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Photoinduced Storage and Thermal Release of Singlet Oxygen from 1,2-Dihydropyridine Endoperoxides

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Supporting information for this article is given via a link at the end of the document.

Abstract: The quest for molecules able to trap, store and release singlet oxygen is of utmost interest due to their applicability in various domains such as materials science and photomedicine. The aim of this study was to prepare and to study a new family of singlet oxygen donors based on the 1,2-dihydropyridine motif. The experiments demonstrated the influence of substituents and solvents on the photooxygenation rate constants. The process can be operated reversibly by thermolysis of the *in-situ* formed endoperoxide leading to a release of singlet oxygen and formation of the parent 1,2-dihydropyridine compound. A bifunctional structure based on a phenalenone photosensitizer covalently connected to a 1,2-dihydropyridine module was synthesized *via* a multi-step sequence. Upon irradiation with blue light, singlet oxygen was produced leading to the formation of the endoperoxide intermediate. In the dark cycle, the endoperoxide underwent cycloreversion reaction affording the parent 1,2-dihydropyridine unit paving the way to a continuous production of singlet oxygen during the light/dark cycles.

Introduction

In the past decades, singlet oxygen ($^1\text{O}_2$) – that is the lowest excited state of molecular oxygen – has attracted considerable attention by the scientific community.^[1] The electrophilicity and oxidizing power of singlet oxygen have been harnessed in various fields such as photodynamic therapy,^[2] materials science,^[3] and synthetic chemistry.^[4] The most common strategy to produce singlet oxygen lies in the combination of a photosensitizer, light and oxygen (type II photooxygenation).^[5] This approach involves triplet-triplet energy transfer between the excited photosensitizer and ground state oxygen. Despite many advantages offered by the photosensitization of oxygen molecules, the limitations inherent to this strategy have prompted the researchers to consider other alternatives. Side reactions induced by light irradiation or the opacity of the reaction medium are situations for which photooxygenation could be an inappropriate method. In addition, the delivery of a precise amount of singlet oxygen to the chemical or biological target is an arduous task in photooxygenation. Within this context, the chemical or thermal release of singlet oxygen from endoperoxides is an appealing alternative to photooxygenation.^[6] This strategy is based upon the release of singlet oxygen from endoperoxides derived from cycloaddition of singlet oxygen to dienes, arenes, or heteroarenes (Scheme 1). In 1967, Wasserman and Scheffer shared the first report highlighting the generation of singlet oxygen through thermolysis of 9,10-diphenylanthracene endoperoxide and further reaction

with singlet oxygen acceptors.^[7] Building from this seminal work, further research has identified relevant polycyclic aromatic hydrocarbons which can undergo addition of singlet oxygen at room temperature or below to form stable endoperoxides which can regenerate singlet oxygen upon thermolysis or chemical activation.^[8] For instance, anthracenes,^[9] naphthalenes^[9a,10] or other acenes^[9h,11] are efficient singlet oxygen traps (Scheme 1). The *dark* generation of singlet oxygen through the decomposition of endoperoxides derived from acenes has found applications in materials science,^[2b,d,12] switchable organic cages^[13] or photodynamic therapy.^[14] Heterocyclic architectures have received less attention as reversible sources of singlet oxygen compared to polycyclic aromatic hydrocarbons owing to the low stability of the corresponding endoperoxides.^[15] Nevertheless, endoperoxides derived from *N*-substituted 2-pyridones have emerged as a privileged chemical source of singlet oxygen due to their ease of synthesis *via* photooxygenation, relative stability, modularity and their ability to release singlet oxygen under biocompatible conditions.^[16] Therefore, the 2-pyridone motif has been connected to various photosensitizers enabling a photochemical and chemical generation of singlet oxygen for the destruction of cancer cells.^[17] While major advancements have been made in developing endoperoxides derived from acenes, examples of heterocyclic structures as chemical sources of singlet oxygen remain scarce in literature.^[16-18] Within this context, the current work aims at developing a new family of heterocyclic architectures able to trap, store and release $^1\text{O}_2$ (Scheme 1).

Scheme 1. Capture and release of singlet oxygen from acenes and heterocycles.

The 1,2-dihydropyridine motif is known to react with singlet oxygen furnishing a reactive endoperoxide intermediate prone to undergo regio- and stereoselective ring-opening transformations with various nucleophiles.^[19] For instance, indoles, pyrroles, enol

ethers or sodium cyanoborohydride in the presence of stannous chloride have been used as nucleophiles to produce the corresponding functionalized nitrogen-containing heterocycles. It is recognized that electron withdrawing groups stabilize endoperoxides derived from 2-pyridones^[16a] and we surmised that the introduction of such substituents on the 1,2-dihydropyridine core could lead to more stable endoperoxide structures for further application in *dark photooxygenation*.^[20] Here, we show that easily prepared 1,2-dihydropyridines bearing a dicyanomethylene group at the 2-position can react reversibly with singlet oxygen to generate the corresponding endoperoxides as new chemical sources of singlet oxygen.

Results and Discussion

With the aim of developing a straightforward synthetic route while introducing electron withdrawing groups on the 1,2-dihydropyridine units, the formation of C-C bonds at the 2-position of pyridinium salts have been investigated at the pivotal step of our strategy (Scheme 2). Different electron withdrawing groups have been introduced to study their influence on the photooxygenation rate and the endoperoxide stability.

Scheme 2. Synthetic routes towards 1,2-dihydropyridine compounds **1-5**. Reaction conditions: a) NaH (1.2 equiv.), THF, Ar, r.t., 4 h; b) Bis-(toluene-4-sulfonyl)methane (1.2 equiv.), NaH (1.2 equiv.), THF, Ar, 0 °C to r.t., 18 h; c) Dimethylmalonate (1.2 equiv. for the preparation of **4**) or malononitrile (1.2 equiv. for the preparation of **5**), THF, Ar, 0 °C to r.t., 2 h.

The desired 1,2-dihydropyridines **1-5** were readily synthesized starting from commercially or readily available 2-substituted 1-methylpyridinium iodide derivatives following two synthetic approaches. Under basic conditions, the 1,2-dihydropyridines **1** and **2** bearing only one electron withdrawing group were selectively obtained in 90% and 99% yields, respectively. The reaction of 2-chloro-1-methylpyridinium iodide with the corresponding activated methylene reagents in the presence of sodium hydride afforded the heterocycles **3-5** in good-to-excellent yields after chromatography on silica gel.

Having prepared the compounds **1-5**, we examined their reactivity towards photosensitized singlet oxygen (Scheme 3). The photooxygenation of **1-5** was carried out under oxygen atmosphere in the presence of a catalytic amount of a diiodo-BODIPY photocatalyst which is an efficient triplet sensitizer.^[21]

Scheme 3. Photooxygenation of **1-5**.

Unfortunately, the photooxidation of heterocycles **1-4** led to complex reaction mixtures and in spite of extensive efforts, no traces of the desired endoperoxides were detected in the crude. Starting from the nitrile derivative **5**, we were pleased to observe the formation of **5-O₂** by photooxygenation with a conversion of 95% determined by ¹H NMR. Full analyses were carried out to confirm the structure of **5-O₂** (see supporting information for details). The endoperoxide turned out to be stable in solution but attempts to isolate **5-O₂** by column chromatography (stationary phase: silica or alumina) or crystallization were unsuccessful. It is known from literature that 2-pyridone substitution has a profound impact on the endoperoxide stability^[16b] and we investigated the preparation of methyl analogues of **5** in order to study the influence of methyl substituents borne by the heterocycle on the capture and release of singlet oxygen (Scheme 4).^[22]

Scheme 4. Preparation of 1,2-dihydropyridines **6-9**.

The compounds **6-9** were prepared following a two-step synthetic route. Alkylation of 2-chloropyridine derivatives with methyl iodide followed by reaction with malononitrile in the presence of sodium hydride afforded the structures **6-9** after chromatography on silica gel. The compounds **7-9** were obtained in good yields over two steps whereas the 1,2-dihydropyridine **6** was isolated in only 10% yield. This disappointing result could be explained by the weak reactivity of 2-chloro-6-methylpyridine towards *N*-methylation likely due to steric constraints imposed by the methyl group at 6-position. In order to shed the light on the reactivity of these heterocycles towards singlet oxygen, a series of photooxygenation

experiments were carried out at 23 °C under green light irradiation in different solvents (Table 1).

Table 1. Photooxygenation of heterocycles **5-9** and *N*-methyl 2-pyridone **10**.^[a]

<div style="display: flex; align-items: center; justify-content: center;"> <div style="margin-right: 20px;"> <p>5, R = H, X = C(CN)₂</p> <p>6, R = 6-Me, X = C(CN)₂</p> <p>7, R = 5-Me, X = C(CN)₂</p> <p>8, R = 4-Me, X = C(CN)₂</p> <p>9, R = 3-Me, X = C(CN)₂</p> <p>10, R = H, X = O</p> </div> <div style="text-align: center;"> </div> </div>							
Entry	Trap	Time (min), CDCl ₃ ^[b]	Time (min), DCE ^[b]	Time (min), MeCN ^[b]	<i>k</i> _{rel} (CDCl ₃) ^[c]	<i>k</i> _{rel} (DCE) ^[c]	<i>k</i> _{rel} (MeCN) ^[c]
1	5	90	600	480	1.00±0.07, [1.0] ^[d]	1.00±0.11	1.0±0.05
2	6	30	120	75	3.62±0.06	8.64±0.49	6.59±0.37
3	7	15	90	45	7.58±0.08, [8.5] ^[d]	14.89±0.86	12.69±0.67
4	8	— ^[e]	— ^[e]	— ^[e]	— ^[e]	— ^[e]	— ^[e]
5	9	90	420	480	1.05±0.02	1.74±0.24	1.31 ± 0.14
6	10	20	n.d.	n.d.	[5.4] ^[d]	n.d.	n.d.

[a] Experimental procedure: **5-10** (55 μmol), sensitizer (2.75 μmol), solvent (10 mL), O₂, Green LEDs (1.9 mW.cm⁻², 535 nm), 23 °C. The kinetics were performed three times for each substance. [b] Time until complete conversion into the corresponding endoperoxide. The photooxygenations were run in different solvents (CDCl₃, 1,2-dichloroethane and MeCN). n.d., non determined. [c] Relative rate constants determined by UV-Visible spectroscopy. See supporting information for further details. [d] Relative rate constants determined by ¹H NMR in CDCl₃. [e] Endoperoxide **8-O₂** was not stable leading to the formation of by-products.

The kinetic experiments were performed by UV-Visible spectroscopy with the disappearance of the absorption band at 385-407 nm for **5-9** (Figure 1).

Figure 1. Absorbance spectra (CHCl₃, 3.3 10⁻⁵ mol.L⁻¹) of the photooxygenation under green LED irradiation (535 nm) in CDCl₃ of **5** to form **5-O₂** showing the disappearance of the band (downward arrow) at 385 nm.

To get a better understanding of the changes in the absorption bands upon photooxygenation, TD-DFT and DFT calculations were carried out on **5** and **5-O₂** (see supporting information for further details). Theory predicts two low-lying electronic transitions for **5** associated to S₀→S₁ and S₀→S₂ transitions located at 355 nm (*f* = 0.17) and 287 nm (*f* = 0.46), respectively. These vertical transitions correspond to the experimental absorption bands observed at 398 nm and 313 nm in CHCl₃.

The computed electron density difference corresponding to these two transitions are depicted in Figure 2. The S₀→S₁ absorption induce a change in the conjugated triene part with the nitrogen atom playing a minor role while the S₀→S₂ absorption does not involve a major change in the cyclic diene part. Therefore, the reaction of singlet oxygen with the diene part involve the disappearance of the S₀→S₁ absorption band as observed experimentally. Thus, theory predicts two vertical transitions at 299 nm (*f* = 0.11) and 283 nm (*f* = 0.15) for the endoperoxide **5-O₂**. Therefore, the analysis of the disappearance of the band around 400 nm is relevant for determining the conversion of **5** into the corresponding endoperoxide **5-O₂**.

Figure 2. Electronic density differences between S₀ and S₁ (a) and between S₀ and S₂ (b) calculated at the PCM-PBE0/defTZVP//PCM-M06-2X/6-31G(d). Blue (positive) and green (negative) regions represent increase and decrease of electron density upon excitation, respectively (isoval: 0.003 a.u.).

Kinetic experiments revealed the dramatic effect of the solvent on the formation of the endoperoxides. For instance, full

conversion of **5-O₂** was observed after 90 minutes in CDCl₃ while much longer reaction times were required using 1,2-dichloroethane or acetonitrile as solvents (entry 1). Similar results were obtained starting from 1,2-dihydropyridine derivatives **6-9** (entries 2-5). A significantly longer singlet oxygen lifetime in CDCl₃ compared to 1,2-dichloroethane or MeCN could explain the increase of reaction rate in CDCl₃.^[23] For the relative rate constants (k_{rel}), the compound **5** was used as a reference (entry 1). Substitution of the heterocycle by a methyl group had a beneficial impact on the reactivity with singlet oxygen. For example, the relative rate constant in CDCl₃ for **7** turned out to be 7.58 faster than **5** (entry 3) and k_{rel} were determined at 3.62 for **6** (entry 5) and 1.05 for **9** (entry 5). A similar reactivity order was observed for the photooxygenation in 1,2-dichloroethane and acetonitrile. It is worthwhile mentioning that photooxygenation of **8** led to a non-stable endoperoxide which tends to decompose into by-products (entry 4). In line with previous studies on other singlet oxygen traps,^[10c,e] the introduction of electron-donating methyl groups induces a higher reactivity towards electrophilic singlet oxygen. Furthermore, the reactivities of **5** and **7** were compared to *N*-Methyl-2-pyridone **10**, a benchmark singlet oxygen trap,^[16] by performing kinetic experiments (entries 1, 3 and 6). The relative rate constants using **5** as a reference were determined by ¹H NMR spectroscopy. The results indicated a k_{rel} for **7** at 8.5 in CDCl₃ using this protocol which is in good agreement with the value determined by UV-Visible spectroscopy ($k_{\text{rel}} = 7.58$, entry 3). Measurement of the relative photooxygenation rate showed that oxidation of **7** into the endoperoxide **7-O₂** was faster than *N*-methyl-2-pyridone (entries 3 and 6). At this stage, we studied by UV-Visible spectroscopy the thermal decomposition of the *in-situ* formed endoperoxides as new chemical sources of singlet oxygen (Figure 3). The endoperoxides turned out to be stable at room temperature and as a result, the cycloreversion was performed at 50 °C in 1,2-dichloroethane in the dark. The half-lives ($\tau_{1/2}$) were estimated by using the equation $\tau_{1/2} = \ln(2)/k$ where k is the first-order rate constant determined by following the increase of the absorption band at the same wavelength as described for the photooxygenation (Figure 3, see supporting

information for further details).

Figure 3. Plot of $\ln(A_{\text{end}} - A_t)$ versus time (min) for the thermolysis experiments of endoperoxides derived from **5-7**, **9** monitored by UV-Visible spectroscopy (the kinetics were performed three times for each substance). A_{end} , A_t are the absorbances of the reappearing parent forms at $t = \text{end}$ and at $t = 0$, respectively. The wavelengths for recording the absorbances A_t are as follows: **5** (388 nm), **6** (394 nm), **7** (397 nm), and **9** (407 nm). Reactions were carried out in 1,2-dichloroethane at 50 °C in the dark.

Examination of the stability of the endoperoxides revealed different behaviours depending on the methyl substitution (Figure 4).

Figure 4. Half-lives of endoperoxides determined in 1,2-dichloroethane at 50 °C in the dark.

For instance, endoperoxides **9-O₂** bearing a methyl group at the 3-position was the most stable derivatives ($\tau_{1/2} = 58$ h). The steric interactions between the methyl groups and the dicyanomethylene moiety may provide a possible explanation for the higher stability of **9-O₂**. The formation of the endoperoxide leads to a change of hybridization of the carbon bearing the methyl group from sp^2 to sp^3 which would significantly reduce the steric constraints in the endoperoxide **9-O₂** compared to the parent heterocycle **9**.^[16b] This behaviour was supported by theoretical calculations (see supporting information for further details). The endoperoxide **7-O₂**, which was found to be the best ¹O₂ trap, demonstrated a faster cycloreversion reaction compared to other analogues **5-O₂** and **6-O₂** exhibiting similar stabilities but the cycloreversion of **7-O₂** remains slower than **10-O₂** (Figure 3). In light of the above-mentioned results, the introduction of a methyl group at the 5-position of the 1,2-dihydropyridine core enhanced the reactivity toward singlet oxygen and accelerated the cycloreversion of **7-O₂** paving the way to a promising singlet oxygen chemical source. To confirm the formation of singlet oxygen by thermolysis of **7-O₂**, the endoperoxide was prepared *in-situ* by photooxygenation of **7** following the protocol described above (Scheme 3) and the dark generation of singlet oxygen was applied to the Schenck-ene reaction with 2,3-dimethylbut-2-ene **11** (Scheme 5).^[24]

Scheme 5. Qualitative singlet oxygen trapping by reaction of **7-O₂** with 2,3-dimethylbut-2-ene **11**. NMR yields are given using MeSO₂Ph as an internal standard.

The reaction of the *in-situ* formed endoperoxide **7-O₂** with 2,3-dimethylbut-2-ene **11** in CDCl₃ at 50 °C afforded the desired hydroperoxide **12** in 70% ¹H NMR yield after 32 h reaction time in the dark. Under these conditions, the formation of **7** was observed with a good yield (70%) which demonstrated that the release of singlet oxygen was the main decomposition pathway during the thermolysis of **7-O₂**.

The combination of a unit able to trap, store and release ¹O₂ and a photosensitizer into the same molecular architecture holds great promise in fractional photodynamic therapy.^[17,25] This strategy is based on intermittent irradiation of the cancer tissue to prevent oxygen depletion and side-effects due to light

exposure. Light irradiation enables the photosensitized generation of cytotoxic singlet oxygen and *in-situ* formation of the endoperoxide as a ¹O₂ carrier. Upon cessation of irradiation, singlet oxygen is chemically produced by release from the endoperoxide ensuring continuous production of the reactive oxygen species throughout the treatment. To assess whether the 1,2-dihydropyridine compounds could be suitable ¹O₂ carriers, we synthesized a bifunctional compound **18** containing a phenalenone-based photosensitizer unit covalently connected to a motif derived from **7** able to trap, store and release singlet oxygen (Scheme 6).

Scheme 6. Multistep synthetic route towards photosensitizer **18**.

Scheme 7. a) Generation of singlet oxygen in CDCl₃ by photosensitization and thermal cycloreversion at 50 °C in the dark. b) Partial ¹H NMR spectra in CDCl₃ demonstrating the reversible cycling between **18** and **18-O₂**. The spectrum A (t=0 min) corresponds to the compound **18** where relevant peaks were marked with orange stars. After photooxygenation under blue light (3.7 mW.cm⁻², 470 nm), the spectrum B was obtained for which relevant ¹H NMR signals were marked with green crosses. At this stage, only compound **18-O₂** was present in solution. The spectra C and D were recorded after 24 h and 48 h, respectively. The thermolysis was performed in the dark at 50 °C. After 48 h, the reaction mixture was irradiated for 15 min. under an oxygen atmosphere leading to the spectrum E similar to the spectrum B. c) The conversion was determined by integration of the relevant ¹H NMR peaks of **18** and **18-O₂**. Relative percentages of **18** and the intermediate **18-O₂** are given in the table.

Recent works from our group demonstrated that phenalenone **13** was an efficient photosensitizer for the generation of singlet oxygen.^[26] To connect this photosensitizer to the singlet oxygen trap, the synthetic route started by the reduction of **13** into the alcohol **14** in 90% yield. Alcohol **14** was not converted into tosylate with tosyl chloride but the chloro derivative **15** was isolated in 75% yield. The treatment of **15** with 1.5 equiv. of sodium azide produced the compound **16** which underwent a copper-catalyzed Huisgen 1,3-dipolar cycloaddition with **17**, readily prepared according to a similar synthetic route as for **7** (Scheme 4). Under these conditions, the bifunctional photosensitizer **18** was isolated in 77% yield and we then investigated the reversible storage capacity of ¹O₂ under irradiation followed by thermal conditions (Scheme 7a).

The trap and delayed release of singlet oxygen of **18** was monitored by ¹H NMR analyses in CDCl₃. As depicted in Scheme 7b (spectrum A), the signals at $\delta = 7.22$ ppm and $\delta = 7.28$ ppm correspond to two protons on the 1,2-dihydropyridine framework. After 15 min of irradiation at 470 nm in the presence of oxygen (spectrum B), these two signals disappeared and the chemical NMR shifts at $\delta = 5.91$ ppm and $\delta = 6.27$ ppm are attributable to the protons of the endoperoxide framework based on the full characterization of **[5-7]-O₂** and **9-O₂** (Figure 4). The chemical NMR shifts of the phenalenone are also affected by the formation of the endoperoxide as exemplified by the singlet at $\delta = 8.64$ ppm for **18** which is found at $\delta = 8.55$ ppm for **18-O₂**. These results clearly indicate the full conversion of **18** into its endoperoxide form **18-O₂** after 15 min of irradiation. The irradiation was then stopped and the sample was heated at 50 °C in the dark (Figures 7b and 7c). The NMR data show the gradual formation of **18** with a ratio of 28/72 (**18/18-O₂**, spectrum C) after 24 h and 56/44 (spectrum D). These results confirm the interconversion of **18-O₂** and **18** by thermolysis. It is interesting to note that the cycloreversion of **18-O₂** to **18** is slower than **7** to **7-O₂** which indicates that the phenalenone influences the stability of the endoperoxide. After 48 h, the sample was irradiated at 450 nm under an oxygen atmosphere and the full formation of **18-O₂** was observed by NMR (spectrum E) which confirmed the ability of **18** to trap, store and release singlet oxygen.

Conclusion

To conclude, we have prepared a new family of singlet oxygen traps based on the 1,2-dihydropyridine framework. These compounds were easily prepared by a two-step synthetic sequence involving an alkylation of substituted 2-chloropyridines followed by a reaction with malononitrile under basic conditions. A series of methyl-substituted 1,2-dihydropyridine compounds were fully characterized and their ability to trap singlet oxygen was studied by kinetic experiments using UV-Visible spectroscopy. In the presence of a catalytic amount of diiodo-BODIPY as the photosensitizer, green LED irradiation of the 1,2-dihydropyridine compounds in the presence of oxygen led to the formation of the corresponding endoperoxides which turned out to be stable at room temperature in solution. The results reveal the influence of methyl substitution pattern on the capture of singlet oxygen. In addition, the reaction solvent plays a crucial role on the reaction kinetics with the best results obtained in CDCl₃ which could be explained by the longer singlet oxygen

lifetime in this solvent. The stability of the endoperoxides was also studied by UV-Visible spectroscopy. As can be seen from photooxygenation experiments, thermolysis in the dark of the endoperoxides performed at 50 °C in 1,2-dichloroethane showed the influence of the methyl substitution position on the stability of the endoperoxides. The release of singlet oxygen was confirmed by reacting endoperoxide **7-O₂** with 2,3-dimethylbut-2-ene at 50 °C in CDCl₃ leading to the corresponding hydroperoxide. To assess whether this new family of singlet oxygen carriers could find future applications in photomedicine, a bifunctional photosensitizer containing a phenalenone unit covalently connected to a 1,2-dihydropyridine framework through a copper-catalyzed Huisgen 1,3-dipolar cycloaddition was synthesized in good overall yields. The NMR analyses reveal that the 1,2-dihydropyridine unit was able to capture singlet oxygen under irradiation and to undergo cycloreversion reaction at 50 °C under dark conditions. Our results are promising and future work should focus on the application of this new family of singlet oxygen carriers in synthetic chemistry and photomedicine.

Experimental Section

General methods

¹H NMR and ¹³C spectra were recorded on a Pulse 300 MHz BRUKER (300 MHz for ¹H and 75 MHz for ¹³C), a BRUKER Avance III 400 MHz (400 MHz for ¹H and 100 MHz for ¹³C) or Avance HD 700 MHz Bruker (700 MHz for ¹H and 175 MHz for ¹³C) at room temperature on samples dissolved in CDCl₃, Acetone-d₆ or DMSO-d₆ and referenced to residual solvent peak. Chemical shifts (δ) are given in parts per million and coupling constants are given as absolute values expressed in Hertz. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). UV-Visible spectra were recorded on an Analytik Jena specord 210. High-resolution mass spectrometry (HRMS) analyses were recorded on a XEVO G2-XS QTOF (Waters). Infrared spectra were recorded with a Bruker Tensor 27 FT ATR spectrometer. Melting points were determined on a Stuart melting point SMP3 apparatus. Thin-layer chromatography (TLC) was carried out on aluminium sheets precoated with silica gel 60 F₂₅₄ (Merck). Column chromatography separations were performed using Merck Kieselgel 60 (0.040-0.060 mm). The chemicals and solvents were purchased from commercial suppliers without further purification. The 2-(cyanomethyl)-1-methylpyridin-1-ium iodide,^[27] 1-methyl-2-(2-oxo-2-phenylethyl)pyridin-1-ium iodide,^[28] diiodo-BODIPY photosensitizer,^[29] and phenalenone **13**^[26] were prepared according to literature procedures.

General procedure for the synthesis of compounds **1** and **2**:

Under argon atmosphere, the pyridinium iodide derivative (1 equiv.) was introduced in anhydrous THF (0.2 mol.L⁻¹) and NaH (60 wt.% in mineral oil; 1.2 equiv.) was then added by portion at 0 °C. The reaction mixture was left to stir at room temperature for 4 hours at which point the reaction was quenched with water and then extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. The crude compound was

purified by column chromatography on silica gel to afford the corresponding product.

(E)-2-(1-methylpyridin-2(1H)-ylidene)acetonitrile 1: 114.3 mg (90%) of **1** (pasty solid) was obtained from 2-(cyanomethyl)-1-methylpyridin-1-ium iodide (250 mg, see Supporting Information for a detailed synthesis) and NaH (38.5 mg). The compound was purified by column chromatography on silica gel (95/5, DCM/MeOH). R_f = 0.38 (DCM/MeOH, 95/5); ^1H (300 MHz, CDCl_3) δ 3.19 ppm (s, 3H), 3.46 (s, 1H), 5.85 (td, J = 6.7, 1.4 Hz, 1H), 6.90-6.82 (m, 2H), 7.04-7.03 (m, 1H); ^{13}C (75 MHz, CDCl_3) δ 41.6 ppm, 52.2, 106.0, 120.7, 123.0, 132.6, 138.2, 155.4; IR (ATR, cm^{-1}) 3097, 2919, 2159, 1638, 1545, 1509, 1458, 1186; HRMS (ASAP+) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_8\text{H}_9\text{N}_3$ 133.0766; Found 133.0768.

(E)-2-(1-methylpyridin-2(1H)-ylidene)-1-phenylethan-1-one 2: 111 mg (99%) of **2** (dark orange solid) was obtained from 1-methyl-2-(2-oxo-2-phenylethyl)pyridin-1-ium iodide (180 mg, see Supporting Information for a detailed synthesis) and NaH (25.4 mg). The compound was purified by column chromatography on silica gel (90/10, DCM/MeOH).

R_f = 0.40 (DCM/MeOH, 90/10); M.p. degradation; ^1H (300 MHz, CDCl_3) δ 3.52 ppm (s, 3H), 5.58 (s, 1H), 6.24 (td, J = 6.7, 1.5 Hz, 1H), 7.25-7.21 (m, 2H), 7.40-7.36 (m, 3H), 7.89-7.87 (m, 2H), 9.20 (dd, J = 10.1, 1.5 Hz, 1H); ^{13}C (75 MHz, CDCl_3) δ 43.0 ppm, 85.4, 110.1, 122.9, 127.1 (2C), 128.1 (2C), 129.8, 135.6, 138.7, 143.7, 154.3, 185.3; IR (ATR, cm^{-1}) 3085, 2921, 1635, 1510, 1495, 1210, 1120, 865; HRMS (ASAP+) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{14}\text{NO}$ 212.1075; Found 212.1077.

General procedure for the synthesis of compounds 3-5:

Under argon atmosphere, the activated methylene reagent (2.11 mmol, 1.2 equiv.) was introduced in anhydrous THF (6 mL) and NaH (60 wt.% in mineral oil; 84.4 mg, 2.11 mmol, 1.2 equiv.) was then added by portion at 0 °C. The mixture was then allowed to warm to room temperature and stirred for 10 minutes, followed by the addition of 2-chloro-1-methylpyridinium iodide (450 mg, 1.76 mmol, 1 equiv.). After stirring until completion of the reaction at room temperature monitored by TLC, the reaction mixture was quenched with water and then extracted with dichloromethane. The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude compound was purified by column chromatography on silica gel to afford the corresponding product.

2-(ditosylmethylene)-1-methyl-1,2-dihydropyridine 3: 475.7 mg (65%) of **3** (pale yellow solid) was obtained from bis(p-toluenesulfonyl)methane (684.5 mg). The compound was purified by column chromatography on silica gel (95/5, DCM/MeOH). R_f = 0.33 (DCM/MeOH, 95/5); M.p. degradation; ^1H (400 MHz, CDCl_3) δ 2.37 ppm (s, 6H), 4.13 (s, 3H), 7.19 (d, J = 8.1 Hz, 4H), 7.42 (td, J = 7.1, 1.8 Hz, 1H), 7.77 (d, J = 8.1 Hz, 4H), 8.05-7.96 (m, 2H), 8.21 (d, J = 5.6 Hz, 1H); ^{13}C (100 MHz, CDCl_3) δ 21.5 ppm (2C), 47.8, 80.5, 122.8, 126.6 (4C), 129.2 (4C), 135.6, 141.5 (2C), 141.6, 143.6, 145.0 (2C), 156.2; IR (ATR, cm^{-1}) 3059, 2919, 1656, 1561, 1498, 1299, 1268, 1179, 1119; HRMS (ASAP+) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_4\text{S}_2$ 416.0990; Found 416.0985.

dimethyl 2-(1-methylpyridin-2(1H)-ylidene)malonate 4: 357.8 mg (91%) of **4** (pale yellow solid) was obtained from dimethyl malonate (0.24 mL). The compound was purified by column chromatography on silica gel (90/10, DCM/MeOH).

R_f = 0.35 (DCM/MeOH, 90/10); M.p. 175-177 °C; ^1H (400 MHz, CDCl_3) δ 3.67 ppm (s, 6H), 3.92 (s, 3H), 7.08 (td, J = 7.1, 1.4 Hz, 1H), 7.73-7.68 (m, 1H), 7.93 (dd, J = 8.6, 1.4 Hz, 1H), 7.98 (d, J = 7.1 Hz, 1H); ^{13}C (100 MHz, CDCl_3) δ 45.7 ppm, 50.5 (2C), 79.0, 119.0 (2C), 133.7, 138.2, 140.9, 162.0, 167.8; IR (ATR, cm^{-1}) 3055, 2944, 1686, 1622, 1593, 1550, 1508, 1433, 1058; HRMS (ASAP+) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{14}\text{NO}_4$ 224.0923; Found 224.0927.

2-(1-methylpyridin-2(1H)-ylidene)malononitrile 5: 249.2 mg (90%) of **5** (pale yellow solid) was obtained from malononitrile (139.4 mg). The compound was purified by column chromatography on silica gel (95/5, DCM/MeOH). R_f = 0.38 (DCM/MeOH, 95/5); M.p. 201-203 °C; ^1H (400 MHz, $\text{DMSO}-d_6$) δ 4.00 ppm (s, 3H), 6.84 (td, J = 6.6, 1.5 Hz, 1H), 7.21 (ddd, J = 8.8, 1.5, 0.5 Hz, 1H), 7.68 (ddd, J = 8.8, 6.6, 1.5 Hz, 1H), 8.00 (app. d, J = 6.6 Hz, 1H); ^{13}C (100 MHz, $\text{DMSO}-d_6$) δ 38.7 ppm, 45.2, 141.1, 119.6 (2C), 120.4, 139.1, 143.1, 154.8; IR (ATR, cm^{-1}) 3086, 3050, 2190, 2164, 1633, 1554, 1501, 1439; HRMS (ASAP+) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_9\text{H}_8\text{N}_3$ 158.0718; Found 158.0722.

General procedure for the synthesis of compounds 6-9:

Step 1. Under argon atmosphere, the 2-chloropyridine derivative (500 mg, 3.92 mmol, 1 equiv.) and MeI (2.44 mL, 39.2 mmol, 10 equiv.) were introduced in anhydrous acetone (2 mL) into a sealed tube. The reaction mixture was left to stir at 56 °C for 48 hours. The solid precipitated was filtered, washed with cold acetone and dried under reduced pressure. The crude compound was used in the next step without further purification.

Step 2. Under argon atmosphere, malononitrile (310.8 mg, 4.70 mmol, 1.2 equiv.) was introduced in anhydrous THF (20 mL) and NaH (60 wt.% in mineral oil; 188.1 mg, 4.70 mmol, 1.2 equiv.) was then added by portion at 0 °C. The mixture was then allowed to warm to room temperature and stirred for 10 minutes followed by the addition of the crude compound from Step 1. After stirring until completion of the reaction at room temperature monitored by TLC, the reaction mixture was quenched with water and then extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude compound was purified by column chromatography on silica gel to afford the corresponding product.

2-(1,6-dimethylpyridin-2(1H)-ylidene)malononitrile 6: 67.1 mg (10% overall yield) of **6** (yellowish solid). The compound was purified by column chromatography on silica gel (98/2, DCM/MeOH). R_f = 0.33 (DCM/MeOH, 98/2); M.p. 183-185 °C; ^1H (300 MHz, Acetone- d_6) δ 2.63 ppm (s, 3H), 3.97 (s, 3H), 6.81 (d, J = 7.0 Hz, 1H), 7.21 (d, J = 9.0 Hz, 1H), 7.55 (dd, J = 9.0, 7.0 Hz, 1H); ^{13}C (75 MHz, Acetone- d_6) δ 21.6 ppm, 41.4, 41.7, 116.2, 120.1 (2C), 120.2, 138.9, 151.8, 159.3; IR (ATR, cm^{-1}) 3068, 2980, 2186, 2158, 1626, 1564; HRMS (ASAP+) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{10}\text{H}_{10}\text{N}_3$ 172.0875; Found 172.0875.

2-(1,5-dimethylpyridin-2(1H)-ylidene)malononitrile 7: 342.2 mg (51% overall yield) of **7** (yellowish solid). The compound was purified by column chromatography on silica gel (98/2, DCM/MeOH). R_f = 0.31 (DCM/MeOH, 98/2); M.p. 184-186 °C; ^1H (400 MHz, $\text{DMSO}-d_6$) δ 2.14 ppm (s, 3H), 3.96 (s, 3H), 7.16 (app. d, J = 9.0 Hz, 1H), 7.59 (dd, J = 9.0, 1.8 Hz, 1H), 7.91 (s, 1H); ^{13}C (100 MHz, $\text{DMSO}-d_6$) δ 16.4 ppm, 37.5, 45.1, 120.0 (2C), 120.2, 123.7, 141.1, 141.2, 152.9; IR (ATR, cm^{-1})

3079, 3045, 2926, 2186, 2158, 1646, 1555; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{10}H_{10}N_3$ 172.0875; Found 172.0876.

2-(1,4-dimethylpyridin-2(1*H*)-ylidene)malononitrile 8: 355.6 mg (53% overall yield) of **8** (yellowish solid). The compound was purified by column chromatography on silica gel (95/5, DCM/MeOH). R_f = 0.51 (DCM/MeOH, 95/5); M.p. 185–187 °C; 1H (400 MHz, DMSO- d_6) δ 2.29 ppm (s, 3H), 3.95 (s, 3H), 6.72 (dd, J = 6.8, 1.8 Hz, 1H), 7.00 (app. s, 1H), 7.90 (d, J = 6.8 Hz, 1H); ^{13}C (100 MHz, DMSO- d_6) δ 20.8 ppm, 37.6, 44.7, 116.1, 118.9, 119.9 (2C), 142.5, 151.1, 154.3; IR (ATR, cm^{-1}) 3090, 2954, 2168, 2163, 1642, 1544; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{10}H_{10}N_3$ 172.0875; Found 172.0878.

2-(1,3-dimethylpyridin-2(1*H*)-ylidene)malononitrile 9: 328.8 mg (49% overall yield) of **9** (yellow solid). The compound was purified by column chromatography on silica gel (95/5, DCM/MeOH). R_f = 0.42 (DCM/MeOH, 95/5); M.p. 155–157 °C; 1H (300 MHz, $CDCl_3$) δ 2.53 ppm (s, 3H), 4.06 (s, 3H), 6.91 (t, J = 7.0 Hz, 1H), 7.50 (d, J = 7.0 Hz, 1H), 7.71 (d, J = 7.0 Hz, 1H); ^{13}C (75 MHz, $CDCl_3$) δ 21.9 ppm, 36.2, 47.7, 116.9, 120.4 (2C), 135.4, 140.2, 140.9, 156.1; IR (ATR, cm^{-1}) 3095, 3048, 2945, 2182, 2147, 1617, 1560; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{10}H_{10}N_3$ 172.0875; Found 172.0882.

Typical procedure for the photooxygenation experiments monitored by UV-Visible spectroscopy: The exact mass of 2-(1-methylpyridin-2(1*H*)-ylidene)malononitrile **5** (8.64 mg, 55 μ mol, 1 equiv.) and sensitizer (2.75 μ mol, 1.58 mg, 5 mol%) were dissolved in $CDCl_3$ (10 mL) to obtain a concentration of 5.5 mmol.L $^{-1}$. From this solution 5 mL was put into a glass tube. The reaction medium was gently bubbled with dioxygen for 5 minutes and was then left under atmospheric pressure of dioxygen throughout the reaction time. The homogenous solution was irradiated with two green LEDs (1.9 mW.cm $^{-2}$, 535 nm typical wavelength). The distance from light source irradiation cells was 3 cm without the use of any filters. The reaction was left to stir at 23°C. Periodically, an aliquot (30 μ L) was taken from the reaction mixture and was then diluted with $CHCl_3$ to obtain a final concentration of 3.3 10 $^{-5}$ mol.L $^{-1}$. The consumption of the substrate was followed by UV-Visible spectroscopy. The absorption maxima A were taken to monitor the disappearance of the substrate at λ = 385 nm. The relative pseudo first order rates constants were obtained from plotting the logarithm (A_t/A_0) against time (compound **5** was used as a reference). The experiments were carried out three times. [For the characterization data, the photooxygenation was carried out in $CDCl_3$ starting from 55 μ mol of **5-7** and **9**. At the end of the reaction monitored by UV-Visible spectroscopy, the solution was concentrated by bubbling O_2 gas in the solution to reach a volume of ca 1.5 mL]

2-(5-methyl-2,3-dioxo-5-azabicyclo[2.2.2]oct-7-en-6-ylidene)malononitrile 5-O₂: 1H (400 MHz, $CDCl_3$) δ 3.58 ppm (s, 3H), 5.51 (ddd, J = 5.3, 1.7, 0.7, 1H), 5.67 (ddd, J = 6.1, 1.8, 0.7 Hz, 1H), 6.83 (ddd, J = 7.9, 6.1, 1.7 Hz, 1H), 6.97 (ddd, J = 7.9, 5.3, 1.8 Hz, 1H); ^{13}C (100 MHz, $CDCl_3$) δ 38.6 ppm, 53.9, 72.8, 86.1, 113.9, 114.4, 128.4, 133.9, 165.5; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_9H_8N_3O_2$ 190.0617; Found 190.0623.

2-(4,5-dimethyl-2,3-dioxo-5-azabicyclo[2.2.2]oct-7-en-6-ylidene)malononitrile 6-O₂: 1H (400 MHz, $CDCl_3$) δ 1.81 ppm (s, 3H), 3.44 (s, 3H), 5.64 (dd, J = 6.1, 1.7 Hz, 1H), 6.70 (dd, J = 7.8, 1.7 Hz, 1H), 6.81 (dd, J = 7.8, 6.1 Hz, 1H); ^{13}C (100 MHz, $CDCl_3$) δ 17.9 ppm, 33.3, 53.6, 73.1, 89.1, 114.6, 115.2, 128.4,

139.1, 167.0; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{10}H_{10}N_3O_2$ 204.0773; Found 204.0780.

2-(5,8-dimethyl-2,3-dioxo-5-azabicyclo[2.2.2]oct-7-en-6-ylidene)malononitrile 7-O₂: 1H (400 MHz, $CDCl_3$) δ 2.10 ppm (d, J = 1.9 Hz, 3H), 3.57 (s, 3H), 5.23 (dd, J = 1.9, 0.5 Hz, 1H), 5.57 (dd, J = 5.9, 0.5 Hz, 1H), 6.38 (dq, J = 5.9, 1.9 Hz, 1H); ^{13}C (100 MHz, $CDCl_3$) δ 18.0 ppm, 38.7, 53.5, 73.3, 90.4, 114.0, 114.4, 120.8, 146.0, 166.4; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{10}H_{10}N_3O_2$ 204.0773; Found 204.0777.

2-(1,5-dimethyl-2,3-dioxo-5-azabicyclo[2.2.2]oct-7-en-6-ylidene)malononitrile 9-O₂: 1H (400 MHz, $CDCl_3$) δ 1.99 ppm (s, 3H), 3.57 (s, 3H), 5.46 (dd, J = 5.3, 1.6 Hz, 1H), 6.49 (dd, J = 7.9, 1.6 Hz, 1H), 6.94 (dd, J = 7.9, 5.3 Hz, 1H); ^{13}C (100 MHz, $CDCl_3$) δ 18.4 ppm, 40.8, 54.5, 79.1, 86.2, 114.8, 115.0, 133.5, 134.0, 170.2; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{10}H_{10}N_3O_2$ 204.0773; Found 204.0781.

Typical procedure for the thermolysis experiments: A solution of **5-O₂** (5.5 mmol.L $^{-1}$) in 1,2-dichloroethane was introduced into a glass tube. The thermolysis was carried out at 50 °C in the dark. Periodically, an aliquot (30 μ L) was taken from the reaction mixture and was then diluted with 1,2-dichloroethane to obtain a final concentration of 3.3 10 $^{-5}$ mol.L $^{-1}$. The formation of **5** was followed by UV-Visible spectroscopy. The absorption maxima A_t were taken to monitor the increase of absorption intensity of **5** at λ = 388 nm. The first order rates constants were obtained from plotting the logarithm of ($A_{end}-A_t$) against time. The half-lives were calculated as follows: $t_{1/2} = \ln 2/k$.

Trapping experiment with 2,3-dimethylbut-2-ene 11: To a sealed tube was introduced 10 mL of a degassed solution of **7-O₂** (5.5 mmol.L $^{-1}$, 55 μ mol, 1 equiv.) in $CDCl_3$. Methyl phenyl sulfone (4.30 mg, 27.5 μ mol, 0.5 equiv.) as an internal standard and 2,3-dimethylbut-2-ene **11** (7.2 μ L, 60.5 μ mol, 1.1 equiv.) were then added. The reaction was left to stir at 50 °C for the appropriate reaction time and an aliquot (0.2 mL) was taken from the reaction mixture at different reaction times. The aliquot was diluted with $CDCl_3$ (0.2 mL) and nitrogen was bubbled through the solution to remove oxygen. The samples were then analyzed by 1H NMR to determine the yield and product formation.

8-(hydroxymethyl)-6-methoxy-7-phenyl-1*H*-phenalen-1-one 14: 6-methoxy-1-oxo-7-phenyl-1*H*-phenalene-8-carbaldehyde **13** (250 mg, 0.80 mmol, 1 equiv.) was introduced in absolute ethanol (8 mL) and $NaBH_4$ (36.3 mg, 0.96 mmol, 1.2 equiv.) was then added at 0 °C. The reaction mixture was then allowed to warm to room temperature and was left to stir for 3 hours. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution and then extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude compound was purified by column chromatography on silica gel (6/4, DCM/Et $_2$ O) to afford the corresponding product **14** as an orange solid (227 mg, 90%). R_f = 0.38 (DCM/Et $_2$ O, 6/4); M.p. 170–172 °C; 1H (300 MHz, $CDCl_3$) δ 3.45 ppm (s, 3H), 4.53 (s, 2H), 6.63 (d, J = 9.6 Hz, 1H), 6.75 (d, J = 8.1 Hz, 1H), 7.20–7.17 (m, 2H), 7.45–7.37 (m, 3H), 7.70–7.64 (m, 2H), 8.84 (s, 1H); ^{13}C (75 MHz, $CDCl_3$) δ 55.7 ppm, 63.2, 106.3, 121.1, 123.6, 126.0, 126.8, 127.7 (2C), 127.8 (2C), 128.8, 129.3, 130.9, 133.8, 139.0, 141.4, 142.5, 144.4, 161.7, 185.7; IR (ATR, cm^{-1}) 3397, 3025, 2932, 1623, 1546, 1506, 1459, 1257,

1219, 1063; HRMS (ES+) m/z : $[M+H]^+$ Calcd for $C_{21}H_{17}O_3$ 317.1178; Found 317.1163.

8-(chloromethyl)-6-methoxy-7-phenyl-1*H*-phenalen-1-one 15: 8-(hydroxymethyl)-6-methoxy-7-phenyl-1*H*-phenalen-1-one **14** (170 mg, 0.54 mmol, 1 equiv.), triethylamine (0.15 mL, 1.08 mmol, 2 equiv.) and then *p*-toluenesulfonyl chloride (154.4 mg, 0.81 mmol, 1.5 equiv.) were introduced in DCM (3 mL). The reaction mixture was left to stir for 16 h at room temperature and water was added. The mixture was then extracted with CH_2Cl_2 . The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude compound was purified by column chromatography on silica gel (6/4, Cyclohexane/EtOAc) to afford the corresponding product **15** as a yellow solid (135 mg, 75%). R_f = 0.48 (Cyclohexane/EtOAc, 6/4); M.p. 210-212 °C; 1H (400 MHz, $CDCl_3$) δ 3.45 ppm (s, 3H), 4.46 (s, 2H), 6.65 (d, J = 9.7 Hz, 1H), 6.77 (d, J = 8.1 Hz, 1H), 7.24-7.21 (m, 2H), 7.44-7.40 (m, 3H), 7.68 (d, J = 5.1 Hz, 1H), 7.70 (d, J = 6.7 Hz, 1H), 8.83 (s, 1H); ^{13}C (100 MHz, $CDCl_3$) δ 44.3 ppm, 55.8, 106.7, 121.0, 123.9, 126.0, 127.1, 127.6 (2C), 127.9 (2C), 129.2, 129.7, 132.7, 134.3, 135.6, 140.7, 142.7, 145.4, 161.7, 185.2; IR (ATR, cm^{-1}) 3023, 2970, 2925, 2849, 1632, 1557, 1509, 1459, 1398, 1223, 1113, 833; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{21}H_{16}ClO_2$ 335.0839; Found 335.0838.

8-(azidomethyl)-6-methoxy-7-phenyl-1*H*-phenalen-1-one 16: Under argon atmosphere, 8-(chloromethyl)-6-methoxy-7-phenyl-1*H*-phenalen-1-one **15** (80 mg, 0.24 mmol, 1 equiv.) and NaN_3 (23.4 mg, 0.36 mmol, 1.5 equiv.) were introduced in a MeCN/DCM, 9/1 mixture (2.5 mL). The reaction was left to stir at reflux for 24 hours. Then, the reaction temperature was brought to room temperature and water was added. The mixture was then extracted with DCM. The organic layer was extracted dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude compound was purified by column chromatography on silica gel (98/2, DCM/EtOAc) to afford the corresponding product **16** as an orange solid (72 mg, 88%). R_f = (DCM/EtOAc, 98/2); M.p. 147-149 °C; 1H (700 MHz, $CDCl_3$) δ 3.45 ppm (s, 3H), 4.25 (s, 2H), 6.64 (d, J = 8.0 Hz, 1H), 6.77 (d, J = 7.2 Hz, 1H), 7.16 (d, J = 7.2 Hz, 2H), 7.39 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.4 Hz, 2H), 7.71-7.61 (m, 2H), 8.76 (s, 1H); ^{13}C (175 MHz, $CDCl_3$) δ 52.7 ppm, 55.7, 106.6, 121.0, 123.9, 126.0, 127.0, 127.8 (2C), 127.9 (2C), 129.1, 129.5, 131.6, 133.6, 134.1, 141.0, 142.6, 145.4, 161.6, 185.3; IR (ATR, cm^{-1}) 3189, 3039, 2994, 2921, 1634, 1575, 1550, 1510, 1459, 1422, 1261, 1219, 1011; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{21}H_{16}N_3O_2$ 342.1243; Found 342.1242.

Synthesis of 2-(5-methyl-1-(prop-2-yn-1-yl)pyridin-2(1*H*)-ylidene)malononitrile 17: Step 1. Under argon atmosphere, 2-chloro-5-methylpyridine (0.26 mL, 2.35 mmol, 1 equiv.) and propargyl bromide (1.78 mL, 23.5 mmol, 10 equiv.) were introduced into a sealed tube. The reaction mixture was left to stir at 60 °C for 72 hours. The solid precipitated was filtered, washed with cold acetone and dried under reduced pressure. The crude compound was used in the next step without further purification. **Step 2.** Under argon atmosphere, malononitrile (246.5 mg, 2.82 mmol, 1.2 equiv.) was introduced in anhydrous THF (12 mL) and NaH (60 wt.% in mineral oil) (112.8 mg, 2.82 mmol, 1.2 equiv.) was then added by portion at 0 °C. The

mixture was then allowed to warm to room temperature and stirred for 10 minutes, followed by the addition of the crude compound from Step 1. After stirring until completion of the reaction at room temperature, the reaction mixture was quenched with water and then extracted with dichloromethane. The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude compound was purified by column chromatography on silica gel (98/2, DCM/MeOH) to afford the corresponding product **17** as a dark orange solid (202 mg, 44% overall yield). R_f = 0.35 (DCM/MeOH, 98/2); M.p. degradation; 1H (400 MHz, Acetone- d_6) δ 2.22 ppm (s, 3H), 3.32 (t, J = 2.6 Hz, 1H), 5.29 (d, J = 2.6 Hz, 2H), 7.26 (d, J = 9.2 Hz, 1H), 7.56 (d, J = 9.2, 1.8 Hz, 1H), 7.87-7.86 (m, 1H); ^{13}C (100 MHz, Acetone- d_6) δ 16.9 ppm, 41.6, 46.6, 77.1, 79.3, 119.5 (2C), 122.4, 124.8, 139.6, 141.8, 154.2; IR (ATR, cm^{-1}) 3374, 3082, 3048, 2952, 2194; 2165, 2121, 1664, 1552, 1503; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{12}H_{10}N_3$ 196.0875; Found 196.0876.

Synthesis of 2-(1-((6-methoxy-1-oxo-7-phenyl-1*H*-phenalen-8-yl)methyl)-1*H*-1,2,3-triazol-4-yl)methyl)-5-methylpyridin-2(1*H*)-ylidene)malononitrile 18: 8-(azidomethyl)-6-methoxy-7-phenyl-1*H*-phenalen-1-one **16** (50 mg, 0.15 mmol, 1 equiv.) and 2-(5-methyl-1-(prop-2-yn-1-yl)pyridin-2(1*H*)-ylidene)malononitrile **17** (58.6 mg, 0.30 mmol, 2 equiv.) were introduced in a H_2O /THF, 1/2 mixture (3 mL). Sodium ascorbate (11.9 mg, 0.06 mmol, 0.4 equiv.) and copper sulfate pentahydrate (3.7 mg, 15 μ mol, 0.1 equiv.) were then added. The reaction mixture was left to stir at room temperature for 30 hours and water was added. The mixture then was extracted with DCM. The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude compound was purified by column chromatography on silica gel (90/10, DCM/MeOH) to afford the corresponding product **18** as an orange solid (60 mg, 77%). R_f = 0.48 (DCM/MeOH, 90/10); M.p. degradation; 1H (400 MHz, $CDCl_3$) δ 2.16 ppm (s, 3H), 3.45 (s, 3H), 5.45 (s, 2H), 5.54 (s, 2H), 6.60 (d, J = 9.7 Hz, 1H), 6.79 (d, J = 8.1 Hz, 1H), 7.18-7.12 (m, 2H), 7.22 (d, J = 9.2, 1.8 Hz, 1H), 7.28 (d, J = 9.2 Hz, 1H), 7.45-7.40 (m, 3H), 7.69-7.68 (m, 2H), 7.73-7.71 (m, 2H), 8.61 (s, 1H); ^{13}C (100 MHz, $CDCl_3$) δ 17.4 ppm, 41.0, 50.1, 52.2, 55.8, 106.8 (2C), 119.8, 120.9, 122.5, 124.0, 124.2, 125.2, 125.9, 127.5, 127.6 (2C), 128.3 (2C), 129.3, 129.7, 131.6, 131.8, 134.6, 139.2, 139.7, 140.4, 140.5, 142.8, 146.7, 153.2, 161.6, 185.0; IR (ATR, cm^{-1}) 3048, 2921, 2849, 2190, 2159, 1635, 1551, 1506, 1458, 1424, 1397, 1220, 1100, 1047, 1008; HRMS (ASAP+) m/z : $[M+H]^+$ Calcd for $C_{33}H_{25}N_6O_2$ 537.2039; Found 537.2039.

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Keywords: Singlet Oxygen • Photochemistry • Endoperoxide • Phenalenone • Photooxygenation

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Entry for the Table of Contents

A new family of heterocycles able to trap, store and release singlet oxygen has been developed. UV-Visible and NMR spectroscopic studies have shown the influence of substituents and solvent on the photooxygenation rate. Thermolysis experiments have demonstrated the potential of *in-situ* formed endoperoxides for *dark photooxygenation*.

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