JOC The Journal of Organic Chemistry

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Preparation of 3-Aryl-2-aminoindoles via Rhodium-Catalyzed Coupling Reaction between 2-Arylpyridines and 3-Diazoindolin-2-imines

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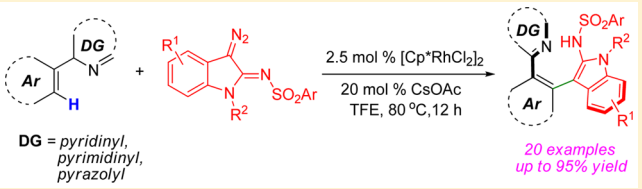
Supporting Information

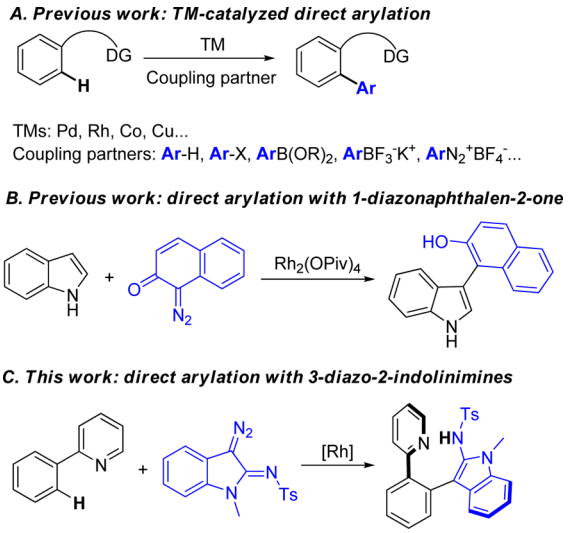
ABSTRACT: Rhodium-catalyzed coupling reaction of 3-diazoindolin-2-imines with 2-arylpyridines, 2-phenylpyrimidines, or 1-phenylpyrazoles furnished the corresponding 3-aryl-2-aminoindoles in moderate to excellent yields. A variety of functional groups were tolerant to the reaction conditions.



Biaryls are privilege scaffolds in a variety of natural compounds,[1,2] bioactive pharmaceuticals[3,4] as well as optoelectronic materials.[5−7] The restricted free rotation of the carbon−carbon bond between two aryl rings of biaryls is believed to be the key factor for the aggregation induced emission effect (AIE)[8] and the axial chirality of 2,2′-disubstituted biphenyl molecules.[9] Moreover, biaryl compounds are an important class of synthetic intermediates for the preparation of several helicenes which exhibit extraordinary optical and electronic properties in material science.[10] Therefore, preparation of specific biaryls and heterocyclic-aryl compounds, especially including indole is a unique challenge in the discovery of drugs, fluorophores, and chiral reagents.

Transition-metal-catalyzed aryl−aryl coupling reactions represent a powerful tool for the synthesis of biaryls.[11] The common methods for this transformation can be classified into two categories according to the starting materials. One starts from aryl halides, such as the well-known copper-catalyzed Ullmann coupling, the palladium-catalyzed Suzuki, Stille, Negishi as well as Hiyama couplings, and the nickel-catalyzed Kumada coupling. Another starts from arenes via direct C−H activation/arylation (Scheme 1A). In this blooming branch, a number of coupling partners have been applied, including arenes,[12] aryl halides,[13] arylboron,[14] and aryldiazonium salts.[15] Recently, α-diazo carbonyl compounds were also demonstrated to be excellent partners for some transition-metal-catalyzed coupling reactions, including alkylation,[16] alkenylation,[17] and the directing group (DG) participated heterocyclization.[18] Among these transformations, however, only one example involving the direct arylation of a metal-activated C−H bond is the rhodium(II)-catalyzed coupling of indoles with 1-diazonaphthalen-2-ones (Scheme 1B).[19] In continuation of our interest in the chemistry of 3-diazoindolin-2-imines,[20] we herein report an efficient preparation of 3-aryl-2-aminoindoles through a rhodium-catalyzed coupling reaction between 2-arylpyridines and 3-diazoindolin-2-imines (Scheme 1C). This transformation involves the direct arylation of a metal-activated C−H bond with diazo compounds as arylation reagent.[21]

Scheme 1. Previous TM-Catalyzed Direct Arylation and Our Work

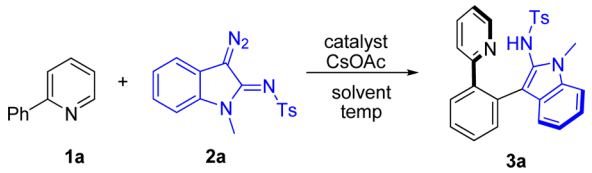


We initiated our investigation with the reaction between 2-phenylpyridine (**1a**) and 3-diazoindolin-2-imine (**2a**) as the model reaction. After the reaction was conducted in the presence of $[Cp^*RhCl_2]_2$ (2.5 mol %) and CsOAc (0.2 equiv) in 2,2,2-trifluoroethanol (TFE) at 80 °C for 12 h, the arylated product **3a** was isolated in 95% yield (Table 1, entry 1). The structure of **3a** was established by ^{1}HNMR, ^{13}CNMR, and HRMS. Further confirmation was done by X-ray crystallographic analysis of its analogue **3c** (see the Supporting Information). Single crystals of compound **3c** were grown from hexane/ethyl acetate (6:1), and the structure is attractive

Received: July 13, 2016
Published: September 12, 2016

DOI: 10.1021/acs.joc.6b01678
J. Org. Chem. 2016, 81, 9433−9437

Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a

entry	catalyst	solvent	temp (°C)	yield (%)[b]
1	2.5 mol % $[Cp^*RhCl_2]_2$	TFE	80	95
2	5.0 mol % $RhCl_3 \cdot 3H_2O$	TFE	80	trace
3	5.0 mol % $Pd(OAc)_2$	TFE	80	trace
4	5.0 mol % $Ni(OAc)_2$	TFE	80	NR
5	5.0 mol % $Cu(OTf)_2$	TFE	80	ND
6	2.5 mol % $[RuCl_2(p\text{-cymene})]_2$	TFE	80	ND
7	2.5 mol % $[Cp^*RhCl_2]_2$	MeOH	80	73
8	2.5 mol % $[Cp^*RhCl_2]_2$	DCE	80	52
9	2.5 mol % $[Cp^*RhCl_2]_2$	MeCN	80	NR
10	2.5 mol % $[Cp^*RhCl_2]_2$	MePh	80	NR
11	2.5 mol % $[Cp^*RhCl_2]_2$	TFE	60	74
12	1.0 mol % $[Cp^*RhCl_2]_2$	TFE	80	68

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (1−5 mol %), CsOAc (0.04 mmol), solvent (2 mL), air, 12 h. [b]Isolated yield.

with three aryls standing in a helix. The dihedral angles for pyridine/benzene and benzene/indole are 47.9° and 53.2°, respectively. Two molecules attract each other through intermolecular hydrogen bonding arising from the sulfonamide functional group and exist as a dimer. Delighted by this preliminary result, the reaction conditions were screened. This reaction was quite sensitive to the catalyst. Altering the catalyst to rhodium trichloride or palladium acetate, **3a** could only be detected by thin layer chromatography (TLC) and was not isolable (Table 1, entries 2 and 3). When nickel acetate was used as catalyst, no reaction occurred (Table 1, entry 4). Altering the catalyst to $Cu(OTf)_2$ or $[RuCl_2(p\text{-cymene})]_2$, the starting materials reacted but **3a** was not detectable (Table 1, entries 5 and 6). Moreover, the reaction was solvent-dependent. Altering the solvent to methanol and 1,2-dichloroethane (DCE), **3a** was obtained in 73% and 52% yields, respectively (Table 1, entries 7 and 8). However, no reaction occurred in acetonitrile or toluene (Table 1, entries 9 and 10). Decreasing the reaction temperature or decreasing the catalyst loading amount significantly decreased the yield (Table 1, entries 11 and 12). Finally, the optimal reaction conditions were established (Table 1, entry 1).

With the optimized reaction conditions in hand, we investigated the scope of the biaryl formation with different groups substituted on the 2-phenylpyridine (Figure 1). With the methyl group occupied on the *ortho* position of the benzene ring in 2-phenylpyridine, 2-(*o*-tolyl)pyridine afforded the desired product **3b** in relatively lower yield (62%) because of the steric hindrance. 2-Phenylpyridines bearing an electron-withdrawing or electron-donating group on the *para* position of the benzene ring afforded the corresponding products **3c−i** in apparently decreased yields (77%−86%) in comparison with the yield of the naked **3a**. Among these examples, relatively higher yields were observed for those substrates with an electron-withdrawing group (**3c−g**) where the acidity of the *ortho* C−H bond was increased. It was also noticeable that the formyl and ester groups could tolerate the reaction conditions and survived after the reaction completed. 2-(Thiophen-2-yl)pyridine and 2-(benzo[*b*]thiophen-2-yl)pyridine could work well in this transformation to afford **3j** and **3k** in 89% and 77%

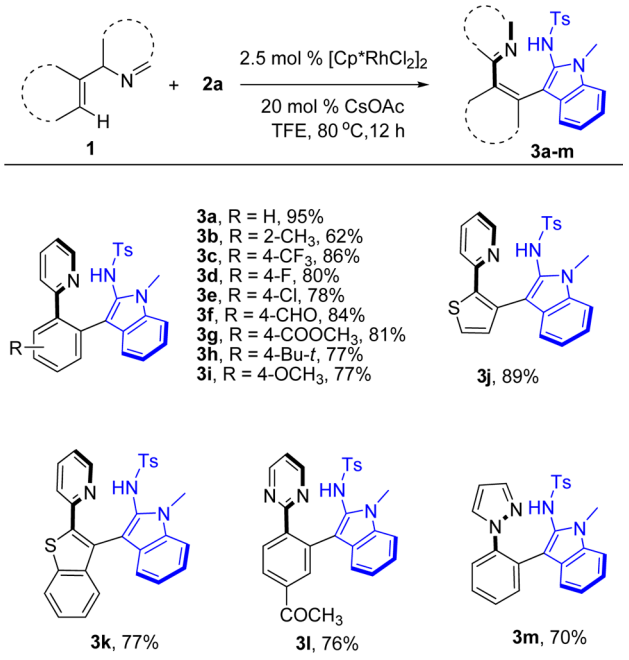


Figure 1. Preparation of compounds **3a−m**.

yields, respectively. Furthermore, pyrimidinyl and pyrazolyl could be used as the directing group. Thus, **3l** (76% yield) and **3m** (70% yield) were prepared from 2-(4-acetylphenyl)pyrimidine and 1-phenylpyrazole, respectively.

Subsequently, we tested the scope of 3-diazoindolin-2-imines **2**. As shown in Figure 2, substituents on the 1-position of the indole ring could be altered to isopropyl (**3n**, 73% yield) and benzyl (**3o**, 62% yield). The 5-position of indole could be substituted by either an electron-donating group or an electron-withdrawing group. Thus, compounds **3p−s** were isolated in 60−77% yields. The electronic effect of these substituents was not apparent. Moreover, the sulfonyl group could be changed into benzenesulfonyl (**3t**, 50% yield).

On the basis of these results and the published works,[18,22] a catalytic cycle was proposed as shown in Scheme 2. First,

DOI: 10.1021/acs.joc.6b01678
J. Org. Chem. 2016, 81, 9433−9437

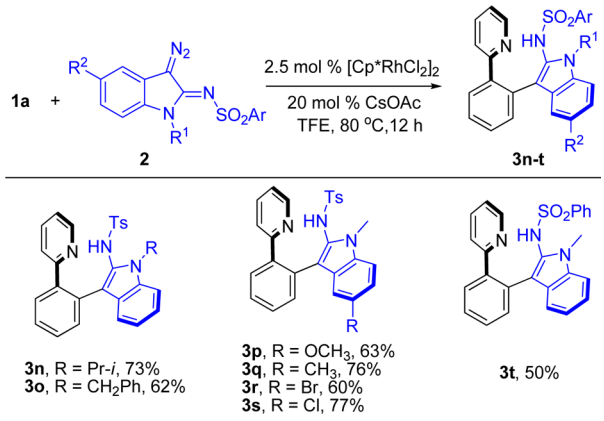
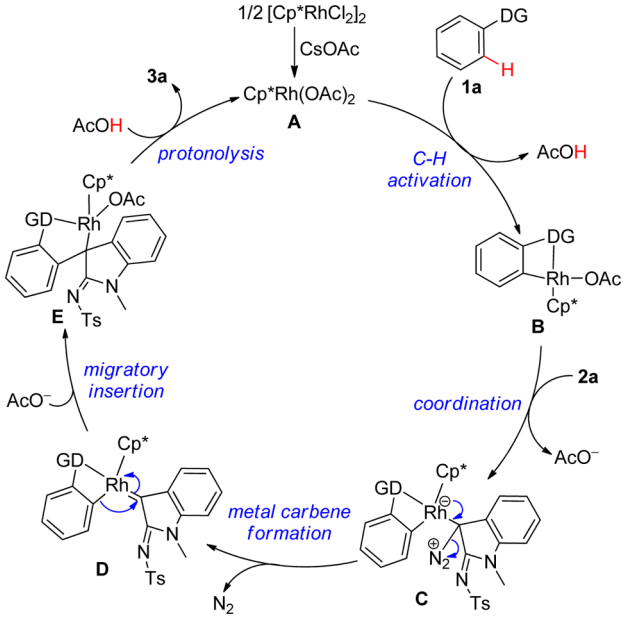


Figure 2. Preparation of compounds **3n−t**.

Scheme 2. Proposed Mechanism for the Formation of 3a



$[Cp^*RhCl_2]_2$ undergoes ligand exchange with CsOAc to form active rhodium species **A**.[18a,22] Then, **1a** coordinates to the rhodium center and the *ortho* C−H bond adjacent to the pyridinyl group is cleaved to give the rhodacyclic complex **B**,[18b] which coordinates with the diazo compound **2a** to form the diazonium intermediate **C**.[18c,22] Subsequently, extrusion of nitrogen from **C** may afford Rh-carbene **D**, which undergoes a 1,2-migratory insertion to generate complex **E**. Finally, protonolysis of **E** provides **3a**.

In conclusion, we have developed a rhodium-catalyzed coupling reaction of 3-diazoindolin-2-imines with 2-arylpyridines, 2-phenylpyrimidines, or 1-phenylpyrazoles, which furnished 3-aryl-2-aminoindoles in moderate to excellent yields. The reaction proceeds through a catalytic cycle involving C−H bond activation as well as possible metal carbene formation and subsequent 1,2-migratory insertion. Furthermore, a variety of functional groups were tolerant to the reaction conditions.

EXPERIMENTAL SECTION

General Information. Melting points were measured with a micro melting point apparatus. ^{1}H NMR spectra were obtained at 600 or 400 MHz. The chemical shifts were quoted in parts per million (ppm) and referenced to 0 ppm for internal tetramethylsilane (TMS). ^{13}C NMR spectra were obtained at 150 or 100 MHz and referenced to the center line of a triplet at 77.0 ppm of $CDCl_3$. The following abbreviations are used to describe peak patterns as appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants J were reported in hertz unit (Hz). Infrared spectra were obtained with an FTIR spectrometer. All high-resolution mass spectra (HRMS) were recorded by using an electron ionization time-of-flight (EI-TOF) mass spectrometer. Flash column chromatography was performed employing 300−400 mesh silica gel.

Substrates **1a−l** were prepared according to the published procedures.[23] Compound **1m** is commercially available. Compounds **2a−h** were prepared using the published procedures.[20a,b]

General Procedure for the Reaction of 2-Arylpyridine and 3-Diazoindolin-2-imines. A 25 mL round-bottom flask was charged with 2-arylpyridine (0.2 mmol), 3-diazoindolin-2-imine (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.005 mmol), and TFE (2 mL). The reaction mixture was stirred at 80 °C (oil bath) for 12 h. After cooling to room temperature, the resulted mixture was evaporated under reduced pressure and the residue was purified by flash column chromatography on a silica gel with petroleum ether/ethyl acetate (3:1) to give pure product.

*4-Methyl-N-(1-methyl-3-(2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)-benzenesulfonamide (**3a**).* Yellow solid; yield 95% (86 mg); mp 181−182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.58 (s, 1H), 8.60 (d, J = 4.8 Hz, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.30−7.28 (m, 5H), 7.24−7.13 (m, 4H), 7.01−6.96 (m, 2H), 6.80 (d, J = 7.7 Hz, 2H), 6.58 (d, J = 7.5 Hz, 1H), 3.87 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 147.0, 142.7, 139.1, 137.4, 136.5, 134.8, 132.7, 131.0, 130.2, 129.8, 129.0, 127.8, 127.0, 126.7, 126.1, 125.1, 122.3, 122.0, 119.6, 119.1, 109.9, 109.5, 29.9, 21.5. IR (film): 3057, 2885, 1593, 1561, 1475, 1330, 1184, 1091, 711, 749, 677 cm^{-1}. HRMS (EI-TOF) calcd for $C_{27}H_{23}N_3O_2S$ $[M]^+$ 453.1511, found 453.1509.

*4-Methyl-N-(1-methyl-3-(3-methyl-2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)benzenesulfonamide (**3b**).* White solid; yield 62% (57 mg); mp 179−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.13 (s, 1H), 8.63−8.52 (m, 1H), 7.36 (td, J = 7.7, 1.8 Hz, 1H), 7.21−7.18 (m, 3H), 7.16−7.14 (m, 1H), 7.12−7.06 (m, 2H), 7.00 (d, J = 7.6 Hz, 1H), 6.95−6.91 (m, 1H), 6.80−6.73 (m, 4H), 6.30 (d, J = 7.6 Hz, 1H), 3.64 (s, 3H), 2.25 (s, 3H), 1.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 148.3, 142.7, 139.4, 137.1, 136.2, 136.0, 134.9, 131.1, 129.04, 128.99, 128.5, 127.9, 127.4, 126.7, 126.4, 124.9, 122.4, 122.0, 119.5, 119.1, 110.5, 109.5, 29.9, 21.5, 20.4. IR (film): 3055, 2848, 1590, 1562, 1471, 1331, 1160, 1092, 793, 736, 671 cm^{-1}. HRMS (EI-TOF) calcd for $C_{28}H_{25}N_3O_2S$ $[M]^+$ 467.1667, found 467.1659.

*4-Methyl-N-(1-methyl-3-(2-(pyridin-2-yl)-5-(trifluoromethyl)-phenyl)-1H-indol-2-yl)benzenesulfonamide (**3c**).* White solid; yield 86% (89 mg); mp 183−185 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.36 (s, 1H), 8.66 (dd, J = 5.0, 0.8 Hz, 1H), 7.66 (td, J = 7.8, 1.8 Hz, 1H), 7.51 (dd, J = 8.1, 1.4 Hz, 1H), 7.42 (d, J = 8.1 Hz, 1H), 7.33−7.28 (m, 4H), 7.25−7.21 (m, 1H), 7.15 (dd, J = 7.9, 3.2 Hz, 2H), 7.06−7.02 (m, 2H), 6.84 (d, J = 8.1 Hz, 2H), 3.88 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 147.5, 143.4, 142.5, 137.7, 136.7, 134.9, 132.3, 131.0, 130.1, 130.0 (q, J = 32.5 Hz), 129.6 (q, J = 3.8 Hz), 129.0, 126.8, 126.7, 126.4 (q, J = 273.5 Hz), 125.2, 123.14 (q, J = 3.6 Hz), 123.06, 122.4, 120.1, 118.7, 109.8, 108.5, 30.1, 21.2. IR (film): 3057, 2885, 1592, 1563, 1476, 1319, 1164, 1126, 1087, 794, 746, 675 cm^{-1}. HRMS (EI-TOF) calcd for $C_{28}H_{22}F_3N_3O_2S$ $[M]^+$ 521.1385, found 521.1384.

*N-(3-(5-Fluoro-2-(pyridin-2-yl)phenyl)-1-methyl-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3d**).* White solid; yield 80% (75 mg); mp 201−202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.54 (s, 1H), 8.60−8.58 (m, 1H), 7.61 (td, J = 7.7, 1.7 Hz, 1H), 7.29 (d, J = 8.3 Hz, 3H), 7.26−7.20 (m, 3H), 7.19−7.16 (m, 1H), 7.11 (d, J = 7.9 Hz, 1H), 7.01−6.94 (m, 2H), 6.87 (d, J = 8.0 Hz, 2H), 6.24 (dd, J = 9.9, 2.7 Hz, 1H), 3.87 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 160.9, 158.9, 147.1, 143.5, 137.5, 136.5, 135.5, 134.8, 133.6 (d, J = 8.9 Hz), 131.9 (d, J = 8.8 Hz), 129.9, 128.0 (d, J = 215.1 Hz), 126.6, 125.1, 122.3 (d, J = 28.4 Hz), 119.9, 119.1 (d, J = 21.1 Hz), 118.8, 113.4 (d, J = 21.3 Hz), 109.6, 108.9, 30.0, 21.2 (d, J = 2.5 Hz). IR (film): 3057, 2913, 1596, 1566, 1472, 1329, 1267, 1162, 1090, 789,

DOI: 10.1021/acs.joc.6b01678
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736, 675 cm^{-1}. HRMS (EI-TOF) calcd for $C_{27}H_{22}FN_3O_2S$ $[M]^+$ 471.1417, found 471.1419.

*N-(3-(5-Chloro-2-(pyridin-2-yl)phenyl)-1-methyl-1H-indol-2-yl)-4-methylbenzenesulfonamide(**3e**).* White solid; yield 78% (76 mg); mp 185−186 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 11.51 (s, 1H), 8.61 (d, J = 4.7 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 7.31 (t, J = 7.8 Hz, 3H), 7.25−7.20 (m, 4H), 7.17 (d, J = 7.9 Hz, 1H), 7.13 (d, J = 7.9 Hz, 1H), 7.03 (t, J = 7.5 Hz, 1H), 6.91 (d, J = 7.9 Hz, 2H), 6.64 (s, 1H), 3.87 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.7, 147.2, 143.5, 137.7, 137.6, 136.5, 134.8, 134.0, 133.0, 132.6, 131.5, 130.1, 129.1, 126.9, 126.7, 126.6, 125.1, 122.7, 122.2, 119.9, 118.9, 109.7, 108.6, 30.0, 21.8. IR (film): 3055, 2913, 1592, 1568, 1472, 1329, 1161, 1091, 788, 735, 675 cm^{-1}. HRMS (EI-TOF) calcd for $C_{27}H_{22}ClN_3O_2S$ $[M]^+$ 487.1116, found 487.1115.

*N-(3-(5-Formyl-2-(pyridin-2-yl)phenyl)-1-methyl-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3f**).* White solid; yield 84% (80 mg); mp 227−228 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 11.32 (s, 1H), 9.80 (s, 1H), 8.65 (d, J = 4.3 Hz, 1H), 7.79 (dd, J = 8.0, 1.7 Hz, 1H), 7.68 (td, J = 7.8, 1.6 Hz, 1H), 7.46 (d, J = 7.9 Hz, 1H), 7.31 (dd, J = 14.5, 8.2 Hz, 4H), 7.26−7.18 (m, 2H), 7.12 (d, J = 7.3 Hz, 2H), 7.03 (dd, J = 11.0, 3.9 Hz, 1H), 6.80 (d, J = 8.1 Hz, 2H), 3.89 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.5, 158.4, 147.4, 143.0, 137.8, 136.8, 135.6, 134.9, 132.5, 131.2, 130.1, 129.1, 127.0, 126.7, 126.0, 125.1, 123.1, 122.4, 120.0, 118.7, 109.8, 108.6, 30.1, 21.5. IR (film): 3055, 2885, 2721, 1698, 1592, 1580, 1475, 1273, 1188, 1090, 749, 676 cm^{-1}. HRMS (EI-TOF) calcd for $C_{28}H_{23}N_3O_3S$ $[M]^+$ 481.1460, found 481.1463.

*Methyl 3-(1-Methyl-2-(4-methylphenylsulfonamido)-1H-indol-3-yl)-4-(pyridin-2-yl)benzoate (**3g**).* Light red solid; yield 81% (82 mg); mp 170−171 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 11.43 (s, 1H), 8.65−8.64 (m, 1H), 7.93 (dd, J = 8.1, 1.7 Hz, 1H), 7.66 (td, J = 7.8, 1.7 Hz, 1H), 7.37−7.35 (m, 2H), 7.33−7.27 (m, 4H), 7.25−7.20 (m, 1H), 7.16 (t, J = 8.4 Hz, 2H), 7.02 (t, J = 7.5 Hz, 1H), 6.79 (d, J = 8.0 Hz, 2H), 3.93 (s, 3H), 3.88 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 158.8, 147.3, 142.9, 137.7, 136.6, 134.9, 134.3, 131.5, 130.5, 130.0, 129.5, 129.0, 127.3, 126.8, 125.2, 122.9, 122.2, 119.9, 119.0, 109.6, 109.0, 52.1, 30.0, 21.2. IR (film): 3056, 2847, 1720, 1591, 1473, 1434, 1331, 1286, 1240, 1162, 1090, 744, 675 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{25}N_3O_4S$ $[M]^+$ 511.1566, found 511.1570.

*N-(3-(5-(tert-Butyl)-2-(pyridin-2-yl)phenyl)-1-methyl-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3h**).* Light yellow solid; yield 77% (78 mg); mp 198−199 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 12.02 (s, 1H), 8.63 (d, J = 4.2 Hz, 1H), 7.63 (td, J = 7.8, 1.6 Hz, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.32−7.28 (m, 3H), 7.24−7.18 (m, 4H), 7.03−6.99 (m, 2H), 6.83 (d, J = 8.1 Hz, 2H), 3.87 (s, 3H), 2.23 (s, 3H), 1.24 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 150.9, 146.9, 142.1, 137.8, 137.5, 136.4, 135.0, 130.7, 130.5, 130.1, 129.7, 128.9, 127.3, 126.7, 125.5, 123.7, 122.2, 121.9, 119.7, 119.2, 110.3, 109.5, 34.4, 31.2, 30.1, 21.7. IR (film): 3056, 2967, 1594, 1571, 1473, 1329, 1160, 1091, 743, 676 cm^{-1}. HRMS (EI-TOF) calcd for $C_{31}H_{31}N_3O_2S$ $[M]^+$, 509.2137, found 509.2140.

*N-(3-(5-Methoxy-2-(pyridin-2-yl)phenyl)-1-methyl-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3i**).* White solid; yield 77% (74 mg); mp 227−228 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 11.98 (s, 1H), 8.58 (dd, J = 5.0, 0.9 Hz, 1H), 7.61 (td, J = 7.7, 1.8 Hz, 1H), 7.30 (dd, J = 8.6, 2.3 Hz, 3H), 7.24−7.17 (m, 4H), 7.14 (d, J = 7.9 Hz, 1H), 7.02−6.98 (m, 1H), 6.84−6.80 (m, 3H), 6.10 (d, J = 2.4 Hz, 1H), 3.88 (s, 3H), 3.65 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 159.0, 146.9, 142.9, 137.4, 136.9, 134.8, 132.6, 131.6, 129.9, 128.8, 126.9, 125.2, 121.99, 121.96, 119.6, 119.1, 116.5, 113.2, 110.0, 109.5, 54.8, 29.9, 21.2. IR (film): 3054, 2888, 1597, 1562, 1471, 1328, 1277, 1226, 1161, 1090, 746, 676 cm^{-1}. HRMS (EI-TOF) calcd for $C_{28}H_{25}N_3O_3S$ $[M]^+$ 483.1617, found 483.1614.

*4-Methyl-N-(1-methyl-3-(2-(pyridin-2-yl)thiophen-3-yl)-1H-indol-2-yl)benzenesulfonamide (**3j**).* Yellow solid; yield 89% (81 mg); mp 198−199 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 12.59 (s, 1H), 8.65−8.63 (m, 1H), 7.70 (td, J = 7.8, 1.8 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.29−7.20 (m, 5H), 7.07−7.01 (m, 2H), 6.85 (d, J = 8.1 Hz, 2H), 6.41 (d, J = 5.1 Hz, 1H), 3.96 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 147.8, 142.7, 137.8, 136.4, 135.3, 134.9, 132.8, 131.7, 131.0, 128.8, 126.7, 126.6, 125.2, 124.2, 122.2, 122.1, 119.8, 119.3, 109.7, 105.1, 30.1, 21.5. IR (film): 3054, 2699, 1589, 1525, 1474, 1324, 1159, 1091, 736, 670 cm^{-1}. HRMS (EI-TOF) calcd for $C_{25}H_{21}N_3O_2S_2$ $[M]^+$ 459.1075, found 459.1075.

*4-Methyl-N-(1-methyl-3-(2-(pyridin-2-yl)benzo[b]thiophen-3-yl)-1H-indol-2-yl)benzenesulfonamide (**3k**).* Light yellow solid; yield 77% (90 mg); mp 198−199 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 12.13 (s, 1H), 8.67 (d, J = 4.4 Hz, 1H), 7.74−7.71 (m, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.33−7.27 (m, 2H), 7.24−7.17 (m, 3H), 7.10−7.07 (m, 1H), 6.97−6.92 (m, 3H), 6.42 (d, J = 8.1 Hz, 2H), 4.00 (s, 3H), 1.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 148.1, 141.9, 140.3, 138.4, 137.7, 136.3, 135.8, 134.9, 131.8, 128.5, 127.2, 126.1, 125.9, 125.8, 125.1, 123.7, 122.8, 122.1, 121.3, 120.4, 119.6, 109.8, 103.4, 30.1, 21.4. IR (film): 3056, 2885, 1589, 1521, 1476, 1334, 1161, 1092, 745, 665 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{23}N_3O_2S_2$ $[M]^+$ 509.1232, found 509.1232.

*N-(3-(5-Acetyl-2-(pyrimidin-2-yl)phenyl)-1-methyl-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3l**).* Light red solid; yield 76% (75 mg); mp 218−219 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 10.82 (s, 1H), 8.80 (d, J = 5.0 Hz, 2H), 7.93 (dd, J = 8.2, 1.8 Hz, 1H), 7.79 (d, J = 8.2 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.30−7.28 (m, 3H), 7.24−7.21 (m, 2H), 7.08 (d, J = 7.8 Hz, 1H), 7.01 (t, J = 7.1 Hz, 1H), 6.81 (d, J = 8.1 Hz, 2H), 3.94 (s, 3H), 2.48 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9, 166.0, 156.8, 143.2, 141.8, 136.7, 136.6, 134.8, 133.6, 131.8, 131.5, 130.0, 129.1, 127.1, 126.8, 125.8, 122.4, 120.1, 119.6, 119.1, 109.6, 108.8, 30.0, 26.6, 21.3. IR (film): 3053, 2885, 1684, 1569, 1423, 1271, 1162, 1090, 743, 677 cm^{-1}. HRMS (EI-TOF) calcd for $C_{28}H_{24}N_4O_3S$ $[M]^+$ 496.1569, found 496.1566.

*N-(3-(2-(1H-Pyrazol-1-yl)phenyl)-1-methyl-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3m**).* White solid; yield 70% (62 mg); mp 192−193 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.73 (d, J = 1.7 Hz, 1H), 7.34−7.31 (m, 3H), 7.27 (d, J = 1.2 Hz, 1H), 7.25−7.21 (m, 3H), 7.17 (d, J = 2.3 Hz, 1H), 7.08−7.03 (m, 2H), 6.82 (d, J = 8.0 Hz, 2H), 6.71 (dd, J = 7.7, 1.1 Hz, 1H), 6.25 (t, J = 2.1 Hz, 1H), 3.83 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 140.5, 138.8, 136.2, 135.0, 132.9, 131.9, 129.5, 129.15, 129.08, 128.2, 127.1, 127.0, 126.8, 126.3, 122.6, 120.0, 118.8, 109.9, 107.1, 106.8, 30.0, 21.5. IR (film): 3056, 2885, 1598, 1564, 1516, 1476, 1395, 1330, 1163, 1091, 944, 749, 672 cm^{-1}. HRMS (EI-TOF) calcd for $C_{25}H_{22}N_4O_2S$ $[M]^+$ 442.1463, found 442.1468.

*N-(1-Isopropyl-3-(2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3n**).* Light yellow solid; yield 73% (70 mg); mp 177−178 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 11.29 (s, 1H), 8.58 (dd, J = 5.0, 0.8 Hz, 1H), 7.63−7.55 (m, 2H), 7.32−7.25 (m, 4H), 7.24−7.19 (m, 1H), 7.15−7.11 (m, 3H), 6.99−6.93 (m, 2H), 6.81 (d, J = 8.1 Hz, 2H), 6.55 (d, J = 7.6 Hz, 1H), 5.41−5.30 (m, 1H), 2.32 (s, 3H), 1.84 (d, J = 7.0 Hz, 3H), 1.39 (d, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 146.8, 142.7, 137.4, 136.5, 132.7, 132.5, 131.3, 130.0, 129.1, 129.0, 127.9, 126.8, 126.2, 125.2, 122.3, 121.4, 119.4, 119.1, 112.1, 110.1, 46.8, 21.5, 21.2, 21.1. IR (film): 3056, 2884, 1701, 1593, 1458, 1385, 1271, 1162, 1092, 799, 749, 675 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{27}N_3O_2S$ $[M]^+$ 481.1824, found 481.1826.

*N-(1-Benzyl-3-(2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3o**).* White solid; yield 62% (65 mg); mp 191−192 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 11.12 (s, 1H), 8.36 (dd, J = 5.0, 0.8 Hz, 1H), 7.60 (td, J = 7.7, 1.7 Hz, 1H), 7.33−7.26 (m, 4H), 7.20−7.07 (m, 8H), 7.03−6.94 (m, 2H), 6.83 (d, J = 8.1 Hz, 2H), 6.77 (d, J = 6.9 Hz, 2H), 6.59 (d, J = 7.5 Hz, 1H), 6.04 (d, J = 16.7 Hz, 1H), 5.33 (d, J = 16.7 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 147.2, 142.8, 138.1, 137.3, 136.5, 134.3, 132.3, 131.0, 129.9, 129.6, 129.1, 128.3, 127.9, 127.2, 126.9, 126.8, 126.4, 126.3, 125.1, 122.3, 122.1, 119.8, 119.1, 111.1, 110.4, 46.5, 21.5. IR (film): 3056, 2885, 1699, 1593, 1567, 1459, 1330, 1266, 1160, 1091, 734, 673 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{27}N_3O_2S$ $[M]^+$ 529.1824, found 529.1824.

*N-(5-Methoxy-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3p**).* White solid; yield 63% (60 mg); mp 175−176 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 11.46 (s, 1H), 8.60 (d, J = 4.4 Hz, 1H), 7.62 (td, J = 7.7, 1.6 Hz, 1H), 7.30−7.21 (m, 5H),

DOI: 10.1021/acs.joc.6b01678
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7.17 (t, J = 8.9 Hz, 2H), 7.02−6.98 (m, 1H), 6.85 (dd, J = 8.8, 2.4 Hz, 1H), 6.80 (d, J = 8.1 Hz, 2H), 6.60−6.58 (m, 2H), 3.83 (s, 3H), 3.68 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 154.2, 147.1, 142.7, 139.1, 137.4, 136.6, 132.6, 131.2, 130.3, 130.13, 130.08, 129.0, 127.9, 127.1, 126.7, 126.1, 125.1, 122.3, 112.1, 110.3, 109.6, 101.0, 55.9, 30.1, 21.5. IR (film): 3057, 2886, 1623, 1593, 1486, 1271, 1197, 1091, 753 cm^{-1}. HRMS (EI-TOF) calcd for $C_{28}H_{25}N_3O_3S$ [M]$^+$ 483.1617, found 483.1624.

*N-(1,5-Dimethyl-3-(2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3q**).* Light yellow solid; yield 76% (71 mg); mp 168−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (s, 1H), 8.60 (dd, J = 5.0, 0.8 Hz, 1H), 7.61 (td, J = 7.7, 1.7 Hz, 1H), 7.28−7.25 (m, 4H), 7.23−7.13 (m, 3H), 7.03−6.98 (m, 2H), 6.93 (s, 1H), 6.79 (d, J = 8.1 Hz, 2H), 6.57 (d, J = 7.6 Hz, 1H), 3.83 (s, 3H), 2.31 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 147.1, 142.7, 139.2, 137.4, 136.5, 133.2, 132.8, 131.2, 130.2, 129.7, 129.0, 128.9, 127.7, 127.1, 126.8, 126.0, 125.1, 123.5, 122.3, 118.7, 109.4, 109.3, 30.0, 21.5, 21.3. IR (film): 3055, 2885, 1593, 1566, 1488, 1326, 1161, 1090, 752, 658 cm^{-1}. HRMS (EI-TOF) calcd for $C_{28}H_{25}N_3O_2S$ [M]$^+$ 467.1667, found 467.1671.

*N-(5-Bromo-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3r**).* Light yellow solid; yield 60% (63 mg); mp 209−210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.77 (s, 1H), 8.60 (d, J = 4.3 Hz, 1H), 7.66 (td, J = 7.8, 1.6 Hz, 1H), 7.28−7.24 (m, 7H), 7.20−7.14 (m, 2H), 7.03−6.99 (m, 1H), 6.81 (d, J = 8.1 Hz, 2H), 6.52 (d, J = 7.7 Hz, 1H), 3.85 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 147.0, 142.9, 139.2, 137.6, 136.5, 133.5, 132.7, 130.9, 130.32, 130.30, 129.1, 128.6, 128.0, 126.7, 126.4, 125.2, 124.8, 122.5, 121.5, 113.0, 111.1, 109.5, 30.2, 21.5. IR (film): 3057, 2913, 1702, 1593, 1563, 1472, 1327, 1269, 1162, 1090, 793, 750, 675 cm^{-1}. HRMS (EI-TOF) calcd for $C_{27}H_{22}BrN_3O_2S$ [M]$^+$, 531.0616, found 531.0616.

*N-(5-Chloro-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)-4-methylbenzenesulfonamide (**3s**).* Light yellow solid; yield 77% (75 mg); mp 216−217 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.75 (s, 1H), 8.59 (d, J = 4.2 Hz, 1H), 7.65 (td, J = 7.7, 1.7 Hz, 1H), 7.28−7.22 (m, 5H), 7.20−7.17 (m, 2H), 7.13−7.08 (m, 2H), 7.03−6.98 (m, 1H), 6.80 (d, J = 8.1 Hz, 2H), 6.52 (d, J = 7.7 Hz, 1H), 3.85 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 147.0, 142.9, 139.1, 137.6, 136.5, 133.2, 132.6, 131.0, 130.4, 130.3, 129.1, 128.0, 127.9, 126.7, 126.4, 125.4, 125.1, 122.5, 122.2, 118.4, 110.7, 109.6, 30.2, 21.5. IR (film): 3056, 2886, 1701, 1593, 1564, 1473, 1267, 1161, 739, 690 cm^{-1}. HRMS (EI-TOF) calcd for $C_{27}H_{22}ClN_3O_2S$ [M]$^+$ 487.1121, found 487.1119.

*N-(1-Methyl-3-(2-(pyridin-2-yl)phenyl)-1H-indol-2-yl)benzenesulfonamide (**3t**).* Yellow solid; yield 50% (44 mg); mp 97−98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.74 (s, 1H), 8.60 (d, J = 4.9 Hz, 1H), 7.61 (t, J = 7.7 Hz, 1H), 7.41−7.39 (m, 2H), 7.30−7.26 (m, 3H), 7.24−7.19 (m, 3H), 7.17−7.14 (m, 2H), 7.04−6.95 (m, 4H), 6.55 (d, J = 7.7 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 147.0, 139.5, 139.1, 137.5, 134.9, 132.6, 132.2, 131.0, 130.2, 129.6, 128.39, 128.36, 127.0, 126.8, 126.4, 125.1, 122.4, 122.0, 119.6, 119.1, 110.0, 109.5, 30.0. IR (film): 3058, 2885, 1592, 1565, 1475, 1328, 1270, 1164, 1091, 749 cm^{-1}. HRMS (EI-TOF) calcd for $C_{26}H_{21}N_3O_2S$ [M]$^+$ 439.1354, found 439.1351.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01678.

^{1}H NMR and ^{13}C NMR spectra for all new compounds (PDF)

X-ray crystallography of **3c** (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (Nos. 21472164, 21472173) for the financial support.

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DOI: 10.1021/acs.joc.6b01678
J. Org. Chem. 2016, 81, 9433−9437