

## Photoswitches

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Sensitized Two-NIR-Photon  $Z \rightarrow E$  Isomerization of a Visible-Light-Addressable Bistable Azobenzene Derivative

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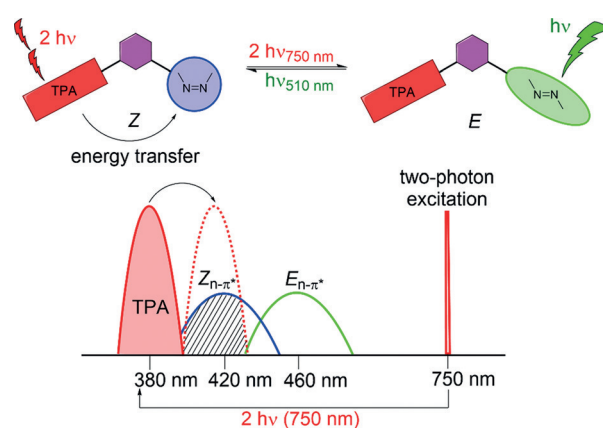
**Abstract:** Two-NIR-photon-triggered  $Z \rightarrow E$  isomerization of an azobenzene was accomplished by covalently linking a two-photon-harvesting triarylamine antenna to a thermally stable *ortho*-fluorinated azobenzene derivative. The obtained photo-switch is fully addressable with visible and NIR light by using one-photon and two-photon excitation, respectively, with the latter offering enhanced penetration depth and improved spatial resolution.

**R**eversibility is one of the most striking features of novel responsive materials, since it enables the repeated and dynamic alteration of their properties on demand.<sup>[1]</sup> Light as a stimulus offers very high spatial, temporal, and energetic resolution. In addition, light of the appropriate wavelength can penetrate into materials and tissues owing to its non-invasive nature. However, a fundamental limitation is encountered at the nanoscale owing to Abbe's law of diffraction, which limits the maximum spatial resolution to half the wavelength of the light used.<sup>[2]</sup> One way to overcome this limitation involves the use of nonlinear optics.<sup>[3]</sup> In this approach, two-photon excitation of chromophores is possible with photon energies corresponding to only half of the one-photon absorption band, thereby reducing photobleaching, material damage, and also cellular damage in biological samples.<sup>[4]</sup> Importantly, the rate of two-photon absorption shows a square dependence on the excitation intensity,<sup>[5]</sup> and therefore two-photon absorption can only occur in the focal point of a focused laser beam (typically involving ultrashort pulses).

Optimization of azobenzenes capable of efficiently responding to two-photon excitation is a widely investigated field of research. Specifically, much effort has been put into the design of azobenzenes, which are capable of intrinsically performing the  $E \rightarrow Z$  isomerization by means of direct two-photon excitation.<sup>[6]</sup> Thus far, mostly azobenzenes with strong push-pull substitution patterns in the *para* positions have been studied.<sup>[7]</sup> However, such push-pull-substituted azobenzene derivatives inherently suffer from thermal instability and hence short half-lives of their *Z* isomers,<sup>[8]</sup> thus rendering them not suitable for many applications in which bistable systems are required. Another approach relies on the indirect

two-photon excitation of an azobenzene through energy transfer from a suitable two-photon-absorbing antenna. By following this strategy, it was possible to achieve the  $E \rightarrow Z$  isomerization of azobenzenes by means of intermolecular<sup>[9]</sup> or intramolecular<sup>[10]</sup> two-photon-induced FRET. Despite its conceptual elegance, photoconversion in the latter system was limited to the generation of 25 % *Z* isomer only and more importantly,  $Z \rightarrow E$  photoisomerization of the thermally unstable *Z* isomer necessitates excitation by harmful UV light.

Herein, we describe a thermally bistable azobenzene photoswitch that can be operated using two-photon near infrared (NIR) excitation, as well as one-photon visible-light excitation to reset the system, which imparts the photochromic system with bistability and high spatial resolution, as well as addressability in the visible and NIR region for enhanced penetration and improved photostability. Our approach is based on an *ortho*-fluorinated azobenzene derivative equipped with a two-photon-absorbing antenna (Figure 1). The antenna is able to harvest low energy 750 nm



**Figure 1.** Illustration of the operating principle based on two-NIR-photon sensitized  $Z \rightarrow E$  photoisomerization and one-visible-photon direct  $E \rightarrow Z$  photoisomerization of a thermally bistable *ortho*-fluorinated azobenzene with well separated  $n \rightarrow \pi^*$  bands (TPA = two-photon antenna).

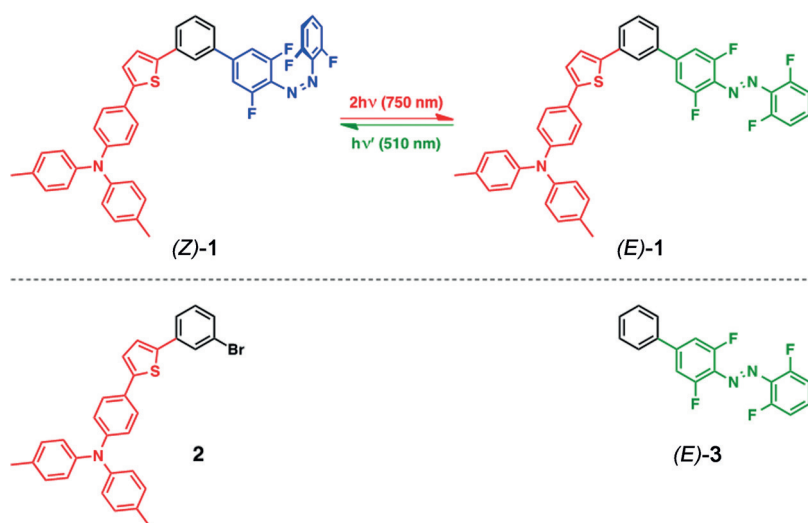
NIR photons and subsequently transfer its excitation energy to the blue-shifted *Z* azobenzene to induce  $Z \rightarrow E$  isomerization. Importantly, the system can be switched back selectively and quantitatively to the *Z* isomer by using 510 nm green light.

Recently, our group reported the superior photochromic and thermal stability of *ortho*-fluorinated azobenzenes, which have well separated  $n \rightarrow \pi^*$  bands that enable selective  $E \rightarrow Z$

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isomerization with visible light ( $\lambda > 500$  nm).<sup>[11]</sup> Furthermore, the thermal half-life of the *Z* isomer has been reported to be as high as two years at room temperature for certain derivatives. Such azobenzenes offer the unique opportunity to achieve the desired molecular properties, since the *Z* isomer can be readily generated in high yield by using visible light, and its thermal stability facilitates the study of the sensitized two-photon-triggered *Z*→*E* isomerization. A triarylamine moiety, which is known to be an excellent two-photon-absorbing chromophore,<sup>[12]</sup> was chosen as the antenna. To allow selective excitation of the antenna, both a thiophene unit and a *meta*-phenylene linkage were introduced into the targeted triarylamine–azobenzene dyad **1** (Scheme 1, top). While the thiophene and the phenylene



**Scheme 1.** Triarylamine–azobenzene dyad **1** (top) and the antenna (**2**) and azobenzene reference (**3**) compounds.

units elongate the  $\pi$ -conjugated system of the antenna to shift its absorption band to the 380 nm region, where the azobenzene exhibits negligible absorption, the *meta*-configured linkage ensures decoupling in the ground state<sup>[13]</sup> and hence selective excitation and spectroscopic identity of each individual component. Importantly, overlap of the emission of the antenna<sup>[14]</sup> with the  $n \rightarrow \pi^*$  absorption band of the (*Z*-configured) azobenzene should facilitate the envisioned energy-transfer mechanism (Figure 1).

The synthesis of the desired triarylamine–azobenzene dyad **1** was accomplished in a convergent fashion. Initial halogen–metal exchange of antenna **2**<sup>[14]</sup> with *n*BuLi at  $-78^\circ\text{C}$  followed by borylation with  $\text{B}(\text{O}i\text{Pr})_3$  and reaction under Suzuki cross-coupling conditions with the corresponding 4-bromo-2,2',6,6'-tetrafluoroazobenzene afforded target compound **1**. Further details of the synthesis and compound characterization are provided in the Supporting Information.

The UV/Vis absorption spectra of dyad **1**, in the *E* as well as *Z* configuration, resemble the spectral signatures of both individual components, as illustrated by comparison with the sum spectra of reference compounds **2** and **3** (Figure 2). The long-wavelength absorption maxima at 460 nm [(*E*)-**1**] and

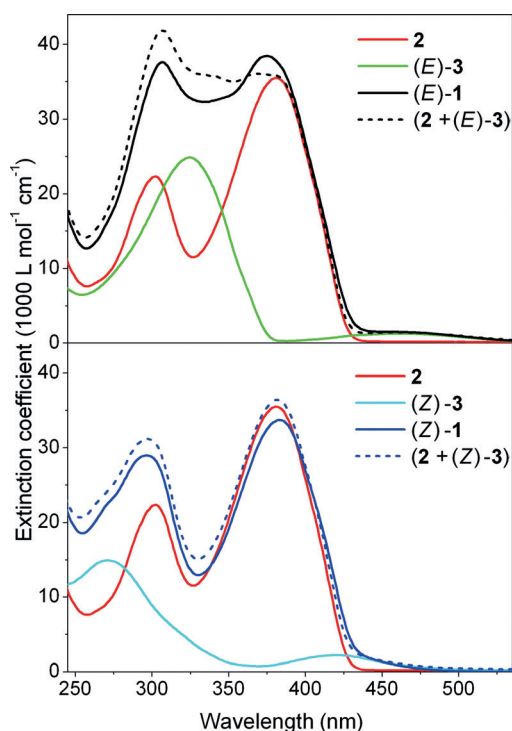
420 nm [(*Z*)-**1**] are assigned to the typical  $n \rightarrow \pi^*$  band of the *ortho*-fluorinated azobenzene, while the maxima at about 320 nm [(*E*)-**1**] and 270 nm [(*Z*)-**1**] are attributed to the azobenzene  $\pi \rightarrow \pi^*$  band. The strong absorption bands at 300 nm and 380 nm are associated with the antenna and exhibit no spectral change upon photoisomerization, thus further illustrating decoupling of the two chromophore subunits in the ground state in both isomers. Interestingly, the parent azobenzene **3** exhibits significant solvatochromism,<sup>[15]</sup> which however only caused a bathochromic shift of the  $\pi \rightarrow \pi^*$  band upon increasing solvent polarity, while the  $n \rightarrow \pi^*$  band remained unaltered. As a consequence, the shape of the absorption spectrum of dyad **1** changes upon varying solvent polarity, that is, upon going from *n*-hexane (Figure 2 and

Figure S4 in the Supporting Information) to acetonitrile (Figure S5) solution. Note that the antenna itself (**2**) does not display notable solvatochromism.<sup>[14]</sup>

Dyad **1** as well as the parent azobenzene **3** exhibit fully reversible photochromism. Upon irradiation with green light ( $\lambda > 500$  nm), the  $n \rightarrow \pi^*$  band of the *E* isomer is selectively excited, thereby leading to high photoconversion with 92% and 96% *Z* isomer content in the photostationary state (PSS) for **1** and **3**, respectively. These values are similar to those observed for other previously reported *ortho*-fluorinated azobenzenes.<sup>[11]</sup> It can thus be assumed that the *meta*-linked antenna has no electronic influence over the  $n \rightarrow \pi^*$  band of the azobenzene, thus ensuring the possibility to selectively address each individual component of the molecular dyad **1**.

In contrast to their similar spectroscopic properties, the *Z* isomers of compounds **1** and **3** display substantially different thermal stability. Interestingly, (*Z*)-**1** exhibits a markedly elongated thermal half-life ( $t_{1/2} = 522$  days at room temperature, see Table S2) compared to (*Z*)-**3** ( $t_{1/2} = 48$  days). Detailed analysis involving experimental determination of the activation parameters for the thermal *Z*→*E* isomerization of **1** and **3** suggests that the observed effect is mostly enthalpic in origin (Table S2).

In the excited state, efficient communication between the antenna and azobenzene moieties in the dyad was observed, as manifested by the relative fluorescence quantum yields (in *n*-hexane) of **1** ( $\Phi = 3.9 \times 10^{-3}$ ) compared to **2**<sup>[14]</sup> ( $\Phi = 0.12$ ). The negligible fluorescence emission of the antenna in the dyad is clear evidence for an efficient intramolecular quenching process. Assuming energy transfer from the excited antenna to the azobenzene moiety to be the origin of the observed quenching, *Z*→*E* isomerization experiments were conducted with compounds **1** and **3** upon 380 nm irradiation (see Figure S7). Indeed, when the highly *Z*-enriched PSS mixtures were subjected to identical irradiation conditions, *Z*→*E* isomerization in the dyad **1** proceeded much faster ( $\Phi_{Z \rightarrow E} = 0.38$  for **1** vs.  $\Phi_{Z \rightarrow E} = 0.09$  for **3**, see Table S1) and a significantly higher *E* content in the PSS was achieved compared to the parent azobenzene **3** (*E*/*Z* = 76:24 for **1** vs.



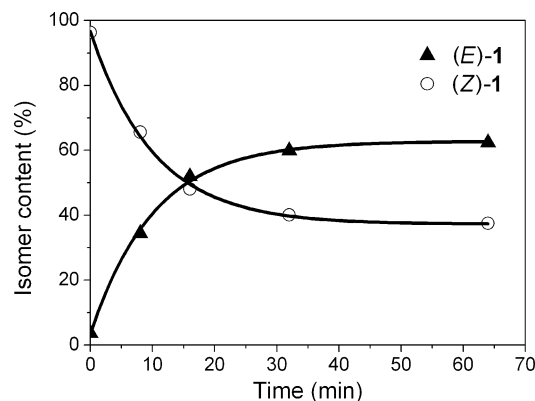
**Figure 2.** UV/Vis spectra in *n*-hexane of (*E*)-1 (black line), (*Z*)-1 (blue line), **2** (red line), (*E*)-3 (green line), and (*Z*)-3 (cyan line);  $c = 10^{-5}$  M, 25 °C. Direct sum spectra (**2** + (*E*)-3, dotted black line) or (**2** + (*Z*)-3, dotted blue line) nearly coincide with the spectra of the dyad **1**, thus suggesting weak ground-state coupling of the triarylamine and the azobenzene units.

$E/Z = 23:77$  for **3**, see Figure S7). Evidently, efficient sensitization of the azobenzene switch by the attached triarylamine antenna takes place in dyad **1**.

To elucidate the nature of the sensitization mechanism, oxidation and reduction potentials of all compounds were determined by cyclic voltammetry (Figure S11 and Table S3). Additionally, spectroelectrochemistry of **1** and **3** was carried out to assign the spectroscopic signatures of the charge-separated species generated upon increasing the applied negative potential (Figures S12, S13). Subsequently, fs time-resolved absorption spectroscopy measurements on (*Z*)-**1** were performed to discern the excited-state dynamics after excitation of the antenna moiety (380 nm) or the  $n \rightarrow \pi^*$  band (440 nm) of the azobenzene moiety (Figures S14, S15). Examination of the observed transients following 380 nm excitation clearly shows that upon irradiation of the triarylamine moiety, the excitation energy is predominantly transferred to the azobenzene unit and subsequent isomerization gives the *E*-configured photoproduct. Note that upon direct irradiation of the  $n \rightarrow \pi^*$  band (440 nm), negligible excited-state absorption could be assigned to the antenna and the isomerization proceeds along the conventional azobenzene pathway.<sup>[15,16]</sup> While the obtained reduction and oxidation potentials of the components support photoinduced electron transfer from the excited antenna to the azobenzene moiety, no charge-separated species could be detected in the time-resolved measurements. Therefore, sensitization can be attributed to energy transfer. In view of the close spatial

proximity of the components, their HOMO and LUMO levels, and the weak oscillator strength of the  $n \rightarrow \pi^*$  band of the azobenzene acceptor, a Dexter-type exchange mechanism most likely operates in dyad **1**.<sup>[17,18]</sup>

After establishing efficient one-photon-driven switching through direct *E* → *Z* isomerization and indirect/sensitized *Z* → *E* isomerization, the two-photon photochromism of dyad **1** was probed. For this purpose, the sensitized *Z* → *E* isomerization of **1**, triggered by 750 nm NIR light from a focused fs laser beam, was monitored by ultraperformance liquid chromatography (UPLC, Figure S16). These experiments clearly prove *Z* → *E* isomerization upon indirect two-photon excitation (Figure 3). Due to the nature of the mostly indirect

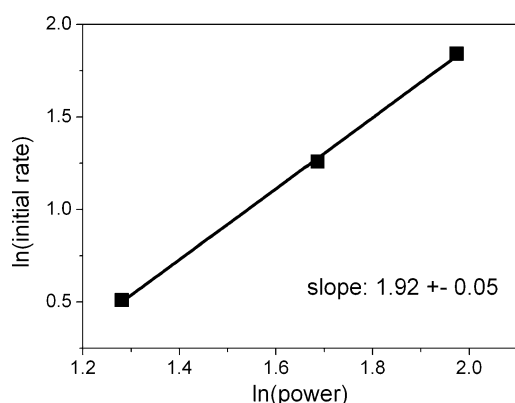


**Figure 3.** Two-photon sensitized *Z* → *E* isomerization of **1** ( $c = 10^{-4}$  M in *n*-hexane, *Z*-enriched PSS mixture) as a function of irradiation time ( $\lambda_{\text{irr}} = 750$  nm,  $E_p = 8$  mJ) as monitored by UPLC. Concentrations of the *E* (solid triangles) and *Z* (empty circles) isomer are expressed as a percentage of the total mixture (lines show exponential fit,  $R = 0.9965$ ).

excitation via the triarylamine antenna, the degree of photoconversion that can be achieved by two-photon excitation (65% *E* isomer content in the PSS) is comparable to that obtained by the corresponding one-photon irradiation (77% *E* isomer content in the PSS). Furthermore, no decomposition products could be detected by UPLC, thereby excluding irradiation damage.

A photoisomerization mechanism involving two-photon excitation must obey an inverse square power law.<sup>[3]</sup> In order to investigate this relationship, the rates of photoisomerization were determined as a function of the applied laser power (Figure S17). Indeed, a double logarithmic plot of the initial rates of *Z* → *E* isomerization versus the applied irradiation power shows a linear relationship with a slope of 1.92 (Figure 4), which is compelling evidence for a two-photon process. The slight deviation from the ideal value of 2 is probably due to competing saturation or photobleaching, as described previously.<sup>[5]</sup>

In summary, we have designed a bistable azobenzene that can undergo sensitized two-photon-triggered *Z* → *E* isomerization. This was achieved by linking a two-photon-absorbing triarylamine antenna to an *ortho*-fluorinated azobenzene core, and it allows the use of low energy NIR-photons (750 nm) with high spatial resolution. Importantly, direct one-



**Figure 4.** Rate–power dependence: Natural logarithm of the initial rate of (*E*)-1 isomer formation (monitored by UPLC) as a function of the natural logarithm of the laser power (750 nm, 100 fs pulse width, 500 Hz repetition rate). The black line shows a linear fit ( $R=0.9986$ ) of the data (see also Figure S17).

photon-triggered  $E \rightarrow Z$  isomerization with visible light (500 nm) quantitatively regenerates the *Z* isomer, which displays a superior thermal half-life of more than 500 days at room temperature. We are currently focusing on improving the efficiency of our system (by increasing the two-photon-absorption cross-section of the antenna and the photoconversion) and on integrating it into more complex molecular architectures to control their properties and functions with light and subdiffraction resolution.

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