

# Mechanically Gated Formation of Donor–Acceptor Stenhouse Adducts Enabling Mechanochemical Multicolor Soft Lithography

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**Mechanochromism is one of the most widely developed areas in the quickly emerging field of polymer mechanochemistry. Stress-sensitive molecules called mechanophores are designed to undergo productive chemical transformations in response to mechanical force including changes in color that are useful for sensing and patterning. A variety of mechanochromic mechanophores have been developed, but modulating the photophysical properties of the mechanically generated dyes generally requires the independent preparation of discrete derivatives. Here we introduce a mechanophore platform enabling mechanically gated multicolor chromogenic reactivity. The mechanophore is based on an activated furan precursor to donor–acceptor Stenhouse adducts (DASAs) masked as a hetero-Diels–Alder adduct. Mechanochemical activation of the mechanophore unveils the DASA precursor and subsequent reaction with a secondary amine generates an intensely colored DASA photoswitch. Critically, the color and photochemical properties of the DASA are controlled by the identity of the amine and thus a single mechanophore can be differentiated post-activation to produce a wide range of functionally diverse DASA compounds. We highlight the unique reactivity of this system by establishing the concept of mechanochemical multicolor soft lithography whereby a complex multicolor composite image is printed into a mechanochemically active elastomer through an iterative process of localized compression and reaction with different amines. Our results demonstrate the first example of multicolor pattern reproduction from a single mechanophore, empowering the fabrication of complex stimuli-responsive materials and paving the way for applications in patterning, sensing, and encryption.**

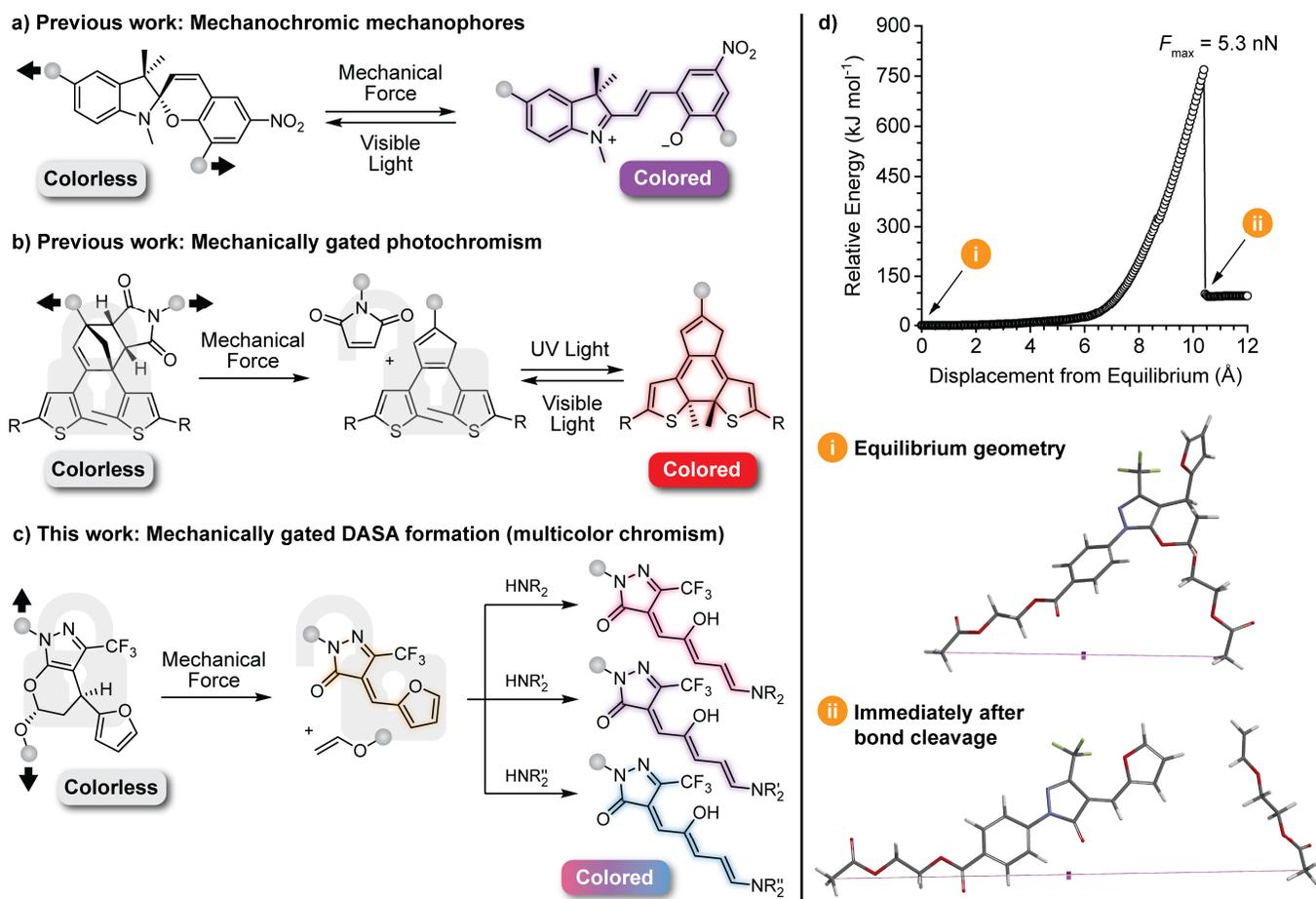
Covalent polymer mechanochemistry has enabled many exciting opportunities for the design of force-responsive polymeric materials.<sup>1,2</sup> Mechanical force typically leads to the degradation of materials by rupturing covalent bonds in the backbones of polymers. By covalently incorporating stress-sensitive molecules called mechanophores into polymer chains, however, force is transduced selectively to weak bonds in the mechanophore to elicit a productive chemical transformation.<sup>3</sup> Mechanical force is a ubiquitous and versatile stimulus that can be applied using a variety of methods including solution-phase ultrasonication,<sup>4</sup> focused ultrasound,<sup>5</sup> and tension, compression, or shear in solid polymeric materials.<sup>6–8</sup> The spatiotemporal control afforded by many mechanochemical activation techniques makes mechanical force an attractive stimulus for a wide range of materials applications including the release of small molecules,<sup>9</sup> structural transformations such as changes in conductivity<sup>10</sup> or crosslinking,<sup>11</sup> and changes in color or luminescence,<sup>6</sup> among many others.<sup>12</sup>

Mechanochromic mechanophores, in particular, have been widely developed as molecular force probes, empowering the visualization of critical stress and/or strain in materials.<sup>13</sup> These same attributes also make force-induced color changes in polymeric materials appealing for patterning and encryption. Pioneering research by Davis *et al.* demonstrated the force-induced ring-opening reaction of spiropyran in polymeric materials activated under tension and compression to generate a highly colored merocyanine dye (Fig. 1a).<sup>6</sup> While many different mechanochromic mechanophores have now been developed with a range of structures and reactivity, modulating the photophysical properties of the dyes typically requires distinct derivatives to be synthesized independently, which is a general limitation of this class of compounds. In an alternative approach to achieving mechanochromic functionality, our group developed the concept of mechanochemically gated photoswitching.<sup>14,15</sup> This strategy overcomes disadvantages of reversibility and a lack of mechanochemical specificity encountered with typical

mechanochromic mechanophores by using mechanical force to unmask a latent photoswitch, which is then converted to a colored species via a photoisomerization reaction (Fig. 1b). An enticing feature of this general molecular design strategy is that mechanochemical activation of the mechanophore is decoupled from the ultimate functional response, which provides a high degree of modularity to the system. Nevertheless, while the absorption properties of the dye can be modified by late-stage diversification of the mechanophore, several synthetic manipulations are still required to prepare each distinct polymer.<sup>15</sup> Moreover, the differential mechanochemical activation of mechanophores with intrinsically different reactivity has proved challenging in the solid state.<sup>16,17</sup>

Donor–Acceptor Stenhouse Adducts (DASAs) are a recently established class of highly modular, optically tunable, and robust visible-light photoswitches.<sup>18</sup> Since being introduced by Read de Alaniz and coworkers in 2014, DASAs have been widely developed and used in a variety of applications including sensing,<sup>19</sup> drug release,<sup>20</sup> and photoactuation.<sup>21</sup> Their synthetic accessibility and simple diversification coupled with excellent photophysical properties have driven their rapid adoption.<sup>22</sup> DASAs are derived from simple activated furan precursors that react with secondary amines to produce an intensely colored extended triene donor–acceptor scaffold with extinction coefficients around  $100,000 \text{ M}^{-1} \text{ cm}^{-1}$ .<sup>18</sup> Importantly, the color, stability, and photoswitching behavior of DASAs are strongly influenced by the identity of the secondary amine in addition to the electron-withdrawing acceptor group of the activated furan precursor.<sup>23,24</sup>

Similar to the approach employed for mechanically gated photoswitching, we hypothesized that a DASA precursor could be masked as a mechanochemically active hetero-Diels–Alder adduct (Figure 1c). In this case, a mechanically promoted retro-[4+2] cycloaddition reaction would reveal the activated furan, which could then be easily differentiated to generate a wide variety of highly colored and functionally diverse DASAs simply



**Fig. 1 | Evolution in the design of mechanochromic mechanophores and a platform enabling mechanically gated DASA formation.** (a) The reaction of a prototypical spiropyran mechanophore under mechanical force generates a colored merocyanine dye. (b) Mechanical force unmasks a diarylethene photoswitch via a retro-[4+2] cycloaddition reaction, gating the photoisomerization reaction that produces the colored ring-closed form. (c) Mechanically triggered retro-[4+2] cycloaddition reaction reveals an activated furan that reacts with a secondary amine to form a DASA photoswitch. (d) Density functional theory (DFT) calculations using the constrained geometries simulate external force (CoGEF) method predict the desired retro-[4+2] cycloaddition reaction upon mechanical elongation of a hetero-Diels–Alder adduct similar to the model in part (c) with a rupture force of 5.3 nN. Calculations were performed at the B3LYP/6-31G\* level of theory.

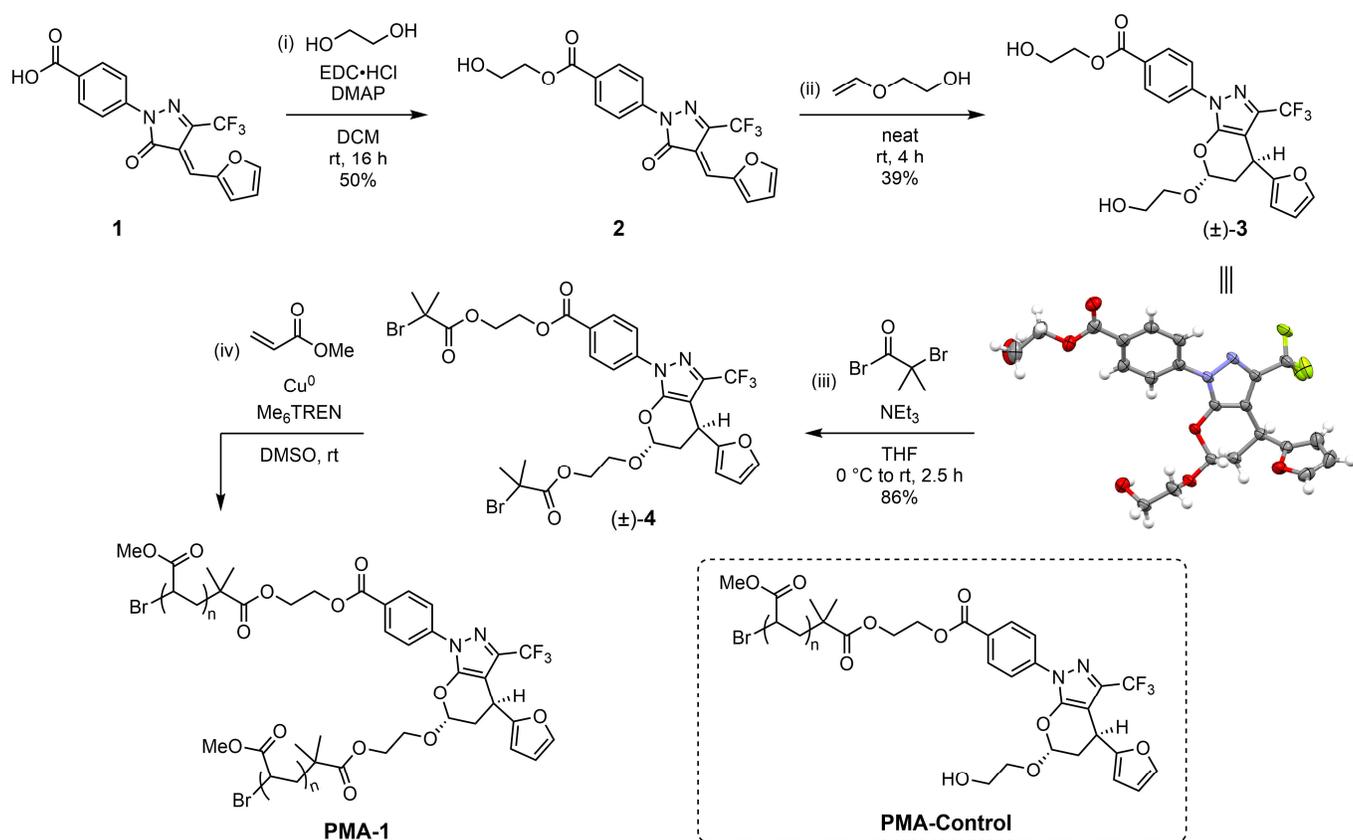
by treatment with different secondary amines. Here, we describe a unique mechanophore platform based on a masked DASA precursor that enables a mechanochemical multicolor chromogenic response. Mechanochemical activation is achieved in solution using ultrasonication and in solid polymeric materials under tension and compression. After mechanical activation, the addition of various secondary amines produces a chromogenic reaction leading to distinctly colored DASAs — all from a single mechanophore. We demonstrate the power of this mechanochemical platform by establishing the concept of mechanochemical multicolor soft lithography, whereby the iterative application of mechanical force and amine developer is used to print a complex multicolor image in an elastomeric polydimethylsiloxane (PDMS) film.

## Results and discussion

**Mechanophore Design and Synthesis.** We first identified a third-generation DASA photoswitch bearing a  $\text{CF}_3$ -pyrazolone acceptor, which shifts the thermal equilibrium of the DASA nearly completely to the triene (colored) form and provides excellent photophysical characteristics including high molar absorptivity.<sup>23</sup> Due to the electron deficiency of the activated

furan DASA precursor, we proposed that an inverse electron demand hetero-Diels–Alder reaction between the  $\alpha,\beta$ -unsaturated carbonyl of the pyrazolone and an electron-rich vinyl ether would generate the desired cycloadduct (see Fig. 1c).<sup>25</sup> The regiochemistry of Diels–Alder mechanophores is paramount in determining their force-sensitivity, with proximal polymer attachment points directing force more efficiently to a single scissile bond in the adduct.<sup>26</sup> Although only bicyclic mechanophores have been investigated, we anticipated that the electronically favored regioisomer would be mechanochemically competent. Indeed, DFT calculations using the constrained geometries simulate external force (CoGEF) method<sup>27</sup> predict that mechanical elongation of the hetero-Diels–Alder adduct results in the expected retro-[4+2] cycloaddition reaction to reveal the DASA precursor with an accessible rupture force of 5.3 nN (Fig. 1d).<sup>28</sup>

Following the successful computational prediction, synthesis of the putative mechanophore was accomplished in a straightforward fashion (Figure 2). Activated furan **1** was synthesized on gram scale in two steps from commercially available materials.<sup>21</sup> Next, carbodiimide coupling using EDC with ethylene glycol produced DASA precursor **2** in 50% yield,



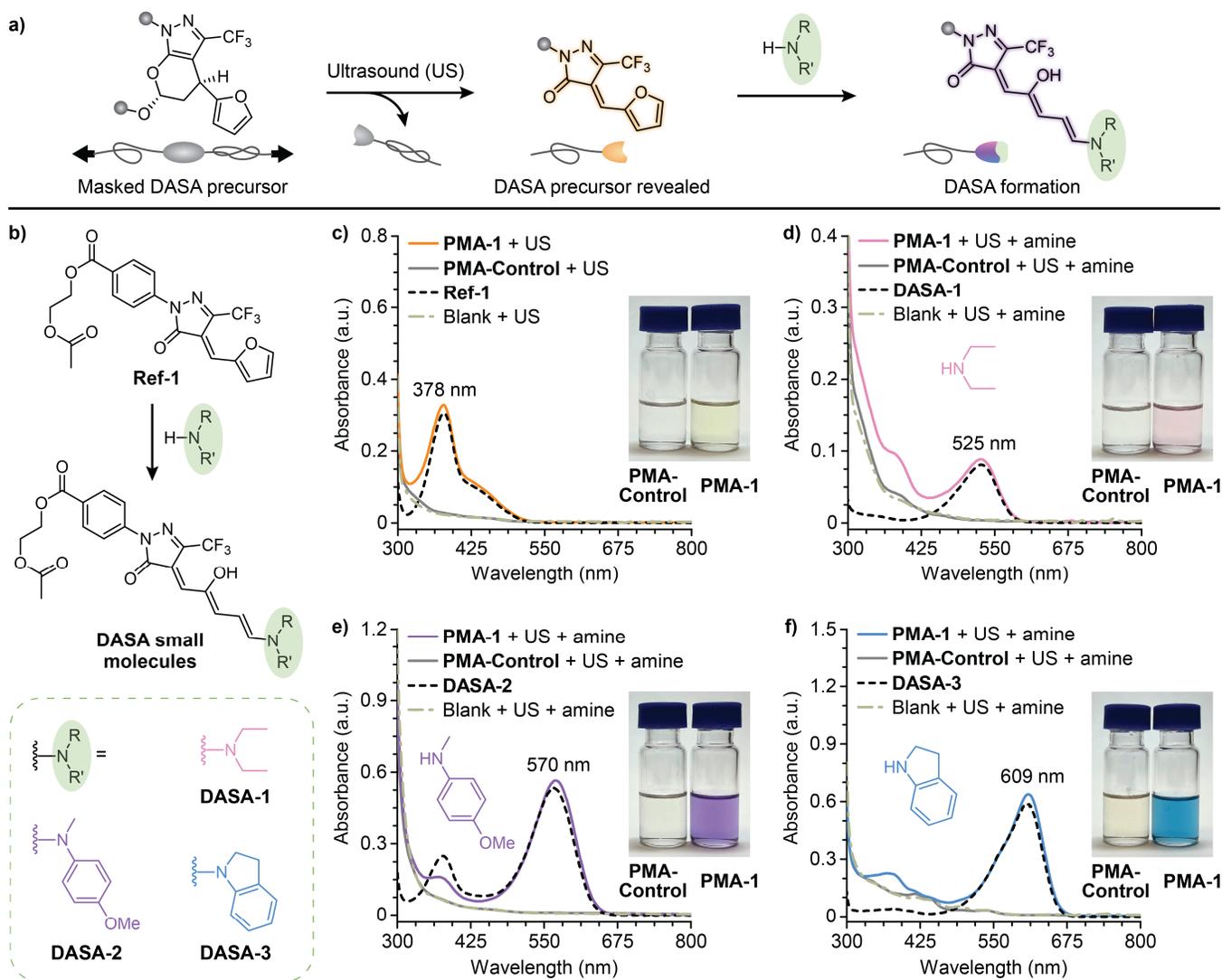
**Fig. 2 | Synthesis of linear poly(methyl acrylate) polymers containing the masked DASA precursor at the chain midpoint (PMA-1) and at the chain-end (PMA-Control) for ultrasonication experiments.** (i) Ethylene glycol (9.6 equiv.), *N*-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC•HCl, 1.2 equiv.), 4-dimethylaminopyridine (DMAP, 0.07 equiv.), CH<sub>2</sub>Cl<sub>2</sub>, room temperature, 16 h, 50%. (ii) Ethylene glycol vinyl ether (33 equiv.), room temperature, 4 h, 39%. (iii) α-Bromoisobutyryl bromide (4.4 equiv.), triethylamine (3.9 equiv.), tetrahydrofuran, 0 °C to room temperature, 2.5 h, 86%. (iv) Methyl acrylate (2030 equiv.), copper wire, tris[2-(dimethylamino)ethyl]amine (Me<sub>6</sub>TREN, 3.0 equiv.), dimethyl sulfoxide, room temperature, 1.5 h.

followed by an inverse electron demand hetero-Diels–Alder reaction with ethylene glycol vinyl ether to generate cycloadduct (±)-3 as a racemic mixture in 39% yield. The structure of the hetero-Diels-Alder adduct, which contains two terminal hydroxyl groups for further functionalization to facilitate its incorporation into polymers, was confirmed by single crystal X-ray diffraction. The thermal stability of (±)-3 was also confirmed by heating the compound in toluene-*d*<sub>8</sub> at 80 °C for 3 h, which resulted in negligible change to the <sup>1</sup>H NMR spectrum (Fig. S1). When dilute polymer solutions are subjected to ultrasonication, cavitation-induced solvodynamic shear results in the rapid extension of the polymers and mechanical force is maximized near the center of the chain.<sup>4</sup> Following conventional methods, diol (±)-3 was esterified with α-bromoisobutyryl bromide to afford (±)-4, which was used as a bis-initiator in the controlled radical polymerization of methyl acrylate to give mechanophore chain-centered poly(methyl acrylate) polymer **PMA-1** with *M*<sub>n</sub> = 125 kDa and *D* = 1.15. Separately, a derivative of (±)-3 containing a single α-bromoisobutyryl ester was used to synthesize control polymer **PMA-Control** incorporating the masked DASA precursor at the chain-end, which is not subjected to mechanical force during ultrasonication.

**Mechanochemical activation using solution-phase ultrasonication and chromogenic reactivity.** The reactivity of the masked DASA precursor in **PMA-1** was initially evaluated by

subjecting a dilute polymer solution (5 mg/mL in THF, 30 mM BHT) to 60 min of pulsed ultrasonication (6–9 °C, 1 s on/2 s off, 13.6 W cm<sup>-2</sup>) followed by treatment with various secondary amines (Fig. 3a). First, aliquots were removed during sonication at regular intervals for analysis by gel permeation chromatography (GPC) and UV–vis spectroscopy to characterize the mechanochemical transformation of the hetero-Diels–Alder adduct (Fig. S2 and S3). Ultrasound-induced mechanical activation of **PMA-1** results in the appearance of a new absorption peak at 378 nm that matches the absorption spectrum of small molecule reference compound **Ref-1** that was independently prepared to model the expected activated furan product (Fig. 3b and 3c). Furthermore, <sup>1</sup>H NMR spectra acquired after ultrasonication of **PMA-1** demonstrate the appearance of resonances corresponding to the retro-Diels–Alder products (Fig. S4). In contrast, no reaction was observed upon ultrasonication of **PMA-Control** under the same conditions, confirming that the reaction of the masked DASA precursor is mechanochemical in nature.

We next investigated DASA formation and the accompanying chromogenic response upon treatment of the mechanochemically generated DASA precursor with different secondary amines as illustrated schematically in Fig. 3a. Small molecule DASA model compounds **DASA-1**, **DASA-2**, and **DASA-3** were prepared by reaction of **Ref-1** with diethylamine, 4-methoxy-*N*-methylaniline, or indoline, respectively, for spectral comparison as before



**Fig. 3 | Characterization of mechanically gated DASA formation via solution-phase ultrasonication.** (a) Scheme illustrating mechanochemical activation upon ultrasonication (US) of a chain-centered polymer. Mechanical force induces the retro-[4+2] cycloaddition reaction producing the activated furan, which is converted to a highly colored DASA upon treatment with a secondary amine. (b) Structures of small molecule model compounds used as analytical references. (c–f) UV–vis absorption spectra of **PMA-1**, **PMA-Control**, or a blank solution after 60 min of ultrasonication. Samples were concentrated and then redissolved in 4:1 DCM/HFIP prior to addition of the indicated amine. Spectra of **PMA-1** after ultrasound-induced mechanical activation and amine addition match the spectra of the small molecule models, while similar treatment of **PMA-Control** does not lead to DASA formation. Photographs of the solutions of **PMA-Control** and **PMA-1** after addition of the amine.

(Figure 3b). The sonicated solution of **PMA-1** was concentrated and then redissolved in a 4:1 (v/v) mixture of dichloromethane (DCM) and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), which promotes DASA formation and stabilizes the triene (colored) form.<sup>29</sup> The addition of the same secondary amines as above to the mechanically-activated polymer solutions results in the generation of new absorption peaks that match the UV–vis absorption spectra of the corresponding DASA model compounds (Fig. 3d–f). Significantly, the colors of the DASA products derived from the same activated mechanophore vary widely from pink ( $\lambda_{\text{max}} = 525 \text{ nm}$ ) to purple ( $\lambda_{\text{max}} = 570 \text{ nm}$ ) to blue ( $\lambda_{\text{max}} = 609 \text{ nm}$ ) depending on the identity of the secondary amine used in the DASA-forming step. The absorption spectra recorded after the same treatment of **PMA-Control** are indistinguishable from the blanks in all cases, confirming that DASA formation proceeds

only after mechanochemical activation of the masked DASA precursor.

**Mechanochemical activation and chromogenic reactivity in solid polymeric materials.** After confirming the mechanochemical and chromogenic reactivity of the hetero-Diels–Alder mechanophore in solution, we sought to demonstrate mechanophore activation and DASA formation in bulk polymeric materials. Crosslinker ( $\pm$ )-**5a** and monofunctional control molecule ( $\pm$ )-**5b** equipped with two or one terminal vinyl group(s), respectively, were covalently incorporated into elastomeric PDMS materials (2.5 wt% loading) via platinum-catalyzed hydrosilylation (Fig. 4a and 4b, see SI for details).<sup>7</sup> The films were optically clear and colorless. Application of tensile force to a strip of **PDMS-1** containing the mechanophore as a



**Mechanochemical multicolor soft lithography.** The unique mechanically gated chromogenic reactivity of the mechanophore presents exciting opportunities for patterning soft materials. We envisioned an iterative process in which the localized application of compressive force using a stamp would reveal the DASA precursor with spatiotemporal precision and the pattern could be “developed” by subsequent treatment with an appropriate amine to generate the colored DASA photoswitch in the regions of mechanical activation. This process, which we refer to as Spatiotemporally Templated Activation for Mechanochemical Multicolor Printing, or STAMMP, is illustrated schematically in Fig. 4d for the production of a tricolor flower image using three different stamps and three different amines. To reproduce this sequence in the laboratory, a hydraulic press and 3D-printed stamps were used to print the composite image of a flower into a 4 cm<sup>2</sup> film of **PDMS-1** (Fig. 4e). First, a stamp embossed with a flower petal pattern was applied to the PDMS film, generating the yellow-colored DASA precursor in the regions of compression. Next, the film was immersed in a solution of diethylamine (0.5 vol% in DCM) for 90 s, converting the activated furan to the DASA and transforming the color of the petal pattern from yellow to purple. After rinsing the film repeatedly with DCM to remove excess amine and then drying *in vacuo*, the sequence was repeated using separate stamps to form the flower stem and the center of the flower, which were developed using indoline (blue) and 4-methoxy-*N*-methylaniline (green) in 9:1 DCM/HFIP, respectively. We note that the color of DASAs is strongly dependent on the environment.<sup>30</sup> As expected, the identical procedure applied to a film of **PDMS-Control** did not produce an image (Fig. 4f and S8). This demonstration illustrates the concept of mechanochemical multicolor soft lithography in which mechanical activation through localized compression reveals a DASA precursor that can be differentiated to generate a diverse range of DASA photoswitches in the same material simply by treatment with different amines.

## Conclusion

We have designed a mechanophore based on a masked DASA precursor that enables a mechanically gated multicolor chromogenic response in polymeric materials. Mechanical force supplied to the mechanophore via solution-phase ultrasonication or tension/compression in solid materials promotes a retro-Diels–Alder reaction to reveal an activated furan species. Subsequent reaction with a secondary amine produces an intensely colored DASA photoswitch. Significantly, the chromogenic response is highly dependent upon the identity of the secondary amine and thus a variety of DASAs with diverse photophysical and photochemical properties can be generated from a single mechanophore. We leverage the unique reactivity of this system to introduce the concept of mechanochemical multicolor soft lithography whereby a complex multicolor composite image is printed into a mechanophore-crosslinked elastomer through an iterative sequence of localized compression and amine development. This novel mechanochemical platform affords unprecedented control and modularity over dye formation using mechanical force and shows great promise for a diverse range of patterning, encryption, and sensing applications. Combined with the unique photoswitching properties of DASAs, we anticipate that this chemistry will empower the creation of new materials with complex stimuli-responsive functionality.

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#### Data Availability

All data are available in the manuscript or the Supplementary Information. Experimental data and characterization data for all new compounds prepared in the course of these studies are provided in the Supplementary Information of this manuscript. The X-ray crystallographic coordinates for compound ( $\pm$ )-**3** have been deposited at the Cambridge Crystallographic Data Center (CCDC) with deposition #2163133. These data can be obtained free of charge from the Cambridge Crystallographic Data Center via [www.ccdc.cam.ac.uk/structures/](http://www.ccdc.cam.ac.uk/structures/).

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#### Author Contributions

M.J.R. conceptualized the project and provided guidance during all stages. A.C.O. and M.J.R. designed the research. A.C.O. and W.G.R. performed the experiments. A.C.O., W.G.R., and M.J.R. analyzed the data. A.C.O. and M.J.R. wrote the manuscript.

#### Competing Interests

The authors declare no competing financial interests.

#### Additional Information

Supplementary information is available for this paper. Correspondence and requests for materials should be addressed to M.J.R. (mrobb@caltech.edu)