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Metal-free visible-light photocatalytic tandem radical addition-cyclization strategy for the synthesis of sulfonyl-containing isoquinolinediones

Kai-Li Zuo,[a] Yan-Hong He*[a] and Zhi Guan*[a]

Abstract: A mild radical cascade reaction for the synthesis of sulfonyl-containing isoquinolinediones has been developed, in which sulfonyl radicals can be accessed from simple sodium sulfinates under visible light and eosin Y catalysis. This tandem approach features a broad range of substrates and functional group tolerance. With this strategy, trifluoromethylated isoquinolinedione was also obtained.

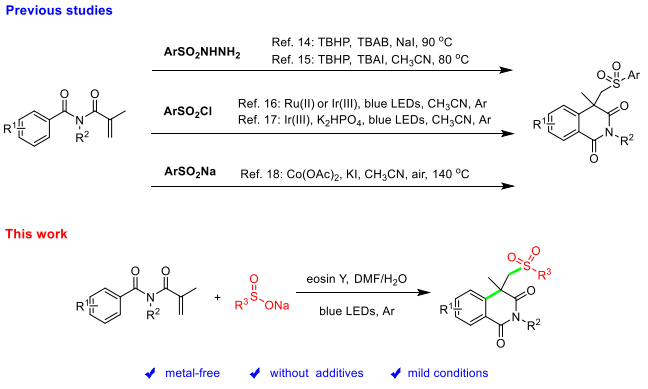
Introduction

Visible-light, as an abundant and sustainable clean energy source, has attracted wide attention from synthetic organic chemists in the past few years.[1] Visible-light photoredox catalysis provides a green and environmentally benign synthetic platform for the formation of C-C or C-heteroatom bonds.[2] Photocatalysts, as a kind of medium, play an important role in photoredox reaction since most organic molecules cannot directly utilize visible light. Organic dyes, such as eosin Y and rose Bengal, as a class of organic photocatalysts, are relatively inexpensive and non-toxic. They have a wider range of absorption compared to metal complex photocatalysts that contain ruthenium (II) and iridium (III), and have been widely used in photoredox transformations.[3]

Many sulfonyl-containing compounds display various bioactivities and are therefore of great significance in the development of agrochemicals and pharmaceuticals.[4] Accordingly, the methods of forming sulfonyl radicals are also greatly expanded. Visible-light photoredox catalysis provides a powerful and versatile tool for the formation of free radical species.[5] The precursors which are currently capable of producing sulfonyl radicals include sulfinic acids[6], sodium sulfinates[7], sulfonyl chlorides[8], sulfonyl hydrazides[9], SO_2[10] and so on[11]. Sodium sulfinates are stable, non-irritating and commercially available at low cost when used as a source of sulfonyl radicals in photoredox reactions, which has attracted our interest.

As a class of important skeleton, isoquinolinediones have been the focus of research.[12] Given their unique chemical, biological and pharmaceutical activities, a series of isoquinolinedione derivatives[13] including sulfonyl-containing isoquinolinediones have been synthesized. A general, concise strategy that enables direct synthesis of sulfonyl-containing isoquinolinedione derivatives by addition of sulfonyl radicals to *N*-methyl-*N*-methacryloylbenzamides followed by cyclization has attracted great interest. Several research groups used different methods to obtain sulfonyl radicals to successfully apply this strategy. In 2015, Zhou's group[14] and Xu's group[15] used $ArSO_2NHNH_2$ as the precursors and tert-butyl hydroperoxide (TBHP) as an oxidant in the presence of tetrabutylammonium bromide (TBAB) + NaI at 90 °C or tetrabutylammonium iodide (TBAI) at 80 °C to generate sulfonyl radicals, respectively. In 2016, Xia's group[16] and Sun's group[17] employed $ArSO_2Cl$ as the sulfonyl sources to produce sulfonyl radicals through visible light photoredox catalysis using $Ru(bpy)_3Cl_2$ or $[Ir(ppy)_2dtbbpy]PF_6$ as the photocatalyst under blue LEDs, respectively. In 2017, Zhou's group[18] utilized $ArSO_2Na$ as the sulfonyl sources to generate sulfonyl radicals with a combined catalyst system composed of $Co(OAc)_2•4H_2O$ and KI at 140 °C. (**Scheme 1**) These efforts have greatly improved and enriched this reaction. However, the existing methods still have some drawbacks, such as the use of excessive amounts of oxidants, irritating reagents, noble metals, high temperatures, etc. Therefore, it is still necessary to develop mild, environmentally friendly and simple methods for this useful reaction.

Scheme 1. Methods for constructing sulfonyl-containing isoquinolinediones



Herein, we report a mild and metal-free method for the

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http://222.198.118.160/s/chemistry/szxx/20151222/180919.html
http://222.198.118.160/s/chemistry/szxx/20151222/180909.html

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synthesis of sulfonyl-containing isoquinolinediones from *N*-alkyl-*N*-methacryloyl benzamides in which sulfonyl radicals can be easily accessed from stable, low cost and non-irritating sodium sulfinates by visible light photoredox catalysis using an inexpensive organic dye, eosin Y, as a photocatalyst.

Results and Discussion

In our initial investigation, the reaction of *N*-methyl-*N*-methacryloylbenzamide (**1a**) and sodium benzenesulfinate (**2a**) was chosen as a model reaction. Rose Bengal was first used as a photocatalyst for the model reaction in DMF under irradiation of 7 W blue light-emitting diodes (LEDs) in an argon atmosphere. To our delight, the desired product **3a** was obtained in 45% yield (**Table 1**, entry 1). On this basis, we investigated the effect of adding water on the reaction and found that adding a small amount of water to the reaction system can increase the reaction yield (see Supporting Information (SI), **Table S1**), possibly due to the addition of water that promotes dissolution of **2a**. A yield of 56% was obtained in a mixed solvent of of DMF (2 mL)/H_2O (50 μL) (**Table 1**, entry 2). We then investigated the effect of substrate molar ratio on the reaction and found that when 3.0 equivalents of **2a** were used, a yield of 60% was obtained (**Table 1**, entry 3; for details, see SI, **Table S2**). Thus, reaction conditions of a mixed solvent of DMF (2 mL)/H_2O (50 μL) and 3.0 equivalents of **2a** were used for further investigations. Next, other photocatalysts such as eosin Y, Na_2-eosin Y, eosin B and $Ru(bpy)_3Cl_2{\cdot}6H_2O$ were examined for the reaction (**Table 1**, entries 4-7). The reaction with eosin Y gave the best yield of 70% (**Table 1**, entry 4). Therefore, eosin Y was selected as the photocatalyst for the reaction. After screening the eosin Y loading, 5 mol % of eosin Y was selected as the optimal condition (SI, **Table S3**). Evaluation of different solvents revealed that DMF was the best choice for this process (**Table 1**, entries 4 and 8-11). In order to test the effect of oxygen on the reaction, the model reaction was carried out under O_2 and air atmosphere respectively; the desired product was not obtained, indicating that oxygen is harmful to this reaction (**Table 1**, entries 12 and 13). Using green LEDs or compact fluorescent lamp (CFL) instead of blue LEDs in the presence of eosin Y did not give better results (**Table 1**, entries 14 and 15). Moreover, control experiments proved that both photocatalyst and visible light were required for this conversion because no reaction was observed in the absence of visible-light or photocatalyst (**Table 1**, entries 16 and 17). Therefore, based on the experimental results, it was found that the optimized reaction conditions (for a 0.2 mmol scale of **1a**) consisted of 5 mol% of eosin Y, **1a**/**2a** = 1 : 3 (molar ratio), 7 W blue LEDs, DMF (2 mL)/H_2O (50 μL) and argon atmosphere.

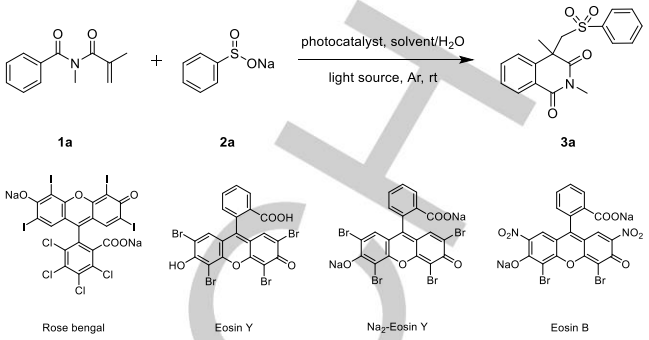


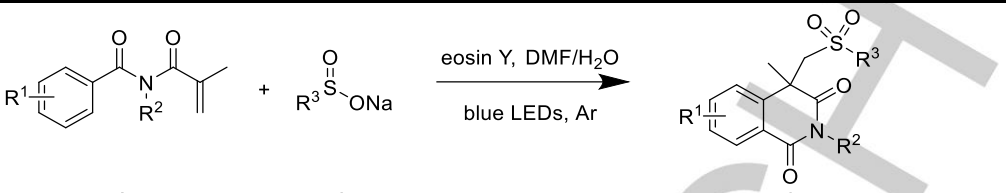
Table 1. Selected optimization experiments and control experiments.[a]

Entry	Photocatalyst	Solvent	Note	Yield (%)[b]
1	rose Bengal	DMF	**2a** (2.0 equiv), without H_2O	45
2	rose Bengal	DMF	**2a** (2.0 equiv)	56
3	rose Bengal	DMF	--	60
4	eosin Y	DMF	--	70
5	Na_2- eosin Y	DMF	--	50
6	eosin B	DMF	--	53
7	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	DMF	--	56
8	eosin Y	DMSO	--	60
9	eosin Y	THF	--	51
10	eosin Y	MeCN	--	42
11	eosin Y	EtOH	--	trace
12	eosin Y	DMF	under air atmosphere	trace
13	eosin Y	DMF	under O_2 atmosphere	NR[c]
14	eosin Y	DMF	7 W green LEDs	40
15	eosin Y	DMF	32 W CFL	59
16	eosin Y	DMF	in the dark	NR
17	--	DMF	--	NR

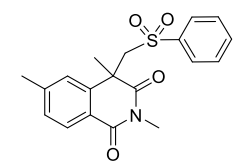
[a] Unless otherwise noted, reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.6 mmol, 3.0 equiv), photocatalyst (5 mol %), H_2O (50 μL) and solvent (2 mL) stirred under irradiation of 7 W blue LEDs in argon atmosphere at RT (25-30 °C) for 24 h. [b] Yield of isolated product. [c] No reaction.

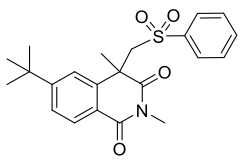
Using the optimized conditions (**Table 1**, entry 4), we investigated substrate scope of the reaction (**Table 2**). The transformation was first extended to various substituted *N*-methyl-*N*-methacryloylbenzamides. Several groups such as methyl, tertiary butyl, methoxyl, fluoro, chloro, bromo, trifluoromethyl and ester group at different position of benzene ring were able to survive under the optimized conditions to produce corresponding products (**3b-3l**). The presence of an electron-donating group and an electron-withdrawing group on the benzene ring of compounds **1** had no significant effect on the reaction. 3,4-Dichlorobenzamide and naphthamide also could participate in the reaction delivering desired isoquinolinediones **3m** and **3n**. However, to our disappointment, when the aromatic ring of compound **1** is thiophene, the transformation failed. The methacryloyl benzamides **1** with different *N*-substituents were also examined and the corresponding products were obtained in moderate yields (**3o-3t**). A series of sodium sulfinates were then investigated in this reaction and the desired products were obtained in good yields (**3u-3y**).

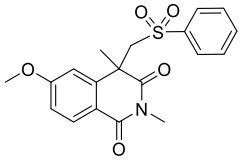
Table 2. Substrate scope.[a,b]

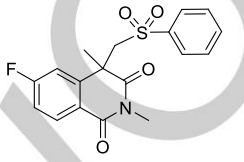


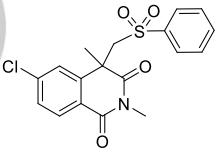
1 **2** **3**

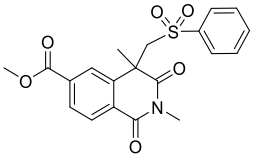

3b, 74%

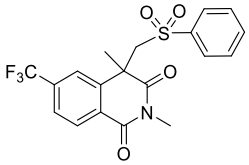

3c, 46%

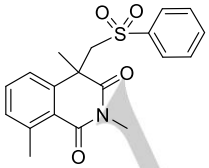

3d, 61%

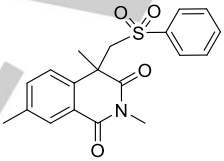

3e, 67%

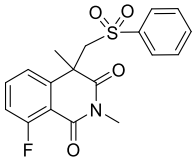

3f, 67%

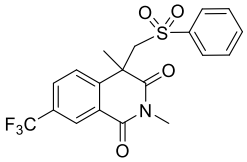

3g, 54%

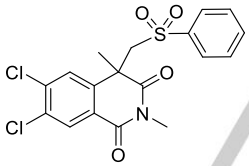

3h, 60%

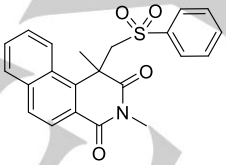

3i, 69%

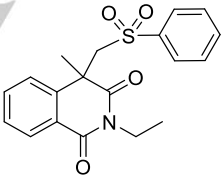

3j, 52%

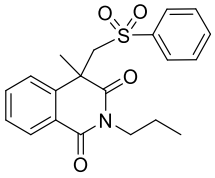

3k, 65%

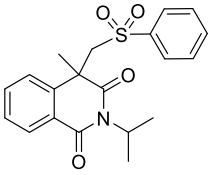

3l, 58%

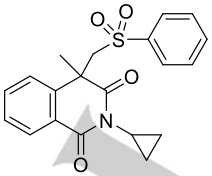

3m, 40%

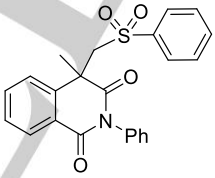

3n, 32%

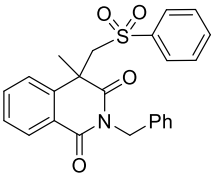

3o, 60%

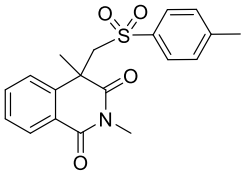

3p, 62%

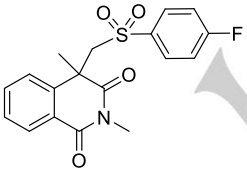

3q, 57%

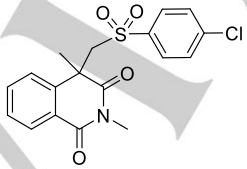

3r, 69%

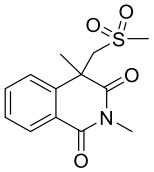

3s, 51%

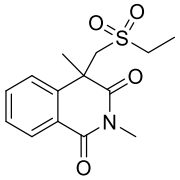

3t, 57%


3u, 65%


3v, 51%


3w, 82%


3x, 76%

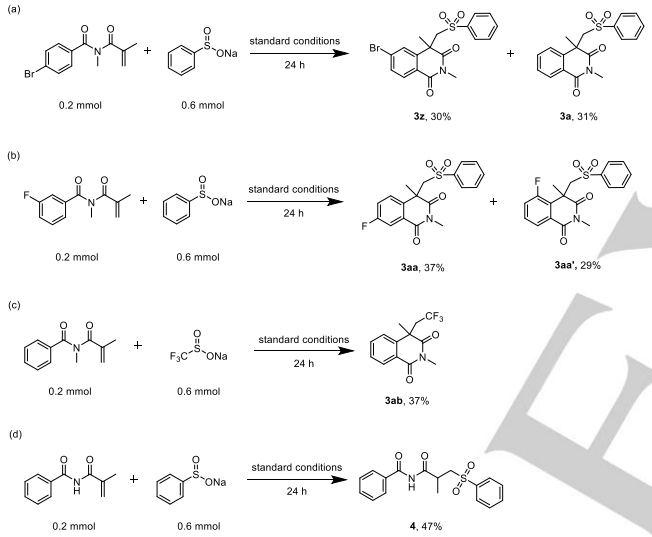

3y, 58%

[a]Reaction conditions: **1** (0.2 mmol, 1.0 equiv), **2** (0.6 mmol, 3.0 equiv), eosin Y (5 mol %), H_2O (50 μL) and DMF (2 mL) stirred under irradiation of 7 W blue LEDs in argon atmosphere at RT (25-30 ^oC) for 24 h. [b]Yield of the isolated product after chromatography on silica gel.

Interestingly, when a bromo substituted substrate **1** was used, it not only gave the desired product (**3z**), but also produced a yield of 30% of compound **3a** in which the bromine atom was removed (**Scheme 2,** a). When a *meta*-fluoro substituted substrate **1** was used, two regioisomers **3aa** (37%) and **3aa'** (29%) were obtained, which were formed by cyclization at the

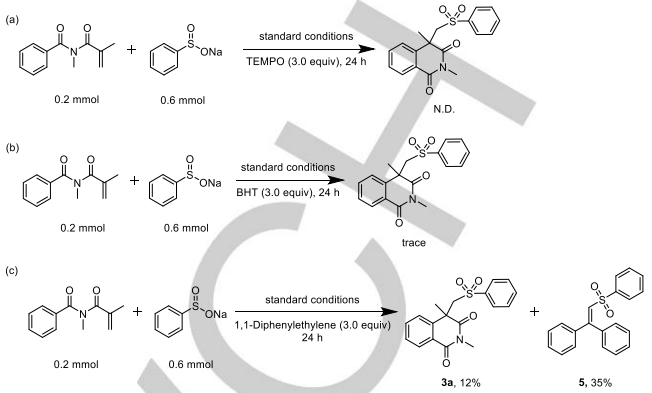
para and *ortho* positions, respectively (**Scheme 2,** b). However, the above-mentioned examples of *meta*-CH_3 or CF_3 substituted substrate **1** only gave a single product (**Table 2, 3j** and **3l**) which was formed by cyclization at the *para* position, probably because CH_3 and CF_3 are bulkier than F. Additionally, when sodium trifluoromethanesulfinate was used, the trifluoromethylsulfonylation product was not formed, but trifluoromethylated isoquinolinedione **3ab** was obtained in a yield of 37% (**Scheme 2,** c).[19] When R^2 is hydrogen atom, the desired cyclized product cannot be achieved, but the radical addition product **4** was obtained (**Scheme 2,** d). When R^2 is a sulfonyl group or the nitrogen atom of *N*-methacryloylbenzamides is replaced with O, the starting material was decomposed, and no desired product was detected.

Scheme 2. Exceptional examples



Next, to gain more mechanistic insight, we performed some control experiments (**Scheme 3**). 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) and 2,6-*di-tert-butyl*-4-methylphenol (BHT) are a class of radical scavengers. When 3.0 equivalents of TEMPO or BHT was added to the model reaction system under optimized reaction conditions, no desired product was obtained (**Scheme 3,** a and b). In addition, 1,1-diphenylethylene has been widely used in photochemistry due to its ability to trap radicals. When 3.0 equivalents of 1,1-diphenylethylene were present in the reaction system, the yield of product **3a** was lowered to 12% and the product **5** which captured the sulfonyl radical was obtained in a yield of 35% (**Scheme 3,** c). All of the results revealed that this reaction should involve a radical process, and sulfonyl radical is a key intermediate.

Scheme 3. Control experiments



In order to understand the effect of photo-irradiation, the reaction with the light on/off over time was carried out (**Figure 1**(**a**)). The results indicated that continuous irradiation of visible light is essential, and radical-chain propagation is not a critical pathway in this reaction. Further, to verify which substrate can quench the excited photocatalyst, a series of fluorescence quenching experiments of eosin Y with substrates were performed (see SI, **Figure S2-S4**), and the Stern-Volmer plot is shown in **Figure 1(b)**. The experiments showed that sodium benzenesulfinate **2a** caused a strong fluorescence quenching of excited eosin Y, while almost no any quenching effect was observed for *N*-methyl-*N*-methacryloylbenzamide **1a**. Additionally, we tested the reaction system with pH test paper before and after the reaction, and the results showed that a base was generated during the reaction (see SI, **Figure S6**).

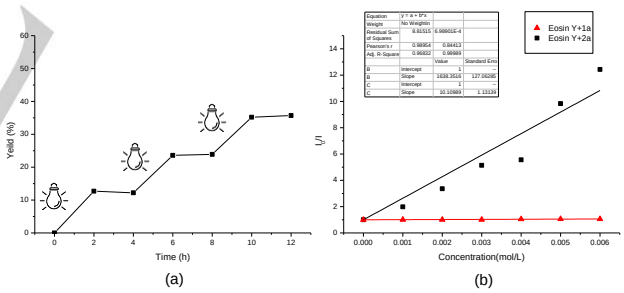
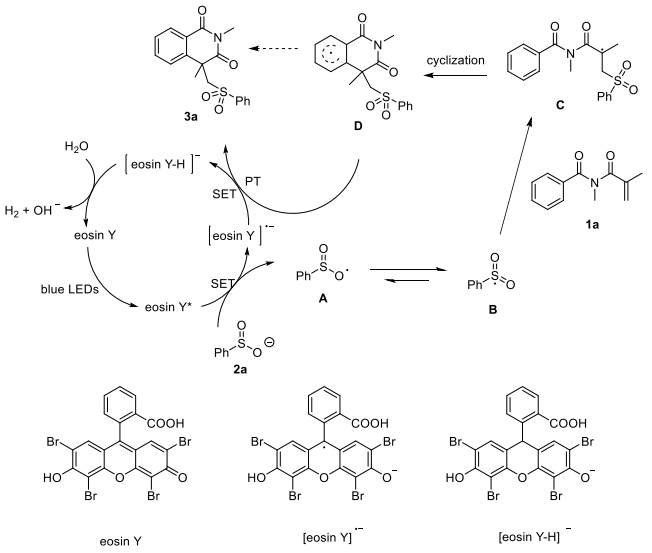


Figure 1. a) Light ON/OFF experiment; b) Sterm-Volmer profile of eosin Y by various concentrations of **1a** and **2a**

On the basis of above mechanistic studies and related literature[20], we proposed a plausible process for the current photocatalytic radical addition/cyclization reaction (**Scheme 4**). First, the excited state of photocatalyst, eosin Y*, which is formed reversibly upon visible light irradiation, is reductively quenched by the sulfinate **2a** ($E_{1/2}$ = 0.47 V vs.SCE, see SI, **Figure S5**) to afford [eosin Y]$^{\cdot-}$ ($E_{1/2\ red}$ [eosin Y*/eosin Y$^{\cdot-}$] = +0.83 V vs.SCE)[21] and sulfonate radical **A**. There is a resonance between the oxygen-centered sulfonyl radical **A** and the corresponding sulfur-centered sulfonyl radical **B**. Next, radical **B** undergoes a radical addition to alkene **1a** generating new radical **C**, which can be intramolecularly cyclized to form intermediate **D**. Product **3a** and eosin Y-H hydride[20b] are then given from intermediate **D** and eosin Y radical anion by single electron transfer (SET) and proton transfer (PT). Finally, the

eosin Y-H hydride reacts with proton to release H_2 and regenerate eosin Y to complete the photocatalytic cycle.

Scheme 4. Proposed Reaction Mechanism



Conclusions

In summary, a general visible-light photocatalytic protocol for the synthesis of sulfonyl-containing isoquinolinediones via radical tandem C-S/C-C bond formation has been developed. In this strategy, stable, non-irritating and cheap sodium sulfinates were used as radical precursors, and a relatively inexpensive and non-toxic organic dye eosin Y was used as a photocatalyst. This tandem approach features a broad range of substrates and functional group tolerances. With this method, trifluoromethylated isoquinolinedione was also obtained. Compared to previously reported methods, this protocol is more environmentally friendly, milder and more economical, avoiding the use of excessive amounts of oxidants, additives, irritating reagents, noble metals and high temperatures. Therefore, we believe that this work is a useful complement to existing methods.

Experimental Section

General information: *N*-Alkyl-*N*-methacryloyl benzamides **1** were prepared according to the literature[22]. Eosin Y was purchased from J&K Scientific Ltd. L520P26-5g. DMF was dried over 3A molecular sieves. 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. Fluorescence emission was determined by fluorescence spectrophotometer (F-2500 Hitachi, Tokyo, Japan). High-resolution mass spectra were obtained by using ESI ionization sources. Melting points were taken on a WPX-4 apparatus and were uncorrected (Yice instrument equipment Co Ltd, Shanghai). Cyclic voltammetry was performed using electrochemical workstation (CHI700E, Shanghai Chenhua Instrument Co., Ltd. Shanghai).

General procedure for the synthesis of products 3: A round bottom flask was charged with eosin Y (5 mol %), *N*-alkyl-*N*-methacryloyl benzamide **1** (0.2 mmol) and sodium sulfinate **2** (0.6 mmol). The flask was evacuated and backfilled with Ar (three times). Then DMF (2 mL) and H_2O (50 μL) were added under Ar. The resultant mixture was stirred at room temperature under irradiation of 7 W blue LEDs. After completion of the reaction, as monitored by TLC, brine (5 mL) was added. The resulting mixture was extracted with ethyl acetate (5 mL × 3). The organic layer was combined, and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo, and the residue was purified by flash column chromatography (petroleum ether/EtOAc 3/1-1/2, v/v) to afford the desired product 3.

2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3a):[16] White solid (48.0 mg, 70%), m.p. 175.2-176.8 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.1 Hz, 1H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 2H), 7.42-7.36 (m, 4H), 7.17 (d, *J* = 7.4 Hz, 1H), 4.46 (d, *J* = 14.7 Hz, 1H), 3.90 (d, *J* = 14.7 Hz, 1H), 3.40 (s, 3H), 1.59 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.3, 163.7, 140.3, 139.1, 133.4, 129.3, 129.1, 128.1, 127.6, 125.8, 124.9, 64.8, 45.4, 31.6, 27.5 ppm.

2,4,6-trimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3b): White solid (52.5 mg, 74%), m.p. 178.1-179.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 1H), 6.82 (s, 1H), 4.47 (d, *J* = 14.8 Hz, 1H), 3.89 (d, *J* = 14.8 Hz, 1H), 3.40 (s, 3H), 2.17 (s, 3H), 1.57 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.4, 163.8, 144.4, 140.4, 138.9, 133.3, 129.3, 129.2, 128.9, 127.5, 126.3, 122.5, 64.8, 45.3, 31.5, 27.4, 21.6 ppm. HRMS (ESI) calc. for C19H19NO4S $(M+Na)^+$: 380.0927, found: 380.0929.

6-(tert-butyl)-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3c): White solid (36.4 mg, 46%), m.p. 183.8-184.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.3 Hz, 1H), 7.51-7.44 (m, 4H), 7.37-7.35 (m, 2H), 7.19 (d, *J* = 3.8 Hz, 1H), 4.49 (d, *J* = 14.7 Hz, 1H), 3.94 (d, *J* = 14.7 Hz, 1H), 3.38 (s, 3H), 1.59 (s, 3H), 1.24-1.23 (m, 9H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.6, 163.8, 157.4, 140.4, 138.9, 133.5, 129.1, 129.0, 127.7, 125.6, 122.4, 122.3, 65.0, 45.7, 35.2, 31.8, 30.9, 27.4 ppm. HRMS (ESI) calc. for C22H25NO4S $(M+Na)^+$: 422.1397, found: 422.1395.

6-methoxy-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3d): White solid (45.4 mg, 61%), m.p. 159.7-160.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.8 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 6.89 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.51 (d, *J* = 2.2 Hz, 1H), 4.47 (d, *J* = 14.8 Hz, 1H), 3.86 (d, *J* = 14.7 Hz, 1H), 3.71 (s, 3H), 3.38 (s, 3H), 1.57 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.4, 163.7, 163.4, 141.2, 140.4, 133.3, 131.6, 129.0, 127.6, 117.9, 114.1, 111.1, 64.8, 55.4, 45.7, 31.7, 27.4 ppm. HRMS (ESI) calc. for C19H19NO5S $(M+Na)^+$: 396.0876, found: 396.0875.

6-fluoro-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3e): White solid (48.3 mg, 67%), m.p. 241.3-242.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 8.5, 5.9 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.10 (t, *J* = 7.9 Hz, 1H), 6.83 (d, *J* = 9.1 Hz, 1H), 4.46 (d, *J* = 14.7 Hz, 1H), 3.82 (d, *J* = 14.7 Hz, 1H), 3.40 (s, 3H),

1.59 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8, 166.7, 165.0, 162.8, 142.1 (d, *J* = 8.6 Hz), 133.7, 132.3 (d, *J* = 9.7 Hz), 129.2, 127.5, 121.3, 116.2, 116.1, 113.0, 112.8, 64.7, 45.6, 31.4, 27.6 ppm. HRMS (ESI) calc. for C18H16FNO4S (M+Na)$^+$: 384.0676, found: 384.0679.

6-chloro-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3f): White solid (50.7 mg, 67%), m.p. 218.5-219.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.5 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.35 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.06 (d, *J* = 1.1 Hz, 1H), 4.46 (d, *J* = 14.8 Hz, 1H), 3.85 (d, *J* = 14.8 Hz, 1H), 3.42 (s, 3H), 1.58 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.7, 162.9, 140.7, 140.2, 140.1, 133.8, 130.8, 129.1, 128.8, 127.4, 126.2, 123.4, 64.6, 45.4, 31.3, 27.6 ppm. HRMS (ESI) calc. for C18H16ClNO4S (M+Na)$^+$: 400.0381, found: 400.0380.

methyl 2,4-dimethyl-1,3-dioxo-4-((phenylsulfonyl)methyl)-1,2,3,4-tetrahydroisoquinoline-6-carboxylate (3g): White solid (43.0 mg, 54%), m.p. 223.2-223.9 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.73 (s, 1H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 4.48 (d, *J* = 14.8 Hz, 1H), 3.98 (d, *J* = 14.8 Hz, 1H), 3.91 (s, 3H), 3.44 (s, 3H), 1.63 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 165.3, 163.0, 140.2, 139.08, 134.3, 133.2, 129.5, 129.1, 128.8, 128.2, 127.4, 64.8, 52.5, 45.4, 31.2, 27.7 ppm. HRMS (ESI) calc. for C20H19NO6S (M+Na)$^+$: 424.0825, found: 424.0825.

2,4-dimethyl-4-((phenylsulfonyl)methyl)-6-(trifluoromethyl)isoquinoline-1,3(2*H*,4*H*)-dione (3h): White solid (49.1 mg, 60%), m.p. 226.3-226.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.45 (d, *J* = 7.3 Hz, 2H), 7.38-7.38 (m, 3H), 4.50 (d, *J* = 14.8 Hz, 1H), 3.91 (d, *J* = 14.8 Hz, 1H), 3.46 (s, 3H), 1.63 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.6, 162.7, 140.0, 139.9, 135.0 (q, *J* = 32.9 Hz), 133.8, 130.2, 129.2, 127.9, 127.3, 125.0 (q, *J* = 32.9 Hz), 123.9, 123.0 (q, *J* = 3.7 Hz), 122.1, 64.8, 45.5, 31.2, 27.8 ppm. HRMS (ESI) calc. for C19H16F3NO4S (M+Na)$^+$: 434.0644, found: 434.0640.

2,4,8-trimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3i): White solid (49.2 mg, 69%), m.p. 211.1-212.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54-7.53 (m, 3H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.27-7.24 (m, 1H), 7.20 (d, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 4.47 (d, *J* = 14.6 Hz, 1H), 3.90 (d, *J* = 14.6 Hz, 1H), 3.38 (s, 3H), 2.82 (s, 3H), 1.58 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0, 164.3, 143.0, 140.4, 133.4, 132.3, 132.2, 129.0, 127.6, 124.2, 123.0, 65.0, 45.6, 32.1, 27.5, 24.1 ppm. HRMS (ESI) calc. for C19H19NO4S (M+Na)$^+$: 380.0927, found: 380.0931.

2,4,7-trimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3j): White solid (37.2 mg, 52%), m.p. 159.2-159.8 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.53-7.46 (m, 3H), 7.36-7.33 (m, 2H), 7.13-7.12 (m, 1H), 7.04-7.02 (m, 1H), 4.42 (d, *J* = 14.6 Hz, 1H), 3.88 (d, *J* = 14.6 Hz, 1H), 3.39 (s, 3H), 2.38 (s, 3H), 1.56 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.4, 163.9, 140.3, 138.1, 136.2, 134.4, 133.2, 129.3, 129.0, 127.6, 125.8, 124.6, 65.0, 45.1, 31.5, 27.5, 21.0. HRMS (ESI) calc. for C19H19NO4S (M+Na)$^+$: 380.0927, found: 380.0930.

8-fluoro-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3k): White solid (47.0 mg, 65%), m.p. 213.3-214.3 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61-7.56 (m, 3H), 7.46-7.42 (m, 3H), 7.14-7.09 (m, 2H), 4.48 (d, *J* = 14.6 Hz, 1H), 3.88 (d, *J* = 14.6 Hz, 1H), 3.38 (s, 3H), 1.60 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5, 162.7 (d, *J* = 266.2 Hz), 160.6, 141.7, 140.3, 134.5 (d, *J* = 10.5 Hz), 133.6, 129.2, 127.6, 121.9 (d, *J* = 4.2 Hz), 116.7 (d, *J* = 22. 2Hz), 113.9 (d, *J* = 4.2 Hz), 64.8, 45.4, 31.8, 27.4. HRMS (ESI) calc. for C18H16FNO4S (M+Na)$^+$: 384.0676, found: 384.0677.

2,4-dimethyl-4-((phenylsulfonyl)methyl)-7-(trifluoromethyl)isoquinoline-1,3(2*H*,4*H*)-dione (3l): White solid (47.6 mg, 58%), m.p. 151.9-152.6 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.58-7.54 (m, 2H), 7.48 (d, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 1H), 4.50 (d, *J* = 14.8 Hz, 1H), 3.92 (d, *J* = 14.8 Hz, 1H), 3.45 (s, 3H), 1.62 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5, 162.6, 142.7, 140.0, 133.7, 130.8 (q, *J* = 33.7 Hz), 130.7, 129.6 (q, *J* = 3.4 Hz), 129.3, 127.5, 126.8, 126.6 (q, *J* = 3.8 Hz), 125.6, 124.2 122.4, 64.6, 45.5, 31.2, 27.8. HRMS (ESI) calc. for C19H16F3NO4S (M+Na)$^+$: 434.0644, found: 434.0641.

6,7-dichloro-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3m): White solid (33.0 mg, 40%), m.p. 237.7-238.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.14 (s, 1H), 4.45 (d, *J* = 14.8 Hz, 1H), 3.81 (d, *J* = 14.9 Hz, 1H), 3.42 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.3, 162.0, 139.9, 138.4, 138.3, 133.8, 133.4, 130.9, 129.2, 128.2, 127.3, 124.8, 64.9, 45.0, 31.0, 27.8. HRMS (ESI) calc. for C18H15Cl2NO4S (M+Na)$^+$: 433.9991, found: 433.9993.

1,3-dimethyl-1-((phenylsulfonyl)methyl)benzo[f]isoquinoline-2,4(1*H*,3*H*)-dione (3n): White solid (24.8 mg, 32%), m.p. 189.8-190.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.6 Hz, 1H), 8.06-8.05 (m, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.69-7.67 (m, 1H), 7.45-7.43 (m, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 7.3 Hz, 2H), 6.88 (t, *J* = 7.8 Hz, 2H), 4.75 (d, *J* = 15.0 Hz, 1H), 4.68 (d, *J* = 15.1 Hz, 1H), 3.51 (s, 3H), 2.02 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.6, 164.1, 136.6, 135.9, 132.6, 130.2, 130.1, 129.2, 128.1, 127.6, 126.8, 126.7, 125.1, 124.4, 124.2, 63.7, 46.6, 29.1, 27.8 ppm. HRMS (ESI) calc. for C22H19NO4S (M+Na)$^+$: 416.0927, found: 416.0928.

2-ethyl-4-methyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3o):[14] White solid (42.8 mg, 60%), m.p. 175.8-177.1 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30-8.28 (m, 1H), 7.53-7.49 (m, 3H), 7.41-7.36 (m, 4H), 7.16-7.14 (m, 1H), 4.47 (d, *J* = 14.6 Hz, 1H)., 4.09 (q, *J* = 7.0 Hz, 2H), 3.91 (d, *J* = 14.6 Hz, 1H), 1.57 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 163.3, 140.5, 139.2, 133.3, 133.3, 129.3, 129.1, 128.1, 127.5, 125.7, 125.0, 64.7, 45.4, 36.1, 31.5, 12.7 ppm.

4-methyl-4-((phenylsulfonyl)methyl)-2-propylisoquinoline-1,3(2*H*,4*H*)-dione (3p): White solid (46.0 mg, 62%), m.p. 116.0-116.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.7 Hz, 1H), 7.54-7.49 (m, 3H), 7.41-7.34 (m, 4H), 7.15 (d, *J* = 7.7 Hz, 1H), 4.48 (d, *J* = 14.7 Hz, 1H), 4.03-3.97 (m, 2H), 3.92 (d, *J* = 14.7 Hz, 1H), 1.78-1.70 (m, 2H), 1.57 (s, 3H), 1.00 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.1, 163.5, 140.5, 139.2, 133.4, 133.3, 129.3, 129.1, 128.1, 127.5, 125.7, 124.9, 45.5, 42.5, 31.7, 20.9, 11.4 ppm. HRMS (ESI) calc. for C20H20NO4S (M+Na)$^+$: 394.1083, found: 394.1086.

2-isopropyl-4-methyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3q): [14] White solid (42.5 mg, 57%), m.p. 156.2-156.6 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.0 Hz, 1H), 7.53-7.48 (m, 3H), 7.39-7.35 (m, 3H), 7.33-7.29 (m, 1H), 7.10-7.09 (m, 1H), 5.30-5.23 (m, 1H), 4.46 (d, *J* = 14.6 Hz, 1H), 3.88 (d, *J* = 14.6 Hz, 1H), 1.58-1.53 (m, 9H) ppm. ^{13}C NMR (150 MHz,

$CDCl_3$) δ 174.3, 163.9, 140.8, 139.1, 133.3, 133.1, 129.3, 129.3, 129.1, 128.0, 127.4, 125.5, 64.8, 45.9, 45.7, 31.4, 19.6, 19.2 ppm.

2-cyclopropyl-4-methyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3r): White solid (50.6 mg, 69%), m.p 177.8-180.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27-8.25 (m, 1H), 7.54-7.50 (m, 3H), 7.40-7.34 (m, 4H), 7.15 (d, *J* = 7.7 Hz, 1H), 4.44 (d, *J* = 14.6 Hz, 1H), 3.87 (d, *J* = 14.6 Hz, 1H), 2.81-2.77 (m, 1H), 1.55 (s, 3H), 1.22-1.15 (m, 2H), 0.97-0.93 (m, 1H), 0.72-0.68 (m, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.1, 164.6, 140.5, 139.1, 133.4, 133.3, 129.2, 129.1, 128.1, 127.5, 125.8, 125.5, 64.7, 45.7, 31.3, 24.8, 8.4, 8.3 ppm. HRMS (ESI) calc. for $C_{20}H_{19}NO_4S$ $(M+Na)^+$: 392.0927, found: 392.0929.

4-methyl-2-phenyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3s): White solid (41.4 mg, 51%), m.p. 246.2-247.7 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.55-7.51 (m, 5H), 7.48-7.35 (m, 7H), 7.22 (d, *J* = 7.5 Hz, 1H), 4.47 (d, *J* = 14.6 Hz, 1H), 3.97 (d, *J* = 14.6 Hz, 1H), 1.70 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.4, 163.8, 140.6, 139.3, 135.6, 133.7, 133.4, 129.7, 129.3, 129.2, 128.7, 128.5, 128.3, 127.5, 126.0, 125.1, 65.2, 45.9, 31.4 ppm. HRMS (ESI) calc. for $C_{23}H_{19}NO_4S$ $(M+Na)^+$: 428.0927, found: 428.0928.

2-benzyl-4-methyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3t): White solid (48.2 mg, 57%), m.p. 149.8-151.4 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (d, *J* = 4.0 Hz, 1H), 7.52-7.46 (m, 5H), 7.40-7.36 (m, 4H), 7.30 (m, 2H), 7.25-7.20 (m, 2H), 5.23 (q, *J* = 14.0 Hz, 2H), 4.48 (d, *J* = 14.6 Hz, 1H), 3.94 (d, *J* = 14.4 Hz, 1H), 1.53 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.2, 163.5, 140.6, 139.4, 137.0, 133.6, 133.4, 129.6, 129.1, 128.5, 128.4, 128.1, 127.6, 127.6, 125.8, 124.8, 64.4, 45.9, 44.1, 31.7 ppm. HRMS (ESI) calc. for $C_{24}H_{21}NO_4S$ $(M+Na)^+$: 442.1083, found: 442.1088.

2,4-dimethyl-4-(tosylmethyl)isoquinoline-1,3(2*H*,4*H*)-dione (3u):[16] White solid (46.5 mg, 65%), m.p. 140.7-141.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29-8.27 (m, 1H), 7.42-7.40 (m, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.21-7.19 (m, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 4.44 (d, *J* = 14.6 Hz, 1H), 3.87 (d, *J* = 14.6 Hz, 1H), 3.39 (s, 3H), 2.39 (s, 3H), 1.58 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.3 163.8, 144.5, 139.2, 137.3, 133.4, 129.6, 129.3, 128.0, 127.7, 125.9, 124.8, 64.9, 45.4, 31.6, 27.5, 21.5 ppm.

4-(((4-fluorophenyl)sulfonyl)methyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3v):[16] White solid (36.7 mg, 51%), m.p. 176.9-177.6 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31-8.29 (m, 1H), 7.51-7.49 (m, 2H), 7.44-7.42(m, 2H), 7.19-7.17 (m, 1H), 7.04 (t, *J* = 8.5 Hz, 2H), 4.47 (d, *J* = 14.7 Hz, 1H), 3.90 (d, *J* = 14.7 Hz, 1H), 3.42 (s, 3H), 1.59 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.3, 165.59 (d, *J* = 256.7 Hz), 163.7, 139.1, 136.4, 133.5, 130.5 (d, *J* = 9.6 Hz), 129.4, 128.2, 125.7, 124.9, 116.34 (d, *J* = 22.7 Hz), 65.0, 45.5, 31.5, 27.6 ppm.

4-(((4-chlorophenyl)sulfonyl)methyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3w):[16] White solid (61.9 mg, 82%), m.p. 156.7-158.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29-8.29 (m, 1H), 7.44-7.40 (m, 4H), 7.33-7.32 (m, 2H), 7.16 (d, *J* = 7.5 Hz, 1H), 4.46 (d, *J* = 14.7 Hz, 1H), 3.89 (d, *J* = 14.7 Hz, 1H), 3.41 (s, 3H), 1.58 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.2, 163.7, 140.3, 139.0, 138.7, 133.5, 129.4, 129.4, 129.1, 128.2, 125.7, 124.9, 64.9, 45.4, 31.5, 27.6 ppm.

2,4-dimethyl-4-((methylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3x):[15] White solid (42.6 mg, 76%), m.p. 123.4-124.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.69-7.68 (m, 1H), 7.53-7.49 (m, 2H), 4.31 (d, *J* = 14.7 Hz, 1H), 3.82 (d, *J* = 14.7 Hz, 1H), 3.43 (s, 3H), 2.61 (s, 3H), 1.65 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.6, 163.7, 140.0, 133.9, 129.8, 128.4, 125.2, 124.9, 63.5, 45.6, 43.9, 31.3, 27.5 ppm.

4-((ethylsulfonyl)methyl)-2,4-dimethylisoquinoline-1,3(2*H*,4*H*)-dione (3y): White solid (34.0 mg, 58%), m.p. 153.0-154.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.69-7.69 (m, 1H), 7.52-7.48 (m, 2H), 4.27 (d, *J* = 14.4 Hz, 1H), 3.74 (d, *J* = 14.5 Hz, 1H), 3.42 (s, 3H), 2.78-2.67(m, 2H), 1.64 (s, 3H), 1.28 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.7, 163.8, 140.1, 133.8, 129.7, 128.3, 125.2, 124.8, 60.5, 50.2, 45.5, 31.5, 27.5, 6.3 ppm. HRMS (ESI) calc. for $C_{14}H_{17}NO_4S$ $(M+Na)^+$: 318.0770, found: 318.0773.

6-bromo-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3z): White solid (26.4 mg, 31%), m.p. 244.3-245.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.4 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.51 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.47 (d, *J* = 7.9 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.20 (d, *J* = 1.6 Hz, 1H), 4.46 (d, *J* = 14.8 Hz, 1H), 3.83 (d, *J* = 14.8 Hz, 1H), 3.42 (s, 3H), 1.58 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.6, 163.1, 140.7, 140.1, 133.9, 131.7, 130.8, 129.2, 129.1, 128.8, 127.3, 123.9, 64.7, 45.3, 31.3, 27.7 ppm. HRMS (ESI) calc. for $C_{18}H_{16}BrNO_4S$ $(M+Na)^+$: 443.9876, found: 443.9873.

5-fluoro-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3aa): White solid (26.4 mg, 37%), m.p. 171.6-172.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.58-7.56 (m, 1H), 7.53-7.51 (m, 2H), 7.43-7.40 (m, 2H), 7.17 (dd, *J* = 8.7, 4.8 Hz, 1H), 7.10-7.06 (m, 1H), 4.45 (d, *J* = 14.7 Hz, 1H), 3.86 (d, *J* = 14.7 Hz, 1H), 3.41 (s, 3H), 1.58 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0, 162.7 (d, *J* = 2.5 Hz), 162.0 (d, *J* = 247.9 Hz) 140.14, 134.9 (d, *J* = 3.3 Hz), 133.6, 129.2, 128.1 (d, *J* = 7.9 Hz), 127.6, 127.0 (d, *J* = 7.8 Hz), 121.0 (d, *J* = 22.6 Hz), 115.4 (d, *J* = 23.4 Hz), 64.9, 45.1, 31.5, 27.7 ppm. HRMS (ESI) calc. for $C_{18}H_{16}FNO_4S$ $(M+Na)^+$: 384.0676, found: 384.0679.

7-fluoro-2,4-dimethyl-4-((phenylsulfonyl)methyl)isoquinoline-1,3(2*H*,4*H*)-dione (3aa'):White solid (21.0 mg, 29%), m.p. 166.4-168.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.9 Hz, 1H), 7.55-7.50 (m, 3H), 7.42-7.36 (m, 3H), 7.03-7.00 (m, 1H), 4.39 (d, *J* = 14.6 Hz, 1H), 4.24 (d, *J* = 14.6 Hz, 1H), 3.41 (s, 3H), 1.68 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 162.8 (d, *J* = 3.2 Hz), 159.7 (d, *J* = 248.7 Hz), 139.6, 133.5, 129.9 (d, *J* = 9.3 Hz), 129.0, 127.6, 126.9 (d, *J* = 3.5 Hz), 126.0 (d, *J* = 12.1 Hz), 125.5 (d, *J* = 2.9 Hz), 120.9, 120.7, 62.3 (d, *J* = 6.1 Hz), 43.4 (d, *J* = 3.1 Hz), 27.9 (d, *J* = 2.9 Hz), 27. 8 ppm. HRMS (ESI) calc. for $C_{18}H_{16}FNO_4S$ $(M+Na)^+$: 384.0676, found: 384.0679.

2,4-dimethyl-4-(2,2,2-trifluoroethyl)isoquinoline-1,3(2*H*,4*H*)-dione (3ab):[16] Colorless liquid (20.0 mg, 37%)**.** ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30-8.28 (m, 1H), 7.66 (d, *J* = 0.9 Hz, 1H), 7.50-7.47 (m, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 3.41 (s, 3H), 3.40-3.32 (m, 1H), 2.84-2.77 (m, 1H), 1.66 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.5, 163.7, 140.4, 133.8, 129.3, 128.7, 128.5, 128.0, 127.7, 125.6, 125.0 (q, *J* = 277.0 Hz), 124.3, 44.41 (q, *J* = 27.5 Hz), 43.6, 31.1, 27.4 ppm.

***N*-(2-methyl-3-(phenylsulfonyl)propanoyl)benzamide (4):** White solid (31.0 mg, 47%), m.p. 137.4-138.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (s, 1H),

7.92-7,87 (m, 4H), 7.66-7.61 (m, 2H), 7.55-7.50 (m, 4H), 4.23 (s, 1H), 3.97 (dd, *J* = 14.3, 9.0 Hz, 1H), 3.13 (dd, *J* = 14.3, 3.3 Hz, 1H), 1.36 (d, *J* = 7.0 Hz, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.1, 165.3, 139.3, 133.9, 133.4, 132.6, 129.3, 129.0, 128.2, 127.9, 58.7, 35.5, 18.1 ppm. HRMS (ESI) calc. for C17H17NO4S $(M+Na)^+$: 354.0770, found: 354.0773.

(2-(phenylsulfonyl)ethene-1,1-diyl)dibenzene (5):[23] White solid (67.0 mg, 35%), m.p. 114.8-115.9 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.3 Hz, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.38-7.33 (m, 4H), 7.31-7.27 (m, 4H), 7.22-7.20 (m, 2H), 7.08-7.07 (m, 2H), 7.02 (s, 1H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.2, 141.6, 139.2, 135.5, 132.8, 130.3, 129.8, 128.9, 128.8, 128.7, 128.6 128.2, 127.9, 127.7 ppm.

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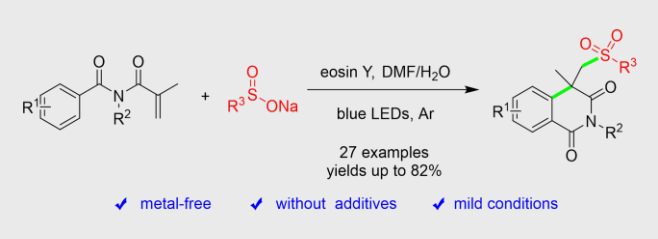

Key Topic: Photochemistry

Kai-Li Zuo, Yan-Hong He and Zhi Guan**

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Metal-free visible-light photocatalytic tandem radical addition-cyclization strategy for the synthesis of sulfonyl-containing isoquinolinediones

A mild visible-light photocatalytic C-S/C-C bond forming radical tandem reaction for the synthesis of sulfonyl-containing isoquinolinediones has been developed using sodium sulfinates as a sulfonyl radical source and eosin Y as an organic photocatalyst without any additives.