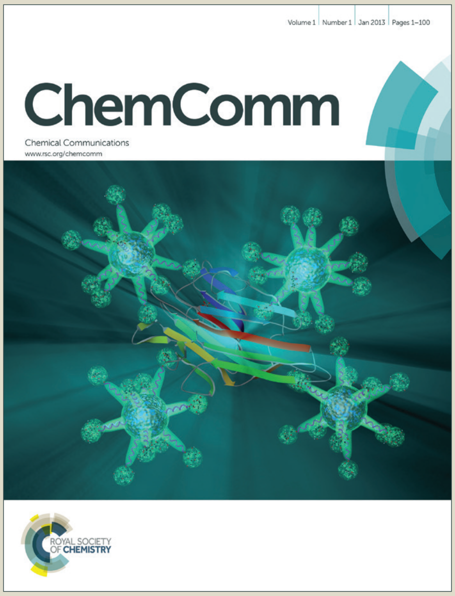
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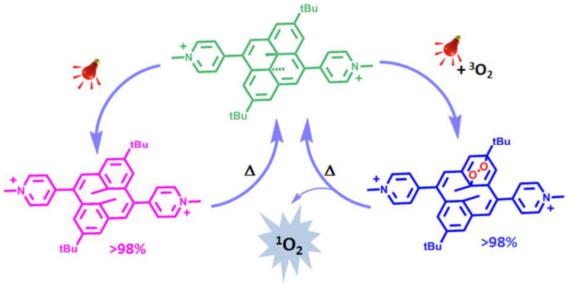

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Reactivity of a Pyridinium-Substituted Dimethyldihydropyrene switch under Aerobic conditions: Self-Sensitized Photo-Oxygenation and Thermal Release of Singlet Oxygen†

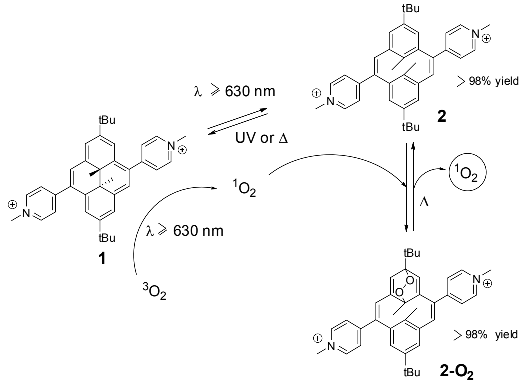
Saioa Cobo,[a] Frédéric Lafolet,[a] Eric Saint-Aman,[a] Christian Philouze,[a] Christophe Bucher,[b] Serena Silvi,[c] Alberto Credi*[c] and Guy Royal*[a]

The behavior of a pyridinium-substituted dimethyldihydropyrene photo-switch under aerobic conditions was investigated. During irradiation with red light (λ ≥ 630 nm), this compound plays the role of oxygen sensitizer and is quantitatively converted into an endoperoxide derivative. The photo-produced endoperoxide then thermally releases singlet oxygen to regenerate the starting compound.

The control of trapping and release of singlet oxygen ($^1\Delta_g$) is of great interest for many applications for example in materials science, wastewater treatment, optical imaging, or therapy.[1-14] This objective may be achieved by the use of specific polyaromatic compounds (often based on the 1,4-dimethylnaphthalene and 9,10-diphenylanthracene motifs[11,12,15-24]) that can be converted to endoperoxides (EPOs) through a formal [4+2] cycloaddition reaction when irradiated with light in the presence of an external photo-sensitizer (e.g. methylene blue or porphyrin derivatives). The photogenerated EPOs can then thermally release $^1O_2$ under dark conditions.[21] In these processes, the efficiency of the oxygen storage and release as well as the stability of the compounds towards degradation (oxidation) can be modulated by chemical functionalization. In addition, compounds capable of forming EPOs by irradiation at low energy (red light)[25,26] or the direct conversion (*i.e.* without use of exogenous sensitizers) of anthracene derivatives to EPOs in solid films by UV light irradiation[19] have been reported.

Another elegant strategy to regulate the production of $^1O_2$ relies on the use of molecular switches.[27,28] Supramolecular species and solid materials based on spiropyran[29] and dithienylethene[9,30] photochromic compounds associated to metal complexes playing the role of oxygen photo-sensitizer were used for the reversible control of $^1O_2$ generation. In these studies, the production of singlet oxygen is governed by the state (ON or OFF) of the photochromic unit.

Following on from our works on the dimethyldihydropyrene-cyclophanediene (DHP-CPD) photochromic couple, we have now focused on the reactivity of a bis-pyridinium-substituted DHP (**1**, Scheme 1) towards O_2. Therein we report that, using optical and thermal stimuli and following a reversible three state process, this system can act as an efficient oxygen carrier and singlet oxygen producer.



Scheme 1 Conversion processes between **1, 2** and **2-O$_2$**.

The DHP-CPD photochromic couple belongs to the family of diarylethenes.[31-36] The colored DHP ("closed" form) unit features a planar aromatic skeleton having 14 delocalized π electrons and two methyl groups pointing in opposite directions on either side of the plane. Under visible-light irradiation, the colorless CPD isomer ("open" state) is formed through the cleavage of the central carbon-carbon bond. The reverse conversion (CPD⟶DHP) may then be accomplished either by irradiation in the UV range or thermally. Importantly, the properties of this molecule can be finely tuned by chemical functionalization, a feature that has enabled the recent development of very promising DHP-based multi-functional materials and opto-electronic devices.[10,37-44]

We have recently investigated the behavior of **1** (closed isomer as PF_6^- salt, Scheme 1) under an inert atmosphere.[45] The presence

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[a] *Université Joseph Fourier Grenoble I, Département de Chimie Moléculaire, UMR CNRS-5250, BP 53, 38041 Grenoble Cedex 9, France.*
E-mail : guy.royal@ujf-grenoble.fr
[b] *Laboratoire de Chimie (UMR 5182), École Normale Supérieure de Lyon/CNRS Université de Lyon 1, Lyon, France.*
[c] *Photochemical Nanosciences Laboratory and SolarChem center, Dipartimento di Chimica ''G. Ciamician'', Universita` di Bologna, via Selmi 2, 40126 Bologna, Italy.*
E-mail: alberto.credi@unibo.it

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of the pyridinium substituents on the DHP core has been shown to significantly improve the photoisomerization efficiency in terms of photoconversion rate and to allow a significant decrease of the irradiation energy (from green to red light). As a follow-up to these early findings, our most recent investigations have now brought to light the great reactivity of this class of compounds towards dioxygen. When irradiated in air-saturated CH_3CN solution,[46] we have observed that the colorless endoperoxide **2-O₂**, formally obtained by cycloaddition of one O_2 entity onto the open isomer **2** (Scheme 1), can be produced quantitatively at room temperature and that the back reaction is also complete.

Compounds **2** and **2-O₂** can thus be produced quantitatively by direct irradiation at $\lambda \geq 630$ nm of a solution of **1** in the absence or presence of air respectively. These two compounds can be easily isolated as powders by evaporation of the solvent. They have been characterized by UV-visible absorption spectroscopy, mass spectrometry (see SI) and also by solid state X-ray diffraction analysis. Indeed, co-crystals containing both **2** and **2-O₂** with a ratio close to 1:1[‡] have been obtained upon slow diffusion of diethyl ether in a CH_3CN solution of freshly prepared **2-O₂** (the presence of **2** in the crystals will be discussed below). The solid-state structures of both species are depicted in Fig. 1, as well as the structure of the starting material **1**.[45]

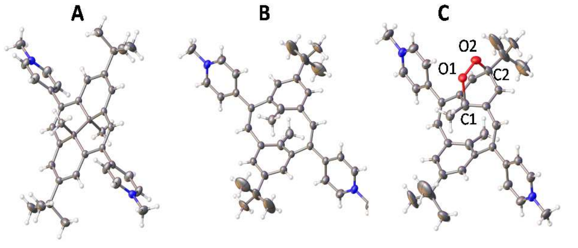

Fig. 1 Molecular structure of **1** (**A**), **2** (**B**) and **2-O₂** (**C**). Thermal ellipsoids are scaled to a 50% probability level. Anions have been omitted for clarity.

In contrast to **1**, featuring a fully planar aromatic skeleton, **2** and **2-O₂** both exhibit highly distorted structures (Fig. 1B,C). For steric reasons, the O_2 adduct in **2-O₂** is only located onto one exo side of the cyclophane. The O1-O2 and the C2-O2 bond lengths in **2-O₂** are 1.49 Å and 1.50 Å, respectively, which are close to the distances measured in analogous metacyclophane endoperoxides,[47] while a much longer distance (1.79 Å) is observed between the C1 and O1 atoms. In order to observe the effect of temperature, annealing experiments have been conducted on a co-crystal of **2** and **2-O₂**. Upon warming at 297 K for 2 days followed by cooling back to 200 K, **2** and **2-O₂** species were no more present and only the structure of the pure parent form **1** was found in the crystal. The regeneration of **1** and the concomitant release of oxygen are thus both achieved at the solid state.

This three-state system has been thoroughly characterized in solution by ^{1}H-NMR spectroscopy (see SI). One key feature is that the opening of the central C–C bond (**1**⟶**2**) results in a large low-field shift of the signal attributed to the chemically equivalent internal methyl groups, *i.e.* from –3.6 ppm to +1.5 ppm. The presence of oxygen on one single benzene ring in **2-O₂** leads to a loss of symmetry which is logically reflected in the observation of two distinct peaks for the internal methyl groups at –0.05 ppm and +2.03 ppm. From integration of the signals, it is seen that photo-irradiation of a 2 mM solution of **1** (as PF_6^- salt) in CD_3CN for 40 min at $\lambda \geq 630$ nm, either under inert atmosphere or in the presence of air (1 atm) led respectively to the formation of **2** and **2-O₂**, both in very high yields (>98%).

The ^{1}H-NMR signals attributed to the terminal N^+-CH_3 substituents can also be conveniently used as diagnostic signals allowing to follow the respective formation of **2** and **2-O₂**. The changes involving these signals observed during irradiation carried out either under argon or in the presence of air are shown in Fig. 2A and 2B

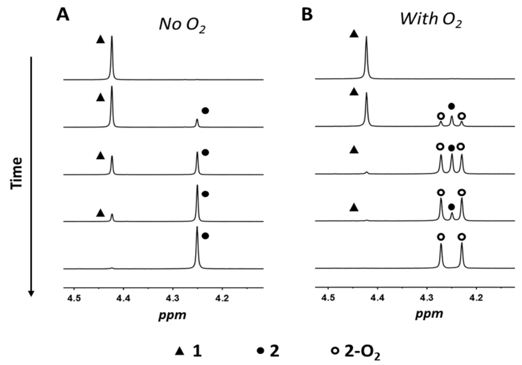

Fig.2 Evolution of the ^{1}H-NMR signals of the N^+-CH_3 groups during irradiation ($\lambda \geq 630$ nm, 200W, 8°C) of **1** (Conc. = 2 mM) in CD_3CN. **A**: under nitrogen and **B**: under air. Black triangles: **1**; black circles: **2**; open circles: **2-O₂**. Final time of irradiation: 30 min.

Under an inert atmosphere (Fig. 2A), the peak observed at +4.43 ppm in the spectrum of **1** progressively vanishes at the expense of a single signal at 4.26 ppm attributed to the terminal N^+-CH_3 substituents in the cyclophanediene **2**. In the presence of air (1 atm, Fig. 2B), both **2** and **2-O₂** are produced in the early stage of the experiment. On a longer time scale, further irradiation leads to a progressive and quantitative conversion of **2** into the oxygenated adduct **2-O₂** which is found as the sole final product, as demonstrated by the observation of two signals only at $\delta = +4.24$ and +4.28 ppm.

This experiment can be interpreted with the mechanism proposed in equations 1-4, which also takes into account the mechanistic data available for this class of photochromes.[36] Visible irradiation of the closed isomer **1** in the ground state (S_0) produces its singlet excited state **1**(S_1) which isomerizes to **2** (eq. 1). The **1**(S_1) level, however, can also undergo intersystem crossing to generate the triplet **1**(T_1) (eq. 2) which is efficiently quenched by oxygen; thus, **1** also plays the role of O_2 sensitizer (eq. 3).[≠] The photogenerated singlet oxygen $O_2(S_1)$ rapidly reacts with **2** to afford the corresponding endoperoxide **2-O₂** (eq. 4). It should be noted that **2** does not absorb the irradiation light and does not react with ground-state oxygen $O_2(T_0)$ under dark conditions. Most importantly, no traces of **1** or **2** have been detected in the final irradiated solution, which further supports the conclusion that the production of $O_2(S_1)$ and its reaction with cyclophanediene **2** are quite efficient. This result, which was *a priori* unexpected because the rate of cycloaddition reactions generally increases when fused rings are involved,[21] can be explained by the large structural constraints occurring within the closed isomer **2**. Formation of the oxygenated bridge in **2-O₂** indeed leads to a drastic change in the hybridization states of the carbon atoms involved in the cycloaddition, from sp^2 to sp^3, which then releases the strain of the twisted 6-membered rings in **2**. Such an effect was previously observed with helianthrene[48] and cyclophanes.[47]

(1) $\mathbf{1}(S_0) + h\nu \rightarrow \mathbf{1}(S_1) \rightarrow \mathbf{2}$
(2) $\mathbf{1}(S_1) \rightarrow \mathbf{1}(T_1)$
(3) $\mathbf{1}(T_1) + O_2(T_0) \rightarrow \mathbf{1}(S_0) + O_2(S_1)$
(4) $O_2(S_1) + \mathbf{2} \rightarrow \mathbf{2\text{-}O_2}$
(5) $\mathbf{2\text{-}O_2} \rightarrow \mathbf{2} + O_2(S_1)$
(6) $O_2(S_1) \rightarrow O_2(T_0) + h\nu'$

It is important to note that, whereas the production of endoperoxide from the simple dimethyldihydropyrene proceeds with low yields and is not workable,[49] the high efficiency of the cycloaddition reaction from **1** demonstrates the utmost importance of the electron withdrawing pyridinium substituents on the oxygen trapping/releasing process. This effect is attributed to a modification of the states order in the DHP photochromic unit upon introduction of the pyridinium groups, *i.e., to a* situation where the electronic excited state initiating the DHP→CPD conversion becomes the lowest excited state.[45] This inversion allows a fast and quantitative formation of the EPO, while operating at low radiant energies and under mild conditions.

The thermal release of O_2 from **2-O₂** (eq. 5) was then investigated using UV-Vis absorption spectroscopy. Upon heating at 35°C, the colorless solution of **2-O₂** in acetonitrile was found to gradually turn red and the UV-visible spectrum of the parent closed form **1** could be fully recovered within a few hours (see SI). The O_2 binding process is thus fully reversible. The cleavage of the peroxidic group has also been monitored by ^{1}H NMR spectroscopy. Fig. 3 displays the relative amount of the different species as a function of time during thermolysis at 35°C.

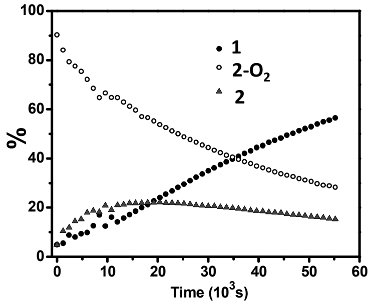

Fig. 3 Evolution of a freshly prepared solution of **2-O₂** (2 mM in CD_3CN) at T = 35°C: plot of the relative concentrations of **1**, **2** and **2-O₂** against time. Percentages of **1** (triangles), **2** (full circles) and **2-O₂** (open circles) were determined by ^{1}H NMR.

The EPO **2-O₂** first releases its O_2 molecule to give the cyclophanediene form **2** which then thermally reverts to the initial DHP form **1** without degradation or formation of rearrangement products. Five cycles of irradiation/oxygenation followed by thermal release have been successfully achieved without notable degradation of the reagents.§

EPR spin trapping experiments[50] have been carried out upon heating a freshly prepared acetonitrile solution of **2-O₂** in the dark and in the presence of 2,2,6,6-tetramethyl-4-piperidone (TEMPD). The production of singlet oxygen was unambiguously demonstrated through the observation of a typical EPR signal assigned to the nitroxide radical generated from the reaction of $^1O_2$ with TEMPD (see SI). This result was further confirmed by luminescence measurements (Fig. 4). A CD_3CN solution of **1** has been exhaustively irradiated to generate quantitatively **2-O₂** and the luminescence in the NIR region has then been monitored at 60°C. As shown in Fig. 4 (inset), the typical phosphorescence peak at 1270 nm corresponding to the spin forbidden transition of singlet oxygen to its ground state (eq. 6)[29,51,52] is observed, confirming that $O_2(S_1)$ has been thermally produced. Under the employed experimental conditions, the phosphorescence signal decayed within *ca.* 50 min.

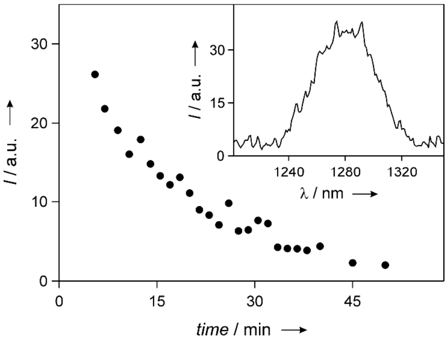

Fig. 4 Time-dependent changes of the luminescence intensity at 1270 nm observed at 60°C for a CD_3CN solution of **2-O₂** (1.9×10^{-3} M), obtained *in situ* upon exhaustive irradiation of **1** with visible light. The emission spectrum of the same solution (inset) shows the characteristic phosphorescence band of $O_2(S_1)$. All these measurements were performed without photo-excitation.

The amount of singlet oxygen produced was quantified using NMR trapping experiments.[18] A freshly prepared solution of **2-O₂** (3 mM) was left at 35°C in the dark in the presence of 2,3-dimethyl-2-butene (90 mM), which is known to react with $O_2(S_1)$ to give a hydroperoxide. Upon thermal relaxation of the EPO solution under dark conditions, the starting **1** was fully recovered and the amount of produced hydroperoxide was quantified by ^{1}H-NMR. A yield of 85±10 % was measured (see SI). Considering that the reaction of $O_2(S_1)$ with 2,3-dimethyl-2-butene is certainly not complete, the amount of singlet oxygen delivered by **2-O₂** is very significant.

In summary, we have used a pyridinium-substituted dimethyldihydropyrene-type reversible molecular photoswitch to capture molecular oxygen and release it in the singlet excited state. Three interconverting forms have been produced and isolated, and a clean oxygen binding and release is evidenced. In comparison with existing similar compounds, this system combines together a number of important practical features: (i) it does not need an external $^1O_2$ photosensitiser, (ii) it uses low energy (red) light, (iii) it is perfectly reversible, and (iv) its physicochemical properties can be finely tuned through subtle modifications of its substitution pattern. Replacing the peripheral methyl groups by functional moieties (grafting groups, polyether chains…) could for instance be used for the preparation of advanced materials or to modify the solubility of the system. Further experiments are currently in progress to accurately investigate the mechanism and kinetics associated with the light- and thermally-induced processes involving these compounds under aerobic conditions.

Notes and references

‡ Note: it has been possible to treat mainly the resulting statistically averaged data as the sum of **2** and **2-O$_2$** with a ratio close to 50%-50%. It is worth noticing that from the X-ray experiment alone, due to symmetry, one could also suppose a third species such as a doubled oxygenated compound, but this hypothesis is clearly rejected from the NMR and the mass spectrometry experiments.

§ Irradiation of **2-O$_2$** by UV light led to a degradation of the system.

≠ Trapping experiments in CD$_3$CN using 3-dimethyl-2-butene as a singlet oxygen trap confirmed that O$_2$(S$_1$) is formed upon irradiation of **1** in the visible region. The final NMR spectrum (see ESI) displays the resonances of free **2** only, confirming the participation of singlet oxygen in the first step of the mechanism.

1 C. Pierlot, J.-M. Aubry, K. Briviba, H. Sies and P. D. Mascio, *in Methods in Enzymology*, Academic Press, 2000.
2 L. F. Agnez-Lima, J. T. A. Melo, A. E. Silva, A. H. S. Oliveira, A. R. S. Timoteo, K. M. Lima-Bessa, G. R. Martinez, M. H. G. Medeiros, P. Di Mascio, R. S. Galhardo and C. F. M. Menck, *Mutat. Res., Rev. Mutat. Res.*, 2012, **751**, 15-28.
3 M. C. DeRosa and R. J. Crutchley, *Coord. Chem. Rev.*, 2002, **233-234**, 351-371.
4 W. Fudickar, A. Fery and T. Linker, *J. Am. Chem. Soc.*, 2005, **127**, 9386-9387.
5 P. R. Ogilby, *Chem. Soc. Rev.*, 2010, **39**, 3181-3209.
6 C. Schweitzer and R. Schmidt, *Chem. Rev.*, 2003, **103**, 1685-1758.
7 A. P. Castano, P. Mroz and M. R. Hamblin, *Nat. Rev. Cancer*, 2006, **6**, 535-545.
8 A. Dewilde, C. Pellieux, S. Hajjam, P. Wattre, C. Pierlot, D. Hober and J.-M. Aubry, *J. Photochem. Photobiol., B*, 1996, **36**, 23-29.
9 J. Park, D. Feng, S. Yuan and H.-C. Zhou, *Angew. Chem. Int. Ed.*, 2015, **54**, 430-435.
10 Y. Tsuji and R. Hoffmann, *Angew. Chem., Int. Ed.*, 2014, **53**, 4093-4097.
11 D. Zehm, W. Fudickar and T. Linker, *Angew. Chem., Int. Ed.*, 2007, **46**, 7689-7692.
12 D. Zehm, W. Fudickar, M. Hans, U. Schilde, A. Kelling and T. Linker, *Chem. Eur. J.*, 2008, **14**, 11429-11441.
13 W. Fudickar and T. Linker, *Langmuir*, 2009, **25**, 9797-9803.
14 W. Fudickar and T. Linker, *Chem. Eur. J.*, 2006, **12**, 9276-9283.
15 V. Nardello and J.-M. Aubry, *Tetrahedron Lett.*, 1997, **38**, 7361-7364.
16 M. Klaper and T. Linker, *Angew. Chem., Int. Ed.*, 2013, **52**, 11896-11899.
17 W. Fudickar and T. Linker, *J. Am. Chem. Soc.*, 2012, **134**, 15071-15082.
18 W. Fudickar and T. Linker, *Chem. Eur. J.*, 2011, **17**, 13661-13664.
19 W. Fudickar and T. Linker, *Langmuir*, 2010, **26**, 4421-4428.
20 W. Fudickar and T. Linker, *Chem. Commun.*, 2008, 1771-1773.
21 J.-M. Aubry, C. Pierlot, J. Rigaudy and R. Schmidt, *Acc. Chem. Res.*, 2003, **36**, 668-675.
22 C. Pierlot and J.-M. Aubry, *Chem. Commun.*, 1997, 2289-2290.
23 J.-M. Aubry, B. Mandard-Cazin, M. Rougee and R. V. Bensasson, *J. Am. Chem. Soc.*, 1995, **117**, 9159-9164.
24 J. Zhang, Z. C. Smith and S. W. Thomas, *J. Org. Chem.*, 2014, **79**, 10081-10093.
25 J. M. Baumes, J. J. Gassensmith, J. Giblin, J.-J. Lee, A. G. White, W. J. Culligan, W. M. Leevy, M. Kuno and B. D. Smith, *Nat. Chem.*, 2010, **2**, 1025-1030.
26 P. Salice, J. Arnbjerg, B. W. Pedersen, R. Toftegaard, L. Beverina, G. A. Pagani and P. R. Ogilby, *J. Phys. Chem. A*, 2010, **114**, 2518-2525.
27 V. Balzani, M. Venturi and A. Credi, *Molecular Devices and Machines*, Wiley-VCH: Weinheim, 2008.
28 B. L. Feringa, W. R. Browne and Editors, *Molecular Switches: Second, Completely Revised And Enlarged Edition*, Wiley-VCH Verlag GmbH & Co. KGaA, 2011.
29 S. Silvi, E. C. Constable, C. E. Housecroft, J. E. Beves, E. L. Dunphy, M. Tomasulo, F. M. Raymo and A. Credi, *Chem. Commun.*, 2009, 1484-1486.
30 L. Hou, X. Zhang, T. C. Pijper, W. R. Browne and B. L. Feringa, *J. Am. Chem. Soc.*, 2014, **136**, 910-913.
31 H. R. Blattmann, D. Meuche, E. Heilbronner, R. J. Molyneux and V. Boekelheide, *J. Am. Chem. Soc.*, 1965, **87**, 130-131.
32 R. H. Mitchell, *Eur. J. Org. Chem.*, 1999, 2695-2703.
33 R. H. Mitchell, T. R. Ward, Y. Chen, Y. Wang, S. A. Weerawarna, P. W. Dibble, M. J. Marsella, A. Almutairi and Z.-Q. Wang, *J. Am. Chem. Soc.*, 2003, **125**, 2974-2988.
34 R. H. Mitchell and S. Bandyopadhyay, *Org. Lett.*, 2004, **6**, 1729-1732.
35 R. H. Mitchell, C. Bohne, Y. Wang, S. Bandyopadhyay and C. B. Wozniak, *J. Org. Chem.*, 2006, **71**, 327-336.
36 C. Bohne and R. H. Mitchell, *J. Photochem. Photobiol., C*, 2011, **12**, 126-137.
37 S. Muratsugu, S. Kume and H. Nishihara, *J. Am. Chem. Soc.*, 2008, **130**, 7204-7205.
38 S. Muratsugu, M.-a. Kishida, R. Sakamoto and H. Nishihara, *Chem. Eur. J.*, 2013, **19**, 17314-17327.
39 M.-a. Kishida, T. Kusamoto and H. Nishihara, *J. Am. Chem. Soc.*, 2014, **136**, 4809-4812.
40 S. Muratsugu and H. Nishihara, *New J. Chem.*, 2014, **38**, 6114-6124.
41 D. Roldan, V. Kaliginedi, S. Cobo, V. Kolivoska, C. Bucher, W. Hong, G. Royal and T. Wandlowski, *J. Am. Chem. Soc.*, 2013, **135**, 5974-5977.
42 S. G. Robinson, V. A. Sauro and R. H. Mitchell, *J. Org. Chem.*, 2009, **74**, 6592-6605.
43 K. Ayub, R. Li, C. Bohne, R. V. Williams and R. H. Mitchell, *J. Am. Chem. Soc.*, 2011, 4040–4045.
44 D. Gust, J. Andreasson, U. Pischel, T. A. Moore and A. L. Moore, *Chem. Commun.*, 2012, **48**, 1947-1957.
45 D. Roldan, S. Cobo, F. Lafolet, N. Vilà, C. Bochot, C. Bucher, E. Saint-Aman, M. Boggio-Pasqua, M. Garavelli and G. Royal, *Chem. Eur. J.*, 2015, **21**, 455-467.
46 M. Quaranta, M. Murkovic and I. Klimant, *Analyst*, 2013, **138**, 6243-6245.
47 T. Sawada, K. Mimura, T. Thiemann, T. Yamato, M. Tashiro and S. Mataka, *J. Chem. Soc. Perkin Trans. 1*, 1998, 1369-1372.
48 M. Seip and H. D. Brauer, *J. Am. Chem. Soc.*, 1992, **114**, 4486-4490.
49 H. Cerfontain, A. Koeberg-Telder, B. H. Bakker, R. H. Mitchell and M. Tashiro, *Liebigs Ann.*, 1997, 873-878.
50 É. Hideg, Z. Deák, M. Hakala-Yatkin, M. Karonen, A. W. Rutherford, E. Tyystjärvi, I. Vass and A. Krieger-Liszkay, *Biochim. Biophys. Acta*, 2011, **1807**, 1658-1661.
51 A. U. Khan and M. Kasha, *Proc. Natl. Acad. Sci.*, 1979, **76**, 6047-6049.
52 H. Wu, Q. Song, G. Ran, X. Lu and B. Xu, *Trends Anal. Chem.*, 2011, **30**, 133-141.