Support information for

Synthesis of functionalized 1,4-Dihydropyridines containing benzosultams catalyzed by lipase

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Materials and Methods

General Information.

PPL (porcine pancreas lipase, 5600 U/g), PSL (*Pseudomonas sp.* lipase, 8500U/g), CalB (Lipase B from *Candida antarctica*, 10,000U/mL), CSL (*Candida sp.* lipase, 6400U/g) was purchased from Shanghai Yuan Ye Biological Technology Company and MML (*Mucor miehei lipase*, 7300 U/g), were purchased from Sigma-Aldrich China Co. (Beijing, China). One unit of the enzyme activity was defined as the amount of enzyme required to hydrolyze 1 μmol of p-nitrophenyl acetate per minute at 30 °C. All the other chemical reagents were purchased from commercial suppliers (Bide Pharmatech, Aladdin, Energy Chemical). All the commercially available reagents and solvents were used without further purification. Proton nuclear magnetic resonance (1H NMR) spectra were recorded on a 400 MHz spectrometer in $CDCl_3$ or DMSO. Chemical shifts for protons are reported in parts per million downfield from tetramethyl silane (TMS) and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.26 ppm, DMSO = δ 2.50 ppm). NMR data are presented as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Hertz (Hz), integration. HRMS was determined on a Q-TOF Micro LC/MS System ESI spectrometer. The experiments were performed triplicate, and all data were obtained based on the average values.

General Procedure for the synthesis of 4.

To a stirred solution of **1** (0.3 mmol), **2** (0.4 mmol) and **4** (0.4 mmol) in water (1.0 mL) at 40 °C, was added PPL (200 U) in one portion and stirred for 36h or 48h. The progress of the reaction was monitored by TLC. The reaction mixture was then concentrated in vacuo and purified by flash column chromatography (acetone/DCM = 1/50-1/20) on silica gel to give products **4**.

General Procedure for the synthesis of 6.

To a stirred solution of **1** (0.3 mmol) and **5** (0.3 mmol) in water (1.0 mL) at 40 °C, was added PPL (200 U) in one portion and stirred for 36h or 48h. The progress of the reaction was monitored by TLC. The reaction mixture was then concentrated in vacuo and purified by flash column chromatography (acetone/DCM = 1/50-1/20) on silica gel to give products **6**.

Data of Products

For known compounds, spectral data are identical to literature.[1]

4a

^{1}H NMR (400 MHz, DMSO) δ 10.75 (s, 1H), 8.21 (d, *J* = 7.9 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.93 – 7.85 (m, 1H), 7.84 – 7.77 (m, 1H), 7.36 – 7.19 (m, 1H), 7.07 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.56 (s, 2H), 6.16 (s, 1H). **ESI HRMS**: calcd. For $C_{19}H_{12}N_4O_3S$[M+H]+ 377.0693, found 377.0697.

4b

^{1}H NMR (400 MHz, DMSO) δ 11.01 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.91 (td, *J* = 7.7, 1.2 Hz, 1H), 7.86 – 7.77 (m, 1H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.09 – 7.03 (m, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.62 (s, 2H), 6.17 (s, 1H). ^{13}C NMR (101 MHz, DMSO-D_6) δ 177.20, 149.46, 143.55, 135.59, 132.41, 131.75, 131.62, 131.14, 130.09, 128.85, 126.73, 123.56, 121.92, 118.06, 109.65, 100.58, 59.29,

52.18. **ESI HRMS**: calcd. For $C_{19}H_{11}N_4O_3SCl$[M+H]+ 411.0323 and 413.0294, found 411.0322 and 413.0291.

4c

^{1}H NMR (400 MHz, DMSO) δ 10.88 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.10 (d, *J* = 7.9 Hz, 1H), 7.90 (td, *J* = 7.6, 1.2 Hz, 1H), 7.85 – 7.77 (m, 1H), 7.39 – 7.33 (m, 2H), 7.02 – 6.93 (m, 1H), 6.63 (s, 2H), 6.16 (s, 1H). **ESI HRMS**: calcd. For $C_{19}H_{11}N_4O_3SCl$[M+H]+ 411.0303 and 413.0274, found 411.0302 and 413.0271.

4d

^{1}H NMR (400 MHz, DMSO) δ 10.88 (s, 1H), 8.23 (d, *J* = 7.9 Hz, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.95 – 7.87 (m, 1H), 7.85 – 7.79 (m, 1H), 7.53 – 7.45 (m, 2H), 6.91 (d, *J* = 8.2 Hz, 1H), 6.62 (s, 2H), 6.16 (s, 1H). **ESI HRMS**: calcd. For $C_{19}H_{11}N_4O_3SBr$[M+H]+ 454.9808 and 456.9788, found 454.9808 and 456.9776.

4e

^{1}H NMR (400 MHz, DMSO) δ 10.64 (s, 1H), 8.21 (d, *J* = 7.9 Hz, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.89 (td, *J* = 7.7, 1.1 Hz, 1H), 7.84 – 7.76 (m, 1H), 7.14 – 7.03 (m, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.53 (s, 2H), 6.14 (s, 1H), 2.27 (s, 3H). **ESI HRMS**: calcd. For $C_{20}H_{14}N_4O_3S$[M+H]+ 391.0859, found 391.0860.

4f

^{1}H NMR (400 MHz, DMSO) δ 10.91 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.90 (td, *J* = 7.7, 1.2 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.28 (dd, *J* = 8.3, 5.5 Hz, 1H), 6.86 (ddd, *J* = 10.1, 8.2, 2.4 Hz, 1H), 6.78 (dd, *J* = 9.1, 2.4 Hz, 1H), 6.59 (s, 2H), 6.16 (s, 1H). **ESI HRMS**: calcd. For $C_{19}H_{11}N_4O_3SF$[M+H]+ 395.0609, found 395.0607.

4g

^{1}H NMR (400 MHz, DMSO) δ 10.91 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.09 (d, *J* = 7.9 Hz, 1H), 7.90 (td, *J* = 7.7, 1.2 Hz, 1H), 7.85 – 7.76 (m, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.11 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.97 (d, *J* = 1.9 Hz, 1H), 6.63 (s, 2H), 6.16 (s, 1H). **ESI HRMS**: calcd. For $C_{19}H_{11}N_4O_3SCl$[M+H]+ 411.0313 and 413.0284, found 411.0312 and 413.0281.

4h

^{1}H NMR (400 MHz, DMSO) δ 10.75 (s, 1H), 8.21 (d, *J* = 7.9 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.93 – 7.85 (m, 1H), 7.83 – 7.76 (m, 1H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 7.06 (td, *J* = 7.6, 1.0 Hz, 1H), 6.56 (s, 2H), 6.16 (s, 1H). **ESI HRMS**: calcd. For $C_{19}H_{11}N_4O_3SBr$[M+H]+ 454.9808 and 456.9788, found 454.9808 and 456.9776.

4i

^{1}H NMR (400 MHz, DMSO) δ 10.70 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.92 – 7.87 (m, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 6.93 (s, 1H), 6.86 (s, 1H), 6.51 (s, 2H), 6.14 (s, 1H), 2.24 (s, 6H). ^{13}C NMR (101 MHz, DMSO-D_6) δ 177.95, 148.66, 141.18, 135.62, 135.50, 132.87, 132.46, 131.20, 128.87, 126.85, 124.94, 123.06, 121.94, 118.14, 102.93, 102.65, 61.08, 52.83, 32.68, 29.54. **ESI HRMS**: calcd. For $C_{21}H_{16}N_4O_3S$[M+H]+ 405.0943, found 405.0977.

6a

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.8 Hz, 1H), 7.78 – 7.73 (m, 1H), 7.72 – 7.65 (m, 2H), 7.44 – 7.39 (m, 2H), 7.34 (t, *J* = 6.7 Hz, 3H), 5.87 (d, *J* = 4.6 Hz, 1H), 4.50 (d, *J* = 4.6 Hz, 1H). **ESI HRMS**: calcd. For $C_{18}H_{13}N_3O_2S$[M+H]+ 336.0801 found 336.0798.

6b

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.8 Hz, 1H), 7.78 – 7.64 (m, 3H), 7.34 (td, *J* = 7.6, 1.8 Hz, 2H), 7.24 – 7.18 (m, 1H), 7.16 – 7.07 (m, 1H), 5.88 (d, *J* = 4.7 Hz, 1H), 4.89 (d, *J* = 4.7 Hz, 1H). ^{13}C

NMR (101 MHz, DMSO-D_6) δ 161.77, 159.32, 147.66, 135.32, 132.37, 131.95, 130.39, 130.26, 129.55, 128.66, 127.35, 125.56, 123.53, 122.86, 121.73, 121.41, 119.79, 116.67, 112.64, 105.19, 62.29, 32.65, 32.58. **ESI HRMS**: calcd. For $C_{18}H_{12}N_3O_2SF$[M+H]+354.0703 found 354.0701.

6c

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.8 Hz, 1H), 7.77 – 7.63 (m, 3H), 7.45 – 7.32 (m, 3H), 7.26 (td, *J* = 7.5, 1.8 Hz, 1H), 5.91 (d, *J* = 4.7 Hz, 1H), 5.07 (d, *J* = 4.7 Hz, 1H). **ESI HRMS**: calcd. For $C_{18}H_{12}N_3O_2SCl$[M+H]+370.0412 and 372.0382, found 370.0411 and 372.0386.

6d

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.8 Hz, 1H), 7.74 – 7.63 (m, 3H), 7.28 (d, *J* = 5.9 Hz, 2H), 7.02 (s, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 5.90 (d, *J* = 4.9 Hz, 1H), 4.94 (d, *J* = 4.8 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, DMSO-D_6) δ 147.66, 146.98, 142.12, 141.11, 137.15, 135.26, 132.39, 129.95, 129.58, 128.12, 127.37, 126.37, 122.74, 121.70, 107.16, 73.81, 40.67, 40.46, 40.25, 40.04, 39.83, 39.62, 39.41, 32.70, 21.18, 14.61. **ESI HRMS**: calcd. For $C_{19}H_{15}N_3O_3S$[M+H]+ 366.0801 found 366.0798.

6e

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.8 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.74 – 7.67 (m, 2H), 7.40 – 7.35 (m, 1H), 7.13 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.07 – 6.99 (m, 2H), 5.84 (d, *J* = 4.5 Hz, 1H), 4.51 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (101 MHz,) δ 161.59, 160.91, 146.35, 135.30, 131.33, 131.16, 130.85, 130.69, 130.55, 130.23, 130.14, 129.56, 127.41, 127.36, 125.93, 122.92, 121.73, 119.89, 116.16, 116.08, 106.73, 62.74, 32.68. **ESI HRMS**: calcd. For $C_{18}H_{12}N_3O_2SF$[M+H]+354.3714 found 354.3712.

6f

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.8 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.34 (dd, *J* = 13.5, 5.8 Hz, 2H), 7.26 – 7.21 (m, 1H), 5.81 (d, *J* = 4.5 Hz, 1H), 4.49 (d, *J* = 4.5 Hz, 1H). **ESI HRMS**: calcd. For $C_{18}H_{12}N_3O_2SCl$[M+H]+370.0412 and 372.0382, found 370.0411 and 372.0386.

6g

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.9 Hz, 1H), 7.80 – 7.67 (m, 3H), 7.31 (s, 1H), 7.29 – 7.27 (m, 1H), 7.09 (t, *J* = 8.4 Hz, 2H), 5.83 (d, *J* = 4.5 Hz, 1H), 4.49 (d, *J* = 4.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-D_6) δ 163.87, 160.97, 146.37, 141.77, 135.32, 131.92, 131.34, 131.03, 130.61, 127.37, 126.83, 122.93, 121.86, 119.84, 116.68, 115.55, 106.26, 63.50. **ESI HRMS**: calcd. For $C_{18}H_{12}N_3O_2SF$[M+H]+354.0634 found 354.0631.

6h

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 7.0 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 5.82 (d, *J* = 4.5 Hz, 1H), 4.49 (d, *J* = 4.5 Hz, 1H). **ESI HRMS**: calcd. For $C_{18}H_{12}N_3O_2SCl$[M+H]+370.0412 and 372.0382, found 370.0411 and 372.0386.

6i

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 7.0 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 2H), 7.56 – 7.52 (m, 2H), 7.21 (d, *J* = 8.3 Hz, 2H), 5.81 (d, *J* = 4.5 Hz, 1H), 4.47 (d, *J* = 4.5 Hz, 1H). **ESI HRMS**: calcd. For $C_{18}H_{12}N_3O_2SBr$[M+H]+413.9906 and 415.9886, found 413.9904 and 415.9883.

6j

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.72 (dd, *J* = 7.6, 4.0 Hz, 4H), 7.46 (d, *J* = 8.0 Hz, 2H), 5.80 (d, *J* = 4.6 Hz, 1H), 4.58 (d, *J* = 4.5 Hz, 1H). **ESI HRMS**: calcd. For $C_{19}H_{12}N_4O_2S$[M+H]+ 360.3910 found 360.3907.

6k

^{1}H NMR (400 MHz, DMSO) δ 8.06 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.79 (dt, *J* = 35.6, 7.6 Hz, 2H), 7.17 (s, 1H), 7.13 (s, 1H), 6.16 (d, *J* = 5.2 Hz, 3H), 4.43 (d, *J* = 4.7 Hz, 1H). ^{13}C NMR (101

MHz, DMSO-D_6) δ 157.15, 147.92, 135.14, 132.39, 131.65, 131.09, 129.25, 128.66, 127.51, 126.88, 122.71, 121.63, 120.11, 112.02, 106.24, 73.83, 35.10, 32.70, 14.60. **ESI HRMS**: calcd. For $C_{19}H_{15}N_3O_2S$[M+H]+ 350.0695 found 350.0692.

6l

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.8 Hz, 1H), 7.80 – 7.66 (m, 3H), 6.93 – 6.85 (m, 2H), 6.82 (d, *J* = 1.8 Hz, 1H), 5.86 (d, *J* = 4.5 Hz, 1H), 4.45 (d, *J* = 4.5 Hz, 1H), 3.91 (d, *J* = 1.9 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-D_6) δ 149.45, 148.71, 146.96, 136.57, 135.27, 131.76, 131.38, 127.59, 126.19, 122.76, 121.72, 120.25, 112.80, 111.95, 107.43, 67.56, 56.05, 32.68, 25.66. **ESI HRMS**: calcd. For $C_{20}H_{17}N_3O_4S$[M+H]+ 396.4330 found 396.4327.

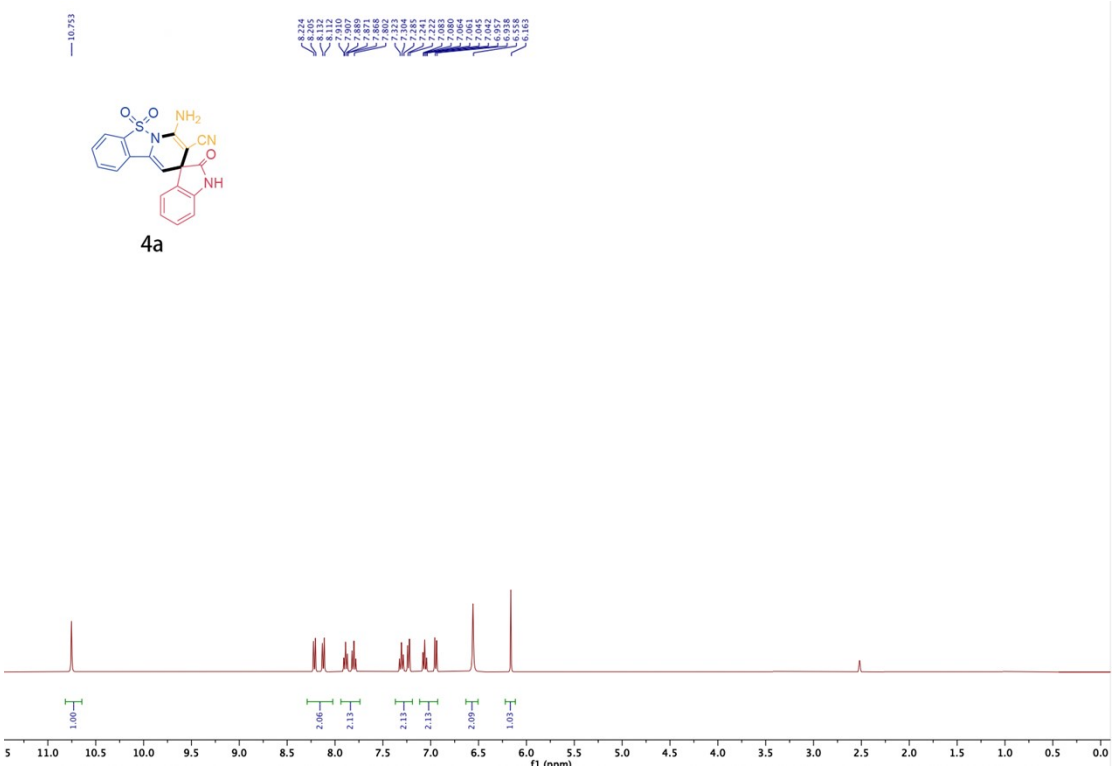
6m

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.8 Hz, 1H), 7.80 – 7.66 (m, 3H), 7.31 (d, *J* = 1.5 Hz, 1H), 7.07 – 7.01 (m, 2H), 5.93 (d, *J* = 4.6 Hz, 1H), 4.83 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-D_6) δ 148.81, 146.86, 142.11, 141.00, 135.40, 132.00, 131.34, 127.37, 127.29, 126.47, 126.37, 125.20, 122.89, 121.86, 119.83, 106.28, 64.42, 35.75. **ESI HRMS**: calcd. For $C_{16}H_{11}N_3O_2S_2$[M+H]+ 342.0293 found 342.0291.

6n

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (ddd, *J* = 13.3, 6.6, 2.7 Hz, 3H), 7.78 – 7.72 (m, 2H), 7.71 – 7.65 (m, 2H), 7.56 – 7.49 (m, 2H), 7.48 – 7.39 (m, 2H), 5.91 (d, *J* = 4.6 Hz, 1H), 4.67 (d, *J* = 4.5 Hz, 1H).
^{13}C NMR (101 MHz, DMSO-D_6) δ 147.65, 142.10, 135.30, 132.91, 132.42, 131.90, 129.58, 129.30, 128.68, 128.29, 128.14, 127.40, 127.03, 126.63, 126.48, 125.97, 122.84, 121.75, 120.05, 106.78, 60.32. **ESI HRMS**: calcd. For $C_{22}H_{15}N_3O_2S$[M+H]+ 386.0885 found 386.0882.

Spectra of Products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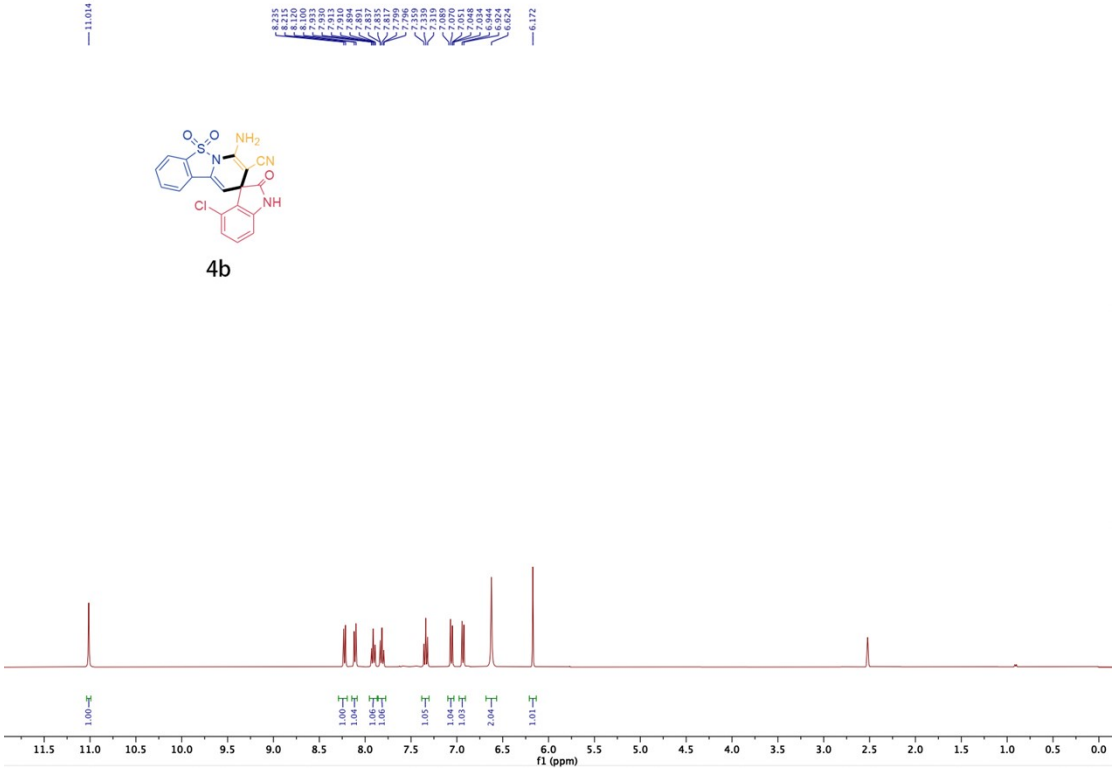
4a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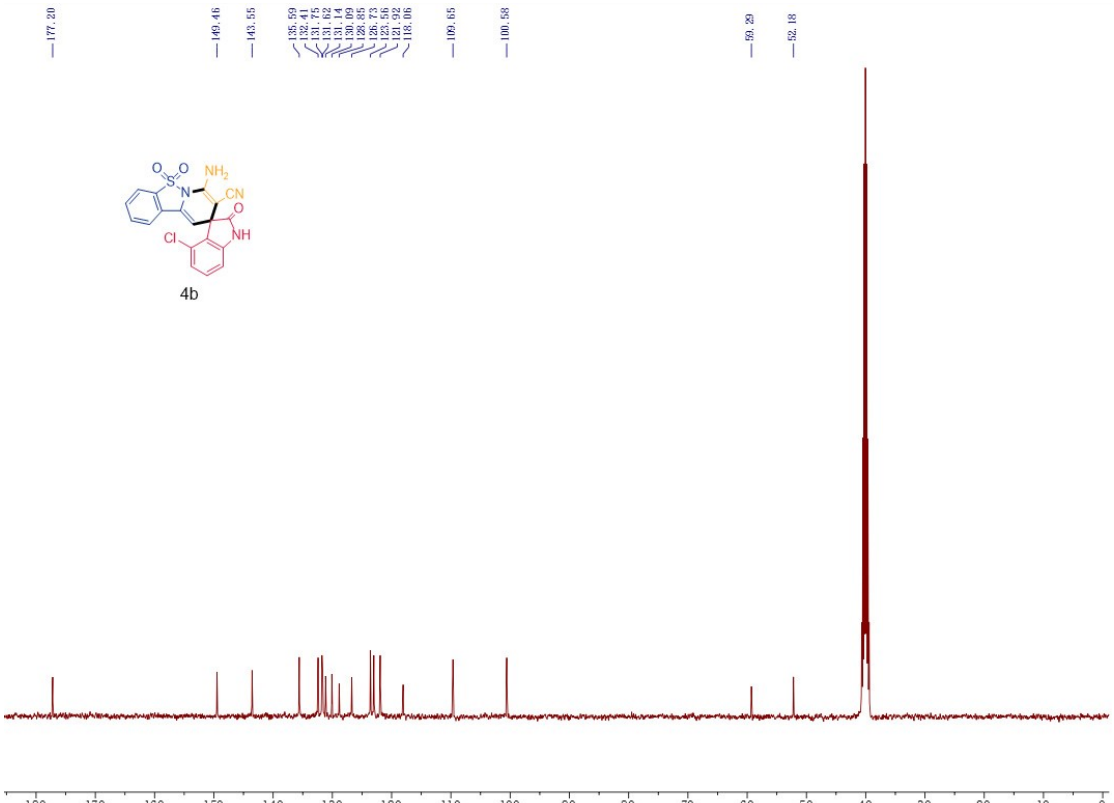
f1 (ppm)

4b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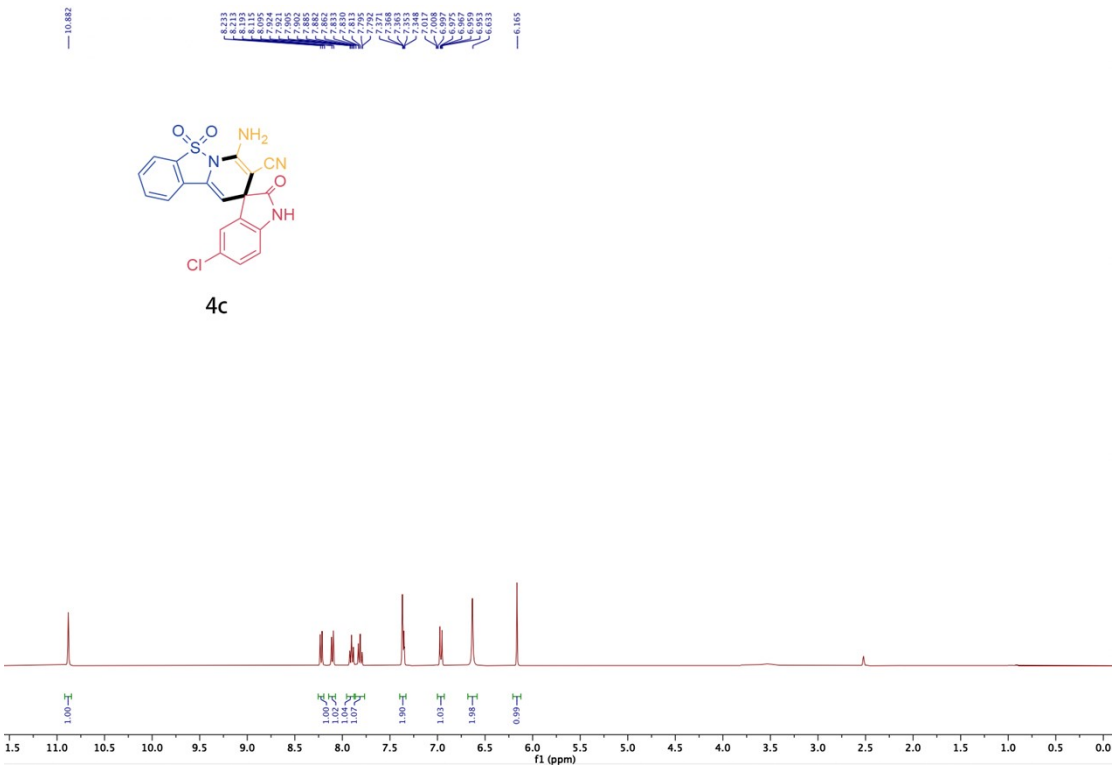
4b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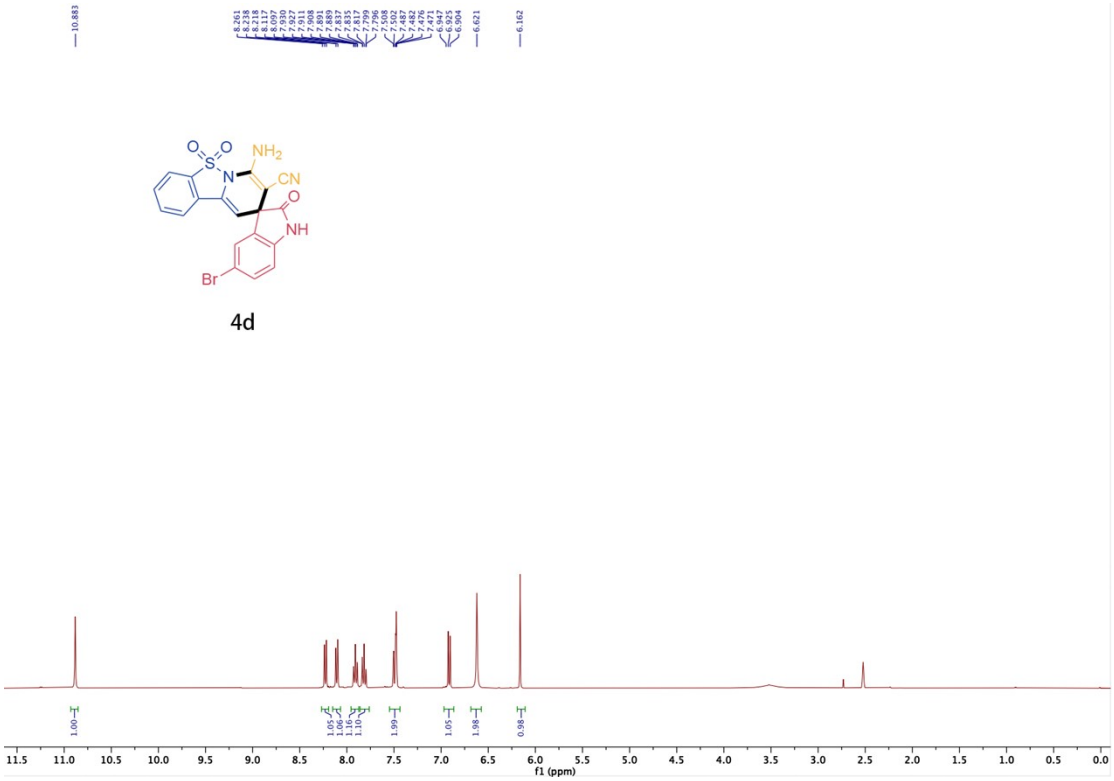
f1 (ppm)

4c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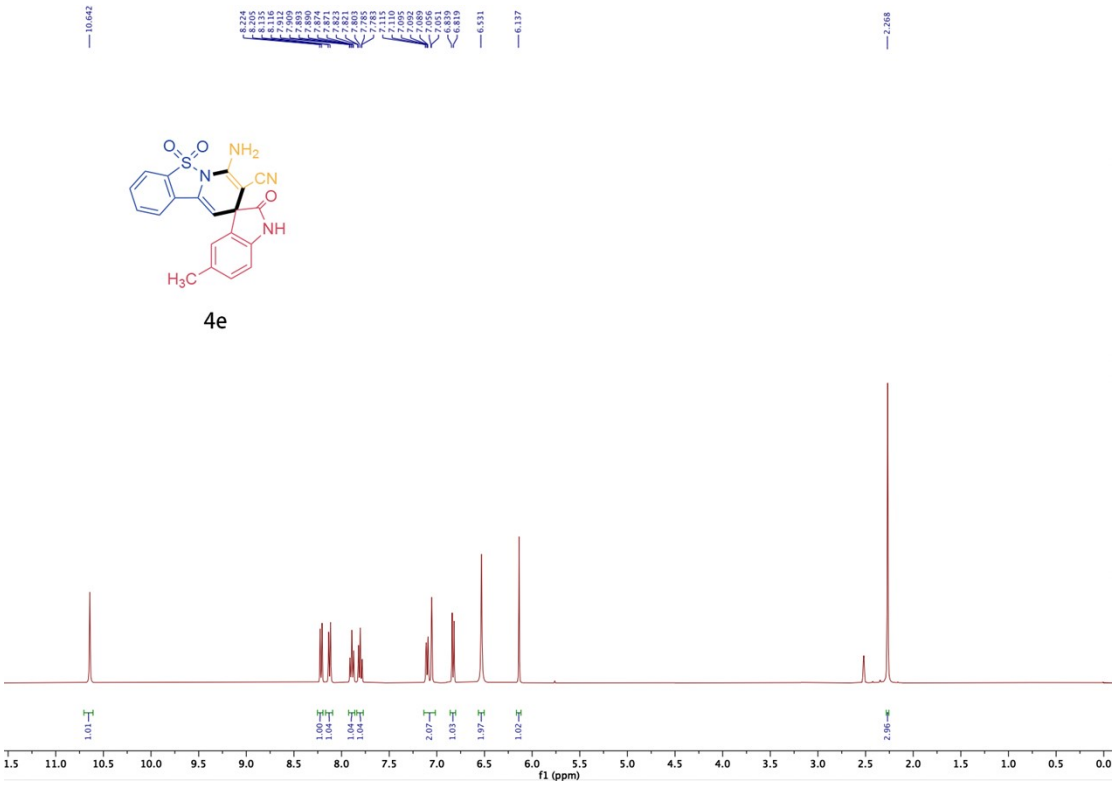
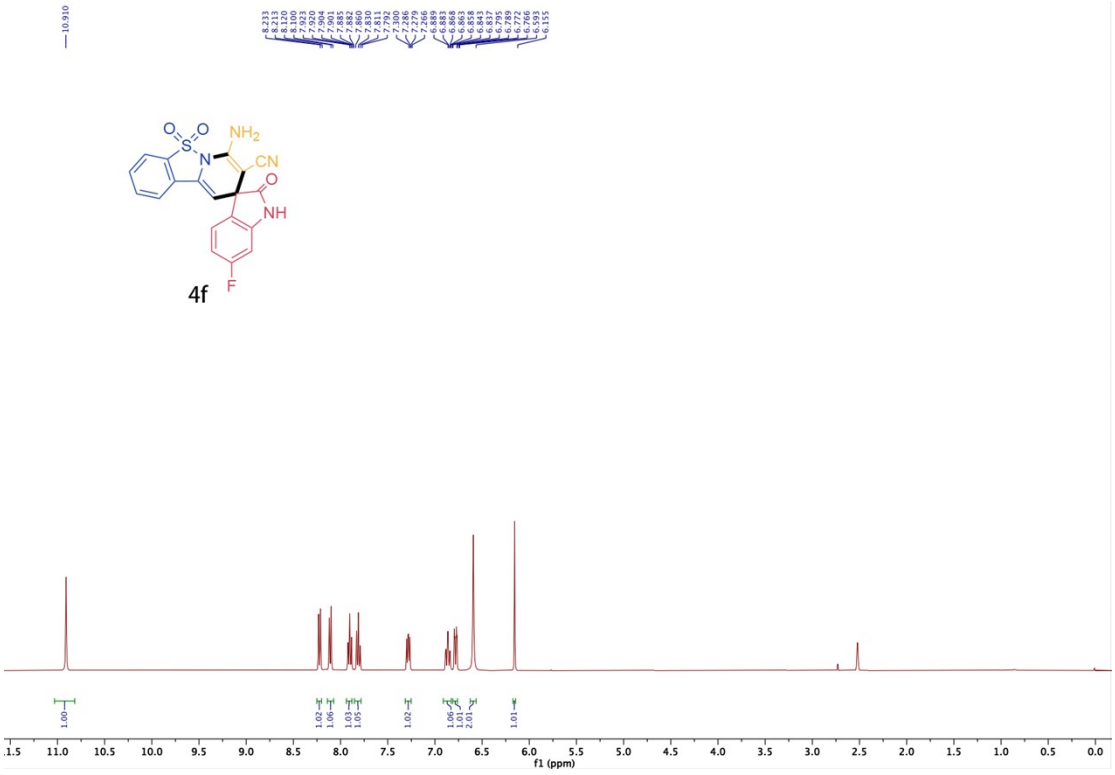
1.06
1.10
1.99
1.05
1.98
0.58
f1 (ppm)

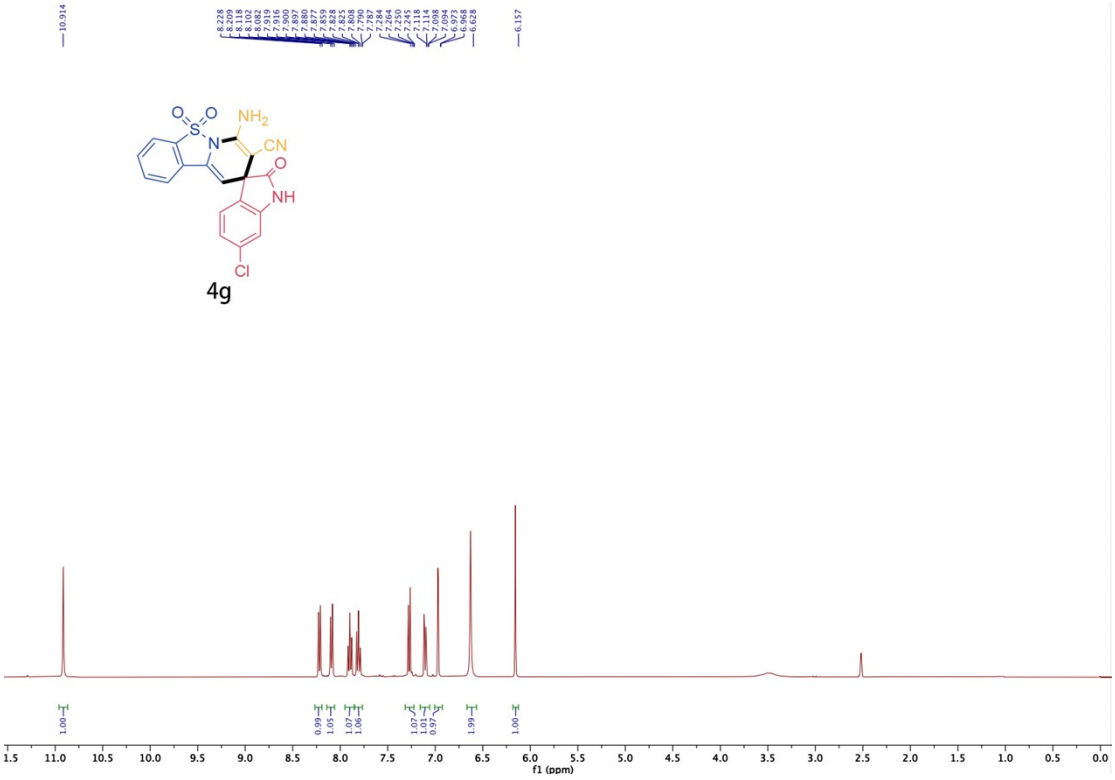
4d


10.642
8.224
8.205
8.135
8.116
7.912
7.909
7.893
7.889
7.874
7.871
7.852
7.821
7.803
7.795
7.783
7.115
7.110
7.095
7.092
7.088
7.056
7.051
6.839
6.819
6.531
6.137
2.268
NH2
CN
O
NH
H3C
1.01
1.00
1.04
1.04
1.04
2.07
1.03
1.97
1.02
2.96
f1 (ppm)

4e

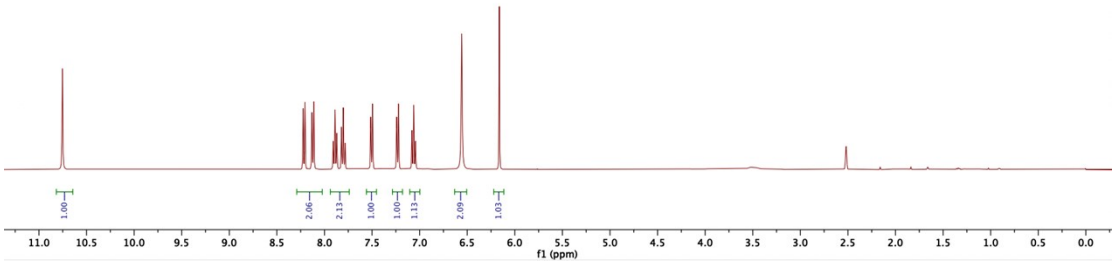

10.910
8.233
8.213
8.120
8.100
7.923
7.920
7.904
7.901
7.885
7.882
7.860
7.810
7.811
7.792
7.300
7.286
7.279
6.886
6.883
6.868
6.865
6.858
6.843
6.837
6.795
6.779
6.777
6.766
6.591
6.155
NH2
CN
O
NH
F
1.00
1.02
1.06
1.03
1.05
1.02
1.06
1.01
2.01
1.01
f1 (ppm)

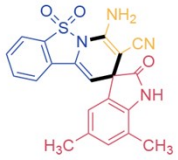
4f


10.914
8.228
8.209
8.118
8.102
8.082
7.919
7.916
7.900
7.897
7.880
7.877
7.859
7.828
7.825
7.808
7.790
7.787
7.284
7.264
7.250
7.235
7.118
7.114
7.098
7.094
6.973
6.968
6.628
6.157
NH2
CN
O
NH
Cl
1.00
0.99
1.05
1.07
1.06
1.07
1.01
0.97
1.99
1.00
f1 (ppm)

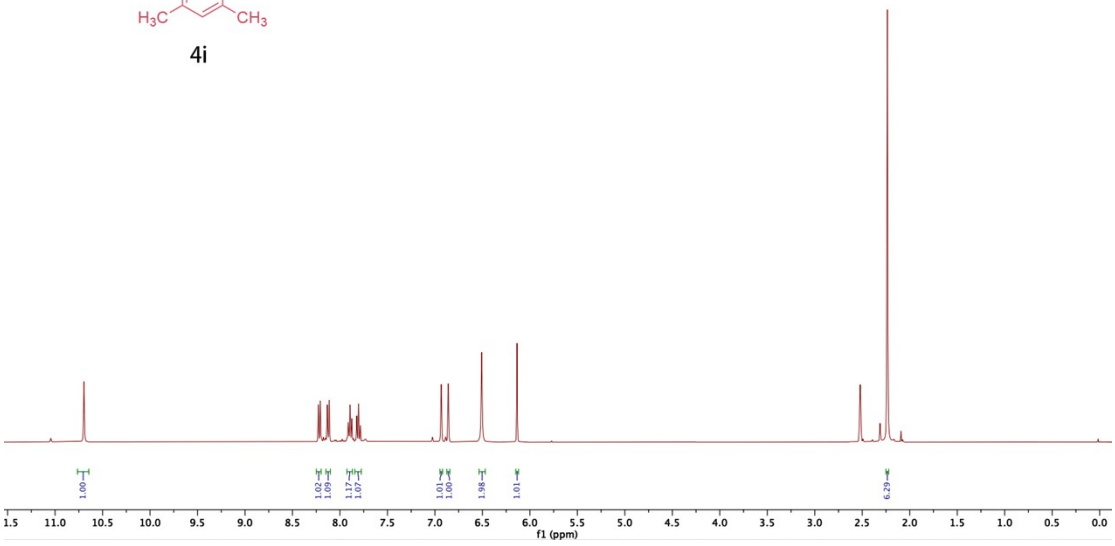
4g

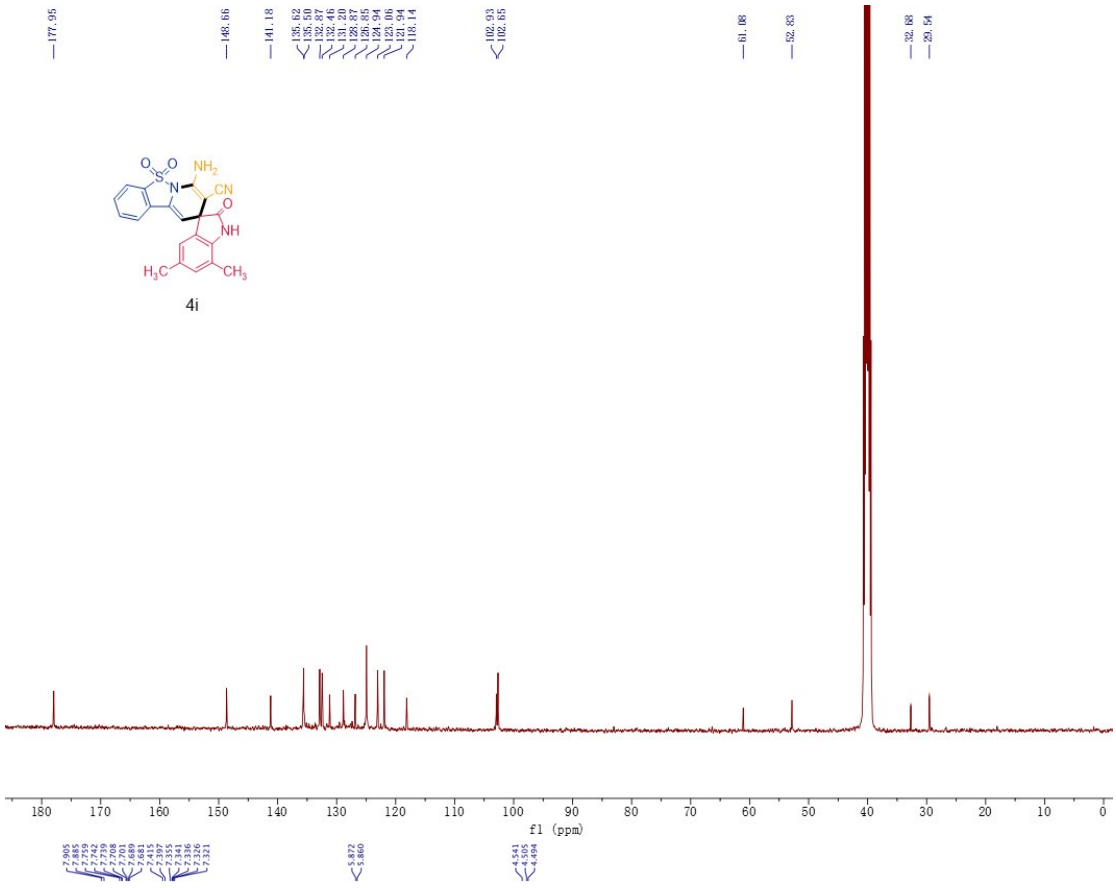
4h

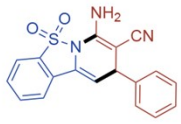




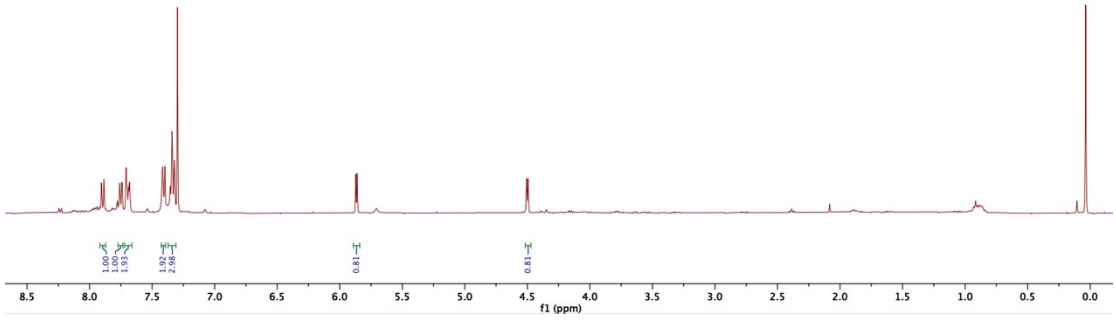
4i

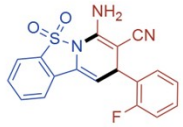



177.95
148.66
141.18
135.62
135.50
132.87
132.46
131.20
128.87
128.65
124.94
123.06
121.94
118.14
102.93
102.65
61.08
52.83
32.88
29.54
NH2
CN
O
NH
H3C
CH3
4i
f1 (ppm)
7.905
7.885
7.759
7.742
7.729
7.708
7.701
7.689
7.681
7.415
7.397
7.355
7.341
7.336
7.326
7.321
5.872
5.860
4.541
4.505
4.494

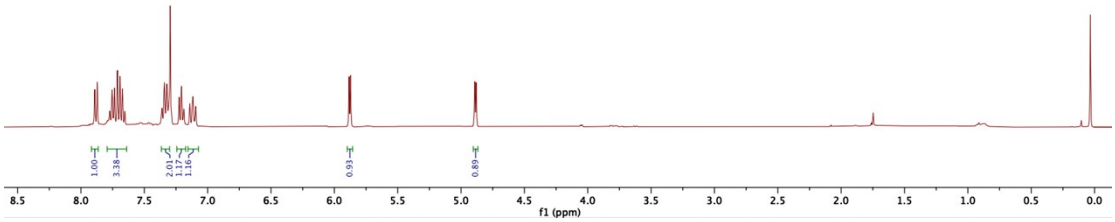

NH2
CN
O
S
N

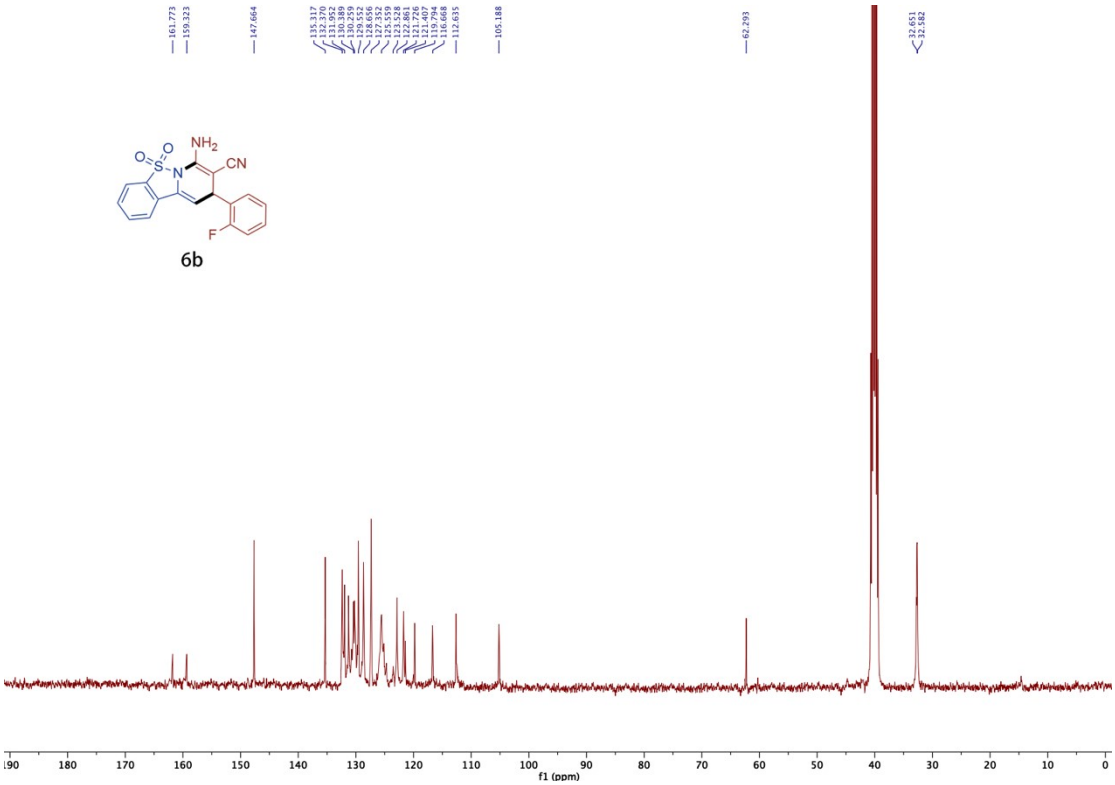
6a


1.00
1.05
1.93
1.92
2.98
0.81
0.81
f1 (ppm)



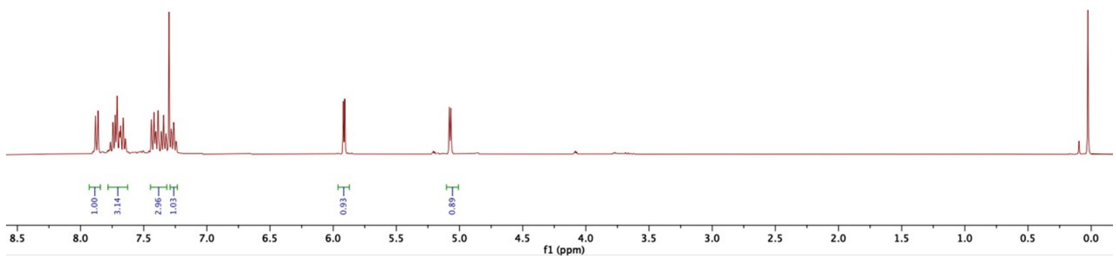
6b

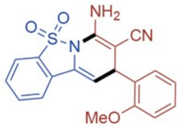




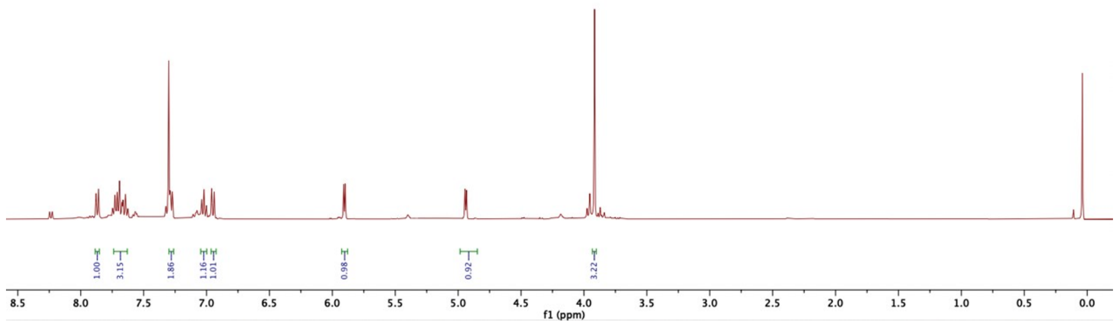
6b

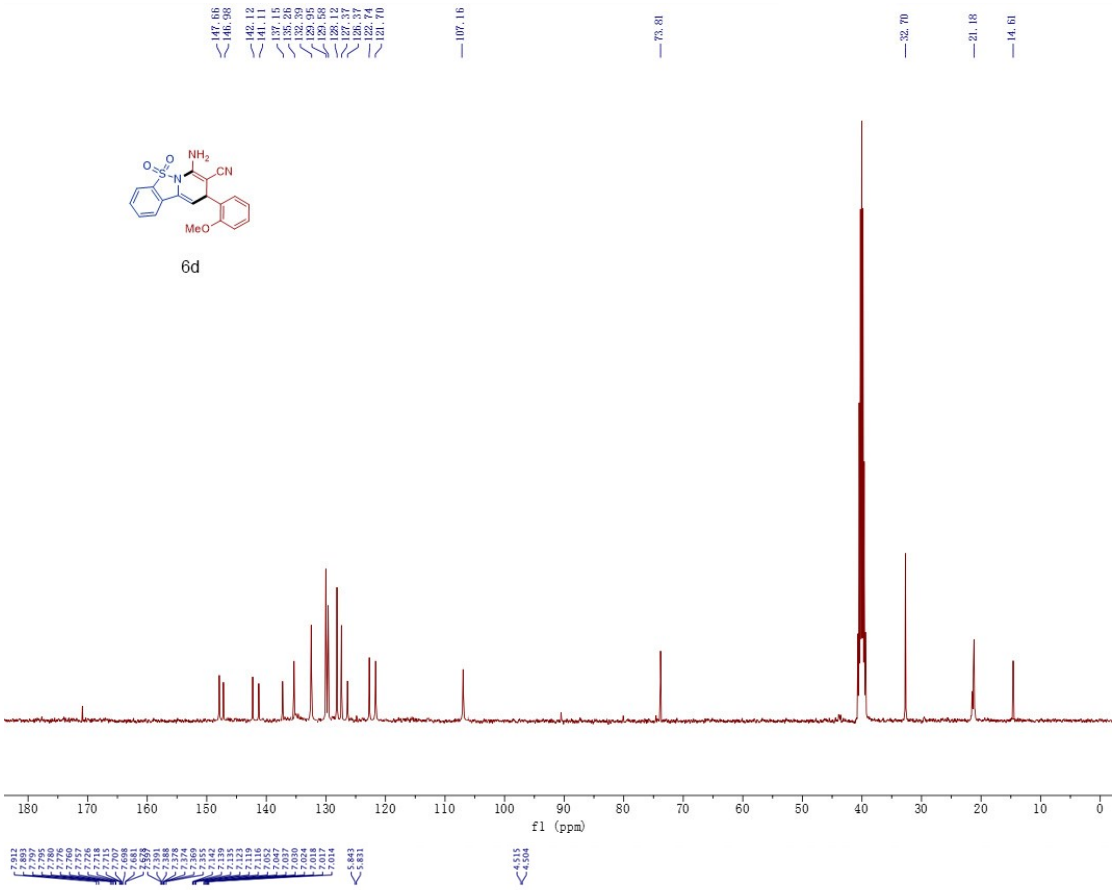
6c



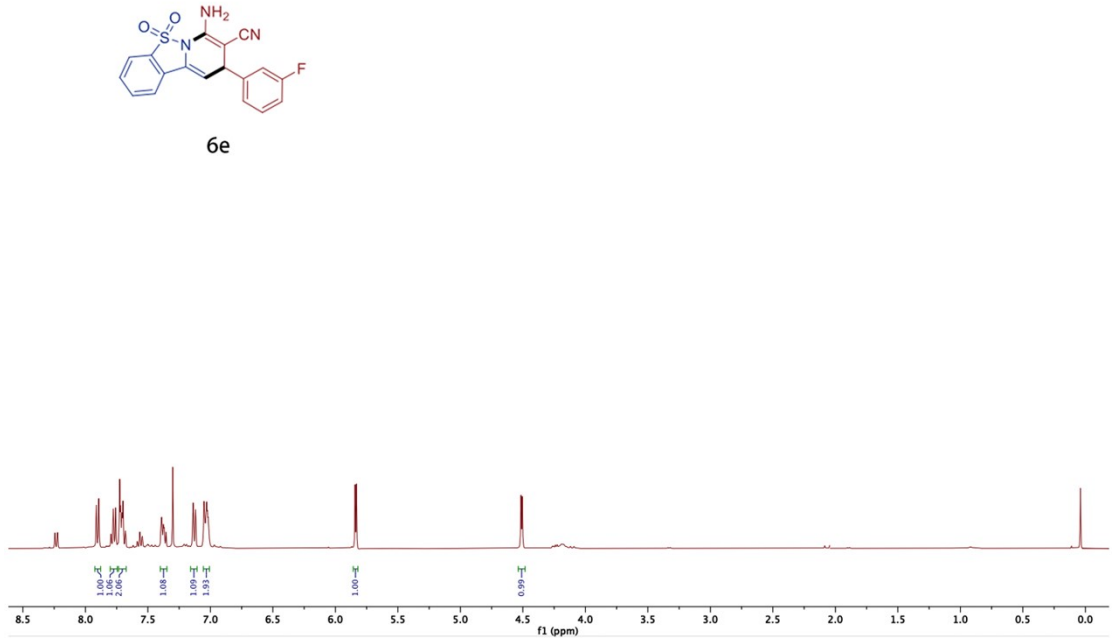


6d

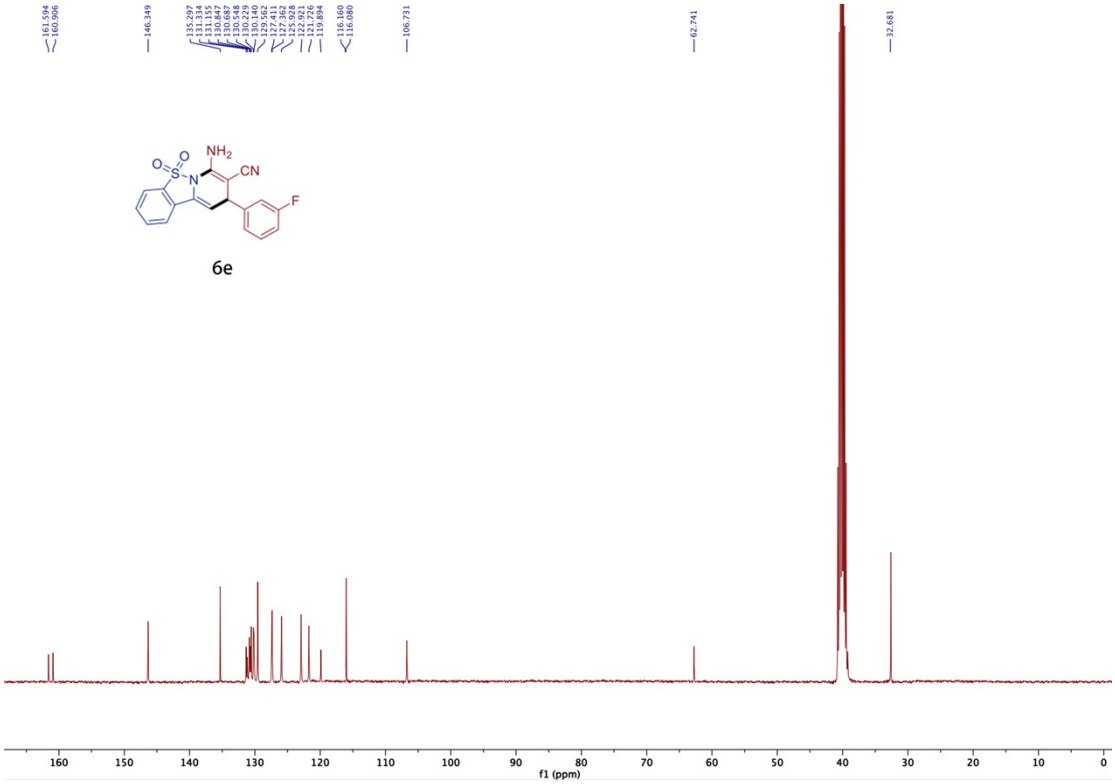



147.66
146.98
142.12
141.11
137.15
135.26
132.39
129.95
129.58
128.12
127.37
126.37
122.74
121.70
107.16
73.81
32.70
21.18
14.61
NH2
CN
MeO
f1 (ppm)

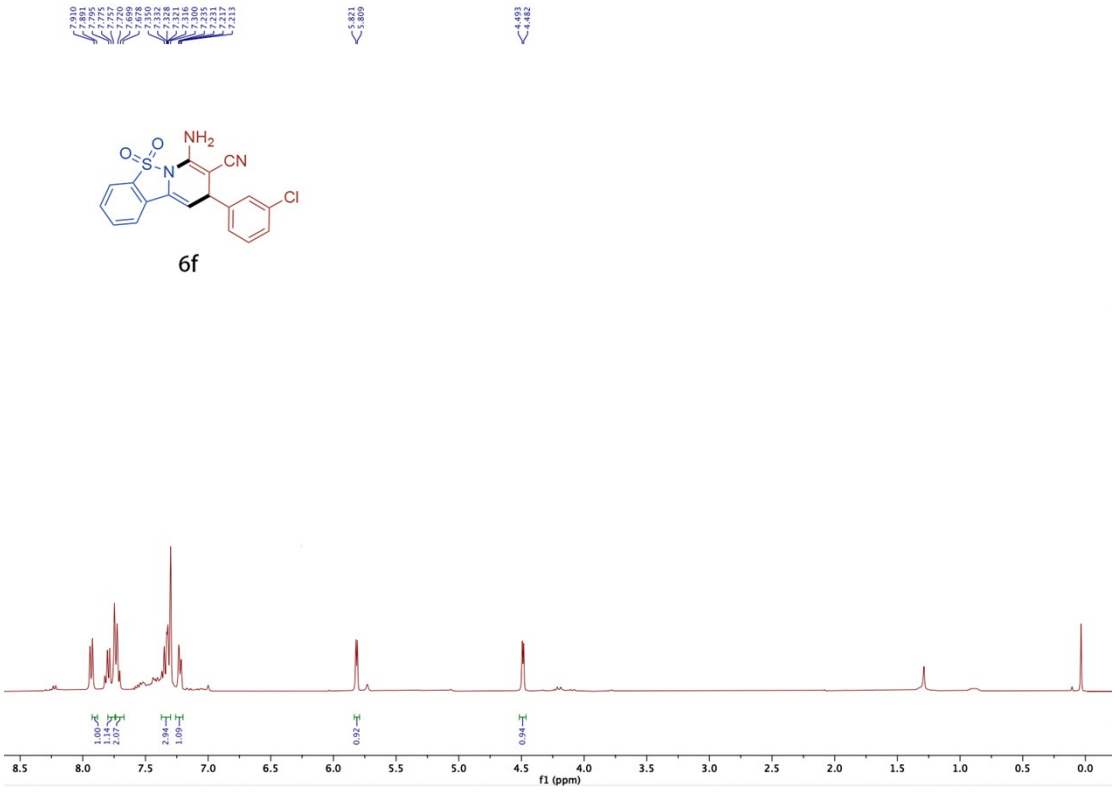
6d


NH2
CN
F
f1 (ppm)

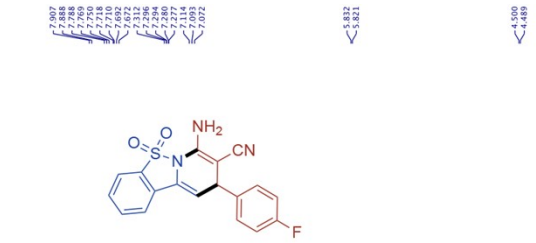
6e


161.594
160.996
146.349
135.297
131.374
131.155
130.847
130.737
130.548
130.229
129.740
129.562
127.411
127.253
125.928
122.921
122.756
113.894
116.160
116.000
106.731
62.741
32.681
NH2
CN
O
O
S
N
F
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

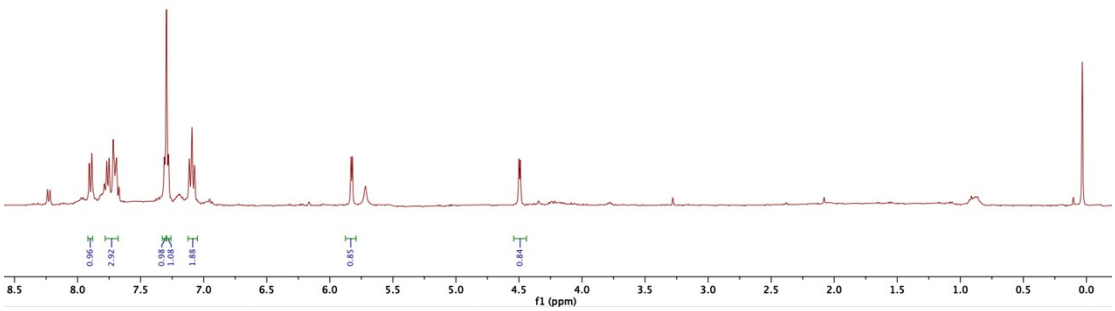
6e

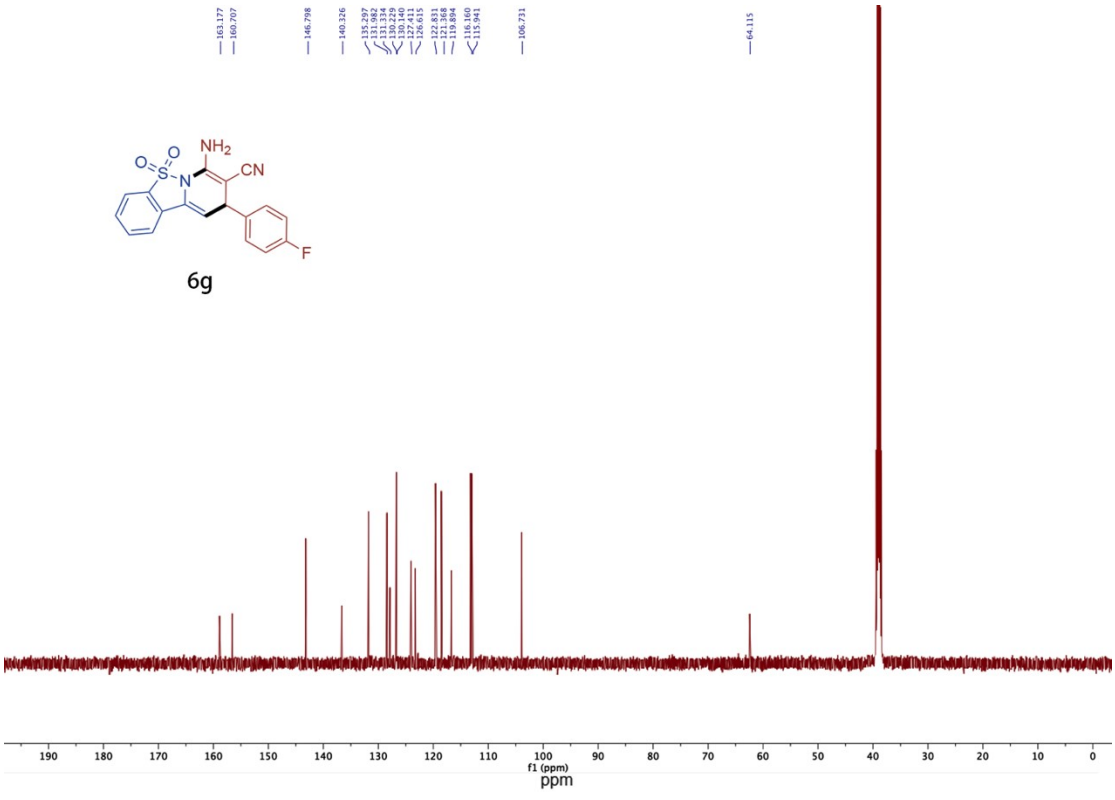

7.910
7.891
7.795
7.775
7.757
7.720
7.699
7.678
7.350
7.332
7.321
7.316
7.300
7.235
7.231
7.217
7.213
5.821
5.809
4.493
4.482
NH2
CN
O
O
S
N
Cl
1.00
1.14
2.07
2.94
1.09
0.92
0.94
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

6f


7.907
7.888
7.788
7.769
7.730
7.710
7.718
7.692
7.672
7.312
7.296
7.284
7.280
7.277
7.114
7.093
7.072
5.832
5.821
4.500
4.489
NH2
CN
O
S
N
F

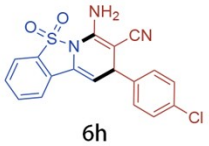
6g


0.96
2.92
0.98
1.08
1.88
0.85
0.84
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

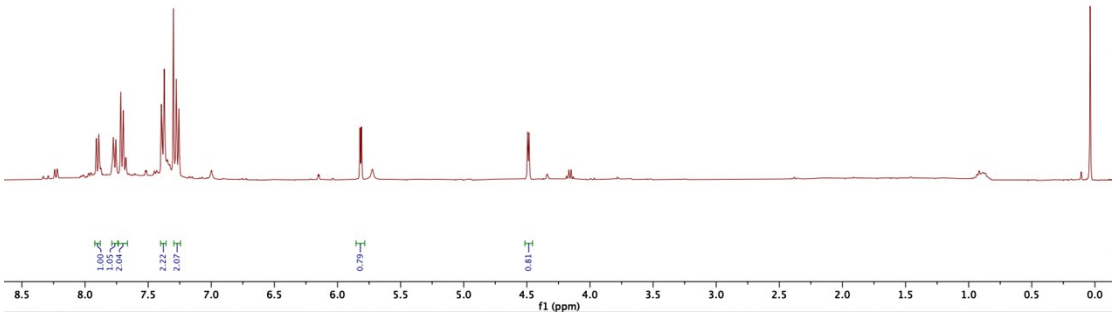

163.177
160.707
146.798
140.326
135.297
131.982
131.334
130.239
130.140
127.411
126.615
122.831
121.368
119.894
116.160
115.941
106.731
64.115
NH2
CN
O
S
N
F
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

6g

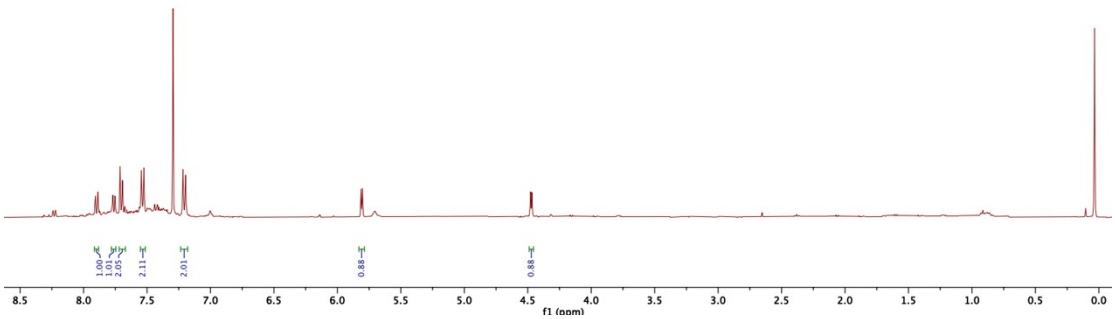
ppm

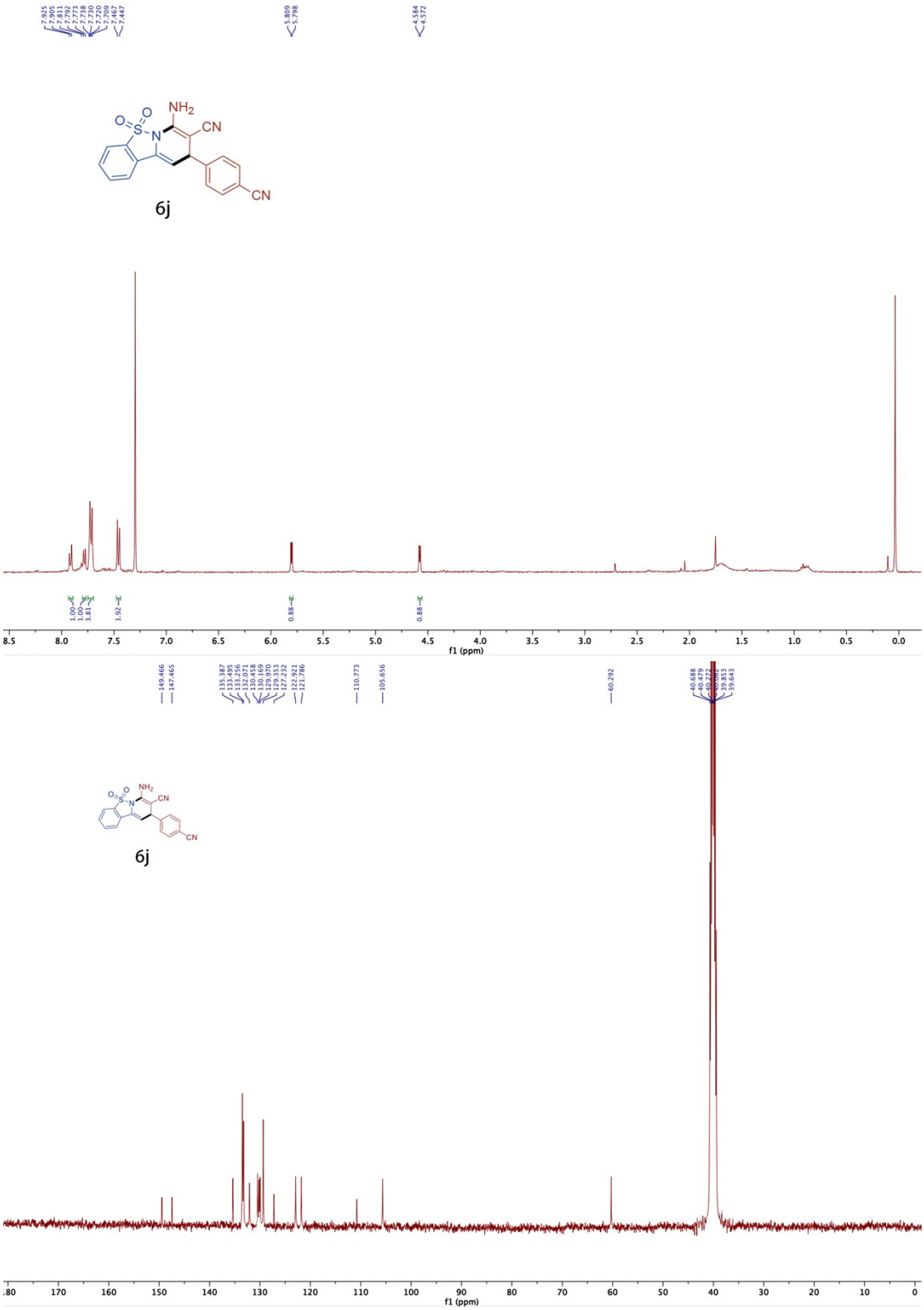


6h

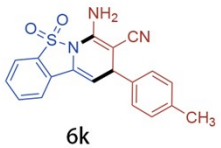


6i

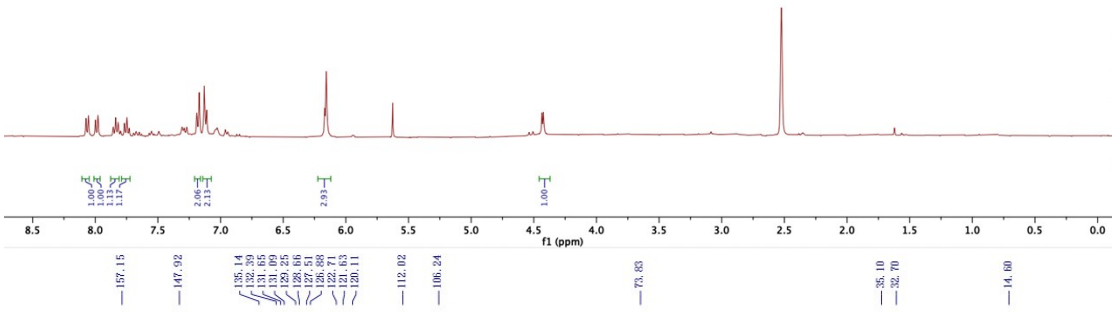


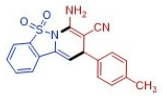

7.925
7.905
7.811
7.792
7.773
7.738
7.720
7.709
7.467
7.447
5.809
5.798
4.584
4.572
NH2
CN
CN
O
O
S
N
6j
1.00
1.00
3.81
1.92
0.88
0.88
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
149.466
147.465
135.387
133.495
133.256
132.271
130.458
130.169
129.970
129.353
127.232
122.921
121.786
110.773
105.656
60.292
40.688
40.479
40.272
40.062
39.853
39.643
6j
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.074
8.054
7.998
7.979
7.956
7.838
7.818
7.797
7.767
7.748
7.729
7.170
7.130
6.170
6.157
4.435
4.423

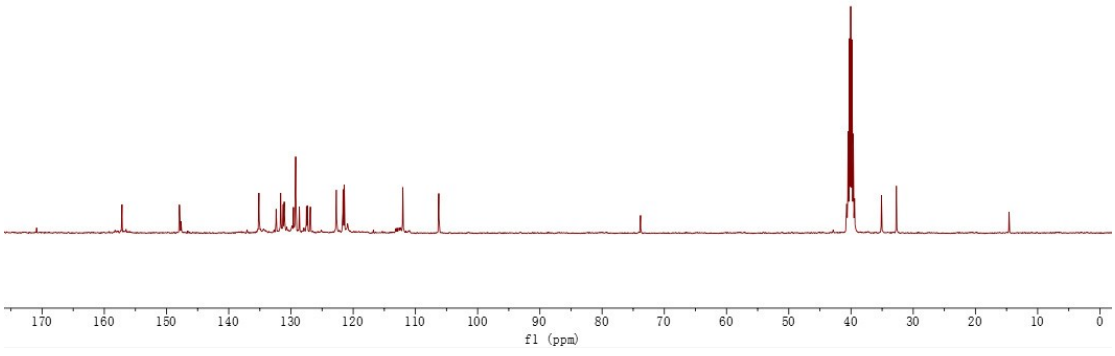

NH2
CN
O
O
S
N
CH3

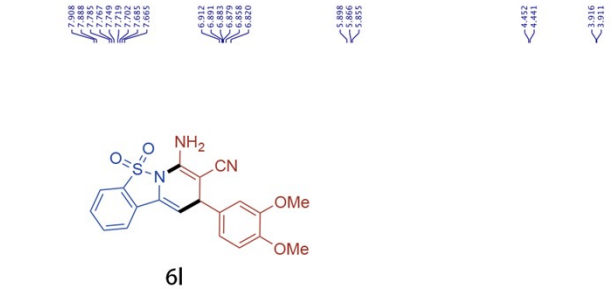
6k


1.00
1.00
1.13
1.17
2.06
2.13
2.93
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
157.15
147.92
135.14
132.39
131.65
131.09
129.25
128.61
127.71
126.88
122.71
121.63
120.11
112.02
106.24
73.83
35.10
32.70
14.60

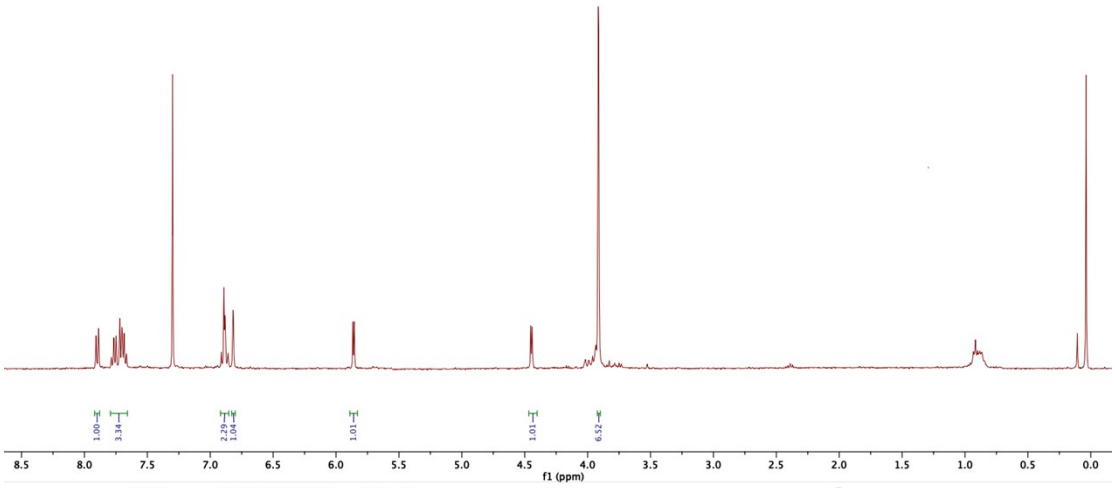

NH2
CN
O
O
S
N
CH3

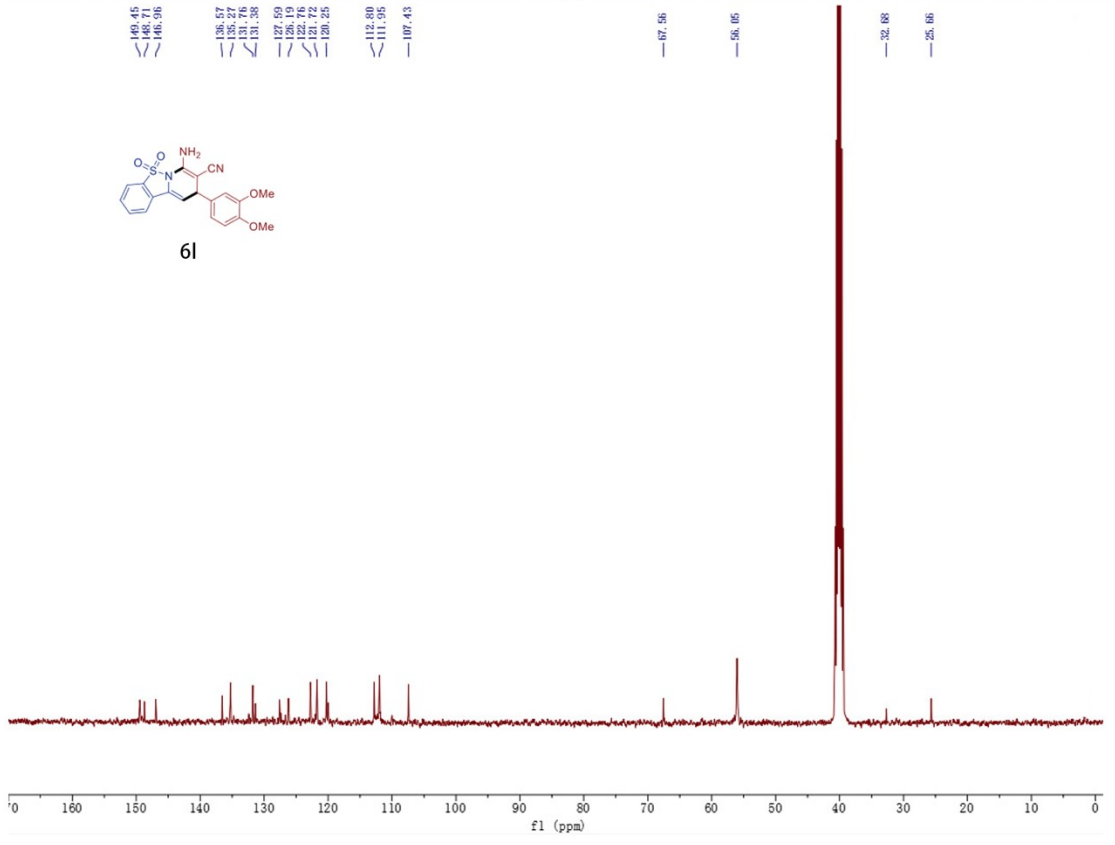
6k


170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.908
7.888
7.785
7.749
7.719
7.692
7.668
7.665
6.912
6.901
6.883
6.879
6.858
6.820
5.898
5.866
5.855
4.452
4.441
3.916
3.911
NH2
CN
OMe
OMe

6l


1.00
3.34
2.29
1.04
1.01
1.01
6.52
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


149.45
148.71
146.96
136.57
135.27
131.76
131.38
127.59
126.19
122.76
121.72
120.25
112.60
111.95
107.43
67.56
56.05
32.68
25.66
NH2
CN
OMe
OMe
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

6l


7.899
7.880
7.795
7.777
7.774
7.759
7.757
7.741
7.722
7.710
7.707
7.690
7.671
7.309
7.305
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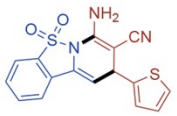
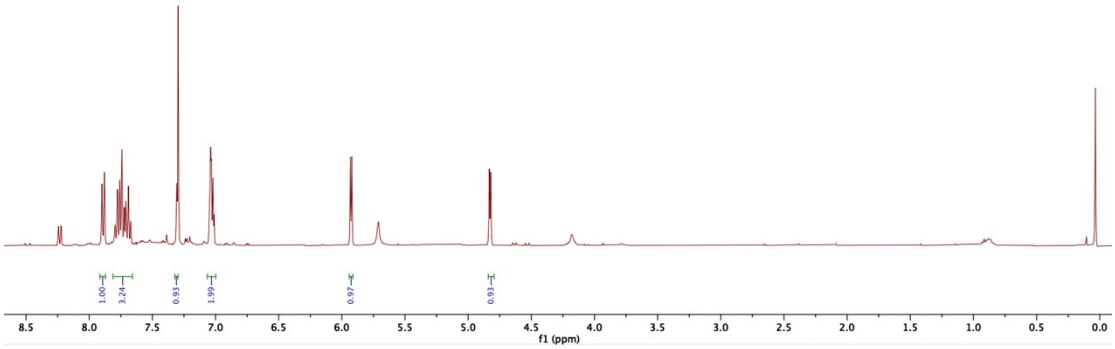
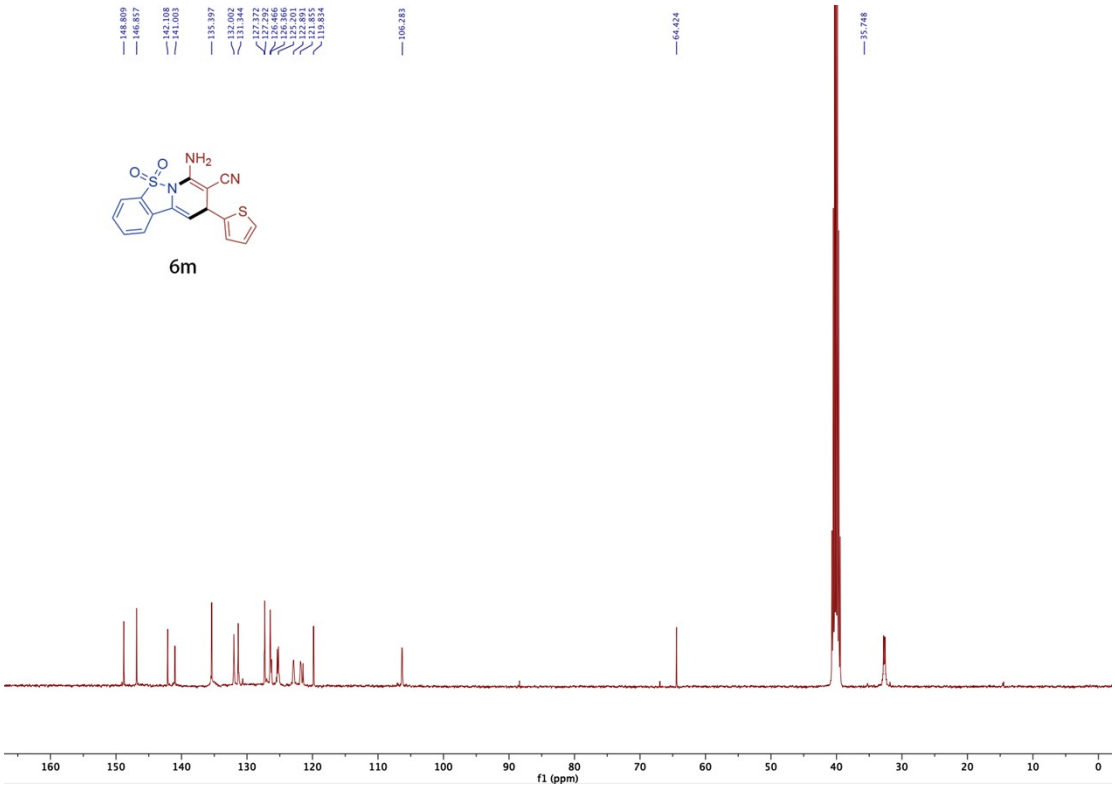
7.011
5.933
5.921
4.832
4.821


NH2
CN
O
S
O
N
S

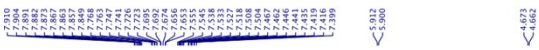
6m

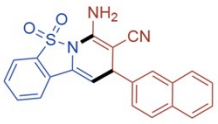

1.00
3.24
0.93
1.99
0.97
0.93
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


148.809
146.857
142.108
141.003
135.397
132.002
131.344
127.372
127.292
126.466
126.366
126.301
122.891
121.855
119.834
106.283
64.424
35.748
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

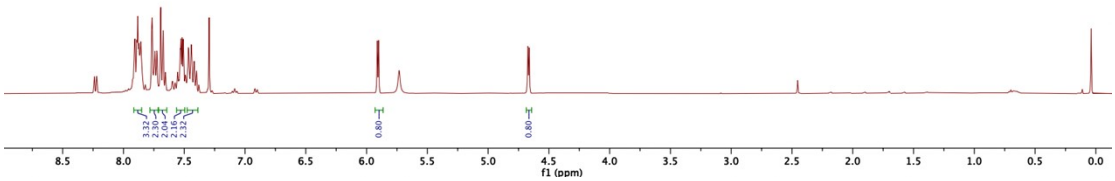
NH2
CN
O
S
O
N
S

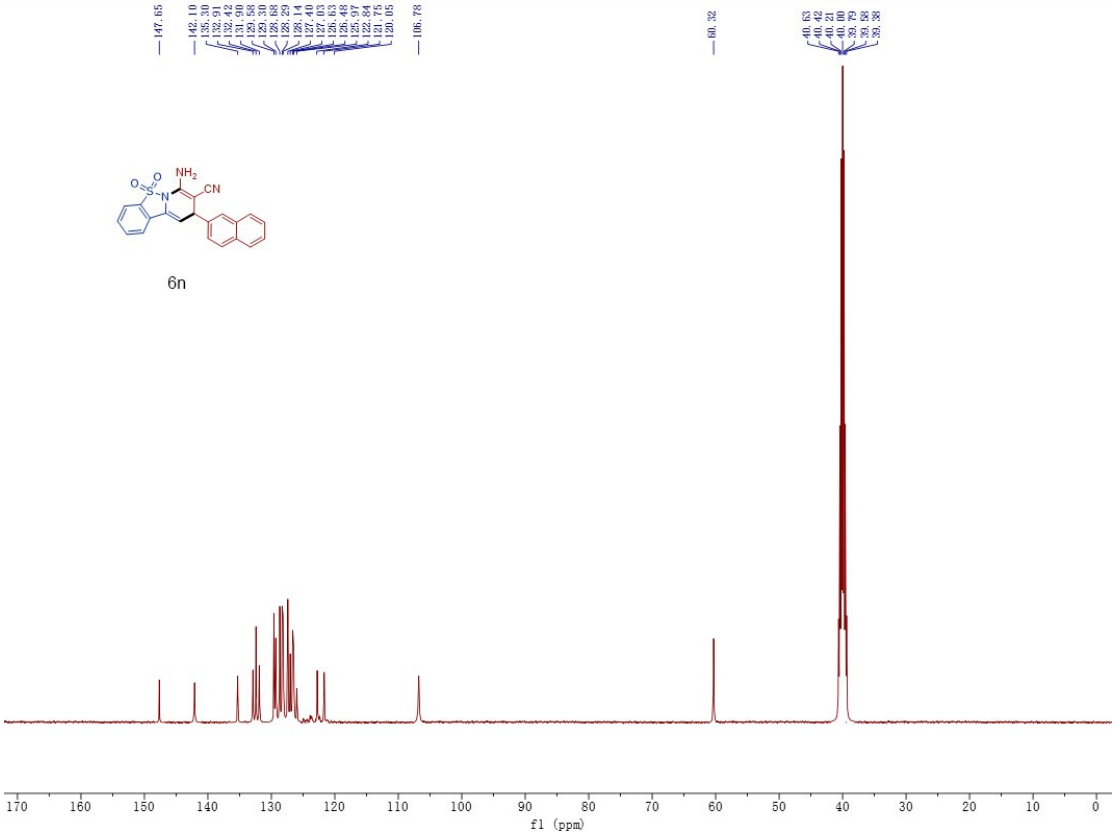
6m





6n





6n

1. Xu, Z.-H.; Jia, S.-K.; Chang, Z.-R.; Hua, Y.-Z.; Wang, M.-C.; Mei, G.-J., Facile Access to Saccharin-Fused 1,4-Dihydropyridines through [3+3] Annulation Reactions. *Eur. J. Org. Chem.* **2022,** *2022* (7), e202101423.