Photoswitches

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An Isolable, Photoswitchable N-Heterocyclic Carbene: On-Demand Reversible Ammonia Activation

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Abstract: *The first isolable, photoswitchable N-heterocyclic carbene was synthesized and found to undergo reversible electrocyclic isomerization upon successive exposure to UV and visible radiation. The UV-induced ring closure afforded substantial changes to the electronic structure of the dithienylethene-based NHC, as evidenced by changes in the corresponding UV/Vis absorption and ^{13}C NMR spectra. Likewise, molecular orbital calculations revealed diminished electron density at the carbene nucleus upon photocyclization, consistent with the enhanced electrophilicity displayed by the ring-closed form. The photoswitchable NHC was successfully switched between its ring-opened and ring-closed states with high fidelity over multiple cycles. Furthermore, the ring-closed isomer was found to undergo facile N−H bond activation, allowing for the controlled capture and release of ammonia upon cycling between its isomeric states.*

The ability to remotely modulate the outcome of chemical reactions constitutes a powerful and convenient means to achieve enhanced control and selectivity. Light represents an attractive external stimulus for such purposes as it is non-invasive, offers excellent spatial and temporal resolution, and can be precisely tuned through the judicious selection of radiation wavelength and power. Furthermore, the ability to discriminate amongst specific wavelengths of light allows for selective excitation, minimizing inadvertent side reactions from ostensible spectator species. As such, the introduction of light-responsive functional groups into known catalysts may enable the toggling between multiple catalytically active states and thus an ability to switch the intrinsic activity and/or selectivity on demand over the course of a chemical reaction.[1]

An attractive class of substrates for incorporating light-responsive groups are the N-heterocyclic carbenes (NHCs) as they have been used in a broad range of organometallic and organocatalysts.[2] As the activities and selectivities displayed by such catalysts are intrinsically linked to the electronic properties of the NHCs, the structural modulation of such moieties has been intensely pursued.[3] We recently developed a photoswitchable NHC by incorporating a photochromic[4] dithienylethene (DTE)[5] unit into an imidazolylidene backbone, and found that the corresponding carbene functioned as a photoswitchable organocatalyst for transesterification and transamidation[6] reactions as well as for ring-opening polymerizations.[7] Similarly, a Rh catalyst bearing the same NHC was found to catalyze hydroborations.[8] All of these catalysts were effectively switched between "off" (inactive) and "on" (active) states by irradiation with UV or visible light, respectively. Although other DTE-functionalized NHCs have been reported,[9] the corresponding free carbenes have hitherto not been isolable and required in situ generation. We envisioned introducing steric bulk about the photoswitchable carbene center to facilitate its isolation and to gain insight into the effects of the photoisomerization processes. Access to isolable, photoswitchable NHCs may also facilitate the selective, reversible activation of small molecules (e.g., NH_3, H_2, CO) in a controlled manner.[10] Herein, we report the first isolable, photoswitchable NHC and demonstrate the remote modulation of its electronic properties in the free carbene state as well as its utility in the on-demand capture and release of ammonia.

As shown in Scheme 1, the synthesis of an NHC precursor bearing *N*- and *N'*-mesityl groups, **1**-HCl, was achieved in three steps from known acyloin **2**.[6,11] Oxidation of **2** with 2-iodoxybenzoic acid (IBX) afforded diketone **3**,[6] which was condensed with 2,4,6-trimethylaniline to afford diazabutadiene **4**.[12] Acid-catalyzed formylative cyclization of **4** with $(CH_2O)_n$ afforded **1**-HCl, as evidenced in part by the appearance of the diagnostic imidazolium ^1H NMR signal at $\delta = 11.8$ ppm ($CDCl_3$). Exposure of **1**-HCl to AgOTf afforded **1**-HOTf as a crystalline solid (see the Supporting Information).

Treatment of **1**-HCl with sodium hexamethyldisilazide (NaHMDS) in C_6H_6 followed by solvent removal and trituration with *n*-pentane afforded the corresponding free NHC **1o**, as evidenced by the absence of the aforementioned imidazolium ^1H NMR signal and the observation of a new ^{13}C NMR resonance at $\delta = 219.4$ ppm (C_6D_6), which was assigned to the newly formed carbene nucleus. Single crystals suitable for X-ray diffraction were obtained by slowly

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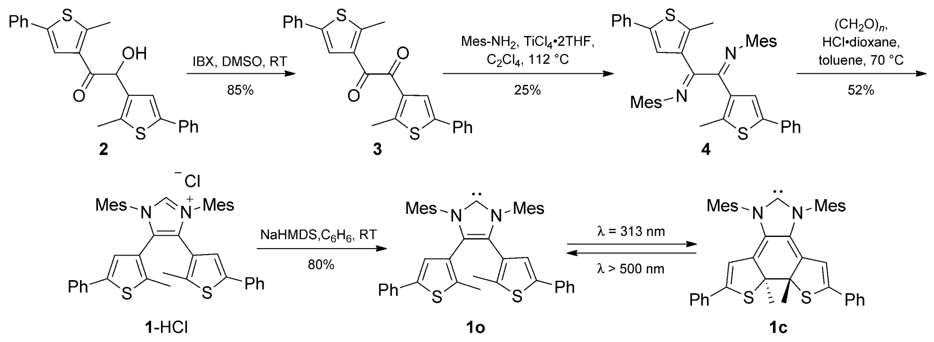


Scheme 1. Synthesis and photochromism of **1o**.

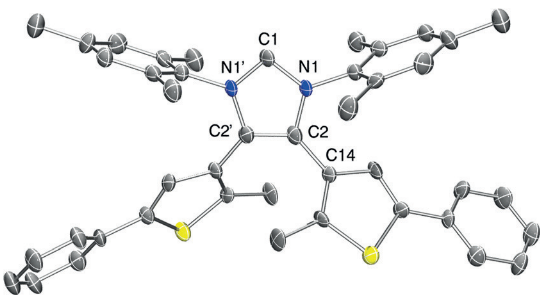


Figure 1. POV-ray representation of **1o**; ellipsoids set at 50% probability. Solvent molecules and H atoms were omitted for clarity. Selected distances (Å) and angles (°): C1–N1 1.369(7), N1–C2 1.410(8), C2–C2′ 1.370(12), C2–C14 1.460(8); N1-C1-N1′ 100.5(7), C1-N1-C2 114.6(5), C2′-C2-N1 105.1(3), N1-C2-C14 123.7(5), C2′-C2-C14 131.0(3).

evaporating a concentrated solution of **1o** in Et_2O and used to confirm the structural assignment (Figure 1). Under an atmosphere of dry nitrogen, **1o** was found to be stable in solution over the course of several weeks or in the solid state for months.

The UV/Vis spectrum recorded for a solution of **1o** in benzene exhibited an intense absorption band centered at 293 nm, which was assigned to a combination of the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions of the N-heterocycle and thiophene systems, respectively. Exposure of a C_6H_6 solution of **1o** ($[\mathbf{1o}]_0 = 3.5 \times 10^{-5}$ M) to UV radiation ($\lambda_{Irr} = 313$ nm) resulted in a color change from pale yellow to deep purple (see the Supporting Information). In agreement with the formation of an extended π-conjugated system, the change in color was accompanied by a decrease in the intensity of the absorption band centered at 293 nm and the appearance of a new band centered at 574 nm (Figure 2).[13] Furthermore, an isosbestic point was observed at 328 nm, which indicated that the photoisomerization proceeded without appreciable side product formation. The spectral changes subsided as the photostationary state (PSS) was reached after 60 s of UV irradiation and were calculated to reflect a 54% conversion[14–16] of **1o** into **1c**. Subsequent visible-light irradiation ($\lambda_{Irr} > 500$ nm) resulted in attenuation of the broad low-energy absorption bands and decoloration of the solution. The UV/Vis spectrum of **1o** was 95% restored after 360 s of irradiation with visible light, which was consistent with reversion of **1c** into the ring-opened isomer **1o**.[17] To probe the fatigue resistance of **1**, a sample was cyclically exposed to UV and visible radiation. As shown in Figure 2c, minimal variation (ca. 10%) was observed upon interconverting between the ring-opened and ring-closed states over multiple cycles.

Having demonstrated the reversible photoisomerization of **1o**, the effects of the process were further quantified by ^{13}C NMR spectroscopy, as the aforementioned changes in electron density at the carbene center should result in a modulation of its chemical shift. To facilitate these studies, an analogue of **1o** that contained an isotopically labeled ^{13}C atom at the C2 position ([^{13}C]-**1o**) was synthesized by an analogous route to that employed for **1o**, with the exception that ($^{13}CH_2O)_n$ was used in the formylative cyclization step; [^{13}C]-**1o** displayed a ^{13}C NMR resonance at $\delta = 219.5$ ppm (C_6D_6).

Exposure of a C_6D_6 solution of [^{13}C]-**1o** ($[[^{13}\mathrm{C}]\text{-}\mathbf{1o}]_0 = 1.0 \times 10^{-3}$ M) to UV light ($\lambda_{Irr} = 313$ nm) for 60 min produced

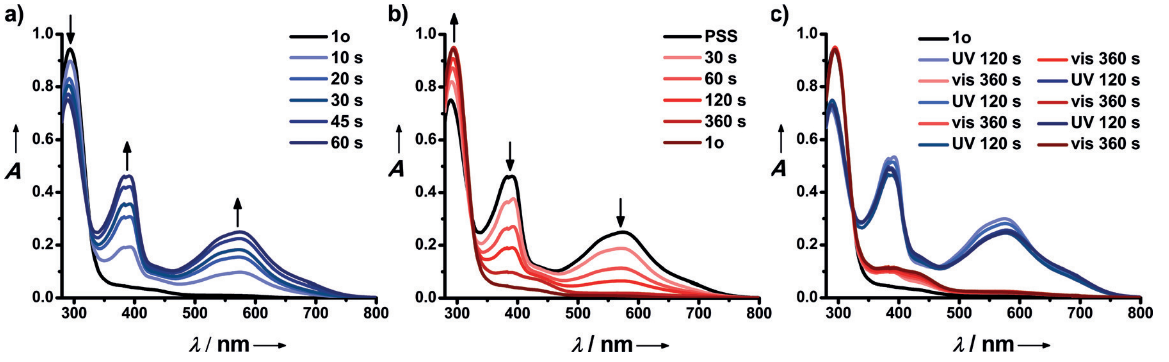


Figure 2. a) UV/Vis spectral changes of **1o** in C_6H_6 upon UV irradiation ($\lambda_{Irr} = 313$ nm). b) UV/Vis spectrum of the photostationary state (PSS) reached after UV irradiation of **1o** for 60 s, and spectral changes of the PSS over time upon visible-light irradiation ($\lambda_{Irr} > 500$ nm). The arrows point to the evolution of spectral changes over time ($[\mathbf{1o}]_0 = 3.5 \times 10^{-5}$ M). c) UV/Vis spectral changes of **1o** in C_6H_6 ($[\mathbf{1o}]_0 = 3.5 \times 10^{-5}$ M) upon successive UV ($\lambda_{Irr} = 313$ nm) and visible-light ($\lambda_{Irr} > 500$ nm) irradiation. The spectra were recorded after 120 s and 360 s, respectively (indicated).

a color change analogous to that observed with **1o**, indicative of photoisomerization to [^{13}C]-**1c**. The cyclization was later confirmed by ^{1}H NMR analysis of the concentrated product mixture, which showed the expected upfield shifts of the proton signals corresponding to the phenyl and thiophene rings and a downfield shift of the signals assigned to the protons associated with the mesityl rings. Integration of the respective signals revealed that 82 % of [^{13}C]-**1o** had been converted into [^{13}C]-**1c** upon photocyclization (see the Supporting Information). Moreover, as shown in Figure 3, ^{13}C NMR analysis revealed a substantial downfield shift of the resonance that corresponded to the carbene nucleus, from $\delta =$ 219.5 ppm to 243.5 ppm upon conversion of [^{13}C]-**1o** into [^{13}C]-**1c**, indicative of the formation of a more electron-deficient NHC. For comparison, the well-known NHC 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes) and its saturated analogue (SIMes) exhibit ^{13}C NMR resonances at $\delta = 219.7$ and 243.8 ppm (C_6D_6), respectively.[18] Subsequent exposure of the UV-irradiated solution to visible light ($\lambda_{Irr} >$ 500 nm) decolorized the solution, consistent with cycloreversion into [^{13}C]-**1o**. The ^{1}H NMR spectrum of the sample irradiated with visible light matched the spectrum of [^{13}C]-**1o** and signified the cycloreversion of [^{13}C]-**1c** into [^{13}C]-**1o**. Similarly, ^{13}C NMR analysis showed the disappearance of the resonance at 243.5 ppm and the growth of an upfield resonance at 219.3 ppm.[19]

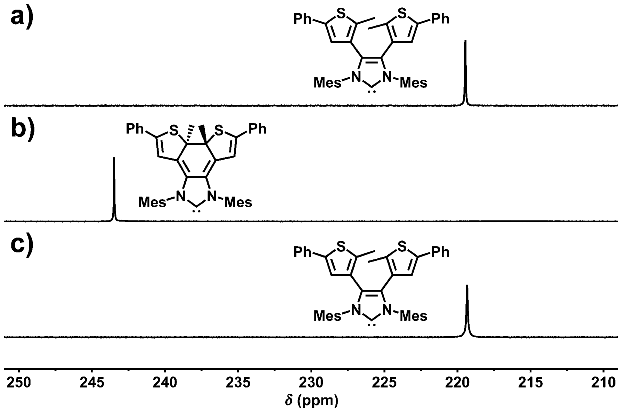


Figure 3. ^{13}C NMR spectra recorded in C_6D_6 over the course of the following experiment: A sample of a) [^{13}C]-**1o** isotopically labeled at the C2 position b) was exposed to UV radiation for 60 min ($\lambda_{Irr} = 313$ nm, $[[^{13}C]\text{-}\mathbf{1o}]_0 = 1.0 \times 10^{-3}$ M), and c) subsequently exposed to visible radiation for 3 h ($\lambda_{Irr} > 500$ nm).

To clarify the electronic structure differences between **1o** and **1c**, a series of molecular orbital calculations were performed. Considering the extended conjugated backbone of **1c**, we expected less electron density to be localized at the carbene nucleus than in the ring-opened isomer **1o**. Indeed, the former was found to display a significantly smaller HOMO coefficient at the carbene center along with a significantly larger LUMO coefficient, as compared to **1o** (Figure 4). The smaller HOMO and larger LUMO coefficients of the ring-closed form were in accordance with its decreased donating ability as compared to its ring-opened isomer.[19] Moreover, the calculated ^{13}C NMR resonances of the carbene nuclei for **1o** (225 ppm) and **1c** (245 ppm) were in good agreement with the experimental values, validating the computational method employed.

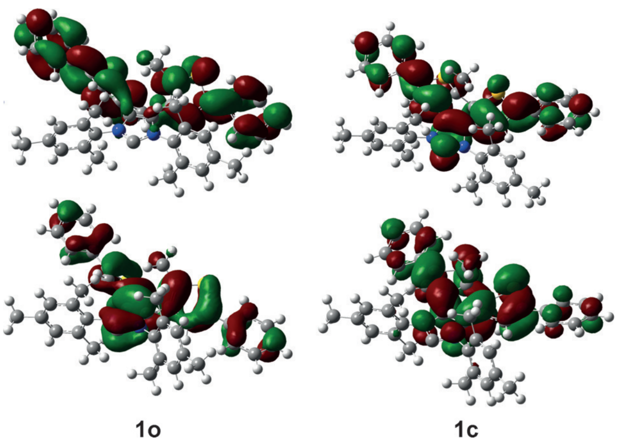
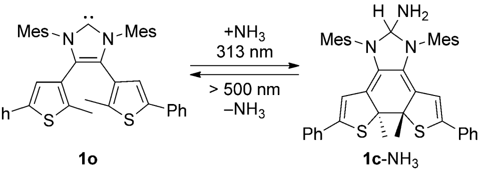


Figure 4. HOMO (bottom) and LUMO (top) of **1o** and **1c**.

To ascertain how the modular electronic structure of **1** influences its intrinsic chemical reactivity, we explored the capture of ammonia with **1o** and **1c**. The activation of NH_3 remains an important yet challenging synthetic endeavor due to the relatively high basicity[20] of the compound (p$K_a = 38$) and N−H bond strength[21] (107 kcal mol^{-1}); indeed, few isolable carbenes are known to activate NH_3.[10] The addition of gaseous NH_3 to a C_6D_6 solution of **1o** produced no noticeable change, as determined by ^{1}H NMR spectroscopy. In contrast, exposure of NH_3(g) to a C_6D_6 solution of **1c** resulted in an immediate color change from deep blue ($\lambda_{max} =$ 574 nm) to dark purple ($\lambda_{max} = 547$ nm), concomitant with the appearance of new ^{1}H NMR signals at $\delta = 5.68$ ppm (t, CH) and 1.28 ppm (d, NH_2) and consistent with the formation of **1c**-NH_3 (Scheme 2).[10]



Scheme 2. Photoswitchable ammonia activation.

Building on these results, we reasoned that the capture and subsequent release of NH_3 over the course of a single experiment should be possible by utilizing the distinct electronic states of **1**. To test this hypothesis, a C_6D_6 solution of **1o** was transferred to a quartz low-pressure NMR tube equipped with a Teflon screw cap and cooled to −78 °C. The tube was then evacuated and the atmosphere was replaced with NH_3 upon warming to ambient temperature. After confirming that no reaction was observed by ^{1}H NMR spectroscopy, the sample was subjected to UV radiation ($\lambda_{Irr} = 313$ nm) for 30 min, which resulted in a color change

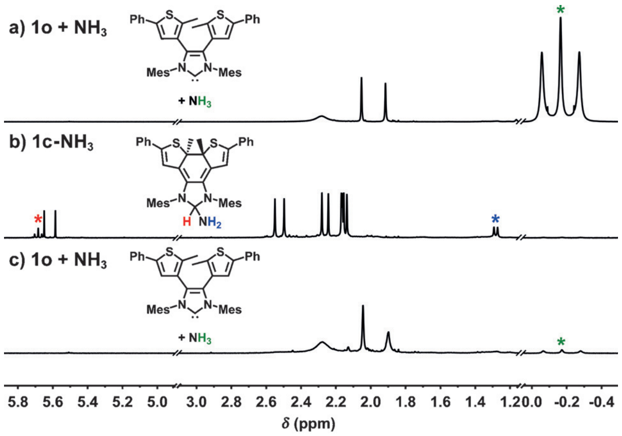


Figure 5. ^{1}H NMR spectra recorded in C_6D_6 over the course of the following experiment: A sample of a) **1o** under an atmosphere of ammonia b) was exposed to UV radiation for 30 min ($\lambda_{Irr} = 313$ nm, $[\mathbf{1o}]_0 = 2.0 \times 10^{-3}$ M), and c) subsequently exposed to visible radiation for 100 min ($\lambda_{Irr} > 500$ nm).

from pale yellow to dark purple. As shown in Figure 5, the ^{1}H NMR spectrum recorded after the excess ammonia had been removed from the reaction mixture matched that previously observed for **1c**-NH$_3$. Subsequent visible-light irradiation ($\lambda_{Irr} > 500$ nm) for 100 min followed by ^{1}H NMR analysis resulted in a spectrum similar to that expected for **1o** along with a new signal at $\delta = -0.17$ ppm (t, 3H), which was attributed to liberated NH$_3$.[22] The presence of NH$_3$ was confirmed by high-resolution mass spectrometry of the reaction-mixture headspace (see the Supporting Information).

In summary, we have developed the first isolable, photoswitchable NHC. The free NHC **1o** was found to undergo photoinduced electrocyclization to its ring-closed isomer **1c** upon exposure to UV light, as evidenced by UV/Vis and NMR spectroscopy. The free NHC **1c** exhibited a substantially different electronic structure, including a more electron-deficient carbene nucleus than **1o**, as revealed by its downfield-shifted ^{13}C NMR resonance ($\Delta\delta = +24$ ppm). Subsequent exposure to visible light restored the electronic structure of the ring-opened NHC. Molecular orbital calculations supported a shift in electron density away from the carbene center upon ring closure, revealing a significantly more electrophilic NHC. Finally, the distinct electronic states of **1o** and **1c** enabled the capture and subsequent release of ammonia over the course of a single experiment. The on-demand N–H bond activation constitutes the first example of its kind and was demonstrated with an unprecedented degree of control (i.e., the process was not mediated by a chemical equilibrium). Given the ubiquity of NHCs, access to an isolable, photoswitchable derivative coupled with the facile tuning of its electronic structure using light is expected to drive the design and development of photoswitchable transformations.

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