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Polysquaramides

Debabrata Konar, Kevin A. Stewart, Jack Moerschel, John F. Rynk, and Brent S. Sumerlin*

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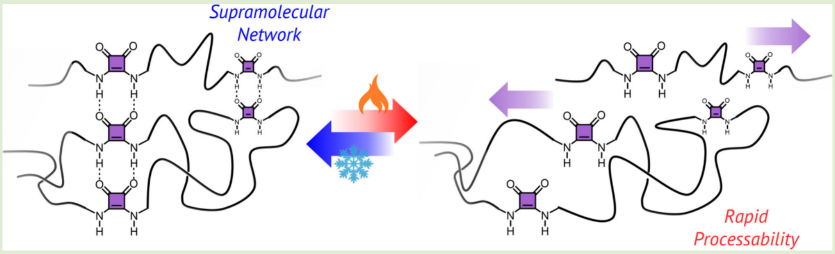

ABSTRACT: Thermoplastics, while advantageous for their processability and recyclability, often compromise thermochemical stability and mechanical strength compared to thermosets. Addressing this limitation, we introduce an innovative approach employing reversibly cross-linked polymers, utilizing squaramide moieties to reconcile recyclability and robustness. Herein, we detail the synthesis of supramolecularly cross-linked polysquaramides through the condensation polymerization of diethyl squarate with primary and secondary diamines. This methodology embeds hydrogen-bonding squaramide motifs into the polymer chains, yielding materials with significantly enhanced storage moduli, reaching up to 1.2 GPa. Material characterization via dynamic mechanical analysis, creep-recovery, and stress relaxation experiments delineate a distinctive rubbery plateau across a broad temperature range, excellent creep resistance, and multimodal viscoelastic flow, respectively, attributable to the dynamic nature of the supramolecular cross-links. Additionally, the study showcases the modulation of glass transition temperature (T_g) by altering the monomer composition and stoichiometry, demonstrating the tunability of polymer viscoelastic properties through precise control over hydrogen bonding interactions. Overall, the incorporation of squaramide motifs not only provides the structural integrity and mechanical performance of these thermoplastics but also leads to engineering materials with tailored viscoelastic characteristics.

Polymer networks, distinguished by chemical or physical cross-links can be described as thermosets, elastomers, or gels and exhibit desirable properties, including elasticity, mechanical strength, and high porosity. Incorporating dynamic cross-links into these networks introduces characteristics like self-healing, recyclability, and stimuli responsiveness. These dynamic networks are categorized into two classes based on the nature of their cross-links: supramolecular networks, which rely on noncovalent interactions, and covalent adaptable networks (CANs), featuring reversible covalent bonds.[1] Supramolecular networks benefit from a myriad of noncovalent forces including hydrogen bonding, $\pi-\pi$ interactions, van der Waals forces, and electrostatic attractions.[2,3] In particular, macromolecules that reversibly associate via hydrogen bonds are especially important, providing the mechanical integrity of both biomacromolecules such as DNA, proteins (e.g., collagen, silk), and cellulose (e.g., wood) and commercial engineering plastics-such as polyamides (e.g., Nylon, Kevlar) and polyureas (e.g., Spandex) through intermolecular hydrogen bonding between polymer chains. CANs, distinguished by their bond exchange mechanism, are divided into dissociative and associative types. Dissociative CANs, when triggered by stimuli (e.g., heat or light), have their cross-links break down into reactive components that diffuse and then recombine, regenerating the network.[4−7] Whereas associative CANs (i.e., vitrimers) break and reform cross-links simultaneously through an associative intermediate, where a reactive group within the network swaps with an existing cross-link.[8−12]

Recent advancements have focused on the integration of unique hydrogen-bonding motifs to enhance the material properties of polymer networks. For instance, Aida et al. reported robust, self-healable polythioureas, where a zig-zag arrangement of hydrogen bonds conferred an amorphous nature to the network, in contrast to the semicrystalline nature typical of analogous polyurea with linear hydrogen bond arrangement.[13] This structural alteration facilitated chain mobility and enabled self-healing properties. Sanjayan, Sumerlin, and coworkers[14] integrated Janus-faced triazine-based guanine-cytosine bases (GCB)[15,16] into acrylate polymers, establishing a directional hydrogen bonding array that led to supramolecular networks with an extended rubbery

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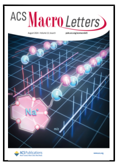

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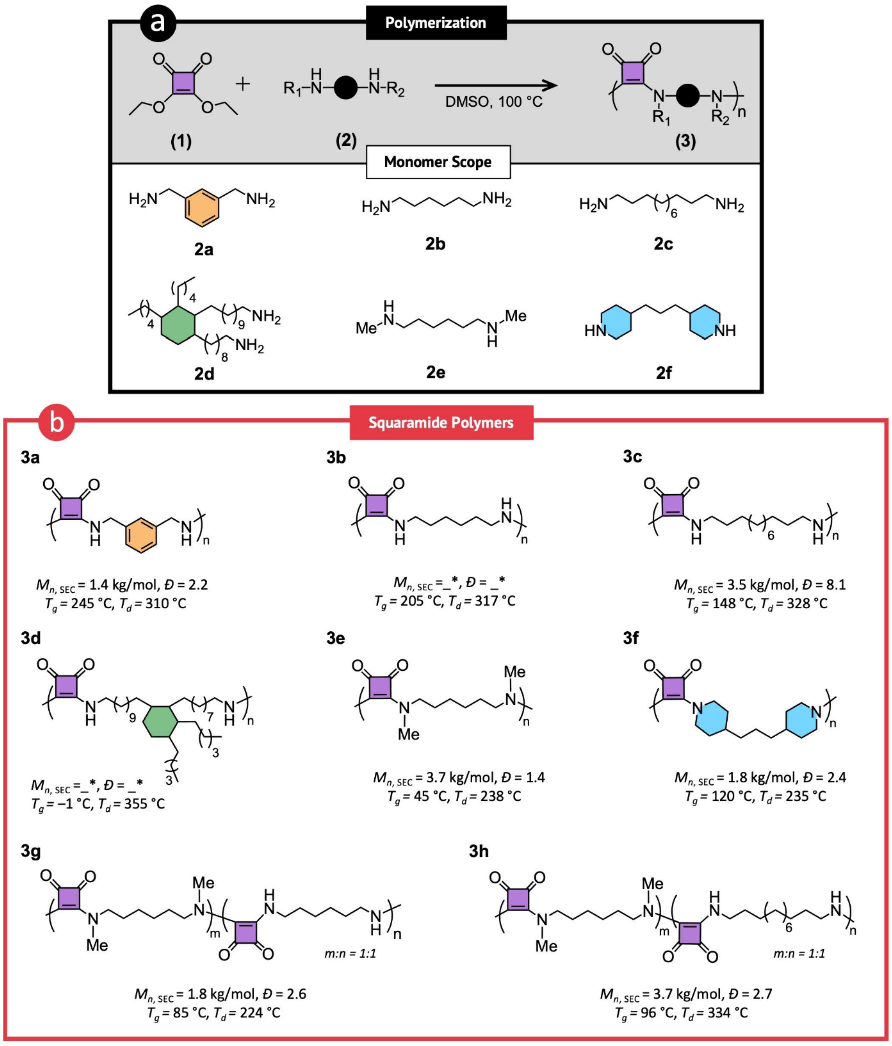

Figure 1. (a) Condensation polymerization of diethyl squarate with primary diamines (**2a**−**d**) and secondary diamines (**2e**,**f**); (b) Library of synthesized polysquaramide homopolymers (**3a**−**f**) and copolymers (**3g**−**h**). M_n and Đ were determined by GPC (HFIP) using poly(methyl methacrylate) standards. T_d = 5% weight loss temperature. *Sample insoluble in HFIP for GPC analysis.

plateau temperature range. The self-complementary hydrogen bonding cross-links promoted high cooperativity and network integrity. Moreover, the introduction of hydrogen bonding motifs such as 2-ureido-4-[1*H*]-pyrimidinone (UPy),[17,18] thioctic acid (TA),[19] and thioctic acylhydrazine (TAH)[20] into synthetic materials has led to the development of robust and dynamic supramolecular polymers. This study explores the potential of squaramides as hydrogen bonding motifs in creating reversibly cross-linked dynamic materials, aiming to reconcile recyclability with enhanced thermochemical stability and mechanical strength.

Squaramides, a subset of vinylogous amides, can be synthesized through the efficient condensation of diethyl squarate with primary or secondary amines. Recognized for their role in drug design, squaramides serve as bioisosteric replacements for heteroatomic groups such as urea, thiourea, guanidine, and cyanoguanidine, facilitating the creation of innovative histamine receptor antagonists.[21] Characterized by their ditopic hydrogen bonding structure, squaramides comprise two carbon−oxygen hydrogen bond acceptors and two nitrogen−hydrogen bond donors, positioned on a structurally rigid cyclobutene ring. The delocalization of the nitrogen lone electron pairs into the cyclobutenedione ring (Hückel's rule ([$4n + 2$] π electrons, with $n = 0$), coupled with the planarity of the carbamoyl groups, endows squaramides with aromatic characteristics.[22,23] This delocalization enables squaramides to act both as hydrogen bond donors and acceptors, a feature that can be leveraged in both material science and organic chemistry.[24,25]

One of the most notable features of squaramides is the capacity to form robust hydrogen bonds, which enhances aromaticity beyond that observed in their non-hydrogen bonded state. This increase in aromaticity is substantiated by nucleus-independent chemical shift (NICS) calculations, with squaramide in a nonhydrogen bonded state showing a NICS (0.6) value of −6.3 ppm, which further decreases to −8.1 ppm when hydrogen-bonded to an ammonium cation complex, indicating more pronounced aromaticity in the bonded state.[26] The combination of enhanced aromaticity and the broad scope for hydrogen bond acceptor interactions, a result of the dual-carbonyl configuration in squaramides, distinguishes squaramides from close congeners like urea and amide.[27,28] Furthermore, the intrinsic capability of squaramides to form head-to-tail hydrogen bonds contributes to their thermodynamic stability via an increase in aromaticity, making them

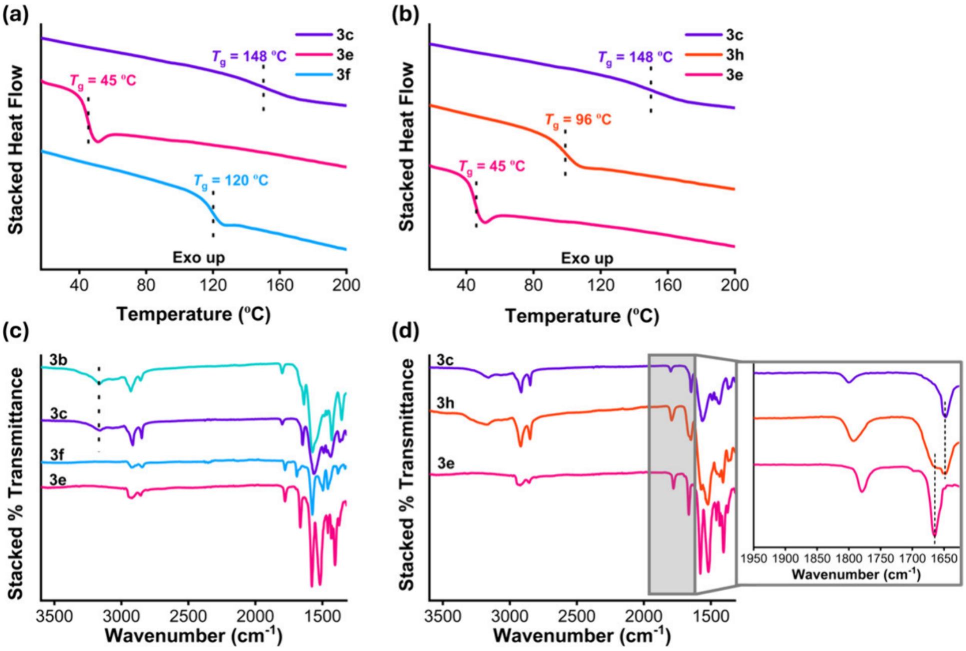

Figure 2. (a) DSC curves of polysquaramide homopolymers from primary diamine (**3c**) and secondary diamine (**3e**, **3f**); (b) DSC curves for polysquaramide copolymer (**3h**) and homopolymer (**3c**, **3e**) showing modulation of T_g; (c) FTIR spectra for polysquaramide homopolymers from primary diamine (**3b**, **3c**) and secondary diamine (**3e**, **3f**); and (d) FTIR spectra for polysquaramide copolymer (**3h**) and homopolymer (**3c**, **3e**).

invaluable for self-assembling supramolecular polymers[29,30] and molecular recognition.[31,32]

Leveraging the aromaticity gain observed in small molecule squaramides, Kieltyka et al. developed robust supramolecular polymers from bis(squaramide) bolaamphiphiles. These polymers self-assemble into stiff, micron-sized fibers in water and undergo rapid depolymerization in hexafluoroisopropanol (HFIP).[33] The bolaamphiphiles exhibit increased aromatic character like that of small molecular squaramides, alongside a higher thermodynamic stability compared to both the bis(squaramide) monomer and urea/amide analogs. By varying the hydrophilic and hydrophobic block lengths of the bis(squaramide) bolaamphiphiles, a morphological transition from fibers to spherical nanoparticles was achieved, leading to potential applications in nanomedicine.[30] Additionally, tripodal squaramide-based monomers self-assembled into fibrillar supramolecular polymers form self-healing hydrogels under physiological conditions and have been successfully utilized as 3D cell culture media.[29] In addition to their self-assembly ability, squaramides function as effective gelators and covalent probes, as illustrated by their use in forming gelatin-based hydrogels[34] and amine-reactive probes[35] through efficient cross-linking and regioselective reaction of lysine residues with squarates.

One of the earliest studies on polysquaramides, polymers featuring repeating squaramide units, dates to the 1970s, with Neuse et al. pioneering the polycondensation of *p*-phenylenediamine with diethyl squarate or squaryl dichloride. These polymers were insoluble and received limited characterization.[36] Taylor et al. described the synthesis of polysquaramides through the Lewis acid-catalyzed polycondensation of diethyl squarate and difunctional aniline derivatives.[32,37] The resulting polymers exhibited a significant increase in affinity for dihydrogen phosphate ($H_2PO_4^-$) anion binding, surpassing that of their nonpolymeric counterparts, along with notable anion sensing selectivity even in competitive environments.[37] Moreover, the utility of squaramide synthons in chemically responsive materials with macroscopic actuation was highlighted by Wezenberg et al., developing anion-binding gels through free-radical polymerization of *N*,*N*-dimethylacrylamide (DMA) with squaramide cross-linkers.[31] Recently, ring-opening metathesis polymerization of strained alkenes from squaramides has allowed tailoring of molecular and material properties by simultaneous integration of rigid and flexible segments into the polymer chain.[38] These advancements suggest the potential of squaramide-based materials as responsive materials.

Previous studies have emphasized the use of squaramides in pharmaceuticals and organocatalysis, yet the synthesis of polysquaramides remains notably sparse, impeding a comprehensive understanding of their structure-property relationships and restricting their use primarily to anion-sensing and nanoparticle formation. Additionally, the role of polysquaramides in dynamic supramolecular networks—a critical area of polymer science—has been largely unexplored. This study introduces a series of polysquaramides synthesized via condensation of diethyl squarate with various primary and secondary diamines. Thermal analysis demonstrated the ability to adjust the glass-transition temperature (T_g) across a broad spectrum by altering monomer stoichiometry. Notably, we report the first polysquaramide with a high biomass content (~90%), which exhibits notable malleability, creep resistance, and multi-modal viscoelastic behavior, marking a significant addition to the burgeoning field of supramolecular cross-linked networks.

We explored the condensation polymerization of diethyl squarate (**1**) with various diamines (**2**) in DMSO, employing primary diamines viz. *m*-xylene diamine (**2a**), hexamethylene diamine (**2b**), 1,12-diaminododecane (**2c**), Priamine 1074 (**2d**), and secondary diamines viz. *N*,*N*′-dimethyl-1,6-hexanediamine (**2e**) and 1,3-bis(4-piperidinyl)propane (**2f**) in the presence of DIPEA. This process generated a library of

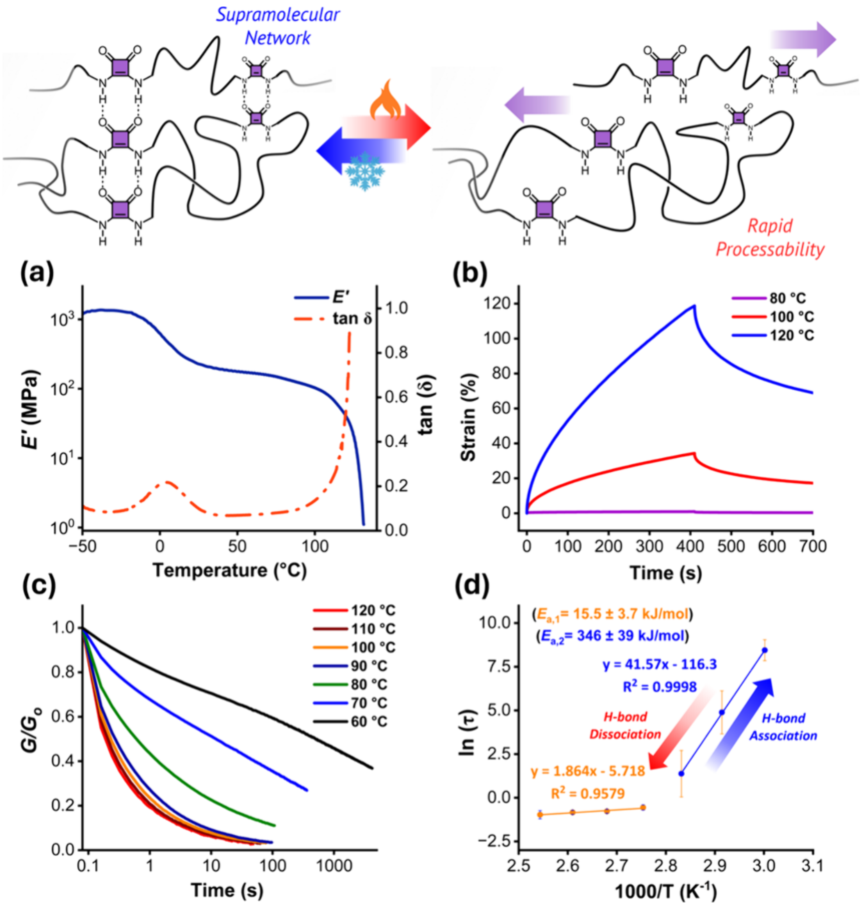

Figure 3. (a) DMA temperature sweep showing storage modulus (E') and tan (δ); (b) Creep-recovery experiments at 80, 100, and 120 °C at a constant stress of 5 kPa; (c) Normalized stress relaxation (0.3% strain) traces at varying temperatures; and (d) Arrhenius plot of stress relaxation (τ at $G/G_o = 1/e$, in 10 °C increments), with activation energies ($E_{a,1}$ and $E_{a,2}$).

polysquaramides (**3a–h**), as depicted in Figure 1a,b. A 1:1 molar ratio of amine to ester was maintained for all polymerizations, resulting in polymers with number-average molecular weights (M_n) between 1.4 and 3.7 kg/mol, as determined by gel permeation chromatography (GPC) in hexafluoroisopropanol (HFIP) with poly(methyl methacrylate) standards (Figures S1 and S2). Notably, polysquaramides derived from secondary diamines (**3e–f**) were soluble in dimethyl sulfoxide (DMSO) and were successfully characterized by ^{1}H NMR spectroscopy, confirming the presence of expected structural peaks (Figures S10–S13).

Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) were used to assess the thermal properties of the polymers, showing high thermal stability with decomposition temperatures (T_d) spanning from 235 (**3f**) to 355 °C (**3d**), as shown in Figure S3. DSC analysis revealed a wide range of T_g values for homopolymers **3a–d** (from primary diamines) and **3e–f** (from secondary diamines), as depicted in Figure S4. T_g values of up to 245, 205, and 148 °C were observed for **3a**, **3b**, and **3c**, respectively, attributed to the intermolecular hydrogen bonding between squaramide units facilitated by hydrogen-bond donors and acceptors (Figure S4a). In contrast, **3d**, with its longer aliphatic segments, exhibited a significantly lower T_g of −1 °C. Remarkably lower T_g values of 45 and 120 °C for **3e** and **3f**, respectively, were attributed to the lack of intermolecular hydrogen bonding, a consequence of missing hydrogen bond donors in these structures (Figure 2a and S4b). The rigidity of cyclic motifs in the repeating units accounts for the higher T_g of **3f** compared to **3e** (Figure 2a). Copolymers **3g** and **3h**, synthesized from (**1**) and an equimolar mixture of secondary and primary diamines, showed T_g values of 85 and 96 °C, respectively, demonstrating the ability to modulate T_g across a wide range, bridging the gap between homopolymers with secondary diamine, **3e** (T_g = 45 °C) and primary diamines, **3b** (T_g = 205 °C) and **3c** (T_g = 148 °C) (Figure 2b and S4c,d). These results demonstrate that T_g can be modulated by varying polymer molecular structure, specifically through the integration of *N*,*N*′-dimethyl-1,6-hexanediamine (**2e**), which reduces intermolecular hydrogen bonding, highlighting the adaptable T_g based on molecular composition.

FTIR spectroscopy highlighted the hydrogen bonding characteristics of the polymers. Homopolymers **3a–d** showed a broad N–H stretching band (3400–3165 cm^{-1}), characteristic of squaramide units (Figures 2c and S5), unlike **3e–f**, indicating the absence of hydrogen bonding N–H units (Figure 2c). However, all samples exhibited a squaramide unit ring-breathing band (1780–1798 cm^{-1}) and C═O stretching in the amide I region (1640–1690 cm^{-1}; Figures 2c and S5). Notably, the presence of diverse molecular structures from primary and secondary amine-derived squaramide motifs was confirmed in copolymer **3h** featuring a broad N–H stretching band (3390–3100 cm^{-1}), indicative of hydrogen bonding N–H units and two distinct C═O stretching vibrations (1650 and 1665 cm^{-1}) correlated with the C═O stretching of **3c** (1649 cm^{-1}) and **3e** (1666 cm^{-1}; Figure 2d).

Due to its low T_g and exceptional moldability, the elastomeric polymer **3d**, derived from Priamine 1074, was chosen for further rheological and material characterization of the supramolecular cross-linked polysquaramide network. This polymer, notable for its high biomass content (∼90%), represents one of the first instances of a bioderived polysquaramide. The polymer was successfully compression molded into disks and bars at 80 °C under vacuum. After 1 h, the materials emerged fully healed, with minimal defects and excellent transparency (Figure S6).

The thermomechanical properties of **3d** were assessed using dynamic mechanical analysis (DMA) (Figure 3a), which revealed a supramolecular cross-linked network through the observation of a pseudo-rubbery plateau at temperatures up to ∼120 °C. Above this temperature, a sharp decline in the storage modulus (E') was observed, indicative of network dissociation. This behavior is attributed to the hydrogen bonding capability of the squaramide units that foster strong intermolecular associations among polymer chains. These supramolecular interactions result in a consistent cross-link density until the observed rapid decrease in E' occurs via hydrogen bond dissociation. Further evidence of the reversible cross-linking was demonstrated by the consistently lower magnitude of the elastic loss modulus (E'') compared to E', especially past the T_g (Figure S7).

Strain-sweep coupled with frequency-sweep experiments conducted at different temperatures (75, 100, and 125 °C) revealed a crossover point at 125 °C, signifying a transition from a viscoelastic solid ($G'' < G'$) to a viscoelastic fluid ($G'' > G'$), due to polymer chain (de)cross-linking (Figures S8 and S9). Remarkably, a high rubbery plateau modulus of 100 MPa was consistent with a dense network structure of **3d**, attributable to the high degree of connectivity and rigidity imparted by the intermolecular hydrogen bonding among the squaramide units.

The susceptibility of the supramolecular cross-links to dissociation at elevated temperatures was assessed through creep-recovery experiments at varying temperatures (80, 100, and 120 °C), applying a constant force (5 kPa) for 400 s, followed by a recovery period of 300 s. **3d** demonstrated exceptional creep resistance at temperatures lower than 120 °C (Figure 3b). At 80 and 100 °C, it exhibited maximum deformations of 1% and 35%, respectively, with high recoveries of 65% and 50%. Notably, at 120 °C, the deformation exceeded 100%, consistent with the sharp decrease in E' observed by DMA at temperatures above 120 °C (Figure 3a). These data suggest intermolecular association via the squaramide units imparts excellent creep resistance at temperatures below which the hydrogen bonds are stable.

The viscoelastic properties of **3d** were explored through stress-relaxation experiments (0.3% strain) across a temperature range of 60 to 120 °C (Figure 3c). The material effectively dissipated stress at all tested temperatures, offering evidence of the dynamic nature of squaramide associations. Using a single-component Maxwell model, the natural log of the characteristic relaxation time (τ) was plotted versus inverse temperature ($1/T$), according to the Arrhenius equation. The activation energy for viscous flow (E_a), derived from the slope of the Arrhenius plot, quantifies the temperature sensitivity of viscous flow. Figure 3d further illustrates the multi-modal viscoelastic behavior for **3d**, marked by a significant increase in viscous flow when heating from 60 to 90 °C ($E_{a,2}$ = 346 kJ/mol). Above 90 °C, the viscous flow behavior demonstrates a significantly lower temperature dependence ($E_{a,1}$ = 15.5 kJ/mol). We attribute this dramatic difference between the two flow regimes to the supramolecular network architecture, characterized by intermolecular hydrogen bonds between the squaramide motifs and their rapid dissociation at elevated temperatures. This dual-temperature responsivity, resulting from the equilibrium of associated and dissociated supramolecular cross-links, suggests potential utility in applications where high E_a could ensure robust dimensional stability at operating temperatures but a significant viscosity reduction at higher temperatures, allowing for on-demand (re)processing.

The ability of a material to undergo damage, heal, and be reprocessed holds significant value, especially for dynamic materials with high biomass content. The reprocessability of **3d** was examined through two additional destruction and compression (i.e., reprocessing) molding cycles. The samples were broken into small pieces and compression molded at 80 °C to produce the reprocessed samples. The resulting materials were analyzed by DMA and FTIR spectroscopy to assess any notable changes in their mechanical properties and chemical characteristics through successive reprocessing cycles. DMA revealed negligible changes in the rubbery plateau of E' or tan(δ), suggesting a consistent cross-linking density across multiple reprocessing cycles (Figure 4a).

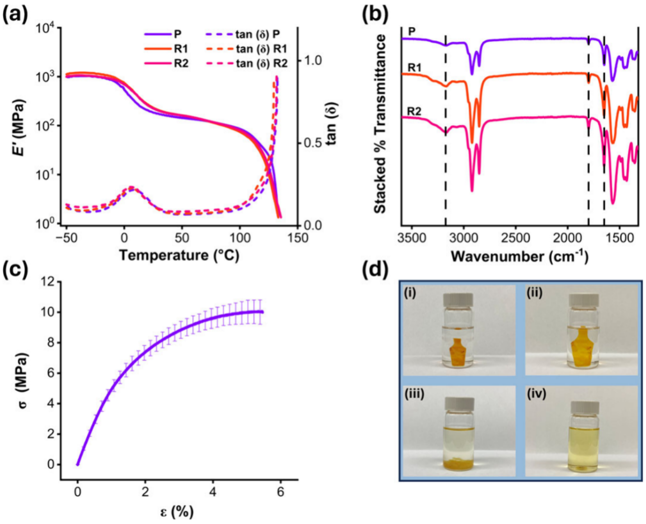

Figure 4. (a) Storage modulus (E') and tan(δ) for reprocessed samples over two compression cycles; (b) FTIR spectra of processed (P) and reprocessed (R) samples, showing retention of the squaramide stretching frequencies; (c) Stress−strain curves from tensile testing (strain rate = 5.0 mm/min until failure); and (d) Representative chemical degradation in the presence of *n*-butylamine in THF.

Additionally, FTIR analyses confirmed the presence of characteristic stretching frequencies of the squaramide motif in the reprocessed samples (Figure 4b). Notably, an increase in the intensity of the N−H stretching band was observed for the reprocessed samples, indicating the further formation of squaramides by the reaction of amine and squarate ester end-groups at elevated temperatures. The tensile properties of **3d** were also evaluated in triplicate, with specimens prepared by compression molding at 100 °C for 1 h under vacuum. At room temperature, **3d** exhibited good tensile strength and moderate extensibility, with an average stress (σ) and strain (ε)

at break of 10 ± 1.3 MPa and 5 ± 1.5%, respectively (Figure 4c).

A characteristic feature of dynamic networks is their potential for chemical degradation, facilitating efficient end-of-life management. Literature reports the successful chemical degradation of enaminone bonds in the presence of an excess of monofunctional amine.[39] To explore this, **3d** was swollen in tetrahydrofuran (THF) for 24 h, during which it showed no signs of dissolution or compromised structural integrity. However, adding *n*-butylamine led to a notable loss of structural integrity, culminating in dissolution of the polymer upon heating at 50 °C, albeit with some remaining insoluble solids. This experiment highlights the effective degradation of **3d** under relatively mild conditions, demonstrating its potential for chemical recycling (Figure 4d).

The step-growth synthesis of polysquaramides broadens the compositional scope of high-performance polymers and elucidates the intricate structure−property relationships inherent in these materials. By systematically varying monomer structure and stoichiometry, we have developed a modular platform that allows precise tuning of thermomechanical properties over a wide range. The distinction in intermolecular interactions between polymers derived from primary and secondary diamines demonstrates the influence of molecular architecture on viscoelastic behavior. The introduction of a polysquaramide with nearly 90% biomass content represents an opportunity for the integration of sustainability within high-performance materials. These findings contribute valuable insights to the domain of supramolecularly cross-linked networks and offer opportunities for the exploration of polysquaramides in applications demanding dynamic, environmentally friendly materials. Future research could explore the practical implications of these materials and investigate the long-term environmental benefits of integrating supramolecular reinforcement into bio-based polymeric materials.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsmacrolett.4c00383.

Instrumentation; Materials; Experimental Procedure; Supplementary figures (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Brent S. Sumerlin − *George and Josephine Butler Polymer Research Laboratory, Center for Macromolecular Science and Engineering, Department of Chemistry, University of Florida, Gainesville, Florida 32611, United States;* orcid.org/0000-0001-5749-5444; Email: sumerlin@chem.ufl.edu

Authors

Debabrata Konar − *George and Josephine Butler Polymer Research Laboratory, Center for Macromolecular Science and Engineering, Department of Chemistry, University of Florida, Gainesville, Florida 32611, United States*

Kevin A. Stewart − *George and Josephine Butler Polymer Research Laboratory, Center for Macromolecular Science and Engineering, Department of Chemistry, University of Florida, Gainesville, Florida 32611, United States*

Jack Moerschel − *George and Josephine Butler Polymer Research Laboratory, Center for Macromolecular Science and Engineering, Department of Chemistry, University of Florida, Gainesville, Florida 32611, United States*

John F. Rynk − *George and Josephine Butler Polymer Research Laboratory, Center for Macromolecular Science and Engineering, Department of Chemistry, University of Florida, Gainesville, Florida 32611, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsmacrolett.4c00383

Author Contributions

D.K. and J.M. synthesized and characterized the polymers by NMR, IR, TGA, DSC, and GPC. D.K. and K.A.S. performed DMA, shear, and oscillatory rheology experiments. K.A.S. performed stress relaxation experiments. B.S.S. directed the research and edited the manuscript. The manuscript was written through the contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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