Photoswitching Using Visible Light: A New Class of Organic Photochromic Molecules

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Ⓢ *Supporting Information*

ABSTRACT: A versatile new class of organic photochromic molecules that offers an unprecedented combination of physical properties including tunable photoswitching using visible light, excellent fatigue resistance, and large polarity changes is described. These unique features offer significant opportunities in diverse fields ranging from biosensors to targeted delivery systems while also allowing non-experts ready synthetic access to these materials.

In the field of adaptable and responsive materials, the ability of organic photochromic compounds to reversibly undergo changes in spectral absorption, volume, and solubility is of particular importance for applications in energy storage and chemical sensing and for controlling the conformation and activity of biomolecules.[1] These switches are particularly valuable because their property changes are triggered by light, the most widely available, non-invasive, and environmentally benign external stimulus. Significantly, light also provides unique opportunities for spatial and temporal resolution.

Among the classes of organic photochromic materials, azobenzenes, spiropyrans and diarylethenes have received the most attention because of their excellent performance and broad utility. Specifically, azobenzene has been extensively employed for its change in volume, resulting from a *trans* to *cis* isomerization, upon irradiation.[2] Similarly, the change in spectral properties of spiropyrans and diarylethenes upon photoswitching has been exploited in a number of applications,[3] with spiropyran exhibiting the added benefit of a solubility switch, or a conversion from a hydrophobic to a hydrophilic form, upon irradiation.[4] Despite their ubiquity and broad utility, these privileged classes of photochromes typically all require the use of high-energy UV light to trigger their photochemical reactions. This hinders their potential use in biomedical applications and material science because UV light can be damaging to healthy cells and results in degradation for many macromolecular systems. Fatigue resistance is also a primary concern for UV-based photochromic switches.

A common design principle to address this problem is to make synthetic modifications to these known classes of photochromic compounds that enable the use of visible light.[5] Herein, we describe a conceptually different approach in which we designed a new class of visible light activated photochromes, termed donor−acceptor Stenhouse adducts

(DASAs).[6] These derivatives switch from a conjugated, colored, and hydrophobic form to a ring-closed, colorless, and zwitterionic structure on irradiation with visible light and have high fatigue resistance under ambient conditions (Figure 1). In addition, the potential of this photoswitch in materials
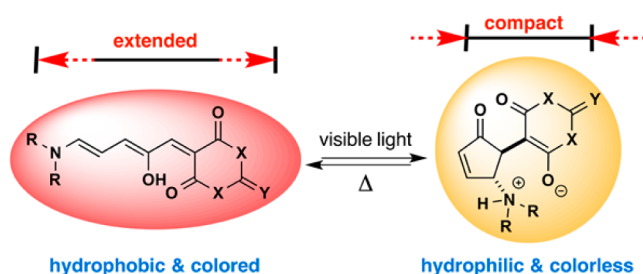

Figure 1. DASAs, a new platform of visible light organic photoswitches.

science is highlighted through the synthesis of a functional amphiphile that displays light-mediated micelle disassembly and cargo release.

Our interest in the cascade rearrangements of activated furans[7] and a pioneering report by Honda[8] played a critical role in our development of these novel negative (colored to colorless) photochromic materials.[5e,3b] The synthetic design of these DASA photoswitches takes advantage of furfural (**1**), a commodity chemical derived from plant byproducts, as a renewable and readily available starting material and employs highly efficient reactions amenable to the rapid synthesis of a broad range of materials. Facile activation of **1** by an "on water" condensation with cyclic 1,3-dicarbonyl compounds provides intermediates that undergo ring-opening at room temperature with a wide variety of secondary amines in the absence of catalysts or other reagents (Scheme 1).[9]

The highly modular nature of this approach enables the rapid synthesis of a library of DASA materials with a variety of furan activating groups and secondary amines in high yields. For example, activation of furfural, **1**, could be accomplished with either Meldrum's acid to form furan **2** or with 1,3-dimethyl barbituric acid to form **3**. Treatment of these activated furans with secondary aliphatic, cyclic, or functional amine derivatives, such as diethylamine, diallylamine, and tetrahydroisoquinoline

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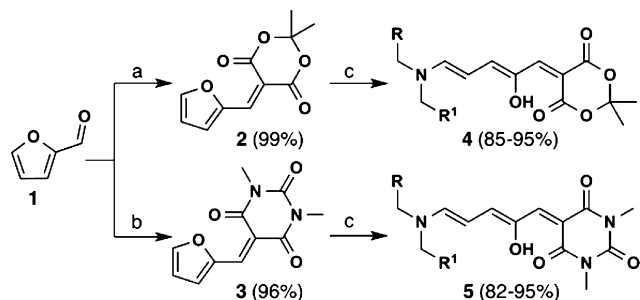
Scheme 1[a]

[a](a) Meldrum's acid, H_2O, 75 °C; (b) 1,3-dimethylbarbituric acid, H_2O, rt; (c) amine (1–1.5 equiv), THF, rt. See Table S1 for amine derivatives investigated.

provide DASA photoswitches with the general structure **4** and **5** (Table S1). These derivatives are routinely accessed at the multigram scale in yields >85% over the two-step procedure. Inherent in the versatility and overall usefulness of these DASA photoswitches is the high yielding and simple nature of the synthetic procedures, which allows nonexperts easy access to more complex or functional substrates that are attractive for tailored applications in materials science. Having efficient access to the triene derivatives, the photophysical properties were examined with the diethyl amine derived adducts as model systems (Scheme 2).

Scheme 2. Photoswitching and Thermal Reversion of Trienes 4a and 5a to Cyclopentenones 4b and 5b
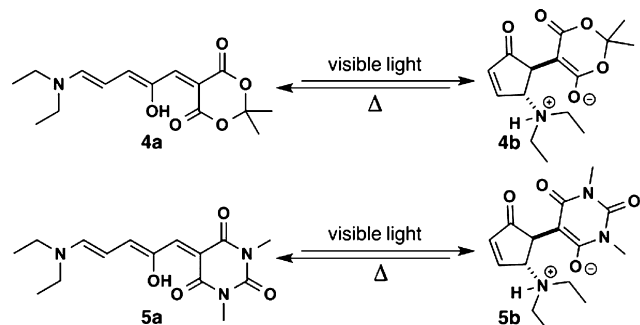
We began by examining the unidirectional conversion of the colored triene **4a** to its colorless zwitterionic cyclopentenone isomer **4b** using NMR spectroscopy in a deuterated methanolic solution (Figure 2A). Exposure of **4a** to a standard incandescent bulb or hand-held fluorescent lamp results in a decrease over the course of 4 h in the NMR peaks corresponding to **4a** and a concomitant increase in the peaks for **4b**. Similarly, this process was also studied using UV–visible spectroscopy for **5a** in methanol (Figure 2B). Again, irradiation with visible light leads to a decrease of the absorption of **5a** as it is converted to **5b** over 50 min.[10] The isosbestic point was determined to occur at 280 nm for both compounds (see Supporting Information (SI) for absorption spectra of **4a** to **4b**).

Having controlled access to both structural forms, we next determined conditions that would facilitate rapid, quantitative, and fully reversible switching between the triene and cyclopentenone forms. Similar to spiropyrans and diarylethenes, reversible photoswitching of DASAs was found to be solvent dependent.[11] We found aromatic solvents to be
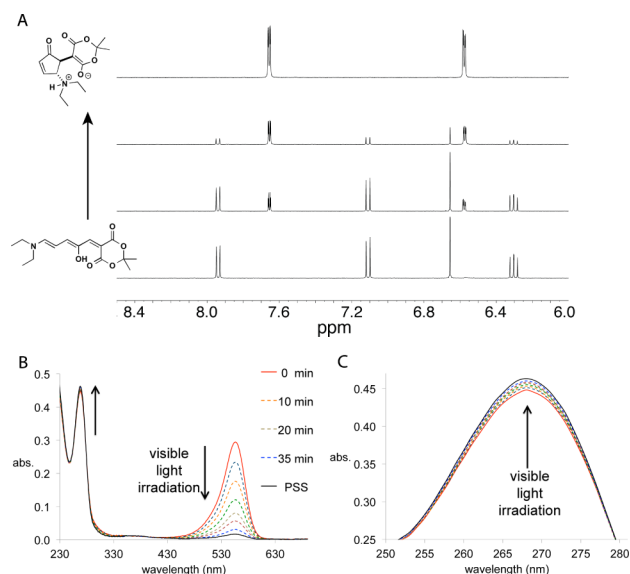

Figure 2. (A) Conversion of **4a** to **4b** by ^{1}H NMR in CD_3OD over 4 h. (B) Absorption spectra of **5a** to **5b** on irradiation with visible light in CH_3OH. (C) Expanded view of absorption spectra of **5a** to **5b** between 250 and 280 nm.

ideal, providing conversion of the triene to cyclopentenone upon irradiation with visible light with thermal reversion from the meta-stable cyclopentenone back to the triene when irradiation is stopped.

With reversible conditions identified, the relative rates of interconversion between the triene and cyclopentenone isomer were evaluated in toluene for the two photoswiches (**4a** and **5a**) bearing different acceptor groups. As illustrated in Figure 3A both derivatives undergo conversion from the open triene isomer (**4a** and **5a**) to the closed zwitterionic cyclopentenone isomer (**4b** and **5b**) at approximately the same rate. A more dramatic rate difference was observed in the thermal recoloration, upon cessation of irradiation, where the 1,3-dimethyl barbituric acid derivative (**5a**) reverted back
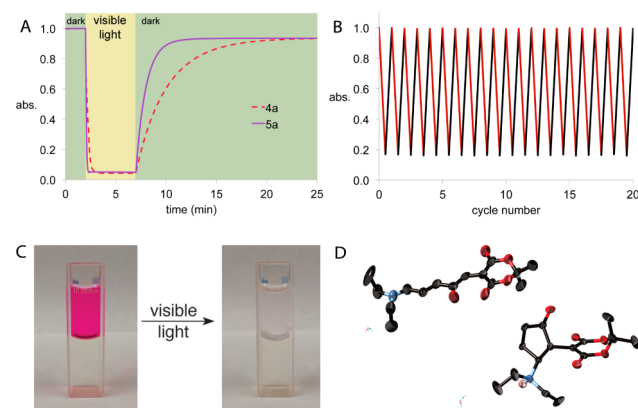

Figure 3. (A) *In situ* kinetic plot of the switching cycle of **4a** and **5a** in PhMe, monitored at λ_{max} of 545 and 570 nm, respectively. (B) Multiple photoswitching cycles of **5a** in PhMe (0.16 mM), alternative irradiation at 570 nm (red) and dark (black). (C) Photographs illustrating the concomitant photoswitching and phase transfer of **4a** upon irradiation with visible light. (D) ORTEP drawings of **4a** (top) and **4b** (bottom) (50% probability ellipsoids, hydrogen atoms omitted for clarity).
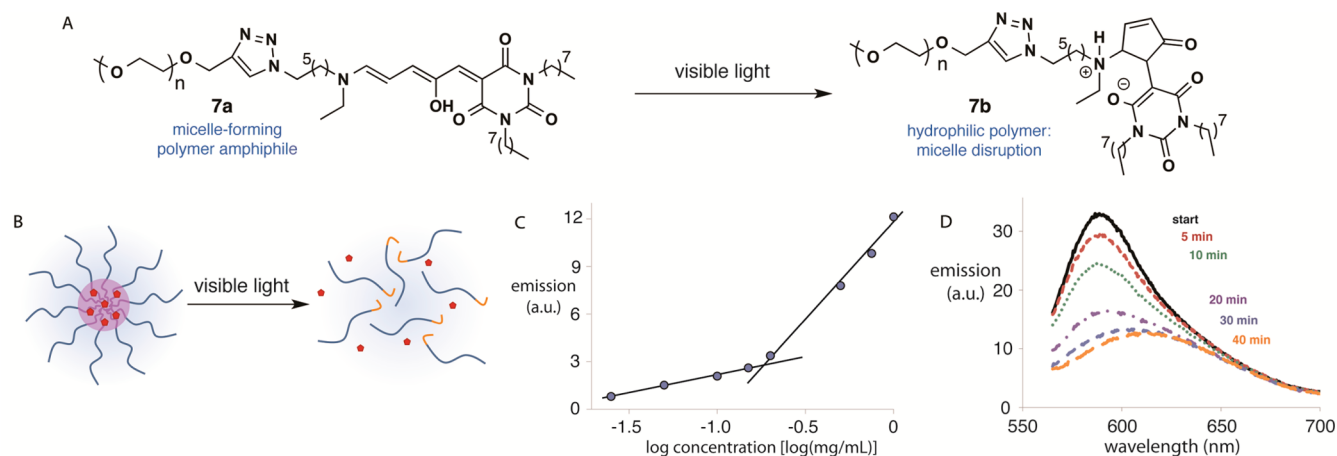
Figure 4. (A) Photoswitching of micelle-forming polymer amphiphile. (B) Schematic of micelle formation and hydrophobic cargo encapsulation by functional amphiphile **7a** and micelle disruption and cargo release on visible light irradiation. (C) Fluorescence intensity (Em at 588 nm) vs log concentration (mg/mL) of **7a**. (D) Fluorescence emission spectra of Nile Red in 0.50 mg/mL **7a** in water at various times of visible light irradiation.

approximately twice as fast. This process is solvent and temperature dependent (details in SI),[12] but it is worth noting that in polar protic solvent thermal reversion was not observed. We also found that the choice of acceptor group has an effect on the λ_{max} and associated color of the triene. For example, in toluene the Meldrum's acid derived triene **4** displays a λ_{max} of 545 nm, changing the acceptor to the more electron-withdrawing 1,3-dimethyl barbituric acid, **5**, results in a bathochromic shift to 570 nm. In both cases these derivatives are excellent organic dyes with extinction coefficients determined to be ~100,000 M^{-1} cm^{-1} for the triene form (details in SI).

Fatigue resistance is a key characteristic for gauging the potential of photochromic materials, thus the performance of DASA photoswitches was tested (Figure 3B).[13] Rapid and complete switching of **5a** was consistently observed when irradiating with visible light centered at the λ_{max} of our DASA with negligible material degradation (<0.05% loss per cycle), as measured by the intensity of absorbance.[14,1b] Fatigue experiments were conducted in ambient conditions without the need to exclude oxygen or water, demonstrating the robust nature of this process.

From related studies, the mechanism of switching is proposed to occur via a reversible Nazarov-type 4π electrocyclization.[7] Importantly, conversion to the zwitterionic cyclopentenone (**4** and **5**) results in bleaching of all derivatives studied, providing colorless, water-soluble materials. A dramatic realization of this solubility change is demonstrated through dynamic phase transfer. Derivative **4a** dissolved in toluene was layered over water; the biphasic system was then irradiated with visible light (Figure 3C). The highly colored organic phase underwent rapid loss of color, correlating to the formation of **4b**. Complete migration of **4b** to the aqueous phase was confirmed by ${}^1H$ NMR analysis of the layers after photoswitching.

Further structural characterization of the two isomeric states was provided by single crystal X-ray diffraction (Figure 3D), which revealed the ring-open Stenhouse adduct **4a** to be a conjugated, linear, hydrophobic material with an amine "donor" and a 1,3-dicarbonyl "acceptor". In contrast, the water-soluble cyclopentenone **4b** is a zwitterion, with the amine substituent protonated and one of the ester (or amide) functionalities in the 1,3-dicarbonyl moiety being a formal enolate.

A powerful aspect of the modular design of DASAs is the ability to rapidly modify their structure, critical for the adoption of these photoswitches into complex systems that require on-demand property changes. Accordingly, we sought to develop a functional polymer system to exploit the visible-light-mediated solubility switch of DASAs. The development of a general, stimuli-responsive micellar system with external control over assembly has been a long-standing goal in polymer chemistry with potential applications in biological settings.[15] The characteristics of these photoswitches are therefore perfectly suited to provide such a function, as visible light mediates structural and property changes from the hydrophobic, linear derivative to the fully hydrophilic, cyclic derivative.

The facile and modular synthesis of DASA-functionalized amphiphilic polymer is detailed in the SI, briefly, a DASA bearing a terminal azide and 1,3-di-n-octyl barbituric acid, was coupled to alkyne terminated monomethyl poly(ethylene glycol) (PEG) (M_w = 3000 g/mol, PDI = 1.1) to form the desired end-functionalized polymer, **7a** (Figure 4A). The amphiphilic nature of **7a** induced micelle formation in aqueous environments (Figure 4B), as determined by Nile Red encapsulation experiments and dynamic light scattering, confirming that Nile Red is successfully encapsulated and solubilized in water and that the critical micelle concentration for this system is 49 μM (Figure 4C, see SI for details). Upon visible light irradiation, the absorption peak of **7a** at 550 nm decreased steadily, indicating the photoswitching of the DASA to its cyclic, hydrophilic state (details in SI). Concurrently, the fluorescence emission of encapsulated Nile Red showed a sharp decrease in intensity and red shift, indicating that the hydrophobic dye was released into the aqueous phase (Figure 4D).[16] These results are consistent with a disruption in the micellar structure and a release of hydrophobic cargo caused by the light-induced photoswitching of **7a** to the fully hydrophilic derivative **7b**. This simple but powerful application of DASAs illustrates the significant potential of these photochromic moieties.

In conclusion, we have introduced a new class of photoswitchable molecules that are synthetically versatile and exhibit a unique combination of physical and chemical properties. These DASAs show reverse photochromism under visible light, which is complementary to previous classes of photoswitches, and display excellent fatigue resistance under ambient

conditions. The potential of these photoswitches in materials science was demonstrated through the synthesis of a functional amphiphile that displays on-demand light-mediated disassembly and cargo release.

ASSOCIATED CONTENT

Supporting Information

Synthetic procedures and experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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