JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Force-Rate Characterization of Two Spiropyran-Based Molecular Force Probes

Gregory R. Gossweiler, Tatiana B. Kouznetsova, and Stephen L. Craig*

Department of Chemistry, Duke University, Durham, North Carolina 27708, United States

Supporting Information

ABSTRACT: The mechanically accelerated ring-opening reaction of spiropyran to a colored merocyanine provides a useful method by which to image the molecular scale stress/strain distribution within a polymer, but the magnitude of the forces necessary for activation has yet to be quantified. Here, we report single molecule force spectroscopy studies of two spiropyran isomers. Ring opening on the time scale of tens of milliseconds is found to require forces of ~240 pN, well below that of previously characterized covalent mechanophores. The lower threshold force is a combination of a low force-free activation energy and the fact that the change in rate with force (activation length) of each isomer is greater than that inferred in other systems. Finally, regiochemical effects on mechanochemical coupling are characterized, and increasing force reverses the relative ring opening rates of the two isomers.

In recent years, covalent mechanochemistry in polymers has led to new stress-responsive behavior in materials[1,2] including small molecule release,[3−5] mechanoradical production,[6] network remodeling,[7−9] and electro-mechanochemically responsive display devices.[10] The fundamentals of force transmission are critical to the development of these materials, and spiropyran (SP) derivatives have served as valuable colorimetric and fluorescent probes of molecular scale mechanochemical events for several synthetic polymers and mechanisms of deformation,[11−18] notably uncovering the role of chain orientation,[19−21] chain-mobility and plasticization,[22−24] and deformation rate[22,25,26] on local force accumulation. The stress/strain distributions mapped by the force-induced conversion of SP to its merocyanine (MC) isomer (Figure 1) have already provided numerous insights, but the actual forces involved in its activation of SP have yet to be characterized experimentally. Such quantitative studies would be useful because they would help to connect the stress/strain mapping to the force-rate relationships derived for a wide range of mechanophores so that SP activation studies might enable the rational design of covalent mechanochemical response in a given class of materials.

We chose to characterize two SP force probes, the seminal isomer, **SP1**, introduced by Davis et al.,[27] and a second isomer, **SP2**, possessing attachment points similar to a number of other demonstrations.[4,12,15,16,24,28] Our approach follows that employed in recent studies of other mechanophores.[29,30] We began by synthesizing copolymers of varying SP content

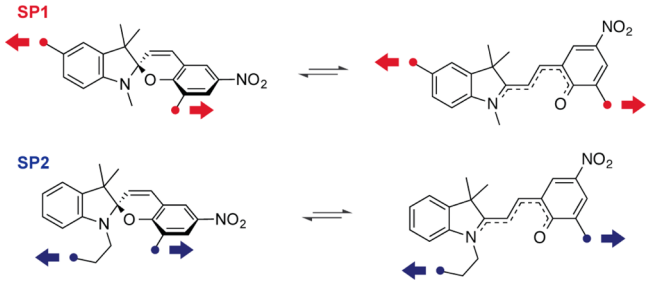


Figure 1. SP can be pulled open to an extended merocyanine isomer, revealing a visibly colored merocyanine form and indicating a local tensile force.

through an entropically driven ring opening metathesis copolymerization[31−33] of SP-containing macrocycles **SP1** and **SP2** with 9-oxabicyclo[6.1.0]non-4-ene (epoxy-COD) (Figure 2). The comonomer is employed because it promotes adhesion with the atomic force microscope (AFM) tip,[29] perhaps through covalent attachments.[34] The copolymers are deposited onto a surface by evaporation of a dilute polymer solution in tetrahydrofuran (THF).

Approach/withdraw cycles at varying velocities result in force curves that display a characteristic transition around 260 ± 15 pN for **SP1** and 240 ± 15 pN for **SP2**. This transition is due to the mechanical conversion of SP to MC, as supported by the following observations: (i) polymer extension scales with initial contour length; (ii) extension is proportional to SP content; and (iii) extension matches theoretical values from simulations (Table 1).

End-to-end lengths were calculated for each of the extended merocyanine isomers possible from a mechanical mechanism (Table 1). Ab initio molecular dynamics simulations performed previously by Cremar et al. predict CTC and TTC to be the major MC isomers for **SP1**, and TCC, TTC, and some CTC isomers for **SP2**.[35] Here, computationally determined extension ratios (for details, see Supporting Information) for each of the copolymers were compared against experimental results (Table 1). In the case of **SP1**, the differences in extension ratio among all isomers are too narrow to comment on the exact identity. For **SP2**, however, computational length changes for the CTC and TTT match well with the experimental observations.

The ring opening is under kinetic rather than thermodynamic control, as revealed by hysteresis in force curves (Supporting Information). The parameters governing the

Received: March 9, 2015
Published: April 28, 2015

DOI: 10.1021/jacs.5b02492
J. Am. Chem. Soc. 2015, 137, 6148−6151

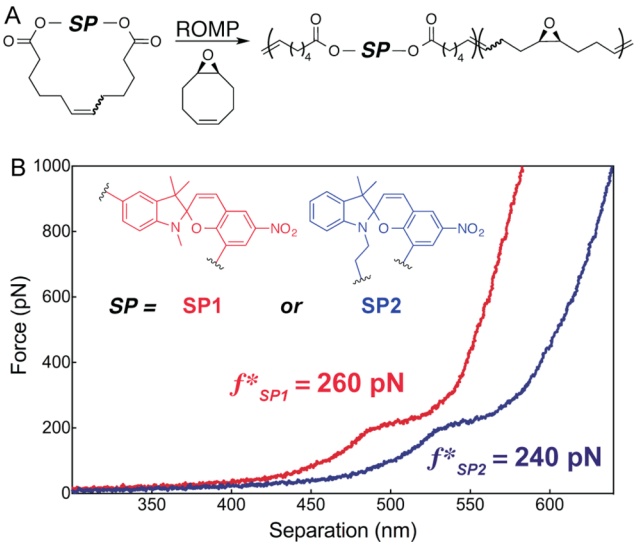


Figure 2. Macrocycles incorporating **SP1** or **SP2** are copolymerized with epoxy-COD to obtain a series of copolymers of varying SP content (A). Representative single molecule force–extension curves of copolymers containing **SP1** (red) or **SP2** (blue) of a 1:1 ratio SP/epoxy-COD (B). The plateau shown is characteristic of the mechanically induced ring-opening of SP to the extended MC form. Values of f^* shown correspond to the average value of the midpoint of the plateau for multiple force extension curves (tip velocity = 300 nm s^{-1}). For additional force curves, see Supporting Information.

conversion were obtained by fitting curves obtained from different polymer lengths and tip velocities to a 1:1 transition from SP to MC (Table 2). Force-free activation energies and rate constants k_0 were obtained independently for both **SP1** and **SP2** (Supporting Information) and used in the fitting. Two fits were done, assuming either a Bell[36] (eq 1) or Cusp[37] (eq 2) model for the force-coupled reaction coordinate. Alkene stereochemistry can influence mechanochemical coupling,[30] but here, the alkenes are too far removed to have a measurable impact on the reactivity.[38]

$$k(F) = k_0 e^{F\Delta x^{\ddagger}/k_B T} \quad (1)$$

$$k(F) = k_0\left(1 - \frac{F\Delta x^{\ddagger}}{2\Delta G^{\ddagger}}\right) e^{F\Delta x^{\ddagger}/k_B T - (F^{\ddagger}\Delta x^{\ddagger})^2/4\Delta G^{\ddagger} k_B T} \quad (2)$$

Table 2. SMFS Parameters Obtained by Modeling Force–Extension Curves[a]

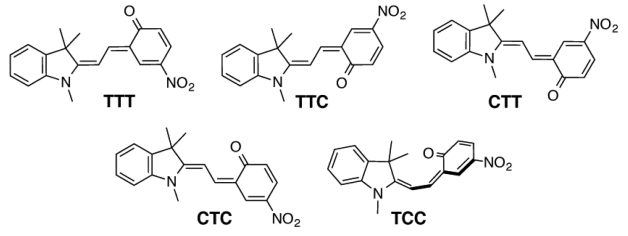
		$\Delta x^{\ddagger}$ (Å)	
entry	k_0 (s^{-1})[b]	Bell-Evans	Cusp
SP1	8.5×10^{-6}	1.79 ± 0.18	1.96 ± 0.22
SP2	1.8×10^{-6}	1.93 ± 0.12	2.14 ± 0.13

[a]Values obtained at a retraction velocity of 300 nm s^{-1}. [b]Force-free rate constants correspond to activation energies of 24.0 and 24.8 kcal mol^{-1} for **SP1** and **SP2**, respectively (see Supporting Information).

The parameters derived from the fits are given in Table 2 and were consistent across all polymer lengths and SP content. Two molecular insights emerge. First, the magnitude of the $\Delta x^{\ddagger}$ values, ~2 Å, is greater than the ~1.6 Å activation length found in polynorbornene embedded dichlorocyclopropanes,[29] the previous record for a covalent mechanophore. As $\Delta x^{\ddagger}$ effectively constitutes the force dependence of a reaction rate, this makes the SP derivatives especially sensitive force probes. Second, while **SP1** opens slightly more readily than **SP2** in the absence of force (k_0 = 8.5×10^{-6} and 1.8×10^{-6} s^{-1}, respectively), its threshold forces for activation under the conditions of the SMFS experiments are on average about 10% higher than those of **SP2**. The regiochemistry of the attachments in **SP2** provides a greater mechanical advantage that leads to a reversal in the relative rates of activation with increasing force.

In addition to the molecular insights, the rate–force parameters in Table 2 provide useful benchmarks for interpreting the results of SP activation in various materials

Table 1. Ratio of Polymer Lengths before and after Plateau as a Function of Incorporated SP Content[a]



		$L_{final}/L_{initial}$[c]					
		SMFS[b]	modeling[c]				
isomer	SP monomer content[a]		CTT	CTC	TTC	TTT	TCC
SP1	0.54	1.13 ± 0.05	1.14	1.12	1.13	1.13	1.03
	0.42	1.11 ± 0.03	1.12	1.10	1.11	1.11	1.03
	0.28	1.09 ± 0.03	1.09	1.08	1.08	1.08	1.02
SP2	0.45	1.15 ± 0.02	1.11	1.11	1.13	1.16	1.13
	0.27	1.09 ± 0.03	1.08	1.08	1.09	1.11	1.09
	0.16	1.07 ± 0.03	1.05	1.05	1.06	1.08	1.06
	0.13	1.05 ± 0.03	1.04	1.04	1.05	1.06	1.05

[a]Mole fraction of SP in copolymer determined from ^{1}H NMR integration. [b]Reported values are averages of the ratio of contour length before and after transition determined by fitting to the freely jointed chain model. [c]Computational contour lengths determined for each of three MC isomers (for details, see Supporting Information).

DOI: 10.1021/jacs.5b02492
J. Am. Chem. Soc. 2015, 137, 6148–6151

and device contexts. The appearance of mechanically driven MC color or fluorescence on the time scale of seconds or faster, for example, involves forces of >200 pN being delivered to the activated mechanophore. The forces involved in SP activation on such time scales, therefore, suggest that the active cross-links or stress-bearing subchains into which the SP is incorporated are strained beyond their contour length and into the overstressed enthalpic distortion regime.[39,40]

Conclusion. Rate−force relationships for SP isomerization should facilitate quantitative, retrospective analyses of previously demonstrated mechanical SP activation and provide a new benchmark for future structure−activity relationships in mechanochemically active materials, especially the relationship between macroscale stress and molecular force distributions. The fact that the forces required correspond to local, molecular strains beyond the purely entropic deformation limit is consistent with the observations that SP activation usually occurs only at large macroscopic strains, often (but not always[4]) in concert with irreversible plastic deformation[12,16,17,25−27] and with orientation along the vector of macroscopic deformation.[19−21] On a molecular level, the atomic motions associated with activation are coupled to large geometry changes in polymer contour length and reinforce existing design principles for highly effective mechanophores. In addition, the two isomers studied represent the first quantitation of regiochemical effects in mechanochemical activation, complementing prior studies of stereochemical effects.[30,41]

Finally, we anticipate that the already extensive utility of colorimetric SP stress probes might be furthered by allowing extrapolation of their behavior to that of other mechanophores. The SP molecule is able to serve as a colorimetric "scout" that permits an operative force to be characterized for a given material and deformation mode. Such interpretations are only valid, of course, if the rate limiting step in SP activation is the molecular force response rather than being limited by material relaxation processes. It is important to be mindful that such might not always be the case, since plastic deformation has its own intrinsic time scale and may become the rate-limiting step,[18,22] and in such a case, the force derived from activation kinetics would represent a minimum value. Prospects for quantitative molecular force mapping should be enhanced through the development and quantification of additional mechanophore reporters including but not limited to modifications of SP, for example, any number of stereoelectronic factors, different isomers/attachment points, steric cluttering, and substituent effects.

■ ASSOCIATED CONTENT

Supporting Information

Synthetic procedures, SMFS fitting analysis, SMFS curves, and additional details. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b02492.

■ AUTHOR INFORMATION

Corresponding Author

*stephen.craig@duke.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This material is based on work supported by the U.S. Army Research Laboratory and the Army Research Office (ARO) (W911NF-11-1-0071).

■ REFERENCES

(1) Caruso, M. M.; Davis, D. A.; Shen, Q.; Odom, S. A.; Sottos, N. R.; White, S. R.; Moore, J. S. *Chem. Rev.* **2009**, *109*, 5755.
(2) Black, A. L.; Lenhardt, J. M.; Craig, S. L. *J. Mater. Chem.* **2011**, *21*, 1655.
(3) Diesendruck, C. E.; Steinberg, B. D.; Sugai, N.; Silberstein, M. N.; Sottos, N. R.; White, S. R.; Braun, P. V.; Moore, J. S. *J. Am. Chem. Soc.* **2012**, *134*, 12446.
(4) Gossweiler, G. R.; Hewage, G. B.; Soriano, G.; Wang, Q. M.; Welshofer, G. W.; Zhao, X. H.; Craig, S. L. *ACS Macro Lett.* **2014**, *3*, 216.
(5) Larsen, M. B.; Boydston, A. J. *J. Am. Chem. Soc.* **2013**, *135*, 8189.
(6) Baytekin, H. T.; Baytekin, B.; Grzybowski, B. A. *Angew. Chem.* **2012**, *124*, 3656.
(7) Ramirez, A. L. B.; Kean, Z. S.; Orlicki, J. A.; Champhekar, M.; Elsakr, S. M.; Krause, W. E.; Craig, S. L. *Nat. Chem.* **2013**, *5*, 757.
(8) Kean, Z. S.; Hawk, J. L.; Lin, S.; Zhao, X.; Sijbesma, R. P.; Craig, S. L. *Adv. Mater.* **2014**, *26*, 6013.
(9) Black, A. L.; Orlicki, J. A.; Craig, S. L. *J. Mater. Chem.* **2011**, *21*, 8460.
(10) Wang, Q.; Gossweiler, G. R.; Craig, S. L.; Zhao, X. *Nat. Commun.* **2014**, *5*, 4899.
(11) Lee, C. K.; Diesendruck, C. E.; Lu, E.; Pickett, A. N.; May, P. A.; Moore, J. S.; Braun, P. V. *Macromolecules* **2014**, *47*, 2690.
(12) O'Bryan, G.; Wong, B. M.; McElhanon, J. R. *ACS Appl. Mater. Interfaces* **2010**, *2*, 1594.
(13) Zhang, H.; Chen, Y.; Lin, Y.; Fang, X.; Xu, Y.; Ruan, Y.; Weng, W. *Macromolecules* **2014**, *47*, 6783.
(14) Kingsbury, C. M.; May, P. A.; Davis, D. A.; White, S. R.; Moore, J. S.; Sottos, N. R. *J. Mater. Chem.* **2011**, *21*, 8381.
(15) Hong, G. N.; Zhang, H.; Lin, Y. J.; Chen, Y. J.; Xu, Y. Z.; Weng, W. G.; Xia, H. P. *Macromolecules* **2013**, *46*, 8649.
(16) Chen, Y.; Zhang, H.; Fang, X.; Lin, Y.; Xu, Y.; Weng, W. *ACS Macro Lett.* **2014**, 141.
(17) Celestine, A.-D. N.; Beiermann, B. A.; May, P. A.; Moore, J. S.; Sottos, N. R.; White, S. R. *Polymer* **2014**, *55*, 4164.
(18) Lee, C. K.; Davis, D. A.; White, S. R.; Moore, J. S.; Sottos, N. R.; Braun, P. V. *J. Am. Chem. Soc.* **2010**, *132*, 16107.
(19) Beiermann, B. A.; Kramer, S. L. B.; Moore, J. S.; White, S. R.; Sottos, N. R. *ACS Macro Lett.* **2011**, *1*, 163.
(20) Lee, C. K.; Beiermann, B. A.; Silberstein, M. N.; Wang, J.; Moore, J. S.; Sottos, N. R.; Braun, P. V. *Macromolecules* **2013**, *46*, 3746.
(21) Beiermann, B. A.; Kramer, S. L. B.; May, P. A.; Moore, J. S.; White, S. R.; Sottos, N. R. *Adv. Funct. Mater.* **2014**, *24*, 1529.
(22) Degen, C. M.; May, P. A.; Moore, J. S.; White, S. R.; Sottos, N. R. *Macromolecules* **2013**, *46*, 8917.
(23) Beiermann, B. A.; Davis, D. A.; Kramer, S. L. B.; Moore, J. S.; Sottos, N. R.; White, S. R. *J. Mater. Chem.* **2011**, *21*, 8443.
(24) Fang, X. L.; Zhang, H.; Chen, Y. J.; Lin, Y. J.; Xu, Y. Z.; Weng, W. G. *Macromolecules* **2013**, *46*, 6566.
(25) Grady, M. E.; Beiermann, B. A.; Moore, J. S.; Sottos, N. R. *ACS Appl. Mater. Interfaces* **2014**, *6*, 5350.
(26) Hemmer, J. R.; Smith, P. D.; van Horn, M.; Alnemrat, S.; Mason, B. P.; de Alaniz, J. R.; Osswald, S.; Hooper, J. P. *J. Polym. Sci., Part B: Polym. Phys.* **2014**, *52*, 1347.
(27) Davis, D. A.; Hamilton, A.; Yang, J.; Cremar, L. D.; Van Gough, D.; Potisek, S. L.; Ong, M. T.; Braun, P. V.; Martinez, T. J.; White, S. R.; Moore, J. S.; Sottos, N. R. *Nature* **2009**, *459*, 68.
(28) Jiang, S. C.; Zhang, L. X.; Xie, T. W.; Lin, Y. J.; Zhang, H.; Xu, Y. Z.; Weng, W. G.; Dai, L. Z. *ACS Macro Lett.* **2013**, *2*, 705.
(29) Klukovich, H. M.; Kouznetsova, T. B.; Kean, Z. S.; Lenhardt, J. M.; Craig, S. L. *Nat. Chem.* **2013**, *5*, 110.

DOI: 10.1021/jacs.5b02492
J. Am. Chem. Soc. 2015, 137, 6148−6151

(30) Wang, J.; Kouznetsova, T. B.; Kean, Z. S.; Fan, L.; Mar, B. D.; Martinez, T. J.; Craig, S. L. *J. Am. Chem. Soc.* **2014**, *136*, 15162.
(31) Xue, Z.; Mayer, M. F. *Soft Matter* **2009**, *5*, 4600.
(32) Strandman, S.; Gautrot, J. E.; Zhu, X. X. *Polym. Chem.* **2011**, *2*, 791.
(33) Hodge, P. *Chem. Rev.* **2014**, *114*, 2278.
(34) Kothe, M.; Muller, M.; Simon, F.; Komber, H.; Jacobasch, H. J.; Adler, H. J. *Colloids Surf., A* **1999**, *154*, 75.
(35) Cremar, L. D. *Insights for Designing Mechanochromic Spiropyrans from First Principles Dynamics and Minimum Energy Pathways*. Doctoral Thesis, University of Illinois at Urbana-Champaign, Champaign, IL, 2012.
(36) Bell, G. I. *Science* **1978**, *200*, 618.
(37) Dudko, O. K.; Hummer, G.; Szabo, A. *Phys. Rev. Lett.* **2006**, *96*, 108101.
(38) Ribas-Arino, J.; Shiga, M.; Marx, D. *J. Am. Chem. Soc.* **2010**, *132*, 10609.
(39) Kausch, H. H.; Plummer, C. J. G. *Polymer* **1994**, *35*, 3848.
(40) Ortiz, C.; Hadziioannou, G. *Macromolecules* **1999**, *32*, 780.
(41) Wang, J.; Kouznetsova, T. B.; Niu, Z.; Ong, M. T.; Klukovich, H. M.; Rheingold, A. L.; Martinez, T. J.; Craig, S. L. *Nat. Chem.* **2015**, *7*, 323.

DOI: 10.1021/jacs.5b02492
J. Am. Chem. Soc. 2015, 137, 6148−6151