Electronic Supplementary Information

Pd-mediated construction of cyclopentane ring fused with indoles

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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. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution by using 400 and 100 MHz spectrometers (VARIAN 400 MR), 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), t (triplet), dd (doublet of doublet), td (triplet of doublet) and m (multiplet) as well as bs (broad). Coupling constants (*J*) are given in hertz. Infrared spectra were recorded on a FT-IR spectrometer (FT/IR-4200, JASCO). Melting points were determined by using melting point apparatus (Buchi melting point B-540) and are uncorrected. MS spectra were obtained on a mass spectrometer (AGILENT 6430 triple quardrupole LC-MS). Chromatographic purity by HPLC (Agilent 1200 series Chem Station software) was determined by using area normalization method and the condition specified in each case: column, mobile phase (range used), flow rate, detection wavelength, and retention times.

Experimental Section

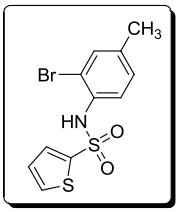
Chemistry

General procedure for the preparation of *N*-(1-allyl-5-substituted-1*H*-indol-2-yl)-*N*-(2-iodo-4-substitutedphenyl)thiophene-2-sulfonamide (3):

To a mixture of *N*-(2-halophenyl)thiophene-2-sulfonamide derivative[1] **1** (1.0 mmol)**,** Cs_2CO_3 (1.5 mmol), I_2 (1mmol) in acetonitrile (CH_3CN) (2.5 mL) was added indole derivative[2] **2** (1.2 mmol) and, the mixture was stirred at room temperature for 4 h under nitrogen. The progress of the reaction was monitored by TLC. Upon completion, the reaction was quenched with a saturation solution of $Na_2S_2O_3$ (5 mL) and then extracted with ethyl acetate (3 × 10 mL). The combined organic phases were washed with brine (20 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**.

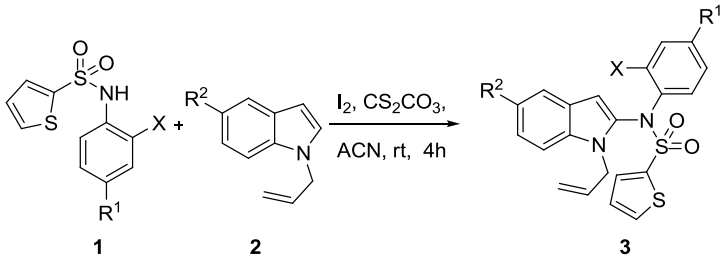
Characterization Data of 1f

***N*-(2-bromo-4-methylphenyl)thiophene-2-sulfonamide (1f)**

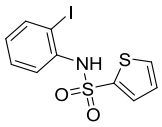
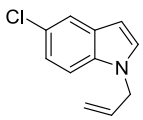
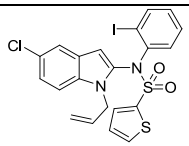
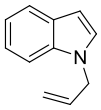
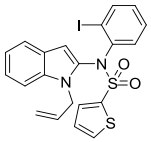


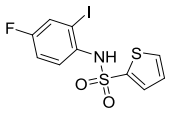
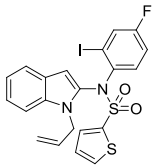
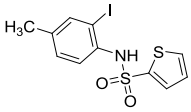
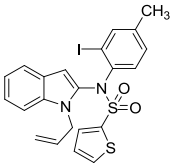
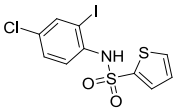
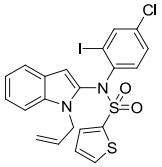
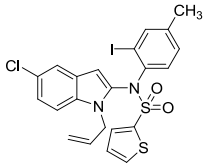
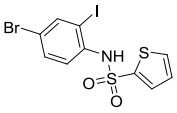
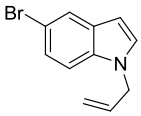
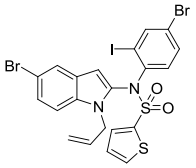
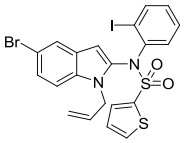
White solid; yield: 87%; mp: 78-80 °C; R_f (10% EtOAc-*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 8.4 Hz, 1H), 7.56 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.46 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.27 (s, 1H), 7.13 (d, *J* = 8.8 Hz, 1H), 7.02 (t, *J* = 4.0 Hz, 1H), 6.90 (bs, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.4, 132.9, 132.8, 132.8, 131.6, 129.3, 127.3, 123.9, 123.8, 116.6, 20.6; IR (KBr, cm^{-1}): 3263, 3099, 2919, 1492, 1338, 1162; MS (ES mass): *m*/*z* 329.4 (M-1).

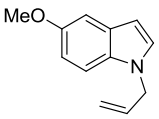
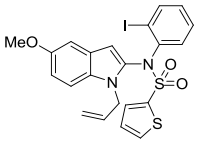
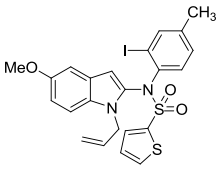
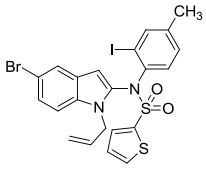
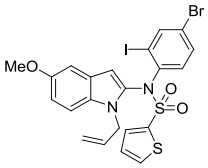
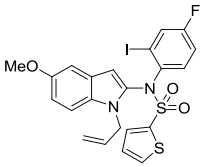
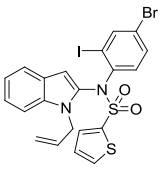
Table S-1: Iodine mediated synthesis of *N*-(1-allyl-5-substituted-1*H*-indol-2-yl)-*N*-(2-iodo-4-substitutedphenyl)thiophene-2-sulfonamide.[a]

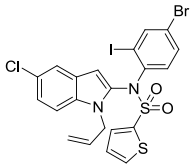
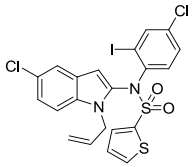
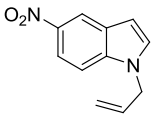
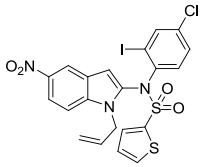
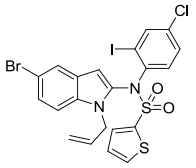
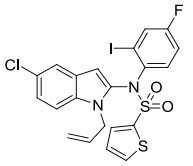
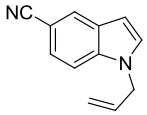
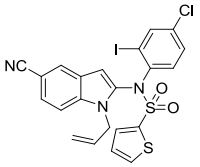


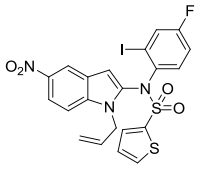
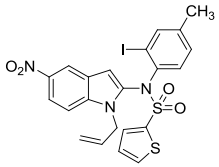
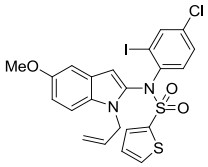
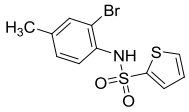
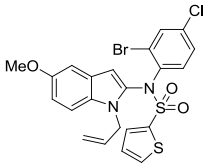
1 **2** **3**

Entry	Iodo anilides (**1**)	Indole (**2**)	Product (**3**)	Yield[b] (%)
1	 **1a**	 **2a**	 **3a**	58
2	**1a**	 **2b**	 **3b**	58

3	 **1b**	**2b**	 **3c**	56
4	 **1c**	**2b**	 **3d**	60
5	 **1d**	**2b**	 **3e**	52
6	**1c**	**2a**	 **3f**	55
7	 **1e**	 **2c**	 **3g**	51
8	**1a**	**2c**	 **3h**	47

9	**1a**	 **2d**	 **3i**	50
10	**1c**	**2d**	 **3j**	48
11	**1c**	**2c**	 **3k**	44
12	**1e**	**2d**	 **3l**	43
13	**1b**	**2d**	 **3m**	46
14	**1e**	**2b**	 **3n**	42

15	**1e**	**2a**	 **3o**	46
16	**1d**	**2a**	 **3p**	50
17	**1d**	 **2e**	 **3q**	45
18	**1d**	**2c**	 **3r**	48
19	**1b**	**2a**	 **3s**	45
20	**1d**	 **2f**	 **3t**	48

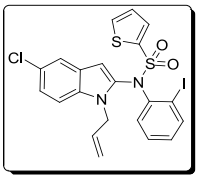
21	**1b**	**2e**	 **3u**	48
22	**1c**	**2e**	 **3v**	43
23	**1d**	**2d**	 **3w**	48
24	 **1f**	**2d**	 **3x**	60

[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]Isolated yield.

Characterization Data of compounds 3a-3t

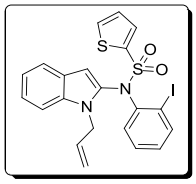
N-(1-Allyl-5-chloro-1*H*-indol-2-yl)-*N*-(2-iodophenyl)thiophene-2-sulfonamide (3a)



Off white solid; yield: 58%; mp: 132-134 °C; R_f (10% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 4.8 Hz, 1H), 7.51 (d, *J* = 6.1 Hz, 2H),

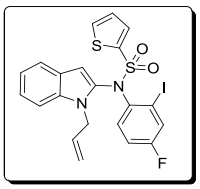
7.36-7.30 (m, 2H), 7.25-7.21 (m, 1H), 7.17-7.13 (m, 2H), 7.07-7.00 (m, 1H), 6.42 (s, 1H), 5.90-5.80 (m, 1H), 5.19 (s, 2H), 5.07 (d, *J* = 10.4 Hz, 1H), 4.89 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.2, 141.3, 137.1, 135.4, 135.3, 134.0, 133.7, 133.2, 130.3, 130.2, 128.9, 127.4, 126.7, 125.9, 123.3, 120.3, 116.6, 112.3, 101.5, 100.6, 47.1; 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, 0.5/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 235 nm, retention time 4.84 min; IR (KBr, cm^{-1}): 3097, 2921, 1457, 1372, 1102; MS (ES mass): *m*/*z* 554.7 (M+1).

_N_-(1-Allyl-1_H_-indol-2-yl)-_N_-(2-iodophenyl)thiophene-2-sulfonamide (3b)



Off white solid; yield: 58%; mp: 160-162 °C; R_f (15% EtOAc-*n*-Hexane) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.70 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.57-7.52 (m, 2H), 7.39 (dd, *J* = 8.05, 1.2 Hz, 1H), 7.32-7.29 (m, 2H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.12 (td, *J* = 13.9, 5.5 Hz, 2H), 7.04-7.00 (m, 1H), 6.49 (s, 1H), 5.92-5.82 (m, 1H), 5.19 (s, 2H), 5.05 (dd, *J* = 10.3, 1.2 Hz, 1H), 4.91 (d, *J* = 17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.2, 141.2, 137.3, 135.3, 134.9, 134.2, 134.0, 133.8, 130.3, 130.1, 128.9, 127.3, 125.8, 122.9, 121.0, 120.1, 116.3, 111.1, 101.5, 101.1, 46.8; 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 (Isocratic) 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 4.66 min; IR (KBr, cm^{-1}): 3087, 1458, 1362, 1163; MS (ES mass): *m*/*z* 520.9 (M+1).

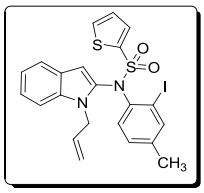
_N_-(1-Allyl-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)thiophene-2-sulfonamide (3c)



Off white solid; yield: 56%; mp: 150-152 °C; R_f (15% EtOAc-*n*-Hexane) 0.48; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.67 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.55-7.53 (m,

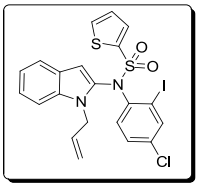
2H), 7.35 (dd, *J* = 8.9, 5.2 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.25-7.20 (m, 1H), 7.15-7.09 (m, 2H), 7.05-7.00 (m, 1H), 6.46 (s, 1H), 5.92-5.82 (m, 1H), 5.17 (s, 2H), 5.06 (dd, *J* = 10.3, 0.9 Hz, 1H), 4.87 (dd, *J* = 17.2, 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5 (d, C-F *J* = 253.6 Hz), 138.8 (d, C-F *J* = 3.4 Hz), 137.0, 135.4, 134.9, 134.1, 134.0, 133.9, 131.0 (d, C-F *J* = 9.0 Hz), 128.0, 127.8, 127.4, 125.7, 123.0, 120.9, 120.2, 116.3, 116.0 (d, C-F *J* = 22.2 Hz), 111.1, 100.9, 46.7; IR (KBr, cm^{-1}): 3082, 2944, 1498, 1356, 1176; MS (ES mass): *m*/*z* 538.9 (M+1).

_N_-(1-Allyl-1_H_-indol-2-yl)-_N_-(2-iodo-4-methylphenyl)thiophene-2-sulfonamide (3d)



White solid; yield: 60%; mp: 170-172 °C; R_f (12% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (s, 1H), 7.70 (dd, *J* = 4.6, 1.2 Hz, 1H), 7.55-7.52 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 8.4 Hz, 2H), 7.14-7.09 (m, 3H), 6.46 (s, 1H), 5.94-5.84 (m, 1H), 5.21 (s, 2H), 5.08 (d, *J* = 10.4 Hz, 1H), 4.95 (d, *J* = 17.2 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.5, 140.6, 139.8, 137.3, 135.3, 134.8, 134.4, 134.2, 133.7, 129.7 (2C), 127.3, 125.8, 122.8, 120.9, 116.3, 111.1, 101.2, 100.8, 46.9, 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.84 min; IR (KBr, cm^{-1}): 3091, 2916, 1466, 1367, 1159; MS (ES mass): *m*/*z* 534.2 (M+1).

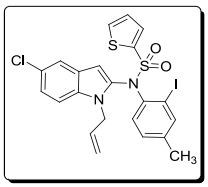
_N_-(1-Allyl-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)thiophene-2-sulfonamide (3e)



Off white solid; yield: 52%; mp: 158-160 °C; R_f (15% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (s, 1H), 7.72 (d, *J* = 5.2 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.30-7.27 (m, 3H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.16-7.08 (m, 2H), 6.44 (s, 1H), 5.91-5.82 (m, 1H), 5.16 (s, 2H), 5.06 (d, *J* = 10.5 Hz, 1H), 4.86 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.1, 140.4, 137.0, 135.5, 135.1, 134.9, 134.0, 133.9, 133.8, 130.6, 129.0, 127.4, 125.7, 123.0, 121.0,

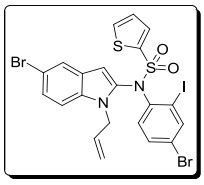
120.2, 116.3, 111.1, 101.8, 101.1, 46.6; HPLC: 99.0%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 0.5/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 4.92 min; IR (KBr, cm^{-1}): 3087, 2920, 1458, 1367, 1159; MS (ES mass): *m*/*z* 554.8 (M+1).

_N_-(1-Allyl-5-chloro-1_H_-indol-2-yl)-_N_-(2-iodo-4-methylphenyl)thiophene-2-sulfonamide (3f)



Off white solid; yield: 55%; mp: 150-152 °C; R_f (10% EtOAc-*n*-Hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (s, 1H), 7.71 (d, *J* = 4.4 Hz, 1H), 7.59-7.55 (m, 1H), 7.52-7.50 (m, 2H), 7.24-7.20 (m, 1H), 7.17-7.10 (m, 3H), 6.39 (s, 1H), 5.92-5.82 (m, 1H), 5.19 (s, 2H), 5.11 (d, *J* = 10.4 Hz, 1H), 4.93 (d, *J* = 17.6 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.6, 140.8, 139.3, 137.1, 135.3, 133.9, 133.8, 133.2, 130.3, 129.7, 129.6, 127.3, 126.7, 125.8, 123.7, 123.2, 120.2, 116.6, 112.3, 100.4, 47.1, 20.4; HPLC: 93.7%; 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, 0.5/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 235 nm, retention time 5.09 min; IR (KBr, cm^{-1}): 3094, 2922, 1465, 1370, 1161; MS (ES mass): *m*/*z* 568.9 (M+1).

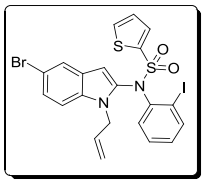
_N_-(1-Allyl-5-bromo-1_H_-indol-2-yl)-_N_-(4-bromo-2-iodophenyl)thiophene-2-sulfonamide (3g)



Light green solid; yield: 51%; mp: 180-182 °C; R_f (10% EtOAc-*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (s, 1H), 7.73 (d, *J* = 4.2 Hz, 1H), 7.67 (s, 1H), 7.52 (d, *J* = 1.2 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.21-7.15 (m, 3H), 6.37 (s, 1H), 5.88-5.81 (m, 1H), 5.14 (s, 2H), 5.07 (d, *J* = 10.4 Hz, 1H), 4.84 (d, *J* = 17.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.2, 141.3, 136.7, 135.5, 134.7, 134.3, 134.2, 133.4, 132.1, 130.9, 127.5, 127.2, 126.0, 123.5, 123.4, 116.6, 113.6, 112.7, 102.3, 100.5, 46.8; HPLC: 92.4%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN

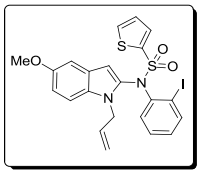
(Isocratic) T/B% : 0/20, 0.5/20, 3/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.55 min; IR (KBr, cm^{-1}): 3087, 2925, 1457, 1364, 1160; MS (ES mass): *m*/*z* 678.7 (M+1).

_N_-(1-Allyl-5-bromo-1_H_-indol-2-yl)-_N_-(2-iodophenyl)thiophene-2-sulfonamide (3h)



Off white solid; yield: 47%; mp: 138-140 °C; R_f (10% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, *J* = 7.6 Hz, 1H), 7.72 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.67 (d, *J* = 1.6 Hz, 1H), 7.52-7.51 (m, 1H), 7.34 (d, *J* = 2.0 Hz, 1H), 7.32 (dd, *J* = 6.8, 0.8 Hz, 1H), 7.28 (d, *J* = 1.6 Hz, 1H), 7.18 (d, *J* = 8.8 Hz, 1H), 7.14 (t, *J* = 4.8 Hz, 1H), 7.04 (td, *J* = 8.0, 2.0 Hz, 1H), 6.42 (s, 1H), 5.90-5.80 (m, 1H), 5.18 (d, *J* = 2.40 Hz, 2H), 5.06 (d, *J* = 10.0 Hz, 1H), 4.88 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.2, 141.3, 137.1, 135.4, 135.2, 134.0, 133.7, 133.5, 130.3, 130.2, 128.9, 127.4, 127.3, 125.8, 123.4, 116.6, 113.5, 112.7, 101.5, 100.5, 47.0; 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 (Gradient) T/B% : 0/20, 0.5/20, 3/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.13 min; IR (KBr, cm^{-1}): 3089, 2928, 1458, 1366, 1160; MS (ES mass): *m*/*z* 599.7 (M+1).

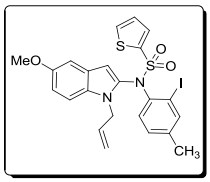
_N_-(1-Allyl-5-methoxy-1_H_-indol-2-yl)-_N_-(2-iodophenyl)thiophene-2-sulfonamide (3i)



Off white solid; yield: 50%; mp: 165-167 °C; R_f (15% EtOAc-*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.76 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.61-7.60 (m, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 8.8 Hz, 1H), 7.20 (t, *J* = 4.8 Hz, 1H), 7.09 (t, *J* = 8.4 Hz, 1H), 7.06-7.05 (m, 1H), 6.94 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.48 (s, 1H), 5.96-5.87 (m, 1H), 5.22 (dd, *J* = 2.8, 1.2 Hz, 2H), 5.12 (d, *J* = 10.0 Hz, 1H), 4.96 (d, *J* = 18.0 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.4, 142.4, 141.2, 137.4, 135.3,

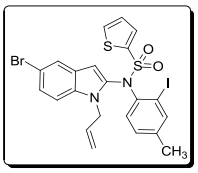
134.3, 134.2, 133.8, 130.3, 130.2, 130.1, 128.9, 127.3, 126.1, 116.3, 113.5, 112.0, 102.4, 101.5, 100.8, 55.8, 46.9; HPLC: 99.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 3/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.75 min; IR (KBr, cm^{-1}): 3093, 2920, 1467, 1366, 1162; MS (ES mass): *m*/*z* 551.0 (M+1).

_N_-(1-Allyl-5-methoxy-1_H_-indol-2-yl)-_N_-(2-iodo-4-methylphenyl)thiophene-2-sulfonamide (3j)



Off white solid; yield: 48%; mp: 150-152 °C; R_f (15% EtOAc-*n*-Hexane) 0.31; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.78 (s, 1H), 7.69 (d, *J* = 4.8 Hz, 1H), 7.52 (d, *J* = 3.6 Hz, 1H), 7.21 (t, *J* = 8.4 Hz, 2H), 7.14-7.08 (m, 2H), 6.98 (d, *J* = 2.4 Hz, 1H), 6.88 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.38 (s, 1H), 5.91-5.82 (m, 1H), 5.16 (s, 2H), 5.07 (d, *J* = 10.4 Hz, 1H), 4.94 (d, *J* = 17.2 Hz, 1H), 3.82 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.3, 141.6, 140.6, 139.9, 137.5, 135.2, 134.5, 134.3, 133.7, 130.1, 129.7 (2C), 127.3, 126.2, 116.4, 113.4, 112.1, 102.4, 101.3, 100.6, 55.8, 47.0, 20.5; 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% : 0/20, 0.5/20, 3/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.90 min; IR (KBr, cm^{-1}): 3091, 2918, 2022, 1476, 1363, 1163; MS (ES mass): *m*/*z* 564.7 (M+1).

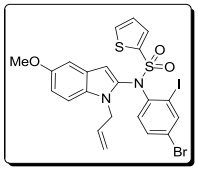
_N_-(1-Allyl-5-bromo-1_H_-indol-2-yl)-_N_-(2-iodo-4-methylphenyl)thiophene-2-sulfonamide (3k)



Off white solid; yield: 44%; mp: 148-150 °C; R_f (10% EtOAc-*n*-Hexane) 0.32; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, *J* = 0.8 Hz, 1H), 7.70 (dd, *J* = 5.2, 1.6 Hz, 1H), 7.65 (d, *J* = 1.6 Hz, 1H), 7.50 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.28 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.20-7.17 (m, 2H), 7.14-7.09 (m, 2H), 6.39 (s, 1H), 5.90-5.81 (m, 1H), 5.19 (s, 2H), 5.08 (dd, *J* = 10.8, 1.2 Hz, 1H), 4.91 (d, *J*

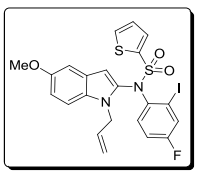
= 16.4 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.6, 140.8, 139.6, 137.2, 135.4, 135.3 (2C), 133.9, 133.8, 133.4, 129.8, 129.6, 127.4, 125.8, 123.4, 116.6, 113.4, 112.7, 101.2, 100.4, 47.1, 20.5; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 3/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.34 min; IR (KBr, cm^{-1}): 3085, 2922, 1468, 1365, 1158; MS (ES mass): *m*/*z* 613.9 (M+1).

_N_-(1-Allyl-5-methoxy-1_H_-indol-2-yl)-_N_-(4-bromo-2-iodophenyl)thiophene-2-sulfonamide (3l)



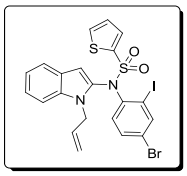
Off white solid; yield: 43%; mp: 157-159 °C; R_f (15% EtOAc-*n*-Hexane) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (d, *J* = 2.2 Hz, 1H), 7.71 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.54 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.43 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.23-7.18 (m, 2H), 7.14 (dd, *J* = 4.8, 3.6 Hz, 1H), 6.98 (d, *J* = 2.0 Hz, 1H), 6.89 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.36 (s, 1H), 5.89-5.80 (m, 1H), 5.10 (s, 2H), 5.05 (d, *J* = 10.4 Hz, 1H), 4.86 (d, *J* = 17.2 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.4, 143.1, 141.6, 137.0, 135.4, 134.1, 134.0, 133.8, 132.0, 131.0, 130.6, 127.4, 126.0, 123.2, 116.3, 113.6, 112.0, 109.9, 102.3, 100.7, 55.7, 46.8; 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, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.49 min; IR (KBr, cm^{-1}): 3087, 2924, 1466, 1358, 1160; MS (ES mass): *m*/*z* 629.7 (M+1).

_N_-(1-Allyl-5-methoxy-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)thiophene-2-sulfonamide (3m)



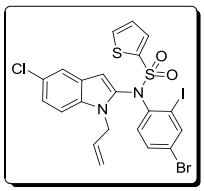
Off white solid; yield: 46%; mp: 158-160 °C; R_f (15% EtOAc-*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.66 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.53 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.34 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.20 (d, *J* = 8.8 Hz, 1H), 7.14 (dd, *J* = 5.2, 4.0 Hz, 1H), 7.05-6.98 (m, 2H), 6.89 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.38 (s, 1H), 5.90-5.81 (m, 1H), 5.13 (s, 2H), 5.04 (d, *J* = 10.0 Hz, 1H), 4.87 (dd, *J* = 17.2, 1.0 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5 (d, C-F *J* = 253.7 Hz), 138.6 (d, C-F *J* = 3.5 Hz), 137.1, 135.4, 134.2, 134.0, 131.0 (d, C-F *J* = 8.9 Hz), 130.1, 128.0 (d, C-F *J* = 24.4 Hz), 127.4, 126.0, 121.0, 120.3, 116.3, 116.0 (d, C-F *J* = 22.1 Hz), 113.6, 112.0, 102.3, 101.6 (d, C-F *J* = 8.4 Hz), 100.6, 55.7, 46.8; 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 (Isocratic) 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 5.02 min; IR (KBr, cm^{-1}): 3089, 2989, 1473, 1358, 1164; MS (ES mass): *m*/*z* 568.9 (M+1).

_N_-(1-Allyl-1_H_-indol-2-yl)-_N_-(4-bromo-2-iodophenyl)thiophene-2-sulfonamide (3n)



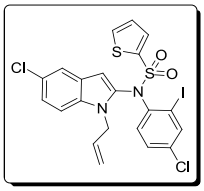
Off white solid; yield: 42%; mp: 148-150 °C; R_f (10% EtOAc-*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (d, *J* = 2.1 Hz, 1H), 7.72 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.55-7.53 (m, 2H), 7.43 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.24-7.21 (m, 2H), 7.15-7.09 (m, 2H), 6.43 (s, 1H), 5.92-5.81 (m, 1H), 5.16 (d, *J* = 2.4 Hz, 2H), 5.04 (d, *J* = 10.4 Hz, 1H), 4.83 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.1, 141.6, 136.9, 135.5, 134.8, 134.1, 133.8, 133.7, 132.0, 131.0, 127.4, 125.7, 123.2, 123.0, 121.0, 120.2, 116.3, 111.1, 102.3, 101.1, 46.6; HPLC: 96.5%; 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, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.62 min; IR (KBr, cm^{-1}): 3087, 2914, 1460, 1359, 1160; MS (ES mass): *m*/*z* 598.1 (M-1).

_N_-(1-Allyl-5-chloro-1_H_-indol-2-yl)-_N_-(4-bromo-2-iodophenyl)thiophene-2-sulfonamide (3o)



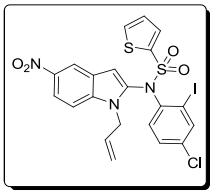
Off white solid; yield: 46%; mp: 160-162 °C; R_f (15% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (s, 1H), 7.73 (d, *J* = 4.8 Hz, 1H), 7.52-7.50 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.23-7.14 (m, 4H), 6.37 (s, 1H), 5.88-5.80 (m, 1H), 5.14 (s, 2H), 5.07 (d, *J* = 10.3 Hz, 1H), 4.84 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.2, 141.3, 136.7, 135.6, 134.8, 134.3, 133.5, 133.2, 132.1, 130.9, 127.5, 126.5, 126.0, 123.5, 123.4, 120.3, 116.6, 112.3, 102.3, 100.6, 46.9; HPLC: 97.2%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 6.22 min; IR (KBr, cm^{-1}): 3086, 2924, 1457, 1364, 1159; MS (ES mass): *m*/*z* 634.9 (M+1).

_N_-(1-Allyl-5-chloro-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)thiophene-2-sulfonamide (3p)



Light brown solid; yield: 50%; mp: 178-180 °C; R_f (10% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 2.0 Hz, 1H), 7.74 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.52-7.50 (m, 2H), 7.32-7.26 (m, 2H), 7.24-7.18 (m, 2H), 7.16-7.14 (m, 1H), 6.38 (s, 1H), 5.91-5.80 (m, 1H), 5.16 (s, 2H), 5.08 (d, *J* = 10.2 Hz, 1H), 4.85 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.9, 140.5, 136.7, 135.6, 135.3, 134.9, 134.3, 133.6, 133.2, 130.5, 129.2, 127.5, 126.6, 126.0, 123.5, 120.3, 116.6, 112.3, 101.9, 100.6, 46.9; 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 (Isocratic) 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 5.89 min; IR (KBr, cm^{-1}): 3090, 2923, 1459, 1361, 1159; MS (ES mass): *m*/*z* 589.8 (M+1).

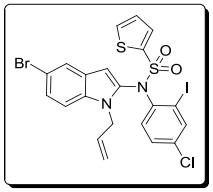
_N_-(1-Allyl-5-nitro-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)thiophene-2-sulfonamide (3q)



Light yellow solid; yield: 45%; mp: 175-177 °C; R_f (15% EtOAc-*n*-Hexane) 0.29; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.52 (d, *J* = 2.0 Hz, 1H), 8.13 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.97 (d, *J* = 2.2 Hz,

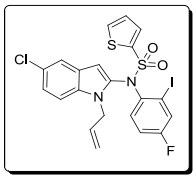
1H), 7.78 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.54-7.53 (m, 1H), 7.37-7.32 (m, 2H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.20-7.17 (m, 1H), 6.62 (s, 1H), 5.94-5.85 (m, 1H), 5.25-5.24 (m, 2H), 5.14 (d, *J* = 10.8 Hz, 1H), 4.89 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.1, 140.6, 140.5, 137.6, 136.9, 135.8, 135.7, 134.6, 132.9, 130.4, 129.2, 127.7, 124.7, 118.5, 118.2, 117.2, 111.3, 109.9, 103.2, 101.8, 47.2; 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 (Gradient) T/B% : 0/50, 0.5/50, 3/95, 10/95, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 4.72 min; IR (KBr, cm^{-1}): 3093, 2933, 1528, 1433, 1345, 1159; MS (ES mass): *m*/*z* 599.7 (M+1).

_N_-(1-Allyl-5-bromo-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)thiophene-2-sulfonamide (3r)



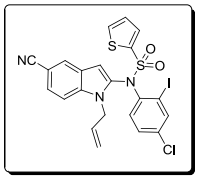
Light brown solid; yield: 48%; mp: 146-148 °C; R_f (15% EtOAc-*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.68-7.65 (m, 2H), 7.52 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.32-7.28 (m, 2H), 7.20-7.14 (m, 2H), 7.07-7.02 (m, 1H), 6.39 (s, 1H), 5.90-5.81 (m, 1H), 5.16 (s, 2H), 5.08 (d, *J* = 10.2 Hz, 1H), 4.85 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.6, 135.5, 135.0, 134.2, 133.5, 133.4, 130.8, 130.7, 128.1, 127.8, 127.5, 127.2, 125.9, 123.4, 116.6, 116.1, 115.9, 113.5, 112.7, 100.3, 46.8; HPLC: 93.1%; 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, 0.5/50, 3/95, 10/95, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.12 min; IR (KBr, cm^{-1}): 3071, 2922, 1462, 1348, 1153; MS (ES mass): *m*/*z* 634.2 (M+1).

_N_-(1-Allyl-5-chloro-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)thiophene-2-sulfonamide (3s)



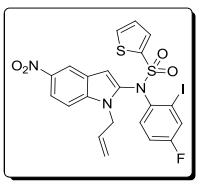
Off white solid; yield: 45%; mp: 168-170 °C; R_f (15% EtOAc-*n*-Hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69-7.64 (m, 1H), 7.61 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.48-7.43 (m, 2H), 7.23 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.18-7.15 (m, 1H), 7.13-7.07 (m, 2H), 7.01-6.95 (m, 1H), 6.32 (s, 1H), 5.84-5.74 (m, 1H), 5.10 (s, 2H), 5.01 (d, *J* = 10.4 Hz, 1H), 4.79 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.6 (d, C-F *J* = 254.2 Hz), 138.5 (d, C-F *J* = 4.5 Hz), 136.7, 135.5, 135.0, 134.2, 133.5, 133.4, 130.8 (d, C-F *J* = 7.0 Hz), 128.1 (d, C-F *J* = 24.5 Hz), 127.5, 127.2, 125.9, 123.4, 116.6, 116.1 (d, C-F *J* = 22.2 Hz), 113.5, 112.7, 101.7 (d, C-F *J* = 8.5 Hz), 100.3, 46.8; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.89 min; IR (KBr, cm^{-1}): 3084, 2921, 1452, 1348, 1152; MS (ES mass): *m*/*z* 573.0 (M+1).

_N_-(1-Allyl-5-cyano-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)thiophene-2-sulfonamide (3t)



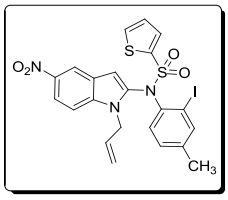
Off white solid; yield: 48%; mp: 142-144 °C; R_f (15% EtOAc-*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 2.4 Hz, 1H), 7.90 (s, 1H), 7.77 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.53-7.51 (m, 1H), 7.45 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.38 (d, *J* = 8.8 Hz, 1H), 7.33 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.19-7.17 (m, 1H), 6.54 (s, 1H), 5.93-5.83 (m, 1H), 5.22 (s, 2H), 5.13 (d, *J* = 10.8 Hz, 1H), 4.88 (d, *J* = 16.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.6, 140.5, 136.4, 136.3, 136.2, 135.7, 135.6, 134.5, 133.0, 130.5, 129.2, 127.6, 126.6, 125.7, 125.3, 120.2, 117.1, 112.1, 103.5, 101.8, 101.7, 47.1; HPLC: 91.2%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 240 nm, retention time 5.70 min; IR (KBr, cm^{-1}): 3093, 2921, 2222, 1466, 1364, 1165; MS (ES mass): *m*/*z* 579.8 (M+1).

N-(1-Allyl-5-nitro-1H-indol-2-yl)-N-(4-fluoro-2-iodophenyl)thiophene-2-sulfonamide (3u)



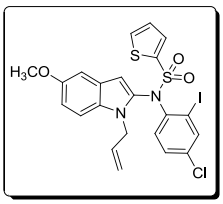
Light yellow solid; yield: 48%; mp: 192-194 °C; R_f (20% EtOAc-*n*-Hexane) 0.34; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.60 (d, *J* = 1.6 Hz, 1H), 8.19 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.84 (d, *J* = 4.8 Hz, 1H), 7.76 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.59 (d, *J* = 4.0 Hz, 1H), 7.43 (d, *J* = 9.2 Hz, 1H), 7.37 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.25 (t, *J* = 4.4 Hz, 1H), 7.19-7.11 (m, 1H), 6.70 (s, 1H), 6.01-5.91 (m, 1H), 5.33 (s, 2H), 5.21 (d, *J* = 10.4 Hz, 1H), 4.97 (d, *J* = 17.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.8 (d, C-F *J* = 254.9 Hz), 142.0, 138.1 (d, C-F *J* = 3.9 Hz), 137.6, 137.2, 136.3, 135.7, 134.6, 132.9, 130.9 (d, C-F *J* = 9.0 Hz), 128.2 (d, C-F *J* = 24.4 Hz), 127.7, 124.7, 118.4, 118.2, 117.2, 116.2 (d, C-F *J* = 22.2 Hz), 111.3, 103.1, 101.6 (d, C-F *J* = 9.1 Hz), 47.3; HPLC: 93.1%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 270 nm, retention time 5.57 min; IR (KBr, cm^{-1}): 3079, 1520, 1343, 1160; MS (ES mass): *m*/*z* 583.7 (M+1).

_N_-(1-Allyl-5-nitro-1_H_-indol-2-yl)-_N_-(2-iodo-4-methylphenyl)thiophene-2-sulfonamide (3v)



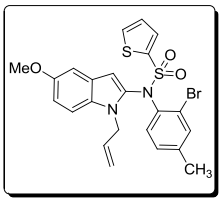
Light yellow solid; yield: 43%; mp: 150-152 °C; R_f (20% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.52 (d, *J* = 2.4 Hz, 1H), 8.12 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.82 (s, 1H), 7.76 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.54-7.52 (m, 1H), 7.38 (d, *J* = 9.2 Hz, 1H), 7.21-7.13 (m, 3H), 6.64 (s, 1H), 5.95-5.87 (m, 1H), 5.29 (s, 2H), 5.17 (d, *J* = 10.2 Hz, 1H), 4.99 (d, *J* = 17.3 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.9, 141.7, 141.2, 139.1, 137.6, 137.5, 136.7, 135.5, 134.3, 133.2, 129.8, 129.5, 127.5, 124.8, 118.2, 118.1, 117.2, 111.3, 103.0, 101.1, 47.3, 20.4; HPLC: 93.7%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.68 min; IR (KBr, cm^{-1}): 3098, 2927, 1516, 1336, 1160; MS (ES mass): *m*/*z* 580.0 (M+1).

_N_-(1-Allyl-5-methoxy-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)thiophene-2-sulfonamide (3w)



Off white solid; yield: 48%; mp: 171-173 °C; R_f (15% EtOAc-*n*-Hexane) 0.30; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (s, 1H), 7.72 (d, *J* = 4.9 Hz, 1H), 7.54 (d, *J* = 3.6 Hz, 1H), 7.30-7.28 (m, 2H), 7.20 (d, *J* = 9.2 Hz, 1H), 7.15 (t, *J* = 3.8 Hz, 1H), 6.99 (s, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 6.37 (s, 1H), 5.90-5.81 (m, 1H), 5.13 (s, 2H), 5.06 (d, *J* = 10.4 Hz, 1H), 4.86 (d, *J* = 17.2 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.5, 141.2, 140.5, 137.1, 135.6, 135.2, 134.2, 134.1, 134.0, 130.7, 130.2, 129.2, 127.5, 126.1, 116.4, 113.8, 112.1, 102.4, 102.0, 100.8, 55.8, 46.9; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.80 min; IR (KBr, cm^{-1}): 3085, 2923, 1466, 1360, 1160; MS (ES mass): *m*/*z* 585.0 (M+1).

_N_-(1-Allyl-5-methoxy-1_H_-indol-2-yl)-_N_-(2-bromo-4-methylphenyl)thiophene-2-sulfonamide (3x)



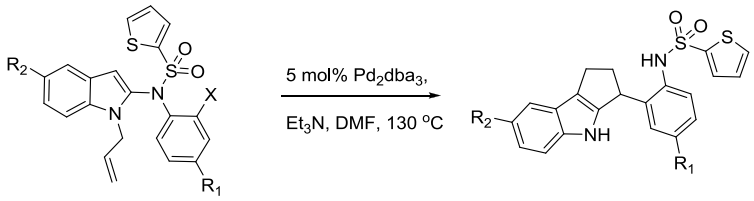
Off white solid; yield: 60%; mp: 100-102°C; R_f (15% EtOAc-*n*-Hexane) 0.34; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.53 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.49 (s, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.20 (d, *J* = 8.8 Hz, 1H), 7.14 (t, *J* = 4.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 2.0 Hz, 1H), 6.88 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.37 (s, 1H), 5.88-5.79 (m, 1H), 5.09 (d, *J* = 4.0 Hz, 2H), 5.05 (d, *J* = 10.4 Hz, 1H), 4.92 (d, *J* = 17.2 Hz, 1H), 3.82 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.2, 140.7, 136.3, 134.9, 134.8 (2C), 134.1, 134.0, 133.6, 130.4, 130.1, 128.8, 127.3, 126.1, 124.9, 116.3, 113.4, 111.9, 102.3, 100.5, 55.7, 46.2, 20.7; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.68 min; IR (KBr, cm^{-1}): 3082, 2917, 1441, 1370, 1156; MS (ES mass): *m*/*z* 518.3 (M+1).

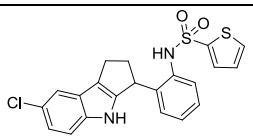
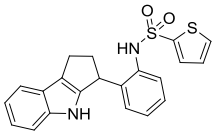
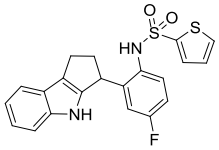
General procedure for preparation of *N*-(2-(7-substituted-1,2,3,4-tetrahydrocyclopenta[b]indol-3-yl)-4-substitutedphenyl)thiophene-2-sulfonamide (4):

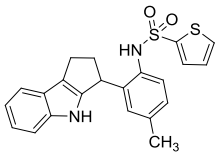
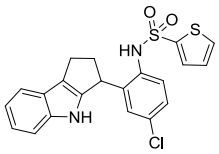
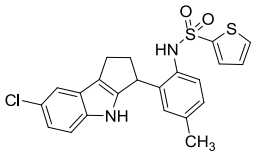
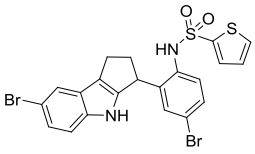
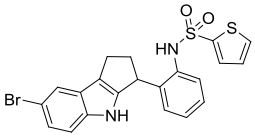
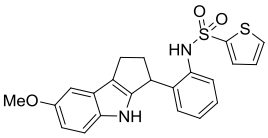
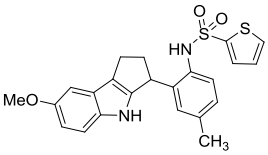
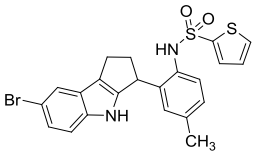
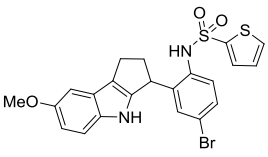
A mixture of *N*-(1-allyl-5-substituted-1*H*-indol-2-yl)-*N*-(2-iodo-4-substitutedphenyl)thiophene-2-sulfonamide **3**, (0.4 mmol), $Pd_2(dba)_3$ (5 mol%), Et_3N (1.2 mmol), and anhydrous DMF (2 mL) was stirred at 130 °C for 7h under a nitrogen atmosphere. The progress of the reaction was monitored by TLC. Upon completion, the mixture was cooled to room temperature and filtered to remove the solid seperated. The filtrate was extracted with ethyl acetate (3 x 10 mL). The combined organic phases were washed with brine (20 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 **4**.

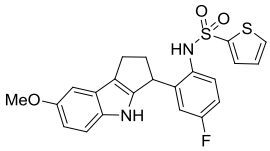
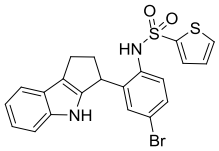
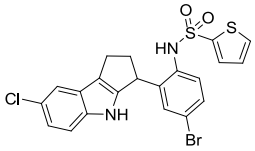
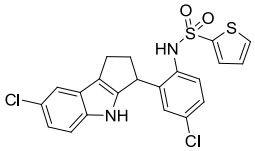
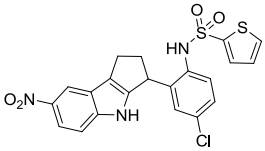
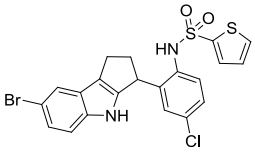
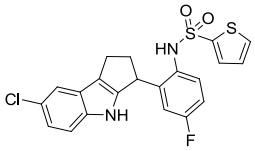
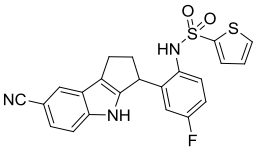
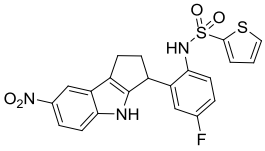
Note: In most of the cases a minute quantity of the ligand (1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one (**L**) dissociated from $Pd_2(dba)_3$ was isolated.

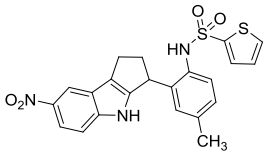
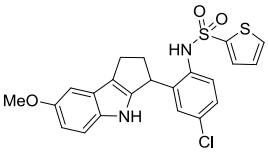
Table S-2: Pd catalyzed synthesis of *N*-(2-(7-substituted-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)-4-substitutedphenyl)thiophene-2-sulfonamide.[a]



S.No.	Compound (**3**)	Product (**4**)	Yield[b](%)
1	**3a**	 **4a**	80
2	**3b**	 **4b**	81
3	**3c**		71

		4c	
4	**3d**		76
		4d	
5	**3e**		78
		4e	
6	**3f**		68
		4f	
7	**3g**		83
		4g	
8	**3h**		72
		4h	
9	**3i**		70
		4i	
10	**3j**		81
		4j	
11	**3k**		80
		4k	
12	**3l**		68
		4l	

13	**3m**	 **4m**	62
14	**3n**	 **4n**	78
15	**3o**	 **4o**	70
16	**3p**	 **4p**	71
17	**3q**	 **4q**	66
18	**3r**	 **4r**	68
19	**3s**	 **4s**	68
20	**3t**	 **4t**	59
21	**3u**	 **4u**	62

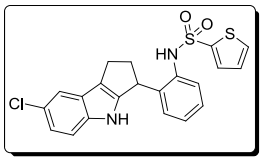
22	**3v**	 **4v**	73
23	**3w**	 **4w**	69
24	**3x**	No product	-

[a]All the reactions were performed using **3** (0.4 mmol), $Pd_2(dba)_3$ (5 mol%) and Et_3N (1.2 mmol) in DMF (2 mL) at 130 °C for 7 h under N_2.

[b]Isolated yield.

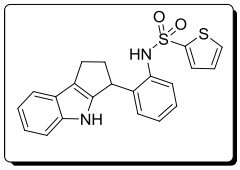
Characterization Data of compounds 4a-4w

***N*-(2-(7-Chloro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4a):**



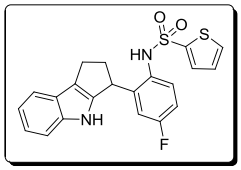
Off white solid; yield: 80%; mp: 152-154 °C; R_f (15% EtOAc-*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 4.8 Hz, 1H), 7.48-7.46 (m, 2H), 7.21-7.10 (m, 6H), 7.07 (t, *J* = 4.0 Hz, 1H), 6.46 (s, 1H), 5.89 (s, 1H), 4.75 (t, *J* = 8.4 Hz, 1H), 4.23 (td, *J* = 9.6, 3.6 Hz, 1H), 4.06 (q, *J* = 7.6 Hz, 1H), 3.06-2.97 (m, 1H), 2.44-2.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.4, 139.9, 138.7, 133.8, 133.2, 133.1, 132.6, 131.1, 128.9, 127.9, 127.8, 127.5, 126.2, 125.2, 121.0, 120.1, 110.4, 93.3, 43.4, 38.8, 37.7; 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 (Isocratic) T/B% : 0/50, 0.5/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 235 nm, retention time 4.21 min; IR (KBr, cm^{-1}): 3246, 2933, 2885, 1457, 1341, 1156; MS (ES mass): *m*/*z* 429.0 (M+1).

***N*-(2-(1,2,3,4-Tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4b)**



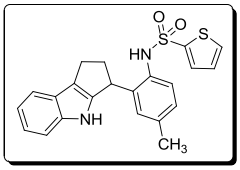
Light brown solid; yield: 81%; mp: 158-160 °C; R_f (20% EtOAc-*n*-Hexane) 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, *J* = 4.8 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.46 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.22-7.14 (m, 5H), 7.10-7.04 (m, 2H), 6.67 (s, 1H), 5.93 (s, 1H), 4.68 (t, *J* = 8.0 Hz, 1H), 4.25-4.19 (m, 1H), 4.07-4.00 (m, 1H), 3.01-2.93 (m, 1H), 2.39-2.30 (m, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.8, 139.9, 138.6, 133.3, 132.9, 132.9, 132.7, 132.6, 128.9, 127.7 (2C), 127.5, 126.0, 120.7 (2C), 119.4, 109.6, 93.5, 43.1, 38.7, 37.7; 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 (Isocratic) T/B% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.15 min; IR (KBr, cm^{-1}): 3337, 3087, 2923, 1851, 1458, 1358, 1162; MS (ES mass): *m*/*z* 395.0 (M+1).

_N_-(4-Fluoro-2-(1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4c)



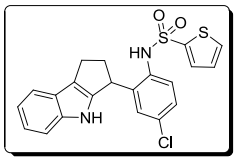
Off white solid; yield: 71%; mp: 145-147 °C; R_f (20% EtOAc-*n*-Hexane) 0.29; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 2.4 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.19-7.06 (m, 4H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.60 (s, 1H), 5.93 (s, 1H), 4.70 (t, *J* = 7.9 Hz, 1H), 4.22 (td, *J* = 10.0, 3.6 Hz, 1H), 4.03 (q, *J* = 7.6 Hz, 1H), 3.04-2.96 (m, 1H), 2.38-2.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.2 (d, C-F *J* = 247.0 Hz), 145.1, 142.7 (d, C-F *J* = 7.6 Hz), 139.7, 135.1, 133.1, 132.8, 132.7, 128.9 (d, C-F *J* = 3.0 Hz), 128.8 (d, C-F *J* = 8.7 Hz), 127.5, 124.9, 120.9 (d, C-F *J* = 9.1 Hz), 119.5, 115.6 (d, C-F *J* = 23.4 Hz), 114.7 (d, C-F *J* = 22.7 Hz), 109.5, 93.7, 43.1, 38.7, 37.7; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.19 min; IR (KBr, cm^{-1}): 3324, 3091, 2921, 1439, 1344, 1169; MS (ES mass): *m*/*z* 413.0 (M+1).

_N_-(4-Methyl-2-(1,2,3,4-tetrahydrocyclopenta[_b_]indol-3-yl)phenyl)thiophene-2-sulfonamide (4d)



White solid; yield: 76%; mp: 133-135 °C; R_f (20% EtOAc-_n_-Hexane) 0.29; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, _J_ = 5.2 Hz, 1H), 7.54 (d, _J_ = 8.0 Hz, 1H), 7.46-7.45 (m, 1H), 7.30 (d, 1H), 7.17 (t, _J_ = 7.2 Hz, 1H), 7.10-7.05 (m, 2H), 7.04 (d, _J_ = 8.4 Hz, 1H), 6.99-6.96 (m, 2H), 6.46 (s, 1H), 5.93 (s, 1H), 4.69 (t, _J_ = 8.0 Hz, 1H), 4.26-4.21 (m, 1H), 4.07-4.01 (m, 1H), 3.01-2.93 (m, 1H), 2.40-2.30 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.2, 140.1, 139.2, 138.1, 132.9, 132.9, 132.7, 132.5, 130.5, 129.3, 128.4, 127.4, 126.5, 120.7, 120.6, 119.4, 109.6, 93.4, 43.2, 38.5, 37.9, 21.1; HPLC: 95.9%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.28 min; IR (KBr, cm^{-1}): 3300, 3091, 2901, 1706, 1482, 1372, 1162; MS (ES mass): _m/z_ 409.0 (M+1).

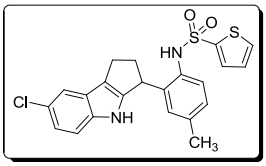
_N_-(4-Chloro-2-(1,2,3,4-tetrahydrocyclopenta[_b_]indol-3-yl)phenyl)thiophene-2-sulfonamide (4e)



Off white solid; yield: 78%; mp: 160-162 °C; R_f (20% EtOAc-_n_-Hexane) 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (d, _J_ = 8.0 Hz, 1H), 7.55 (d, _J_ = 7.6 Hz, 1H), 7.47 (d, = 2.8 Hz, 1H), 7.30 (d, _J_ = 8.4 Hz, 1H), 7.20-7.16 (m, 4H), 7.12-7.07 (m, 2H), 6.44 (s, 1H), 5.95 (s, 1H), 4.63 (t, _J_ = 8.2 Hz, 1H), 4.24 (td, _J_ = 10.2, 3.6 Hz, 1H), 4.04 (q, _J_ = 7.6 Hz, 1H), 3.01-2.93 (m, 1H), 2.38-2.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.7, 140.6, 139.6, 133.5, 133.1, 132.9, 132.8, 132.7, 131.8, 128.9, 127.9, 127.5, 127.4, 121.0, 120.8, 119.6, 109.6, 93.8, 43.1, 38.6, 37.5; HPLC: 98.8%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 0.5/50, 3/98, 10/98, 10.5/50, 12/50;

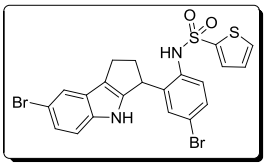
flow rate: 1.0 mL/min; UV 220 nm, retention time 4.25 min; IR (KBr, cm^{-1}): 3361, 3091, 2922, 1474, 1335, 1159; MS (ES mass): *m*/*z* 428.9 (M+1).

_N_-(2-(7-Chloro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)-4-methylphenyl)thiophene-2-sulfonamide (4f)



Off white solid; yield: 68%; mp: 125-127 °C; R_f (15% EtOAc-*n*-Hexane) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 4.4 Hz, 1H), 7.49 (s, 1H), 7.47 (d, *J* = 1.6 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.13-7.10 (m, 1H), 7.07 (t, *J* = 4.4 Hz, 1H), 6.97-6.95 (m, 3H), 6.35 (s, 1H), 5.89 (s, 1H), 4.77 (t, *J* = 8.0 Hz, 1H), 4.25 (td, *J* = 9.6, 3.6 Hz, 1H), 4.08-4.01 (m, 1H), 3.06-2.96 (m, 1H), 2.45-2.35 (m, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.8, 140.0, 139.3, 138.3, 133.9, 133.0, 132.5, 131.1, 130.4, 129.3, 128.5, 127.4, 126.7, 125.1, 120.9, 120.1, 110.4, 93.2, 43.4, 38.7, 37.9, 21.1; 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 (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 4.88 min; IR (KBr, cm^{-1}): 3254, 2925, 1459, 1399, 1159; MS (ES mass): *m*/*z* 443.0 (M+1).

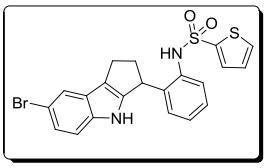
***N*-(4-Bromo-2-(7-bromo-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4g)**



White solid; yield: 83%; mp: 183-185 °C; R_f (15% EtOAc-*n*-Hexane) 0.27; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (s, 1H), 7.65 (d, *J* = 4.8 Hz, 1H), 7.50 (d, *J* = 3.6 Hz, 1H), 7.34 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.30-7.29 (m, 2H), 7.17 (d, *J* = 8.8 Hz, 1H), 7.10 (t, *J* = 4.0 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.44 (s, 1H), 5.92 (s, 1H), 4.72 (t, *J* = 8.0 Hz, 1H), 4.26 (td, *J* = 10.0, 3.2 Hz, 1H), 4.09-4.02 (m, 1H), 3.06-2.98 (m, 1H), 2.44-2.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.2, 140.8, 139.5, 134.4, 133.2, 132.9, 132.3, 131.8, 131.4, 131.0, 127.8, 127.6, 123.8, 123.2,

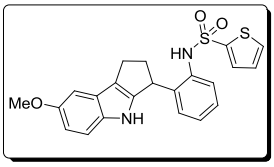
121.7, 112.9, 110.9, 93.5, 43.3, 38.7, 37.6; HPLC: 99.8%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.27 min; IR (KBr, cm^{-1}): 3258, 2938, 2885, 1465, 1394, 1159; MS (ES mass): *m*/*z* 552.8 (M+1).

_N_-(2-(7-Bromo-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4h)



Light yellow solid; yield: 72%; mp: 171-173 °C; R_f (15% EtOAc-*n*-Hexane) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 1.6 Hz, 1H), 7.61 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.48-7.45 (m, 1H), 7.25-7.23 (m, 1H), 7.20-7.17 (m, 3H), 7.13-7.11 (m, 2H), 7.09-7.05 (m, 1H), 6.48 (s, 1H), 5.88 (s, 1H), 4.76 (t, *J* = 7.8 Hz, 1H), 4.26-4.20 (m, 1H), 4.08-4.02 (m, 1H), 3.06-2.97 (m, 1H), 2.44-2.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.3, 138.8, 134.4, 133.2, 133.1, 132.6, 131.3, 128.8, 128.0, 127.8, 127.5, 126.3, 123.5, 123.1, 112.7, 110.9, 109.9, 93.2, 43.4, 38.7, 37.8; HPLC: 93.2%; 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 230 nm, retention time 4.79 min; IR (KBr, cm^{-1}): 3243, 3098, 1455, 1338, 1157; MS (ES mass): *m*/*z* 473.9 (M+1).

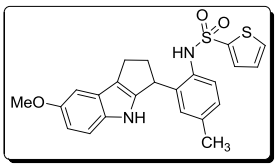
_N_-(2-(7-Methoxy-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4i)



Off white solid; yield: 70%; mp: 135-137 °C; R_f (20% EtOAc-*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, *J* = 4.4 Hz, 1H), 7.46 (d, *J* = 2.9 Hz, 1H), 7.24-7.13 (m, 5H), 7.07-7.05 (m, 1H), 7.01 (d, *J* = 2.0 Hz, 1H), 6.83 (dd, *J* = 8.6, 2.0 Hz, 1H), 6.56 (s, 1H), 5.86 (s, 1H), 4.65 (t, *J* = 7.7 Hz, 1H), 4.22-4.15 (m, 1H), 4.05-3.97 (m, 1H), 3.84 (s, 3H), 2.99-2.91 (m, 1H), 2.37-

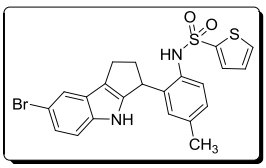
2.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.0, 146.2, 140.0, 138.4, 133.3, 133.2, 132.9, 132.5, 128.9, 128.1, 127.7, 127.6, 127.4, 125.9, 110.8, 110.2, 102.8, 93.2, 55.9, 43.3, 39.0, 37.6; HPLC: 96.0%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/50, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.01 min; IR (KBr, cm^{-1}): 3257, 3092, 2913, 1482, 1336, 1159; MS (ES mass): *m*/*z* 425.0 (M+1).

_N_-(2-(7-Methoxy-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)-4-methylphenyl)thiophene-2-sulfonamide (4j)



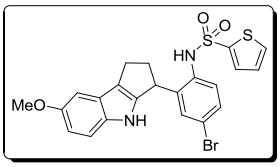
Light green solid; yield: 81%; mp: 141-143 °C; R_f (20% EtOAc-*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.46 (dd, *J* = 3.6, 0.8 Hz, 1H), 7.19 (d, *J* = 8.8 Hz, 1H), 7.07-7.04 (m, 1H), 7.02-7.00 (m, 2H), 6.99-6.96 (m, 2H), 6.83 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.46 (s, 1H), 5.85 (s, 1H), 4.66 (t, *J* = 8.0 Hz, 1H), 4.23-4.16 (m, 1H), 4.05-3.94 (m, 1H), 3.84 (s, 3H), 2.98-2.90 (m, 1H), 2.36-2.29 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.0, 146.7, 139.1, 138.0, 133.3, 132.9, 132.4, 130.4, 129.4, 128.4, 128.0, 127.4, 126.4, 110.7, 110.2, 109.9, 102.7, 93.1, 55.9, 43.4, 38.8, 37.8, 21.0; HPLC: 95.5%; 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, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.25 min; IR (KBr, cm^{-1}): 3266, 3092, 2926, 1484, 1333, 1156; MS (ES mass): *m*/*z* 439.1 (M+1).

_N_-(2-(7-Bromo-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)-4-methylphenyl)thiophene-2-sulfonamide (4k)



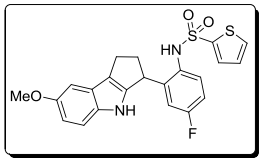
Off white solid; yield: 80%; mp: 193-195 °C; R_f (15% EtOAc-*n*-Hexane) 0.19; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 1.4 Hz, 1H), 7.61 (d, *J* = 4.0 Hz, 1H), 7.47 (d, *J* = 2.8 Hz, 1H), 7.25 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.16 (d, *J* = 8.5 Hz, 1H), 7.09-7.06 (m, 1H), 7.00-6.96 (m, 2H), 6.94 (s, 1H), 6.39 (s, 1H), 5.88 (s, 1H), 4.77 (t, *J* = 8.0 Hz, 1H), 4.27-4.19 (m, 1H), 4.07-4.00 (m, 1H), 3.05-2.97 (m, 1H), 2.40-2.32 (m, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.8, 139.8, 139.4, 138.3, 134.5, 133.0, 132.5, 131.2, 130.4, 129.2, 128.5, 127.5, 126.7, 123.3, 123.0, 112.6, 110.9, 93.1, 43.4, 38.5, 38.0, 21.1; 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 (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 5.03 min; IR (KBr, cm^{-1}): 3255, 2884, 1335, 1158; MS (ES mass): *m*/*z* 486.8 (M-1).

_N_-(4-Bromo-2-(7-methoxy-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4l)



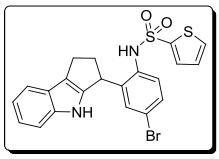
Off white solid; yield: 68%; mp: 149-150 °C; R_f (20% EtOAc-*n*-Hexane) 0.17; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, *J* = 4.4 Hz, 1H), 7.49-7.46 (m, 1H), 7.36-7.29 (m, 2H), 7.19 (d, *J* = 8.8 Hz, 1H), 7.13-7.06 (m, 2H), 7.02 (s, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.47 (s, 1H), 5.89 (s, 1H), 4.59 (d, *J* = 8.2 Hz, 1H), 4.25-4.18 (m, 1H), 4.06-3.98 (m, 1H), 3.85 (s, 3H), 2.99-2.90 (m, 1H), 2.35-2.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.2, 145.1, 140.3, 139.7, 133.3, 133.1, 132.7, 132.5, 131.9, 130.9, 128.2, 127.5, 127.3, 121.2, 111.2, 110.2, 102.9, 93.5, 55.9, 43.3, 39.0, 37.4; HPLC: 95.5%; 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, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.57 min; IR (KBr, cm^{-1}): 3424, 2953, 1478, 1333, 1160; MS (ES mass): *m*/*z* 504.0 (M+1).

_N_-(4-Fluoro-2-(7-methoxy-1,2,3,4-tetrahydrocyclopenta[b]indol-3-yl)phenyl)thiophene-2-sulfonamide (4m)



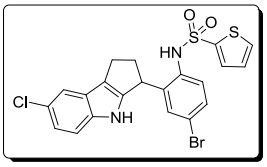
Light yellow solid; yield: 62%; mp: 125-127 °C; R_f (20% EtOAc-*n*-Hexane) 0.28; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, *J* = 4.4 Hz, 1H), 7.47-7.46 (m, 1H), 7.34-7.31 (m, 2H), 7.19 (d, *J* = 8.8 Hz, 1H), 7.13-7.08 (m, 2H), 7.02 (s, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.47 (s, 1H), 5.88 (s, 1H), 4.59 (t, *J* = 8.2 Hz, 1H), 4.24-4.19 (m, 1H), 4.04-3.98 (m, 1H), 3.85 (s, 3H), 2.99-2.90 (m, 1H), 2.36-2.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.2 (d, C-F *J* = 246.7 Hz), 154.1, 142.8 (d, C-F *J* = 7.3 Hz), 139.7, 133.3, 133.2, 132.8, 128.9, 128.8, 128.1, 127.6, 115.7 (d, C-F *J* = 2.1 Hz), 115.5, 114.8 (d, C-F *J* = 22.5 Hz), 111.0, 110.3, 102.8, 93.3, 55.9, 43.3, 38.9, 37.7; HPLC: 93.1%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.09 min; IR (KBr, cm^{-1}): 3037, 2921, 1467, 1339, 1152; MS (ES mass): *m*/*z* 442.9 (M+1).

_N_-(4-Bromo-2-(1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4n)



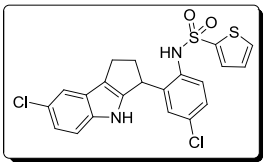
Off white solid; yield: 78%; mp: 185-187 °C; R_f (15% EtOAc-*n*-Hexane) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63-7.61 (m, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 2.8 Hz, 1H), 7.34-7.29 (m, 3H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.14-7.07 (m, 3H), 6.49 (s, 1H), 5.96 (s, 1H), 4.63 (t, *J* = 8.0 Hz, 1H), 4.25 (dt, *J* = 9.8, 3.4 Hz, 1H), 4.08-4.00 (m, 1H), 3.01-2.93 (m, 1H), 2.38-2.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.6, 140.6, 133.2, 132.9, 132.8, 132.7, 132.4, 131.8, 130.9, 127.6, 127.5, 121.4, 121.0, 120.8, 119.6, 109.9, 109.6, 93.8, 43.1, 38.6, 37.6; HPLC: 96.9%; 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, 0.5/50, 4/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.85 min; IR (KBr, cm^{-1}): 3363, 3294, 3084, 2883, 1477, 1332, 1161; MS (ES mass): *m*/*z* 473.9 (M+1).

_N_-(4-Bromo-2-(7-chloro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4o)



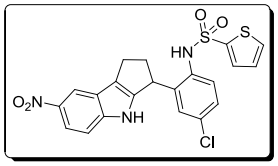
Off white solid; yield: 70%; mp: 166-167 °C; R_f (20% EtOAc-*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 4.5 Hz, 1H), 7.50-7.47 (m, 2H), 7.33-7.28 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.13-7.07 (m, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.55 (s, 1H), 5.89 (s, 1H), 4.70 (t, *J* = 8.0 Hz, 1H), 4.23 (td, *J* = 8.8, 2.8 Hz, 1H), 4.06-4.00 (m, 1H), 3.05-2.97 (m, 1H), 2.41-2.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.4, 140.8, 139.4, 133.7, 133.3, 132.9, 132.3, 131.8, 131.1, 131.0, 127.8, 127.6, 125.3, 121.7, 121.2, 120.2, 110.5, 93.5, 43.3, 38.7, 37.6; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.69 min; IR (KBr, cm^{-1}): 3074, 2921, 1455, 1343, 1161; MS (ES mass): *m*/*z* 508.4 (M+1).

_N_-(4-Chloro-2-(7-chloro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4p)



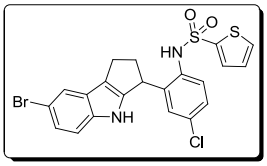
Light brown solid; yield: 71%; mp: 146-148 °C; R_f (20% EtOAc-*n*-Hexane) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (d, *J* = 4.8 Hz, 1H), 7.51 (s, 1H), 7.48 (d, *J* = 4.0 Hz, 1H), 7.21-7.18 (m, 1H), 7.16-7.12 (m, 3H), 7.10-7.07 (m, 2H), 6.41 (s, 1H), 5.91 (s, 1H), 4.71 (t, *J* = 8.2 Hz, 1H), 4.28-4.21 (m, 1H), 4.08-4.02 (m, 1H), 3.03-2.98 (m, 1H), 2.40-2.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.6, 140.9, 139.5, 133.8, 133.3, 132.9, 131.8, 131.1, 128.9, 128.0, 127.8, 127.6 (2C), 125.2, 121.2, 120.2, 110.5, 93.5, 43.4, 38.7, 37.7; HPLC: 91.7%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.62 min; IR (KBr, cm^{-1}): 3280, 2923, 1720, 1467, 1337, 1159; MS (ES mass): *m*/*z* 463.0 (M+1).

_N_-(4-Chloro-2-(7-nitro-1,2,3,4-tetrahydrocyclopenta[_b_]indol-3-yl)phenyl)thiophene-2-sulfonamide (4q)



Light yellow solid; yield: 66%; mp: 142-144 °C; R_f (25% EtOAc-*n*-Hexane) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50 (d, *J* = 1.9 Hz, 1H), 8.10 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.66 (d, *J* = 4.0 Hz, 1H), 7.50 (d, *J* = 2.6 Hz, 1H), 7.30 (d, *J* = 8.9 Hz, 1H), 7.19-7.14 (m, 2H), 7.13 (t, *J* = 4.4 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.60 (s, 1H), 6.15 (s, 1H), 4.91 (t, *J* = 8.0 Hz, 1H), 4.37-4.31 (m, 1H), 4.17-4.11 (m, 1H), 3.17-3.09 (m, 1H), 2.51-2.42 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 149.0, 141.5, 141.4, 139.2, 135.4, 134.2, 133.4, 133.0, 131.9, 131.7, 128.7, 128.3, 128.1, 127.6, 117.9, 116.7, 109.3, 96.5, 43.6, 38.4, 37.9; HPLC: 90.8%; 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, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 3.99 min; IR (KBr, cm^{-1}): 3271, 3032, 2932, 1456, 1321, 1149; MS (ES mass): *m*/*z* 474.0 (M+1).

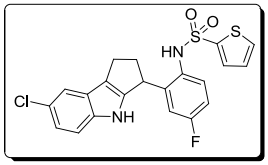
_N_-(2-(7-Bromo-1,2,3,4-tetrahydrocyclopenta[_b_]indol-3-yl)-4-chlorophenyl)thiophene-2-sulfonamide (4r)



Off white solid; yield: 68%; mp: 155-150 °C; R_f (20% EtOAc-*n*-Hexane) 0.26; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (d, *J* = 1.5 Hz, 1H), 7.61 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.47-7.46 (m, 1H), 7.23-7.11 (m, 5H), 7.08-7.06 (m, 1H), 6.48 (s, 1H), 5.88 (s, 1H), 4.76 (t, *J* = 7.8 Hz, 1H), 4.25-4.20 (m, 1H), 4.08-4.02 (m, 1H), 3.05-2.97 (m, 1H), 2.44-2.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.3, 138.8, 134.4, 133.2, 133.1, 132.6, 131.3, 128.8, 128.0, 127.8, 127.5, 126.3, 123.5, 123.1, 112.7, 110.9, 109.9, 93.2, 43.4, 38.7, 37.8; HPLC: 97.2%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm,

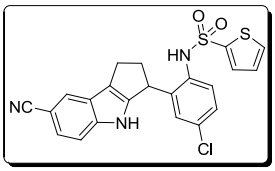
retention time 5.73 min; IR (KBr, cm^{-1}): 3268, 3072, 2932, 1455, 1338, 1155; MS (ES mass): *m*/*z* 508.2 (M+1).

_N_-(2-(7-Chloro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)-4-fluorophenyl)thiophene-2-sulfonamide (4s)



Off white solid; yield: 68%; mp: 149-151 °C; R_f (20% EtOAc-*n*-Hexane) 0.29; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, *J* = 4.7 Hz, 1H), 7.43 (s, 1H), 7.40 (d, *J* = 3.6 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 7.06-7.02 (m, 2H), 6.96 (dd, *J* = 8.4, 5.2 Hz, 1H), 6.83-6.76 (m, 2H), 6.32 (s, 1H), 5.82 (s, 1H), 4.71 (t, *J* = 7.8 Hz, 1H), 4.19-4.13 (m, 1H), 4.01-3.95 (m, 1H), 3.01-2.93 (m, 1H), 2.35-2.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.1 (d, C-F *J* = 163.2 Hz), 148.1, 137.6, 134.6, 133.3, 132.8 (d, C-F *J* = 3.0 Hz), 131.7, 127.6 (d, C-F *J* = 6.3 Hz), 126.8, 124.6, 122.5, 121.1, 120.3, 120.1, 115.6 (d, C-F *J* = 23.0 Hz), 114.9 (d, C-F *J* = 22.4 Hz), 110.9, 93.4, 44.1, 38.7, 37.4; HPLC: 91.2%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.13 min; IR (KBr, cm^{-1}): 3298, 2921, 1452, 1342, 1148; MS (ES mass): *m*/*z* 447.4 (M+1).

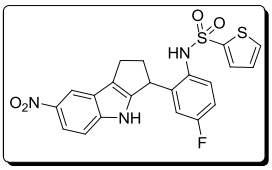
_N_-(2-(7-Cyano-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)-4-fluorophenyl)thiophene-2-sulfonamide (4t)



Light yellow solid; yield: 59%; mp: 171-173 °C; R_f (20% EtOAc-*n*-Hexane) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 2.8 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.20-7.16 (m, 3H), 7.12-7.07 (m, 2H), 6.44 (s, 1H), 5.95 (s, 1H), 4.63 (t, *J* = 8.2 Hz, 1H), 4.24 (td, *J* = 10.2, 3.6 Hz, 1H), 4.04 (q, *J* = 7.6 Hz, 1H), 3.01-2.93 (m, 1H), 2.38-2.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.7, 140.6, 139.6, 133.5, 133.1, 132.9, 132.8, 132.7, 131.8, 128.9, 127.9, 127.5, 127.4, 121.0, 120.8, 119.6, 109.6, 102.2, 93.8, 43.1,

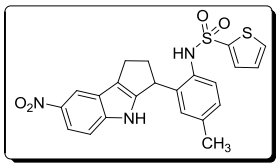
38.6, 37.5; HPLC: 94.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Isocratic) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.01 min; IR (KBr, cm^{-1}): 3293, 2922, 2223, 1437, 1333, 1167; MS (ES mass): *m*/*z* 454.4 (M+1).

_N_-(4-Fluoro-2-(7-nitro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4u)



Light yellow solid; yield: 62%; mp: 145-147 °C; R_f (25% EtOAc-*n*-Hexane) 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.49 (d, *J* = 2.0 Hz, 1H), 8.08 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.66 (d, *J* = 3.6 Hz, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 7.10 (t, *J* = 4.0 Hz, 1H), 6.94-6.85 (m, 3H), 6.44 (s, 1H), 6.15 (s, 1H), 4.97 (t, *J* = 8.2 Hz, 1H), 4.36-4.29 (m, 1H), 4.14 (td, *J* = 10.2, 7.8 Hz, 1H), 3.18-3.11 (m, 1H), 2.51-2.41 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.5 (d, C-F *J* = 247.9 Hz), 149.2, 143.1, 141.5, 139.3, 135.4, 133.4, 133.0, 131.9, 129.5 (d, C-F *J* = 8.8 Hz), 128.9 (d, C-F *J* = 3.0 Hz), 127.6, 117.9, 116.7, 115.6 (d, C-F *J* = 23.7 Hz), 115.1 (d, C-F *J* = 22.8 Hz), 109.3, 96.5, 43.6, 38.6, 38.0; HPLC: 95.2%; 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 210 nm, retention time 4.09 min; IR (KBr, cm^{-1}): 3297, 3078, 2922, 1453, 1323, 1157; MS (ES mass): *m*/*z* 455.9 (M-1).

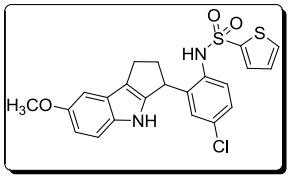
_N_-(4-Methyl-2-(7-nitro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4v)



Light yellow solid; yield: 75%; mp: 125-127 °C; R_f (25% EtOAc-*n*-Hexane) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.31 (d, *J* = 1.6 Hz, 1H), 8.11 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.65 (d, *J* = 4.8 Hz, 1H), 7.51 (d, *J* = 3.6 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.11-7.09 (m, 1H), 6.98 (d, *J* = 7.6 Hz,

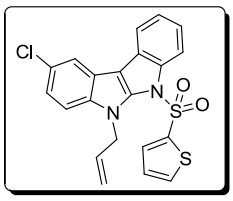
1H), 6.85 (s, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 6.46 (s, 1H), 5.03 (t, *J* = 8.0 Hz, 1H), 4.45-4.39 (m, 1H), 4.24-4.16 (m, 1H), 3.27-3.18 (m, 1H), 2.64-2.56 (m, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.3, 139.9, 139.3, 138.9, 136.4, 133.5, 132.8, 130.6, 129.6, 129.4, 128.9, 127.7, 118.1, 117.7, 116.6, 110.0, 109.3, 96.4, 44.6, 38.6, 38.4, 21.3; HPLC: 91.2%; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 5.29 min; IR (KBr, cm^{-1}): 3268, 2930, 1732, 1509, 1326, 1156; MS (ES mass): *m*/*z* 453.9 (M+1).

_N_-(4-Chloro-2-(7-methoxy-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (4w)



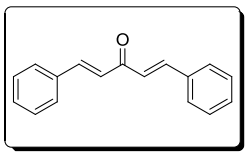
Off white solid; yield: 69%; mp: 153-155 °C; R_f (20% EtOAc-*n*-Hexane) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.45 (dd, *J* = 4.2, 1.2 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.10-7.05 (m, 1H), 7.03-7.00 (m, 2H), 6.99-6.96 (m, 2H), 6.83 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.44 (s, 1H), 5.87 (s, 1H), 4.68 (t, *J* = 8.2 Hz, 1H), 4.23-4.17 (m, 1H), 4.05-3.97 (m, 1H), 3.84 (s, 3H), 2.98-2.90 (m, 1H), 2.37-2.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.0, 146.7, 139.1, 138.0, 133.3, 132.9, 132.4, 130.4, 129.4, 128.4, 128.0, 127.4, 126.4, 110.7, 110.2, 109.9, 102.7, 93.1, 55.9, 43.4, 38.8, 37.8; 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 (Isocratic) 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 4.57 min; IR (KBr, cm^{-1}): 3424, 2953, 1478, 1333, 1160; MS (ES mass): *m*/*z* 458.9 (M+1).

5-Allyl-2-chloro-6-(thiophen-2-ylsulfonyl)-5,6-dihydroindolo[2,3-*b*]indole (5)



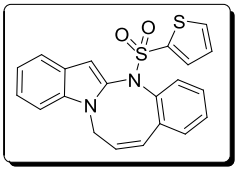
White solid; mp: 180-182 °C; R_f (10% EtOAc-*n*-Hexane) 0.68; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.15 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 8.8 Hz, 1H), 7.38-7.33 (m, 2H), 7.29-7.27 (m, 1H), 7.25-7.24 (m, 2H), 6.77 (t, *J* = 4.8 Hz, 1H), 6.17-6.08 (m, 1H), 5.30-5.25 (m, 3H), 5.19 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.6, 140.6, 139.6, 133.9, 133.6, 133.4, 133.3, 126.9, 126.8, 126.7, 126.1, 125.6, 122.9, 122.5, 121.3, 118.9, 118.5, 118.1, 117.2, 112.8, 49.5; 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% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 240 nm, retention time 6.15 min; IR (KBr, cm^{-1}): 3097, 2897, 1439, 1375, 1173; MS (ES mass): *m*/*z* 427.4 (M+1).

(1*E*,4*E*)-1,5-Diphenylpenta-1,4-dien-3-one (L)



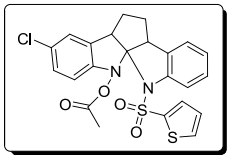
Off white solid; mp: 110-112 °C; R_f (20% EtOAc-*n*-Hexane) 0.82; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75 (d, *J* = 15.6 Hz, 1H), 7.64-7.62 (m, 2H), 7.43-7.41 (m, 3H), 7.10 (d, *J* = 15.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 188.9, 143.3, 134.7, 130.5, 128.9 (2C), 128.4 (2C), 125.4.

Compound **6:**



White solid; mp: 156-158 °C; R_f (15% EtOAc-*n*-Hexane) 0.36; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.57-7.55 (m, 2H), 7.39-7.35 (m, 2H), 7.33 (s, 1H), 7.32-7.28 (m, 2H), 7.25-7.22 (m, 1H), 7.11-7.09 (m, 2H), 6.79 (d, *J* = 11.2 Hz, 1H), 6.62 (s, 1H), 6.04-5.97 (m, 1H), 4.92-4.87 (m, 1H), 4.07 (dd, *J* = 15.6, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.6, 138.1, 136.8, 135.1, 133.7 (2C), 132.7, 132.6, 130.0, 129.5, 129.3, 129.2, 127.1, 126.6, 125.8, 122.4, 121.1, 120.2, 109.3, 99.7, 41.7; MS (ES mass): *m*/*z* 392.5 (M+1).

Compound 7:



Off white solid; R_f (15% EtOAc-*n*-Hexane) 0.46; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (d, *J* = 2.9 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.55 (d, *J* = 4.4 Hz, 1H), 7.33-7.29 (m, 2H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.99-6.96 (m, 2H), 6.67 (d, *J* = 8.4 Hz, 1H), 4.27 (d, *J* = 8.4 Hz, 1H), 3.32 (dd, *J* = 11.3, 6.9 Hz, 1H), 2.56 (td, *J* = 12.4, 5.2 Hz, 1H), 2.15 (s, 3H), 2.11-2.03 (m, 2H), 1.96-1.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.4(C=O), 149.6, 141.1, 139.5, 133.9, 133.0, 130.2, 129.8, 128.5, 126.3, 126.2, 125.8, 124.6, 124.5, 123.9, 113.6, 111.7, 104.9, 79.6, 51.8, 47.0 (-CH_2-), 33.3 (-CH_2-), 20.9 (CH_3); IR (KBr, cm^{-1}): 2927, 1729, 1466, 1358, 1167; MS (ES mass): *m*/*z* 487.0 (M+1).

References:

1. B. Prasad; R. Adepu; S. Sandra; D. Rambabu; G. R. Krishna; C. M. Reddy; G. S. Deora; P. Misra; M. Pal, *Chem. Commun*. **2012**, *48*, 10434.
2. H. S. Kim; H. S. Lee; S. H. Kim; J. N. Kim, *Tetrahedron Lett.* **2009**, *50*, 3154.

Single crystal X-ray data for compound 4b.

Single crystals suitable for X-ray diffraction of **4b** were 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 **4b:** Molecular formula = $C_{21}H_{18}N_2O_2S_2$, formula weight = 394.10, crystal system = Triclinic, space group = *P*-1, *a* = 8.814 (5) Å, *b* = 10.987 (6) Å, *c* = 11.7256 (12) Å, *V* = 947.9 (9) $Å^3$, *T* = 298 K, *Z* = 2, D_c = 1.382 Mg m^{-3}, μ(Mo-Kα) = 0.30 mm^{-1}, 6911 reflections measured, 4456 independent reflections, 1925 observed reflections [I > 2.0 σ (I)], R_1_obs = 0.045, Goodness of fit = 1.11. Crystallographic data (excluding structure factors) for **4b** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC 918746.

Reference

1. Bruker SADABS V2008-1, Bruker AXS.: Madison, WI, USA, **2008**.
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Pharmacology

PDE4B protein production and purification

PDE4B1 cDNA was sub-cloned into pFAST Bac HTB vector (Invitrogen) and transformed into DH10Bac (Invitrogen) competent cells. Recombinant bacmids were tested for integration by PCR analysis. Sf9 cells were transfected with bacmid using Lipofectamine 2000 (Invitrogen) according to manufacturer's instructions. Subsequently, P3 viral titer was amplified, cells were infected and 48 h post infection cells were lysed in lysis buffer (50 mM Tris-HCl pH 8.5, 10 mM 2-mercaptoethanol, 1 % protease inhibitor cocktail (Roche), 1 % NP40). Recombinant His-tagged PDE4B protein was purified as previously described elsewhere.[19a] Briefly, lysate was centrifuged at 10,000 rpm for 10 min at 4 ºC and supernatant was collected. Supernatant was mixed with Ni-NTA resin (GE Life Sciences) in a ratio of 4:1 (v/v) and equilibrated with binding buffer (20 mM Tris-HCl pH 8.0, 500 mM-KCl, 5 mM imidazole, 10 mM 2-mercaptoethanol and 10 % glycerol) in a ratio of 2:1 (v/v) and mixed gently on rotary shaker for 1 hour at 4 ºC. After incubation, lysate-Ni-NTA mixture was centrifuged at 4,500 rpm for 5 min at 4 ºC and the supernatant was collected as the flow-through fraction. Resin was washed twice with wash buffer (20 mM Tris-HCl pH 8.5, 1 M KCl, 10 mM 2-mercaptoethanol and 10% glycerol). Protein was eluted sequentially twice using elution buffers (Buffer I: 20 mM Tris-HCl pH 8.5, 100 mM KCl, 250 mM

imidazole, 10 mM 2-mercaptoethanol, 10% glycerol, Buffer II: 20 mM Tris-HCl pH 8.5, 100 mM KCl, 500 mM imidazole, 10 mM 2-mercaptoethanol, 10% glycerol). Eluates were collected in four fractions and analyzed by SDS-PAGE. Eluates containing PDE4B protein were pooled and stored at -80 ºC in 50% glycerol until further use.

PDE4 enzymatic assay

The inhibition of PDE4 enzyme was measured using PDElight HTS cAMP phosphodiesterase assay kit (Lonza) according to manufacturer's recommendations. Briefly, 10 ng of in house purified PDE4B1 or 0.5 ng commercially procured PDE4D2 enzyme was pre-incubated either with DMSO (vehicle control) or compound for 15 min before incubation with the substrate cAMP (5 µM) for 1 hour. The reaction was halted with stop solution and reaction mix was incubated with detection reagent for 10 minutes in dark. Dose response studies were performed at 13 different concentrations ranging from 200 µM to 0.001 µM. Luminescence values (RLUs) were measured by a Multilabel Plate Reader (PerklinElmer 1420 Multilabel Counter). The percentage of inhibition was calculated using the following formula and the IC_{50} values were determined by a nonlinear regression analysis from dose response curve using Graphpad Prism software (San Diego, U.S.A). IC_{50} values are presented as mean ± SD.

$$\%\ inhibition = \frac{(RLU\ of\ vehicle\ control - RLU\ of\ inhibitior)}{RLU\ of\ vehicle\ control} X\ 100$$

Some of the synthesized compounds were tested for their PDE4B inhibitory potential *in vitro* at 30 μM using PDE4B enzyme[1] and rolipram as a reference compound.

Reference

1. P. Wang, J. G. Myers, P. Wu, B. Cheewatrakoolpong, R. W. Egan and M. M. Billah, *Biochem. Biophys. Res. Commun.* **1997**, *234*, 320

Molecular Modeling Studies

The molecular docking Simulation was performed using Chemical Computing Group's Molecular Operating Environment (MOE) software 2008.10 Version, "DOCK" application

Module. The molecule **E** was docked into the PDE4B protein and its docking score as well as interactions were observed.

The purpose of the Dock application was to search for favorable binding configurations in macromolecular target, which is usually a protein. For each ligand, a number of configurations called *poses* are generated and scored in an effort to determine favorable binding modes.

The Dock workflow involves Conformational Analysis, Placement, scoring, and Force field method of Refinement.

Procedure: The PDE4B protein in complex with Rolipram (PDB code-1XMY) was used for our docking studies. The original PDE Protein's PDB file containing crystallized Zn and Mn metal ions were retrieved from PDB Database and Protonated (Addition of Hydrogen atoms) with Protonation 3D application in MOE. Connolly Molecular surface was generated around the ligand site of the protein, Gasteiger Partial charges was added to the protein and finally energy was minimized to relieve bad crystallographic contacts. The "Active site finder" function of the MOE software was used to denote potential docking pockets within the Protein crystal structure. The test molecule was placed in the active site pocket of the protein by the "Triangle Matcher" Method, which generates poses by aligning the ligand triplet of atoms with the triplet of alpha spheres in cavities of tight atomic packing. The Dock scoring was carried out with London dG method after retaining and scoring the best 10 poses of the molecule. The Preparation of ligand for Docking Simulation involves the Energy minimization with Molecular Mechanics Force-field MMFF94x (Merck Molecular Force Field 94×) and then the molecule was subjected to conformational search in MOE using the Conformational Stochastic search module to find the lowest energy conformers.

The docking results appeared as docking score in which the docking poses are ranked by the Molecular Mechanics and Generalized Born solvation model (MM/GBVI) binding free energy.

For all scoring functions, lower scores indicate more favorable binding poses. The unit for all scoring functions is K.cal/mol. The final energy was calculated using the Generalized Born solvation model. Poses for each ligand were scored based on complementarity with binding pocket.

The London dG scoring function estimates the free energy of binding of the ligand from a given pose. The functional form is a sum of terms:

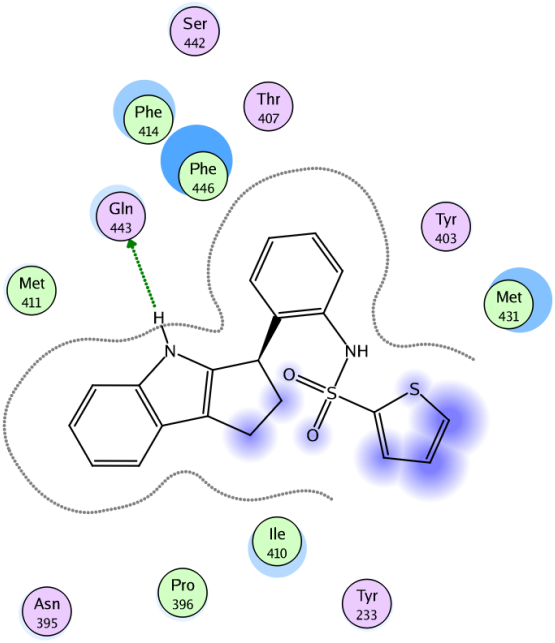
$$\Delta G = c + E_{flex} + \sum_{h-bonds} c_{HB} f_{HB} + \sum_{m-lig} c_M f_M + \sum_{atoms\ i} \Delta D_i$$

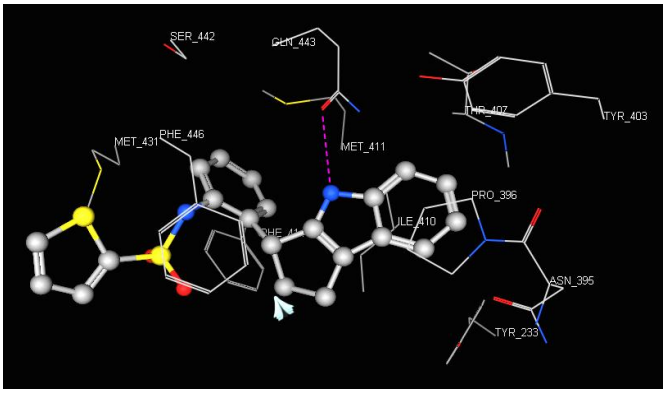
where *c* represents the average gain/loss of rotational and translational entropy; E_{flex} is the energy due to the loss of flexibility of the ligand (calculated from ligand topology only); f_{HB} measures geometric imperfections of hydrogen bonds and takes a value in [0,1]; c_{HB} is the energy of an ideal hydrogen bond; f_M measures geometric imperfections of metal ligations and takes a value in [0,1]; c_M is the energy of an ideal metal ligation; and D_i is the desolvation energy of atom *i*.

To validate the Docking accuracy of the program used, the native co-crystallized Rolipram ligand was docked back into its binding site of PDE4B protein.

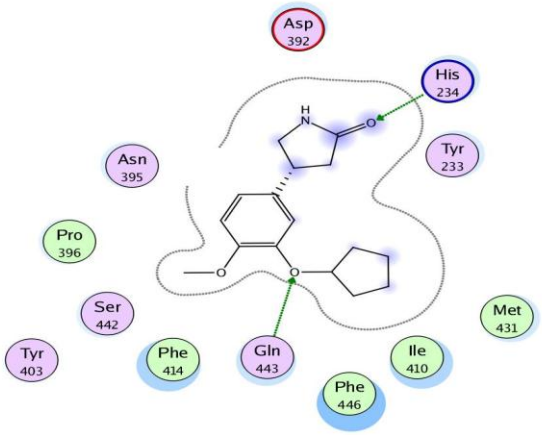
Protein-Molecular Interactions in Docking Pose:

Molecule **4b**_PDE4B:-





Rolipram_PDE4B protein:



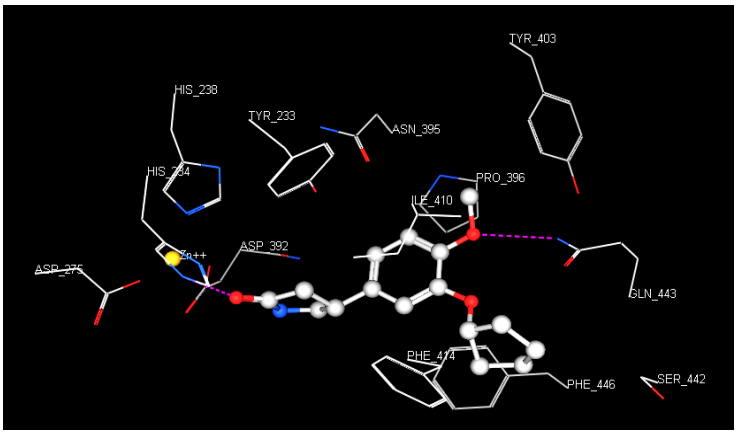


Table S-3: Molecular interactions Summary of top-ranked docking poses of Rolipram and the molecule **4b**.

	H-bond interactions
Compounds	**PDE4B**
Rolipram	His234, Gln443
Molecule **4b**	Gln443

	MOE Dockscore (K.cal/mol)
Compounds	PDE4B
Rolipram	-22.94
Molecule **4b**	-18.22

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3. Annalisa Tait, Amedeo Luppi, Armin Hatzelmann, Paola Fossa and Luisa Mosti, Synthesis, biological evaluation and molecular modelling studies on benzothiadiazine derivatives as PDE4 selective inhibitors, *Bioorg. Med. Chem.* **2004,** *68*, 2087-2094.
4. Chidochangu P. Mpamhanga, Beining Chen, Iain M. McLay, Daniel L. Ormsby, And Mika K. Lindvall, Retrospective Docking Study of PDE4B Ligands and an Analysis of the Behavior of Selected Scoring Functions, *J. Chem. Inf. Model*. **2005**, *45*, 1061-1074.