

Bicyclo[3.2.0]heptane Mechanophores for the Non-scissile and Photochemically Reversible Generation of Reactive Bis-enones

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S Supporting Information

ABSTRACT: Force-induced transformations of polymer-bound functionalities have the potential to produce a rich array of stress-responsive behavior. One area of particular interest is the activation of non-scissile mechanophores in which latent reactivity can be unveiled that, under the appropriate conditions, could lead to constructive bond formation in materials exposed to typically destructive stress. Here, the mechanical activation of a bicyclo[3.2.0]heptane (BCH) mechanophore is demonstrated via selective labeling of bis-enone products. BCH ring-opening produces large local elongation (>4 Å) and products that are reactive to conjugate additions under mild conditions. Subsequent photocyclization regenerates the initial BCH functionality, providing switchable structure and reactivity along the polymer backbone in response to stress and visible light.

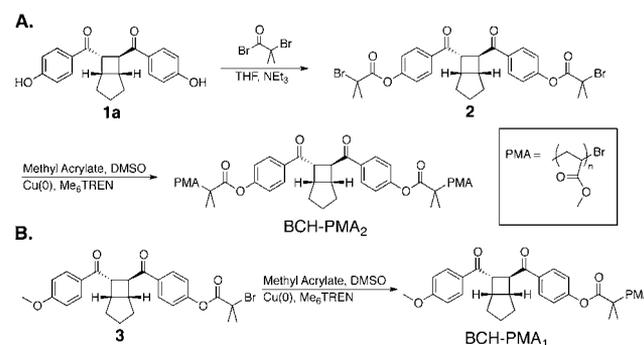
Mechanochemically active polymers have the potential to create a new generation of stress-responsive and self-healing materials.^{1,2} It has been proposed that stress-induced degradation of polymer chains on the molecular level, a mechanism that contributes to failure in bulk materials, could potentially be attenuated by incorporating latent reactive groups that can elicit constructive bond-forming reactions in regions of high stress. Additionally, non-scissile mechanochemical ring-opening events may create “on-demand” regions of local slack under applied mechanical load, thus preventing catastrophic failure.^{3,4} Many examples of stress-responsive mechanophores have been reported,^{5–15} and they have proved invaluable in studying the rich array of reactivity and stereochemical outcomes available through mechanochemistry. Despite this progress, most mechanophores to date, when activated, result in scission of their parent polymer chain. Examples of non-scissile mechanophores include benzocyclobutenes (BCBs),^{5,6} binols,⁷ epoxides,¹⁶ cyclobutene molecular force probes,¹⁷ and *gem*-dihalocyclopropanes (gDHCs).¹³ These generally offer only modest (1–2 Å) and sometimes transient extensions, and only select gDHCs and cyclobutenes generate products with both good stability and significant elongations.

We therefore set out to construct a non-scissile mechanophore with substantial stored length and a stable activation product that is cross-reactive with uncharged reagents. The extensive palette of existing scissile mechanophores provided a rich set of reactivities from which to draw inspiration. In particular, we took note of the recent report by Moore,¹⁸ in

which cyclobutenes were mechanically cleaved to enones. We hypothesized that the mechanophores could be converted from scissile to non-scissile by incorporating them into a fused, bicyclic framework such as a bicyclo[3.2.0]heptane (BCH). In addition to non-scissile behavior and good product reactivity, we envisaged that this design would give large extensions compared to the aforementioned examples, as well as allow for new, two-way switching behavior via photochemical reversion of the bis-enone products to the starting BCH mechanophore. Here, we report the synthesis and mechanochemical activation of a BCH mechanophore. Features of this system include non-scissile activation, generation of reactive enones, large local elongation, and photochemical reversibility.

To access the BCH architecture, we looked to the simple and efficient synthesis of such molecules by Yoon.¹⁹ Bisphenol **1a** was reacted with α -bromoisobutyryl bromide to yield **2**, a BCH-centered difunctional initiator (Scheme 1A). Reaction of

Scheme 1. Synthesis of BCH-Linked PMA via SET-LRP of Di-initiator **2, and End-Functional Control BCH-PMA₁**



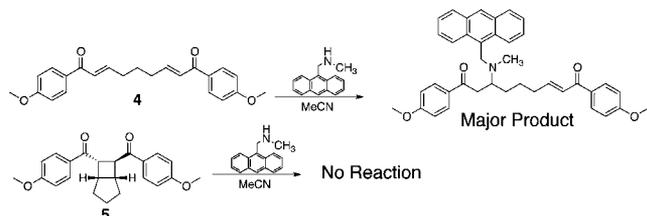
2 under standard SET-LRP conditions^{20,21} resulted in chain-centered BCH-PMA_{2,N} (PMA = poly(methyl acrylate)) with various molecular weights ($N = MW$). Additionally, a similar strategy was used to access monofunctional initiator **3**, for the synthesis of end-functional control polymer BCH-PMA₁ (Scheme 1B). Chain-end linked mechanophores are commonly used as control systems in pulsed ultrasound as shear stresses accumulate toward the center of the chain, precluding activation at the chain end. The low mechanophore content in these systems generally precludes direct observation of the reaction outcome by ¹H NMR, and the most common strategy to detect activation is to label the reaction products with UV-

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active functionalities.^{5,8,10,22} To ensure orthogonal labeling of the proposed bis-enone product over the starting BCH functionality, we explored the use of conjugate addition by secondary amines (Scheme 2).²³ When small-molecule

Scheme 2. Orthogonal Labeling Demonstrated by Small-Molecule Reactivity



analogue **5**²² was exposed to 9-(methylaminomethyl)-anthracene (MAMA; 5 equiv, 0.25 M) in MeCN overnight, no change was observed in the ¹H NMR spectrum. Alternatively, when a bis-enone analogue **4** was subjected to identical conditions, the primary product observed was the mono-MAMA adduct (see Supporting Information). These observations motivated our experimental design, whereby activation of the BCH functionality by pulsed ultrasound could be tracked by the addition of MAMA to bis-enone products.

When BCH-PMA_{2,151k} is subjected to pulsed ultrasound in acetonitrile (6–9 °C) and subsequently treated with 0.09 M MAMA, the integral of the UV absorbance (365 nm) increases with increasing sonication time (Figure 1). After 120 min this

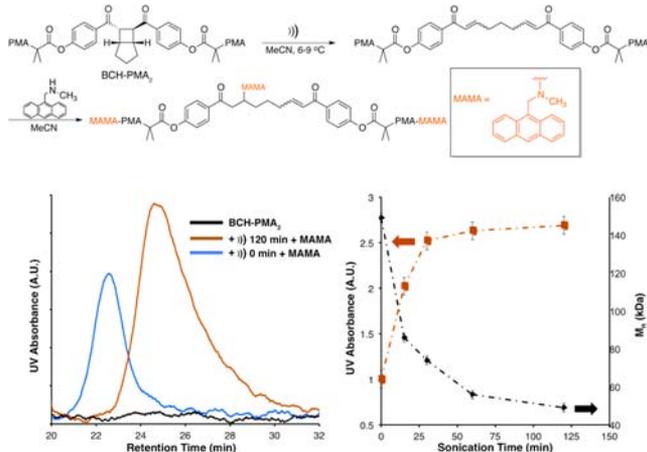


Figure 1. Sonochemical activation and subsequent labeling of bis-enone with MAMA (top). GPC-UV traces (365 nm, left) show no absorbance in the native polymer (BCH-PMA₂) (black), the absorbance of the unsonicated polymer treated with MAMA (blue), and the absorbance of the sonicated (120 min) polymer treated with MAMA (orange). Increasing UV absorbance and concurrent MW degradation is plotted at various time points during sonication (right).

increase levels off at a ratio of 2.7:1 vs the unsonicated sample (0 min) or a value of $\chi_{\text{MAMA}} = 0.81$ (Table 1), which we define as additional molecules of MAMA incorporated per initial chain relative to an unsonicated control (see Supporting Information). Because the MAMA concentration used with the polymers is lower than that used with small-molecule analogue **4**, we expect that the labeling is dominated by formation of the mono-MAMA adduct.

Table 1. Summary of PMA Sonication and Labeling Experiments^a

polymer	M_n	PDI	$M_{n, \text{GPC}}$	Abs _{init}	Abs _{son}	χ_{MAMA}
BCH-PMA _{2,151k}	151	1.11	49	0.039	0.119	0.81
PMA _{CRP,149k}	149	1.11	54	0.073	0.088	0.15
PMA _{FRP,157k}	157	2.12	51	n/a	0.006	0.12
BCH-PMA _{2,23k}	23	1.08	23	0.210	0.279	0.11
BCH-PMA _{1,158k}	158	1.12	61	0.021	0.030	0.09

^aPolymers of number-average molecular weight M_n were subjected to pulsed ultrasound [indicated by “(son)”] in acetonitrile (6–9 °C) for 120 min and subsequently treated with MAMA (0.09 M) overnight. Absorbance (365 nm) is given for the polymer treated with MAMA with (Abs_{son}) and without (Abs_{init}) sonication.

We note the presence of UV absorbance in the unsonicated control polymer after treatment with MAMA (Table 1, BCH-PMA_{2,151k}). This can be attributed to addition of the secondary amine to the chain-end α -bromoesters that result from the SET-LRP process. Due both to terminal group reactivity and to the non-scissile nature of the mechanophore, the change in absorbance does not directly correlate with MW degradation, as mechanophore activation can occur independently from chain scission. For this reason, the absorbance is seen to increase in both the high (unbroken chains) and low (broken chains) MW regions of the GPC trace (Figures S7–S9 in Supporting Information).

The terminal bromide is highly susceptible to nucleophilic attack, as demonstrated by the “click” reaction with thiophenols described by the Percec group.²⁴ In support of this mechanism, the PMA homopolymer (PMA_{CRP,149k}) produced by the same method shows a similar increase in absorbance when reacted with MAMA, with minimal additional increase after sonication ($\chi_{\text{MAMA}} = 0.15$). We note that the modest increase in UV absorbance in the control sample is not unusual and has been observed after sonication in similar labeling experiments.²² Alternatively, PMA prepared by conventional free radical polymerization (PMA_{FRP,157k}) shows no UV absorbance due to lack of halogenated end groups. Low-molecular-weight BCH-PMA_{2,23k} also exhibits an increase in absorbance upon treatment with MAMA, and, upon purification by preparatory GPC, its ¹H NMR spectrum shows no change in the BCH functionality. Upon sonication, this polymer exhibits only a mild increase in UV absorbance ($\chi_{\text{MAMA}} = 0.11$). Similar behavior is observed when control polymer BCH-PMA₁ bearing chain-end BCH functionality is subjected to identical conditions, yielding a χ_{MAMA} value of 0.09, both results indicating that mechanochemical rather than thermal processes drive this ring-opening reaction.

These results demonstrate that the mechanochemical activity of the fused BCH is qualitatively similar to that of Moore’s cyclobutanes that inspired the design. Polymer¹⁶ and mechanophore^{18,25} architecture can have significant and sometimes unexpected effects on mechanical activity, however, and we turned to CoGEF calculations²⁶ to quantify the impact of the BCH framework on mechanical activity of the cyclobutane. In the CoGEF calculations, the BCH functionality is seen to transform into the corresponding bis-enone product via a formal retro [2+2] cycloaddition at 4.08 Å elongation. Both this extension at break and the associated force (6.01 nN) are in excellent agreement with those of similar *trans*-substituted cyclobutane mechanophores previously reported by the Moore group.¹⁸

The second ring system appears to fulfill its desired role as an otherwise inert source of stored length. That stored length has the potential to generate large amounts of local slack and increased strain windows between activation and rupture in polymer chains or sub-chains,⁴ concepts that motivated our design. Quantitatively, we are able to estimate the elongation upon activation using our CoGEF force–displacement relationship. The contour lengths before and after activation were calculated at 100 pN of simulated force (estimating the force necessary to exhaust conformational entropy of a single polymer chain), showing a local elongation of 4.31 Å, which to our knowledge is the largest extension of any non-scissile mechanophore to date (see Supporting Information).

That extension in contour length can only be realized, however, if the mechanophore is truly non-scissile. That is, the stored length that is released by the retro-cycloaddition must survive the forces required for ring-opening. That this is the case is demonstrated by recycling the bis-enone under the same Ru(bpy)₃Cl₂-sensitized photocyclization used to generate the starting BCH small molecule **1a** (product C, Figure 2).¹⁹

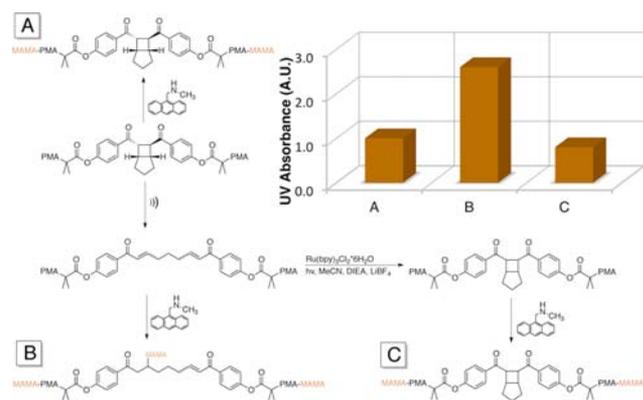


Figure 2. Summary of activation and recycling experiment. (A) Initial polymer treated with MAMA. (B) After sonication and treatment with MAMA. (C) After recycling and treatment with MAMA. Absorbance intensity returns to pre-sonication level after photochemical recycling (inset).

Sonication and reaction with MAMA (product B) generates a ~2.6-fold increase in absorbance over the control (product A), whereas the final UV absorbance from product C drops appreciably to ~0.8 vs the control. The photoreversion occurs without a change in MW, confirming an intramolecular, rather than intermolecular, addition of the enones. The chain scission process is therefore spatially and temporally distinct from the BCH activation. Reversible mechanochemistry has been demonstrated for several scissile mechanophores,^{8,10,15,27} but reversibility in non-scissile mechanophores has been limited to the mechanical *cis/trans* isomerization of *gem*-difluorocyclopropanes,^{14,28} switching that comes with no significant difference in intrinsic reactivity between the two states. We believe the BCH mechanophore to be the first example of reversible, non-scissile mechanophores with states of qualitatively different chemical reactivity, and the first example of photoreversion of an activated mechanophore of any type.

In conclusion, we have demonstrated the mechanochemical generation of bis-enones via the formal retro [2+2] cycloaddition of a non-scissile bicyclo[3.2.0]heptane-based mechanophore. The functionality generated upon activation can participate in conjugate additions that we envision could allow

for application in stress-responsive and/or self-healing materials. Furthermore, this reaction is reversible under photochemical conditions, demonstrating a platform where damage due to stress-induced ring-opening potentially could be reversed by ambient sunlight. Currently we are pursuing the synthesis of high mechanophore content analogues²⁹ of this system for applications along these lines.

■ ASSOCIATED CONTENT

📄 Supporting Information

Synthetic details; NMR, GPC, and UV characterization; control experiments; CoGEF calculations; and additional details. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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