

Syntheses of Polyglycolide via Polycondensation: A Reinvestigation

Hans R. Kricheldorf,* Steffen M. Weidner, and Andreas Meyer

The Na salt of chloroacetic acid is condensed in suspension. Furthermore, glycolic acid is condensed in bulk or in concentrated solution by means of SnCl_2 or 4-toluene sulfonic acid (TSA) as catalysts. The temperatures are varied from 160 to 200 °C and the time from 1 to 5 days. Low molar mass cyclic poly(glycolic acid) (PGA) is detected by means of matrix-assisted laser desorption ionization time-of-flight (MALDI TOF) mass spectrometry in most PGAs. A predominance of certain cycles having an even number of repeat units is observed suggesting a thermodynamically favored formation of extended-ring crystals. Extremely high melting temperatures (up to 237.5 °C) and high melting enthalpies are found for polycondensations with TSA in 1,2-dichlorobenzene.

The first synthesis of high molar mass PGA was described by Higgins in a patent of DuPont^[7] hundred years after the first publication.^[1] In that patent glycolic acid served as monomer (Scheme (b)), and molecular weights sufficient for the extrusion of films were achieved, when the primary polycondensation process was combined with solid state polycondensation at temperatures between 215 and 220 °C. In the following 70 years, several publications appeared dealing with syntheses of PGA via polycondensation methods, either using chloroacetic acid salts^[8–10] or glycolic acid^[11–13] as monomers. Partially because a suitable analytical method

1. Introduction

Poly(glycolic acid) (PGA) was prepared by two quite different polymerization strategies, namely by ring-opening polymerization of glycolide and by polycondensation of glycolic acid or haloacetic acids. The history of PGA begins with polycondensation chemistry, because glycolide was not available for a long time. The first synthesis of (low molecular mass) PGA was achieved by polycondensation of hydroxy malonic acid which upon heating lost CO_2 yielding glycolic acid, which was the true monomer.^[1] The following publications were all dealing with polycondensations of bromo or chloroacetic acid salts (Scheme 1a).^[2–6]

was lacking and partially because the researchers working after 1998 did not use MALDI TOF mass spectrometry, the question was never discussed, whether the afore-mentioned polycondensation processes involve formation of cyclic PGA or not. Another open question concerns the molecular weights of PGAs prepared from sodium (or potassium) chloroacetate. The research groups that used this method purified their reaction products by washing with water to remove the inorganic salts prior to characterization of the PGAs. Yet, since PGA is highly sensitive to hydrolysis such a purification will reduce the molecular weights due to partial hydrolysis. In this context, the first objective of this work was to find out whether the syntheses of PGA by the above-mentioned polycondensation methods are accompanied by cyclization. A second objective was to identify the end groups of the linear PGAs prepared by polycondensation of sodium chloroacetate. The third objective of this work was to elucidate the molecular masses of virgin PGAs prepared by polycondensation of sodium chloroacetate. Fourth, the properties of PGAs prepared by polycondensation of Na-chloroacetate should be compared with those obtained by polycondensation of glycolic acid.

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DOI: 10.1002/macp.202300397

2. Experimental Section

2.1. Materials

Glycolic acid and chloroacetic acid, SnCl_2 and toluene sulfonic acid (TSA) monohydrate, were all purchased from Alfa-Aesar (Thermo-Scientific Fisher, Kandel or Schwerte Germany) and used as received. Anhydrous dichloromethane (CH_2Cl_2), 1,2-dichlorobenzene (1,2-DCB) and 1,2,4-trichlorobenzene (1,2,4-TCB) were also purchased from Thermo-Scientific-Fisher (Schwerte, Germany) and used as received.

Table 1. Polycondensation of sodium chloroacetate in suspension^{a)}.

Exp. No.	Reaction medium	Temp. [°C]	Time [h]	T_m [°C]	ΔH_m^b [J g ⁻¹]
1A	1,2-DCB	160	4	–	–
1B	1,2-DCB	160	24	207.4 + 220.2	52.4
2	1,2-DCB	180	4	209.5 + 221.4	53.4
3	1,2,4-TCB	180	4	207.2 + 220.0	53.7
4	1,2,4-TCB	200	4	219.6	57.8

^{a)} Due to the content of NaCl calculation of yields was not feasible; ^{b)} Due to the content of NaCl calculation of crystallinity was not possible.

Table 2. Polycondensation of glycolic acid in bulk or in 1,2-DCB at 180 °C/24 h.

Exp. No.	Catalyst	Solvent	T_m [°C]	ΔH_m^a [J g ⁻¹]	Cryst. [%]
1	SnCl ₂	–	221.5	135.3	66
2	TSA	–	226.1 + 230.0	143.4	70
3	SnCl ₂ +TSA	–	220.1	136.5	66
5	Bi-triflate	–	219.0	105.1	51
6	SnCl ₂	+++	219.6	142.3	69
7	TSA	+++	233.1 + 236.6	138.5	67
8	SnCl ₂ +TSA	+++	219.2	114.6	56

^{a)} Calculated with $\Delta H_m^0 = 206$ J g⁻¹.

2.2. Polycondensation of Sodium Chloroacetate (Table 1)

Sodium chloroacetate (40 mmol) was weighed into a 50 mL Erlenmeyer flask, 1,2-DCB or 1,2,4-TCB (20 mL) and a magnetic bar were added. The reaction vessel was immersed into an oil bath thermostated at 160, 180, or 200 °C. Finally, the cold suspension was diluted with ≈50 mL of dichloromethane, the product was isolated by filtration, washed with dichloromethane, and dried at 80 °C in vacuo.

2.3. Polycondensations of Glycolic Acid in Bulk or in 1,2-DCB (Table 2)

A) Polycondensations in Bulk:

A catalyst (0.6 mmol) and glycolic acid (60 mmol) were weighed into a 50 mL round-bottom flask under a blanket of argon. A magnetic bar was added. The reaction vessel was closed with a kind of glass-stopper having a hole with a diameter of 3 mm allowing for the evaporation of water. The reaction vessel was placed into an oil bath thermostated at 180 °C. A few minutes after dissolution of the glycolic acid, evaporation of water became detectable. After 24 h SbCl₂ and TSA·H₂O were added in equimolar amounts, each catalyst in a quantity of 0.5 mmol.

B) Polycondensations in 1,2-Dichlorobenzene

These polycondensations were performed analogously, but 20 mL of 1,2-DCB were added prior to heating. After cooling the precipitated PGA was washed twice with dichloromethane and dried at 80 °C in vacuo.

2.4. Polycondensation of Glycolic Acid in Solution Catalyzed by TSA (Table 3)

A catalyst (0.5 mmol) and glycolic acid (50 mmol) were weighed into a 50 mL round-bottom flask under a blanket of argon, and

a magnetic bar and 1,-dichlorobenzene (20 mL) were added. The reaction vessel was closed with a kind of stopper having an opening with a diameter of 3 mm. The reaction vessel was placed into an oil bath thermostated at 180 °C. The evaporation of water became detectable within the first 51 min and the formation of solid particles began within the first hour. After cooling the precipitated PGA was washed twice with dichloromethane and dried at 80 °C in vacuo. Since part of the PGA stuck to the glass walls, it did not make sense to determine yields. The PGAs listed in Table 3 had an ochre color when prepared in anisole or a grey color when prepared in chlorinated benzenes.

2.5. Measurements

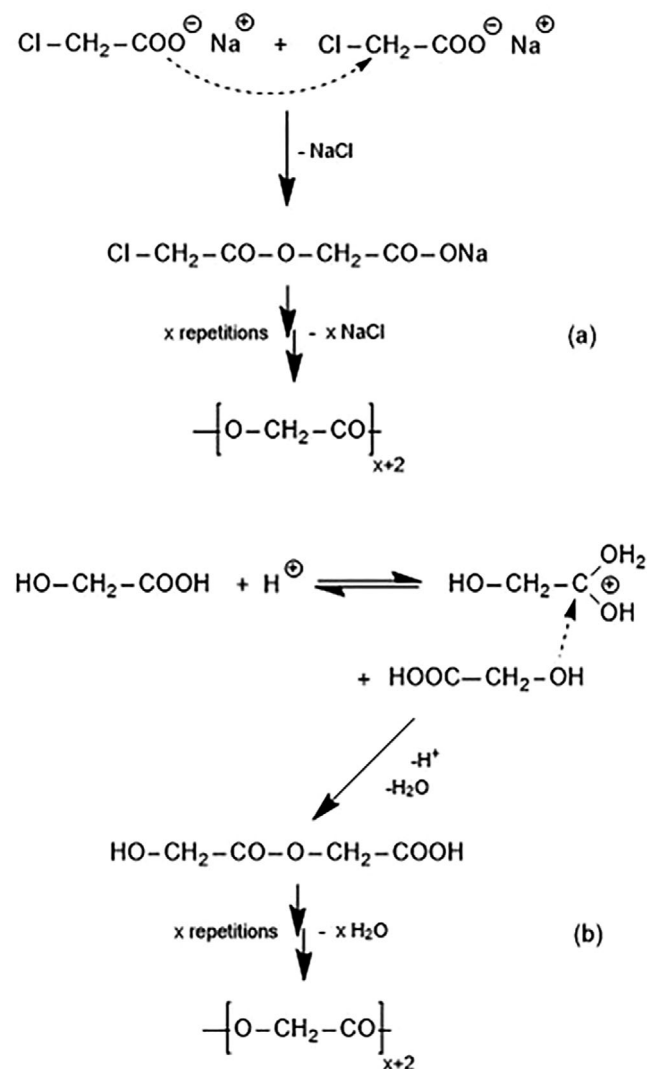
The MALDI TOF mass spectra were measured with Autoflex maX mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with a Smartbeam laser ($\lambda = 355$ nm). All spectra were recorded in the positive ion linear mode. The MALDI stainless steel targets were prepared from solutions of PGA in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) and doped with potassium trifluoroacetate (2 mg mL⁻¹). Typically, 20 μ L of sample the solution, 2 μ L of the potassium salt solution and 50 μ L of a solution of trans-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene] malononitrile (DCTB, 20 mg mL⁻¹ in HFIP) serving as matrix were mixed in an Eppendorf vial. 1 μ L of the corresponding solution was deposited on the MALDI target. FlexControl (Bruker Daltonik GmbH) was used to record spectra by accumulating 2000 single laser shots recorded at 4 different positions.

The GPC measurements were performed in a modular system kept at 30 °C consisting of an isocratic pump (Agilent, USA) running with a flow rate of 0.5 mL min⁻¹ and a refractive index detector (RI-501-Shodex). HFIP was used as eluent. Samples were manually injected (100 μ L, ≈2–4 mg mL⁻¹). For instrument control and data calculation WinGPC software (Polymer Standard

Table 3. TSA-catalyzed polycondensations in solution with variation of solvent, temperature, and time.

Exp. No.	Solvent	LA/Cat	Temp. [°C]	Time [h]	T_m [°C]	ΔH_m [J g ⁻¹]	Cryst. ^{a)} [%]	L [nm]
1b ^{b)}	Anisole	200/1	160	48	211.6	105.3	52	–
1B	Anisole	200/1	160	120	218.6	149.0	72	8.0
2A ^{c)}	1,2-DCB	200/1	180	24	221.3	156.9	76/69	8
2B	1,2-DCB	200/1	180	48	223.3	153.2	74	8
2C	1,2-DCB	200/1	180	120	222.8	168.2	81	8
2C ^{d)}	1,2-DCB	200/1	180	120	225.3	172.1	83	8
3A	1,2-DCB	100/1	180	24	223.6	156.0	76	8
3B	1,2-DCB	100/1	180	48	235.7 + 237.7	152.6	74	8
4	1,2-DCB	400/1	180	24	206.8 + 211.0 + 213.5	130.3	52	8
5A	1,2,4-TCB	200/1	200	24	222.0 + 228.1	127.5	51	–
5B	1,2,4-TCB	200/1	200	48	234.7	132.5	63	8

^{a)} Calculated with $\Delta H_m^0 = 206 \text{ J g}^{-1}$; ^{b)} $M_n = 3500/M_w = 14 \text{ 500}$; ^{c)} $M_n = 3100/M_w = 10 \text{ 100}$; ^{d)} Tris(4-nonylphenyl)phosphite was added.



Service-PSS now Agilent, Mainz, Germany) was used. The calibration was performed using a polymethylmethacrylate (PMMA) standard set (Polymer Standards Service – PSS, Mainz).

The DSC heating traces were recorded on a (with indium and zinc freshly 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. The crystallinities were calculated with a ΔH_m max of -206 J g^{-1} .

The SAXS measurements were performed using our in-house SAXS/WAXS apparatus equipped with an Incoatec X ray source I μ S and Quazar Montel optics. The wavelength of the X ray beam was 0.154 nm and the focal spot size at the sample position was 0.6 mm^2 . The samples were measured in transmission geometry and were recorded with a Rayonix SX165 CCD-Detector. The SAXS measurements were performed at sample-detector distance of 1.6 m and the accumulation was 1200 s for each position. DPDAK, a customizable software for reduction and analysis of X-ray scattering data sets was used for gathering 1D scattering curves.^[14] For the evaluation of the crystallinity of the samples the data were imported in Origin and analyzed with the curve fitting module. The SAXS curves were converted into Kratky plots. The long periods of the lamellar domains were determined by the q values of the reflection maxima.

3. Results and Discussion

3.1. Polycondensation of Sodium Chloroacetate

The polycondensation of sodium-chloroacetate is known to be an extremely exothermic process with the consequence of local overheating and discoloration when quantities larger than 5 g are used. Therefore, it has been recommended to “dilute” the monomer with copper shavings. In the present work it was attempted to control the heat flow by performing the polycondensation in suspension using an inert, high-boiling reaction medium such as 1,2-dichlorobenzene (1,2-DCB) or 1,2,4-trichlorobenzene (1,2,4-TCB). This attempt proved successful and no severe discoloration was observed meaning the color of the reaction product was off-white or slightly gray. The crude reaction mixture was characterized to avoid hydrolysis of the PGA by washing with water as it was usually conducted by other research groups. After 4 h

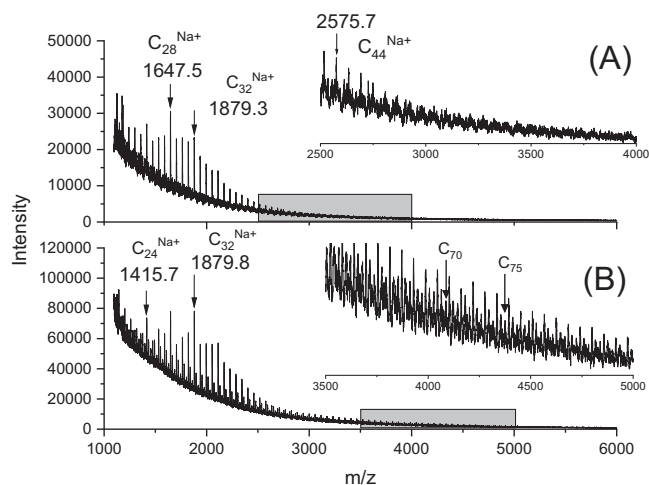


Figure 1. MALDI TOF mass spectra of PGAs prepared by polycondensation of Na-chloroacetate in suspension: A) 1,2-DCB, 160 °C /24 h (1B, Table 1), B) 1,2,4-TCB, 200 °C/4 h (No. 4, Table 1).

at 160 °C the conversion was still low as indicated by the observation that the vast majority of the material was still soluble in water. After 24 h (1B, Table 1) the conversion of Na-chloroacetate was almost complete as indicated by the insolubility of the reaction product in water. Complete conversion was also observed for all experiments at higher temperatures. Unfortunately, it was impossible to retrieve molecular weight data because the virgin reaction products were almost completely insoluble in HFIP. The samples were milled, and the resulting powders were stirred in HFIP at 50 °C for 20 h, but without success. This negative result is remarkable, because two other research groups reported on GPC measurements of PGAs dissolved in HFIP. However, the preparative procedures of other research groups were somewhat different and, presumably more important, the work-up procedure was quite different. Other research groups washed the crude reaction products intensively with water to remove the sodium chloride.^[9,10] Yet, GA is highly sensitive to hydrolysis, and thus, the virgin reaction products were characterized in the present study.

As expected from the strong electronic interactions between the densely packed PGA chains, it was difficult to obtain useful MALDI TOF mass spectra. Nonetheless, these mass spectra yielded the desired information. As demonstrated in **Figure 1**, the mass peaks of cycles dominated in the mass range below m/z 3 000 whereas the peaks of linear chains having one HO-CH₂- and one COOH end group were the prevalent species at higher masses. The mass spectra of PGAs isolated from experiments 2 – 4 (Table 1) were quite similar. A quite similar pattern was also found for the PGAs prepared from glycolic acid as will be discussed below. In the mass range below m/z 3000 an unusual and unexpected pattern of mass peaks was found with a slight predominance of certain even-numbered cycles having degrees of polymerization (DPs) of 24, 28 and 32 (labeled C₂₄, C₂₈ and/or C₃₂ in the mass spectra). Despite the poor signal-to-noise ratio (s/n), cycles up to DPs in the range of 75–80 were detected in the mass range above m/z 3 000 (Figure 1B). These results prove that the cyclization tendency in these polycondensation is quite high

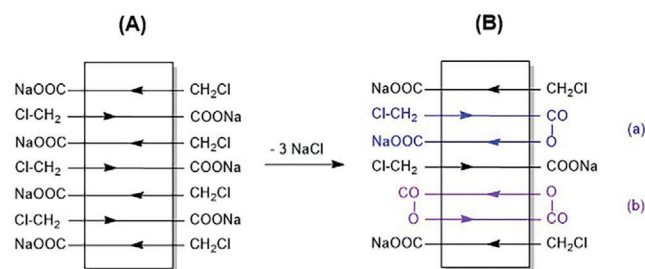


Figure 2. Schematic illustration of loop formation A) and cyclization B) via reactions of functional end groups on the surface of crystallites.

despite the high monomer concentration and despite a relatively low mobility of the PGA chains in the solid state. Polyglycolide is an extremely fast crystallizing polymer and even short oligomers can crystallize. Hence, it is unlikely that all the cycles with DPs in the range of 20–80 cyclized in the melt prior to crystallization.

The authors, therefore, propose an additional cyclization process which proceeds in the solid state and complements the cyclization reactions going on in the melt. This second cyclization process is schematically illustrated in **Figure 2**. PGA like polylactide crystallize for thermodynamic reasons with an antiparallel alignment of their chains. This statement is based on the X-ray analyses of crystalline PGAs and PLAs contributed by other research groups.^[15–17] In the case of PLA, which in contrast to PGA has been the subject of numerous studies on kinetic and thermodynamic aspects of crystallization, there is a general consensus that the α -modification with antiparallel helical chains is the most thermodynamically stable crystal modification.^[17] Polypeptides also adopt an antiparallel orientation in the β -sheet structure. The antiparallel alignment of the PGA chains results in an alternating arrangement of the two functional end groups is formed on both surfaces. Hence, a certain fraction of COONa- and ClCH₂- end groups will be in favorable position for formation of loops ((a) in Figure 2), and formation of loops on both sides of the crystallites may result in a formation of cycles ((b)). Not all end groups can react in this way, because their distance from the surface certainly varies and because their concentration is lowered by the loops of folded chains and will further be reduced by the formation of new loops.

In the case of polylactides the authors have recently found convincing evidence for this type of loop formation and cyclization,^[18] but the insolubility of most PGA samples hinders a more detailed study of this problem in the case of PGA. Regardless of the cyclization mechanism, these measurements justify the decision to characterize the virgin sample without washing with water, because hydrolytic cleavage of one single ester group in a cycle suffices to change the topology completely.

The DSC measurements yielded two types of heating traces. All PGAs prepared at 160 or 180 °C displayed two melting endotherms with peaks around 203–205 °C and 220 °C as exemplarily illustrated in **Figure 3A**. This pattern suggests that two populations of crystallites with different perfection or thickness were formed. This suggestion was confirmed by the heating trace of the 200 °C experiment, which exclusively displayed the “high-temperature” endotherm at 219.6 °C (Figure 3B). A discussion of the melting enthalpies (ΔH_m) does not make sense, since the virgin samples contain stoichiometric amounts of NaCl.

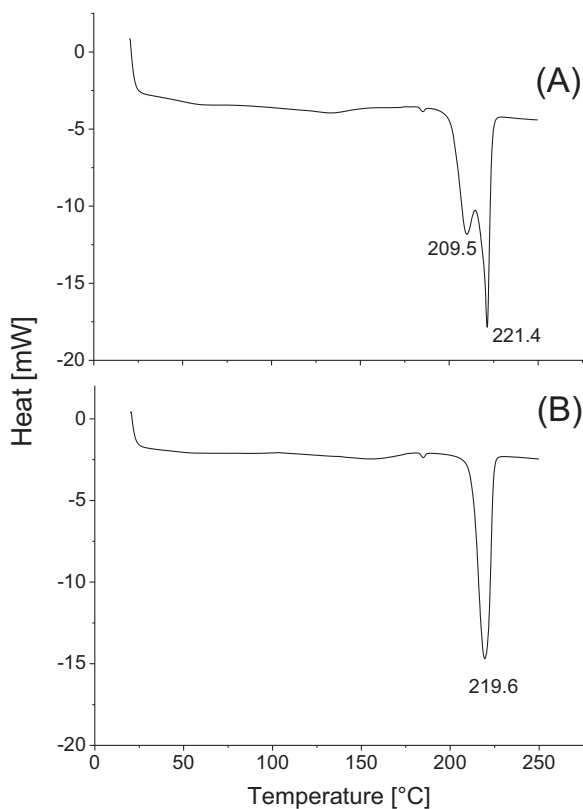


Figure 3. DSC heating traces (1st heating) of PGAs prepared by polycondensation of Na-chloroacetate: A) 180 °C/4 h (No. 2, Table 1), B) 200 °C/4 h (No. 4, Table 1).

3.2. Polycondensation of Glycolic Acid (GA)

As catalysts for the polycondensation of GA four protic acids or Lewis acids were mentioned in recent publications: trifluoromethane sulfonic acid (triflic acid), TSA, SnCl_2 and a 1:1 combination of TSA and SnCl_2 . Therefore, these catalysts were also used in the present work, but with triflic acid the reaction mixture turned black within 30 min and the reaction product was not characterized and this experiment was not listed in Table 2. Unfortunately, only two samples listed in Table 3 (see footnotes) were soluble enough for GPC measurements, and these samples gave low number average (M_n) and weight average (M_w) molecular weights.

The MALDI TOF mass spectrum of the PGAs prepared with SnCl_2 alone or in combination with TSA had in common that the mass peaks of cycles along with several unidentified mass peaks resulting from side reactions **Figure 4A**.

However, all PGAs prepared with TSA alone gave rather “clean” mass spectra exclusively displaying peaks of cycles as exemplarily illustrated in **Figure 4B**. Particularly interesting is the predominance of peaks having DPs of 20, 24, 28 and 32. Since the polycondensation of GA is reversible as long as water is present in the reaction mixture, and since rapid transesterification reactions should occur at 160 °C or above, the high abundance of the even-numbered cycles is certainly a thermodynamically controlled effect. Furthermore, these results agree with those ob-

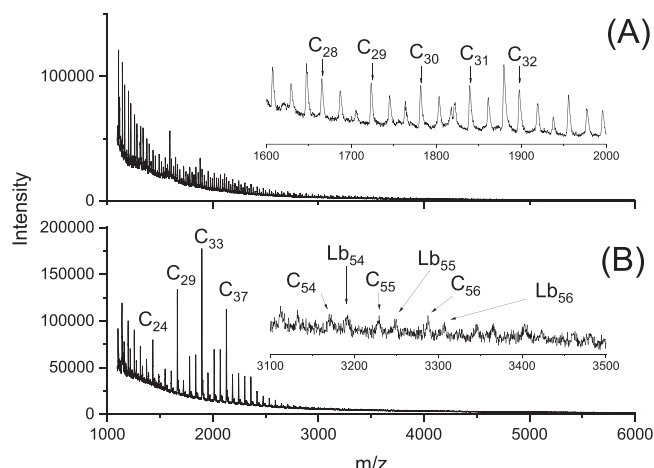


Figure 4. MALDI TOF mass spectra of PGAs prepared by polycondensation of glycolic acid: A) TSA in 1,2-DCB, 180 °C/120 h (2C, Table 3), B) TSA+ SnCl_2 in bulk 180 °C/24 h (No. 3, Table 2).

tained by polycondensation of Na-chloroacetate and thus, confirm that the predominant formation of the even-membered cycles C20-C32 is independent of the reaction mechanism. Despite the low signal-to-noise ratio above m/z 2 000, peaks of cycles up to a DP of 60 were detectable indicating that the cyclization tendency was not limited to oligomers. Furthermore, weak peaks of linear chains having one HO- CH_2 end group and one COOH group were found as may be expected for a polycondensate of glycolic acid (**Figure 4B**).

The S/N-ratio of the mass spectra recorded from samples prepared at 200 °C was extremely poor and only a few peaks of cycles below m/z 2 000 were observable. This low S/N ratios is a result of the relatively high molecular masses, which have the consequence that the fraction of PGAs in the mass range below m/z 5 000 is relatively low. Due to the insolubility of the samples prepared at 200 °C molecular masses were not measurable.

The DSC measurements of several samples prepared by TSA catalyzed polycondensations displayed endotherms with a somewhat unusual shape, in contrast to DSC traces presented in the literature, which all showed a simple, monomodal curves.^[13,19–21] As illustrated in **Figure 5**, the endotherms were rather broad, but had two sharp tips around or above 230 °C.

In two cases T_m values even slightly above 233 °C were found, the highest values reported in the literature were 231–232 °C.^[12,22] However, for two reasons this result is not unexpected. First, the polycondensation experiments of Ayyoob et al.^[12] have already demonstrated that polycondensations of GA may give higher T_m and ΔH_m values than ring-opening polymerizations of glycolide. Second, Yu et al. have calculated the maximum T_m of perfect PGA crystals via the (standard) Hoffman–Weeks method, and they have extrapolated a T_m^0 of 252 °C.^[18] When a T_m above 232° was found in experiment No. 7, Table 2, the authors decided to study TSA-catalyzed polycondensations in more detail. The results were listed in Table 3, but a T_m above 237 °C was not found.

The PGAs prepared from GA enabled a discussion of the melting enthalpies (ΔH_m), which were listed in Tables 2 and 3. Only

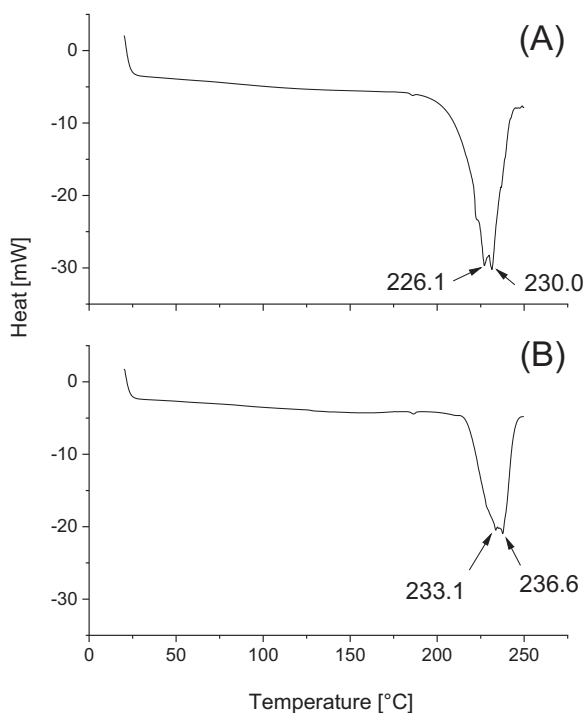


Figure 5. DSC heating traces (1. heat) of PGAs prepared by TSA-catalyzed polycondensation of glycolic acid: A) in bulk, 180 °C/1 d (No. 2, Table 2), B) in 1,2-DCB, 180 °C/1 d (No. 7, Table 2).

few research groups reported ΔH_m values and, unfortunately, no research group has compared crystallinities determined by the WAXS method with crystallinities calculated from DSC measurements. ΔH_m values can only be used for a determination of crystallinities, when ΔH_m^0 , the value of a perfect crystal, is known.

Unfortunately, an accurate and trustworthy ΔH_m^0 of PGA has not been published yet. A ΔH_m of 139.7 J g⁻¹ was mentioned in publications of Shawe et al.^[23] and of Nakka et al.,^[19] but this value was extracted from a Handbook of Polymer Data,^[20] and its origin is not clear. More important, this value is much too low as demonstrated by the experimental ΔH_m values published by Ayyoob et al.^[12] and by the ΔH_m values presented in this work. More recently a considerably higher value of 206 J g⁻¹ was mentioned by Ayyoob et al.^[12] and Ramdhanie et al.^[21] However, this value was calculated from a single ΔH_m value and a single crystallinity value given in a data sheet of the manufacturer of the “DEXON” fiber (its name was not mentioned). Hence, this value is based on one pair of data only, and it is not evident, how the crystallinity of the DEXON fiber was determined. Nonetheless, a ΔH_m of 206 J g⁻¹ seems reasonable, since the crystallinities calculated with this value roughly agree with crystallinities (53–63%) determined by Yu et al.^[18] using WAXS for a series of PGAs crystallized at different temperatures. The WAXS method was also used by Schmidt et al.^[24] for numerous samples prepared by ROP of glycolide in supercritical CO₂, and values between 9 and 95% were found. However, crystallinities above 85% and certainly around or above 90% are unlikely and raise the question if those authors correctly evaluated the WAXS method. Since those authors did not report DSC data, a comparison of both methods and a comparison with

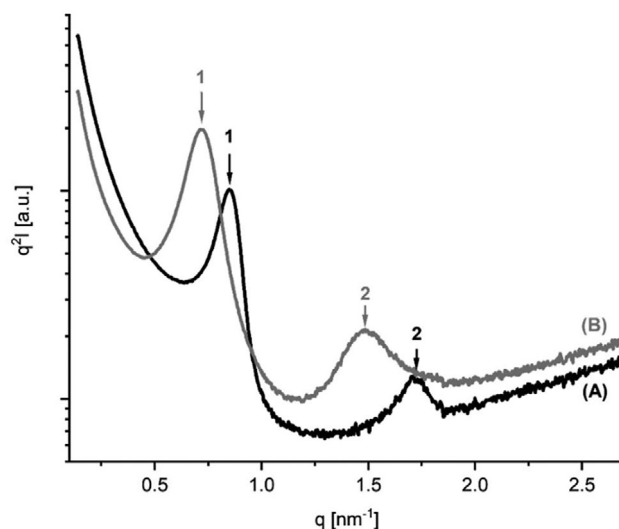


Figure 6. SAXS measurements (Kratky plots) of PGAs catalyzed by TSA: A) in anisole at 160 °C (1B, Table 3), B) in 1,2-DCB at 180 °C (2B, Table 3).

the DSC based crystallinities data of the present work is not feasible.

Finally, a couple of SAXS measurements of the samples listed in Table 3 were performed to find out, if the high T_m s of the PGAs prepared with TSA are a consequence of higher crystal thickness. Two representative examples are presented in Figure 6. They display a second order reflection, which indicates a rather high level of 3d-order of the crystallites inside the spherulites. However, the long period L was almost identical for all measured samples within the range of 7.6–8.2 nm. For PGA prepared by ROP of glycolide a L -value of 7.2 nm has been reported by Zubov et al.^[25] and values between 6.2 and 7.5 nm by Yu^[18] in good agreement with the L -data found in this work. Yet, L values for PGAs prepared by polycondensation were not reported. Quite similar L -values (6.9–7.6 nm) were found by the authors in their ongoing work on ROP of glycolide.

Hence it may be concluded that in the case of PGA the L -values depend little on the preparative method and on the thermal history. This result is quite different from the properties of poly(L-lactide), where L -values on the range of 12–40 nm were found depending on the thermal history of the samples.^[25] Apparently, the dense packing of the PGA chains hinders extensive transesterification and chain-growth reactions resulting in a significant growth of the crystal thickness.

4. Conclusion

The results of this work prove that both standard polycondensation methods involve a significant tendency of cyclization reactions not reported in the previous literature. Furthermore, it was found that certain cyclic PGAs possess an unusual thermodynamic stability. At temperatures below 180 °C the mass peaks of cyclic PGAs show a so-called “saw-tooth pattern” which indicates the formation of crystallites exclusively consisting of extended cycles.

Acknowledgements

The authors wish to thank Dipl. Ing A Myxa for her attempts to perform GPC measurements, and Stefan Bleck for the DSC measurements. Furthermore, the authors thank Dr. S. Rost (Elantas/Altana SE, Hamburg) for financial support.

Open access funding enabled and organized by Projekt DEAL.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords

cyclization, MALDI TOF mass-spectrometry, poly(glycolic acid), polycondensation

Received: November 3, 2023

Revised: February 6, 2024

Published online:

- [1] V. Dessaignes, *Ann. Chem. Pharm.* **1854**, 89, 339.
- [2] A. Kekule, *Ann. Chem. Pharm.* **1858**, 105, 286.
- [3] T. H. Norton, J. Tscherniak, *Bull. Soc. Chim. France* **1878**, 30, 102.
- [4] C. Bischoff, P. Walden, *Ber. Dtsch. Chem. Ges.* **1893**, 26, 262.

- [5] R. Anschütz, *Ber. Dtsch. Chem. Ges.* **1893**, 26, 262.
- [6] C. Bischoff, P. Walden, *Liebigs Ann. Chem.* **1894**, 279, 45.
- [7] US 2676945, **1954**, inv. N. A. Higgins.
- [8] A. Pinkus, R. Subramanyam, *J. Polym. Sci.: Polym. Chem. Ed.* **1984**, 22, 1131.
- [9] K. Schwarz, M. Epple, *Macromol. Chem. Phys.* **1999**, 200, 2221.
- [10] O. Herzberg, R. Gehrke, M. Epple, *Polymer* **1999**, 40, 507.
- [11] K. Takahashi, I. Taniguchi, M. Miyamoto, Y. Kimura, *Polymer* **2000**, 41, 8725.
- [12] M. Ayyoob, D. H. Lee, J. H. Kim, S. W. Nam, Y. J. Kim, *Fibers Polym.* **2017**, 18, 407.
- [13] V. Sanko, I. Sahin, U. Aydemir Sezer, S. Sezer, *Polym. J.* **2019**, 51, 637.
- [14] G. Benecke, W. Wagermaier, C. Li, M. Schwartzkopf, G. Flucke, R. Hoerth, I. Zizak, M. Burghammer, E. Metwalli, P. Müller-Buschbaum, *J. Appl. Crystallogr.* **2014**, 47, 1797.
- [15] Y. Chatani, K. Suehiro, Y. Okita, H. Tadokoro, K. Chujo, *Die Makromol. Chem.* **1968**, 113, 215.
- [16] P. DeSantis, A. J. Kovacs, *Biopolymers* **1968**, 6, 299.
- [17] B. Lotz, in *Synthesis, Structure and Properties of Poly (Lactic Acid)* (Eds.: M.L. Di Lorenzo, R. Androsch), Springer, Cham, **2017**, p. 273.
- [18] C. Yu, J. Bao, Q. Xie, G. Shan, Y. Bao, P. Pan, *CrystEngComm* **2016**, 18, 7894.
- [19] R. R. Nakka, V. R. Thumu, R. R. SVS, S. R. Buddhiraju, *Radiat. Eff. Defects Solids* **2015**, 170, 439.
- [20] L. Lu, A. G. Mikas, *Polymer Data Handbook*, (Ed.: J.E. Mark), Oxford University Press, Oxford/New York, **1999**, p. 566.
- [21] L. I. Ramdhanie, S. R. Aubuchon, E. D. Boland, D. C. Knapp, C. P. Barnes, D. G. Simpson, G. E. Wnek, G. L. Bowlin, *Polym. J.* **2006**, 38, 1137.
- [22] Y. Chen, K. Xie, Y. He, W. Hu, *Polymers* **2021**, 13, 891.
- [23] S. Shawe, F. Buchanan, E. Harkin-Jones, D. Farrar, *J. Mater. Sci.* **2006**, 41, 4832.
- [24] C. Schmidt, M. Behl, A. Lendlein, S. Beuermann, *RSC Adv.* **2014**, 4, 35099.
- [25] Y. A. Zubov, V. I. Selikhova, V. S. Shirets, I. A. Chebotareva, D. K. Polyakov, *Vysokomol. Soedin.* **1995**, 37, 1784.