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KI-Promoted Oxidative Coupling of Styrenes with Indoles under Metal-Free Conditions: Facile Access to C-3 Dicarbonyl Indoles

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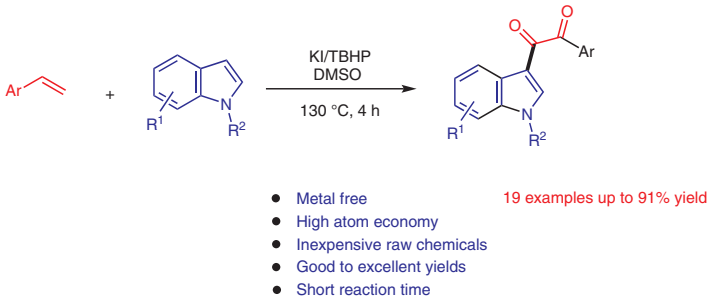

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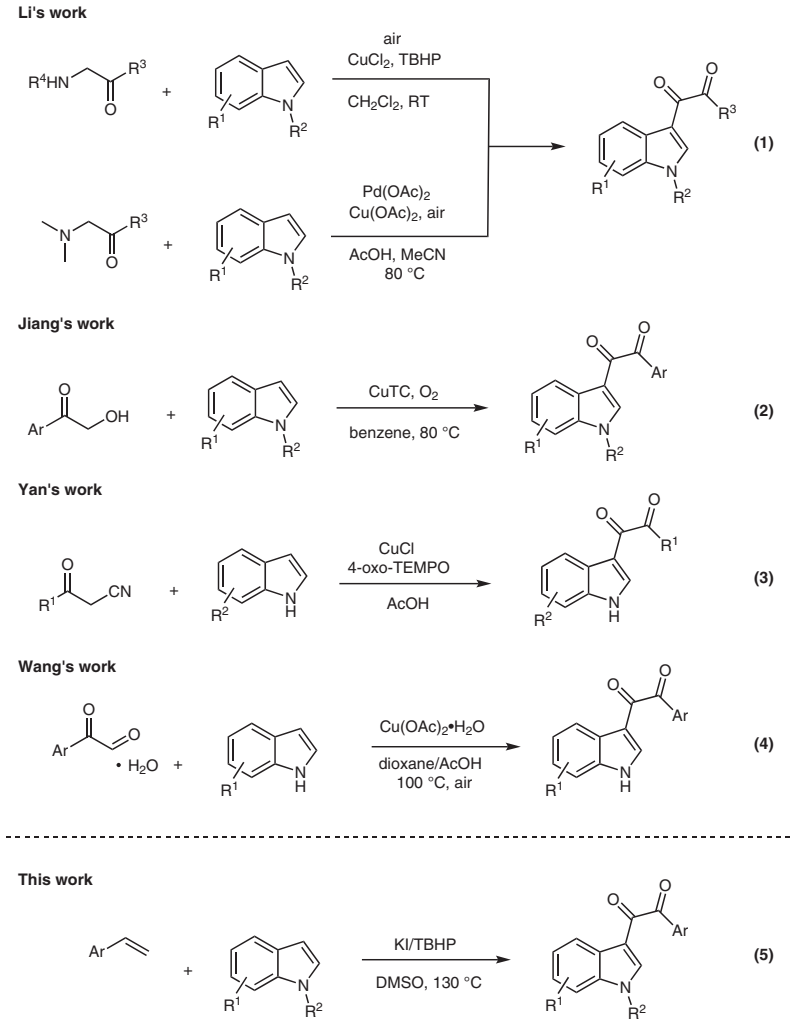
Abstract A new and efficient method for the synthesis of C-3 dicarbonyl indoles via oxidative cross-coupling of styrenes with indoles under metal-free conditions has been developed. Moreover, a broad scope of C-3 dicarbonyl indoles in moderate to good yields were obtained, and a plausible mechanism is proposed based on control and isotope-labeling experiments.

Key words styrenes, metal free, dicarbonyl indoles, synthetic methods

Indoles, a class of valuable synthetic precursors in organic synthesis, are widespread in bioactive natural products, pharmaceutical molecules, and functional materials.[1] Meanwhile, the C-3 acylation of indoles has been widely studied because of the versatile chemical reactions of 3-acylindoles and their significant applications in pharmaceuticals and natural products.[2,3] Furthermore, heteroaryl 1,2-diketones are a kind of versatile and powerful structural unit in organic synthesis, and an ideal choice to prepare heterocyclic compounds with pharmacological properties; for instance, pyrimidine-1,2-diketones are involved in the preparation of orally bioavailable p38 MAP kinase inhibitors.[4] Therefore, it is of great significance to explore new strategies for the direct dicarbonylation of indoles to generate C-3 dicarbonyl indoles.[1a,5]

In the past few years, protocols for the synthesis of C-3 dicarbonyl indoles have been well developed.[2b,5c] Importantly, two methods were reported by Li's group: (1) Cu-catalyzed C–H bond oxidation/cross-coupling of secondary anilines with indoles; (2) Pd-catalyzed oxidative cross-coupling of indoles with α-amino carbonyl compounds (Scheme 1, eq 1).[2b,5c] In addition, Jiang's group reported a route to C-3 dicarbonyl indoles by the Cu-catalyzed aerobic oxidative coupling of indoles with α-hydroxy ketones (Scheme 1, eq 2).[6] Yan and co-workers developed a process for the synthesis of dicarbonyl indoles involving a Cu-catalyzed α-oxonation Friedel–Crafts reaction of indoles and β-carbonyl nitriles (Scheme 1, eq 3).[7] Recently, Wang and co-workers reported a protocol for the Cu-catalyzed C–H bond oxidation/coupling of indoles with arylglyoxal hydrates to construct indolyl diketones (Scheme 1, eq 4).[8] Although such significant advances have been realized, there are still some drawbacks with these protocols: (1) relatively low atom economy; (2) environmentally unfriendly metal catalysts; (3) starting materials which are not easy to obtain. Hence, it is highly desirable to develop suitable and highly efficient methods to prepare C-3 dicarbonyl indoles using easily available starting materials. Herein, we present a novel and efficient KI-catalyzed oxidative coupling of styrenes with indoles for the synthesis of C-3 dicarbonyl indoles, which has high atomic economy, employing readily available styrenes as starting materials, and TBHP together with DMSO as co-oxidant (Scheme 1, eq 5).

At the beginning of our study, the reaction of styrene (**1a**) with 1-methylindole (**2a**) was selected as the model reaction to identify appropriate reaction conditions through screening a series of reaction parameters. The results are presented in Table 1. Firstly, the model reaction was carried out in the presence of various iodine source catalysts, such as I_2, TBAI, NIS, and KI, in DMSO (3 mL) at 120 °C for 4 hours (Table 1, entries 1–4). To our delight, TBAI and KI both presented catalytic efficiency, affording the desired product 1-

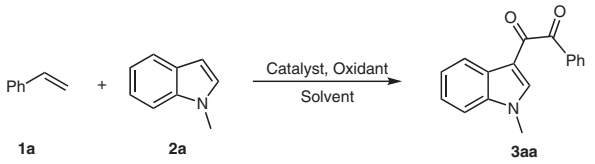


Scheme 1 Previous work and KI-promoted oxidative coupling of ethenylarenes with indoles (this work) to prepare C-3 dicarbonyl indoles

(1-methyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (**3aa**) in 52% and 63% yield, respectively (Table 1, entries 2 and 4). Then, the reaction was conducted with oxidants other than TBHP, such as TBPB, $K_2S_2O_8$, O_2, and IBX, and the results showed that TBHP is the best oxidant (Table 1, entries 5–8). Subsequently, a series of solvents was screened, affording no target product **3aa** when DMSO was replaced, demonstrating that DMSO acts not only as solvent but also plays some other important role (Table 1, entries 9–12). Then, a reaction temperature of 100–140 °C was also screened (Table 1, entries 13–16). Gratifyingly, when the reaction temperature was increased to 130 °C, a 91% yield of the target product **3aa** was obtained (Table 1, entry 15). Finally, different amounts of KI and TBHP were also evaluated (Table 1, entries 17–22). Based on these investigating experiments, the optimized reaction conditions were determined as styrene (**1a**, 1.0 mmol), 1-methylindole (**2a**, 1.0 mmol), KI (20 mol%), and TBHP (3 mmol) dissolved in DMSO (3 mL), with stirring at 130 °C for 4 hours in a sealed tube.

The substrate scope of both styrenes **1** and indoles **2** was then studied under the optimized conditions. As shown in Scheme 2, styrenes bearing various electron-withdrawing and electron-donating groups reacted smoothly with 1-methylindole (**2a**), providing the corresponding products **3aa**–**3ia** in moderate to good yields. However, styrene bearing a nitro substituent was converted into the desired product **3ea** in trace yield, probably owing to the strong electron-withdrawing inductive effect of nitro, resulting in the electron density and reactivity of the double bond decreasing. Notably, styrene with a methyl group performed greatly better than that with a methoxy group, likely for the reason that the strong electron-donating conjugation of the methoxy group causes a decrease in

Table 1 Screening for the Optimal Conditions[a]



Entry	Catalyst (equiv)	Oxidant[b] (equiv)	Solvent	Temp (°C)	Yield[c] (%)
1	I_2 (0.2)	TBHP (3.0)	DMSO	120	trace
2	TBAI (0.2)	TBHP (3.0)	DMSO	120	52
3	NIS (0.2)	TBHP (3.0)	DMSO	120	0
4	KI (0.2)	TBHP (3.0)	DMSO	120	63
5	KI (0.2)	TBPB (3.0)	DMSO	120	0
6	KI (0.2)	$K_2S_2O_8$ (3.0)	DMSO	120	34
7	KI (0.2)	O_2 (3.0)	DMSO	120	0
8	KI (0.2)	IBX (3.0)	DMSO	120	0
9	KI (0.2)	TBHP (3.0)	DMF	120	0
10	KI (0.2)	TBHP (3.0)	1,4-dioxane	120	0
11	KI (0.2)	TBHP (3.0)	toluene	120	0
12	KI (0.2)	TBHP (3.0)	MeCN	120	0
13	KI (0.2)	TBHP (3.0)	DMSO	100	trace
14	KI (0.2)	TBHP (3.0)	DMSO	110	42
15	KI (0.2)	TBHP (3.0)	DMSO	130	91
16	KI (0.2)	TBHP (3.0)	DMSO	140	74
17	KI (0.1)	TBHP (3.0)	DMSO	130	84
19	KI (0.3)	TBHP (3.0)	DMSO	130	79
20	KI (0.2)	TBHP (1.0)	DMSO	130	33
21	KI (0.2)	TBHP (2.0)	DMSO	130	52

[a] Reaction conditions, unless otherwise noted: **1a** (1.0 mmol), **2a** (1.0 mmol) catalyst, oxidant, solvent (3 mL), stirred, 130 °C, 4 h, sealed tube.
[b] TBHP = *tert*-butyl hydroperoxide, TBPB = *tert*-butyl peroxybenzoate, $K_2S_2O_8$ = potassium persulfate, IBX = *o*-iodoxybenzoic acid.
[c] Isolated yield.

the electrophilicity of the double bond unsaturated carbon (**3fa**, **3ga**). Further, the position (ortho, meta, or para) of the methyl substituent had no evident influence on the efficiency of this transformation (**3ga**–**3ia**). Next, olefins with polycyclic aromatic and heterocyclic substituents were also subjected to the optimized conditions. 1-Ethenylnaphthalene, 2-ethenylthiophene, 2-ethenylfuran, and 2-ethenylpyridine were all suitable reaction partners for this transformation (53–75% yield, **3ja**–**3ma**).

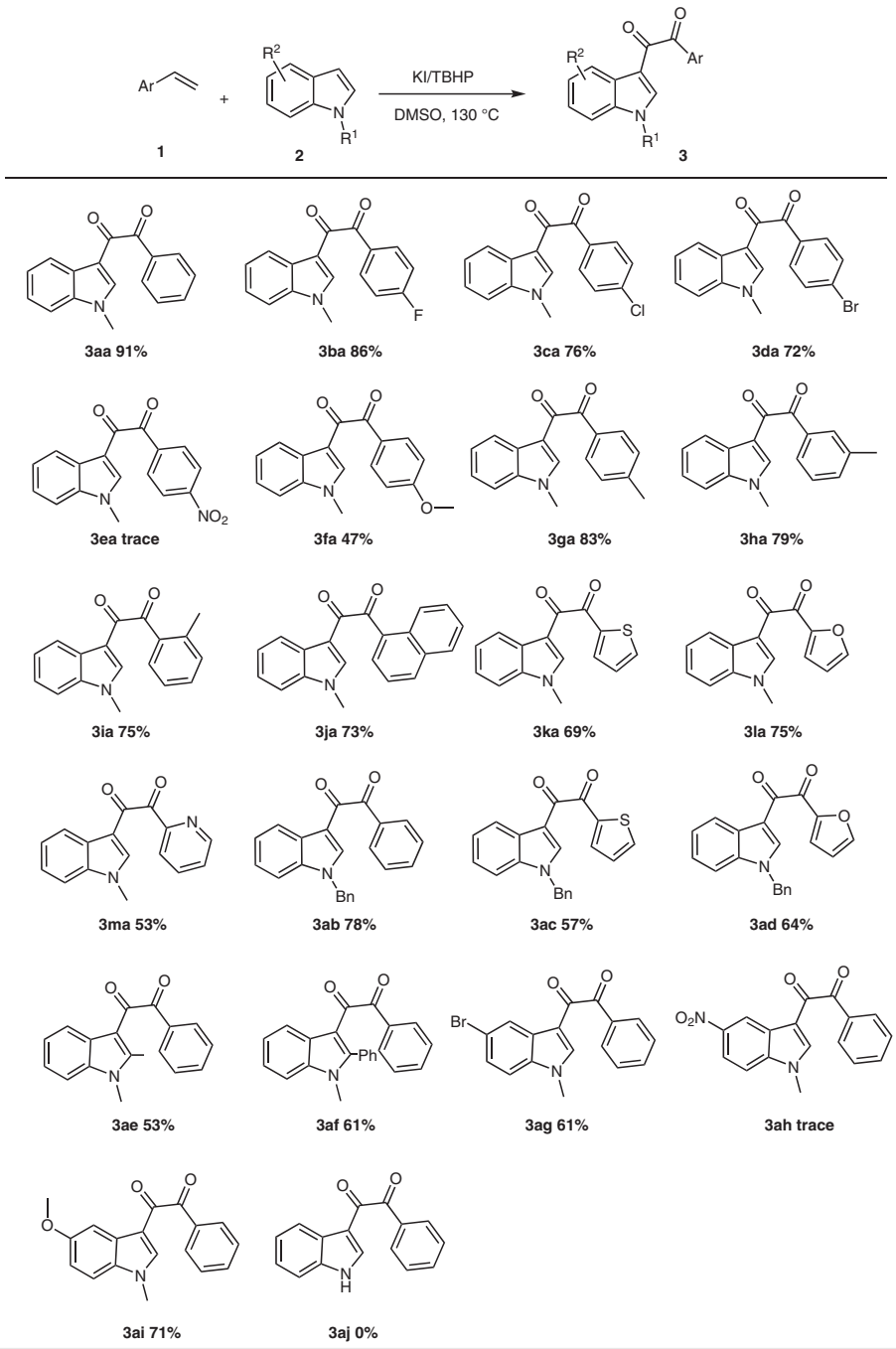
Subsequently, the scope with respect to indoles **2** was examined under the optimized reaction conditions. It was observed that indoles with an *N*-benzyl group could be transformed smoothly into the corresponding desired products **3ab**–**3ad**, in 57–78% yield (Scheme 2). The benzyl group is not deprotectable and dicarbonyl products with an *N*-benzylindole moiety have been reported to act as either negative or positive modulators of the human A_{2B} adenosine receptor (A_{2B}AR), and their C-3 diketo indole scaffold could be useful in the design of new analogues, which could be smoothly obtained through our method.[9] Moreover, 2-substituted and 5-substituted indoles reacted with **1a** to produce the corresponding products **3ae**–**3ag** and **3ai** in 53–71% yield. Unfortunately, this method failed to afford the target product 1-(1*H*-indol-3-yl)-2-phenylethane-1,2-dione (**3aj**) likely due to the low C-3 activity of *N*-H indole **2** (R^1 = H), and no other byproduct was provided.

In order to explore the mechanism of this reaction, a few control experiments were carried out (Scheme 3). When the radical scavenger TEMPO was added to this reaction under the optimized conditions, the transformation was strongly inhibited, indicating that the oxidative process goes through a radical pathway (Scheme 3a). To demonstrate that TBHP is involved in the formation of α-iodoacetophenone (**A**), a key intermediate, the reaction of styrene (**1a**) with KI and TBHP proceeded smoothly to produce **A**, and then DMSO was added to give phenylglyoxal (**B**) (Scheme 3b). However, when we treated styrene (**1a**) with KI and DMSO, the transformation failed to give α-iodoacetophenone (**A**) thereby indicating that TBHP plays an important role in the formation of **A**, through a radical intermediate (Scheme 3c). Consequently, TBHP together with DMSO is the co-oxidant. α-Iodoacetophenone (**A**) reacted with 1-methylindole (**2a**) in DMSO affording 1-(1-methyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (**3aa**) exclusively (Scheme 3d). In the presence of additional KI, phenylglyoxal (**B**) reacted with 1-methylindole (**2a**) to produce product **3aa** in 95% yield (Scheme 3e). These results clearly show that α-iodoacetophenone (**A**) and phenylglyoxal (**B**) are the key intermediates in this process. Finally, control experiments e and f (Scheme 3) showed that KI is indispensable in this transformation.

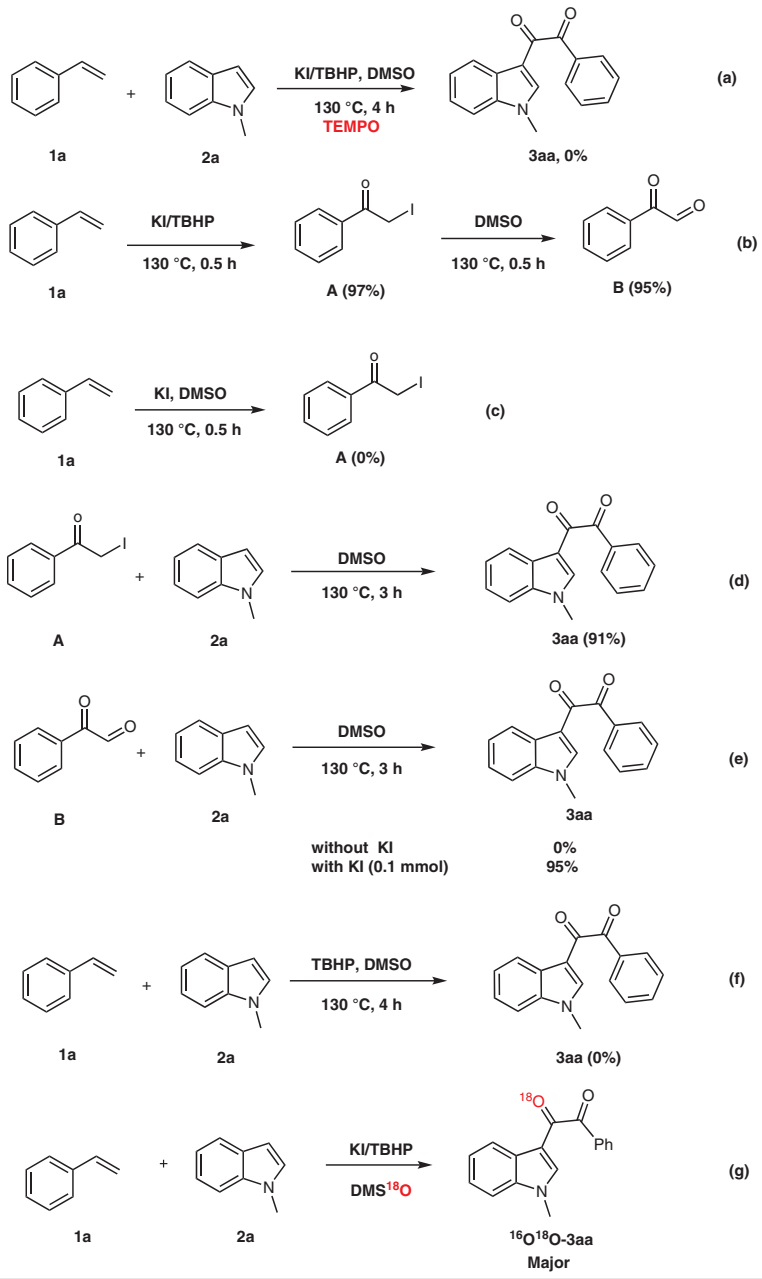
In order to explore the role of DMSO in this process, an ^{18}O-isotope-labeling experiment was carried out (Scheme 3g). When the model reaction of styrene (**1a**) with 1-methylindole (**2a**) was carried out under KI/TBHP and ^{18}O-labeled DMSO conditions, the product $^{16}O^{18}O$-**3aa** was clearly detected by ESI-MS analysis at $[M + H]^+$ 266.1056 and $[M + Na]^+$ 288.0872, indicating that DMSO performs as an oxygen donor in the formation of C-3 dicarbonyl indoles.

On the basis of results above and previous reports, a possible mechanism is proposed (Scheme 4).[5e,10] The initial reaction of KI/TBHP with styrene (**1a**) results in the formation of 1-phenylethanol radical, which eventually is iodinated to the key intermediate, α-iodoacetophenone (**A**). Then, **A** is further transformed to phenylglyoxal (**B**) through Kornblum oxidation. The activated aldehyde group of **B** would react with 1-methylindole (**2a**) to provide intermediate **C** directly, which is followed by further rapid oxidation by KI to afford 1-(1-methyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (**3aa**).

In summary, a novel and efficient method for the preparation of dicarbonyl indoles via oxidative cross-coupling of styrenes with indoles under metal-free conditions has been developed. This transformation proceeds under mild conditions with high atom economy and a broad substrate scope. A possible reaction mechanism has been proposed on the basis of a series of control and isotope-labeling experiments. Further studies on the synthetic applications of this process are underway in our laboratory.

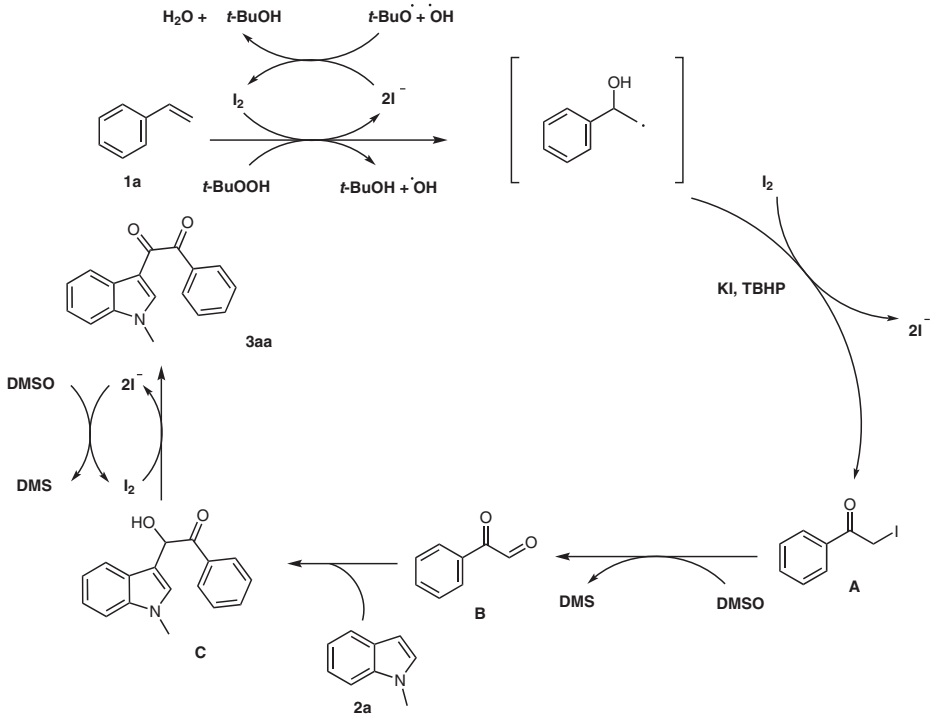


Scheme 2 Substrate scope of ethenylarenes **1** and indoles **2**. *Reagents and conditions*: **1** (1 mmol), **2** (1 mmol), KI (20 mol%), TBHP (3 mmol), DMSO (3 mL), stirred, 130 °C, 4 h, sealed tube; isolated yields are given.



Scheme 3 Control experiments

All general reagents and solvents were commercially available and used as received. ^{1}H and ^{13}C NMR spectra were measured on a magnet system 400/54 Ascend instrument purchased from Bruker BioSpin AG. Chemical data for protons are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual proton in the NMR solvent ($CDCl_3$, 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (standard abbreviations), coupling constant (*J*) in hertz (Hz), and integration. ^{13}C NMR spectra were recorded at 100 MHz. Chemical data for carbons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the NMR solvent. Column chromatography was generally performed on SiliCycle silica gel (200–300 mesh). LC-MS analysis was performed on an Agilent 6520 Accurate-Mass Q-TOF LC/MS (Agilent Technologies, USA) triple-stage quadrupole mass spectrometer equipped with electrospray ionization. Analytical TLC was performed on 0.2 mm coated silica gel plates (HSGF254) and the course of reactions was visualized using UV light (254 or 365 nm).



Scheme 4 Proposed mechanism

C-3 Dicarbonyl Indoles 3; General Procedure

Ethenylarene **1** (1.0 mmol), indole **2** (1.0 mmol), KI (20 mol%), and TBHP (3 mmol) were dissolved in DMSO (3 mL) and the mixture was stirred at 130 °C for 4 h in a sealed tube. To estimate the status of the reaction, it was screened by TLC. After reaction completion, the reaction mixture was cooled to room temperature, then quenched with saturated $NaHSO_3$ solution and extracted with ethyl acetate. The organic layer was washed with saturated NaCl solution and dried over anhydrous Na_2SO_4. Removal of the organic solvent in vacuo followed by flash column chromatography on silica gel (hexane/ethyl acetate, 30:1) afforded the desired product **3** in good yield (47–91%).

1-(1-Methyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (3aa)

Light yellow solid; yield: 0.239 g (91%); mp 88–90 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54–8.40 (m, 1 H), 8.10 (d, *J* = 7.4 Hz, 2 H), 7.81 (s, 1 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.49 (t, *J* = 7.7 Hz, 2 H), 7.39 (m, 3 H), 3.84 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.89, 187.70, 139.65, 137.87, 134.42, 133.62, 130.46, 128.88, 126.52, 124.36, 123.64, 122.85, 113.04, 110.12, 33.91.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{13}NO_2$: 286.0838; found: 286.0832.

1-(4-Fluorophenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3ba)

Light yellow solid; yield: 0.242 g (86%); mp 112–113 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51–8.40 (m, 1 H), 8.18–8.11 (m, 2 H), 7.82 (d, *J* = 5.1 Hz, 1 H), 7.38 (dd, *J* = 5.4, 2.6 Hz, 3 H), 7.15 (t, *J* = 8.7 Hz, 2 H), 3.83 (d, *J* = 10.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.09, 187.14, 167.87, 165.32, 139.76, 137.86, 133.32, 133.22, 130.10, 130.07, 126.53, 124.41, 123.70, 122.78, 116.23, 116.01, 112.90, 110.17, 33.92.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{12}FNO_2$: 304.0744; found: 304.0747.

1-(4-Chlorophenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3ca)

Light yellow solid; yield: 0.226 g (76%); mp 125–127 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52–8.39 (m, 1 H), 8.03 (d, *J* = 8.6 Hz, 2 H), 7.80 (s, 1 H), 7.44 (d, *J* = 8.6 Hz, 2 H), 7.37 (dd, *J* = 6.2, 3.4 Hz, 3 H), 3.81 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.35, 186.80, 140.95, 139.77, 137.83, 131.98, 131.81, 129.19, 126.50, 124.42, 123.71, 122.76, 112.83, 110.16, 33.91.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{12}ClNO_2$: 320.0449; found: 320.0443.

1-(4-Bromophenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3da)

Light brown solid; yield: 0.245 g (72%); mp 144–146 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53–8.37 (m, 1 H), 7.95 (d, *J* = 8.6 Hz, 2 H), 7.80 (s, 1 H), 7.61 (d, *J* = 8.6 Hz, 2 H), 7.37 (dd, *J* = 6.4, 3.7 Hz, 3 H), 3.81 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.58, 186.76, 139.82, 137.87, 132.42, 132.22, 131.89, 129.86, 126.52, 124.46, 123.75, 122.79, 112.86, 110.20, 33.95.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{12}BrNO_2$: 363.9944; found: 363.9939.

1-(4-Methoxyphenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3fa)

Light yellow solid; yield: 0.138 g (47%); mp 114–116 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51–8.42 (m, 1 H), 8.12–8.06 (m, 2 H), 7.79 (s, 1 H), 7.40–7.35 (m, 3 H), 6.98–6.93 (m, 2 H), 3.87 (s, 3 H), 3.81 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.60, 188.24, 164.66, 139.58, 137.79, 132.87, 126.57, 126.51, 124.21, 123.49, 122.77, 114.17, 113.09, 110.04, 55.69, 33.83.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NO_3$: 316.0944; found: 316.0947.

1-(1-Methyl-1*H*-indol-3-yl)-2-(*p*-tolyl)ethane-1,2-dione (3ga)

Light yellow solid; yield: 0.230 g (83%); mp 80–82 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50–8.38 (m, 1 H), 7.96 (d, *J* = 8.2 Hz, 2 H), 7.74 (s, 1 H), 7.37–7.30 (m, 3 H), 7.24 (t, *J* = 6.5 Hz, 2 H), 3.76 (s, 3 H), 2.39 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.76, 188.18, 145.67, 139.70, 137.91, 131.20, 130.63, 129.69, 126.56, 124.36, 123.62, 122.84, 113.11, 110.21, 33.94, 22.08.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NO_2$: 300.0995; found: 300.0996.

1-(1-Methyl-1*H*-indol-3-yl)-2-(*m*-tolyl)ethane-1,2-dione (3ha)

Light yellow solid; yield: 0.219 g (79%); mp 88–90 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47 (dd, *J* = 5.5, 2.8 Hz, 1 H), 7.97–7.83 (m, 2 H), 7.83–7.71 (m, 1 H), 7.45–7.35 (m, 5 H), 3.85–3.79 (m, 3 H), 2.39 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.18, 187.98, 139.58, 138.72, 137.82, 135.25, 133.57, 130.79, 128.76, 127.63, 126.43, 124.29, 123.56, 122.76, 113.00, 110.10, 33.85, 21.39.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NO_2$: 300.0995; found: 300.0995.

1-(1-Methyl-1*H*-indol-3-yl)-2-(*o*-tolyl)ethane-1,2-dione (3ia)

Light yellow solid; yield: 0.208 g (75%); mp 97–99 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51–8.35 (m, 1 H), 7.83 (s, 1 H), 7.75 (d, *J* = 7.8 Hz, 1 H), 7.44–7.19 (m, 6 H), 3.83 (s, 3 H), 2.64 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.48, 188.22, 140.86, 139.32, 137.71, 133.10, 133.01, 132.72, 132.18, 126.53, 125.79, 124.20, 123.47, 122.73, 33.80, 21.66.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NO_2$: 300.0995; found: 300.0993.

1-(1-Methyl-1*H*-indol-3-yl)-2-(naphthalen-1-yl)ethane-1,2-dione (3ja)

Light yellow solid; yield: 0.228 g (73%); mp 104–106 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.12 (d, *J* = 8.6 Hz, 1 H), 8.54–8.45 (m, 1 H), 8.07 (d, *J* = 7.3 Hz, 2 H), 7.92 (d, *J* = 8.1 Hz, 1 H), 7.87 (s, 1 H), 7.73–7.67 (m, 1 H), 7.59 (t, *J* = 7.5 Hz, 1 H), 7.48 (t, *J* = 7.7 Hz, 1 H), 7.43–7.38 (m, 3 H), 3.83 (d, *J* = 8.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.71, 188.43, 139.47, 137.82, 135.12, 134.39, 134.19, 131.47, 130.00, 128.96, 128.86, 126.89, 126.63, 126.06, 124.58, 124.33, 123.62, 122.88, 113.34, 110.10, 33.93.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{15}NO_2$: 336.0995; found: 336.0993.

1-(1-Methyl-1*H*-indol-3-yl)-2-(thiophen-2-yl)ethane-1,2-dione (3ka)

Light yellow solid; yield: 0.186 g (69%); mp 91–93 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51–8.47 (m, 1 H), 8.15 (s, 1 H), 8.10 (dd, *J* = 3.8, 1.1 Hz, 1 H), 7.78 (dd, *J* = 4.9, 1.1 Hz, 1 H), 7.40–7.36 (m, 3 H), 7.17 (dd, *J* = 4.8, 3.9 Hz, 1 H), 3.84 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.63, 184.59, 140.38, 139.44, 137.56, 136.76, 136.72, 128.43, 127.02, 124.21, 123.58, 122.81, 112.16, 110.03, 33.86.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{11}NO_2S$: 292.0403; found: 292.0402.

1-(Furan-2-yl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3la)

Light yellow solid; yield: 0.190 g (75%); mp 106–108 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49–8.44 (m, 1 H), 8.13 (s, 1 H), 7.74 (d, *J* = 0.8 Hz, 1 H), 7.65 (d, *J* = 3.6 Hz, 1 H), 7.39–7.36 (m, 3 H), 6.60 (dd, *J* = 3.6, 1.6 Hz, 1 H), 3.84 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.18, 179.94, 150.34, 148.77, 140.35, 137.59, 127.00, 124.25, 124.14, 123.62, 122.77, 112.92, 112.24, 110.09, 33.91.

HRMS (TOF): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{11}NO_3$: 254.0812; found: 254.0813.

1-(1-Methyl-1*H*-indol-3-yl)-2-(pyridin-2-yl)ethane-1,2-dione (3ma)

Light yellow solid; yield: 0.140 g (53%); mp 103–105 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (d, *J* = 4.6 Hz, 1 H), 8.48–8.38 (m, 1 H), 8.16 (d, *J* = 7.8 Hz, 1 H), 7.88 (td, *J* = 7.7, 1.6 Hz, 1 H), 7.71 (s, 1 H), 7.47 (ddd, *J* = 7.5, 4.7, 1.0 Hz, 1 H), 7.34 (dd, *J* = 6.5, 3.3 Hz, 3 H), 3.78 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.46, 188.23, 152.21, 149.95, 139.15, 137.81, 137.12, 127.59, 126.21, 124.28, 124.21, 123.42, 122.83, 113.06, 109.96, 33.81.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{12}N_2O_2$: 287.0791; found: 287.0804.

1-(1-Benzyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (3ab)

Light yellow solid; yield: 0.264 g (78%); mp 82–84 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47 (d, *J* = 7.8 Hz, 1 H), 8.09–8.04 (m, 2 H), 7.87 (s, 1 H), 7.57 (t, *J* = 7.4 Hz, 1 H), 7.44 (t, *J* = 7.7 Hz, 2 H), 7.36–7.24 (m, 6 H), 7.17–7.07 (m, 2 H), 5.27 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.70, 187.82, 139.08, 137.41, 135.32, 134.47, 133.61, 130.53, 129.25, 128.91, 128.52, 127.18, 126.82, 124.49, 123.74, 122.93, 113.49, 110.86, 51.32.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{17}NO_2$: 362.1151; found: 362.1134.

1-(1-Benzyl-1*H*-indol-3-yl)-2-(thiophen-2-yl)ethane-1,2-dione (3ac)

Light yellow solid; yield: 0.197 g (57%); mp 100–102 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (d, *J* = 7.9 Hz, 1 H), 8.25 (s, 1 H), 8.10 (dd, *J* = 3.9, 1.1 Hz, 1 H), 7.77 (dd, *J* = 4.9, 1.1 Hz, 1 H), 7.37–7.27 (m, 6 H), 7.16 (dd, *J* = 8.4, 3.7 Hz, 3 H), 5.34 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.71, 184.42, 139.81, 139.41, 137.08, 136.84, 136.81, 135.33, 129.18, 128.46, 128.44, 127.32, 127.10, 124.34, 123.67, 122.95, 112.66, 110.72, 51.29.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{15}NO_2S$: 368.0716; found: 368.0712.

1-(1-Benzyl-1*H*-indol-3-yl)-2-(furan-2-yl)ethane-1,2-dione (3ad)

Light yellow solid; yield: 0.211 g (64%); mp 113–115 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (d, *J* = 7.8 Hz, 1 H), 8.23 (s, 1 H), 7.72 (d, *J* = 1.1 Hz, 1 H), 7.66 (dd, *J* = 3.6, 0.6 Hz, 1 H), 7.37–7.27 (m, 6 H), 7.15 (dd, *J* = 7.5, 1.8 Hz, 2 H), 6.59 (dd, *J* = 3.6, 1.7 Hz, 1 H), 5.33 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.26, 179.67, 150.26, 148.74, 139.68, 137.04, 135.23, 129.14, 128.41, 127.21, 127.14, 124.31, 124.15, 123.64, 122.84, 112.88, 112.65, 110.69, 51.24.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{15}NO_3$: 352.0944; found: 352.0957.

1-(1,2-Dimethyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (3ae)

Light yellow solid; yield: 0.147 g (53%); mp 152–155 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 7.2 Hz, 2 H), 7.86 (d, *J* = 7.7 Hz, 1 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.46 (t, *J* = 7.7 Hz, 2 H), 7.28–7.16 (m, 3 H), 3.65 (s, 3 H), 2.61 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.54, 190.15, 147.68, 137.16, 134.51, 133.48, 130.16, 129.08, 126.24, 123.17, 123.15, 120.94, 110.71, 109.73, 29.92, 12.87.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NO_2$: 300.0993; found: 300.0995.

1-(1-Methyl-2-phenyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (3af)

Light yellow solid; yield: 0.207 g (61%); mp 108–110 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58–8.45 (m, 1 H), 7.55 (dd, *J* = 8.2, 1.1 Hz, 2 H), 7.44 (t, *J* = 7.4 Hz, 1 H), 7.37 (dd, *J* = 6.8, 3.1 Hz, 3 H), 7.27–7.21 (m, 3 H), 7.11–7.01 (m, 4 H), 3.46 (d, *J* = 0.9 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.84, 191.12, 149.86, 137.20, 133.64, 133.55, 131.05, 129.76, 129.32, 129.02, 128.26, 127.97, 126.51, 124.17, 123.68, 122.64, 112.55, 110.02, 31.01.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{17}NO_2$: 362.1151; found: 362.1132.

1-(5-Bromo-1-methyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (3ag)

Light yellow solid; yield: 0.208 g (61%); mp 184–186 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (d, *J* = 1.8 Hz, 1 H), 8.11–8.07 (m, 2 H), 7.81 (s, 1 H), 7.64 (t, *J* = 7.4 Hz, 1 H), 7.53–7.46 (m, 3 H), 7.26 (s, 1 H), 3.83 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.42, 187.21, 140.13, 136.49, 134.54, 133.39, 130.47, 128.89, 128.08, 127.36, 125.47, 117.42, 112.47, 111.52, 34.06.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{12}BrNO_2$: 363.9944; found: 363.9951.

1-(5-Methoxy-1-methyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (3ai)

Light yellow solid; yield: 0.208 g (71%); mp 153–155 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10–8.06 (m, 2 H), 7.95 (d, *J* = 2.4 Hz, 1 H), 7.71 (s, 1 H), 7.63–7.58 (m, 1 H), 7.47 (t, *J* = 7.7 Hz, 2 H), 7.26–7.22 (m, 1 H), 6.98 (dd, *J* = 8.9, 2.5 Hz, 1 H), 3.92 (s, 3 H), 3.77 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.89, 187.58, 157.23, 139.48, 134.34, 133.61, 132.68, 130.39, 128.82, 127.40, 114.65, 112.66, 110.98, 104.03, 55.94, 34.04.

HRMS (TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}NO_3$: 316.0944; found: 316.0947.

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Supporting Information

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