϵ -Caprolactone and Poly(L,L or D,L)Lactide by Aluminum Alkoxides. *Macromolecules* **1991**, *24* (11), 3027–3034.
- (20) Hofman, A.; Slomkowski, S.; Penczek, S. Polymerization of ϵ -Caprolactone with Kinetic Suppression of Macrocyces. *Makromol. Chem. Rapid Commun.* **1987**, *8* (8), 387–391.
- (21) Perret, R.; Skoulios, A. Synthèse et caractérisation de quelques poly- ϵ -caprolactones. *Makromol. Chem.* **1972**, *152* (1), 291–303.
- (22) Perret, R.; Skoulios, A. Synthèse et caractérisation de copolymères séquencés polyoxyéthylène/poly- ϵ -caprolactone. *Makromol. Chem.* **1972**, *156* (1), 143–156.
- (23) Kurcok, P.; Matuszowicz, A.; Jedliński, Z.; Kricheldorf, H. R.; Dubois, P.; Jérôme, R. Substituent Effect in Anionic Polymerization of β -Lactones Initiated by Alkali Metal Alkoxides. *Macromol. Rapid Commun.* **1995**, *16* (7), 513–519.
- (24) Jedlinski, Z.; Kowalczyk, M.; Kurcok, P. Polymerization of β -Lactones Initiated by Alkali Metal Naphthalenides. A Convenient Route to Telechelic Polymers. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **1992**, *29* (12), 1223–1230.
- (25) Jedlinski, Z.; Kowalczyk, M.; Glowkowski, W.; Grobelny, J.; Szwarc, M. Novel Polymerization of β -Butyrolactone Initiated by Potassium Naphthalenide in the Presence of a Crown Ether or a Cryptand. *Macromolecules* **1991**, *24* (2), 349–352.
- (26) Jedlinski, Z.; Kurcok, P.; Kowalczyk, M.; Matuszowicz, A.; Dubois, P.; Jerome, R.; Kricheldorf, H. R. Anionic Polymerization of Pivalolactone Initiated by Alkali Metal Alkoxides. *Macromolecules* **1995**, *28* (21), 7276–7280.
- (27) Matuszowicz, A.; Jedlinski, Z.; Gawron, M.; Kosturkiewicz, Z. Synthesis of Macro cyclic Oligomers of Pivalolactone. Crystal Structure and Properties of Tetrolide. *J. Org. Chem.* **1995**, *60* (21), 6826–6828.

- (28) Nomura, R.; Ueno, A.; Endo, T. Anionic Ring-Opening Polymerization of Macroyclic Esters. *Macromolecules* **1994**, *27* (2), 620–621.
- (29) Jedliński, Z.; Juzwa, M.; Adamus, G.; Kowalczyk, M.; Montaudo, M. Anionic Polymerization of Pentadecanolide. A New Route to a Potentially Biodegradable Aliphatic Polyester. *Macromol. Chem. Phys.* **1996**, *197* (9), 2923–2929.
- (30) Grobelny, Z.; Jurek-Suliga, J.; Golba, S. New Way of Anionic Ring-Opening Copolymerization of β -Butyrolactone and ϵ -Caprolactone: Determination of the Reaction Course. *J. Polym. Res.* **2020**, *27* (12), No. 359, DOI: 10.1007/s10965-020-02333-9.
- (31) D'Auria, I.; D'Alterio, M. C.; Tedesco, C.; Pellicchia, C. Tailor-Made Block Copolymers of L-, D- and Rac-Lactides and ϵ -Caprolactone via One-Pot Sequential Ring Opening Polymerization by Pyridylamidozinc(II) Catalysts. *RSC Adv.* **2019**, *9* (56), 32771–32779.
- (32) Duda, A.; Biela, T.; Libiszowski, J.; Penczek, S.; Dubois, P.; Mecerreyes, D.; Jérôme, R. Block and Random Copolymers of ϵ -Caprolactone. *Polym. Degrad. Stab.* **1998**, *59* (1), 215–222.
- (33) Labet, M.; Thielemans, W. Synthesis of Polycaprolactone: A Review. *Chem. Soc. Rev.* **2009**, *38* (12), 3484–3504.
- (34) Ito, K.; Hashizuka, Y.; Yamashita, Y. Equilibrium Cyclic Oligomer Formation in the Anionic Polymerization of ϵ -Caprolactone. *Macromolecules* **1977**, *10* (4), 821–824.
- (35) Sipos, L.; Zsuga, M. Anionic Polymerization of L-Lactide Effect of Lithium and Potassium as Counterions. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **1997**, *34* (7), 1269–1284.
- (36) Bhaw-Luximon, A.; Jhurry, D.; Spassky, N.; Pensec, S.; Belleney, J. Anionic Polymerization of d,l-Lactide Initiated by Lithium Diisopropylamide. *Polymer* **2001**, *42* (24), 9651–9656.
- (37) Oshimura, M.; Okazaki, R.; Hirano, T.; Ute, K. Ring-Opening Polymerization of ϵ -Caprolactone with Dilithium Tetra-Tert-Butylzincate under Mild Conditions. *Polym. J.* **2014**, *46* (12), 866–872.
- (38) Miola-Delaite, C.; Hamaide, T.; Spitz, R. Anionic Coordinated Polymerization of ϵ -Caprolactone with Aluminium, Zirconium and Some Rare Earths Alkoxides as Initiators in the Presence of Alcohols. *Macromol. Chem. Phys.* **1999**, *200* (7), 1771–1778.
- (39) Deffieux, A.; Boileau, S. Use of Cryptates in Anionic Polymerization of Lactones. *Macromolecules* **1976**, *9* (2), 369–371.
- (40) Ito, K.; Yamashita, Y. Propagation and Depropagation Rates in the Anionic Polymerization of ϵ -Caprolactone Cyclic Oligomers. *Macromolecules* **1978**, *11* (1), 68–72.
- (41) Ouhadi, T.; Stevens, C.; Teyssié, P. Mechanism of ϵ -Caprolactone Polymerization by Aluminum Alkoxides. *Makromol. Chem.* **1975**, *1* (S19751), 191–201.
- (42) Sosnowski, S.; Słomkowski, S.; Penczek, S.; Reibel, L. Kinetics of ϵ -Caprolactone Polymerization and Formation of Cyclic Oligomers. *Makromol. Chem.* **1983**, *184* (10), 2159–2171.
- (43) Lin, B.; Jadrlich, C. N.; Pane, V. E.; Arrechea, P. L.; Erdmann, T.; Dausse, C.; Hedrick, J. L.; Park, N. H.; Waymouth, R. M. Ultrafast and Controlled Ring-Opening Polymerization with Sterically Hindered Strong Bases. *Macromolecules* **2020**, *53* (20), 9000–9007.
- (44) Hodge, P. Entropically Driven Ring-Opening Polymerization of Strainless Organic Macrocycles. *Chem. Rev.* **2014**, *114* (4), 2278–2312.
- (45) Jacobson, H.; Stockmayer, W. H. Intramolecular Reaction in Polycondensations. I. The Theory of Linear Systems. *J. Chem. Phys.* **1950**, *18* (12), 1600–1606.
- (46) Ito, K.; Tomida, M.; Yamashita, Y. Ring-Chain Equilibrium in the Anionic Polymerization of δ -Valerolactone. *Polym. Bull.* **1979**, *1* (8), 569–573.
- (47) Shannon, R. D. Revised Effective Ionic Radii and Systematic Studies of Interatomic Distances in Halides and Chalcogenides. *Acta Crystallogr., Sect. A* **1976**, *32* (5), 751–767.
- (48) Penczek, S.; Słomkowski, S. Progress in Anionic Ring-Opening Polymerization. In *Recent Advances in Anionic Polymerization*; Hogen-Esch, T. E.; Smid, J., Eds.; Springer: Dordrecht, 1987; pp 275–295.
- (49) McGrath, J. E. *Ring-Opening Polymerization*, ACS Symposium Series; American Chemical Society: Washington, DC, 1985; p 286.
- (50) Clarson, S. J.; Semlyen, J. A. *Siloxane Polymers*; Prentice Hall: Englewood Cliffs, NJ, 1993.
- (51) Kazanskii, K. S.; Solovyanov, A. A.; Entelis, S. G. Polymerization of Ethylene Oxide by Alkali Metal-Naphthalene Complexes in Tetrahydrofuran. *Eur. Polym. J.* **1971**, *7* (10), 1421–1433.
- (52) Szwarc, M. Living Polymers and Mechanisms of Anionic Polymerization. *Living Polymers and Mechanisms of Anionic Polymerization*, Advances in Polymer Science; Springer, 1983; Vol. 49, pp 1–177.
- (53) Herzberger, J.; Niederer, K.; Pohlit, H.; Seiwert, J.; Worm, M.; Wurm, F. R.; Frey, H. Polymerization of Ethylene Oxide, Propylene Oxide, and Other Alkylene Oxides: Synthesis, Novel Polymer Architectures, and Bioconjugation. *Chem. Rev.* **2016**, *116* (4), 2170–2243.
- (54) Van Beylen, M.; Bywater, S.; Smets, G.; Szwarc, M.; Worsfold, D. J. Developments in Anionic Polymerization—A Critical Review. *Polysiloxane Copolymers/Anionic Polymerization*, Advances in Polymer Science; Springer: Berlin, Heidelberg, 1988; pp 87–143.
- (55) Jeuck, H.; Müller, A. H. E. Kinetics of the Anionic Polymerization of Methyl Methacrylate in Tetrahydrofuran Using Lithium and Potassium as Counterions. *Makromol. Chem. Rapid Commun.* **1982**, *3* (2), 121–125.
- (56) Dainton, F. S.; East, G. C.; Harpell, G. A.; Hurworth, N. R.; Ivin, K. J.; Laffair, R. T.; Pallen, R. H.; Hui, K. M. The Kinetics of Anionic Polymerization of Styrene and α -Methylstyrene. Effects of Counter-Ion and Solvent. *Makromol. Chem.* **1965**, *89* (1), 257–262.
- (57) Myers, D.; Witt, T.; Cyriac, A.; Bown, M.; Mecking, S.; K Williams, C. Ring Opening Polymerization of Macrolactones: High Conversions and Activities Using an Yttrium Catalyst. *Polym. Chem.* **2017**, *8* (37), 5780–5785.
- (58) Nieboer, V.; Fanjul-Mosteirín, N.; Olsén, P.; Odelius, K. Linear Not Cyclic – Unravelling an Anionic Initiation Pathway for Lewis Pair Polymerization of Lactones. *Polym. Chem.* **2023**, *14* (20), 2485–2493.
- (59) Duda, A.; Penczek, S. Polymerization of ϵ -Caprolactone Initiated by Aluminum Isopropoxide Trimer and/or Tetramer. *Macromolecules* **1995**, *28* (18), 5981–5992.
- (60) Nieboer, V.; Fanjul-Mosteirín, N.; Olsén, P.; Odelius, K. Lewis-Pair Derived Activated Lactone Initiator (ALI) Complex for Rapid, Controlled, Bench Stable and Selective Ring-Opening Polymerization of (Macro)Lactones. *Eur. Polym. J.* **2023**, *201*, No. 112594.
- (61) Bouyahyi, M.; Pepels, M. P. F.; Heise, A.; Duchateau, R. ω -Pentadecalactone Polymerization and ω -Pentadecalactone/ ϵ -Caprolactone Copolymerization Reactions Using Organic Catalysts. *Macromolecules* **2012**, *45* (8), 3356–3366.
- (62) Bouyahyi, M.; Duchateau, R. Metal-Based Catalysts for Controlled Ring-Opening Polymerization of Macrolactones: High Molecular Weight and Well-Defined Copolymer Architectures. *Macromolecules* **2014**, *47* (2), 517–524.
- (63) Wang, B.; Pan, L.; Ma, Z.; Li, Y. Ring-Opening Polymerization with Lewis Pairs and Subsequent Nucleophilic Substitution: A Promising Strategy to Well-Defined Polyethylene-like Polyesters without Transesterification. *Macromolecules* **2018**, *51* (3), 836–845.
- (64) Huang, Y.-T.; Wang, W.-C.; Hsu, C.-P.; Lu, W.-Y.; Chuang, W.-J.; Chiang, M. Y.; Lai, Y.-C.; Chen, H.-Y. The Ring-Opening Polymerization of ϵ -Caprolactone and L-Lactide Using Aluminum Complexes Bearing Benzothiazole Ligands as Catalysts. *Polym. Chem.* **2016**, *7* (26), 4367–4377.
- (65) Endo, M.; Aida, T.; Inoue, S. Immortal Polymerization of ϵ -Caprolactone Initiated by Aluminum Porphyrin in the Presence of Alcohol. *Macromolecules* **1987**, *20* (12), 2982–2988.
- (66) Kitayama, T.; Yamaguchi, H.; Kanzawa, T.; Hirano, T. Living Ring-Opening Polymerization of ϵ -Caprolactone with Combinations of Tert-Butyllithium and Bilky Aluminium Phenoxides. *Polym. Bull.* **2000**, *45* (2), 97–104.
- (67) Pepels, M. P. F.; Hofman, W. P.; Kleijnen, R.; Spoelstra, A. B.; Koning, C. E.; Goossens, H.; Duchateau, R. Block Copolymers of “PE-Like” Poly(Pentadecalactone) and Poly(L-Lactide): Synthesis, Properties, and Compatibilization of Polyethylene/Poly(L-Lactide) Blends. *Macromolecules* **2015**, *48* (19), 6909–6921.

(68) Bai, J.-H.; Wang, J.-H.; Zhang, L.-F. Isothiourea-Based Lewis Pairs for Homopolymerization and Copolymerization of 2,2-Dimethyltrimethylene Carbonate with ϵ -Caprolactone and ω -Pentadecalactone. *J. Polym. Sci., Part A: Polym. Chem.* **2019**, *57* (23), 2349–2355.

(69) Focarete, M. L.; Gazzano, M.; Scandola, M.; Kumar, A.; Gross, R. A. Copolymers of ω -Pentadecalactone and Trimethylene Carbonate from Lipase Catalysis: Influence of Microstructure on Solid-State Properties. *Macromolecules* **2002**, *35* (21), 8066–8071.

(70) Duda, A.; Kowalski, A.; Penczek, S.; Uyama, H.; Kobayashi, S. Kinetics of the Ring-Opening Polymerization of 6-, 7-, 9-, 12-, 13-, 16-, and 17-Membered Lactones. Comparison of Chemical and Enzymatic Polymerizations. *Macromolecules* **2002**, *35* (11), 4266–4270.

(71) Wilson, J. A.; Hopkins, S. A.; Wright, P. M.; Dove, A. P. Synthesis of ω -Pentadecalactone Copolymers with Independently Tunable Thermal and Degradation Behavior. *Macromolecules* **2015**, *48* (4), 950–958.

(72) Bai, J.-H.; Wang, X.-Q.; Wang, J.-H.; Zhang, L.-F. Homo- and Random Copolymerizations of ω -Pentadecalactone with ϵ -Caprolactone Using Isothiourea-Based Dual Catalysis. *J. Polym. Sci., Part A: Polym. Chem.* **2019**, *57* (11), 1189–1196.

(73) Kumar, A.; Garg, K.; Gross, R. A. Copolymerizations of ω -Pentadecalactone and Trimethylene Carbonate by Chemical and Lipase Catalysis. *Macromolecules* **2001**, *34* (11), 3527–3533.

(74) Nuyken, O.; Pask, S. D. Ring-Opening Polymerization—An Introductory Review. *Polymers* **2013**, *5* (2), 361–403.

(75) Carlotti, S.; Peruch, F. Cyclic Monomers: Epoxides, Lactide, Lactones, Lactams, Cyclic Silicon-Containing Monomers, Cyclic Carbonates, and Others. In *Anionic Polymerization: Principles, Practice, Strength, Consequences and Applications*; Hadjichristidis, N.; Hirao, A., Eds.; Springer: Tokyo, 2015; pp 191–305.

(76) Sudo, A. Anionic Ring-Opening Polymerization. In *Encyclopedia of Polymeric Nanomaterials*; Kobayashi, S.; Müllen, K., Eds.; Springer: Berlin, Heidelberg, 2021; pp 1–11.



CAS BIOFINDER DISCOVERY PLATFORM™

**PRECISION DATA
FOR FASTER
DRUG
DISCOVERY**

CAS BioFinder helps you identify targets, biomarkers, and pathways

Unlock insights

CAS
A Division of the
American Chemical Society