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Eosin Y catalyzed difunctionalization of styrenes using O_2 and CS_2: a direct access to 1,3-oxathiolane-2-thiones†

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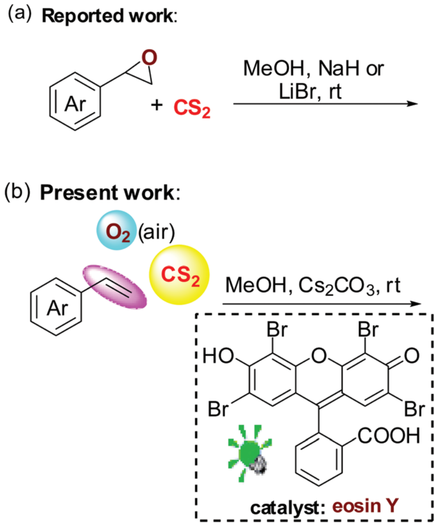
Visible light promoted straightforward highly regioselective synthesis of 1,3-oxathiolane-2-thiones (cyclic dithiocarbonates) starting directly from styrenes, CS_2 and air (O_2) is reported. The protocol utilizes eosin Y as an organophotoredox catalyst and clean resources like visible light and air (O_2) as sustainable reagents at room temperature in a one-pot procedure. Additionally, the approach is advantageous in terms of step economy as it skips the prefunctionalization of styrenes to oxiranes, which has been inevitable in commonly used syntheses of 1,3-oxathiolane-2-thiones.

Introduction

The utilization of clean, cheapest and unending natural resources like air, water and light is among the basic demands of green and sustainable chemistry.[1] During the last two decades, free radical reactions have played a crucial role in the construction of useful molecular frameworks.[2] This is mainly because of the availability of new methods for producing radicals, which have allowed the targeted use of these reactive intermediates in organic syntheses. The recent research on visible light promoted synthetically useful photoredox reactions has opened up a new facet of free radical chemistry.[3] Advantageously, several visible light photoredox catalyzed reactions utilize atmospheric dioxygen to complete the catalytic cycle and the resulting superoxide radical ($O_2^{\bullet-}$) acts as an oxidant required in the synthesis.[4]

The 1,3-oxathiolane moiety is present in a variety of biologically active compounds and natural products.[5] They show antibacterial, tuberculostatic, antifungal,[5c–f] and neuroprotective activities.[5,6] Moreover, 1,3-oxathiolane-2-thiones (cyclic dithiocarbonates) are useful intermediates for the synthesis of alkanes, alkenes, and thiols and have found application in materials science.[7] One of the most efficient methods available for the synthesis of cyclic dithiocarbonates involves the ring opening of oxiranes catalyzed by alkali metals or alcoholates (Scheme 1a).[8] However, all of these methods suffer from one or more drawbacks, such as low efficiency and yields, requirement of high pressure, high catalyst loading and above all, the formation of regioisomeric products, which limit their synthetic applications. Thus, the development of a highly regioselective, efficient and convenient method for the synthesis of 1,3-oxathiolane-2-thiones will be a valuable contribution to this field.



Scheme 1 Synthesis of 1,3-oxathiolane-2-thiones.

Styrenes are readily available substrates, which allow the introduction of two functional groups in a single step. Consequently, several communications have appeared exploring the difunctionalization of styrenes.[3a,9,10b] Recently, anionic species like $ArSO_2^-$,[10a] NCS^- [10b,c] and $RN{=}CRS^-$ [10d] have been converted to the corresponding radicals under photoredox catalysis.[10] Inspired by the fact that sulfur compounds can be

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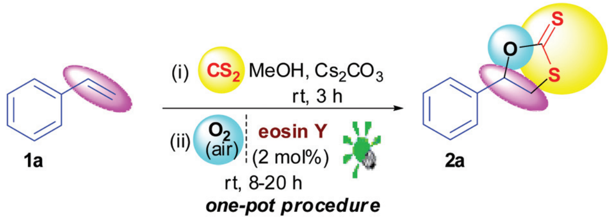
easily converted into radicals employing eosin Y (EY) as a visible light photoredox catalyst,[10,11] we hypothesized that the xanthate anion formed *in situ* from CS_2 and alcoholates could be converted into its radicals, which could be trapped with styrenes and finally cyclized under aerobic conditions to give 1,3-oxathiolane-2-thiones.

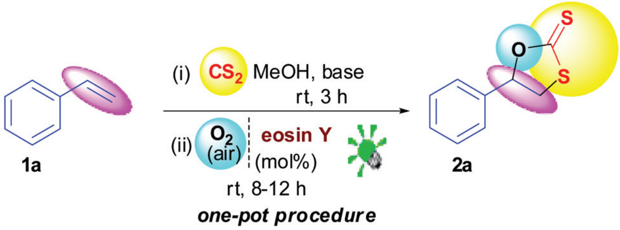
Table 1 Control experiments[a]



Entry	Visible light	Eosin Y	MeOH	Base	CS_2	Air (O_2)	Time[b] (h)	Yield[c] (%)
1	+	+	+	+	+	+	20	90[d]
2	+	+	+	+	+	+	8	92
3	–	+	+	+	+	+	12	n.d.
4	+	–	+	+	+	+	12	n.d.
5	+	+	–	+	+	+	12	n.d.[e]
6	+	+	+	–	+	+	12	Trace
7	+	+	+	+	–	+	12	n.d.
8	+	+	+	+	+	N_2	12	Trace
9	+	+	+	+	+	O_2	8	92[f]
10	+	+	+	+	+	+	12	60[g]

[a] Reaction conditions: CS_2 (1.0 mmol), Cs_2CO_3 (1.0 equiv.) and MeOH (3 mL) were taken in a closed flask and stirred for 3 h at rt, then **1a** (1.0 mmol) and eosin Y (2 mol%) were added and the flask was opened to air. Now, the reaction mixture was irradiated using Luxeon Rebel high power green LEDs [2.50 W, λ = 535 nm] under an air atmosphere at rt for 8–20 h (for the general procedure, see the ESI). [b] Time required for photo-irradiation. [c] Isolated yield of the pure product **2a**; n.d. = not detected. [d] A mixture of **1a** (1.0 mmol), an excess amount of CS_2 (1.0 mL), Cs_2CO_3 (1.0 equiv.) and eosin Y (2 mol%) in MeOH (3 mL) was irradiated with green LEDs [2.50 W, λ = 535 nm] under an air atmosphere at rt for 20 h. [e] Acetonitrile was used instead of MeOH. [f] O_2 balloon was used. [g] Reaction mixture was irradiated with a CFL (Philips 18 W).

Table 2 Optimization of reaction parameters[a]



Entry	Catalyst (mol%)	Solvent	CS_2 (mmol)	Base (equiv.)	Time[b] (h)	Yield[c] (%)
1	Eosin Y (2)	MeOH	1.0	Cs_2CO_3 (1.0)	8	92
2	Rose bengal (2)	MeOH	1.0	Cs_2CO_3 (1.0)	8	63
3	Eosin Y (3)	MeOH	1.0	Cs_2CO_3 (1.0)	8	92
4	Eosin Y (1)	MeOH	1.0	Cs_2CO_3 (1.0)	8	60
5	Eosin Y (2)	MeOH	1.0	Cs_2CO_3 (0.5)	12	54
6	Eosin Y (2)	MeOH	1.0	Cs_2CO_3 (1.5)	8	92
7	Eosin Y (2)	MeOH	0.5	Cs_2CO_3 (1.0)	8	44
8	Eosin Y (2)	MeOH	1.5	Cs_2CO_3 (1.0)	8	92
9	Eosin Y (2)	MeOH	1.0	K_2CO_3 (1.0)	12	64
10	Eosin Y (2)	MeOH	1.0	KOH (1.0)	12	67
11	Eosin Y (2)	MeOH	1.0	Na_2CO_3 (1.0)	12	52
12	Eosin Y (2)	MeOH	1.0	NaH (1.0)	12	79

[a] Reaction conditions: CS_2 (0.5–1.5 mmol), Cs_2CO_3 (0.5–1.5 equiv.) and MeOH (3 mL) were taken in a closed flask and stirred for 3 h at rt, then **1a** (1.0 mmol) and eosin Y (1–3 mol%) were added and the flask was opened to air. Now, the reaction mixture was irradiated using Luxeon Rebel high power green LEDs [2.50 W, λ = 535 nm] under an air atmosphere at rt for 8–12 h (for the general procedure, see the ESI). [b] Time required for photo-irradiation. [c] Isolated yield of the pure product **2a**.

In view of the above points and our recent research focused on the aerobic oxidative difunctionalization of alkenes,[9c,10b,12] herein we report a novel synthesis of 1,3-oxathiolane-2-thiones. The present protocol is more advantageous than the available methods in terms of step economy and sustainability because it starts from styrene instead of oxiranes and utilizes atmospheric oxygen and visible light as the greenest reagents (Scheme 1b).

Results and discussion

To test our idea and optimize the reaction conditions, styrene (**1a**) was selected as the model substrate. The key reaction was performed with a mixture of **1a** (1.0 mmol), an excess amount of CS_2 (1.0 mL), Cs_2CO_3 (1.0 equiv.) and a catalytic amount of eosin Y (2 mol%) in MeOH (3 mL). The reaction mixture was irradiated with green LEDs [2.50 W, λ = 535 nm] for 20 h in open air under stirring at room temperature. The desired product 1,3-oxathiolane-2-thione (**2a**) was isolated in 90% yield (Table 1, entry 1). A large excess (1.0 mL) of CS_2 was required probably because of its high volatility and vaporization during the reaction. One of the referees indicated that CS_2 is not really a green compound, and its high volatility is easy to control. This led us to modify the procedure.

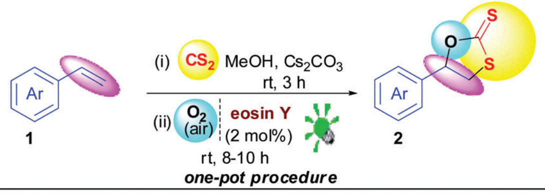
Thus, CS_2 (1.0 mmol), Cs_2CO_3 (1.0 equiv.) and MeOH (3 mL) were taken in a closed flask and stirred at room temperature for 3 h to complete the formation of cesium methyl xanthate ($\mathrm{MeO{-}\overset{\overset{S}{\|}}{C}{-}S^{-}Cs^{+}}$). Then, styrene (**1a**, 1.0 mmol) and eosin Y (2 mol%) were added to the open flask and the reaction mixture was irradiated with green LEDs [2.50 W, λ = 535 nm] for 8 h in open air under stirring at room temperature. We were delighted to get the desired product **2a** in 92% isolated yield (Table 1, entry 2). Then the control experiments were carried out, which show that eosin Y, visible light, air (O_2), CS_2, MeOH and a base are essential for the reaction, because in the absence of any of the reagents/reaction parameters the product was either not detected or formed in traces (Table 1, entry 1 *versus* 3–8).

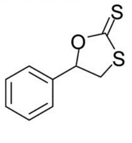
The presence of O_2 (air) is also essential for the reaction because only a trace amount of product was detected under a nitrogen atmosphere (Table 1, entry 8). Notably, the same result was obtained on using O_2 (balloon) instead of an air atmosphere (Table 1, entry 9). Green LEDs [2.50 W, λ = 535 nm] were more effective than fluorescent light (Table 1, entry 10), which shows the higher photocatalytic activity of eosin Y in the presence of high intensity green light.

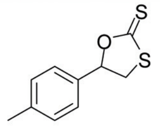
Next, the reaction was optimized for the optimum amount of CS_2, base and catalyst using MeOH as the solvent, which also acts as a reagent for xanthate formation in step i. For the reasonable yield, CS_2 was required in 1.0 mmol (Table 2, entry 1 *versus* 7 and 8). Among the tested bases, Cs_2CO_3 was most efficient (Table 2, entry 1 *versus* 9–12), this is probably because of the greater solubility of Cs_2CO_3 in MeOH and its 1.0 equiv. was required for optimum yield (Table 2, entry 1 *versus* 5 and 6). The optimum catalyst (eosin Y) loading required for the maximum yield was 2 mol%, because on decreasing the amount from 2 mol% to 1 mol% decreases the yield considerably, although the yield was not affected on increasing the catalyst loading from 2 mol% to 3 mol% (Table 2, entry 1 *versus* 3 and 4). The use of rose bengal (2 mol%) was not as effective as eosin Y (Table 2, entry 1 *versus* 2).

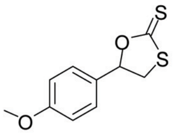
Finally, the generality and scope of the present reaction were investigated across a range of styrenes incorporating various substituents like Me, MeO, NO_2, Cl, Br and F (Table 3).

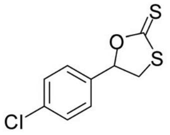
Table 3 Scope of the reaction[a]

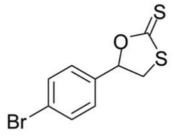


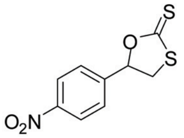

2a: 92%[b,c], 8 h[d]

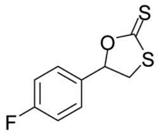

2b: 93%, 8 h

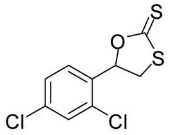

2c: 95%, 8 h

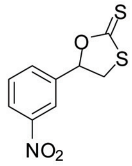

2d: 78%, 10 h

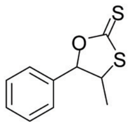

2e: 80%, 10 h

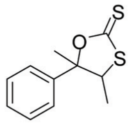

2f: 68%, 10 h

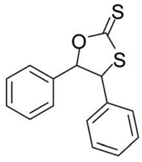

2g: 73%, 10 h

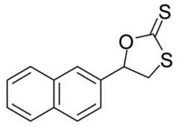

2h: 70%, 10 h

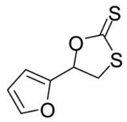

2i: 72%, 10 h

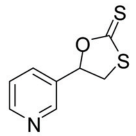

2j: 84%, 8 h


2k: 86%, 8 h


2l: 94%, 8 h


2m: 90%, 8 h


2n: 79 %, 10 h


2o: 70 %, 10 h

[a] Reaction conditions: CS_2 (1.0 mmol), Cs_2CO_3 (1.0 equiv.) in 3 mL MeOH were taken in a closed flask and stirred for 3 h at rt, then **1** (1.0 mmol) and eosin Y (2 mol%) were added and the flask was opened to air. Now, the reaction mixture was irradiated using Luxeon Rebel high power green LEDs [2.50 W, λ = 535 nm] under an air atmosphere at rt for 8–10 h. [b] Isolated yield of the product **2**. [c] For the general procedure, experimental details and characterization data of the products, see the ESI. [d] Time required for photo-irradiation (step (ii)).

The reaction worked well in all the cases and afforded the desired products **2** in good to excellent yields (68–95%). Styrenes **1** with an electron-donating group on the aromatic ring appear to react faster and afford marginally higher yields in comparison with those bearing an electron-withdrawing group (Table 3, products **2b**, **2c** *versus* **2d**–**2i**). However, the reaction does not work with aliphatic alkenes, this is probably because of the less stability of the radical intermediate formed with aliphatic alkenes than that in the case of styrenes. Moreover, the greater stability of the radical formed at the α-position of an aromatic or heteroaromatic ring plausibly governs the high regioselectivity in the formation of product **2**. The efficacy of this reaction was also evaluated on a preparative scale (50 mmol). Thus, a mixture of CS_2 (50.0 mmol, 3.5 mL), Cs_2CO_3 (1.0 equiv., 8.15 g) and MeOH (150 mL) was taken in a closed flask and stirred at room temperature for 3 h. Then, styrene (**1a**, 50.0 mmol, 5.78 g) and eosin Y (2 mol%, 0.652 g) were added and the flask was open to air. The reaction mixture was irradiated with green LEDs [2.50 W, $\lambda = 535$ nm] for 8 h in open air under stirring at room temperature. Interestingly, the product **2a** was isolated in excellent yield (94%, 9.21 g) without compromising the optimized reaction conditions.

Conclusion

In conclusion, we have disclosed a one-pot multicomponent cyclization strategy for a highly regioselective synthesis of 1,3-oxathiolane-2-thiones from styrenes using CS_2, MeOH and Cs_2CO_3 in the presence of eosin Y as a photocatalyst at room temperature. The salient features of the present protocol include the step economy, organophotoredox catalysis and utilization of clean resources, like air (O_2) and visible light as inexpensive, green and sustainable reagents, which make it a superior alternative to the existing approaches to 1,3-oxathiolane-2-thiones.

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Notes and references

1 R. A. Sheldon, *Green Chem.*, 2007, **9**, 1273 and references cited therein.

2 For recent reviews, see: (*a*) J.-T. Yu and C. Pan, *Chem. Commun.*, 2016, **52**, 2220; (*b*) A. Studer and D. P. Curran, *Nat. Chem.*, 2014, **6**, 765; (*c*) C.-L. Sun and Z.-J. Shidx, *Chem. Rev.*, 2014, **114**, 9219.

3 For recent reviews on visible-light-photoredox catalysis, see: (*a*) M.-Y. Cao, X. Ren and Z. Lu, *Tetrahedron Lett.*, 2015, **56**, 3732; (*b*) J. Xiea, H. Jina, P. Xua and C. Zhu, *Tetrahedron Lett.*, 2014, **55**, 36; (*c*) D. A. Nicewicz and T. M. Nguen, *ACS Catal.*, 2014, **4**, 355; (*d*) X. Lang, X. Chen and J. Zhao, *Chem. Soc. Rev.*, 2014, **43**, 473; (*e*) M. Reckenthäler and A. G. Griesbeck, *Adv. Synth. Catal.*, 2013, **355**, 2727; (*f*) D. Rovelli, M. Fagnoni and A. Albini, *Chem. Soc. Rev.*, 2013, **42**, 97; (*g*) J. Hu, J. Wang, T. H. Nguyen and N. Zheng, *Beilstein J. Org. Chem.*, 2013, **9**, 1977; (*h*) Y. Xi, H. Yia and A. Lei, *Org. Biomol. Chem.*, 2013, **11**, 2387; (*i*) J. Xuan, L.-Q. Lu, J.-R. Chen and W.-J. Xiao, *Eur. J. Org. Chem.*, 2013, 6755; (*j*) J. Xuan and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 6828; (*k*) J. W. Tucker and C. R. J. Stephenson, *J. Org. Chem.*, 2012, **77**, 1617; (*l*) L. Shi and W. Xia, *Chem. Soc. Rev.*, 2012, **41**, 7687; (*m*) Y.-Q. Zou, J.-R. Chen, X.-P. Liu, L.-Q. Lu, R. L. Devis, K. A. Jorgensen and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 784; (*n*) S. Maity and N. Zheng, *Synlett*, 2012, 1851; (*o*) J. M. R. Narayanam and C. R. J. Stephenson, *Chem. Soc. Rev.*, 2011, **40**, 102.

4 For recent articles in support of the super oxide radical as the oxidant, see: (*a*) A. K. Yadav and L. D. S. Yadav, *Tetrahedron Lett.*, 2015, **56**, 686; (*b*) A. K. Yadav and L. D. S. Yadav, *Tetrahedron Lett.*, 2015, **56**, 6966; (*c*) A. K. Yadav and L. D. S. Yadav, *Tetrahedron Lett.*, 2014, **55**, 2065; (*d*) V. P. Srivastava, A. K. Yadav and L. D. S. Yadav, *Tetrahedron Lett.*, 2014, **55**, 1788; (*e*) C. L. Mathis, B. M. Gist, C. K. Frederickson, K. M. Midkiff and C. C. Marvin, *Tetrahedron Lett.*, 2013, **54**, 2101; (*f*) S. Zhu and M. Rueping, *Chem. Commun.*, 2012, **48**, 11960; (*g*) D. B. Freeman, L. Furst, A. G. Condie and C. R. J. Stephenson, *Org. Lett.*, 2012, **14**, 94; (*h*) D. A. DiRocco and T. Rovis, *J. Am. Chem. Soc.*, 2012, **134**, 8094; (*i*) G. Zhao, C. Yang, L. Guo, H. Sun, C. Chen and W. Xia, *Chem. Commun.*, 2012, **48**, 2337; (*j*) M. Rueping, R. M. Koenigs, K. Poscharny, D. C. Fabry, D. Leonori and C. Vila, *Chem. – Eur. J.*, 2012, **18**, 5170; (*k*) M. Rueping, S. Zhu and R. M. Koenigs, *Chem. Commun.*, 2011, **47**, 8679; (*l*) M. Rueping, S. Zhu and R. M. Kónigs, *Chem. Commun.*, 2011, **47**, 12709; (*m*) J. Xuan, Y. Cheng, J. An, L.-Q. Lu, X.-X. Zhang and W.-J. Xiao, *Chem. Commun.*, 2011, **47**, 8337.

5 For biological activities of 1,3-oxathiolanes, see: (*a*) M. T. Konieczny, W. Konieczny, M. Sabisz, A. Skladanowski, R. Wakiec, E. Augustynowicz-Kopec and Z. Zwolska, *Chem. Pharm. Bull.*, 2007, **55**, 817; (*b*) J. B. Jaquith, G. Villeneuve, P. Bureau and A. Boudreault, *Worldwide Patent*, 2005012281, 2005; (*c*) T. Kikuchi, T. Mizukoshi and T. T. Niki, *Japanese Patent*, 2002226463, 2002; *Chem. Abstr.*, 2002, **137**, 154930 (*d*) L. D. S. Yadav, R. K. Tripathi, R. Dwivedi and H. Singh, *J. Agric. Foo. Chem.*, 1992, **40**, 1700; (*e*) Y. Aizawa, T. Kanai, K. Hasegawa, T. Yamaguchi, T. Iizuka, T. Iwaoka and T. Yoshioka, *J. Med. Chem.*, 1990, **33**, 1491; (*f*) V. Nair, B. Mathew, A. U. Vinod, J. S. Mathen, S. Ros, R. S. Menon, R. L. Varma and R. Srinivas, *Synthesis*, 2003, 662;

(*g*) K. K. Sowa Denko, *Japanese Patent*, 6006680, 1985.*Chem. Abstr.*, 1985, **102**, 166730.

6 (*a*) F. R. Bisogno, A. Cuetos, I. Lavandera and V. Gotor, *Green Chem.*, 2009, **11**, 452; (*b*) X. Lv, Y. Liu, W. Qian and W. Baoa, *Adv. Synth. Catal.*, 2008, **350**, 2507; (*c*) A. Bellomo and D. Gonzalez, *Tetrahedron Lett.*, 2007, **48**, 3047; (*d*) W. Fathalla, J. Marek and P. Pazdera, *J. Heterocycl. Chem.*, 2002, **39**, 1139; (*e*) M. Noboru, T. Masaaki, M. Osamu, T. Yoshikazu and Y. Shigeo, *Tetrahedron Lett.*, 1989, **30**, 2259; (*f*) L. Raphaelian, H. Hooks and G. Ottmann, *Angew. Chem.*, 1967, **79**, 315, (*Angew. Chem., Int. Ed.*, 1967, **79**, 363).

7 (*a*) M. Isola, E. Ciuffarin and L. Sangromora, *Synthesis*, 1976, 326; (*b*) D. H. R. Barton and S. W. Combie, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1574; (*c*) H. R. Nace, *Org. React.*, 1962, **12**, 57.

8 (*a*) I. Yavari, M. G. Darjani, Z. Hossaini, M. Sabbaghan and N. Hosseini, *Synlett*, 2008, 889; (*b*) N. Kihara, Y. Nakawaki and T. Endo, *J. Org. Chem.*, 1995, **60**, 473.

9 (*a*) L. Song, S. Luo and J.-P. Cheng, *Org. Chem. Front.*, 2016, **3**, 447; (*b*) K. Wang, L.-G. Meng, Q. Zhang and L. Wang, *Green Chem.*, 2016, **18**, 2864; (*c*) T. Keshari, V. K. Yadav, V. P. Srivastava and L. D. S. Yadav, *Green Chem.*, 2014, **16**, 3986; (*d*) D. P. Hari, T. Hering and B. König, *Angew. Chem., Int. Ed.*, 2014, **53**, 725; (*e*) R. Tomita, Y. Yasu, T. Koike and M. Akita, *Angew. Chem., Int. Ed.*, 2014, **53**, 7144; (*f*) A. Carboni, G. Dagousset, E. Magnier and G. Masson, *Org. Lett.*, 2014, **16**, 1240; (*g*) S. H. Oh, Y. R. Malpani, N. Ha, Y.-S. Jung and S. B. Han, *Org. Lett.*, 2014, **16**, 1310; (*h*) B. Sahoo, M. N. Hopkinson and F. Glorius, *J. Am. Chem. Soc.*, 2013, **135**, 5505; (*i*) G. Fumagalli, S. Boyd and M. F. Greaney, *Org. Lett.*, 2013, **15**, 4398; (*j*) Q. Lu, J. Zhang, G. Zhao, Y. Qi and H. Wang, *J. Am. Chem. Soc.*, 2013, **135**, 114; (*k*) Q. Jiang, W. Sheng and C. Guo, *Green Chem.*, 2013, **15**, 2175.

10 (*a*) A. U. Meyer, S. Joger, D. P. Hari and B. Konig, *Adv. Synth. Catal.*, 2015, **357**, 2050; (*b*) A. K. Yadav and L. D. S. Yadav, *Green Chem.*, 2015, **17**, 3515; (*c*) W. Fan, Q. Yang, F. Xu and P. Li, *J. Org. Chem.*, 2014, **79**, 10588; (*d*) Y. Cheng, J. Yang, Y. Qu and P. Li, *Org. Lett.*, 2012, **14**, 98.

11 For photocatalytic applications of eosin Y, see: (*a*) S. Mitra, M. Ghosh, S. Mishra and A. Hajra, *J. Org. Chem.*, 2015, **80**, 8275; (*b*) V. P. Srivastava;, A. K. Yadav and L. D. S. Yadav, *Synlett*, 2013, 465; (*c*) A. K. Yadav;, V. P. Srivastava and L. D. S. Yadav, *New J. Chem.*, 2013, **37**, 4119; (*d*) M. Majek and A. J. von Wanglin, *Chem. Commun.*, 2013, **49**, 5507; (*e*) D. P. Hari and B. König, *Org. Lett.*, 2011, **13**, 3852.

12 (*a*) A. K. Singh, R. Chawla and L. D. S. Yadav, *Tetrahedron Lett.*, 2014, **55**, 4742; (*b*) A. K. Singh, R. Chawla, T. Keshari, V. K. Yadav and L. D. S. Yadav, *Org. Biomol. Chem.*, 2014, **12**, 8550; (*c*) R. Chawla, A. K. Singh and L. D. S. Yadav, *Eur. J. Org. Chem.*, 2014, 2032; (*d*) A. K. Singh, R. Chawla and L. D. S. Yadav, *Tetrahedron Lett.*, 2014, **55**, 2845.