Supplementary Information

Non-Directed Copper-Catalyzed Regioselective C-H Sulfonylation of Phenothiazines

Caiyan Liu, Yongli Shen and Kedong Yuan*

Tianjin Key Laboratory of Advanced Functional Porous Materials, Institute for New Energy Materials & Low-Carbon Technologies, School of Materials Science and Engineering, Tianjin University of Technology, Tianjin 300384, P. R. China.

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General information

Unless otherwise noted, all reactions were handled under air atmosphere, refluxed in 25 mL flame-dried Schlenk tubes placed in a preheated oil bath. CuI (99.995%, 99.5% purity) were used for reaction optimization and substrate scope studies. HPLC grade solvents, 1,4-dioxane, DMF, m-xylene, 1,2-dichloroethane (DCE), Diethyl carbonate (DEC) were purchased from commercial sources and used without further purification. All new compounds were fully characterized. \(^1\)H NMR spectra were recorded on a Bruker GPX 400 MHz spectrometer. Chemical shifts (\(\delta\)) were reported in parts per million relative to residual chloroform (7.26 ppm for \(^1\)H NMR; 77.0 ppm for \(^{13}\)C NMR), Coupling constants were reported in Hertz. \(^1\)H NMR assignment abbreviations were the following: singlet (s), broad singlet (bs), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). \(^{13}\)C NMR spectra were recorded at 100 MHz on the same spectrometer and reported in ppm. Melting point were measured on SGW-4A microscopic melting point apparatus. Mass spectra were conducted at Agilent Technologies 5973N (EI).

General procedure for synthesis of \(N\)-alkyl-phenothiazines 1a, 1b, 1d-f

To a phenothiazine DMF solution (10-50 mmol, 1.0 equiv. Conc. \(\approx 0.5\) M) at room temperature, sodium hydride (1.05 equiv.) was slowly added and the mixture was stirred for 10 minutes under nitrogen atmosphere. Alky-Br (1.2 equiv.) was added dropwise and the reaction was monitored by TLC until the full conversion of phenothiazines. The reaction mixture was washed by diethyl ether and brine. The combined organic layer was dried over Na\(_2\)SO\(_4\) and purified by silica column chromatography using petroleum ether as eluent to afford the corresponding \(N\)-alkyl-phenothiazines 1a, 1b, 1d-f.

10-butyl-10H-phenothiazine\(1a\)^1

\[
\text{Compound 1a was prepared on 50 mmol (9.95 g) scale following the general procedure, purified by petroleum ether as a brown oil, 11.6 g, 91% yield.}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.22 (dd, \(J = 8.5\) Hz, 1.6 Hz, 2H), 7.20 (dt, \(J = 7.4\), 1.3 Hz, 2H), 6.96 (td, \(J = 7.5\), 1.3 Hz, 2H), 6.92 (dd, \(J = 8.5\), 1.2 Hz, 2H), 3.90 (t, \(J = 7.1\) Hz, 2H), 2.02 – 1.71 (m, 2H), 1.52 (h, \(J = 7.4\) Hz, 2H), 1.00 (t, \(J = 7.4\) Hz, 3H).
Compound 1b was prepared on 5 mmol scale following the general procedure, purified by petroleum ether as a brown oil, 1.28 g, 83% yield.  
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32 (d, $J = 6.5$ Hz, 4H), 7.28 – 7.22 (m, 1H), 7.09 (dd, $J = 7.6$, 1.5 Hz, 2H), 6.97 (td, $J = 7.7$, 1.6 Hz, 2H), 6.89 – 6.81 (m, 2H), 6.65 (d, $J = 8.1$ Hz, 2H), 5.09 (s, 2H).

Compound 1c was prepared on 5 mmol scale following the general procedure, purified by petroleum ether as a colorless oil, 1.28 g, 63% yield.  
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.68 (dd, $J = 6.9$, 1.9 Hz, 1H), 7.24 – 7.15 (m, 3H), 7.11 (dd, $J = 7.5$, 1.6 Hz, 2H), 6.99 (td, $J = 7.7$, 1.7 Hz, 2H), 6.89 (td, $J = 7.5$, 1.2 Hz, 2H), 6.55 (dd, $J = 8.2$, 1.3 Hz, 2H), 5.07 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 143.84, 134.83, 133.07, 128.79, 128.65, 127.37, 127.22, 126.76, 122.83, 122.60, 122.37, 115.12, 53.58.

Compound 1e was prepared on 5 mmol scale following the general procedure, purified by petroleum ether as a white solid, 1.03 g, 75% yield.  
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.18 (d, $J = 1.6$ Hz, 0H), 7.14 (ddd, $J = 9.2$, 7.6, 1.6 Hz, 1H), 7.02 (d, $J = 8.2$ Hz, 0H), 6.93 (td, $J = 7.5$, 1.2 Hz, 0H), 6.87 (ddd, $J = 9.9$, 8.2, 1.6 Hz, 1H), 6.82 (d, $J = 2.1$ Hz, 0H), 3.78 (t, $J = 7.1$ Hz, 1H), 1.82 (h, $J = 7.3$ Hz, 1H), 1.01 (t, $J = 7.4$ Hz, 2H).
10-benzyl-3-(methylthio)-10H-phenothiazine(1f)

Compound 1f was prepared in 5 mmol scale following the general procedure, purified by ethyl acetate/petroleum ether as a colorless oil, 888 mg, 53% yield.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.33 (d, \(J = 6.4\) Hz, 4H), 7.26 (td, \(J = 6.1, 5.6, 2.4\) Hz, 1H), 7.09 (dd, \(J = 7.5, 1.5\) Hz, 1H), 6.99 (dt, \(J = 7.7, 3.7\) Hz, 2H), 6.87 (t, \(J = 7.4\) Hz, 1H), 6.78 (dd, \(J = 8.1, 1.8\) Hz, 1H), 6.68 (d, \(J = 8.1\) Hz, 1H), 6.55 (d, \(J = 1.8\) Hz, 1H), 5.08 (s, 1H), 2.23 (s, 2H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 144.89, 144.33, 137.40, 136.47, 128.74, 127.22, 127.11, 126.86, 126.61, 123.41, 122.65, 121.04, 120.24, 115.62, 114.38, 52.70, 16.09.

Synthesis of N-alkyl-phenothiazines 1c:

To a 100 mL Schlenk tube charged with phenothiazine (1.0 g, 5 mmol), K\(_2\)CO\(_3\) (1.38 g, 10 mmol), bromobenzene (0.79 g, 5 mmol), Pd(OAc)\(_2\) (33.6 mg, 0.15 mmol), PPh\(_3\) (157 mg, 0.6 mmol) and 15 mL toluene was subsequently added. The mixture was evacuated and backfilled with nitrogen for three times. Then, the reaction tube was set at 120 °C oil bath for 20 hours. The cooling reaction mixture was directly purified by ethyl acetate/petroleum ether after vacuum concentration to afford a white solid, 0.7 g, 51% yield. The analytical information was consistent with the previous report.\(^4\)

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.61 (t, \(J = 7.7\) Hz, 2H), 7.48 (t, \(J = 7.5\) Hz, 1H), 7.40 (d, \(J = 7.5\) Hz, 2H), 7.03 (dd, \(J = 6.8, 2.4\) Hz, 2H), 6.84 (d, \(J = 7.9\) Hz, 4H), 6.22 (d, \(J = 7.9\) Hz, 2H).

General procedure for synthesis of 3a -3w:

As a typical reaction, phenothiazines 1a-1f (0.5 mmol, 1.0 equiv.), R-SO\(_2\)Cl (0.75 mmol, 1.5 equiv.), Cul (19 mg, 0.1 mmol), Li\(_2\)CO\(_3\) (74 mg, 1.0 mmol), 1,2-dichloroethane (0.25 M, 2 mL) were subsequently added to an oven dried 25 mL Schlenk tube and sealed with a Teflon screw-cap under air atmosphere. The reaction was allowed to reflux in a preheated (120 °C) oil bath for 18 h with rigid stirring. Upon the reaction completed, the crude reaction mixture was...
concentrated and directly purified by using silica chromatography (ethyl acetate/petroleum ether) as eluent to afford 3a-3w.

10-butyl-3-tosyl-10H-phenothiazine(3a)

\[
\begin{array}{c}
\text{N} \\
\text{S} \\
\text{Me}
\end{array}
\]

Compound 3a was prepared on 2 mmol scale following the general procedure, purified by ethyl acetate/petroleum ether (1:9) as a pale yellow solid, 678 mg, 83% yield. Melting point: 136.6-139.1 °C. The crystal of 3a was obtained by slow evaporation of ether solution.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.78 (d, $J = 8.3$ Hz, 2H), 7.68 (dd, $J = 8.6$, 2.2 Hz, 1H), 7.59 (d, $J = 2.2$ Hz, 1H), 7.26 (d, $J = 8.3$ Hz, 2H), 7.14 (td, $J = 7.7$, 1.6 Hz, 1H), 7.07 (dd, $J = 7.7$, 1.5 Hz, 1H), 6.94 (td, $J = 7.5$, 1.1 Hz, 1H), 6.84 (d, $J = 8.6$ Hz, 2H), 3.83 (t, $J = 7.1$ Hz, 2H), 2.37 (s, 3H), 1.73 (qd, $J = 7.5$, 5.8 Hz, 2H), 1.42 (h, $J = 7.4$ Hz, 2H), 0.92 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 149.55, 143.76, 143.51, 139.14, 134.76, 129.79, 127.61, 127.48, 127.33, 127.13, 126.33, 125.64, 123.55, 123.49, 115.91, 114.80, 47.43, 28.66, 21.45, 19.95, 13.65.

HRMS calculated for C$_{23}$H$_{23}$NO$_2$S$_2$Na$^+$: [M+Na]$^+$ 432.1068, found 432.1069.

10-butyl-3-((4-methoxyphenyl)sulfonyl)-10H-phenothiazine(3b)

\[
\begin{array}{c}
\text{N} \\
\text{S} \\
\text{OMe}
\end{array}
\]

Compound 3b was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:5) as a yellow oil, 151 mg, 71% yield.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.78 (d, $J = 8.2$ Hz, 2H), 7.68 (dd, $J = 8.6$, 2.2 Hz, 1H), 7.59 (d, $J = 2.2$ Hz, 1H), 7.26 (d, $J = 8.2$ Hz, 2H), 7.14 (td, $J = 7.7$, 1.6 Hz, 1H), 7.07 (dd, $J = 7.7$, 1.5 Hz, 1H), 6.94 (td, $J = 7.5$, 1.1 Hz, 1H), 6.84 (dd, $J = 8.6$, 2.2 Hz, 2H), 3.83 (t, $J = 7.1$ Hz, 1H), 2.37 (s, 2H), 1.73 (qd, $J = 7.5$, 5.8 Hz, 1H), 1.42 (h, $J = 7.4$ Hz, 1H), 0.92 (t, $J = 7.4$ Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.15, 149.44, 143.62, 135.29, 133.74, 129.51, 127.62, 127.52, 126.95, 126.22, 125.71, 123.67, 123.49, 115.93, 114.82, 114.43, 55.57, 47.48, 28.74, 19.99, 13.65.

HRMS calculated for C$_{23}$H$_{23}$NO$_3$S$_2$Na$^+$: [M+Na]$^+$ 448.1017, found 448.1028.

N-(4-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)phenyl)acetamide(3c)
Compound 3c was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:1) as a yellow solid, 206 mg, 91% yield. Melting point: 171-173 °C.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.32 (s, 1H), 7.81 – 7.72 (d, $J = 8.7$ Hz, 2H), 7.65 (dd, $J = 8.7$, 2H), 7.65 (dd, $J = 7.5$, 2.1 Hz, 1H), 7.62 (d, $J = 3.3$ Hz, 1H), 7.55 (d, $J = 3.3$ Hz, 1H), 7.14 (ddd, $J = 8.4$, 7.4, 1.6 Hz, 1H), 7.06 (dd, $J = 7.7$, 1.6 Hz, 1H), 6.93 (td, $J = 7.5$, 1.1 Hz, 1H), 6.87 – 6.75 (m, 2H), 3.82 (t, $J = 7.2$ Hz, 2H), 2.14 (s, 3H), 1.72 (ddt, $J = 12.3$, 8.1, 3.7 Hz, 2H), 1.41 (q, $J = 7.5$ Hz, 2H), 0.90 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 169.33, 149.82, 143.49, 142.71, 136.18, 134.35, 128.51, 127.75, 127.59, 127.15, 126.19, 125.83, 123.67, 123.48, 119.68, 116.07, 115.00, 47.55, 29.70, 28.72, 20.03, 13.73.

HRMS calculated for C$_{24}$H$_{25}$N$_2$O$_3$S: [M+H]$^+$ 453.1306, found 453.1317.

10-butyl-3-(naphthalen-2-ylsulfonyl)-10H-phenothiazine (3d)

Compound 3d was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:9) as a yellow oil, 169 mg, 76% yield.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.67 (dd, $J = 8.6$, 1.2 Hz, 1H), 8.45 (dd, $J = 7.4$, 1.3 Hz, 1H), 8.06 (d, $J = 8.2$ Hz, 1H), 7.88 (dd, $J = 8.2$, 1.5 Hz, 1H), 7.76 (dd, $J = 8.6$, 2.2 Hz, 1H), 7.59 (qd, $J = 6.1$, 4.4 Hz, 3H), 7.56 – 7.49 (m, 1H), 7.12 (ddd, $J = 8.4$, 7.4, 1.6 Hz, 1H), 7.04 (dd, $J = 7.7$, 1.6 Hz, 1H), 6.93 (dd, $J = 7.5$, 1.2 Hz, 1H), 6.82 (dd, $J = 8.4$, 2.3 Hz, 2H), 3.81 (t, $J = 7.2$ Hz, 2H), 1.78 – 1.64 (m, 2H), 1.48 – 1.32 (m, 2H), 0.90 (t, $J = 7.3$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 149.59, 143.42, 136.27, 134.88, 134.50, 134.20, 129.59, 128.98, 128.33, 128.31, 127.61, 127.48, 127.35, 127.16, 126.79, 126.27, 125.53, 124.35, 123.51, 123.48, 115.90, 114.58, 47.48, 28.65, 19.97, 13.65.

HRMS calculated for C$_{26}$H$_{23}$NO$_2$S$_2$Na$: [M+Na]$^+$ 468.1068, found 468.1081.

4-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)benzonitrile(3e)
Compound 3e was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:5) as a yellow oil, 160 mg, 76% yield.

\[
\text{^1H NMR (400 MHz, CDCl}_3\text{)} \delta 8.00 (d, J = 8.5 Hz, 2H), 7.77 (d, J = 8.5 Hz, 2H), 7.67 (dd, J = 8.6, 2.3 Hz, 1H), 7.58 (d, J = 2.3 Hz, 1H), 7.16 (ddd, J = 8.5, 7.4, 1.6 Hz, 1H), 7.08 (dd, J = 7.7, 1.5 Hz, 0H), 6.97 (td, J = 7.5, 1.1 Hz, 1H), 6.86 (d, J = 8.7 Hz, 2H), 3.85 (t, J = 7.2 Hz, 2H), 1.75 (tt, J = 7.7, 6.4 Hz, 2H), 1.44 (h, J = 7.4 Hz, 2H), 0.93 (t, J = 7.4 Hz, 3H).
\]

\[
\text{^13C NMR (101 MHz, CDCl}_3\text{)} \delta 150.58, 146.46, 143.24, 133.05, 132.59, 127.98, 127.85, 127.79, 127.66, 126.77, 126.19, 123.93, 123.37, 117.26, 116.58, 116.14, 115.00, 47.66, 28.72, 20.04, 13.72.
\]

HRMS calculated for C_{23}H_{20}N_2O_2S_2Na^+: [M+Na]^+ 443.0864, found 443.0870.

10-butyl-3-((4-(trifluoromethyl)phenyl)sulfonyl)-10H-phenothiazine(3f)

Compound 3f was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:9) as a yellow oil, 183 mg, 79% yield.

\[
\text{^1H NMR (400 MHz, CDCl}_3\text{)} \delta 8.03 (d, J = 8.1 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.70 (dd, J = 8.6, 2.2 Hz, 1H), 7.61 (d, J = 2.2 Hz, 1H), 7.16 (t, J = 7.7 Hz, 1H), 7.08 (dd, J = 7.7, 1.6 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 6.86 (dd, J = 8.4, 3.0 Hz, 2H), 3.84 (t, J = 7.4 Hz, 2H), 1.74 (h, J = 6.7, 6.0 Hz, 2H), 1.43 (h, J = 7.4 Hz, 2H), 0.92 (t, J = 7.4 Hz, 3H).
\]

\[
\text{^19F NMR (376 MHz, CDCl}_3\text{)} \delta -63.12.
\]

\[
\text{^13C NMR (101 MHz, CDCl}_3\text{)} \delta 150.37, 145.79, 143.33, 134.52 (q, J = 33.0 Hz), 133.12, 127.91, 127.82, 127.70, 127.64, 126.70, 126.42 (q, J = 3.7 Hz), 126.05, 124.54 (q, J = 274.7 Hz), 123.83, 123.42, 116.13, 115.02, 47.62, 28.72, 20.04, 13.73.
\]

HRMS calculated for C_{23}H_{21}NO_2S_2F_3+: [M+H]^+ 464.0966, found 464.0958.

10-butyl-3-((4-fluorophenyl)sulfonyl)-10H-phenothiazine(3g)
Compound 3g was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:9) as a yellow solid, 159 mg, 77% yield. Melting point: 90-93°C.

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.97 - 7.86 \text{ (m, 2H), 7.67 (dd, } J = 8.6, 2.2 \text{ Hz, 1H), 7.59 (d, } J = 2.2 \text{ Hz, 1H), 7.20 - 7.12 \text{ (m, 3H), 7.08 (dd, } J = 7.7, 1.5 \text{ Hz, 1H), 6.95 (td, } J = 7.5, 1.2 \text{ Hz, 1H), 6.85 (dd, } J = 8.5, 1.7 \text{ Hz, 2H), 3.84 (t, } J = 7.2 \text{ Hz, 2H), 1.75 (p, } J = 7.5 \text{ Hz, 2H), 1.43 (h, } J = 7.4 \text{ Hz, 2H), 0.92 (t, } J = 7.3 \text{ Hz, 3H).} \]

\[ \text{F NMR (376 MHz, CDCl}_3\text{)} \delta -104.68. \]

\[ \text{C NMR (101 MHz, CDCl}_3\text{)} \delta 165.21 \text{ (d, } J_{C\text{-F}} = 255.5 \text{ Hz), 149.88, 143.43, 138.22 (d, } J_{C\text{-F}} = 3.1 \text{ Hz), 134.14, 130.10 (d, } J_{C\text{-F}} = 9.5 \text{ Hz), 127.70, 127.56, 127.26, 126.42, 125.86, 123.65, 123.49, 116.46 (d, } J_{C\text{-F}} = 22.7 \text{ Hz), 115.99, 114.88, 47.52, 28.69, 19.99, 13.67. \]

HRMS calculated for C_{22}H_{21}NO_2S_2F^+: [M+H]^+ 414.0997, found 414.1000.

10-butyl-3-((4-chlorophenyl)sulfonyl)-10H-phenothiazine(3h)

Compound 3h was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 116 mg, 51% yield. Melting point: 152-154°C.

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.77 \text{ (dd, } J = 8.8, 2.4 \text{ Hz, 2H), 7.61 (dd, } J = 8.6, 2.3 \text{ Hz, 1H), 7.52 (d, } J = 2.3 \text{ Hz, 1H), 7.38 (dd, } J = 8.8, 2.4 \text{ Hz, 2H), 7.15 - 7.05 \text{ (m, 1H), 7.02 (dd, } J = 7.7, 1.7 \text{ Hz, 1H), 6.93 - 6.85 \text{ (m, 1H), 6.79 (dd, } J = 8.4, 2.4 \text{ Hz, 2H), 3.78 (t, } J = 7.2 \text{ Hz, 2H), 1.80 - 1.58 \text{ (m, 2H), 1.37 (h, } J = 7.3 \text{ Hz, 2H), 0.86 (t, } J = 7.4 \text{ Hz, 3H).} \]

\[ \text{C NMR (101 MHz, CDCl}_3\text{)} \delta 149.98, 143.38, 140.65, 139.49, 133.81, 129.50, 128.78, 127.70, 127.56, 127.34, 126.46, 125.88, 123.68, 123.45, 115.99, 114.88, 47.52, 28.67, 19.99, 13.68. \]

HRMS calculated for C_{22}H_{21}NO_2S_2Cl^+: [M+H]^+ 430.0702, found 430.0703.

3h-disulfonylation: 10-butyl-3,7-bis((4-chlorophenyl)sulfonyl)-10H-phenothiazine
Compound 3h-disulfonylated product was obtained as a yellow oil, 36 mg, 12% yield.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (d, $J$ = 8.6 Hz, 4H), 7.68 (dd, $J$ = 8.7, 2.2 Hz, 2H), 7.56 (d, $J$ = 2.2 Hz, 2H), 7.46 (d, $J$ = 8.6 Hz, 4H), 6.87 (d, $J$ = 8.7 Hz, 2H), 3.84 (t, $J$ = 7.2 Hz, 2H), 1.71 (td, $J$ = 7.8, 5.7 Hz, 2H), 1.41 (h, $J$ = 7.4 Hz, 2H), 0.92 (t, $J$ = 7.4 Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 148.24, 140.29, 139.89, 135.78, 129.65, 128.92, 127.76, 126.74, 125.09, 115.82, 48.04, 28.56, 19.92, 13.59.

HRMS calculated for C$_{28}$H$_{24}$NO$_4$S$_3$Cl$_2$+: [M+H]$^+$ 604.0244, found 604.4106

**3-((4-bromophenyl)sulfonyl)-10-butyl-10H-phenothiazine(3i)**

Compound 3i was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 154mg, 65% yield. Melting point: 163-164 °C.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.76 (d, $J$ = 8.2 Hz, 2H), 7.66 (dd, $J$ = 8.6, 2.2 Hz, 1H), 7.62 (d, $J$ = 1.8 Hz, 1H), 7.59 (dd, $J$ = 7.9, 2.0 Hz, 2H), 7.15 (t, $J$ = 7.7 Hz, 1H), 7.08 (d, $J$ = 7.5 Hz, 1H), 6.95 (t, $J$ = 7.5 Hz, 1H), 6.85 (dd, $J$ = 8.6, 2.8 Hz, 2H), 3.84 (t, $J$ = 7.2 Hz, 2H), 1.75 (p, $J$ = 7.3 Hz, 2H), 1.43 (q, $J$ = 7.5 Hz, 2H), 0.93 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 150.05, 143.44, 141.32, 133.86, 132.53, 128.91, 128.06, 127.77, 127.60, 127.43, 126.49, 125.97, 123.73, 123.53, 116.09, 114.99, 47.59, 28.76, 20.03, 13.72.

HRMS calculated for C$_{22}$H$_{21}$NO$_2$S$_2$Br$: [M+H]$^+$ 474.0197, found 474.0196.

**10-butyl-3-((4-iodophenyl)sulfonyl)-10H-phenothiazine(3j)**

Compound 3j were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 120mg, 45% yield. Melting point: 163-164 °C.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (d, $J$ = 8.3 Hz, 2H), 7.63 (dd, $J$ = 8.7, 2.1 Hz, 2H), 7.37 (t, $J$ = 7.7 Hz, 1H), 7.28 (d, $J$ = 7.2 Hz, 1H), 6.91 (t, $J$ = 7.5 Hz, 1H), 6.75 (dd, $J$ = 8.6, 2.8 Hz, 2H), 3.84 (t, $J$ = 7.2 Hz, 2H), 1.78 (p, $J$ = 7.3 Hz, 2H), 1.43 (q, $J$ = 7.5 Hz, 2H), 0.93 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 150.05, 143.44, 141.32, 133.86, 132.53, 128.91, 128.06, 127.77, 127.60, 127.43, 126.49, 125.97, 123.73, 123.53, 116.09, 114.99, 47.59, 28.76, 20.03, 13.72.

HRMS calculated for C$_{22}$H$_{21}$NO$_2$S$_2$I$: [M+H]$^+$ 474.0197, found 474.0196.
ether as a yellow solid, 151 mg, 58% yield. Melting point: 157-158 °C.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.89 – 7.76 (m, 2H), 7.66 (dd, $J$ = 8.7, 2.3 Hz, 1H), 7.62 – 7.56 (m, 3H), 7.20 – 7.11 (m, 1H), 7.08 (dd, $J$ = 7.7, 1.7 Hz, 1H), 6.96 (t, $J$ = 7.5 Hz, 1H), 6.85 (dd, $J$ = 8.4, 3.9 Hz, 2H), 3.84 (t, $J$ = 7.2 Hz, 1H), 1.75 (p, $J$ = 7.5 Hz, 1H), 1.43 (h, $J$ = 7.4 Hz, 1H), 0.93 (t, $J$ = 7.5 Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 150.01, 143.41, 141.89, 138.48, 133.77, 128.72, 127.71, 127.60, 127.35, 126.49, 125.93, 123.70, 123.50, 116.00, 114.89, 100.57, 47.55, 28.70, 20.01, 13.70.

HRMS calculated for C$_{22}$H$_{21}$NO$_2$S$_2$ I$^+$: [M+H]$^+$ 522.0058, found 522.0057.

3-((2-bromophenyl)sulfonyl)-10-butyl-10H-phenothiazine (3k)

Compound 3k were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 137 mg, 58% yield. Melting point: 113-115 °C. Rotational isomer observed.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.37 (dd, $J$ = 7.9, 1.7 Hz, 1H), 7.79 (dd, $J$ = 8.7, 2.2 Hz, 1H), 7.67 (d, $J$ = 7.9 Hz, 1H), 7.59 (d, $J$ = 2.2 Hz, 1H), 7.54 (t, $J$ = 7.6 Hz, 1H), 7.45 – 7.38 (m, 1H), 7.18 (t, $J$ = 7.7 Hz, 1H), 7.10 (d, $J$ = 7.4 Hz, 1H), 6.98 (t, $J$ = 7.5 Hz, 1H), 6.88 (dd, $J$ = 8.4, 2.9 Hz, 2H), 3.89 (t, $J$ = 7.2 Hz, 2H), 1.79 (p, $J$ = 7.4 Hz, 2H), 1.47 (h, $J$ = 7.4 Hz, 2H), 0.96 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 149.95, 143.43, 140.34, 135.58, 134.30, 134.26, 132.37, 131.99, 131.19, 130.79, 128.78, 127.86, 127.66, 127.54, 127.40, 125.19, 123.62, 120.96, 116.00, 114.31, 114.26, 47.59, 28.70, 20.01, 13.69.

HRMS calculated for C$_{22}$H$_{21}$NO$_2$S$_2$Br$^+$: [M+H]$^+$ 474.0197, found 474.0199.

3k-disulfonylation:

3,7-bis((2-bromophenyl)sulfonyl)-10-butyl-10H-phenothiazine

Compound 3k-disulfonylated product was obtained as a yellow oil, 52 mg, 15% yield.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.34 (dd, $J$ = 8.0, 1.7 Hz, 2H), 7.78 (dd, $J$ = 8.7, 2.2 Hz, 2H), 7.65
(d, J = 7.9 Hz, 2H), 7.58 – 7.47 (m, 4H), 7.41 (td, J = 7.6, 1.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 3.87 (t, J = 7.2 Hz, 2H), 1.75 (h, J = 6.6, 5.9 Hz, 2H), 1.43 (h, J = 7.4 Hz, 2H), 0.93 (t, J = 7.3 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 148.21, 139.96, 135.65, 134.52, 134.11, 131.31, 129.13, 127.98, 127.58, 124.35, 121.02, 115.14, 48.12, 28.51, 19.93, 13.63.

HRMS calculated for C28H24NO4S3Br2+: [M+H]+ 691.9234, found 691.9241

10-butyl-3-((2-(trifluoromethoxy)phenyl)sulfonyl)-10H-phenothiazine(3l)

Compound 3l was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 175 mg, 73% yield. Melting point: 114-117 ºC.

1H NMR (400 MHz, CDCl3) δ 8.25 (dd, J = 7.9, 1.7 Hz, 1H), 7.78 (dd, J = 8.7, 2.2 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.60 (d, J = 2.2 Hz, 1H), 7.46 (t, J = 7.7 Hz, 1H), 7.32 (d, J = 8.3 Hz, 1H), 7.18 (t, J = 7.8 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1H), 6.89 (d, J = 8.4 Hz, 2H), 3.89 (t, J = 7.1 Hz, 2H), 1.79 (p, J = 7.3 Hz, 2H), 1.47 (h, J = 7.4 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H). 19F NMR (376 MHz, CDCl3) δ -56.12. 13C NMR (101 MHz, CDCl3) δ 146.42, 143.52, 135.00, 133.77, 133.18, 130.28, 128.39, 127.68, 127.57, 127.21, 126.58, 125.49, 123.67, 121.47, 120.00, 118.88, 116.03, 114.52, 47.62, 28.73, 20.00, 13.69.

HRMS calculated for C23H21NO3S2F+: [M+H]+ 480.0915, found 480.0916.

10-butyl-3-(quinolin-8-ylsulfonyl)-10H-phenothiazine (3m)

Compound 3m were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, the crystal of 3m was obtained by slow evaporation of ether solution. 152 mg, 69% yield. Melting point: 193-195 ºC.

1H NMR (400 MHz, CDCl3) δ 9.00 (dd, J = 4.2, 1.6 Hz, 1H), 8.65 (dd, J = 7.4, 1.2 Hz, 1H), 8.13 (d, J = 8.3 Hz, 1H), 8.07 (dd, J = 8.7, 2.2 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 2.2 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.42 (dd, J = 8.3, 4.2 Hz, 1H), 7.15 – 7.07 (m, 1H), 7.05 (dd, J = 7.6, 1.2 Hz, 1H), 6.91 (dd, J = 11.0, 3.9 Hz, 1H), 6.82 (t, J = 7.9 Hz, 2H), 3.84 – 3.79 (m, 2H),
1.77 – 1.65 (m, 2H), 1.46 – 1.34 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H). $^1$C NMR (101 MHz, CDCl$_3$) δ 151.04, 149.48, 143.62, 138.33, 136.20, 134.62, 134.24, 131.38, 129.24, 128.87, 128.17, 127.45, 127.42, 125.40, 124.40, 123.85, 123.31, 121.94, 115.84, 114.01, 47.44, 28.72, 19.95, 13.62.

**HRMS** calculated for C$_{25}$H$_{23}$N$_2$O$_2$S$_2^+$: [M+H]$^+$ 447.1201, found 447.1234.

### 6-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)-2H-chromen-2-one(3n)

![Compound 3n](image)

Compound 3n was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow oil, 187 mg, 81% yield.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.09 (d, J = 2.2 Hz, 1H), 7.99 (dd, J = 8.7, 2.2 Hz, 1H), 7.73 (d, J = 9.7 Hz, 1H), 7.69 (dd, J = 8.7, 2.2 Hz, 1H), 7.59 (d, J = 2.1 Hz, 1H), 7.38 (dd, J = 8.6, 1.7 Hz, 1H), 7.15 (td, J = 7.8, 1.6 Hz, 1H), 7.06 (dd, J = 7.7, 1.7 Hz, 1H), 6.95 (t, J = 7.5 Hz, 1H), 6.85 (dd, J = 8.4, 2.9 Hz, 2H), 6.50 (d, J = 9.6 Hz, 1H), 3.84 (t, J = 7.2 Hz, 2H), 1.74 (h, J = 6.6, 6.1 Hz, 2H), 1.42 (h, J = 7.4 Hz, 2H), 0.91 (t, J = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 159.13, 156.44, 150.10, 143.28, 142.38, 138.53, 133.61, 130.36, 127.73, 127.58, 127.53, 127.36, 126.40, 125.99, 123.72, 123.36, 118.99, 118.23, 118.06, 116.03, 114.92, 47.54, 28.67, 19.94, 13.62.

**HRMS** calculated for C$_{25}$H$_{22}$NO$_4$S$_2^+$: [M+H]$^+$ 464.0990, found 464.0989.

### 3-((5-bromothiophen-2-yl)sulfonyl)-10-butyl-10H-phenothiazine(3o)

![Compound 3o](image)

Compound 3o was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow oil, 189 mg, 79% yield.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.69 (dd, J = 8.6, 2.3 Hz, 1H), 7.61 (d, J = 2.3 Hz, 1H), 7.39 (d, J = 4.0 Hz, 1H), 7.16 (td, J = 7.7, 1.7 Hz, 1H), 7.08 (dd, J = 7.6, 1.6 Hz, 1H), 7.01 (d, J = 4.0 Hz,
1H, 6.96 (t, J = 7.5 Hz, 1H), 6.86 (dd, J = 8.7, 2.2 Hz, 2H), 3.85 (t, J = 7.2 Hz, 2H), 1.75 (h, J = 6.6, 5.8 Hz, 2H), 1.44 (h, J = 7.4 Hz, 2H), 0.93 (t, J = 7.3 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 150.08, 144.55, 143.30, 134.11, 132.69, 130.68, 127.69, 127.52, 127.07, 126.11, 125.86, 123.68, 123.41, 121.37, 116.02, 114.85, 47.54, 28.68, 19.96, 13.64.

HRMS calculated for C20H19NO2S3Br+: [M+H]+ 479.9761, found 479.9708.

10-butyl-3-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-10H-phenothiazine(3p)

Compound 3p was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 144 mg, 72% yield. Melting point: 97-100 °C.

1H NMR (400 MHz, CDCl3) δ 7.80 (s, 1H), 7.74 (s, 1H), 7.68 (ddd, J = 8.6, 2.1, 1.2 Hz, 1H), 7.59 (d, J = 2.2 Hz, 1H), 7.15 (ddd, J = 8.6, 7.3, 1.5 Hz, 1H), 7.08 (dq, J = 7.8, 1.8 Hz, 1H), 6.98 – 6.91 (m, 1H), 6.85 (dd, J = 8.6, 2.8 Hz, 2H), 3.88 (s, 3H), 3.85 (t, J = 7.1 Hz, 2H), 1.83 – 1.67 (m, 2H), 1.43 (qd, J = 7.3, 1.7 Hz, 2H), 0.92 (tt, J = 7.4, 3H). 13C NMR (101 MHz, CDCl3) δ 149.63, 143.63, 138.81, 135.78, 132.01, 127.73, 127.57, 126.59, 125.86, 125.79, 125.09, 123.60, 116.03, 114.91, 114.89, 47.54, 39.56, 28.77, 20.03, 13.71.

HRMS calculated for C20H22N3O2S2+: [M+H]+ 400.1153, found 400.1171.

10-butyl-3-(cyclopropylsulfonyl)-10H-phenothiazine(3q)

Compound 3q was obtained following the general procedure but increasing the CuI loading to 50 mol% and temperature at 130 °C. The reaction mixture was purified by ethyl acetate/petroleum ether as a yellow oil, 127 mg, 71% yield.

1H NMR (400 MHz, CDCl3) δ 7.63 (dd, J = 8.6, 2.1 Hz, 1H), 7.57 (d, J = 2.1 Hz, 1H), 7.17 (d, J = 7.7 Hz, 1H), 7.12 (d, J = 7.6 Hz, 1H), 6.98 (d, J = 7.5 Hz, 1H), 6.89 (dd, J = 8.5, 4.1 Hz, 2H), 3.89 (t, J = 7.2 Hz, 2H), 2.42 (tt, J = 8.2, 4.8 Hz, 1H), 1.79 (p, J = 7.3 Hz, 2H), 1.46 (h, J = 7.4 Hz, 2H), 1.30 (dt, J = 7.2, 3.7 Hz, 2H), 1.00 (dt, J = 7.9, 2.3 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 149.88, 143.70, 133.76, 127.68, 127.61, 127.20, 126.48, 125.82,
123.79, 123.59, 116.00, 114.83, 47.57, 33.24, 28.81, 20.04, 13.70, 5.91.

HRMS calculated for C_{19}H_{22}NO_{2}S_{2}^+: [M+H]^+ 360.1092, found 360.1097.

10-benzyl-3-(naphthalen-2-ylsulfonyl)-10H-phenothiazine(3r)

![Chemical Structure](image)

Compound 3r was obtained following the general procedure with higher loading of CuI and temperature reflux (CuI, 50 mol%, 130 °C), purified by ethyl acetate/petroleum ether as a brown oil, 100 mg, 42% yield.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.51 (d, $J = 1.8$ Hz, 1H), 7.99 – 7.93 (m, 1H), 7.90 (d, $J = 8.7$ Hz, 1H), 7.87 – 7.83 (m, 1H), 7.81 (dd, $J = 8.6$, 1.9 Hz, 1H), 7.65 (d, $J = 2.2$ Hz, 1H), 7.62 – 7.57 (m, 2H), 7.55 (dd, $J = 8.7$, 2.3 Hz, 1H), 7.31 (t, $J = 7.3$ Hz, 2H), 7.28 – 7.23 (m, 1H), 7.21 (d, $J = 7.4$ Hz, 2H), 7.03 (dd, $J = 7.6$, 1.6 Hz, 1H), 6.96 (td, $J = 7.7$, 1.7 Hz, 1H), 6.89 (t, $J = 7.4$ Hz, 1H), 6.61 (dd, $J = 11.3$, 8.4 Hz, 2H), 5.04 (s, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 148.82, 143.01, 138.89, 135.36, 134.94, 134.78, 132.27, 129.63, 129.38, 129.03, 128.98, 128.66, 127.92, 127.77, 127.59, 127.50, 127.43, 126.99, 126.35, 125.96, 124.35, 123.83, 122.59, 122.04, 116.04, 115.05, 53.09.

HRMS calculated for C$_{29}$H$_{22}$NO$_2$S$_2^+$: [M+H]$^+$ 480.1092, found 480.1087

4-((10-benzyl-10H-phenothiazin-3-yl)sulfonyl)benzonitrile(3s)

![Chemical Structure](image)

Compound 3t was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a brown oil, 84 mg, 37% yield.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.99 (d, $J = 8.2$ Hz, 1H), 7.77 (d, $J = 8.2$ Hz, 1H), 7.55 (d, $J = 2.2$ Hz, 1H), 7.48 (dd, $J = 8.7$, 2.2 Hz, 1H), 7.34 (dd, $J = 7.9$, 6.4 Hz, 1H), 7.29 (d, $J = 6.9$ Hz, 1H), 7.24 – 7.20 (m, 1H), 7.05 (dd, $J = 7.5$, 1.7 Hz, 1H), 7.00 (td, $J = 7.7$, 1.7 Hz, 1H), 6.93 (td, $J = 7.4$, 1.2 Hz, 1H), 6.66 (d, $J = 8.1$ Hz, 0H), 6.61 (d, $J = 8.7$ Hz, 1H), 5.08 (s, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 149.55, 146.37, 142.80, 135.13, 133.03, 132.93, 129.04, 127.99, 127.92, 127.80, 127.55, 127.05, 126.30, 126.10, 124.80, 124.11, 121.84, 117.23, 116.62, 116.16, 115.15, 53.18.
HRMS calculated for C_{26}H_{19}N_{2}O_{2}S_{2}^{+}: \ [M+H]^+ 455.0888, found 455.0886.

3-((2-bromophenyl)sulfonyl)-10-phenyl-10H-phenothiazine (3t)

Compound 3t was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow oil, 235 mg, 95% yield.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.29 (d, $J = 7.8$ Hz, 1H), 7.61 (t, $J = 7.7$ Hz, 3H), 7.55 - 7.44 (m, 3H), 7.35 (dd, $J = 19.9$, 7.9 Hz, 4H), 7.01 - 6.87 (m, 1H), 6.87 - 6.76 (m, 2H), 6.11 (t, $J = 7.1$ Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 148.43, 142.57, 140.23, 139.58, 135.51, 134.20, 132.24, 131.07, 130.60, 129.04, 128.25, 127.80, 127.23, 126.71, 126.61, 123.66, 120.82, 120.11, 118.58, 116.35, 114.46.

HRMS calculated for C_{24}H_{17}BrNO_{2}S_{2}: \ [M+H]^+ 493.9884, found 493.9885

10-(2-bromobenzyl)-3-tosyl-10H-phenothiazine(3u)

Compound 3u was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 138 mg, 53% yield. Melting point: 180-182 ºC.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (d, $J = 8.1$ Hz, 2H), 7.68 - 7.63 (m, 1H), 7.56 (d, $J = 2.2$ Hz, 1H), 7.47 (dd, $J = 8.6$, 2.2 Hz, 1H), 7.27 (d, $J = 8.1$ Hz, 2H), 7.21 - 7.14 (m, 2H), 7.04 (ddd, $J = 9.0$, 6.2, 2.5 Hz, 2H), 6.96 (td, $J = 7.8$, 1.8 Hz, 1H), 6.90 (t, $J = 7.3$ Hz, 1H), 6.51 (d, $J = 8.0$ Hz, 1H), 6.46 (d, $J = 8.7$ Hz, 1H), 5.00 (s, 2H), 2.38 (s, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 148.04, 143.94, 142.54, 139.08, 135.42, 133.70, 133.44, 129.89, 129.16, 128.38, 127.83, 127.65, 127.47, 127.32, 127.00, 125.78, 124.08, 123.96, 122.38, 121.86, 115.76, 114.77, 54.06, 21.55.

HRMS calculated for C_{26}H_{21}NO_{2}S_{2}Br: \ [M+H]^+ 522.0197, found 522.0188.

7-((4-bromophenyl)sulfonyl)-2-chloro-10-propyl-10H-phenothiazine(3v)
Compound 3v were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 133 mg, 54% yield. Melting point: 152-155 °C.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.75 (d, $J = 8.4$ Hz, 2H), 7.67 (dd, $J = 8.7$, 2.2 Hz, 1H), 7.61 (d, $J = 8.4$ Hz, 2H), 7.57 (d, $J = 2.2$ Hz, 1H), 6.97 (d, $J = 8.2$ Hz, 1H), 6.92 (dd, $J = 8.2$, 1.9 Hz, 1H), 6.85 (d, $J = 8.7$ Hz, 1H), 6.80 (d, $J = 1.9$ Hz, 1H). 3.77 (t, $J = 7.1$ Hz, 2H), 1.77 (h, $J = 7.3$ Hz, 2H), 0.98 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 149.27, 144.69, 141.05, 134.50, 133.71, 132.50, 128.88, 128.13, 128.02, 127.46, 126.48, 125.89, 123.47, 122.06, 116.43, 115.40, 49.63, 19.85, 11.06.

HRMS calculated for C$_{21}$H$_{18}$NO$_2$S$_2$BrCl$^+$: [M+H]$^+$ 493.9651, found 493.9644.

3-((4-bromophenyl)sulfonyl)-2-chloro-10-propyl-10H-phenothiazine(3w)

Compound 3w were obtained in the same reaction as 3v, purified by ethyl acetate/petroleum ether as a yellow solid, 74 mg, 30% yield. Melting point: 133-134 °C.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.95 (s, 1H), 7.79 (d, $J = 8.6$ Hz, 2H), 7.62 (d, $J = 8.6$ Hz, 2H), 7.21 – 7.15 (dt, 7.1, 1.6 Hz, 1H), 7.11 (dd, $J = 7.7$, 1.6 Hz, 1H), 6.99 (t, $J = 7.7$ Hz, 1H), 6.85 (d, $J = 8.0$ Hz, 1H), 6.75 (s, 1H), 3.76 (t, $J = 7.1$ Hz, 2H), 1.79 (h, $J = 7.3$ Hz, 2H), 0.99 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 150.87, 142.70, 139.79, 132.16, 132.10, 130.46, 129.81, 128.89, 128.40, 127.83, 127.72, 124.10, 123.41, 117.43, 116.26, 49.65, 19.89, 11.10.

HRMS calculated for C$_{21}$H$_{18}$NO$_2$S$_2$BrCl$^+$: [M+H]$^+$ 493.9651, found 493.9647.

10-benzyl-2-(methylthio)-3-((3-(trifluoromethoxy)phenyl)sulfonyl)-10H-phenothiazine (3x)
Compound 3x were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 129 mg, 46% yield. Melting point: 171-173 °C.

$^1$H NMR (400 MHz, Chloroform-d) δ 7.90 (s, 1H), 7.89 – 7.84 (m, 2H), 7.52 (t, $J = 8.0$ Hz, 1H), 7.41 (d, $J = 8.3$ Hz, 1H), 7.35 (d, $J = 7.3$ Hz, 2H), 7.32 – 7.24 (m, 4H), 7.12 (d, $J = 7.7$ Hz, 1H), 7.06 (t, $J = 7.7$ Hz, 1H), 6.98 (t, $J = 7.4$ Hz, 1H), 6.75 (d, $J = 8.1$ Hz, 1H), 6.35 (s, 1H), 5.11 (s, 2H), 1.86 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -57.88. $^{13}$C NMR (101 MHz, CDCl$_3$) δ 148.96, 148.85, 143.17, 143.03, 139.65, 139.65, 135.42, 135.42, 130.25, 129.96, 129.07, 128.43, 127.81, 127.60, 127.14, 126.31, 125.27, 125.21, 123.98, 122.31, 120.98, 119.73, 115.95, 113.52, 53.34, 15.73.

HRMS calculated for C$_{27}$H$_{21}$NF$_3$O$_3$: [M+H]$^+$ 560.0635, found 560.0632.

**Synthesis of heteroarene 3y**

To an oven-dried 25 mL Schlenk tube, compound 3k (95 mg, 0.2 mmol), KOAc (59 mg, 0.6 mmol) and Pd(OAc)$_2$ solution (0.45 mg in 2 mL DMAc) were subsequently added. The mixture was bubbled under nitrogen flow for 3 minutes. Then the reaction tube was sealed and set in a preheated oil bath at 150 °C for 16 hours. Upon the reaction completed, the reaction mixture was washed by water and ethyl acetate. The combined organic layer was dried over Na$_2$SO$_4$ and purified by column chromatography using ethyl acetate/petroleum ether to afford 3y as yellow oil, 59 mg, 75% yield.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.68 (d, $J = 7.6$ Hz, 1H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.40 (s, 1H), 7.36 (t, $J = 7.5$ Hz, 1H), 7.21 (t, $J = 7.8$ Hz, 1H), 7.14 (d, $J = 7.6$ Hz, 1H), 7.05 (s, 1H), 7.01 (t, $J = 7.5$ Hz, 1H), 6.92 (d, $J = 8.1$ Hz, 1H), 3.95 (t, $J = 7.1$ Hz, 2H), 1.79 (p, $J = 7.2$ Hz, 2H), 1.48 (h, $J = 7.4$ Hz, 2H), 0.95 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 150.71, 143.52, 138.26, 133.52, 131.52, 131.25, 130.53, 130.02, 127.91, 127.76, 127.62, 123.85, 123.76, 121.87, 120.88, 120.57, 116.33, 107.23, 47.69, 28.80, 20.00, 13.72.

HRMS calculated for C$_{22}$H$_{20}$NO$_2$S$_2$: [M+H]$^+$ 394.0935, found 394.0938.
Synthesis of heteroarene 3z

To an oven-dried 25 mL Schlenk tube, compound 3u (104 mg, 0.2 mmol), Cs$_2$CO$_3$ (65 mg, 0.4 mmol), BzMe$_3$NBr (98 mg, 0.4 mmol) and Pd(OAc)$_2$ solution (0.45 mg in 2 mL DMAc) were subsequently added. The mixture was bubbled under oxygen flow for 3 minutes. Then the reaction tube was sealed and set in a preheated oil bath at 130 $^\circ$C for 16 hours. Upon the reaction completed, the reaction mixture was washed by water and ethyl acetate. The combined organic layer was dried over Na$_2$SO$_4$ and purified by column chromatography using ethyl acetate/petroleum ether to afford 3z as yellow oil, 40 mg, 45% yield.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.77 (d, $J = 8.0$ Hz, 2H), 7.56 (d, $J = 2.2$ Hz, 1H), 7.48 (dd, $J = 8.6, 2.2$ Hz, 1H), 7.39 – 7.31 (m, 3H), 7.22 (d, $J = 7.4$ Hz, 2H), 7.04 (dd, $J = 7.5, 1.7$ Hz, 1H), 6.98 (td, $J = 7.7, 1.7$ Hz, 1H), 6.90 (t, $J = 7.4$ Hz, 1H), 6.63 (d, $J = 8.1$ Hz, 1H), 6.59 (d, $J = 8.6$ Hz, 1H), 5.06 (s, 2H), 2.38 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 148.57, 143.85, 143.00, 139.04, 135.31, 135.07, 129.83, 128.93, 127.71, 127.40, 127.37, 127.19, 126.92, 126.29, 125.74, 124.14, 123.74, 121.98, 115.93, 114.91, 53.03, 21.51.

HRMS calculated for C$_{26}$H$_{20}$NO$_2$S$_2$: [M+H]$^+$ 442.0935, found 442.0952.

References

NMR data

10-(2-bromobenzyl)-10H-phenothiazine (1d)
10-butyl-3-tosyl-10H-phenothiazine(3a)

13C NMR, 100 MHz, CDCl3

1H NMR, 400 MHz, CDCl3
10-butyl-3-((4-methoxyphenyl)sulfonyl)-10H-phenothiazine(3b)
N-(4-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)phenyl)acetamide (3c)
10-butyl-3-(naphthalen-2-ylsulfonyl)-10H-phenothiazine (3d)
4-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)benzonitrile (3e)
10-butyl-3-((4-(trifluoromethyl)phenyl)sulfonyl)-10H-phenothiazine(3f)
10-butyl-3-((4-fluorophenyl)sulfonyl)-10H-phenothiazine(3g)
10-butyl-3-((4-chlorophenyl)sulfonyl)-10H-phenothiazine(3h)
10-butyl-3,7-bis((4-chlorophenyl)sulfonyl)-10H-phenothiazine
10-benzyl-3-((4-bromophenyl)sulfonyl)-10H-phenothiazine(3i)
10-butyl-3-((4-iodophenyl)sulfonyl)-10H-phenothiazine(3j)

13C NMR, 100 MHz, CDCl₃

H NMR, 400 MHz, CDCl₃

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3-((2-bromophenyl)sulfonyl)-10-butyl-10H-phenothiazine(3l)

{C NMR, 100 MHz, CDCl₃

{H NMR, 400 MHz, CDCl₃
3,7-bis((2-bromophenyl)sulfonyl)-10-butyl-10H-phenothiazine
10-butyl-3-((2-(trifluoromethoxy)phenyl)sulfonyl)-10H-phenothiazine(3l)
$^{19}$F NMR, 376 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
6-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)-2H-chromen-2-one(3n)

$^1$H NMR, CDCl$_3$, 400 MHz

$^{13}$C NMR, 100 MHz, CDCl$_3$
3-((5-bromothiophen-2-yl)sulfonyl)-10-butyl-10H-phenothiazine(3o)

^1H NMR, 400 MHz, CDCl₃

^13C NMR, 100 MHz, CDCl₃
10-butyl-3-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-10H-phenothiazine (3P)

νH NMR, 400 MHz, CDCl₃

13C NMR, 100 MHz, CDCl₃

10-butyl-3-(cyclopropylsulfonyl)-10H-phenothiazine (3q)
10-benzyl-3-(naphthalen-2-ylsulfonyl)-10H-phenothiazine(3r)

$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$
4-((10-benzyl-10H-phenothiazin-3-yl)sulfonyl)benzonitrile (3s)

$^1$H NMR, 400 MHz, CDCl$_3$

$^{13}$C NMR, 100 MHz, CDCl$_3$

3-((2-bromophenyl)sulfonyl)-10-phenyl-10H-phenothiazine (3t)
10-(2-bromobenzyl)-3-tosyl-10H-phenothiazine(3u)
7-((4-bromophenyl)sulfonyl)-2-chloro-10-propyl-10H-phenothiazine(3v)
3-((4-bromophenyl)sulfonyl)-2-chloro-10-propyl-10H-phenothiazine(3w)
10-benzyl-2-(methylthio)-3-((3-(trifluoromethoxy)phenyl)sulfonyl)-10H-phenothiazine(3x)
12-butyl-12H-benzo[4,5]thieno[3,2-b]phenothiazine 5,5-dioxide (3y)
10-tosyl-14H-isoquinolino[4,3,2-kl]phenothiazine (3z)
Crystal structure information

**Fig.1** 10-butyl-3-tosyl-10H-phenothiazine (3a)

Empirical formula \( \text{C}_{23}\text{H}_{23}\text{NO}_{2}\text{S}_{2} \)

Formula weight 409.54

Temperature 150 K
Crystal system, space group: Monoclinic, P 1 21/c 1

Unit cell dimensions:
\[ a = 12.0587(8) \, \text{Å} \quad \alpha = 90^\circ \]
\[ b = 15.5180(13) \, \text{Å} \quad \beta = 117.134(2)^\circ \]
\[ c = 12.0126(8) \, \text{Å} \quad \gamma = 90^\circ \]

Volume: 2000.5(3) \, \text{Å}^3

Z, Calculated density: 4, 1.360 (g. cm\(^{-3}\))

Absorption coefficient: 0.285 mm\(^{-1}\)

F(000): 864

Crystal size: 0.410 x 0.170 x 0.030 mm

Crystal color: colorless

Reflections collected / unique: 19822 / 4600 [R(int) = 0.0898]

Reflections [I>2sigma(I)]: 3311

Completeness to theta_max: 0.996

Absorption correction type: multi-scan

Max. and min. transmission: 0.991, 0.722

Refinement method: Full-matrix least-squares on F^2

Data / restraints / parameters: 4600 / 0 / 255

Goodness-of-fit: 1.035

Fig 2. 10-butyl-3-(quinolin-8-ylsulfonyl)-10H-phenothiazine (3m)

Empirical formula: C\(_{25}\)H\(_{22}\)N\(_2\)O\(_2\)S\(_2\)

Formula weight: 446.11

Temperature: 299.83 K

Crystal system, space group: Monoclinic, P 1 21/c 1

Unit cell dimensions:
\[ a = 12.5619(2) \, \text{Å} \quad \alpha = 90^\circ \]
\[ b = 19.6420(4) \text{ Å} \quad \beta = 100.832(2)^\circ \]
\[ c = 9.1574(2) \text{ Å} \quad \gamma = 90^\circ \]

Volume \( 2219.25(8) \text{ Å}^3 \)

Z, Calculated density \( 4, 1.312 \text{ (g.cm}^{-3}\text{)} \)

radiation_wavelength \( 1.54184 \)

Absorption coefficient \( 0.887 \text{ mm}^{-1} \)

F(000) \( 926 \)

Crystal color \( \text{colorless} \)

Reflections [I>2sigma(I)] \( 3311 \)

Completeness to theta_max \( 78.5110 \)

Absorption correction type \( \text{multi-scan} \)

reflns_number \( 13319 \)

measured_fraction_full \( 0.967 \)

measured_fraction_max \( 0.948 \)

reflns_theta_full \( 67.684 \)

reflns_theta_max \( 79.371 \)

reflns_theta_min \( 3.582 \)

environment \( \text{air} \)

detector \( \text{CCD plate} \)