Journal of Applied Polymer Science

Random Polyesteramides Based on ε-Caprolactone and Glycine

Abdoulkader Ali Mohamed,[1,2,3] Slim Salhi,[3] Souhir Abid,[3] Rachid El Gharbi,[3] Alain Fradet[1,2]

[1]Sorbonne Universités, UPMC Univ Paris 06, UMR 7610, Laboratoire de Chimie des Polymères, 3 rue Galilée, 94200 Ivry-sur-Seine, France

[2]CNRS, UMR 7610, Laboratoire de Chimie des Polymères, Courrier 184, 4 Place Jussieu, 75252 Paris Cedex 05, France

[3]Université de Sfax, Faculté des Sciences, Laboratoire de Chimie Appliquée H.C.G.P., 3038 Sfax, Tunisia

Correspondence to: A. Fradet (E-mail: alain.fradet@upmc.fr)

ABSTRACT: A series of random polyesteramides (PEAs) based on ε-caprolactone and glycine were synthesized by a direct melt polycondensation method. Their structure was fully characterized by NMR spectroscopy. High molar mass PEAs were obtained for glycine contents lower than 15 mol-%. The resulting copolymers are semi-crystalline and present increasing glass transition temperatures but decreasing melting points at increasing glycine contents. Some of these PEAs exhibit better thermal stability and higher Young's modulus and ultimate tensile strength than PCL homopolymer. © 2014 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2014**, *131*, 40573.

KEYWORDS: copolymers; polyamides; polycondensation; polyesters

Received 17 December 2013; accepted 8 February 2014
DOI: 10.1002/app.40573

INTRODUCTION

Aliphatic polyesters, especially polylactide (PLA), polyglycolide (PGA), poly(ε-caprolactone) (PCL), and their copolymers, are the most commonly used synthetic biodegradable polymers for biomedical applications, such as sutures, drug delivery systems, or tissue engineering.[1,2] Aliphatic polyesters can also be used as substitutes for some convenience plastics in daily life.[3] However, aliphatic polyesters generally exhibit properties that do not allow their use as engineering plastics. On the other hand, aliphatic polyesteramides (PEAs) present an interesting combination of properties: good mechanical properties, due to intermolecular hydrogen bonding of amide groups, and degradability, due to the presence of hydrolyzable ester groups.[4,5] The applications of aliphatic PEAs reported so far include biodegradable convenience materials for waste bags, agricultural films or plant pots,[6] as well as functional biomaterials for, e.g., drug delivery systems[5,7–11] or tissue engineering scaffolds.[5,12]

Various monomers and various synthetic strategies can be used for the preparation of PEAs exhibiting alternating,[13] block,[14] or random[15,16] structures. Alternating PEAs are prepared by polycondensation of diol or diacid derivatives with intermediate compounds, such as diamine-terminated diesters or diester-terminated diamides,[17–24] or by the ring-opening polymerization of morpholine-2,5-diones deriving from natural α-amino acids and α-hydroxy acids.[25–29] The synthesis of polyester-block-polypeptides can be carried out by the ring-opening polymerization of ε-caprolactone initiated by amine-terminated peptides or by the ring-opening polymerization of α-amino acid N-carboxyanhydrides (NCAs) initiated by amine-terminated polylactide or poly ε-caprolactone.[30–33]

On the other hand, random PEAs can be prepared by simple procedures that do not require the use of solvents or expensive monomers like NCAs or morpholine-2,5-diones. Random PEAs were synthesized by polycondensation of monomers such as adipic acid, hexamethylene diamine, butanediol and diethylene glycol, by reaction of mixtures of linear and cyclic monomers, like caprolactam, butanediol and adipic acid,[6] or by the ring-opening copolymerization of lactones and lactams.[15,34] Some studies have reported the use of amino acids in the bulk synthesis of PEAs, e.g., 6-aminohexanoic acid and 11-aminoundecanoic acid.[35–37] Improved thermal and mechanical properties and better biological properties can reasonably be expected when using shorter amino acids, such as naturally occurring α-amino acids.[5] However, only very few studies discuss the synthesis of such copolymers, namely the syntheses of poly(D,L-lactic acid–glycine)[38] and poly(D,L-lactic acid–glycolic acid-L-glutamic acid)[39] by direct bulk polycondensation.

To our best knowledge, no study has yet been reported on the bulk synthesis of random polyesteramides based on α-amino acids and lactones. The aim of the present work is to study the synthesis and properties of random polyesteramides prepared by the bulk copolymerization of inexpensive ε-caprolactone and glycine, using a simple one-step procedure.

EXPERIMENTAL

Materials

Glycine (Gly, >99%), ε-caprolactone (CL, 97%), tetrabutoxytitanium ($Ti(OBu)_4$, 97%), and trifluoroacetic anhydride (TFA, ≥99%) were purchased from Sigma–Aldrich and were used as received.

Synthesis of Poly(ε-caprolactone–glycine) (PEA-*x*/*y*)

The synthesis of PEA-*x*/*y*, where *x*/*y* represents the CL/Gly molar ratio, is described below for PEA-70/30 as an example. A total of 78.01 g of CL (0.683 mol) and 21.99 g of Gly (0.293 mol) were mixed in a 200 mL reactor fitted with a mechanical stirrer, a nitrogen inlet, distillation side arm, and a vacuum line and reacted at 200°C under nitrogen for 1 h. Eight milliliters of a 25 g/L solution of tetrabutoxytitanium in methylene chloride was carefully added. The mixture was stirred at 200°C for 1 h and under vacuum for 2 h. The other PEA-*x*/*y* were synthesized by the same method, starting from the corresponding *x*/*y* CL/Gly mol ratio. All polymers were characterized without further purification.

Synthesis of Poly(ε-caprolactone) (PCL)

The synthesis of PCL was carried out using the same conditions of PEAs synthesis, by the ring-opening polymerization of CL. CL (20.0 g) and 0.2 wt-% of $Ti(OBu)_4$ were heated at 200°C, first under nitrogen for 1 h, then under vacuum for 2 h.

NMR and FTIR Characterizations

The NMR spectra were recorded on a Bruker Avance 500 spectrometer at 500 MHz (^{1}H-NMR) or 125 MHz (^{13}C-NMR) using a 5 mm inverse probe. 2D ^{13}C–^{1}H HSQC correlation spectra were recorded using a phase-sensitive gradient-enhanced 2D HSQC echo–antiecho experiment (HSQCETGP sequence). 2D ^{13}C–^{1}H long-distance correlation HMBC spectra were recorded using a heteronuclear zero and double quantum coherence experiment (HMBCGPLPNDQF sequence). The samples were dissolved in $CDCl_3$/TFA solutions (2/1 vol/vol). Chemical shifts are referenced to residual $CHCl_3$ peak (7.26 ppm, ^{1}H) and to the central peak of $CDCl_3$ (77.16 ppm, ^{13}C).

The FTIR spectra were recorded in the range 4000–400 cm^{-1} using a Nicolet iS10 spectrometer equipped with a Ge ATR accessory.

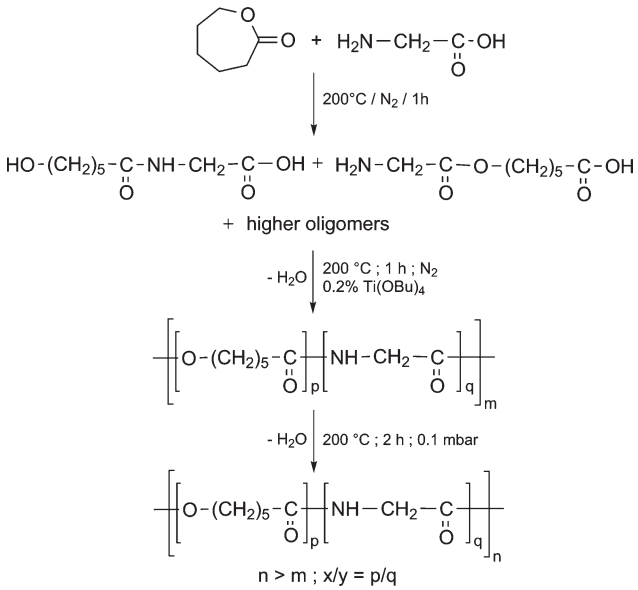
Thermal Properties

Differential Scanning Calorimetry (DSC) analyses were carried out under nitrogen on a TA Instruments DSC Q2000 system. The samples (15 mg) were heated from −80°C to 200°C, then cooled to −80°C and finally heated to 200°C (cooling and heating rates: 10°C/min). Melting and glass transition temperatures (T_m and T_g) were measured from the second heating curves.

Thermogravimetric analyses (TGA) were carried out on a TA instruments Q50 system at 10°C/min under nitrogen atmosphere from room temperature to 800°C.

Size Exclusion Chromatography (SEC)

SEC analyses were performed at 60°C on a column set consisting of two PSS GRAM 1000 Å columns (8 × 300 mm; separation limits: 1–1000 kg mol^{-1}) and one PSS GRAM 30 Å (8 × 300 mm; separation limits: 0.1–10 kg mol^{-1}) connected to a Viscotek VE5111 injector, VE7510 pump, and TDA 305 RI detector. DMF (containing 1 g/L LiBr,) was used as eluent (0.8 $mL.min^{-1}$). A total of 100 µL of filtrated polymer solutions in DMF (5mg/mL) were injected. The chromatograms were processed using the OmniSEC software. Poly(methyl methacrylate) standards (Polymer Laboratories) were used for the calibration.



Scheme 1. Synthesis of PEA-*x*/*y* copolymer.

Tensile Properties

Tensile tests were performed at room temperature according to ISO 527-2 using 5A-type dumbbell tensile specimens and a T2000 mechanical testing machine (Alpha Technologies) operating at 50 mm/min. The specimens were molded on a Thermo-Haake Minijet II injection molder set at 200°C with a mold temperature of 75°C.

RESULTS AND DISCUSSION

The reactions of ε-caprolactone (CL) and glycine (Gly) were carried out in the bulk at high temperature as illustrated in Scheme 1. Glycine and ε-caprolactone react rapidly, leading to oligomers with hydroxy- and carboxy end-groups or amino- and carboxy end-groups, depending on whether caprolactone first reacts on the carboxy- or the amine groups of glycine. The resulting oligomer mixture was then reacted in the presence of tetrabutoxytitanium catalyst under vacuum to yield high molar mass copolymers. PEAs with various compositions in CL and Gly units were obtained. They are denoted as PEA-*x*/*y*, where *x*/*y* is the starting CL/Gly molar ratio.

The weight-average molar mass (M_w) and the molar-mass dispersity (M_w/M_n) of the PEAs were determined using SEC. With the exception of PEA-98/2, all copolymers exhibit lower molar masses than the PCL synthesized in the same conditions (Table I). The increase in glycine molar fraction in the initial mixture leads to a molar mass decrease and a noticeable distribution broadening. When glycine molar fraction increases from 2 to 15 mol-%, PEA molar mass decreases by ca. 30%. This negative effect on molar mass becomes dramatic at 20 mol-% of glycine

Table I. Results of Size Exclusion Chromatography and Thermal Analyses (DSC, TGA) of PCL and PEA-*x*/*y*: Mass-Average Molar Mass (M_w), Molar-Mass Dispersity (M_w/M_n), Glass Transition Temperature (T_g), Melting Point (T_m), Crystallization Temperature (T_c), Melting Enthalpy (ΔH_m), and 5% Mass Loss Temperature ($T_{d,5\%}$)

Polymer	M_w (g/mol)	M_w/M_n	T_g (°C)	T_m (°C)	T_C (°C)	ΔH_m (J/g)	$T_{d,5\%}$ (°C)
PEA-70/30	8200	2.33	−44	30	−3	25.7	319
PEA-80/20	18400	2.55	−39	35	-	44.8	324
PEA-85/15	118800	4.67	−46	45	-	41.5	335
PEA-90/10	101600	3.18	−51	46	-	41.8	336
PEA-93/7	125800	3.64	−54	50	-	43.7	331
PEA-95/5	106500	2.73	−59	51	-	46.6	331
PEA-98/2	158000	3.25	−60	58	-	54.3	329
PCL	136400	1.98	−64	55	32	49.8	293

and above, leading to very low molar mass for PEA-80/20 and PEA-70/30 (Table I). A similar molar mass decrease at increasing amino acid content has been reported for the synthesis of PEAs based on CL and 11-aminoundecanoic acid[35] and on L-lactic acid and glycine,[38] but no interpretation was proposed to explain this phenomenon. In our case, partial catalyst deactivation may occur due to interactions between titanium and amine and/or amide groups present during the reaction.

The FTIR spectra of PEA-*x*/*y* copolymers exhibit the expected features (Figure 1), with absorptions corresponding to amide NH (a), amide I (d), and amide II (e) at 3387, 1677, and 1521 cm^{-1}, to aliphatic CH (b) at 2945 cm^{-1}, ester carbonyl (c) and amide carbonyl (amide I, (d)) at 1726 and 1677 cm^{-1}, respectively, and C–O simple bond at 1171 cm^{-1}. Their relative intensities vary in the expected way when the CL/Gly mol ratio changes. For instance increasing Gly content clearly leads to an increase of the amide I absorption at 1677 cm^{-1} (peak (d)).

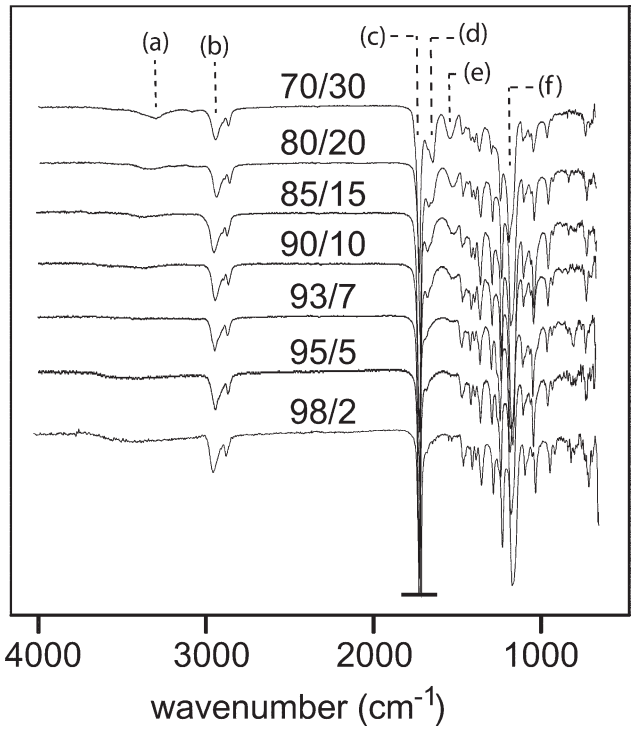


Figure 1. FTIR spectra of PEA-*x*/*y*. See text for comments on absorptions (a)–(f).

The ^{1}H-NMR and ^{13}C-NMR spectra of PEA-*x*/*y* are in good agreement with the expected structure. 2D NMR spectra (HSQC and HMBC) of PEA-70/30 were used to assign the various signals. The ^{1}H-NMR spectrum of PEA-70/30 is given in Figure 2. The various triads observed in this spectrum and the corresponding atoms numbering are summarized in Table II. The presence of CC dyads corresponding to PCL sequences in CCC, CCG, and GCC triads is reflected by the signals at 4.12 and 2.38 ppm, corresponding to the protons of 1cc and 5cc, respectively. The signals of connected CL and Gly units appear at 4.18 and 2.93 ppm (1cg and 5cg, respectively) and at 4.67 and 4.51 ppm (1gcg and 1gcc, respectively). The proton resonances of the three methylenes inside CL units (2c, 3c and 4c) are not affected by the nature of the neighboring units and are observed at 1.68 ppm (2c, 4c) and 1.41 ppm (3c). The GG

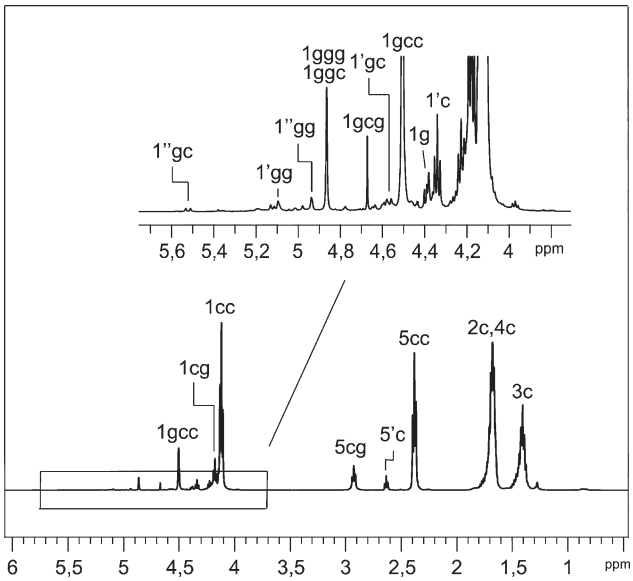
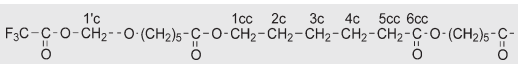
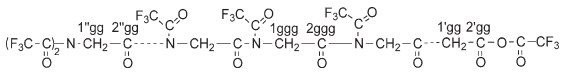
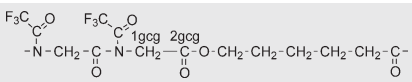
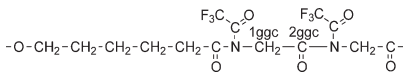
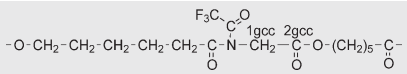
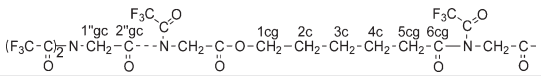
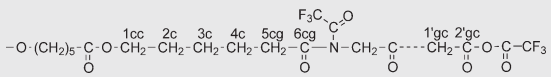
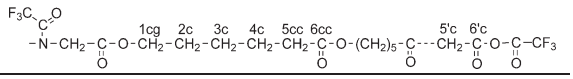


Figure 2. ^{1}H-NMR spectrum of PEA-70/30 (500 MHz; $CDCl_3$/TFA 2/1 vol/vol, ref δ ($CHCl_3$) = 7.26 ppm).

Table II. Triads Present in CL-Gly Copolymers and the Corresponding Atom Numbering (C = CL Unit and G = Gly Unit)

CCC	
GGG	
GGC	
CGG	
CGC	
GCG	
CCG	
GCC	

dyads give two signals: one at 4.86 ppm (1ggg, 1ggc) corresponding to the GG dyads of GGG and CGG triads and another at 4.67 ppm (1gcg) corresponding to GGC triads. The resonances of CL end units, 5′c and 1′c, are not influenced by the nature of unit linked to CL unit and appear, respectively, at 2.64 and 4.34 ppm. The four end-groups of Gly units, denoted 1′gc, 1″gc, 1′gg, and 1″gg, were also identified in the ^{1}H-NMR spectrum at 4.57, 5.52, 5.11, and 4.93 ppm, respectively, with the help of 2D ^{1}H–^{13}C HMBC NMR. These assignments are discussed below. The signal appearing at 4.38 ppm (1g) corresponds to unreacted glycine.

The ^{13}C-NMR spectrum of PEA-70/30 is given in Figure 3. The resonances of CC dyads appear at 65.40, 34.41, and 176.36 ppm (1cc and 5cc methylene carbons and 6cc ester carbonyl of CL units, respectively). Connected CL and Gly units are easily detected at 66.32, 38.69, and 175.88 ppm (respectively 1cg and 5cg methylene- and 6cg amide carbons of CL units) and 168.26 ppm (2gcc Gly ester carbonyl). The resonances of the three inner methylenes of CL units, 2c, 3c, and 4c appear at 28.24, 25.56, and 24.66 ppm, respectively, regardless of the nature of the neighboring units. Similarly, the resonances of Gly methylenes are not affected by the nature of neighboring units (1ggg = 1gcg = 1ggc = 1gcc) and appear at 45.01 ppm. The two Gly amide carbonyls of GG dyads appearing in GGG and CGG triads also give only one signal at 165.31 ppm (2ggg, 2ggc). The carbon resonances relative to CL end units appear at 68.04 ppm (1′c, methylene of hydroxy end-groups), 34.81 ppm (5′c, methylene of carboxy end-groups) and 165.60 ppm (COOH carbonyl).

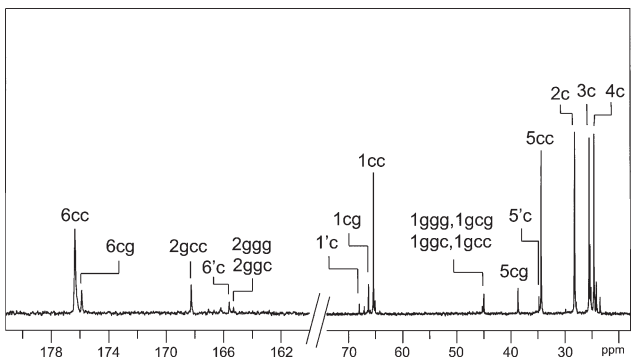


Figure 3. ^{13}C-NMR spectrum of PEA-70/30 (500 MHz, $CDCl_3$/TFA 2/1 vol/vol, ref δ ($CDCl_3$) = 77.16 ppm).

Four different Gly end units may be present, depending on the nature of the end-group (amine or carboxy) and the nature of the neighboring unit (CL or Gly). The assignments of the corresponding resonances require a close examination of the 2D ^{1}H–^{13}C HMBC spectrum in the carbonyl resonance area (160–180 ppm, Figure 4).

The methylene protons of trifluoroacetylated –Gly–NH_2 end units, 1″gg and 1″gc, respectively, connected to Gly and CL units, are identified at 4.93 and 5.52 ppm by their couplings with the corresponding glycine chain carbonyls at 165.31 (2ggg and 2ggc) and 168.26 ppm (2gcc). Similarly, two correlations appear between two Gly methylene and two carbonyl resonances of very low intensity, assigned to COOH end-groups. Since the 1ggg methylene protons of Gly units in GGG triads are more deshielded than the 1gcc Gly methylene protons of CGC triads, 1′gg signal is assigned to the proton resonance of higher chemical shift (5.11 ppm) and 1′gc at 4.57 ppm, allowing the attribution of the corresponding two carboxy resonances of –Gly–COOH end units (2′gg and 2′gc).

Three reactions can take place in the first step, when the CL/Gly initial mixture is heated without catalyst: Gly dimerization, leading to dimer D1, and CL aminolysis and acidolysis, leading to dimers D2 and D3, respectively (Scheme 2).

The presence of four Gly end-group resonances (two amine and two carboxy) and of the CL hydroxy and carboxy end-group resonances in the spectra of PEA-70/30 show that all of these

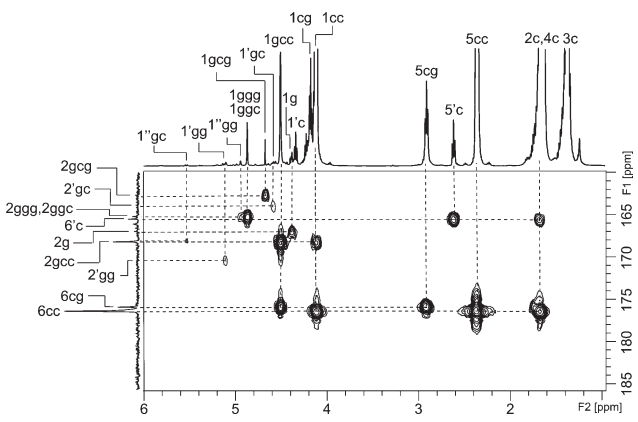
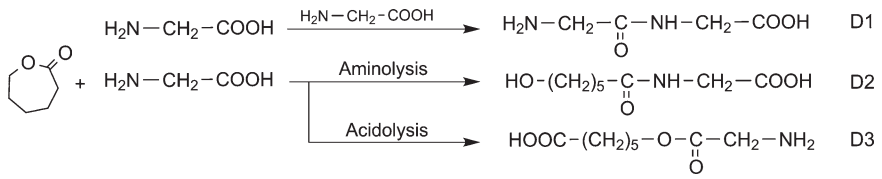


Figure 4. Carbonyl area of 2D ^{1}H–^{13}C HMBC spectrum of PEA-70/30 (500 MHz, $CDCl_3$/ATFA 2/1 vol/vol, ref $\delta(CHCl_3)$ = 7.26 ppm; ref $\delta(CDCl_3)$ = 77.16 ppm).



Scheme 2. Possible monomer reactions.

reactions take place. The resulting dimers then react with each other or with residual caprolactone or glycine, to form oligomers, which in turn lead to random PEAs via polycondensation and interchange reactions in the last step of reaction.

The CL/Gly mol fraction present in final PEAs was evaluated by the integration of ^{1}H-NMR peaks: 5cc and 5cg for CL units and 1gcc, 1ggg, 1ggc, and 1gcg for Gly units. For PEA-*x*/*y* with low Gly unit content (Gly $\leq$ 10 mol-%) the experimental CL/Gly ratio is very close to the theoretical one, as shown in Table III. For the highest Gly contents, there is a large discrepancy between these values. Some glycine loss was observed during the course of reaction, forming a white deposit on reactor walls, which became increasingly important at the highest glycine contents.

The degree of randomness R was determined from the ^{1}H-NMR peak integrations of 5cc, 5cg, 1gcc, 1ggg, 1ggc, and 1gcg. R is defined as the probability of finding mixed CG dyads (P_{cg}) divided by the product of the probabilities of finding the CL and Gly units in PEA chains (P_c and P_g):

$$R = P_{cg}/\left(P_c \cdot P_g\right),$$

$$P_{cg} = I_{5cg}/\left(I_{5cg}+I_{5cc}+I_{1gcc}+I_{1gcg}+\mathrm{I}_{1ggg\,,1ggc}\right)$$

$$P_c = \left(I_{5cg}+I_{5cc}\right)/\left(I_{5cg}+I_{5cc}+I_{1gcc}+I_{1gcg}+I_{1ggg\,,1ggc}\right)$$

$$P_g = \left(I_{1gcc}+I_{1gcg}+I_{1ggg\,,1ggc}\right)/\left(I_{5cg}+I_{5cc}+I_{1gcc}+I_{1gcg}+I_{1ggg\,,1ggc}\right)$$

$R = 1$ for random copolymers, $R < 1$ for copolymers with a blocky microstructure and $1 < R \leq 2$ for copolymers with an alternating tendency. The number-average sequence lengths, defined as the ratio of the number of CL (or Gly) units present in PEA chains to the number of CL-Gly dyads, can also be determined by ^{1}H-NMR peak integrations:

$$L_{n,g} = \left(I_{1gcc}+I_{1gcg}+I_{1ggg\,,1ggc}\right)/I_{5cg}$$

$$L_{n,c} = \left(I_{5cg}+I_{5cc}\right)/I_{5cg}$$

The results are summarized in Table III. The degree of randomness is close to 1 for all PEAs, indicating that the distribution of CL and Gly units in the chains follows a Bernoullian statistics.

Table III. Experimental Molar Composition, Degree of Randomness (R), and Number-Average Sequence Lengths (L_{nc} $L_{n,g}$) for PEA-*x*/*y*

Polymer	CL/Gly experimental	R	L_{nc}	$L_{n,g}$
PEA-70/30	82/18	1.08	5.3	1.12
PEA-80/20	86/14	1.11	6.6	1.04
PEA-85/15	89/11	1.09	9.1	1.02
PEA-90/10	91/9	1.05	11.1	1.04
PEA-93/7	94/6	1.07	16.0	0.99
PEA-95/5	96/4	1.06	21.2	0.98
PEA-98/2	98/2	1.05	60.9	0.96

The DSC results are summarized in Table I and Figure 5. As expected, the incorporation of rigid Gly units PCL chains results in increasing glass transition temperatures (T_g), due to the formation of intermolecular hydrogen bonds. On the other hand, with the exception of PEA-98/2, the melting points of PEAs are lower than that of PCL, reflecting the disturbance generated in PCL chains by the insertion of Gly units: increasing Gly unit content results in decreasing PCL block length and, consequently, in a decrease of the corresponding melting temperature. PEA-70/30 presents a crystallization peak at −3°C and the lowest melting point, but it is difficult to compare this polymer to the others, due to its comparatively low molar mass.

All PEAs are more thermally stable than PCL, and exhibit 5% mass loss temperatures exceeding that of PCL by more than 25°C (Figure 6). This, again, can be assigned to the formation of intermolecular hydrogen bonds between the glycine units of PEA chains.

Tensile tests were carried out on specimens of PEAs and PCL prepared by injection molding (Figure 7 and Table IV). PEA-80/20 and PEA −70/30 were very brittle, probably due to their low molar mass, and tensile specimens of these polymers could not be prepared. For the other PEAs, increasing Gly contents results

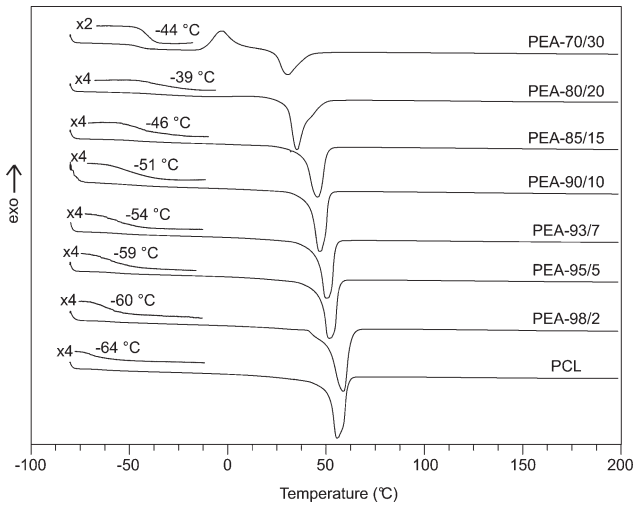


Figure 5. DSC curves of the PEA-*x*/*y* copolymers with vertical expansion (two or four times) in the T_g zone.

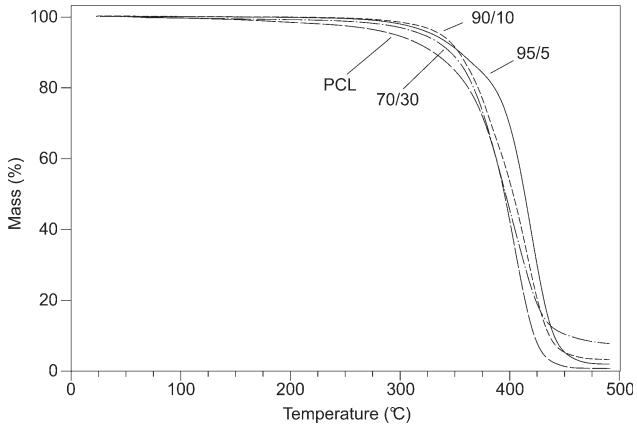


Figure 6. TGA curves of PCL, PEA-70/30, PEA-90/10, and PEA-95/5.

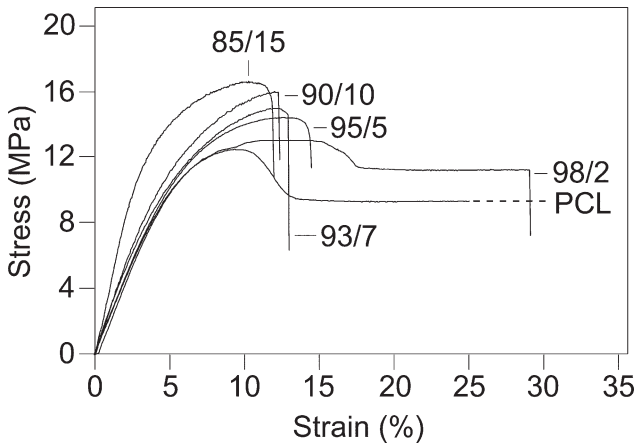


Figure 7. Tensile curves of PCL and PEA-*x*/*y* (*x*/*y* from 98/2 to 85/15).

in increasing Young's modulus (E), ultimate tensile strength (R_m), and stress at break (σ_r), while elongation at break (ε_r) decreases, as expected for materials with increasing rigid unit content and intermolecular H-bond density.

CONCLUSION

A series of polyesteramides were successfully synthesized by simple direct polymerization of mixtures of ε-caprolactone and 2–30 mol-% glycine in the bulk. The NMR results are fully consistent with their anticipated chemical structures. All types of possible glycine end units are present at the end of the first step of reaction, showing that the ring-opening of ε-caprolactone proceeds by reactions involving the $–NH_2$ and –COOH groups of glycine. These PEAs are random copolymers and present increasing glass transition temperatures but decreasing melting points at increasing glycine content. The incorporation of 20 mol-% of glycine and above resulted in low molar mass, brittle polymers. On the other hand, the PEAs with 7, 10, and 15 mol-% glycine content presented higher Young's modulus and ultimate tensile strength than PCL homopolymer.

Table IV. Results of Tensile Test Analysis for PCL and PEA-*x*/*y* (*x*/*y* from 98/2 to 85/15): Young's Modulus (E), Ultimate Tensile Strength (R_m), Stress at Break (σ_r), and Strain at Break (ε_r)

Polymer	E (MPa)	R_m (MPa)	σ_r (MPa)	ε_r (%)
PEA-85/15	400	16.5	15.3	11.8
PEA-90/10	267	15.9	15.9	12.3
PEA-93/7	256	14.9	14.5	13.0
PEA-95/5	233	14.5	13.7	14.4
PEA-98/2	236	13.3	11.3	29.1
PCL	250	12.7	10.4	287.5

ACKNOWLEDGMENTS

The Présidence and the Ministère de l'Enseignement Supérieur et de la Recherche of Djibouti are gratefully acknowledged for AAM's doctoral fellowship.

REFERENCES

1. Albertsson, A.-C.; Varma, I. K. In Degradable Aliphatic Polyesters; Advances in Polymer Science; Springer: Berlin, Heidelberg, **2002**, pp 1–40.
2. Albertsson, A.-C.; Varma, I. K. *Biomacromolecules* **2003**, *4*, 1466.
3. Bastioli, C. *Polym. Degrad. Stab.* **1998**, *59*, 263.
4. Rodriguez-Galan, A.; Franco, L.; Puiggali, J. *Polymers* **2010**, *3*, 65.
5. Sun, H.; Meng, F.; Dias, A. A.; Hendriks, M.; Feijen, J.; Zhong, Z. *Biomacromolecules* **2011**, *12*, 1937.
6. Grigat, E.; Koch, R.; Timmermann, R. *Polym. Degrad. Stab.* **1998**, *59*, 223.
7. Duncan, R.; Kopeček, J. In Polymers in Medicine; Advances in Polymer Science; Springer: Berlin, Heidelberg, **1984**; pp 51–101.
8. Guo, K.; Chu, C. C. *J Biomed Mater Res Part B Appl Biomater* **2009**, *89B*, 491.
9. Del Valle, L. J.; Roca, D.; Franco, L.; Puiggalí, J.; Rodríguez-Galán, A. *J Appl Polym Sci* **2011**, *122*, 1953.
10. He, P.; Tang, Z.; Lin, L.; Deng, M.; Pang, X.; Zhuang, X.; Chen, X. *Macromol Biosci* **2012**, *12*, 547.
11. Wu, J.; Chu, C.-C. *J. Mater. Chem. B* **2013**, *1*, 353.
12. Karimi, P.; Rizkalla, A. S.; Mequanint, K. *Materials* **2010**, *3*, 2346.
13. Song, H.; Chu, C. C. *J Appl Polym Sci* **2012**, *124*, 3840.
14. Cakir, S.; Kierkels, R.; Koning, C. *J. Polym. Sci. Part Polym. Chem.* **2011**, *49*, 2823.
15. Chromcová, D.; Baslerová, L.; Roda, J.; Brožek, J. *Eur Polym J* **2008**, *44*, 1733.
16. Deshayes, G.; Delcourt, C.; Verbruggen, I.; Trouillet-Fonti, L.; Touraud, F.; Fleury, E.; Degée, P.; Destarac, M.; Willem, R.; Dubois, P. *Macromol. Chem. Phys.* **2009**, *210*, 1033.
17. Asín, L.; Armelin, E.; Montané, J.; Rodríguez-Galán, A.; Puiggalí, J. *J Polym Sci Part Polym Chem* **2001**, *39*, 4283.
18. Paredes, N.; Rodriguez-Galán, A.; Puiggalí, J.; Peraire, C. *J. Appl. Polym. Sci.* **1998**, *69*, 1537.

19. Rodríguez-Galán, A.; Pelfort, M.; Aceituno, J. E.; Puiggalí, J. *J Appl Polym Sci* **1999**, *74*, 2312.
20. Wu, J.; Mutschler, M. A.; Chu, C.-C. *J. Mater. Sci. Mater. Med.* **2011**, *22*, 469.
21. Deng, M.; Wu, J.; Reinhart-King, C. A.; Chu, C.-C. *Acta Biomater.* **2011**, *7*, 1504.
22. Guo, K.; Chu, C. C. *J. Appl. Polym. Sci.* **2010**, *117*, 3386.
23. Pang, X.; Wu, J.; Reinhart-King, C.; Chu, C.-C. *J. Polym. Sci. Part Polym. Chem.* **2010**, *48*, 3758.
24. Casas, M. T.; Gestí, S.; Puiggalí, J. *Cryst. Growth Des.* **2005**, *5*, 1099.
25. Feng, Y.; Klee, D.; Keul, H.; Höcker, H. *Macromol. Chem. Phys.* **2000**, *201*, 2670.
26. Feng, Y.; Guo, J. *Int. J. Mol. Sci.* **2009**, *10*, 589.
27. Wang, D.; Feng, X.-D. *Macromolecules* **1997**, *30*, 5688.
28. Ouchi, T.; Seike, H.; Nozaki, T.; Ohya, Y. *J. Polym. Sci. Part Polym. Chem.* **1998**, *36*, 1283.
29. Franz, N.; Klok, H.-A. *Macromol. Chem. Phys.* **2010**, *211*, 809.
30. Fan, Y.; Chen, G.; Tanaka, J.; Tateishi, T. *Biomacromolecules* **2005**, *6*, 3051.
31. Motala-Timol, S.; Jhurry, D.; Zhou, J.; Bhaw-Luximon, A.; Mohun, G.; Ritter, H. *Macromolecules* **2008**, *41*, 5571.
32. Kricheldorf, H. R.; Hauser, K. *Biomacromolecules* **2001**, *2*, 1110.
33. Hrkach, J. S.; Ou, J.; Lotan, N.; Langer, R. *Macromolecules* **1995**, *28*, 4736.
34. Bernášková, A.; Chromcová, D.; Brožek, J.; Roda, J. *Polymer* **2004**, *45*, 2141.
35. Qian, Z.; Li, S.; He, Y.; Li, C.; Liu, X. *Polym. Degrad. Stab.* **2003**, *81*, 279.
36. He, Y.; Du, Y. R.; Liu, X. B. *Adv. Mater. Res.* **2011**, *287–290*, 1538.
37. Qian, Z.; Li, S.; He, Y.; Zhang, H.; Liu, X. *Colloid Polym. Sci.* **2004**, *282*, 1083.
38. Wang, Z.; Hou, X.; Mao, Z.; Ye, R.; Mo, Y.; Finlow, D. E. *Iran Polym J* **2008**, *17*, 791.
39. Lu, D.; Ren, Z.; Zhou, T.; Wang, S.; Lei, Z. *J. Appl. Polym. Sci.* **2008**, *107*, 3638.