Mechanical Force Enables an Anomalous Dual Ring-Opening Reaction of Naphthodipyran

Molly E. McFadden, Skylar K. Osler, Yan Sun, and Maxwell J. Robb*

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States

ABSTRACT: Multimodal mechanophores that exhibit complex mechanochromic behavior beyond the typical binary response are capable of distinguishing between multiple stress states through discrete changes in color. Naphthodipyran photoswitches contain two pyran rings fused to a central naphthalene core and represent a potentially promising framework for multimodal reactivity. However, the concurrent ring opening of both pyran moieties has previously proven inaccessible via photochemical activation. Here, we demonstrate that mechanical force supplied to naphthodipyran through covalently bound polymer chains generates the elusive dual ring-opened dimerocyanine product with unique near-infrared absorption properties. Trapping with boron trifluoride renders the merocyanine dyes thermally persistent and reveals unusual sequential ring-opening behavior that departs from the reactivity of previously studied mechanophores under the high strain rates imposed by ultrasound-induced solvodynamic chain extension.

Mechanical force has been demonstrated to promote unusual reaction pathways that often diverge from those obtained under more conventional thermal or photochemical processes. Stress-sensitive molecules termed mechanophores are designed to selectively transduce mechanical force into a wide variety of productive chemical transformations. The development of mechanochromic mechanophores in particular has attracted significant interest as these molecular force probes enable the straightforward detection of stress and/or strain in polymers through changes in color. Naphthodipyran derivatives are molecular switches that undergo a ring-opening reaction upon external stimulation to generate intensely colored merocyanine dyes. The photochemical reactivity of naphthodipyran has been studied extensively, producing a rich array of structurally diverse and commercially important photoswitches. More recently, it was discovered that the ring-opening reaction of naphthodipyran can be achieved using mechanical force. While relatively rare, multimodal mechanophores that exhibit more complex mechanochromic behavior beyond a binary on–off response are capable of distinguishing between different stress states through discrete visual cues. To this end, our group previously developed a bis-naphthopyran mechanophore incorporating two separate naphthopyran subunits joined by a conjugated linker that displays transient changes in color via a force-dependent dynamic equilibrium.

Naphthodipyran derivatives are compounds that contain two separate pyran rings fused to a central naphthalene nucleus. In contrast to bis-naphthopyrans, however, concurrent ring opening of both pyran units is inaccessible upon photochemical activation. Given the proclivity for mechanical force to facilitate otherwise unattainable reactions, we hypothesized that mechanochemical activation of naphthodipyran could enable the ring-opening reactions of both pyrans to produce the elusive dimerocyanine species with extended π-conjugation. The potential reactivity of naphthodipyran endowed with two mechanochromically active pyran rings and distinctly colored merocyanine states would render it an alluring new multimodal mechanophore.

The 3H-naphthodipyran scaffold was identified as an ideal target as it possesses the requisite geometry for transmitting force selectively across the C–O bonds in each pyran ring. We initiated our investigation by examining the computationally predicted mechanochemical reactivity of a series of 3H-naphthodipyran derivatives using the \textit{ab initio} constrained geometries simulate external force (CoGEF) method. The calculations revealed that several substituted naphthodipyran derivatives were predicted to undergo a dual ring-opening reaction upon mechanical elongation, including a model incorporating aryl substituents with \textit{para}-pyrrolidine groups. Conveniently, merocyanine dyes derived from simple 3H-naphthopyran derivatives can be trapped using BF$_3$·Et$_2$O, precluding possible complications in reaction analysis due to fast thermal reversion processes.

With these insights, we set out to experimentally investigate the mechanochemical reactivity of naphthodipyran using solution-phase ultrasonication for direct comparison to the photochemical reactivity under ultraviolet (UV) light. Polymers in dilute solution subjected to high intensity ultrasound underwent rapid extension with elongational forces maximized near the chain midpoint. Therefore, we designed and synthesized a naphthodipyran bis-initiator that...
was used in the controlled radical polymerization of methyl acrylate to generate linear PMA-1 (Mn = 185 kDa, Đ = 1.23) incorporating the naphthodipyran motif near the center of the polymer chain (Figure 1b, see SI for details). A continuous flow setup enabled monitoring of both mechanochemical and photochemical reactions in real-time by UV–vis–near-infrared absorption spectroscopy. \(^{13,21}\) Photoirradiation of PMA-1 (5.8 µM in CH\(_3\)CN stabilized with 30 mM BHT) with 365 nm UV light in the presence of BF\(_3\)·Et\(_2\)O (1.5 mM) generates a thermally persistent merocyanine dye with a single visible absorption peak at 625 nm (Figure 2a and Figure S3). Additional irradiation with UV light does not produce any further spectral changes (Figure S4). The absorption spectrum is consistent with the expected BF\(_3\)-coordinated monomerocyanine (NDPO·C·nBF\(_3\)) wherein one pyran ring has opened and the other remains closed (Figure 1b). The absorption maximum is bathochromically shifted by 65 nm in comparison to the spectrum acquired after photoirradiation of PMA-1 in the absence of BF\(_3\)·Et\(_2\)O (Figure S5), in excellent agreement with similar experiments performed on a simple 3H-naphthopyran.\(^{19}\)

In contrast to the photochemical reaction, ultrasound-induced mechanochemical activation of PMA-1 with BF\(_3\)·Et\(_2\)O produces a unique absorption spectrum with longer wavelength features that extend into the near-infrared region, consistent with generation of the dimerocyanine product in which both pyran rings have opened (NDPO·O·nBF\(_3\)) (Figure 2a). Again, the mechanochemical reaction product is thermally persistent (Figure S6). This unique absorption is not observed without BF\(_3\)·Et\(_2\)O, consistent with the anticipated transience of the untrapped dimerocyanine (Figure S7). Intriguingly, the kinetics of mechanochemical activation observed for the naphthodipyran mechanophore report colorimetrically on temporal exposure to ultrasound-induced mechanical force (Figure 2b). At early reaction times, only monomerocyanine product NDPO·C·nBF\(_3\) is observed; the longer wavelength absorption features associated with dimerocyanine NDPO·O·nBF\(_3\) emerge later in the reaction.
and increase with extended sonication time. This apparent sequential ring-opening behavior juxtaposes the mechanochemical reactivity of our previously studied bis-naphthopyran mechanophore. In that system, bis-naphthopyran is converted directly to the bis-merocyanine species, consistent with recently discovered dynamic effects whereby the momenta derived from extrinsic force drive reaction trajectories that completely bypass reactive intermediates. While the observed kinetic behavior of naphthodipyrans is effectively indistinguishable from a sequential ring-opening mechanism, we speculate that both pyran rings open during a single chain extension event; however, the lifetime of the free dimero-cyanine may be too transient for efficient trapping. Instead, rapid reversion of the dimero-cyanine species to the more stable monomerocyanine upon chain relaxation would permit BF$_3$ coordination. A second chain extension is then primed for a relatively facile intramolecular trapping process to form dimero-cyanine NDPO–O·nBF$_3$ (Scheme S1). Although we cannot rule out that BF$_3$ coordination is necessary for the second ring-opening reaction, this hypothesis is inconsistent with the observed photochemical reactivity of monomerocyanine NDPO–C·nBF$_3$ as well as DFT calculations employing an explicit BF$_3$-binding model (Figure S8).

Control experiments confirmed that the spectral changes ascribed to the dual ring-opening reactions of naphthodipyrans are uniquely enabled by mechanical activation. First, negligible changes in absorption were observed upon sonication of control polymer PMA-Control ($M_n = 173$ kDa, $\bar{D} = 1.20$) incorporating the naphthodipyrans moiety at the chain-end, which is not subjected to mechanical force (Figure S9). Given the unprecedented nature of the second ring-opening reaction, we sought additional evidence to support that the transformation attributed to the conversion of NDPO–C·nBF$_3$ to NDPO–O·nBF$_3$ observed for PMA-1 was indeed mechanochemically mediated (Figures 3a and S10). A solution of PMA-1 in the presence of BF$_3$·Et$_2$O was irradiated with 365 nm UV light to generate the trapped monomerocyanine species, NDPO–C·nBF$_3$, near the center of the polymer chains (Figure 3b). After 10 min, UV light was turned off and ultrasonication was applied to the solution, causing the attenuation of the absorption peak at 625 nm and the concurrent appearance of longer wavelength absorption features, consistent with the conversion of NDPO–C·nBF$_3$ to dimerocyanine NDPO–O·nBF$_3$. In direct contrast, the same experiment performed on PMA-Control, in which NDPO–C·nBF$_3$ is photochemically generated at the polymer chain-end, resulted in no changes to the absorption spectrum after initiation of ultrasound (Figure 3c). The time-dependent changes in absorbance at characteristic wavelengths of 625 nm (NDPO–C·nBF$_3$) and 820 nm (NDPO–O·nBF$_3$) clearly illustrate the divergent reactivity of PMA-1 and PMA-Control upon ultrasonication and the critical role of mechanical force in the activation of the putative second ring-opening reaction (Figure 3d).

To confirm the identity of the photochemical and mechanochemical reaction products, a series of characterization experiments were performed on the small molecule naphthodipyrans bis-initiator used to prepare PMA-1. Photoirradiation of the naphthodipyrans (0.5 mM in CD$_3$CN) with 365 nm UV light in the presence of BF$_3$·Et$_2$O (1.5 mM) produces an absorption spectrum with a peak at 625 nm that matches the spectrum obtained upon similar treatment of PMA-1 (Figure 4a). Analysis of the same sample by $^1$H NMR spectroscopy supports the photochemical generation of monomerocyanine NDPO–C·nBF$_3$ and dimero-cyanine NDPO–O·nBF$_3$, respectively.

![Figure 2.](image-url)

Figure 2. a) UV–vis–near-infrared absorption spectra of PMA-1 (5.8 $\mu$M in CH$_3$CN, 30 mM BHT, 1.5 mM BF$_3$·Et$_2$O) before and after photiodrivation with 365 nm UV light (15 min, −30 °C) or ultrasonication (180 min, −15 °C). The photograph shows the two solutions after activation with UV light or ultrasound (US). b) Spectral evolution during sonication of PMA-1 and time-dependent absorption profiles at 625 nm and 820 nm characteristic of monomerocyanine NDPO–C·nBF$_3$ and dimero-cyanine NDPO–O·nBF$_3$, respectively.
Figure 4c. We found that at sufficiently high concentrations of BF₃·Et₂O, photochemically-generated monomero-cyanine NDP O–C·ₙBF₃ is thermally converted to trapped dimerocyanine NDP O–O·ₙBF₃ (Figure S11). This behavior is not unexpected²⁴ and is similar to the strong thermodynamic driving force responsible for acidochromic and metallocromatic phenomena commonly observed for spiropyran.²⁵ After increasing the concentration of BF₃·Et₂O to 3 mM, additional photoirradiation replenished the monomero-cyanine, which is thermally transient without a sufficient stoichiometric excess of trapping agent. The ¹H NMR spectrum slowly transformed in the dark at room temperature with loss of the resonances associated with monomero-cyanine NDP O–C·ₙBF₃ and the concomitant appearance of a new doublet at 9.19 ppm (J = 14.8 Hz) consistent with the formation of dimerocyanine NDP O–O·ₙBF₃ (Figure 4d and Figure S12). As illustrated in Figure 4a, the absorption spectrum of this chemically-generated small molecule closely matches the spectrum acquired after extended ultrasonication of PMA-1, providing further support that the mecha-nochemical reaction product is the same dimerocyanine species.

High resolution mass spectrometry provided additional insight into the structure of trapped dimerocyanine NDP O–O·ₙBF₃. Analysis of a solution containing a mixture of small molecule naphthodipyran bis-initiator and chemically-generated NDP O–O·ₙBF₃ analogous to the sample that produced the ¹H NMR spectrum in Figure 4d provided the expected [M+H]⁺ peaks of the naphthodipyran as well as new signals corresponding to [M+BF₂]⁺ (Figure 4e). In addition, synchronous visible–near-infrared absorption measurements demonstrated the concomitant increase of the long-wavelength spectral features characteristic of the trapped dimerocyanine product (Figure S13). We hypothesize that the 1,2-diketone subunit of the dimerocyanine species forms a thermally and hydrolytically stable 5-membered difluoroborocyclic motif upon reaction with BF₃, which is presumably charge-balanced by a BF₄⁻ counterion (Figure 4e). Taken together, these results provide compelling support for the mecha-nochemical generation of an unprecedented dimerocyanine species from naphthodipyran.

Mechanical force has been demonstrated to bias reaction pathways, promoting chemical transformations that are not attainable using light or heat alone. Our results complement previous work revealing that mecha-nochemical activation can formally override orbital symmetry rules conventionally governing the electrocyclic ring-opening reactions of benzocyclobutene and gem-dihalocyclopropanes to yield products with unexpected stereochemistry.¹²⁶ Here, we show that mechanical force promotes a previously elusive and photochemically inaccessible dual ring-opening
reaction of naphthodipyran to generate a unique dimerocy-
anine species with near-infrared absorption. More broadly,
we envision that the newly unveiled multimodal reactivity
of naphthodipyran coupled with unusual mechanochemical
activation kinetics will enable the design and study of addi-
tional mechanophores and force-responsive polymers with
multicolor mechanochromic function.

ASSOCIATED CONTENT
The Supporting Information is available free of charge on the
ACS Publications website: Experimental details, synthetic pro-
cedures, DFT calculations, GPC chromatograms, UV-vis absorp-
tion and mass spectrometry data, and NMR spectra.

AUTHOR INFORMATION

Corresponding Author
mrobb@caltech.edu

Authors
Molly E. McFadden; Skylar K. Osler; Yan Sun; Maxwell J. Robb.

Notes
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