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Report Title

Final Report: Mechanochemical Activation of Small Ring Cyclopolymers

ABSTRACT

With the support of this award, we were able to explore mechanochemical activation of small ring cyclopolymers, which ultimately led to the discovery of flex activated mechanophores. These mechanophores take advantage of bond bending motions induced by polymer chain elongation, rather than more traditional bond stretching modes of activation. We found that flex activated mechanophores were uniquely capable of releasing small organic molecules upon activation, without bond scission occurring in the polymer main chain. Using this mechanophore design, we also demonstrated successive mechanophore activation upon consecutive loading cycles in an elastomeric material. In our investigation of other flex activated mechanophore designs, we embarked on related projects in the areas of triggered depolymerization and mechanochemistry of star polymers. Key results from these areas include mechanochemically- and thermally-triggered self-immolative polymers, a quantitative kinetic analysis of mechanical degradation of star versus linear polymers, and a practical approach for modeling chain scission in star polymers.

Enter List of papers submitted or published that acknowledge ARO support from the start of the project to the date of this printing. List the papers, including journal references, in the following categories:

(a) Papers published in peer-reviewed journals (N/A for none)

<u>Received</u>	<u>Paper</u>
08/27/2013	2.00 Andrew J. Boydston, Michael B. Larsen. "Flex-Activated" Mechanophores: Using Polymer Mechanochemistry To Direct Bond Bending Activation, <i>Journal of the American Chemical Society</i> , (06 2013): 8189. doi: 10.1021/ja403757p
08/30/2012	1.00 Gregory I. Peterson, Michael B. Larsen, Andrew J. Boydston. Controlled Depolymerization: Stimuli-Responsive Self-Immolative Polymers, <i>Macromolecules</i> , (08 2012): 0. doi: 10.1021/ma300817v
10/31/2014	5.00 Charles E. Diesendruck, Gregory I. Peterson, Heather J. Kulik, Joshua A. Kaitz, Brendan D. Mar, Preston A. May, Scott R. White, Todd J. Martínez, Andrew J. Boydston, Jeffrey S. Moore. Mechanically triggered heterolytic unzipping of a low-ceiling-temperature polymer, <i>Nature Chemistry</i> , (04 2014): 0. doi: 10.1038/nchem.1938
10/31/2014	6.00 Michael B. Larsen, Andrew J. Boydston. Successive Mechanochemical Activation and Small Molecule Release in an Elastomeric Material, <i>Journal of the American Chemical Society</i> , (01 2014): 0. doi: 10.1021/ja411891x
10/31/2014	7.00 Gregory I. Peterson, Andrew J. Boydston. Kinetic Analysis of Mechanochemical Chain Scission of Linear Poly(phthalaldehyde), <i>Macromolecular Rapid Communications</i> , (09 2014): 0. doi: 10.1002/marc.201400271
10/31/2014	8.00 Derek C. Church, Gregory I. Peterson, Andrew J. Boydston. Comparison of Mechanochemical Chain Scission Rates for Linear versus Three-Arm Star Polymers in Strong Acoustic Fields, <i>ACS Macro Letters</i> , (07 2014): 0. doi: 10.1021/mz5003068
10/31/2014	3.00 Gregory I. Peterson, Derek C. Church, Neal A. Yakelis, Andrew J. Boydston. 1,2-oxazine linker as a thermal trigger for self-immolative polymers, <i>Polymer</i> , (09 2014): 0. doi: 10.1016/j.polymer.2014.09.048
10/31/2014	4.00 Gregory I. Peterson, Andrew J. Boydston. Modeling the Mechanochemical Degradation of Star Polymers, <i>Macromolecular Theory and Simulations</i> , (07 2014): 0. doi: 10.1002/mats.201400045
TOTAL:	8

Number of Papers published in peer-reviewed journals:

(b) Papers published in non-peer-reviewed journals (N/A for none)

Received Paper

TOTAL:

Number of Papers published in non peer-reviewed journals:

(c) Presentations

248th National Meeting of the American Chemical Society, San Francisco, CA, August 2014. Seminar Title: Development of Flex Activated Mechanophores.

Collaborative Conference on Materials Research, Incheon, South Korea, June 2014. Seminar Title: Development of Flex Activated Mechanophores and Mechanically-Triggered Self-Immolative Polymers.

97th Canadian Chemistry Conference, Vancouver, B. C., June 2014. Seminar Title: Development of Flex-Activated Mechanophores for Non-Destructive Small-Molecule Release.

247th National Meeting of the American Chemical Society, Dallas, TX, March 2014. Invited Young Investigator Symposium (PMSE) Seminar Title: Mechanochemical Flex Activation and Mechano-Responsive Self-Immolative Polymers.

244th National Meeting of the American Chemical Society, Philadelphia, PA, August 2012. Seminar Title: Novel Responses in Polymer Mechanochemistry: Dual Activation and Force-Induced Rehybridization. Michael B. Larsen and Andrew J. Boydston.

Number of Presentations: 5.00

Non Peer-Reviewed Conference Proceeding publications (other than abstracts):

Received Paper

TOTAL:

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Number of Peer-Reviewed Conference Proceeding publications (other than abstracts):

(d) Manuscripts

Received Paper

TOTAL:

Number of Manuscripts:

Books

Received Book

TOTAL:

Received

Book Chapter

TOTAL:

Patents Submitted

“Thermally-Triggered Self-Immolative Polymers” Andrew J. Boydston, Neal A. Yakelis, Ronald Berenson, Derek C. Church, Gregory I. Peterson, Provisional U.S. Patent Application Filed on December 7, 2012.

Patents Awarded

Awards

Cottrell Scholar Award (Andrew Boydston)

Eastman Chemical Student Award in Applied Polymer Science (Michael Larsen)

Graduate Students

<u>NAME</u>	<u>PERCENT SUPPORTED</u>	Discipline
Greg Peterson	0.12	
Derek Church	0.15	
Mike Larsen	0.19	
Kelli Ogawa	0.01	
FTE Equivalent:	0.47	
Total Number:	4	

Names of Post Doctorates

<u>NAME</u>	<u>PERCENT SUPPORTED</u>
Chang-Uk Lee	0.03
FTE Equivalent:	0.03
Total Number:	1

Names of Faculty Supported

<u>NAME</u>	<u>PERCENT SUPPORTED</u>	National Academy Member
Andrew Boydston	0.06	
FTE Equivalent:	0.06	
Total Number:	1	

Names of Under Graduate students supported

<u>NAME</u>	<u>PERCENT SUPPORTED</u>	Discipline
Madeline Wong	0.04	chemistry
Dorothy Ackerman	0.00	chemsistry
Se-Ah Yoon	0.00	chemistry
Stephanie Wang	0.00	chemistry
Gedion Yitref	0.00	chemistry
FTE Equivalent:	0.04	
Total Number:	5	

Student Metrics

This section only applies to graduating undergraduates supported by this agreement in this reporting period

The number of undergraduates funded by this agreement who graduated during this period: 5.00

The number of undergraduates funded by this agreement who graduated during this period with a degree in science, mathematics, engineering, or technology fields:..... 5.00

The number of undergraduates funded by your agreement who graduated during this period and will continue to pursue a graduate or Ph.D. degree in science, mathematics, engineering, or technology fields:..... 5.00

Number of graduating undergraduates who achieved a 3.5 GPA to 4.0 (4.0 max scale):..... 4.00

Number of graduating undergraduates funded by a DoD funded Center of Excellence grant for Education, Research and Engineering:..... 0.00

The number of undergraduates funded by your agreement who graduated during this period and intend to work for the Department of Defense 0.00

The number of undergraduates funded by your agreement who graduated during this period and will receive scholarships or fellowships for further studies in science, mathematics, engineering or technology fields:..... 0.00

Names of Personnel receiving masters degrees

<u>NAME</u>
Total Number:

Names of personnel receiving PHDs

<u>NAME</u>
Total Number:

Names of other research staff

<u>NAME</u>	<u>PERCENT SUPPORTED</u>
FTE Equivalent:	
Total Number:	

Sub Contractors (DD882)

Inventions (DD882)

Scientific Progress

See Attachment

Technology Transfer

Andrew Boydston, Department of Chemistry, University of Washington, Seattle, WA 98195
Grant Number: W911NF-11-1-0289

Statement of the Problem Studied:

This Young Investigator Program award enabled research into the area of polymer mechanochemistry. A primary focus was to determine whether bond bending/flexing motions induced by tensile force within a polymer main chain could be used to activate mechanophores toward specific chemical reactivity. This deviation from traditional bond-stretching approaches to mechanophore activation ultimately gave rise to the first polymer mechanophore capable of fragmenting to release a small organic molecule and a preserved macromolecular structure. Moreover, the flex activation mechanism accomplishes scission of bonds that are not integral components of the polymer main chain, and therefore not directed elongated by tensile forces in the polymer. Other key investigations addressed basic research in the area of triggered depolymerizations and mechanochemical chain scission in star polymers.

Summary of Most Important Research Results:

Flex Activated Mechanophores

We have demonstrated the first example of a polymer mechanophore capable of fragmentation to release a small organic molecule from an intact macromolecular structure.¹ This is an important first step toward mechanoresponsive materials that can resist macroscopic failure upon application of mechanical load, yet still undergo bond scission that release small molecules such as therapeutics, catalysts, high-energy compounds, etc. This capability was realized through the design of a mechanophore that takes advantage of bond bending distortions induced along a polymer main chain under extensional force. The general design and envisioned mechanism is depicted in Figure 1, and involves an oxanorbornadiene-based mechanophore that is covalently linked to a macromolecular network through an ene-diester moiety. Elongation and linearization of the ene-diester moiety presumably facilitates cycloreversion via bond scissions orthogonal to the polymer main chain.

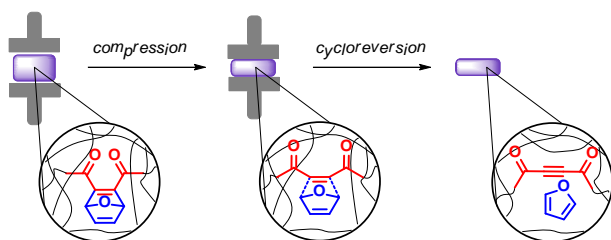
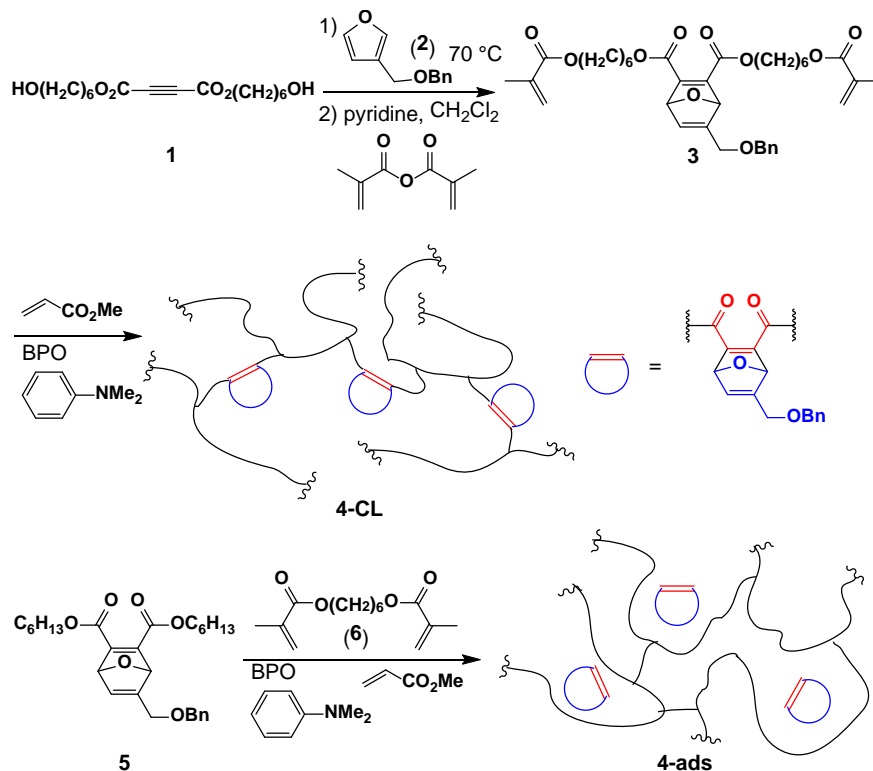


Figure 1. Generalized depiction of mechanophore activation via bond “flexing” motions induced by application of force.

We prepared two types of crosslinked networks each comprising oxanorbornadiene mechanophores (Scheme 1): one in which the mechanophore was used as a crosslinking unit that would experience extensional force upon application of stress, and another in which the mechanophore was adsorbed into a crosslinked material. Diol **1** was prepared from acetylene dicarboxylic acid and 1,6-hexanediol via Fischer esterification. Benzyl furfuryl ether (**2**) was chosen as the diene in place of furan to avoid issues of volatility with the latter. Diol **1** and furan **2** reacted smoothly via [4+2] cycloaddition to provide the corresponding oxanorbornadiene (not shown) in moderate yield. Subsequent reaction with methacryloyl anhydride furnished difunctionalized crosslinker mechanophore **3**. Formation of crosslinked network **4-CL** was prepared via radical polymerization and crosslinking. For a control comparison, we also prepared a mechanophore (**5**) incapable of functioning as a crosslinking unit during acrylate polymerization. For this control system, 1,6-hexanediol dimethacrylate (**6**) was used as a crosslinker to ultimately provide a material in which the oxanorbornadiene mechanophore was adsorbed into the material, but not covalently attached (**4-ads**).



Scheme 1. Synthesis of network with mechanophore crosslinking units (**4-CL**), and control network with grafted mechanophore units (**4-ads**).

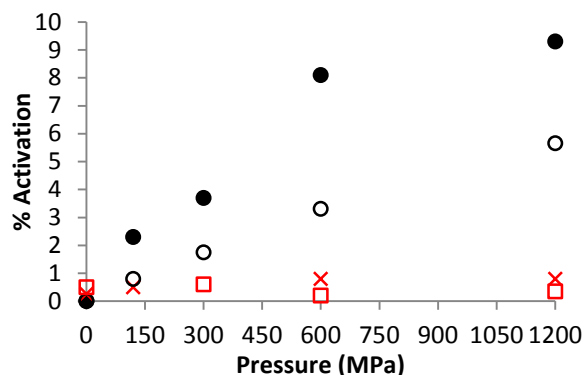


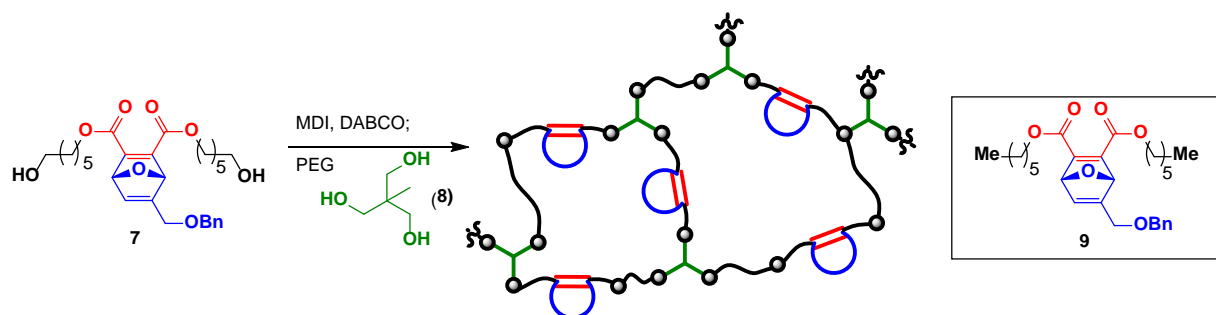
Figure 2. Plot of applied pressure versus activation of mechanophore, as judged by GC/MS analysis of soak solutions after compression of **4-CL** with 14 mol% **3** (●), **4-CL** with 5 mol% **3** (○), **4-ads** with 17 mol% **5** and 19 mol% **6** (×), and **4-ads** with 7 mol% **5** and 11 mol% **6** (□). Each data point is an average of two independent compression experiments.

To evaluate the mechanochemical reactivity of each network, we conducted compression experiments of each sample at different pressures. Without applied stress, no furan was observed indicating to us that no background amount of furan was released. Over the range of 0 to 1200 MPa of applied pressure, we observed a monotonic increase in the % activation of the crosslinked mechanophore for both samples of **4-CL**. While the same trend was observed for **4-CL** containing **5** and 14 mol% of mechanophore **3**, greater activation was observed from the network having a greater density of **3**. Compression of **4-CL** for 1 min at 600 MPa gave essentially the same % activation (3.0%) as a 30-min

compression (3.3%), consistent with mechanical activation mechanisms. Importantly, compression and analysis of each **4-ads** sample resulted in little or no activation, further supporting the mechanochemical origins of the cycloreversion reaction. These results suggested to us that released amounts of **2** detected in compression experiments could not be attributed to thermal or pressure-induced activation.

Notably, the compressive force necessary for mechanochemical transduction in crosslinked PMA led to macroscopic failure of the sample. As a result, the amount of activated mechanophore was limited to that achieved in a single compression, and the relative inability of the polymer matrix to withstand mechanochemically-relevant pressures limits its use in practical applications. Adaptation of this system to an elastomeric scaffold able to recover its initial shape after experiencing forces necessary for activation would enable multiple compression-activation cycles, thereby increasing the conversion of mechanophores in a dose-responsive fashion.

To obtain a material with a lower elastic modulus than the crosslinked PMA networks, we incorporated the flex activated mechanophore into an elastomeric segmented polyurethane network.² These networks comprise flexible polyether segments joined by short, hard diisocyanates and diol chain extenders, resulting in the phase separation between hard and soft segments responsible for their superior strength and elasticity. Toward this end, diol **7** was first reacted with an excess of methylene diphenyldiisocyanate (MDI) to form a diisocyanate-capped mechanophore (Scheme 2). Polymerization and crosslinking was effected via addition of dihydroxy-terminated poly(ethylene glycol) and triol **8** to the reaction mixture, resulting in full gelation of the network within 48 h. After curing at 30 °C, solid materials were obtained with a mechanophore concentration of 6.7 wt% (0.13 mmol of mechanophore 1 per gram of material), based upon the feed ratios. Comparison of analogous non-crosslinked (i.e., linear polymers) systems revealed excellent mechanophore stability during polymerization and curing. A control system was also prepared, in which mechanophore chain extender **7** was replaced by inert 1,6-hexanediol and mechanophore **9** was physically adsorbed into the material, thus enabling determination of the mechanical (as opposed to thermal or pressure-induced) activation.



Scheme 2. Synthesis of polyurethane networks.

The mechanochemical reactivity of each network cured at 30 °C was evaluated by subjecting each to compression in a hydraulic press at sustained pressures as indicated in Figure 5. After 1 min of sustained stress, the sample was placed in CH₂Cl₂ to facilitate diffusion of released small molecules. The CH₂Cl₂ solutions were then analyzed by GC-MS in the presence of an internal standard. Without applied stress, only a small amount of benzyl furfuryl ether was observed in the soak solution, corresponding to activation of roughly 1% of the incorporated mechanophores. As the pressure was increased in each subsequent experiment using fresh samples of the polyurethane material, we observed a monotonic increase in the % activation of the crosslinked mechanophore up 176 MPa of applied pressure. At higher pressures, we saw consistent % activation but no additional increase. Importantly, the control network only gave ca. 2% activation, and we observed no increase in the % activation with increasing pressure. Collectively, these results confirmed the mechanical origins of the cycloreversion reaction.

We next explored the feasibility of using multiple compressions to achieve iterative increases in the % mechanophore activation from the same sample of material. Samples were compressed at 35 or 88

MPa for 1 min, and pressure was then released and the sample was folded before subjecting to another 1-min compression. The process was repeated for each fresh sample until the target number of compressions was reached, at which point the sample was soaked in CH_2Cl_2 and the soak solution analyzed by GC-MS. As shown in Figure 6, we observed a discernible positive correlation between the number of compressions and the % activation. The amount gained with each compression began to diminish, which we speculate is likely due to a strain softening effect (see below). When compressed at either 35 or 88 MPa, increases in activation were apparent up to 9 compression-activation cycles, reaching a maximum of 6 – 7% activation. The material clearly resisted permanent physical deformation, as shown in Figure 7. In comparison, however, no increase in % activation was observed for > 1 compression when using the previously reported PMA networks, nor the polyurethane control networks containing **9**.

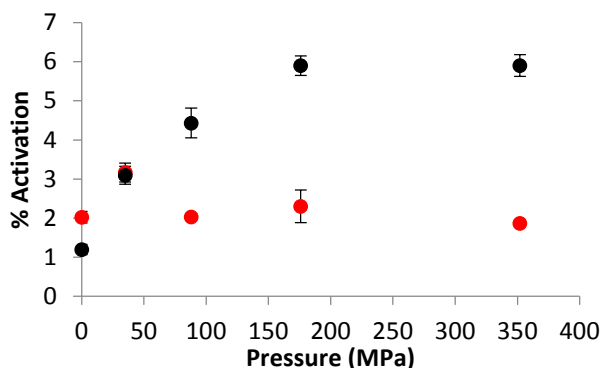


Figure 5. Plot of applied pressure versus activation of crosslinking (●) and control (●) mechanophore, as judged by GC-MS analysis of soak solutions after compression. Error bars represent standard deviations.

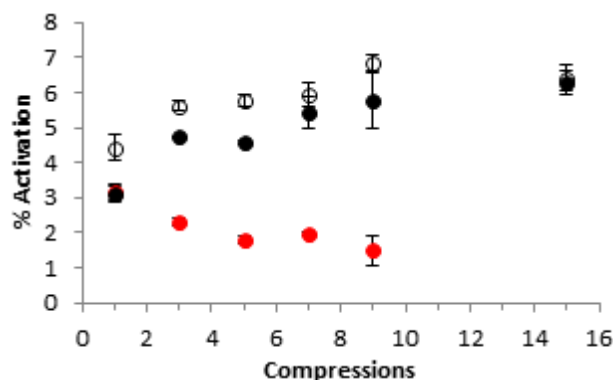


Figure 6. Plot of % activation of mechanophores versus number of successive compressions (1 min each) at 35 (●) and 88 MPa (○). Control network (●) was compressed at 35 MPa. Error bars represent standard deviations.

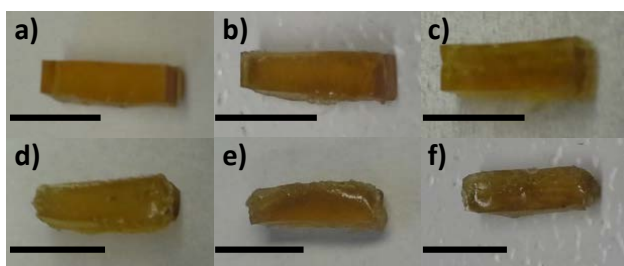


Figure 7. Polyurethane material after compressions at 35 MPa. Images a) through f) were taken after 0, 1, 3, 5, 7, and 9 compressions, respectively, of the same sample piece. Scale bars = 5 mm.

Mechanochemically-Triggered Self-Immolative Polymers

We have also explored the ability to trigger depolymerization of a low ceiling temperature (T_c) polymer, poly(phthalaldehyde) (PPA).^{3,4} The successful mechanochemical chain scission and rapid subsequent depolymerization signifies the ability to: 1) have an amplified response to a mechanochemical reaction, 2) reconfigure a material from macromolecular to small molecule, and 3) depolymerize in such a way that true monomeric species are produced, thus potentiating repolymerization into macromolecular forms. We prepared linear PPA via phosphazine super base mediated polymerization using propargyl alcohol as initiator and TBS-Cl as an end-capping agent. Mechanochemical chain scission was accomplished in solution using ultrasonic irradiation (13.7 W/cm² and an internally monitored temperature between 10 and 15 °C). As shown in Figure 8, we observed a gradual decrease in PPA concentration and number average molecular weight (M_n) as a function of sonication time for an initially 32 kDa ($\mathcal{D} = 1.6$) PPA sample.

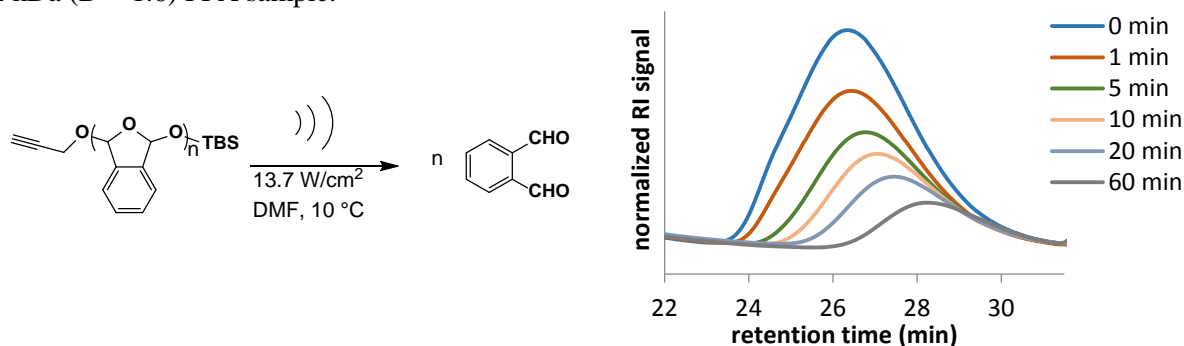


Figure 8. GPC traces of 32 kDa PPA with increasing sonication time. Times indicate total “on time” of ultrasound using a duty cycle of 1 s on, 9 s off. A 200 kDa polystyrene internal standard (3.0 mg/mL) was added to each sample prior to injection for RI normalization and retention time referencing.

We next determined rate constants for activation as a function of PPA molecular weight. The absence of lower molecular weight byproducts, combined with the sonication of a polydisperse sample, enabled us to determine rate constants of activation for multiple molecular weight ranges from a single sonication experiment. We analyzed a PPA sample with $M_n = 27$ kDa and $\mathcal{D} = 1.5$. Sectional analysis using 5 kDa ranges between 35 and 75 kDa was performed on each GPC trace taken throughout the sonication experiment, using the area of each section (determined by RI signal intensity) as an indication of residual PPA of the corresponding M_n . First-order plots were prepared for each M_n (Figure 9). A linear dependence of the rate constant on molecular weight was observed over the range of 35 to ca. 65 kDa.

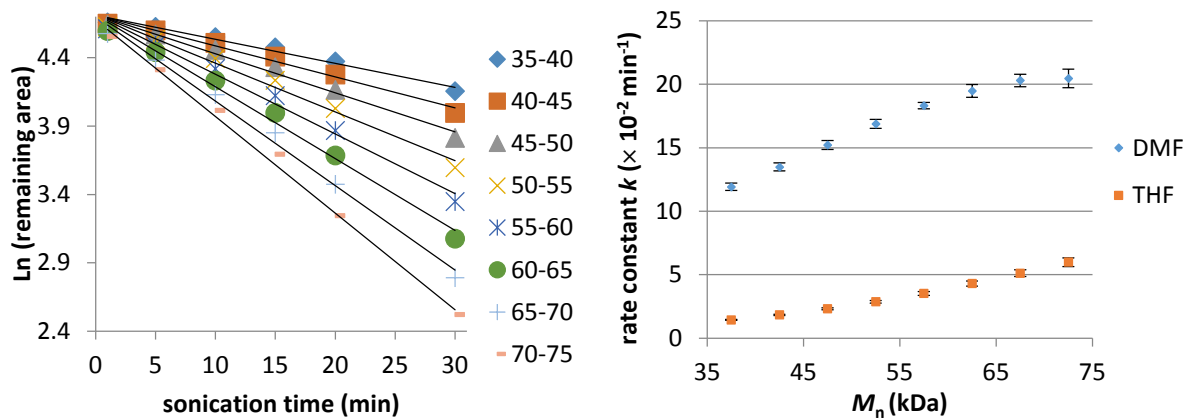
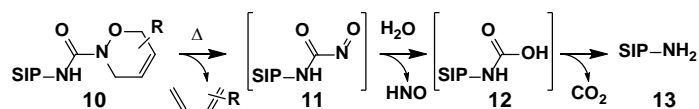


Figure 9. (left) Representative example of a set of first-order plots for molecular weight sections analyzed via GPC. The R^2 values for each M_n range are as follows: 35-40, 0.9817; 40-45, 0.9826; 45-50, 0.984; 50-55, 0.9856; 55-60, 0.9876; 60-65, 0.99; 65-70, 0.9929; 70-75, 0.9956. (right) Plot of rate constant vs M_n (average of three runs with error bars indicating one standard deviation).

Thermally-Triggered Self-Immolative Polymers

Additional efforts toward achieving triggered depolymerizations revealed 1,2-oxazines as viable thermally-responsive triggers for self-immolative polymers (SIPs).⁵ The envisioned mechanism of action, from responsive SIP diblock **10** to activated SIP with electron-rich end group (**13**) is depicted in Scheme 3. Thermal cycloreversion of the oxazine moiety was expected to liberate carbamoylnitroso species **11**, which would be subject to rapid hydrolysis to give **12**. Decarboxylation would ultimately give the activated SIP **13**.



Scheme 3. Proposed Mechanism of Action of a Thermally-Activated SIP Trigger

We considered polyurethane-based SIPs derived from *p*-aminobenzyl alcohol to be an attractive and versatile platform since they can be readily adapted for small-molecule release from side chain functionalities, turn-on fluorescence reporting, and solubility in water. We were able to install the oxazine unit at the junction of an AB diblock copolymer (**14**), achieving an overall *A-trigger-B* architecture. We also prepared a control system (**15**) absent the oxazine trigger to assess the relative contributions of hydrolysis to the overall depolymerization (Figure 10). To avoid complications arising from insolubility of the SIP block after detachment from the PDMA, we conducted thermal triggering and depolymerization experiments in DMSO-*d*₆/D₂O mixtures (9:1 v/v). Figure 10 shows the amount of SIP depolymerization over time as **14** and **15** were each heated at various temperatures. At RT, we observed gradual activation leading to 22% depolymerization after 65 d. As expected, at 40 °C more rapid activation and depolymerization was observed, reaching 61% depolymerization after ca. 71 d. At 60 and 85 °C, nearly full depolymerization was observed after ca. 47 and 5 d, respectively. We observed only 17% or 18% depolymerization when **15** was heated at RT or 40 °C for 81 d, respectively. At 60 and 85 °C, the rate of depolymerization was clearly much less for **15** than for the oxazine trigger variant (**14**), consistent with different mechanisms of activation between the two. The results from the control polymer suggest that hydrolysis plays a fairly significant role in the degradation of the SIP above 60 °C.

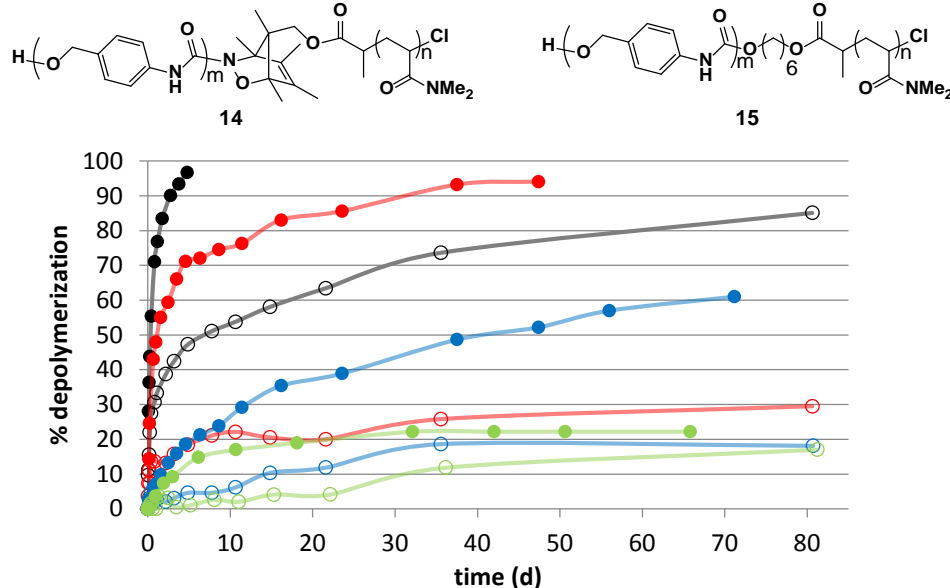


Figure 10. Thermal activation and depolymerization of SIPs **14** (filled circles) and **15** (empty circles) in DMSO-*d*₆/D₂O (9:1 v/v) at 85 °C (●,○), 60 °C (●,○), 40 °C (●,○), and RT (●,○). The % depolymerization = 100 - % SIP repeat units remaining, as determined by ¹H NMR spectroscopy using 1,4-dicyanobenzene as an internal standard. Average of two runs. The colored lines are for visual aid only

Comparison of Mechanochemical Chain Scission in Linear and Three-Arm Star Polymers

Our previous reports described investigations into the mechanochemical reactivity of three-arm star polymer built upon an isocyanurate core. We have since found the isocyanurate to be mechanochemically inert under our ultrasonication conditions. This result led us to consider how the overall structure and molecular weight distribution of a polymer influence mechanochemical transduction.⁶ To probe this, we synthesized complementary linear and three-arm star polymers in which the single arm building blocks can be thought of as 20- or 30-kDa units, thus achieving approximately 40, 60, and 90 kDa polymers varying in structure between linear and three-arm architectures. Specific structures are depicted in Figure 11. The notations are **S** for star, **L** for linear, and subscripts indicate either a planar (p) or tetrahedral (t) core geometry followed by the M_n (kDa) of the polymer. Each linear and star polymer was subjected to sonication in DMF, and aliquots were analyzed by gel-permeation chromatogram (GPC) over time (Figure 12, left is a representative example). Kinetic analyses were conducted by following the refractive index (RI) signal intensity of a single section (retention time) of the insipient portion of the GPC over the course of the sonication experiment. Monitoring the RI signal intensity at that retention time over the course of the sonication experiment provided a first-order rate constant (k_{RI}) for the consumption of the polymer species. Fitting

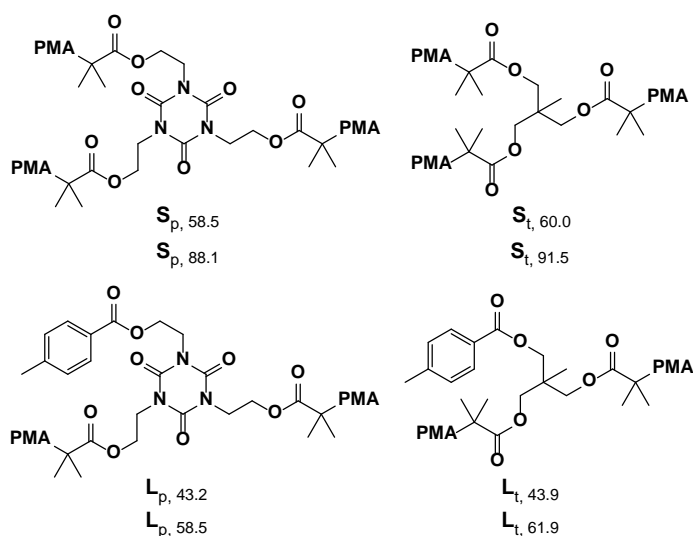


Figure 11. Structures of star and linear polymers used in this study. For each polymer, $\bar{D} < 1.1$.

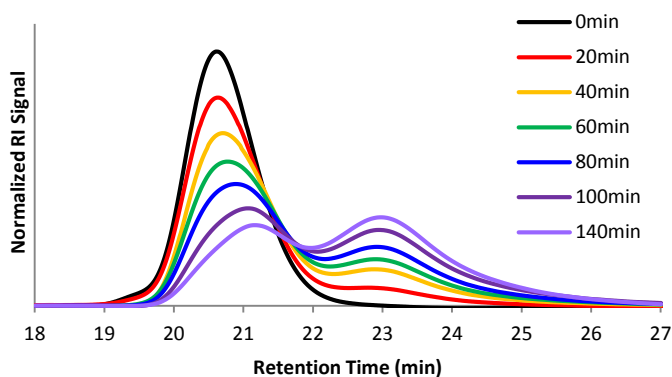


Figure 12. (Left) GPC traces of S_{t,60.0} during ultrasonication. Sonication conditions: polymer concentration of 5 mg/mL in DMF, 13.8 W/cm², duty cycle of 1 s on 9 s off.

Applying the same sonication conditions and analyses to each of the polymers in the series provided k_{RI} values as listed in Table 1. The trends are consistent with the rate of chain scission being dictated by the arm molecular weight (M_{arm}) as opposed to the total molecular weight (M_{total}) of the polymer. While two sequential chain scission events are operative in the mechanochemical degradation of three-arm star polymers, k_{RI} for consumption of each star polymer closely matches that of the corresponding linear counterpart of equal M_{arm} . For polymers with M_{arm} of ca. 20 kDa, k_{RI} were all similar, ranging from 1.02 to $1.26 \times 10^{-2} \text{ min}^{-1}$. The same general trend was observed from the polymers bearing ~ 30 kDa arms, with k_{RI} clustered between 2.38 and $2.66 \times 10^{-2} \text{ min}^{-1}$.

Table 1. Summary of k_{RI} for mechanochemical chain scission of three-arm star and linear polymers.

Polymer	M_{total} (kDa)	M_{arm} (kDa)	$k_{\text{RI}} (\times 10^{-2} \text{ min}^{-1})$
S _{p,58.5}	58.5	19.5	1.07 ± 0.01
S _{t,60.0}	60.0	20.0	1.16 ± 0.06
L _{p,43.2}	43.2	21.6	1.26 ± 0.03
L _{t,43.9}	43.9	21.9	1.25 ± 0.08
<hr/>			
L _{p,58.5}	58.5	29.2	2.38 ± 0.12
S _{p,88.1}	88.1	29.3	2.62 ± 0.09
S _{t,91.5}	91.5	30.5	2.90 ± 0.10
L _{t,61.9}	61.9	30.9	2.63 ± 0.06

^a M_{total} (M_n values) determined by GPC analysis using multi-angle laser light scattering (MALS) to give M_w values from which M_n values were calculated. M_{arm} were assumed to be one-third M_{total} for stars, and one-half M_{total} for linear polymers. Rate constants were calculated from linear regression of the RI signal intensity at the M_p retention time of the virgin sample versus ultrasonication “on time” and are an average of three runs \pm one standard deviation. The dashed line segregates 20- and 30-kDa M_{arm} polymers.

To investigate site-selective mechanophore activation as a function of polymer shape, we also prepared and analyzed a linear (**L**_{DA, 61.6}) and star polymer (**S**_{DA, 85.9}) pair that each contained an anthracene-maleimide Diels-Alder adduct mechanophore (Figure 13). Importantly, the average M_{arm} was similar in each polymer. The mechanophore, which has been extensively studied by Bielawski and coworkers, is capable of mechanochemical UV-vis and photoluminescence (PL) “turn-on” response upon mechanically-facilitated cycloreversion to generate an anthracene moiety.

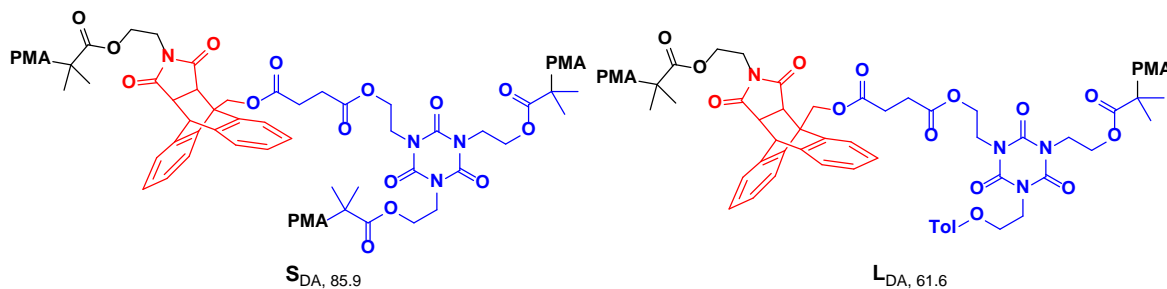


Figure 13. Mechanophore-containing star (**S**_{DA, 85.9}) and linear (**L**_{DA, 61.6}) polymers.

After subjecting **L**_{DA, 61.6} and **S**_{DA, 85.9} each to sonication as described above, the formation of anthracene was confirmed by UV-vis and photoluminescence (PL) spectroscopies. Monitoring the consumption of initial polymer via GPC-RI to give k_{RI} , and production of anthracene via PL spectroscopy (to give k_{PL}), provided corroborating data for consistent chain scission rate constants

between the two polymer structures. As in the previous series, we found k_{RI} for the linear and star analogues to be very similar, consistent with their similar M_{arm} values (Table 2). Additionally, the k_{PL} values for each polymer were also similar to one another, and to the k_{RI} values. The similarity between the k_{RI} and k_{PL} values is consistent with high selectivity for initial chain scission occurring at the mechanophore.

Table 2. Rate constants for mechanochemical chain scission for $S_{DA, 85.9}$ and $L_{DA, 61.6}$.^a

Polymer	M_{total} (kDa)	M_{arm} (kDa)	$k_{RI} (\times 10^{-2} \text{ min}^{-1})$	$k_{PL} (\times 10^{-2} \text{ min}^{-1})$
$S_{DA, 85.9}$	85.9	28.6	3.13 ± 0.11	3.24 ± 0.23
$L_{DA, 61.6}$	61.6	30.8	3.27 ± 0.38	3.26 ± 0.09

^a M_{total} (M_n values) determined by GPC analysis using MALS to give M_w values from which M_n values were calculated. M_{arm} were assumed to be one-third M_{total} for stars, and one-half M_{total} for linear polymers. Rate constants calculated from linear regression of the RI signal intensity at the M_p retention time of the virgin sample versus ultrasonication “on time” for k_{RI} , and from a linear regression of the PL intensity at 411 nm ($\lambda_{ex} = 360$ nm) for k_{PL} . Rate constants are an average of three runs \pm one standard deviation.

Modeling of Mechanochemical Chain Scission in Star Polymers

We developed a model to predict the molecular weight distributions of star polymers having arms of equal length,⁷ the following general formula is provided:

$$f_n(t+1, M) = \frac{\left\{ \sum_{a=3}^n \frac{(N+t)S^a(t, M) - P_{Sa}(t, M) + \left\{ \sum_{y=M+1}^{\infty} P_{Sa}(t, y) Q_{Sa_1}(y, M) \right\} + \left\{ \sum_{y=M+1}^{\infty} P_{Sa}(t, y) Q_{Sa_2}(y, M) \right\}}{N+t+1} \right\} + \frac{(N+t)L_n(t, M) - P_{Ln}(t, M) + 2 \left\{ \sum_{y=M+1}^{\infty} P_{Ln}(t, y) Q(y, M) \right\}}{N+t+1}}{N+t+1} \quad (1)$$

Here, n and a are the number of arms and the Q_{Sa} distributions are equal to:

$$Q_{Sa_1}(y, M) = \frac{1}{ry\sqrt{2\pi}} e^{\left(-\frac{\left(M - \frac{y}{a} \right)^2}{2r^2y^2} \right)} \quad (2)$$

and

$$Q_{Sa_2}(y, M) = \frac{1}{ry\sqrt{2\pi}} e^{\left(-\frac{\left(M - \frac{y}{a} \right)^2}{2r^2y^2} \right)} \quad (3)$$

The P_{Sa} distribution is equal to:

$$P_{Sa}(t, M) = C(t) \left(\frac{2}{a} (M - M_{lim}) \right)^S S_a(t, M) \quad (4)$$

Each P distribution needs the same normalization coefficient, $c(t)$, such that the sum of all P distributions equals unity. We anticipated that this model would be able to accurately predict the MWDs of n -arm star polymer degradation. To verify this model, we modeled the distributions of 86 and 62 kDa three-arm star polymers undergoing mechanochemical degradation via ultrasonication (Figure 14B and 14D). As shown in Figure 14, the predicted MWDs for both star polymers are visually in good agreement with the experimental findings. Additionally, as shown in Figure 15, the predicted M_n for each MWD closely matches those of the experimental results for each polymer. Molecular weight comparisons were made assuming that each sequential $f_n(t, M)$ distribution corresponded to about 5 min or 9 min of sonication time for the 86 and 62 kDa polymers, respectively.

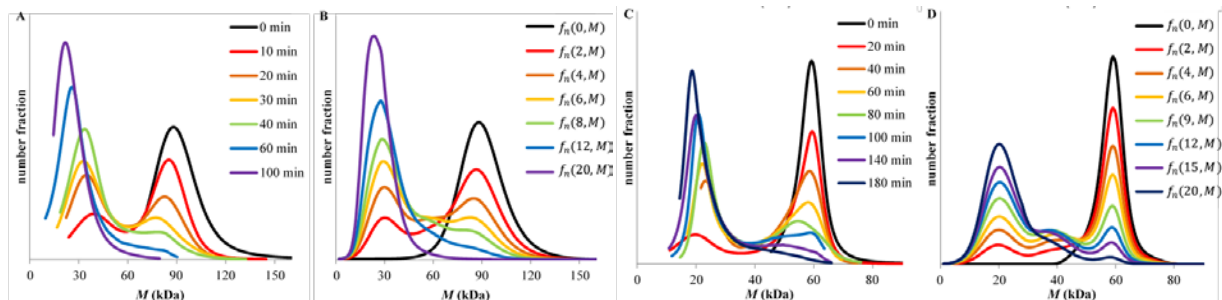


Figure 14. (A) Number fraction plots for a 86 kDa PMA undergoing ultrasonic degradation at various time points; (B) Predicted MWDs for the same polymer using the three-arm degradation model ($r = 0.1$, $M_{\text{lim}} = 28$ kDa, $N = 8$); (C) Number fraction plots for a 62 kDa PMA undergoing ultrasonic degradation at various time points; (D) Predicted MWDs for the same polymer using the three-arm degradation model ($r = 0.1$, $M_{\text{lim}} = 28$ kDa, $N = 14$).

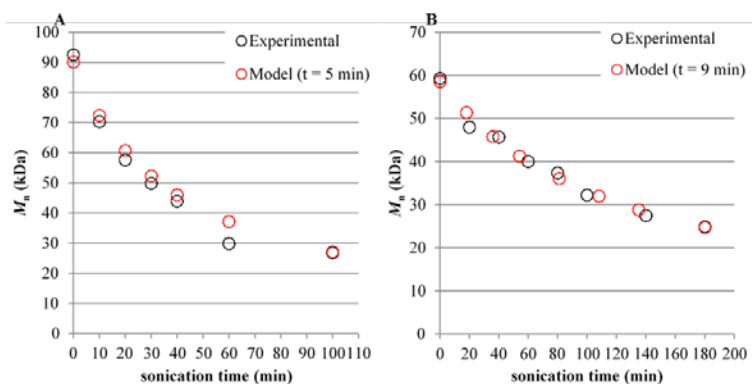


Figure 15. Experimental and predicted M_n values for the ultrasonic degradation of a (A) 86 kDa three-arm star polymer and (B) 62 kDa three-arm star polymer. The predicted M_n values were calculated from the $f_n(t, M)$ distributions assuming that t corresponded to approximately 5 min (for the 86 kDa star polymer) or 9 min (for the 62 kDa star polymer) of sonication time.

Bibliography

- 1) Larsen, M. B.; Boydston, A. J. *J. Am. Chem. Soc.* **2013**, *135*, 8189-8192.
- 2) Larsen, M. B.; Boydston, A. J. *J. Am. Chem. Soc.* **2014**, *136*, 1276-1279.
- 3) Diesendruck, C. E.; Peterson, G. I.; Kulik, H. J.; Kaitz, J. A.; Mar, B. D.; May, P. A.; White, S. R.; Martínez, T. J.; Boydston, A. J.; Moore, J. S. *Nature Chem.* **2014**, *6*, 623-628.
- 4) Peterson, G. I.; Boydston, A. J. *Macrol. Rapid Commun.* **2014**, *35*, 1611-1614.
- 5) Peterson, G. I.; Church, D. C.; Yakelis, N. A.; Boydston, A. J. *Polymer*, in press (DOI: 10.1016/j.polymer.2014.09.048).
- 6) Church, D. C.; Peterson, G. I.; Boydston, A. J. *ACS Macro Lett.* **2014**, *3*, 648-651.
- 7) Peterson, G. I.; Boydston, A. J. *Macromol. Theory Simul.* **2014**, in press (DOI: 10.1002/mats.201400045).