Tunable Shape Memory Polymers from \(\alpha\)-Amino Acid-Based Poly(ester urea)s

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Supporting Information

ABSTRACT: The thermal shape memory behavior of poly(ester urea)s (PEUs) composed of \(\alpha\)-amino acids and linear diols has been explored. The thermal, mechanical, and shape memory properties of PEUs are shown to be controlled by changing the amino acid and diol components of the polymer, without negatively affecting the shape memory performance of the polymer in most cases. These materials display triple-shape memory behavior and temperature memory properties due to a broad glass transition temperature interval. The versatility of the shape memory behavior of PEUs was explored by demonstrating shape transformations of thin films, salt leached scaffolds, and larger constructs. Overall good shape memory behavior in combination with the tunable properties of PEU materials makes them prime candidates for use as shape memory materials in biomedical applications.

Introduction

Shape memory polymers (SMPs) provide materials that can change shape upon application of a stimulus and have shown considerable promise for use in biomedical applications. \(^{1-6}\) Self-tightening sutures, \(^{7}\) deployable structures in medical devices, \(^{8}\) shape changing scaffolds and surfaces, \(^{9,10}\) and drug delivery systems \(^{11}\) represent some of the potential uses of SMPs. The advantages of using polymers, as opposed to shape memory alloys, \(^{12,13}\) include the potential for biodegradability, lower cost, larger achievable strains during shape actuation, and tunable material properties. Considering the broad range of tissue types and corresponding mechanical properties encountered in the body, the ability to tune a material’s properties to meet the demands of a particular application is vital.

The simplest SMPs are dual-shape memory materials that require, first, programming a temporary shape, followed by application of an appropriate stimulus (heat being the most common) to trigger recovery of the permanent shape. \(^{14-18}\) Other stimuli can be used such as light, chemical impetus, or various methods of indirect heating (e.g., photo-, electro-, and magneto-thermal transduction). The two basic requirements for a thermal SMP are possessing: 1) a reversible thermal transition (i.e., glass or melt transition) to activate and suppress chain slippage and set the permanent shape. \(^{18}\) In addition, important design considerations for SMPs in biomedical applications include biodegradability, biocompatibility, compatible mechanical properties, and sterilizability. \(^{5}\) A wide range of thermal SMPs, including polyesters, polyurethanes, and polyacrylates, have been identified as viable candidates for biomedical applications, \(^{1,4,5,19,20}\) although the extent to which these materials meet the design considerations lacks a comprehensive study.

\(\alpha\)-Amino acid-based poly(ester urea)s (PEUs) have recently emerged as an important class of tunable materials for biomedical applications. These materials are biodegradable, sterilizable, nontoxic, have nontoxic degradation products, and lead to no inflammatory response during degradation \textit{in vivo}. \(^{11}\) Their mechanical properties can be tuned for use in both hard and soft tissues, such as bone and blood vessels. \(^{12-24}\) Additionally, the materials can be prepared with various functionalities for specific applications, such as peptides for bone growth, \(^{25}\) iodine for radiopacity, \(^{26}\) catechols for adhesion, \(^{27}\) fluorescent probes for visualization, \(^{28}\) and therapeutics for drug delivery. \(^{29}\) The main advantages of PEUs over many other biodegradable polymers include simple scalable synthesis, tunable degradation and mechanical properties, and mechanical properties derived from hydrogen bonding rather than crystallinity. This versatility, and the previously demonstrated examples of biocompatibility, makes PEUs viable candidates for a wide range of biomedical applications.

We recently demonstrated that \(\text{i}-\text{valine (VAL)-based PEUs}

\[ \begin{align*}
\text{N} & \quad \text{O} & \quad \text{N} \\
\text{O} & \quad \text{R} & \quad \text{N} \\
\text{O} & \quad \text{R} & \quad \text{N} \\
\end{align*} \]

\text{N} & \quad \text{O} & \quad \text{N} \\
\text{O} & \quad \text{R} & \quad \text{N} \\
\text{O} & \quad \text{R} & \quad \text{N} \\
\end{align*} \]

\]
backbone. In this article, we explore the effect of amino acid and diol lengths on the shape memory behavior of PEUs prepared from L-alanine (ALA), L-isoleucine (ILE), L-phenylalanine (PHE), and the unnatural amino acid L-2-aminobutyric acid (ABA).

EXPERIMENTAL SECTION

Materials. Chloroform was either obtained from an Inert Pure Solv solvent purification system or dried over calcium hydride overnight and then distilled. All other reagents and solvents were used as obtained from commercial sources.

Characterization. NMR spectra were collected with Varian NMR spectrometers (300 and 500 MHz). All chemical shifts were reported in ppm (δ) and referenced to the chemical shifts of the residual solvent resonances (1H NMR, dimethyl sulfoxide (DMSO)-d6: 2.50 ppm; 13C NMR DMSO-d6: 39.50 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Number-average molecular mass (Mn) and postprecipitation molecular mass distribution (Dn) were determined by size exclusion chromatography (SEC), and molecular mass values were determined relative to polystyrene standards. The SEC analyses were performed using a TOSOH HLC-8320 gel permeation chromatography system equipped with a TOSOH HLC-8320 gel permeation chromatograph instrument with dimethylformamide (DMF) (containing 0.1 M LiBr) as eluent (flow rate of 1 mL/min and temperature of 50°C) and a refractive index detector. The Tg of polymers was determined by differential scanning calorimetry (DSC, TA Q2000, scan rate of 20°C/min) or dynamic mechanical analysis (DMA, TA Q800, 3°C/min and a frequency of 1 Hz). X-ray diffraction (XRD) data were collected on a Rigaku Ultima IV X-ray diffractometer. IR spectra of monomers and polymers were collected on a Nicolet iS50 FT-IR (Thermo Scientific) after dissolution in chloroform and application to a KBr salt plate (32 scans, 8 cm⁻¹ resolution).

Synthesis of VAL- and PHE-Based PEUs. The VAL- and PHE-based PEUs were prepared and characterized as previously described.25-27

General Procedure for Synthesis of PEU Monomers. Either 1,6-hexanediol, 1,8-octanediol, 1,10-decanediol, or 1,12-dodecanediol (1.0 mol equiv), a L-amino acid (2.3 mol equiv), 1,6-hexanediol, 1,8-octanediol, 1,10-decanediol, or 1,12-dodecanediol (2.4 mol equiv), and toluene (1 mL per gram of TsOH) (1.0 mol equiv), a L-amino acid (2.3 mol equiv), L-alanine (ALA), L-isoleucine (ILE), L-phenylalanine (PHE), and the unnatural amino acid L-2-aminobutyric acid (ABA). In this article, we explore the e...
The monomer was prepared on a 90 mmol scale (based on the diol) and obtained with an 85% yield. The monomer was prepared on a 70 mmol scale (based on the diol) and obtained with a 92% yield. The monomer was prepared on a 28 mmol scale (based on the diol), and obtained with an 86% yield. The monomer was prepared on a 70 mmol scale (based on the diol) and obtained with a 92% yield.

Synthesis of m(1-ILE-6). The monomer was synthesized as described in the general procedure described above. The monomer was prepared on a 90 mmol scale (based on the diol) and obtained with an 85% yield. The monomer was prepared on a 70 mmol scale (based on the diol) and obtained with a 92% yield. The monomer was prepared on a 28 mmol scale (based on the diol), and obtained with an 86% yield. The monomer was prepared on a 70 mmol scale (based on the diol) and obtained with a 92% yield.

Synthesis of m(1-ILE-8). The monomer was synthesized as described in the general procedure described above. The monomer was prepared on a 90 mmol scale (based on the diol) and obtained with an 85% yield. The monomer was prepared on a 70 mmol scale (based on the diol) and obtained with a 92% yield. The monomer was prepared on a 28 mmol scale (based on the diol), and obtained with an 86% yield. The monomer was prepared on a 70 mmol scale (based on the diol) and obtained with a 92% yield.

Synthesis of m(1-ILE-10). The monomer was synthesized as described in the general procedure described above. The monomer was prepared on a 90 mmol scale (based on the diol) and obtained with an 85% yield. The monomer was prepared on a 70 mmol scale (based on the diol) and obtained with a 92% yield. The monomer was prepared on a 28 mmol scale (based on the diol), and obtained with an 86% yield. The monomer was prepared on a 70 mmol scale (based on the diol) and obtained with a 92% yield.

The polymer was prepared by following the general procedure described above with the exception the number of triphosgene addition steps. To further increase the molecular mass of the polymer, the amount of triphosgene in the second addition was increased to 0.16 mol equiv, and a third addition of triphosgene (0.16 mol equiv, in chloroform, 1 mL per mmol of monomer) was added after 2 h from the second addition. The polymer was prepared on a 33 mmol scale (based on monomer), stirred for 17 h after the third triphosgene addition, and obtained with a 70% yield. The polymer was prepared on a 30 mmol scale (based on monomer), stirred for 17 h after the third triphosgene addition, and obtained with a 71% yield. The polymer was prepared on a 30 mmol scale (based on monomer), stirred for 17 h after the third triphosgene addition, and obtained with an 84% yield. The polymer was prepared on a 30 mmol scale (based on monomer), stirred for 17 h after the third triphosgene addition, and obtained with an 89% yield.

After the second triphosgene addition, and obtained with an 84% yield. The polymer was prepared on a 30 mmol scale (based on monomer), stirred for 17 h after the third triphosgene addition, and obtained with a 71% yield. The polymer was prepared on a 30 mmol scale (based on monomer), stirred for 17 h after the third triphosgene addition, and obtained with an 89% yield.

After 2 h from the second addition. The polymer was prepared on a 33 mmol scale (based on monomer), stirred for 17 h after the third triphosgene addition, and obtained with a 70% yield. The polymer was prepared on a 30 mmol scale (based on monomer), stirred for 5 h after the second triphosgene addition, and obtained with a 90% yield. The polymer was prepared on a 33 mmol scale (based on monomer), stirred for 17 h after the third triphosgene addition, and obtained with a 70% yield. The polymer was prepared on a 30 mmol scale (based on monomer), stirred for 5 h after the second triphosgene addition, and obtained with a 90% yield.
Figure 1. Synthesis and nomenclature of amino acid-based poly(ester urea)s. Diamine monomers are prepared by Fischer esterification between various amino acids and diols with varying carbon chain lengths. Monomers are polymerized with triphosgene in an interfacial polymerization. Nomenclature is based on the amino acid and diol from which its structure is derived.

Table 1. Molecular Mass, Thermal Properties, and Shape Memory Performance Characterization for PEUs

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Side Chain</th>
<th>Mₘ (kDa)</th>
<th>Dₘ</th>
<th>Tₛ (°C)ᵇ</th>
<th>Tₘₖₐₜ (°C)ᵇ</th>
<th>ΔR (%)ᵇ</th>
<th>R (%)ᵇ</th>
<th>Strain (%)ᵈ</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(1-ALA-6)ᵉ</td>
<td>ALA</td>
<td>12</td>
<td>1.4</td>
<td>10.6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>p(1-ALA-8)ᵉ</td>
<td>ALA</td>
<td>14</td>
<td>1.6</td>
<td>-13.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>p(1-ALA-10)ᵉ</td>
<td>ABA</td>
<td>25</td>
<td>1.7</td>
<td>27.6±3.1</td>
<td>48.0±1.4</td>
<td>87.7±4.3 f</td>
<td>95.0±1.5</td>
<td>5.5±1.1</td>
</tr>
<tr>
<td>p(1-ALA-12)ᵉ</td>
<td>VAL</td>
<td>34</td>
<td>1.7</td>
<td>27.3±0.6</td>
<td>47.4±0.4</td>
<td>79.8±13.0</td>
<td>88.5±5.4</td>
<td>5.5±1.1</td>
</tr>
<tr>
<td>p(1-ABA-6)ᵇ</td>
<td>VAL</td>
<td>18</td>
<td>1.7</td>
<td>55.4±1.0</td>
<td>71.6±1.9</td>
<td>90.4±2.3</td>
<td>92.3±2.2</td>
<td>4.1±0.5</td>
</tr>
<tr>
<td>p(1-ABA-8)ᵇ</td>
<td>ILE</td>
<td>31</td>
<td>2.0</td>
<td>21.8±4.7</td>
<td>47.2±3.3</td>
<td>87.3±2.2</td>
<td>85.4±1.6</td>
<td>6.1±1.0</td>
</tr>
<tr>
<td>p(1-ABA-10)ᵇ</td>
<td>ILE</td>
<td>27</td>
<td>1.9</td>
<td>32.9±0.2</td>
<td>21.1±1.2</td>
<td>99.3±1.0</td>
<td>83.4±0.7</td>
<td>159±12</td>
</tr>
<tr>
<td>p(1-ABA-12)ᵇ</td>
<td>PHE</td>
<td>28</td>
<td>1.9</td>
<td>25.8±1.8</td>
<td>22.5±1.4</td>
<td>99.1±0.2</td>
<td>87.4±2.3</td>
<td>94±11</td>
</tr>
<tr>
<td>p(1-VAL-6)ᵇ</td>
<td>ALA</td>
<td>39</td>
<td>1.8</td>
<td>73.1±0.5</td>
<td>65.9±2.2</td>
<td>99.2±0.1</td>
<td>98.3±0.3</td>
<td>222±13</td>
</tr>
<tr>
<td>p(1-VAL-8)ᵇ</td>
<td>VAL</td>
<td>70</td>
<td>1.7</td>
<td>62.1±1.8</td>
<td>57.0±0.2</td>
<td>99.2±0.1</td>
<td>95.8±0.5</td>
<td>106±5</td>
</tr>
<tr>
<td>p(1-VAL-10)ᵇ</td>
<td>VAL</td>
<td>50</td>
<td>1.8</td>
<td>47.5±1.4</td>
<td>39.6±1.0</td>
<td>98.9±0.1</td>
<td>97.2±0.9</td>
<td>204±3</td>
</tr>
<tr>
<td>p(1-VAL-12)ᵇ</td>
<td>VAL</td>
<td>18</td>
<td>1.6</td>
<td>43.7±1.9</td>
<td>32.8±1.4</td>
<td>98.3±0.1</td>
<td>97.0±0.7</td>
<td>162±8</td>
</tr>
<tr>
<td>p(1-ILE-6)ᵇ</td>
<td>ILE</td>
<td>41</td>
<td>1.5</td>
<td>67.3±1.1</td>
<td>68.8±0.3</td>
<td>96.4±0.5</td>
<td>99.2±0.1</td>
<td>186±12</td>
</tr>
<tr>
<td>p(1-ILE-8)ᵇ</td>
<td>ILE</td>
<td>34</td>
<td>1.4</td>
<td>54.4±0.7</td>
<td>53.9±1.6</td>
<td>96.2±0.3</td>
<td>99.1±0.1</td>
<td>112±13</td>
</tr>
<tr>
<td>p(1-ILE-10)ᵇ</td>
<td>ILE</td>
<td>17</td>
<td>1.7</td>
<td>47.2±0.9</td>
<td>34.6±1.9</td>
<td>95.4±0.1</td>
<td>98.9±0.1</td>
<td>216±42</td>
</tr>
<tr>
<td>p(1-ILE-12)ᵇ</td>
<td>ILE</td>
<td>16</td>
<td>1.5</td>
<td>37.8±0.5</td>
<td>34.9±0.9</td>
<td>95.9±0.8</td>
<td>97.6±0.1</td>
<td>130±13</td>
</tr>
<tr>
<td>p(1-PHE-6)ᵇ</td>
<td>PHE</td>
<td>18</td>
<td>3.0</td>
<td>71.3±1.1</td>
<td>83.9±1.1</td>
<td>86.2±5.0</td>
<td>92.8±3.6</td>
<td>5.0±2.4</td>
</tr>
<tr>
<td>p(1-PHE-8)ᵇ</td>
<td>PHE</td>
<td>48</td>
<td>1.9</td>
<td>58.2±0.8</td>
<td>52.4±5.2</td>
<td>97.7±0.2</td>
<td>99.7±1.0</td>
<td>206±60</td>
</tr>
<tr>
<td>p(1-PHE-10)ᵇ</td>
<td>PHE</td>
<td>35</td>
<td>2.0</td>
<td>47.0±0.7</td>
<td>40.0±2.4</td>
<td>96.6±0.1</td>
<td>99.4±0.1</td>
<td>241±46</td>
</tr>
<tr>
<td>p(1-PHE-12)ᵇ</td>
<td>PHE</td>
<td>38</td>
<td>1.7</td>
<td>31.8±1.8</td>
<td>25.9±2.0</td>
<td>90.1±2.3</td>
<td>98.3±0.3</td>
<td>120±48</td>
</tr>
</tbody>
</table>

“Tₛ” from E,, “Tₘₖₐₜ” determined from the onset of shape recovery in the third cycle. Fixity and recovery parameters reported for the third cycle.

“From the third cycle. “Tₛ” determined from DSC, shape memory performance was not able to be characterized due to sample failure upon any appreciable sample extension.”

ΔTₘₖₐₜ = 50°C. Fixity and recovery parameters reported for the second cycle, samples failed in third cycle. “Tₖ = 70°C. “Tₖ = 81°C. Values with errors are an average of three runs ± one standard deviation.

NMR (300 MHz, DMSO-d₆, δ): 6.37 (d, J = 8.0 Hz, NH), 4.04 (m, CH₂ and CH), 1.60 (m, CH₂), 1.24 (m, CH₂), 0.84 (m, CH₃). IR (cm⁻¹): 1562, 1638 (–NH–(CO)–NH–), 1738 (–C–(CO)–O–), 3352 (–NH–(CO)–NH–).

Synthesis of p(1-ILE-6). The polymer was synthesized as described in the general procedure described above. The polymer was prepared on a 70 mmol scale (based on monomer), stirred for 2 h after the second triphosgene addition, and obtained with an 85% yield.

¹H NMR (500 MHz, DMSO-d₆, δ): 6.37 (d, J = 8.9 Hz, NH), 4.04 (m, CH₂ and CH), 1.71 (m, CH), 1.55 (s, CH₂), 1.34 (m, CH₂), 0.84 (m, CH₃). IR (cm⁻¹): 1547, 1631 (–NH–(CO)–NH–), 1732 (–C–(CO)–O–), 3356 (–NH–(CO)–NH–).

Synthesis of p(1-ILE-8). The polymer was synthesized as described in the general procedure described above. The polymer was prepared on a 50 mmol scale (based on monomer), stirred for 2 h after the second triphosgene addition, and obtained with a 92% yield.

¹H NMR (500 MHz, DMSO-d₆, δ): 6.38 (d, J = 6.9 Hz, NH), 4.03 (m, CH₂ and CH), 1.71 (m, CH), 1.53 (s, CH₂), 1.33 (m, CH₂). 0.86 (m, CH₃). IR (cm⁻¹): 1554, 1631 (–NH–(CO)–NH–), 1738 (–C–(CO)–O–), 3356 (–NH–(CO)–NH–).

Synthesis of p(1-ILE-10). The polymer was synthesized as described in the general procedure described above. The polymer was prepared on a 30 mmol scale (based on monomer), stirred for 20 h after the second triphosgene addition, and obtained with an 89% yield.

¹H NMR (500 MHz, DMSO-d₆, δ): 6.43 (d, J = 7.6 Hz, NH), 4.06 (m, CH₂ and CH), 1.71 (m, CH), 1.53 (s, CH₂), 1.29 (m, CH₂), 0.86 (m, CH₃). IR (cm⁻¹): 1554, 1631 (–NH–(CO)–NH–), 1738 (–C–(CO)–O–), 3356 (–NH–(CO)–NH–).
Shape Memory Characterization. Rectangular test specimens (2 x 8 x 0.5 mm) were prepared by compression molding. ABA-based PEU test specimens were annealed at their T_g for 72 h to ensure complete crystallization was achieved (only the ABA-based PEUs exhibited this behavior). Cyclic thermomechanical testing was conducted using a DMA Q800 instrument. Testing was completed in controlled force mode with heating and cooling rates of 10 °C min⁻¹. Dual-shape memory testing was completed with three sequential runs, repeated three times with independent test specimens. The deformation temperature (T_D) was equal to the T_g determined from the peak in loss modulus (unless otherwise noted). Tripe-shape memory testing was completed with one cycle, repeated three times with independent test specimens. The fixity and recovery parameters for dual- and triple-shape memory were calculated using the standard shape memory equations previously published.¹⁵ Temperature memory effect testing was completed in duplicate. The plot of strain recovery rate in Figure 5C was obtained by fitting the plot of recovery parameter vs time with a sigmoidal function and taking its derivative.

Preparation of Specimens for Visual Demonstrations. Thin films were prepared by compression molding of powdered PEU using a stainless steel mold sandwiched between Kapton film and metal plates. Salt leached scaffolds were prepared by first adding a concentrated polymer solution (50% w/v of DMF) into a 0.5 cm thick layer of NaCl (sieved to a size of 250 μm) in a 6 cm aluminum dish. The samples were air-dried for 72 h and then vacuum-dried for 168 h to remove any residual solvent. The polymer–salt composites were then soaked in deionized water (the water was changed every 12 h, and a AgNO₃ solution was used to check for the presence of NaCl until no white precipitation was found) to leach out the salt and provide the desired scaffold. The tube construct was prepared via melt extrusion using powdered PEU.

Results and Discussion

PEUs composed of varying amino acids and diol chain lengths were prepared in a two-step synthesis (Figure 1).²²⁻²⁴ Diamine monomers were prepared via Fischer esterification of amino acids and a diol with a chain length of 6, 8, 10, or 12 methylene units. The yields of the monomers ranged from 67 to 95%. Polymers were prepared via an interfacial step-growth polymerization between the monomers and triphosgene, with yields ranging from 70 to 97%. The M_n and D_M of PEUs ranged from 12 to 70 kDa and 1.4 to 3.0, respectively (see Table 1). Dispersities significantly lower than 2.0 can likely be attributed to fractionation during postpolymerization precipitation of polymers. The p(1-ALA-6) and p(1-ALA-8) PEUs were obtained with lower molecular weights (12 and 14 kDa, respectively), likely due to poor solubility of the polymers during polymerization), prohibiting the preparation of sample specimens for shape memory characterization.

The thermal properties of the PEUs were studied by DMA. Of particular interest was the T_g, which indicates the minimum temperature for shape programming and recovery, and the storage modulus (E') at room and physiological temperatures, which provides an indication of the stiffness of the material. In accord with other studies, the T_g of all PEUs increased with decreasing diol chain length,²²⁻²⁴ with T_g values ranging from 21 to 73 °C, and providing a set of materials whose shape changes could be triggered at or near physiological temperatures. The modulus was shown to increase with decreasing diol chain length (Figure 2). The PHE-based PEUs showed the highest modulus values, likely due to π–π stacking between the aromatic side chains. The ABA-, VAL-, and ILE-based PEUs generally showed the same modulus trends, with the exceptions (including the ALA-based PEUs) being attributed to enhanced crystallinity (see below). Overall, these results illustrate the broad tunability of the thermomechanical response of these materials. By simply changing the amino acid and diol, the T_g can be tuned over a range of nearly 55 °C and the modulus over a range of nearly 2.5 GPa.

DMA curves are a good indicator of the thermal shape memory behavior of a material.¹⁸ The drop in modulus at the T_g provides an indication of the extent of chain mobility (with a large modulus drop indicating that a material can be easily programmed into a temporary shape), and a rubbery plateau above the T_g indicates the presence of a network capable of maintaining shape recovery. The decreasing slope of the plateau, prior to melt/failure, is likely a result of the dynamic nature of the hydrogen bonding (i.e., some chain slippage occurs). While all PEUs showed a rubbery plateau, the magnitude of the modulus drop did have some variance between polymers. For example, p(1-PHE-6) showed a small modulus drop (ca. 1 order of magnitude, Figure 3A) while the remaining polymers in the PHE series showed a large drop (at...
We attributed the behavior of p(1-PHE-6) to the increased crystallinity of the material (as apparent from the XRD curves of PHE-based PEUs, Figure 3C). We found this trend to hold true for all other PEUs and that only those with an increased degree of crystallinity (p(1-ALA-10), p(1-ALA-12), p(1-ABA-6), and p(1-ABA-8)) exhibited a small modulus drop (this is especially apparent when comparing PEUs with a consistent diol length, Figure 3D−F). These results suggested that all of the PEUs, regardless of amino acid or diol, should exhibit shape memory behavior. However, the materials with a small modulus drop are likely to have diminished performance.

The dual-shape memory properties of PEUs were studied by cyclic thermomechanical testing with a DMA. A single cycle consists of programming a temporary shape and recovering the permanent shape. The temporary shape was programmed by elongating the sample at a $T_d$ equal to the $T_g$ of the material (as determined from the peak in the plot of loss modulus vs temperature), cooling below the $T_g$ and removing the tensile load. The permanent shape was recovered by simply reheating the material above the $T_g$ in the absence of a tensile load. Three back-to-back cycles were completed to remove the effects of the thermal processing and to demonstrate the fidelity of shape memory performance (Figure 4A). The strain fixity and recovery parameters, $R_f$ and $R_r$, respectively, are used to characterize the efficacy of the programming and recovery steps.\(^\text{15}\) We observed that the VAL-, ILE-, and PHE-based PEUs with a large drop in storage modulus had high $R_f$ (>90%) and $R_r$ (>95%) values. In these materials the incorporated amino acid or diol had little effect on those parameters (Table 1). The PEUs with a small modulus drop demonstrated decreases in $R_f$ (79−90%) and $R_r$ (85−95%) values; however, the largest decrease in performance was the strain achievable during the shape programming step. The maximum achievable strain for these materials was less than 10%, even with increased $T_d$ temperatures (applying higher strains led to failure of the materials), in contrast to achievable strains of greater than 90% for PEUs with a large modulus drop. The ABA-based PEUs with a large modulus drop (p(1-ABA-10) and p(1-ABA-12) had high $R_f$ values but decreased $R_r$ values. This could be attributed to the low storage modulus, manifested in the material storing less energy for shape actuation. The molecular weight of PEUs is not expected to have a significant effect on the shape memory properties of PEUs, unless it were to drop below the least 2 orders in magnitude).
entanglement molecular weight (decreasing the degree of physical cross-linking). For instance, a 33 and 99 kDa p(1-PHE-10) were compared head-to-head and shown to have $R_f$ values of 97 and 99%, respectively, and both had $R_s$ values of 99%. It is, however, expected that the molecular weight would have a small impact on the $T_g$.

As shape fixing and recovery are based on the $T_g$, we observed that the transition temperature ($T_{trans}$) of shape recovery; see Table 1 trended well with the $T_g$, as expected. Overall, PEUs showed good to excellent shape memory performance across all amino acids and diol combinations studied, except when the materials were crystalline. This is a significant finding as being able to tune the mechanical properties without significantly impacting the shape memory performance is an advantageous feature of these materials.

PEUs exhibit a broad $T_g$ range (>20 °C), which is a common feature of many multishape memory polymers. We previously demonstrated that p(1-VAL-8) had good triple-shape memory performance. We further subjected p(1-ILE-8) and p(1-PHE-8) to thermomechanical testing to determine how the amino acid might affect the SMP performance. In triple-shape memory testing, two temporary shapes are programmed at two different $T_g$s above the $T_g$, followed by recovery of the first temporary shape and permanent shape by heating at the two $T_g$s consecutively (Figure 4B). Each polymer showed good $R_s$ and $R_f$ parameters (Table 2). During the recovery of the first shape of p(1-PHE-8), a $R_f > 100$% was obtained due to partial recovery of the second temporary shape. This is primarily due to having used only a 20 °C difference between $T_g$s (as opposed to 30 °C for VAL and ILE). This adjustment was required as the width of the thermal transition for p(1-PHE-8) is narrower than the other two polymers (see Figure S1 in the Supporting Information).

Another common feature of SMPs with broad thermal transitions is that they often have temperature memory properties. The temperature memory effect (TME) was explored in p(1-VAL-8), a representative PEU. We first looked at the stress-based TME. In this test, multiple samples were heated at various $T_g$s and then stretched to 100% strain. The samples were then held in an isostrain state and heated, and the recovery stress was monitored as a function of temperature. We observed a steady increase in the peak recovery stress (Figure 5), indicating the material had ”memorized” the $T_g$. With the exception of the tests completed using a $T_g$ of 30 °C, which is below the $T_g$ of the material, the peak recovery stress was within ca. 5 °C from the $T_g$, which is consistent with other temperature memory materials. To confirm that the material would also show a strain-based TME, multiple samples were heated at various $T_g$s and then stretched to 100% strain; then the samples were heated in the absence of a tensile load, and the recovery of the permanent shape was monitored as a function of time and temperature. We observed that the recovery profile of the material shifted to higher temperatures with increasing $T_g$. The peak in recovery rate also trended toward higher temperatures as higher $T_g$s were used. This confirmed that p(1-VAL-8) exhibited both stress- and strain-based temperature memory properties. Given that the diol and amino generally had minimal effect on the dual- and triple-shape memory properties of PEUs, it would follow that the other PEUs would also exhibit the TME.

To explore the shape memory behavior of PEUs in constructs that might be relevant to biomedical applications, several specimens were prepared to explore the effect of shape changes outside the realm of pure tensile elongation. For instance, we demonstrated multidirectional unfolding of a box into a thin film (Figure 6A). The same specimen could also be reprogrammed to fold from the flat film to the box. Shape recovery, in both cases, occurred in 3 s or less. We next looked at the surface topology of a thin film, which was altered and recovered (Figure 6C). Shape changes of larger constructs such as a salt-leached scaffold or a thick cylindrical specimen could also be achieved. These demonstrations show the versatility of the shape memory effect in PEUs.

**CONCLUSIONS**

New PEUs with differing amino acid and diol compositions were prepared and shown to have unique and tunable...
thermomechanical properties. The $T_g$s of PEUs covered a range of nearly 55 °C, and the storage moduli, a range of nearly 2.5 GPa. We found that most of the studied PEUs demonstrated shape memory behavior with excellent shape memory characteristics. The main inhibitor of SMP performance was found to be associated with the appearance of a crystalline morphology, leading to a reduction in chain mobility and very low achievable strains. Because of the broad glass transition temperature of these materials, we found them to exhibit triple-shape memory and temperature memory behavior. The overall shape memory performance together with tunable mechanical properties and previous demonstrations of biocompatibility make PEUs prime candidates for use as SMPs in various biomedical applications.

Figure 5. (A) Stress generated by p(1-VAL-8) when heated after programming a temporary shape with 100% strain. The strain is fixed, and the temperature is increased from 10 °C at a rate of 5 °C/min until sample failure occurs. Each plot corresponds to the $T_g$ used to program the temporary shape. The peak in recovery stress increases with increasing $T_g$, demonstrating stress-based TME properties. (B) Strain recovery profiles of p(1-VAL-8) specimens that were programmed to 100% strain. Samples were heated at 5 °C/min to 90 °C. (C) Strain recovery rates obtained from the recovery profiles in (B). The peak in recovery rate increases with increasing $T_d$, demonstrating strain-based TME properties. The arrow on the x-axis indicates the temperature corresponding to the $T_g$ of the material.

Figure 6. (A) Demonstration of dual-shape memory actuation in a p(1-ILE-8) thin film. A ca. 1 cm³ cube is programmed to open to a flat film upon heating. The shape change occurred over ca. 2 s. (B) The same p(1-ILE-8) thin film programmed to close into the shape of a 1 cm³ cube upon heating. The shape change occurred over ca. 3 s. (C) Changing surface roughness of a p(1-ILE-6) thin film. The film in i is the starting polymer, ii is after applying roughness to the sample, and iii is after heating the sample, showing recovery of the smooth surface. (D) Bending of a p(1-VAL-8) salt leached scaffold. The scaffold in i is prior to deformation, ii is after bending, and iii is after heating the scaffold. (E) Shape change of a large tube construct of p(1-PHE-6). The tube in i is the original shape, ii is after deformation, and iii is the recovered shape. Shape recovery was triggered by gentle heating with a heat gun. All scale bars represent 1 cm.

ASSOCIATED CONTENT *

Supporting Information
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Figure S1, SEC plots, IR spectra, and ¹H/¹³C NMR spectra for all new monomers and polymers (PDF)

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Notes
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### ABBREVIATIONS

ABA, 1,2-aminobutyric acid; ALA, L-alanine; $D_{\text{M}}$, molecular mass distribution/dispersity; DMA, dynamic mechanical analysis; DMF, dimethylformamide; DMSO, dimethyl sulfoxide; DSC, differential scanning calorimetry; $M_\text{n}$, number-average molecular weight; PEU, poly(ester urea); PHE, L-phenylalanine; ILE, i-isoleucine; $R_\text{f}$, fatty acid parameter; SEC, size exclusion chromatography; SMP, shape memory polymer; $T_\text{d}$, deformation temperature; $T_\text{g}$, glass transition temperature; TME, temperature memory effect; TsOH, p-toluene sulfonic acid; $T_{\text{trans}}$, transition temperature; VAL, L-valine; XRD, X-ray diffraction.

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