ChemComm

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: M. Uygur, T. Danelzik and O. García Mancheño, *Chem. Commun.*, 2019, DOI: 10.1039/C8CC10239B.

Volume 52 | Number 1 | 4 January 2016 | Pages 1–216

ChemComm

Chemical Communications
www.rsc.org/chemcomm

ISSN 1359-7345

COMMUNICATION
Marilyn M. Olmstead, Alan L. Balch, Josep M. Poblet, Luis Echegoyen et al.
Reactivity differences of $Sc_3N@C_{2n}$ (2n = 68 and 80). Synthesis of the first methanofullerene derivatives of $Sc_3N@D_{5h}$-C_{80}

175 YEARS

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemcomm

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

COMMUNICATION

Metal-Free Desilylative C-C Bond Formation by Visible Light Photoredox Catalysis

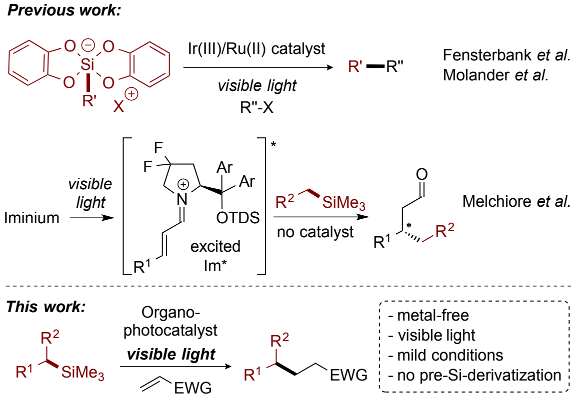
Mustafa Uygur,[a] Tobias Danelzik[a] and Olga García Mancheño*[a]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

A newly developed methodology for the use of organosilanes as radical precursors under metal-free and visible light conditions is presented. The strong oxidant character of the 9-mesityl-10-methylacridinium salt in its excited state enables the transformation of simple silanes to the corresponding carbon-centered radicals, which were trapped by various acceptor molecules.

Visible light photoredox catalysis has gained significant importance in synthetic organic chemistry in the past few years.[1] While a great diversity of photocatalysts for photoreductions and oxidations already exists, the number of substrates acting as alkyl C-radical precursors is still limited.[2] In this regard, halide-containing precursors provide the corresponding radical upon reductive conditions, but they often lead to the formation of halogenated side-products (e.g. via atom transfer radical addition (ATRA) process) and require sacrificial electron donors like amines in excess to close the catalytic cycle.[3] Changing the reactivity to the photooxidation pathway enables the access to alkylic C-radicals by using carboxylic acids (E_{ox} = ~ +1.3 – 2.0 V vs. SCE)[4] and organotrifluoroborates (E_{ox} ~ +1.4 V vs. SCE)[5] in the presence of strong photooxidants, such as Ir(dF-CF$_3$ppy)$_2$(dtbpy)$_3$PF$_6$ ($E^*_{1/2}$ (Ir(III)*/ Ir(II)) = +1.21 V vs. SCE)[6] or 9-mesityl-10-methyl-acridinium salt ($E^*_{1/2}$ (Mes-Acr^{+*}/Mes-Acr$^{\circ}$) = +2.06 V vs. SCE).[7] However, photocatalytic decarboxylation reactions require a base as additive in superstoichiometric amounts, as well as sacrificial electron acceptors such as diphenyldisulfide, which can form further undesired thiol-containing waste during the photoredox process. The problematic production of toxic and corrosive side- compounds, such as BF$_3$, might also appear if the substrate is switched to organotrifluoroborates, which additionally show poor solubility in organic solvents.

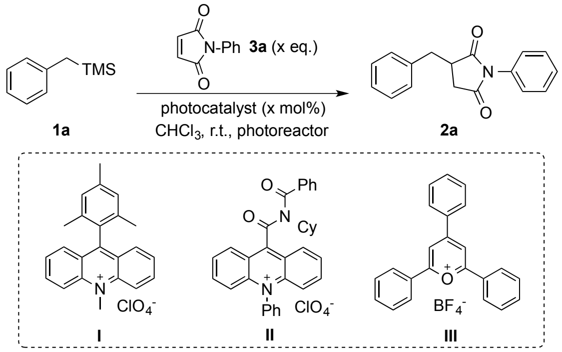
In 2015 and 2016, the groups of Fensterbank[8] and Molander[9] published new methods for the use of organosilicon compounds under visible light conditions (Scheme 1, top).[10] These approaches require an additional synthetic step, which implies the transformation of the organosilanes to the corresponding activated bis(catecholato)silicates. Besides the addition to Michael acceptors,[8a] these intermediates allowed the performance of a broad variety of C-Csp^3 couplings in the presence of additional nickel catalyst.[8-9] Unfortunately, after the photocatalytic transfer of the corresponding alkyl-group, the resulting catecholatosilane/silicate and the stabilizing potassium 18-crown-6 or ammonium counterion remain as waste, which points out a suboptimal atom economy of this methodology. Moreover, expensive Ir(III) or Ru(II) complexes are used as photocatalysts, which leads to another drawback as far as up-scaling of this process is considered. Alternatively, Melchiorre and coworkers reported a photocatalyst-free approach, in which an in situ formed chiral iminium excited species was used to cleave the C-Si bond of organosilanes and allow enantioselective β-alkylation reactions of aldehydes (Scheme 1, middle).[11] In order to address some of the current limitations and expand the use of simple organosilanes as alkyl-radical precursors, we aimed at developing a visible light mediated C-C bond forming methodology in the presence of an organophotocatalyst, without the necessity of a derivatization step at the Si-atom and further additives (Scheme 1, bottom).



Scheme 1. Organosilicon compounds as alkyl-radical precursors.

We started our investigations with the optimization of the oxidative C-Si bond cleavage of the commercially available, cheap and bench-stable benzyltrimethylsilane (**1a**) (Table 1). The redoxpotential of this compound is reported as E_{ox} = +1.68 V vs. SCE in the literature,[12] which induced us to use organophotocatalysts with a highly oxidizing excited state. Therefore, the 9-mesityl-10-methylacridinium perchlorate salt **I** ($E^*_{1/2}$ = +2.06 vs. SCE),[7] the imido-acridinium perchlorate salt **II** ($E^*_{1/2}$ = +2.40 vs. SCE),[13] which was previously developed in our group, and the triphenylpyrylium tetrafluoroborate salt **III** ($E^*_{1/2}$ = +1.9 vs. SCE)[14] were explored. In the presence of organo-photocatalyst **I-III** (10 mol%) and the Michael acceptor *N*-phenylmaleimide (**3a**) (3 equiv.) as trapping reagent, the reaction mixture was stirred for 18 h in CHCl$_3$ under N$_2$ atmosphere by irradiation with a stripe of blue LEDs in the photoreactor. To our

Table 1. Optimization of the photocatalytic C-Si bond cleavage.[a]



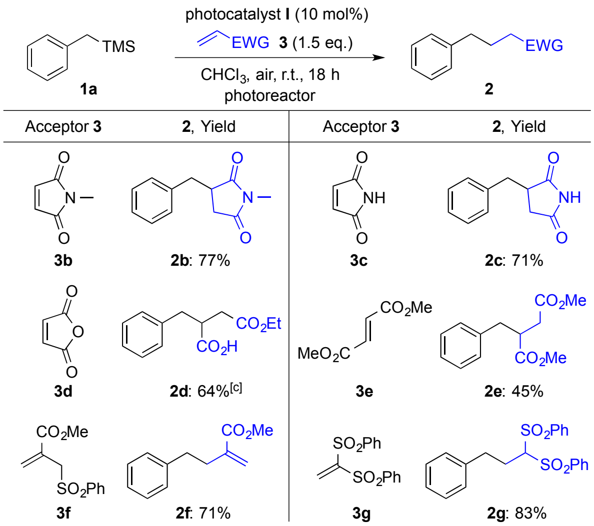
Entry	Cat. (x mol%)	**3a** (x eq.)	Atm.	Yield (%)[b]
1	**I** (10)	3	N_2	30
2	**II** (10)	3	N_2	36
3	**III** (10)	3	N_2	16
4	Na_2-Eosin Y (10)	3	N_2	--[c]
5	Ru(bpy)$_3$(PF$_6$)$_2$ (10)	3	N_2	--[c]
6	**I** (10)	3	air	49
7	**I** (10)	3	O_2	17
8	**I** (5)	3	air	46
9	**I** (2.5)	3	air	35
10	**I** (10)	1.5	air	78

[a] Reactions in 0.2 mmol scale. [b] Isolated yields. [c] Determined by GC-MS.

delight, the desired product could be obtained in all three cases in moderate yields (Table 1, entries 1-3). Both acridinium salts **I** and **II** led to similar results (30 and 36% yield, respectively), while the pyrylium catalyst **III** showed the lowest catalytic activity (16%). Moreover, as expected, the reaction with Na$_2$-Eosin Y ($E^*_{1/2}$ ($EY^{\circ *}/EY^{\circ -}$) = +0.83 V *vs.* SCE).[15] or Ru(bpy)$_3$(PF$_6$)$_2$ ($E^*_{1/2}$ (Ru(III)*/Ru(II)) = +0.77 V *vs.* SCE)[6] gave no conversion (entries 4-5). Due to the availability as well as its better solubility in chloroform, catalyst **I** was used for further optimization. The atmosphere was then changed from nitrogen to air and oxygen (entries 6-7), which resulted in an increase of the yield to 49% when air was used. However, a significant drop to 17% was obtained when the reaction was performed under oxygen. We assume that the regeneration efficiency of the reduced photocatalyst is enhanced by the reaction with oxygen that leads to the in situ formation of the super-oxide radical anion ($O_2^{\bullet -}$),[16] which might be generated in too high concentrations under pure oxygen atmosphere, leading to a large number of undesired side-products by radical chain processes. Next, the catalyst loading was evaluated (entries 8-9). A small decrease of the yield was obtained when 5 mol% of catalyst **I** was used, while 2.5 mol% gave **2a** in only 35%. Pleasantly, a decrease to 1.5 equivalents of **3a** gave the best results of 78% yield (entry 10). Furthermore, a short solvent screening showed that in comparison to CHCl$_3$ all the other tested solvents gave the desired product in notably lower yields (see S.I. for details).

With these results in hand, the scope of applicable Michael acceptors was explored (Table 2). Thus, the *N*-methyl protected (**3b**) and the unprotected maleimide (**3c**) gave the corresponding products **2** in good yields (71-77%). Switching to the closely related maleic anhydride (**3d**), as well as to the open form dimethyl fumarate (**3e**), gave us the dicarboxylic and diacid monoester[17] coupling products in moderate to good yields. Furthermore, the functional group tolerance was tested by the use of the acceptor molecules phenylsulfonylmethylacrylate (**3f**) and sulfonylethylene (**3g**). In both cases, the desired compounds **2f** and **2g** were obtained in high yields (71 and 83%, respectively) without the occurrence of any side-products from the interaction of either the silane **1a** or the radical intermediate with the functional groups.

Table 2. Scope of the Michael trapping reagents **3**.[a],[b]



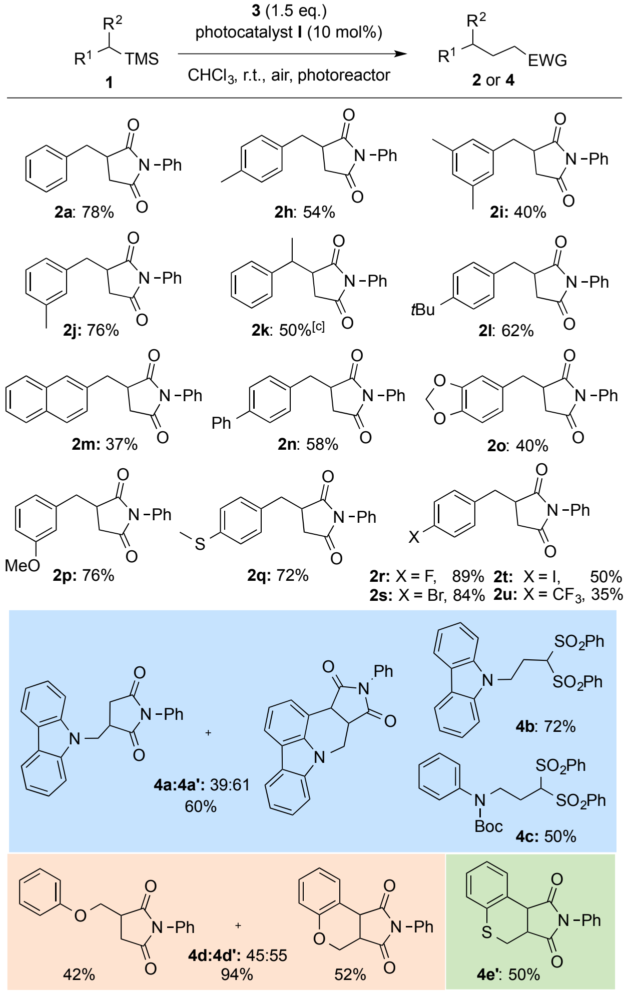
[a] All reactions in a 0.2 mmol scale. [b] Isolated yields. [c] From ring-opening and esterification of **3d** (Note: the used p.a. CHCl$_3$ contains 0.5-1% EtOH).

Under the optimized conditions, a library of alkyl-trimethylsilanes with various substitution patterns and electronic properties were next applied in the desilylative C-C bond formation reaction with **3a** (Table 3). We were pleased to see that the coupling products could be obtained in moderate to good yields for neutral and electron-rich benzylsilanes **1h-r**. Different methyl substituted derivatives were initially investigated, showing that mainly all the positions at the aromatic system (**2h-j**, 40-76%) as well as at the benzylic site (**2k**, 50%) were well tolerated. This might be not only caused by the higher production of side-products, but also by the steric hindrance of the formed radical by the neighbouring methyl group. The reaction with other alkyl (4-*t*BuC$_6$H$_4$, **1l**) and aryl (2-naphtyl, **1m** or 4-PhC$_6$H$_4$, **1n**) substituted benzylsilanes also proceeded smoothly, providing the corresponding products **2l-n**. Furthermore, the reaction of benzylsilanes with strong electron-donating cyclic ketal (**1o**), methoxy (**1p**) and methylsulfide (**1q**) substituents, which are known to lower the redoxpotential of the aromatic system and lead to further side-products in the presence of strongly oxidizing conditions, led to the desired products in up to 76% yield. Additionally, excellent chemo-selectivity was observed in the case of **1q**, which occurred without formation of the corresponding sulfoxide by oxidation of the functional group. Halogen-substituents, such as fluoride, bromide and iodine, led to the coupling products in good yields (**2r-t**, 89%, 84% and 50%, respectively), while the more demanding electron-poor substrates,

View Article Online
DOI: 10.1039/C8CC10239B

such as the 4-CF$_3$ derivative **1u** provided **2u** in a moderate 35% yield. Finally, other organosilanes bearing an amine, thioether or ether functionality were also efficiently enrolled (50-94% overall yields, **4a-e**). Interestingly, in the reactions between **3a** and this type of substrates with electron rich aromatic substituents, a subsequent ring-closing process was observed, leading to a tricyclic species **4a'**, **4d'** and **4e'** as the major or sole product.

Table 3. Scope of the benzyltrimethylsilane derivatives **1**.[a],[b]



[a] Reactions in a 0.2 mmol scale. [b] Isolated yields. [c] Obtained in a 79:21 d.r.

Motivated by these results, we decided to analyse the mechanism of the photocatalytic process (Scheme 2). Initially, fluorescence experiments were carried out by excitation of catalyst Mes-Acr **I** at 420 nm and measuring the corresponding fluorescence in the presence of different amounts of silane **1a** as quencher (Q) (Figure 2).[18] As already predicted, a decay in the fluorescence was observed upon addition of increasing concentrations of the quencher, which also evidences that the singlet excited state of the photocatalyst is responsible for the reactivity. To prove that the reaction is photocatalyzed and not initiated by radical chain processes caused by the homolytic cleavage of the C-Cl-bond of chloroform to the corresponding chlorine and trichloromethane radical, a test reaction in BrCCl$_3$ as a radical starter was next performed (Scheme 2, eq. 1).[19] No conversion of **1a** could be achieved in the absence of the photocatalyst and only traces of product could be obtained in the presence of **I**.[20] Moreover, we determined the fluorescence quantum yield for the standard reaction as 0.92 (see S.I.), which confirms our presumption that a radical chain propagation is not the predominant pathway ($\Phi \leq 1$). We then focused on the detection of the radical intermediate formed by the oxidation of the C-Si bond. Therefore, the standard reaction of **1a** with **3a** in the presence of the photocatalyst **I** under visible light irradiation was conducted with 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO) (1.1 equiv.) of as additive (Scheme 2). We were pleased to observe the TEMPO-adduct **6** of the radical-intermediate **5**, as well as the homo-coupling **7**, by GC-MS analysis. However, we were not able to detect the TEMPO adduct of intermediate **8**, since the reactivity of this species is much higher than that of the radical **5**.

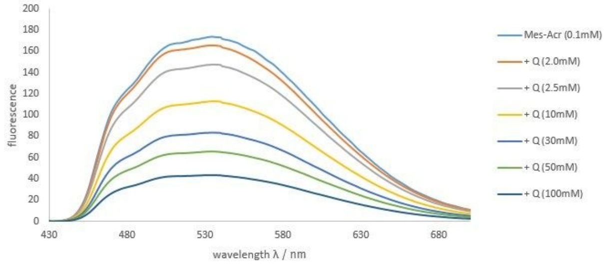


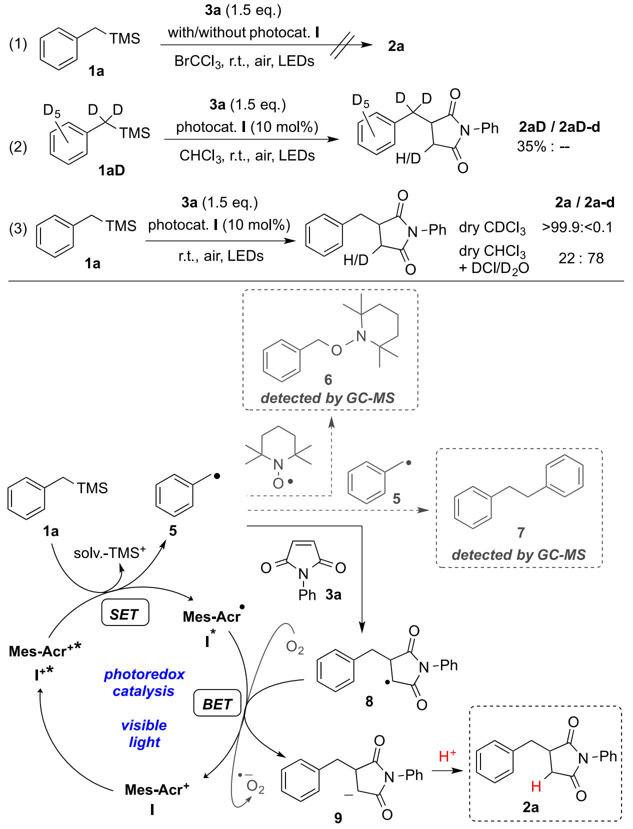
Figure 2. Fluorescence quenching of **I** by different concentrations of **1a** (Q).

Our control experiments (see S.I., Table S7) indicated the importance of the presence of small amounts of HCl, formed presumably by the decomposition of CHCl$_3$ over the time under light and moisture exposure. Thus, when freshly distilled CHCl$_3$ was used, low conversions and the formation of 8% of the radical homocoupling product **7** were observed. Moreover, extra-added H$_2$O generally hampered the reaction (see S.I. TS6-7).[21] We were then interested in identifying the source of the necessary proton for the formation of the products **2** and **4a-c**. Therefore, deuterium-labelling experiments were carried out. While the formation of the deuterated product **2aD-d** or **2a-d** was not observed in the reaction with benzylTMS-d7 (Scheme 2, eq. 2) or with dry CDCl$_3$ as solvent (Scheme 2, eq. 3), the use of CHCl$_3$ in the presence of DCl in D$_2$O resulted in the formation of **2a-d** as the major compound in a **2a**:**2a-d** 22:78 ratio (Scheme 2, eq. 3).[21] Moreover, the blank reaction using HCl as potential promoter without the presence of the catalyst and light irradiation did not proceed (see S.I., TS7).

With these results in hand, a postulated reaction mechanism is outlined in Scheme 2 (bottom). The excitation of the catalyst in its ground state Mes-Acr$^+$ **I** by absorption of visible light generates the photoexcited state **I**$^{+*}$. In this state, **I**$^{+*}$ is able to oxidize the C-Si bond of **1** by a single electron transfer (SET) to form the radical intermediate **5** and the reduced catalyst **I**$^{\bullet}$ after desilylation promoted by a weak nucleophilic solvent (e.g. 0.5-1% of EtOH present in CHCl$_3$ or water).[22] Radical **5** adds to the double bond of the acceptor **3** to form the radical **7**. Then, a back-electron transfer (BET) from **I**$^{\bullet}$ to **8**, forming the anionic intermediate **9** and regenerating the photocatalyst **I** in its ground state, closes the catalytic cycle.[16] Finally, the product **2** is formed after the protonation of **9** by traces of HCl present in the solvent.

Conclusions

In summary, we were able to develop a novel application of simple organosilanes as radical precursors in visible light photoredox aerobic catalysis in the presence of an organophotocatalyst for C-C bond formation reactions, without the necessity of an additional Si-atom derivatization/activation step or external additives. The scope of the applied organosilanes and Michael acceptors proved the excellent functional group tolerance of this process. In addition, quenching and deuterium experiments were performed to enlighten the reaction mechanism, in which the singlet excited state of the catalyst is responsible for the reactivity and traces of HCl in the solvent might facilitate the final protonation step.



Scheme 2. Mechanistic investigations and proposed mechanism. Solv: solvent or H_2O

Notes and references

[a] *Münster University, Organic Chemistry Institute, Corrensstraße 40, 48149 Münster, Germany. Fax: +49 251 83 36503; E-mail: olga.garcia@uni-muenster.de*

† Electronic Supplementary Information (ESI) available: Full optimization screeing, experimental procedure and mechanistic studies, analytical data and NMR collection of new compounds. See DOI: 10.1039/b000000x/

WWU Münster is gratefully acknowledged for generous support.

1 a) C. R. J. Stephenson, T. P. Yoon and D. W. C. MacMillan, *Visible Light Photocatalysis in Organic Chemistry*, Wiley-VCH, 2018, Weinheim. Selected reviews: a) K. Zeitler, *Angew. Chem. Int. Ed.*, 2009, **48**, 9785-9789; b) J. M. R. Narayanam and C. R. J. Stephenson, *Chem. Soc. Rev.*, 2011, **40**, 102-113; c) J. Xuan and W.-J. Xiao, *Angew. Chem. Int. Ed.*, 2012, **51**, 6828-6838; d) D. Ravelli, M. Fagnoni and A. Albini, *Chem. Soc. Rev.*, 2013, **42**, 97-113; e) C. K. Prier, D. A. Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322-5363; f) X. Lang, J. Zhao and X. Chen, *Chem. Soc. Rev.*, 2016, **45**, 3026-3038; g) J. Xie, H. Jinb and A. S. K. Hashmi, *Chem. Soc. Rev.*, 2017, **46**, 5193-5203; h) I. K. Sideri, E. Voutyritsaa and C. G. Kokotos, *Org. Biomol. Chem.*, 2018, **16**, 4596-4614. See also: i) Special Issue on photoredox catalysis: *Eur. J. Org. Soc.*, 2017, issue **15**, 1978.

2 a) L. Fensterbank, J.-P. Goddard and C. Ollivier, *Visible-Light-Mediated Free Radical Synthesis*, In *Visible Light Photocatalysis in Organic Chemistry*, Wiley-Blackwell, 2018, p. 25-71; b) J.-P. Goddard, C. Ollivier and L. Fensterbank, *Acc. Chem. Res.*, 2016, **49**, 1924-1936; c) J. D. Nguyen, E. M. D'Amato, J. M. R. Narayanam and C. R. J. Stephenson, *Nat. Chem.*, 2012, **4**, 854-859.

3 See e.g.: a) T. Courant and G. Masson, *J. Org. Chem.* 2016, **81**, 6945-6952; b) L. Marzo, S. K. Pagire, O. Reiser and B. König, *Angew. Chem. Int. Ed.*, 2018, **57**, 10034-10072.

4 See e.g.: J. D. Griffin, M. A. Zeller and D. A. Nicewicz, *J. Am. Chem. Soc.*, 2015, **137**, 11340-11348.

5 See e.g.: I. Karakaya, D. N. Primer and G. A. Molander, *Org. Lett.*, 2015, **17**, 3294-3297.

6 C. K. Prier, D. A Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322-5363.

7 a) S. Fukuzumi, H. Kotani, K. Ohkubo, S. Ogo, N. V. Tkachenko and H. Lemmetyinen, *J. Am. Chem. Soc.*, 2004, **126**, 1600-1601; b) A. Joshi-Pangu, F. Lévesque, H. G. Roth, S. F. Oliver, L.-C. Campeau, D. Nicewicz and D. A. DiRocco, *J. Org. Chem.*, 2016, **81**, 7244-7249.

8 a) V. Corcé, L.-M. Chamoreau, E. Derat, J.-P. Goddard, C. Olliver and L. Fensterbank, *Angew. Chem. Int. Ed.*, 2015, **54**, 11414-11418. See also: b) C. Lévêque, L. Chenneberg, V. Corcé, C. Ollivier and L. Fensterbank, *Chem. Commun.*, 2016, **52**, 9877-9880; c) C. Lévêque, L. Chenneberg, V. Corcé, J.-P. Goddard, C. Ollivier and L. Fensterbank, *Org. Chem. Front.*, 2016, **3**, 462-465; d) L. Chenneberg, C. Lévêque, V. Corcé, A. Baralle, J.-P. Goddard, C. Ollivier and L. Fensterbank, *Synlett,* 2016, **27**, 731-735; e) C. Lévêque, V. Corcé, L. Chenneberg, C. Ollivier and L. Fensterbank, *Eur. J. Org. Chem.*, 2017, 2118-2121.

9 a) M. Jouffroy, D. N. Primer and G. A. Molander, *J. Am. Chem. Soc.*, 2016, **138**, 475-478. See also: b) N. R. Patel, C. B. Kelly, M. Jouffroy and G. A. Molander, *Org. Lett.*, 2016, **18**, 764-767; c) M. Jouffroy, G. H. M. Davies and G. A. Molander, *Org. Lett.,* 2016, **18**, 1606-1609; d) N. R. Patel and G. A. Molander, *J. Org. Chem.*, 2016, **81**, 7271-7275; e) K. Lin, R. J. Wiles, C. B. Kelly, G. H. M. Davies and G. A. Molander, *ACS Catal.*, 2017, **7**, 5129-5133; f) S. Zheng, D. N. Primer and G. A. Molander, *ACS Catal.*, **2017**, **7**, 7957-7961.

10 See also: T. Guo, L. Zhang, X. Liu, Y. Fang, X. Jin, Y. Yang, Y. Li, B. Chen and M. Ouyang, *Adv. Synth. Catal.*, 2018, **360**, 4459-4463. For a UV-mediated photocatalytic C-Si cleavage/coupling, see: S. Montanaro, D. Ravelli, D. Merli, M. Fagnoni and A. Albini, *Org. Lett.*, 2012, **14**, 4218-4221.

11 a) M. Silvi, C. Verrier, Y. P. Rey, L. Buzzetti and P. Melchiorre, *Nat. Chem.*, 2017, **9**, 868-873. For an intramolecular organophoto-catalytic reaction with imines, see: b) M. K. Jackl, L. Legnani, B. Morandi and J. W. Bode, *Org. Lett.*, 2017, **19**, 4696-4699.

12 T. Maruyama, Y. Mizuno, I. Shimizu, S. Suga and J.-I. Yoshida, *J. Am. Chem. Soc.*, 2007, **129**, 1902-1903.

13 A. Gini, M. Uygur, T. Rigotti, J. Alemán and O. García Mancheño, *Chem. Eur. J.*, 2018, **24**, 12509-12514.

14 N. A. Romero and D. A. Nicewicz, *Chem. Rev.*, 2016, **116**, 10075-10166.

15 D. P. Hari and B. König, *Chem. Commun.*, 2014, **50**, 6688-6699.

16 S. Fukuzumi and K. Ohkubo, *Org. Biomol. Chem.*, 2014, **12**, 6059-6071. Mechanistically O_2 is not required, but beneficial to facilitate the regeneration of the catalysts into its ground state.

17 Exposure of the maleic anhydride to the standard reaction conditions led to the maleic acid mono-ethylester, as the actual Michael acceptor.

18 It is reported that the excited-state of **I** is only able to oxidize electron-rich olefins, not being quenched by acceptors like **3**: K. A. Margrey and D. A. Nicewicz, *Acc. Chem. Res.*, 2016, **49**, 1997-2006.

19 J. F. Franz, W. B. Klaus and K. Zeitler, *Chem. Commun.*, 2015, **51**, 8280-8283.

20 No conversion of **1a** was observed in the presence of H_2O_2, which could be produced in the catalytic cycle under aerobic conditions.

21 Freshly distilled dry solvents or the presence of H_2O led to notable lower yields (14-23% vs. 78%), whereas the addition of aq. HCl did not improve the outcome (see TS6 in S.I.), suggesting that as much as ~1-2% vol. of HCl and/or H_2O hampers the reaction.

22 K. P. Dockery, J. P. Dinnocenzo, S. Farid, J. L. Goodman, I. R. Gould and W. P. Todd, *J. Am. Chem. Soc.* 1997, **119**, 1876-1883.