

Supplementary Information

Non-Directed Copper-Catalyzed Regioselective C-H Sulfonation 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.

General information	S2
General procedure for synthesis of <i>N</i>-alkyl-phenothiazines 1a, 1b, 1d-f:	S2
Synthesis of <i>N</i>-alkyl-phenothiazines 1c	S4
General procedure for synthesis of 3a -3w	S4
Synthesis of heteroarene 3y	S16
Synthesis of heteroarene 3z	S17
References	S17
NMR data	S18
Crystal structure information	S50

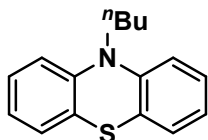
General information

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. ¹H NMR spectra were recorded on a Bruker GPX 400 MHz spectrometer. Chemical shifts (δ) were reported in parts per million relative to residual chloroform (7.26 ppm for ¹H NMR; 77.0 ppm for ¹³C NMR), Coupling constants were reported in Hertz. ¹H 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). ¹³C 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 Na₂SO₄ and purified by silica column chromatography using petroleum ether as eluent to afford the corresponding *N*-alkyl-phenothiazines **1a**, **1b**, **1d-f**.

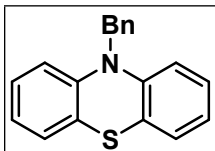
10-butyl-10H-phenothiazine(**1a**)¹



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.

¹H NMR (400 MHz, CDCl₃) δ 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).

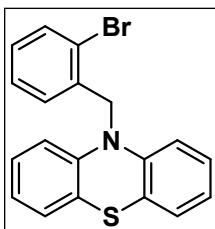
10-benzyl-10H-phenothiazine(1b)²



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.

¹H NMR (400 MHz, CDCl₃) δ 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).

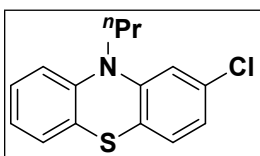
10-(2-bromobenzyl)-10H-phenothiazine (1d)



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.

¹H NMR (400 MHz, CDCl₃) δ 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). ¹³C NMR (101 MHz, CDCl₃) δ 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.

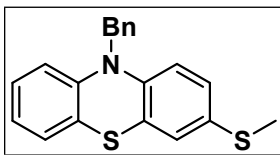
2-chloro-10-propyl-10H-phenothiazine(1e)³



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.

¹H NMR (400 MHz, CDCl₃) δ 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).

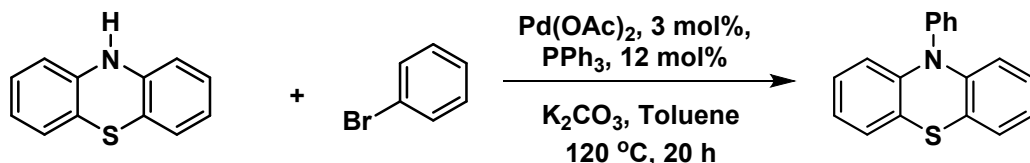
10-benzyl-3-(methylthio)-10H-phenothiazine(1f)



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.

^1H NMR (400 MHz, CDCl_3) δ 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) δ 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_2CO_3 (1.38 g, 10 mmol), bromobenzene (0.79 g, 5 mmol), $\text{Pd}(\text{OAc})_2$ (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

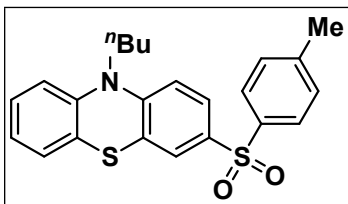
^1H NMR (400 MHz, CDCl_3) δ 7.61 (t, $J = 7.7$ Hz, 2H), 7.48 (t, $J = 7.5$ Hz, 1H), 7.40 (d, $J = 7.5$ Hz, 2H), 7.03 (dd, $J = 6.8, 2.4$ Hz, 2H), 6.84 (d, $J = 7.9$ Hz, 4H), 6.22 (d, $J = 7.9$ Hz, 2H).

General procedure for synthesis of 3a -3w:

As a typical reaction, phenothiazines **1a-1f** (0.5 mmol, 1.0 equiv.), $\text{R-SO}_2\text{Cl}$ (0.75 mmol, 1.5 equiv.), CuI (19 mg, 0.1 mmol), Li_2CO_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**)

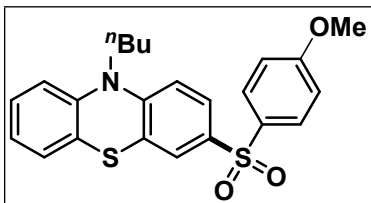


Compound **3a** was prepared on 2 mmol scale following the general procedure, purified by ethyl acetate/petroleum ether (1:9) as a pale yellow solid, 678 mg, 83% yield. Melting point: 136.6-139.1 °C. The crystal of **3a** was obtained by slow evaporation of ether solution.

¹H NMR (400 MHz, CDCl₃) δ 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). ¹³C NMR (101 MHz, CDCl₃) δ 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 C₂₃H₂₃NO₂S₂Na⁺: [M+Na]⁺ 432.1068, found 432.1069.

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

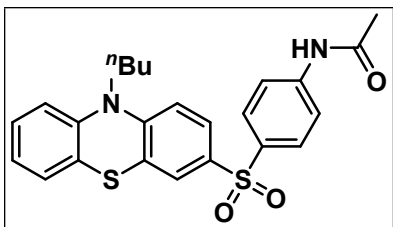


Compound **3b** was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:5) as a yellow oil, 151 mg, 71% yield.

¹H NMR (400 MHz, CDCl₃) δ 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). ¹³C NMR (101 MHz, CDCl₃) δ 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 C₂₃H₂₃NO₃S₂Na⁺: [M+Na]⁺ 448.1017, found 448.1028.

N-(4-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)phenyl)acetamide(**3c**)

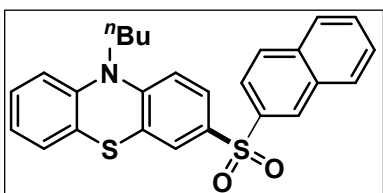


Compound **3c** was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:1) as a yellow solid, 206 mg, 91% yield. Melting point: 171-173 °C.

¹H NMR (400 MHz, CDCl₃) 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* = 2.3 Hz, 1H), 7.55 (d, *J* = 2.3 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). ¹³C NMR (101 MHz, CDCl₃) 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 C₂₄₃H₂₅N₂O₃S⁺: [M+H]⁺ 453.1306, found 453.1317.

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

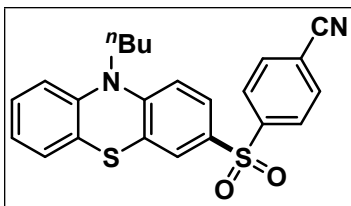


Compound **3d** was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:9) as a yellow oil, 169 mg, 76% yield.

¹H NMR (400 MHz, CDCl₃) 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). ¹³C NMR (101 MHz, CDCl₃) 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 C₂₆H₂₃NO₂S₂Na⁺: [M+Na]⁺ 468.1068, found 468.1081.

4-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)benzamide (**3e**)

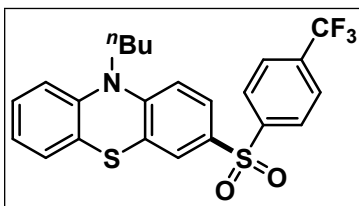


Compound **3e** was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:5) as a yellow oil, 160 mg, 76% yield.

^1H NMR (400 MHz, CDCl_3) δ 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). ^{13}C NMR (101 MHz, CDCl_3) δ 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 $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_2\text{S}_2\text{Na}^+$: $[\text{M}+\text{Na}]^+$ 443.0864, found 443.0870.

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

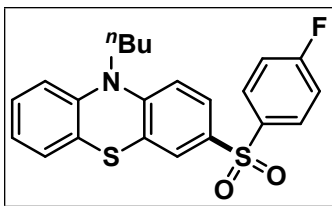


Compound **3f** was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:9) as a yellow oil, 183 mg, 79% yield.

^1H NMR (400 MHz, CDCl_3) δ 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). ^{19}F NMR (376 MHz, CDCl_3) δ -63.12. ^{13}C NMR (101 MHz, CDCl_3) δ 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 $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{S}_2\text{F}_3^+$: $[\text{M}+\text{H}]^+$ 464.0966, found 464.0958.

10-butyl-3-((4-fluorophenyl)sulfonyl)-10H-phenothiazine(3g)

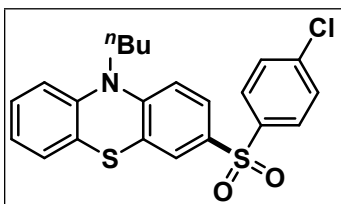


Compound **3g** was obtained following the general procedure, purified by ethyl acetate/petroleum ether (1:9) as a yellow solid, 159 mg, 77% yield. Melting point: 90-93 °C.

^1H NMR (400 MHz, CDCl_3) δ 7.97 – 7.86 (m, 2H), 7.67 (dd, $J = 8.6, 2.2$ Hz, 1H), 7.59 (d, $J = 2.2$ Hz, 1H), 7.20 – 7.12 (m, 3H), 7.08 (dd, $J = 7.7, 1.5$ Hz, 1H), 6.95 (td, $J = 7.5, 1.2$ Hz, 1H), 6.85 (dd, $J = 8.5, 1.7$ Hz, 2H), 3.84 (t, $J = 7.2$ Hz, 2H), 1.75 (p, $J = 7.5$ Hz, 2H), 1.43 (h, $J = 7.4$ Hz, 2H), 0.92 (t, $J = 7.3$ Hz, 3H). ^{19}F NMR (376 MHz, CDCl_3) δ -104.68. ^{13}C NMR (101 MHz, CDCl_3) δ 165.21 (d, $J_{\text{C-F}} = 255.5$ Hz), 149.88, 143.43, 138.22 (d, $J_{\text{C-F}} = 3.1$ Hz), 134.14, 130.10 (d, $J_{\text{C-F}} = 9.5$ Hz), 127.70, 127.56, 127.26, 126.42, 125.86, 123.65, 123.49, 116.46 (d, $J_{\text{C-F}} = 22.7$ Hz), 115.99, 114.88, 47.52, 28.69, 19.99, 13.67.

HRMS calculated for $\text{C}_{22}\text{H}_{21}\text{NO}_2\text{S}_2\text{F}^+$: $[\text{M}+\text{H}]^+$ 414.0997, found 414.1000.

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



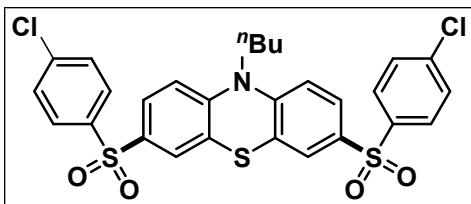
Compound **3h** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 116 mg, 51% yield. Melting point: 152-154 °C.

^1H NMR (400 MHz, CDCl_3) δ 7.77 (dd, $J = 8.8, 2.4$ Hz, 2H), 7.61 (dd, $J = 8.6, 2.3$ Hz, 1H), 7.52 (d, $J = 2.3$ Hz, 1H), 7.38 (dd, $J = 8.8, 2.4$ Hz, 2H), 7.15 – 7.05 (m, 1H), 7.02 (dd, $J = 7.7, 1.7$ Hz, 1H), 6.93 – 6.85 (m, 1H), 6.79 (dd, $J = 8.4, 2.4$ Hz, 2H), 3.78 (t, $J = 7.2$ Hz, 2H), 1.80 – 1.58 (m, 2H), 1.37 (h, $J = 7.3$ Hz, 2H), 0.86 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 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 $\text{C}_{22}\text{H}_{21}\text{NO}_2\text{S}_2\text{Cl}^+$: $[\text{M}+\text{H}]^+$ 430.0702, found 430.0703.

3h-disulfonylation:

10-butyl-3,7-bis((4-chlorophenyl)sulfonyl)-10H-phenothiazine



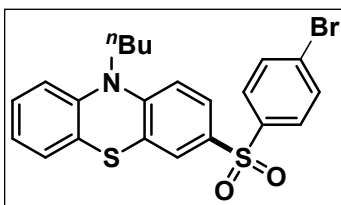
Compound **3h**-disulfonylated product was obtained as a yellow oil, 36 mg, 12% yield.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 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).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 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 $\text{C}_{28}\text{H}_{24}\text{NO}_4\text{S}_3\text{Cl}_2^+$: $[\text{M}+\text{H}]^+$ 604.0244, found 604.4106

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

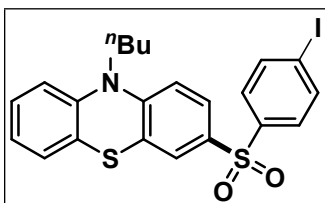


Compound **3i** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 154mg, 65% yield. Melting point: 163-164 °C.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 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). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 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 $\text{C}_{22}\text{H}_{21}\text{NO}_2\text{S}_2\text{Br}^+$: $[\text{M}+\text{H}]^+$ 474.0197, found 474.0196.

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



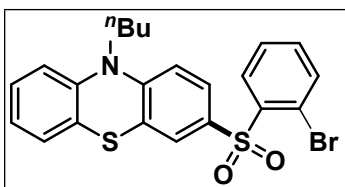
Compound **3j** were obtained following the general procedure, purified by ethyl acetate/petroleum

ether as a yellow solid, 151 mg, 58% yield. Melting point: 157-158 °C.

^1H 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 $\text{C}_{22}\text{H}_{21}\text{NO}_2\text{S}_2\text{I}^+$: $[\text{M}+\text{H}]^+$ 522.0058, found 522.0057.

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



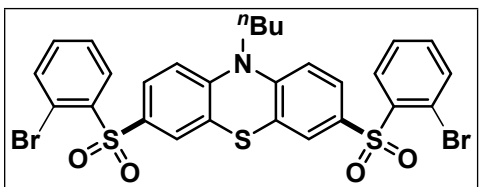
Compound **3k** were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 137 mg, 58% yield. Melting point: 113-115 °C. Rotational isomer observed.

^1H 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 $\text{C}_{22}\text{H}_{21}\text{NO}_2\text{S}_2\text{Br}^+$: $[\text{M}+\text{H}]^+$ 474.0197, found 474.0199.

3k-disulfonylation:

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



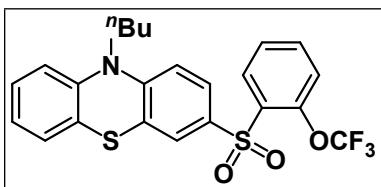
Compound **3k**-disulfonylated product was obtained as a yellow oil, 52 mg, 15% yield.

^1H 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). ^{13}C NMR (101 MHz, CDCl_3) 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 $\text{C}_{28}\text{H}_{24}\text{NO}_4\text{S}_3\text{Br}_2^+$: $[\text{M}+\text{H}]^+$ 691.9234, found 691.9241

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

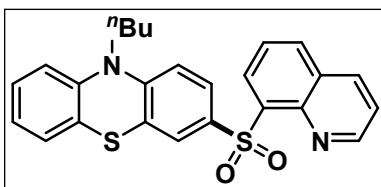


Compound **3l** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 175 mg, 73% yield. Melting point: 114-117 °C.

^1H NMR (400 MHz, CDCl_3) 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). ^{19}F NMR (376 MHz, CDCl_3) δ -56.12. ^{13}C NMR (101 MHz, CDCl_3) 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 $\text{C}_{23}\text{H}_{21}\text{NO}_3\text{S}_2\text{F}^+$: $[\text{M}+\text{H}]^+$ 480.0915, found 480.0916.

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



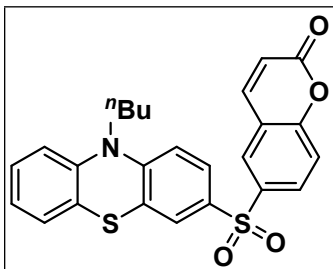
Compound **3m** were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, the crystal of **3m** was obtained by slow evaporation of ether solution. 152 mg, 69% yield. Melting point: 193-195 °C.

^1H NMR (400 MHz, CDCl_3) 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). ^{13}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 $\text{C}_{25}\text{H}_{23}\text{N}_2\text{O}_2\text{S}_2^+$: $[\text{M}+\text{H}]^+$ 447.1201, found 447.1234.

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

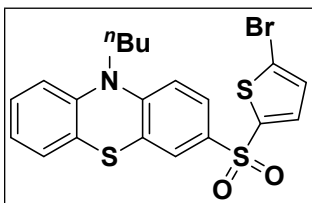


Compound **3n** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow oil, 187 mg, 81% yield.

^1H 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 $\text{C}_{25}\text{H}_{22}\text{NO}_4\text{S}_2^+$: $[\text{M}+\text{H}]^+$ 464.0990, found 464.0989.

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



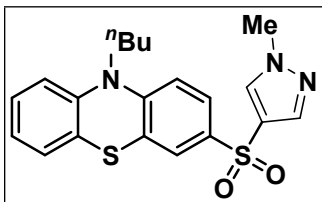
Compound **3o** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow oil, 189 mg, 79% yield.

^1H 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). ^{13}C NMR (101 MHz, CDCl_3) 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 $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{S}_3\text{Br}^+$: $[\text{M}+\text{H}]^+$ 479.9761, found 479.9708.

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

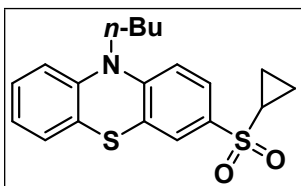


Compound **3p** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 144 mg, 72% yield. Melting point: 97-100 °C.

^1H NMR (400 MHz, CDCl_3) δ 7.80 (s, 1H), 7.74 (s, 1H), 7.68 (ddd, $J = 8.6, 2.2, 1.2$ 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, $J = 7.4, 3\text{H}$). ^{13}C NMR (101 MHz, CDCl_3) 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 $\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_2\text{S}_2^+$: $[\text{M}+\text{H}]^+$ 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.

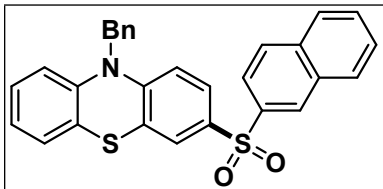
^1H NMR (400 MHz, CDCl_3) δ 7.63 (dd, $J = 8.6, 2.1$ Hz, 1H), 7.57 (d, $J = 2.1$ Hz, 1H), 7.17 (d, $J = 7.7$ Hz, 1H), 7.12 (d, $J = 7.6$ Hz, 1H), 6.98 (d, $J = 7.5$ Hz, 1H), 6.89 (dd, $J = 8.5, 4.1$ Hz, 2H), 3.89 (t, $J = 7.2$ Hz, 2H), 2.42 (tt, $J = 8.2, 4.8$ Hz, 1H), 1.79 (p, $J = 7.3$ Hz, 2H), 1.46 (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).

^{13}C NMR (101 MHz, CDCl_3) 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 $C_{19}H_{22}NO_2S_2^+$: $[M+H]^+$ 360.1092, found 360.1097.

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

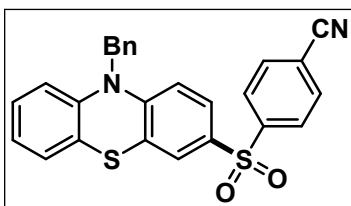


Compound **3r** was obtained following the general procedure with higher loading of CuI and temperature reflux (CuI, 50 mol%, 130 °C), purified by ethyl acetate/petroleum ether as a brown oil, 100 mg, 42% yield.

1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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 $C_{29}H_{22}NO_2S_2^+$: $[M+H]^+$ 480.1092, found 480.1087

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

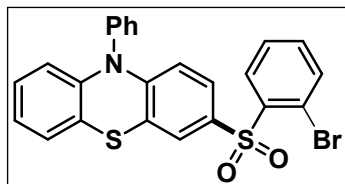


Compound **3t** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a brown oil, 84 mg, 37% yield.

1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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 $C_{26}H_{19}N_2O_2S_2^+$: $[M+H]^+$ 455.0888, found 455.0886.

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

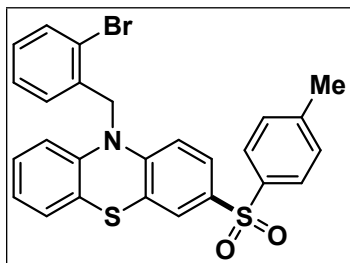


Compound **3t** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow oil, 235 mg, 95% yield.

1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 148.43, 142.57, 140.23, 139.58, 135.51, 134.20, 132.24, 131.12, 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 $C_{24}H_{17}BrNO_2S_2$: $[M+H]^+$ 493.9884, found 493.9885

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



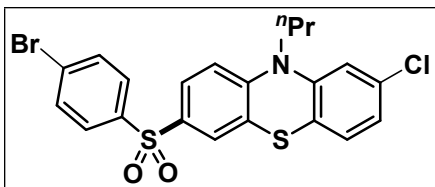
Compound **3u** was obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 138 mg, 53% yield. Melting point: 180-182 °C.

1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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 $C_{26}H_{21}NO_2S_2Br^+$: $[M+H]^+$ 522.0197, found 522.0188.

7-((4-bromophenyl)sulfonyl)-2-chloro-10-propyl-10H-phenothiazine(3v)

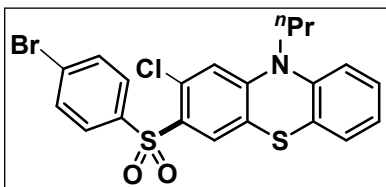


Compound **3v** were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 133 mg, 54% yield. Melting point: 152-155 °C.

^1H NMR (400 MHz, CDCl_3) δ 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) δ 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 $\text{C}_{21}\text{H}_{18}\text{NO}_2\text{S}_2\text{BrCl}^+$: $[\text{M}+\text{H}]^+$ 493.9651, found 493.9644.

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

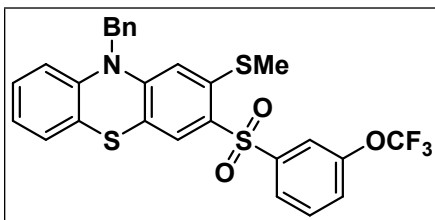


Compound **3w** were obtained in the same reaction as **3v**, purified by ethyl acetate/petroleum ether as a yellow solid, 74 mg, 30% yield. Melting point: 133-134 °C.

^1H NMR (400 MHz, CDCl_3) δ 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) δ 150.87, 142.70, 139.79, 132.16, 132.10, 130.46, 129.81, 128.89, 128.40, 127.83, 127.72, 124.10, 123.84, 123.41, 117.43, 116.26, 49.65, 19.89, 11.10.

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

10-benzyl-2-(methylthio)-3-((3-(trifluoromethoxy)phenyl)sulfonyl)-10H-phenothiazine (**3x**)

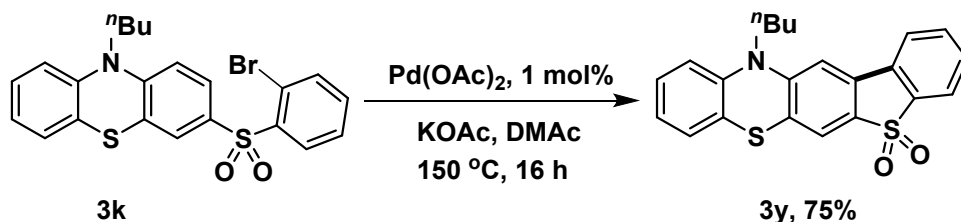


Compound **3x** were obtained following the general procedure, purified by ethyl acetate/petroleum ether as a yellow solid, 129 mg, 46% yield. Melting point: 171-173 °C.

^1H 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, 130.25, 129.96, 129.07, 128.43, 127.81, 127.60, 127.14, 126.31, 126.27, 125.21, 123.98, 122.31, 120.98, 119.73, 115.95, 113.52, 53.34, 15.73.

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

Synthesis of heteroarene **3y**

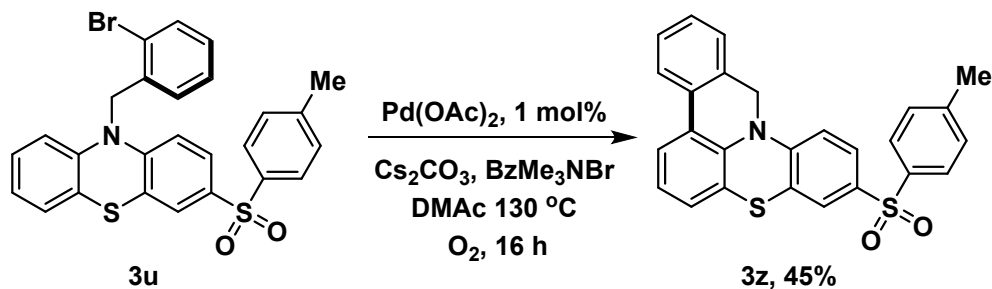


To an oven-dried 25 mL Schlenk tube, compound **3k** (95 mg, 0.2 mmol), KOAc (59 mg, 0.6 mmol) and Pd(OAc)_2 solution (0.45 mg in 2 mL DMAc) were subsequently added. The mixture was bubbled under nitrogen flow for 3 minutes. Then the reaction tube was sealed and set in a preheated oil bath at 150 °C 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_2SO_4 and purified by column chromatography using ethyl acetate/ petroleum ether to afford **3y** as yellow oil, 59 mg, 75% yield.

^1H 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 $\text{C}_{22}\text{H}_{20}\text{NO}_2\text{S}_2^+$: $[\text{M}+\text{H}]^+$ 394.0935, found 394.0938.

Synthesis of heteroarene **3z**



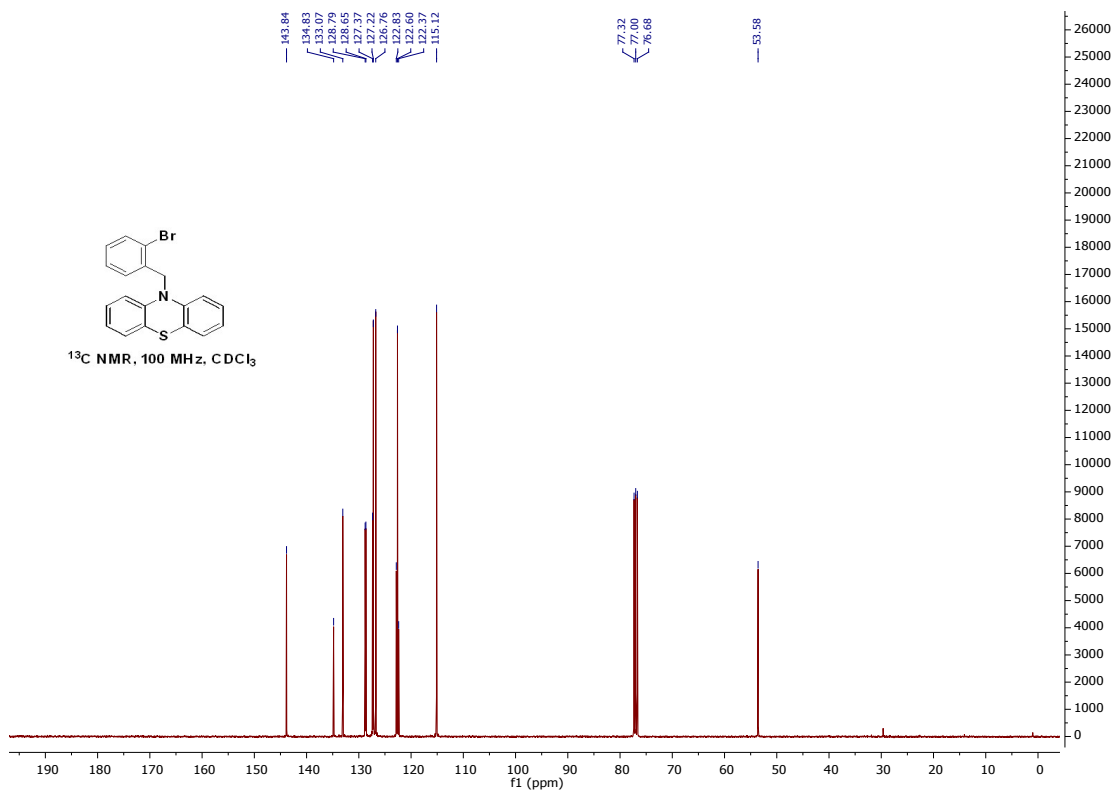
To an oven-dried 25 mL Schlenk tube, compound **3u** (104 mg, 0.2 mmol), Cs_2CO_3 (65 mg, 0.4 mmol), BzMe_3NBr (98 mg, 0.4 mmol) and $\text{Pd}(\text{OAc})_2$ solution (0.45 mg in 2 mL DMAc) were subsequently added. The mixture was bubbled under oxygen flow for 3 minutes. Then the reaction tube was sealed and set in a preheated oil bath at 130 °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_2SO_4 and purified by column chromatography using ethyl acetate/petroleum ether to afford **3z** as yellow oil, 40 mg, 45% yield.

^1H NMR (400 MHz, CDCl_3) δ 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) δ 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.

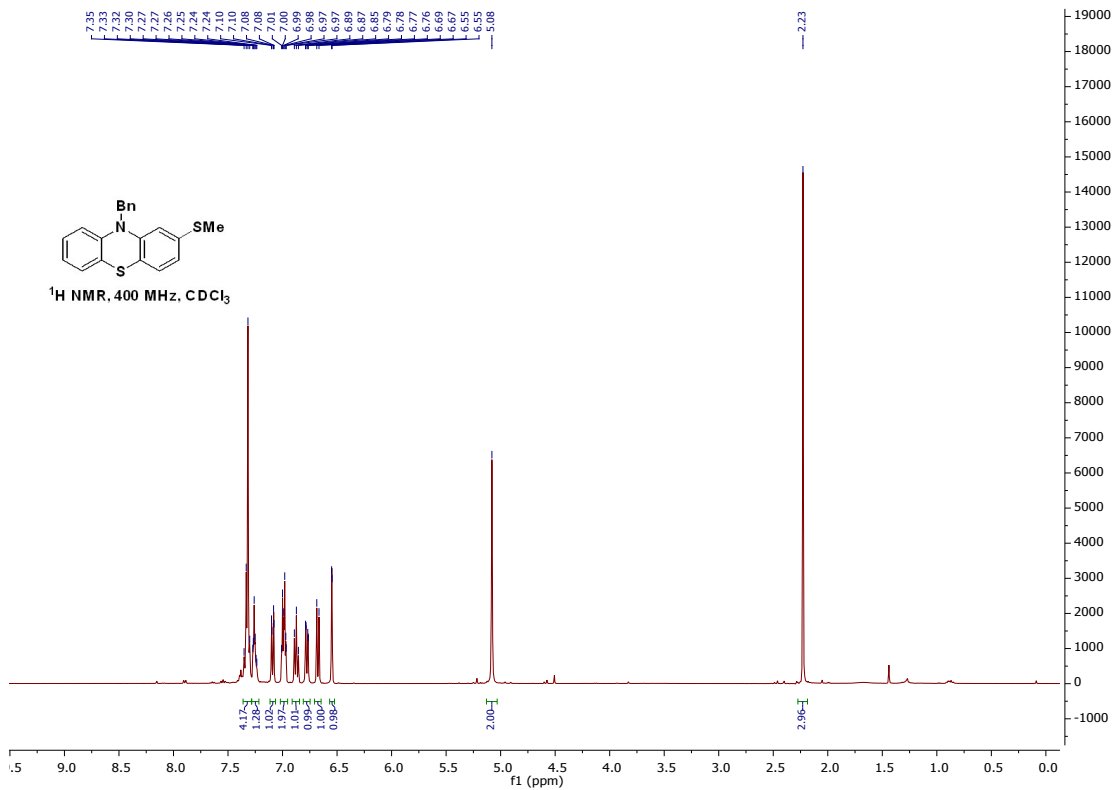
HRMS calculated for $\text{C}_{26}\text{H}_{20}\text{NO}_2\text{S}_2^+$: $[\text{M}+\text{H}]^+$ 442.0935, found 442.0952.

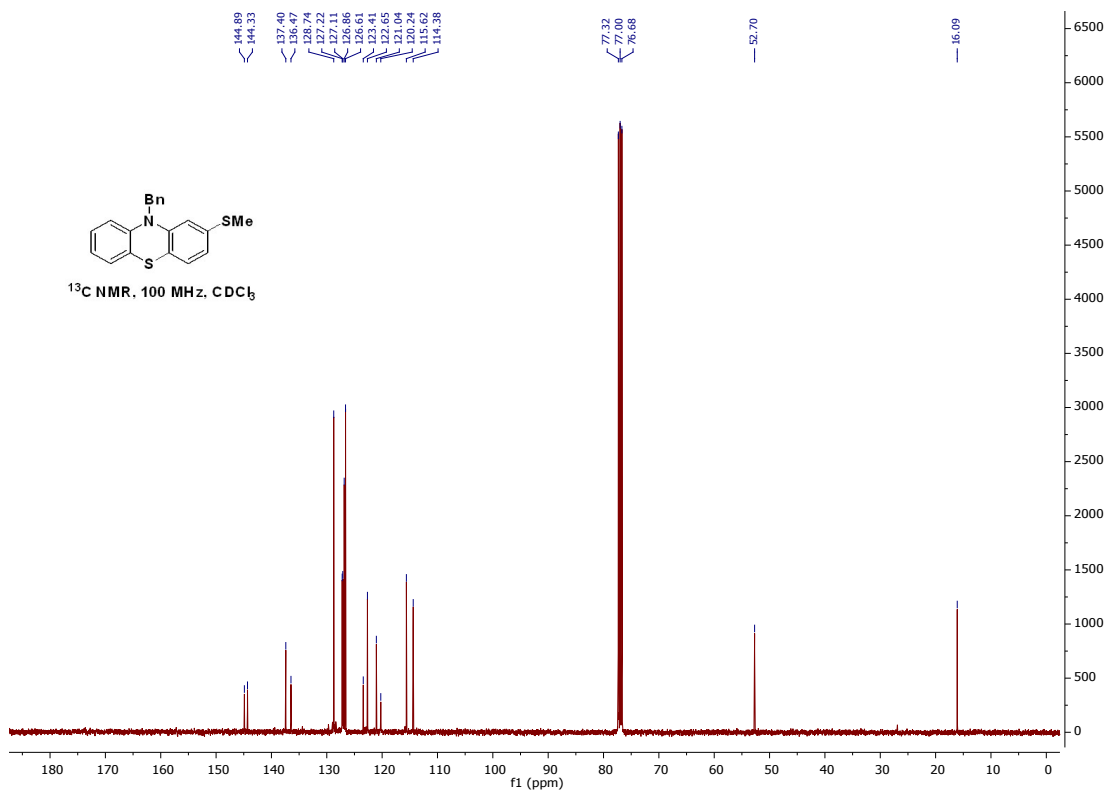
References

1. Sanap, A. K.; Sanap, K. K.; Shankarling, G. S., *Dyes and Pigments* **2015**, *120*, 190-199.
2. Orsi, D. L.; Easley, B. J.; Lick, A. M.; Altman, R. A., *Org. Lett.* **2017**, *19*, 1570-1573.
3. Kastrinsky, D. B.; Sangodkar, J.; Zaware, N.; Izadmehr, S.; Dhawan, N. S.; Narla, G.; Ohlmeyer, M., *Bioorg. Med. Chem.* **2015**, *23*, 6528-34.
4. Discekici, E. H.; Treat, N. J.; Poelma, S. O.; Mattson, K. M.; Hudson, Z. M.; Luo, Y.; Hawker, C. J.; Read de Alaniz, J., *Chem. Commun.* **2015**, *51*, 11705-8.

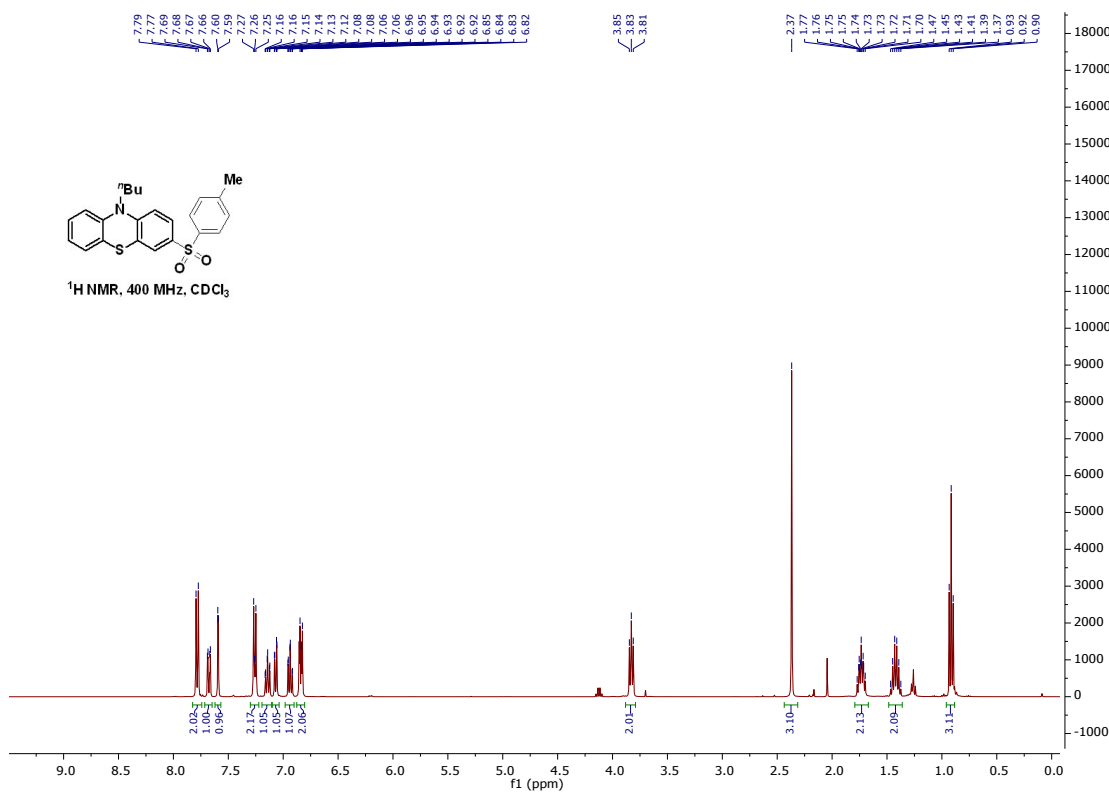


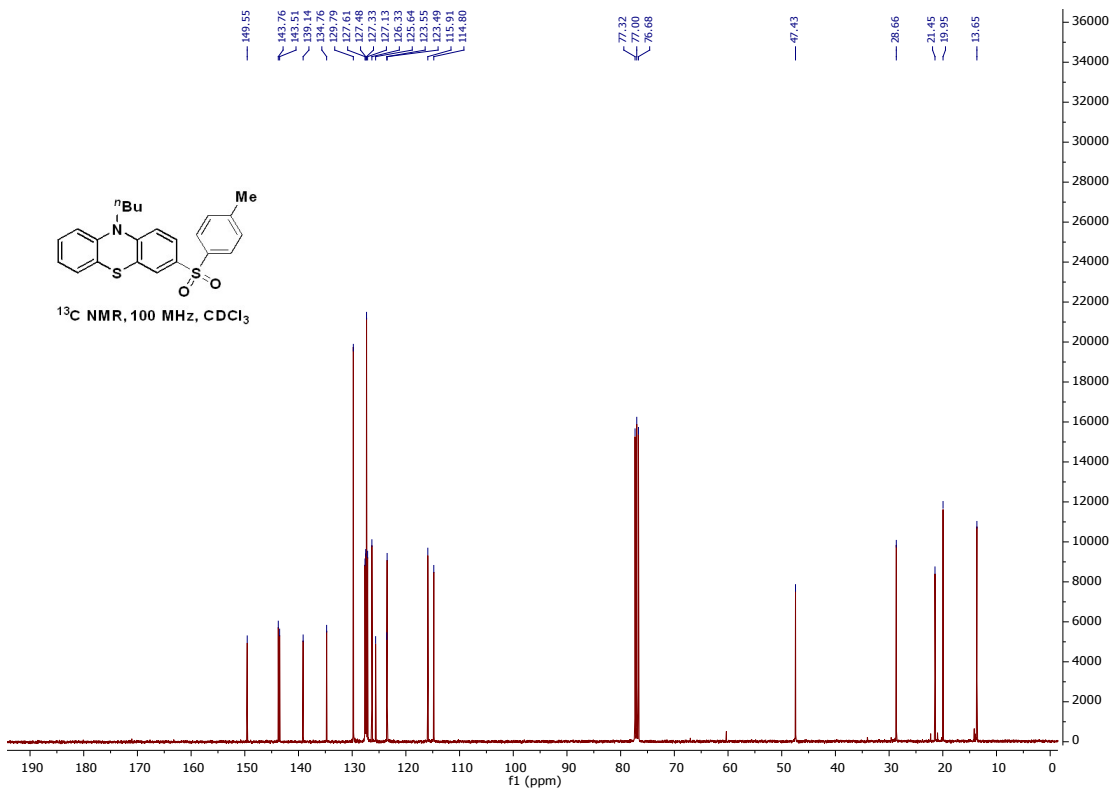
10-benzyl-3-(methylthio)-10H-phenothiazine(1f)



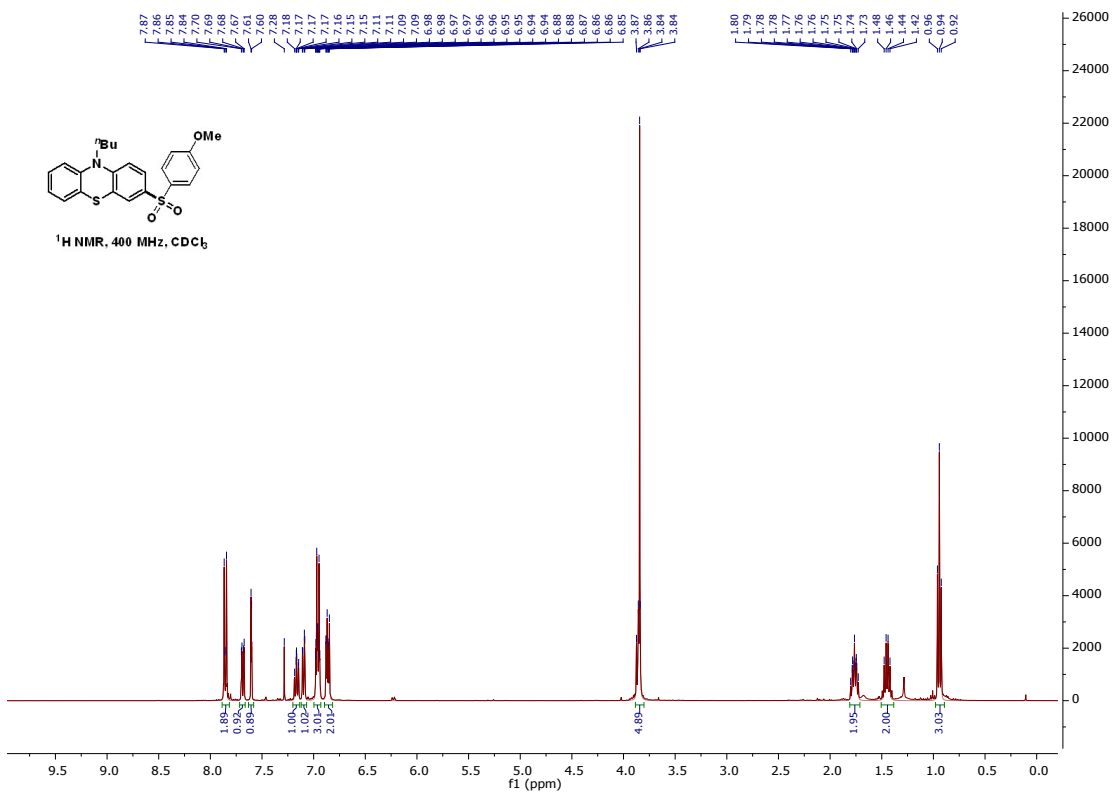


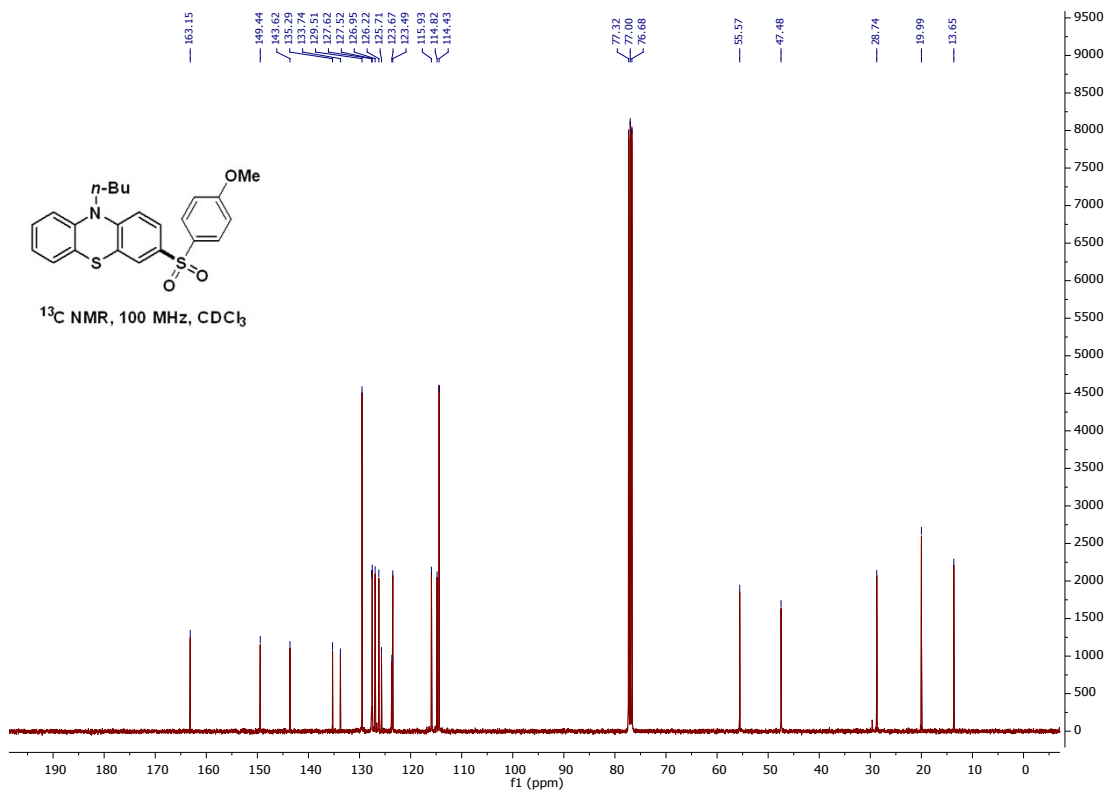
10-butyl-3-tosyl-10H-phenothiazine(3a)



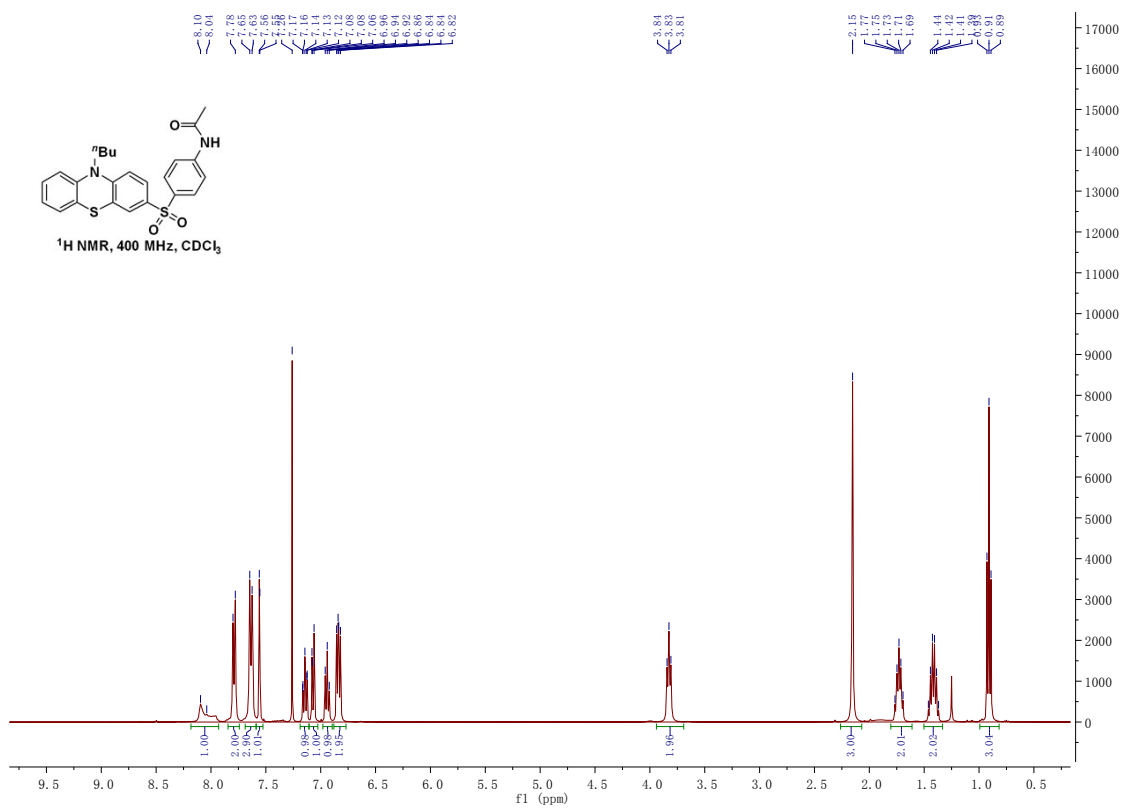


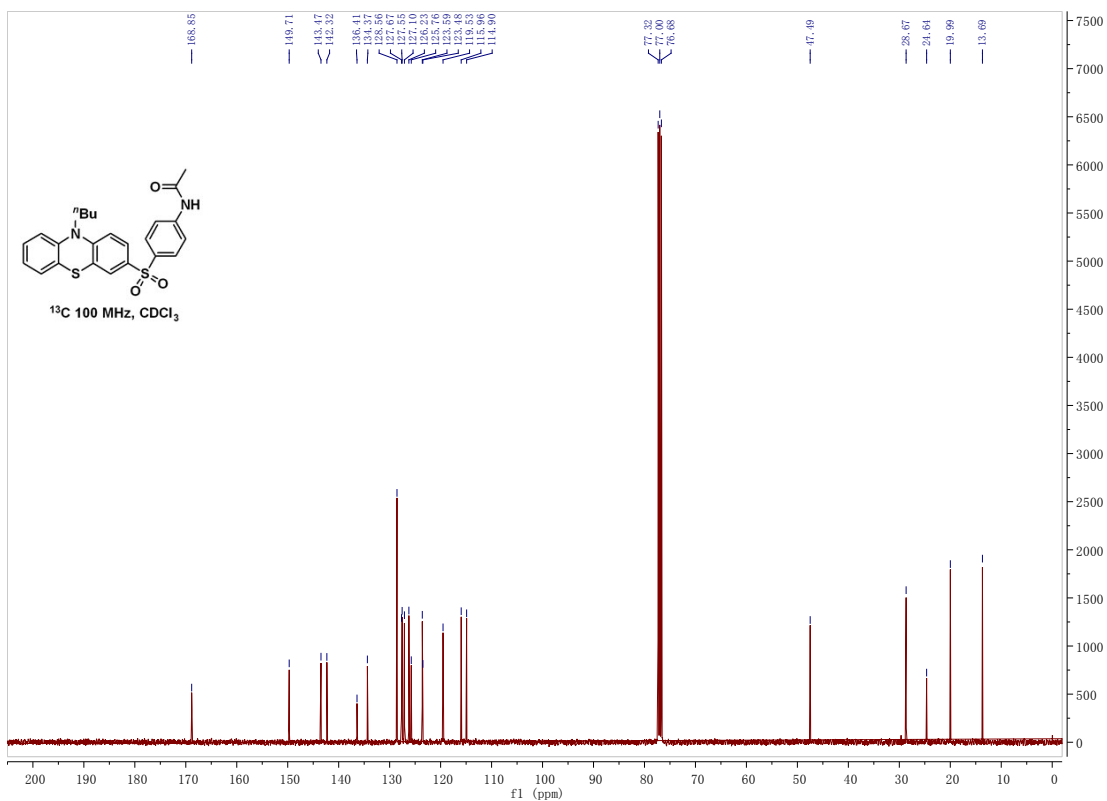
10-butyl-3-((4-methoxyphenyl)sulfonyl)-10H-phenothiazine(3b)



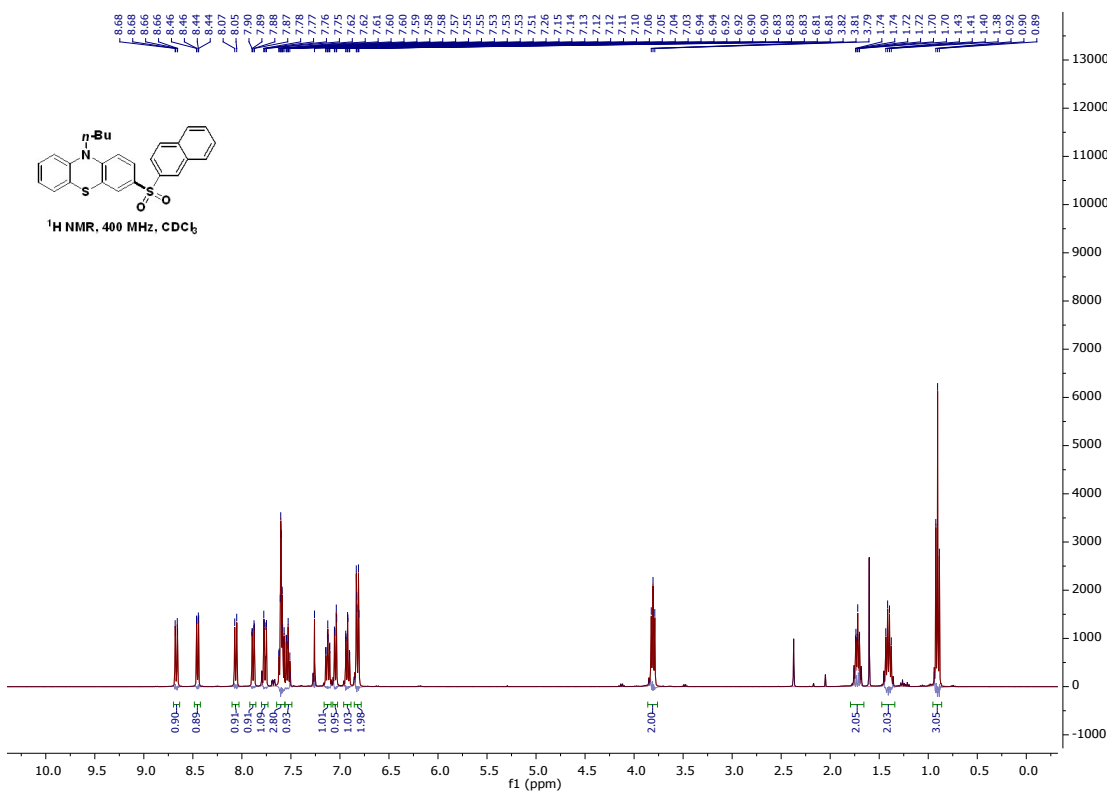


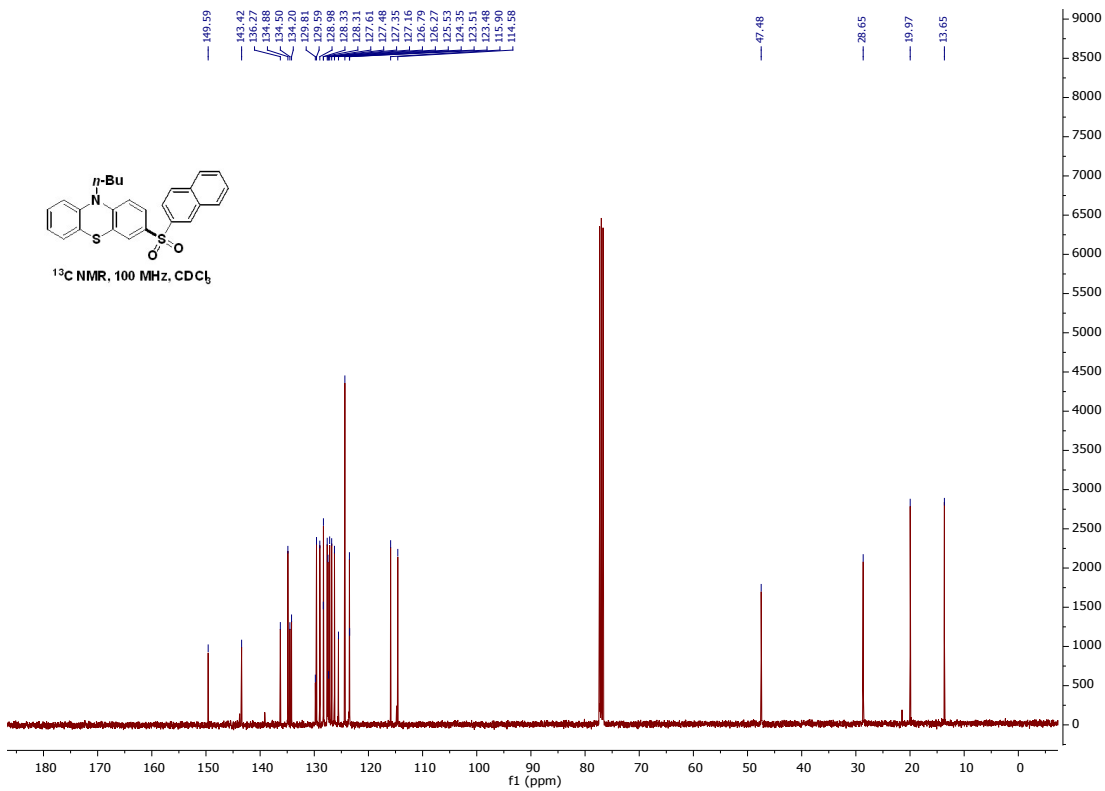
N-(4-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)phenyl)acetamide (3c)



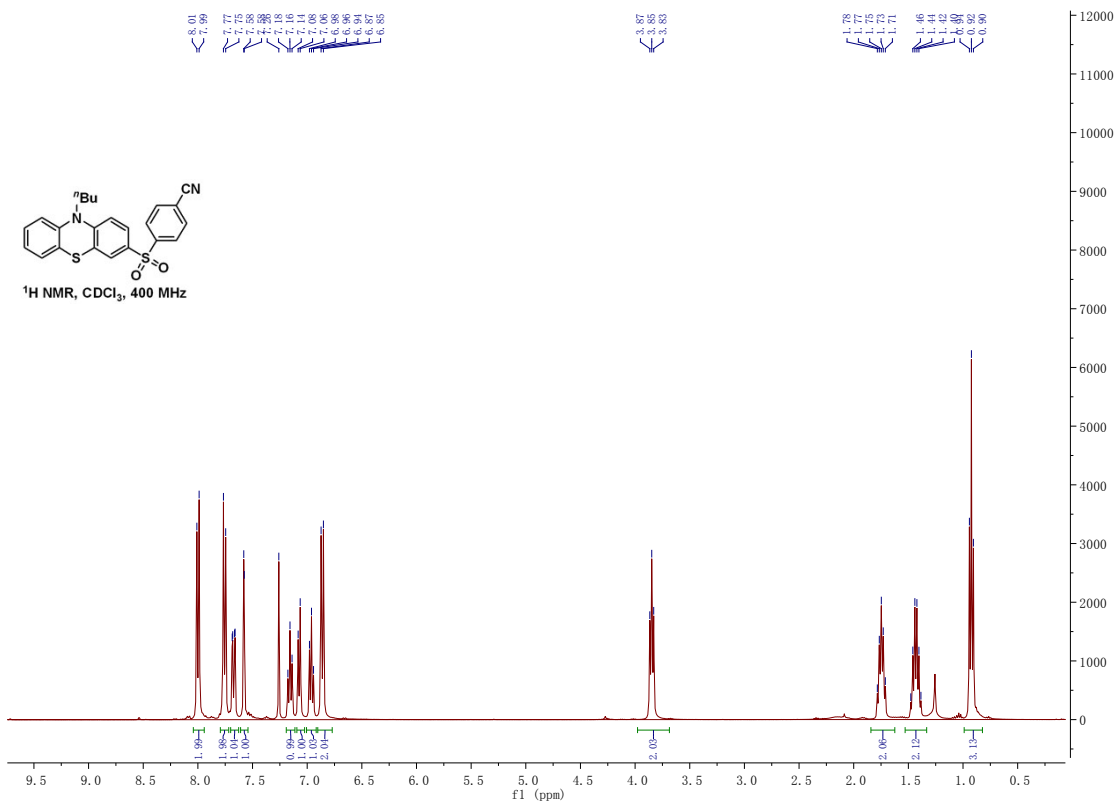


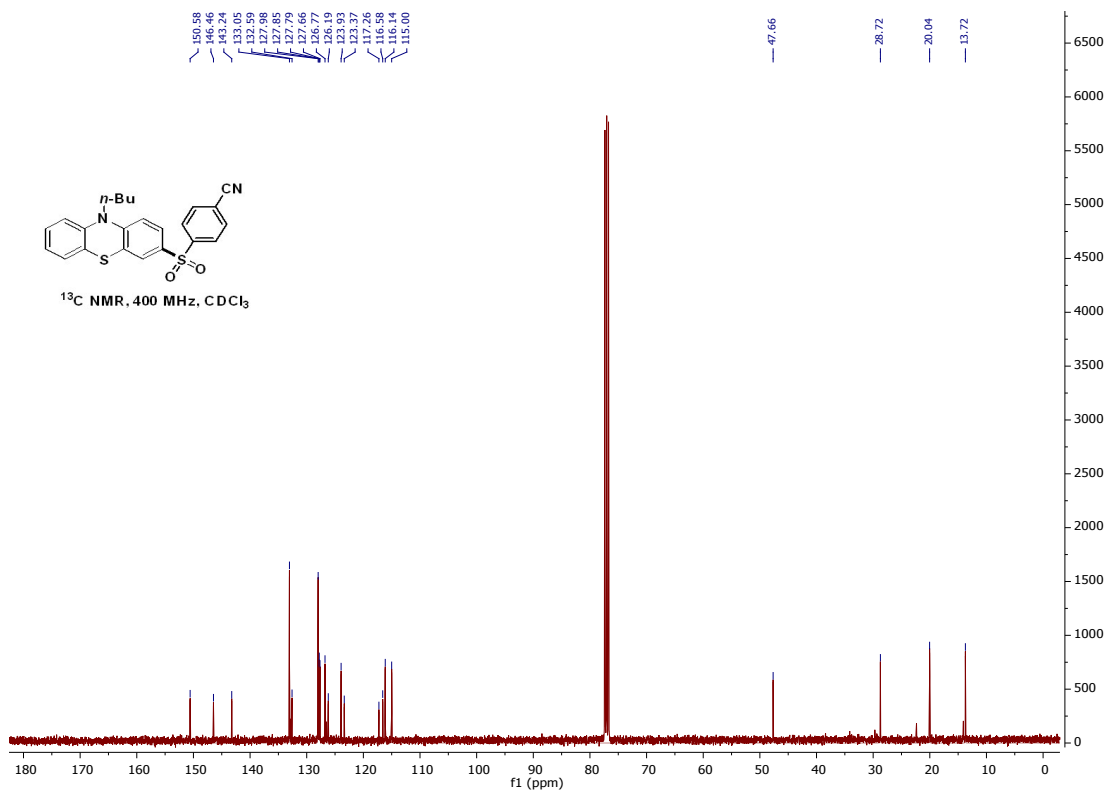
10-butyl-3-(naphthalen-2-ylsulfonyl)-10H-phenothiazine (3d)



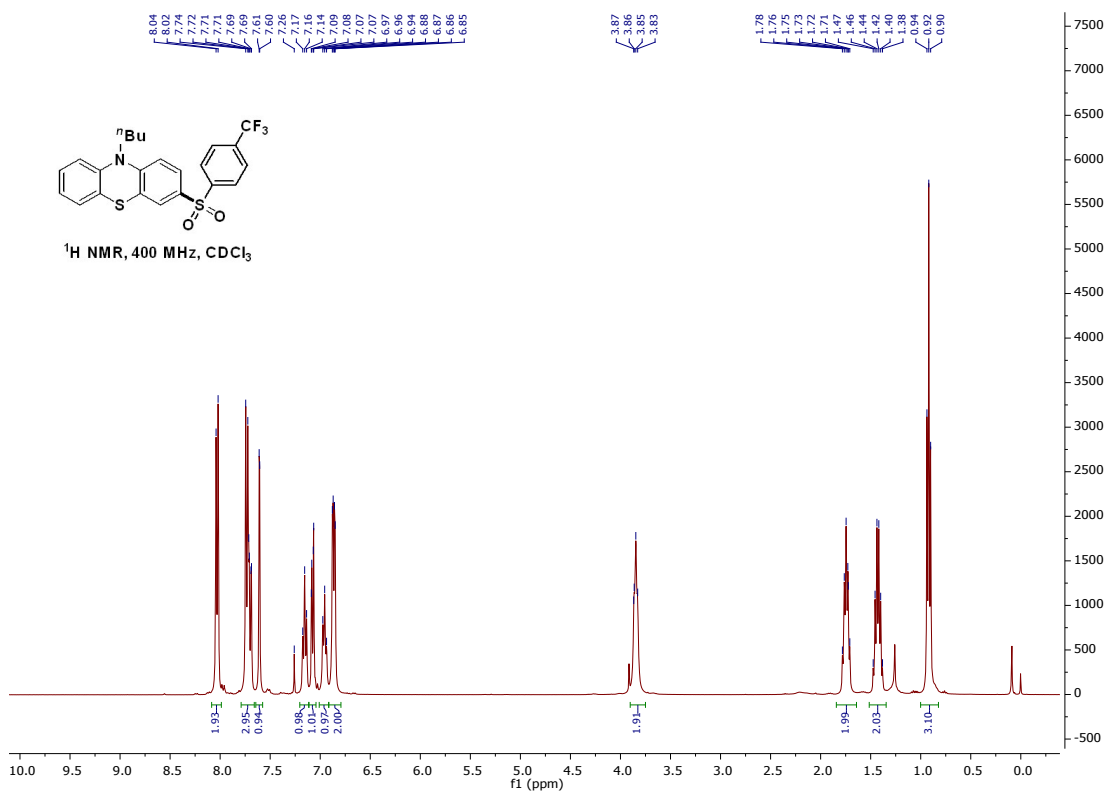


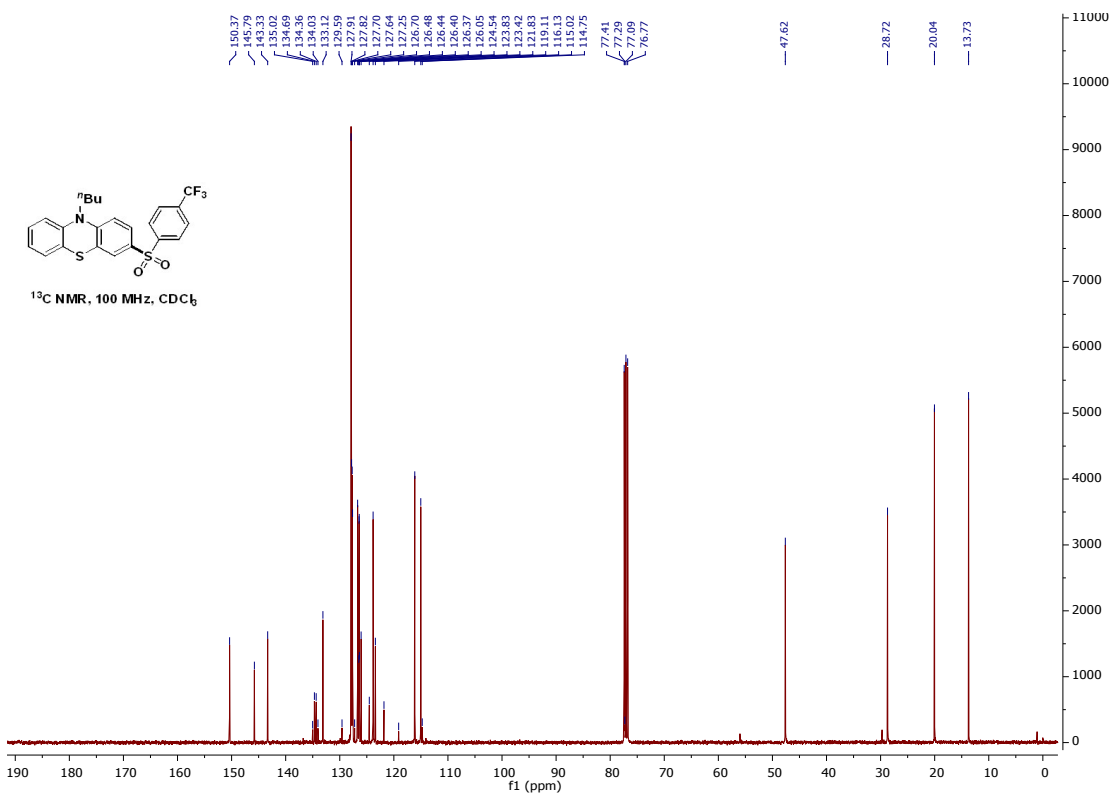
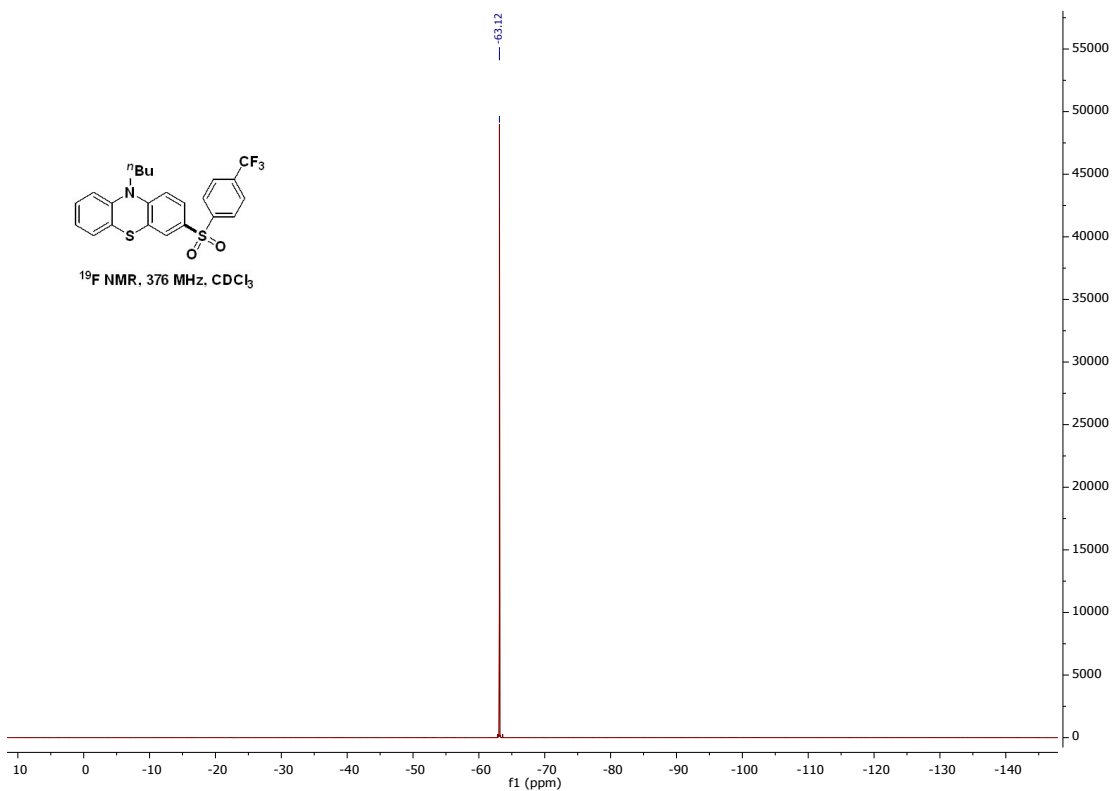
4-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)benzotrile(3e)



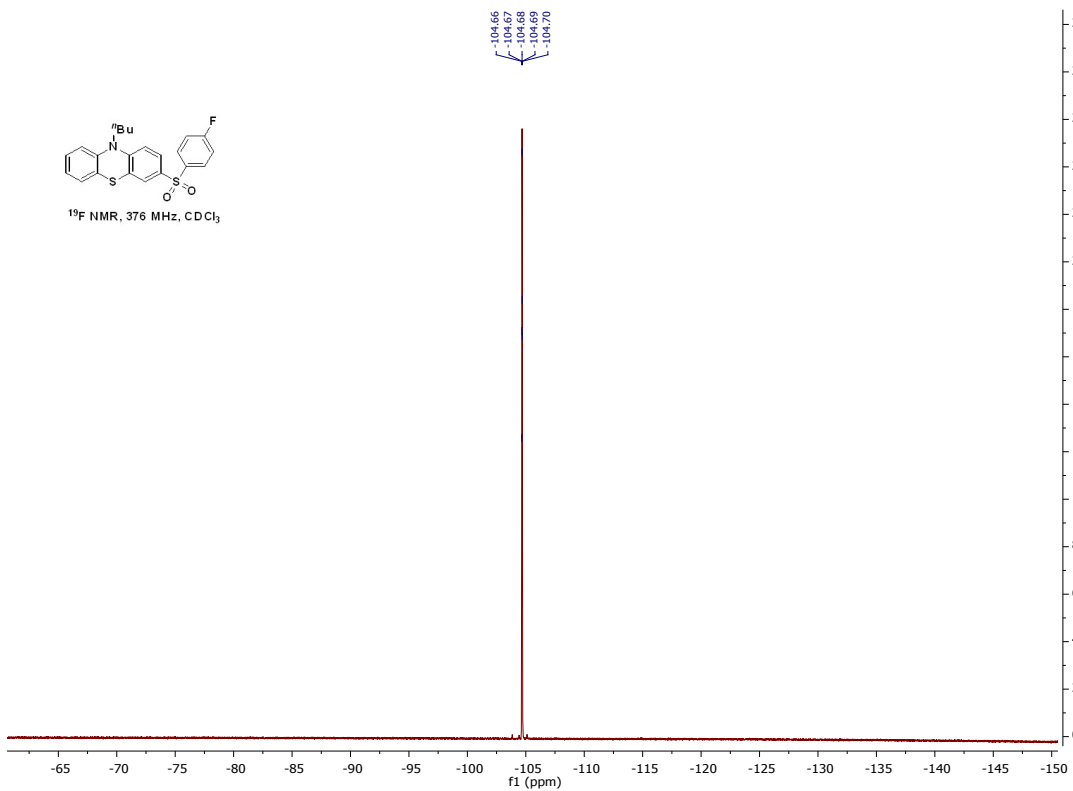
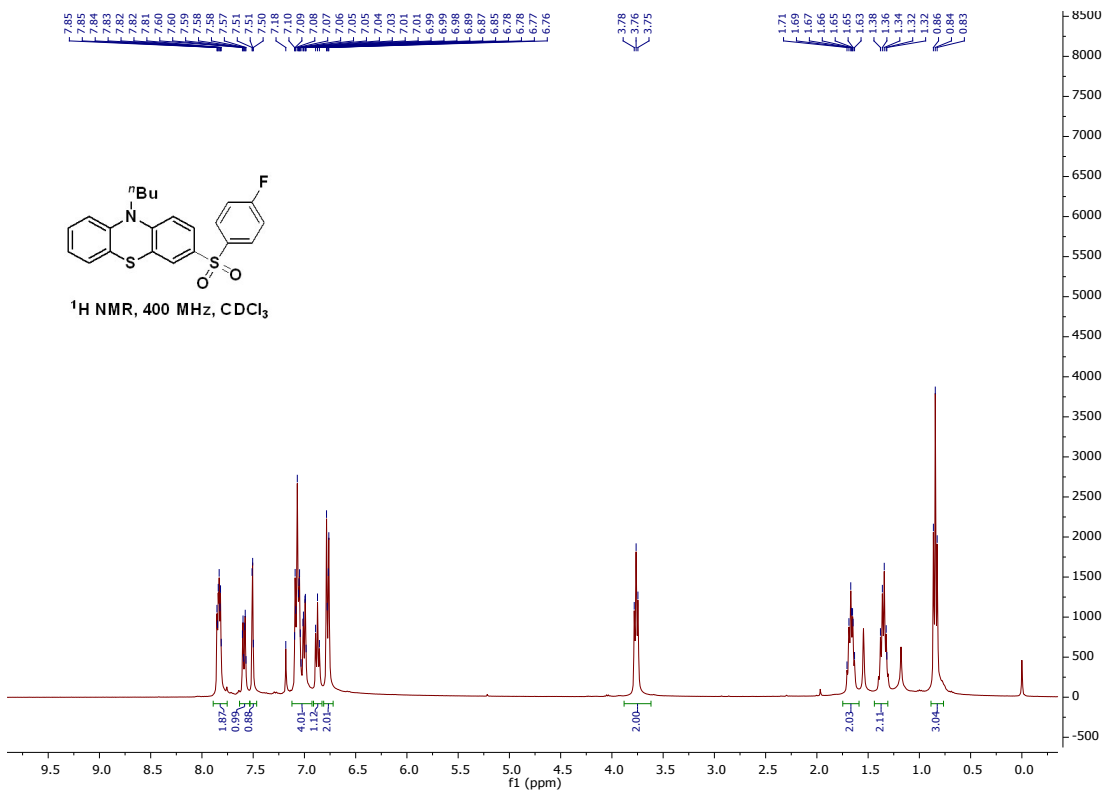


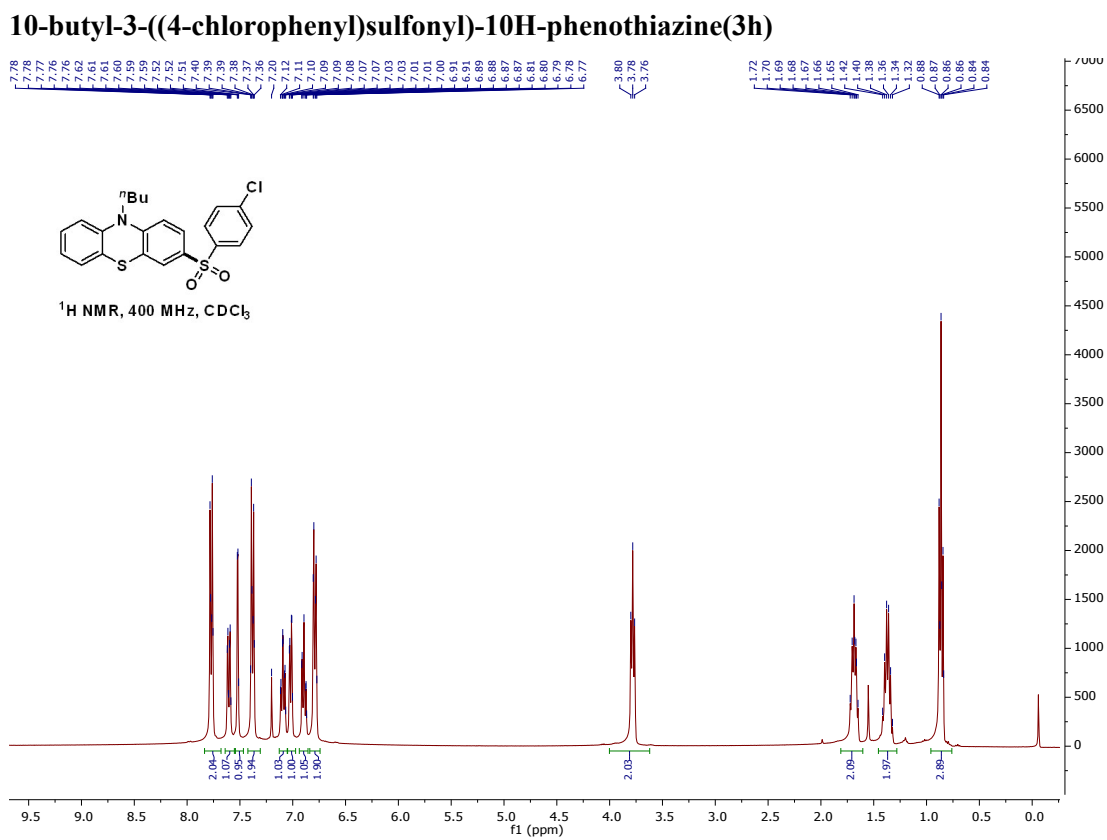
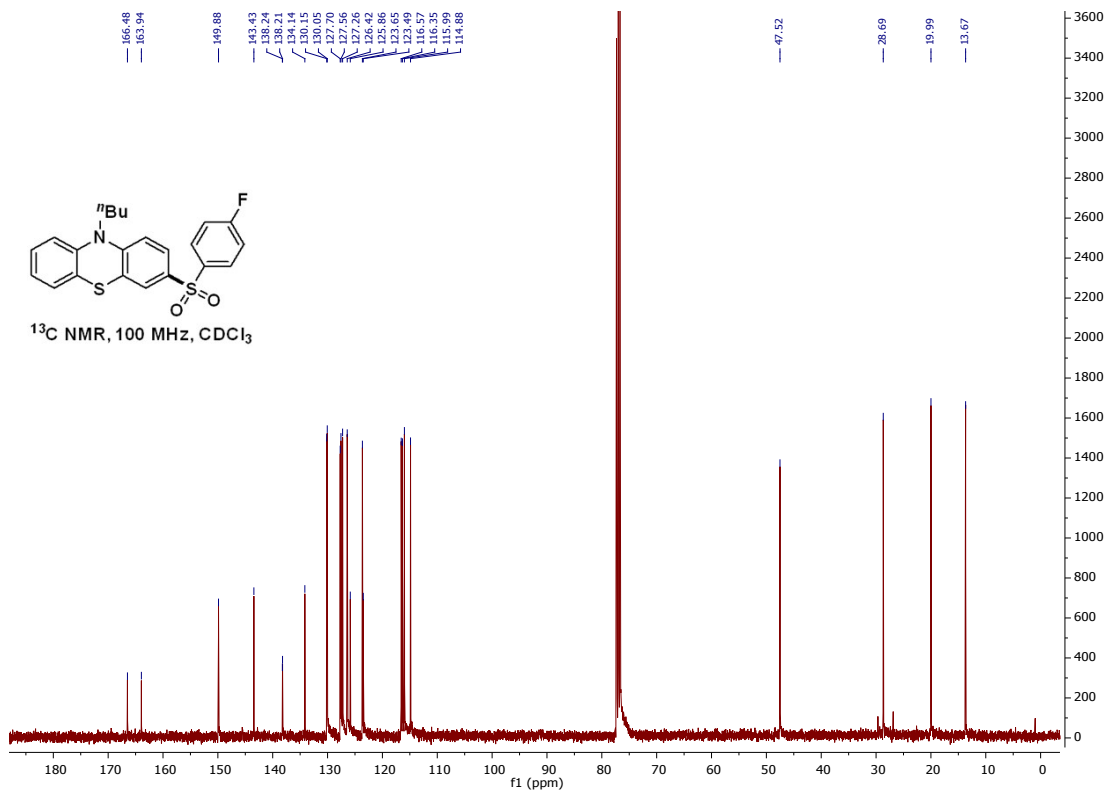
10-butyl-3-((4-(trifluoromethyl)phenyl)sulfonyl)-10H-phenothiazine(3f)

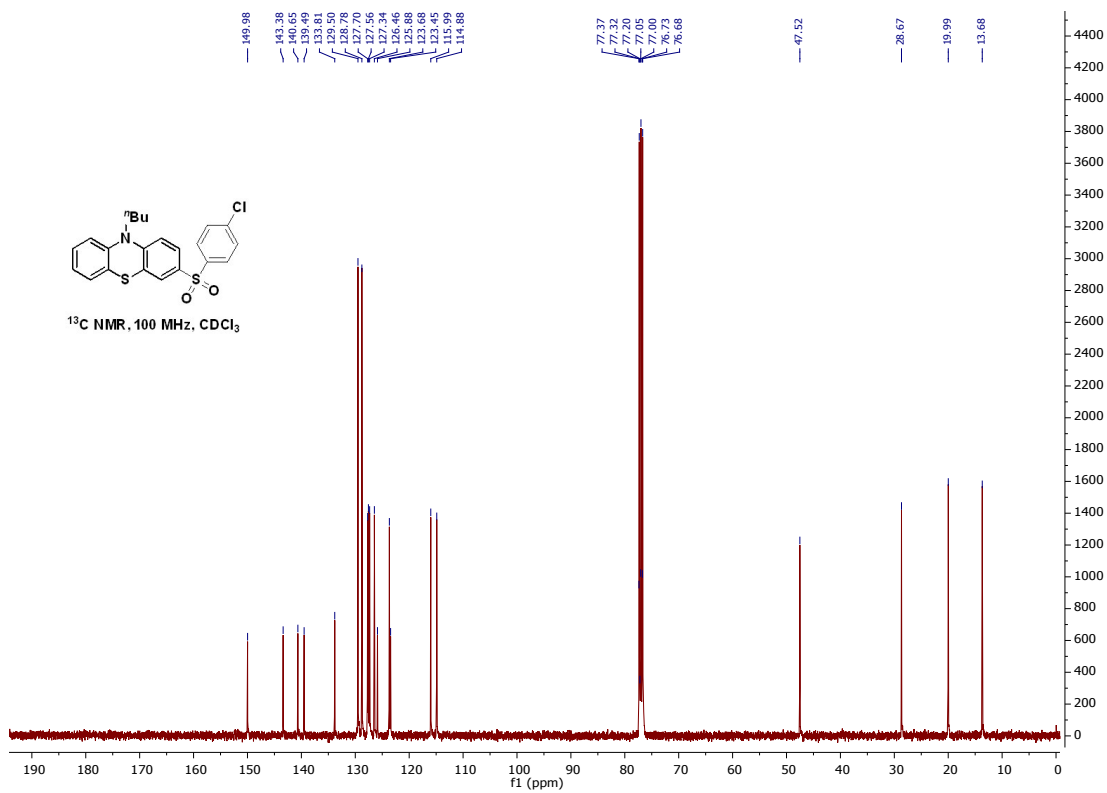




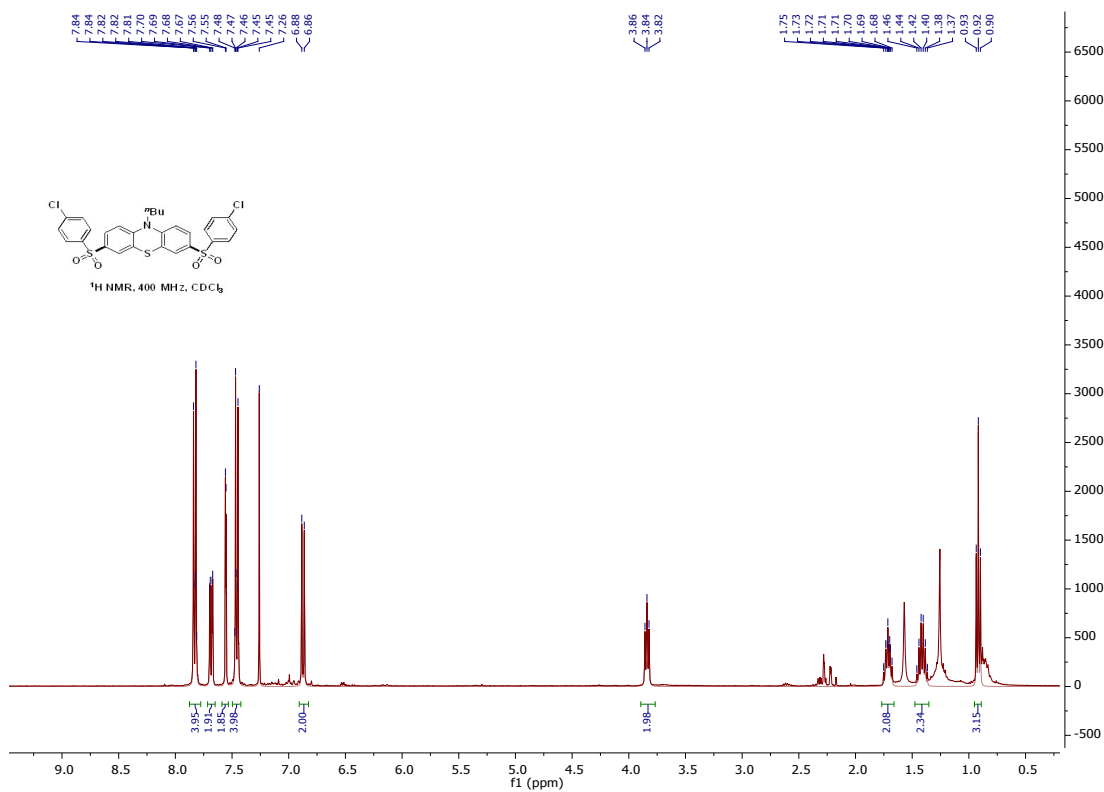
10-butyl-3-((4-(trifluoromethyl)phenyl)sulfonyl)-10H-phenothiazine(3g)

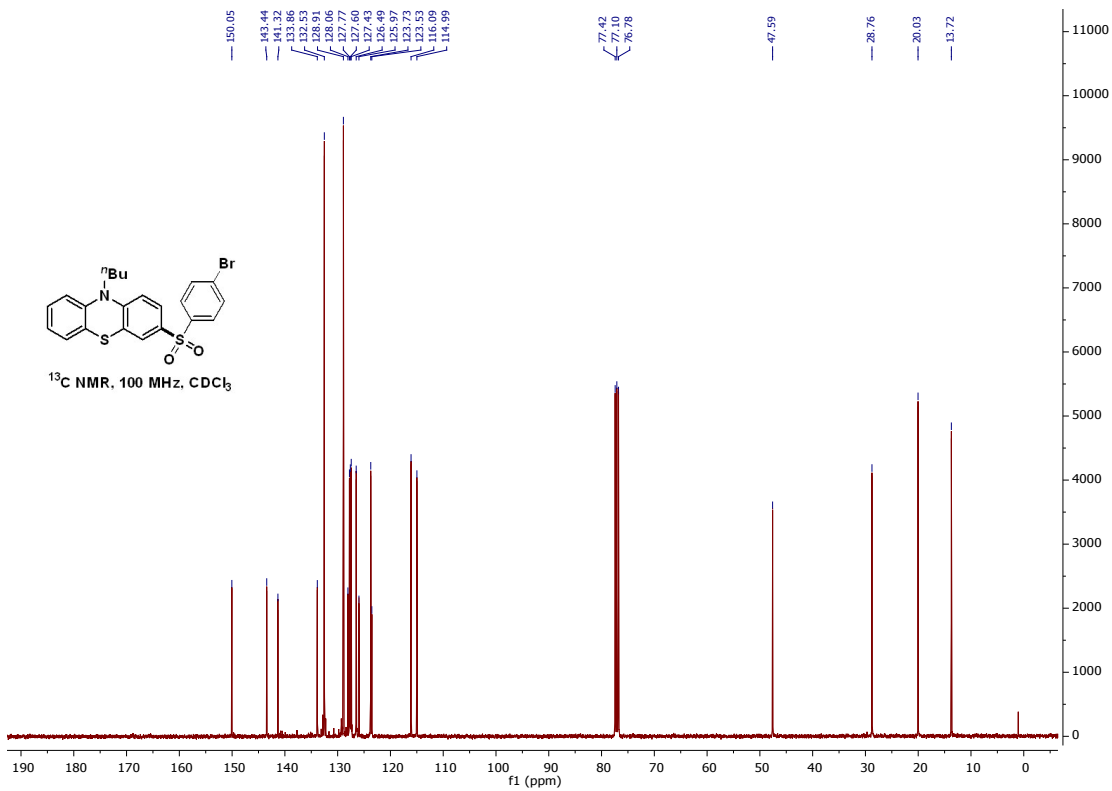




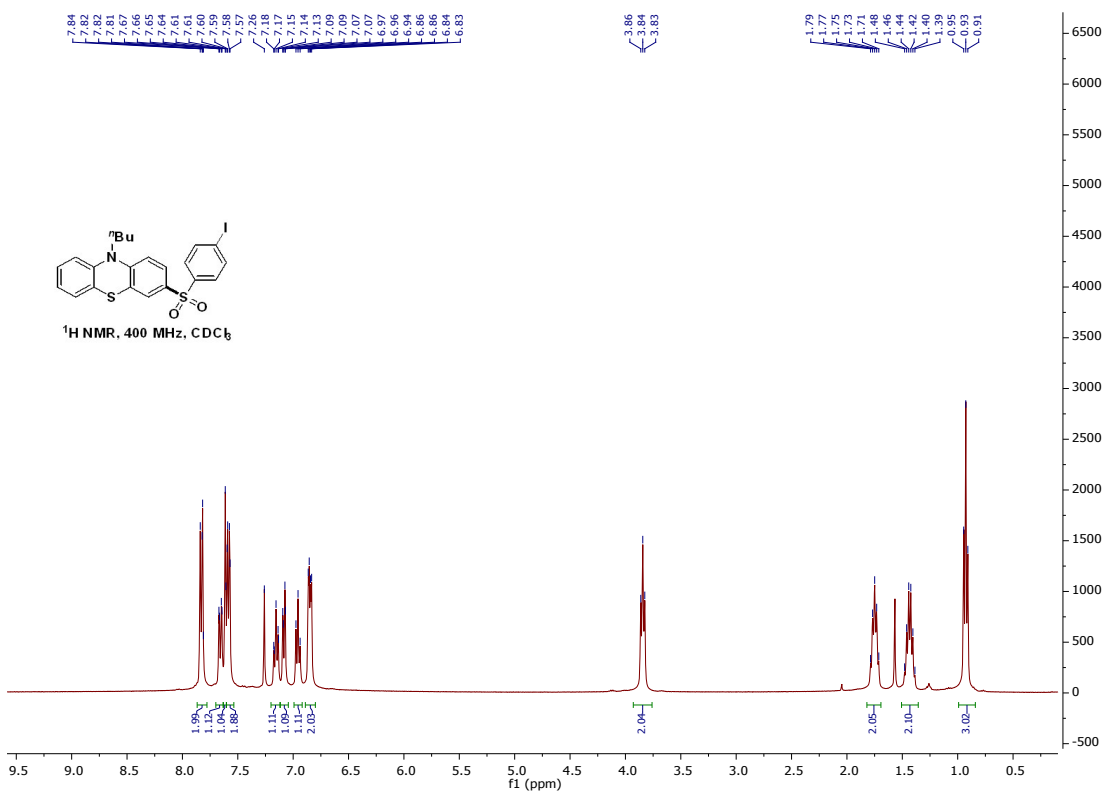


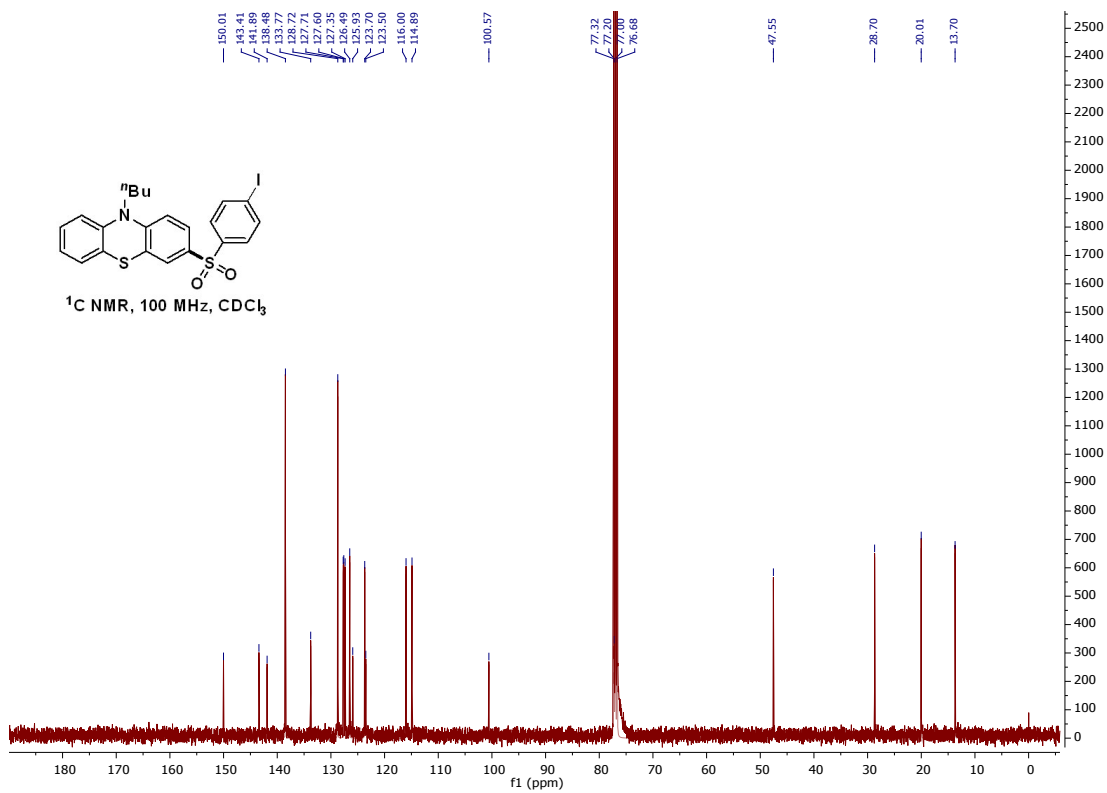
10-butyl-3,7-bis((4-chlorophenyl)sulfonyl)-10H-phenothiazine



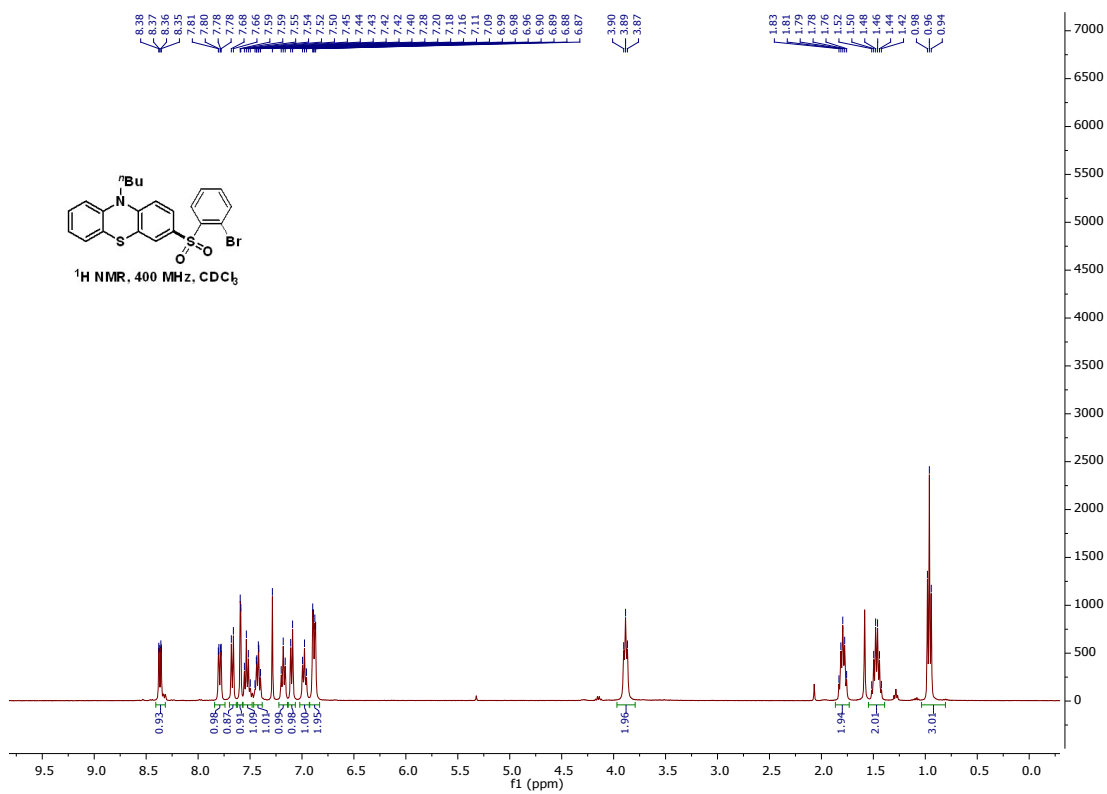


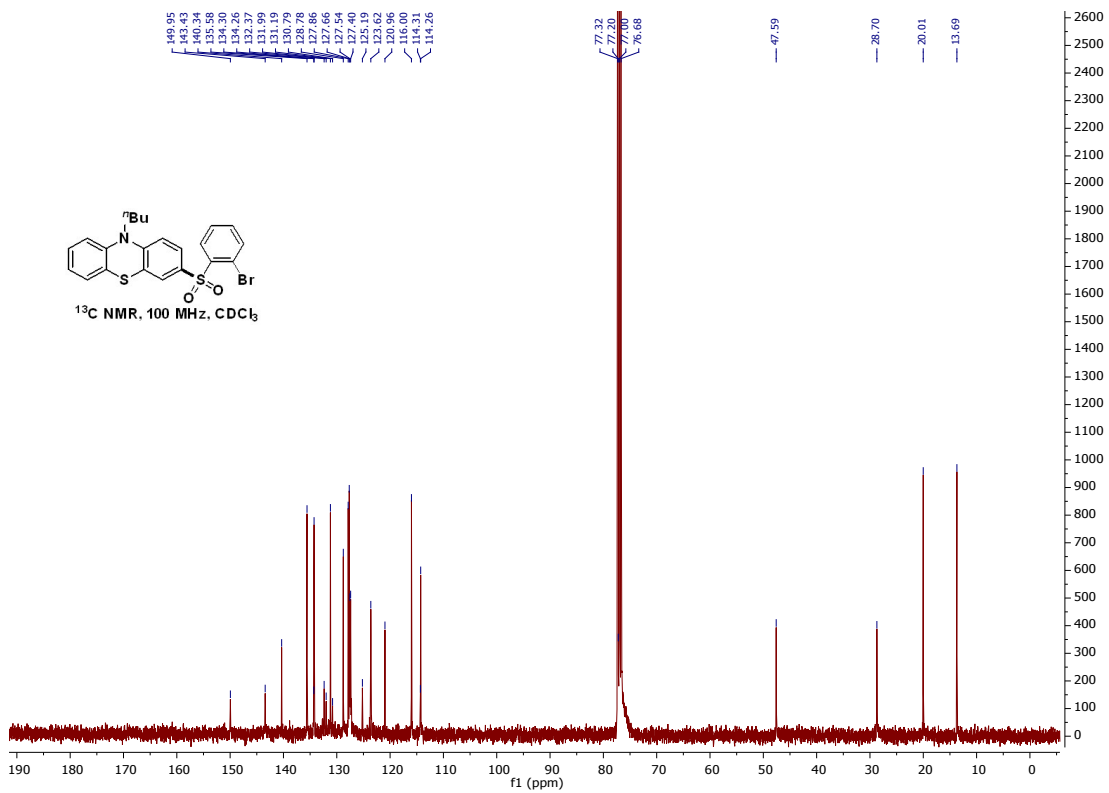
10-butyl-3-((4-iodophenyl)sulfonyl)-10H-phenothiazine(3j)



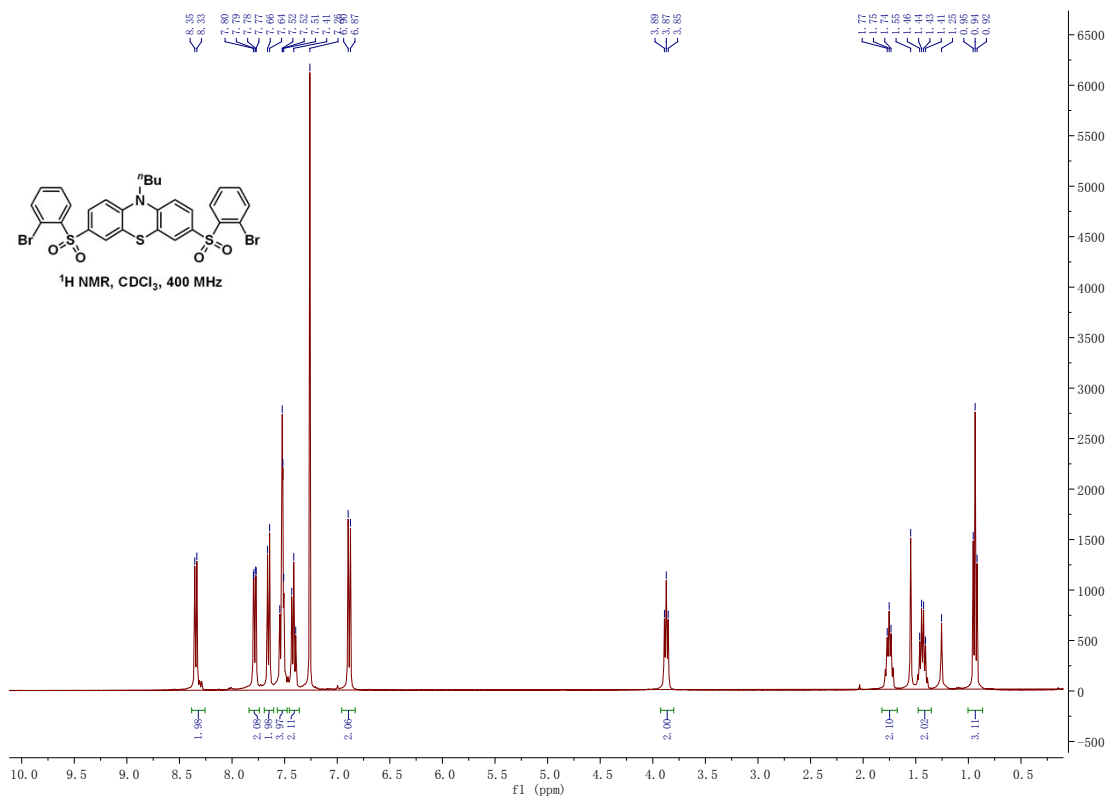


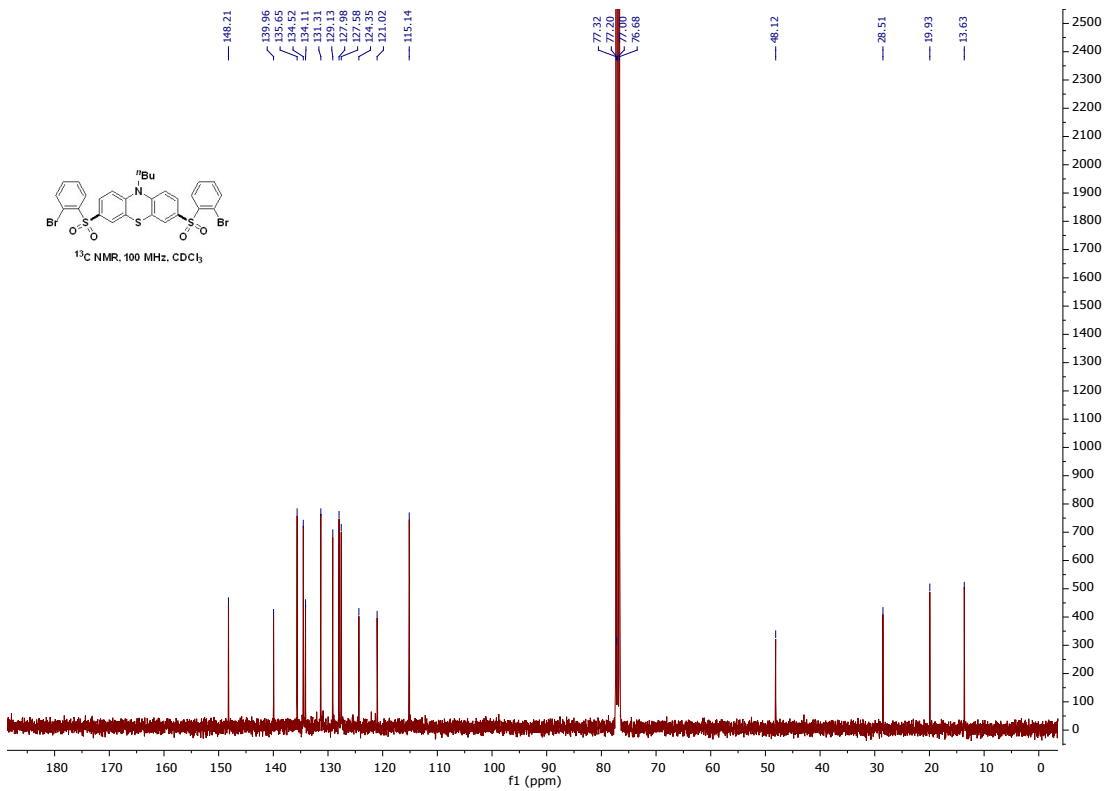
3-((2-bromophenyl)sulfonyl)-10-butyl-10H-phenothiazine(31)



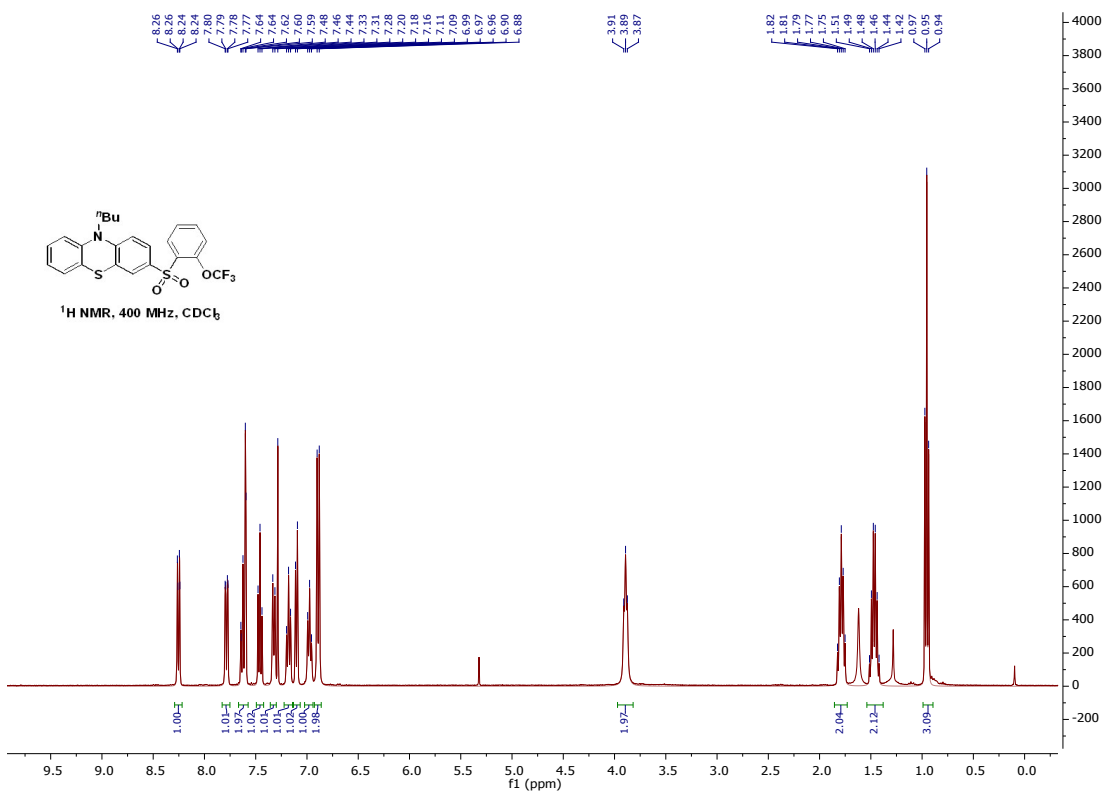


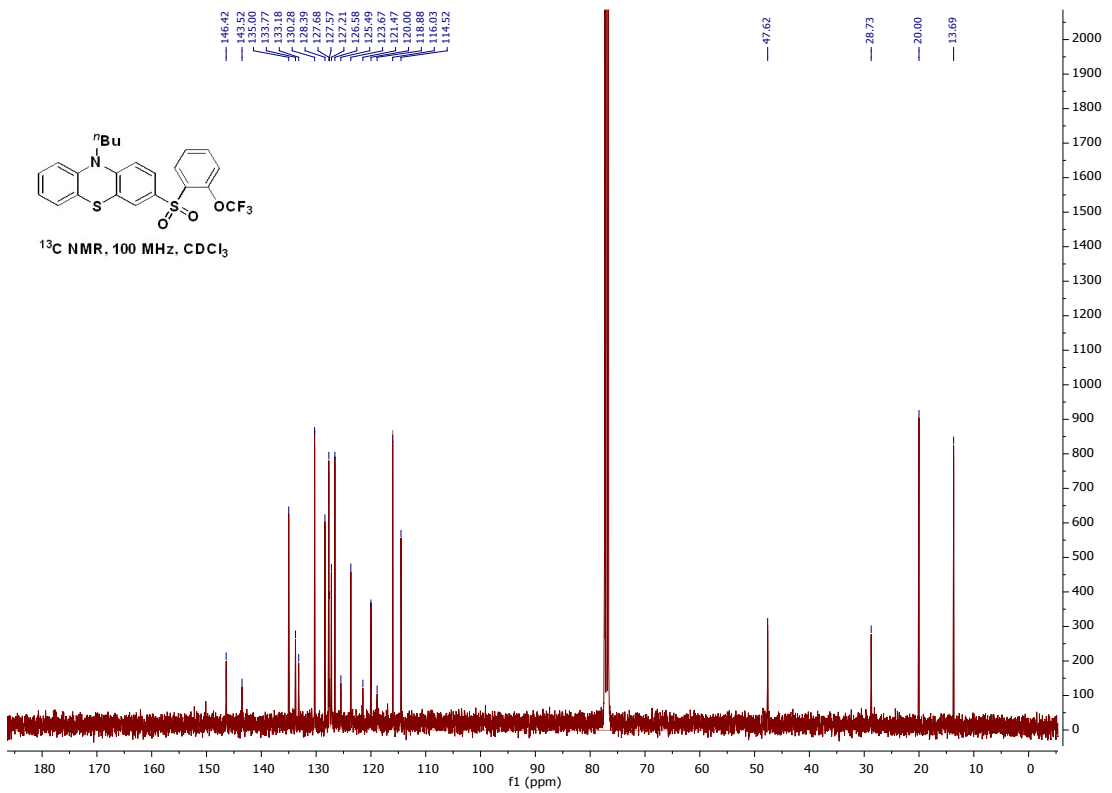
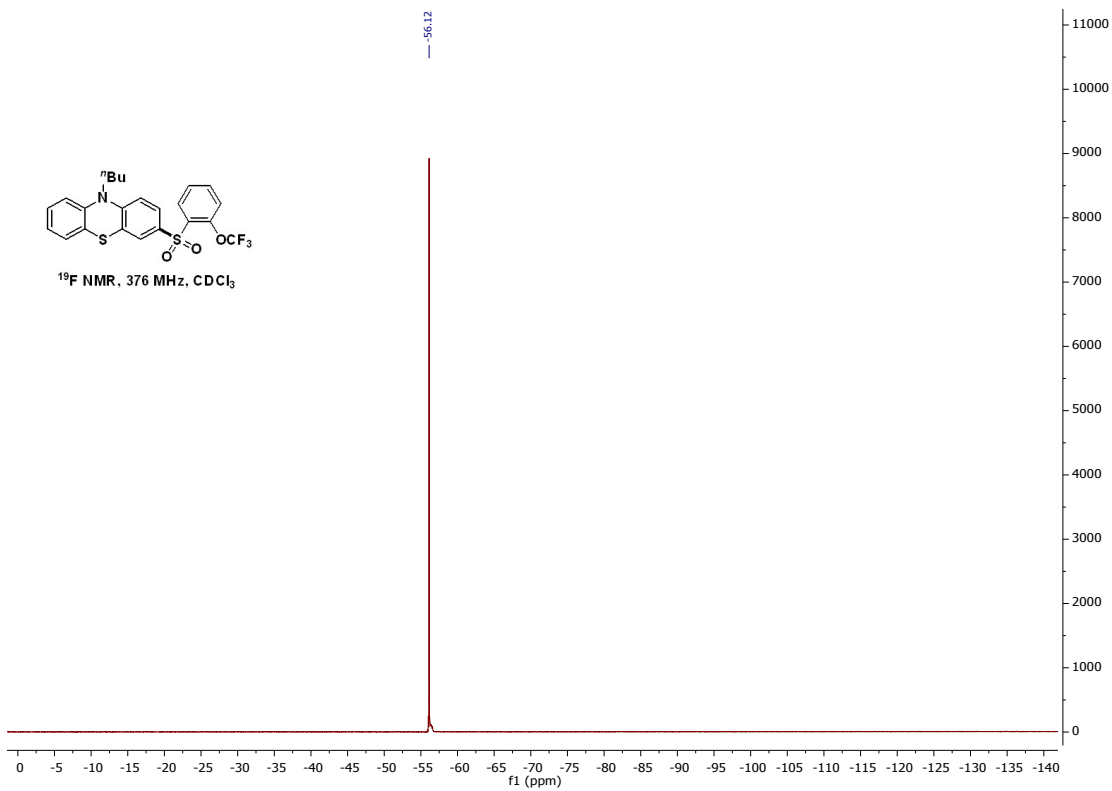
3,7-bis((2-bromophenyl)sulfonyl)-10-butyl-10H-phenothiazine



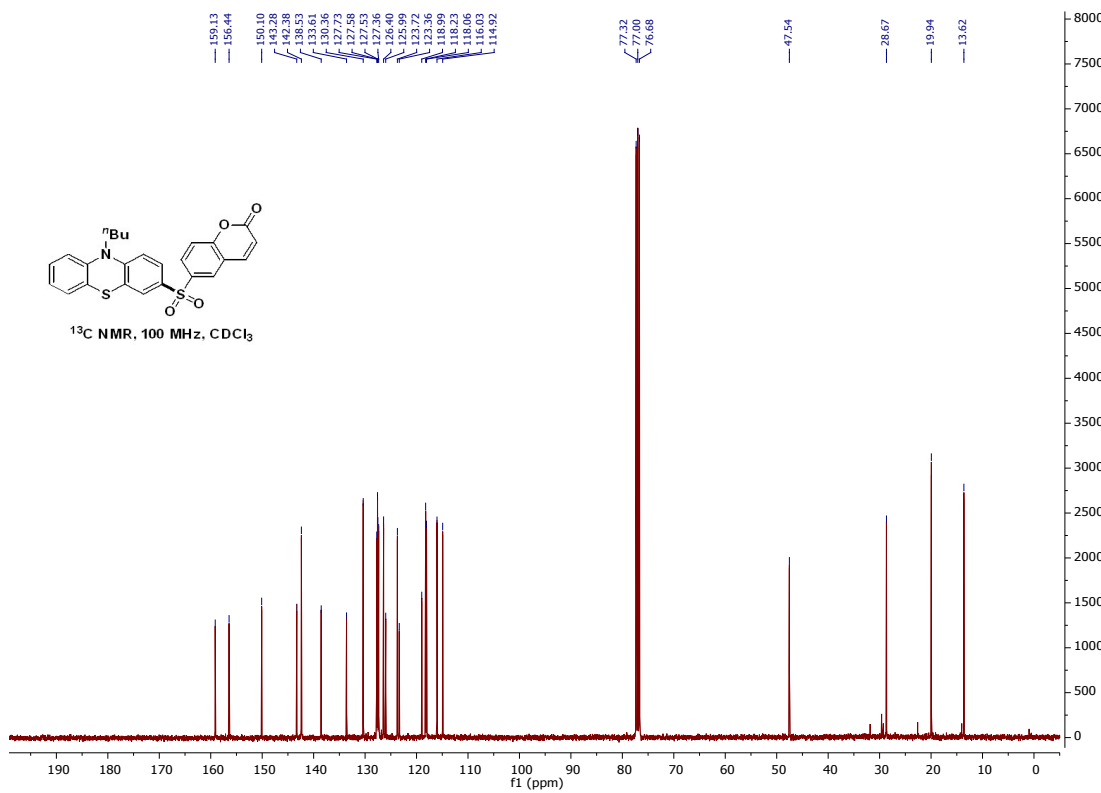
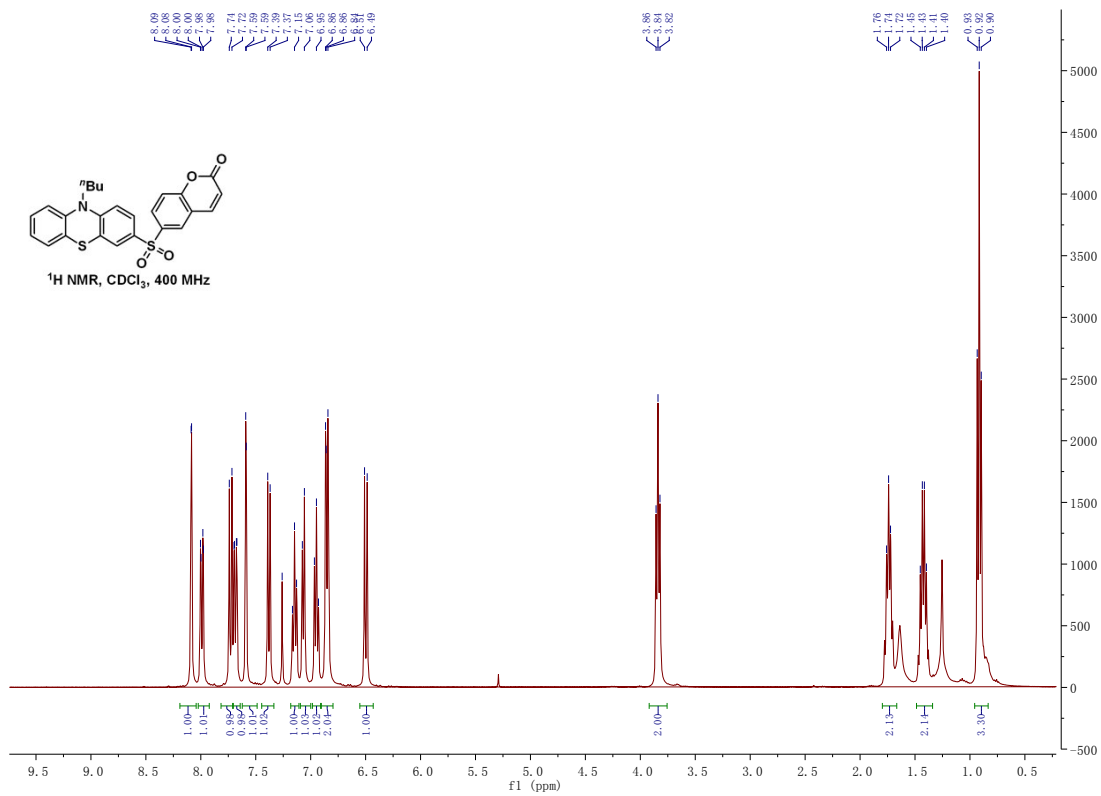


10-butyl-3-((2-(trifluoromethoxy)phenyl)sulfonyl)-10H-phenothiazine(3)

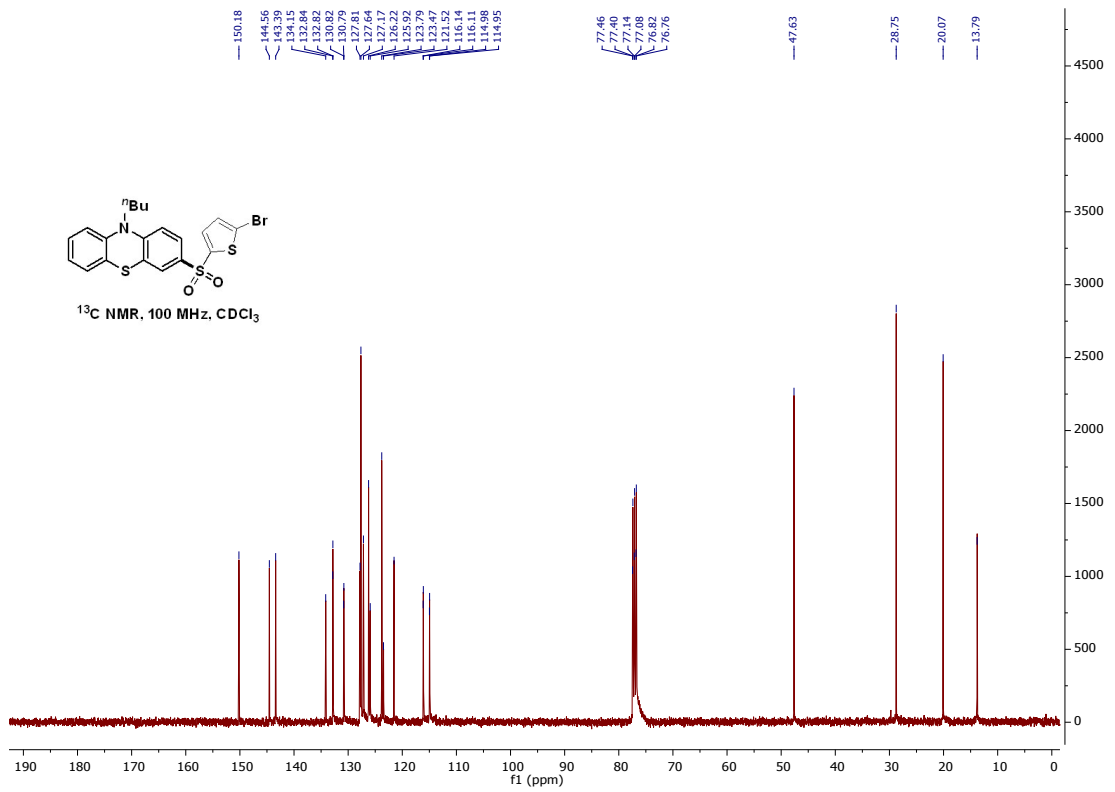
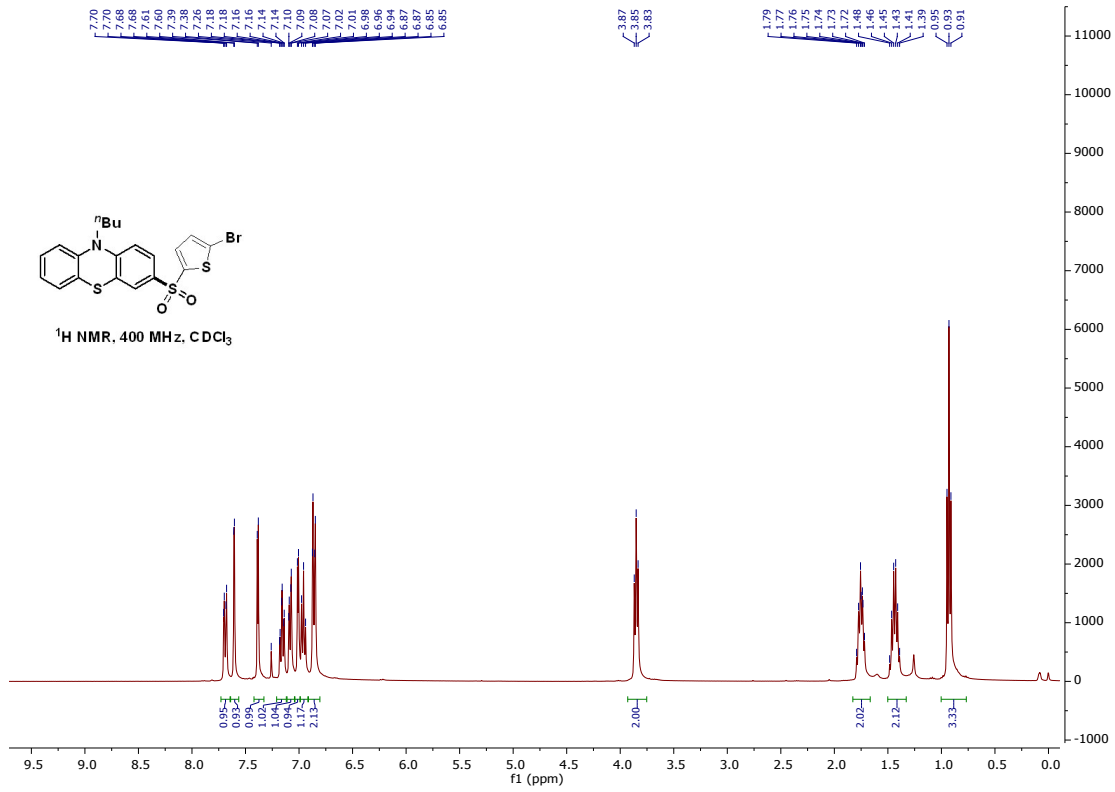


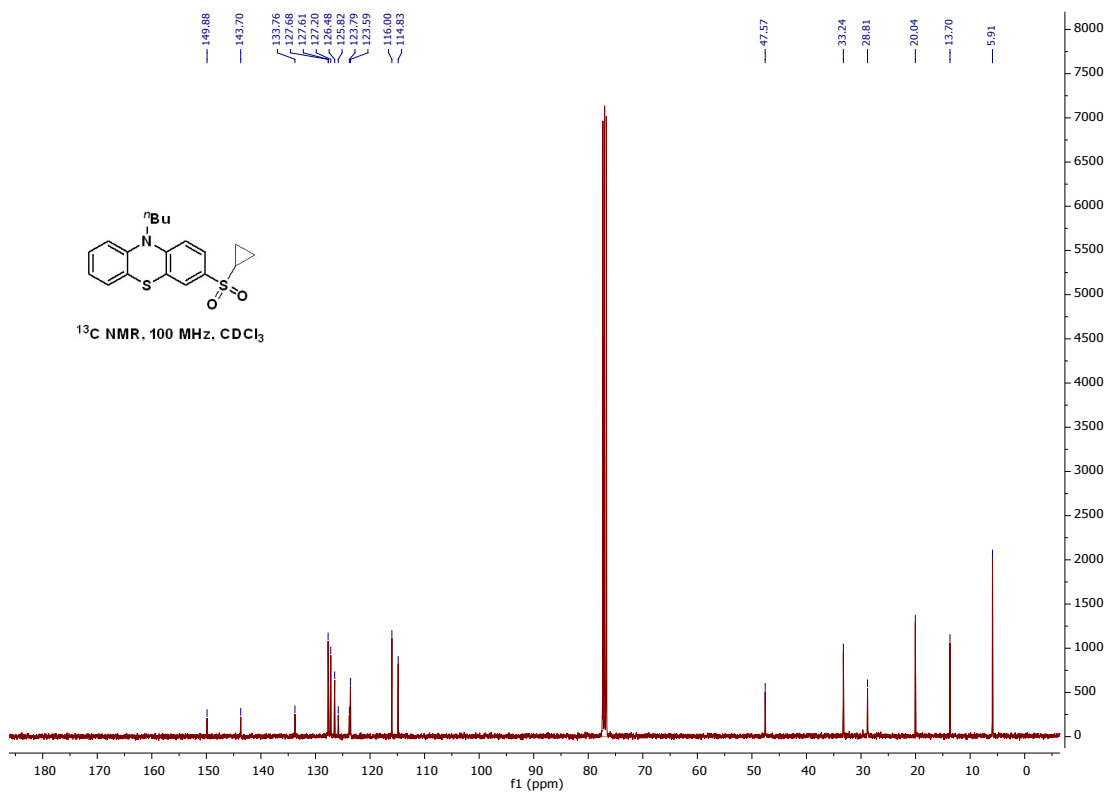
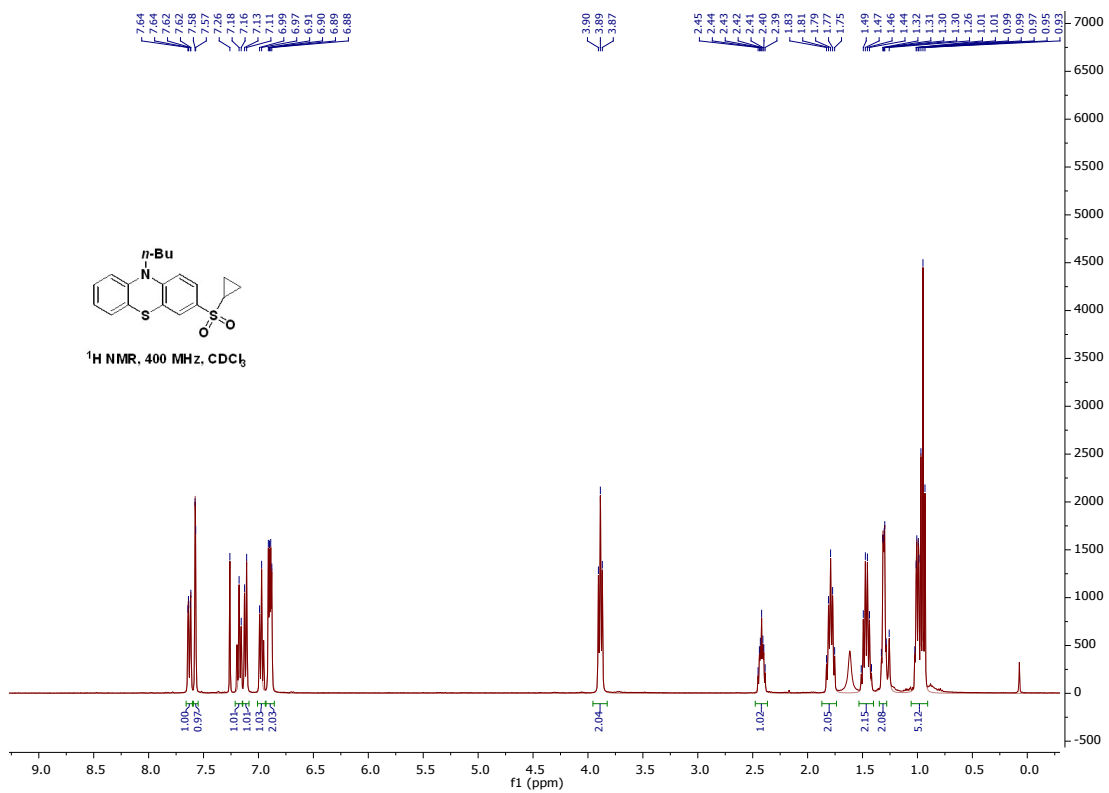


6-((10-butyl-10H-phenothiazin-3-yl)sulfonyl)-2H-chromen-2-one(3n)

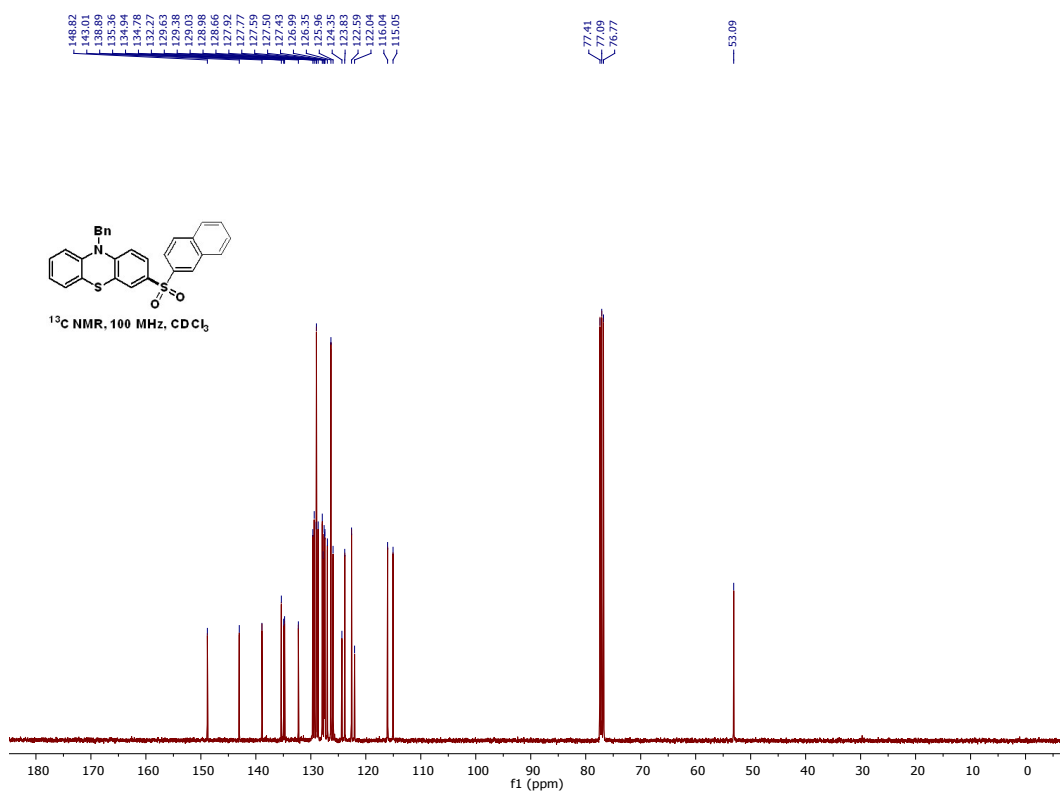
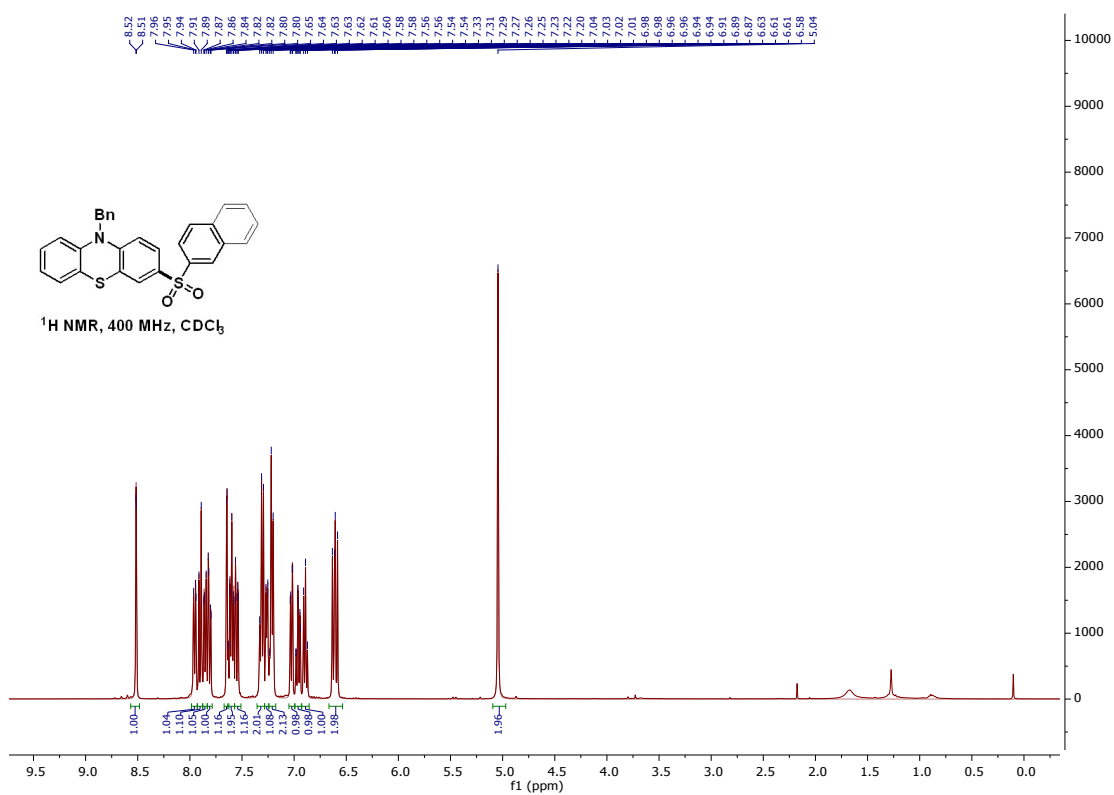


3-((5-bromothiophen-2-yl)sulfonyl)-10-butyl-10H-phenothiazine(3o)

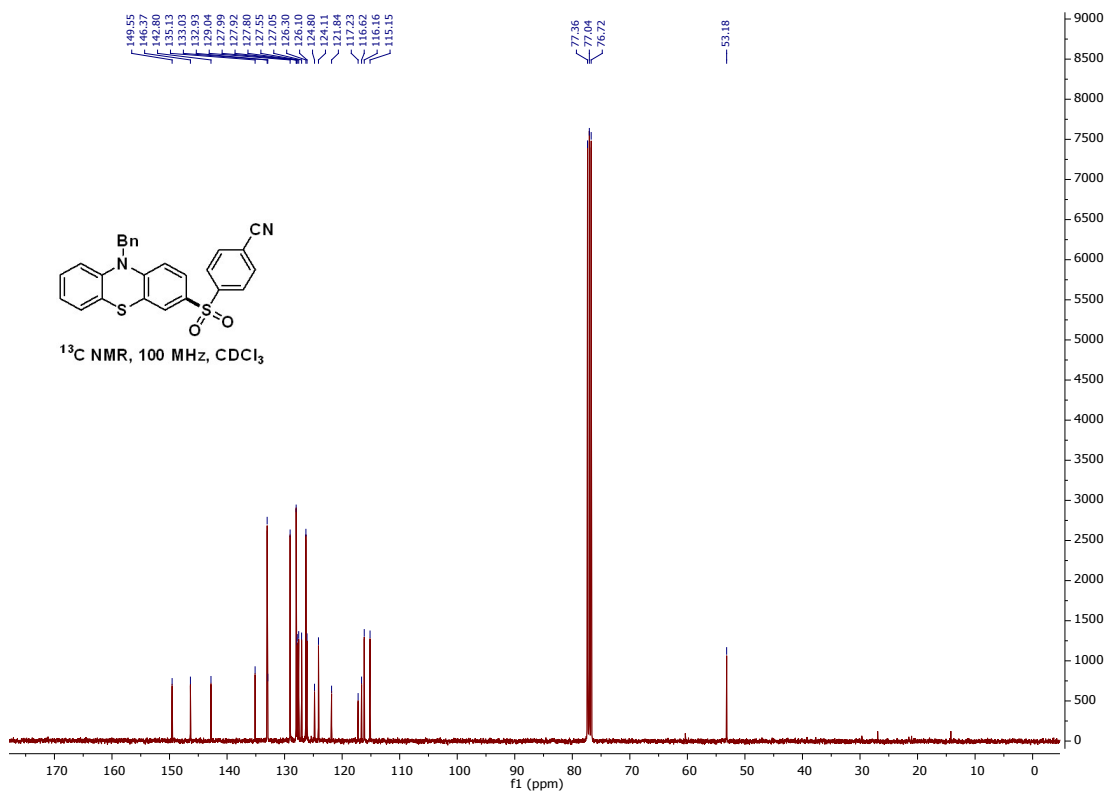
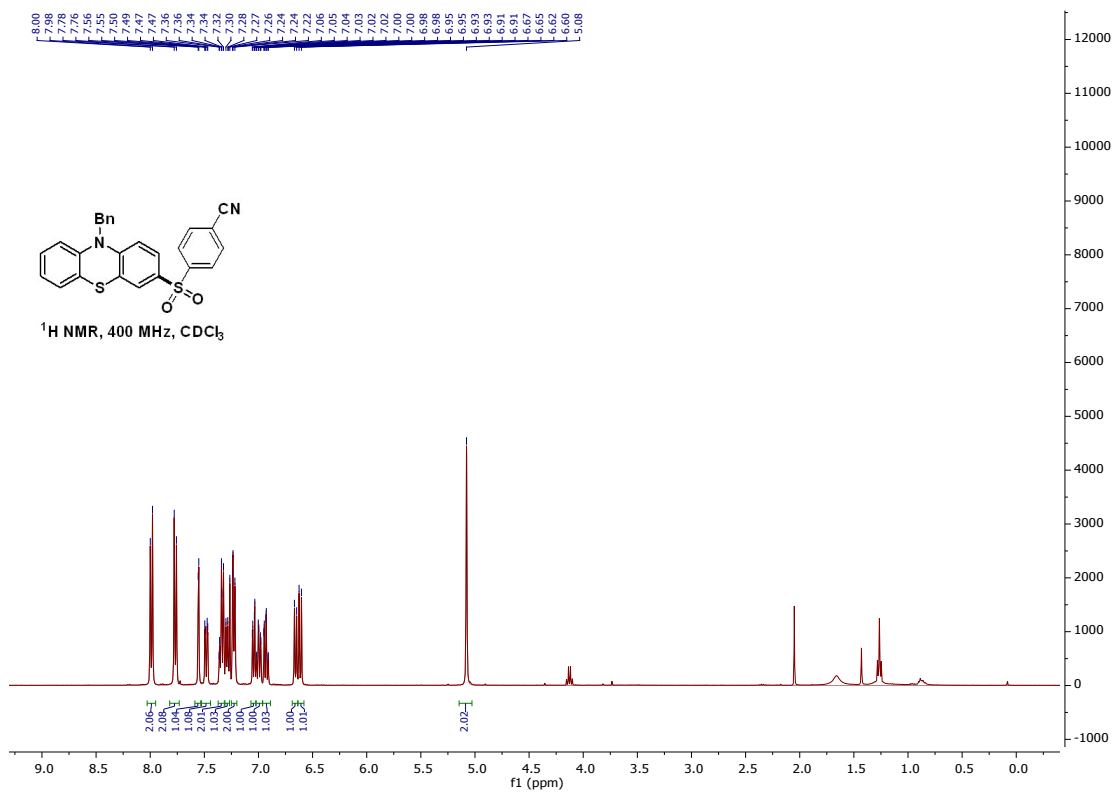




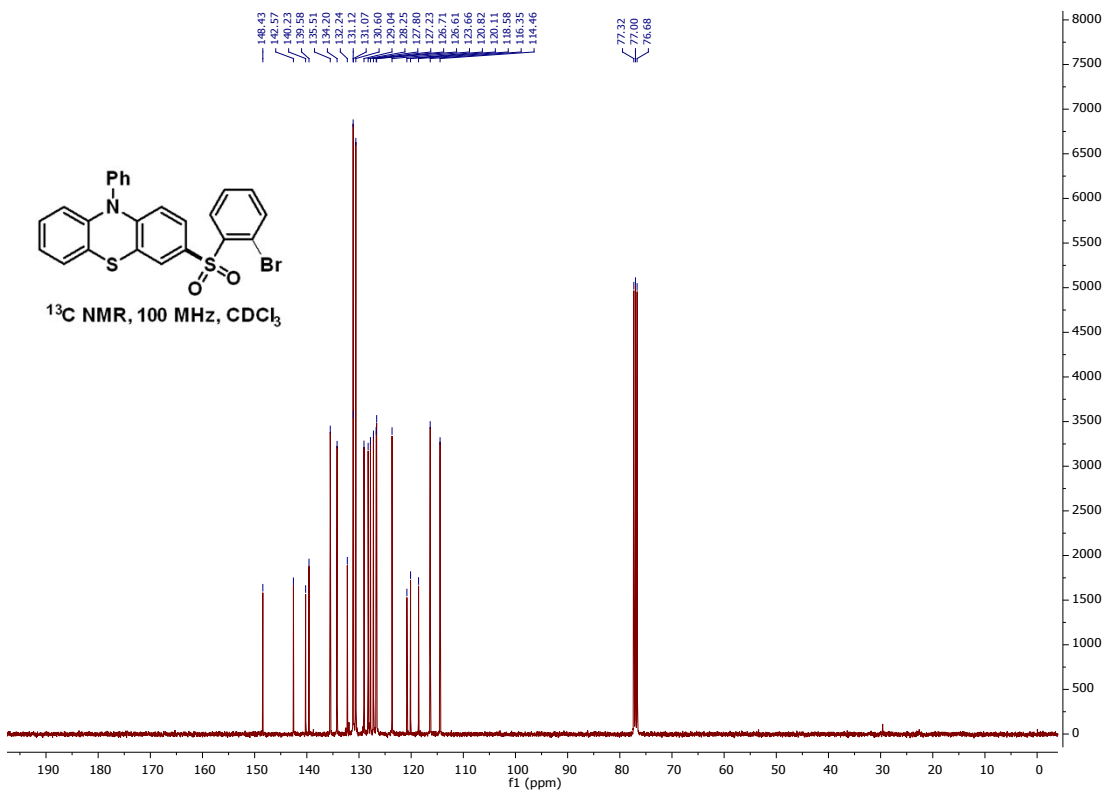
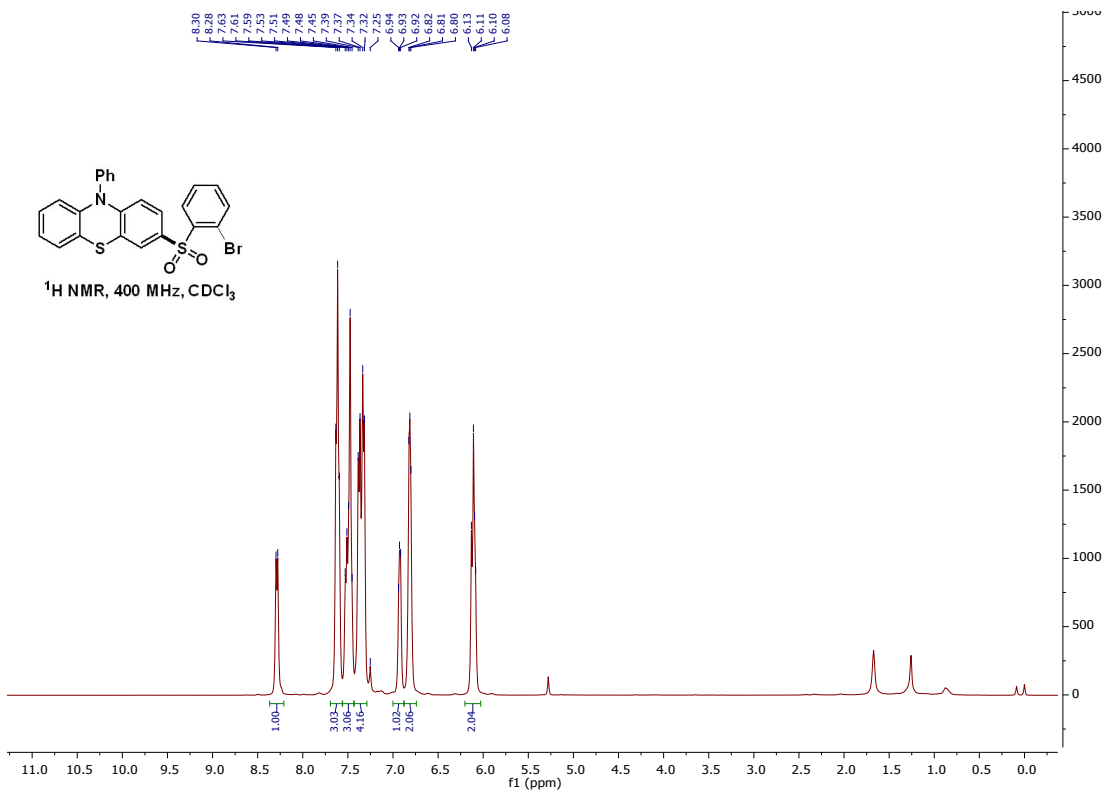
10-benzyl-3-(naphthalen-2-ylsulfonyl)-10H-phenothiazine(3r)



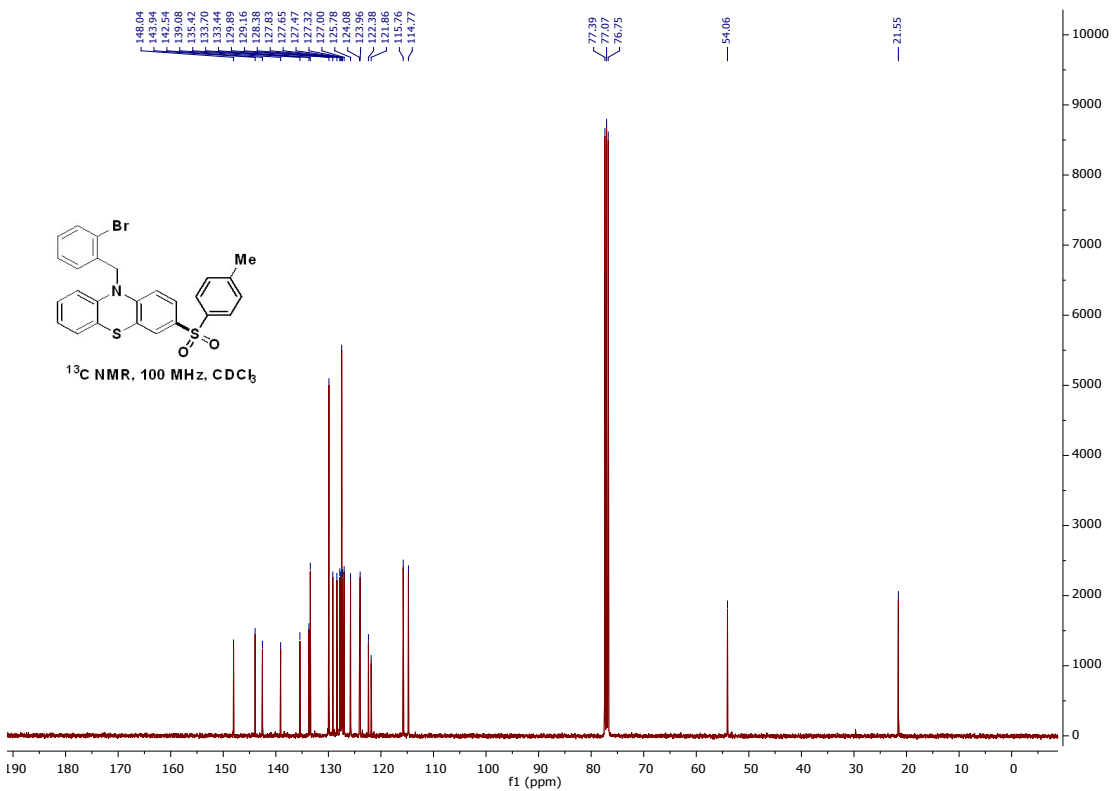
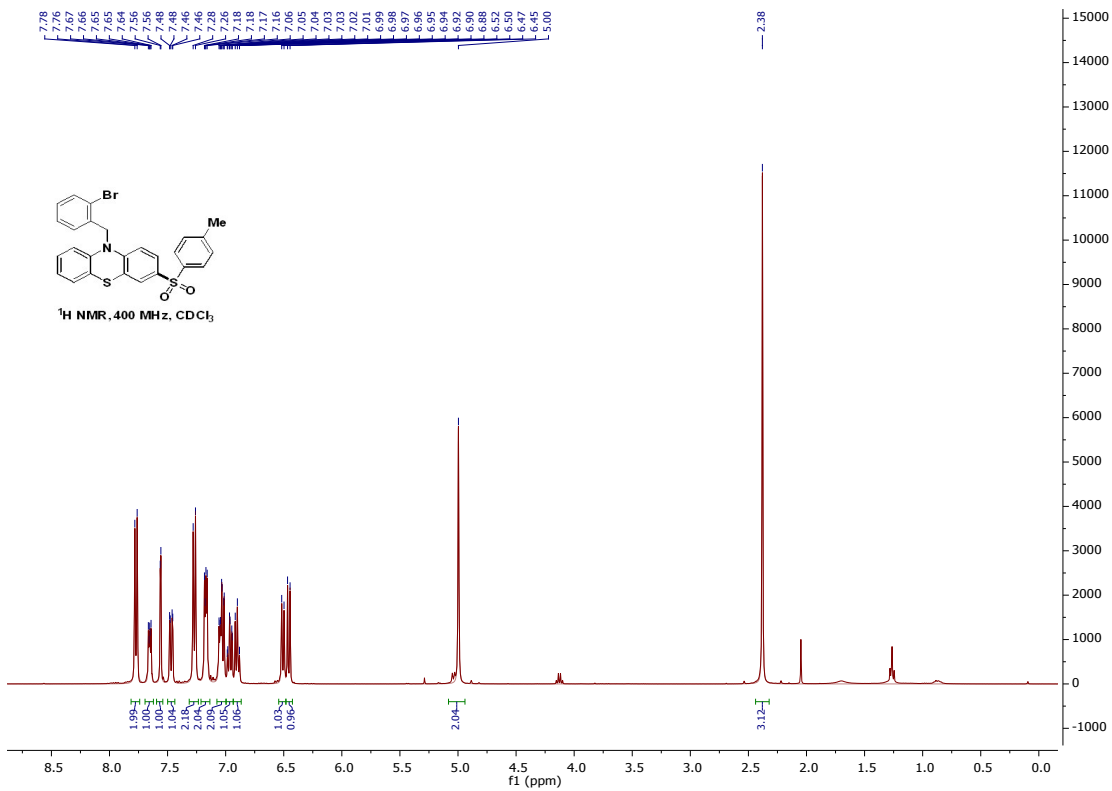
4-((10-benzyl-10H-phenothiazin-3-yl)sulfonyl)benzonitrile(3s)



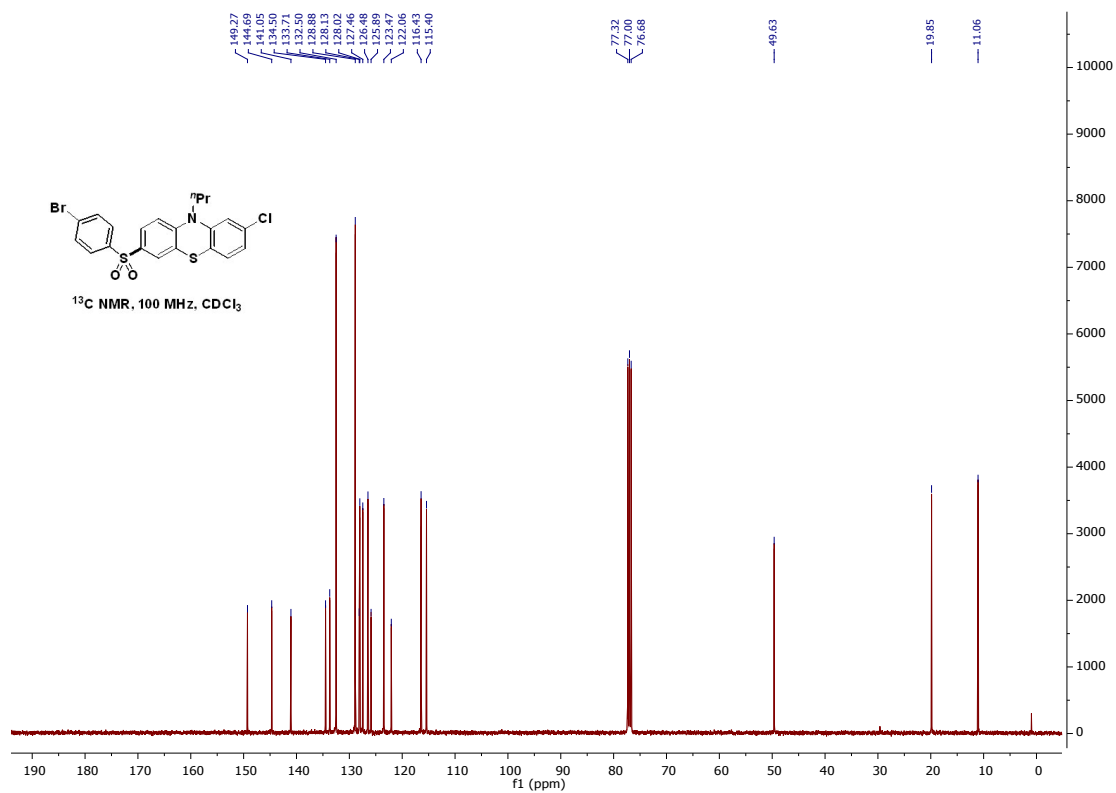
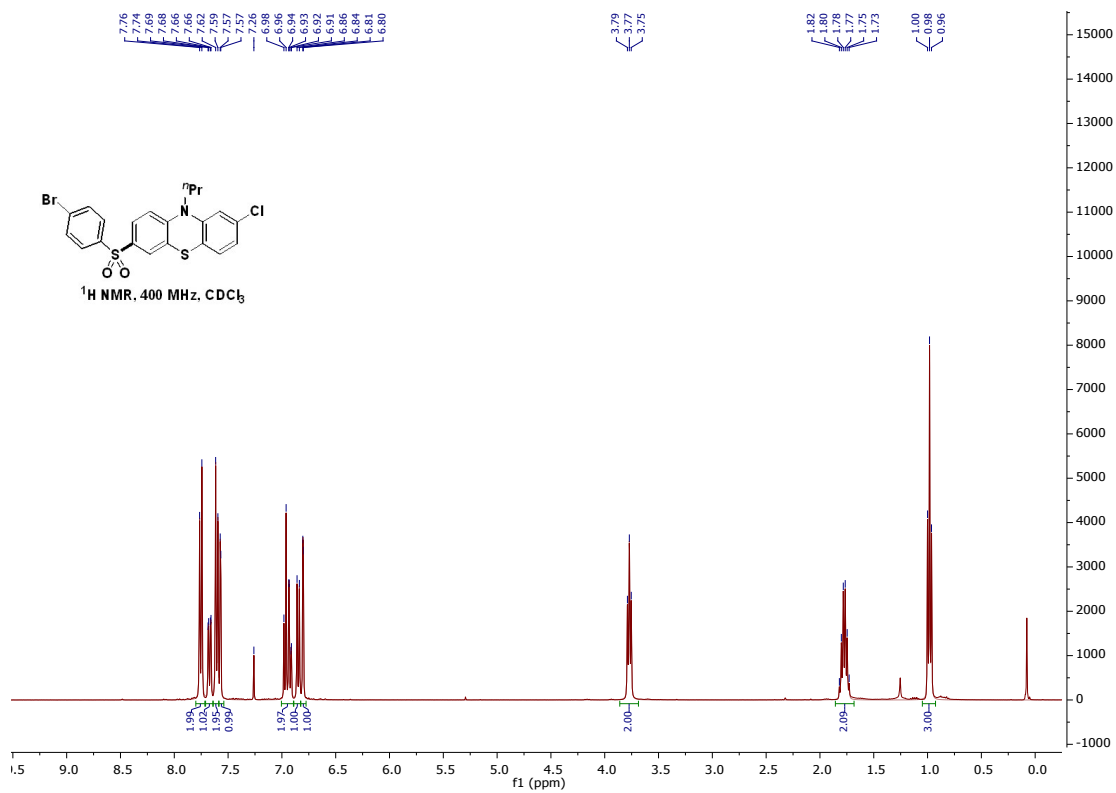
3-((2-bromophenyl)sulfonyl)-10-phenyl-10H-phenothiazine (3t)



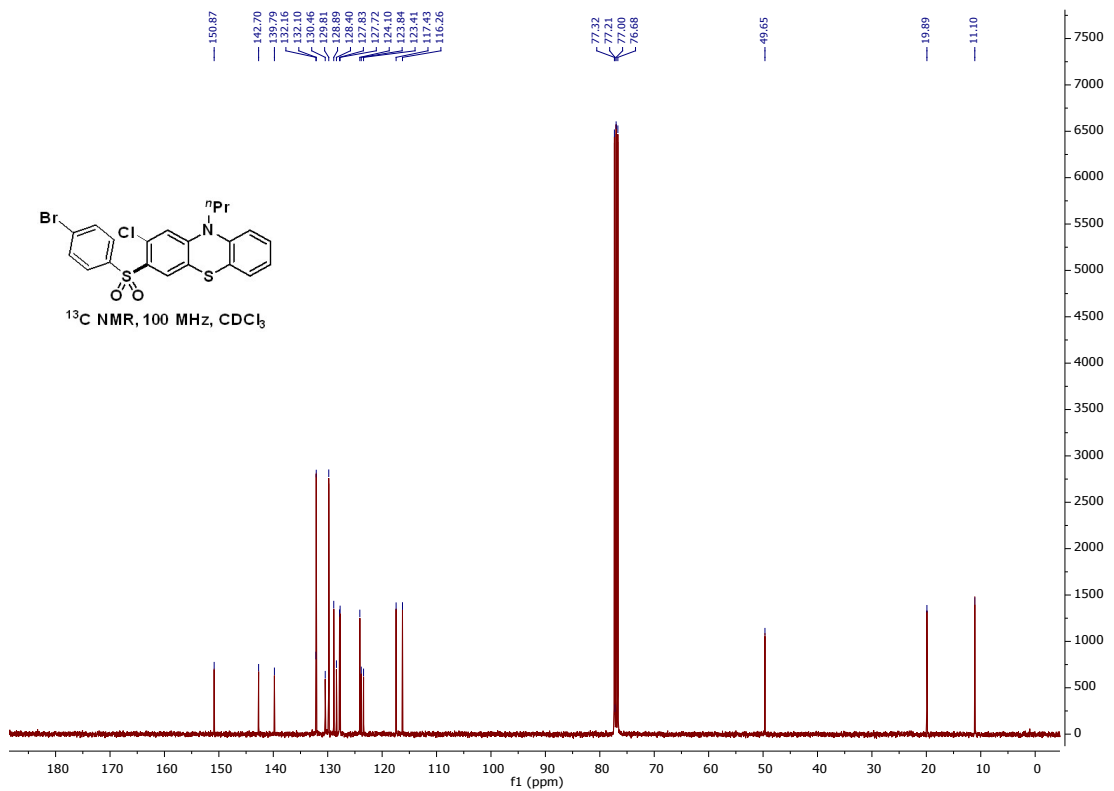
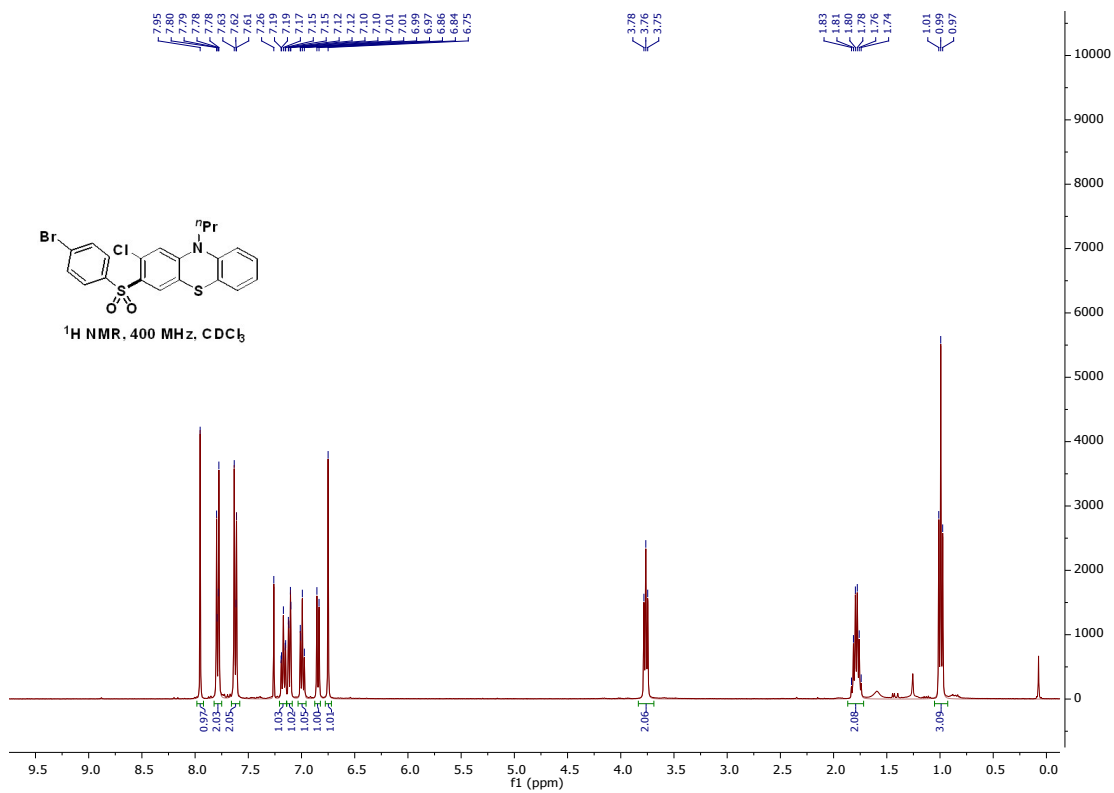
10-(2-bromobenzyl)-3-tosyl-10H-phenothiazine(3u)



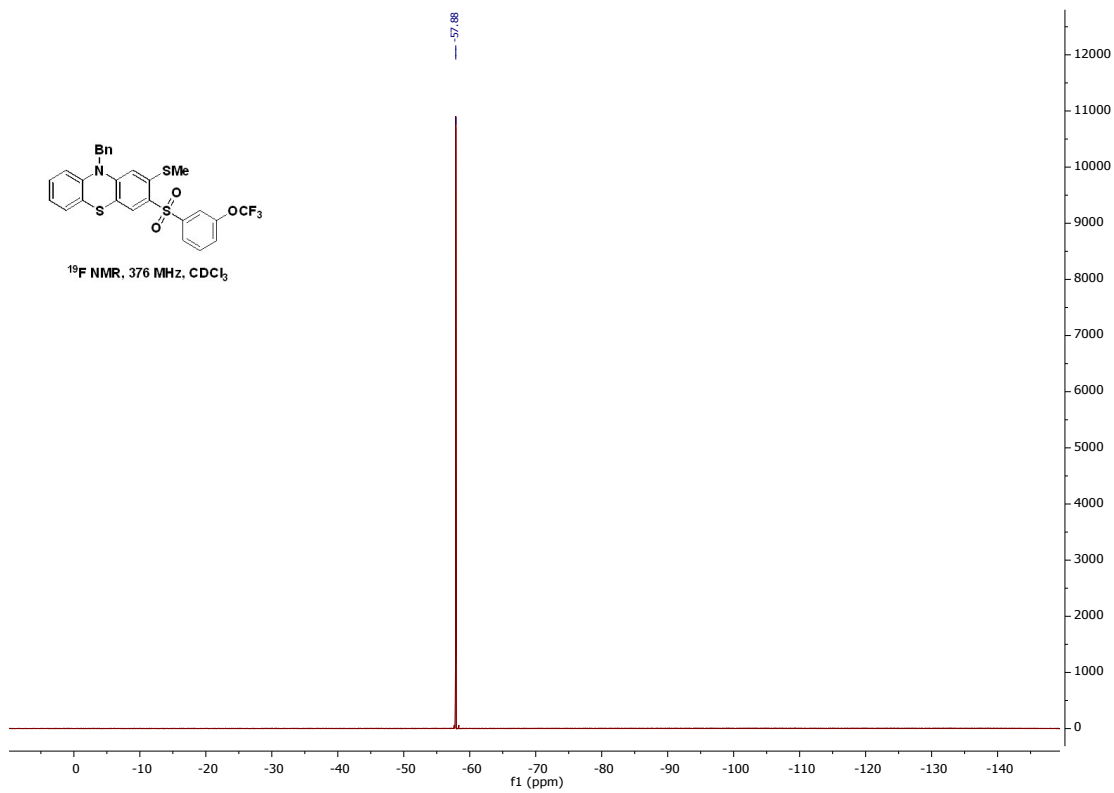
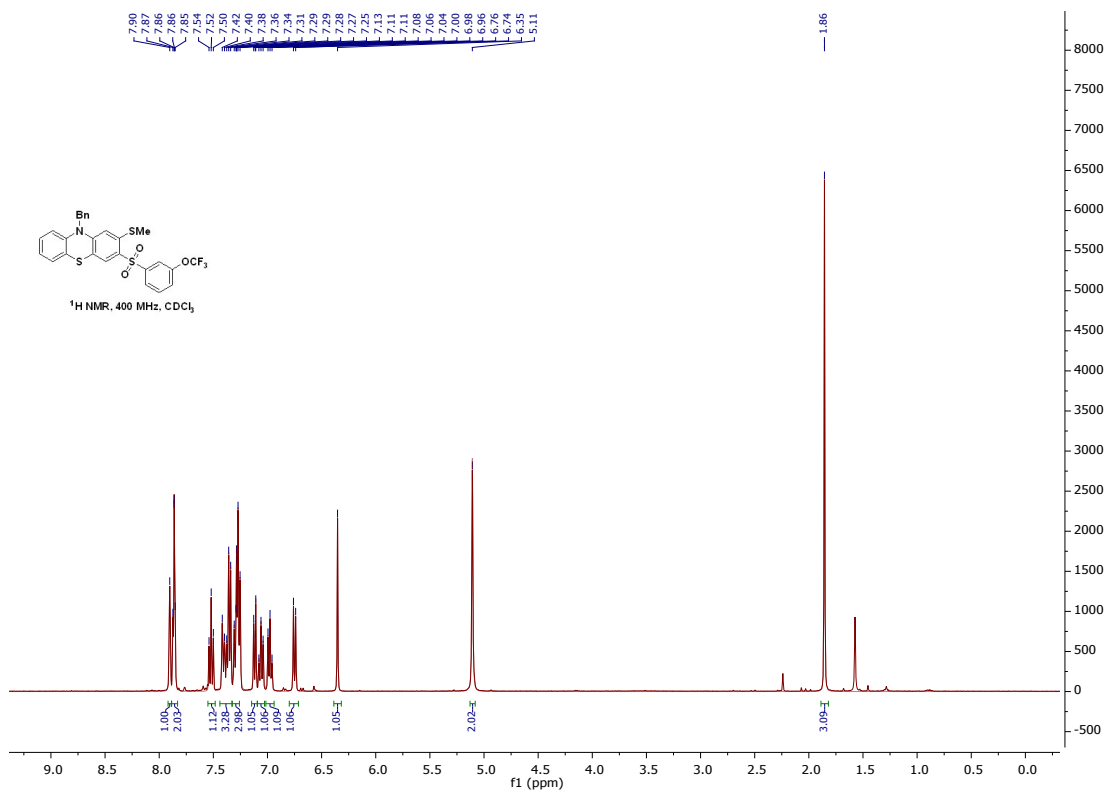
7-((4-bromophenyl)sulfonyl)-2-chloro-10-propyl-10H-phenothiazine(3v)

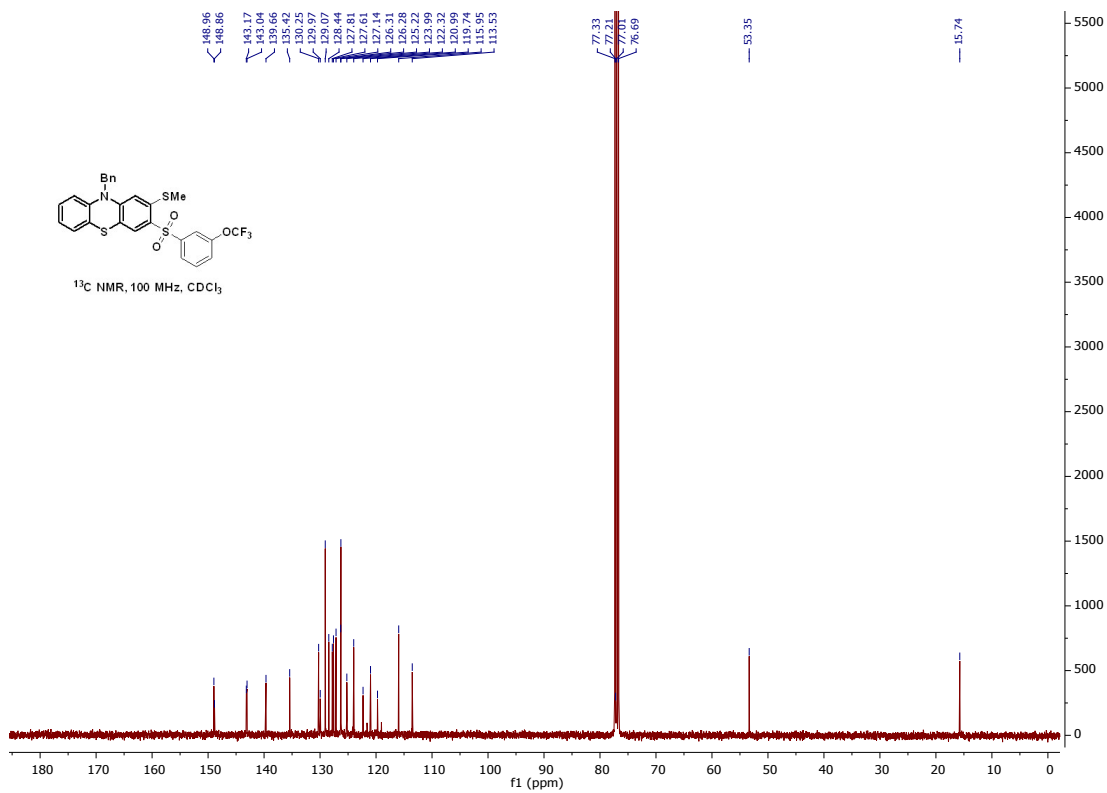


3-((4-bromophenyl)sulfonyl)-2-chloro-10-propyl-10H-phenothiazine(3w)

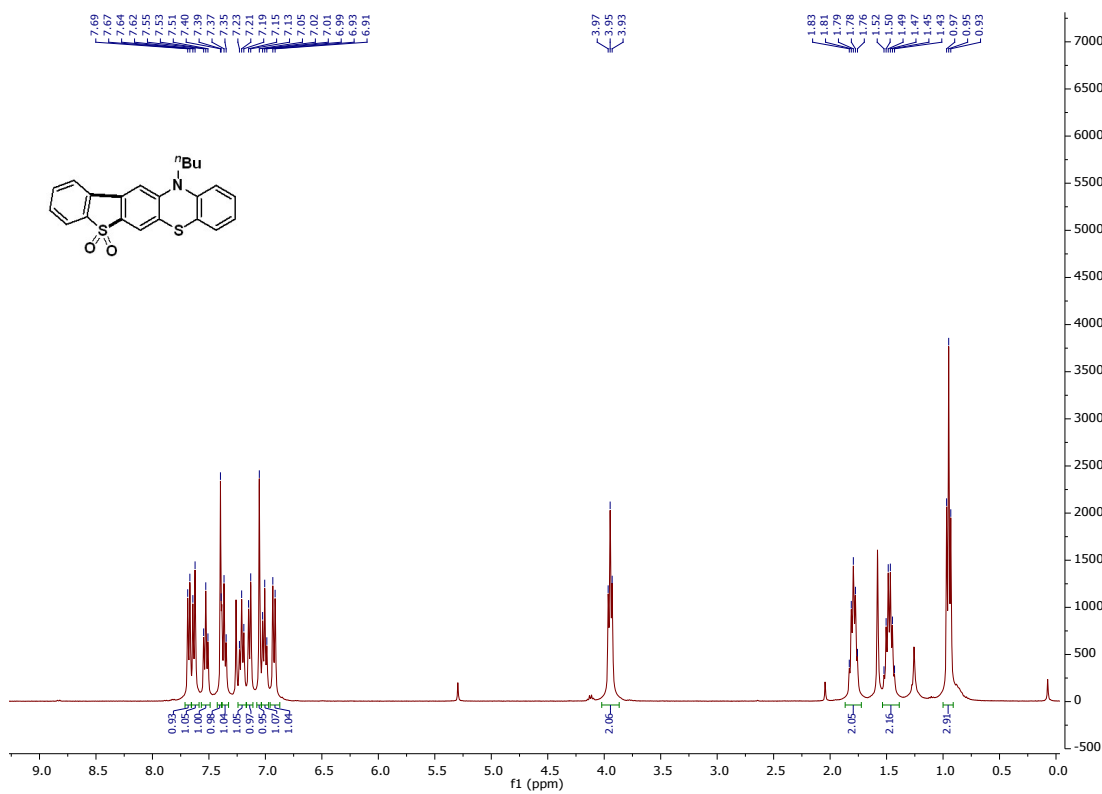


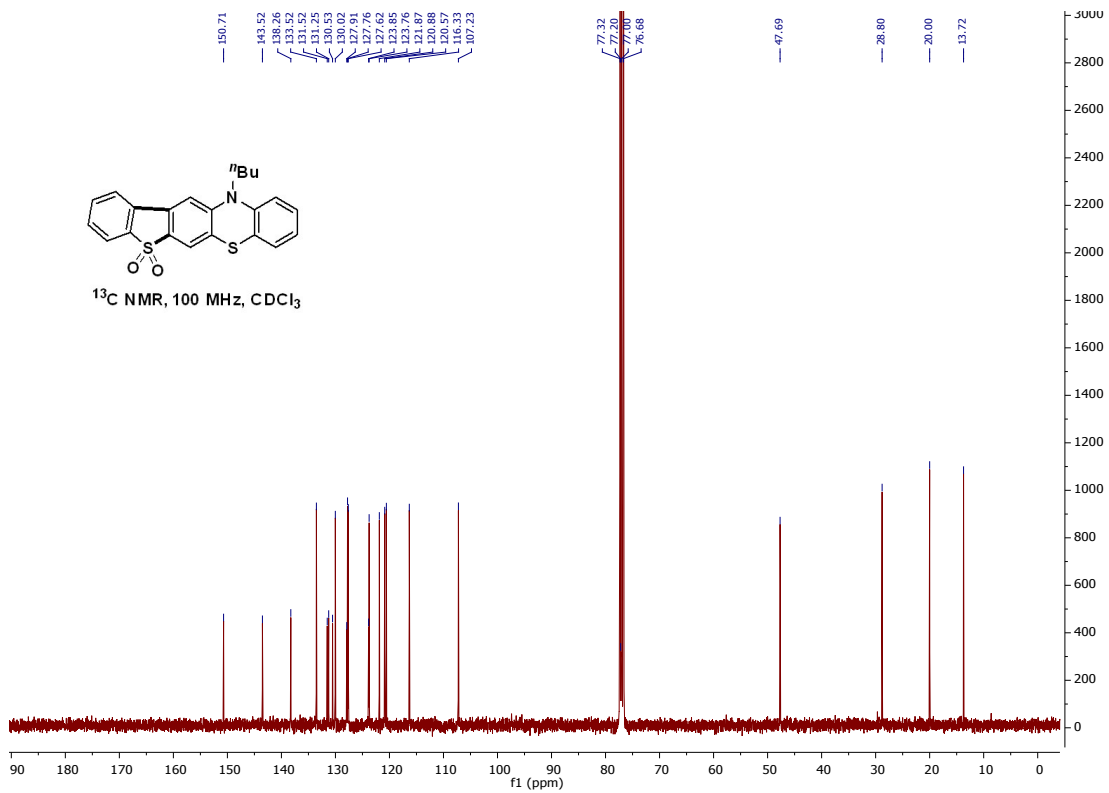
10-benzyl-2-(methylthio)-3-((3-(trifluoromethoxy)phenyl)sulfonyl)-10H-phenothiazine(3x)



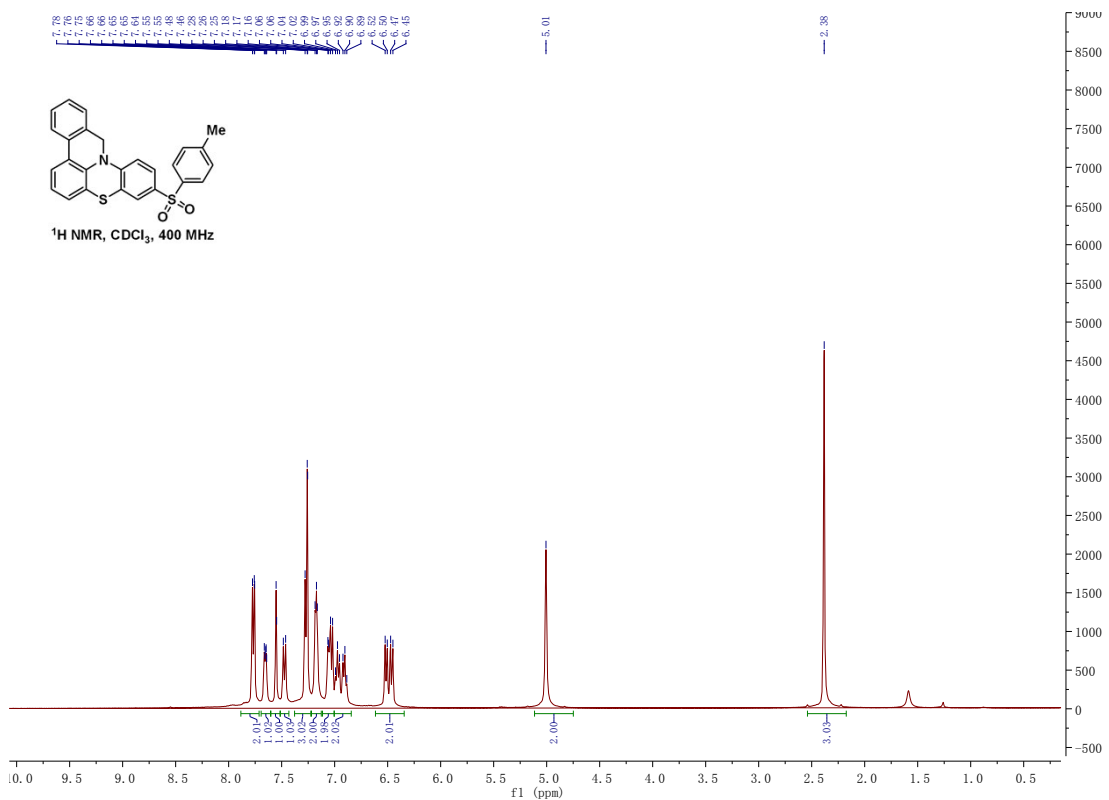


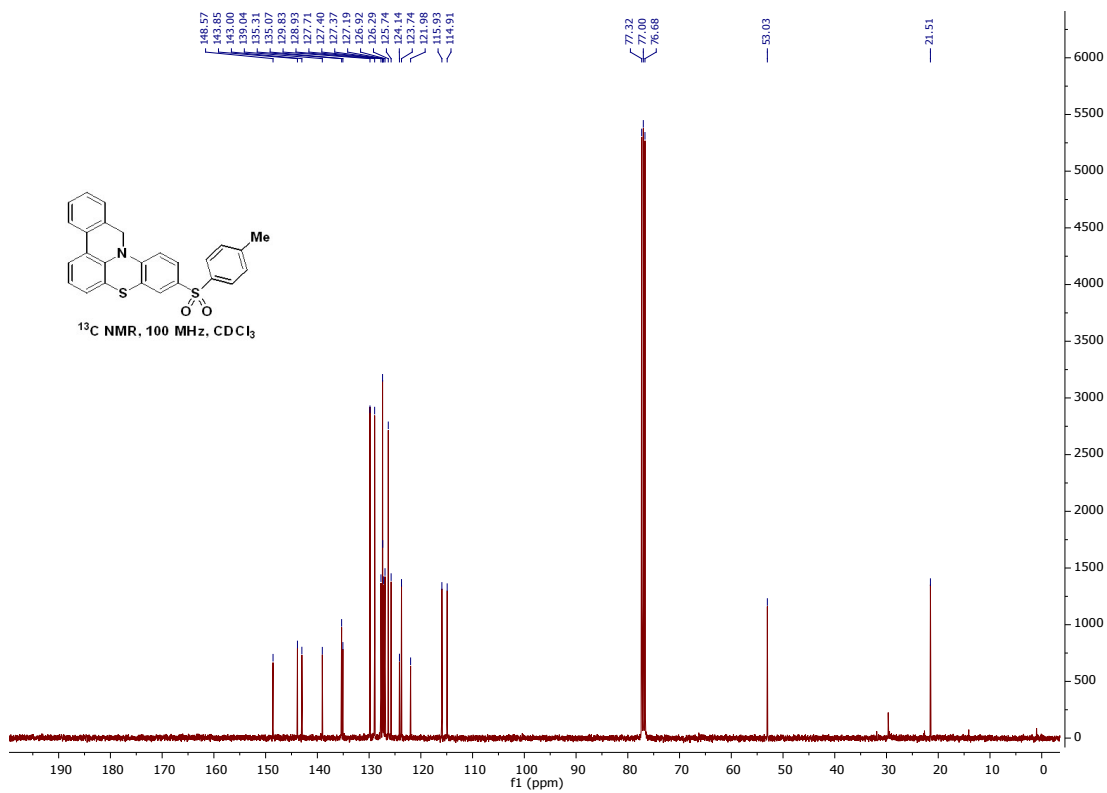
12-butyl-12H-benzo[4,5]thieno[3,2-b]pheno-thiazine 5,5-dioxide (3y)





10-tosyl-14H-isoquinolino[4,3,2-k]phenothiazine (3z)





Crystal structure information

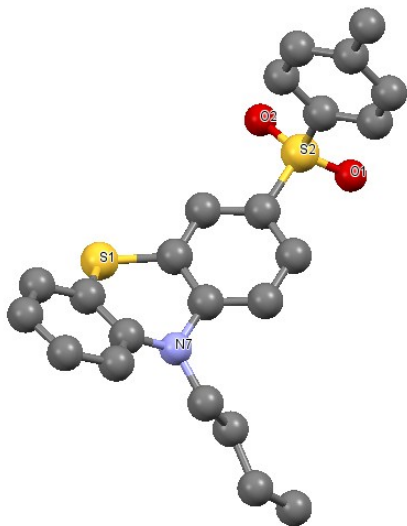


Fig.1 10-butyl-3-tosyl-10H-phenothiazine (**3a**)

Empirical formula C₂₃H₂₃NO₂S₂

Formula weight 409.54

Temperature 150 K

Crystal system, space group	Monoclinic, P 1 21/c 1
Unit cell dimensions	a = 12.0587(8) Å $\alpha = 90^\circ$ b = 15.5180(13) Å $\beta = 117.134(2)^\circ$ c = 12.0126(8) Å $\gamma = 90^\circ$
Volume	2000.5(3) 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 > 2 σ (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

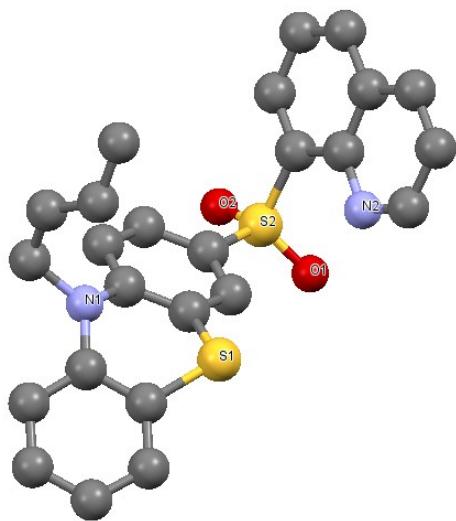


Fig 2. 10-butyl-3-(quinolin-8-ylsulfonyl)-10H-phenothiazine (**3m**)

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) Å $\alpha = 90^\circ$

b = 19.6420(4) Å β = 100.832(2)°

c = 9.1574(2) Å γ = 90°

Volume	2219.25(8) Å ³
Z, Calculated density	4, 1.312 (g.cm ⁻³)
radiation_wavelength	1.54184
Absorption coefficient	0.887 mm ⁻¹
F(000)	926
Crystal color	colorless
Reflections [I>2sigma(I)]	3311
Completeness to theta_max	78.5110
Absorption correction type	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	air
detector	CCD plate