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Communication

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Mechanogeneration of Acid from Oxime Sulfonates

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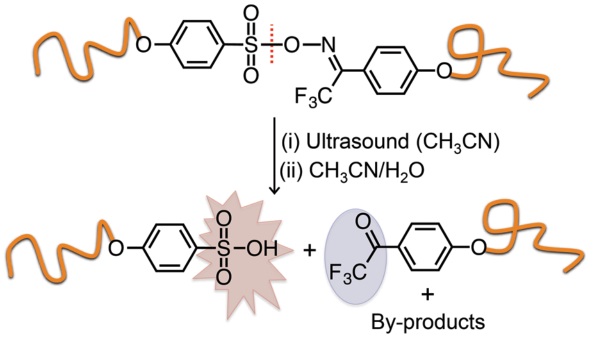
Supporting Information

ABSTRACT: The generation of acid under mechanical force is potentially useful for initiating proton-catalyzed changes in polymeric materials. Here we demonstrate that oxime sulfonates—known photoacid generators—are also acid generators when activated mechanically. NMR analysis of products suggests that the ultrasound-induced mechanochemical scission of the oxime sulfonate mechanophore also generates a ketone functional moiety, in addition to acid. Both acid and ketone moieties are useful for developing stress-responsive polymeric materials for autonomous self-healing applications.

Scheme 1. Oxime Sulfonate Mechanophore Generates a Trifluoromethyl Ketone Moiety and an Acid Constituent, Presumed To Be an Aryl Sulfonic Acid, upon Ultrasound-Induced Mechanical Scission



Acid-catalyzed reactions such as functional group deprotection, ester hydrolysis, and ring-opening polymerization are ubiquitous.[1] Coupling mechanical stress to acid catalysis holds great promise for modifying macroscopic polymer properties and may lead to unprecedented mechanoresponsive materials and self-healing applications.[2] Designing mechanoacids, i.e., mechanophores that undergo force-promoted reaction to produce acid from an initially nonacidic group, is the first step toward realizing such mechanoresponsive materials.

Mechanophore design has progressed considerably during the past decade.[3] Mechanophores that elicit a wide array of productive chemistry, such as mechanochromism,[4] mechanoluminescence,[5] activation of latent metal catalysts,[6] and generation of reactive species (radicals, alkenes, ketenes, etc.),[3b,7] are well developed. Mechanoacids, however, are still relatively scarce. There is only one known example of a mechanoacid.[6a] The known mechanoacid, based on a *gem*-dichlorocyclopropanated indene, is thermally unstable (degrades above 40 °C), which limits its practical utility for materials applications due to poor processability.

While mechanoacids are scarce, photoacids[8] are well known. Several classes of photoacids exist,[8b,c] and a majority of them contain weak bonds such as C−S, S−O,C−S, S−O, and C−I that may be mechanically activated. In addition, many photoacids display good thermal stability (100 °C < T_{dec} < 225 °C).[9] Activating photoacids under mechanical stress opens up numerous possibilities to design thermally stable mechanoacids. Herein, we demonstrate, using an oxime sulfonate photoacid as a mechanophore, that certain photoacids are activatable by mechanical means to generate acid (Scheme 1).

We hypothesized that the "S−O" (ca. 63 kcal/mol)[10] or "N−O" (ca. 48 kcal/mol)[10] bonds in oxime sulfonates, which are weaker than the C−C (ca. 83 kcal/mol)[10] or C−O (ca. 85 kcal/mol)[10] bonds, are mechanically sensitive toward bond homolysis, generating sulfonyloxyl ($RSO_3^•$) or sulfonyl ($RSO_2^•$) radicals similar to photolytic activation (Scheme 2).[8e] These radicals in the presence of water lead to acid generation, presumably via an aryl sulfonic acid. For ease of synthesis, the mechanophore (**5**, Chart 1) design included two symmetrical oxime sulfonate groups, but since the mode of proton formation involves a chain scission event, only one of the groups is expected to respond to force activation. Given that there is only a single mechanophore per polymer chain and it requires analytical characterization of the products' end-groups using ^1H and ^{13}C NMR or other techniques,[11] $-CF_3$ was chosen as a substituent to take advantage of the highly sensitive fluorine NMR for end-group analysis. CoGEF (Constrained Geometries simulate External Force) calculations,[12] which model the effect of external force on a mechanophore placed near the center of a polymer chain, predict preferential activation of the "S−O" bond in the oxime sulfonate mechanophore under mechanical stress (Figure S1), thus supporting our hypothesis.

Scheme 2. Proposed Pathways of Sulfonic Acid Generation via Photolysis of Oxime Sulfonates

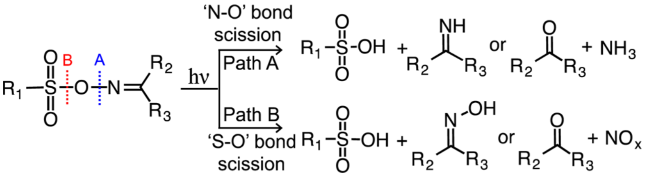


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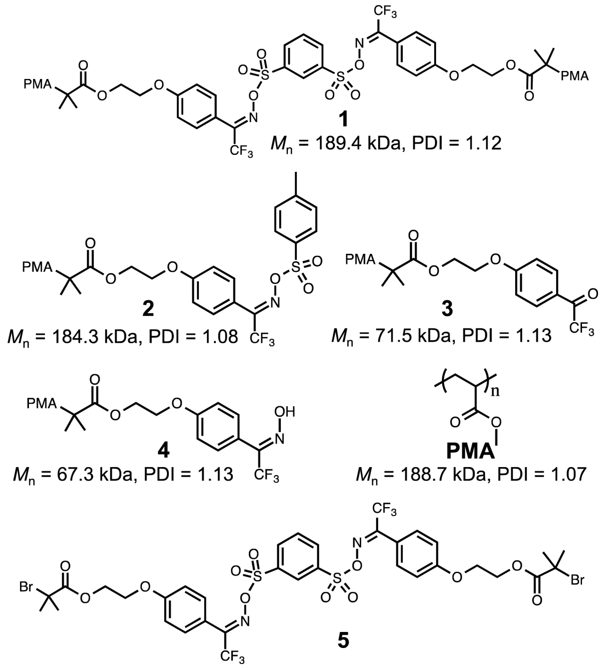
Chart 1. Structures of Polymers and Bifunctional Initiator



To experimentally verify mechanical activation of the oxime sulfonate mechanophore, we synthesized a series of polymers shown in Chart 1 using Cu (0) mediated single-electron-transfer living-radical polymerization (SET-LRP) (see the Supporting Information for synthetic details). The oxime may exist as (*E*) and (*Z*) isomers. To exclude effects of the stereochemical configuration on mechanochemical scission rates,[10] the oxime sulfonate mechanophore **5** was obtained exclusively as (*E*,*E*)-isomer starting from the corresponding (*E*)-oxime. We chose to synthesize the (*E*,*E*)-isomer of the mechanophore since the (*E*)- and (*Z*)-isomers of the precursor oxime were obtained in 9:1 ratio, respectively. Stereochemistry of the oxime and the oxime sulfonate mechanophore is confirmed by X-ray crystal structure, and ^{1}H and ^{19}F NMR data (see the Supporting Information for details). Polymer **1** exhibits excellent thermal stability in both solution and solid-state (Figure S2).

Pulsed ultrasound was used to probe mechanochemical activation of the polymers. Aliquots of sonicated polymer solution removed at regular intervals were analyzed by gel permeation chromatography (GPC). Polymer **1** with "chain-centered" mechanophore showed an expected decrease in molecular weight (MW) with sonication time, and the MW reached to approximately one-half (M_n = 103.2 kDa) the original polymer MW (M_n = 189.4 kDa) in about 30 min (Figure S3). In contrast, the low MW polymer $\mathbf{1}_{\text{low MW}}$ (M_n = 38.2 kDa; PDI = 1.13) for which chain scission is less susceptible to mechanochemical activation showed negligible change in MW (M_n = 36.7 kDa) upon ultrasonication for 60 min, which confirms that the activation is indeed of mechanical origin. Furthermore, the rate of chain scission in polymer **1** is significantly faster compared to that of the **PMA** control (M_n = 188.7 kDa; PDI = 1.07) of comparable MW but without a mechanophore (Figure 1). Under identical sonication conditions, the rate constant for cleavage of polymer **1** ($k' = 13.6 \times 10^{-5}$ min^{-1} kDa^{-1}), determined from the slope of the curve, is nearly twice as larger as that for the **PMA** control ($k' = 7.1 \times 10^{-5}$ min^{-1} kDa^{-1}), which provides substantial evidence for preference to cleavage at the mechanophore versus random cleavage along the polymer backbone.

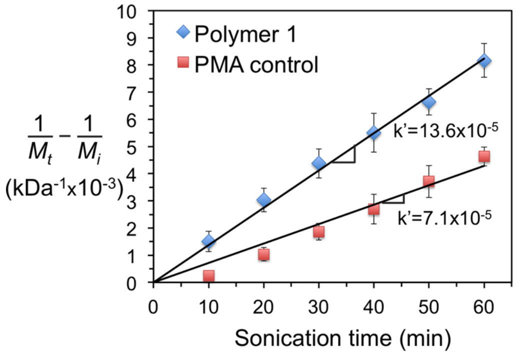


Figure 1. Rate of polymer chain scission under pulsed ultrasound. A 1 mg/mL polymer solution was sonicated with pulsed ultrasound (8.7 W cm^{-2}) under argon atmosphere at 6–9 °C. Measurements were performed in triplicate, and the error bars represent standard deviation at each data point.

Mechanochemical activation of the oxime sulfonate mechanophore in polymer **1** was further confirmed by using ^{19}F NMR spectroscopy. Upon ultrasonication, polymer **1** shows two new peaks at −66.60 and −71.53 ppm in the ^{19}F NMR spectrum (Figure 2). The intensity of these two peaks increases steadily with increasing sonication time, with a concomitant decrease in the intensity of the peak at −66.53 ppm corresponding to the uncleaved polymer **1** (Figure S4). These results clearly confirm that the scission occurred with high mechanochemical selectivity at or in close proximity to the mechanophore since fluorine signal in **1** comes from only the oxime sulfonate mechanophore and not the **PMA** polymer backbone. Furthermore, no new peaks were observed in ^{19}F NMR spectra upon ultrasonication of four different controls, which include (i) polymer $\mathbf{1}_{\text{low MW}}$; (ii) polymer **2** with "chain-end" mechanophore; (iii) small molecule mechanophore **5**; and (iv) a physical mixture of **5** and **PMA** polymer (Figure S5).

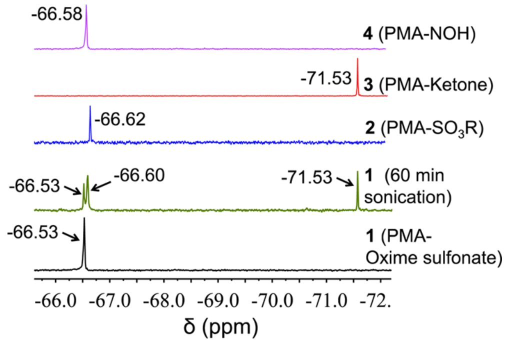


Figure 2. ^{19}F NMR spectra of polymers. CFCl$_3$ (δ = 0 ppm) was used as an internal standard.

To test acid generation upon ultrasonication of polymer **1**, pH measurements were carried out in CH_3CN/H_2O (99:1 v/v) mixture using a pH meter for organic solvents equipped with a H$^+$ ion sensitive glass electrode. Solutions of polymer **1** showed a steady decrease in pH with increasing sonication time and the pH changed from 6.0 to 3.6 in 60 min (Figure 3). In sharp contrast, **PMA** control showed a minimal change in pH (6.0 to 5.7) upon ultrasonication for 60 min. These results provide our

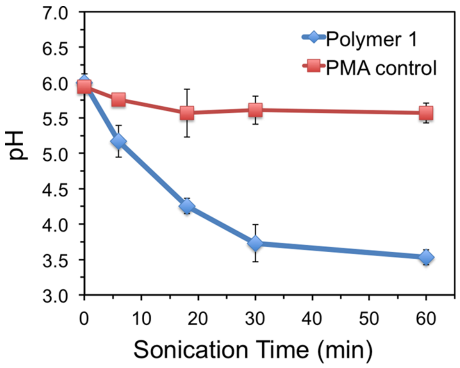


Figure 3. Change in pH with sonication time. The ultrasonicated polymer solution (1 mg/mL in CH_3CN) was concentrated, dried under vacuum, and CH_3CN/H_2O (99:1 v/v) was added to obtain a 3 mg/mL polymer solution for pH measurements. Measurements were performed in triplicate, and the error bars represent standard deviation at each data point.

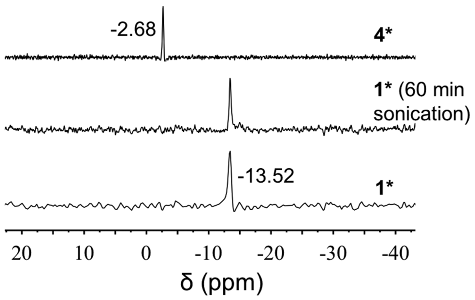


Figure 4. ^{15}N NMR spectra of polymers **1*** (before and after sonication) and **4***. The chemical shifts are reported relative to CH_3NO_2 standard.

best evidence for the generation of acid upon mechanical activation of the oxime sulfonate mechanophore.

We now turn to analyze the products formed from mechanochemical scission of the oxime sulfonate mechanophore in polymer **1**. A detailed study of the scission products is underway. Our preliminary findings are presented here. ^{19}F and ^{15}N NMR techniques are valuable in identifying some of the scission products. Mechanochemical scission of the oxime sulfonate mechanophore in polymer **1** exhibits two new peaks at −66.60 and −71.53 ppm in the ^{19}F NMR spectrum (Figure 2). The peak at −71.53 ppm matches well with that of authentically prepared trifluoromethyl ketone-terminated polymer **3** (Chart 1), thus confirming the formation of a ketone moiety. Ketones are also the most commonly observed byproducts of the photolysis of oxime sulfonates.[8] The peak at −66.60 ppm is tentatively assigned to the sulfonic acid-terminated PMA polymer. Since the chemical shifts of the authentically prepared sulfonate ester-terminated polymer **2** (−66.62) and the authentically prepared (*E*)-oxime-terminated polymer **4** (−66.58) are very close, it was difficult to unequivocally assign the peak at −66.60 ppm to either a sulfonic acid- or an (*E*)-oxime-terminated polymer based on the ^{19}F NMR data. Hence, ^{15}N NMR was employed.

Following similar synthetic procedures, analogous ^{15}N-labeled polymers **1*** (M_n = 162.6 kDa; PDI = 1.11) and **4*** (M_n = 68.2 kDa; PDI = 1.15) were synthesized using ^{15}N-labeled hydroxylamine (see the Supporting Information for details). Due to the low sensitivity of ^{15}N NMR as well as the low concentration of ^{15}N atoms per polymer chain, gel-phase NMR was used to record ^{15}N NMR.[13] The authentically prepared (*E*)-oxime-terminated polymer **4*** shows a peak at −2.68 ppm in the ^{15}N NMR spectrum (Figure 4). However, upon ultrasonication, polymer **1*** exhibits no peak at −2.68 ppm, confirming that the oxime-terminated moiety is not one of the products that we isolated.

Based on the proposed path B in Scheme 2, NO is another possible byproduct. A peak corresponding to NO (ca. 400 to 600 ppm) was not observed in the ^{15}N NMR spectrum of the ultrasonicated polymer 1*. NO is a gaseous, short-lived, open shell structure known to convert into other nitrogenous compounds upon reaction with oxygen or water, which make its detection difficult. Failure to observe peaks corresponding to imine (ca. −60 to −80 ppm), NH_3 (ca. −380 ppm) or NH_4^+ (ca. −360 ppm) in the ^{15}N NMR spectrum of the ultrasonicated polymer **1*** disfavors the "N−O" bond scission path A (Scheme 2), which is consistent with the prediction of CoGEF simulations. Low concentration of byproducts, coupled with low sensitivity of ^{15}N NMR, also limit the detection ability. We are currently investigating alternate detection methods to identify other possible byproducts.

In conclusion, we have demonstrated that an oxime sulfonate photoacid is also mechanically activatable to generate acid. This finding suggests that a thorough exploration of the photoacids is a reasonable approach to discover new mechanoacids that are thermally stable. Given the alignment of our experimental results with CoGEF calculations, a reasonable first step in this pursuit is to computationally survey the known photoacids for their tendency to undergo mechanochemically induced bond homolysis.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b00097.

Experimental details, synthetic procedures, and characterization data (^1H, ^{13}C, and ^{19}F NMR, and MS) (PDF)

X-ray crystallographic data for compounds **9** (CCDC 1443858), **15** (CCDC 1443857), and **16** (CCDC 1443856) (CIF)

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Notes

The authors declare no competing financial interest.

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