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Molecularly Shielded, On-Demand, Ultrasound-Cured Polymer Networks

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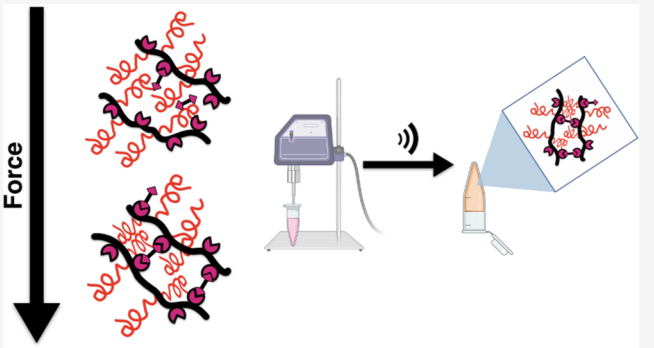
ABSTRACT: Networks formed from polymers can range from soft hydrogels to ultrahard protective coatings, making them useful for a wide range of applications, from cell culture to highly bonded adhesives. Polymer networks are commonly cross-linked via heat or high-energy light, and recently mechanical force has also been used to induce the formation of cross-links in preexisting networks. Here, we demonstrate a new strategy to use mechanical deformation and ultrasound to induce liquid-to-solid cross-linking. We synthesized graft copolymers with large poly(ethylene glycol) (PEG) side chains acting as molecular shielding groups to protect otherwise highly reactive epoxide groups. Solutions of highly shielded polymers could remain as a liquid solution when left undisturbed, and we could initiate gelation of these solutions with ultrasound in 20 s. These ultrasound-sensitive polymers are particularly useful in light- and heat-sensitive applications and where precise control over the gelation time is required.



INTRODUCTION

Polymer networks can be cross-linked via permanent covalent bonds. Polymer networks can include supersoft hydrogels that mimic human tissue,[1] protective ultrahard coatings,[2] and highly bonded adhesives.[3] Highly cross-linked lightweight networks, such as those formed with epoxide, are crucial in industrial applications like transportation, where reducing vehicle weight improves passenger safety and reduces harmful greenhouse gas emissions. The process of cross-linking or "curing" polymers is typically accomplished via (a) mixing, (b) heat, (c) high-energy light, or (d) electron beams.[4] Heat and light are popular routes, as they facilitate curing on-demand, allowing liquid application to a substrate. However, light and heat are not always feasible as light cannot pass through opaque materials, and heat can damage delicate or flammable substrates. Electron beams are also popular industrially due to their high energy efficiency and excellent uniformity; however, transmittance through metals can be challenging.

Alternatively, natural polymers (e.g., peptides, saccharides, nucleic acids) can form networks in response to temperature, light, and solvents by partially unfolding, thus exposing previously buried, or "cryptic", binding sites. Of particular interest to us, these cryptic binding sites can also be revealed in response to a mechanical stimulus.[5,6] For example, fibronectin will dynamically unfold and polymerize into fibrils in response to cell-generated forces.[7−9] In contrast, synthetic polymers commonly weaken or even rupture under force.[10]

Inspired by the unfolding triggered cross-linking of proteins like fibronectin, we sought to develop a new method of installing mechanosensitivity within synthetic polymer networks. Recently, we developed organogels[11] and hydrogels[12] with mechano-responsive properties, both based on preformed diacrylate cross-links with reactive pendent thiols for postpolymerization cross-linking. Both systems begin as a cross-linked network and respond to compression, strengthening several hundreds of kPa in elastic modulus over repeated cycles. The mechanosensitivity results from long poly(ethylene glycol) (PEG) molecular shielding groups grafted to the polymer backbone, which prevent the reactive thiol groups from cross-linking until compression brings them together.

To date, the most successful method of creating synthetic mechanosensitive polymers that undergo liquid-to-solid transition is by inserting weak bonds, "mechanophores," within polymer chains that are converted to an active intermediate in response to force, capable of strengthening the material.[13−15] Still other approaches to designing force-sensitive materials involve the design of small molecules with several ways of

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participating in intermolecular interactions such as hydrogen bonding, $\pi-\pi$ stacking, and van der Waals forces. Peptide-based isomers functionalized with cholesterol and naphthalic groups have been shown to create micellar assemblies that undergo a gel-gel transition with the application of ultrasound.[16] This work, in contrast, uses the shielding group concept, starting with un-cross-linked, shielded polymers that can undergo a rapid liquid-to-solid transition upon application of force. To accomplish this, graft polymers bearing reactive epoxide[17] groups are mixed with small-molecule amine/thiol cross-linkers. Ultrasonic irradiation is used to apply high strain rates to the shielded polymers. Straining of the graft polymers overcomes their steric barrier to interaction with the small-molecule cross-linkers, facilitating a reaction that rapidly strengthens the material. The resultant materials achieve elastic modulus values comparable to ultrahard commercial epoxy coatings. We anticipate that these shielded polymers will be useful as extremely hard and solvent-resistant coatings and as adhesives that can be cured by focusing ultrasound through the surfaces to which the adhesive is bound.

MATERIALS AND METHODS

Chemicals and Polymer Sourcing. Materials were purchased from Sigma-Aldrich unless otherwise mentioned. Poly(ethylene glycol) methyl ether methacrylate (500 and 950 g/mol, PEGMA500 and PEGMA950, respectively), glycidyl methacrylate (97%, GMA), and 2-methoxyethyl methacrylate (99%, MEMA) were passed through a column of neutral alumina to remove inhibitors before use. 2,2′-(Ethylenedioxy)diethanethiol (95%, EDT), ethylene diamine (99%, EDA), 2-phenyl-2-propyl benzodithioate (99%, PPB), 4-cyano-4-(phenylcarbonothioylthio)pentanoic acid (98%, CPA), 2-(azo(1-cyano-1-methylethyl))-2-methylpropane nitrile (98%, AIBN), 1-butanol (99.9%, BuOH), 1,4-dioxane (99%, dioxane), and *N*,*N*-dimethylformamide (99.8%, DMF) were used as received. Diethyl ether (99%, ether), lithium hydroxide monohydrate (98.5%, LiOH), and acetonitrile (99%, MeCN) were purchased from Fisher Chemical and used as received. Basic alumina 60−325 mesh was purchased from Fisher Scientific and used as received.

Representative Polymer Synthesis. Poly(GMA-*co*-PEGMA) and poly(GMA-*co*-MEMA) of all molar ratios and degrees of polymerization (DP) were synthesized by reversible addition−fragmentation chain transfer (RAFT) polymerization. The targeted monomer ratios and DP are described in Table 1. Each reaction was fed 0.01 mol of monomer total. For example, 0.71 g (0.005 mol) of GMA, 0.72 g (0.005 mol) of MEMA, 0.0559 g of CPA (0.2 mmol), 6.6 mg of AIBN (0.04 mmol) ([50]:[1]:[0.2] [M]/[CTA]/[I], where [M]/[CTA] defines the DP), 4 mL of 1,4-dioxane, and a stir bar were added to a 20 mL scintillation vial. The vial was sealed with a rubber septum, and the solution was purged with N_2 (g) for ca. 20−30 min in an ice bath to prevent solvent and monomer evaporation (PEGMA solutions were bubbled in cool water to prevent PEG crystallization). Subsequently, the vial was placed in a thermostated aluminum reaction block at 60 °C on top of a magnetic stir/hot plate. The reaction mixture was stirred overnight, yielding a viscous liquid. The solution was removed from the heat and exposed to air to terminate the polymerization. The solution was precipitated into cold (−20 °C) ether, and the solid was washed twice more with cold ether and dried at 0.01 mbar overnight.

Polymer Characterization. Polymer DP and the comonomer incorporation ratio were determined through ^{1}H NMR on a Bruker Avance 500 at 500 MHz in $CDCl_3$ (Figures S1−S10).[18] The ratio of monomers was determined by integration of ^{1}H spectral resonances of the PEGMA/MEMA methoxy protons and the methanetriyl proton of the GMA glycidyl ring, normalized to the aromatic proton peak at the para position of the CPA phenyl ring, assuming there is one Z group[19] on every polymer chain.

Table 1. Polymers Used in Each Experiment, Their Target DP, Comonomer Feed Ratio, Actual DP, and Actual Comonomer Ratio as Determined by ^{1}H NMR

name	target DP	feed ratio	actual DP	actual ratio
50:50 GMA/MEMA	50	1:1	73	55:45
50:50 GMA/PEGMA500	50	1:1	122	51:49
50:50 GMA/PEGMA950	50	1:1	91	56:44
60:40 GMA/PEGMA950	50	60:40	102	62:38
70:30 GMA/PEGMA950	50	70:30	87	72:28
30:70 GMA/PEGMA500	50	30:70	76	30:70
60:40 GMA/PEGMA950	50	60:40	119	60:40
70:30 GMA/PEGMA500	50	70:30	95	68:32
60:40 GMA/MEMA	50	60:40	134	60:40
70:30 GMA/MEMA	50	70:30	140	70:30
50:50 GMA/PEGMA950 25DP	25	1:1	34	1:1
50:50 GMA/PEGMA950 50DP	50	1:1	61	54:46
50:50 GMA/PEGMA950 100DP	100	1:1	93	1:1
50:50 GMA/PEGMA950 150DP	150	1:1	130	52:48
50:50 GMA/PEGMA950 200DP	200	1:1	191	57:43

Copolymer Solution Preparation. Polymer solutions were initially prepared to be 50 wt % polymer. For example, 0.3 g of polymer was dissolved in 0.3 g of solvent, and cross-linker was added such that the nucleophilic functional group was equimolar with the total epoxide concentration. To control for the concentration of cross-linking points in solution, polymers were subsequently formulated to be 1 M of epoxide in solution. For copolymers containing PEGMA2000, solutions were formulated in MeCN at 0.5 M epoxide functional units due to the large pendant chains dominating the overall mass of the sample and cross-linked with EDT catalyzed by LiOH. Each sample was vortexed for 5 s to ensure complete mixing before proceeding with rheometry or sonication.

For all experiments cross-linked with amines, reactions were conducted in a solvent system of 1:1 BuOH/DMF. Alcohols are known to catalyze the reaction between amines and epoxides through the formation of a trimolecular complex.[20] Thiol-cross-linked reactions were conducted in MeCN with 10 μL of 2 M LiOH as a catalyst, necessary to deprotonate the thiols in order to perform a nucleophilic attack on the epoxide ring.[21]

Parallel Plate Rheology. Gelation times and storage moduli (G'), and tan δ of polymer solutions/gels, were determined on a Kinexus Pro parallel plate rheometer (Netzsch, Selb, Bayern, Germany). Measurements were run on a 20 mm plate with a 1 mm gap at 1% strain and a 1−100 rad s^{-1} frequency sweep. Each frequency sweep lasted approximately 5 min, and the entire measurement lasted approximately 15 h. The gel point was defined using the Winter−Chambon criterion, for which the time of gelation is defined as the point at which tan δ becomes frequency-independent at small frequencies.[22−24] For samples with very high moduli, the elastic modulus was determined using compressive rheology by taking the slope of the stress−strain curve of cured gels with a 4 mm diameter. Rheological experiments were analyzed using IRIS Rheo-Hub (IRIS Development, Amherst, MA).[25]

Sonication-Induced Gelation of Shielded Copolymers. Polymer solutions were sonicated using a QSonica Q500 with a microtip attachment. The microtip QSonica probe was immersed in a polymer solution in MeCN. Water was flowed across the outer surface of the tube using a custom-made jacketed beaker to control the bulk temperature (Video S1) (University of Massachusetts Amherst Scientific Glassblowing Laboratory, Amherst, MA). Temperature was monitored with an IRT205 IR thermometer (General Tools, Secaucus, NJ) and confirmed with a mercury thermometer. This

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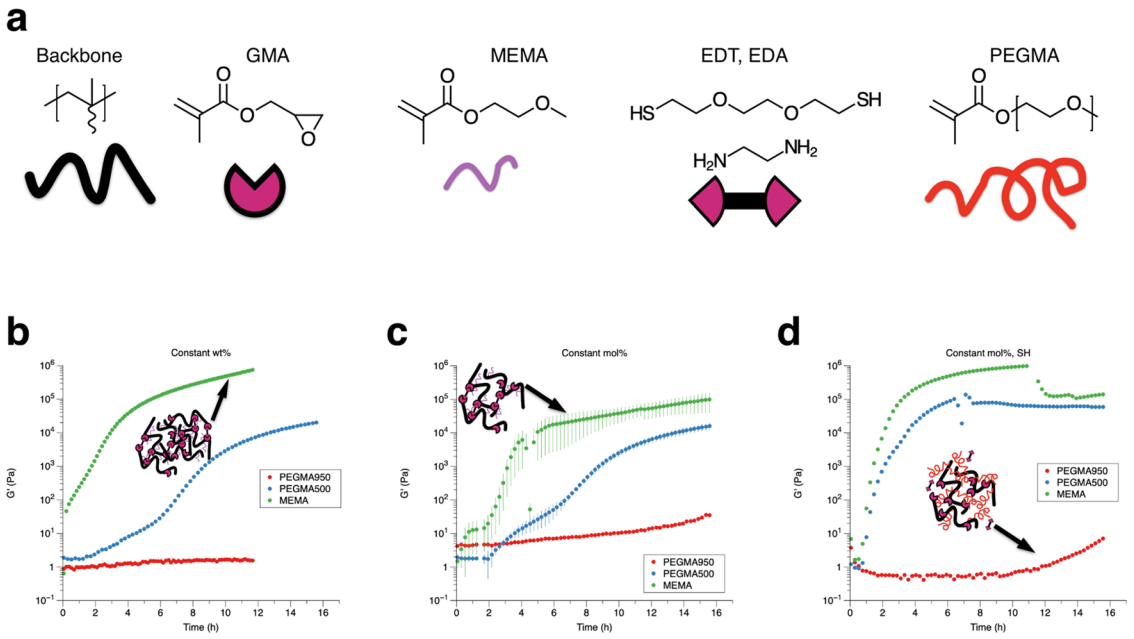

Figure 1. Large molecular shields inhibit or delay cross-linking. (a) Illustrations of polymer components are used throughout the paper. (b) Effect of shielding group functionality on storage modulus (G') over time with amine cross-links at constant 50 wt % polymer, reacting with EDA. Inset depicts high-density poly(GMA-*co*-MEMA) with many epoxy groups. (c) Effect of shielding group functionality on storage modulus over time with amine cross-links at constant 1 M concentration epoxy, reacting with EDA. The inset depicts low-density poly(GMA-*co*-MEMA) with a fixed amount of epoxy groups. (d) Effect of shielding group functionality on storage modulus over time with thiol cross-links at constant 1 M concentration epoxy, reacting with EDT. The inset depicts poly(GMA-*co*-PEGMA950) with a fixed amount of epoxy groups and large shielding groups preventing cross-linking. For all experiments, a 1:1 ratio of GMA/MEMA, PEGMA500, or PEGMA950 was used. Error bars show the standard deviation of G' at each time point (n = 3). For all conditions, including the enhanced kinetics provided by the thiol-epoxy reaction, a latency period before gelation at static conditions is present.

cooling setup was not sufficient to control temperature after 2 min and 40 s of sonication. Samples were sonicated at 10% amplitude and 20 kHz for 5 s at a time, with 10 s breaks in between pulses to avoid probe overheating. Gelation was determined by the point at which the power output would drop to ∼0 W and noise from vibrations would cease when the polymer had formed a solid gel. Samples were then immediately moved to the adjacent needle-induced cavitation (NIC) setup to determine the elastic modulus immediately post sonication.

Differential Scanning Calorimetry. Differential scanning calorimetry (DSC, Q200, TA Instruments) was used for the crystallization characterization. A sample (3−5 mg) was sealed in a standard aluminum hermetic pan using a TZERO press (TA Instruments) before being added to the calorimeter with an identical empty reference pan. The equipment was lowered to −90 °C and heated to 100 °C at a rate of 5 °C/min to remove the thermal history of the sample. The equipment was then lowered to −90 °C again and heated to 100 °C at the same rate, where enthalpy of melting (ΔH_m) was obtained from the area of the melting curve divided by the sample weight.[26] Thermogravimetric analysis (TGA, Q50, TA Instruments) was used to determine the degradation of the samples before running DSC to meet the criteria of a maximum 1.5 wt % loss.

Needle-Induced Cavitation. Characterization of elastic modulus of sonicated gels was done with needle-induced cavitation (NIC) using a custom-made setup with water as the fluid, pressurized with a NE 1000 syringe pump (New Era, Farmingdale, NY), contained in a 6 mL disposable syringe with a 27-gauge stainless steel disposable needle, microstand, and Px409−015 GUSBH pressure gauge (Omega, Norwalk, CT). Data collected from NIC was recorded on a Surface Mini using a custom LabView program to interface with the pressure sensor and record the pressure values (Crosby Lab, University of Massachusetts Amherst, Amherst, MA). When calculating the elastic modulus of gels, the effects of surface tension were ignored and values were computed using eq 1.[27,28] Each NIC experiment lasted on average from 30 to 90 s.

$$E = \frac{6P_c}{5} \tag{1}$$

RESULTS AND DISCUSSION

Gelation Kinetics of Polymers under Static Conditions. Our goal was to create a polymer network that was shelf-stable and would gel in response to force. First, we created a suite of polymers with varying cross-linker to comonomer ratios. Shielded and control copolymers were synthesized using RAFT polymerization of PEGMA (molecular shielder, grafting-through process)[29] or MEMA (control) with GMA monomers. Poly(GMA-*co*-PEGMA) and poly(GMA-*co*-MEMA) were synthesized with varying monomer ratios (30:70 GMA/PEGMA/MEMA to 70:30 GMA/PEGMA/MEMA) and shield lengths (1, ∼10, and ∼20 PEG repeats for MEMA, PEGMA500, and PEGMA950, respectively) to determine their effect on gelation. Additionally, the DP for each composition was varied to determine the effect of polymer length on force sensitivity.

When developing these materials, we imagined a polymer system that would be easily spread onto a substrate as a liquid that would then undergo a transition to a solid state after the introduction of mechanical stimuli. The final solid material should be bonded together permanently with covalent cross-links. To achieve this goal, we selected monomer GMA for its robust epoxide reactive group. Epoxides are known to undergo a ring-opening reaction in the presence of nucleophiles, such as amines and thiols. To introduce mechanosensitivity, we sought to copolymerize our epoxide functional monomers with monomers functionalized with groups that could provide steric hindrance. Toward this goal, GMA was copolymerized

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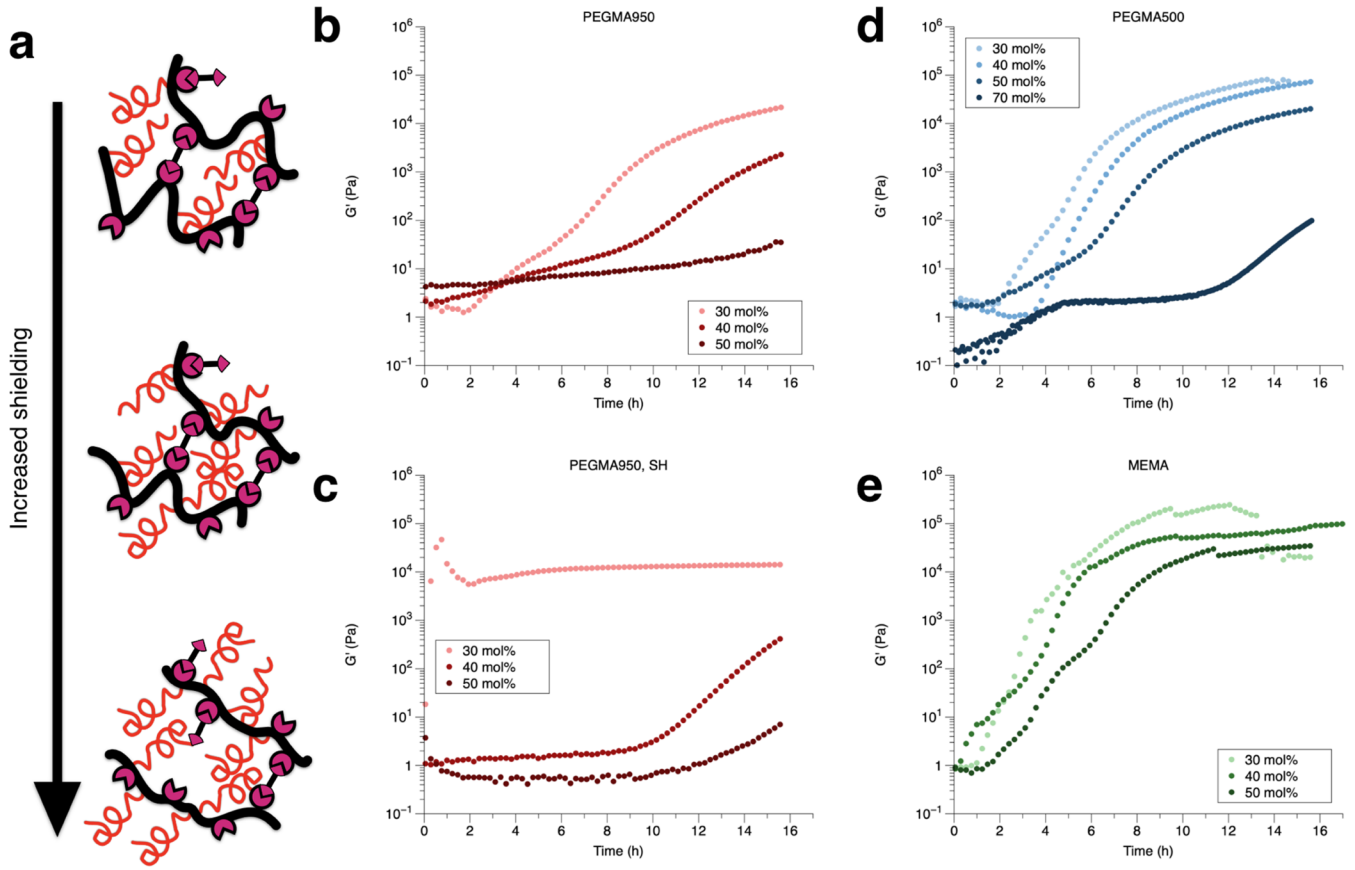

Figure 2. Ratio of pendent shields to reactive groups controls the gelation time. (a) Illustrations of polymers at different GMA/PEGMA molar ratios, showing the change in backbone flexibility and exposed reactive sites. (b–e) Storage modulus evolution over time for: (b–c) varying mole percentage of PEGMA950 with a diamine (b) or dithiol (c) cross-linker; (d) varying mole percentage of PEGMA500; and (e) MEMA with a diamine cross-linker. Arrows represent trends in shielding resulting from the increased ratio of shielding monomer.

with PEGMA of varied molecular weights from 140 to 950 g/mol that we hypothesized could provide a steric hindrance to cross-linking via their ether side chains.

Synthesis of this suite of polymers proceeded as expected, with final DPs and incorporation ratios closely matching the targeted DP and feed ratio when conducted in dioxane (Table 1). Successful incorporation and molar ratio of constituent monomers were confirmed using ^{1}H NMR spectroscopy (Figures S1–S10). DP and incorporation ratios of poly(GMA-*co*-PEGMA) samples were less consistent compared to their MEMA counterparts, attributed to the inherent dispersity of PEGMA macromonomers, skewing the actual molar amount added to reactions. After successfully synthesizing the desired copolymers, we moved on to assess their gelation kinetics.

For our cross-linkers, we chose EDT due to its nonvolatile nature and reasonable stability in air, and EDA as it is commonly used to cure epoxy resins. Amines and thiols were chosen as two candidates both because they are frequently used in commercial epoxy formulations and because they compare the effects of different reaction kinetics on the shielded copolymer system. We sought to determine a molecular weight of shielding groups that would facilitate delayed cross-linking of the epoxide groups in the presence of a bifunctional nucleophile without preventing it entirely. In our experiments, we tested a range of effects, including varying the DP of grafted chains from 1 to 20, varying the DP of the polymer backbone from 25 to 670, adjusting nucleophilic attack kinetics, and varying the ratio of comonomers from 30 to 70% GMA concentration. The monomers used to form the copolymers and the different cross-linkers in these experiments are represented in Figure 1a.

First, the effect of pendent shield size on cross-linking was assessed at constant weight percent and static conditions (Figure 1b). When solutions are formulated at 50 wt % of polymer with EDA, poly(GMA-*co*-MEMA) cross-links very quickly (1 h) and reaches a final G' on the order of 10^6 Pa. Conversely, poly(GMA-*co*-PEGMA500) cross-links more slowly (8 h) and reaches a final G' on the order of 10^4 Pa, and poly(GMA-*co*-PEGMA950) shows no change in modulus indicating no cross-linking occurred. At a constant 50 wt % of polymer in solution, the concentration of epoxide for unshielded samples (MEMA) is very high compared to the shielded polymers (PEGMA). At this fixed concentration, the overall mass for the shielded polymer solutions is dominated by the presence of ether in the PEGMA side chains, skewing the sample in favor of unreactive ether and decreasing the number of possible cross-links. The lack of an increase in modulus with PEGMA950 may be due to this ether dominance preventing the formation of a volume-spanning network. Additionally, the relatively large mass of the ether side chains decreases the amount of reactive epoxy in solution.

To control for the effect of variable epoxide concentration, samples were next formulated at a constant epoxide molar concentration (Figure 1c). Epoxide concentration was set to 1 M, resulting in variable weight percent polymer in solution: control polymer samples with low (25%) and shielded samples

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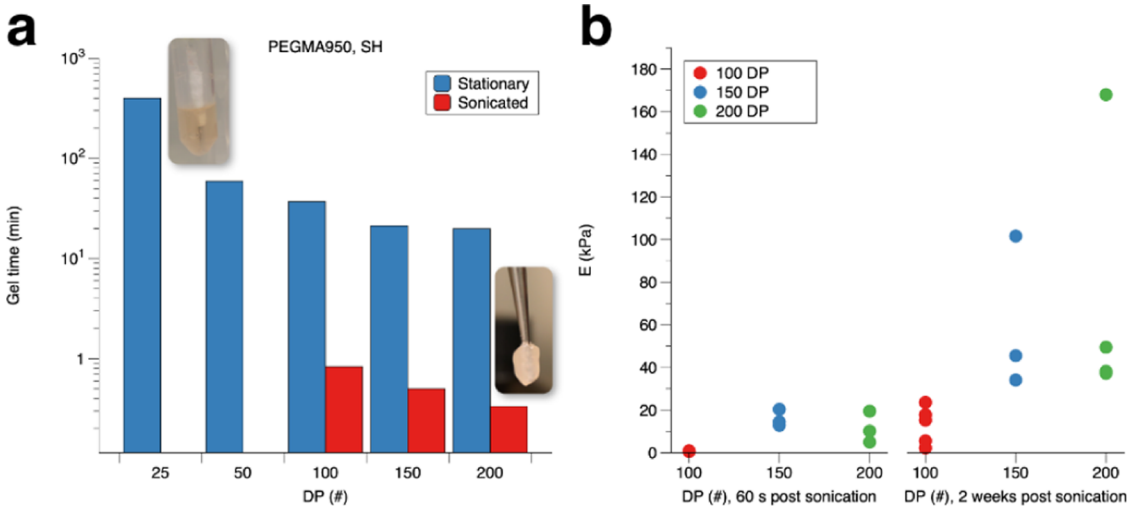

Figure 3. Sonication induces shielded polymer cross-linking. (a) Gel time of poly(GMA-*co*-PEGMA950) under static and sonicated conditions at varying DP with a 1:1 molar ratio. Samples at 25 and 50 DP did not form a gel. The insets show a liquid polymer solution during a bubble test and a polymer cured through sonication, still attached to the sonicator probe. (b) Elastic modulus of poly(GMA-*co*-PEGMA950) cured with sonication as measured via NIC. Samples were cross-linked with a 1:1 molar ratio of thiol to epoxy and at a DP of 100, 150, or 200 and measured 60 s post sonication and after 2 weeks.

with high (61%) weight percent. At 25 wt %, poly(GMA-*co*-MEMA) cross-links more slowly (2 h) than at 50 wt % and reaches a lower final G' on the order of 10^5 Pa. For poly(GMA-*co*-PEGMA950), wt % changes from 50 to 61 and expectedly shows only a small increase in G' of 35 Pa. For poly(GMA-*co*-PEGMA500) samples, 1 M epoxide concentration is equal to 50 wt % of polymer. Trends in the effect of shielding groups are the same at constant wt % polymer or mol % epoxides: as the shielding group MW increases, the time to gelation and the final modulus both decrease.

Finally, the effect of more reactive nucleophiles on cross-linking was investigated by replacing EDA with EDT and keeping the mol % epoxide constant (Figure 1d). Thiols are known to be stronger nucleophiles than primary amines, and the ring-opening reaction between thiols and epoxides proceeds orders of magnitude faster than between amines and epoxides.[30] At a constant 1 M epoxide concentration, poly(GMA-*co*-MEMA) with EDT cross-linked more rapidly (30 min) than the amine condition and attained a similar final G'. Poly(GMA-*co*-PEGMA500) samples cross-linked rapidly (42 min) with EDT, but more slowly than the MEMA copolymer and attained a final modulus on the order of 10^4 Pa. Poly(GMA-*co*-PEGMA950) samples still did not show any signs of gelation, increasing only to a final modulus of 10 Pa. Even with faster reaction kinetics, the PEGMA950 shielding groups suppress gelation.

For permanently cross-linked polymer networks, the equilibrium modulus of the cured material can be predicted by Flory's theory of rubber elasticity[31,32] and is proportional to the number of elastically effective chains in the network.[33,34] As the number of elastically effective chains increases, so does the equilibrium modulus; therefore, a low equilibrium modulus implies the presence of unreacted cross-links. With the same number of cross-links possible in MEMA, PEGMA500, and PEGMA950 samples, and taking the equilibrium modulus of the MEMA polymer in Figure 1c, PEGMA500 and PEGMA950 can be inferred to be have a lower cross-linking density due to the protective effects of the polyether chains. This led us to believe that 950 g/mol shielding groups are most effective at creating a steric barrier to reaction, preventing cross-linking between adjacent polymers and resulting in lower final G' values.

Controlling Gel Time through Shield Graft Density. We next aimed to determine the minimum molar ratio of shielding groups necessary to prevent spontaneous cross-linking by varying the ratio of GMA/PEGMA (Figure 2a). We expected that high contents of shielding monomer would entirely inhibit gelation over the measurement time, eventually prohibiting cross-linking even under force. To assess the minimum molar ratio necessary for preventing gelation without applied mechanical stimulus, the mole percent of PEGMA950 (~20 repeat units) and PEGMA500 (~10 repeat units) shielding monomers within each polymer chain was varied from 30 to 50 mol %. Variations in mole percent of MEMA copolymers were assessed as a negative control. The total concentration of epoxides in solution remained constant at 1 M.

In the presence of EDA or EDT with shielding group concentrations at mol 50% (PEGMA950), a negligible increase in G' was seen; at 40%, a very slow increase in G' with a final value on the order of 10^3 Pa was demonstrated; and at 30%, a rapid increase in G' with a final G' of 10^4 Pa was observed (Figure 2b,c). At higher shielding monomer percentages, gelation was entirely inhibited over the measurement time, even with the quick cross-linking EDT. In both the thiol and amine cases, the trend toward decreasing gel time with increasing PEGMA950 content is the same.

Next, polymers with PEGMA500 shielding units (~10 repeat units) were varied from 30 to 70 mol % shielding monomer content while keeping the total epoxide group concentration in solution constant at 1 M (Figure 2d) with EDA. When the shielding group concentration was 30 and 40 mol %, the material cross-links rapidly and reaches final G' values on the order of 10^5 Pa. At 50% concentration of shielding groups, the material reaches a lower final modulus on the order of 1×10^4 Pa. At the maximum tested 70% molar ratio of shielding group to reactive group, the shielded polymers still form a gel, but do not attain an equilibrium

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modulus during the experimental time frame. The PEGMA500 shielding groups do not provide a sufficient steric barrier to reaction but do provide some hindrance to reaction evidenced by the decreased final modulus values compared to control samples.

Finally, polymers with one repeat unit pendent chain (MEMA) were varied between 30 and 50 mol % control monomer and reacted in the presence of EDA. Increasing the control monomer ratio from 30 to 50% slightly decreased the rate at which the material cross-linked and the final modulus, from 10^5 Pa at 30 and 40 mol % control monomer to just above 10^4 Pa at 50 mol % control monomer (Figure 2e). As expected, the small size of the MEMA comonomer did not contribute significantly to suppressing the cross-linking kinetics of the cross-linking polymers.

At low ratios of shielding monomer to reactive monomer, there are statistically likely to be more stretches of reactive monomer with no steric effects to prevent them from cross-linking, as well as increased backbone flexibility. At high ratios of shielding monomer to reactive monomer, there are far fewer reactive monomer sequences as well as a straighter backbone due to pendent chains preventing backbone flexing. In summary, only the poly(GMA-*co*-PEGMA950) compositions achieved this with a high degree of shielding. Gelation was completely inhibited at a 1:1 ratio of reactive to shielding groups. This composition was selected as the most promising candidate for force-activated gelation.

Force-Induced Gelation of Shielded Copolymers. We hypothesized that sonication would be a facile method to mechanically induce gelation of shielded polymer. Sonication can achieve enormous strain rates approaching 10^8 s^{-1}.[35] This enormous strain rate arises from cavitations introduced during ultrasonic irradiation, nearly instantaneously creating and destroying microscopic bubbles that in turn create pressure gradients that can apply force through fast solvent flows to polymers of sufficient size. The force accumulated along the polymer backbone results in overstretched regions, which is what is generally accepted to drive conventional mechanochemical reactions.[36]

Cross-linking of shielded polymers induced via sonication was assessed at DP of 25 to 200 monomer units per chain (Figure 3a). Each polymer sample was prepared at 1 M epoxide group concentration and reacted with EDT catalyzed by LiOH. Utilizing an ultrasonic probe immersed in polymer solutions, samples were subjected to ultrasonic waves for 5 s at a time, with 10 s of pause in between to prevent probe overheating. All conditions have delayed gelation at static conditions, allowing for the characterization of faster cross-linking with induced strain. At DP equal to or greater than 100, samples gelled within 60 s of sonication time. At 100 DP, we observed a 2 orders of magnitude decrease in gelation time when comparing unperturbed samples with sonicated samples. Samples of DP 150 and 200 gelled more rapidly, within 30 and 20 s of sonication time, respectively. Poly(GMA-*co*-PEGMA950) of lower DP (25 and 50) did not show any strain responsiveness, and the solution boiled before any gelation or viscosity change was observed due to the heat generated by the ultrasonic probe, reaching a temperature of 56 °C measured through an IR thermometer, at which point the solution began to boil while sonication was being applied. Counterintuitively, the heat generated by sonication is counterproductive to the gelation of this system, possibly due to changes in the conformation of PEGMA shielding groups at higher temperatures (Figure S11). It is well understood that PEGMA copolymers have a lower critical solution temperature in water that is dependent on the polyether length and the ionic strength of the environment,[37] but it is not clear that this behavior extends into aprotic organic solvents. Gelation time under static conditions decreased as a function of DP like that of sonicated samples but showed a leveling off after 150 DP unlike that of the sonicated samples. This decrease in gel time is likely due to the longer backbone lengths of the polymers beginning closer to the percolation threshold for gelation, resulting in fewer epoxide-thiol reactions needing to take place to form a volume spanning elastic path and a shorter time to the critical gel.[38,39]

It has been shown that polymers of sufficient molecular weight are sensitive to shear forces. The large size of polymers results in the restriction of bond angle conformers available due to chain and bond torsional strain, meaning polymers can accumulate force along their backbone as entropic potential energy.[40−43] High-molecular-weight polymers undergo chain scission in response to strong shear forces generating two distinct carbon-centered radicals.[44,45] These sufficiently strong shear forces result in overstreched segments of polymer adjacent to the chain center, generating a tensile force that drives mechanochemical reactions.[36] The chain scission rate increases with molecular weight.[46] This molecular weight dependence is more accurately described as a polymer length dependence.[47] It follows that shielded poly(GMA-*co*-PEGMA950) of sufficient DP is more easily influenced by shear forces in solution if the chain length is long enough, surpassing at least 100 units in length. The increased DP of the polymer also increased the viscosity of the sample. The literature has shown that highly viscous media decreases the effectiveness of ultrasonic micromixing,[48] making it less likely that the dependence of gel time on DP is a result of mixing phenomena. This study does not elucidate the mechanism for this system's strain sensitivity. It is not clear what aspect of cross-linking is sped up by the application of ultrasound, the addition of EDT to polymer, or the addition of polymer + EDT to another polymer. Future studies using monothiols functionalized with UV tags would shed light on the precise molecular mechanism of strain-sensitive cross-linking.

Cavitation rheology was used to assess postgelation elastic moduli of gels formed via sonication (Figure 3b). NIC has previously been shown to be effective at extracting elastic modulus information from soft materials.[27] Sonicated samples were measured to have an elastic modulus near 1 kPa for samples starting at 100 DP, and 20 kPa for samples between 150 and 200 DP as measured by NIC. After a week of resting in a sealed tube to allow for residual epoxides to be consumed by thiols, the modulus of each sample increased to an average of 20 kPa for samples starting at 100 DP and 60 kPa for samples starting at 150 to 200 DP. The final modulus for 150 and 200 DP polymers had a wide range, varying from 30 to 170 kPa. This variance is likely an error from cavitation rheology, which tends to have a higher variance for samples with higher elastic moduli.[49,50] The modulus derived from NIC shows that polymers shielded with PEGMA950 cure into relatively weak materials.

Ultrahard Materials from Shielded Copolymers. Conventional epoxy resins and composites can attain G' values approaching and surpassing 10^9 Pa.[51,52] Choosing this value as a benchmark for comparison, we formulated poly(GMA-*co*-PEGMA2000) copolymers at a 1:1 monomer

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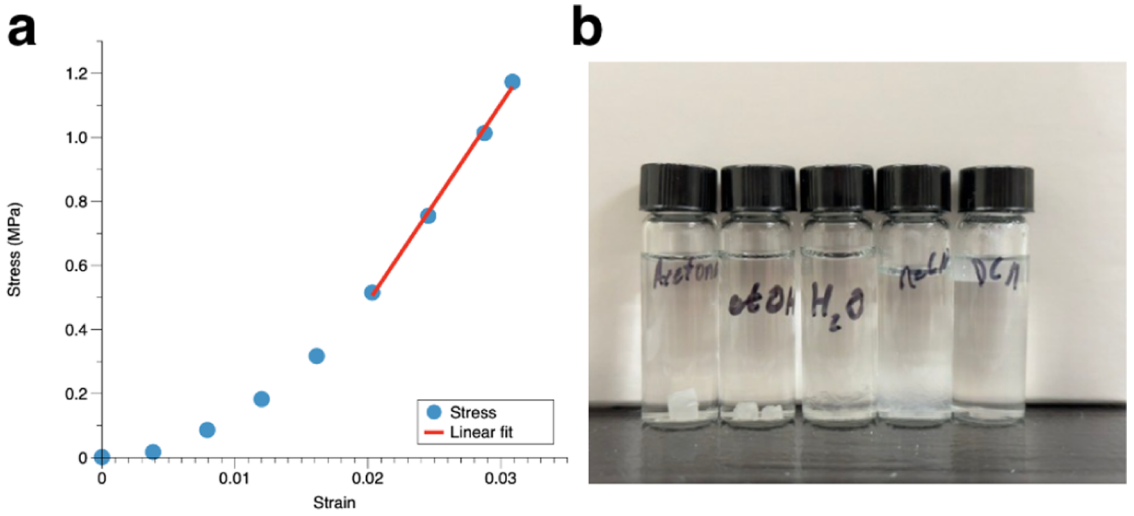

Figure 4. Shielded copolymers create ultrahard and durable materials. (a) Compression modulus of a fully cured poly(GMA-*co*-PEGMA2000) with a 1:1 molar ratio of monomers. Elastic modulus is calculated by taking the slope during the linear portion of the stress−strain curve. Red lines show the linear best fit through four points. (b) Fully cured poly(GMA-*co*-PEGMA2000) gels were immersed in acetone, ethanol, water, acetonitrile, and dichloromethane.

ratio and 670 DP. The extremely long shielding group and long DP were chosen to provide a material that had both maximum latency and sensitivity to ultrasound. After sonicating these samples and leaving them to cure for 48 h, the polymer cross-linked into an opaque white solid. Samples were prepared as 5 × 4 mm^2 cylinders, and their moduli were assessed on a rheometer via compression with a 4 mm diameter plate. An elastic modulus value of 62 MPa was extracted from the resultant stress−strain curve (Figure 4a), approaching that of conventional epoxy materials. Immersing gels of this copolymer into acetone and ethanol showed no visible change in the material, but in MeCN, DCM, and water, the gels crumbled into insoluble chunks (Figure 4b), leading us to conclude that the material's strength comes from a combination of epoxide-thiol covalent cross-links and PEG side-chain crystallization. It is well known that graft copolymers with crystallizable side chains will form crystal domains.[53,54] Using DSC we were able to measure the melting temperature for a cured GMA/PEGMA2000 sample, confirming the material is partially crystallized (Figure S12). Using a steric shielding approach, we created an ultrahard material through an unexpected combination of crystallinity and covalent bonding.

CONCLUSIONS

We synthesized novel strain-sensitive shielded polymers containing both reactive epoxides and molecular shields. These shielding PEG chains provide a steric barrier to an otherwise powerful and efficient cross-linking reaction between amines or thiols and epoxides. This approach to creating strain-sensitive materials provides a facile route to creating strain-responsive coatings and adhesives using well-known and commercially available monomers. Through this, we demonstrated, for the first time, a liquid-to-solid transition accelerated under force using shielded reactive polymers. We showed that force-stimulated gelation could be achieved with ultrasound. We further showed that steric shielding can create ultrahard materials. Suppressed gelation without force, combined with ultrasound sensitivity, makes this polymer an ideal candidate for an adhesive in a heat- or light-sensitive application.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.macromol.4c00315.

Example sonication setup (Video S1) (MOV)

^{1}H NMR spectra, temperature control rheology, and DSC thermogram (PDF)

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Notes

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