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Electronic Supplementary Information

Creation of molecular complexities via a Cu-catalyzed new cascade reaction: A direct access to novel 2,2'-spirobiindole derivatives

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Supporting Information

General Experimental Procedures: S3

X-ray data: S28

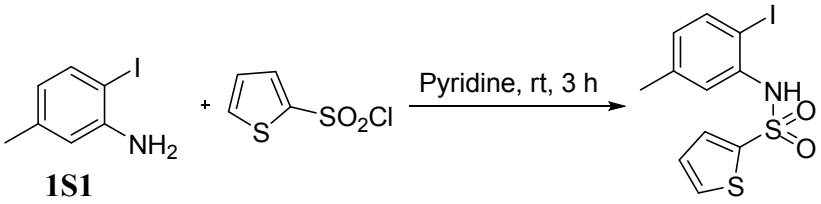
Reference: S29

Copies of Spectra: .....

General Experimental Procedures:

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 a 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). 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.

Procedure for preparation of 3-substituted *N*-(2-iodophenyl)thiophene-2-sulfonamide (1S2):

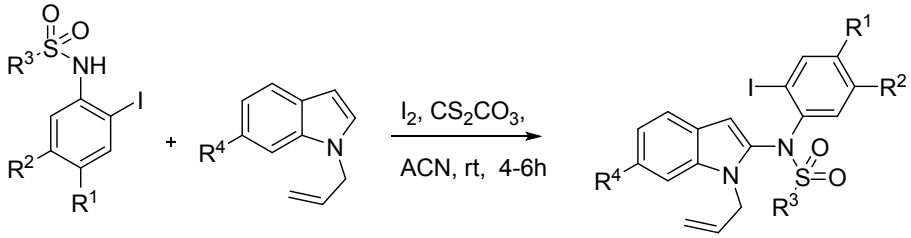


1S1 **1S2**

Thiophene-2-sulfonyl chloride (1.2 mmol) was slowly added to compound **1S1** (1 mmol) in pyridine (5mL) at 0 °C under nitrogen atmosphere. Then, the reaction mixture stirred at rt for 3 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 **1S2.**
Off white solid; yield: 80%; mp: 140-141 °C; R_f (5% EtOAc/*n*-Hexane) 0.62; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57-7.52 (m, 3H), 7.46 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.01 (dd, *J* = 5.2, 4.0 Hz,

1H), 6.79 (s, 1H), 6.72 (dd, J = 7.8, 1.6 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 139.9, 138.6, 136.8, 132.9, 132.8, 128.5, 127.4, 124.1, 88.9, 21.1; MS (ES mass): *m*/*z* 378.0 (M-1).

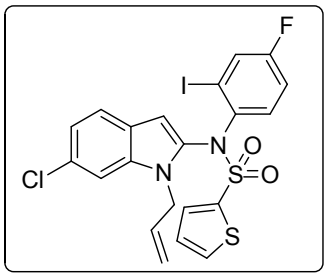
General procedure for the preparation of sulfonamide (1S4):



1S2 **1S3** **1S4**

To a mixture of *N*-(2-iodophenyl)methane/4-methylbenzene/thiophene-2-sulfonamide derivative **1S2** (1.0 mmol)**,** Cs_2CO_3 (1.5mmol), I_2 (1mmol) in acetonitrile (2.5 mL) was added indole derivative **1S3** (1.2 mmol). Then the mixture was stirred at room temperature under nitrogen for 4-6 h. The progress of the reaction was monitored by TLC. Upon completion, the reaction was quenched with a saturation solution of $Na_2S_2O_3$ (5 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under a reduced pressure. The residue was purified by column chromatography over silica gel using ethyl acetate–hexane to give the desired product (**1S4)**.

***N*-(1-allyl-6-chloro-1*H*-indol-2-yl)-*N*-(4-fluoro-2-iodophenyl)thiophene-2-sulfonamide (1S4r)**

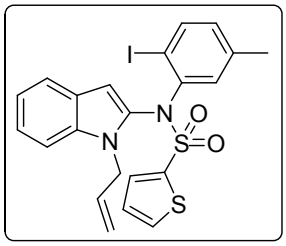


1S4r was prepared according to the general procedure as mentioned above.

Light yellow solid; yield: 48%; mp: 142-144 °C; R_f (20% EtOAc-*n*-Hexane) 0.51; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (dd, J = 5.2, 1.2 Hz, 1H), 7.68 (dd, J = 7.6, 2.8 Hz, 1H), 7.53 (dd, J = 3.6, 0.9 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.34 (dd, J = 9.2, 3.6 Hz, 1H), 7.30 (d, J = 0.4 Hz, 1H),

7.15 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.09 (dd, *J* = 8.8, 1.2 Hz, 1H), 7.06-7.02 (m, 1H), 6.47 (s, 1H), 5.91-5.81 (m, 1H), 5.13-5.08 (m, 3H), 4.88 (d, *J* = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.6 (d, C-F *J* = 254.1 Hz), 138.5 (d, C-F *J* = 3.5 Hz), 136.9, 135.5, 135.2, 134.7, 134.2, 133.4, 131.0 (d, C-F *J* = 8.9 Hz), 129.0, 128.1 (d, C-F *J* = 24.5 Hz), 127.5, 124.2, 122.0, 121.1, 116.8, 116.1 (d, C-F *J* = 22.2 Hz), 111.0, 101.6, 101.2, 46.8; MS (ES mass): *m*/*z* 573.1 (M+1).

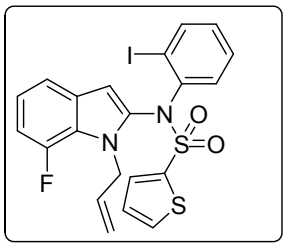
_N_-(1-allyl-6-chloro-1_H_-indol-2-yl)-_N_-(4-fluoro-2-iodophenyl)thiophene-2-sulfonamide (1S4s)



1S4s was prepared according to the general procedure as mentioned above.

Light yellow solid; yield: 50%; mp: 170-172 °C; R_f (20% EtOAc-*n*-Hexane) 0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (d, *J* = 8.0 Hz, 1H), 7.69 (dd, *J* = 4.9, 1.3 Hz, 1H), 7.58-7.54 (m, 2H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.22 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.20-7.18 (m, 1H), 7.15-7.08 (m, 2H), 6.85 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.56 (s, 1H), 5.88-5.78 (m, 1H), 5.16 (d, *J* = 3.5 Hz, 2H), 5.05 (dd, *J* = 10.3, 1.2 Hz, 1H), 4.90 (dd, *J* = 17.2, 1.2 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.9, 140.6, 139.2, 137.5, 135.3, 134.8, 134.2, 133.9, 133.7, 131.2, 131.1, 127.2, 125.8, 122.8, 120.9, 120.1, 116.2, 111.0, 101.0, 97.0, 46.7, 20.8; MS (ES mass): *m*/*z* 535.1 (M+1).

_N_-(1-allyl-1_H_-indol-2-yl)-_N_-(2-iodo-5-methylphenyl)thiophene-2-sulfonamide (1S4t)

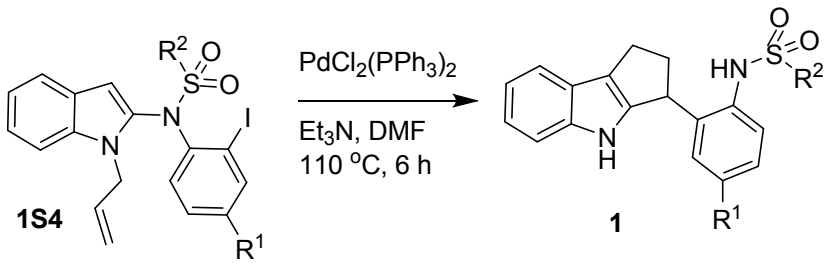


1S4t was prepared according to the general procedure as mentioned above.

Light yellow solid; yield: 47%; mp: 189-191 °C; R_f (15% EtOAc-*n*-Hexane) 0.29; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.70 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.56 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.43 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.35-7.28 (m, 2H), 7.13 (t, *J* = 4.0 Hz, 1H), 7.05-6.95 (m, 2H), 6.90-6.85 (m, 1H), 6.59 (d, *J* = 2.0 Hz, 1H), 5.86-5.76 (m, 1H), 5.22 (d, *J* = 2.4

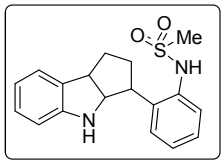
Hz, 2H), 4.86 (dd, *J* = 10.4, 0.9 Hz, 1H), 4.60 (d, *J* = 17.2 Hz, 1H); MS (ES mass): *m*/*z* 539.1 (M+1).

General procedure for the preparation of compound 1:



A mixture of sulfonamide **1S4**, (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 6 h under a nitrogen atmosphere. The progress of the reaction was monitored by TLC. Upon completion, 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 **1**.

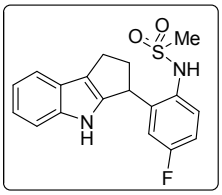
Compound 1a



Compound **1a** was prepared according to above general procedure using **S1a** (R^1 = H, R^2 = Me) as starting compound.

Off white solid; yield: 45%; mp: 187-189 °C; R_f (15% EtOAc-*n*-Hexane) 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (d, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.32-7.27 (m, 2H), 7.26-7.24 (m, 1H), 7.22-7.16 (m, 2H), 7.11-7.07 (m, 1H), 6.44 (s, 1H), 6.07 (s, 1H), 4.87 (t, *J* = 7.9 Hz, 1H), 4.33-4.28 (m, 1H), 4.13-4.06 (m, 1H), 3.17-3.09 (m, 1H), 3.07 (s, 3H), 2.6-2.5 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.7, 137.8, 133.9, 132.9, 132.8, 129.4, 128.0, 127.4, 125.0, 120.8, 120.7, 119.5, 109.6, 93.5, 43.2, 40.2, 39.0, 37.6; MS (ES mass): *m*/*z* 327.1 (M+1).

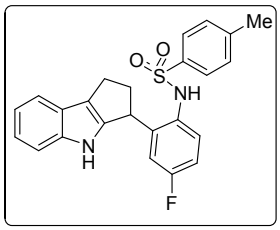
Compound 1f



Compound **1f** was prepared according to above general procedure using **S1f** (R^1 = F, R^2 = Me) as starting compound.

Off white solid; yield: 43%; mp: 160-162 °C; R_f (15% EtOAc-*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.48-7.43 (m, 2H), 7.40-7.31 (m, 2H), 6.95 (td, *J* = 8.8, 1.2 Hz, 1H), 6.18 (bs, 1H), 5.98 (bs, 1H), 4.92 (t, *J* = 8.0 Hz, 1H), 4.3 (td, *J* = 10.0, 3.2 Hz, 1H), 4.08 (dd, *J* = 17.2, 7.6 Hz, 1H), 3.15-3.09 (m, 1H), 3.07 (s, 3H), 2.59-2.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.3 (d, C-F *J* = 241.5 Hz), 143.6, 141.3, 136.6, 128.4, 122.7, 121.3, 119.9, 119.3, 118.3 (d, C-F *J* = 9.6 Hz), 110.9, 109.6 (d, C-F *J* = 24.4 Hz), 105.4 (d, C-F *J* = 25.1 Hz), 92.7, 43.4, 40.2, 39.0, 37.8; MS (ES mass): *m*/*z* 345.1 (M+1).

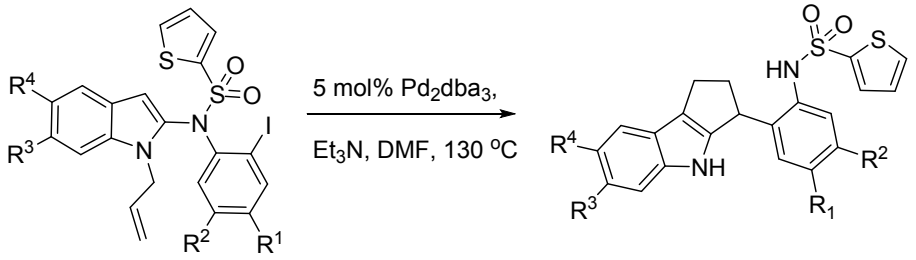
Compound 1g



Compound **1g** was prepared according to above general procedure using **S1g** (R^1 = F, R^2 = C_6H_4Me-*p*) as starting compound.

Off white solid; yield: 30%; mp: 120-122 °C; R_f (15% EtOAc-*n*-Hexane) 0.24; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.28-7.27 (m, 3H), 7.18-7.14 (m, 1H), 7.10-7.08 (m, 1H), 7.07-7.02 (m, 1H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.35 (s, 1H), 5.86 (s, 1H), 4.63 (t, *J* = 8.0 Hz, 1H), 4.23-4.17 (m, 1H), 4.05-3.99 (m, 1H), 3.00-2.92 (m, 1H), 2.43 (s, 3H), 2.38-2.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.9 (d, C-F *J* = 246.3), 145.3, 144.2, 142.4 (d, C-F *J* = 7.3), 136.1, 132.9, 132.6, 129.8 (2C), 129.3 (d, C-F *J* = 3.1), 128.9 (d, C-F *J* = 8.8), 127.3 (2C), 120.8, 120.7, 119.5, 115.5 (d, C-F *J* = 23.5), 114.6 (d, C-F *J* = 22.5), 109.6, 93.6, 43.1, 38.6, 37.7, 21.6; MS (ES mass): *m*/*z* 421.2 (M+1).

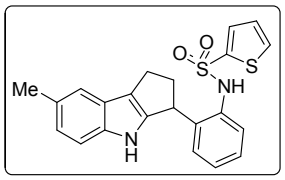
General procedure for preparation of *N*-(2-(8-substituted-1,2,3,4-tetrahydrocyclopenta[b]indol-3-yl)-3-4-substitutedphenyl)thiophene-2-sulfonamide (3.14):



1S4 **1**

A mixture of *N*-(1-allyl-5-substituted-1*H*-indol-2-yl)-*N*-(2-iodo-4-substitutedphenyl)thiophene-2-sulfonamide **1S4**, (0.4mmol), $Pd_2(dba)_3$ (5mol%), and Et_3N (1.2 mmol), in anhydrous DMF (2 mL) was stirred at 130 °C for 7h under a nitrogen atmosphere. The progress of the reaction was monitored by TLC. Upon completion, the mixture was cooled to room temperature and filtered to remove the solid separated. The filtrate was extracted with ethyl acetate (3 x 10 mL).The combined organic phases were washed with brine (20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under a reduced pressure. The residue was purified by column chromatography over silica gel using ethyl acetate-hexane to give the desired product **1**.

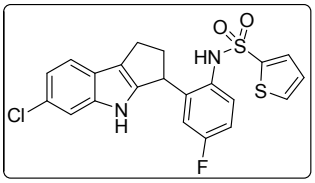
***N*-(2-(7-methyl-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)-phenyl)thiophene-2-sulfonamide (1e)[1]**



1e was prepared from **1S4e** according to the general procedure as presented above.

Off white solid; yield: 68%; mp: 165-167 °C; R_f (15% EtOAc-*n*-Hexane) 0.26; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.46 (d, *J* = 2.4 Hz, 1H), 7.32 (s, 1H), 7.24-7.22 (m, 1H), 7.20-7.18 (m, 2H), 7.16-7.11 (m, 2H), 7.06 (t, *J* = 4.2 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.55 (s, 1H), 5.85 (s, 1H), 4.64 (t, *J* = 8.0 Hz, 1H), 4.23-4.17 (m, 1H), 4.06-3.99 (m, 1H), 2.99-2.91 (m, 1H), 2.44 (s, 3H), 2.37-2.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.5, 140.1, 138.2, 133.3, 133.2, 132.9, 132.5, 131.1, 129.0, 128.7, 127.7, 127.6, 127.4, 125.8, 122.4, 120.5, 109.2, 93.0, 43.2, 38.9, 37.5, 21.5; MS (ES mass): *m*/*z* 409.1 (M+1).

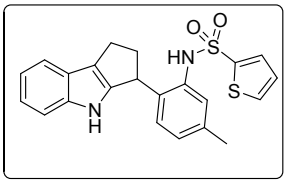
***N*-(2-(6-chloro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)-4-fluorophenyl)thiophene-2-sulfonamide (1r)**



1r was prepared from **1S4r** according to the general procedure as presented above.

Off white solid; yield: 65%; mp: 148-150 °C; R_f (20% EtOAc-*n*-Hexane) 0.26; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.49 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.28 (d, *J* = 1.5 Hz, 1H), 7.12-7.04 (m, 3H), 6.92-6.83 (m, 2H), 6.69 (s, 1H), 5.93 (s, 1H), 4.77 (t, *J* = 8.0 Hz, 1H), 4.22-4.16 (m, 1H), 4.04-3.97 (m, 1H), 3.09-2.99 (m, 1H), 2.39-2.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.2 (C-F *J* = 247.1 Hz), 146.3, 142.9 (C-F *J* = 7.5 Hz), 139.4, 133.2, 132.9, 132.8, 131.3, 129.1 (C-F *J* = 8.7 Hz), 128.9 (C-F *J* = 3.0 Hz), 127.6, 126.6, 121.5, 120.1, 115.5 (C-F *J* = 23.3 Hz), 114.8 (C-F *J* = 22.6 Hz), 109.6, 93.8, 43.1, 38.4, 37.9; MS (ES mass): *m*/*z* 447.1 (M+1).

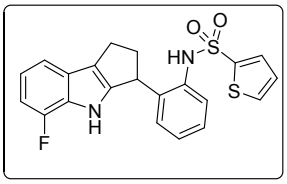
***N*-(5-methyl-2-(1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (1s)**



1s was prepared from **1S4s** according to the general procedure as presented above.

Off white solid; yield: 70%; mp: 211-213 °C; R_f (20% EtOAc-*n*-Hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.47 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.11-7.05 (m, 3H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.50 (s, 1H), 5.91 (s, 1H), 4.60 (t, *J* = 7.9 Hz, 1H), 4.24-4.18 (m, 1H), 4.06-4.00 (m, 1H), 2.98-2.88 (m, 1H), 2.38-2.29 (m, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.7, 140.0, 137.7, 135.1, 133.0, 132.9, 132.8, 132.6, 132.4, 128.6, 128.4, 127.3, 126.4, 120.6 (2C), 119.4, 109.5, 93.4, 43.1, 38.4, 37.6, 20.9; MS (ES mass): *m*/*z* 409.1 (M-+1).

***N*-(2-(5-fluoro-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)phenyl)thiophene-2-sulfonamide (1t)**



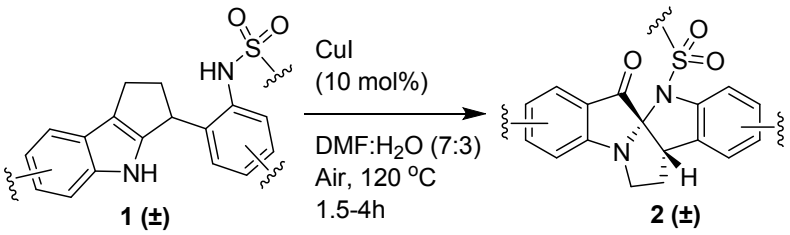
1t was prepared from **1S4t** according to the general procedure as presented above.

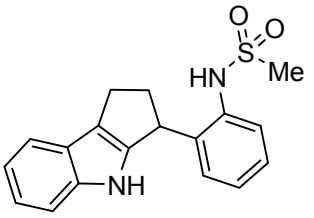
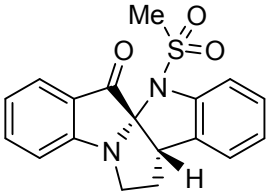
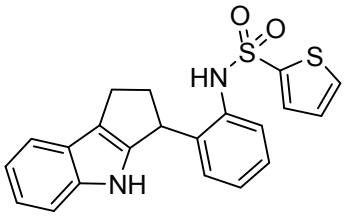
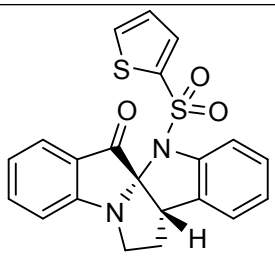
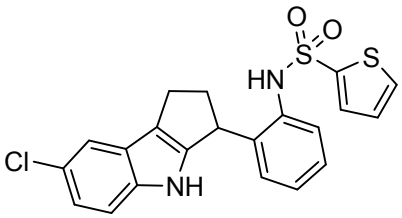
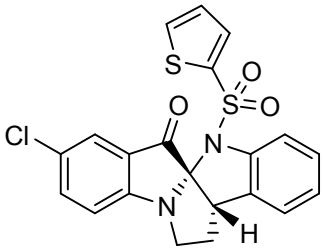
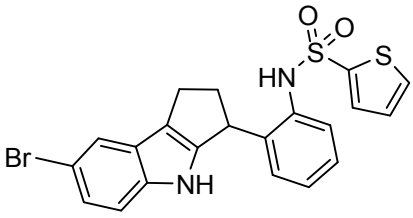
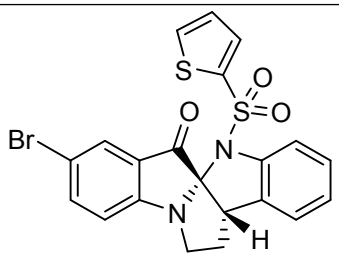
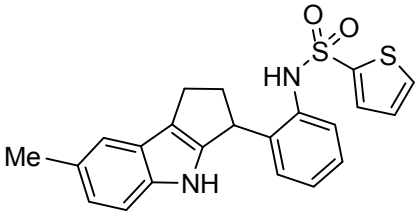
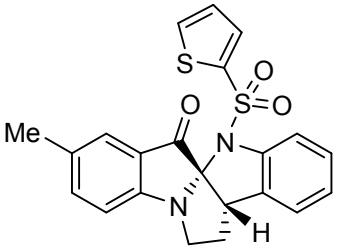
Off white solid; yield: 71%; mp: 172-173 °C; R_f (15% EtOAc-*n*-Hexane) 0.19; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.48 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.27-7.26 (m, 1H), 7.20-7.18 (m, 3H), 7.15-7.13 (m, 1H), 7.08-7.06 (m, 1H), 6.97-6.92 (m, 1H), 6.85-6.81 (m, 1H), 6.51 (s, 1H), 5.96-5.94 (m, 1H), 4.71 (t, *J* = 8.4 Hz, 1H), 4.48-4.42 (m, 1H), 4.30-4.22 (m, 1H), 3.02-2.93 (m, 1H), 2.41-3.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.8 (C-F *J* = 241.7 Hz), 146.9, 139.7, 138.7, 136.5 (C-F *J* = 5.9 Hz), 133.1, 133.0, 132.6, 128.8, 127.9, 127.7, 127.5, 126.3, 119.6 (C-F *J* = 6.2 Hz), 116.4, 116.4, 105.9 (C-F *J* = 16.2 Hz), 94.1 (C-F *J* = 1.8 Hz), 45.3, 38.2, 38.1; MS (ES mass): *m*/*z* 411.2 (M-1).

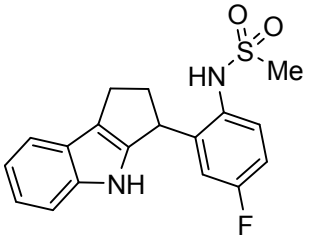
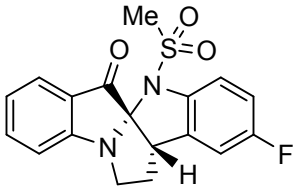
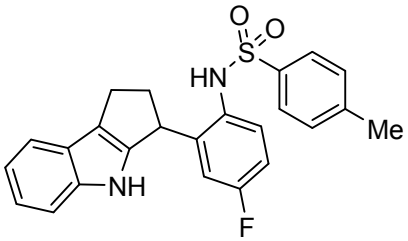
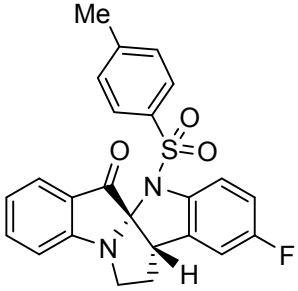
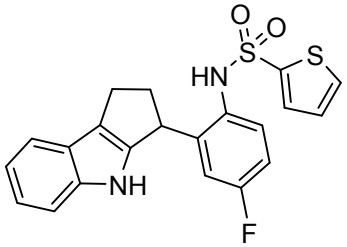
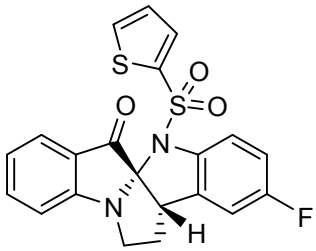
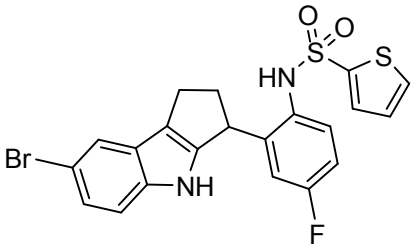
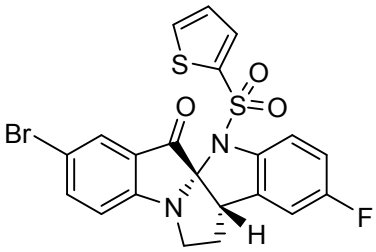
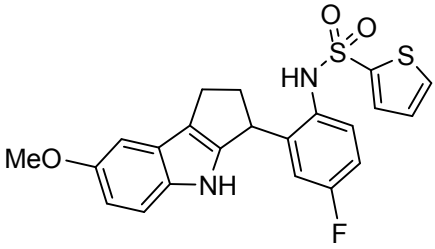
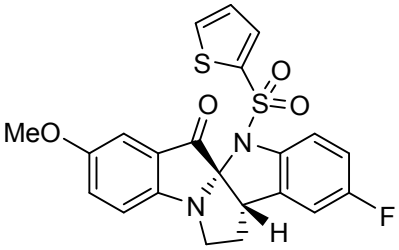
General procedure for preparation of 2,2'-spirobi[indolin]-3-one derivatives (2):

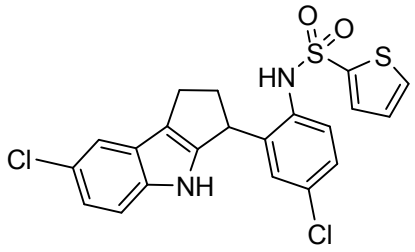
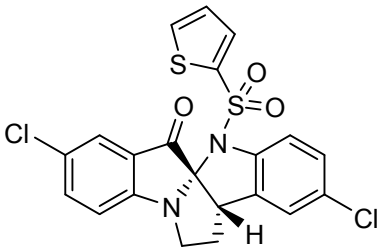
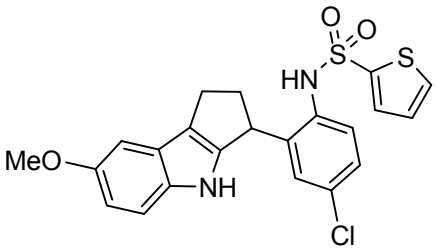
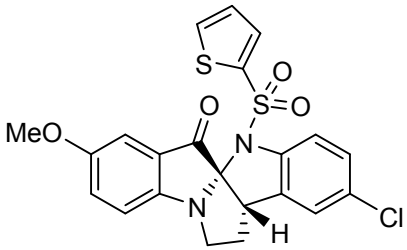
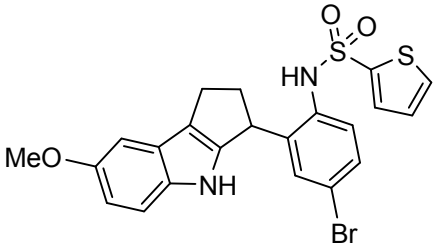
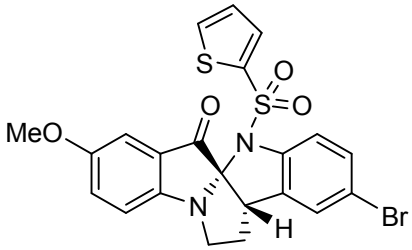
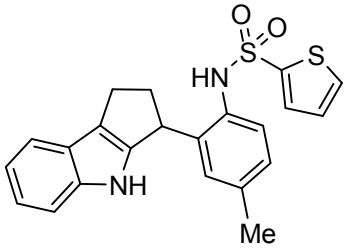
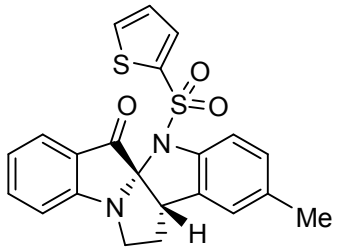
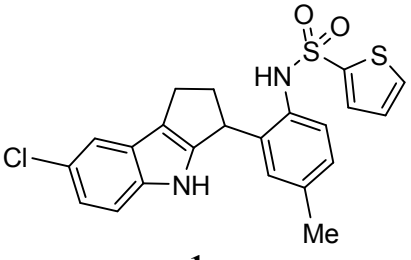
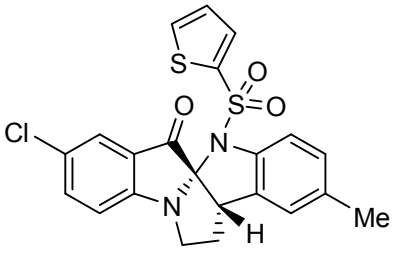
A round bottom (RB) flask containing the compound **1** in DMF:H_2O (7:3) was fitted with a condenser through which cold water was circulated. Then 10 mol% of CuI was added and the reaction mixture was stirred for 1.5-4 h at 120 °C in the presence of open air (the top end of the water condenser was kept open to allow free exchange of air). The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled to room temperature and filtered to remove the solid separated. The filtrate was extracted with ethyl acetate (3 x 10 mL). The combined organic phases were collected, 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 **2**.

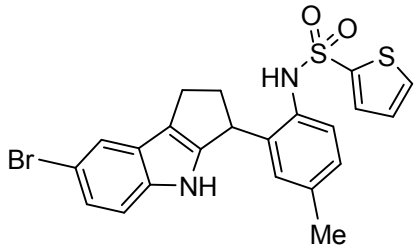
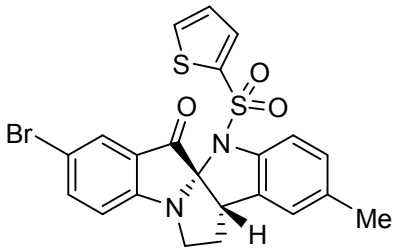
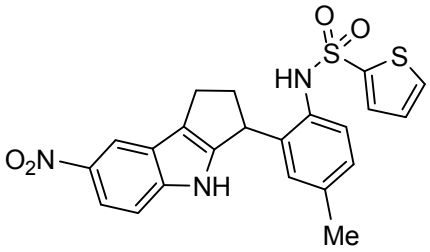
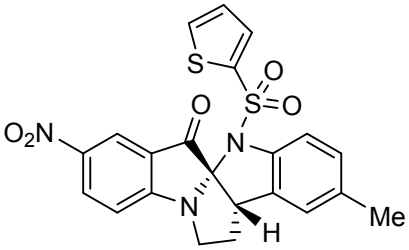
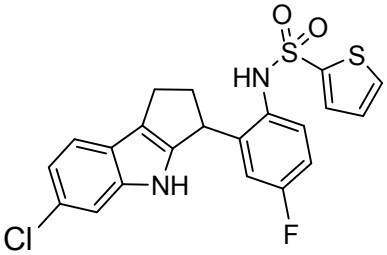
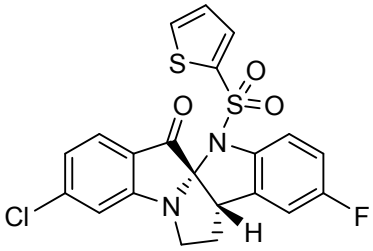
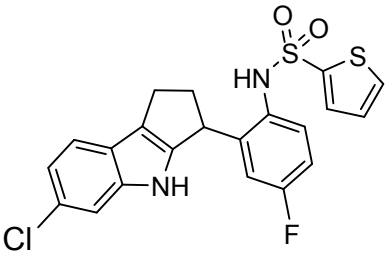
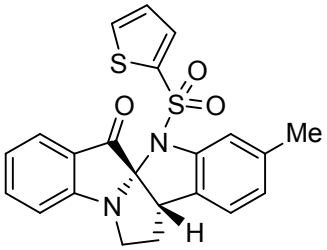
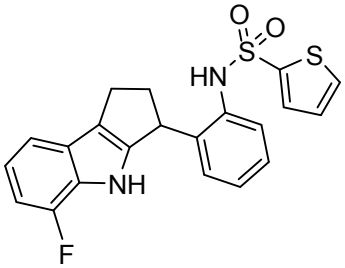
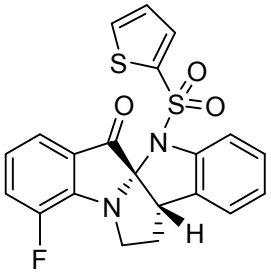
Table S1: Cu catalyzed synthesis of 2,2'-spirobi[indolin]-3-one derivatives.[a]



S.No.	Compound (**1**)	Product (**2**)	Time (h)	Yield[b] (%)
1	 **1a**	 **2a**	2	66
2	 **1b**	 **2b**	1.5	66
3	 **1c**	 **2c**	1.5	72
4	 **1d**	 **2d**	2	59
5	 **1e**	 **2e**	2	63

6	 **1f**	 **2f**	1.5	54
7	 **1g**	 **2g**	2	65
8	 **1h**	 **2h**	1.5	64
9	 **1i**	 **2i**	2	60
10	 **1j**	 **2j**	1.5	66

11	 **1k**	 **2k**	2	52
12	 **1l**	 **2l**	1.5	62
13	 **1m**	 **2m**	1.5	64
14	 **1n**	 **2n**	2	61
15	 **1o**	 **2o**	1.5	63

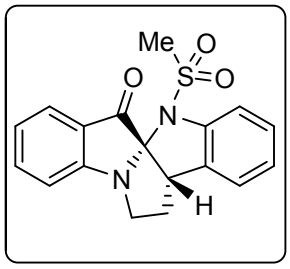
16	 **1p**	 **2p**	2	57
17	 **1q**	 **2q**	4	42
18	 **1r**	 **2r**	4	56
19	 **1s**	 **2s**	3	60
20	 **1t**	 **2t**	3	35

[a]All the reactions were performed using **1** (0.1 mmol), 10 mol% of CuI in DMF+H_2O (7:3) (1.5 mL) at 120 °C for 1.5-4h in the presence of air.

[b]Isolated yield.

Spectral data of compound 2:

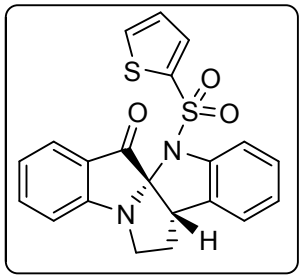
Compound 2a



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

Light yellow solid; yield: 66%; mp: 201-203 °C; R_f (15% EtOAc-*n*-Hexane) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 7. 6 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.10-7.02 (m, 3H), 3.97 (d, *J* = 8.0 Hz, 1H), 3.70 (dd, *J* = 12. 4, 6.0 Hz, 1H), 3.26-3.20 (m, 1H), 3.18 (s, 3H), 2.15-2.07 (m, 1H), 2.03 (dd, *J* = 12.8, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.2, 161.5, 142.4, 137.8, 129.6, 129.1, 125.3, 124.9, 123.6, 123.3, 122.4, 113.9, 111.9, 95.9, 50.3, 49.9, 39.7, 32.6; HPLC: 96.4%; column: Symmetry C-18 250*4.6 mm, 5µm, mobile phase A: 5mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 12.23 min; MS (ES mass): *m/z* 341.0 (M+1); HRMS: *m/z* calcd for $C_{18}H_{17}O_3N_2S$ $[M + H]^+$ 341.09554, found 341.09512.

Compound 2b

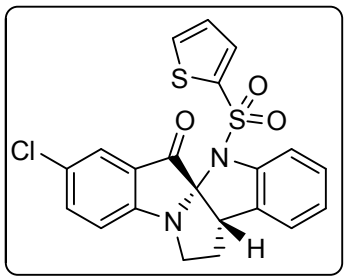


Compound **2b** was prepared from **1b** according to the above general procedure.

Light yellow solid; yield: 66%; mp: 217-219 °C; R_f (20% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 8.00 Hz, 1H), 7.58 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.25-7.23 (m, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.07-7.02 (m, 3H), 3.95 (d, *J* = 8.4 Hz, 1H), 3.58 (dd, *J* = 12.4, 6.8 Hz, 1H), 2.90 (td, *J* = 12.4, 6.8 Hz, 1H), 2.12-2.04 (m, 1H), 1.96 (dd, *J* = 12.4, 4.8 Hz,

1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.2, 161.4, 141.6, 139.1, 137.6, 134.6, 133.4, 129.7, 128.7, 126.7, 125.1, 124.9, 123.7, 123.6, 122.3, 113.6, 112.7, 95.9, 50.2, 49.7, 32.6; HPLC: 97.8%; column: Symmetry C-18 250*4.6 mm, 5µm, mobile phase A: 0.1 % 5mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 13.14 min; IR (KBr, cm^{-1}): 3399, 2926, 1718, 1604, 1469, 1356, 1163; MS (ES mass): *m/z* 409.1 (M+1); HRMS: *m/z* calcd for $C_{21}H_{17}O_3N_2S_2$ $[M + H]^+$ 409.06751, found 409.06598.

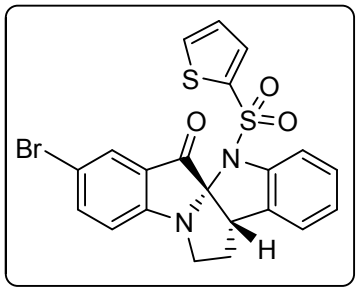
Compound 2c



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

Light yellow solid; yield: 72%; mp: 231-233 °C; R_f (20% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 1.6 Hz, 1H), 7.59-7.55 (m, 2H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.25-7.22 (m, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 7.06-6.99 (m, 3H), 3.94 (d, *J* = 8.0 Hz, 1H), 3.53 (dd, *J* = 12.4, 6.8 Hz, 1H), 2.90 (td, *J* = 12.4, 5.2 Hz, 1H), 2.12-2.02 (m, 1H), 1.97 (dd, *J* = 12.8, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.1, 159.6, 141.4, 138.9, 137.4, 134.6, 133.5, 129.4, 128.8, 127.9, 126.8, 124.9, 124.7, 124.5, 123.8, 114.9, 112.6, 96.1, 50.3, 49.7, 32.7; HPLC: 99.1%; column: Symmetry C-18 250*4.6 mm, 5µm, mobile phase A: 5mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 13.8 min; IR (KBr, cm^{-1}): 2927, 1729, 1607, 1466, 1358, 1167; MS (ES mass): *m/z* 442.3 (M+1); HRMS: *m/z* calcd for $C_{21}H_{16}O_3N_2ClS_2$ $[M + H]^+$ 443.02854, found 443.02747.

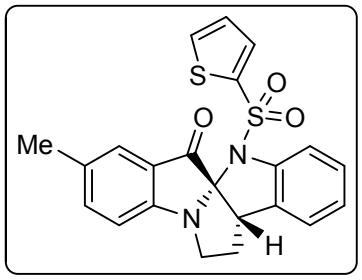
Compound 2d



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

Light yellow solid; yield: 59%; mp: 219-221 °C; R_f (15% EtOAc-*n*-Hexane) 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 2.0 Hz, 1H), 7.81 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.70 (dd, *J* = 8.4, 2.00 Hz, 1H), 7.59 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.25-7.23 (m, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 4.0 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 3.94 (d, *J* = 8.0 Hz, 1H), 3.53 (dd, *J* = 12.4, 6.4 Hz, 1H), 2.94-2.88 (m, 1H), 2.11-2.01 (m, 1H), 1.98 (dd, *J* = 12.8, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.8, 159.9, 141.5, 140.1, 139.1, 134.5, 133.4, 129.4, 128.8, 127.6, 126.8, 125.2, 124.9, 123.8, 115.2, 114.9, 112.6, 95.9, 50.2, 49.7, 32.7; HPLC: 99.0%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.16 min; IR (KBr, cm^{-1}): 2967, 1725, 1467, 1353, 1157; MS (ES mass): *m/z* 488.3 (M+1); HRMS: *m/z* calcd for $C_{21}H_{16}O_3N_2BrS_2$ $[M + H]^+$ 486.97802, found 486.97598.

Compound 2e

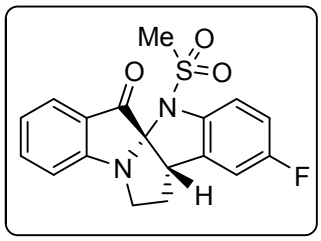


Compound **2e** was prepared from **1e** according to the above general procedure..

Light yellow solid; yield: 63%; mp: 145-147 °C; R_f (15% EtOAc-*n*-Hexane) 0.24; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, *J* = 3.2 Hz, 1H), 7.57 (d, *J* = 4.8 Hz, 1H), 7.54 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.24-7.22 (m, 1H), 7.14 (d, *J* = 7.2 Hz, 1H), 7.06-7.01 (m, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 3.92 (d, *J* = 8.0 Hz, 1H), 3.52 (dd, *J* = 12.0, 6.4 Hz, 1H), 2.86 (dd, *J* = 12.4, 4.8 Hz, 1H),

2.37 (s, 3H), 2.09-2.01 (m, 1H), 1.94 (dd, J = 13.2, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.4, 159.6, 141.7, 139.2, 138.9, 134.6, 133.4, 132.1, 129.8, 128.7, 126.7, 124.9, 124.7, 123.7, 123.6, 113.5, 112.7, 96.2, 50.3, 49.7, 31.9, 29.7; HPLC: 90.4%; column: Symmetry C-18 250*4.6 mm, 5µm, mobile phase A: 0.1 % 5mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 13.49 min; MS (ES mass): *m/z* 423.1 (M+1); HRMS: *m/z* calcd for $C_{22}H_{19}O_3N_2S_2$ $[M + H]^+$ 423.08316, found 423.08314.

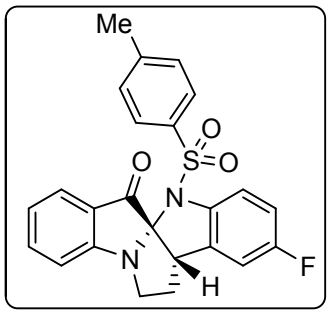
Compound 2f



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

Light yellow solid; yield: 54%; mp: 188-190 °C; R_f (20% EtOAc-*n*-Hexane) 0.24; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, J = 7.2 Hz, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.38-7.35 (m, 1H), 7.10-6.99 (m, 3H), 6.94 (d, J = 7.6 Hz, 1H), 3.95 (d, J = 8.0 Hz, 1H), 3.75-3.70 (m, 1H), 3.27-3.20 (m, 1H), 3.16 (s, 3H), 2.19-2.08 (m, 1H), 2.03-2.00 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:196.9, 161.4, 160.8 (d, C-F J = 241.1), 138.4 (d, C-F J = 2.1), 137.9, 125.0, 123.2, 122.6, 116.6 (d, C-F J = 22.7), 115.7 (d, C-F J = 23.3), 113.9, 112.8 (d, C-F J = 8.2), 112.7 (d, C-F J = 24.3), 96.3, 50.3, 49.7, 39.6, 32.5; HPLC: 96.8%; column: Symmetry C-18 250*4.6 mm, 5µm, mobile phase A: 5mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 12.34 min; MS (ES mass): *m/z* 358.6 (M+1); HRMS: *m/z* calcd for $C_{18}H_{16}O_3N_2FS$ $[M + H]^+$ 359.08602, found 359.08619.

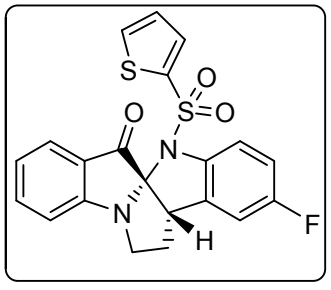
Compound 2g



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

Off white solid; yield: 65%; mp: 228-230 °C; R_f (20% EtOAc-*n*-Hexane) 0.28; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.30-7.27 (m, 3H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.90 (td, *J* = 8.8, 2.8 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 3.88 (d, *J* = 8.4 Hz, 1H), 3.54 (dd, *J* = 12.4, 6.4 Hz, 1H), 2.80 (td, *J* = 12.8, 5.2 Hz, 1H), 2.41 (s, 3H), 2.09-2.01 (m, 1H), 1.91 (dd, *J* = 8.0, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:197.2, 161.1, 144.1, 138.2 (d, C-F *J* = 2.5), 137.7, 136.2, 129.3 (2C), 128.2 (2C), 125.1, 123.3, 122.3, 115.3 (d, C-F *J* = 23.3), 113.4, 113.0, 112.9, 112.3, 112.1, 96.1, 49.7, 49.5, 32.7, 21.6; HPLC: 99.3%; column: Symmetry C-18 250*4.6 mm, 5µm, mobile phase A: 5mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 13.71 min; IR (KBr, cm^{-1}): 3072, 2938, 1732, 1474, 1361, 1161; MS (ES mass): *m/z* 435.2 (M+1); HRMS: *m/z* calcd for $C_{24}H_{20}O_3N_2FS$ $[M + H]^+$ 435.11732, found 435.11597.

Compound 2h

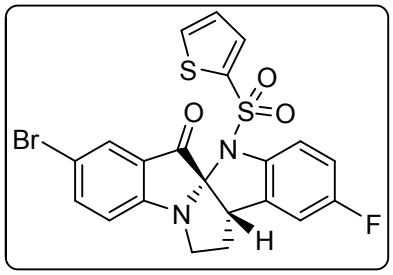


Compound **2h** was prepared from **1h** according to the above general procedure.

Light yellow solid; yield: 64%; mp: 208-210 °C; R_f (20% EtOAc-*n*-Hexane) 0.29; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (s, 1H), 7.76 (d, *J* = 6.8 Hz, 1H), 7.67-7.61 (m, 2H), 7.41 (d, *J* = 7.6, 4.0 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 7.08-7.06 (m, 2H), 6.99-6.94 (m, 1H), 6.89 (d, *J* = 6.4 Hz,

1H), 3.93 (d, *J* = 8.0 Hz, 1H), 3.62-3.57 (m, 1H), 2.92-2.85 (m, 1H), 2.10-2.06 (m, 1H), 1.97-1.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:196.9, 161.3, 160.8 (d, C-F *J* = 241.2), 138.8, 137.8, 137.6 (d, C-F *J* = 2.1), 134.6, 133.5, 131.6 (d, C-F *J* = 8.1), 126.8, 125.2, 123.4, 122.5, 115.5 (d, C-F *J* = 23.3), 113.5, 113.5 (d, C-F *J* = 8.2), 112.7 (d, C-F *J* = 24.2), 96.2, 50.2, 49.5, 32.5; HPLC: 97.9%; column: Symmetry C-18 250*4.6 mm, 5µm, mobile phase A: 0.1 % 5mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 13.24 min; MS (ES mass): *m*/*z* 427.1 (M+1).

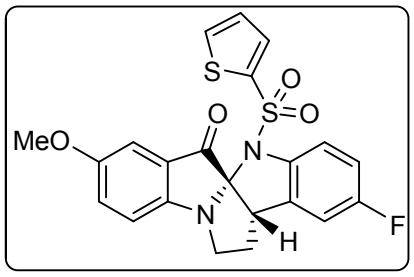
Compound 2i



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

Light yellow solid; yield: 60%; mp: 220-222 °C; R_f (15% EtOAc-*n*-Hexane) 0.19; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 1.9 Hz, 1H), 7.78 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.70 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.61 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.39 (dd, *J* = 8.8, 4.0 Hz, 1H), 7.04 (t, *J* = 4.4 Hz, 1H), 6.97-6.92 (m, 2H), 6.87 (dd, *J* = 7.6, 1.6 Hz, 1H), 3.92 (d, *J* = 8.4 Hz, 1H), 3.54 (dd, *J* = 12.4, 6.8 Hz, 1H), 2.92-2.84 (m, 1H), 2.12-2.02 (m, 1H), 1.95 (dd, *J* = 12.8, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.5, 159.8, 140.2, 138.6, 137.4, 134.6, 133.6, 131.2 (d, C-F *J* = 7.9), 127.7, 126.8, 125.0, 115.6, 115.4, 115.2, 115.1, 113.4 (d, C-F *J* = 8.4), 112.4 (d, C-F *J* = 24.3), 96.2, 50.2, 49.5, 32.5; HPLC: 95.9%; column: Symmetry C-18 75*4.6 mm, 3µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 235 nm, retention time 3.96 min; IR (KBr, cm^{-1}): 2918, 1732, 1434, 1335, 1163; MS (ES mass): *m*/*z* 504.9 (M+1); HRMS: *m/z* calcd for $C_{21}H_{14}O_3N_2BrFS_2$ $[M + H]^+$ 504.96860, found 504.96989.

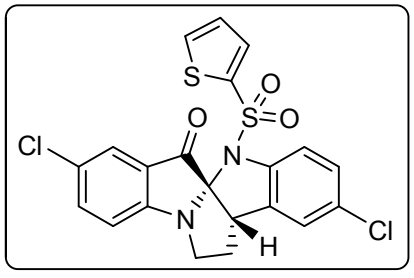
Compound 2j



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

Light yellow solid; yield: 66%; mp: 200-202 °C; R_f (20% EtOAc-*n*-Hexane) 0.27; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.60 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.40 (dd, *J* = 8.8, 4.4 Hz, 1H), 7.28-7.26 (m, 1H), 7.18 (d, *J* = 2.8 Hz, 1H), 7.03 (t, *J* = 4.0 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.94 (td, *J* = 8.8, 2.0 Hz, 1H), 6.86 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.90 (d, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 3.50 (dd, *J* = 12.4, 6.4 Hz, 1H), 2.85 (td, *J* = 12.8, 5.0 Hz, 1H), 2.10-2.01 (m, 1H), 1.92 (dd, *J* = 12.8, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:197.1, 160.8 (d, C-F *J* = 241.3), 156.3, 155.7, 138.8, 137.7, 134.7, 133.6, 131.6 (d, C-F *J* = 8.0), 127.7, 126.7, 123.8, 115.5 (d, C-F *J* = 23.4), 115.0, 113.5 (d, C-F *J* = 8.3), 112.4 (d, C-F *J* = 24.2), 105.4, 96.9, 55.8, 50.5, 49.7, 32.2; HPLC: 94.2%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 4.93 min; IR (KBr, cm^{-1}): 3064, 2935, 1735, 1465, 1365, 1159; MS (ES mass): *m/z* 457.0 (M+1); HRMS: *m/z* calcd for $C_{22}H_{17}O_4N_2FS_2$ $[M + H]^+$ 457.06865, found 457.06889.

Compound 2k

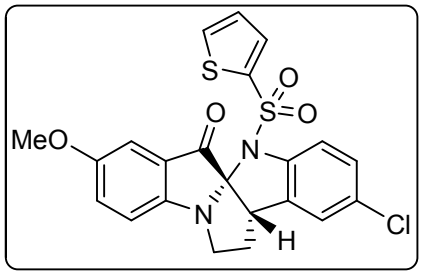


Compound **2k** was prepared from **1k** according to the above general procedure.

Light yellow solid; yield: 52%; mp: 284-286 °C; R_f (20% EtOAc-*n*-Hexane) 0.20; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80-7.79 (m, 1H), 7.70 (d, *J* = 2.00 Hz, 1H), 7.62 (d, *J* = 5.2 Hz, 1H), 7.58 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.23 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.14 (s, 1H), 7.05

(t, J = 4.0 Hz, 1H), 7.01 (d, J = 8.8 Hz, 1H), 3.92 (d, J = 12.8, 6.8 Hz, 1H), 2.93-2.85 (m, 1H), 2.89 (s, 1H), 2.12-2.03 (m, 1H), 1.98 (dd, J = 12.8, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.6, 159.5, 140.2, 137.6, 134.8, 133.8, 131.4, 129.1, 128.9, 128.1, 126.9, 125.2, 124.6, 124.5, 122.9, 114.9, 113.6, 96.4, 50.3, 49.4, 32.6; HPLC: 96.5%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.20 min; IR (KBr, cm^{-1}): 2967, 1746, 1452, 1342, 1144; MS (ES mass): m/z 476.9 (M+1); HRMS: m/z calcd for $C_{21}H_{14}O_3N_2Cl_2S_2$ $[M + H]^+$ 476.98957, found 476.99155.

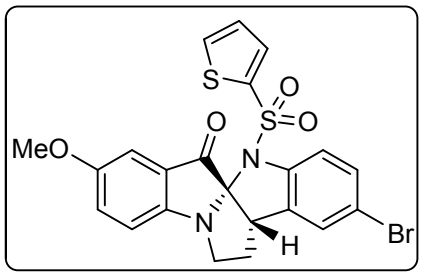
Compound 2l



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

Light yellow solid; yield: 62%; mp: 226-228 °C; R_f (20% EtOAc-*n*-Hexane) 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (dd, J = 4.0, 1.2 Hz, 1H), 7.61 (dd, J = 5.2, 1.2 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.29-7.27 (m, 1H), 7.22-7.20 (m, 1H), 7.18 (d, J = 2.8 Hz, 1H), 7.13 (s, 1H), 7.05-7.03 (m, 1H), 7.00 (d, J = 8.8 Hz, 1H), 3.91 (d, J = 8.4 Hz, 1H), 3.83 (s, 3H), 3.51 (dd, J = 12.4, 7.2 Hz, 1H), 2.89-2.81 (m, 1H), 2.10-2.02 (m, 1H), 1.93 (dd, J = 12.8, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.9, 156.3, 155.7, 140.4, 138.8, 134.8, 133.7, 131.7, 128.9, 128.8, 127.7, 126.7, 125.1, 123.8, 114.9, 113.6, 105.5, 96.9, 55.8, 50.5, 49.6, 32.2; HPLC: 99.3%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; UV 235 nm, retention time 9.37 min; MS (ES mass): m/z 473.0 (M+1).

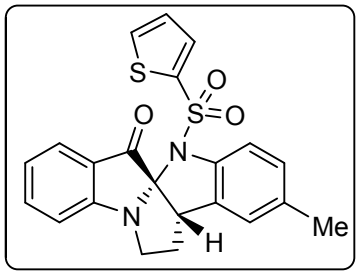
Compound 2m



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

Light yellow solid; yield: 64%; mp: 235-237 °C; R_f (20% EtOAc-*n*-Hexane) 0.21; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.61 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.37-7.32 (m, 2H), 7.28-7.27 (m, 2H), 7.18 (d, *J* = 2.4 Hz, 1H), 7.04 (t, *J* = 4.8 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 1H), 3.91 (d, *J* = 8.4 Hz, 1H), 3.83 (s, 3H), 3.51 (dd, *J* = 12.4, 6.8 Hz, 1H), 2.89-2.81 (m, 1H), 2.12-2.02 (m, 1H), 1.94 (dd, *J* = 12.8, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.9, 156.3, 155.7, 140.9, 138.6, 134.8, 133.7, 132.0, 131.6, 127.9, 127.7, 126.7, 123.8, 116.2, 114.9, 114.1, 105.4, 96.8, 55.8, 50.5, 49.5, 32.2; HPLC: 97.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 2/20, 10/95, 20/95, 22/20, 25/20; flow rate: 1.0 mL/min; UV 235 nm, retention time 9.52 min; IR (KBr, cm^{-1}): 3087, 2943, 1732, 1454, 1342, 1161; MS (ES mass): *m*/*z* 518.8 (M+1).

Compound 2n

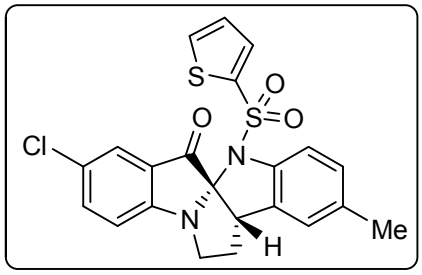


Compound **2n** was prepared from **1n** according to the above general procedure.

Light yellow solid; yield: 61%; mp: 262-264 °C; R_f (20% EtOAc-*n*-Hexane) 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 8.4 Hz, 1H), 7.56 (dd, *J* = 5.2, 1.6 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.07-7.00 (m, 3H), 6.96 (s, 1H), 3.90 (d, *J* = 8.4 Hz, 1H), 3.55 (dd, *J* = 12.4, 6.4 Hz, 1H), 2.88 (td, *J* = 12.4, 5.2 Hz, 1H), 2.29 (s, 3H), 2.08-2.00 (m, 1H), 1.93 (dd, *J* = 12.8, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.2, 161.4, 139.4, 137.5, 134.3, 133.4, 133.0, 129.7, 129.2, 126.6, 125.4,

125.0, 123.6, 122.2, 113.4, 112.4, 109.9, 95.9, 50.2, 49.7, 32.6, 20.8; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.05 min; IR (KBr, cm^{-1}): 3094, 2922, 1722, 1611, 1477, 1362, 1161; MS (ES mass): *m/z* 422.4 (M+1); HRMS: *m/z* calcd for $C_{22}H_{19}O_3N_2S_2$ $[M + H]^+$ 423.08316, found 423.08247.

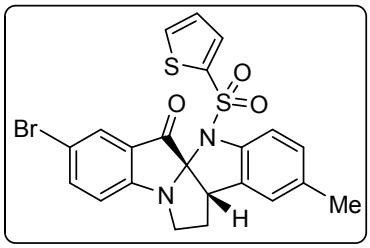
Compound 2o



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

Light yellow solid; yield: 63%; mp: 282-284 °C; R_f (15% EtOAc-*n*-Hexane) 0.24; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.79 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.69 (d, *J* = 2.4 Hz, 1H), 7.58-7.55 (m, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.06-7.02 (m, 2H), 7.01-6.98 (m, 1H), 6.96 (s, 1H), 3.91 (d, *J* = 8.0 Hz, 1H), 3.52 (dd, *J* = 12.4, 6.4 Hz, 1H), 2.93-2.85 (m, 1H), 2.30 (s, 3H), 2.09-2.00 (m, 1H), 1.96 (dd, *J* = 12.4, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:196.2, 159.6, 139.2, 139.1, 137.4, 134.5, 133.6, 133.4, 129.5, 129.4, 127.9, 126.7, 125.5, 124.7, 124.5, 114.9, 112.4, 96.2, 50.3, 49.7, 32.6, 20.8; HPLC: 98.5%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 4/98, 10/98, 10.5/20, 12/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 5.28 min; IR (KBr, cm^{-1}): 2942, 1736, 1475, 1354, 1156; MS (ES mass): *m/z* 457.0 (M+1); HRMS: *m/z* calcd for $C_{22}H_{17}O_3N_2ClS_2$ $[M + H]^+$ 457.04419, found 457.04469.

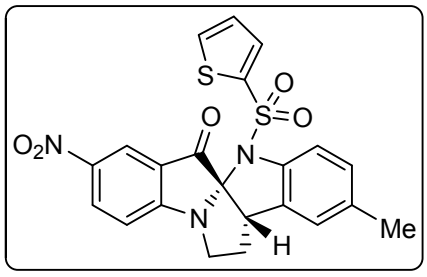
Compound 2p



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

Light yellow solid; yield: 57%; mp: 256-258 °C; R_f (20% EtOAc-*n*-Hexane) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 1.6 Hz, 1H), 7.79 (d, *J* = 3.6 Hz, 1H), 7.69 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.57 (d, *J* = 5.2 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.06-7.01 (m, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 3.90 (d, *J* = 8.0 Hz, 1H), 3.52 (dd, *J* = 12.4, 6.7 Hz, 1H), 2.92-2.84 (m, 1H), 2.29 (s, 3H), 2.07-2.01 (m, 1H), 1.96 (dd, *J* = 12.4, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.9, 159.9, 140.1, 139.1, 139.0, 134.4, 133.6, 133.3, 129.4, 129.3, 127.6, 126.7, 125.5, 125.2, 115.2, 114.9, 112.4, 96.0, 50.2, 49.7, 32.6, 29.7; HPLC: 93.5%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 1/20, 6/98, 10/98, 12/20, 15/20; flow rate: 1.0 mL/min; UV 235 nm, retention time 6.88 min; IR (KBr, cm^{-1}): 3095, 2953, 1736, 1452, 1371, 1148; MS (ES mass): *m*/*z* 502.8 (M+1).

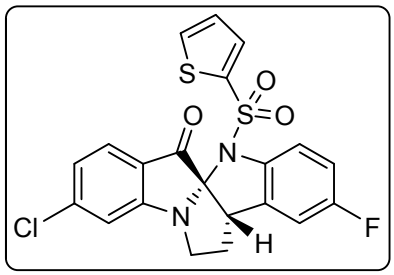
Compound 2q



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

Light yellow solid; yield: 42%; mp: 294-296 °C; R_f (25% EtOAc-*n*-Hexane) 0.15; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.60 (d, *J* = 2.0 Hz, 1H), 8.51 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.77 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.60 (dd, *J* = 5.2, 1.6 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.10-7.04 (m, 3H), 6.98 (s, 1H), 3.96 (d, *J* = 8.0 Hz, 1H), 3.65 (dd, *J* = 12.4, 6.0 Hz, 1H), 3.03-2.95 (m, 1H), 2.31 (s, 3H), 2.12-2.07 (m, 1H), 2.03 (dd, *J* = 12.4, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.3, 164.1, 142.7, 138.9, 134.4, 133.9, 133.4, 132.5, 129.6, 129.1, 127.9, 126.9, 125.6, 123.4, 121.6, 113.1, 112.4, 96.1, 49.7, 49.3, 33.5, 20.8; MS (ES mass): *m*/*z* 468.0 (M+1).

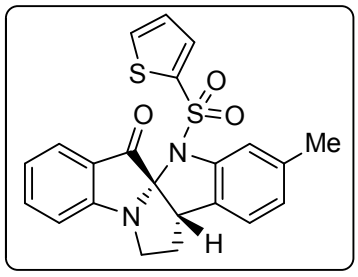
Compound 2r



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

Light yellow solid; yield: 56%; mp: 242-244 °C; R_f (20% EtOAc-*n*-Hexane) 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (dd, *J* = 3.6, 1.0 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 8.1, 1H), 7.40 (dd, *J* = 8.5, 4.3 Hz, 1H), 7.10-7.03 (m, 3H), 6.95 (td, *J* = 8.5, 2.4 Hz, 1H), 6.87 (dd, *J* = 7.8, 1.8 Hz, 1H), 3.91 (d, *J* = 8.3 Hz, 1H), 3.54 (dd, *J* = 12.2, 6.7 Hz, 1H), 2.87 (td, *J* = 12.3, 5.2 Hz, 1H), 2.15-2.05 (m, 1H), 1.96 (dd, *J* = 12.4, 4.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 195.4, 161.7, 160.9 (C-F *J* = 241.7 Hz), 144.2, 138.7, 137.5, 134.6, 133.6, 131.3 (C-F *J* = 8.1 Hz), 126.8, 126.1, 123.2, 121.9, 115.6 (C-F *J* = 23.6 Hz), 113.9, 113.5 (C-F *J* = 8.2 Hz), 112.4 (C-F *J* = 24.4 Hz), 96.3, 50.2, 49.4, 32.7; HPLC: 96.7%; column: X-Terra C-18 250*4.6 mm, 5μm, mobile phase A: 5 mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 0.1 mL/min; UV 230 nm, retention time 14.16 min; MS (ES mass): *m*/*z* 461.2 (M+1).

Compound 2s

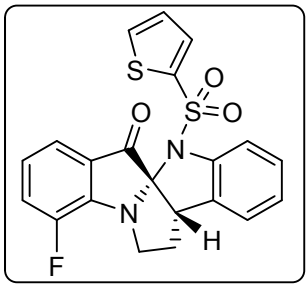


Compound **2s** was prepared from **1s** according to the above general procedure.

Light yellow solid; yield: 60%; mp: 182-184 °C; R_f (20% EtOAc-*n*-Hexane) 0.1; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, *J* = 2.7 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.65-7.55 (m, 2H), 7.29 (s, 1H), 7.10-7.01 (m, 4H), 6.86 (d, *J* = 7.3 Hz, 1H), 3.89 (d, *J* = 8.1 Hz, 1H), 3.55 (dd, *J* = 12.3, 6.6 Hz, 1H), 2.89 (tb, *J* = 12.4, 5.1 Hz, 1H), 2.35 (s, 3H), 2.10-1.98 (m, 1H), 1.91 (dd, *J* = 12.6,

5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.2, 161.3, 141.7, 139.3, 138.9, 137.5, 134.3, 133.2, 126.7, 126.6, 125.0, 124.5, 124.4, 123.5, 122.2, 113.5, 113.3, 96.1, 50.1, 49.3, 32.7, 21.6; HPLC: 98.7%; column: X-Terra C-18 250*4.6 mm, 5µm, mobile phase A: 5 mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 230 nm, retention time 13.67 min; MS (ES mass): *m*/*z* 423.1 (M+1).

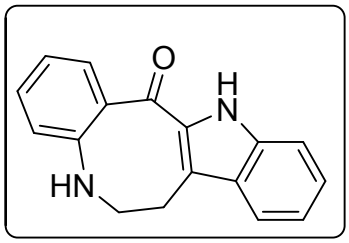
Compound 2t



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

Light yellow solid; yield: 35%; mp: 194-196 °C; R_f (15% EtOAc-*n*-Hexane) 0.17; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.85 (dd, *J* = 4.0, 1.6 Hz, 1H), 7.61 (dd, *J* = 5.2, 1.6 Hz, 1H), 7.56 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.37-7.32 (m, 1H), 7.28-7.26 (m, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 3.9 Hz, 1H), 7.06-7.03 (m, 2H), 3.98 (d, *J* = 8.0 Hz, 1H), 3.86 (dd, *J* = 12.8, 6.6 Hz, 1H), 2.87 (td, *J* = 12.8, 5.2 Hz, 1H), 2.19-2.09 (m, 1H), 2.02 (dd, *J* = 12.8, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.5, 152.4 (C-F *J* = 246.9 Hz), 148.1 (C-F *J* = 10.2 Hz), 141.6, 138.7, 134.7, 133.6, 129.4, 128.8, 127.2 (C-F *J* = 5.9 Hz), 126.7, 124.8, 123.8, 123.6, 123.2 (C-F *J* = 5.7 Hz) , 120.8 (C-F *J* = 3.8 Hz), 112.6, 95.8, 50.1, 49.5 (C-F *J* = 4.4 Hz), 32.7; HPLC: 99.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1% TFA in water, mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 0.5/20, 2/95, 8/95, 10/20, 12/20; flow rate: 1.0 mL/min; Diluent: ACN: Water (90:10); UV 230 nm, retention time 3.61 min; MS (ES mass): *m*/*z* 427.1 (M+1).

Preparation of compound 3:



Compound **3a** (0.08 mmol) was dissolved in 10 mL of 5% methanolic potassium hydroxide and refluxed for 6 h.[2] After completion of the reaction, the solvent was evaporated under vacuum. The residue was diluted with water and extracted with ethyl acetate (3 x 10 mL). The combined organic phases were collected, washed with brine (20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under a reduced pressure. The crude product was purified by column chromatography over silica gel using ethyl acetate-hexane to give the desired product **3**.

Off white solid; yield: 90%; mp: 226-228 °C; R_f (15% EtOAc-*n*-Hexane) 0.22; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.42 (bs, 1H), 7.80 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.56-7.52 (m, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.42-7.38 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.28-7.24 (m, 1H), 7.19-7.15 (m, 1H), 3.85 (bs, 1H), 3.36 (t, *J* = 6.0 Hz, 2H), 2.86 (t, *J* = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 184.5, 147.4, 136.8, 135.3, 135.2, 132.9, 130.2, 127.4, 126.9, 126.3, 124.5, 120.9, 120.5, 119.2, 111.9, 53.3, 23.5; HPLC: 99.5%; column: Symmetry C-18 250*4.6 mm, 5μm, mobile phase A: 5mm Ammonium Acetate in water mobile phase B: CH_3CN (Gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 210 nm, retention time 12.36 min; MS (ES mass): *m/z* 263.1 (M+1); HRMS: *m/z* calcd for $C_{17}H_{15}ON_2$ $[M + H]^+$ 263.11789, found 263.11757.

Single crystal X-ray data for compound 2j:

Single crystals suitable for X-ray diffraction of **2j** were grown from methanol. The crystals were carefully chosen using a stereo zoom microscope supported by a rotatable polarizing stage. The data were collected at room temperature on Bruker's KAPPA APEX II CCD Duo with graphite monochromated Mo-Kα radiation (0.71073 Å). The crystals were glued to a thin glass fibre using FOMBLIN immersion oil and mounted on the diffractometer. The intensity data were processed using Bruker's suite of data processing programs (SAINT), and absorption corrections were applied using SADABS.[3] The crystal structures were solved by direct methods using

SHELXS-97 and refined by full matrix least-squares refinement on F^2 with anisotropic displacement parameters for non-H atoms, using SHELXL-97.[4]

Crystal data of **2j**: Molecular formula = $C_{22}H_{17}FN_2O_4S_2$, formula weight = 456.50, crystal system = Monoclinic, space group = *P2(1)/c*, a = 9.0012 (2) Å, b = 11.6897 (3) Å, c = 19.0204 (5) Å, V = 1999.06 (9) Å^3, T = 296 K, Z = 4, D_x = 1.517 Mg m^{-3}, μ(Mo-Kα) = 0.31 mm^{-1}, 14591 reflections measured, 3409 independent reflections, 2957 observed reflections [I > 2.0 σ (I)], R_{int} = 0.027, Goodness of fit = 1.05. Crystallographic data (excluding structure factors) for **2j** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC 993261.

Reference

1. B. Prasad, B. Y. Sreenivas, G. R. Krishna, R. Kapavarapu and M. Pal, *Chem. Commun.,* 2013, **49**, 6716.
2. R. J. Sundberg and J. P. Laurino, *J. Org. Chem.,* 1984, **49**, 253.
3. Bruker SADABS V2008-1, Bruker AXS.: Madison, WI, USA, **2008**.
4. Sheldrick, G. M.; SHELX-97, Program for Crystal Structure Determination, University of Göttingen, **1997**.