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Reactivity-Gated Photochromism of 1,2-Dithienylethenes for Potential Use in Dosimetry Applications

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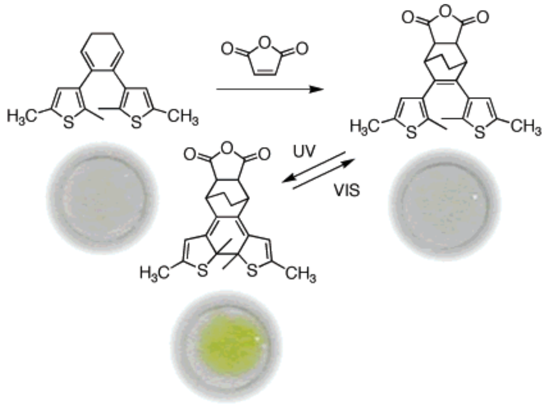
ABSTRACT



A novel molecular switching system based on reactivity-gated photochromism operates because a butadiene undergoes a [4 + 2] cycloaddition reaction with a dienophile to produce the photoresponsive 1,2-dithienylethene backbone. The reversible change in color when samples are irradiated with appropriate wavelengths of light occurs only after the Diels–Alder cycloaddition reaction takes place.

The thermally irreversible photocyclization reactions of 1,2-dithienylethene (DTE) derivatives are becoming increasingly significant to the Materials Science community.[1−3] Because the two isomers that are interconverting when DTE derivatives are stimulated with appropriate wavelengths of light have distinctly different optical and electronic characteristics, compounds containing this 6π-electron backbone have the potential to advance optoelectronic technologies such as optical information processing. However, the use of the versatile DTE architecture in sensing and dosimetry applications has not been extensively discussed in the literature.[4] This is surprising since the large variety of electronic properties that are accessible by synthetically tailoring the DTE backbone offer a wide range of useful read-out signals. Our research interests in this area involve taking advantage of the concept of reactivity-gated photochromism to develop methods to recognize specific chemical species on the basis of how they behave in common organic reactions.

In gated photochromism, light does not trigger the molecular transformation unless another external stimulus such as electricity, other photons, heat, or a chemical is also applied.[5] This concept has been described in reports that illustrate how the complexation to a saccharide[6] or a metal ion,[7] the reversible formation of intramolecular hydrogen

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(1) Special issue on photochromism: Irie, M. *Chem. Rev.* **2000**, *100*, 1685.

(2) Tian, H.; Yang, S. *Chem. Soc. Rev.* **2004**, *33*, 85.

(3) Irie, M. In *Molecular Switches*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, Germany, 2001; p 37.

(4) Although sensing was not directly addressed, some reports have described DTEs that may be used for this application. See refs 6−8 and: Kawai, S. H. *Tetrahedron Lett.* **1998**, *39*, 4445.

(5) Yokoyama, Y.; Yamane, T.; Kurita, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 1722.

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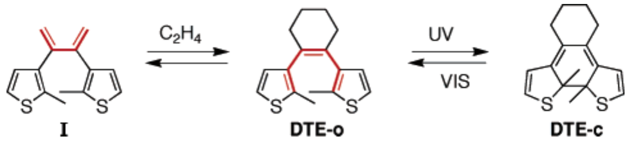
bonds,[8] or the action of a reducing agent[8] regulates the photochemistry of DTE derivatives. In each of these cases, the "gate" input dictates whether the 1,3,5-hexatriene portion of the photoswitch can adopt the appropriate conformation to undergo the conrotatory 6π-electron photocyclization. In this communication, we describe an example of reactivity-gated photochromism based on the creation of the DTE substructure by a mild and spontaneous reaction with an external chemical species. The concept is illustrated in Scheme 1 and represents a particularly appealing approach to sensing and dosimetry applications because of the diverse synthetically accessible "made-to-order" output signals.

Scheme 1. Reversible Photocyclization Gated by [4 + 2] Cycloaddition

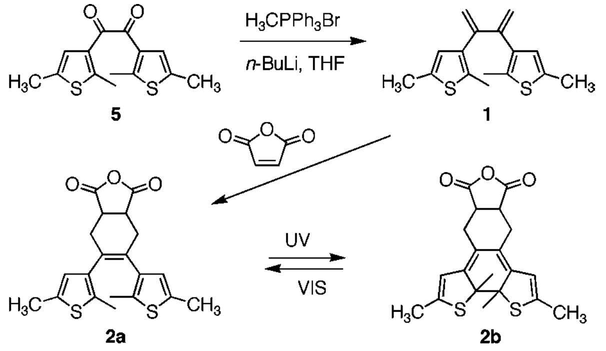


Compound **I** possesses a butadiene backbone (highlighted in red in Scheme 1) that cannot undergo the pericyclic photoreaction. The cyclohexene (**DTE-o**) generated when diene **1** reacts with a dienophile now contains the 1,3,5-hexatriene system and resembles the well-known photoresponsive DTE architecture. Irradiation should trigger the cyclization reaction and produce **DTE-c**, which can be detected using the numerous output signals available when using these derivatives (e.g., absorption, emission, redox properties). We decided to use the thermal Diels−Alder cycloaddition reaction to demonstrate our approach because it tends to proceed under mild conditions with minimal side reactions and with no intermediates. It is also reversible. This last point is an appealing property in dosimetry applications, as it allows for the resetting of the device.

The reversibility of the thermal [4 + 2] reaction shown in Scheme 1 is limited only to the ring-open form of the photoswitch (**DTE-o**). This implies that the initially targeted dienophile is liberated and the device is reset only after the photoreaction is reversed (**DTE-c** → **DTE-o**). This can be achieved using visible light and provides an effective mechanism to trap the chemical being targeted and to filter it from the environment.

To demonstrate our new concept, we present two butadiene derivatives, **1** and **3**. The acyclic version **1** is obtained from the known diketone **5**[9,10] by condensing it with the ylide obtained from methyltriphenylphosphonium bromide and *n*-butyllithium (−78 °C in THF) as shown in Scheme 2.[11]

Scheme 2. Synthesis and Diels−Alder Reaction of Diene **1** and Photochromism of Hexatriene **2a**



The conjugated diene **1** is isolated by column chromatography using silica gel and ethyl acetate/hexanes (1:9) as the eluent mixture.

As expected, irradiation of **1** with light of various wavelengths did not induce a photochromic response as proven by the absence of significant changes in the UV−vis absorption spectrum. Butadiene **1** undergoes a cycloaddition reaction with maleic anhydride but only when the reaction mixture is heated to 70 °C in the absence of a solvent. The need for these relatively harsh and limiting conditions can be attributed to the fact that only a small amount of the necessary s-cis conformer of **1** will exist at any given time. The major conformer will clearly be the s-trans isomer, which is not appropriately positioned to undergo the [4 + 2] cycloaddition reaction. The cyclohexene (**2a**) produced when diene **1** reacts with maleic anhydride is photoactive and spontaneously ring-closes when exposed to UV light (313 nm)[12] to produce **2b**. This is illustrated in Figure 1, which shows a decrease in the high-energy absorption bands that correspond to the ring-open isomer and the appearance of lower energy absorptions for the ring-closed form. Subsequent irradiation of this ring-closed isomer with light of wavelengths greater than 415 nm regenerates the ring-open isomer and establishes that the reactivity-gated photochromism has been successful in this preliminary example.

An improved system is based on cyclic diene **3** (Scheme 3), which eliminates the rotational freedom in the butadiene fragment and is more suitable for developing dosimetry applications. 2,3-Bis(2′,5′-dimethyl-3′-thienyl)cyclohexadiene **3** is synthesized from diketone **5** using a procedure that is analogous to the one used to prepare **1** but replacing the 2 molar equiv of methyltriphenylphosphonium bromide with 1 molar equiv of 1,4-butanebis(triphenylphosphonium) dibromide.[11] In this case, the bis(ylide) is best obtained by using potassium *t*-butoxide as the base (20 °C in dry

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(6) Takeshita, M.; Uchida, K.; Irie, M. *Chem. Commun.* **1996**, 1807.

(7) Takeshita, M.; Soong, C. F.; Irie, M. *Tetrahedron Lett.* **1998**, *39*, 7717.

(8) Irie, M.; Miyatake, O.; Uchida, K.; Eriguchi, T. *J. Am. Chem. Soc.* **1994**, *116*, 9894.

(9) Ivanov, S. N.; Lichitskii, B. V.; Dudinov, A. A.; Martynkin, A. Y.; Krayushkin, M. M. *Chem. Heterocycl. Cmpds.* **2001**, *37*, 85.

(10) Uchida, K.; Masuda, G.; Aoi, Y.; Nakayama, K.; Irie, M. *Chem. Lett.* **1999**, 1071.

(11) See Supporting Information for details.

(12) Standard lamps used for visualizing TLC plates (Spectroline E-series, 470 $\mu W/cm^2$) were used to carry out the ring-closing reaction of both photochromic compounds used in this study (313 nm light source). The ring-opening reactions were carried out using the light of a 150 W tungsten source that was passed through a 415 nm cutoff filter to eliminate higher energy light.

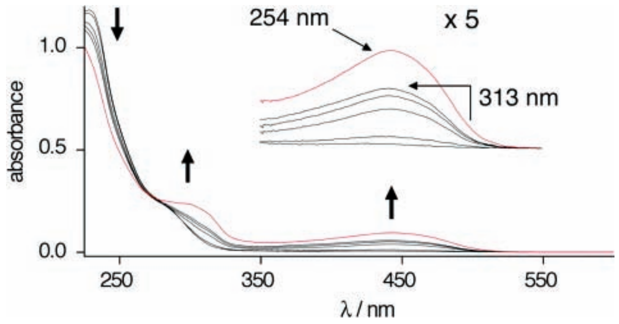
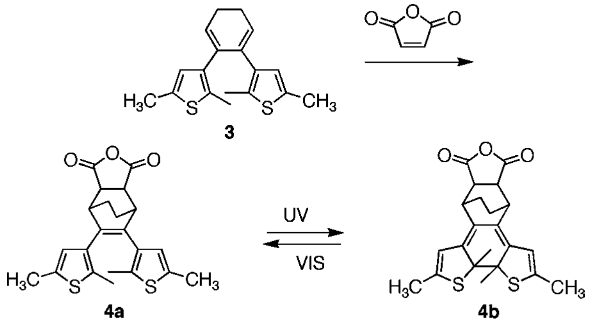


Figure 1. Changes in the UV−vis absorption spectra when an acetonitrile solution (2×10^{-5} M) of **2a** is irradiated with 313 nm light for 5, 15, 25, and 45 s (black traces) and 254 nm light for 45 s (red trace).

benzene). The diene product **3** can be purified by column chromatography using silica gel and ethyl acetate/hexanes (1:9) as the eluent mixture.

Scheme 3. Diels−Alder Reaction of Cyclohexadiene **3** and Photochromism of Hexatriene **4a**



By locking the butadiene into its productive s-cis conformation, the cycloaddition now occurs under milder conditions. When the colorless, photoinert butadiene **3** is treated with maleic anhydride in solution (acetone) at 65 °C, it undergoes the [4 + 2] cycloaddition reaction and produces a photochromic compound, **4a**. The reaction also proceeds at room temperature, albeit over a much longer period. The reaction is quantitative, and no side products are formed as measured by ^{1}H NMR spectroscopy. When an acetonitrile solution (2×10^{-5} M) of the colorless ring-open form (**4a**) is irradiated with 313 nm light,[12] absorption bands in the visible region appear, and the solution turns yellow as a result of the ring-closing reaction to produce the corresponding ring-closed form **4b** (Figure 2). ^{1}H NMR spectroscopic studies performed on a $CDCl_3$ (1×10^{-3} M) solution of **4a** reveal that the photostationary state contains 31% of the ring-closed isomer. This is not the case for diene **3**, which undergoes no significant changes when irradiated under identical conditions. The photogenerated solutions of **4b** can be bleached by irradiating them with visible light of wavelengths greater than 415 nm to induce the ring-opening reaction and regenerate **4a**. In the absence of visible light, the color persists, attesting to the thermal stability of the photochromic compound. Figure 2 also illustrates that using 254 nm light produces a greater amount of photocyclization. This comes at the expense of stability, however, and some degradation is observed when this higher-energy light is used.

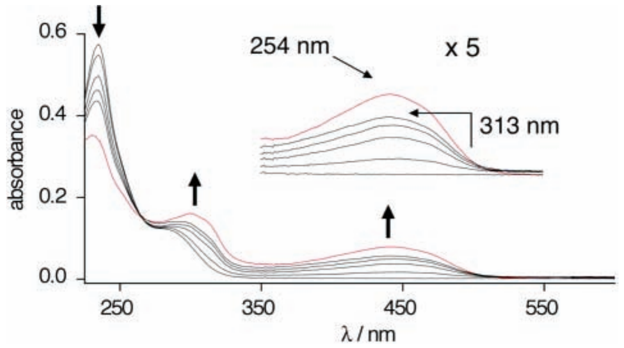


Figure 2. Changes in the UV−vis absorption spectra when an acetonitrile solution (2×10^{-5} M) of **4a** is irradiated with 313 nm light for 5, 15, 25, and 45 s (black traces) and 254 nm light for 45 s (red trace).

Figure 3 highlights the visible color changes in the reactivity-gated system. In this demonstration, a small amount of the cyclohexadiene **3** (1 mg) was added to pure DMSO (1 mL) and simultaneously to the same volume of a saturated DMSO solution of maleic anhydride. Both solutions were kept in the dark overnight. As shown in Figure 3, irradiation with 313 nm light only produces a color change in the solution containing both **3** and the analyte. Irradiation with light of wavelengths greater than 415 nm bleaches the sample back to its original colorless state.

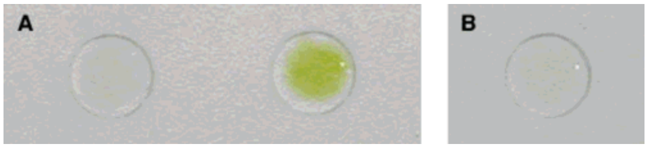


Figure 3. (A) Color change that occurs when a DMSO solution of diene **3** and excess maleic anhydride are mixed and exposed to 313 nm light (right spot). The left spot is a sample containing only the diene **3** that has been simultaneously irradiated. (B) The same sample of diene **3** and maleic anhydride after bleaching with greater than 415 nm light.

It is anticipated that further improvements with respect to the amount of the ring-closed isomer in the photostationary state and the color of this ring-closed form can be achieved by replacing the two methyl groups on the 5-positions of the thiophene heterocycles with groups that are more amenable to photochromic sensing. These and other modifications are currently underway and will be reported in due course. Preliminary targeting of other dienophiles such as quinones and electron-deficient acetylene derivatives has also been successful and will be included in future reports.

This novel example of reactivity-gated photochromism has the potential to significantly impact dosimetry applications and the concept of controlled release of chemical species. The approach could be used to identify toxic dienophiles such as Lewisite (2-chlorovinyldichloroarsine), a blistering agent similar to mustard gas and a compound that is a powerful respiratory irritant when inhaled (Figure 4). Another highly toxic dienophile is the pesticide 1,3-dichloropropene. The DTE derivatives described in this communication also have the potential to interface with many biologically relevant dienophiles such as those found in the membrane-bound "quinone pool" (bacterial enzyme cofactors phylloquinone and menaquinone, etc.) and the numerous quinone intermediates in the biosynthesis of antibiotics such as tetracycline. Finally, it offers new sites and mechanisms to further functionalize photoresponsive molecular switches based on the DTE scaffold and provides synthetic access to unprecedented and innovative systems.

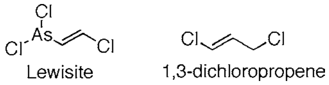


Figure 4. Chemical warfare agent Lewisite and the toxic pesticide 1,3-dichloropropene.

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Supporting Information Available: Synthetic details and photochemical characterizations for compounds **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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