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## Communication

# Photochromic Hydrazone Switches with Extremely Long Thermal Half-Lives

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# Photochromic Hydrazone Switches with Extremely Long Thermal Half-Lives

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Supporting Information Placeholder

**ABSTRACT:** A family of easily accessible light-activated hydrazone switches has been developed having thermal halflives of up to 2700 years! Structure-property analysis shows that replacing the rotor pyridyl group of our typical hydrazone switch with a phenyl one leads to the long-live negative photochromic compounds. The switching properties of the hydrazones in both toluene and DMSO were assessed offering insights into the kinetics and thermodynamics of the switching process.

One of the most important characteristics of a photochromic compound<sup>1</sup> is its thermal isomerization half-life. This property defines the type of application the switch can be used for; if long then it can be used in optical data storage<sup>2</sup>, on the other hand if it is short then photodriven oscillators come into play.<sup>3</sup> Then there is a sea of opportunities in between. The search for photochromic compounds where the back-isomerization process can only be addressed photochemically (i.e., the process is practically thermally irreversible) have yielded only a handful of systems. Most notable are Irie's diarylethylene derivatives<sup>4</sup> whose ring opening step can have half-lives of up to 450,000 years at 303 K. As for thermally stable configurational photochromic compounds, two recent azo-based examples by Hecht<sup>5</sup> and Fuchter<sup>6</sup> showed that half-lives of 700 and 1000 days at 298 K can be accessible. Given this limited space, the development of new photochromic compounds with long isomerization half-lives is imperative for the development of new functions, and accessing new opportunities.

As part of our efforts in developing light- and chemicallyactivated hydrazone-based switches,<sup>7</sup> we revisited the photoswitching of the parent hydrazone 1 (Scheme 1). Our initial studies indicated that this system cannot be appreciably and effectively switched using light.<sup>8</sup> This finding was in contrast with the pioneering work done by Courtot,<sup>9</sup> showing that  $\beta$ ketoesterhydrazones can be switched photochemically. We concluded that the intramolecular H-bond with the pyridyl ring was hindering the photochemical isomerization. This hypothesis was supported by work by Lehn,<sup>10</sup> who showed that certain acylhydrazones <sup>11</sup> can be photochemically switched to the *Z* isomer as long as they are stabilized through an intramolecular H-bond with a pyridyl group. However, this stabilization turned out to be detrimental to the photochemical back-isomerization, and only the application of acid at elevated temperatures could revert the Z isomer back to the E one.

Herein, we report on a new family of photochromic hydrazone switches (3 and 4) with extraordinarily long half-lives (Scheme 1). These systems are based on our previously reported pH activated switches.<sup>7</sup> The structures were altered, however, to tweak the intramolecular H-bond with the pyridyl ring, or completely eliminate it by replacing it with a phenyl one. This strategy yielded efficient negativephotochromic compounds having thermal half-lives as long as 2700 years! To the best our knowledge, these systems have the slowest thermal back isomerization lifetimes (at room temperature) among all configurational photochromic compounds. Moreover, their ease of synthesis and derivatization, photostability and quantum yields make them highly competitive with another family of bistable photochromic compounds, i.e., diarylethylenes.<sup>12</sup> This novel family of lightactivated switches is an important addition to the limited toolbox of bistable photochromic compounds, and can open the door to many new opportunities.

#### Scheme 1. Structures of hydrazones 1-4



Hydrazone **2** was first reported as a pH sensitive multistate switch.<sup>13</sup> Based on single crystal structure analysis (i.e., N-H...N bond lengths) the intramolecular H-bond with in **2** is bifurcated. To assess whether this property will lead to a photoresponsive system we studied its light-induced switching. The <sup>1</sup>H NMR spectrum of an equilibrated solution of **2** consist of a 90:10 mixture of *E* and *Z* isomers, respectively (Figure S22a in the Supporting Information). Upon irradiation with a 442 nm light source, a photostationary state (PSS) is obtained consisting of 95% of the *Z* isomer (Figure S22b in the Supporting Information). The quantum yield ( $\phi$ ) of this photoisomerization process was calculated to be 3.7 ± o.6%.<sup>6,14</sup> Unfortunately, the overlap of the UV spectra of the **2**-*E* ( $\lambda_{max} = 398$  nm) and **2**-*Z* ( $\lambda_{max} = 390$  nm) isomers (Figure S17 in the Supporting Information) made it difficult to find an optimal irradiation wavelength to photochemically reverse the isomerization process.<sup>15</sup> Nonetheless, this result shows that tweaking the intramolecular H-bond with the pyridyl ring indeed leads to a photoisomerizable hydrazone switch.



**Figure 1**. a) Light induced *Z* /*E* isomerization of hydrazone **3**; b) UV-Vis spectra (1.0 × 10<sup>-5</sup> M) of **3**-*E* (colorless) and **3**-*Z* (yellow) isomers in toluene; c) Isomerization cycles of **3** in toluene upon alternating irradiation using 442 and 340 nm light sources. The absorbance change at  $\lambda_{max} = 398$  nm (**3**-*Z*) was monitored.

Next we replaced the pyridyl ring with a phenyl one (**3**) to study the effect of completely removing the intramolecular H-bond with the former ring. Switch **3** was synthesized through the condensation reaction between quinolinyl hydrazine and the corresponding ketone (Scheme Si in the Supporting Information).<sup>7f</sup> After column chromatography, both the *E* and *Z* isomers were separated (48 and 28 % yield, respectively) and then fully characterized using NMR spectroscopy, mass spectrometry and X-ray crystallography (Figures S<sub>3</sub>–15, and 8<sub>3</sub> in the Supporting Information). The hydrazone N-H proton signal of 3-E resonates at 10.49 ppm in toluene- $d_8$  (Figure S23a in the Supporting Information), indicating the presence of a weak intramolecular H-bond with the quinolinyl ring. This conclusion was corroborated with the analysis of the single crystal structure of 3-E (Figure S83 in the Supporting Information).<sup>16</sup> Switch 3-Z on the other hand has a characteristic (for these systems) N-H proton resonance at 13.96 ppm (Figure S23b in the Supporting Information), indicating that the N-H is H-bonded with both the quinolinyl nitrogen and carbonyl oxygen. Intriguingly, the <sup>1</sup>H NMR spectrum of each individual isomer of 3 reveals only a set of proton signals, and no interconversion between the two isomers is observed even after a week of equilibration at r.t. This fact is an indication that the barrier for E/Zisomerization in 3 is very high.

The UV spectra of 3-*E* and 3-*Z* were measured separately (Figure 1b and Table 1). The  $\lambda_{max}$  (373 nm; absorption coefficient constant ( $\varepsilon$ ) of 13637 M<sup>-1</sup>·cm<sup>-1</sup>) of 3-*E* is shifted hypsochromically by 25 nm as compared to 2-*E*,<sup>17</sup> while in 3-*Z* the absorption band is shifted bathochromically by 8 nm to  $\lambda_{max}$  = 398 nm ( $\varepsilon$  = 17267 M<sup>-1</sup>·cm<sup>-1</sup>). The separation in the absorption bands caused by these shifts allowed us to photochemically address both the forward and backward *E*/*Z* isomerization processes of 3.

Table 1. Photophysical data for compounds 2-4 in toluene.

Hydrazone	λ <sub>max</sub> /nm	$\Phi^{a}_{E \rightarrow Z}$	$\Phi^{a}_{Z \to E}$
<b>2</b> - <i>E</i>	398	$a = \pm a 60$	Ь
<b>2-</b> Z	390	$3.7 \pm 0.0\%$	-
<b>3-</b> <i>E</i>	373	$2.4 \pm 0.2\%$	$a^{2} + a^{10}$
<b>3-</b> Z	398	2.4 ± 0.3%	$0.3 \pm 0.170$
<b>4</b> - <i>E</i>	334	$10.2 \pm 0.1\%$	$17 \pm 0.1\%$
<b>4</b> -Z	367	$10.2 \pm 0.170$	1.7 ± 0.170

<sup>*a*</sup> Photoisomerization quantum yield; <sup>*b*</sup> Because of the poor band separation an optimal irradiation wavelength was not found to initiate the  $Z \rightarrow E$  isomerization process.

The photoisomerization efficiency of 3 was studied using <sup>1</sup>H NMR spectroscopy. Upon 340 nm light irradiation a sample of 100% 3-E yields a PSS consisting of 76% 3-Z isomer (Figure S23b in the Supporting Information). The quantum yield of the process was determined to be  $2.4 \pm 0.3\%$ . Irradiation of the obtained sample with 442 nm light yields a PSS consisting of 91% **3**-*E* isomer with  $\Phi_{Z \to E}$  of 0.3 ± 0.1% (Figure S23c in the Supporting Information). During the isomerization from 3-Z to 3-E isomer (Figure 1b) a significant color change from yellow to colorless was observed. This behavior, which is known as negative photochromism, is quite rare and can be used in many interesting applications.<sup>18</sup> We used UV/Vis spectroscopy (Figure 1c) to study the fatigue resistance of the switch, and did not observe any photodegradation up to 50 isomerization cycles. This result attests to the robustness of the photochromic hydrazone switch. Next, we studied the thermal isomerization process of switch 3. It was surprising to find that at elevated temperatures, pure 3-Eisomerizes to 3-Z with an extremely slow first-order rate

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Hydrazone (Solvent)	$k^a$ / s <sup>-1</sup>	$\tau_{1/2}^{b}$ / year	E <sub>a</sub> / kcal∙mol⁻¹	∆H <sup>‡c</sup> / kcal∙mol⁻¹	$\Delta S^{\ddagger c}$ / cal·mol <sup>-1</sup> ·K <sup>-1</sup>	$\Delta G^{\ddagger c}$ kcal·
<b>2</b> (Toluene) <sup>e</sup>	$(4.3 \pm 0.2) \times 10^{-7}$	$0.052\pm0.002$	$14.8\pm0.1$	14.1 ± 0.4	-40.2 ± 1.1	26.1
<b>2</b> (DMSO) <sup><i>e</i></sup>	$(4.5 \pm 0.1) \times 10^{-7}$	$0.049 \pm 0.001$	16.0 ± 0.1	15.3 ± 0.4	-36.3 ± 1.1	26.1
<b>3</b> (Toluene) <sup>d</sup>	$(8.2 \pm 0.4) \times 10^{-12}$	2,700 ± 100	$32.8\pm0.6$	32.0±0.9	-1.6 ± 2.3	32.5 :
<b>3</b> (DMSO) <sup>d</sup>	$(8.3 \pm 0.2) \times 10^{-11}$	265 ± 6	$28.7\pm0.1$	$27.7\pm0.8$	-11.1±2.0	31.1 ±
<b>4</b> (Toluene) <sup>d</sup>	$(8.6 \pm 0.8) \times 10^{-11}$	255 ± 19	$30.5\pm0.7$	29.6 ± 0.6	-4.7 ± 1.6	31.1 ±
$4 (DMSO)^d$	$(9.6 \pm 0.5) \times 10^{-10}$	23 ± 1	$28.3\pm0.2$	$27.5\pm0.5$	-7.4 ± 1.2	29.6

Table 2. Kinectic data and activation parameters for the thermal isomerization of compounds 2–4 in different

(Table 2) (Figures S53–66 in the Supporting Information). This finding shows that the Z isomer is the thermodynamically more stable isomer, and not a kinetically trapped configuration obtained during synthesis. This conclusion is corroborated by DFT calculations (B3LYP/6-311G\*\*) that show that the Z isomer is 2.74 kcal/mol more stable than the E one (Figures S81-82 in the Supporting Information). The intramolecular H-bond in the Z isomer, and the steric effect between the rotor phenyl ring (red) and N-H proton in the E configuration can explain this unusual stability. The temperature dependency of the thermal isomerization of 3-E was studied in both toluene and DMSO and the activation energy barriers were determined to be 32.8  $\pm$  0.6 and 28.7  $\pm$  0.1 kcal·mol<sup>-1</sup>, respectively (Table 2).<sup>19</sup> These barriers are much higher than the barriers found for hydrazone 2 (14.8  $\pm$  0.1 and 16.0  $\pm$  0.1 kcal·mol<sup>-1</sup> in toluene and DMSO, respectively), where thermal isomerization occurs from Z to E.<sup>13</sup> Extrapolation of the obtained Arrhenius plot yields an extraordinarily slow isomerization rate  $(8.2 \times 10^{-12} \text{ s}^{-1})$  for 3 in toluene, which translates into an isomerization half-life  $(\tau_{1/2})$  of 2,700 ± 100 years at 298 K! Even in DMSO, the estimated half-life ( $\tau_{1/2}$  =  $265 \pm 6$  years) of 3 is ca. 138 and 97 times longer than the systems developed by Hecht (o-fluoroazobenzene)<sup>5</sup> and Fuchter (arylazopyrazole),<sup>6</sup> respectively. The difference in isomerization kinetics of 3 in toluene and DMSO might originate from the latter's competition with, and hence weakening of the intramolecular H-bond. The lower  $\Delta H^{\ddagger}$  value and larger negative  $\Delta S^{\ddagger}$  value in DMSO, which can indicate disruption of intramolecular H-bond, and more solvent reorganization in transition state, supports this conclusion. A direct comparison with 2 is not possible because it's thermal isomerization process (i.e.,  $Z \rightarrow E$  and not the other way round) and mechanism are different. We have previously proposed tautomerization-followed-by-rotation as the mechanism for thermal isomerization is such intramolecularly Hbonded hydrazone switches.7a The thermodynamic data and solvent dependency of 2 match well with this mechanism.

In order to have a better understanding of the effect of the intramolecular H-bond with the quinolinyl ring on isomerization half-life, we synthesized compound 4 (Figure S16 in the Supporting Information). The replacement of the quinolinvl with a phenyl ring induces a hypochromic shift of 39 and 31 nm in 4-*E* and 4-*Z*, respectively (Figure 2 and Table 1). The Z isomer was found to be the thermally stable configuration in 4 as well (Figures S67-80 in the Supporting Information). The photoisomerization of 4 is achieved using 340 and 412 nm light sources. Irradiation with a 412 nm light, leads to **4**-*E* with a  $\Phi_{Z \rightarrow E}$  = 1.7 ± 0.1%, and PSS<sub>412</sub> of 95% (Table 1 and Figure S23b in the Supporting Information). Irradiation with 340 nm light leads to 76% of 4-Z (PSS<sub>340</sub>), with  $\Phi_{E\to Z}$  =  $10.2 \pm 0.1\%$ . This photoisomerization process can be repeated multiple times (up to 10 cycles were tried) without any signs of fatigue (Figure S25 in the Supporting Information).



**Figure 2**. UV spectra  $(1 \times 10^{-5} \text{ M})$  of **4**-*E* and **4**-*Z* isomers in toluene

The thermal isomerization rate of 4-*E* was also studied as a function of temperature, and its half-life determined to be  $255 \pm 19$  years in toluene, and  $23 \pm 1$  years in DMSO (Table 2). Compared to 3 in toluene, switch 4 has a smaller  $\Delta H^{\ddagger}$  value  $(29.6 \pm 0.6 \text{ vs } 32.0 \pm 0.9 \text{ kcal·mol}^{-1}$ , respectively) and a similar  $\Delta S^{\ddagger}$  value (-4.7 ± 1.6 vs -1.6 ± 2.3 cal·mol<sup>-1</sup>·K<sup>-1</sup>, respectively). These data indicate that the 10 fold decrease in half-life in 4 compared to 3 is mainly an enthalpy driven one. We attribute this effect to the absence of the intramolecular H-bond with the quinolinyl ring in 4. In DMSO, which can compete with the quinolinyl ring over the H-bond, a similar  $\Delta H^{\pm}$  value  $(27.5 \pm 0.5 \text{ vs } 27.7 \pm 0.8 \text{ kcal·mol}^{-1} \text{ for } 4 \text{ and } 3$ , respectively)

but a less negative  $\Delta S^{\ddagger}$  value (-7.4 ± 1.2 *vs* -11.1 ± 2.0 cal·mol<sup>-1</sup>·K<sup>-1</sup> for **4** and **3**, respectively) are obtained indicating that less solvent reorganization happens in the transition state of **4** (i.e., the non-intramolecularly H-bonded molecule). This effect again explains the 10 fold decrease in the half-life for **4** compared to **3** in DMSO. In the same vein, the intramolecular H-bond (or the lack of) in addition to a hypothesized polar transition state that is affected by the solvent polarity, can explain the 10 fold changes in half-lives of **3** and **4** when going from toluene to DMSO.<sup>20</sup>

In conclusion, we developed a new family of photochromic hydrazone-based compounds. These systems exhibit extraordinary thermal stability, with half-lives as long as 2700 years. This property, in addition to their ease of synthesis and derivatization, very good band separation, very high photostationary states, and good quantum yields will make these switches highly valuable tools in the development of responsive and adaptive materials. We are currently working on optimizing the properties of the switches, and incorporating them in bulk materials.

#### ASSOCIATED CONTENT

#### **Supporting Information**

General methods, experimental procedures, NMR spectra of key compounds, photoisomerization studies, kinetic studies, DFT calculations, and crystallographic data (CIF). This material is available free of charge via the internet at <a href="http://pubs.acs.org">http://pubs.acs.org</a>.

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#### Notes

The authors declare no competing financial interest

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(15) The poor band separation was observed in both toluene and DMSO (Figure S18 in the Supporting Information).

(16) Each asymmetric single crystal unit contains two crystallographically independent molecules (Figure S69 in the Supporting Information). Unfortunately, we could not obtain single crystals of **3**-*Z* that were suitable for X-ray crystallography analysis.

(17) The X-ray analysis shows that the phenyl ring in **3**-*E* is twisted out of the plane of the rest of the molecule, which may lower the conjugation in the molecule and lead to this blue-shift.

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(19) We chose these two solvents because elevated temperatures (>90 °C) were required to study the isomerization kinetics of 3 and 4.
(20) Hydrazones 3 and 4 can also be efficiently switched (i.e., multiple cycles without any signs of fatigue) in protic solvents such as MeOH, and in the presence of acid and base (Figure S26–33 in the Supporting Information).



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