Electronic Supplementary Information

$AlCl_3$ mediated unexpected migration of sulfonyl group: regioselective synthesis of 7-sulfonyl indoles of potential pharmacological interest

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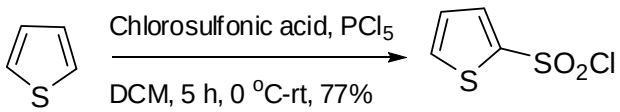
Experimental

Chemistry

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

Typical procedure for preparation of thiophene-2-sulfonyl chloride (11)

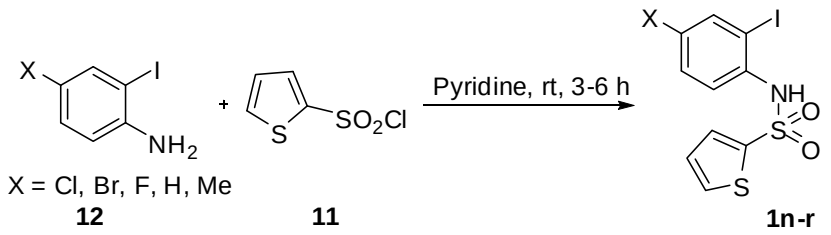


10 **11**

Chlorosulfonic acid (4.7 mL, 71.4 mmol) was slowly added to thiophene **10** (2.8 mL, 35.7 mmol) in dry DCM (25 mL) at 0 °C under nitrogen atmosphere. Then, phosphorus pentachloride (0.75 g, 3.57 mmol) was added slowly to the reaction mixture and stirred at room temperature for 5 h. After completion of reaction, saturated $NaHCO_3$ solution (100 mL) was slowly added to reaction mixture. Then, the residue was diluted with water (100 mL) and extracted with DCM (150 mL). The organic layers were collected, combined, washed with brine solution (100 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give the desired product **13** (5 mL, 77%) which was used further without any purification.

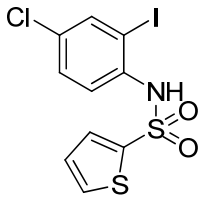
Preparation of 4-substituted *N*-(2-iodophenyl) methane/4-methylbenzene sulfonamide (1a-m): These compounds were prepared according to the procedure described in literature.[1]

General procedure for preparation of 4-substituted *N*-(2-iodophenyl)thiophene-2-sulfonamide (1n-r):



Thiophene-2-sulfonyl chloride **11** (1.2 mmol) was slowly added to compound **12** (1 mmol) in pyridine (5 mL) at 0 °C under nitrogen atmosphere. Then, the reaction mixture stirred at rt for 3-6 h. After completion of reaction monitored by TLC, the reaction mixture was diluted with ethyl acetate (30 mL), washed with 2N HCl solution (25 mL) followed by brine solution (25 mL) and dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography using ethyl acetate-hexane to give the desired product **1**.

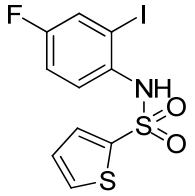
***N*-(4-chloro-2-iodophenyl)thiophene-2-sulfonamide (1n)**



White solid; yield: 85%; mp: 115-117 °C; R_f (10% EtOAc/*n*-Hexane) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, *J* = 2.0 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 3.4 Hz, 1H), 7.47 (d, *J* = 3.6 Hz, 1H), 7.34 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.03 (t, *J* = 4.2 Hz, 1H), 6.79 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.7, 138.2, 135.9, 133.2 (2C), 132.0, 129.6, 127.5, 124.0, 93.0; HPLC: 98.9%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate: 01.0

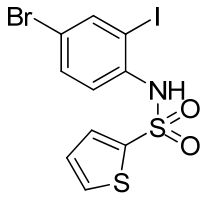
mL/min; UV 220 nm, retention time 6.91 min; IR (KBr, cm^{-1}): 3251, 3093, 1567, 1466; MS (ES mass): *m*/*z* 397.7 (M-1).

_N_-(4-fluoro-2-iodophenyl)thiophene-2-sulfonamide (1o)



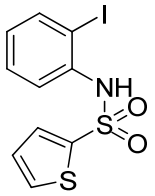
White floppy solid; yield: 87%; mp: 110-112 °C; R_f (10% EtOAc/*n*-Hexane) 0.72; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99-7.66 (m, 1H), 7.58 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.44-7.40 (m, 2H), 7.14-7.09 (m, 1H), 7.04-7.02 (m, 1H), 6.68 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.9 (C-F *J* = 250.3 Hz), 138.8, 133.6, 133.1 (C-F *J* = 4.7 Hz), 127.5 (2C), 125.7 (C-F *J* = 24.9 Hz), 125.4 (C-F *J* = 8.3 Hz), 116.6 (C-F *J* = 22.0 Hz), 93.4 (C-F *J* = 8.5 Hz); HPLC: 99.3%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/50, 2/50, 9/95, 14/95, 16/50, 18/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.09 min; IR (KBr, cm^{-1}): 3259, 3083, 1588, 1481; MS (ES mass): *m*/*z* 381.8 (M-1).

_N_-(4-bromo-2-iodophenyl)thiophene-2-sulfonamide (1p)



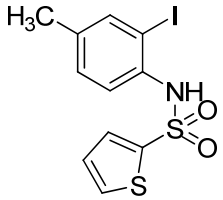
White solid; yield: 71%; mp: 125-127 °C; R_f (10% EtOAc/*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, *J* = 2.0 Hz, 1H), 7.59-7.56 (m, 2H), 7.49-7.46 (m, 2H), 7.05-7.02 (m, 1H), 6.80 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.9, 138.7, 136.4, 133.2 (2C), 132.6, 127.6, 124.3, 119.5, 93.4; HPLC: 97.3%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/40, 2/40, 9/95, 14/95, 16/40, 18/40; flow rate: 1.0 mL/min; UV 230 nm, retention time 7.01 min; IR (KBr, cm^{-1}): 3250, 3102, 1581, 1398; MS (ES mass): *m*/*z* 443.7 (M-1).

***N*-(2-iodophenyl)thiophene-2-sulfonamide (1q)**



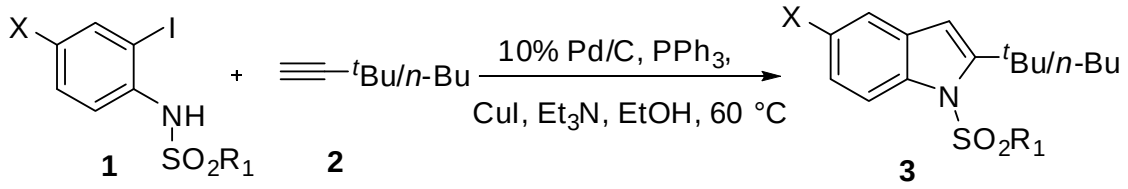
White solid; yield: 89%; mp: 88-90 °C; R_f (5% EtOAc/*n*-Hexane) 0.30; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.72-7.68 (m, 2H), 7.56 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.47 (dd, *J* = 4.5, 1.2 Hz, 1H), 7.37-7.33 (m, 1H), 7.02-7.00 (m, 1H), 6.90-6.88 (m, 1H), 6.86 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 139.1, 139.0, 137.1, 133.0, 132.9, 129.5, 127.4 (2C), 123.3, 92.9; HPLC: 96.6%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/40, 2/40, 9/95, 14/95, 16/40, 18/40; flow rate: 1.0 mL/min; UV 210 nm, retention time 6.99 min; IR (KBr, cm^{-1}): 3249, 3108, 1574, 1393; MS (ES mass): *m*/*z* 363.8 (M-1).

***N*-(2-iodo-4-methylphenyl)thiophene-2-sulfonamide (1r)**



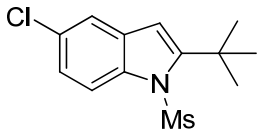
White floppy solid; yield:83%; mp: 72-74 °C; R_f (5% EtOAc/*n*-Hexane) 0.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57-7.54 (m, 2H), 7.51 (s, 1H), 7.43 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.02-6.99 (m, 1H), 6.73 (bs, 1H), 2.26 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 139.3, 139.0, 137.8, 134.5, 133.0, 132.8, 130.3, 127.4, 123.8, 93.4, 20.3; HPLC: 99.7%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/40, 2/40, 9/95, 14/95, 16/40, 18/40; flow rate: 1.0 mL/min; UV 230 nm, retention time 7.85 min; IR (KBr, cm^{-1}): 3249, 3079, 1589, 1486; MS (ES mass): *m*/*z* 377.8 (M-1).

General procedure for the synthesis of 2-alkyl-1-(alkyl/aryl/heteroaryl sulfonyl)-1*H*-indole (3):



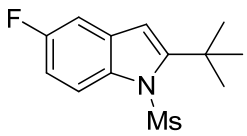
To a solution of 4-substituted ortho iodoanilides **1** (0.31 mmol) in ethanol (5.0 ml), 10% Pd/C (0.03 mmol), CuI (0.06 mmol), PPh_3 (0.12 mmol) and triethylamine (0.62 mmol) was added under nitrogen atmosphere. The reaction mixture was allowed to stir at room temperature for 15 min, and then added corresponding alkyne **2** (0.68 mmol). The mixture was stirred at 60 °C for 3-6 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was diluted with saturated NH_4Cl solution (15 mL) and the product was extracted with ethyl acetate (3 x 15 mL). The organic layers were collected, combined, dried over anhydrous Na_2SO_4, filtered and concentrated under a reduced pressure. The residue was purified by column chromatography over silica gel using ethyl acetate–hexane to give the desired product **3**.

2-*tert*-butyl-5-chloro-1-(methylsulfonyl)-1*H*-indole (3a)



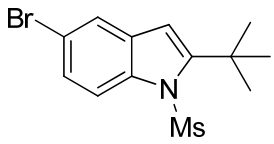
White solid; mp 105-107 °C; R_f (10% EtOAc/*n*-Hexane) 0.78; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, *J* = 9.2 Hz, 1H), 7.45 (s, 1H), 7.23 (d, *J* = 9.2 Hz, 1H), 6.55 (s, 1H), 2.94 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.4, 136.8, 130.7, 129.6, 124.5, 120.0, 116.5, 109.3, 39.7, 34.8, 30.7 (3C); HPLC: 99.6%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/70, 2/70, 8/98, 13/98, 15/70, 18/70; flow rate: 1.0 mL/min; UV 260 nm, retention time 6.12 min; IR (KBr, cm^{-1}): 3022, 2953, 1598, 1452, 1361, 1328; MS (ES mass): *m*/*z* 286.5 (M+1).

2-*tert*-butyl-5-fluoro-1-(methylsulfonyl)-1*H*-indole (3b)



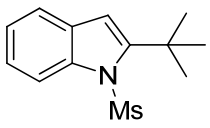
White solid; mp: 50-52 °C; R_f (10% EtOAc/*n*-hexane) 0.82; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (dd, *J* = 9.2, 3.6 Hz, 1H), 7.13 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.00 (td, *J* = 9.2, 2.4 Hz, 1H), 6.58 (s, 1H), 2.92 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.5 (C-F *J* = 239 Hz), 153.6, 134.7, 130.6, 116.6 (C-F *J* = 8.5 Hz), 112.1 (C-F *J* = 24.8 Hz), 110.0 (C-F *J* = 3.7 Hz), 106.0 (C-F *J* = 24.0 Hz), 39.5, 34.8, 30.8 (3C); HPLC: 96.2%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/60, 2/60, 9/98, 13/98, 15/60, 18/60; flow rate: 0.8 mL/min; UV 220 nm, retention time 8.02 min; IR (KBr, cm^{-1}): 3024, 2962, 1609, 1480, 1460, 1361; MS (ES mass): *m*/*z* 270.1 (M+1).

5-Bromo-2-*tert*-butyl-1-(methylsulfonyl)-1*H*-indole (3c)



Brown solid; mp: 110-112 °C; R_f (5% EtOAc/*n*-Hexane) 0.80; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 2.0 Hz, 1H), 7.55 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.54 (s, 1H), 2.94 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.3, 137.3, 131.2, 127.2, 123.1, 117.3, 116.8, 109.2, 39.8, 34.8, 30.8 (3C); HPLC: 98.7%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/75, 2/75, 10/98, 14/98, 17/75, 20/75; flow rate: 1.0 mL/min; UV 260 nm, retention time 5.48 min; IR (KBr, cm^{-1}): 3019, 2949, 1591, 1453, 1361, 1186; MS (ES mass): *m*/*z* 251.0 (M-SO_2Me+1).

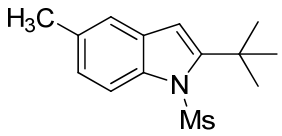
2-*tert*-butyl-1-(methylsulfonyl)-1*H*-indole (3d)



Semi solid; R_f (10% EtOAc/*n*-Hexane) 0.90; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.32-7.25 (m, 2H), 6.63 (s, 1H), 2.94 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 151.8, 138.5, 129.4, 124.4, 123.8, 120.5, 115.3, 110.1, 39.4, 34.6, 30.8 (3C); HPLC: 99.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 13/98, 15/50,

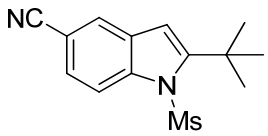
18/50; flow rate: 1.0 mL/min; UV 255 nm, retention time 8.38 min; IR (KBr, cm^{-1}): 3030, 2987, 1521, 1355, 1186; MS (ES mass): *m*/*z* 251.9 (M+1).

2-*tert*-butyl-5-methyl-1-(methylsulfonyl)-1*H*-indole (3e)



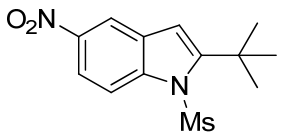
Semi solid; R_f (10% EtOAc/*n*-Hexane) 0.85; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 8.8 Hz, 1H), 7.27 (s, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 6.55 (s, 1H), 2.90 (s, 3H), 2.42 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 151.9, 136.8, 133.5, 129.7, 125.8, 120.4, 115.1, 110.1, 39.4, 34.6, 30.8 (3C), 21.0; HPLC: 98.7, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/70, 2/70, 9/98, 13/98, 15/70, 18/70; flow rate: 1.0 mL/min; UV 260 nm, retention time 5.82 min; IR (KBr, cm^{-1}): 3024, 2962, 1609, 1480, 1460, 1361; MS (ES mass): *m*/*z* 266.1 (M+1).

2-*tert*-butyl-5-cyano-1-(methylsulfonyl)-1*H*-indole (3f)



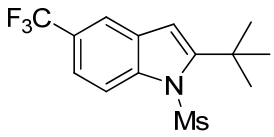
White solid; mp: 193-195 °C; R_f (10% EtOAc/*n*-Hexane) 0.82; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.19 (d, *J* = 8.8 Hz, 1H), 7.82 (s, 1H), 7.54 (d, *J* = 8.8 Hz, 1H), 6.65 (s, 1H), 3.05 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.4, 140.2, 129.4, 127.4, 125.1, 123.7, 115.9, 108.9, 107.3, 40.7, 34.9, 30.7 (3C); HPLC: 98.7%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 13/98, 15/50, 18/50; flow rate: 1.0 mL/min; UV 235 nm, retention time 7.56 min; IR (KBr, cm^{-1}): 3011, 2957, 2258, 1582, 1455, 1333; MS (ES mass): *m*/*z* 277.1 (M+1).

2-*tert*-butyl-5-nitro-1-(methylsulfonyl) -1*H*-indole (3g)



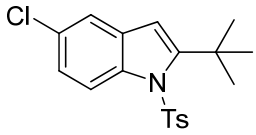
White solid; mp: 165-167 °C; R_f (10% EtOAc/*n*-Hexane) 0.85; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 1.6 Hz, 1H), 8.28-8.10 (m, 2H), 6.73 (s, 1H), 3.08 (s, 3H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.2, 144.4, 141.4, 129.2, 119.5, 116.5, 115.4, 109.5, 40.9, 35.0, 30.7 (3C); HPLC: 99.8%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/60, 2/60, 9/98, 13/98, 15/60, 18/60; flow rate: 0.8 mL/min; UV 255 nm, retention time 7.59 min; IR (KBr, cm^{-1}): 3027, 2955, 1598, 1517, 1174; MS (ES mass): *m*/*z* 251.8 (M-NO_2).

2-*tert*-butyl-1-(methylsulfonyl)-5-(trifluoromethyl)-1*H*-indole (3h)



Brown solid; mp: 60-62 °C; R_f (10% EtOAc/*n*-Hexane) 0.75; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.20 (d, *J* = 9.2 Hz, 1H), 7.77 (s, 1H), 7.52 (d, *J* = 9.2 Hz, 1H), 6.68 (s, 1H), 3.01 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.8, 140.0, 129.1, 121.2, 117.9 (2C), 117.8, 115.5, 109.5, 40.3, 34.9, 30.7 (3C); HPLC: 92.2%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/60, 2/60, 9/98, 13/98, 15/60, 18/60; flow rate: 0.8 mL/min; UV 220 nm, retention time 9.4 min; IR (KBr, cm^{-1}): 3023, 2965, 1555, 1455, 1369, 1339; MS (ES mass): *m*/*z* 320.1 (M+1).

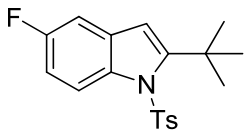
2-*tert*-butyl-5-chloro-1-tosyl-1*H*-indole (3i)



Semi solid; R_f (30% EtOAc/*n*-Hexane) 0.80; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94 (d, *J* = 9.2 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.36-7.35 (m, 1H), 7.13-7.10 (m, 3H), 6.54 (s, 1H), 2.31 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.3, 144.3, 137.2, 136.6, 130.5, 129.6 (2C), 129.3, 125.9 (2C), 124.2, 119.8, 117.1, 109.8, 35.1, 31.2 (3C), 21.5; HPLC: 98.9%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.05 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/90, 2/90, 9/95, 12/95, 15/90, 18/90; flow rate: 0.8 mL/min; UV 222

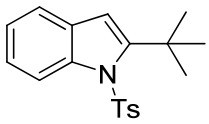
nm, retention time 5.18 min; IR (KBr, cm^{-1}): 3032, 2963, 1455, 1363, 1184; MS (ES mass): *m*/*z* 362.1 (M+1).

2-*tert*-butyl-5-fluoro-1-tosyl-1*H*-indole (3j)



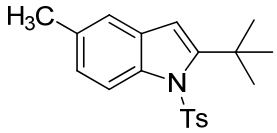
Semi solid; R_f (10% EtOAc/*n*-Hexane) 0.87; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (dd, *J* = 9.1, 4.4 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.03 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.91-6.86 (m, 1H), 6.56 (s, 1H), 2.30 (s, 3H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.9 (C-F *J* = 239.2 Hz), 154.5, 144.2, 136.5, 135.2, 130.4 (C-F *J* = 10.0 Hz), 129.5 (2C), 125.9 (2C), 117.3 (C-F *J* = 9.0 Hz), 111.9, 110.6 (C-F *J* = 3.7 Hz), 105.6 (C-F *J* = 23.4 Hz), 35.1, 31.3 (3C), 21.5; HPLC: 97.0%, column: Zorbax XDB C-18 150*4.6 mm 5µ, mobile phase A: 0.05 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/80, 2/80, 9/98, 12/98, 15/80, 18/80; flow rate: 1.0 mL/min; UV 222 nm, retention time 6.74 min; IR (KBr, cm^{-1}): 2932, 2868, 1462, 1365, 1303; MS (ES mass): *m*/*z* 346.1 (M+1).

2-*tert*-butyl-1-tosyl-1*H*-indole (3k)



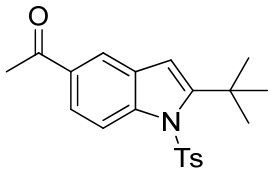
Semi solid; R_f (30% EtOAc/*n*-Hexane) 0.80; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02-8.00 (m, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.40-7.38 (m, 1H), 7.17-7.15 (m, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.60 (s, 1H), 2.28 (s, 3H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.7, 143.9, 138.9, 136.8, 129.4 (2C), 129.2, 125.9 (2C), 124.1, 123.6, 120.3, 116.1, 110.7, 34.9, 31.3 (3C), 21.5; HPLC: 96.4%, column: Zorbax XDB C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/90, 2/90, 9/98, 12/98, 15/90, 18/90; flow rate: 0.8 mL/min; UV 222 nm, retention time 4.75 min; IR (KBr, cm^{-1}): 3019, 2956, 1465, 1363, 1184; MS (ES mass): *m*/*z* 327.5 (M+1).

2-*tert*-butyl-5-methyl-1-tosyl-1*H*-indole (3l)



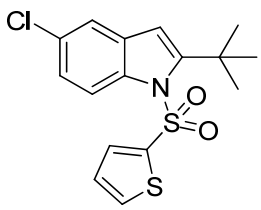
Yellow solid; mp: 88-90 °C; R_f (10% EtOAc/*n*-Hexane) 0.82; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (d, *J* = 8.8 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.17 (s, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 1H), 6.53 (s, 1H), 2.31 (s, 3H), 2.29 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.7, 143.9, 137.2, 136.9, 133.1, 129.4 (3C), 125.9 (2C), 125.5, 120.2, 115.8, 110.6, 34.9, 31.1 (3C), 21.4, 21.1; HPLC: 96.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/80, 2/80, 9/98, 13/98, 15/80, 18/80; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.31 min; IR (KBr, cm^{-1}): 2956, 2911, 1601, 1465, 1363; MS (ES mass): *m*/*z* 342.1 (M+1).

1-(2-*tert*-butyl-1-tosyl-1*H*-indol-5-yl)ethanone (3m)



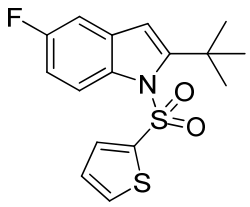
Semi solid; R_f (10% EtOAc/*n*-Hexane) 0.86; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (dd, *J* = 9.1, 1.8 Hz, 2H) 7.79 (dd, *J* = 8.8, 1.5 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 6.68 (s, 1H), 2.59 (s, 3H), 2.29 (s, 3H), 1.60 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.8, 154.5, 144.5, 141.5, 136.6, 132.9, 129.7 (2C), 128.9, 125.9 (2C), 124.2, 121.3, 115.8, 110.5, 35.1, 31.2 (3C), 26.6, 21.5; HPLC: 94.5%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 13/98, 15/50, 18/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 7.82 min; IR (KBr, cm^{-1}): 3014, 2943, 1656, 1454, 1342; MS (ES mass): *m*/*z* 370.0 (M+1).

2-*tert*-butyl-5-chloro-1-(thiophen-2-ylsulfonyl)-1*H*-indole (3n)



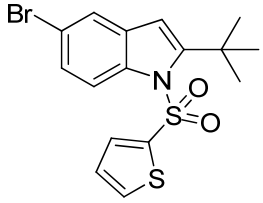
Light brown solid; mp: 105-107 °C; R_f (5% EtOAc/*n*-Hexane) 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, *J* = 8.6 Hz, 1H), 7.47-7.43 (m, 2H), 7.36 (d, *J* = 1.1 Hz, 1H), 7.21 (dd, *J* = 8.6, 1.2 Hz, 1H), 6.92-6.90 (m, 1H), 6.54 (s, 1H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.7, 138.3, 137.0, 132.7, 132.6, 131.1, 129.8, 126.6, 124.4, 119.9, 117.5, 111.2, 35.1, 31.1 (3C); HPLC: 97.8%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/50, 2/50, 9/95, 16/95, 18/50, 20/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 11.52 min; IR (KBr, cm^{-1}): 3110, 2965, 1596, 1451; MS (ES mass): *m*/*z* 353.8 (M+1).

2-*tert*-butyl-5-fluoro-1-(thiophen-2-ylsulfonyl)-1*H*-indole (3o)



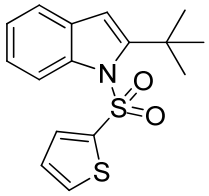
White solid; mp: 105-107 °C; R_f (10% EtOAc/*n*-Hexane) 0.85; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12-8.08 (m, 1H), 7.45-7.41 (m, 2H), 7.04 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.97-6.94 (m, 1H), 6.89 (t, *J* = 4.8 Hz, 1H), 6.56 (s, 1H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.1 (C-F *J* = 240.0 Hz), 154.1, 134.9, 132.6 (C-F *J* = 15.1 Hz), 131.0, 126.6 (2C), 117.7 (C-F *J* = 9.1 Hz), 111.9, 111.8 (C-F *J* = 24.8 Hz), 109.9, 106.0 (C-F *J* = 23.5 Hz), 35.1, 31.2 (3C); HPLC: 98.5%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/50, 2/50, 9/95, 16/95, 18/50, 20/50; flow rate: 1.0 mL/min; UV 254 nm, retention time 10.52 min; IR (KBr, cm^{-1}): 3099, 2957, 1605, 1458; MS (ES mass): *m*/*z* 337.8 (M+1).

5-Bromo-2-*tert*-butyl-1-(thiophen-2-ylsulfonyl)-1*H*-indole (3p)



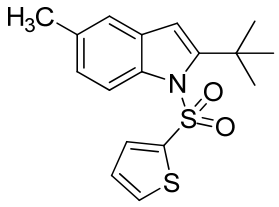
Light brown solid; mp: 125-127 °C; R_f (8% EtOAc/*n*-Hexane) 0.60; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (d, *J* = 8.8 Hz, 1H), 7.51 (d, *J* = 1.6 Hz, 1H), 7.46-7.43 (m, 2H), 7.35 (dd, *J* = 8.8, 1.8 Hz, 1H), 6.92-6.90 (m, 1H), 6.53 (s, 1H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.6, 138.2, 137.3, 132.8, 132.7, 131.6, 127.1, 126.7, 123.0, 117.9, 117.6, 111.0, 35.0, 31.1 (3C); HPLC: 98.5%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/50, 2/50, 9/95, 16/95, 18/50, 20/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 11.78 min; IR (KBr, cm^{-1}): 3100, 2965, 1592, 1450; MS (ES mass): *m*/*z* 399.7 (M+1).

2-*tert*-butyl-1-(thiophen-2-ylsulfonyl)-1*H*-indole (3q)



Brown color solid; mp: 78-80 °C; R_f (3% EtOAc/*n*-Hexane) 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.15 (d, *J* = 8.2 Hz, 1H), 7.45-7.44 (m, 1H), 7.40-7.38 (m, 2H), 7.28-7.26 (m, 1H), 7.22-7.20 (m, 1H), 6.88-6.86 (m, 1H), 6.60 (s, 1H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.2, 138.7, 132.5, 132.3, 129.9, 126.5, 124.3, 124.1, 120.4, 116.5, 112.1, 112.0, 34.9, 31.3 (3C); HPLC: 95.6%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/60, 2/60, 9/95, 14/95, 16/60, 18/60; flow rate: 1.0 mL/min; UV 220 nm, retention time 8.57 min; IR (KBr, cm^{-1}): 3101, 2922, 1455, 1371; MS (ES mass): *m*/*z* 319.8 (M+1).

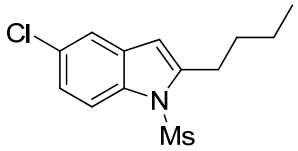
2-*tert*-butyl-5-methyl-1-(thiophen-2-ylsulfonyl)-1*H*-indole (3r)



Light yellow solid; mp: 102-104 °C; R_f (4% EtOAc/*n*-Hexane) 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (d, *J* = 8.6 Hz, 1H), 7.43 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.37 (d, *J* = 8.6, 1.2 Hz, 1H),

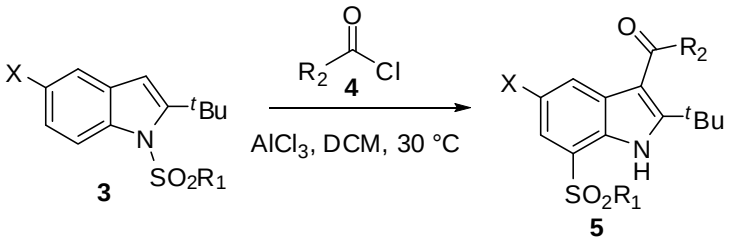
7.17 (s, 1H), 7.07 (dd, *J* = 8.6, 1.2 Hz, 1H), 6.88-6.86 (m, 1H), 6.53 (s, 1H), 2.38 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.2, 138.5, 136.8, 133.8, 132.4, 132.2, 130.1, 126.4, 125.6, 120.3, 116.2, 112.0, 34.9, 31.2 (3C), 21.1; HPLC: 98.8%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAc in water mobile phase B: CH_3CN (gradient) T/B%: 0/40, 2/40, 9/95, 18/95, 22/40, 25/40; flow rate: 1.0 mL/min; UV 255 nm, retention time 11.52 min; IR (KBr, cm^{-1}): 3097, 2963, 1465, 1364; MS (ES mass): *m*/*z* 333.9 (M+1).

2-*n*-Butyl-5-chloro-1-(methylsulfonyl)-1*H*-indole (3s)



Semi solid; R_f (10% EtOAc/*n*-Hexane) 0.85; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (d, *J* = 9.2 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 7.18 (dd, *J* = 9.2, 2.0 Hz, 1H), 6.36 (s, 1H), 2.96 (s, 3H), 2.90 (t, *J* = 7.6 Hz, 2H), 1.74-1.66 (m, 2H), 1.46-1.37 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.9, 135.1, 131.0, 129.4, 124.0, 119.8, 115.2, 107.7, 40.6, 30.8, 28.5, 22.4, 13.9; HPLC : 99.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/70, 2/70, 9/98, 14/98, 16/70, 18/70; flow rate: 1.0 mL/min; UV 225 nm, retention time 6.59 min; IR (KBr, cm^{-1}): 3026, 2948, 2932, 1448, 1354; MS (ES mass): *m*/*z* 285.9 (M+1).

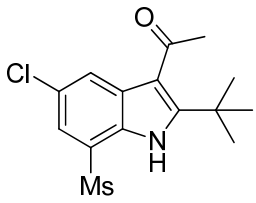
General procedure for preparation of 1-(2-*tert*-butyl-5-substituted-7-(alkyl/aryl/heteroaryl sulfonyl)-1*H*-indol-3-yl)alkanone (5):



A mixture of $AlCl_3$ (3.50 mmol) and acid chloride (5.25 mmol) was stirred at 0 ºC in dry DCM (5 mL) for 10 min. To this indole **3** (1.75 mmol) in DCM (3 mL) was added and the reaction mixture was stirred at 30 °C for 6-8 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was diluted with DCM (20 mL), washed with water (10 mL) and brine solution (10 mL). The organic layer was collected, dried over

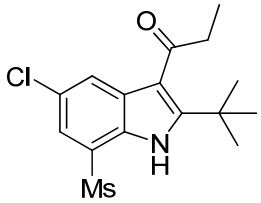
anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using ethyl acetate-hexane to give the desired product **5**.

1-(2-*tert*-butyl-5-chloro-7-(methylsulfonyl)-1*H*-indol-3-yl)ethanone (5a)



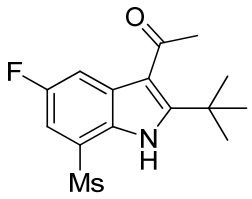
White solid; mp: 168-170 ^{o} C; R_f (10% EtOAc/*n*-Hexane) 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.10 (bs, 1H), 8.05 (d, *J* = 1.6 Hz, 1H), 7.65 (d, *J* = 2.0 Hz, 1H), 3.18 (s, 3H), 2.70 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.5, 156.2, 131.2, 128.1, 127.3, 125.8, 123.1, 121.7, 114.2, 45.3, 34.3, 32.6, 28.4 (3C); HPLC: 99.7%, column: X Bridge C-18 150*4.6 mm 5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/95, 12/95, 15/15, 18/50; flow rate: 1.0 mL/min; UV 229 nm, retention time 7.28 min; IR (KBr, cm^{-1}): 3441, 3001, 2958, 1599, 1452, 1358, 1176; MS (ES mass): *m*/*z* 327.4 (M+1).

1-(2-*tert*-butyl-5-chloro-7-(methylsulfonyl)-1*H*-indol-3-yl)propan-1-one (5b)



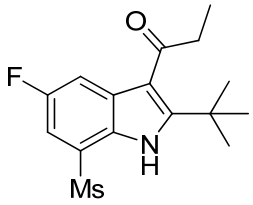
White solid; mp: 150-152 ºC; R_f (20% EtOAc/*n*-Hexane) 0.42; ^{1}H-NMR (400 MHz, $CDCl_3$): 10.06 (s, 1H), 8.02 (d, *J* = 1.4 Hz, 1H), 7.65 (d, *J* = 1.5 Hz, 1H), 3.19 (s, 3H), 3.01 (q, *J* = 7.2 Hz, 2H), 1.54 (s, 9H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.7, 155.5, 130.8, 128.1, 127.1, 125.8, 123.0, 121.6, 114.1, 45.3, 37.6, 34.2, 28.6 (3C), 8.5; HPLC: 94.5%, column: X Bridge C-18 150*4.6 mm 5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/95, 12/95, 15/15, 18/50; flow rate: 1.0 mL/min; UV 229 nm, retention time 8.95 min; IR (KBr, cm^{-1}): 3451, 3004, 2950, 1588, 1435, 1358, 1166; MS (ES mass): *m*/*z* 340.0 (M-1).

1-(2-*tert*-butyl-5-fluoro-7-(methylsulfonyl)-1*H*-indol-3-yl)ethanone (5c)



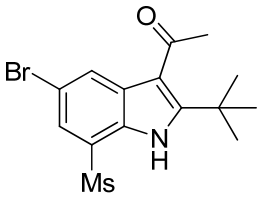
White solid; mp: 143-145 ^{o}C; R_f (10% EtOAc/*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.10 (s, 1H), 7.79 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.43 (dd, *J* = 8.0, 2.2 Hz, 1H), 3.18 (s, 3H), 2.69 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.4, 157.5 (C-F *J* = 240.1 Hz), 156.8, 131.0, 130.9 (C-F *J* = 25.1 Hz), 126.4, 122.6, 112.5 (C-F *J* = 25.1 Hz), 109.6 (C-F *J* = 27.9 Hz), 45.2, 34.3, 32.4, 28.3 (3C); HPLC: 98.5%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 10/95, 15/95, 18/50, 20/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.41 min; IR (KBr, cm^{-1}): 3446, 3069, 2965, 1652, 1429, 1317; MS (ES mass): *m*/*z* 311.9 (M+1).

1-(2-*tert*-butyl-5-fluoro-7-(methylsulfonyl)-1*H*-indol-3-yl)propan-1-one (5d)



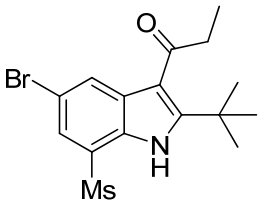
White solid; mp: 115-117 ^{o}C; R_f (15% EtOAc/*n*-Hexane) 0.60; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.06 (bs, 1H), 7.76 (dd, *J* = 9.7, 1.5 Hz, 1H), 7.43 (dd, *J* = 7.6, 1.6 Hz, 1H), 3.18 (s, 3H), 2.99 (q, *J* = 7.2 Hz, 2H), 1.54 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.4, 157.4 (C-F *J* = 240.0 Hz), 156.2, 130.5 (C-F *J* = 9.0 Hz), 126.4, 122.4 (C-F *J* = 8.1 Hz), 114.5 (C-F *J* = 27.9 Hz),112.5 (C-F *J* = 25.3 Hz), 109.6 (C-F *J* = 25.3 Hz), 45.2, 37.4, 34.3, 28.5 (3C), 8.6; HPLC: 99.6%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 5mM NH_4OAC in water B: CH_3CN (gradient) T/B% : 0/50,3/50, 12/95, 16/95, 18/50, 20/50; flow rate: 1.0 mL/min; UV 225 nm, retention time 8.72 min; IR (KBr, cm^{-1}): 3425, 3012, 2966, 1659, 1477, 1305; MS (ES mass): *m*/*z* 324.7 (M-1).

1-(5-Bromo-2-*tert*-butyl-7-(methylsulfonyl)-1*H*-indol-3-yl)ethanone (5e)



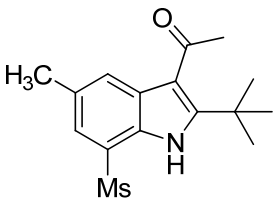
White solid; mp: 148-150 °C; R_f (15% EtOAc/*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.11 (bs, 1H), 8.20 (d, *J* = 1.4 Hz, 1H), 7.78 (d, *J* = 1.4 Hz, 1H), 3.19 (s, 3H), 2.70 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.6, 156.0, 131.7, 128.8, 128.4, 124.3, 123.5, 114.4, 114.1, 45.3, 34.3, 32.6, 28.4 (3C); HPLC: 99.4%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 10/95, 15/95, 18/50, 20/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 7.60 min; IR (KBr, cm^{-1}): 3423, 3079, 2915, 1644, 1423, 1308; MS (ES mass): *m*/*z* 372.8 (M+1).

1-(5-Bromo-2-*tert*-butyl-7-(methylsulfonyl)-1*H*-indol-3-yl)propan-1-one (5f)



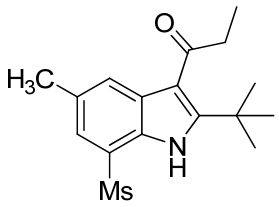
White solid; mp: 145-147 ºC; R_f (10% EtOAc/*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.05 (s, 1H), 8.16 (d, *J* = 1.2 Hz, 1H), 7.76 (d, *J* = 1.5 Hz, 1H), 3.18 (s, 3H), 3.00 (q, *J* = 7.2 Hz, 2H), 1.53 (s, 9H), 1.27 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.7, 155.2, 131.3, 128.7, 128.4, 124.2, 123.4, 114.0, 109.9, 45.3, 37.7, 34.2, 28.6 (3C), 8.5; HPLC: 99.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 10/95, 15/95, 18/50, 20/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 8.92 min; IR (KBr, cm^{-1}): 3424, 3074, 2918, 1654, 1412, 1312; MS (ES mass): *m*/*z* 385.8 (M-1).

1-(2-*tert*-butyl-5-methyl-7-(methylsulfonyl)-1*H*-indol-3-yl)ethanone (5g)



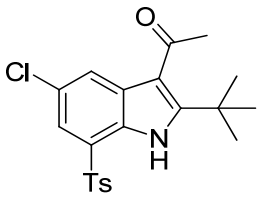
White solid; mp: 115-117 ºC; R_f (10% EtOAc/*n*-Hexane) 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.02 (s, 1H), 7.88 (s, 1H), 7.49 (s, 1H), 3.15 (s, 3H), 2.72 (s, 3H), 2.55 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.2, 155.0, 131.4, 130.4, 127.9, 126.5, 122.8, 121.8, 114.0, 45.3, 32.6, 29.8, 28.4 (3C), 21.6; HPLC: 95.6%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/10, 2/10, 9/95, 16/95, 17/10, 20/10; flow rate: 1.0 mL/min; UV 210 nm, retention time 9.77 min; IR (KBr, cm^{-1}): 3442, 2967, 2932, 1652, 1479; MS (ES mass): *m*/*z* 307.9 (M+1).

1-(2-*tert*-butyl-5-methyl-7-(methylsulfonyl)-1*H*-indol-3-yl)propan-1-one (5h)



White solid; mp: 110-112 ºC; R_f (10% EtOAc/*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.96 (s, 1H), 7.84 (s, 1H), 7.48 (s, 1H), 3.15 (s, 3H), 3.03 (q, *J* = 7.2 Hz, 2H), 2.54 (s, 3H), 1.53 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 199.3, 154.2, 131.1, 130.0, 128.1, 126.5, 122.7, 121.7, 113.9, 45.2, 37.6, 34.1, 28.6 (3C), 21.6, 8.6; HPLC: 97.6%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/10, 2/10, 9/95, 16/95, 17/10, 20/10; flow rate: 1.0 mL/min; UV 210 nm, retention time 10.38 min; IR (KBr, cm^{-1}): 3423, 2955, 2924, 1665, 1458; MS (ES mass): *m*/*z* 322.3 (M+1).

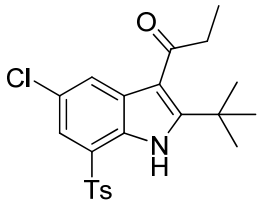
1-(2-*tert*-butyl-5-chloro-7-tosyl-1*H*-indol-3-yl)ethanone (5i)



White solid; mp: 120-122 ºC; R_f (10% EtOAc/*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.22 (s, 1H), 7.94 (d, *J* = 1.4 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 1.6 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 2.66 (s, 3H), 2.41 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.5, 156.1, 145.2, 138.2, 131.2, 130.2 (2C), 127.9, 127.3, 127.1 (2C), 125.3, 124.7, 121.9,

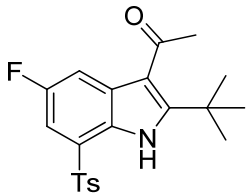
114.1, 34.3, 32.5, 28.4 (3C), 21.6; HPLC: 99.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 10/98, 15/98, 18/50, 20/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 10.59 min; IR (KBr, cm^{-1}): 3430, 2925, 1665, 1458, 1309; MS (ES mass): *m*/*z* 404.8 (M+1).

1-(2-*tert*-butyl-5-chloro-7-tosyl-1*H*-indol-3-yl)propan-1-one (5j)



White solid; mp: 110-112 ºC; R_f (10% EtOAc/*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.17 (s, 1H), 7.91 (d, *J* = 1.4 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 1.7 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 2.96 (q, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 1.56 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.6, 155.3, 145.2, 138.1, 130.7, 130.2 (2C), 128.0, 127.2, 127.1, 127.0, 125.3, 124.6, 121.9, 113.9, 37.5, 34.2, 28.6 (3C), 21.6, 8.5; HPLC: 98.6%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/70, 2/70, 9/95, 15/95, 18/70, 20/70; flow rate: 1.0 mL/min; UV 210 nm, retention time 9.73 min; IR (KBr, cm^{-1}): 3430, 2956, 2925, 1669, 1457; MS (ES mass): *m*/*z* 418.4 (M+1).

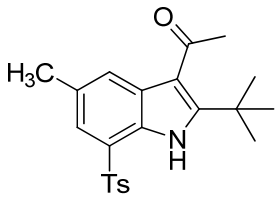
1-(2-*tert*-butyl-5-fluoro-7-tosyl-1*H*-indol-3-yl)ethanone (5k)



White solid; mp: 128-130 ºC; R_f (10% EtOAc/*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.21 (s, 1H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.68 (dd, *J* = 9.9, 2.1 Hz, 1H), 7.35 (d, *J* = 2.4 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 2.65 (s, 3H), 2.41 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.3, 157.6 (C-F *J* = 240.0 Hz), 156.6, 145.1, 138.1, 130.8 (C-F *J* = 9.1 Hz), 130.2 (2C), 127.1 (2C), 126.2, 124.2 (C-F *J* = 8.2 Hz), 114.5, 111.9 (C-F *J* = 25.2 Hz), 110.0 (C-F *J* = 28.1 Hz), 34.3, 32.4, 28.3 (3C), 21.6; HPLC: 96.3%, column: X Bridge C-18 150*4.6 mm 5µ, mobile

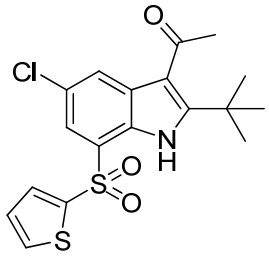
phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/70, 2/70, 9/98, 14/98, 15/70, 18/70; flow rate: 1.0 mL/min; UV 215 nm, retention time 5.91 min; IR (KBr, cm^{-1}): 3430, 2925, 1665, 1458, 1309; MS (ES mass): *m*/*z* 387.8 (M+1).

1-(2-*tert*-butyl-5-methyl-7-tosyl-1*H*-indol-3-yl)ethanone (5l)



White solid; HPLC mp: 140-142 ºC; R_f (10% EtOAc/*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.13 (s, 1H), 7.83 (d, *J* = 8.2 Hz, 2H), 7.78 (s, 1H), 7.43 (s, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 2.68 (s, 3H), 2.48 (s, 3H), 2.39 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.1, 154.8, 144.5, 138.9, 131.3, 130.3, 129.9 (2C), 129.3, 127.9, 126.9 (2C), 126.1, 123.2, 113.9, 34.2, 32.6, 29.9, 28.4 (3C), 21.7; HPLC : 98.6%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/70, 2/70, 9/98, 14/98, 15/70, 18/70; flow rate: 1.0 mL/min; UV 215 nm, retention time 5.99 min; IR (KBr, cm^{-1}): 3430, 2925, 1665, 1458, 1309; MS (ES mass): *m*/*z* 383.9 (M+1).

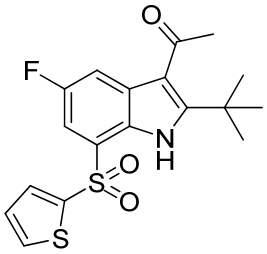
1-(2-*tert*-butyl-5-chloro-7-(thiophen-2-ylsulfonyl)-1*H*-indol-3-yl)ethanone (5m)



White solid; mp: 112-115 °C; R_f (20% EtOAc/*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.01 (bs, 1H), 7.80 (d, *J* = 2.2 Hz, 1H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.70-7.64 (m, 2H), 7.12 (t, *J* = 4.4 Hz, 1H), 2.67 (s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.8, 153.1, 131.6, 131.2, 131.0 (2C), 128.3, 126.9, 123.8, 122.9, 119.9, 112.2, 111.3, 34.0, 32.2, 30.0 (3C); HPLC: 97.2%; column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate: 01.0

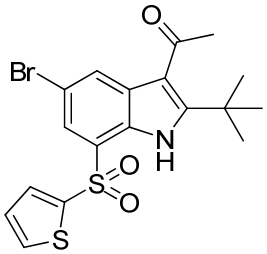
mL/min; UV 230 nm, retention time 5.85 min; IR (KBr, cm^{-1}) 3228, 2957, 1673, 1427; MS (ES mass): *m*/*z* 394.8 (M-1).

1-(2-*tert*-butyl-5-fluoro-7-(thiophen-2-ylsulfonyl)-1*H*-indol-3-yl)ethanone (5n)



White solid; mp: 138-140 ºC; R_f (25% EtOAc/*n*-Hexane) 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.09 (s, 1H), 7.75-7.67 (m, 3H), 7.48 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.13-7.10 (m, 1H), 2.67 (s, 3H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.3, 158.8, 156.6, 142.2, 134.3, 133.4, 130.9, 128.2, 125.8, 112.4, 112.2, 109.9, 109.6, 34.3, 32.4, 28.3 (3C); HPLC : 95.8%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 16/98, 18/50, 18/50, 20/50; flow rate: 1.0 mL/min; UV 270 nm, retention time 8.53 min; IR (KBr, cm^{-1}): 3425, 3091, 2950, 1659, 1426; MS (ES mass): *m*/*z* 379.8 (M+1).

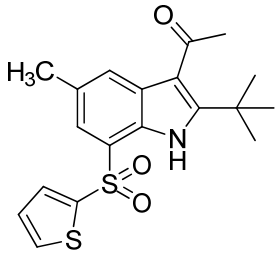
1-(5-Bromo-2-*tert*-butyl-7-(thiophen-2-ylsulfonyl)-1*H*-indol-3-yl)ethanone (5o)



White solid; mp: 145-147 °C; R_f (20% EtOAc/*n*-Hexane) 0.30; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.65 (bs, 1H), 7.67 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 2.2 Hz, 1H), 7.37-7.30 (m, 2H), 7.00 (t, *J* = 4.8 Hz, 1H), 2.64 (s, 3H), 1.66 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.9, 154.5, 145.2, 134.2, 133.5, 131.8, 129.7, 128.3, 124.9, 123.2, 123.1, 115.3, 112.7, 34.1, 32.7, 28.3 (3C); HPLC: 96.3%; column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate:

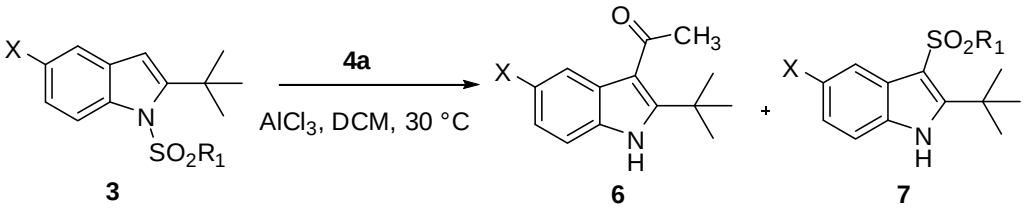
1.0 mL/min; UV 245 nm, retention time 11.21 min; IR (KBr, cm^{-1}): 3343, 3013, 1675, 1354; MS (ES mass): *m*/*z* 439.6 (M-1).

1-(2-*tert*-butyl-5-methyl-7-(thiophen-2-ylsulfonyl)-1*H*-indol-3-yl)ethanone (5p)



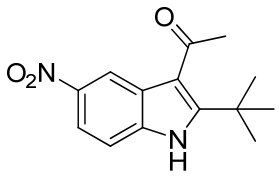
White solid; mp: 180-182 °C; R_f (20% EtOAc/*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.69 (bs, 1H), 7.99 (s, 1H), 7.77 (s, 1H), 7.68 (dd, *J* = 4.6, 1.0 Hz, 1H), 7.48 (dd, *J* = 4.8, 1.0 Hz, 1H), 7.00-6.98 (m, 1H), 2.64 (s, 3H), 2.60 (s, 3H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.0, 154.6, 146.3, 133.1, 132.4, 131.5, 131.1, 130.5, 129.6, 126.9, 122.7, 113.6, 111.2, 34.6, 29.9 (3C), 29.5, 22.4; HPLC: 95.6%; column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate: 1.0 mL/min; UV 250 nm, retention time 10.12 min; IR (KBr, cm^{-1}) 3325, 2963, 1673, 1315; MS (ES mass): *m*/*z* 373.9 (M-1).

Procedure for preparation of compounds (6-7):



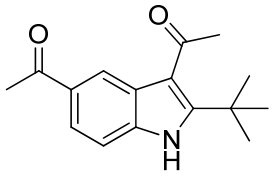
A mixture of $AlCl_3$ (3.50 mmol) and acetyl chloride (5.25 mmol) was stirred at 0 ºC in dry DCM (5 mL) for 10 min. To this indole **3** (1.75 mmol) in DCM (3 mL) was added and the reaction mixture was stirred at 30 °C for 6-8 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was diluted with DCM (20 mL), washed with water (10 mL) and brine solution (10 mL). The organic layer was collected, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using ethyl acetate-hexane to give the desired products **6** and **7**.

1-(2-*tert*-butyl-5-nitro-1*H*-indol-3-yl)ethanone (6a)



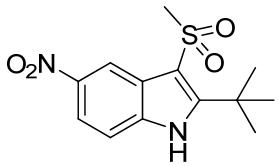
White solid; mp: 183-185 °C; R_f (10% EtOAc/*n*-Hexane) 0.59; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.86 (s, 1H), 8.80 (d, *J* = 1.6 Hz, 1H), 8.14 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.45 (d, *J* = 89.2 Hz, 1H), 2.79 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.5, 155.2, 144.4, 141.4, 129.2, 119.5, 116.5, 115.4, 109.5, 34.3, 32.6, 28.3 (3C); HPLC : 98.9%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/95, 14/95, 17/50, 19/50; flow rate: 1.0 mL/min; UV 210 nm, retention time 6.12 min; IR (KBr, cm^{-1}): 3402, 2992, 2942, 1652, 1453; MS (ES mass): *m*/*z* 261.2 (M+1).

1,1'-(2-*tert*-butyl-1*H*-indole-3,5-diyl)diethanone (6b)



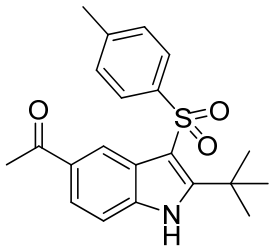
White solid; mp: 182-184 °C; R_f (10% EtOAc/*n*-Hexane) 0.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.79 (s, 1H), 8.52 (s, 1H), 7.86 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 2.78 (s, 3H), 2.69 (s, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.2, 195.4, 154.5, 135.8, 131.3, 127.6, 122.7, 121.9, 115.2, 110.9, 34.1, 28.4, 26.8 (3C), 26.7; HPLC : 96.9%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate: 1.0 mL/min; UV 245 nm, retention time 4.08 min; IR (KBr, cm^{-1}): 3391, 2967, 2930, 1685, 1642, 1482; MS (ES mass): *m*/*z* 258.1 (M+1).

2-*tert*-butyl-3-(methylsulfonyl)-5-nitro-1*H*-indole (7a)



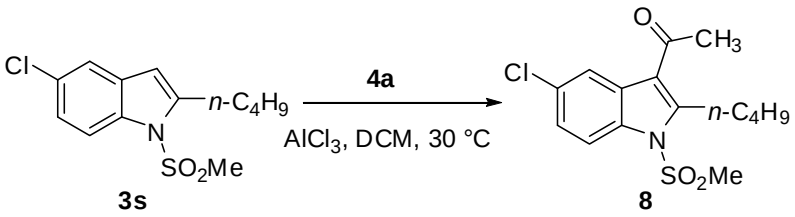
White solid; mp: 215-217 °C; R_f (10% EtOAc/*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.03 (s, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 3.19 (s, 3H), 1.67 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.7, 143.7, 135.5, 127.3, 126.9, 118.9, 117.1, 113.2, 34.5, 29.6 (3C), 22.7; HPLC : 97.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/95, 14/95, 16/50, 18/50; flow rate: 1.0 mL/min; UV 255 nm, retention time 6.09 min; IR (KBr, cm^{-1}): 3409, 2977, 2924, 1444; MS (ES mass): *m*/*z* 297.2 (M+1).

1-(2-*tert*-butyl-3-tosyl-1*H*-indol-5-yl)ethanone (7b)



White solid; mp: 179-181 °C; R_f (10% EtOAc/*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.79 (s, 1H), 8.52 (s, 1H), 7.86 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 2H) 7.42 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.78 (s, 3H), 2.69 (s, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 198.2, 153.3, 143.2, 141.6, 135.3, 131.9, 129.6, 129.3, 127.1, 126.2, 125.9, 123.1, 122.9, 122.7, 111.9, 34.5, 30.0, 26.9 (3C), 22.7; HPLC : 96.9%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate: 1.0 mL/min; UV 245 nm, retention time 4.08 min; IR (KBr, cm^{-1}): 3411, 2979, 2927, 1681, 1455; MS (ES mass): *m*/*z* 370.1 (M+1).

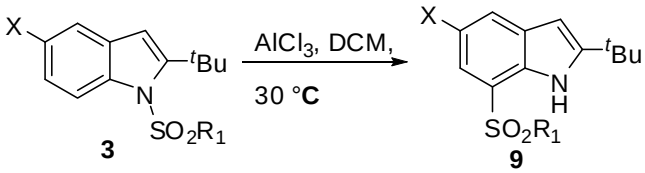
Typical procedure for preparation of 1-(2-butyl-5-chloro-1-(methylsulfonyl)-1*H*-indol-3-yl)ethanone (8):



A mixture of $AlCl_3$ (2.1 mmol) and acetyl chloride (5.25 mmol) was stirred at 0 ºC in dry DCM (5 mL) for 10 min. To this indole **3s** (1.75 mmol) in DCM (3 mL) was added and the reaction mixture was stirred at 30 °C temperature for 6 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was diluted with DCM (20 mL), washed with water (10 mL) and brine solution (10 mL). The organic layer was collected, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using ethyl acetate-hexane to give the desired product **8**.

White solid; mp: 120-122 °C; R_f (10% EtOAc/*n*-Hexane) 0.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (d, *J* = 8.8 Hz, 1H), 7.94 (d, *J* = 2.0 Hz, 1H), 7.31 (dd, *J* = 9.0, 2.0 Hz, 1H), 3.33-3.29 (m, 2H), 3.15 (s, 3H), 2.67 (s, 3H), 1.75-1.68 (m, 2H), 1.53-1.44 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.0, 149.4, 133.8, 130.6, 128.5, 125.1, 120.8, 119.6, 115.3, 41.8, 32.9, 31.9, 26.8, 22.9, 13.6; HPLC : 99.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/70, 2/70, 9/98, 14/98, 16/70, 18/70; flow rate: 0.8 mL/min; UV 220 nm, retention time 6.29 min; IR (KBr, cm^{-1}): 3008, 2961, 1645, 1379; MS (ES mass): *m*/*z* 327.8 (M+1).

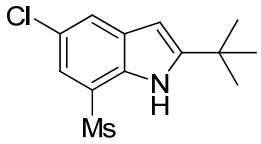
General procedure for preparation of 2-*tert*-butyl-5-substituted-7-(alkyl/ary/heteroaryl sulfonyl)-1*H*-indole (9):



A mixture of $AlCl_3$ (2.10 mmol) and indole **3** (1.75 mmol) stirred at 0 ºC in dry DCM (5 mL) for 10 min. Then, the reaction mixture was stirred at 30 °C for 4-5 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was diluted with DCM (20 mL), washed with water (10 mL) and brine solution (10 mL). The organic layer was collected, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The

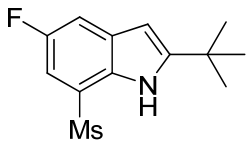
residue was purified by column chromatography using ethyl acetate-hexane to give the desired product **9**.

2-*tert*-butyl-5-chloro-7-(methylsulfonyl)-1*H*-indole (9a)



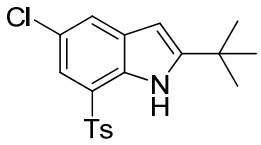
White solid; mp: 95-97 °C; R_f (10% EtOAc/*n*-Hexane) 0.70; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.34 (s, 1H), 7.73 (d, *J* = 1.6 Hz, 1H), 7.55 (d, *J* = 1.6 Hz, 1H), 6.32 (s, 1H), 3.15 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.0, 131.7, 128.8, 128.3, 124.3, 123.5, 114.3, 114.1, 45.3, 32.6, 28.4 (3C); HPLC: 96.4%; column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/95, 14/95, 16/50, 18/50; flow rate: 1.0 mL/min; UV 265 nm, retention time 9.12 min; IR (KBr, cm^{-1}): 3441, 2962, 2920, 1652, 1451; MS (ES mass): *m*/*z* 286.0 (M+1).

2-*tert*-butyl-5-fluoro-7-(methylsulfonyl)-1*H*-indole (9b)



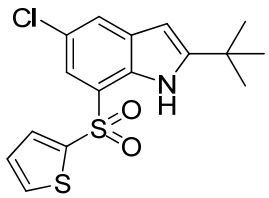
White solid; mp: 84-85 °C; R_f (10 % EtOAc/*n*-Hexane) 0.72; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.29 (s, 1H), 7.45 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.33 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.34 (s, 1H), 3.15 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.6 (C-F *J* = 237.3 Hz), 153.3, 131.6 (C-F *J* = 9.2 Hz), 128.9, 111.6 (C-F *J* = 23.3 Hz), 108.6, 108.3, 97.8, 44.9, 32.1, 30.1 (3C); HPLC : 98.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/60, 2/60, 9/95, 14/95, 16/60, 18/60; flow rate: 0.8 mL/min; UV 225 nm, retention time 6.74 min; IR (KBr, cm^{-1}): 3383, 2967, 2930, 1486; MS (ES mass): *m*/*z* 269.8 (M+1).

2-*tert*-butyl-5-chloro-7-tosyl-1*H*-indole (9c)



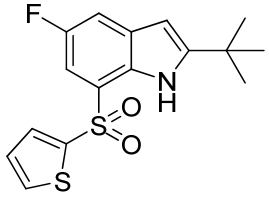
White solid; mp: 103-105 °C; R_f (15% EtOAc/*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.65 (s, 1H), 8.11 (d, *J* = 1.2 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.28-7.25 (m, 3H), 6.32 (s, 1H), 2.36 (s, 3H), 1.61 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.3, 145.2, 138.1, 130.7, 130.2 (2C), 128.0, 127.2, 127.1, 127.0, 125.3, 124.6, 121.9, 113.9, 34.2, 28.6 (3C), 21.6; HPLC : 99.1%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/70, 2/70, 9/95, 14/95, 16/70, 17/70; flow rate: 1.0 mL/min; UV 245 nm, retention time 10.09 min; IR (KBr, cm^{-1}): 3441, 2962, 2920, 1652, 1451; MS (ES mass): *m*/*z* 362.4 (M+1).

2-*tert*-butyl-5-chloro-7-(thiophen-2-ylsulfonyl)-1*H*-indole (9d)



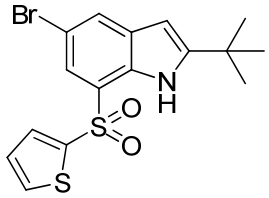
Off white solid; mp: 95-97 °C; R_f (20% EtOAc/*n*-Hexane) 0.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.58 (bs, 1H), 7.68 (d, *J* = 2.4 Hz, 1H), 7.48 (d, *J* = 2.2 Hz, 1H), 7.22-7.15 (m, 2H), 7.01-6.99 (m, 1H), 6.49 (s, 1H), 1.67 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.8, 131.4, 131.3, 131.0, 128.0, 127.0, 123.7, 123.6, 120.0, 112.2, 111.1, 96.9, 34.4, 29.9 (3C); HPLC: 95.9%; column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate: 1.0 mL/min; UV 280 nm, retention time 5.48 min; IR (KBr, cm^{-1}) 3251, 2985, 1545, 1466; MS (ES mass): *m*/*z* 353.9 (M+1).

1-(2-*tert*-butyl-5-fluoro-7-(thiophen-2-ylsulfonyl)-1*H*-indol-3-yl)propan-1-one (9e)



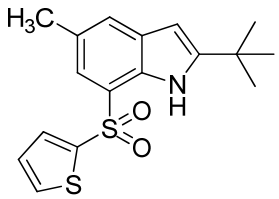
White solid; mp: 105-107 ºC; R_f (25% EtOAc/*n*-Hexane) 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.72 (s, 1H), 7.82 (dd, *J* = 9.1, 2.0 Hz, 1H), 7.68 (d, *J* = 2.6 Hz, 1H), 7.48 (d, *J* = 5.2 Hz, 1H), 7.31-7.28 (m, 1H), 7.01-6.94 (m, 2H), 1.65 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.3, 157.9, 153.2, 146.3, 131.4, 131.1, 129.1, 126.9, 112.4, 111.8, 111.6, 106.1, 34.4, 29.9 (3C); HPLC : 98.5%, column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 16/98, 18/50, 18/50, 20/50; flow rate: 1.0 mL/min; UV 280 nm, retention time 6.77 min; IR (KBr, cm^{-1}): 3372, 3104, 2962, 1478, 1448; MS (ES mass): *m*/*z* 337.9 (M+1).

5-Bromo-2-*tert*-butyl-7-(thiophen-2-ylsulfonyl)-1*H*-indole (9f)



Light red solid; mp: 198-200 °C; R_f (20% EtOAc/*n*-Hexane) 0.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.37 (bs, 1H), 7.81 (d, *J* = 1.0 Hz, 1H), 7.72-7.71 (m, 2H), 7.61(dd, *J* = 5.8, 1.0 Hz, 1H), 7.08 (t, *J* = 4.8 Hz, 1H), 6.28 (s, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.6, 142.9, 133.7, 132.9, 132.6, 130.4, 128.2, 127.9, 123.7, 123.1, 111.9, 97.3, 32.1, 30.0 (3C); HPLC: 93.9%; column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate: 1.0 mL/min; UV 230 nm, retention time 10.45 min; IR (KBr, cm^{-1}): 3364, 2986, 1521, 1432; MS (ES mass): *m*/*z* 399.8 (M+1).

2-*tert*-butyl-5-methyl-7-(thiophen-2-ylsulfonyl)-1*H*-indole (9g)



Light green solid; mp: 170-172 °C; R_f (20% EtOAc/*n*-Hexane) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.92 (bs, 1H), 7.98 (s, 1H), 7.79-7.75 (m, 2H), 7.66-7.64 (m, 1H), 7.06-7.04 (m, 1H), 6.40 (s, 1H), 2.61 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.4, 132.0, 131.6,

130.9, 130.1, 124.4, 123.0 (2C), 122.3, 113.9, 113.6, 96.8, 32.7, 28.3 (3C), 22.8; HPLC: 98.9%; column: X Bridge C-18 150*4.6 mm 5µ, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 2/50, 9/98, 14/98, 16/50, 18/50; flow rate: 1.0 mL/min; UV 245 nm, retention time 6.24 min; IR (KBr, cm^{-1}): 3334, 3012, 1532, 1387; MS (ES mass): *m*/*z* 333.8 (M+1).

Reference

1. A. Nakhi, B. Prasad, R. M. Rao, U. Reddy, S. Sandra, R. Kapavarapu, D. Rambabu, G. R. Krishna, C. M. Reddy, R. Kishore, P. Misra, J. Iqbal and M. Pal, *Med Chem Commun.* 2011**, 2,** 1006.

Single crystal X-ray data for compound 5a

Single crystals suitable for X-ray diffraction of **5a** were grown from methanol. The crystals were carefully chosen using a stereo zoom microscope supported by a rotatable polarizing stage. The data was 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 structure was solved by direct methods using SHELXS-97 and the data was 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 **5a**: Molecular formula = $C_{15}H_{18}ClNO_3S$, Formula weight = 327.81, Crystal system = Monoclinic, space group = P2(1)/n, a = 10.815 (5) Å, b = 9.725 (4) Å, c = 14.935 (7) Å, V = 1570.22 (12) $Å^3$, T = 296 K, Z = 4, Dc = 1.387 Mg m^{-3}, µ(Mo-Kα) = 0.39 mm^{-1}, 19884 reflections measured, 3429 independent reflections, 2873 observed reflections [I > 2.0 σ (I)], R1_obs = 0.032, Goodness of fit = 0.876. Crystallographic data (excluding structure factors) for 3a have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC 859365.

Reference

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

2. Sheldrick, G. M.; SHELX-97, Program for Crystal Structure Determination, University of Göttingen, **1997**.

Pharmacology

Chorismate mutase activity assay[1,2]

Mycobacterium *tuberculosis* chorismate mutase (MtCM) gene was PCR amplified and cloned into expression vector pET22b. MtCM was purified from over expressed culture of BL21 (DE3) harboring pET22b/ MtCM by Ni-NTA affinity chromatography.

Activity of chorismate mutase enzyme is based on the direct observation of conversion of chorismate to prephenate Spectrophotometrically at OD_{274}. The reaction volume of 100 µl contained 50 mM Tris-HCl (pH 7.5), 0.5 mM EDTA, 0.1 mg/ml bovine serum albumin, and 10 mM β-Mercaptoethanol, and chorismic acid 4 mM. The reaction was started by adding 180 pmol of purified protein to the pre-warmed chorismic acid solution. Inhibitory screening of the test compounds against chorismate mutase activity was measured at 30 µM concentration of the effectors. The reaction was allowed to proceed at 37 °C and was terminated after 5 min with 100 µl of 1 N HCl. A blank with no enzyme for every reaction was kept as a control to account for the non enzymatic conversion of chorismate to prephenate.

The percentage of enzyme inhibition caused by the test compound is calculated by the following formula

% inhibition = 100 – residual activity of CM

$$\text{Residual Activity of CM} = \frac{A_{274}\,(S + (E' + C)) - A_{274}\,(S + C)}{A_{274}\,(S + E) - A_{274}\,(S)} \times 100$$

S = Absorbance of the substrate (chorismic acid) at 274 nm

E’ = Absorbance of the enzyme (CM) at 274 nm with compound

E = Absorbance of the enzyme (CM) at 274 nm without compound

C = Test compound

(A_{274} indicates absorbance at 274 nm)

References

1. S. K.Kim, S. K.; Reddy, B. C. Nelson, G. B. Vasquez, A. Davis, A. J. Howard, S. Patterson, G. L. Gilliland, J. E. Ladner and P. T. Reddy, *J. Bacteriol.* 2006, **188**, 8638.
2. S. Sasso, C. Ramakrishnan, M. Gamper, D. Hilvert and P. Kast, *FEBS J.* 2005, **272**, 375.

Docking study

Method: Docking simulations of molecules were performed using the Schrodinger software suite (Maestro, version 9.2).[1] The compounds were sketched in 3D format using build panel and were prepared for docking using ligprep application. The Protein (Chorismate mutase; PDB ID: 2F6L)[2] for docking study was retrieved from protein data bank (PDB). The protein was prepared by giving preliminary treatment like adding hydrogen, adding missing residues, refining the loop with prime and finally minimized by using OPLS-2005 force field. Grids for molecular docking were generated by selecting 15 Å residues, around the binding site of protein. Compounds were docked using Glide in extra-precision mode,[3] with up to three poses saved per molecule.

Docking Discussion:

The docking studies were performed to predict the interactions and binding mode of synthesized molecules with the binding site of chorismate mutase enzyme. In both molecules **5a** and **5m** carbonyl-group interacted well with the binding site residues of protein. The carbonyl oxygen of molecules made perfect hydrogen bond bridge with Glutamine-76 and Arginine-72 (Figure 1), but in case of **5m**, thiophene ring was aligned towards the highly charged surface **(**Figure 2) of the binding pocket (Asp-138, Arg-134), which requires a complementary features in ligand (H-Bond donor/acceptor). The lack of these complementary features in **5m** might be the reason for its relatively inferior in vitro activity compared to **5a**. Figure 3 and 4 represents the hydrophobic and hydrophilic mapping of molecules and reflecting their chemical nature.

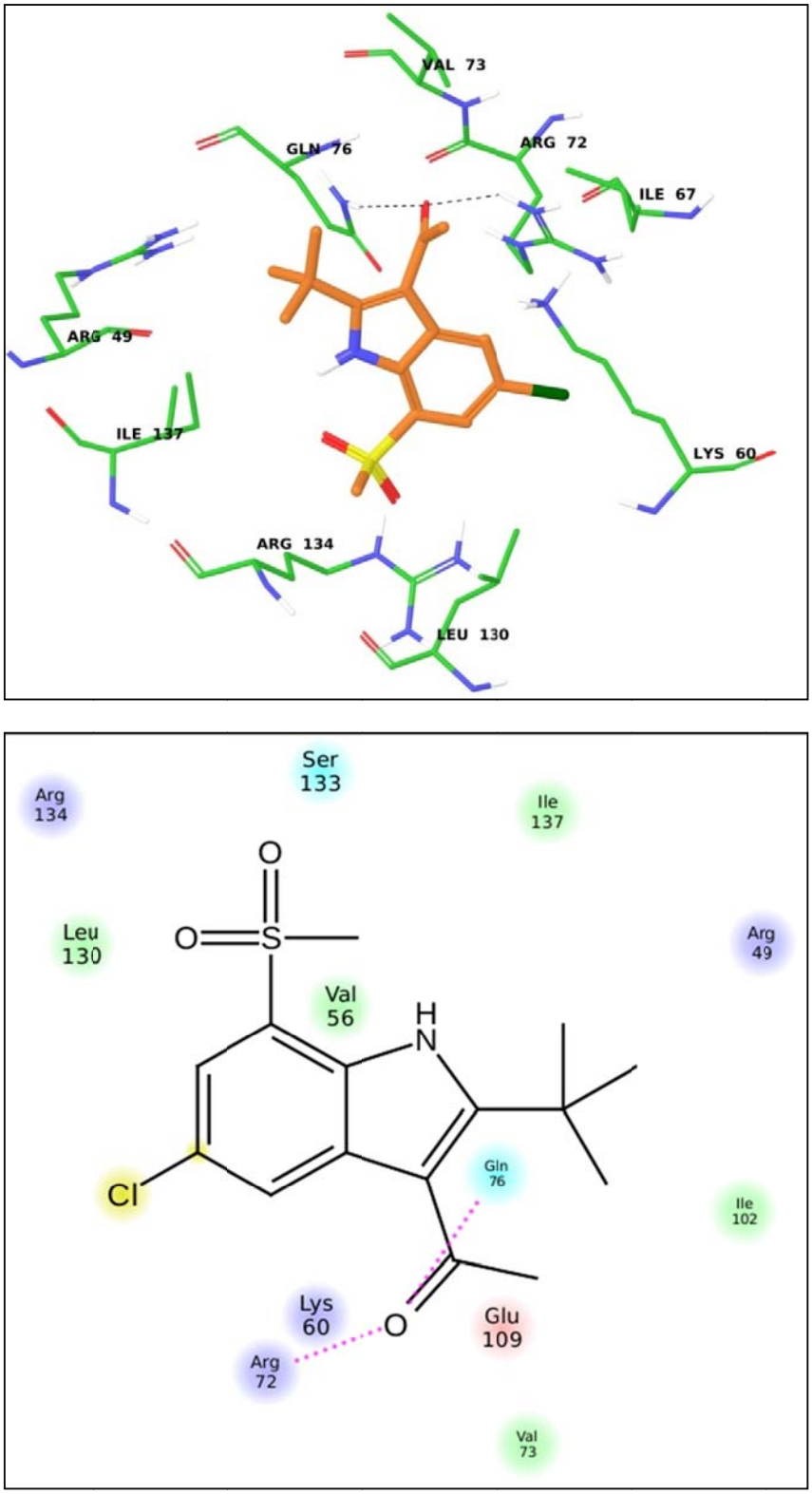


Figure 1. Binding pose and interaction of compound **5a** at the binding site of chorismate mutase enzyme.

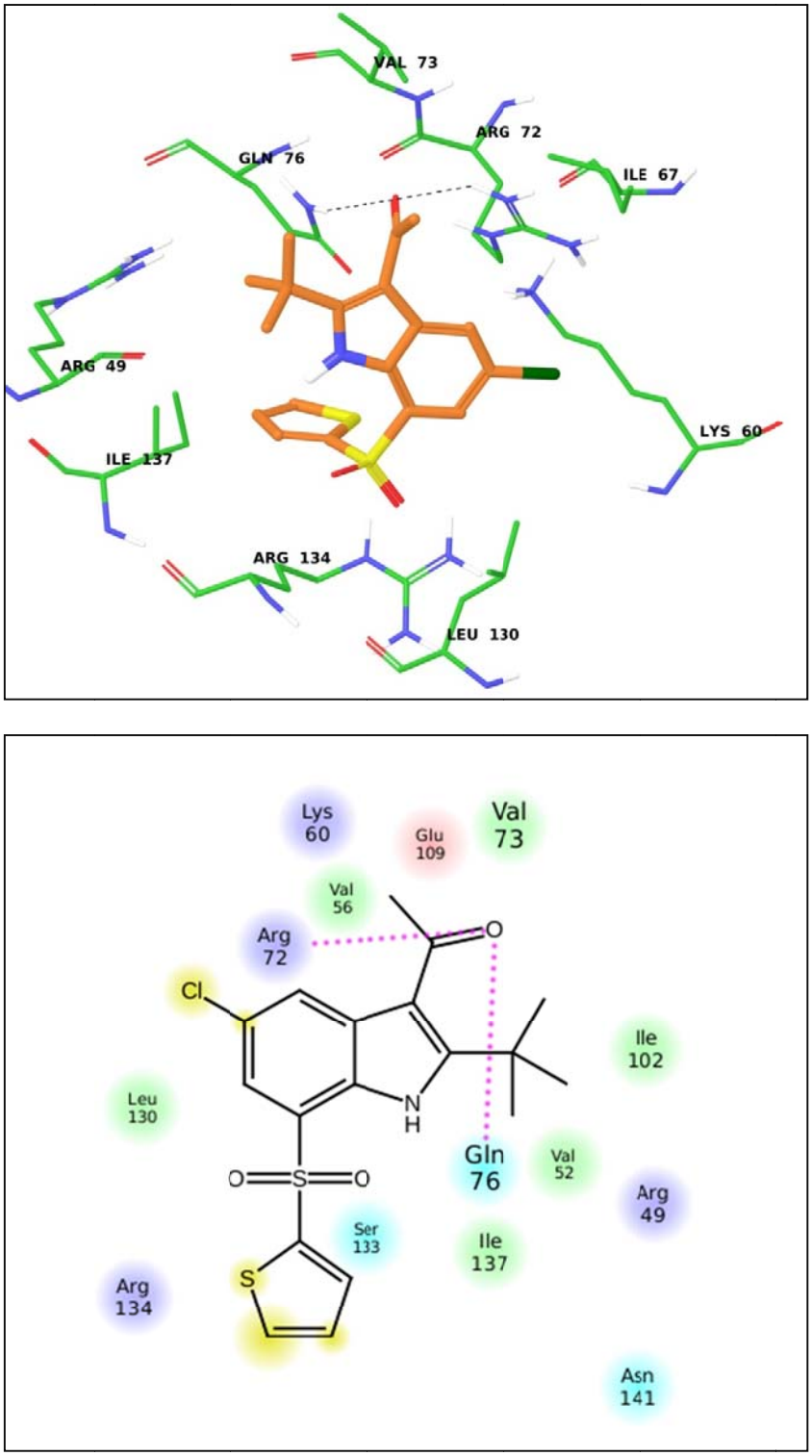


Figure 2. Binding pose and interaction of compound **5m** at the binding site of chorismate mutase enzyme.

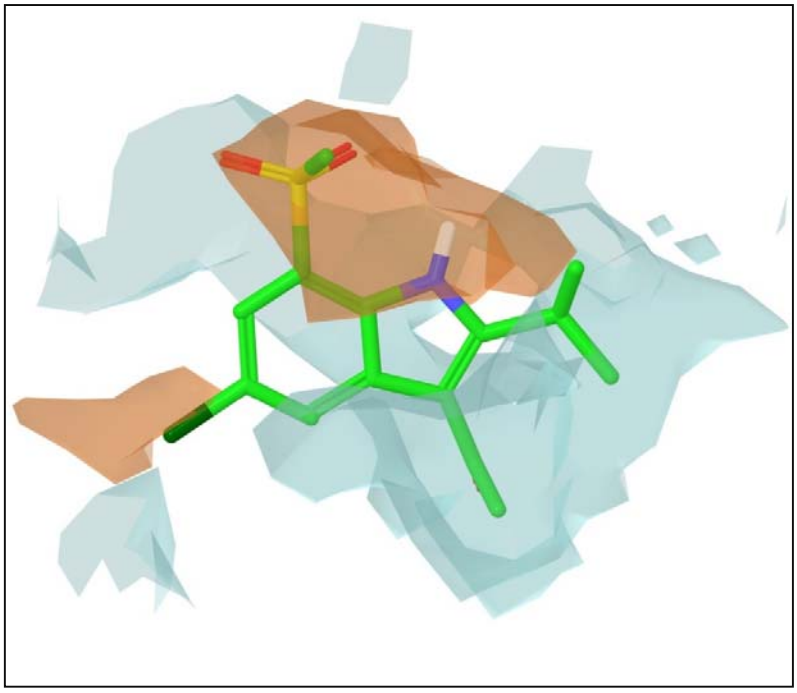


Figure 3. Hydrophobic/hydrophilic (Orange: hydrophilic region, Turquoise: Hydrophobic region) mapping of **5a**.

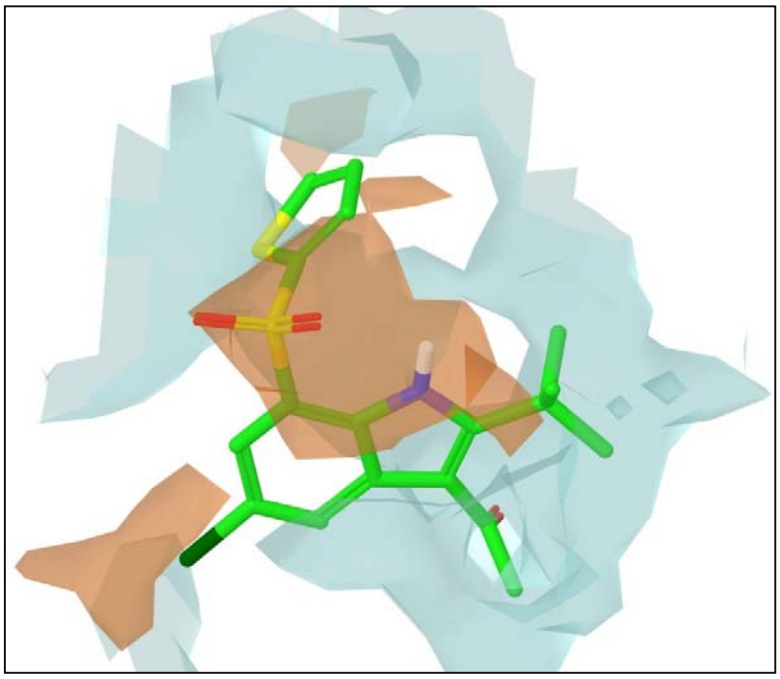


Figure 4. Hydrophobic/hydrophilic (Orange: hydrophilic region, Turquoise: Hydrophobic region) mapping of **5m.**

Reference:

1. Maestro, version 9.2; Schrodinger, LLC: New York, NY, 2012.
2. S. K. Kim, S. K. Reddy, B. C. Nelson, G. B. Vasquez, A. Davis, A. J. Howard, S. Patterson, G. L. Gilliland, J. E. Ladner and P. T. Reddy, *J. Bacteriol.* 2006, **188**, 8638.
3. Glide, version 5.7; Schrodinger, LLC: New York, NY, 2012.