Metal-free visible-light-promoted intermolecular [2+2]-cycloaddition of 3-ylideneoxindoles

Ling-Ling Wu, Gao H. Yang, Zhi Guan, Yan-Hong He

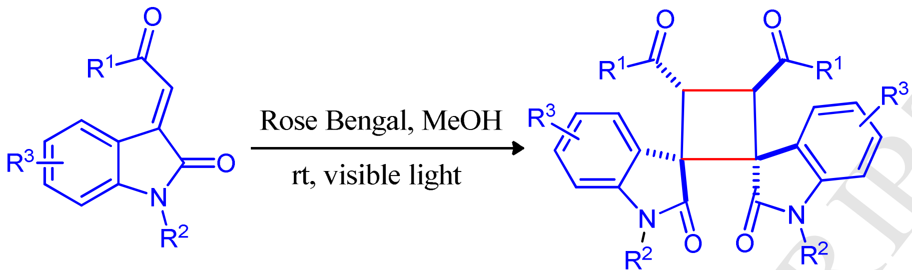
PII: S0040-4020(17)30174-6
DOI: 10.1016/j.tet.2017.02.035
Reference: TET 28476

To appear in: *Tetrahedron*

Received Date: 24 January 2017
Revised Date: 15 February 2017
Accepted Date: 17 February 2017

Please cite this article as: Wu L-L, Yang GH, Guan Z, He Y-H, Metal-free visible-light-promoted intermolecular [2+2]-cycloaddition of 3-ylideneoxindoles, *Tetrahedron* (2017), doi: 10.1016/j.tet.2017.02.035.

Graphical Abstract



1a-n

R^1 = OMe, OEt, OPr, Me, Ph

R^2 = H, Me, Bn

R^3 = H, 5-Me, 5-OMe, 5-F, 5-Br,
5-I, 7-F, 7-Cl

2a-n

14 examples, yields: 30-93%

Metal-free visible-light-promoted intermolecular [2+2]-cycloaddition of 3-ylideneoxindoles

Ling-Ling Wu[a], Gao H. Yang[b], Zhi Guan[a,]* and Yan-Hong He[a,]*

[a] *Key Laboratory of Applied Chemistry of Chongqing Municipality, School of Chemistry and Chemical Engineering, Southwest University, Chongqing 400715, PR China*

[b] *Chemistry Department, College of Saint Benedict and Saint John's University, MN 56374, USA*

E-mails: guanzhi@swu.edu.cn (for Z. Guan); heyh@swu.edu.cn (for Y.-H. He)

Abstract: The Rose Bengal sensitized intermolecular [2+2]-cycloaddition of 3-ylideneoxindoles for the synthesis of spirocyclic oxindoles was developed successfully under visible light irradiation conditions. The cycloaddition products were obtained in good yields (up to 93%) with excellent diastereoselectivity and regioselectivity by using a low loading of Rose Bengal (0.125 mol%) as a triplet sensitizer. This work demonstrates the potential benefits of Rose Bengal in visible light catalysis.

Key words: visible light; Rose Bengal; 3-ylideneoxindoles; [2+2]-cycloaddition; spirocyclic oxindoles

1. Introduction

Among many green chemical approaches, visible light photocatalysis can serve as a valuable application since light can be considered as an ideal reaction condition for environmentally friendly and green chemical synthesis.[1] Using visible light and either ruthenium or iridium complexes as photosensitizers[2, 3e] have been reported for the formation of fundamental and useful chemical transformations[3]. However, the potential toxicity and the limited availability of the ruthenium or the iridium salts hinder the production of fine chemicals and pharmaceuticals.[4] Organic dyes could serve as promising catalysts in the field of visible light-induced reactions due to their high absorption within the visible spectrum.[5] Moreover, they are inexpensive, low toxic,[4a, 6] and widely available. For example, commercially readily available Rose Bengal presents a viable alternative to inorganic photocatalysts.[7] The photocatalytic activity of Rose Bengal is similar to ruthenium or iridium complexes in some reactions such as alkylation reaction,[4a] photoredox oxidative reaction,[4b, 6b, 7b, 8] oxyamination reaction,[9] sulfoxidation reaction[10] and thiocyanation reaction.[11] In consideration of the advantages of Rose Bengal as a photosensitizer in visible light catalysis, it is necessary to further explore its application in the field of photocatalysis.

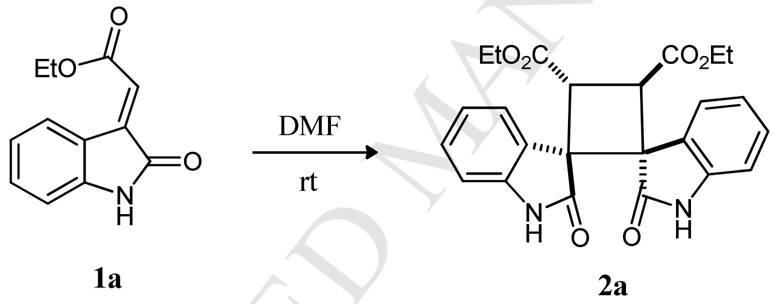
Spirocyclic oxindoles have emerged as attractive synthetic targets in chemical science because they are widespread in the bioactive alkaloids and pharmacologically important compounds.[12] They display various biological activities and have been exploited as insecticidal, antitumor and antibacterial agents.[13] For this reason, this family of oxindole has been extensively researched.[14] A number of synthetic methods have been developed in pursuit of this kind of structure, including rearrangements,[15] cascade Michael-aldol reactions,[16] conjugate additions,[17] cycloadditions[18] et al. Although considerable progress has been described toward their synthesis, the potential biological activities of spirocyclic oxindole skeleton have led to a demand for efficient and novel synthetic methods.

Since Ciamician et al. reported the first example of a photoinitiated intramolecular [2+2] enone cycloaddition in 1908,[19] some research groups have further reported [2+2] cycloaddition reactions initiated by photoredox catalysis under visible light irradiation.[18d, 20-22] In recent decades, allenoates have received significant attention in organic synthesis due to its facile preparation and versatile reactivity.[23] They have proven to be valuable building blocks in many types of cycloaddition reactions.[24] Xiao group[18d] and Yan group[18e] reported the successful photoinitiated intermolecular [2+2]-cycloaddition reactions of 3-ylideneoxindoles by ruthenium complex for the synthesis of spirocyclic oxindoles. However, to the best of our knowledge, organic dyes have rarely been applied as photosensitizers in photoinitiated [2+2]-cycloadditions.[22b, 22d, 22e, 25] In this context, we are interested in the development of the intermolecular [2+2]-cycloaddition reactions of 3-ylideneoxindoles using Rose Bengal as a photocatalyst. In Xiao and Yan groups' work, they mainly used N-protected 3-ylideneoxindoles as substrates and $Ru(bpy)_3^{2+}$ served as a photosensitizer. In this work, 3-ylideneoxindoles were used directly without protection in most cases and Rose Bengal was used as a cheap and easily available metal-free photosensitizer. Various cycloaddition products were obtained with good yields (up to 93%) in the presence of a low loading of Rose Bengal (0.125 mol%). The excellent diastereoselectivity (only one diastereomer was observed) and regioselectivity (only head-to-head product was observed) were achieved. Among the obtained products, 11 products are new compounds, and a representative product was determined by single-crystal X-ray analysis to confirm the stereochemistry.

2. Results and Discussion

Initially, the intermolecular [2+2]-cycloaddition of 3-ylideneoxindole (**1a**) was selected as a model reaction. To verify if visible light and Rose Bengal are necessary in this catalytic process, some control experiments were conducted (**Table 1**). The data indicated that irradiating a DMF solution of **1a** containing 2 mol% of Rose Bengal with a 32 W compact fluorescent light bulb (λ= 405-577 nm) gave cycloadduct **2a** in 64% yield (**Table 1**, entry 1). A low yield of 16% was obtained without Rose Bengal under visible light irradiation (**Table 1**, entry 2), indicating that Rose Bengal can promote the reaction. No product was observed without visible light irradiation in the presence of Rose Bengal (**Table 1**, entry 3), confirming that visible light was necessary for the reaction. The product was obtained with an excellent diastereoselectivity (only one diastereomer **2a** was observed) and regioselectivity (only head-to-head product was observed) determined by ^{1}H NMR and ^{13}C NMR in comparison with known compound.[18d]

Table 1. Control experiments[a]



Entry	Visible light	Rose Bengal	Yield (%)[b]
1	+[c]	+[c]	64
2	+[c]	-[d]	16
3	-[d]	+[c]	0

[a] Unless otherwise noted, reaction conditions: A mixture of **1a** (0.2 mmol) and Rose Bengal (2 mol%) in DMF (1.0 mL) was irradiated by a 32 W CFL bulb at rt for 36 h.

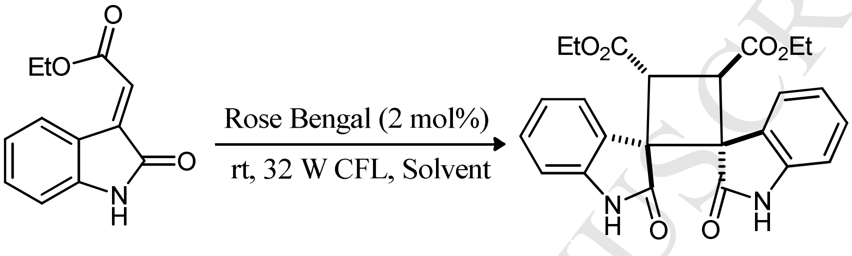
[b] Isolated yield.

[c] "+" means the corresponding substance was used.

[d] "-" means the corresponding substance was not used.

Encouraged by these important results, different solvents were screened (**Table 2**). The data confirmed the significant roles of solvents in the model reaction. The reaction in MeOH gave the best yield of 87% after 36 h (**Table 2**, entry 1), and a good yield of 82% was obtained in EtOH (**Table 2**, entry 2). The other tested solvents such as EtOAc, MeCN and CH_2Cl_2 gave low yields (**Table 2**, entries 6-8). Therefore, MeOH was chosen as an optimal solvent for the following studies.

Table 2. Solvent screening[a].



1a **2a**

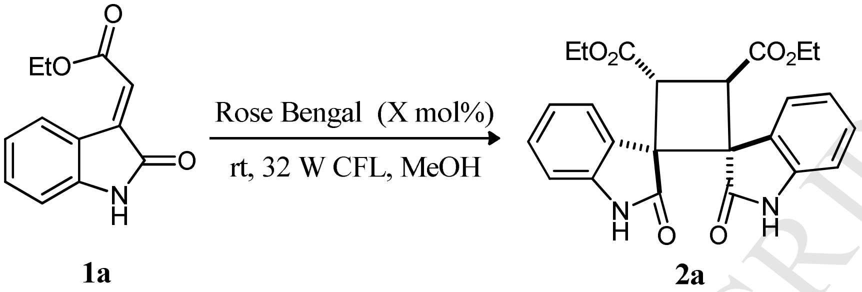
Entry	Solvent	Yield (%)[b]
1	MeOH	87
2	EtOH	82
3	*i*-PrOH	69
4	DMSO	69
5	DMF	64
6	EtOAc	53
7	MeCN	46
8	CH_2Cl_2	19

[a] Reaction conditions: A mixture of **1a** (0.2 mmol) and Rose Bengal (2 mol%) in solvent (1.0 mL) was irradiated by a 32 W CFL bulb at rt for 36 h.

[b] Isolated yield.

Subsequently, to find out a suitable Rose Bengal loading for the reaction, Rose Bengal loading from 0.125 mol% [2 mol% (4 mg) of Rose Bengal was dissolved in 16 mL of MeOH, and then 1.0 mL of this solution was used for the reaction] to 4 mol% was screened for the cycloaddition reaction (**Table 3**). It is surprising that the reaction can give good yields by using a low amount of Rose Bengal (**Table 3**, entries 5-7). Taking into consideration of the yield and cost of the reaction, 0.125 mol% of Rose Bengal was chosen as an optimal amount of catalyst for the further experiments.

Table 3. Screening of Rose Bengal loading[a].



Entry	Rose Bengal loading (mol%)	Yield (%)[b]
1	4	89
2	3	87
3	2	87
4	1	86
5	0.5	85
6	0.25	85
7	0.125	85
8	0	16

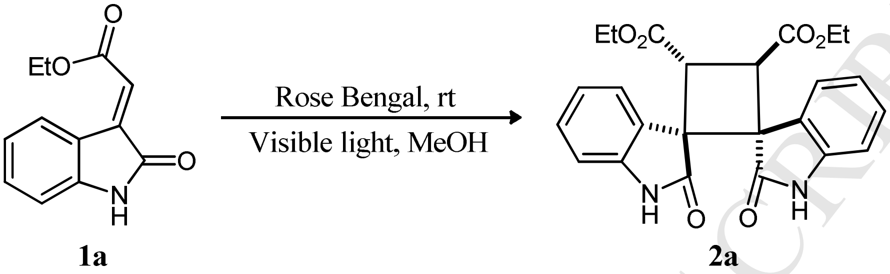
[a] Reaction conditions: A mixture of **1a** (0.2 mmol) and Rose Bengal in MeOH (1.0 mL) was irradiated by a 32 W CFL bulb at rt for 36 h.

[b] Isolated yield.

Additionally, solvent volume, wattage of lamp and reaction time may also affect the model reaction. Therefore, the effects of different solvent volume, wattage of lamp and reaction time on the model reaction were investigated (**Table 4**). It can be seen that when increasing the solvent volume from 0.5 mL to 2.0 mL, the yield of **2a** increased (**Table 4**, entries 1-4). By increasing the solvent volume to 2.5 mL, the yield of **2a** decreased slightly (**Table 4**, entry 5). Next, the wattages of lamp ranged from 5 W to 45 W were investigated. It can be seen that 32 W CFL bulb was suitable for the model reaction (**Table 4**, entry 4). Subsequently, we investigated the time course of the model reaction, as shown in **Table 4**. Extending the reaction time led to an increase of the yield (**Table 4**, entries 4, 11-13), and the best yield of 90% was obtained after 36 h (**Table 4**, entry

4). Thus, 2.0 mL of MeOH and 32 W CFL bulb were chosen as the optimum conditions for the model reaction.

Table 4. Solvent volume, wattage of lamp and reaction time investigation[a].



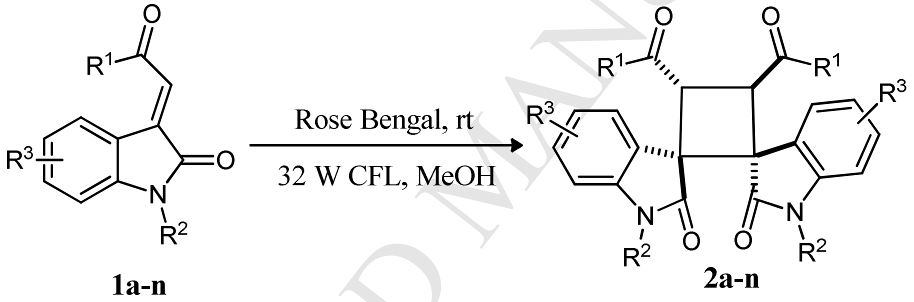
Entry	MeOH (mL)	Wattage of lamp (W)	Time (h)	Yield (%)[b]
1	0.5	32	36	84
2	1.0	32	36	85
3	1.5	32	36	86
4	2.0	32	36	90
5	2.5	32	36	89
6	2.0	5	36	63
7	2.0	12	36	72
8	2.0	20	36	78
9	2.0	23	36	80
10	2.0	45	36	73
11	2.0	32	8	49
12	2.0	32	12	67
13	2.0	32	24	89
14	2.0	32	48	83

[a] Reaction conditions: A mixture of **1a** (0.2 mmol) and Rose Bengal (0.125 mol%) in MeOH (0.5-2.5 mL) was irradiated by a 5-45 W CFL bulb at rt for 8-48 h.

[b] Isolated yield.

With the optimized conditions in hand, the substrate scope of this intermolecular [2+2]-cycloaddition was explored. As shown in **Table 5**, [2+2]-cycloaddition reactions of a variety of substituted 3-ylideneoxindoles proceed smoothly to give the corresponding products in the presence of a low amount of Rose Bengal. Both esters (R^1 = OMe, OEt, OPr) and ketones (R^1 = CH_3, Ph) of 3-ylideneoxindoles can participate in the reaction very well. The reaction can be applied to N-protected (R^2 = CH_3, Bn) and unprotected 3-ylideneoxindoles. 3-Ylideneoxindoles with either electron-withdrawing (R^3 = 5-F, 5-Br, 5-I, 7-F, 7-Cl) or electron-donating (R^3 = 5-CH_3, 5-OCH_3) substituents in benzene ring can take part in the reaction. The highest yield of 93% was obtained (**Table 5,** entry 6). In all cases**,** products obtained were with excellent diastereoselectivity (only one diastereomer was observed) and regioselectivity (only head-to-head product was observed). To the best of our knowledge, all the products we obtained except **2b**, **2f** and **2g** are new compounds. To confirm the stereochemistry, product **2m** as a representative example was determined by single-crystal X-ray analysis (**Fig. 1**).

Table 5. Substrate scope[a].



Entry	R^1	R^2	R^3	Product	Time (h)	Yield (%)[b]
1	OMe	H	H	**2a**	24	91
2	OEt	H	H	**2b**	24	89
3	OPr	H	H	**2c**	24	80
4[c]	CH_3	H	H	**2d**	18	75
5[c]	Ph	H	H	**2e**	35	70
6	OEt	CH_3	H	**2f**	24	93
7	OEt	Bn	H	**2g**	27	86
8	OEt	H	5-CH_3	**2h**	17	87
9	OEt	H	5-OCH_3	**2i**	18	88
10[c]	OEt	H	5-F	**2j**	16	87
11	OEt	H	5-Br	**2k**	26	39
12[c]	OEt	H	5-I	**2l**	26	30
13[c]	OEt	H	7-F	**2m**	25	43
14[c]	OEt	H	7-Cl	**2n**	36	70

[a] Unless otherwise noted, reaction conditions: A mixture of **1a-n** (0.2 mmol) and Rose Bengal (0.125 mol%) in MeOH (2.0 mL) was irradiated by a 32 W CFL bulb at rt.

[b] Isolated yield.

[c] Rose Bengal (1 mol%) was used.

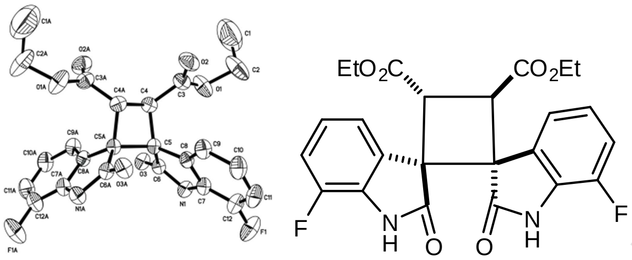
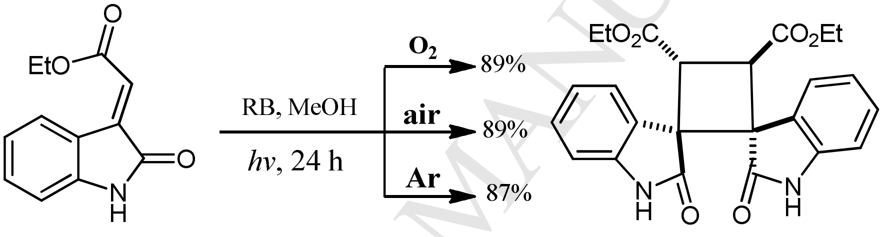


Fig. 1. X-ray crystal structure of **2m**.

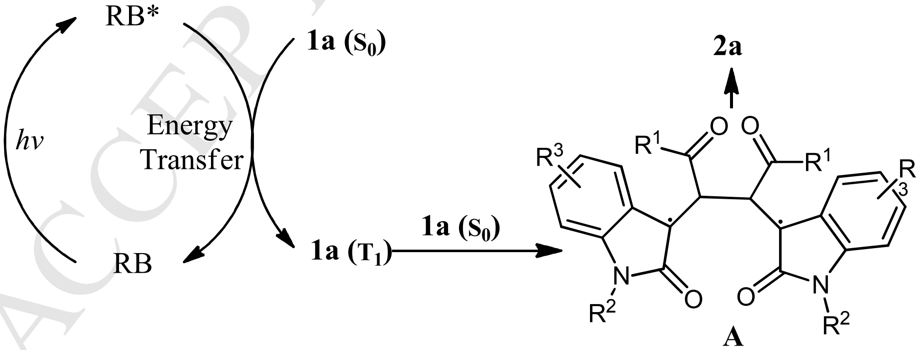
In order to understand the mechanism of this visible light-promoted intermolecular [2+2]-cycloaddition of 3-ylideneoxindoles, fluorescence experiments with Rose Bengal and **1a** were performed. Rose Bengal exhibited a strong absorption in the visible light region at λ= 563 nm (ε = 3926 L·mol^{-1}·cm^{-1}). **1a** exhibited a weak absorption in the visible light region at λ = 415 nm (ε = 37 L·mol^{-1}·cm^{-1}) (the spectrum shown in the Supporting information). We speculated that **1a** could be a light absorber, and the reaction without catalyst can still give a yield. This has been proven by the control experiments, in which a yield of 16% was obtained without the presence of a catalyst (**Table 1**, entry 2).

Xiao et al. proposed that the [2+2]-cycloaddition reaction promoted by Ru(bpy)$_3$Cl$_2$·6H$_2$O likely takes place via a pathway involving energy transfer from Ru*(bpy)$_3^{2+}$ to the ground state **1a** as described in their article or by a single electron transfer (SET) mechanism discussed in their Supporting information, but the precise mechanism of the reaction was uncertain.[18d] They revealed that **1a** has a significantly high oxidation peak potential (E_p^{ox} = 1.5-2.0 V vs SCE in MeCN). Thus, in the present reaction it is impossible for **1a** to reductively quench the excited state of Rose Bengal ($E_{1/2}{}^{RB*/RB^{\cdot-}}$ = 0.99 V vs SCE in MeCN).[26] Rose Bengal is well known as a singlet oxygen sensitizer,[27] and the photocycle is always accomplished by single electron transfer[28] or energy transfer[29] from excited state of Rose Bengal to oxygen. Thus, comparison experiments were conducted under O_2, Ar and air, respectively, and the reaction gave the similar yields (**Scheme 1**), indicating that O_2 is not involved in the reaction. Therefore, we propose that the reaction likely takes place via a pathway involving energy transfer from excited state of Rose Bengal to substrate (**Scheme 2**) instead of a SET process. Rose Bengal may be play the role of triplet sensitizer[22d, 22e, 30] and the energy transfers from RB***** to the ground state **1a** (S_0) (**Scheme 2**)[18d]. Then, the triplet state **1a** (T_1) is formed through triplet sensitization, which reacts with **1a** (S_0) to form a biradical intermediate **A** that then undergoes the cyclization to afford the adduct **2a**.



1a **2a**

Scheme 1. Comparison experiments



Scheme 2. Proposed mechanism.

3. Conclusion

In conclusion, Rose Bengal was used as a triplet sensitizer for the first time in the intermolecular [2+2]-cycloaddition for the synthesis of spirocyclic oxindoles from 3-ylideneoxindoles under the irradiation of visible light. The cycloaddition products were obtained in good yields (up to 93%) with excellent diastereoselectivity and regioselectivity by using a low loading of Rose Bengal (0.125 mol%). This work demonstrates the potential benefits of Rose Bengal as an inexpensive, low-toxic, and widely available metal-free photosensitizer in visible light catalysis.

4. Experimental Section

4.1.General experimental details

Rose bengal was purchased from aladdin industrial corporation Shanghai, China. R104993-1g, 95%. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Reactions were monitored by thin-layer chromatography (TLC) with Haiyang GF 254 silica gel plates (Qingdao Haiyang chemical industry Co Ltd, Qingdao, China) using UV light and vanillic aldehyde as visualizing agents. Flash column chromatography was performed using 200-300 mesh silica gel at increased pressure. ^{1}H NMR spectra and ^{13}C NMR spectra were respectively recorded on 600 MHz and 150 MHz NMR spectrometers. Chemical shifts (δ) were expressed in ppm with TMS as the internal standard, and coupling constants (*J*) were reported in Hz. High-resolution mass spectra were obtained by using ESI ionization sources (Varian 7.0 T FTICR-MS). Melting points were taken on a WPX-4 apparatus and were uncorrected (Yice instrument equipment Co Ltd, Shanghai). X-ray crystal structures were tested by Bruker Apex-II.

*4.2. General procedure for the synthesis of compounds **1***[31]

To a stirred solution of ethyl 2-(triphenylphosphoranylidene) acetate[32] (22 mmol, 1.1 eq.) in anhydrous THF (50 mL), dione (20 mmol, 1.0 eq.) was added at 0 °C. The mixture was stirred at the same temperature until the reaction was completed monitored by TLC analysis. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethylacetate 5:1). Compound **1a-n** was obtained as a red or yellow solid.

*4.3. General procedure for the synthesis of compounds **2***

A mixture of 3-ylideneoxindoles **1** (0.20 mmol) and Rose Bengal [0.125 mol% (6 mg of Rose Bengal was dissolved in 16 mL of MeOH, and then 1.0 mL of this solution was transferred into the reaction bottle) or 1.0 mol%] in MeOH (2.0 mL) was stirred under irradiation of a 32 W fluorescent light bulb (The parallel distance between the bulb and the reaction flask was about 2 cm) for the specified reaction time, and monitored by TLC. The MeOH was removed under reduced pressure. The crude products were purified by column chromatography on a silica gel (petroleum ether/EtOAc: 8/1~5/1) to give the desired [2+2]-cycloaddition adducts as white solids.

*4.3.1. Compound **2a***

White solid; 91% yield (37 mg); m.p. 144.7-145.1 °C; R_f = 0.25 (PE/EtOAc, 5:1); ^{1}H NMR (600 MHz, DMSO-d_6): δ = 10.26 (s, 2H), 7.39 (d, J = 7.6 Hz, 2H), 7.18-7.16 (m, 2H), 6.94-6.91 (m, J = 7.6 Hz, 2H), 6.73 (d, J = 7.6 Hz, 2H), 4.34 (s, 2H), 3.40 (s, 6H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$): δ = 174.4, 169.6, 142.4, 129.6, 127.9, 124.1, 120.7, 109.8, 55.3, 52.3, 42.1. HRMS (ESI) calc. for $C_{22}H_{18}N_2O_6$ $(M+Na)^+$: 429.1057, found: 429.1064.

*4.3.2. Compound **2b***[18d]

White solid; 89% yield (39 mg); m.p. 135.0-135.2 °C; R_f = 0.25 (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ = 10.27 (s, 2H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.19-7.16 (m, 2H), 6.94-6.91 (m, *J* = 7.6 Hz, 2H), 6.75 (d, *J* = 7.6 Hz, 2H), 4.30 (s, 2H), 3.94-3.91 (m, 2H), 3.85-3.81 (m, 2H),0.72 (t, J = 7.1 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$): δ = 174.3, 169.1, 142.5, 129.5, 128.3, 124.0, 120.5, 109.7, 61.0, 55.0, 42.4, 14.0.

*4.3.3. Compound **2c***

White solid; 80% yield (37 mg); m.p. 140.0-140.2 °C; R_f = 0.25 (PE/EtOAc, 4:1); ^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ = 10.29 (s, 2H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.18-7.16 (m, 2H), 6.94-6.91 (m, 2H), 6.73 (d, *J* = 7.6 Hz, 2H), 4.31 (s, 2H), 3.83-3.81 (m, 2H), 3.74-3.73 (m, 2H), 1.21-1.19 (m, , 2H), 1.09-1.07 (m, 2H), 0.45 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$): δ = 174.3, 169.2, 142.5, 129.5, 128.2, 124.1, 120.6, 109.8, 66.5, 55.1, 42.4, 21.6, 10.1. HRMS (ESI) calc. for $C_{26}H_{26}N_2O_6$ $(M+Na)^+$: 485.1683, found: 485.1687.

*4.3.4. Compound **2d***

White solid; 75% yield (28 mg); m.p. 155.9-156.5 °C; R_f = 0.30 (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ = 10.34 (s, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 7.19-7.18 (m, 2H), 6.93-6.90 (m, 2H), 6.77 (d, *J* = 7.6 Hz, 2H), 4.40 (s, 2H), 1.64 (s, 6H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$): δ = 203.9, 174.5, 142.3, 129.5, 128.4, 123.8, 120.6, 109.9, 55.0, 48.3, 28.2. HRMS (ESI) calc. for $C_{22}H_{18}N_2O_4$ $(M+Na)^+$: 397.1159, found: 397.1163.

*4.3.5. Compound **2e***

White solid; 70% yield (35 mg); m.p. 135.2-135.5 °C; R_f = 0.30 (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ = 10.36 (s, 2H), 7.67 (d, *J* = 7.6 Hz, 4H), 7.53-7.50 (m, 2H), 7.45-7.36 (m, 6H), 7.00-6.98 (m, 2H), 6.82-6.80 (m, 2H), 6.54 (d, *J* = 7.6 Hz, 2H), 5.48 (s, 2H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$): δ = 196.2, 174.8, 142.0, 135.3, 134.3, 129.3, 129.2, 128.8, 128.1, 123.6, 120.5, 109.6, 56.4, 43.5. HRMS (ESI) calc. for $C_{32}H_{22}N_2O_4$ $(M+H)^+$: 499.1652, found: 499.1657.

4.3.6. Compound ***2f***[18d]

White solid; 93% yield (43 mg); m.p. 148.4-148.9 °C; R_f = 0.30 (PE/EtOAc, 5:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 7.7 Hz, 2H), 7.28-7.25 (m, 2H), 7.10-7.07 (m, 2H), 6.71 (d, *J* = 7.7 Hz, 2H), 4.54 (s, 2H), 3.92-3.91 (m, 2H), 3.82-3.81 (m, 2H), 3.02 (s, 6H), 0.75 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.9, 168.8, 143.6, 129.2, 128.4, 123.3, 121.3, 107.5, 60.7, 54.3, 44.1, 26.5, 13.7.

4.3.7. Compound ***2g***[18d]

White solid; 86% yield (53 mg); m.p. 144.9-145.2 °C; R_f = 0.30 (PE/EtOAc, 6:1); ^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ = 7.59 (d, *J* = 7.7 Hz, 2H), 7.24-7.22 (m, 2H), 7.10-7.08 (m, 2H), 7.05-7.00 (m, 6H), 6.83 (d, *J* = 7.7 Hz, 2H), 6.78-6.77 (m, 4H), 4.78 (d, *J* = 16.0 Hz, 2H), 4.63 (d, *J* = 16.0 Hz, 2H), 4.52 (s, 2H), 3.98-3.97 (m, 2H), 3.89-3.86 (m, 2H), 0.69 (s, 6H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$): δ = 173.0, 169.0, 142.8, 135.9, 129.7, 128.7, 128.0, 127.5, 126.9, 123.2, 121.5 (s), 109.4, 61.2, 55.1, 43.1, 42.3, 14.0. HRMS (ESI) calc. for $C_{38}H_{34}N_2O_6$ $(M+Na)^+$: 637.2309, found: 637.2313.

4.3.8. Compound ***2h***

White solid; 87% yield (40 mg); m.p. 151.3-151.8 °C; R_f = 0.30 (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d*$_6$): δ = 10.12 (s, 2H), 7.25 (s, 2H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.62 (d, *J* = 7.8

Hz, 2H), 4.28 (s, 2H), 3.98-3.96 (m, 2H), 3.86-3.83 (m, 2H), 3.34 (s, 3H), 0.75 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-*d$_6$*): δ = 174.5, 169.2, 140.0, 129.6, 129.0, 128.9, 124.2, 109.3, 70.0, 55.2, 42.2, 21.3, 14.0. HRMS (ESI) calc. for $C_{26}H_{26}N_2O_6$ $(M+Na)^+$: 485.1683, found: 485.1691.

4.3.9. Compound ***2i***

White solid; 88% yield (43 mg); m.p. 136.7-137.0 ^{o}C; R_f = 0.30 (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d$_6$*): δ = 10.13 (s, 2H), 7.09 (s, 2H), 6.78 (d, *J* = 8.4, 2.2 Hz, 2H), 6.67 (d, *J* = 8.4 Hz, 2H), 4.30 (s, 2H), 3.99-3.96 (m, 2H), 3.88-3.85 (m, 2H), 3.72 (s, 6H), 0.78 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-*d$_6$*): δ = 174.4, 169.1, 153.8, 135.9, 125.3, 115.9, 114.2, 109.8, 61.0, 56.0, 55.4, 42.3, 14.1. HRMS (ESI) calc. for $C_{26}H_{26}N_2O_8$ $(M+Na)^+$: 517.1581, found: 517.1585.

4.3.10. Compound ***2j***

White solid; 87% yield (41 mg); m.p. 155.0-155.5 ^{o}C; R_f = 0.30 (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d$_6$*): δ = 10.46 (s, 2H), 7.30-7.27 (m, 2H), 7.07-7.06 (m, 2H), 6.78-6.76 (m, 2H), 4.31 (s, 2H), 4.01-3.96 (m, 2H), 3.89-3.84 (m, 2H), 0.77 (t, *J* = 7.1 Hz, 6H).; ^{13}C NMR (150 MHz, DMSO-*d$_6$*): δ = 174.2, 168.7, 157.0 (d, $^1J_{C\text{-}F}$ =234.1 Hz), 138.8, 125.3 (d, *J* = 8.9 Hz), 116.1 (d, 7.6 Hz), 116.0 (d, *J* = 10.3 Hz), 110.5 (d, *J* = 8.0 Hz), 61.2, 55.0, 42.6, 14.0. HRMS (ESI) calc. for $C_{24}H_{20}F_2N_2O_6$ $(M+Na)^+$: 493.1182, found: 493.1184.

4.3.11. Compound ***2k***

White solid; 39% yield (23 mg); m.p. 166.0-166.3 ^{o}C; R_f = 0.25 (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d$_6$*): δ = 10.58 (s, 2H), 7.57 (d, *J* = 1.5 Hz, 2H), 7.41 (dd, *J* = 8.3, 1.8 Hz, 2H), 6.75 (d, *J* = 8.3 Hz, 2H), 4.28 (s, 2H), 4.04-4.00 (m, 2H), 3.89-3.86 (m, 2H), 0.79 (t, *J* = 7.1 Hz, 6H).; ^{13}C NMR (150 MHz, DMSO-*d$_6$*): δ = 173.9, 168.7, 141.8, 132.4, 131.1, 125.9, 112.6, 111.8, 61.3, 54.7, 42.5, 14.1. HRMS (ESI) calc. for $C_{24}H_{20}Br_2N_2NO_6$ $(M+Na)^+$: 612.9580, found: 612.9585.

*4.3.12. Compound **2l***

White solid; 30% yield (21 mg); m.p. 143.4-143.9 °C; $R_f = 0.25$ (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d6*): δ = 10.53 (s, 2H), 7.71 (s, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 6.63 (d, *J* = 8.1 Hz, 2H), 4.24 (s, 2H), 4.04-4.01 (m, 2H), 3.88-3.85 (m, 2H), 0.80 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-*d6*): δ = 173.8, 168.7, 142.2, 138.2, 136.6, 126.2, 112.3, 61.4, 54.5, 42.3, 14.2. HRMS (ESI) calc. for $C_{24}H_{20}Br_2N_2NO_6$ $(M+Na)^+$: 612.9580, found: 612.9585. HRMS (ESI) calc. for $C_{24}H_{20}I_2N_2O_6$ $(M+Na)^+$: 708.9303, found: 708.9308.

*4.3.13. Compound **2m***

White solid; 43% yield (20 mg); m.p. 156.9-160.2 °C; $R_f = 0.30$ (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d6*): δ = 10.91 (s, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 7.17-7.14 (m, 2H), 7.00-6.97 (m, 2H), 4.32 (s, 2H), 3.97-3.92 (m, 2H), 3.87-3.82 (m, 2H), 0.75 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-*d6*): δ = 173.8, 168.7, 146.7 (d, $^1J_{C\text{-}F}$ =240.4 Hz), 129.7 (d, *J* =12.6 Hz), 126.5, 124.4, 121.4 (d, *J* =5.4 Hz), 116.7 (d, *J* =16.6 Hz), 61.2, 55.2, 42.5, 14.0. HRMS (ESI) calc. for $C_{24}H_{20}F_2N_2O_6$ $(M+Na)^+$: 493.1182, found: 493.1186.

*4.3.14. Compound **2n***

White solid; 70% yield (35 mg); m.p. 160.8-161.1 °C; $R_f = 0.30$ (PE/EtOAc, 3:1); ^{1}H NMR (600 MHz, DMSO-*d6*): δ = 10.82 (s, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.02-7.00 (m, 2H), 4.33 (s, 2H), 3.97-3.94 (m, 2H), 3.87-3.84 (m, 2H), 0.75 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-*d6*): δ = 173.8, 168.7, 140.1, 129.7, 126.9, 125.4, 122.0, 114.2, 61.2, 55.7, 42.5, 14.07. HRMS (ESI) calc. for $C_{24}H_{20}C_{l2}N_2O_6$ $(M+Na)^+$: 525.0591, found: 525.0595.

Acknowledgements

This work was financially supported by the Basic and Frontier Research Project of Chongqing (cstc2015jcyjBX0106), and the National Natural Science Foundation of China (No. 21672174 and No. 21472152).

References

1. (a) Roth HD. *Angew. Chem., Int. Ed. Engl*. 1989;28:1193-1207;

   (b) Tundo P, Anastas P, Black DS, Breen J, Collins T, Memoli S, Miyamoto J, Poliakoff M, Tumas W. *Pure Appl. Chem*. 2000;72:1207-1228;

   (c) Albini A, Fagnoni M. *Green Chem*. 2004;6:1-6;

   (d) Yoon TP, Ischay MA, Du J. *Nat. Chem*. 2010;2:527-532.

2. (a) Shi L, Xia WJ. *Chem. Soc. Rev*. 2012;41:7687-7697;

   (b) Xi YM, Yi H, Lei AW. *Org. Biomol. Chem*. 2013;11:2387-2403;

   (c) Prier CK, Rankic DA, MacMillan DWC. *Chem. Rev*. 2013;113:5322-5363;

   (d) Schultz DM, Yoon TP. *Science*. 2014;343:1239176.

3. (a) Gust D, Moore TA. *Acc. Chem. Res*. 1993;26:198-205;

   (b) Zeitler K. *Angew. Chem., Int. Ed*. 2009;48:9785-9789;

   (c) Ravelli D, Dondi D, Fagnoni M, Albini A. *Chem. Soc. Rev*. 2009;38:1999-2011;

   (d) Yoon TP, Ischay MA, Du J. *Nat. Chem*. 2010;2:527-532;

   (e) Narayanam JMR, Stephenson CRJ. *Chem. Soc. Rev*. 2011;40:102-113;

   (f) Xuan J, Xiao WJ. *Angew. Chem. Int. Ed*. 2012;51:6828-6838;

(g) Ravelli D, Fagnoni, M. *ChemCatChem*. 2012;4:169-171;

(h) Yoon TP. *ACS Catal*. 2013;3:895-902.

4. (a) Fidaly K, Ceballos C, Falguières A, Veitia MSI, Guy A, Ferroud C. Green Chem. 2012;14:293-1297;

(b) Shen ZC, Yang P, Tang Y. *J. Org. Chem*. 2016;81:309-317.

5. (a) Oelgemöller M, Healy N, de Oliveira L, Jung C, Mattay J. *Green Chem*. 2006;8:831-834;

(b) Clennan EL, Pace A. *Tetrahedron*. 2005;61:6665-6691;

(c) Shinkarenko NV, Aleskovskii VB. *Russ. Chem. Rev*. 1981;50:406-428;

(d) Fidaly K, Ceballos C, Falguières A, Sylla-Iyarreta Veitia M, Guy A, Ferroud C. *Green Chem*. 2012;14:1293-1297;

(e) Romero NA, Nicewicz DA. *Chem. Rev*. 2016;116:10075-10166.

6. (a) Gu X, Li X, Chai Y, Yang Q, Li P, Yao Y. *Green Chem*. 2013;15;357-361;

(b) Li X, Gu X, Li Y, Li P. *ACS Catal*. 2014;4:1897-1900;

(c) Majek M, Von Wangelin, A. J. *Angew. Chem., Int. Ed*. 2015; 54: 2270-2274.

7. (a) Esser P, Pohlmann B, Scharf HD. *Angew. Chem., Int. Ed. Engl*. 1994;33:2009-2023;

(b) Oelgemöller M, Jung C, Ortner J, Mattay J, Zimmermann E. *Green Chem*. 2005;7:35-38;

(c) Oelgemöller M, Healy NI, de Oliveira L, Jung C. J. Mattay, *Green Chem*. 2006;8: 831-834;

(d) Dondi D, Protti S, Albini A, Carpio SM. Fagnoni M. *Green Chem*. 2009;11:1653-1659.

8. (a) Vila C, Lau J, Rueping M, *Beilstein J. Org. Chem*. 2014;10:1233-1238;

(b) Gandy MN, Raston CL, Stubbs KA. *Chem. Commun*. 2015;51:11041-11044;

(c) Pan Y-H, Kee CW, Chen L, Tan C-H. *Green Chem*. 2011;13;2682-2685;

(d) Fidaly K, Ceballos C, Falguières A, Veitia MSI, Guy A, Ferroud C. *Green Chem*. 2012;

14:1293-1297;

(e) Vallejo SB, Yerien DE, Postigo A. *Eur. J. Org. Chem*. 2015;2015:7869-7875.

9. Liu H-J, Feng W, Kee CW, Zhao Y-J, Leow DS, Pan Y-H, Tan C-H. *Green Chem*. 2010;12: 953-956.

10. Gu X-Y, Li X, Chai Y-H, Yang Q, Li P-X, Yao Y-M. *Green Chem*. 2013;15:357-361.

11. Fan W-G, Yang Q, Xu F-S, Li P-X, *J. Org. Chem*. 2014;79:10588-10592.

12. (a) Galliford CV, Scheidt KA. *Angew. Chem., Int. Ed*. 2007;46:8748-8758;

(b) Zhou F, Liu Y-L, Zhou J. *Adv. Synth. Catal*. 2010;352:1381-1407.

13. (a) Venkatesan H, Davis MC, Altas Y, Snyder JP, Liotta DC. *J. Org. Chem*. 2001;66: 3653-3661;

(b) Greshock TJ, Grubbs AW, Jiao P, Wicklow DT, Gloer JB, Williams RM. *Angew. Chem., Int. Ed*. 2008;47:3573-3577;

(c) Kumar RR, Perumal S, Senthilkumar P, Yogeeswari P, Sriram D. *Eur. J. Med. Chem*. 2009; 44:3821-3829;

(d) Kotha S, Deb AC, Lahiri K, Manivannan E. *Synthesis*. 2009;2:165-193.

14. (a) Edmondson S, Danishefsky SJ, Sepp-Lorenzino L. Rosen N. *J. Am. Chem. Soc*. 1999;121:2147-2155;

(b) Marti C, Carreira EM. *J. Am. Chem. Soc*. 2005;127:11505-11515;

(c) Trost BM, Cramer N, Bernsmann H. *J. Am. Chem. Soc*. 2007;129:3086-3087;

(d) Franz AK, Dreyfuss PD, Schreiber SL. *J. Am. Chem. Soc*. 2007;129:1020-1021;

(e) Trost BM, Cramer N, Silverman SM. *J. Am. Chem. Soc.* 2007;129:12396-12397;

(f) Shangary S. *Proc. Natl. Acad. Sci. USA*. 2008;105:3933-3938;

(g) Chen XH, Wei Q, Luo SW, Xiao H, Gong LZ. *J. Am. Chem. Soc*. 2009;131:13819-13825;

(h) Trost BM, Brennan MK. *Synthesis*. 2009;18:3003-3025.

15. (a) Mao Z, Baldwin SW. *Org. Lett*. 2004;6:2425-2428;

(b) Nakazaki A, Miyamoto H, Henmi K, Kobayashi S. *Synlett*. 2005;9:1417-1420;

(c) Miyamoto H, Okawa Y, Nakazaki A, Kobayashi S. *Angew. Chem. Int. Ed*. 2006;45:2274-2277.

16. (a) Duan S-W, Li Y, Liu Y-Y, Zou Y-Q, Shi D-Q, Xiao W-J. *Chem. Commun*. 2012;48: 5160-5162;

(b) Tan B, Candeias NR, Barbas CF. *Nat. Chem*. 2011;3:473-477.

17. (a) Zhu X, Chiba S. *Chem. Commun*. 2016;52:2473-2476;

(b) He Y-H, He T, Guo J-T, Li R, Xiang Y, Yang D-C, Guan Z. *Catal. Sci. Technol*. 2016;6: 2239-2248.

18. (a) Beccalli EM, Clerici F, Gelmi ML. *Tetrahedron*. 2003;59:4615-4622;

(b) Yong SR, Williams MC, Pyne SG, Ung AT, B. SkeltonW, White AH, Turner P, *Tetrahedron*. 2005;61:8120-8129;

(c) Tan B, Candeias NR, Barbas CF. *J. Am. Chem. Soc*. 2011;133:4672-4675;

(d) Zou Y-Q, Duan S-W, Meng X-G, Hu X-Q, Gao S, Chen J-R, Xiao W-J. *Tetrahedron*. 2012;68:6914-6919;

(e) Jiang Y-H, Yang R-Y, Sun J, Yan C-G. *Heterocycl. Commun*. 2016;22:151-156.

19. Ciamician G, Silber P. *Chem. Ber*. 1908;1:071-1080.

20. (a) Ischay MA, Anzovino ME, Du J, Yoon TP. *J. Am. Chem. Soc*. 2008;130:12886-12887;

(b) Du J, Yoon TP. *J. Am. Chem. Soc*. 2009;131:14604-14605;

(c) Ischay MA, Lu Z, Yoon TP. *J. Am. Chem. Soc*. 2010;132:8572-8574.

21. (a) Austin KAB, Herdtweck E, Bach T. *Angew. Chem. Int. Ed*. 2011;50:8416-8419;

(b) Müller C, Bauer A, Maturi MM, Cuquerella MC, Miranda MA, Bach T. *J. Am. Chem. Soc*. 2011;133:16689-16697;

(c) Bach T, Bergmann H, Harms K. *Angew. Chem., Int. Ed*. 2000;39:2302-2304;

(d) Bach T, Bergmann H. *J. Am. Chem. Soc*. 2000;122:11525-11526;

(e) lonso R, Bach T. *Angew. Chem.* 2014;126:4457-4460;

(f) Maturi MM, Bach T. *Angew. Chem. Int. Ed*. 2014;53:7661-7664;

(g) Mayr F, Brimioulle R, Bach T. *J. Org. Chem*. 2016;81:6965-6971.

22. (a) Neumann M, Zeitler K. *Chem. Eur. J.* 2013;19:6950-6955;

(b) Riener M, Nicewicz DA. *Chem. Sci.* 2013;4:2625-2629;

(c) Liu Y, Song RJ, Li JH. *Sci. China Chem*. 2016;59:161-170;

(d) Xuan J, Lu LQ, Chen JR, Xiao WJ. *Eur. J. Org. Chem*. 2013;2013:6755-6770;

(e) Chen JR, Hu XQ, Lu LQ, Xiao WJ, *Acc. Chem. Res*. 2016;49:1911-1923.

23. (a) López F, Mascareñas JL. *Chem. Soc. Rev*. 2014;43:2904-2915;

(b) Ma S. *Acc. Chem. Res*. 2009;42:1679-1688;

(c) Alcaide B, Almendros P, Martínez del Campo T. *Chem. Eur. J*. 2010;16:5836-5842;

(d) Aubert C, Fensterbank L, Garcia P, Malacria M, Simonneau A. *Chem. Rev*. 2011;111: 1954-1993;

(e) Soriano E, Fernández I. *Chem. Soc. Rev*. 2014;43:3041-3105;

(f) López F, Mascareñas JL. *Chem. Eur. J*. 2011;17:418-428;

(g) Inagaki F, Kitagaki S, Mukai C. *Synlett*. 2011;2011:594-614.

24. (a) Danis J-B, Masson G, Retailleau P, Zhu J. *Angew. Chem., Int. Ed*. 2011;50:5356-5360;

(b) Xu S, Zhou L, Ma R, Song H, He Z. *Chem.Eur. J*. 2009;15:8698-8702;

(c) Rout L, Harned AM. *Chem. Eur. J*. 2009;15:12926-12928;

(d) Zhao G-L, Huang J-W, Shi M. *Org. Lett*. 2003;5:4737-4739;

(e) Zhang Q, Yang L, Tong X, *J. Am. Chem. Soc*. 2010;132:2550-2551;

(f) Clavier H, Jeune KL, de Riggi I, Tenaglia A, Buono G. *Org. Lett*. 2011;13:308-311.

25. Mojr V, Svobodová E, Straková K, Neveselý T, Chudoba J, Dvorˇákováb H, Cibulka R. *Chem. Commun*. 2015;51:12036-12039.

26. Ravelli D, Fagnoni M, Albini A. *Chem. Soc. Rev*. 2013;42:97-113.

27. (a) Lambert CR, Kochevar IE. *Photochem.Photobiol*.1997;66:15-25;

(b) Fischer BB, Krieger-Liszkay A, Eggen RIL. *Environ. Sci. Technol*. 2004;38:6307-6313.

28. (a) Li X, Gu XY, Li YJ, Li PX. *ACS Catal*. 2014;4:1897-1900;

(b) Pan YH, Wang SA, Kee CW, Dubuisson E, Yang YY, Loha KP, CH Tan. *Green Chem*. 2011;13:3341-3344.

29. (a) Sun JG, Yang H, Li P, Zhang B, *Org. Lett*. 2016;18:5114-5117;

(b) Shi Q, Li P, Zhu X, Wang L. *Green Chem*, 2016;18:4916-4923;

(c) Tung CH, Wu LZ, Zhang LP, Chen B. *Acc. Chem. Res*. 2003;36:39-47;

(d) Ghogare AA, Greer A. *Chem. Rev*. 2016;116:994-10034.

30. (a) Herder M, Schmidt BM, Grubert L, Pätzel M, Schwarz J, Hecht S. *J. Am. Chem. Soc*. 2015;137:2738-2747;

(b) Zhou J, Guo X, Katz HE. Bragg AE. *J. Am. Chem. Soc*. 2015;137:10841-10850.

31. Duan SW, Li Y, Liu YY, Zou YQ, Shi DQ, Xiao WJ. *Chem. Commun*. 2012;48:5160-5162.

32. Xu SB. Li CJ, Jia XS. Li J. *J. Org. Chem*. 2014;79:11161-11169.