

A Photobasic Functional Group

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S Supporting Information

ABSTRACT: Controlling chemical reactivity using light is a longstanding practice within organic chemistry, yet little has been done to modulate the basicity of compounds. Reported herein is a triazabutadiene that is rendered basic upon photoisomerization. The pH of an aqueous solution containing the water-soluble triazabutadiene can be adjusted with 350 nm light. Upon synthesizing a triazabutadiene that is soluble in aprotic organic solvents, we noted a similar light-induced change in basicity. As a proof of concept we took this photobase and used it to catalyze a condensation reaction.

The ability to control chemical reactions and reactivity using light has been of interest to organic chemists since Klinger's first forays into photochemical reactions in cloud-bedeveloped Germany.¹ Since its inception, the synthetic power of photochemistry has been used to elegantly solve numerous synthetic riddles,^{2,3} but much less has been done in an area of chemistry so intrinsic to its core, namely basicity. Whereas Brønsted photoacids that dissociate more rapidly in the singlet excited state than the ground state are known,⁴ there are fewer examples of Lewis photoacids,⁵ and an analogous photobase has thus far escaped exposure. Our work fills in this last remaining gap. To be sure, bases protected with photolabile groups have been reported, but generally the photochemistry is being used to break apart a mask, not change the inherent property of the molecule (Figure 1a).^{6,7} Following with a more recent trend to utilize the photoinduced *E/Z* isomerization of azobenzene compounds, Hecht cleverly employed a steric wall to block access to a basic nitrogen atom's lone pair of electrons (Figure 1b).^{8,9} To the best of our knowledge, the Lewis basicity of a functional group has yet to be altered with photochemistry (Figure 1c). Herein we report a water-soluble compound that, upon photoirradiation, is rendered significantly more basic in a reversible fashion. Furthermore, an organic-soluble derivative is used to catalyze a Henry reaction in a light-dependent manner.

We recently reported a triazabutadiene scaffold, **1** (Figure 2a), which was water-soluble and reacted with hydronium ions to liberate a protected aryl diazonium species under physiologically relevant, mild conditions.¹⁰ Inspired by Fanghanel's report establishing that this general class of compounds readily photoisomerize to a more reactive *Z*-form,¹¹ we irradiated a pH 9 buffered solution of **1**. Indeed, with a simple hand-held UV lamp ("365 nm", measured at 350 nm), we observed complete consumption of **1** after only a few hours.¹² The non-irradiated reaction under similar conditions was stable for days. We hypothesized that, if a two-electron

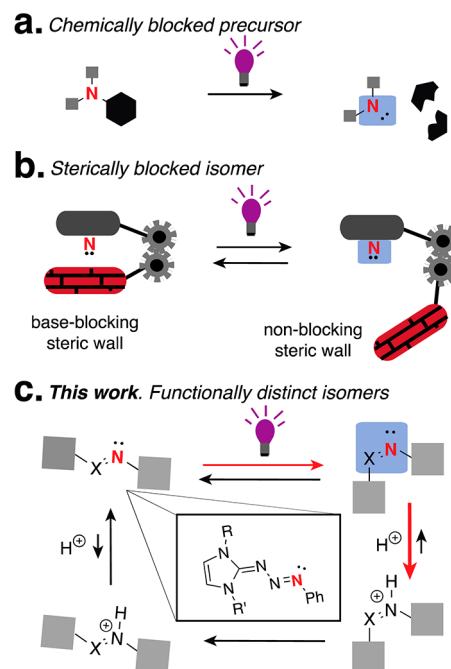


Figure 1. Photochemically generated bases. (a) Upon exposure to light, the protecting group of a masked base decomposes to reveal a basic nitrogen atom. (b) The basic nitrogen atom of a molecule is obscured by a steric wall that is reversibly swung away in a photochemically triggered fashion. (c) The intrinsic basicity of a nitrogen-containing functional group is altered by a photochemical event.

process (illustrated in Scheme S1) is occurring, then **1-Z** must be more basic than **1-E**. Initial NMR analysis of samples post-irradiation clearly showed cyclic guanidine **2** (Figure 2a), but we did not observe evidence of a benzene diazonium species or phenol/azobenzene products derived therefrom. We conducted a trapping experiment with resorcinol because it can serve a dual role as a radical scavenger and a trap for the benzene diazonium species that could be formed. In the event, we added an excess of resorcinol to a pH 9 borate-buffered solution of **1** and irradiated the mixture with light (Scheme S2). Gratifyingly, the known azobenzene, Sudan Orange G, was formed in a 65% yield (versus 4% for the non-irradiated reaction).¹³

We observed that non-buffered solutions became basic upon exposure to light in a time-dependent manner. This increase in pH correlated with the appearance of **2**, which is mildly basic.

Received: April 27, 2015

Published: July 27, 2015

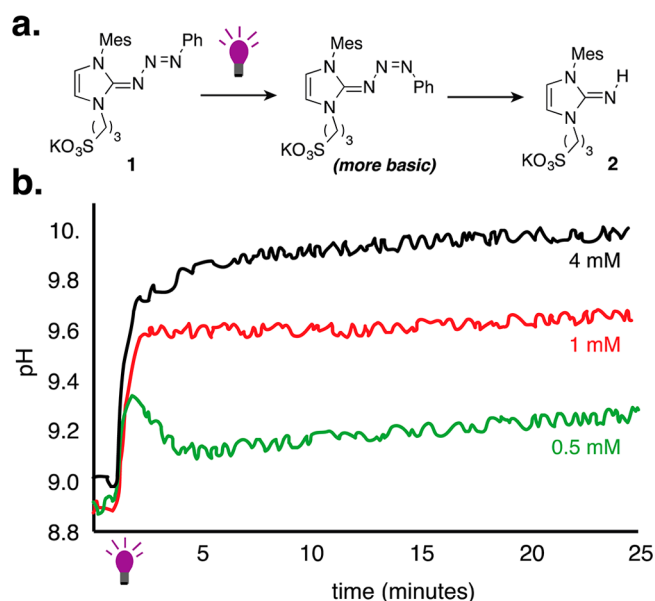


Figure 2. (a) Compound **1** is rendered more basic upon exposure to light. (b) Constant UV irradiation of dilute solutions shows a quick spike in pH (presumably from **1-Z**) followed by a leveling off resulting from complete conversion of **1** to **2**.

To assess the basicity of **1-Z**, a non-buffered solution of water was irradiated with light while the pH was monitored in real-time. Compound **1** was dissolved in water, and the pH was adjusted to ~ 9 to prevent the formation of **2** in the absence of light. Upon exposure to 350 nm light, the solution rapidly spiked up to a pH of 9.8 over the course of several minutes; upon longer exposure, it slowly became more basic (black line, Figure 2b). At a low concentration of **1**, these spikes were followed by a decrease in pH (green line). These data suggest that **1-Z** is more basic than **2**, a fact that is corroborated by the finding that **1** is able to deprotonate water absent of hydronium ions.¹⁴ Once the more basic **Z** isomer is formed, it can go on to form **2** or revert to **1**. Assuming that 10% of **1** is isomerized in the first 30 s of irradiation¹⁵ and that **1** is completely consumed at 25 min, the relative pK_b values of **1-Z** and **2** in water were found to be 5.1 and 6.0, respectively (see the Supporting Information for the calculations).

In spite of the jump in pH suggesting its existence, **1-Z** remained uncharacterized by NMR in water, even at low temperatures. Attributing this to a low steady-state concentration of **1-Z** that both decomposes and thermally reverts the inability to directly observe the elusive **1-Z** in water prompted a swapping of solvents to DMSO. As noted previously, **1** is quite stable to an excess of acetic acid in DMSO,¹⁰ showing only 12% degradation to **2** over 14 h at room temperature. Upon irradiation with light, **1** was completely converted to **2** over the same time frame. Gratifyingly, irradiation of **1** in acid-free DMSO for ~ 2 h provided a mixture of two compounds, the starting material and what appeared to be its isomer (**1-E** and **1-Z**, respectively). Moreover, unlike what we assumed was occurring in water, the thermal reversion from **Z** to **E** in pure DMSO is slow, with a half-life on the order of days. This long half-life enabled NOESY experiments that delivered a clear picture of the identity and conformation of the two isomers (Figures 3 and S1). To bolster our contention that the new species in DMSO was the phantom **Z**-isomer, AcOH was added to a 70:30 (**E:Z**) mixture in the absence of light, and within 2

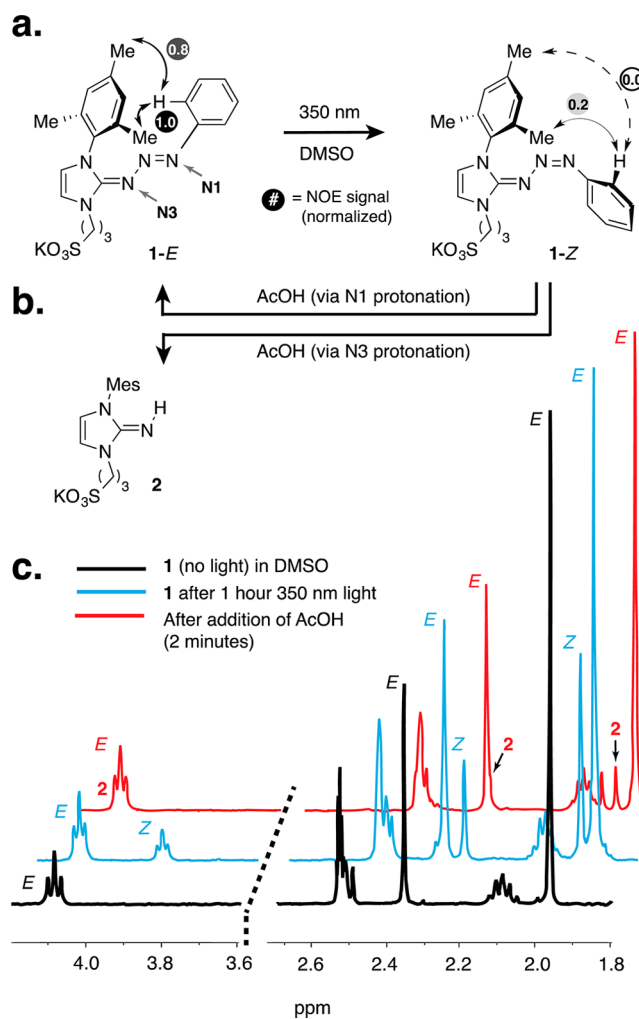


Figure 3. (a) Compound **1** in DMSO was irradiated with UV light for 1.75 h and analyzed by NOESY. Signals were normalized to the strongest NOE observed (numbers in circles) taking into consideration relative concentrations of **E** and **Z**. (b,c) A solution of **1** in DMSO (black spectrum) was treated with UV light for 1 h and analyzed by NMR (blue spectrum). The solution was treated with 10 equiv of AcOH, and an NMR spectrum was collected after 2 min (red spectrum). The **Z** isomer was consumed within this time.

min the **Z** isomer was gone (Figure 3b,c). The speed of its disappearance was remarkable, and all that remained was a mixture of the **E** isomer and newly formed **2** in a 92:8 ratio. We draw from this two conclusions: (1) **1-Z** is significantly more basic than **1-E**, and (2) the differentially basic **N1** and **N3** nitrogen atoms provide two pathways of reaction for **1-Z**, and proton-catalyzed reversion to **1-E** (likely from **N1**-protonation) is dominant.¹⁶ Indeed Fanghänel had previously reported that an **N1** alkylated triazabutadiene was able to isomerize thermally.¹⁷

To the best of our knowledge, this phenomenon of an isomerization-induced pK_b change has escaped the eyes of watchful chemists, as it almost did ours. Unlike the case where Hecht's compound is rendered basic upon irradiation by way of moving a steric wall (Figure 1b),⁸ it is unlikely that steric factors play a significant role in our chemistry, especially in water. Our current rationale for this effect is that the **E** isomer has a stable conjugated π -system with alternating non- π -involved lone pairs of electrons,^{18,19} whereas the **Z** isomer lacks

these features and has a higher energy HOMO. This higher energy HOMO stems from a break in the conjugation between the phenyl ring and the nitrogen π -system of the *Z* isomer (consistent with NOE data, Figure 3a, and diminution of UV-vis spectrum compared with the *E* isomer, Figure S3) and repulsion between the two adjacent lone pairs of electrons on the N1–N2 nitrogen atoms. These factors render the N1-nitrogen atom more electron rich than in the *E* isomer, and thus more basic. This model is bolstered by ^{15}N NMR data collected on the same general class of compounds in the early 1980s.^{20–22} These studies observed a significant upfield shift in the N1-nitrogen signal with a minimal effect on the N3-nitrogen upon examination of the *E* vs *Z* isomer. Data from the same study suggest that a similar effect is true of simple azobenzenes, but these compounds are generally so much less basic than **1**²³ that the switching occurs in a less synthetically useful or observable range. This hypothesis is corroborated by derivatives of **1** with electron-withdrawing groups that were synthesized and irradiated with light in a buffered solution (Figure S4). Whereas these compounds decomposed to form **2**, when tested in pure water an initial rapid spike in pH was not observed, but simply a slow increase due to **2** forming.

Seeing the potential utility of **1** as a photocatalytic²⁴ base in the context of organic reactions, we desired to test its ability to catalyze a simple condensation reaction. Due to the limited organic solubility of **1**, we synthesized **3**, a compound previously reported by Bielawski (Figure 4a).²⁵ With **3** we noted similar light-induced acid sensitivity in DMSO and slow thermal isomerization. As such, we used what we had learned

from **1** to select a proof-of-concept reaction. Based on the apparent $\text{p}K_{\text{b}}$ of **3**,²⁶ we matched $\text{p}K_{\text{a}}$ values to condensation substrates. A Henry reaction between nitroethane (**4**) and *p*-nitrobenzaldehyde (**5**) was chosen to demonstrate the virtues of **3** (Figure 4b).²⁷ Indeed, the reaction between **4** and **5** occurred rapidly at room temperature in a light- and catalyst-dependent manner (Figure 4c). The reaction with 25 mol% **3** in the absence of light was exceedingly slow. Likewise, the reaction with light but no catalyst also failed to proceed (Figure S5). The cyclic guanidine was not observed during a post-reaction analysis of the components from a 25 mol% **3** run, indicating that the *Z*-isomer of **3** is likely to be the catalytically active species in solution.²⁸ Worried that a trace of cyclic guanidine could catalyze the reaction, we treated a mixture of **4** and **5** with 1% guanidine and found that it did indeed catalyze the reaction to near completion with 3 h (Figure S5). In order to discriminate between *Z*-**3** and guanidine as the relevant catalyst that we were observing, we ran a reaction with light and turned it off once the slope matched that of the guanidine-catalyzed reaction. True to our model, the reaction slowed and stopped, presumably as *Z*-**3** became protonated and thermally isomerized (Figure S5). Interestingly, the reaction photocatalyzed with **3** was significantly faster than the same reaction reported by Hecht.⁸

In closing, we have reported a remarkable transformation whereby a molecule is rendered basic upon photoisomerization. Steric arguments cannot be employed to explain the dramatic change, but instead loss of conjugation in a π -system and coplanar lone pairs of electrons on adjacent nitrogen atoms appear to be the key differences. These findings are guiding ongoing divergent efforts in our research to (1) better control the release of diazonium species and (2) design a photobase with long-term stability. The operational ease by which these compounds are rendered basic should allow them to find their way into other applications. Furthermore, we hope that these findings will promote a better understanding of factors that should be assessed when examining Lewis basicity and will inspire researchers in the area of catalysis, both organic and organometallic.

■ ASSOCIATED CONTENT

📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b04367.

Synthesis and characterization of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Profs. Richard Glass, Jon Njardarson, Elisa Tomat, Michael Heien, and Jeffrey Pyun for fruitful discussions regarding this work, Drs. Neil Jacobsen and Jixun Dai for assistance with analysis of NMR data, and the NSF for a generous departmental instrumentation grant for the NMR facility (CHE-0840336). We also thank Dr. Kevin Bao for assistance with UV-LED array design and development, and the general chemistry laboratories at the University of Arizona for use of their pH meter. This work was funded in part by an ACS

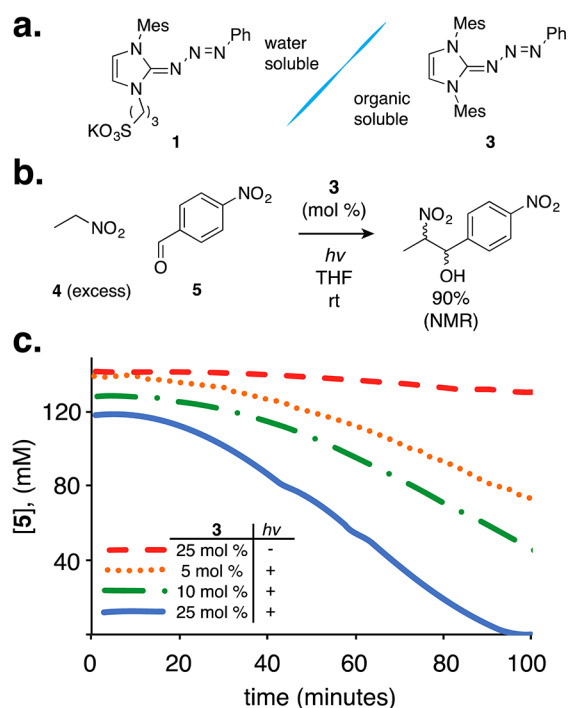


Figure 4. Using the photobase as a catalyst. (a) Structures of water-soluble **1** versus organic-soluble **3**. (b) The Henry reaction between **4** and **5** was carried out at room temperature and with varying amounts of catalyst. (c) The reactions were monitored by a ReactIR (Mettler Toledo) in situ spectroscopy system, following consumption of aldehyde **5**. Red line = 25 mol% **3** with no light. Orange line = 5 mol% **3** + light. Green line = 10 mol% **3** + light. Blue line = 25 mol% **3** + light.

PRF grant to J.C.J. and start-up funds provided by the Arizona Board of Regents to J.C.J.

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- (12) We have since made a home-built UV-LED system for more controlled irradiation. The device is described in the [Supporting Information](#).
- (13) This yield is similar to that for the non-irradiated reaction carried out in a pH 6 buffer.
- (14) Indeed, compound **1** decomposed in the presence of 1.0 N NaOH upon exposure to light.
- (15) A conservative estimate based on 8% isomer observed after irradiating a solution in DMSO for 1 min and analyzing by NMR.
- (16) In aqueous solutions we observed a drop in pH upon turning off the UV light. This effect was amplified with the addition of copper sulfate, presumably acting as a Lewis acid ([Figure S2](#)).
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- (26) **Z-1** is able to deprotonate AcOH in DMSO, so it can remove protons from substrates of at least $pK_a = 12.6$.
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- (28) If **3** is exposed to light for prolonged times (>4 h), degradation is observed.