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Solution and Solid-State Emission Toggling of a Photochromic Hydrazone

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Supporting Information Placeholder

ABSTRACT: The proliferation of light-activated switches in recent years has enabled their use in a broad range of applications encompassing an array of research fields and disciplines. All current systems, however, have limitations (e.g., from complicated synthesis to incompatibility in biologically relevant media and lack of switching in the solid-state) that can stifle their real-life application. Here we report on a system that packs most, if not all, the desired, targeted and sought-after traits from photochromic compounds (bistability, switching in various media ranging from serum to solid-state, while exhibiting ON/OFF fluorescence emission switching, and two-photon assisted near infrared light toggling) in an easily accessible structure.

Photochromic compounds¹ play a key role in diverse areas of science and technology as they enable the control over (bio)molecular processes,² properties, assemblies, and functions³ with the high temporal and spatial resolution of light. These capabilities have allowed for their incorporation in responsive materials and surfaces,⁴ catalysis and separation,⁵ information storage,⁶ energy conversion,⁷ and drug design,⁸ and have made them an integral part of the field of artificial molecular switches and machines.⁹ Several prominent photoswitches have been investigated throughout the years (e.g., azobenzenes,¹⁰ diarylethenes,¹¹ spiropyrans,¹² and fulgides¹³) and while great strides have been made in their development, optimization, and use, a few drawbacks hinder their deployment in real-life applications. Depending on the system, these shortcomings include complicated synthesis, low thermal and/or photochemical stability, undesired spectral features (e.g., UV light activation), inefficient photoconversion, lack of solid-state switching and/or fluorescence emission, small amplitude geometrical changes, pH and/or oxygen sensitivity, reduction by glutathione, and more commonly inadequate (if any) switching in aqueous media.

Considering the prevalent and prospective use of photochromic compounds in a broad range of fields and disciplines, the development of new systems that can overcome some, if not all these short-

comings is a sought-after goal. This necessity explains the surge witnessed in the past decade in the development of new photochromic compounds,¹⁴ with an emphasis on visible-light activated ones.¹⁵

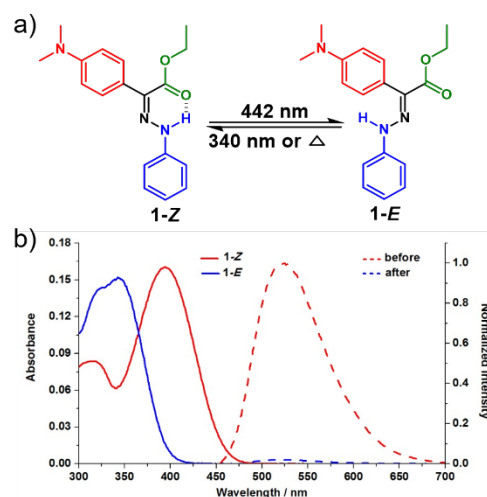


Figure 1. (a) Light induced E/Z isomerization of hydrazone **1**; (b) Solid lines: UV-Vis spectra (1.0×10^{-5} M) of **1-Z** and **1-E** isomers in toluene; Dashed lines: Fluorescence emission spectra (5.0×10^{-6} M; $\lambda_{\text{ex}} = 420$ nm) of **1** in toluene, before (red) and after irradiation (blue).

As part of our effort to address the drawbacks associated with photochromic compounds,¹⁶ we report here on an easy-to-make, robust, bistable, hydrazone-based¹⁷ photochromic compound (**1**; Scheme 1) whose functions in organic solutions, which include fluorescence ON/OFF switching under both 1-photon and 2-photon excitation (i.e., near infrared (NIR) light), are maintained in serum and in the solid-state. This compound combines together the most significant properties of widely used photoswitches (i.e., the large geometrical changes of azobenzenes, the bistability and solid-state switching of diarylethenes, and the emission toggling of spiropyrans) while circumventing their shortcomings (e.g., reduction with

glutathione, complicated synthesis, and low photochemical stability and switching in aqueous media, etc.).

Hydrazone **1** was synthesized as described in Scheme S1 and fully characterized using NMR spectroscopy, mass spectrometry and X-ray crystallography (Figures S2, S3 and S43). An equilibrated solution (Toluene; under dark) of **1** shows an absorption maximum (λ_{max}) at 395 nm, with a molar absorption coefficient (ϵ) of $14600 \text{ M}^{-1}\cdot\text{cm}^{-1}$ (Figure 1b). The absorption maximum of **1-Z** is shifted bathochromically by 28 nm compared to a previously reported hydrazone lacking the NMe_2 electron donating group ($\lambda_{\text{max}} = 367 \text{ nm}$).^{16c} Irradiation of the solution of **1** with a 442 nm light source induces a $Z \rightarrow E$ photoisomerization (photostationary state (PSS) of $> 99\% E$; $\Phi_{Z \rightarrow E} = 9.1 \pm 0.2\%$; Figure S12), accompanied by the appearance of a new absorption band at $\lambda_{\text{max}} = 343 \text{ nm}$ ($\epsilon = 13800 \text{ M}^{-1}\cdot\text{cm}^{-1}$), and a color change from light yellow to colorless (Figure 1b). The reverse process ($E \rightarrow Z$) can be triggered by using a 340 nm light source ($\text{PSS}_{340} = 82\% \text{ 1-Z}$; $\Phi_{E \rightarrow Z} = 13.6 \pm 1.0\%$; Figure S13) the system can be cycled between the two isomers by alternating 442 and 340 nm irradiation (Figures S15 and S16). The thermal $E \rightarrow Z$ back-isomerization (Figure S41) was found to be very slow ($k_{E \rightarrow Z} = (1.1 \pm 0.1) \times 10^{-6} \text{ h}^{-1}$). The isomerization half-life ($\tau_{1/2}$) at 298 K is 75 ± 3 years, which is about 3 times smaller than that of the previously reported hydrazone ($\tau_{1/2} = 255 \pm 19$ years).^{16c}

The introduction of the NMe_2 group drastically enhanced the emission of the Z isomer compared to the parent system which is not emissive (Figure S32). Upon excitation with blue light ($\lambda_{\text{ex}} = 420 \text{ nm}$) the toluene solution of **1-Z** exhibits an intense emission band (λ_{em}) at 525 nm (Stokes shift of 130 nm; Figure 1b). The fluorescence lifetime (Figure S28) and fluorescence quantum yield of the process were determined to be $193 \pm 2 \text{ ps}$ and $0.7 \pm 0.1\%$, respectively. Switching **1-Z** to **1-E** using 442 nm light leads to quenching of fluorescence. Irradiation of the E -dominant solution with 340 nm light leads to a Z -dominant solution, which turns the emission ON again. Such an ON-OFF fluorescence response in photochromic compounds, especially those that function upon configurational changes, is highly unusual.¹⁸ The fluorescence modulation can be cycled 10 times with no signs of photobleaching (Figure S30).

As part of our solvent screening studies (Figures S17 and S35), we found that **1** can undergo photoisomerization in fetal bovine serum (FBS) buffer (Figure S17). An equilibrated solution of **1** in 10% FBS buffer (PBS with 10% DMSO, pH = 7.4) shows an absorption maximum at 395 nm, which shifts to $\lambda_{\text{max}} = 343 \text{ nm}$ upon isomerization with 442 nm light ($\text{PSS}_{442} = 96\% \text{ 1-E}$; $\Phi_{Z \rightarrow E} = 6.5 \pm 0.1\%$). These observations highlight the transformation of the initially present **1-Z** form into the E isomer. The back $E \rightarrow Z$ isomerization process ($\text{PSS}_{340} = 76\% \text{ 1-Z}$; $\Phi_{E \rightarrow Z} = 6.9 \pm 0.3\%$) can be triggered by irradiating with 340 nm light, reverting the system to its original state. More interestingly, the emission of **1-Z** in the serum buffer is maintained ($\tau_{1/2} = 2.16 \pm 0.02 \text{ ns}$ and $\Phi_{\text{FL}} = 3.5 \pm 0.4\%$) with a maximum emission band at 525 nm ($\lambda_{\text{ex}} = 420 \text{ nm}$). This behavior is contrary to the diminished fluorescence intensity observed for **1-Z** in polar protic solvents and aqueous solutions (Figures S17 and S35), most likely because **1-Z** interacts with the protein components of the FBS buffer (Figure S20).¹⁹ Similar to what happens in organic solvents, repeated switching between **1-Z** and

1-E leads to emission turn OFF and ON. The switching in serum prompted us to also test the sensitivity of **1** towards glutathione reduction. We found that **1** and its switching process are not affected by GSH (Figure S21).

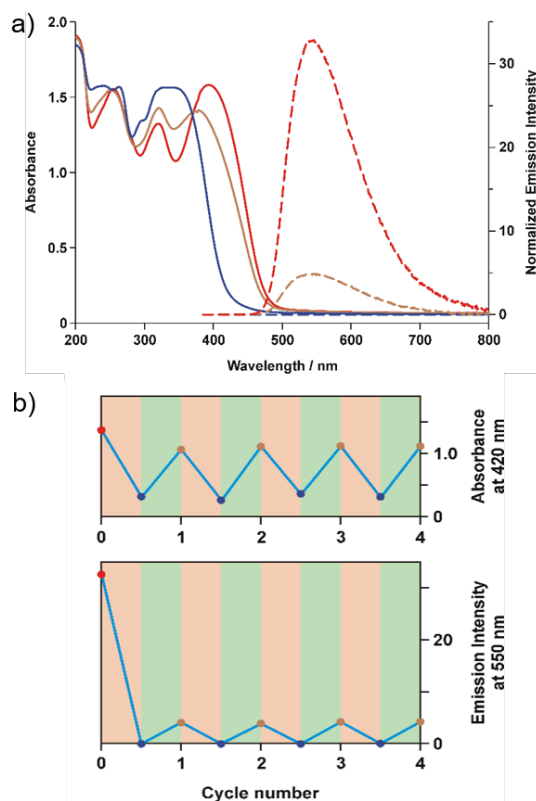


Figure 2. a) Absorption spectra (solid lines, left scale) and emission spectra (dashed lines, right scale; $\lambda_{\text{ex}} = 380 \text{ nm}$, isobestic point) of a drop casted film of **1**. The red lines are of **1-Z**, the blue lines correspond to PSS_{450} ($> 90\% \text{ 1-E}$), and the brown lines depict the bands at PSS_{360} ; b) Absorbance (top) and emission (bottom) changes of a drop casted film of **1-Z** subjected to alternative irradiation cycles at 450 and 360 nm. Orange areas: irradiation at 450 nm for 20 min. Green areas: irradiation at 360 nm for 20 min.

We were pleasantly surprised to find that the photoswitching behavior of **1** also takes place in drop-casted films (1 mg in 1 mL dichloromethane, *ca.* 0.5-1 micron thickness films). The absorption and emission spectra ($\lambda_{\text{ex}} = 370 \text{ nm}$, isobestic point) of **1-Z** in the solid film (Figure 2a) are very similar to those recorded in solution (Figure 1b) indicating that the *same* isomerization process is taking place in the solid-state. Irradiation of the film at 450 nm brings about absorption spectral changes that are almost identical to those observed in solution, indicating efficient $Z \rightarrow E$ isomerization in the solid-state. From an analysis of the absorption spectra it can be estimated that at the photostationary state (PSS_{450}), more than 90% of **1-Z** is converted to the E configuration.

Remarkably, the emission of the Z isomer is maintained in the solid-state (i.e., there is no aggregation-caused quenching),²⁰ and so is the toggling between the ON/OFF states, which is also highly uncommon.²¹ The characteristic emission of the Z form at $\lambda_{\text{max}} = 560 \text{ nm}$ is quenched at the photostationary state, confirming that the **1-E** form is non-emissive also in the solid-state. We hypothesize, based on an analysis of the single-crystal structure of **1-Z** (Figure S43) that the absence of π - π interactions is responsible for the un-

sual emission observed in the solid-state. Unfortunately, we could not grow suitable crystals of **1-E** for crystallographic analysis.

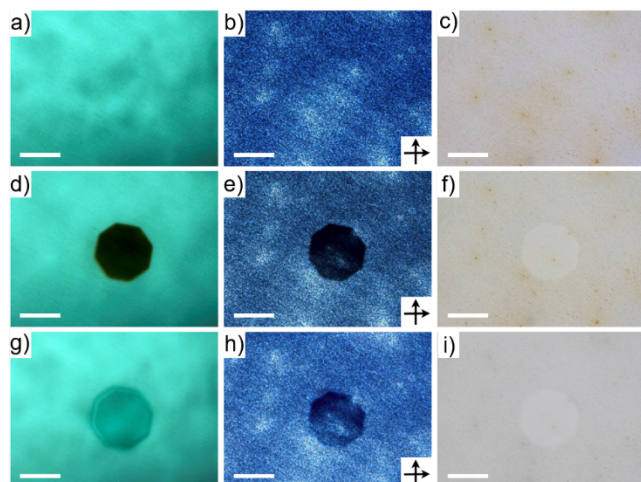


Figure 3. Optical micrographs obtained with 360-nm excited fluorescence (left), cross-polarized (central), and bright field (right) light illumination. (a, b, c) The as-prepared film; (d, e, f) the film after blue light irradiation (430–470 nm) in a central spot for 10 min; (g, h, i) the film in (d, e, f) after near-UV light irradiation (330–380 nm) in the same central spot for 10 min. Scale bar, 100 μm . The black arrows in b, e and h represent the relative orientation of the polarizer and analyzer.

No changes in the absorption spectrum of the **1-E** film were observed after one month at room temperature, proving that the thermal *E* to *Z* back isomerization is exceedingly slow also in the solid-state. On the other hand, exposing the **1-E** enriched film to 360 nm light causes spectral changes consistent with *E* \rightarrow *Z* photoisomerization ($\text{PSS}_{360} = 70\%$ **1-Z**; Figure 2a). The initial absorption and fluorescence spectra cannot be fully recovered by irradiation at 360 nm because of the extensive overlap, at this wavelength, between the absorption spectra of the *E* and *Z* forms. Nevertheless, the system displays high fatigue resistance in the solid-state, as its absorption and emission characteristics can be reversibly switched multiple times by alternate irradiation at 450 and 360 nm (Figure 2b). A decrease in the emission intensity is observed after the first switching cycle, which stabilizes in subsequent cycles. This effect might be attributed to an annealing effect (e.g., reorganization of the solid-state structure) that the film undergoes after the first switching cycle.

To get a better insight into what is happening to the drop casted film upon photoswitching, we imaged it with an epifluorescence polarizing optical microscope. The film exhibits a strong fluorescence emission when excited with 360 nm light (Figure 3a), and significant optical birefringence under cross-polarized light illumination (Figure 3b), confirming an ordered arrangement of the molecules in the solid that gives rise to anisotropic crystals. Upon irradiation with high intensity blue light in a central spot, the morphology of the film changes (Figure 3c-f) and both the optical birefringence (Figure 3e) and fluorescence emission (Figure 3d) disappear in the irradiated area. This observation suggests that isomerization induces a phase transition leading to a loss of crystalline order, that is, amorphization of the material. The emission intensity and birefringence of the material are partially restored upon irradiation with high intensity near-UV light. This result confirms the reversible nature of the light induced switching process, and rules out local thermal effects as the cause of the observed phenomenon.

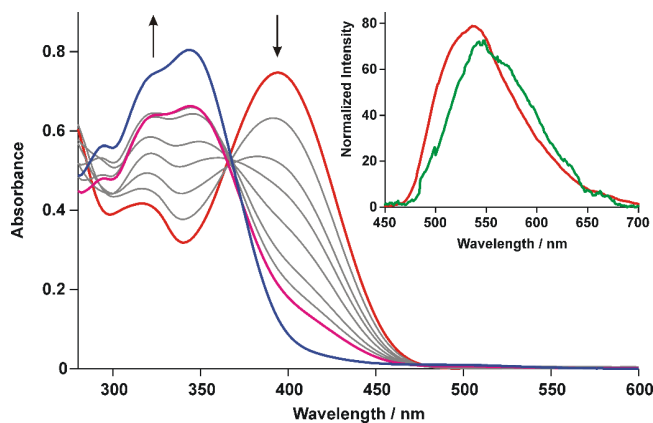


Figure 4. Absorption spectral changes of a toluene solution of **1-Z** (red line) upon irradiation at 800 nm for 3 h (purple line) and successive rest in the dark for 3 d (blue line). Inset: emission spectra of **1-Z** in solution (red line) and in a solid film (green line) upon excitation at 800 nm.

We also investigated the two photon absorption properties of **1** in both solution and the solid-state. Indeed, the relevant excited-state manifestations of **1** – namely, luminescence and isomerization – can be triggered by the absorption of two near infrared photons (i.e., 750 and 800 nm), similarly to what we observed upon conventional one-photon excitation. This property is also highly unusual, considering that most small molecules have negligible 2-photon absorption, and that our compound was not specifically designed for this purpose (Figure 4, Figures S53-S56).

Finally, to demonstrate how easily **1**, and its solution and solid-state properties can be taken advantage of, and as a proof of principle, we devised two simple experiments (Figures S45 and S50). In the first one a laser pointer was used to reversibly draw sustained structures in a toluene solution of **1** (Video S1). The other is a “sketch-and-etch” type application where a laser pointer is used to write on a hydrazone covered transparency slide (Video S3), while UV is used to erase the writing.

In conclusion, we developed an easy-to-make photochromic hydrazone that features configurational switching and fluorescence toggling with one- or two-photon irradiation in solution (organic and aqueous solutions including serum) and solid-state; the toggled state is stable for years in the dark at rt. All these properties are unprecedented for an individual compound! The combination of the desirable characteristics of several families of photochromic species in a single, easily accessible system, will enable the development of new adaptive functions and systems. For example, the simple molecular structure of **1**, that does not require additional structural manipulation for it to be emissive²² or water soluble,²³ can open the way for theranostics,²⁴ where diagnostics (by following the distribution and localization of the drug using super-resolution fluorescence microscopy²⁵) and therapy (using photopharmacology²⁶) are combined.

ASSOCIATED CONTENT

Supporting Information

The supporting material is available free of charge on ACS Publications Website at DOI: <http://pubs.acs.org>.

General methods, experimental procedures, NMR spectra of compounds, photoisomerization studies, kinetic studies, and solution and solid-state emission studies (PDF)

Crystallographic data for **1-Z** (CIF)
Crystallographic data for **2-Z** (CIF)
Real-time writing in solution (AVI)
Diffusion in solution (AVI)
Real-time writing in solid-state (AVI)

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Notes

The authors declare no competing financial interest

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