Polymer Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/polymers

Depolymerizable, Adaptive Supramolecular Polymer Nanoparticles and Networks

Joshua A. Kaitz[1], Catherine M. Possanza[1], Yang Song[1], Charles E. Diesendruck[1], A. Jolanda H. Spiering[2], E. W. Meijer[2], and Jeffrey S. Moore[1]*

1. Department of Chemistry and Beckman Institute for Advanced Science and Technology; University of Illinois at Urbana-Champaign, Urbana, Illinois 61801, United States. 2. Institute for Complex Molecular Systems and Laboratory of Macromolecular and Organic Chemistry; Eindhoven University of Technology, 5600 MB Eindhoven, the Netherlands. *e-mail: jsmoore@illinois.edu

KEYWORDS *phthalaldehyde, poly(phthalaldehyde), 2-ureido-pyrimidinone, supramolecular polymers, anionic polymerization, polymer networks, polymer nanoparticles.*

ABSTRACT

Incorporation of supramolecular cross-linking motifs into low-ceiling temperature (T_c) polymers allows for the possibility of remendable polymeric networks and nanoparticles whose structure and chemical backbones can be dynamically modified or depolymerized as desired. Herein, we demonstrate the synthesis of phthalaldehyde-benzaldehyde copolymers bearing a pendant dimerizing 2-ureido-pyrimidinone (UPy) motif. The UPy moiety promotes single-chain polymeric nanoparticle formation through non-covalent cross-linking at intermediate concentrations and results in reversible polymer network formation at high concentrations. Furthermore, due to the low T_c polymer backbone within such macromolecules, the materials depolymerize to monomer under appropriate conditions. We envision that the synthesis of such depolymerizable, adaptive supramolecular polymeric materials may find use in materials capable of self-healing and remodeling as well as in triggered release applications or the development of nanoporous structures.

Introduction

Stimuli-responsive materials that utilize reversible and dynamic supramolecular interactions have generated strong interest in recent years.[1] These materials acquire their unique properties from non-covalent interactions and have promise in self-healing applications.[2] Moreover, they have been employed for the controlled formation of single-chain polymeric architectures.[3] The quadruple hydrogen-bond dimerizing 2-ureido-pyrimidinone (UPy) motif has been introduced towards the synthesis of robust supramolecular polymers and nanoparticles.[4] The UPy motif, which dimerizes by a self-complementary DDAA (donor-donor-acceptor-acceptor) hydrogen bonding array, exhibits a dimerization constant greater than 10^7 M^{-1} in chloroform at room temperature.[4c] Due to its ease of synthesis as well as its strong affinity for non-covalent cross-linking, the UPy motif has been incorporated into polymers either at the chain-end or as a pendant functionality to form stable yet reversible non-covalent cross-links and facilitate the formation of various architectures and nanostructures.[4]

Low ceiling temperature (T_c) polymers have likewise garnered significant interest in recent years, being attractive materials for triggered release, lithography, and degradable nanostructures.[5-7] By virtue of being above the polymer's ceiling temperature, yet kinetically stabilized from depolymerization by end-capping, these polymers represent a unique class of materials capable of rapid and complete head-to-tail depolymerization upon removal of the end-cap.[6] Poly(phthalaldehyde) (PPA) is one such low T_c polymer that has been extensively studied due to its ease of synthesis and fast, complete depolymerization upon triggering.[7] We recently demonstrated the copolymerization of phthalaldehyde with various substituted benzaldehydes towards the preparation of more complex, depolymerizable nanostructures.[8a] We have also demonstrated the ability to dynamically modify backbone polyacetal linkages within the PPA backbone under cationic polymerization conditions.[8b-c]

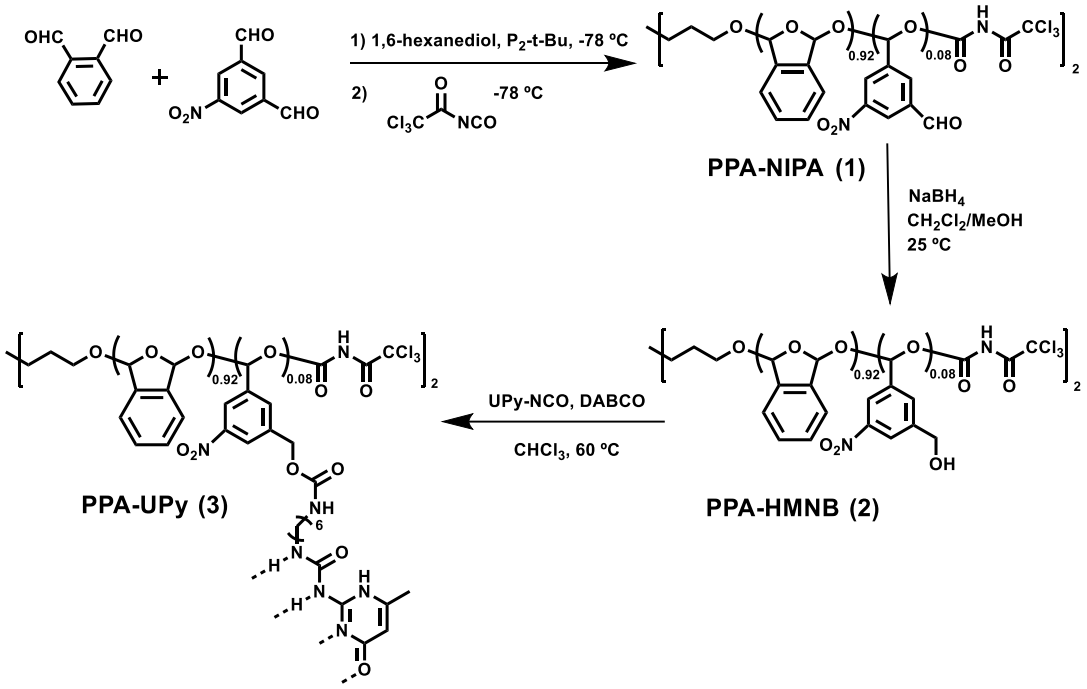
Using these synthetic methods, we sought to make materials which combine the dynamic, reversible nature of supramolecular interactions and the stimuli-responsive capabilities of low T_c polymers. To the best of our knowledge, there are no examples incorporating supramolecular cross-linking units into depolymerizable polymers towards the development of dynamic polymer nanoparticles or networks. Here we report the synthesis of phthalaldehyde-benzaldehyde copolymers modified with pendant UPy dimerizing functionalities, the characterization of the resulting morphologies, and the demonstration of their dynamic reversibility and triggered depolymerization.

Results and Discussion

Phthalaldehyde copolymer synthesis and functionalization with supramolecular cross-linker

Anionic copolymerization of *o*-phthalaldehyde with a substituted benzaldehyde monomer, 5-nitroisophthalaldehyde (NIPA), was carried out in order to prepare a PPA that could be further functionalized with a supramolecular cross-linking motif (Scheme 1). UPy-functionalized benzaldehyde could not be copolymerized directly with *o*-phthalaldehyde, as the copolymerization requires strongly electron-withdrawing substituents for incorporation of the benzaldehyde comonomer.[8a] To prepare polymers of suitably high molecular weight, the copolymerization was initiated by 1,6-hexanediol in conjunction with phosphazene base P_2-*t*-Bu, per literature precedent.[7i] The copolymerization yielded PPA-NIPA (**1**) random copolymers in three hours with a degree of polymerization of ca. 110 and 8% incorporation of the NIPA monomer, as determined by ^{1}H NMR (See Figure S1). At this molecular weight and composition, we expect an average of 8 to 9 UPy units per chain, assuming near quantitative conversion of each step of post-polymerization modification. The pendant aldehyde of the PPA-NIPA copolymer was then quantitatively reduced to a benzylic alcohol by reaction with sodium borohydride, affording PPA-HMNB polymer (**2**, HMNB = 3-hydroxymethyl-5-nitrobenzaldehyde) in high yield. A slight increase in molecular weight and a decrease in polydispersity were observed in this polymer, which was attributed to the removal of low molecular weight species after repeated precipitations (See Table 1).

Finally, PPA-HMNB was functionalized with the 2-ureido-pyrimidinone (UPy) motif by reaction with an isocyanate terminated UPy.[4e] Due to the high sensitivity of PPA polymers towards acid, 1,4-diazabicyclo[2.2.2]octane (DABCO) was employed as a catalyst rather than the tin (II) catalysts typically used in the reaction.[9] The PPA-UPy (**3**) polymers thus produced show characteristic peaks in the ^{1}H NMR spectrum corresponding to the three hydrogen-bonded protons in UPy at δ 10.2 ppm, 11.8 ppm, and 13.1 ppm (Figure 1). Molecular weights and yields of polymers used in this study are summarized in Table 1.



Scheme 1 | Synthesis of UPy-functionalized PPA polymers. *Polymer yields and molecular weights are summarized in Table 1.*

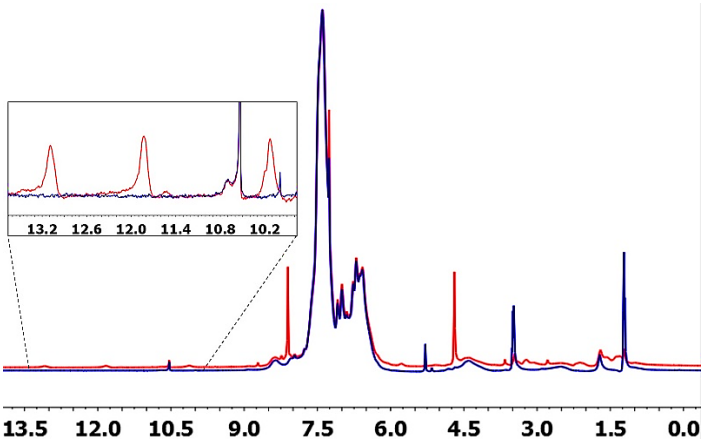


Figure 1 | NMR characterization of polymers in chloroform*: PPA-HMNB (Polymer 2, blue trace) overlayed with PPA-UPy (Polymer 3, red trace). Characteristic hydrogen-bonded protons corresponding to UPy are observed at δ 10.2, 11.8, and 13.1 ppm.*

Table 1 | Characterization data for Polymers 1-3.[a]

Polymer	*Name*	*Yield*	M_n *(kDa)*[b]	M_w *(kDa)*[b]	*PDI*[b]	R_h *(nm)*[c]
1	PPA-NIPA	68%	13.5	20.0	1.49	- - -
2	PPA-HMNB	72%	15.7	21.0	1.34	5.9
3	PPA-UPy	85%	15.3	20.1	1.31	4.9

[a]*o*-Phthalaldehyde purified before use according to literature procedure.[7i] [b]Average molecular weights and polydispersity determined by gel permeation chromatography (GPC), calibrated with monodisperse polystyrene standards. [c]Hydrodynamic radius determined by dynamic light scattering.

Characterization of supramolecular single-chain polymeric nanoparticles

In order to investigate PPA-UPy intramolecular folding into well-defined polymeric nanoparticles, triple-detector GPC, dynamic light scattering (DLS), and atomic force microscopy (AFM) characterization techniques were utilized. It has previously been demonstrated that at low concentration, UPy functionalized polymers undergo reversible intramolecular folding to form single-chain polymeric nanoparticles (SCPNs).[4] To investigate this phenomenon in PPA-UPy polymers, the polymers were injected onto a triple-detector GPC at 9 mg/mL in THF. A slight increase in retention time was observed for PPA-UPy compared to PPA-HMNB when comparing the raw chromatograms, indicative of a decreased hydrodynamic radius and a more compact structure (Figure 2a). Even more significant, when absolute molecular weights of the two polymers are plotted versus retention time, PPA-UPy gives a greater retention time than PPA-HMNB at all molecular weights (Figure 2b). Again, this suggests a collapse in hydrodynamic radius consistent with intramolecular association to produce PPA SCPNs. Interestingly, the polymer M_n absolute values increase from 20.8 kDa to 22.4 kDa after functionalization of PPA-HMNB with UPy, consistent with covalent functionalization of between five and six UPy units per polymer chain (corresponding to a 63% incorporation of UPy; See Table S4). Dynamic light scattering analysis confirmed this decrease in hydrodynamic radius, as the particles shrank from number-weighted average radii of 5.9 nm to 4.9 nm after functionalization with UPy. The observed 17% decrease in hydrodynamic radius is consistent with previous findings for intramolecular folding of SCPNs in THF.[3e,4e]

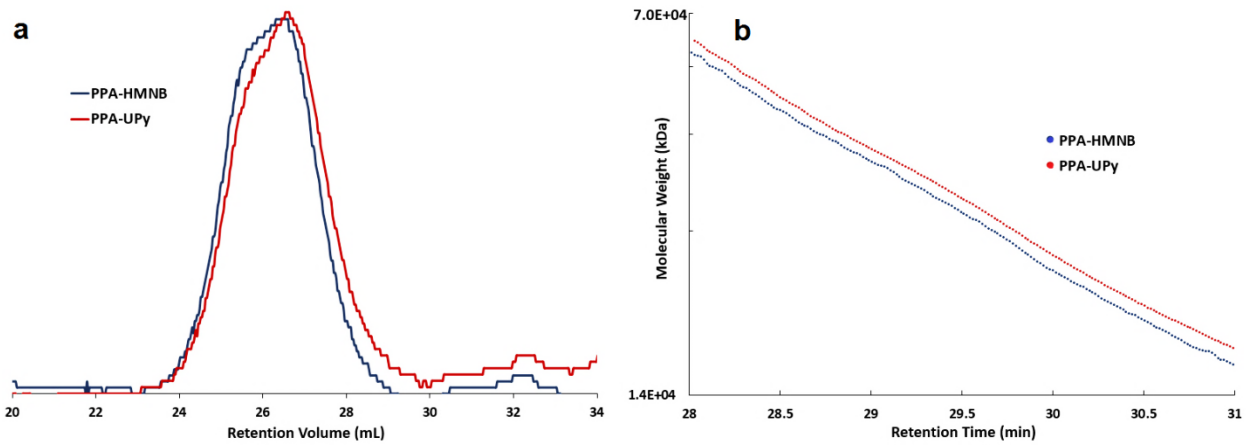


Figure 2 | Triple-detection GPC characterization of polymers*: (a) Normalized GPC chromatograms of PPA-HMNB (Polymer 2, blue trace) overlayed with PPA-UPy (Polymer 3, red trace) in THF at 1 mg/mL. (b) Triple detector plot of absolute molecular weight versus retention time for PPA-HMNB (Polymer 2, blue trace) and PPA-UPy (Polymer 3, red trace) in THF at 9 mg/mL. Both plots reveal longer retention times for PPA-UPy, suggesting a smaller hydrodynamic radius due to intramolecular UPy dimerization.*

In order to further characterize the SCPNs, we utilized AFM to visualize their size, morphology, and dispersity. Samples were prepared by casting extremely dilute solutions (0.1 µg/mL in THF) on freshly cleaved mica and allowing them to air dry under ambient conditions. The low concentration is critical to minimize nanoparticle aggregation.[4d] The micrographs demonstrate that the PPA SCPNs exhibit a spherical/round morphology and display a monodisperse distribution, as expected (Figure 3). The particle heights were found to be 4.2 nm on average, with an average diameter of 46.5 nm. Assuming a half-ellipsoid geometry of nanoparticles under AFM conditions[4d], the radius of unflattened nanoparticle spheres is calculated to be about 16.5 nm. That this radius does not correlate well with DLS results is not surprising, as SCPN radii extracted from AFM images are known to yield larger values than expected.[3f] The AFM images, however, serve to qualitatively corroborate GPC and DLS analytical techniques and confirm the presence of monodisperse, spherical SCPNs.

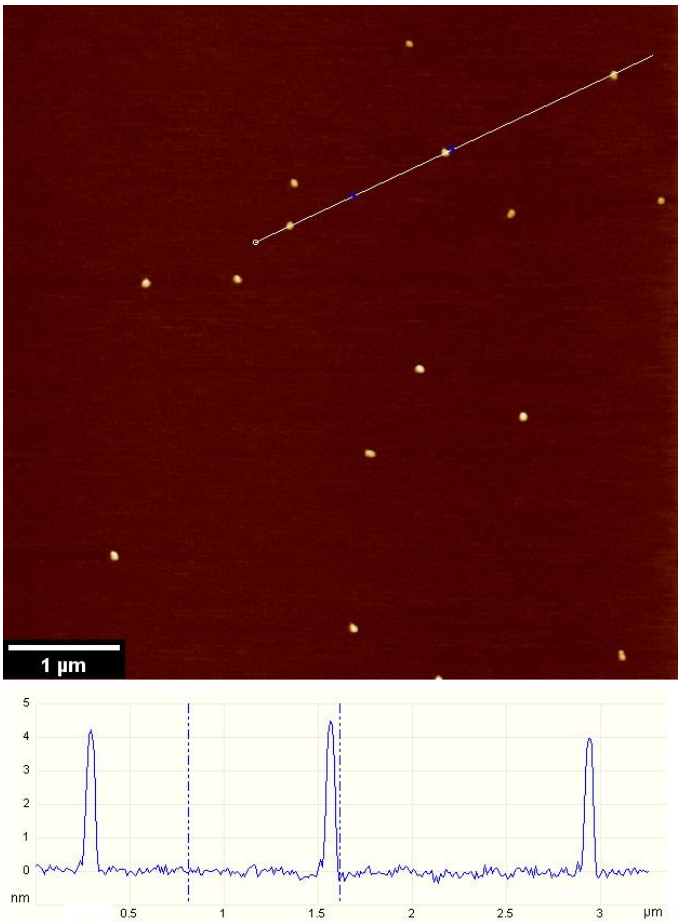
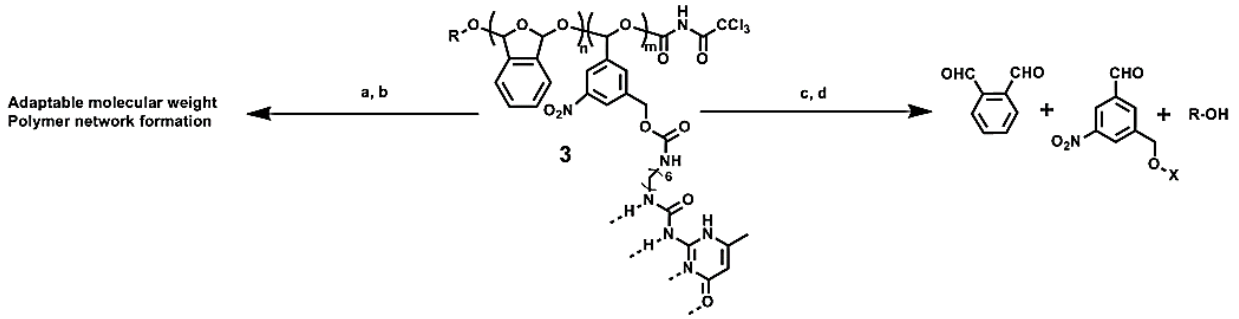


Figure 3 | AFM micrograph of single-chain polymeric nanoparticles*: PPA-UPy (Polymer 3) nanoparticles on mica, casted from a 0.1 µg/mL solution in THF. Nanoparticles are spherical and monodisperse, with heights of approximately 4 nm and average diameters of 46 nm.*

Dynamic reconstitution of low T_c polymeric nanostructures and polymer network formation

The utility of PPA as the polymer scaffold was probed by exploring the depolymerization and reconstitution of PPA SCPNs. PPA is known to depolymerize when exposed to acid or chemical reagents appropriate to the end-group structure.[7] Further, we have shown that PPA can be subjected to cationic initiators in appropriate conditions and the molecular weight and architecture of the polymer backbone is dynamically modified.[8] With this knowledge at hand, we exposed PPA-UPy to the Lewis acid boron trifluoride etherate at room temperature. As expected, immediate depolymerization to monomer was observed and confirmed by NMR (Scheme 2c-d; Figures 4, S6). Triggered depolymerization of polymeric nanoparticles provides a simple approach towards the development of nanoporous structures, where pore size is defined by nanoparticle size and number of pores is determined by the concentration of nanoparticles in solution.[10]



Scheme 2 | Supramolecular polymer reconstitution and depolymerization*: a) $BF_3{\cdot}OEt_2$, CH_2Cl_2, -78 °C; b) Pyridine, -78 °C. c) $BF_3{\cdot}OEt_2$, CH_2Cl_2, 25 °C; d) Pyridine, 25 °C. X represents pendant ureidopyrimidinone functionality.*

In order to test the reconstitution of the PPA nanoparticle backbone, PPA-UPy was exposed to boron trifluoride etherate at -78 °C (Scheme 2a-b), a temperature below the PPA T_c (ca. -40 °C).[7a] When the reaction is conducted at low concentration, i.e., below 0.7 M with respect to polymer repeat units, a shift towards lower molecular weight is observed in the GPC (Figures 4, S7). The molecular weight of the product is tuned by varying the initial concentration, as previously demonstrated.[8b] Interestingly, this process makes it possible to dynamically modify supramolecular polymers to achieve desired molecular weights, even after their initial formation. These unique polymers can therefore be reversibly tuned by two chemically orthogonal methods; both the UPy cross-linker as well as the PPA backbone itself can be dynamically controlled.

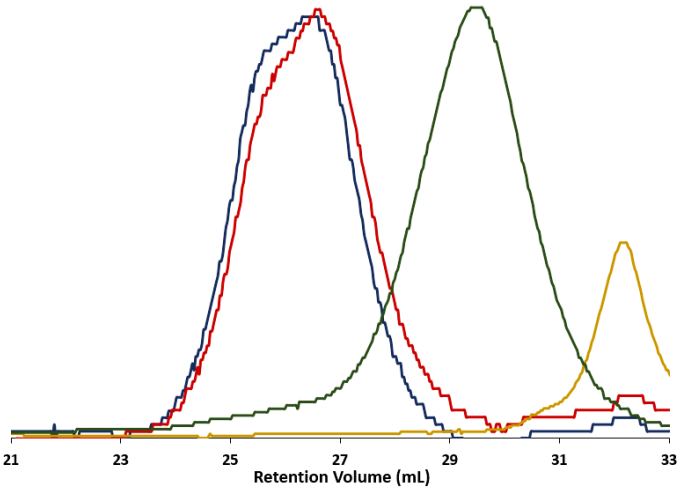


Figure 4 | GPC chromatograms of polymer reconstitution and depolymerization reactions*: GPC traces of PPA-HMNB (Polymer 2, blue trace), PPA-UPy (Polymer 3, red trace), PPA-UPy reconstituted to lower molecular weight (green trace), and after depolymerization (yellow trace). The peak at 32 mL corresponds to remainder small molecule in the void volume.*

Remarkably, an insoluble supramolecular polymer network is formed when PPA-UPy is subjected to reconstitution at high concentration, i.e., greater than 1.0 M. The white solid thus collected swelled but remained insoluble in typical solvents for PPA, specifically chloroform, dichloromethane, THF, and dimethyl sulfoxide. When reconstitution at high concentration is attempted on PPA-HMNB, however, the polymer remains soluble throughout the reaction, confirming that the supramolecular UPy cross-linker promotes polymer network formation. Figure 5 demonstrates triggered degradation of these supramolecular polymer networks. The cross-linked samples were initially swollen in deuterated chloroform, remaining insoluble opaque gels (Figure 5a). A drop of trifluoroacetic acid (TFA), which can hydrolyze the backbone acetal linkages, was then added to a single sample, and the polymer sample immediately shrunk in size, completely disappearing within 2 min (Figure 5b-c, right). The solution was collected and analyzed by NMR (Figure S8), confirming depolymerization to monomer. The control sample, on the other hand, remains unchanged (Figure 5b-c, left). This experiment demonstrates that supramolecular PPA networks are not only easily constructed, but unlike typical thermosets, this cross-linked polymer is rapidly deconstructed in response to an external stimulus.

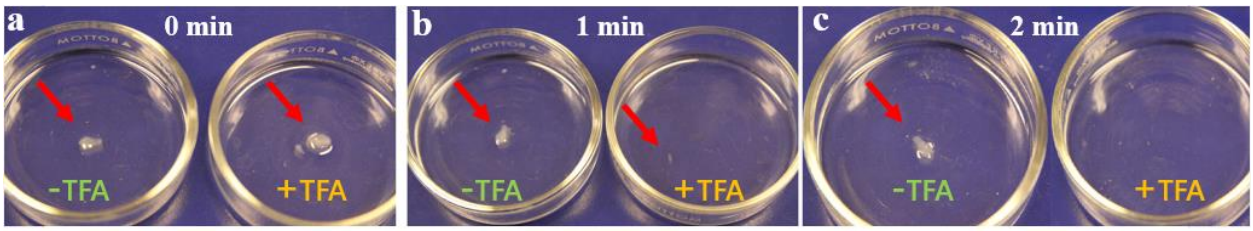


Figure 5 | Supramolecular PPA-UPy Network and Triggered Depolymerization of Polymer Backbones*: (a) Image of PPA-UPy polymer networks suspended in $CDCl_3$ before addition of trifluoroacetic acid (TFA); (b) Image of PPA-UPy polymer network after one minute exposure to TFA (right) and without exposure to TFA (left); and (c) Image of fully depolymerized PPA-UPy network after two minute exposure to acid (right) and without exposure to acid (left).*

Conclusions

The results presented here serve as an initial foray into combining reversible supramolecular cross-linking reagents with dynamic low T_c polymers. Supramolecular PPA-UPy polymers were prepared by taking advantage of a previously reported phthalaldehyde-benzaldehyde copolymerization approach. The PPA-UPy polymers exhibit two distinct levels of control, as both the UPy dimerizing motif and the PPA backbone are capable of dynamic reorganization. The supramolecular cross-linker was shown to permit the preparation of both single-chain polymeric nanoparticles as well as degradable polymer networks. The polymer nanoparticles were then reconstituted to various molecular weights, and the polymer networks were shown to depolymerize by reaction with an external signal. We envision a wide range of applications

for such polymers, from the development of nanoporous structures to potential self-healing materials that are also fully recyclable and capable of structural remodeling.

Experimental

Materials

Unless otherwise stated, all starting materials were obtained from commercial suppliers and used without further purification. Anhydrous tetrahydrofuran, dichloromethane, and methanol were obtained from an Anhydrous Solvent Delivery System (SDS) equipped with activated alumina columns. *o*-Phthalaldehyde (98%, Alfa-Aesar) was purified according to a literature procedure.[7i] 1,6-hexanediol (99% Aldrich) was dissolved in THF over CaH_2, filtered after stirring overnight, and collected by evaporation of the solvent.[7e] 5-nitroisophthalaldehyde and 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydro-pyrimidin-2-yl)urea were prepared according to literature procedures.[11, 1c] All reactions were performed in oven dried glassware under N_2 atmosphere unless otherwise indicated.

Techniques

^{1}H and ^{13}C NMR spectra were obtained with a Varian 400 or Varian 500 MHz spectrometer in the School of Chemical Sciences NMR laboratory at the University of Illinois at Urbana-Champaign. Chemical shifts are reported in δ (ppm) relative to the residual solvent peak. Coupling constants (J) are expressed in Hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), m (multiplet), and b (broad).

Analytical gel permeation chromatography (GPC) analyses were performed on either of two systems. Most GPC analyses were performed on a system composed of a Waters 515 HPLC pump, a Thermoseparations Trace series AS100 autosampler, a series of three Waters HR Styragel columns (7.8’ 300 mm, HR3, HR4, and HR5), and a Viscotek TDA Model 300 triple detector array, in HPLC grade THF (flow rate = 0.9 mL/min) at 25 °C. The GPC was calibrated using a series of monodisperse polystyrene standards. Triple detector analysis was carried out in Waters 1515 Isocratic HPLC pump, with a Waters (2707) 96-well autosampler, and a series of 4 Waters HR Styragel columns (7.8 X 300mm, HR1, HR3, HR4, and HR5) in THF at 30 °C, coupled to 4 detectors in sequence: Waters (2998) Photodiode Array Detector, a Waters (2414) Refractive Index Detector, Wyatt mini-DAWN TREOS multi-angle laser light-

scattering, and a Wyatt Viscostar II viscometer. Analysis of the data was done using Wyatt's Astra 6 software. PPA dn/dc was calculated online to be 0.1515 as an average of three 100% mass-recovery experiments and was used for all samples.

Thermal gravimetric analysis (TGA) was done using a Mettler-Toledo TGA/DSC1 LF. Scans were collected in the range of 25 °C – 400 °C with a ramping rate of 10 °C/min under a dry nitrogen atmosphere. Hydrodynamic radii where determined by dynamic light scattering (DLS) on a Malvern Zetasizer Nano ZS. The laser power was 20mW at 633 nm. The polymer solutions were prepared by dissolving the polymer in THF at 1 mg/mL and filtering over a 0.45 μm filter before being analyzed by DLS. Infrared spectra (percent transmittance) were acquired on a SmartITR ATR accessory for a Nicolet Nexus 670 FT-IR spectrometer.

Atomic force microscopy (AFM) was performed under ambient conditions on a Bruker Multimode NanoScope VIII. A silicon tip cantilever (SCANASYST-AIR, 50-90 kHz, 0.4 N/m from Bruker) was used in ScanAsyst mode with a scan size of 1-4 μm, a 1 Hz scan rate and 512 scan lines. Atomic force microscopy samples were prepared by dropcasting 2 μl of solution (0.1-10 μg/mL in THF, filtered over a 0.45 μm filter) on freshly cleaved mica in ambient conditions and allowing the sample to air dry.

Synthetic Procedures

Synthesis of PPA-NIPA (Polymer 1).

In a glovebox, purified *o*-PA (2.62 g, 19.5 mmol) and 5-nitroisophthalaldehyde (1.01 g, 5.6 mmol) were weighed into a Schlenk flask and dissolved in THF (35 mL). The solution was removed from the glovebox and degassed by three freeze-pump-thaw cycles. Then, 1,6-hexanediol in THF (0.80 mL of a 0.03 M solution, 24 μmol) was added, and the solution stirred 2 minutes then cooled to -78 °C. Finally, P_2-t-Bu phosphazene base in THF (0.05 mL of a 2.0 M solution, 100 μmol) was added to initiate polymerization. The reaction was left stirring at -78 °C for 3 h, then the polymer end-capped by adding trichloroacetyl isocyanate (0.65 mL, 5.5 mmol) and allowing the mixture to stir an additional 2 h at -78 °C. The reaction mixture was then brought to room temperature and polymer precipitated by pouring into methanol (100 mL) and collected by filtration. Polymer **1** was further purified by dissolving in dichloromethane and re-precipitating from methanol and washed in diethyl ether (2.46 g, 68%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.25-9.75 (b, 1H, aldehyde), 8.80-8.15 (b, 3H, benzaldehyde), 7.75-7.05 (b, 4H, phthalaldehyde), 7.05-6.25 (b, acetal). GPC (RI): M_n = 13.5 kDa, PDI = 1.49.

Synthesis of PPA-HMNB (Polymer 2).

To a Schlenk flask were added 2.41 g PPA-NIPA (Polymer 1, 1.4 mmol –CHO) and sodium borohydride (0.10 g, 2.6 mmol). The solids were dissolved in dichloromethane (40 mL) and methanol (8 mL), and the reaction mixture left stirring 1 h at room temperature. Polymer **2** was then precipitated into excess methanol (200 mL) and washed in methanol and diethyl ether (1.74 g, 72%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45-7.75 (b, 3H, benzaldehyde), 7.75-7.05 (b, 4H, phthalaldehyde), 7.05-6.25 (b, acetal), 5.70-5.40 (b, CH_2-O*H*), 4.75-4.25 (b, -C*H*$_2$-OH). GPC (RI): M_n = 15.7 kDa, PDI = 1.34.

Synthesis of PPA-UPy (Polymer 3).

In a glovebox, PPA-HMNB (Polymer 2, 0.20 g, 88 μmol –OH) and 1-(6-isocyanatohexyl)-3-(6-methyl-4-oxo-1,4-dihydro-pyrimidin-2-yl)urea (UPy-NCO, 28 mg, 95 μmol) were weighed into a Schlenk flask and dissolved in chloroform (60 mL, neutralized by stirring over K_2CO_3). To this solution was added 1,4-diazabicyclo[2.2.2]octane (DABCO, 0.65 mL of a 8.8 mM solution, 6 μmol) and the flask was closed and warmed to 60 °C overnight (18 hours). After overnight reaction, 1,6-hexanediamine (50 mg) was added to quench the PPA-UPy and the mixture filtered and concentrated in vacuo. The residue was dissolved in dichloromethane (20 mL) and filtered, then precipitated into methanol (150 mL) and washed in methanol and diethyl ether (0.17 g, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.3-12.9 (b, NH), 12.0-11.7 (b, NH), 10.3-9.9 (b, NH), 8.50-7.75 (b, 3H, benzaldehyde), 7.75-7.05 (b, 4H, phthalaldehyde), 7.05-6.25 (b, acetal), 4.75-4.00 (b, -C*H*$_2$-O), 4.00-0.50 (b, aliphatic –C*H*$_2$-). GPC (RI): M_n = 15.3 kDa, PDI = 1.31.

Depolymerization of PPA-UPy.

In a Schlenk flask, PPA-UPy (Polymer 3, 40 mg) was dissolved in dichloromethane (0.4 mL). To the solution was added boron trifluoride etherate (1 drop, ~0.04 mmol) and the reaction stirred for 5 min at room temperature, turning deep yellow immediately. To the mixture was then added pyridine (0.10 mL, 1.2 mmol) and left stirring 2 h. The reaction mixture was concentrated in vacuo and collected as a yellow oil, identified as majority *o*-PA by ^{1}H NMR. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.54 (s, 2H, CHO), 7.98 (q, 2H, Ar-H), 7.78 (q, 2H, Ar-H). GPC (RI): No polymer.

Reconstitution of PPA-UPy.

In a Schlenk flask, PPA-UPy (Polymer 3, 40 mg) was dissolved in dichloromethane (0.4 mL). The solution was cooled to -78 °C, and boron trifluoride etherate (1 drop, ~0.04 mmol) was added. The reaction was

stirred for 2 h at -78 °C, then quenched by adding pyridine (0.10 mL, 1.2 mmol) and left stirring 2 h. The solution was then warmed to room temperature and polymer collected by precipitation into methanol (50 mL) and washing in methanol and diethyl ether (30 mg, 75%). GPC (RI): M_n = 2.5 kDa, PDI = 2.00.

Formation of PPA-UPy Supramolecular Networks.

In a Schlenk flask, PPA-UPy (Polymer 3, 70 mg) was dissolved in dichloromethane (0.4 mL). The solution was cooled to -78 °C, and boron trifluoride etherate (0.01 mL, 0.08 mmol) was added. The reaction gels almost immediately, but was left for 2 h at -78 °C before quenching with pyridine (0.10 mL, 1.2 mmol) and left stirring 2 h. The solution was brought to room temperature and the resulting solid polymer was washed in excess methanol and diethyl ether (71 mg, quantitative recovery). The white solid was insoluble in chloroform, dichloromethane, THF, and dimethyl sulfoxide (all good solvents for PPA-UPy).

As a control reaction, the above procedure was repeated with PPA-HMNB (Polymer 2, 70 mg in 0.4 mL dichloromethane). The reaction mixture remains soluble and colorless, and the polymer was collected as a white powder (34 mg, 49% yield). The polymer is soluble in all typical solvents for PPA. GPC (RI): M_n = 2.0 kDa, PDI = 1.80.

Depolymerization of PPA-UPy Supramolecular Networks (Figure 5).

Cross-linked PPA-UPy (10-20 mg) was suspended in $CDCl_3$ (~3 mL) in a small glass dish, turning to an opaque gel. To the suspension was added three drops trifluoroacetic acid. The solid sample shrank in size immediately and disappeared completely within 2 min. The solution was collected for analysis and identified as majority *o*-PA monomer by ^{1}H NMR. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.54 (s, 2H, CHO), 7.98 (q, 2H, Ar-H), 7.78 (q, 2H, Ar-H).

ASSOCIATED CONTENT

Supporting Information. Experimental details, synthetic procedures, NMR spectra, GPC data, AFM images, and TGA data. This material is available via the Internet as an electronic supplementary information file.

AUTHOR INFORMATION

Corresponding Author

*Email jsmoore@illinois.edu (J.S.M.).

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work was supported as part of the Center for Electrical Energy Storage, an Energy Frontier Research Center funded by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences under Award Number DOE ANL 9F-31921J. J.A.K. thanks the Springborn Endowment for a graduate fellowship. E.W.M. thanks the Gravity Program 024.001.035.

REFERENCES

(1) (a) Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. *Chem. Rev.* **2001**, 101, 4071-4098. (b) Aida, T.; Meijer, E. W.; Stupp, S. I. *Science* **2012**, 335, 813-817. (c) Folmer, B. J. B.; Sijbesma, R. P.; van der Rijt, J. A. J.; Meijer, E. W. *Adv. Mater.* **2000**, 12, 874-878. (d) Sijbesma, R. P.; Meijer, E. W. *Chem. Commun.* **2003**, 5-16. (e) De Greef, T. F. A.; Smulders, M. M. J.; Wolffs, M.; Schenning, A. P. H. J.; Sijbesma, R. P.; Meijer, E. W. *Chem. Rev.* **2009**, 109, 5687-5754.

(2) (a) Hart, L. R.; Harries, J. L.; Greenland, B. W.; Colquhoun, H. M.; Hayes, W. *Polym. Chem.* **2013**, 4, 4860-4870. (b) Burnworth, M.; Tang, L.; Kumpfer, J. R.; Duncan, A. J.; Beyer, F. L.; Fiore, G. L.; Rowan, S. J.; Weder, C. *Nature* **2011**, 472, 334-337. (c) Cordier, P.; Tournilhac, F.; Soulie-Ziakovic, C.; Leibler, L. *Nature* **2008**, 451, 977-980. (d) Chen, Y.; Kushner, A. M.; Williams, G. A.; Guan, Z. *Nat. Chem.* **2012**, 4, 467-472. (e) Hentschel, J.; Kushner, A. M.; Ziller, J.; Guan, Z. *Angew. Chem. Int. Ed.* **2012**, 51, 10561-10565. (f) Burattini, S.; Greenland, B. W.; Merino, D. H.; Weng, W.; Seppala, J.; Colquhoun, H. M.; Hayes, W.; Mackay, M. E.; Hamley, I. W.; Rowan, S. J. *J. Am. Chem. Soc.* **2010**, 132, 12051-12058.

(3) (a) Ouchi, M.; Badi, N.; Lutz, J.-F.; Sawamoto, M. *Nat. Chem.* **2011**, 3, 917-924. (b) Altintas, O.; Barner-Kowollik, C. *Macromol. Rapid. Commun.* **2012**, 33, 958-971. (c) Seo, M.; Beck, B. J.; Paulusse, J. M. J.; Hawker, C.; Kim, S. Y. *Macromolecules*, **2008**, 41, 6413-6418. (d) Altintas, O.;

Lejeune, E.; Gerstel, P.; Barner-Kowollik, C. *Polym. Chem.* **2012**, 3, 640-651. (e) Mavila, S.; Diesendruck, C. E.; Linde, S.; Amir, L.; Shikler, R.; Lemcoff, N. G. *Angew. Chem. Int. Ed.* **2013**, 52, 5767-5770. (f) Altintas, O.; Willenbacher, J.; Wuest, K. N. R.; Oehlenschlager, K. K.; Krolla-Sidenstein, P.; Gliemann, H.; Barner-Kowollik, C. *Macromolecules* **2013**, 46, 8092-8101.

(4) (a) Sijbesma, R. P.; Beijer, F. H.; Brunsveld, L.; Folmer, B. J. B.; Hirschberg, J. H. K. K.; Lange, R. F. M.; Lowe, J. K. L.; Meijer, E. W. *Science* **1997**, 278, 1601-1604. (b) Beijer, F. H.; Sijbesma, R. P.; Kooijman, H.; Spek, A. L.; Meijer, E. W. *J. Am. Chem. Soc.* **1998**, 120, 6761-6769. (c) Sontjens, S. H. M.; Sijbesma, R. P.; van Genderen, M. H. P.; Meijer, E. W. *J. Am. Chem. Soc.* **2000**, 122, 7487-7493. (d) Foster, E. J.; Berda, E. B.; Meijer, E. W. *J. Am. Chem. Soc.* **2009**, 131, 6964-6966. (e) Stals, P. J. M.; Gillissen, M. A. J.; Nicolay, R.; Palmans, A. R. A.; Meijer, E. W. *Polym. Chem.* **2013**, 4, 2584-2597. (f) Berda, E. B.; Foster, E. J.; Meijer, E. W. *Macromolecules* **2010**, 43, 1430-1437. (g) Hosono, N.; Gillissen, M. A. J.; Li, Y.; Sheiko, S. S.; Palmans, A. R. A.; Meijer, E. W. *J. Am. Chem. Soc.* **2013**, 135, 501-510.

(5) (a) Peterson, G. I.; Larsen, M. B.; Boydston, A. J. *Macromolecules* **2012**, 45, 7317-7328. (b) Esser-Kahn, A. P.; Odom, S. A.; Sottos, N. R.; White, S. R.; Moore, J. S. *Macromolecules* **2011**, 44, 5539-5553. (c) Wong, A. D.; DeWit, M. A.; Gillies, E. R. *Adv. Drug Delivery Rev.* **2012**, 64, 1031-1045.

(6) (a) Sagi, A.; Weinstain, R.; Karton, N.; Shabat, D. *J. Am. Chem. Soc.* **2008**, 130, 5434-5435. (b) Weintain, R.; Sagi, A.; Karton, N.; Shabat, D. *Chem. Eur. J.* **2008**, 14, 6857-6861. (c) DeWit, M. A.; Gillies, E. R. *J. Am. Chem. Soc.* **2009**, 131, 18327-18334. (d) Chen, E. K. Y.; McBride, R. A.; Gillies, E. R. *Macromolecules* **2012**, 45, 7364-7374. (e) Dewit, M. A.; Beaton, A.; Gillies, E. R. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, 48, 3977-3985. (f) McBride, R. A.; Gillies, E. R. *Macromolecules* **2013**, 46, 5157-5166. (g) Robbins, J. S.; Schmid, K. M.; Phillips, S. T. *J. Org. Chem.* **2013**, 78, 3159-3169. (h) Olah, M. G.; Robbins, J. S.; Baker, M. S.; Phillips, S. T. *Macromolecules* **2013**, 46, 5924-5928. (i) Wang, W.; Alexander, C. *Angew. Chem. Int. Ed.* **2008**, 47, 7804-7806. (j) Esser-Kahn, A. P.; Sottos, N. R.; White, S. R.; Moore, J. S. *J. Am. Chem. Soc.* **2010**, 132, 10266-10268.

(7) (a) Chuji, A.; Tagami, S.; Kunitake, T. *J. Polym. Sci. Part A* **1969**, 7, 497-511. (b) Chuji, A.; Tagami, S. *Macromolecules* **1969**, 2, 414-419. (c) Willson, C. G.; Ito, H.; Frechet, J. M. J.; Tessier, T. G.; Houlihan, F. M. *J. Electrochem. Soc.* **1986**, 133, 181-187. (d) Ito, H.; Willson, C. G. *Polym. Eng. Sci.* **1983**, 23, 1012-1018. (e) Coulembier, O.; Knoll, A.; Pires, D.; Gotsmann, B.; Duerig, U.; Frommer, J.; Miller, R. D.; Dubois, P.; Hedrick, J. L. *Macromolecules* **2010**, 43, 572-574. (f) Knoll, A. W.; Pires, D.; Coulembier, O.; Dubois, P.; Hedrick, J. L.; Frommer, J.; Duerig, U. *Advanced Materials* **2010**, 22, 3361-3365. (g) Seo, W.; Phillips, S. T. *J. Am. Chem. Soc.* **2010**, 132,

9234-9235 (h) Zhang, H.; Yeung, K.; Robbins, J. S.; Pavlick, R. A.; Wu, M.; Liu, R.; Sen, A.; Phillips, S. T. *Angew. Chem. Int. Ed.* **2012**, 51, 2400-2404. (i) Dilauro, A. M.; Robbins, J. S.; Phillips, S. T. *Macromolecules* **2013**, 46, 2963-2968. (j) Dilauro, A. M.; Abbaspourrad, A.; Weitz, D. A.; Phillips, S. T. *Macromolecules* **2013,** 46, 3309-3313.

(8) (a) Kaitz, J. A.; Moore, J. S.; *Macromolecules* **2013**, 46, 608-612. (b) Kaitz, J. A.; Diesendruck, C. E.; Moore, J. S. *J. Am. Chem. Soc.* **2013**, 135, 12755-12761. (c) Kaitz, J. A.; Diesendruck, C. E.; Moore, J. S. *Macromolecules* **2013**, 46, 8121-8128.

(9) Smith, H. A. *J. Appl. Polym. Sci.* **1963**, 7, 85-95.

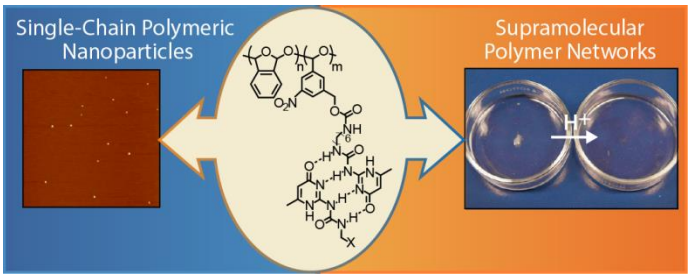
(10) (a) Hou, X.; Guo, W.; Jiang, L. *Chem. Soc. Rev.* **2011**, 40, 2385-2401. (b) Fan, J.-B.; Huang, C.; Jiang, L.; Wang, S. *J. Mater. Chem. B* **2013**, 1, 2222-2235. (c) Dekker, C. *Nat. Nanotech.* **2007**, 2, 209-215.

(11) Company, A.; Gomez, L.; Mas-Balleste, R.; Korendovych, I. V.; Ribas, X.; Poater, A.; Parella, T.; Fontrodona, X.; Benet-Buchholz, J.; Sola, M.; Que, L.; Rybak-Akimova, E. V.; Costas, M. *Inorg. Chem.* **2007**, 46, 4997-5012.

Table of Contents use only:

Depolymerizable, adaptive supramolecular polymer nanoparticles and networks

Joshua A. Kaitz, Catherine M. Possanza, Yang Song, Charles E. Diesendruck, A. Jolanda H. Spiering, E. W. Meijer, and Jeffrey S. Moore



Depolymerizable polymers are appended with supramolecular cross-linking motifs to enable preparation of tunable single-chain polymeric nanoparticles and degradable polymer networks.