

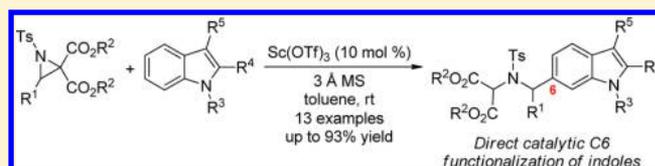
# Catalytic C6 Functionalization of 2,3-Disubstituted Indoles by Scandium Triflate

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**S** Supporting Information

**ABSTRACT:** We report herein an unprecedented direct catalytic C6 functionalization reaction of 2,3-disubstituted indoles with various N-Ts aziridines catalyzed by  $\text{Sc}(\text{OTf})_3$  under mild conditions. Mechanistic studies revealed that a kinetically favored but reversible formal [3 + 2] annulation occurs initially. The direct C6 functionalization, although having a relatively higher energetic barrier, delivers the thermodynamically favorable products.

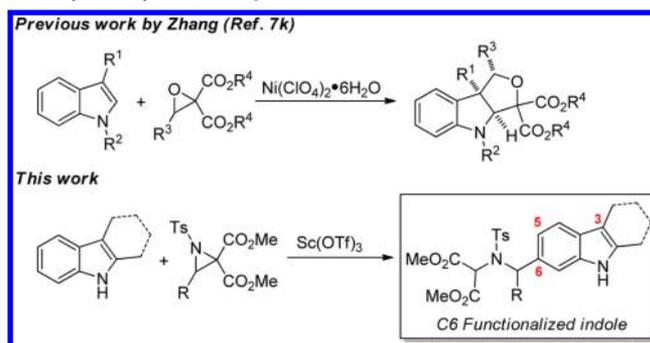


## INTRODUCTION

Indoles are among the most privileged structures that are widely distributed in natural products as well as molecules of pharmaceutical interest.<sup>1</sup> Therefore, direct functionalization of indoles has attracted tremendous attention and numerous methods to achieve this goal have been reported in the past several decades.<sup>2</sup> Nonetheless, most of these reactions occur at the more reactive pyrrole ring and the reactions involving the fused benzene motif are relatively less developed. One strategy for the functionalization at the benzene ring of indoles is to link the other reaction partner and the indole core with a proper tether to construct the peri-annulated products in an intramolecular way.<sup>3</sup> Other methods<sup>4</sup> include taking advantage of a directing group,<sup>4a–f</sup> using a preinstalled functionality<sup>4g–j</sup> or carrying out enzyme-catalyzed reactions.<sup>4k–p</sup> Recently, Garg and co-workers<sup>5</sup> reported an elegant method to access various C4-, C5-, C6-, or C7-substituted indoles via indolyne intermediates. However, to the best of our knowledge, direct catalytic C6 functionalization of indoles has not been reported to date.<sup>6</sup>

The annulation of indoles with 1,3-dipolar equivalents has been found to be an efficient method to deliver polycyclic indole derivatives by diverse catalytic systems.<sup>7</sup> As part of our ongoing program on exploring the dearomatization of substituted indoles,<sup>8</sup> we envisaged that 2,3-disubstituted indoles might undergo annulation with donor–acceptor aziridines, affording pyrroloindoline products possessing two consecutive quaternary chiral centers by a Lewis acid catalyst.<sup>9</sup> To our surprise, the C6-functionalized indoles were obtained as the major products in the presence of a catalytic amount of  $\text{Sc}(\text{OTf})_3$  for a series of substrates (Scheme 1). A plausible mechanism involving a reversible [3 + 2] annulation prior to the direct C6 functionalization was proposed for this transformation on the basis of further experiments and DFT calculations. Herein, we wish to report our results on this subject.

## Scheme 1. C6 Functionalization of 2,3-Disubstituted Indole Catalyzed by $\text{Sc}(\text{OTf})_3$

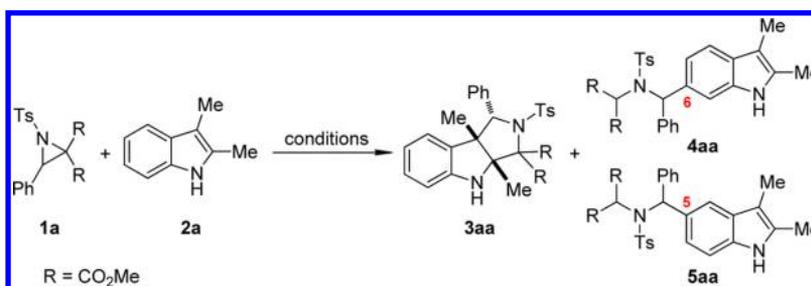


## RESULTS AND DISCUSSION

At the outset, the N-Ts aziridine **1a** and 2,3-dimethylindole (**2a**) were chosen as the model substrates. In the presence of 10 mol % of  $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  and activated 4 Å molecular sieves (MS), the annulation product **3aa** was obtained in 60% yield, along with 21% of the C6-functionalized product **4aa** under mild conditions. No reaction was observed without 4 Å MS (Table 1, entries 1 and 2).<sup>10</sup> With these results in hand, a series of Lewis acids were screened. **3aa** was afforded as the major or the sole product when using  $\text{Sn}(\text{OTf})_2$  or  $\text{Fe}(\text{OTf})_3$  (Table 1, entries 5 and 6), while employing  $\text{Co}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ ,  $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ , or  $\text{Sc}(\text{OTf})_3$  led to **4aa** predominantly (Table 1, entries 3, 4, and 8). The utilization of  $\text{In}(\text{OTf})_3$  resulted in a mixture of **3aa** and **4aa** (Table 1, entry 7). In some cases, a small amount of C5-substituted indole derivative **5aa** was also isolated. The structures of **3aa**, **4aa**, and **5aa** were confirmed unambiguously by single crystal X-ray diffraction analyses.<sup>11</sup> With  $\text{Sc}(\text{OTf})_3$  as the optimal catalyst, various solvents such as

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Table 1. Optimization of Reaction Conditions<sup>a</sup>

entry	catalyst	solvent	MS	time (h)	yield (%) of 3aa, 4aa <sup>b</sup>	3aa:4aa:5aa <sup>c</sup>
1	Ni(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O	PhMe	none	12	no reaction	ND <sup>d</sup>
2	Ni(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O	PhMe	4 Å	3	60, 21	30:10:<1
3	Co(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O	PhMe	4 Å	3	ND, 55	1:10:1
4	Zn(ClO <sub>4</sub> ) <sub>2</sub> ·6H <sub>2</sub> O	PhMe	4 Å	2	ND, 66	0:9:1
5	Sn(OTf) <sub>2</sub>	PhMe	4 Å	3	79, trace	>20:1:<1
6	Fe(OTf) <sub>3</sub>	PhMe	4 Å	3	76, ND	1:0:0
7	In(OTf) <sub>3</sub>	PhMe	4 Å	3	30, 29	10:10:<1
8	Sc(OTf) <sub>3</sub>	PhMe	4 Å	1.5	ND, 75	0:9.5:1
9	Sc(OTf) <sub>3</sub>	DCM	4 Å	0.5	ND, 76	0:6.3:1
10	Sc(OTf) <sub>3</sub>	DCE	4 Å	0.5	ND, 75	0:6.7:1
11	Sc(OTf) <sub>3</sub>	MeCN	4 Å	0.5	ND, 14	0:2.5:1
12	Sc(OTf) <sub>3</sub>	THF	4 Å	24	no reaction	ND
13	Sc(OTf) <sub>3</sub>	PhMe	3 Å	0.5	ND, 80	0:9:1
14	Sc(OTf) <sub>3</sub>	PhMe	5 Å	24	20, ND	1:0:0
15	Sc(OTf) <sub>3</sub>	PhMe	none	0.25	ND, 50	0:9:1
16 <sup>e</sup>	Sc(OTf) <sub>3</sub>	PhMe	3 Å	3	ND, 70	0:11.5:1
17 <sup>f</sup>	Sc(OTf) <sub>3</sub>	PhMe	3 Å	0.75	ND, 77	0:12:1

<sup>a</sup>Conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (10 mol %), and activated MS (100 mg) in anhydrous solvent (2 mL) at room temperature.

<sup>b</sup>Isolated yields. <sup>c</sup>The ratio **3aa:4aa:5aa** was determined by <sup>1</sup>H NMR of the crude reaction mixture. <sup>d</sup>ND = not determined. <sup>e</sup>The loading of catalyst was reduced to 5 mol %. <sup>f</sup>0.4 mmol of **2a** was used.

## Scheme 2. Control Experiments

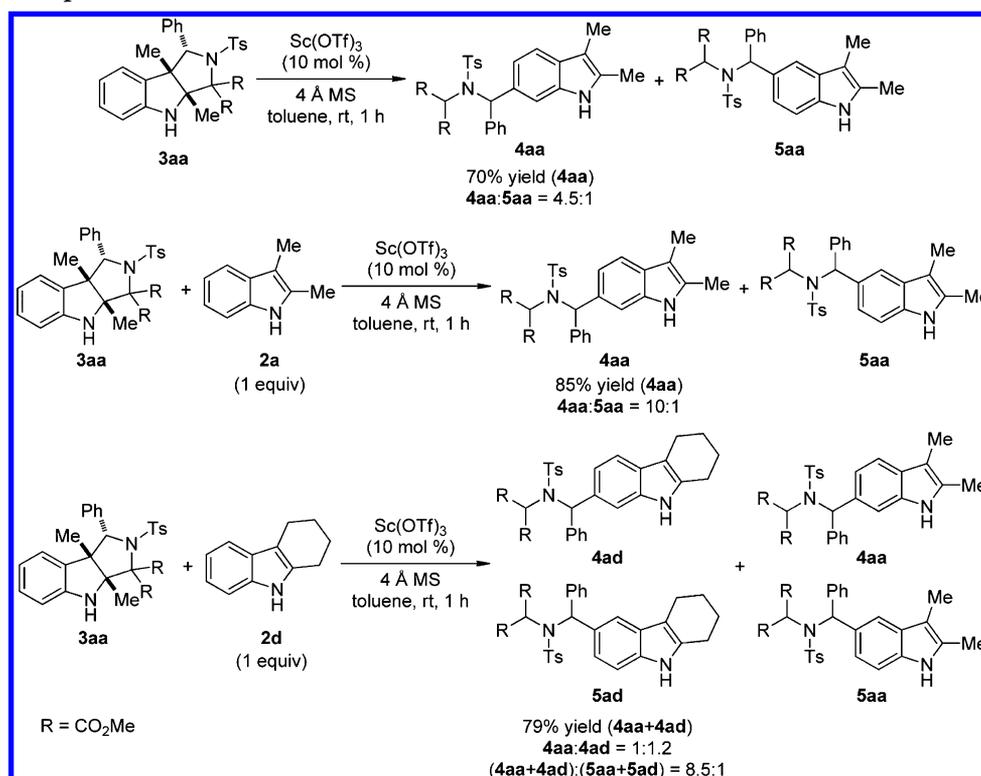
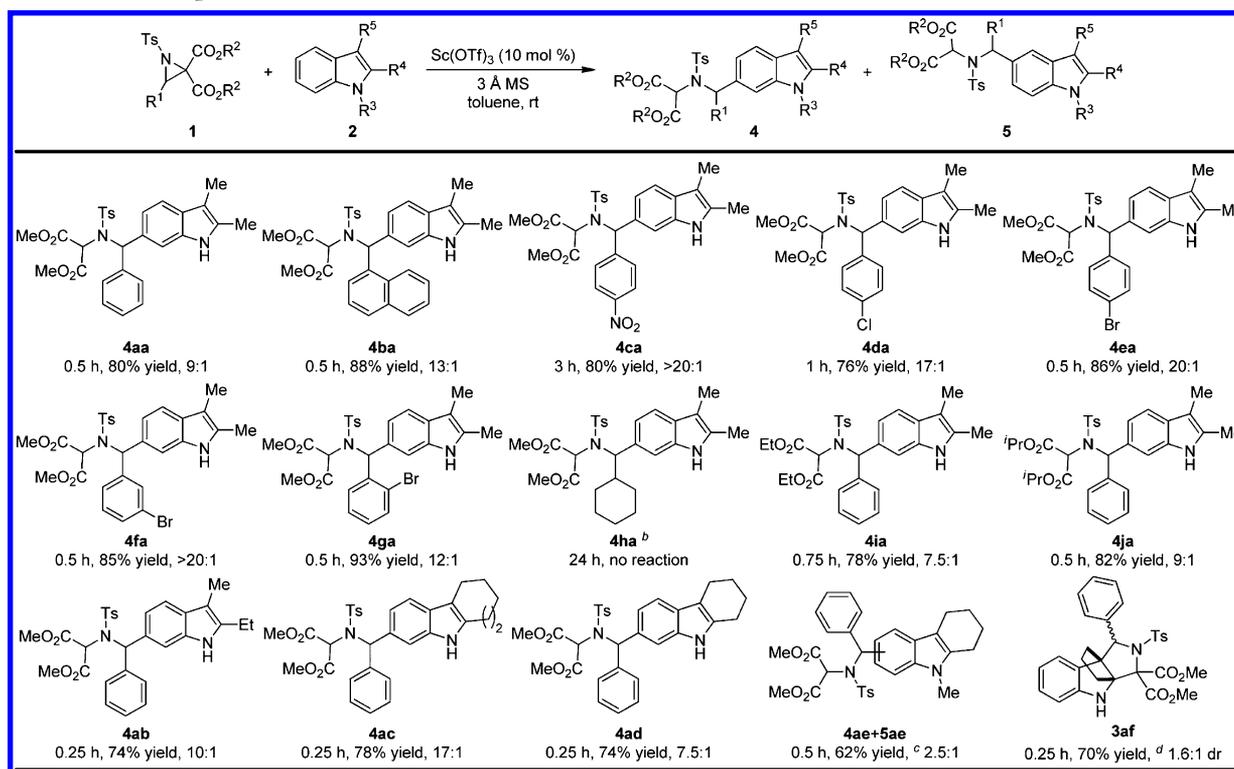
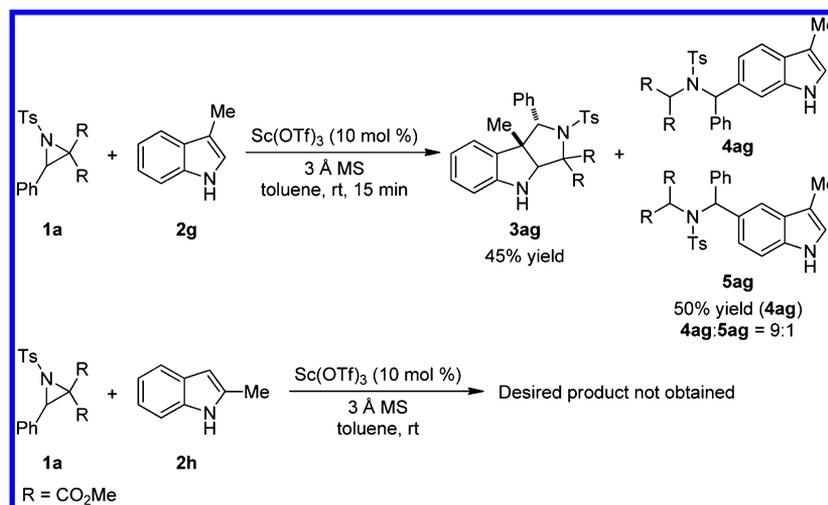


Table 2. Substrate Scope<sup>a</sup>

<sup>a</sup>Conditions: **1** (0.2 mmol), **2** (0.3 mmol), Sc(OTf)<sub>3</sub> (10 mol %), and activated 3 Å MS (100 mg) in anhydrous toluene (2 mL) at room temperature. The isolated yield of **4** is reported. The ratio **4**:**5** was determined by <sup>1</sup>H NMR of the crude reaction mixture. <sup>b</sup>The reaction was carried out at 80 °C for 24 h. <sup>c</sup>Combined yield of **4ae** and **5ae**. <sup>d</sup>Combined yield of the two diastereomers of **3af**.

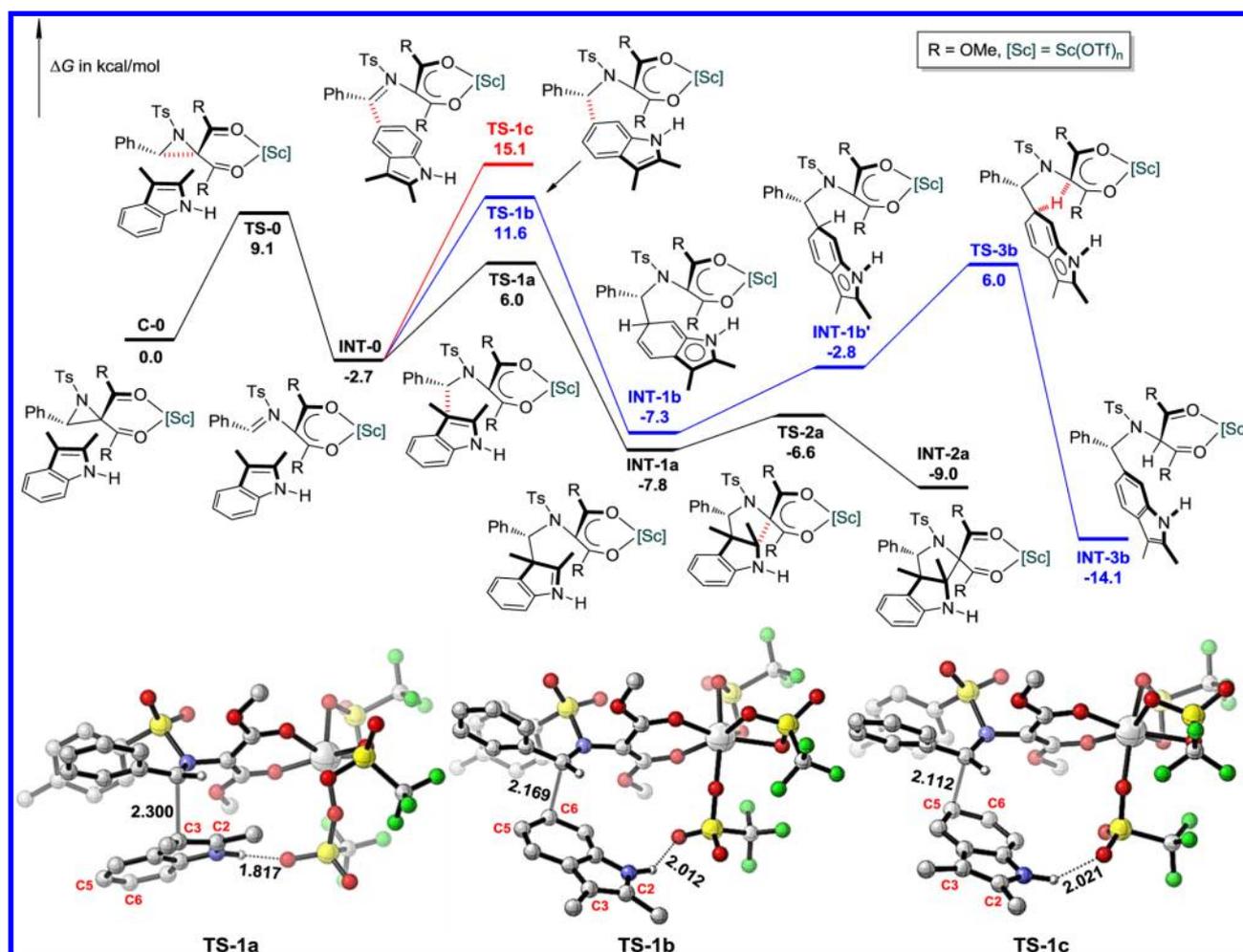
## Scheme 3. Reactions of Monosubstituted Indoles



toluene, DCM, DCE, CH<sub>3</sub>CN, and THF were examined (Table 1, entries 8–12), and toluene was still found to be the optimal solvent with a relatively higher regioselectivity favored for **4aa** (Table 1, entry 8). To further optimize the reaction conditions, different types of MS and catalyst loadings were tested (Table 1, entries 13–16). The addition of 3 Å MS with 10 mol % of Sc(OTf)<sub>3</sub> gave the best results. In addition, increasing the loading of **2a** enhanced the regioselectivity without affecting the yield of **4aa** (Table 1, entry 17). Finally, the optimal reaction conditions were identified as described in Table 1, entry 13.

TLC monitoring of the reaction suggested that the annulation products **3aa** were always generated initially during

the course of the C6 functionalization. The amount of **3aa** decreased gradually while those of **4aa** and **5aa** increased. Thus, several control experiments were carried out to check whether **4aa** and **5aa** were transformed from **3aa** (Scheme 2). In the presence of 10 mol % of Sc(OTf)<sub>3</sub>, **3aa** was converted smoothly to **4aa** in 70% yield and the ratio **4aa**:**5aa** was 4.5:1. When 1 equiv of **2a** was added, the yield of **4aa** was increased to 85%, with the ratio **4aa**:**5aa** was enhanced to 10:1. Moreover, when 1 equiv of tetrahydrocarbazole **2d** was added instead of **2a**, the crossover products **4ad** and **5ad** were afforded along with **4aa** and **5aa**. The combined yield of **4aa** and **4ad** was 79%, with a ratio of **4aa** to **4ad** of 1:1.2. These



**Figure 1.** Calculated reaction pathways and optimized structures of the three key transition states. The  $\Delta G$  values are in kcal/mol. The bond distances are in Å. Most of the hydrogen atoms are omitted for the sake of clarity.

results implicated that the C6 functionalization products were converted from the annulation products and the transformation probably goes through an intermolecular path rather than intramolecular rearrangement.

Next, various N-Ts aziridines **1** and 2,3-disubstituted indoles **2** were subjected to the optimized conditions to evaluate the scope of the reaction (Table 2). In most cases, the desired C6 alkylation products **4** could be generated smoothly in good to excellent yields. Aziridines with different aryl substituents or ester groups were well tolerated, with up to 93% yield of **4aa–4ga** and >20:1 regioselectivity. On the other hand, different indoles led to different outcomes. The reaction of indoles **2b–d** worked well to afford the corresponding **4ab–4ad** with up to 78% yield and 17:1 ratio of **4**:**5**. When N-Me tetrahydrocarbazole **2e** was employed, the ratio of **4ae** and **5ae** decreased dramatically to 2.5:1. Notably, when tetrahydrocyclopenta[*b*]indole **2f** was used, only the annulation product **3af** could be obtained in 70% yield with 1.6:1 dr. Prolonged reaction time or elevated temperature did not lead to the formation of the desired C6 functionalization products. In addition, monosubstituted indole substrates were also tested (Scheme 3). Under the optimized conditions, 3-methylindole **2g** was converted to the corresponding annulation product **3ag** (45% yield) and C6-functionalized product **4ag** (50% yield), as well as a trace amount of C5-functionalized product **5ag** (**4ag**:**5ag** = 9:1). However, 2-methylindole (**2h**) was not a

suitable substrate, because no desired product could be obtained when **2h** was subjected to the standard conditions.

DFT calculations were performed to shed light on the reaction mechanism. As shown in Figure 1, the complex **C-0** (0.0 kcal/mol) of  $\text{Sc}(\text{OTf})_3$ -coordinated N-Ts aziridine **1a** and 2,3-dimethylindole (**2a**) was set as the starting point of the calculations. A weak interaction between the indole N-H moiety and one triflate anion of  $\text{Sc}(\text{OTf})_3$  could be observed.<sup>12</sup> The C–C bond of the aziridine ring is cleaved very easily through **TS-0** (9.1 kcal/mol) to yield the azomethine ylide **INT-0** (–2.7 kcal/mol). The following attack of the indole C3 position at the N-Ts iminium carbon is quite facile (**TS-1a**, 6.0 kcal/mol). The possibility of the direct attack of the indole C3 position at the aziridine ring via  $\text{S}_{\text{N}}2$  displacement or an intimate ion pair was also considered. This kind of mechanism was suggested by Johnson for the cycloaddition reactions of donor–acceptor cyclopropanes.<sup>13</sup> However, such a transition state could not be located in the current system. The 3,3-disubstituted indolenine intermediate **INT-1a** (–7.8 kcal/mol) then undergoes a subsequent ring-closing process (**TS-2a**, –6.6 kcal/mol), leading to **INT-2a** (–9.0 kcal/mol), which is the  $\text{Sc}(\text{OTf})_3$ -coordinated annulation product. The calculated low energetic barrier for the formation of the annulation product is in agreement with the fast formation of **3aa** observed experimentally. Notably, the energetic barrier between **INT-2a** and **TS-1a** is not high (15.0 kcal/mol), indicating that the

annulation process could be reversible. Therefore, other possible reaction pathways of INT-0 were investigated. The transition state for the direct attack of the indole C6 position at the N-Ts iminium carbon was located (TS-1b, 11.6 kcal/mol). The proton at the indole C6 position is then abstracted by the  $\alpha$  carbanion intramolecularly (TS-3b, 6.0 kcal/mol) after a minor conformational switch (INT-1b  $\rightarrow$  INT-1b'), giving the more stabilized final complex INT-3b (-14.1 kcal/mol). These calculation results confirmed that the annulation reaction is kinetically more favored but is reversible. The functionalization at the C6 position, although with a higher energetic barrier, is a thermodynamically favorable process.<sup>14</sup> In addition, the energetic barrier of TS-1b, the rate-determining step of the C6 functionalization process, is 20.6 kcal/mol relative to INT-2a, which is also in accord with the fact that most reactions were complete within 0.5 h at room temperature.

The reaction pathway of the C5 functionalization was also investigated computationally. The energetic barrier of the direct attack of the indole C5 position at the N-Ts iminium carbon (TS-1c) is higher than that of TS-1b by 3.5 kcal/mol. In order to probe the origin of the high regioselectivity favoring C6 over C5 functionalization, a molecular orbital analysis of 2a was conducted. The contribution of the  $2p_z$  orbital of C6 to the HOMO of 2a was estimated to be 12.5%, which is more significant in comparison with the contribution of the  $2p_z$  orbital of C5 (<1%). The sharp difference in the HOMO distributions implies that the nucleophilicity at the C6 position of 2a might be much stronger than that at the C5 position. Further calculations on a series of model substrates revealed that an electron-donating group at the C2 position of indoles might play an important role in enhancing the nucleophilicity at the C6 position.<sup>11</sup>

## CONCLUSIONS

In summary, we have disclosed an unprecedented direct C6 functionalization of 2,3-disubstituted indoles with N-Ts aziridines catalyzed by Sc(OTf)<sub>3</sub>. Mechanistic investigations suggested that the initial formation of the annulation products is a kinetically favored but reversible process while direct C6 functionalization has a relatively higher energetic barrier but leads to more stabilized products. Future studies will be focused on expanding the substrate scope as well as developing asymmetric variants of these novel transformations.

## EXPERIMENTAL SECTION

**General Methods.** Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were freshly distilled according to standard methods prior to use. <sup>1</sup>H NMR spectra were obtained at 300, 400, or 600 MHz and recorded relative to tetramethylsilane signal (0 ppm) or residual protio solvent. <sup>13</sup>C NMR spectra were obtained at 75, 100, or 150 MHz, and chemical shifts were recorded relative to the solvent resonance (CDCl<sub>3</sub>, 77.0 ppm; DMSO-*d*<sub>6</sub>, 39.5 ppm). Data for <sup>1</sup>H NMR are recorded as follows: chemical shift ( $\delta$ , ppm) (multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet), coupling constant(s) in Hz, integration). Data for <sup>13</sup>C NMR are reported in terms of chemical shift ( $\delta$ , ppm).

**General Procedure for the Preparation of Aziridines 1.** The aziridines 1a–j were prepared according to the reported procedures.<sup>15</sup> The characterization data of the two new compounds 1b,h are summarized below.

**Dimethyl 3-(naphthalen-1-yl)-1-tosylaziridine-2,2-dicarboxylate (1b):** white solid, 0.90 g, 68% yield; mp 130–132 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.21 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 2H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.80–7.75 (m, 1H), 7.61–7.55 (m,

1H), 7.54–7.47 (m, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.34–7.29 (m, 2H), 5.31 (s, 1H), 4.01 (s, 3H), 3.23 (s, 3H), 2.46 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  163.8, 162.8, 145.2, 135.5, 133.1, 131.1, 129.8, 129.2, 128.5, 128.0, 126.9, 126.3, 126.1, 125.01, 124.97, 123.0, 56.6, 54.1, 52.8, 48.2, 21.7; IR (thin film):  $\nu_{\max}$  (cm<sup>-1</sup>) 3013, 2956, 2849, 1740, 1594, 1434, 1335, 1162, 1119, 910, 804, 735, 679; HRMS (ESI-TOF) calcd for C<sub>23</sub>H<sub>25</sub>N<sub>2</sub>O<sub>6</sub>S [M + NH<sub>4</sub>]<sup>+</sup> 457.1428, found 457.1442.

**Dimethyl 3-cyclohexyl-1-tosylaziridine-2,2-dicarboxylate (1h):** colorless oil, 1.01 g, 85% yield; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.79 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 3.76 (s, 3H), 3.69 (s, 3H), 3.39 (d, *J* = 9.2 Hz, 1H), 2.35 (s, 3H), 1.74–1.38 (m, 5H), 1.15–0.85 (m, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  164.1, 163.8, 144.6, 135.6, 129.4, 127.7, 55.0, 53.6, 53.1, 52.7, 36.8, 30.4, 28.7, 25.6, 24.9, 24.8, 21.4; IR (thin film):  $\nu_{\max}$  (cm<sup>-1</sup>) 2929, 2853, 1750, 1436, 1337, 1224, 1163, 1120, 1090, 917, 815, 680; HRMS (ESI-TOF) calcd for C<sub>19</sub>H<sub>26</sub>NO<sub>6</sub>S [M + H]<sup>+</sup> 396.1475, found 396.1493.

**Procedure for the Preparation of the Annulation Product 3aa.** To a mixture of 2a (29 mg, 0.2 mmol), Fe(OTf)<sub>3</sub> (10 mg, 0.02 mmol), and 4 Å MS (100 mg) in anhydrous DCM (0.8 mL) was added 1a (117 mg, 0.3 mmol) in DCM (1.2 mL) with stirring. The reaction mixture was stirred at room temperature and monitored by TLC. After the reaction was complete, the mixture was directly subjected to silica gel column chromatography purification (petroleum ether/ethyl acetate 5/1) to afford the desired product 3aa.

**(1S,3aR,8bR)-Dimethyl 3a,8b-dimethyl-1-phenyl-2-tosyl-1,3a,4,8b-tetrahydropyrrolo[3,4-b]indole-3,3(2H)-dicarboxylate (3aa):** white solid, 101 mg, 95% yield; mp 169–171 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.18 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 4.2 Hz, 2H), 6.90–6.85 (m, 1H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.74 (td, *J* = 7.4, 0.8 Hz, 1H), 6.38–6.24 (m, 4H), 6.19 (d, *J* = 7.0 Hz, 1H), 5.40 (s, 1H), 3.99 (s, 6H), 3.73 (s, 1H), 2.21 (s, 3H), 1.74 (s, 3H), 1.48 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.5, 167.8, 146.7, 142.4, 137.7, 137.3, 132.2, 128.8, 128.3, 128.2, 127.7, 127.6, 127.2, 126.8, 126.7, 124.4, 118.9, 109.1, 84.7, 80.0, 77.5, 59.7, 52.9, 52.6, 22.6, 21.2, 20.1; IR (thin film):  $\nu_{\max}$  (cm<sup>-1</sup>) 3341, 2921, 1761, 1602, 1492, 1257, 1144, 1062, 871, 749, 702, 657; HRMS (ESI-TOF) calcd for C<sub>29</sub>H<sub>30</sub>N<sub>2</sub>NaO<sub>6</sub>S [M + Na]<sup>+</sup> 557.1717, found 557.1708.

**General Procedure for the Reaction of 2,3-Disubstituted Indoles with Aziridines by Sc(OTf)<sub>3</sub>.** To a mixture of 2 (0.3 mmol), Sc(OTf)<sub>3</sub> (10 mg, 0.02 mmol), and 4 Å MS (100 mg) in toluene (2 mL) was added 1 (0.2 mmol) with stirring. The reaction mixture was stirred at room temperature and monitored by TLC. After the reaction was complete, the crude reaction mixture was filtered through a pad of silica gel and washed with ethyl acetate. The solvents were removed under reduced pressure. The ratio 4:5 was determined by <sup>1</sup>H NMR of the crude reaction mixture. Then the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 4/1) to afford the desired product 4 (and 3 or 5 in some cases).

**Dimethyl 2-(N-((2,3-dimethyl-1H-indol-6-yl)(phenyl)methyl)-4-methylphenylsulfonamido)malonate (4aa):** white solid, 86 mg, 80% yield; mp 144–145 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.85 (d, *J* = 8.3 Hz, 2H), 7.70 (s, 1H), 7.33–7.22 (m, 4H), 7.22–7.15 (m, 3H), 7.12 (d, *J* = 8.2 Hz, 2H), 6.76 (d, *J* = 8.2 Hz, 1H), 6.30 (s, 1H), 4.86 (s, 1H), 3.66 (s, 3H), 3.38 (s, 3H), 2.33 (s, 3H), 2.31 (s, 3H), 2.17 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  167.3, 167.1, 143.3, 138.4, 136.8, 134.8, 132.0, 129.7, 128.9, 128.6, 127.9, 127.2, 120.4, 117.2, 111.9, 106.5, 64.9, 62.6, 53.0, 52.5, 21.4, 11.4, 8.4; IR (thin film):  $\nu_{\max}$  (cm<sup>-1</sup>) 3392, 2924, 2854, 1756, 1737, 1434, 1132, 1247, 1155, 1026, 808, 786, 665; HRMS (ESI-TOF) calcd for C<sub>29</sub>H<sub>34</sub>N<sub>3</sub>O<sub>6</sub>S [M + NH<sub>4</sub>]<sup>+</sup> 552.2163, found 552.2159.

**Dimethyl 2-(N-((2,3-dimethyl-1H-indol-5-yl)(phenyl)methyl)-4-methylphenylsulfonamido)malonate (5aa):** white solid, 9 mg, 9% yield; mp 125–127 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.90 (d, *J* = 8.3 Hz, 2H), 7.76 (s, 1H), 7.35–7.31 (m, 2H), 7.25–7.18 (m, 4H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.81 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.31 (s, 1H), 4.87 (s, 1H), 3.67 (s, 3H), 3.42 (s, 3H), 2.32 (s, 3H), 2.31 (s, 3H), 2.10 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  167.3, 167.1, 143.3, 138.5, 136.9, 134.6, 131.4, 129.1, 129.0, 128.80, 128.78, 128.0, 127.7, 127.4, 122.5, 119.2, 109.6, 107.2, 65.1, 62.6, 53.0, 52.5, 21.5, 11.5, 8.3; IR (thin film):  $\nu_{\max}$  (cm<sup>-1</sup>) 3403, 2948, 1744,

1597, 1435, 1336, 1247, 1151, 1042, 909, 808, 730, 668; HRMS (ESI-TOF) calcd for  $C_{29}H_{34}N_3O_6S [M + NH_4]^+$  552.2163, found 552.2155.

**Dimethyl 2-(N-((2,3-dimethyl-1H-indol-6-yl)(naphthalen-1-yl)methyl)-4-methylphenylsulfonamido)malonate (4ba):** white solid, 103 mg, 88% yield; mp 177–179 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.97 (d,  $J = 7.2$  Hz, 1H), 7.71 (d,  $J = 8.2$  Hz, 2H), 7.69–7.58 (m, 4H), 7.33–7.16 (m, 4H), 7.11 (s, 1H), 7.04 (s, 1H), 6.84 (d,  $J = 8.2$  Hz, 2H), 6.75 (d,  $J = 7.8$  Hz, 1H), 4.92 (s, 1H), 3.73 (s, 3H), 3.19 (s, 3H), 2.25 (s, 3H), 2.14 (s, 3H), 2.13 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.5, 167.3, 143.0, 136.7, 134.9, 133.9, 133.5, 132.2, 130.4, 129.9, 129.4, 128.5, 128.33, 128.30, 127.8, 125.9, 125.1, 124.9, 123.9, 121.0, 117.7, 112.5, 106.7, 63.7, 63.1, 53.2, 52.1, 21.2, 11.5, 8.3; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3395, 2959, 1753, 1736, 1469, 1338, 1249, 1155, 1016, 804, 760, 666; HRMS (ESI-TOF) calcd for  $C_{33}H_{36}N_3O_6S [M + NH_4]^+$  602.2319, found 602.2309.

**Dimethyl 2-(N-((2,3-dimethyl-1H-indol-6-yl)(4-nitrophenyl)methyl)-4-methylphenylsulfonamido)malonate (4ca):** Yellow solid, 93 mg, 80% yield; mp 165–167 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.99 (d,  $J = 8.8$  Hz, 2H), 7.89 (s, 1H), 7.77 (d,  $J = 8.3$  Hz, 2H), 7.53 (d,  $J = 8.7$  Hz, 2H), 7.28 (d,  $J = 8.2$  Hz, 1H), 7.17 (s, 1H), 7.12 (d,  $J = 8.2$  Hz, 2H), 6.63 (dd,  $J = 8.2, 1.2$  Hz, 1H), 6.40 (s, 1H), 4.83 (s, 1H), 3.79 (s, 3H), 3.20 (s, 3H), 2.31 (two s, 6H), 2.17 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.3, 166.7, 146.9, 146.5, 143.9, 136.6, 134.8, 132.7, 129.6, 129.1, 128.9, 128.5, 128.4, 123.0, 120.7, 117.7, 112.6, 106.9, 64.7, 62.8, 53.4, 52.4, 21.5, 11.5, 8.4; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3399, 1758, 1746, 1512, 1326, 1152, 1032, 839, 727, 671; HRMS (ESI-TOF) calcd for  $C_{29}H_{33}N_4O_8S [M + NH_4]^+$  597.2014, found 597.2004.

**Dimethyl 2-(N-((4-chlorophenyl)(2,3-dimethyl-1H-indol-6-yl)methyl)-4-methylphenylsulfonamido)malonate (4da):** white solid, 87 mg, 76% yield; mp 122–124 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.89 (s, 1H), 7.81 (d,  $J = 8.2$  Hz, 2H), 7.30–7.21 (m, 4H), 7.15–7.09 (m, 4H), 6.70 (d,  $J = 7.8$  Hz, 1H), 6.27 (s, 1H), 4.82 (s, 1H), 3.71 (s, 3H), 3.28 (s, 3H), 2.32 (s, 3H), 2.29 (s, 3H), 2.16 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.3, 166.9, 143.6, 137.1, 136.7, 134.8, 133.0, 132.2, 129.9, 129.19, 129.17, 129.0, 128.5, 128.0, 120.4, 117.4, 112.0, 106.7, 64.5, 62.6, 53.2, 52.5, 21.4, 11.5, 8.4; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3373, 2953, 1763, 1747, 1492, 1244, 1148, 1013, 810, 741, 726, 664; HRMS (ESI-TOF) calcd for  $C_{29}H_{33}ClN_3O_6S [M + NH_4]^+$  586.1773, found 586.1766.

**Dimethyl 2-(N-((4-bromophenyl)(2,3-dimethyl-1H-indol-6-yl)methyl)-4-methylphenylsulfonamido)malonate (4ea):** white solid, 105 mg, 86% yield; mp 133–135 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.88 (s, 1H), 7.80 (d,  $J = 8.1$  Hz, 2H), 7.29–7.21 (m, 4H), 7.18 (d,  $J = 8.3$  Hz, 2H), 7.12 (d,  $J = 7.9$  Hz, 2H), 6.70 (d,  $J = 8.1$  Hz, 1H), 6.25 (s, 1H), 4.82 (s, 1H), 3.72 (s, 3H), 3.28 (s, 3H), 2.33 (s, 3H), 2.29 (s, 3H), 2.16 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.3, 166.9, 143.6, 137.6, 136.7, 134.8, 132.3, 130.9, 130.2, 129.2, 129.1, 129.0, 128.5, 121.2, 120.4, 117.4, 112.1, 106.7, 64.5, 62.6, 53.2, 52.5, 21.5, 11.5, 8.4; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3373, 3033, 2953, 1762, 1746, 1433, 1317, 1245, 1148, 1027, 830, 749, 670; HRMS (ESI-TOF) calcd for  $C_{29}H_{33}BrN_3O_6S [M + NH_4]^+$  630.1268, found 630.1258.

**Dimethyl 2-(N-((3-bromophenyl)(2,3-dimethyl-1H-indol-6-yl)methyl)-4-methylphenylsulfonamido)malonate (4fa):** white solid, 104 mg, 85% yield; mp 156–158 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.86–7.77 (m, 3H), 7.45 (s, 1H), 7.29 (d,  $J = 8.1$  Hz, 2H), 7.22–7.18 (m, 2H), 7.14 (d,  $J = 8.0$  Hz, 2H), 7.03 (t,  $J = 7.9$  Hz, 1H), 6.73 (dd,  $J = 8.2, 1.4$  Hz, 1H), 6.28 (s, 1H), 4.80 (s, 1H), 3.77 (s, 3H), 3.28 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H), 2.17 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.2, 166.9, 143.6, 140.9, 136.6, 134.8, 132.2, 131.2, 130.2, 129.5, 129.3, 129.1, 128.5, 127.1, 122.2, 120.7, 117.6, 112.1, 106.9, 64.6, 62.6, 53.3, 52.5, 21.5, 11.6, 8.4; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3413, 1762, 1735, 1598, 1434, 1330, 1259, 1154, 1046, 787, 728, 669; HRMS (ESI-TOF) calcd for  $C_{29}H_{33}BrN_3O_6S [M + NH_4]^+$  630.1268, found 630.1259.

**Dimethyl 2-(N-((2-bromophenyl)(2,3-dimethyl-1H-indol-6-yl)methyl)-4-methylphenylsulfonamido)malonate (4ga):** white solid, 114 mg, 93% yield; mp 170–172 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.89 (d,  $J = 7.7$  Hz, 1H), 7.77 (s, 1H), 7.73 (d,  $J = 8.3$  Hz, 2H), 7.33–7.25 (m, 2H), 7.17 (td,  $J = 7.6, 1.1$  Hz, 1H), 7.04–6.96 (m, 4H), 6.64 (d,  $J = 8.3$  Hz, 1H), 6.59 (s, 1H), 4.81 (s, 1H), 3.82 (s, 3H), 3.21 (s,

3H), 2.31 (s, 3H), 2.25 (s, 3H), 2.16 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.6, 167.3, 143.2, 138.3, 136.3, 134.9, 132.6, 132.4, 129.5, 128.7, 128.5, 128.4, 128.2, 128.0, 126.9, 123.0, 120.9, 117.6, 113.0, 106.8, 65.1, 63.6, 53.4, 52.1, 21.3, 11.5, 8.4; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3397, 3033, 2936, 1760, 1744, 1471, 1329, 1251, 1156, 1018, 786, 725, 666; HRMS (ESI-TOF) calcd for  $C_{29}H_{33}BrN_3O_6S [M + NH_4]^+$  630.1268, found 630.1258.

**Diisopropyl 2-(N-((2,3-dimethyl-1H-indol-6-yl)(phenyl)methyl)-4-methylphenylsulfonamido)malonate (4ia):** white solid, 88 mg, 78% yield; mp 163–165 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.87 (d,  $J = 8.3$  Hz, 2H), 7.76 (s, 1H), 7.34–7.21 (m, 4H), 7.20–7.14 (m, 3H), 7.10 (d,  $J = 6.6$  Hz, 2H), 6.76 (d,  $J = 8.1$  Hz, 1H), 6.30 (s, 1H), 4.81 (s, 1H), 4.22–4.06 (m, 2H), 3.94–3.82 (m, 1H), 3.75–3.63 (m, 1H), 2.30 (two s, 6H), 2.16 (s, 3H), 1.24 (t,  $J = 7.1$  Hz, 3H), 0.99 (t,  $J = 7.1$  Hz, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  166.8, 166.7, 143.2, 138.6, 137.0, 134.8, 131.8, 130.0, 129.0, 128.9, 128.7, 128.6, 127.8, 127.2, 120.6, 117.3, 111.9, 106.7, 64.9, 62.9, 62.2, 61.7, 21.4, 13.8, 13.4, 11.5, 8.4; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3398, 1751, 1735, 1470, 1332, 1252, 1148, 1021, 808, 785, 665; HRMS (ESI-TOF) calcd for  $C_{31}H_{38}N_3O_6S [M + NH_4]^+$  580.2476, found 580.2487.

**Diisopropyl 2-(N-((2,3-dimethyl-1H-indol-6-yl)(phenyl)methyl)-4-methylphenylsulfonamido)malonate (4ja):** white solid, 97 mg, 82% yield; mp 173–174 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.90 (d,  $J = 8.3$  Hz, 2H), 7.74 (s, 1H), 7.32–7.26 (m, 2H), 7.25–7.20 (m, 2H), 7.17–7.11 (m, 3H), 7.07 (d,  $J = 8.0$  Hz, 2H), 6.73 (dd,  $J = 8.2, 1.4$  Hz, 1H), 6.27 (s, 1H), 5.02–4.92 (m, 1H), 4.72 (s, 1H), 4.66–4.57 (m, 1H), 2.29 (s, 3H), 2.26 (s, 3H), 2.13 (s, 3H), 1.26 (d,  $J = 6.2$  Hz, 3H), 1.18 (d,  $J = 6.3$  Hz, 3H), 1.12 (d,  $J = 6.2$  Hz, 3H), 0.79 (d,  $J = 6.3$  Hz, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  166.5, 166.2, 143.1, 138.7, 137.0, 134.8, 131.8, 130.1, 129.0, 128.9, 128.8, 128.5, 127.8, 127.1, 120.7, 117.4, 112.0, 106.7, 70.2, 69.6, 64.8, 63.1, 21.5, 21.4, 21.3, 20.9, 11.5, 8.3; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3388, 1751, 1728, 1469, 1324, 1248, 1151, 1022, 786, 703, 668, 640; HRMS (ESI-TOF) calcd for  $C_{33}H_{42}N_3O_6S [M + NH_4]^+$  608.2789, found 608.2799.

**Dimethyl 2-(N-((2-ethyl-3-methyl-1H-indol-6-yl)(phenyl)methyl)-4-methylphenylsulfonamido)malonate (4ab):** white solid, 81 mg, 74% yield; mp 148–150 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.85 (d,  $J = 8.3$  Hz, 2H), 7.81 (s, 1H), 7.32–7.24 (m, 4H), 7.20–7.14 (m, 3H), 7.10 (d,  $J = 8.1$  Hz, 2H), 6.75 (dd,  $J = 8.4, 1.3$  Hz, 1H), 6.31 (s, 1H), 4.86 (s, 1H), 3.65 (s, 3H), 3.36 (s, 3H), 2.70 (q,  $J = 7.6$  Hz, 2H), 2.29 (s, 3H), 2.18 (s, 3H), 1.22 (t,  $J = 7.6$  Hz, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.3, 167.1, 143.3, 138.5, 137.7, 136.9, 134.8, 129.9, 129.0, 128.9, 128.7, 128.6, 127.9, 127.3, 120.6, 117.5, 111.9, 105.8, 65.0, 62.7, 53.0, 52.5, 21.4, 19.3, 13.9, 8.3; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3388, 2953, 1762, 1750, 1436, 1328, 1148, 1038, 815, 783, 664; HRMS (ESI-TOF) calcd for  $C_{30}H_{36}N_3O_6S [M + NH_4]^+$  566.2319, found 566.2313.

**Dimethyl 2-(N-((5,6,7,8,9,10-hexahydrocyclohepta[b]indol-3-yl)(phenyl)methyl)-4-methylphenylsulfonamido)malonate (4ac):** white solid, 90 mg, 78% yield; mp 135–137 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.85 (d,  $J = 8.3$  Hz, 2H), 7.74 (s, 1H), 7.30–7.23 (m, 4H), 7.19–7.14 (m, 3H), 7.11 (d,  $J = 8.1$  Hz, 2H), 6.75 (dd,  $J = 8.3, 1.4$  Hz, 1H), 6.30 (s, 1H), 4.85 (s, 1H), 3.65 (s, 3H), 3.37 (s, 3H), 2.80–2.70 (m, 4H), 2.30 (s, 3H), 1.91–1.81 (m, 2H), 1.79–1.68 (m, 4H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.3, 167.2, 143.3, 138.6, 138.4, 136.8, 133.8, 129.5, 129.0, 128.8, 128.7, 128.6, 127.9, 127.3, 120.5, 117.1, 113.4, 111.9, 64.9, 62.6, 53.0, 52.6, 31.7, 29.5, 28.7, 27.4, 24.6, 21.4; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3390, 2923, 1759, 1740, 1434, 1322, 1245, 1149, 1023, 911, 800, 730, 701; HRMS (ESI-TOF) calcd for  $C_{32}H_{38}N_3O_6S [M + NH_4]^+$  592.2476, found 592.2466.

**Dimethyl 2-(4-methyl-N-(phenyl(2,3,4,9-tetrahydro-1H-carbazol-7-yl)methyl)phenylsulfonamido)malonate (4ad):** white solid, 83 mg, 74% yield; mp 123–125 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.81 (d,  $J = 8.3$  Hz, 2H), 7.73 (s, 1H), 7.26–7.19 (m, 4H), 7.15–7.10 (m, 3H), 7.07 (d,  $J = 8.3$  Hz, 2H), 6.71 (dd,  $J = 8.2, 1.4$  Hz, 1H), 6.26 (s, 1H), 4.83 (s, 1H), 3.61 (s, 3H), 3.35 (s, 3H), 2.68–2.56 (m, 4H), 2.26 (s, 3H), 1.88–1.74 (m, 4H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.2, 167.1, 143.3, 138.5, 136.9, 135.34, 135.28, 129.9, 128.9, 128.7, 128.6, 127.9, 127.4, 127.3, 120.6, 117.1, 112.0, 109.7, 65.1, 62.6, 53.0, 52.6, 23.2, 23.1, 21.4, 20.8; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 2952, 1743, 1435,

1335, 1151, 1030, 907, 811, 730, 666; HRMS (ESI-TOF) calcd for  $C_{31}H_{36}N_3O_6S$  [ $M + NH_4$ ] $^+$  578.2319, found 578.2310.

**Dimethyl 2-(4-methyl-N-((9-methyl-2,3,4,9-tetrahydro-1H-carbazol-7-yl)(phenyl)methyl)phenylsulfonamido)malonate (4ae):** white solid, 48 mg, 42% yield; mp 167–169 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.92 (d,  $J = 8.3$  Hz, 2H), 7.34–7.19 (m, 7H), 7.13 (d,  $J = 8.0$  Hz, 2H), 6.68 (d,  $J = 8.2$  Hz, 1H), 6.34 (s, 1H), 4.86 (s, 1H), 3.58 (s, 3H), 3.52 (s, 3H), 3.51 (s, 3H), 2.71–2.63 (m, 4H), 2.30 (s, 3H), 1.97–1.77 (m, 4H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.12, 167.09, 143.3, 138.4, 136.9, 136.6, 136.4, 129.3, 129.1, 128.9, 128.7, 127.9, 127.6, 126.4, 119.8, 117.1, 109.3, 108.9, 65.0, 62.4, 52.80, 52.77, 28.8, 23.1, 22.0, 21.4, 21.0; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 2916, 2840, 1764, 1745, 1469, 1334, 1289, 1156, 1030, 813, 666; HRMS (ESI-TOF) calcd for  $C_{33}H_{38}N_3O_6S$  [ $M + NH_4$ ] $^+$  592.2476, found 592.2479.

**Dimethyl 2-(4-methyl-N-((9-methyl-2,3,4,9-tetrahydro-1H-carbazol-6-yl)(phenyl)methyl)phenylsulfonamido)malonate (5ae):** white solid, 23 mg, 20% yield; mp 142–144 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.90 (d,  $J = 8.3$  Hz, 2H), 7.35–7.29 (m, 2H), 7.24–7.18 (m, 4H), 7.14 (d,  $J = 8.0$  Hz, 2H), 7.07 (d,  $J = 8.5$  Hz, 1H), 6.86 (dd,  $J = 8.4, 1.7$  Hz, 1H), 6.31 (s, 1H), 4.86 (s, 1H), 3.67 (s, 3H), 3.57 (s, 3H), 3.45 (s, 3H), 2.68 (t,  $J = 5.9$  Hz, 2H), 2.58 (t,  $J = 6.0$  Hz, 2H), 2.32 (s, 3H), 1.96–1.88 (m, 2H), 1.84–1.78 (m, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  167.3, 167.0, 143.3, 138.6, 137.0, 136.4, 136.2, 128.9, 128.83, 128.77, 127.9, 127.3, 127.2, 126.8, 122.0, 118.9, 109.4, 108.0, 65.1, 62.5, 53.0, 52.6, 29.0, 23.12, 23.07, 22.0, 21.4, 20.9; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 2925, 2851, 1744, 1434, 1337, 1245, 1152, 1042, 807, 701, 668; HRMS (ESI-TOF) calcd for  $C_{32}H_{35}N_2O_6S$  [ $M + H$ ] $^+$  575.2210, found 575.2214.

**(3aR,8bR,9S)-Dimethyl 9-phenyl-10-tosyl-1,2,3,4-tetrahydro-3a,8b-(methanoiminomethano)cyclopenta[b]indole-11,11-dicarboxylate (3af-1, minor diastereoisomer of 3af):** white solid, 30 mg, 27% yield; mp 273–274 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.26–7.15 (m, 4H), 6.92 (tt,  $J = 7.3, 1.2$  Hz, 1H), 6.83–6.74 (m, 3H), 6.36 (d,  $J = 7.8$  Hz, 1H), 6.29 (t,  $J = 7.5$  Hz, 1H), 6.22 (td,  $J = 7.5, 0.9$  Hz, 1H), 6.10 (d,  $J = 7.9$  Hz, 1H), 5.86 (d,  $J = 7.5$  Hz, 1H), 5.68 (s, 1H), 4.00 (s, 3H), 3.99 (s, 3H), 3.96 (s, 1H), 2.66–2.56 (m, 1H), 2.37–2.18 (m, 2H), 2.21 (s, 3H), 2.02–1.86 (m, 2H), 1.69–1.52 (m, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  170.1, 167.7, 148.8, 142.5, 137.8, 137.2, 131.5, 129.7, 129.0, 128.6, 127.8, 127.7, 127.1, 127.01, 127.00, 124.9, 119.2, 108.6, 88.1, 85.1, 75.7, 70.5, 53.1, 52.7, 40.64, 40.59, 28.6, 21.3; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3353, 2952, 1761, 1599, 1489, 1334, 1231, 1154, 1037, 750, 700; HRMS (ESI-TOF) calcd for  $C_{30}H_{31}N_2O_6S$  [ $M + H$ ] $^+$  547.1897, found 547.1907.

**(3aR,8bR,9R)-Dimethyl 9-phenyl-10-tosyl-1,2,3,4-tetrahydro-3a,8b-(methanoiminomethano)cyclopenta[b]indole-11,11-dicarboxylate (3af-2, major diastereoisomer of 3af):** white solid, 47 mg, 43% yield; mp 208–209 °C;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.45 (d,  $J = 7.5$  Hz, 1H), 7.37 (t,  $J = 7.4$  Hz, 1H), 7.31 (d,  $J = 8.4$  Hz, 2H), 7.21–7.16 (m, 1H), 7.10 (dd,  $J = 7.4, 0.7$  Hz, 1H), 7.04 (td,  $J = 7.7, 1.2$  Hz, 1H), 6.95 (d,  $J = 8.1$  Hz, 2H), 6.82–6.76 (m, 3H), 6.53 (d,  $J = 7.6$  Hz, 1H), 5.76 (s, 1H), 4.19 (br, 1H), 4.00 (s, 3H), 3.42 (s, 3H), 2.33 (s, 3H), 1.97 (dd,  $J = 12.7, 5.2$  Hz, 1H), 1.80–1.70 (m, 2H), 1.60–1.42 (m, 2H), 1.20 (dd,  $J = 13.1, 6.7$  Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  168.6, 168.1, 149.1, 143.0, 137.8, 137.3, 130.6, 129.3, 128.9, 128.3, 128.1, 127.9, 127.5, 127.3, 122.9, 119.7, 108.1, 85.4, 84.0, 74.8, 66.9, 52.8, 51.6, 40.3, 40.1, 24.8, 21.4; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3378, 2949, 2870, 1752, 1599, 1484, 1340, 1249, 1154, 1052, 920, 746, 704, 667; HRMS (ESI-TOF) calcd for  $C_{30}H_{31}N_2O_6S$  [ $M + H$ ] $^+$  547.1897, found 547.1904.

**(1S,3aR,8bS)-Dimethyl 8b-methyl-1-phenyl-2-tosyl-1,3a,4,8b-tetrahydropyrrolo[3,4-b]indole-3,3(2H)-dicarboxylate (3ag):** white solid; mp 215–216 °C, 47 mg, 45% yield.  $^1H$  NMR (600 MHz,  $DMSO-d_6$ , 80 °C)  $\delta$  7.20 (d,  $J = 7.8$  Hz, 2H), 6.92 (d,  $J = 8.4$  Hz, 2H), 6.85 (t,  $J = 6.6$  Hz, 1H), 6.68–6.86 (m, 5H), 6.36 (d,  $J = 7.2$  Hz, 1H), 6.09 (t,  $J = 7.2$  Hz, 1H), 5.95 (d,  $J = 7.8$  Hz, 1H), 5.78 (br, 1H), 5.11 (s, 1H), 4.51 (d,  $J = 4.8$  Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 2.21 (s, 3H), 1.66 (s, 3H);  $^{13}C$  NMR (150 MHz,  $DMSO-d_6$ , 80 °C)  $\delta$  168.6, 166.4, 149.1, 142.1, 137.3, 136.7, 131.9, 128.1, 127.8, 127.5, 126.9, 126.3, 126.2, 123.6, 117.1, 108.4, 81.5, 77.3, 76.8, 57.3, 52.3, 52.0, 26.7, 20.3; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3354, 3055, 2953, 1764, 1735, 1609,

1455, 1287, 1145, 1051, 990, 737, 678; HRMS (ESI-TOF) calcd for  $C_{28}H_{29}N_2O_6S$  [ $M + H$ ] $^+$  521.1741, found 521.1738.

**Dimethyl 2-(4-methyl-N-((3-methyl-1H-indol-6-yl)(phenyl)methyl)phenylsulfonamido)malonate (4ag):** white solid; mp 144–145 °C, 52 mg, 50% yield.  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  9.45 (s, 1H), 7.57 (d,  $J = 8.1$  Hz, 2H), 7.42 (d,  $J = 7.8$  Hz, 1H), 7.33–7.12 (m, 7H), 7.10–6.97 (m, 3H), 6.35 (s, 1H), 5.06 (s, 1H), 3.62 (s, 3H), 3.47 (s, 3H), 2.22 (s, 3H), 1.79 (s, 3H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  167.9, 166.8, 143.8, 136.4, 136.0, 135.6, 129.8, 129.01, 128.96, 128.9, 128.4, 128.2, 127.8, 122.0, 119.0, 118.3, 111.1, 109.8, 62.6, 58.7, 53.5, 52.9, 21.4, 8.7; IR (thin film):  $\nu_{max}$  ( $cm^{-1}$ ) 3392, 2943, 1766, 1737, 1493, 1339, 1265, 1143, 1047, 763, 663; HRMS (ESI-TOF) calcd for  $C_{28}H_{29}N_2O_6S$  [ $M + H$ ] $^+$  521.1741, found 521.1744.

**Computational Methods.** All calculations in this paper were performed with the Gaussian09 package.<sup>16</sup> The density functional theory (DFT) method was employed using the M06 functional.<sup>17</sup> SDD basis sets<sup>18</sup> with the associated effective core potential was used for Sc and the 6-31G(d) basis sets<sup>19</sup> for other atoms. The key word “Sd” was specified to use five pure d functions in the calculations. Optimizations were conducted without any constraint using the SMD model<sup>20</sup> in toluene ( $\epsilon = 2.3741$ ). Frequency analyses were carried out to confirm each structure being a minimum (no imaginary frequency) or a transition state (only one imaginary frequency). The energies were further estimated by single-point calculations at the M06/SDD/6-311++G(d,p) level of theory. The Gibbs free energies in toluene ( $\Delta G$ ) were discussed throughout this paper. The orbital composition analyses were conducted using Multiwfn.<sup>21</sup> All figures of the calculated 3D structures were prepared using CYLview.<sup>22</sup> Details of the computational work can be found in the Supporting Information.

## ■ ASSOCIATED CONTENT

### ☉ Supporting Information

Figures, tables, text, and CIF files giving  $^1H$  and  $^{13}C$  NMR spectra of all new compounds, crystallographic data for **3aa**, **4aa**, and **5aa**, complete citation of ref 16, computational details (including the figures not presented in the text), 3D structures, and Cartesian coordinates of all calculated stationary points. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

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