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# The fast and efficient KI/H<sub>2</sub>O<sub>2</sub> mediated 2-sulfonylation of indoles and *N*-methylpyrrole in water†

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The rapid and efficient KI/H<sub>2</sub>O<sub>2</sub>-mediated 2-sulfonylation of substituted indoles and *N*-methylpyrrole was established. The corresponding 2-sulfonylation products are synthesized from readily available sulfur sources, namely arylsulfonyl hydrazides, 4-methylbenzenesulfinic acid and sodium 4-methylbenzenesulfinate in good to excellent yields in only 5 min. Moreover, the aqueous solution of hydrogen peroxide is used as both oxidant and solvent. Mechanistic studies demonstrated that 2,3-diiodoindoline was the main sulfonylation intermediate.

## Introduction

Indole is a widely used building block and is found in many natural products, pharmaceuticals and fine chemicals.<sup>1</sup> 2-Sulfonylindoles are an important class of indole derivatives due to the sulfonyl moiety which can enhance bioactivity<sup>2</sup> and acts as a useful vehicle for the development of new strategies for synthesis.<sup>3</sup> Generally, 2-sulfonylindoles are synthesized *via* the oxidation of the corresponding arylthioindoles.<sup>4</sup> In recent years, a series of simple, efficient and direct 2-sulfonylations of indoles with sodium sulfinates have been reported for the synthesis of 2-arylsulfonyl indoles. For example, Deng and co-workers developed the I<sub>2</sub>-catalyzed 2-sulfonylation of indoles using sodium sulfinates, with TBHP as the oxidant and HOAc as the solvent.<sup>5</sup> Around the same time Kuhakarn and co-workers proposed a similar catalytic process in the absence of oxidants.<sup>6</sup> This provoked the development of numerous catalytic systems, such as NH<sub>4</sub>I–TBHP in HOAc<sup>7</sup> and KI-oxones (2KHSO<sub>5</sub>–KHSO<sub>4</sub>–K<sub>2</sub>SO<sub>4</sub>) in H<sub>2</sub>O.<sup>8</sup> Recently, Yu and co-workers presented the electrochemical-sulfonylation of 1*H*-indoles using sodium sulfinates under chemical oxidant-free conditions with TBAI as the catalyst.<sup>9</sup> In addition, sulfonyl hydrazides are environmentally friendly sulfur sources, and have been extensively employed in organic reaction because they are stable, readily accessible, odor-free.<sup>10</sup> Barman and co-workers reported the elegant sulfonylation of sulfonyl hydrazides and indoles using TBHP/I<sub>2</sub> as the catalyst and DCE as solvent.<sup>11</sup> However, drawbacks still remain, such as prolonged reaction

times, the use of organic solvents and large amounts of acid, non-green oxidant, and a relatively expensive iodine source. Therefore, a more environmentally benign protocol for the synthesis of 2-sulfonylindoles is highly desirable. Herein, we report a rapid and efficient KI-mediated 2-sulfonylation of substituted indoles and *N*-methylpyrrole using 30% H<sub>2</sub>O<sub>2</sub> solution as both oxidant and solvent. Importantly, this transformation can be completed within 5 min and features a broad substrate scope.

## Results and discussion

As our model reaction for the optimization study 1*H*-indole (**1a**, 0.5 mmol) and *p*-toluenesulfonyl hydrazide (TsNHNH<sub>2</sub>, **2a**, 1.0 mmol) were used (Table 1). When the reaction was first conducted using 10% KI and 1 equiv. of H<sub>2</sub>O<sub>2</sub> in HOAc at 60 °C for 2 h, 2-tosyl-1*H*-indole **3a** was obtained in only 15% yield (entry 1). With the addition of EtOH as the solvent product **3a** was isolated in 20% yield (entry 2). However, by increasing the KI content to 20%, and with the slow addition of 30% H<sub>2</sub>O<sub>2</sub> solution to the reaction, we found that the 2-sulfonylation of indole can occur rapidly resulting in 53% yield of product **3a** in only 5 min (entry 3). The main reason for the increase in yield may be that a large amount of heat is released due to the addition of hydrogen peroxide to the mixture of 1*H*-indole and TsNHNH<sub>2</sub> in absence of any other solvent, and the high temperature generated promotes the progress of the 2-sulfonylation. Moreover, by increasing the amount of KI, the reaction yield rose significantly (entries 4 and 5). In the case of altering the substrate ratio of compounds **1a** and **2a**, no significant change in the reaction yield was observed (entries 6 and 7). When 70% TBHP was used as the oxidant product **3a** was produced in 65% yield (entry 8). A similar yield was observed when NH<sub>4</sub>I was employed as the iodine source, furnishing product **3a** in 69% yield (entry 9). Since KI is substantially greener and has lower-cost, it was

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Table 1 Optimization of the reaction conditions<sup>a</sup>

Entry	Catalyst	Oxidation/solvent	Time (min)	Yield <sup>b</sup> (%)
1 <sup>c</sup>	KI (10%)	H <sub>2</sub> O <sub>2</sub> (1 equiv.)/HOAc(1 mL)	120	15
2 <sup>c</sup>	KI (10%)	H <sub>2</sub> O <sub>2</sub> (2 equiv.)/EtOH(1 mL)	120	20
3	KI (20%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/—	5	53
4	KI (40%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/—	5	58
5	KI (60%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/—	5	71
6 <sup>d</sup>	KI (60%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/—	5	60
7 <sup>e</sup>	KI (60%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/—	5	48
8	KI (60%)	TBHP (1 mL)/—	5	65
9	NH <sub>4</sub> I (60%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/—	5	69
10	KI (100%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/—	5	81
11	KI (120%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/—	5	83
12	KI (100%)	H <sub>2</sub> O <sub>2</sub> (1 mL)/EtOH(1 mL)	5	63

<sup>a</sup> Reaction conditions: 1*H*-indole (**1a**, 0.5 mmol), TsNHNH<sub>2</sub> (**2a**, 1 mmol). <sup>b</sup> Isolated yield. <sup>c</sup> 60 °C. <sup>d</sup> 0.50 mmol of **2a** was used. <sup>e</sup> 0.75 mmol of **1a** was used.

selected as the iodine source and H<sub>2</sub>O<sub>2</sub> as the oxidant. Finally, by using excess KI, 1.0 and 1.2 equiv. of KI, the reaction yield reached 81% and 83% of compound **3a**, respectively (entries 10 and 11). Meanwhile, we also tried the reaction at room temperature using ethanol as a solvent, but only to give a yield of 63% (entry 12). On the basis of the above experiments, the optimized reaction conditions are as follows: 1*H*-indole (**1a**, 0.5 mmol), TsNHNH<sub>2</sub> (**2a**, 1 mmol), KI (1.0 equiv.), H<sub>2</sub>O<sub>2</sub> (1 mL), for 5 min under air.

With the optimized reaction conditions in hand, we next investigated the scope of the reaction with a series of indoles, which are summarized in Table 2. The electronic nature of the substituents on the indole was found to have a considerable effect on the reaction yield. Electron-donating substituents (1-Me, 3-Me, 5-Me, 7-Me, 4-MeO, 5-MeO, and 7-MeO) gave better reactivity and provided the corresponding 2-sulfonylated products **3a**, **3b**, and **3e–j** in 78–89% yields. In addition, 4-(benzyloxy)-1*H*-indole furnished product **3k** in 60% yield. Whereas, 6-bromo- and 7-bromoindoles gave products **3l** and **3m** in 78% and 52% yield, respectively. To our delight, 2-methyl-1*H*-indole showed good reactivity and C-3 regioselectivity, providing product **3n** in 88% yield. Unfortunately, when 1-ethyl or 1-benzyl-substituted indole was used as the reactant, the desired product **3c** or **3d** was obtained in a low yield.

Encouraged by the above results, we further explored our sulfonylation method using a variety of arylsulfonyl hydrazides with 1*H*-indole **1a** under optimum conditions (Table 3). The reaction of benzenesulfonyl hydrazide with 1*H*-indole gave product **3o** in only 55% yield. A similar result was obtained for the substituted benzenesulfonyl hydrazide bearing electron-withdrawing groups 4-F, 4-Br, 4-CF<sub>3</sub>. However, 4-Cl or 4-NO<sub>2</sub> substituted substrates were converted into 2-sulfonylated products **3q** and **3t** in good yields. Electron-donating substrates 4-<sup>t</sup>Bu, and 4-OMe gave 2-sulfonylated products **3u** and **3v** in 76% and 51% yield, respectively. Furthermore, the method was also

extended to 2-naphthylsulfonyl hydrazide, producing product **3w** in 81% yield.

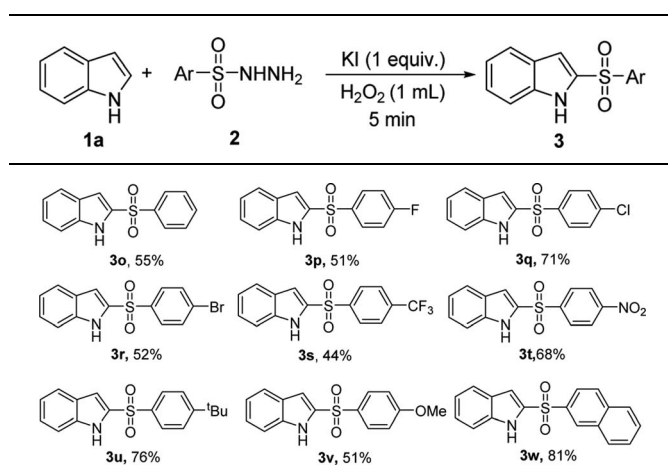
In our scope studies, 4-methylbenzenesulfinic acid and sodium 4-methylbenzenesulfinate were also examined under the optimized conditions, as shown in Table 4. Weather

Table 2 KI/H<sub>2</sub>O<sub>2</sub>-mediated 2-sulfonylation of substituted indoles and TsNHNH<sub>2</sub><sup>a</sup>

<b>3a</b> , 81%	<b>3b</b> , R = Me, 80%	<b>3e</b> , 81%
<b>3f</b> , 78%	<b>3c</b> , R = Et, 42%	<b>3h</b> , 82%
<b>3i</b> , 89%	<b>3d</b> , R = CH <sub>2</sub> Ph, 26%	<b>3j</b> , 82%
<b>3l</b> , 78%		<b>3k</b> , 60%
<b>3m</b> , 52%		<b>3n</b> , 88%

<sup>a</sup> Reaction conditions: **1** (0.5 mmol), **2a** (1.0 mmol), KI (1 equiv.), H<sub>2</sub>O<sub>2</sub> (1 mL), reaction time 5 min. The yields of isolated products are given.

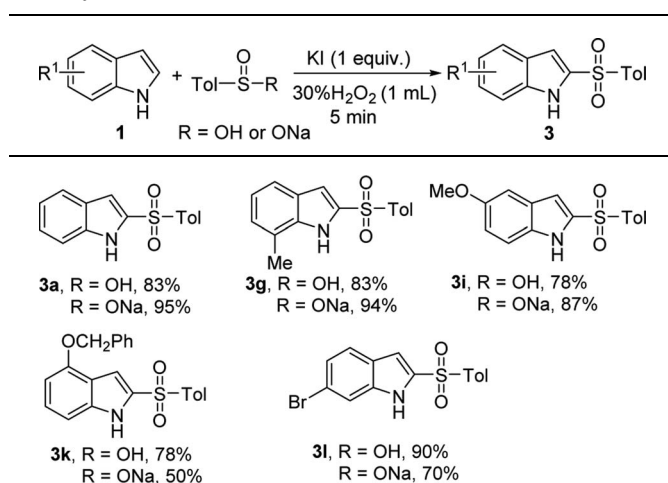


**Table 3** KI/H<sub>2</sub>O<sub>2</sub>-mediated 2-sulfonylation of 1*H*-indole and arylsulfonyl hydrazides<sup>a</sup>

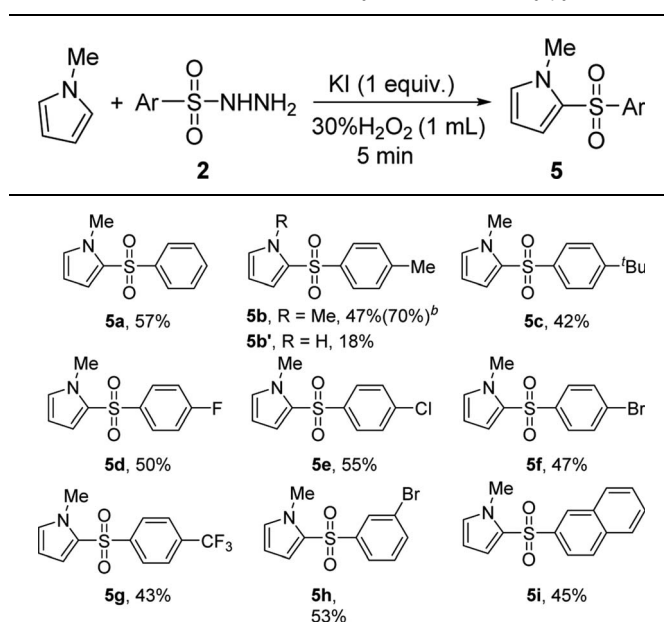
<sup>a</sup> Reaction conditions: 1a (0.5 mmol), 2 (1.0 mmol), KI (1 equiv.), H<sub>2</sub>O<sub>2</sub> (1 mL), reaction time 5 min. The yields of isolated products are given.

electron-donating or withdrawing groups were employed the reactions performed well, giving the desired products in high yields. In this case, the electronic nature of the substituent had no significant influence on the reactivity. Compared with the reported methods,<sup>5–9</sup> operational simplicity, short reaction time and good yield are the key advantages of this protocol.

To the best of our knowledge, the 2-sulfonylation of *N*-methylpyrrole has rarely been reported, with unstable sulfur sources and complex reaction conditions often required.<sup>12,13</sup> Gratifyingly, various arylsulfonyl hydrazides showed good results with *N*-methylpyrrole, giving the desired products 5a–i in 42–57% yields (Table 5). We also found that when 4-

**Table 4** 2-Sulfonylation of 4-methylbenzenesulfonic acid or sodium 4-methylbenzenesulfinate as sulfur sources<sup>a</sup>

<sup>a</sup> Reaction conditions: 1a (0.5 mmol), 4-methylbenzenesulfonic acid or sodium 4-methylbenzenesulfinate (1.0 mmol), KI (1 equiv.), H<sub>2</sub>O<sub>2</sub> (1 mL), reaction time 5 min (0.5 mL HOAc was added, when sodium 4-methylbenzenesulfinate is used as sulfur source). The yields of isolated products are given.

**Table 5** KI/H<sub>2</sub>O<sub>2</sub>-mediated 2-sulfonylation of *N*-methylpyrrole<sup>a</sup>

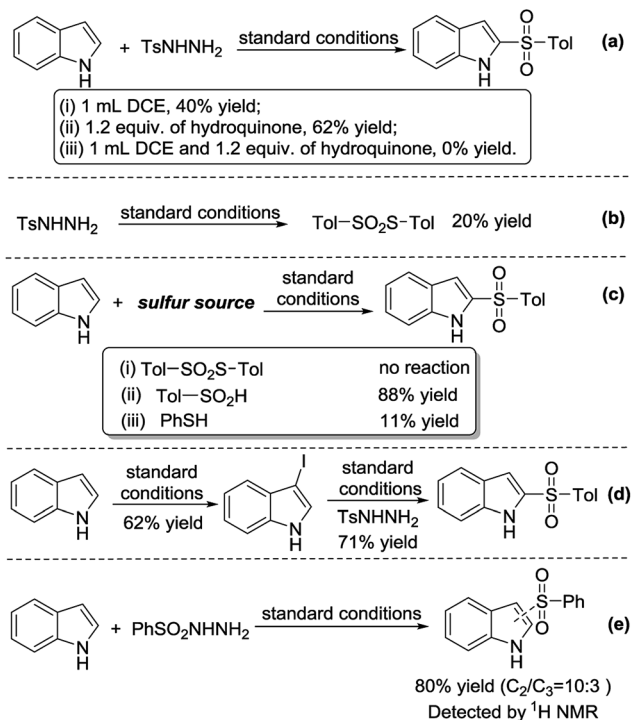
<sup>a</sup> Reaction conditions: *N*-methylpyrrole (0.5 mmol), 2 (1.0 mmol), KI (1 equiv.) in H<sub>2</sub>O<sub>2</sub> (1 mL), reaction time 5 min. The yields of isolated products are given. <sup>b</sup> 4-Methylbenzenesulfonic acid as sulfur source.

methylbenzenesulfonic acid was used as the sulfur source, the reaction yield (5b) significantly improved. In addition, 1*H*-pyrrole as a substrate reacted with *p*-toluenesulfonyl hydrazide to afford the desired product 5b' in only 18% yield.

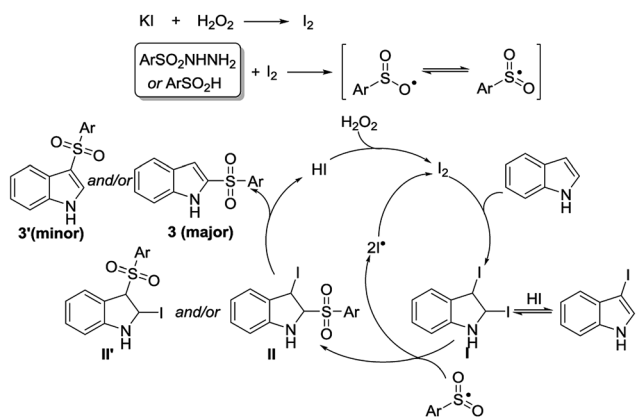
A series of experiments were conducted to uncover the reaction mechanism. In order to confirm that the reaction was radical, a radical scavenger, 1.2 equiv. of hydroquinone, was added to the reaction mixture. Dichloroethane was also added to aid in solubility of the scavenger. We found that the reaction did not proceed; hence, the reaction was radical (Scheme 1a). In the absence of 1*H*-indole, *p*-toluenesulfonyl hydrazide underwent a self-coupling reaction to form *S-p*-tolyl 4-methylbenzenesulfonothioate (Scheme 1b). However, when *S-p*-tolyl 4-methylbenzenesulfonothioate was used as the sulfur source, the 2-sulfonylation reaction did not proceed. This result indicates that *S-p*-tolyl 4-methylbenzenesulfonothioate is not an intermediate of the reaction. Subsequently, we tested other sulfur sources, such as sodium 4-methylbenzenesulfinate and thiophenol, giving the 2-sulfonylated product under standard conditions in 88% and 11% yield, respectively (Scheme 1c). 1*H*-Indole underwent iodination to form 3-iodo-1*H*-indole in the absence of *p*-toluenesulfonyl hydrazide in 62% yield, and 3-iodo-1*H*-indole reacted with *p*-toluenesulfonyl hydrazide to give 3a in 71% yield under standard conditions (Scheme 1d). In addition, we found an important experimental fact that benzenesulfonyl hydrazide reacted with 1*H*-indole to afford C<sub>2</sub>- and C<sub>3</sub>-sulfonylation products, which were detected by <sup>1</sup>H NMR in a ratio of 10 : 3 (80% conversion, Scheme 1e).

According to the above results, as well as support from previous reports,<sup>5–9,11</sup> a plausible radical mechanism is





Scheme 1 Control experiments.



Scheme 2 Proposed mechanism.

proposed (Scheme 2). KI is first oxidized by H<sub>2</sub>O<sub>2</sub> to form molecular iodine, which reacts quickly with *p*-toluenesulfonyl hydrazide to produce the active sulfonyl radical. Meanwhile, the addition of molecular iodine to indole occurs and generates a key intermediate **I** (2,3-diiodoindole). Subsequently, intermediate **I** reacts with the sulfonyl radical to produce intermediate **II**, **II'**, and iodine radical. Then, HI elimination takes place to provide 2- or 3-sulfonylindole. Meanwhile, the molecular iodine can be re-generated *via* the coupling of two iodine radicals or the oxidation of HI by H<sub>2</sub>O<sub>2</sub>. This mechanism provides a reasonable explanation for the generation of C<sub>2</sub>- and/or C<sub>3</sub>-sulfonylation products (Scheme 1e), and even product **3n** (Table 2).

## Conclusions

In summary, we have developed a simple KI-mediated 2-sulfonylation of substituted indoles and *N*-methylpyrrole using 30% H<sub>2</sub>O<sub>2</sub> solution as the oxidant and the solvent in presence of various sulfur sources. This method provides a fast and efficient approach to produce diversified 2-sulfonylation products in good to excellent yields within 5 min. This protocol has great advantages including short reaction time, green oxidant and solvent, cheap iodine source, avoiding the use of acid, and broad substrate scope. Notably, 2,3-diiodoindole maybe the main sulfonylation intermediates in this transformation. Studies to further investigate this catalytic system to other related reactions are currently underway in our laboratory.

## Experimental

### Materials and instruments

Chemicals were obtained commercially and used as received. All products were isolated by short chromatography on a silica gel (200–300 mesh) column using petroleum ether (60–90 °C) and ethyl acetate. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Bruker Avance III HD 400 MHz spectrometer in CDCl<sub>3</sub> solution. All chemical shifts were reported in ppm (δ) relative to the internal standard TMS (0 ppm). ESI-mass spectrum was measured on an Agilent 6210 ESI/TOF MS.

### General procedure for a KI/H<sub>2</sub>O<sub>2</sub> mediated 2-sulfonylation of indoles and *N*-methylpyrrole in water

A mixture of substituted indole or *N*-methylpyrrole (0.5 mmol), sulfur source (1.0 mmol, arylsulfonyl hydrazides or 4-methylbenzenesulfinic acid or sodium 4-methylbenzenesulfinate + 0.5 mL HOAc) and KI (0.5 mmol) was stirred at room temperature under air. Subsequently, 30% H<sub>2</sub>O<sub>2</sub> solution (1 mL) was slowly added to the above system (note: a large amount of heat is generated during this process) and the reaction stirred for an additional 5 min. The solution was quenched the saturated solution of sodium thiosulfate (5 mL) and extracted with EtOAc (3 × 10 mL). The combined EtOAc extracts were dried over anhydrous MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel using PE/EtOAc as the eluent.

### The characterization data of products

**4-Methoxy-2-tosyl-1*H*-indole (3h)**. White solid, 123 mg, 82% yield, mp 155–158 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.90 (s, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 7.1 Hz, 3H), 7.23 (d, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.52 (d, *J* = 7.8 Hz, 1H), 3.92 (s, 3H), 2.38 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 154.65, 144.52, 130.06, 127.45, 127.20, 106.80, 105.11, 100.55, 55.52, 21.72; HRMS(ESI): *m/z* calcd for C<sub>16</sub>H<sub>15</sub>NO<sub>3</sub>S (M)<sup>+</sup>: 301.0767, found: 301.0763.

**7-Methoxy-2-tosyl-1*H*-indole (3j)**. White solid, 123 mg, 82% yield, mp 149–151 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.00 (s, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.28 (s, 2H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.16–7.03 (m, 3H), 6.73 (d, *J* = 7.7 Hz, 1H), 3.95 (s, 3H), 2.38 (s,



3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  146.65, 144.52, 138.77, 134.40, 130.04, 127.47, 122.15, 114.85, 109.09, 104.80, 55.60, 21.71; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}_3\text{S}$  ( $\text{M}^+$ ): 301.0767, found: 301.0769.

**4-(Benzyloxy)-2-tosyl-1H-indole (3k).** White solid, 113 mg, 60% yield, mp 136–139 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.97 (s, 1H), 7.87 (d,  $J = 8.3$  Hz, 2H), 7.47 (d,  $J = 7.2$  Hz, 2H), 7.37 (dt,  $J = 24.0, 7.0$  Hz, 4H), 7.28 (s, 1H), 7.22 (t,  $J = 8.1$  Hz, 1H), 6.58 (d,  $J = 7.8$  Hz, 1H), 5.18 (s, 2H), 2.38 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  153.74, 138.79, 138.54, 136.92, 133.16, 130.07, 128.72, 128.15, 127.44, 107.00, 105.38, 101.85, 70.11, 21.72; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{22}\text{H}_{19}\text{NO}_3\text{S}$  ( $\text{M}^+$ ): 377.1080, found: 377.1075.

**6-Bromo-2-tosyl-1H-indole (3l).** Brown solid, 136 mg, 78% yield, mp 181–182 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.25 (s, 1H), 7.88 (d,  $J = 8.3$  Hz, 2H), 7.61–7.48 (m, 2H), 7.33–7.27 (m, 3H), 2.39 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  144.99, 138.28, 137.75, 135.32, 130.24, 127.50, 126.01, 125.30, 123.96, 119.78, 115.35, 108.91, 21.77; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{12}\text{BrNNaO}_2\text{S}$  ( $\text{M} + \text{Na}^+$ ): 371.9664, found: 371.9653.

**7-Bromo-2-tosyl-1H-indole (3m).** Dark red solid, 91 mg, 52% yield, mp 155–158 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.86 (s, 1H), 7.91 (d,  $J = 8.3$  Hz, 2H), 7.60 (d,  $J = 8.1$  Hz, 1H), 7.51–7.47 (m, 1H), 7.33 (d,  $J = 8.1$  Hz, 2H), 7.22 (d,  $J = 2.2$  Hz, 1H), 7.06 (t,  $J = 7.8$  Hz, 1H), 2.41 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  144.87, 138.14, 135.77, 135.57, 130.10, 128.20, 128.02, 127.51, 122.67, 121.87, 109.60, 105.32, 21.64; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{12}\text{BrNNaO}_2\text{S}$  ( $\text{M} + \text{Na}^+$ ): 371.9664, found: 371.9661.

**2-Methyl-3-tosyl-1H-indole (3n).** White solid, 125 mg, 88% yield; mp 179–181 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.26 (s, 1H), 7.97 (d,  $J = 8.5$  Hz, 1H), 7.83 (d,  $J = 8.3$  Hz, 2H), 7.24–7.10 (m, 5H), 2.64 (s, 3H), 2.32 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.38, 141.52, 141.19, 134.54, 129.75, 126.15, 125.40, 123.10, 122.17, 119.28, 111.42, 111.27, 21.57, 13.04. HRMS(ESI):  $m/z$  calcd for  $\text{C}_{16}\text{H}_{16}\text{NO}_2\text{S}$  ( $\text{M} + \text{H}^+$ ): 286.0896, found: 286.0900.

**2-((4-Nitrophenyl)sulfonyl)-1H-indole (3t).** Light yellow solid, 102 mg, 68% yield, mp 129–132 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.90 (s, 1H), 8.36–8.34 (m, 1H), 8.33 (d,  $J = 2.1$  Hz, 1H), 8.20–8.15 (m, 2H), 7.69 (d,  $J = 8.1$  Hz, 1H), 7.46–7.42 (m, 1H), 7.41–7.37 (m, 1H), 7.29 (dd,  $J = 2.1, 0.8$  Hz, 1H), 7.22 (ddd,  $J = 8.0, 6.8, 1.1$  Hz, 1H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  150.40, 147.18, 137.49, 132.20, 129.24, 128.58, 127.15, 126.92, 124.61, 124.46, 122.97, 122.12, 112.35, 110.85. HRMS(ESI):  $m/z$  calcd for  $\text{C}_{14}\text{H}_{10}\text{N}_2\text{NaO}_4\text{S}$  ( $\text{M} + \text{Na}^+$ ): 325.0253, found: 325.0251.

**2-((4-(tert-Butyl)phenyl)sulfonyl)-1-methyl-1H-pyrrole (5c).** Pale yellow solid, 58 mg, 42% yield, mp 59–61 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.80 (d,  $J = 8.7$  Hz, 2H), 7.50 (d,  $J = 8.7$  Hz, 2H), 7.02 (dd,  $J = 4.0, 1.9$  Hz, 1H), 6.75 (t,  $J = 2.2$  Hz, 1H), 6.16 (dd,  $J = 4.0, 2.6$  Hz, 1H), 3.72 (s, 3H), 1.32 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.84, 139.25, 129.56, 128.43, 127.16, 126.33, 118.64, 108.33, 35.79, 35.30, 31.18; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{20}\text{NO}_2\text{S}$  ( $\text{M} + \text{H}^+$ ): 278.1209, found: 278.1208.

**1-Methyl-2-((4-(trifluoromethyl)phenyl)sulfonyl)-1H-pyrrole (5g).** Pale yellow solid, 62 mg, 43% yield, mp 66–68 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 8.2$  Hz, 2H), 7.77 (d,  $J = 8.3$  Hz, 2H), 7.09 (dd,  $J = 4.1, 1.9$  Hz, 1H), 6.81 (t,  $J = 2.2$  Hz, 1H), 6.21 (dd,  $J = 4.1, 2.6$  Hz, 1H), 3.73 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  145.96, 134.76, 134.43, 130.61, 127.77, 126.85, 126.53, 126.50,

124.63, 121.92, 119.92, 108.94, 35.87; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{12}\text{H}_{11}\text{F}_3\text{NO}_2\text{S}$  ( $\text{M} + \text{H}^+$ ): 290.0457, found: 290.0457.

**2-((3-Bromophenyl)sulfonyl)-1-methyl-1H-pyrrole (5h).** Pale yellow solid, 79 mg, 53% yield, mp 55–58 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (t,  $J = 1.8$  Hz, 1H), 7.81 (d,  $J = 7.9$  Hz, 1H), 7.68 (d,  $J = 8.0$  Hz, 1H), 7.38 (t,  $J = 7.9$  Hz, 1H), 7.05 (dd,  $J = 4.1, 1.9$  Hz, 1H), 6.80 (t,  $J = 2.2$  Hz, 1H), 6.20 (dd,  $J = 4.1, 2.6$  Hz, 1H), 3.72 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  144.26, 136.02, 130.86, 130.36, 130.09, 127.11, 125.78, 123.25, 119.62, 108.77, 35.85; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{11}\text{H}_{10}\text{BrNO}_2\text{S}$  ( $\text{M}^+$ ): 298.9688, found: 298.9690.

**1-Methyl-2-(naphthalen-2-ylsulfonyl)-1H-pyrrole (5i).** Pale yellow solid, 60 mg, 45% yield, mp 60–63 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.50 (s, 1H), 7.93 (td,  $J = 17.0, 16.6, 7.8$  Hz, 3H), 7.80 (dd,  $J = 8.7, 1.9$  Hz, 1H), 7.66–7.57 (m, 2H), 7.10 (dd,  $J = 4.0, 1.9$  Hz, 1H), 6.75 (t,  $J = 2.2$  Hz, 1H), 6.19 (dd,  $J = 4.0, 2.6$  Hz, 1H), 3.72 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  139.13, 135.02, 132.30, 129.85, 129.73, 129.47, 129.15, 128.33, 128.06, 127.72, 122.71, 119.14, 108.54, 35.81; HRMS(ESI):  $m/z$  calcd for  $\text{C}_{15}\text{H}_{14}\text{NO}_2\text{S}$  ( $\text{M} + \text{H}^+$ ): 272.0740, found: 272.0745.

## Conflicts of interest

There are no conflicts to declare.

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## Notes and references

- (a) E. C. Taylor, in *The Chemistry of Heterocyclic Compounds*, ed. J. E. Saxton, Wiley-Interscience, New York, 1994; (b) Y. Ban, Y. Murakami, Y. Iwasawa, M. Tsuchiya and N. Takano, *Med. Res. Rev.*, 1988, **8**, 231; (c) A. R. Katritzky and A. F. Pozharskii, *Handbook of Heterocyclic Chemistry*, Pergamon Press, Oxford, 2000; (d) G. R. Humphrey and J. T. Kuethe, *Chem. Rev.*, 2006, **106**, 2875; (e) P. N. Craig, in *Comprehensive Medicinal Chemistry*, ed. C. J. Drayton, Pergamon, New York, 1991, vol. 8; (f) R. J. Sundberg, *Indoles*, Academic Press, New York, 1996; (g) T. Kawasaki and K. Higuchi, *Nat. Prod. Rep.*, 2005, **22**, 761; (h) F. Ban, E. Leblanc, H. Li, R. S. Munuganti, K. Frewin, P. S. Rennie and A. Cherkasov, *J. Med. Chem.*, 2014, **57**, 6867; (i) H. Yan, H. L. Wang, X. C. Li, X. Y. Xin, C. X. Wang and B. S. Wan, *Angew. Chem., Int. Ed.*, 2015, **54**, 10613; (j) A. J. Kochanowska-Karamyan and M. T. Hamann, *Chem. Rev.*, 2010, **110**, 4489.
- (a) N. S. Simpkins, in *Sulfones in Organic Synthesis*, ed. J. E. Baldwin, Pergamon Press, Oxford, UK, 1993; (b) B. M. Trost, *Comprehensive Organic Chemistry*, Pergamon Press, Oxford, UK, 1991; (c) H. Y. Lee, S. L. Pan, M. C. Su,



- Y. M. Liu, C. C. Y. Kuo, T. Chang, J. S. Wu, C. Y. Nien, S. Mehndiratta, C. Y. Chang, S. Y. Wu, M. J. Lai, J. Y. Chang and J. P. Liou, *J. Med. Chem.*, 2013, **56**, 8008; (d) O. Cazorla, A. Lacampagne, J. Fauconnier and G. Vassort, *Br. J. Pharmacol.*, 2003, **139**, 99; (e) T. Asai, T. Takeuchi, J. Diffenderfer and D. L. Sibley, *Antimicrob. Agents Chemother.*, 2002, **46**, 2393; (f) F. Dol, P. Schaeffer, I. Lamarche, A. Mares, P. Chatelain and J. Herbert, *Eur. J. Pharmacol.*, 1995, **280**, 135.
- 3 (a) S. Caddick, K. Aboutayab and R. West, *Synlett*, 1993, **3**, 231; (b) W. A. Carroll and P. A. Grieco, *J. Am. Chem. Soc.*, 1993, **115**, 1164; (c) D. R. Stuart, E. Villemure and K. Fagnou, *J. Am. Chem. Soc.*, 2007, **129**, 12072; (d) J. E. Taylor, M. D. Jones, J. M. J. Williams and S. D. Bull, *Org. Lett.*, 2010, **12**, 5740; (e) R. Rahaman and P. Barman, *Synlett*, 2017, **28**, 684.
- 4 (a) R. Bernotas, S. Antane, B. Harrison, S. Lenicek, J. Coupet, L. Schechter, D. Smith and G. M. Zhang, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 5499; (b) G. Broggini, D. Diliddo and G. Zecchi, *J. Heterocycl. Chem.*, 1991, **28**, 89; (c) E. Vedejs and J. D. Little, *J. Org. Chem.*, 2004, **69**, 1794; (d) C. Shen, P. Zhang, Q. Sun, S. Bai, T. S. A. Hor and X. Liu, *Chem. Soc. Rev.*, 2015, **44**, 291; (e) C.-F. Lee, Y.-C. Liu and S. S. Badsara, *Chem.-Asian J.*, 2014, **9**, 706.
- 5 F. Xiao, H. Chen, H. Xie, S. Chen, L. Yang and G.-J. Deng, *Org. Lett.*, 2014, **16**, 50.
- 6 P. Katrun, C. Mueangkaew, M. Pohmakotr, V. Reutrakul, T. Jaipetch, D. Soorukram and C. Kuhakarn, *J. Org. Chem.*, 2014, **79**, 1778.
- 7 Y. Yang, W. Li, C. Xia, B. Ying, C. Shen and P. Zhang, *ChemCatChem*, 2016, **8**, 304.
- 8 H. Li, X. Wang and J. Yan, *New J. Chem.*, 2017, **41**, 4277.
- 9 M. L. Feng, L. Y. Xi, S. Y. Chen and X. Q. Yu, *Eur. J. Org. Chem.*, 2017, **82**, 2746.
- 10 (a) G. Rong, J. Mao, H. Yan, Y. Zheng and G. Zhang, *J. Org. Chem.*, 2015, **80**, 4697; (b) M. Zhang, P. Xie, W. Zhao, B. Niu, W. Wu, Z. Bian, C. U. Pittman and A. Zhou, *J. Org. Chem.*, 2015, **80**, 4176; (c) W. Yu, P. Hu, Y. Fan, C. Yu, X. Yan, X. Li and X. Xu, *Org. Biomol. Chem.*, 2015, **13**, 3308; (d) K. Xu, V. Khakyzadeh, T. Bury and B. Breit, *J. Am. Chem. Soc.*, 2014, **136**, 16124; (e) J. Zhang, Y. Shao, H. Wang, Q. Luo, J. Chen, D. Xu and X. Wan, *Org. Lett.*, 2014, **16**, 3312; (f) S. Guo, W. He, J. Xiang and Y. Yuan, *Chem. Commun.*, 2014, **50**, 8578; (g) F.-L. Yang, F.-X. Wang, T.-T. Wang, Y.-J. Wang and S.-K. Tian, *Chem. Commun.*, 2014, **50**, 2111; (h) R. Singh, D. S. Raghuvanshi and K. N. Singh, *Org. Lett.*, 2013, **15**, 4202; (i) X. Li, X. Xu, P. Hu, X. Xiao and C. Zhou, *J. Org. Chem.*, 2013, **78**, 7343; (j) X. Li, Y. Xu, W. Wu, C. Jiang, C. Qi and H. Jiang, *Chem.-Eur. J.*, 2014, **20**, 7911.
- 11 R. Rahaman and P. Barman, *Synlett*, 2017, **28**, 684.
- 12 S. K. Pagire, A. Hossain and O. Reiser, *Org. Lett.*, 2018, **20**, 648.
- 13 N. Margraf and G. Manolikakes, *J. Org. Chem.*, 2015, **80**, 2582.

