

Functional polyesters via ring-opening copolymerization of α -hydroxy- γ -butyrolactone and ϵ -caprolactone: $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ as an efficient coordination-insertion catalyst

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Abstract

The growing awareness of environmental concerns and the fossil resources depletion have raised the need to develop sustainable and degradable polymers such as aliphatic polyesters. γ -Lactone-based polyesters are of great interest today due to their ability to depolymerize. The introduction of functional groups appeared also useful to tune the properties of such polyesters. This can be addressed by the use of functional monomers such as the sugar-based α -hydroxy- γ -butyrolactone (HBL). In this study, the synthesis of random copolyesters of HBL and ϵ -caprolactone (ϵ -CL) was investigated via ring-opening copolymerization in the presence of $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ as a catalyst. High polymerization temperature (80°C) was required for fast and high monomer conversions. The characterization of the copolyesters and kinetic investigations provided better insight into the polymerization mechanism and formation of various HBL monomer units (cyclic, linear and branched). $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ catalyst afforded high HBL conversion ratio (over 85 %) for the copolymerization reaction enabling the synthesis of copolyesters with a ratio of HBL units ranging from 9 to 63 %.

Keywords

Ring-opening (co)polymerization, α -hydroxy- γ -butyrolactone, functional polyesters, sustainable polymers, organometallic catalysis

Introduction

In recent years, aliphatic polyesters have shown a particular relevance in the development of sustainable and degradable polymers to face the environmental concerns [1–3]. Thanks to their biodegradable and biocompatible properties, these polymers are already used in many fields as in packaging, biomedical (tissue engineering, drug delivery systems, regenerative medicine...) or 3D printing applications [4–9]. However, their application range can be extended with the use of functional monomers. Indeed, these latter enable to design tailor-made copolyesters thanks to the introduction of pendant functionalities to the polymer backbone ready for post-modification reactions such as chain extension, cross-linking, or functionalization with peptides [10–12]. To achieve the synthesis of polyesters, the ring-opening (co)polymerization (ROP/ROCP) of cyclic esters (lactones and lactides), which is a powerful tool to design the structure and architecture of polymers, has been promoted [13,14]. Moreover, the growing awareness of environmental concerns together with the fossil resources depletion have raised the need to develop bio-based polymers [15–18] as, nowadays, most of the polyesters are derived from petroleum. γ -Lactones are an important class of monomers that count many bio-based and functional lactones. Nevertheless, ROP of γ -lactones [19–22] faces thermodynamic challenges [23–27]. Because of their low strain energy, this class of monomer has been considered as “non-polymerizable”. In this particular case, the ROP under ambient pressure results in a low negative change of enthalpy (ΔH_p) which is too small to counterbalance the large negative entropic (ΔS_p) change, thus, resulting in a positive polymerization free energy (ΔG_p). In 2016, Chen *et al.* achieved the polymerization of the five-membered γ -butyrolactone (γ -BL) using $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ as catalyst under specific reaction conditions: polymerization at low temperature (below the ceiling temperature (T_c)) and at high monomer concentration [28]. The γ -BL is a well-known monomer as the poly(γ -butyrolactone) is a polyester that can be totally depolymerized. Another strategy to overcome the thermodynamic issues is to perform the random copolymerization of γ -lactones with high ring strain energy monomers, such as the seven-membered ϵ -caprolactone (ϵ -CL) [21]. The random copolymerization is also a good method to tune the polyester degradability by

playing on the chemical nature of the comonomers and their rate of incorporation. As an example, increasing the number of γ -BL units in a PBL-co-PCL copolymer facilitates the thermal and hydrolytic degradation of the poly(ϵ -caprolactone) (PCL) chains [29]. Organometallic catalysts have been widely used for the synthesis of (co)polyesters through a coordination/insertion mechanism [30–32]. Several metal-based systems [33–46] and more specifically Lanthanum (La) based catalyst [28,47–53] showed a high efficiency for the ROP and ROCP of the γ -BL and its derivatives yielding high molar mass (co)polyesters which drove the presented work.

Among the γ -lactone family, α -hydroxy- γ -butyrolactone (HBL) is a bioderived monomer from glucose [54][55] analogue to the γ -BL and bearing a hydroxyl function. The presence of this rare function on the monomer is of particular interest for the synthesis of functionalized polymers that can be post-modified. The incorporation of HBL units into a polyester can change its thermomechanical properties by decreasing the crystallinity. Hydroxyl function can also provide hydrophilicity to the polymer which may enhance the degradability of the final material. Only a few articles discuss the HBL polymerization. HBL oligomers were first obtained using Lewis and Brønsted acids in bulk [56]. Its copolymerization with ϵ -CL was also performed using $\text{Sn}(\text{Oct})_2$ as a catalyst and led to the formation of branched copolymers with a maximum HBL incorporation ratio of 14% [57]. Indeed, the HBL polymerization remains to be explored further.

In this project, the synthesis of functional copolyesters via the ROCP of HBL and ϵ -CL monomers using $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ as the catalyst was studied. The polymerization mechanism was elucidated thanks to a kinetic study and to precise characterization of the polymer microstructure. In order to optimize the polymerization conditions, the influence of different reaction parameters was investigated allowing the synthesis of copolyesters with various amounts of HBL.

Materials and methods

Materials

α -hydroxy- γ -butyrolactone (HBL) was given by ADISSEO, put under dynamic vacuum at 40°C and stirred overnight. Then the monomer was purified by distillation, only the second fraction was kept, the first and last fractions were removed. Tri[N,N-bis(trimethylsilyl)amide] lanthanum(III) was purchased from Sigma-Aldrich, stored into a glovebox and used as received. Benzyl alcohol and ϵ -caprolactone were purchased from Alfa Aesar, dried over CaH₂ overnight and vacuum-distilled. The solvents were dried on alumina column and cryo-distilled: THF over Na/benzophenone and toluene over polystyryl lithium.

General polymerization method(s)

All polymerizations were performed in a flame-dried Schlenk. For a typical copolymerization: ratio M/C/I = 400/1/1; [M1 + M2] = 8 M; THF; ϵ -CL/HBL ratio = 77/23, the Schlenk was first introduced into an argon-filled glovebox, charged with a predetermined amount of catalyst (1 equivalent; 0.021 mmol; 13 mg.) and closed with a rotaflow stopcock. The reactors were taken out from the glovebox and connected to a dual-manifold Schlenk line. Under argon atmosphere, the initiator (1 equivalent; 0.021 mmol; 26 μ L of a solution in THF at 0.8 M) and the solvent (0.15 mL) were added to the reactor and stirred for 10 min. Then, the pre-mixed monomers (400 equivalents; ϵ -CL: 6.39 mmol, 0.71 mL; HBL: 1.91 mmol, 0.15 mL) were added to the blend under argon atmosphere. The reactors were closed and placed in a bath at the desired temperature. After a given period of time the polymerizations were quenched by addition of 2.2 mL methanol acidified with HCl. The polymers were solubilized in CHCl₃, precipitated in methanol and dried overnight under vacuum. Both monomer conversions were determined from ¹H NMR spectra of the crude products. The ϵ -CL conversion was calculated using the integration of the polymer signals N, J' and the CH₂ signal of the unreacted monomer. The HBL conversion, composition and copolymer composition were determined

according to procedure on the Figure S8. The degree of branching (DB) was calculated in the case of copolymerization of AB₂ with AB monomers according to the formula [58]:

$$DB = \frac{2D}{2D + LAB_2 + LAB}$$

With D the branched HBL, L_{AB₂} the linear HBL and L_{AB} the opened caprolactone (Procedure Figure S9).

Polymerization kinetic studies

The kinetic was performed in a flame-dried Schlenk and inside an argon-filled glovebox. A first batch was prepared by mixing the catalyst, initiator and solvent. After 10 min of stirring, the pre-mixed monomers were added to the mixture and the first batch was separated into different Schlenk tubes. The reactors were taken out of the glovebox and placed in a pre-heated bath at 80°C. After a chosen period of time the Schlenk tubes were quenched, and an aliquot was taken for NMR and SEC analyses.

Characterization

For conversion calculations, the samples were analyzed by liquid-state ¹H NMR recorded at 298 K on a Bruker Advance 400 spectrometer operating at 400 MHz in CDCl₃. For the identification of the structure, liquid-state ¹H NMR, ¹H-¹³C HSQC NMR, ¹H-¹H COSY NMR, ¹H-¹H TOCSY NMR and DOSY NMR spectra were recorded at 298 K on a Bruker Prodigy spectrometer operating at 400 MHz in CDCl₃.

Size exclusion chromatography (SEC) has been used for the determination of the polymer number-average molar masses (\overline{Mn}) and dispersities ($D = \overline{Mw}/\overline{Mn}$). Measurements were performed using tetrahydrofuran (THF) as the eluent and on an Ultimate 3000 system from ThermoScientific equipped with diode array detector DAD. The system also includes a multi-angles light scattering detector MALS and differential refractive index detector dRI from Wyatt technology. Polymers were separated on three G2000, G3000 and G4000 TOSOH HXL gel columns (300 x 7.8 mm) (exclusion

limits from 1000 Da to 400 000 g/mol) at a flowrate of 1 mL/min. Columns temperature was held at 40°C. Polystyrene was used as the standard.

Differential scanning calorimetry (DSC) measurements of copolyesters samples (≈ 5 mg) were performed using a DSC Q100 RCS apparatus from TA Instruments. First, the samples were heated from -80°C to 100°C at 10°C/min and equilibrated at this temperature for 2 min in order to remove the residual solvent. The samples were then cooled to -80°C at 5°C/min and held for 2 min, and finally reheated to 100°C at 10°C/min. The thermograms were obtained from third cycle.

Results and discussion

Based on γ -BL thermodynamics, the homopolymerization of HBL was first investigated at low temperature (-40°C) and also at 80°C in the presence of a very small amount of THF, keeping a Monomer/Catalyst/Initiator (M/C/I) ratio of 100/1/1 and a monomer concentration of 8 M. In both cases, no polymer was formed in line with thermodynamic issues. Therefore, HBL copolymerization with ϵ -CL, a commonly used lactone for copolymerizations, was studied.

As a starting investigation, a 1/0.3 eq (77/23 %) ϵ -CL/HBL ratio was chosen to check a possible incorporation of HBL into the PCL. the influence of the temperature in the range 0-100°C was first studied keeping all the reaction parameters constant (Table 1). At 0°C, low conversions of both monomers were obtained: 12 % for ϵ -CL and 5 % for HBL with mainly the formation of dimers or trimers. Increasing the temperature to 25°C raises the HBL conversion to 52 %. A slight raise of the molar mass follows this conversion increase but remains limited. Indeed, as the initial feed ratio is only composed of 23 % of HBL, its conversion increase is not sufficient to reach high molar masses. At higher temperatures (70°C and 80°C), the HBL conversion reaches 90 % whereas the one of ϵ -CL levels off to 56 % and 70 %, respectively. SEC analyses reveal a mix of oligomers and polymer chains with average molar masses around 700 g/mol and 950 g/mol and dispersity of 3.4 and 4.9, respectively. At 100°C, the ϵ -CL conversion continues to grow reaching 81 % and a slight decrease

of HBL one. This temperature appeared to be unfavourable for the HBL ring-opening. The molar mass and dispersity of this sample remain in the same range. From 25°C to 80 °C, the HBL incorporation remains high between 59 % and 28 %, higher than the HBL feed, as its conversion is higher as compared to the ϵ -CL one. At 100°C the conversion gap between the two monomers reduces and the HBL incorporation decreases to 22%.

These preliminary experiments confirm the importance of the temperature parameter. The copolymerization at room temperature for a longer polymerization time was also tested (Table S1). After 7 days of reaction, the monomer conversions reached 49 % for ϵ -CL and 91 % for HBL. The so-formed copolymer contains 36 % of HBL monomer units and exhibits a molar mass of 1 300 g/mol with a dispersity of 3.1. The copolymerization at room temperature was possible but with a very slow kinetic profile. Therefore, the progress of the copolymerization indicates that active species are not dead but react much slower in this case.

For the rest of the study, the temperature was set at 80°C as it was considered as the best compromise between high monomer conversions, higher molar masses and reasonable polymerization times.

Table 1: ϵ -CL/HBL copolymerization with $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ at different temperatures. Ratio M/C/I = 400/1/1; $[\text{M1}+\text{M2}] = 8\text{M}$; THF; ϵ -CL/HBL ratio = 77/23; time = 3h

Run	Temperature (°C)	Conversion ^a		HBL incorporation (mol.%) ^a	\overline{M}_n SEC (g/mol) ^b	\mathcal{D}^b
		ϵ -CL (mol.%)	HBL (mol.%)			
1	0	12	5	11	170	1.3
2	25	11	52	59	230	1.6
3	70	56	90	32	700	3.4
4	80	70	90	28	950	4.9
5	100	81	78	22	1 090	4.1

^aCalculated from ¹H NMR of the crude product. ^bObtained from SEC analysis in THF with polystyrene standards.

The percentages indicated in the article are in mol.%.

In order to have a better insight of the copolymerization mechanism, NMR analyses were performed on the prepared copolymers (Figure 1 and Figures S1-S4). The structural analysis showed the presence of monomer units from both monomers: in green the ϵ -CL units and in blue the HBL units which include different structural patterns.

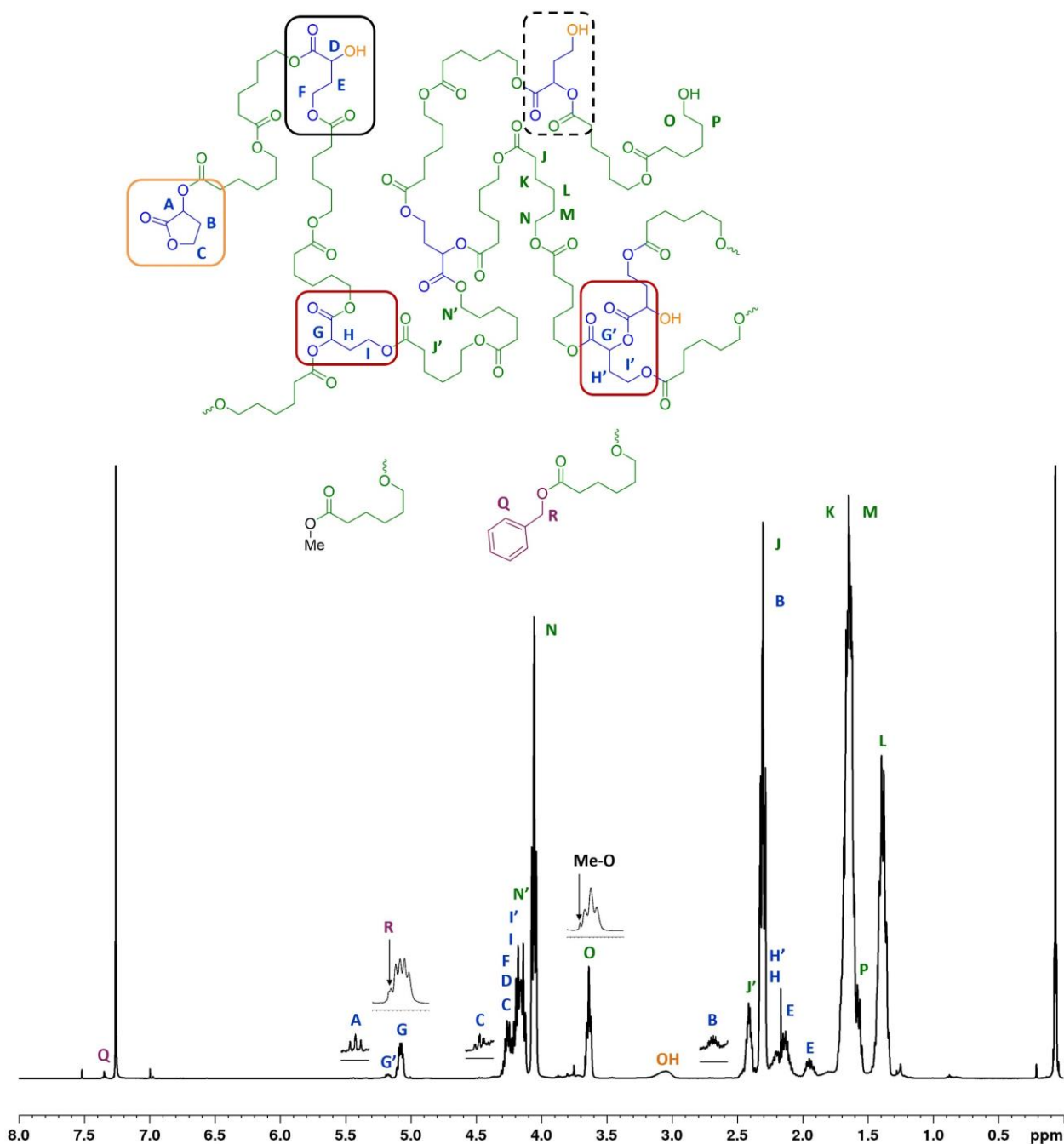


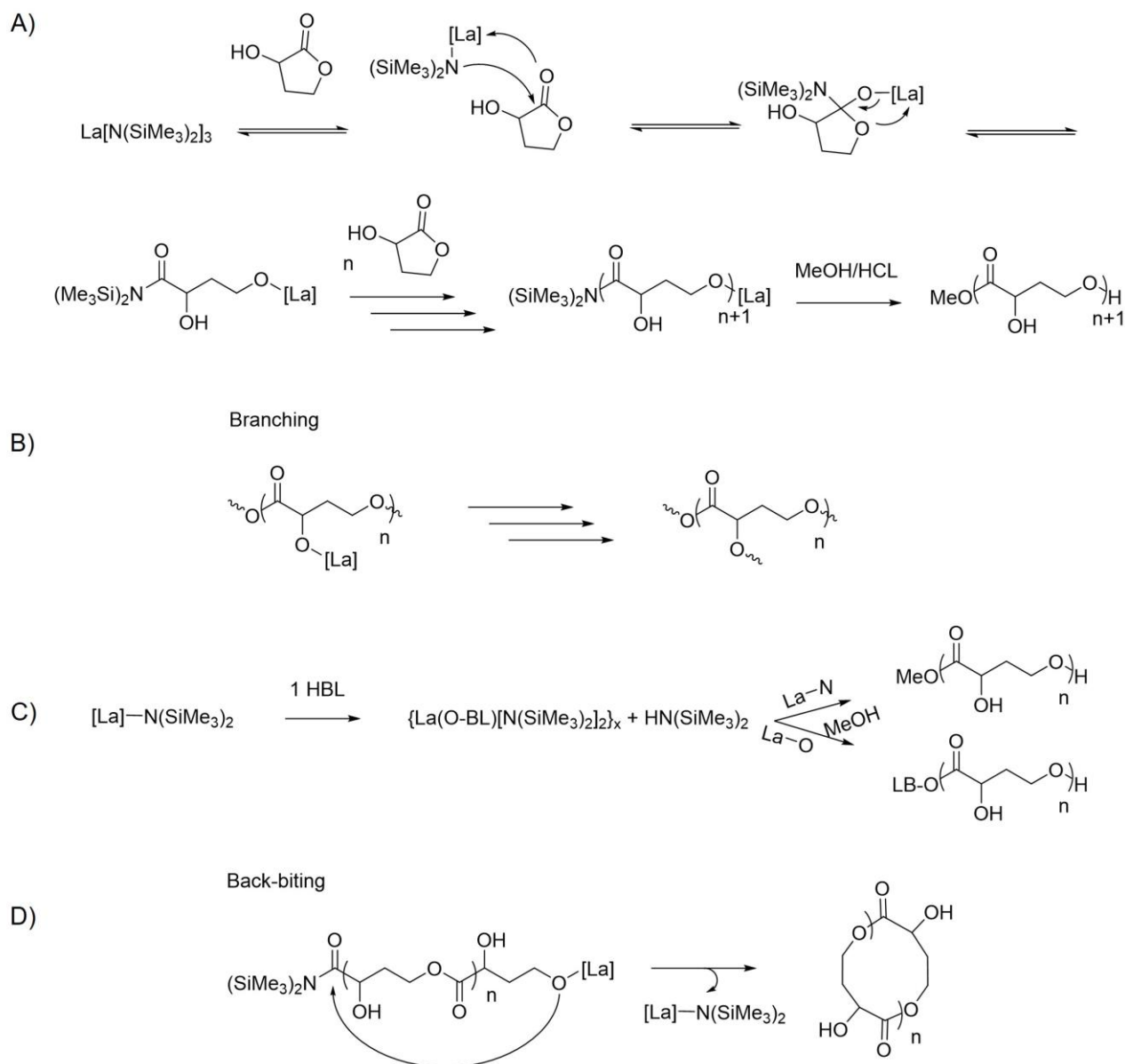
Figure 1: ^1H NMR spectrum and proposed structure of HBL/ ϵ -CL copolymers (Table 1, run 4).

The ^1H NMR spectrum shows the opened forms of HBL, which have been referred as “linear HBL” on the structure (black rectangle, Figure 1). During the polymerization process, a secondary hydroxyl function is formed by the ring-opening of HBL. The switch of the La catalyst from the primary alcohol to the secondary one generating a primary alcohol can be considered. Such motive (black rectangle in dash dots, Figure 1) was not identified by NMR but cannot be excluded.

In addition, the presence of branching points in the structure (red rectangle, Figure 1) as reported before [57], was also confirmed and referred as “branched HBL”. Indeed, according to the mechanism (Scheme 1A), the ring-opening of HBL leads to the formation of pendant free hydroxyl functions which can react further with the catalyst (Scheme 1B) to generate branches.

As also evidenced by NMR analysis, several chain ends are produced during the copolymerization process. One can note the formation of MeO- chain-end which has already been observed [28] with the $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ and $\gamma\text{-BL}$. As an example, when no alcohol is used as an initiator, the chain-ends are: $-\text{N}(\text{SiMe}_3)_2$ and $[\text{La}]^-$. The quenching step with acidified MeOH leads to the production of MeO-termini (Scheme 1A). However, when benzyl alcohol is used as an initiator, a metal alkoxide species is formed which produces BnO- chain-ends, as observed on the NMR spectra. It was reported [28] that, depending on the La/BnOH ratio, both MeO- and BnO- chain ends can be formed. Finally, the formation of cyclic HBL terminated chains (-OBL) was reported [57] and was also evidenced here and referred as “cyclic HBL” (orange rectangle, Figure 1). The presence of -OBL units as chain ends means that the monomer acts also as an initiator (inimer) thanks to its secondary hydroxyl group. In comparison to the reaction between $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ and benzyl alcohol, the presence of -OBL chain ends testifies the occurrence of a similar reaction between the catalyst and HBL according to the proposed mechanism (Scheme 1C). Furthermore, it was also observed (Figure S4) the duplication of the cyclic HBL proton (in α position of the carbonyl) when the initial $\epsilon\text{-CL}/\text{HBL}$ ratio is decreased. It is speculated that at high $\epsilon\text{-CL}$ amount, there is only initiation of $\epsilon\text{-CL}$ by HBL. However, the self-initiation of HBL can be observed with higher amount of HBL in the feed.

Finally, the formation of macrocycles caused by back-biting reactions known in the γ -lactones polymerization [28], could not be demonstrated in this study but cannot be excluded (Scheme 1D).



Scheme 1: proposed mechanism of the different polymerization steps of HBL with $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$. A) Usual expected mechanism of HBL ROP without initiator. B) Formation of branched HBL. C) Formation of cyclic HBL. D) Back-biting reaction.

In order to simplify the mechanism, the ϵ -CL incorporation is not represented in this scheme.

The successful incorporation of HBL units into the copolymers was also confirmed by DOSY analysis (Figure S5). As can be seen, a single diffusion coefficient is observed for the signals of the ϵ -CL and HBL units confirming the formation of only true copolyesters.

To have a better insight on the copolymerization mechanism, a kinetic study was performed at the following conditions: ratio M/C/I = 400/1/1; $[M1+M2] = 8M$; THF; ϵ -CL/HBL ratio = 77/23; $T=80^{\circ}C$ (Figure 2). The variation of the monomer conversion and the types of HBL monomer units (cyclic, linear and branched) were determined. As several HBL motives have been identified, only the linear and branched units were considered for the calculation of HBL conversion as the conversion refers to the monomer ring-opening.

The results show that HBL was converted faster than ϵ -CL. Indeed, after 1h reaction, the HBL conversion reached its maximum, 90 %, while ϵ -CL converted slower, *i.e.* conversion of 77 % after 3 h reaction (Figure 2A). The molar masses also increased from 230 g/mol to 1 700 g/mol with the conversion (Figure S6, Table S2), as well as the dispersity from $D=1.7$ to $D=6.6$. The shape of the chromatograms and the dispersity values are in agreement with the occurrence of branching reactions.

The variation with time of HBL motive, *i.e.* cyclic, linear or branched units within the copolymers was also investigated (Figure 2B). At very low reaction time (5 min), the majority of the reacted HBL is under its cyclic form: 17 % against 5 % for the linear and 13 % for the branched forms. This feature shows that most of the HBL first reacts as an initiator through its secondary alcohol function. After 15 min reaction, the linear and branched forms become predominant (30 % and 23 % respectively) showing that HBL is consumed as a monomer. Over time, the chain-end cyclic HBL motives gradually decline from 17 % to 3-5 % due to their ring-opening. In the meantime, the branching points gradually increased during the polymerization to reach more than 50 % while the linear HBL units decreased to about 25 %. Overall, such kinetic investigation shows that the majority of HBL motive is the branched form as the linear and cyclic units can react during the polymerization.

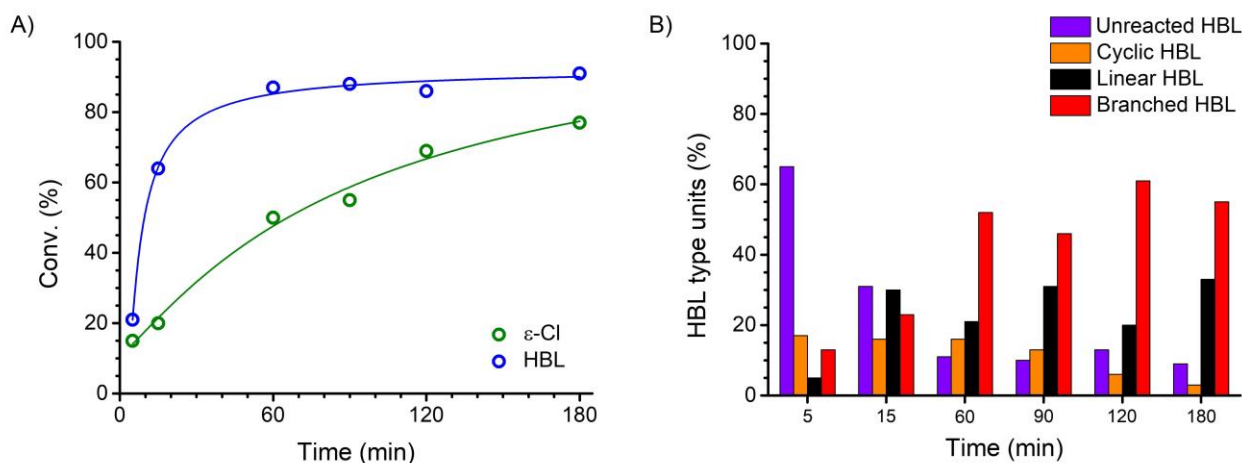


Figure 2: kinetic study A) conversion of ϵ -CL and HBL vs time B) Type of HBL motive vs time.

In a second step, the influence of the monomers feed ratio was studied (Table 2). A wide a range of initial ϵ -CL/HBL ratios from 9 % to 50 % of HBL was investigated which led to the formation of copolyesters with a content of HBL motives ranging from 9 % to 63 %. For all the experiments, the HBL conversion remains high, between 85 % and 90 %. By decreasing the ϵ -CL/HBL ratio, the ϵ -CL conversion decreased from 89 % to 54 %. Indeed, at high HBL content in the feed, a decrease in the polymerization rate is suggested due to the difference in the monomer reactivities. The decrease in the ϵ -CL conversion is accompanied by a decrease of the copolyester molar masses from \overline{Mn} = 3400 g/mol to 850 g/mol. Therefore, such copolyesters exhibit high HBL incorporation ratio and low molar masses. The variation in the type of incorporated HBL motive (linear, branched, cyclic) was also evaluated as a function of the initial monomer concentration. By varying the HBL concentration from 9 % to 50 %, the HBL-linear units in the polymer chains raise from 23 % to 67 % and reversibly, the HBL-branched units diminish from 73 % to 26 %. Indeed, by keeping the same reaction time, the higher the HBL concentration, the higher the HBL linear forms and the lower the branching points. The reduction of branching points is also reflected by the dispersity value which also declines from 7.8 to 3.4.

The degree of branching (DB) was also calculated to evidence the evolution of the amount of branching points with the HBL incorporation. For highly branched polymers, the DB tends towards DB=1, while the DB is closer to 0 for polymers with low amount of branching. The DB was calculated according to the formula [58] applied to the copolymerization case between AB₂ and AB monomers with the HBL (linear and branched) and ε-CL (linear) units. The increase in the HBL incorporation in the copolymers from 9 % to 43 % was followed by a gradual raise in DB from 0.12 to 0.31. Although the branched HBL decreased (from 73 % to 42 %), the increase in HBL incorporation is so high that the amount of branched units incorporated increases the DB. In contrast, the DB is decreased to 0.24 with the highest HBL incorporation, 63 %. In this case, even though the HBL incorporation is high, the amount of branched units incorporated (26 %) is not enough to overcome the high amount of linear HBL (67 %), which decreases the DB.

The thermal properties of the copolyesters were investigated by performing DSC analyses on different samples: the PCL used as a reference and several copolymers with various HBL incorporation ratios (Figure S7). A decrease of the melting temperature and crystallinity ratio of the copolymers was observed with an increase of the HBL content. The copolymer with 9% of HBL showed a broad and split melting peak with a shift toward lower temperature values, 30°C and 38°C. As reported [57], the HBL incorporation in the copolymer breaks the order of crystalline domains of poly(ε-caprolactone). Indeed, the split peak is related to the formation of different kind of domains. This phenomenon is accentuated with the increase in HBL incorporation to 18 % which leads to a broadening of the crystallisation peak and a decrease of its melting temperature, 16°C. Finally, above 28 % of incorporated HBL in the copolymers, the crystallization was no longer observed, proof of the random structure of these copolyesters.

Table 2: ϵ -CL/HBL copolymerization with $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ and various monomers feed ratios. Ratio M/C/I = 400/1/1; $[\text{M1}+\text{M2}] = 8\text{M}$; THF; time = 3h; $T=80^\circ\text{C}$.

Run	ϵ -CL/HBL ratio	Conv. ϵ -CL (mol.%) ^a	Conv. HBL (mol.%) ^a	HBL incorporation (mol.%) ^a	HBL type units ^a			$\overline{\text{Mn}}_{\text{SEC}}$ (g/mol) ^b	\overline{D}^b	DB ^a
					Cyclic HBL (mol.%)	Linear HBL (mol.%)	Branched HBL (mol.%)			
6	91/9	89	87	9	4	23	73	3 400	7.8	0.12
7	83/17	80	87	18	4	24	72	1 700	6.1	0.20
8	71/29	53	86	40	14	42	44	740	4.0	0.28
9	67/33	55	85	43	12	47	42	800	3.3	0.31
10	50/50	54	90	63	7	67	26	850	3.4	0.24

^aCalculated from ^1H NMR of the crude product. ^bObtained from SEC analysis in THF with polystyrene standards.

In addition, other experimental parameters such as the reaction time, M/C/I ratio, solvent and monomer concentration were also studied (Table 3). Increasing polymerisation time to 48h slightly increased the molar masses (Table 3, run 12) but is not really significant. In the ROP of γ -lactones, it has been shown that the presence of primary alcohol together with $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ enhanced considerably the catalytic activity due to the formation of metal alkoxide species. As HBL behaves as an inimer, we performed the copolymerization without using BnOH (Table 3, run 13) as an initiator. It was observed that ϵ -CL conversion remained unchanged around 70 %. The conversion of HBL decreased to 84 % as a fraction of HBL served as initiator. This is confirmed by the copolyester analysis which indicates a content of the cyclic HBL motive of 9 %. A higher amount of branched HBL was also noticed (70 %) in opposition to linear HBL motives (21 %). Therefore, no significant effect with the use or not of benzyl alcohol was observed on the catalytic activity, as its amount in the M/C/I ratio is low in regard to the HBL amount.

Finally, the nature of the solvent to perform polymerizations is also an important factor such as the polarity which may affect the reaction rate. As an example, in the case of γ -butyrolactone polymerization with $\text{La}[\text{N}(\text{SiMe}_3)_2]_3$ as catalyst, the highest yield was obtained in THF. Achieving the reaction in a non-polar solvent, e.g. toluene, (Table 3, run 14), resulted in similar monomer

conversion and HBL incorporation ratios. The reaction was also performed in bulk ($[M1+M2] = 9.68$ M) and similar results were obtained (Table 3, run 15) showing the possibility to perform a solvent-free reaction. The low influence of the solvent may be explained by its low amount.

DB calculations were also carried out for the different synthesized copolyesters. For runs 11 and 13 to 15, the DB values are almost identical, around 0.26, as the monomer conversion and HBL incorporation ratios and compositions (linear and branched) are in the same range.

Table 3: ϵ -CL/HBL copolymerization with $La[N(SiMe_3)_2]_3$ and various reaction conditions (Reaction time, M/C/I ratio, solvent, monomer concentration). Ratio M/C/I = 400/1/1; $[M1+M2] = 8M$; THF; ϵ -CL/HBL ratio = 77/23; time = 3h; $T=80^\circ C$

Run	Solvent	Time (h)	Conv. ϵ -CL (mol.%) ^c	Conv. HBL (mol.%) ^c	HBL incorporation (mol.%) ^c	HBL type units ^c			\overline{Mn}_{SEC} (g/mol) ^d	\overline{D} ^d	DB ^c
						Cyclic HBL (mol.%)	Linear HBL (mol.%)	Branched HBL (mol.%)			
11	THF	3	70	90	28	5	32	63	950	4.9	0.27
12	THF	48	80	79	23	3	43	54	2 000	6.9	0.18
13 ^a	THF	3	70	84	26	9	21	70	1 100	3.9	0.27
14	Toluene	3	69	89	28	10	25	65	1 500	5.7	0.26
15 ^b	-	3	67	89	28	4	39	57	990	4.0	0.25

^aRatio M/C/I = 400/1/0. ^bBulk, $[M1+M2]=9.68M$. ^cCalculated from ¹H NMR of the crude product. ^dObtained from SEC analysis in THF with polystyrene standards.

Conclusion

Copolyesters based on ϵ -CL and HBL monomers were synthesized in the presence of $La[N(SiMe_3)_2]_3$. The temperature was the key parameter to get high monomer conversions and molar masses. At $80^\circ C$ in THF and after 3h of reaction, the monomer conversions reached 70 % for ϵ -CL and 90 % for HBL, generating copolyesters with \overline{Mn} values of 950 g/mol and $\overline{D}=4.9$. The kinetic of the polymerization under these conditions revealed a faster conversion of HBL in comparison to ϵ -CL. Analysis of the copolyester microstructure and monitoring of the HBL conversion allowed us to

have a better insight with respect to the polymerization mechanism. Indeed, HBL first behaves as an initiator and then as a monomer leading to the formation of linear units with pendant free hydroxyl groups together with branched units. Finally, by tuning the initial monomer ratios, copolyesters with incorporated HBL units from 9 % to 63 % could be obtained. As a general trend, low molar masses were obtained due to the low conversion of ϵ -CL. The high insertion of HBL units in the copolymers and the presence of free hydroxyl pendant groups on the polymer backbone opens the way for post-modification reactions in order to design original polymeric materials and target various applications.

Supporting Information

The supplementary information is available online at:

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Declaration of competing interest

There are no conflicts of interest.

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Data availability

Some raw/processed data required to reproduce these findings cannot be shared at this time as the data also forms part of an ongoing study, but others are present in the Supplementary Information file linked to this manuscript.

References

- [1] M.A. Hillmyer, W.B. Tolman, Aliphatic polyester block polymers: Renewable, degradable, and sustainable, *Acc Chem Res.* 47 (2014) 2390–2396. <https://doi.org/10.1021/ar500121d>.
- [2] D.K. Schneiderman, M.A. Hillmyer, Aliphatic Polyester Block Polymer Design, *Macromolecules.* 49 (2016) 2419–2428. <https://doi.org/10.1021/acs.macromol.6b00211>.

- [3] A. Larrañaga, E. Lizundia, A review on the thermomechanical properties and biodegradation behaviour of polyesters, *Eur Polym J.* 121 (2019). <https://doi.org/10.1016/j.eurpolymj.2019.109296>.
- [4] R.P. Brannigan, A.P. Dove, Synthesis, properties and biomedical applications of hydrolytically degradable materials based on aliphatic polyesters and polycarbonates, *Biomater Sci.* 5 (2017) 9–21. <https://doi.org/10.1039/c6bm00584e>.
- [5] K.E. Washington, R.N. Kularatne, V. Karmegam, M.C. Biewer, M.C. Stefan, Recent advances in aliphatic polyesters for drug delivery applications, *Wiley Interdiscip Rev Nanomed Nanobiotechnol.* 9 (2017). <https://doi.org/10.1002/wnan.1446>.
- [6] F. Asghari, M. Samiei, K. Adibkia, A. Akbarzadeh, S. Davaran, Biodegradable and biocompatible polymers for tissue engineering application: a review, *Artif Cells Nanomed Biotechnol.* 45 (2017) 185–192. <https://doi.org/10.3109/21691401.2016.1146731>.
- [7] X. Zhang, B.H. Tan, Z. Li, Biodegradable polyester shape memory polymers: Recent advances in design, material properties and applications, *Materials Science and Engineering C.* 92 (2018) 1061–1074. <https://doi.org/10.1016/j.msec.2017.11.008>.
- [8] I. Chiulan, A.N. Frone, C. Brandabur, D.M. Panaitescu, Recent advances in 3D printing of aliphatic polyesters, *Bioengineering.* 5 (2018). <https://doi.org/10.3390/bioengineering5010002>.
- [9] M.P. Arrieta, M.D. Samper, M. Aldas, J. López, On the use of PLA-PHB blends for sustainable food packaging applications, *Materials.* 10 (2017). <https://doi.org/10.3390/ma10091008>.
- [10] I. Taniguchi, W.A. Kuhlman, A.M. Mayes, L.G. Griffith, Functional modification of biodegradable polyesters through a chemoselective approach: Application to biomaterial surfaces, *Polym Int.* 55 (2006) 1385–1397. <https://doi.org/10.1002/pi.2139>.
- [11] G. Becker, F.R. Wurm, Functional biodegradable polymers: Via ring-opening polymerization of monomers without protective groups, *Chem Soc Rev.* 47 (2018) 7739–7782. <https://doi.org/10.1039/c8cs00531a>.
- [12] T.J. Farmer, J.W. Comerford, A. Pellis, T. Robert, Post-polymerization modification of bio-based polymers: maximizing the high functionality of polymers derived from biomass, *Polym Int.* 67 (2018) 775–789. <https://doi.org/10.1002/pi.5573>.
- [13] S. Penczek, M. Cypryk, A. Duda, P. Kubisa, S. Słomkowski, Living ring-opening polymerizations of heterocyclic monomers, *Progress in Polymer Science (Oxford).* 32 (2007) 247–282. <https://doi.org/10.1016/j.progpolymsci.2007.01.002>.
- [14] C. Jérôme, P. Lecomte, Recent advances in the synthesis of aliphatic polyesters by ring-opening polymerization, *Adv Drug Deliv Rev.* 60 (2008) 1056–1076. <https://doi.org/10.1016/j.addr.2008.02.008>.
- [15] K.M. Zia, A. Noreen, M. Zuber, S. Tabasum, M. Mujahid, Recent developments and future prospects on bio-based polyesters derived from renewable resources: A review, *Int J Biol Macromol.* 82 (2016) 1028–1040. <https://doi.org/10.1016/j.ijbiomac.2015.10.040>.
- [16] Z. Wang, M.S. Ganewatta, C. Tang, Sustainable polymers from biomass: Bridging chemistry with materials and processing, *Prog Polym Sci.* 101 (2020). <https://doi.org/10.1016/j.progpolymsci.2019.101197>.

- [17] K. Nomura, N.W. Binti Awang, Synthesis of Bio-Based Aliphatic Polyesters from Plant Oils by Efficient Molecular Catalysis: A Selected Survey from Recent Reports, *ACS Sustain Chem Eng.* 9 (2021) 5486–5505. <https://doi.org/10.1021/acssuschemeng.1c00493>.
- [18] Q. Zhang, M. Song, Y. Xu, W. Wang, Z. Wang, L. Zhang, Bio-based polyesters: Recent progress and future prospects, *Prog Polym Sci.* 120 (2021). <https://doi.org/10.1016/j.progpolymsci.2021.101430>.
- [19] M. Danko, J. Mosnázek, Ring-opening polymerization of γ -butyrolactone and its derivatives: A review, *Polimery/Polymers.* 62 (2017) 272–282. <https://doi.org/10.14314/polimery.2017.272>.
- [20] Q. Song, J. Zhao, G. Zhang, F. Peruch, S. Carlotti, Ring-opening (co)polymerization of γ -butyrolactone: a review, *Polym J.* 52 (2020) 3–11. <https://doi.org/10.1038/s41428-019-0265-5>.
- [21] Q. Song, C. Pascouau, J. Zhao, G. Zhang, F. Peruch, S. Carlotti, Ring-opening polymerization of γ -lactones and copolymerization with other cyclic monomers, *Prog Polym Sci.* 110 (2020) 101309. <https://doi.org/10.1016/j.progpolymsci.2020.101309>.
- [22] Y. Liu, J. Wu, X. Hu, N. Zhu, K. Guo, Advances, Challenges, and Opportunities of Poly(γ -butyrolactone)-Based Recyclable Polymers, *ACS Macro Lett.* 10 (2021) 284–296. <https://doi.org/10.1021/acsmacrolett.0c00813>.
- [23] W. Saiyasombat, R. Molloy, T.M. Nicholson, A.F. Johnson, I.M. Ward, S. Poshyachinda, Ring strain and polymerizability of cyclic esters, *Polymer (Guildf).* 39 (1998) 5581–5585. [https://doi.org/10.1016/S0032-3861\(97\)10370-6](https://doi.org/10.1016/S0032-3861(97)10370-6).
- [24] K.N. Houk, A. Jabbari, H.K. Hall, C. Alemán, Why δ -valerolactone polymerizes and γ -butyrolactone does not, *Journal of Organic Chemistry.* 73 (2008) 2674–2678. <https://doi.org/10.1021/jo702567v>.
- [25] C. Alemán, O. Betran, J. Casanovas, K.N. Houk, H.K. Hall, Thermodynamic control of the polymerizability of five-, six-, and seven-membered lactones, *Journal of Organic Chemistry.* 74 (2009) 6237–6244. <https://doi.org/10.1021/jo9010969>.
- [26] P. Dubois, O. Coulembier, J.M. Raques, *Handbook of Ring-Opening Polymerization*, Wiley, 2009. <https://doi.org/10.1002/9783527628407>.
- [27] P. Olsén, K. Odelius, A.C. Albertsson, Thermodynamic Presynthetic Considerations for Ring-Opening Polymerization, *Biomacromolecules.* 17 (2016) 699–709. <https://doi.org/10.1021/acs.biomac.5b01698>.
- [28] M. Hong, E.Y.X. Chen, Completely recyclable biopolymers with linear and cyclic topologies via ring-opening polymerization of γ -butyrolactone, *Nat Chem.* 8 (2016) 42–49. <https://doi.org/10.1038/nchem.2391>.
- [29] M. Hong, X. Tang, B.S. Newell, E.Y.X. Chen, “nonstrained” γ -Butyrolactone-Based Copolyesters: Copolymerization Characteristics and Composition-Dependent (Thermal, Eutectic, Cocrystallization, and Degradation) Properties, *Macromolecules.* 50 (2017) 8469–8479. <https://doi.org/10.1021/acs.macromol.7b02174>.
- [30] W. Kuran, Coordination polymerization of heterocyclic and heterounsaturated monomers, *Prog Polym Sci.* 23 (1998) 919–992. [https://doi.org/10.1016/S0079-6700\(97\)00031-2](https://doi.org/10.1016/S0079-6700(97)00031-2).

- [31] E. Stirling, Y. Champouret, M. Visseaux, Catalytic metal-based systems for controlled statistical copolymerisation of lactide with a lactone, *Polym Chem.* 9 (2018) 2517–2531. <https://doi.org/10.1039/c8py00310f>.
- [32] H. Li, R.M. Shakaroun, S.M. Guillaume, J.F. Carpentier, Recent Advances in Metal-Mediated Stereoselective Ring-Opening Polymerization of Functional Cyclic Esters towards Well-Defined Poly(hydroxy acid)s: From Stereoselectivity to Sequence-Control, *Chemistry - A European Journal.* 26 (2020) 128–138. <https://doi.org/10.1002/chem.201904108>.
- [33] R. Hatamvand, A. Shams, E. Mohammadifar, A. Yari, M. Adeli, Synthesis of boronic acid-functionalized poly(glycerol-oligo γ -butyrolactone): Nano-networks for efficient electrochemical sensing of biosystems, *J Polym Sci A Polym Chem.* 57 (2019) 1430–1439. <https://doi.org/10.1002/pola.29406>.
- [34] J. Zhou, A.M. Schmidt, H. Ritter, Bicomponent transparent polyester networks with shape memory effect, *Macromolecules.* 43 (2010) 939–942. <https://doi.org/10.1021/ma901402a>.
- [35] M. Gagliardi, F. di Michele, B. Mazzolai, A. Bifone, Chemical synthesis of a biodegradable PEGylated copolymer from ϵ -caprolactone and γ -valerolactone: evaluation of reaction and functional properties, *Journal of Polymer Research.* 22 (2015). <https://doi.org/10.1007/s10965-015-0661-2>.
- [36] M. Gagliardi, A. Bifone, Ring-opening copolymerization thermodynamics and kinetics of γ -valerolactone/ ϵ -caprolactone, *PLoS One.* 13 (2018) 1–15. <https://doi.org/10.1371/journal.pone.0199231>.
- [37] A. Bhaw-Luximon, D. Jhurry, S. Motala-Timol, Y. Lochee, Polymerization of ϵ -caprolactone and its copolymerization with γ -butyrolactone using metal complexes, *Macromol Symp.* 231 (2005) 60–68. <https://doi.org/10.1002/masy.200590025>.
- [38] Y. Hori, A. Yamaguchi, T. Hagiwara, Chemical synthesis of high molecular weight poly(3-hydroxybutyrate-co-4-hydroxybutyrate), *Polymer (Guildf).* 36 (1995) 4703–4705. [https://doi.org/10.1016/0032-3861\(95\)96838-Y](https://doi.org/10.1016/0032-3861(95)96838-Y).
- [39] M. Danko, M. Basko, S. Ďurkáčová, A. Duda, J. Mosnáček, Functional Polyesters with Pendant Double Bonds Prepared by Coordination-Insertion and Cationic Ring-Opening Copolymerizations of ϵ -Caprolactone with Renewable Tulipalin A, *Macromolecules.* 51 (2018) 3582–3596. <https://doi.org/10.1021/acs.macromol.8b00456>.
- [40] J. Zhu, E.Y. -X. Chen, Catalyst-Sidearm-Induced Stereoselectivity Switching in Polymerization of a Racemic Lactone for Stereocomplexed Crystalline Polymer with a Circular Life Cycle, *Angewandte Chemie.* 131 (2019) 1190–1194. <https://doi.org/10.1002/ange.201813006>.
- [41] Y. Liu, J. Wu, H. Liang, Z. Jin, L. Sheng, X. Hu, N. Zhu, K. Guo, Organomagnesium towards efficient synthesis of recyclable polymers, *Eur Polym J.* 130 (2020) 109659. <https://doi.org/10.1016/j.eurpolymj.2020.109659>.
- [42] P. Olsén, J. Undin, K. Odelius, A.C. Albertsson, Establishing α -bromo- γ -butyrolactone as a platform for synthesis of functional aliphatic polyesters-bridging the gap between ROP and SET-LRP, *Polym Chem.* 5 (2014) 3847–3854. <https://doi.org/10.1039/c4py00148f>.
- [43] X. Xi, G. Jiang, X. Wang, R. Hu, R. Wang, Synthesis, characterization and degradation properties of poly(α -angelica lactone-co- ϵ -caprolactone) copolymers, *Polymers from Renewable Resources.* 4 (2013) 49–60. <https://doi.org/10.1177/204124791300400201>.

- [44] T. Chen, Z. Qin, Y. Qi, T. Deng, X. Ge, J. Wang, X. Hou, Degradable polymers from ring-opening polymerization of α -angelica lactone, a five-membered unsaturated lactone, *Polym Chem.* 2 (2011) 1190–1194. <https://doi.org/10.1039/c1py00067e>.
- [45] P. Catchpole, R.H. Platel, Copolymerisation of β -butyrolactone and γ -butyrolactone using yttrium amine bis(phenolate) Catalysts, *Polym Int.* (2022). <https://doi.org/10.1002/pi.6429>.
- [46] Y. Liu, X. Yuan, J. Wu, X. Hu, N. Zhu, K. Guo, Access to high-molecular-weight poly(γ -butyrolactone) by using simple commercial catalysts, *Polym Chem.* 13 (2022) 439–445. <https://doi.org/10.1039/d1py01340h>.
- [47] M. Hong, E.Y.X. Chen, Coordination ring-opening copolymerization of naturally renewable α -methylene- γ -butyrolactone into unsaturated polyesters, *Macromolecules.* 47 (2014) 3614–3624. <https://doi.org/10.1021/ma5007717>.
- [48] J.B. Zhu, E.Y.X. Chen, Living Coordination Polymerization of a Six-Five Bicyclic Lactone to Produce Completely Recyclable Polyester, *Angewandte Chemie - International Edition.* 57 (2018) 12558–12562. <https://doi.org/10.1002/anie.201808003>.
- [49] J.B. Zhu, E.M. Watson, J. Tang, E.Y.X. Chen, A synthetic polymer system with repeatable chemical recyclability, *Science* (1979). 360 (2018) 398–403. <https://doi.org/10.1126/science.aar5498>.
- [50] A. Sangroniz, J.B. Zhu, X. Tang, A. Etxeberria, E.Y.X. Chen, H. Sardon, Packaging materials with desired mechanical and barrier properties and full chemical recyclability, *Nat Commun.* 10 (2019) 1–7. <https://doi.org/10.1038/s41467-019-11525-x>.
- [51] X. Tang, M. Hong, L. Falivene, L. Caporaso, L. Cavallo, E.Y.X. Chen, The Quest for Converting Biorenewable Bifunctional α -Methylene- γ -butyrolactone into Degradable and Recyclable Polyester: Controlling Vinyl-Addition/Ring-Opening/Cross-Linking Pathways, *J Am Chem Soc.* 138 (2016) 14326–14337. <https://doi.org/10.1021/jacs.6b07974>.
- [52] C. Shi, Z.C. Li, L. Caporaso, L. Cavallo, L. Falivene, E.Y.X. Chen, Hybrid monomer design for unifying conflicting polymerizability, recyclability, and performance properties, *Chem.* 7 (2021) 670–685. <https://doi.org/10.1016/j.chempr.2021.02.003>.
- [53] Y. Chen, Y.J. Chen, Y. Qi, H.J. Zhu, X. Huang, Y.R. Wang, R.X. Yang, Y.H. Kan, S.L. Li, Y.Q. Lan, Boosting Highly Ordered Porosity in Lanthanum Metal–Organic Frameworks for Ring-Opening Polymerization of γ -Butyrolactone, *Chem.* 7 (2021) 463–479. <https://doi.org/10.1016/j.chempr.2020.11.019>.
- [54] K.K. Hong, J.H. Kim, J.H. Yoon, H.M. Park, S.J. Choi, G.H. Song, J.C. Lee, Y.L. Yang, H.K. Shin, J.N. Kim, K.H. Cho, J.H. Lee, O-Succinyl-L-homoserine-based C4-chemical production: succinic acid, homoserine lactone, γ -butyrolactone, γ -butyrolactone derivatives, and 1,4-butanediol, *J Ind Microbiol Biotechnol.* 41 (2014) 1517–1524. <https://doi.org/10.1007/s10295-014-1499-z>.
- [55] T. Walther, C.M. Topham, R. Irague, C. Auriol, A. Baylac, H. Cordier, C. Dressaire, L. Lozano-Huguet, N. Tarrat, N. Martineau, M. Stodel, Y. Malbert, M. Maestracci, R. Huet, I. André, M. Remaud-Siméon, J.M. François, Construction of a synthetic metabolic pathway for biosynthesis of the non-natural methionine precursor 2,4-dihydroxybutyric acid, *Nat Commun.* 8 (2017). <https://doi.org/10.1038/ncomms15828>.
- [56] M. Bednarek, Cationic oligomerization of α -hydroxy- γ -butyrolactone, *Polimery/Polymers.* 53 (2008) 377–383. <https://doi.org/10.14314/polimery.2008.377>.

- [57] G. Hua, J. Franzén, K. Odelius, One-pot inimer promoted ROCP synthesis of branched copolyesters using α -hydroxy- γ -butyrolactone as the branching reagent, *J Polym Sci A Polym Chem*. 54 (2016) 1908–1918. <https://doi.org/10.1002/pola.28048>.
- [58] M. Bednarek, Branched aliphatic polyesters by ring-opening (co)polymerization, *Prog Polym Sci*. 58 (2016) 27–58. <https://doi.org/10.1016/j.progpolymsci.2016.02.002>.