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# Visible-light-induced radical cascade sulfonation/cyclization towards indole-fused pyridine derivatives†

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Indole-fused pyridines are an important motif in pharmaceuticals and functional molecules. A visible-light induced Ru(bpy)<sub>3</sub>Cl<sub>2</sub>·6H<sub>2</sub>O catalyzed radical cascade sulfonation/cyclization strategy for the synthesis of indole-fused pyridine derivatives was developed. Diverse indole-fused pyridines bearing different functional groups were obtained in moderate to good yields. Compared with previous work, the easily accessible starting materials, molecular nitrogen as byproduct, and eco-friendly visible light as an energy source all make this transformation more sustainable and practical.

## Introduction

Indole-fused heterocycles are widely found in a large number of natural products, drug molecules, and artificial functional materials.<sup>1,2</sup> Among them, indole-fused pyridines have attracted huge attention from medicinal chemists because of their biological activities and medicinal value. For example, compound **a** acts as an HDAC6 inhibitor and anti-tumoral agent, and compound **b** is a histamine H1 antagonist (Fig. 1).<sup>3</sup> Therefore, developing efficient pathways to construct indole-fused pyridine compounds is of great importance. By viewing the literature, synthetic methods to construct indole-fused pyridines remain rare, only Mita and co-workers reported a cyclization reaction of a doubly carboxylated compound with methylamine to provide the corresponding indole-fused pyridine products in 2018 (Scheme 1a).<sup>4</sup> However, the high reaction temperature, inaccessible starting materials, and long reaction time remain major shortcomings of this methodology, which may impede its wide application in more complex organic syntheses. Thus, the exploration of novel and more efficient strategies to synthesize indole-fused pyridine derivatives from cheap and readily available starting materials is still highly desirable.

In recent years, the photoinduced radical cascade reaction has emerged as an appealing platform for multiple bond formation because of the inexhaustible, mild and inexpensive nature of the visible-light.<sup>5</sup> In this context, the photoinduced

direct C–H functionalization of *N*-acrylamide provides a versatile strategy for the synthesis of various functionalized nitrogen heterocycles.<sup>6,7</sup> Commonly, these reactions are initiated by radical addition to unsaturated bonds and then followed by cyclization reaction. Very recently, we also developed a method of visible-light-induced organic dye-catalyzed alkoxyacylation/cyclization of 2-aryl indoles with methyl carbazates to obtain diverse indolo[2,1-*a*]isoquinolin-6(5*H*)-ones.<sup>8</sup> On the other hand, sulfone-containing molecules are widely applied in medicinal chemistry and agrochemistry because of their remarkable anticancer and antibacterial activities.<sup>9</sup> The sulfones can also serve as versatile building blocks in

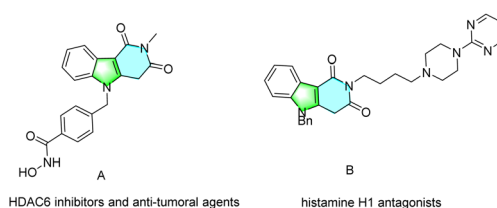
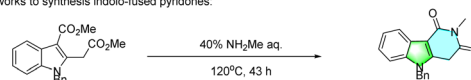
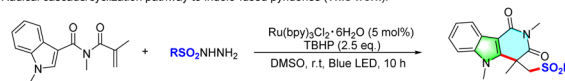


Fig. 1 Representative examples of indolo-fused pyridines.

(a) Previous works to synthesis indolo-fused pyridones:



(b) Radical cascade/cyclization pathway to indolo-fused pyridones (This work):



- ✓ Easily-accessible starting materials
- ✓ Good functional group tolerance
- ✓ Eco-friendly visible-light as energy source
- ✓ Milder reaction conditions
- ✓ Molecular nitrogen as byproduct
- ✓ Dual C-C bond formation

Scheme 1 Strategies for the synthesis of indolo-fused pyridones.

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organic synthesis.<sup>10</sup> Considering the importance of indole-fused pyridines and sulfones synthesis, it was hypothesized that indole-derived *N*-acrylamide may act as a radical acceptor *via* a similar addition/cyclization process to prepare a variety of indole-fused pyridines. Herein we report a novel and practical protocol for the synthesis of sulfonated indole-fused pyridines *via* visible-light initiated tandem reaction of *N*-methacryloyl-*N*,1-dimethyl-1*H*-indole-3-carboxamide with sulfonylhydrazides under mild reaction conditions (Scheme 1b).<sup>11</sup> Compared with previous work, the reported reaction exhibits several advantages, such as easily-accessible starting materials, good functional group tolerance, molecular nitrogen as byproduct and eco-friendly visible-light as energy source, which make the present methodology more attractive and practical.

## Results and discussion

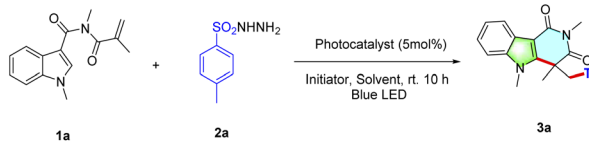
We initiated our hypothesis by first exploring the model reaction of *N*-methacryloyl-*N*,1-dimethyl-1*H*-indole-3-carboxamide (**1a**) with 4-methylbenzenesulfonylhydrazide (**2a**) under different reaction conditions (Table 1). After extensive evaluation of various photocatalyst, such as Eosin B, Fluorescein, Rose Bengal and Na<sub>2</sub>-Eosin Y, Ru(bpy)<sub>3</sub>Cl<sub>2</sub>·6H<sub>2</sub>O was found to be the best and provided indole-fused pyridine **3a** in 65% yield (entries 1–5). Subsequently, several solvents, such as dichloromethane

(DCM), DMF, THF, EtOH, CH<sub>3</sub>CN, 1,2-dichloroethane (DCE), CH<sub>3</sub>OH and 1,4-dioxane, were screened. In most of these cases, a trace of or lower yield of **3a** was observed (entries 6–9, 11 and 12). While 1,2-dichloroethane (DCE) was used as a solvent, product **3a** could be isolated in 57% yield (entry 10). Decreasing the loading of **2a** leads to a reduction in the yield of **3a** (entry 13). In contrast, increasing the amount of 4-methylbenzenesulfonylhydrazide (**2a**) and oxidant TBHP to 2.5 equivalent, an enhancement in yield of **3a** was observed (73%, entry 14). Finally, several control experiments were conducted. When the reaction was performed under without irradiation, or in the absence of photocatalyst, or oxidant, the reaction did not proceed at all, no desired product **3a** was detected (entries 15–17). These results indicates that both the visible-light, photocatalyst and oxidant play a crucial role in the reaction.

With the optimized condition in hand, we next investigated the substrate scope of *N*-methacryloyl-1*H*-indole-3-carboxamides with sulfonylhydrazides (Table 2). The effect of *N*-protecting groups on the indole ring were first examined. It was found that a variety of *N*-methacryloyl-1*H*-indole-3-carboxamides bearing different groups at R<sub>1</sub> position, such as methyl, ethyl, phenyl and benzyl, were compatible with the reaction conditions, giving the desired indole-fused pyridine products **3a–3d** in 61–75% yields, respectively. The amide group bearing different substituents at R<sub>2</sub> position was then evaluated. We were pleased to discover that a variety of aliphatic groups at R<sub>2</sub>-position including ethyl, isopropyl, cyclopropyl, propargyl, cyanoethyl, phenyl and benzyl were well compatible with the transformation (**3e–3k**). It is worth noting that alkynyl and cyano were retained in the reaction, which were suitable for potential further functionalization. Moreover, substrates bearing different groups at the C5 and C7 position of the indole ring were found to be well compatible under standard conditions, delivering the desired products in moderate to good yields (**3l**, 61%; **3m**, 58%; **3n**, 53%; **3o**, 58%, respectively). The reaction also worked well when R<sub>3</sub> position was substituted by phenyl or benzyl group, generating the target products **3p** and **3q** in 61% and 50% yields, respectively. Finally, the feasibility of a variety of substituted sulfonylhydrazides in this reaction system were tested. To our delight, sulfonylhydrazides bearing different substituents at aromatic ring such as OMe, CO<sub>2</sub>Me, Cl, Br, CF<sub>3</sub> and CN could all participate in the reaction efficiently to deliver the corresponding products **3r–3x** in 53–78% yields. Moreover, the alkyl-, thiophene- and naphthalene-substituted sulfonylhydrazides were also tolerated, giving the products **3y–4b** in moderate to good yields. However, the use of *N*-acryloyl-*N*,1-dimethyl-1*H*-indole-3-carboxamide and *N*-methacryloyl-*N*,1,2-trimethyl-1*H*-indole-3-carboxamide as reactants, no desired products were detected.

In order to understand the mechanism of this protocol, several control experiments were further conducted. To verify if the radical pathway is involved in the present transformation, 3.0 equiv. of radical scavenger [2,2,6,6-tetramethylpiperidoxyl (TEMPO) or butylated hydroxytoluene (BHT)] was added to the reaction. The formation of **3a** was completely inhibited and the TEMPO-Ts adduct was detected by EI-MS (Scheme 2a). Furthermore, the addition of 3.0 equiv. of 1,1-diphenylethylene

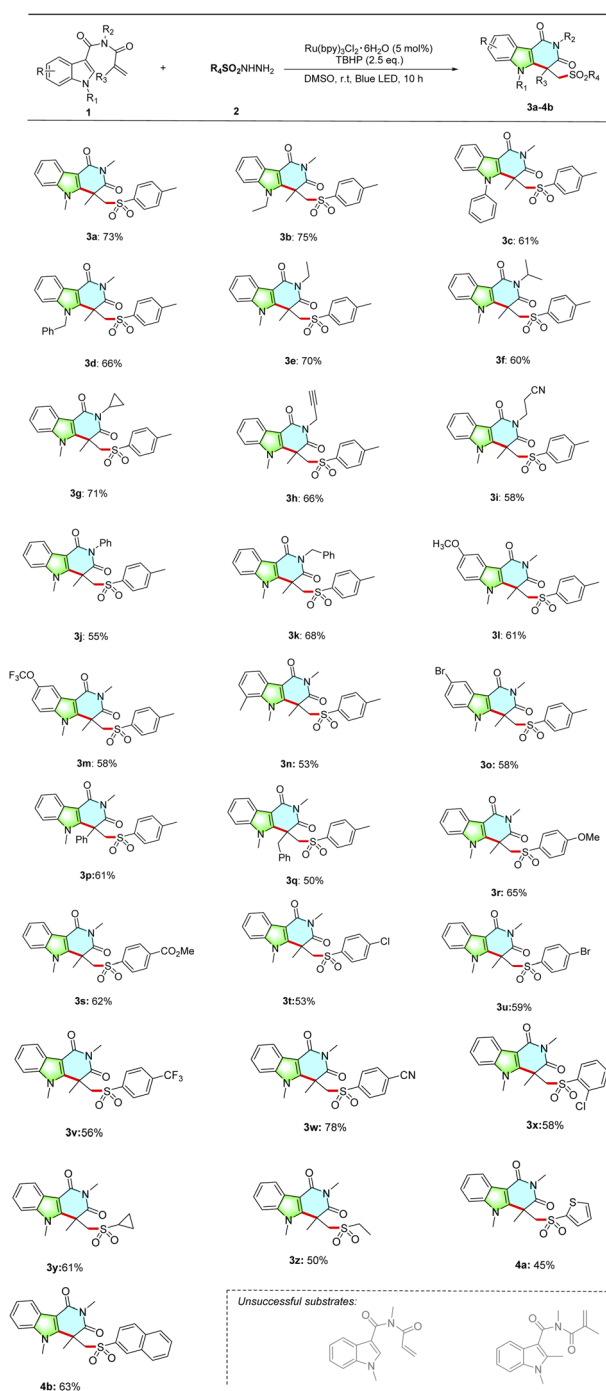
Table 1 Optimization of reaction conditions<sup>a,b</sup>



Entry	Photocatalyst	Solvent	Yield <sup>b</sup> (%)
1	Eosin B	DMSO	25
2	Fluorescein	DMSO	38
3	Rose Bengal	DMSO	48
4	Na <sub>2</sub> -Eosin Y	DMSO	46
5	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DMSO	65
6	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DCM	35
7	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DMF	15
8	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	THF	0
9	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	CH <sub>3</sub> CN	10
10	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DCE	57
11	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	CH <sub>3</sub> OH	23
12	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	1,4-Dioxane	40
13 <sup>c</sup>	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DMSO	57
14 <sup>d</sup>	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DMSO	73
15 <sup>e</sup>	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DMSO	0
16 <sup>f</sup>	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DMSO	0
17 <sup>g</sup>	Ru(bpy) <sub>3</sub> Cl <sub>2</sub> ·6H <sub>2</sub> O	DMSO	0

<sup>a</sup> Reaction conditions: **1a** (0.25 mmol), **2a** (0.5 mmol, 2.0 eq.), photocatalyst (5 mol%) TBHP (2.0 eq., 70% aqueous solution) and DMSO (2 mL) were stirred under 10 W blue LED (460–465 nm) irradiation at room temperature under air for 10 h. <sup>b</sup> Isolated yield. <sup>c</sup> 1.5 eq. of **2a** was used. <sup>d</sup> 2.5 eq. of **2a** and 2.5 eq. of TBHP were used. <sup>e</sup> Without 10 W blue LED (460–465 nm) irradiation. <sup>f</sup> Without photocatalyst. <sup>g</sup> Without TBHP.

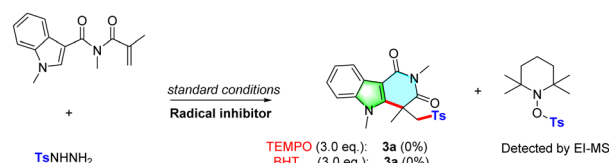


Table 2 The scope of reactions<sup>ab</sup>

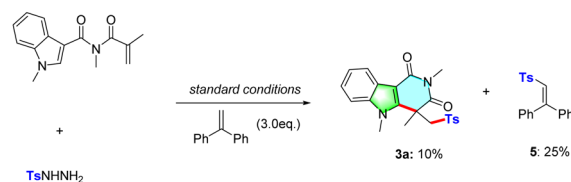
<sup>a</sup> Reaction conditions: **1** (0.25 mmol), **2** (0.625 mmol, 2.5 eq.), Ru(bpy)<sub>3</sub>Cl<sub>2</sub>·6H<sub>2</sub>O (5 mol%), TBHP (2.5 eq., 70% aqueous solution) and DMSO (2 mL) were stirred under 10 W blue LED (460–465 nm) irradiation at room temperature in air for 10 h. <sup>b</sup> Isolated yield.

as the probe afforded adduct **5** in 25% yield (Scheme 2b). These results suggested that the sulfonyl radical may be an intermediate of this photocatalytic transformation. To gain insight into the photocatalytic cycle, a Stern–Volmer luminescence quenching experiment was further conducted by mixing

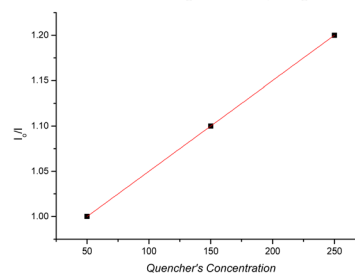
## (a) The radical trapping experiments



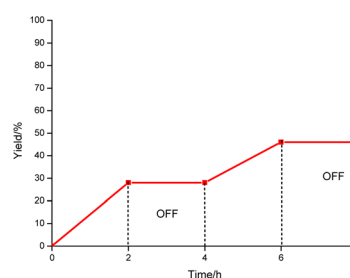
## (b) 1,1-Diphenylethylene as radical scavenger



## (c) Stern–Volmer luminescence quenching experiment



## (d) Light on/off experiment

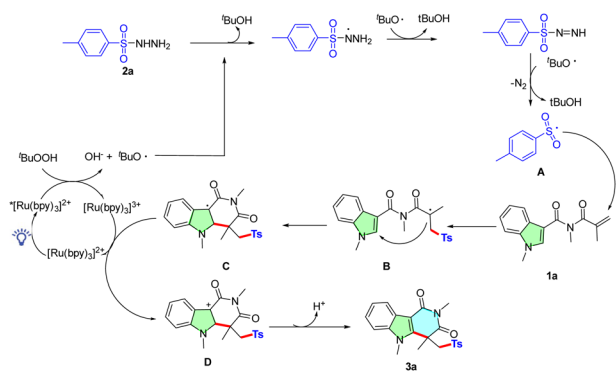


Scheme 2 Control experiments.

Ru(bpy)<sub>3</sub>Cl<sub>2</sub>·6H<sub>2</sub>O with different concentrations of TBHP. It was observed that the excited-state  $^*[\text{Ru}(\text{bpy})_3]^{2+}$  was quenched by the addition of TBHP, suggesting a strong interaction between the photocatalyst and TBHP (Scheme 2c). Finally, an on/off light experiment was conducted. The formation of product **3a** was totally suppressed in the absence of light, demonstrating that the continuous light radiation was indispensable for this transformation and the radical chain reaction pathway is not involved in the present transformation (Scheme 2d).

Based on the results of mechanistic studies and previously reported results,<sup>6,7,11–14</sup> a plausible reaction mechanism is depicted in Scheme 3. First, visible-light irradiation of photocatalyst  $[\text{Ru}(\text{bpy})_3]^{2+}$  forms the excited state species  $^*[\text{Ru}(\text{bpy})_3]^{2+}$ . Then, the single electron transfer (SET) from  $^*[\text{Ru}(\text{bpy})_3]^{2+}$  to oxidant *t*-BuOOH forms radical *t*-BuO<sup>•</sup>, along with the oxidation of  $^*[\text{Ru}(\text{bpy})_3]^{2+}$  to  $[\text{Ru}(\text{bpy})_3]^{3+}$ . Next, the radical *t*-BuO<sup>•</sup> abstract hydrogen atoms from sulfonylhydrazide





Scheme 3 Proposed preliminary mechanisms.

to generate sulfonyl radical with the release of molecular nitrogen. Subsequently, sulfonyl radical attacks the C=C bond of **1a**, followed by intramolecular cyclization to afford radical intermediate **C**. Intermediate **C** was further oxidized to carbocation **D** by  $[\text{Ru}(\text{ppy})_3]^{3+}$  via SET process. Finally, the deprotonation of intermediate **D** affording the desired product **3a**.

## Conclusions

In conclusion, we have developed a novel radical cascade cyclization strategy for the synthesis of indole-fused pyridines by using  $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$  as photocatalyst and TBHP as oxidant. With visible light irradiation, a variety of indole-fused pyridine derivatives bearing different functional groups were obtained in moderate to good yields. Compared with previous work, the easily-accessible starting materials, molecular nitrogen as byproduct and eco-friendly visible-light as energy source make this transformation more sustainable and practical, and may find applications in organic, materials and pharmaceutical chemistry in future.

## Experimental section

### General information

All reagents and solvents were purchased from commercial suppliers and used without purifications. TLC was performed on silica gel plates (200–300 mesh) using UV light (254/365 nm) for detection and column chromatography was performed on silica gel (200–300 mesh). The  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded at 25 °C in  $\text{CDCl}_3$  at 400 and 100 MHz, respectively, with TMS as the internal standard. Chemical shifts ( $\delta$ ) are expressed in ppm and coupling constants  $J$  are given in Hz. All reactions were performed on the photoreaction instrument (WP-TEC-1020SL), which are purchased from WATTCAS, China. High resolution mass spectra (HRMS) were obtained on a TOF MS instrument with ESI source. Melting points were measured with X-4B digital point apparatus and not corrected. All the starting materials are known compounds.

### General experimental procedure for the synthesis of **3a–4b**

To a stirred solution of **1** (0.25 mmol) in DMSO (2.0 mL) were added **2** (2.5 eq., 0.625 mmol),  $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$  (5 mol%) and

TBHP (70% aqueous solution, 2.5 eq., 0.625 mmol). The resulting mixture was stirred in air under a 10 W blue LEDs (460–465 nm) and irradiated for 10 h. The temperature was maintained at 20–25 °C when the LED light was on. After the reaction was complete, the reaction mixture was diluted with a brine solution (25 mL) and extracted with EtOAc (30 mL  $\times$  3). The combined organic phase was dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to afford the desired products **3a–4b**.

**2,4,5-Trimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3a)**.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.31 (d,  $J = 6.6$  Hz, 1H), 7.41–7.21 (m, 4H), 7.19–7.09 (m, 1H), 6.92 (d,  $J = 7.8$  Hz, 2H), 4.46 (d,  $J = 14.9$  Hz, 1H), 3.95 (d,  $J = 14.9$  Hz, 1H), 3.55 (s, 3H), 3.23 (s, 3H), 2.26 (s, 3H), 1.66 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.77, 161.59, 145.12, 142.03, 138.56, 135.02, 129.42, 127.89, 124.21, 124.07, 122.92, 121.57, 109.42, 104.62, 77.44, 76.80, 62.43, 43.75, 31.94, 27.17, 26.80, 21.50. HRMS (ESI) calcd for  $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 411.1379, found 411.1374.

**5-Ethyl-2,4-dimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3b)**. Pale yellow solid; m.p. 257–258 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.36 (dd,  $J = 15.0$ , 7.4 Hz, 1H), 7.59–7.02 (m, 6H), 6.90 (dd,  $J = 15.0$ , 7.7 Hz, 1H), 4.47 (d,  $J = 14.9$  Hz, 1H), 4.18–3.77 (m, 3H), 3.25 (s, 3H), 2.24 (s, 3H), 1.74 (s, 3H), 1.53–1.37 (m, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.79, 161.58, 144.82, 143.17, 141.08, 137.28, 135.13, 129.27, 127.67, 123.98, 122.85, 121.94, 109.92, 104.77, 62.99, 43.96, 40.54, 29.79, 27.71, 26.83, 14.65. HRMS (ESI) calcd for  $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 425.1535, found 425.1533.

**2,4-Dimethyl-phenyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3c)**. Pale yellow liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.38 (d,  $J = 7.9$  Hz, 1H), 7.87 (d,  $J = 7.7$  Hz, 1H), 7.76–7.49 (m, 5H), 7.34 (q,  $J = 7.2$  Hz, 2H), 7.25 (d,  $J = 7.9$  Hz, 3H), 6.76 (d,  $J = 8.3$  Hz, 1H), 3.99 (d,  $J = 14.4$  Hz, 1H), 3.40 (d,  $J = 14.3$  Hz, 1H), 3.13 (s, 3H), 2.40 (s, 3H), 1.52 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.55, 161.88, 145.24, 143.52, 141.12, 136.77, 136.02, 130.36, 130.23, 130.15, 130.04, 129.76, 129.72, 128.21, 124.35, 123.83, 123.09, 121.31, 110.86, 105.26, 62.63, 44.16, 28.36, 26.66, 21.60. HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 473.1535, found 473.1531.

**5-Benzyl-2,4-dimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3d)**. Pale yellow liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.45–8.22 (m, 1H), 7.37–7.10 (m, 8H), 6.94–6.74 (m, 4H), 5.28–4.98 (m, 2H), 4.42 (d,  $J = 19.3$  Hz, 1H), 3.93 (d,  $J = 10.2$  Hz, 1H), 3.15 (s, 3H), 2.20 (s, 3H), 1.42 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 172.75, 160.53, 144.07, 140.75, 137.16, 134.13, 133.90, 128.70, 128.35, 128.10, 126.98, 126.86, 124.50, 123.33, 122.06, 120.72, 109.53, 61.52, 47.89, 43.04, 28.69, 25.80, 20.49. HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{27}\text{N}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 487.1692, found 487.1688.

**2-Ethyl-4,5-dimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3e)**. White solid; m.p. 217–218 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.25 (d,  $J = 5.8$  Hz, 1H), 7.35–7.13 (m, 4H), 7.04 (d,  $J = 6.7$  Hz, 1H), 6.84 (d,  $J = 7.8$  Hz, 2H), 4.43 (d,  $J = 3.1$  Hz, 1H), 3.86 (dd,  $J = 15.9$ , 5.1 Hz, 3H), 3.44 (s, 3H), 2.18 (s, 3H), 1.59 (s, 3H), 1.17 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.34, 161.35, 145.03, 141.96, 138.49, 135.30,



129.44, 127.80, 124.29, 124.03, 122.90, 121.64, 109.32, 104.76, 62.51, 43.74, 35.34, 31.84, 27.15, 21.50, 12.95. HRMS (ESI) calcd for  $C_{23}H_{25}N_2O_4S$  ( $[M + H]^+$ ) 425.1535, found 425.1532.

**2-Isopropyl-4,5-dimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3f).** Colourless oil liquid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  ppm 8.49–8.29 (m, 1H), 7.58–7.21 (m, 5H), 7.05 (s, 1H), 6.86 (d,  $J = 7.8$  Hz, 1H), 5.25 (p,  $J = 9.2$ , 6.7 Hz, 1H), 4.48 (d,  $J = 15.0$  Hz, 1H), 3.89 (d,  $J = 15.0$  Hz, 1H), 3.43 (s, 3H), 2.23 (s, 3H), 1.77–1.47 (m, 9H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  ppm 173.74, 162.13, 144.84, 141.66, 138.43, 135.70, 129.42, 127.61, 124.47, 123.92, 122.82, 121.71, 109.17, 105.11, 62.60, 44.94, 44.05, 31.64, 27.04, 21.45, 19.53. HRMS (ESI) calcd for  $C_{24}H_{27}N_2O_4S$  ( $[M + H]^+$ ) 439.1692, found 439.1689.

**2-Cyclopropyl-4,5-dimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3g).** Pale yellow liquid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  ppm 8.33 (d,  $J = 6.5$  Hz, 1H), 7.45–7.21 (m, 4H), 7.13 (d,  $J = 8.1$  Hz, 1H), 7.05–6.84 (m, 2H), 4.45 (d,  $J = 14.8$  Hz, 1H), 3.91 (d,  $J = 14.7$  Hz, 1H), 3.52 (s, 3H), 2.99 (d,  $J = 15.1$  Hz, 1H), 2.25 (s, 3H), 1.65 (s, 3H), 1.32–1.07 (m, 2H), 0.84 (d,  $J = 91.4$  Hz, 2H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  ppm 174.78, 162.39, 145.03, 141.73, 138.49, 135.31, 129.45, 127.77, 124.29, 124.04, 122.92, 121.69, 109.25, 105.09, 62.51, 44.03, 42.67, 31.80, 26.94, 24.11, 21.50, 8.43, 8.19. HRMS (ESI) calcd for  $C_{24}H_{25}N_2O_4S$  ( $[M + H]^+$ ) 437.1535, found 437.1532.

**4,5-Dimethyl-2-(prop-2-yn-1-yl)-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3h).** Colourless oil liquid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  ppm 8.28 (t,  $J = 15.4$  Hz, 1H), 7.40–7.18 (m, 4H), 7.08 (d,  $J = 7.1$  Hz, 1H), 6.87 (d,  $J = 7.8$  Hz, 2H), 4.71 (d,  $J = 15.7$  Hz, 1H), 4.42 (d,  $J = 16.0$  Hz, 2H), 3.89 (d,  $J = 14.2$  Hz, 1H), 3.50 (s, 3H), 2.20 (s, 3H), 2.10 (s, 1H), 1.64 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  ppm 171.85, 159.18, 144.09, 141.03, 137.55, 134.16, 128.43, 126.88, 123.20, 122.08, 120.65, 108.35, 103.44, 77.53, 69.35, 61.30, 42.96, 30.93, 28.15, 25.98, 20.48. HRMS (ESI) calcd for  $C_{24}H_{23}N_2O_4S$  ( $[M + H]^+$ ) 435.1379, found 435.1375.

**3-(4,5-Dimethyl-1,3-dioxo-4-(tosylmethyl)-1,3,4,5-tetrahydro-2H-pyrido[4,3-*b*]indol-2-yl)propanenitrile (3i).** Colourless oil liquid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  ppm 8.29 (d,  $J = 6.2$  Hz, 1H), 7.40–7.24 (m, 4H), 7.09 (d,  $J = 7.6$  Hz, 1H), 6.89 (d,  $J = 7.9$  Hz, 2H), 4.43 (d,  $J = 15.3$  Hz, 2H), 4.21 (d,  $J = 19.9$  Hz, 1H), 3.97 (d,  $J = 14.3$  Hz, 1H), 3.48 (s, 3H), 3.07–2.92 (m, 2H), 2.24 (s, 3H), 1.72 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  ppm 173.73, 160.72, 145.14, 141.95, 138.50, 135.21, 129.48, 127.55, 124.33, 124.12, 123.24, 121.60, 117.76, 109.37, 104.27, 62.75, 43.87, 35.42, 31.82, 26.71, 21.48, 15.92. HRMS (ESI) calcd for  $C_{24}H_{24}N_3O_4S$  ( $[M + H]^+$ ) 450.1488, found 450.1486.

**4,5-Dimethyl-2-phenyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3j).** Pale yellow solid; m.p. 178–179 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  ppm 8.30 (d,  $J = 8.6$  Hz, 1H), 7.64–7.28 (m, 9H), 7.12 (d,  $J = 8.9$  Hz, 1H), 6.92 (d,  $J = 7.8$  Hz, 2H), 4.52 (d,  $J = 14.9$  Hz, 1H), 4.00 (d,  $J = 15.0$  Hz, 1H), 3.56 (s, 3H), 2.26 (s, 3H), 1.83 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  ppm 174.00, 161.58, 145.04, 142.10, 138.57, 135.63, 135.50, 129.95, 129.22, 128.77, 128.53, 127.67, 124.44, 124.20, 123.16, 121.90, 109.17, 62.99, 44.23, 31.85, 29.71, 27.04, 21.48. HRMS (ESI) calcd for  $C_{27}H_{25}N_2O_4S$  ( $[M + H]^+$ ) 473.1535, found 473.1531.

**2-Benzyl-4,5-dimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3k).** Colourless oil liquid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.39–8.28 (m, 1H), 7.42 (d,  $J = 7.6$  Hz, 2H), 7.36–7.27 (m, 6H), 7.22–7.12 (m, 2H), 6.97 (d,  $J = 7.9$  Hz, 2H), 5.16 (s, 1H), 4.89 (d,  $J = 14.0$  Hz, 1H), 4.51 (d,  $J = 14.9$  Hz, 1H), 3.94 (d,  $J = 15.0$  Hz, 1H), 3.57 (s, 3H), 2.29 (s, 3H), 1.62 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  173.57, 161.25, 145.08, 142.10, 138.56, 137.42, 135.30, 129.92, 129.45, 128.35, 128.30, 127.96, 127.18, 124.09, 122.95, 121.68, 109.36, 104.62, 62.28, 43.99, 43.25, 31.90, 27.28, 21.52. HRMS (ESI) calcd for  $C_{28}H_{27}N_2O_4S$  ( $[M + H]^+$ ) 487.1692, found 487.1689.

**8-Methoxy-2,4,5-trimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3l).** Colourless oil liquid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.72 (d,  $J = 6.3$  Hz, 1H), 7.30–7.16 (m, 2H), 7.09–6.80 (m, 4H), 4.41 (d,  $J = 8.8$  Hz, 1H), 4.10–3.97 (m, 1H), 3.87 (s, 3H), 3.48 (s, 3H), 3.13 (s, 3H), 2.23 (s, 3H), 1.60 (s, 3H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  172.67, 160.69, 155.50, 144.07, 140.78, 134.04, 132.40, 128.41, 126.98, 123.93, 113.54, 109.26, 103.24, 101.55, 61.46, 54.84, 42.80, 31.01, 26.26, 25.69, 20.49. HRMS (ESI) calcd for  $C_{23}H_{25}N_2O_5S$  ( $[M + H]^+$ ) 441.1484, found 441.1480.

**2,4,5-Trimethyl-4-(tosylmethyl)-8-(trifluoromethoxy)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3m).** Pale yellow solid; m.p. 205–206 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.11 (s, 1H), 7.24 (d,  $J = 7.9$  Hz, 2H), 7.15–7.06 (m, 2H), 6.92 (d,  $J = 7.9$  Hz, 2H), 4.40 (d,  $J = 14.9$  Hz, 1H), 3.88 (d,  $J = 14.9$  Hz, 1H), 3.58 (s, 3H), 3.14 (s, 3H), 2.21 (s, 3H), 1.62 (s, 3H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  172.41, 160.20, 144.29, 144.18 (d,  $J = 2$  Hz), 142.58, 135.75, 133.91, 128.45, 126.86, 123.52, 119.67 (d,  $J = 255$  Hz), 116.98, 113.06, 109.30, 103.85, 61.14, 42.78, 31.26, 26.04, 25.79, 20.41. HRMS (ESI) calcd for  $C_{23}H_{22}F_3N_2O_5S$  ( $[M + H]^+$ ) 495.1202, found 495.1206.

**2,4,5,6-Tetramethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3n).** White solid; m.p. 227–228 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.25 (d,  $J = 8.0$  Hz, 1H), 7.22 (dd,  $J = 23.9, 8.2$  Hz, 3H), 7.02 (d,  $J = 7.2$  Hz, 1H), 6.94 (d,  $J = 7.8$  Hz, 2H), 4.54 (d,  $J = 15.0$  Hz, 1H), 3.96 (d,  $J = 15.1$  Hz, 1H), 3.79 (s, 3H), 3.23 (s, 3H), 2.62 (s, 3H), 2.30 (s, 3H), 1.70 (s, 3H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  173.85, 161.41, 144.92, 141.77, 137.10, 135.11, 129.37, 128.02, 127.62, 125.32, 122.93, 121.16, 119.86, 104.60, 62.70, 43.93, 35.14, 27.13, 21.46, 20.58. HRMS (ESI) calcd for  $C_{23}H_{25}N_2O_4S$  ( $[M + H]^+$ ) 425.1535, found 425.1531.

**8-Bromo-2,4,5-trimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3o).** White solid; m.p. 240–241 °C;  $^1H$  NMR (400 MHz,  $DMSO-d_6$ )  $\delta$  ppm 8.23 (d,  $J = 13.0$  Hz, 1H), 7.61–7.19 (m, 4H), 7.01 (dd,  $J = 12.9, 7.7$  Hz, 2H), 4.73 (t,  $J = 16.7$  Hz, 1H), 4.19 (t,  $J = 16.3$  Hz, 1H), 3.58 (s, 3H), 3.16 (s, 3H), 2.23 (s, 3H), 1.68 (s, 3H).  $^{13}C$  NMR (100 MHz,  $DMSO-d_6$ )  $\delta$  ppm 174.12, 161.36, 144.91, 143.99, 137.58, 135.60, 129.61, 127.51, 126.48, 125.59, 122.77, 115.52, 113.00, 103.45, 61.80, 43.74, 32.45, 26.86, 26.10, 21.42. HRMS (ESI) calcd for  $C_{22}H_{22}BrN_2O_4S$  ( $[M + H]^+$ ) 489.0484, found 489.0480.

**2,5-Dimethyl-4-phenyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3p).** White solid; m.p. 286–287 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  ppm 8.40 (d,  $J = 7.8$  Hz, 1H), 7.43–7.27 (m, 7H), 7.11–7.00 (m, 3H), 6.93 (d,  $J = 7.9$  Hz, 2H),



5.17 (d,  $J = 14.4$  Hz, 1H), 4.24 (d,  $J = 14.5$  Hz, 1H), 3.20 (s, 3H), 3.09 (s, 3H), 2.26 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 171.73, 161.72, 145.06, 140.89, 138.39, 137.66, 135.10, 129.60, 129.34, 128.98, 127.81, 126.11, 124.19, 123.03, 121.75, 109.47, 106.82, 61.71, 50.36, 31.18, 26.99, 21.48. HRMS (ESI) calcd for  $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 473.1535, found 473.1528.

**4-Benzyl-2,5-dimethyl-4-(tosylmethyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3q).** Colourless oil liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.17 (d,  $J = 7.7$  Hz, 1H), 7.79 (d,  $J = 7.9$  Hz, 2H), 7.42–7.26 (m, 6H), 7.00 (dd,  $J = 17.0$ , 7.6 Hz, 2H), 6.92 (t,  $J = 7.5$  Hz, 1H), 6.43 (d,  $J = 7.5$  Hz, 1H), 4.68 (d,  $J = 15.0$  Hz, 1H), 4.14 (d,  $J = 14.8$  Hz, 1H), 3.78 (s, 3H), 3.36–3.25 (m, 2H), 2.90 (s, 3H), 2.29 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 172.30, 160.97, 145.22, 144.58, 139.57, 138.51, 135.08, 133.12, 129.94, 129.40, 128.98, 128.25, 128.17, 127.91, 124.06, 124.00, 122.81, 121.59, 61.74, 50.12, 46.10, 32.39, 26.13, 21.60. HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{27}\text{N}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 487.1692, found 487.1688.

**4-(((4-Methoxyphenyl)sulfonyl)methyl)-2,4,5-trimethyl-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3r).** Colourless oil liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.47–8.27 (m, 1H), 7.31 (dd,  $J = 29.6$ , 13.4 Hz, 5H), 6.63 (d,  $J = 9.2$  Hz, 2H), 4.62–4.47 (m, 1H), 3.96 (d,  $J = 8.7$  Hz, 1H), 3.73 (d,  $J = 8.3$  Hz, 3H), 3.22 (d,  $J = 8.5$  Hz, 3H), 1.71 (d,  $J = 8.4$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.80, 163.75, 161.62, 142.10, 138.59, 130.48, 130.20, 129.15, 127.44, 124.04, 122.91, 121.60, 114.54, 113.90, 109.43, 104.67, 62.57, 55.63, 43.82, 31.99, 27.20, 26.87. HRMS (ESI) calcd for  $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_5\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 427.1328, found 427.1325.

**Methyl-4-(((2,4,5-trimethyl-1,3-dioxo-2,3,4,5-tetrahydro-1H-pyrido[4,3-*b*]indol-4-yl)methyl)sulfonyl)benzoate (3s).** White solid; m.p. 167–168 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.45–7.91 (m, 2H), 7.88–7.04 (m, 6H), 3.90 (d,  $J = 7.3$  Hz, 3H), 3.37 (d,  $J = 7.4$  Hz, 3H), 2.44 (d,  $J = 14.3$  Hz, 1H), 2.17 (d,  $J = 7.3$  Hz, 1H), 1.75 (d,  $J = 7.4$  Hz, 3H), 0.59 (d,  $J = 7.6$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 176.46, 162.39, 161.64, 157.68, 146.70, 138.71, 130.56, 130.18, 127.08, 126.66, 124.46, 123.67, 122.76, 121.38, 109.33, 105.99, 104.66, 48.03, 32.93, 32.04, 26.46, 25.66, 9.88. HRMS (ESI) calcd for  $\text{C}_{23}\text{H}_{23}\text{N}_2\text{O}_6\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 455.1277, found 455.1274.

**4-(((4-Chlorophenyl)sulfonyl)methyl)-2,4,5-trimethyl-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3t).** White solid; m.p. 209–210 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.34 (d,  $J = 7.0$  Hz, 1H), 7.63–7.30 (m, 5H), 7.18 (dd,  $J = 20.0$ , 8.7 Hz, 2H), 4.55 (d,  $J = 15.5$  Hz, 1H), 3.96 (d,  $J = 15.1$  Hz, 1H), 3.65 (s, 3H), 3.24 (s, 3H), 1.71 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.53, 161.37, 141.67, 140.84, 138.48, 136.38, 129.43, 129.12, 124.44, 124.08, 123.14, 121.64, 109.38, 104.71, 62.49, 43.75, 31.99, 27.25, 26.82. HRMS (ESI) calcd for  $\text{C}_{21}\text{H}_{20}\text{ClN}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 431.0832, found 431.0828.

**4-(((4-Bromophenyl)sulfonyl)methyl)-2,4,5-trimethyl-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3u).** White solid; m.p. 209–210 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.34 (d,  $J = 8.0$  Hz, 1H), 7.38 (d,  $J = 5.9$  Hz, 2H), 7.34–7.25 (m, 4H), 7.21 (t,  $J = 4.5$  Hz, 1H), 4.52 (d,  $J = 15.0$  Hz, 1H), 3.95 (d,  $J = 15.0$  Hz, 1H), 3.62 (s, 3H), 3.25 (s, 3H), 1.71 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.55, 161.40, 141.65, 138.47, 136.90, 132.12, 129.49, 129.41, 124.50, 124.06, 123.16, 121.62, 109.43, 104.72, 62.50, 43.74, 31.99, 27.19, 26.84. HRMS (ESI) calcd for  $\text{C}_{21}\text{H}_{20}\text{BrN}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 475.0327, found 475.0324.

**2,4,5-Trimethyl-4-(((4-(trifluoromethyl)phenyl)sulfonyl)methyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3v).** White solid; m.p. 270–271 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.27 (d,  $J = 3.7$  Hz, 1H), 7.49 (d,  $J = 8.4$  Hz, 2H), 7.41–7.23 (m, 4H), 7.07 (d,  $J = 8.9$  Hz, 1H), 4.52 (d,  $J = 15.1$  Hz, 1H), 3.93 (d,  $J = 14.9$  Hz, 1H), 3.53 (s, 3H), 3.18 (s, 3H), 1.66 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 172.48, 160.33, 140.45, 137.29, 127.58, 124.89, 123.50, 121.86 (d,  $J = 234$  Hz), 122.26, 108.33, 103.79, 91.57, 61.61, 42.71, 30.90, 26.13, 25.82. HRMS (ESI) calcd for  $\text{C}_{22}\text{H}_{20}\text{F}_3\text{N}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 465.1096, found 465.1093.

**4-(((2,4,5-Trimethyl-1,3-dioxo-2,3,4,5-tetrahydro-1H-pyrido[4,3-*b*]indol-4-yl)methyl)sulfonyl)benzonitrile (3w).** White solid; m.p. 150–151 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.27 (d,  $J = 3.6$  Hz, 1H), 7.90–7.68 (m, 1H), 7.48 (d,  $J = 8.1$  Hz, 2H), 7.40–7.30 (m, 3H), 7.15–7.05 (m, 1H), 4.49 (d,  $J = 15.0$  Hz, 1H), 3.93 (d,  $J = 15.1$  Hz, 1H), 3.56 (s, 3H), 3.23 (s, 3H), 1.68 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 172.39, 160.30, 159.54, 148.56, 140.95, 140.31, 137.25, 131.29, 127.46, 123.75, 122.99, 122.43, 120.80, 116.34, 115.61, 108.25, 103.88, 61.62, 42.67, 30.95, 28.69, 25.98. HRMS (ESI) calcd for  $\text{C}_{22}\text{H}_{20}\text{F}_3\text{N}_3\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 422.1175, found 422.1171.

**4-(((2-Chlorophenyl)sulfonyl)methyl)-2,4,5-trimethyl-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3x).** White solid; m.p. 260–261 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.27 (d,  $J = 7.0$  Hz, 1H), 7.45–7.25 (m, 4H), 7.20 (t,  $J = 8.4$  Hz, 1H), 7.06 (d,  $J = 7.4$  Hz, 1H), 6.72 (t,  $J = 7.7$  Hz, 1H), 4.59 (d,  $J = 15.2$  Hz, 1H), 4.39 (d,  $J = 15.3$  Hz, 1H), 3.68 (s, 3H), 3.29 (s, 3H), 1.78 (s, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.67, 161.61, 141.57, 138.32, 135.35, 134.59, 132.11, 131.27, 130.99, 126.84, 124.08, 123.02, 121.67, 109.25, 105.01, 60.76, 43.67, 42.69, 32.01, 26.90, 26.67. HRMS (ESI) calcd for  $\text{C}_{21}\text{H}_{20}\text{ClN}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 431.0832, found 431.0828.

**4-(((Cyclopropylsulfonyl)methyl)-2,4,5-trimethyl-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3y):<sup>11</sup>** Colourless oil liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.43–8.23 (m, 1H), 7.37 (d,  $J = 11.1$  Hz, 3H), 4.49 (d,  $J = 14.8$  Hz, 1H), 3.96 (d,  $J = 7.9$  Hz, 1H), 3.90 (s, 3H), 3.40 (s, 3H), 1.73 (s, 3H), 1.04 (d,  $J = 4.9$  Hz, 2H), 0.88 (s, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 174.26, 161.59, 142.95, 138.67, 124.38, 124.10, 122.93, 121.62, 109.55, 104.17, 59.92, 43.60, 32.17, 30.75, 27.42, 26.94, 5.03, 4.92.

**4-(((Ethylsulfonyl)methyl)-2,4,5-trimethyl-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (3z):<sup>11</sup>** Pale yellow liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.31 (d,  $J = 6.5$  Hz, 1H), 7.53–7.27 (m, 3H), 4.40 (d,  $J = 13.9$  Hz, 1H), 3.93 (s, 3H), 3.80 (d,  $J = 14.2$  Hz, 1H), 3.40 (s, 3H), 3.04–2.78 (m, 2H), 1.73 (s, 3H), 1.31 (t,  $J = 7.0$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 174.34, 161.58, 142.88, 138.68, 124.46, 124.04, 122.91, 121.66, 109.56, 104.24, 57.76, 49.42, 43.39, 32.16, 27.50, 26.96, 6.24.

**2,4,5-Trimethyl-4-(((thiophen-2-ylsulfonyl)methyl)-4,5-dihydro-1H-pyrido[4,3-*b*]indole-1,3(2H)-dione (4a).** Pale yellow liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.34 (d,  $J = 8.8$  Hz, 1H), 7.58 (d,  $J = 4.9$  Hz, 1H), 7.43–7.28 (m, 3H), 7.09 (d,  $J = 3.8$  Hz, 1H), 6.80 (t,  $J = 4.4$  Hz, 1H), 4.66 (d,  $J = 15.0$  Hz, 1H), 4.07 (d,  $J = 15.1$  Hz, 1H), 3.73 (s, 3H), 3.26 (s, 3H), 1.73 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.57, 161.53, 141.97, 139.18, 138.57, 134.97, 134.80, 127.76, 124.28, 124.22, 123.03, 121.69, 109.47, 104.79, 63.56, 43.96, 42.67, 27.49, 26.92. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_4\text{S}_2$  ( $[\text{M} + \text{H}]^+$ ) 403.0786, found 403.0782.



**2,4,5-Trimethyl-4-((naphthalen-2-ylsulfonyl)methyl)-4,5-dihydro-1H-pyrido[4,3-b]indole-1,3(2H)-dione (4b).** White solid; m.p. 180–181 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.34 (d,  $J = 7.9$  Hz, 1H), 7.78 (d,  $J = 10.8$  Hz, 3H), 7.68–7.38 (m, 4H), 7.33 (d,  $J = 7.7$  Hz, 1H), 7.18 (d,  $J = 7.9$  Hz, 1H), 6.87 (d,  $J = 6.7$  Hz, 1H), 4.62 (d,  $J = 15.3$  Hz, 1H), 4.04 (d,  $J = 12.3$  Hz, 1H), 3.49 (s, 3H), 3.04 (s, 3H), 1.69 (d,  $J = 12.0$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 173.67, 161.45, 141.82, 138.37, 135.00, 134.58, 131.58, 130.22, 129.54, 129.49, 129.18, 127.68, 127.54, 124.23, 124.17, 123.00, 122.28, 121.48, 109.20, 104.72, 62.38, 43.85, 31.84, 27.29, 26.63. HRMS (ESI) calcd for  $\text{C}_{25}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$  ( $[\text{M} + \text{H}]^+$ ) 447.1379, found 447.1375.

## Data availability

The authors confirm that the data supporting the findings of this study are available within the article [and/or its ESI†].

## Conflicts of interest

The authors declare no competing financial interest.

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