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Synthesis of 2,3-Disubstituted Indoles and Benzofurans by the Tandem Reaction of Rhodium(II)-Catalyzed Intramolecular C–H Insertion and Oxygen-Mediated Oxidation

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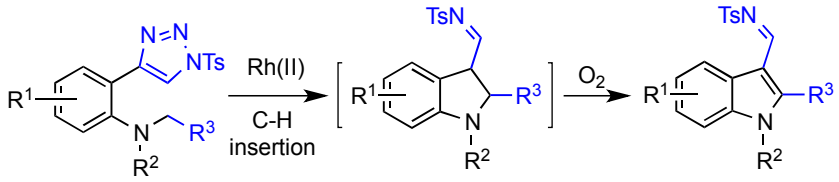


ABSTRACT: A highly effective and straightforward method to construct a wide range of functionalized 2,3-disubstituted indoles has been developed. The method involves the tandem reaction of rhodium(II)-catalyzed denitrogenative annulation of triazole-based benzyl anilines and oxygen-mediated oxidative aromatization. The developed method can also be used to synthesize 2,3-disubstituted benzofurans by replacing the benzyl anilines with benzyl phenols.

Introduction

2,3-Disubstituted indoles are ubiquitous in biologically active natural products and medicinal agents, and they are an important class of heterocycles.[1] Therefore, development of practical and efficient procedures to prepare functionalized indoles has long been an area of intensive research.[2]

Among the reported methods,[3] transition-metal-catalyzed C–H insertion of metal carbene followed by oxidation with DDQ or chloranil provides a novel pathway to prepare functionalized 2,3-disubstituted indoles (eq 1, Figure 1).[4]

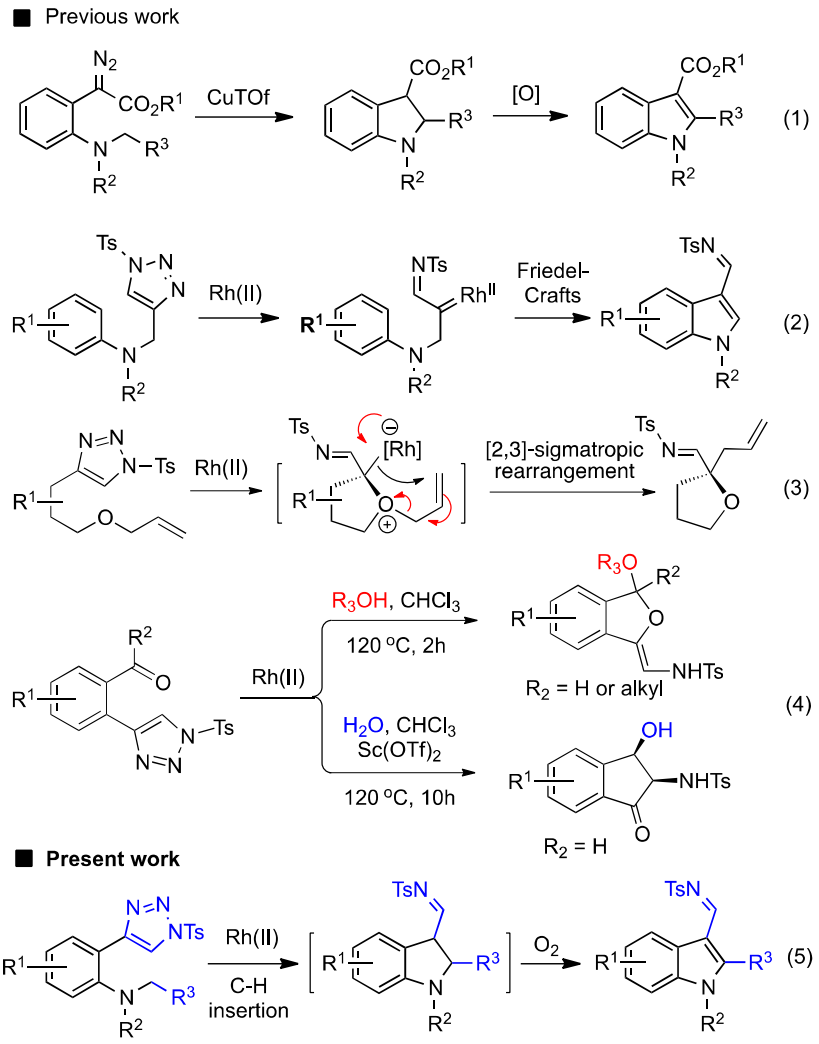


Figure 1. Synthesis of heterocycles utilizing Rh(II) azavinyl carbene.

In this context, *N*-sulfonyl 1,2,3-triazole can be regarded as a masked diazo compound.[5] Upon treatment with a Rh(II) catalyst, *N*-sulfonyl 1,2,3-triazole transforms to Rh(II) azavinyl carbene,[6] which allows *N*-sulfonyl triazole to be a surrogate of the diazo compound in Rh(II)-carbenoid-promoted reactions, such as cyclopropanation,[7] transannulation,[8] C–H insertion,[9] dehydrogenative rearrangement,[10] and other rhodium carbene-based reactions.[11]

Recently, Lin and co-workers developed a simple approach[12] to synthesize 3-indolylimines from *N*-propargyl aniline-derived triazoles by a tandem reaction involving Rh(II)-catalyzed denitrogenative annulation of the substituted triazole followed by an intramolecular Friedel–Crafts reaction (eq 2, Figure 1).

We recently developed synthetic methods to construct core heterocycles in complex natural products using Rh(II)-catalyzed annulation of substituted triazoles as the key step, and the developed chemistry allows construction of the core structures of oxaspirocycles[13] (eq 3, Figure 1), dihydroisobenzofurans, and indanones[14] (eq 4, Figure 1).

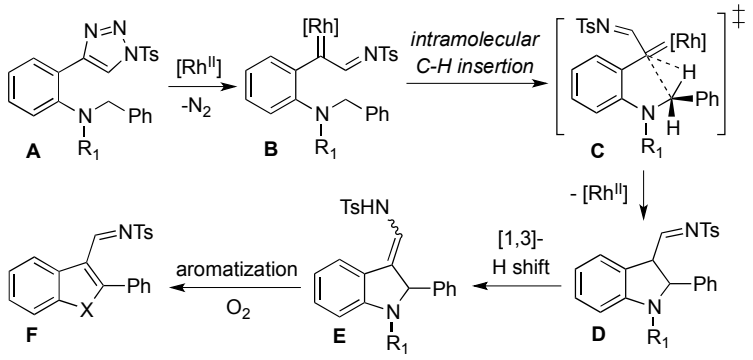


Figure 2. Rational proposal for the synthesis of 2,3-disubstituted indoles via Rh-catalyzed *N*-sulfonyl-1,2,3-triazole-based anilines.

Based on our previous experience in Rh-catalyzed denitrogenative annulation of substituted triazoles, we wanted to apply this chemistry to synthesize 2,3-disusbtittued indoles. We envisioned that triazole-based *N*-benzyl aniline **A** (Figure 2) might undergo Rh-catalyzed denitrogenation to form Rh(II) azavinyl carbene **B**. **B** could then undergo sequential intramolecular C–H insertion and a 1,3-hydrogen shift through transition state **C**[15a, b] and intermediate **D** to give intermediate **E**, followed by oxygen-mediated oxidative aromatization to give 2,3-disubstituted indole **F**.

Herein, we report our recent results for the synthesis of 2,3-disubstituted indoles from *N*-benzyl-*N*-(2-(*N*-sulfonyl-1,2,3-triazole-4-yl)-phenyl) acetamide by the tandem reaction of

Rh-catalyzed denitrogenative annulation and oxygen-mediated oxidation.[16] The developed chemistry provides an alternative way to synthesize this important scaffold.

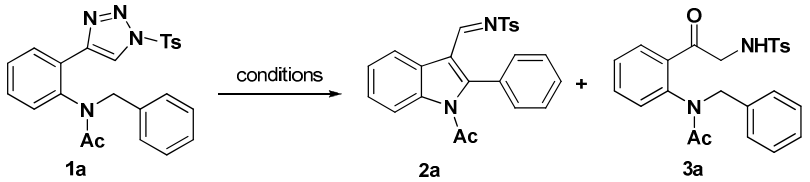
RESULTS AND DISCUSSION

Our research began with evaluation of the substrate *N*-benzyl-*N*-(2-(*N*-sulfonyl-1,2,3-triazole -4-yl)-phenyl) acetamide (**1a**) in the Rh-catalyzed tandem reaction. Initially, **1a** was treated with $Rh_2(Oct)_4$ (5 mol %) in 1,2-dichloroethane (DCE) at room temperature for 2 h, however, no desired product **2a** was obtained, and starting material **1a** was recovered (entry 1 in Table 1). We then carried out the reaction at a higher temperature (70 °C) for 2 h, under these conditions product **2a** was obtained in 30% yield, in addition to a hydrolyzed product **3a** in 50% yield[11a] (entry 2). We later found out that the yield of **2a** could be improved up to 42% in the presence of oxygen under the conditions listed in entry 2 (entry 3).

To improve the yield, we then carried out a systematic evaluation of the effects of reaction parameters on the outcomes of the annulation. In the event, when the reaction was performed in dichloromethane (DCM) at 40 ^oC in the presence of 4Å MS,[11a] only a trace amount of product **2a** was obtained because of the lower reaction temperature (entry 4). On the other hand, when the reaction was carried out at 70 ^oC in the presence of 4Å MS in DCE and $CHCl_3$, the corresponding product **2a** was formed in 50% and 54%, respectively, and product **3a** could not be observed (entries 5 and 6). We then changed the catalyst from $Rh_2(Oct)_4$ to $Rh_2(OAc)_4$ or $Rh_2(TFA)_4$, and run the reactions in $CHCl_3$, however, product **2a** were obtained in 0% and 20%, respectively (entries 7 and 8), indicating $Rh_2(Oct)_4$ is an effective catalyst for this reaction. We therefore selected $Rh_2(Oct)_4$ as a catalyst, and ran the reaction in the solvents of DCE and $CHCl_3$ at 100 ^oC in a sealed tube, as expected product **2a** was obtained in 75% and 80% yields, respectively (entries 9 and 10). We finally performed the reaction at

120 °C in toluene for 1 h under N_2, and then at 90 °C for another 1 h in the presence of O_2,[17] to our delight, the desired product **2a** could be obtained in 89% yield (entry 11).

Table 1. Conditions for the Rh-catalyzed annulation of **1a** for the syntheses of 2,3-disubstituted indole **2a**[a]



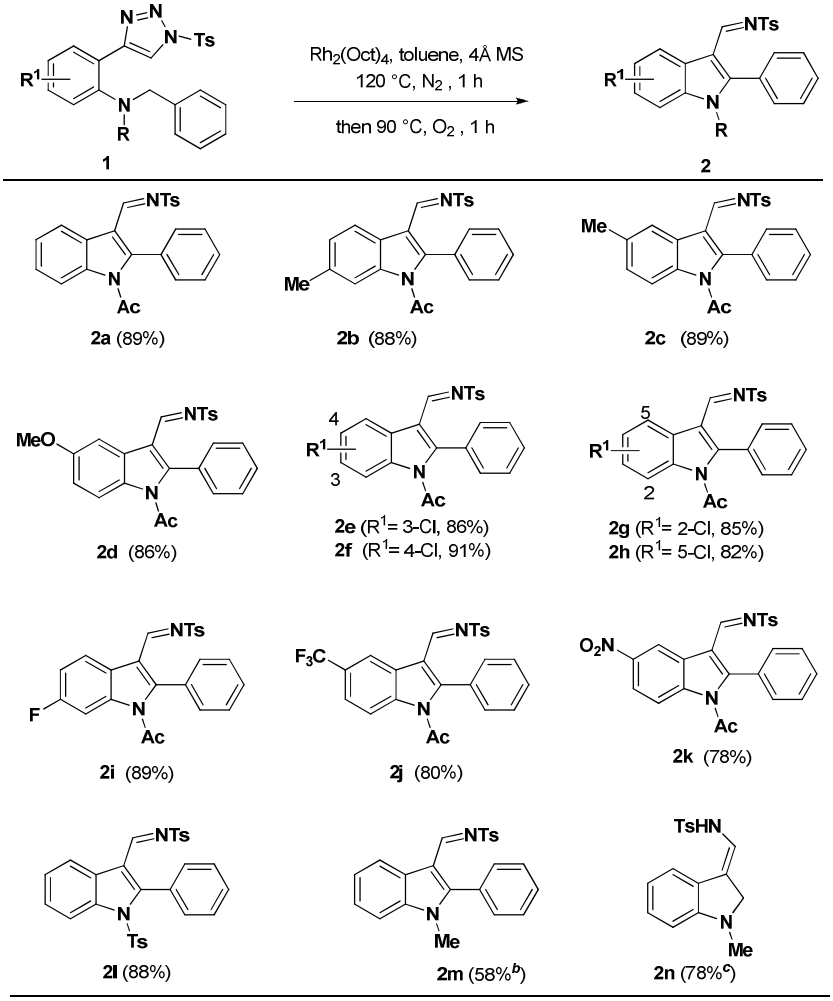
1a 2a 3a

Entry[a]	Catalyst	Additive	Solvent	Temperature	Time	Yield of **2a** / **3a**[b]
1	$Rh_2(Oct)_4$	-	DCE	rt	2 h	0
2	$Rh_2(Oct)_4$	-	DCE	70 °C	2 h	30%/50%
3	$Rh_2(Oct)_4$	-	DCE	70 °C	2 h[c]	42%/45%
4	$Rh_2(Oct)_4$	4ÅMS	DCM	40 °C	2 h[c]	trace
5	$Rh_2(Oct)_4$	4ÅMS	DCE	70 °C	2 h[c]	50%/0
6	$Rh_2(Oct)_4$	4ÅMS	$CHCl_3$	70 °C	2 h[c]	54%/0
7	$Rh_2(OAc)_4$	4ÅMS	$CHCl_3$	70 °C	2 h[c]	0
8	$Rh_2(OCOCF_3)_4$	4ÅMS	toluene	70 °C	2 h[c]	20%/0
9	$Rh_2(Oct)_4$	4ÅMS	DCE	100 °C	2 h[c]	75%/0
10	$Rh_2(Oct)_4$	4ÅMS	$CHCl_3$	100 °C	2 h[c]	80%/0
11	$Rh_2(Oct)_4$	4ÅMS	toluene	120 °C-90 °C	2 h[d]	89%/0

[a]Reaction agents and conditions: **1a** (90 mg, 0.2 mmol), solvent (0.025 M for substrate), catalyst (5 mol%), 4Å MS (180 mg, 200 wt. %, powder) unless otherwise noted; [b]Yield of isolated product; [c]The mixture was carried out under an oxygen atmosphere; [d]The reaction was carried out under a nitrogen atmosphere for 1 h, then under an oxygen atmosphere at 90 °C for another 1 h.

We next investigated the substrate scope of this Rh(II)-catalyzed annulation reaction. To this end, substrates **1b**–**1n** were synthesized (see Experimental Section for details), and annulated under the optimized reaction conditions listed in entry 12 in Table 1. The results are listed in Figure 3.

Figure 3. Rh(II)-catalyzed denitrogenative annulation with different substituents on the aniline aromatic ring.[a]



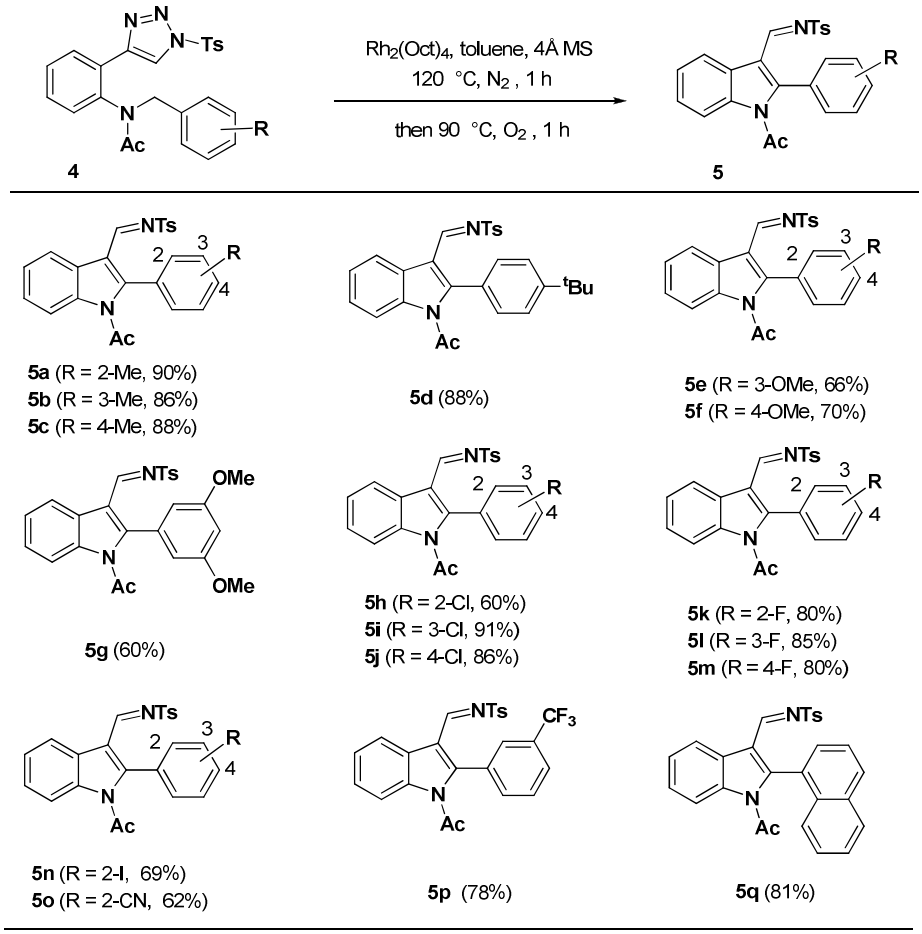
[a]Isolated yield. [b]Reaction time 5 h. [c]Reaction time 4 h.

From the results, we can make the following observations: (1) When the nitrogen atom of aniline in the substrate is protected as its acetamide, both electron-rich and electron-deficient substrates can smoothly undergo Rh-catalyzed denitrogenative annulation to give the corresponding products **2a**–**2k** in good to excellent yields (Figure 3). In addition, the substitution pattern did not greatly change the product yield (**2e** vs. **2f** and **2g** vs. **2h**). (2) When the nitrogen atom of the aniline in substrates **1l** and **1m** is protected with Ts and Me groups, respectively, the corresponding annulation proceeds to give the desired annulated products **2l** and **2m** in good yields. (3) When the nitrogen atom of the aniline is

protected with two Me groups, the resultant substrate can also undergo the desired reaction to give annulated product **2n** in 78% yield.

We then investigated the effect of substituents on the benzyl ring on Rh-catalyzed annulation. Substrates **4a**–**4q** were prepared (see Experimental Section form details) and then annulated under the optimized conditions. The results are shown in Figure 4. Accordingly, when the benzyl ring contained an alkyl substituent, such as a methyl or tertiary butyl group (**4a**–**4d**), annulation gave the corresponding products **5a**–**5d** in good yields (86%–90%). In contrast, when the benzyl ring contained electron-donating substituents (one or two methoxyl groups, **4e**–**4g**), annulation gave low yields of products **5e**–**5g** (60%–70%), indicating that electron-donating groups are unfavorable for annulation. Presumably, the electron-rich benzyl ring could result in some unexpected side reactions in the presence of Rh(II) azavinyl carbene.[15] When the benzene ring of the substrate contained an electron-withdrawing substituent (Cl, F, or CF_3, **5h**–**5m** and **5p**) annulation proceeded smoothly to give the corresponding products in good yields. It should be mentioned that when electron-withdrawing groups were located at the C-2 position (**5h**, **5n**, and **5o**), relatively low yields were obtained because of steric hindrance, which prevents formation of transition state **C**. Interestingly, the naphthalene ring was also suitable for this reaction sequence and gave the desired annulated product **5q** in 81% yield.

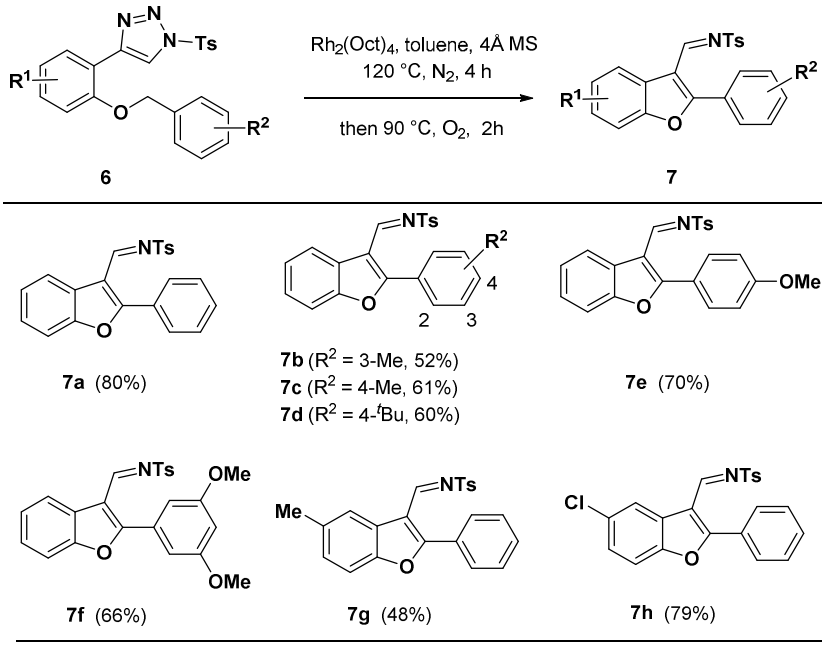
Figure 4. Rh(II)-catalyzed denitrogenative annulation with different substituents on the benzyl aromatic ring.[a]



[a]Isolated yield.

To increase the reaction scope, we used this methodology to synthesize 2,3-disubstituted benzofurans by replacing the benzyl anilines in the triazole-based substrates with benzyl phenols. Substrates **6a**–**6h** were synthesized (see Experimental Section for details) and then subjected to the optimized Rh-catalyzed annulation reaction conditions. The results are listed in Figure 5. As expected, all of the selected substrates smoothly underwent annulation to give 2-3-disubstituted benzofurans **7a**–**7h** in good to acceptable yields (48%–80%). Interestingly, all of the reactions needed to be carried out for 6 h, indicating that formation of benzofurans is more difficult than the corresponding indoles.

Figure 5. Sequential Rh(II)-catalyzed C–H insertion and oxidation to produce 2,3-disubstituted benzofurans.[a]



[a]Isolated yield.

CONCLUSIONS

In summary, we have developed a simple method to synthesize structurally diverse 2,3-disubstituted indoles by a tandem reaction involving Rh-catalyzed denitrogenative annulation of triazole-based benzyl anilines and oxygen-mediated oxidative aromatization. This method can also synthesize certain types of 2,3-disubstituted benzofurans.

EXPERIMENTAL SECTION

General Experimental Information. All of the reactions were performed under an argon atmosphere with dry solvents under anhydrous conditions. Unless otherwise specified, all of the reagents and starting materials were purchased from commercial sources and used as received. The chromatography solvents were technical grade and distilled prior to use. Flash chromatography was performed using 200−300 mesh silica gel with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel plates. The developed chromatograms were visualized by UV absorbance (254 nm). The ^{1}H and ^{13}C NMR data were recorded on 400 MHz NMR and 500 MHz NMR spectrometers, unless otherwise specified. The

following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. HRMS (ESI) analysis with a quadrupole time-of-flight mass spectrometer yielded ion mass/charge (m/z) ratios in atomic mass units. IR spectra were measured as dry films (KBr), and peaks are reported in terms of wavenumber (cm^{-1}).

General procedure for the synthesis of triazole substrates 1a-1n, 4a-4q:

To a stirred solution of 2-iodoaniline (1.0 g, 4.6 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was sequentially added pyridine (0.7 mL, 6.8 mmol, 1.5 equiv) and acetic anhydride (0.6 mL, 6.9 mmol, 1.51 equiv) in a dropwise manner at 0˚C under argon, and the mixture was then allowed to warm to room temperature, and stirred for 1h. The reaction was worked up by addition of water (10 mL), and the mixture was extracted with CH_2Cl_2 (10 mL x 3). Combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was filtered off, and the filtrate was concentrated under vacuum. The residue was purified by a flash column chromatography on silica gel (PE: EA = 4:1) to give *N*-(2-iodophenyl)acetamide **1-1** (1.06 g, 4.05 mmol) [18] in 88% yield as a crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.75 (s, 1H), 7.50 (s, 1H), 7.31 (m, 1H), 6.83 (m, 1H), 2.22 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 138.8, 138.2, 129.2, 126.1, 122.5, 24.7 ppm; IR ν_{max} (film): 3065, 3035, 2929, 2864, 2758, 1684, 1598, 1483, 1458, 1454, 1285, 1239, 1161, 1103, 1005, 758, 737, 696, 658 cm^{-1}; HRMS (ESI) m/z calcd for C_8H_9INO $[M+H]^+$: 261.9729; found: 261.9721.

To a flame dried round-bottom flask containing *N*-(2-iodophenyl)acetamide **1-1** (2.0 g, 7.66 mmol, 1.0 equiv) was added $Pd(Ph_3P)_2Cl_2$ (105 mg, 0.15 mmol, 0.02 equiv.) and CuI (15 mg, 0.08 mmol, 0.01 equiv), and degassed with argon for 3 times. To this flask was added dried THF (25 mL, 0.3 M for substrate), Et_3N (4.3 mL, 30.6 mmol, 4.0 equiv) and (trimethylsilyl)acetylene (1.6 mL, 11.5 mmol, 1.5 equiv.), and the resultant reaction mixture was then stirred at 50 °C for 16 h. After cooled to

ambient temperature, the mixture was filtered off through a celite pad, and the filtrate was concentrated under vacuum. The residue was purified by a flash column chromatography on silica gel (PE: EA = 16:1) to give *N*-(2-((trimethylsilyl)ethynyl)phenyl)- acetamide **1-2**[13] (1.51 g, 6.51 mmol) in 85% yield as a yellow viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.4 Hz, 1H), 8.00 (s, 1H), 7.40 (dd, J = 7.6, 1.2 Hz, 1H), 7.36 – 7.29 (m, 1H), 7.01 (m, 1H), 2.21 (s, 3H), 0.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 139.5, 131.4, 129.9, 123.1, 118.9, 111.5, 102.2, 100.3, 24.8, -0.1 ppm; IR ν_{max} (film): 3064, 3042, 2915, 2814, 2766, 1572, 1435, 1368, 1324, 1319, 1161, 1153, 789, 765, 688, 628 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{18}NOSi$ $[M+H]^+$: 232.1158; found: 232.1153.

To a stirred solution of *N*-(2-((trimethylsilyl)ethynyl)phenyl)acetamide **1-2** (2.74 g, 11.1 mmol, 1.0 equiv) in THF (60 mL) was added NaH (666 mg, 16.65 mmol, 1.5 equiv, 60% w/w) at 0 °C, and the resultant reaction mixture was allowed to warm up to room temperature, and stirred for 30 min. To this solution was added benzyl bromide (1.23 mL, 14.43mmol, 1.3 equiv) and tetrabutyl ammonium iodide (408 mg, 1.11 mmol, 0.1 equiv) at room temperature, and the mixture was stirred at the same temperature for 3h. The reaction mixture was quenched by addition of a saturated aqueous solution of ammonium chloride, and the mixture was extracted with ethyl acetate (2 x 30 mL), and the combined extracts were dried over Na_2SO_4. The extract was filtered off, and the filtrate as concentrated under vacuum. The residue was purified by a flash column chromatography on silica gel (PE: EA = 8:1) afforded *N*-benzyl-*N*-(2-(1-tosyl-1H- triazol-4-yl)phenyl)acetamide **1-3** [13] (2.07 g, 8.33 mmol) in 75% yield as a white oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, J = 7.2 Hz, 1H), 7.21 (m, 7H), 6.76 (d, J = 7.4 Hz, 1H), 5.51 (d, J = 14.3 Hz, 1H), 4.23 (d, J = 14.3 Hz, 1H), 3.25 (s, 1H), 1.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 144.3, 137.2, 133.9, 129.7, 129.5, 129.1, 128.3, 128.1, 127.4, 121.8, 82.8, 79.4, 51.7, 22.4 ppm; IR *vmax* (film): 3258, 3223,3046, 3030, 1648, 1486, 1448, 1387, 1358, 1289,

1261, 1216, 1070, 749, 703 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{15}NNaO$ $[M+Na]^+$: 272.1051; found: 272.1045.

Following the procedure published by Fokin[19]: To a solution of *N*-benzyl-*N*-(2-(1-tosyl-1H-triaz-ol-4-yl)phenyl)acetamide **1-3** (2.0 g, 8.03 mmol, 1.0 equiv) in dry toluene (80 mL) was added copper(I) thiophene-2-carboxylate (CuTC, 152 mg, 0.80 mmol, 0.1 equiv), followed by addition of tosyl azide (1.24 mL, 8.03 mmol, 1.0 equiv) in a dropwise manner at ambient temperature. The reaction mixture was then stirred at the same temperatue for 3 h. The reaction mixture was was worked up by addition of a saturated aqueous solution of ammonium chloride (60 mL), and then extracted with ethyl acetate (2 x 20 mL). The combined organic extracts were washed with brine, and dried over Na_2SO_4. The extract was filtered off, and the residue was concentrated under vacuum, and the residue was purified by a flash column chromatography on silica gel (PE: EA = 4:1) to give *N*-benzyl-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide **1a** (3.04 g, 6.83 mmol) in 85% yield as an orange solid; m p 101-102 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.84 (m, 4H), 7.29 (m, 3H), 7.21 (td, J = 7.7, 1.4 Hz, 1H), 7.07 – 6.95 (m, 5H), 6.84 (d, J = 7.2 Hz, 1H), 5.07 (d, J = 14.0 Hz, 1H), 4.18 (d, J = 14.0 Hz, 1H), 2.31 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 147.6, 143.4, 139.4, 136.4, 132.8, 130.5, 130.2, 129.8, 129.2, 128.8, 128.5, 128.3, 127.6, 127.6, 120.7, 51.9, 22.5, 21.7 ppm; IR ν_{max} (film): 3142, 3085, 3064, 2925, 1662, 1392, 1195, 1176, 989, 763, 751, 701, 672, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}N_4NaO_3S$ $[M+Na]^+$: 469.1310; found: 469.1301.

Synthesis of *N*-benzyl-*N*-(5-methyl-2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1b): **1b** (1.5 g) was obtained in 90% yield as a yellow solid; m p 95-96 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H), 7.79 – 7.70 (m, 2H), 7.24 (d, J = 8.3 Hz, 2H), 7.05 (d, J = 7.9 Hz, 1H), 7.01 – 6.90 (m, 5H), 6.64 (s, 1H), 4.95 (d, J = 14.0 Hz, 1H), 4.21 (d, J = 14 Hz, 1H), 2.25 (s, 3H), 2.10 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 147.4, 143.6, 140.6, 139.3, 136.5, 132.9, 130.5, 130.5,

129.6, 129.5, 129.2, 128.5, 128.2, 127.5, 124.7, 120.3, 52.0, 22.4, 21.7, 20.9 ppm; IR νmax (film): 3152, 3005, 2929, 2900, 1652, 1492, 1165, 1186, 969, 768, 741, 700, 692, 588, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{25}N_4O_3S$ [M+H]+: 461.1647; found: 461.1642.

Synthesis of *N*-benzyl-*N*-(4-methyl-2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1c): **1c** (1.0 g) was obtained in 91% yield as an orange solid; m p 89-90 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 2H), 7.91 (d, J = 1.2 Hz, 1H), 7.85 (s, 1H), 7.41 (d, J = 8.4 Hz, 2H), 7.23 – 7.14 (m, 3H), 7.14 – 7.06 (m, 3H), 6.76 (d, J = 8.0 Hz, 1H), 5.20 (d, J = 13.6 Hz, 1H), 4.19 (d, J = 13.6 Hz, 1H), 2.45 (s, 3H), 2.39 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 170.7, 147.4, 143.4, 138.9, 136.8, 136.5, 133.0, 130.8, 130.5, 130.2, 129.9, 129.4, 128.7, 128.4, 127.7, 127.2, 120.4, 51.9, 22.4, 21.8, 21.1 ppm; IR νmax (film): 3036, 3011, 2928, 2925, 2858, 1659, 1654, 1394, 1194, 1179, 989, 814, 750, 702, 672, 583, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{25}N_4O_3S$ [M+H]+: 461.1647; found: 461.1641.

Synthesis of *N*-benzyl-*N*-(4-methoxy-2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1d): **1d** (1.05 g) was obtained in 85% yield as orange solid; m p 100-101 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 2H), 7.89 (s, 1H), 7.60 (d, J = 2.8 Hz, 1H), 7.38 (d, J = 8.4 Hz, 2H), 7.20 – 7.10 (m, 3H), 7.08 (m, 2H), 6.78 (m, 2H), 5.19 (d, J = 13.8 Hz, 1H), 4.16 (d, J = 13.8 Hz, 1H), 3.79 (s, 3H), 2.41 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 159.3, 147.6, 143.2, 136.5, 132.8, 132.1, 131.3, 130.5, 129.4, 128.6, 128.5, 128.4, 127.7, 120.6, 116.0, 113.9, 55.6, 52.0, 22.4, 21.8 ppm; IR νmax (film): 3148, 3088, 3064, 2961, 2934, 2839, 1654, 1594, 1503, 1494, 1395, 1327, 1291, 1195, 1777, 1093, 996, 968, 814, 746, 702, 671, 589, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{24}N_4NaO_4S$ [M+Na]+: 499.1416; found: 499.1412.

Synthesis of *N*-benzyl-*N*-(5-chloro-2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1e): **1e** (2.0 g) was obtained in 90% yield as an orange solid; m p 99-100 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 –

8.00 (m, 1H), 7.98 (d, *J* = 7.2 Hz, 2H), 7.83 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 3H), 7.23 – 7.14 (m, 3H), 7.08 (d, *J* = 7.2 Hz, 2H), 6.93 (d, *J* = 2.0 Hz, 1H), 5.11 (d, *J* = 13.9 Hz, 1H), 4.33 (d, *J* = 13.9 Hz, 1H), 2.43 (s, 3H), 1.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 147.6, 142.4, 140.3, 135.9, 135.4, 132.8, 130.8, 130.6, 130.2, 129.3, 129.2, 128.7, 128.6, 128.0, 126.6, 120.6, 52.0, 22.5, 21.9 ppm; IR ν_{max} (film): 3391, 3146, 3088, 3064, 3031, 2927, 1665, 1653, 1595, 1572, 1394, 1324, 1282, 1196, 1177, 1158, 1086, 990, 813, 763, 737, 702, 671, 594, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{21}ClN_4NaO_3S$ $[M+Na]^+$: 503.0921; found: 503.0916.

Synthesis of *N*-benzyl-*N*-(4-chloro-2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1f): **1f** (2.5 g) was obtained in 88% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 2.4 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.92 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.23 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.16 – 7.11 (m, 3H), 7.05 (d, *J* = 7.2 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 1H), 5.16 (d, *J* = 13.9 Hz, 1H), 4.20 (d, *J* = 13.9 Hz, 1H), 2.41 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 147.7, 142.2, 137.8, 136.1, 134.7, 132.7, 131.6, 130.6, 130.1, 129.5, 129.4, 129.3, 128.7, 128.5, 127.8, 121.1, 51.8, 22.5, 21.8 ppm; IR ν_{max} (film): 3290, 3140, 3076, 3044, 3011, 2900, 1643, 1600, 1590, 1562, 1304, 1298, 1280, 1096, 1160, 11543, 1076, 980, 816, 735, 678, 588, 560 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}ClN_4O_3S$ $[M+H]^+$: 481.1101; found: 481.1096.

Synthesis of *N*-benzyl-*N*-(3-chloro-2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1g): **1g** (1.5 g) was obtained in 92% yield as an orange solid; m p 114-115 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.85 (s, 1H), 7.48 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 2H), 6.97 (d, *J* = 7.2 Hz, 2H), 6.92 (dd, *J* = 8.0, 0.8 Hz, 1H), 4.73 (d, *J* = 14.4 Hz, 1H), 4.22 (d, *J* = 14.4 Hz, 1H), 2.46 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 147.6, 143.3, 140.3, 136.4, 135.2, 132.9, 130.9, 130.5, 130.0, 129.1, 129.0, 128.6, 128.4, 128.0, 127.6, 123.6, 52.4, 23.0, 21.8 ppm; IR ν_{max} (film): 3149, 3065, 2954, 2926,

1669, 1452, 1392, 1343, 1195, 1176, 998, 965, 766, 701, 670, 590, 537 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}ClN_4O_3S$ $[M+H]^+$: 481.1101; found: 481.1098.

Synthesis of *N*-benzyl-*N*-(2-chloro-6-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1h): **1h** (1.1 g) was obtained in 88% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.36(m, 3H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 2H), 6.88 (d, *J* = 11.6 Hz, 2H), 5.17 (d, *J* = 13.8 Hz, 1H), 4.24 (d, *J* = 13.8 Hz, 1H), 2.46 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 147.5, 142.8, 136.8, 135.2, 134.9, 132.9, 131.2, 131.0, 130.5, 129.9, 129.7, 128.8, 128.4, 128.1, 127.8, 120.9, 51.2, 22.3, 21.8 ppm; IR ν_{max} (film): 3156, 3105, 2854, 2726, 1696, 1466, 1460, 1366, 1295, 1186, 996, 968, 765, 703, 660, 580, 557 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}ClN_4O_3S$ $[M+H]^+$: 481.1101; found: 481.1096.

Synthesis of *N*-benzyl-*N*-(5-fluoro-2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1i): **1i** (1.04 g) was obtained in 82% yield as an orange solid; m p 110-111 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 8.8, 6.0 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 2H), 7.82 (s, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.24 – 7.12 (m, 4H), 7.10 (dd, *J* = 7.6, 1.2 Hz, 2H), 6.64 (dd, *J* = 8.9, 2.6 Hz, 1H), 5.19 (d, *J* = 13.9 Hz, 1H), 4.25 (d, *J* = 13.9 Hz, 1H), 2.45 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 162.8 (d, $^1J_{C-F}$ = 251.3 Hz), 147.6, 142.5, 140.9, 140.8, 136.0, 132.9, 131.4, 131.3, 130.5, 129.3, 128.7, 128.6, 128.0, 124.3, 124.3, 120.3, 117.4, 117.2, 116.4, 116.2, 51.9, 22.4, 21.8 ppm; IR ν_{max} (film):3356, 3308, 3147, 2926, 2852, 1663, 1593, 1431, 1392, 1293, 1202, 1179, 990, 813, 747, 703, 672, 625, 584, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}FN_4O_3S$ $[M+H]^+$: 465.1397; found: 465.1390.

Synthesis of *N*-benzyl-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)-4-(trifluoromethyl)phenyl)acetamide (1j): **1j** (900 mg) was obtained in 92% yield as an orange solid; m p 79-80 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.08 – 7.90 (m, 3H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.23 – 7.14 (m, 3H), 7.07–7.10 (m, 3H), 5.22 (dd, *J* = 14.0, 1.2 Hz, 1H), 4.27 (d, *J* = 14.0 Hz, 1H),

2.44 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 147.8, 142.3, 142.0, 136.0, 132.6, 131.1, 130.6, 129.3, 128.9, 128.7, 128.6, 128.0, 127.6, 127.4, 127.0, 126.9, 126.8, 126.3, 123.3 (q, $^1J_{C-F}$ = 271.1 Hz), 121.2, 51.9, 22.5, 21.8 ppm; IR ν_{max} (film): 3395, 3150, 3090, 3065, 2929, 1668, 1653, 1594, 1394, 1339, 1306, 1266, 1196, 1174, 1131, 1083, 1027, 997, 914, 815, 755, 736, 720, 702, 672, 588, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{22}F_3N_4O_3S$ $[M+H]^+$: 515.1365; found: 515.1357.

Synthesis of *N*-benzyl-*N*-(4-nitro-2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (1k): **1k** (1.2 g) was obtained in 86% yield as an orange solid; m p 143-144 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 2.4 Hz, 1H), 8.14 (dd, *J* = 8.8, 2.4 Hz, 1H), 8.06 – 7.91 (m, 3H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.26 – 7.16 (m, 3H), 7.07 –7.11 (m, 3H), 5.24 (d, *J* = 14.0 Hz, 1H), 4.30 (d, *J* = 14.0 Hz, 1H), 2.46 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 147.9, 147.5, 144.5, 141.4, 135.7, 132.5, 131.7, 130.6, 129.8, 129.3, 128.8, 128.7, 128.2, 125.0, 124.6, 121.4, 51.9, 22.6, 21.9 ppm; IR ν_{max} (film): 3418, 3364, 3334, 3238, 2925, 2854, 2700, 1786, 1616, 1275, 1261, 1177, 1125, 1036, 1011, 763, 749, 683, 569 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}N_5O_5S$ $[M+H]^+$: 492.1342; found: 492.1334.

Synthesis of *N*-benzyl-4-methyl-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)benzenesulfonamide (1l): **1l** (1.0 g) was obtained in 80% yield except that tosyl chloride[20] was used to replace the acetic anhydride as an orange solid; m p 119-120 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.04 (d, J = 8.3 Hz, 2H), 7.94 (d, J = 6.9 Hz, 1H), 7.64 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.2 Hz, 2H), 7.34 (t, J = 8.9 Hz, 3H), 7.25 (dd, J = 10.8, 3.6 Hz, 2H), 7.05 (t, J = 7.4 Hz, 1H), 6.90 (t, J = 7.6 Hz, 2H), 6.76 (dd, J = 14.8, 7.6 Hz, 3H), 5.04 (d, J = 12.9 Hz, 1H), 4.20 – 4.04 (m, 1H), 2.47 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 144.3, 143.3, 136.5, 135.3, 133.9, 133.5, 131.8, 130.4, 129.8, 129.3, 129.3, 129.0, 128.6, 128.5, 128.2, 128.1, 128.1, 123.1, 56.7, 21.8, 21.6 ppm; IR ν_{max} (film): 3031, 3010, 2924, 2870, 1595, 1442, 1393, 1345, 1195, 1176, 1163, 1091, 1042, 987, 862, 814, 763,

751, 727, 672, 591, 561, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{29}H_{26}N_4O_4S_2$ $[M+H]^+$: 559.1474; found: 559.1468.

Synthesis of *N*-benzyl-*N*-methyl-2-(1-tosyl-1H-1,2,3-triazol-4-yl)aniline (1m): **1m** (1.0 g) was obtained in 91% yield except that methylation[21] reaction was used instead of acylation reaction as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.22 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.32 (m, 6H), 7.19 (m, 4H), 4.05 (s, 2H), 2.53 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 147.1, 144.7, 137.6, 133.4, 130.4, 129.6, 129.1, 128.9, 128.5, 128.4, 127.3, 124.3, 124.1, 122.1, 121.5, 60.5, 41.8, 21.8 ppm; IR ν_{max} (film):3174, 3063, 2921, 2848, 2799, 1595, 1489, 1392, 1194, 1174, 1090, 983, 813, 701, 674, 591, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{23}N_4O_2S$ $[M+H]^+$: 419.1542; found: 419.1538.

Synthesis of *N*,*N*-dimethyl-2-(1-tosyl-1H-1,2,3-triazol-4-yl)aniline (1n): **1n** (1.16 g) was obtained in 86% yield expect for acylation[21] as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.18 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.31 (t, J = 7.6 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.11 (t, J = 7.5 Hz, 1H), 2.63 (s, 6H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 147.2, 144.8, 133.3, 130.4, 129.6, 128.9, 128.5, 123.5, 123.5, 121.9, 119.6, 44.3, 21.8 ppm; IR ν_{max} (film): 3165, 3033, 2925, 2923, 2789, 1492, 1391, 1200, 1175, 983, 673, 592, 542 cm-1; HRMS (ESI) m/z calcd for $C_{17}H_{19}N_4O_2S$ $[M+H]^+$: 343.1229; found: 343.1222.

Synthesis of *N*-(2-methylbenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4a): **4a** (2.65 g) was obtained in 95% yield as an orange solid; m p 136-137 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 2H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.81 (s, 1H), 7.40 (m, 3H), 7.32 (td, *J* = 7.6, 1.6 Hz, 1H), 7.08 (m, 1H), 6.99 – 6.87 (m, 4H), 5.04 (d, *J* = 14.0 Hz, 1H), 4.56 (d, *J* = 14.0 Hz, 1H), 2.46 (s, 3H), 1.98 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 147.5, 143.4, 139.3, 137.0, 134.2, 133.0, 130.6, 130.5, 130.2, 130.2, 129.8, 128.8, 128.7, 128.2, 127.8, 125.8, 120.4, 48.7, 22.7,

21.8, 19.0 ppm; IR ν_{max} (film): 3144, 3064, 2954, 2926, 2861, 1660, 1653, 1444, 1393, 1349, 1176, 1096, 989, 759, 739, 672, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{25}N_4O_3S$ $[M+H]^+$: 461.1647; found: 461.1645.

Synthesis of *N*-(3-methylbenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4b): **4b** (3.12 g) was obtained in 89% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.6 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.86 (s, 1H), 7.36 (t, *J* = 7.6 Hz, 3H), 7.27 (t, *J* = 7.2 Hz, 1H), 6.89 – 7.00 (m, 3H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 6.4 Hz, 1H), 5.12 (d, *J* = 14.0 Hz, 1H), 4.19 (d, *J* = 14.0 Hz, 1H), 2.37 (s, 3H), 2.18 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 147.5, 143.4, 139.5, 138.2, 136.4, 132.9, 130.6, 130.2, 130.1, 129.8, 128.9, 128.6, 128.5, 128.3, 127.7, 126.3, 120.7, 52.0, 22.5, 21.8, 21.3 ppm; IR ν_{max} (film): 3142, 3092, 3063, 2925, 2868, 1661, 1594, 1443, 1393, 1199, 1176, 1096, 989, 760, 672, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{24}N_4NaO_3S$ $[M+Na]^+$: 483.1467; found: 483.1458.

Synthesis of *N*-(4-methylbenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4c): **4c** (1.02 g) was obtained in 86% yield as an orange solid; m p 114-115 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.82 (s, 1H), 7.45 – 7.36 (m, 3H), 7.32 (td, *J* = 7.6, 1.2 Hz, 1H), 6.98 (s, 4H), 6.91 (d, *J* = 7.6 Hz, 1H), 5.12 (d, *J* = 13.8 Hz, 1H), 4.24 (d, *J* = 13.8 Hz, 1H), 2.44 (s, 3H), 2.28 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 147.5, 143.3, 139.4, 137.5, 133.3, 133.0, 130.5, 130.2, 130.2, 129.8, 129.3, 129.1, 128.8, 128.6, 127.7, 120.6, 51.7, 22.5, 21.8, 21.1 ppm; IR ν_{max} (film): 3242, 3098, 3066, 2900, 2878, 1761, 1694, 1543, 1496, 1299, 1076, 1026, 999, 780, 682, 598, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{25}N_4O_3S$ $[M+H]^+$: 461.1647; found: 461.1644.

Synthesis of *N*-(4-tert-butylbenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4d): **4d** (2.0 g) was obtained in 90% yield as an orange solid; m p 101-102 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ

8.12 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.89 (s, 1H), 7.38 –7.43 (m, 3H), 7.33 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 7.6 Hz, 1H), 5.17 (d, *J* = 14.0 Hz, 1H), 4.21 (d, *J* = 14.0 Hz, 1H), 2.43 (s, 3H), 1.67 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 150.7, 147.5, 143.3, 139.5, 133.3, 133.0, 130.6, 130.2, 130.2, 129.8, 129.1, 128.9, 128.7, 127.7, 125.4, 120.7, 51.7, 34.5, 31.3, 22.5, 21.9 ppm; IR ν_{max} (film): 3144, 2962, 2933, 2868, 1662, 1394, 1195, 1176, 1096, 989, 813, 762, 672, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{31}N_4O_3S$ $[M+H]^+$: 503.2117; found: 503.2111.

Synthesis of *N*-(3-methoxybenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4e): **4e** (1.06 g) was obtained in 87% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.83 (s, 1H), 7.39 – 7.45 (m, 3H), 7.33 – 7.36 (m, 1H), 7.09 (t, *J* = 7.8 Hz, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.77 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.72 (s, 1H), 6.66 (d, *J* = 7.6 Hz, 1H), 5.16 (d, *J* = 13.9 Hz, 1H), 4.25 (d, *J* = 13.9 Hz, 1H), 3.72 (s, 3H), 2.44 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 159.5, 147.5, 143.3, 139.5, 137.9, 132.8, 130.5, 130.2, 130.1, 129.8, 129.4, 128.9, 128.6, 127.7, 121.5, 120.6, 114.6, 113.5, 55.1, 52.0, 22.4, 21.8 ppm; IR ν_{max} (film): 3000, 2954, 2852, 2839, 2795, 1738, 1161, 1513, 1318, 1248, 1212, 1176, 1123, 1033, 1009, 966, 816, 764, 682, 568 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{24}N_4NaO_4S$ $[M+Na]^+$: 499.1416; found: 499.1409.

Synthesis of *N*-(4-methoxybenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4f): **4f** (1.09 g) was obtained in 85% yield as a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.5 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.79 (s, 1H), 7.36 – 7.41 (m, 3H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 5.04 (d, *J* = 13.9 Hz, 1H), 4.28 (d, *J* = 13.9 Hz, 1H), 3.73 (s, 3H), 2.41 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 159.1, 147.4, 143.2, 139.4, 132.9, 130.7, 130.5, 130.1, 129.7, 128.7, 128.6, 128.5, 127.8, 120.5, 113.8, 55.1, 51.4, 22.4, 21.7 ppm; IR ν_{max} (film): 3011, 2900, 2868, 2855, 2800, 1768, 1666, 1613, 1436, 1348,

1238, 1216, 1166, 1133, 1008, 968, 818, 766, 688, 566 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{24}N_4NaO_4S$ $[M+Na]^+$: 499.1416; found: 499.1408.

Synthesis of *N*-(3,5-dimethoxybenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide(4g): **4g** (2.01 g) was obtained in 84% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.81 (s, 1H), 7.47 – 7.18 (m, 4H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.36 – 6.13 (m, 3H), 5.01 (d, *J* = 13.9 Hz, 1H), 4.26 (d, *J* = 13.9 Hz, 1H), 3.61 (s, 6H), 2.37 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 160.8, 147.5, 143.4, 139.6, 138.6, 132.9, 130.5, 130.3, 130.0, 129.8, 128.9, 128.6, 127.8, 120.7, 107.1, 100.0, 55.2, 52.3, 22.4, 21.8 ppm; IR ν_{max} (film): 3109, 2933, 2900, 2888, 2816, 1868, 1766, 1656, 1488, 1348, 1338, 1266, 1188, 1133, 1009, 966, 816, 768, 698, 666 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{26}N_4NaO_5S$ $[M+Na]^+$: 529.1522; found: 529.1517.

Synthesis of *N*-(2-chlorobenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4h): **4h** (1.08 g) was obtained in 95% yield as an orange solid; m p 118-119 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 8.8 Hz, 3H), 7.21 – 7.25 (m, 2H), 6.98 – 7.03 (m, 3H), 6.93 (d, *J* = 8.0 Hz, 1H), 5.15 (d, *J* = 14.4 Hz, 1H), 4.47 (d, *J* = 14.4 Hz, 1H), 2.36 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 147.6, 143.6, 139.3, 134.0, 133.9, 132.8, 131.4, 130.6, 130.3, 130.1, 129.9, 129.2, 129.1, 129.0, 128.6, 127.8, 126.9, 120.7, 48.5, 22.6, 21.8 ppm; IR ν_{max} (film): 3629, 3387, 3322, 3287, 2959, 2926, 2855, 2468, 1662, 1394, 1267, 1199, 1175, 988, 749, 672, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{21}ClN_4NaO_3S$ $[M+Na]^+$: 503.0921; found: 503.0914.

Synthesis of *N*-(3-chlorobenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4i): **4i** (1.08 g) was obtained in 87% yield as an orange solid; m p 129-130 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.04 – 7.95 (m, 3H), 7.47 – 7.37 (m, 3H), 7.32 (td, *J* = 7.6, 1.2 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.08 – 7.12 (m, 2H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 5.27 (d, *J* =

14.4 Hz, 1H), 4.01 (d, *J* = 14.4 Hz, 1H), 2.44 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 147.6, 143.3, 139.2, 138.6, 134.2, 132.8, 130.6, 130.3, 130.3, 130.0, 129.7, 129.3, 129.1, 128.7, 127.9, 127.5, 120.5, 51.4, 22.5, 21.9 ppm; IR ν_{max} (film): 3149, 3092, 3064, 2927, 2855, 2588, 2285, 1661, 1594, 1490, 1442, 1393, 1349, 1291, 1195, 1176, 1095, 990, 813, 761, 701, 673, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{21}ClN_4NaO_3S$ $[M+Na]^+$: 503.0921; found: 503.0911.

Synthesis of *N*-(4-chlorobenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4j): **4j** (1.09 g) was obtained in 91% yield as an orange solid; m p 136-138 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.97 (m, 2H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.31 – 7.35 (m, 3H), 7.30 – 7.20 (m, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.87 – 6.79 (m, 1H), 5.11 (d, *J* = 14.0 Hz, 1H), 4.09 (d, *J* = 14.0 Hz, 1H), 2.34 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 147.6, 143.3, 139.2, 135.1, 133.3, 132.7, 130.7, 130.6, 130.3, 130.2, 129.9, 129.0, 128.6, 128.4, 127.5, 120.7, 51.2, 22.4, 21.8 ppm; IR ν_{max} (film): 3064, 2954, 2924, 2854, 2361, 2325, 1700, 1391, 1347, 1296, 1195, 1176, 1096, 990, 761, 672, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}ClN_4O_3S$ $[M+H]^+$: 481.1101; found: 481.1095.

Synthesis of *N*-(2-fluorobenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4k): **4k** (2.01 g) was obtained in 87% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 7.90 (m, 4H), 7.39 (d, *J* = 8.0 Hz, 3H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.24 (t, *J* = 8.2 Hz, 1H), 7.13 (dd, *J* = 13.2, 6.4 Hz, 1H), 6.94 (dd, *J* = 12.4, 7.2 Hz, 2H), 6.75 (t, *J* = 9.0 Hz, 1H), 5.09 (d, *J* = 14.2 Hz, 1H), 4.47 (d, *J* = 14.2 Hz, 1H), 2.42 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 160.9 (d, $^1J_{C-F}$ = 245.8 Hz), 147.6, 143.4, 139.3, 132.9, 131,9, 131.8, 130.6, 130.2, 130.0, 129.98, 129.7, 129.6, 129.0, 128.7, 127.7, 124.2, 124.2, 123.3, 123.3, 120.6, 115.2, 114.9, 44.8, 44.8, 22.6, 21.8 ppm; IR ν_{max} (film): 3627, 3357, 3318, 2920, 2849, 2257, 1661, 1647, 1492, 1393, 1195, 1176, 990, 759, 672, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{21}FN_4NaO_3S$ $[M+Na]^+$: 487.1216; found: 487.1210.

Synthesis of *N*-(3-fluorobenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4l): **4l** (2.01 g) was obtained in 85% yield as an orange solid; m p 116-117 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.00 (m, 1H), 8.00 – 7.92 (m, 3H), 7.37 – 7.41 (m, 3H), 7.26 – 7.30 (m, 1H), 7.15 – 7.04 (m, 1H), 6.85 (m, 4H), 5.22 (d, *J* = 14.1 Hz, 1H), 4.07 (d, *J* = 14.1 Hz, 1H), 2.40 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 162.5 (d, $^{1}J_{C-F}$ = 245.0 Hz) , 147.6, 143.4, 139.3, 139.1, 139.0, 132.8, 130.6, 130.3, 130.2, 130.0, 129.9, 129.9, 129.5, 129.1, 128.6, 127.5, 126.3, 124.9, 124.9, 120.6, 116.2, 115.9, 114.7, 114.5, 51.5, 22.4, 21.8 ppm; IR ν_{max} (film): 3147, 3064, 3037, 2927, 2853, 1660, 1653, 1466, 1393,1348, 1295, 1200, 1176, 990, 761, 672, 588, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}FN_4O_3S$ $[M+H]^+$: 465.1397; found: 465.1392.

Synthesis of *N*-(4-fluorobenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4m): **4m** (1.08 g) was obtained in 86% yield as an orange solid; m p 98-99 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.92 (t, *J* = 4.2 Hz, 3H), 7.35 (t, *J* = 8.0 Hz, 3H), 7.27 (ddd, *J* = 7.6, 6.4, 1.2 Hz, 1H), 7.00 (dd, *J* = 8.8, 5.6 Hz, 2H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.74 (t, *J* = 8.6 Hz, 2H), 5.07 (d, *J* = 14.0 Hz, 1H), 4.17 (d, *J* = 14.0 Hz, 1H), 2.36 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 162.1 (d, $^{1}J_{C-F}$ = 244.7 Hz), 147.6, 143.3, 139.2, 132.7, 132.5, 132.4, 131.1, 131.0, 130.6, 130.2, 130.2, 129.8, 128.9, 128.6, 127.6, 120.6, 115.2, 115.0, 51.2, 22.5, 21.7 ppm; IR ν_{max} (film): 3166, 3064, 3044, 2928, 2866, 1666, 1653, 1638, 1468, 1399, 1368, 1296, 1200, 1166, 990, 766, 672, 589, 556, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}FN_4O_3S$ $[M+H]^+$: 465.1397; found: 465.1390.

Synthesis of *N*-(2-iodobenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4n): **4n** (1.08 g) was obtained in 81% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 7.85 (m, 4H), 7.67 – 7.51 (m, 1H), 7.47 – 7.33 (m, 4H), 7.30 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.25 – 7.13 (m, 1H), 6.98 – 6.74 (m, 2H), 5.31 (dd, *J* = 14.4, 6.4 Hz, 1H), 4.37 (d, *J* = 14.4 Hz, 1H), 2.44 (s, 3H), 1.81 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 147.5, 143.6, 139.2, 139.1, 132.9, 130.8, 130.5, 130.5, 130.3, 130.0,

129.3, 129.0, 128.7, 128.6, 128.0, 120.6, 100.1, 55.1, 22.5, 21.9 ppm; IR ν_{max} (film): 3122, 3068, 2966, 1665, 1660, 1651, 1396, 1390, 1349, 1328, 1302, 1198, 1176, 1166, 1126, 1096, 1073, 990, 813, 766, 705, 671, 589, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}IN_4O_3S$ $[M+H]^+$: 573.0451; found: 573.0451.

Synthesis of *N*-(2-cyanobenzyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)acetamide (4o): **4o** (980 mg) was obtained in 85% yield as an orange solid; m p 116-127 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 – 7.92 (m, 3H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.45 – 7.30 (m, 6H), 7.27 – 7.24 (m, 1H), 6.92 (d, *J* = 11.2 Hz, 1H), 5.25 (d, *J* = 14.6 Hz, 1H), 4.52 (d, *J* = 14.6 Hz, 1H), 2.42 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 147.6, 143.7, 140.0, 138.9, 133.0, 132.7, 132.3, 130.7, 130.6, 130.3, 130.3, 129.3, 128.7, 128.2, 127.8, 120.8, 116.8, 112.5, 49.3, 22.5, 21.8 ppm; IR ν_{max} (film): 3096, 3088, 2968, 1666, 1660, 1651, 1496, 1396, 1369, 1326, 1312, 1198, 1186, 1166, 1128, 1074, 998, 816, 766, 676, 588, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{22}N_5O_3S$ $[M+H]^+$: 472.1443; found: 472.1438.

Synthesis of *N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)-*N*-(3-(trifluoromethyl)benzyl)acetamide (4p): **4p** (1.26 g) was obtained in 86% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 1H), 8.05 – 7.95 (m, 3H), 7.47 – 7.36 (m, 5H), 7.35 – 7.27 (m, 3H), 6.90 – 6.68 (m, 1H), 5.35 (d, *J* = 14.4 Hz, 1H), 4.09 (d, *J* = 14.4 Hz, 1H), 2.45 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 147.7, 143.4, 139.1, 137.6, 132.8, 130.7, 130.7, 130.6, 130.4, 130.4, 130.3, 130.1, 130.0, 129.2, 129.0, 128.8, 127.5, 126.0, 126.0, 125.9, 125.9, 125.9, 124.9 (q, $^1J_{C-F}$ = 269.3 Hz), 124.5, 124.5, 124.5, 124.1, 120.5, 51.4, 22.5, 21.8 ppm; IR ν_{max} (film): 3067, 2828, 1663, 1660, 1650, 1395, 1392, 1349, 1329, 1303, 1196, 1176, 1166, 1124, 1098, 1074, 990, 813, 762, 703, 671, 589, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{21}F_3N_4NaO_3S$ $[M+Na]^+$: 537.1184; found: 537.1197.

Synthesis of *N*-(naphthalen-1-ylmethyl)-*N*-(2-(1-tosyl-1H-1,2,3-triazol-4-yl)phenyl)aceta-

mide (4q): **4q** (1.07 g) was obtained in 87% yield as an orange solid; m p 99-100 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.99 – 7.84 (m, 3H), 7.85 – 7.76 (m, 1H), 7.73 – 7.69 (m, 2H), 7.52 (s, 1H), 7.49 – 7.40 (m, 3H), 7.40 – 7.32 (m, 3H), 7.28 – 7.21 (m, 1H), 6.90 – 6.76 (m, 1H), 5.52 (d, *J* = 13.9 Hz, 1H), 4.26 (d, *J* = 13.9 Hz, 1H), 2.43 (s, 3H), 1.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 147.5, 143.3, 139.3, 134.1, 133.1, 132.9, 132.8, 130.5, 130.3, 130.1, 129.8, 128.9, 128.7, 128.3, 128.3, 127.9, 127.7, 127.6, 127.2, 126.1, 126.0, 120.5, 52.0, 22.5, 21.8 ppm; IR ν_{max} (film): 3147, 3058, 3030, 2925, 2849, 1661, 1394, 1289, 1195, 1176, 1096, 990, 813, 761, 670, 588, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{25}N_4O_3S$ $[M+H]^+$: 497.1647; found: 497.1644.

General procedure for the synthesis of triazole substrates 6a-6h:

To a stirred solution of commercial available compound salicylaldehyde (1.50 g, 12.30 mmol, 1.0 equiv) in THF (60 mL) at 0 °C was added NaH (798 mg, 19.96 mmol, 1.5 equiv, 60% w/w). The reaction mixture was allowed to warm up to ambient temperature, and stirred for 30 min. Benzyl bromide (1.36 mL, 15.99 mmol, 1.3 equiv) was added, followed by the addition of tetrabutyl ammonium iodide (452 mg, 1.23 mmol, 0.1 equiv). Upon TLC showed complete consumption of the starting material (about 3 h), the reaction was quenched with saturated aqueous ammonium chloride, extracted twice with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (PE: EA = 16:1) afforded 2-(benzyloxy)benzaldehyde **6-1**[13] (1.96 g, 9.23 mmol) in 75% yield as a white oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (s, 1H), 7.89 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.57 – 7.50 (m, 1H), 7.48 – 7.36 (m, 5H), 7.10 – 7.01 (m, 2H), 5.18 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7, 161.1, 136.1, 136.0, 128.8, 128.4, 128.3, 127.3, 125.2, 121.0, 113.1, 70.5 ppm; IR ν_{max} (film): 3358, 3266, 3146, 3030, 1666, 1586, 1448, 1386, 1368, 1289, 1266, 1226, 1076, 766, 749, 703, 566, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{12}NaO_2$ $[M+Na]^+$: 235.0735; found: 235.0730.

To a flame dried round-bottom flask containing CBr_4 (6.12g, 18.46 mmol, 2.0 equiv) and PPh_3 (9.68g, 36.92 mmol, 4.0 equiv) in DCM (150 mL) was added 2-(benzyloxy)benzaldehyde **6-1** (1.96 g, 9.23 mmol, 1.0 equiv). The reaction mixture was stirred at 0 °C for 1 h and TLC showed the starting 2-(benzyloxy)benzaldehyde **6-1** was completely consumed. Then *n*-hexane was added to the reaction mixture until solid was completely precipitated. The mixture was filtered through celite, and the filtrate was concentrated *in vacuo*. Further purification by flash column chromatography (PE: EA = 30:1) gave desired 1-(benzyloxy)-2-(2,2-dibromovinyl)benzene **6-2** (2.87 g, 7.85 mmol) in 85% yield [22] as a yellow viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.72 (s, 1H), 7.48 – 7.42 (m, 4H), 7.40 – 7.31 (m, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 5.14 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 136.8, 133.0, 130.0, 129.3, 128.7, 128.0, 127.2, 125.0, 120.6, 112.4, 89.9, 70.4 ppm; IR ν_{max} (film): 3460, 3322, 3214, 3166, 3030, 1666, 1586, 1445, 1366, 1332, 1286, 1267, 1216, 1076, 766, 749, 703, 566, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{15}H_{12}Br_2NaO$ $[M+Na]^+$: 388.9153; found: 388.9156.

To a stirred solution of 1-(benzyloxy)-2-(2,2-dibromovinyl)benzene **6-2** (2.87 g, 7.85 mmol, 1.0 equiv) in THF (50 mL) at -78 °C was added CH_3Li (12.27 mg, 19.63 mmol, 2.5 equiv. 1.6 M) dropwise slowly. The reaction mixture was allowed to stir at -78 °C for 1 h. Upon TLC showed complete consumption of the starting dibromide product **6-2**, the reaction was quenched with saturated aqueous ammonium chloride, extracted twice with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (PE: EA = 50:1) afforded 1-(benzyloxy)-2-ethynylbenzene **6-3** (1.23 g, 5.89 mmol) in 75% yield [22] as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.5 Hz, 1H), 7.67 (d, *J* = 7.5 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 5.24 (s, 2H), 3.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 137.1, 134.4, 130.5, 128.9, 128.1, 127.3, 121.1,

112.9, 112.4, 82.3, 80.6, 70.4 ppm; IR ν_{max} (film): 3268, 3266, 3146, 3030, 1668, 1466, 1458, 1386, 1368, 1287, 1265, 1215, 1060, 749, 703, 666, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{15}H_{13}O$ $[M+H]^+$: 209.0966; found: 209.0961.

According to the procedure published by Professor Fokin[19]: To a solution of 1-(benzyloxy)-2-ethynylbenzene **6-3** (1.23 g, 5.91 mmol, 1.0 equiv) in dry toluene (60 mL) was added copper(I) thiophene-2-carboxylate (CuTc, 112 mg, 0.59 mmol, 0.1 equiv). Then tosyl azide (0.91 mL, 5.91 mmol, 1.0 equiv) was added dropwise at ambient temperature, and the reaction mixture was allowed to stir for 3 h. The reaction was diluted with saturated aqueous ammonium chloride (60 mL), extracted twice with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (PE: EA = 6:1) to afford 4-(2-(benzyloxy)phenyl)-1-tosyl-1H-1,2,3-triazole **6a** (2.11 g, 5.20 mmol) in 88% yield as a white solid; m p 118-119 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.33 (d, J = 7.6 Hz, 1H), 7.89 (d, J = 8.0 Hz, 2H), 7.47 (s, 5H), 7.33 (d, J = 7.6 Hz, 3H), 7.10 – 7.04 (m, 2H), 5.20 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 147.0, 142.9, 136.4, 133.4, 130.3, 129.9, 128.8, 128.4, 128.0, 127.7, 122.4, 121.3, 118.0, 112.1, 70.7, 21.8 ppm; IR ν_{max} (film): 3175, 2988, 2920, 2848, 2587, 1393, 1200, 1174, 985, 812, 752, 701, 670, 590, 539 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_3NaO_3S$ $[M+Na]^+$: 428.1045; found: 428.1039.

Synthesis of 4-(2-(3-methylbenzyloxy)phenyl)-1-tosyl-1H-1,2,3-triazole (6b): **6b** (1.25 g) was obtained in 78 % yield as a white solid; m p 103-104 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.35 (dd, J = 7.6, 1.2 Hz, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.41 – 7.30 (m, 5H), 7.26 (d, J = 7.2 Hz, 2H), 7.07 (dd, J = 12.8, 7.6 Hz, 2H), 5.17 (s, 2H), 2.47 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 147.0, 142.9, 138.7, 136.3, 133.4, 130.3, 129.9, 129.2, 128.7, 128.4, 128.4, 128.0, 124.7, 122.5, 121.2, 118.0, 112.1, 70.7, 21.8, 21.5 ppm; IR ν_{max} (film): 3472, 3334, 3176, 3063, 2922, 2588, 2126,

1594, 1505, 1393, 1325, 1285, 1240, 1194, 1174, 1150, 1085, 1026, 989, 961, 810, 739, 700, 670, 591, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{22}N_3O_3S$ $[M+H]^+$: 420.1382; found: 420.1376.

Synthesis of 4-(2-(4-methylbenzyloxy)phenyl)-1-tosyl-1H-1,2,3-triazole (6c): **6c** (1.08 g) was obtained in 90 % yield as a white solid; m p 125-126 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.33 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.34 (t, *J* = 8.4 Hz, 5H), 7.30 – 7.27 (m, 2H), 7.07 (dd, *J* = 14.2, 7.6 Hz, 2H), 5.17 (s, 2H), 2.44 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 147.0, 142.9, 138.2, 133.4, 133.4, 130.3, 129.8, 129.5, 128.4, 128.0, 127.7, 122.4, 121.2, 118.1, 112.2, 70.6, 21.8, 21.3 ppm; IR ν_{max} (film): 3355, 3176, 2956, 2900, 2869, 2853, 1742, 1456, 1377, 1287, 1245, 1194, 1175, 1088, 1016, 985, 850, 801, 667, 591 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{22}N_3O_3S$ $[M+H]^+$: 420.1382; found: 420.1376.

Synthesis of 4-(2-(4-tert-butylbenzyloxy)phenyl)-1-tosyl-1H-1,2,3-triazole (6d): **6d** (985 mg) was obtained in 87 % yield as a white solid; m p 121-122 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.35 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.36 – 7.32 (m, 3H), 7.08 (dd, *J* = 7.2, 4.4 Hz, 2H), 5.19 (s, 2H), 2.42 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 151.6, 147.0, 143.0, 133.6, 133.4, 130.4, 129.9, 128.4, 128.0, 127.7, 125.8, 122.6, 121.2, 118.1, 112.2, 70.5, 34.7, 31.4, 21.8 ppm; IR ν_{max} (film): 3175, 2962, 2869, 1500, 1488, 1394, 1246, 1195, 1175, 985, 813, 753, 701, 673, 590, 540 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{28}N_3O_3S$ $[M+H]^+$: 462.1851; found: 462.1847.

Synthesis of 4-(2-(4-methoxybenzyloxy)phenyl)-1-tosyl-1H-1,2,3-triazole (6e): **6e** (2.62 g) was obtained in 90 % yield as a white oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.32 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.34 – 7.32 (m, 3H), 7.11 – 7.03 (m, 2H), 7.03 – 6.96 (m, 2H), 5.13 (s, 2H), 3.88 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 155.2, 147.0, 142.9, 133.4, 130.3, 129.8, 129.4, 128.5, 128.4, 128.0, 122.4, 121.2, 118.1, 114.2, 112.2, 70.5,

55.4, 21.8 ppm; IR ν_{max} (film): 3852, 3668, 3571, 3147, 2920, 2452, 1500, 1391, 1243, 1174, 986, 810, 753, 670, 589, 546 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{22}N_3O_4S$ $[M+H]^+$: 436.1331; found: 436.1324.

Synthesis of 4-(2-(3,5-dimethoxybenzyloxy)phenyl)-1-tosyl-1H-1,2,3-triazole (6f): **6f** (1.85 g) was obtained in 95 % yield as a white oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.33 (d, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 7.6 Hz, 3H), 7.16 – 6.88 (m, 2H), 6.61 (s, 2H), 6.53 (s, 1H), 5.13 (s, 2H), 3.84 (s, 6H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 155.1, 146.9, 142.9, 138.7, 133.4, 130.3, 129.8, 128.5, 128.1, 122.4, 121.3, 118.1, 112.1, 105.5, 100.2, 70.7, 55.4, 21.8 ppm; IR ν_{max} (film): 3866, 3768, 3591, 3222, 3167, 2929, 2452, 1600, 1500, 1396, 1244, 1176, 966, 810, 756, 677, 589, 546 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{24}N_3O_5S$ $[M+H]^+$: 466.1437; found: 466.1427.

Synthesis of 4-(2-(benzyloxy)-5-methylphenyl)-1-tosyl-1H-1,2,3-triazole (6g): **6g** (2.24 g) was obtained in 90 % yield as a white solid; m p 122-123 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.15 (d, *J* = 2.0 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.53 – 7.41 (m, 5H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.12 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 5.16 (s, 2H), 2.41 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 147.0, 143.1, 136.6, 133.4, 130.6, 130.4, 128.8, 128.4, 128.4, 128.4, 127.7, 122.4, 117.7, 112.2, 70.8, 21.8, 20.5 ppm; IR ν_{max} (film): 3852, 3571, 3176, 3030, 2921, 2869, 2125, 1504, 1392, 1284, 1240, 1194, 1174, 989, 962, 810, 739, 700, 670, 590, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{22}N_3O_3S$ $[M+H]^+$: 420.1382; found: 420.1379.

Synthesis of 4-(2-(benzyloxy)-5-chlorophenyl)-1-tosyl-1H-1,2,3-triazole (6h): **6h** (2.65 g) was obtained in 85 % yield as a white solid; m p 169-170 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.30 (d, *J* = 2.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.51 – 7.40 (m, 5H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 2.4 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 1H), 5.19 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 147.1, 141.7, 135.9, 133.2, 130.4, 129.3, 128.9, 128.6, 128.5, 127.7, 127.7, 126.5, 122.8, 119.6,

113.4, 71.1, 21.8 ppm; IR ν_{max} (film): 3856, 3561, 3166, 3130, 2931, 2889, 2126, 1506, 1395, 1248, 1199, 1172, 990, 957, 809, 726, 674, 591, 539 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{19}ClN_3O_3S$ $[M+H]^+$: 440.0836; found: 440.0830.

General procedure for the synthesis of 2,3-disubstituted indoles 2a-2n, 5a-5q: To a solution of triazole (0.20 mmol, 1.0 equiv) in dry toluene (8 mL) was added $Rh_2(Oct)_4$ (7.8 mg, 0.010 mmol, 0.05 equiv) and 4ÅMs (200 wt. %, powder) at room temperature. The resultant mixture was degassed with nitrogen for 3 times, and then stirred under a balloon pressure of nitrogen at 120 °C for 1 h. The reaction mixture was cooled down to RT and was degassed with oxygen for 3 times, and then stirred under a balloon pressure of oxygen at 90 °C for another 1 h. The reaction was worked by removal of the reaction solvent toluene under vacuum, and the residue was purified by a flash column chromatography on silica gel to give the corresponding 2,3-disubstituted indoles.

Synthesis of *N*-((1-acetyl-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfonamide (2a): **2a** (74 mg) was obtained in 89% yield as a yellow solid; mp: 212-213 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.44 (d, *J* = 6.8 Hz, 1H), 8.25 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 7.2 Hz, 2H), 7.62 – 7.56 (m, 3H), 7.48 – 7.40 (m, 4H), 7.32 (d, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 164.2, 150.0, 144.1, 136.9, 135.9, 130.9, 130.3, 129.7, 129.6, 129.4, 127.7, 126.8, 125.4, 125.3, 122.8, 116.2, 115.4, 27.7, 21.6 ppm; IR ν_{max} (film): 3418, 3386, 3364, 3244, 2923, 1645, 1568, 1449, 1331, 1275, 1153, 1085, 736, 705, 546, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{20}N_2NaO_3S$ $[M+Na]^+$: 439.1092; found: 439.1084

Synthesis of *N*-((1-acetyl-6-methyl-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfonamide (2b): **2b** (76 mg) was obtained in 88% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 8.07 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.65 – 7.54 (m, 3H), 7.46 (d, *J* = 6.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 2.51 (s, 3H), 2.42 (s, 3H),

2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 164.3, 149.5, 144.0, 137.2, 137.1, 136.0, 130.8, 130.3, 129.7, 129.6, 129.3, 127.7, 126.8, 123.0, 122.3, 116.3, 115.4, 27.7, 22.0, 21.6 ppm: IR ν_{max} (film): 3188, 3089, 3034, 2933, 2864, 2737, 1801, 1629, 1600, 1492, 1466, 1333, 1268, 1106, 1088, 813, 766, 698, 549, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{22}N_2NaO_3S$ $[M+Na]^+$ = 453.1249; found: 453.1245.

Synthesis of *N*-((1-acetyl-5-methyl-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzene-sulfonamide (2c): **2c** (76 mg) was obtained in 89% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.22 (s, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.71 – 7.51 (m, 3H), 7.45 (d, *J* = 6.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 10.5 Hz, 1H), 2.47 (s, 3H), 2.42 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 164.5, 150.1, 144.0, 135.9, 135.3, 135.1, 130.8, 130.3, 129.7, 129.6, 129.3, 128.1, 127.7, 125.4, 122.5, 116.1, 115.1, 27.6, 21.6, 21.5 ppm; IR ν_{max} (film): 3188, 3099, 3034, 2926, 2853, 2737, 1800, 1628, 1598, 1492, 1466, 1336, 1268, 1166, 1088, 812, 767, 698, 549, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{23}N_2O_3S$ $[M+H]^+$: 431.1429; found: 431.1423.

Synthesis of *N*-((1-acetyl-5-methoxy-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenze-nesulfonamide (2d): **2d** (77 mg) was obtained in 86% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 2.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.67 – 7.52 (m, 3H), 7.45 (d, *J* = 6.8 Hz, 2H), 7.34 – 7.24 (m, 2H), 7.10 – 6.92 (m, 1H), 3.86 (s, 3H), 2.41 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 164.1, 157.6, 150.2, 144.1, 135.9, 131.5, 130.8, 130.3, 129.6, 129.6, 129.3, 127.7, 126.3, 116.5, 116.1, 115.3, 104.9, 55.6, 27.6, 21.6 ppm; IR ν_{max} (film): 3060, 3000, 2955, 2929, 2834, 2592, 1722, 1717, 1611, 1591, 1569, 1480, 1459, 1434, 1366, 1346, 1131, 1284, 1275, 1259, 1196, 1154, 1085, 1033, 1011, 861, 832, 814, 768, 737, 655, 633, 551 cm-1; HRMS (ESI) m/z calcd for $C_{25}H_{23}N_2O_4S$ $[M+H]^+$: 447.1379; found: 447.1381.

Synthesis of *N*-((1-acetyl-6-chloro-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzene-sulfonamide (2e): **2e** (77 mg) was obtained in 86% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.36 – 8.26 (m, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.65 – 7.57 (m, 3H), 7.47 (d, *J* = 6.8 Hz, 2H), 7.35 – 7.31 (m, 3H), 2.43 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 163.8, 150.2, 144.3, 137.2, 135.6, 132.7, 131.1, 130.3, 129.7, 129.5, 129.2, 127.8, 125.9, 123.7, 123.5, 115.9, 115.8, 76.7, 27.6, 21.6 ppm; IR ν_{max} (film): 3063, 2955, 2925, 2853, 2468, 1717, 1589, 1568, 1467, 1418, 1367, 1323, 1314, 1266, 1236, 1211, 1155, 1086, 1017, 889, 852, 814, 791, 766, 723, 686, 649, 632, 557, 548 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{20}ClN_2O_3S$ $[M+H]^+$: 451.0883; found: 451.0902.

Synthesis of *N*-((1-acetyl-5-chloro-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzene-sulfonamide (2f): **2f** (82 mg) was obtained in 91% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.37 (d, *J* = 2.0 Hz, 1H), 8.16 (d, *J* = 8.9 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.61 (td, *J* = 8.9, 4.5 Hz, 3H), 7.47 (dd, *J* = 7.7, 1.2 Hz, 2H), 7.37 – 7.28 (m, 3H), 2.42 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 163.8, 150.7, 144.3, 135.5, 135.2, 131.1, 131.0, 130.3, 129.8, 129.5, 129.1, 127.8, 126.9, 126.4, 122.2, 116.7, 115.4, 27.6, 21.6 ppm; IR ν_{max} (film): 3066, 2998, 2926, 1777, 1596, 1595, 1477, 1429, 1401, 1365, 1329, 1314, 1290, 1208, 1117, 1030, 855, 730, 689, 664, 580 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{20}ClN_2O_3S$ $[M+H]^+$: 451.0883; found: 451.0880.

Synthesis of *N*-((1-acetyl-7-chloro-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzene-sulfonamide (2g): **2g** (76 mg) was obtained in 85% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.41 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.65 – 7.54 (m, 3H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.32 – 7.29 (m, 3H), 2.41 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 163.7, 150.5, 144.0, 136.2, 132.6, 131.1, 130.8, 129.7, 129.1, 127.9, 127.6, 127.1, 126.6, 125.4, 121.9, 117.7, 113.0, 29.7, 21.6 ppm; IR ν_{max} (film): 3063, 2954, 2850, 1729, 1595, 1530,

1426, 1316, 1287, 1274, 1155, 1086, 1017, 761, 663, 551 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}ClN_2NaO_3S$ $[M+Na]^+$: 473.0703; found: 473.0692.

Synthesis of *N*-((1-acetyl-4-chloro-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzene-sulfonamide (2h): **2h** (74 mg) was obtained in 82% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.52 – 7.46 (m, 1H), 7.43 – 7.31 (m, 7H), 7.23 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 163.6, 144.5, 143.8, 137.5, 135.5, 130.7, 130.2, 129.3, 128.5, 127.7, 126.5, 126.1, 125.9, 124.5, 114.3, 27.8, 21.6 ppm; IR ν_{max} (film): 3061, 2954, 2924, 1766, 1599, 1595, 1477, 1429, 1402, 1364, 1329, 1314, 1290, 1268, 1208, 1117, 1087, 1030, 852, 788, 730, 703, 689, 664, 550 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}ClN_2NaO_3S$ $[M+Na]^+$: 473.0703; found: 473.0695.

Synthesis of *N*-((1-acetyl-6-fluoro-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzene-sulfonamide (2i): **2i** (77 mg) was obtained in 89% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.36 (dd, *J* = 8.4, 5.6 Hz, 1H), 8.03 (dd, *J* = 10.0, 2.0 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.66 – 7.56 (m, 3H), 7.47 (d, *J* = 6.8 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 3H), 7.13 (td, *J* = 8.8, 2.0 Hz, 1H), 2.43 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 163.9, 162.0 (d, $^1J_{C-F}$ = 242.2 Hz), 150.1, 144.2, 137.3, 137.1, 135.7, 131.0, 130.3, 129.7, 129.4, 129.3, 127.8, 123.8, 123.7, 121.5, 116.1, 113.7, 113.5, 103.3, 103.0, 27.5, 21.6 ppm; IR ν_{max} (film): 3063, 2923, 2855, 2398, 1727, 1585, 1568, 1447, 1366, 1332, 1315, 1302, 1275, 1211, 1155, 1087, 1015, 856, 812, 765, 718, 691, 548 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}FN_2NaO_3S$ $[M+Na]^+$: 457.0998; found: 457.0992.

Synthesis of *N*-((1-acetyl-2-phenyl-5-(trifluoromethyl)-1*H*-indol-3-yl)methylene)-4-methylbenzene sulfonamide (2j): **2j** (77 mg) was obtained in 80% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.70 (s, 1H), 8.36 (d, *J* = 8.8 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.68 – 7.61 (m, 4H), 7.49 (d, *J* = 6.8 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H), 2.02 (s, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 170.9, 163.5, 151.0, 144.4, 138.3, 135.5, 131.3, 130.3, 129.7, 129.6, 129.0, 128.0, 127.8, 127.7, 127.3, 127.0, 125.6, 125.1, 124.3(q, $^1J_{C-F}$ = 200.5 Hz), 123.5, 120.2, 120.1, 115.9, 115.9, 27.6, 21.6 ppm; IR ν_{max} (film): 3500, 3208, 3064, 2926, 2855, 1729, 1591, 1575, 1461, 1367, 1329, 1299, 1281, 1211, 1156, 1121, 1087, 861, 825, 814, 768, 696, 546 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{20}F_3N_2O_3S$ $[M+H]^+$: 485.1147; found: 485.1141.

Synthesis of *N*-((1-acetyl-5-nitro-2-phenyl-1*H*-indol-3-yl)methylene)-4-methylbenzene -sulfonamide (2k): **2k** (72 mg) was obtained in 78% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 9.17 (d, *J* = 2.0 Hz, 1H), 8.80 (s, 1H), 8.32 (d, *J* = 9.2 Hz, 1H), 8.23 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.71 – 7.61 (m, 3H), 7.52 (d, *J* = 6.8 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 162.9, 151.8, 145.2, 144.6, 139.6, 135.4, 131.5, 130.2, 129.8, 129.7, 128.6, 127.9, 125.4, 121.7, 118.8, 115.9, 27.6, 21.6 ppm; IR ν_{max} (film): 3621, 3529, 3347, 2919, 2849, 1730, 1576, 1448, 1320, 1275, 1211, 1155, 1085, 1016, 764, 748, 692, 551, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{20}N_3O_5S$ [M+H]+: 462.1124; found: 462.1123.

Synthesis of 4-methyl-*N*-((2-phenyl-1-tosyl-1*H*-indol-3-yl)methylene)benzenesulfonam- ide (2l): **2l** (93 mg) was obtained in 88% yield as a yellow solid; m p: 96-97 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.44 – 8.32 (m, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 3H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.36 – 7.25 (m, 7H), 7.12 (d, *J* = 8.0 Hz, 2H), 2.40 (s, 3H), 2.33 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 151.8, 145.9, 144.2, 137.0, 135.5, 134.9, 131.8, 130.6, 129.8, 129.7, 129.0, 128.3, 127.8, 127.8, 127.6, 127.0, 126.6, 126.0, 125.6, 123.0, 117.5, 115.4, 21.6, 21.6 ppm: IR ν_{max} (film): 3360, 3262, 3060, 2953, 2924, 2852, 1669, 1596, 1448, 1403, 1380, 1336, 1307, 1257, 1214, 1191, 1178, 1163, 1127, 1093, 1081, 974, 813, 789, 752, 702, 681, 662, 572, 542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{29}H_{25}N_2O_4S_2$ $[M+H]^+$: 529.1256; found: 529.1250.

Synthesis of 4-methyl-*N*-((1-methyl-2-phenyl-1*H*-indol-3-yl)methylene)benzenesulfona- mide (2m): **2m** (45 mg) was obtained in 58% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.48 (d, *J* = 7.2 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 3.6 Hz, 3H), 7.40 – 7.36 (m, 4H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.29 – 7.25 (m, 2H), 3.66 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 153.3, 143.2, 138.1, 137.4, 130.7, 130.3, 129.5, 129.0, 127.9, 127.3, 125.2, 124.6, 123.7, 123.2, 111.1, 110.2, 31.6, 21.5 ppm: IR ν_{max} (film): 3088, 3066, 2966, 2925, 2867, 1777, 1645, 1600, 1500, 1456, 1366, 1285, 1263, 1219, 1166, 1085, 1033, 936, 775, 681, 608, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{21}N_2O_2S$ $[M+H]^+$: 389.1324; found: 389.1316.

Synthesis of 4-methyl-*N*-((1-methyl-1*H*-indol-3-yl)methylene)benzenesulfonamide (2n): **2n** (49 mg) was obtained in 78 % yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.32 – 7.26 (m, 2H), 7.18 – 7.00 (m, 2H), 6.89 – 6.85 (m, 1H), 6.81 – 6.78 (m, 2H), 5.71 (d, *J* = 9.6 Hz, 1H), 4.66 (s, 2H), 2.91 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 143.8, 136.8, 132.3, 129.8, 127.1, 126.9, 126.2, 125.8, 121.1, 117.0, 112.7, 67.4, 40.0, 21.5 ppm; IR ν_{max} (film): 3064, 3030, 2955, 2925, 2855, 1729, 1634, 1596, 1495, 1443, 1348, 1286, 1266, 1219, 1166, 1087, 1044, 936, 775, 754, 681, 606, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{19}N_2O_2S$ $[M+H]^+$: 315.1167; found: 315.1159.

Synthesis of 4-methyl-*N*-((1-methyl-1*H*-indol-3-yl)methylene)benzenesulfonamide (2o): **2o** (20 mg) was obtained in 25 % yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 2H), 7.38 – 7.17 (m, 8H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.92 – 6.76 (m, 3H), 5.73 (d, *J* = 10.0 Hz, 1H), 4.49 (s, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 143.9, 138.3, 136.6, 132.2, 129.9, 128.6, 127.1, 127.0, 126.9, 126.8, 126.8, 126.3, 121.6, 119.1, 111.8, 65.3, 56.8, 29.7, 21.5 ppm; IR ν_{max} (film): 3082, 2968, 2935, 2866, 1777, 1666, 1600, 1505, 1454, 1356, 1274, 1255, 1209, 1168, 1080,

1032, 933, 776, 686, 608, 541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{23}N_2O_2S$ $[M+H]^+$: 391.1480; found: 391.1476.

Synthesis of *N*-((1-acetyl-2-(*o*-tolyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfona- mide (5a): **5a** (77 mg) was obtained in 90% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.44 (d, *J* = 7.2 Hz, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.46 – 7.39 (m, 4H), 7.35 – 7.28 (m, 3H), 2.41 (s, 3H), 2.16 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 163.7, 149.7, 144.1, 137.8, 136.9, 135.8, 131.1, 130.8, 129.7, 129.3, 127.7, 126.7, 126.7, 125.4, 125.4, 122.6, 116.4, 116.1, 26.7, 21.6, 19.9 ppm; IR ν_{max} (film): 3116, 3057, 2923, 2859, 1718, 1589, 1570, 1448, 1368, 1325, 1286, 1211, 1154, 1085, 1015, 798, 759, 693, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{23}N_2O_3S$ $[M+H]^+$: 431.1429; found: 431.1422.

Synthesis of *N*-((1-acetyl-2-(*m*-tolyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfona- mide (5b): **5b** (74 mg) was obtained in 86% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.43 (d, *J* = 7.2 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.50 – 7.36 (m, 4H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.27 (s, 2H), 2.48 (s, 3H), 2.42 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 164.4, 150.3, 144.0, 139.4, 136.8, 136.0, 131.7, 130.8, 129.7, 129.5, 129.2, 127.7, 127.5, 126.7, 125.3, 125.3, 122.7, 116.1, 115.4, 27.7, 21.6, 21.4 ppm; IR ν_{max} (film): 3216, 3157, 2926, 2869, 1724, 1592, 1570, 1449, 1329, 1284, 1273, 1154, 1085, 1017, 811, 779, 719, 691, 5456 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{23}N_2O_3S$ $[M+H]^+$: 431.1429; found: 431.1425.

Synthesis of *N*-((1-acetyl-2-(*p*-tolyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfona- mide (5c): **5c** (76 mg) was obtained in 88% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.42 (d, *J* = 7.2 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.29 (m, 8H), 2.50 (s, 3H), 2.42 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 164.5, 150.5, 144.0, 141.4, 136.8, 136.1, 130.2, 130.1, 129.7, 127.7, 126.7, 126.5, 125.3, 122.7, 116.1, 115.3, 27.7, 21.6,

21.5 ppm; IR ν_{max} (film): 3063, 3047, 3004, 2954, 2927, 2840, 1606, 1594, 1581, 1565, 1560, 1502, 1452, 1355, 1306, 1262, 1176, 1155, 1077, 1027, 916, 774, 752, 669, 554, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{23}N_2O_3S$ $[M+H]^+$: 431.1429; found: 431.1421.

Synthesis of *N*-((1-acetyl-2-(4-(*tert*-butyl)phenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfonamide (5d): **5d** (83 mg) was obtained in 88% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.43 (d, *J* = 7.2 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.37 (m, 4H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.41 (s, 3H), 1.99 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 164.4, 154.5, 150.5, 144.0, 136.8, 136.1, 130.1, 129.7, 127.7, 126.6, 126.4, 126.4, 125.3, 125.3, 122.7, 115.9, 115.2, 35.1, 31.2, 27.6, 21.6 ppm; IR ν_{max} (film): 3058, 2963, 2929, 2869, 1723, 1589, 1569, 1449, 1366, 1329, 1288, 1275, 1212, 1155, 1085, 1018, 867, 786, 748, 694, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{29}N_2O_3S$ $[M+H]^+$: 473.1899; found: 473.1898.

Synthesis of *N*-((1-acetyl-2-(3-methoxyphenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfonamide (5e): **5e** (59 mg) was obtained in 66% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.43 (d, *J* = 7.6 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.52 – 7.40 (m, 3H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.14 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.97 (s, 1H), 3.89 (s, 3H), 2.42 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 164.3, 160.0, 149.7, 144.1, 136.8, 135.9, 130.7, 130.5, 129.7, 127.7, 126.8, 125.4, 125.2, 122.7, 122.7, 116.3, 116.2, 116.0, 115.4, 55.6, 27.5, 21.6 ppm; IR ν_{max} (film): 3197, 3004, 2956, 2925, 2854, 1716, 1608, 1589, 1568, 1376, 1330, 1288, 1277, 1208, 1154, 1085, 1040, 1017, 896, 809, 753, 720, 692, 667, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{23}N_2O_4S$ $[M+H]^+$: 447.1379; found: 447.1374.

Synthesis of *N*-((1-acetyl-2-(4-methoxyphenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfonamide (5f): **5f** (62 mg) was obtained in 70% yield as a yellow oil; ^1H NMR (400 MHz,

$CDCl_3$) δ 8.80 (s, 1H), 8.41 (d, *J* = 7.2 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.34 (m, 4H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 3.92 (s, 3H), 2.41 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 164.5, 161.6, 150.4, 144.0, 136.8, 136.1, 131.7, 129.7, 127.7, 126.6, 125.3, 122.6, 121.3, 115.9, 115.3, 114.9, 55.5, 27.7, 21.6 ppm; IR ν_{max} (film): 3196, 3000, 2966, 2925, 2858, 1716, 1608, 1589, 1577, 1375, 1330, 1288, 1278, 1155, 1066, 1040, 898, 809, 766, 720, 692, 668, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{23}N_2O_4S$ $[M+H]^+$: 447.1379; found: 447.1374.

Synthesis of N-((1-acetyl-2-(3,5-dimethoxyphenyl)-1H-indol-3-yl)methylene)-4-methylbenzenesulfonamide (5g): **5g** (57 mg) was obtained in 60% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.45 – 7.37 (m, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 6.66 (t, *J* = 2.2 Hz, 1H), 6.57 (d, *J* = 2.0 Hz, 2H), 3.86 (s, 6H), 2.42 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 164.3, 161.3, 149.7, 144.1, 136.8, 135.9, 131.1, 129.7, 127.7, 126.8, 125.4, 125.2, 122.7, 116.1, 115.4, 108.8, 102.4, 55.7, 27.3, 21.6 ppm; IR ν_{max} (film): 3198, 3000, 2966, 2936, 2858, 1716, 1592, 1570, 1454, 1340, 1317, 1278, 1206, 1153, 1086, 825, 752, 720, 688, 544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{25}N_2O_5S$ $[M+H]^+$: 477.1484; found: 477.1478.

Synthesis of *N*-((1-acetyl-2-(2-chlorophenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfonamide (5h): **5h** (54 mg) was obtained in 60% yield as a yellow oil; ^{1}H NMR 400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.44 (d, *J* = 7.6 Hz, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.62 – 7.57 (m, 2H), 7.53 – 7.40 (m, 4H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 163.4, 146.2, 144.2, 136.8, 135.7, 134.8, 132.4, 132.3, 130.5, 129.7, 129.2, 127.8, 127.6, 127.0, 125.4, 125.3, 122.9, 116.9, 115.9, 26.5, 21.6 ppm; IR ν_{max} (film): 3322, 3243, 3060,

2920, 2849, 1725, 1599, 1500, 1446, 1367, 1329, 1286, 1211, 1155, 1086, 862, 786, 757, 735, 691, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{20}ClN_2O_3S$ $[M+H]^+$: 451.0883; found: 451.0879.

Synthesis of *N*-((1-acetyl-2-(3-chlorophenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfonamide (5i): **5i** (82 mg) was obtained in 91% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 2.0 Hz, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.60 – 7.52 (m, 2H), 7.48 – 7.35 (m, 4H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 163.5, 147.8, 144.3, 136.8, 135.4, 131.4, 131.0, 130.6, 130.2, 129.7, 128.5, 127.8, 127.1, 125.5, 125.1, 122.8, 116.6, 115.4, 27.8, 21.6 ppm; IR ν_{max} (film): 3062, 2956, 2925, 2854, 1725, 1592, 1568, 1448, 1366, 1329, 1283, 1261, 1211, 1186, 1086, 1035, 790, 717, 666, 546 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}ClN_2NaO_3S$ $[M+Na]^+$: 473.0703; found: 473.0697.

Synthesis of *N*-((1-acetyl-2-(4-chlorophenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzene sulfonamide (5j): **5j** (77 mg) was obtained in 86% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.47 – 7.38 (m, 4H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 163.6, 148.3, 144.3, 137.4, 136.8, 135.6, 131.5, 129.7, 129.7, 128.0, 127.8, 127.0, 125.5, 125.2, 122.8, 116.5, 115.3, 27.9, 21.6 ppm; IR ν_{max} (film): 3083, 3058, 2955, 2925, 2853, 1723, 1589, 1569, 1486, 1447, 1367, 1329, 1285, 1264, 1211, 1155, 1085, 1017, 821, 786, 732, 712, 690, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}ClN_2NaO_3S$ $[M+Na]^+$: 473.0703; found: 473.0698.

Synthesis of *N*-((1-acetyl-2-(2-fluorooorophenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzenesulfonamide (5k): **5k** (69 mg) was obtained in 80% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.45 (d, *J* = 7.6 Hz, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.48 – 7.35 (m, 1H), 7.49 – 7.39 (m, 4H), 7.36 – 7.29 (m, 3H), 2.43 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 163.6, 159.9 (d, $^1J_{C-F}$ = 248.2 Hz), 158.7, 144.2, 143.3, 137.0, 135.7, 133.3,

133.2, 132.2, 129.7, 127.8, 126.9, 125.4, 125.3, 125.2, 125.1, 122.9, 118.0, 117.8, 117.1, 116.7, 116,5, 115.4, 26.5, 21.6 ppm; IR ν_{max} (film): 3320, 3200, 3175, 3060, 2922, 2389, 1725, 1598, 1574, 1484, 1453, 1447, 1366, 1334, 1285, 1268, 1225, 1208, 1153, 1085, 1016, 866, 811, 763, 738, 712, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{20}FN_2O_3S$ $[M+H]^+$: 435.1179; found: 435.1173.

Synthesis of *N*-((1-acetyl-2-(3-fluorooorophenyl)-1*H*-indol-3-yl)methylene)-4-methylbenz-enesulfonamide (5l): **5l** (74 mg) was obtained in 85% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.43 (d, *J* = 7.6 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 2H), 7.67 – 7.53 (m, 1H), 7.47 – 7.38 (m, 2H), 7.35 – 7.29 (m, 4H), 7.19 (d, *J* = 8.4 Hz, 1H), 2.43 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 163.6, 162.7(d, $^1J_{C-F}$ = 249.5 Hz), 147.8, 144.2, 136.8, 135.6, 131.6, 131.5, 131,3, 131.2, 129.7, 127.8, 127.0, 126.3, 126.3, 125.5, 125.1, 122.8, 118.1, 117.9, 117.6, 117.4, 116.5, 115.4, 27.6, 21.6 ppm; IR ν_{max} (film): 3628, 3517, 3454, 2924, 2893, 2357, 1729, 1587, 1450, 1330, 1279, 1267, 1151, 1086, 1016, 817, 763, 752, 719, 866, 544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{20}FN_2O_3S$ $[M+H]^+$: 435.1179; found: 435.1173.

Synthesis of *N*-((1-acetyl-2-(4-fluorooorophenyl)-1*H*-indol-3-yl)methylene)-4-methylbenz-enesulonamide (5m): **5m** (69 mg) was obtained in 80% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.42 (d, *J* = 7.2 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.67 – 7.53 (m, 4H), 7.33 – 7.28 (m, 4H), 2.43 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.70, 164.1 (d, $^1J_{C-F}$ = 251.9 Hz), 163.8, 148.6, 144.2, 136.8, 135.7, 132.4, 132.3, 129.7, 127.8, 126.9, 125.6, 125.6, 125.5, 125.2, 122.7, 116.9, 116.7, 116.5, 115.4, 27.8, 21.6 ppm; IR ν_{max} (film): 3200, 2955, 2922, 2850, 1724, 1593, 1573, 1448, 1367, 1329, 1288, 1274, 1268, 1229, 1153, 1085, 1012, 828, 763, 752, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}FN_2NaO_3S$ $[M+Na]^+$: 457.0998; found: 457.0991.

Synthesis of *N*-((1-acetyl-2-(2-iodophenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzene-sulfonamid (5n): **5n** (75 mg) was obtained in 69% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$)

δ 8.56 (s, 1H), 8.44 (d, *J* = 7.6 Hz, 1H), 8.35 (d, *J* = 8.2 Hz, 1H), 8.03 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.58 (td, *J* = 7.2, 0.8 Hz, 1H), 7.50 – 7.40 (m, 3H), 7.34 – 7.29 (m, 3H), 2.42 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 163.5, 150.4, 144.2, 139.9, 136.6, 135.6, 135.5, 132.1, 131.8, 129.7, 128.8, 127.9, 127.1, 125.5, 125.2, 122.9, 116.6, 116.2, 100.6, 27.1, 21.6 ppm; IR ν_{max} (film): 3277, 3059, 2954, 2924, 2853, 1723, 1594, 1568, 1444, 1366, 1329, 1318, 1285, 1209, 1154, 1086, 1014, 860, 814, 786, 757, 730, 709, 687, 544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{20}IN_2O_3S$ $[M+H]^+$: 543.0239; found: 543.0233.

Synthesis of *N*-((1-acetyl-2-(2-cyanophenyl)-1*H*-indol-3-yl)methylene)-4-methylbenzene-sulfonamide (5o): **5o** (55 mg) was obtained in 62% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.47 (d, *J* = 7.6 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.90 – 7.84 (m, 3H), 7.84 – 7.76 (m, 1H), 7.70 (td, *J* = 8.0, 1.0 Hz, 1H), 7.55 (d, J = 7.6 Hz, 1H), 7.53 – 7.46 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 162.8, 144.9, 144.4, 136.4, 135.4, 133.9, 133.5, 133.2, 131.6, 130.6, 129.8, 127.9, 127.2, 125.7, 125.5, 123.5, 117.6, 116.7, 114.8, 113.8, 27.0, 21.6 ppm; IR ν_{max} (film): 3282, 2957, 2922, 2849, 2802, 2740, 2394, 2226, 1729, 1593, 1569, 1451, 1366, 1329, 1283, 1268, 1216, 1154, 1086, 1015, 789, 764, 745, 692, 544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{20}N_3O_3S$ $[M+H]^+$: 442.1225; found: 442.1217.

Synthesis of *N*-((1-acetyl-2-(3-(trifluoromethyl)phenyl)-1*H*-indol-3-yl)methylene)-4-met-hylbenzenesulfonamide (5p): **5p** (76 mg) was obtained in 78% yield as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 2H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 8.8 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 163.3, 147.4, 144.3, 136.8, 135.4 133.6, 132.2, 132.0, 131.6, 131.4 130.7, 130.0, 129.7, 127.8, 127.4, 127.4, 127.2, 127.1, 125.6, 125.2, 123.3 (q, $^1J_{C-F}$ = 271.2 Hz), 122.9, 116.9, 115.4, 27.8, 21.6 ppm; IR ν_{max}

(film): 3464, 3064, 2923, 2851, 1738, 1595, 1572, 1367, 1337, 1300, 1213, 1180, 1129, 1110, 807, 751, 719, 701, 544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{20}F_3N_2O_3S$ $[M+H]^+$: 485.1147; found: 485.1142.

Synthesis of *N*-((1-acetyl-2-(naphthalen-1-yl)-1*H*-indol-3-yl)methylene)-4-methylbenzen-esulfonamide (5q): **5q** (76 mg) was obtained in 81% yield as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.48 (d, *J* = 7.2 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.99 – 7.96 (m, 3H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.72 – 7.64 (m, 2H), 7.53 – 7.42 (m, 3H), 7.26 (d, *J* = 6.8 Hz, 2H), 2.37 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 164.2, 150.0, 144.1, 137.0, 135.6, 133.8, 132.7, 130.5, 129.6, 129.3, 128.5, 128.2, 128.1, 127.8, 127.7, 126.8, 126.8, 126.6, 125.4, 125.4, 122.8, 116.5, 115.4, 27.8, 21.5 ppm; IR ν_{max} (film): 3281, 3058, 3032, 2957, 2925, 2854, 1719, 1590, 1580, 1447, 1366, 1317, 1281, 1210, 1153, 1085, 1017, 821, 754, 714, 673, 545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{23}N_2O_3S$ [M+H]+: 467.1429; found: 467.1425.

General procedure for the synthesis of 2, 3-disubstituted benzufurans 7a-7h: To a solution of a triazole (0.20 mmol, 1.0 equiv) in dry toluene (8 mL) was added $Rh_2(Oct)_4$ (7.8 mg, 0.01 mmol, 0.05 equiv) and 4ÅMs (200 wt. %, powder) at room temperature. The resultant mixture was degassed with nitrogen for 3 times, and then stirred under a balloon pressure of nitrogen at 120 °C for 4 h. The reaction mixture was cooled down to RT and was degassed with oxygen for 3 times, and then stirred under a balloon pressure of oxygen at 90 °C for another 2 h. The reaction was worked by removal of the reaction solvent toluene under vacuum, and the residue was purified by a flash column chromatography on silica gel to give the corresponding 2,3-disubstituted benzofurans.

Synthesis of 4-methyl-*N*-((2-phenylbenzofuran-3-yl) methylene)benzenesulfonamide (7a): **7a** (60 mg) was obtained in 80% yield as a white solid; mp: 130-131; ^1H NMR (400 MHz, $CDCl_3$) δ 9.38 (s, 1H), 8.30 (d, *J* = 7.2 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 2H), 7.80 (dd, *J* = 6.4, 3.2 Hz, 2H), 7.65 – 7.53 (m,

4H), 7.44 – 7.34 (m, 4H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 163.5, 154.4, 144.3, 135.8, 131.5, 129.8, 129.4, 129.1, 128.2, 127.8, 126.4, 125.1, 124.9, 123.6, 113.2, 111.2, 21.6 ppm; IR ν_{max} (film): 3176, 3030, 2955, 2923, 2853, 2735, 2245, 1597, 1580, 1499, 1331, 1318, 1292, 1184, 1156, 1100, 1000, 812, 772, 751, 667, 625, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{18}NO_3S$ $[M+H]^+$: 376.1007; found: 376.1002.

Synthesis of 4-methyl-*N*-((2-(*m*-tolyl)benzofuran-3-yl) methylene)benzenesulfonamide (7b): **7b** (40 mg) was obtained in 52% yield as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.34 – 8.25 (m, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.60 – 7.55 (m, 3H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.44 – 7.34 (m, 5H), 2.49 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 163.6, 154.4, 144.2, 139.3, 135.8, 132.3, 129.7, 129.5, 129.3, 128.1, 127.8, 126.4, 126.3, 125.2, 124.8, 123.6, 113.1, 111.1, 21.6, 21.5 ppm; IR ν_{max} (film): 3065, 3032, 3008, 2922, 2849, 1609, 1507, 1332, 1295, 1262, 1200, 1153, 1110, 1017, 814, 745, 663, 574 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{20}NO3S$ $[M+H]^+$: 390.1164; found: 390.1157.

Synthesis of 4-methyl-*N*-((2-(*p*-tolyl)benzofuran-3-yl) methylene)benzenesulfonamide (7c): **7c** (47 mg) was obtained in 61% yield as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37 (s, 1H), 8.29 (d, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.43 – 7.32 (m, 6H), 2.49 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 163.6, 154.4, 144.2, 142.2, 136.0, 130.1, 129.7, 129.0, 127.8, 126.2, 125.4, 125.2, 124.8, 123.5, 112.8, 111.1, 21.6 ppm; IR ν_{max} (film): 3066, 3032, 3008, 2955, 2922, 2849, 1595, 1581, 1451, 1320, 1289, 1155, 1088, 1076, 916, 816, 755, 751, 669, 552 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{20}NO_3S$ $[M+H]^+$: 390.1164; found: 390.1155.

Synthesis of *N*-((2-(4-(tert-butyl)phenyl)benzofuran-3-yl)methylene)-4-methylbenzene -sulfonamide (7d): **7d** (52 mg) was obtained in 60% yield as a white oil; ^{1}H NMR (400 MHz, $CDCl_3$)

δ 9.39 (s, 1H), 8.32 – 8.19 (m, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.32 (m, 5H), 2.44 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 163.7, 155.2, 154.4, 144.1, 136.0, 129.7, 128.9, 127.8, 126.4, 126.2, 125.3, 125.2, 124.8, 123.5, 112.8, 111.1, 35.1, 31.3, 31.1, 21.6 ppm; IR ν_{max} (film): 3068, 3033, 3008, 2958, 2925, 2853, 1594, 1580, 1451, 1321, 1254, 1156, 1100, 1096, 918, 851, 815, 781, 751, 669, 551 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{26}NO_3S$ $[M+H]^+$: 432.1633; found: 432.1626.

Synthesis of *N*-((2-(4-methoxyphenyl)benzofuran-3-yl)methylene)-4-methylbenzene- sulfonamide (7e): **7e** (57 mg) was obtained in 70% yield as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.32 – 8.22 (m, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.33 (m, 4H), 7.09 (d, *J* = 8.8 Hz, 2H), 3.92 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 163.6, 162.3, 154.2, 144.1, 136.1, 130.7, 129.7, 127.8, 126.1, 125.3, 124.8, 123.4, 120.6, 114.9, 112.1, 111.0, 55.6, 21.6 ppm; IR ν_{max} (film): 3006, 2966, 2921, 2856, 1600, 1588, 1456, 1318, 1261, 1157, 1066, 1056, 803, 763, 760, 671, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{20}NO_4S$ $[M+H]^+$: 406.1113; found: 406.1108.

Synthesis of *N*-((2-(3,5-dimethoxyphenyl)benzofuran-3-yl)methylene)-4-methylbenzen-esulfonamide (7f): **7f** (57 mg) was obtained in 66% yield a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.29 (d, *J* = 7.2 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.47 – 7.33 (m, 4H), 6.89 (d, *J* = 2.0 Hz, 2H), 6.68 (t, *J* = 2.2 Hz, 1H), 3.90 (s, 6H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.7, 161.3, 154.3, 144.3, 135.8, 129.8, 129.6, 127.8, 126.4, 125.1, 124.9, 123.6, 113.3, 111.2, 107.0, 103.8, 55.7, 21.6 ppm; IR ν_{max} (film): 3004, 2957, 2921, 2849, 1596, 1560, 1456, 1318, 1280, 1261, 1157, 1046, 803, 763, 750, 670, 549 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}NO_5S$ $[M+H]^+$: 436.1219; found: 436.1211.

Synthesis of 4-methyl-*N*-((5-methyl-2-phenylbenzofuran-3-yl)methylene)benzenesulfo- namide (7g): **7g** (37 mg) was obtained in 48% yield as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H), 8.09 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.78 (dd, *J* = 6.2, 3.0 Hz, 2H), 7.64 – 7.54 (m, 3H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 1H), 2.47 (s, 3H), 2.45 (s, 3H); 13C NMR (100 MHz, $CDCl_3$) δ 166.7, 163.8, 152.9, 144.2, 135.9, 134.7, 131.3, 129.7, 129.3, 129.1, 128.3, 127.8, 127.6, 125.1, 123.4, 113.0, 110.7, 21.6, 21.5 ppm; IR ν_{max} (film): 3333, 3176, 2954, 2924, 1600, 1573, 1400, 1321, 1260, 1155, 1088, 866, 768, 751, 661, 547 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{20}NO_3S$ $[M+H]^+$: 390.1164; found: 390.1160.

Synthesis of *N*-(5-chloro-2-phenylbenzofuran-3-yl methylene)-4-methylbenzenesulfon-amide (7h): **7h** (65 mg) was obtained in 79% yield as a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.34 (s, 1H), 8.26 (d, *J* = 1.5 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.82 – 7.74 (m, 2H), 7.62 – 7.58 (m, 3H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.39 – 7.33 (m, 3H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 163.1, 152.8, 144.5, 135.6, 131.8, 130.7, 129.9, 129.5, 129.2, 128.0, 127.9, 126.8, 126.6, 123.3, 112.7, 112.3, 21.7 ppm. IR ν_{max} (film): 3125, 3036, 2954, 2850, 1606, 1505, 1456, 1331, 1295, 1262, 1153, 1109, 1084, 1017, 813, 749, 573, 543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{17}ClNO_3S$ $[M+H]^+$: 410.0618; found: 410.0608.

ASSOCIATED CONTENT

Supporting Information. Compound characterization data-are available free of charge via the Internet at http://pubs.acs.org.

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