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Masked Cyanoacrylates Unveiled by Mechanical Force

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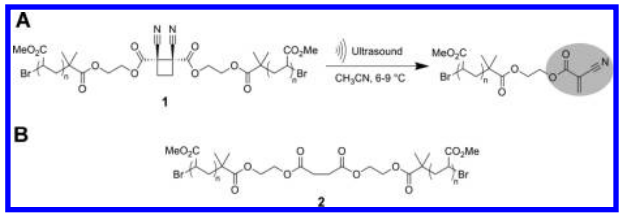
Mechanochemistry is the study of force-induced scission of covalent bonds.[1] Selective force-induced bond scission has been demonstrated in a variety of chemical moieties called mechanophores.[2a−i] Solution sonication studies and mechanical analysis of solid polymers has allowed for the identification of these inherently reactive molecular structures. Although several mechanophores have been identified, few examples have produced reactive species that can be utilized for self-healing applications. Here we demonstrate the mechanically-induced generation of reactive alkenes upon fragmentation of a strained dicyano-substituted cyclobutane ring (polymer **1**, Scheme 1A), which cleaves faster and more selectively than a control (polymer **2**, Scheme 1B). Trapping experiments with a Michael donor are consistent with of a formal retro [2 + 2] cleavage of **1**, yielding cyanoacrylate functional groups. Since cyanoacrylates are known to readily undergo addition reactions under mildly basic conditions, it may be possible to incorporate this mechanophore into solid polymers that selectively react and autonomically repair themselves upon application of mechanical force.

In order to probe the ability of a strained ring to produce cyanoacrylates under the application of mechanical force, poly(methyl acrylate) (PMA) incorporating a chain-centered dicyano-substituted cyclobutane mechanophore (**1**) and a control polymer (**2**) were formed using single-electron-transfer living-radical polymerization (SET-LRP)[3] of the corresponding small molecules containing α-bromoester initiators [see the Supporting Information (SI)]. Polymers ranging from 60 to 160 kDa were prepared using the two initiators. To determine the rates of cleavage, dilute solutions of polymers were exposed to controlled ultrasonic pulses under an argon atmosphere (6−9 °C). Aliquots removed at regular intervals were analyzed by gel permeation chromatography (GPC).

Scheme 1. (A) Ultrasound-Induced Cleavage of Mechanophore **1** To Yield Cyanoacrylate-Terminated Polymers; (B) Control Polymer **2**



A variety of models have been developed to measure the rate of polymer cleavage during sonication in solution;[4a] in this communication, the model developed by Malhotra[4b] was used because of its simplicity and ability to reliably model ultrasonic cleavage of linear polymers. Comparison of the rates of fragmentation versus molecular weight showed a significant enhancement of the scission rate for mechanophore-containing polymer **1** relative to control polymer **2** (see the SI). We propose that this increase in reactivity is due to a lower barrier to cleavage in the cyclobutane-containing mechanophore.

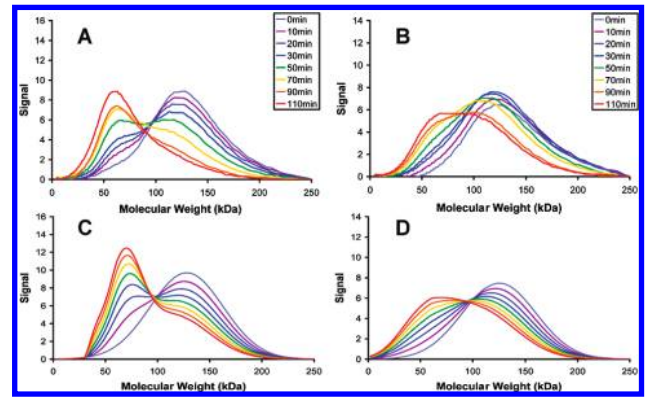


Figure 1. GPC traces showing the effects of ultrasound on **1** and **2**. A 0.75 mg/mL solution of **1** or **2** in acetonitrile was exposed to ultrasound, and aliquots were removed at the specified times. (A) Change in MWD for **1** (100 kDa). (B) Change in MWD for **2** (120 kDa). (C) Simulated MWD for **1** obtained using a center-selective cleavage model. (D) Simulated MWD for **2** obtained using a Gaussian cleavage model. See the SI for details of the simulations.

In addition to greater reactivity for **1** than its control, GPC traces of sonicated polymer **1** showed more selective cleavage than in polymer **2** (Figure 1A vs Figure 1B). Modeling of the GPC traces showed a peak evolution for **1** (100 kDa) that is comparable to the simulated change in the molecular weight distribution (MWD) for selective cleavage (Figure 1C), whereas the traces of **2** (120 kDa) were best modeled by unselective Gaussian cleavage near the polymer chain center (Figure 1D). For the control polymer, this trend matches those predicted for sonicated homopolymers.[4c]

After this demonstration that **1** contains a selectively cleavable moiety, the sonication products were analyzed to probe for cyanoacrylate formation. Sonicated polymers are often analyzed through trapping or isotope-labeling experiments.[1] In this work, UV-active 9-(methylaminomethyl)anthracene (MAMA) was suitable for trapping the cyanoacrylate-functionalized PMA product because of the potential Michael-type conjugate addition reaction of the secondary amine with the cyanoacrylate (Figure 2A). Upon sonication of the polymers with 1200 equiv of MAMA, GPC analysis of **1** (100 kDa) showed a significant increase in the UV signal, whereas **2** (120 kDa) displayed only a slight increase in the UV signal under the same conditions (Figure 2B,C). The absorption

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spectrum of the isolated polymer matched the spectrum of MAMA, confirming that the increase in UV signal for sonicated **1** was due to the incorporation of the trap and not to other background reactions (see the SI), thus supporting the mechanically induced formation of cyanoacrylates upon mechanophore cleavage. The percentage of cleaved polymer that reacted with MAMA was estimated by recording the absorption spectra of the isolated polymers at known dilutions and comparing them to the molar absorptivity of MAMA in the same solvent (THF). Over three runs, we found an average of 24% incorporation of MAMA into the product, assuming complete and selective chain scission. It is possible that other mechanically active reactions occurred, forming products that did not react with the trap. Also, this calculation did not take into account potential loss of the polymer during isolation or potential side reactions of the generated cyanoacrylate with molecules other than the trap.

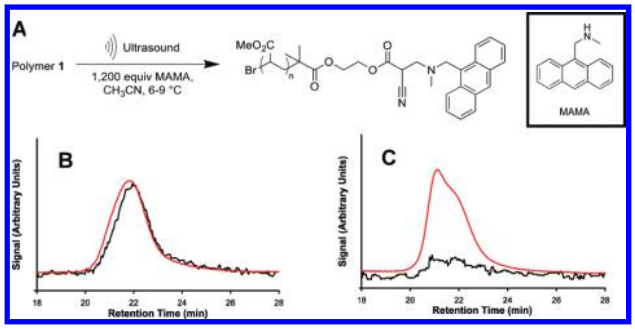

Figure 2. Results of trapping experiments. A 0.75 mg/mL solution of **1** or **2** in acetonitrile containing 1200 equiv of MAMA was sonicated for 90 min; the resulting polymers were analyzed by GPC. (A) Reaction of sonicated **1** with MAMA. (B) Refractive index (RI) trace (red) and UV−vis (365 nm) trace (black) for **1** after sonication. (C) RI (red) and UV−vis (black) traces for **2**.

Control studies were needed to confirm that MAMA incorporation occurred as a result of mechanophore fragmentation. Exposure of **1** (100 kDa) to the trap under the same conditions but without sonication showed no incorporation of MAMA. Low-molecular-weight **1** (30 kDa), which does not fragment under sonication conditions,[1] was sonicated in the presence of MAMA and showed no incorporation of the trapping molecule. These studies showed that chain cleavage is necessary for the reaction with MAMA to occur.

Computational modeling can be used to determine the likely effects of mechanical force on potential mechanophores. Here we employed the ab initio steered molecular dynamics (AI-SMD) method developed previously.[5] Computational modeling was performed using small-molecule methyl ester derivatives of **1** and **2**. A constant-force, fixed-pulling scheme was used in which the two methyl ester carbons were pulled toward two opposing fixed points under a constant-magnitude force. The simulations were performed for 1 ps or until cleavage occurred. The calculations predicted more rapid cleavage for the mechanophore in **1**, which selectively yields two cyanoacrylates (Figure 3A). Out of 20 trajectories sampled using a force of 3 nN, all resulted in cleavage of the cyclobutane ring. Sequential bond rupture occurred wherein a C−C single bond within the ring (r1) was cleaved, followed by a second C−C single bond (r2) (Figure 3). In direct contrast, only one trajectory out of 20 for the control (the methyl ester analogue of **2**) showed any bond rupture at a force of 3 nN (see the SI). The results for the control suggest that the central C−C single bond of

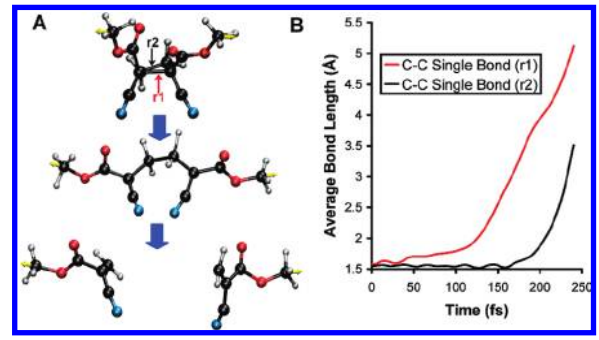

Figure 3. AI-SMD simulations of **1** using a force of 3 nN. (A) Snapshots along one trajectory for **1** showing selective cleavage ($t = 0$, 200, and 286 fs top to bottom). (B) Average bond lengths of 20 trajectories as a function of time for **1**, indicating sequential bond rupture of r1 and r2.

2 requires more force, and hence more energy, for bond rupture, and that dicyanocyclobutane is dramatically more reactive than its control.

In conclusion, we have shown that sonication of polymer **1** results in selective cleavage of the chain-centered mechanophore, forming reactive cyanoacrylates. Our conclusions are supported by the increased rate of cleavage upon sonication relative to the rate for a control polymer as well as the reaction of the products with a secondary amine trap. Furthermore, our experimental results are corroborated by computational studies that not only predict both selectivity and rate enhancement for the dicyanocyclobutane mechanophore relative to the control but also predict cyanoacrylate formation. Because of the inherent reactivity of cyanoacrylates, our future work will investigate the use of this mechanophore in self-healing polymers.

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Supporting Information Available: Experimental details, synthetic procedures, cleavage rate data, UV−vis spectra, control experiments, and details on the computational modeling of polymer cleavage. This material is available free of charge via the Internet at http://pubs.acs.org.

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