

Supporting information

Bio-Inspired Self-Healing Polyurethanes with Multiple Stimulus

Responsiveness

Zhijun Yang,^a Fenfen Wang,^a Chi Zhang,^a Jian Li,^a Rongchun Zhang,^{*b} Qiang Wu,^a Tiehong Chen^c
and Pingchuan Sun^{*a,d}

^aKey Laboratory of Functional Polymer Materials of the Ministry of Education and College of Chemistry, Nankai University, Tianjin 300071, P. R. China

^bSouth China Advanced Institute for Soft Matter Science and Technology (AISMST), South China University of Technology, Guangzhou, 510640, China

^cInstitute of New Catalytic Material Science, School of Materials Science and Engineering, Key Laboratory of Advanced Energy Materials Chemistry (MOE), Nankai University, Tianjin, 300350, P. R. China

^dCollaborative Innovation Center of Chemical Science and Engineering (Tianjin), Tianjin 300071, P. R. China

*Corresponding Authors:

Rongchun Zhang, Email: zhangcr@scut.edu.cn

Pingchuan Sun, E-mail: spclbh@nankai.edu.cn

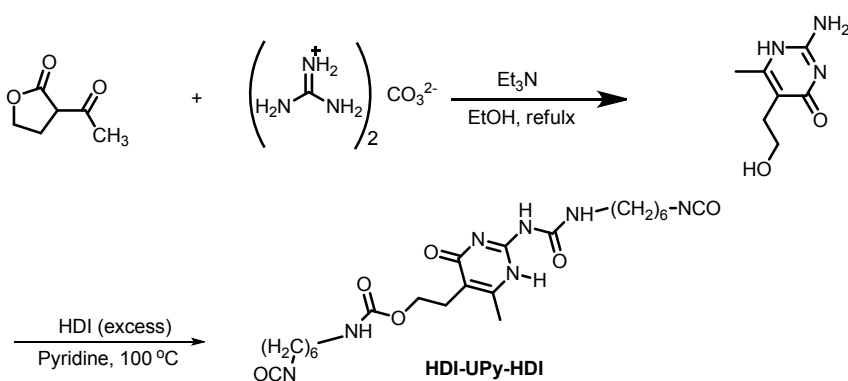
Experimental Section

1. Materials.

Triethylamine (Et_3N), 2-acetylbutyrolactone, guanidine carbonate and dibutyltin dilaurate were purchased from Sigma-Aldrich (Shanghai China). 3-mercaptopropane-1,2-diol (95%) and hexamethylene diisocyanate (HDI, 98%) were both obtained from TCI Chemicals Co., Ltd. (Tianjin, China). Polycaprolactone (PCL-2000, $M_n \sim 2000$ g/mol) and N,N-dimethylformamide (DMF) were purchased from Acros Organics (Beijing, China), while all the other reagents were purchased from Alfa Aesar Tianjin Chemical Reagent Co., China. Prior to use, DMF and Et_3N were both distilled in the presence of 4 Å molecular sieves and calcium hydride, respectively, after which both were stored in the dry nitrogen atmosphere. 3-mercaptopropane-1,2-diol and HDI were also both distilled before used. PCL-2000 sample was dried in vacuum at 120 °C for three hours prior to use. 2,2'-(methylenebis(4,1-phenylene))bis(cyclopent-4-ene-1,3-dione) was purified by recrystallization from dichloromethane/methanol (DCM/MeOH, v/v = 20 :1) mixture solution. N-hexane and absolute ethanol were distilled under atmospheric pressure in the presence of 4 Å molecular sieves. All other reagents were used as received without further purification.

2. Synthesis and sample preparation

2.1 Synthesis of UPy-containing monomer, HDI-UPy-HDI



Scheme S1. Schematic synthesis pathway of HDI-UPy-HDI.

(1) Synthesis of 5-(2-hydroxyethyl)-6-methyl-2-aminouracil: The synthesis procedure of UPy precursor was adapted from the work of Gangjee et al.¹, as shown in Scheme S1 above. A mixture of 2-acetylbutyrolactone (5.12 g, 40 mmol,) and guanidine carbonate (3.6 g, 40

mmol) was refluxed in absolute ethanol (40 mL) in the presence of Et₃N (11.0 mL, 80 mmol) for 1 h. Then the mixture became clear, and the reaction continued for 3 h. The final obtained product was precipitated and filtered to yield a light yellow solid, which was further washed with ethanol for three times and dried in vacuum to obtain a white powder solid, i.e. 5-(2-hydroxyethyl)-6-methyl-2-aminouracil. The chemical structure was confirmed by ¹H-NMR (Figure S1) and HRMS (Figure S2) below.

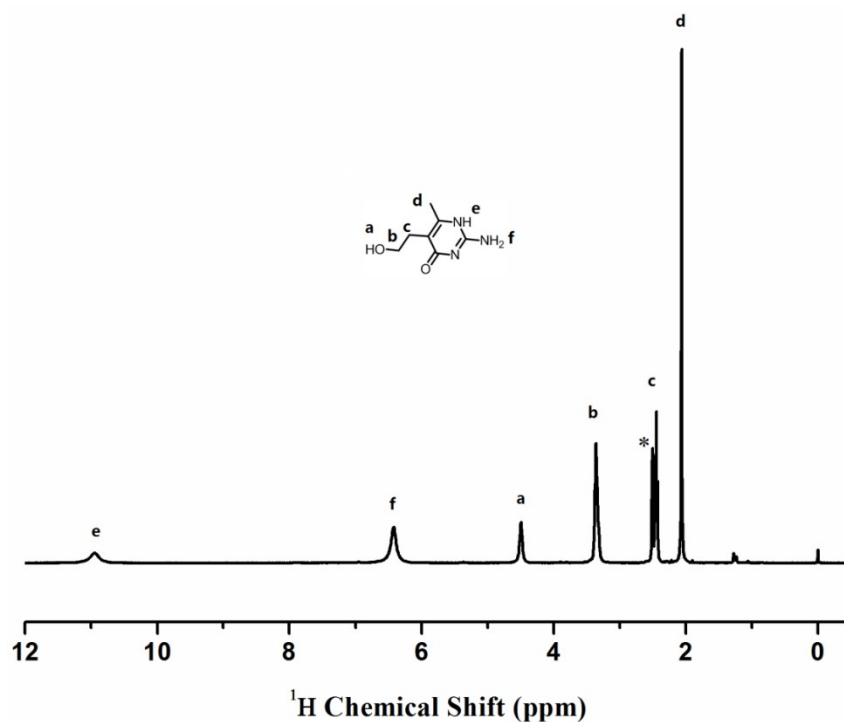


Figure S1. ¹H NMR spectrum of UPy precursor in DMSO-d₆. “*” denotes the proton signals of DMSO-d₆. ¹H (400 MHz, DMSO, δ ppm): 10.95 (s, 1H, NH, exch), 6.42 (s, 2H, NH₂, exch), 4.49 (s, 1H, OH, exch), 3.36 (t, 2H, $J = 7.2$ Hz), 2.45 (t, 2H, $J = 7.2$ Hz), 2.06 (s, 3H).

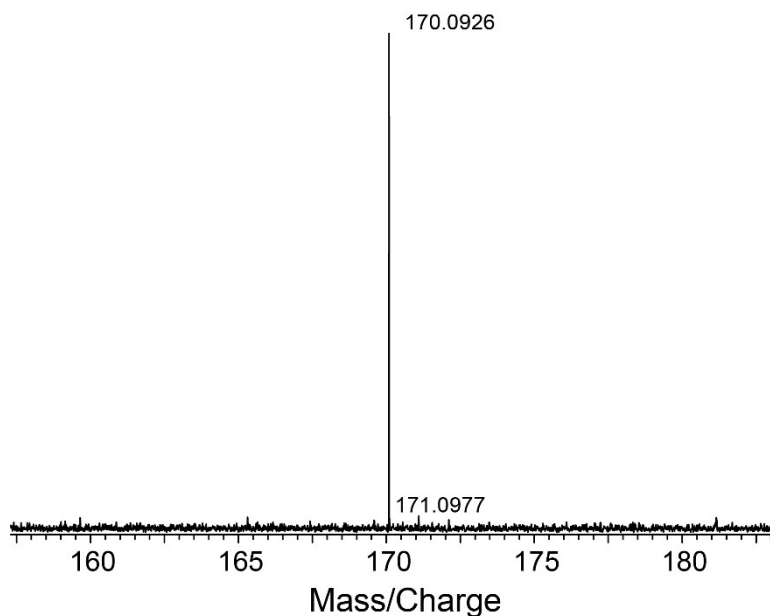


Figure S2. ESI-HRMS spectrum recorded for UPy precursor, 5-(2-hydroxyethyl)-6-methyl-2-aminouracil. The ESI-HRMS m/z calcd for $C_7H_{12}N_3O_2^+ [M + H]^+$: 170.0924, found 170.0926.

(2) Synthesis of HDI-UPy-HDI (UPy diisocyanate): The synthesis procedure of UPy was adapted from the work of Meijer *et al.*², as also shown in Scheme S1. The 5-(2-hydroxyethyl)-6-methyl-2-aminouracil (0.85 g, 5.0 mmol) was dissolved in a mixture of 10 mL of 1,6-diisocyanatohexane (HDI) and 1 mL of pyridine under a nitrogen atmosphere. The mixture solution was stirred at 100 °C for 1.5 h followed by precipitation into ten-fold excess of petroleum ether. The resulting solid was then washed with pentane and dried in vacuum to yield a white powder. The chemical structure of HDI-UPy-HDI was confirmed by 1H and ^{13}C NMR spectra as shown in Figure S3 and S4, respectively.

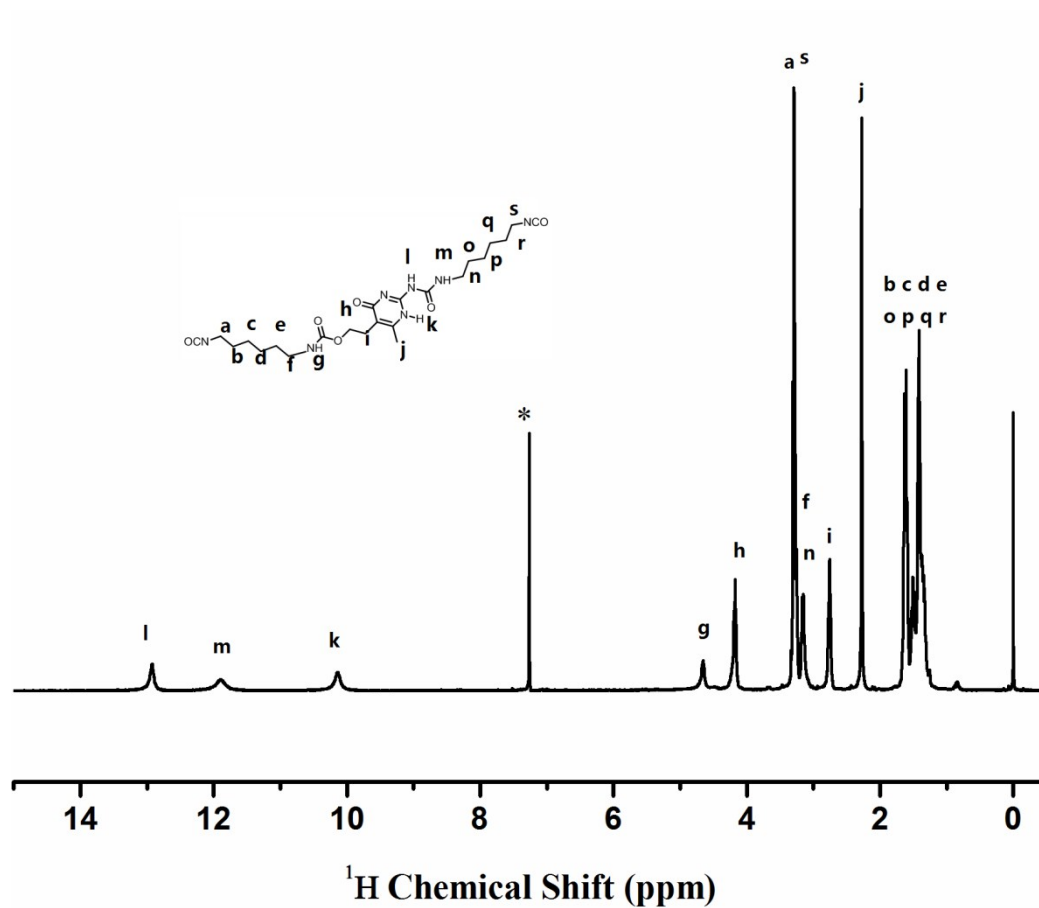


Figure S3. ^1H NMR spectrum of HDI-UPy-HDI in CDCl_3 , “*” denotes the solvent signal. ^1H (400 MHz, CDCl_3 , δ ppm): 12.93 (s, 1H), 11.90 (s, 1H), 10.12 (s, 1H), 4.65 (s, 1H), 4.18 (t, $J = 6.4$ Hz, 2H), 3.29 (t, $J = 6.4$ Hz, 4H), 3.25 (m, 2H), 3.15 (m, 2H), 2.76 (t, $J = 6.0$ Hz, 2H), 2.27 (s, 3H), 1.6-1.3 (m, 16H).

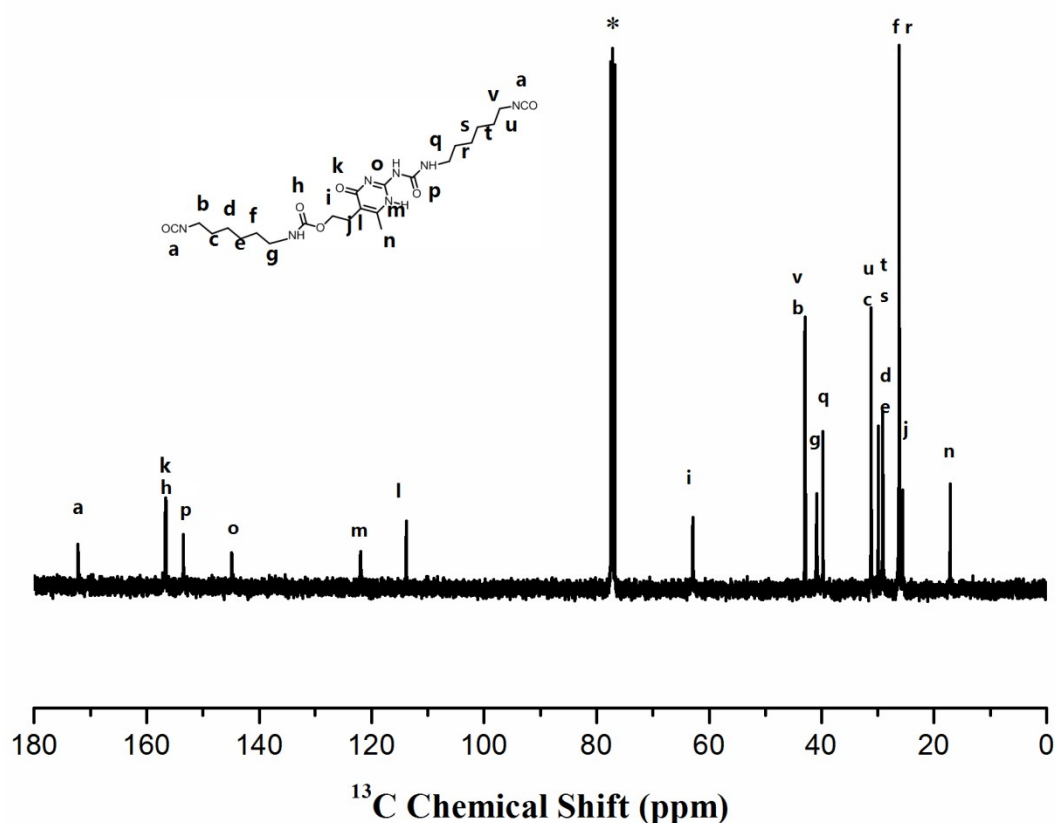
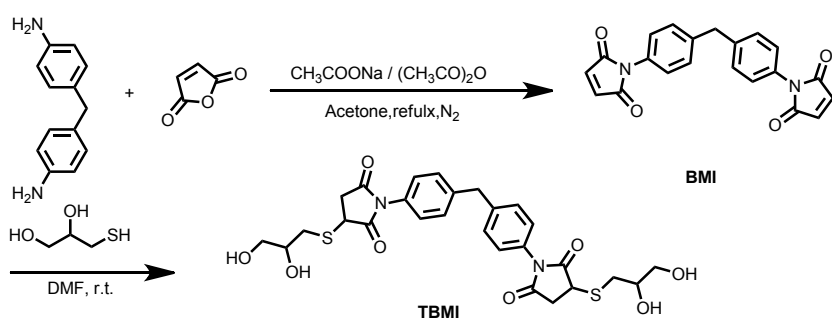


Figure S4. ^{13}C NMR spectrum of HDI-UPy-HDI in CDCl_3 . “*” denotes the solvent signal.

^{13}C (100 MHz, CDCl_3 , δ ppm): 172.2, 156.7, 156.6, 153.5, 144.8, 121.9, 113.8, 62.9, 42.96, 42.88, 40.9, 39.7, 31.2, 31.1, 29.9, 29.1, 26.3, 26.2, 26.1, 25.6, 17.2.

2.2 Synthesis of the Thiol-Michael Adduct Cross-linker, TBMI.



Scheme S2. Schematic synthesis pathway of TBMI.

(1) Synthesis of bismaleimides (BMI). The BMI were prepared by the method as reported in literature,³ as also shown in Scheme S2. 4,4'-Diaminodiphenylmethane (3.96 g, 20 mmol) was firstly dissolved in 80 mL dry acetone under a vigorously stirring condition, and then the maleic anhydride (4.3 g, 44 mmol) in dry acetone was added dropwise under nitrogen

atmosphere at 5 °C in 45 mins. The pale yellow precipitate of bismaleimic acid was obtained with the addition of maleic anhydride. The reaction mixture was vigorously stirred for 1 h after complete addition of maleic anhydride solution, and then kept for 0.5 h at room temperature. Sodium acetate (1.5 g, 18 mmol) and acetic anhydride (17.5 mL) were further added into the mixture to induce the cyclodehydration reaction of bismaleimic acid under continuous stirring condition. Then the reaction mixture was refluxed for about 3 h under nitrogen atmosphere until the solution became clear. The clear solution was then poured into crushed ice and repeatedly washed with water, and filtered to obtain the yellow precipitate. The precipitate was then dissolved in the DCM solution and dried over anhydrous MgSO_4 in vacuum. Further purification by flash column chromatography (DCM/MeOH, v/v = 50:1) was performed to yield the desired products. The chemical structure of BMI was confirmed by ^1H and ^{13}C solution NMR spectra (Figure S5 and S6) and ESI-HRMS (Figure S7).

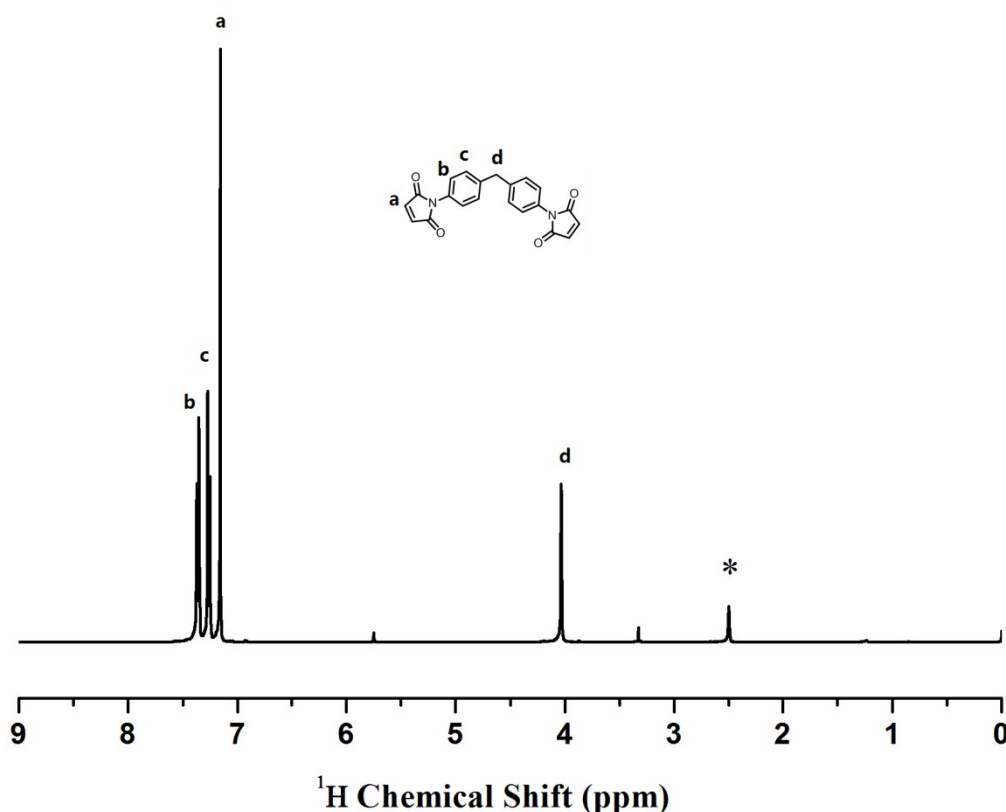


Figure S5. ^1H -NMR spectrum of BMI in DMSO-d_6 . “*” denotes the solvent signal. ^1H (400 MHz, DMSO , δ ppm): 7.36 (d, 4H, $J = 8.4$ Hz), 7.26 (d, 4H, $J = 8.4$ Hz), 7.16 (s, 4H), 4.03 (s, 2H).

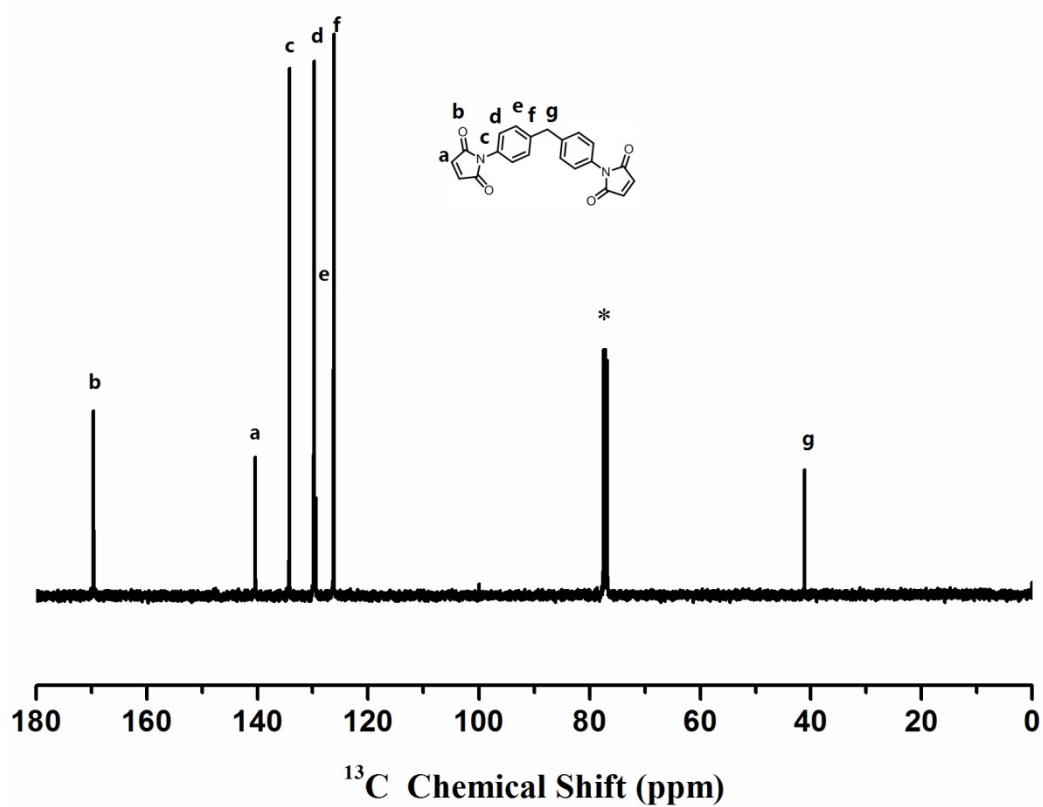


Figure S6. ^{13}C -NMR spectrum of BMI in CDCl_3 . “*” denotes the solvent signal. ^{13}C (100 MHz, CDCl_3 , δ ppm): 169.6, 140.4, 134.2, 129.8, 129.5, 126.2, 41.1.

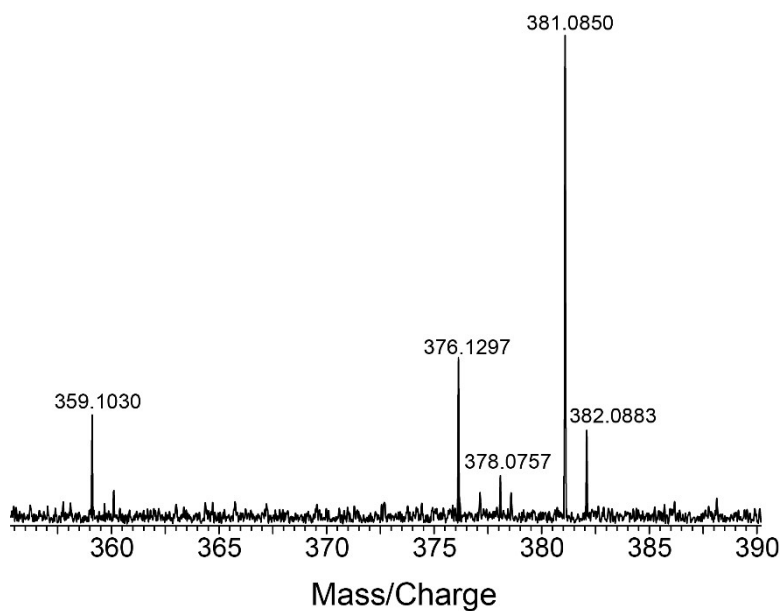


Figure S7. ESI-HRMS spectrum recorded for BMI. ESI-HRMS m/z calcd for $\text{C}_{21}\text{H}_{14}\text{N}_2\text{NaO}_4^+$ [$\text{M} + \text{Na}$] $^+$: 381.0846, Found 381.0850.

(2) Synthesis of the Thiol-Michael Adduct Cross-linker, TBMI. 3-Mercapto-1, 2-

propanediol (2.16 g, 20 mmol) was dissolved in the DMF solution in a 100 mL round-bottom flask under magnetic stirring, and then bismaleimides (3.58 g, 10 mmol) was added slowly in five minutes. The mixture in the flask capped with a glass stopper was stirred for 0.5 h at room temperature, and the solvent was removed by evaporation in vacuum at 50 °C to obtain a pale yellow viscous liquid. The yellow liquid was then washed with water/MeOH mixture for three times, and the solvents were again removed by evaporation in a vacuum oven at room temperature. The obtained residue was further purified by flash column chromatography (DCM/MeOH = 3:1), and the fractions containing the desired product were collected. The dry TBMI compound was finally obtained by further solvent evaporation in a vacuum oven. The chemical structure of TBMI compound was confirmed by ^1H and ^{13}C NMR spectra (Figure S8 and S9) as well as ESI-HRMS (Figure S10).

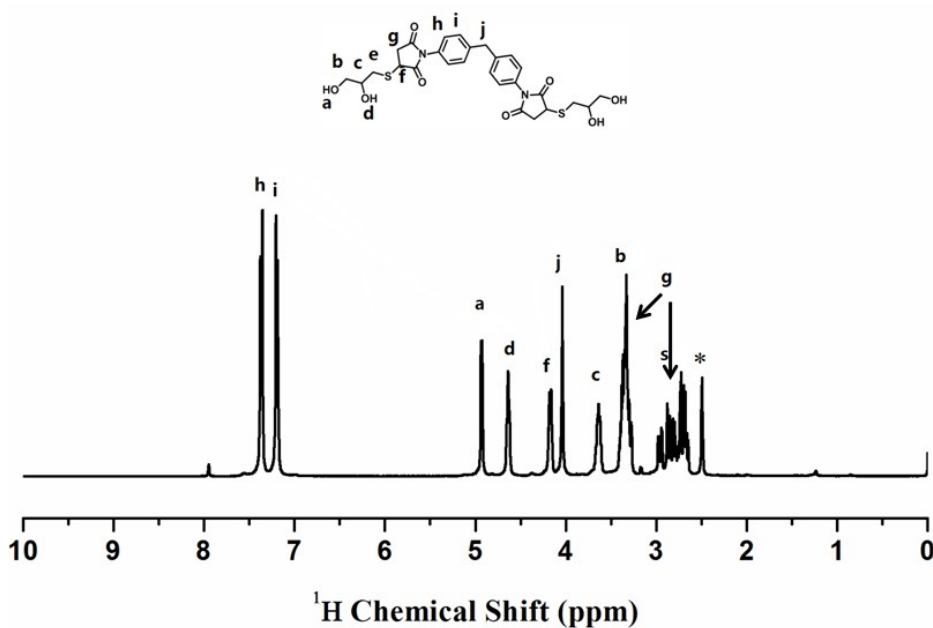


Figure S8. ^1H NMR spectrum of TBMI in DMSO- d_6 . “*” denotes the solvent signal. ^1H (400 MHz, DMSO, δ ppm): 7.37 (d, 4H, J = 8.0 Hz), 7.20 (d, 4H, J = 8.0 Hz), 4.94 (s, 2H), 4.65 (s, 2H), 4.04 (s, 4H), 3.63 (m, 2H), 3.40-3.28 (m, 6H), 2.98-2.65 (m, 6H).

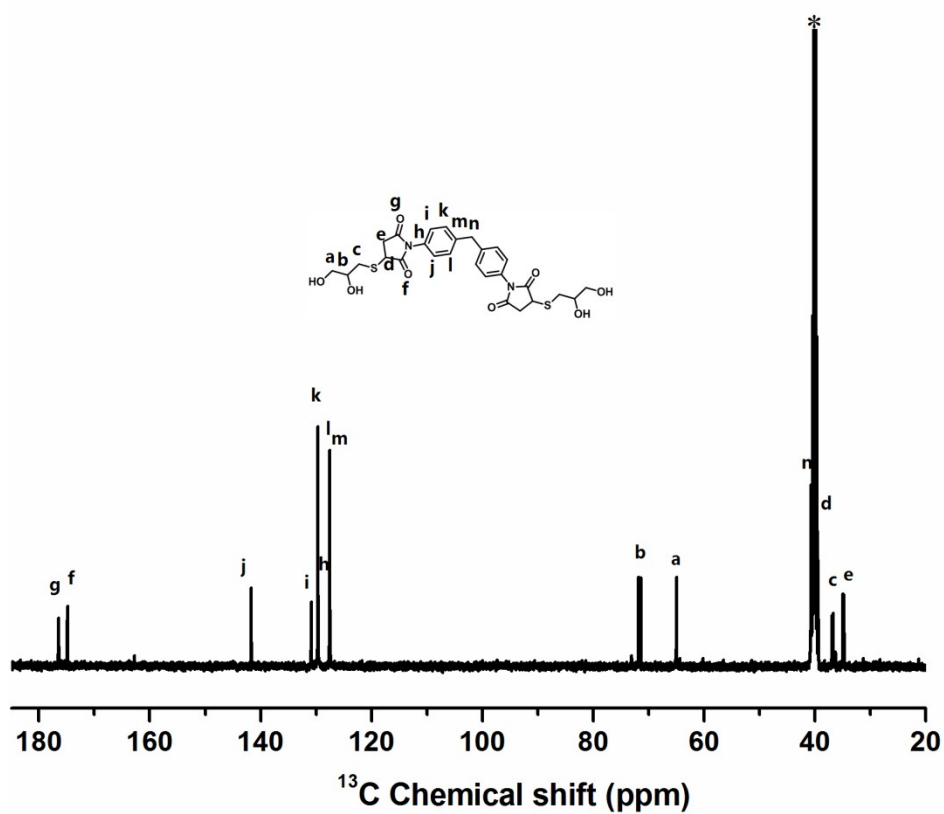


Figure S9. ¹³C-NMR spectrum of TBMI in DMSO-d₆. “*” denotes the solvent signal. ¹³C (100 MHz, DMSO, δ ppm): 176.5, 174.9, 141.7, 130.9, 129.7, 127.5, 71.8, 64.9, 40.7, 39.4, 36.7, 34.8.

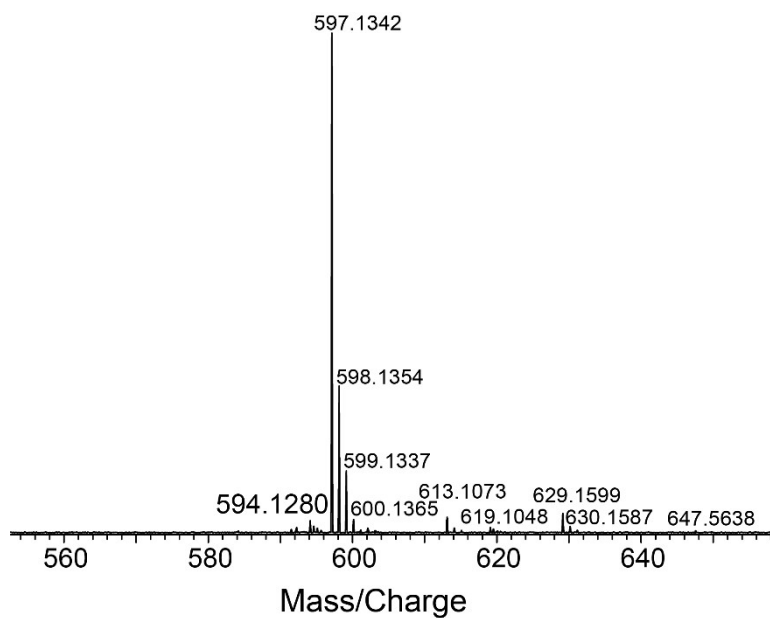
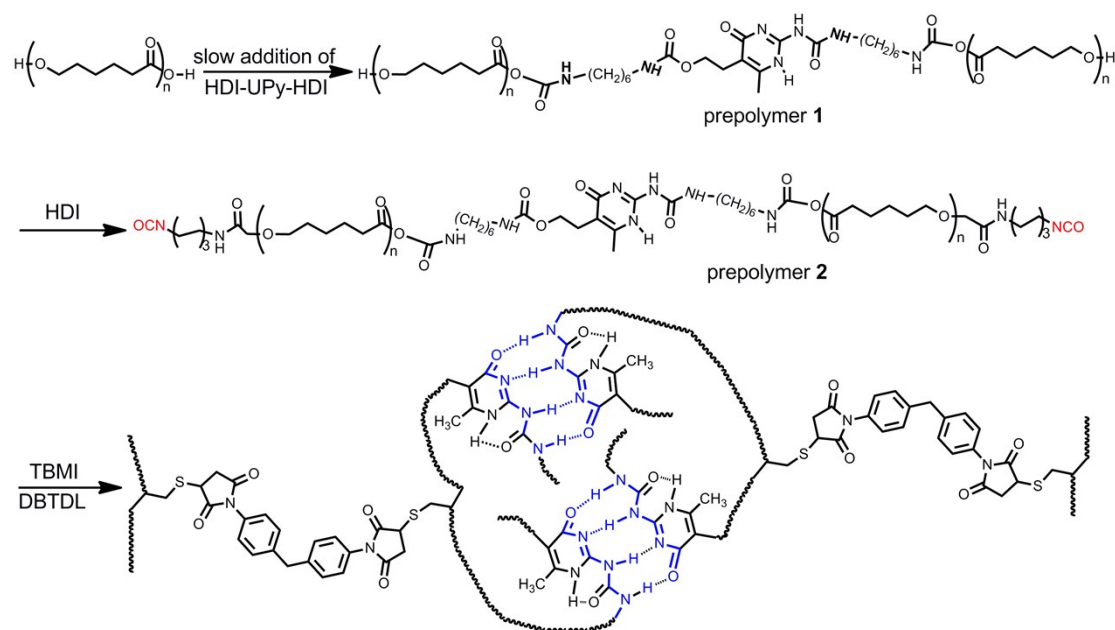


Figure S10. ESI-HRMS spectrum recorded for TBMI. ESI-HRMS m/z calcd for C₂₇H₃₀N₂O₈S₂Na⁺ [M + Na]⁺: 597.1341, found 597.1342.

2.3 Synthesis of Polyurethanes



Scheme S3. Schematic synthesis pathway of self-healing cross-linked PU.

PCL-2000 (8.0 g, 4.0 mmol) firstly reacted with HDI-UPy-HDI (1.010 g, 2 mmol) in anhydrous *N,N*-dimethylacetamide (DMAc, 15 ml) at 70 °C under nitrogen atmosphere for 1 h, yielding a prepolymer. Subsequently, 1,6-hexamethylene diisocyanate (0.64 ml, 4 mmol) was slowly injected into the above reaction solution, and then the reaction was conducted at 70 °C for another 0.5 h. Finally, the cross-linker TBMI (0.574 g, 1 mmol) and the catalyst dibutyltin dilaurate (DBTDL, 0.5 mol% for isocyanate or alcohol units) were added into the above mixture, which was allowed to react at 70 °C for 15 mins. Then, the solution was transferred onto a Teflon mold, kept at 70 °C for another 16 h in a vacuum oven. Finally, the cross-linked polymer was immersed in an acetonitrile with 10% methanol for 24 h. After another 5 days' drying in the vacuum oven, a transparent yellow solid (i.e. PU material) can be obtained. Monomer conversion was determined by gravimetry analysis and was found to be greater than 92%.

3. Characterization techniques

Nuclear Magnetic Resonance (NMR). Solution NMR experiments were performed on a Bruker AVANCE III NMR spectrometer with a proton resonance frequency of 400.13 MHz. The samples were dissolved in deuterated chloroform or DMSO-*d*₆ with a small amount of TMS as the internal reference standard.

Fourier Transform Infrared Spectroscopy. The infrared spectra were recorded with a resolution of 8 cm⁻¹ and 16 scans per sample, using a Bio-Rad FTS6000 spectrometer and UMA600 microscope equipped with a Linkam FTIR600 heat stage.

Mechanical Testing. Stress-strain curves were measured on an UTM6103 mechanical testing instrument (Shenzhen Suns Technology Stock Co., LTD., China) in tensile mode under a strain rate of 100 mm/min at room temperature. Dog-bone-shaped test strips were prepared from the PU films using a gauge dimension of: 50 mm x 4 mm and thickness of 1.5-1.8 mm measured for each sample with SFJ digital thickness tester.

Differential Scanning Calorimetry (DSC). DSC measurements were performed on a Mettler-Toledo DSC1 differential scanning calorimeter with a heating rate of 10 °C/min under nitrogen atmosphere. About 10 mg samples were encapsulated in 40 µL aluminum pans before measurements.

X-Ray Diffraction. XRD measurement was carried out on a Bruker Model D8 FOCUS X-ray diffractometer with Cu K α irradiation ($\lambda=1.5406$ Å) at a generator voltage of 40 kV and a current of 40 mA.

Small Angle X-ray Scattering (SAXS) Measurement. The SAXS experiments were performed at room temperature using a Bruker Nanostar SAXS system with a 2D detector (Bruker Histar) operated at 40 kV and 35 mA. The wavelength of the incident X-ray beam from Cu K α radiation was $\lambda=0.154$ nm. The distance between sample and the detector was 67.2 cm, which was calibrated by silver behenate. The long period d is inversely relate to the wave vector at the scattering peak, $d=2\pi/q$.

Dynamical Mechanical Analysis

Dynamical mechanical analysis (DMA) and stress relaxation experiments were performed on a TA Q800 instrument in “multi-frequency-strain” and “strain rate” mode, respectively. The heating rate in DMA tests was set as 5 °C min⁻¹.

High Performance Liquid Chromatography (HPLC)

High Performance Liquid Chromatography experiments were performed on an Agilent-1260 instrument with a DAD detector using H₂O/CH₃CN (95%, v:v) and CH₃CN as the mixed eluent.

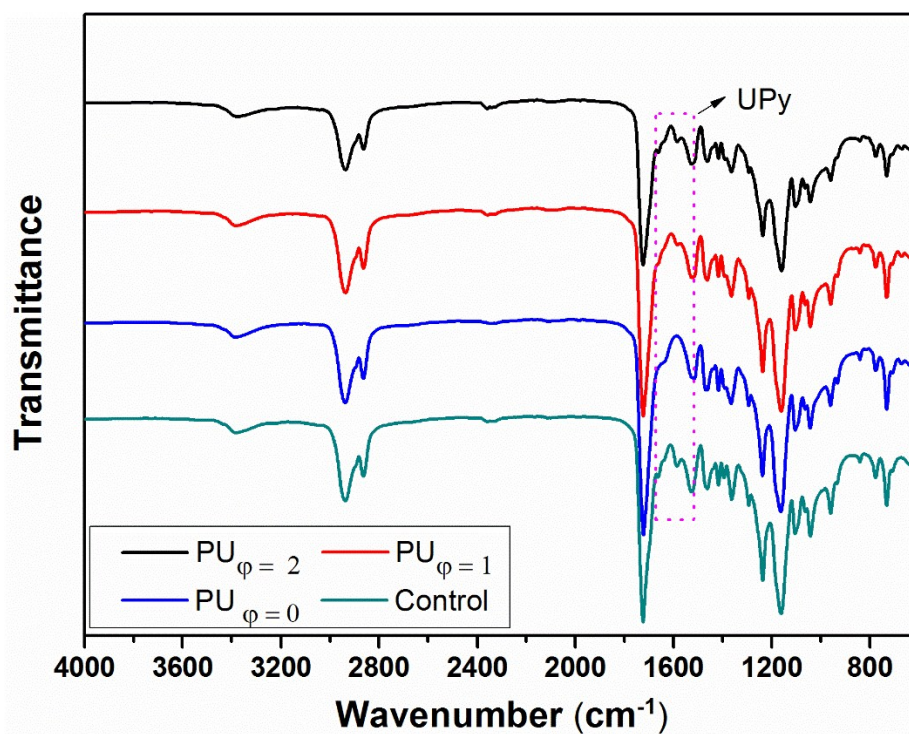


Figure S11. FTIR spectra of PUs with variable molar ratio of $n_{\text{UPy}}/n_{\text{TBMI}}$ as well as the $\text{PU}_{\text{control}}$ sample. The IR peak indicated by the dash pink rectangle represents a characteristic peak of UPy motif.

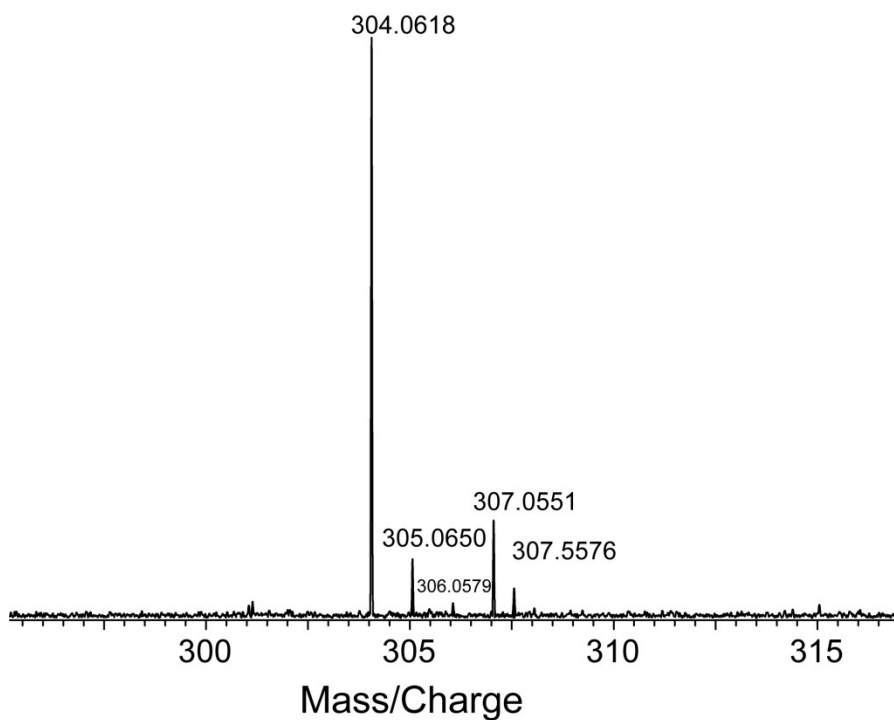


Figure S12. ESI-HRMS spectrum recorded for TMI. ESI-HRMS m/z calcd for $\text{C}_{13}\text{H}_{15}\text{NO}_4\text{SNa}^+ [\text{M}^+ \text{Na}]^+$: 304.0614, found 304.0618.

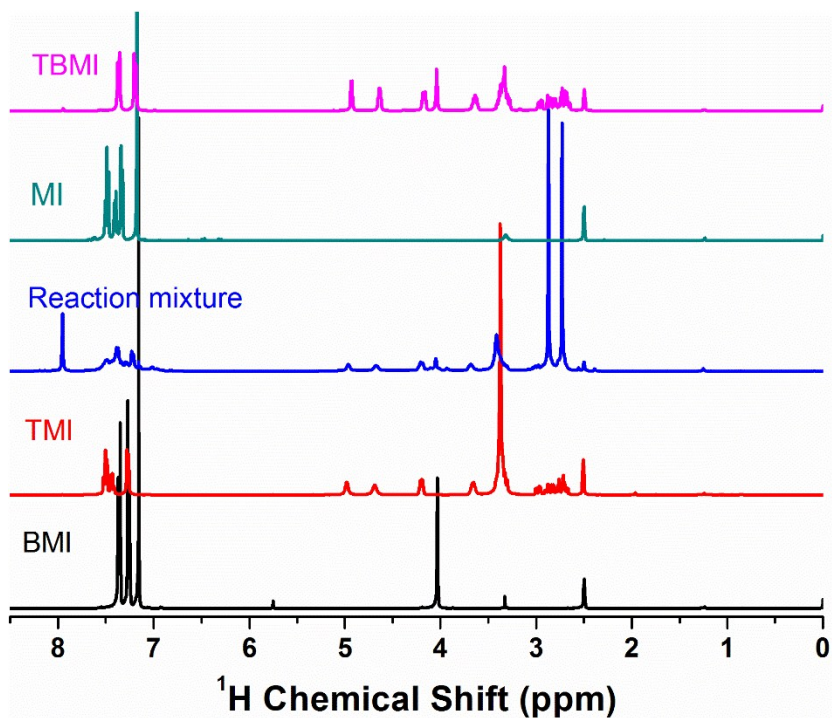


Figure S13. Solution ^1H NMR spectra of TBMI, MI, TMI, BMI and the reaction mixture in DMSO- d_6 as depicted in Figure 1.

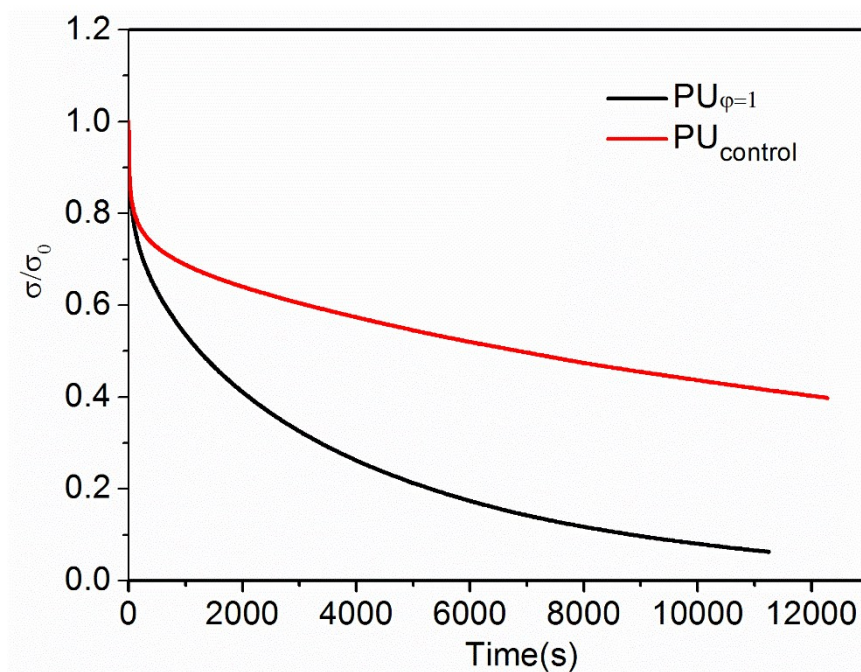


Figure S14. Stress relaxation curves of $\text{PU}_{\varphi=1}$ and $\text{PU}_{\text{control}}$ samples at a temperature of 100 °C. A 5% strain was firstly applied after the temperature equilibrium in 5 mins.

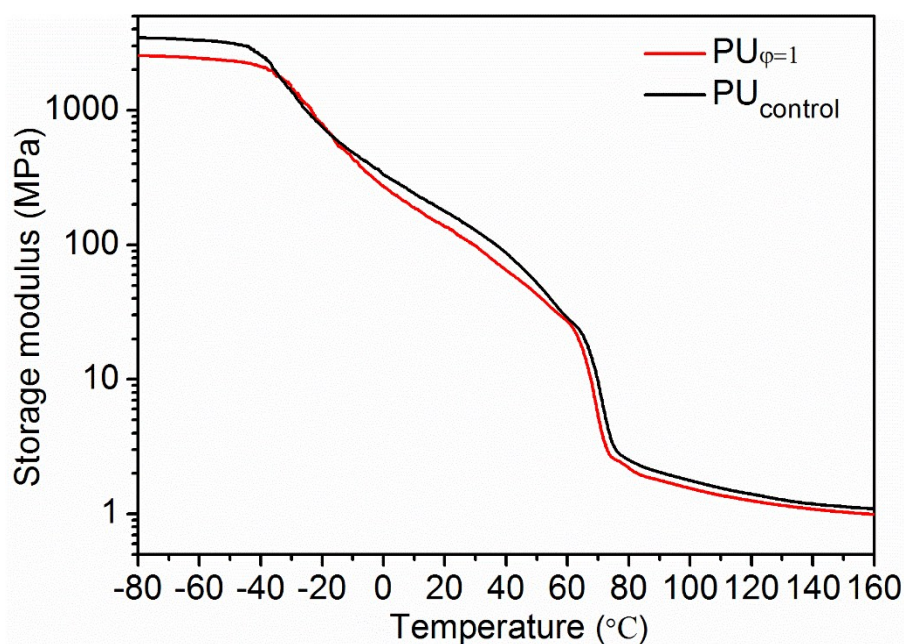


Figure S15. Storage modulus as a function of the temperature for $\text{PU}_{\varphi=1}$ and $\text{PU}_{\text{control}}$ crosslinked by permanent chemical crosslinker pentaerythro instead of TBMI. Samples were measured from -80 to 160 °C at a heating rate of 5 °C /min, a strain amplitude of 5 μm , and a frequency of 1 Hz.

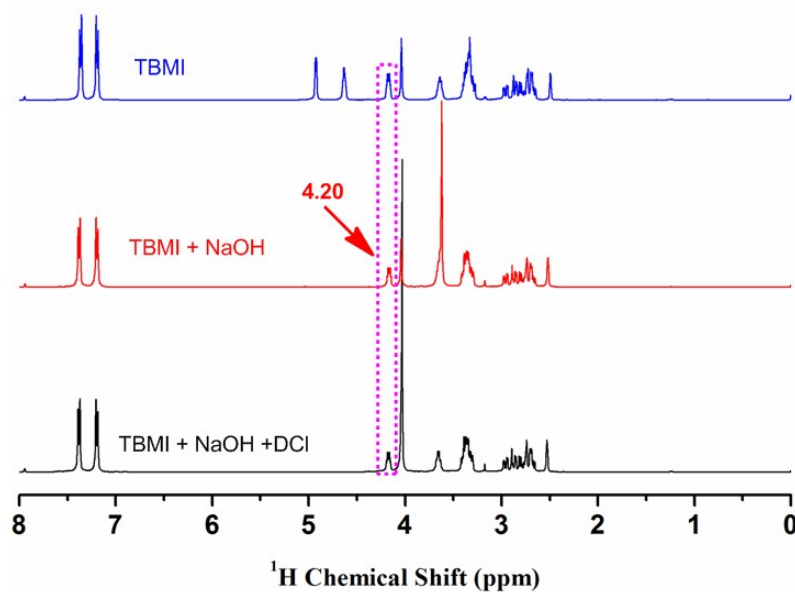


Figure S16. Solution ^1H NMR spectra corresponding to (a) TBMI solution in DMSO-d_6 (top), (b) TBMI solution in DMSO-d_6 with the addition of 0.05 ml 0.1 mol/L NaOH aqueous solution (middle), (c) TBMI solution in DMSO-d_6 by adding 30wt% DCl aqueous solution drop by drop into the above base TBMI solution until it became transparent (bottom). The peak at 4.2 ppm was ascribed to the proton of $-\text{CH}$ group bonded to sulphur atom. The peak intensity changed with the addition of base and acid solution well confirmed that TBMI may undergo a keto-enol tautomerism under acid/base conditions shown in Figure 3e.

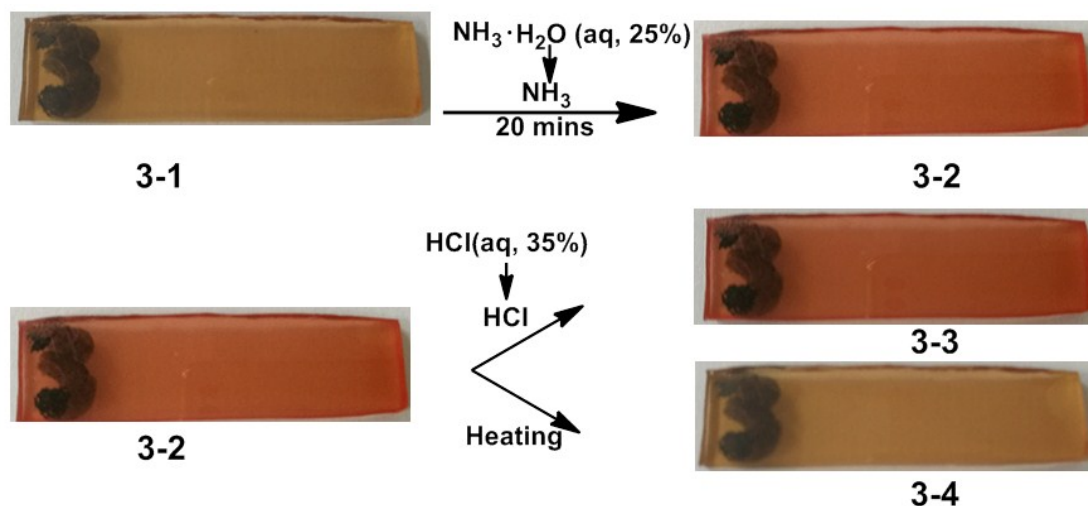


Figure S17. The responsive behavior of PU $_{\phi=1}$ to the HCl gas. A 25wt% NH_3 aqueous solution is adapted for creating ammonia gas environment through natural volatilization. As is clearly shown, brown solid PU sample will become light red at the ammonia gas environment in 20 mins (top row). However, when this sample was put into the HCl environment, it will not change back to original color. But once the sample was kept at 90 °C for 20 mins, the color was the same as the original as-synthesized one.

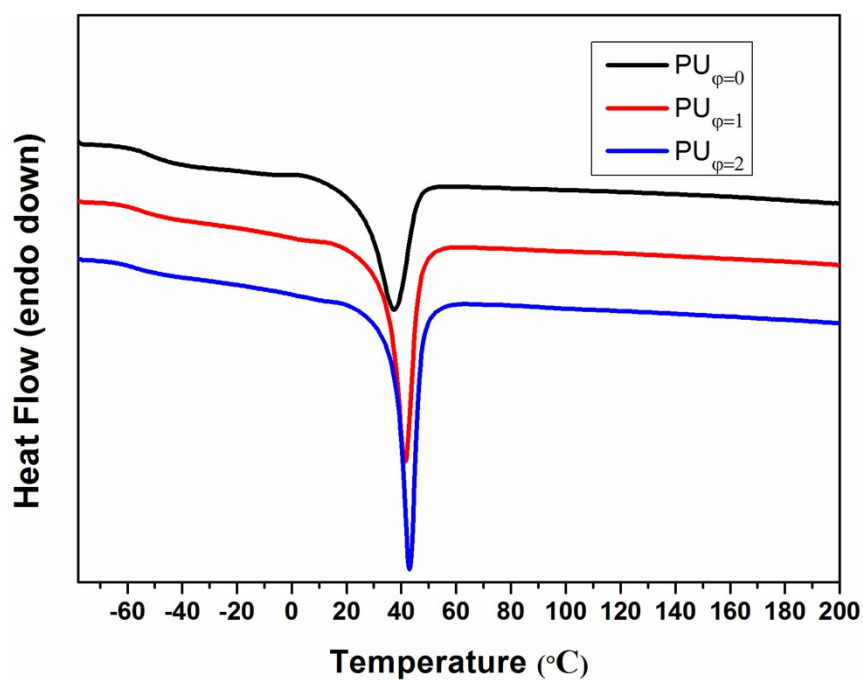


Figure S18. DSC thermograms of PUs for the second heating flow at a heating and cooling rate of 10 °C/min.

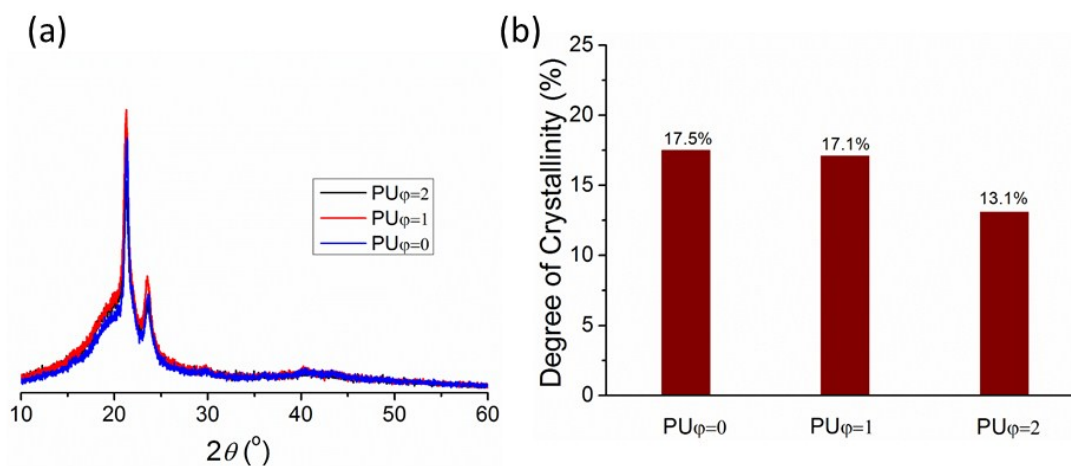


Figure S19. (a) XRD curves of PU samples, and (b) the degree of crystallinity determined by the deconvolution of peaks.

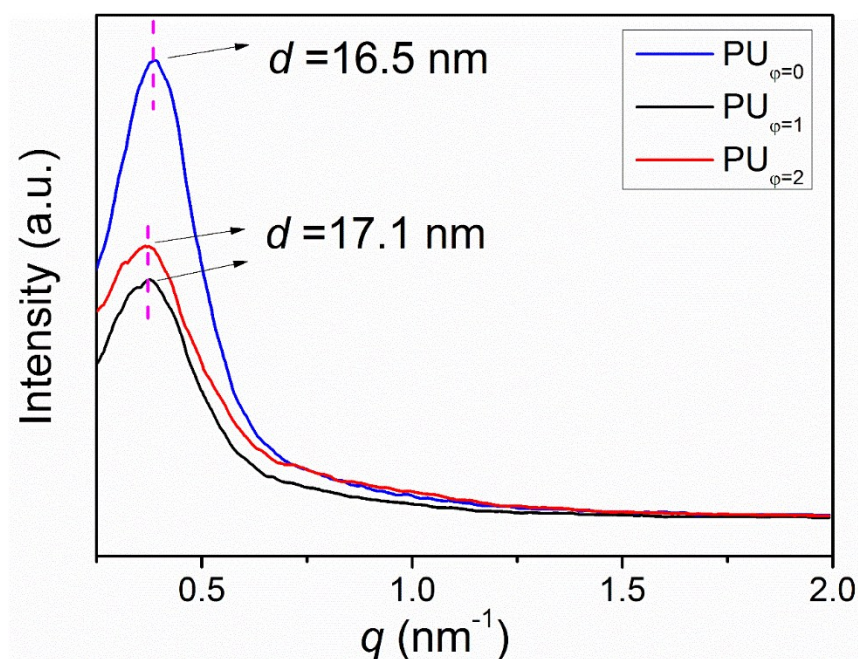


Figure S20. SAXS curves of PU samples. It is clearly observed that with the incorporation of UPy motifs in the backbone chains, the microphase-separated domain size in the PU sample only slightly increased by ca. 0.6nm, since the UPy dimers are dispersed in the hard domains.

4. References

- (1) Gangjee, A.; Yu, J.; McGuire, J. J.; Cody, V.; Galitsky, N.; Kisliuk, R. L.; Queener, S. F. Design, synthesis, and X-ray crystal structure of a potent dual inhibitor of thymidylate synthase and

dihydrofolate reductase as an antitumor agent. *J. Med. Chem.* **2000**, *43*, 3837-3851.

(2) Guo, M.; Pitet, L. M.; Wyss, H. M.; Vos, M.; Dankers, P. Y. W.; Meijer, E. W. Tough Stimuli-Responsive Supramolecular Hydrogels with Hydrogen-Bonding Network Junctions. *J. Am. Chem. Soc.* **2014**, *136*, 6969-6977.

(3) Patel, B. K.; Patel, H. S. Synthesis, Characterization, and Glass Reinforcement of Flame Retardant Acrylated Poly(Ester-Amide) and Flame Retardant Poly(Ester-Imide) Resins Based on Brominated Epoxy Resin. *Int. J. Polym. Mater. Polym. Biomater.* **2013**, *62*, 455-461.