Synthesis and Characterization of Three-Arm Poly(ε-caprolactone)-Based Poly(ester−urethanes) with Shape-Memory Effect at Body Temperature

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Received October 31, 2008; Revised Manuscript Received December 22, 2008

ABSTRACT: Novel biodegradable star poly(ester−urethanes) containing three-arm poly(ε-caprolactone) (PCL) as switching segment were prepared as shape-memory polymers (SMPs) with switching temperature (T_s) around body temperature. PCL-triols with molecular weight (M_n) of 2700−4200 g/mol and T_m of 45−47 °C were synthesized in 55−67% yield by Novozym 435-catalyzed ring-opening polymerization of ε-caprolactone with glycerol as initiator, and their three-arm structures were confirmed by ^{1}H and ^{13}C NMR analysis. Reaction of the PCL-triols with methylene diphenyl 4,4′-diisocyanate isocynate and 1,6-hexanediol gave three-arm PCL-based poly(ester−urethane)s (*t*PCL-PUs) in 83−92% yield, with 65−75% soft segment. The structure of *t*PCL-PUs was confirmed by ^{1}H NMR analysis, and the thermal properties were analyzed by DSC with T_s of 36−39 °C. *t*PCL-PUs showed excellent shape-memory effects at 38 °C during cyclic thermomechanical tensile tests: shape recovery within 10 s, shape fixity rate of 92%, and shape recovery rate of 99%. The novel biodegradable star SMPs are potentially useful in biomedical applications.

Introduction

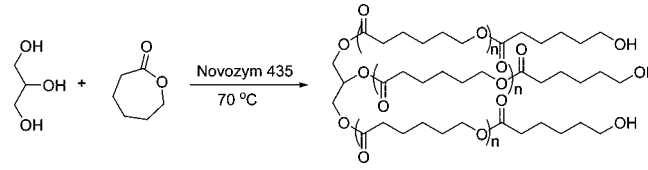
Shape-memory polymers (SMPs) possess the capability to remember and return to the predefined original shape when exposed to external stimulus, such as light[1,2] and temperature.[3] SMPs have a wide application in biomedical fields[4,5] such as drug delivery,[6] biosensors and biomedical devices,[7] and implant materials.[8] Thermally induced SMPs are better than shape-memory alloys (SMAs) as implant materials, since SMAs have limitations in deformation rate, programming, and degradability.[9] The development of degradable SMPs as implant materials has become more and more important due to the advantages such as minimally invasive surgery and no needs for a second surgery to remove implant materials.[10] For such application, the switching temperature (T_s) should be around body temperature: the temporary shape of the implant material can be created by deformation at temperature higher than T_s, fixed at temperature below T_s, and finally returned to its original shape when temperature becomes higher than T_s after implanted into the human body.

Thermally induced shape-memory effects can be achieved by using chemically cross-linked networks[11−13] or physically cross-linked copolymers.[14−16] The latter SMPs are often linear block copolymers containing hard and switching segments.[17] Hard segment with higher thermal transition stabilizes the permanent shape, while switching segment with lower thermal transition fixes the temporary shape. T_s can be either the glass transition temperature (T_g)[18−20] or melting temperature (T_m),[21,22] but T_m is preferred due to a sharper transition and better shape recovery.[23] Polyurethanes (PUs) are often used as biodegradable hard segments for their wide variation of mechanical properties.[24] On the other hand, the selection of appropriate switching segments for biodegradable SMPs with T_s around body temperature is a significant challenge. Poly(ε-caprolactone) (PCL), poly(lactide) (PLA), and polyglycolide (PGC) are three known biodegradable polymers in biomedical applications.[23,25,26] PLA has a T_g of 60 °C, which could be adjusted to 35−50 °C by modifying with PGC.[27] However, T_g triggered shape-memory effect is less preferred, as mentioned above. From this aspect, PCL is a better choice as switching segments: it has a T_m of 60 °C,[28] and the T_m can be decreased by reducing the molecular weight (M_n).[29] PCL-diols with low M_n were used for the preparation of thermally induced SMPs.[17] In a successful example, low-molecular-weight PCL-diols incorporated with a crystallizable hard segment gave a linear block copolymer with shape-memory effect at 37−40 °C.[30] However, when noncrystallizable PUs were used as hard segment, the T_s of the resulting linear PCL−PU copolymers could not reach body temperature:[10,21,31,32] a T_s of 43 °C was achieved by using PCL-diols with a T_m of 53 °C and a M_n of 2000 g/mol as the soft segment, and no T_s was observed when PCL-diols with a T_m of 46 °C and a M_n of 1000 g/mol were used, possibly due to the too low molecular weight and crystallinity of the PCL-diols.[10]

We are interested in preparing star polymers as thermally induced biodegradable SMPs. The higher excluded volume of star polymers may improve the shape-memory properties, in comparison with the linear block copolymers. On the other hand, the T_s may be easily adjusted to body temperature by the use of a three-arm soft segment such as PCL-triols. Comparing to PCL-diols with a T_m of 46 °C, three-arm PCL-triols with the same T_m may have sufficiently high M_n and good crystallinity to give a T_s around body temperature for the corresponding star SMP.

Here we report the enzymatic syntheses of three-arm PCL-triols with well-defined structure, controlled molecular weight, and desired thermal properties, the chemical preparation of three-arm PCL-based poly(ester−urethanes), the characterization of

Scheme 1. Synthesis of Three-Arm PCL-Triols via Enzyme-Catalyzed ROP of ε-Caprolactone with Glycerol



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10.1021/ma802437f CCC: $40.75
Published on Web 01/23/2009

Table 1. Novozym 435-Catalyzed ROP of ε-Caprolactone with Glycerol at 70 °C under Different Reaction Conditions

entry	CL/G[a] (mol/mol)	CL/E[b] (w/w)	CL:sol[c] (mL/mL)	time (h)	yield (%)	M_n(GPC)[e] (g/mol)	M_n(NMR) (g/mol)	M_w/M_n (GPC)[e]	T_m (°C)	X_c[d] (%)	code
1	10:1	10:1	NS[f]	1.5	67	2700	2720	1.56	(40)[g] 45	55	A
2	10:1	10:1	1:2	4	86	2900		1.46	46 (50)[g]	57	B
3	30:1	10:1	1:2	3	72	4900	5600	1.42	53	68	C
4	30:1	10:1	1:3	3	55	3200	4200	1.38	47	64	D
5	30:1	10:1	1:3	2	50	3000		1.35	46	61	E

[a] CL for ε-caprolactone, G for glycerol. [b] E for Novozym 435. [c] Sol for solvent, dioxane. [d] M_n was determined by GPC with polystyrene as standards in THF. [e] $X_c$was calculated according to the equation $X_c = (\Delta H_m/\Delta H_{100\%}) \times 100\%$, where $\Delta H_{100\%}$ is the theoretical heat of fusion of PCL (135 J/g). [f] NS for no solvent. [g] Shoulder near the major melting peak in the DSC curve.

Table 2. Synthesis of *t*PCL-PU by Polymerization of PCL-Triols, MDI, and HD with Dibutyltin Dilaurate as Catalyst in DMF

entry	PCL-triols code	PCL-triols:MDI:HD[a] (mol/mol/mol)	SS[b] (%)	*t*PCL-PU code	yield (%)	M_n(GPC)[c] (g/mol)	T_m (°C)	T_g (°C)	X_c (%)
1	A	1.0:7.1:5.6	55	F	95	43 700	NT[d]		
2	A	1.0:6.1:4.6	60	G	95	32 600	NT[d]		
3	A	1.0:4.6:3.1	65	H	92	24 600	38	−46	19
4	A	1.0:4.0:2.5	70	I	85	18 400	36	−46	22
5	A	1.0:3.2:1.7	75	J	80	13 100	38	−45	28
6	D	1.0:6.6:5.1	65	K	90	26 200	39	−43	22
7	D	1.0:5.4:3.9	70	L	85	19 500	38	−42	31
8	D	1.0:4.2:2.7	75	M	83	13 900	38	−42	33
9	C	1.0:7.0:5.5	70	N	88	19 600	48		
10	C	1.0:4.3:2.8	80	O	70	14 200	50		

[a] The polymerization consists of two steps: (1) PCL-triols were reacted with MDI in the presence of dibutyltin dilaurate in DMF at 65 °C for 6 h; (2) HD and dibutyltin dilaurate were added and the reaction was continued at 65 °C for 6 h. [b] SS for soft segment of *t*PCL-PU; the percentage was calculated based on the feed ratio. [c] M_n was determined by GPC with polystyrene as standards in DMF with 0.05 M LiBr at 55 °C. [d] NT for no T_m.

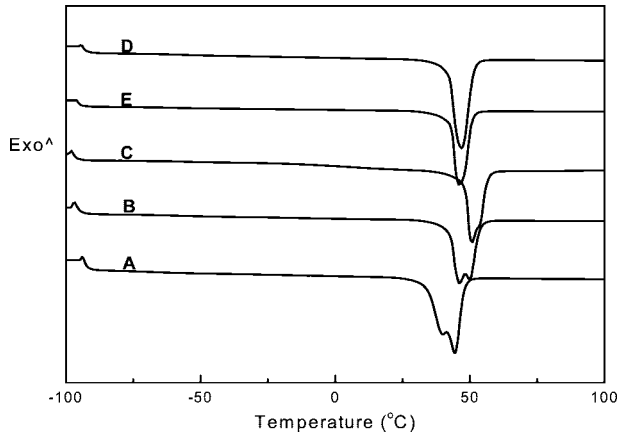


Figure 1. DSC spectra of PCL-triols (samples A to E).

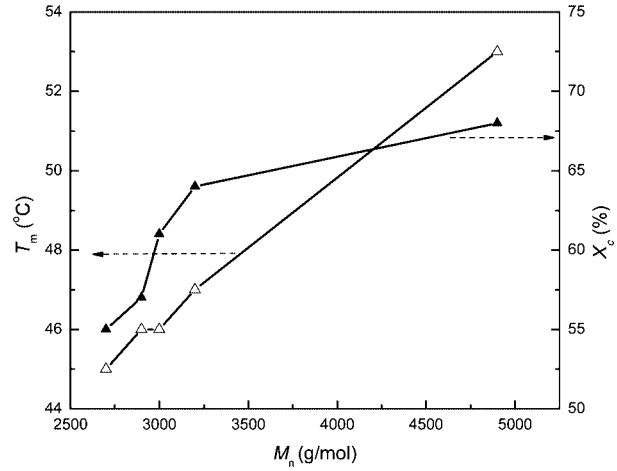


Figure 2. Dependence of the T_m and X_c on the M_n of PCL-triols.

polymers structure, thermal, and mechanical properties, and the investigation of shape-memory behavior of the star polymers at 38 °C.

Experimental Section

Materials. All solvents and reagents were purchased from Aldrich, and Novozym 435 (immobilized *Candida Antarctica* lipase B, 10 000 PLU/g) (CALB) was obtained from Novozymes. ε-Caprolactone (99%), *N*,*N*-dimethylformamide (DMF, 99%), and 1,4-dioxane (99.8%) were dried with CaH_2 for 24 h and freshly distillated before use. Glycerol (>99%) was dried by azeotropic distillation in toluene before use. Methylene diphenyl 4,4′-diisocyanate isocynate (MDI), 1,6-hexanediol (HD), and Novozym 435 were dried in a vacuum oven for 12 h at 40 °C.

General Procedure for the Preparation of Three-Arm PCL-Triols by Enzymatic Ring-Opening Polymerization of ε-Caprolactone with Glycerol. Novozym 435, ε-caprolactone, glycerol, and dioxane were added into a dried Schlenck tube with a magnetic stirring bar. The mixture was stirred at 70 °C under argon. Reaction conditions were summarized in Table 1. After polymerization, the reaction was stopped by adding chloroform. Novozym 435 was separated by filtration, and chloroform was removed by evaporation under reduced pressure. The crude product was dissolved into chloroform and precipitated in a mixture of chloroform and methanol (1:5) at −20 °C. The product was collected by filtration and dried in vacuum oven at 40 °C for 24 h.

Preparation of Three-Arm PCL-Triols (Sample D). Novozym 435 (2.06 g), ε-caprolactone (20 mL), and glycerol (0.55 g) were added into a 250 mL two-necked reaction tube with a magnetic stirring bar. The reaction was carried out in 1,4-dioxane (60 mL) at 70 °C under argon. After 3 h polymerization, the reaction was stopped by adding chloroform (50 mL). Novozym 435 was removed by filtration, and 1,4-dioxane as well as chloroform was removed by evaporation under reduced pressure. The raw product was dissolved in chloroform (15 mL) and precipitated by adding methanol (75 mL) for 12 h. The product was collected by filtration and dried under vacuum oven at 40 °C for 24 h. This gave 11.4 g (55% yield) of PCL-triol (sample D). The three-arm structure was confirmed by ^1H and ^{13}C NMR. M_n was determined by GPC as 3200 g/mol and calculated by ^1H NMR analysis as 4200 g/mol. T_m of 47 °C was obtained from DSC curve, and X_c of 64% was calculated based on data from DSC.

General Procedure for Synthesis of Three-Arm PCL-Based Poly(ester−urethane)s (*t*PCL-PUs). Dry MDI in DMF and dibutyltin dilaurate were added in a three-necked round bottle

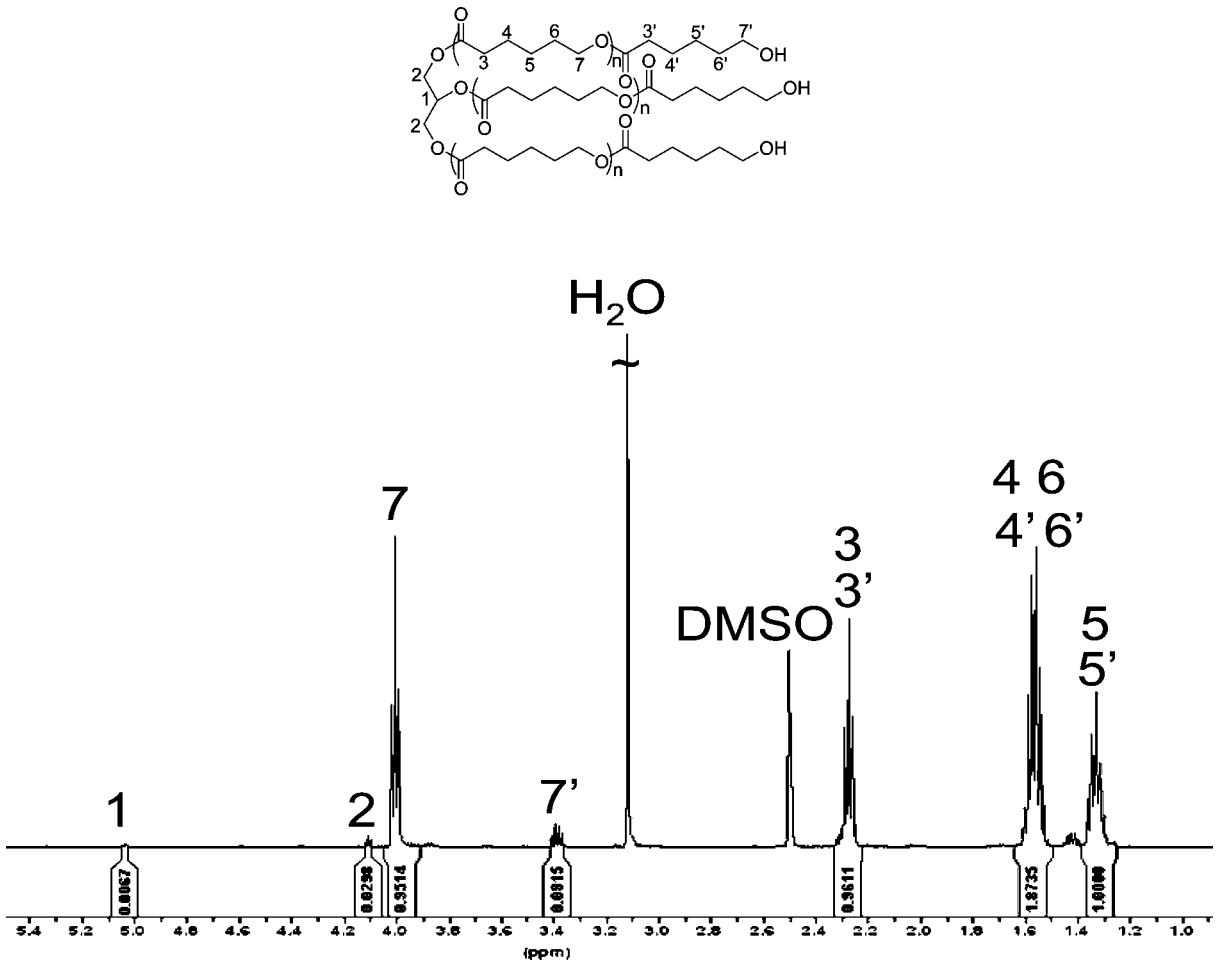


Figure 3. ^{1}H NMR spectrum of PCL-triols (sample D) in DMSO-d_6 at 333 K.

equipped with mechanical stirrer, and a solution of PCL-triols in DMF was added dropwise. The mixture was stirred at 65 °C under argon for 6 h. Another portion of dibutyltin dilaurate was added, followed by dropwise addition of a solution of HD in DMF. The mixture was stirred at 65 °C for another 6 h. Reaction conditions are summarized in Table 2. After the reaction, the hot viscous solution was poured into methanol (1:2 v/v) and magnetically stirred for 1 h at room temperature. The *t*PCL-PUs were precipitated, collected by filtration, washed by DMF/methanol (1:2 v/v) mixture solution three times, and dried in a vacuum oven at 80 °C for 24 h.

Preparation of Three-Arm PCL-Based Poly(ester−urethane) (*t*PCL-PU) (Sample M). According to the general procedure for *t*PCL-PUs synthesis, MDI (0.51 g) in DMF (15 mL) and dibutyltin dilaurate (40 mg) were added in a 250 mL three-necked round bottle equipped with a mechanical stirrer. A solution of PCL-triol (sample D, 2.0 g) in DMF (30 mL) was added dropwise at 65 °C. After 6 h polymerization, dibutyltin dilaurate (20 mg) and a solution of HD (0.16 g) in DMF (10 mL) were added. The reaction was continued at 65 °C for another 6 h. After reaction, the mixture was poured into methanol (110 mL) and *t*PCL-PU was then precipitated. The product was collected by filtration and washed by DMF/methanol (1:2, 60 mL) three times. After drying in vacuum oven for 24 h at 80 °C, 2.2 g (83%) of *t*PCL-PU was obtained. The polymer structure was confirmed by ^{1}H NMR, and M_n was deduced as 6800 g/mol by NMR analysis. T_m of 38 °C, T_g of −42 °C, and X_c of 33% for *t*PCL-PU were obtained from DSC.

Gel Permeation Chromatography (GPC). The analysis of molecular weight (M_n and polydispersity index M_w/M_n) was performed by GPC using a Waters instrument, with a Waters 510 pump, a Waters 410 refractive index detector, and Waters HR4E, HR5E, and HR6 columns placed in series. THF was used as the eluent at a flow rate of 1.0 mL/min at 30 °C for analyzing PCL-triols. DMF containing 0.05 M LiBr was used as the eluent at a flow rate of 1.0 mL/min at 55 °C for the analysis of *t*PCL-PUs. Sample concentration was about 0.1% (w/v), and the injection volume was 100 μL. Polystyrene standards with M_n of 370, 2970, 13 900, 30 200, 197 000, and 696 000 g/mol were used to generate a calibration curve.

Nuclear Magnetic Resonance (NMR). ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded with a Bruker AMX500 NMR instrument in DMSO-d_6 at 333 K. Chemical shifts were referred to TMS at 0 ppm.

Differential Scanning Calorimetry (DSC). The thermal properties of polymers were measured on a Mettler Toledo DSC 822 system. Nitrogen was used as purge gas with a flow rate of 20 mL/min. 6−12 mg samples were used for DSC analysis. For the measurement of PCL-triols, samples were heated from −20 to 100 °C with a heating rate of 20 °C/min, cooled down to −100 °C with a cooling rate of −20 °C/min, and then heated again to 100 °C at the same heating rate. For analyzing *t*PCL-PUs, samples were heated from −20 to 250 °C, cooled down to −100 °C, and heated again to 250 °C at the same heating and cooling rate as that used for the analysis of PCL-triols. T_m and T_g of samples were obtained from the second heating curves.

Film Preparation. 1.5 g of *t*PCL-PU was dissolved in 15 mL of DMF, and the solution was cast onto a PTFE plate and kept at 65 °C for 4 h to remove DMF. *t*PCL-PU film was further dried in a vacuum oven at 65 °C for 48 h. Finally, dog-bone-shaped specimens [50 mm (length) × 3.14 mm (width) × 0.5 mm (thickness)] were prepared for cyclic thermomechanical tensile tests.

Strain−Stress and Cyclic Thermomechanical Tensile Tests. The tests were carried out on Microforce Tester, Instron 8848 (Instron). The films prepared before were used for strain−stress test at 25 and 60 °C, respectively. The shape-memory properties

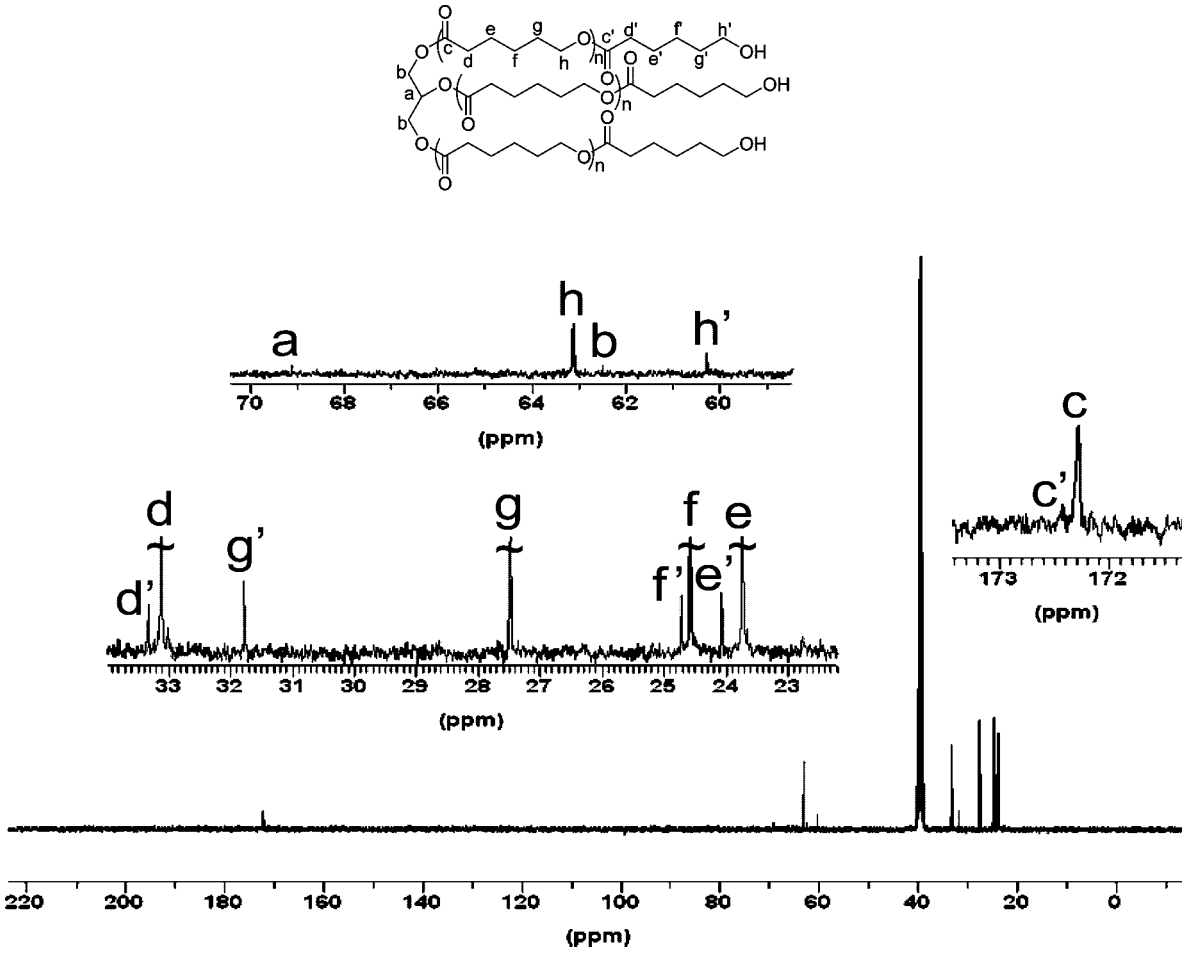


Figure 4. ^{13}C NMR spectrum of PCL-triols (sample D) in DMSO-d_6 at 333 K.

of *t*PCL-PUs were investigated by cyclic thermomechanical tensile tests equipped with thermochamber and temperature controller.

The cyclic thermomechanical tensile tests were performed with four steps: (1) heating the sample to 60 °C for 5 min, stretching the sample to extension of 100% (ε_m) with a strain rate of 20 mm/min, and holding for 5 min; (2) cooling to 15 °C with 10 K/min while keeping the strain under constant ε_m and holding for 15 min; (3) unloading the sample and holding for 2 min; (4) heating the sample to 38 °C and holding for 30 s. This cycle was repeated three times. The shape recovery rate (R_r) and the shape fixity rate (R_f) were calculated by using the following equations:

$$R_f = \left[\frac{\varepsilon_u(N)}{\varepsilon_m}\right] \times 100\%$$

and

$$R_r(N) = \left[\frac{\varepsilon_m - \varepsilon_p(N)}{\varepsilon_m - \varepsilon_p(N-1)}\right] \times 100\%$$

where N denotes the Nth cycle.

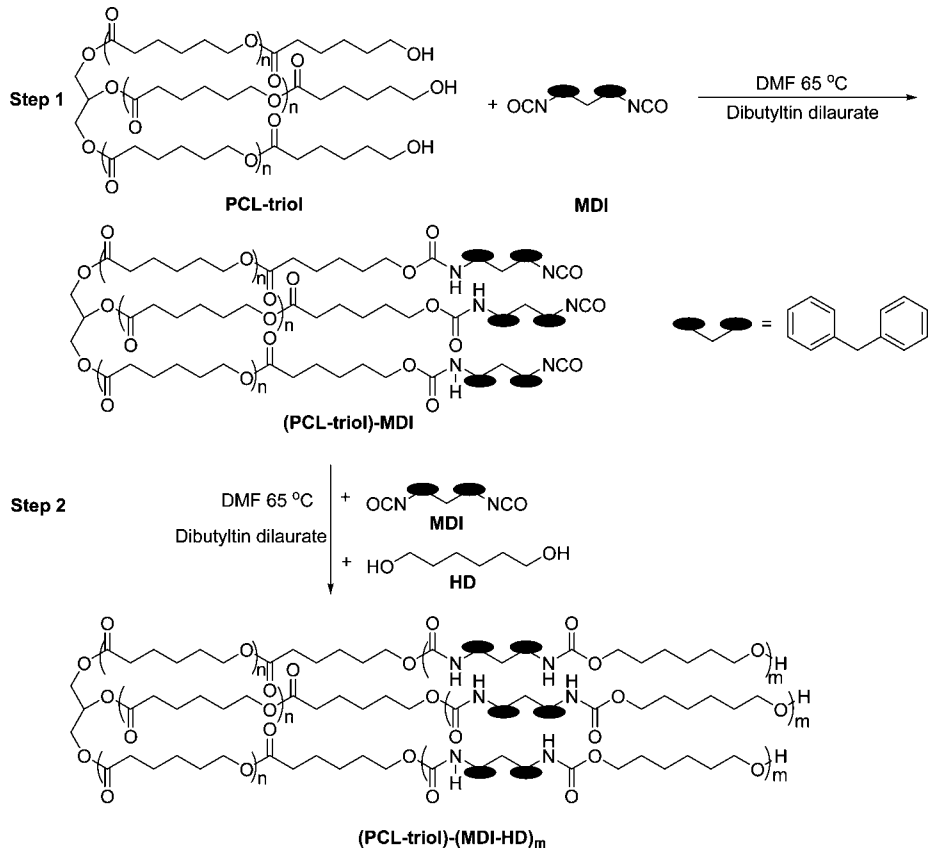
The photos of sample M in three states during the test of shape-memory behavior were taken: (a) the original state; (b) the sample stretched at 60 °C and then fixed at 15 °C; (c) the sample returned to the original shape after soaking into 38 °C water.

Results and Discussion

Enzymatic Synthesis of Three-Arm PCL-Triols. *Synthesis.* Previously, it was found that the T_s of PCL-based linear block copoly(ester−urethanes) was about 10 °C lower than the T_m of PCL-diols used as starting materials.[10] Therefore, we target at the preparation of three-arm PCL-triols with a T_m of 45−48 °C to achieve a T_s of body temperature for the corresponding star SMPs. PCL-triols was previously synthesized by stannous octoate-catalyzed ring-opening polymerization (ROP) of ε-caprolactone with glycerol as initiator.[33] However, it was difficult to obtain PCL-triols in pure form, and the prepared PCL-triols mixture showed more than one T_m.[33] On the other hand, enzyme-catalyzed reactions are often highly selective, and enzyme-catalyzed ROPs have been well established.[34−40] Therefore, we explored the enzymatic ROP of ε-caprolactone (CL) with glycerol (G) as initiator to prepare three-arm PCL-triols with defined structure, M_n, and T_m (Scheme 1).

Novozym 435 [immobilized *Candida Antarctica* lipase B (CALB)][34−37] was chosen as the enzyme for the target ROP, since it is well-known for high catalytic activity, good solvent resistance, and high stability for this type of transformation.[38,39] The enzymatic reaction was performed at 70 °C, which is the optimal temperature for Novozym 435.[38−40] 1,4-Dioxane was used as solvent due to the good solubility for both starting materials and product. To avoid water-initiated ROP, an anhydrous system under the protection of argon atmosphere was utilized. Different reaction conditions including the ratios of CL/G, CL/E, CL/sol, and reaction time were investigated to synthesize PCL-triols with a T_m of 45−48 °C. The reactions were followed by GPC analysis of samples taken at different time points. PCL-triols were separated from the immobilized enzyme by filtration, precipitated in a mixture of chloroform and methanol (1:5) at −20 °C, and dried in a vacuum oven at 40 °C. The yields were 50−86%. The reaction conditions and results are summarized in Table 1. In entries 1 and 2, the ratio

Scheme 2. Synthesis of *t*PCL-PU from PCL-Triols, MDI, and HD via Two-Step Reactions



of CL/G and CL/E were all fixed at 10:1, while bulk and solution polymerization were compared. In both cases, M_n of the product increased during the reaction, indicating the happening of ROP. Bulk polymerization gave PCL-triols with a M_n of 2700 g/mol (GPC) at 1.5 h, whereas solution polymerization gave the product with a M_n of 2900 g/mol at 4 h. Obviously, the ROP in dioxane was slower, thus being more easily controlled to obtain desired PCL-triols. Moreover, it offered a relatively narrow polydispersity of PCL-triols. However, PCL-triols prepared in both cases showed a major T_m peak and a shoulder in DSC (curves A and B in Figure 1), indicating the existence of mixed structures of different types of PCL-triols due to the incomplete reaction of three hydroxyl groups in one glycerol molecule with CL. To solve this problem, the ratio of CL/G was increased to 30:1 (entries 3−5). Under this condition, the effects of ratio of CL/sol and reaction time on the ROP were studied. In entries 3 and 4, the reaction time was kept for 3 h while the ratios of CL/sol of 1:2 and 1:3 were compared. In the latter case, more solvent was used, which reduced the reaction speed and led to a decrease of M_n of PCL-triols from 4900 to 3200 g/mol. On the other hand, reduction of the reaction time from 3 to 2 h (entry 5 vs 4) did not change too much the M_n of PCL-triols. All three PCL-triols prepared with a ratio of CL/G of 30:1 (entries 3−5) showed only a single melting peak in the corresponding DSC curves (Figure 1), with a T_m of 53, 47, and 46 °C, respectively.

The enzyme-catalyzed ROP of CL with glycerol is much faster than the stannous octoate-catalyzed ROP which, for instance, required 48 h to reach polymer M_n of 2980 g/mol at the CL/G ratio of 10:1.[33] In addition, PCL-triols prepared by using metal catalyst showed two T_m even if the ratio of CL/G was increased to 40:l. Therefore, the enzymatic ROP was the only choice for the synthesis of PCL-triols with well-defined three-arm structure and single T_m.

The relationship between the T_m and M_n of PCL-triols prepared by enzymatic ROP is shown in Figure 2. T_m of PCL-triols decreased linearly with the decrease of the M_n. The desired T_m of 46−47 °C was observed in the PCL-triols with a M_n of 3000−3200 g/mol (GPC). In comparison, linear PCL-diols with a T_m of 45.8 °C had a M_n of only 1000 g/mol, which is too low to show any T_m for the block copoly(ester−urethane) prepared with such PCL-diols.[10] Obviously, PCL-triols have much higher M_n than PCL-diols at the same T_m (46−47 °C). This is very important, since the increased molecular weight of PCL-triols could promote the crystallization of PCL switching segment in the corresponding SMPs to show the melting point. The crystallinity of PCL-triols was estimated based on the enthalpy determined by DSC and the theoretical heat of fusion of PCL (135 J/g).[41] PCL-triols with T_m of 46−47 °C and M_n of 3000−3200 g/mol had X_c of 61−64%. Further decreasing M_n of PCL-triol significantly decreased the X_c, shown in Figure 2.

Structure Analysis. The chemical structure of all PCL-triols was determined by NMR analyses in DMSO-d_6 at 333 K. ^{1}H and ^{13}C NMR spectra of PCL-triols (sample D) with T_m of 47 °C and M_n of 3200 g/mol (GPC) are shown in Figures 3 and 4, respectively. In the ^{1}H NMR spectrum, each signal could be assigned to the corresponding proton of the proposed structure of three-arm PCL-triols (Figure 3). There are three OH groups in glycerol, and the disappearance of OH signals (4.70 ppm) from glycerol indicated the reaction of OH groups with CL. If part of OH groups was not reacted, it could form a mixture of mono-, di-, and triesters of glycerol with H-(1) signal in three different regions, 5.22−5.32, 5.02−5.12, and 4.91−4.99 ppm.[33] For sample D, H-(1) signal appeared in the region of 5.05−5.12 ppm, suggesting a pure triester structure. H-(7′) of the CH_2−OH end group of PCL-triol absorbed at 3.35−3.51 ppm, and other protons of PCL repeating unit such as H-(3−7) were observed in the corresponding area indicated in Figure 3. On the basis of

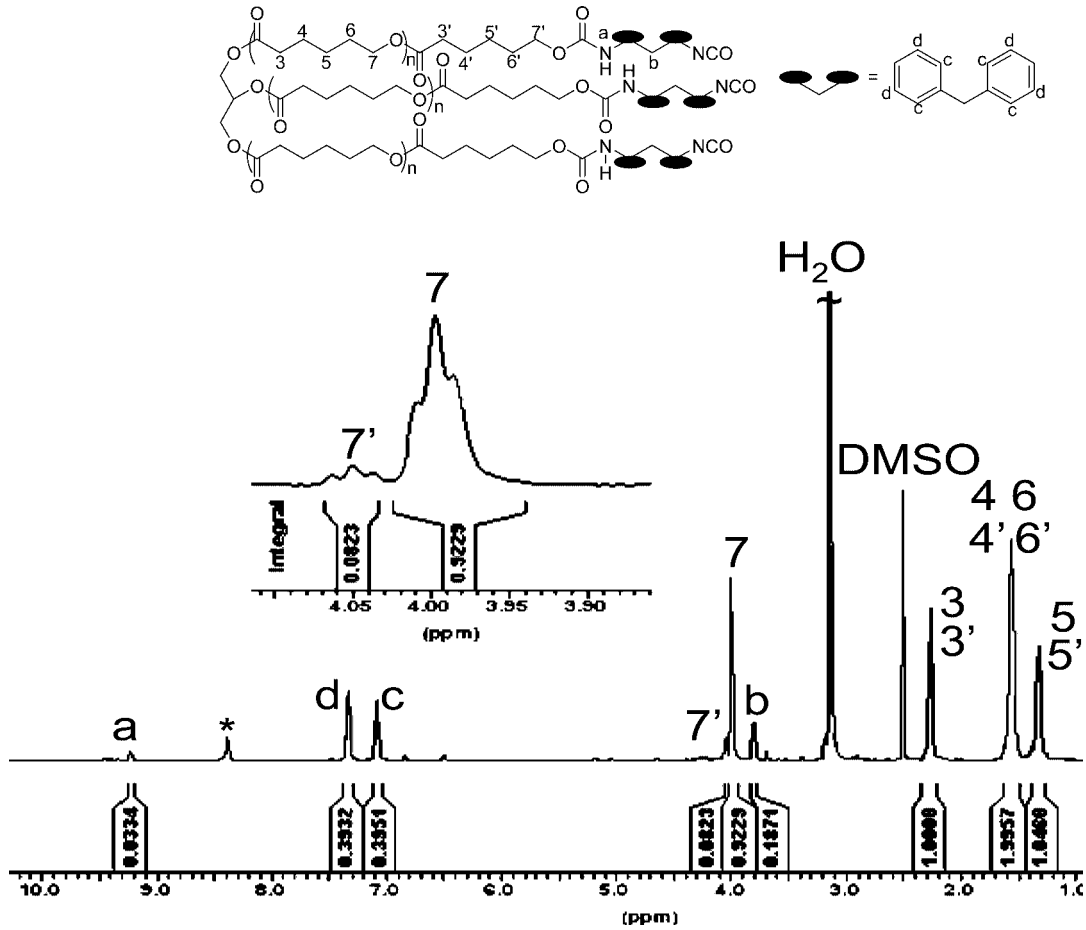


Figure 5. ^{1}H NMR spectrum of PCL-MDI, an intermediate after reaction step 1 for the preparation of *t*PCL-PU (sample M) in DMSO-d_6 at 333 K (signal * existed also in the ^{1}H NMR spectrum of pure MDI).

this analysis, the structure of the product sample D was the proposed three-arm PCL-triols in Scheme 1. From the intensity of signal H-(7) and H-(7′), the number of repeating units (n) was established as 11.7. Thus, M_n of PCL-triols was deduced as 4200 g/mol, which was comparable with the M_n determined by GPC (3200 g/mol).

The structure of three-arm PCL-triols was further confirmed by ^{13}C NMR analysis. As shown in Figure 4, all signals could be assigned to the carbons of PCL-triols. The signal intensity for the repeating unit [C-(c−h)] was much higher than that for the terminal carbons [C-(c′−h′)]. The carbon C-(h′) of the end group CH_2−OH was clearly observed at 60.2 ppm. C-(a) and C-(b) from glycerol absorbed at 69.1 and 62.5 ppm, respectively. The signal of the carbonyl group C-(c) was also clearly visible at 172.5 ppm.

Preparation and Structure Analysis of Three-Arm PCL-Based Poly(ester−urethanes) (*t*PCL-PUs). *Synthesis.* Three-arm PCL-triols with T_m of 45 °C (sample A), 47 °C (sample D), and 53 °C (sample C) were used for the preparation of the corresponding three-arm PCL-based poly(ester−urethanes). The polymerization was carried out by two-step reactions, shown in Scheme 2. In step 1, PCL-triol was reacted with methylene diphenyl 4,4′-diisocyanate isocynate (MDI) using dibutyltin dilaurate as catalyst, and the reaction was performed in DMF at 65 °C for 6 h. To control the three-arm structure and avoid the possible cross-linking, PCL-triols in DMF were slowly added into a DMF solution containing MDI in excess. Moreover, the ratio of MDI/PCL-triols between 4.3:1 and 7.1:1 was used, which is larger than the ratio at equivalent of 1.5:1 for the reaction step 1. In step 2, 1,6-hexanediol (HD) and some dibutyltin dilaurate in DMF were added to the mixture of step 1, and the reaction was continued at 65 °C for 6 h. The amount of HD added was theoretically equivalent to the remaining MDI after the reaction step 1. As listed in Table 2, a different feed ratio of PCL-triols/MDI/HD was applied to prepare the final polymer with 55−80% switching segment. After the polymerization, the reaction mixture was poured into methanol, and the product was precipitated. The polymer (*t*PCL-PUs) was dried in vacuum oven overnight to give a nonsticky solid material, with an over yield of 70−95% for two-step syntheses.

Structure Analysis. All *t*PCL-PUs were characterized by ^{1}H NMR analysis. The spectra of the intermediate after reaction step 1 and final product *t*PCL-PU (sample M) from entry 8 of Table 2 are shown in Figures 5 and 6, respectively. The intermediate was obtained by taking sample after the first step reaction, precipitating in methanol, filtrating, and drying in a vacuum oven. In the ^{1}H spectrum of the intermediate, the peak at 3.36 ppm corresponding to H-(7′) of the end group (−CH_2−OH) from PCL-triols (Figure 3) disappeared, and a new peak in the range of 4.03−4.09 ppm was observed for H-(7′) due to the transformation of the ending group (−CH_2−OH) into −CH_2−OR via the reaction with MDI. Moreover, a peak at 9.23 ppm corresponding to NH-(a) group was observed, which further indicated that the reaction happened between PCL-triols and MDI. Based on the three-arm structure, the theoretical ratio of H-(3,3′)/NH-(a) should be 26, calculated from $2(n + 1)/1$ with n of 11.7. The ratio of H-(3,3′)/NH-(a) was determined as 29.9 from Figure 5, which was very close to the theoretical value. This suggested the three-arm structure of the intermediate after reaction step 1. During the preparation of intermediate sample, unreacted MDI was also precipitated in methanol, thus

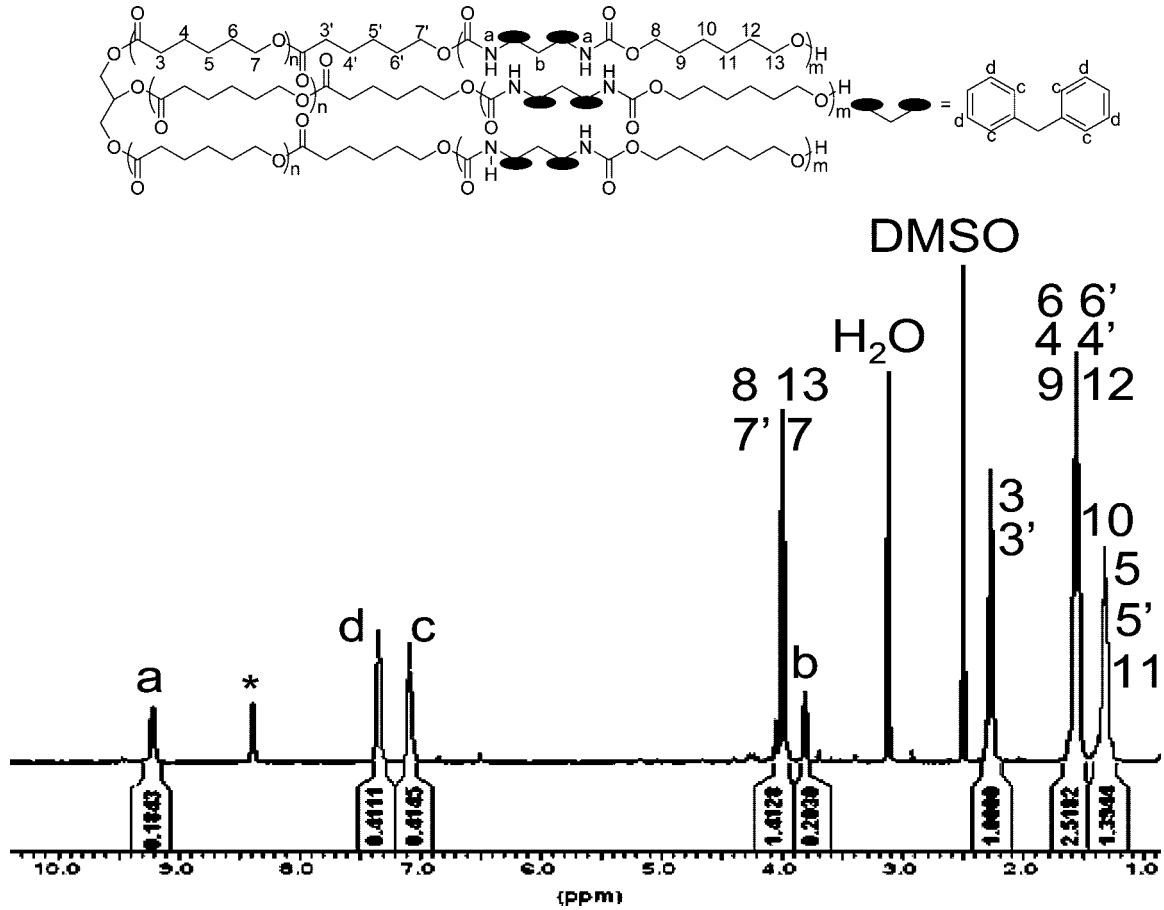


Figure 6. ^{1}H NMR spectrum of *t*PCL-PU (sample M) in DMSO-d_6 at 333 K (signal * existed also in the ^{1}H NMR spectrum of pure MDI).

existing in the intermediate sample. Therefore, H-(b,c,d) could not be used for the structure analysis.

In the ^{1}H NMR spectrum of *t*PCL-PU sample M in Figure 6, the ratio of peak at 9.23 ppm for NH-(a) and those for H-(b,c,d) was much bigger (nearly 1:2) than that in Figure 5, which indicated that the reaction in step 2 happened. The number of repeating units (*m*) in the hard segment (MDI + HD) could be calculated based on the intensity of NH-(a) and H-(3,3′). The ratio of NH-(a)/H-(3,3′) should be *m*/12.7, and ratio of the signal intensity was determined as 0.19:1 from Figure 6. Therefore, *m* was established as 2.4. The intensity of signals at 1.2−1.47 ppm for H-(5,5′,10,11), 1.5−1.7 ppm for H-(4,4′,6,6′,9,12), and 3.95−4.08 ppm for H-(7,7′,8,13) related to that at 2.2−2.4 ppm for H-(3,3′) was increased in comparison with those in Figure 5. This further confirmed the taking place of the reaction in step 2. In Figure 6, the ratio of the signals at 1.2−1.47 ppm for H-(5,5′,10,11) and 2.2−2.4 ppm for H-(3,3′) is 1.40:1, while the ratio of the signals at 1.2−1.47 ppm for H-(5,5′) and 2.2−2.4 ppm for H-(3,3′) in Figure 5 for the intermediate is 1.06:1. Thus, the signal ratio of H-(10,11)/H-(3,3′) for the *t*PCL-PU is 0.34:1. This value equals to (2 × *m*)/12.7, giving rise to *m* of 2.2, which was nearly the same as the above established value. M_n of the polymer was thus deduced to be 6600 g/mol. This is comparable with the M_n of 5600 g/mol for a three-arm polymer estimated based on the feed ratio of the reactants and the M_n (4200, NMR) of PCL-triols used. Thus, the NMR analysis supported the three-arm structure of *t*PCL-PUs in Scheme 2. The M_n of all polymers was also analyzed by GPC, but the values obtained are not accurate due to the use of polystyrene for the calibration.

Thermal Properties of *t*PCL-PUs. The thermal transitions of *t*PCL-PUs were determined by DSC, the curves from the second heating run are shown in Figure 7, and T_m, T_g, and X_c are listed in Table 2. *t*PCL-PUs containing 65−75% PCL segment derived from PCL-triols (sample A or D) with a T_m of 45−47 °C showed a T_m of 36−39 °C, thus reaching the desired and designed switching temperature. On the other hand, the use of PCL-triols with T_m of 53 °C (sample C) as switching segment gave the corresponding polymer with a T_m between 48 and 50 °C, even with 80% soft segments. In general, T_m of *t*PCL-PUs was lower than T_m of PCL-triols, possibly caused by the decreased crystallinity of PCL segment and the inhibited crystal formation via the incorporation of hard segment. T_m was also

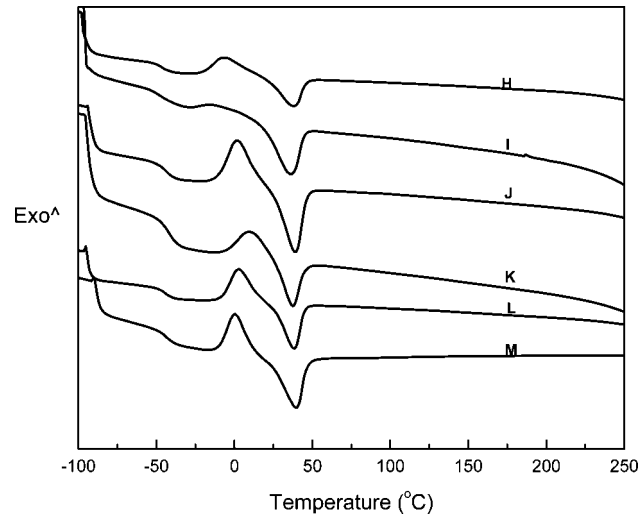


Figure 7. DSC spectra of *t*PCL-PUs (samples H−O) from second heating.

Table 3. Mechanic and Shape-Memory Properties of *t*PCL-PU (Sample H to M) Determined by Thermomechanical Tensile Test

*t*PCL-PU code	R_f (%)			R_r (%)			E^a (MPa) 25 °C	$\varepsilon_R{}^b$ (%) 25 °C	$\sigma_m{}^c$ (MPa) 25 °C	E^a (MPa) 60 °C	$\varepsilon_R{}^b$ (%) 60 °C	$\sigma_m{}^c$ (MPa) 60 °C
	N(1)[d]	N(2)[d]	N(3)[d]	N(1)[d]	N(2)[d]	N(3)[d]						
H	81	82	82	91	95	98						
I	83	83	84	92	97	99						
J	84	84	84	93	98	99	18	229	10	3.9	143	3.6
K	90	91	91	94	97	99						
L	90	90	91	95	98	99						
M	91	92	92	95	98	99	23	357	12	4.6	272	4.4

[a] *E* for Yong's modulus. [b] ε_R for elongation at break. [c] σ_m for tensile strength at maximum. [d] *N*(*x*) for cycle *x* in the cyclic thermomechanical tensile tests.

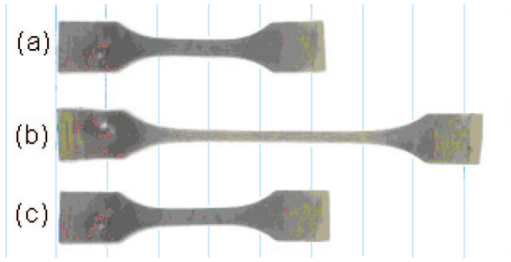


Figure 8. *t*PCL-PU (sample M) showing shape-memory effect at 38 °C: (a) initial state; (b) deformed state (stretched at 60 °C and fixed at 15 °C); (c) recovered state after 10 s (soaked into 38 °C water).

dependent on the percentage of switching segment in the polymer: using the same PCL-triols (sample A), *t*PCL-PUs containing lower than 60% PCL segments did not show any T_m. From DSC curves, a clear T_g between −46 and −42 °C was observed for all *t*PCL-PUs with a T_m of 36−39 °C. For comparison, PCL-triols did not show any T_g. Thus, the incorporation of PCL with hard segment makes T_g detectable.

Mechanical and Shape-Memory Properties of *t*PCL-PUs. The mechanical property of *t*PCL-PUs was examined by tensile tests at 25 and 60 °C, and the results for sample J and M are given in Table 3. In both cases, Young's modulus (*E*), tensile strength at maximum (σ_m), and elongation at break (ε_R) were higher at higher temperature: while *E* of 18−23 MPs, σ_m of 10−12 MPa, and ε_R of 229−357% were observed at 25 °C, *E*, σ_m, and ε_R decreased to 3.9−4.6 MPa, 3.6−4.4 MPa, and 143−272%, respectively, at 60 °C.

As an example, the shape deformation and recovery process for *t*PCL-PU sample M are shown in Figure 8. The sample was first stretched to the deformed state at 60 °C, the temporary shape was then fixed at 15 °C, and finally the temperature was raised to 38 °C to recover the original state. The shape-memory behavior was clearly observed.

To further quantify shape-memory properties, samples were analyzed by cyclic thermomechanical tensile tests. Stress−strain curves in the first cycle for *t*PCL-PU (sample M) at T_s of 38 °C are shown in Figure 9. During the test, the sample was heated to 60 °C for 5 min and stretched to extension of 100% (ε_m) by applying a deformation stress (step 1). ε_m was correspondingly recorded. It was then cooled down to 15 °C while keeping the strain under constant ε_m, and a decrease in stress was observed (step 2). The stress was unloaded, and the temporary shape was fixed after release the stress (step 3). ε_u was recorded. Finally, the sample was heated to 38 °C, and the original shape was quickly recovered in about 10 s (step 4). ε_p was recorded. The shape recovery rate (R_r) and shape fixity rate (R_f) in the first cycle could be calculated as 95% and 91% based on the equations $R_r(1) = [(\varepsilon_m - \varepsilon_p)/\varepsilon_m] \times 100\%$ and $R_f(1) = (\varepsilon_u/\varepsilon_m) \times 100\%$. Samples K−M from PCL-triols with T_m of 47 °C and M_n of 4200 g/mol showed R_f of 90−91%, while samples H−J from PCL-triols with T_m of 45 °C and M_n of 2720 g/mol showed lower R_f of 81−84% (Table 3) in the first cycle. The increase in molecular weight of PCL segment promoted the crystallization and thus increased R_f. However, the increase of molecular weight and crystallinity of PCL-triols showed only a small effect on R_r, with 94−95% for samples K−M and 91−93% for samples H−J. With the increased number of test cycles, R_r increased slightly and reached 99% in the third cycle, while R_f was almost the same for all three cycles. The percentage of switching segment between 65% and 75% had a negligible influence on R_f and R_r in all samples. During the shape-memory transition, all *t*PCL-PUs produced stress in the range of 2−3 MPa, which resembles the mechanical stresses in soft tissue.[30] This suggests that our shape-memory polymer might be useful in tissue engineering.

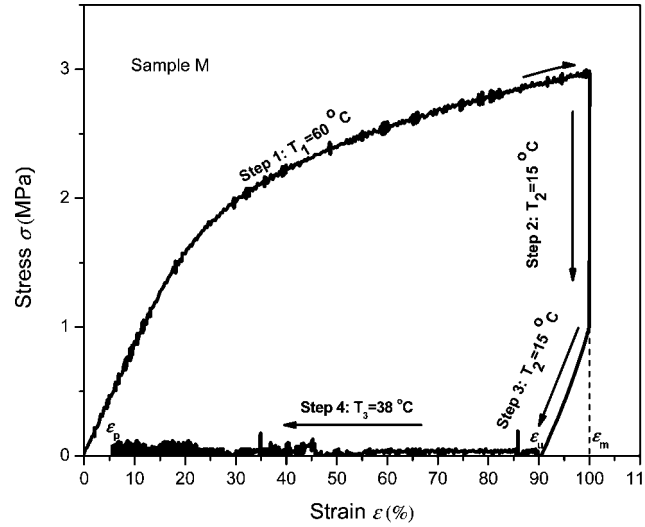


Figure 9. Strain−stress curve of *t*PCL-PU (sample M) from cyclic thermomechanical tensile tests with $\varepsilon = 100\%$.

Conclusion

Three-arm PCL-triols were developed as biodegradable switching segment for the preparation of star polymer with shape-memory effect around body temperature. Enzymatic ring-opening polymerization of ε-caprolactone with glycerol as initiator gave the corresponding PCL-triols with high purity and good yield. PCL-triols with T_m of 45−47 °C were obtained by controlling the M_n between 2720 and 4200 g/mol. The three-arm structure of PCL-triols was established by ^{1}H and ^{13}C NMR analyses.

Star SMPs were prepared in high yield by polymerization of PCL-triols with MDI and subsequently with HD in the presence of dibulytin dilaurate. The three-arm structures of *t*PCL-PU and its synthetic intermediate were confirmed by NMR analysis. T_s of *t*PCL-PUs could be adjusted by using PCL-triols with different T_m. T_s of 36−39 °C was achieved by using PCL-triols with T_m of 45−47 °C and M_n of 2720−4200 g/mol. Excellent shape-memory properties of *t*PCL-PU were demonstrated in cyclic thermomechanical tensile tests at 38 °C, with shape recovery in 10 s, shape fixity rate of 91−92%, and shape

recovery rate of 95−99%. The prepared three-arm biodegradable shape-memory polymers with switching temperature at body temperature are potentially useful materials for biomedical applications.

Acknowledgment. This work is supported by Ministry of Education of Singapore through an AcRF Tier 1 Grant (Project No. R-279-000-225-112).

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MA802437F