JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Regioselective C2 Sulfonylation of Indoles Mediated by Molecular Iodine

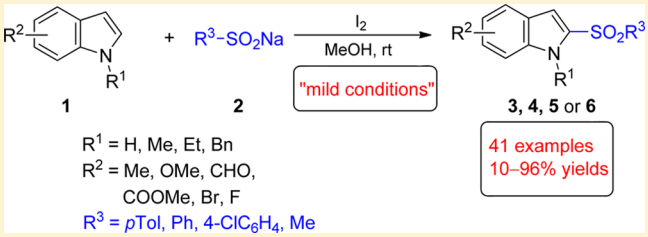
Praewpan Katrun,[†] Charoensak Mueangkaew,[†] Manat Pohmakotr,[†] Vichai Reutrakul,[†] Thaworn Jaipetch,[‡] Darunee Soorukram,[†] and Chutima Kuhakarn*[,†]

[†]Department of Chemistry and Center of Excellence for Innovation in Chemistry (PERCH-CIC), Faculty of Science, Mahidol University, Rama VI Road, Bangkok 10400, Thailand

[‡]Mahidol University, Kanchanaburi Campus, Saiyok, Kanchanaburi 71150, Thailand

Supporting Information

ABSTRACT: A facile and general method for regioselective C2 sulfonylation reaction of indoles mediated by iodine is described. The 2-sulfonylated products were obtained up to 96% yield under mild reaction conditions (room temperature, 2 h).



INTRODUCTION

Indole represents an important structural scaffold omnipresent in naturally occurring compounds and pharmacologically important agents (Figure 1).[1,2] Therefore, new approaches directing synthesis of indole nucleus have long inspired synthetic organic chemists.[3] In addition to the state of the art with synthetic strategy toward construction of the indole motif, development of novel methods for indole functionalization has also received remarkable attention.[4] In this context, it has been widely proven that the C3 position of indole has priority in functionalization over the C2 position. Hence, the direct C2 functionalization of indole has been more difficult and less studied.

The presence of a sulfur moiety either as a sulfanyl, a sulfinyl, or a sulfonyl in a molecular motif adds variety to its chemical architecture and also enhances the biological activity of the compound.[5] In particular, the 2-sulfanylindoles possess an inhibitory effect toward nucleoside triphosphate hydrolase enzyme, and a sulfonyl group in 2-sulfonylindoles serves as a temporary functional group that can be later removed by β-elimination.[6] Literature methods available for accessing 2-sulfanylindoles and 2-sulfonylindoles are not straightforward; they require multistep synthesis, moisture-sensitive alkyllithium reagent, or metal-mediated reactions.[7] Therefore, an exploration of a facile method for a direct regioselective installation of the sulfur moiety to the indole scaffold would be highly desirable. Recently, Liang and co-workers reported an elegant work on regioselective C2 amination of indole and derivatives.[8] During our investigation on mechanistic study and the process of preparation of this manuscript, a report on the use of the reagent combination $ArSO_2Na$, I_2, TBHP in AcOH for regioselective 2-sulfonylation of indoles was disclosed by Deng and co-workers.[9] This prompted us to report our findings. We report herein a direct C2 sulfonylation of indoles in a highly regioselective manner via a molecular iodine-mediated reaction.

RESULTS AND DISCUSSION

In order to achieve optimum reaction conditions, a series of reaction parameters including reagent stoichiometry and solvents were screened employing indole as a prototype (Table 1). To our delight, treatment of indole (**1a**) and sodium *p*-toluenesulfinate (**2a**, 1 equiv) with iodine (1 equiv) in methanol at room temperature for 2 h gave 2-(*p*-toluenesulfonyl)indole (**3a**) in 42% yield (Table 1, entry 1). Higher yields were obtained when **2a** was employed in excess amount (2 equiv) and the reaction time was prolonged from 2 to 8 h (Table 1, entries 2 and 3). When the amount of iodine was increased to 1.5 equiv, 64% yield of **3a** was obtained after 2 h (Table 1, entry 4). Increasing the stoichiometry of **2a** from 2 equiv to 3 and 4 equiv led to a significant increase in product yields (Table 1, entries 5 and 6). Next, the effect of solvent on the reaction efficiency was examined (Table 1, entries 7−16). It was found that methanol was the most suitable solvent for the present transformation, possibly due to an intrinsically better solubility of the sodium *p*-toluenesulfinate in methanol. It is worth mentioning that the order of reagent addition has significant effect on the reaction profile. If indole was exposed to iodine prior to the addition of sodium *p*-toluenesulfinate or the iodine and sodium *p*-toluenesulfinate was premixed before the addition of indole, the yields of **3a** slightly dropped (Table 1, entries 17 and 18). Finally, if an indole was stirred with iodine for 1 h, followed by the addition of sodium *p*-toluenesulfinate, and the reaction was further stirred for 2 h, product **3a** was obtained in only 14% yield while the starting

Received: December 20, 2013

   dx.doi.org/10.1021/jo402831k | J. Org. Chem. XXXX, XXX, XXX−XXX

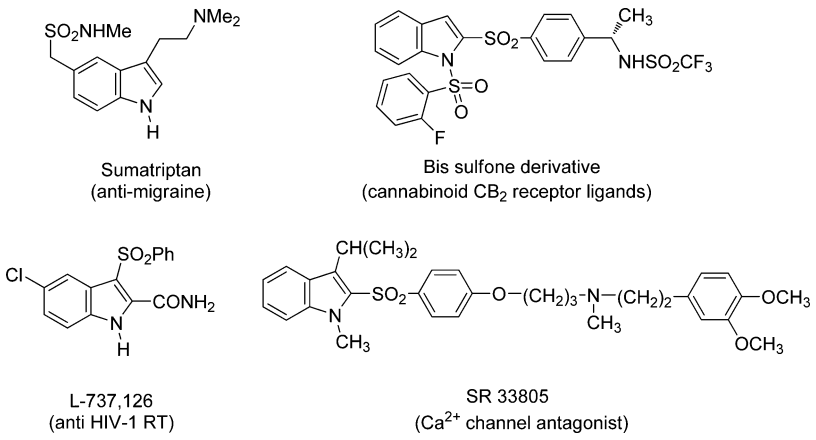
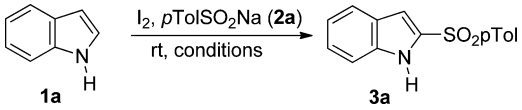


Figure 1. Representative examples of biologically active indolyl aryl sulfones.

Table 1. Optimization of the Reaction Conditions for Iodine-Mediated *C*2 Sulfonylation Reaction of Indole (1a)[a]



entry	I_2 (equiv)	**2a** (equiv)	solvent	time (h)	yield[b] (%)
1	1	1	MeOH	2	42
2	1	2	MeOH	2	56
3	1	2	MeOH	8	69
4	1.5	2	MeOH	2	64
5	1.5	3	MeOH	2	85
6	1.5	4	MeOH	2	90
7	1.5	3	EtOH	2	74
8	1.5	3	CH_3CN	2	32
9	1.5	3	CH_2Cl_2	2	54
10	1.5	3	$ClCH_2CH_2Cl$	2	45
11	1.5	3	EtOAc	2	26
12	1.5	3	acetone	2	17
13	1.5	3	THF	2	18
14	1.5	3	DMSO	2	trace
15	1.5	3	Et_2O	2	32
16	1.5	3	H_2O	2	[c]
17[d]	1.5	3	MeOH	2	70
18[e]	1.5	3	MeOH	2	68
19[f]	1.5	3	MeOH	3	14

[a]Conditions: **1a** (0.5 mmol) in 0.25 M of solvent at room temperature. [b]Isolated yield. [c]Reaction did not occur. [d]Iodine was added to a solution of **1a** in methanol prior to the addition of sodium *p*-toluenesulfinate. [e]Iodine and sodium *p*-toluenesulfinate were premixed prior to the addition of **1a**. [f]Compound **1a** was stirred with iodine for 1 h followed by the addition of sodium *p*-toluenesulfinate.

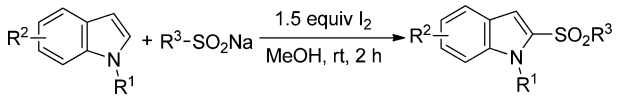
indole was totally consumed (Table 1, entry 19). On the basis of the experimental results shown in Table 1, the optimized reaction conditions were chosen as follows: **1a** (1 equiv), I_2 (1.5 equiv), **2a** (3 equiv) in methanol at room temperature for 2 h (Table 1, entry 5).

Having accomplished the optimized reaction conditions in hand, we next explored the substrate scope and limitations of the procedure. Indoles possessing electronically different substituents and sodium sulfinates including sodium *p*-toluenesulfinate, sodium benzenesulfinate, sodium 4-chlorobenzenesulfinate, and sodium methanesulfinate were employed. As shown in Table 2, the electronic nature of the substituents on the benzene unit of indoles was found to have considerable effect on the reaction efficiency. Electron-donating substituents (5-Me, 7-Me, and 5-MeO) gave better reactivity and provided the corresponding 2-sulfonylated products in good to excellent yields (76−96%, Table 2, entries 2−4). In contrast, the 5-bromo- and 5-fluoroindoles (**1e**,**f**) furnished products in low to moderate yields (22−58%, Table 2, entries 5 and 6). In case of 5-formylindole (**1g**) and methyl 1*H*-indole-5-carboxylate (**1h**), low yields (10−31%) were obtained with all the sulfinate salts tested and **1g** and **1h** were recovered in all cases (Table 2, entries 7 and 8). The reaction did not proceed when 5-nitroindole (**1i**) was employed as a substrate (Table 2, entry 9). Compound **1i** remained untouched and the corresponding methyl sulfonates were detected as major components. In an effort to improve the yields of the sulfonylated products derived from **1e**−**i**, the reactions were carried out at elevated temperature (refluxing methanol). Unfortunately, no improvement in the yields was observed. *N*-Methylindole (**1j**), *N*-ethylindole (**1k**), and *N*-benzylindole (**1l**) gave moderate to high yields (54−93%) of the products (Table 2, entries 10−12). To our surprise, 3-methylindole (**1m**) gave poor reactivity, providing the corresponding products in low to moderate yields (30−60%), and **1m** was recovered in a range of 20−60%, (Table 2, entry 13). However, **3m** was obtained in higher yield (68% yield vs 50% yield) when the reaction was carried out for 8 h. The reactions of sodium *p*-toluenesulfinate with *N*-protected indoles, including *N*-Cbz-, *N*-Bz-, and *N*-Ms-, did not proceed under standard reaction conditions or at prolonged reaction time (from 2 to 8 h). In all cases, the starting materials were recovered and the methyl *p*-toluenesulfonate was detected as a major component. Most importantly, when 2-methylindole was employed as a substrate to react with sodium *p*-toluenesulfinate, our reaction conditions failed to provide any sulfonylated adduct and methyl *p*-toluenesulfonate was detected as a major component. Finally, no reaction was observed with the less reactive benzothiophene, benzofuran, and electron-poor quinoline as substrates, under standard reaction conditions; methyl *p*-toluenesulfonate was obtained in all cases.

At this point, the reaction mechanism should be addressed. It has long been known that sulfonyl iodide prepared from the reaction of sodium sulfinate and molecular iodine can react with unsaturated systems through a radical process to yield *β*-iodosulfones with an anti-Markovnikov fashion.[10] In an effort to elucidate the reaction mechanism, a series of probing

dx.doi.org/10.1021/jo402831k | *J. Org. Chem.* XXXX, XXX, XXX−XXX

Table 2. Iodine-Mediated *C*2 Sulfonylation of Indole Derivatives[a]

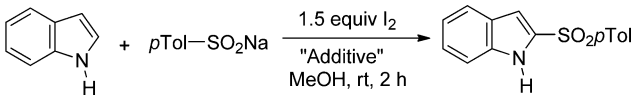


1 2 3, 4, 5 or 6

	substrate			product; R^3 =; yield[b] (%)			
entry		R^1 =	R^2 =	*p*Tol, **3**	Ph, **4**	4-Cl-C_6H_4, **5**	Me, **6**
1	**1a**	H	H	**3a**; 85	**4a**; 89	**5a**; 88	**6a**; 70
2	**1b**	H	5-Me	**3b**; 81	**4b**; 90	**5b**; 92	**6b**; 88
3	**1c**	H	7-Me	**3c**; 87	**4c**; 92	**5c**; 94	**6c**; 76
4	**1d**	H	5-OMe	**3d**; 89	**4d**; 96	*g*	**6d**; 77
5	**1e**	H	5-Br	**3e**; 43	**4e**; 46	**5e**; 33	**6e**; 29
6	**1f**	H	5-F	**3f**; 58	**4f**; 54	*g*	**6f**; 22
7[c]	**1g**	H	5-CHO	**3g**; 21[d]	**4g**; 31[d]	*g*	**6g**; 20[d]
8[c]	**1h**	H	5-CO_2Me	**3h**; 13[d]	**4h**; 22[d]	*g*	**6h**; 10[d]
9	**1i**	H	5-NO_2	*e*	*e*	*g*	*e*
10	**1j**	Me	H	**3j**; 86	**4j**; 87	**5j**; 75	**6j**; 72
11	**1k**	Et	H	**3k**; 90	**4k**; 93	*g*	**6k**; 74
12	**1l**	Bn	H	**3l**; 75	**4l**; 79	*g*	**6l**; 54
13	**1m**	H	3-Me	**3m**; 50[f] (68)[h]	**4m**; 60[f]	*g*	**6m**; 30[f]

[a]Unless otherwise noted. Conditions: **1** (0.5 mmol), **2** (3 equiv), I_2 (1.5 equiv) in MeOH (0.25 M), rt, 2 h. [b]Isolated yield. [c]Reaction time = 3 h. [d]About 30−40% of **1g** and **1h** were recovered. [e]Reactions did not occur. [f]About 20−60% of **1m** was recovered. [g]Reaction was not performed. [h]Reaction time = 8 h.

Table 3. Effect of Additives on Iodine-Mediated *C*2 Sulfonylation of Indole (1a) with Sodium *p*-Toluenesulfinate (2a)[a]

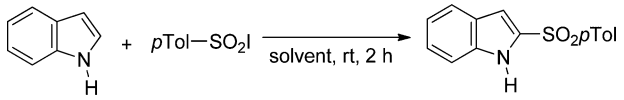


1a 2a 3a

entry	additive (equiv)	**3a**, yield[b] (%)
1	none (normal reaction)	85
2	none (dark, 30−32 °C)	75
3	none (dark, 15−20 °C)	69
4	none (light, rt)[c]	79
5	TEMPO (0.2, dark)	74
6	TEMPO (0.2)	73
7	TEMPO (1)	45
8	TEMPO (3)	29
9	TEMPO (5)	trace

[a]Unless otherwise noted. Conditions: **1a** (0.5 mmol), **2a** (3 equiv), I_2 (1.5 equiv) in MeOH (0.25 M), rt, 2 h. [b]Isolated yield. [c]Irradiated with light (100 W tungsten filament bulb) during and after addition of reagents.

Table 4. Reaction of 1a with *p*-Toluenesulfonyl Iodide[a]



1a 3a

entry	*p*-Tol-SO_2I (equiv)	solvent	**3a**, yield[b] (%)
1	1	CH_2Cl_2	45
2	1.5	CH_2Cl_2	54
3	3	CH_2Cl_2	58
4	3	MeOH	23[c]

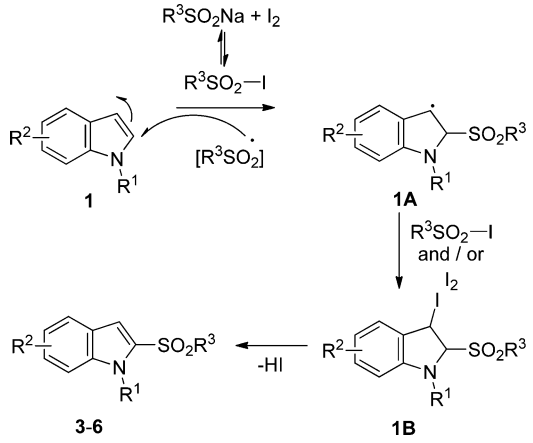
[a]Conditions: **1a** (0.5 mmol) in MeOH (0.25 M), rt, 2 h. [b]Isolated yield. [c]Methyl *p*-toluenesulfonate was isolated in 29% yield.

experiments employing the reactions of **1a** and **2a** were carried out (Tables 3 and 4). Reactions carried out in the dark either at room temperature (30−32 °C) or at lower temperature (15−20 °C) were less efficient, leading to **3a** in 75% and 69% yields, respectively (Table 3, entries 2 and 3). The yield of **3a** was not improved when the reaction was carried out under irradiated light (100 W tungsten filament bulb), and **3a** was isolated in 79% yield (Table 3, entry 4). The addition of TEMPO had considerable effects on the yields. When a catalytic amount of TEMPO (0.2 equiv) was added to the reactions carried out either in the dark or under standard reaction conditions, a slight decrease in the yields of **3a** was observed (Table 3, entries 5 and 6). The yield of **3a** dropped significantly when TEMPO was employed in stoichiometric amounts (Table 3, entries 7 and 8). The reaction ceased when TEMPO (5 equiv) was employed (Table 3, entry 9). As the presence of TEMPO drastically reduced the yield of **3a**, these observations implied that the reaction may be proceeding through a radical intermediate. Additionally, we found that **3a** was obtained in moderate yields (45−58%) when indole (**1a**) was allowed to react with a freshly prepared *p*-toluenesulfonyl iodide (yellowish solid) using dichloromethane as the solvent (Table 4, entries 1−3).[10g] It is worth noting that **3a** was obtained in 54% yield when the reaction carried out in CH_2Cl_2 with the in situ generation of *p*-toluenesulfonyl iodide (Table 1, entry 9). However, when methanol was employed as the solvent, **3a** and methyl *p*-toluenesulfonate were obtained in 23% and 29% yields, respectively (Table 4, entry 4).

On the basis of the control experiments in Tables 3 and 4 and relevant reports on the iodosulfonylation−dehydroiodination of alkenes mediated by sulfonyl iodide, we proposed possible reaction pathways for regioselective *C*2 sulfonylation of indole and derivatives as shown in Scheme 1. The sulfinate sodium salt reacts with iodine to give sulfonyl iodide intermediate that could undergo homolytic cleavage to yield a sulfonyl radical.[10] Addition of the sulfonyl radical to the indole nucleus takes place chemoselectively to form a benzylic radical

dx.doi.org/10.1021/jo402831k | J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 1. Proposed Reaction Mechanism



1A. Subsequently, **1A** abstracts the iodine radical either from the sulfonyl iodide[10b] or the molecular iodine[9] providing **1B**, which readily undergoes HI elimination to provide the observed products **3**–**6**.

CONCLUSION

We have developed a convenient and highly efficient method for direct *C*2 sulfonylation reaction of indoles mediated by iodine using sodium sulfinate as a reagent. The reactions proceed under mild reaction conditions in a neutral solvent allowing a broad scope of 2-sulfonylindole derivatives being prepared. This protocol should be very useful in organic synthesis because of the ease of operation and its wide scope.

EXPERIMENTAL SECTION

General Procedure. All isolated compounds were characterized on the basis of ^{1}H NMR and ^{13}C NMR spectroscopic data, IR spectra, and HRMS data. ^{1}H NMR and ^{13}C NMR chemical shifts are reported in ppm using tetramethylsilane (TMS) as an internal standard or residual nondeuterated solvent peak as an internal standard.

General Procedure for the Synthesis of 2-Sulfonylindole. Iodine (190.5 mg, 0.75 mmol) was added to a solution of indole (0.5 mmol) and sodium arenesulfinate or sodium methanesulfinate (1.5 mmol) in MeOH (2 mL; 0.25 M), and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was quenched by the addition of satd aq $Na_2S_2O_3$ (5 mL). Further stirring was followed by extraction with EtOAc (2 × 20 mL). The combined organic extracts were washed with H_2O (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and concentrated (aspirator). The residue was purified by column chromatography using EtOAc/hexanes as eluent to afford the corresponding product.

2-[(4-Methylphenyl)sulfonyl]-1H-indole (**3a**):[7c] white solid (114.3 mg, 85% yield); mp = 194–195 °C (lit.[7c] mp 196 °C) ; TLC (20% EtOAc in hexanes) R_f = 0.26; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.37 (br s, 1 H), 7.90 (d, J = 8.3 Hz, 2 H), 7.65 (d, J = 8.1 Hz, 1 H), 7.41 (d, J = 8.4 Hz, 1 H), 7.33–7.25 (m, 3 H), 7.18–7.14 (m, 2 H), 2.37 (s, 3 H) ppm. ^{13}C NMR (100 MHz; $CDCl_3$) δ 144.5 (C), 138.5 (C), 137.2 (C), 134.4 (C), 130.0 (2 × CH), 127.3 (2 × CH), 127.0 (C), 125.9 (CH), 122.5 (CH), 121.4 (CH), 112.4 (CH), 108.8 (CH), 21.5 (CH_3) ppm; IR (KBr) ν 3398 (N–H), 1320 and 1146 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{13}NO_2SNa$ 294.0565, found 294.0566.

2-(Phenylsulfonyl)-1H-indole (**4a**):[11] white solid (119.3 mg, 92% yield); mp = 137–138 °C; TLC (20% EtOAc in hexanes) R_f = 0.23; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.92 (br s, 1 H), 8.02 (d, J = 8.0 Hz, 2 H), 7.63 (d, J = 8.1 Hz, 1 H), 7.49–7.38 (m, 4 H), 7.27–7.24 (m, 2 H), 7.12 (t, J = 7.5 Hz, 1 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.3 (C), 137.4 (C), 133.7 (C), 133.4 (CH), 129.3 (2 × CH), 127.1 (2 × CH), 126.8 (C), 125.9 (CH), 122.4 (CH), 121.4 (CH), 112.5 (CH), 109.2 (CH) ppm; IR (KBr) ν 3392 (N–H), 1321 and 1146 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{14}H_{11}NO_2SNa$ 280.0408, found 280.0409.

2-[(4-Chlorophenyl)sulfonyl]-1H-indole (**5a**):[9] white solid (128.4 mg, 88% yield); mp = 159–160 °C; TLC (20% EtOAc in hexanes) R_f = 0.31; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.63 (br s, 1 H), 7.93 (d, J = 8.7 Hz, 2 H), 7.65 (d, J = 8.1 Hz, 1 H), 7.43–7.38 (m, 3 H), 7.33–7.29 (m, 1 H), 7.23 (d, J = 1.3 Hz, 1 H), 7.16 (t, J = 7.9 Hz, 1 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 140.1 (C), 139.8 (C), 137.5 (C), 133.2 (C), 129.6 (2 × CH), 128.6 (2 × CH), 126.9 (C), 126.2 (CH), 122.6 (CH), 121.6 (CH), 112.5 (CH), 109.6 (CH) ppm; IR (KBr) ν 3389 (N–H), 1332 and 1155 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{14}H_{10}ClNO_2SNa$ 314.0018, found 314.0017.

2-(Methylsulfonyl)-1H-indole (**6a**):[12] white solid (67.0 mg, 70% yield); mp = 167–168 °C; TLC (40% EtOAc in hexanes) R_f = 0.34; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.47 (br s, 1 H), 7.71 (d, J = 8.1 Hz, 1 H), 7.49 (d, J = 8.4 Hz, 1 H), 7.40–7.36 (m, 1 H), 7.26–7.20 (m, 2 H), 3.22 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 137.4 (C), 133.4 (C), 126.4 (C), 125.6 (CH), 122.4 (CH), 121.1 (CH), 112.6 (CH), 108.1 (CH), 45.1 (CH_3) ppm; IR (KBr) ν 3378 (N–H), 1308 and 1140 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_9H_9NO_2SNa$ 218.0252, found 218.0260.

5-Methyl-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3b**): pale yellow solid (115.1 mg, 81% yield); mp = 150–151 °C; TLC (20% EtOAc in hexanes) R_f = 0.26; ^{1}H NMR (500 MHz; $CDCl_3$) δ 9.21 (br s, 1 H), 7.91 (d, J = 8.2 Hz, 2 H), 7.45 (s, 1 H), 7.34–7.29 (m, 3 H), 7.17 (d, J = 8.5 Hz, 1 H), 7.13 (s, 1 H), 2.44 (s, 3 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (125 MHz; $CDCl_3$) δ 144.4 (C), 138.7 (C), 135.6 (C), 134.3 (C), 130.9 (C), 129.9 (2 × CH), 127.9 (CH), 127.4 (C), 127.3 (2 × CH), 121.8 (CH), 112.0 (CH), 108.4 (CH), 21.5 (CH_3), 21.3 (CH_3) ppm; IR (KBr) ν 3433 (N–H), 1324 and 1143 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{16}H_{15}NO_2SNa$ 308.0721, found 308.0713.

5-Methyl-2-(phenylsulfonyl)-1H-indole (**4b**): pale yellow solid (109.5 mg, 90% yield); mp = 116–117 °C; TLC (40% EtOAc in hexanes) R_f = 0.49; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.43 (br s, 1 H), 8.02–7.99 (m, 2 H), 7.55–7.51 (m, 1 H), 7.47–7.42 (m, 3 H), 7.31 (d, J = 8.5 Hz, 1 H), 7.14–7.12 (m, 2 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.5 (C), 135.8 (C), 133.6 (C), 133.3 (CH), 130.9 (C), 129.3 (2 × CH), 128.0 (CH), 127.2 (C), 127.1 (2 × CH), 121.7 (CH), 112.1 (CH), 108.8 (CH), 21.3 (CH_3) ppm; IR (KBr) ν 3387 (N–H), 1316 and 1146 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{13}NO_2SNa$ 294.0565, found 294.0560.

2-[(4-Chlorophenyl)sulfonyl]-5-methyl-1H-indole (**5b**): pale yellow solid (140.7 mg, 92% yield); mp = 152–153 °C; TLC (20% EtOAc in hexanes) R_f = 0.31; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.58 (br s, 1 H), 7.91 (d, J = 8.6 Hz, 2 H), 7.41–7.37 (m, 3 H), 7.30 (d, J = 8.5 Hz, 1 H), 7.14–7.12 (m, 2 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 139.96 (C), 139.94 (C), 135.9 (C), 133.0 (C), 131.1 (C), 129.6 (2 × CH), 128.5 (2 × CH), 128.2 (CH), 127.1 (C), 121.7 (CH), 112.1 (CH), 109.1 (CH), 21.3 (CH_3) ppm; IR (KBr) ν 3344 (N–H), 1321 and 1157 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{12}ClNO_2SNa$ 328.0175, found 328.0172.

5-Methyl-2-(methylsulfonyl)-1H-indole (**6b**): white solid (91.6 mg, 88% yield); mp = 159–160 °C; TLC (40% EtOAc in hexanes) R_f = 0.34; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.02 (br s, 1 H), 7.46 (s, 1 H), 7.35 (d, J = 8.5 Hz, 1 H), 7.20 (dd, J = 8.5, 1.2 Hz, 1 H), 7.10 (d, J = 1.5 Hz, 1 H), 3.17 (s, 3 H), 2.43 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 135.3 (C), 133.1 (C), 131.2 (C), 128.2 (CH), 127.2 (C), 121.9 (CH), 112.0 (CH), 108.2 (CH), 45.5 (CH_3), 21.4 (CH_3) ppm; IR (KBr) ν 3318 (N–H), 1303 and 1157 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{10}H_{11}NO_2SNa$ 232.0408, found 232.0416.

7-Methyl-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3c**): white solid (125.9 mg, 87% yield); mp =177–178 °C; TLC (20% EtOAc in hexanes) R_f = 0.25; ^{1}H NMR (500 MHz; $CDCl_3$) δ 9.57 (br s, 1 H), 7.97 (d, J = 8.4 Hz, 2 H), 7.50 (d, J = 7.6 Hz, 1 H), 7.29 (d, J = 8.2 Hz, 2 H), 7.22 (d, J = 2.2 Hz, 1 H), 7.12–7.06 (m, 2 H), 2.48 (s, 3 H),

dx.doi.org/10.1021/jo402831k | J. Org. Chem. XXXX, XXX, XXX–XXX

2.38 (s, 3 H) ppm; ^{13}C NMR (125 MHz; $CDCl_3$) δ 144.4 (C), 138.7 (C), 137.2 (C), 134.1 (C), 129.9 (2 × CH), 127.3 (2 × CH), 126.7 (C), 126.1 (CH), 122.0 (C), 121.7 (CH), 120.1 (CH), 109.5 (CH), 21.5 (CH_3), 16.7 (CH_3) ppm; IR (KBr) ν 3375 (N−H), 1314 and 1149 (SO_2) cm^{-1}; IR (KBr) ν 3375 (N−H), 1314 and 1149 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{16}H_{15}NO_2SNa$ 308.0721, found 308.0716.

*7-Methyl-2-(phenylsulfonyl)-1H-indole (**4c**):*[9] pale yellow solid (120.0 mg, 92% yield); mp = 139−140 °C; TLC (40% EtOAc in hexanes) R_f = 0.51; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.95 (br s, 1 H), 8.10−8.08 (m, 2 H), 7.52−7.42 (m, 4 H), 7.25 (d, J = 2.1 Hz, 1 H), 7.08−7.02 (m, 2 H), 2.45 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.5 (C), 137.4 (C), 133.5 (C), 133.3 (CH), 129.3 (2 × CH), 127.1 (2 × CH), 126.5 (C), 126.2 (CH), 122.2 (C), 121.6 (CH), 120.0 (CH), 109.9 (CH), 16.7 (CH_3) ppm; IR (KBr) ν 3372 (N−H), 1309 and 1148 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{13}NO_2SNa$ 294.0565, found 294.0567.

*7-Methyl-2-(methylsulfonyl)-1H-indole (**6c**):* pale yellow solid (78.4 mg, 76% yield); mp = 141−142 °C; TLC (40% EtOAc in hexanes) R_f = 0.33; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.44 (br s, 1 H), 7.53 (d, J = 7.8 Hz, 1 H), 7.22 (d, J = 2.1 Hz, 1 H), 7.17−7.09 (m, 2 H), 3.23 (s, 3 H), 2.51 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 137.1 (C), 132.8 (C), 126.4 (CH), 126.3 (C), 122.1 (C), 121.9 (CH), 120.2 (CH), 109.4 (CH), 45.4 (CH_3), 16.8 (CH_3) ppm; IR (KBr) ν 3309 (N−H), 1323 and 1135 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{10}H_{11}NO_2SNa$ 232.0408, found 232.0413.

*5-Methoxy-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3d**):*[13] white solid (132.9 mg, 89% yield); mp = 159−160 °C; TLC (40% EtOAc in hexanes) R_f = 0.45; ^{1}H NMR (400 MHz; $CDCl_3\delta$ 9.04 (br s, 1 H), 7.87 (d, J = 8.3 Hz, 2 H), 7.31−7.26 (m, 3 H), 7.09 (dd, J = 2.0, 0.7 Hz, 1 H), 7.03 (d, J = 2.3 Hz, 1 H), 6.99 (dd, J = 9.0, 2.4 Hz, 1 H), 3.82 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 155.1 (C), 144.4 (C), 138.6 (C), 134.5 (C), 132.4 (C), 129.9 (2 × CH), 127.5 (C), 127.2 (2 × CH), 117.6 (CH), 113.3 (CH), 108.4 (CH), 102.5 (CH), 55.7 (CH_3), 21.5 (CH_3) ppm; IR (KBr) ν 3369 (N−H), 1327 and 1148 (SO_2), 1292 and 1100 (C−O) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{16}H_{15}NO_3SNa$ 324.0670, found 324.0671.

*5-Methoxy-2-(phenylsulfonyl)-1H-indole (**4d**):*[9] white solid (142.4 mg, 96% yield); mp = 121−122 °C; TLC (40% EtOAc in hexanes) R_f = 0.41; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.86 (br s, 1 H), 8.00 (d, J = 7.3 Hz, 2 H), 7.50−7.46 (m, 1 H), 7.42−7.38 (m, 2 H), 7.30 (d, J = 9.0 Hz, 1 H), 7.16 (d, J = 1.4 Hz, 1 H), 7.02 (d, J = 2.3 Hz, 1 H), 6.95 (dd, J = 9.0, 2.4 Hz, 1 H), 3.79 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 155.2 (C), 141.6 (C), 134.1 (C), 133.4 (CH), 132.5 (C), 129.3 (2 × CH), 127.5 (C), 127.2 (2 × CH), 117.8 (CH), 113.3 (CH), 108.8 (CH), 102.5 (CH), 55.7 (CH_3) ppm; IR (KBr) ν 3359 (N−H), 1326 and 1151 (SO_2), 1293 and 1099 (C−O) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{13}NO_3SNa$ 310.0514, found 310.0519.

*2-[(4-Chlorophenyl)sulfonyl]-5-methoxy-1H-indole (**5d**):* white solid (151.2 mg, 94% yield); mp = 124−125 °C; TLC (20% EtOAc in hexanes) R_f = 0.24; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.66 (br s, 1 H), 7.90 (d, J = 8.6 Hz, 2 H), 7.36 (d, J = 8.6 Hz, 2 H), 7.29 (d, J = 9.0 Hz, 1 H), 7.13 (d, J = 1.2 Hz, 1 H), 7.02 (d, J = 1.9 Hz, 1 H), 6.97 (dd, J = 9.0, 2.4 Hz, 1 H), 3.80 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 155.1 (C), 139.94 (C), 139.88 (C), 133.3 (C), 132.8 (C), 129.5 (2 × CH), 128.5 (2 × CH), 127.3 (C), 118.0 (CH), 113.4 (CH), 109.0 (CH), 102.3 (CH), 55.6 (CH_3) ppm; IR (KBr) ν 3380 (N−H), 1332 and 1151 (SO_2), 1293 and 1091 (C−O) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{12}ClNO_3SNa$ 344.0124, found 344.0125.

*5-Methoxy-2-(methylsulfonyl)-1H-indole (**6d**):* white solid (86.4 mg, 77% yield); mp = 177−178 °C; TLC (40% EtOAc in hexanes) R_f = 0.26; ^{1}H NMR (400 MHz; acetone-d_6) δ 11.02 (br s, 1 H), 7.47 (d, J = 9.0 Hz, 1 H), 7.18 (d, J = 2.4 Hz, 1 H), 7.07 (dd, J = 2.2, 0.8 Hz, 1 H), 7.01 (dd, J = 9.0, 2.4 Hz, 1 H), 3.81 (s, 3 H), 3.22 (s, 3 H) ppm; ^{13}C NMR (100 MHz; acetone-d_6) δ 156.0 (C), 135.9 (C), 133.6 (C), 128.1 (C), 117.9 (CH), 114.5 (CH), 107.9 (CH), 103.2 (CH), 55.8 (CH_3), 45.3 (CH_3) ppm; IR (KBr) ν 3286 (N−H), 1325 and 1165 (SO_2), 1295 and 1096 (C−O) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{10}H_{11}NO_3SNa$ 248.0357, found 248.0352.

*5-Bromo-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3e**):* pale yellow solid (74.6 mg, 43% yield); mp = 193−194 °C; TLC (40% EtOAc in hexanes) R_f = 0.50; ^{1}H NMR (400 MHz; acetone-d_6) δ 11.44 (br s, 1 H), 7.91 (d, J = 8.4 Hz, 2 H), 7.88 (d, J = 1.8 Hz, 1 H), 7.46 (d, J = 8.8 Hz, 1 H), 7.41−7.38 (m, 3 H), 7.20 (dd, J = 2.2, 0.8 Hz, 1 H), 2.35 (s, 3 H) ppm; ^{13}C NMR (100 MHz; acetone-d_6) δ 145.7 (C), 139.7 (C), 137.9 (C), 137.3 (C), 130.9 (2 × CH), 129.3 (C), 129.1 (CH), 128.3 (2 × CH), 125.6 (CH), 115.4 (CH), 114.6 (C), 108.1 (CH), 21.5 (CH_3) ppm; IR (KBr) ν 3348 (N−H), 1328 and 1153 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{12}BrNO_2SNa$ 371.9670, found 371.9679.

*5-Bromo-2-(phenylsulfonyl)-1H-indole (**4e**):*[9] pale yellow solid (76.8 mg, 46% yield); mp = 158−159 °C; TLC (40% EtOAc in hexanes) R_f = 0.45; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.77 (br s, 1 H), 8.03−8.00 (m, 2 H), 7.77 (d, J = 1.8 Hz, 1 H), 7.59−7.55 (m, 1 H), 7.51−7.47 (m, 2 H), 7.37 (dd, J = 8.8, 1.8 Hz, 1 H), 7.30 (d, J = 8.8 Hz, 1 H), 7.13 (dd, J = 2.1, 0.7 Hz, 1 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.0 (C), 135.8 (C), 135.1 (C), 133.7 (CH), 129.5 (2 × CH), 129.1 (CH), 128.5 (C), 127.3 (2 × CH), 124.9 (CH), 114.7 (C), 114.0 (CH), 108.3 (CH) ppm; IR (KBr) ν 3363 (N−H), 1322 and 1157 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{14}H_{10}BrNO_2SNa$ 357.9513, found 357.9510.

*5-Bromo-2-[(4-chlorophenyl)sulfonyl]-1H-indole (**5e**):* brown solid (61.2 mg, 33% yield); mp = 184−185 °C; TLC (20% EtOAc in hexanes) R_f = 0.28; ^{1}H NMR (400 MHz; acetone-d_6) δ 11.57 (br s, 1 H), 8.04 (d, J = 8.7 Hz, 2 H), 7.90 (d, J = 1.2 Hz, 1 H), 7.65 (d, J = 8.8 Hz, 2 H), 7.48 (d, J = 8.8 Hz, 1 H), 7.42 (dd, J = 8.8, 1.8 Hz, 1 H), 7.26 (s, 1 H) ppm; ^{13}C NMR (100 MHz; acetone-d_6) δ 141.3 (C), 140.4 (C), 137.3 (C), 136.6 (C), 130.6 (2 × CH), 130.0 (2 × CH), 129.4 (CH), 129.2 (C), 125.6 (CH), 115.4 (CH), 114.7 (C), 108.8 (CH) ppm; IR (KBr) ν 3344 (N−H), 1323 and 1142 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{14}H_9BrClNO_2SNa$ 393.9103, found 393.9101.

*5-Bromo-2-(methylsulfonyl)-1H-indole (**6e**):* pale yellow solid (38.3 mg, 29% yield); mp = 188−189 °C; TLC (40% EtOAc in hexanes) R_f = 0.29; ^{1}H NMR (400 MHz; acetone-d_6) δ 11.37 (br s, 1 H), 7.94 (d, J = 1.9 Hz, 1 H), 7.55 (d, J = 8.8 Hz, 1 H), 7.46 (dd, J = 8.8, 1.9 Hz, 1 H), 7.16 (dd, J = 2.2, 0.7 Hz, 1 H), 3.27 (s, 3 H) ppm; ^{13}C NMR (100 MHz; acetone-d_6) δ 137.4 (C), 137.0 (C), 129.3 (C), 129.1 (CH), 125.7 (CH), 115.6 (CH), 114.6 (C), 107.6 (CH), 45.2 (CH_3) ppm; IR (KBr) ν 3293 (N−H), 1303 and 1126 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_9H_8BrNO_2SNa$ 295.9357, found 295.9341.

*5-Fluoro-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3f**):* white solid (78.5 mg, 58% yield); mp = 142−143 °C; TLC (40% EtOAc in hexanes) R_f = 0.48; ^{1}H NMR (400 MHz; acetone-d_6) δ 11.41 (br s, 1 H), 7.92 (d, J = 8.4 Hz, 2 H), 7.52 (dd, J = 9.1, 4.5 Hz, 1 H), 7.42 (d, J = 7.9 Hz, 3 H), 7.21 (d, J = 1.6 Hz, 1 H), 7.13 (td, J = 9.2, 2.6 Hz, 1 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (100 MHz; acetone-d_6) δ 159.1 (d, J = 234 Hz, C), 145.6 (C), 139.9 (C), 138.2 (C), 135.5 (C), 131.0 (2 × CH), 128.3 (2 × CH), 128.0 (d, J = 11 Hz, C), 115.3 (d, J = 27 Hz, CH), 115.0 (d, J = 9 Hz, CH), 108.7 (d, J = 5 Hz, CH), 107.4 (d, J = 24 Hz, CH), 21.5 (CH_3) ppm; IR (KBr) ν 3273 (N−H), 1308 and 1157 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{12}FNO_2SNa$ 312.0470, found 312.0477.

*5-Fluoro-2-(phenylsulfonyl)-1H-indole (**4f**):* pale yellow solid (74.7 mg, 54% yield); mp = 144−145 °C; TLC (40% EtOAc in hexanes) R_f = 0.44; ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.80 (br s, 1 H), 8.01 (d, J = 8.7 Hz, 2 H), 7.57−7.53 (m, 1 H), 7.48−7.45 (m, 2 H), 7.36 (dd, J = 9.1, 4.4 Hz, 1 H), 7.26 (dd, J = 9.1, 2.4 Hz, 1 H), 7.15 (d, J = 1.4 Hz, 1 H), 7.05 (td, J = 9.0, 2.5 Hz, 1 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 158.3 (d, J = 237 Hz, C), 141.0 (C), 135.3 (C), 133.9 (C), 133.6 (CH), 129.4 (2 × CH), 127.2 (2 × CH), 127.1 (C), 115.3 (d, J = 27 Hz, CH), 113.6 (d, J = 10 Hz, CH), 108.9 (d, J = 5 Hz, CH), 106.8 (d, J = 24 Hz, CH) ppm; IR (KBr) ν 3326 (N−H), 1327 and 1146 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{14}H_{10}FNO_2SNa$ 298.0314, found 298.0332.

dx.doi.org/10.1021/jo402831k | J. Org. Chem. XXXX, XXX, XXX−XXX

5-Fluoro-2-(methylsulfonyl)-1H-indole (**6f**): pale yellow solid (23.5 mg, 22% yield); mp = 157−158 °C; TLC (40% EtOAc in hexanes) R_f = 0.30; ^{1}H NMR (400 MHz; acetone-d_6) δ 11.32 (br s, 1 H), 7.60 (dd, J = 9.0, 4.5 Hz, 1 H), 7.46 (dd, J = 9.4, 2.5 Hz, 1 H), 7.21−7.16 (m, 2 H), 3.27 (s, 3 H) ppm; ^{13}C NMR (100 MHz; acetone-d_6) δ 159.2 (d, J = 234 Hz, C), 137.7 (C), 135.1 (C), 127.9 (d, J = 11 Hz, C), 115.2 (d, J = 25 Hz, CH), 115.1 (d, J = 7 Hz, CH), 108.1 (d, J = 6 Hz, CH), 107.4 (d, J = 24 Hz, CH), 45.2 (CH_3) ppm; IR (KBr) ν 3311 (N−H), 1326 and 1159 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_9H_8FNO_2SNa$ 236.0157, found 236.0146.

2-[(4-Methylphenyl)sulfonyl]-1H-indole-5-carbaldehyde (**3g**): pale yellow solid (31.9 mg, 21% yield); mp = 174−174 °C; TLC (40% EtOAc in hexanes) R_f = 0.55; ^{1}H NMR (300 MHz; DMSO-d_6) δ 12.88 (br s, 1 H), 9.96 (s, 1 H), 8.31, (d, J = 0.8 Hz, 1 H), 7.89 (d, J = 8.3 Hz, 2 H), 7.78 (dd, J = 8.7, 1.5 Hz, 1 H), 7.56 (dd, J = 8.7, 0.5 Hz, 1 H), 7.44−7.41 (m, 3 H), 2.33 (s, 3 H) ppm; ^{13}C NMR (75 MHz; DMSO-d_6) δ 192.5 (C═O of aldehyde), 144.9 (C), 140.8 (C), 137.9 (C), 137.0 (C), 130.4 (C), 130.3 (2 × CH), 128.6 (CH), 127.3 (2 × CH), 125.8 (C), 124.2 (CH), 113.7 (CH), 109.6 (CH), 21.2 (CH_3) ppm; IR (KBr) ν 3293 (N−H), 2855 (C−H of aldehyde), 1671 (C═O), 1324 and 1144 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{16}H_{13}NO_3SNa$ 322.0514, found 322.0515.

2-(Phenylsulfonyl)-1H-indole-5-carbaldehyde (**4g**): pale yellow solid (43.7 mg, 31% yield); mp = 159−160 °C; TLC (40% EtOAc in hexanes) R_f = 0.50; ^{1}H NMR (300 MHz; DMSO-d_6) δ 12.92 (br s, 1 H), 9.96 (s, 1 H), 8.31 (s, 1 H), 8.02 (d, J = 8.2 Hz, 2 H), 7.78 (dd, J = 8.7, 1.3 Hz, 1 H), 7.70−7.55 (m, 4 H), 7.44 (d, J = 1.2 Hz, 1 H) ppm; ^{13}C NMR (75 MHz; DMSO-d_6) δ 192.4 (C═O of aldehyde), 140.9 (C), 140.8 (C), 136.6 (C), 134.1 (CH), 130.4 (C), 129.8 (2 × CH), 128.6 (CH), 127.2 (2 × CH), 125.8 (C), 124.2 (CH), 113.7 (CH), 109.9 (CH) ppm; IR (KBr) ν 3306 (N−H), 2834 and 2740 (C−H of aldehyde), 1678 (C═O), 1331 and 1147 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{11}NO_3SNa$ 308.0357, found 308.0354.

2-(Methylsulfonyl)-1H-indole-5-carbaldehyde (**6g**): pale yellow solid (22.7 mg, 20% yield); mp = 167−168 °C; TLC (40% EtOAc in hexanes) R_f = 0.39; ^{1}H NMR (300 MHz; acetone-d_6) δ 11.66 (br s, 1 H), 10.05 (s, 1 H), 8.37 (t, J = 0.7 Hz, 1 H), 7.89 (dd, J = 8.7, 1.5 Hz, 1 H), 7.71 (d, J = 9.0 Hz, 1 H), 7.38 (dd, J = 2.1, 0.7 Hz, 1 H), 3.30 (s, 3 H) ppm; ^{13}C NMR (75 MHz; acetone-d_6) δ 192.3 (C═O of aldehyde), 141.2 (C), 138.0 (C), 132.0 (C), 129.0 (CH), 127.2 (C), 124.9 (CH), 114.3 (CH), 109.8 (CH), 45.0 (CH_3) ppm; IR (KBr) ν 3298 (N−H), 2818 and 2769 (C−H of aldehyde), 1686 (C═O), 1310 and 1124 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{10}H_9NO_3SNa$ 246.0201, found 246.0202.

Methyl 2-[(4-methylphenyl)sulfonyl]-1H-indole-5-carboxylate (**3h**): white solid (21.1 mg, 13% yield); mp = 219−220 °C; TLC (40% EtOAc in hexanes) R_f = 0.41; ^{1}H NMR (400 MHz; acetone-d_6) δ 11.68 (br s, 1 H), 8.44 (t, J = 0.7 Hz, 1 H), 7.95−7.92 (m, 3 H), 7.57 (d, J = 8.8 Hz, 1 H), 7.43−7.37 (m, 3 H), 3.87 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (100 MHz; acetone-d_6) δ 167.6 (C═O of ester), 145.8 (C), 141.1 (C), 139.7 (C), 138.4 (C), 131.0 (2 × CH), 128.4 (2 × CH), 127.3 (C), 126.9 (CH), 126.3 (CH), 124.3 (C), 113.5 (CH), 110.1 (CH), 52.3 (CH_3), 21.5 (CH_3) ppm; IR (KBr) ν 3302 (N−H), 1699 (C═O), 1261 and 1102 (C−O), 1328 and 1149 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{17}H_{15}NO_4SNa$ 352.0619, found 352.0625.

Methyl 2-(phenylsulfonyl)-1H-indole-5-carboxylate (**4h**): white solid (33.9 mg, 22% yield); mp = 237−238 °C; TLC (40% EtOAc in hexanes) R_f = 0.38; ^{1}H NMR (400 MHz; DMSO-d_6) δ 12.83 (br s, 1 H), 8.41 (d, J = 1.0 Hz, 1 H), 8.04−8.02 (m, 2 H), 7.88 (dd, J = 8.8, 1.6 Hz, 1 H), 7.71−7.61 (m, 3 H), 7.53 (d, J = 8.8 Hz, 1 H), 7.43 (s, 1 H), 3.82 (s, 3 H) ppm; ^{13}C NMR (100 MHz; DMSO-d_6) δ 166.6 (C═O of ester), 140.8 (C), 140.1 (C), 136.2 (C), 134.0 (CH), 129.8 (2 × CH), 127.1 (2 × CH), 125.7 (CH), 125.6 (C), 125.4 (CH), 122.5 (C), 112.9 (CH), 109.6 (CH), 51.9 (CH_3) ppm; IR (KBr) ν 3256 (N−H), 1693 (C═O), 1264 and 1110 (C−O), 1329 and 1155 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{16}H_{13}NO_4SNa$ 338.0463, found 338.0464.

Methyl 2-(methylsulfonyl)-1H-indole-5-carboxylate (**6h**): pale yellow solid (12.8 mg, 10% yield); mp = 167−168 °C; TLC (40% EtOAc in hexanes) R_f = 0.21; ^{1}H NMR (400 MHz; acetone-d_6) δ 11.53 (br s, 1 H), 8.49 (d, J = 0.5 Hz, 1 H), 7.99 (dd, J = 8.8, 1.6 Hz, 1 H), 7.65 (d, J = 8.8 Hz, 1 H), 7.34 (d, J = 1.8 Hz, 1 H), 3.89 (s, 3 H), 3.30 (s, 3 H) ppm; ^{13}C NMR (100 MHz; acetone-d_6) δ 167.7 (C═O of ester), 140.6 (C), 137.8 (C), 127.2 (C), 126.8 (CH), 126.3 (CH), 124.3 (C), 113.6 (CH), 109.6 (CH), 52.3 (CH_3), 45.1 (CH_3) ppm; IR (KBr) ν 3323 (N−H), 1702 (C═O), 1262 and 1099 (C−O), 1314 and 1138 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{11}H_{11}NO_4SNa$ 276.0306, found 276.0318.

1-Methyl-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3j**): white solid (122.4 mg, 86% yield); mp = 152−153 °C; TLC (20% EtOAc in hexanes) R_f = 0.35; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.83 (d, J = 8.4 Hz, 2 H), 7.67 (d, J = 8.0 Hz, 1 H), 7.35−7.26 (m, 5 H), 7.17−7.13 (m, 1 H), 3.81 (s, 3 H), 2.36 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 144.4 (C), 139.3 (C), 138.0 (C), 135.0 (C), 129.8 (2 × CH), 127.5 (2 × CH), 125.5 (CH), 125.0 (C), 122.6 (CH), 121.0 (CH), 110.2 (CH), 110.1 (CH), 30.8 (CH_3), 21.4 (CH_3) ppm; IR (KBr) ν 1320 and 1150 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{16}H_{15}NO_2SNa$ 308.0721, found 308.0703.

1-Methyl-2-(phenylsulfonyl)-1H-indole (**4j**):[11b] pale yellow solid (121.9 mg, 87% yield); mp = 118−119 °C; TLC (20% EtOAc in hexanes) R_f = 0.31; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.96 (d, J = 8.1 Hz, 2 H), 7.70 (d, J = 8.1 Hz, 1 H), 7.60−7.49 (m, 3 H), 7.38−7.29 (m, 3 H), 7.18 (t, J = 7.1 Hz, 1 H), 3.84 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.2 (C), 139.5 (C), 134.7 (C), 133.4 (CH), 129.3 (2 × CH), 127.6 (2 × CH), 125.7 (CH), 125.1 (C), 122.8 (CH), 121.1 (CH), 110.8 (CH), 110.2 (CH), 31.0 (CH_3) ppm; IR (KBr) ν 1323 and 1157 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{13}NO_2SNa$ 294.0565, found 294.0572.

2-[(4-Chlorophenyl)sulfonyl]-1-methyl-1H-indole (**5j**): pale yellow solid (114.7 mg, 75% yield); mp = 135−136 °C; TLC (20% EtOAc in hexanes) R_f = 0.40; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.88 (d, J = 8.6 Hz, 2 H), 7.69 (d, J = 8.1 Hz, 1 H), 7.46 (d, J = 8.6 Hz, 2 H), 7.39−7.35 (m, 2 H), 7.30 (d, J = 8.4 Hz, 1 H), 7.18 (t, J = 7.5 Hz, 1 H), 3.83 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 139.9 (C), 139.6 (C), 139.5 (C), 134.1 (C), 129.5 (2 × CH), 129.0 (2 × CH), 125.9 (CH), 125.0 (C), 122.8 (CH), 121.2 (CH), 111.0 (CH), 110.2 (CH), 30.9 (CH_3) ppm; IR (KBr) ν 1327 and 1156 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{12}ClNO_2SNa$ 328.0175, found 328.0170.

1-Methyl-2-(methylsulfonyl)-1H-indole (**6j**): pale yellow solid (78.2 mg, 72% yield); mp = 104−105 °C; TLC (40% EtOAc in hexanes) R_f = 0.39; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.68 (d, J = 8.1 Hz, 1 H), 7.43−7.36 (m, 2 H), 7.25 (s, 1 H), 7.24−7.18 (m, 1 H), 4.00 (s, 3 H), 3.16 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 139.4 (C), 134.5 (C), 125.9 (CH), 125.0 (C), 122.9 (CH), 121.3 (CH), 110.32 (CH), 110.30 (CH), 45.3 (CH_3), 31.0 (CH_3) ppm; IR (KBr) ν 1311 and 1143 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{10}H_{11}NO_2SNa$ 232.0408, found 232.0421.

1-Ethyl-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3k**): yellow viscous oil (134.6 mg, 90% yield); TLC (20% EtOAc in hexanes) R_f = 0.40; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.85 (d, J = 8.3 Hz, 2 H), 7.71 (d, J = 8.0 Hz, 1 H), 7.38−7.31 (m, 5 H), 7.20−7.17 (m, 1 H), 4.38 (q, J = 7.2 Hz, 2 H), 2.41 (s, 3 H), 1.17 (t, J = 7.2 Hz, 3 H) ppm; ^{13}C NMR (125 MHz; $CDCl_3$) δ 144.4 (C), 138.39 (C), 138.35 (C), 134.6 (C), 129.8 (2 × CH), 127.7 (2 × CH), 125.5 (CH), 125.4 (C), 122.9 (CH), 121.0 (CH), 110.6 (CH), 110.5 (CH), 39.6 (CH_2), 21.5 (CH_3), 14.9 (CH_3) ppm; IR (neat) ν 2981 (C−H), 1317 and 1155 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{17}H_{17}NO_2SNa$ 322.0878, found 322.0870.

1-Ethyl-2-(phenylsulfonyl)-1H-indole (**4k**): yellow viscous oil (127.4 mg, 93% yield); TLC (20% EtOAc in hexanes) R_f = 0.36; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.98−7.95 (m, 2 H), 7.71 (d, J = 8.0 Hz, 1 H), 7.60−7.56 (m, 1 H), 7.53−7.49 (m, 2 H), 7.38−7.31 (m, 3 H), 7.20−7.16 (m, 1 H), 4.37 (q, J = 7.2 Hz, 2 H), 1.15 (t, J = 7.2 Hz, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.3 (C), 138.4 (C), 134.1 (C), 133.4 (CH), 129.3 (2 × CH), 127.6 (2 × CH), 125.7 (CH), 125.4 (C), 123.0 (CH), 121.1 (CH), 111.0 (CH), 110.5 (CH),

dx.doi.org/10.1021/jo402831k | J. Org. Chem. XXXX, XXX, XXX−XXX

39.6 (CH_2), 14.9 (CH_3) ppm; IR (neat) ν 2981 (C−H), 1338 and 1155 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{16}H_{15}NO_2SNa$ 308.0721, found 308.0728.

*1-Ethyl-2-(methylsulfonyl)-1H-indole (**6k**):* yellow viscous oil (76.9 mg, 74% yield); TLC (40% EtOAc in hexanes) R_f = 0.46; ^1H NMR (300 MHz; $CDCl_3$) δ 7.60 (d, J = 8.1 Hz, 1 H), 7.31 (d, J = 3.8 Hz, 2 H), 7.14−7.08 (m, 2 H), 4.43 (q, J = 7.1 Hz, 2 H), 3.09 (s, 3 H), 1.36 (t, J = 7.1 Hz, 3 H) ppm; ^{13}C NMR (75 MHz; $CDCl_3$) δ 138.2 (C), 133.9 (C), 125.8 (CH), 125.3 (C), 123.0 (CH), 121.2 (CH), 110.6 (CH), 110.4 (CH), 45.5 (CH_3), 39.8 (CH_2), 15.4 (CH_3) ppm; IR (neat) ν 2983 (C−H), 1317 and 1144 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{11}H_{13}NO_2SNa$ 246.0565, found 246.0567.

*1-Benzyl-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3l**):* white solid (136.2 mg, 75% yield); mp =133−134 °C; TLC (20% EtOAc in hexanes) R_f = 0.45; ^1H NMR (300 MHz; $CDCl_3$) δ 7.78 (d, J = 7.9 Hz, 1 H), 7.67 (d, J = 8.3 Hz, 2 H), 7.53 (d, J = 0.7 Hz, 1 H), 7.33−7.06 (m, 8 H), 6.72 (d, J = 6.9 Hz, 2 H), 5.69 (s, 2 H), 2.32 (s, 3 H) ppm; ^{13}C NMR (75 MHz; $CDCl_3$) δ 144.0 (C), 139.2 (C), 137.6 (C), 136.4 (C), 135.5 (C), 129.5 (2 × CH), 128.3 (2 × CH), 127.6 (2 × CH), 126.8 (CH), 125.8 (CH), 125.7 (2 × CH), 125.3 (C), 122.7 (CH), 121.3 (CH), 111.1 (CH), 111.0 (CH), 47.6 (CH_2), 21.4 (CH_3) ppm; IR (KBr) ν 2976 (C−H), 1316 and 1159 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{22}H_{19}NO_2SNa$ 384.1034, found 384.1036.

*1-Benzyl-2-(phenylsulfonyl)-1H-indole (**4l**):* white solid (121.7 mg, 79% yield); mp = 116−117 °C; TLC EtOAc in hexanes) R_f (20% = 0.39; ^1H NMR (400 MHz; $CDCl_3$) δ 7.76−7.73 (m, 3 H), 7.51 (d, J = 0.8 Hz, 1 H), 7.40−7.36 (m, 1 H), 7.28−7.24 (m, 3 H), 7.20−7.03 (m, 5 H), 6.69 (d, J = 6.8 Hz, 2 H), 5.65 (s, 2 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 140.7 (C), 139.4 (C), 136.4 (C), 135.1 (C), 133.0 (CH), 128.9 (2 × CH), 128.4 (2 × CH), 127.5 (2 × CH), 127.1 (CH), 126.0 (CH), 125.7 (2 × CH), 125.3 (C), 122.8 (CH), 121.4 (CH), 111.6 (CH), 111.2 (CH), 47.7 (CH_2) ppm; IR (KBr) ν 2921 (C−H), 1321 and 1157 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{17}NO_2SNa$ 370.0878, found 370.0863.

*1-Benzyl-2-(methylsulfonyl)-1H-indole (**6l**):* white solid (77.6 mg, 54% yield); mp = 126−127 °C; TLC (40% EtOAc in hexanes) R_f = 0.54; ^1H NMR (400 MHz; $CDCl_3$) δ 7.67 (d, J = 8.0 Hz, 1 H), 7.34−7.28 (m, 3 H), 7.23−7.14 (m, 4 H), 6.98 (d, J = 6.9 Hz, 2 H), 5.68 (s, 2 H), 2.65 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 139.4 (C), 136.9 (C), 134.4 (C), 128.9 (2 × CH), 127.9 (CH), 126.4 (2 × CH), 126.3 (CH), 125.1 (C), 123.0 (CH), 121.5 (CH), 111.7 (CH), 110.9 (CH), 47.3 (CH_2), 45.2 (CH_3) ppm; IR (KBr) ν 2996 (C−H), 1314 and 1150 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{16}H_{15}NO_2SNa$ 308.0721, found 308.0725.

*3-Methyl-2-[(4-methylphenyl)sulfonyl]-1H-indole (**3m**):* white solid (71.8 mg, 50% yield); mp = 124−125 °C; TLC (20% EtOAc in hexanes) R_f = 0.30; ^1H NMR (400 MHz; $CDCl_3$) δ 9.02 (br s, 1 H), 7.86 (d, J = 8.3 Hz, 2 H), 7.59 (d, J = 8.1 Hz, 1 H), 7.39 (d, J = 8.3 Hz, 1 H), 7.34−7.27 (m, 3 H), 7.17−7.13 (m, 1 H), 2.52 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 144.3 (C), 139.0 (C), 135.8 (C), 129.9 (2 × CH), 129.5 (C), 128.3 (C), 126.9 (2 × CH), 126.0 (CH), 120.7 (2 × CH), 118.4 (C), 112.1 (CH), 21.5 (CH_3), 8.9 (CH_3) ppm; IR (KBr) ν 3377 (N−H), 1316 and 1154 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{16}H_{15}NO_2SNa$ 308.0721, found 308.0722.

*3-Methyl-2-(phenylsulfonyl)-1H-indole (**4m**):*[14] white solid (79.0 mg, 60% yield); mp = 156−157 °C; TLC (20% EtOAc in hexanes) R_f = 0.28; ^1H NMR (400 MHz; $CDCl_3$) δ 9.57 (br s, 1 H), 8.01−7.98 (m, 2 H), 7.57 (d, J = 8.1 Hz, 1 H), 7.52−7.48 (m, 1 H), 7.45−7.38 (m, 3 H), 7.30−7.26 (m, 1 H), 7.14−7.10 (m, 1 H), 2.54 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.9 (C), 136.0 (C), 133.2 (CH), 129.3 (2 × CH), 129.0 (C), 128.2 (C), 126.8 (2 × CH), 126.2 (CH), 120.69 (CH), 120.67 (CH), 118.9 (C), 112.2 (CH), 8.9 (CH_3) ppm; IR (KBr) ν 3360 (N−H), 1302 and 1148 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{15}H_{13}NO_2SNa$ 294.0565, found 294.0579.

*3-Methyl-2-(methylsulfonyl)-1H-indole (**6m**):* white solid (31.6 mg, 30% yield); mp = 144−145 °C; TLC (40% EtOAc in hexanes) R_f = 0.40; ^1H NMR (400 MHz; $CDCl_3$) δ 9.14 (br s, 1 H), 7.66 (d, J = 8.1 Hz, 1 H), 7.44 (d, J = 8.3 Hz, 1 H), 7.40−7.36 (m, 1 H), 7.23−7.19 (m, 1 H), 3.17 (s, 3 H), 2.60 (s, 3 H) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 135.7 (C), 128.4 (C), 128.0 (C), 126.3 (CH), 120.83 (CH), 120.76 (CH), 118.5 (C), 112.3 (CH), 45.1 (CH_3), 8.8 (CH_3) ppm; IR (KBr) ν 3364 (N−H), 1299 and 1145 (SO_2) cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{10}H_{11}NO_2SNa$ 232.0408, found 232.0404.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H and ^{13}C NMR spectra for all 2-sulfonylindole derivatives presented in Table 2. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: chutima.kon@mahidol.ac.th.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the Thailand Research Fund (TRF-DBG5480017), the Center for Innovation in Chemistry (PERCH-CIC), the Office of the Higher Education Commission, Mahidol University under the National Research Universities Initiative and the Development and Promotion of Science and Technology Talent Project (DPST), and the Institute for the Promotion of Teaching Science and Technology for financial support. We also thank Professor Chi Wi Ong, National Sun Yat-sen University, and Professor Günter Grampp, Technical University of Graz, and Dr. Soraya Pornsuwan and Asst. Prof. Noppawan Phumala Morales, Mahidol University, for discussions on the mechanistic study.

■ REFERENCES

(1) (a) Ban, Y.; Murakami, Y.; Iwasawa, Y.; Tsuchiya, M.; Takano, N. *Med. Res. Rev.* **1988**, *8*, 231. (b) Katritzky, A. R.; Pozharskii, A. F. *Handbook of Heterocyclic Chemistry*; Pergamon Press: Oxford, 2000. (c) Seigler, D. S. *Plant Secondary Metabolism*; Springer: New York, 2001; pp 628−667. (d) Hibino, S.; Choshi, T. *Nat. Prod. Rep.* **2002**, *19*, 148. (e) Takayama, H.; Tsutsumi, S. I.; Kitajima, M.; Santiarworn, D.; Liawruangrath, B.; Aimi, N. *Chem. Pharm. Bull.* **2003**, *51*, 232. (f) Humphrey, G. R.; Tsutumi, J. T. *Chem. Rev.* **2006**, *106*, 2875. (g) Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489.

(2) (a) Bentley, J. M.; Bickerdike, M. J.; Hebeisen, P.; Kennett, G. A.; Lightowler, S.; Mattei, P.; Mizrahi, J.; Morley, T. J.; Plancher, J.-M.; Richter, H. et al. WO20020704, 2002. (b) Campbell, J. A.; Bordunov, V.; Borka, C. A.; Browner, M. F.; Kress, J. M.; Mirzadegan, T.; Ramesha, C.; Sanpablo, B. F.; Stabler, R.; Takahara, P.; Villasenor, A.; Walker, K. A. M.; Wang, J.-H.; Welch, M.; Weller, P. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 4741. (c) Holenz, J.; Pauwels, P. J.; Diaz, J. L.; Mercè, R.; Codony, X.; Buschmann, H. *Drug Discovery Today* **2006**, *11*, 283. (d) Tong, L.; Shankar, B. B.; Chen, L.; Rizvi, R.; Kelly, J.; Gilbert, E.; Huang, C.; Yang, D.-Y.; Kozlowski, J. A.; Shih, N.-Y.; Gonsiorek, W.; Hipkin, R. W.; Malikzay, A.; Lunn, C. A.; Lundell, D. J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 6785. (e) Williams, T. M.; Ciccarone, T. M.; MacTough, S. C.; Rooney, C. S.; Balani, S. K.; Condra, J. H.; Emini, E. A.; Goldman, M. E.; Greenlee, W. J.; Kauffman, L. R.; O'Brien, J. A.; Sardana, V. V.; Schleif, W. A.; Theoharides, A. D.; Anderson, P. S. *J. Med. Chem.* **1993**, *36*, 1291. (f) Romey, G.; Lazdunski, M. *J. Pharmacol. Exp. Ther.* **1994**, *271*, 1348.

(3) (a) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Bird, C. W., Eds.; Pergamon Press: Oxford, UK, 1996; Vol. 2, pp 119−206.

(b) Sundberg, R. J. *Indoles*; Academic Press: London, 1996. (c) Gribble, G. W. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Bird, C. W., Eds.; Pergamon Press: Oxford, UK, 1996; Vol. 2, pp 207−257. (d) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (e) Taber, D. F.; Tirunahari, P. K. *Tetrahedron* **2011**, *67*, 7195.

(4) For recent C−C functionalization, see: (a) Ackermann, L.; Dell'Acqua, M.; Fenner, S.; Vicente, R.; Sandmann, R. *Org. Lett.* **2011**, *13*, 2358. (b) England, D. B.; Padwa, A. *Org. Lett.* **2008**, *10*, 3631. For recent C−O functionalization, see: (c) Liu, K.; Wen, P.; Liu, J.; Huang, G. *Synthesis* **2010**, 3623. (d) Choy, P. Y.; Lau, C. P.; Kwong, F. Y. *J. Org. Chem.* **2011**, *76*, 80. (e) Lubriks, D.; Sokolovs, I.; Suna, E. *Org. Lett.* **2011**, *13*, 4324. For recent C−N functionalization, see: (f) Lubriks, D.; Sokolovs, I.; Suna, E. *J. Am. Chem. Soc.* **2012**, *134*, 15436. For recent C−S functionalization, see: (g) Chen, M.; Huang, Z.-T.; Zheng, Q.-Y. *Chem. Commun.* **2012**, *48*, 11689. (h) Ge, W.; Wei, Y. *Green Chem.* **2012**, *14*, 2066.

(5) (a) Simpkins, N. S. In *Sulfones in Organic Synthesis*; Baldwin, J. E., Ed.; Pergamon Press: Oxford, UK, 1993. (b) Trost, B. M. In *Comprehensive Organic Chemistry*; Pergamon Press: Oxford, UK, 1991.

(6) (a) Asai, T.; Takeuchi, T.; Diffenderfer, J.; Sibley, D. L. *Antimicrob. Agents Ch.* **2002**, *46*, 2393. (b) Caddick, S.; Aboutayab, K.; West, R. *Synlett* **1993**, 231.

(7) (a) Hamel, P.; Girard, Y.; Atkinson, J. G. *J. Org. Chem.* **1992**, *57*, 2694. (b) Katritzky, A. R.; Lue, P.; Chen, Y.-X. *J. Org. Chem.* **1990**, *55*, 3688. (c) Caddick, S.; Shering, C. L.; Wadman, S. N. *Tetrahedron* **2000**, *56*, 465. (d) Stella, N.; Kline, T. Preparation of Naphthoylindole Derivatives for Treating Glioblastoma. Int. Appl. WO 2012024670, February 23, 2012. (e) Tocco, G.; Begala, M.; Esposito, F.; Caboni, P.; Cannas, V.; Tramontano, E. *Tetrahedron Lett.* **2013**, *54*, 6237. (f) Stokes, B. J.; Liu, S.; Driver, T. G. *J. Am. Chem. Soc.* **2011**, *133*, 4702. (g) Boroujeni, K. P. *Bull. Korean Chem. Soc.* **2010**, *31*, 1887. (h) Boroujeni, K. P. *J. Sulfur Chem.* **2010**, *31*, 197. (i) Yadav, J. S.; Reddy, B. V. V; Krishna, A. D.; Swamy, T. *Tetrahedron Lett.* **2003**, *44*, 6055.

(8) (a) Liu, X.-Y.; Gao, P.; Shen, Y.-W.; Liang, Y.-M. *Org. Lett.* **2011**, *13*, 4196. (b) Li, Y.-X.; Wang, H.-X.; Ali, S.; Xia, X.-F.; Liang, Y.-M. *Chem. Commun.* **2012**, *48*, 2343.

(9) Xiao, F.; Chen, H.; Xie, H.; Chen, S.; Yang, L.; Deng, G.-J. *Org. Lett.* **2014**, *16*, 50.

(10) (a) da Silva Corrêa, C. M. M.; Waters, W. A. *J. Chem. Soc. C* **1968**, 1874. (b) Truce, W. E.; Wolf, G. C. *J. Org. Chem.* **1971**, *36*, 1727. (c) Truce, W. E.; Heuring, D. L.; Wolf, G. C. *J. Org. Chem.* **1974**, *39*, 238. (d) Liu, L. K.; Chi, Y.; Jen, K.-Y. *J. Org. Chem.* **1980**, *45*, 406. (e) Harwood, L. M.; Julia, M.; Thuillier, G. L. *Tetrahedron* **1980**, *36*, 2483. (f) Barluenga, J.; Martínez-Gallo, J. M.; Nájera, C.; Yus, M.; Fananas, F. J. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2605. (g) Nájera, C.; Baldó, B.; Yus, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1029. (h) da Silva Corrêa, C. M. M.; Fleming, M. D. C. M.; Oliveira, M. A. B. C. S. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1993. (i) Nájera, C.; Sansano, J. M.; Yus, M. *J. Chem. Educ.* **1995**, *72*, 664. (j) Craig, D. C.; Edwards, G. L.; Muldoon, C. A. *Synlett* **1997**, 1441.

(11) (a) Stokes, B. J.; Liu, S.; Driver, T. G. *J. Am. Chem. Soc.* **2011**, *113*, 4702. (b) Karchava, A. V.; Shuleva, I. S.; Ovcharenko, A. A.; Yurovskaya, M. A. *Khim. Geterotsikl. Soedin.* **2010**, 373; *Chem. Heterocycl. Compd.* **2010**, *46*, 291.

(12) Pfister, J. R.; Clarke, D. E. N-aryloxyalkyl tryptamine alpha 1-adrenergic receptor antagonists. US5436264 (A), July 25, 1995.

(13) Tsotinis, A.; Panoussopoulou, M.; Sivananthan, S.; Sugden, D. *Il Farm.* **2001**, *56*, 725.

(14) (a) Wenkert, E.; Moeller, P. D. R.; Piettre, S. R. *J. Org. Chem.* **1987**, *52*, 3404. (b) Qian, D. C.; Alford, P. E.; Kishbaugh, T. L. S.; Jones, S. T.; Gribble, G. W. *ARKIVOC* **2010**, *iv*, 66.