

# Physical Characterization of Poly( $\omega$ -pentadecalactone) Synthesized by Lipase-Catalyzed Ring-Opening Polymerization

MARIA LETIZIA FOCARETE,<sup>1</sup> MARIANELLA SCANDOLA,<sup>1</sup> AJAY KUMAR,<sup>2</sup> RICHARD A. GROSS<sup>2</sup>

<sup>1</sup>G. Ciamician and Centro di Studio per la Fisica delle Macromolecole del Consiglio Nazionale delle Ricerche, Department of Chemistry, University of Bologna, Via Selmi 2, 40126 Bologna, Italy

<sup>2</sup>National Science Foundation Industry/University Cooperative Research Center, Center for Biocatalysis and Bioprocessing of Macromolecules, Department of Chemistry and Chemical Engineering, Polytechnic University, Six Metrotech Center, Brooklyn, New York 11201

Received 10 January 2001; revised 20 April 2001; accepted 25 April 2001

**ABSTRACT:** The *Candida antarctica* lipase B (Novozyme-435)-catalyzed ring-opening polymerization of  $\omega$ -pentadecalactone in toluene was performed. Poly( $\omega$ -pentadecalactone) [poly(PDL)] was obtained in a 93% isolated yield in 4 h with a number-average molecular weight of  $64.5 \times 10^3$  g/mol and a polydispersity index of 2.0. The solid-state properties of poly(PDL) were investigated by thermogravimetric analysis (TGA) coupled with mass spectrometry, differential scanning calorimetry (DSC), stress-strain measurements, wide-angle X-ray diffraction, and dynamic mechanical and dielectric spectroscopies. Poly(PDL) is a crystalline polymer that melts around 100 °C. The polyester shows good thermal stability, with a main TGA weight loss centered at 425 °C. Because of the high degree of poly(PDL) crystallinity, the glass transition ( $-27$  °C) is revealed by relaxation techniques such as dynamic mechanical and dielectric spectroscopies, rather than by DSC. In addition to the glass transition, the viscoelastic spectrum of poly(PDL) also shows two low-temperature secondary relaxations centered at  $-130$  ( $\gamma$ ) and  $-90$  °C ( $\beta$ ). They are attributed to local motions of the long methylene sequence ( $\gamma$ ) and complex units involving water associated with the ester groups ( $\beta$ ). The mechanical properties of poly(PDL) are typical of a hard, tough material, with an elastic modulus and yield parameters comparable to those of low-density polyethylene. © 2001 John Wiley & Sons, Inc. *J Polym Sci Part B: Polym Phys* 39: 1721–1729, 2001

**Keywords:** poly( $\omega$ -pentadecalactone); thermal analysis; dynamic mechanical spectroscopy; crystallinity; lipase catalysis

## INTRODUCTION

Recently, enzymatic polymerization in nonaqueous or nontraditional media has been receiving increased attention as a new tool for building polymer chains.<sup>1</sup> A rapidly increasing number of publications now exist that showcase the potential of *in vitro* enzyme catalysis to provide a wide

range of polymer structures.<sup>2–8</sup> Examples that illustrate attractive features of biocatalytic synthetic methods include the following: (1) they offer mild reaction conditions, (2) they circumvent the use of heavy metals and other nondesirable chemical catalyst substances, and (3) they provide synthetic routes to complex structures that would not be available or would be impractical to prepare with conventional chemical methods. Earlier investigations of enzymatic polyester syntheses were focused on using whole-cell synthetic methods.<sup>9</sup>

Correspondence to: R. A. Gross

*Journal of Polymer Science: Part B: Polymer Physics*, Vol. 39, 1721–1729 (2001)  
© 2001 John Wiley & Sons, Inc.

For 4- to 7-membered lactones, traditional chemical catalysts are already known that are capable of achieving high polymerization efficiencies. In contrast to smaller cyclic lactones that have ring strain, macrolactones are difficult to polymerize by traditional chemical methods. Polymerizations of macrolactones proceed slowly and give low molecular weight polymers.<sup>10</sup> However, *in vitro* enzyme-catalyzed polymerizations of macrolactones have thus far proved advantageous relative to chemical preparative routes. Kobayashi and coworkers<sup>3(d-f)</sup> were first to investigate the enzyme-catalyzed polymerization of  $\omega$ -undecanolide,  $\omega$ -dodecanolide, and  $\omega$ -pentadecalactone (PDL; 12-, 13-, and 16-membered lactones). Later studies by us showed that Novozyme-435 (immobilized *Candida antarctica* lipase B) catalyzed polymerization of PDL at 70 °C in toluene (1:1 w/v monomer:toluene) gave poly( $\omega$ -pentadecalactone) [poly(PDL)] in a greater than 90% yield with a number-average weight ( $M_n$ ) of 86,400 g/mol and a weight-average molecular weight/number-average molecular weight ( $M_w/M_n$ ) ratio of 2.3 within 2 h.<sup>2(b)</sup>

The properties and potential applications of poly(PDL) have attracted little attention since; before recent work with lipase-catalyzed polymerizations, only relatively low molecular weight poly(PDL) was available. Thus, on the basis of the very recent availability of high molecular weight poly(PDL) by lipase catalysis, the properties of poly(PDL) were revisited. Among biodegradable polyesters studied for use in medical science,<sup>11</sup> poly( $\epsilon$ -caprolactone) has received considerable attention,<sup>12,13</sup> despite its low melting temperature ( $T_m$ ; ca. 60 °C) that limits its use in applications that require dimensional stability above room temperature. In contrast, poly(PDL), with 14 methylene units per ester group, melts at temperatures close to 100 °C. Furthermore, its properties should lie between those of polycaprolactone and polyethylene. Earlier characterization studies on poly(PDL) focused on the thermal properties of the polymer synthesized by chemical methods.<sup>14-17</sup> This article describes a thorough investigation of the solid-state properties of poly(PDL) synthesized by *C. antarctica* lipase B catalysis.

## EXPERIMENTAL

### Material and Methods

The monomer PDL (98%) was purchased from Aldrich Chemical Co., used without further puri-

fication, and characterized by <sup>1</sup>H NMR [CDCl<sub>3</sub>,  $\delta$ : 4.15 (2H, t), 2.35 (2H, t), 1.64 (4H, m), 0.85 (22H, brs) ppm]. Anhydrous toluene and chloroform-*d* were purchased from Aldrich Chemical. Toluene was dried over calcium hydride and distilled under a nitrogen atmosphere. Novozyme-435 (specified activity = 7000 PLU/g) was a gift from Novo Nordisk Co. All liquid chemical transfers were performed with a syringe through rubber septum caps under a nitrogen atmosphere.

### Novozyme-435-Catalyzed Ring-Opening Polymerization of PDL

Novozyme-435 (6 g) dried in a vacuum desiccator (0.1 mmHg, 25 °C, 24 h) was transferred under a nitrogen atmosphere into an oven-dried, 500-mL, round-bottom flask containing PDL (60 g). The vials were stoppered with rubber septa and sealed with Teflon tape. Toluene (120 mL) was subsequently added via syringe under nitrogen into the reaction vial. The vial was then placed into a constant-temperature (70 °C) oil bath with stirring for 4 h. Reactions were rapidly terminated with the addition of an excess of cold chloroform and the removal of the enzymes by filtration (glass-fritted filter, medium-pore porosity). The insoluble portion was washed several times with hot chloroform. The chloroform filtrates were combined, much of the chloroform was removed by rotary evaporation, and the remaining concentrated polymer solution was precipitated in methanol. The precipitate was isolated by filtration and then dried in a vacuum oven (0.1 mmHg, 50 °C, 24 h). The isolated yield,  $M_n$ , and polydispersity index (PDI;  $M_w/M_n$ ) of the isolated poly(PDL) was 93%,  $64.5 \times 10^3$  g/mol, and 2.0, respectively.

### Instrumental Methods

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker Instruments, Inc. DPX300 spectrometer at 300 and 75.13 MHz, respectively. The chemical shifts in parts per million for <sup>1</sup>H and <sup>13</sup>C NMR spectra were referenced relative to tetramethylsilane as an internal reference at 0.00. NMR spectra of poly(PDL),  $[-O=C-CH_2^b-CH_2^c-(CH_2^d-CH_2^d)_5-CH_2-CH_2^a-O-]$  ( $M_n = 64.5 \times 10^3$  g/mol, PDI = 2.0), was as follows.

<sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 4.07 (t, J 6.5 Hz, CH<sub>2</sub><sup>a</sup>O), 3.61 (t, J 6.5 Hz, CH<sub>2</sub>OH), 2.31 (t, J 7.5 Hz, CH<sub>2</sub><sup>b</sup>CO), 1.65, 1.30 (brs, CH<sub>2</sub><sup>c,d</sup>) ppm. <sup>13</sup>C NMR (CDCl<sub>3</sub>,  $\delta$ ): 173.9 (COCH<sub>2</sub>), 64.4 (CH<sub>2</sub><sup>a</sup>O), 34.4

( $\text{OCOCH}_2^b$ ), 29.6–29.1, 28.6, 25.9, 25.0 (all other carbons) ppm.

Molecular weights were determined by gel permeation chromatography (GPC) with a Waters high performance liquid chromatography (HPLC) system equipped with a model 510 pump, a Waters model 717 autosampler, a model 410 refractive-index detector, and a model T-50/T-60 detector from Viscotek Corp. with 500-,  $10^3$ -,  $10^4$ -, and  $10^5$ -Å ultrastyrigel columns in series. Trisec GPC software (version 3) was used for calculations. Chloroform was used as the eluent at a flow rate of 1.0 mL/min. Sample concentrations of 0.2 w/v % and injection volumes of 100  $\mu\text{L}$  were used. Molecular weights were determined on the basis of conventional calibration curves generated by narrow molecular weight polystyrene standards obtained from Aldrich Chemical.

Thermogravimetric analysis (TGA) measurements were performed with a TA Instruments TGA2950 thermogravimetric analyzer (purge gas = helium, scan rate = 10  $^\circ\text{C}/\text{min}$ ). The released volatile products were directly transferred to a quadrupole mass spectrometer (Balzers ThermoStar GSD 300T; temperature setting of the interface = 200  $^\circ\text{C}$ , mass range = 10–300 amu, CH-tron detector = 1400 V). A TA Instruments DSC2910 was used for calorimetric analysis from –100 to 150  $^\circ\text{C}$ .

Dynamic mechanical measurements were carried out on injection-molded bars (8 mm  $\times$  1.5 mm  $\times$  30 mm) in the dual-cantilever bending mode with a dynamic mechanical thermal analyzer (DMTA) MkII (Polymer Laboratories Ltd.) from –150 to +70  $^\circ\text{C}$  (heating rate = 3  $^\circ\text{C}/\text{min}$ , frequency = 3 Hz).

Multifrequency dielectric measurements from –140 to +40  $^\circ\text{C}$  were carried out on compression-molded films (0.11 mm thick) with dielectric thermal analyzer (DETA) (Polymer Laboratories) at a heating rate of 1  $^\circ\text{C}/\text{min}$ .

Wide-angle X-ray scattering (WAXS) spectra were collected with a Philips PW1050/81 powder diffractometer controlled by a PW1710 unit, with nickel-filtered Cu K $\alpha$  radiation ( $\lambda = 0.1542$  nm, 40 kV, 30 mA).

An Instron 4465 tensile testing machine (gauge length = 20 mm, crosshead speed = 1 mm/min) was used for the mechanical testing of rectangular specimens (5 mm wide) die-cut from compression-molded sheets (0.3 mm thick).

## RESULTS AND DISCUSSION

Figure 1 shows the TGA curve of poly(PDL). The polymer thermal degradation occurs above 350  $^\circ\text{C}$  and is composed of a main step (I), where about 90% of the initial weight is lost, followed by a minor loss (II), appearing as a shoulder in the derivative curve. The two degradation events are centered at 425 and 475  $^\circ\text{C}$ , respectively. No solid residue remains above 500  $^\circ\text{C}$ . The mass spectra collected during the TGA measurement show the presence of water and its fragmentation products both in the main degradation step (I) and from room temperature to about 150  $^\circ\text{C}$ . The latter water loss is too small to be revealed as a weight change by conventional TGA measurements but can be determined by the combined TGA–mass spectrometry (MS) technique. In degradation step I, in addition to water, the main volatile product is carbon dioxide, whereas in step II, a cluster of higher mass products analogous to those released in TGA–MS of low-density polyethylene<sup>18</sup> is observed, attributed to degradation of the hydrocarbon part of poly(PDL) chain. When the thermal stability of poly(PDL) is compared with that of other polylactones [cf. the main degradation of polyglycolic acid centered at 380  $^\circ\text{C}$ <sup>19</sup> and that of poly( $\epsilon$ -caprolactone) at 400  $^\circ\text{C}$ <sup>19</sup>], it turns out that poly(PDL) is a quite stable polyester. As a result, if required, poly(PDL) can be thermally processed at rather high temperatures.

Calorimetric analysis of poly(PDL) shows as the only appreciable thermal transition a melting endotherm at  $T_m = 97$   $^\circ\text{C}$  (peak value); it is associated with a quite large melting enthalpy ( $\Delta H_m$ ; Table I). Figure 2 shows  $T_m$  for linear polyhydroxy acids and lactones as a function of the methylene-to-ester group ratio, that is, of the repeating unit length. According to a well-known behavior of aliphatic polyesters, after an initial steep drop caused by a reduction of intermolecular polar interactions with increasing repeating unit length,  $T_m$  slowly increases, reflecting the predominant effect of dilution of the flexible ester group along the polymer chain when  $n(\text{CH}_2)/n(\text{COO}) > 3$ . Figure 2 shows that  $T_m$  of poly(PDL) fits the increasing trend of  $T_m$  toward the limiting value of polyethylene (dotted line). The degree of crystallinity ( $\chi_c$ ) of poly(PDL), calculated from the experimental  $\Delta H_m$  and literature data for  $\Delta H_m$  of the 100% crystalline polymer,<sup>14</sup> is reported in Table I. All melting parameters of the lipase-catalyzed poly(PDL) investigated in this work agree

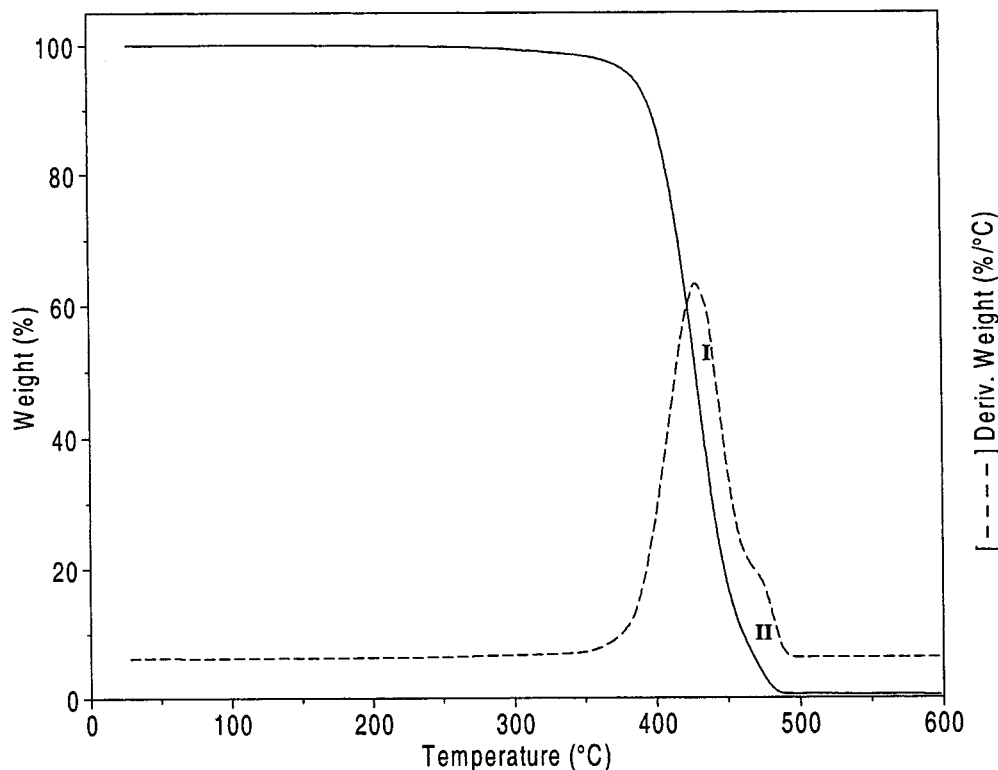


Figure 1. Thermogravimetric curve of poly(PDL).

with those earlier obtained on the polymer synthesized by traditional chemical methods.<sup>14-17,20</sup>

A powder X-ray diffraction spectrum of poly(PDL) is shown in Figure 3, and  $\chi_c$ , calculated by Ruland's method,<sup>21</sup> is reported in Table I. The difference between the  $\chi_c$  values obtained from differential scanning calorimetry (DSC) and WAXS measurements is expected and reflects the known underestimation of  $\chi_c$  by the latter method, which does not appreciate the scattering contribution from very small-dimension crystalline domains. Further studies on oriented film samples to establish the unit cell parameters of poly(PDL) crystals are underway and will be reported in due time.

Because of the high crystallizability of poly(PDL), fast cooling in DSC did not quench a considerable fraction of the polymer in the amorphous state, and no glass transition was appreciable in the DSC curve of a subsequent heating run from  $-100$  °C. Conversely, the glass-transition temperature ( $T_g$ ) of semicrystalline poly(PDL) was easily revealed by relaxation techniques, such as dynamic mechanical and dielectric spectroscopies. Figure 4 reports the DMTA spectrum of the polyester, where the loss modulus ( $E''$ ) shows three relaxation phenomena ( $\alpha$ ,  $\beta$ , and  $\gamma$  in order of decreasing temperature). The  $\alpha$  relaxation is the glass transition of the amorphous fraction of poly(PDL), and its temperature (Table

Table I. Thermal and Mechanical Properties of Poly(PDL)

$T_m$ (°C) <sup>a</sup>	$\Delta H_m$ (J/g) <sup>a</sup>	$\chi_c$ (%)	$T_g$ (°C) <sup>d</sup>	$\sigma_y$ (MPa) <sup>e</sup>	$\varepsilon_y$ (%) <sup>e</sup>	$E$ (MPa) <sup>e</sup>	
97	149	64 <sup>b</sup>	54 <sup>c</sup>	-27	14.5	12	370

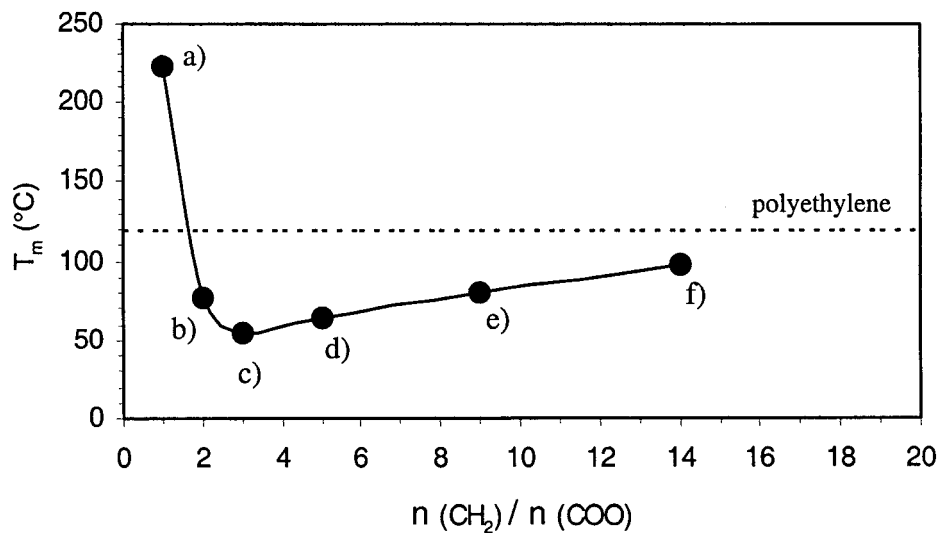
<sup>a</sup> From DSC.

<sup>b</sup> From DSC ( $\pm 2\%$ ) with  $\Delta H_m^\circ = 233$  J/g for 100% crystalline poly(PDL).<sup>14</sup>

<sup>c</sup> From WAXS ( $\pm 5\%$ ).

<sup>d</sup> From DMTA.

<sup>e</sup> From stress-strain measurements:  $\sigma_y$  = stress at yield,  $\varepsilon_y$  = elongation at yield, and  $E$  = tensile modulus.

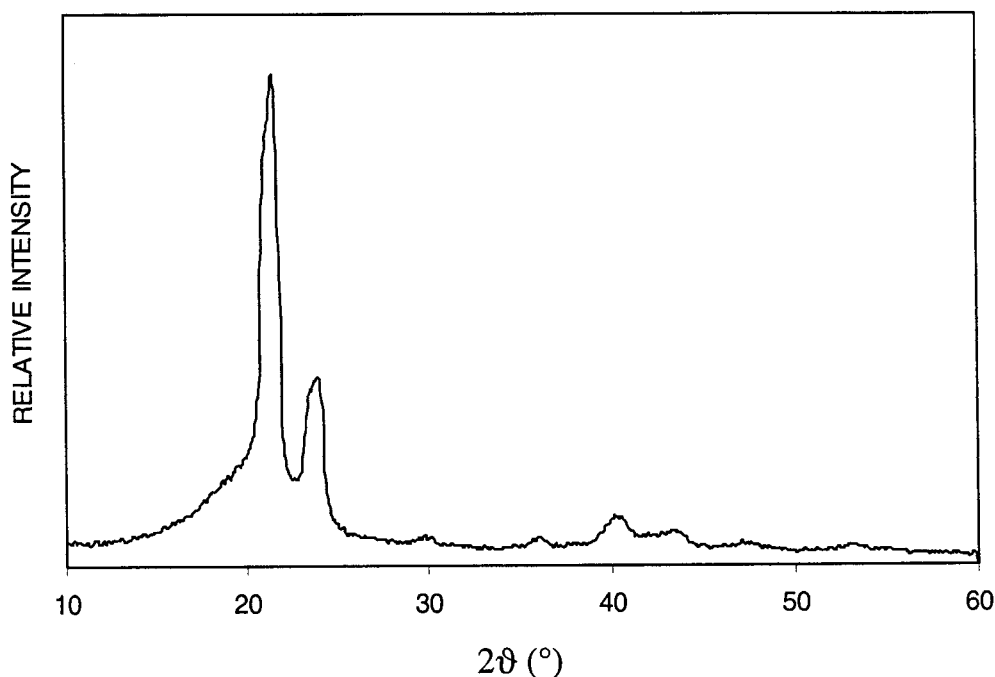


**Figure 2.**  $T_m$  of linear polyhydroxy acids and lactones as a function of the methylene-to-ester group ratio: (a) polyglycolic acid,<sup>30</sup> (b) poly(3-hydroxypropionate),<sup>31</sup> (c) poly(4-hydroxybutyrate),<sup>32</sup> (d) poly( $\epsilon$ -caprolactone),<sup>30</sup> (e) poly(10-hydroxycapric acid),<sup>30</sup> and (f) poly(PDL). The dotted line indicates  $T_m$  of polyethylene.<sup>30</sup>

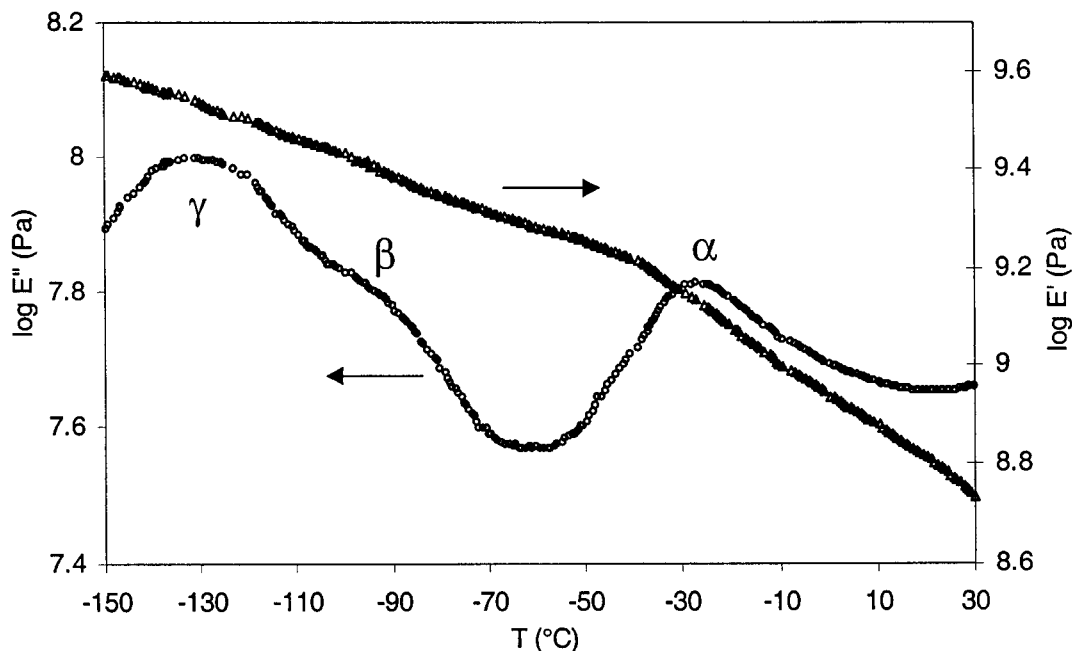
I) agrees with earlier results obtained from heat capacity measurements.<sup>14,15</sup> Poly(PDL) is a crystalline polymer, and the crystalline fraction imparts rigidity to the sample above  $T_g$ . For this reason, the storage elastic modulus ( $E'$ ) shows a limited decrease at the  $\alpha$  relaxation compared

with the drop typical of totally amorphous polymers (0.5 vs ca. 3 orders of magnitude).

In Figure 4, the low-temperature  $\gamma$  peak, centered at  $-130$  °C, is a local-mode secondary relaxation commonly found in polymers containing a sequence of three or more methylene groups in



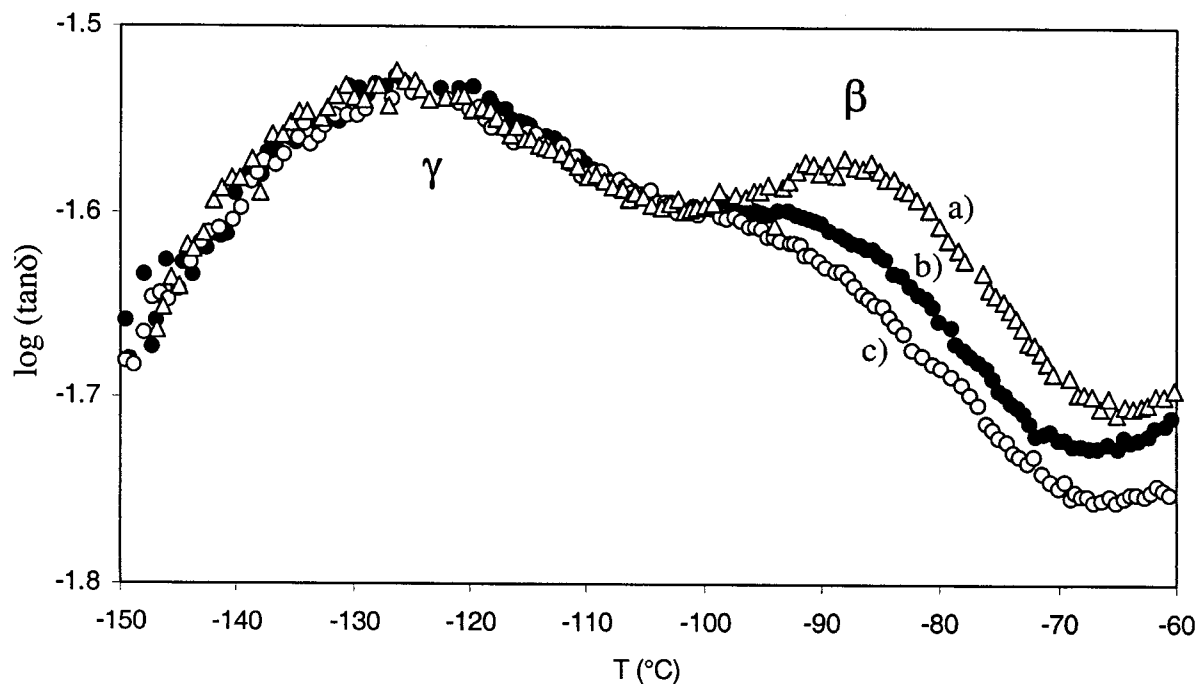
**Figure 3.** WAXS spectrum of poly(PDL).



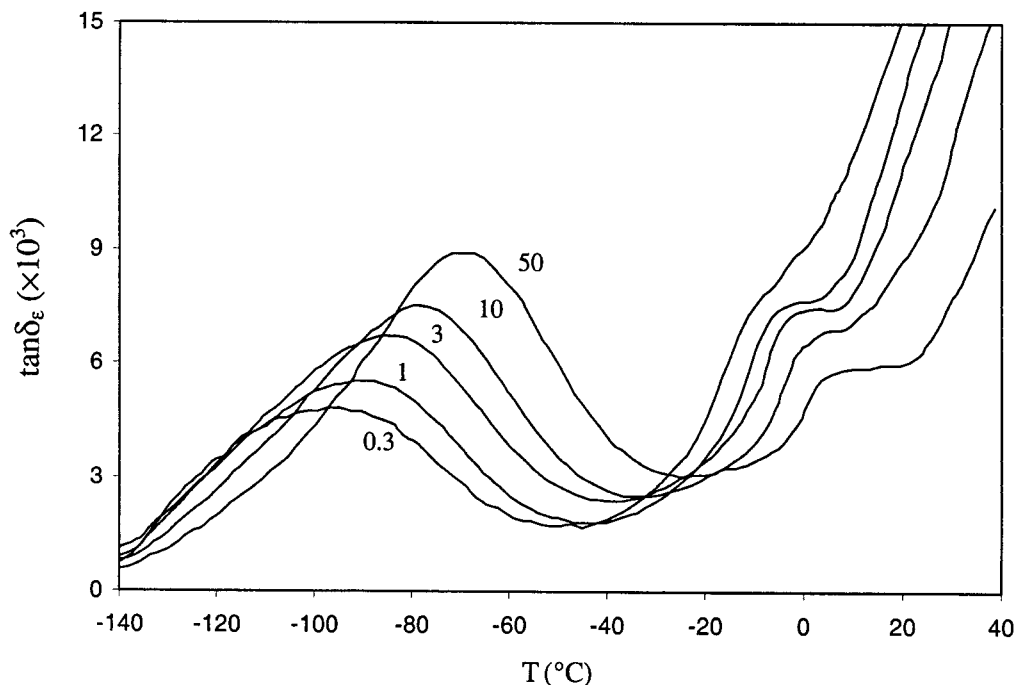
**Figure 4.** Dynamic mechanical spectrum of poly(PDL): (○)  $E''$  and (△)  $E'$ .

the repeating unit. For poly(PDL), it is attributed to the motion of the long main-chain methylene sequence. As revealed by TGA-MS, a small amount of water that is likely bound to the ester

groups of poly(PDL) is present in the polymer in normal room-humidity conditions. The  $\beta$ -dissipation process, located at about  $-90^\circ\text{C}$  and appearing as a shoulder on the high-temperature side of



**Figure 5.** Dynamic mechanical spectrum of poly(PDL) (low-temperature range) after different humidity conditioning (see the text).



**Figure 6.** Multifrequency dielectric spectra of poly(PDL). The numbers on the curves are frequencies in kilohertz.

the  $\gamma$  relaxation (Fig. 4), is affected by the water content of the polyester. This phenomenon is illustrated in Figure 5, which shows the loss tangent ( $\tan \delta$ ) of three poly(PDL) samples run after the following conditioning procedures: (a) 5 days at room temperature in saturated water vapor, (b) room humidity (the same as in Fig. 4), and (c) heating to 70 °C in DMTA and cooling to -150 °C under a dry  $N_2$  flow. In the case of curve c, the DMTA measurement was carried out under a dry  $N_2$  purge to avoid water absorption from the environment. Figure 5 shows that the intensity of the  $\beta$  relaxation increases with the water content of the poly(PDL) sample ( $c < b < a$ ), suggesting that the mechanical dissipation arises from the motion of units involving water associated with the macromolecule through polar interactions. Low-temperature dissipation phenomena, the so-called diluent-induced relaxations,<sup>22</sup> are common features in the viscoelastic spectrum of polar polymers that interact with the ubiquitous water molecules in the environment. The existence of water-dependent secondary relaxations in polyesters,<sup>23,24</sup> polysaccharides,<sup>25,26</sup> and other hydrophilic polymers<sup>27</sup> is well documented. The amount of water absorbed by poly(PDL) is limited by the hydrophobic character of its long methylene sequences and by the presence of a large

crystalline fraction. Nevertheless, the changes with conditioning shown by the spectra in Figure 5 confirm both the molecular origin of the  $\beta$  peak (water-dependent relaxation) and the presence of some water in room-conditioned poly(PDL) revealed by TGA-MS.

Dielectric spectroscopy, a relaxation technique applicable to polymers containing polar groups, was used to further extend the solid-state characterization of poly(PDL). The dielectric spectrum of the polyester at five selected frequencies is shown in Figure 6, where a broad dissipation region is observed in the low-temperature range. It is well known that in relaxation techniques the peak resolution capacity decreases with increasing frequency. For this reason, the  $\gamma$  and  $\beta$  relaxations that are well resolved in the DMTA curves of Figures 4 and 5 (frequency = 3 Hz) overlap in the DETA spectra of Figure 6 (frequency = 0.3–50 kHz). At the lowest dielectric frequency (0.3 kHz), the  $\gamma$  and  $\beta$  relaxations have already merged into a broad loss process, whereas at the highest frequency (50 kHz), the low-temperature  $\gamma$  relaxation, hidden by the  $\beta$  peak, is barely distinguishable. The high degree of uncertainty associated with deconvolution of the DETA curves does not allow the calculation of the activation energy of

the low-temperature relaxations of poly(PDL) from Arrhenius plots.

An additional dielectric relaxation from  $-10$  to  $+10$  °C (depending on the measurement frequency) is observed in the DETA spectra of Figure 6, which favorably compares with the  $\alpha$  relaxation of the DMTA spectrum (Fig. 4) and corresponds to the glass transition of poly(PDL). As commonly found in polymers, the steep increase of  $\tan \delta_\epsilon$  above the glass transition (Fig. 6) indicates the onset of direct-current conductivity, interfacial polarization phenomena, or both.<sup>28</sup> These results confirm the ability of relaxation techniques such as DMTA and DETA to reveal the glass-to-rubber transition of the amorphous phase in highly crystalline polymers.

The mechanical properties of the lipase-catalyzed polyester were also investigated, from the perspective of practical applications of poly(PDL) as a material. The polymer shows a stress-strain curve (not shown) that reflects a typical hard and tough behavior. In the experimental conditions applied, the sample elongates up to about 100–200%. The elastic modulus and yield parameters reported in Table I are comparable to those of a widely used polyolefin (low-density polyethylene),<sup>29</sup> indicating that poly(PDL) is a promising polymer for applications in a variety of fields.

Good mechanical properties associated with the presence along the polymer chain of hydrolyzable ester linkages suggest the consideration of poly(PDL) as a biodegradable material for diversified purposes, including biomedical applications.

A. Kumar and R. A. Gross are grateful to the industrial members (BASF, Cargill-Dow, DSM, EcoSynthetix, Nalco, Novozymes, and Maxygen) of the National Science Foundation Industrial/University Cooperative Research Center for Biocatalysis and Bioprocessing of Macromolecules at Polytechnic University for their encouragement and financial support of this research. In addition, M. L. Focarete and M. Scandola gratefully acknowledge partial support of this work by the Italian Ministry for University and Research.

## REFERENCES AND NOTES

- (a) Tokiwa, Y.; Kitagawa, M.; Fan, H.; Takao, R.; Yoichi, H.; Shibatani, S.; Kurane, R. *Biotechnol Tech* 1999, 13, 173; (b) Kline, B. J.; Beckman, E. J.; Russel, A. J. *J Am Chem Soc* 1998, 120, 9475; (c) Noda, S.; Kamiya, N.; Goto, M.; Nakashio, F. *Biotechnol Lett* 1997, 19, 307; (d) Patil, D. R.; Reth-
- wisch, D. G.; Dordick, J. S. *Biotechnol Bioeng* 1991, 37, 639; (e) Knani, D.; Gutman, A. L.; Kohn, D. H. *J Polym Sci Part A: Polym Chem* 1993, 31, 1221; (f) Knani, D.; Kohn, D. H. *J Polym Sci Part A: Polym Chem* 1993, 31, 2887.
- (a) Kumar, A.; Gross, R. A. *J Am Chem Soc* 2000, 122, 11767; (b) Kumar, A.; Kalra, B.; Dekhterman, A.; Gross, R. A. *Macromolecules* 2000, 33, 6303; (c) Kumar, A.; Gross, R. A. *Biomacromolecules* 2000, 1, 133; (d) *Enzymes in Polymer Synthesis*; Gross, R. A.; Kaplan, D. L.; Swift, G., Eds.; ACS Symposium Series 684; American Chemical Society: Washington, DC, 1998; (e) Deng, F.; Bisht, K. S.; Gross, R. A.; Kaplan, D. L. *Macromolecules* 1999, 32, 5159; (f) Deng, F.; Gross, R. A. *Int J Biol Macromol* 1999, 25, 153; (g) Bisht, K. S.; Deng, F.; Gross, R. A.; Kaplan, D. L.; Swift, G. *J Am Chem Soc* 1998, 120, 1363; (h) Bisht, K. S.; Henderson, L. A.; Gross, R. A.; Kaplan, D. L.; Swift, G. *Macromolecules* 1997, 30, 2705; (i) Henderson, L. A.; Svirkin, Y. Y.; Gross, R. A. *Macromolecules* 1996, 29, 7759; (j) Svirkin, Y. Y.; Xu, J.; Gross, R. A.; Kaplan, D. L.; Swift, G. *Macromolecules* 1996, 29, 4591; (k) MacDonald, R.; Pulapura, S.; Svirkin, Y. Y.; Gross, R. A.; Kaplan, D. L.; Akkara, J.; Swift, G. *Macromolecules* 1995, 28, 73.
- (a) Kobayashi, S.; Uyama, H.; Namekawa, S.; Hayakawa, H. *Macromolecules* 1998, 31, 5655; (b) Kobayashi, S.; Kiyosada, T.; Shoda, S. *J Am Chem Soc* 1996, 118, 13113; (c) Kobayashi, S.; Wen, X.; Shoda, S. *Macromolecules* 1996, 29, 2698; (d) Uyama, H.; Kikuchi, H.; Takeya, K.; Kobayashi, S. *Acta Polym* 1996, 47, 357; (e) Uyama, H.; Takeya, K.; Kobayashi, S. *Bull Chem Soc Jpn* 1995, 68, 56; (f) Uyama, H.; Takeya, K.; Hoshi, N.; Kobayashi, S. *Macromolecules* 1995, 28, 7046; (g) Uyama, H.; Kobayashi, S. *Chem Lett* 1993, 1149; (h) Kobayashi, S.; Kashiwa, K.; Kawasaki, T.; Shoda, S. *J Am Chem Soc* 1991, 113, 3079.
- Wong, C. H.; Chen, S. T.; Hennen, W. J.; Bibbs, J. A.; Wang, Y. F.; Lics, L. C.; Pantolino, M. W.; Whitlow, M.; Bryan, P. N. *J Am Chem Soc* 1990, 112, 945.
- Akkara, J. A.; Senecal, K. J.; Kaplan, D. L. *J Polym Sci Part A: Polym Chem* 1991, 29, 1561.
- Patil, D. R.; Dordick, J. S.; Rethwisch, D. G. *Macromolecules* 1991, 24, 3462.
- Wallace, J. S.; Morrow, C. J. *J Polym Sci Part A: Polym Chem* 1989, 27, 2553.
- Cordova, A.; Hult, A.; Hult, K.; Ihre, H.; Iversen, T.; Malmstrom, E. *J Am Chem Soc* 1998, 120, 13521.
- (a) Wallace, J. S.; Morrow, C. J. *J Polym Sci Part A: Polym Chem* 1989, 27, 3271; (b) Morrow, C. J.; Wallace, J. S. U.S. Patent 5,147,791, Sept 15, 1993.
- Nomura, R.; Ueno, A.; Endo, T. *Macromolecules* 1994, 27, 620.
- Biomaterials Science: An Introduction to Materials in Medicine*; Ratner, B. D.; Hoffman, A. S.; Schoen, F. J.; Lemons, J. E., Eds.; Academic: London, 1996.

12. Pitt, C. *Drugs Pharm Sci* 1990, 45, 71
13. Datta, R.; Tsai, S. P.; Bonsignore, P.; Moon, S. H.; Frank, J. R. *FEMS Microbiol Rev* 1995, 16, 221.
14. Lebedev, B.; Yevstropov, A. *Makromol Chem* 1984, 185, 1235.
15. Skoglund, P.; Fransson, Å. *Polymer* 1998, 39, 1899.
16. Skoglund, P.; Fransson, Å. *Polymer* 1998, 39, 3143.
17. Zhong, Z.; Dijkstra, P. J.; Feijen, J. *Macromol Chem Phys* 2000, 201, 1329.
18. Statheropoulos, M.; Kyriakou, S.; Tzamtzis, N. *Thermochim Acta* 1998, 322, 167.
19. Focarete, M. L.; Scandola, M. Unpublished results.
20. Jedlinski, Z.; Juzwa, M.; Adamus, G.; Kowalczuk, M. *Macromol Chem Phys* 1996, 197, 2923.
21. Ruland, W. *Acta Crystallogr* 1961, 14, 1180.
22. Kolarik, J. *Adv Polym Sci* 1982, 46, 119.
23. Scandola, M.; Pizzoli, M.; Ceccorulli, G.; Cesaro, A.; Paoletti, S.; Navarini, L. *Int J Biol Macromol* 1988, 10, 373.
24. Scandola, M.; Ceccorulli, G.; Doi, Y. *Int J Biol Macromol* 1990, 12, 113.
25. Pizzoli, M.; Ceccorulli, G.; Scandola, M. *Carbohydr Res* 1991, 222, 205.
26. Scandola, M.; Ceccorulli, G.; Pizzoli, M. *Int J Biol Macromol* 1991, 13, 254.
27. Pizzoli, M.; Scandola, M. In *Polymeric Materials Encyclopedia*; CRC: Boca Raton, FL, 1996; Vol. 7.
28. *Dielectric Spectroscopy of Polymeric Materials*; Runt, J. P.; Fitzgerald, J. J., Eds.; American Chemical Society: Washington, DC, 1997.
29. *Physical Properties of Polymers Handbook*; Mark, J. E., Ed.; American Institute of Physics: Woodbury, NY, 1996.
30. *Polymer Handbook*, 4th ed.; Brandrup, J.; Immergut, E. H.; Grulke, E. A., Eds.; Wiley Interscience: New York, 1999.
31. Shimamura, E.; Scandola, M.; Doi, Y. *Macromolecules* 1994, 27, 4429.
32. Nakamura, S.; Doi, Y.; Scandola, M. *Macromolecules* 1992, 25, 4237.