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Reactive Cross-Talk between Adjacent Tension-Trapped Transition States

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Supporting Information

ABSTRACT: Tension along a polymer chain traps neighboring *s-trans*/*s-trans*-1,3-diradicals from the mechanically induced ring opening of *gem*-difluorocyclopropanes (*g*DFCs). The diradicals correspond to the transition states of the force-free thermal isomerization reactions of *g*DFCs, and the tension trapping allows a new disproportionation reaction between two simultaneously trapped diradicals to take place.

We recently reported that the tension along a polymer main chain can be used to trap species that are at or very near the transition state of a chemical reaction,[1] namely, the *s-trans*/*s-trans*-1,3-diradicals that form during the isomerization of 2,3-disubstituted *gem*-difluorocyclopropanes[2,3] (*g*DFCs) on polybutadiene (PB) scaffolds. The underlying reactivity is shown in Figure 1. The thermal activation of a *trans*-*g*DFC proceeds in a formally disrotatory process to the *s-cis*/*s-trans* diradical transition state, which undergoes ring closure by the same mechanism to regenerate the *trans*-*g*DFC (Figure 1a). An analogous process occurs for *cis*-*g*DFCs, but the transition-state structure is the *s-trans*/*s-trans* diradical (Figure 1b). Applying a large mechanical force through sonochemical shear fundamentally changes the potential energy surface, causing the ring opening to proceed in a conrotatory fashion to the *s-trans*/*s-trans* diradical, which, despite being the transition state of a thermal reaction,[2,3] is a global minimum on the force-coupled potential energy surface. Once the transient shear event ends, the diradical closes in the normal, force-free disrotatory manner to the *cis* isomer. Here we report that large numbers of these diradicals can be trapped simultaneously and in proximity to each other, enabling a new fragmentation reaction between two diradicals to take place.

In our previous study, well over 100 *trans*-*g*DFC isomerization reactions were typically observed to occur by the time the polymer M_n was cut in half [i.e., in one scission cycle; see the Supporting Information (SI)] in a competing mechanochemical process.[1] Unexpectedly, however, the extent of isomerization depends on the *g*DFC content of the copolymer (Figure 2), which was prepared by difluorocarbene addition to *cis*/*trans*-PB using known methods.[4,5] The mechanical activation of *g*DFCs was induced by pulsed ultrasound (11.3 W cm^{-2}) in an ice water bath (6−9 °C) under an inert N_2 atmosphere and monitored by ^{19}F NMR spectroscopy, and the molecular weight degradation was determined from multiangle light scattering (MALS) gel-permeation chromatography (GPC). Critical for the work reported here is that both isomerization and scission of the polymer were observed; for convenience, we define ϕ_1 to be the fraction of *trans*-*g*DFCs that isomerize during the first scission cycle. Normalizing the extent of isomerization in terms of the scission cycle is a robust and convenient mechanism to account for variations in the magnitude of the forces generated as a result of, for example, polymer molecular weight, *g*DFC content, and fluctuations in sonication power.[6] We note that the variation in absolute polymer scission rates was much too small to account for the differences reported here (see the SI).

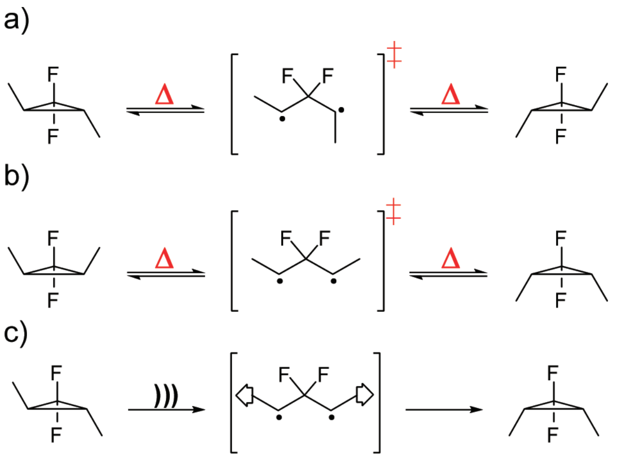

Figure 1. Thermally, both (a) *trans*- and (b) *cis*-*g*DFCs preferentially open and close through a disrotatory process via a 1,3-diradical transition state. (c) Application of a large mechanical force leads to the formation and trapping of the *s-trans*/*s-trans*-1,3-diradical "transition state", which closes to the *cis*-*g*DFC once the force is removed.

In the random *g*DFC copolymers, higher *g*DFC content gave lower levels of isomerization (Figure 2). For example, $\phi_1 = 0.41$ and 0.19 for copolymers of 97 kDa/3.8% *g*DFC and 88 kDa/59% *g*DFC, respectively. The inverse dependence of isomerization rate on copolymer loading was observed for polymers with *g*DFC loadings of up to 95%, spanning ϕ_1 from 0.07 to 0.41 (Figure 2c).

The decrease in isomerization efficiency with increasing *g*DFC incorporation suggested participatory effects of neighboring ring-

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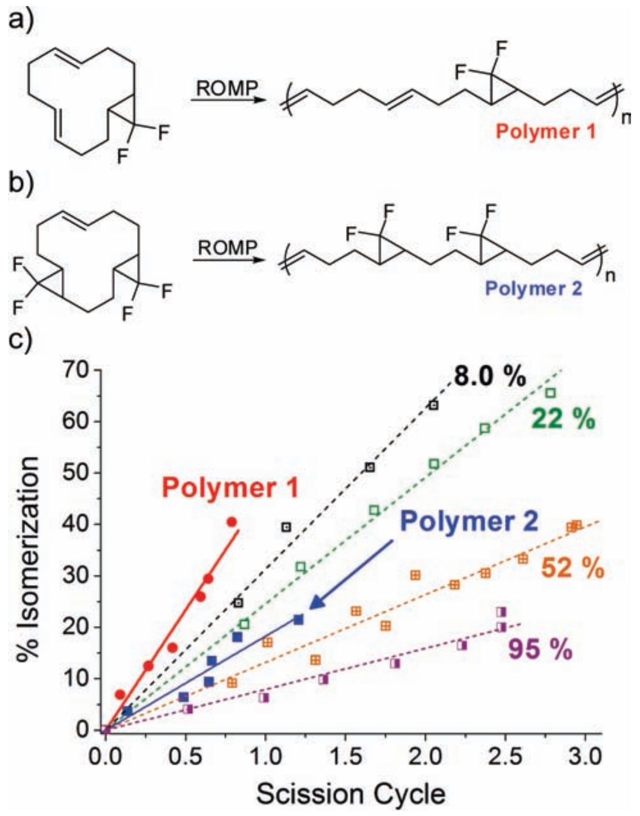

Figure 2. (a, b) Ring-opening metathesis polymerization yields (a) polymer **1** (33.3% *g*DFC) and (b) polymer **2** (66.7% *g*DFC). (c) Fraction of *trans*-*g*DFC converted to *cis*-*g*DFC as a function of difluorocarbene addition to PB. Points are experimental values taken from ^{19}F NMR integrations and have an estimated uncertainty of ±3%. Lines are linear fits constrained through the origin and are used to extrapolate the % isomerization to one scission cycle.

opened 1,3-diradicals along the polymer backbone. This was confirmed by ring-opening metathesis polymerization (ROMP) of a mono-*g*DFC-cyclododecatriene to yield a 66 kDa copolymer with 33.3% *trans*-*g*DFC content and no adjacent *g*DFCs (Figure 2a, polymer **1**). Sonication of **1** led to the highest normalized extent of isomerization, over twice that of an equivalently functionalized random copolymer (319 kDa, 32% *g*DFC−PB).

A likely explanation is that as the polymer is stretched under tension, the peak force along the polymer backbone increases and more and more *g*DFCs are pulled into the diradicals that correspond to force-free transition states. Both the peak force and activated zone continue to grow until the polymer snaps, halting subsequent *g*DFC activation. This picture of multiple transformations occurring in a single extension event is consistent with our earlier observations on the related mechanical activation of *gem*-dichlorocyclopropanes (*g*DCCs) under similar conditions.[7] The influence of neighboring *g*DFCs would then be explained by the mechanism shown in Figure 3a. Activation of adjacent *g*DFCs leads to a tetraradical that disproportionates at a lower force than the rest of the polymer backbone, halting the mechanical activation prematurely.

Bernoullian statistical analysis[8] supports this picture. The probabilities of adjacent *g*DFCs [P_{FF} = (% *g*DFC)^2] were calculated assuming a random distribution of *g*DFCs. The probability of generating and breaking a weak bond at any point in the extension event, as proposed in Figure 3a, is proportional to the absolute number of adjacent *g*DFCs in the mechanically active zone of the polymer, the size of which is in turn proportional to the degree of polymerization (DP). Importantly, the isomerization efficiencies correlate almost perfectly with $P^* = P_{FF} \cdot \mathrm{DP}$ (Figure 3b) as opposed to P_{FF} alone (Figure S94 in the SI). These analyses included polymers of varying molecular weights, *g*DFC content, and controlled *g*DFC microstructure (including polymer **2** in Figure 2b) beyond those for which data is shown in Figure 2c (Table S1 in the SI). Additional experimental support for the mechanism was provided by ^{1}H and ^{19}F NMR spectroscopy of the reaction products generated by the sonication of 95% *g*DFC−PB. The chemical shifts and coupling patterns of new resonances in the ^{1}H and ^{19}F NMR spectra agree with those of model compounds with terminal 3,3-difluoroalkenes, and the relative intensities of the new peaks are consistent with the 3,3-difluoroalkenes being the dominant product of chain scission (Figures S81−S93).

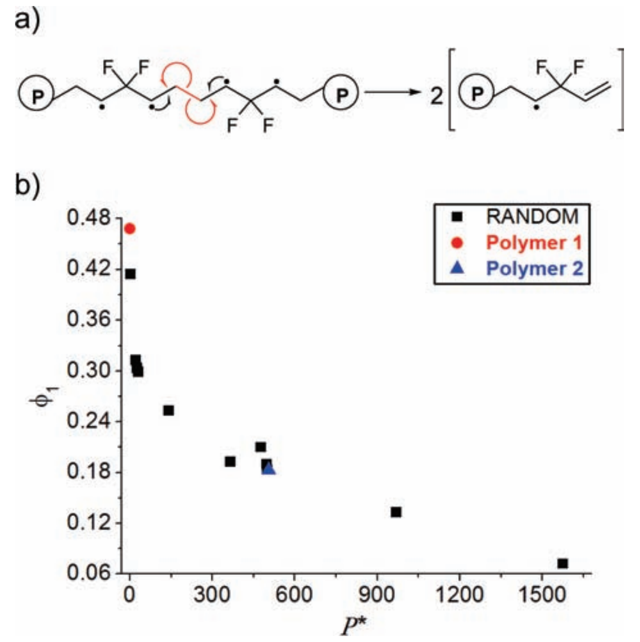

Figure 3. (a) Proposed mechanism for the force-induced fractionation of neighboring 1,3-diradicals; **P** denotes the polymer chain. (b) Extent of *trans*-to-*cis* isomerization efficiency at one scission cycle (ϕ_1) as a function of P^*.

An alternative explanation is that a weak bond is created simply by generating one diradical next to an intact cyclopropane. To address this possibility, a 36% *g*DFC−PB was reacted with dichlorocarbene to yield a mixed *g*DFC−*g*DCC−PB polymer with 36% *g*DFC and 26% *g*DCC content. The 36% *g*DFC polymer had the same ϕ_1 value (0.20) with or without the added *g*DCCs. Much stronger support was provided by ab initio steered molecular dynamics (AISMD) calculations under simulated force.[1,11] The AISMD simulations confirmed that once one *g*DFC opens to the diradical, the ring opening of an adjacent *g*DFC precedes bond scission between the open diradical and closed *g*DFC (Figure 4). A total of 20 trajectories were run on *g*DFC dimers (*cis*,*trans*) under simulated forces of 3 nN. The mixed *cis*,*trans* dimers were chosen to confirm that both isomers open prior to bond scission and that the subsequent reactivity is independent of the initial stereochemistry because both isomers generate the same diradical.[1]

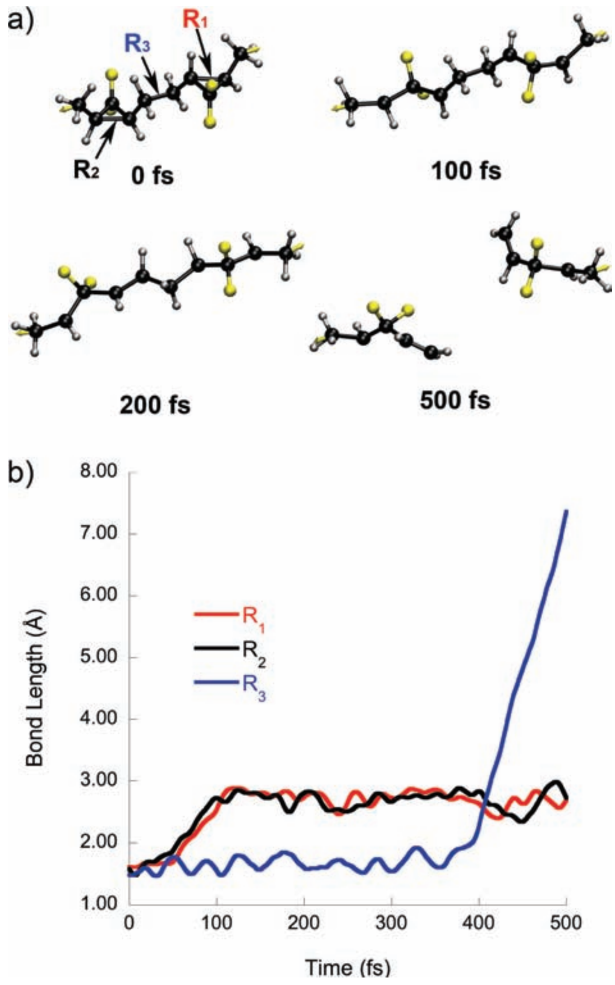

Figure 4. (a) Representative time points taken from an AISMD simulation of a *g*DFC dimer under a simulated force of 3 nN. The dominant process is ring opening of the *g*DFCs into their respective 1,3-diradicals, which occurred in all 20 simulated trajectories, as shown in the snapshots at 100 and 200 ps of simulation time. In two out of 20 trajectories, including the one shown here, a secondary bond scission process occurred, giving alkene-terminated products. (b) Bond lengths associated with *g*DFC ring opening and bond scission as functions of time for the MD simulation corresponding to (a).

In all 20 trajectories, the primary process was ring opening; both *g*DFCs rapidly and irreversibly formed the associated diradicals before any bond scission reaction was observed. In 18 of the trajectories, the adjacent diradicals remained intact for the 1 ps duration of the simulation. In two of the 20 trajectories, however, the adjacent diradicals disproportionated via the mechanism shown in Figure 3a. The simulated force of 3 nN was probably an overestimate of the peak force in the sonication experiments, as suggested by the following analysis. Similar sonication conditions lead to covalent bond scission in PB and other covalent polymers,[7] a process that requires several nanonewtons of force[9] to build on the approximately microsecond time scale of bubble collapse. Dividing the change in the force by the time scale of collapse gives a lower limit (full extension and chain scission may not require the full time of the bubble collapse) of $\sim 10^{10}$ pN s^{-1} for the effective loading rate of force during extension. The force builds until the rate of force-accelerated chain scission is comparable to the loading rate. For example, from the Bell–Evans theory, $k(F) = r_F/f_\beta$, where r_F is the loading rate and f_β describes the characteristic force dependence of the rate constant [the inverse slope of a plot of ln $k(F)$ vs F].[10] Use of the f_β value for Si–C bond scission, which has been previously reported to be $\sim 10^2$ pN,[9] suggests that the force should continue to build until the rate of bond scission is $>10^8$ s^{-1}. (It should be noted that we provide this analysis for rough "order of magnitude" purposes of discussion only. We recognize that many questions exist regarding the specific dynamics of loading and reaction. Nonetheless, we regard this estimate as a likely lower limit for the case at hand.)

In the simulations, two out of 20 dimers broke in 1 ps at 3 nN, meaning that the rate constant of the chain scission reaction at 3 nN approaches 10^{12} s^{-1}. On the basis of the discussion above, the typical peak force for chain scission is therefore likely less than 3 nN, but not dramatically so. Because ring opening is much faster than chain scission at both zero force (thermal isomerization of the *g*DFCs was observed without chain scission[1]) and 3 nN, however, we infer that the same relative reactivity observed in the simulations applies to the experimental conditions. The AISMD simulations are therefore consistent with a mechanism in which adjacent diradicals are formed prior to bond scission, which subsequently occurs at the site proposed in Figure 3a.

In conclusion, tension trapping allows the reactivity between two diradicals that closely resemble the transition states of force-free reactions to occur. This mode of reactivity represents a new method by which to engineer covalent mechanochemistry in polymers and polymeric materials. In addition, the use of mechanical force to characterize the chemistry of species whose existence is otherwise fleeting expands its application as a tool for physical organic chemistry, as applied previously in strained macrocycles[12] and in the sonochemically directed anti-Woodward–Hoffmann ring-openings of benzocyclobutene[13] and the *gem*-difluorocyclopropanes discussed here.[1] With the increasing interest in the synthesis of new mechanophores and the characterization of their behavior in severe stress fields,[14–18] we anticipate that numerous challenges to conventional notions of reactivity will continue to appear.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Details of syntheses, characterization data, NMR spectra, and details of molecular dynamics simulations. This material is available free of charge via the Internet at http://pubs.acs.org.

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