Supporting Information

A Mannich/Cyclization Cascade Process for the Asymmetric Synthesis of Spirocyclic Thioimida-zolidinexoindoles

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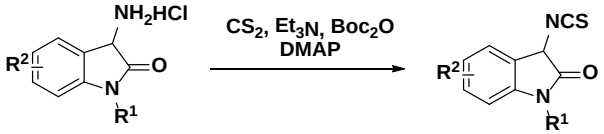
1. Gerenal Information

Toluene used in reactions was freshly distilled from sodium. All other chemicals were of commercial grade and used without further purification. Analytical thin-layer chromatography (TLC) was performed on HSGF 254 (0.15-0.2 mm thickness), visualized by irradiation with UV light (254 nm). Column Chromatography was performed with Combi*Flash*® companion system (Teledyne Isco. cn), silica gel was purchased from qingdaohaiyang (300-400 mesh). ^{1}H-NMR and ^{13}C-NMR were recorded on 300 or 400 MHz spectrometer. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated, s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); coupling constants (J) are in Hertz (Hz). HPLC was performed on a JASCO 2000 instrument by using Daicel columns. LC-MS was performed on an Agilent 1100 instrument by column Eclipse XDB-C18 (4.6 × 150 mm, 5 μm) or Extend-C18 (4.6 × 150 mm, 5 μm).

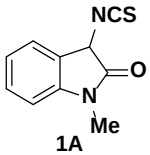
2. Preparation and Characterization of Compounds

2.1 General Procedure for Synthesis of 3-isothiocyanato oxindole 1A~D

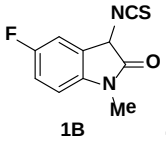


Hydrochlorate **5** was prepared according to literature procedure[1]. 3-isothiocyanato oxindole **1A~D** were prepared according to revised literature procedure[2]: To a suspension of hydrochlorate **5** (4.61 mmol) in EtOH (10 mL) were added CS_2 (3.51 g, 46.1 mmol) and Et_3N (1.87g, 18.4 mmol). The reaction mixture was stirred for 45 min at toom temperature and then cooled on an ice bath. Then Boc_2O (1.01 g, 4.61 mmol) and DMAP (10 mol %), dissolved in 2 mL of EtOH, were added. The reaction mixture was kept in the ice bath for 5 min, and then stirred for another 15 min at room temperature. Then, 10% HCl (5 mL) was added, and the mixture was extracted with DCM. The combined organic layers were dried over Na_2SO_4, concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to obtain **1A~F**.

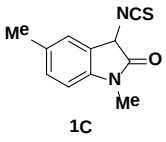
2.2 Characterization data of 1A~F



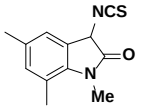
1A 61% yield, soild; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 7.54 – 7.43 (m, 2H), 7.22 – 7.13 (m, 2H), 3.20 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 193.84, 169.43, 144.10, 132.08, 127.95, 125.01, 124.52, 110.48, 91.33, 27.58. HRMS (EI): Calculated for $C_{10}H_8N_2NaOS$ [M+Na]$^+$: 227.0250, found: 227.0253.



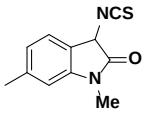
1B 35% yield, solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.04 (s, 1H), 7.62 (dd, J = 7.9, 2.7 Hz, 1H), 7.37 (td, J = 9.1, 2.7 Hz, 1H), 7.22 (dd, J = 8.7, 4.1 Hz, 1H), 3.20 (s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 194.12 , 169.37 , 159.45 (d, J = 240.4 Hz), 140.45 , 129.00 (d, J = 9.0 Hz), 118.42 (d, J = 23.6 Hz), 113.56 (d, J = 26.2 Hz), 111.56 (d, J = 7.9 Hz), 91.06 , 27.77; HRMS (EI): Calculated for $C_{10}H_7FN_2NaOS$ [M+Na]$^+$: 245.0155, found: 245.0149.



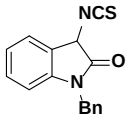
1C 66% yield, solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.34 – 7.26 (m, 3H), 7.09 (d, J = 8.4 Hz, 1H), 3.18 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 193.75, 169.39, 141.66, 133.92, 132.18, 128.02, 125.35, 110.24, 91.48, 27.57, 20.89. HRMS (EI): Calculated for $C_{11}H_{10}N_2NaOS$ [M+Na]$^+$: 241.0406, found: 241.0395.



1D 60% yield, solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.02 (s, 1H), 7.05 (s, 1H), 7.03 (s, 1H), 3.40 (s, 3H), 2.51 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 193.13, 169.51, 138.71, 135.32, 133.25, 128.21, 122.57, 120.89, 90.70, 30.06, 20.07, 18.13; HRMS (EI): Calculated for $C_{12}H_{12}N_2NaOS$ [M+Na]$^+$: 255.0563, found: 255.0559.



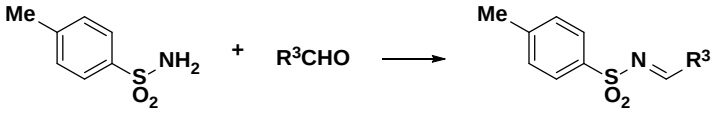
1E 68% yield; soild; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.01 (s, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.01 (s, 1H), 6.95 (d, J = 7.3 Hz, 1H), 3.16 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 193.20, 169.17, 143.65, 141.81, 124.60, 124.34, 124.19, 110.64, 90.84, 27.01, 21.50; HRMS (EI): Calculated for $C_{11}H_{10}N_2NaOS$ [M+Na]$^+$: 241.0406, found: 241.0405.



1F

57% yield, solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.25 (s, 1H), 7.51 (d, J = 7.5 Hz, 1H), 7.44 – 7.38 (m, 1H), 7.37 (d, J = 4.4 Hz, 4H), 7.34 – 7.26 (m, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 7.9 Hz, 1H), 5.06 – 4.89 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6)) δ 193.96, 169.67, 143.20, 135.55, 132.00, 129.10, 128.14, 128.01, 127.67, 125.29, 124.61, 111.04, 91.26, 43.96, 40.47. HRMS (EI): Calculated for $C_{16}H_{12}N_2NaOS$ $[M+Na]^+$: 303.0563, found: 303.0570.

2.3 General Procedure for the Synthesis of sulfonimides 2a~2q



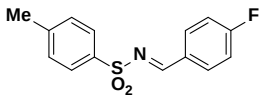
6 **7a~q** **2a~q**

Method A: A mixture of aliphatic or aromatic aldehyde (1.0 equiv), *p*-Toluenesulfonamide (1.0 equiv) , activated 4 Å molecular sieves and catalytic amount of Amberlyst 15 was heated to reflux in toluene with a Dean-Stark apparatus for 12 h. The mixture was cooled to room temperature, filtered, washed with DCM and the filtrate was concentrated under vacuum.

Method B: A mixture of aldehyde (1.0 equiv), *p*-Toluenesulfonamide (1.0 equiv) and tetraethoxysilane (1.05 equiv) was heated at 160 °C for 5 h, and then cooled to room temperature. The mixture was crystallized with ethyl acetate and petroleum ether (4:1), filtrate to get the solid.

Method C: A mixture of aldehyde (10 mmol, 1equiv), *p*-toluenesulfonamide and sodium *p*-toluenesulfinate (10mool, 1.0 equiv) in formic acid (15 mL) and H_2O (15 mL) was stirred over night at room temperature. The resulting white precipitate was filtered off, washed with H_2O and pentane, and then dissolved in CH_2Cl_2 (100 mL). Saturated aqueous $NaHCO_3$ (70 mL) was added and the mixture was stirred at room temperature for 2 h. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to yield the corresponding crude imines.

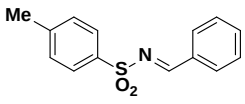
2.4 Characterization data of sulfonimides 2a~2q



2a

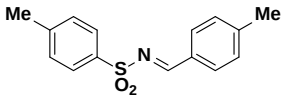
Method A, 98% yield, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.18 (s, 1H), 7.90 (d, J = 7.7 Hz, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 8.4 Hz, 1H), 7.64 (td, J = 8.0, 5.6 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.49 (d, J = 8.6 Hz, 2H), 7.37 (d, J = 8.2 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.43 , 164.03 (d, J = 245.9 Hz), 146.71 , 136.36 (d, J = 4.5 Hz), 133.38 (d, J = 7.5 Hz), 132.01 ,

131.18 , 129.66 , 127.49 , 123.88 (d, *J* = 21.0 Hz), 118.95 (d, *J* = 22.5 Hz), 23.01; MS (ESI): Calculated for $C_{14}H_{13}FNO_2S^+$ $[M+H]^+$: 278.3, found: 277.9.



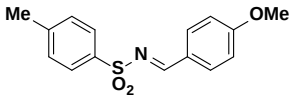
2b

Method A,90% yield, white solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.03 (s, 1H), 7.95 – 7.86 (m, 4H), 7.61 (ddt, *J* = 8.7, 7.1, 1.3 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.37 – 7.32 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.18, 144.65, 134.97, 132.36, 131.33, 129.83, 129.16, 128.11, 126.46, 21.69; MS (ESI): Calculated for $C_{14}H_{14}NO_2S^+$ $[M+H]^+$: 260.3, found: 260.3.



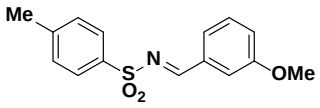
2c

Method A, 90% yield, white solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.00 (s, 1H), 7.94 – 7.86 (m, 2H), 7.83 (d, *J* = 8.1 Hz, 2H), 7.37 – 7.33 (m, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 2.44 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.43, 147.85, 145.88, 132.87, 131.36, 131.20, 129.44, 127.88, 23.45, 23.10, 1.44; MS (ESI): Calculated for $C_{15}H_{16}NO_2S^+$ $[M+H]^+$: 274.4, found: 274.4.



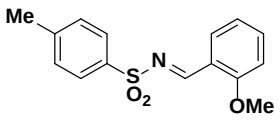
2d

Method A, 95% yield, Beige solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.95 (s, 1H), 7.92 – 7.86 (m, 4H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.01 – 6.94 (m, 2H), 3.90 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.62, 166.69, 145.66, 137.16, 135.14, 131.14, 129.32, 126.64, 116.09, 57.10, 23.05, 1.42; MS (ESI): Calculated for $C_{15}H_{16}NO_3S^+$ $[M+H]^+$: 290.4, found: 290.4.



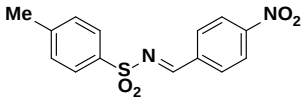
2e

Method A, 89% yield, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.12 (s, 1H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.62 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.55 (dd, *J* = 2.7, 1.5 Hz, 1H), 7.50 – 7.44 (m, 3H), 7.30 – 7.25 (m, 1H), 3.80 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 171.91, 160.09, 145.11, 135.24, 133.96, 130.91, 130.56, 129.74, 128.16, 124.62, 122.23, 115.10, 55.90, 21.56; MS (ESI): Calculated for $C_{15}H_{16}NO_3S^+$ $[M+H]^+$: 290.4, found: 290.4.



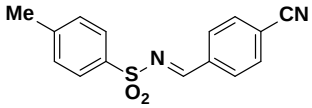
2f

Method B, 68% yield, white solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.57 (s, 1H), 8.07 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.93 – 7.88 (m, 2H), 7.58 (ddd, *J* = 8.4, 7.3, 1.8 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.04 – 6.94 (m, 2H), 3.94 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.40, 161.71, 144.27, 136.93, 135.65, 129.72, 129.34, 127.98, 126.47, 120.89, 111.45, 55.75, 21.66, 21.55, 0.03; MS (ESI): Calculated for $C_{15}H_{16}NO_3S^+$ $[M+H]^+$: 290.4, found: 290.4.



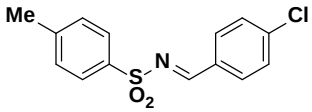
2g

Method B, 65% yield, yellow solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.29 (s, 1H), 8.41 – 8.33 (m, 2H), 8.31 – 8.23 (m, 2H), 7.93 – 7.85 (m, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 170.44, 151.21, 145.52, 137.93, 134.56, 132.74, 130.64, 128.41, 124.59, 21.61; MS (ESI): Calculated for $C_{14}H_{13}N_2O_4S^+$ $[M+H]^+$: 305.3, found: 305.3.



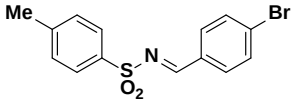
2h

Method B, 63% yield, white solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.08 (s, 1H), 8.06 (d, *J* = 8.3 Hz, 2H), 7.94 – 7.87 (m, 2H), 7.84 – 7.76 (m, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 2.47 (s, 3H)； ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.82, 145.29, 135.91, 134.20, 132.78, 131.32, 130.01, 128.35, 117.65, 99.98, 21.75, 0.02; MS (ESI): Calculated for $C_{15}H_{13}N_2O_2S^+$ $[M+H]^+$: 285.3, found: 285.3.



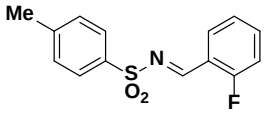
2i

Method A, 92% yield, white solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.01 (s, 1H), 7.94 – 7.84 (m, 4H), 7.51 – 7.45 (m, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.03, 146.21, 142.87, 136.33, 133.77, 132.25, 131.28, 131.03, 129.57, 23.10, 1.42; MS (ESI): Calculated for $C_{14}H_{13}ClNO_2S^+$ $[M+H]^+$: 294.8, found: 294.8.



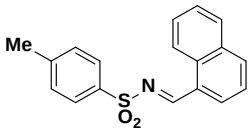
2j

Method A, 95% yield, white solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.98 (s, 1H), 7.91 – 7.85 (m, 2H), 7.81 – 7.75 (m, 2H), 7.66 – 7.60 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.80, 144.83, 134.82, 132.60, 132.40, 131.21, 130.27, 129.88, 128.16, 21.71; MS (ESI): Calculated for $C_{14}H_{13}BrNO_2S^+$ $[M+H]^+$: 339.2, found: 339.2.



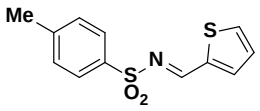
2k

Method B,64% yield, Beige solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.37 (s, 1H), 8.09 (ddd, *J* = 8.1, 7.0, 1.8 Hz, 1H), 7.96 – 7.88 (m, 2H), 7.67 – 7.58 (m, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 15.2 Hz, 1H), 7.19 (ddd, *J* = 9.7, 8.4, 1.1 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.30 (d, *J* = 259.9 Hz), 163.65 (d, *J* = 6.2 Hz), 144.84 , 137.05 (d, *J* = 9.2 Hz), 134.72 , 129.88 , 129.35 , 128.23 , 126.45 , 124.86 (d, *J* = 3.6 Hz), 120.47 (d, *J* = 8.8 Hz), 116.40 (d, *J* = 20.9 Hz), 21.71; MS (ESI): Calculated for $C_{14}H_{13}FNO_2S^+$ $[M+H]^+$: 278.3, found: 278.3.



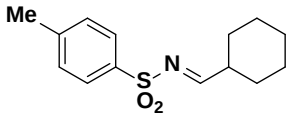
2l

Method A, 78% yield, white solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.63 (s, 1H), 9.01 (d, *J* = 8.5 Hz, 1H), 8.15 (dd, *J* = 25.4, 7.7 Hz, 2H), 7.95 (dd, *J* = 15.7, 8.0 Hz, 3H), 7.69 (dd, *J* = 8.6, 6.8 Hz, 1H), 7.60 (q, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 7.9 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.26, 145.98, 137.59, 136.85, 136.64, 135.22, 133.26, 131.28, 130.50, 130.38, 129.48, 129.05, 128.41, 126.55, 125.71, 23.12, 1.45; MS (ESI): Calculated for $C_{18}H_{16}NO_2S^+$ $[M+H]^+$: 310.4, found: 310.4.



2m

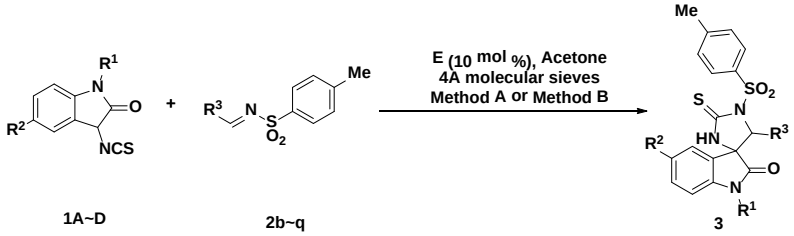
Method B, 65% yield, yellow solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.13 (s, 1H), 7.93 – 7.86 (m, 2H), 7.80 (d, *J* = 4.2 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.23 (t, *J* = 4.4 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.25, 144.49, 139.10, 138.17, 136.76, 135.39, 129.79, 129.72, 128.89, 127.96, 21.68, 18.47, 0.03; MS (ESI): Calculated for $C_{12}H_{12}NO_2S_2^+$ $[M+H]^+$: 266.4, found: 266.4.



2n

Method C, 70% yield, white solid; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.64 (d, *J* = 1.4 Hz, 0H), 7.87 – 7.79 (m, 2H), 7.34 (dd, *J* = 9.6, 8.1 Hz, 2H), 4.92 (s, 1H), 2.45 (s, 3H), 1.97 – 1.84 (m, 2H), 1.78 (dt, *J* = 8.8, 4.5 Hz, 2H), 1.68 (dddq, *J* = 11.1, 6.3, 3.3, 1.7 Hz, 2H), 1.50 – 1.24 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.11, 129.79, 129.72, 128.06, 126.46, 43.69, 28.36, 25.09, 21.67, 21.55; MS (ESI): Calculated for $C_{14}H_{20}NO_2S^+$ $[M+H]^+$: 266.4, found: 266.4.

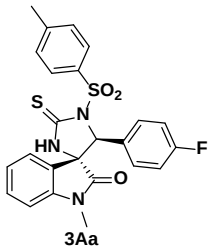
2.5 General Procedure for the Snthesis of Spirooxindole 3Aa~3Aq, 3Ba,3Bb, 3Bd, 3Cb, 3Db



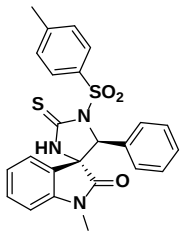
Method A: To a mixture of **1** (0.2 mmol), **2** (0.3 mmol) and 4 Å molecular sieves in acetone (2 mL) were added catalyst E (0.02 mmol) and additive p-CNC_6H_4COOH (o.o2 mmol). The mixture was stirred at -20℃ for 12 h, and then allowed to warm to room temperature, stirred until complete as monitored by TLC analysis, then diluted with additional CH_2Cl_2 to dissolve all soluble chemicals. The solution was filtered through a filter paper, concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1).

Method B: To a mixture of 1 (0.2 mmol), 2 (0.3 mmol) and 4 Å molecular sieves in acetone (2 mL) was added catalyst E (0.02 mmol). The mixture was stirred at -20℃ for 24 h, and then allowed to warm to room temperature, stirred until complete as monitored by TLC analysis, then diluted with additional CH_2Cl_2 to dissolve all soluble chemicals. The solution was filtered through a filter paper, concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1).

2.6 Characterization data of Spirooxindole 3Aa~3Aq, 3Ba,3Bb, 3Bd, 3Cb, 3Db

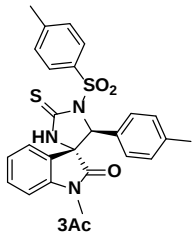


Method A, 90% yield, >99% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.93 (s, 1H), 7.91 (dd, J = 8.3, 1.7 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.38 – 7.30 (m, 1H), 7.24 (td, J = 7.7, 1.3 Hz, 1H), 7.00 (t, J = 7.7 Hz, 3H), 6.67 (td, J = 7.5, 1.1 Hz, 1H), 6.05 (d, J = 1.7 Hz, 1H), 5.94 (dd, J = 7.5, 1.3 Hz, 1H), 3.33 (s, 1H), 3.18 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 181.76 , 175.97 , 163.96 (d, J = 245.2 Hz), 146.45 , 146.17 , 137.43 , 134.74 , 132.45 (d, J = 9.2 Hz), 132.30 , 130.90 , 130.65 , 129.54 (d, J = 9.0 Hz), 127.57 , 123.87 , 123.69 , 117.25 (d, J = 22.1 Hz), 116.91 (d, J = 21.2 Hz), 110.94 , 70.87 , 69.29 , 28.40 , 23.04; HRMS (ESI): Calculated for $C_{24}H_{20}FN_3NaO_3S_2$ $[M+Na]^+$: 504.0828, found: 504.0840. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 10.975 min (major) and 18.950 min (minor).



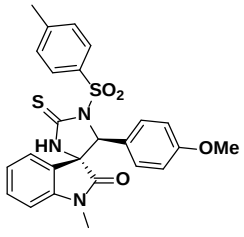
3Ab

Method A, 92% yield, 95% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.91 (s, 1H), 7.90 (dq, J = 8.4, 1.9 Hz, 2H), 7.49 (t, J = 7.7 Hz, 1H), 7.41 (d, J = 8.0 Hz, 3H), 7.34 (dd, J = 8.0, 6.6 Hz, 1H), 7.22 (td, J = 7.7, 1.3 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 7.8 Hz, 1H), 6.89 (d, J = 8.1 Hz, 1H), 6.59 (t, J = 7.6 Hz, 1H), 6.00 (s, 1H), 5.90 – 5.81 (m, 1H), 3.18 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.96, 174.17, 144.48, 144.23, 136.41, 135.60, 130.32, 128.97, 128.79, 128.73, 128.40, 128.13, 125.66, 125.52, 121.88, 108.98, 69.76, 67.41, 26.50, 21.15; HRMS (ESI): Calculated for $C_{24}H_{21}N_3NaO_3S_2$ $[M+Na]^+$: 486.0922, found: 486.0918. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 11.805 min (major) and 27.522 min (minor).



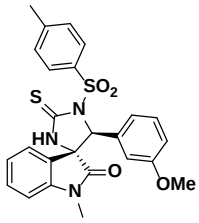
3Ac

Method A, 88% yield, 85% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 7.88 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.30 – 7.16 (m, 3H), 6.96 (dd, J = 20.9, 8.1 Hz, 2H), 6.75 (d, J = 7.8 Hz, 1H), 6.60 (t, J = 7.6 Hz, 1H), 5.92 (d, J = 5.9 Hz, 2H), 3.16 (s, 3H), 2.41 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.40, 174.68, 144.85, 144.65, 138.41, 136.12, 133.94, 130.72, 129.37, 129.21, 126.23, 125.95, 122.38, 109.38, 70.20, 67.86, 26.92, 21.58, 21.25; HRMS (ESI): Calculated for $C_{25}H_{23}N_3NaO_3S_2$ $[M+Na]^+$: 500.1079, found: 500.1077. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 10.277 min (major) and 20.976 min (minor).



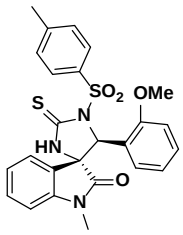
3Ad

Method A, 85% yield, 96% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.86 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.31 – 7.17 (m, 2H), 7.00 (dd, J = 16.2, 7.5 Hz, 2H), 6.82 (d, J = 8.2 Hz, 1H), 6.73 – 6.59 (m, 2H), 6.04 – 5.85 (m, 2H), 3.73 (s, 3H), 3.16 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.39, 174.68, 159.86, 144.81, 144.70, 136.16, 130.73, 130.21, 129.36, 129.21, 128.83, 126.30, 122.41, 122.38, 114.20, 113.84, 109.37, 69.97, 67.95, 55.65, 26.90, 21.57; HRMS (ESI): Calculated for $C_{25}H_{23}N_3NaO_4S_2$ $[M+Na]^+$: 516.1028, found: 516.1032. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 13.711 min (major) and 27.881 min (minor).



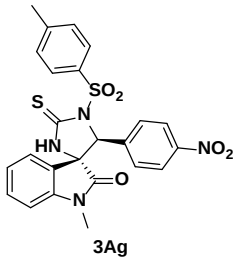
3Ae

Method A, 91% yield, 98% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 7.90 (dd, J = 17.2, 8.0 Hz, 2H), 7.40 (q, J = 6.9, 6.3 Hz, 3H), 7.29 – 7.20 (m, 1H), 7.11 – 6.95 (m, 2H), 6.93 – 6.82 (m, 1H), 6.63 (q, J = 6.8 Hz, 1H), 6.52 – 6.42 (m, 1H), 5.94 (d, J = 13.9 Hz, 2H), 3.71 (s, 1H), 3.49 (s, 1H), 3.33 (s, 1H), 3.18 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 182.59, 176.83, 161.90, 146.87, 140.71, 138.32, 133.02, 132.06, 131.64, 131.47, 128.24, 124.65, 124.57, 123.37, 120.39, 116.83, 116.40, 114.37, 111.64, 72.39, 70.12, 57.74, 29.19, 23.83; HRMS (ESI): Calculated for $C_{25}H_{23}N_3NaO_4S_2$ [M+Na]$^+$: 516.1028, found: 516.1042. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 85:15, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 18.728 min (major) and 47.277 min (minor).



3Af

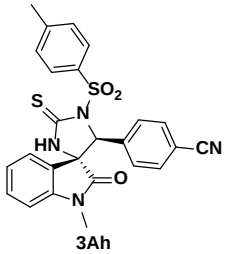
Method A, 90% yield, 97% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.96 (s, 1H), 8.07 – 7.89 (m, 2H), 7.44 (dd, J = 21.5, 7.7 Hz, 3H), 7.34 – 7.20 (m, 2H), 7.15 – 7.02 (m, 2H), 6.69 (d, J = 8.2 Hz, 1H), 6.61 (t, J = 7.7 Hz, 1H), 5.99 (s, 1H), 5.89 (d, J = 7.7 Hz, 1H), 3.24 (s, 3H), 3.10 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.28, 174.46, 155.36, 144.67, 144.08, 135.21, 130.03, 129.80, 129.10, 128.74, 125.41, 124.88, 124.59, 123.16, 121.79, 120.33, 110.70, 108.59, 67.25, 66.25, 54.83, 26.44, 21.13; HRMS (ESI): Calculated for $C_{25}H_{23}N_3NaO_4S_2$ [M+Na]$^+$: 516.1028, found: 516.1013. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 12.076 min (major) and 21.294 min (minor).



3Ag

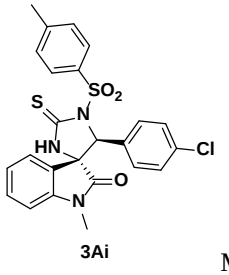
Method A, 85% yield, 89% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.98 (d, J = 19.7 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.71 (tq, J = 16.0, 7.8 Hz, 2H), 7.41 (dd, J = 17.8, 8.1 Hz, 3H), 7.34 – 7.18 (m, 2H), 7.02 (d, J = 7.9 Hz, 1H), 6.59 (dt, J = 15.4, 7.7 Hz, 1H), 6.20 (d, J = 11.6 Hz, 1H), 5.73 (d, J = 7.6 Hz, 1H), 3.17 (s, 3H), 2.41 (d, J = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.32, 174.30, 145.13, 144.75, 138.55, 135.83, 133.13, 130.90, 130.06, 129.86, 129.52, 129.22, 125.72, 121.97, 109.60, 69.26, 67.85, 27.00, 21.58; HRMS (ESI): Calculated for $C_{24}H_{20}N_4NaO_5S_2$ [M+Na]$^+$: 531.0773, found: 531.0774. HPLC conditions:

chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 15.136 min (major) and 40.613 min (minor).



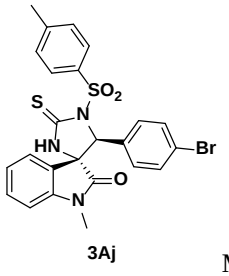
3Ah

Method A, 88% yield, 96% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.01 (s, 1H), 8.03 (d, J = 8.1 Hz, 1H), 7.94 (d, J = 8.0 Hz, 2H), 7.61 (dd, J = 28.0, 8.3 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 7.25 (t, J = 8.0 Hz, 1H), 7.16 (d, J = 8.1 Hz, 1H), 7.02 (d, J = 7.9 Hz, 1H), 6.66 (t, J = 7.7 Hz, 1H), 6.18 (s, 1H), 5.91 (d, J = 7.5 Hz, 1H), 3.18 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.19, 174.31, 145.20, 144.71, 142.51, 135.72, 133.15, 132.48, 131.03, 129.79, 129.54, 129.21, 126.97, 126.00, 122.52, 121.93, 118.96, 111.79, 109.62, 69.34, 67.62, 27.02, 21.60; HRMS (ESI): Calculated for $C_{25}H_20N_4NaO_3S_2$ [M+Na]$^+$: 511.0875, found: 511.0864. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 18.766 min (major) and 40.976 min (minor).



3Ai

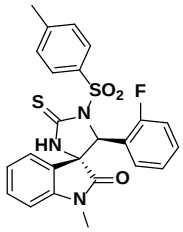
Method A, 87% yield, 87% ee, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.96 (s, 1H), 7.93 (d, J = 7.9 Hz, 2H), 7.65 – 7.55 (m, 1H), 7.42 (dd, J = 14.4, 7.6 Hz, 3H), 7.30 – 7.17 (m, 2H), 7.00 (dd, J = 24.2, 8.3 Hz, 2H), 6.69 (t, J = 7.6 Hz, 1H), 6.07 (s, 1H), 5.99 (d, J = 7.5 Hz, 1H), 3.18 (s, 4H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.29, 174.51, 145.09, 144.75, 136.15, 135.94, 133.71, 130.96, 130.73, 129.52, 129.22, 128.62, 127.92, 126.15, 122.51, 122.19, 109.59, 69.42, 67.75, 49.07, 27.00, 21.63; HRMS (ESI): Calculated for $C_{24}H_{20}ClN_3NaO_3S_2$ [M+Na]$^+$: 520.0532, found: 520.0530. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 85:15, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 16.559 min (major) and 42.679 min (minor).



3Aj

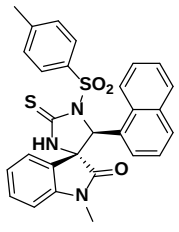
Method B, 87% yield, 98% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.94 (s, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.3 Hz, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.35 (t, J = 8.7 Hz, 2H), 7.25 (t, J = 7.5 Hz, 1H), 7.02 (d, J = 7.8 Hz, 1H), 6.90 (d, J = 8.1 Hz, 1H), 6.68 (t, J = 7.6 Hz, 1H), 6.06 – 5.95 (m, 2H), 3.17 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.27, 174.48, 145.04, 136.53, 135.92, 131.90, 131.50, 130.92, 129.48, 129.18, 128.20, 126.12, 122.29, 109.54, 69.49, 67.66, 26.97, 21.59; HRMS (ESI): Calculated for $C_{24}H_{20}BrN_3NaO_3S_2$ [M+Na]$^+$: 564.0027, found:

564.0043. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 11.863 min (major) and 25.638 min (minor).



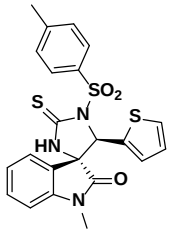
3Ak

Method A, 90% yield, 75% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.06 (s, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.54 – 7.35 (m, 5H), 7.34 – 7.25 (m, 1H), 7.03 (dd, J = 27.6, 7.8 Hz, 2H), 6.67 (td, J = 7.5, 1.0 Hz, 1H), 6.01 (d, J = 8.4 Hz, 2H), 3.21 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.50 , 174.04 , 158.70 (d, J = 245.9 Hz), 144.89 , 144.11 , 134.95 , 131.01 (d, J = 8.3 Hz), 129.01 (d, J = 25.6 Hz), 127.06 , 125.20 , 124.81 (d, J = 2.9 Hz), 123.71 (d, J = 13.4 Hz), 122.23 , 121.71 , 115.26 (d, J = 20.9 Hz), 66.97 , 64.29 , 26.54 , 21.15; HRMS (ESI): Calculated for $C_{24}H_{20}FN_3NaO_3S_2$ [M+Na]$^+$: 504.0828, found: 504.0831. HPLC conditions: chiralpak IA, hexane/iso-PrOH = 90:10, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 21.296 min (major) and 40.994 min (minor).



3Al

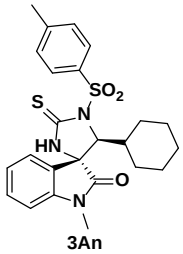
Method A, 86% yield, 99% ee; white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.01 (s, 1H), 8.03 (d, J = 8.0 Hz, 2H), 7.97 – 7.90 (m, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.66 (d, J = 4.8 Hz, 2H), 7.46 (dd, J = 8.5, 4.5 Hz, 3H), 7.34 (t, J = 7.5 Hz, 1H), 7.21 (t, J = 7.7 Hz, 1H), 6.95 (t, J = 7.7 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.69 (s, 1H), 6.21 (t, J = 7.6 Hz, 1H), 5.66 (d, J = 7.5 Hz, 1H), 3.25 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.28, 174.61, 145.13, 144.33, 135.80, 130.65, 129.61, 129.48, 128.75, 126.78, 126.11, 125.44, 125.30, 124.26, 122.48, 121.94, 109.17, 67.77, 67.24, 27.14, 21.62; HRMS (ESI): Calculated for $C_{28}H_{23}N_3NaO_3S_2$ [M+Na]$^+$: 536.1079, found: 536.1076. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 11.938 min (major) and 19.275 min (minor).



3Am

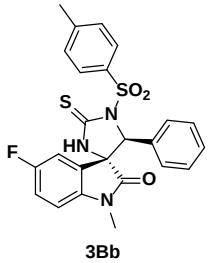
Method A, 95% yield, 92% ee, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.96 (s, 1H), 7.89 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 5.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.30 (t, J = 7.7 Hz, 1H), 7.07 – 6.97 (m, 2H), 6.96 – 6.90 (m, 1H), 6.73 (t, J = 7.6 Hz, 1H), 6.29 (s, 1H), 6.19 (d, J = 7.5 Hz, 1H), 3.18 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.92, 174.25, 144.96, 144.79, 135.98, 131.04, 129.39, 129.33, 127.66, 127.35, 127.01, 125.54, 122.64, 122.24, 109.51, 68.05, 66.37, 26.95, 21.63; HRMS (ESI): Calculated for $C_{22}H_{19}N_3NaO_3S_3$ [M+Na]$^+$: 492.0486, found: 492.0483.

HPLC conditions: chiralpak IA, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 12.607 min (major) and 27.921 min (minor).



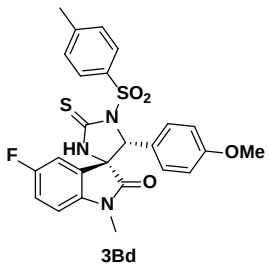
3An

Method B, 84% yield, 52% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.07 (d, J = 8.0 Hz, 2H), 7.58 – 7.37 (m, 4H), 7.24 – 7.08 (m, 2H), 5.76 (d, J = 0.6 Hz, 0H), 4.56 (d, J = 4.5 Hz, 1H), 3.15 (s, 3H), 2.41 (s, 3H), 2.04 (d, J = 12.5 Hz, 1H), 1.82 (q, J = 12.8 Hz, 2H), 1.64 – 1.48 (m, 2H), 1.43 – 1.31 (m, 1H), 1.24 (t, J = 12.8 Hz, 2H), 1.08 (s, 1H), 0.93 (t, J = 12.8 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.18, 175.21, 144.81, 144.66, 135.84, 131.25, 130.26, 129.02, 126.63, 123.27, 123.16, 109.98, 72.69, 68.14, 28.11, 26.92, 26.25, 26.09, 25.87, 21.59; HRMS (ESI): Calculated for $C_{24}H_{27}N_3NaO_3S_2$ [M+Na]$^+$: 492.1392, found: 492.1399. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 10.120 min (major) and 23.017 min (minor).



3Bb

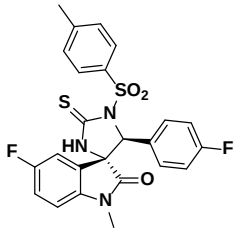
Method B, 86% yield, 70% ee, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.91 (d, J = 1.9 Hz, 1H), 7.96 – 7.86 (m, 2H), 7.51 (t, J = 7.5 Hz, 1H), 7.43 – 7.35 (m, 4H), 7.19 (t, J = 7.6 Hz, 1H), 7.09 (td, J = 8.9, 2.7 Hz, 1H), 7.01 (dd, J = 8.7, 4.3 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H), 6.04 (d, J = 2.0 Hz, 1H), 5.59 (dt, J = 8.6, 2.4 Hz, 1H), 3.17 (d, J = 1.2 Hz, 3H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.32 , 174.39 , 158.01 (d, J = 238.0 Hz), 144.93 , 140.86, 136.47 , 135.86 , 129.36 , 129.16 , 128.90 , 128.68 (d, J = 9.0 Hz), 124.08 (d, J = 8.3 Hz), 116.98 (d, J = 23.2 Hz), 113.69 (d, J = 26.1 Hz), 110.25 (d, J = 8.1 Hz), 69.98 , 67.77 , 27.04 , 21.50 ; HRMS (ESI): Calculated for $C_{24}H_{20}FN_3NaO_3S_2$ [M+Na]$^+$: 504.0828, found: 504.0825. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 10.424 min (major) and 43.045 min (minor).



3Bd

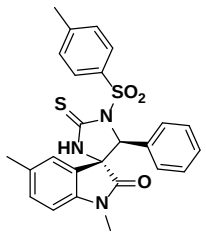
Method B, 90% yield, 66% ee, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.88 (s, 1H), 7.90 – 7.84 (m, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.28 (dq, J = 8.8, 2.8 Hz, 1H), 7.11 (td, J = 8.9, 2.7 Hz, 1H), 7.07 – 7.04 (m, 1H), 7.01 (dd, J = 8.6, 4.3 Hz, 1H), 6.88 (d, J = 9.0 Hz, 1H), 6.80 – 6.72 (m, 1H), 5.97 (s, 1H), 5.69 (ddd, J = 8.4, 4.1, 2.4 Hz, 1H), 3.75 (s, 3H), 3.16 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.30 , 174.45 , 159.98 , 158.04 (d, J = 238.3 Hz), 144.84 ,

140.90 , 135.96 , 130.11 , 129.32 , 129.13 , 128.44 , 127.27 , 124.19 (d, *J* = 8.3 Hz), 116.96 (d, *J* = 23.1 Hz), 113.96 (d, *J* = 6.1 Hz), 110.21 (d, *J* = 8.2 Hz), 69.72 , 67.88 , 55.66 , 27.00 , 21.50 ; HRMS (ESI): Calculated for $C_{25}H_{22}FN_3NaO_4S_2$ $[M+Na]^+$: 534.0933, found: 534.0930. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 13.583 min (major) and 31.714 min (minor).



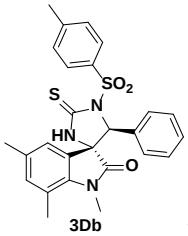
3Ba

Method B, 88% yield, 58% ee, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.96 (s, 1H), 7.94 – 7.88 (m, 2H), 7.58 (td, *J* = 8.2, 6.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.28 – 7.18 (m, 2H), 7.12 (td, *J* = 9.2, 2.9 Hz, 1H), 7.09 – 7.01 (m, 1H), 6.85 (dd, *J* = 48.5, 8.3 Hz, 1H), 6.10 (d, *J* = 23.9 Hz, 1H), 5.74 (s, 1H), 3.17 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.16 , 174.22 , 162.15 (d, *J* = 244.5 Hz), 158.07 (d, *J* = 238.1 Hz), 145.11 (d, *J* = 10.9 Hz), 140.90 (d, *J* = 6.3 Hz), 135.67 (d, *J* = 14.5 Hz), 131.09 (d, *J* = 8.7 Hz), 117.16 (d, *J* = 22.9 Hz), 115.51 (d, *J* = 22.6 Hz), 113.46 (d, *J* = 26.2 Hz), 110.45 (d, *J* = 9.4 Hz), 69.18 , 67.62 , 27.08 , 21.50 ; HRMS (ESI): Calculated for $C_{24}H_{19}F_2N_3NaO_3S_2$ $[M+Na]^+$: 522.0734, found: 522.0728. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 15.874 min (major) and 46.300 min (minor).



3Cb

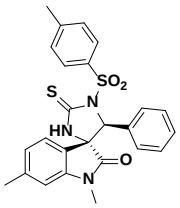
Method B, 88% yield, 86% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.91 (s, 1H), 8.02 – 7.87 (m, 2H), 7.49 – 7.37 (m, 4H), 7.02 (dd, *J* = 23.9, 10.8 Hz, 3H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.03 (s, 1H), 5.67 (s, 1H), 3.15 (s, 3H), 2.43 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.91, 174.03, 144.44, 141.73, 136.42, 135.62, 130.75, 130.24, 128.95, 128.75, 128.53, 128.42, 128.25, 127.96, 126.59, 125.50, 121.85, 108.53, 69.77, 67.52, 26.47, 21.12, 20.19; HRMS (ESI): Calculated for $C_{25}H_{23}N_3NaO_3S_2$ $[M+Na]^+$: 500.1079, found: 500.1074. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 75:25, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 9.791 min (major) and 31.131 min (minor).



3Db

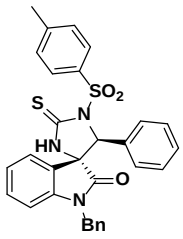
Method A, 90% yield, 92% ee, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.88 (s, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.59 – 7.45 (m, 1H), 7.45 – 7.23 (m, 5H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.77 (s, 1H), 5.91 (s, 1H), 3.42 (s, 3H), 2.45 (s, 3H), 2.42 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.38, 175.24, 144.93, 139.75, 136.80, 136.11, 134.50, 131.04,

129.76, 129.45, 129.27, 128.68, 128.46, 128.24, 126.08, 125.05, 122.92, 119.99, 70.62, 67.47, 30.11, 21.62, 20.39, 18.76; HRMS (ESI): Calculated for $C_{26}H_{25}N_3NaO_3S_2$ $[M+Na]^+$: 514.1235, found: 514.1248. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 9.732 min (major) and 20.232 min (minor).



3Eb

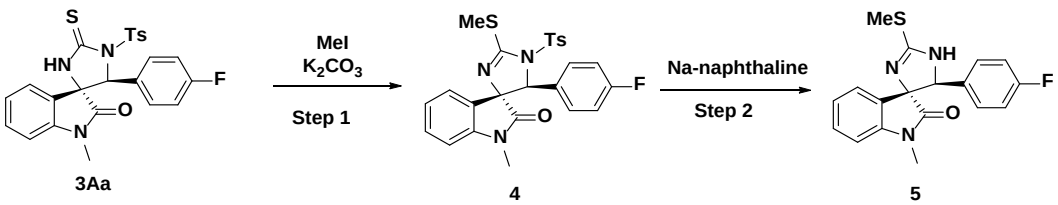
Method A, 91% yield, 98% ee, white solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.90 (s, 1H), 7.90 (d, J = 8.3 Hz, 2H), 7.56 – 7.28 (m, 5H), 7.25 – 7.07 (m, 1H), 6.91 (d, J = 7.8 Hz, 1H), 6.84 (d, J = 1.4 Hz, 1H), 6.40 (d, J = 7.7 Hz, 1H), 5.96 (s, 1H), 5.72 (d, J = 7.7 Hz, 1H), 3.16 (s, 3H), 2.42 (s, 2H), 2.21 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.36, 174.88, 144.91, 144.77, 140.81, 136.93, 136.12, 129.43, 129.25, 129.19, 128.99, 128.81, 128.63, 125.98, 125.92, 122.81, 119.27, 110.24, 70.15, 67.79, 26.91, 21.73; HRMS (ESI): Calculated for $C_{25}H_{23}N_3NaO_3S_2$ $[M+Na]^+$: 500.1079, found: 500.1063. HPLC conditions: chiralpak AD-H, hexane/iso-PrOH = 85:15, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 16.386 min (major) and 28.403 min (minor).



3Fb

Method B, 92% yield, 94% ee, white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 7.92 (dt, J = 8.7, 1.9 Hz, 2H), 7.56 – 7.47 (m, 1H), 7.43 (t, J = 6.9 Hz, 3H), 7.40 – 7.32 (m, 5H), 7.20 – 7.07 (m, 3H), 6.93 – 6.86 (m, 1H), 6.83 (d, J = 7.9 Hz, 1H), 6.57 (td, J = 7.6, 1.0 Hz, 1H), 6.09 (d, J = 1.5 Hz, 1H), 5.92 (dt, J = 7.6, 1.2 Hz, 1H), 5.08 (d, J = 16.0 Hz, 1H), 4.84 (d, J = 15.9 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.91, 174.45, 144.51, 143.17, 136.30, 135.60, 135.53, 130.22, 128.97, 128.80, 128.76, 128.60, 128.41, 127.46, 127.20, 125.90, 122.00, 121.94, 109.62, 70.00, 67.47, 43.13, 21.11; HRMS (ESI): Calculated for $C_{30}H_{25}N_3NaO_3S_2$ $[M+Na]^+$: 562.1235, found: 562.1232. HPLC conditions: chiralpak IA, hexane/iso-PrOH = 80:20, flow rate = 1.0 mL/min, λ= 254 nm, retention time: 12.567 min (major) and 17.731 min (minor).

2.7 Transformation of Mannich adduct 3Aa into spirobrassinin imidazolidine analogues



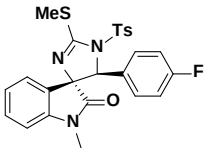
3Aa 4 5

Step 1: To mixture of **3Aa** (130 mg, 0.27 mmol) and anhydrous K_2CO_3 (42 mg, 0.3 mmol) in 5.0 mL of

acetone was added CH_3I (42 mg, 0.3 mmol) at 0 °C. Then the reaction was stirred at room temperature overnight and diluted with 5 mL of water. The residue was collected by filtration, then purified by flash column chromatography on silica gel (hexane/ethyl acetate 4:1) to give compound **4** 127 mg (yield 95%) as pale yellow solid.

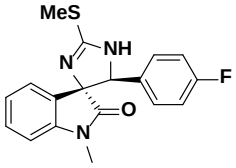
Step 2: Naphthalene (188 mg, 1.45 mmol) was dissolved in previously degassed DME (4 mL). Sodium (34 mg, 1.45 mmol) was added and the mixture was sonicated for 30 min and then stirred at room temperature for 2 h in order to obtain dark green Na-naphthalenide solution. N-tosyl derative **4** (100 mg, 0.2 mmol) was dissolved in DME (1 mL) and the resulting solution was cooled to -78 °C. The Na-naphthalenide was then added dropwise until the reaction mixture stayed permanently dark green. The mixture was stirred at -78 °C for 30 min and at room temperature for 30 min, before quenching with 1 M $NaHCO_3$. The aqueous layer was extracted with EtOAc for 3 times. The combined organic layers were dried over $NaSO_4$, concentrated *in vacuo.* Purfication by column chromatography (PE/EA 2:1 to 1:1) afford compound **5** 53 mg (yield 76%) as pale yellow solid.

2.8 Characterization data of spirobrassinin deratives 4 and 5



4

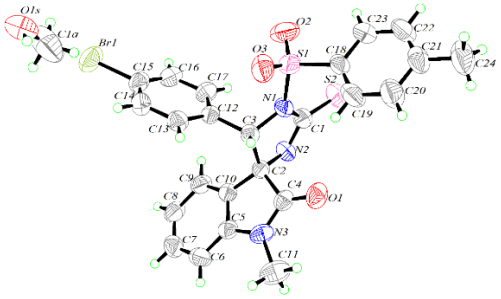
95% yield, pale yellow solid; ^{1}H NMR (300 MHz, DMSO- d_6) δ 9.93 (s, 1H), 7.88 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.1 Hz, 2H), 7.40 (m, 1H), 7.16 (t, J = 7.8 Hz, 2H), 6.91 (d, J = 7.8 Hz, 3H), 6.64 (t, J = 7.5 Hz, 1H), 6.09 (d, J = 7.5 Hz, 1H), 5.65 (s, 1H), 3.08 (s, 3H), 2.45 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.96, 161.56 (d, J = 242.2 Hz), 161.54 , 144.84, 143.79, 134.47,133.48 (d, J = 2.3 Hz), 129.68 (d, J = 8.3 Hz), 129.37, 127.97 , 125.75 (d, J = 18.0 Hz), 121.75, 108.62, 77.68, 69.60, 26.30, 21.11, 14.98; HRMS (ESI): Calculated for $C_{25}H_{23}FN_3O_3S_2^+$ $[M+H]^+$: 496.1159, found: 496.1165.

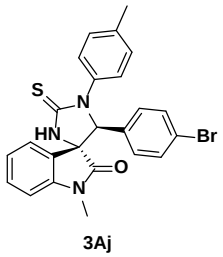


5

81% yield, pale yellow solid; ^{1}H NMR (300 MHz, DMSO- d_6) δ 7.09 (dt, J = 7.5, 1.9 Hz, 1H), 7.05 – 7.00 (m, 2H), 7.97 – 6.92 (m, 2H), 6.85 (d, J = 7.5 Hz,1H), 6.71 (t, J = 7.5 Hz, 1H), 6.56 (d, J = 6.9 Hz, 1H), 6.64 (t, J = 7.5 Hz, 1H), 6.09 (d, J = 7.5 Hz, 1H), 5.25 (s, 1H), 3.15 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 177.00, 161.11 (d, J = 241.5 Hz), 142.63 , 134.35, 128.78, 128.1 (d, J = 7.5 Hz), 125.1, 121.8, 114.6 (d, J = 21.0 Hz), 108.21, 62.38, 26.27, 22.11, 13.26; HRMS (ESI): Calculated for $C_{18}H_{17}FN_3OS^+$ $[M+H]^+$: 342.1071, found: 342.1077.

3. Single-Crystal X-ray Crystallography of Product 3Aj





3Aj

Table 1. Sample and crystal data for 2013390.

Identification code	2013390	
Chemical formula	$C_{25}H_{19}BrN_3O_3S_2$	
Formula weight	553.46	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal size	0.050 x 0.100 x 0.150 mm	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 8.9006(5) Å	α = 90°
	b = 16.8997(9) Å	β = 90°
	c = 17.3802(10) Å	γ = 90°
Volume	2614.3(3) $Å^3$	
Z	4	
Density (calculated)	1.406 Mg/cm^3	
Absorption coefficient	1.763 mm^{-1}	
F(000)	1124	

Table 2. Data collection and structure refinement for 2013390.

Theta range for data collection	1.68 to 27.61°
Index ranges	-11<=h<=11, -22<=k<=22, -22<=l<=20
Reflections collected	45041
Independent reflections	6063 [R(int) = 0.0841]
Coverage of independent reflections	99.8%

Absorption correction	multi-scan	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick, 2008)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-97 (Sheldrick, 2008)	
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	6063 / 0 / 320	
Goodness-of-fit on F^2	1.152	
Δ/σ_{max}	0.057	
Final R indices	3435 data; $I>2\sigma(I)$	R1 = 0.0435, wR2 = 0.0629
	all data	R1 = 0.1076, wR2 = 0.0724
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0000P)^2+0.0000P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	0.0(0)	
Largest diff. peak and hole	0.261 and -0.247 eÅ^{-3}	
R.M.S. deviation from mean	0.044 eÅ^{-3}	

4. Bioactivity test of compounds 3Aa-3Db

The HDACs inhibition activities of **3Aa**-**3Db** were preliminarily tested (Table 1).

Table 1 *In vitro* inhibition rate against HDACs of **3Aa-3Db**[a]

Entry	Compound	Inhibition rate*		
		HDAC1	HDAC2	HDAC3
1	**3Aa**	17.86±2.17	11.08±11.39	9.49±9.59
2	**3Ab**	15.50±2.95	7.98±5.63	5.80±2.59
3	**3Ac**	12.69±1.58	6.92±6.39	3.24±13.21
4	**3Ad**	11.45±2.00	3.16±1.12	3.05±3.67
5	**3Ae**	4.92±1.75	-1.65±4.09	-0.55±4.59
6	**3Af**	4.28±3.33	0.64±2.98	-2.01±5.96
7	**3Ag**	5.50±1.87	-1.08±8.69	3.23±4.63
8	**3Ah**	-0.89±1.40	-0.45±7.28	-3.87±3.01
9	**3Ai**	1.64±0.09	-10.44±2.92	0.02±1.16
10	**3Aj**	3.40±0.03	2.33±0.56	2.26±3.83
11	**3Ak**	4.21±5.14	-0.34±3.18	3.86±4.90
12	**3Al**	5.16±0.41	-6.28±1.26	2.67±3.44
13	**3Am**	23.40±9.43	5.20±0.27	11.97±14.45
14	**3An**	16.91±5.34	10.15±0.18	6.16±1.44
15	**3Bb**	8.48±6.18	2.29±4.65	4.92±4.58
16	**3Bd**	5.75±4.41	10.13±4.23	14.68±2.43
17	**3Ba**	-0.67±8.92	1.25±2.92	13.73±2.03
18	**3Cb**	-5.54±8.16	3.09±2.65	2.97±3.67
19	**3Db**	12.14±6.07	5.54±9.80	10.48±11.44
20	**3Eb**	7.62±0.13	9.47±3.27	10.54±1.01
21	**3Fb**	-4.10±1.92	0.96±1.27	11.47±4.16

[a] Inhibition rate were tested at the concentration of 20 μg/mL.

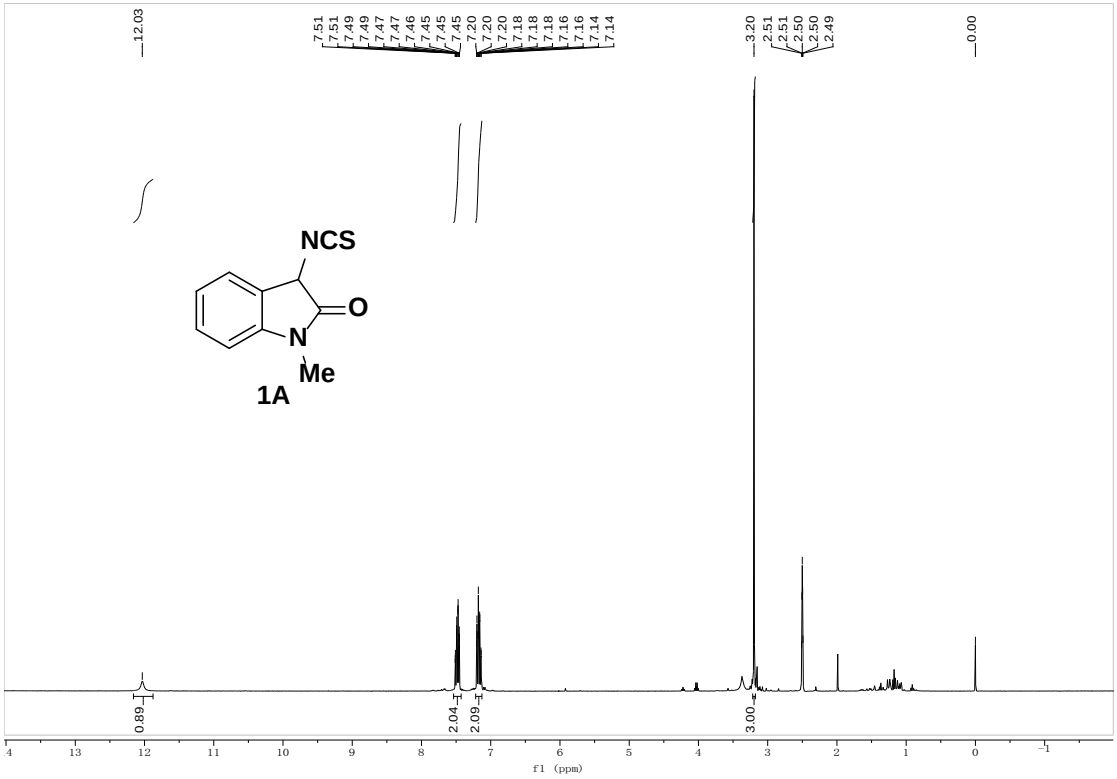
5. Reference

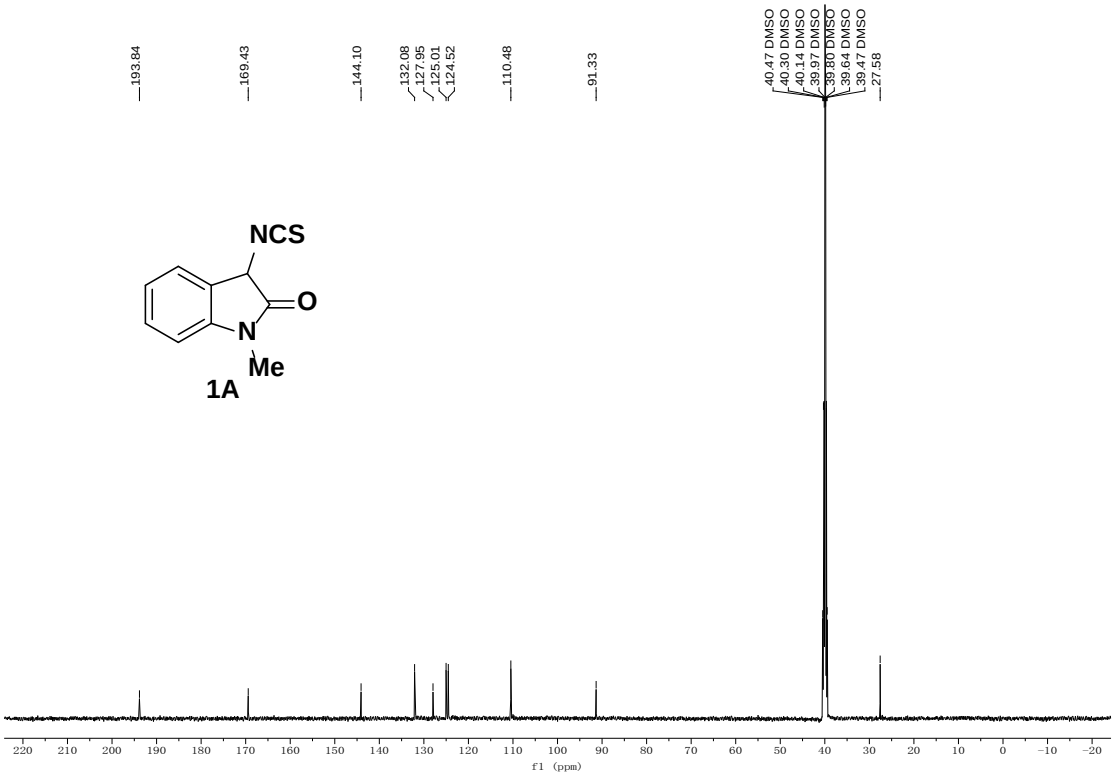
1. Chen, W.-B.; Wu, Z.-J.; Hu, J.; Cun, L.-F.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2011,** *13*, 2472-2475.

2. Munch, H.; Hansen, J. S.; Pittelkow, M.; Christensen, J. B.; Boas, U. *Tetrahedron Lett.* **2008,** *49*, 3117-3119.

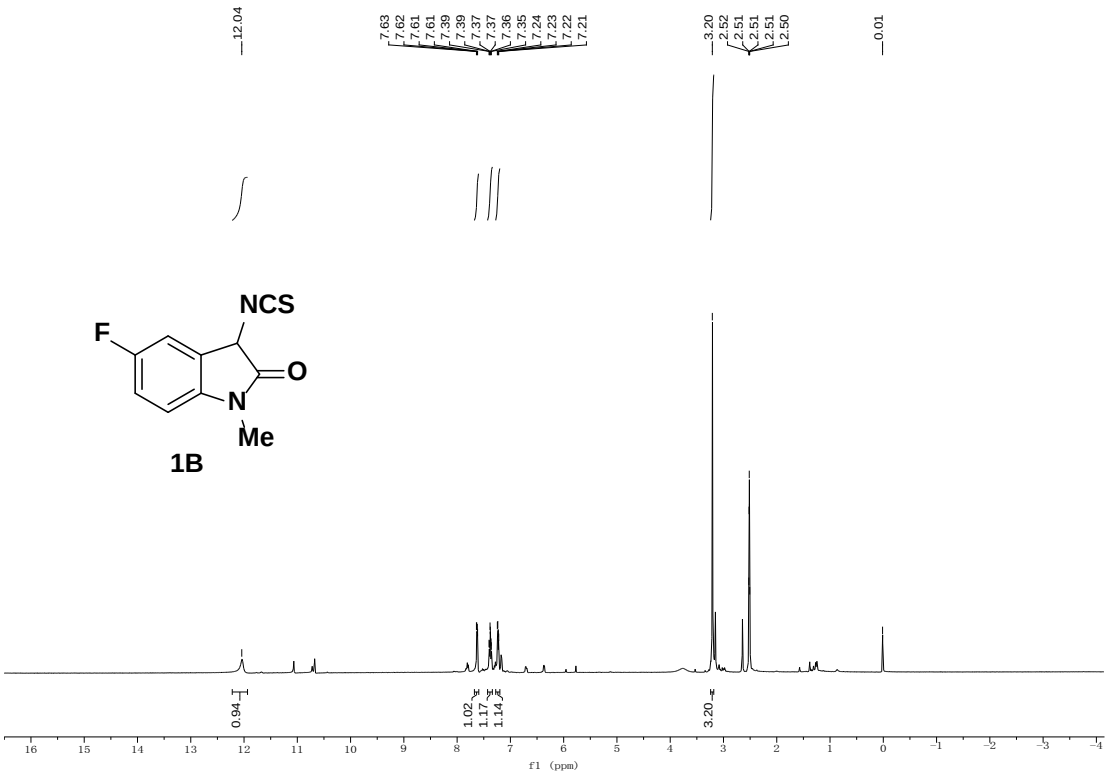
6. NMR and HPLC Spectrum Spectra

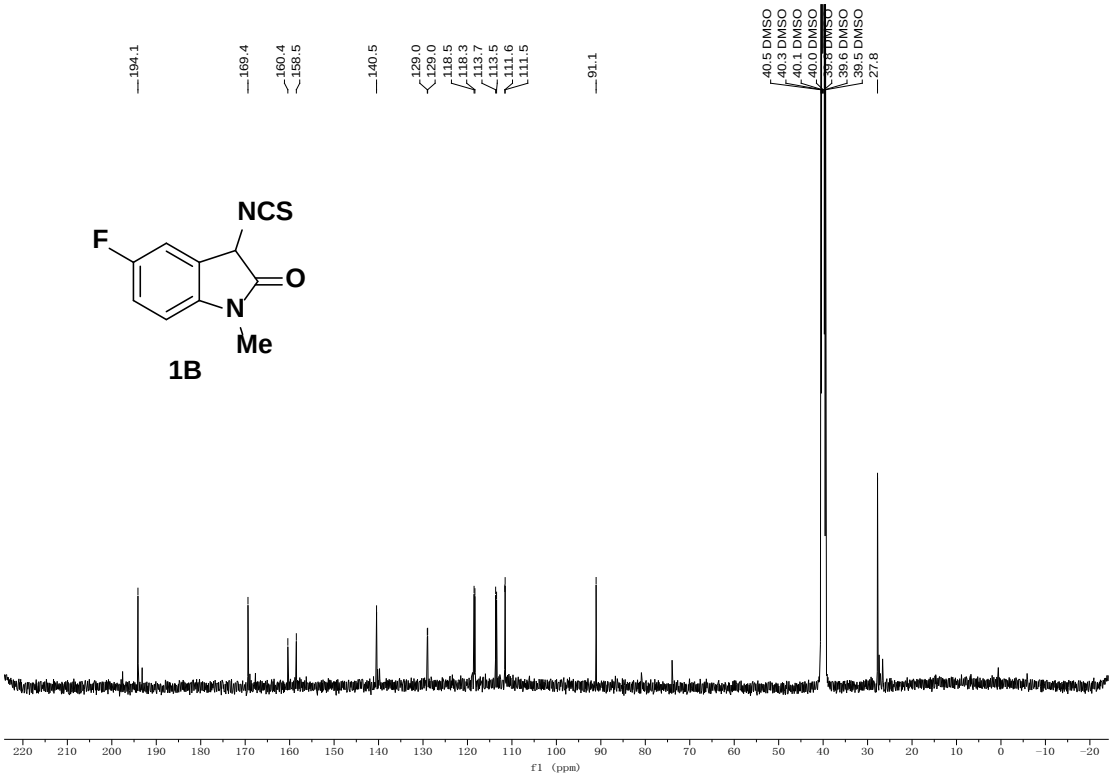
Product of **1A**



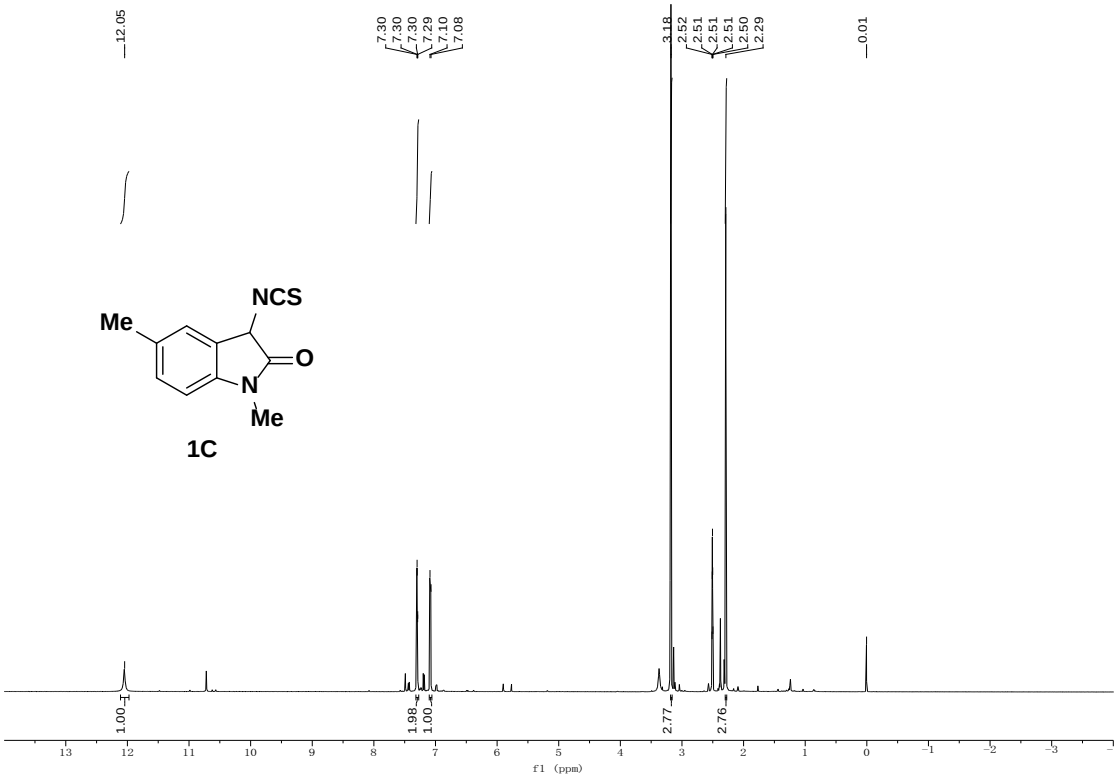


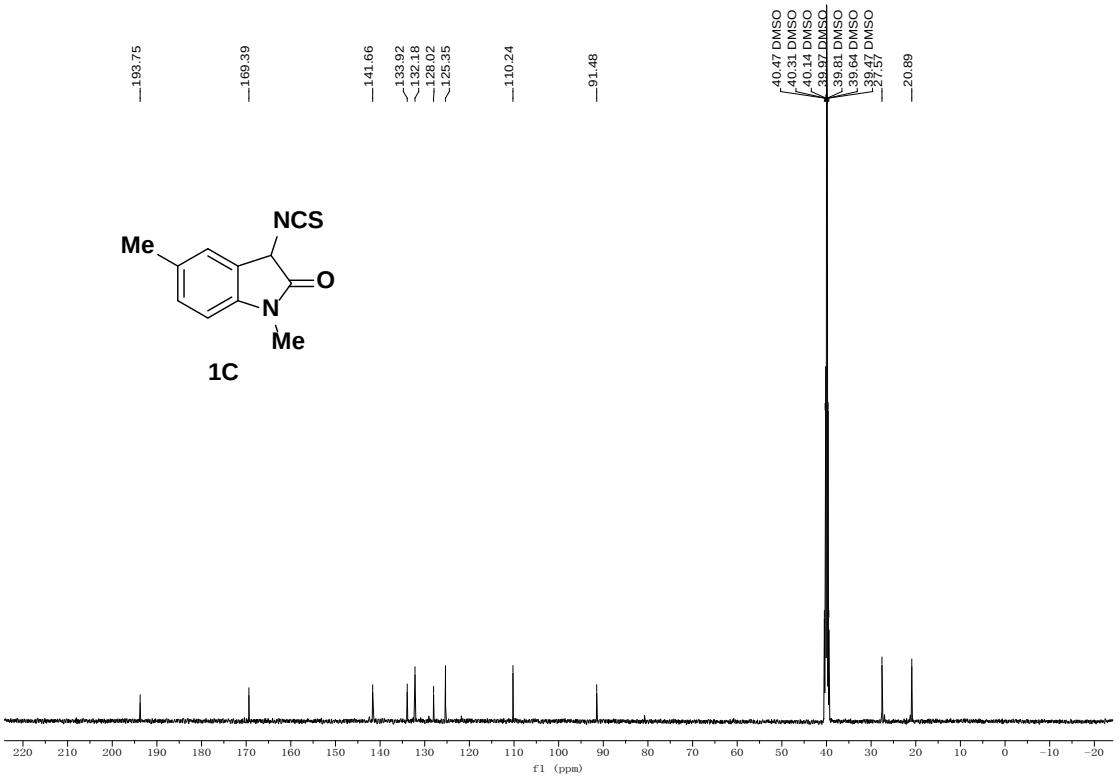
Product of **1B**



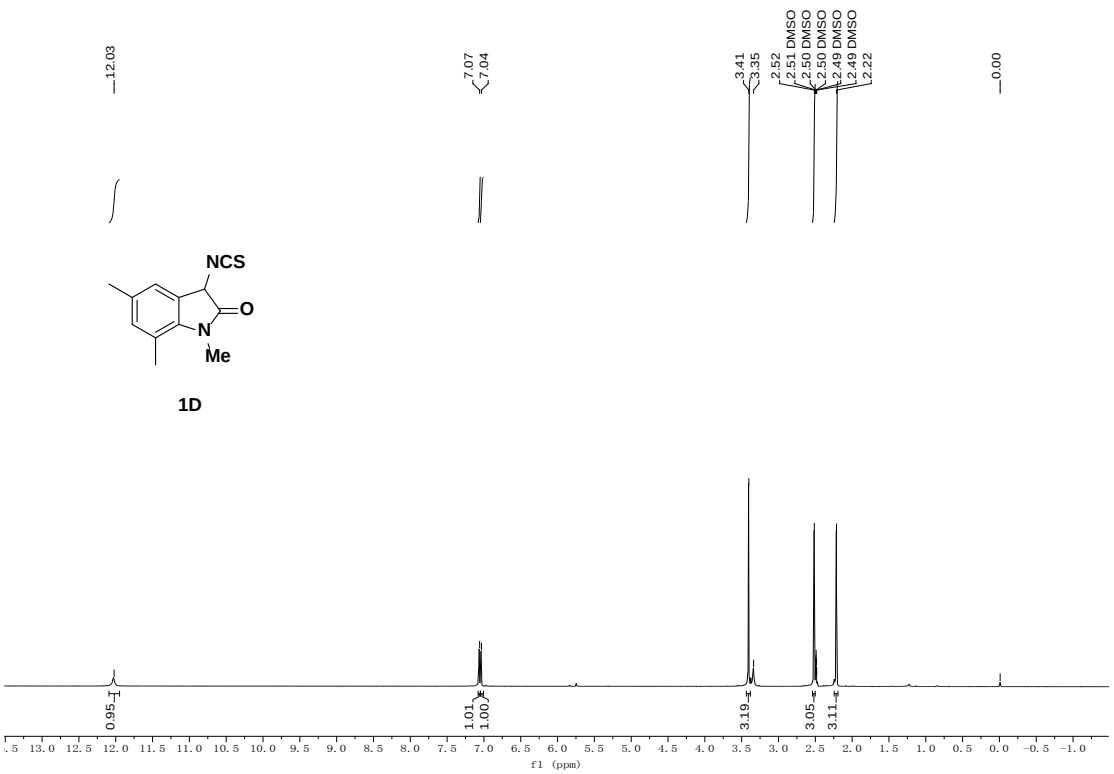


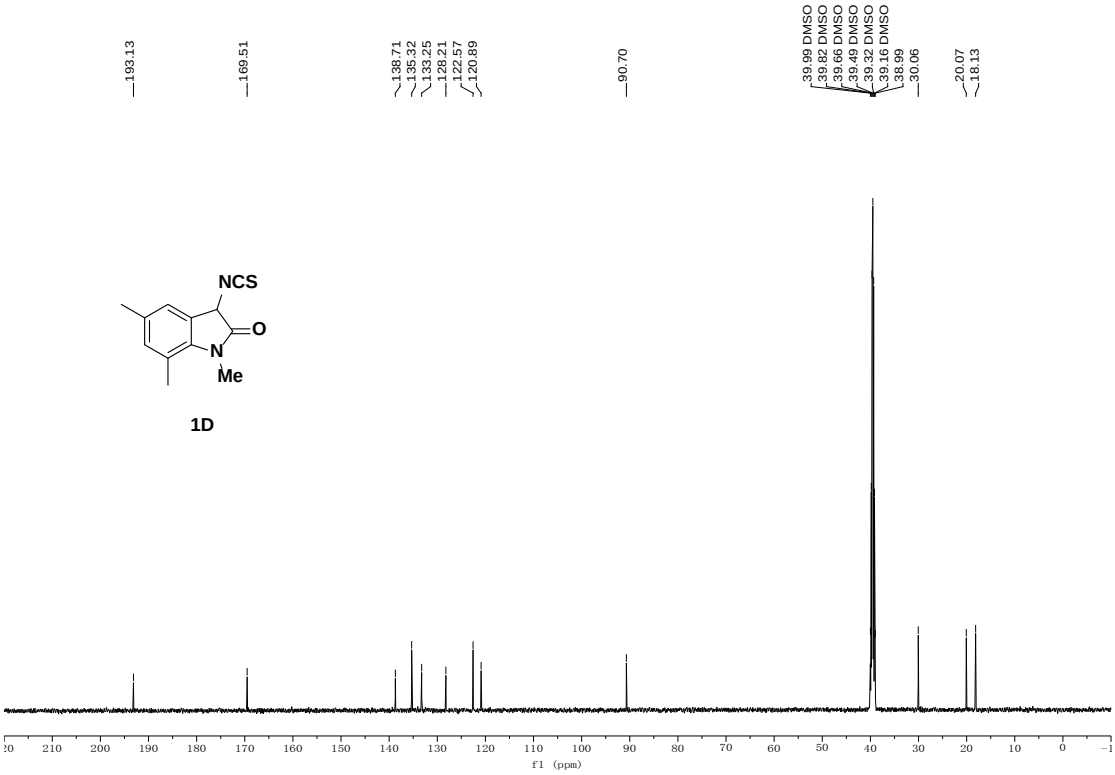
Product of **1C**





Product of **1D**





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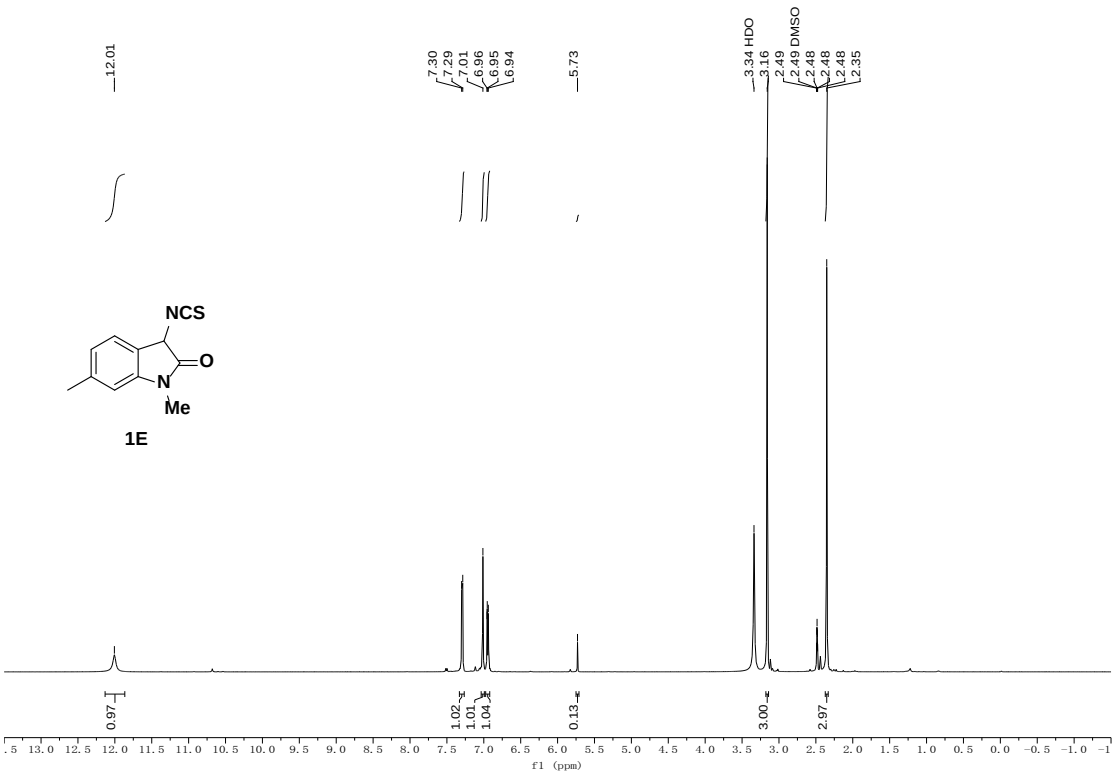

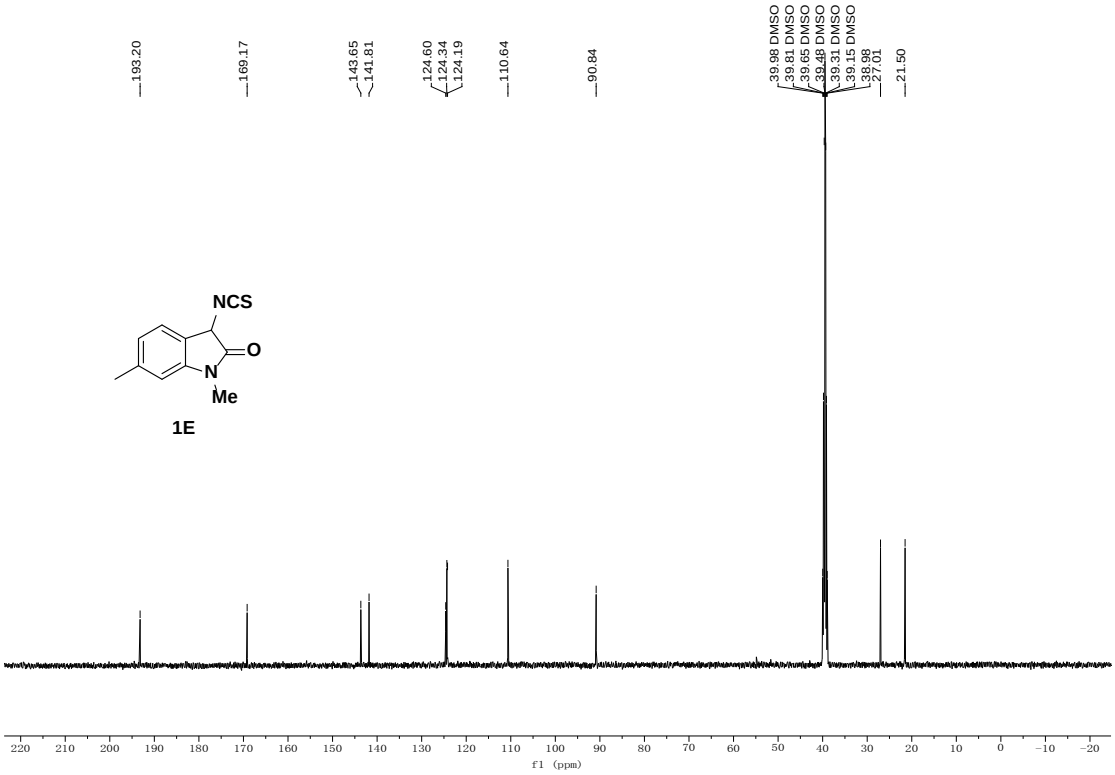

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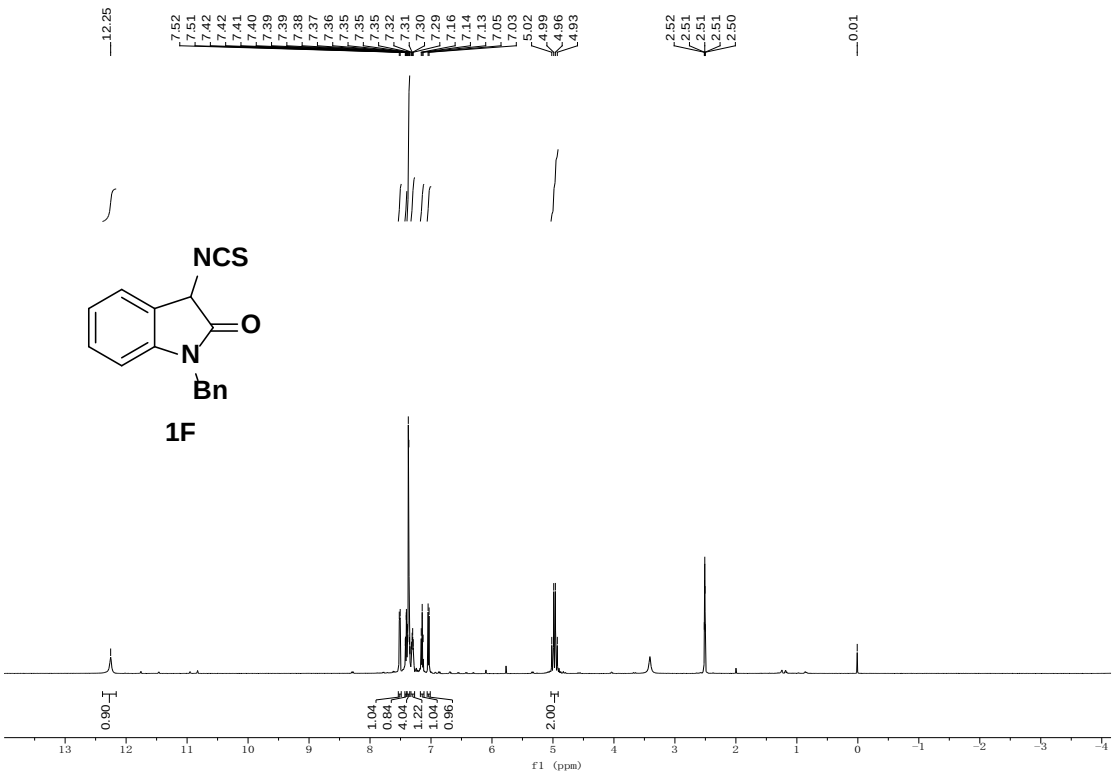
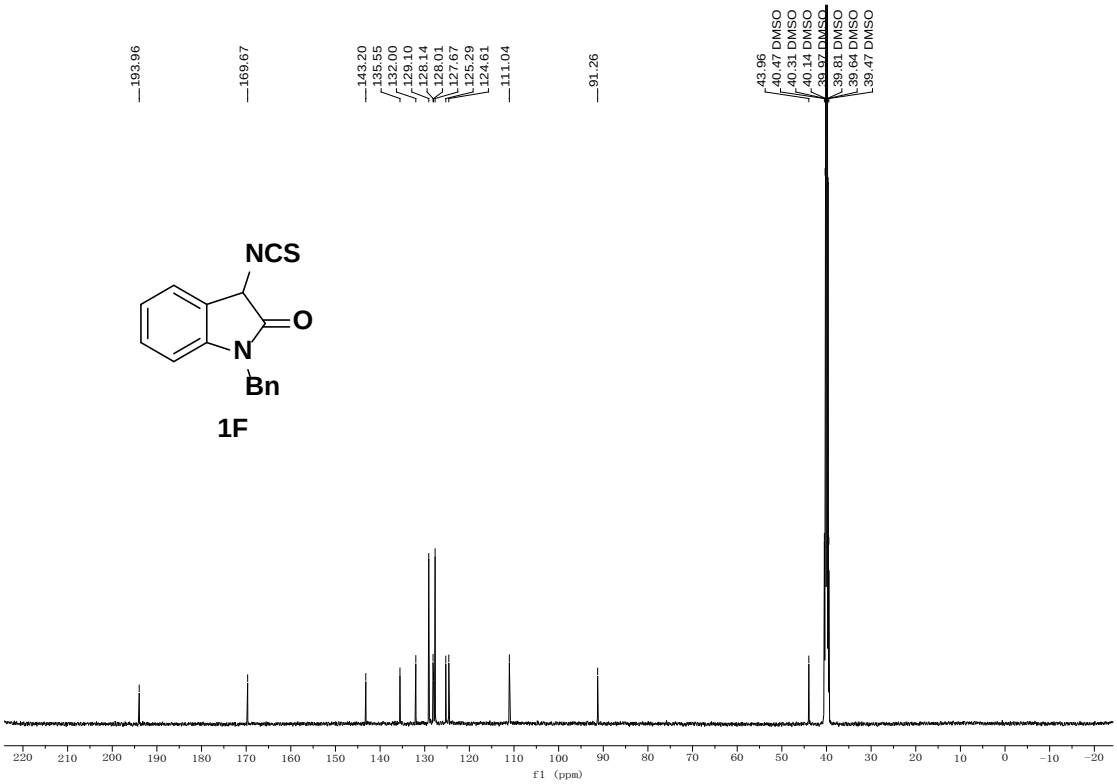
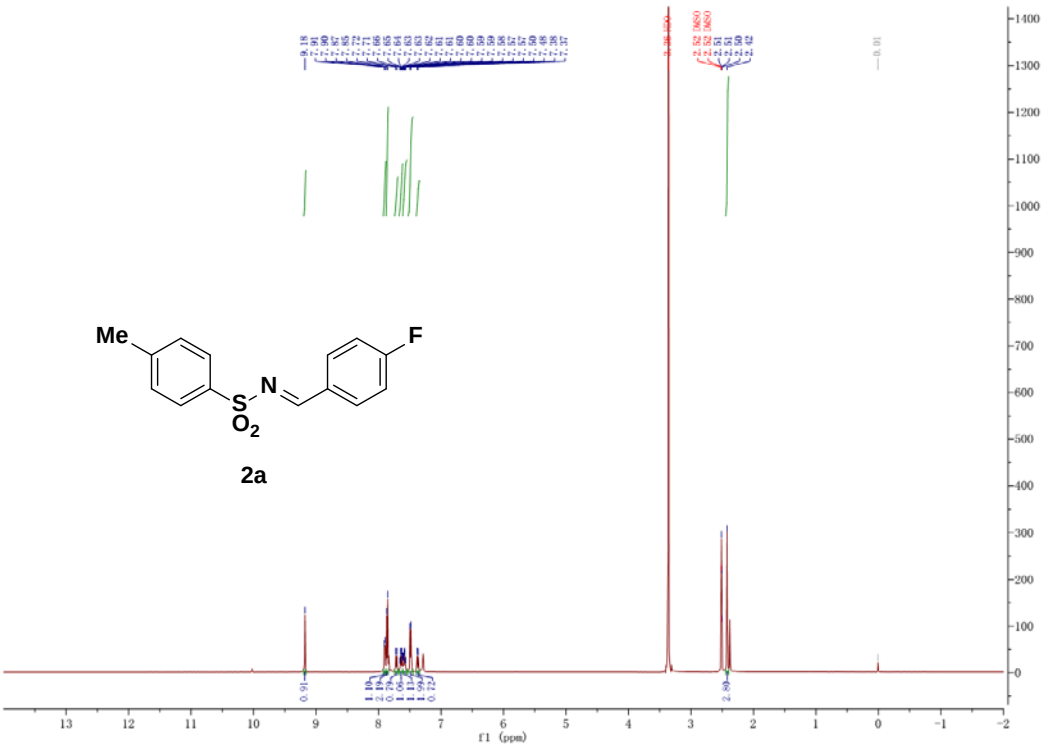
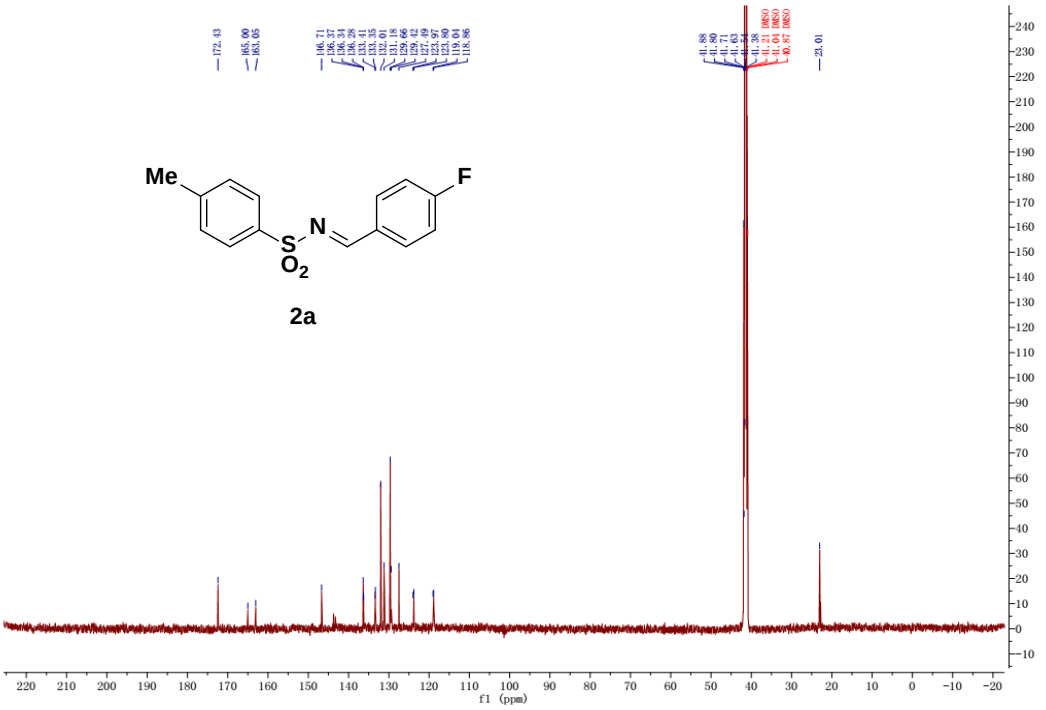


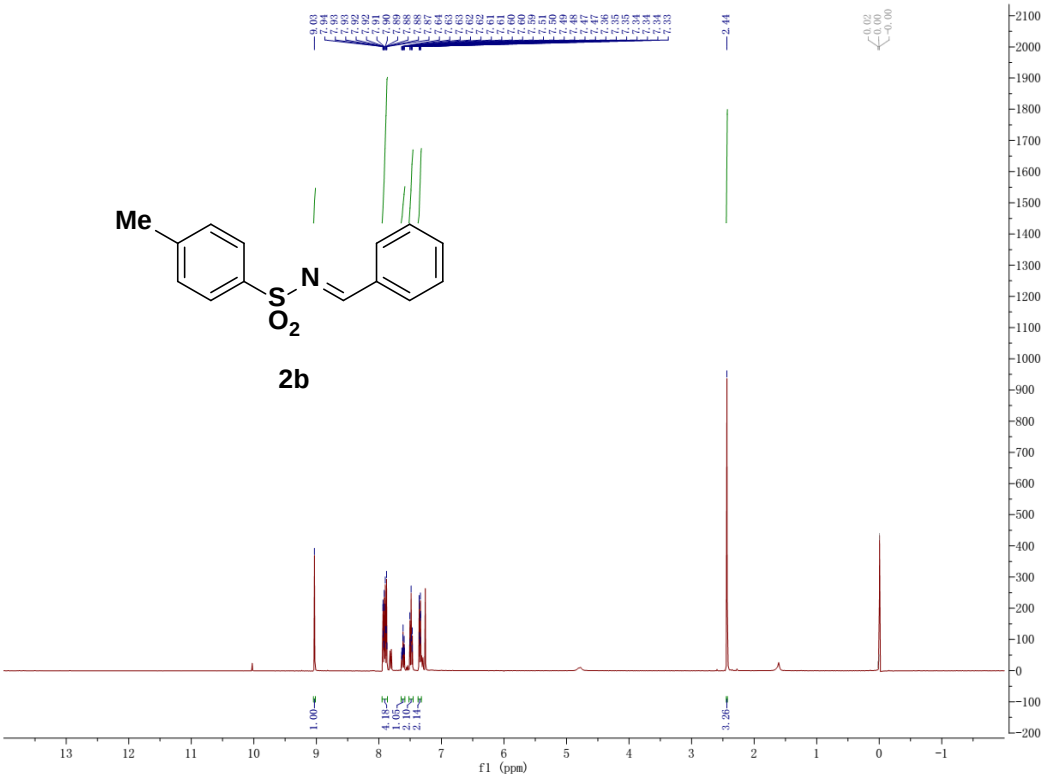


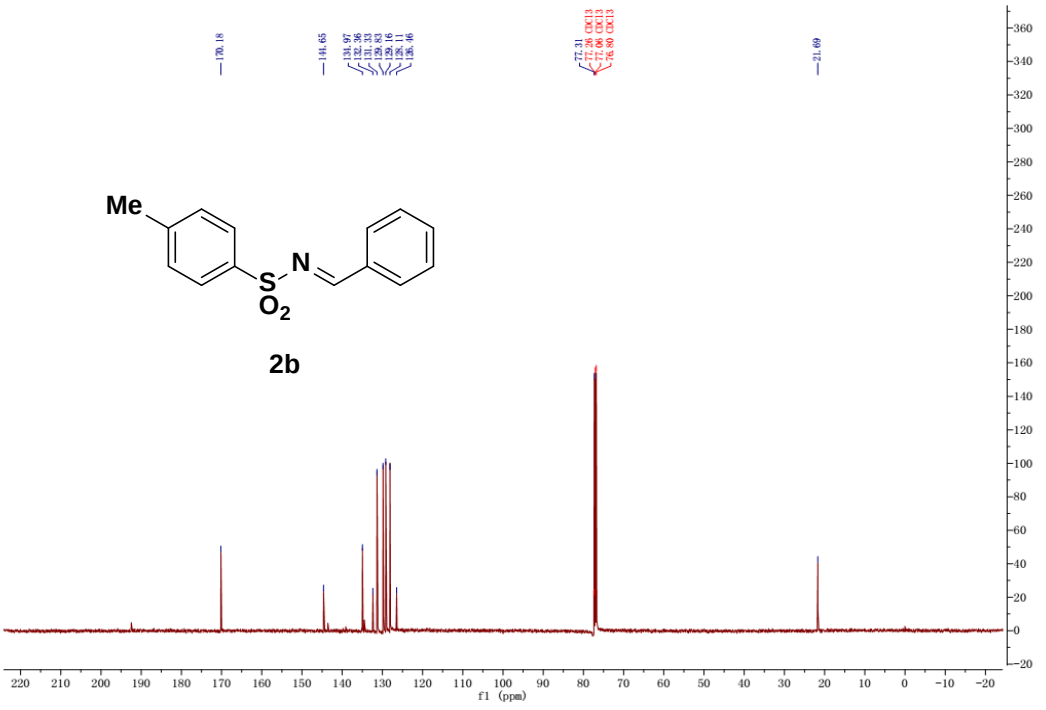
Product of **2a**





Product of **2b**





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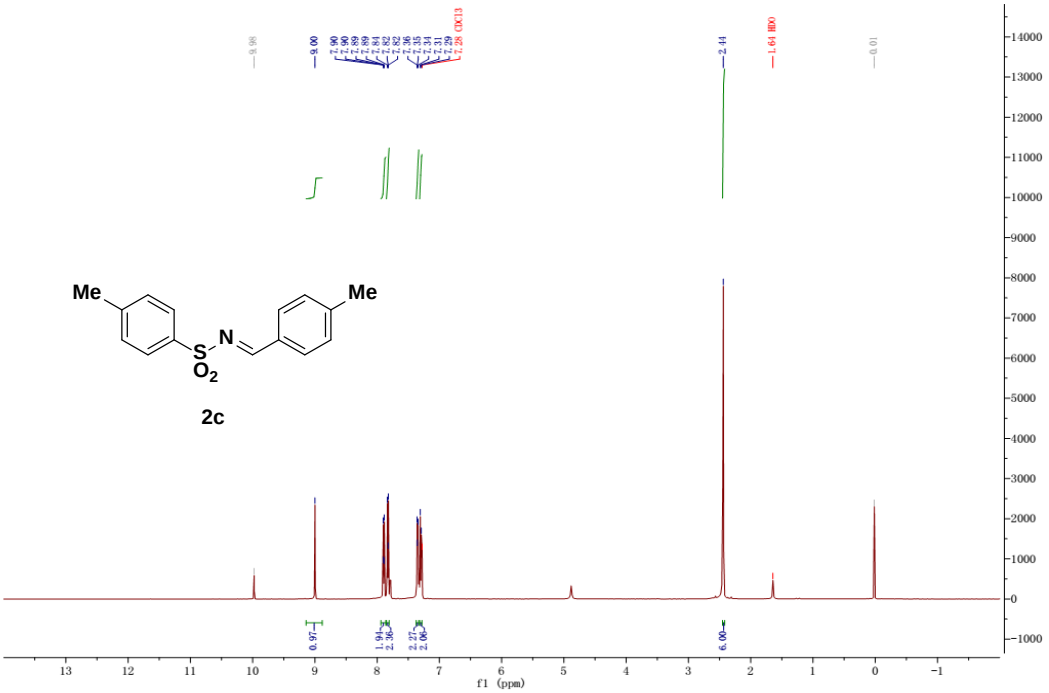

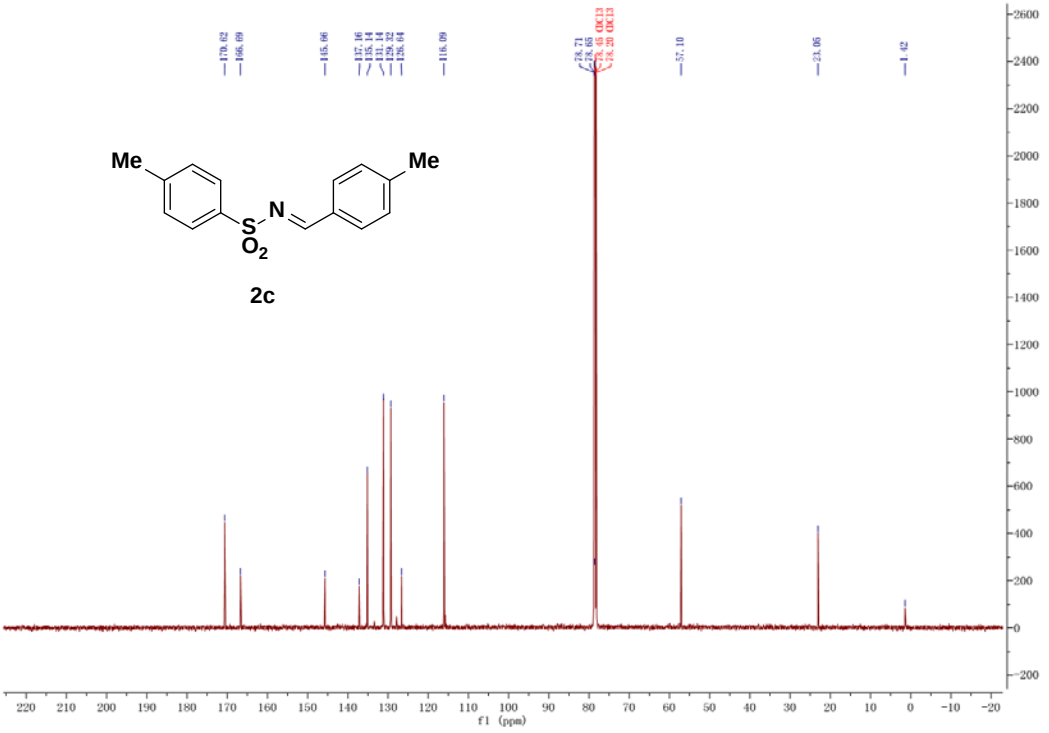

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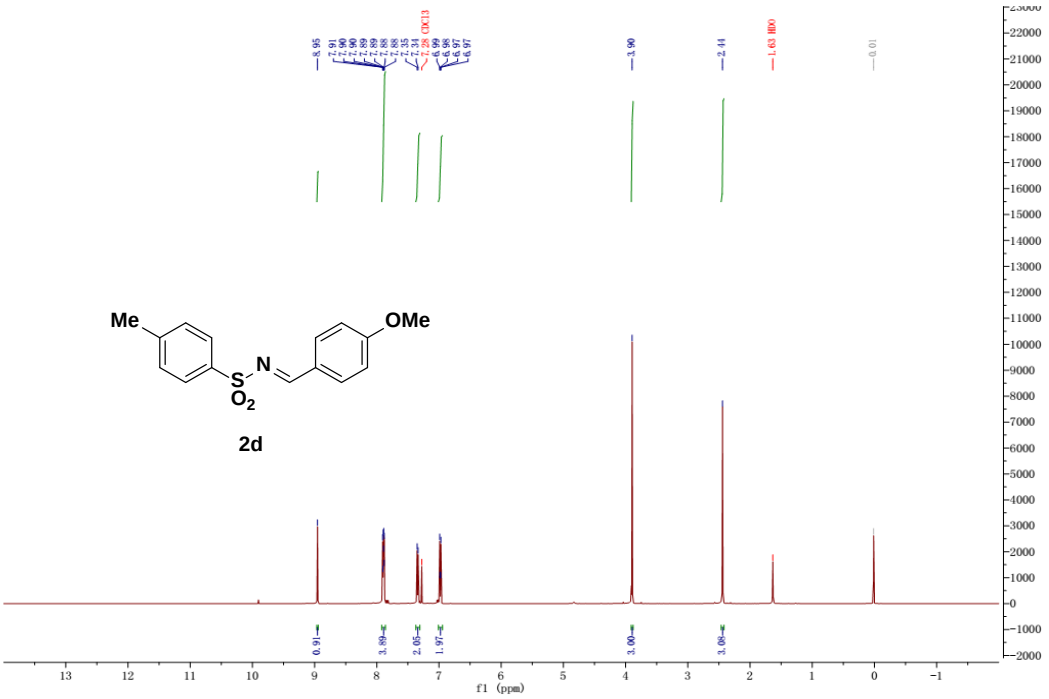

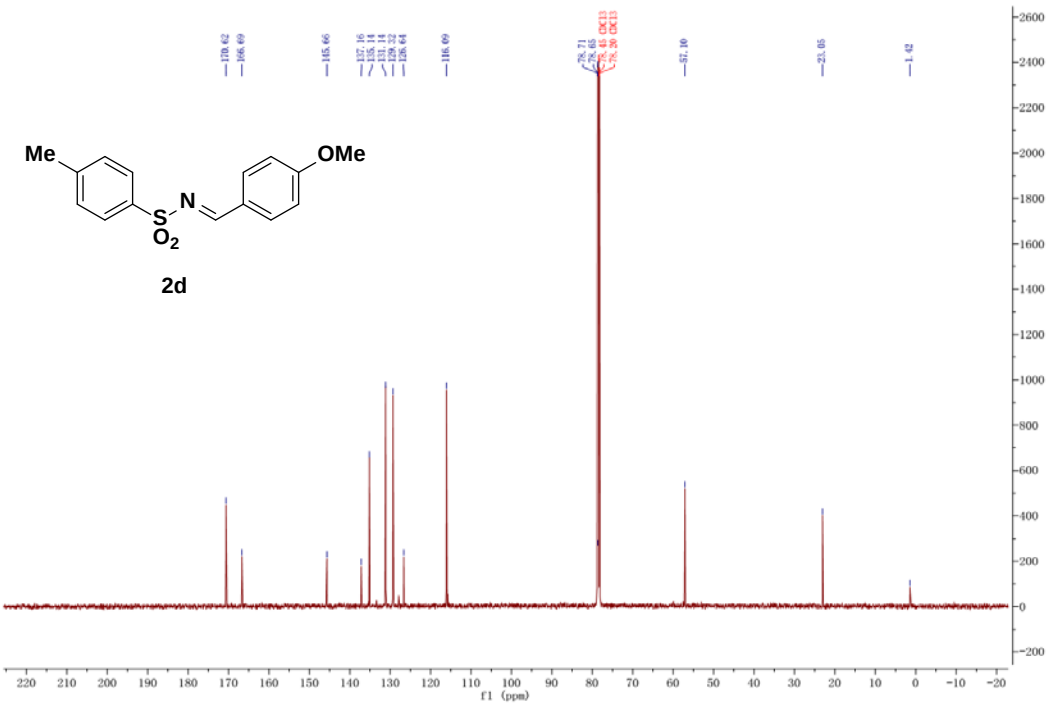

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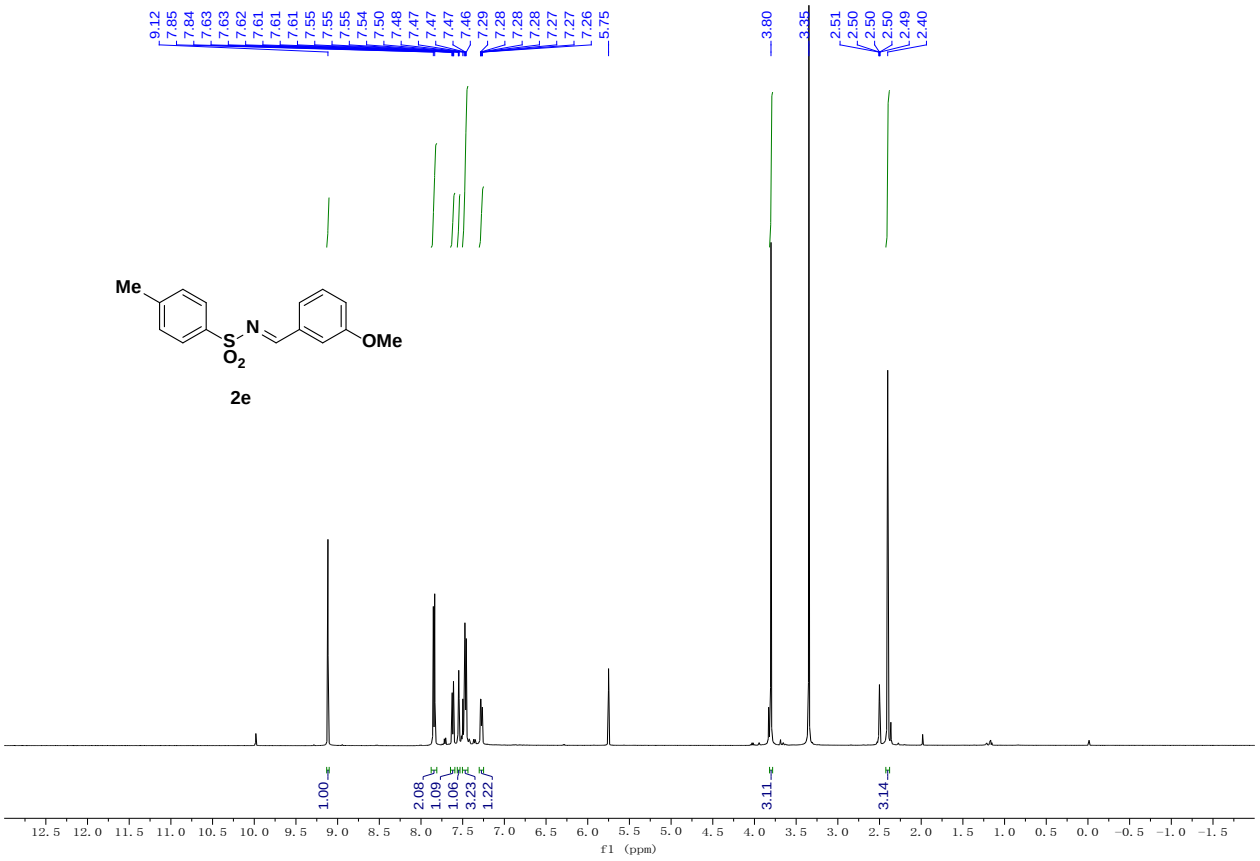
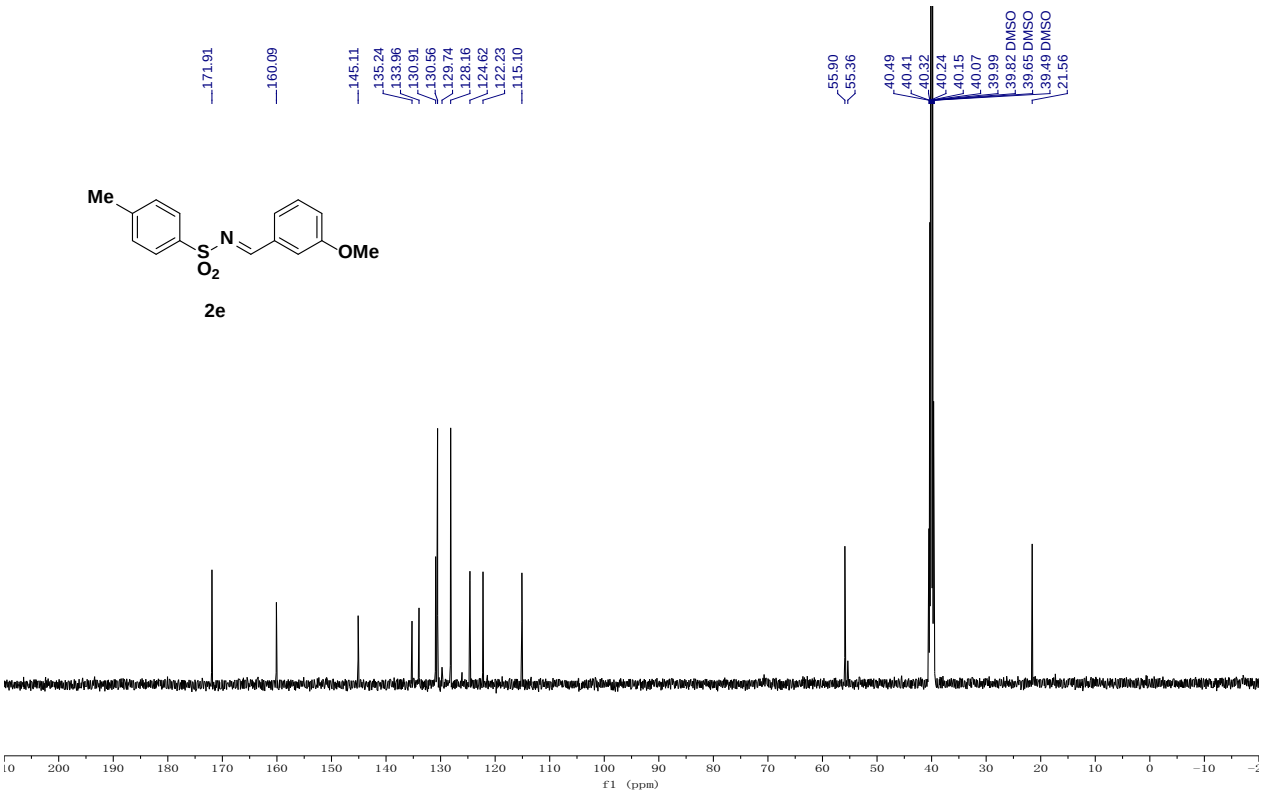
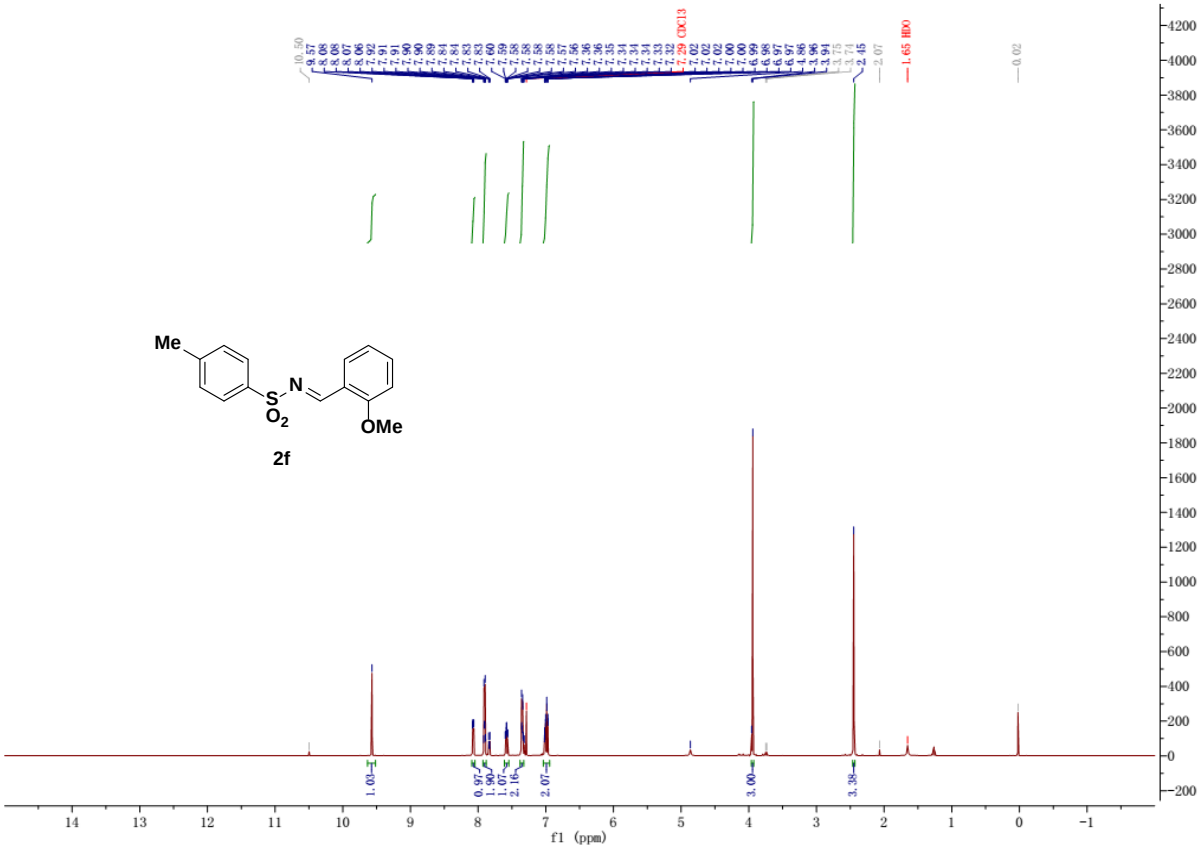
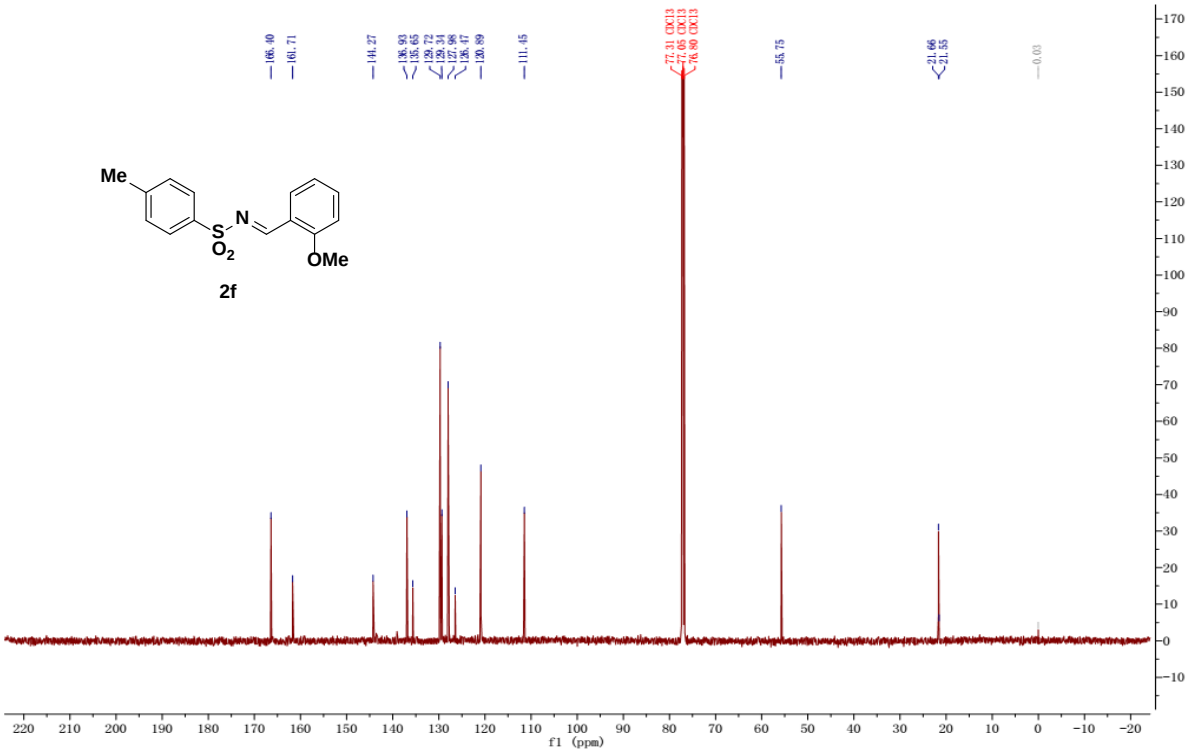


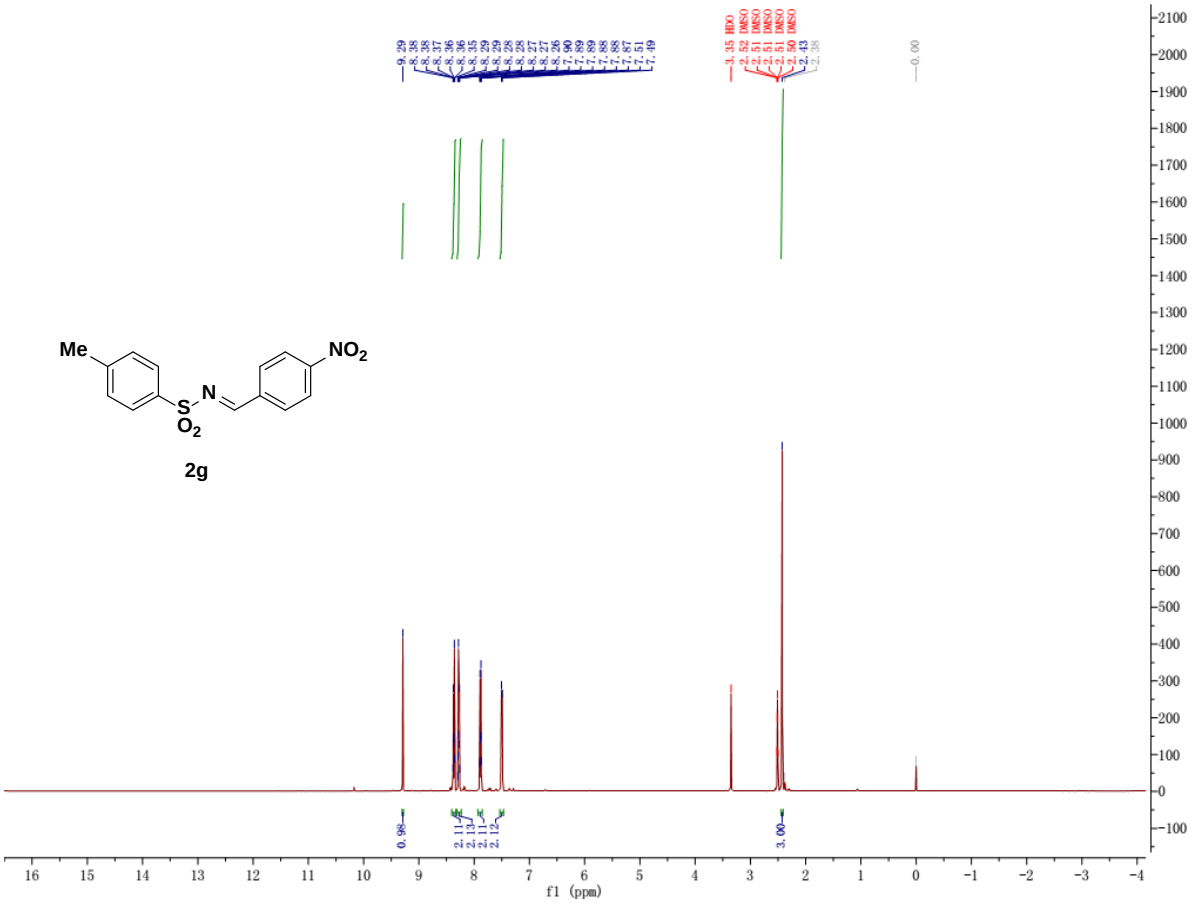


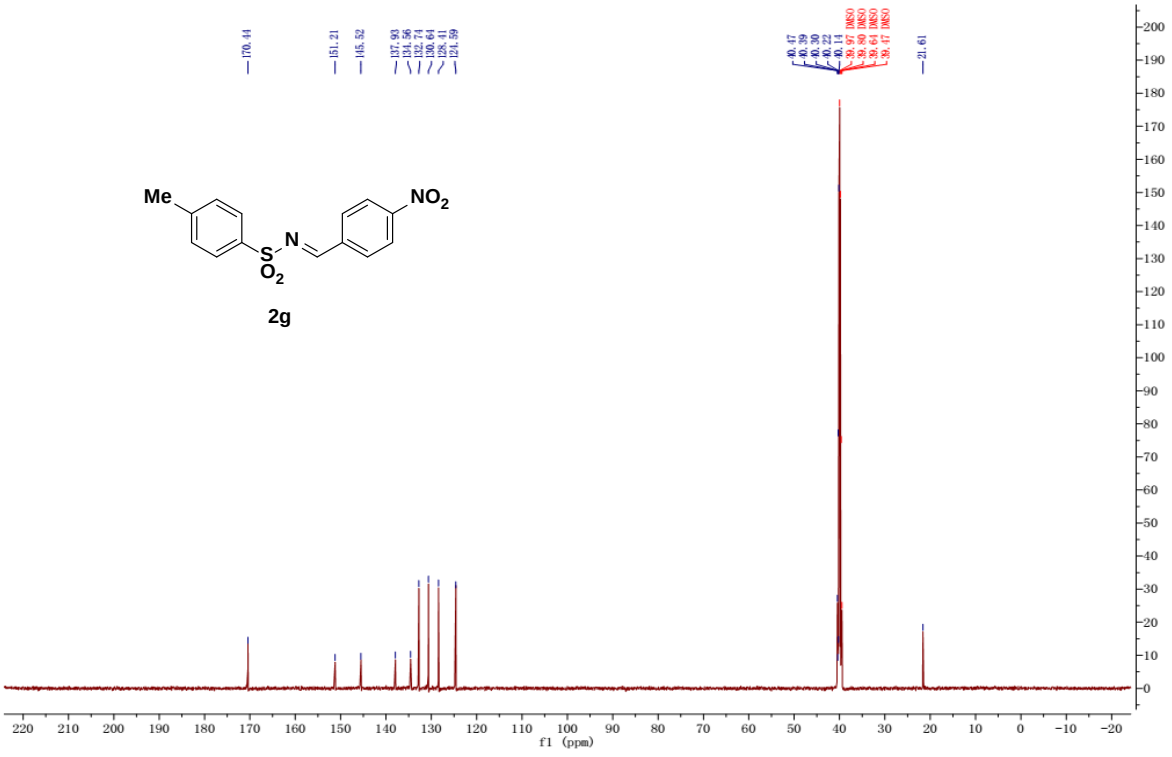
Product of **2f**



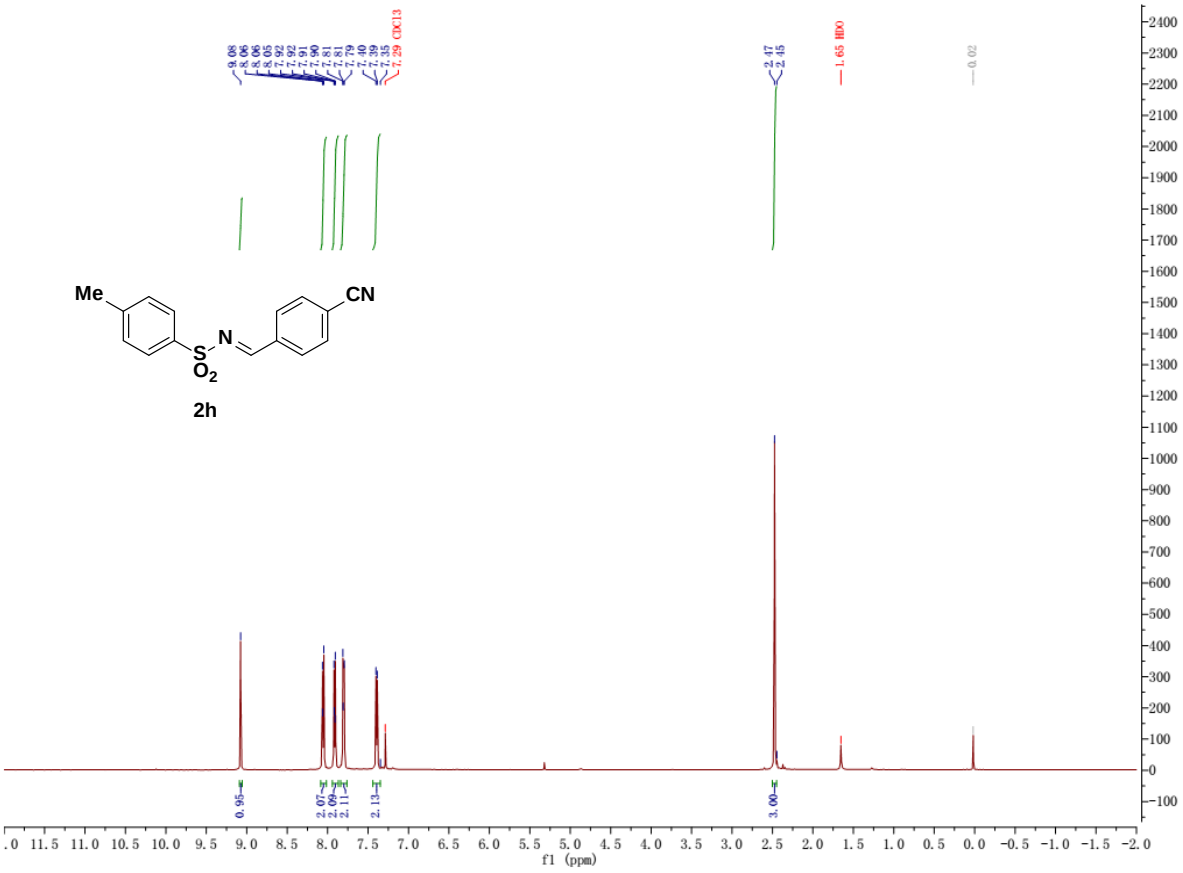


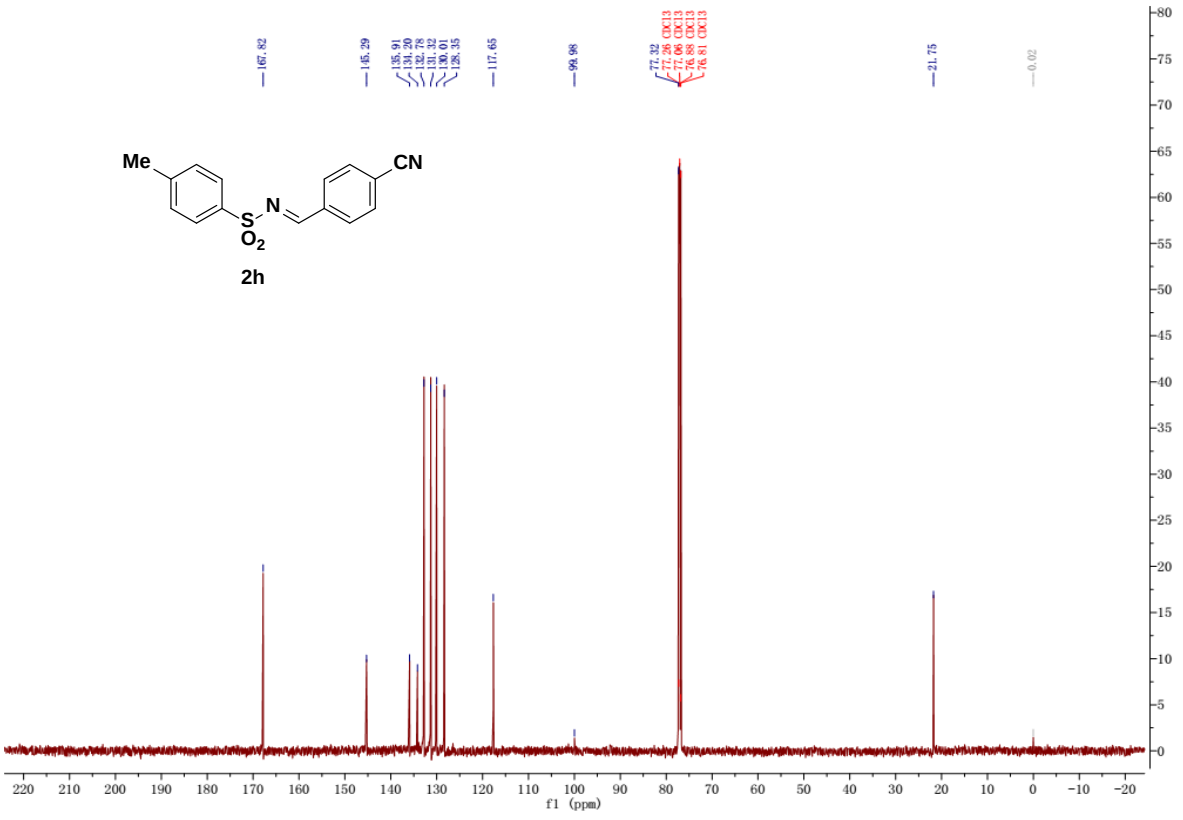
Product of **2g**


Me
NO2
S
O2
N
2g
f1 (ppm)

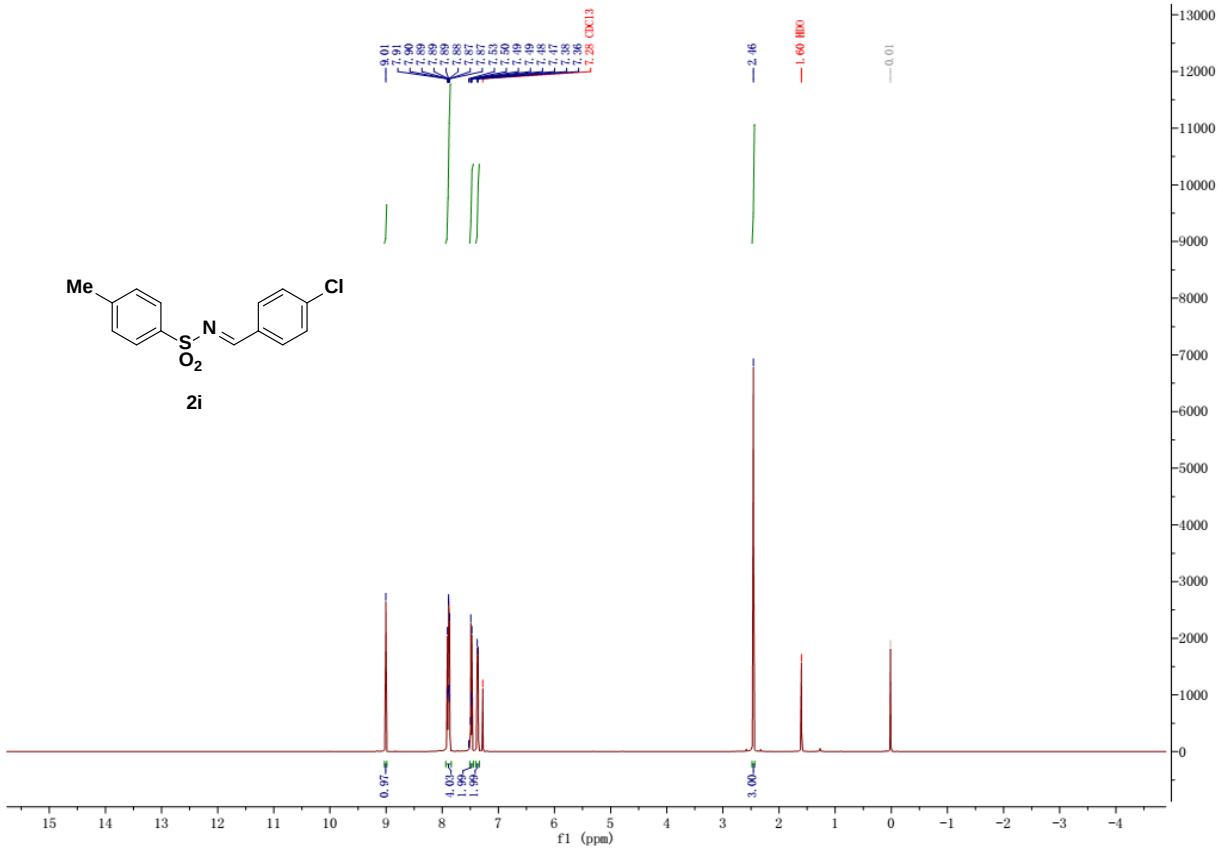

Me
NO2
S
O2
N
2g
f1 (ppm)

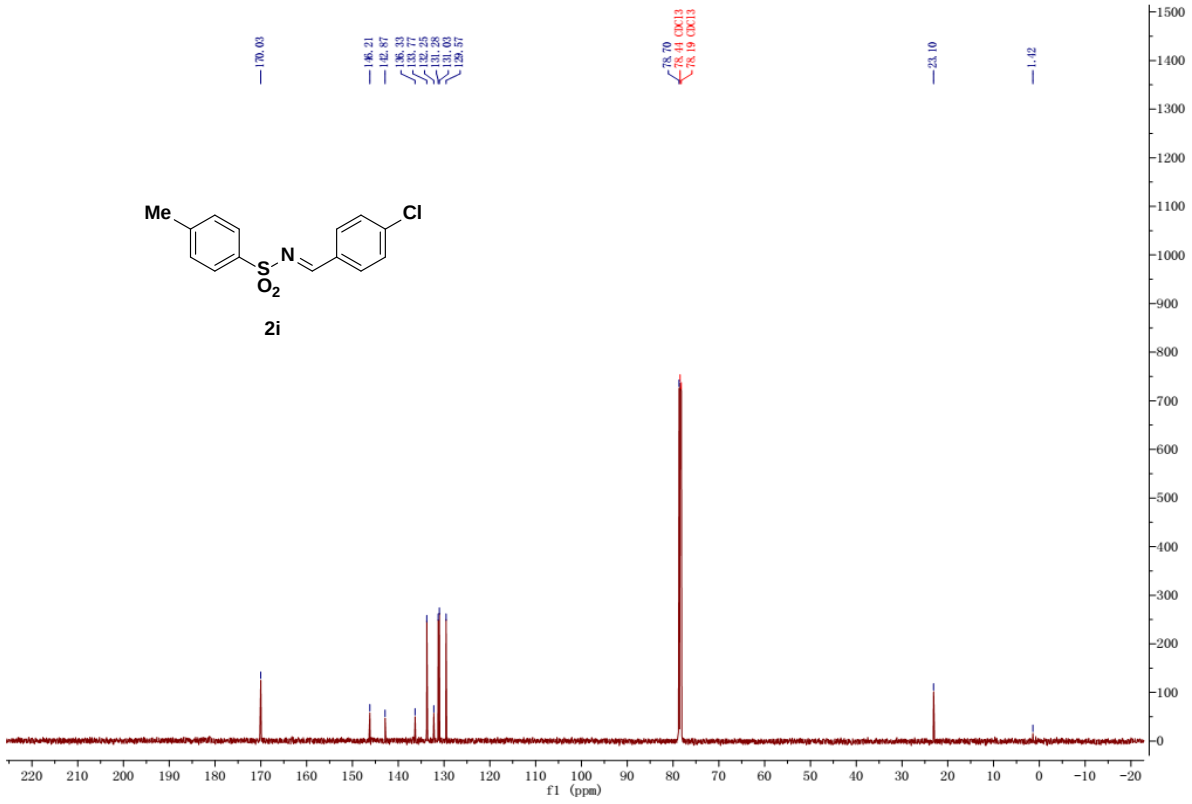
Product of **2h**



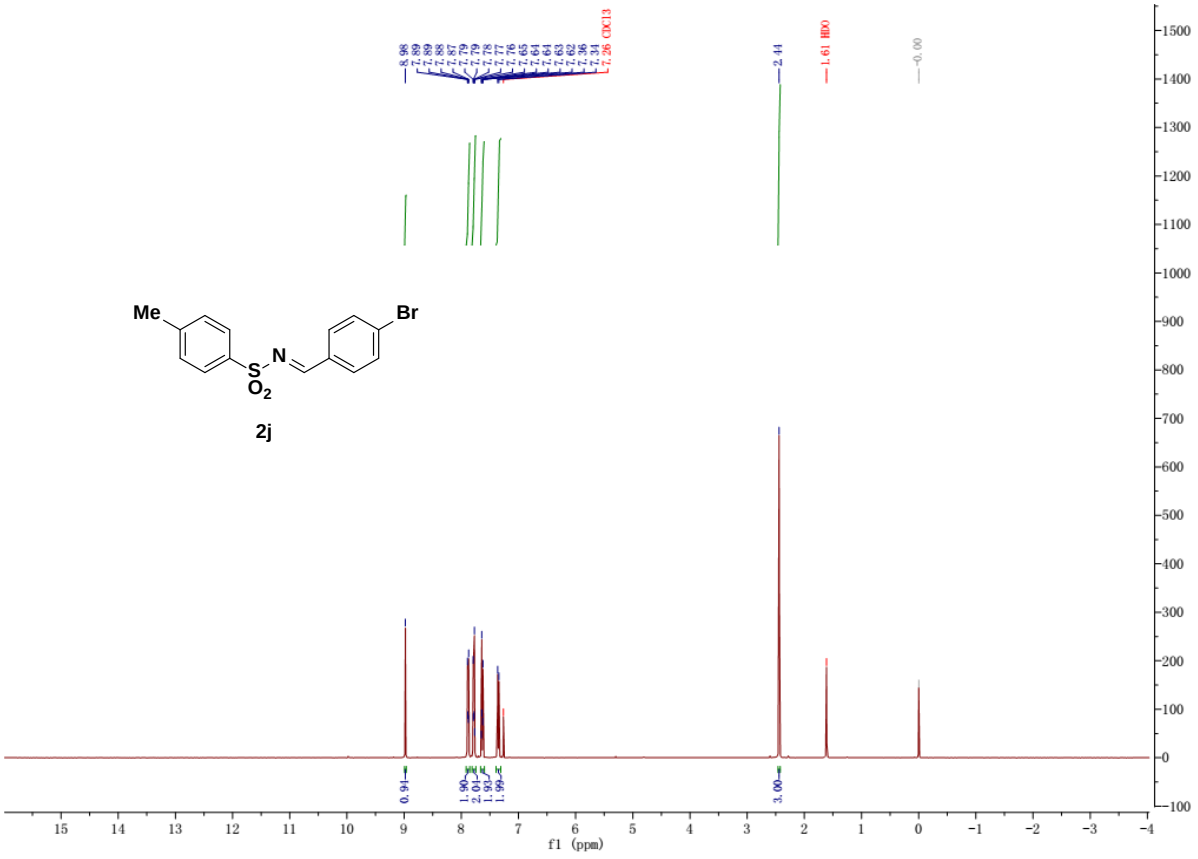


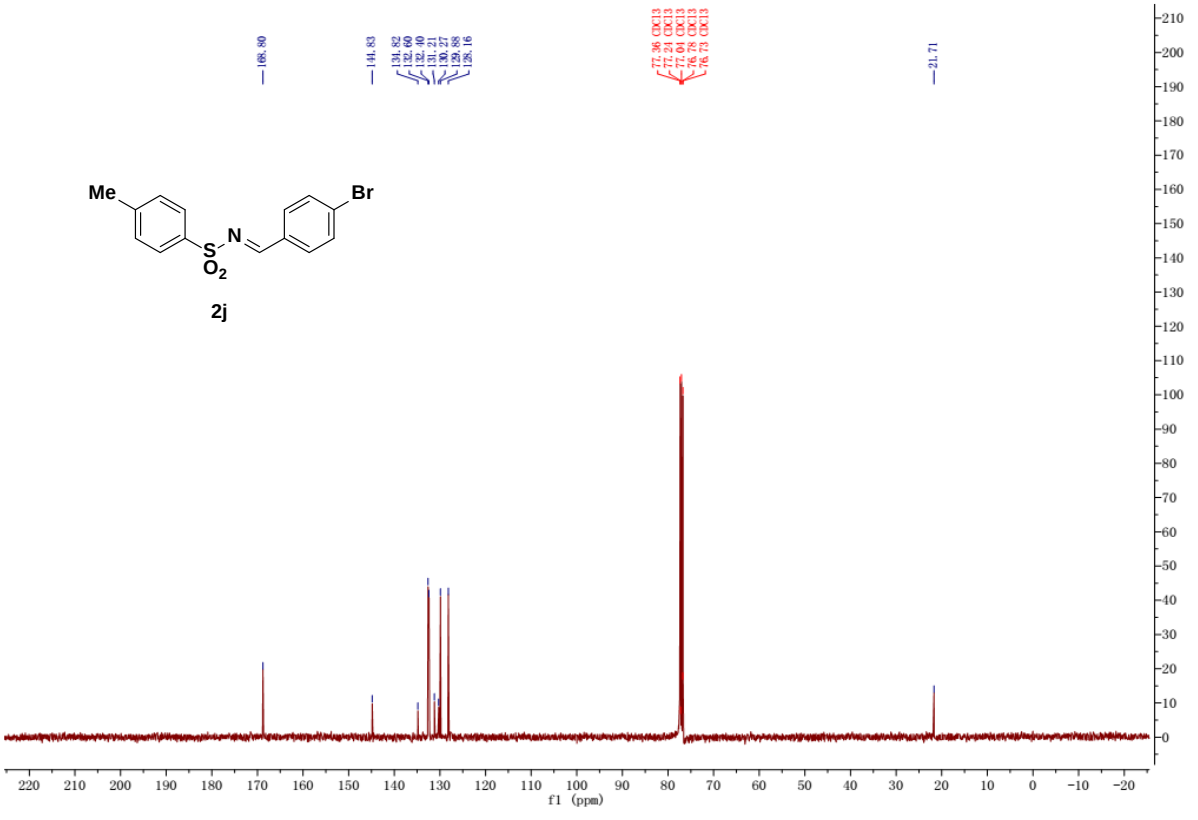
Product of **2i**



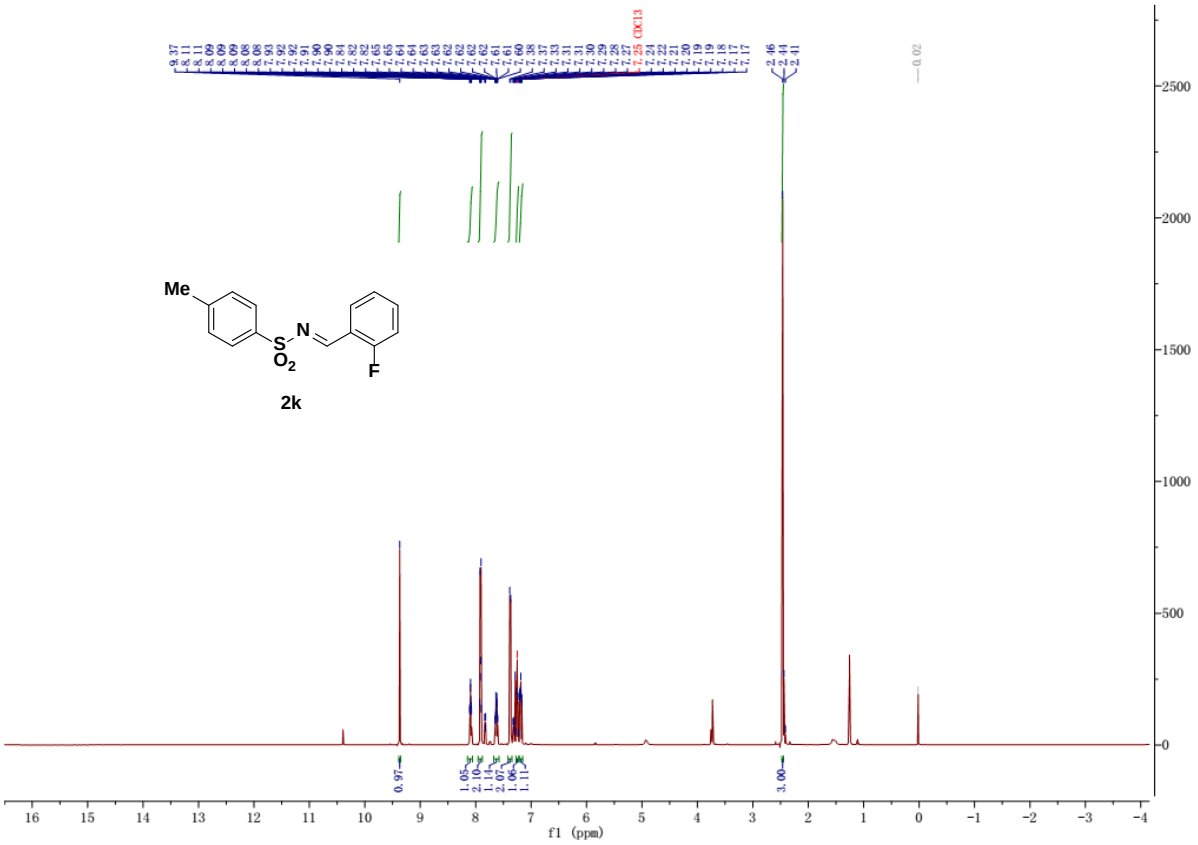


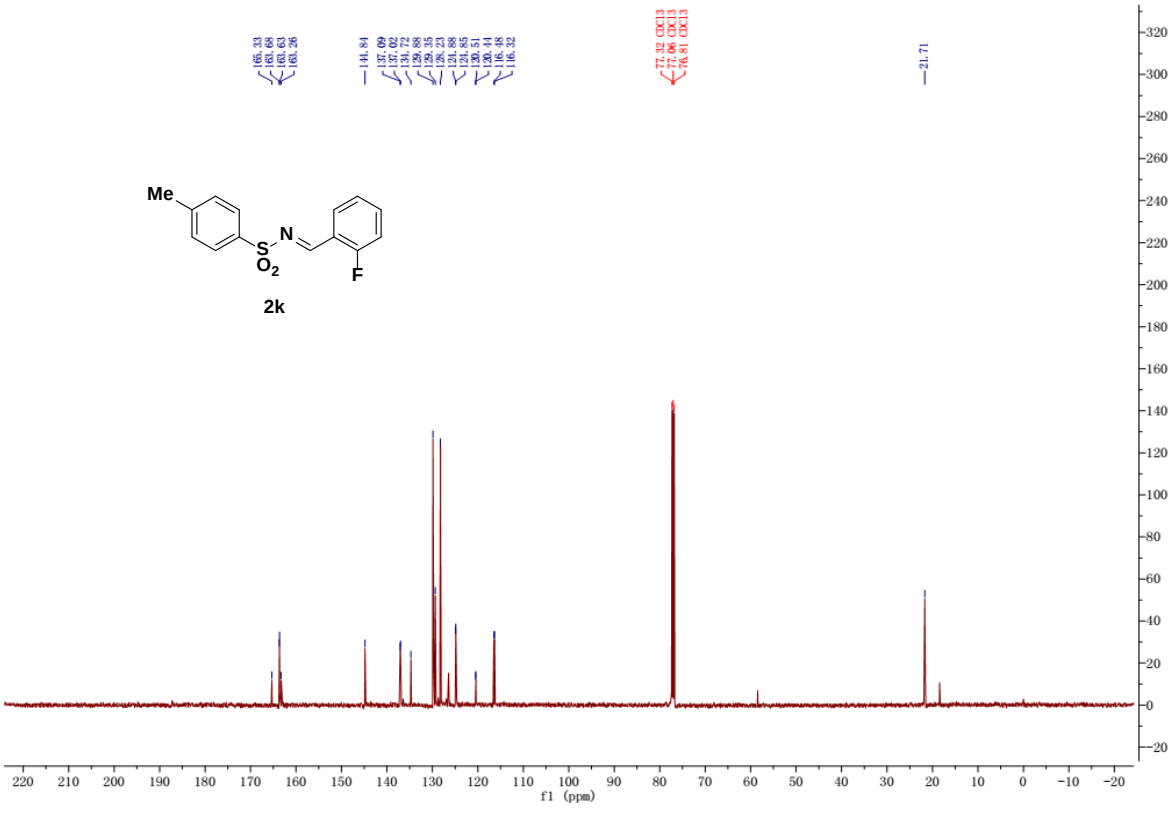
Product of **2j**



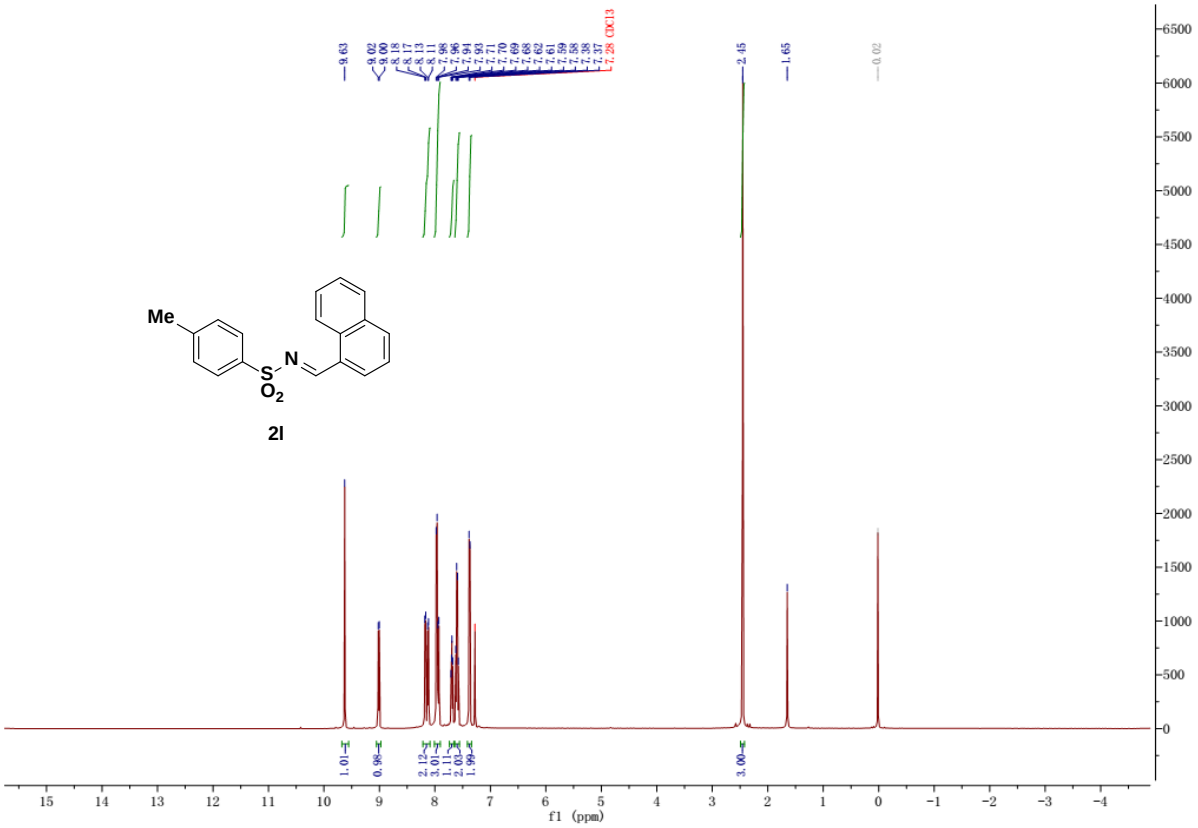


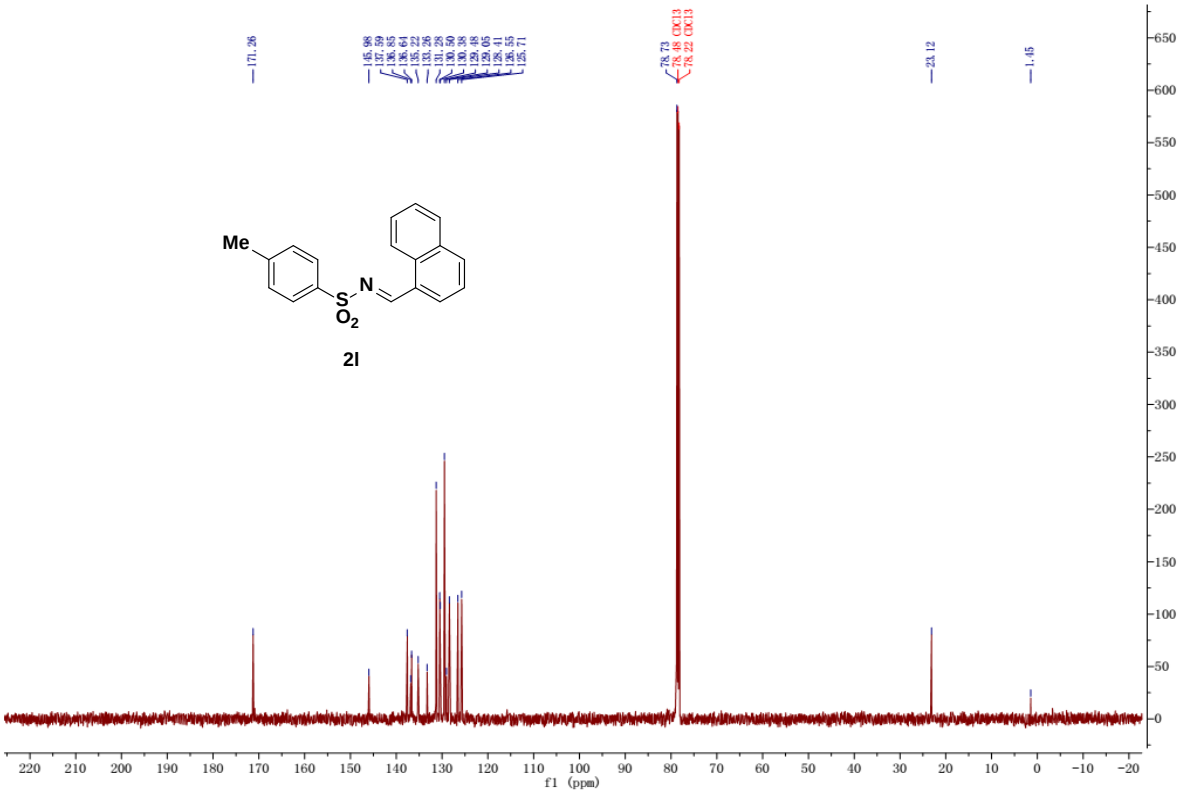
Product of **2k**



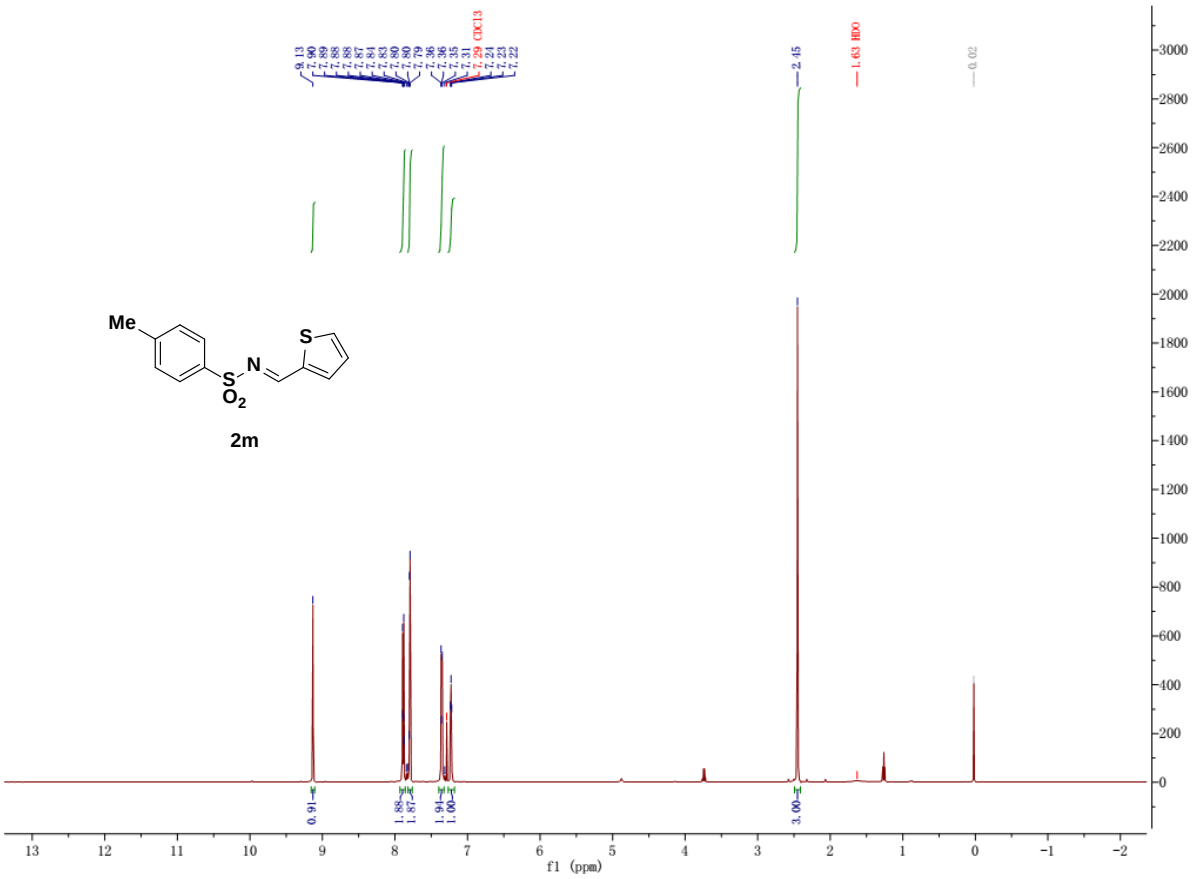


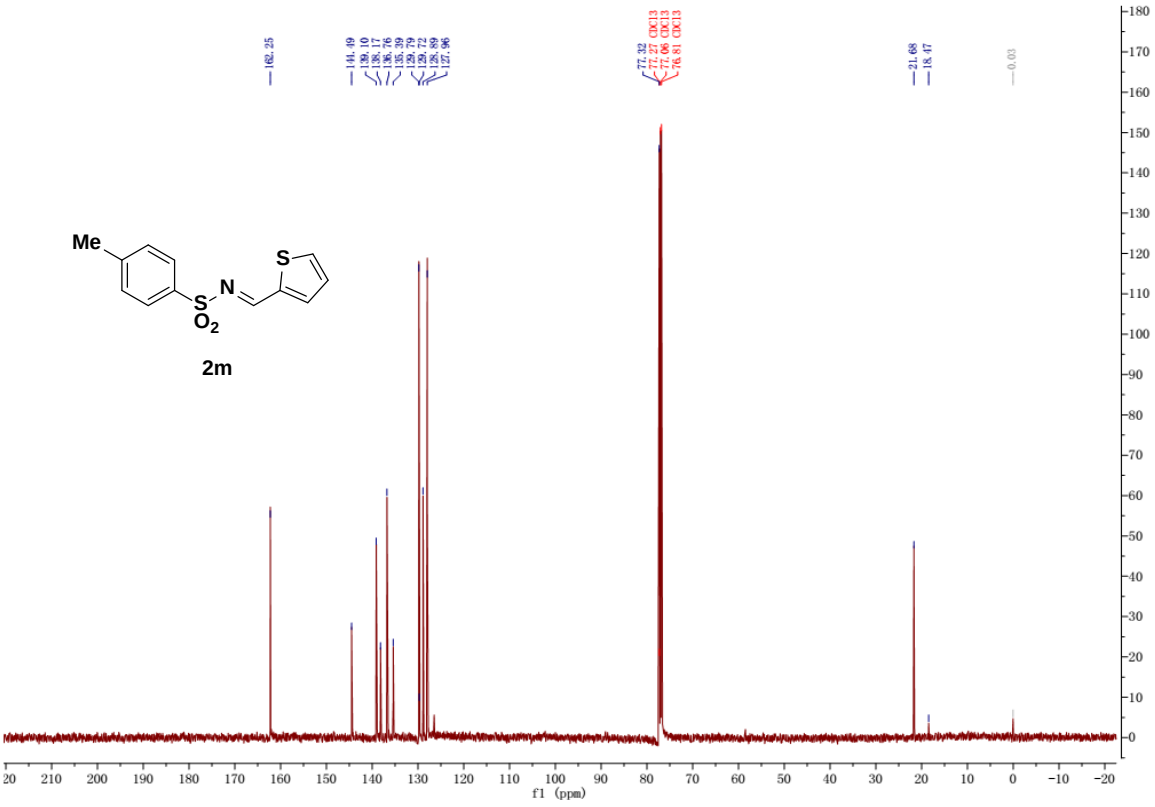
Product of **2l**



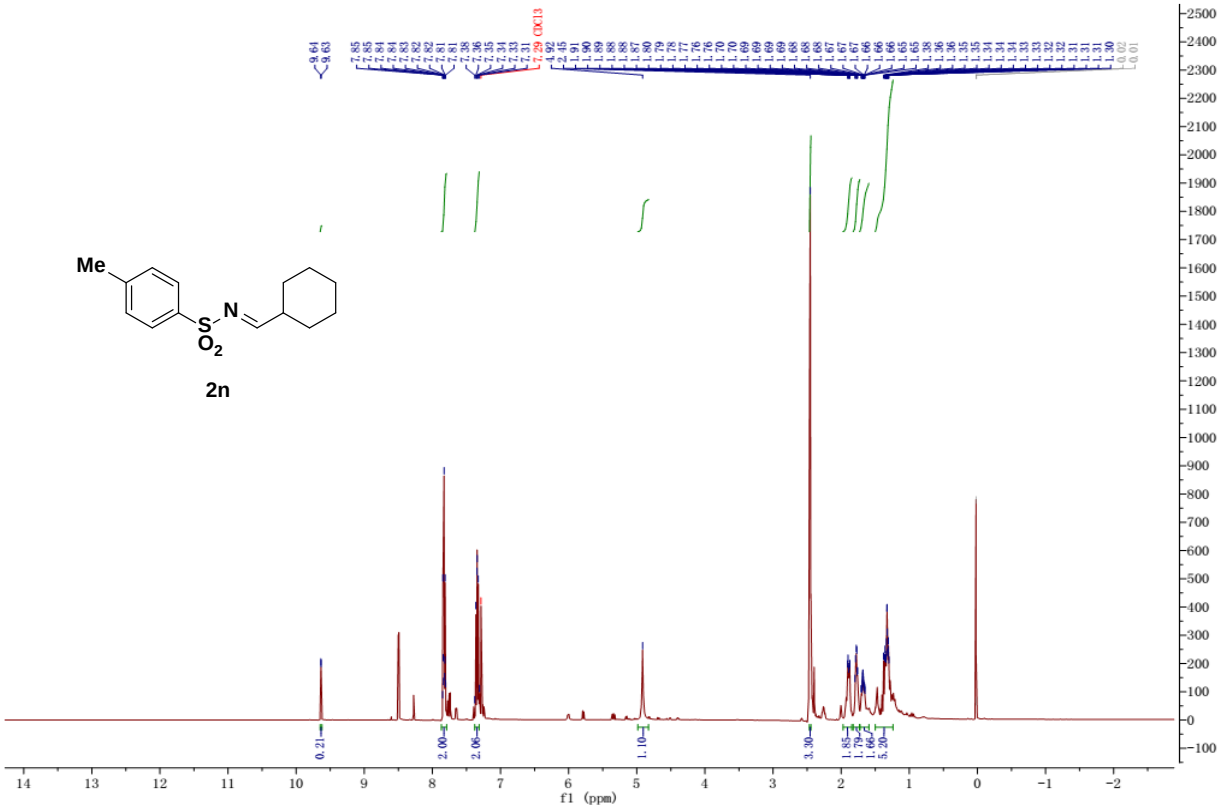


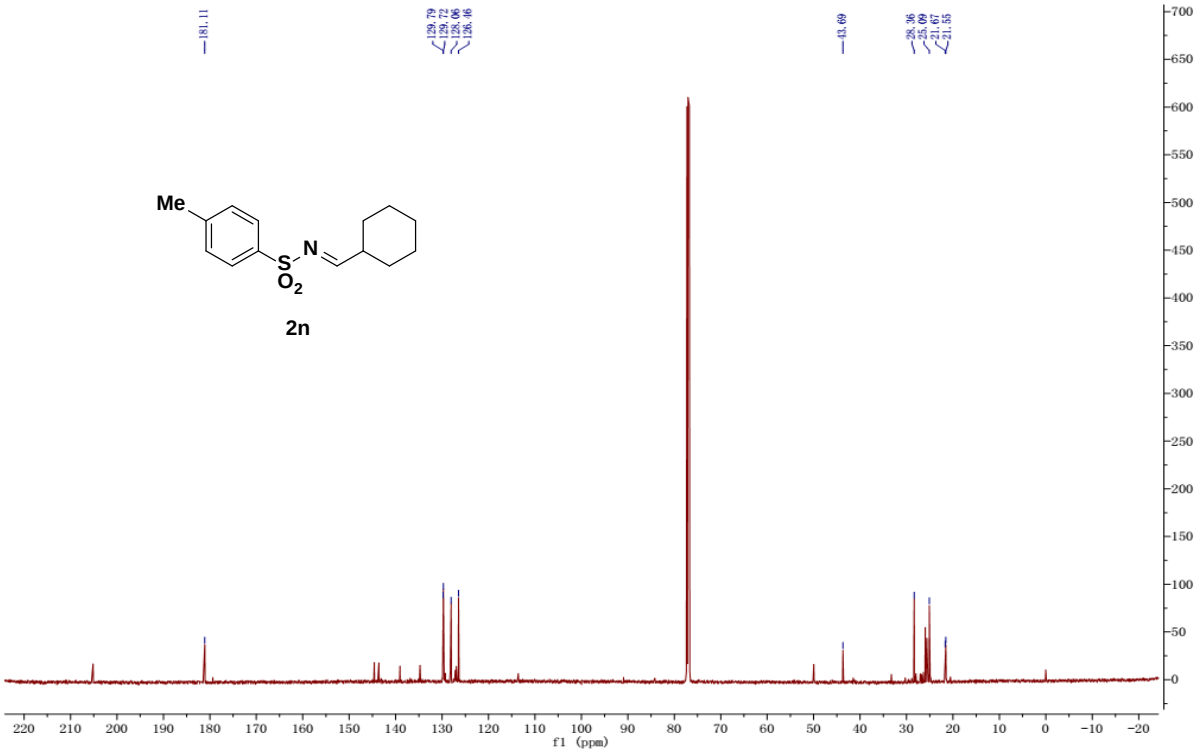
Product of **2m**


Me
S
N
O2
2m
f1 (ppm)

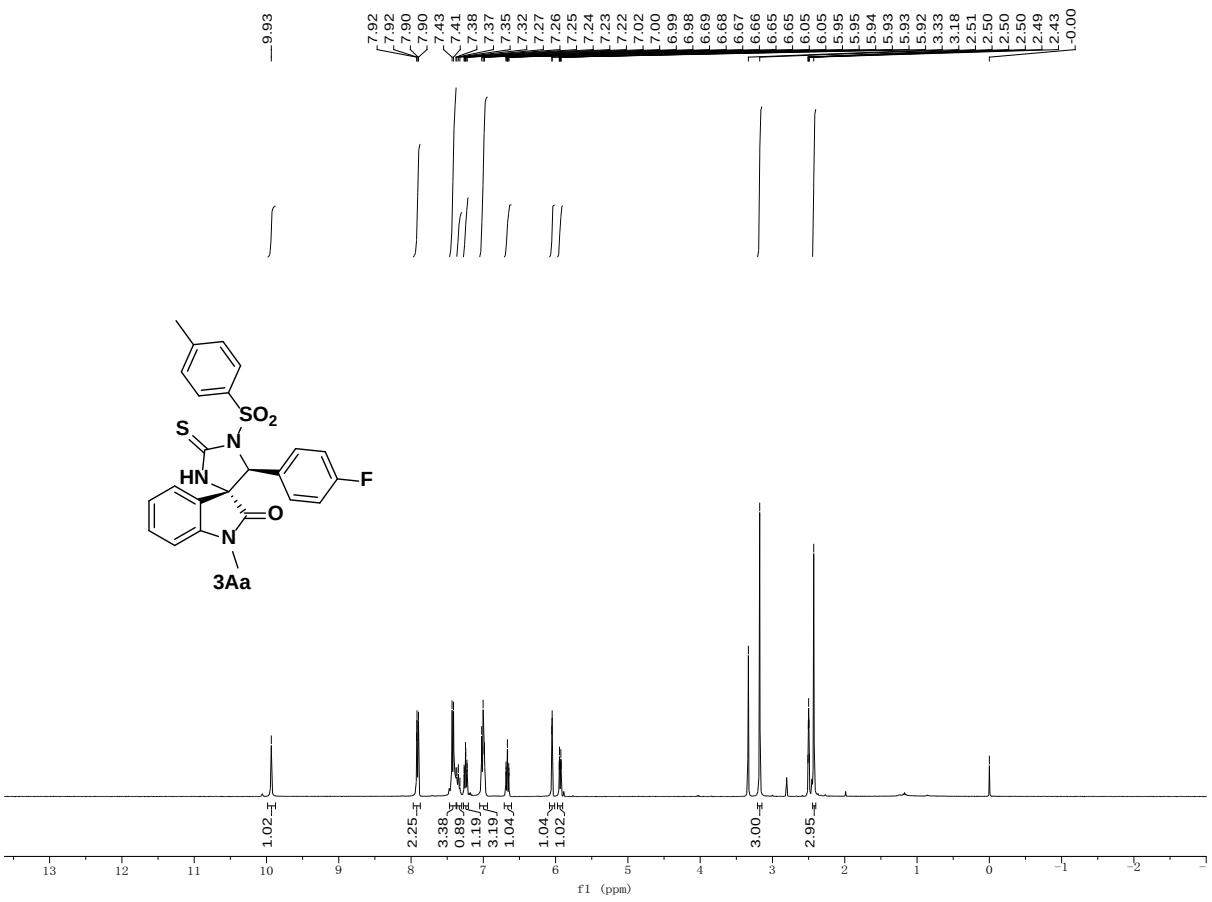

Me
S
N
O2
2m
f1 (ppm)

Product of **2n**





Product of **3Aa**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7.92
7.90
7.90
7.43
7.41
7.38
7.37
7.35
7.32
7.27
7.26
7.25
7.24
7.23
7.22
7.02
7.00
6.99
6.98
6.69
6.68
6.67
6.66
6.65
6.65
6.05
6.05
5.95
5.95
5.94
5.93
5.93
5.92
3.33
3.18
2.51
2.50
2.50
2.50
2.49
2.43
-0.00
SO2
S
N
HN
F
O
N
3Aa
1.02
2.25
3.38
0.89
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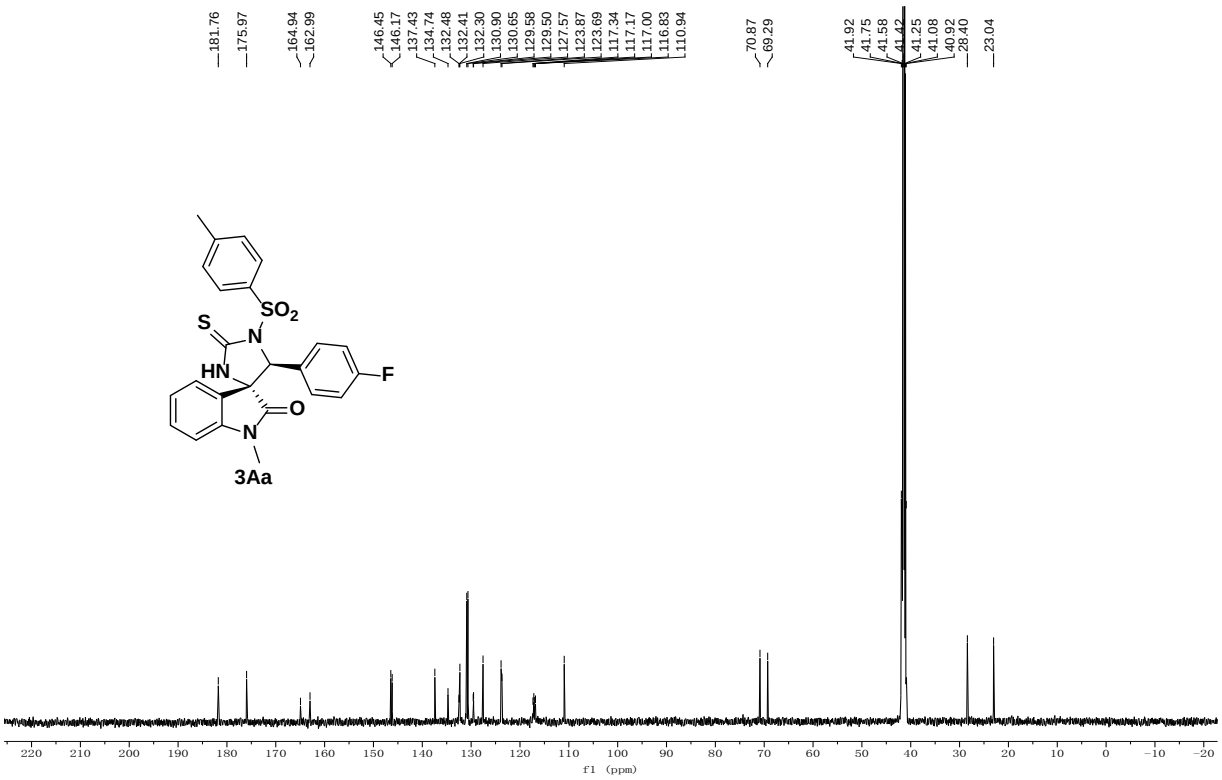
3.19
1.04
1.04
1.02
3.00
2.95
f1 (ppm)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146.45
146.17
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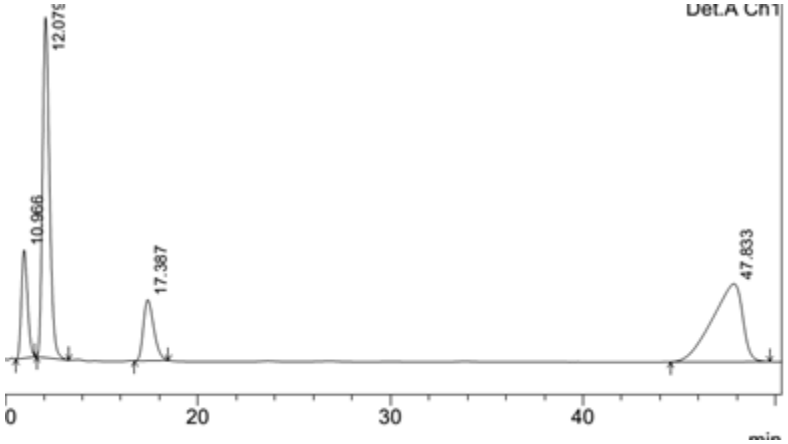
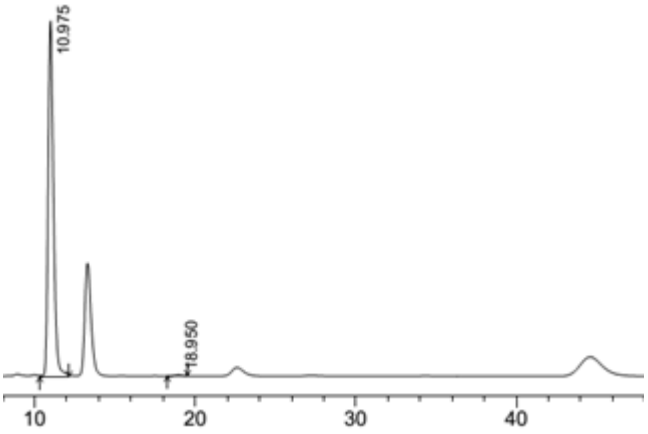
134.74
132.48
132.41
132.30
130.90
130.65
129.58
129.50
127.57
123.87
123.69
117.34
117.17
117.00
116.83
110.94
70.87
69.29
41.92
41.75
41.58
41.42
41.25
41.08
40.92
28.40
23.04
SO2
S
N
HN
F
O
N
3Aa
f1 (ppm)



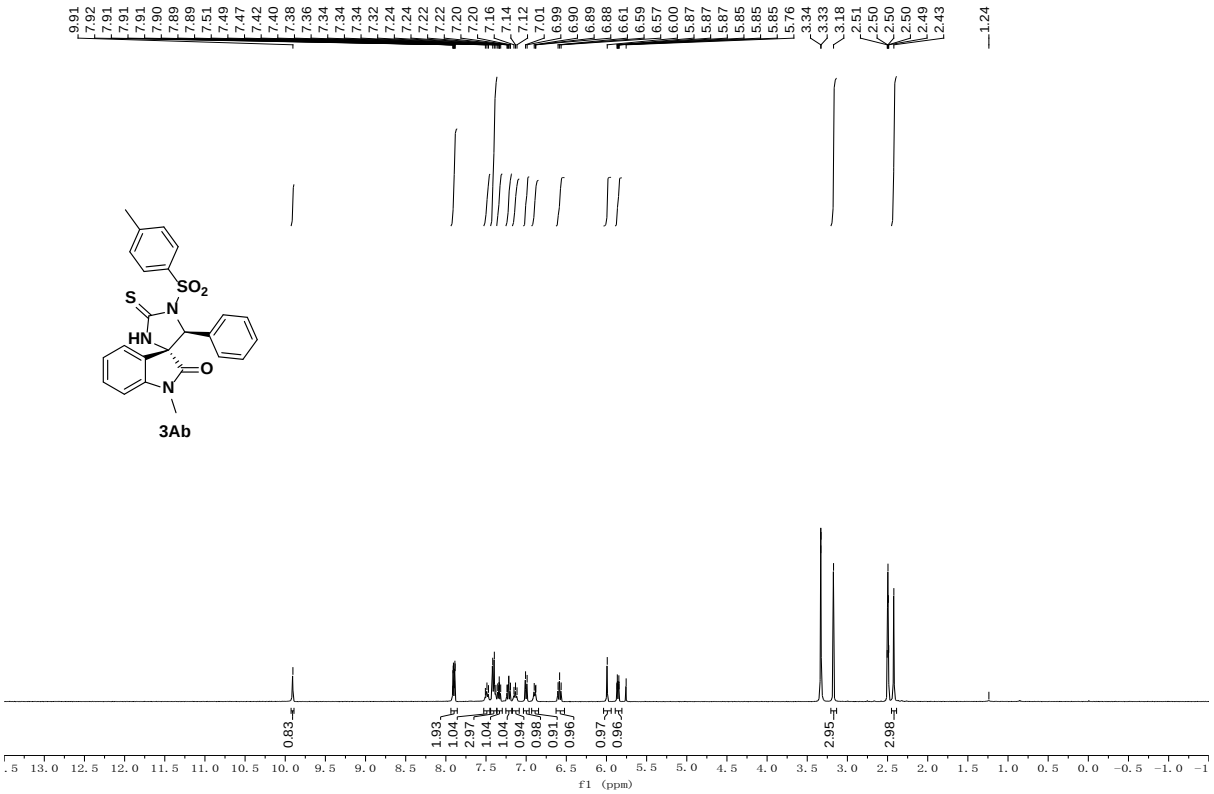
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.966	2797121	125892	11.004	18.408
2	12.079	9949322	396313	39.140	57.949
3	17.387	2679261	70848	10.540	10.359
4	47.833	9994129	90852	39.316	13.284
Total		25419833	683905	100.000	100.000



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.975	8317224	359074	99.571	99.721
2	18.950	35847	1006	0.429	0.279
Total		8353071	360080	100.000	100.000

Product of **3Ab**


9.91
7.92
7.91
7.91
7.91
7.90
7.89
7.89
7.51
7.49
7.47
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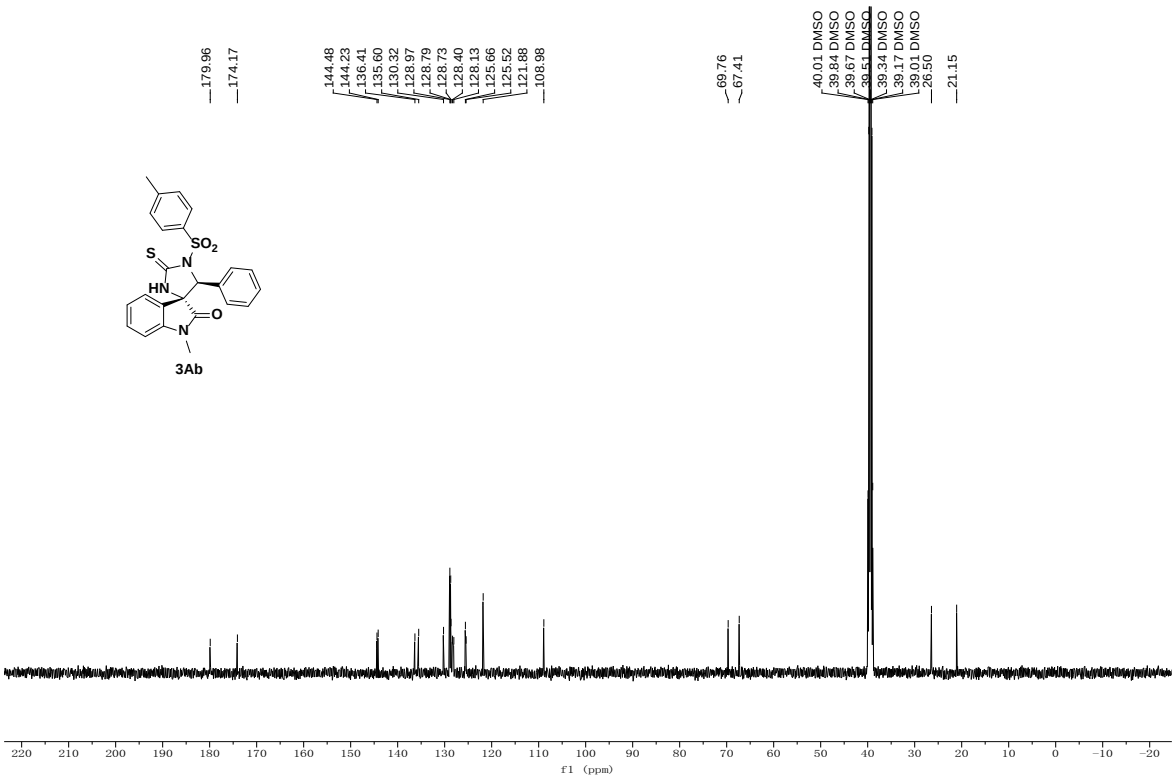
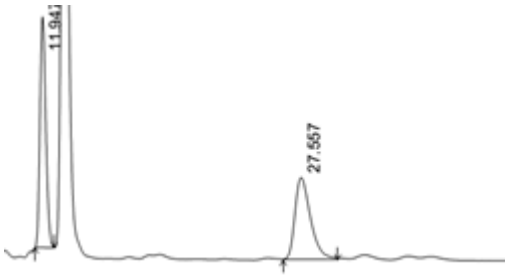
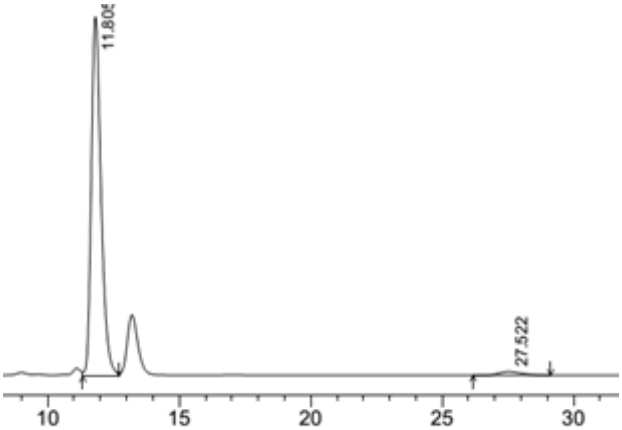
7.40
7.38
7.36
7.34
7.34
7.34
7.32
7.24
7.24
7.22
7.22
7.20
7.20
7.16
7.14
7.12
7.01
6.99
6.90
6.89
6.88
6.61
6.59
6.57
6.00
5.87
5.87
5.85
5.85
5.85
5.76
3.34
3.33
3.18
2.51
2.50
2.50
2.50
2.49
2.43
1.24
SO2
S
N
HN
O
N
3Ab
0.83
1.93
1.04
2.97
1.04
1.04
0.94
0.98
0.91
0.96
0.97
0.96
2.95
2.98
f1 (ppm)





Detector A Ch1 254nm

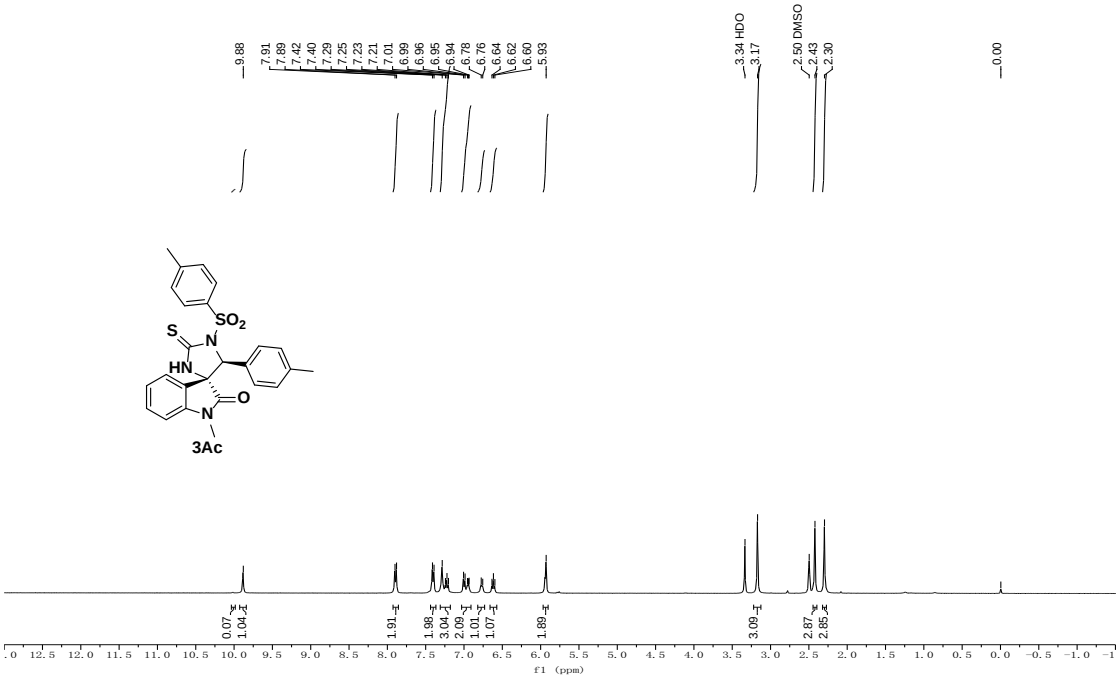
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.947	1028236	41860	50.940	73.690
2	27.557	990281	14946	49.060	26.310
Total		2018517	56805	100.000	100.000

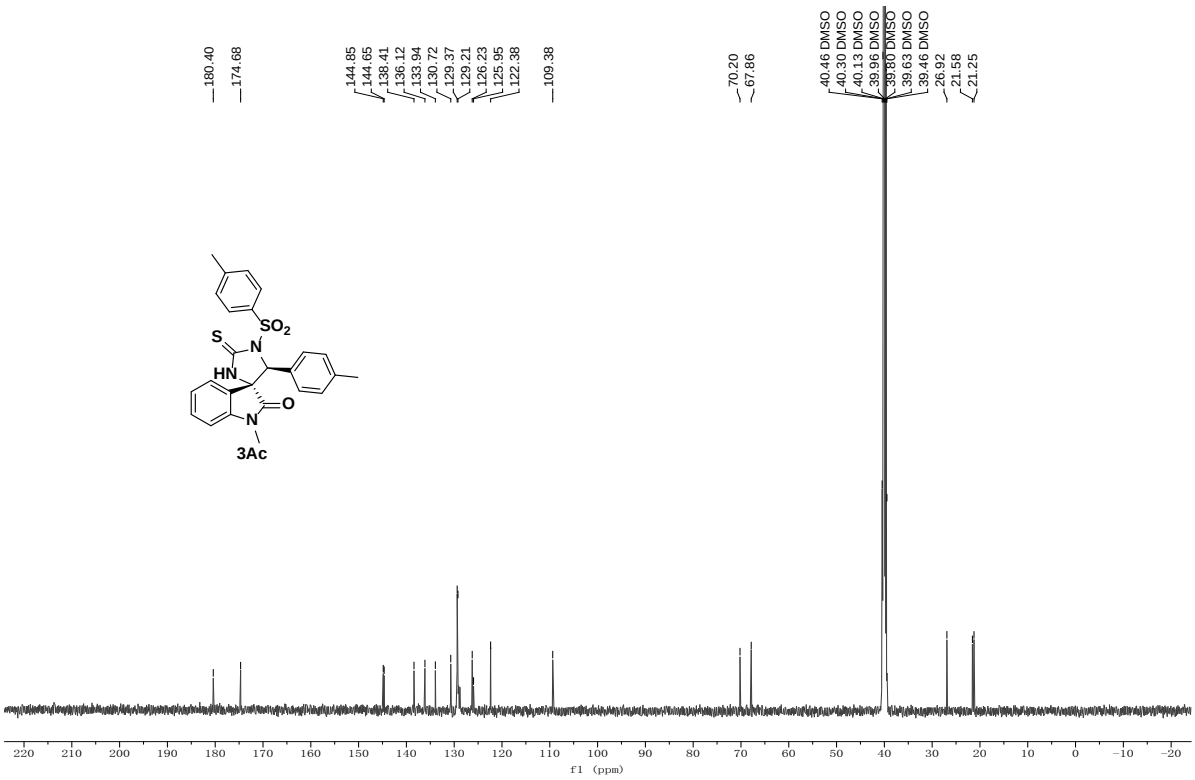


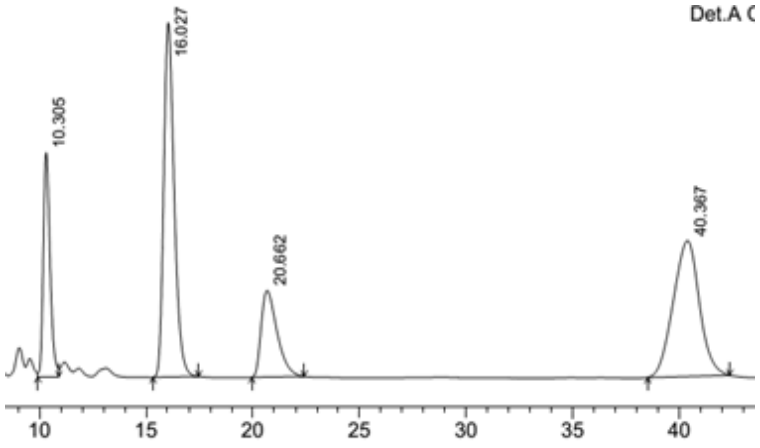
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.805	11814546	457391	97.635	99.009
2	27.522	286153	4578	2.365	0.991
Total		12100698	461969	100.000	100.000

Product of **3Ac**

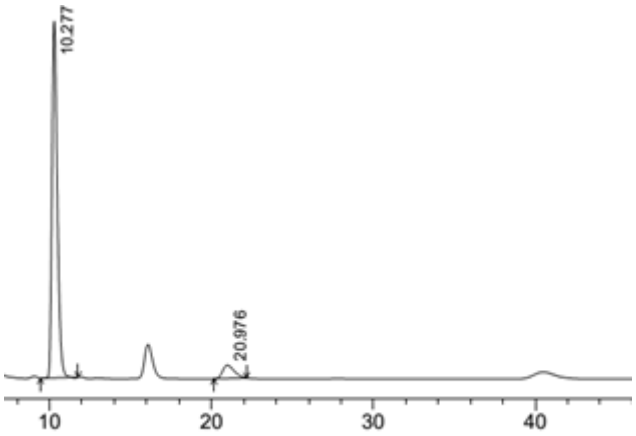






Detector A Ch1 254nm

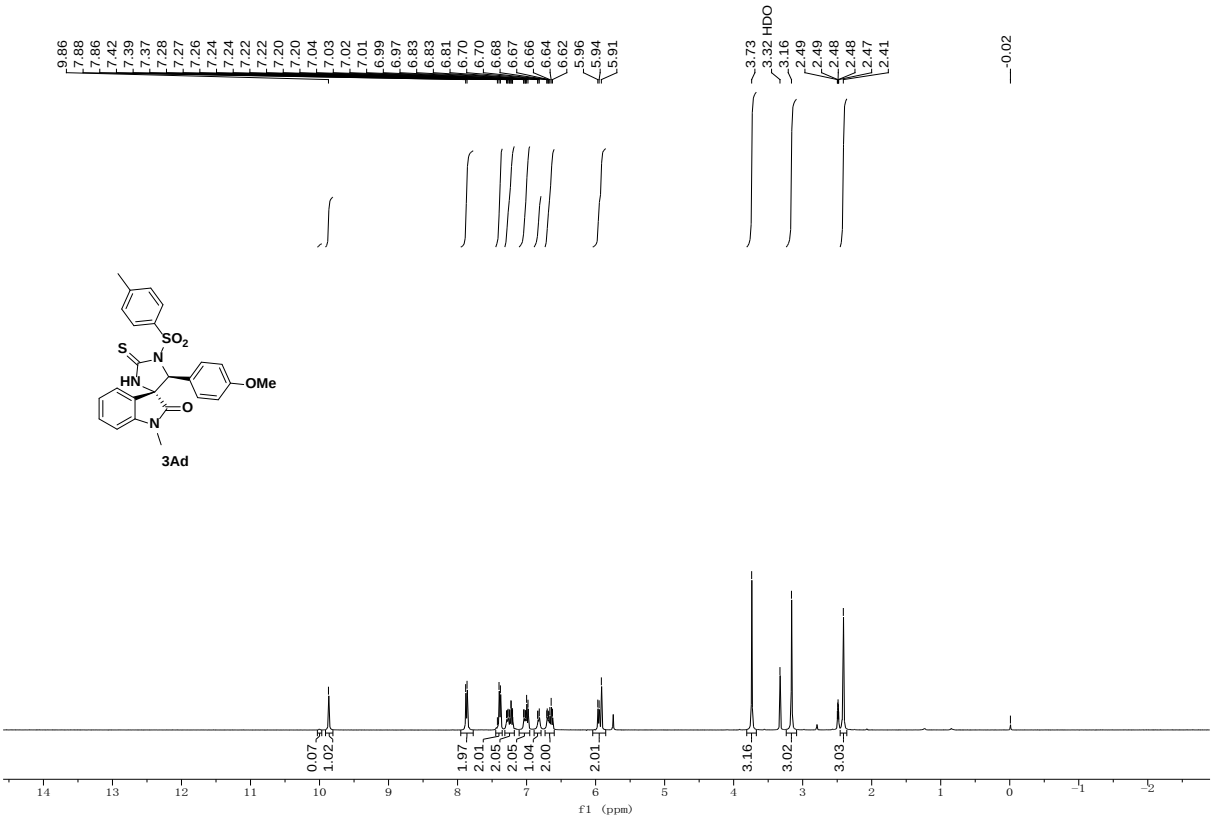
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.305	3650906	165144	14.967	27.998
2	16.027	8896914	261145	36.473	44.274
3	20.662	3316586	63686	13.596	10.797
4	40.367	8529069	99870	34.965	16.932
Total		24393475	589844	100.000	100.000

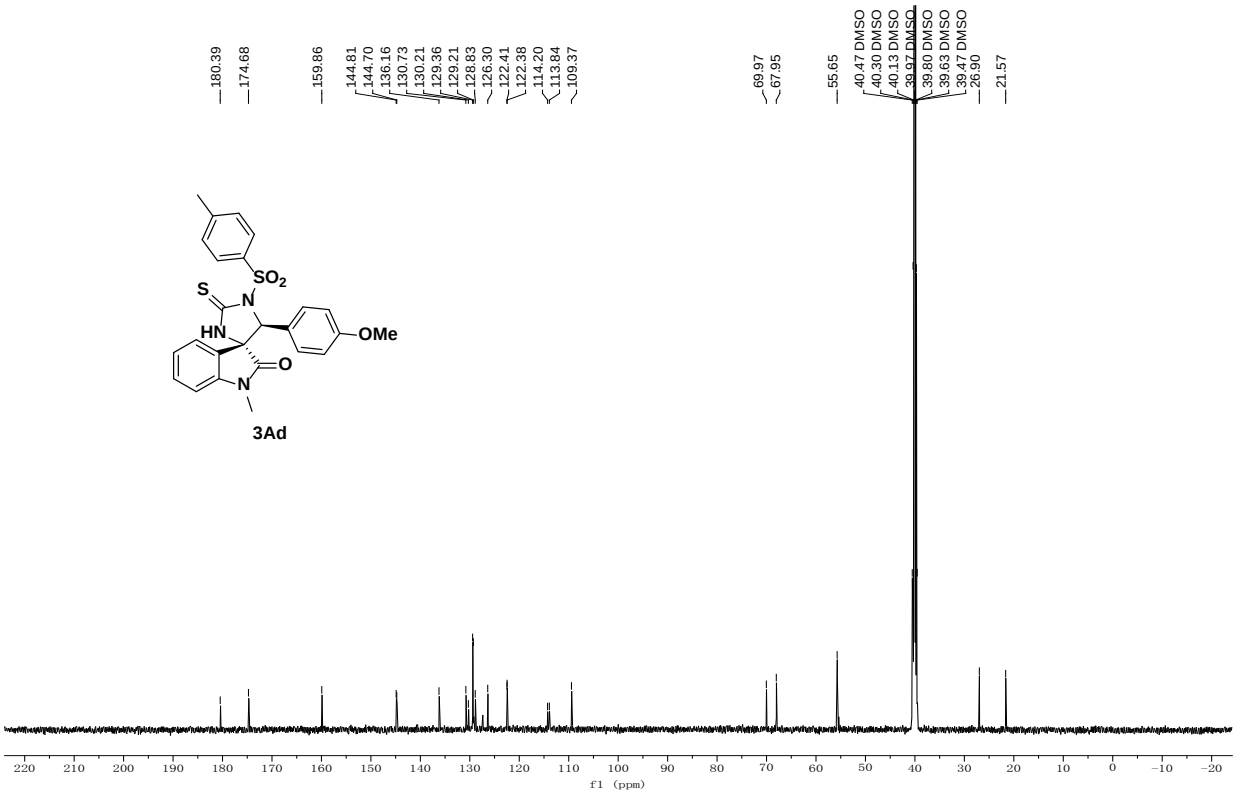


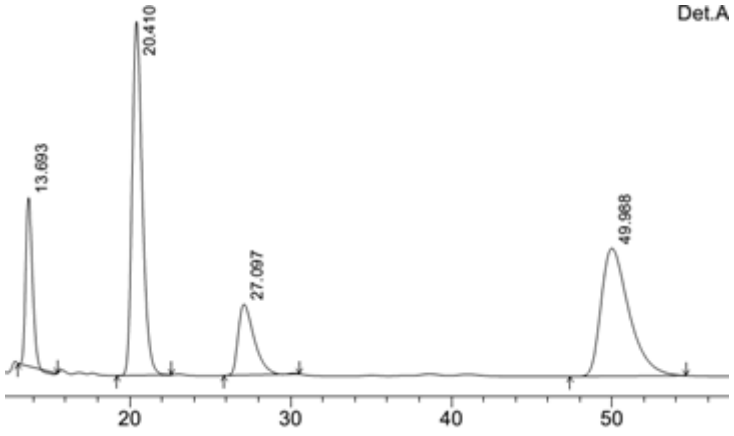
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.277	16605064	727660	92.551	96.434
2	20.976	1336536	26904	7.449	3.566
Total		17941599	754564	100.000	100.000

Product of **3Ad**



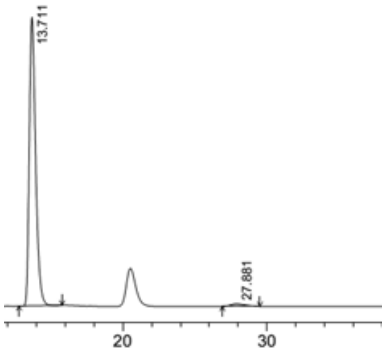




PeakTable

Detector A Ch1 254nm

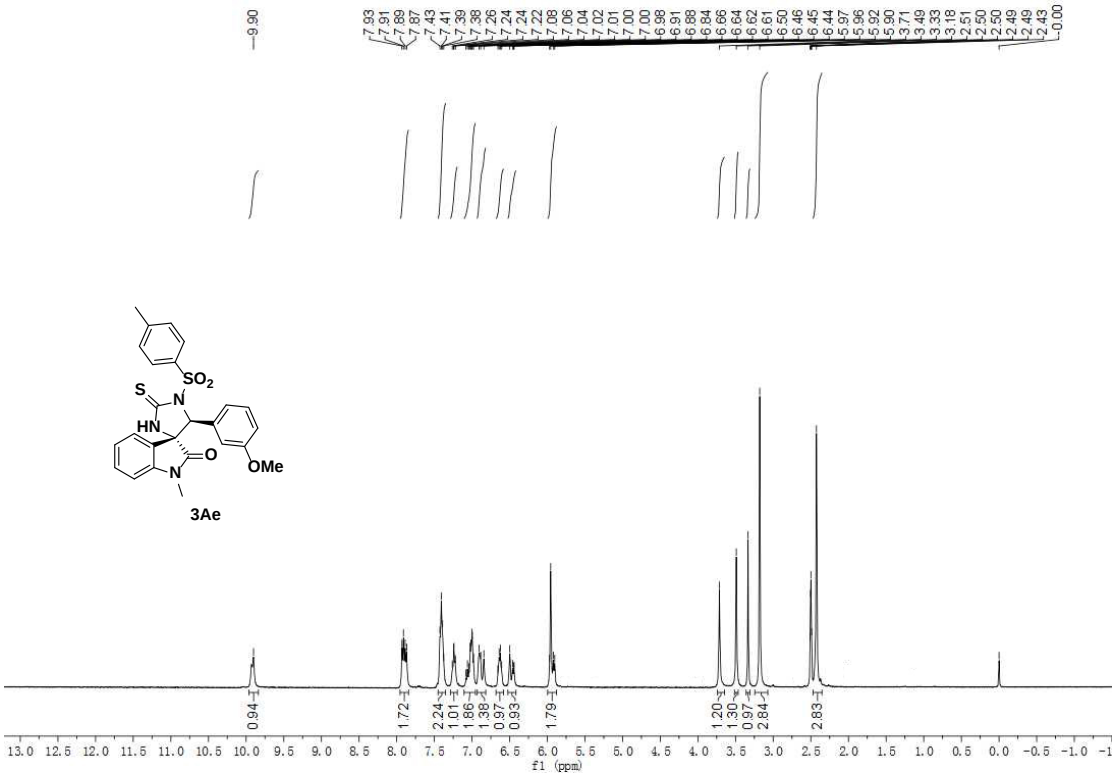
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.693	2712194	94569	11.841	23.378
2	20.410	8770747	198471	38.291	49.062
3	27.097	2758242	39667	12.042	9.806
4	49.988	8664582	71821	37.827	17.754
Total		22905766	404527	100.000	100.000

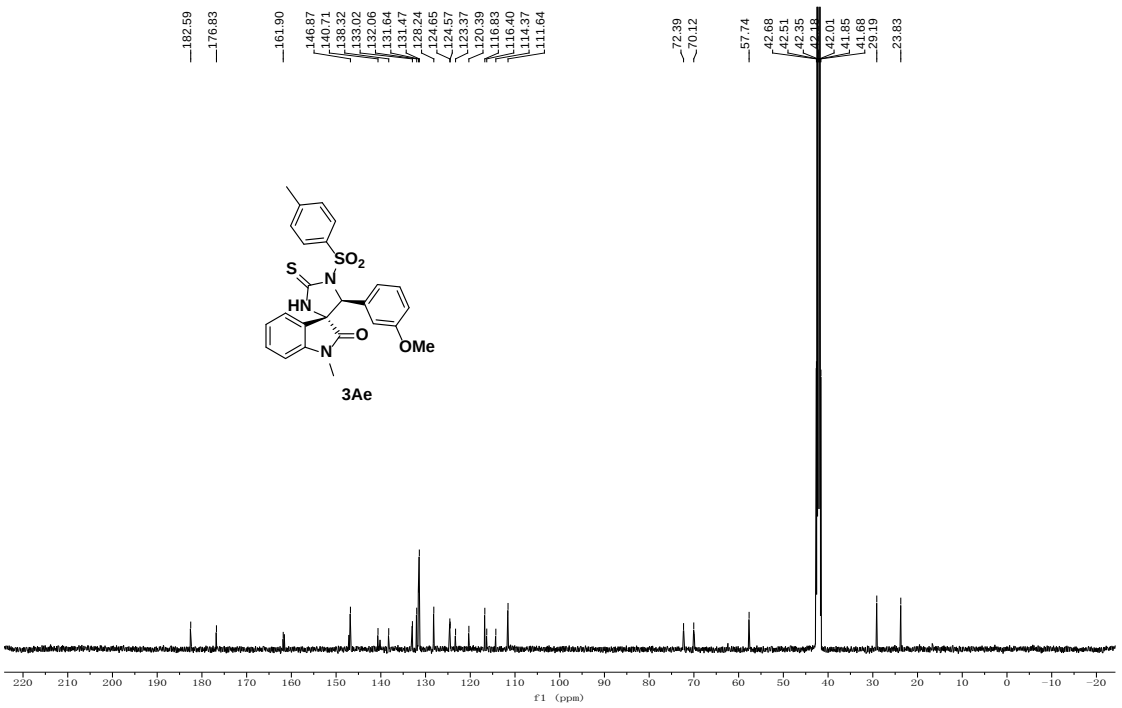


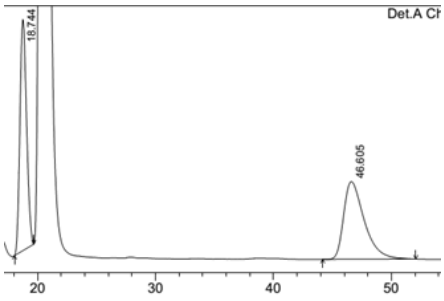
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.711	21378620	701651	98.157	99.157
2	27.881	401515	5966	1.843	0.843
Total		21780135	707617	100.000	100.000

Product of **3Ae**

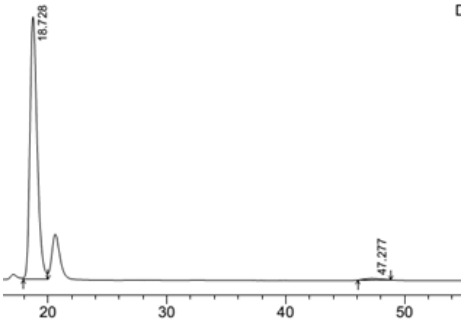






Detector A Ch1 254nm

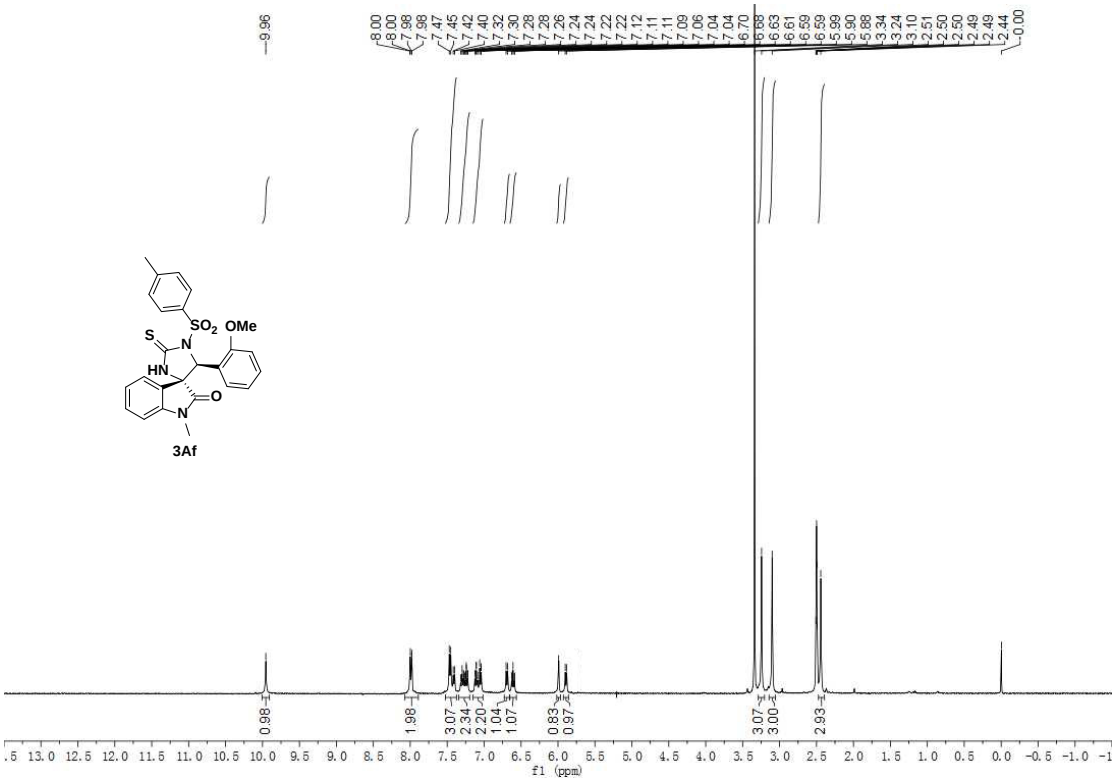
Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.744	1340128	34174	49.042	74.864
2	46.605	1392462	11474	50.958	25.136
Total		2732590	45648	100.000	100.000

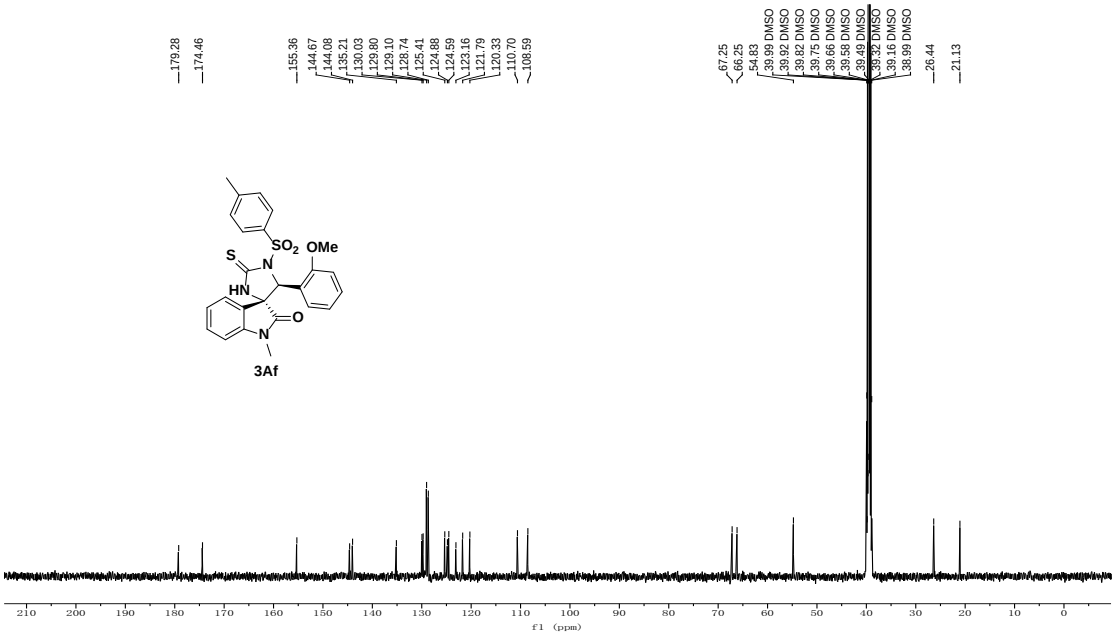


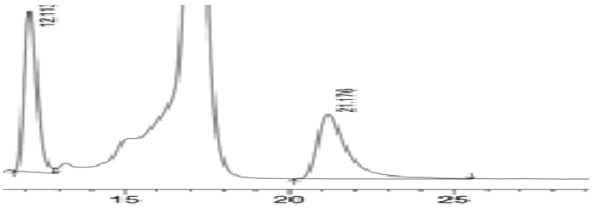
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.728	5014123	117849	98.771	99.427
2	47.277	62368	679	1.229	0.573
Total		5076491	118528	100.000	100.000

Product of **3Af**

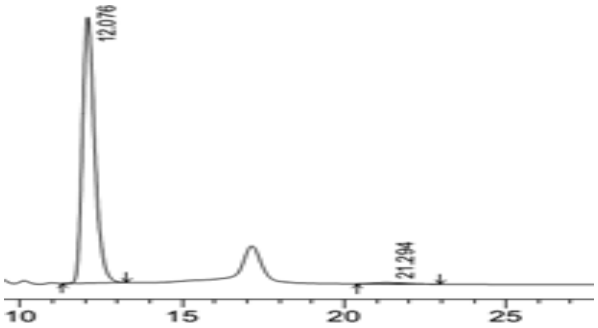






Detector A Ch1 254nm

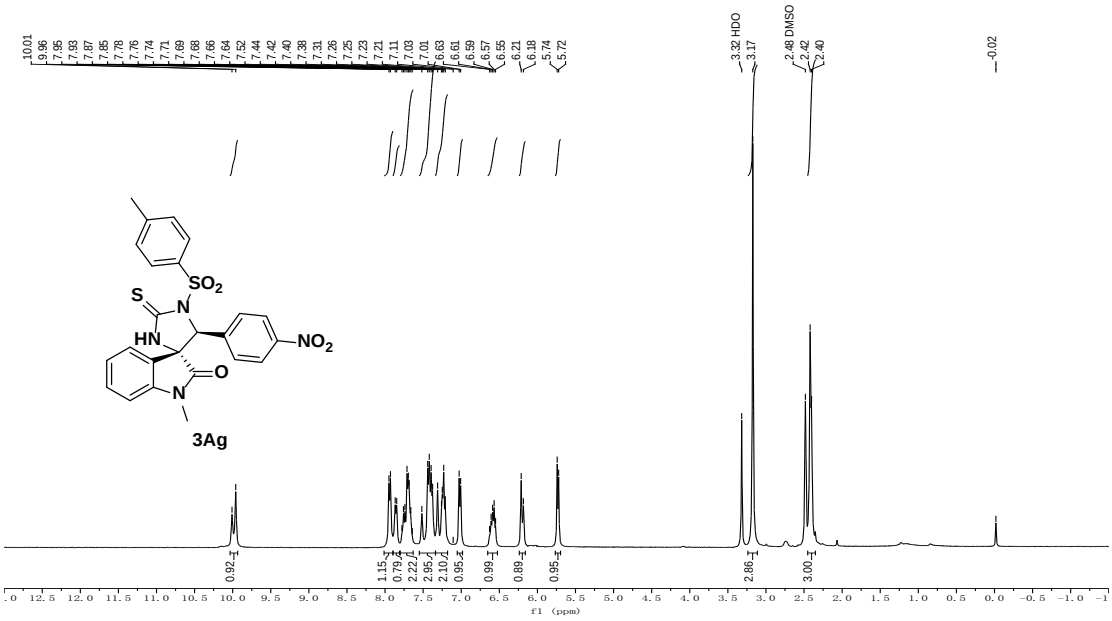
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.113	1282784	48650	50.649	71.425
2	21.176	1249889	19463	49.351	28.575
Total		2532672	68113	100.000	100.000

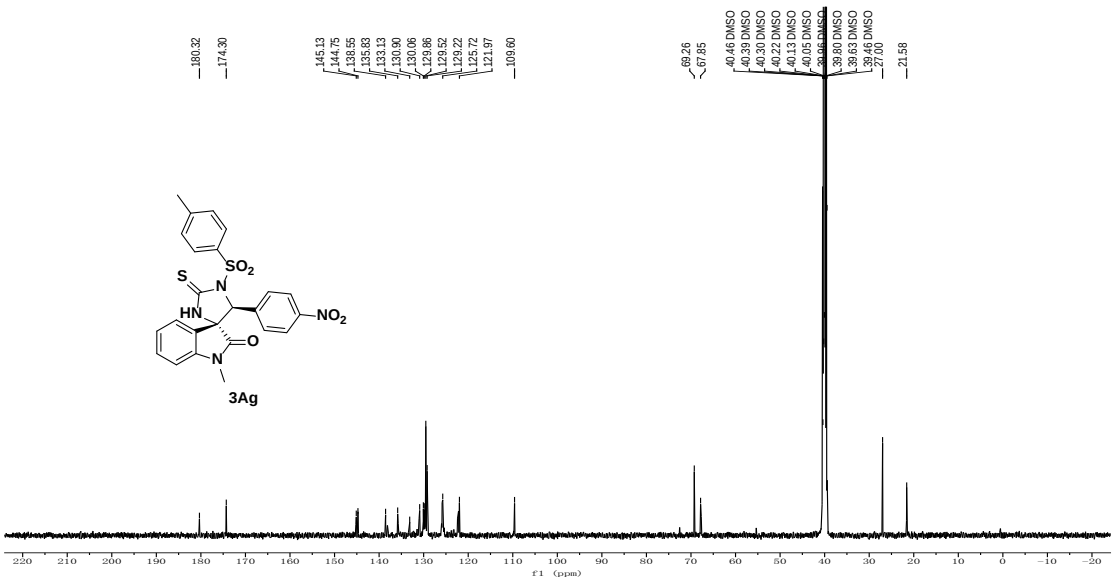


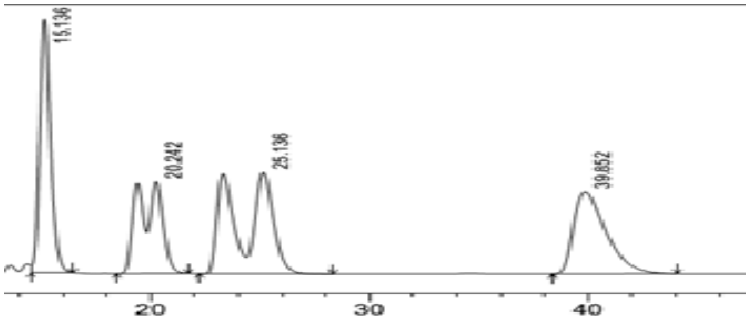
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.076	13655469	520487	98.852	99.497
2	21.294	158588	2630	1.148	0.503
Total		13814057	523117	100.000	100.000

Product of **3Ag**



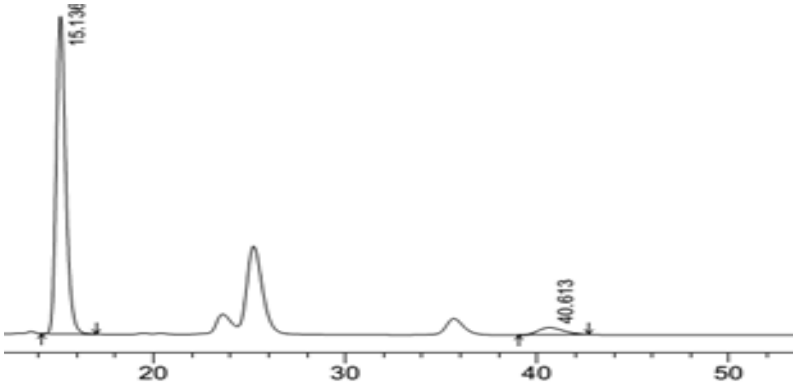




PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.136	13769439	395530	24.808	47.942
2	20.242	11024739	143519	19.863	17.396
3	25.136	17432653	157962	31.408	19.147
4	39.852	13276241	128006	23.920	15.516
Total		55503071	825018	100.000	100.000

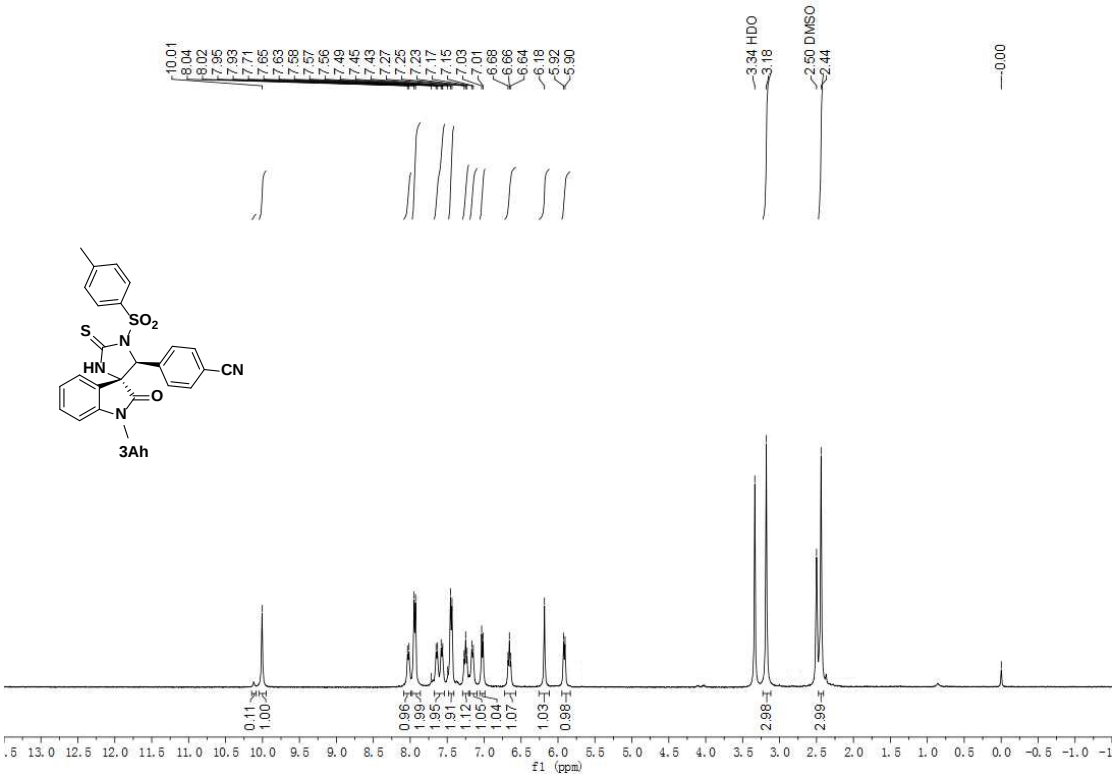


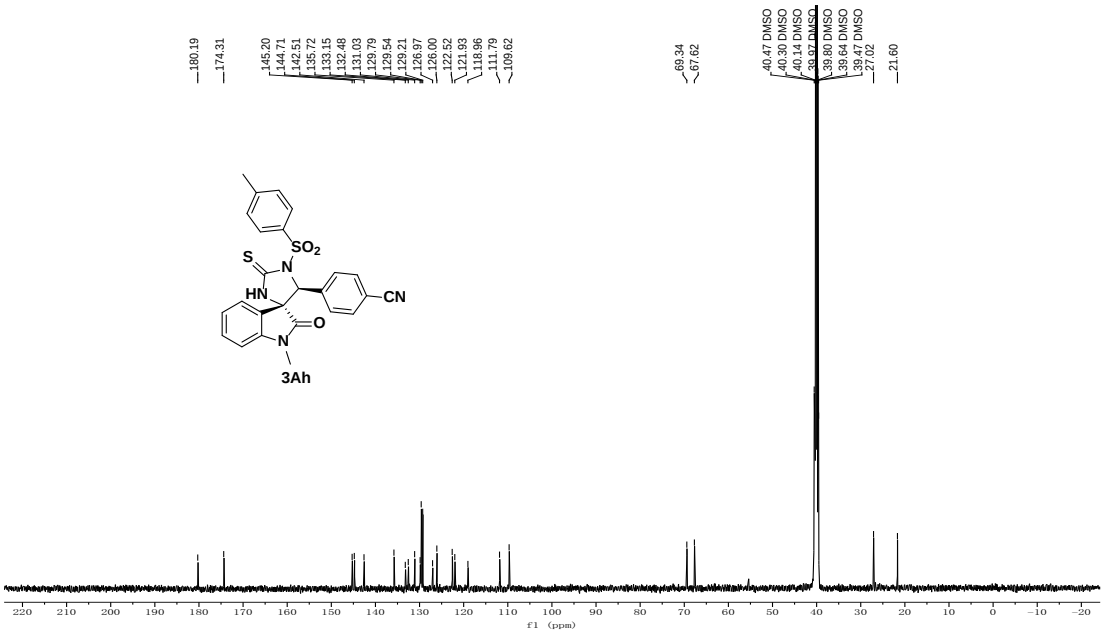
PeakTable

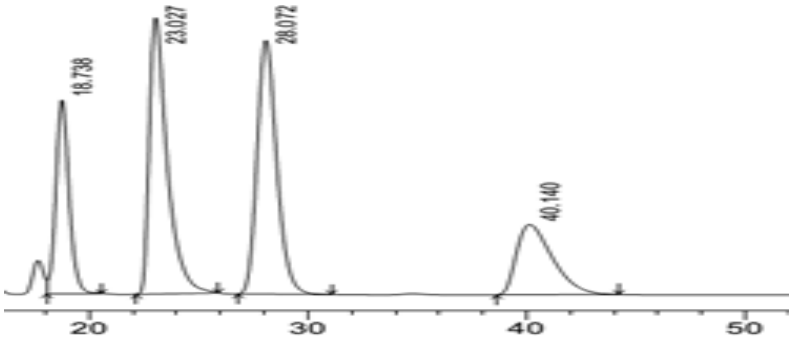
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.136	11624735	338855	94.363	97.825
2	40.613	694428	7533	5.637	2.175
Total		12319163	346388	100.000	100.000

Product of **3Ah**



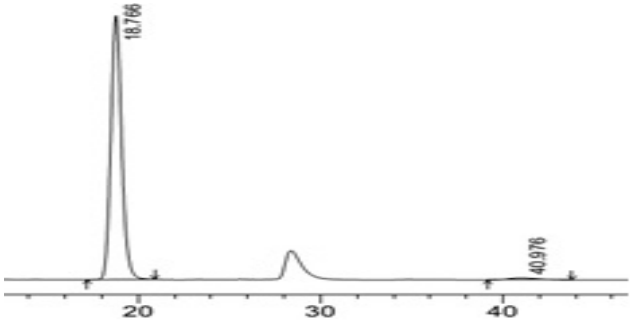




PeakTable

Detector A Ch1 254nm

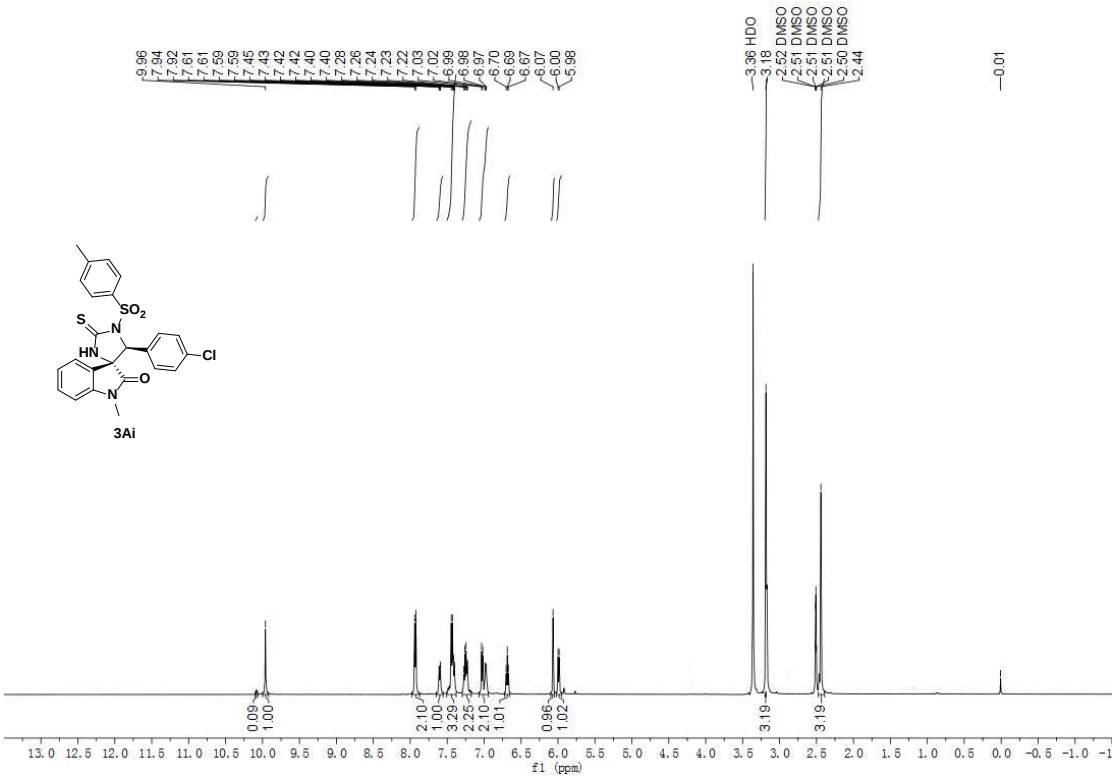
Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.738	6904160	163352	17.122	24.405
2	23.027	13265833	232913	32.899	34.798
3	28.072	13386371	213908	33.198	31.959
4	40.140	6766638	59153	16.781	8.838
Total		40323002	669326	100.000	100.000

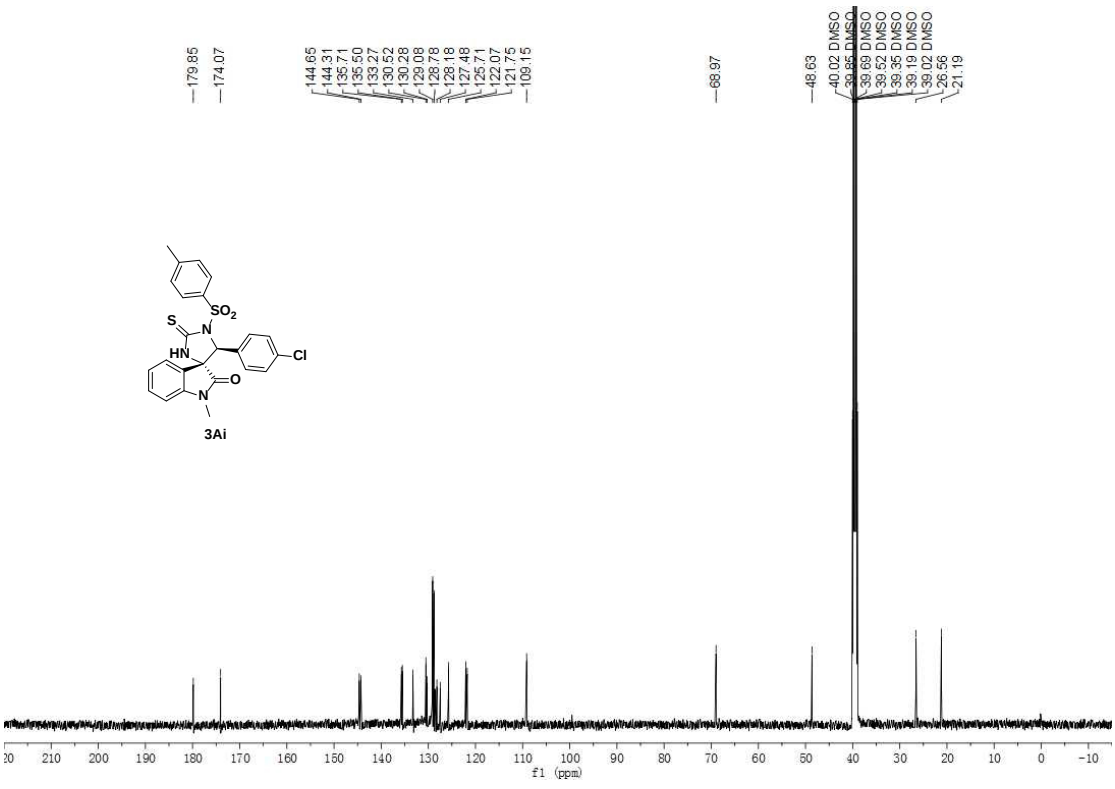


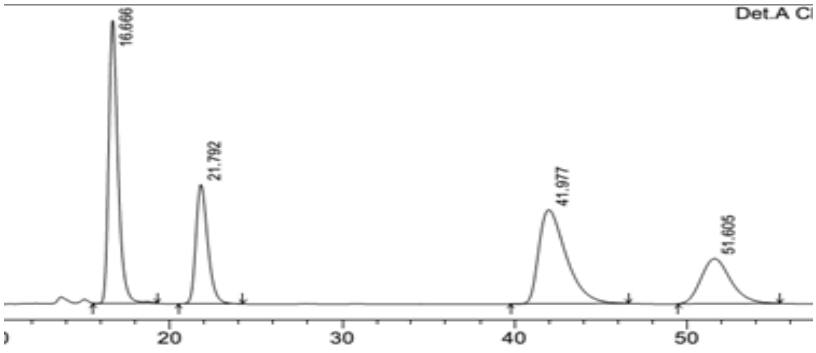
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.766	14906604	361735	98.176	99.265
2	40.976	276906	2678	1.824	0.735
Total		15183510	364412	100.000	100.000

Product of **3Ai**

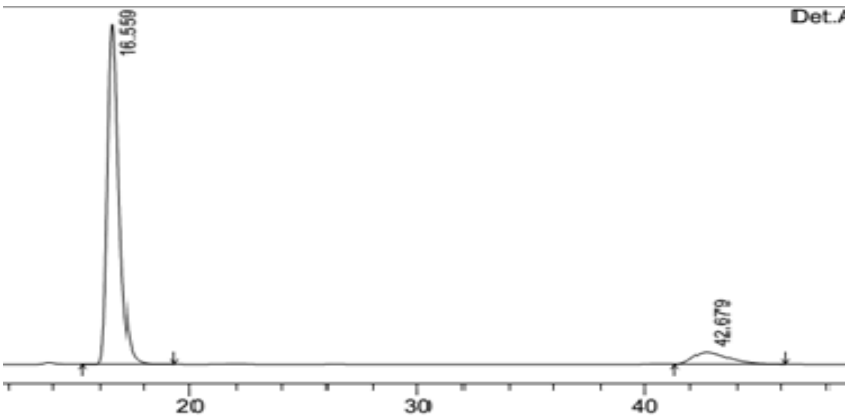

9.96
7.94
7.92
7.61
7.61
7.59
7.59
7.45
7.43
7.42
7.42
7.40
7.40
7.28
7.26
7.24
7.23
7.22
7.03
7.02
6.98
6.98
6.97
6.70
6.69
6.67
6.07
6.00
5.98
3.36 HDO
3.18
2.62 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.44
0.01
SO2
S
N
HN
Cl
O
N
3Ai
0.09
1.00
2.10
1.00
3.29
2.25
2.10
1.01
0.96
1.02
3.19
3.19
f1 (ppm)


179.85
174.07
144.65
144.31
135.71
135.50
133.27
130.52
130.28
129.08
128.78
128.18
127.48
125.71
122.07
121.75
109.15
68.97
48.63
40.02 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
39.35 DMSO
39.19 DMSO
39.02 DMSO
26.56
21.19
SO2
S
N
HN
Cl
O
N
3Ai
f1 (ppm)



Detector A Ch1 254nm

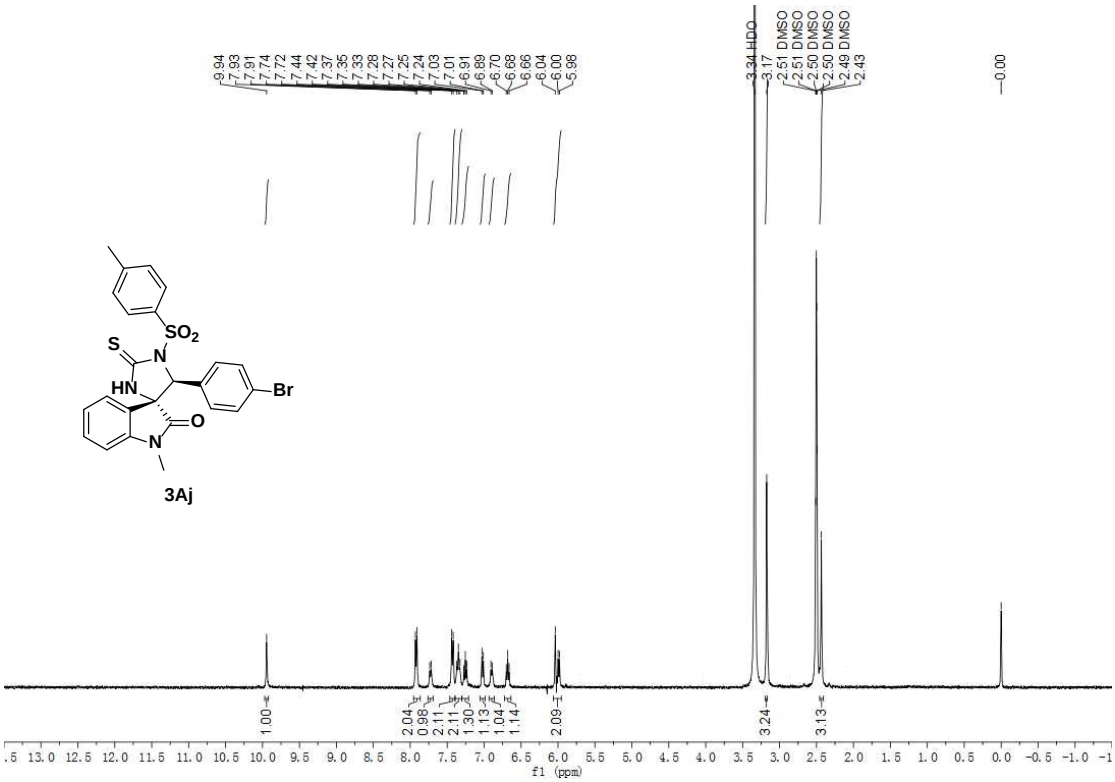
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.666	5208499	137060	33.354	52.287
2	21.792	2754013	57714	17.636	22.018
3	41.977	5046317	45526	32.315	17.368
4	51.605	2607122	21829	16.695	8.327
Total		15615952	262129	100.000	100.000

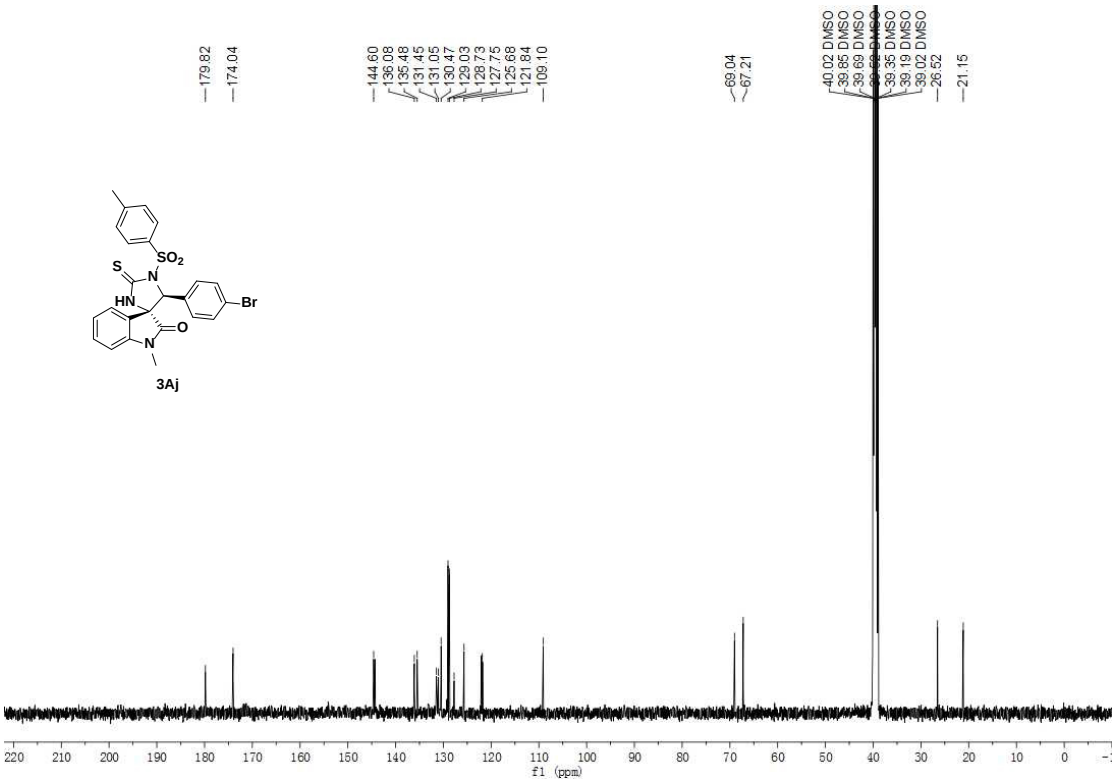


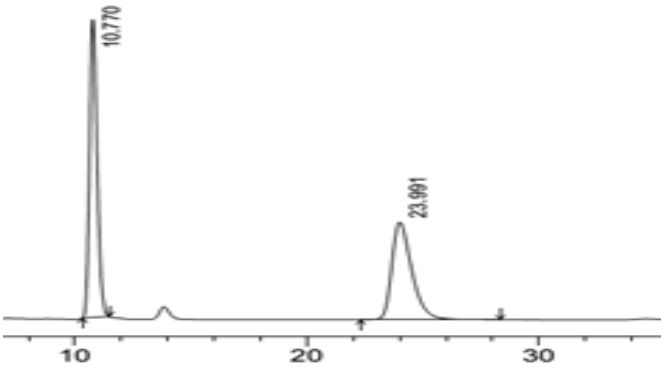
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.559	18873435	507391	90.445	96.526
2	42.679	1993863	18260	9.555	3.474
Total		20867298	525651	100.000	100.000

Product of **3Aj**

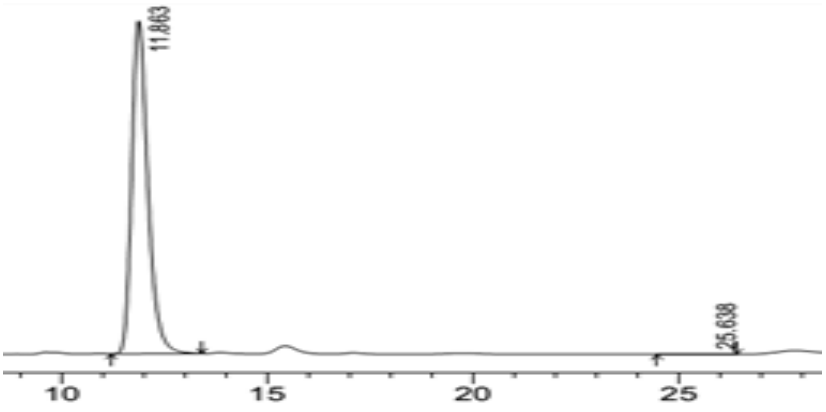

9.94
7.93
7.91
7.74
7.72
7.44
7.42
7.37
7.35
7.33
7.28
7.27
7.25
7.24
7.03
7.01
6.91
6.89
6.70
6.68
6.66
6.04
6.00
5.98
3.34 HDO
3.17
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
2.43
0.00
SO2
S
N
HN
Br
O
N
3Aj
1.00
2.04
0.98
2.11
2.11
1.30
1.13
1.04
1.14
2.09
3.24
3.13
f1 (ppm)


179.82
174.04
144.60
136.08
135.48
131.45
131.05
130.47
129.03
128.73
127.75
125.68
121.84
109.10
69.04
67.21
40.02 DMSO
39.85 DMSO
39.69 DMSO
39.35 DMSO
39.19 DMSO
39.02 DMSO
26.52
21.15
SO2
S
N
HN
Br
O
N
3Aj
f1 (ppm)



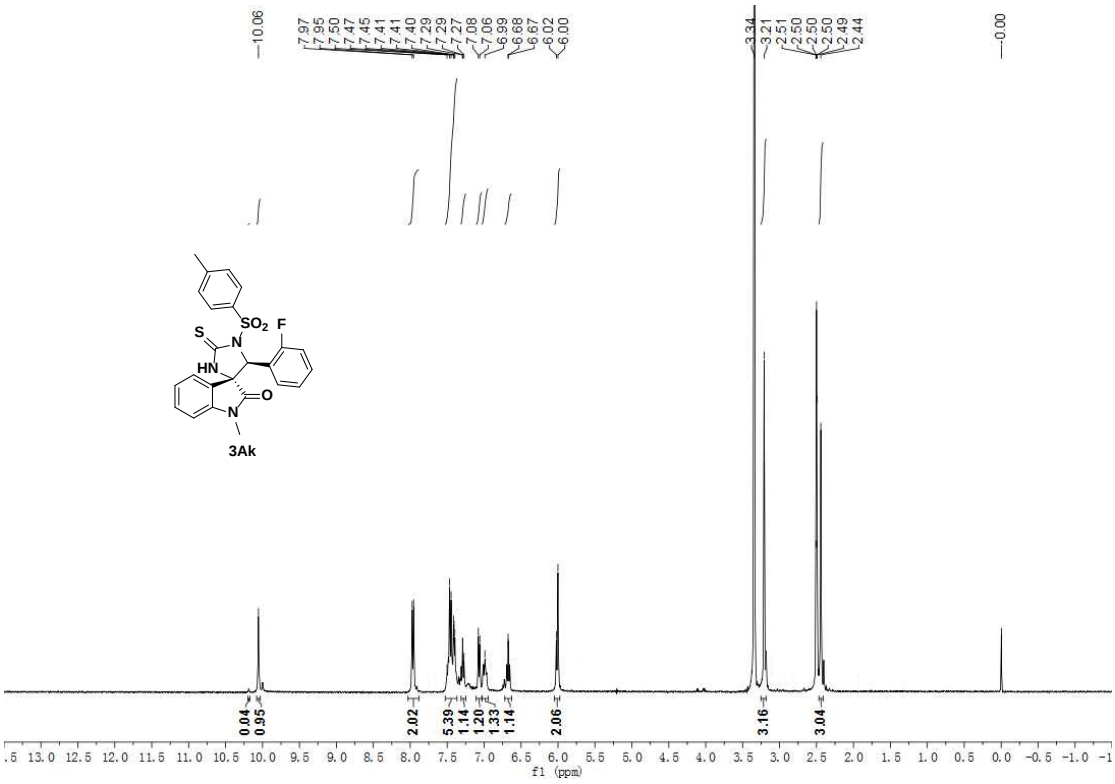
Detector A Ch1 254nm

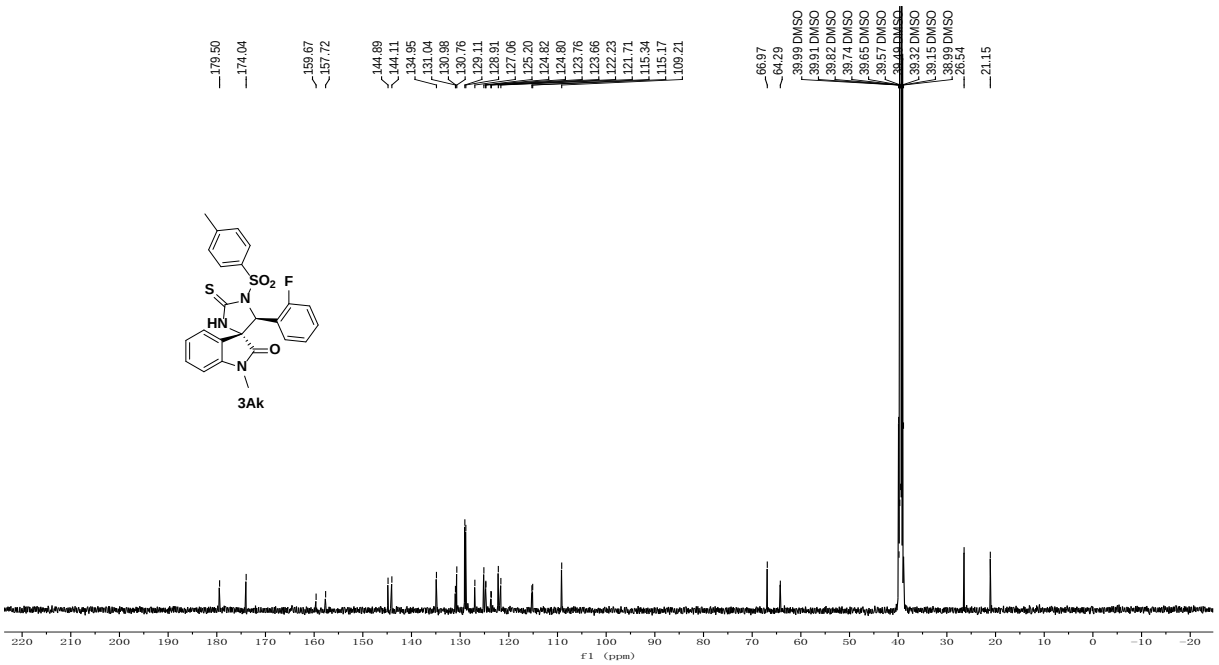
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.770	3438744	149993	53.729	75.356
2	23.991	2961362	49053	46.271	24.644
Total		6400107	199046	100.000	100.000

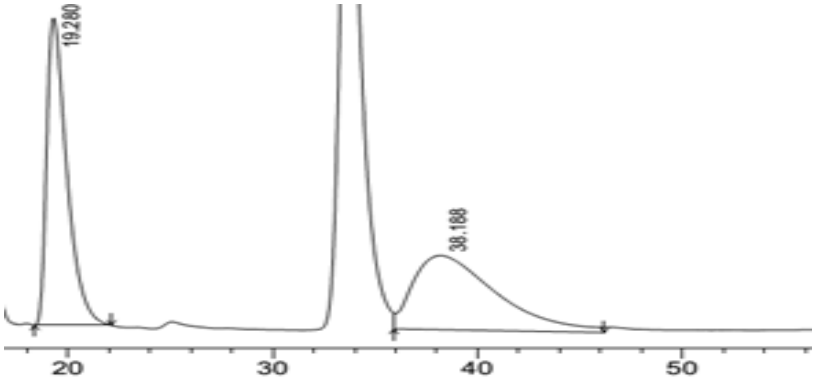


Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.863	6938645	254456	99.937	99.970
2	25.638	4379	77	0.063	0.030
Total		6943024	254533	100.000	100.000

Product of **3Ak**

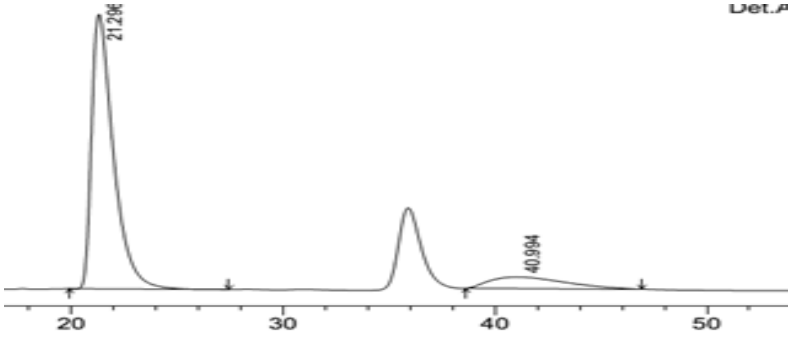

10.06
7.97
7.95
7.50
7.47
7.45
7.41
7.41
7.40
7.29
7.29
7.27
7.08
7.06
6.99
6.68
6.67
6.02
6.00
3.34
3.21
2.51
2.50
2.50
2.50
2.49
2.44
0.00
SO2 F
S
N
HN
O
N
3Ak
0.04
0.95
2.02
5.39
1.14
1.20
1.33
1.14
2.06
3.16
3.04
f1 (ppm)


179.50
174.04
159.67
157.72
144.89
144.11
134.95
131.04
130.98
130.76
129.11
128.91
127.06
125.20
124.82
124.80
123.76
123.66
122.23
121.71
115.34
115.17
109.21
66.97
64.29
39.99 DMSO
39.91 DMSO
39.82 DMSO
39.74 DMSO
39.65 DMSO
39.57 DMSO
39.49 DMSO
39.32 DMSO
39.15 DMSO
38.99 DMSO
26.54
21.15
SO2 F
S
N
HN
O
N
3Ak
f1 (ppm)



Detector A Ch1 254nm

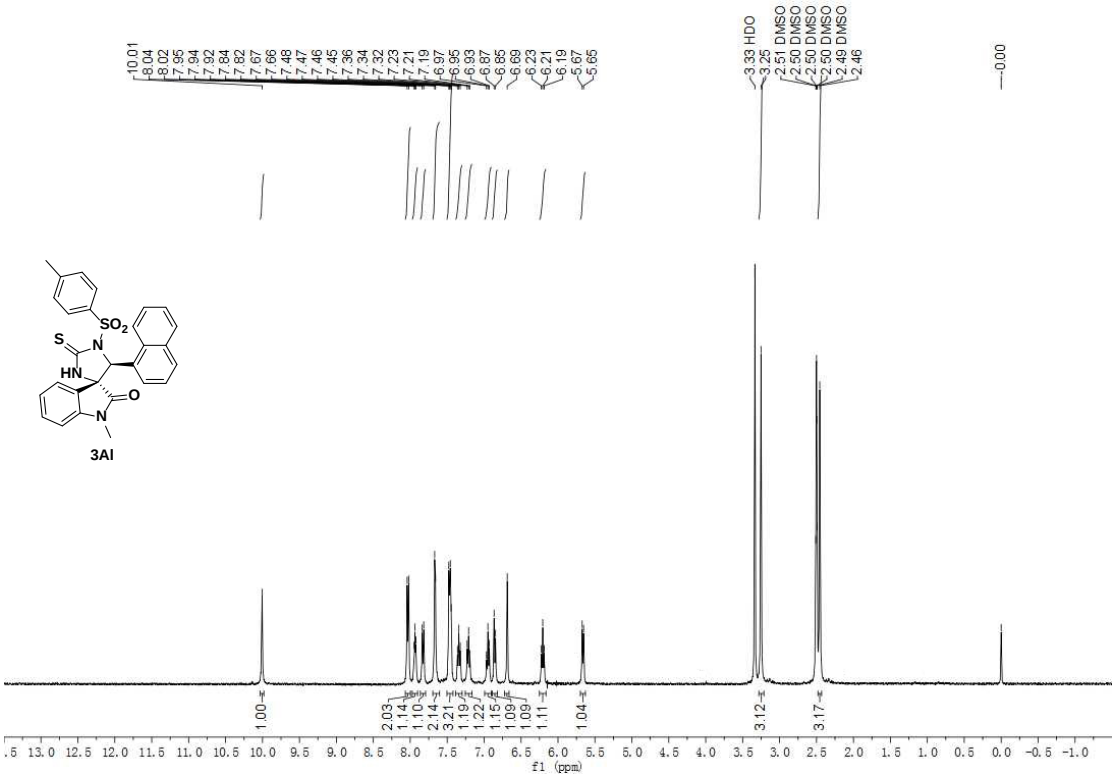
Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.280	7446027	108830	49.921	80.539
2	38.188	7469679	26297	50.079	19.461
Total		14915706	135127	100.000	100.000

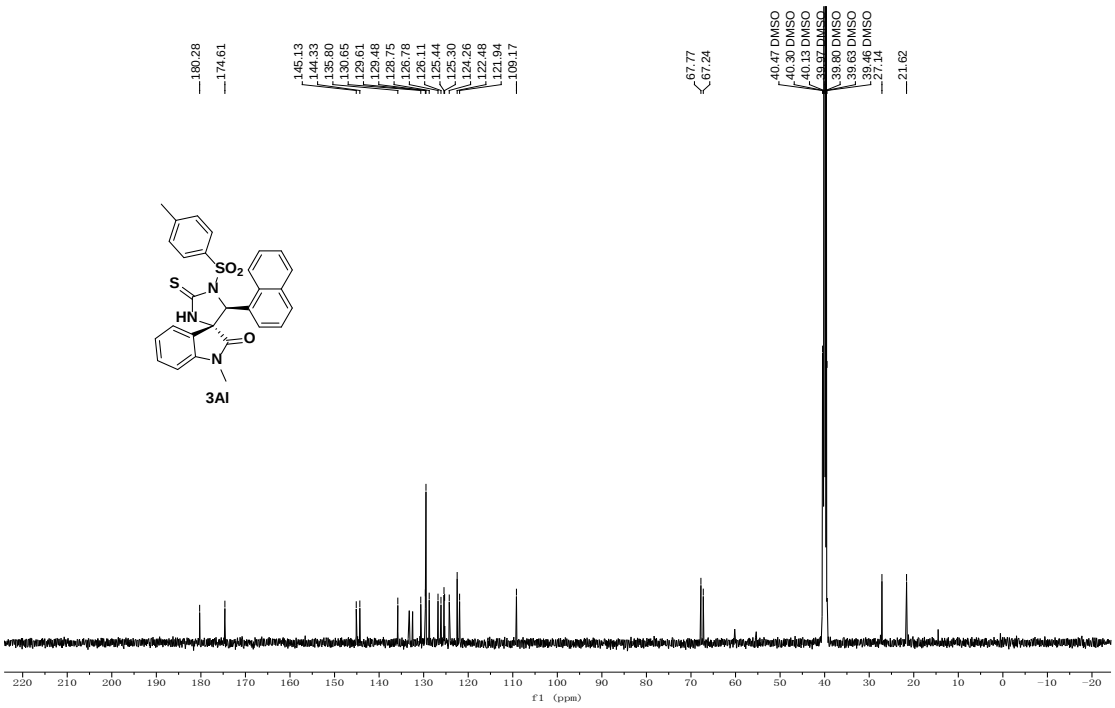


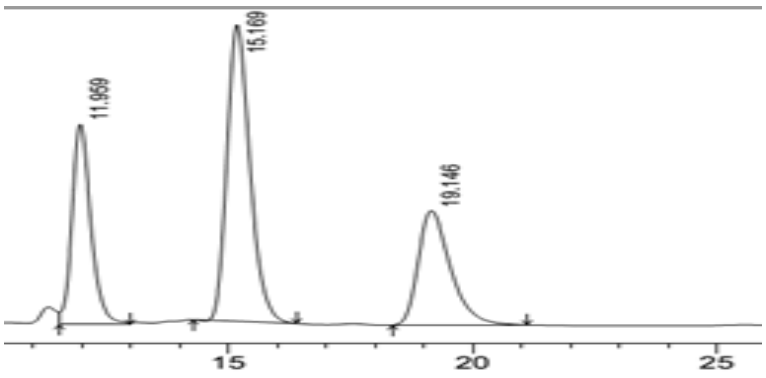
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.296	11202889	155953	87.297	95.953
2	40.994	1630233	6578	12.703	4.047
Total		12833122	162531	100.000	100.000

Product of **3Al**

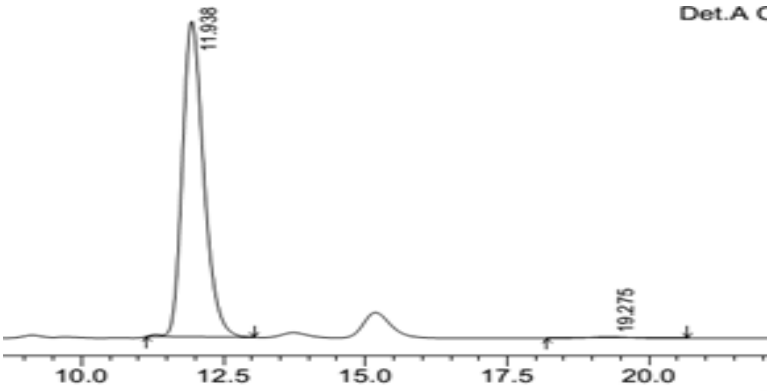






Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.959	2401369	89245	26.553	32.788
2	15.169	4314401	132075	47.707	48.523
3	19.146	2327859	50869	25.740	18.689
Total		9043629	272189	100.000	100.000

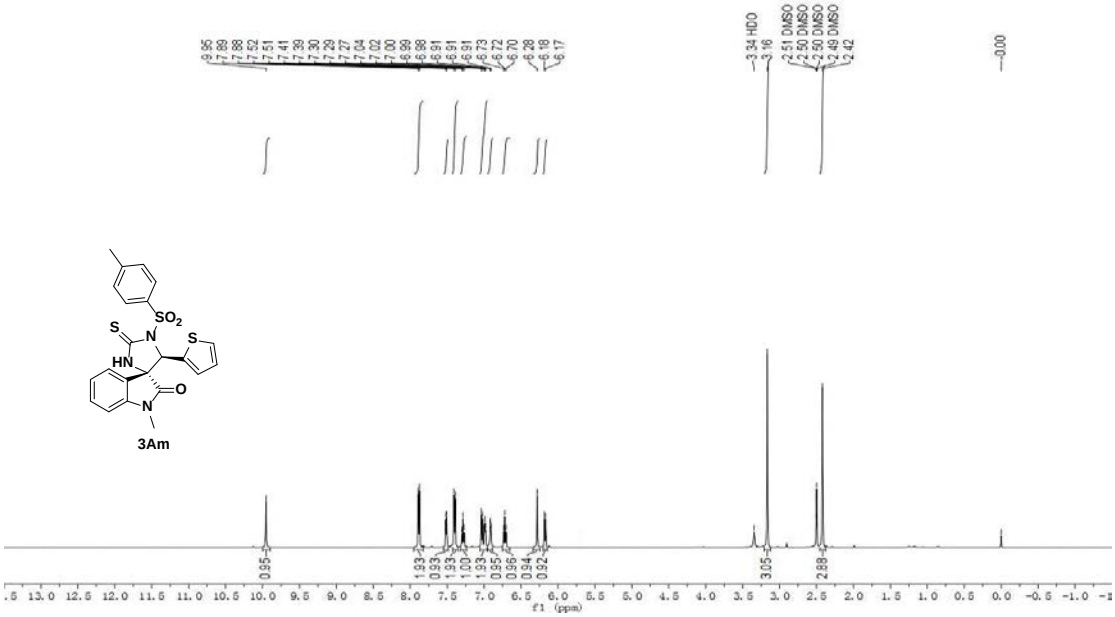


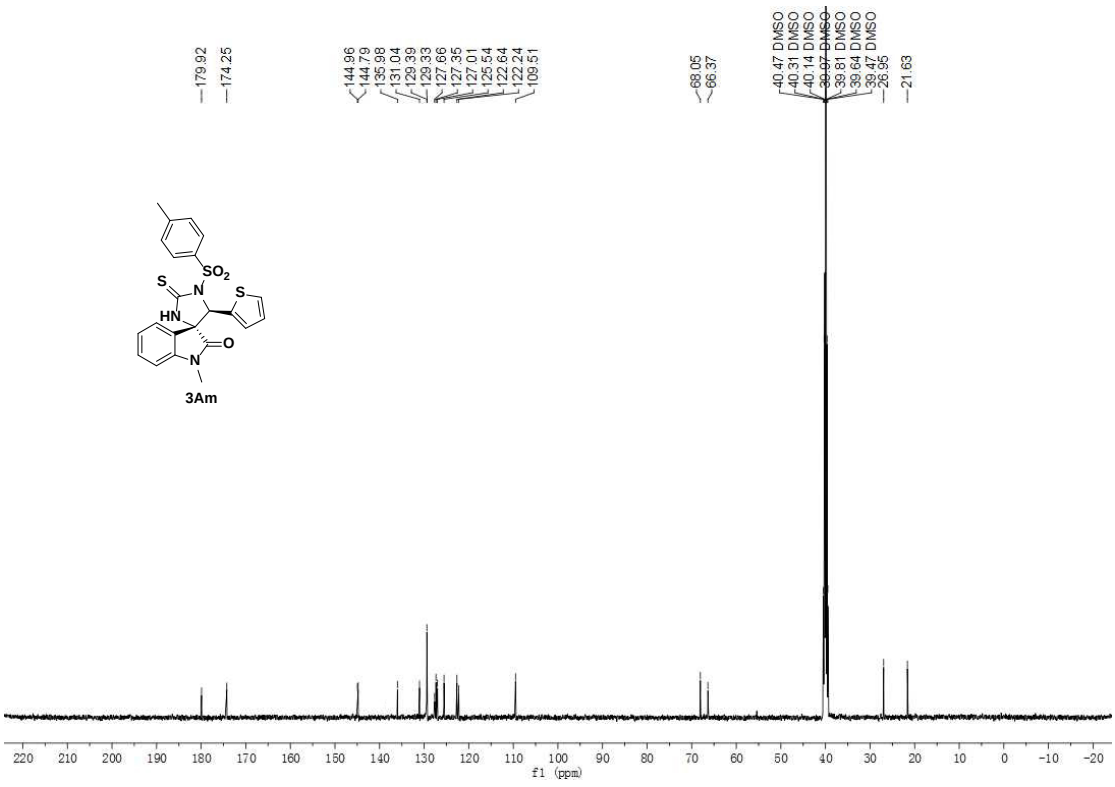
PeakTable

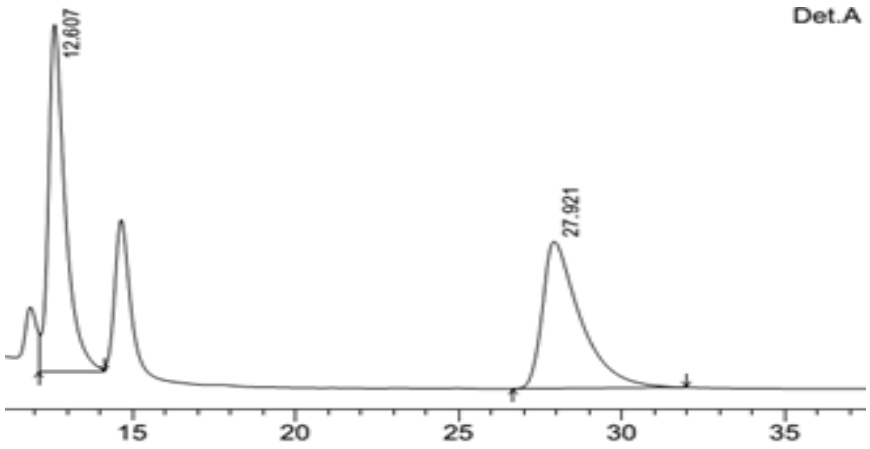
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.938	20617157	784847	99.296	99.636
2	19.275	146101	2868	0.704	0.364
Total		20763258	787715	100.000	100.000

Product of **3Am**

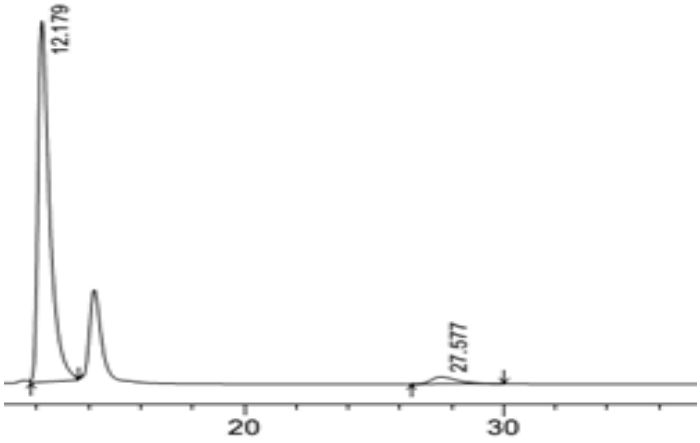

3Am


3Am



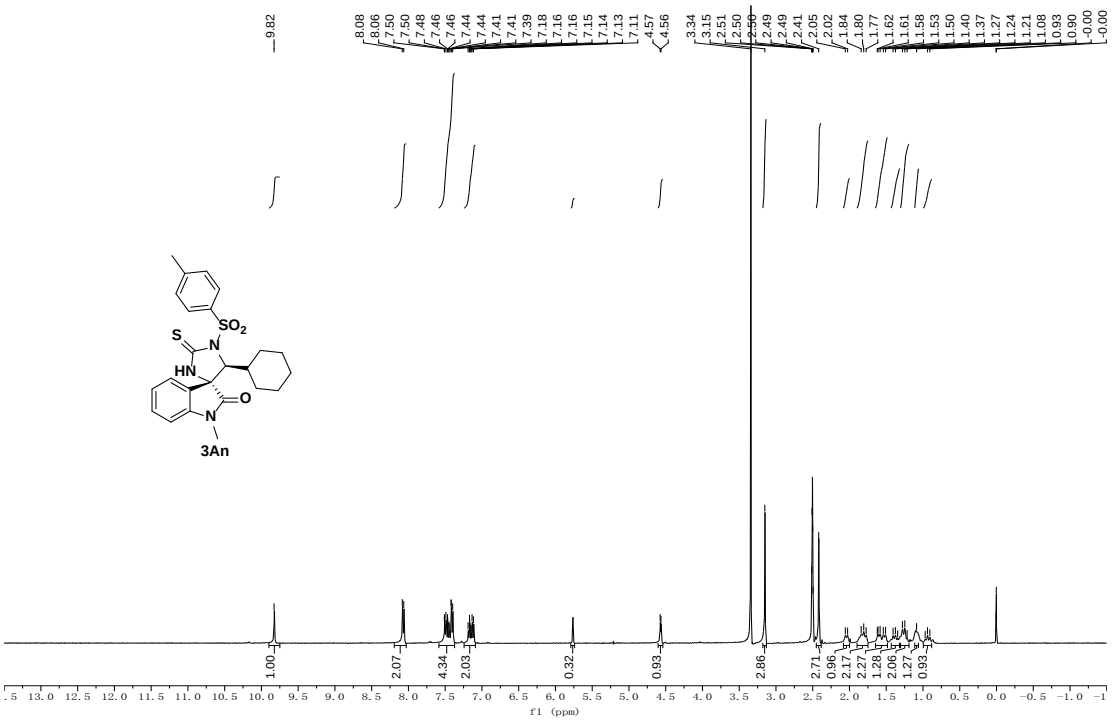
Detector A Ch1 254nm

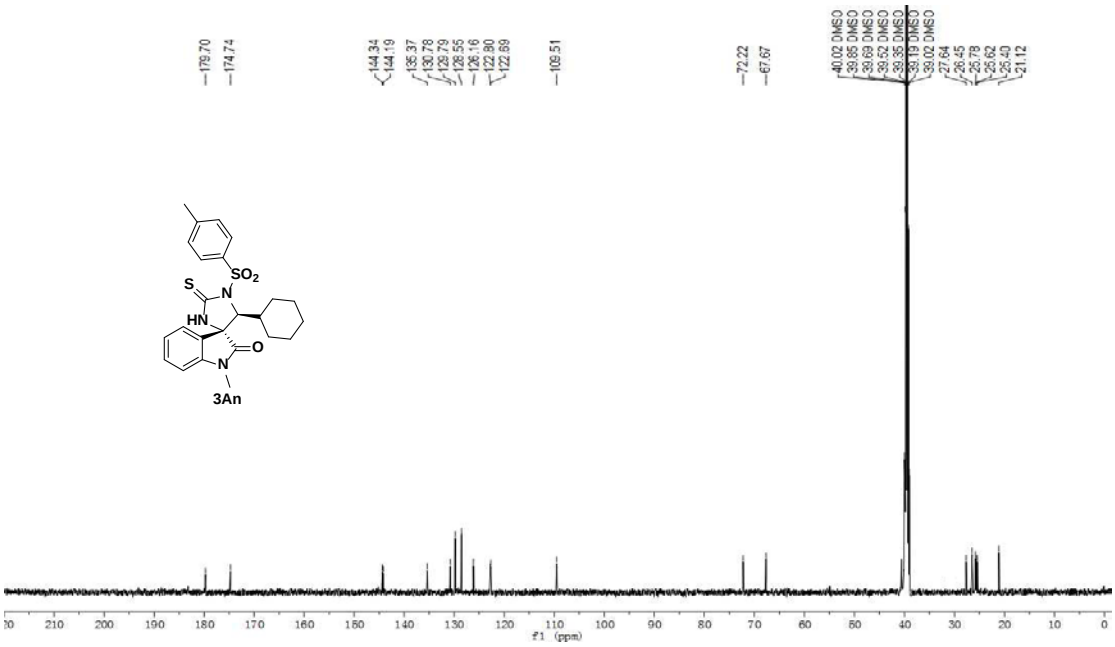
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.607	10374623	286975	51.334	70.285
2	27.921	9835375	121329	48.666	29.715
Total		20209998	408304	100.000	100.000

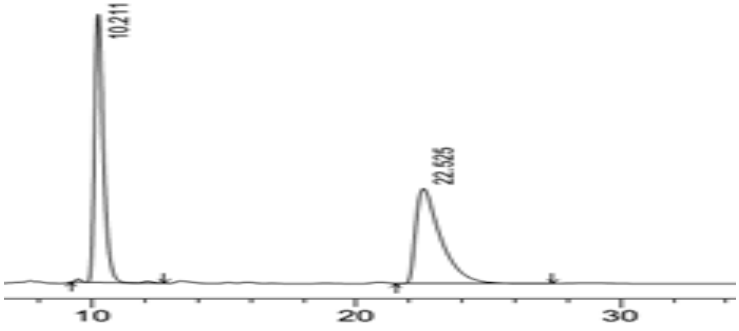


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.179	14994353	477703	95.758	98.076
2	27.577	664309	9370	4.242	1.924
Total		15658661	487073	100.000	100.000

Product of **3An**

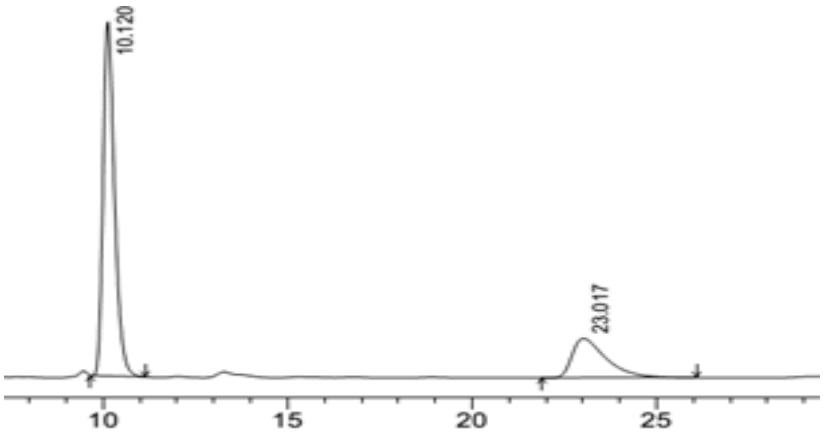

3An
f1 (ppm)


3An
f1 (ppm)


10.211
22.525

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.211	14405741	615499	50.428	73.864
2	22.525	14161387	217790	49.572	26.136
Total		28567128	833289	100.000	100.000

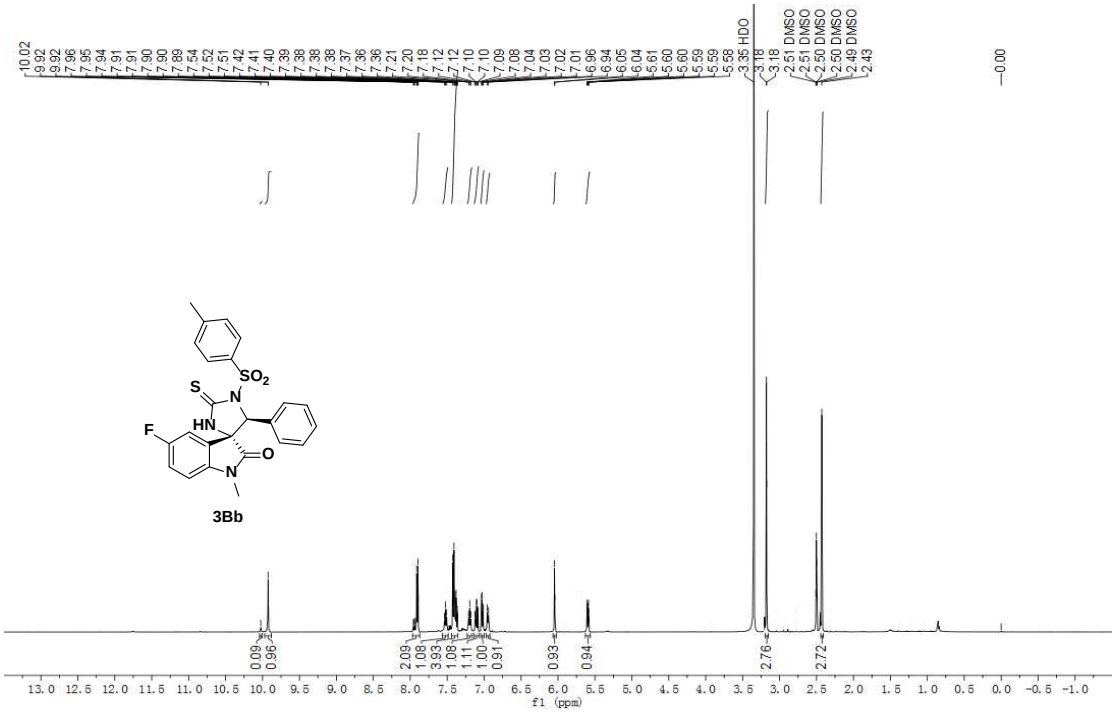


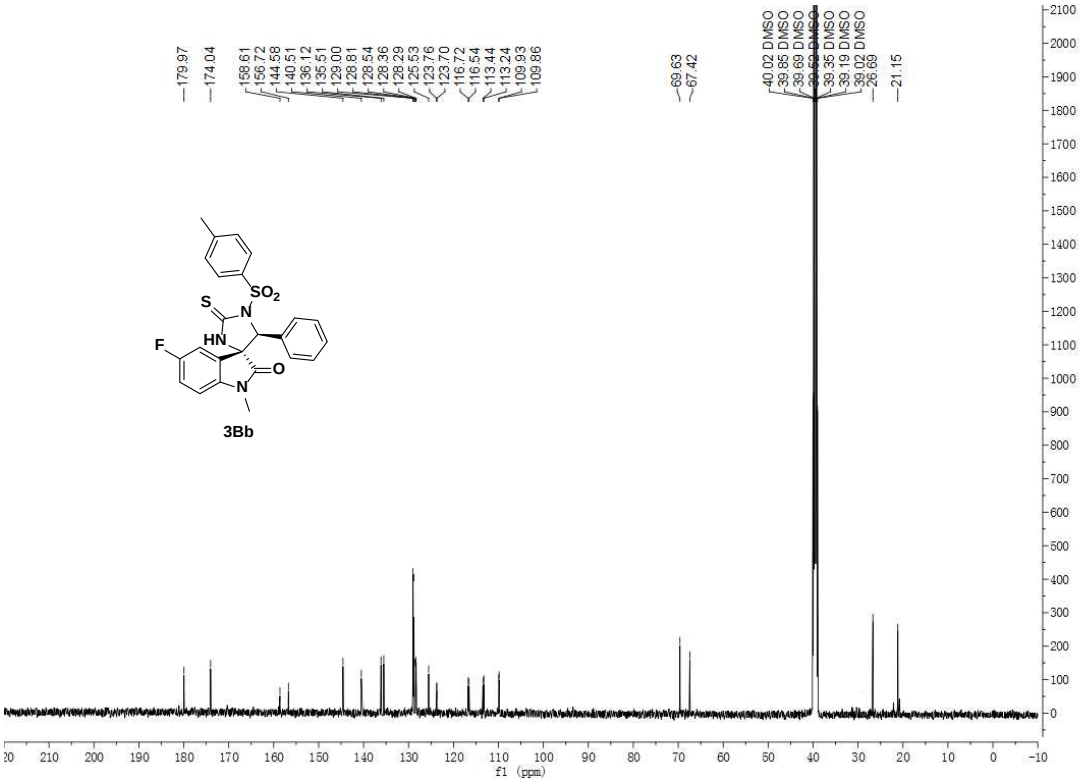
PeakTable

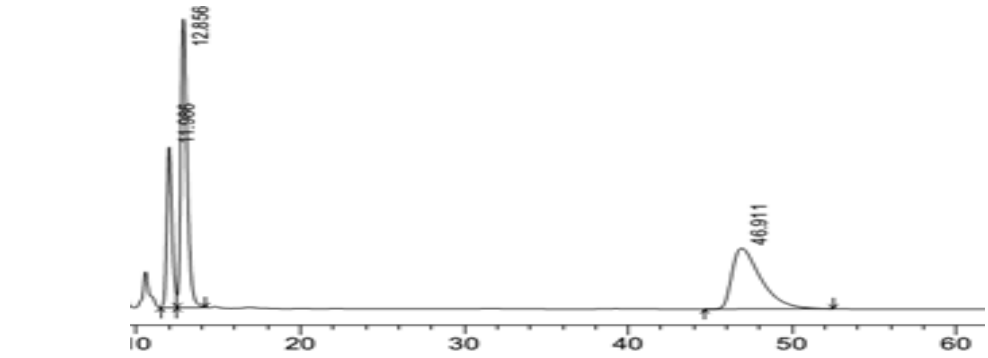
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.120	6665737	308586	75.252	90.008
2	23.017	2192172	34256	24.748	9.992
Total		8857909	342843	100.000	100.000

Product of **3Bb**

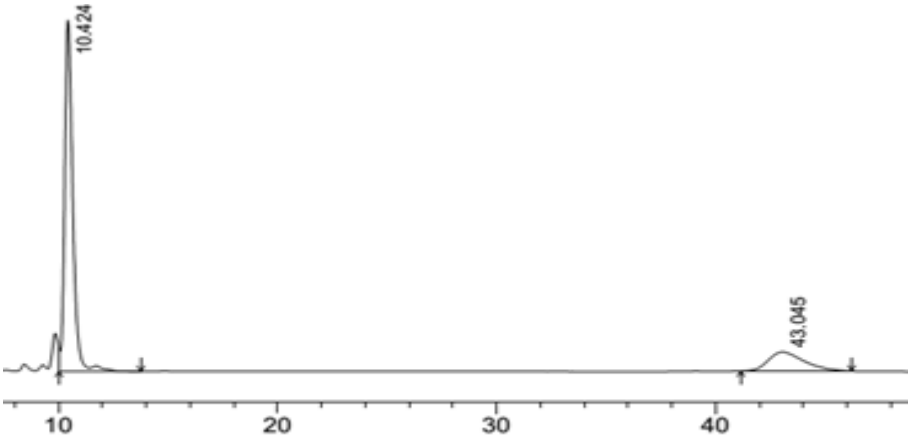






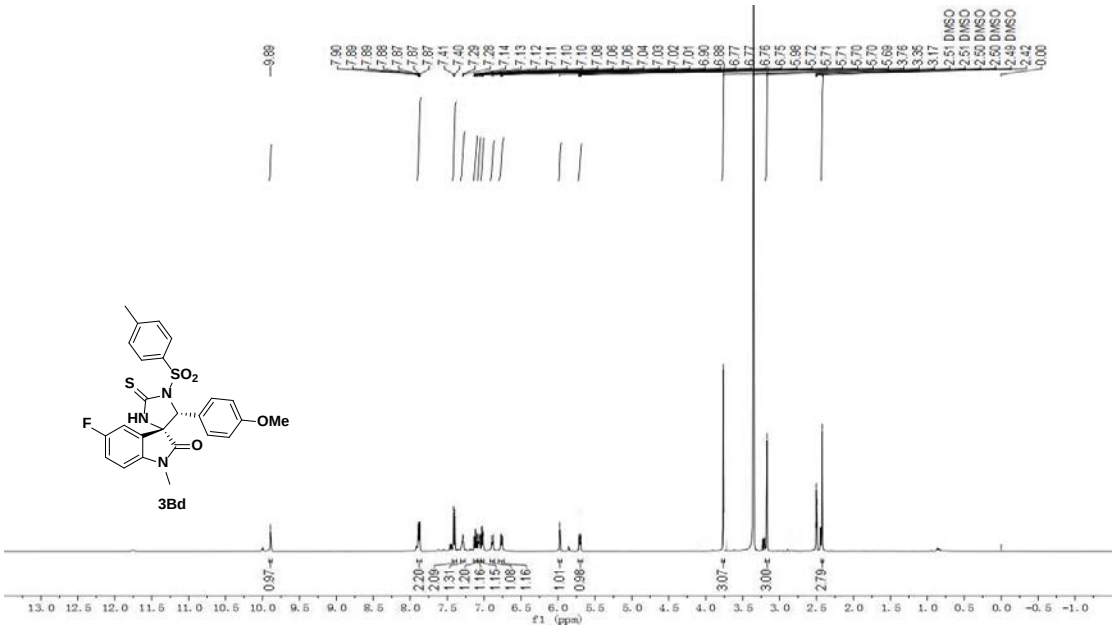
Detector A Ch1 254nm

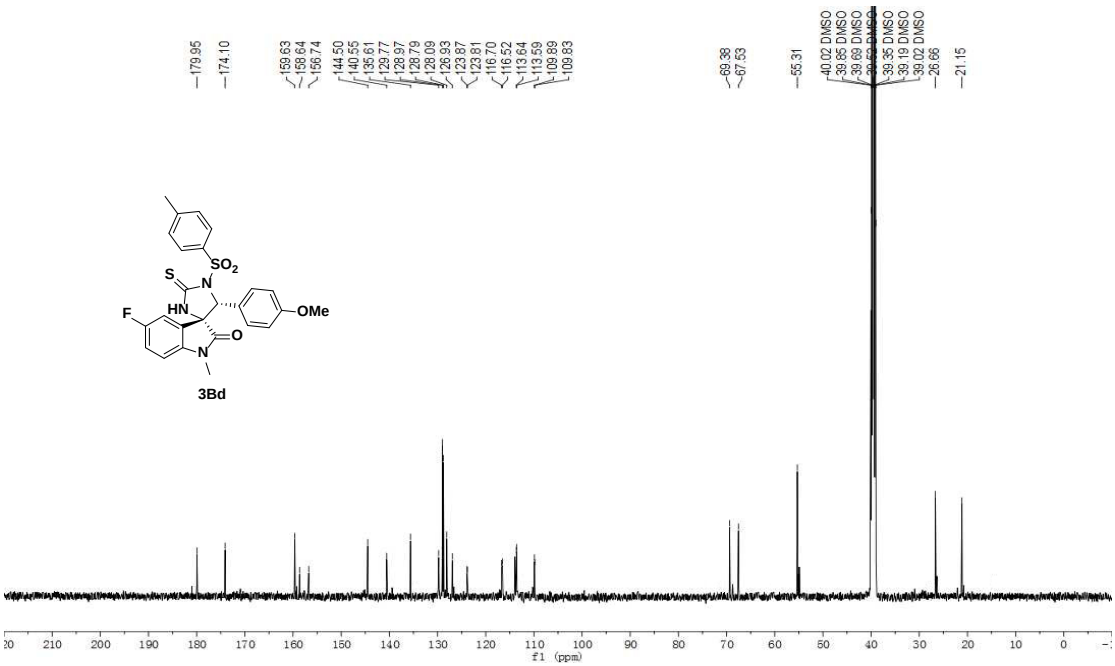
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.986	4593746	203500	19.373	31.442
2	12.856	9686284	366595	40.849	56.640
3	46.911	9432639	77138	39.779	11.918
Total		23712669	647232	100.000	100.000

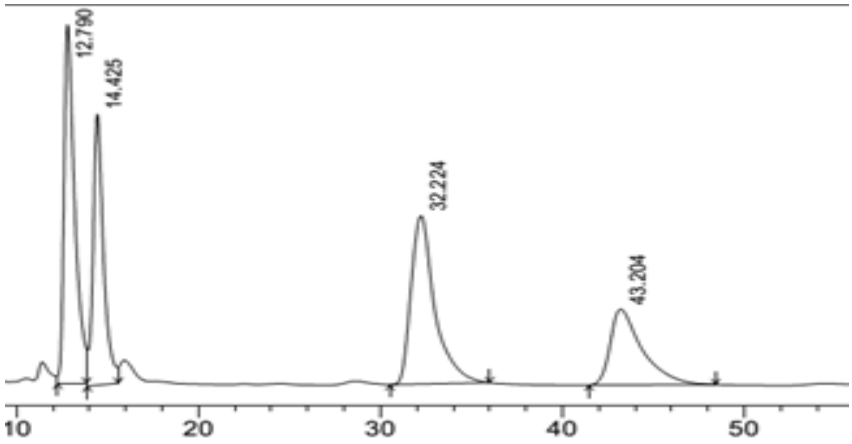


Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.424	12515062	482566	81.010	94.920
2	43.045	2933806	25828	18.990	5.080
Total		15448868	508394	100.000	100.000

Product of **3Bd**

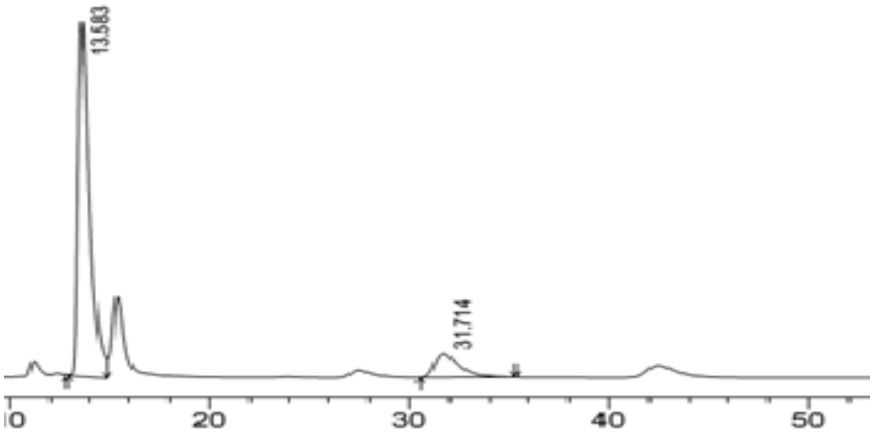






Detector A Ch1 254nm

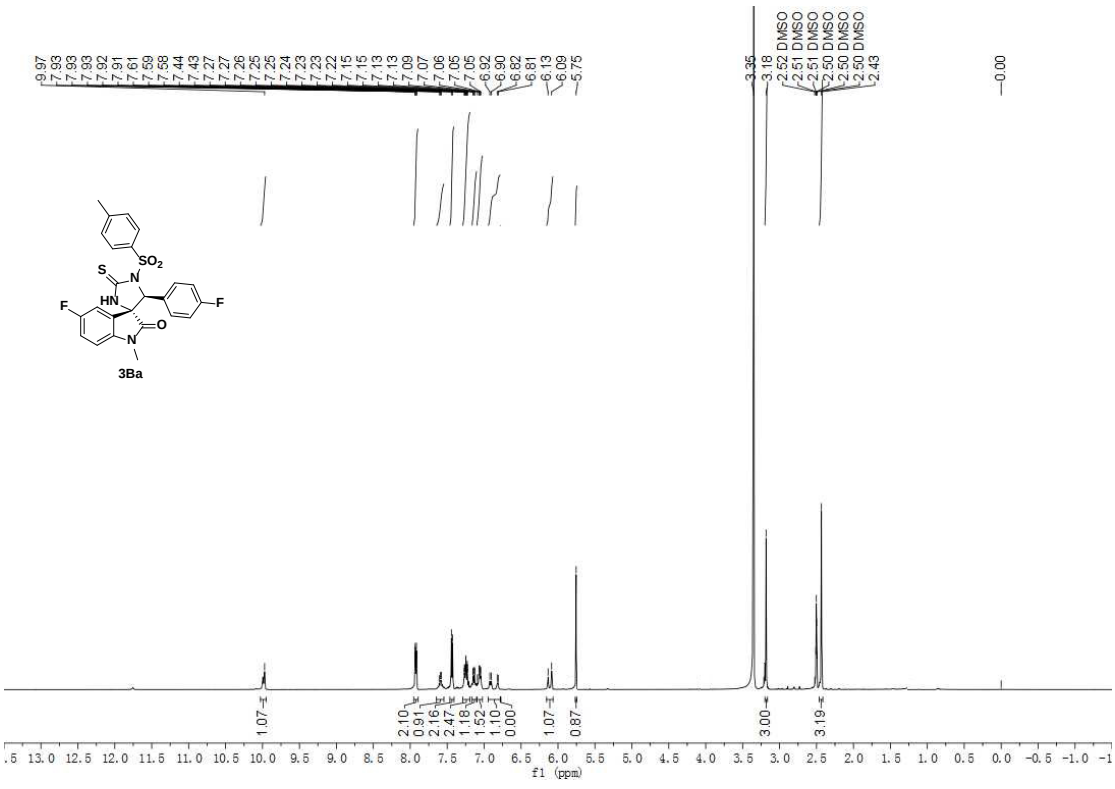
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.790	20653862	505023	29.340	41.038
2	14.425	15207464	381772	21.603	31.023
3	32.224	21532155	237116	30.587	19.268
4	43.204	13001823	106708	18.470	8.671
Total		70395304	1230619	100.000	100.000

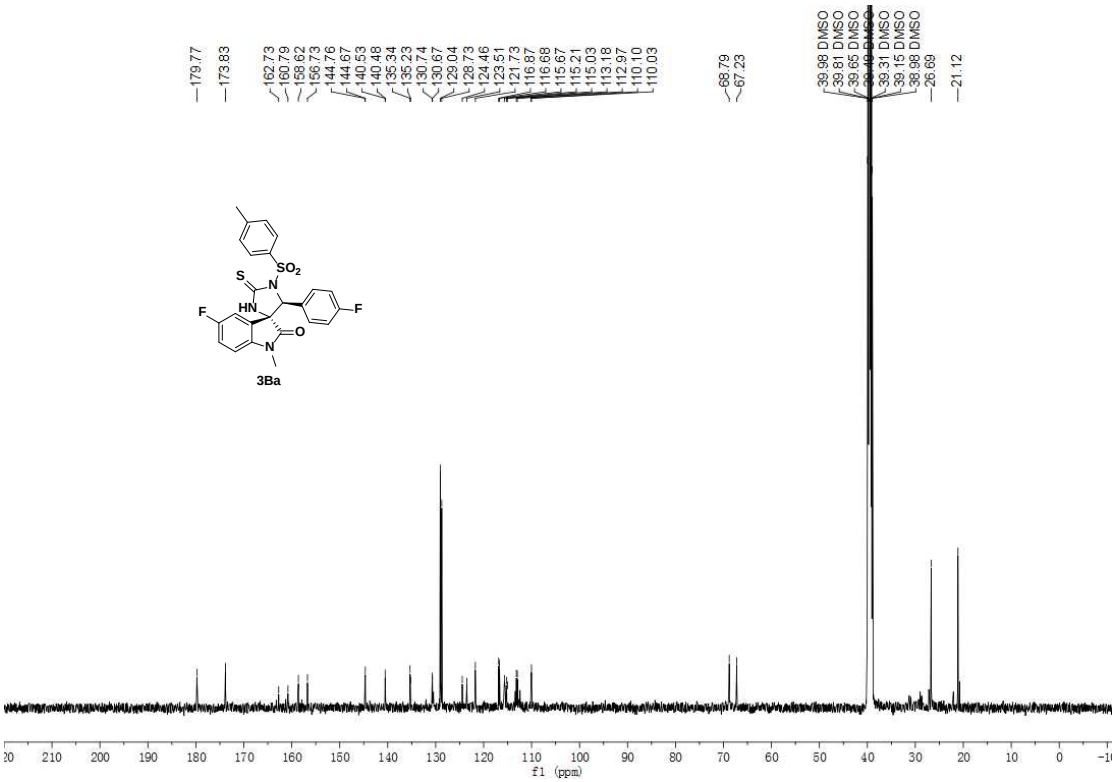


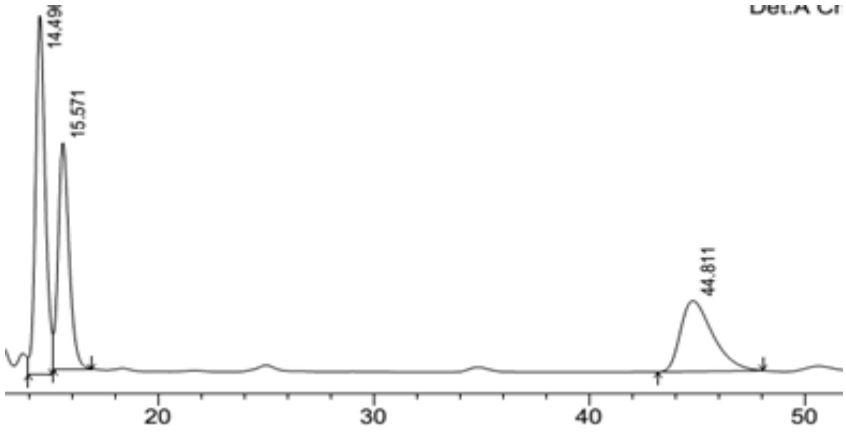
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.583	14578027	377189	87.335	93.841
2	31.714	2113982	24755	12.665	6.159
Total		16692009	401944	100.000	100.000

Product of **3Ba**



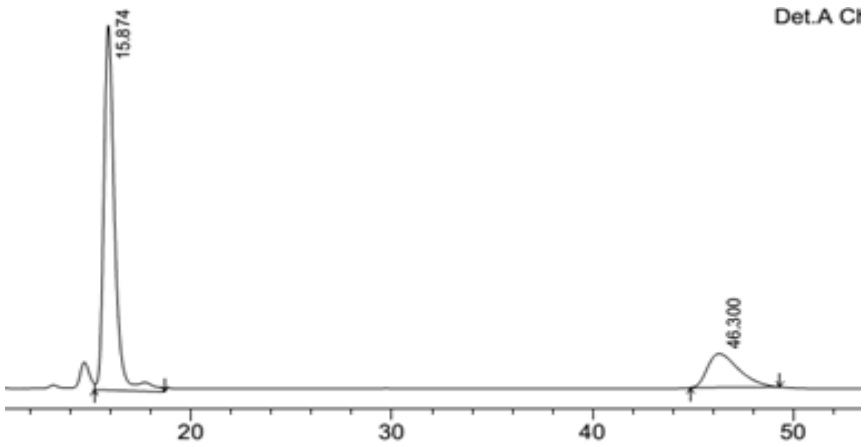




PeakTable

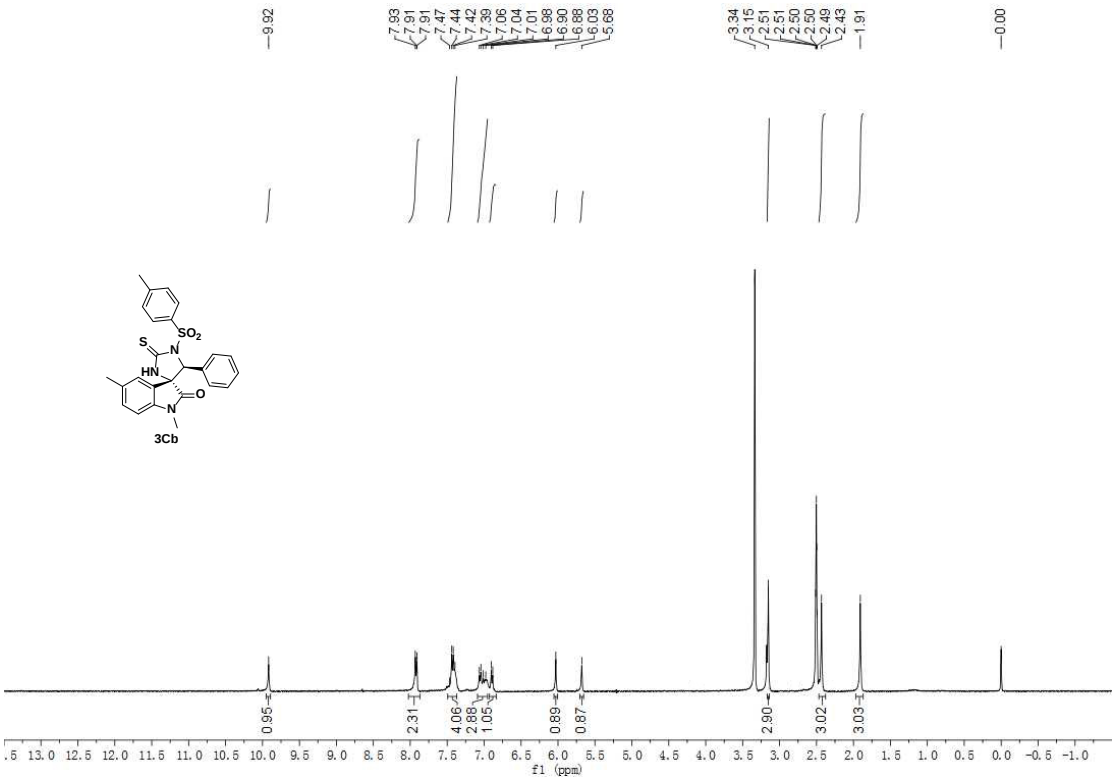
Detector A Ch1 254nm

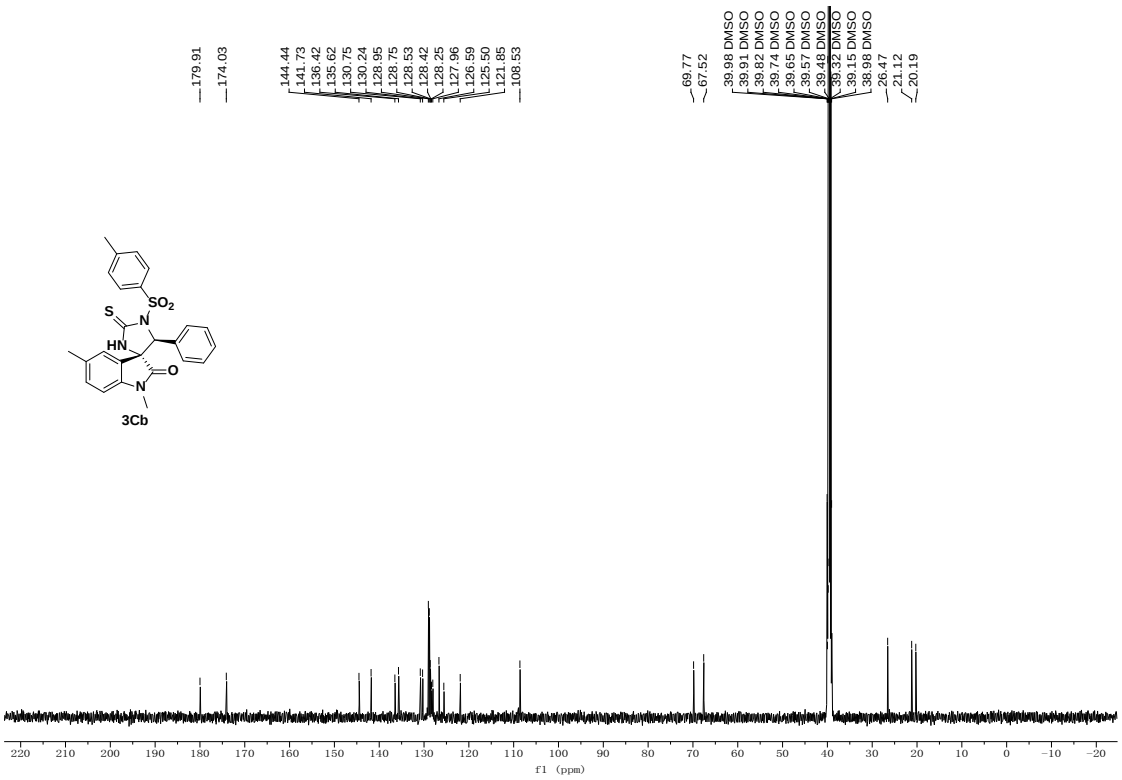
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.496	5078149	162700	42.175	54.693
2	15.571	3620108	102717	30.066	34.529
3	44.811	3342397	32061	27.759	10.777
Total		12040654	297478	100.000	100.000

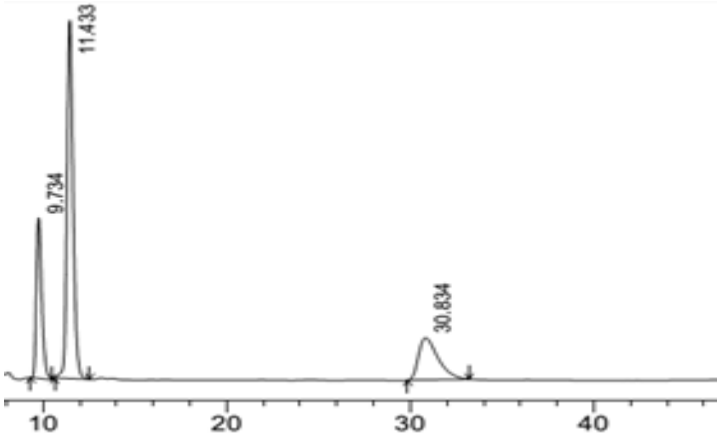


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.874	23649478	627065	78.826	91.500
2	46.300	6352558	58255	21.174	8.500
Total		30002036	685320	100.000	100.000

Product of **3Cb**

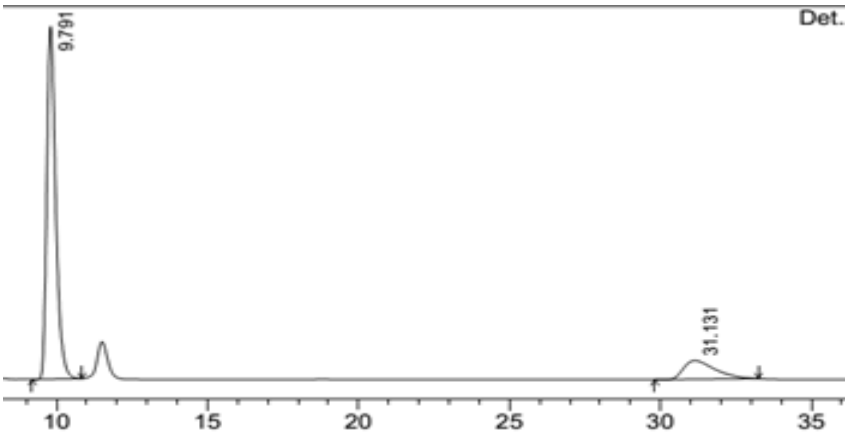






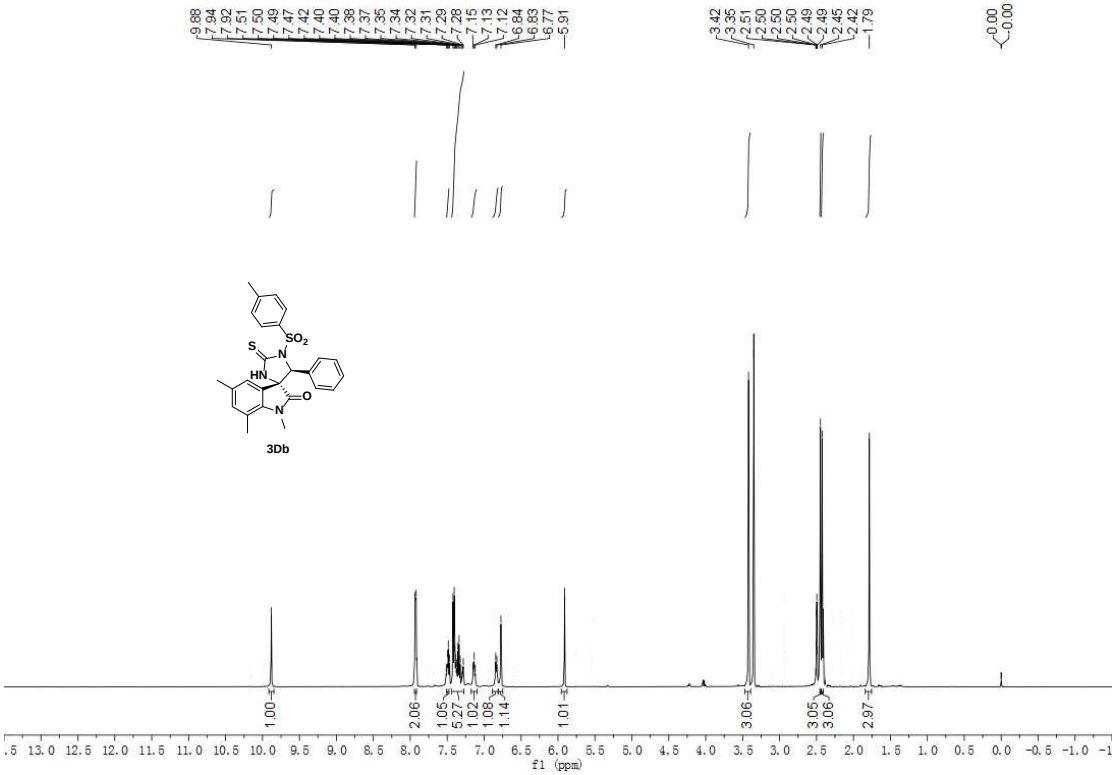
Detector A Ch1 254nm

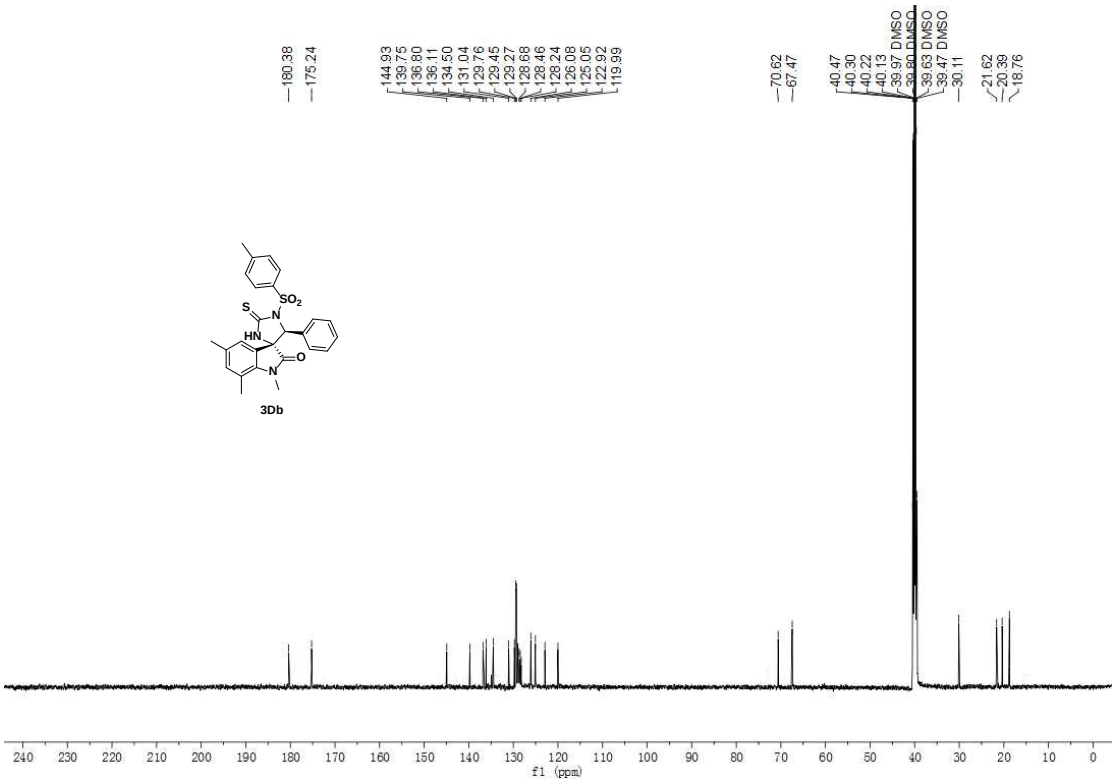
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.734	6494676	314516	22.451	28.628
2	11.433	16341231	701926	56.488	63.891
3	30.834	6092913	82181	21.062	7.480
Total		28928821	1098622	100.000	100.000

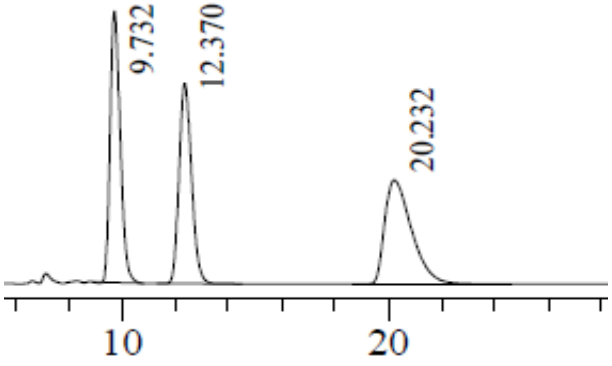


Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.791	40931945	1983869	84.272	94.967
2	31.131	7639492	105148	15.728	5.033
Total		48571437	2089016	100.000	100.000

Product of **3Db**



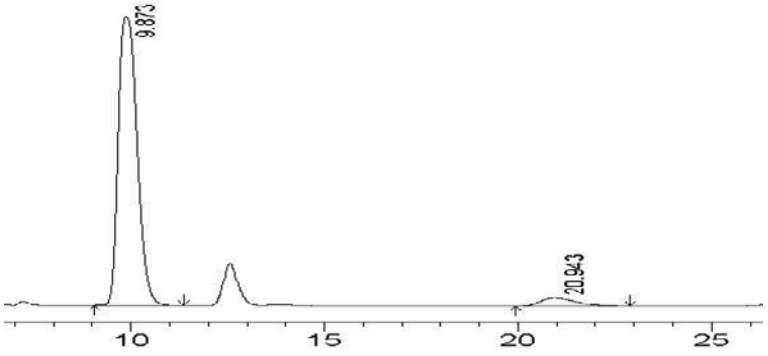




PeakTable

Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.732	45278473	1712447	34.276	47.142
2	12.370	41031165	1265223	31.061	34.831
3	20.232	45790622	654843	34.664	18.027
Total		132100260	3632512	100.000	100.000

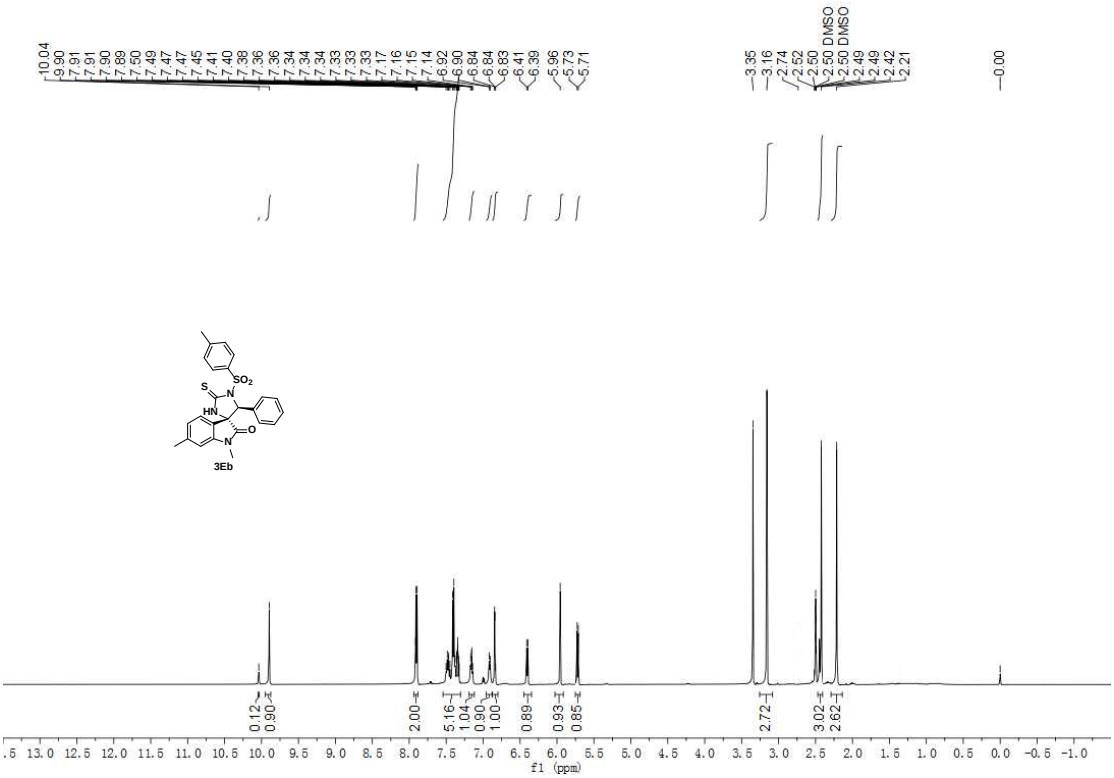


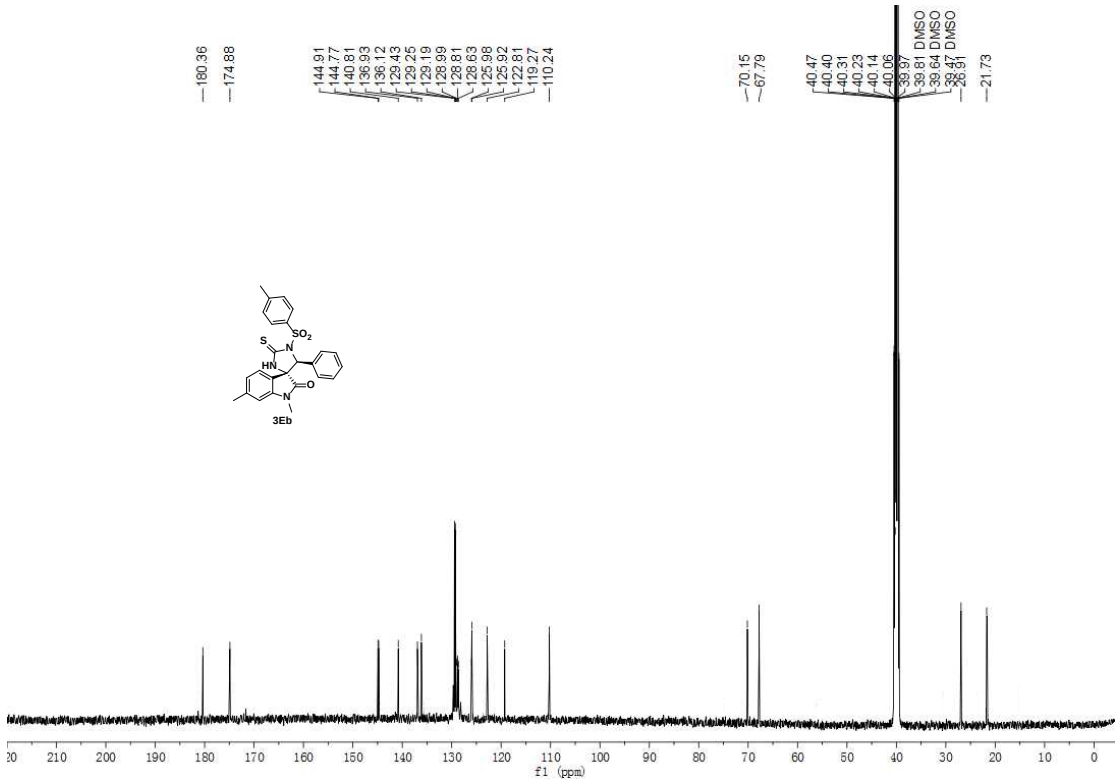
PeakTable

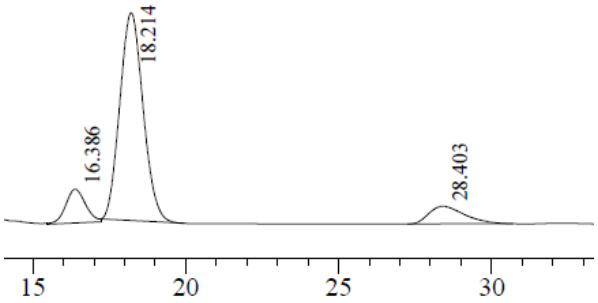
Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.873	106836307	3148222	95.223	97.403
2	20.943	5359263	83930	4.777	2.597
Total		112195570	3232152	100.000	100.000

Product of **3Eb**

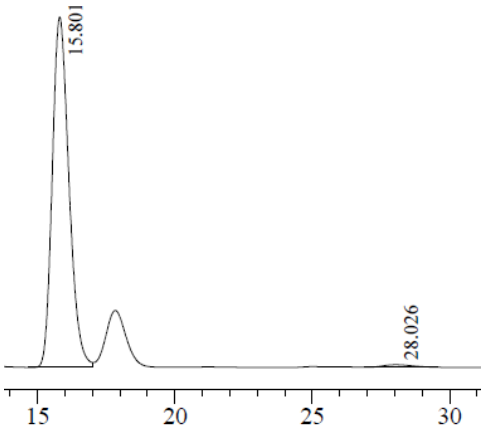






Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.386	5897810	130771	10.902	13.031
2	18.214	42719338	804806	78.963	80.199
3	28.403	5483319	67937	10.135	6.770
Total		54100467	1003515	100.000	100.000

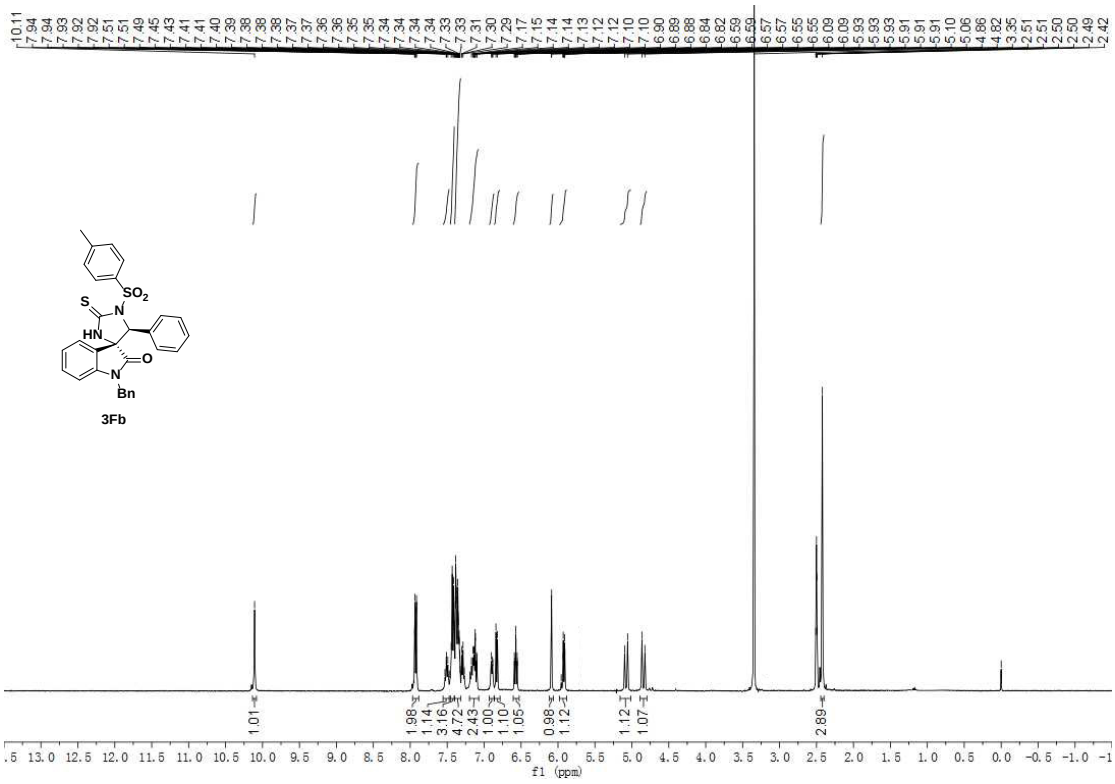


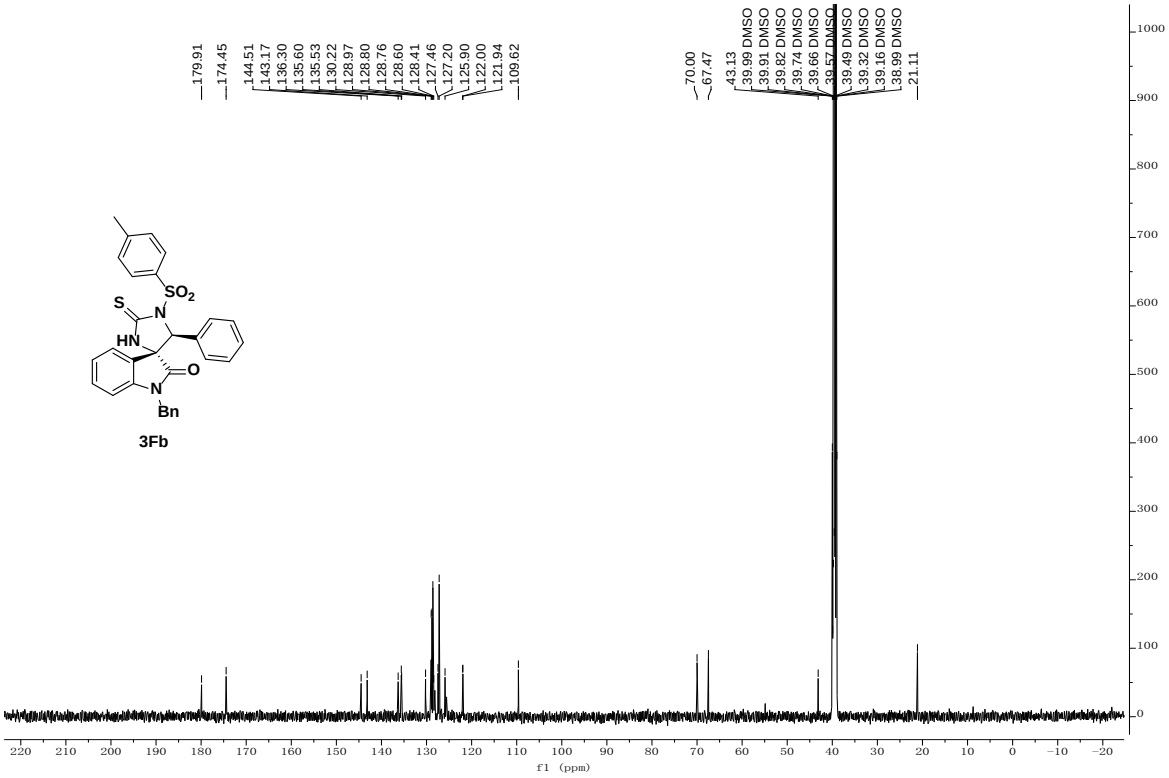
PeakTable

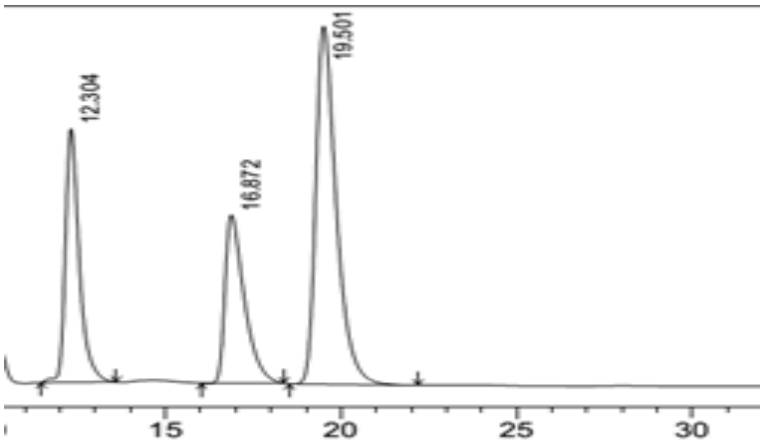
Detector A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.801	27215416	646775	98.717	99.250
2	28.026	353713	4885	1.283	0.750
Total		27569129	651660	100.000	100.000

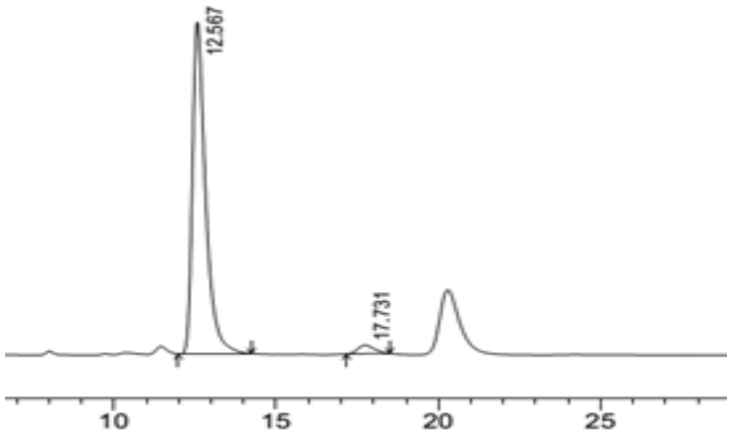
Product of **3Fb**







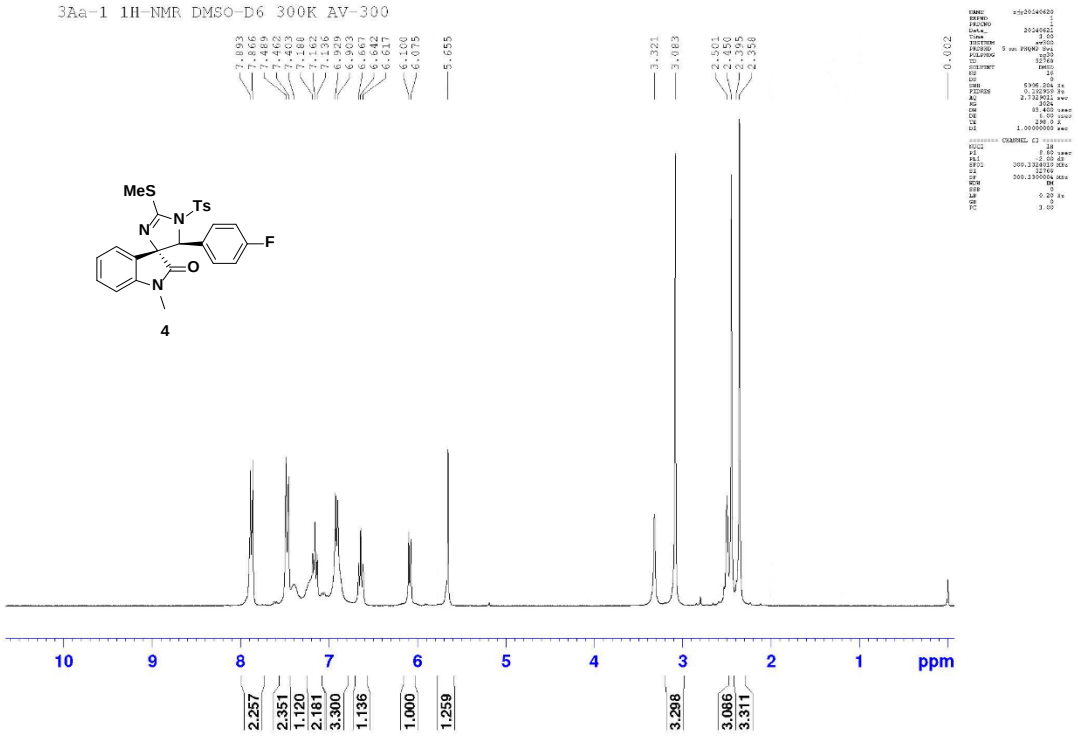
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.304	6164167	224015	24.975	32.529
2	16.872	5668461	148551	22.966	21.571
3	19.501	12848829	316096	52.059	45.900
Total		24681458	688662	100.000	100.000

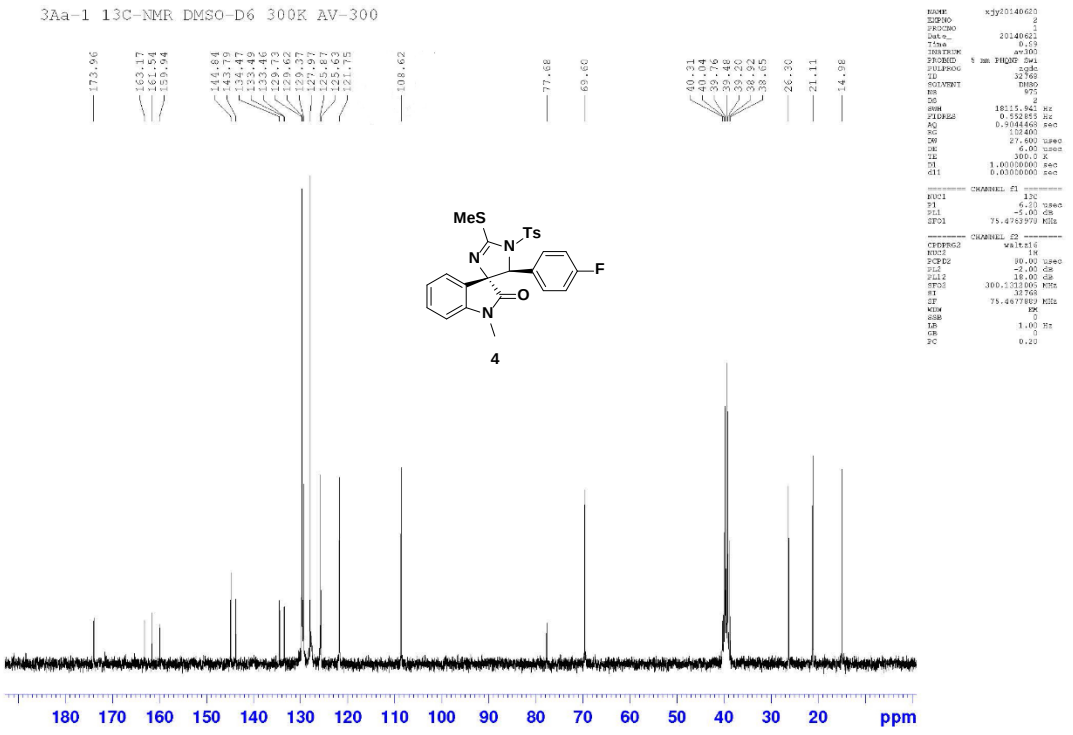


Detector A Ch1 254nm

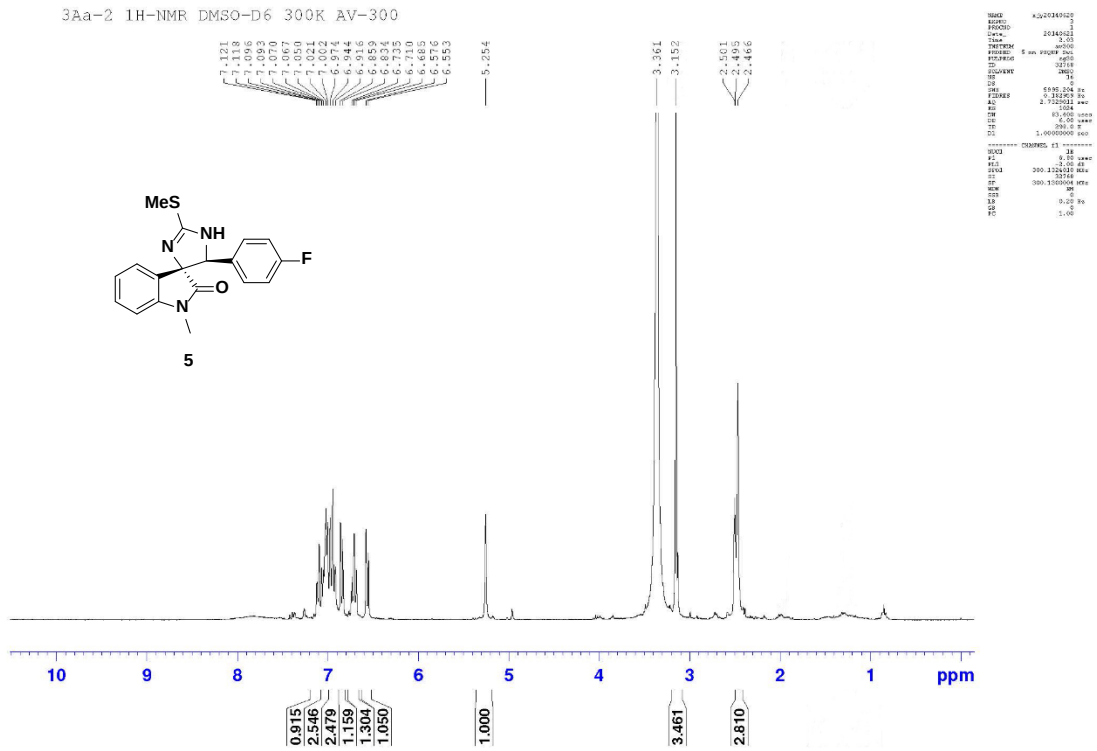
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.567	12491279	443319	96.824	97.493
2	17.731	409676	11400	3.176	2.507
Total		12900955	454719	100.000	100.000

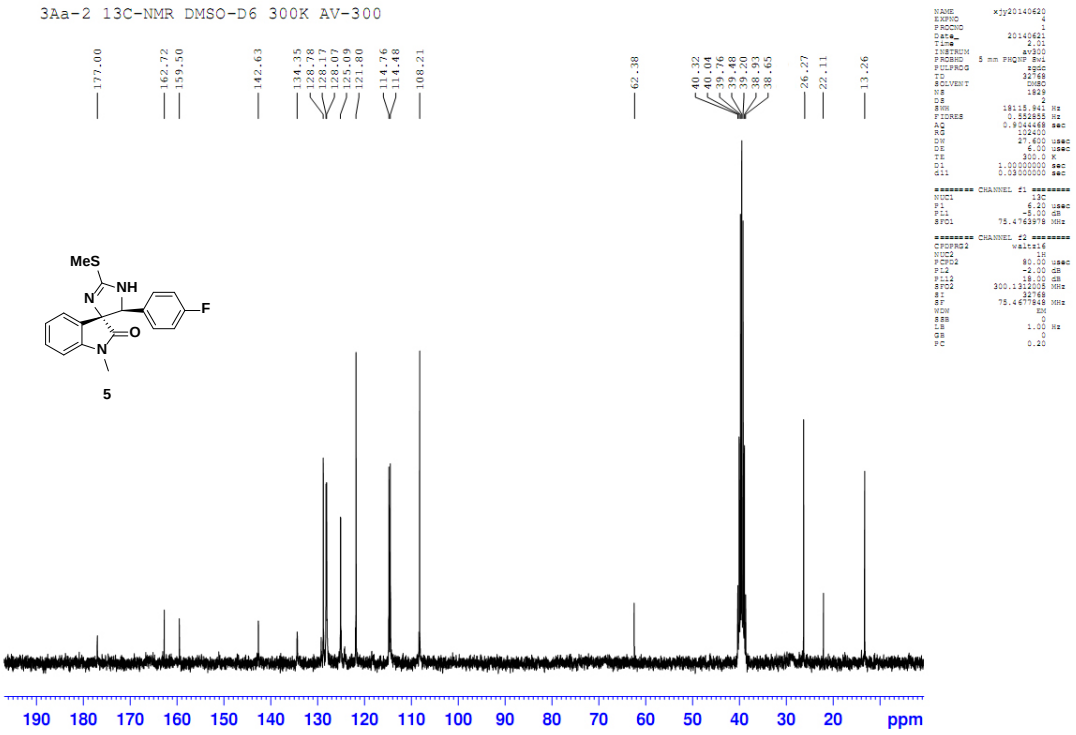
4




3Aa-1 13C-NMR DMSO-D6 300K AV-300
MeS
Ts
N
N
F
O
N
4
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

5


3Aa-2 1H-NMR DMSO-D6 300K AV-300
MeS
NH
N
F
O
N
5
10 9 8 7 6 5 4 3 2 1 ppm
0.915
2.546
2.479
1.159
1.304
1.050
1.000
3.461
2.810


3Aa-2 13C-NMR DMSO-D6 300K AV-300
177.00
162.72
159.50
142.63
134.35
128.78
128.17
128.07
125.09
121.80
114.76
114.48
108.21
62.38
40.32
40.04
39.76
39.48
39.20
38.93
38.65
26.27
22.11
13.26
MeS
NH
N
F
O
N
5
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm