Supplementary Information for:

Sulfenylnitrene-Mediated Aminative Cyclization for the Diastereoselective Synthesis of Fused Bicyclic Indolines

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1. General Information

Reagents and Solvents

Reagents and solvents were obtained from Sigma-Aldrich (www.sigma-aldrich.com), ChemImpex (www.chemimpex.com) or Acros Organics (www.fishersci.com) and used without further purification unless otherwise indicated. Dry solvents (acetonitrile, dichloroethane, and chlorobenzene) were obtained from Acros Organics (www.fishersci.com), and dichloromethane was distilled over CaH_2 under N_2 unless otherwise indicated. THF purchased from Sigma-Aldrich was distilled over Na metal with benzophenone indicator.

Reactions

All reactions were performed in flame-dried glassware under positive N_2 pressure with magnetic stirring unless otherwise noted. Liquid reagents and solutions were transferred through rubber septa via syringes flushed with N_2 prior to use. Cold baths were generated as follows: 0 °C with wet ice/water, –5 °C with Julabo (MeOH as a coolant), and −78 °C with dry ice/acetone.

Chromatography

TLC was performed on 0.25 mm E. Merck silica gel 60 F254 plates and visualized under UV light (254 nm) or by staining with potassium permanganate (KMnO4), cerium ammonium molybdenite (CAM), phosphomolybdic acid (PMA), and ninhydrin. Silica flash chromatography was performed on Sorbtech 230–400 mesh silica gel 60.

Analytical Instrumentation

NMR spectra were recorded on a Varian VNMRS 400, 500, and 600 MHz NMR spectrometer in CDCl3 unless otherwise indicated. Chemical shifts are expressed in ppm relative to solvent signals: CDCl3 (^{1}H, 7.26 ppm, 13C, 77.0 ppm); coupling constants are expressed in Hz. NMR spectra were processed using Mnova (www.mestrelab.com/software/mnova-nmr). Mass spectra were obtained at the OU Analytical Core Facility.

2. Synthesis of Indole Starting Materials

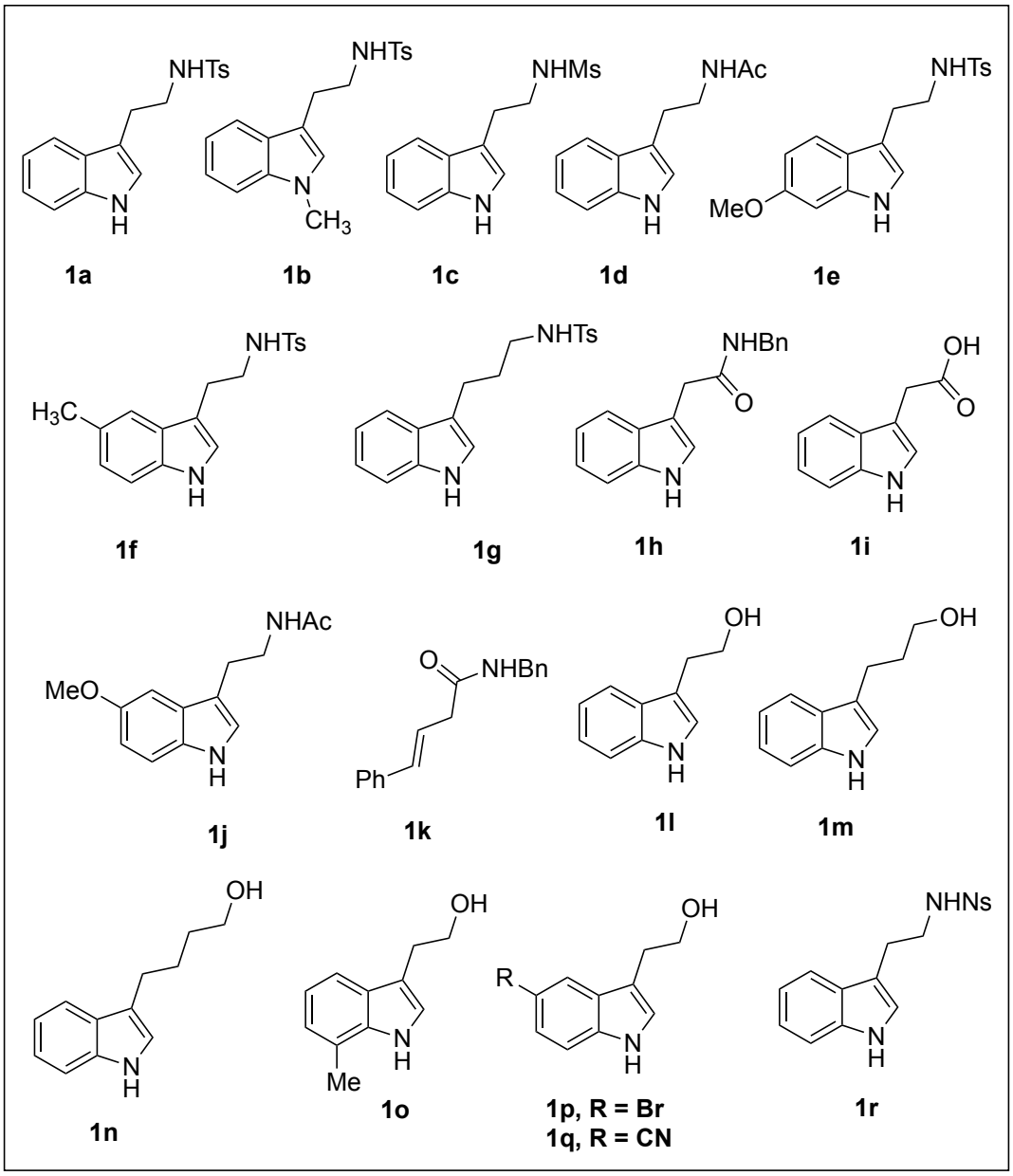


Table S1: Substrate scope of indoles

Compounds **1a**, **1b**, **1c**, **1d**, **1e**, **1f**, **1g**, **1h**, **1i**, **1k**, **1l**, **1m**, **1n, 1o, 1p, 1q**, and **1r** were synthesized using literature known protocols. Compounds **1j** (CAS No: 73-31-4) is commercially available from Ambeed.

3. Sulfenylnitrene Precursors and Their Synthesis

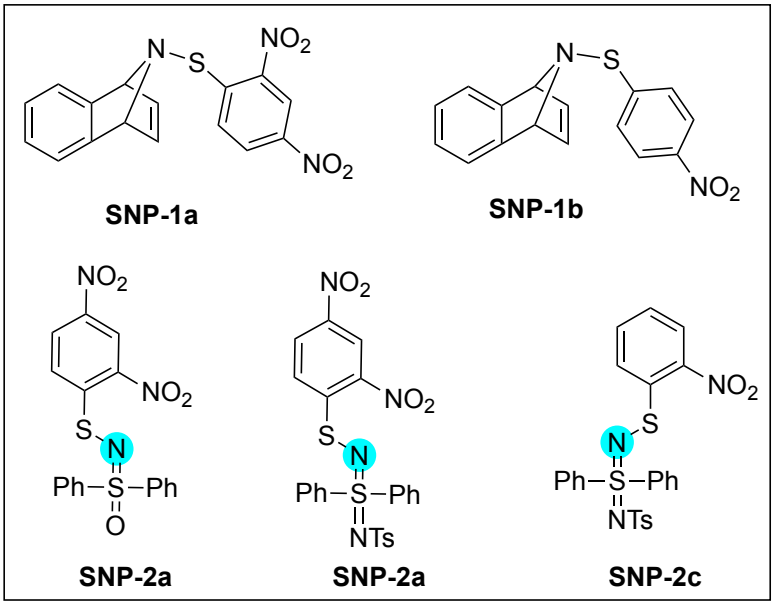
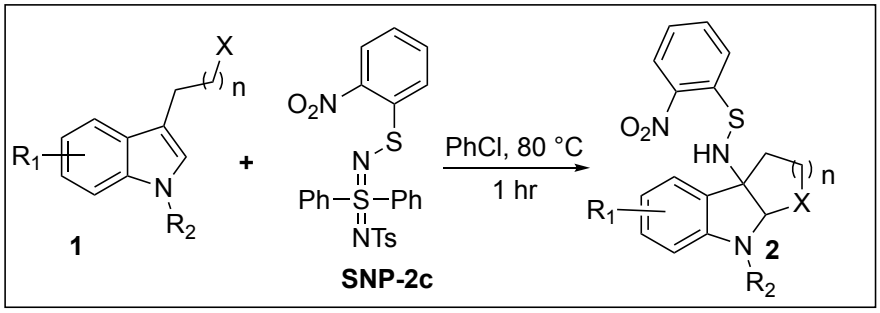


Table S2: List of sulfenylnitrene precursors

Compounds **SNP-1a,**(1) **SNP-1b,**(1) **SNP-2a,**(2) **SNP-2b,**(2) and **SNP-2c**(2) were synthesized using literature known protocols.

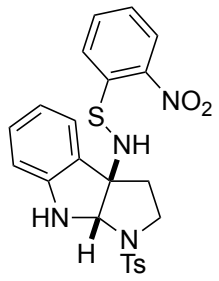
4. General Procedure for Aminocyclization

General procedure-1 (GP-1)



To a solution of indole (1 equiv.) in PhCl (0.1 M), **SNP-2** (1 equiv.) was added and heated to 80 °C for 1 hour. The reaction was then cooled to room temperature. The crude was concentrated under reduced pressure (700 mmHg, bath temperature: 50 °C). The products were purified by silica-gel flash column chromatography.

***S*-(2-nitrophenyl)-*N*-((3a*S*,8a*R*)-1-tosyl-2,3,8,8a-tetrahydropyrrolo[2,3-*b*]indol-3a(1*H*)-yl)thiohydroxylamine (2a):**



2a

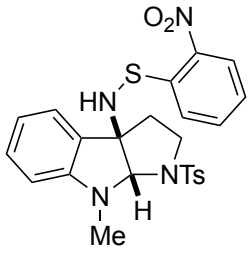
Title compound **2a** was prepared using the **GP-1** for aminocyclization on 20 μmol scale yielding a yellow oil in 96% isolated yield. (9.5 mg, **TLC:** R_f = 0.4 in 30% ethyl acetate/hexanes).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.03 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.65 – 7.61 (m, 3H), 7.28 (dd, *J* = 7.0, 1.4 Hz, 2H), 7.25 – 7.21 (m, 3H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.73 (d, *J* = 7.9 Hz, 1H), 5.09 (s, 1H), 4.94 (s, 1H), 3.42 (ddd, *J* = 10.6, 8.2, 2.1 Hz, 1H), 3.15 (td, *J* = 10.7, 6.2 Hz, 1H), 3.02 (s, 1H), 2.42 (s, 3H), 2.25 – 2.08 (m, 2H).

^{13}C NMR: (100 MHz, $CDCl_3$) δ 149.84, 145.12, 144.22, 142.60, 135.21, 134.06, 130.88, 129.93, 128.49, 127.03, 125.74, 125.18, 124.67, 123.58, 119.77, 110.74, 80.95, 47.13, 33.75, 21.58.

LRMS(ESI): calculated for $C_{23}H_{23}N_4O_4S_2(M+H)^+$: 483.1; found: 483.2.

***N*-((3a*S*,8a*R*)-8-methyl-1-tosyl-2,3,8,8a-tetrahydropyrrolo[2,3-*b*]indol-3a(1*H*)-yl)-*S*-(2-nitrophenyl)thiohydroxylamine (3b):**



2b

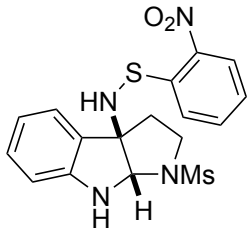
Title compound **2b** was prepared using the **GP-1** for aminocyclizations on 20 μmol scale yielding a yellow oil in 65% isolated yield. (6.5 mg, **TLC:** R_f = 0.35 in 30% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 11.3 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.65 – 7.60 (m, 1H), 7.30 (d, *J* = 5.3 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 4H), 6.79 – 6.69 (m, 1H), 6.52 (d, *J* = 10.7 Hz, 1H), 5.22 (s, 1H), 3.55 – 3.47 (m, 1H), 3.06 (s, 3H), 2.98 (s, 2H), 2.39 (s, 3H), 1.92 (d, *J* = 7.0 Hz, 1H), 1.89 – 1.80 (m, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 151.47, 145.31, 144.10, 142.55, 135.93, 134.00, 131.07, 129.92, 128.65, 127.41, 125.80, 125.19, 124.46, 123.19, 118.04, 107.13, 86.80, 47.79, 34.48, 31.36, 21.55.

HRMS(ESI): calculated for $C_{24}H_{25}N_4O_4S_2(M+H)^+$: 497.1317; found: 497.1318.

***N*-((3a*S*,8a*R*)-1-(methylsulfonyl)-2,3,8,8a-tetrahydropyrrolo[2,3-*b*]indol-3a(1*H*)-yl)-*S*-(2-nitrophenyl)thiohydroxylamine (2c):**



2c

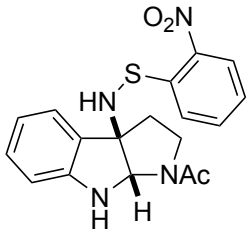
Title compound **2c** was prepared using the **GP-1** for aminocyclizations on 20 μmol scale yielding a yellow oil in 45% isolated yield. (4.0 mg, **TLC:** R_f = 0.7 in 50% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.29 (d, J = 8.2 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.36 (d, J = 8.9 Hz, 1H), 7.30 (t, J = 7.1 Hz, 1H), 7.22 (t, J = 7.7 Hz, 1H), 6.87 (t, J = 6.9 Hz, 1H), 6.73 (d, J = 7.9 Hz, 1H), 5.33 (s, 1H), 4.88 (s, 1H), 3.60 – 3.54 (m, 1H), 3.21 (s, 1H), 3.16 – 3.09 (m, 1H), 2.91 (s, 3H), 2.62 – 2.54 (m, 1H), 2.33 (dd, J = 11.7, 5.1 Hz, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 149.61, 144.84, 142.74, 134.13, 130.93, 128.88, 125.90, 125.29, 124.75, 123.86, 120.24, 110.88, 81.33, 77.64, 46.57, 38.48, 34.61.

HRMS(ESI): calculated for $C_{17}H_{19}N_4O_4S_2(M+H)^+$: 407.0848; found: 407.0837.

1-((3a*S*,8a*R*)-3a-(((2-nitrophenyl)thio)amino)-3,3a,8,8a-tetrahydropyrrolo[2,3-*b*]indol-1(2*H*)-yl)ethan-1-one (2d):



2d

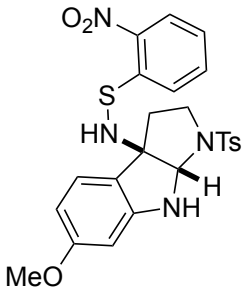
Title compound **2d** was prepared using the **GP-1** for aminocyclizations on 25 μmol scale yielding a yellow oil in 52% isolated yield. (4.8 mg, **TLC:** R_f = 0.4 in 50% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.68 – 7.62 (m, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.81 (t, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 7.9 Hz, 1H), 5.37 (s, 1H), 5.30 (s, 1H), 3.60 (t, *J* = 9.3 Hz, 1H), 3.18 (td, *J* = 10.7, 6.3 Hz, 1H), 3.11 (s, 1H), 2.65 (td, *J* = 11.8, 8.5 Hz, 1H), 2.33 (dd, *J* = 12.6, 6.3 Hz, 1H), 1.96 (s, 3H).

^{13}C NMR: (125 MHz, $CDCl_3$) δ 170.58, 150.11, 145.56, 134.11, 130.78, 128.68, 125.86, 125.16, 124.82, 123.73, 119.34, 110.44, 78.53, 75.17, 46.70, 32.93, 22.32.

HRMS(ESI): calculated for $C_{18}H_{19}N_4O_4S(M+H)^+$: 371.1178; found: 371.1173.

***N*-((3a*S*,8a*R*)-6-methoxy-1-tosyl-2,3,8,8a-tetrahydropyrrolo[2,3-*b*]indol-3a(1*H*)-yl)-*S*-(2-nitrophenyl)thiohydroxylamine (2e):**



2e

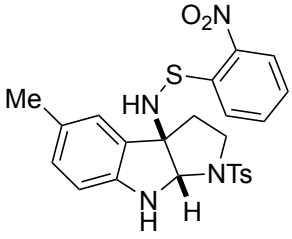
Title compound **2e** was prepared using the **GP-1** for aminocyclizations on 20 μmol scale yielding a yellow oil in 53% isolated yield. (5.5 mg, **TLC:** R_f = 0.75 in 50% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.27 (d, J = 8.3 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H), 7.63 (d, J = 8.3 Hz, 3H), 7.30 (s, 1H), 7.23 (d, J = 8.3 Hz, 2H), 7.16 (d, J = 10.3 Hz, 1H), 6.37 (d, J = 10.5 Hz, 1H), 6.29 (s, 1H), 5.09 (s, 1H), 3.79 (s, 3H), 3.44 – 3.38 (m, 1H), 3.20 – 3.13 (m, 1H), 2.98 (s, 1H), 2.42 (s, 3H), 2.19 – 2.12 (m, 1H), 2.09 – 2.03 (m, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 162.46, 151.42, 145.22, 144.21, 142.61, 135.28, 134.03, 129.93, 127.00, 125.73, 125.14, 124.68, 124.22, 120.70, 105.66, 96.46, 81.39, 55.55, 47.17, 33.67, 21.58.

HRMS(ESI): calculated for $C_{24}H_{25}N_4O_5S_2(M+H)^+$: 5123.1265; found: 513.1256.

***N*-((3a*S*,8a*R*)-5-methyl-1-tosyl-2,3,8,8a-tetrahydropyrrolo[2,3-*b*]indol-3a(1*H*)-yl)-*S*-(2-nitrophenyl)thiohydroxylamine (2f):**



2f

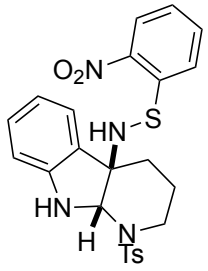
Title compound **2f** was prepared using the **GP-1** for aminocyclizations on 20 μmol scale yielding a yellow oil in 50% isolated yield. (4.9 mg, **TLC:** R_f = 0.75 in 30% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.28 (d, J = 9.2 Hz, 1H), 8.04 (d, J = 8.3 Hz, 1H), 7.64 (dd, J = 15.2, 6.8 Hz, 3H), 7.29 (t, J = 7.7 Hz, 1H), 7.22 (d, J = 6.2 Hz, 2H), 7.08 (s, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 5.07 (s, 1H), 3.45 – 3.38 (m, 1H), 3.15 (td, J = 10.9, 5.0 Hz, 1H), 3.01 (s, 1H), 2.41 (s, 3H), 2.30 (s, 3H), 2.22 – 2.14 (m, 1H), 2.10 (dd, J = 13.5, 5.0 Hz, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 147.90, 145.51, 144.47, 142.92, 135.56, 134.35, 131.72, 130.21, 129.56, 128.99, 127.34, 126.03, 125.46, 125.03, 124.30, 111.02, 81.49, 47.45, 33.94, 21.88, 21.25.

HRMS(ESI): calculated for $C_{24}H_{24}N_4O_4S_2(M+H)^+$: 497.1317; found: 497.1318.

***S*-(2-nitrophenyl)-*N*-((4a*S*,9a*R*)-1-tosyl-1,2,3,4,9,9a-hexahydro-4a*H*-pyrido[2,3-*b*]indol-4a-yl)thiohydroxylamine (2g):**



2g

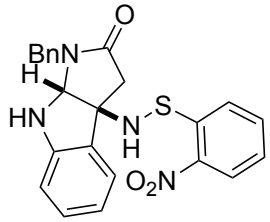
Title compound **2g** was prepared using the **GP-1** for aminocyclizations on 20 µmol scale yielding a yellow oil in 35% isolated yield. (3.5 mg, **TLC:** R_f = 0.4 in 50% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.33 – 8.28 (m, 1H), 8.25 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.70 – 7.64 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.25 (s, 1H), 7.18 – 7.08 (m, 2H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 5.47 (s, 1H), 4.21 (s, 1H), 3.49 (dt, *J* = 12.0, 6.1 Hz, 1H), 3.22 (s, 1H), 3.13 (ddd, *J* = 12.2, 7.6, 5.3 Hz, 1H), 2.45 (s, 3H), 1.97 (ddd, *J* = 13.1, 8.9, 3.9 Hz, 1H), 1.86 (ddd, *J* = 13.2, 8.0, 3.9 Hz, 1H), 1.79 (dd, *J* = 14.7, 8.6 Hz, 1H), 1.47 (dp, *J* = 13.8, 4.7 Hz, 1H).

^{13}C NMR: (125 MHz, $CDCl_3$) δ 147.81, 145.33, 144.13, 142.57, 136.15, 134.12, 130.82, 130.16, 130.12, 129.70, 129.66, 127.39, 127.35, 125.76, 125.72, 125.60, 124.93, 122.69, 119.95, 119.91, 110.54, 76.39, 67.68, 40.10, 31.54, 21.77, 19.38.

HRMS(ESI): calculated for $C_{24}H_{25}N_4O_4S_2(M+H)^+$: 497.1317; found: 497.1312.

(3a*S*,8a*R*)-1-benzyl-3a-(((2-nitrophenyl)thio)amino)-3,3a,8,8a-tetrahydropyrrolo[2,3-*b*]indol-2(1*H*)-one (2h):



2h

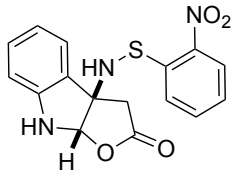
Title compound **2h** was prepared using the **GP-1** for aminocyclizations on 20 µmol scale yielding a yellow oil in 61% isolated yield. Preparative TLC was employed to obtain a spectroscopically pure compound. (5.5 mg, **TLC:** R_f = 0.75 in 30% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.28 (d, J = 8.2 Hz, 1H), 8.12 (d, J = 9.6 Hz, 1H), 7.66 (t, J = 7.7 Hz, 1H), 7.40 (d, J = 7.4 Hz, 1H), 7.34 – 7.29 (m, 4H), 7.25 – 7.21 (m, 3H), 6.91 (t, J = 7.4 Hz, 1H), 6.64 (d, J = 7.9 Hz, 1H), 5.12 (s, 1H), 4.87 (d, J = 15.2 Hz, 1H), 4.27 (d, J = 15.3 Hz, 1H), 3.18 (s, 1H), 3.08 – 2.88 (m, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 171.71, 148.50, 144.51, 143.10, 136.12, 134.38, 131.69, 131.24, 129.31, 128.23, 126.29, 125.63, 124.96, 124.64, 121.29, 112.30, 81.15, 70.72, 44.28, 40.75.

HRMS(ESI): calculated for $C_{23}H_{21}N_4O_3S(M+H)^+$: 433.1334; found: 433.1327.

(3a*S*,8a*R*)-3a-(((2-nitrophenyl)thio)amino)-3,3a,8,8a-tetrahydro-2*H*-furo[2,3-*b*]indol-2-one (2i):



2i

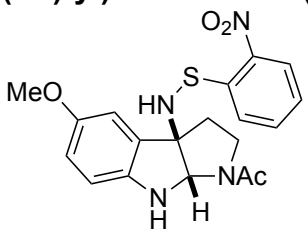
Title compound **2i** was prepared using the **GP-1** for aminocyclizations on 25 µmol scale yielding a yellow oil in 72% isolated yield. (6.3 mg, **TLC:** R_f = 0.5 in 50% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.33 (d, J = 8.3 Hz, 1H), 8.09 (d, J = 8.3 Hz, 1H), 7.76 – 7.70 (m, 1H), 7.38 – 7.32 (m, 1H), 7.29 (d, J = 7.6 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H), 6.78 (d, J = 7.9 Hz, 1H), 5.87 (s, 1H), 5.07 (s, 1H), 3.25 (d, J = 15.8 Hz, 1H), 3.20 (s, 1H), 2.98 (d, J = 17.5 Hz, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 172.57, 147.30, 143.56, 134.08, 131.37, 128.31, 125.94, 125.47, 124.31, 124.09, 120.89, 110.68, 96.55, 72.19, 37.34.

HRMS(ESI): calculated for $C_{16}H_{13}N_3O_4S(M+H)^+$: 344.0705; found: 344.0705.

1-((3a*S*,8a*R*)-5-methoxy-3a-(((2-nitrophenyl)thio)amino)-3,3a,8,8a-tetrahydropyrrolo[2,3-*b*]indol-1(2*H*)-yl)ethan-1-one (2j):



2j

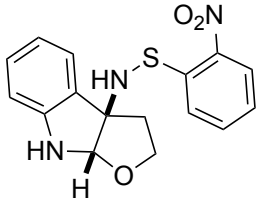
Title compound **2j** was prepared using the **GP-1** for aminocyclizations on 85 µmol scale yielding a yellow oil in 77% isolated yield. (29mg, **TLC:** R_f = 0.4 in 80% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.4, 1.4 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.66 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1H), 7.31 – 7.27 (m, 1H), 6.94 (d, *J* = 2.6 Hz, 1H), 6.78 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 5.32 (s, 1H), 3.77 (s, 3H), 3.61 (ddd, *J* = 10.2, 8.6, 1.4 Hz, 1H), 3.20 (td, *J* = 10.6, 6.4 Hz, 1H), 2.62 (ddd, *J* = 12.5, 11.1, 8.5 Hz, 1H), 2.36 – 2.28 (m, 1H), 1.97 (s, 3H).

^{13}C NMR: (125 MHz, $CDCl_3$) δ 170.57, 153.83, 145.51, 144.00, 142.77, 134.10, 130.00, 125.84, 125.15, 124.83, 115.82, 111.20, 110.26, 79.36, 75.44, 56.28, 46.66, 32.93, 22.35.

HRMS(ESI): calculated for $C_{19}H_{21}N_4O_4S(M+H)^+$: 401.1284; found: 401.1288.

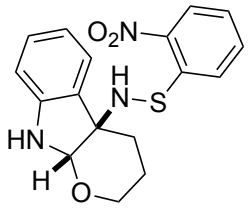
***S*-(2-nitrophenyl)-*N*-((3a*S*,8a*R*)-2,3,8,8a-tetrahydro-3a*H*-furo[2,3-*b*]indol-3a-yl)thiohydroxylamine (2l)**



2l

Title compound **2l** was prepared using the **GP-1** for aminocyclizations on 30 µmol scale yielding a yellow oil in 96% isolated yield. (9.8 mg, **TLC:** R_f = 0.6 in 30% ethyl acetate/hexanes).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.30 – 8.22 (m, 2H), 7.71 – 7.65 (m, 1H), 7.36 (d, J = 7.4 Hz, 1H), 7.28 (s, 1H), 7.20 – 7.13 (m, 1H), 6.83 – 6.78 (m, 1H), 6.65 (d, J = 4.4 Hz, 1H), 5.50 (s, 1H), 4.66 (s, 1H), 4.05 – 3.98 (m, 1H), 3.67 – 3.59 (m, 1H), 3.26 (s, 1H), 2.53 – 2.44 (m, 1H), 2.25 (d, J = 13.7 Hz, 1H).
^{13}C NMR: (126 MHz, $CDCl_3$) δ 150.24, 145.87, 143.00, 134.21, 130.54, 130.02, 126.10, 125.25, 124.41, 119.78, 109.73,77.33, 97.59, 67.56, 38.49.
HRMS(ESI): calculated for $C_{16}H_{16}N_3O_3S(M+H)^+$: 330.0912; found: 330.0906.

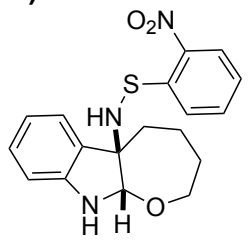
***S*-(2-nitrophenyl)-*N*-((4a*S*,9a*R*)-3,4,9,9a-tetrahydropyrano[2,3-*b*]indol-4a(2*H*)-yl)thiohydroxylamine (2m):**



2m

Title compound **2m** was prepared using the **GP-1** for aminocyclizations on 60 µmol scale yielding a yellow oil in 63% isolated yield. (13 mg, **TLC:** R_f = 0.4 in 40% ethyl acetate/hexanes).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.22 (ddd, *J* = 15.9, 8.4, 1.4 Hz, 2H), 7.59 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1H), 7.29 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.20 (dtd, *J* = 21.8, 7.3, 1.3 Hz, 2H), 6.83 (td, *J* = 7.4, 1.0 Hz, 1H), 6.76 (d, *J* = 7.7 Hz, 1H), 4.95 (s, 1H), 4.43 (s, 1H), 3.68 (dddd, *J* = 11.5, 4.6, 3.0, 1.6 Hz, 1H), 3.46 (td, *J* = 11.2, 2.7 Hz, 1H), 3.10 (s, 1H), 2.37 (dtd, *J* = 13.7, 4.0, 1.6 Hz, 1H), 2.18 – 2.10 (m, 1H), 1.58 (dt, *J* = 8.1, 2.2 Hz, 1H), 1.51 – 1.38 (m, 1H).
^{13}C NMR: (125 MHz, $CDCl_3$) δ 149.93, 146.41, 133.70, 129.98, 125.60, 125.48, 124.72, 123.36, 119.87, 110.91, 92.80, 65.89, 62.67, 26.92, 22.04.
HRMS(ESI): calculated for $C_{17}H_{18}N_3O_3S(M+H)^+$: 344.1068; found: 344.1058.

***N*-((5a*S*,10a*R*)-2,3,4,5,10,10a-hexahydro-5a*H*-oxepino[2,3-*b*]indol-5a-yl)-*S*-(2-nitrophenyl)thiohydroxylamine (2n):**

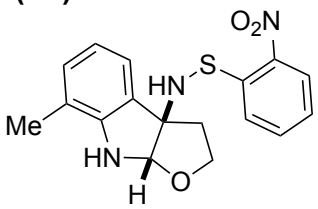


2n

Title compound **2n** was prepared using the **GP-1** for aminocyclizations on 25 µmol scale yielding a yellow oil in 32% isolated yield. (3.2 mg, **TLC:** R_f = 0.25 in 30% ethyl acetate/hexanes).
^{1}H NMR: (500 MHz, $CDCl_3$**)** δ 8.18 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.46 – 7.41 (m, 1H), 7.15 (d, J = 10.6 Hz, 2H), 7.06 (t, J = 7.6 Hz, 1H), 6.64 (t, J = 6.8 Hz, 2H),

4.94 (s, 1H), 4.51 (s, 1H), 3.88 (s, 1H), 3.59 – 3.52 (m, 1H), 3.22 (s, 1H), 2.56 – 2.48 (m, 1H), 2.02 (d, J = 11.0 Hz, 1H), 1.72 (d, J = 11.3 Hz, 2H), 1.26 (s, 1H), 0.84 (s, 1H).
^{13}C NMR: (126 MHz, $CDCl_3$) δ 149.05, 146.37, 142.82, 133.65, 130.20, 129.81, 125.70, 125.61, 124.74, 119.05, 108.96, 99.94, 73.90, 34.54, 32.22, 23.66.
HRMS(ESI): calculated for $C_{18}H_{20}N_3O_3S(M+H)^+$: 358.1225; found: 358.1232.

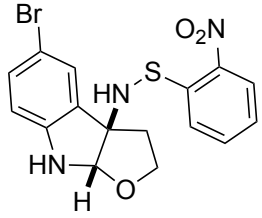
***N*-((3a*S*,8a*R*)-7-methyl-2,3,8,8a-tetrahydro-3a*H*-furo[2,3-*b*]indol-3a-yl)-*S*-(2-nitrophenyl)thiohydroxylamine (2o):**



2o

Title compound **2o** was prepared using the **GP-1** for aminocyclizations on 57 µmol scale yielding a yellow oil in 87% isolated yield. (17.0 mg, **TLC:** R_f = 0.30 in 30% ethyl acetate/hexanes).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.26 (ddd, *J* = 9.8, 8.2, 1.3 Hz, 2H), 7.68 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 5.52 (s, 1H), 4.49 (s, 1H), 4.01 (td, *J* = 8.4, 1.8 Hz, 1H), 3.63 (ddd, *J* = 11.0, 8.7, 5.1 Hz, 1H), 3.25 (s, 1H), 2.49 (td, *J* = 11.3, 7.6 Hz, 1H), 2.27 – 2.20 (m, 1H), 2.17 (s, 3H).
^{13}C NMR: (126 MHz, $CDCl_3$) δ 148.58, 145.70, 142.71, 133.96, 131.02, 129.23, 125.84, 124.99, 124.96, 121.49, 119.75, 119.00, 97.33, 78.15, 67.27, 38.17, 16.77.
HRMS(ESI): calculated for $C_{17}H_{18}N_3O_3S(M+H)^+$: 344.1069; found: 344.1058.

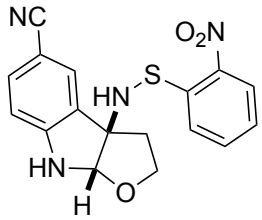
***N*-((3a*S*,8a*R*)-5-bromo-2,3,8,8a-tetrahydro-3a*H*-furo[2,3-*b*]indol-3a-yl)-*S*-(2-nitrophenyl)thiohydroxylamine (2p):**



2p

Title compound **2p** was prepared using the **GP-1** for aminocyclizations on 22 µmol scale yielding a yellow oil in 77% isolated yield. (6.5 mg, **TLC:** R_f = 0.30 in 30% ethyl acetate/hexanes).
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.3, 1.3 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.70 (ddd, *J* = 8.4, 7.1, 1.5 Hz, 1H), 7.41 (d, *J* = 2.1 Hz, 1H), 7.29 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1H), 7.23 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.52 (d, *J* = 8.3 Hz, 1H), 5.51 (s, 1H), 4.02 (ddd, *J* = 9.2, 7.6, 1.7 Hz, 1H), 3.63 (ddd, *J* = 11.0, 8.9, 5.1 Hz, 1H), 3.28 (s, 1H), 2.51 – 2.41 (m, 1H), 2.23 (ddd, *J* = 12.1, 5.1, 1.7 Hz, 1H).
^{13}C NMR: (126 MHz, $CDCl_3$) δ 149.05, 145.05, 142.76, 134.03, 132.98, 131.84, 127.26, 125.89, 125.18, 124.92, 110.83, 110.75, 97.62, 77.81, 67.22, 38.43.
HRMS(ESI): calculated for $C_{16}H_{15}BrN_3O_3S(M+H)^+$: 408.0018; found: 409.0014.

(3a*S*,8a*R*)-3a-(((2-nitrophenyl)thio)amino)-3,3a,8,8a-tetrahydro-2*H*-furo[2,3-*b*]indole-5-carbonitrile (2q):



2q

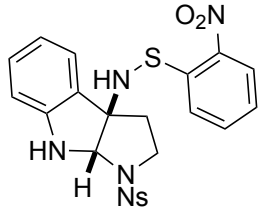
Title compound **2q** was prepared using the **GP-1** for aminocyclizations on 37 µmol scale yielding a yellow oil in 68% isolated yield. (8.5 mg, **TLC:** R_f = 0.20 in 30% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$**)** δ 8.27 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.19 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.56 (d, *J* = 1.9 Hz, 1H), 7.42 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.34 – 7.29 (m, 1H), 6.61 (d, *J* = 8.3 Hz, 1H), 5.59 (s, 1H), 5.10 (br, 1H) 4.06 (ddd, *J* = 9.2, 7.6, 1.5 Hz, 1H), 3.61 (ddd, *J* = 11.3, 9.1, 5.0 Hz, 1H), 3.34 (s, 1H), 2.49 (td, *J* = 11.8, 7.6 Hz, 1H), 2.24 (dd, *J* = 12.1, 3.7 Hz, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 153.44, 144.46, 135.35, 134.08, 130.24, 128.47, 125.93, 125.39, 124.86, 119.93, 108.73, 101.27, 97.45, 77.41, 67.17, 47.68, 39.02.

LRMS(ESI): calculated for $C_{17}H_{15}N_4O_3S(M+H)^+$: 355.1; found: 355.2.

***S*-(2-nitrophenyl)-*N*-((3a*S*,8a*R*)-1-((4-nitrophenyl)sulfonyl)-2,3,8,8a tetrahydro pyrrolo[2,3-*b*]indol-3a(1*H*)-yl)thiohydroxylamine (2r):**



2r

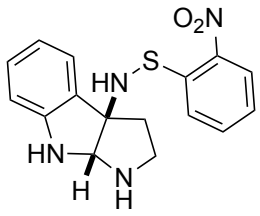
Title compound **2r** was prepared using the **GP-1** for aminocyclizations on 2.90 mmol scale yielding a yellowish solid in 68% isolated yield. (0.98g, **TLC:** R_f = 0.30 in 30% ethyl acetate/hexanes).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.8 Hz, 2H), 8.25 (d, *J* = 8.3 Hz, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 8.8 Hz, 2H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.30 (dd, *J* = 7.4, 3.7 Hz, 2H), 7.22 (t, *J* = 7.7 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 5.29 (s, 1H), 4.93 (s, 1H), 3.49 (ddd, *J* = 10.4, 8.1, 2.0 Hz, 1H), 3.16 (td, *J* = 10.8, 6.0 Hz, 1H), 3.11 (s, 1H), 2.29 (td, *J* = 11.7, 8.1 Hz, 1H), 2.19 (ddd, *J* = 12.6, 6.0, 2.0 Hz, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 150.31, 149.42, 144.54, 144.39, 142.73, 134.15, 131.16, 128.39, 128.20, 125.94, 125.45, 124.62, 123.82, 120.23, 110.71, 81.42, 77.62, 47.12, 34.03.

HRMS(ESI): calculated for $C_{22}H_{20}N_5O_6S_2(M+H)^+$: 514.0852; found: 514.0841.

***S*-(2-nitrophenyl)-*N*-((3a*S*,8a*S*)-2,3,8,8a-tetrahydropyrrolo[2,3-*b*]indol-3a(1*H*)-yl)thiohydroxylamine (3):**



3

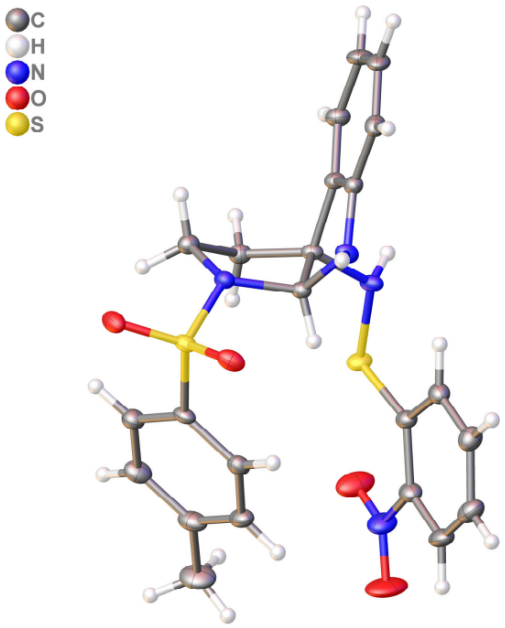
To a solution of compound **2r** (40 mg) in CH_3CN (0.1 M), 4-methylbenzenethiol (2.0 equiv.) and K_2CO_3 (4.0 equiv.) was added and stirred at room temperature overnight until the completion of reaction. After the completion of reaction, crude mixture was filtered through the short pad of celite and purified by silica gel chromatography to obtain the title compound as a yellowish oil in 72% isolated yield. (18.5 mg, **TLC:** R_f = 0.30 in 20% MeOH/CH_2Cl_2).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.3 Hz, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 7.68 (t, *J* = 7.7 Hz, 1H), 7.25 (d, *J* = 7.3 Hz, 2H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 5.48 – 5.38 (m, 1H), 3.64 (s, 1H), 3.34 (d, *J* = 10.5 Hz, 1H), 2.91 (s, 1H), 2.46 (d, *J* = 7.2 Hz, 1H), 2.29 (d, *J* = 8.1 Hz, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$)δ 150.06, 145.23, 142.63, 134.07, 130.39, 125.75, 125.33, 125.00, 124.05, 119.84, 110.26, 83.18, 44.71, 38.65, 29.86.

HRMS(ESI): calculated for $C_{16}H_{17}N_4O_2S(M+H)^+$: 329.1072; found: 329.1061.

5. X-Ray Crystallographic Data of 2a



Formula unit.
The inverted structure was also found in the packing.
Thermal ellipsoids are drawn at 50% probability level.

Empirical formula	$C_{23}H_{22}N_4O_4S_2$	
Formula weight	482.56	
Crystal color, shape, size	yellow plate, 0.598 × 0.202 × 0.078 mm^3	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system, space group	Monoclinic, $P2_1/c$	
Unit cell dimensions	a = 21.5245(9) Å	α = 90°
	b = 8.0424(3) Å	β = 97.0210(10)°
	c = 12.9761(5) Å	γ = 90°
Volume	2229.43(15) $Å^3$	
Z	4	
Density (calculated)	1.438 Mg/m^3	
Absorption coefficient	0.278 mm^{-1}	
F(000)	1008	

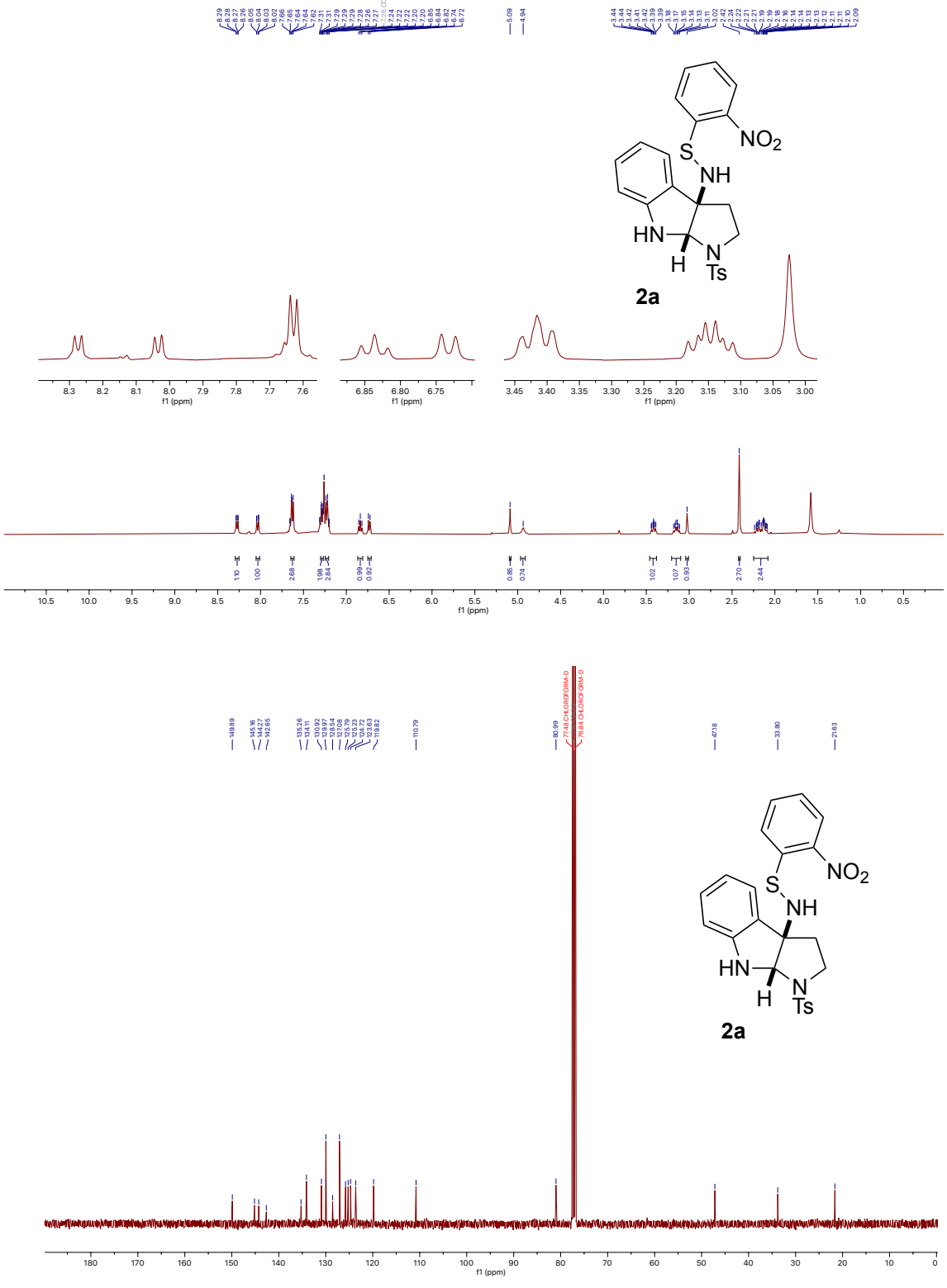
Data collection

Diffractometer	D8 QUEST, Bruker
Source	IμS 2.0, Incoatec
Detector	PHOTON II
Theta range for data collection	2.706 to 26.020°
Index ranges	-26<=h<=26, -9<=k<=9, -14<=l<=16
Reflections collected	44956
Independent reflections	4350 [R_{int} = 0.0639]
Observed Reflections	4099
Completeness to theta = 25.242°	99.4 %

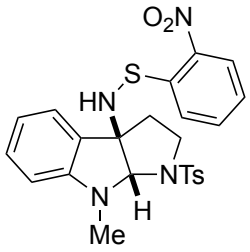
Solution and Refinement

Absorption correction	Multi-Scan
Max. and min. transmission	0.7454 and 0.4358
Solution	Intrinsic methods
Refinement method	Full-matrix least-squares on F^2
Weighting scheme	$w = [\sigma^2 Fo^2 + AP^2 + BP]^{-1}$, with
	$P = (Fo^2 + 2\,Fc^2)/3$, A = 0.0465, B = 1.9118
Data / restraints / parameters	4350 / 0 / 307
Goodness-of-fit on F^2	1.065
Final R indices [I>2σ(I)]	R1 = 0.0375, wR2 = 0.0985
R indices (all data)	R1 = 0.0396, wR2 = 0.1004
Extinction coefficient	n/a
Largest diff. peak and hole	0.436 and -0.552 $e.Å^{-3}$

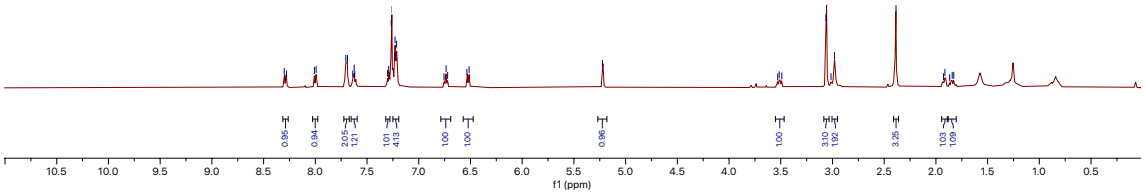
6.NMR Spectras

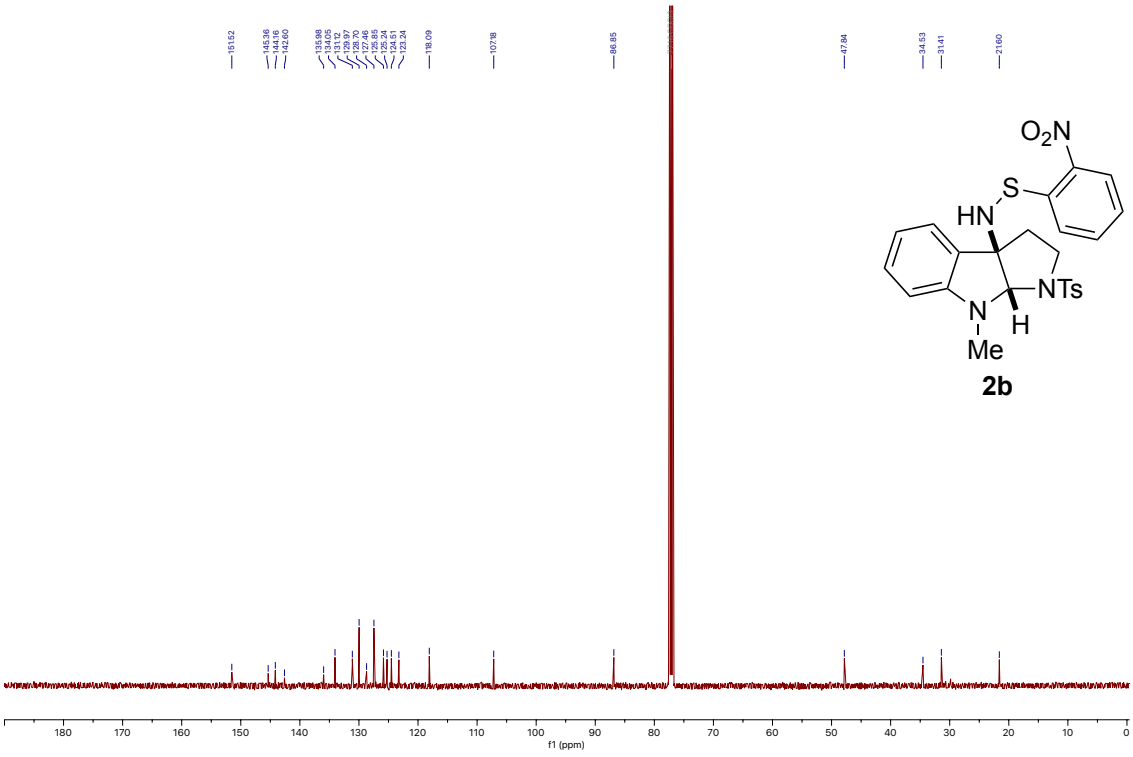



8.30
8.28
8.00
7.99
7.71
7.69
7.64
7.62
7.62
7.60
7.29
7.27
7.24
7.24
7.23
7.21
6.76
6.74
6.72
6.53
6.51
5.22
3.53
3.52
3.49
3.06
3.01
2.98
2.39
1.93
1.91
1.87
1.84
1.83


O2N
S
HN
NTs
N
H
Me

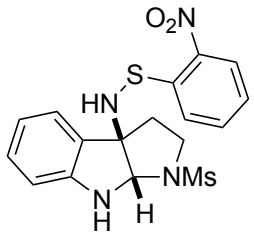
2b


0.95
0.94
2.05
1.21
1.01
4.13
1.00
1.00
0.96
1.00
3.10
1.92
3.25
1.03
1.09
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

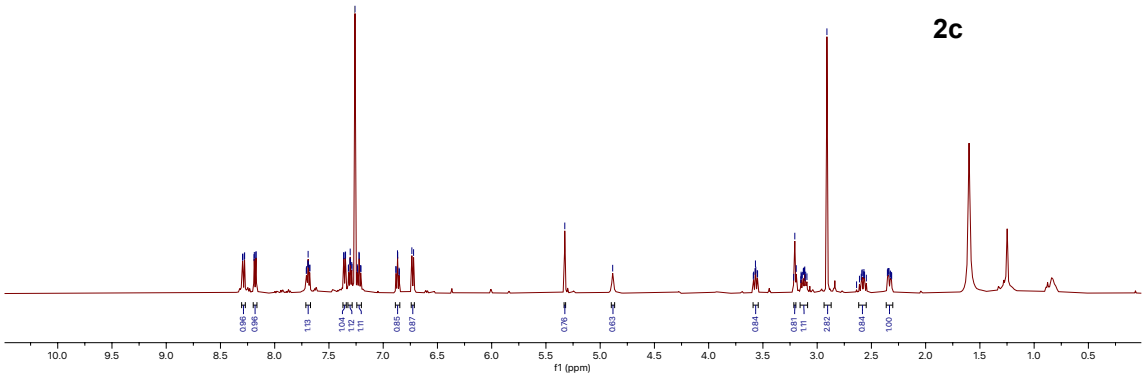

151.52
143.36
141.45
142.60
135.98
134.05
131.12
129.90
128.70
127.46
126.85
125.24
124.51
123.24
118.09
107.18
86.85
47.84
34.53
31.41
21.60
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

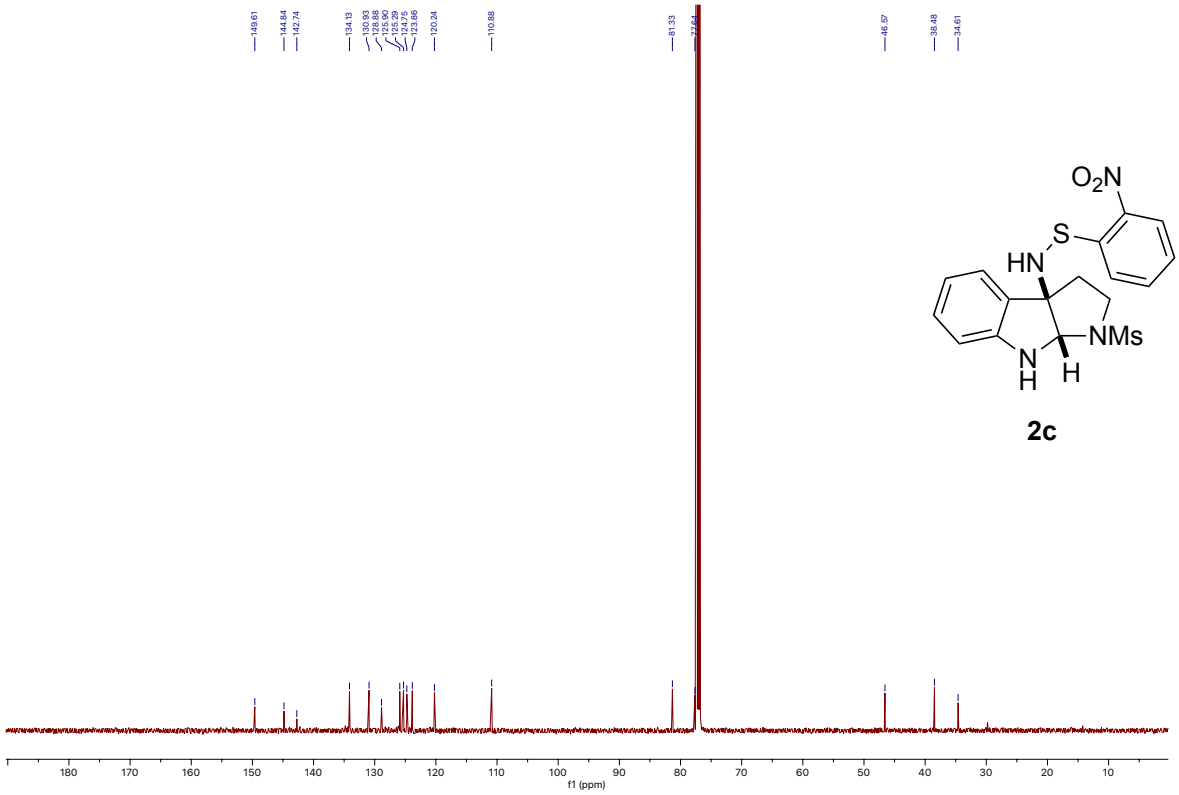
O2N
S
HN
NTs
N
H
Me

2b

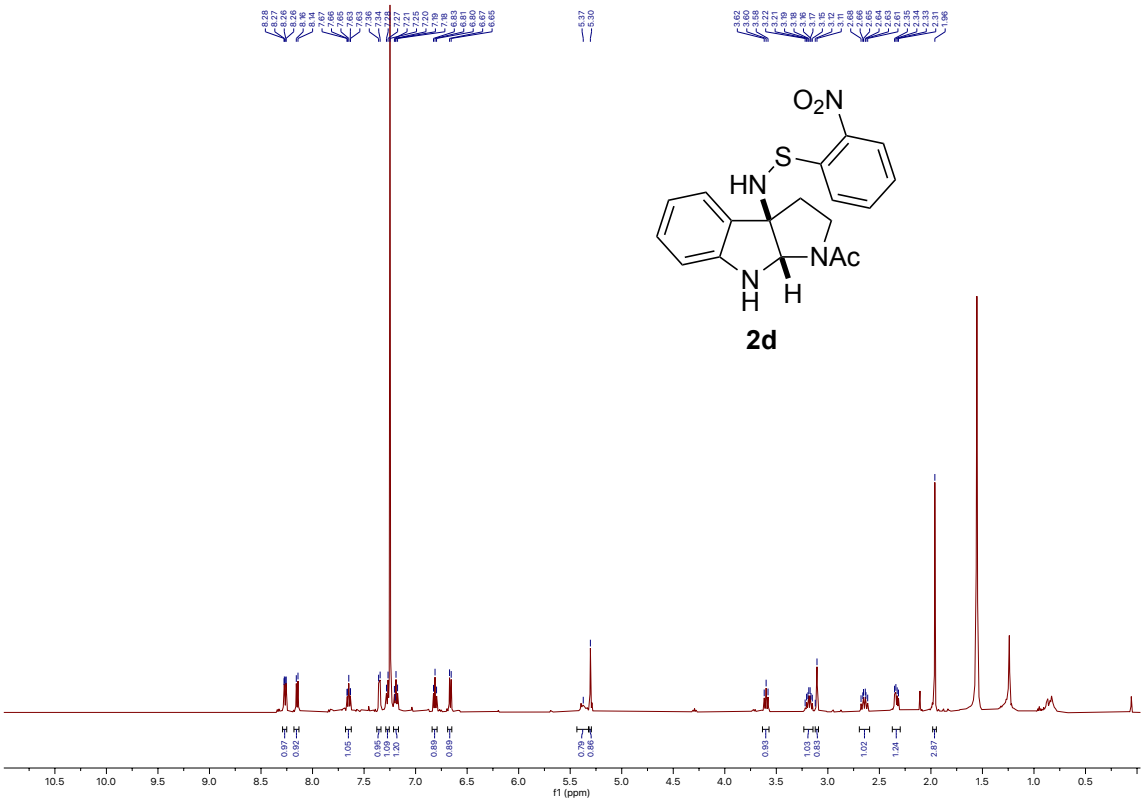


2c

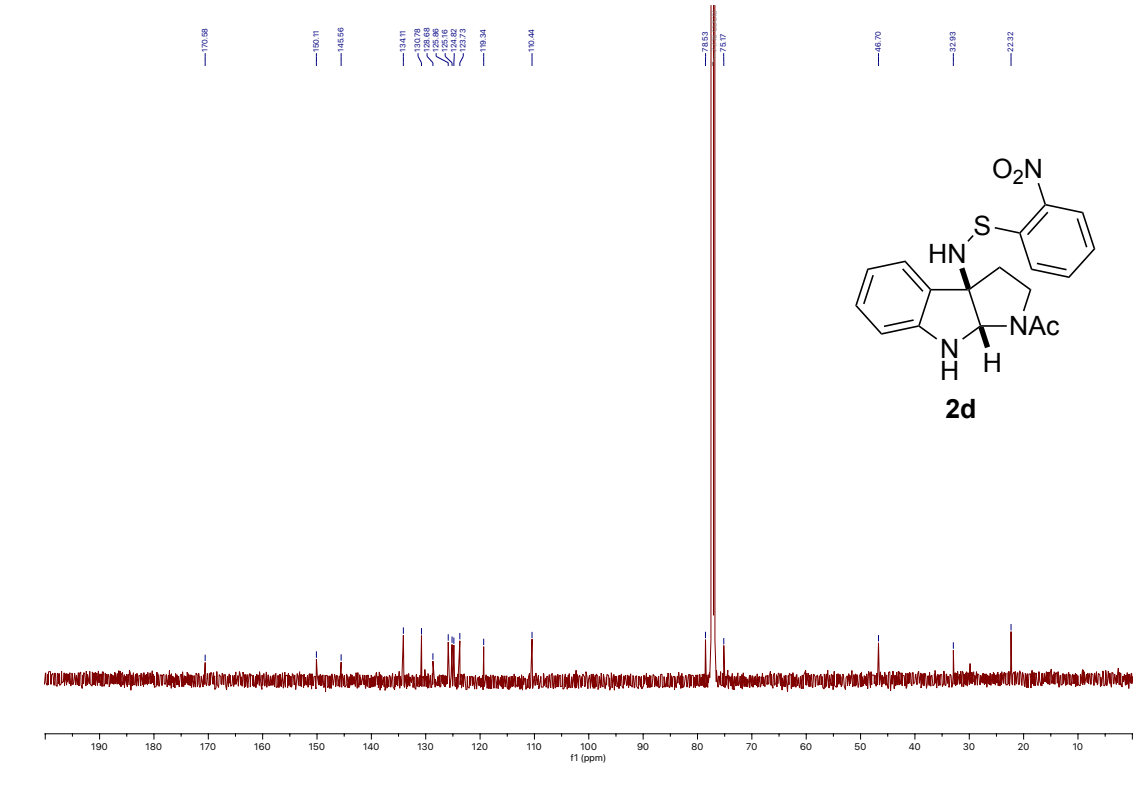




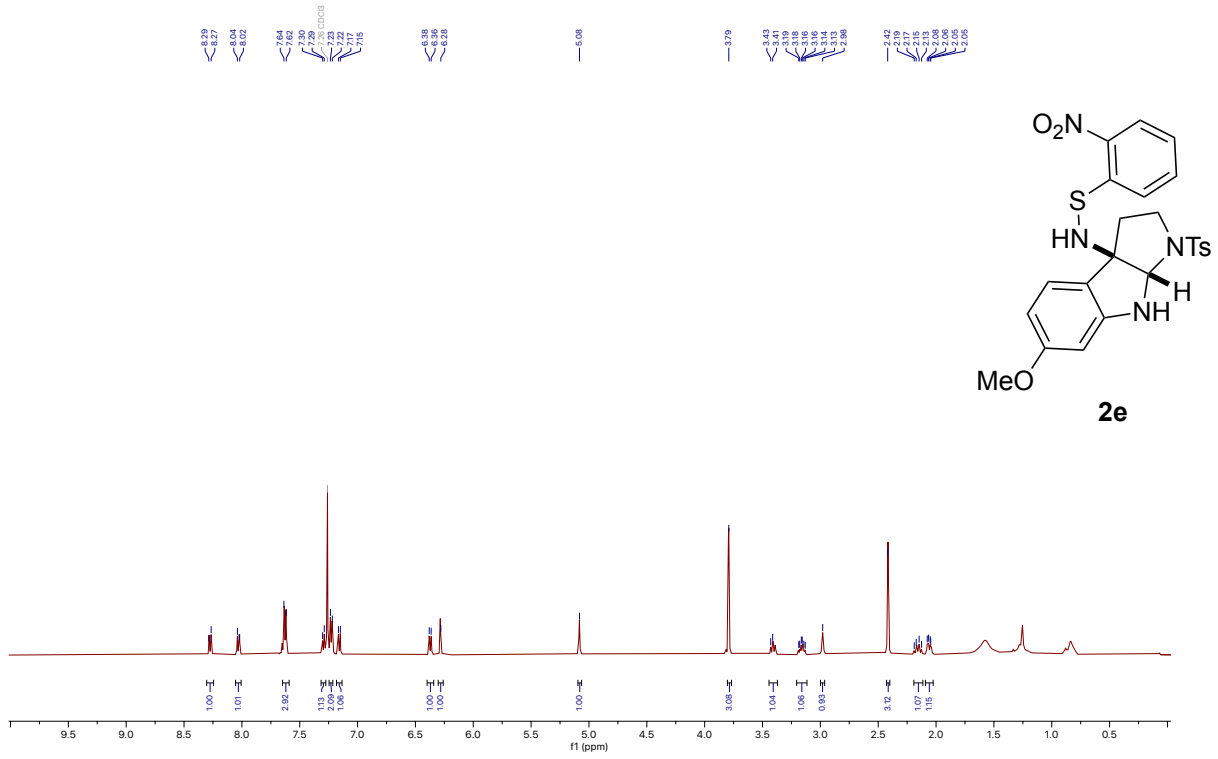
2c

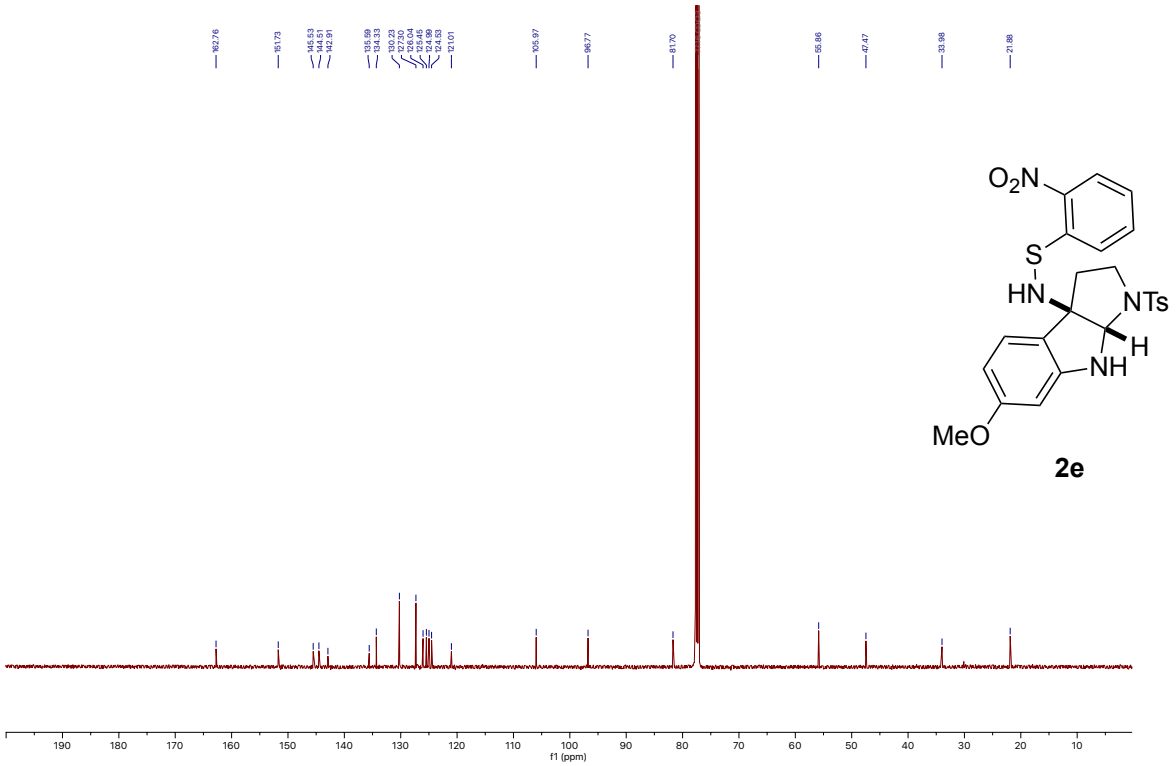


2d



2d


O2N
S
HN
NTs
H
NH
MeO
2e
f1 (ppm)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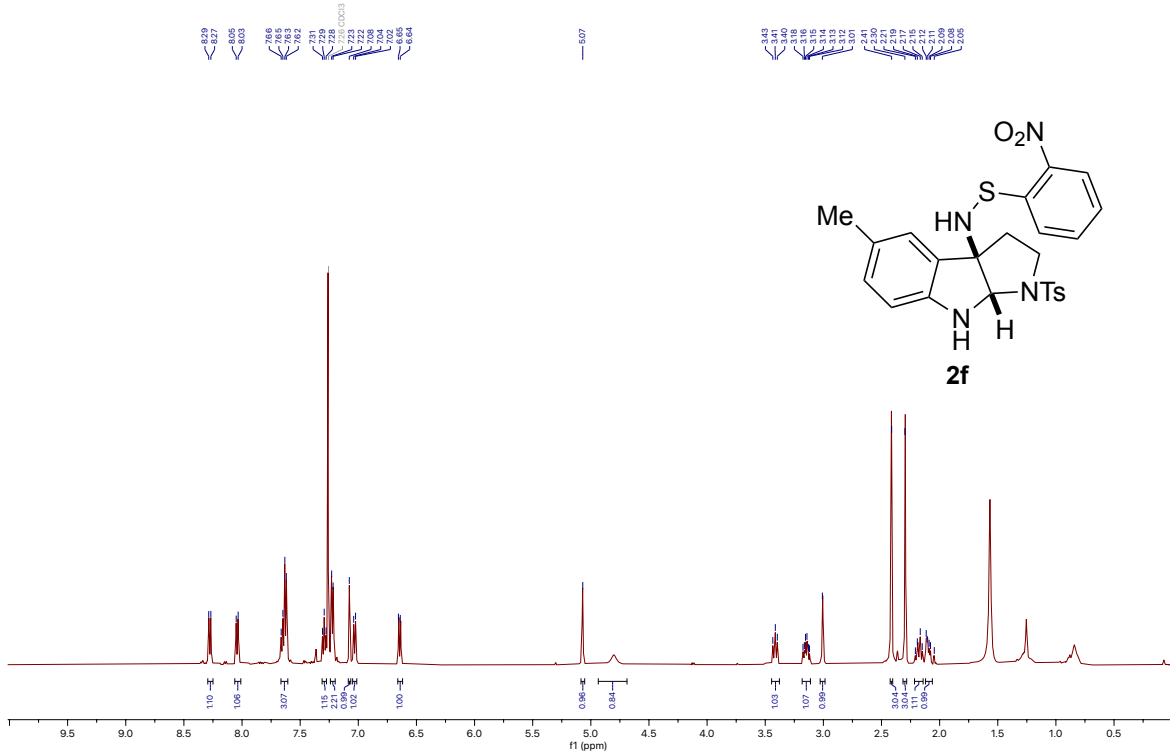
NTs
H
NH
MeO
2e
f1 (ppm)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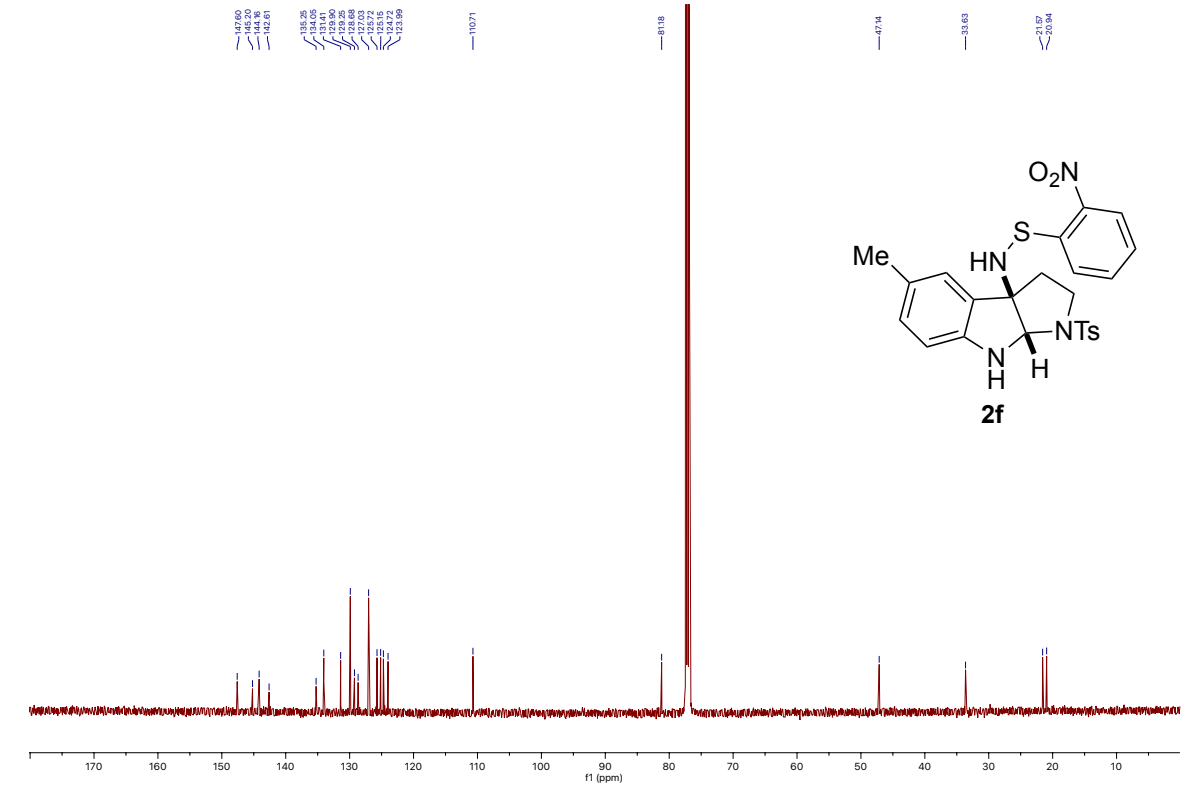
7.08
7.04
7.02
6.65
6.64
5.07
3.43
3.41
3.40
3.18
3.16
3.15
3.14
3.13
3.12
3.01
2.41
2.30
2.21
2.19
2.17
2.16
2.12
2.11
2.09
2.08
2.05
1.10
1.06
3.07
1.15
2.21
0.99
1.02
1.00
0.96
0.84
1.03
1.07
0.99
3.04
3.04
1.11
0.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
O2N
S
HN
Me
NTs
N
H
H
2f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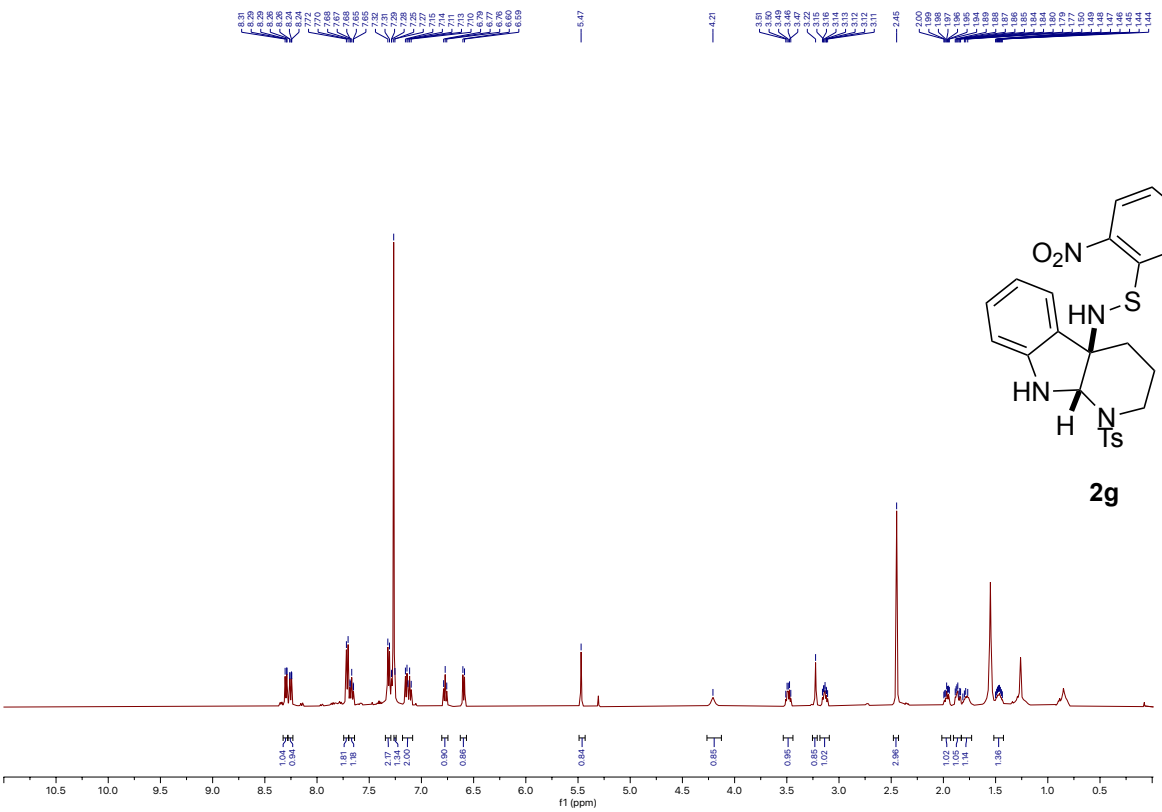
127.03
125.72
125.15
124.72
123.99
110.71
81.18
47.14
33.63
21.57
20.94
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)
O2N
S
HN
Me
NTs
N
H
H
2f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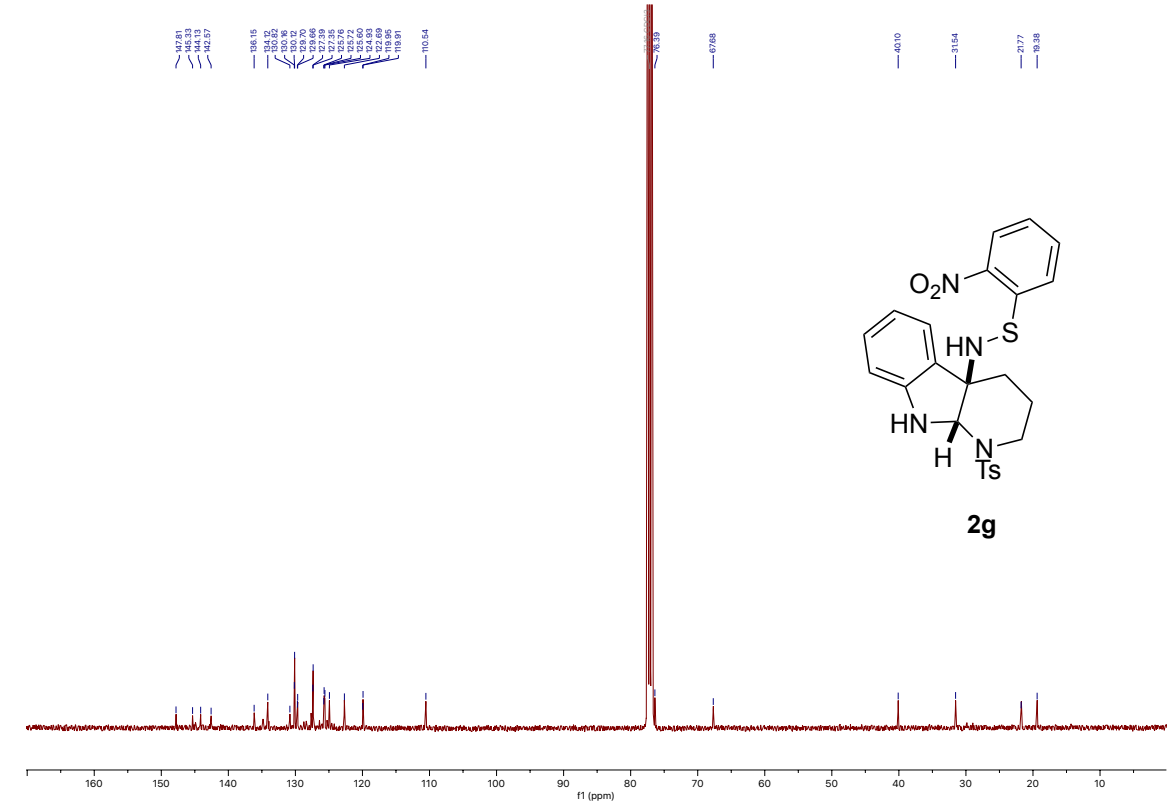
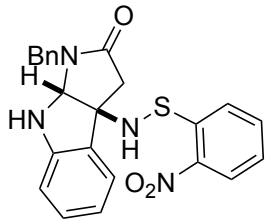
HN
S
HN
H
N
Ts
2g
f1 (ppm)


O2N
HN
S
HN
H
N
Ts
2g
f1 (ppm)



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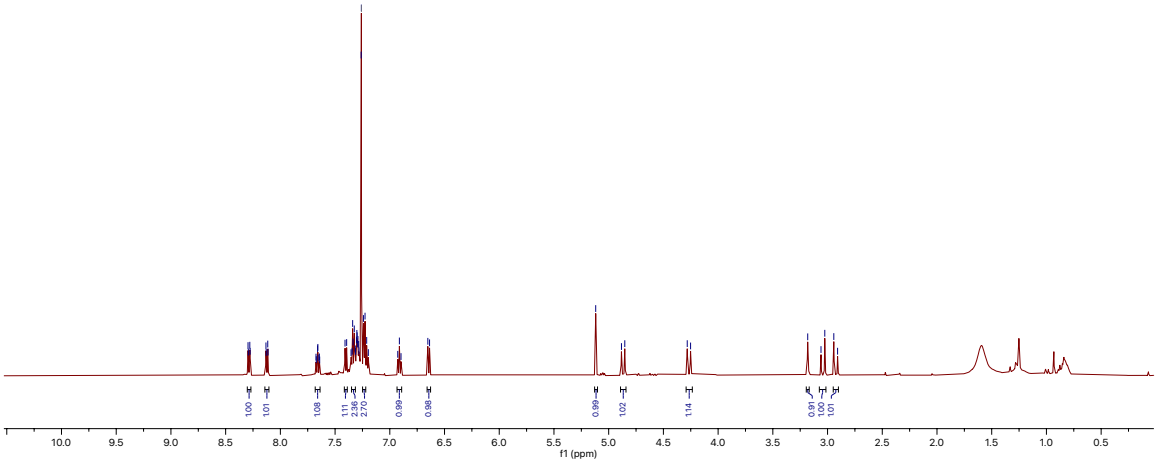

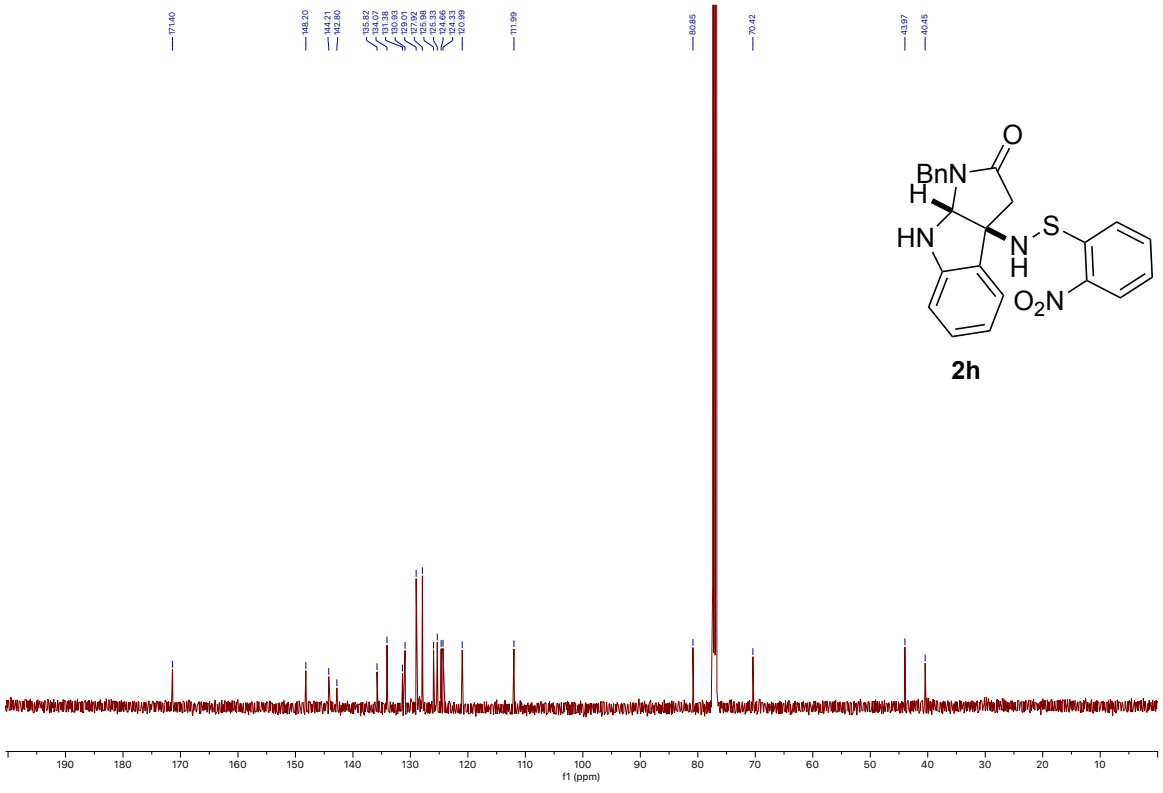

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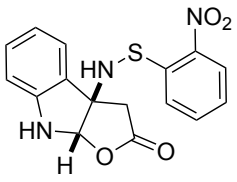

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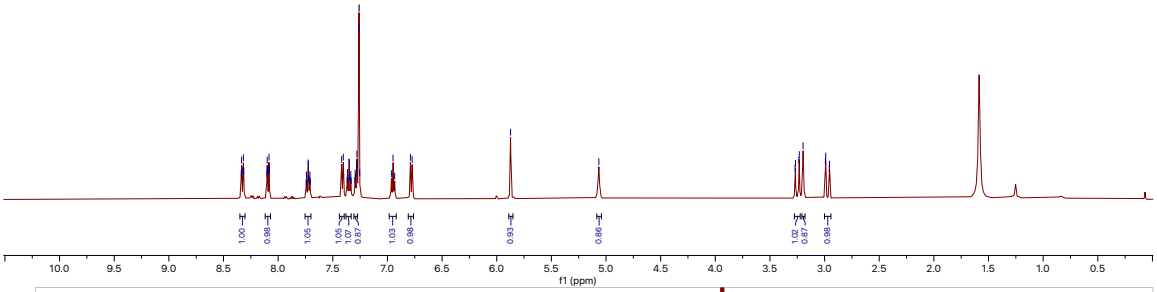

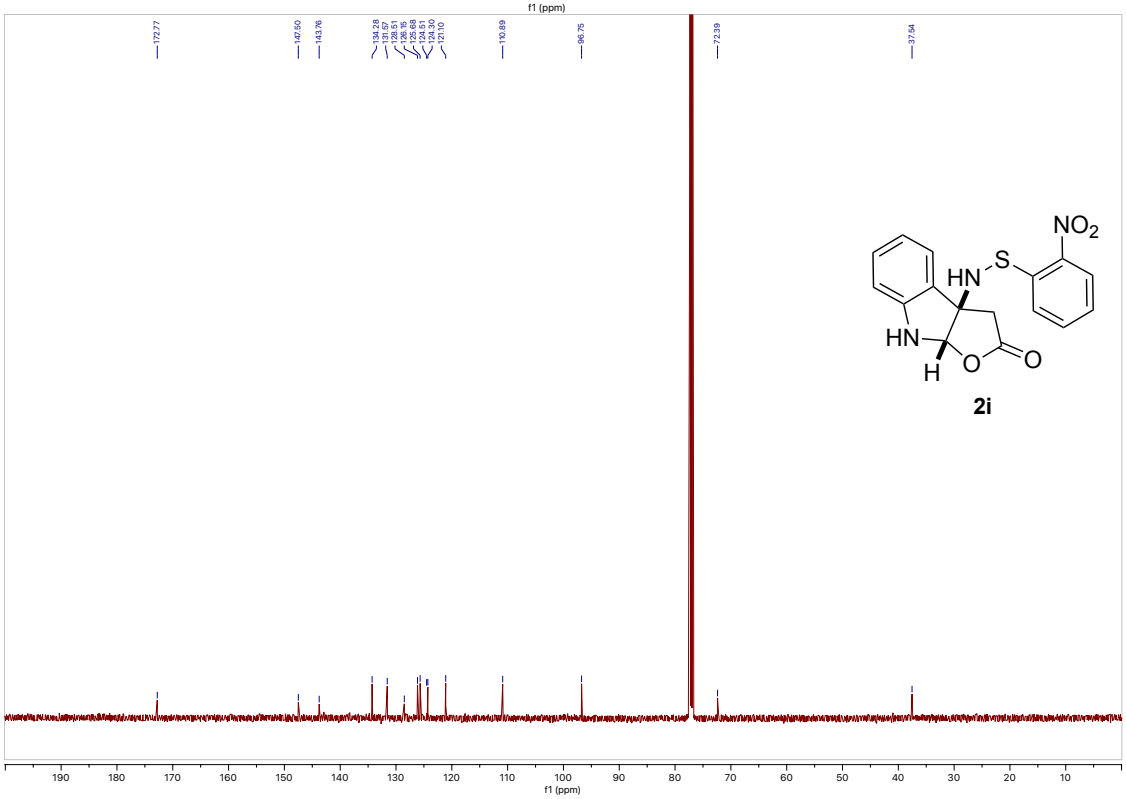

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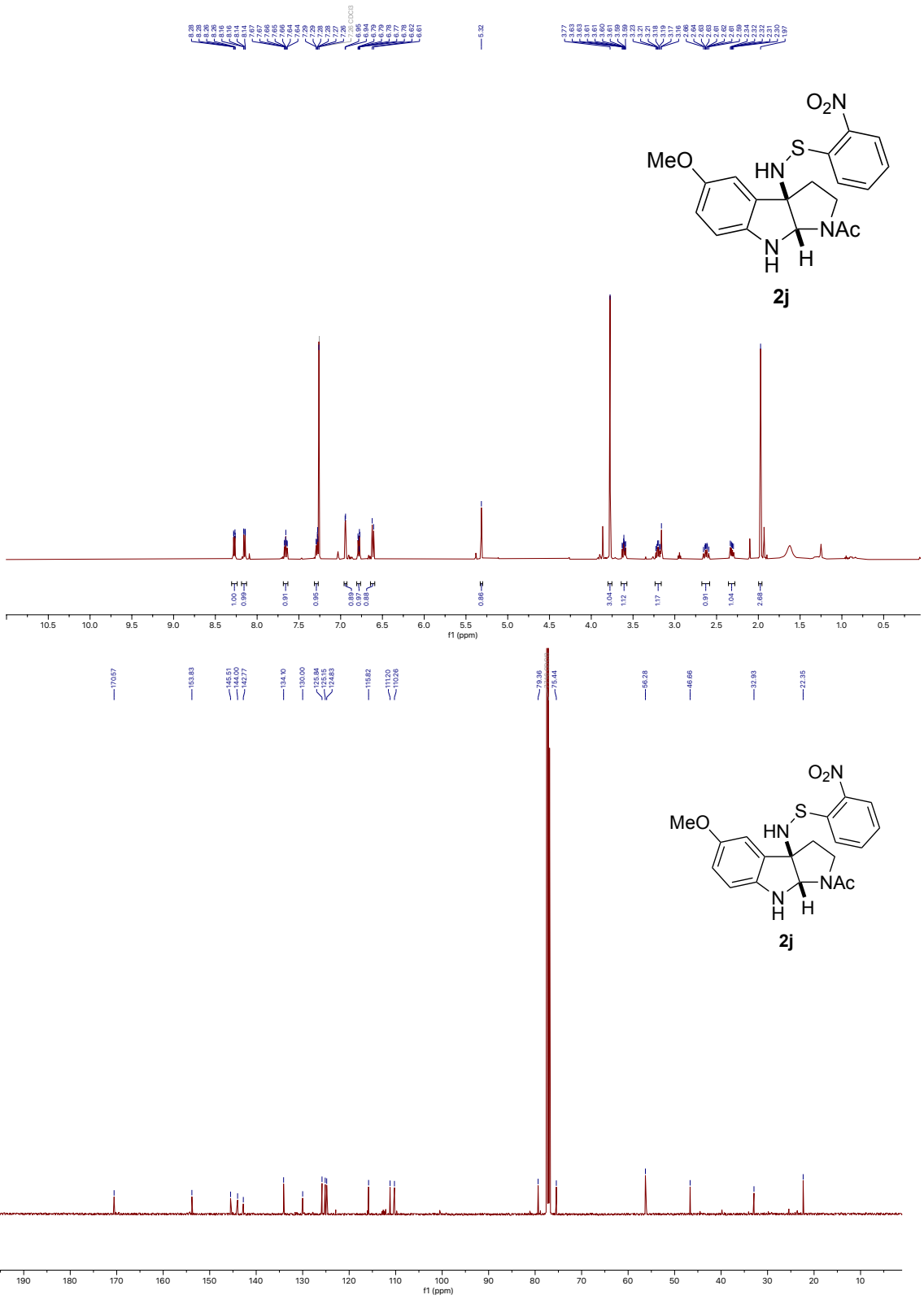
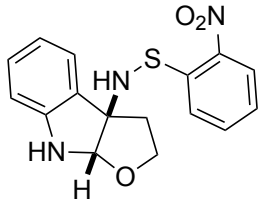

O2N
S
MeO
HN
NAc
N
H
H
2j
f1 (ppm)
O2N
S
MeO
HN
NAc
N
H
H
2j
f1 (ppm)



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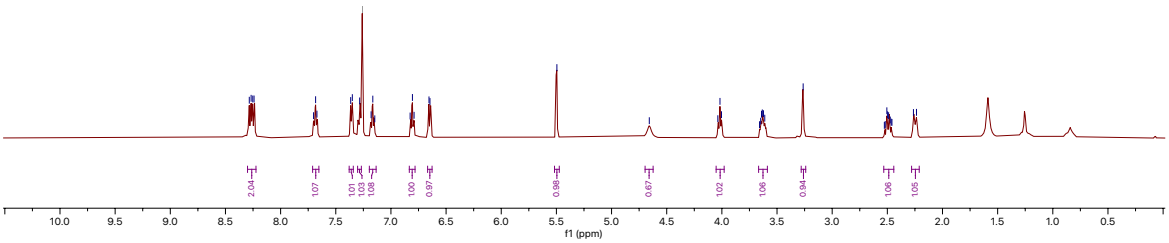

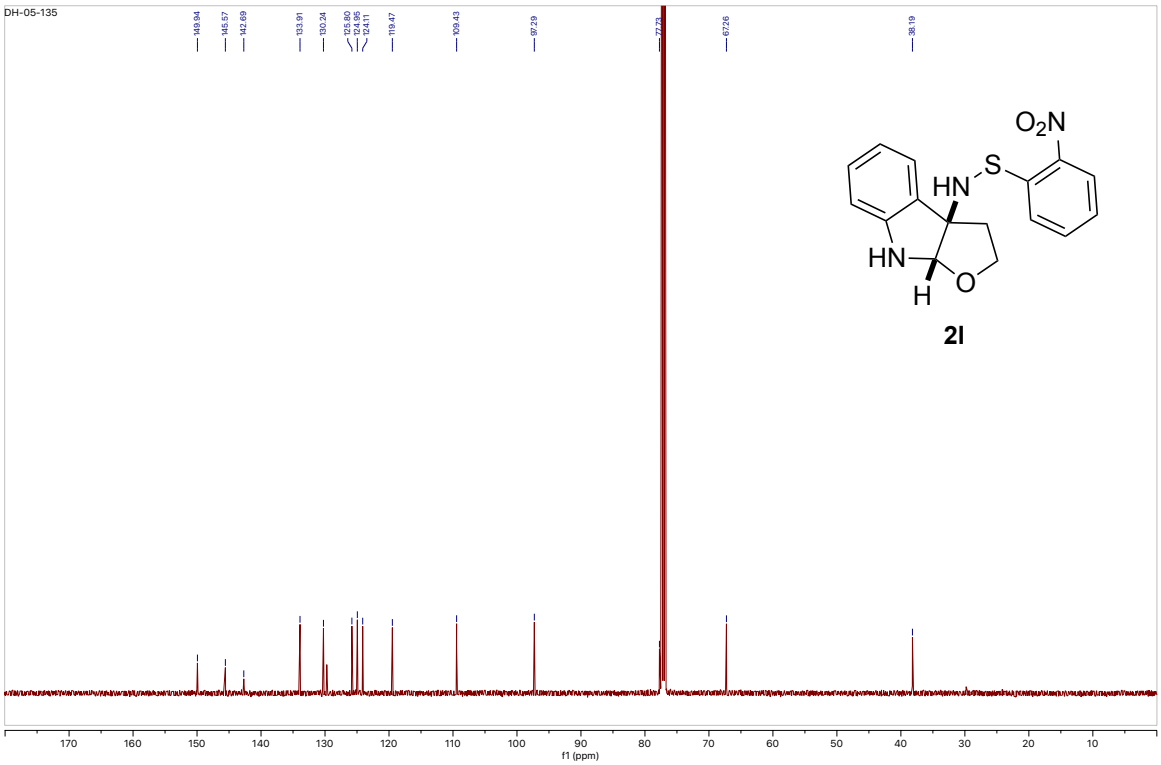

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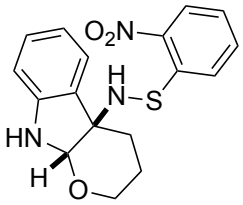

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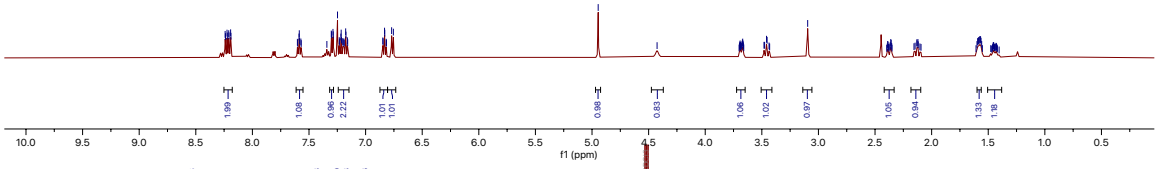

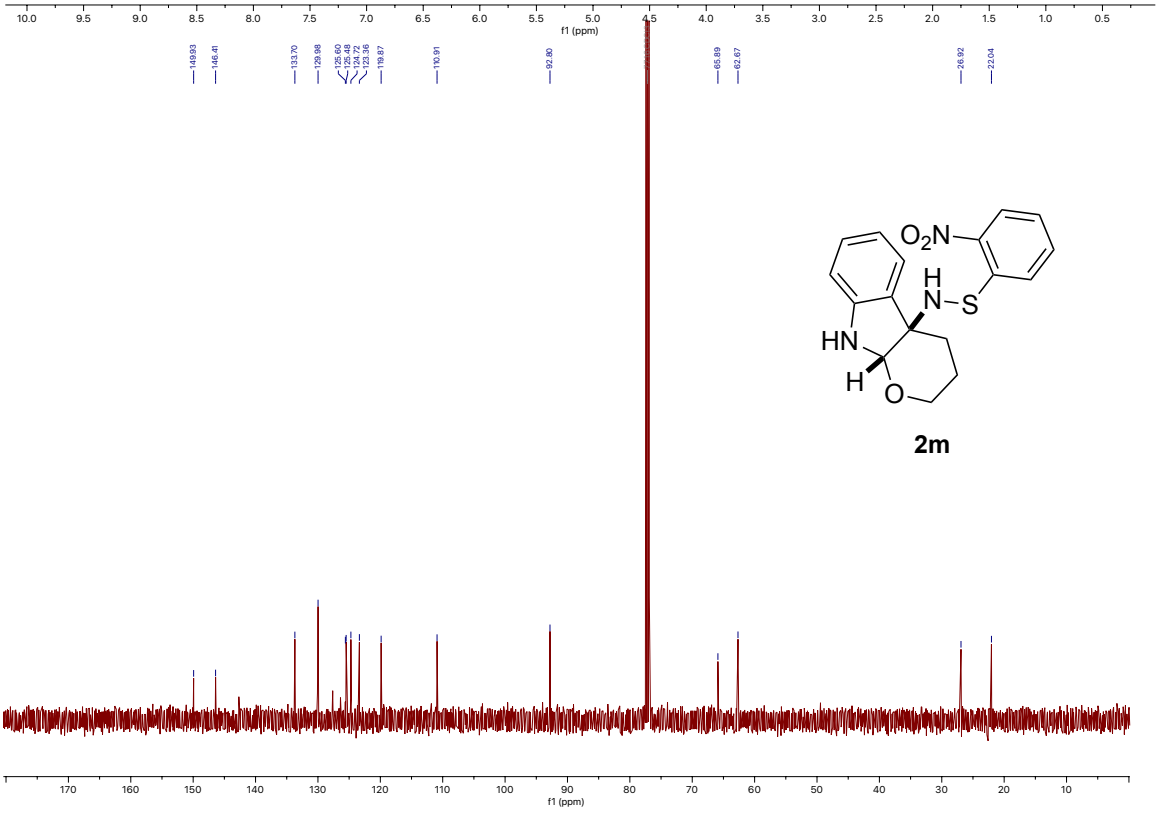

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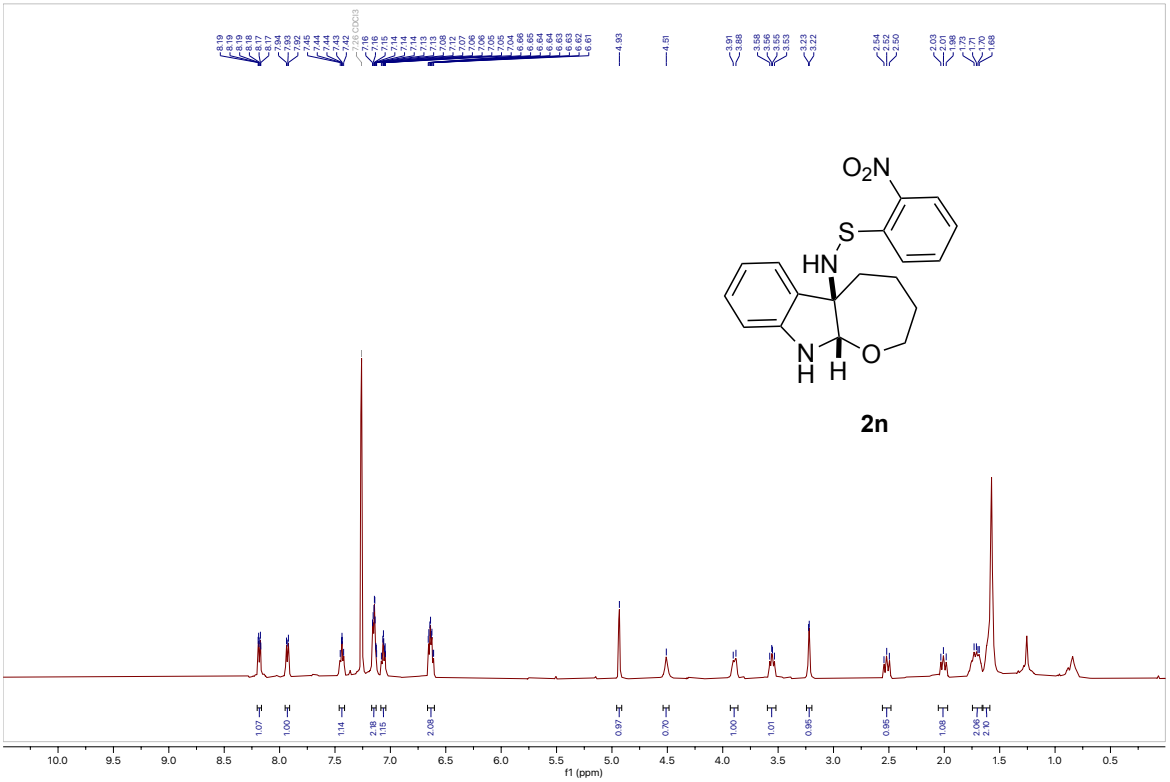
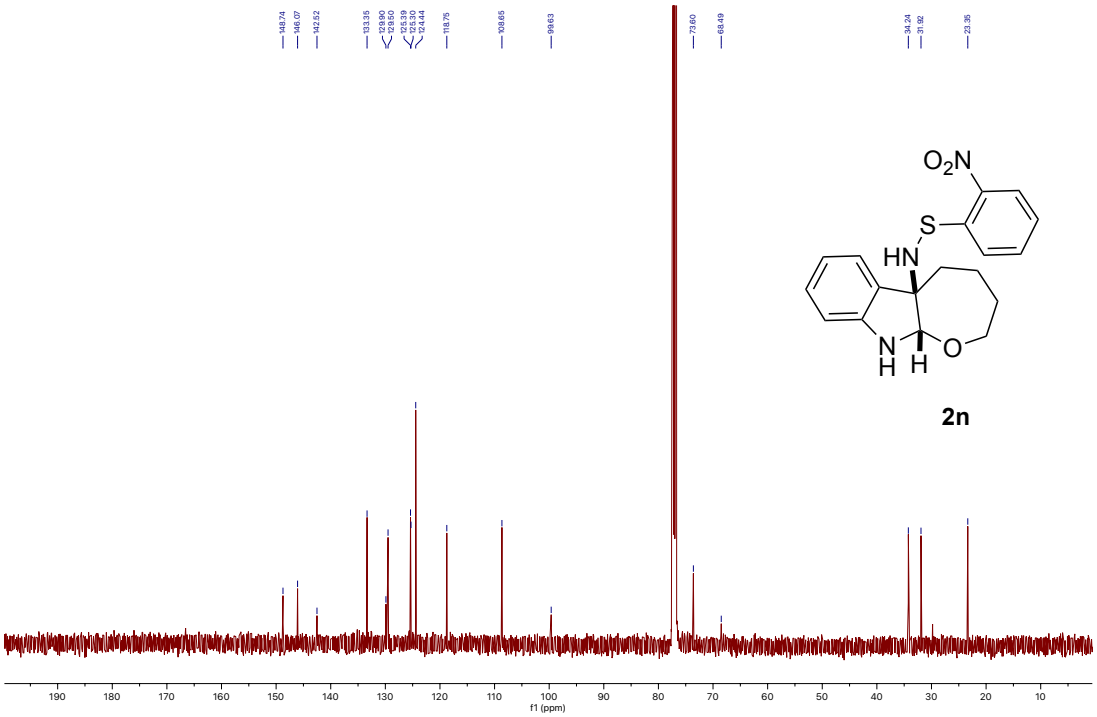
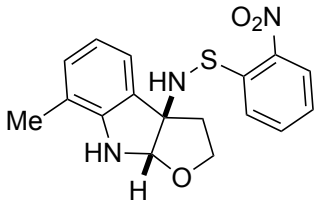
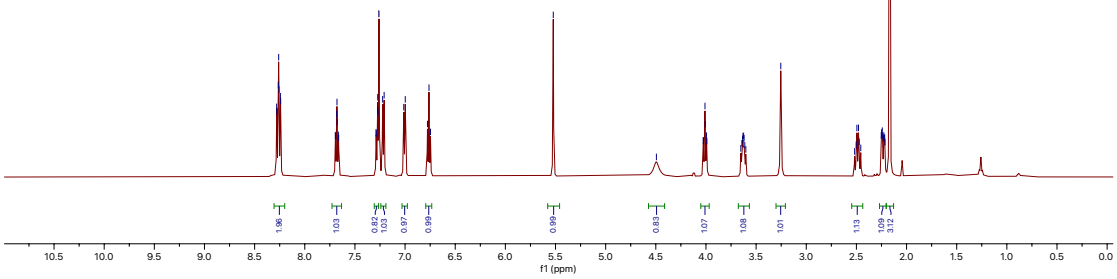

O2N
S
HN
N
H
H
O
2n
f1 (ppm)


O2N
S
HN
N
H
H
O
2n
f1 (ppm)


O_2N
S
HN
Me
HN
O
H

2o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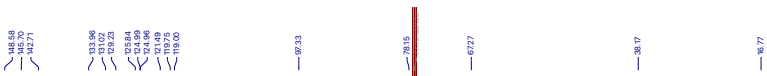
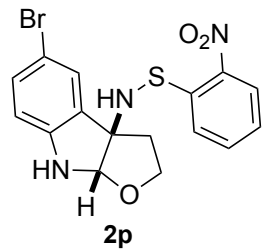
1.13
1.09
3.12
f1 (ppm)



f1 (ppm)

O_2N
S
HN
Me
HN
O
H

2o



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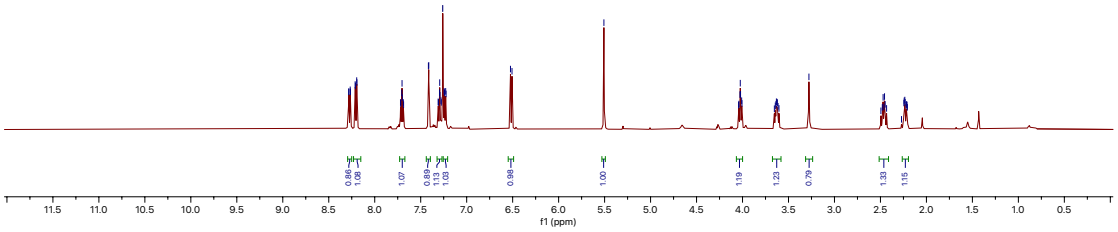

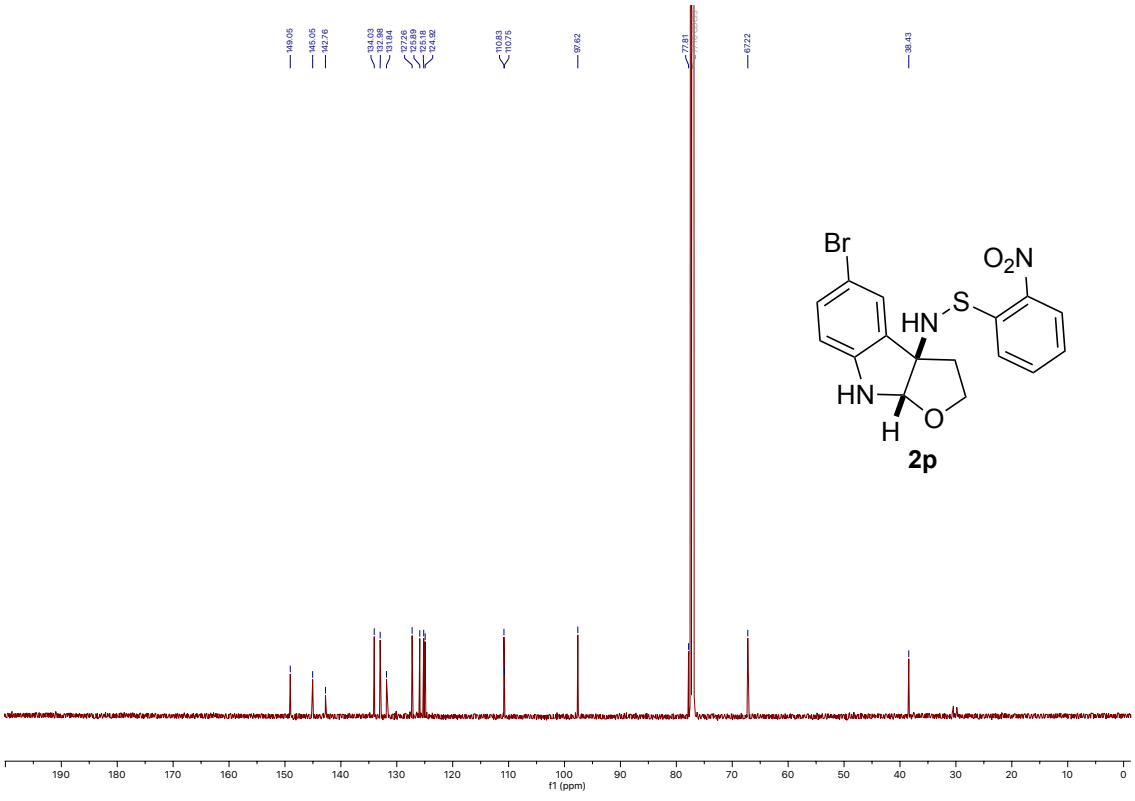

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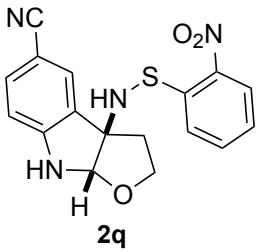

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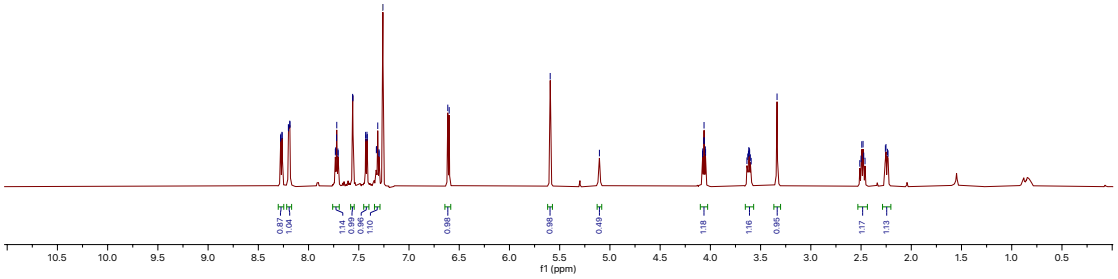

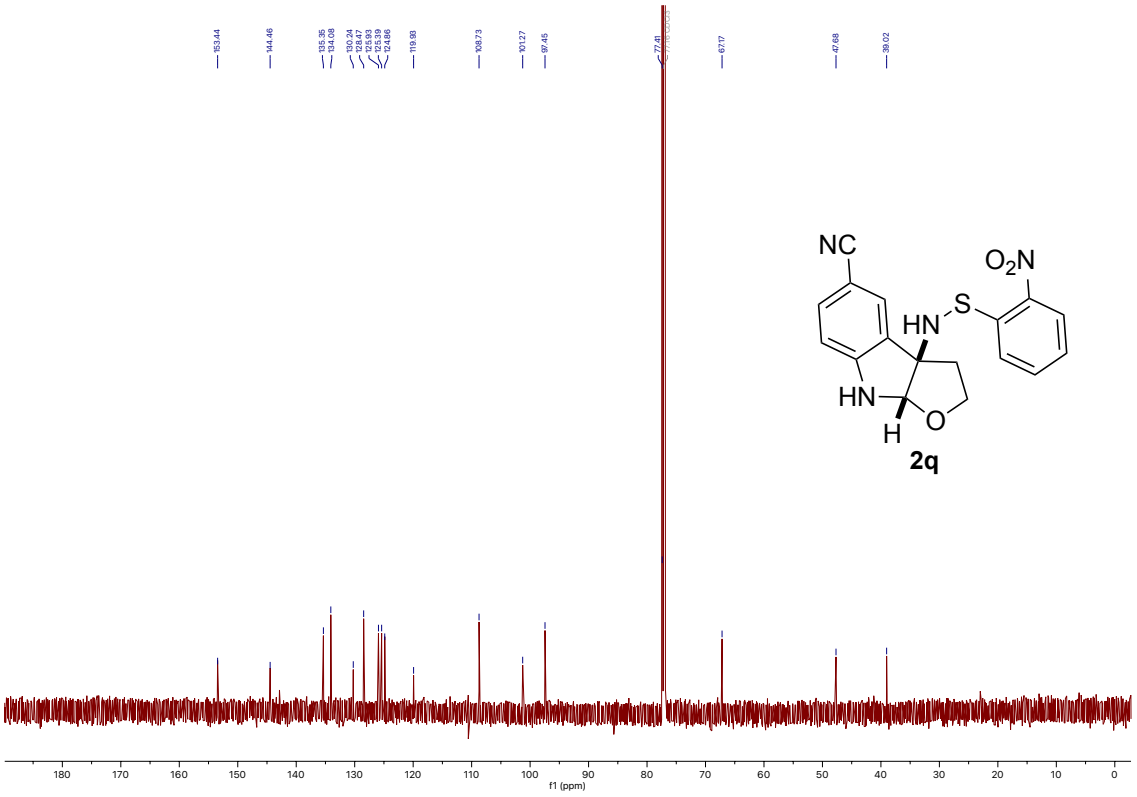

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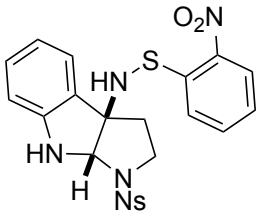

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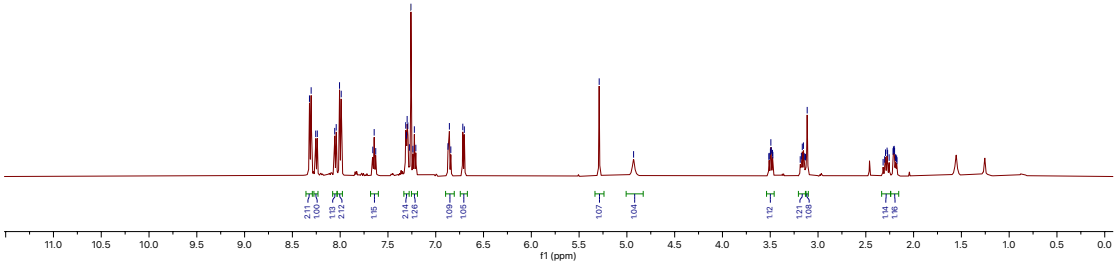

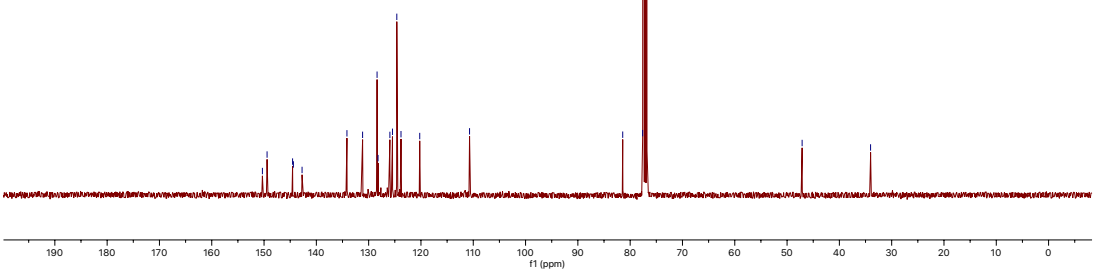

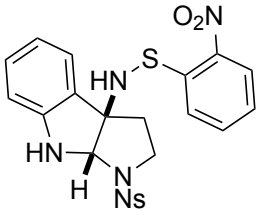

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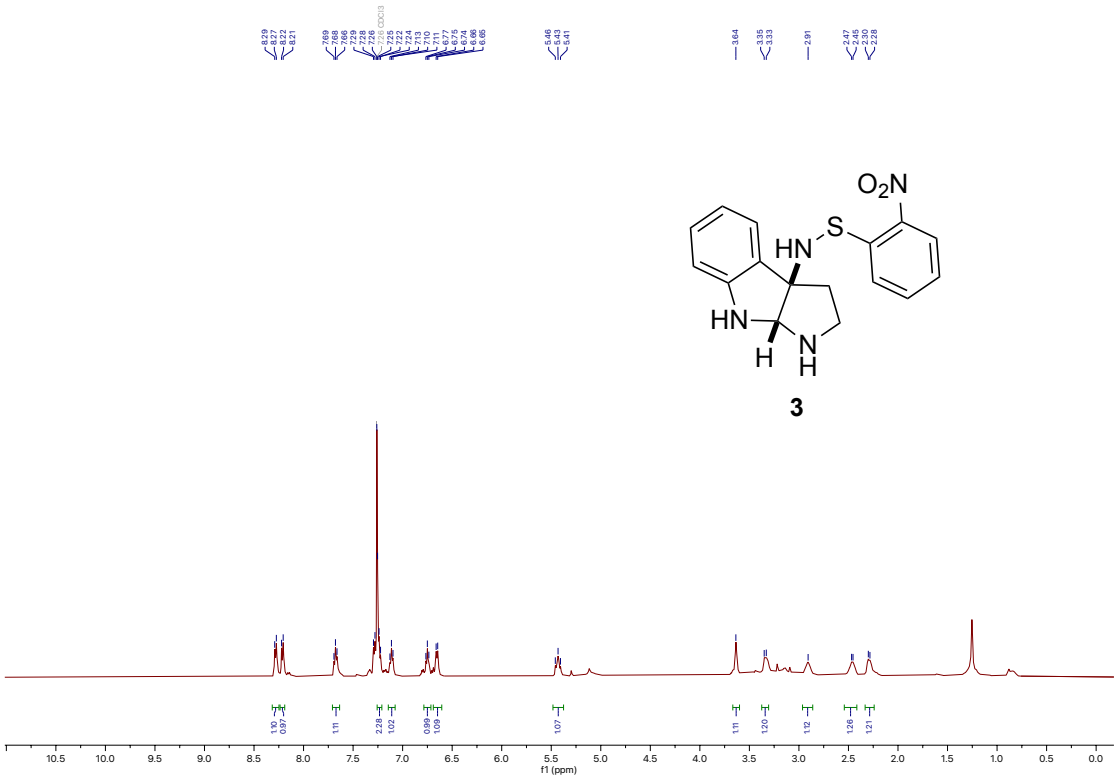
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7.22
7.14
7.10
7.10
6.77
6.75
6.74
6.66
6.65
5.46
5.43
5.41
3.64
3.35
3.33
2.91
2.47
2.46
2.30
2.28
O2N
S
HN
HN
H
N
H
3
1.00
0.97
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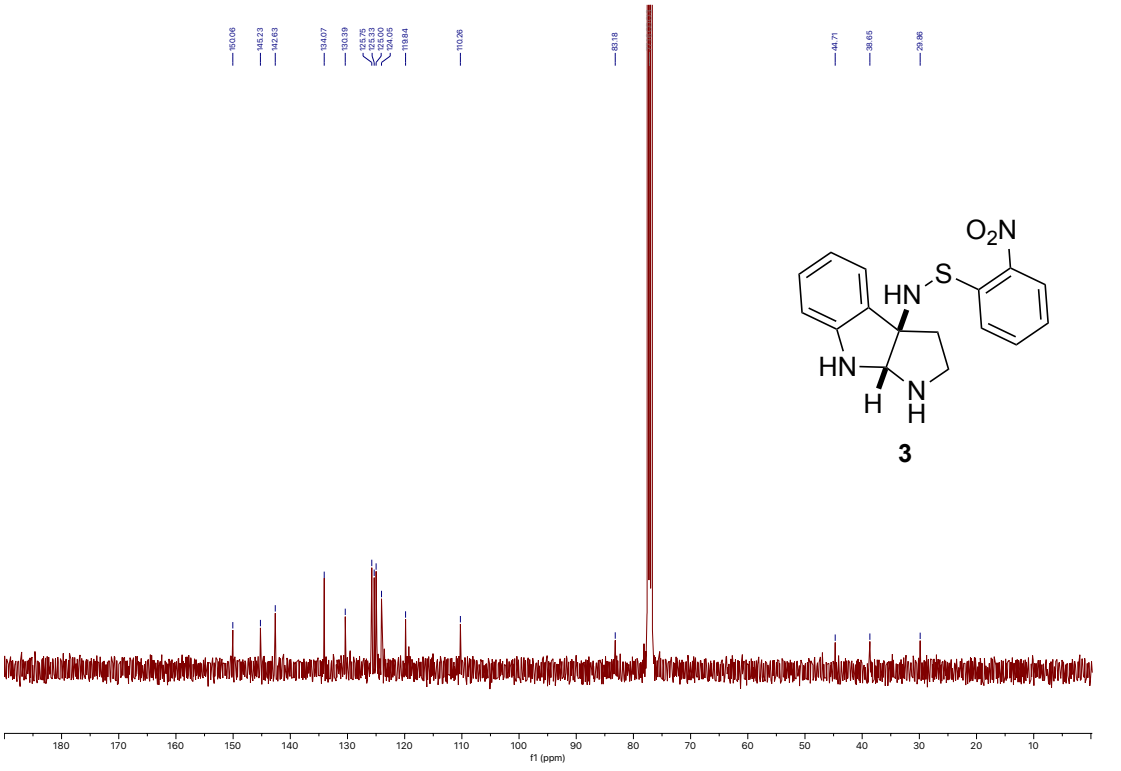
0.99
1.00
1.07
1.11
1.20
1.12
1.26
1.21
f1 (ppm)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110.26
83.18
44.71
38.65
29.86
O2N
S
HN
HN
H
N
H
3
f1 (ppm)

7. References

1. Ghosh B, Kafle P, Mukherjee R, Welles R, Herndon D, Nicholas KM, et al. Sulfenylnitrene-mediated nitrogen-atom insertion for late-stage skeletal editing of N-heterocycles. Science. 2025;387(6729):102-7.
2. Kafle P, Kharel P, Nilson D, Herndon D, Yasuda S, Sharma I. Photolysis-generated sulfenylnitrenes enable site-selective nitrogen-atom insertion into N-heterocycles. Chem. 2025:102753.