Electronic Supplementary Information

Conformationally restricted functionalized heteroaromatics: A direct access to novel indoloindoles via Pd-mediated reaction

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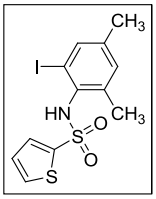
Experimental Section

Chemistry

General methods: Unless stated otherwise, reactions were performed under nitrogen atmosphere using oven dried glassware. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254), visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (230-400 mesh) using distilled hexane, ethyl acetate. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution by using 400 or 100 MHz spectrometers, respectively. Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, δ = 0.00) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), dd (doublet of doublet), td (triplet of doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants (*J*) are given in hertz. Infrared spectra were recorded on a FT- IR spectrometer. Melting points were determined by using melting point apparatus and are uncorrected. MS spectra were obtained by using Agilent 6430 series Triple Quard LC-MS / MS spectrometer. Melting points (mp) were by using Buchi B-540 melting point appratus.

General Procedure for the preparation of starting materials: Starting materials **1a**−**1l** were prepared according to the procedure described in literature.[1] The compound **1m** was prepared according to a procedure (i.e. bromination followed by tosylation) described in the literature[2,3]. Other starting materials i.e. **2a**−**2d** were prepared via methylation, benzylation and allylation of the corresponding indoles according to a known procedure.[4]

***N*-(2-Iodo-4,6-dimethylphenyl)thiophene-2-sulfonamide (1l)**

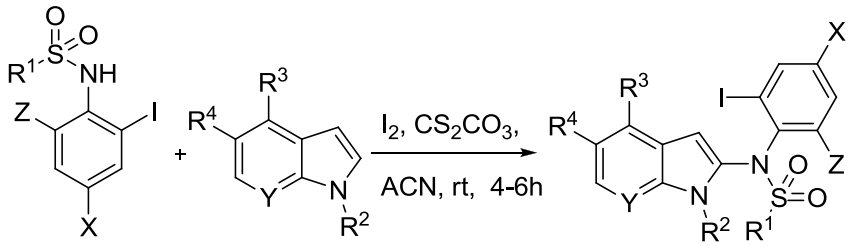


White solid; yield: 80%; mp: 143-145 °C; R_f (12% EtOAc-*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.43-7.42 (m, 2H), 7.09-7.08 (m, 2H), 6.22 (s, 1H), 2.51 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.6, 139.7, 139.5, 137.5, 133.2, 132.9, 132.8, 132.7, 127.6, 99.8, 20.6, 20.3; IR (KBr, cm^{-1}): 3290, 3100, 2924, 1336, 1157; MS (ES mass): *m*/*z* 394.3 (M+1).

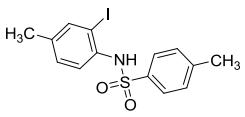
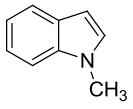
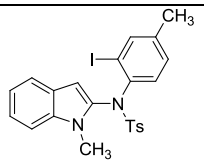
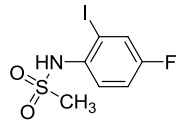
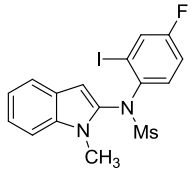
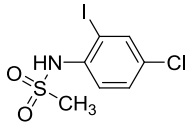
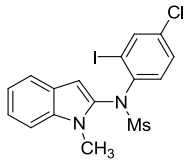
General procedure for the preparation of *N*-(4-substituted-2-iodophenyl)-*N*-(1-alkyl-1*H*-indol-2-yl)alkane/arene/heteroarene sulfonamide (3):

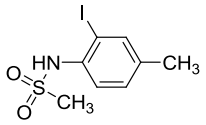
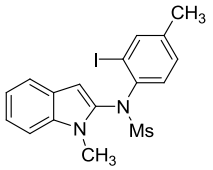
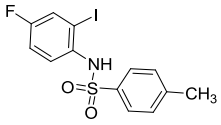
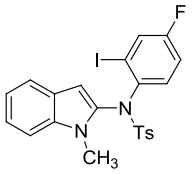
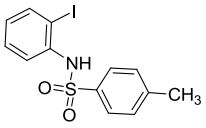
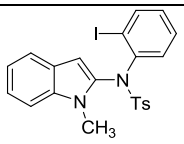
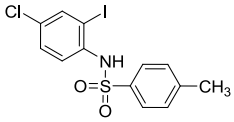
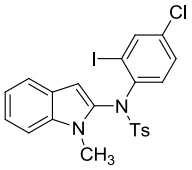
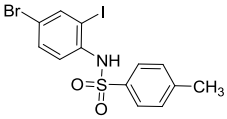
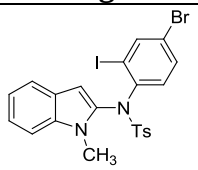
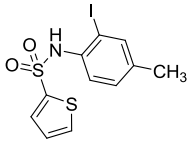
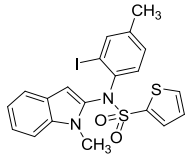
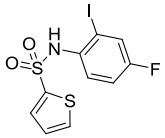
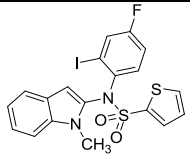
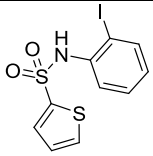
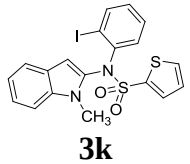
To a mixture of *N*-(2-iodophenyl) methane/4-methylbenzene/thiophene-2-sulfonamide derivative **1** (1.0 mmol)**,** Cs_2CO_3 (1.5 mmol), I_2 (1 mmol) in acetonitrile (2.5 mL) added indole derivative **2** (1.2 mmol), Then stirred at room temperature under nitrogen for 4-6 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction was quenched with a saturated solution of $Na_2S_2O_3$ (5 mL) and extracted with ethyl acetate (3 × 30 mL). The organic layers were collected, combined, washed with brine (50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under a reduced pressure. The residue was purified by column chromatography over silica gel using ethyl acetate–hexane to give the desired product (**3)**.

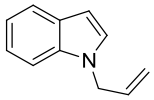
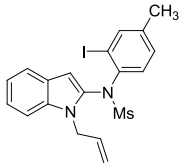
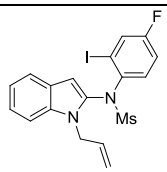
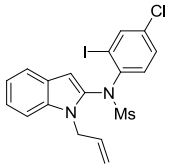
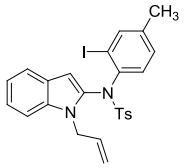
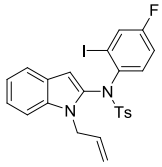
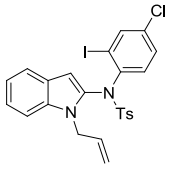
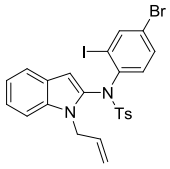
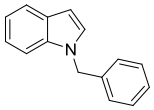
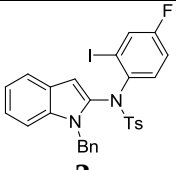
Table S1: Iodine mediated synthesis of *N*-(4-substituted-2-iodophenyl)-*N*-(1-alkyl-1*H*-indol-2-yl)alkane/arene/heteroarene sulfonamide.[a]

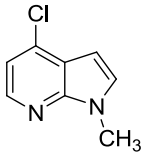
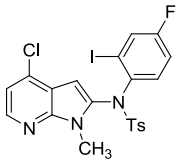
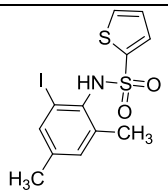
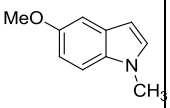
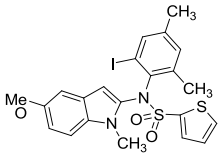
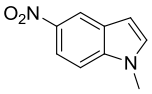
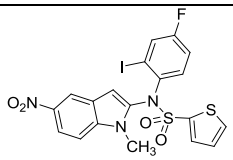
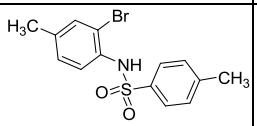
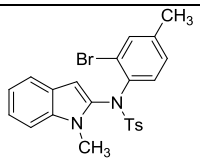


1 **2** **3**

Entry	Iodo anilides (**1**)	Indole (**2**)	Time/h[b]	Product (**3**)	Yield[c] (%)
1	 **1a**	 **2a**	4	 **3a**	75
2	 **1b**	**2a**	6	 **3b**	60
3	 **1c**	**2a**	6		62

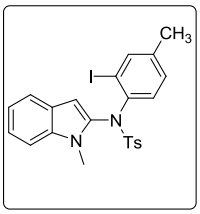
				3c	
4	 **1d**	**2a**	4	 **3d**	70
5	 **1e**	**2a**	5	 **3e**	72
6	 **1f**	**2a**	4.5	 **3f**	74
7	 **1g**	**2a**	4.5	 **3g**	63
8	 **1h**	**2a**	4.5	 **3h**	62
9	 **1i**	**2a**	5	 **3i**	75
10	 **1j**	**2a**	5	 **3j**	75
11	 **1k**	**2a**	5	 **3k**	76

12	**1d**	 **2b**	5	 **3l**	62
13	**1b**	**2b**	6	 **3m**	61
14	**1c**	**2b**	6	 **3n**	65
15	**1a**	**2b**	6	 **3o**	61
16	**1e**	**2b**	5	 **3p**	64
17	**1g**	**2b**	5	 **3q**	58
18	**1h**	**2b**	6	 **3r**	61
19	**1e**	 **2c**	6	 **3s**	58

20	**1e**	 **2d**	6	 **3t**	66
21	 **1l**	 **2e**	6	 **3u**	65
22	**1j**	 **2f**	6	 **3v**	55
23	 **1m**	**2a**	6	 **3w**	80

[a]All the reactions were carried out using **1** (1.0 mmol), **2** (1.2 mmol), I_2 (1.0 mmol) and Cs_2CO_3 (1.5 mmol) in acetonitrile (5.0 mL), at room temperature under nitrogen. [b]After adding indole **2**. [c]Isolated yield.

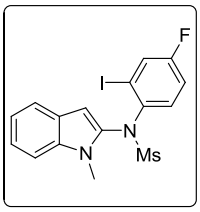
N-(2-Iodo-4-methylphenyl)-4-methyl-*N*-(1-methyl-1*H*-indol-2-yl)benzenesulfonamide (3a)



Light brown solid; yield: 75%; mp: 173-175 °C; R_f (15% EtOAc-*n*-Hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.29-7.24 (m, 3H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 2H), 6.21 (s, 1H), 4.13 (s, 3H), 2.48 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.5, 141.4, 140.7, 140.5, 135.4, 135.3, 134.3, 129.7, 129.5, 129.4 (2C), 129.2 (2C), 125.6, 122.6, 120.8, 119.9, 109.9, 101.4, 100.1, 32.1, 21.7, 20.4; HPLC: 95.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50,

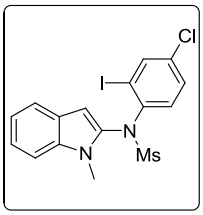
1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.07 min; IR (KBr, cm^{-1}): 3041, 2923, 1476, 1358, 1166; MS (ES mass): *m*/*z* 516.9 (M+1).

_N_-(4-Fluoro-2-iodophenyl)-_N_-(1-methyl-1_H_-indol-2-yl)methanesulfonamide (3b)



Off white solid; yield: 60%; mp: 165-167 °C; R_f (10% EtOAc-*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.67 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.32-7.28 (m, 2H), 7.17-7.10 (m, 2H), 6.92 (s, 1H), 3.97 (s, 3H), 3.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5 (d, C-F *J* = 253.8 Hz), 138.6 (d, C-F *J* = 3.4 Hz), 135.5, 134.1, 131.7 (d, C-F *J* = 8.9 Hz), 128.1 (d, C-F *J* = 24.4 Hz), 125.7, 123.1, 121.0, 120.3, 116.6 (d, C-F *J* = 22.3 Hz), 109.9, 100.9, 100.8 (d, C-F *J* = 8.6 Hz), 39.2, 31.5; HPLC: 98.2%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.25 min; IR (KBr, cm^{-1}): 3065, 2960, 1473, 1343; MS (ES mass): *m*/*z* 444.8 (M-+1).

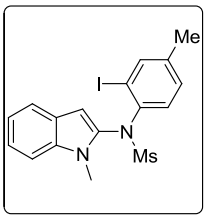
_N_-(4-Chloro-2-iodophenyl)-_N_-(1-methyl-1_H_-indol-2-yl)methanesulfonamide (3c)



Off white solid; yield: 62%; mp: 168-170 °C; R_f (10% EtOAc-*n*-Hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 2.0 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.40 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.32-7.28 (m, 2H), 7.16-7.12 (m, 1H), 6.92 (s, 1H), 3.95 (s, 3H), 3.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.5, 140.8, 139.6, 135.5, 134.5, 130.4, 130.2, 125.8, 122.9, 120.9, 120.2, 109.9, 100.8, 100.5, 39.1, 31.6; HPLC: 94.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm,

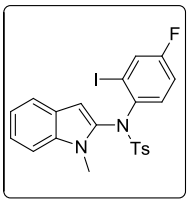
retention time 4.53 min; IR (KBr, cm^{-1}): 3073, 2932, 1355, 1463, 1166; MS (ES mass): *m*/*z* 461.2 (M+1).

_N_-(2-Iodo-4-methylphenyl)-_N_-(1-methyl-1_H_-indol-2-yl)methanesulfonamide (3d)



Off white solid; yield: 70%; mp: 201-203 °C; R_f (10% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, *J* = 0.8 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.31-7.28 (m, 2H), 7.24-7.21 (m, 1H), 7.14-7.10 (m, 1H), 6.92 (s, 1H), 3.98 (s, 3H), 3.27 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.5, 140.8, 139.6, 135.5, 134.5, 130.4, 130.2, 125.8, 122.9, 120.9, 120.2, 109.9, 100.8, 100.5, 39.1, 31.6, 20.4; HPLC: 98.9%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 4.39 min; IR (KBr, cm^{-1}): 3129, 3020, 2938, 1469, 1347, 1155; MS (ES mass): *m*/*z* 440.9 (M+1).

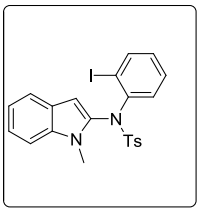
_N_-(4-Fluoro-2-iodophenyl)-4-methyl-_N_-(1-methyl-1_H_-indol-2-yl)benzenesulfonamide (3e)



Light pink color solid; yield: 72%; mp: 150-152 °C; R_f (10% EtOAc-*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.35-7.27 (m, 4H), 7.14-7.08 (m, 2H), 7.00 (dd, *J* = 7.2, 2.4 Hz, 1H), 6.19 (s, 1H), 4.11 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5 (d, C-F *J* = 253.6 Hz), 144.8, 139.7, 135.3 (d, C-F *J* = 23.6 Hz), 133.9, 130.9 (d, C-F *J* = 8.9 Hz), 129.4 (2C), 129.3 (2C), 128.4, 127.9 (d, C-F *J* = 24.4 Hz), 125.6, 125.8, 122.8, 120.8, 120.0, 115.9 (d, C-F *J* = 22.2 Hz), 110.0, 100.1, 32.1, 21.7; HPLC: 90.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98,

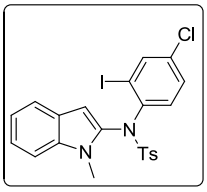
10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.91 min; IR (KBr, cm^{-1}): 3072, 2961, 1421, 1354; MS (ES mass): *m*/*z* 521.1 (M+1).

_N_-(2-Iodophenyl)-4-methyl-_N_-(1-methyl-1_H_-indol-2-yl)benzenesulfonamide (3f)



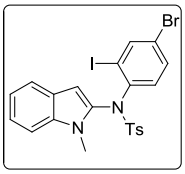
Brown solid; yield: 74%; mp: 190-192 °C; R_f (10% EtOAc-*n*-Hexane) 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.29-7.26 (m, 3H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.16 (d, *J* = 8.0 Hz,1H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.22 (s, 1H), 4.12 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.5, 141.4, 140.7, 140.5, 135.4, 135.3, 134.3, 129.7, 129.5, 129.4 (2C), 129.2 (2C), 125.6, 122.6, 120.8, 119.9, 109.9, 101.4, 100.1, 32.1, 21.7; HPLC: 99.3%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 4.84 min; IR (KBr, cm^{-1}): 3072, 2961, 1491, 1155; MS (ES mass): *m*/*z* 503.2 (M+1).

_N_-(4-Chloro-2-iodophenyl)-4-methyl-_N_-(1-methyl-1_H_-indol-2-yl)benzenesulfonamide (3g)



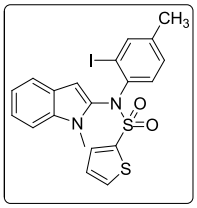
Light pink solid; yield: 63%; mp: 152-154 °C; R_f (10% EtOAc-*n*-Hexane) 0.51; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 2.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.35-7.28 (m, 4H), 7.23 (d, *J* = 2.0 Hz, 1H), 7.13-7.08 (m, 2H), 6.19 (s, 1H), 4.10 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.9, 142.0, 140.3, 135.3, 135.1, 134.8, 133.9, 130.6, 129.4 (2C), 129.3 (2C), 128.9, 125.5, 122.9, 120.8, 120.1, 110.0, 102.0, 100.3, 32.0, 21.7; HPLC: 97.9%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.23 min; IR (KBr, cm^{-1}): 3132, 3059, 2938, 1463, 1356, 1165; MS (ES mass): *m*/*z* 537.8 (M+1).

_N_-(4-Bromo-2-iodophenyl)-4-methyl-_N_-(1-methyl-1_H_-indol-2-yl)benzenesulfonamide (3h)



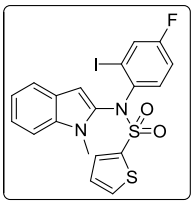
Light brown solid; yield: 62%; mp: 163-165 °C; R_f (10% EtOAc-*n*-Hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 2.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.39 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.34-7.27 (m, 4H), 7.10 (t, *J* = 7.2 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.17 (s, 1H), 4.09 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.9, 143.0, 142.5, 135.3, 134.7, 133.9, 131.9, 131.0, 129.4 (2C), 129.3 (2C), 125.5, 123.2, 122.9, 120.8, 120.1, 110.0, 102.5, 100.3, 32.0, 21.7; HPLC: 98.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.22 min; IR (KBr, cm^{-1}): 3123, 2987, 1453, 1395, 1154; MS (ES mass): *m*/*z* 582.7 (M+1).

_N_-(2-Iodo-4-methylphenyl)-_N_-(1-methyl-1_H_-indol-2-yl)thiophene-2-sulfonamide (3i)



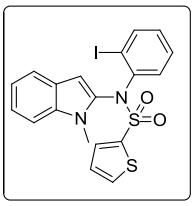
White solid; yield: 75%; mp: 180-182 °C; R_f (10% EtOAc-*n*-Hexane) 0.57; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (s, 1H), 7.70 (d, *J* = 5.2 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 2.8 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.28-7.25 (m, 1H), 6.38 (s, 1H), 7.16-7.13 (m, 2H), 7.10 (d, *J* = 7.6 Hz, 2H), 4.12 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.4, 140.6, 140.2, 137.3, 135.2, 134.9, 134.6, 133.5, 129.5, 129.4, 127.2, 125.5, 122.6, 120.7, 119.8, 109.9, 101.0, 100.0, 31.9, 20.3; HPLC: 99.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.75 min; IR (KBr, cm^{-1}): 3083, 2935, 1475, 1364; MS (ES mass): *m*/*z* 508.9 (M+1).

_N_-(4-Fluoro-2-iodophenyl)-_N_-(1-methyl-1_H_-indol-2-yl)thiophene-2-sulfonamide (3j)



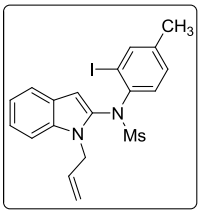
Off white solid; yield: 75%; mp: 168-170 °C; R_f (15% EtOAc-*n*-Hexane) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72-7.71 (m, 1H), 7.67 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.49-7.48 (m, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.25 (d, *J* = 6.8 Hz, 1H), 7.16-7.09 (m, 2H), 7.05-7.00 (m, 1H), 6.35 (s, 1H), 4.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.7 (d, C-F *J* = 253.8 Hz), 139.3 (d, C-F *J* = 3.7 Hz), 136.9, 135.4, 135.3, 134.4, 133.9, 130.8 (d, C-F *J* = 8.9 Hz), 128.0 (d, C-F *J* = 24.5 Hz), 127.5, 125.5, 123.0, 120.9, 120.1, 116.0 (d, C-F *J* = 22.2 Hz), 110.0, 101.6 (d, C-F *J* = 8.6 Hz), 100.2, 32.0; HPLC: 98.4%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 4.89 min; IR (KBr, cm^{-1}): 3057, 2951, 1504, 1368, 1176; MS (ES mass): *m*/*z* 512.9 (M+1).

_N_-(2-Iodophenyl)-_N_-(1-methyl-1_H_-indol-2-yl)thiophene-2-sulfonamide (3k)



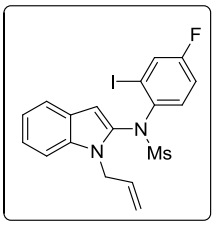
Light brown solid; yield: 76%; mp: 185-187 °C; R_f (10% EtOAc-*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 7.6 Hz, 1H), 7.70 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.49 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.35-7.29 (m, 4H), 7.16-7.08 (m, 2H), 7.06-7.01 (m, 1H), 6.39 (s, 1H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.9, 141.2, 137.3, 135.4, 135.2, 134.5, 133.8, 130.3, 130.2, 128.9, 127.4, 125.6, 122.9, 120.9, 120.1, 110.0, 101.4, 100.4, 32.1; HPLC: 99.0%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.52 min; IR (KBr, cm^{-1}): 3076, 2931, 1492, 1351, 1176; MS (ES mass): *m*/*z* 494.9 (M+1).

***N*-(1-Allyl-1*H*-indol-2-yl)-*N*-(2-iodo-4-methylphenyl)methanesulfonamide (3l)**



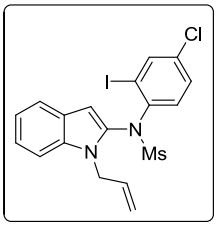
Light yellow semi solid; yield: 62%; R_f (20% EtOAc-*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (s, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.28-7.27 (m, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.18-7.11 (m, 2H), 7.06 (s, 1H), 5.84-5.75 (m, 1H), 5.07-5.02 (m, 3H), 4.85 (d, *J* = 17.2 Hz, 1H), 3.26 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.4, 140.6, 138.9, 135.1, 134.2, 133.5, 130.5, 130.1, 126.0, 122.9, 121.1, 120.3, 116.4, 110.8, 101.4, 100.6, 46.3, 39.4, 20.4; HPLC: 98.5%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 4.54 min; IR (KBr, cm^{-1}): 3078, 3026, 2924, 1472, 1345; MS (ES mass): *m/z* 466.9 (M+1).

***N*-(1-Allyl-1*H*-indol-2-yl)-*N*-(4-fluoro-2-iodophenyl)methanesulfonamide (3m)**



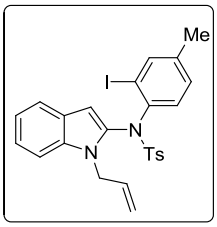
Semi solid; yield: 61%; R_f (7% EtOAc-*n*-Hexane) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66-7.61 (m, 3H), 7.27-7.25 (m, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.11-7.07 (m, 2H), 5.83-5.74 (m, 1H), 5.03-5.00 (m, 3H), 4.76 (d, *J* = 17.2 Hz, 1H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5 (d, C-F *J* = 253.3 Hz), 137.8, 135.1, 133.9, 133.2, 131.8 (d, C-F *J* = 8.4 Hz), 127.9 (d, C-F *J* = 24.6 Hz), 125.9, 123.2, 121.2, 120.5, 116.5 (d, C-F *J* = 22.0 Hz), 116.3, 110.7, 101.5, 100.1 (d, C-F *J* = 7.5 Hz), 46.1, 39.5; HPLC: 98.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.41 min; IR (KBr, cm^{-1}): 3072, 2924, 1586, 1470, 1348; MS (ES mass): *m/z* 470.8 (M+1).

***N*-(1-Allyl-1*H*-indol-2-yl)-*N*-(4-chloro-2-iodophenyl)methanesulfonamide (3n)**



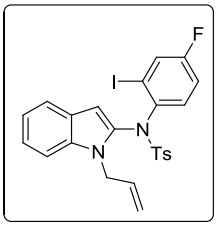
Semi solid; yield: 65%; R_f (20% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (d, *J* = 2.4 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 1H), 7.34 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.28 (s, 1H), 7.24-7.22 (m, 1H), 7.17-7.13 (m, 1H), 7.08 (s, 1H), 5.83-5.74 (m, 1H), 5.03-5.02 (m, 3H), 4.76 (d, *J* = 17.2 Hz, 1H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.3, 140.2, 135.1, 135.0, 133.7, 133.1, 131.4, 129.5, 125.9, 123.3, 121.2, 120.6, 116.4, 110.7, 101.7, 101.2, 46.1, 39.6; HPLC: 98.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 4.64 min; IR (KBr, cm^{-1}): 3073, 2932, 1355, 1463, 1166; MS (ES mass): *m*/*z* 487.2 (M+1).

_N_-(1-Allyl-1_H_-indol-2-yl)-_N_-(2-iodo-4-methylphenyl)-4-methylbenzenesulfonamide (3o)



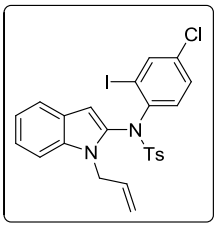
semi solid; yield: 61%; R_f (10% EtOAc-*n*-Hexane) 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (s, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.30-7.27 (m, 3H), 7.21-7.17 (m, 1H), 7.13-7.04 (m, 3H), 6.28 (s, 1H), 5.93-5.83 (m, 1H), 5.20 (s, 2H), 5.06 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.93 (dd, *J* = 17.2, 1.2 Hz, 1H), 2.46 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.6, 141.5, 140.4, 140.2, 134.9, 134.8, 134.3, 129.8, 129.6, 129.5 (2C), 129.2 (2C), 127.5, 125.8, 122.6, 120.8, 119.9, 116.3, 111.1, 101.4, 100.8, 46.9, 21.7, 20.4; HPLC: 95.8%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.11 min; IR (KBr, cm^{-1}): 2956, 1464, 1362, 1155; MS (ES mass): *m*/*z* 542.8 (M+1).

_N_-(1-Allyl-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (3p)



Light pink solid; yield: 64%; mp: 167-169 °C; R_f (10% EtOAc-*n*-Hexane) 0.67; ^{1}H NMR (400MHz, $CDCl_3$) δ: 7.68 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.32-7.29 (m, 3H), 7.27-7.21 (m, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.04-6.98 (m, 1H), 6.31 (s, 1H), 5.95-5.85 (m, 1H), 5.19 (d, *J* = 0.4 Hz, 2H), 5.07 (d, *J* = 10.4 Hz, 1H), 4.89 (d, *J* = 17.6 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5 (d, C-F *J* = 253.4 Hz), 144.9, 139.2 (d, C-F *J* = 3.6 Hz), 134.8, 134.6, 134.1, 133.9, 131.1 (d, C-F *J* = 8.9 Hz), 129.5 (2C), 129.4 (2C), 127.9 (d, C-F *J* = 24.3 Hz), 125.7, 122.9, 120.9, 120.2, 116.2, 115.9 (d, C-F *J* = 22.1 Hz), 111.1, 101.8 (d, C-F *J* = 8.4 Hz), 100.9, 46.7, 21.7; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.91 min; IR (KBr, cm^{-1}): 3357, 3072, 2923, 1567, 1465, 1368; MS (ES mass): *m*/*z* 546.9 (M+1).

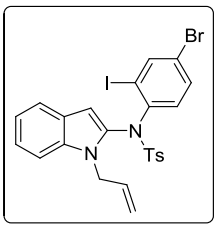
_N_-(1-Allyl-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)-4-methylbenzenesulfonamide (3q)



Light pink solid; yield: 58%; mp: 160-162 °C; R_f (10% EtOAc-*n*-Hexane) 0.48; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 2.4 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 3H), 7.24-7.23 (m, 1H), 7.19 (t, *J* = 8.0 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.27 (s, 1H), 5.91-5.82 (m, 1H), 5.15 (d, *J* = 2.0 Hz, 2H), 5.05 (d, *J* = 11.2 Hz, 1H), 4.85 (d, *J* = 17.2 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.9, 141.6, 140.3, 134.9, 134.8, 134.3, 134.0, 133.9, 130.7, 129.5 (2C), 129.4 (2C), 128.9, 125.7, 122.9, 120.9, 120.2, 116.3, 111.1, 102.0, 101.1, 46.7, 21.7; HPLC: 99.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50,

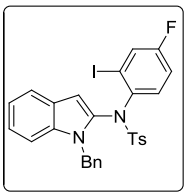
1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.20 min; IR (KBr, cm^{-1}): 3066, 2920, 1458, 1363, 1165; MS (ES mass): *m*/*z* 563.4 (M+1).

***N*-(1-Allyl-1H-indol-2-yl)-*N*-(4-bromo-2-iodophenyl)-4-methylbenzenesulfonamide (3r)**



White solid; yield: 62%; mp: 173-175 °C; R_f (10% EtOAc-*n*-Hexane) 0.54; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (d, *J* = 2.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.40 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 3H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.12-7.13 (m, 2H), 6.27 (s, 1H), 5.92-5.82 (m, 1H), 5.17-5.15 (m, 2H), 5.06-5.04 (m, 1H), 4.86 (d, *J* = 17.2 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.9, 143.1, 142.1, 134.8, 134.3, 134.0, 133.9, 131.9, 131.1, 129.5 (2C), 129.4 (2C), 125.7, 123.0, 122.9, 120.9, 120.2, 116.3, 111.1, 102.5, 101.1, 46.7, 21.7; HPLC: 99.1%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.35 min; IR (KBr, cm^{-1}): 3078, 2972, 1435, 1352; MS (ES mass): *m*/*z* 608.7 (M+1).

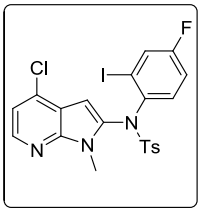
***N*-(1-Benzyl-1*H*-indol-2-yl)-*N*-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (3s)**



Light pink solid; yield: 58%; mp: 181-183 °C; R_f (10% EtOAc-*n*-Hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 8.0 Hz, 2H), 7.56-7.54 (m, 2H), 7.29-7.24 (m, 3H), 7.14-7.07 (m, 5H), 6.97-6.92 (m, 2H), 6.77 (d, *J* = 6.4 Hz, 2H), 6.47 (s, 1H), 5.74 (s, 2H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.4 (d, C-F *J* = 252.6 Hz), 144.9, 138.8, 137.3, 135.3, 134.8, 133.9, 131.3 (d, C-F *J* = 8.1 Hz), 129.5 (2C), 129.4 (2C), 128.3 (2C), 127.8, 127.6, 126.8, 126.1 (2C), 125.8, 123.0, 120.9, 120.3, 115.8 (d, C-F *J* = 22.2 Hz), 111.2, 101.2, 47.6, 21.7; HPLC: 98.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow

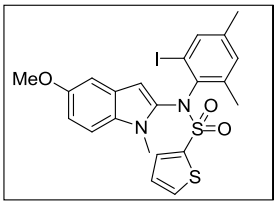
rate: 1.0 mL/min; UV 210 nm, retention time 5.00 min; IR (KBr, cm^{-1}): 3164, 2978, 1431, 1356; MS (ES mass): *m*/*z* 596.9 (M+1).

_N_-(4-Chloro-1-methyl-1_H_-pyrrolo[2,3-b]pyridin-2-yl)-_N_-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (3t)



White solid; yield: 66%; mp: 232-234 °C; R_f (10% EtOAc-*n*-Hexane) 0.51; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.28 (d, *J* = 4.8 Hz, 1H), 7.67 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.59 (d, *J* = 8. 4 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.26-7.23 (m, 1H), 7.11 (d, *J* = 5.2 Hz, 1H), 7.09-7.04 (m, 1H), 6.36 (s, 1H), 4.18 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.7 (d, C-F *J* = 254.3 Hz), 146.6, 145.3, 144.4, 138.7 (d, C-F *J* = 3.7 Hz), 136.3, 135.9, 133.8, 131.4 (d, C-F *J* = 8.9 Hz), 129.6 (2C), 129.3 (2C), 128.1 (d, C-F *J* = 24.3 Hz), 127.8, 118.1, 116.6, 116.1, 115.9, 101.6 (d, C-F *J* = 8.4 Hz), 97.2, 31.3, 21.7; HPLC: 99.8%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 4.98 min; IR (KBr, cm^{-1}): 3077, 2987, 1584, 1476, 1368; MS (ES mass): *m*/*z* 582.3 (M+1).

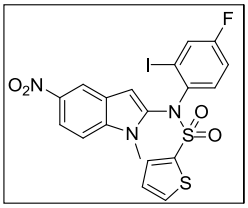
_N_-(2-Iodo-4,6-dimethylphenyl)-_N_-(5-methoxy-1-methyl-1_H_-indol-2-yl)thiophene-2-sulfonamide (3u)



Off white solid; yield: 65%; mp: 100-102 °C; R_f (12% EtOAc-*n*-Hexane) 0.33; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87 (d, *J* = 4.0 Hz, 1H), 7.72 (s, 1H), 7.58 (d, *J* = 4.0 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 7.06-7.02 (m, 3H), 6.99 (s, 1H), 6.86 (dd, *J* = 9.2, 2.0 Hz, 1H), 3.86 (s, 3H), 3.53 (s, 3H), 2.48 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.2, 141.2, 140.3, 140.1, 138.8, 137.0, 135.5, 134.3, 133.5 (2C), 130.5, 126.6, 126.0, 112.3, 110.0, 102.8, 102.2, 100.4, 55.7, 31.9, 21.4, 20.3; HPLC: 96.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase

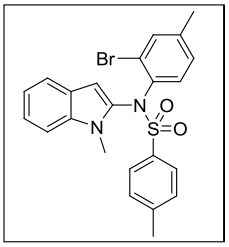
A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.20 min; IR (KBr, cm^{-1}): 3099, 2930, 1614, 1473, 1349, 1161; MS (ES mass): *m*/*z* 553.0 (M+1).

_N_-(4-Fluoro-2-iodophenyl)-_N_-(1-methyl-5-nitro-1_H_-indol-2-yl)thiophene-2-sulfonamide (3v)



Light yellow solid; yield: 55%; mp: 215-217 °C; R_f (15% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.52 (d, *J* = 1.6 Hz, 1H), 8.20 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.80 (d, *J* = 4.8 Hz, 1H), 7.71 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.50 (d, *J* = 3.6 Hz, 1H), 7.41 (d, *J* = 9.2 Hz, 1H), 7.24-7.20 (m, 2H), 7.14-7.06 (m, 1H), 6.55 (s, 1H), 4.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.9, 142.0, 138.6, 138.1, 137.6, 136.3, 135.6, 135.0, 134.5, 130.7 (d, C-F *J* = 9.0 Hz), 128.2, 127.9, 127.7, 124.5, 118.5 (d, C-F *J* = 28.5 Hz), 116.2 (d, C-F *J* = 22.1 Hz), 110.2, 102.6, 32.7; HPLC: 97.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.84 min; IR (KBr, cm^{-1}): 3081, 2924, 2860, 1475, 1326, 1160; MS (ES mass): *m*/*z* 555.7 (M-1).

_N_-(2-Bromo-4-methylphenyl)-4-methyl-_N_-(1-methyl-1_H_-indol-2-yl)benzenesulfonamide (3w)



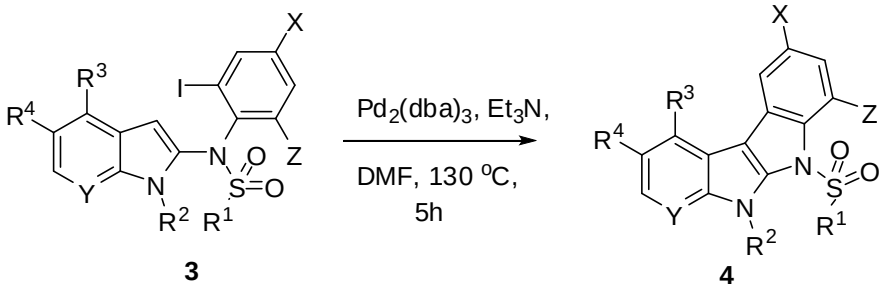
Off white solid; yield: 80%; mp: 148-150 °C; R_f (10% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.32-7.25 (m, 4H), 7.12-7.09 (m, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.24 (s, 1H), 4.04 (s, 3H), 2.49 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.4, 140.5, 137.1, 135.2, 135.0, 134.7, 134.6, 130.4, 129.3 (2C), 129.2

(2C), 128.7, 125.6, 124.9, 122.6, 120.8, 119.8, 109.9, 100.2, 30.8, 21.7, 20.7; HPLC: 99.4%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.57 min; IR (KBr, cm^{-1}): 3046, 2932, 1476, 1357, 1163; MS (ES mass): *m*/*z* 471.0 (M+1).

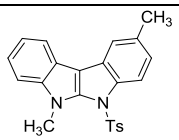
General procedure for preparation of 2-substituted-6-methyl-5-(alkyl/aryl/hetero arylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4):

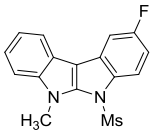
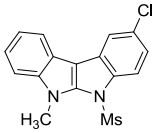
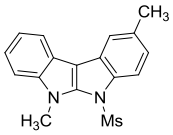
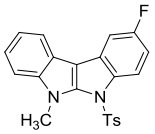
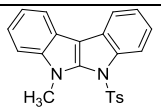
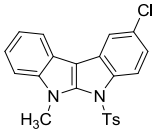
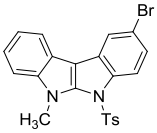
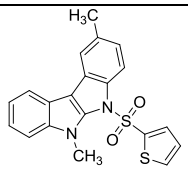
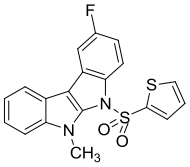
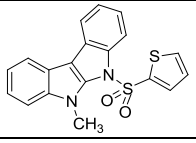
A mixture of *N*-(4-substituted-2-iodophenyl)-*N*-(1-alkyl-1*H*-indol-2-yl)alkane/arene/heteroarene sulfonamide (**3**) (0.4 mmol), $Pd_2(dba)_3$ (5 mol%), Et_3N (1.0 mmol), and anhydrous DMF (1 mL) was stirred at 130 °C under nitrogen atmosphere for 5 h. The progress of the reaction was monitored by TLC. Upon completion, the mixture was cooled to room temperature, filtered to remove the solid materials. The filtrate was extracted with ethyl acetate (3 x 15 mL). The organic layers were collected, combined, dried over anhydrous Na_2SO_4, filtered and concentrated under a reduced pressure. The residue was purified by column chromatography over silica gel using ethyl acetate–hexane to give the desired product **4**.

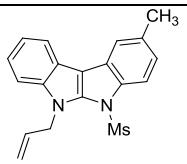
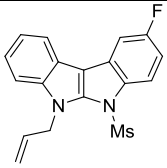
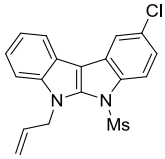
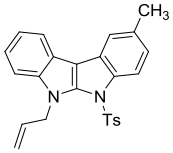
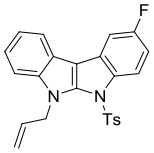
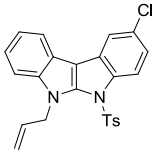
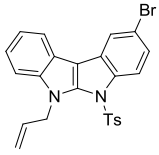
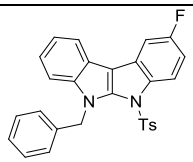
Table S2: Pd catalyzed synthesis of 2-substituted-6-methyl-5-(alkyl/aryl/hetero aryl sulfonyl)-5,6-dihydroindolo[2,3-*b*]indole.[a]

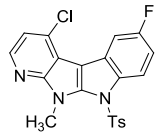
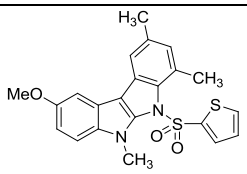
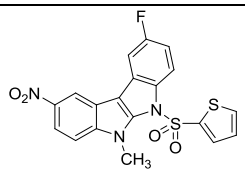


3 **4**

S. No.	Compound (**3**)	Product (**4**)	Yield[b] (%)
1	**3a**	 **4a**	85

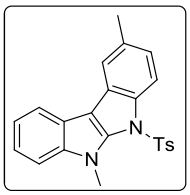
2	**3b**	 **4b**	78
3	**3c**	 **4c**	76
4	**3d**	 **4d**	80
5	**3e**	 **4e**	85
6	**3f**	 **4f**	83
7	**3g**	 **4g**	81
8	**3h**	 **4h**	68
9	**3i**	 **4i**	87
10	**3j**	 **4j**	84
11	**3k**		80

		4k	
12	**3l**	 **4l**	74
13	**3m**	 **4m**	70
14	**3n**	 **4n**	78
15	**3o**	 **4o**	78
16	**3p**	 **4p**	76
17	**3q**	 **4q**	70
18	**3r**	 **4r**	69
19	**3s**	 **4s**	75

20	**3t**	 **4t**	70
21	**3u**	 **4u**	74
22	**3v**	 **4v**	68
23	**3w**	**4a**	38[c]

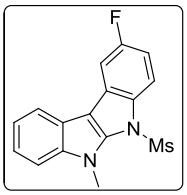
[a]All the reactions were performed using **3** (1.0 mmol), $Pd_2(dba)_3$ (5 mol%) and Et_3N (2.5 mmol) in DMF (5 mL) at 130 °C for 5 h under N_2. [b]Isolated yield. [c]after 12 h.

2,6-Dimethyl-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4a)



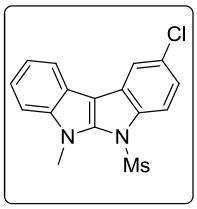
White solid; yield: 85%; mp: 165-167 °C; R_f (15% EtOAc-*n*-Hexane) 0.62; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.31 (s, 1H), 7.28-7.22 (m, 3H), 7.19-7.16 (m, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.12 (s, 3H), 2.35 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.7, 142.9, 141.4, 138.4, 135.1, 132.3, 129.2 (2C), 127.2, 126.8 (2C), 123.2, 121.9, 120.6, 120.3, 119.2, 118.7, 117.3, 110.7, 108.8, 33.7, 29.7, 21.5; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 8/98, 10/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.72 min; IR (KBr): 3051, 2947, 1528, 1367, 1174 cm^{-1}; MS (ES mass): *m*/*z* 388.8 (M+1).

2-Fluoro-6-methyl-5-(methylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4b)



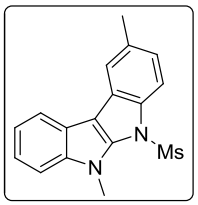
Floppy white solid; yield: 78%; mp: 148-150 °C; R_f (5% EtOAc-*n*-Hexane) 0.71; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.48-7.43 (m, 2H), 7.40-7.31 (m, 2H), 6.95 (td, *J* = 8.8, 1.2 Hz, 1H), 4.06 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.3 (d, C-F *J* = 241.5 Hz), 143.6, 141.3, 136.6, 128.4, 122.7, 121.3, 119.9, 119.3, 118.3 (d, C-F *J* = 9.6 Hz), 110.9, 109.6 (d, C-F *J* = 24.4 Hz), 108.0, 105.4 (d, C-F *J* = 25.1 Hz), 36.1, 29.7; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.45 min; IR (KBr, cm^{-1}): 3018, 2928, 1449, 1365, 1168; MS (ES mass): *m*/*z* 317.2 (M+1).

2-Chloro-6-methyl-5-(methylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4c)



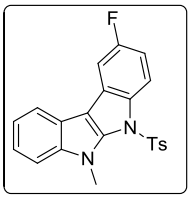
Floppy white solid; yield: 76%; mp: 161-163 °C; R_f (10% EtOAc-*n*-Hexane) 0.69; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 8.8 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 1.6 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.41-7.31 (m, 2H), 7.22 (dd, *J* = 8.8, 1.6 Hz, 1H), 4.07 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.1, 141.4, 138.8, 131.8, 128.3, 122.7, 122.4, 121.3, 119.9, 119.3, 118.6, 118.0, 110.9, 107.5, 36.4, 33.7; HPLC: 99.9%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 235 nm, retention time 4.75 min; IR (KBr, cm^{-1}): 3054, 2932, 1564, 1152; MS (ES mass): *m*/*z* 333.8 (M+1).

2,6-Dimethyl-5-(methylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4d)



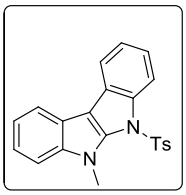
Light brown solid; yield: 80%; mp: 165-167 °C; R_f (10% EtOAc-*n*-Hexane) 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90-7.87 (m, 2H), 7.59 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.36-7.28 (m, 2H), 7.06 (d, *J* = 8.4 Hz, 1H), 4.05 (s, 3H), 2.59 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.7, 141.3, 138.8, 135.8, 127.3, 123.7, 122.3, 120.9, 120.2, 119.4, 119.2, 116.8, 110.7, 108.4, 35.8, 33.6, 21.5; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.49 min; IR (KBr, cm^{-1}): 3057, 2951, 1504, 1368, 1176; MS (ES mass): *m*/*z* 313.9 (M+1).

2-Fluoro-6-methyl-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4e)



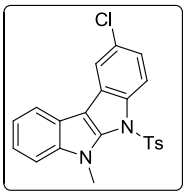
Off white solid; yield: 85%; mp: 140-142 °C; R_f (10% EtOAc-*n*-Hexane) 0.72; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (dd, *J* = 8.8, 4.4 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.28-7.25 (m, 3H), 7.21 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.87 (td, *J* = 9.2, 2.8 Hz, 1H), 4.19 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.3 (d, C-F *J* = 240.7 Hz), 145.0, 143.9, 141.4, 136.4 , 136.3, 131.8, 129.3 (2C), 128.5 (d, C-F *J* = 10.7 Hz), 126.8 (2C), 122.4, 121.0, 120.1, 119.2, 118.8 (d, C-F *J* = 9.6 Hz), 110.8, 109.1 (d, C-F *J* = 24.6 Hz), 105.0 (d, C-F *J* = 25.0 Hz), 33.8, 21.5; HPLC: 99.8%; column: Symmetry C-18 75*4.6 mm 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 8/98, 10/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.55 min; IR (KBr, cm^{-1}): 3005, 2954, 1604, 1444, 1175; MS (ES mass): *m*/*z* 392.9 (M+1).

5-Methyl-6-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4f)



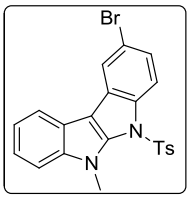
Light brown solid; yield: 83%; mp: 160-162 °C; R_f (10% EtOAc-*n*-Hexane) 0.62; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.15 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.36-7.24 (m, 5H) 7.20 (t, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 2H), 4.21 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.8, 142.8, 141.5, 140.5, 132.2, 129.2 (2C), 127.1, 126.8 (2C), 125.4, 122.2, 122.1, 120.7, 120.3, 119.3, 118.3, 117.7, 110.7, 108.9, 33.8, 21.5; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.49 min; IR (KBr, cm^{-1}): 3057, 2951, 1504, 1368, 1176; MS (ES mass): *m*/*z* 374.8 (M+1).

2-Chloro-6-methyl-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4g)



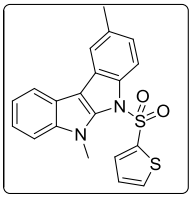
White solid; yield: 81%; mp: 178-180 °C; R_f (10% EtOAc-*n*-Hexane) 0.68; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.31-7.27 (m, 3H), 7.14 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 2H), 4.20 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.1, 143.5, 141.5, 138.6, 132.1, 131.2, 129.4 (2C), 128.3, 126.8 (2C), 122.5, 121.9, 121.1, 119.9, 119.3, 118.5, 118.2, 110.8, 108.0, 29.7, 21.5; HPLC: 99.4%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.31 min; IR (KBr, cm^{-1}): 3059, 2929, 1530, 1367, 1171; MS (ES mass): *m*/*z* 409.5 (M+1).

2-Bromo-6-methyl-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4h)



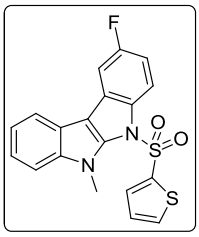
White solid; yield: 68%; mp: 193-195 °C; R_f (10% EtOAc-*n*-Hexane) 0.58; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.36 (td, *J* = 8.4, 1.0 Hz, 1H), 7.32-7.28 (m, 4H), 6.98 (d, *J* = 8.4 Hz, 2H), 4.20 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.2, 143.4, 141.5, 139.1, 132.1, 129.4 (2C), 128.7, 126.8 (2C), 124.8, 122.5, 121.1, 121.0, 119.9, 119.3, 119.1, 118.9, 110.8, 109.9, 33.8, 21.5; HPLC: 96.2%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.46 min; IR (KBr, cm^{-1}): 3063, 2943, 1529, 1366, 1171; MS (ES mass): *m*/*z* 454.8 (M+1).

2,6-Dimethyl-5-(thiophen-2-ylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4i)



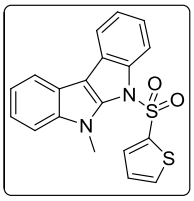
Light green solid; yield: 87%; mp: 213-215 °C; R_f (10% EtOAc-*n*-Hexane) 0.67; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.41 (s, 1H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.31-7.23 (m, 2H), 7.19 (d, *J* = 4.1 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.76-6.73 (t, *J* = 4.4 Hz, 1H), 4.15 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.6, 141.4, 138.6, 135.7, 134.3, 133.3, 133.1, 127.7, 126.8, 123.4, 122.1, 120.7, 120.2, 119.4, 118.9, 117.7, 110.7, 109.4, 33.6, 21.5; HPLC: 99.9%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 235 nm, retention time 4.89 min; IR (KBr, cm^{-1}): 3098, 2953, 1532, 1368, 1173; MS (ES mass): *m*/*z* 380.8 (M+1).

2-Fluoro-6-methyl-5-(thiophen-2-ylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4j)



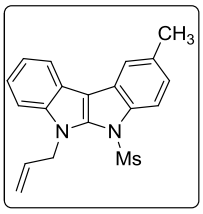
Light yellow solid; yield: 84%; mp: 188-190 °C; R_f (15% EtOAc-*n*-Hexane) 0.61; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.38-7.33 (m, 2H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.25-7.23 (m, 1H), 7.18 (d, *J* = 3.2 Hz, 1H), 6.92 (td, *J* = 8.8, 2.4 Hz, 1H), 6.76 (t, *J* = 4.8 Hz, 1H), 4.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.6 (d, C-F *J* = 241.4 Hz), 143.5, 141.4, 136.5, 133.9, 133.7, 133.3, 129.1(d, C-F *J* = 10.7 Hz), 126.9, 122.6, 121.1, 119.9, 119.3, 119.2, 119.1, 110.8, 109.3 (d, C-F *J* = 24.5 Hz), 105.2 (d, C-F *J* = 25.1 Hz), 33.7; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.49 min; IR (KBr, cm^{-1}): 3057, 2951, 1504, 1368, 1176; MS (ES mass): *m*/*z* 385.0 (M+1).

5-Methyl-6-(thiophen-2-ylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4k)



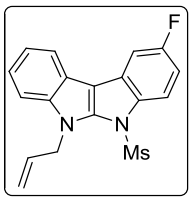
Light yellow solid; yield: 80%; mp: 162-164 °C; R_f (10% EtOAc-*n*-Hexane) 0.48; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.36-7.31 (m, 2H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.26-7.21 (m, 2H), 7.19 (d, *J* = 3.2 Hz, 1H), 6.73 (t, *J* = 4.4 Hz, 1H), 4.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.4, 141.4, 140.6, 134.2, 133.5, 133.2, 127.7, 126.8, 125.9, 122.5, 122.3, 120.8, 120.2, 119.4, 118.4, 118.1, 110.7, 109.5, 33.7; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.49 min; IR (KBr, cm^{-1}): 3057, 2951, 1504, 1368, 1176; MS (ES mass): *m*/*z* 367.1 (M+1).

6-Allyl-2-methyl-5-(methylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4l)



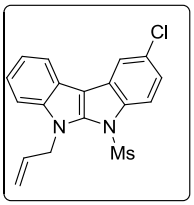
Floppy white solid; yield: 74%; mp: 170-172 °C; R_f (20% EtOAc-*n*-Hexane) 0.56; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, *J* = 8.2 Hz, 2H), 7.62 (s, 1H), 7.47-7.45 (m, 1H), 7.34-7.29 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.10-6.00 (m, 1H), 5.21-5.17 (m, 3H), 5.06 (d, *J* = 16.8 Hz, 1H), 2.64 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.9, 141.1, 138.7, 135.7, 133.9, 126.9, 123.8, 122.4, 121.1, 120.5, 119.4, 119.2, 116.8, 116.5, 111.6, 108.7, 48.8, 36.1, 21.5; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.49 min; IR (KBr, cm^{-1}): 3057, 2951, 1504, 1368, 1176; MS (ES mass): *m*/*z* 338.8 (M+1).

6-Allyl-2-fluoro-5-(methylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4m)



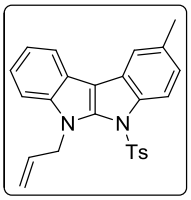
Floppy white solid; yield: 70%; mp: 175-177 °C; R_f (7% EtOAc-*n*-Hexane) 0.54; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (dd, *J* = 9.2, 4.4 Hz, 1H), 7.88 (dd, *J* = 6.4, 2.8 Hz, 1H), 7.47 (dd, *J* = 7.6, 2.4 Hz, 2H), 7.37-7.31 (m, 2H), 6.97 (td, *J* = 9.2, 2.8 Hz, 1H), 6.11-6.01 (m, 1H), 5.22-5.2 (m, 3H), 5.06 (d, *J* = 17.7 Hz, 1H), 2.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.4 (d, C-F *J* = 241.5 Hz), 142.6, 140.9, 136.3, 133.6, 128.0 (d, C-F *J* = 10.7 Hz), 122.6, 121.3, 120.1, 119.1, 118.8 (d, C-F *J* = 9.5 Hz), 116.5, 111.6, 109.4 (d, C-F *J* = 24.5 Hz), 108.2, 105.2 (d, C-F *J* = 25.0 Hz), 48.7, 36.2; HPLC: 99.5%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.63 min; IR (KBr, cm^{-1}): 2928, 1443, 1356, 1165; MS (ES mass): *m*/*z* 343.2 (M+1).

6-Allyl-2-chloro-5-(methylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4n)



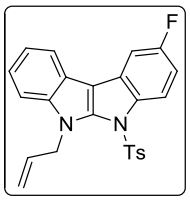
White solid; yield: 78%; mp: 188-190 °C; R_f (10% EtOAc-*n*-Hexane) 0.61; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, *J* = 8.8 Hz, 1H), 7.91 (dd, *J* = 6.8, 3.2 Hz, 1H), 7.79 (d, *J* = 1.6 Hz, 1H), 7.50-7.48 (m, 1H), 7.39-7.33 (m, 2H), 7.25 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.12-6.03 (m, 1H), 5.23-5.21 (m, 3H), 5.03 (d, *J* = 17.2 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.3, 141.1, 138.6, 133.8, 131.6, 127.9, 122.8, 122.6, 121.5, 120.1, 119.3, 118.5, 117.9, 116.6, 111.7, 107.9, 48.8, 36.7; HPLC: 97.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.89 min; IR (KBr, cm^{-1}): 3057, 2951, 1504, 1368, 1176; MS (ES mass): *m*/*z* 359.2 (M+1).

6-Allyl-2-methyl-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4o)



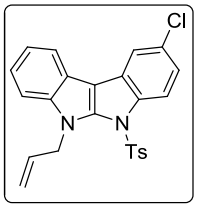
Light brown solid; yield: 78%; mp: 140-142 °C; R_f (10% EtOAc-*n*-Hexane) 0.62; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (d, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.39 (s, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.26-7.23 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.20-6.10 (m, 1H), 5.32 (d, *J* = 4.8 Hz, 2H), 5.26 (d, *J* = 10.4 Hz, 1H), 5.19 (d, *J* = 20.4 Hz, 1H), 2.42 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.7, 142.4, 141.4, 138.5, 137.5, 135.1, 133,7, 131.9, 129.8, 129.2, 126.9, 126.4, 124.2, 123.4, 122.1, 120.8, 119.3, 118.8, 117.4, 116.8, 111.7, 109.4, 49.3, 29.7, 21.5; HPLC: 96.4%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 235 nm, retention time 5.28 min; IR (KBr, cm^{-1}): 3014, 2967, 1514, 1342, 1167; MS (ES mass): *m*/*z* 415.2 (M+1).

6-Allyl-2-fluoro-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4p)



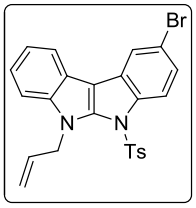
Yellowish white solid; yield: 76%; mp: 133-135 °C; R_f (10% EtOAc-*n*-Hexane) 0.68; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.35-7.27 (m, 4H), 7.23 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.89 (td, *J* = 9.2, 2.8 Hz, 1H), 6.21-6.11(m, 1H), 5.31 (d, *J* = 5.2 Hz, 2H), 5.29 (d, *J* = 10.4 Hz, 1H), 5.22 (d, *J* = 17.2 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.2 (d, C-F *J* = 240.8 Hz), 145.0, 143.5, 141.4, 136.4, 133.5, 131.9, 129.2 (2C), 128.4 (d, C-F *J* = 10.7 Hz), 126.9 (2C), 122.5, 121.2, 120.4, 119.2, 118.8 (d, C-F *J* = 9.6 Hz), 117.1, 111.8, 109.9, 109.2 (d, C-F *J* = 24.5 Hz), 105.0 (d, C-F *J* = 25.0 Hz), 49.3, 21.5; HPLC: 99.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.14 min; IR (KBr, cm^{-1}): 3070, 2950, 1474, 1442, 1176; MS (ES mass): *m*/*z* 418.8 (M+1).

6-Allyl-2-chloro-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4q)



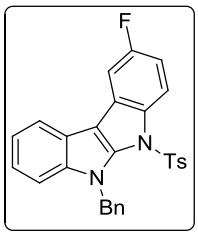
White solid; yield: 70%; mp: 155-157 °C; R_f (10% EtOAc-*n*-Hexane) 0.51; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.8 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 1.6 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.35-7.25 (m, 4H), 7.15 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.20-6.10 (m, 1H), 5.32-5.27 (m, 3H), 5.21 (d, *J* = 17.2 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.2, 143.1, 141.5, 138.7, 133.5, 132.1, 131.2, 129.4 (2C), 128.2, 126.9 (2C), 122.6, 122.1, 121.3, 120.4, 119.3, 118.6, 118.2, 117.1, 111.9, 108.5, 49.4, 21.5; HPLC: 99.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.44 min; IR (KBr, cm^{-1}): 3026, 2923, 1491, 1332, 1176; MS (ES mass): *m*/*z* 435.3 (M+1).

6-Allyl-2-bromo-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4r)



White solid; yield: 69%; mp: 160-162 °C; R_f (10% EtOAc-*n*-Hexane) 0.61; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 1.6 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 3H), 7.30-7.27 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.20-6.10 (m, 1H), 5.32 (d, *J* = 4.8 Hz, 2H), 5.28 (d, *J* = 10.8 Hz, 1H), 5.20 (d, *J* = 17.2 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.2, 142.9, 141.5, 139.1, 133.5, 132.1, 129.4 (2C), 128.6, 126.9 (2C), 124.9, 122.6, 121.3, 121.2, 120.4, 119.3, 119.1, 118.9, 117.1, 111.8, 108.4, 49.4, 21.5; HPLC: 98.4%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.53 min; IR (KBr, cm^{-1}): 3053, 2919, 1430, 1370, 1175; MS (ES mass): *m*/*z* 479.9 (M+1).

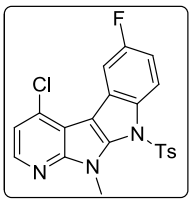
6-Benzyl-2-fluoro-5-tosyl-5,6-dihydroindolo[2,3-*b*]indole (4s)



Light yellow solid; yield: 75%; mp: 150-152 °C; R_f (10% EtOAc-*n*-Hexane) 0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.78-7.76 (m, 1H), 7.40 (dd, *J* = 7.6, 3.2 Hz, 1H), 7.28-7.23 (m, 6H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 6.8 Hz, 2H), 6.92-6.87 (m, 3H), 5.99 (s, 2H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.2 (d, C-F *J* = 240.8 Hz), 145.0, 143.4, 141.4, 137.4, 136.4, 132.2, 129.2 (2C), 128.6 (2C), 128.2 (d, C-F *J* = 10.5 Hz), 127.3, 126.9 (2C), 126.4 (2C), 122.7, 121.3, 120.5, 119.3, 118.8 (d, C-F *J* = 9.5 Hz), 111.9, 109.4 (d, C-F *J* = 24.6 Hz), 109.3, 105.1(d, C-F *J* = 24.9 Hz), 49.8, 21.5; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min;

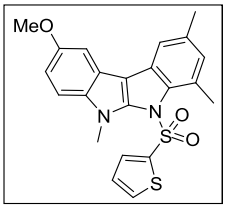
UV 230 nm, retention time 5.49 min; IR (KBr, cm^{-1}): 3057, 2951, 1504, 1368, 1176; MS (ES mass): *m*/*z* 469.1 (M+1).

Compound 4t



Off white solid; yield: 70%; mp: 203-205 °C; R_f (10% EtOAc-*n*-Hexane) 0.36; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.27 (d, *J* = 5.2 Hz, 1H), 8.14 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.67 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 5.2 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.95 (td, *J* = 8.8, 2.4 Hz, 1H), 4.32 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.7, 151.9, 145.5, 143.4, 142.8, 135.6, 135.6, 134.3, 132.2, 129.6 (2C), 127.1 (d, C-F *J* = 11.0 Hz), 126.8 (2C), 118.4 (d, C-F *J* = 9.6 Hz), 117.5, 113.5, 110.3 (d, C-F *J* = 24.5 Hz), 107.1 (d, C-F *J* = 25.8 Hz), 32.9, 21.5; HPLC: 99.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.40 min; IR (KBr, cm^{-1}): 3029, 2959, 1481, 1349, 1173; MS (ES mass): *m*/*z* 428.0 (M+1).

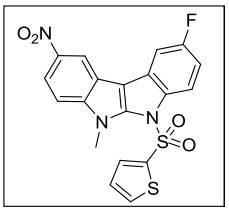
9-Methoxy-2,4,6-trimethyl-5-(thiophen-2-ylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4u)



Light yellow solid; yield: 74%; mp: 184-186 °C; R_f (10% EtOAc-*n*-Hexane) 0.51; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 (d, *J* = 8.8 Hz, 1H), 7.29 (d, *J* = 4.0 Hz, 1H), 7.13 (d, *J* = 2.0 Hz, 1H), 7.06 (s, 1H), 6.95 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.82 (s, 1H), 6.80-6.79 (m, 1H), 6.67 (t, *J* = 4.0 Hz, 1H), 4.06 (s, 3H), 3.90 (s, 3H), 2.71 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.7, 145.7, 139.7, 136.7, 135.9, 133.6 (2C), 131.2, 131.3, 131.1, 126.6, 126.4, 120.5, 116.3, 11.4, 111.3, 110.5, 101.9, 55.8, 33.3, 21.3, 20.4; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% :

0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.51 min; IR (KBr, cm^{-1}): 3098, 2928, 1453, 1372, 1171; MS (ES mass): *m*/*z* 425.1 (M+1).

2-Fluoro-6-methyl-9-nitro-5-(thiophen-2-ylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (4v)



Light yellow solid; yield: 68%; mp: 245-247 °C; R_f (15% EtOAc-*n*-Hexane) 0.56; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.70 (d, *J* = 2.4 Hz, 1H), 8.27 (dd, *J* = 9.2, 2.4, 1H), 8.13 (dd, *J* = 9.2, 4.4 Hz, 1H), 7.55 (d, *J* = 9.2 Hz, 1H), 7.41 (d, *J* = 4.8 Hz, 1H), 7.36 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.24 (d, *J* = 4.0 Hz, 1H), 7.03 (td, *J* = 8.8, 2.4 Hz, 1H), 6.82 (d, *J* = 4.4 Hz, 1H), 4.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.7 (d, C-F *J* = 243.6 Hz), 145.2, 143.9, 142.5, 136.6 (d, C-F *J* = 1.7 Hz), 134.1, 133.7, 127.2, 127.1, 120.5, 119.4 (d, C-F *J* = 9.9 Hz), 119.1, 118.0, 115.9, 110.7 (d, C-F *J* = 22.0 Hz), 110.8, 105.8 (d, C-F *J* = 25.1 Hz), 34.3, 29.6; HPLC: 98.2%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.02 min; IR (KBr, cm^{-1}): 3082, 2924, 1475, 1326, 1170; MS (ES mass): *m*/*z* 430.4 (M+1).

Reference

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Single crystal X-ray data for compound 4p.

Single crystals suitable for X-ray diffraction of **4p** was grown from methanol. The crystals were carefully chosen using a stereo zoom microscope supported by a rotatable polarizing stage. The data were collected at room temperature on Bruker's KAPPA APEX II CCD Duo with graphite monochromated Mo-Kα radiation (0.71073 Å). The crystals were glued to a thin glass fibre using FOMBLIN immersion oil and mounted on the diffractometer. The intensity data were processed using Bruker's suite of data processing programs (SAINT), and absorption corrections were applied using SADABS.[1] The crystal structures were solved by direct methods using SHELXS-97 and refined by full matrix least-squares refinement on F^2 with anisotropic displacement parameters for non-H atoms, using SHELXL-97.[2]

Crystal data of **4p:** Molecular formula = $C_{24}H_{19}FN_2O_2S$, formula weight = 418.48, crystal system = Triclinic, space group = *P*-1, *a* = 8.4548 (9) Å, *b* = 11.3819 (12) Å, *c* = 11.7256 (12) Å, *V* = 1021.48 (19) Å^3, *T* = 296 K, *Z* = 2, D_c = 1.361 Mg m^{-3}, μ(Mo-Kα) = 0.19 mm^{-1}, 18280 reflections measured, 4932 independent reflections, 3687 observed reflections [I > 2.0 σ (I)], R_1_obs = 0.028, Goodness of fit =1.04. Crystallographic data (excluding structure factors) for **3a** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC 903580.

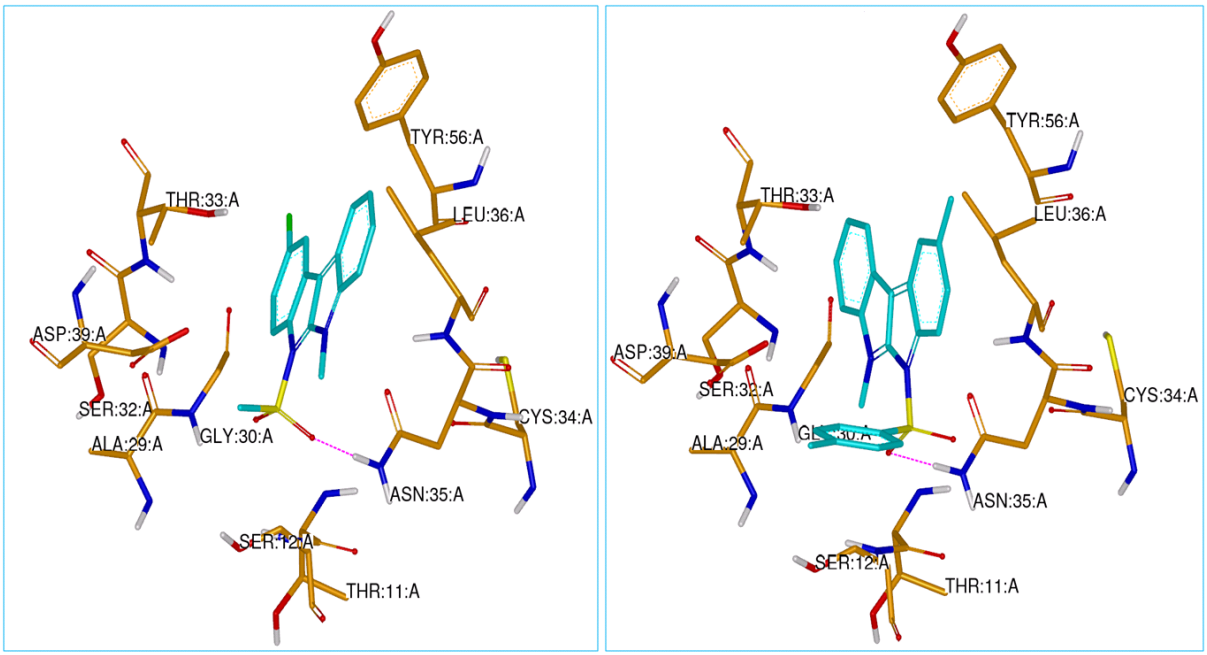
Reference

1. Bruker SADABS V2008-1, Bruker AXS.: Madison, WI, USA, **2008**.
2. Sheldrick, G. M.; SHELX-97, Program for Crystal Structure Determination, University of Göttingen, **1997**.

Molecular Docking Studies

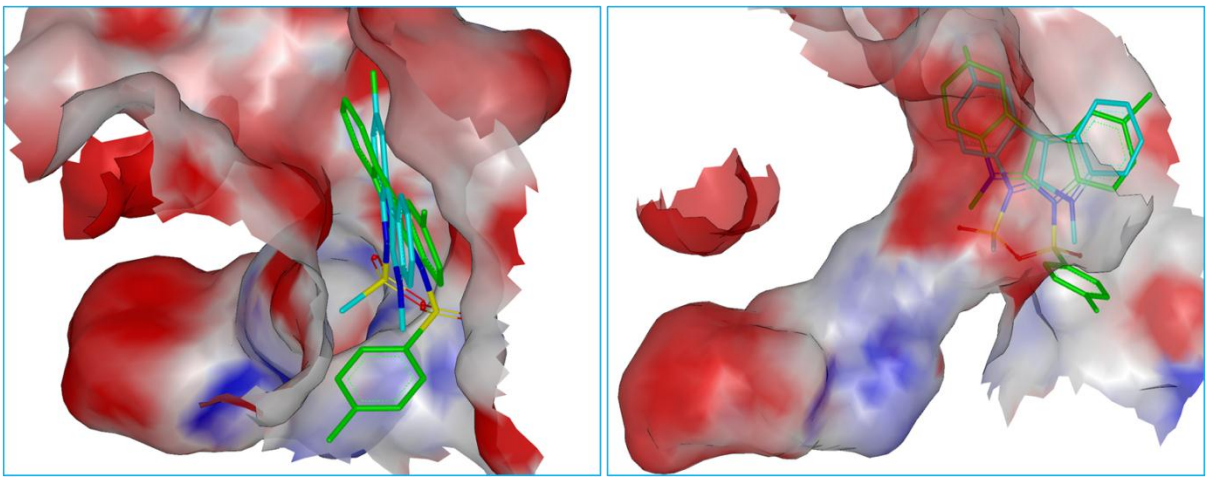
The crystal structure of yeast Sir2 protein in ternary complex with 2'-O-acetyl ADP ribose and histone peptide (PDB ID: 1Q1A) [1] was chosen for the present docking studies. In order to understand the binding modes of **4a** and **4b** at the catalytic site of yeast Sir2, molecular docking studies were performed by FRED v3.0 [2, 3] implemented from OpenEye Scientific Software. The multi-conformer database of the inhibitors was generated through OMEGA v1.7.7 [4].

The binding pose of inhibitors **4b** in the catalytic pocket of yeast Sir2 was shown in Fig. 1a. In its docked conformation oxygen from sulfonyl group of inhibitor **4b**, makes hydrogen bond interaction with the side chain amino group of ASN 35. This same kind of interaction was observed between inhibitor **4a** and yeast Sir2 (Fig. 1b). Due to the presence of smaller substituent (N-Ms) inhibitor **4b** was found entering deep in to the active site (Fig 2a). Whereas, the presence of bulky group (N-Ts) group had restricted the entry of inhibitors **4a** and therefore it enters partially in to the catalytic site (Fig. 2b). The docking results for the compounds are given in Table 1, which are ranked on the basis of their chemguass 3 docking scores.



a b

Figure 1: (a) Binding mode of **4b** in yeast Sir2 (PDBID: 1Q1A), showing hydrogen bonding with ASN 35; (b) Binding mode of **4a** in yeast Sir2 showing same hydrogen bonding as **4b** with ASN 35



a b

Figure 2: a) Front view of inhibitor **4b** (cyan) and **4a** (green) bound at yeast Sir2 active site b) Lateral view of inhibitor bound **4b** (cyan) and 1 (green) bound at yeast Sir2 active site. The protein was represented as surface and mapped with electrostatic property (blue = positive potential, red = negative potential).

Table 1: Docking results of compounds **4a** and **4b**

Molecules	Dock Score[a]	Steric	Protein Desolvation	Ligand Desolvation H-Bond	Clash	Ligand Desolvation	Hydrogen bond
4a	-6.0	-11.7	4.8	-0.18	0.54	1.02	-0.62
4b	-5.8	-10.6	4.2	-0.23	0.24	0.97	-0.44

[a]FRED Chemgauss4 score.

References:

1. K. Zhao, R. Harshaw, X. Chai, R. Marmorstein (2004) Structural basis for nicotinamide cleavage and ADP-ribose transfer by NAD(+)-dependent Sir2 histone/protein deacetylases. Proc Natl Acad Sci USA 101: 8563.
2. G. B. McGaughey, R. P. Sheridan, C. I. Bayly, J. C. Culberson, C. Kreatsolas, S. Lindsley, V. Maiorov, J.-F. Truchon and W. D. Cornell, "Comparison of Topological, Shape, and Docking Methods in Virtual Screening"**,** *J. Chem. Inf. Model.*, **2007**, *47* pp 1504-1519
3. M. McGann, "FRED Pose Prediction and Virtual Screening Accuracy"**,** J. Chem. Inf. Model., **2011**, 51, 578-596

4. Paul C.D. Hawkins, A. Geoffrey Skillman, Gregory L. Warren, Benjamin A. Ellingson, and Matthew T. Stahl. Conformer Generation with OMEGA: Algorithm and Validation Using High Quality Structures from the Protein Databank and Cambridge Structural Database**.** J. Chem. Inf. Model., **2010**, 50, 572-584

Pharmacology

A yeast cell based assay[1] for identification of potential inhibitors of HDAC Sir2

Reporter silencing assay: In this assay a yeast strain (TEL::URA3 strain (MATα ura3-52 lys2-801 ade2-101 trpΔ63 his3Δ200 leu3Δ200 leu2-Δ1 TEL adh4::URA) was used in which, a reporter gene URA3 was inserted in the silenced telomeric region where it is silenced by yeast Sir2 protein. A compound having the Sir2 protein inhibitory effect will inhibit the Sir2 protein, and thus the URA3 gene will be expressed and this will result in the death of the yeast cell in presence of 5-fluoro orotic acid (5-FOA) through formation of toxic 5-fluorouracil. This assay can also test the toxicity of compounds. The cells when grown in absence of 5-FOA should grow if the compound is not toxic. However in case of a toxic compound yeast cells would die.

The yeast strain was inoculated in 5.0 mL of YPDA media. The cells growing at the exponential phase were dispensed in the round bottom 96-well plate using cell dispenser. A Stock concentration of 10% 5-FOA was used to make a final concentration of 0.3% 5-FOA in the wells of 96-well plate. The compounds at a concentration of 50 uM were added to each well and the plates were incubated at 30 ^{0}C. Absorbance at 590 was measured using 96 well plate reader after 24 and 48 h. The inhibitory effect of compounds was analyzed after plotting the OD vs concentration of the compound in Excel data sheet. Splitomicin was used as a control (data not shown).

Reference

1. C. M. Grozinger, E. D. Chao, H. E. Blackwell, D. Moazed, S. L. Schreiber, *J. Biol. Chem.* **2001**, *276*, 38837.