

Single-Molecule Observation of a Mechanically Activated *Cis*-to-*Trans* Cyclopropane Isomerization

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ABSTRACT: The mechanochemical activation of *cis*-gem-difluorocyclopropane (*cis*-gDFC) mechanophore in toluene was characterized with single-molecule force spectroscopy. Unlike previously reported behavior in methyl benzoate (MB), two transitions are observed in the force vs extension curves of *cis*-gDFC polymers in toluene. The first transition occurs at the same force of ~ 1300 pN observed previously in MB, but a second transition is observed at forces of ~ 1800 pN that reveal the partial formation of the *trans*-gDFC isomer. The behavior is attributed to competing reactions of the *cis*-gDFC at the 1300 pN plateau: addition of oxygen to a ring-opened diradicaloid intermediate, and isomerization of *cis*-gDFC to its *trans* isomer.

Covalent polymer mechanochemistry¹ has received considerable attention in recent years, due in large part to its potential to unlock reactivity that is otherwise inaccessible. In this regard, a promising application is “tension trapping” of transition states and intermediates, which enables studies of reactivity and reaction dynamics.² For example, large forces can be used to trap the 1,3-diradicaloid transition state of *gem*-difluorocyclopropane (gDFC) inversion as the global minimum on the force-coupled potential energy surface.^{2a} The trapped diradicaloid undergoes intermolecular addition with nitroxide radical^{2a} and intramolecular disproportionation with adjacent tension-trapped diradicaloids.³

Recently, we used single-molecule force spectroscopy (SMFS) to quantify the force required for *cis*-gDFC ring opening to occur on the ~ 100 ms time scale of the experiment, and a representative force–extension curve is shown in Figure 1a (blue line). Those studies employed methyl benzoate (MB) as the solvent for SMFS, and the force-coupled reactivity observed at a single plateau force of $f^* \approx 1290$ pN was consistent with theoretical predictions.⁴ The extension at the plateau is attributed to the irreversible consumption of the mechanically generated 1,3-diyl, for example via an addition reaction. Here we report that when toluene, instead of MB, is used as the solvent for the same SMFS experiment, the consumption of the diyl is suppressed, leading to an unusual combination of reaction dynamics observed at the single-molecule level: the first observation of a covalently limited *cis*-to-*trans* isomerization triggered by mechanical force, and the first direct observation of competing reaction paths in a single-molecule experiment of this type.

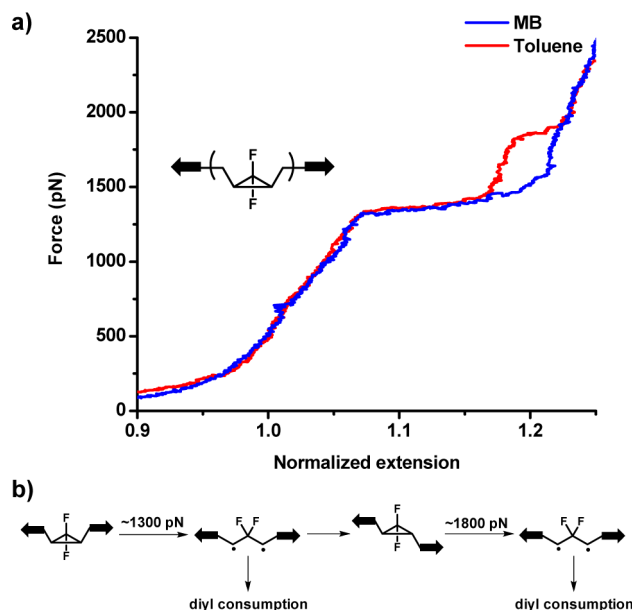


Figure 1. (a) Representative SMFS force curves of *cis*-gDFC polymer obtained in methyl benzoate (blue) and toluene (red), at a retraction velocity of 300 nm/s. The force curves are normalized to the stress-bearing sub-chain’s contour length at 500 pN. (b) The mechanistic scheme for *cis*-gDFC when the SMFS experiment is performed in toluene. At ~ 1300 pN, *cis*-gDFC is pulled open into a 1,3-diyl, which undergoes competing reactions between irreversible diyl consumption and conrotatory ring closing to the *trans* isomer. When the force further increases to 1800 pN, the *in situ* formed *trans*-gDFC is pulled open to 1,3-diradicaloid and fully consumed.

A typical SMFS force curve for a *cis*-gDFC-functionalized poly(butadiene) (*cis*-gDFC content is 50% of the butadiene repeats) in toluene is shown in Figure 1. Two plateaus are observed: the first occurs at a plateau force of $f_1^* \approx 1300$ pN, as expected from the previous work in MB, but we were surprised to see that (a) the length of the plateau is shorter than in MB, and (b) an unexpected second plateau is observed at $f_2^* \approx 1800$ pN. The second plateau occurs reproducibly on different days with different batches of polymer. We note that the precise values of f^* are rate and contour length dependent, and they are used here for illustrative purposes only; when desired, kinetic data are obtained by fitting the entire force curve as described previously.⁵ As shown in the overlaid force curves in

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Figure 1, the total relative extension from the two plateaus in the force curve obtained in toluene is equivalent to that of the single plateau in the force curve obtained in MB. The identical extension suggests the ultimate formation of the same product, but through different processes.

The nature of the ring opening in toluene is suggested by the value of $f_2^* \approx 1800$ pN, which is indistinguishable from that of the ring opening for *trans*-gDFC (Figure 2). We therefore

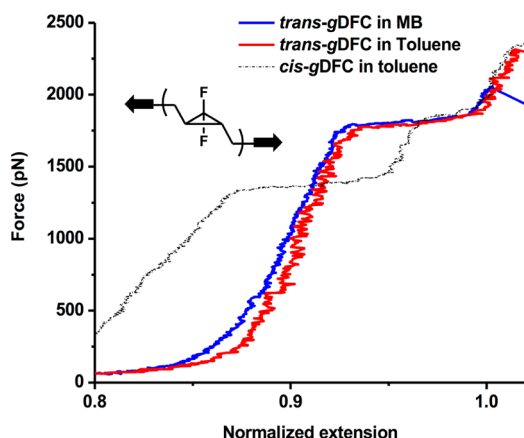


Figure 2. Representative SMFS force curves of *trans*-gDFC polymer obtained in methyl benzoate (blue) and toluene (red), at a retraction velocity of 300 nm/s. The force curves are normalized to the stress-bearing sub-chain's contour length at 2000 pN. The *cis*-gDFC force curve in toluene (dashed line) from Figure 1 is provided for comparison. The differences in extensions are due largely to the difference in mechanophore contents (50% of poly(butadiene) repeats for the *cis*-gDFC, 33% for *trans*-gDFC).

conclude that some *cis*-to-*trans* ring isomerization is occurring at the first plateau. Figure 2 also shows that in the case of *trans*-gDFC, only one plateau is obtained at ~ 1800 pN in both toluene and MB, and that the force curves in those solvents are indistinguishable.

The contour lengths of *cis*-gDFC and *trans*-gDFC repeats were obtained by modeling (see Supporting Information). For each gDFC, *cis*-to-*trans* isomerization produces only a $\sim 4\%$ extension in the contour length. If all of the *cis*-gDFCs isomerized into their *trans* counterparts at the first plateau and then underwent ring opening to form the diradicaloid, the extension at the second plateau would be much larger than that at the first plateau. Instead, the observed extensions at the two plateaus are comparable (Figure 1), indicating that only a fraction of the *cis*-gDFCs undergo *cis*-to-*trans* isomerization at the ~ 1300 pN plateau under these experimental conditions. Based on a comparison of the experimental extensions at the plateaus and the theoretical extension produced by each pathway, the branching ratios of the two pathways are roughly $\sim 60\%$ isomerization and $\sim 40\%$ diyl consumption. To the best of our knowledge, this is the first SMFS characterization of either a covalent isomerization or of directly competing covalent reaction outcomes from the same mechanophore.

While the identity of the ultimate ring opened product is not central to the core conclusion of unexpected *cis*-to-*trans* isomerization, we considered the nature of the process that consumes the ring opened diyl. Possibilities include the migration of fluoride (similar to what has been observed in dichloro- and dibromocyclopropane mechanophores^{5,6}), hydrogen atom abstraction from solvent, or oxygen addition. Both

fluoride migration and oxygen addition are plausibly enhanced by the polarity of MB relative to toluene. To test the importance of solvent polarity, we conducted identical experiments in diphenyl ether, whose dielectric constant ($\epsilon = 3.7$)⁷ is intermediate to that of MB and toluene ($\epsilon = 6.7$ and 2.4, respectively).⁷ A second plateau of intermediate length is observed (see Supporting Information), supporting the role of solvent polarity.

Between fluoride migration and oxygen addition, intermolecular reaction with ambient O_2 , potentially forming a 5-membered peroxide ring (Figure 3) and associated downstream

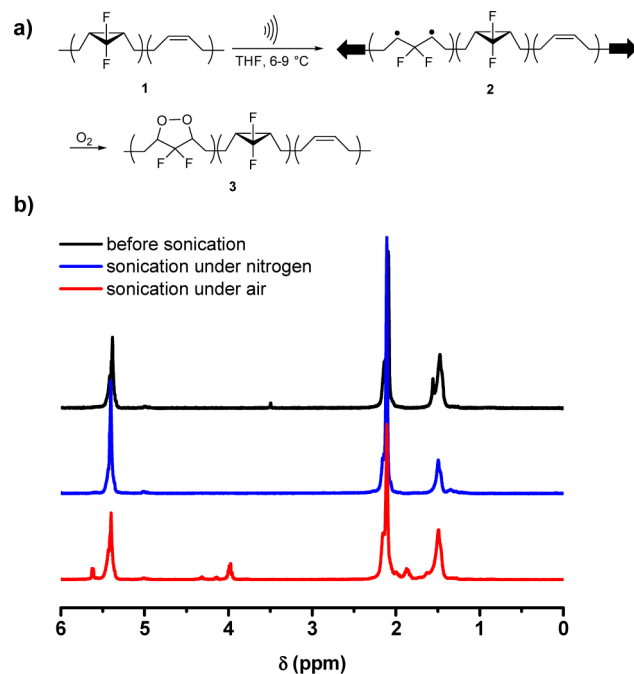


Figure 3. (a) Proposed mechanistic scheme for oxygen addition during sonication of gDFC-PB in an air atmosphere. Mechanically activated gDFC ring opening leads to a tension-trapped diradical that undergoes an intermolecular addition with ambient oxygen to form a 5-membered-ring peroxide. (b) 1H NMR of gDFC-PB before sonication (black), after sonication under nitrogen (blue) and after sonication under air (red). The peak at 4.0 ppm that is formed in the presence of O_2 is consistent with expectations based on other 5-membered-ring peroxides.

products, has been reported previously in similar diradicaloid species,⁸ and rapid addition of oxygen is expected from previously reported rate constants of oxygen addition ($k \approx 10^6$ $M^{-1} s^{-1}$) to similar singlet 1,3-diyls⁸ and $[O_2] \approx 0.01$ M in toluene.⁹ The expected $k[O_2] \approx 10^4$ s^{-1} is therefore fast relative to the rate of the force-coupled ring opening reaction (~ 10 s^{-1} at 1300 pN), as required for diyl formation to remain the rate-determining step. It is obviously not possible to characterize the product of the SMFS experiment, but further support for oxygen addition is found by sonicating *cis*-gDFC polymer in an atmosphere of air (Figure 3; see Supporting Information for details). Both 1H and ^{13}C NMR spectra show new peaks that are not found when the polymer is sonicated under an N_2 atmosphere, and that are consistent with oxygenated fluorocarbons.¹⁰ No fluoride migration is observed in the sonication experiments, and so the addition of oxygen to the trapped diyl is more rapid than fluoride migration in that

setting; we therefore favor it as the more likely event in the SMFS experiments.

The origin of the two plateaus obtained in toluene is different from previous reports in which two different sets of reactants are embedded along the same polymer backbone and differential reactivity exists before the force is applied.^{4,11} The mechanically induced *cis*-to-*trans* isomerization itself is rare, joining that observed previously in proline isomerization of polypeptides as a mechanism for mechanical chain extension.¹² The direct *cis*-to-*trans* isomerization stands in contrast to the complementary *trans*-to-*cis* isomerization enabled by “catch-and-release” ratcheting under high strain rate/high force transient extensions,^{2a,c} and provides a potential mechanism for probing stress/strain history in complex mechanical environments. The concept of multi-step, *in situ* formation and activation of a new mechanophore with differential mechanochemical activity might also be useful for other applications of covalent polymer mechanochemistry, including stress-sensing,¹³ release of small molecules,¹⁴ stress-induced remodeling of polymeric materials,^{6,15} catalysis,¹⁶ and soft devices.¹⁷

■ ASSOCIATED CONTENT

📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b06452.

AFM and sonication experiments; modeling data (PDF)

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Notes

The authors declare no competing financial interest.

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