

# Iridium(III)-Catalyzed Regioselective C7-Amination of *N*-Pivaloylindoles with Sulfonylazides

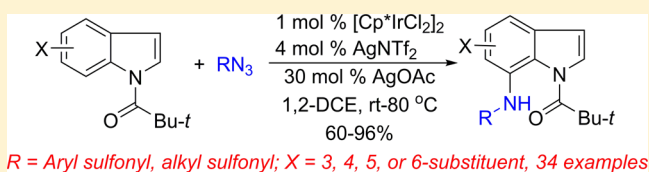
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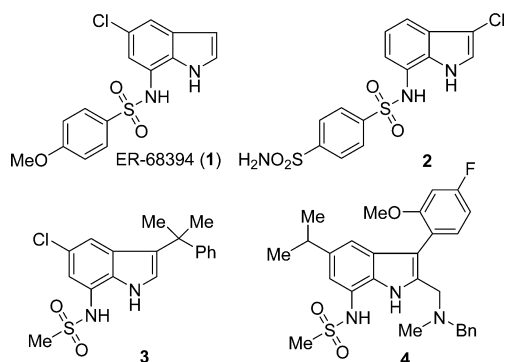
**S** Supporting Information

**ABSTRACT:** Direct C7-amination of *N*-pivaloylindoles has been achieved using a combination of [Cp\*IrCl<sub>2</sub>]<sub>2</sub>, AgNTf<sub>2</sub>, and AgOAc as the catalyst and sulfonylazides as the nitrogen source. The reaction proceeded at room temperature to 80 °C to afford 7-sulfonamidoindoles in good to excellent yields. The reaction is broadly applicable to the C7-amination of a wide variety of 3-, 4-, 5-, and 6-substituted *N*-pivaloylindoles with either alkyl or aryl sulfonylazides.



## INTRODUCTION

7-Sulfonamidoindole moiety is a key substructure found in numerous biologically important compounds such as the tubulin polymerization and cell proliferation inhibitors ER-68394 (**1**),<sup>1</sup> E-7070 (**2**),<sup>2</sup> and compound **3**<sup>3</sup> and the glucocorticoid receptor antagonist compound **4**.<sup>4</sup> Indoles **1**, **2**, and **3** have potential for treatment of congestive heart diseases, and **4** lowers LDL while raising HDL in a hamster model of dyslipidemia (Figure 1). Traditionally, these molecules were



**Figure 1.** Biologically important compounds that contain the 7-sulfonamidoindole moiety.

synthesized from substituted 7-nitroindoles.<sup>3c,5</sup> Since these special heterocycles are not conveniently available, development of straightforward and general methods for assembling 7-sulfonamidoindoles is highly desired.<sup>6,7</sup> Recently, we discovered that regioselective C7-functionalization of indoles could be achieved by simply using *N*-pivaloyl as a directing group.<sup>8,9</sup> As an extension of this work, we explored the possibility of using our substrates for other C7-functionalization reactions and discovered that Ir-catalyzed direct functionalization of *N*-

pivaloylindoles with sulfonylazides could proceed smoothly to afford 7-sulfonamidoindoles.<sup>10–15</sup> During the preparation of this manuscript, similar reactions with different conditions were disclosed by the groups of Chang<sup>10a</sup> and Antonchick.<sup>10b</sup> Chang and co-workers described that they could carry out the reaction at room temperature but needed to use 5 mol % of Cp\*Ir(OAc)<sub>2</sub> as the catalyst and 10 mol % of AgNTf<sub>2</sub> as the additive,<sup>10a</sup> while Antonchick found that the reaction completed at 120 °C even with 4 mol % of [Cp\*IrCl<sub>2</sub>]<sub>2</sub> as the catalyst and 16 mol % of AgNTf<sub>2</sub> and 40 mol % of LiOAc as the additives.<sup>10b</sup> In our hands, we discovered that only 1 mol % of [Cp\*IrCl<sub>2</sub>]<sub>2</sub> was required to complete the reaction at rt to 80 °C if 4 mol % of AgNTf<sub>2</sub> and 30 mol % of AgOAc were employed as the additives. These relatively practical reaction conditions and expanded substrate scope, together with a preliminary mechanism study, are disclosed here.

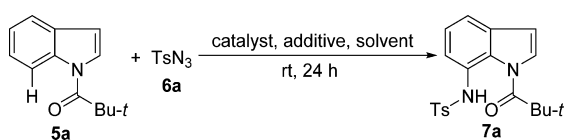
## RESULTS AND DISCUSSION

We commenced our amination research by employing our standard olefination conditions of *N*-pivaloylindoles by treatment of **5a** with tosyl azide **6a** in the presence of [Cp\*RhCl<sub>2</sub>]<sub>2</sub>, AgNTf<sub>2</sub>, and Cu(OAc)<sub>2</sub> in DCE at 80 °C.<sup>8</sup> However, no desired product was obtained, and **5a** was recovered completely. We then turned our attention to Ir catalysts.<sup>13</sup> As indicated in Table 1, in the presence of [Cp\*IrCl<sub>2</sub>]<sub>2</sub>, AgNTf<sub>2</sub>, and NaOAc, the reaction of *N*-pivaloylindole **5a** with tosyl azide **6a** took place at room temperature but with only a trace amount of the desired product **7a** owing to poor conversion (entry 1). Changing one of the additives from NaOAc to pivalic acid or CsOAc gave similar results (entries 2 and 3). However,

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**Table 1.** Condition Screening for Reaction of *N*-Pivaloylindole with Tosyl Azide<sup>a</sup>


entry	catalyst (mol %)	additives (mol %)	solvent	yield <sup>b</sup> (%)
1	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/NaOAc (30)	1,2-DCE	2
2	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/PivOH (30)	1,2-DCE	0
3	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/CsOAc (30)	1,2-DCE	0
4	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	1,2-DCE	95
5	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/Cu(OAc) <sub>2</sub> ·H <sub>2</sub> O (30)	1,2-DCE	55
6	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/Ag <sub>2</sub> CO <sub>3</sub> (30)	1,2-DCE	25
7	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgSbF <sub>6</sub> (16)/AgOAc (30)	1,2-DCE	30 (73) <sup>c</sup>
8	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgOTf (16)/AgOAc (30)	1,2-DCE	45 (81) <sup>c</sup>
9	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgO <sub>2</sub> CCF <sub>3</sub> (16)/AgOAc (30)	1,2-DCE	0 (0) <sup>c</sup>
10	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgOTs (16)/AgOAc (30)	1,2-DCE	0 (0) <sup>c</sup>
11	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (0)/AgOAc (30)	1,2-DCE	0 (0) <sup>c</sup>
12	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	C <sub>6</sub> H <sub>5</sub> CF <sub>3</sub>	88
13	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	CH <sub>2</sub> Cl <sub>2</sub>	93
14	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	<i>t</i> -AmOH	15
15	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	MeCN	0
16	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	dioxane	5
17	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	1,2-DCE	0
18	[Ru( <i>p</i> -cymene)Cl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	1,2-DCE	9
19	Cp*Co(CO)I <sub>2</sub>	AgNTf <sub>2</sub> (16)/AgOAc (30)	1,2-DCE	0
20	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (4)/AgOAc (30)	1,2-DCE	93 <sup>d</sup>
21	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (4)/ AgOAc (0)	1,2-DCE	5 <sup>d</sup>
22	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	AgNTf <sub>2</sub> (0)/ AgOAc (30)	1,2-DCE	0 <sup>d</sup>

<sup>a</sup>5a (0.2 mmol), 6a (0.3 mmol), catalyst (4.0 mol %), and DCE (1.0 mL) at room temperature for 24 h. <sup>b</sup>Yields based on <sup>1</sup>H NMR analysis of the crude mixture (1,3,5-trimethoxybenzene; internal standard). <sup>c</sup>Reaction temperature was 80 °C. <sup>d</sup>[Cp\*IrCl<sub>2</sub>]<sub>2</sub> (1.0 mol %) and DCE (0.2 mL) was used.

when AgOAc was used, complete conversion was observed, and 7a was obtained in 95% yield (entry 4). If AgOAc was switched to Cu(OAc)<sub>2</sub>·H<sub>2</sub>O or Ag<sub>2</sub>CO<sub>3</sub>, the reaction yields were greatly decreased (entries 5 and 6). Further investigations revealed that the use of AgNTf<sub>2</sub> is critical to the reaction efficiency. No desired product was obtained without AgNTf<sub>2</sub> or by replacing it with AgO<sub>2</sub>CCF<sub>3</sub> and AgOTs even at 80 °C (entries 9–11). Interestingly, when AgNTf<sub>2</sub> was replaced with either AgSbF<sub>6</sub> or AgOTf, poor yields were obtained at room temperature but acceptable yields were realized at 80 °C (entries 7 and 8).

Using the combination of [Cp\*IrCl<sub>2</sub>]<sub>2</sub>, AgNTf<sub>2</sub>, and AgOAc, we examined several polar solvents and found that (trifluoromethyl)benzene and methylene chloride afforded 7a in 88–93% yields (entries 12 and 13), while *t*-amylOH, MeCN, and dioxane gave poor yields or no conversion (entries 14–16). Additionally, we discovered that Ir catalyst was also essential for this reaction, and little conversion was observed when [Cp\*RhCl<sub>2</sub>]<sub>2</sub>,<sup>12</sup> [Ru(*p*-cymene)Cl<sub>2</sub>]<sub>2</sub>,<sup>14</sup> and Cp\*Co(CO)I<sub>2</sub><sup>15</sup> were used as the catalyst (entries 17–19). We were pleased that the catalyst loading could be reduced to 1 mol % without decreasing the reaction yield with the optimized reaction conditions (entry 4 vs 20). Noteworthy is that the combination of two silver salts was essential to ensure complete conversion because using AgNTf<sub>2</sub> or AgOAc alone gave a poor yield or no conversion (entries 21 and 22).

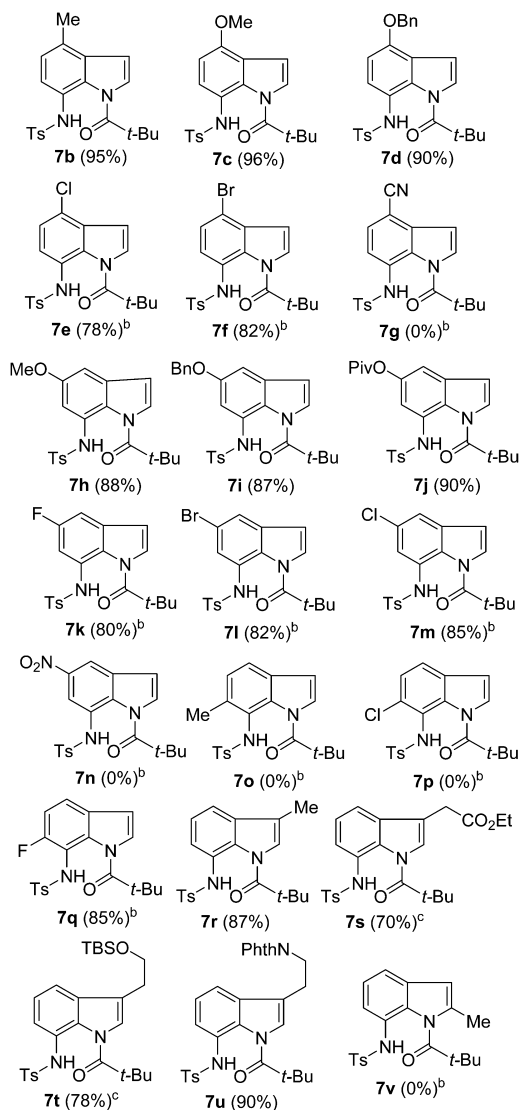
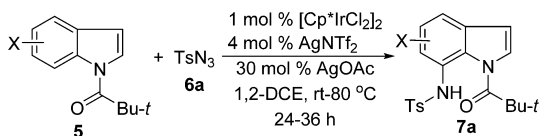
With the optimized conditions in hand, we next explored the substrate scope using different substituted indoles. As summarized in Table 2, indoles bearing an electron-donating group at the 4- or 5-position worked well at room temperature, leading to the formation of 7b–d and 7h–j in 87–95% yields. Halogen-substituted indoles were less reactive and required increased reaction temperature (80 °C) to afford 7e,f,k–m in good yields. However, more electron-deficient substrates like 4-cyano-*N*-pivaloylindole and 5-nitro-*N*-pivaloylindole gave no conversion even at 80 °C. The present reaction is very sensitive to the steric hindrance of the 6-position in *N*-pivaloylindoles. No product was obtained when 6-methyl-*N*-pivaloylindole or 6-chloro-*N*-pivaloylindole was utilized as the substrate. In contrast, 6-fluoro-*N*-pivaloylindole that possesses a small F at the 6-position delivered the amination product 7q in 85% yield.

In addition, substrates with both simple and functionalized alkyl substituents at the 3-position of *N*-pivaloylindoles underwent the amination smoothly, producing 7r–u in 70–90% yields. The additional functional groups in the side chain of these products should be useful for further conversion to pharmaceutically important molecules. However, 2-methyl-*N*-pivaloylindole was inert under the present reaction conditions, presumably because the steric hindrance at this position could inhibit the formation of the active metal complex intermediates.

The reaction was successfully conducted on gram scale without any difficulty. Thus, 1.6 g of the desired amination product 7w was obtained in 88% yield from the tryptophan derivative 5w (Scheme 1). Interestingly, the phthaloyl protecting group in 5w was essential for this transformation, as Boc-protected tryptophan derivative 5x and dipeptide 5y were inert under the same reaction conditions. This phenomenon indicated that the free NH moiety in the substrates might bond to the metal in a way that blocked the catalytic reaction.

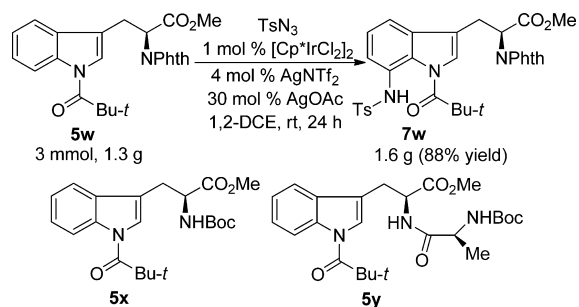
We also evaluated the reaction scope using different sulfonyl azides, and the results are summarized in Table 3. Aryl sulfonyl azides with electron-donating groups, in general, were more reactive, giving complete conversion and excellent yields at room temperature, while aryl sulfonyl azides with electron-withdrawing groups required elevated temperature to reach complete conversion. Alkyl sulfonyl azides also worked well, and 8k and 8l were obtained in 88% and 81% yields, respectively. Using methylsulfonyl azide as the reagent, we examined several substituted *N*-pivaloylindoles and were pleased that all of them proceeded smoothly to afford the desired products 8o–s in good to excellent yields.

The application of the current methodology is demonstrated by the successful preparation of a known tubulin polymer-

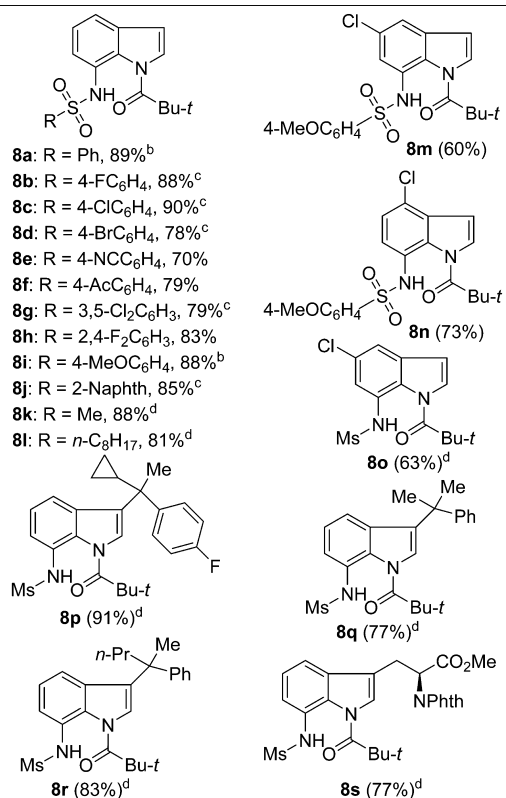
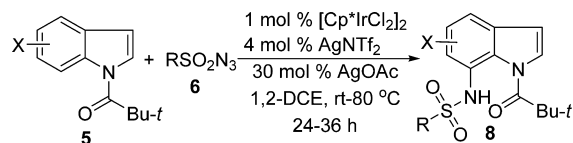
Table 2. Substrate Scope of Indoles<sup>a</sup>

<sup>a</sup>5 (0.2 mmol), 6a (0.3 mmol), DCE (0.2 mL) at room temperature for 24–36 h. <sup>b</sup>At 80 °C. <sup>c</sup>At 50 °C.

Scheme 1. Gram-Scale Reaction of a Tryptophan Derivative



ization and cell proliferation inhibitor **1** (ER-68394)<sup>1</sup> and **9**, a compound with interesting activity against congestive heart

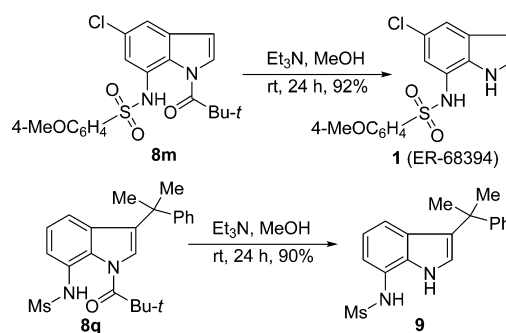
Table 3. Scope of Sulfonyl Azides<sup>a</sup>

<sup>a</sup>5 (0.2 mmol), 6 (0.3 mmol), DCE (0.2 mL) at 80 °C for 24–36 h in pressure tubes. <sup>b</sup>At room temperature. <sup>c</sup>At 50 °C. <sup>d</sup>[IrCp\*Cl<sub>2</sub>]<sub>2</sub> (4 mol %), AgNTf<sub>2</sub> (16 mol %), DCE (1.0 mL) at 80 °C.

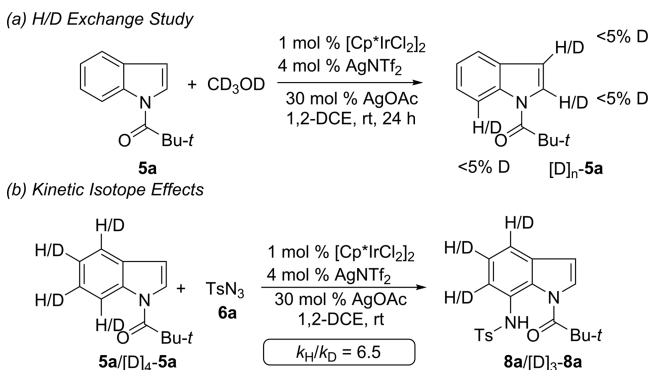
diseases.<sup>3</sup> Thus, treatment of **8m** and **8q**, prepared as discussed above, with our standard mild deprotection conditions (Et<sub>3</sub>N in MeOH, room temperature)<sup>8</sup> afforded **1** and **9** in 92% and 90% yield, respectively (Scheme 2).

To obtain mechanistic insights into the present Ir-catalyzed direct C–H amination, we conducted some deuteration experiments as depicted in Scheme 3. No significant H/D exchange was observed when **5a** was treated with CD<sub>3</sub>OD in the presence of [IrCp\*Cl<sub>2</sub>]<sub>2</sub>, AgNTf<sub>2</sub>, and AgOAc, indicating that the C–H activation step might be irreversible. Addition-

Scheme 2. Deprotection of the Amidation Products



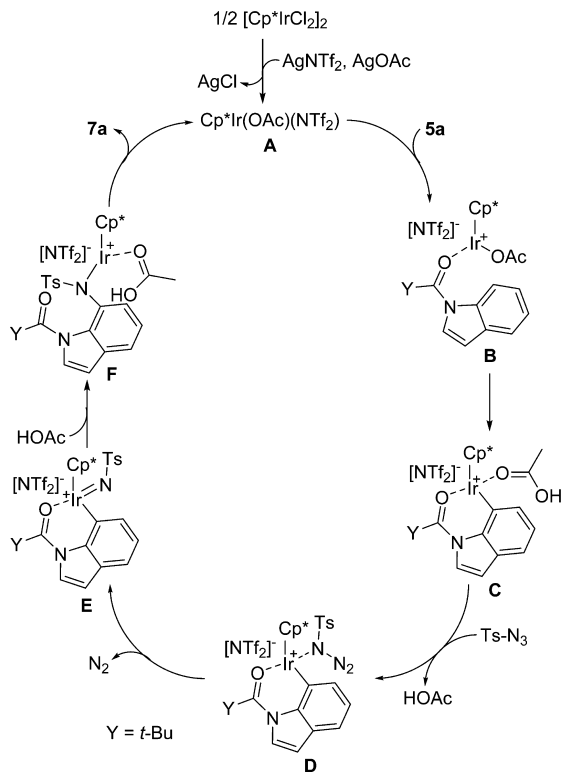
## Scheme 3. Preliminary Mechanistic Studies



ally, kinetic isotope effect (KIE) experiments on parallel reactions of **6a** with **5a** and  $[D]_4$ -**5a** in separate vessels were carried out under the standard reaction conditions, giving the KIE value of  $k_H/k_D = 6.5$ . This result implied that the C–H bond cleavage might occur in the rate-limiting stage.

On the basis of the above mechanistic studies and known reports on metal-catalyzed directing group assisted C–H amidation,<sup>11–15</sup> a plausible mechanism is proposed as shown in Scheme 4. First, treatment of the dimeric precursor

## Scheme 4. Proposed Mechanistic Pathway



$[IrCp^*Cl_2]_2$  with  $AgNTf_2$  and  $AgOAc$  generates the cationic Ir(III) catalyst **A**. The coordination of **A** to the *N*-pivaloyl group of **5a** forms **B**, which accordingly undergoes an irreversible C–H activation at the C7 position of indole substrate to result the six-membered iridacycle **C**. The latter step may be the rate-limiting step based on KIE studies. Next, coordination of sulfonoazide gives the complex **D**, which may undergo release of  $N_2$  to provide a metal–nitrenoid intermediate **E**. The subsequent intramolecular insertion of

nitrenoid moiety into iridacycle forms a new C–N bond to deliver complex **F**, upon coordination with acetic acid. Finally, protonolysis of **F** affords the desired product **7a** and regenerates the catalyst **A**. Further efforts to explore the detailed mechanistic insights of the present regioselective amination reaction are ongoing in our group.

In summary, we have developed a straightforward and general method for preparing 7-sulfonamidoindoles from conveniently available starting materials through Ir-catalyzed C–H activation. The key is an iridium(III)-catalyzed, C7-selective amidation of *N*-pivaloylindole derivatives. High efficiency and regioselectivity are achieved even at room temperature with considerably low catalyst loading. A number of functional groups are tolerated under these reaction conditions, thus allowing synthesizing 7-sulfonamidoindoles in a diverse manner. The usage of this method has been illustrated by quick access to some pharmaceutically important molecules.

## EXPERIMENTAL SECTION

**General Information.** All of the reactions were carried out under inert atmosphere. All of the solvents used for the reactions were dried according to standard procedures. All commercial materials were used as received unless otherwise noted. All of the *N*-pivaloylindoles were synthesized according to the literature procedure.<sup>16,17</sup> All the sulfonoazides were synthesized according to the literature procedure.<sup>18</sup> All of the reactions were monitored by thin-layer chromatography (TLC, silica gel Merck 60 F<sub>254</sub>). The spots were visualized by UV light. Purification of products was conducted by flash chromatography on silica gel (particle size 40–63  $\mu$ m, 230–400 mesh SiliaFlash P60 (Silicycle, Inc.)). Optical rotations were measured at room temperature with a digital polarimeter.  $CDCl_3$  was used as NMR solvents. Chemical shifts were given relative to  $CDCl_3$  (7.24 ppm for  $^1H$  NMR, 77.23 ppm for  $^{13}C$  NMR). For the characterization of the observed signal multiplicities, the following abbreviations were applied: s (singlet), d (doublet), dd (double doublet), t (triplet), td (triple doublet), q (quartet), m (multiplet), as well as br (broad). High-resolution mass spectra were acquired using the ESI-FTMS method. Melting points were measured with an X-4 Melting-point apparatus with microscope.

**General Procedure for the Ir-Catalyzed Amidation with Sulfonoazides.** A sealed tube was charged with indole substrates (0.2 mmol),  $[IrCp^*Cl_2]_2$  (1.6 mg, 0.002 mmol),  $AgOAc$  (10.0 mg, 0.06 mmol),  $AgNTf_2$  (2.0 mg, 0.008 mmol), and sulfonoazides (0.3 mmol). The tube was evacuated and backfilled with argon before 0.2 mL of 1,2-DCE was added. The reaction mixture was stirred for 24–36 h at the indicated temperatures. After being cooled to room temperature, the mixture was diluted with dichloromethane, filtered through a plug of diatomite, and concentrated under vacuum, and the residue was purified by chromatography on silica with a gradient eluent of petroleum ether and ethyl acetate to give the corresponding products.

**Large-Scale Preparation of **7w**.** A sealed tube was charged with indole **5e** (1.3 g, 3.0 mmol),  $[IrCp^*Cl_2]_2$  (23.9 mg, 0.03 mmol),  $AgOAc$  (150 mg, 0.9 mmol),  $AgNTf_2$  (30.7 mg, 0.12 mmol), and *p*-toluenesulfonyl azide (887 mg, 4.5 mmol). The tube was evacuated and backfilled with argon before 3.0 mL of 1,2-DCE was added. The reaction mixture was stirred at room temperature for 40 h. Then the mixture was diluted with dichloromethane, filtered through a plug of diatomite, and concentrated under vacuum, and the residue was purified by chromatography on silica with a gradient eluent of petroleum ether and ethyl acetate to give 1.6 g (88%) of **7w**.

**4-Methyl-*N*-(1-pivaloyl-1*H*-indol-7-yl)benzenesulfonamide (**7a**):** white solid (67 mg, 90%); mp 119–121  $^{\circ}C$ ;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  9.21 (s, 1H), 7.52–7.48 (m, 2H), 7.39–7.35 (m, 3H), 7.30 (t,  $J = 7.7$  Hz, 1H), 7.07 (d,  $J = 8.0$  Hz, 2H), 6.56 (d,  $J = 3.9$  Hz, 1H), 2.28 (s, 3H), 1.35 (s, 9H);  $^{13}C\{^1H\}$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  179.5, 143.3, 137.7, 132.4, 129.6, 129.5, 127.0, 126.7, 125.4, 125.4, 123.0,



119.0, 109.5, 41.8, 29.2, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{20}H_{23}N_2O_3S$  ( $M + H$ )<sup>+</sup> 371.1424, found 371.1426.

**4-Methyl-N-(4-methyl-1-pivaloyl-1H-indol-7-yl)-benzenesulfonamide (7b)**: white solid (73 mg, 95%); mp 162–164 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.95 (s, 1H), 7.47 (d,  $J = 3.9$  Hz, 1H), 7.40–7.35 (m, 3H), 7.10–7.04 (m, 3H), 6.58 (d,  $J = 3.9$  Hz, 1H), 2.45 (s, 3H), 2.28 (s, 3H), 1.33 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.5, 143.2, 137.8, 131.6, 129.6, 129.5, 128.6, 127.0, 126.0, 125.8, 123.7, 122.9, 107.7, 41.8, 29.2, 21.6, 18.3; HRMS (ESI)  $m/e$  calcd for  $C_{21}H_{25}N_2O_3S$  ( $M + H$ )<sup>+</sup> 385.1580, found 385.1586.

**N-(4-Methoxy-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7c)**: white solid (77 mg, 96%); mp 155–157 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.64 (s, 1H), 7.44 (d,  $J = 8.6$  Hz, 1H), 7.35 (d,  $J = 3.9$  Hz, 1H), 7.30 (d,  $J = 8.3$  Hz, 2H), 7.04 (d,  $J = 8.0$  Hz, 2H), 6.76 (d,  $J = 8.6$  Hz, 1H), 6.68 (d,  $J = 3.9$  Hz, 1H), 3.92 (s, 3H), 2.27 (s, 3H), 1.29 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.3, 151.7, 143.2, 137.7, 131.5, 129.5, 127.0, 125.8, 125.0, 122.0, 118.02, 106.2, 105.4, 55.9, 41.7, 29.1, 21.6. HRMS (ESI)  $m/e$  calcd for  $C_{21}H_{25}N_2O_4S$  ( $M + H$ )<sup>+</sup> 401.1530, found 401.1532.

**N-(4-(Benzyloxy)-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7d)**: brown solid (86 mg, 90%); mp 156–158 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.66 (s, 1H), 7.46–7.29 (m, 9H), 7.05 (d,  $J = 8.0$  Hz, 2H), 6.83 (d,  $J = 8.6$  Hz, 1H), 6.74 (d,  $J = 3.9$  Hz, 1H), 5.18 (s, 2H), 2.27 (s, 3H), 1.30 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.3, 150.7, 143.2, 137.6, 136.9, 131.5, 129.5, 128.8, 128.3, 127.6, 127.0, 125.6, 125.1, 122.4, 118.2, 106.9, 106.3, 70.5, 41.7, 29.0, 21.5; HRMS (ESI)  $m/e$  calcd for  $C_{27}H_{29}N_2O_4S$  ( $M + H$ )<sup>+</sup> 477.1843, found 477.1844.

**N-(4-Chloro-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7e)**: white solid (63 mg, 78%); mp 144–146 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.97 (s, 1H), 7.54 (d,  $J = 3.9$  Hz, 1H), 7.44–7.39 (m, 3H), 7.29 (d,  $J = 8.4$  Hz, 1H), 7.10 (d,  $J = 8.0$  Hz, 2H), 6.70 (dd,  $J = 3.9, 0.9$  Hz, 1H), 2.29 (s, 3H), 1.35 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.7, 143.6, 137.4, 130.7, 130.2, 129.6, 127.2, 126.9, 124.9, 124.1, 124.0, 123.8, 107.5, 41.9, 29.0, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{20}H_{22}N_2O_3Cl$  ( $M + H$ )<sup>+</sup> 405.1034, found 405.1038.

**N-(4-Bromo-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7f)**: brown solid (74 mg, 82%); mp 141–143 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.99 (s, 1H), 7.55 (d,  $J = 3.9$  Hz, 1H), 7.44–7.35 (m, 4H), 7.10 (d,  $J = 8.0$  Hz, 2H), 6.66 (d,  $J = 3.9$  Hz, 1H), 2.29 (s, 3H), 1.35 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.8, 143.6, 137.5, 132.6, 130.0, 129.7, 128.2, 127.2, 127.0, 124.7, 123.9, 112.4, 109.4, 42.0, 29.1, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{20}H_{22}N_2O_3BrS$  ( $M + H$ )<sup>+</sup> 449.0529, found 449.0525.

**N-(5-Methoxy-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7h)**: white solid (70 mg, 88%); mp 125–127 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.63 (s, 1H), 7.48–7.45 (m, 3H), 7.14 (d,  $J = 2.5$  Hz, 1H), 7.09 (d,  $J = 8.1$  Hz, 2H), 6.79 (d,  $J = 2.5$  Hz, 1H), 6.47 (d,  $J = 3.9$  Hz, 1H), 3.82 (s, 3H), 2.28 (s, 3H), 1.35 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.0, 157.6, 143.4, 137.5, 133.3, 129.5, 127.5, 127.0, 126.2, 123.8, 109.6, 109.5, 102.0, 55.9, 41.7, 29.2, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{21}H_{25}N_2O_4S$  ( $M + H$ )<sup>+</sup> 401.1530, found 401.1534.

**N-(5-(Benzyloxy)-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7i)**: white solid (83 mg, 87%); mp 157–159 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.64 (s, 1H), 7.47–7.41 (m, 5H), 7.38–7.29 (m, 3H), 7.26 (d,  $J = 2.4$  Hz, 1H), 7.07 (d,  $J = 8.0$  Hz, 2H), 6.86 (d,  $J = 2.5$  Hz, 1H), 5.10 (s, 2H), 2.28 (s, 3H), 1.35 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.0, 156.7, 143.4, 137.5, 137.0, 133.2, 129.5, 128.8, 128.2, 127.7, 127.5, 127.1, 126.3, 124.0, 110.2, 109.6, 103.5, 70.7, 41.7, 29.2, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{27}H_{29}N_2O_4S$  ( $M + H$ )<sup>+</sup> 477.1843, found 477.1849.

**7-(4-Methylphenylsulfonamido)-1-pivaloyl-1H-indol-5-yl pivalate (7j)**: white solid (85 mg, 90%); mp 145–147 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.39 (s, 1H), 7.51 (d,  $J = 3.9$  Hz, 1H), 7.43 (d,  $J = 8.2$  Hz, 2H), 7.26 (d,  $J = 2.3$  Hz, 1H), 7.08–7.06 (m, 3H), 6.50 (d,  $J = 3.9$  Hz, 1H), 2.27 (s, 3H), 1.36 (s, 9H), 1.34 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.3, 177.2, 148.5, 143.5, 137.2, 132.7, 129.5, 127.7, 127.1, 127.0, 126.0, 116.3, 111.4, 109.5, 41.8, 39.3, 29.1, 27.3, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{25}H_{31}N_2O_5S$  ( $M + H$ )<sup>+</sup> 471.1948, found 471.1951.

**N-(5-Fluoro-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7k)**: white solid (62 mg, 80%); mp 128–130 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.56 (s, 1H), 7.57 (d,  $J = 3.9$  Hz, 1H), 7.50 (d,  $J = 8.1$  Hz, 2H), 7.30 (dd,  $J = 10.6, 2.5$  Hz, 1H), 7.12 (d,  $J = 8.2$  Hz, 2H), 6.99 (dd,  $J = 7.5$  Hz, 2.5 Hz, 1H), 6.52 (d,  $J = 3.9$  Hz, 1H), 2.30 (s, 3H), 1.38 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.5, 161.5 ( $J_{C-F} = 240.8$  Hz), 143.7, 137.4, 133.2 ( $J_{C-F} = 11.1$  Hz), 129.7, 128.2, 127.1, 126.8 ( $J_{C-F} = 11.9$  Hz), 125.5 ( $J_{C-F} = 1.8$  Hz), 109.50 ( $J_{C-F} = 32.2$  Hz), 109.46, 104.1 ( $J_{C-F} = 23.4$  Hz), 42.0, 29.2, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{20}H_{22}N_2O_3FS$  ( $M + H$ )<sup>+</sup> 389.1330, found 389.1334.

**N-(5-Bromo-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7l)**: brown solid (74 mg, 82%); mp 165–167 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.30 (s, 1H), 7.63 (d,  $J = 1.9$  Hz, 1H), 7.52 (d,  $J = 3.9$  Hz, 1H), 7.47–7.45 (m, 3H), 7.11 (d,  $J = 8.0$  Hz, 2H), 6.50 (d,  $J = 3.9$  Hz, 1H), 2.30 (s, 3H), 1.36 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (125 MHz, CDCl<sub>3</sub>) δ 179.6, 143.7, 137.3, 133.7, 129.7, 128.3, 127.8, 127.0, 126.5, 124.7, 121.3, 118.2, 108.8, 42.0, 29.1, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{20}H_{22}N_2O_3BrS$  ( $M + H$ )<sup>+</sup> 449.0529, found 449.0525.

**N-(5-Chloro-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7m)**: white solid (69 mg, 85%); mp 149–151 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.36 (s, 1H), 7.54 (d,  $J = 3.9$  Hz, 1H), 7.50 (d,  $J = 2.0$  Hz, 1H), 7.47 (d,  $J = 8.2$  Hz, 2H), 7.30 (d,  $J = 2.0$  Hz, 1H), 7.11 (d,  $J = 8.1$  Hz, 2H), 6.50 (d,  $J = 3.9$  Hz, 1H), 2.30 (s, 3H), 1.36 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (125 MHz, CDCl<sub>3</sub>) δ 179.6, 143.7, 137.4, 133.3, 130.8, 129.7, 127.9, 127.8, 127.1, 126.3, 121.9, 118.2, 108.9, 42.0, 29.2, 21.6; HRMS (ESI)  $m/e$  calcd for  $C_{20}H_{22}N_2O_3ClS$  ( $M + H$ )<sup>+</sup> 405.1034, found 405.1032.

**N-(6-Fluoro-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7q)**: white solid (66 mg, 85%); mp 129–131 °C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.84 (s, 1H), 7.56–7.53 (m, 3H), 7.40 (dd,  $J = 8.5, 4.9$  Hz, 1H), 7.17 (d,  $J = 8.0$  Hz, 2H), 7.13 (dd,  $J = 10.0, 8.6$  Hz, 1H), 6.56 (d,  $J = 3.9$  Hz, 1H), 2.35 (s, 3H), 1.40 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (125 MHz, CDCl<sub>3</sub>) δ 179.5, 158.7 ( $J_{C-F} = 245.6$  Hz), 143.7, 137.7, 132.9 ( $J_{C-F} = 3.7$  Hz), 129.5, 128.2 ( $J_{C-F} = 1.9$  Hz), 127.4, 127.1 ( $J_{C-F} = 3.8$  Hz), 120.5 ( $J_{C-F} = 9.8$  Hz), 113.8 ( $J_{C-F} = 24.1$  Hz), 113.5 ( $J_{C-F} = 17.3$  Hz), 108.5 ( $J_{C-F} = 1.4$  Hz), 41.8, 29.0, 21.7; HRMS (ESI)  $m/e$  calcd for  $C_{20}H_{22}N_2O_3FS$  ( $M + H$ )<sup>+</sup> 389.1330, found 389.1323.

**4-Methyl-N-(3-methyl-1-pivaloyl-1H-indol-7-yl)-benzenesulfonamide (7r)**: yellow solid (67 mg, 87%); mp 129–131 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.45 (s, 1H), 7.53 (dd,  $J = 7.0, 1.9$  Hz, 1H), 7.40 (d,  $J = 8.2$  Hz, 2H), 7.30–7.24 (m, 3H), 7.06 (d,  $J = 8.0$  Hz, 2H), 2.28 (s, 3H), 2.19 (d,  $J = 1.1$  Hz, 3H), 1.33 (s, 9H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.0, 143.3, 137.7, 133.4, 129.8, 129.5, 127.0, 125.4, 125.1, 123.5, 122.8, 118.3, 116.7, 41.7, 29.1, 21.6, 9.9; HRMS (ESI)  $m/e$  calcd for  $C_{21}H_{25}N_2O_3S$  ( $M + H$ )<sup>+</sup> 385.1580, found 385.1585.

**Ethyl 2-(7-(4-methylphenylsulfonamido)-1-pivaloyl-1H-indol-3-yl)acetate (7s)**: yellow semisolid (64 mg, 70%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.34 (s, 1H), 7.62 (s, 1H), 7.53–7.51 (m, 1H), 7.40 (d,  $J = 7.0$  Hz, 2H), 7.30–7.28 (m, 2H), 7.07 (d,  $J = 8.1$  Hz, 2H), 4.19 (q,  $J = 7.1$  Hz, 2H), 3.64 (d,  $J = 1.0$  Hz, 2H), 2.28 (s, 3H), 1.36 (s, 9H), 1.27 (t,  $J = 7.2$  Hz, 3H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.3, 170.7, 143.4, 137.6, 132.2, 129.5 (2C), 126.9 (2C), 125.5, 125.3, 122.9, 116.6, 114.9, 61.3, 41.8, 30.7, 29.1, 21.6, 14.4; HRMS (ESI)  $m/e$  calcd for  $C_{24}H_{29}N_2O_5S$  ( $M + H$ )<sup>+</sup> 457.1792, found 457.1794.

**N-(3-(2-(tert-Butyldimethylsilyloxy)ethyl)-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7t)**: brown semisolid (82 mg, 78%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.41 (s, 1H), 7.52 (dd,  $J = 6.7, 2.0$  Hz, 1H), 7.39–7.38 (m, 3H), 7.31–7.25 (m, 2H), 7.06 (d,  $J = 8.0$  Hz, 2H), 3.87 (t,  $J = 6.1$  Hz, 2H), 2.81 (t,  $J = 6.0$  Hz, 2H), 2.27 (s, 3H), 1.33 (s, 9H), 0.83 (s, 9H), –0.06 (s, 6H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 179.1, 143.2, 137.7, 132.9, 129.6, 129.5, 127.0, 125.4, 125.0, 124.3, 122.8, 120.1, 116.7, 62.4, 41.7, 29.1, 28.5, 26.1, 21.6, 18.4, –5.2; HRMS (ESI)  $m/e$  calcd for  $C_{28}H_{40}N_2O_4SSiNa$  ( $M + Na$ )<sup>+</sup> 551.2370, found 551.2365.

**N-(3-(2-(1,3-Dioxoisindolin-2-yl)ethyl)-1-pivaloyl-1H-indol-7-yl)-4-methylbenzenesulfonamide (7u)**: white solid (98 mg, 90%); mp 167–169 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.26 (s, 1H), 7.81–7.79 (m, 2H), 7.70–7.68 (m, 2H), 7.50–7.48 (m, 1H), 7.44–7.42 (m, 1H), 7.38–7.36 (m, 3H), 7.31 (t,  $J = 7.8$  Hz, 1H), 7.06 (d,  $J = 8.1$  Hz, 1H), 3.98 (t,  $J = 7.2$  Hz, 2H), 3.06 (t,  $J = 7.2$  Hz, 2H), 2.26 (s, 3H), 1.29 (s,

9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.2, 168.4, 143.3, 137.7, 134.4, 132.3, 132.1, 129.8, 129.5, 126.9, 125.4, 125.3, 123.7, 123.5, 123.1, 118.8, 116.7, 41.7, 37.2, 29.0, 24.1, 21.6; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{30}\text{H}_{30}\text{N}_3\text{O}_3\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  544.1901, found 544.1902.

(*S*)-Methyl 2-(1,3-dioxoisindolin-2-yl)-3-(7-(4-methylphenylsulfonamido)-1-pivaloyl-1H-indol-3-yl)propanoate (**7w**): white semisolid (1.6 g, 88%);  $[\alpha]_{\text{D}} -101.9$  ( $c$  0.2,  $\text{CH}_3\text{OH}$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.23 (s, 1H), 7.77–7.75 (m, 2H), 7.70–7.68 (m, 2H), 7.46 (d,  $J = 7.8$  Hz, 1H), 7.34–7.23 (m, SH), 7.01 (d,  $J = 8.0$  Hz, 2H), 5.21–5.18 (m, 1H), 3.76 (s, 3H), 3.62–3.59 (m, 2H), 2.22 (s, 3H), 1.19 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  179.1, 169.2, 167.6, 143.2, 137.7, 134.6, 132.0, 131.7, 129.7, 129.5, 126.9, 125.5, 125.3, 124.5, 123.7, 123.1, 117.6, 116.3, 53.3, 51.3, 41.6, 28.9, 24.6, 21.5; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{32}\text{H}_{32}\text{N}_3\text{O}_7\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  602.1955, found 602.1945.

*N*-(1-Pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8a**): white solid (63 mg, 89%); mp 125–127 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.26 (s, 1H), 7.54–7.48 (m, 4H), 7.42–7.36 (m, 2H), 7.31–7.25 (m, 3H), 6.55 (d,  $J = 3.9$  Hz, 1H), 1.35 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.5, 140.5, 132.6, 132.4, 129.6, 128.9, 126.9, 126.7, 125.4, 125.2, 123.1, 119.1, 109.5, 41.8, 29.2; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{19}\text{H}_{21}\text{N}_2\text{O}_3\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  357.1267, found 357.1269.

4-Fluoro-*N*-(1-pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8b**): white solid (66 mg, 88%); mp 116–118 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.34 (s, 1H), 7.54–7.49 (m, 4H), 7.39 (dd,  $J = 7.7, 1.2$  Hz, 1H), 7.31 (t,  $J = 7.7$  Hz, 1H), 6.97–6.93 (m, 2H), 6.57 (d,  $J = 3.9$  Hz, 1H), 1.38 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.5, 166.4 ( $J_{\text{C-F}} = 253.2$  Hz), 136.6 ( $J_{\text{C-F}} = 2.8$  Hz), 132.5, 129.7 ( $J_{\text{C-F}} = 9.2$  Hz), 129.6, 126.9, 125.5, 125.0, 122.9, 119.2, 116.2 ( $J_{\text{C-F}} = 22.3$  Hz), 109.7, 41.9, 29.3; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{19}\text{H}_{20}\text{FN}_2\text{O}_3\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  375.1173, found 375.1181.

4-Chloro-*N*-(1-pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8c**): white solid (70 mg, 90%); mp 112–114 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.37 (s, 1H), 7.53 (d,  $J = 3.9$  Hz, 1H), 7.51 (dd,  $J = 7.8, 1.1$  Hz, 1H), 7.45–7.41 (m, 2H), 7.39 (dd,  $J = 7.7, 1.2$  Hz, 1H), 7.32 (t,  $J = 7.7$  Hz, 1H), 7.25–7.23 (m, 2H), 6.58 (d,  $J = 3.9$  Hz, 1H), 1.37 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.5, 139.1, 138.9, 132.5, 129.5, 129.1, 128.4, 126.8, 125.5, 124.9, 123.0, 119.3, 109.7, 41.9, 29.2; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_3\text{ClS}$  ( $\text{M} + \text{H}$ ) $^+$  391.0878, found 391.0884.

4-Bromo-*N*-(1-pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8d**): white solid (68 mg, 78%); mp 118–120 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.38 (s, 1H), 7.53 (d,  $J = 3.9$  Hz, 1H), 7.51 (dd,  $J = 7.8, 0.9$  Hz, 1H), 7.42–7.37 (m, 3H), 7.36–7.33 (m, 2H), 7.32 (t,  $J = 7.7$  Hz, 1H), 6.58 (d,  $J = 3.9$  Hz, 1H), 1.37 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.5, 139.5, 132.5, 132.1, 129.5, 128.5, 127.6, 126.8, 125.5, 124.8, 123.0, 119.4, 109.7, 41.9, 29.2; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{19}\text{H}_{20}\text{BrN}_2\text{O}_3\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  435.0372, found 435.0376.

4-Cyano-*N*-(1-pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8e**): brown semisolid (53 mg, 70%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.58 (s, 1H), 7.64–7.62 (m, 2H), 7.59–7.56 (m, 2H), 7.54 (d,  $J = 3.9$  Hz, 1H), 7.49–7.47 (m, 1H), 7.40–7.38 (m, 1H), 7.32 (t,  $J = 7.8$  Hz, 1H), 6.59 (d,  $J = 3.9$  Hz, 1H), 1.38 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.7, 144.7, 132.69, 132.65, 129.4, 127.7, 126.9, 125.7, 124.5, 122.5, 119.6, 117.4, 116.3, 109.9, 42.0, 29.3; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}_3\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  382.1220, found 382.1220.

4-Acetyl-*N*-(1-pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8f**): brown semisolid (63 mg, 79%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.49 (s, 1H), 7.83 (d,  $J = 8.4$  Hz, 2H), 7.60 (d,  $J = 8.4$  Hz, 2H), 7.50–7.48 (m, 2H), 7.37 (d,  $J = 7.0$  Hz, 1H), 7.30–7.26 (m, 1H), 6.55 (d,  $J = 3.9$  Hz, 1H), 2.52 (s, 3H), 1.34 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  196.9, 179.6, 144.3, 139.9, 132.5, 129.4, 128.7, 127.3, 126.8, 125.5, 124.7, 122.5, 119.3, 109.7, 41.9, 29.2, 27.0; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  399.1373, found 399.1378.

3,5-Dichloro-*N*-(1-pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8g**): brown solid (67 mg, 79%); mp 108–110 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.59 (s, 1H), 7.56 (d,  $J = 3.9$  Hz, 1H), 7.52 (dd,  $J = 7.8, 1.1$  Hz, 1H), 7.43 (dd,  $J = 7.7, 1.2$  Hz, 1H), 7.36–7.31 (m, 4H), 6.61 (d,  $J = 3.9$  Hz, 1H), 1.41 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.7, 143.1, 135.8, 132.7, 132.5, 129.6, 126.9, 125.7, 125.4,

124.4, 123.0, 119.8, 109.9, 41.9, 29.2; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_3\text{Cl}_2\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  425.0488, found 425.0487.

2,4-Difluoro-*N*-(1-pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8h**): white semisolid (65 mg, 83%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.62 (s, 1H), 7.77–7.72 (m, 1H), 7.64 (d,  $J = 3.9$  Hz, 1H), 7.47–7.45 (m, 1H), 7.30–7.28 (m, 1H), 7.22 (t,  $J = 7.8$  Hz, 1H), 6.82–6.77 (m, 1H), 6.74–6.69 (m, 1H), 6.57 (d,  $J = 3.9$  Hz, 1H), 1.51 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.9, 167.2 ( $J_{\text{C-F}} = 256.0, 11.3$  Hz), 161.0 ( $J_{\text{C-F}} = 256.7, 12.7$  Hz), 133.0 ( $J_{\text{C-F}} = 10.4, 1.4$  Hz), 132.6, 128.8, 127.0, 125.4, 124.8, 124.5 ( $J_{\text{C-F}} = 26.2, 14.0$  Hz), 120.4, 118.7, 112.0 ( $J_{\text{C-F}} = 21.7, 3.8$  Hz), 109.6, 105.6 ( $J_{\text{C-F}} = 25.7, 24.6$  Hz), 42.1, 29.3; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_3\text{SF}_2$  ( $\text{M} + \text{H}$ ) $^+$  393.1079, found 393.1082.

4-Methoxy-*N*-(1-pivaloyl-1H-indol-7-yl)benzenesulfonamide (**8i**): white solid (68 mg, 88%); mp 119–121 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.19 (s, 1H), 7.48–7.46 (m, 2H), 7.40 (d,  $J = 8.8$  Hz, 2H), 7.33 (d,  $J = 7.0$  Hz, 1H), 7.26–7.21 (m, 1H), 6.70 (d,  $J = 8.9$  Hz, 2H), 6.53 (d,  $J = 3.9$  Hz, 1H), 3.70 (s, 3H), 1.34 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.5, 162.8, 132.4, 132.1, 129.5, 129.0, 126.7, 125.4, 125.3, 122.9, 118.9, 114.0, 109.5, 55.7, 41.8, 29.2; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  387.1372, found 387.1376.

*N*-(1-Pivaloyl-1H-indol-7-yl)naphthalene-2-sulfonamide (**8j**): brown semisolid (69 mg, 85%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.39 (s, 1H), 8.14 (s, 1H), 7.77–7.74 (m, 2H), 7.67 (d,  $J = 8.6$  Hz, 1H), 7.58–7.48 (m, 3H), 7.37–7.28 (m, 4H), 6.50 (d,  $J = 3.9$  Hz, 1H), 1.16 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.4, 137.4, 134.8, 132.4, 132.2, 129.6, 129.3, 129.0, 128.9, 128.1, 127.9, 127.6, 126.7, 125.4, 125.2, 123.2, 122.3, 119.2, 109.5, 41.6, 28.9; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{23}\text{H}_{22}\text{N}_2\text{O}_3\text{SNa}$  ( $\text{M} + \text{Na}$ ) $^+$  429.1243, found 429.1250.

*N*-(1-Pivaloyl-1H-indol-7-yl)methanesulfonamide (**8k**): white solid (52 mg, 88%); mp 160–162 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.03 (s, 1H), 7.72 (d,  $J = 3.9$  Hz, 1H), 7.50 (d,  $J = 7.8$  Hz, 1H), 7.41–7.39 (m, 1H), 7.32 (t,  $J = 7.8$  Hz, 1H), 6.67 (d,  $J = 3.9$  Hz, 1H), 2.90 (s, 3H), 1.54 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  180.1, 132.9, 129.1, 127.0, 125.6, 125.5, 120.8, 118.8, 109.7, 42.2, 39.9, 29.4; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_3\text{SNa}$  ( $\text{M} + \text{Na}$ ) $^+$  317.0930, found 317.0928.

*N*-(1-Pivaloyl-1H-indol-7-yl)octane-1-sulfonamide (**8l**): brown semisolid (64 mg, 81%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.93 (s, 1H), 7.71 (d,  $J = 3.9$  Hz, 1H), 7.51 (dd,  $J = 7.8, 1.0$  Hz, 1H), 7.38 (dd,  $J = 7.7, 1.2$  Hz, 1H), 7.31 (t,  $J = 7.8$  Hz, 1H), 6.66 (d,  $J = 3.9$  Hz, 1H), 3.00–2.96 (m, 2H), 1.78–1.71 (m, 2H), 1.54 (s, 9H), 1.32–1.18 (m, 10H), 0.85 (t,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  180.1, 132.9, 128.9, 127.0, 125.9, 125.5, 120.0, 118.4, 109.7, 52.2, 42.2, 31.8, 29.4, 29.1, 29.0, 28.3, 23.5, 22.7, 14.2; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{21}\text{H}_{33}\text{N}_2\text{O}_3\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  393.2206, found 393.2209.

*N*-(5-Chloro-1-pivaloyl-1H-indol-7-yl)-4-methoxybenzenesulfonamide (**8m**): white solid (51 mg, 60%); mp 151–153 °C;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.34 (s, 1H), 7.56 (d,  $J = 4.0$  Hz, 1H), 7.53 (d,  $J = 9.0$  Hz, 2H), 7.48 (d,  $J = 2.0$  Hz, 1H), 7.29 (d,  $J = 2.0$  Hz, 1H), 6.78 (d,  $J = 9.0$  Hz, 2H), 6.5 (d,  $J = 4.0$  Hz, 1H), 3.75 (s, 3H), 1.39 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  179.6, 163.1, 133.4, 131.9, 130.8, 129.2, 128.0, 127.8, 126.5, 121.7, 118.1, 114.2, 108.9, 55.8, 42.0, 29.3; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_4\text{ClS}$  ( $\text{M} + \text{H}$ ) $^+$  421.0983, found 421.0981.

*N*-(4-Chloro-1-pivaloyl-1H-indol-7-yl)-4-methoxybenzenesulfonamide (**8n**): brown semisolid (61 mg, 73%);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.95 (s, 1H), 7.56 (d,  $J = 4.0$  Hz, 1H), 7.46 (d,  $J = 9.0$  Hz, 2H), 7.41 (d,  $J = 8.5$  Hz, 1H), 7.27 (d,  $J = 8.4$  Hz, 1H), 6.76 (d,  $J = 9.0$  Hz, 2H), 6.70 (d,  $J = 4.0$  Hz, 1H), 3.75 (s, 3H), 1.38 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  179.7, 163.0, 132.0, 130.8, 130.3, 129.1, 127.2, 124.9, 124.1, 124.0, 123.7, 114.2, 107.5, 55.8, 42.0, 29.2; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_4\text{ClS}$  ( $\text{M} + \text{H}$ ) $^+$  421.0983, found 421.0985.

*N*-(5-Chloro-1-pivaloyl-1H-indol-7-yl)methanesulfonamide (**8o**): white semisolid (41 mg, 63%);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.24 (s, 1H), 7.74 (d,  $J = 4.0$  Hz, 1H), 7.48 (d,  $J = 2.0$  Hz, 1H), 7.34 (d,  $J = 2.0$  Hz, 1H), 6.60 (d,  $J = 4.0$  Hz, 1H), 2.96 (s, 3H), 1.53 (s, 9H);



$^{13}\text{C}\{^1\text{H}\}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  180.2, 133.8, 131.0, 128.3, 127.2, 126.7, 119.5, 117.9, 109.1, 42.3, 40.2, 29.4. HRMS (ESI)  $m/e$  calcd for  $\text{C}_{14}\text{H}_{17}\text{ClN}_2\text{O}_3\text{SNa}$  ( $\text{M} + \text{Na}$ ) $^+$  351.0541, found 351.0543.

*N*-(3-(1-Cyclopropyl-1-(4-fluorophenyl)ethyl)-1-pivaloyl-1*H*-indol-7-yl)methanesulfonamide (**8p**): brown semisolid (83 mg, 91%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.16 (s, 1H), 7.86 (s, 1H), 7.37 (d,  $J = 7.8$  Hz, 1H), 7.20–7.17 (m, 2H), 7.05 (t,  $J = 7.9$  Hz, 1H), 6.94 (t,  $J = 8.7$  Hz, 2H), 6.63 (d,  $J = 7.8$  Hz, 1H), 2.93 (s, 3H), 1.58 (s, 2H), 1.49–1.45 (m, 1H), 0.57–0.48 (m, 2H), 0.31–0.27 (m, 1H), 0.14–0.11 (m, 1H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  179.9, 162.6 ( $J_{\text{C-F}} = 243.8$  Hz), 140.7 ( $J_{\text{C-F}} = 3.2$  Hz), 131.5 ( $J_{\text{C-F}} = 89.3$  Hz), 130.3, 129.3, 129.2, 125.8, 124.8, 124.3, 120.1, 119.2, 115.1 ( $J_{\text{C-F}} = 20.9$  Hz), 42.3, 41.8, 40.2, 29.5, 25.1, 22.1, 1.8, 1.5; HRMS (ESI)  $m/e$  calcd for  $\text{C}_{23}\text{H}_{29}\text{FN}_2\text{O}_3\text{SNa}$  ( $\text{M} + \text{Na}$ ) $^+$  479.1775, found 479.1774.

*N*-(3-(2-Phenylpropan-2-yl)-1-pivaloyl-1*H*-indol-7-yl)methanesulfonamide (**8q**): brown semisolid (64 mg, 77%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.07 (s, 1H), 7.59 (s, 1H), 7.38 (dd,  $J = 0.9, 7.8$  Hz, 1H), 7.28–7.27 (m, 4H), 7.20–7.18 (m, 1H), 7.07 (t,  $J = 7.9$  Hz, 1H), 6.78 (dd,  $J = 1.1, 7.9$  Hz, 1H), 2.92 (s, 3H), 1.74 (s, 6H), 1.57 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.9, 147.7, 131.7, 131.6, 130.5, 128.6, 126.5, 126.3, 125.7, 124.9, 123.1, 120.3, 119.3, 42.2, 40.2, 39.1, 30.1, 29.5. HRMS (ESI)  $m/e$  calcd for  $\text{C}_{23}\text{H}_{29}\text{N}_2\text{O}_3\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  413.1893, found 413.1894.

*N*-(3-(2-Phenylpropan-2-yl)-1-pivaloyl-1*H*-indol-7-yl)methanesulfonamide (**8r**): brown semisolid (73 mg, 83%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.14 (s, 1H), 7.59 (s, 1H), 7.38 (d,  $J = 7.8$  Hz, 1H), 7.29–7.26 (m, 4H), 7.21–7.18 (m, 1H), 7.06 (t,  $J = 7.9$  Hz, 1H), 6.75 (d,  $J = 7.9$  Hz, 1H), 2.94 (s, 3H), 2.14–2.02 (m, 2H), 1.70 (s, 3H), 1.59 (s, 9H), 1.13–1.10 (m, 2H), 0.90 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.9, 146.9, 131.7, 130.7, 130.2, 128.5, 126.9, 126.4, 125.6, 124.9, 123.8, 120.1, 119.3, 43.4, 42.5, 42.2, 40.2, 29.5, 27.0, 17.9, 14.9. HRMS (ESI)  $m/e$  calcd for  $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_3\text{SNa}$  ( $\text{M} + \text{Na}$ ) $^+$  463.2026, found 463.2018.

(*S*)-Methyl 2-(1,3-dioxisoindolin-2-yl)-3-(7-(methylsulfonamido)-1-pivaloyl-1*H*-indol-3-yl)propanoate (**8s**): White semisolid (81 mg, 77%);  $[\alpha]_{\text{D}} -140.3$  (c 0.2,  $\text{CH}_3\text{OH}$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  9.09 (s, 1H), 7.78–7.75 (m, 2H), 7.70–7.68 (m, 2H), 7.54 (s, 1H), 7.46 (d,  $J = 7.8$  Hz, 1H), 7.38 (dd,  $J = 1.0, 7.8$  Hz, 1H), 7.31 (t,  $J = 7.8$  Hz, 1H), 5.27–5.23 (m, 1H), 3.79 (s, 3H), 3.67–3.65 (m, 2H), 2.83 (s, 3H), 1.38 (s, 9H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  179.7, 169.2, 167.7, 134.7, 132.5, 131.7, 129.2, 125.9, 125.6, 124.8, 123.8, 120.9, 117.9, 116.2, 53.4, 51.1, 42.0, 39.9, 29.1, 24.8. HRMS (ESI)  $m/e$  calcd for  $\text{C}_{26}\text{H}_{27}\text{N}_3\text{O}_7\text{SNa}$  ( $\text{M} + \text{Na}$ ) $^+$  548.1462, found 548.1452.

*N*-(5-Chloro-1*H*-indol-7-yl)-4-methoxybenzenesulfonamide (**1**). To a solution of **8m** (84 mg, 0.2 mmol) in 1.0 mL of methanol was added  $\text{Et}_3\text{N}$  (1.0 mL) dropwise at room temperature. The reaction mixture was stirred for 24 h before it was concentrated under vacuum. The residue was purified by chromatography on silica with a gradient eluent of petroleum ether and ethyl acetate to give 62 mg (92%) of **1** as white solid: mp 142–144 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.35 (s, 1H), 7.63 (d,  $J = 9.0$  Hz, 2H), 7.42 (d,  $J = 1.3$  Hz, 1H), 7.26–7.25 (m, 1H), 7.15 (s, 1H), 6.85 (d,  $J = 9.0$  Hz, 2H), 6.54 (d,  $J = 1.6$  Hz, 1H), 6.46–6.44 (m, 1H), 3.79 (s, 3H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  163.7, 130.8, 130.0, 129.7, 129.0, 126.8, 124.8, 121.0, 119.1, 117.5, 114.6, 102.7, 55.8. HRMS (ESI)  $m/e$  calcd for  $\text{C}_{15}\text{H}_{14}\text{ClN}_2\text{O}_3\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  337.0408, found 337.0402.

*N*-(3-(2-Phenylpropan-2-yl)-1*H*-indol-7-yl)methanesulfonamide (**9**). Following the same procedure for preparing **1** from **8m**, **9** was obtained in 90% yield (yellow solid, 59 mg) from **8q**: mp 161–163 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.02 (s, 1H), 7.33–7.31 (m, 2H), 7.25–7.21 (m, 2H), 7.18–7.13 (m, 2H), 6.98 (s, 1H), 6.96 (d,  $J = 8.0$  Hz, 1H), 6.90 (d,  $J = 7.3$  Hz, 1H), 6.82 (t,  $J = 7.8$  Hz, 1H), 3.00 (s, 3H), 1.75 (s, 6H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  149.8, 133.1, 128.6, 128.2, 126.54, 126.53, 125.8, 122.1, 120.9, 119.9, 119.2, 117.5, 39.0, 38.8, 30.8. HRMS (ESI)  $m/e$  calcd for  $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_2\text{S}$  ( $\text{M} + \text{H}$ ) $^+$  329.1318, found 329.1314.

## ■ ASSOCIATED CONTENT

### § Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01856.

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectrum of products, X-ray diffraction parameters and data of **7a**, and detailed deuteration experiments (PDF)

X-ray data for compound **7a** (CIF)

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