Electronic Supplementary Information

A Pd-based regioselective strategy to indole-1,2-fused 8 and 9 membered rings: Their evaluation as new and potential scaffolds for apoptosis in zebrafish

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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 MHz spectrometer (VARIAN 400 MR). 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).

Experimental Section

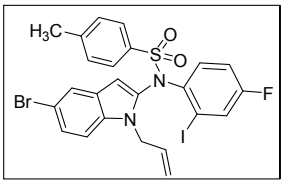
Chemistry

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

To a mixture of *N*-(2-halophenyl)alkyl/aryl/heteroarylsulfonamide derivative[1] (1.0 mmol) **1,** Cs_2CO_3 (1.5 mmol), I_2 (1mmol) in acetonitrile (CH_3CN) (2.5 mL) was added indole derivative[2] (1.2 mmol) **2.** The mixture was then stirred at room temperature for 4 h under nitrogen. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was quenched with a saturated 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**. Compounds **1a-1f**, **1h-1j**, **1r** were reported by our group.[3,4]

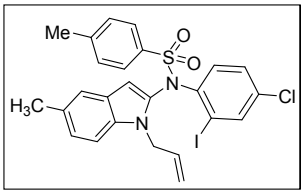
Characterization data of 1g, 1k-1q, 1s-1x.

N-(1-Allyl-5-bromo-1*H*-indol-2-yl)-*N*-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (1g)



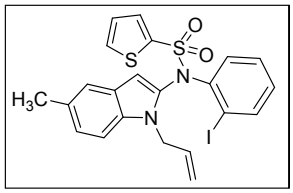
Off white solid; yield: 47%; mp: 146-148 °C; R_f (15% EtOAc-*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.63 (d, *J* = 1.6 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 3H), 7.21-7.15 (m, 2H), 7.03-6.98 (m, 1H), 6.22 (s, 1H), 5.90-5.81 (m, 1H), 5.16 (d, *J* = 1.2 Hz, 2H), 5.07 (d, *J* = 11.2 Hz, 1H), 4.84 (d, *J* = 17.2 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5 (d, C-F *J* = 253.8 Hz), 145.1, 138.9 (d, C-F *J* = 3.7 Hz), 135.6, 134.3, 133.7, 133.4, 130.9 (d, C-F *J* = 9.1 Hz), 129.4 (2C), 129.4 (2C), 127.9, 127.7, 127.3, 125.8, 123.3, 116.5, 115.9 (d, C-F *J* = 22.1 Hz), 113.5, 112.7, 100.3, 46.9, 21.7; MS (ES mass): *m*/*z* 624.7 (M+1).

_N_-(1-Allyl-5-methyl-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)-4-methylbenzenesulfonamide (1k)



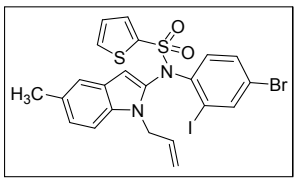
Off white solid; yield: 52%; mp: 136-138 °C; R_f (15% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (d, *J* = 2.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.41 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 3H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.18 (s, 1H), 5.92-5.82 (m, 1H), 5.15 (s, 2H), 5.05 (d, *J* = 10.4 Hz, 1H), 4.84 (d, *J* = 16.0 Hz, 1H), 2.49 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.9, 143.0, 142.1, 134.5, 134.1, 133.9, 131.9, 131.1, 129.4 (2C), 129.3 (2C), 125.8, 124.6, 122.9, 120.4, 116.1, 115.9, 115.6, 110.8, 102.5, 100.5, 46.6, 21.7, 21.4; MS (ES mass): *m*/*z* 577.4 (M+1).

_N_-(1-Allyl-5-methyl-1_H_-indol-2-yl)-_N_-(2-iodophenyl)thiophene-2-sulfonamide (1l)



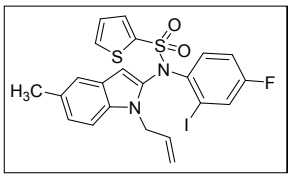
Off white solid; yield: 52%; mp: 108-110 °C; R_f (15% EtOAc-*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 4.8 Hz, 1H), 7.54 (d, *J* = 4.0 Hz, 1H), 7.38 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.33-7.29 (m, 2H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.13 (t, *J* = 4.4 Hz, 1H), 7.06-7.01 (m, 2H), 6.39 (s, 1H), 5.89-5.80 (m, 1H), 5.17 (s, 2H), 5.03 (d, *J* = 10.4 Hz, 1H), 4.87 (d, *J* = 17.2 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.4, 141.2, 137.3, 135.3, 134.1, 134.0, 133.8, 133.2, 130.2, 130.1, 129.4, 128.9, 127.3, 125.9, 124.6, 120.5, 116.2, 110.8, 101.5, 100.6, 46.8, 21.4; MS (ES mass): *m*/*z* 534.5 (M+1).

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



Light brown solid; yield: 53%; mp: 132-134 °C; R_f (15% EtOAc-*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (d, *J* = 2.2 Hz, 1H), 7.71-7.70 (m, 1H), 7.52 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.42 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.32 (s, 1H), 7.22 (d, *J* = 8.6 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.12 (t, *J* = 4.8 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.33 (s, 1H), 5.89-5.79 (m, 1H), 5.12 (bs, 2H), 5.03 (d, *J* = 10.3 Hz, 1H), 4.82 (d, *J* = 17.2 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.1, 141.6, 136.9, 135.5, 134.0, 133.9, 133.6, 133.2, 132.0, 130.9, 129.6, 127.4, 125.9, 124.8, 123.2, 120.5, 116.2, 110.8, 102.4, 100.6, 46.6, 21.4; IR (KBr, cm^{-1}): 3088, 2914, 1563, 1458, 1365, 1162; MS (ES mass): *m*/*z* 614.1 (M+1).

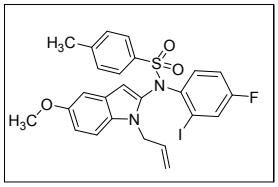
_N_-(1-Allyl-5-methyl-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)thiophene-2-sulfonamide (1n)



Light pink solid; yield: 51%; mp: 170-172 °C; R_f (15% EtOAc-*n*-Hexane) 0.43; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.74-7.73 (m, 1H), 7.68 (dd, *J* = 8.0, 2.8 Hz, 1H), 7.56-7.55 (m, 1H), 7.38-7.35 (m, 2H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.17-7.15 (m, 1H), 7.09-7.07 (m, 1H), 7.06-7.03 (m, 1H), 6.39 (s, 1H), 5.93-5.83 (m, 1H), 5.17 (s, 2H), 5.07 (d, *J* = 10.4 Hz, 1H), 4.87 (d, *J* = 17.6 Hz, 1H), 2.44 (s, 3H); ^{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

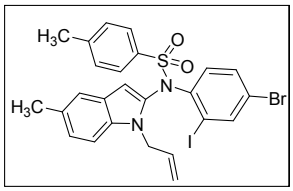
Hz), 137.0, 135.4, 134.9, 134.1, 134.0, 133.9, 131.0 (d, C-F J = 9.0 Hz), 128.0, 127.8, 127.4, 125.7, 123.0, 120.9, 120.2, 116.3, 116.0 (d, C-F J = 22.2 Hz), 111.1, 100.9, 46.7, 21.7; MS (ES mass): m/z 552.8 (M+1).

_N_-(1-Allyl-5-methoxy-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (1o)



Light red solid; yield: 57%; mp: 154-156 °C; R_f (15% EtOAc-*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (dd, J = 8.0, 3.2 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.23-7.18 (m, 2H), 7.01-6.97 (m, 1H), 6.96 (d, J = 2.3 Hz, 1H), 6.88 (dd, J = 9.2, 2.4 Hz, 1H), 6.21 (s, 1H), 5.91-5.81 (m, 1H), 5.14 (bs, 2H), 5.05 (d, J = 10.4 Hz, 1H), 4.87 (d, J = 17.4 Hz, 1H), 3.82 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.4 (d, C-F J = 253.5 Hz), 154.3, 144.8, 139.1 (d, C-F J = 3.7 Hz), 134.7, 134.2, 133.9, 131.1 (d, C-F J = 8.9 Hz), 129.9, 129.4 (2C), 129.3 (2C), 127.8 (d, C-F J = 24.3 Hz), 126.0, 116.3, 115.7 (d, C-F J = 22.1 Hz), 113.4, 112.0, 102.3, 101.8 (d, C-F J = 8.3 Hz), 100.5, 55.7, 46.8, 21.7; MS (ES mass): m/z 577.2 (M+1).

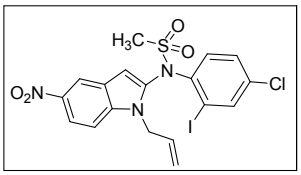
_N_-(1-Allyl-5-methyl-1_H_-indol-2-yl)-_N_-(4-bromo-2-iodophenyl)-4-methylbenzenesulfonamide (1p)



Light brown solid; yield: 55%; mp: 108-110 °C; R_f (15% EtOAc-*n*-Hexane) 0.46; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (d, J = 2.4 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.41 (dd, J = 8.8, 2.4 Hz, 1H), 7.31-7.29 (m, 3H), 7.20 (d, J = 8.4 Hz, 1H), 7.13 (d, J = 8.4 Hz, 1H), 7.07-7.05 (m, 1H), 6.18 (s, 1H), 5.92-5.82 (m, 1H), 5.15 (bs, 2H), 5.05 (d, J = 10.3 Hz, 1H), 4.85 (d, J = 17.2 Hz, 1H), 2.49 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.9, 143.0, 142.1, 134.1,

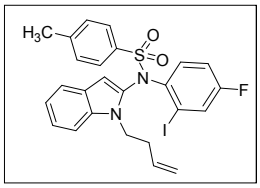
133.9, 133.1, 131.9, 131.0, 129.4 (2C), 129.3 (2C), 125.9, 124.6, 124.5, 122.9, 120.4, 116.1, 115.9, 110.8, 102.5, 100.5, 46.6, 21.7, 21.4; MS (ES mass): *m*/*z* 620.5 (M+1).

_N_-(1-Allyl-5-nitro-1_H_-indol-2-yl)-_N_-(4-chloro-2-iodophenyl)methanesulfonamide (1r)



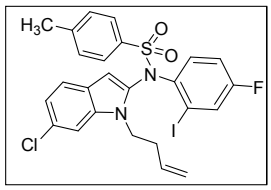
Light yellow solid; yield: 52%; mp: 116-118 °C; R_f (15% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.60 (d, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.96 (d, *J* = 2.3 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.40 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.32 (d, *J* = 9.2 Hz, 1H), 7.25 (s, 1H), 5.84-5.76 (m, 1H), 5.11-5.07 (m, 3H), 4.78 (d, *J* = 17.3 Hz, 1H), 3.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.3, 140.6, 139.7, 137.9, 136.7, 135.7, 132.2, 131.5, 129.7, 125.0, 118.6, 118.3, 117.2, 111.0, 103.8, 100.9, 46.7, 39.8; MS (ES mass): *m*/*z* 529.5 (M-1).

_N_-(1-(But-3-enyl)-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (1s)



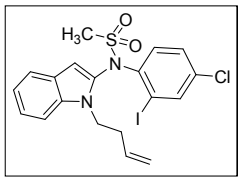
Light brown solid; yield: 55%; mp: 138-140 °C; R_f (15% EtOAc-*n*-Hexane) 0.39; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (dd, *J* = 7.7, 2.8 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.32-7.27 (m, 4H), 7.25-7.22 (m, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.03-6.98 (m, 1H), 6.25 (s, 1H), 5.91-5.79 (m, 1H), 5.13 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.06 (d, *J* = 10.4 Hz, 1H), 4.50-4.49 (m, 2H), 2.47 (s, 3H), 2.45-2.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.3 (d, C-F *J* = 253.5 Hz), 144.9, 139.1 (d, C-F *J* = 3.6 Hz), 134.6, 134.3, 134.2, 133.8, 131.1 (d, C-F *J* = 37.6 Hz), 129.5 (2C), 129.3 (2C), 128.0 (d, C-F *J* = 24.2 Hz), 125.7, 122.9, 121.0, 120.0, 117.0, 115.9 (d, C-F *J* = 22.1 Hz), 110.4, 101.7 (d, C-F *J* = 8.5 Hz), 101.1, 42.8, 33.9, 21.7; MS (ES mass): *m*/*z* 561.3 (M+1).

_N_-(1-(But-3-enyl)-6-chloro-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (1t)



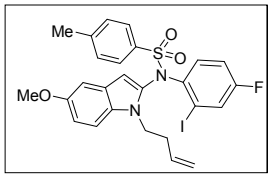
Light red solid; yield: 51%; mp: 116-118 °C; R_f (15% EtOAc-*n*-Hexane) 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.29-7.24 (m, 4H), 7.08-7.00 (m, 2H), 6.27 (s, 1H), 5.88-5.77 (m, 1H), 5.13 (d, *J* = 17.2 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 4.46-4.42 (m, 2H), 2.47 (s, 3H), 2.46-2.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.4 (d, C-F *J* = 253.7 Hz), 145.0, 138.8 (d, C-F *J* = 3.4 Hz), 134.9, 134.5, 134.2, 133.7, 131.0 (d, C-F *J* = 8.8 Hz), 129.4 (2C), 129.3 (2C), 128.8, 128.1, 127.9, 124.1, 122.0, 120.8, 117.3, 116.0 (d, C-F *J* = 22.2 Hz), 110.3, 101.3, 42.9, 33.7, 21.7; MS (ES mass): *m*/*z* 594.8 (M+1).

_N_-(4-Chloro-2-iodophenyl)-_N_-(1-(but-3-enyl)-_1H_-indol-2-yl)methanesulfonamide (1u)



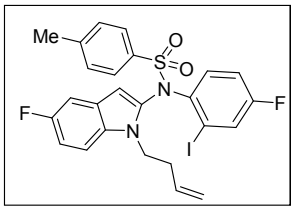
Light red semi solid; yield: 52%; R_f (15% EtOAc-*n*-Hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 (d, *J* = 2.4 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.6 Hz, 1H), 7.38-7.35 (m, 1H), 7.33-7.29 (m, 2H), 7.18 (t, *J* = 6.8 Hz, 1H), 7.09 (s, 1H), 5.87-5.77 (m, 1H), 5.13-5.06 (m, 2H), 4.40 (t, *J* = 8.0 Hz, 2H), 3.28 (s, 3H), 2.34-2.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.4, 140.1, 135.0, 134.5, 134.1, 133.5, 131.2, 129.5, 125.9, 123.2, 121.3, 120.4, 117.4, 110.2, 101.6, 101.1, 42.7, 39.3, 34.0; MS (ES mass): *m*/*z* 500.7 (M+1).

_N_-(1-(But-3-enyl)-5-methoxy-_1H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (1v)



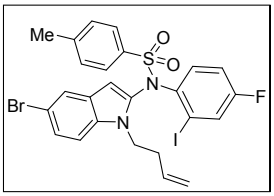
Light brown semi solid; yield: 55%; R_f (15% EtOAc-*n*-Hexane) 0.39; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.29-7.27 (m, 3H), 7.20 (d, *J* = 9.2 Hz, 1H), 7.03-6.98 (m, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.19 (s, 1H), 5.88-5.77 (m, 1H), 5.11 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.04 (dd, *J* = 10. 4, 1.6 Hz, 1H), 4.52 (t, *J* = 8.0 Hz, 2H), 3.82 (s, 3H), 2.46 (s, 3H), 2.43-2.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.4 (d, C-F *J* = 253.4 Hz), 154.3, 144.8, 139.1 (d, C-F *J* = 3.6 Hz), 134.6, 134.4, 133.9, 131.1 (d, C-F *J* = 9.1 Hz), 129.5 (2C), 129.4, 129.3, 128.0 (d, C-F *J* = 24.4 Hz), 127.7, 127.4, 125.9, 117.0, 115.9 (d, C-F *J* = 22.0 Hz), 113.5, 111.4, 102.3, 100.7, 55.7, 42.9, 34.1, 21.7; MS (ES mass): *m*/*z* 574.8 (M-Me).

_N_-(1-(But-3-enyl)-5-fluoro-_1H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (1w)



Light brown solid; yield: 47%; mp: 140-142 °C; R_f (15% EtOAc-*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.25-7.22 (m, 2H), 7.16 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.04-6.97 (m 2H), 6.21 (s, 1H), 5.88-5.78 (m, 1H), 5.12 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.06 (d, *J* = 10.4 Hz, 1H), 4.52-4.48 (m, 2H), 2.47 (s, 3H), 2.43-2.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.4 (d, C-F *J* = 253.7 Hz), 159.1 (d, C-F *J* = 234.3 Hz), 145.0, 138.9 (d, C-F *J* = 3.6 Hz), 135.5, 134.4, 133.7, 131.0 (d, C-F *J* = 8.9 Hz), 130.8, 129.4 (2C), 129.3 (2C), 128.1 (d, C-F *J* = 24.4 Hz), 125.7 (d, C-F *J* = 10.4 Hz), 117.1, 116.0 (d, C-F *J* = 22.0 Hz), 111.6 (d, C-F *J* = 35.4 Hz), 111.4, 105.8 (d, C-F *J* = 23.3 Hz), 101.7 (d, C-F *J* = 8.5 Hz), 101.0 (d, C-F *J* = 4.4 Hz), 43.0, 33.9, 21.7; MS (ES mass): *m*/*z* 578.9 (M+1).

_N_-(5-Bromo-1-(but-3-enyl)-_1H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (1x)

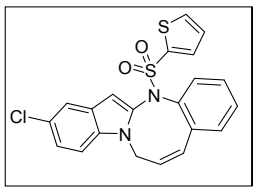


Light brown solid; yield: 51%; mp: 135-137 °C; R_f (15% EtOAc-*n*-Hexane) 0.46; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (dd, *J* = 8.0, 3.2 Hz, 1H), 7.65 (d, *J* = 2.4 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.34-7.29 (m, 3H), 7.26-7.24 (m, 1H), 7.19 (d, *J* = 8.8 Hz, 1H), 7.06-7.01 (m, 1H), 6.21 (s, 1H), 5.87-5.77 (m, 1H), 5.11 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.05 (dd, *J* = 10.4, 1.4 Hz, 1H), 4.51-4.47 (m, 2H), 2.48 (s, 3H), 2.43 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.4 (d, C-F *J* = 253.6 Hz), 145.1, 138.8 (d, C-F *J* = 3.4 Hz), 135.3, 134.3, 133.7, 132.9, 131.0 (d, C-F *J* = 8.9 Hz), 129.5 (2C), 129.4 (2C), 128.1 (d, C-F *J* = 24.4 Hz), 127.2, 125.8, 123.5, 117.3, 116.0 (d, C-F *J* = 22.2 Hz), 113.3, 112.0, 101.6, 100.6, 43.0, 33.9, 21.7; MS (ES mass): *m*/*z* 640.1 (M+1).

General procedure for preparation of indole-1,2-fused 8 and 9 membered rings (2):

A mixture of *N*-(1-allyl-5-substituted-1*H*-indol-2-yl)-*N*-(2-iodo-4-substitutedphenyl)sulfonamide **1**, (0.2 mmol), $Pd(PPh_3)_2Cl_2$ (5 mol%), Et_3N (0.4 mmol) in anhydrous DMF (2 mL) was stirred at 110 °C for 2-6 h under a nitrogen atmosphere. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled to room temperature, diluted with ethylacetate (20 mL) and passed through celite. The filtrate was washed with water (2 x 10 mL), followed by 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 **2**.

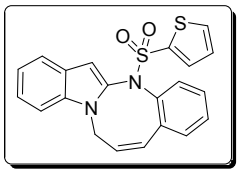
Compound **2a**



2a was prepared according to the general procedure from **1a.**

Off white solid; yield: 63%; mp: 152-154 °C; R_f (20% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.56 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.53 (d, *J* = 1.2 Hz, 1H), 7.39 (d, *J* = 1.2 Hz, 1H), 7.37 (s, 1H), 7.35-7.32 (m, 2H), 7.19-7.16 (m, 2H), 7.11-7.09 (m, 1H), 6.82 (d, *J* = 11.4 Hz, 1H), 6.57 (s, 1H), 6.02-5.96 (m, 1H), 4.86-4.80 (m, 1H), 4.03-3.97 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.2, 140.5, 137.0, 135.5, 135.2, 134.9, 134.1, 133.9, 133.8, 130.6, 129.0, 127.4, 125.7, 123.1, 121.0, 120.2, 116.3, 111.1, 101.8, 101.1, 46.6; IR (KBr, cm^{-1}): 3100, 2924, 2875, 1554, 1457, 1352, 1161; MS (ES mass): *m*/*z* 427.4 (M+1).

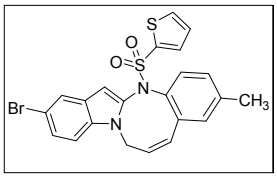
Compound **2b**



2b was prepared according to the general procedure from **1b**.

White solid; yield: 61%; 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; IR (KBr, cm^{-1}): 3097, 2897, 1511, 1439, 1375, 1173; MS (ES mass): *m*/*z* 392.5 (M+1).

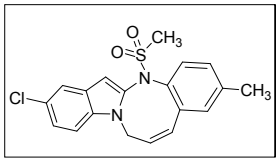
Compound **2c**



2c was prepared according to the general procedure from **1c**.

Light brown solid; yield: 54%; mp: 115-117 °C; R_f (20% EtOAc-*n*-Hexane) 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (d, *J* = 1.6 Hz, 1H), 7.64 (d, *J* = 4.9 Hz, 1H), 7.54 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.31-7.27 (m, 2H), 7.17-7.14 (m, 3H), 7.09 (t, *J* = 4.8 Hz, 1H), 6.80 (d, *J* = 11.2 Hz, 1H), 6.58 (s, 1H), 6.00-5.93 (m, 1H), 4.81 (dd, *J* = 15.2, 6.4 Hz, 1H), 3.98 (dd, *J* = 15.6, 8.3 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.4, 139.6, 137.9, 134.6, 133.7 (2C), 133.6, 133.4, 132.8, 130.3, 130.2, 129.4, 128.1, 127.1, 125.1, 124.9, 123.4, 113.2, 110.7, 98.8, 41.7, 21.2; IR (KBr, cm^{-1}): 3100, 2924, 2875, 1554, 1457, 1352, 1161; MS (ES mass): *m*/*z* 484.2 (M-+1).

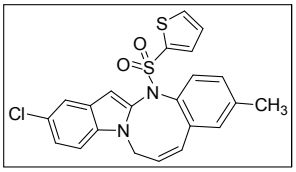
Compound **2d**



2d was prepared according to the general procedure from **1d**.

Light brown solid; yield: 45%; mp: 120-122 °C; R_f (20% EtOAc-*n*-Hexane) 0.36; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56 (s, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.18 (d, *J* = 5.6 Hz, 2H), 7.02 (d, 1H), 6.74 (s, 1H), 6.22-6.16 (m, 1H), 4.82(dd, *J* = 14.4, 6.8 Hz, 1H), 3.94 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.07 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 139.6, 137.8, 134.8, 134.5, 133.4, 133.2, 130.4, 129.9, 129.8, 127.6, 125.8, 124.9, 122.5, 120.3, 110.2, 98.6, 41.6, 40.4, 21.1; MS (ES mass): *m*/*z* 373.3 (M+1).

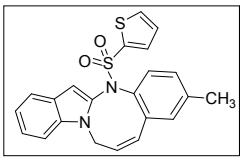
Compound **2e**



2e was prepared according to the general procedure from **1e**.

Light brown solid; yield: 62%; mp: 120-122 °C; R_f (20% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (d, *J* = 3.9 Hz, 1H), 7.72 (d, *J* = 4.8 Hz, 1H), 7.72 (d, *J* = 2.0 Hz, 1H), 7.44-7.41 (m, 1H), 7.38 (d, *J* = 8.8 Hz, 1H), 7.34 (d, *J* = 1.9 Hz, 1H), 7.32 (d, *J* = 5.6 Hz, 2H), 7.27 (t, *J* = 4.0 Hz, 1H), 6.97 (d, *J* = 11.2 Hz, 1H), 6.75 (s, 1H), 6.18-6.11 (m, 1H), 4.97 (dd, *J* = 15.2, 6.8 Hz, 1H), 4.18-4.12 (m, 1H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.5, 139.5, 137.9, 134.7, 133.7, 133.6, 133.4, 133.3, 132.7, 130.3, 130.1, 129.4, 127.4, 127.1, 125.7, 124.9, 122.5, 120.3, 110.3, 98.9, 41.7, 21.2; IR (KBr, cm^{-1}): 2922, 2859, 1734, 1460, 1165; MS (ES mass): *m*/*z* 440.3 (M+1).

Compound **2f**

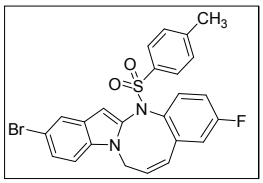


2f was prepared according to the general procedure from **1f**.

Off white solid; yield: 58%; mp: 148-150 °C; R_f (20% EtOAc-*n*-Hexane) 0.43; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.57-7.56 (m, 1H), 7.55 (s, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.26-7.25 (m, 1H), 7.22 (t, *J* = 6.8 Hz, 1H), 7.12 (d, *J* = 5.4 Hz, 2H), 7.10-7.07 (m,

2H), 6.76 (d, *J* = 11.2 Hz, 1H), 6.62 (s, 1H), 6.01-5.94 (m, 1H), 4.86 (dd, *J* = 15.2, 6.1 Hz, 1H), 4.03 (dd, *J* = 15.3, 8.2 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.7, 139.3, 137.8, 135.0, 134.1, 133.8, 133.6, 132.9, 132.6, 130.4, 130.0, 129.3, 127.0, 126.6, 125.5, 122.3, 121.1, 120.1, 109.9, 99.5, 41.6, 21.2; IR (KBr, cm^{-1}): 3092, 3038, 2930, 1546, 1459, 1354; MS (ES mass): *m*/*z* 406.4 (M+1).

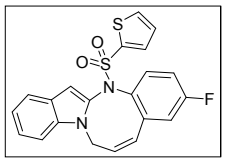
Compound **2g**



2g was prepared according to the general procedure from **1g**.

White solid; yield: 65%; mp: 155-157 °C; R_f (15% EtOAc-*n*-Hexane) 0.23;^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66-7.64 (m, 3H), 7.31-7.27 (m, 4H), 7.14 (d, *J* = 8.8 Hz, 1H), 7.03-6.99 (m, 2H), 6.70 (d, *J* = 11.6 Hz, 1H), 6.42 (s, 1H), 6.04-5.97 (m, 1H), 4.81 (dd, *J* = 15.6, 6.4 Hz, 1H), 3.98 (dd, *J* = 15.2, 8.4 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.4 (d, C-F *J* = 249.2 Hz), 144.2, 140.5 (d, C-F *J* = 8.9 Hz), 136.9, 134.8, 133.6, 132.7 (d, C-F *J* = 3.3 Hz), 132.3, 131.6 (d, C-F *J* = 9.2 Hz), 129.5 (2C), 128.1, 128.0 (2C), 126.2, 125.2, 123.4, 116.5 (d, C-F *J* = 6.1 Hz), 116.2 (d, C-F *J* = 6.0 Hz), 113.3, 110.7, 98.8, 41.7, 21.6; IR (KBr, cm^{-1}): 2923, 2871, 1582, 1460, 1346, 1161; MS (ES mass): *m*/*z* 496.3 (M+1).

Compound **2h**

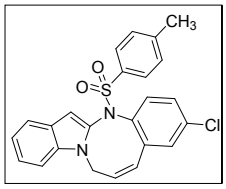


2h was prepared according to the general procedure from **1h**.

Light brown solid; yield: 70%; mp: 120-122 °C; R_f (20% EtOAc-*n*-Hexane) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.60 (m, 2H), 7.40-7.37 (m, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.25 (dd, *J* = 11.8, 4.5 Hz, 1H), 7.16-7.10 (m, 2H), 7.08-7.00 (m, 2H), 6.76 (d, *J* = 11.3 Hz, 1H), 6.63 (s, 1H), 6.10-6.02 (m, 1H), 4.90 (dd, *J* = 15.3, 6.3 Hz, 1H), 4.06 (dd, *J* = 15.3, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.3 (d, C-F *J* = 249.0 Hz), 140.4 (d, C-F *J* = 8.9 Hz), 133.6, 133.5, 133.4 (d, C-F *J* = 5.6 Hz), 132.9, 132.7, 131.6, 131.5 (d, C-F *J* = 9.2 Hz), 129.5,

127.3, 127.0 (d, C-F J = 30.4 Hz), 126.8, 124.1, 120.7, 118.1, 116.5 (d, C-F J = 21.2 Hz), 116.0, 108.9, 99.5, 41.7; IR (KBr, cm^{-1}): 3099, 2918, 1576, 1462, 1358, 1160; MS (ES mass): m/z 410.4 (M+1).

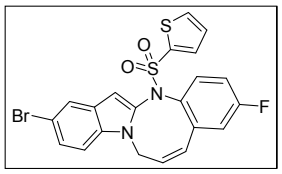
Compound **2i**



2i was prepared according to the general procedure from **1i**.

Off white solid; yield: 54%; mp: 119-121 °C; R_f (20% EtOAc-*n*-Hexane) 0.34; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68-7.64 (m, 3H), 7.34-7.29 (m, 3H), 7.28-7.27 (m, 2H), 7.18 (d, J = 8.6 Hz, 1H), 7.03-6.99 (m, 2H), 6.70 (d, J = 11.0 Hz, 1H), 6.42 (s, 1H), 6.02-5.95 (m, 1H), 4.83 (dd, J = 15.6, 6.4 Hz, 1H), 3.95 (dd, J = 15.4, 8.2 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.2, 140.5, 136.9, 134.8, 133.5, 132.7, 132.3, 131.6, 131.5, 129.5 (2C), 128.1, 128.0 (2C), 126.1, 125.1, 123.4, 116.4, 116.2, 113.2, 110.7, 98.8, 41.7, 21.6; MS (ES mass): m/z 434.9 (M+1).

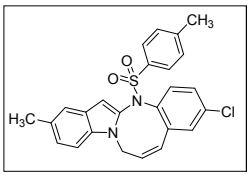
Compound **2j**



2j was prepared according to the general procedure from **1j**.

Off white solid; yield: 60%; mp: 168-170 °C; R_f (20% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.74 (dd, J = 15.1, 3.3 Hz, 2H), 7.61 (d, J = 4.0 Hz, 1H), 7.44-7.41 (m, 1H), 7.38 (dd, J = 8.8, 2.0 Hz, 1H), 7.22 (d, J = 8.8 Hz, 1H), 7.17 (dd, J = 5.7, 3.0 Hz, 1H), 7.13-7.08 (m, 2H), 6.83 (d, J = 11.0 Hz, 1H), 6.63 (s, 1H), 6.11-6.05 (m, 1H), 4.88 (dd, J = 14.9, 6.0 Hz, 1H), 4.04 (dd, J = 15.1, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.5 (d, C-F J = 249.5 Hz), 140.5 (d, C-F J = 9.0 Hz), 140.0, 134.2, 133.9, 133.6, 133.0, 132.4 (d, C-F J = 2.5 Hz), 131.7(d, C-F J = 9.3 Hz), 128.0 127.2, 126.0, 125.3, 123.5, 116.5 (d, C-F J = 8.0 Hz), 116.3 (d, C-F J = 8.3 Hz), 113.3, 110.7, 109.9, 99.1, 41.6; MS (ES mass): m/z 490.8 (M+1).

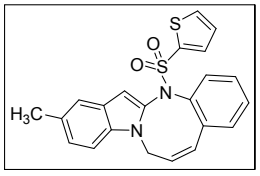
Compound **2k**



2k was prepared according to the general procedure from **1k**.

White solid; yield: 52%; mp: 152-154 °C; R_f (20% EtOAc-*n*-Hexane) 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.40-7.39 (m, 2H), 7.37-7.36 (m, 2H), 7.32-7.31 (m, 2H), 7.24 (d, *J* = 7.6 Hz, 1H), 6.71 (d, *J* = 11.5 Hz, 1H), 6.45 (s, 1H), 6.12-6.05 (m, 1H), 4.91(dd, *J* = 16.4, 5.6 Hz, 1H), 4.17-4.11 (m, 1H), 2.55 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.0, 139.6, 137.4, 134.7, 133.9, 133.5, 131.0, 130.8, 129.9, 129.6, 129.5 (2C), 129.2, 128.1 (2C), 127.8, 127.2, 124.0, 120.7, 117.9, 108.9, 99.4, 41.9, 21.6, 21.3; MS (ES mass): *m*/*z* 448.9 (M+1).

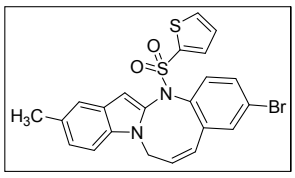
Compound **2l**



2l was prepared according to the general procedure from **1l**.

Off white solid; yield: 55%; mp: 158-160 °C; R_f (25% EtOAc-*n*-Hexane) 0.43; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 5.1 Hz, 1H), 7.57 (d, *J* = 3.0, 1H), 7.40-7.31 (m, 5H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.10-7.03 (m, 2H), 6.78 (d, *J* = 11.6 Hz, 1H), 6.54 (s, 1H), 6.02-5.95 (m, 1H), 4.83 (dd, *J* = 14.8, 6.4 Hz, 1H), 4.04 (dd, *J* = 15.2, 8.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.0, 136.9, 133.6, 133.5, 133.3, 132.5, 132.4, 130.0, 129.5, 129.4, 129.2, 129.0, 128.5, 126.9, 126.8, 125.8, 123.9, 120.7, 108.9, 99.3, 41.8, 21.2; IR (KBr, cm^{-1}): 2922, 2853, 1547, 1482, 1360, 1163; MS (ES mass): *m*/*z* 406.4 (M+1).

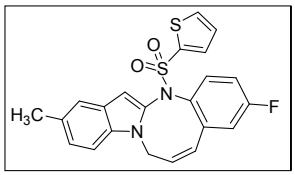
Compound **2m**



2m was prepared according to the general procedure from **1m**.

Off white solid; yield: 51%; mp: 148-150 °C; R_f (20% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.53-7.54 (m, 1H), 7.49-7.43 (m, 2H), 7.35 (d, *J* = 9.2 Hz, 1H), 7.25 (d, *J* = 9.5 Hz, 1H), 7.16 (t, *J* = 8.4 Hz, 1H), 7.11-7.09 (m, 1H), 7.06-7.03 (m, 1H), 6.69 (d, *J* = 11.4 Hz, 1H), 6.51 (s, 1H), 6.04-5.98 (m, 1H), 4.86-4.79 (m, 1H), 4.04 (dd, *J* = 15.4, 8.2 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.3, 139.9, 135.9, 133.8, 133.5, 133.1, 132.9, 132.3, 132.1, 131.3, 313.1, 129.6, 127.4, 127.1, 126.7, 124.2, 123.0, 120.8, 109.0, 99.6, 41.8, 29.7; IR (KBr, cm^{-1}): 3097, 2925, 2858, 1550, 1482, 1362, 1163; MS (ES mass): *m*/*z* 486.3 (M+1).

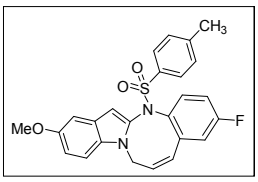
Compound **2n**



2n was prepared according to the general procedure from **1n**.

Off white solid; yield: 63%; mp: 168-170 °C; R_f (20% EtOAc-*n*-Hexane) 0.36; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (d, *J* = 4.8 Hz, 1H), 7.55 (d, *J* = 2.7 Hz, 1H), 7.36 (d, *J* = 8.0Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.11-6.99 (m, 4H), 6.73 (d, *J* = 11.2 Hz, 1H), 6.54 (s, 1H), 6.06-5.98 (m, 1H), 4.85-4.80 (m, 1H), 4.03-3.97 (m, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.3 (d, C-F *J* = 249.0 Hz), 140.4 (d, C-F *J* = 8.9 Hz), 133.6, 133.5, 133.4 (d, C-F *J* = 5.6 Hz), 132.9, 132.7, 131.6, 131.5 (d, C-F *J* = 9.2 Hz), 129.5, 127.3, 127.0 (d, C-F *J* = 30.4 Hz), 126.8, 124.1, 120.7, 118.1, 116.5 (d, C-F *J* = 21.2 Hz), 116.0, 108.9, 99.5, 41.7, 21.2; IR (KBr, cm^{-1}): 2933, 2885, 1532, 1457, 1324, 1158; MS (ES mass): *m*/*z* 425.2 (M+1).

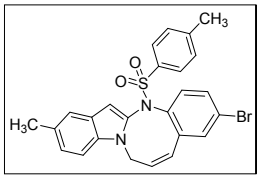
Compound **2o**



2o was prepared according to the general procedure from **1o**.

Off white solid; yield: 64%; mp: 164-166 °C; R_f (20% EtOAc-*n*-Hexane) 0.39; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 3H), 7.16 (d, *J* = 8.8 Hz, 1H), 7.00-6.98 (m, 3H), 6.87 (dd, *J* = 9.2, 2.6 Hz, 1H), 6.65 (d, *J* = 11.2 Hz, 1H), 6.41 (s, 1H), 6.02-5.96 (m, 1H), 4.79 (dd, *J* = 15.6, 6.0 Hz, 1H), 3.98 (dd, *J* = 15.2, 8.0 Hz, 1H), 3.82 (s, 3H) 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.3 (d, C-F *J* = 248.7 Hz), 154.3, 144.0, 137.3, 134.3, 133.1 (d, C-F *J* = 3.0 Hz), 131.7, 131.5 (d, C-F *J* = 9.3 Hz), 130.3, 129.5 (2C), 128.1 (2C), 127.7, 126.9, 126.7, 116.5 (d, C-F *J* = 22.8 Hz), 116.2 (d, C-F *J* = 22.6 Hz), 112.6, 110.2, 102.6, 99.4, 55.8, 41.9, 21.6; MS (ES mass): *m*/*z* 449.2 (M+1).

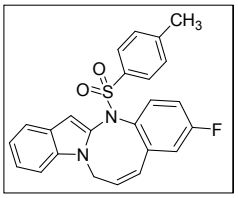
Compound **2p**



2p was prepared according to the general procedure from **1p**.

Off white solid; yield: 52%; mp: 150-152 °C; R_f (25% EtOAc-*n*-Hexane) 0.44; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.45 (t, *J* = 3.8 Hz, 2H), 7.31-7.29 (m, 2H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.16 (dd, *J* = 8.4, 2.6 Hz, 2H), 6.62 (d, *J* = 11.5 Hz, 1H), 6.37 (s, 1H), 6.04-5.96 (m, 1H), 4.83 (dd, *J* = 15.6, 5.6 Hz, 1H), 4.05 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.46 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.2, 136.9, 134.8, 133.5, 132.3, 131.5, 131.2, 129.6, 129.5 (2C), 129.4, 128.0 (2C), 126.1, 125.1, 123.4, 116.4, 116.2, 116.1, 113.2, 110.7, 98.8, 41.7, 29.6, 21.5; MS (ES mass): *m*/*z* 492.8 (M+1).

Compound **2q**

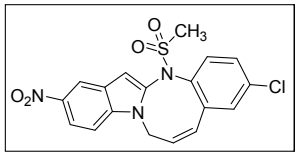


2q was prepared according to the general procedure from **1q**.

Off white solid; yield: 65%; mp: 151-153 °C; R_f (20% EtOAc-*n*-Hexane) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, *J* = 8.4 Hz, 2H), 7.53 (t, *J* = 6.6 Hz, 1H), 7.33-7.25 (m, 5H), 7.23-7.20 (m, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 8.2 Hz, 1H), 6.66 (d, *J* = 11.4 Hz, 1H), 6.46 (s, 1H), 6.04-5.98 (m, 1H), 4.87 (dd, *J* = 15.6, 5.7 Hz, 1H), 4.05 (dd, *J* = 15.5, 8.0 Hz, 1H), 2.45 (s,

3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.3 (d, C-F J = 248.9 Hz), 144.0, 140.4 (d, C-F J = 9 Hz) 137.2, 135.0, 134.0, 133.2 (d, C-F J = 3.3 Hz), 131.7, 131.4 (d, C-F J = 9.2 Hz), 129.5 (2C), 128.1 (2C), 127.7, 126.8, 126.6, 122.4, 121.0 (d, C-F J = 85.4 Hz), 116.6 (d, C-F J = 22.6 Hz), 116.2 (d, C-F J = 22.6 Hz), 109.3, 99.6, 41.7, 21.6; IR (KBr, cm^{-1}): 3064, 2918, 2885, 1578, 1402, 1350, 1162; MS (ES mass): *m*/*z* 419.2 (M+1).

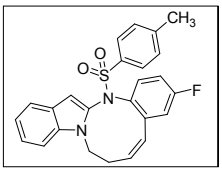
Compound **2r**



2r was prepared according to the general procedure from **1r**.

Light yellow solid; yield: 34%; mp: 168-170 °C; R_f (20% EtOAc-*n*-Hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.55 (d, J = 2.0 Hz, 1H), 8.15 (dd, J = 9.2, 2.1 Hz, 1H), 7.50-7.46 (m, 1H), 7.41-7.35 (m, 3H), 7.04 (d, J = 10.8 Hz, 1H), 6.96 (s, 1H), 6.30-6.23 (m, 1H), 4.93 (dd, J = 14.8, 6.8 Hz, 1H), 4.03 (dd, J = 14.5, 8.4 Hz, 1H), 3.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.1, 139.7, 137.7, 135.9, 135.7, 134.0, 133.9, 131.5, 130.0, 129.5, 125.7, 125.6, 118.1, 118.0, 109.3, 101.1, 40.7, 29.6; MS (ES mass): *m*/*z* 404.2(M+1).

Compound **2s**

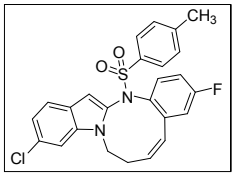


2s was prepared according to the general procedure from **1s**.

Light brown solid; yield: 70%; mp: 170-172 °C; R_f (15% EtOAc-*n*-Hexane) 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 7.6 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.28-7.27 (m, 1H), 7.08 (t, J = 7.6 Hz, 1H), 7.01 (dd, J = 8.8, 2.0 Hz, 1H), 6.82-6.81 (m, 2H), 6.12 (s, 1H), 5.78-5.70 (m, 3H), 4.92-4.87 (m, 1H), 4.59 (dd, J = 11.6, 2.8 Hz, 1H), 3.05 (dd, J = 12.3, 6.0 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.5 (d, C-F J = 250.1 Hz), 144.5, 135.8 (d, C-F J = 3.3 Hz), 135.0, 134.7, 134.1, 132.7, 130.9 (d, C-F J = 10.0 Hz), 130.3, 129.4 (2C), 128.9 (2C), 125.7, 125.1, 122.9, 121.0, 119.9, 117.3 (d, C-F J =

22.2 Hz), 114.3 (d, C-F J = 22.5 Hz), 109.5, 99.5, 37.9, 30.9, 21.6; MS (ES mass): m/z 432.6 (M+1).

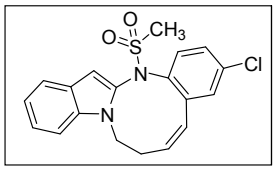
Compound **2t**



2t was prepared according to the general procedure from **1t**.

Light yellow solid; yield: 72%; mp: 210-212 °C; R_f (15% EtOAc-*n*-Hexane) 0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 7.29-7.27 (m, 1H), 7.05-6.99 (m, 2H), 6.79 (d, J = 6.8 Hz, 1H), 6.09 (s, 1H), 5.76-5.69 (m, 3H), 4.88-4.82 (m, 1H), 4.51-4.47 (m, 1H), 3.04 (dd, J = 13.2, 5.6 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.5 (d, C-F J = 250.1 Hz), 144.5, 135.8 (d, C-F J = 3.3 Hz), 135.0, 134.7, 134.1, 132.7, 130.9 (d, C-F J = 10.0 Hz), 130.3, 129.4 (2C), 128.9 (2C), 125.7, 125.1, 122.9, 121.0, 119.9, 117.3 (d, C-F J = 22.2 Hz), 114.3 (d, C-F J = 22.5 Hz), 109.5, 99.5, 37.9, 30.9, 21.6; MS (ES mass): m/z 466.5 (M+1).

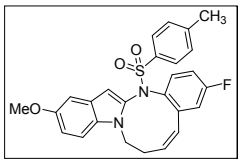
Compound **2u**



2u was prepared according to the general procedure from **1u**.

Off white solid; yield: 54%; mp: 240-242 °C; R_f (20% EtOAc-*n*-Hexane) 0.32; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.31-7.28 (m, 2H), 7.26-7.24 (m, 1H), 7.09 (t, J = 7.6 Hz, 1H), 6.63 (s, 1H), 5.80-5.69 (m, 2H), 5.63 (dd, J = 14.6, 10.2 Hz, 1H), 4.76-4.71 (m, 1H), 4.54 (dd, J = 14.6, 5.6 Hz, 1H), 3.27 (s, 3H), 3.01 (dd, J = 13.2, 6.4 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.5, 138.2, 135.3, 134.3, 134.1, 132.7, 130.9, 130.0, 128.1, 125.7, 125.1, 123.3, 121.1, 120.2, 109.6, 99.5, 37.9, 37.4, 30.7; MS (ES mass): m/z 372.9.

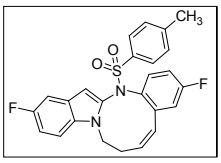
Compound **2v**



2v was prepared according to the general procedure from **1v**.

Off white solid; yield: 68%; mp: 232-234 °C; R_f (20% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.93-6.90 (m, 2H), 6.79 (d, *J* = 6.4 Hz, 2H), 6.03(s, 1H), 5.75-5.65 (m, 3H), 4.89-4.83 (m, 1H), 4.53-4.49 (m, 1H), 3.80 (s, 3H), 3.02 (dd, *J* = 12.4, 6.0 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.4 (d, C-F *J* = 250.0 Hz), 154.1, 144.4, 144.3 (d, C-F *J* = 8.1 Hz), 135.5 (d, C-F *J* = 3.2 Hz), 135.1, 134.7, 132.6, 130.9 (d, C-F *J* =9.1 Hz), 129.4 (2C), 129.3, 128.9 (2C), 125.9, 125.1, 117.3 (d, C-F *J* =22.2 Hz), 114.2 (d, C-F *J* = 22.5 Hz), 113.4, 110.4, 102.5, 99.0, 55.7, 38.0, 30.9, 21.7; MS (ES mass): *m*/*z* 462.5 (M+1).

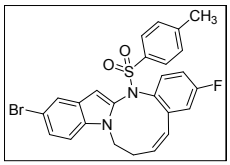
Compound **2w**



2w was prepared according to the general procedure from **1w**.

Off white solid; yield: 61%; mp: 204-206 °C; R_f (15% EtOAc-*n*-Hexane) 0.34; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.32 (dd, *J* = 8.8, 4.4 Hz, 1H), 7.14 (dd, *J* = 9.6, 2.4 Hz, 1H), 7.03-6.98 (m, 2H), 6.79 (d, *J* = 6.8 Hz, 2H), 6.08 (s, 1H), 5.76-5.69 (m, 3H), 4.90-4.84 (m, 1H), 4.56-4.49 (m, 1H), 3.04 (dd, *J* = 13.2, 5.2 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.5 (d, C-F *J* = 249.0 Hz), 158.9 (d, C-F *J* = 233.9 Hz), 144.6, 144.3 (d, C-F *J* = 8.2 Hz), 136.1 (d, C-F *J* = 56.5 Hz), 134.6, 132.9, 130.9 (d, C-F *J* = 9.2 Hz), 130.7, 129.5 (2C), 129.3, 128.8 (2C), 125.8 (d, C-F *J* = 10.4 Hz), 124.8, 117.4 (d, C-F *J* = 22.2 Hz), 114.3 (d, C-F *J* = 22.6 Hz), 111.7 (d, C-F *J* = 26.2 Hz), 110.4 (d, C-F *J* = 9.5 Hz), 105.9 (d, C-F *J* = 23.5 Hz), 99.5 (d, C-F *J* = 4.8 Hz), 38.2, 30.9, 21.7; MS (ES mass): *m*/*z* 450.9 (M+1).

Compound **2x**



2x was prepared according to the general procedure from **1x**.

Off white solid; yield: 65%; mp: 238-240 °C; R_f (20% EtOAc-*n*-Hexane) 0.34; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61-7.58 (m, 3H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.33-7.29 (m, 2H), 7.02 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.81-6.79 (m, 2H), 6.05 (s, 1H), 5.75-5.71 (m, 3H), 4.89-4.83 (m, 1H), 4.54-4.49 (m, 1H), 3.06-3.02 (m, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.2 (d, C-F *J* = 237.0 Hz), 144.7, 135.6 (d, C-F *J* = 38.3 Hz), 134.5, 133.1, 132.7, 130.9 (d, C-F *J* = 9.4 Hz), 129.5 (2C), 129.3, 128.9 (2C), 127.3, 125.9, 124.7, 123.5, 117.5 (d, C-F *J* = 22.5 Hz), 114.4 (d, C-F *J* = 22.2 Hz), 113.0 (d, C-F *J* = 25.3 Hz), 111.1, 109.9, 99.1, 38.2, 30.9, 21.7; MS (ES mass): *m*/*z* 512.9 (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.
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Zebrafish embryo study (apoptotic assay):

Materials and Methods:

Husbandry:

Zebrafish obtained from a local vendor were maintained in in-house built recirculatory system under 14-10hrs light dark cycle and 28˚C temperature as described in (Banote et al., 2013). Breeding was carried out using females and males in ratio of 2:3 and the embryos obtained were collected in petridishes and maintained at 28^0C. (Westerfield et al., 2000, Nakhi et al.,2013).

Apoptosis Assay:

24hpf embryos were de-chorinated manually. 6 embryos were distributed as two sets in each well of 24 well plate with 250 µl of 0.1% DMSO. The working stock solutions were prepared by serial dilution as described earlier. Each well was added with 250µl of respective concentration to obtain final working concentration. Embryos were incubated at 28˚C for 24hrs and 48hrs.

The apoptotic effect was checked at 24 hrs and 48 hrs by washing drug exposed embryos thrice with E3 medium. Acridine orange (2µg/ml) solution of dye in E3 medium was added and incubated for 30 mins. The embryos were rinsed thoroughly twice in fresh E3 medium to wash the acridine orange solution. Stained embryos were anesthetized with tricaine and photographed under UV illumination using Zeiss AxioCamMR camera attached to a Zeiss florescence microscope (GFP filter set : excitation 473,emission 520) under 5X magnification. The Images were taken and analyzed using Image J software.

References

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