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Tension Trapping of Carbonyl Ylides Facilitated by a Change in Polymer Backbone

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Supporting Information

ABSTRACT: Epoxidized polybutadiene and epoxidized polynorbornene were subjected to pulsed ultrasound in the presence of small molecules capable of being trapped by carbonyl ylides. When epoxidized polybutadiene was sonicated, there was no observable small molecule addition to the polymer. Concurrently, no appreciable isomerization (*cis* to *trans* epoxide) was observed, indicating that the epoxide rings along the backbone are not mechanically active under the experimental conditions employed. In contrast, when epoxidized polynorbornene was subjected to the same conditions, both addition of ylide trapping reagents and net isomerization of *cis* to *trans* epoxide were observed. The results demonstrate the mechanical activity of epoxides, show that mechanophore activity is determined not only by the functional group but also the polymer backbone in which it is embedded, and facilitate a characterization of the reactivity of the ring-opened dialkyl epoxide.

The mechanical activation of reactive functional groups (mechanophores) has led to a number of advances,[1−8] including those related to stress-responsive polymers,[9,10] damage detection,[11,12] mechanocatalysis,[13,14] and mechanically exclusive reactivity.[15−17] A particular interest of ours lies in exploiting the concept of "tension trapping" reactive intermediates[17] and transition states.[18] To date, the emphasis in the field has been on the mechanophore, and the polymer scaffold has been regarded as an inactive handle that either is or is not coupled to the reaction coordinate of the mechanophore. Theoretical calculations have postulated the role of the polymer backbone in the mechanophore reactivity,[5,19] but no experimental evidence has been reported. We report here that a change in polymer backbone enables the mechanical activation of epoxides and subsequent trapping of the ring-opened intermediates. The reactivity of the intermediates is that of closed shell ylides, rather than open shell diradicals.

Since 1965, carbonyl ylide intermediates have been the suspected route through which substituted epoxides participate in electrocyclic addition to a variety of π systems.[20] Huisgen has largely been credited with providing the definitive proof of carbonyl ylide intermediate participation in thermal and photochemical cycloaddition of epoxides to dipolarophiles.[21] These intermediates are synthetically significant and versatile.[22] Not only can carbonyl ylides provide access to a host of heterocyclic products through electrocyclic addition reactions,[23,24] but they are also a route to various acetals through addition of alcohol containing compounds.[25,26]

We hypothesized that epoxides might undergo mechanically triggered ring-opening to carbonyl ylides (Figure 1), similar to the previously reported mechanical ring-opening of *gem*-dihalocyclopropanes (gDHCs), which leads to either 2,3-dihaloalkenes[2,27] capable of nucleophilic substitution at the allylic halogen[3] or 1,3-diradicals capable of radical addition.[18] Epoxides undergo a similar electrocyclic ring-opening, and, like gDHCs, epoxides represent minor structural perturbations to a polymer making them potentially interesting mechanophores for stress-responsive polymers.

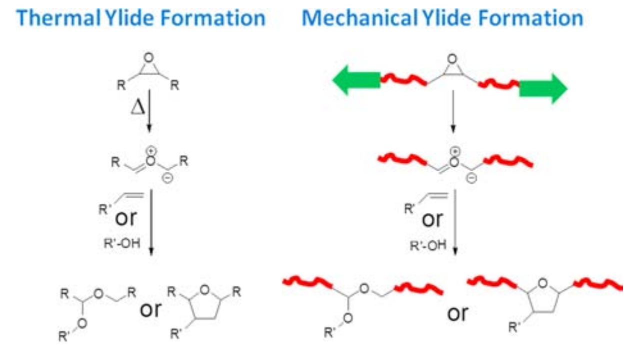

Figure 1. Reactivity of carbonyl ylides. (left) When heated, epoxides can ring open to carbonyl ylide intermediates which can then be trapped by either dipolarophiles or alcoholic solvents. (right) When mechanical force is applied to an epoxide, the same acetal and furan products are formed.

The barrier to ring-opening for unsubstituted epoxides[20] is larger than that for gDHCs[28] (65 kcal/mol vs 30−45 kcal/mol). Ring-opening of epoxides to carbonyl ylide intermediates are facilitated by the addition of charge stabilizing groups on either side of the epoxide ring.[29,30] These stabilizing groups lower the activation energy for ring-opening to within the same range of gDHCs.[20] Polymer scaffolds containing such groups are difficult to prepare and handle (solubility/stability), so we began by investigating whether such charge stabilizing groups were even necessary for mechanochemical activation of epoxides, and if mechanical activity could be realized on readily available polyolefin scaffolds.

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We investigated epoxide reactivity utilizing the large extensional shear forces generated by pulsed ultrasound, a readily accessible and widely used method of mechanically inducing polymer chain scission and screening for mechanophore reactivity.[1,31] Polybutadiene (PB) was epoxidized (60 ± 5% relative to initial alkene; PB-epox **1**, M_{n} = 384 kDa, see SI) and then sonicated to screen for mechanically induced ring-opening through isomerization (*cis* to *trans*). This isomerization would occur if *cis* epoxide rings were pulled open to the *s-trans/s-trans*[18] ylide intermediate which would then preferentially relax to the more stable *trans* epoxide due to a conrotatory ring closing (based on Woodward−Hoffmann rules) once the tension is released after chain scission or at the end of a bubble collapse.[32] No significant isomerization was detectable, however, even after the M_{n} had been reduced to a fraction of the original M_{n} through sonochemical chain scission (final M_{n} = 50 kDa) (Figure 2a).

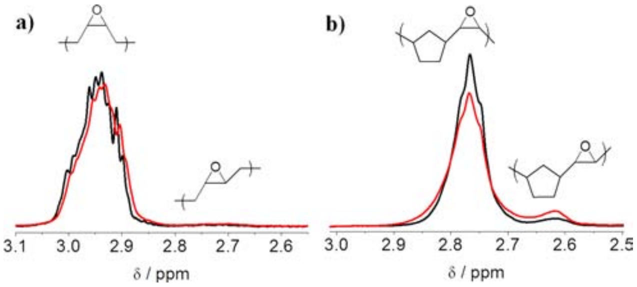
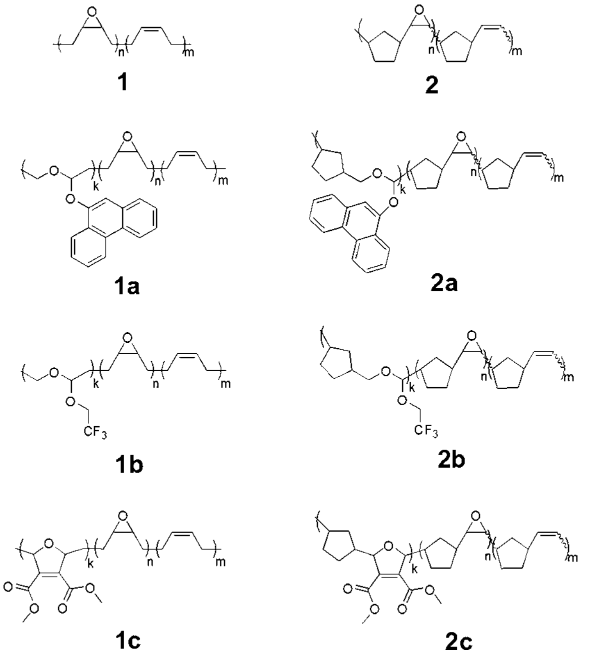


Figure 2. (a) ^{1}H NMR spectra of **1** before (black) and after 120 min of sonication at 30% amplitude (red). (b) ^{1}H NMR spectra of **2** before (black) after 120 min (red) of identical sonication conditions to **1**. Epoxide region normalized to the unreacted alkene resonance.

A different result was found when the polymer backbone was changed. Poly(norbornene) (PNB) was 50 ± 5% epoxidized (PNB-epox **2**, M_{n} = 965 kDa) and sonicated under identical conditions. It was evident, even as the M_{n} approached only half that of the original polymer, that the *cis* isomer content decreased with increasing sonication time (Figure 2b). This decrease is not due solely to selective destruction of *cis* isomers, as the total *trans* epoxide content (by ^{1}H NMR normalized to the alkene resonances) increased from an initial value of 6% to a final value of 11% after the molecular weight had decreased to 48 kDa following 120 min of sonication. The mechanical nature of the isomerization was confirmed by sonicating a low M_{n} (9 kDa, below the limiting M_{n} for sonochemical chain scission) **2** under identical conditions; no isomerization was observed, confirming that the isomerization is mechanically driven (see SI). We note that the difference in mechanical reactivity cannot be attributed to molecular-weight dependent differences in the achieved forces, because isomerization in **2** is observed throughout the scission process, even as the molecular weight drops below 100 kDa (see SI). A more important concern stems from previous work that suggests that the extent of activity can be diminished by the presence of "weak bonds" along the polymer backbone.[33] To test whether **1** had intrinsically weaker backbone bonds than **2**, we normalized the scission profiles to the contour lengths of the polymers. The normalized degradation profiles are quite similar, and if anything suggest a slightly greater degradation rate in **2** than in **1**, confirming that the lack of mechanophore activity in **1** is not due to an intrinsic fragility along the main chain that leads to scission prior to widespread activation (see SI).

In order for this isomerization to occur, the C−C bond of the epoxide must be broken, suggesting the likely formation of a ring-opened ylide intermediate. To test this hypothesis, each polymer was sonicated in the presence of small molecules capable of addition to carbonyl ylides. Chart 1 illustrates the two different polymers that were investigated in this study and the anticipated products from addition of various small molecules to the two carbonyl ylides that might potentially be formed along each of the polymer main chains.

Chart 1. Structures of Epoxidized Polymers and Anticipated Product Structures[a]



[a]Note that multiple stereoisomers are not depicted.

Stress-induced acetal formation was investigated by sonicating both epoxidized polymers in the presence of hydroxyl-containing molecules. Carbonyl ylides are known to react with alcoholic solvents such as methanol,[26,34] and **2** was sonicated for 180 min in a 0.1 M solution of 9-phenanthrol in THF. The GPC/UV spectra indicated that phenanthrene had been incorporated onto the polymer backbone to produce **2a** (Figure 3b). ^{1}H NMR of the sonicated product also confirms the acetal formation (see SI). No evidence of such addition was found for **1** under identical conditions (Figure 3a). Also, when a low M_{n} (13 kDa, below the limiting M_{n} for sonochemical chain scission) **2** was sonicated under identical conditions in the presence of 9-phenanthrol, there was no evidence of **2a** formation (see SI), confirming that the acetal formation is mechanically induced. Hydrolysis of the stress-induced acetal was performed using aqueous HCl. Upon treatment with HCl, the polymer became difficult to work with (mostly insoluble in common organic solvents), but the ^{1}H NMR of the small amount that was soluble indicated there was no longer a phenanthrene acetal attached to the polymer (see SI). Additional acetal formation was observed when polymer **2** was sonicated for 120 min in a 2 M trifluoroethanol (TFE) solution in THF; ^{19}F NMR indicated the formation of acetal **2b** (Figure 3c). In comparison, no addition was observed when a

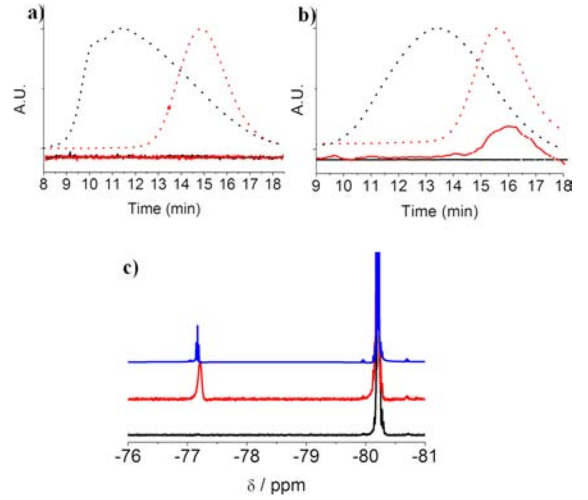


Figure 3. a) GPC-RI/UV traces of **1** stirred (RI, black dots; UV, black; M_n = 250 kDa) and sonicated (RI, red dots; UV, red; M_n = 26 kDa) in a 0.1 M 9-phenanthrol THF solution for 180 min at 30% amplitude. b) GPC-RI/UV traces of **2** stirred (RI, black dots; UV, black; M_n = 250 kDa) and sonicated (RI, red dots; UV, red; M_n = 36 kDa) under identical conditions. c) ^{19}F NMR spectra of **1** (black; initial M_n = 200 kDa, final M_n = 53 kDa) and **2** (red; initial M_n = 250 kDa, final M_n = 54 kDa) after sonication for 120 min in a 2 M TFE solution in THF, and acetal model compound 2-(1-ethoxyethoxy)-1,1,1-trifluoroethane (blue). All sonications were at 30% amplitude. Spectra are referenced to TFE, $\delta = -80.2$.

solution of **2** was stirred for 24 h in a 2 M TFE solution in THF (see SI).

Mechanically assisted cycloaddition was also investigated using the well-known dipolarophile carbonyl ylide trap dimethyl acetylenedicarboxylate (DMAD).[35] After sonication in the presence of DMAD, there was no change in the ^{1}H NMR spectrum of **1** (see SI). When **2**, rather than **1**, was sonicated in the presence of DMAD, however, ^{1}H NMR indicated formation of the expected product **2c** (see SI). The chemical shifts of new resonances at δ = 3.76 and 4.91 ppm are in agreement with published chemical shift values for methyl ester and furan protons, respectively.[36] Similar studies were done on PNB with varying levels of epoxidation (50−80%), and the amount of DMAD addition per epoxide stayed constant (see SI). The dipolarophiles dimethylfumarate and dimethylmaleate were also screened for furan formation when sonicated with **2**, and the ^{1}H NMR spectra showed evidence of addition of these species to the polymer as well (see SI). The different stereochemistry in these isomeric dipolarophiles translates to the addition products. The ^{1}H NMR spectrum from dimethyl maleate addition is consistent with *cis* stereochemistry between carboxymethyl groups in the product, whereas the ^{1}H NMR spectrum from dimethyl fumarate addition is consistent with a *trans* isomer. We therefore conclude that the addition is effectively concerted, as suggested by recent computational studies of related carbonyl ylides.[37]

Control experiments were conducted to account for other possible mechanisms of dipolarophile addition (see SI). First, stirred controls both of an unsonicated and previously sonicated **2** (without dipolarophile) were negative for cycloaddition. Second, sonication of unfunctionalized PNB in the presence of DMAD led to no evidence of polymer addition. Third, the cycloaddition could not be promoted thermally. When **2** was heated to 180 °C for 120 min, almost all of the material was cross-linked and insoluble common organic solvents. Lastly, when a low-molecular-weight polymer (9 kDa, below the limiting molecular weight for sonochemical chain scission) was sonicated under identical conditions to its high-molecular-weight analogue, there was no evidence of **2c** formation.

It is widely accepted that these ylides, often drawn as a zwitterion as in Figure 1, possess a considerable amount of 1,3-diradical character,[20,29] but a complete electronic picture is still a topic of debate. Prior investigations have mainly been theoretical, but mechanical ylide formation provides an opportunity to probe experimentally the diradical character of the opened epoxide in the context of radical addition using methods applied to the 1,3- and 1,4-diradicals formed from *gem*-difluorocyclopropanes (*g*DFCs)[18] and perfluorocyclobutane aryl ethers,[17] respectively. Sonication of **2** in the presence of 32 mM coumarin-2,2,6,6-tetramethylpiperidine-1-oxyl, which efficiently traps carbon-centered radicals,[38] showed levels of CT addition commensurate with addition to newly formed chain ends (based on comparisons to unfunctionalized polymers), without substantial addition to the activated epoxides (see SI). Whereas the trapped carbonyl ylide exhibits observable dipolarophile addition reactivity, it has a lower propensity for radical addition of the sort observed in the analogous 1,3-diradical formed from *g*DFCs. We emphasize that discussions of reactivity should not be confused with different structural outcomes to the ring-opening, because the diradical and zwitterionic depictions are resonance structures that both contribute to a full description of a single intermediate. Rather, these results expand the foundation for relating the complex electronic structure of carbonyl ylides to their reactivity.

Finally, we consider why the change in polymer backbone to PNB from PB affects the mechanical activity of the epoxides. As noted above, a comparison of normalized chain scission rates eliminates the possibility that **2** is simply experiencing higher forces than **1**, for example due to greater viscoelastic coupling. The possibility that the epoxide rings of **1** are opening but simply closing too quickly to be trapped by a bimolecular process is ruled out by the lack of isomerization in **1**. The likely root of the backbone effect is either (a) the epoxidized PNB is intrinsically more reactive than the epoxidized PB, for example due to steric repulsion in the reactant that is relieved upon opening to the transition state (an extra "push" from within), or (b) the polymer backbone might enhance chemomechanical coupling (a more efficient "pull" from without). We addressed the possible contributions of type (a) via electronic structure calculations. Computationally, we find that the reaction energies of the two ring-opening reactions (from epoxide to carbonyl ylide) differ by less than 1 kcal mol^{-1} (see SI). Any relief of steric congestion upon ring-opening should be, if anything, less important in the transition state than in the fully opened ylide, and so the type (a) contributions appear to be minimal. These results therefore suggest that the cyclopentyl groups increase the efficiency of force transduction. Polymer tether effects have been noted previously. Boulatov has recently shown that conformational heterogeneity contributes significantly to reaction chemomechanics[39] and that a given constraining force might couple differently to a local reaction coordinate as a function of polymer tether.[40] The results shown here provide experimental support for this picture, although the nature of the sonochemical studies does not at present permit the effect to be quantified. Such coupling effects might be expected to be relatively modest, but on a qualitative level they are shown here to provide access to tension trapped intermediates that are otherwise inaccessible through sonochemical methodologies. Quantifying the enhanced coupling provided by cyclopentyl tethers in related systems is a subject of ongoing work in our laboratory.

In conclusion, the mechanochemical isomerization of epoxides has been demonstrated, and reactive trapping experiments provide strong evidence for the formation of tension trapped carbonyl ylide intermediates. The synthetic ease and low cost of epoxidation, its minimal structural perturbation, and the rich reactivity of carbonyl ylides offer possibilities as a platform for stress-responsive polymeric materials and also as a tool for studying the physical organic chemistry of ylide intermediates. The isomerization and the capture of the intermediate were made possible by manipulation of the polymer scaffold within which the epoxide mechanophore is embedded. The fact that poly(norbornene) is found to be an enabling scaffold is particularly attractive, given that it and its derivatives are so easily accessed via ring-opening methathesis polymerization.[41] Looking ahead, we will examine the generality of the poly(norbornene) scaffold and look for additional scaffolds as a mechanism to enhance the mechanical activity of known mechanophores and enable the discovery of new mechanophores.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR, GPC, and UV characterizations; computational details; control experiments 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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