Biomimetic Polymer with Unique Combination and Adaptive Mechanical Properties

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Supporting Information

Part I. Synthesis and characterizations of the monomers and polymers

Part II. Thermal, mechanical, and microscopic characterizations of the polymers

Part III. Computer modeling of UPy cross-dimerization
Part I. Synthesis and characterizations of the monomers and polymers

**General Experimental Details:** $^1$H NMR spectra were recorded at 400 and 500 MHz and $^{13}$C NMR spectra were recorded at 125 and 100 MHz on Bruker instruments. $^1$H and $^{13}$C NMR chemical shifts are reported as δ values in ppm relative to TMS or residual solvent: CDCl$_3$ (7.26 ppm). Data is reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet), coupling constants in Hertz (Hz), and integration. Multiplets (m) are reported over the range (ppm) which they appear at the indicated field strength. Carbon NMR spectra were recorded in ppm relative to the solvent signals: CDCl$_3$ (77.23 ppm). Mass spectral data was obtained on Micromass LCT (ES-MS). Dialysis was carried out using Spectrum Labs Spectra/Por® regenerated cellulose dialysis membrane (MWCO: 15000). Gel Permeation Chromatography (GPC) was performed on an Agilent 1100 SEC system using a Polymer Laboratories PLgel Mixed-C column (Amherst, MA) with CHCl$_3$/DMF (9:1 v/v) eluent to determine molecular weights and molecular weight distributions, $M_w/M_n$, of polymer samples with respect to polystyrene (PS) standards purchased from Aldrich (Milwaukee, WI). All commercial reagents were used as received with the following exceptions: CH$_2$Cl$_2$, THF, and toluene were purified by passage through an alumina filtration system according to the method described by Grubbs.$^1$ Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on Fisher silica gel 60 (230-400 mesh). Moisture sensitive reactions were carried out under a nitrogen atmosphere using flame-dried glassware and standard syringe/septa techniques.
Scheme S1: Synthesis of the sample and control monomers and polymers.

a) Diol module 5, 10-undecenoyl chloride, py, THF, rt, 76%. b) Grubbs gen 2, 1,2,4-TCB, 70 ºC, 84%. c) 3, o-NBnBr, K2CO3, DMF, 70 ºC, 52% d) Grubbs gen 2, CHCl3, reflux, 75%.

Bis-olefin monomer (3). Diol module 5 was synthesized as previously described, though the initial benzyl ether halide was switched from butane to propane, resulting in a four rather than five carbon alcohol tether in the final molecule. 5 (1.0 g, 1.0 mmol) was dissolved in THF (10 mL) with heating. After cooling to room temperature, 10-undecenoyl chloride (0.55 mL, 2.6 mmol) was added, followed by pyridine (0.25 mL, 3.1 mmol). A white precipitate quickly formed, and the solution was allowed to stir for 4 h at ambient temperature. The reaction was
diluted with CHCl₃ (25 mL), washed with water (25 mL), sat. NaHCO₃ (25 mL), brine (25 mL),
dried over anhydrous MgSO₄, filtered and evaporated, then subjected to a benzene azeotrope to
remove residual pyridine. The residue was purified by flash column chromatography
(MeOH/DCM, 0:100 – 1:99) and the clean fractions combined and evaporated to afford the
desired bis-olefin module as white wax (1.0 g, 76%). ¹H NMR (toluene-d₆) δ: 13.25 (s, 2H),
12.27, (s, 2H), 10.84 (t, J = 5.0 Hz, 2H), 5.78 (ddt, J = 6.9 Hz, 17.0 Hz, 6.7 Hz, 2H), 5.02 (m,
2H), 4.98 (m, 2H), 3.92 (t, J = 6.2 Hz, 4H), 3.46 (q, J = 6.3 Hz, 4H), 2.46 (t, J = 7.5 Hz, 4H),
2.21 (t, J = 7.5 Hz, 4H), 1.99 (m, 6H), 1.76, (quintet, J = 7.5 Hz, 4H), 1.67-1.57 (m, 8H), 1.5-1.1
(m, 92H); ¹³C NMR (CDCl₃) δ: 174.1, 172.7, 157.0, 153.6, 146.1, 139.4, 118.5, 114.3, 63.6,
40.3, 34.5, 34.0, 30.2, 30.2, 30.1, 30.0, 30.0, 30.0, 30.0, 29.8, 29.7, 29.6, 29.5, 29.5, 29.5,
29.4, 29.3, 29.1, 29.0, 28.8, 28.4, 28.1, 28.0, 27.9,27.8, 27.5, 27.4, 27.3, 27.0, 28.6, 25.1,
24.7; ES-MS m/z calcd for C₇₈H₁₃₉N₈O₈ (M+H)+: 1316.07, found 1316.26.

**Synthesis of polymer (1).**³ Bis-olefin monomer 3 (0.65 g, 0.5 mmol) was dissolved in degassed
1,2,4-trichlorobenzene (2 ml) and heated to 70 °C. Grubbs Gen-2 catalyst (8.4 mg, 0.01 mmol)
was added, and the mixture placed under vacuum while heating. Gentle bubbling ensued, and
after 15 min, the mixture gelled. More 1,2,4-TCB (5 mL) was added to re-dissolve, and the
reaction was poured into a petri dish and placed in a nitrogen-flushed vacuum oven at 70 °C
under vacuum. The solvent evaporated slowly overnight, and the film was removed and re-
dissolved by stirring in hot CHCl₃/ethyl vinyl ether (10:1, 10 mL) for 12 h. The solution was
poured into stirring ether (100 mL) and the suspension was allowed to stand for 10 min. The
supernatant was decanted, and the precipitate dried under high vacuum (0.54 g, 84%). The
polymer was re-dissolved in CHCl₃ (10 mL), poured into a petri-dish, and the solvent was
allowed to evaporate slowly at room temperature. The transparent film was dried at 70 °C overnight under high vacuum, removed from the dish and subjected to mechanical testing. $^1$H NMR (toluene-$d_6$; 348K) δ: 13.20 (s, 2H), 12.13, (s, 2H), 10.59 (t, $J = 5.1$ Hz, 2H), 5.47 (m, 2H), 5.02 (m, 2H), 4.98 (m, 2H), 3.99 (t, $J = 6.2$ Hz, 4H), 3.44 (q, $J = 6.3$ Hz, 4H), 2.49 (t, $J = 7.5$ Hz, 4H), 2.29-2.19 (m, 8H), 2.1-2.0 (m, 4H), 1.79, (quintet, $J = 7.4$ Hz, 4H), 1.67-1.57 (m, 8H), 1.5-1.1 (m, 100H); $M_n = 18.0$ kDa, D = 1.7.

o-NBn protected bis-olefin module (4). To a mixture of bis-olefin monomer 3 (0.4 g, 0.3 mmol) and o-nitrobenzyl bromide (0.2 g, 0.9 mmol) in DMF (3 mL), K$_2$CO$_3$ (0.17 g, 1.2 mmol) was added and the reaction heated to 70 °C overnight. After cooling to room temperature, the mixture was diluted with CHCl$_3$ (15 mL), washed with 1N HCl (10 mL), sat. NaHCO$_3$ (10 mL), brine (10 mL), dried over anhydrous MgSO$_4$, filtered and evaporated. The residue was purified by flash column chromatography (MeOH/DCM, 0:100 – 3:97) and the fractions containing pure product combined and evaporated to afford the desired compound as an off-white solid (0.25 g, 52%). $^1$H NMR (CDCl$_3$) δ: 9.17 (s br, 2H), 8.17 (d, $J = 8.2$ Hz, 2H), 7.71-7.66 (m, 4H), 7.55 (m, 2H), 7.26 (s, 2H), 7.06 (s, 2H), 5.84 (ddt, $J = 6.9$ Hz, 17.0 Hz, 6.7 Hz, 2H), 5.78 (s, 4H), 5.02 (m, 2H), 4.98 (m, 2H), 4.15 (t, $J = 6.2$ Hz, 4H), 3.40 (q, $J = 6.3$ Hz, 4H), 2.73 (t, $J = 7.2$ Hz, 4H), 2.58 (t, $J = 7.5$ Hz, 4H), 2.33 (t, $J = 7.6$ Hz, 4H), 2.07 (q, $J = 6.8$ Hz, 4H) 1.84-1.73 (m, 8H), 1.69-1.57 (m, 8H), 1.5-1.1 (m, 84H); $^{13}$C NMR (CDCl$_3$) δ: 174.0, 167.6, 155.1, 154.6, 139.3, 133.8, 132.8, 129.2, 128.9, 125.3, 114.4, 113.1, 65.3, 64.0, 40.1, 34.5, 34.0, 33.5, 29.9, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.4, 29.3, 29.1, 28.7, 27.3, 25.2, 25.1, 24.7; ES-MS m/z calcd for C$_{92}$H$_{149}$N$_{10}$O$_{12}$ (M+H)$^+$: 1586.14, found 1586.63.
**Synthesis of control polymer (2).** Bis-olefin o-NBn protected module 4 (0.25 g, 0.16 mmol) was dissolved in degassed CHCl₃ (1 ml) and heated to reflux. Grubbs generation 2 catalyst (0.009 g, 0.009 mmol in 0.1 mL CHCl₃) was added. After 1 h, the condenser was removed and ~75% of the solvent removed under a stream of N₂. The condenser was replaced and reaction stirred at reflux for a further 30 min. Ethyl vinyl ether/MeOH/CHCl₃ (1:1:5, 5 mL) was added and the mixture heated until the polymer re-dissolved. The solution was poured into stirring ether (15 mL) and the suspension was allowed to stand for 10 min. The supernatant was decanted, and the precipitate dried under high vacuum. The solid was then dissolved in THF (10 mL) and placed in a dialysis membrane and suspended in a beaker of THF (800 mL). The solvent was removed and replaced with fresh THF every 12 h for 48 h, then the tubing unsealed and the solution removed and evaporated (0.15 g, 75%). The brown powder was re-dissolved in CHCl₃ (3 mL), transferred to a scintillation vial, and the solvent was allowed to evaporate slowly at room temperature. The film was dried at 70 °C overnight under high-vacuum, removed from the vial and subjected to mechanical testing. \(^1\)H NMR (CDCl₃) δ: 9.13 (s br, 2H), 8.10 (d, \(J = 8.5\) Hz, 2H), 7.67-7.60 (m, 4H), 7.49 (m, 2H), 7.25 (s br, 2H), 5.72 (s, 4H), 5.32-5.27 (m, 2H), 4.09 (t, \(J = 6.2\) Hz, 4H), 3.34 (q, \(J = 6.1\) Hz, 4H), 2.67 (t, \(J = 7.2\) Hz, 4H), 2.53 (t, \(J = 7.7\) Hz, 4H), 2.27 (t, \(J = 7.4\) Hz, 4H), 2.00-1.90 (m, 6.8 Hz, 4H) 1.79-1.51 (m, 18H), 1.49-1.41 (m, 4H), 1.40-1.18 (m, 88H); \(M_n = 29.3\) kDa, D = 1.7.
Part II. Thermal, Mechanical, and Microscopic Characterizations of Polymers

**Tensile Testing.** Static multi-cycle tensile measurements were obtained on an MTS Synergie 100 materials testing machine with TestWorks 4 software. “Dogbone” test strips were stamped from the transparent thin films using an ASTM 638 V standard die (gauge dimensions: 30 mm x 3 mm; thickness measured for each sample with Mitutoyo digital calipers) and stretched at room temperature with a 10 mm/min strain rate. The raw data was exported and analyzed with Excel. Modulus was determined according to the ASTM 638 standard, or taken at the steepest point of the initial stress-response slope for later cycles, as result of the initial stress artifact associated with re-straightening the samples (Fig. 1 in the text). For easy visualization of the test cycle, a short movie can be found at: [http://www.youtube.com/watch?v=sKatRwMKZLI](http://www.youtube.com/watch?v=sKatRwMKZLI). One sample was immersed in water for 18 h and again subjected to tensile testing (Fig. S 17).

**Dynamic Mechanical Analysis (DMA).** DMA was performed on the “dogbone” film test strips of modular polymer 1 and control polymer 2 using a TA Instruments DMA 2980 with the cryo accessory attached, with a 15 µm 1 Hz oscillation and 0.1N static force. The raw data was exported and analyzed using Excel. The storage modulus (G’), loss modulus (G”), and tan δ are plotted in Fig. S10, revealing a tan δ peak at ~ 52 °C. This temperature corresponds closely with the T\text{trans} of polymer 1 observed in the subsequent shape-memory studies.

**Shape-memory Property Determination.** Shape-memory studies were carried out using a TA Instruments DMA 2980 with the cryo accessory attached. For the extension cycle, the sample was heated to 80 °C, and a static force of 0.3 N was applied. When the sample reached a strain of 250%, the experiment was stopped and the chamber was cooled quickly to 5 °C. The second
part of the experiment began from the final position of the first stage. 0.003 N of static force was applied and the temperature was held at 5 °C to confirm strain fixity before heating to 80 °C at a rate of 5 °C/min, and the displacement measured. The small force was applied to prevent the sample from bending when heated. The application of this force did not change the $T_{trans}$ from the value observed with a 0 N force. The raw data from the two experiments were exported, combined and analyzed using Excel (Fig. 2 in the text).

**Small angle X-ray scattering (SAXS) and wide angle X-ray scattering (WAXS) analysis.** SAXS/WAXS studies were carried out on polymers 1 and 2 (Fig. S11-14) at the Materials Research Laboratory of the University of California, Santa Barbara. Exact details of the home-built SAXS/WAXS setup can be found at: http://www.mrl.ucsb.edu/mrl/centralfacilities/xray/instruments/saxs.html.

**Dynamic Light Scattering (DLS).** DLS experiments were carried out with a Malvern Zetasizer. Polymer 1 was dissolved 0.5 mg/ml in CHCl$_3$/DMF (9:1 v/v) for characterization (Fig. S9).

**Atomic force microscopy (AFM) analysis.** Intermittent-contact mode (Tapping mode$^TM$) AFM measurements were performed under ambient conditions using a Veeco MultiMode with a Nanoscope IV controller. Standard silicon AFM probes (Nanosensors, PPP-NCH), having cantilever spring constants of 10-130 N/m, resonance frequencies from 204 to 497 kHz, and a typical tip curvature radius of 10 nm were used. Typically, an amplitude set point $A/A_0$ of 0.9 and a scan rate of 1 Hz was used. Samples were prepared by spin-coating films at 1500 rpm from solutions of 10 mg/mL in MeOH/CHCl$_3$ (1:9 v/v) on cleaned glass microscope cover slips. The
cleaning procedure comprises sonication in acetone for 15 min, rubbing briefly with SDS soap solution, sonication in SDS soap solution for 10 min, rinsing in a stream of demi water for 15 min, and finally sonication in isopropanol for 10 min. The AFM samples were measured directly after spin-coating (Fig. S15).\textsuperscript{4}

**Differential scanning calorimetry (DSC):** DSC measurements were performed with a TA Instruments Q2000 on ~5 mg of sample between -50 and 90 °C with a temperature gradient of 10 °C/min (Fig. S16).
Figure S1. $^1$H-NMR spectrum for the biomimetic monomer module (3)
Figure S2. $^{13}$C-NMR spectrum and ES-MS for the biomimetic module monomer (3)
Figure S3. $^1$H-NMR spectrum for the control monomer (4)
Figure S4. $^{13}$C-NMR spectrum and ES-MS mass spectrum for the control monomer (4)
Figure S5. $^1$H-NMR spectrum for the biomimetic modular polymer (1)
Figure S6. $^1$H-NMR spectrum for the control polymer (2)
Figure S7. GPC trace for the biomimetic modular polymer (1)
Figure S8. GPC trace for the control polymer (2)
Figure S9. DLS plot for polymer (1)

Figure S10. DMA plots for polymer (1)
Figure S11. Small angle X-ray scattering (SAXS) data for polymer (1) without pre-stretching treatment
Figure S12. Small angle X-ray scattering (SAXS) data for polymer (1) after deformation to 250% strain at 80 °C followed by cooling to freeze extended shape.
**Figure S13.** Small angle X-ray scattering (SAXS) data for the control polymer (2)

**Figure S14.** Wide-Angle X-Ray Scattering (WAXS) data for polymer (1)
Figure S15. A representative TM-AFM phase image for polymer (1) film spin-coated on clean glass microscope cover slip.

Figure S16. DSC plot for polymer (1) showing lack of crystalline or melting transitions.
**Figure S17.** Stress/strain plot for polymer (1) after incubating in water for 18 hours

**Part III. Computer modeling.**

Computer models of the conformations proposed to explain the observed material mechanical properties at the molecular level were generated using Maestro Modeling software with the AMBER* force field and CHCl₃ solvation. To generate the elongated structure (Fig S19), a 17 angstrom constraint was placed on the terminal methyl groups, a large enough distance to ensure the module was fully unfolded and extended but the bond lengths and angles were not distorted upon energy minimization. The cross-dimerized structure (Fig S20) was generated by separating the dimers from the first structure (Fig S19),
reconnecting the loop arms across the gap, and constraining the terminal methyl’s during minimization.

**Figure S18.** Molecular model illustrating two adjacent folded UPy dimer modules in bulk polymer 1.
Figure S19. Molecular model representing the possible unfolded conformation of two adjacent UPy dimer modules after the bulk material is strained past the yield point.
**Figure S20.** Molecular model illustrating the feasibility of inter-chain cross-dimerization of proximal unfolded UPy units, forming a new temporary network after extension-induced unfolding and relaxation of stress. While this model illustrates cooperative cross-dimerization of two unfolded UPy dimer modules, non-cooperative cross-dimerization between unfolded UPy units should also be feasible.
References:

1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J.


