Green Chemistry

PAPER

View Article Online
View Journal | View Issue

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.

Cite this: *Green Chem.*, 2014, **16**, 3787

Received 10th April 2014,
Accepted 8th May 2014

DOI: 10.1039/c4gc00647j

www.rsc.org/greenchem

Visible-light-induced photocatalytic formyloxylation reactions of 3-bromooxindoles with water and DMF: the scope and mechanism†

You-Quan Zou,[a] Wei Guo,[a] Feng-Lei Liu,[a] Liang-Qiu Lu,[a] Jia-Rong Chen*[a] and Wen-Jing Xiao*[a,b]

The formyloxylation reaction of 3-bromooxindoles with water and *N*,*N*-dimethylformamide (DMF) has been developed in the presence of the photoredox catalyst *fac*-Ir(ppy)$_3$ under irradiation of visible light at ambient temperature. The reaction provides a straightforward approach to pharmaceutically and synthetically useful 3-formyloxyoxindoles in high yields. The mechanism of this transformation was investigated by fluorescence quenching experiments, "on–off" switching of the light source, labeling experiments, mass spectral analyses and *in situ* IR experiments.

Introduction

A major goal for the advancement of modern organic chemistry is the development of efficient, atom economical, sustainable and selective methodologies that allow the rapid construction of structurally complex and functionally diverse molecular architectures from readily available starting materials.[1,2] In this regard, photoredox catalysis using visible light has emerged as a novel and powerful strategy for molecular bond activations to construct intricate molecules, and demonstrated great potential in the past several years.[3] The asymmetric alkylation of aldehydes and the [2 + 2] cycloaddition of enones constitute landmark achievements in this area,[4,5] which enabled other elegant research studies.[6–9] Despite these significant advances, visible light photoredox catalysis has not reached its full potential. The implementation of clean and commercially available compounds in visible light photoredox catalysis toward intricate molecules is highly desirable.

N,*N*-Dimethylformamide (DMF), which often serves as a polar reaction medium, is also widely used as a multipurpose feedstock in organic synthesis.[10] Chemists have developed many new methods for the incorporation of DMF into small molecules forming basic building blocks for elaboration into biologically relevant molecules and pharmaceutically important compounds. For example, Chang *et al.* reported a highly regioselective palladium catalyzed cyanation of aryl C–H bonds by employing DMF as the "C" source and ammonia as the "N" source of the –CN unit.[11] In 2010, the group of Tsuji described an intermolecular hydroamidation of alkynes catalyzed by palladium using DMF as the reaction partner.[12] Notably, Jiao and co-workers realized an alternative way for the direct cyanation of indole and benzofuran rings using DMF as the "CN" source, leading to valuable aryl nitriles with excellent selectivities.[13] Recently, other interesting reactions involving DMF as a precursor were also conducted.[14] The first example applying DMF to visible light photoredox catalysis was reported by the Stephenson group. They successfully converted alcohols to the corresponding bromides and iodides *via* a Vilsmeier–Haack intermediate under mild reaction conditions.[15,16]

On the other hand, water has often been regarded as an ideal reagent as a result of its "green chemistry" features.[17] We envisioned that the development of new multicomponent reactions that assemble DMF, water and other reactants into valuable compounds under the irradiation of visible light should be highly useful. As part of our ongoing research program directed at the applications of visible light photoredox catalysis for organic synthesis,[18] we disclose herein a novel and efficient visible light induced radical addition/oxidation/hydrolysis cascade which gives 3-formyloxyoxindoles from 3-bromooxindoles, DMF and water (Scheme 1). This transformation can directly install a formyloxy group at the C3-position of oxindoles using DMF as the "H, C, O" source and H$_2$O as the "O" source, and the corresponding products can be used in the

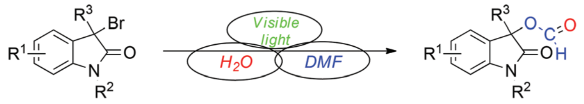
---

[a] *Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, 152 Luoyu Road, Wuhan, Hubei 430079, China. E-mail: wxiao@mail.ccnu.edu.cn; Fax: +86 27 67862041; Tel: +86 27 67862041*

[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

† Electronic supplementary information (ESI) available: Experimental procedures and compound characterisation data, including X-ray crystal data for **2a**. CCDC 937531. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4gc00647j

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.



Scheme 1 Concept of the visible-light-induced photocatalytic formyloxylation reactions of 3-bromooxindoles with water and DMF.

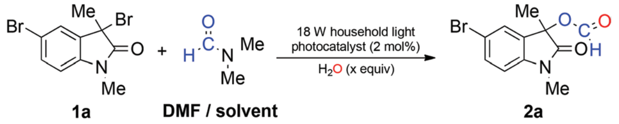
synthesis of natural alkaloids and pharmaceuticals.[19–21] Mechanism studies have been performed by fluorescence quenching experiments, "on–off" switching of the light source, labeling experiments, mass spectral analyses and *in situ* IR experiments.

Results and discussion

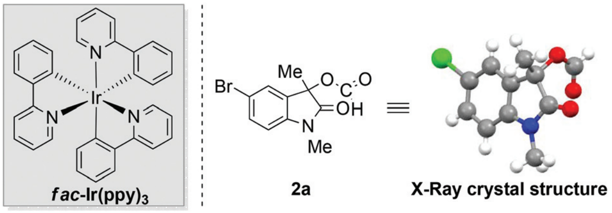
Reaction optimization

We commenced our investigation of the visible light photoredox three-component reaction using 3,5-dibromo-1,3-dimethylindolin-2-one **1a** and DMF, along with 2 mol% photocatalyst *fac*-Ir(ppy)$_3$, and an 18 W fluorescent household light bulb. This initial experiment gave the desired product **2a** in 62% isolated yield after workup (Table 1, entry 1), and the structure of **2a** was unambiguously established by X-ray crystallographic analysis. Control experiments showed that a trace amount of product, or no product at all, was obtained in the absence of either the photocatalyst or the light source, which indicated that this transformation proceeded *via* a visible light catalytic pathway (entries 2 and 3). Encouraged by these preliminary results, we then embarked on optimizing the reaction conditions to improve the yield of **2a**. Firstly, an extensive screening of photocatalysts was conducted and it was found that *fac*-Ir(ppy)$_3$ was still the best choice (entry 1 *vs.* entries 4–9). Subsequent investigation of the light source such as 3 W blue LEDs gave comparable results with somewhat prolonged reaction time (entry 10). When H_2O (5.0 equiv.) was added to the reaction mixture, the model reaction was completed within 4 h and the yield was increased to 70% (entry 11). Finally, doubling the water equivalent further reduced the reaction time to 2.5 h and increased the yield of **2a** to 79%.

Table 1 Results of the experiments on optimization of reaction conditions[a]



Entry	Photocatalyst[b]	H_2O (x)	Time (h)	Yield[c] (%)
1	*fac*-Ir(ppy)$_3$	—	7	62
2	—	—	24	Trace
3[d]	*fac*-Ir(ppy)$_3$	—	24	0
4	[Ru(bpy)$_3$Cl$_2$]·6H_2O	—	24	Trace
5	Ir(ppy)$_2$(dtbbpy)PF$_6$	—	24	44
6	Ir(ppy)$_2$(bpy)PF$_6$	—	24	31
7	[Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)](PF$_6$)	—	24	9
8	Ru(bpm)$_3$(BArF)$_2$	—	24	Trace
9	Eosin Y	—	24	Trace
10[e]	*fac*-Ir(ppy)$_3$	—	8	62
11	*fac*-Ir(ppy)$_3$	5	4	70
12	***fac*-Ir(ppy)$_3$**	**10**	**2.5**	**79**



[a] The reactions were carried out on a 0.2 mmol scale of **1a** with 2 mol% of photocatalyst and H_2O (x equiv.) in DMF (2.0 mL). [b] See the ESI for the detailed structures of the photocatalysts. [c] Isolated yields. [d] Reaction was carried out in the dark. [e] 3 W blue LEDs were used as the light source. DMF: *N*,*N*-dimethylformamide.

Substrate scope

The generality of the visible light induced assembly of 3-bromooxindoles, DMF and water was investigated under the optimal reaction conditions using 2 mol% *fac*-Ir(ppy)$_3$. As shown in Table 2, this reaction tolerates a wide range of 3-bromooxindoles and various 3-formyloxyoxindoles were obtained in moderate to excellent yields upon isolation. For example, electron-withdrawing, electron-neutral and electron-donating substitution patterns on the aromatic rings all performed well, furnishing the corresponding products in 42–87% yields (Table 2, entries 1–8). It is noteworthy that halogen substituents such as F, Cl, and Br on the benzene ring were compatible with the photoredox process. Products **2a**, **2c–2f** might be further modified at the halogenated positions using transition-metal catalyzed cross-coupling reactions.[22] Meanwhile, we have also tested the C-4-Br substituted substrate; unfortunately, we could not detect the desired product. It was also found that the group at the C-3 position of the oxindole skeleton might be extended to ethyl, isopropyl, butyl as well as longer-chain octyl groups. These substrates reacted smoothly to give the desired products in good yields (93–96% yields, entries 9–12). Cyclic substituents such as cyclopentyl and cyclohexyl are also suitable for this transformation and give good results (entries 13 and 14). In addition, the feasibility of this methodology could also be realized for 3-bromooxindoles bearing an allyl or a phenyl group at the C-3 position with somewhat lower yields (entries 15 and 16). Structural variation in the nitrogen protected groups did not affect the reaction efficiency and compounds containing *N*-H, Bn, 4-Me-Bn and allyl groups in **1q–1t** gave the products in 83–91% yields (entries 17–20), while the presence of an acylated group gave a complex mixture (entry 21).

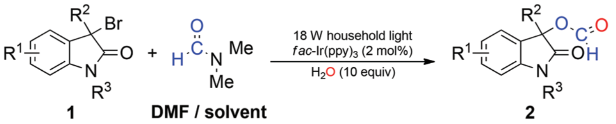
Insight into the catalytic mechanism of the visible light induced formyloxylation reaction

While a precise reaction mechanism awaits further study, we now propose a possible catalytic cycle to explain the generation of 3-formyloxyoxindoles. As illustrated in Scheme 2, the photocatalyst *fac*-Ir(ppy)$_3$ was first excited to the highly active species

This journal is © The Royal Society of Chemistry 2014

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.

Table 2 Substrate scope[a]



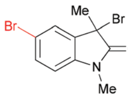
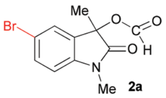
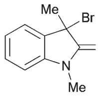
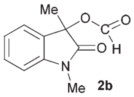
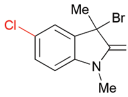
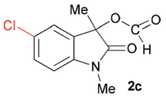
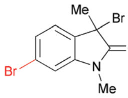
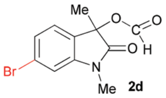
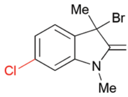
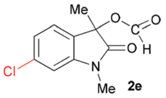
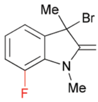
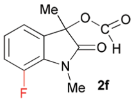
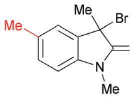
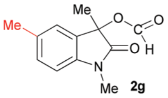
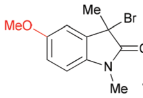
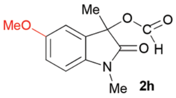
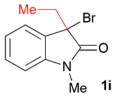
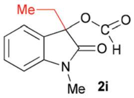
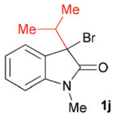
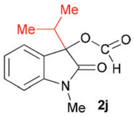
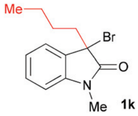
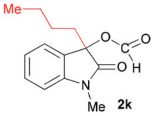
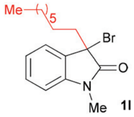
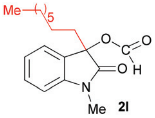
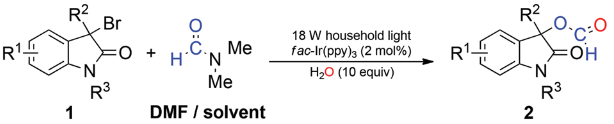
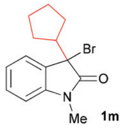
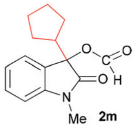
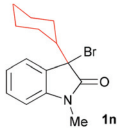
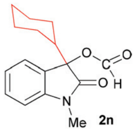
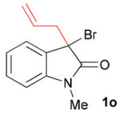
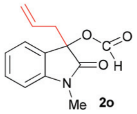
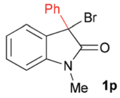
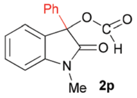
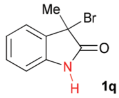
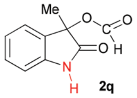
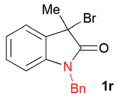
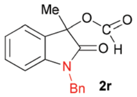
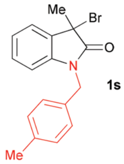
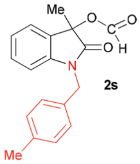
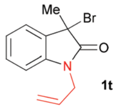
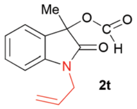
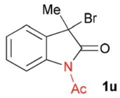
Entry	1	Time (h)	2	Yield[b] (%)
1[c]	 1a	2.5	 2a	79
2	 1b	3	 2b	79
3	 1c	6	 2c	68
4	 1d	2.5	 2d	84
5	 1e	2.5	 2e	83
6	 1f	3.5	 2f	42
7	 1g	2.5	 2g	87
8	 1h	10	 2h	83
9	 1i	3	 2i	96
10	 1j	3	 2j	93
11	 1k	4	 2k	93
12	 1l	8	 2l	93

Table 2 *(Contd.)*



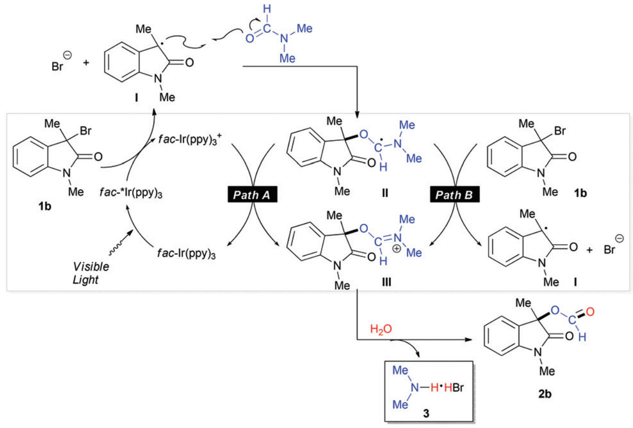
Entry	1	Time (h)	2	Yield[b] (%)
13	 1m	3	 2m	80
14	 1n	3	 2n	88
15	 1o	3.5	 2o	78
16	 1p	11.5	 2p	40
17	 1q	2.5	 2q	83
18	 1r	2.5	 2r	89
19	 1s	3	 2s	86
20	 1t	3	 2t	91
21	 1u	—	—	N.D.

[a] Reactions were carried out on a 0.4 mmol scale of **1** with 2 mol% of *fac*-Ir(ppy)$_3$ and H_2O (10 equiv.) in DMF (2.0 mL). [b] Isolated yields. [c] The reactions were carried out on a 0.2 mmol scale of **1a**. DMF: *N*,*N*-dimethylformamide; N.D.: not determined.

fac-*Ir(ppy)$_3$ by the irradiation of visible light, which was then reacted with alkyl bromide **1b**, resulting in the formation of the radical intermediate **I** with the release of bromide ions and

View Article Online

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.



Scheme 2 Possible mechanism for the visible light induced three-component assembly of 3-bromooxindoles, DMF and water.

fac-Ir(ppy)$_3^+$ by an oxidative quenching cycle. Subsequently, radical addition reaction between the intermediate **I** and *N*,*N*-dimethylformamide took place, giving the radical intermediate **II**. The next step may involve the oxidation of intermediate **II** to the iminium ion **III** by two possible pathways: (a) the intermediate **II** is oxidized by *fac*-Ir(ppy)$_3^+$ regenerating the ground state *fac*-Ir(ppy)$_3$ to complete the catalytic cycle (path A); (b) the intermediate **II** is oxidized by another molecule **1b**, affording the iminium ion **III** and the radical intermediate **I** through a chain-propagation mechanism (path B). Finally, hydrolysis of **III** gave the terminal product **2b** accompanying dimethylaminehydrobromide **3** as the byproduct. It is worth mentioning that an extra base is not needed to neutralize HBr, because the dimethylamine derived from DMF could serve as a base to capture the acid HBr.

In order to shed some light on the above mechanism, a series of experiments including fluorescence quenching experiments, "on–off" switching of the light source and labeling experiments, MS analyses as well as *in situ* IR studies were carried out.

(1) Fluorescence quenching experiments. To gain some insight into the proposed catalytic mechanism in which electron transfer from excited state *fac*-*Ir(ppy)$_3$ to the substrate **1b** would occur, fluorescence quenching experiments (Stern–Volmer studies) of *fac*-Ir(ppy)$_3$ were carried out. We were pleased to observe that the fluorescence intensity decreased with increasing concentration of **1b** (Fig. 1a).[23] The maximum emission wavelength (λ_{em}) for *fac*-Ir(ppy)$_3$ was about 520 nm, and the data at this wavelength were selected for the Stern–Volmer plot (Fig. 1b). As shown in Fig. 1, a linear relationship between I_0/I and the concentration of **1b** was observed at low concentrations (I_0 and I are the fluorescence intensities before and after the addition of **1b**, Fig. 1d). At high concentrations, the Stern–Volmer plot exhibited an upward curvature, concave toward the *y*-axis (Fig. 1c). These results strongly indicate that the photoexcited state *fac*-*Ir(ppy)$_3$ was quenched by **1b** *via* electron transfer, and static and dynamic quenching might occur simultaneously in this reaction system.[24]

(2) "On–off" switching of the light source. As depicted in Scheme 2, a radical-chain propagation process was also possible for this visible light induced transformation (Scheme 2, path B). In order to gain some information about this reaction pathway, we performed the experiment on the on–off switching of the light source in the reaction of **1b**, DMF and water. We initially removed the light source after 20 minutes when the yield of **1b** was approximately 13% under the standard con-

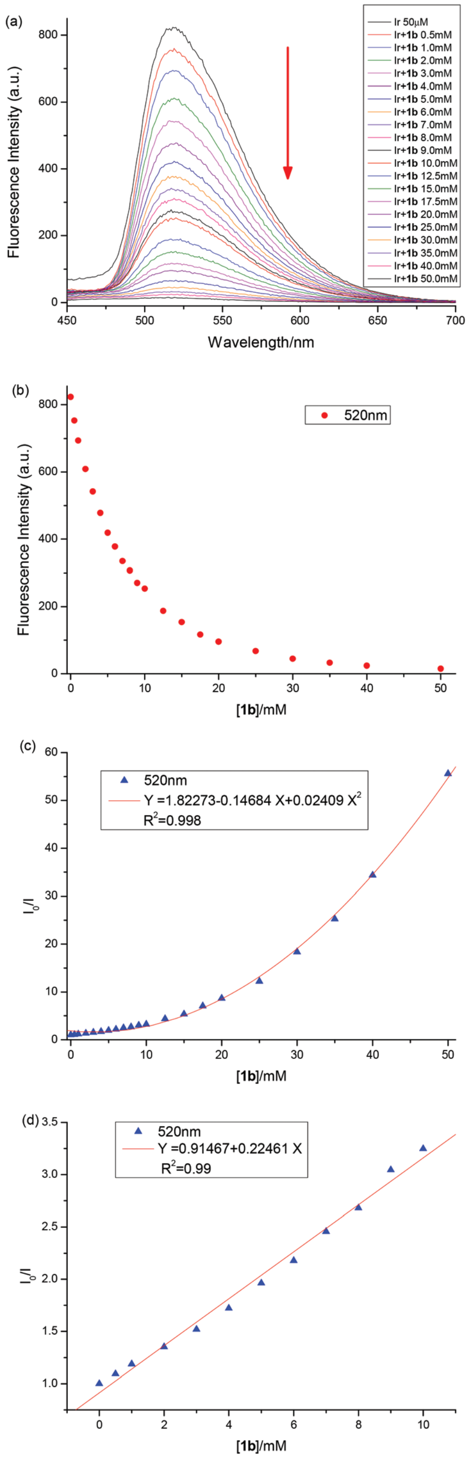


Fig. 1 Fluorescence quenching (Stern–Volmer) studies between *fac*-Ir(ppy)$_3$ and **1b**.

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.

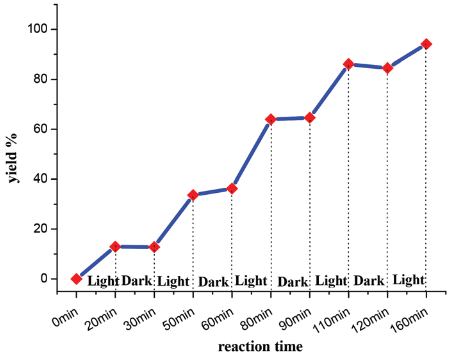
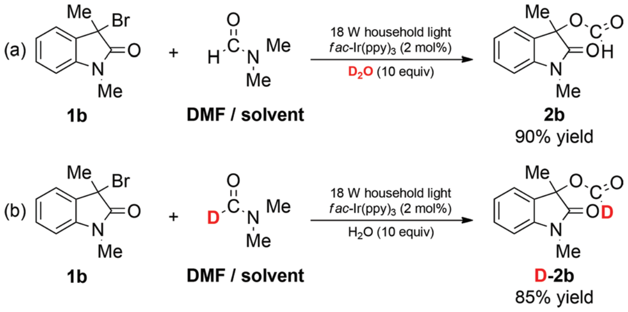


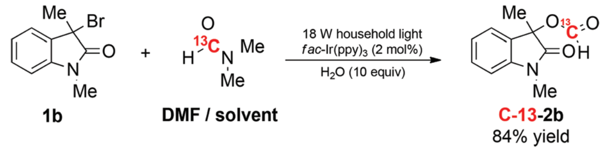
Fig. 2 Time profile of the visible light induced assembly of **1b**, DMF and water.

ditions (GC yield, using *n*-tetradecane as the internal standard).[23] It was found that no further progress was observed after stirring in the dark for 10 minutes (Fig. 2). Importantly, the reintroduction of the visible light source for 20 minutes led to the further conversion of **1b** to the desired product **2b** in 34% yield (GC yield). The "on–off" cycle could be repeated many times until the full consumption of **1b** took place. This phenomenon demonstrated that the visible light induced three-component reactions required continuous irradiation with visible light, although the radical chain mechanism cannot be ruled out in this reaction system.[25]

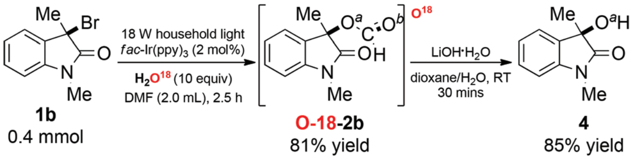
(3) Labeling experiments and ESI-MS analyses. To better understand the "C, H, O" source of the formyloxy group, we performed a series of labeling experiments. Treatment of **1b** with 10 equivalents of deuterium oxide under the optimal reaction conditions resulted in no deuterium product (Scheme 3a). Interestingly, when *N*,*N*-dimethylformamide-d1 (98 atom% D) was used as the reaction partner, almost complete isotope incorporation occurred into the final product **2b** in 85% yield (Scheme 3b). Thus, the hydrogen atom of the formyloxy group unambiguously originated from *N*,*N*-dimethylformamide (DMF). The deuterium product was further confirmed by HRMS analysis.[23]



Scheme 3 Results of deuterium experiments.



Scheme 4 Results of C-13 labeling experiments.



Scheme 5 Results of O-18 labeling experiments.

Next, in order to confirm that the "C" of the formyloxy group at the C3-oxindole position also arose from DMF, we conducted the following C-13 labeling experiment. It was found that the carbon of the formyloxy group was wholly from DMF (Scheme 4), which implied that the carbonyl moiety of DMF is an efficient carbon source of "OCHO" in the present protocol. Meanwhile, mass spectrometric data were also recorded and integrated with the NMR spectroscopic analysis.[23] These results further support our proposed mechanism.

To better understand the source for the two oxygen atoms, we carried out O-18 labeling experiments (Scheme 5). Using water-18O (97% atom) as the reaction partner, the O-18 labeling product was obtained in 81% isolated yield under the optimized reaction conditions. However, we cannot identify which oxygen atom was labeled at this stage. So the O-18 labeling product was further hydrolyzed to the corresponding 3-hydroxyl oxindole **4** under basic conditions, and the O-18 labeling hydrolyzed product was not observed based on HRMS analysis. These results revealed that O^a was from DMF, and O^b originated from water.[23]

(4) Possible byproduct. As depicted in Scheme 2, the possible byproduct is dimethylaminehydrobromide **3**, which might be a salt dissolved in the aqueous phase during the workup process. To validate this proposal, we carefully studied the reaction of **1b** (Table 2, entry 2). After the reaction was complete (monitored by TLC), D_2O was added into the flask, then extracted with ethyl ether, and the aqueous phase was used for the NMR experiment directly. As shown in Fig. 3, besides DMF, only one signal (δ = 2.67 ppm) was observed (Fig. 3c).

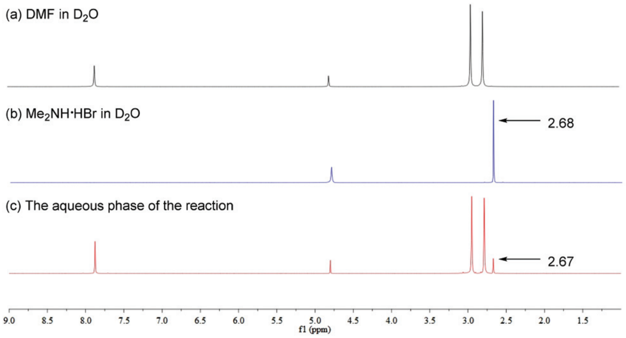


Fig. 3 Results of the byproduct studies.

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.

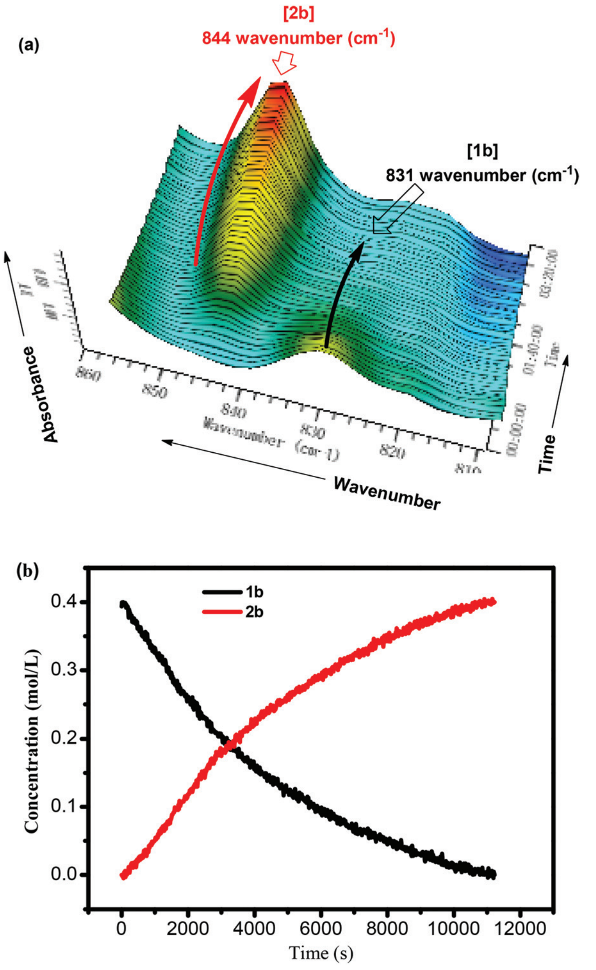


Fig. 4 (a) Overall three-dimensional Fourier transform IR (3D-FTIR) profile of the three-component reaction. (b) Kinetic profile for the three-component reaction.

This signal could be assigned to the two methyl protons of dimethylaminehydrobromide when compared with dimethylaminehydrobromide (δ = 2.68 ppm). On the other hand, dimethylaminehydrobromide **3** might be unstable at high temperatures and released dimethylamine and hydrobromide, which were detected by GC-MS.[23] These results provide compelling evidence that dimethylaminehydrobromide **3** indeed existed in this process.

(5) ***In situ* IR experiments.** In order to gain some insight into the kinetic behaviors of this transformation, the reaction of **1b** with DMF and water was monitored *via in situ* FTIR. It was very clear that from the 3D-FTIR spectrum (Fig. 4a), the product **2b** was formed with the consumption of **1b**. From the kinetic profile of this reaction (Fig. 4b), a linear relationship between the concentration of **2b** and the reaction time was observed at the beginning of this reaction, which indicated that the reaction rate is independent of **1b**. However, a plot of **2b** formation *vs.* time became a curved line with the progress of this reaction, which might result from the catalyst deactivation.[23,26]

Conclusions

In summary, we have developed a visible light induced three component assembly of 3-formyloxyoxindoles from 3-bromooxindoles, DMF and water. Two green and sustainable natural resources, visible light and water, were combined into one reaction system which opened new opportunities to visible light photoredox catalysis. The mild reaction conditions, broad scope of substrates, excellent functional group tolerance and high reaction efficiencies made this new protocol attractive, and a variety of 3-formyloxyoxindole derivatives can be constructed in a highly concise fashion. Moreover, the detailed mechanism of this transformation was investigated based on fluorescence quenching experiments, "on–off" switching of the light source study, labeling experiments, MS studies and *in situ* IR experiments. The application of this strategy to the synthesis of some promising candidates for drug discovery and the biological evaluation of these 3-formyloxyoxindoles are currently ongoing in our laboratory.

Experimental section

General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Flash column chromatography (FC) was performed using 200–300 mesh silica gel. ^{1}H NMR spectra were recorded on Varian Mercury 600 (600 MHz) spectrophotometers. Chemical shifts (δ) are reported in ppm from the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR spectra were recorded on Varian Mercury 400 (100 MHz) spectrophotometers ($CDCl_3$: 77.0 ppm) with complete proton decoupling. IR spectra were recorded on a BRUKER TENSOR 27 FT-IR spectrometer and are reported in terms of the frequency of absorption (cm^{-1}). GC-MS was performed using a Thermo DSQ II 2000. High resolution mass spectra were obtained from the Shanghai Mass Spectrometry Center (Shanghai Institute of Organic Chemistry). Melting points were measured using a Büchi Melting Point B-545. Fluorescence spectra were collected on a Cary Eclipse Fluorescence spectrophotometer. For the ReactIR kinetic experiments, the reaction spectra were recorded using an IC 15 from Mettler-Toledo AutoChem.

General procedure for visible light induced formyloxylation

A 10 mL Schlenk tube equipped with a magnetic stir bar and rubber septum was charged with 3,5-dibromo-1,3-dimethylindolin-2-one **1a** (0.20 mmol, 1.0 equiv.), tris-(2-phenylpyridinato-C2,*N*)iridium(III) (*fac*-Ir(ppy)$_3$) (0.004 mmol, 0.02 equiv.), water (2.0 mmol, 10.0 equiv.), and DMF (2.0 mL). The mixture was degassed *via* the freeze–pump–thaw method and placed at

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.

a distance of ~5 cm from the 18 W household light bulb. After the reaction was complete (2.5 h, monitored by TLC analysis), H_2O (5.0 mL) was added to the reaction mixture. Then, the mixture was extracted with Et_2O and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by FC (silica gel, PE : EtOAc = 10 : 1–5 : 1) to give the desired product 5-bromo-1,3-dimethyl-2-oxoindolin-3-yl formate **2a** (44.8 mg, 79% yield) as a white solid.

Acknowledgements

We are grateful to the National Science Foundation of China (no. 21002036, 21072069, 21232003 and 21202053), the National Basic Research Program of China (2011CB808600), the Program for Changjiang Scholars and Innovative Research Team in University (IRT0953) and the Excellent Doctorial Dissertation Cultivation Grant from Central China Normal University (CCNU13T04094, 2013YBZD22) for support of this research. We thank Prof. Guosheng Liu of Shanghai Institute of Organic Chemistry for helping with HRMS analysis. We also thank Mr Hong Yi and Prof. Ai-Wen Lei of Wuhan University for their help with *in situ* IR experiments, as well as Dr Xiang-Gao Meng and Xiao-Peng Liu of Central China Normal University for their help with X-ray diffraction and NMR analysis.

Notes and references

1 For selected reviews and books, see: (*a*) P. A. Wender and B. L. Miller, *Org. Synth.: Theory Appl.*, 1993, **2**, 27; (*b*) F. Vögtle, J. F. Stoddart and M. Shibasaki, *Stimulating Concepts in Chemistry*, Wiley-VCH, Weinheim, 2000; (*c*) B. M. Trost, *Acc. Chem. Res.*, 2002, **35**, 695; (*d*) A. Fürstner, *Chem. Soc. Rev.*, 2009, **38**, 3208; (*e*) H. Hopf and M. S. Sherburn, *Angew. Chem., Int. Ed.*, 2012, **51**, 2298; (*f*) K. C. Nicolaou, C. R. Hale, C. Nilewski and H. A. Ioannidou, *Chem. Soc. Rev.*, 2012, **41**, 5185; (*g*) M. Shi, J.-M. Lu, Y. Wei and L.-X. Shao, *Acc. Chem. Res.*, 2012, **45**, 641.

2 Representative examples: (*a*) H. Jiang, P. Elsner, K. L. Jensen, A. Falcicchio, V. Marcos and K. A. Jørgensen, *Angew. Chem., Int. Ed.*, 2009, **48**, 6844; (*b*) N. T. Jui, E. C. Lee and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2010, **132**, 10015; (*c*) A. Deagostino, C. Prandi, S. Tabasso and P. Venturello, *Molecules*, 2010, **15**, 2667; (*d*) A. Quintard, A. Alexakis and C. Mazet, *Angew. Chem., Int. Ed.*, 2011, **50**, 2354; (*e*) E. M. Stang and M. C. White, *J. Am. Chem. Soc.*, 2011, **133**, 14892; (*f*) J.-L. Li, S.-L. Zhou, P.-Q. Chen, L. Dong, T.-Y. Liu and Y.-C. Chen, *Chem. Sci.*, 2012, **3**, 1879; (*g*) Y. Wang, Y. Chi, W.-X. Zhang and Z. Xi, *J. Am. Chem. Soc.*, 2012, **134**, 2926.

3 For selected reviews on visible light photoredox catalysis, see: (*a*) D. Gust, T. A. Moore and A. L. Moore, *Acc. Chem. Res.*, 1993, **26**, 198; (*b*) D. Ravelli, D. Dondi, M. Fagnoni and A. Albini, *Chem. Soc. Rev.*, 2009, **38**, 1999; (*c*) K. Zeitler, *Angew. Chem., Int. Ed.*, 2009, **48**, 9785; (*d*) T. P. Yoon, M. A. Ischay and J. Du, *Nat. Chem.*, 2010, **2**, 527; (*e*) J. M. Narayanam and C. R. Stephenson, *Chem. Soc. Rev.*, 2011, **40**, 102; (*f*) F. Teplý, *Collect. Czech. Chem. Commun.*, 2011, **76**, 859; (*g*) N. Hoffmann, *ChemSusChem*, 2012, **5**, 352; (*h*) S. Maity and N. Zheng, *Synlett*, 2012, 1851; (*i*) L. Shi and W. Xia, *Chem. Soc. Rev.*, 2012, **41**, 7687; (*j*) J. Xuan and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 6828; (*k*) Y. You and W. Nam, *Chem. Soc. Rev.*, 2012, **41**, 7061; (*l*) C. K. Prier, D. A. Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322; (*m*) D. Ravelli, M. Fagnoni and A. Albini, *Chem. Soc. Rev.*, 2013, **42**, 97; (*n*) Y. Xi, H. Yi and A. Lei, *Org. Biomol. Chem.*, 2013, **11**, 2387; (*o*) D. P. Hari and B. König, *Angew. Chem., Int. Ed.*, 2013, **52**, 4734; (*p*) M. Reckenthäler and A. G. Griesbeck, *Adv. Synth. Catal.*, 2013, **355**, 2727.

4 D. A. Nicewicz and D. W. C. MacMillan, *Science*, 2008, **322**, 77.

5 M. A. Ischay, M. E. Anzovino, J. Du and T. P. Yoon, *J. Am. Chem. Soc.*, 2008, **130**, 12886.

6 Selected examples through electron transfer, see: (*a*) D. A. Nagib and D. W. C. MacMillan, *Nature*, 2011, **480**, 224; (*b*) M. T. Pirnot, D. A. Rankic, D. B. Martin and D. W. MacMillan, *Science*, 2013, **339**, 1593; (*c*) A. G. Condie, J. C. Gonzalez-Gomez and C. R. Stephenson, *J. Am. Chem. Soc.*, 2010, **132**, 1464; (*d*) J. D. Nguyen, E. M. D'Amato, J. M. Narayanam and C. R. Stephenson, *Nat. Chem.*, 2012, **4**, 854; (*e*) J. Du, L. R. Espelt, I. A. Guzei and T. P. Yoon, *Chem. Sci.*, 2011, **2**, 2115; (*f*) Z. Lu, M. Shen and T. P. Yoon, *J. Am. Chem. Soc.*, 2011, **133**, 1162; (*g*) R. S. Andrews, J. J. Becker and M. R. Gagné, *Angew. Chem., Int. Ed.*, 2010, **49**, 7274; (*h*) D. Kalyani, K. B. McMurtrey, S. R. Neufeldt and M. S. Sanford, *J. Am. Chem. Soc.*, 2011, **133**, 18566; (*i*) M. H. Larraufie, R. Pellet, L. Fensterbank, J. P. Goddard, E. Lacote, M. Malacria and C. Ollivier, *Angew. Chem., Int. Ed.*, 2011, **50**, 4463; (*j*) M. Neumann, S. Füldner, B. König and K. Zeitler, *Angew. Chem., Int. Ed.*, 2011, **50**, 951; (*k*) S. Cai, X. Zhao, X. Wang, Q. Liu, Z. Li and D. Z. Wang, *Angew. Chem., Int. Ed.*, 2012, **51**, 8050; (*l*) D. S. Hamilton and D. A. Nicewicz, *J. Am. Chem. Soc.*, 2012, **134**, 18577; (*m*) D. P. Hari, P. Schroll and B. König, *J. Am. Chem. Soc.*, 2012, **134**, 2958; (*n*) P. Kohls, D. Jadhav, G. Pandey and O. Reiser, *Org. Lett.*, 2012, **14**, 672; (*o*) S. Maity and N. Zheng, *Angew. Chem., Int. Ed.*, 2012, **51**, 9562; (*p*) Y. Ye and M. S. Sanford, *J. Am. Chem. Soc.*, 2012, **134**, 9034; (*q*) S. Zhu, A. Das, L. Bui, H. Zhou, D. P. Curran and M. Rueping, *J. Am. Chem. Soc.*, 2013, **135**, 1823; (*r*) W. P. To, Y. Liu, T. C. Lau and C. M. Che, *Chem. – Eur. J.*, 2013, **19**, 5654; (*s*) J. Xie, Q. Xue, H. Jin, H. Li, Y. Cheng and C. Zhu, *Chem. Sci.*, 2013, **4**, 1281.

7 See also: (*a*) Y. Pan, S. Wang, C. W. Kee, E. Dubuisson, Y. Yang, K. P. Loh and C.-H. Tan, *Green Chem.*, 2011, **13**, 3341; (*b*) Y. Su, L. Zhang and N. Jiao, *Org. Lett.*, 2011, **13**, 2168; (*c*) Z. Xie, C. Wang, K. E. deKrafft and W. Lin, *J. Am. Chem. Soc.*, 2011, **133**, 2056; (*d*) M. Zlotorzynska and G. M. Sammis, *Org. Lett.*, 2011, **13**, 6264; (*e*) Y. Cheng, J. Yang, Y. Qu and P. Li, *Org. Lett.*, 2012, **14**, 98;

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.

(*f*) D. A. DiRocco and T. Rovis, *J. Am. Chem. Soc.*, 2012, **134**, 8094; (*g*) K. Fidaly, C. Ceballos, A. Falguières, M. S.-I. Veitia, A. Guy and C. Ferroud, *Green Chem.*, 2012, **14**, 1293; (*h*) N. Iqbal, S. Choi, E. Kim and E. J. Cho, *J. Org. Chem.*, 2012, **77**, 11383; (*i*) H. Jiang, C. Huang, J. Guo, C. Zeng, Y. Zhang and S. Yu, *Chem. – Eur. J.*, 2012, **18**, 15158; (*j*) X. Ju, D. Li, W. Li, W. Yu and F. Bian, *Adv. Synth. Catal.*, 2012, **354**, 3561; (*k*) X. Ju, Y. Liang, P. Jia, W. Li and W. Yu, *Org. Biomol. Chem.*, 2012, **10**, 498; (*l*) H. Kim and C. Lee, *Angew. Chem., Int. Ed.*, 2012, **51**, 12303; (*m*) D. P. Kranz, A. G. Griesbeck, R. Alle, R. Perez-Ruiz, J. M. Neudorfl, K. Meerholz and H. G. Schmalz, *Angew. Chem., Int. Ed.*, 2012, **51**, 6000; (*n*) Q. Liu, Y. N. Li, H. H. Zhang, B. Chen, C. H. Tung and L. Z. Wu, *Chem. – Eur. J.*, 2012, **18**, 620; (*o*) L. Möhlmann, M. Baar, J. Rieß, M. Antonietti, X. Wang and S. Blechert, *Adv. Synth. Catal.*, 2012, **354**, 1909; (*p*) P. Wu, C. He, J. Wang, X. Peng, X. Li, Y. An and C. Duan, *J. Am. Chem. Soc.*, 2012, **134**, 14991; (*q*) T. Xiao, X. Dong, Y. Tang and L. Zhou, *Adv. Synth. Catal.*, 2012, **354**, 3195; (*r*) G. Zhao, C. Yang, L. Guo, H. Sun, C. Chen and W. Xia, *Chem. Commun.*, 2012, **48**, 2337; (*s*) G.-B. Deng, Z.-Q. Wang, J.-D. Xia, P.-C. Qian, R.-J. Song, M. Hu, L.-B. Gong and J.-H. Li, *Angew. Chem., Int. Ed.*, 2013, **52**, 1535; (*t*) M. E. Weiss, L. M. Kreis, A. Lauber and E. M. Carreira, *Angew. Chem., Int. Ed.*, 2011, **50**, 11125; (*u*) S. Mizuta, S. Verhoog, K. M. Engle, T. Khotavivattana, M. O'Duill, K. Wheelhouse, G. Rassias, M. Medebielle and V. Gouverneur, *J. Am. Chem. Soc.*, 2013, **135**, 2505.

8 Selected examples through energy transfer, see: (*a*) Y.-Q. Zou, S.-W. Duan, X.-G. Meng, X.-Q. Hu, S. Gao, J.-R. Chen and W.-J. Xiao, *Tetrahedron*, 2012, **68**, 6914; (*b*) Z. Lu and T. P. Yoon, *Angew. Chem., Int. Ed.*, 2012, **51**, 10329; (*c*) E. P. Farney and T. P. Yoon, *Angew. Chem., Int. Ed.*, 2014, **53**, 793.

9 For visible light initiated multicomponent reactions, see: (*a*) T. Courant and G. Masson, *Chem. – Eur. J.*, 2012, **18**, 423; (*b*) Y. Yasu, T. Koike and M. Akita, *Angew. Chem., Int. Ed.*, 2012, **51**, 9567; (*c*) M. Rueping and C. Vila, *Org. Lett.*, 2013, **15**, 2092; (*d*) Y. Yasu, T. Koike and M. Akita, *Org. Lett.*, 2013, **15**, 2136; (*e*) H. S. Yoon, X. H. Ho, J. Jang, H. J. Lee, S. J. Kim and H. Y. Jang, *Org. Lett.*, 2012, **14**, 3272.

10 Selected reviews, see: (*a*) J. Muzart, *Tetrahedron*, 2009, **65**, 8313; (*b*) S. Ding and N. Jiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 9226. Selected examples using DMF as the source of the formyloxy group, see: (*c*) F. C. Chang and R. T. Blickenstaff, *J. Am. Chem. Soc.*, 1958, **80**, 2906; (*d*) M. Dakanali, G. K. Tsikalas, H. Krautscheid and H. E. Katerinopoulos, *Tetrahedron Lett.*, 2008, **49**, 1648; (*e*) Y.-P. Zhu, Q.-H. Gao, M. Lian, J.-J. Yuan, M.-C. Liu, Q. Zhao, Y. Yang and A.-X. Wu, *Chem. Commun.*, 2011, **47**, 12700; (*f*) J. C. Lee, Y. S. Jinn and J.-H. Choi, *Chem. Commun.*, 2001, 956.

11 J. Kim and S. Chang, *J. Am. Chem. Soc.*, 2010, **132**, 10272.

12 T. Fujihara, Y. Katafuchi, T. Iwai, J. Terao and Y. Tsuji, *J. Am. Chem. Soc.*, 2010, **132**, 2094.

13 S. Ding and N. Jiao, *J. Am. Chem. Soc.*, 2011, **133**, 12374.

14 (*a*) S. H. Cho, J. Y. Kim, S. Y. Lee and S. Chang, *Angew. Chem., Int. Ed.*, 2009, **48**, 9127; (*b*) R. Arias-Ugarte, H. K. Sharma, A. L. Morris and K. H. Pannell, *J. Am. Chem. Soc.*, 2012, **134**, 848; (*c*) J. Kim, J. Choi, K. Shin and S. Chang, *J. Am. Chem. Soc.*, 2012, **134**, 2528; (*d*) Z. Liu, J. Zhang, S. Chen, E. Shi, Y. Xu and X. Wan, *Angew. Chem., Int. Ed.*, 2012, **51**, 3231; (*e*) E. Yoshioka, S. Kohtani and H. Miyabe, *Angew. Chem., Int. Ed.*, 2011, **50**, 6638; (*f*) Y. Li, D. Xue, C. Wang, Z.-T. Liu and J. Xiao, *Org. Lett.*, 2014, **16**, 66.

15 C. Dai, J. M. Narayanam and C. R. Stephenson, *Nat. Chem.*, 2011, **3**, 140. Formate ester was also observed with the increased steric hindrance of the cyclic alcohol, but DMF is the source of "C, H" of the formate unit. The other part of the ester product is from the alcohol, and bromide was sacrificed.

16 (*a*) M. D. Konieczynska, C. Dai and C. R. Stephenson, *Org. Biomol. Chem.*, 2012, **10**, 4509; (*b*) F. R. Bou-Hamdan and P. H. Seeberger, *Chem. Sci.*, 2012, **3**, 1612.

17 For selected reviews, see: (*a*) M. J. Shultz, T. H. Vu, B. Meyer and P. Bisson, *Acc. Chem. Res.*, 2012, **45**, 15; (*b*) M.-O. Simon and C.-J. Li, *Chem. Soc. Rev.*, 2012, **41**, 1415.

18 (*a*) Y.-Q. Zou, L.-Q. Lu, L. Fu, N.-J. Chang, J. Rong, J.-R. Chen and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2011, **50**, 7171; (*b*) Y.-Q. Zou, J.-R. Chen, X.-P. Liu, L.-Q. Lu, R. L. Davis, K. A. Jørgensen and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 784; (*c*) Y.-Q. Zou, J.-R. Chen and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2013, **52**, 11701.

19 (*a*) T. S. Kam and Y. M. Choo, *J. Nat. Prod.*, 2004, **67**, 547; (*b*) V. C. Pham, J. Ma, S. J. Thomas, Z. Xu and S. M. Hecht, *J. Nat. Prod.*, 2005, **68**, 1147; (*c*) C. V. Galliford and K. A. Scheidt, *Angew. Chem., Int. Ed.*, 2007, **46**, 8748; (*d*) B. Trost and M. Brennan, *Synthesis*, 2009, 3003; (*e*) K. Wang, X.-Y. Zhou, Y.-Y. Wang, M.-M. Li, Y.-S. Li, L.-Y. Peng, X. Cheng, Y. Li, Y.-P. Wang and Q.-S. Zhao, *J. Nat. Prod.*, 2011, **74**, 12.

20 For selected reviews, see: (*a*) G. S. Singh and Z. Y. Desta, *Chem. Rev.*, 2012, **112**, 6104; (*b*) F. Zhou, Y.-L. Liu and J. Zhou, *Adv. Synth. Catal.*, 2010, **352**, 1381. For selected examples, see: (*c*) A. M. Taylor, R. A. Altman and S. L. Buchwald, *J. Am. Chem. Soc.*, 2009, **131**, 9900; (*d*) X. Jiang, Y. Cao, Y. Wang, L. Liu, F. Shen and R. Wang, *J. Am. Chem. Soc.*, 2010, **132**, 15328; (*e*) S. Mouri, Z. Chen, H. Mitsunuma, M. Furutachi, S. Matsunaga and M. Shibasaki, *J. Am. Chem. Soc.*, 2010, **132**, 1255; (*f*) B. Tan, N. R. Candeias and C. F. Barbas III, *J. Am. Chem. Soc.*, 2011, **133**, 4672; (*g*) B. Seashore-Ludlow and P. Somfai, *Org. Lett.*, 2012, **14**, 3858; (*h*) B. Tan, X. Zeng, W. W. Leong, Z. Shi, C. F. III Barbas and G. Zhong, *Chem. – Eur. J.*, 2012, **18**, 63; (*i*) D. Uraguchi, K. Koshimoto and T. Ooi, *J. Am. Chem. Soc.*, 2012, **134**, 6972; (*j*) J. Wang, Y. Yuan, R. Xiong, D. Zhang-Negrerie, Y. Du and K. Zhao, *Org. Lett.*, 2012, **14**, 2210; (*k*) F. Zhong, W. Yao, X. Dou and Y. Lu, *Org. Lett.*, 2012, **14**, 4018; (*l*) J. Zuo, Y.-H. Liao, X.-M. Zhang and W.-C. Yuan, *J. Org. Chem.*, 2012, **77**, 11325; (*m*) Q. H. Deng, T. Bleith, H. Wadepohl and L. H. Gade, *J. Am. Chem. Soc.*, 2013, **135**,

This journal is © The Royal Society of Chemistry 2014

Published on 08 May 2014. Downloaded by York University on 23/10/2014 00:28:54.

5356; (*n*) Z.-K. Xiao, H.-Y. Yin and L.-X. Shao, *Org. Lett.*, 2013, **15**, 1254.

21 Representative work from our group on the oxindoles: (*a*) J.-R. Chen, X.-P. Liu, X.-Y. Zhu, L. Li, Y.-F. Qiao, J.-M. Zhang and W.-J. Xiao, *Tetrahedron*, 2007, **63**, 10437; (*b*) S.-W. Duan, J. An, J.-R. Chen and W.-J. Xiao, *Org. Lett.*, 2011, **13**, 2290; (*c*) S.-W. Duan, Y. Li, Y.-Y. Liu, Y.-Q. Zou, D.-Q. Shi and W.-J. Xiao, *Chem. Commun.*, 2012, **48**, 5160.

22 (*a*) J. F. Hartwig, *Acc. Chem. Res.*, 1998, **31**, 852; (*b*) J. P. Corbet and G. Mignani, *Chem. Rev.*, 2006, **106**, 2651; (*c*) D. Ma and Q. Cai, *Acc. Chem. Res.*, 2008, **41**, 1450; (*d*) N. Marion and S. P. Nolan, *Acc. Chem. Res.*, 2008, **41**, 1440; (*e*) N. Kambe, T. Iwasaki and J. Terao, *Chem. Soc. Rev.*, 2011, **40**, 4937.

23 Please see the ESI† for details.

24 (*a*) H. W. Shih, M. N. Vander Wal, R. L. Grange and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2010, **132**, 13600; (*b*) Y. C. Teo, Y. Pan and C. H. Tan, *ChemCatChem*, 2013, **5**, 235.

25 (*a*) Y. Miyake, K. Nakajima and Y. Nishibayashi, *J. Am. Chem. Soc.*, 2012, **134**, 3338; (*b*) B. P. Fors and C. J. Hawker, *Angew. Chem., Int. Ed.*, 2012, **51**, 8850; (*c*) C. J. Wallentin, J. D. Nguyen, P. Finkbeiner and C. R. Stephenson, *J. Am. Chem. Soc.*, 2012, **134**, 8875; (*d*) Q. Liu, H. Yi, J. Liu, Y. Yang, X. Zhang, Z. Zeng and A. Lei, *Chem. – Eur. J.*, 2013, **19**, 5120.

26 We also investigated the influence of light intensity on the reaction efficiencies, please see the ESI† for details.

This journal is © The Royal Society of Chemistry 2014