Supporting Information For

Masked Cyanoacrylates Unveiled by Mechanical Force

Matthew J. Kryger,[†,‡] *Mitchell T. Ong,*[§] *Susan A. Odom,* [†,‡] *Nancy R. Sottos,*[‖,‡] *Scott R. White,*[⊥,‡] *Todd J. Martinez,*[§] *and Jeffrey S. Moore*[†,‡,*]

† Department of Chemistry, University of Illinois at Urbana-Champaign.
‡ Beckman Institute for Advanced Science and Technology, UIUC.
§ Department of Chemistry, Stanford University.
‖ Department of Materials Science and Engineering, UIUC.
⊥ Department of Aerospace Engineering, UIUC.

*To whom all correspondence should be addressed. Phone: (217) 244-4024.
Fax: (217) 244-8068. E-mail: jsmoore@illinois.edu

Table of Contents

I. General Experimental Details

Unless otherwise stated, all starting materials were obtained from commercial suppliers and used without purification. Anhydrous acetonitrile was obtained for Acros (Acroseal, 99.9%) and used as is. Dry dichloromethane was obtained from an Anhydrous Engineering Solvent Delivery System (SDS) equipped with activated alumina columns. Cu(0) powder (99%, 1-5 μm) was purchased from Sigma-Aldrich. Me_6TREN was synthesized following a literature procedure.[1] All reactions were performed under N_2 atmosphere unless otherwise specified.

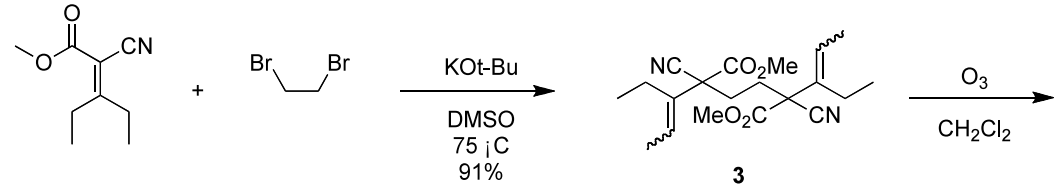
Analytical gel permeation chromatography (GPC) analyses were performed with a Waters 515 HPLC pump, a Viscotek TDA Model 300 triple detector array, a Thermoseparations Trace series AS100 autosampler, and a series of 3 Waters HR Styragel columns (7.8 X 300mm, HR3, HR4, and HR5) in THF at 30 °C. The GPC was calibrated using monodisperse polystyrene standards. Preparatory GPC analyses were performed with a waters 515 HPLC pump, a Waters 2487 UV detector (set at 265 nm), a 410 Differential Diffractometer, and a series of 3 Waters columns (19 X 300 mm, Ultrastyragel 10^4 Å THF, 10^2 Å THF, 500 Å THF) in HPLC grade THF.

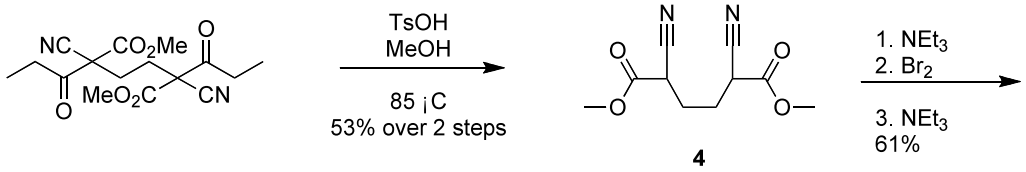
Ultrasound experiments were performed on a Vibra Cell 505 liquid processor with a ½" diameter solid probe from Sonics and Materials. The distance between the titanium tip and bottom of the Suslick cell was 1 cm. The Suslick cells[2] were made by the School of Chemical Sciences' Glass Shop at the University of Illinois.

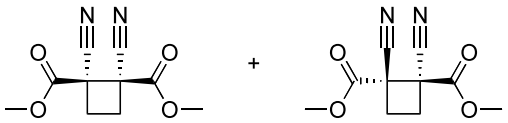
Flash column chromatography was conducted with silica gel 60 (230-400 mesh) from Silicycle. Melting points were obtained using an electrothermal melting temperature apparatus (Mel-Temp, Model 1001). ^{1}H and ^{13}C NMR spectra were obtained using either a Varian 400 or 500 MHz spectrometer in the VOICE NMR laboratory at the University of Illinois; the residual solvent protons were used to reference the chemical shift. Coupling constants (*J*) are reported in Hertz (Hz), and splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad).

UV-vis spectra were recorded using a Shimadzu UV-2401PC. Quartz cells with a path length of 1 cm were used. UV irradiation of samples dissolved in THF was performed with a Model UVG-11 Mineralight lamp (short wave UV – 254 nm). Mass spectra were obtained through the Mass Spectrometry Facility, SCS, University of Illinois and elemental analyses were performed by the University of Illinois MicroAnalytical services. X-ray crystallographic analysis was performed by the George L. Clark X-ray Facility at the University of Illinois.

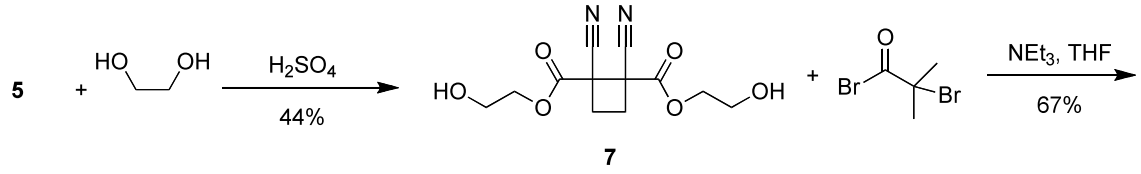
II. Synthetic Procedures

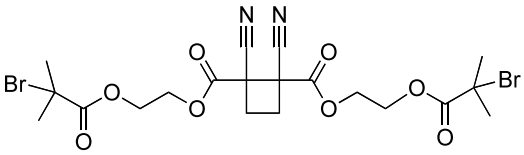




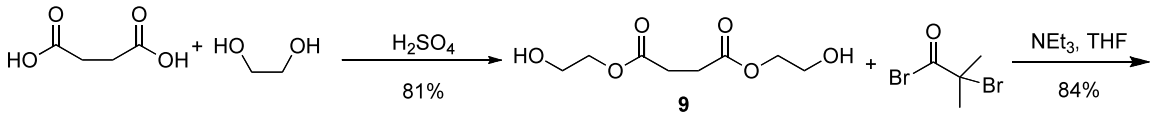


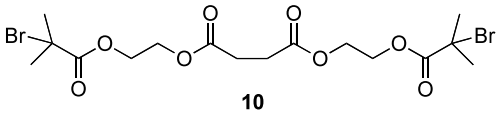
5 1:3 6





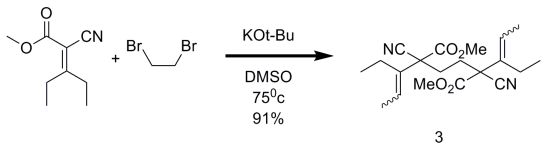
8





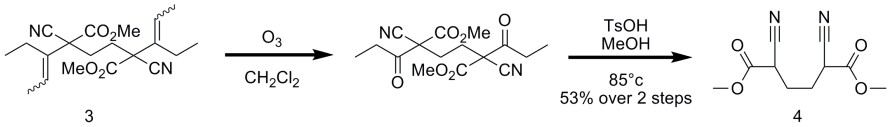
10

Dimethyl 2,5-dicyano-2,5-di(pent-2-en-3-yl)hexanedioate (3) (mixture of isomers)



Compound **3** was prepared using a modified procedure from that reported by Grossman *et al*.[3] Potassium *tert*-butoxide (11.0 g, 98.1 mmol) was dissolved into 60 mL DMSO in a 250 mL round-bottom flask. Methyl 2-cyano-3-ethylpent-2-enoate (15.0 g, 90.0 mmol), prepared according to literature procedure,[4] was added dropwise and the solution was allowed to stir for 45 min. 1,2-dibromoethane (3.51 mL, 40.8 mmol) was added dropwise. The reaction mixture was heated for 18 h at 70 °C. The reaction mixture was dissolved into 1.5 L diethyl ether and washed with 1.2 L H_2O, dried over magnesium sulfate, and the solvent was evaporated *in vacuo*. The crude product was purified via flash column chromatography (0.4% methanol in methylene chloride) yielding a white solid (13.4g, 37.2mmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (q, J = 6.8 Hz, 2H), 3.81 (s, 6H), 1.98-2.22 (m, 8H), 1.73 (s, 3H), 1.72 (s, 3H), 0.98 (t, J = 7.5 Hz, 6H). ^{13}C{^{1}H} NMR (500 MHz, $CDCl_3$) δ 167.9, 134.5, 126.3, 118.0, 54.8, 31.1, 21.2, 14.0, 13.6. HRMS-EI (*m/z*): calcd for $C_{20}H_{28}N_2O_4$ [M+], 360.2049; found, 360.2053. Anal. Calcd for $C_{20}H_{28}N_2O_4$: C, 66.64; H, 7.83; N, 7.77. Found: C, 66.66; H, 8.00; N, 7.77. mp 76-80 °C.

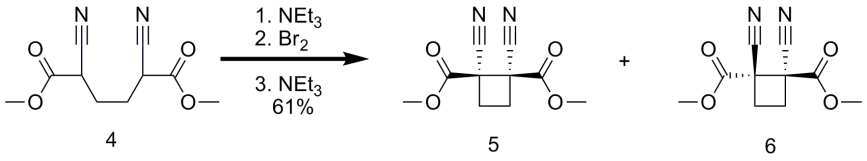
Dimethyl 2,5-dicyanohexanedioate (4)



Compound **4** was prepared using a modified procedure from that reported by Grossman *et al*.[4] Dimethyl 2,5-dicyano-2,5-di(pent-2-en-3-yl)hexanedioate (**3**) (20.0 g, 55.5 mmol) was dissolved in 400 mL methylene chloride in a 500 mL 3-neck round-bottom flask. The solution was sparged with O_3 until a dark blue color appeared and was subsequently sparged with O_2 until colorless. Methylene chloride was removed under N_2 stream, and

the residue was dissolved into 300 mL methanol. Tosic acid (1.50 g, 7.89 mmol) was added, and the solution was refluxed for three days. Methanol was evaporated *in vacuo*, the resulting solid was dissolved into methylene chloride, washed with sodium bicarbonate, dried under magnesium sulfate, and the solvent was removed *via* evaporation. The crude product was recrystallized in hot ethyl acetate to yield white crystals (6.54 g, 29.2 mmol, 53%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (s, 6H), 3.60-3.64 (m, 2H), 2.10-2.25 (m, 4H). $^{13}C\{^{1}H)$ NMR (500 MHz, $CDCl_3$) δ 165.8, 115.6, 54.1, 36.7, 26.8. HRMS-EI (*m/z*): calcd for $C_{10}H_{13}N_2O_4$ (MH^+), 225.08754; found, 225.08720. Anal. Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49. Found: C, 53.60; H, 5.35; N, 12.22. mp: 116.5-118.5 °C

***Cis*- and *trans*-dimethyl 1,2-dicyanocyclobutane-1,2-dicarboxylates (5,6)**



Dimethyl 2,5-dicyanohexanedioate (**4**) (3.00 g, 13.4 mmol) was dissolved into 75 mL of dry methylene chloride in a 250 mL round-bottom flask. Triethylamine (1.35 g, 13.4 mmol) was dissolved in 10 mL methylene chloride and added dropwise. After 10 min of stirring, bromine (2.14 g, 13.4 mmol), dissolved in 10 mL methylene chloride, was added dropwise and the solution was stirred for 45 min. Triethylamine (1.35 g, 13.4 mmol) in 10 mL methylene chloride was added dropwise, and the solution was stirred for 45 min. The resulting solution was dissolved in 600 mL methylene chloride, washed with water, dried with magnesium sulfate, and evaporated *in vacuo*. Crude product was purified using flash column chromatography (methylene chloride) yielding a white solid (1.82 g, 8.20 mmol, 61%) as a 3:1 mixture of *trans*-diester:*cis*-diester (by ^{1}H NMR). The isomers were separated by selective sublimation of the *trans*-diester in the presence of the *cis*-diester and the isomers were identified by single crystal XRD analysis (Figure S1).

(1R,2S)-dimethyl 1,2-dicyanocyclobutane-1,2-dicarboxylate (5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (s, 6H), 2.88-2.98 (m, 2H), 2.75-2.85 (m, 2H). $^{13}C\{^{1}H\}$ NMR (400 MHz,

$CDCl_3$) δ 164.9, 115.5, 54.7, 47.2, 27.9. HRMS-EI (*m/z*): calcd for $C_{10}H_{11}N_2O_4$ [MH+], 223.07189; found, 223.07186. mp 97-100 °C.

(1S,2S)-dimethyl 1,2-dicyanocyclobutane-1,2-dicarboxylate (6). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.02 (s, 6H), 2.88-2.98 (m, 2H), 2.75-2.85 (m, 2H). $^{13}C\{^1H\}$ NMR (500 MHz, $CDCl_3$) δ 164.9, 115.2, 55.2, 47.4, 27.3. HRMS-EI (*m/z*): calcd for $C_{10}H_{10}N_2O_4$ [M+], 222.06406; found, 222.06400.

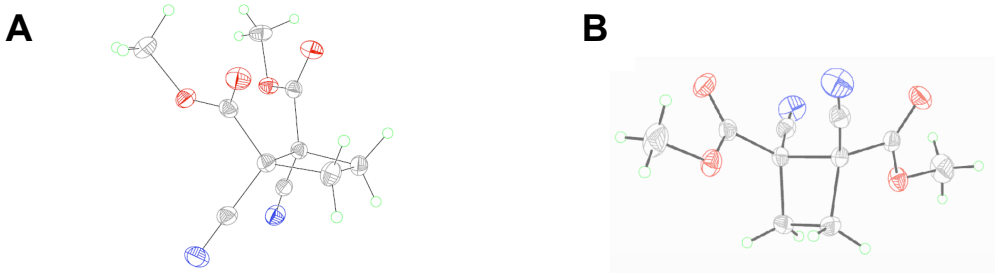
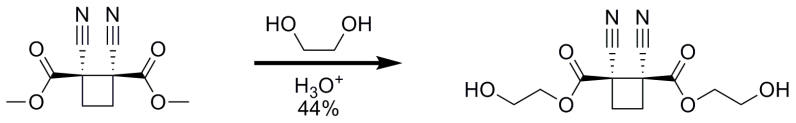


Figure S1. (A) Crystal structure of **5**. (B) Crystal structure of **6**.

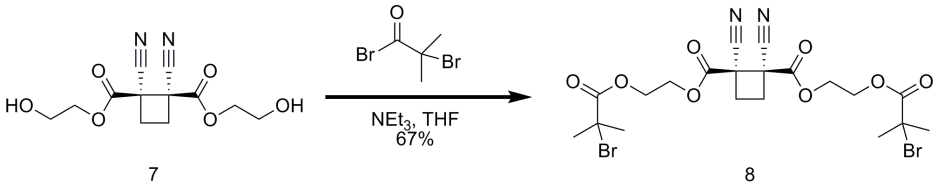
(1R,2S)-bis(2-hydroxyethyl) 1,2-dicyanocyclobutane-1,2-dicarboxylate (7)



5 7

(1R,2S)-dimethyl 1,2-dicyanocyclobutane-1,2-dicarboxylate (**5**) (0.500 g, 2.25 mmol) was dissolved into ethylene glycol (5.58 g, 90.0 mmol). Five drops of H_2SO_4 were added and the solution was heated for three days at 75 °C. The solution was dissolved into 50 mL ethyl acetate, washed with a dilute sodium bicarbonate solution, and the solvent was evaporated *in vacuo*. The resulting liquid was purified via flash chromatography (2% methanol in ethyl acetate) yielding a light brown liquid (0.28 g, 0.81 mmol, 44%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.16-4.26 (m, 4H), 3.57-3.62 (t, J = 4.7Hz, 4H), 2.76-2.88 (m, 4H). $^{13}C\{^1H\}$ NMR (500 MHz, DMSO-d_6) δ 164.2, 116.2, 69.2, 58.4, 46.8, 27.1. HRMS-EI (*m/z*): calcd for $C_{12}H_{15}N_2O_6$ [MH+], 283.09302; found, 283.09340.

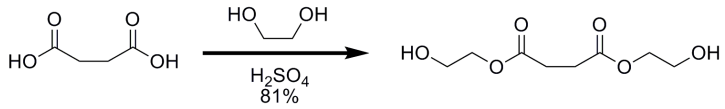
(1R,2S)-bis(2-(2-bromo-2-methylpropanoyloxy)ethyl) 1,2-dicyanocyclo butane-1,2-dicarboxylate (8)



7 8

(1R,2S)-bis(2-hydroxyethyl) 1,2-dicyanocyclobutane-1,2-dicarboxylate (**7**) (0.100 g, 0.354 mmol) was dissolved into 10 mL THF in a 25 mL round-bottom flask and cooled to 0 °C. Triethylamine (0.110g, 1.10 mmol) was added and the solution was stirred for 10 min. 2-Bromo-2-methylpropanoyl bromide (0.250g, 1.06mmol) was added dropwise to the cooled solution and was allowed to warm to room temperature while stirring overnight. The resulting solid salt was removed by filtration, the solvent was removed, and flash column chromatography (2% methanol in methylene chloride) gave a light brown liquid (0.137 g, 0.236 mmol, 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.34-4.59 (m, 8H), 2.87-2.96 (m, 2H), 2.74-2.84 (m, 2H), 1.93 (s, 12H). $^{13}C\{^{1}H\}$ NMR (500 MHz, $CDCl_3$) δ 171.6, 164.4, 65.2, 62.8, 55.5, 47.1, 30.8, 28.1. HRMS-EI (*m/z*): calcd for $C_{20}H_{25}{}^{81}Br_2N_2O_8$ [MH+], 582.99368; found, 582.99411.

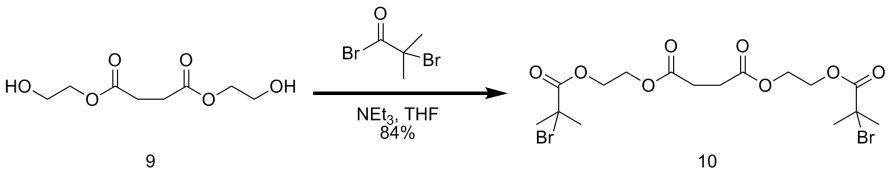
Bis(2-hydroxyethyl) succinate (9)



9

Succinic acid (1.00 g, 8.46 mmol) was dissolved in ethylene glycol (10.5 g, 169 mmol) in a 50 mL round-bottom flask. Two drops of H_2SO_4 were added and the solution was stirred at 70 °C for 15 h. After cooling, the solution was neutralized by adding sodium bicarbonate, and the product was isolated *via* flash chromatography (4% methanol in ethyl acetate) to give a colorless liquid (1.4134 g, 6.85 mmol, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.24-4.26 (m, 4H), 3.82-3.84 (m, 4H), 2.70 (s, 4H) 1.94-2.10 (s, broad, 2H). $^{13}C\{^{1}H\}$ NMR (500 MHz, $CDCl_3$) δ 29.4, 60.7, 66.5, 173.0. HRMS-EI (*m/z*): calcd for $C_8H_{15}O_6$ [MH+], 207.08687; found, 207.08672.

Bis(2-(2-bromo-2-methylpropanoyloxy)ethyl) succinate (10)



9 10

Bis(2-hydroxyethyl) succinate (**9**) (0.20 g, 0.97 mmol) was dissolved into 10 mL of anhydrous THF in a 25 mL round-bottom flask and cooled to 0 °C. Triethylamine (0.304 g, 3.00 mmol) was added and the solution was stirred for 10 min. 2-Bromo-2-methylpropanoyl bromide (0.669 g, 2.90 mmol) was added dropwise and the solution was allowed to warm to room temperature while stirring overnight. The resulting solid salt was removed by filtration, the solvent was removed, and flash chromatography (3% methanol in methylene chloride) gave a colorless liquid (0.4084 g, 0.810 mmol, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.32-4.38 (m, 8H), 2.65 (s, 4H), 1.92 (s, 12H). $^{13}C\{^{1}H\}$ NMR (500 MHz, $CDCl_3$) δ 172.1, 171.7, 63.7, 62.2, 55.7, 30.9, 29.0. HRMS-EI (*m/z*): calcd for $C_{16}H_{25}Br_2O_8$ [MH+], 502.99163; found, 502.99192.

Representative Procedure for the Synthesis of Mechanophore-Linked PMA

DMSO was degassed by freeze-pump-thaw and sparged with argon for 30 min prior to use. Methyl acrylate was filtered through basic alumina to remove inhibitor. Initiator-functionalized *cis*-dicyano cyclobutane (3.73 mg, 0.00643 mmol), Cu(0) (1.76 mg, 0.0277 mmol), and Me_6TREN (7.23 mg, 0.0319 mmol) were weighed on a microbalance and transferred to a 10mL Schlenk flask equipped with a Teflon stir bar. Methyl acrylate (1.00 mL, 11.1 mmol) and DMSO (1 mL) were added. The flask was immediately sealed and three freeze-pump-thaw cycles were applied to remove dissolved oxygen. The flask was backfilled with argon and was allowed to stir in a water bath for 2 h at room temperature. The polymerization was opened to air and 10 mL of THF was added, and the polymer filtered through a pad of silica gel. After solvent was removed *in vacuo*, the polymer was precipitated by dropwise addition to stirring methanol. The resulting polymer was collected and dried under vacuum at room temperature. Molecular weight

and polydispersity indices were recorded using an analytical GPC that had been calibrated with polystyrene standards.

III. ^{1}H NMR Spectra

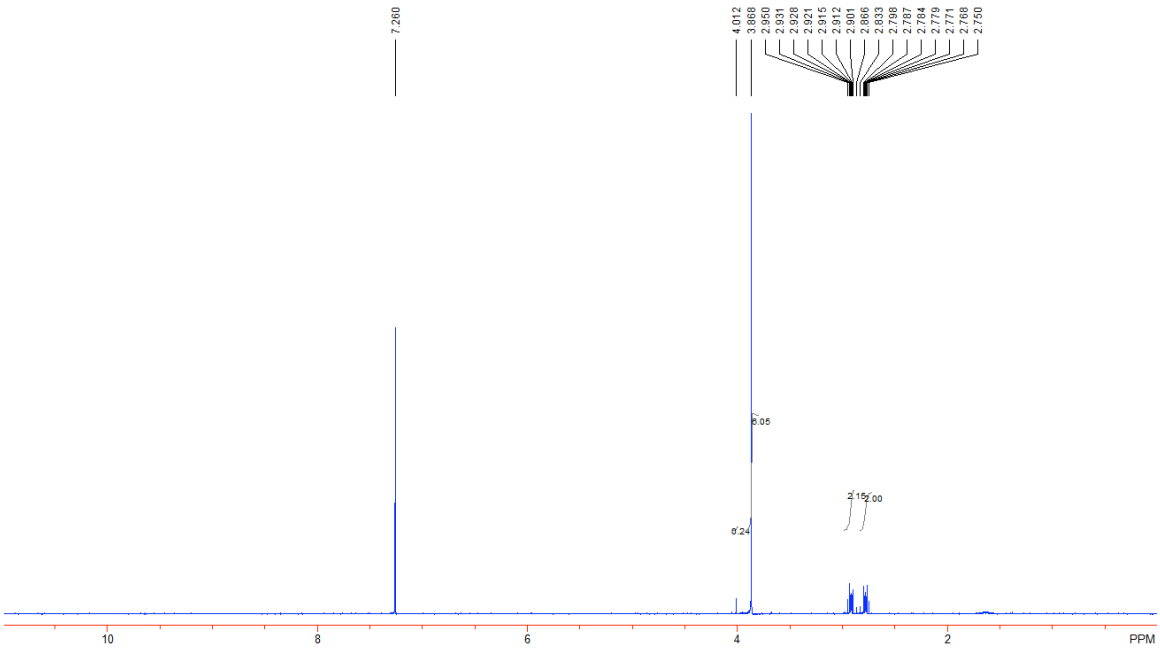


Figure S2. ^{1}H NMR spectra of (1R,2S)-dimethyl 1,2-dicyanocyclobutane-1,2-dicarboxylate (**5**).

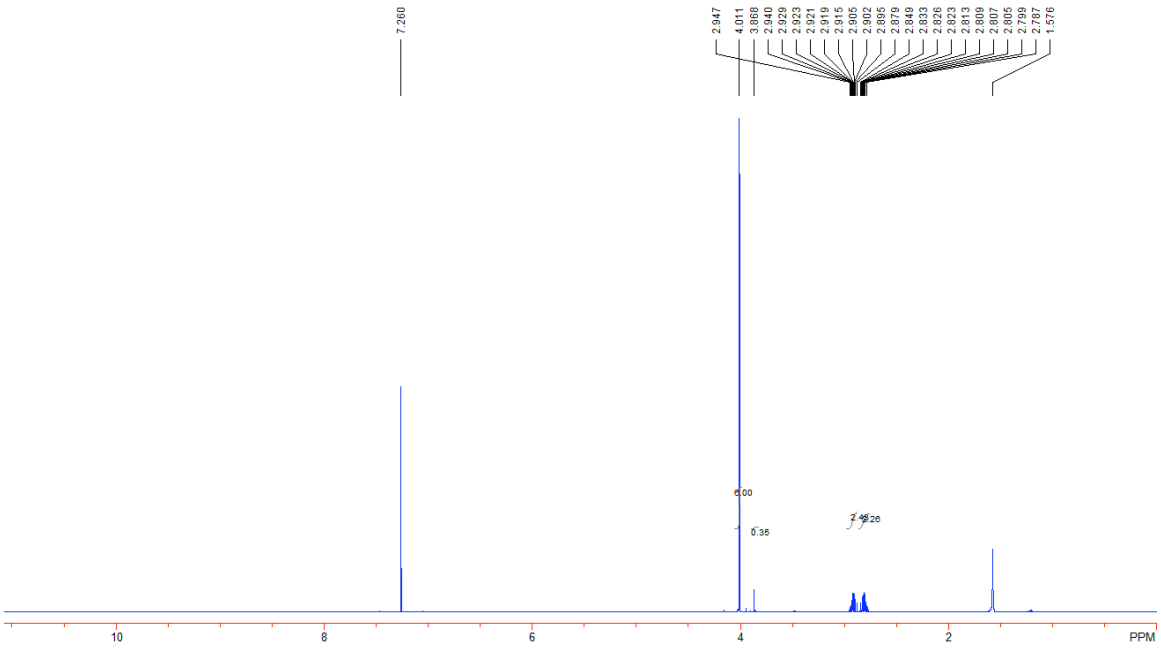


Figure S3. [1]H NMR spectra of (1S,2S)-dimethyl 1,2-dicyanocyclobutane-1,2-dicarboxylate (**6**).

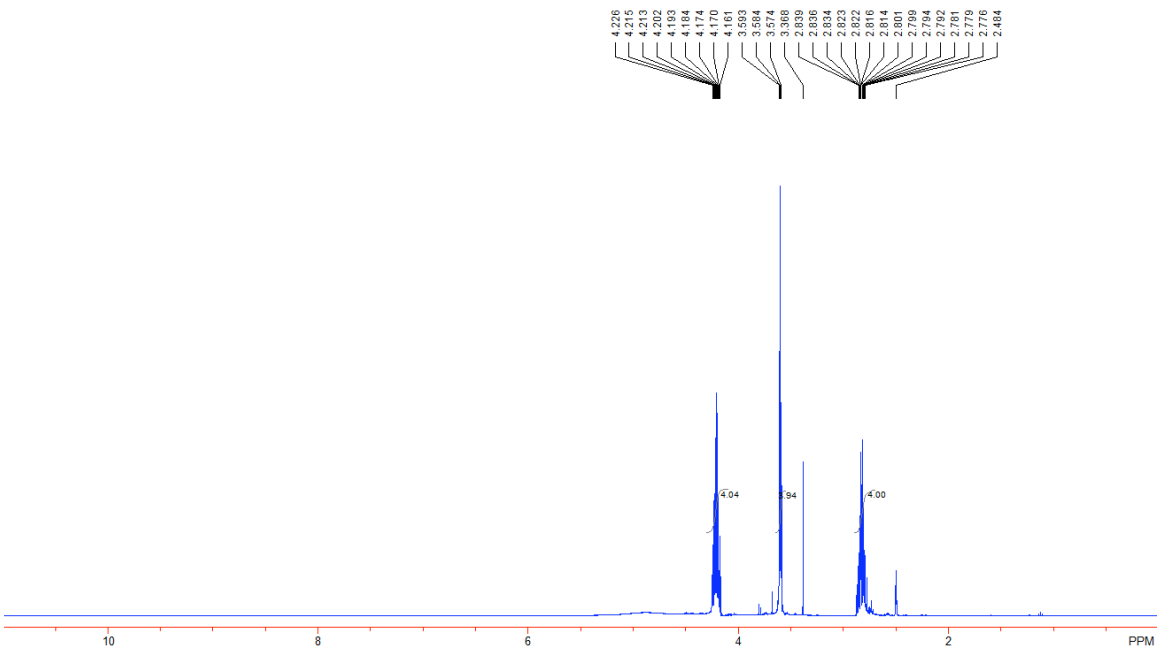


Figure S4. [1]H NMR spectra of (1R,2S)-bis(2-hydroxyethyl) 1,2-dicyanocyclobutane-1,2-dicarboxylate (**7**).

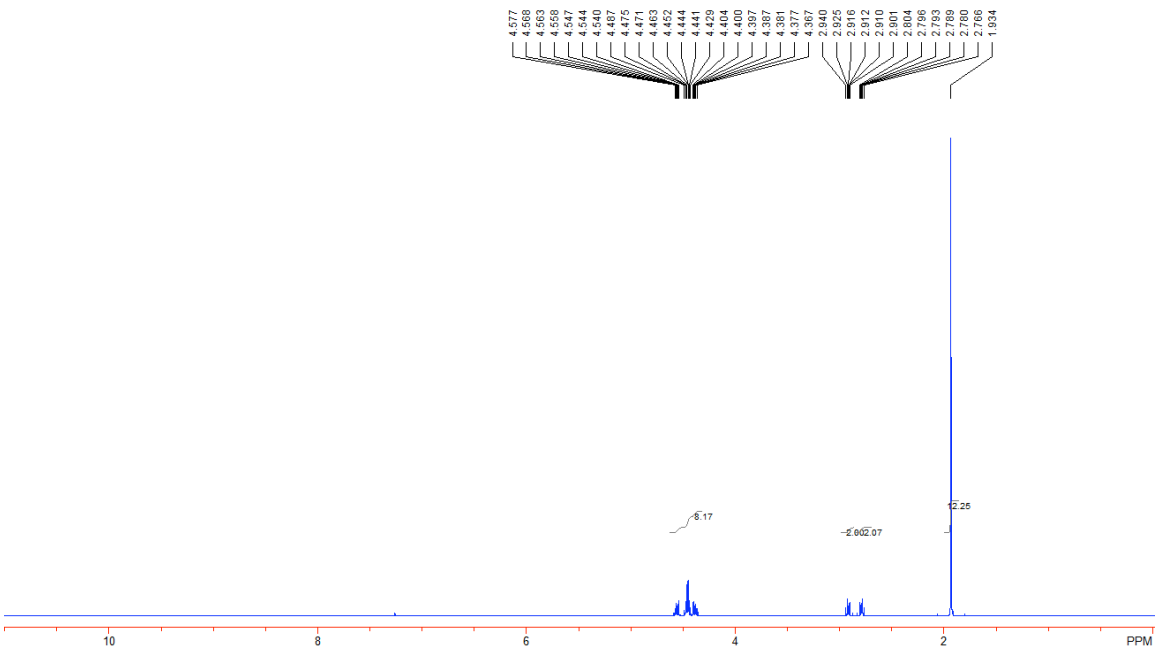


Figure S5. ^{1}H NMR spectra of (1R,2S)-bis(2-(2-bromo-2-methylpropanoyloxy)ethyl) 1,2-dicyanocyclo butane-1,2-dicarboxylate (**8**).

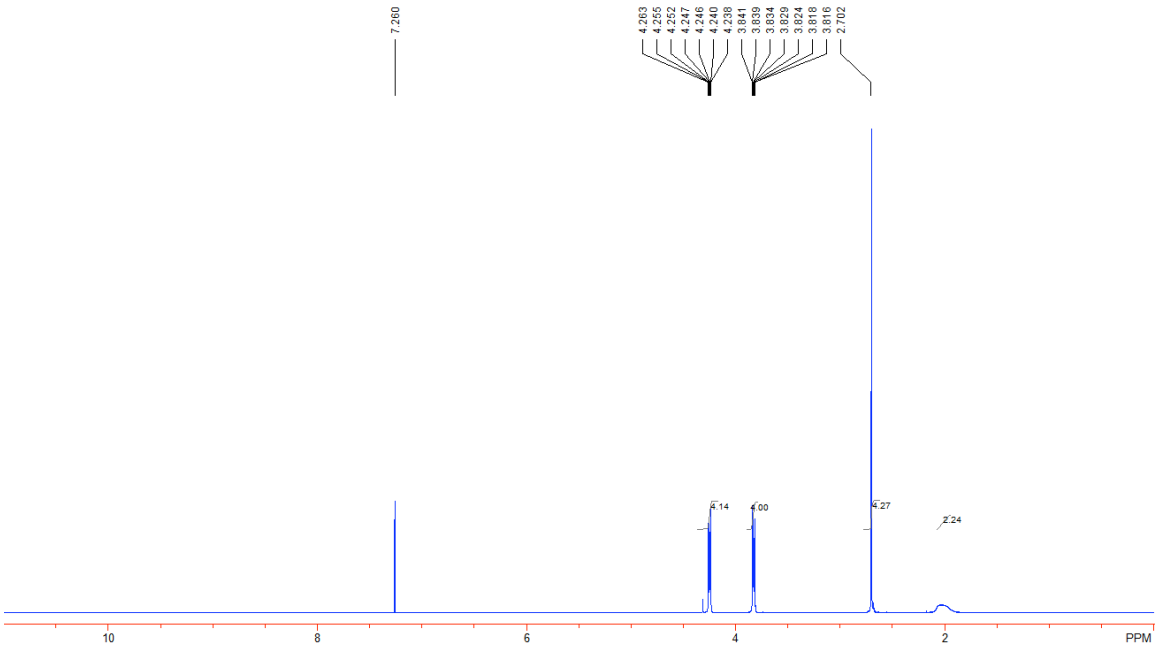


Figure S6. ^{1}H NMR spectra of bis(2-hydroxyethyl) succinate (**9**).

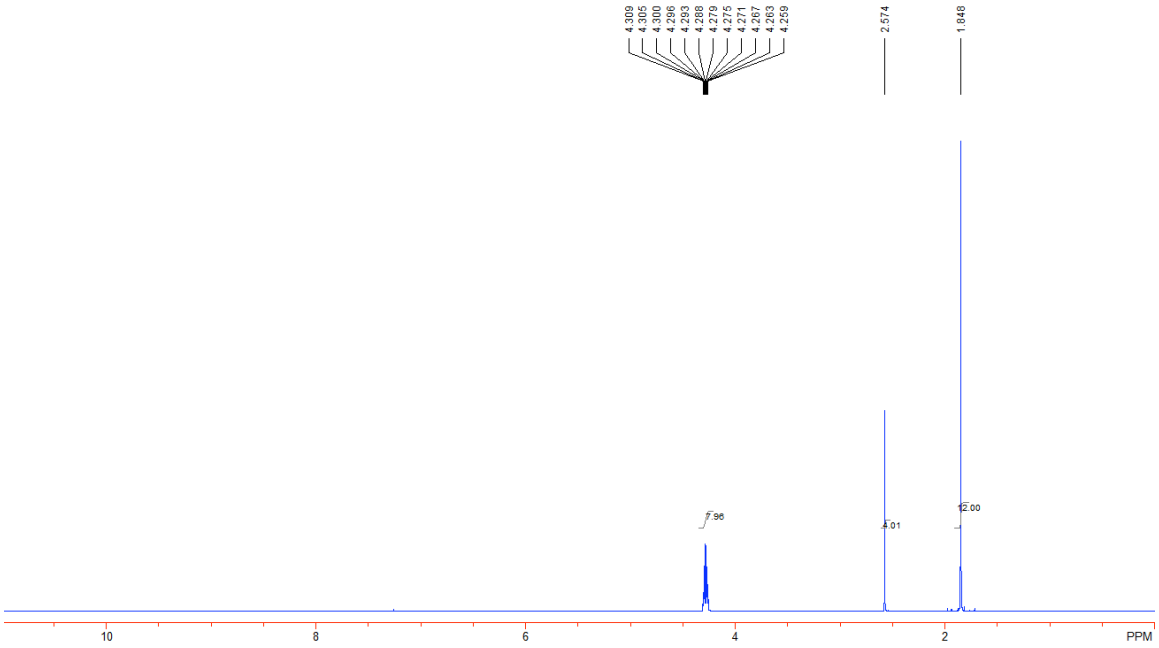


Figure S7. ^{1}H NMR spectra of bis(2-(2-bromo-2-methylpropanoyloxy)ethyl) succinate (**10**).

IV. Sonication Set-Up and Procedures

The general apparatus was assembled as shown in Figure S8. Each sonication reaction took place inside the Suslick cell.

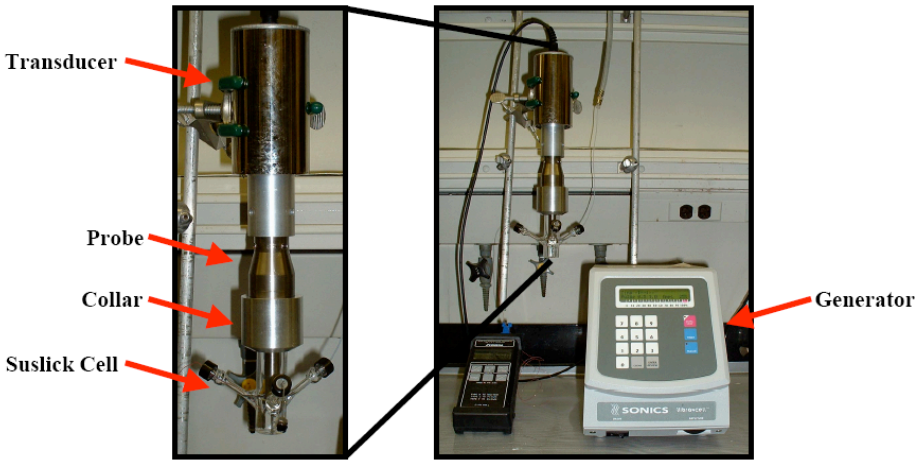


Figure S8. General set-up of the sonication apparatus.

General Procedure for Sonication Experiments

The sonication apparatus was assembled as shown in Figure S8. Polymer dissolved in acetonitrile was transferred to an oven-dried Suslick cell, which was placed into the collar and screwed onto the probe. An argon line and thermocouple were introduced into the cell and argon was sparged through the system for 30 min prior to any sonication runs, as well as during the run itself. A plastic cap was used to seal off the third arm of the Suslick cell. The Suslick cell was cooled with an ice bath throughout the entire sonication in order to maintain a constant temperature of 6-9º C. Pulsed ultrasound (0.5 s on, 1.0 s off, 8.7 W/cm^2) was then applied to the system.

General Procedure for Sonication Kinetics Experiments

For each experiment, mechanophore-containing polymer (7.5 mg) was weighed and dissolved into 10 mL of reagent grade acetonitrile. The polymer solution was added to the Suslick cell, cooled, purged with argon, and then sonication was started. Aliquots of 600 μL were removed at 0, 10, 20, 30, 50, 70, 90, and 110 min and placed into Eppendorf tubes. Solvent was removed by evaporation in air and the polymer was redissolved in 350 μL of THF. The sample was filtered through a syringe filter (PTFE, 0.45μm pore size) and analyzed by GPC.

General Procedure for MAMA Trapping Experiments

For each experiment, polymer (7.5 mg) was dissolved into 10 mL of anhydrous acetonitrile. 9-(methylaminomethyl) anthracene (MAMA) (0.020 g, ~1,200 eq.) was added to the dissolved polymer, and the solution was transferred to an oven-dried Suslick cell. Sonication was conducted for 90 min. The sample was transferred to a scintillation vial and the solvent was removed *via* N_2 stream. The resulting solid was dissolved into 1 mL THF and filtered through a syringe filter (PTFE, 0.45 μm pore size). 500 μL of the resulting solution was injected onto the prep GPC. The UV signal was monitored at 365 nm. When the RI signal corresponding to the polymer appeared, the eluent from the columns was collected and a UV-vis spectrum of the polymer in THF was recorded (Figure S9).

For quantification of the amount of MAMA incorporated into the sonication of the polymer, prep GPC and UV-vis analysis were also used. The molar absorptivity of MAMA in THF was determined through three serial dilutions of MAMA/THF solutions of known concentrations (ε = 8,700 $M^{-1}cm^{-1}$ at 378 nm). Three 90 minute sonications were performed with polymer (7.5 mg) and MAMA (0.020 g, ~1200 eq) in 10 mL of anhydrous acetonitrole. The sample was transferred to a scintillation vial and the solvent was removed *via* N_2 stream. The resulting solid was dissolved into 1 mL THF and filtered through a syringe filter (PTFE, 0.45 μm pore size). 500 μL of the resulting solution was injected onto the prep GPC. As the UV signal (365 nm) increased upon elution of the tagged polymer, the polymer was isolated from the prep GPC. The solution was concentrated by rotary evaporation, and the polymer was redissolved in THF (2.0 mL). The absorption spectrum was recorded, which was corrected for scattering (example spectrum and line used to apply the correction are shown in Figure S#). Using the molar absorptivity value of MAMA and the absorbance of the isolated polymer at 378 nm, the concentration of MAMA in solution was calculated, and from that the number of mmol of MAMA was calculated. This value was compared to the number of mmol of cyanoacrylate produced, assuming 100% selective cyclobutane cleavage. This number, while halved from analyzing half of the original solution, is doubled compared to the initial value from the original polymer because two cyanoacrylates are formed per one mechanophore. Given 7.5 mg of polymer and a Mw = 128,000 g/mol, there are ~5.9×10^{-5} mmol of mechanophore. The average of three runs gave a value of 2.8×10^{-5} mmol of tagged MAMA. Therefore, 2.8×10^{-5} mmol of tagged MAMA molecules / 5.9×10^{-5} mmol potential cyanoacrylate produced gives 24% incorporation of the tag per cyanoacrylate. This value does not take into account potential reaction of cyanoacrylates with residual water in the sonication solution, nor does it take into account potential loss of polymer during filtration.

V. UV-Vis Absorption Spectra

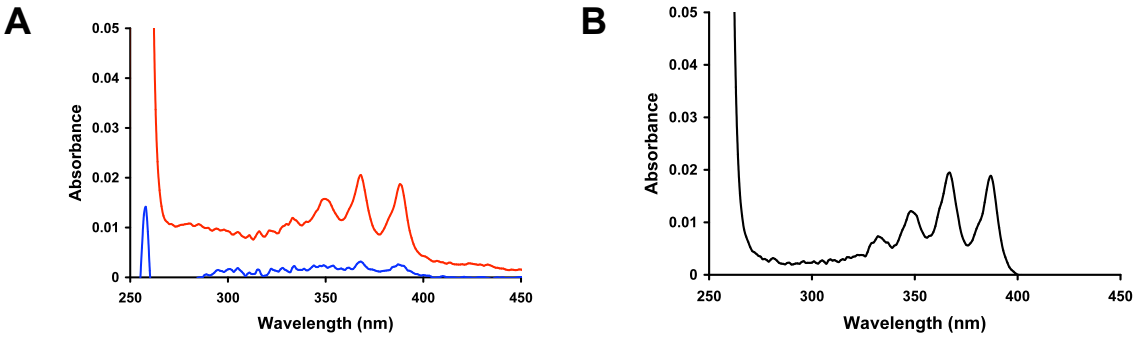


Figure S9. (A) Absorption spectra in THF of isolated **1** (red) and isolated **2** (blue) after sonication in the presence of MAMA (same concentration) (B) UV-vis spectrum of MAMA in THF.

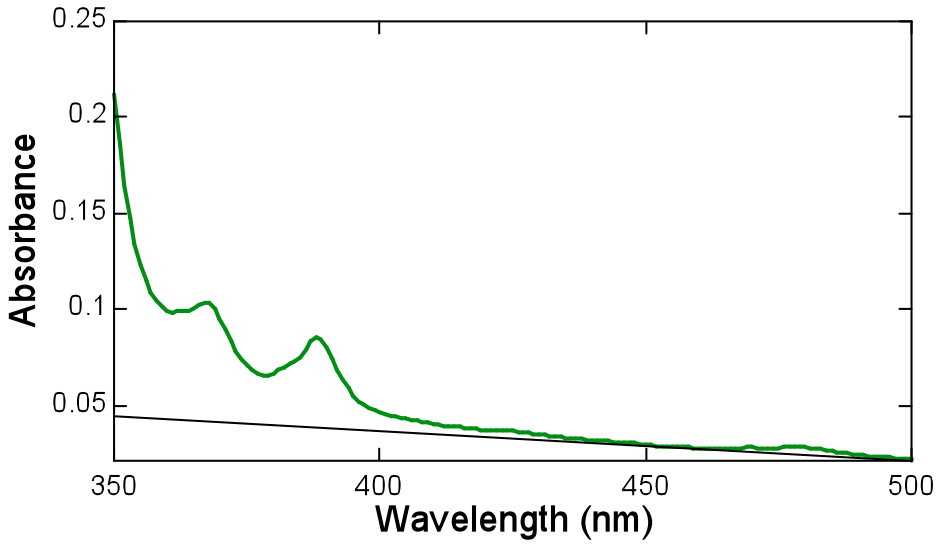


Figure S10. Absorption spectrum of isolated **1** (green) after sonication in the presence of MAMA and correction factor (black line) used for calculations of trapping percent.

VI. Control Experiments

Testing potential reaction between MAMA and non-sonicated polymer

To determine if the incorporation of the chromophoric trap was due to sonication and polymer cleavage, the same polymer that was used in the trapping experiment (and showed trap incorporation) was treated under identical conditions to the trapping experiment without sonication. Upon GPC analysis, it was noted that no incorporation of the trap occurred (Figure S11A).

Sonication of low molecular weight dicyano-functionalized polymer

To determine if trap incorporation is due to fragmentation of the dicyano mechanophore, a low molecular weight polymer (30 kDa) containing the mechanophore at its center was sonicated in the presence of the MAMA trap following the same experimental procedure used for the higher molecular weight polymers. Because this polymer is below the threshold for polymer cleavage, no incorporation of the trap should be seen in the polymer after sonication. Upon GPC analysis, no discernable incorporation of the chromophoric trap was observed (Figure S11B).

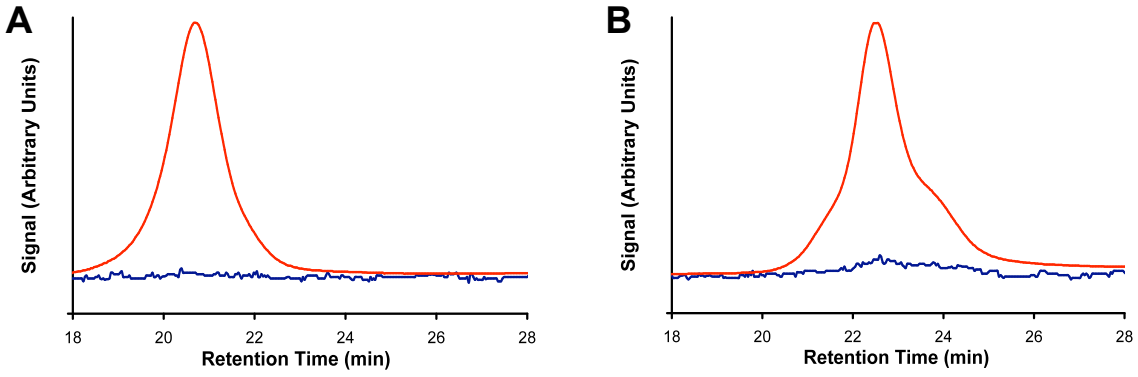


Figure S11. (A) RI (red trace) and UV (blue trace) spectra for unsonicated polymer in the presence of chromophore trap. (B) RI (red trace) and UV (blue trace) spectra for sonicated low molecular weight polymer.

VII. Kinetic Analysis of Polymer Cleavage

Rates of cleavage for both **1** and polymer **2** were calculated using the method developed by Malhotra and co-workers.[5] Relative rates of polymer degradation for molecular weights ranging from 60 kDa to 160 kDa were measured by performing sonication experiments as outlined above and measuring the change in M_n over time. Plots of the relative cleavage rates can be found in Figure S12 below. For a given molecular weight, mechanophore-containing polymer **1** degraded at a faster rate than control polymer **2** in all cases. This increase in cleavage rate is attributed the greater reactivity of the mechanophore polymer in relation to the control polymer. Due to the harsh and energetic nature of sonication, the rate of degradation of the mechanophore containing polymer is on the same order of magnitude as the degradation of the control polymer.

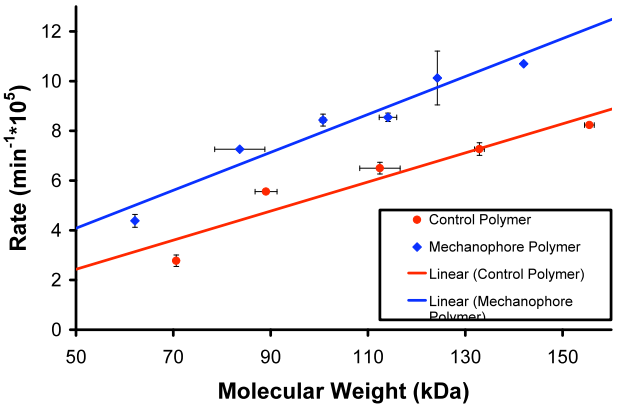


Figure S12. Comparison of the rates of cleavage between **1** (mechanophore polymer) and **2** (control polymer).

VIII. Modeling of Polymer Cleavage/GPC distribution.

Modeling of polymer chain length distribution upon both selective and Gaussian distribution was done using the procedure specified by Glynn and co-workers.[6] In both the selective cleavage model and the Gaussian distribution model, a cleavage threshold of 60 kDa as well as a linear increase in cleavage rate above this threshold were assumed.[7] All calculations were done using Microsoft Excel. In the case of selective cleavage,

polymer chains were split into equal length fragments upon chain scission. In the case of Gaussian scission, polymer fragmentation was assumed to occur in a Gaussian distribution around the center of the polymer using the parameters described by Basedow.[8] Initial polymer distributions for the modeling experiments were calculated by fitting the experimental polymer GPC trace (at time = 0, prior to sonication) with a Gaussian fit. Experimental GPC traces were corrected to account for drift in the refractive index signal.

IX. Computational Studies

Theory

To model the effects of a mechanical force on both dicyano-cyclobutane and the control polymer, we used the *ab initio* steered molecular dynamics (AI-SMD) method developed by Martinez and co-workers.[9] The potential energy surface and forces on the atoms were calculated "on the fly" by solving the electronic Schrödinger equation, which allows for arbitrary bond rearrangement. An external force is added to the *ab initio* internal forces and acts only on the attachment points.

$$\mathbf{F}^{tot} = \mathbf{F}^{\text{ab initio}} + \mathbf{F}^{ext} \qquad [1]$$

We used a constant force, fixed pulling scheme where the expression of the external force is given as:

$$\mathbf{F}_{ext} = \sum_{i}^{N_{attach}} F_0 \mathbf{n}_i \qquad [2]$$

Each attachment point is pulled under a constant magnitude force (F_0) towards a corresponding fixed point. The pulling direction ($\mathbf{n}_i$) for each attachment point is defined as:

$$\mathbf{n}_i = \frac{\mathbf{R}_i^{fix} - \mathbf{R}_i}{\left\| \mathbf{R}_i^{fix} - \mathbf{R}_i \right\|} \qquad [3]$$

where $\mathbf{R}_i^{fix}$ and $\mathbf{R}_i$ represent the positions of the ith fixed point and corresponding attachment point, respectively. The fixed points were chosen such that the attachment points are pulled in opposite directions. This is consistent with the forces the molecule

would feel when embedded in a polymer. Using this framework, the potential energy is adjusted so that it agrees with the AI-SMD forces defined above. The expression for this *force-modified* potential energy surface (FMPES) is:

$$V_{total}(\mathbf{R}) = V_{\text{ab initio}} + F_0 \sum_{i}^{N_{attach}} \left(\left\| \mathbf{R}_i^{fix} - \mathbf{R}_i \right\| - \left\| \mathbf{R}_i^{fix} - \mathbf{R}_i^0 \right\| \right) \quad [4]$$

where $\mathbf{R}_i^0$ is the initial position of the attachment points.

Computational Details

All calculations were done using the JAGUAR software package[10] within a modified version of the *ab initio* multiple spawning (AIMS) molecular dynamics code[11-13]. The electronic structure was solved using restricted Kohn-Sham density functional theory (DFT)[14,15] with the B3LYP[16,17] density functional and 6-31G* basis set. Initial conditions for the position and momentum were randomly sampled from a finite temperature Boltzmann distribution at 280K constructed from DFT/B3LYP/6-31G* vibrational frequencies at the no-force minimum geometry. Low vibrational frequencies under 100 cm^{-1} for the control molecule were ignored when generating this distribution.

AI-SMD Results of the Control

We used AI-SMD to look at a simplified model of control molecule **2**, where each end has been truncated with methyl-ester groups. This molecule can adopt either a *cis* or *trans* conformation with respect to the central C-C bond. Previous *ab initio* studies[18] using Hartree-Fock (HF) and Møller-Plesset second-order perturbation theory (MP2) have shown that the *cis* conformation is slightly more favored by less than 2 kcal/mol. We have performed AI-SMD on the *trans* conformation at 3 nN (Figure S13). Simulations for the *cis* conformation are currently in progress.

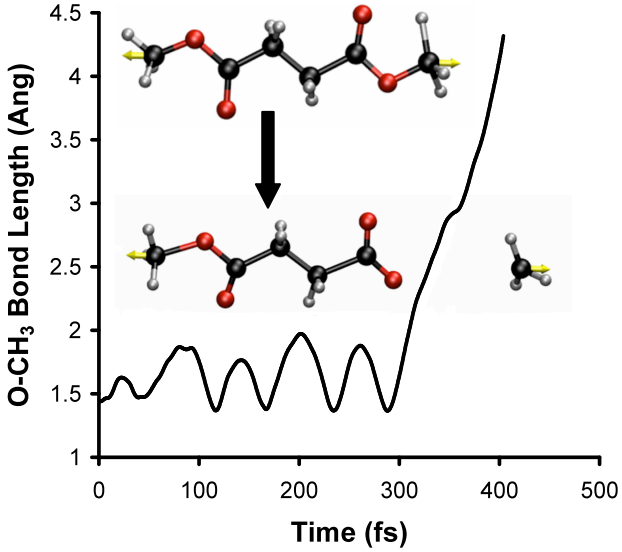


Figure S13. The O-CH_3 bond length plotted as a function of time for the only trajectory for control **2** to show bond rupture at 3 nN out of 20 total trajectories.

Out of 20 trajectories, only one trajectory resulted in a bond rupture event. Here, bond rupture occurred at the O-CH_3 single bond on the ester side chain, which could possibly suggest that bond rupture of this side chain could compete with cleavage of the cyclobutane ring. In fact, four trajectories for dicyano-cyclobutane showed bond rupture of the side ester chain, but this was only *after* cleavage of the cyclobutane ring had already taken place. Furthermore, the dynamics for the control polymer could indicate that the central C-C single bond of the control polymer may require more force to break. Even if it does break at higher forces, rupture of the central C-C single bond will have to compete with rupture at the O-CH_3 single bond. Therefore, it may be difficult to selectively cleave the central C-C single bond for the control polymer with mechanical force.

X. References for Supporting Information

1. Queffelec, J.; Gaynor, S.; Matyjaszewski, K., *Macromolecules* **2000,** 33, 8629-8639.
2. Suslick, K. S.; Goodale, J. W.; Schubert, P. F.; Wang, H. H., *J. Am. Chem. Soc.* **1983,** 105, 5781-5785.

3. Grossman, R. B.; Varner, M. A.; *J. Org. Chem.* **1997**, *62*, 5235-5237.
4. Cope, A. C.; Hofmann, C. M.; Wyckoff, C.; Hardenbergh, E. *J Am. Chem. Soc.* **1941**, *63*, 3452.
5. Malhotra, S. L. *J. Macromol. Sci., Part A.* **1986***, 23*, 729.
6. Glynn, P. A. R.; Van Der Hoff, B. M. E., Reilly, P. M. *J. Macromol. Sci.-Chem.* **1972**, *6*, 1653.
7. Vijayalakshmi, S. P.; Madras, G. *Polym. Degrad. Stab.* **2005**, *90*, 116.
8. Basedow, A. M.; Ebert, K. H. *Adv. Polym. Sci.* **1977**, *22*, 83.
9. Ong, M. T.; Leiding, J.; Tao, H.; Virshup, A. M.; Martinez, T. J. *J. Am. Chem. Soc.* **2009**, *131*, 6377.
10. Jaguar version 7.0 (Schrodinger, LLC, New York, NY, **2007**).
11. Ben-nun, M.; Martinez, T. J. *J. Phys. Chem.* **2000**, *104*, 5161.
12. Ben-nun, M.; Martinez, T. J. *Adv. Chem. Phys.* **2002**, *121*, 439.
13. Levine, B. G.; Coe, J. D.; Virshup, A. M.; Martinez, T. J. *Chem. Phys.* **2008**, *347*, 3.
14. Hohenberg, P.; Koh, W. *Phys. Rev.* **1964**, *136*, B864.
15. Kohn, W.; Sham, L. J. *Phys. Rev.* **1965**, *140*, A1133.
16. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.
17. Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B.* **1988**, *37*, 785.
18. Aleman, C.; Puiggali, J. *J. Org. Chem.* **1997**, *62*, 3076.