



Ring-Expansion Copolymerization of L-Lactide and Glycolide

Steffen M. Weidner, Hans R. Kricheldorf,* and Felix Scheliga

1:1 Copolymerizations of glycolide (GL) and L-lactide (LA) are performed in bulk at 100 °C and at 160 °C with four cyclic tin catalysts. The resulting copolyesters are characterized by size exclusion chromatography measurements, ¹H and ¹³C NMR spectroscopy and by MALDI-TOF mass spectrometry. At 160 °C and longer reaction time (22 h), nearly complete conversion of both monomers is achieved, and cyclic copolymers with nearly random sequences are formed. At shorter times (0.5–3.0 h, depending on catalyst) the conversion of LA is incomplete, and only cyclics having even numbers of lactyl units are obtained. At 100 °C and 22 h again cycles mainly consisting of even numbered lactyl units are formed, but with even and odd numbers of glycolyl units. Copolymerization of lactide at 160 °C with small amounts of GL show that formation of high *T_m* crystallites (*T_m* > 190 °C) is hindered even when only >2% of GL is added. For polyglycolide containing a smaller amount of lactide complete solubility in hexafluoroisopropanol is only observed around and above 20 mol% of lactide.

reviews were published and, therefore, the following references are only a small fraction of representative examples.^[10–21]

Following our recent work on syntheses of cyclic poly(lactides) via ring-expansion polymerization (REP, see Scheme 1)^[22–26] it was the main purpose of this study to explore the synthesis of cyclic glycolide/L-lactide (LA) copolyesters by means of cyclic tin catalysts. Cyclic polyesters have several, although minor, advantages over their linear counterparts, for example a lower hydrodynamic volume with the consequence of lower melt viscosity, which improves thermal processing of high molecular weight materials. Furthermore, absence of reactive and hydrophilic end groups may improve thermal stability and hydrolytic stability upon storage.^[27,28]

1. Introduction

In 1962 polyglycolide was developed as the first reabsorbable medical suture by American Cyanamide.^[1–3] It was commercialized after 1970 under the trademark “Dexon,”^[4–7] immediately followed by a poly(L-lactide) fiber developed by DuPont.^[8] It was found that the polyglycolide fiber had a higher strength, but its strength and brittleness made it difficult for surgeons to make knots. Therefore, less brittle, more flexible materials were developed, and after 1975 a copolymer containing 8 mol% of lactic acid was commercialized under the trademark “Vicryl.”^[9] Since then, copolymerizations of glycolide (GL) and lactides were studied in much detail. The chemical, physical, and physiological properties of the resulting copolyesters were determined and numerous medical and pharmaceutical applications were explored. More than 100 patents, research articles, and

It was not the purpose of this study to develop special copolyesters for certain applications, but to elaborate fundamental information about the copolymerization of both monomers under the influence of cyclic tin catalysts. First, it should be clarified, if the copolyesters possess the expected cyclic architecture. Furthermore, the influence of three experimental parameters on molecular weight, composition, and sequence of the comonomers should be elucidated. The three parameters varied in this work were catalyst, temperature, and polymerization time. The catalysts were selected, so that structure and reactivity varied over a broad range (Scheme 2). Their reactivity obeys the following order: DSTL < BuSnBuCa ≈ BuSnBiph < SnBiph, as observed in homopolymerizations of L-lactide)

2. Results and Discussion

2.1. Copolymerizations at 100 °C

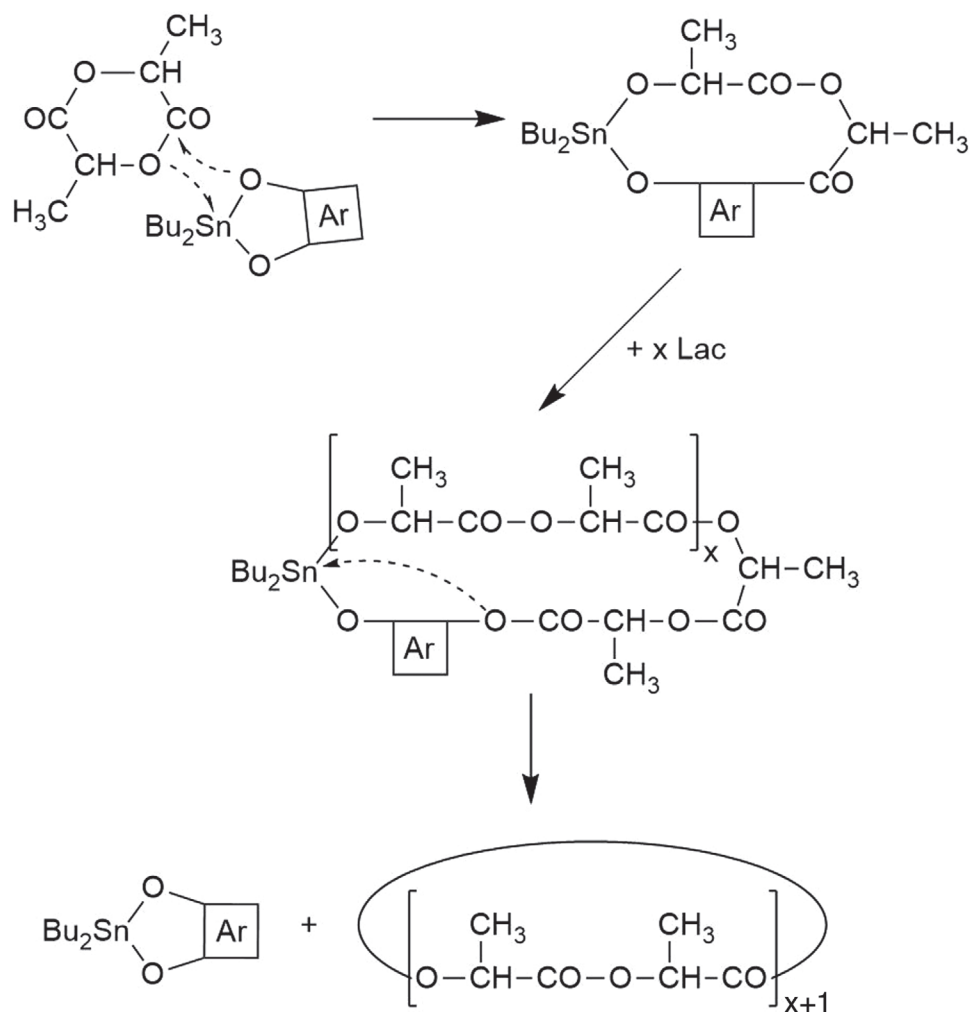
A first series of polymerizations based on the five catalysts depicted in Scheme 2 was performed at 100 °C for the following reasons. 100 °C is the lowest temperature which can be used for polymerizations of L-lactide in bulk, because of its melting temperature (*T_m*) of 98.5–99.0 °C (the frequently reported *T_m* of 95 °C is incorrect). It was of interest to compare the results obtained from the copolymerization with those found for the homopolymerization of L-lactide. For REPs of L-lactide catalyzed by BuSn-BuCa it was found that cyclic polylactides with a predominance of odd-numbered cycles were formed. This was an unexpected result since the normal course of the REP of lactide (or glycolide) should yield even-numbered polylactides, when transesterification reactions such as intercircular back-biting are more or less suppressed (Scheme 1). The other three catalysts yielded

Dr. S. M. Weidner
BAM, Federal Institute for Material Research and Testing
Richard Willstätter Str. 11, Berlin D-12489, Germany
Prof. H. R. Kricheldorf, Dr. F. Scheliga
Institut für Technische und Makromolekulare Chemie
Universität Hamburg
Bundesstr. 45, Hamburg D-20146, Germany
E-mail: hrkricheldorf@aol.de

The ORCID identification number(s) for the author(s) of this article can be found under <https://doi.org/10.1002/macp.202000307>.

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Scheme 1. Syntheses of cyclic poly lactides via ring-expansion polymerization (REP).

equimolar amounts of odd- and even-numbered cycles. Therefore, it was of interest, if, and to what extent, transesterification reactions influence the sequences of the LA/GL copolymers.

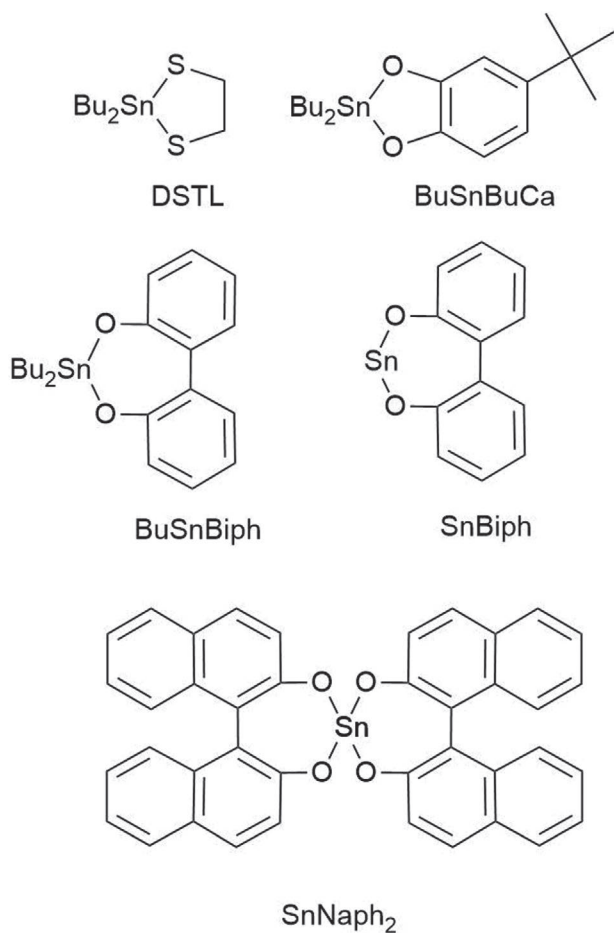
When the copolymerizations at 100 °C were conducted with the more reactive catalysts DSTL, BuSnBuCa, BuSnBiph, and SnBiph (Table 1) only peaks of cyclics were found in the MALDI-TOF mass spectra. These cycles consisted of even and odd numbers of GL units (Figure 1A). However, all cycles mainly consisted of even numbered lactide sequences. In other words, the transesterification activity of these catalysts sufficed to break up the GL-GL bonds in the copolymer backbone, but not the less reactive LA-LA bonds. In the case of the most reactive catalyst (SnBiph) weak peaks of cycles containing odd numbers of LA units were also detectable (Figure 1B). This observation evidences that the most reactive catalysts also cause at least partial transesterification of LA-LA bonds and not only of GL-GL bonds. The correlation of masses and composition of cyclic copolyesters is given in Table S1, Supporting Information.

The ^{13}C NMR spectra of all four poly lactides were quite similar, showing a resolution of tetrads for both comonomers. The following results were obtained. A strong signal originating from unreacted lactide (labeled as Lac in all ^{13}C NMR

spectra, Figure 2 and Figures S2,S3, Supporting Information) indicates incomplete conversion of this monomer. Correspondingly, the tetrad representing a sequence of four LA units was absent, whereas the tetrad indicating blocks of GL units was the strongest signal of all GL tetrad signals (labeled G4). Its intensity compared to that of the other tetrad signals was used to estimate an average block length. These block lengths data are listed in Table 2 and show values around 4–5. In summary, it may be said that a temperature of 100 °C is too low to achieve complete copolymerization of both monomers. Furthermore, transesterification does not involve GL-GL bonds in the copolyester backbone and the resulting sequences are far from randomness.

2.2. Copolymerizations at 160 °C

Two small series of 1:1 copolymerizations were performed in bulk at 160 °C, either with short (0.5–3 h, experiments A, Table 2) or with longer reaction time (22 h, experiments B, Table 2). A first characteristic observation for the short time series was the insolubility of all four copolyesters in neat



Scheme 2. Structure of catalyst discussed in this work.

dichloromethane or chloroform. Addition of hexafluoroisopropanol (HFIP) was necessary to bring all copolyesters into solution. This observation proved that the insolubility was not based on chemical crosslinking, but on physical crosslinking meaning crystallization of GL-blocks.

The short time copolymerizations gave results quite similar to those obtained at 100 °C/22 h, regardless of the catalyst. However, the lower reactivity of DSTL and BuSnBuCa was evident from a longer reaction time needed until the reaction mixture turned viscous. Nonetheless, both, ¹H and ¹³C NMR spectra indicated that the conversions of lactide were below 50% (an exact quantification of the ¹H NMR signals was not feasible because of poor resolution). The ¹³C NMR spectrum of the

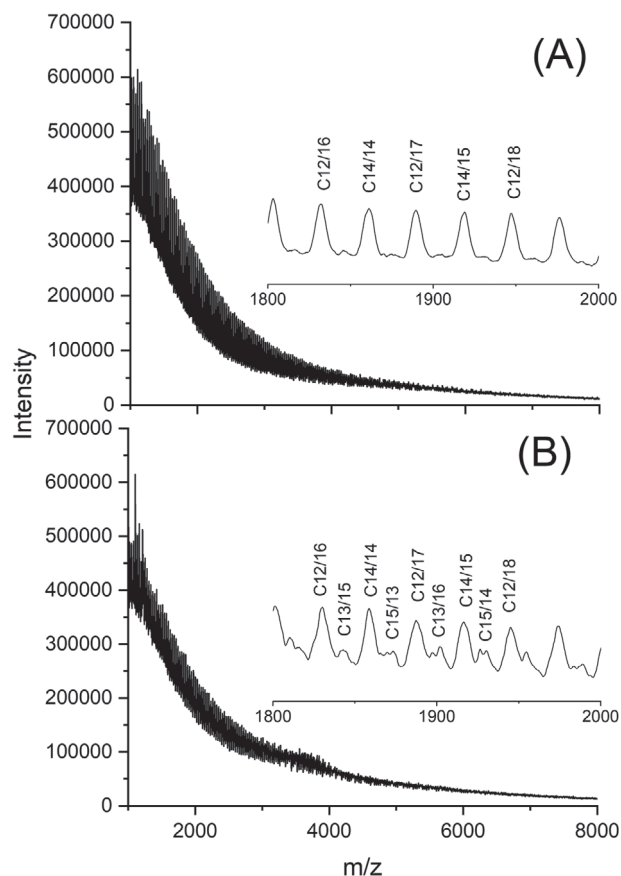


Figure 1. MALDI-TOF mass spectra of copoly(LA-GL)s prepared at 100 °C/22 h: A) with BuSnBi (No. 4, Table 1); B) with SnBiph, (No. 5, Table 1).

poly(lactide) polymerized with BuSnBiph (Figure S4, Supporting Information) illustrates this observation. The excess of GL in these copolyesters has of course the consequence that blocks of several GL units are formed and part of these blocks tend to form tiny instable crystallites. These tiny crystallites were responsible for the insolubility in neat chloroform, but they went into solution, when HFIP was added.

The MALDI-TOF mass spectra demonstrated that almost exclusively cyclics containing even numbers of lactyl units were formed (Figure 3A). Since these cycles contained equal amounts of even and odd numbers of glycolyl units, these mass spectra demonstrate that the intracircular back-biting reactions were highly selective for GL-GL bonds (Scheme 3a). The nearly complete conversion of lactide combined with the

Table 1. Ring-expansion copolymerization of glycolide and L-lactide in bulk at 100 °C with variation of catalyst and (mon/cat ratio = 1000/1; 22 h).

Exp. No.	Catalyst	Conversion LA [%] ^{a)}	GL	Average block length of GL ^{b)}	M _n	M _w
1	DSTL	≈30–35	85–90	≈5	56°400	86°600
2	BuSnBuca	≈40–45	>90	≈4	12°700	30°500
3	BuSnBiph	≈40–45	>95	≈4	67°000	110°700
4	SnBiph	>80	>95	≈4	19°400	46°300

^{a)}mon = sum of both monomers; ^{b)}intensity of GL4 tetrad relative to the averaged intensity of another tetrad.

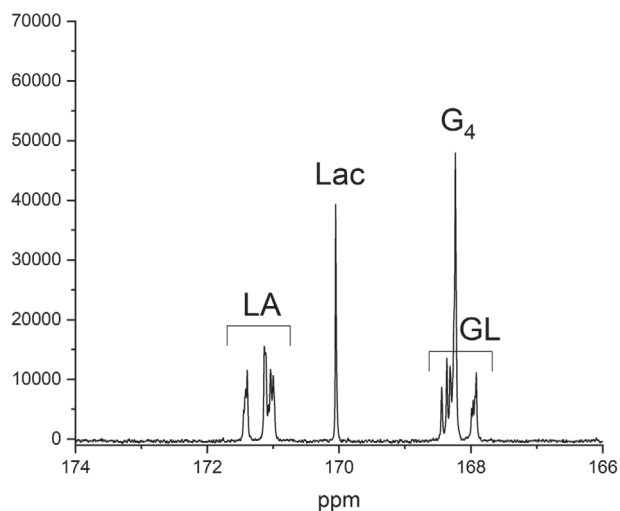


Figure 2. ^{13}C NMR spectrum (CO-signals) of a copoly(LA-GL) polymerized at $100\text{ }^\circ\text{C}/22\text{ h}$ with BuSnBuCa (No. 3, Table 1).

survival of LA-LA bonds also demonstrates again, that the cisoid LA-LA bonds in the dimeric monomer are more reactive than the preferentially transoid ester bonds in the polymer backbone.

When the time was extended to 22 h, both ^1H NMR and ^{13}C NMR spectra indicated that the conversion of both monomers was above 95%. The MALDI-TOF mass spectra displayed peaks of cycles containing even and odd numbers of lactyl units combined with even and odd numbers of glycolyl units, as expected for (nearly) random sequences (Figure 3B and Scheme 3b). Due to formation of cycles based on odd numbers of LA units, the number of cycles doubled, and the mass spectra were more crowded with peaks, so that the signal-to-noise ratio decreased (Figure 3B). Furthermore, the ^{13}C NMR CO-signals, evidenced that in all four experiments nearly random sequences were formed with average block lengths in the range of 2.1–2.8. **Figure 4** is a representative example of such signal pattern (two more examples are presented in Figures S4,S5, Supporting Information). All these analytical data agree with each other and with the afore-mentioned solubility in neat chloroform. Clearly, the long reaction time has favored intensive transesterification.

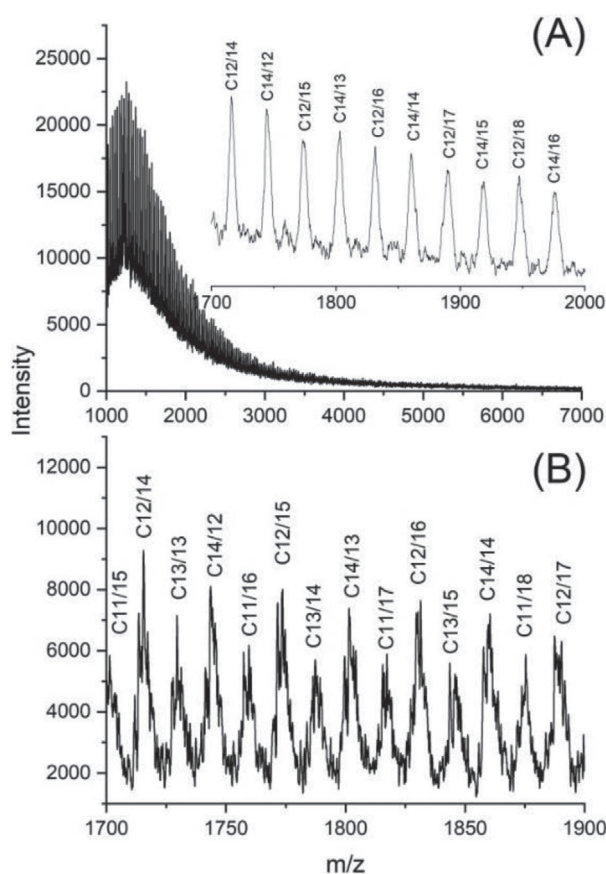


Figure 3. MALDI-TOF mass spectra of copoly(LA-GL) polymerized at $160\text{ }^\circ\text{C}$ with BuSnBuCa: A) stopped after 0.7 h (No. 2A, Table 2); B) after 22 h (No. 2B, Table 2).

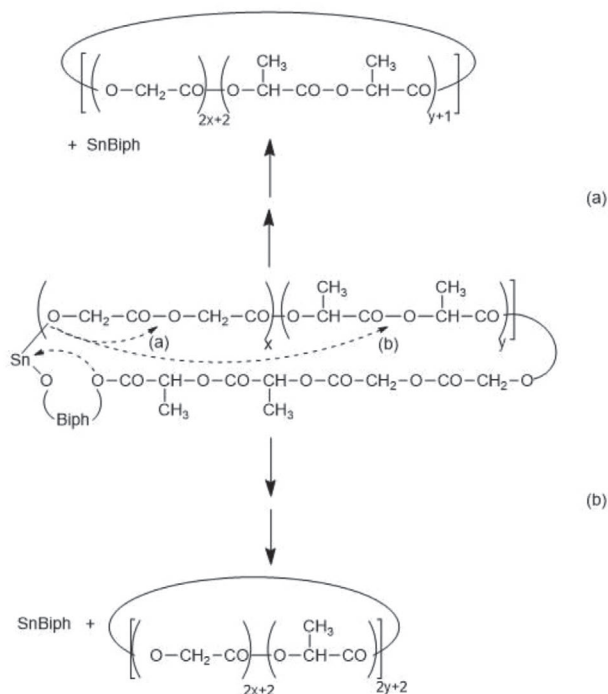
2.3. SEC Measurements

The size exclusion chromatography (SEC) measurements were performed in HFIP, so that the vast majority of the copolyesters were soluble. Particularly interesting was the comparison of the catalyst with the lowest reactivity (DSTL) with the most reactive catalyst (SnBiph). As demonstrated in **Figure 5**, at $100\text{ }^\circ\text{C}$ DSTL yielded only a low molar mass copolyester. In contrast, high molar mass copolyesters were obtained from the

Table 2. Ring-expansion copolymerization of glycolide and L-lactide in bulk at $160\text{ }^\circ\text{C}$ with variation of catalyst and time (mon/cat ratio = 1000/1).

Exp. No.	Catalyst	Time [h]	Conversion LA [%] ^{b)}	GL	Average block length of GL ^{c)}	Single lactyl units	M_n	M_w
1A ^{a)}	DSTL	3	≈40	>90	≈5	no	30°500	56°500
1B		22	>97	>95	≈2.8	yes	5°500	9°000
2A	BuSnBuCa	0.7	≈40	>95	≈4	no	33°000	64°900
2B		2	>95	>95	≈2.7	yes	13°500	37°000
3A	BuSnBiph	0.5	≈40	>95	≈4	no	55°000	113°000
3B		22	>95	>95	≈2.7	yes	18°000	51°200
4A	SnBiph	0.5	≈35	>95	≈5	yes, low conc.	28°300	97°700
4B		22	>95	>95	≈2.1	yes	38°000	78°000

^{a)}mon = sum of both monomers; ^{b)}estimated from ^1H NMR spectra; ^{c)}estimated from ^{13}C NMR spectra.



Scheme 3. Formation of lactide-glycolide copolymers a) without and b) with transesterification of the LA-LA bonds.

SnBiph catalyst under identical conditions (Figure 5B) in agreement with an almost complete conversion of both monomers. When the copolymerization was conducted at 160 °C for 22 h, the SEC curves of the copolyesters prepared by both catalysts were similar (Figure 6A,B) in agreement with almost complete conversion and complete transesterification of both monomers. Conspicuous are two small maxima in the low molar mass region. The multimodal character of these curves has the consequence that calculation of dispersities does not make much sense. The SEC curves of the copolyesters polymerized with

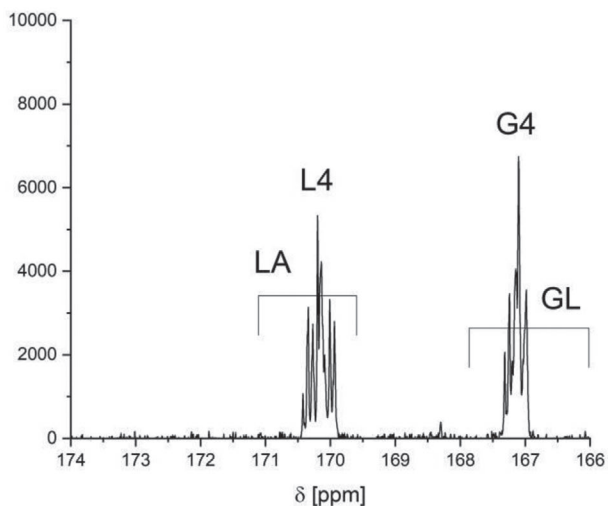


Figure 4. ^{13}C NMR spectrum of the copoly(LA-GL) polymerized at 160 °C/22 h with DSTL (No. 1B, Table 2).

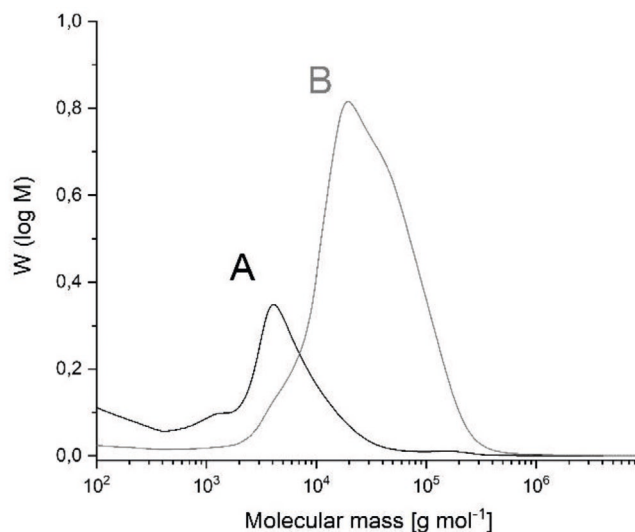


Figure 5. SEC curves of copoly(LA-GL) polymerized at 100 °C/22 h: A) with DSTL (No. 2, Table 1); B) with SnBiph (No. 5, Table 1).

BuSnBuca or BuSnBi are displayed in Figures S3 and S4, Supporting Information. Finally, it should be mentioned, that polystyrene-calibrated SEC measurements of aliphatic polyesters overestimate the real molecular weights by 50–60%, depending on structure and solvent. To what extent such an overestimation also exists for polymethylmethacrylate (PMMA)-calibrated SEC measurements in HFIP is unknown to the best knowledge of the authors.

2.4. Copolymerizations of L-Lactide with Little Glycolide

Copolymerizations of GL and LA with variation of the GL/LA ratio were studied by Gilding and Reed as early as 1979.^[12] Those authors performed these copolymerizations at 200 °C

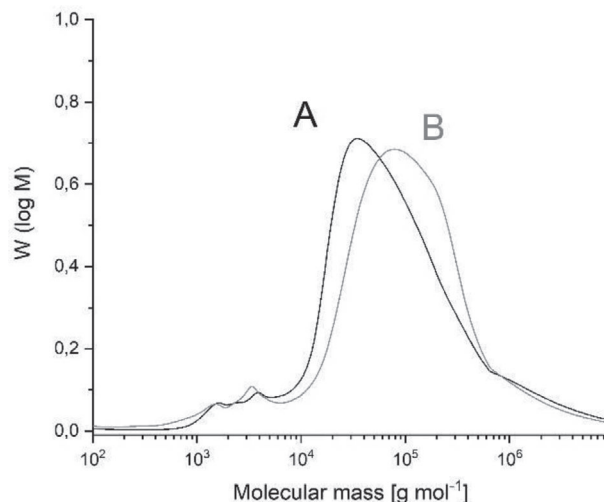


Figure 6. SEC elution curves of copoly(LA-GL) polymerized at 160 °C/22 h: A) with DSTL (No. 1B, Table 2); B) with SnBiph (No. 4B, Table 2).

so that formation of nearly random sequences is highly probable, although not experimentally proven. It was found that between 25 and 70 mol% of glycolide the resulting copolyesters were amorphous. At lower fractions of GL blocks of LA crystallized, whereas at higher fractions of GL blocks of GL crystallized. These and similar studies were all conducted with linear copolymers prepared with alcohol-initiated polymerizations catalyzed by SnOct₂ or zinc powder and zinc complexes. The crystalline blocks of LA adopted the normal orthorhombic crystal lattice first described by Desantis and Kovacs^[29] and formed a morphology with a low degree of 3D order of crystallites. Depending on the content of GL, glass-transition temperatures (T_g values) in the range of 37–57 °C were found.^[12] For poly(L-lactide) annealed in absence of a catalyst or in the presence of poisoned SnOct₂ a T_m of 180 °C is the upper limit as reported by several research groups (so-called LT_m crystallites).^[30–35]

Quite recently, the authors of this study discovered a second, thermodynamically more stable kind of crystallites, which is characterized by higher melting points (189–196 °C, so-called HT_m crystallites).^[30] Furthermore, high degrees of crystallinity (70–90%) and a relatively high 3D order of the crystallites were detected. Moreover, it was found that not only temperature, time, and reactivity of the catalyst play a role for the formation of HT_m crystallites and this morphology, but also the polymerization mechanism. REPs with cyclic tin catalysts turned out to be far more favorable than alcohol initiated ROPs. In this context, it was of interest to elucidate how much GL is compatible with the formation of HT_m crystallites, a question which has not been studied before. Therefore, several copolymerizations with systematic variation of the GL content were performed under conditions optimum for formation of HT_m crystallites. The results summarized in **Table 3** allow for the following conclusions.

First, even the presence of only 2 mol% of GL severely hindered the formation of HT_m crystallites. After 44 h at 160 °C only part of the reaction mixture had crystallized and after crystallization of the majority of the sample at 120 °C two endotherms were observable. The first one at 173 °C corresponds to LT_m crystallites formed at 120 °C, whereas the second one at 189 °C originates from the HT_m crystallites formed at 160 °C (Figure S7A, Supporting Information). With 4% of GL one

Table 3. Ring-expansion copolymerization of LA and little GL in bulk at 160 °C/22 h with variation of the GL/LA ratio; catalyst: SnBiph (mon/cat = 1000/1).

Exp. No.	GL [mol%]	M_n	M_w	T_m [°C]	ΔH_m [J g ⁻¹]	Cryst. [%] ^{c)}
1 ^{a)}	0	68°000	157°000	192.0	66	62
2 ^{b)}	2	57°000	124°000	173.5°+°189.0	46	43
3 ^{b)}	4	55°000	113°000	160/166	36	34
4 ^{b)}	8	51°000	119°000	153.0	37	35
5 ^{b)}	12	47°000	107°000	151.0	23	22
6 ^{b)}	20	39°000	99°000	137.5	1	1
7 ^{b)}	30	35°000	81°000	-	-	-

^{a)}mon means the sum of both monomers; ^{b)}after annealing at 120 °C for 2h; ^{c)}calculated with $\Delta H_{m\max} = -106$ J g⁻¹.

broad endotherm around 166 °C appeared in the DSC trace (Figure S7B, Supporting Information). All samples containing more than 4 mol% of GL were transparent melts after 44 h at 160 °C. After annealing at 120 °C, crystallization was observable for samples containing up to 12 mol% of GL and only one small and broad endotherm appeared in the DSC traces. The T_m and melting enthalpies decreased as expected with higher mol fractions of GL. With 20 mol% of GL only a turbidity resulting from tiny crystallites was observable after 22 h at 20 °C (which disappeared after heating to 170 °C), but no melting endotherm showed up in the DSC heating trace. This means that 20 mol% of GL is the limit above which the GL units prevent crystallization even under optimum conditions. Gilding and Reed reported for linear copolyesters prepared by SnOct₂-catalyzed ROP at 200 °C/5 min, that the crystallinity vanished completely at a GL content of 25 mol%, which is in good agreement with the results obtained in this work.^[12]

The MALDI-TOF mass spectra showed a good resolution of peaks representing cycles with a characteristic individual composition, when the content of GL was low (**Figures 7 and 8A**). The predominant species were cycles bare of GL units which were detectable up to masses around m/z 8000 corresponding to DPs around 110 (Figure 8A). Even and odd cycles were present in equal quantities proving complete transesterification of LA–LA bonds. Cycles containing one or more GL-units were also clearly detectable. With higher mol fractions of GL units the intensities of mass peaks representing GL containing cycles

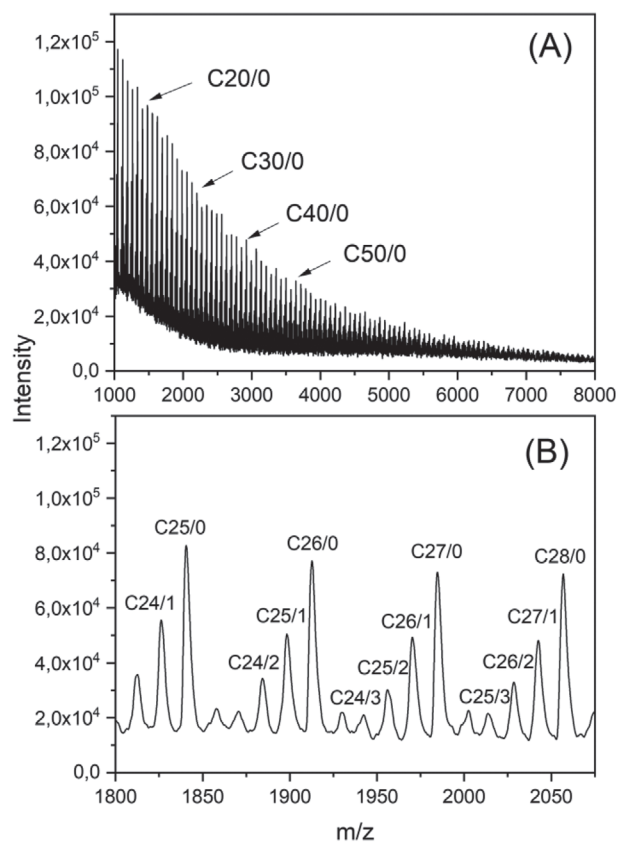


Figure 7. MALDI-TOF mass spectra of copoly(LA–GL) prepared with 2 mol% of GL at 160 °C/22 h catalyzed by SnBiph.

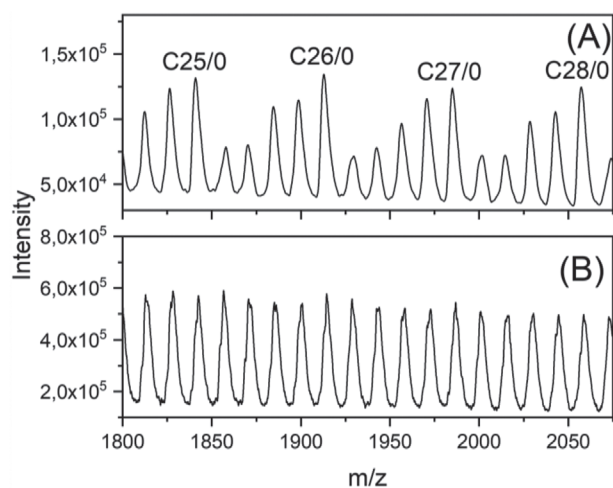


Figure 8. MALDI-TOF mass spectra of copoly(LA-GL) polymerized with SnBiph at 160 °C/22 h: A) containing 4 mol% of GL; B) containing 30 mol% of GL.

increased as evidenced by comparison of Figures 7B and 8A. At higher GL contents the good resolution vanished due to the multitude of cycles with different GL/LA ratios (Figure 8B).

2.5. Copolymerization of Glycolide with Little L-Lactide

Several copolymerizations with high G/L ratios were performed to study the influence of LA on the solubility of polyglycolide. At this point, it is worth noting that the solubility of homopolymers of glycolic acid is a poorly understood phenomenon. Poly(glycolic acid) prepared by polycondensation of glycolic acid is usually soluble in neat HFIP, whereas the polymer prepared by ROP of glycolide is usually partially or completely insoluble. This phenomenon is, for example, documented by the commercial polyesters available from Sigma-Aldrich, which both offers a soluble poly(glycolic acid) and an insoluble polyglycolide. However, this phenomenon has not been studied in detail and explained in the literature.

When neat GL was polymerized with the four catalysts used in this work, the resulting polyglycolides were insoluble in HFIP regardless, if these polymerizations were performed

at 100, 130, 160, or 190 °C. Since all copolymers prepared in this work at 100 or 160 °C were completely soluble, the insolubility of the homopolymers cannot be ascribed to intensive crosslinking, and differences in crystallinity and/or morphology must be responsible for the different solubilities of poly(glycolic acid) and polyglycolide.

The polymerization experiments with increasing fractions of L-lactide were conducted with SnBiph as catalyst at 160 °C for 22 h (Table 4), what means under conditions favoring nearly random sequences of both comonomer (B experiments in Table 2).

Copolyesters containing 2, 4, or 8% of L-lactide were completely insoluble in HFIP. At 12% lactide it was possible to extract a small fraction and to record a MALDI-TOF mass spectrum. However, even the sample containing 20% of L-lactide crystallized at 160 °C and with 30% of L-lactide the sample was almost transparent (but somewhat turbid) indicating the presence of tiny crystallites formed by blocks of glycolide. Only with 40% of L-lactide, the copolyester looked perfectly transparent. Complete solubility in HFIP was achieved with 20% of lactide, but even 40% of lactide did not suffice to enable complete dissolution in chloroform or dichloromethane. Since the crystallinity detectable by DSC measurements vanishes above a content of 20% of L-lactide, the incomplete solubility of the 60/40 copolyester in chloroform must be based on tiny crystallites formed by short blocks of GL units. The size of these crystallites is too small to scatter visible light and their quantity was too low to cause a melting endotherm in the DSC heating trace.

The finding that melting point and melting enthalpy decreased steadily with the molar fraction of L-lactide suggests that lactide was randomly distributed in the polyester chain, perhaps not from the beginning of the polymerization, but due to transesterification during the long period of annealing at 160 °C as discussed above. Three characteristic examples of DSC curves are displayed in Figure S8, Supporting Information. This conclusion is supported by the MALDI-TOF mass spectra of the samples containing 12 or more percentage of lactyl units. Although the reactivity of glycolide is considerably higher than that of LA, cyclic oligoglycolides devoid of LA units were not detectable. Furthermore, cycles containing odd-numbers of lactyl units were present indicating transesterification of the LA-LA bonds.

Table 4. Ring-expansion copolymerization of GL with little LA in bulk at 160 °C/22 h with variation of the GL/LA ratio catalyst SnBi (mon/cat = 1000/1).

Exp. No.	LA [mol%]	Solubility in HFIP at 40–50 °C	M_n	M_w	T_m [°C]	ΔH_m [J g ⁻¹]
1 ^{a)}	0	insol.	-	-	225	-
2	2	insol.	-	-	220	117.5
3	4	insol.	-	-	212–218	113.0
4	8	insol.	-	-	216	108.5
5	12	mainly insol.	31°000	110°000	212	45.0
6	20	mainly gel	59°500	147°000	196.5	33.0
7	30	solution ^o +°gel particles	70°000	185°000	-	-
8	40	soluble	64°500	173°000	-	-

^{a)}mon means the sum of both monomers.

2.6. Discussion of Topology

The MALDI-TOF mass spectra indicate that the copolyesters prepared in this work by REP have cyclic topology in the mass range below m/z 10^6 . This finding and the fact that numerous REPs of neat L-lactide performed under the same conditions with the same catalysts yield cyclic high molar mass polylactides suggest that the high molar mass fraction of the LA/GL copolyesters also consists mainly of cycles. However, a definite proof is difficult to obtain, because a comparison of linear and cyclic copolyesters for instance via their intrinsic viscosity requires identical sequences and compositions. Yet, the polymerization mechanisms yielding linear and cyclic copolymers are different and the solubilities and hydrodynamic volumes of copolyesters derived from glycolide are highly sensitive to slight variations of composition and sequence. A technical problem might be the stability of the analytical equipment against the aggressive solvent HFIP, which is needed for the 1/1 copolyesters.

However, for chloroform soluble copolymers containing only 2 or 4 mol% of GL (Table 3) a linear polylactide, such as the commercial PURAPOL L105, may be acceptable for comparison of the intrinsic viscosities, in as much as such Mark-Houwink-Sakurada (MHS) measurements are not highly accurate anyway. As demonstrated by Figure 9, the MHS measurements of the 2% and 4% copolyesters (Nos. 2 and 3, Table 3) prove that also the high molar mass fraction of these copolyesters almost exclusively consists of cycles. The intrinsic viscosities of the copolyesters are $\approx 30\%$ lower than that of the linear counterpart as expected for $>90\%$ cyclization. Differentiation between 95% and 99% of cycles is impossible in this way, but a more accurate method does not exist. Hence, in agreement with the mass spectra these MHS measurements confirm that ring-expansion copolymerization of glycolide does not hinder formation of cyclic copolyesters, a result that was, in principle predictable.

This view is supported by dn/dc measurements of the three sample numbers 1B, 2B, 3B, and 4B (Table 2). Although composition and sequence were quite similar, their dn/dc values,

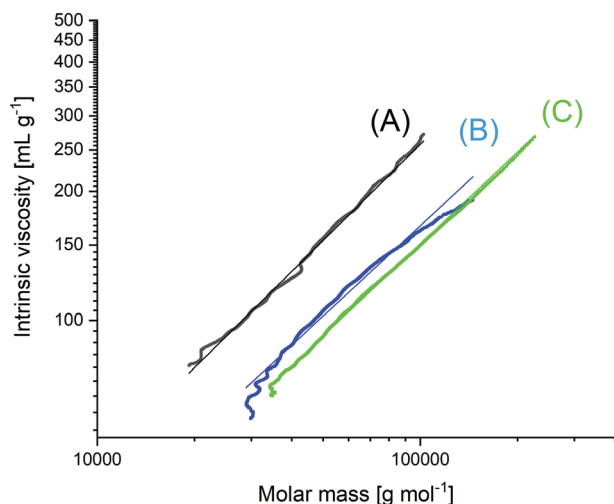


Figure 9. Comparison of intrinsic viscosities of: A) linear poly(L-lactide) Purapol L105 and B,C) copolyesters containing 2% and 4% glycolide (No. 2 and 3, Table 3).

which are sensitive to hydrodynamic volume and composition scattered within the range of 0.159 and 0.162. Therefore, the authors could not definitely prove that the high molar mass fraction of their copolyesters almost completely consists of cycles.

3. Conclusion

Copolymerizations of glycolide and L-lactide at a molar ratio of 1:1 in bulk, catalyzed by DSTL, BuSnBuCa, BuSnBiph, or SnBiph yield copolyesters having molecular weights (M_w) up to 120^6 g mol $^{-1}$. Both composition and sequence depend on the reactivity of the catalyst, on temperature and time, so that solubility and other properties can be varied over a broad range. When these catalysts are used at 160 °C and long reaction times, complete conversion of both monomers and nearly random sequences can be obtained based on total transesterification of both, GL-GL and LA-LA bonds. With short times reaction at 160 °C, the conversion of lactide may be incomplete and the LA-LA bonds do not undergo transesterification, so that cycles exclusively based on even numbers of lactyl units are formed. Under the conditions of total transesterification crystallinity and solubility vary systematically with the LA/GL ratio.

4. Experimental Section

Materials: Glycolide was kindly supplied by Boehringer (Ingelheim/Rhein, Germany). It was recrystallized from a tetrahydrofuran toluene mixture ($v/v = 8/2$), by dropwise addition of toluene at 60 °C until crystallization began. After cooling to room temperature (22 °C) over night, the crystallized glycolide was isolated by filtration under a blanket of argon. L-lactide (a product of PURAC) was kindly supplied by Thyssen-Uhde AG (Berlin) and recrystallized from "Toluene 99.89% extra dry" purchased from ACROS Chem. (Geel, Belgium). The syntheses of the catalysts, SnBiph, BuSnBiph, BuSnBuCa, and DSTL (see Scheme 2) were described previously.^[22–26] Anhydrous tetrahydrofuran was purchased from Alfa Aesar (Karlsruhe, Germany) and HFIP was obtained from Sigma Aldrich (Taufkirchen, Germany).

Copolymerizations: A. At 100 °C: The catalyst (0.2 mmol) was weighed into a flame-dried 50 mL Erlenmeyer flask. Glycolide (20 mmol), L-lactide (20 mmol), and a magnetic bar were added under a blanket of argon. The reaction vessel was immersed into an oil bath thermostated at 100 °C and the resulting crystalline copolyester was isolated after destruction of the reaction vessel.

B. At 160 °C: The catalyst (0.04 mmol) was weighed into a flame dried 50 mL Erlenmeyer flask, a magnetic bar, glycolide (20 mmol), and L-lactide (20 mmol) were added under a blanket of argon. The reaction vessel was immersed into an oil bath preheated 161 °C. After 10 min the temperature was lowered to 160 °C. With exception of DSTL, which needed 20 min to yield a high viscosity, the reaction mixture turned viscous within 10 min. After the reaction vessel was removed from the oil bath, most of the transparent, amorphous looking copolyesters were removed from the reaction vessel by means of a spatula and pincer.

Measurements: The 600 MHz ^1H NMR spectra and the 150.4 MHz ^{13}C NMR spectra were recorded on a Bruker Avance III 600 FT spectrometer in 5 mm sample tubes. A mixture of hexafluoroisopropanol and CDCl_3 ($v/v = 7/3$) served as solvent. The ^{13}C NMR spectra were accumulated over a period of 4 h.

The DSC heating traces were recorded on a (freshly with indium and zinc calibrated) Mettler-Toledo DSC-1 equipped with Stare Software-11 using a heating rate of 10 K min $^{-1}$. Only the first heating traces were evaluated.

MALDI-TOF mass spectra were recorded on an Autoflex Max (Bruker Daltonik, Bremen, Germany). Spectra were recorded in linear mode at

2000 Hz. The matrix solution (DCTB–trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile, 10 mg mL⁻¹, chloroform) was doped (0.5%) with potassium trifluoroacetate (KTFA 2 mg mL⁻¹, water/tetrahydrofuran) to selectively enable the formation of potassium adduct ions. 20 µL of dissolved samples (5 mg mL⁻¹, chloroform) were mixed with 50 µL of the matrix solution. Finally, 1 µL of the combined solutions was deposited on a stainless-steel target. Typically, 8000 single spectra were recorded on four different positions and accumulated for one spectrum. The manufactures software (FlexControl and FlexAnalysis) were used for recording and evaluation.

SEC measurements in chloroform (experiments listed in Table 3) were performed using a modular system consisting of an isocratic pump (chromophore C 1130) running at 1 mL min⁻¹ flow rate. The system was kept at 40 °C. Samples with a concentration of 2–4 mg mL⁻¹ were manually injected by a Rheodyne valve (100 µL). A triple detector combination was used consisting of a refractive index detector RI-501 (Shodex), a multi angle laser light scattering detector DAWN, and a viscometer Viscostar (both Wyatt Germany, Dernbach). Manufacturer software (Clarity GPC extension, DataApex) was used for instrument control and molecular weight calculation, whereas the MHS calculations were performed using ASTRA 6 (Wyatt). The calibration was performed using commercially available polystyrene standard sets (Polymer Standards Service–PSS, Mainz, Germany). In addition, SEC measurements were performed in HFIP (Sigma-Aldrich, Germany). For these experiments, an Agilent 1200 HPLC system (Agilent, USA) with two PFG columns (M7 and A7 from PSS) equipped with a RI detector (Agilent) was used. The flow rate was 1 mL min⁻¹ and 100 µL of a dissolved sample (2–3 mg mL⁻¹ in HFIP) were manually injected. The system temperature was 35 °C. For calibration, a set of PMMA standards from PSS (Mainz, Germany) were applied. WINGPC software (PSS) was used for calibration and to calculate molecular masses. Due to additional small peaks caused by solvent and low mass impurities, the calculation of the number average (M_n) and weight average (M_w) molecular weights and the dispersities \bar{D} started from 1100 g mol⁻¹ onward. Therefore, the molecular mass calculation probably did not include all oligomers, which, however, had only little influence on M_w , but resulted in M_n values that might be too low. Thus, dispersities \bar{D} could be underestimated as well.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

copolymerization L-lactide, crystallization, glycolide, MALDI-TOF mass spectrometry, ring-expansion polymerization

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