Ring-opening copolymerization of (*R,S*)- β -butyrolactone and ϵ -caprolactone using sodium hydride as initiator

M. Monsalve¹, J. M. Contreras^{1*}, E. Laredo², F. López-Carrasquero¹

¹Grupo de Polímeros, Departamento de Química, Facultad de Ciencias, Universidad de Los Andes, Mérida, 5101-A, Venezuela

²Grupo FIMAC, Departamento de Física, Universidad Simón Bolívar, Caracas 1080A, Venezuela

Received 3 March 2010; accepted in revised form 7 May 2010

Abstract. Copolymers of racemic β -butyrolactone ((*R,S*)-BL) and ϵ -caprolactone (CL), were synthesized by ring-opening polymerization initiated by sodium hydride (NaH). The initiator exhibited a satisfactory catalytic activity, producing copolymers whose yields are greatly influenced by the feed monomer ratio, CL/BL. All polymers obtained were characterized by nuclear magnetic resonance (NMR), gel permeation chromatography (GPC), thermogravimetric analysis (TGA), differential scanning calorimetry (DSC) and wide angle X-rays scattering, WAXS. The molar composition of copolyesters determined by ¹H-NMR spectra, showed that the incorporation of CL is favoured over the incorporation of (*R,S*)-BL. Gel permeation chromatography and ¹³C-NMR spectra indicated that CL/BL copolymers had block sequence distribution. The TGA analysis of copolymers showed that these copolymers are stable up to temperatures near 200°C, followed by a decomposition process in two steps; the first one is attributed to the (*R,S*)-BL block degradation and the second to the remaining PCL block. The crystallization process of these copolymers was studied by DSC and WAXS showing that the amorphous (*R,S*)-BL segments chains did not affect the crystallinity of the PCL blocks.

Keywords: biodegradable polymers, sodium hydride, ϵ -caprolactone, β -butyrolactone, block copolymers

1. Introduction

Biodegradable polymers have received much attention as materials for medical applications [1–3]. Linear aliphatic polyesters such as poly(glycolide) (PGL), poly(lactide) (PLA), poly(β -butyrolactone) (PBL) and poly(ϵ -caprolactone) (PCL) and their co- and terpolymers are the most popular bioabsorbable polymers. Because of the wide range of applications in biomedicine, it is necessary for the polyesters to present different mechanical and physical properties to adjust the adequate time of their degradation; in this sense copolymerization constitutes an attractive mean for modulating the basic properties of each homopolymer [4–6]. In particular, block copolymerization may offer a broader spectrum of mechanical and degradation

properties in order to meet the demands of a larger number of applications. Blocks with different physical properties, for example, a soft, amorphous segment together with a hard semicrystalline one, can be used to modulate the thermal and mechanical material behaviour [4, 7–9]. The mechanical properties can be controlled by the hard/soft segment ratio [7] and copolymers with various morphologies such as solid, pasty and waxy states, can be obtained according to the monomer composition [6, 10]. The soft phase provides elasticity and the degradation behaviour, whereas the rigid phase gives mechanical strength and also acts as a physical crosslinker [6].

Polymerization of racemic monomer (*R,S*)- β -butyrolactone ((*R,S*)-BL) has given an atactic poly

*Corresponding author, e-mail: jeco@ula.ve

© BME-PT

(*R,S*)-(β -butyrolactone) ((*R,S*)-PBL) with elastomeric properties because of its low crystallinity [7, 11, 12]. However, for its applications as biodegradable elastomer, it is necessary to decrease their creep behaviour. This has been done by the introduction of a biodegradable hard segment, by means of the successive ring-opening polymerization of (*R,S*)-BL and *L*-lactide [7] or ϵ -caprolactone [8, 13]. The resultant block copolymers, consisting of (*R,S*)-PBL as the soft segment and PLLA or PCL as the hard segment, could be the biodegradable thermoplastic elastomer.

On the other hand, the choice of a proper initiator is another important parameter in the synthesis of polyesters. Many effective catalysts based on tin-compounds, have been employed for this purpose [4, 7, 8, 13–21]. However, many are relatively toxic and impossible to remove completely from the synthesized material, this being undesirable for pharmaceutical or biomedical applications [2, 6].

Therefore, several attempts to use a catalyst based on much less toxic metal compounds are being undertaken [2, 6, 11, 22–27]. The anionic polymerization of β -butyrolactone had been widely studied [27–40], and in general polymers with low molecular weight were obtained. Relatively low toxic alkali metal hydrides are among the initiators used for this purpose [27], nevertheless, they have not been used so far for the synthesis of copolymers of (*R,S*)-BL and CL. It is for this reason that the possibility of utilizing sodium hydride as the initiator of the copolymerization of (*R,S*)-BL and CL is undertaken in this work.

2. Experimental

2.1. Materials

ϵ -caprolactone (CL) and racemic β -butyrolactone ((*R,S*)-BL) (from Aldrich) were dried over calcium hydride for 24 h at room temperature and then distilled under reduced pressure in a nitrogen atmosphere prior use. Sodium hydride (from Aldrich) was used as received.

2.2. Polymerization procedure

CL and (*R,S*)-BL were polymerized in bulk using sodium hydride (NaH) as initiator, in a glass reactor equipped with magnetic stirring bar. The reactors

were charged with the previously established amounts of initiator, CL and (*R,S*)-BL under nitrogen atmosphere, in a dry-box. The sealed reaction vessels were placed into an oil bath preheated at 70°C, for the duration requested. The resultant polymeric products were washed by ethylic ether several times in order to separate (*R,S*)-(butyrolactone) oligomers from the copolymer. Finally, the copolymers obtained were dissolved in chloroform, filtered in order to eliminate the traces of remaining initiator and precipitated into an excess amount of methanol. The precipitated products were then separated by filtration and thoroughly dried at 50°C in vacuum.

2.3. Characterization

^1H -NMR and ^{13}C -NMR spectroscopy was carried out with a Bruker AVANCE DRX 400 Spectrometer. CDCl_3 was used as solvent for the NMR measurements. The GPC measurements were carried out with THF as the eluent using a Waters chromatograph, model 150CV, operated at 40°C and equipped with three columns connected in series and packed with Ultrastaygel 10^3 , 10^4 and 10^5 . Calibration was performed with polystyrene standards with a narrow molecular weight distribution.

Thermogravimetric curves were obtained in a Perkin-Elmer TGA 7, from a heating scan of a sample of about 10 mg from 25 to 500°C, at 10°C/min under a nitrogen atmosphere.

Thermal volatilization analysis (TVA) was carried out in a vacuum line heating the samples of about 100 mg from room temperature to 270°C during 30 minutes under a moderate primary vacuum. Volatile fractions were condensed at room temperature and analyzed by IR and ^1H -NMR.

DSC measurements were carried out with a Perkin-Elmer DSC-7, the sample mass was 10–15 mg and the heating rate was 10°C/min.

Wide angle X-ray scattering (WAXS) experiments were performed in an Analytical X'Pert Pro automatic horizontal θ - θ axis diffractometer with an X'celerator detector, using $\text{CuK}\alpha$ -Ni filtered radiation. The excitation voltage was 45 kV and the tube current 40 mA. Spectra were taken at temperatures ranging from 25 to 70°C in an Anton PAAR Variable Temperature Attachment with the scattering angle 2θ varying from 3 to 50°.

3. Results and discussion

3.1. Synthesis of the copolymers

Among the initiators used in anionic polymerization of BL are the alkali metal hydrides, which give rise to polymers with low yield and low molecular weight [27]. However, to the best of our knowledge, there are no literature reports in which these have been used to start the copolymerization of BL and CL. Results of the copolymerization of a mixture of BL and CL using NaH as the initiator are presented here.

All copolymerizations of CL and (*R,S*)-BL were conducted in bulk with sodium hydride (NaH) as initiator. The effect of monomer to initiator (M/I) molar ratio of on the copolymerization was first examined. As may be seen in Table 1, above M/I = 20 (exp. 3 and exp. 4), no polymer formation was observed even after 72 hours. This fact can be attributed to the copolymerization rate which is suppressed due to a small amount of initiator [24, 25]. Also, the results reported in Table 1 show that for M/I = 4 and 20 the conversion of monomers to copolymer decreases with the increase of M/I; CL content in copolyesters is higher than in (*R,S*)-BL. Taking into account that for M/I = 20 (exp. 2) the product was a stiff white solid, while for M/I = 4

(exp. 1) it was a softer solid, it may be suggested that the molecular weight increases with the content of CL in the copolymers, which increases with molar ratio M/I. On the basis of these results, subsequent polymerizations were carried out at M/I = 20.

The effects of feed ratio on the copolymerization is shown in Table 2 using a constant relation M/I = 20, at 70°C, for 96 h. There it can be seen that the proportion of butyryl units in the copolymers is quite constant regardless the feed ratio; in addition, its content is lower than expected from the feed ratio for (*R,S*)-BL feed content up to 40 mol% (exp. 6 to exp. 8), while for contents lower than 40 mol% (exp. 9 and exp. 10) the instantaneous composition of the copolymers (F_{CL}/F_{BL}) is nearly equal to the monomer feed composition. On the other hand, the increase of CL in the feed mixture raises the copolymers yields. This is consistent with the results of homopolymerization of CL and (*R,S*)-BL (exp. 11 and exp. 5, respectively), in which CL polymerization is much faster than that of (*R,S*)-BL. In general, the molecular weight of the copolymers obtained tends to increase with F_{CL} , and this could be due to the fact that the molecular weight of the PCL homopolymer is higher than that of the

Table 1. Effect of molar ratio of comonomers (M) to initiator (I) on the copolymerization of CL and (*R,S*)-BL^a

Exp. No.	NaH [mmol]	M/I [mol/mol]	F_{CL}^b [%]	$F_{(R,S)-BL}^b$ [%]	Yield ^c [%]	Physical appearance
1	5.20	4	55.00	45.00	87.72	white soft solid
2	1.06	20	66.30	33.70	17.33	white rigid solid
3	0.35	60	–	–	–	–
4	0.21	100	–	–	–	–

^a at 70°C for 72 h, $n_{CL} = 9.02$ mmol ($f_{CL} = 0.42$, 1 mmol = 0.086 g); $n_{(R,S)-BL} = 12.3$ mmol ($f_{(R,S)-BL} = 0.58$, 1 mmol = 0.114 g),

1 mmol NaH = 0.024 g

^b Content of CL and (*R,S*)-BL in copolymer [mol%]

^c Based on initial comonomers

Table 2. Results of the copolymerization of CL and BL at various feed monomer ratios using sodium hydride (NaH) as initiator

Exp. No.	NaH [mmol]	CL/BL [mmol/mmol]	Feed monomer ratio CL/BL [mol%]	F_{CL}/F_{BL}^a [%]	Yield ^b [%]	GPC ^c		
						$\overline{M}_n \cdot 10^{-3}$	$\overline{M}_w \cdot 10^{-3}$	D
5	0.61	12.30	0/100	0/100	19.08	1.94	2.51	1.29
6	2.71	16.24/37.88	30/70	88/12	7.35	18.63	26.26	1.41
7	1.23	12.30/12.30	50/50	75/25	14.96	8.96	13.91	1.55
8	1.50	18.04/12.02	60/40	75/25	37.17	8.67	12.84	1.48
9	1.29	18.04/7.73	70/30	80/20	63.25	11.23	16.46	1.47
10	1.13	18.04/4.51	80/20	83/17	74.17	12.05	16.28	1.35
11	0.45	9.02	100/0	100/0	87.37	32.21	44.21	1.37

M/I = 20, in bulk at 70°C for 96 h

^a Content of CL and BL in copolymer [mol%], obtained by means ¹H-NMR

^b Based on initial comonomers

^c From GPC, measured in THF at 40°C

Figure 1. Gel permeation chromatograms of copolymers obtained using NaH at various molar ratios CL/(*R,S*)-BL: a) PCL, b) block PCL/(*R,S*)-PBL 75/25, c) block PCL/(*R,S*)-PBL 80/20, d) block PCL/(*R,S*)-PBL 83/17, e) (*R,S*)-PBL

(*R,S*)-PBL homopolymer (exp. 11 and exp. 5, respectively). These results are in agreement with the fact the anionic polymerization of (*R,S*)-BL leads to low yield and chains of a relatively low molecular weight [27–33].

Figure 1 displays the GPC chromatograms of the obtained polymers. There it can be noted that the curves show a monomodal pattern which indicates that the polymerization product is a true copolymer not contaminated by PCL and (*R,S*)-PBL.

3.2. Structural analysis of copolymers:

Analysis of copolymer microstructure was performed by means of NMR spectroscopy. The typical ^1H -NMR and ^{13}C -NMR spectra copolymer of CL with BL are shown in Figure 2. The assignments of the peaks were made according to previous results [24, 25, 32]. It can be noted that the copolymers spectra show signals of both homopolymers. The resonances at $\delta = 1.8$ ppm, $\delta = 5.8$ ppm

and $\delta = 6.8$ ppm observed in the ^1H -NMR spectrum, can be attributed to the presence of a crotonyl end-group [32]; this group is formed at the initiation step of the polymerization where the α -proton abstraction of the (*R,S*)-BL could occur resulting in the salt of the unsaturated carboxylic acid as propagating species of reaction, as shown in Figure 3 [27, 33].

To determine the comonomer sequencing (random or in block), the most convenient spectrum range is the corresponding to carbonyl carbon [10, 13, 41]. The expanded ^{13}C -NMR spectrum of the carbonyl (CO) region of the copolymer shown in Figure 2 indicates the formation of a diblock, because the two CO signals of the blocks BL-BL and CL-CL are strong, whereas the signals of the BL-CL and CL-BL sequences are absent [6]. The CO signal of BL-BL sequences exhibits a splitting resulting from isotactic and syndiotactic dyads [13, 41]. This result may be explained, taking into account the higher strain in bond angle in the (*R,S*)-BL with respect to CL; this could facilitate in the medium of reaction the occurrence as first step the anionic polymerization of (*R,S*)-BL via carboxylate anions as propagating species, leading to blocks of PBL of a relatively low molecular weight [27–33]. The latter could then initiate the polymerization of CL through alkoxide anions as propagating species leading to blocks of PCL of a relatively higher molecular weight [5, 23].

3.3. Thermal properties of the obtained copolymers

3.3.1. Thermogravimetric analysis (TGA)

Thermal stability was evaluated by TGA and traces of most of the polymers are shown in Figure 4 where it may be observed that the PCL is significantly more stable than the PBL and the degradation of both polymers occurs in a single stage. On the other hand, the PCL-*block*-(*R,S*)-PBL copolymers exhibit an intermediate stability between both homopolymers and their stability increases with the content of CL. In addition, these copolymers show two stages of degradation where the first one corresponds to a weight-loss comparable to the fraction in weight of the PBL in the copolymer as may be observed in Table 3.

The temperature values and mainly the comparison between the percentage of volatilized material after

Figure 2. NMR spectra of the PCL-*block*-(*R,S*)-PBL 55/45 copolymer. a) ^{13}C -NMR, b) ^1H -NMR

Figure 3. Initiating step in ring-opening copolymerization of (*R,S*)-PBL with CL [27, 33]

each step, and the composition of the copolymers suggest that the first step can be essentially attributed to the degradation of (*R,S*)-PBL moiety and the second one to the remaining PCL fraction.

On the other hand, the analysis by TVA was carried out to examine the volatiles produced during the degradation process. The degradation products were analyzed by ^1H -NMR. Figure 5 depicts the

spectra of volatile fraction produced during the first degradation stage, in the range of 120 to 270°C, and it shows appreciable quantities of crotonic acid, which is well known to be one of the main degradation products of PBL, together with low molecular weight fractions of the (*R,S*)-PBL having crotonyl end groups [28, 42–45]. Additionally, the NMR spectra of the solid residue were identical to the

Figure 4. TGA curves under nitrogen atmosphere (10°C/min) of: a) (*R,S*)-PBL, b) block PCL/(*R,S*)-PBL 75/25, c) block PCL/(*R,S*)-PBL 83/17, d) block PCL/(*R,S*)-PBL 88/12, e) PCL

PCL homopolymer (Figure 6). These results confirm those obtained by TGA, which indicated that thermal degradation involves the occurrence of two distinct processes. The first one mainly involves the degradation of (*R,S*)-PBL block for which it has been proposed a random chain scission by β -elimination [43, 44] or an E1cB mechanism proceeding via α -deprotonation by carboxylate anion [45], both alternatives lead the same products: crotonic acid and oligomers with a crotonate end group [28,

Figure 6. ^1H -NMR spectrum: a) PCL homopolymer (exp. 5, Table 2), b) solid residue obtained in the analysis by TVA

42–45]. The second process is due to the degradation of the remaining PCL block.

3.3.2. Differential scanning calorimetry (DSC) and Wide angle X-ray scattering WAXS

In order to study the effect of the (*R,S*)-PBL blocks in the crystallization of PCL on the copolymer a combined study of DSC and WAXS was carried out.

In the DSC study all copolymers were first heated from -40 to 120°C to erase thermal history and

Table 3. TGA data of PCL, PBL and copolymers

Sample	Composition CL/(<i>R,S</i>)-BL [%p/p]		First step		Second step	
			Ti ^a [°C]	ΔW^b [%]	Ti ^a [°C]*	ΔW^b [%]
PCL	100	–	389.70	97.86	–	–
PCL- <i>block</i> -(<i>R,S</i>)-PBL (88/12)	90.67	9.33	229.35	11.07	411.31	88.85
PCL- <i>block</i> -(<i>R,S</i>)-PBL (83/17)	86.62	13.38	221.53	13.43	340.92	85.46
PCL- <i>block</i> -(<i>R,S</i>)-PBL (80/20)	84.13	15.87	219.65	18.08	327.24	77.85
PCL- <i>block</i> -(<i>R,S</i>)-PBL (75/25)	79.91	20.09	214.40	20.27	309.79	75.75
PBL	–	100	191.18	94.80	–	–

^a Temperature at the inflection point

^b Total weight loss percentage at the end of the step

Figure 5. ^1H -NMR spectrum of volatile fraction obtained in the analysis by TVA

Figure 7. DSC (7-A) cooling and (7-B) second heating curves (10°C/min) of the (R,S)-PBL, PCL and the copolyesters obtained: a) (R,S)-PBL, b) block PCL/(R,S)-PBL 75/25, c) block PCL/(R,S)-PBL 80/20, d) block PCL/(R,S)-PBL 88/12, e) PCL

subsequently cooled to -40°C and heated back to 120°C . Analyses are based on first cooling and second heating and the resulting thermograms are plotted in Figure 7. The transition temperatures values are listed in Table 4. It can be observed in Figure 7A, that, as expected, the (R,S)-PBL do not show any exothermal peak, whereas the PCL shows one at about 33°C ; for the copolyesters the peak moves towards lower temperatures when the butyroyl units content increases. This could be indicating that the (R,S)-PBL segment in the copolyesters may hinder crystallization of the PCL segment as their crystallization needs greater undercooling during the crystallization process. On the other

hand, the DSC heating curves (Figure 7B), for (R,S)-PBL homopolymer doesn't show any melting endotherms, whereas the PCL exhibit a melting endotherm at about 55°C . The copolyesters display endotherms very close to the melting temperature of PCL homopolymer and the melting enthalpies of these are not influenced by the (R,S)-PBL content; they remain about $63\text{ J}\cdot\text{g}^{-1}$.

Additionally, the most striking feature in Figure 7B is that all the DSC melting traces of the copolyesters show bimodal melting peaks, whereas the DSC melting curve of PCL only reveals a single peak in the absence of (R,S)-BL. In general, these peaks are attributed to a crystalline reorganization via melting, re-crystallization and re-melting at higher temperature [8, 46–48].

The lower temperature peak in DSC curves corresponds to the melting of unstable crystals formed during the cooling process due a (R,S)-PBL block in the copolymer. The slight shift of the melting peak to lower temperatures with increased (R,S)-BL content, suggests that crystals with lower thermal stability had been formed [46]. The higher temperature peak should be attributed to crystals recrystallized during the DSC heating process [8, 48].

The DSC results were confirmed by WAXS experiments carried out for some PCL-*block*-(R,S)-PBL copolymers at different temperatures. In Figure 8 the X-ray diffraction patterns of PCL-*block*-(R,S)-PBL, 80/20, recorded at different temperatures are shown. At 45°C the diffractograms are identical to those obtained at room temperature. In Figure 8a, the Bragg peaks characteristic of the orthorhombic PCL crystals [49] (Space group $\text{P2}_1\text{2}_1\text{2}_1$, $a = 7.496\text{ \AA}$, $b = 4.974\text{ \AA}$, $c = 17.297\text{ \AA}$) are observed together with broad bands which correspond to the scattering by disordered regions. At 60°C (Figure 8b) the amount of crystalline regions has decreased significantly and the spectrum recorded at 70°C show a total absence of crystalline order,

Table 4. DSC results of PCL and copolymers in the cooling and second heating scans

Sample	ΔH_{total} [J·g ⁻¹]	T_{m1} [°C]	T_{m2} [°C]	ΔH_c [J·g ⁻¹]	T_c [°C]
PCL	75.04	55.45	–	–72.09	33.13
PCL- <i>block</i> -(R,S)-PBL (88/12)	63.26	54.20	57.03	–63.98	21.47
PCL- <i>block</i> -(R,S)-PBL (80/20)	63.62	47.37	53.20	–61.93	17.47
PCL- <i>block</i> -(R,S)-PBL (75/25)	63.50	46.87	53.03	–60.76	17.47

T_{m2} denotes the melting point of the second peak in the bimodal endotherm

ΔH_{total} denote total heat of melting

ΔH_c denotes heat of crystallization

T_c denotes temperature of crystallization

Figure 8. Diffractograms of copolymer 80/20 at different temperatures: (a) 45°C, (b) 60°C, (c) 70°C

the sample is 100% amorphous as revealed by the sole presence of broad amorphous halos. These results confirm the DSC determinations and show that the melting peaks are due to the PCL blocks whose behaviour is not affected by the presence of PBL blocks. This behaviour is to be expected as the blending [50, 51] or copolymerization of PCL [52] with a broad variety of homopolymers have always preserved the crystalline structure of PCL.

4. Conclusions

Copolymers of CL/(*R,S*)-BL could be synthesized by ring-opening copolymerization using NaH as initiator. NMR spectroscopic analysis show block sequences in these copolyesters, in which the content of (*R,S*)-BL units was in all cases lower than expected from the feed ratio; its proportion in the copolymers is almost constant regardless of the feed ratio. This indicates that in the reaction mixture, the first stage polymerization could consist of BL, thus obtaining relatively short chain segment of PBL with active carboxylate ions which subsequently induce the polymerization of CL via alkoxide ion producing chain segment PCL relatively longer. The catalyst concentration and the monomer feed ratios had strong effects on yield, while the molecular weights do not depend significantly on the feed ratio.

The thermal stability of the prepared copolymers studied by TGA and TVA showed that they are stable up to temperatures near 200°C, when the decomposition process begins in two steps, the first

one due to the (*R,S*)-BL block degradation and the second to the remaining PCL block. The DSC and WAXS results indicate that the copolymers contain one crystallizable block of PCL, which crystallization and melting behaviors are slightly affected by composition.

Acknowledgements

This work has been supported by CDCHT-ULA (grants C-1517-07-08-A and C1522-07-08-F) and by DID-USB (DID-G15) and FONACIT (F2005-000284). The authors also thank the Laboratorio Nacional de RMN Nodo ULA (Mérida Venezuela) for NMR facilities.

References

- [1] Vert M.: Bioresorbable polymers for temporary therapeutic applications. *Die Angewandte Makromolekulare Chemie*, **166**, 155–168 (1989). DOI: [10.1002/apmc.1989.051660111](https://doi.org/10.1002/apmc.1989.051660111)
- [2] Dobrzynski P.: Synthesis of biodegradable copolymers with low-toxicity zirconium compounds. III. Synthesis and chain-microstructure analysis of terpolymer obtained from L-lactide, glycolide, and ϵ -caprolactone initiated by zirconium(IV) acetylacetonate. *Journal of Polymer Science Part A: Polymer Chemistry*, **40**, 3129–3143 (2002). DOI: [10.1002/pola.10401](https://doi.org/10.1002/pola.10401)
- [3] Ashammakhi N., Mäkelä E. A., Vihtonen K., Rokkanen P., Törmälä P.: Effect of self-reinforced polyglycolide membranes on cortical bone: An experimental study on rats. *Journal of Biomedical Materials Research*, **29**, 687–694 (1995). DOI: [10.1002/jbm.820290603](https://doi.org/10.1002/jbm.820290603)
- [4] Stridsberg K., Albertsson A-C.: Controlled ring-opening polymerization of L-lactide and 1,5-dioxepan-2-one forming a triblock copolymer. *Journal of Polymer Science Part A: Polymer Chemistry*, **38**, 1774–1784 (2000). DOI: [10.1002/\(SICI\)1099-0518\(20000515\)38:10<1774::AID-POLA620>3.0.CO;2-F](https://doi.org/10.1002/(SICI)1099-0518(20000515)38:10<1774::AID-POLA620>3.0.CO;2-F)
- [5] Vanhoorne P., Dubois P., Jerome R., Teyssie P.: Macromolecular engineering of polylactones and polylactides. 7. Structural analysis of copolyesters of ϵ -caprolactone and L- or D,L-lactide initiated by triisopropoxyaluminum. *Macromolecules*, **25**, 37–44 (1992). DOI: [10.1021/ma00027a008](https://doi.org/10.1021/ma00027a008)
- [6] Kricheldorf H. R., Rost S.: A-B-A-triblock and multi-block copolyesters prepared from ϵ -caprolactone, glycolide and L-lactide by means of bismuth subsalicylate. *Polymer*, **46**, 3248–3256 (2005). DOI: [10.1016/j.polymer.2005.02.004](https://doi.org/10.1016/j.polymer.2005.02.004)

- [7] Hiki S., Miyamoto M., Kimura Y.: Synthesis and characterization of hydroxy-terminated [RS]-poly(3-hydroxybutyrate) and its utilization to block copolymerization with L-lactide to obtain a biodegradable thermoplastic elastomer. *Polymer*, **41**, 7369–7379 (2000).
DOI: [10.1016/S0032-3861\(00\)00086-0](https://doi.org/10.1016/S0032-3861(00)00086-0)
- [8] Chen C., Peng S., Wu H., Zhuang Y., Chen X., Dong L., Feng Z.: Synthesis and characterization of poly(β -hydroxybutyrate) and poly(ϵ -caprolactone) copolyesters by transesterification. *Journal of Polymer Science Part B: Polymer Physics*, **40**, 1893–1903 (2002).
DOI: [10.1002/polb.10242](https://doi.org/10.1002/polb.10242)
- [9] Zhong Z., Yu D., Meng F., Gan Z., Ping X.: Controlled synthesis of L-lactide-*b*- ϵ -caprolactone block copolymers using a rare earth complex as catalyst. *Polymer Journal*, **31**, 633–636 (1999).
DOI: [10.1295/polymj.31.633](https://doi.org/10.1295/polymj.31.633)
- [10] Fukuzaki H., Yoshida M., Asano M., Kumakura M., Mashimo T., Yuasa H., Imai K., Yamanaka H.: Synthesis of low-molecular-weight copoly(L-lactic acid/ ϵ -caprolactone) by direct copolycondensation in the absence of catalysts, and enzymatic degradation of the polymers. *Polymer*, **31**, 2006–2014 (1990).
DOI: [10.1016/0032-3861\(90\)90031-S](https://doi.org/10.1016/0032-3861(90)90031-S)
- [11] Vivas M., Mejías N., Contreras J.: Ring-opening polymerization of lactones initiated by diphenylzinc-coinitiator systems. *Polymer International*, **52**, 1005–1009 (2003).
DOI: [10.1002/pi.1183](https://doi.org/10.1002/pi.1183)
- [12] Abe H., Matsubara I., Doi Y., Hori Y., Yamaguchi A.: Physical properties and enzymic degradability of poly(3-hydroxybutyrate) stereoisomers with different stereoregularities. *Macromolecules*, **27**, 6018–6025 (1994).
DOI: [10.1021/ma00099a013](https://doi.org/10.1021/ma00099a013)
- [13] Kricheldorf H. R., Lee S.-R.: Polylactones. 35. Macrocyclic and stereoselective polymerization of β -D,L-butyrolactone with cyclic dibutyltin initiators. *Macromolecules*, **28**, 6718–6725 (1995).
DOI: [10.1021/ma00124a004](https://doi.org/10.1021/ma00124a004)
- [14] Kohn F. E., Van Den Berg J., Van De Ridder G.: The ring-opening polymerization of D,L-lactide in the melt initiated with tetraphenyltin. *Journal of Applied Polymer Science*, **29**, 4265–4277 (1984).
DOI: [10.1002/app.1984.070291255](https://doi.org/10.1002/app.1984.070291255)
- [15] Grijpma D. W., Pennings A. J.: Polymerization temperature effects on the properties of L-lactide and ϵ -caprolactone copolymers. *Polymer Bulletin*, **25**, 335–341 (1991).
DOI: [10.1007/BF00316903](https://doi.org/10.1007/BF00316903)
- [16] Storey R. F., Herring K. R., Hoffman D. C.: Hydroxy-terminated poly(ϵ -caprolactone-co- δ -valerolactone) oligomers: Synthesis, characterization, and polyurethane network formation. *Journal of Polymer Science Part A: Polymer Chemistry*, **29**, 1759–1777 (1991).
DOI: [10.1002/pola.1991.080291209](https://doi.org/10.1002/pola.1991.080291209)
- [17] Kricheldorf H. R., Lee S., Scharnagl N.: Polylactones. 28. Syndiotactic poly(β -D,L-hydroxybutyrate) by ring-opening polymerization of β -D,L-butyrolactone with butyltin methoxides. *Macromolecules*, **27**, 3139–3146 (1994).
DOI: [10.1021/ma00090a005](https://doi.org/10.1021/ma00090a005)
- [18] Kricheldorf H.R., Eggerstedt S.: Polylactones: 41. Polymerization of β -D,L-butyrolactone with dialkyltin oxides as initiators. *Macromolecules*, **30**, 5693–5697 (1997).
DOI: [10.1021/ma970244c](https://doi.org/10.1021/ma970244c)
- [19] Nakayama A., Kawasaki N., Maeda Y., Arvanitoyannis I., Aiba S., Yamamoto N.: Study of biodegradability of poly(δ -valerolactone-co-L-lactide)s. *Journal of Applied Polymer Science*, **66**, 741–748 (1997).
DOI: [10.1002/\(SICI\)1097-4628\(19971024\)66:4<741::AID-APP14>3.0.CO;2-U](https://doi.org/10.1002/(SICI)1097-4628(19971024)66:4<741::AID-APP14>3.0.CO;2-U)
- [20] Nakayama A., Kawasaki N., Aiba S., Maeda Y., Arvanitoyannis I., Yamamoto N.: Synthesis and biodegradability of novel copolyesters containing γ -butyrolactone units. *Polymer*, **39**, 1213–1222 (1998).
DOI: [10.1016/S0032-3861\(97\)00401-1](https://doi.org/10.1016/S0032-3861(97)00401-1)
- [21] Kricheldorf H. R., Bornhorst K., Hachmann-Thiessen H.: Bismuth(III) n-hexanoate and Tin (II) 2-ethylhexanoate initiated copolymerizations of ϵ -caprolactone and L-lactide. *Macromolecules*, **38**, 5017–5024 (2005).
DOI: [10.1021/ma047873o](https://doi.org/10.1021/ma047873o)
- [22] Piao L., Deng M., Chen X., Jiang L., Jing X.: Ring-opening of ϵ -caprolactone and L-lactide using organic aminocalcium catalyst. *Polymer*, **44**, 2331–2336 (2003).
DOI: [10.1016/s0032-3861\(03\)00118-6](https://doi.org/10.1016/s0032-3861(03)00118-6)
- [23] Zhong Z., Ankoné M., Dijkstra P. J., Birg C., Westerhausen M., Feijen J.: Calcium methoxide initiated ring-opening polymerization of ϵ -caprolactone and L-lactide. *Polymer Bulletin*, **46**, 51–57 (2001).
DOI: [10.1007/s002890170088](https://doi.org/10.1007/s002890170088)
- [24] Vivas M., Contreras J.: Ring-opening polymerization of ϵ -caprolactone initiated by diphenylzinc. *European Polymer Journal*, **39**, 43–47 (2003).
DOI: [10.1016/S0014-3057\(02\)00190-8](https://doi.org/10.1016/S0014-3057(02)00190-8)
- [25] Contreras J., Dávila D.: Ring-opening copolymerization of L-lactide with ϵ -caprolactone initiated by diphenylzinc. *Polymer International*, **55**, 1049–1056 (2006).
DOI: [10.1002/pi.2050](https://doi.org/10.1002/pi.2050)

- [26] Dobrzynski P.: Synthesis of biodegradable copolymers with low-toxicity zirconium compounds. II. Copolymerization of glycolide with ϵ -caprolactone initiated by zirconium(IV) acetylacetonate and zirconium(IV) chloride. *Journal of Polymer Science Part A: Polymer Chemistry*, **40**, 1379–1394 (2002).
DOI: [10.1002/pola.10222](https://doi.org/10.1002/pola.10222)
- [27] Kurcok P., Matuszowicz A., Jedliński Z.: Anionic polymerization of β -lactones initiated with potassium hydride. A convenient route to polyester macromonomers. *Macromolecular Rapid Communication*, **16**, 201–206 (1995).
DOI: [10.1002/marc.1995.030160308](https://doi.org/10.1002/marc.1995.030160308)
- [28] Kurcok P., Kowalczyk M., Hennek K., Jedliński Z.: Anionic polymerization of β -lactones initiated with alkali-metal alkoxides: Reinvestigation of the polymerization mechanism. *Macromolecules*, **25**, 2017–2020 (1992).
DOI: [10.1021/ma00033a027](https://doi.org/10.1021/ma00033a027)
- [29] Kurcok P., Dubois P., Sikorska W., Jedliński Z., Jérôme R.: Macromolecular engineering of lactones and lactides. 24. Controlled synthesis of (R,S)- β -butyrolactone-*b*- ϵ -caprolactone block copolymers by anionic and coordination polymerization. *Macromolecules*, **30**, 5591–5595 (1997).
DOI: [10.1021/ma970212p](https://doi.org/10.1021/ma970212p)
- [30] Liu K., Goh S., Li J.: Controlled synthesis and characterizations of amphiphilic poly[(R,S)-3-hydroxybutyrate]-poly(ethylene glycol)-poly[(R,S)-3-hydroxybutyrate] triblock copolymers. *Polymer*, **49**, 732–741 (2008).
DOI: [10.1016/j.polymer.2007.12.017](https://doi.org/10.1016/j.polymer.2007.12.017)
- [31] Adamus G., Kowalczyk M.: Anionic ring-opening polymerization of β -alkoxymethyl-substituted β -lactones. *Biomacromolecules*, **9**, 696–703 (2008).
DOI: [10.1021/bm701077v](https://doi.org/10.1021/bm701077v)
- [32] Yu G., Marchessault R. H.: Characterization of low molecular weight poly(β -hydroxybutyrate)s from alkaline and acid hydrolysis. *Polymer*, **41**, 1087–1098 (2000).
DOI: [10.1016/S0032-3861\(99\)00230-X](https://doi.org/10.1016/S0032-3861(99)00230-X)
- [33] Jedliński Z., Kowalczyk M., Kurcok P.: Polymerization of β -lactones initiated by alkali metal naphthalenides. A convenient route to telechelic polymers. *Journal of Macromolecular Science Part A*, **29**, 1223–1230 (1992).
DOI: [10.1080/10601329208054152](https://doi.org/10.1080/10601329208054152)
- [34] Duda A.: Anionic polymerization of 4-methyl-2-oxetanone (β -butyrolactone). *Journal of Polymer Science Part A: Polymer Chemistry*, **30**, 21–29 (1992).
DOI: [10.1002/pola.1992.080300103](https://doi.org/10.1002/pola.1992.080300103)
- [35] 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. *Macromolecular Rapid Communication*, **16**, 513–519 (1995).
DOI: [10.1002/marc.1995.030160709](https://doi.org/10.1002/marc.1995.030160709)
- [36] Jedliński Z., Kowalczyk M., Kurcok P., Adamus G., Matuszowicz A., Sikorska W., Gross R. A., Xu J., Lenz R. W.: Stereochemical control in the anionic polymerization of β -butyrolactone initiated with alkali-metal alkoxides. *Macromolecules*, **29**, 3773–3777 (1996).
DOI: [10.1021/ma951888s](https://doi.org/10.1021/ma951888s)
- [37] Kurcok P., Dubois P., Jérôme R.: Polymerization of β -butyrolactone initiated with $\text{Al}(\text{O}^i\text{Pr})_3$. *Polymer International*, **41**, 479–485 (1999).
DOI: [10.1002/\(SICI\)1097-0126\(199612\)41:4<479::AID-PI652>3.0.CO;2-w](https://doi.org/10.1002/(SICI)1097-0126(199612)41:4<479::AID-PI652>3.0.CO;2-w)
- [38] Kurcok P., Śmiga M., Jedliński Z.: β -butyrolactone polymerization initiated with tetrabutylammonium carboxylates: A novel approach to biomimetic polyester synthesis. *Journal of polymer Science Part A: Polymer Chemistry*, **40**, 2184–2189 (2002).
DOI: [10.1002/pola.10285](https://doi.org/10.1002/pola.10285)
- [39] Arkin A. H., Hazet B., Adamus G., Kowalczyk M., Jedliński Z., Lenz R. W.: Synthesis of poly(2-methyl-3-hydroxyoctanoate) via anionic polymerization of α -methyl- β -pentyl- β -propiolactone. *Biomacromolecules*, **2**, 623–627 (2001).
DOI: [10.1021/bm015528q](https://doi.org/10.1021/bm015528q)
- [40] Kawalec M., Śmiga-Matuszowicz M., Kurcok P.: Counterion and solvent effects on the anionic polymerization of β -butyrolactone initiated with acetic acid salts. *European Polymer Journal*, **44**, 3556–3563 (2008).
DOI: [10.1016/j.eurpolymj.2008.09.008](https://doi.org/10.1016/j.eurpolymj.2008.09.008)
- [41] Kricheldorf H. R., Mang T., Jonté J. M.: Polylactones. 1. Copolymerizations of glycolide and ϵ -caprolactone. *Macromolecules*, **17**, 2173–2181 (1984).
DOI: [10.1021/ma00140a051](https://doi.org/10.1021/ma00140a051)
- [42] Aoyagi Y., Yamashita K., Doi Y.: Thermal degradation of poly[(R)-3-hydroxybutyrate], poly[ϵ -caprolactone], and poly[(S)-lactide]. *Polymer Degradation and Stability*, **76**, 53–59 (2002).
DOI: [10.1016/S0141-3910\(01\)00265-8](https://doi.org/10.1016/S0141-3910(01)00265-8)
- [43] Gonzalez A., Irusta L., Fernández-Berridi M. J., Iriarte M., Irui J. J.: Application of pyrolysis/gas chromatography/Fourier transform infrared spectroscopy and TGA techniques in the study of thermal degradation of poly (3-hydroxybutyrate). *Polymer Degradation and Stability*, **87**, 347–354 (2005).
DOI: [10.1016/j.polymdegradstab.2004.09.005](https://doi.org/10.1016/j.polymdegradstab.2004.09.005)
- [44] Ariffin H., Nishida H., Shirai Y., Hassan M. A.: Determination of multiple thermal degradation mechanisms of poly(3-hydroxybutyrate). *Polymer Degradation and Stability*, **93**, 1433–1439 (2008).
DOI: [10.1016/j.polymdegradstab.2008.05.020](https://doi.org/10.1016/j.polymdegradstab.2008.05.020)
- [45] Kawalec M., Adamus G., Kurcok P., Kowalczyk M., Foltran I., Focarete M. L., Scandola M.: Carboxylate-induced degradation of poly(3-hydroxybutyrate)s. *Biomacromolecules*, **8**, 1053–1058 (2007).
DOI: [10.1021/bm061155n](https://doi.org/10.1021/bm061155n)

- [46] Pearce R., Marchessault R. H.: Multiple melting in blends of isotactic and atactic poly(β -hydroxybutyrate). *Polymer*, **35**, 3990–3997 (1994). DOI: [10.1016/0032-3861\(94\)90285-2](https://doi.org/10.1016/0032-3861(94)90285-2)
- [47] Gunaratne L. M., Shanks R. A.: Multiple melting behaviour of poly(3-hydroxybutyrate-co-hydroxyvalerate) using step-scan DSC. *European Polymer Journal*, **41**, 2980–2988 (2005). DOI: [10.1016/j.eurpolymj.2005.06.015](https://doi.org/10.1016/j.eurpolymj.2005.06.015)
- [48] Yoo E. S., Im S. S.: Melting behavior of poly(butylene succinate) during heating scan by DSC. *Journal of Polymer Science Part B: Polymer Physics*, **37**, 1357–1366 (1999). DOI: [10.1002/\(SICI\)1099-0488\(19990701\)37:13<1357::AID-POLB2>3.0.CO;2-Q](https://doi.org/10.1002/(SICI)1099-0488(19990701)37:13<1357::AID-POLB2>3.0.CO;2-Q)
- [49] Bittiger H., Marchessault R. H., Niegisch W.D.: Crystal structure of poly- ϵ -caprolactone. *Acta Crystallographica*, **B26**, 1923–1927 (1970). DOI: [10.1107/S0567740870005198](https://doi.org/10.1107/S0567740870005198)
- [50] Herrera D., Zamora J-C., Bello A., Grima M., Laredo E., Müller A. J., Lodge T.: Miscibility and crystallization in polycarbonate/poly(ϵ -caprolactone) blends: Application of the self-concentration model. *Macromolecules*, **38**, 5109–5120 (2005). DOI: [10.1021/ma050481c](https://doi.org/10.1021/ma050481c)
- [51] Balsamo V., Newman D., Gouveia L., Herrera L., Grima M., Laredo E.: Molecular dynamics and crystallization kinetics in PSMA14/PCL blends. *Polymer*, **47**, 5810–5820 (2006). DOI: [10.1016/j.polymer.2006.06.019](https://doi.org/10.1016/j.polymer.2006.06.019)
- [52] Laredo E., Hernández M. C., Bello A., Grima M., Müller A., Balsamo V.: Local and segmental dynamics in homopolymer and triblock copolymers with one semicrystalline block. *Physical Review E*, **65**, 021807/1–021807/13 (2002). DOI: [10.1103/PhysRevE.65.021807](https://doi.org/10.1103/PhysRevE.65.021807)