Electronic Supplementary Information

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

Bagineni Prasad, Raju Adepu, Atul Kumar Sharma and Manojit Pal*

Dr. Reddy's Institute of Life Sciences, University of Hyderabad Campus, Gachibowli,
Hyderabad 500 046, India
E-mail: manojitpal@rediffmail.com
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):

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$_2$SO$_4$, 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\(_3\)) \( \delta \): 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):**

To a mixture of \( N \)-(2-iodophenyl)methane/4-methylbenzene/thiophene-2-sulfonamide derivative 1S2 (1.0 mmol), Cs\(_2\)CO\(_3\) (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\(_2\)S\(_2\)O\(_3\) (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\(_3\)) \( \delta \): 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$_3$) $\delta$: 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-$1H$-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$_3$) $\delta$: 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$_3$) $\delta$: 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-$1H$-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$_3$) $\delta$: 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\(_3\))\(_2\)Cl\(_2\) (5 mol%), Et\(_3\)N (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; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \): 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\(_3\)) \( \delta \): 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; ^1H 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); ^13C 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; ^1H 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); ^13C 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):

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\(_3\)N (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)

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-\text{-}n\text{-}Hexane) 0.26; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 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\(_3\)) \(\delta\): 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; Rf (20% EtOAc-n-Hexane) 0.26; 1H NMR (400 MHz, CDCl3) 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); 13C NMR (100 MHz, CDCl3) 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; Rf (20% EtOAc-n-Hexane) 0.23; 1H NMR (400 MHz, CDCl3) 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); 13C NMR (100 MHz, CDCl3) 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; Rf (15% EtOAc-n-Hexane) 0.19; 1H NMR (400 MHz, CDCl3) 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), 3.92-3.20 (m, 1H); 13C NMR (100 MHz, CDCl3) 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:H2O (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.8
<table>
<thead>
<tr>
<th>S.No.</th>
<th>Compound (1)</th>
<th>Product (2)</th>
<th>Time (h)</th>
<th>Yield$^b$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="1a.png" alt="image" /></td>
<td><img src="2a.png" alt="image" /></td>
<td>2</td>
<td>66</td>
</tr>
<tr>
<td>2</td>
<td><img src="1b.png" alt="image" /></td>
<td><img src="2b.png" alt="image" /></td>
<td>1.5</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td><img src="1c.png" alt="image" /></td>
<td><img src="2c.png" alt="image" /></td>
<td>1.5</td>
<td>72</td>
</tr>
<tr>
<td>4</td>
<td><img src="1d.png" alt="image" /></td>
<td><img src="2d.png" alt="image" /></td>
<td>2</td>
<td>59</td>
</tr>
<tr>
<td>5</td>
<td><img src="1e.png" alt="image" /></td>
<td><img src="2e.png" alt="image" /></td>
<td>2</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td><img src="image1f" alt="Molecule 1f" /></td>
<td><img src="image2f" alt="Molecule 2f" /></td>
<td>1.5</td>
<td>54</td>
</tr>
<tr>
<td>---</td>
<td>------------------------</td>
<td>------------------------</td>
<td>-----</td>
<td>----</td>
</tr>
<tr>
<td>6</td>
<td><img src="image1g" alt="Molecule 1g" /></td>
<td><img src="image2g" alt="Molecule 2g" /></td>
<td>2</td>
<td>65</td>
</tr>
<tr>
<td>7</td>
<td><img src="image1h" alt="Molecule 1h" /></td>
<td><img src="image2h" alt="Molecule 2h" /></td>
<td>1.5</td>
<td>64</td>
</tr>
<tr>
<td>8</td>
<td><img src="image1i" alt="Molecule 1i" /></td>
<td><img src="image2i" alt="Molecule 2i" /></td>
<td>2</td>
<td>60</td>
</tr>
<tr>
<td>9</td>
<td><img src="image1j" alt="Molecule 1j" /></td>
<td><img src="image2j" alt="Molecule 2j" /></td>
<td>1.5</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>---</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td></td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td></td>
<td><img src="image6.png" alt="Image" /></td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td><img src="image9.png" alt="Image" /></td>
</tr>
<tr>
<td>11</td>
<td>1k</td>
<td>2k</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>1l</td>
<td>2l</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>1m</td>
<td>2m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>1n</td>
<td>2n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>1o</td>
<td>2o</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1.5</td>
<td>1.5</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>52</td>
<td>62</td>
<td>64</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td><img src="image1.png" alt="Structure 1p" /></td>
<td><img src="image2.png" alt="Structure 2p" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>16</td>
<td><img src="image3.png" alt="Structure 1q" /></td>
<td><img src="image4.png" alt="Structure 2q" /></td>
<td>2</td>
<td>57</td>
</tr>
<tr>
<td>17</td>
<td><img src="image5.png" alt="Structure 1r" /></td>
<td><img src="image6.png" alt="Structure 2r" /></td>
<td>4</td>
<td>42</td>
</tr>
<tr>
<td>18</td>
<td><img src="image7.png" alt="Structure 1s" /></td>
<td><img src="image8.png" alt="Structure 2s" /></td>
<td>4</td>
<td>56</td>
</tr>
<tr>
<td>19</td>
<td><img src="image9.png" alt="Structure 1t" /></td>
<td><img src="image10.png" alt="Structure 2t" /></td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>20</td>
<td><img src="image11.png" alt="Structure 1tp" /></td>
<td><img src="image12.png" alt="Structure 2tp" /></td>
<td>3</td>
<td>35</td>
</tr>
</tbody>
</table>

*a* All the reactions were performed using 1 (0.1 mmol), 10 mol% of CuI in DMF+H2O (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 was prepared from 1a according to the above general procedure. Light yellow solid; yield: 66%; mp: 201-203 °C; Rf (15% EtOAc-n-Hexane) 0.21; 1H NMR (400 MHz, CDCl3) 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); 13C NMR (100 MHz, CDCl3) 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: CH3CN (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 C18H17O3N2S [M + H]+ 341.09554, found 341.09512.

Compound 2b was prepared from 1b according to the above general procedure. Light yellow solid; yield: 66%; mp: 217-219 °C; Rf (20% EtOAc-n-Hexane) 0.31; 1H NMR (400 MHz, CDCl3) 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,
NMR (100 MHz, CDCl$_3$) $\delta$: 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$_3$CN (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$_3$ N$_2$S$_2$ [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$_3$) $\delta$: 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$_3$) $\delta$: 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$_3$CN (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$_3$ N$_2$ClS$_2$ [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; 1H 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); 13C 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_3 N_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; 1H 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$_3$CN (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$_3$N$_2$S$_2$ [M + H]$^+$ 423.08316, found 423.08314.

**Compound 2f**

![Chemical Structure](image)

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$_3$CN (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$_3$N$_2$FS [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\textsubscript{f} (20% EtOAc-n-Hexane) 0.28; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{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); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{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\textsubscript{3}CN (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\textsuperscript{-1}): 3072, 2938, 1732, 1474, 1361, 1161; MS (ES mass): m/z 435.2 (M+1); HRMS: m/z calcd for C\textsubscript{24}H\textsubscript{20}O\textsubscript{3}N\textsubscript{2}FS [M + H]\textsuperscript{+} 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\textsubscript{f} (20% EtOAc-n-Hexane) 0.29; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{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); ¹³C NMR (100 MHz, CDCl₃) 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: CH₃CN (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](image)

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

Light yellow solid; yield: 60%; mp: 220-222 °C; Rₐ (15% EtOAc-n-Hexane) 0.19; ¹H NMR (400 MHz, CDCl₃) 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 = 11.6 Hz, 1H), 3.02-2.84 (m, 1H), 2.12-2.02 (m, 1H), 1.95 (dd, J = 12.8, 5.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) 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: CH₃CN (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 C₂₁H₁₄O₃N₂BrFS₂ [M + H]⁺ 504.96860, found 504.96989.

**Compound 2j**

---

S20
Compound 2j was prepared from 1j according to the above general procedure.
Light yellow solid; yield: 66%; mp: 200-202 °C; Rf (20% EtOAc-n-Hexane) 0.27; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) : 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\(_3\)) \(\delta\) : 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\(_3\)CN (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: \(m/z\) calcld for C\(_{22}\)H\(_{17}\)O\(_4\)N\(_2\)FS\(_2\) [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; Rf (20% EtOAc-n-Hexane) 0.20; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) : 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\textsubscript{3}) \delta: 195.6, 159.5, 140.2, 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\textsubscript{3}CN (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\textsuperscript{-1}): 2967, 1746, 1452, 1342, 1144; MS (ES mass): \textit{m/z} 476.9 (M+1); HRMS: \textit{m/z} calcd for C\textsubscript{21}H\textsubscript{14}O\textsubscript{3}N\textsubscript{2}Cl\textsubscript{2}S\textsubscript{2} [M + H]\textsuperscript{+} 476.98957, found 476.99155.

**Compound 2l**

![Compound 2l Image](image-url)

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

Light yellow solid; yield: 62%; mp: 226-228 °C; R\textsubscript{f} (20% EtOAc-n-Hexane) 0.22; \^{1}H NMR (400 MHz, CDCl\textsubscript{3}) \delta: 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\textsubscript{3}) \delta: 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\textsubscript{3}CN (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): \textit{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; Rf (20% EtOAc-n-Hexane) 0.21; 1H NMR (400 MHz, CDCl₃) 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); 13C NMR (100 MHz, CDCl₃) 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: CH₃CN (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 was prepared from 1n according to the above general procedure.

Light yellow solid; yield: 61%; mp: 262-264 °C; Rf (20% EtOAc-n-Hexane) 0.3; 1H NMR (400 MHz, CDCl₃) 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); 13C NMR (100 MHz, CDCl₃) 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: CH₃CN (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 C₂₂H₁₉O₃N₂S₂ [M + H]⁺ 423.08316, found 423.08247.

**Compound 2o**

![Compound 2o](image)

Compound 2o was prepared from 1o according to the above general procedure. Light yellow solid; yield: 63%; mp: 282-284 °C; Rf (15% EtOAc-n-Hexane) 0.24; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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: CH₃CN (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 C₂₂H₁₇O₃N₂ClS₂ [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; Rf (20% EtOAc-n-Hexane) 0.25; 1H NMR (400 MHz, CDCl₃) 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); 13C NMR (100 MHz, CDCl₃) 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: CH₃CN (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; Rf (25% EtOAc-n-Hexane) 0.15; 1H NMR (400 MHz, CDCl₃) 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); 13C NMR (100 MHz, CDCl₃) 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 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\(_3\)) \(\delta\): 7.79 (dd, \(J = 3.6, 1.0 \text{ Hz}, 1\text{H}\)), 7.66 (d, \(J = 8.1 \text{ Hz}, 1\text{H}\)), 7.61 (d, \(J = 8.1, 1\text{H}\)), 7.40 (dd, \(J = 8.5, 4.3 \text{ Hz}, 1\text{H}\)), 7.10-7.03 (m, 3H), 6.95 (td, \(J = 8.5, 2.4 \text{ Hz}, 1\text{H}\)), 6.87 (dd, \(J = 7.8, 1.8 \text{ Hz}, 1\text{H}\)), 3.91 (d, \(J = 8.3 \text{ Hz}, 1\text{H}\)), 3.54 (dd, \(J = 12.2, 6.7 \text{ Hz}, 1\text{H}\)), 2.87 (td, \(J = 12.3, 5.2 \text{ Hz}, 1\text{H}\)), 2.15-2.05 (m, 1H), 1.96 (dd, \(J = 12.4, 4.9 \text{ Hz}, 1\text{H}\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 195.4, 161.7, 160.9 (C-F \(J = 241.7 \text{ Hz}\)), 144.2, 138.7, 137.5, 134.6, 133.6, 131.3 (C-F \(J = 8.1 \text{ Hz}\)), 126.8, 126.1, 123.2, 121.9, 115.6 (C-F \(J = 23.6 \text{ Hz}\)), 113.9, 113.5 (C-F \(J = 8.2 \text{ Hz}\)), 112.4 (C-F \(J = 24.4 \text{ Hz}\)), 96.3, 50.2, 49.4, 32.7; HPLC: 96.7%; column: X-Terra C-18 250*4.6 mm, 5\(\mu\)m, mobile phase A: 5 mm Ammonium Acetate in water mobile phase B: CH\(_3\)CN (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 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\(_3\)) \(\delta\): 7.82 (d, \(J = 2.7 \text{ Hz}, 1\text{H}\)), 7.73 (d, \(J = 7.5 \text{ Hz}, 1\text{H}\)), 7.65-7.55 (m, 2H), 7.29 (s, 1H), 7.10-7.01 (m, 4H), 6.86 (d, \(J = 7.3 \text{ Hz}, 1\text{H}\)), 3.89 (d, \(J = 8.1 \text{ Hz}, 1\text{H}\)), 3.55 (dd, \(J = 12.3, 6.6 \text{ Hz}, 1\text{H}\)), 2.89 (tb, \(J = 12.4, 5.1 \text{ Hz}, 1\text{H}\)), 2.35 (s, 3H), 2.10-1.98 (m, 1H), 1.91 (dd, \(J = 12.6, 6.6 \text{ Hz}, 1\text{H}\)), 2.35 (s, 3H), 1.91 (dd, \(J = 12.6, 6.6 \text{ Hz}, 1\text{H}\)), 2.10-1.98 (m, 1H), 1.91 (dd, \(J = 12.6, 6.6 \text{ Hz}, 1\text{H}\)), 2.10-1.98 (m, 1H), 1.91 (dd, \(J = 12.6, 6.6 \text{ Hz}, 1\text{H}\)).
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$_3$CN (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$_3$CN (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. 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; Rf (15% EtOAc-n-Hexane) 0.22; 1H NMR (400 MHz, CDCl3) 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); 13C NMR (100 MHz, CDCl3) 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: CH₃CN (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 C₁₇H₁₅ON₂ [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. 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$_2$O$_4$S$_2$, 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$^{-3}$, $\mu$(Mo-Kα) = 0.31 mm$^{-1}$, 14591 reflections measured, 3409 independent reflections, 2957 observed reflections [$I > 2.0 \sigma (I)$], $R_{int} = 0.027$, 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