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Shape Memory Behavior of Novel (L-Lactide−Glycolide−Trimethylene Carbonate) Terpolymers

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Bioresorbable new terpolymers of L-lactide, glycolide, and trimethylene carbonate with different compositions were synthesized via ring-opening polymerization reaction of the cyclic monomers using low-toxicity zirconium(IV) acetylacetonate as initiator. The thermal and mechanical properties were investigated by means of thermogravimetry, differential scanning calorimetry, stress−strain measurements, and dynamical mechanical analysis. The glass transition temperature of the terpolymers changes with composition from 12 to 42 °C in a predictable manner. All terpolymers display shape memory properties and, after undergoing 100% deformation, they recover the permanent shape in a time frame of seconds. Terpolymers with high L-lactide content show a glass transition in the range of 38−42 °C, recovery temperature close to body temperature, and good recovery ratio (>0.89). Low-toxicity bioresorbable terpolymers with shape memory properties are promising new materials for biomedical applications.

Introduction

Shape memory materials are stimuli-responsive compounds that can change their shape as a consequence of an external stimulus, such as variations of temperature, light, pH, etc.[1] Among shape memory materials, thermoresponsive shape memory polymers (SMP) have recently drawn great interest because of their good processability, low cost, and high recovery ability at relatively low temperatures.[1−6] SMPs must be first processed to receive their permanent shape. Afterward, within a given temperature range, SMPs can be easily deformed into a temporary shape that is then fixed by fast cooling: this process is named programming.[1] The sample now displays the given temporary shape, while the permanent shape is stored in the sample "memory". When required, the memorized permanent shape can be regained by reheating.

Usually SMPs display at least two phases, characterized by two distinct thermal transitions. The phase showing the highest transition temperature (associated with either a glass transition or a melting phenomenon) acts as a physical cross-linker of the polymer chains and is responsible for the permanent shape. The second phase, with lower transition temperature, plays the role of a molecular switch. Above and below this "switching temperature" the temporary shape is, respectively, formed and fixed.

Applications of SMPs are widespread and include sensors, self-repairing bodies, actuators, and medical implants.[7−13] In the specific field of medical implants, the shape memory ability is particularly desirable in order to minimize surgical impact. Indeed, the material can be implanted in the human body in a small-size temporary shape, and it is then allowed to recover the original larger shape at body temperature. In biomedical applications, shape memory materials are required to be both biocompatible and to have a recovery temperature near human body temperature. To date the most widely used shape memory materials implanted in the human body are metallic alloys (SMAs).[7] Bioresorbable SMPs are very promising candidates for replacement of SMAs for short-term applications because, contrary to metal implants, they do not require additional removal operation after implantation.

Typical SMPs for biomedical applications reported in the literature are segmented polyurethanes obtained by means of two-stage synthesis. In a first stage macrodiols of cyclic diesters or lactones (oligolactides, oligocaprolactone, oligo(lactide-*co*-glycolide) diols) are prepared; afterward they are condensed with coupling compounds such as diisocyanates and chain extenders to obtain segmented copolymers composed by hard and soft blocks.[2,4,5,14] Depending on the chemical structure, length, and composition of hard and soft blocks, different properties and shape recovery temperatures can be obtained.

A different approach to biocompatible and bioresorbable polymer materials with shape memory properties is the ring-opening polymerization or copolymerization of lactides, lactones, and cyclic carbonates. Aliphatic polyesters and polyestercarbonates are the best known bioresorbable materials, whose biocompatibility has been clinically confirmed, and which are now applied in daily medical practice. These polymers are used as forming elements for osteosynthesis, as threads and wovens for treatment in internal tissue injuries, as carriers in controlled release of drugs, as scaffolds for cell culturing in tissue engineering, etc.[15]

Poly(L-lactide) (PLLA) is one of the most studied polymers for biomedical applications whose shape memory properties have been already reported.[11] However, as an SMP its recovery ratio is relatively low and the recovery temperature is too high

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Table 1. Molecular Weight, Chemical Composition, and Thermal Properties of Terpolymers

sample	time (h)	conversion (%)[a]	composition[a]	M_n (Da)[b]	PDI[b]	$\Delta m_{RT-200°C}$ (%)[c]	T_{max} (°C)[c]	T_g (°C)[d]	T_α (°C)
Zr1	72	90	G34:L20:T46	33700	2.1	0.3	336	12	15[e]
Zr2	72	88	G24:L33:T43	31100	2.3	0.3	336	21	26[e]
Zr3	48	94	G37:L36:T27	53900	2.0	0.7	335	31	37[f]
Zr4	48	95	G25:L53:T22	43500	2.1	1.0	346	39	45[f]
Zr5	36	97	G35:L52:T13	48400	2.0	0.8	341	42	50[f]
Zr5a	36	92	G37:L47:T16	26500	2.3	0.4	324	40	47[f]
Sn5	36	94	G37:L48:T15	24600	2.2	1.0	275	38	47[f]

[a] From ^{1}H NMR. The composition is labeled G*x*:L*y*:T*z* where *x*, *y*, and *z* indicate the content in mol % of glycolidyl (G), lactidyl (L), and trimethylene carbonate (T) units, respectively. [b] From GPC. [c] From TGA. [d] From DSC. [e] From DMTA in bending mode (polymer films sandwiched between two aluminum plates). [f] From DMTA in tensile mode.

for the use in human body.[16,17] Copolymerization is a strategy that can be applied to decrease the glass transition temperature of PLLA and, as a consequence, to lower the recovery temperature of the material in shape memory applications. Earlier investigations showed that copolymerization of L-lactide with other lactones (ϵ-caprolactone and glycolide)[16,18] or with cyclic trimethylene carbonate (TMC)[19,20] is an easy route to materials whose properties can be modulated by changing composition. In particular, materials with glass transition in the physiological temperature range can be obtained by copolymerization.

Ring-opening copolymerization of lactide with other cyclic monomers is commonly carried out using stannous compounds as initiators.[16,20,21] However, these compounds are relatively toxic, and it is practically impossible to totally eliminate them from the final synthesized polymer.[22] A group of significantly less toxic compounds includes zirconium complexes, which are practically inert in human metabolic processes. Moreover, most absorbed zirconium is eliminated from the body in bile, and only small amounts appear in urine.[23,24] The low biological toxicity of zirconium complexes has been confirmed by prolonged survival of selected cell cultures carried out on poly(lactide−glycolide) copolymers synthesized using zirconium(IV) acetylacetonate Zr(Acac)$_4$, compared with shorter survival of cells cultured on the same material polymerized using stannous octanoate Sn(Oct)$_2$ as initiator.[25,26]

Following earlier successful application of Zr(Acac)$_4$ to the synthesis of bioresorbable copolyesters[18,27] and copolyestercarbonates,[19,28] this compound is used in the present work as the initiator of lactide/glycolide/TMC terpolymerization. The obtained polymers show shape memory properties, and they recover the permanent shape near body temperature.

Experimental Section

Materials. The monomers, namely, L-lactide (from Purac), glycolide (from Purac), and 1,3-trimethylene carbonate (from Boehringer Ingelheim), were purified by recrystallization from dry ethyl acetate and were subsequently dried in a vacuum oven at 30 °C. Zirconium(IV) acetylacetonate and stannous(II) octanoate (from Aldrich) were used as initiators, without further purification.

Terpolymerization Procedure. The terpolymerizations of L-lactide, glycolide, and 1,3-trimethylene carbonate (TMC) were conducted in bulk at 120 °C in an argon atmosphere. Weighed amount of glycolide, L-lactide, TMC monomers with the initiator, either Zr(Acac)$_4$ or Sn(Oct)$_2$, were charged into dried glass ampoules, which were then sealed. The ampoules were conditioned at 120 °C in an oil bath equipped with a periodically working shaker. After selected reaction times (Table 1), the ampoules were cooled to room temperature to quench the reaction, and the obtained polymers were discharged.

All obtained samples were purified by means of dissolution in chloroform followed by precipitation in methanol.

Polymer Processing. After purification the terpolymers were dried in an oven at 80 °C under reduced pressure in order to eliminate residual solvent. Sheets (0.3−0.5 mm thickness) were obtained by hot pressing the terpolymer samples at 100 °C between Teflon plates, in a Carver laboratory press. The polymer was allowed to melt for 2 min, then a pressure of 0.56 MPa was applied for 30 s. The obtained sheet was quickly cooled to room temperature in the press, with the aid of cold running water.

Characterization. The molecular weights and polydispersities of the polymers were determined by gel permeation chromatography with a Viscotek RImax chromatograph (chloroform was used as the eluent, the temperature and flow rate were 35 °C and 1 mL/min, respectively, two PL Mixed C columns with a Viscotek model 3580 refractive index detector and injection volume equal to 100 μL were used). The molecular weights were calibrated with polystyrene standards.

The copolymer composition and conversion of the polymerization reaction were determined by ^{1}H NMR spectroscopy. The ^{1}H NMR spectra of the copolymers were recorded at 300 MHz using a Varian Unity Inova spectrometer and a 5 mm sample tube. Dried DMSO-d_6 was used as solvent, and TMS was the internal standard. The spectra were obtained at 50 °C with 32 scans, 3.74 s of acquisition time, and 7 μs pulse width. As an example, Figure 1 shows a representative ^{1}H NMR spectrum of terpolymer Zr3, whose composition and molecular weight are reported in Table 1. The signal assignment shown in Figure 1 is based on previously reported proton spectra of glycolide/L-lactide,[18] glycolide/TMC,[28] and L-lactide/TMC[19] copolymers.

Thermogravimetric analysis (TGA) was performed with a TA Instruments TGA 2950 thermogravimetric analyzer from room temperature to 600 °C, at a heating rate of 10 °C/min, under nitrogen purge. Differential scanning calorimetry (DSC) was carried out using a TA Instruments Q100 DSC equipped with the LNCS low-temperature accessory. The temperature scale was calibrated with high-purity standards. DSC scans were performed at a heating rate of 20 °C/min, in helium atmosphere and in the temperature range from −100 to 200 °C. The glass transition temperature (T_g) was taken at the midpoint of the stepwise specific heat increment. Repeated heating scans were performed in order to verify the reproducibility of results.

Stress−strain measurements were carried out on strips die-cut from hot-pressed sheets (width, 5 mm; average thickness, 0.3 mm) by means of an Instron 4465 tensile testing machine. The measurements were conducted at room temperature (21 °C). The cross-head speed was 5 mm/min, and the gauge length was 20 mm. Dynamic mechanical measurements were carried out on film samples using a DMTA MkII (Polymer Laboratories Ltd.) in tensile mode. The analyses were conducted using a pretensioning force of 0.4 N, a heating rate of 3°/min, and a frequency of 3 Hz, in the temperature range from −150 °C up to above the glass transition of each sample. For particularly soft samples it was difficult to apply the pretension necessary for DMTA measurements in tensile mode. In such cases dynamic mechanical

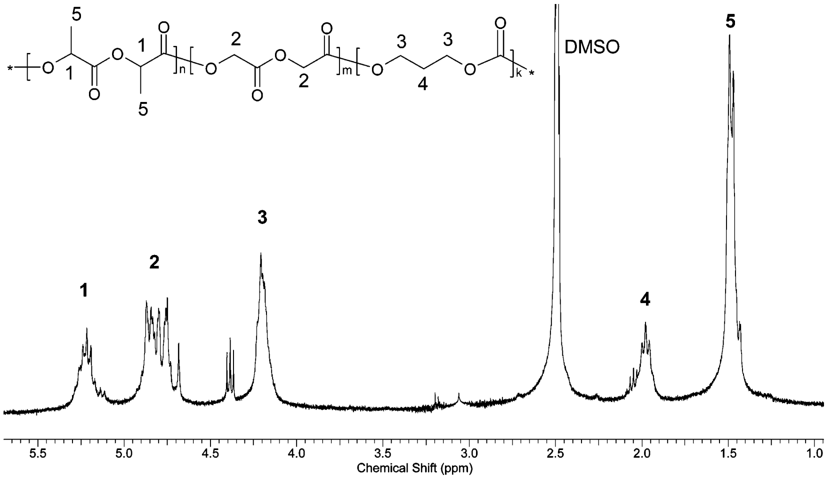

Figure 1. ^{1}H NMR spectrum (in DMSO-d_6) of Zr3 sample.

measurements were performed in bending mode, on sample films sandwiched between aluminum plates, as previously described.[29]

The shape memory behavior of the terpolymers was quantitatively evaluated by a two-step procedure, i.e., deformation and recovery, as described below. At first, by means of the Instron dynamometer a polymer strip (width = 5 mm; thickness ~0.4 mm) was stretched at T = 48 °C up to 100% deformation (strain rate, 60 mm/min; gauge length = 10 mm). Without releasing the sample from the grips, the deformed strip (i.e., the temporary shape) was fixed by quenching the sample to 0 °C with the aid of ice spray. Then the sample was removed from the dynamometer clamps, and it was immediately transferred to the second (recovery) step. Recovery was quantitatively assessed using the DMTA analyzer in tensile mode and applying the following nonconventional procedure: the applied force was set to zero and the change of sample length was recorded during a heating scan at 2°/min from 0 to 70 °C.

Results and Discussion

Synthesis of L-Lactide/Glycolide/TMC terpolymers. Terpolymers with different unit composition (Table 1) were obtained by changing the monomer feed ratio. As a rule, Zr(Acac)$_4$ was used as the reaction initiator, with an initiator-to-monomer molar ratio (I/M) equal to 1:1000 (Table 1, samples Zr1, Zr2, Zr3, Zr4, Zr5). For the sake of comparison, an additional terpolymer with the same composition as Zr5 but using Sn(Oct)$_2$ as initiator was prepared (Sn5, I/M = 1:1000). As evidenced in Table 1, regardless of composition, all samples were obtained with high conversion, but this goal was reached after different reaction times. Among carbonate-based comonomers, TMC has a particularly low reactivity, and this is the reason why terpolymers with increasing TMC content require increasing reaction times to reach high conversion.

It is worth noting that terpolymer Sn5 has a significantly lower molecular weight than the corresponding terpolymer synthesized using Zr(Acac)$_4$ (Zr5). This fact is likely to be due to lower efficiency of Sn(Oct)$_2$ as initiator in the ring-opening terpolymerization. In order to investigate the effect of molecular weight on the terpolymer properties, an additional sample (Zr5a), having the same unit composition as Zr5, was prepared with Zr(Acac)$_4$ using a different I/M ratio (1:500). According to expectations, a higher concentration of initiator (twice as much) produces a polymer with lower molecular weight (roughly halved in Zr5a compared to Zr5). Interestingly, the molar mass of Zr5a (polymerized starting from I/M = 1/500) is similar to that of Sn5, a sample obtained with I/M = 1:1000 using the less efficient Sn(Oct)$_2$ initiator.

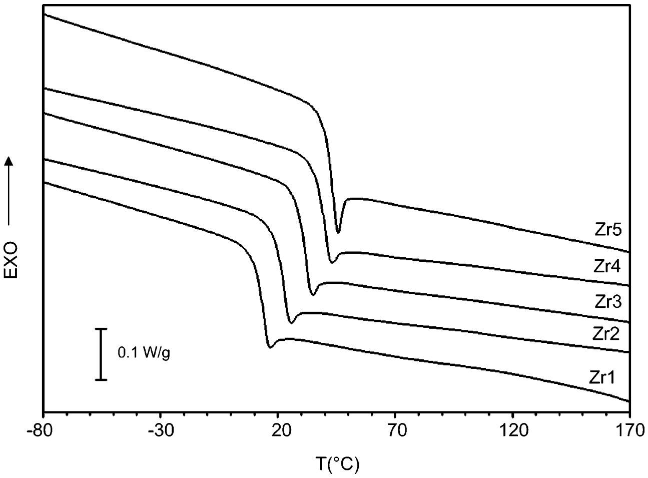

Figure 2. DSC curves after quench cooling from the melt of terpolymers Zr1, Zr2, Zr3, Zr4, and Zr5.

Thermal Properties. Thermogravimetric analysis shows that in the range from room temperature (RT) to 200 °C all investigated terpolymers are quite stable, with a maximum observed weight loss of 1% (Table 1). All samples degrade in a single decomposition step. The temperature of maximum degradation rate (T_{max}) is similar in terpolymers synthesized using Zr(Acac)$_4$ as initiator in a 1:1000 initiator-to-monomer ratio, i.e., Zr1, Zr2, Zr3, Zr4, and Zr5. Therefore, no dependence of thermal stability on composition is observed in this group of terpolymers. However, terpolymers with very similar composition, but different molar mass (Zr5 and Zr5a), exhibit different thermal stability. Sample Zr5a degrades at a significantly lower temperature than Zr5, in agreement with the known dependence on molecular weight of polyesters' thermal stability.[30] It is worth noting that, although Zr5a and Sn5 have similar unit composition and molecular weight, the terpolymer synthesized using Sn(Oct)$_2$ degrades 50 °C lower than Zr5a (compare T_{max} in Table 1). The low thermal stability of Sn5 can be associated with the presence of the Sn(Oct)$_2$ initiator, which is known to catalyze transesterification reactions, particularly back-biting reactions that release volatile byproducts.[31] The TGA results show that Zr(Acac)$_4$ initiator, besides being less toxic than Sn(Oct)$_2$, also leads to terpolymerization products with higher thermal stability.

Figure 2 shows the DSC curves of terpolymer samples with different unit composition. In each DSC curve, the stepwise specific heat increment associated with the glass transition is the only thermal feature observed. The same result (i.e., a single

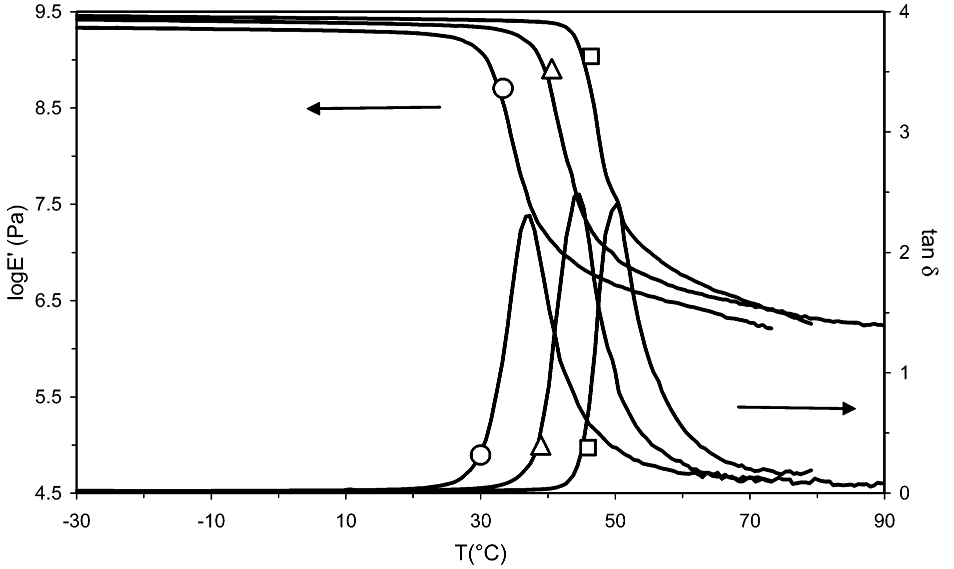

Figure 3. DMTA curves (log *E*′ and tan *δ*) of terpolymers: (□) Zr5, (△) Zr4, and (○) Zr3 (3 Hz, 3 °C/min, tensile mode).

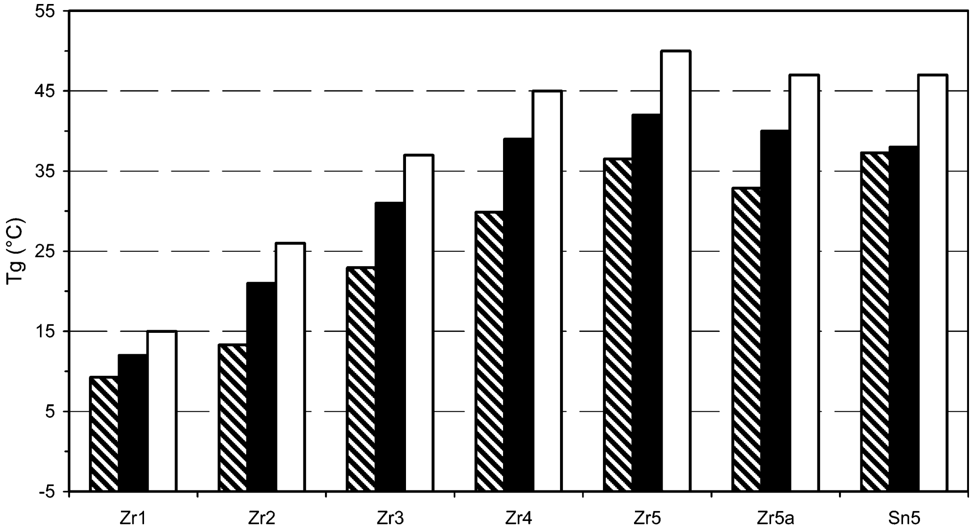

Figure 4. Glass transition temperature of terpolymers: experimental data from DSC (black bars), experimental data from DMTA (white bars), and calculated values from eq 1 (striped bars).

glass transition phenomenon) is obtained for samples Zr5a and Sn5 whose DSC curves, similar to that of Zr5, are not reported for the sake of clarity. The DSC results show that all terpolymers are single-phase amorphous materials with no evidence of phase separation. The glass transition temperatures are collected in Table 1.

Dynamic mechanical spectroscopy was also used to investigate the glass transition phenomenon. As an example Figure 3 shows the DMTA curves (storage modulus E' and loss factor tan δ) of selected terpolymers with different unit composition (Zr5, Zr4, and Zr3). In the low-temperature region of each DMTA curve, the elastic modulus slightly decreases with increasing temperature, as expected, whereas at the glass transition it undergoes an abrupt drop of about 3 orders of magnitude. In correspondence to the modulus step, the tan δ curve displays the α relaxation peak, whose maximum temperature (T_α) is reported in Table 1. Comparison of the T_α's from DMTA with the T_g data from DSC shows that, although the former values are higher than the latter owing to the well-known frequency effect, both T_α and T_g follow a common trend with changing terpolymer composition.

In order to rationalize the glass transition temperature changes with composition in the terpolymers, the well-known Fox equation[32] was modified to account for a three-component system as follows:

$$1/T_{\mathrm{gter}} = w_1/T_{\mathrm{g1}} + w_2/T_{\mathrm{g2}} + w_3/T_{\mathrm{g3}} \qquad (1)$$

where T_{gter} is the glass transition temperature of the terpolymer, the indexes 1, 2, and 3 refer to the three monomers, w is the monomer weight fraction in the terpolymer, and T_{g1}, T_{g2}, and T_{g3} are the glass transition temperatures of the respective homopolymers. Equation 1 was applied to calculate the glass transition of terpolymers with given composition, using the following values (from DSC) for the glass transition temperature of the homopolymers: polyglycolide acid = 309 K;[18] PLLA = 332 K;[19] polytrimethylene carbonate = 261 K.[33] In particular, eq 1 was used to calculate the T_g of terpolymers with the same composition as those investigated in this work, and the obtained values are plotted in a bar graph in Figure 4, where they are compared with the experimental DSC and DMTA data. It is clear that the calculated values (striped bars) follow the same trend with composition as the experimental T_g's, showing that the proposed modified Fox equation (eq 1) can be used to predict with good approximation the glass transition of the terpolymers as a function of comonomer content. A range of glass transition

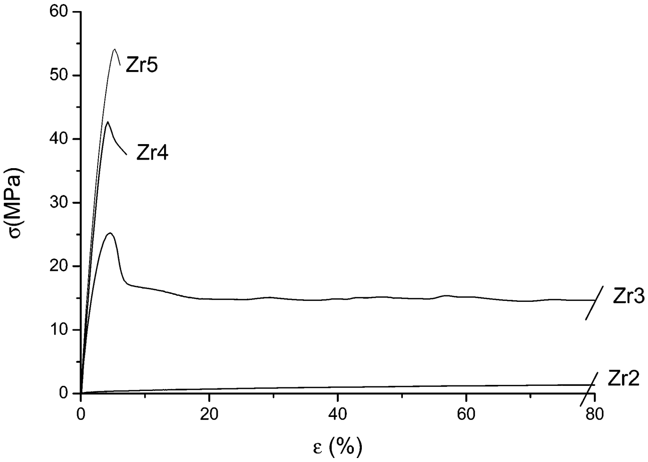

Figure 5. Stress−strain curves (5 mm/min, room temperature) of terpolymers: Zr2, Zr3, Zr4, and Zr5.

temperatures, achieved by targeted variations of the relative content of the three monomers, is accessible to this terpolymer system leading to materials with tunable physical properties.

Mechanical Properties. Figure 5 shows stress−strain curves at RT of terpolymers with different monomer composition (Zr2, Zr3, Zr4, Zr5). The mechanical behavior of these polyesters is markedly different, reflecting the differences of the individual T_g values (Table 1) and particularly the respective glass transition location relative to RT. Samples Zr4 and Zr5, having T_g well above RT (Table 1), are characterized by a high Young's modulus (1353 and 1541 MPa, respectively). They show a yield point at $\epsilon_y = 4.5\%$, with $\sigma_y = 41$ MPa (Zr4) and $\sigma_y = 49$ MPa (Zr5), and a very low strain at break (less than 8%). Zr5a and Sn5, which possess a T_g similar to that of Zr5, display analogous stress−strain curves that are not reported in Figure 5 for the sake of clarity. Terpolymer Zr3, which has a T_g around RT, shows a Young modulus (871 MPa) markedly lower than that of the above samples and, after yielding at $\epsilon_y = 4.7\%$ and σ_y =26 MPa, it breaks well above 100% deformation. Hence, sample Zr3 is much tougher and more ductile than Zr4 and Zr5. Finally, sample Zr2 (having T_g slightly below RT) displays a typical elastomeric behavior: low Young modulus (148 MPa) and no yield point. Terpolymer Zr1, whose glass transition temperature is below RT, displays the lowest modulus of all terpolymers investigated (3 MPa), and its stress−strain curve is not reported in Figure 3 because in the given stress (σ) scale it would be indistinguishable from the *x*-axis.

Shape Memory Properties. A preliminary investigation on the shape memory properties of the terpolymers was carried out by thermally cycling compression-molded film strips between two selected temperatures. The upper temperature (TU) was used to impose a temporary deformed shape to the sample (by stretching), whereas the lower temperature (TL) was used to fix such a shape. For each terpolymer, the TU was at least 6 °C above the respective T_g, whereas the TL was either RT (for Zr5, Zr5a, Sn5, and Zr4) or 0 °C (for Zr1, Zr2, and Zr3). In these preliminary experiments all terpolymers were manually stretched at TU to reach an elongation higher than 100% (step 1), and then they were rapidly cooled down to TL (step 2). It was visually verified that all terpolymers are able to recover the initial shape when returned to TU (step 3), and it was found that this property strongly depends on the procedure adopted in step 1 to impose the temporary shape at TU, particularly on the two combined effects of time and temperature. As an example, the ability of sample Zr5 to completely recover its original shape (in step 3) depends on the specificity of step 1 as follows: at TU = 48 °C the stretching procedure can last up to 1 min, whereas at TU = 52 °C the maximum stretching time allowing total recovery decreases to 15 s, and at TU = 60 °C it is further reduced to 5 s. Longer times at the given temperatures induce a degree of nonrecoverable deformation, as a consequence of material flowing. This result shows that, when the deformation temperature is increased, deformation time must be reduced, in order to allow subsequent full recovery of the original shape. The same experiment was repeated with all terpolymers, and it was found that by applying a suitable deformation program (temperature and time), each sample can totally recover the permanent shape, as estimated by visual observation.

In Figure 6, a picture sequence illustrates, as an example, the shape memory performance of terpolymer Zr5 (T_g = 42 °C, Table 1). The permanent shape of the material (Figure 6a) is a spiral, obtained by keeping the sample strip wrapped around a screwdriver in an oven at 100 °C for 1 h. The spiral is then deformed by unwinding the sample into a water bath at TU = 48 °C for 10 s, and the obtained temporary shape (straight strip, Figure 6b) is fixed by quickly withdrawing the sample from the hot water bath and cooling down at RT. Figure 6c−e illustrating the full shape recovery process are pictures taken, respectively, 2, 3, and 4 s after reimmersion of the sample in the water bath at 48 °C. It is clear from pictures in Figure 6 that, when the deformed strip is dipped again in the water bath at 48 °C, the spiral permanent shape is completely recovered in a matter of seconds (compare Figure 6, parts a and e).

The shape memory behavior of terpolymers having T_g above RT (Zr4, Zr5, Zr5a, and Sn5) was quantitatively assessed by means of a concerted use of the Instron dynamometer and of the DMTA instrument (see the Experimental Section), by which changes of strain (ϵ), stress (σ), and temperature (T) were measured. Figure 7 summarizes the results of a typical shape memory experiment performed on Zr4, in a three-dimensional graph. The initial position A represents the permanent shape at 48 °C (no strain, no stress). Path 1 from position A to position B is a stress−strain curve (σ vs ϵ) at constant temperature (48 °C), i.e., the result of the deformation process carried out in the dynamometer. The 100% strained strip (temporary shape) is indicated by position B and corresponds to the maximum sample strain (ϵ_m). Such temporary ϵ_m deformation is fixed by quenching the sample down to 0 °C. The sample is now at position C in the plot, with no stress applied, and it is ready for the recovery process, carried out at a constant heating rate without stress applied. Recovery is represented by path 2 in Figure 7 and is performed in the DMTA. The final shape (D) indicates that at the end of shape memory experiment the sample displays a small residual strain (ϵ_r). The ability of the sample to recover, hence to "memorize" its permanent shape after one deformation cycle, is quantified by the shape recovery ratio parameter (R_r), defined as follows:

$$R_r = (\epsilon_m - \epsilon_r)/\epsilon_m \qquad (2)$$

where ϵ_m is the strain imposed to the strip at 48 °C and ϵ_r is the measured residual strain after one complete cycle of the shape memory experiment. From the recovery curve (path 2 in Figure 7) additional recovery parameters can be obtained. The maximum slope of the sinusoidal recovery curve (tangent slope at the inflection point) indicates the recovery rate. The intersection of such tangent with the baseline prior to recovery is taken as the initial recovery temperature (IRT). Table 2 collects R_r, recovery rate, and IRT values of the investigated terpolymers. It is evident from Table 2 that in all cases the shape recovery

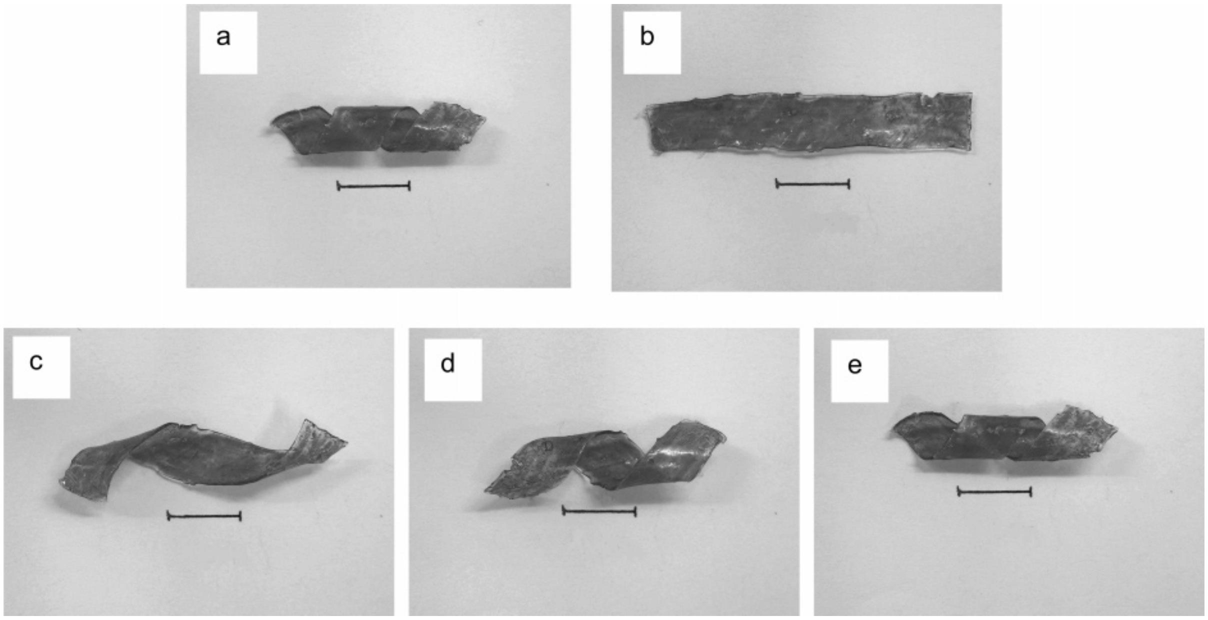

Figure 6. Shape memory experiment on a strip of terpolymer Zr5: the permanent shape (spiral, a); the temporary shape (unwound strip, b); the recovery process at 48 °C (c) after 2 s, (d) after 3 s, and (e) after 4 s; bar = 1 cm.

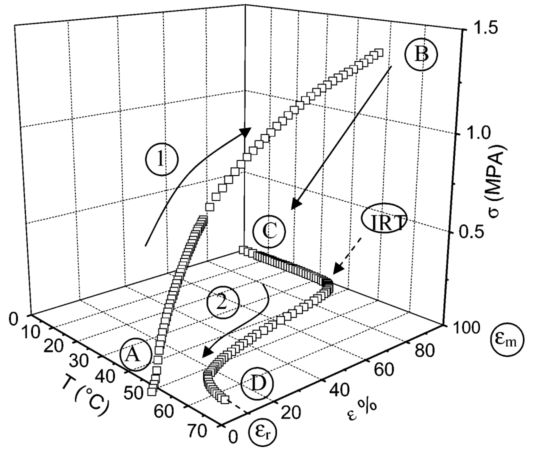

Figure 7. Thermomechanical experiment on a strip of terpolymer Zr4: (1) stress−strain curve at 48 °C (strain rate, 60 mm/min); (2) recovery process (heating rate, 2 °C/min), see text.

Table 2. Recovery Parameters of Terpolymers

sample	T_g (°C)[a]	R_r[b]	recovery rate (%/°C)[c]	IRT (°C)[d]
Zr4	39	0.90	6.7	37
Zr5	42	0.92	10.8	40
Zr5a	40	0.89	8.0	38
Sn5	38	0.95	7.1	40

[a] From DSC. [b] Shape recovery ratio, eq 2. [c] Slope at the inflection point of the sinusoidal recovery curve. [d] Initial recovery temperature, see text.

ratio is at least 0.89 after one deformation cycle. Moreover, among the three samples with similar unit composition (Zr5, Zr5a, Sn5), the fastest recovery is shown by Zr5 that has the highest molecular weight (Table 1).

It is commonly accepted that, in order to show thermally induced shape memory behavior, polymers should possess two components at the molecular level: a fixing phase, constituted by physical or chemical cross-links that impart dimensional stability, and a reversible phase that provides elastomeric properties. Hence, in the broadest sense, thermoresponsive SMPs are networks. As illustrated above, the poly(L-lactide, glycolide, TMC)s investigated in this work show a single and sharp glass-to-rubber transition as the only thermal event in both the DSC and DMTA curves. They are therefore amorphous single-phase materials, with neither chemical cross-links nor crystals that may anchor the polymer chains. In this case the fixing phase responsible for the observed shape recovery must be provided by chain entanglements, whose presence and number is known to depend on polymer molecular weight, and notably, their density under deformation is a function of time and temperature.[34] This is the reason why, as mentioned before, the shape memory properties of the terpolymers depend so strongly on the specific deformation program applied. It is clear that temperature and deformation time must be kept as low as possible to hinder disentanglement of polymeric chains leading to irreversible flow. In keeping with these arguments, the higher recovery rate of sample Zr5 (Table 2) compared with that of terpolymers with analogous unit composition (Zr5a and Sn5) can be explained by the presence of a higher average number of entanglements per molecule in Zr5, due to its higher molecular weight, that enables a faster shape recovery.

Finally it is worth noting that the temperature at which the terpolymers initiate to recover the deformation (IRT in Table 2) is located in the neighborhood of human body temperature. It is therefore concluded that, providing that a tuned and accurate programming is used in order to avoid viscous deformation of the material, some of the analyzed terpolymers of L-lactide, glycolide, and TMC might find interesting clinical applications as shape memory implants.

Conclusions

In the present paper the solid-state properties of new interesting terpolymers poly(L-lactide, glycolide, TMC) with different compositions have been described. The glass transition temperature of the terpolymers changes with unit composition and follows a trend based on the relative amount of the three units. When the terpolymers are deformed at a suitable TU above T_g and the deformation is fixed at a TL below T_g, they are able to recover the initial shape with a shape recovery ratio higher than 0.89, when returning to TU. The shape memory ability strongly depends on the procedure adopted to impose the temporary shape, and it is ascribed to the existence of chain entanglements that act as temporary cross-links. For this reason the deformation program is the crucial point of the shape memory experiment, and it must be accurately applied. However, since terpolymer properties can be tuned during the synthesis, it is expected that continuing research in this field will produce materials allowing easier programming.

Terpolymers that recover their original shape at temperatures located in the neighborhood of human body temperature are now available. Among them, samples initiated with $Zr(Acac)_4$ have the additional advantages of higher thermal stability than those initiated with common stannous initiators and contain a less toxic compound as the initiator residue. It is therefore concluded that the analyzed terpolymers of L-lactide, glycolide, and TMC obtained using $Zr(Acac)_4$ as initiator may find practical medical applications as novel SMPs for devices such as self-expanding stents, new tools for microinvasive surgery, or smart matrices for controlled drug release.

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References and Notes

(1) Lendlein, A.; Kelch, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 2034−2057.
(2) Kim, B. K.; Lee, S. Y.; Xu, M. *Polymer* **1996**, *37*, 5781−5793.
(3) Lendlein, A.; Schmidt, A. M.; Langer, R. *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 842−847.
(4) Ping, P.; Wang, W.; Chen, X.; Jing, X. *Biomacromolecules* **2005**, *6*, 587−592.
(5) Wang, W.; Ping, P.; Chen, X.; Jing, X. *Eur. Polym. J.* **2006**, *42*, 1240−1249.
(6) Xu, J.; Shi, W.; Pang, W. *Polymer* **2006**, *47*, 457−465.
(7) El Feninat, F.; Laroche, G.; Fiset, M.; Mantovani, D. *Adv. Eng. Mater.* **2002**, *4*, 91−104.
(8) Kaway, T; Matsuda, T. Plastic Molded Articles with shape memory properties. U.S. Patent 4950258, 1990.
(9) Lendlein, A.; Langer, R. *Science* **2002**, *296*, 1673−1676.
(10) Lendlein, A; Knischka, R; Kratz, K. Shape memory thermoplastics and polymer networks for tissue engineering. U.S. Patent 2004110285, 2004.
(11) Shikinami, Y. Shape-Memory, biodegradable, absorbable material. U.S. Patent 6281262, 2001.
(12) Venkatraman, S. S.; Tan, L. P.; Joso, J. F. D.; Boey, Y. C. F.; Wang, X. *Biomaterials* **2006**, *27*, 1573−1578.
(13) Yakacki, C. M.; Shandas, R.; Lanning, C.; Rech, B.; Eckstein, A.; Gall, K. *Biomaterials* **2007**, *28*, 2255−2263.
(14) Min, C.; Cui, W.; Bei, J.; Wang, S. *Polym. Adv. Technol.* **2005**, *16*, 608−615.
(15) *Wound Closure Biomaterials and Devices*, 1st ed.; Chun, C. C., von Fraunhofer, J. A., Greisler, H. P., Eds.; CRC Press: Boca Raton, FL, 1996.
(16) Lu, X. L.; Cai, W.; Gao, Z. Y.; Zhao, L. C. *Mater. Sci. Eng., A* **2006**, *438*−*440*, 8 57−861.
(17) Zheng, X.; Zhou, S.; Li, X.; Weng, J. *Biomaterials* **2006**, *27*, 4288−4295.
(18) Dobrzynski, P.; Kasperczyk, J.; Janeczek, H.; Bero, M. *Macromolecules* **2001**, *34*, 5090−5098.
(19) Dobrzynski, P.; Kasperczyk, J. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 3184−3201.
(20) Pospiech, D.; Komber, H.; Jehnichen, D.; Haussler, L.; Eckstein, K.; Scheibner, H.; Janke, A.; Kricheldorf, H. R.; Petermann, O. *Biomacromolecules* **2005**, *6*, 439−446.
(21) Wasserman, D.; Versfelt, C. Use of stannous octoate catalyst in the manufacture of L-lactide−glycolide copolymer sutures. U.S. Patent 3839297, 1974.
(22) Schwach, G.; Coudane, J.; Engel, R.; Vert, M. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 3431−3440.
(23) *Sax's Dangerous Properties of Industrial Materials*, 8th ed.; Levis, R. J., Ed.; Van Nostrand Reinhold: New York, 1992.
(24) IPCSINTOX Databank. http://www.intox.org (accessed 2005).
(25) Czajkowska, B.; Dobrzynski, P.; Bero, M. *J. Biomed. Mater. Res., Part A* **2005**, *75*, 591−597.
(26) Pamula, L. E.; Bacakowa, J.; Buczynska, E.; Filova, L.; Dobrzynski, P.; Bero, M. *Eng. Biomater.* **2004**, *37*, 14−17.
(27) Dobrzynski, P. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3129−3143.
(28) Dobrzynski, P.; Kasperczyk, J. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 98−114.
(29) Ceccorulli, G.; Zini, E.; Scandola, M. *Macromol. Chem. Phys.* **2006**, *207*, 864−869.
(30) Cam, D.; Marucci, M. *Polymer* **1997**, *38*, 1879−1884.
(31) Deege, P.; Dubois, P.; Jacobsen, S.; Fritz, H. G.; Jerome, R. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 2413−2420.
(32) Fox, T. G. *Bull. Am. Phys. Soc.* **1956**, *1*, 123.
(33) Dobrzynski, P.; Pastusiak, M.; Bero, M. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 1913−1922.
(34) Ferry, J. D. *Viscoelastic Properties of Polymers*; John Wiley & Sons: New York, 1980.

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