Electronic Supporting Information

A Practical Sulfenylation of 2,5-Diketopiperazines

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Supporting Information Available

I. Experimental Section

General Methods

All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene, benzene, diethyl ether (Et_2O), *N*,*N*′-dimethylformamide (DMF), and methylene chloride (CH_2Cl_2) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of phosphomolybdic acid and cerium sulfate, and heat as developing agents. E. Merck silica gel (60, particle size 0.040 – 0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker DRX-500 or DRX-600 instruments and calibrated using residual undeuterated solvent ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.0 ppm) as an internal reference. The following abbreviations were used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Infrared (IR) spectra were recorded on a Perkin–Elmer 100 FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI-TOF (time of flight) mass spectrometer using MALDI (matrix-assisted laser desorption ionisation) or ESI (electrospray ionization). Melting points are uncorrected and were recorded on a Thomas-Hoover Unimelt capillary melting point apparatus. Optical rotations were recorded on a Perkin-Elmer Model 343 polarimeter at 589 nm, and are reported in units of 10^{-1} (deg cm^2 g^{-1}).

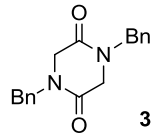
General Procedure A. Preparation of epidithiodiketopiperazines.

Dithiodiketopiperazine 16: To a suspension of elemental sulfur (79.3 mg, 2.48 mmol, 8.0 equiv) in THF (1.6 mL, 0.2 M) at 25 °C under argon was added NaHMDS (0.6 M in PhMe, 1.55 mL, 0.93 mmol, 3.0 equiv) dropwise over a period of 2 min. During the addition, the insoluble yellow S_8 quickly changed color, initially into a dark blue solution, then dark orange and finally light orange solution. This solution was stirred for an additional 1 min, and diketopiperazine **6** (100 mg, 0.31 mmol, 1.0 equiv) dissolved in THF (1.6 mL, 0.2 M) was added dropwise at 25 °C over a 2 min period, at which time the reaction mixture turned to light brown. The mixture was stirred for an additional 1 min, then additional NaHMDS (0.6 M in PhMe, 1.03 mL, 2.0 equiv) was added and the resulting mixture was stirred for 0.5 h at 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford a brownish residue which was taken to the next step without purification. The residue was dissolved in a mixture of degassed THF:EtOH (1:1, 3.1 mL, 0.05 M) at 0 °C and to the stirred solution under argon was added $NaBH_4$ (286 mg, 7.75 mmol, 25 equiv) in small portions over a period of 1 min. The resulting mixture was stirred for 45 min while it was allowed to reach ambient temperature. After this time, the solution was cooled to 0 °C and quenched by careful addition of sat. aq. NH_4Cl solution (20 mL). The resulting mixture was extracted with EtOAc (3 × 20 mL) and to the combined organic extracts was added an aq. solution of KI_3 (10 mL, 1.4 M). This mixture was stirred for 10 min and then quenched with sat. aq. $Na_2S_2O_3$ solution (40 mL), and the resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo to give an oily residue. The so-obtained residue was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:4) to afford pure epidithiodiketopiperazine **16** (82 mg, 0.21 mmol, 69% yield).

General procedure B. Preparation of epidithiodiketopiperazines.

***bis*-Methylthiodiketopiperazine 23**: To a suspension of elemental sulfur (79 mg, 2.48 mmol, 8.0 equiv) in THF (1.6 mL, 0.2 M) at 25 °C under argon was added NaHMDS (0.6 M in PhMe, 1.55 mL, 0.93 mmol, 3.0 equiv) dropwise over a period of 2 min. During the addition, the insoluble yellow S_8 quickly changed color initially into a dark blue solution, then dark orange and finally light orange solution. This solution was stirred for an additional 1 min, and diketopiperazine **6** (100 mg, 0.31 mmol, 1.0 equiv) dissolved in THF (1.6 mL, 0.2 M) was added dropwise at 25 °C over a 2 min period, at which time the reaction mixture turned light brown. The mixture was stirred for an additional 1 min, then additional NaHMDS (0.6 M in PhMe, 1.03 mL, 2.0 equiv) was added and the resulting mixture was stirred for 0.5 h at 25 °C. The reaction mixture was quenched with sat. aq. NH_4Cl solution (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford a brownish residue which was taken to the next step without purification. The residue was dissolved in a mixture of degassed THF:EtOH (1:1, 3.4 mL, 0.05 M) at 0 °C and to the stirred solution under argon was added $NaBH_4$ (287 mg, 7.75 mmol, 25 equiv) in small portions over a period of 1 min. The resulting mixture was stirred for 45 min while it was allowed to reach ambient temperature. After this time, the solution was cooled to 0 °C and then MeI (0.96 mL, 15.5 mmol, 50 equiv) was added and the solution stirred at 25 °C for 15 h. After this time, the solution was quenched by careful addition of sat. aq. NH_4Cl solution (30 mL) and extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo to give an oily residue. The residue so-obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 2:3) to afford pure *bis*-methylthiodiketopiperazine **23** (92 mg, 0.22 mmol, 72% yield).

1,4-Dibenzyl-2,5-diketopiperazine 3: Physical properties match those reported.[1]



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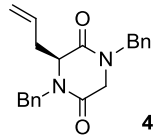
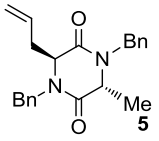
1,4-Dibenzyl-3-allyl-2,5-diketopiperazine 4: To a stirred solution of diketopiperazine **3** (1.37 g, 4.6 mmol, 1.0 equiv) in THF (17 mL) at –10 °C was added NaHMDS (0.6 M in toluene, 8.6 mL, 5.13 mmol, 1.1 equiv). After stirring for 1 h, the reaction mixture was cooled to –78 °C and allyl bromide (0.4 mL, 4.66 mmol, 1.0 equiv) was added. The mixture was allowed to warm to room temperature over 2 h and then quenched with sat. aq. NH_4Cl solution (25 mL). The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The so-obtained residue was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:1) to give diketopiperazine **4** as a white foam (1.0 g, 2.99 mmol, 67% yield). **4**: R_f = 0.41 (silica, EtOAc:hexanes, 1:1); IR ν_{max} (film): 2924w, 1660s, 1453w, 1326w, 725w cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.38 – 7.24 (m, 10 H), 5.64 (ddt, *J* = 17.5, 10.1, 7.5 Hz, 1 H), 5.29 (d, *J* = 14.9 Hz, 1 H), 5.13 (dd, *J* = 17.1, 1.3 Hz, 1 H), 5.08 (dd, *J* = 10.1, 0.8 Hz, 1 H), 4.88 (d, *J* = 14.4 Hz, 1 H), 4.28 (d, *J* = 14.4 Hz, 1 H), 4.03 (dd, *J* = 9.8, 4.9 Hz, 2 H), 3.95 (d, *J* = 17.5 Hz, 1 H), 3.81 (d, *J* = 17.5 Hz, 1 H), 2.67 (dd, *J* = 7.4, 4.1 Hz, 1 H), 2.59 (dd, *J* = 13.7, 7.1 Hz, 1 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 165.9, 164.3, 135.3, 130.7, 128.9, 128.8, 128.55, 128.54, 128.53, 128.38, 128.37, 128.36, 128.19, 128.14, 121.0, 59.0, 49.5, 49.2, 47.1, 36.0 ppm; HRMS calcd for $C_{21}H_{22}N_2O_2H^+$ [*M*+H^+] 335.1754 found 335.1745.



4

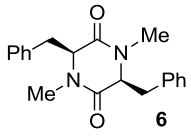
1,4-Dibenzyl-3-allyl-6-methyl-2,5-diketopiperazine 5: To a stirred solution of diketopiperazine **4** (0.39 g, 1.18 mmol, 1.0 equiv) in THF (5.9 mL) at –10 °C was added NaHMDS (0.6 M in toluene, 2.2 mL, 1.3 mmol, 1.1 equiv). After stirring for 1 h, the reaction mixture was cooled to –78 °C and MeI (0.09 mL, 1.42 mmol, 1.2 equiv) was added. The mixture was allowed to warm to room temperature over 2 h and then quenched



5

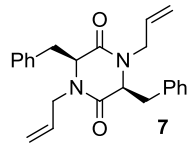
with sat. aq. NH_4Cl solution (10 mL). The mixture was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The so-obtained residue was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:2) to give diketopiperazine **5** as a white foam (0.3 g, 0.86 mmol, 75% yield). **5**: R_f = 0.37 (silica, EtOAc:hexanes, 1:1); IR ν_{max} (film): 2939w, 1651s, 1450m, 1322w, 1168w, 911w, 726s, 698s cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.30 (m, 10 H), 5.79 (ddt, *J* = 17.4, 10.1, 7.4 Hz, 1 H), 5.30 (d, *J* = 15.0 Hz, 1 H), 5.21 – 5.18 (m, 1 H), 5.16 (dd, *J* = 25.1, 8.1 Hz, 2 H), 4.12 (d, *J* = 14.9 Hz, 1 H), 4.05 (d, *J* = 6.6 Hz, 1 H), 4.03 (d, *J* = 2.6 Hz, 1 H), 4.00 (d, *J* = 7.1 Hz, 1 H), 2.80 – 2.61 (m, 2 H), 1.54 (d, *J* = 7.1 Hz, 3 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 167.2, 165.4, 135.7, 135.4, 132.2, 128.89(2C), 128.83(2C), 128.1(2C), 128.03(2C), 128.01. 127.9, 119.8, 58.9, 55.0, 47.3, 47.1, 37.0, 19.7 ppm; HRMS calcd for $C_{22}H_{24}N_2O_2H^+$ [*M*+H^+] 349.1911 found 349.1912.

1,4-Dimethyl-3,6-dibenzyl 2,5-diketopiperazine 6: Physical properties match those reported.[2]



6

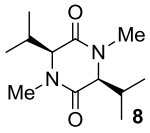
1,4-Diallyl-3,6-dibenzyl 2,5-diketopiperazine 7: To a stirred solution of cyclo (L-Phe-L-Phe) (1.0 g, 3.39 mmol, 1.0 equiv) in DMF (17 mL) at 0 °C was added NaH (60% dispersion, 0.34 g, 8.5 mmol, 2.5 equiv). After stirring for 10 min, allyl bromide (0.44 mL, 7.13 mmol, 2.1 equiv) was added and the mixture was allowed to stir for 15 h at room temperature. The reaction mixture was quenched with sat. aq. NH_4Cl solution (20 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The so-obtained residue was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:2) to give diketopiperazine **7** as a white foam (0.92 g, 2.47 mmol, 73% yield). **7**: R_f = 0.46 (silica, EtOAc:hexanes, 1:1); $[\alpha]_D^{25}$ = –89.0 (*c* = 1.0, $CHCl_3$);



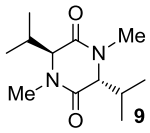
7

IR ν_{max} (film): 2926w, 1654s, 1450m, 1417m, 1262w, 935m, 758m, 731m, 703s cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.24 (dd, *J* = 5.0, 1.8 Hz, 6 H), 7.04 – 7.00 (m, 4 H), 5.25 – 5.16 (m, 2 H), 5.13 – 5.05 (m, 4 H), 4.85 – 4.76 (m, 2 H), 3.69 (t, *J* = 3.8 Hz, 2 H), 3.40 (dd, *J* = 15.0, 8.4 Hz, 2 H), 3.15 (dd, *J* = 14.2, 3.5 Hz, 2 H), 3.02 (dd, *J* = 14.3, 4.1 Hz, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 165.1, 134.7, 131.3, 129.8(2C), 128.4(2C), 127.1, 119.6, 58.0, 45.6, 35.8 ppm; HRMS calcd for $C_{18}H_{26}N_2O_2H^+$ [*M*+H^+] 375.2067 found 375.2071.

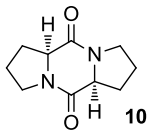
1,4-Dimethyl-3,6-*cis*-diisopropyl 2,5-diketopiperazine 8: Physical properties match those reported.[3]



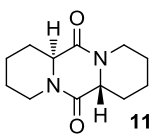
1,4-Dimethyl-3,6-*trans*-diisopropyl 2,5-diketopiperazine 9: Physical properties match those reported.[3]



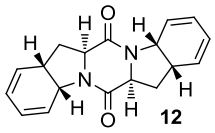
Cycloproline 10: Physical properties match those reported.[4]



Pipecolic acid dimer 11: Physical properties match those reported.[5]

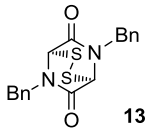


***Bis*-diene 12**: Physical properties match those reported.[6]



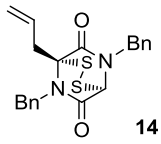
12

Epidithiodiketopiperazine 13:[7] Following general procedure A, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 3:7) to afford pure epidithiodiketopiperazine **13** as a white foam (40% yield). **13**: R_f = 0.55 (silica, EtOAc:hexanes, 3:7); IR ν_{max} (film): 2963w, 1674s, 1420w, 731w cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.41 – 7.35 (m, 6 H), 7.31 – 7.28 (m, 4 H), 5.24 (s, 2 H), 4.86 (d, *J* = 15.0 Hz, 2 H), 4.50 (d, *J* = 15.0 Hz, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 163.7, 134.0, 129.2(2C), 128.6, 128.4(2C), 64.6, 47.6 ppm; HRMS calcd for $C_{18}H_{16}N_2O_2S_2H^+$ [*M*+H^+] 357.0726 found 357.0737.



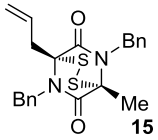
13

Epidithiodiketopiperazine 14: Following general procedure A, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:4) to afford pure epidithiodiketopiperazine **14** as a white foam (63% yield). **14**: R_f = 0.37 (silica, EtOAc:hexanes, 1:4); IR ν_{max} (film): 2918w, 1686s, 1385w, 730w, 697w cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.44 – 7.27 (m, 10 H), 6.13 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.36 (s, 1 H), 5.33 – 5.24 (m, 2 H), 5.11 (d, *J* = 16.1 Hz, 1 H), 4.92 (d, *J* = 14.9 Hz, 1 H), 4.62 (d, *J* = 16.1 Hz, 1 H), 4.52 (d, *J* = 14.9 Hz, 1 H), 4.52 (d, *J* = 14.9 Hz, 1 H), 3.29 – 3.18 (m, 1 H), 3.12 – 3.04 (m, 1 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 164.9, 164.4, 135.8, 134.2, 131.4, 129.14,129.13, 128.75, 128,74(3C), 128.5, 128.4, 127.8, 126.9, 120.7, 74.9, 63.9, 48.4, 45.1, 36.1 ppm; HRMS calcd for $C_{21}H_{20}N_2O_2S_2H^+$ [*M*+H^+] 397.1039 found 397.1046.



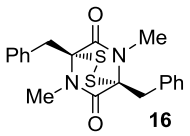
14

Epidithiodiketopiperazine 15: Following general procedure A, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 3:7) to afford pure epidithiodiketopiperazine **15** as a white foam (70% yield). **15**: R_f = 0.39 (silica, EtOAc:hexanes, 3:7); IR ν_{max} (film): 3030w, 2943w, 1678s, 1352m, 1283m, 909m, 727s, 695s cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.36 – 7.27 (m, 10 H), 6.21 – 6.10 (m, 1 H), 5.34 – 5.25 (m, 2 H), 5.19 (d, *J* = 16.1 Hz, 1 H), 4.95 (d, *J* = 16.0 Hz, 1 H), 4.69 (dd, *J* = 16.0, 12.0 Hz, 2 H), 3.34 – 3.25 (m, 1 H), 2.02 (s, 3 H), 3.18 – 3.10 (m, 1 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 166.3, 165.28, 136.2, 135.9, 131.6, 128.7, 128.6, 127.74, 127.71, 126.99, 126.96, 120.6, 74.3, 71.5, 45.9, 45.7, 36.7, 18.79 ppm; HRMS calcd for $C_{22}H_{22}N_2O_2S_2H^+$ [*M*+H^+] 411.1195 found 411.1194.



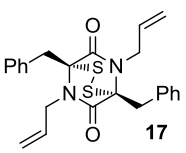
15

Epidithiodiketopiperazine 16:[8] Following general procedure A, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:4) to afford pure epidithiodiketopiperazine **16** as a white crystals (69% yield). **16**: R_f = 0.48 (silica, EtOAc:hexanes, 1:4); m.p. = 151.5 – 152.5 °C (EtOH); IR ν_{max} (film): 3030w, 2935w, 1679s, 1338m, 1258w, 908w, 726s, 697s cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.36 – 7.27 (m, 10 H), 4.14 (d, *J* = 15.8 Hz, 2 H), 3.64 (d, *J* = 15.8 Hz, 2 H), 3.03 (s, 6 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 165.9, 134.3, 129.1, 128.8, 128.7, 127.2, 76.8, 37.0, 29.0 ppm; HRMS calcd for $C_{20}H_{20}N_2O_2S_2H^+$ [*M*+H^+] 385.1039 found 385.1043.



16

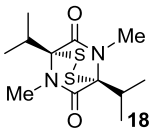
Epidithiodiketopiperazine 17: Following general procedure A, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:5) to afford pure epidithiodiketopiperazine **17** as a white foam (65% yield). **17**: R_f = 0.55 (silica, EtOAc:hexanes, 1:5); IR ν_{max} (film): 2946w, 1685s, 1344m, 1267w, 700w cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.33 (ddd, *J* = 25.5, 22.0, 7.2 Hz, 10 H), 5.89 – 5.82 (m, 2 H), 5.28 (d, *J* = 17.2 Hz, 2 H), 5.22 (d, *J* = 10.3 Hz, 2 H), 4.66 (ddd, *J* = 16.2, 4.2, 2.2 Hz, 2 H),



17

4.00 (d, *J* = 15.4 Hz, 2 H), 3.82 (dd, *J* = 16.2, 7.2 Hz, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 164.7, 134.3, 131.3, 129.5, 128.5(3C), 127.4, 118.2, 75.9, 46.4, 36.2 ppm; HRMS calcd for $C_{24}H_{24}N_2O_2S_2Na^+$ [*M*+Na^+] 459.1171 found 459.1158.

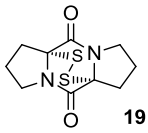
Epidithiodiketopiperazine 18:[3] Following general procedure A, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:5) to afford pure epidithiodiketopiperazine **18** as a white foam (45% yield from **8** or 47% yield from **9**).



18

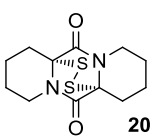
18: R_f = 0.45 (silica, EtOAc:hexanes, 1:5); m.p. = 109 °C (EtOH); IR ν_{max} (film): 2963w, 1663s, 1363m, 1054w cm^{-1}; ^{1}H NMR: ($CDCl_3$, 600 MHz) δ = 3.08 (s, 6 H), 1.55 (s, 2 H), 1.41 (d, *J* = 6.9 Hz, 6 H), 1.09 (d, *J* = 6.9 Hz, 6 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 168.0, 80.5, 35.4, 30.2, 18.6, 18.4 ppm; HRMS calcd for $C_{12}H_{20}N_2O_2S_2H^+$ [*M*+H^+] 289.1039 found 289.1041.

Epidithiodiketopiperazine 19:[4] Following general procedure A, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc) to afford pure epidithiodiketopiperazine **19** as a white crystal (65% yield). **19**: R_f = 0.36 (silica, EtOAc); m.p. = 136 °C (EtOH); IR ν_{max} (film): 2955w, 2890w, 1687s, 1380m cm^{-1}; ^{1}H NMR: ($CDCl_3$, 600 MHz) δ = 3.88 (ddd, *J* = 12.1, 8.7, 3.6 Hz, 2 H), 3.61 – 3.54 (m, 2 H), 3.00 (dd, *J* = 7.7, 4.2 Hz, 2 H), 2.35 (ddd, *J* = 13.7, 9.7, 4.9 Hz, 4 H), 2.28 – 2.18 (m, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 163.3, 77.3, 45.8, 32.2, 23.6 ppm; HRMS calcd for $C_{10}H_{12}N_2O_2S_2H^+$ [*M*+H^+] 257.0413 found 257.0412.



19

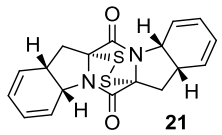
Epidithiodiketopiperazine 20: Following general procedure A, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 3:7) to afford pure epidithiodiketopiperazine **20** as a white powder (68% yield). **20**: R_f = 0.45 (silica, EtOAc:hexanes, 3:7); m.p. = 136 °C; IR ν_{max} (film): 2946w, 2863w, 1686s, 1326w cm^{-}



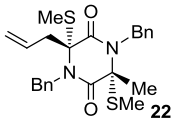
20

[1]; ^{1}H NMR: ($CDCl_3$, 600 MHz) δ = 4.20 – 4.10 (m, 2 H), 2.94 (td, *J* = 13.2, 3.9 Hz, 2 H), 2.49 – 2.37 (m, 2 H), 2.26 – 2.15 (m, 2 H), 2.02 – 1.90 (m, 4 H), 1.83 – 1.71 (m, 2 H), 1.60 – 1.51 (m, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 166.0, 71.7, 40.7, 28.6, 22.2, 19.5 ppm; HRMS calcd for $C_{12}H_{16}N_2O_2S_2H^+$ [*M*+H^+] 285.0726 found 285.0737.

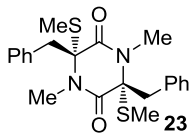
Epidithiodiketopiperazine 21: Physical properties match those reported.[6]



***bis*-Methylthiodiketopiperazine 22**: Following general procedure B, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:2) to afford pure *bis*-methylthiodiketopiperazine **22** as a colorless syrup (70% yield). **22**: R_f = 0.52 (silica, EtOAc:hexanes, 1:2); IR ν_{max} (film): 2922w, 1658s, 1392m cm^{-1}; ^{1}H NMR: ($CDCl_3$, 600 MHz) δ = 7.50 (d, *J* = 7.5 Hz, 2 H), 7.34 (d, *J* = 7.5 Hz, 2 H), 7.32 – 7.20 (m, 6 H), 5.43 – 5.31 (m, 1 H), 5.18 (d, *J* = 15.4 Hz, 1 H), 5.10 (t, *J* = 14.5 Hz, 2 H), 4.87 (d, *J* = 14.6 Hz, 1 H), 4.81 (d, *J* = 14.6 Hz, 1 H), 4.63 (d, *J* = 15.4 Hz, 1 H), 3.20 (dd, *J* = 14.2, 7.9 Hz, 1 H), 2.76 (dd, *J* = 14.1, 6.3 Hz, 1 H), 2.19 (s, 3 H), 1.73 (s, 3 H), 2.08 (s, 3 H ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 166.8, 165.5, 137.6, 137.4, 129.9, 128.5(2C), 128.29(2C), 128.24(2C), 127.7(2C), 127.2, 127.1, 121.8, 73.3, 68.9, 47.9, 47.8, 41.8, 26.0, 14.5, 14.4 ppm; HRMS calcd for $C_{24}H_{28}N_2O_2S_2Na^+$ [*M*+Na^+] 463.1484 found 463.1482.

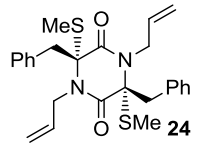


***bis*-Methylthiodiketopiperazine 23**:[9] Following general procedure B, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:1) to afford pure *bis*-methylthiodiketopiperazine **23** as a white crystal (72 % yield). **23**: R_f = 0.30 (silica, EtOAc:hexanes, 3:7); m.p. = 97 – 98 °C (EtOH); IR ν_{max} (film): 3030w,



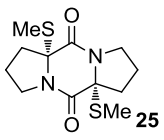
2921w, 1650s, 1367m, 1088m, 697s cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.14 (dd, *J* = 9.7, 3.9 Hz, 6 H), 6.95 (dd, *J* = 7.9, 1.1 Hz, 4 H), 3.31 (d, *J* = 14.3 Hz, 2 H), 3.14 (s, 6 H), 2.90 (d, *J* = 14.3 Hz, 2 H), 2.17 (s, 6 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 165.2, 134.2, 130.0, 128.46, 128.45, 128.44, 127.3, 73.2, 43.0, 31.3, 14.1 ppm; HRMS calcd for $C_{22}H_{26}N_2O_2S_2H^+$ [*M*+Na^+] 437.1328 found 437.1330.

***bis*-Methylthiodiketopiperazine 24**: Following general procedure B, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:4) to afford pure *bis*-methylthiodiketopiperazine **24** as a colorless syrup (63% yield). **24**: R_f = 0.58 (silica, EtOAc:hexanes, 1:4); IR ν_{max} (film): 2920w, 1653s, 1382m, 699s cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.32 – 7.14 (m, 6 H), 7.10 – 6.99 (m, 4 H), 5.94 (dd, *J* = 17.0, 10.3 Hz, 2 H), 5.36 (dd, *J* = 17.2, 1.3 Hz, 2 H), 5.25 – 5.08 (m, 2 H), 4.36 (dd, *J* = 14.0, 6.3 Hz, 2 H), 3.92 (dd, *J* = 14.0, 6.7 Hz, 2 H), 2.86 (d, *J* = 14.2 Hz, 2 H), 2.76 (d, *J* = 14.2 Hz, 2 H), 2.05 (s, 6 H), ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 165.3, 134.3, 132.9, 130.91(2C), 130.90, 128.4, 127.6, 119.3, 75.2, 48.8, 44.1, 13.7 ppm; HRMS calcd for $C_{26}H_{30}N_2O_2S_2Na^+$ [*M*+Na^+] 489.1641 found 489.1647.



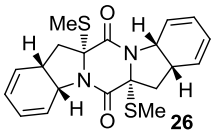
24

***bis*-Methylthiodiketopiperazine 25**:[4] Following general procedure B, the crude residue obtained was purified by flash column chromatography (silica gel, EtOAc) to afford pure *bis*-methylthiodiketopiperazine **25** as a white powder (64% yield). **25**: R_f = 0.47 (silica, EtOAc); IR ν_{max} (film): 2925w, 1657s, 1382m cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 3.72 (dt, *J* = 11.9, 8.9 Hz, 2 H), 3.60 (ddd, *J* = 12.0, 9.9, 2.2 Hz, 2 H), 2.49 (dd, *J* = 13.3, 6.8 Hz, 2 H), 2.32 (ttd, *J* = 12.3, 9.6, 6.7 Hz, 2 H), 2.23 (s, 6 H), 2.09 (ddd, *J* = 13.0, 12.1, 7.7 Hz, 2 H), 2.05 – 1.98 (m, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 164.8, 71.3, 45.3, 34.0, 19.8, 14.6 ppm; HRMS calcd for $C_{12}H_{18}N_2O_2S_2H^+$ [*M*+H^+] 287.0810 found 287.0815.



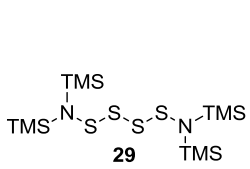
25

***bis*-(Methylthio)diketopiperazine 26**: Physical properties match those reported.[6]



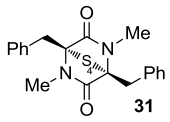
26

***N,N′*-tetrathio-*bis*-trimethylsilyl compound 29**:[10] To a suspension of elemental sulfur (87 mg, 2.72 mmol, 8.0 equiv) in THF (1.7 mL, 0.2 M) at 25 °C under argon was added NaHMDS (0.6 M in PhMe, 1.70 mL, 1.02 mmol, 3.0 equiv) dropwise over a period of 2 min. During the addition, the insoluble yellow S_8 quickly changed color, turned initially into a dark blue solution, then dark orange and finally light orange solution. The reaction mixture was quenched with sat. aq. NH_4Cl solution (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford a brownish residue. The residue was purified by flash column chromatography (silica gel, hexanes) to afford pure *N,N′*-tetrathio-*bis*-trimethylsilyl compound **29** as a yellow syrup (40% yield). **29**: R_f = 0.8 (silica, hexanes); IR ν_{max} (film): 2956w, 1251s, 907s, 842s cm^{-1}; ^1H NMR: ($CDCl_3$, 500 MHz) δ = 0.26 (s, 36 H), ppm; ^{13}C NMR: ($CDCl_3$, 125 MHz) δ = 2.3(6C); HRMS calcd for $C_{12}H_{36}N_2O_2S_4Si_4H^+$ [*M*+H^+] 449.0911 found 449.0908.



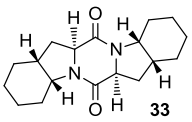
29

Epitetrathiodiketopiperazine 31: Following general procedure A, the crude residue obtained before the $NaBH_4$ reduction was purified by preparative thin layer chromatography (benzene) to afford pure epitetrathiodiketopiperazine **31** as a white crystal (43% yield). **31**: R_f = 0.31 (silica, benzene); m.p. = 167–169 °C (hexanes:CH_2Cl_2) IR ν_{max} (film): 2939s, 1666s, 1360m, 697m cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 7.13 (t, *J* = 7.4 Hz, 2 H), 7.00 (t, *J* = 7.6 Hz, 4 H), 6.85 (d, *J* = 7.6 Hz, 4 H), 3.87 (d, *J* = 14.7 Hz, 2 H), 3.19 (s, 6 H), 3.18 (d, *J* = 14.9 Hz, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 167.4, 133.5, 129.1(2C), 128.7(2C), 127.3, 78.4, 39.4, 31.0 ppm; HRMS calcd for $C_{20}H_{20}N_2O_2S_4H^+$ [*M*+H^+] 449.0480 found 449.0472.

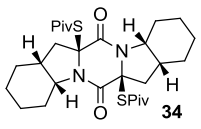


31

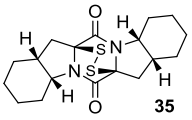
Diketopiperazine 33: To a stirred solution of *bis*-diene **12**[6] (1.0 g, 3.30 mmol, 1.0 equiv) in MeOH (20 mL) was added $Pd(OH)_2/C$ (20% w/w, 100 mg, 0.11 mmol, 0.03 equiv). The mixture was stirred under a hydrogen atmosphere (balloon) at 25 °C for 3 h. The combined solution was filtered through Celite®, and the residue was rinsed with EtOAc several times. The solution was concentrated in vacuo and the crude product was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:1) to give diketopiperazine **33** as a white foam (0.95 g, 3.14 mmol, 93% yield). **33**: R_f = 0.31 (silica, EtOAc:hexanes, 2:3); $[\alpha]_D^{25}$ = –107.0 (*c* = 1.0, $CHCl_3$); IR ν_{max} (film): 2927m, 1657s, 1419m, 751m cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 4.19 (dd, *J* = 9.3, 2.7 Hz, 2 H), 4.06 – 3.99 (m, 2 H), 2.53 (ddd, *J* = 12.6, 7.2, 2.8 Hz, 2 H), 2.21 – 2.14 (m, 2 H), 2.13 – 2.02 (m, 2 H), 1.92 (dd, *J* = 8.9, 4.1 Hz, 2 H), 1.71 – 1.56 (m, 6 H), 1.40 – 1.30 (m, 4 H), 1.26 – 1.15 (m, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 166.3, 58.4, 56.6, 35.2, 27.3, 26.5, 25.6, 23.1, 20.4 ppm; HRMS calcd for $C_{18}H_{26}N_2O_2H^+$ [M+H^+] 303.2067 found 303.2060.



***bis*-Pivthiodiketopiperazine 34**: Following general procedure B, except PivCl (20 equiv) was used instead of MeI in the last step. The crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:1) to afford pure *bis*-Pivthiodiketopiperazine **34** as a colorless syrup (35% yield). **34**: R_f = 0.30 (silica, EtOAc:hexanes, 1:2); $[\alpha]_D^{25}$ = –163.8 (*c* = 1.0, $CHCl_3$); IR ν_{max} (film): 2935m, 1686s, 1382m, 1100m cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 4.07 (d, *J* = 6.7 Hz, 2 H), 3.65 (dd, *J* = 14.0, 7.7 Hz, 2 H), 2.91 (dd, *J* = 12.8, 7.5 Hz, 2 H), 2.53 – 2.47 (m, 2 H), 2.44 – 2.36 (m, 2 H), 2.23 – 2.13 (m, 3 H), 2.12 – 2.03 (m, 3 H), 2.02 – 1.97 (m, 2 H), 1.80 – 1.70 (m, 2 H), 1.55 – 1.46 (m, 2 H), 1.45 – 1.38 (m, 2 H), 1.29 (s, 18 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 203.3, 167.7, 72.4, 57.6, 47.2, 38.9, 33.2, 29.6, 27.1(3C), 25.1, 22.5, 20.0 ppm; HRMS calcd for $C_{28}H_{42}N_2O_4S_2H^+$ [M+H^+] 535.2586 found 535.2590.

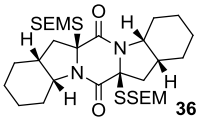


Epidithiodiketopiperazine 35: To a stirred solution of *bis*-Pivthiodiketopiperazine **35** (30 mg, 0.056 mmol, 1.0 equiv) in MeOH (1 mL) at room temperature was added $Mg(OMe)_2$ (8% in MeOH, 1.2 mL, 1.12 mmol, 20 equiv). The mixture was allowed to stir for 2 h at room temperature, followed by bubbling oxygen through the solution. The reaction mixture was quenched with sat. aq. NH_4Cl solution (5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The so-obtained residue was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:1) to give epidithiodiketopiperazine **35** as a white foam (87% yield). **35**: R_f = 0.71 (silica, EtOAc:hexanes, 1:1); $[\alpha]_D^{25}$ = –255.5 (*c* = 1.0, $CHCl_3$); IR ν_{max} (film): 2935m, 1686s, 1382m cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 4.07 – 4.01 (m, 2 H), 3.13 (dd, *J* = 13.3, 7.7 Hz, 2 H), 2.51 (td, *J* = 12.4, 6.1 Hz, 2 H), 2.31 (t, *J* = 12.8 Hz, 2 H), 2.17 – 2.10 (m, 2 H), 1.83 (d, *J* = 14.3 Hz, 2 H), 1.72 (d, *J* = 13.5 Hz, 2 H), 1.70 – 1.61 (m, 4 H), 1.57 (d, *J* = 13.6 Hz, 2 H), 1.43 – 1.33 (m, 2 H), 1.21 – 1.11 (m, 2 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 163.0, 75.4, 57.9, 37.1, 33.0, 26.3, 25.5, 23.1, 20.1 ppm; HRMS calcd for $C_{18}H_{24}N_2O_2S_2H^+$ [*M*+H^+] 365.1352 found 365.1350.



35

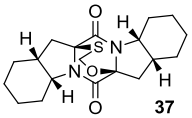
***bis*-SEMthiodiketopiperazine 36**: Following general procedure B, except SEMCl (50 equiv) was used instead of MeI in the last step. The crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:5) to afford pure *bis*-SEMthiodiketopiperazine **36** as a colorless syrup (40 % yield). **36**: R_f = 0.47 (silica, EtOAc:hexanes, 1:5); $[\alpha]_D^{25}$ = –189.4 (*c* = 1.0, $CHCl_3$); IR ν_{max} (film): 2925w, 1661s, 1390m, 1069m, 835s cm^{-1}; ^1H NMR: ($CDCl_3$, 600 MHz) δ = 5.24 (d, *J* = 12.6 Hz, 2 H), 4.67 (d, *J* = 12.6 Hz, 2 H), 4.40 – 4.29 (m, 2 H), 3.81 (ddd, *J* = 11.7, 9.4, 5.2 Hz, 2 H), 3.42 (ddd, *J* = 11.4, 9.4, 5.8 Hz, 2 H), 3.09 (dd, *J* = 14.0, 8.7 Hz, 2 H), 2.97 (dd, *J* = 13.9, 11.7 Hz, 2 H), 2.19 – 2.07 (m, 2 H), 1.98 – 1.84 (m, 4 H), 1.80 – 1.70 (m, 4 H), 1.63 – 1.54 (m, 2 H), 1.54 – 1.46 (m, 2 H), 1.46 – 1.33 (m, 2 H), 1.21 (ddd, *J* = 14.5, 12.7, 7.9 Hz, 2 H), 1.00 (ddd, *J* = 13.6, 11.8, 5.8 Hz, 2 H), 0.91



36

(ddd, *J* = 13.7, 11.5, 5.2 Hz, 2 H), 0.02 (s, 18 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 165.8, 73.0, 70.2, 66.0, 59.3, 40.8, 35.7, 26.2, 25.4, 23.1, 19.9, 17.8, 1.4(3C) ppm; HRMS calcd for $C_{30}H_{54}N_2O_2S_2Si_2Na^+$ [*M*+Na^+] 649.2956 found 649.2957.

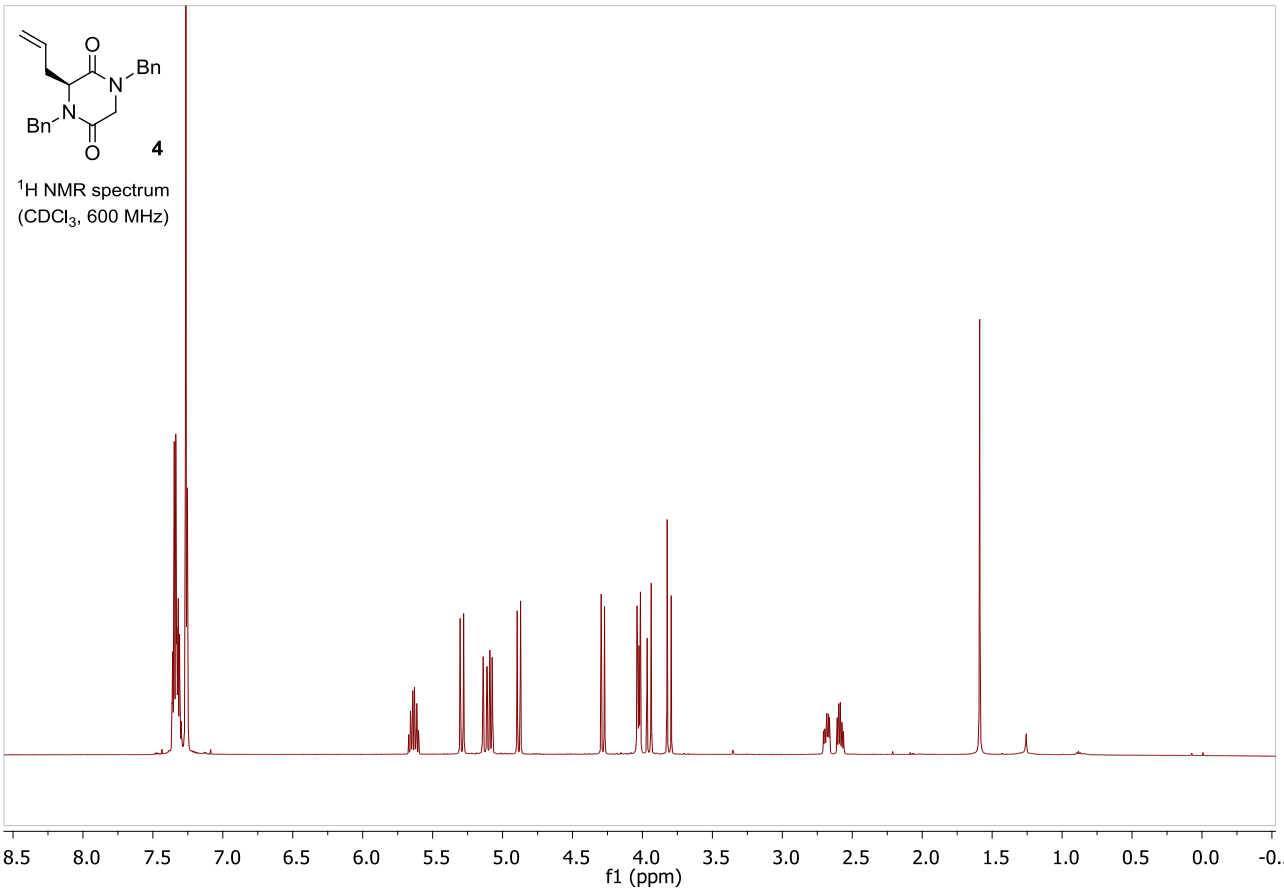
***O,S*-acetal diketopiperazine 37**: To a solution of compound **37** (52 mg, 0.084 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 25 °C was added $SnCl_4$ (1.0 M in CH_2Cl_2, 1.17 mL, 1.17 mmol, 14 equiv). The reaction mixture was stirred for 15 min, then quenched with sat. aq. $NaHCO_3$ solution. (20 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford an incolore oil. The crude residue obtained was purified by flash column chromatography (silica gel, EtOAc:hexanes, 1:2) to afford pure diketopiperazine **37** as white crystals (28 mg, 0.078 mmol, 93 % yield).

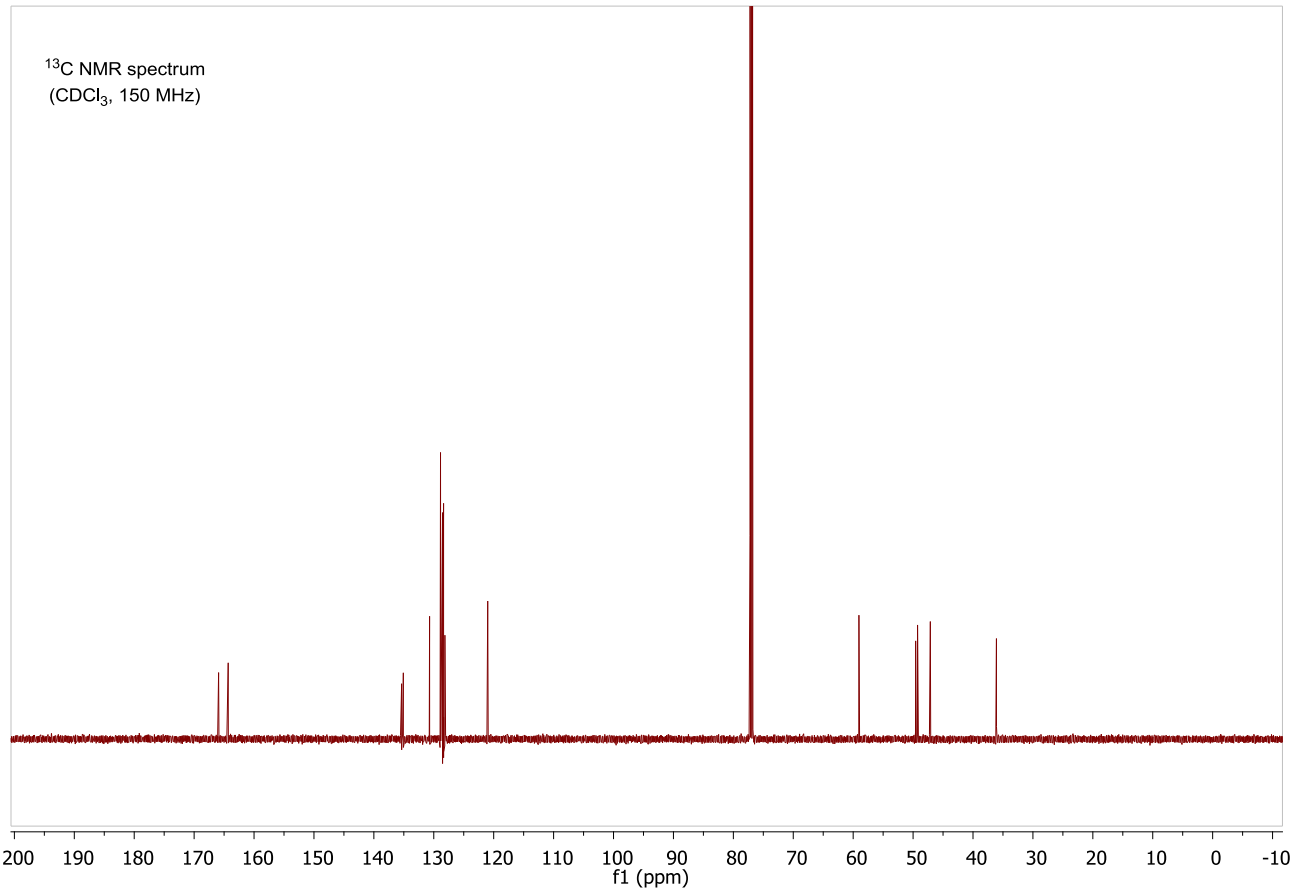


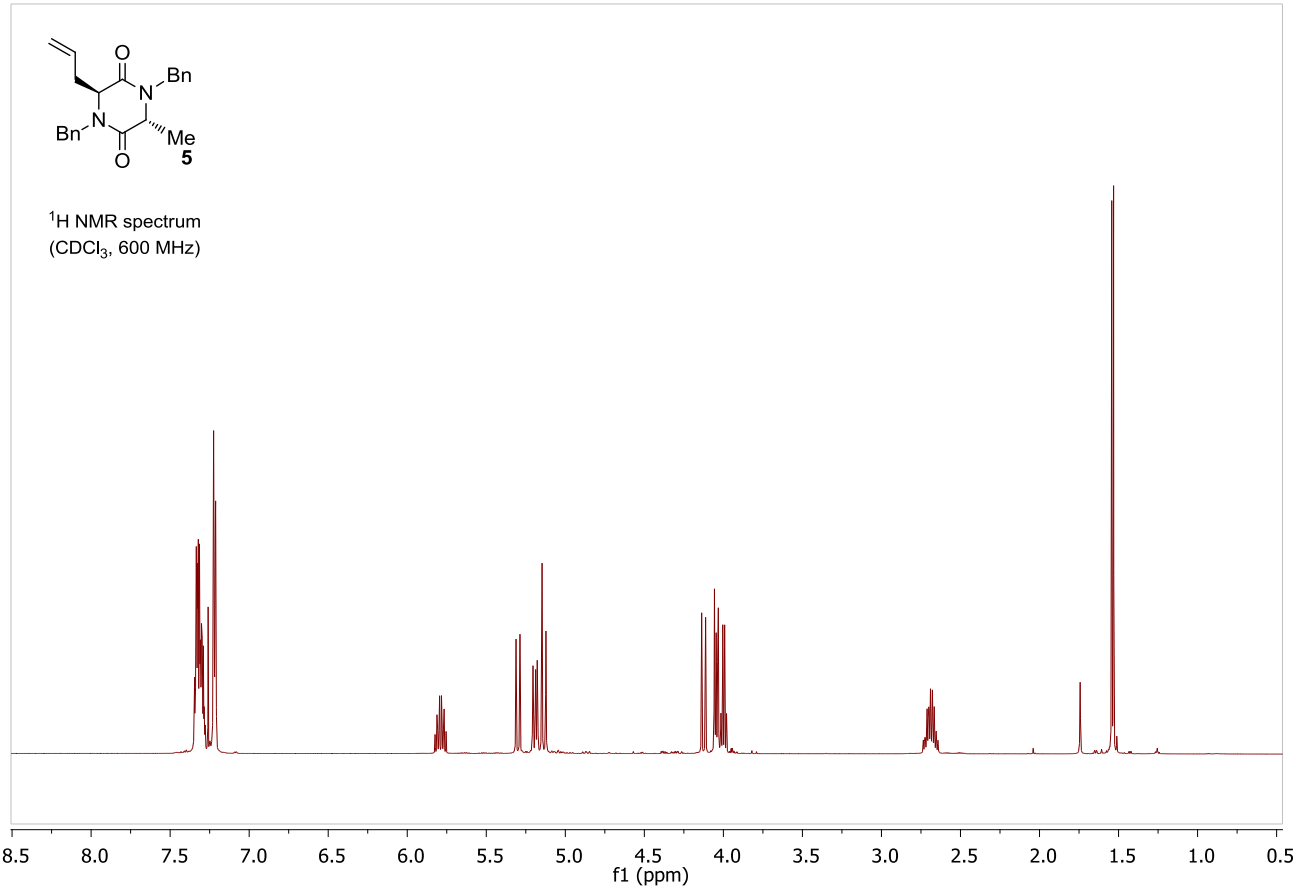
37

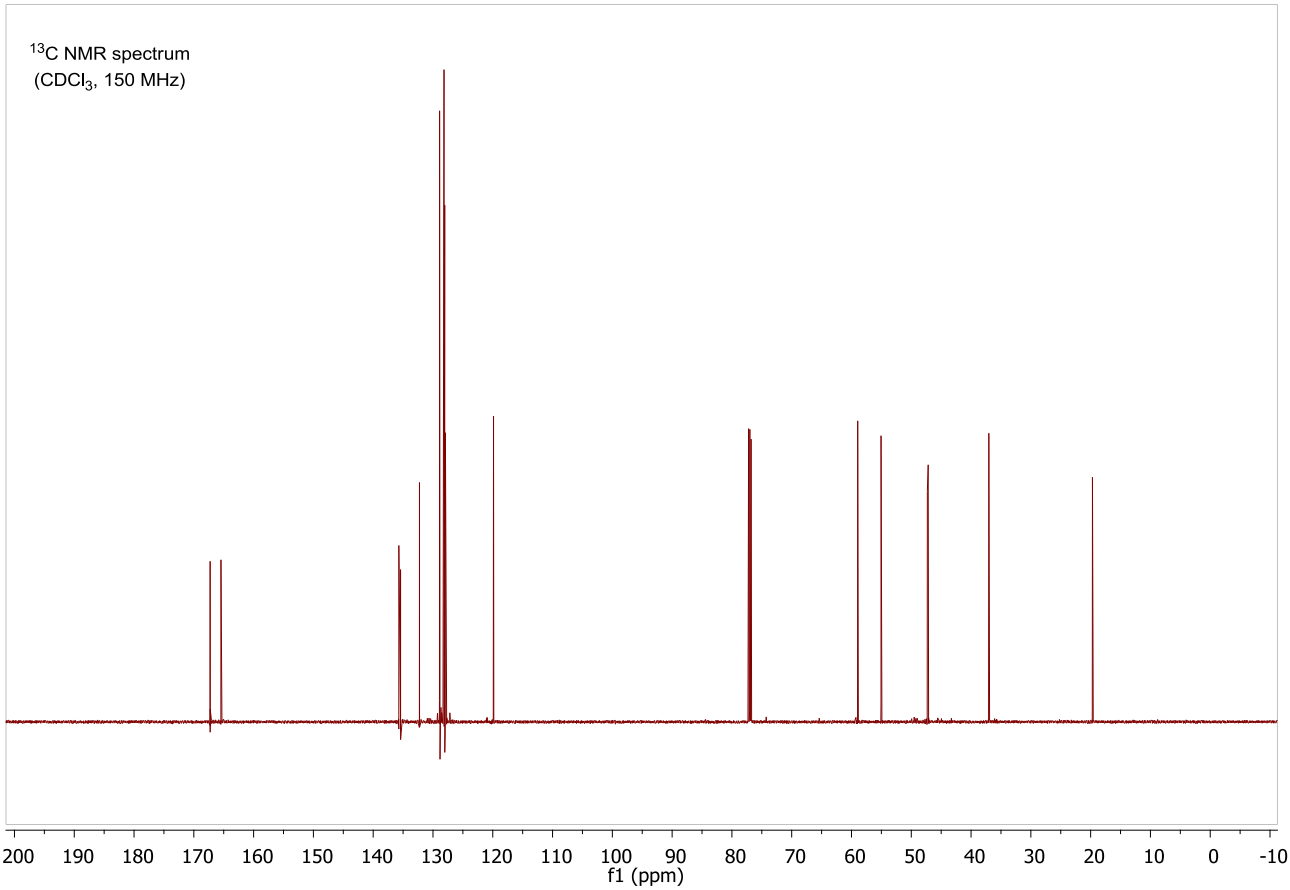
37: R_f = 0.52 (silica, EtOAc:hexanes, 1:2); m.p. = 122–123 °C (CH_2Cl_2\Hexanes); $[\alpha]_D^{25}$ = – 162.3 (*c* = 1.0, $CHCl_3$); IR ν_{max} (film): cm^{-1}; ^{1}H NMR: ($CDCl_3$, 600 MHz) δ = 5.11 (d, *J* = 12.1 Hz, 1 H), 4.97 (d, *J* = 12.1 Hz, 1 H), 4.18 (dt, *J* = 11.0, 5.7 Hz, 1H), 4.08 (dt, *J* = 10.7, 6.5 Hz, 1 H), 2.74 (t, *J* = 9.8 Hz, 2 H), 2.61 (dd, *J* = 13.1, 6.3 Hz, 1 H), 2.44 (t, *J* = 13.6 Hz, 1 H), 2.36 – 2.27 (m, 2 H), 1.98 (dd, *J* = 13.4, 5.9 Hz, 1 H), 5.11 (d, *J* = 12.1 Hz, 1 H), 1.77 – 1.66 (m, 4 H), 1.65 – 1.58 (m, 2 H), 1.57 – 1.48 (m, 2 H), 1.38 – 1.15 (m, 4 H), 1.13 – 1.06 (m, 1 H), 0.98 (ddd, *J* = 24.0, 13.4, 3.6 Hz, 1 H) ppm; ^{13}C NMR: ($CDCl_3$, 150 MHz) δ = 167.3, 164.3, 94.1, 70.5, 67.1, 57.2, 56.7, 36.3, 35.9, 34.2, 33.1, 27.7, 27.2, 25.32, 25.30, 23.0, 22.9, 20.8, 20.5 ppm; HRMS calcd for $C_{19}H_{26}N_2O_3SH^+$ [*M*+H^+] 363.1664 found 363.1666

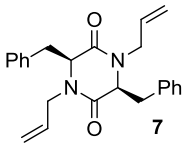
II. ^{1}H and ^{13}C NMR Spectra of Compounds





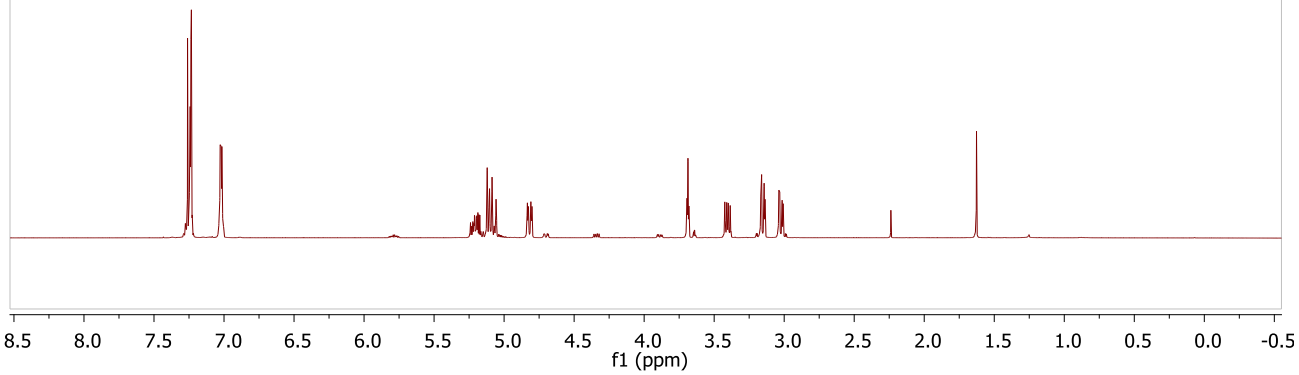

Bn
N
N
Bn
Me
O
O
5
1H NMR spectrum
(CDCl3, 600 MHz)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


13C NMR spectrum
(CDCl3, 150 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

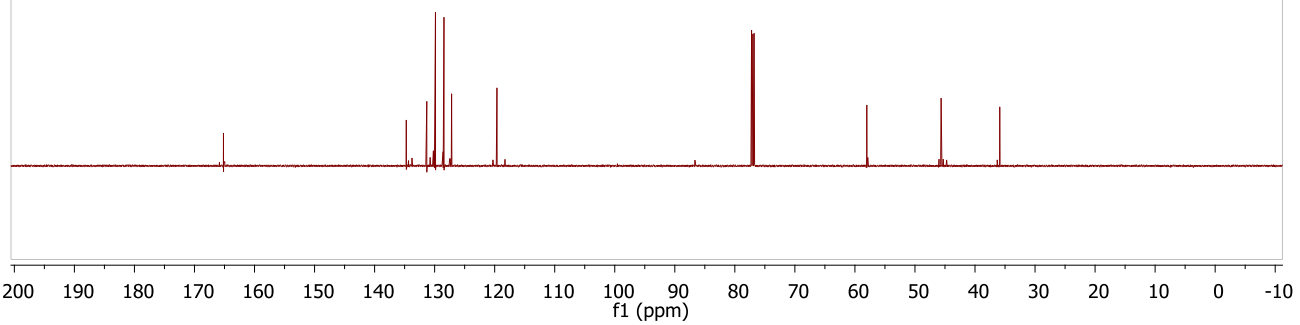


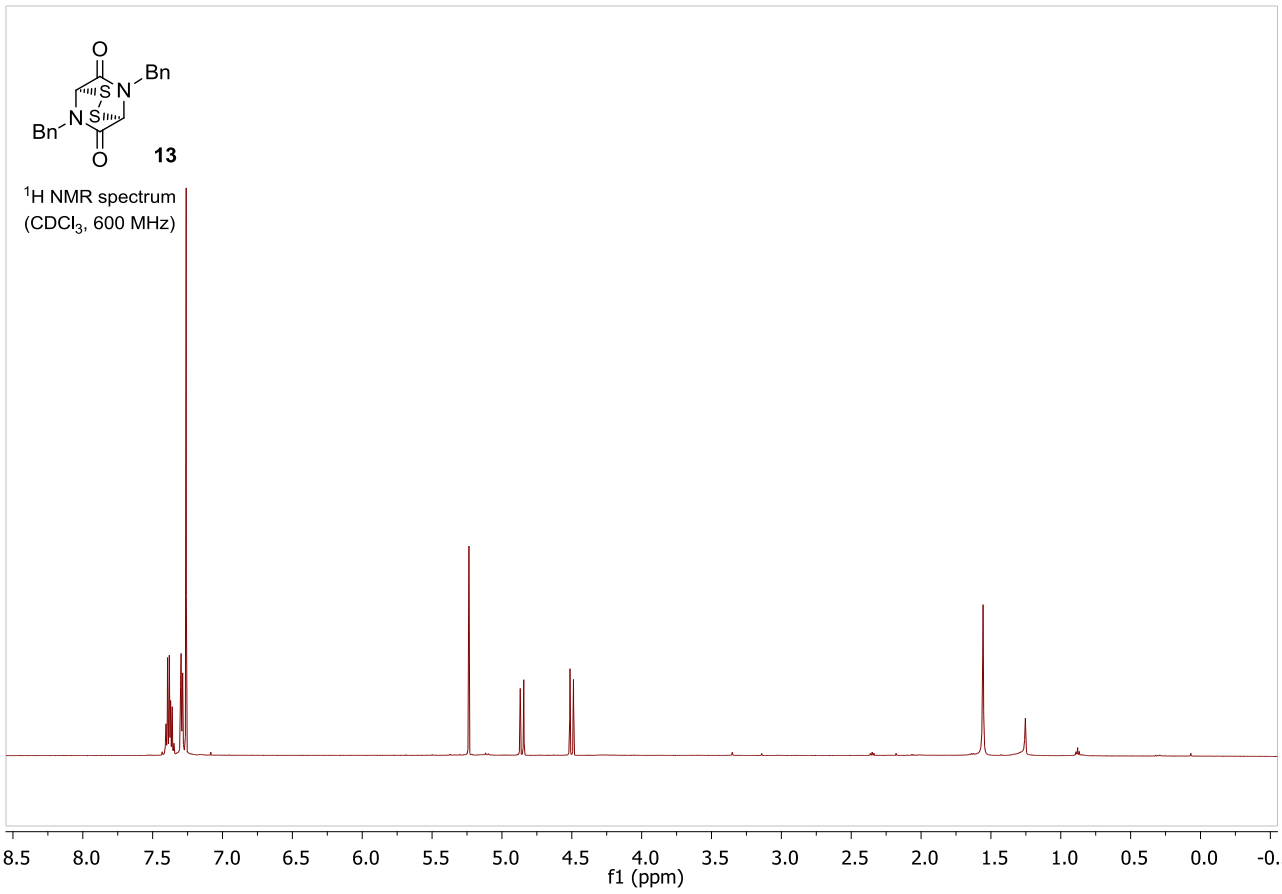
7

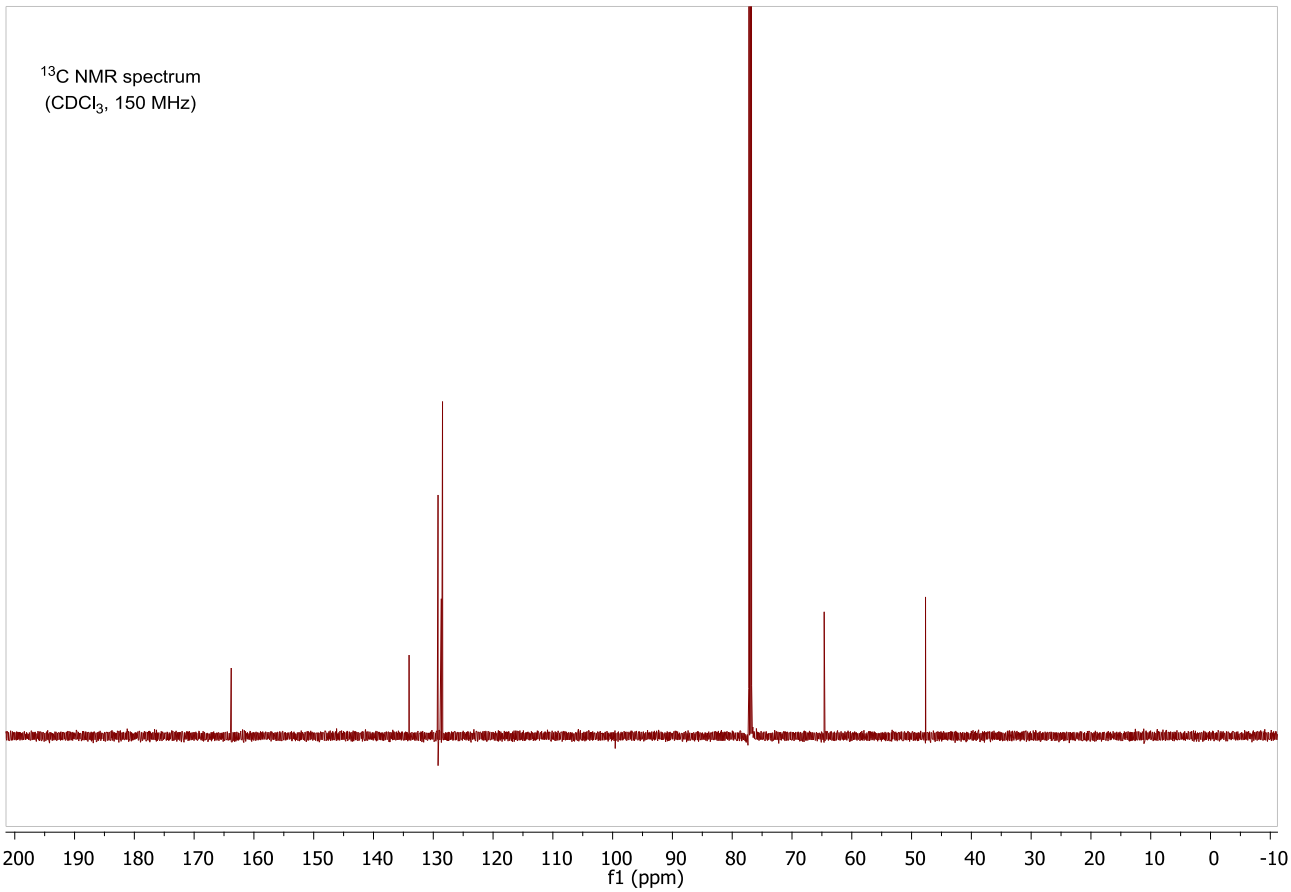
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)

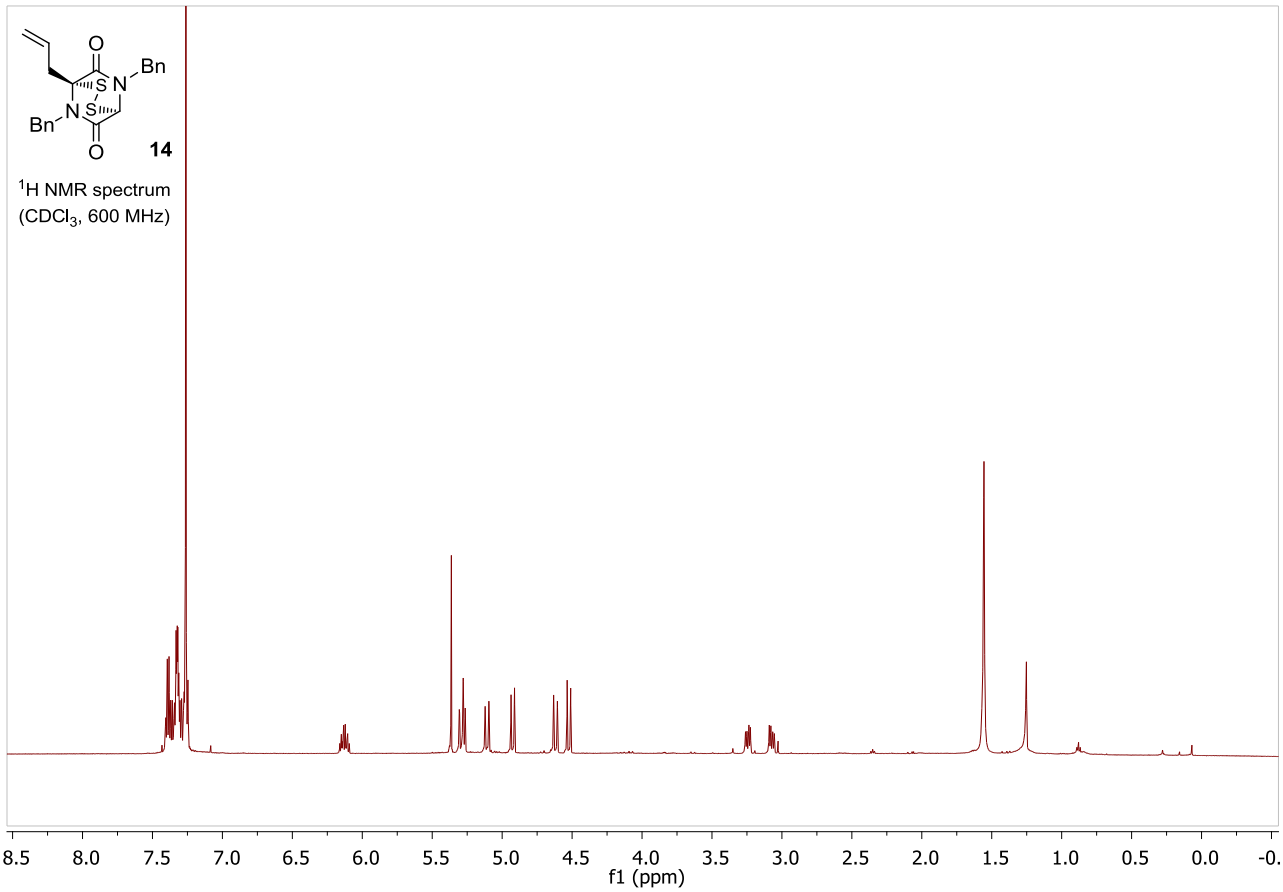


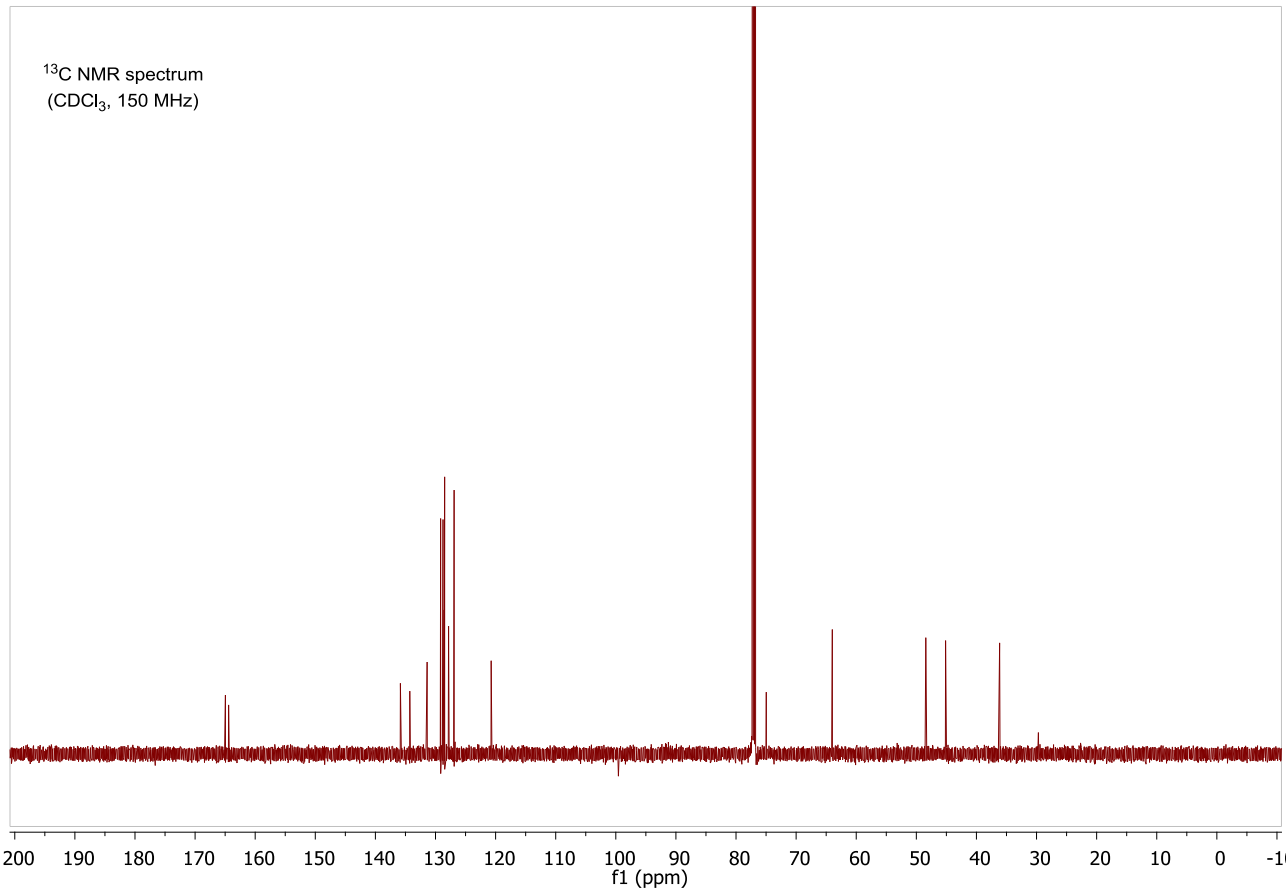
^{13}C NMR spectrum
($CDCl_3$, 150 MHz)

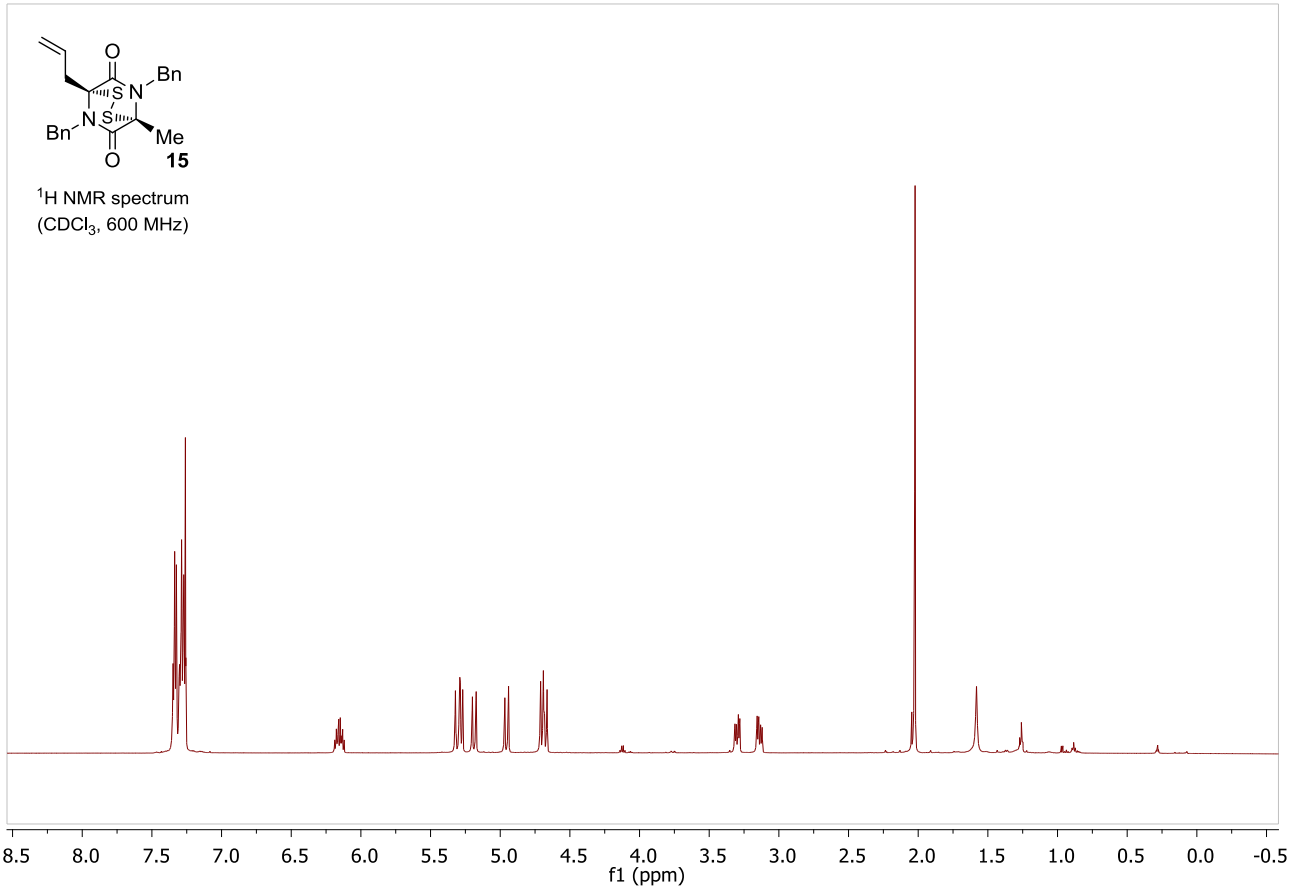


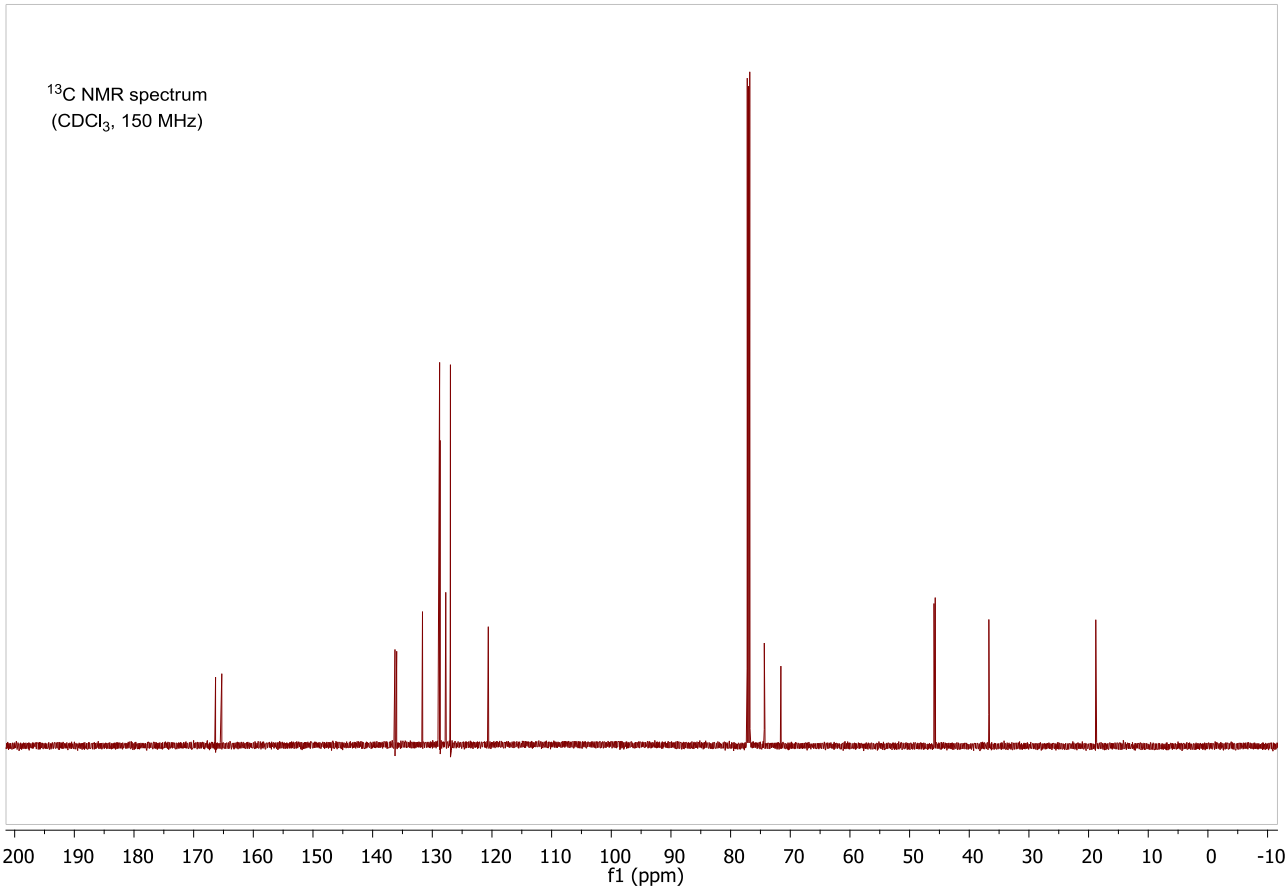

13
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

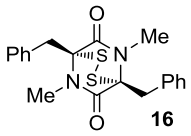

^{13}C NMR spectrum
($CDCl_3$, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Bn
Bn
14
1H NMR spectrum
(CDCl3, 600 MHz)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


13C NMR spectrum
(CDCl3, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

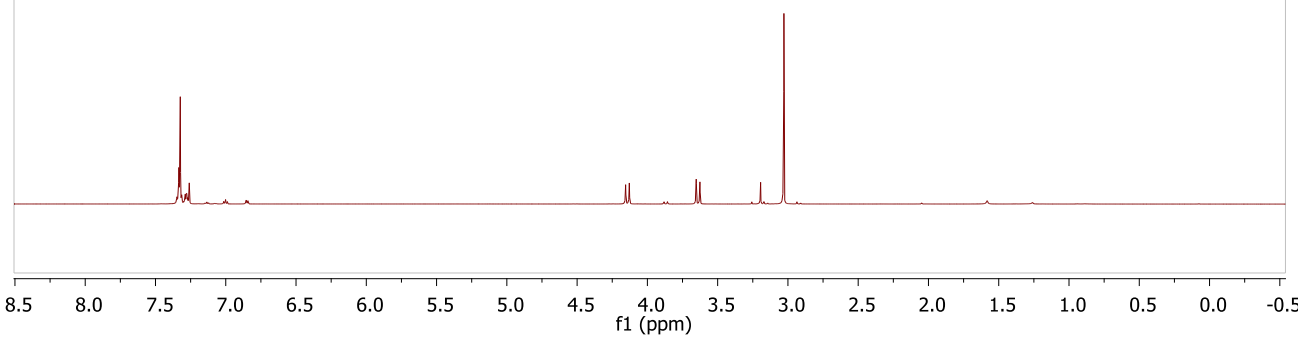

Bn
Bn
Me
15
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


^{13}C NMR spectrum
($CDCl_3$, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

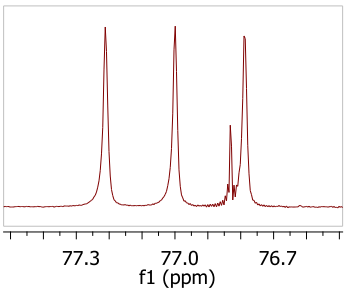


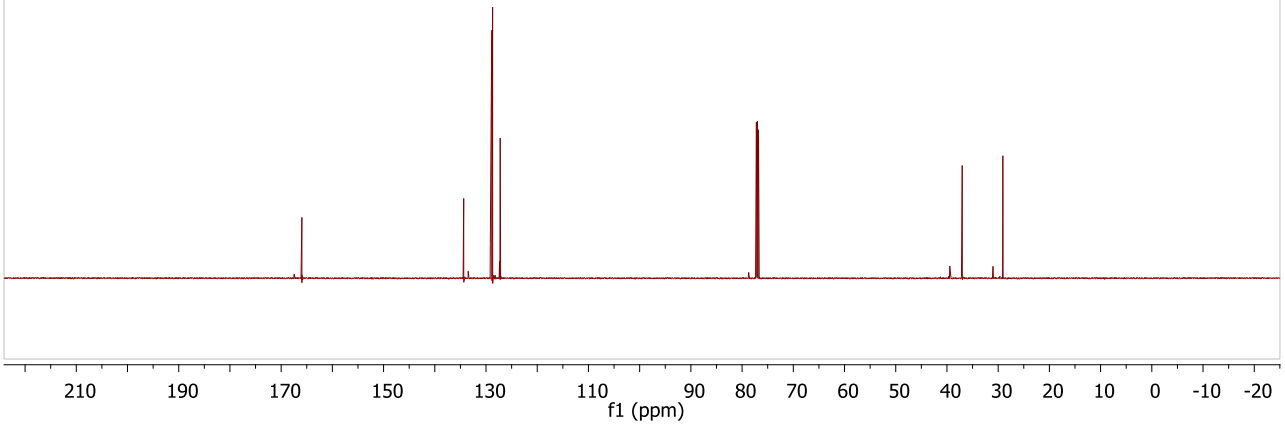
16

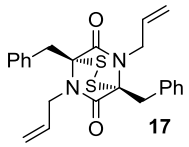
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)



^{13}C NMR spectrum
($CDCl_3$, 150 MHz)

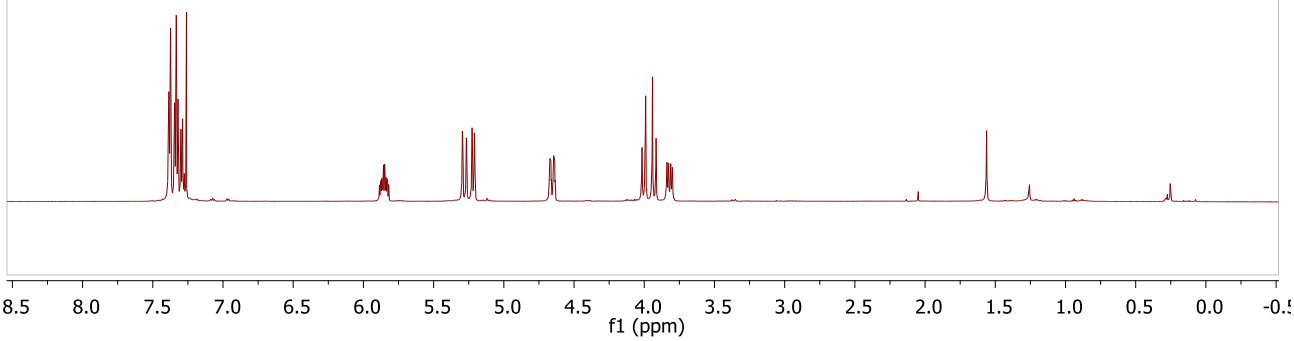




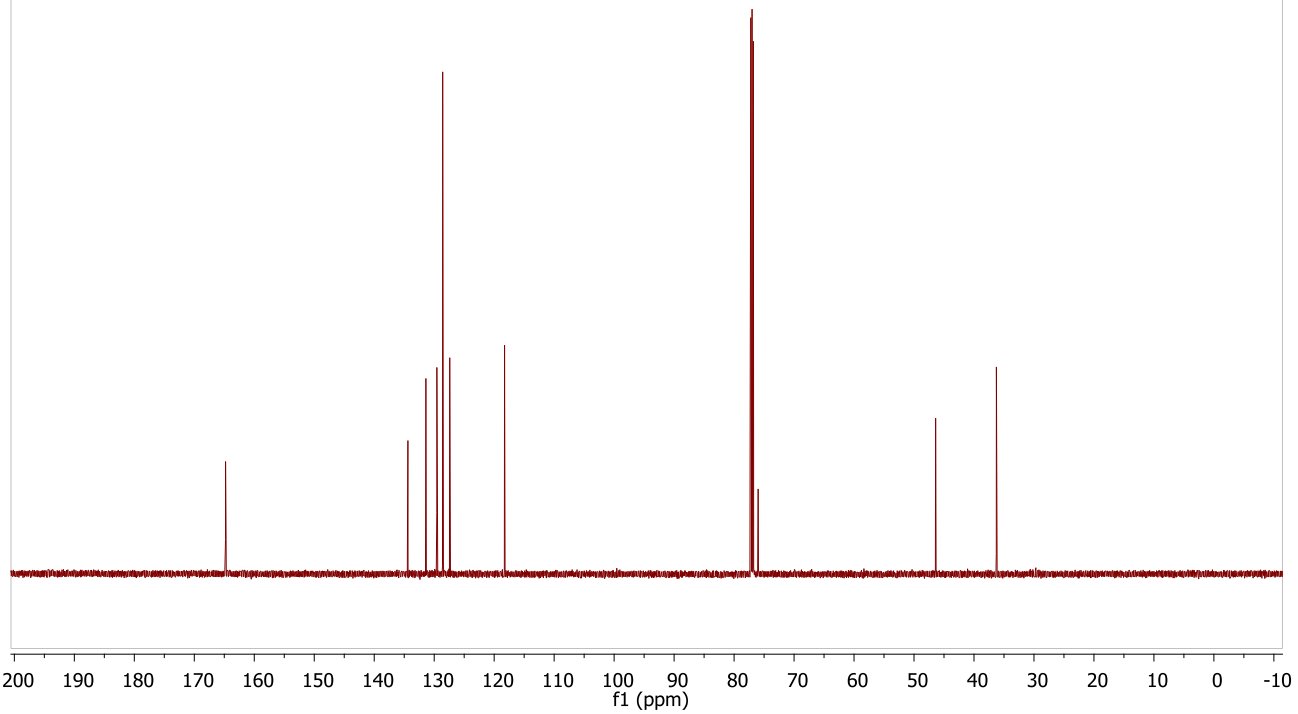


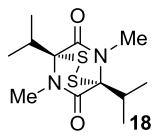
17

^{1}H NMR spectrum
($CDCl_3$, 600 MHz)



^{13}C NMR spectrum
($CDCl_3$, 150 MHz)

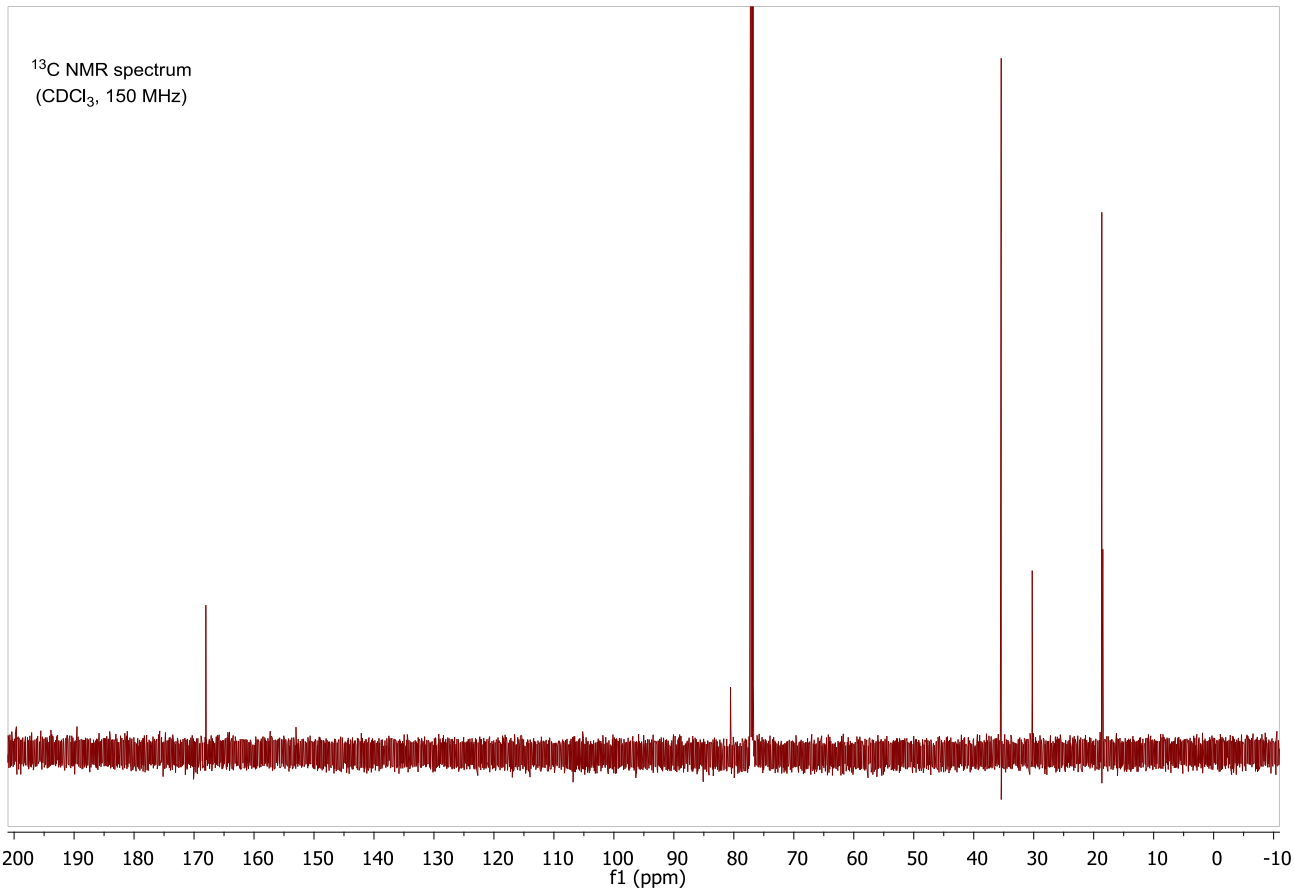


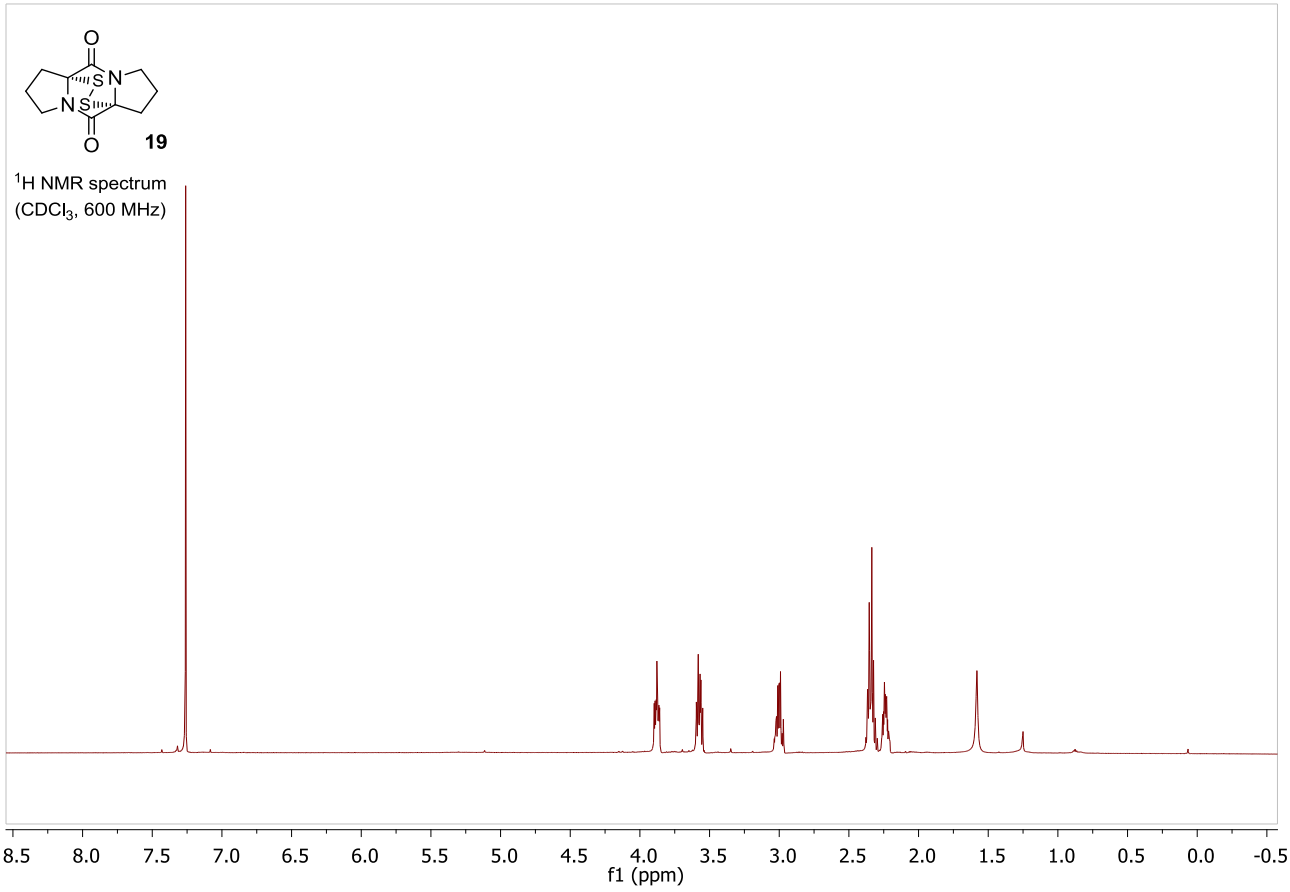


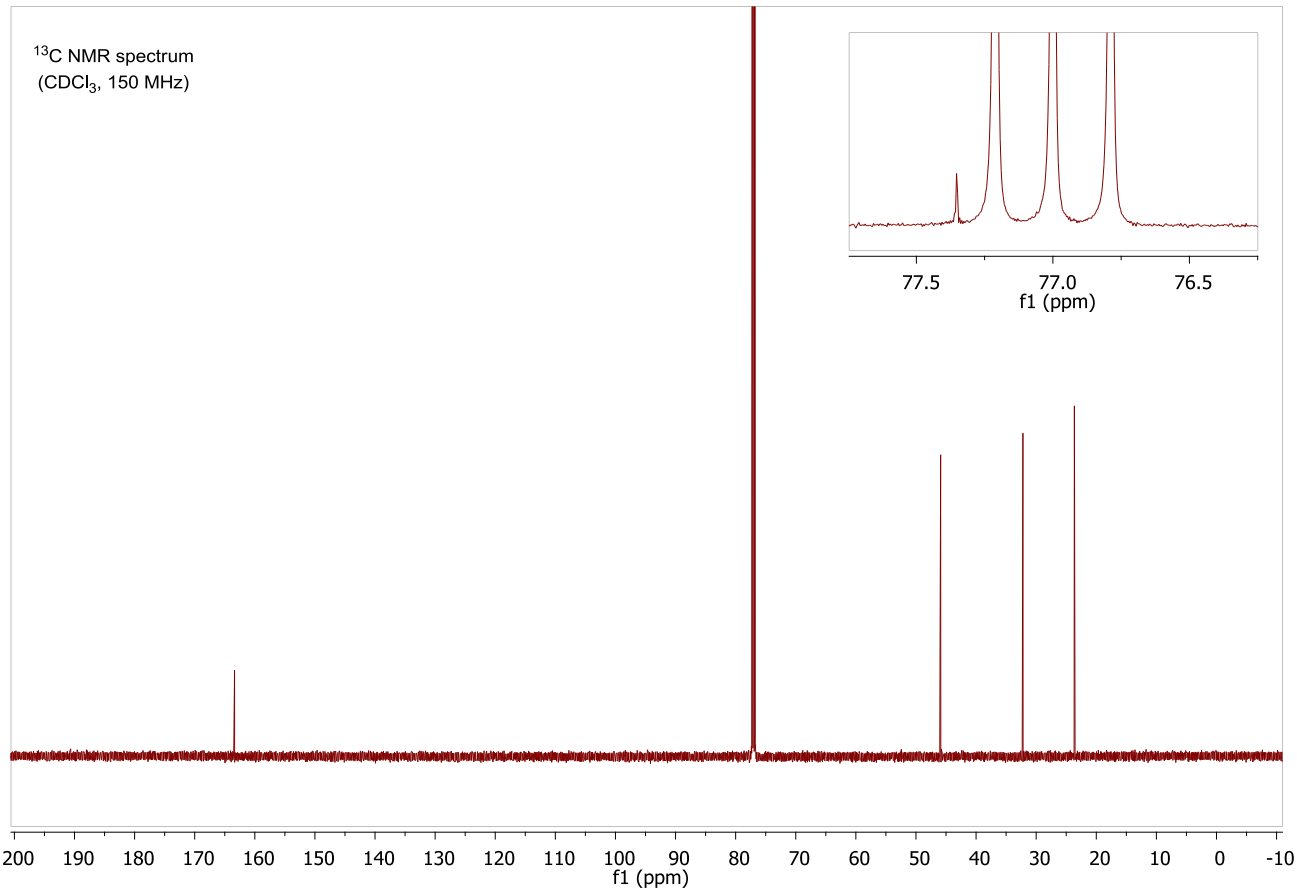
18

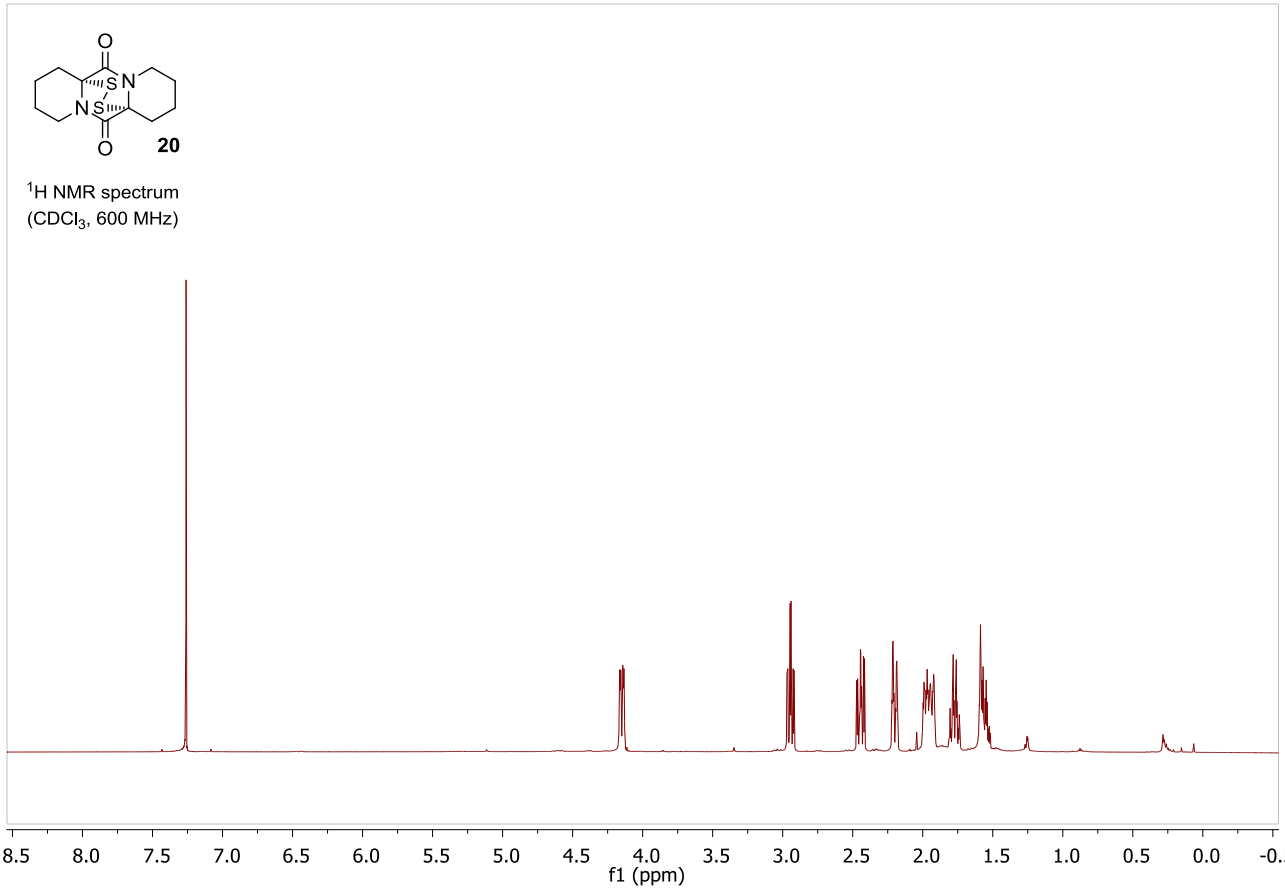
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)

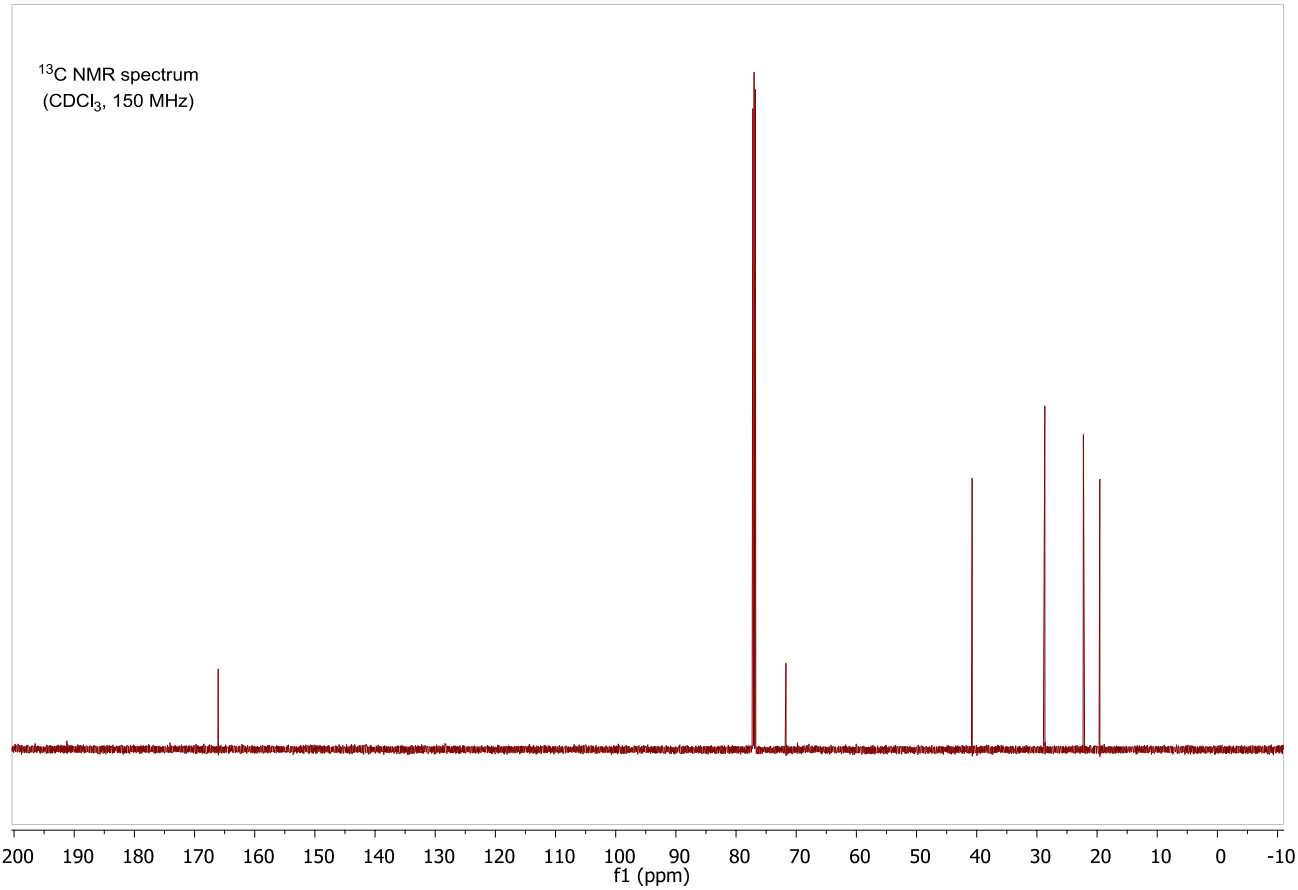
^{13}C NMR spectrum
($CDCl_3$, 150 MHz)

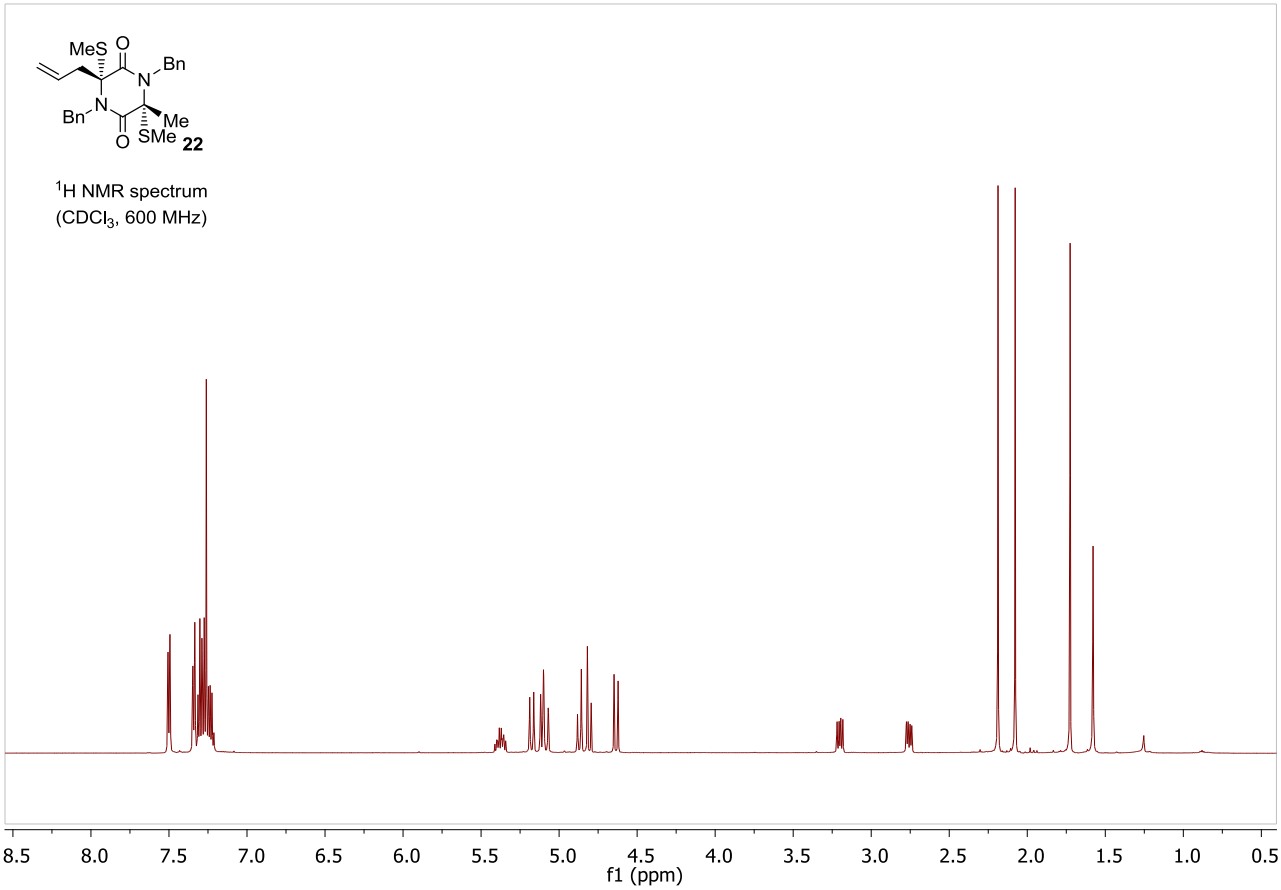


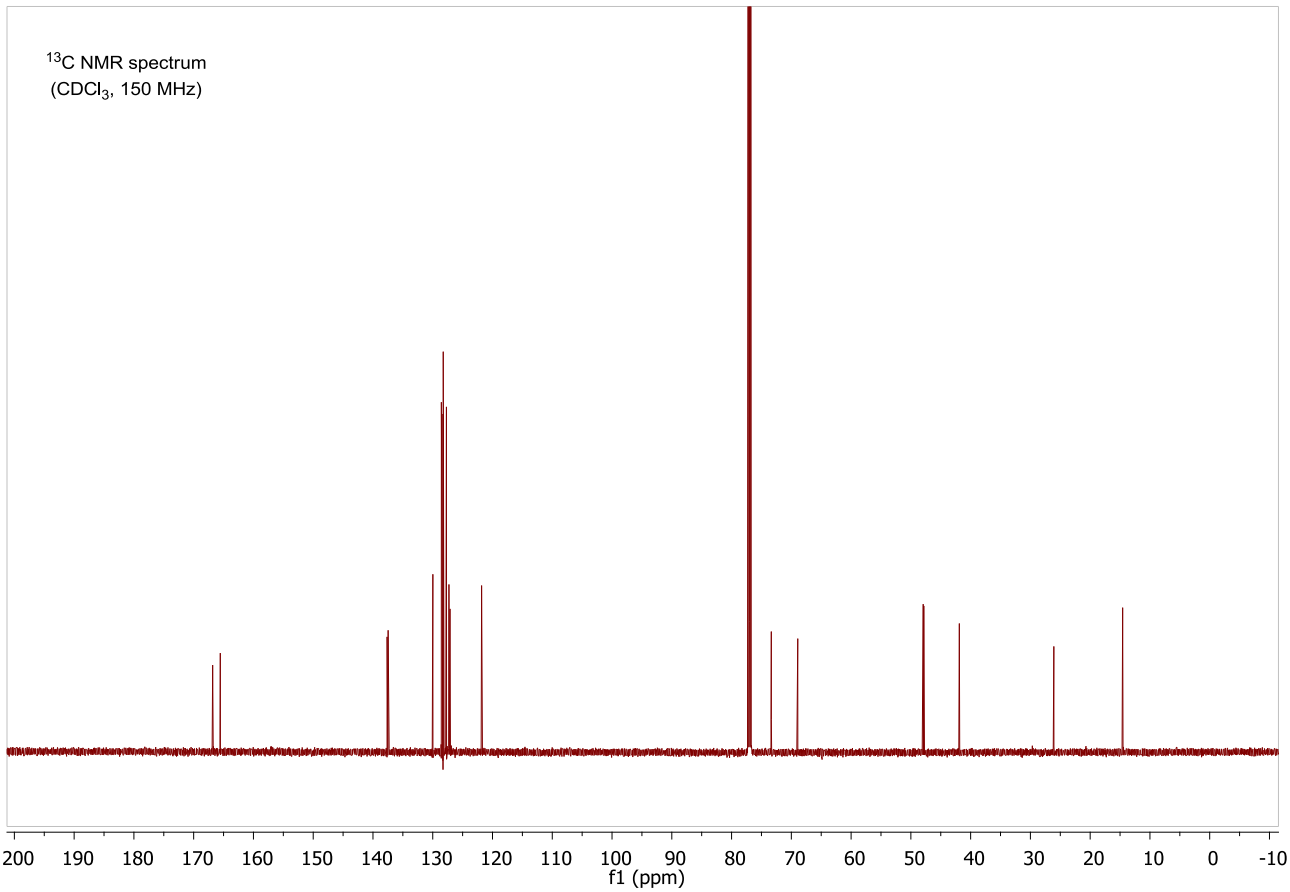

19
^{1}H NMR spectrum
(CDCl$_3$, 600 MHz)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

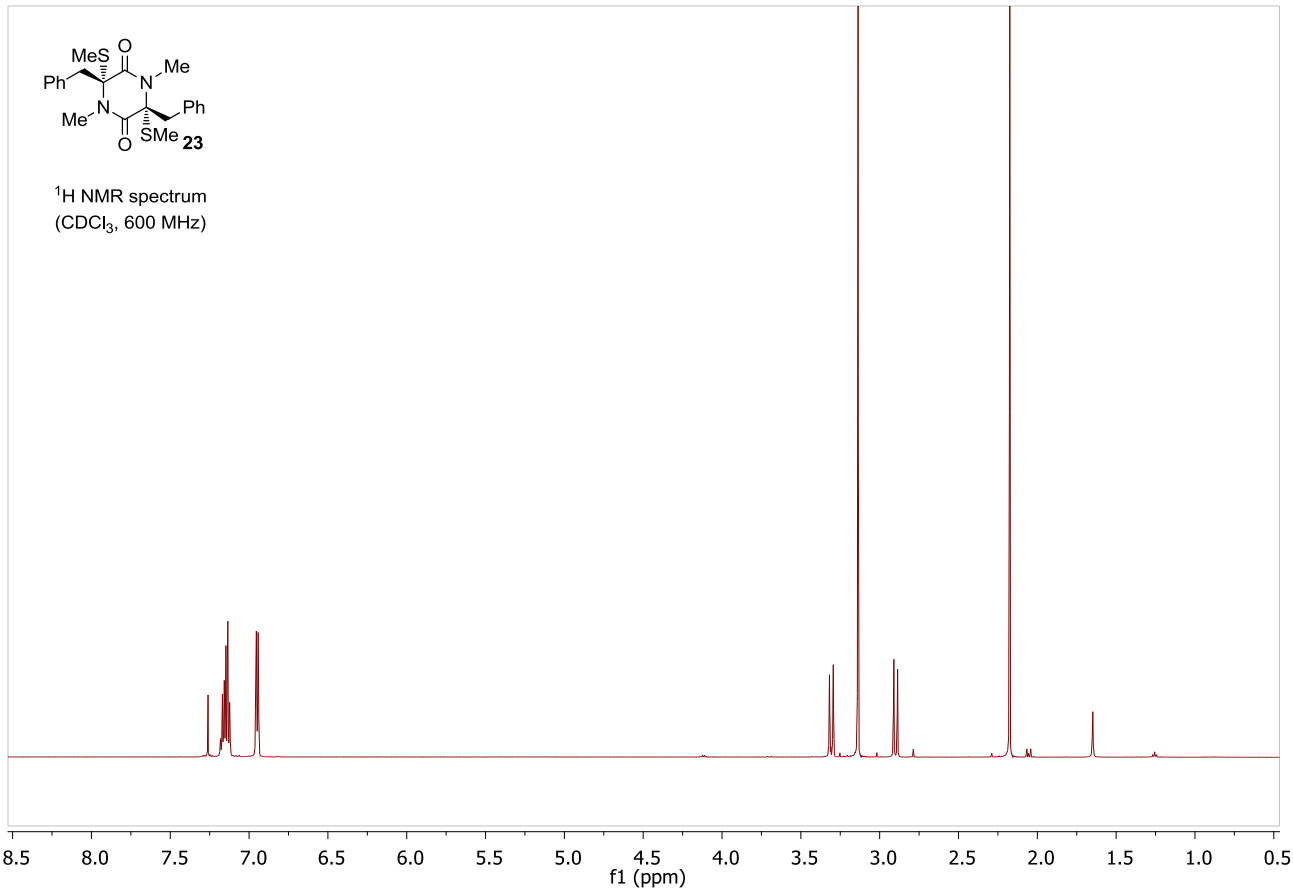

^{13}C NMR spectrum
(CDCl$_3$, 150 MHz)
77.5 77.0 76.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

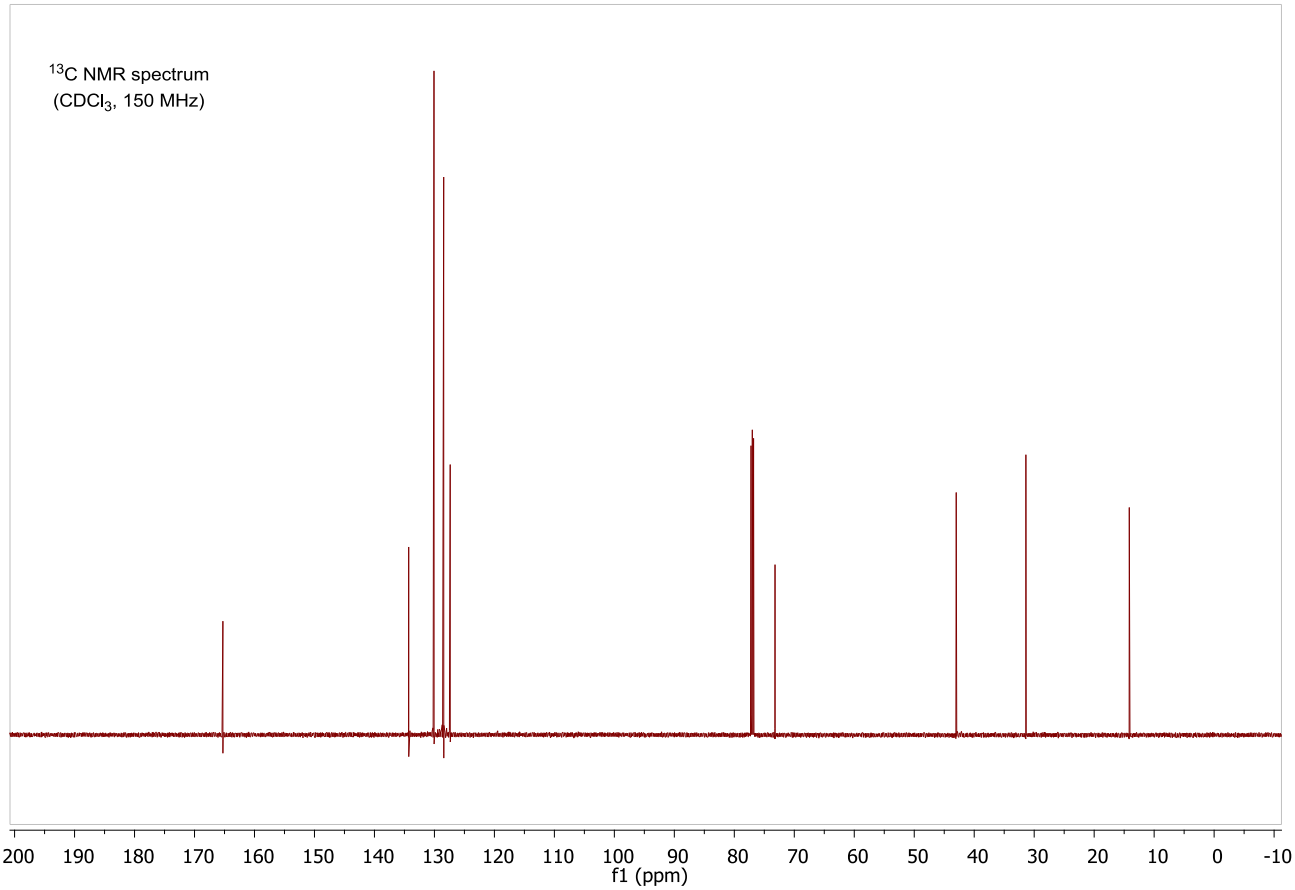

20
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

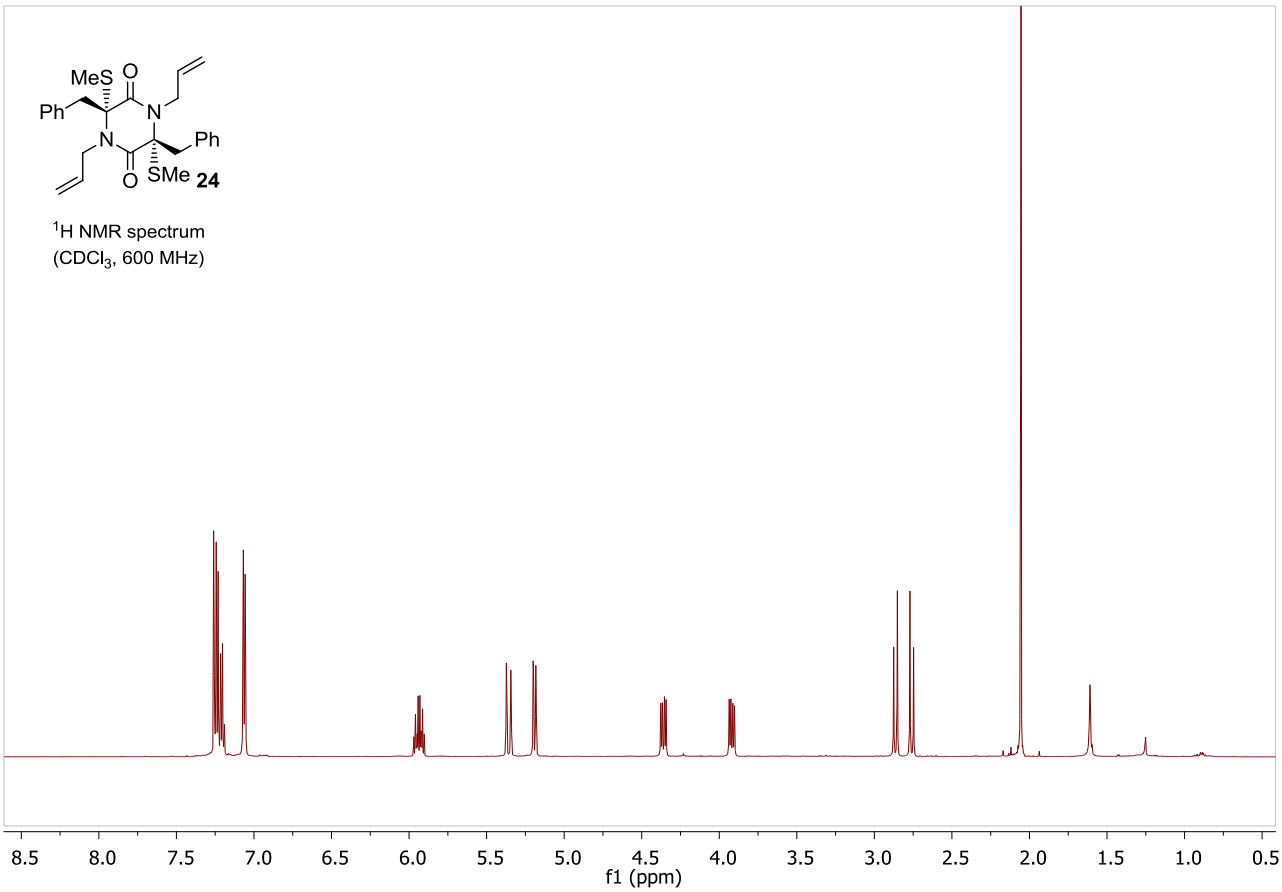

^{13}C NMR spectrum
($CDCl_3$, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

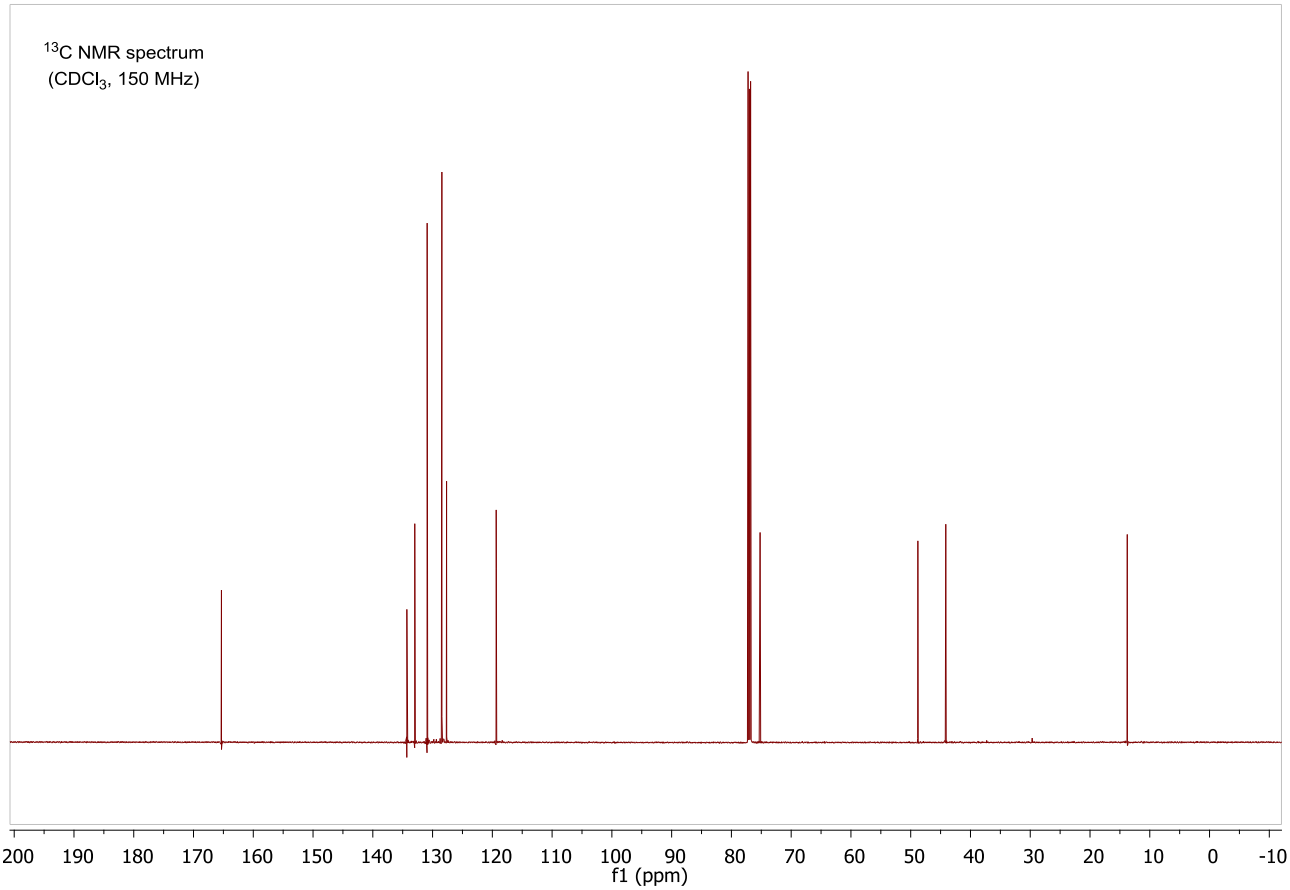

MeS
O
Bn
N
Bn
N
Me
O
SMe
22
^{1}H NMR spectrum
(CDCl$_3$, 600 MHz)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

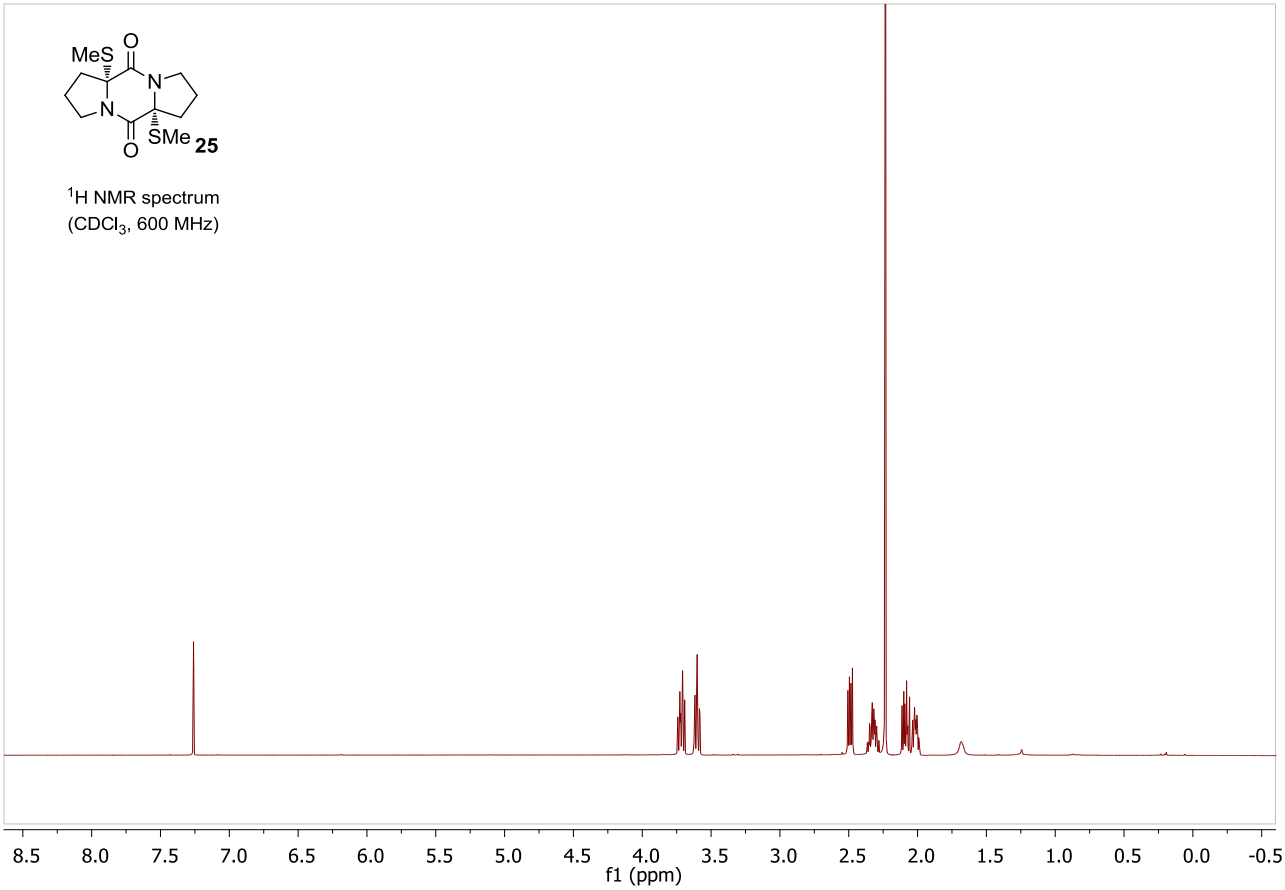

^{13}C NMR spectrum
(CDCl$_3$, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

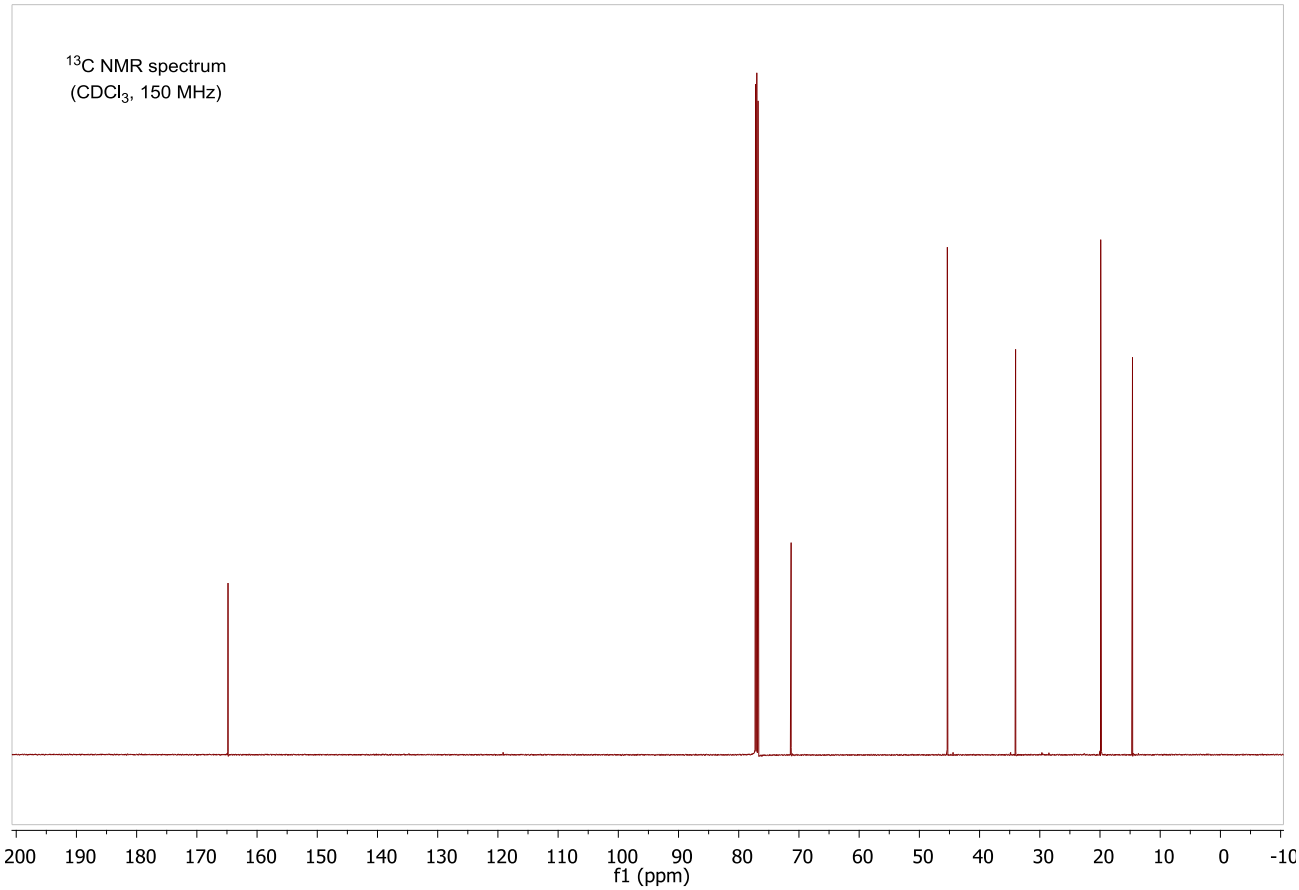

MeS
O
Me
Ph
N
N
Ph
Me
O
SMe
23
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

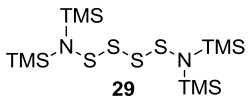

^{13}C NMR spectrum
($CDCl_3$, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


MeS
O
Ph
N
N
Ph
O
SMe
24
1H NMR spectrum
(CDCl3, 600 MHz)
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)


13C NMR spectrum
(CDCl3, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

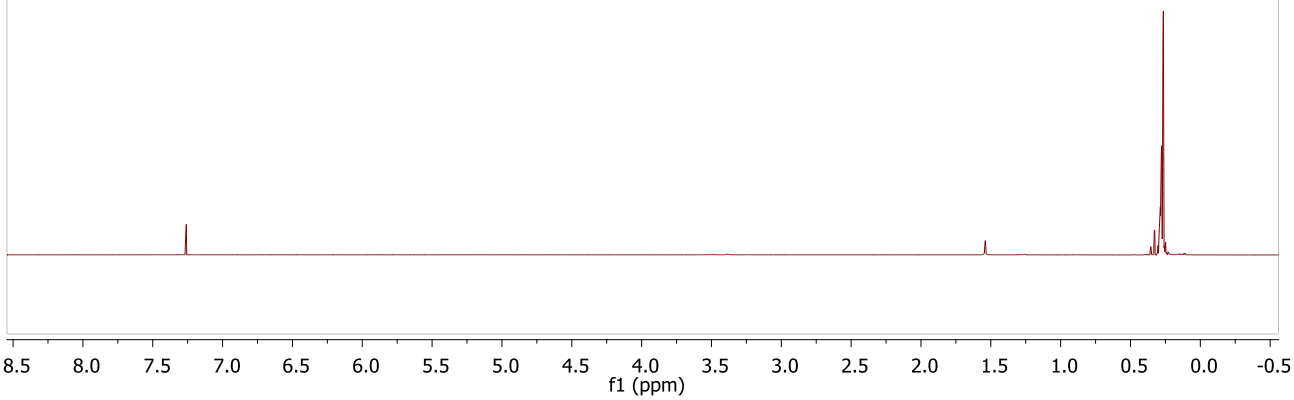

MeS
O
N
N
SMe
O
25
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


^{13}C NMR spectrum
($CDCl_3$, 150 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

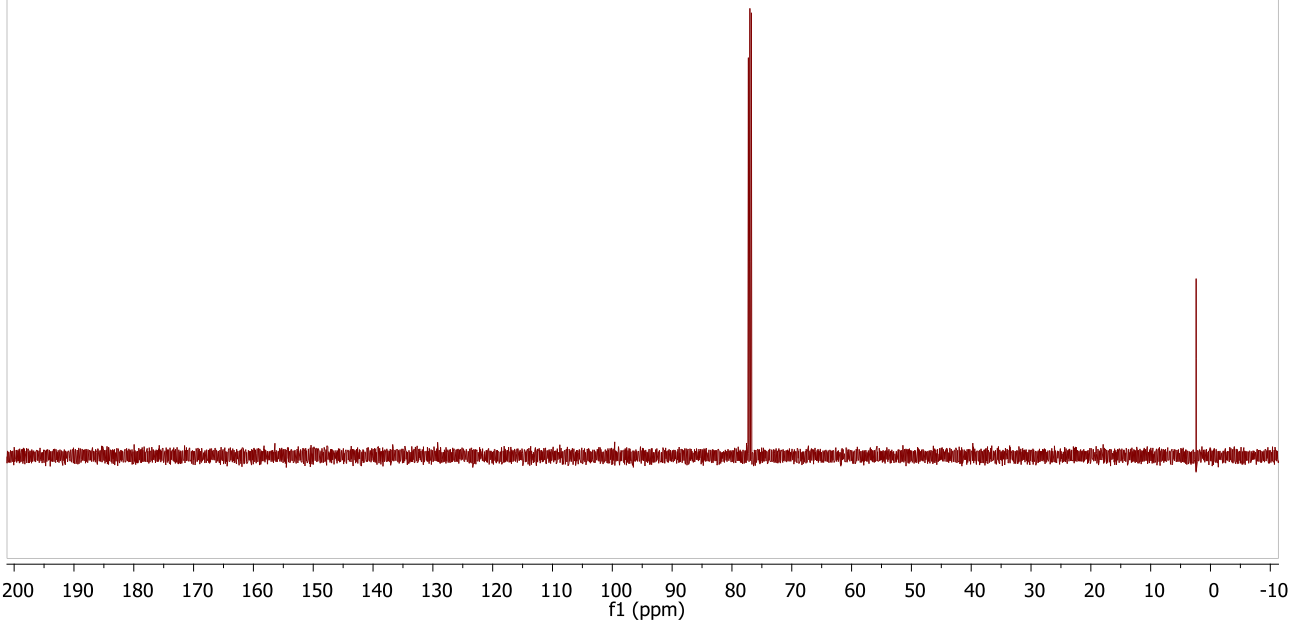


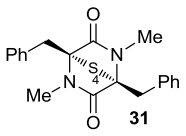
29

^{1}H NMR spectrum
($CDCl_3$, 500 MHz)



^{13}C NMR spectrum
($CDCl_3$, 125 MHz)

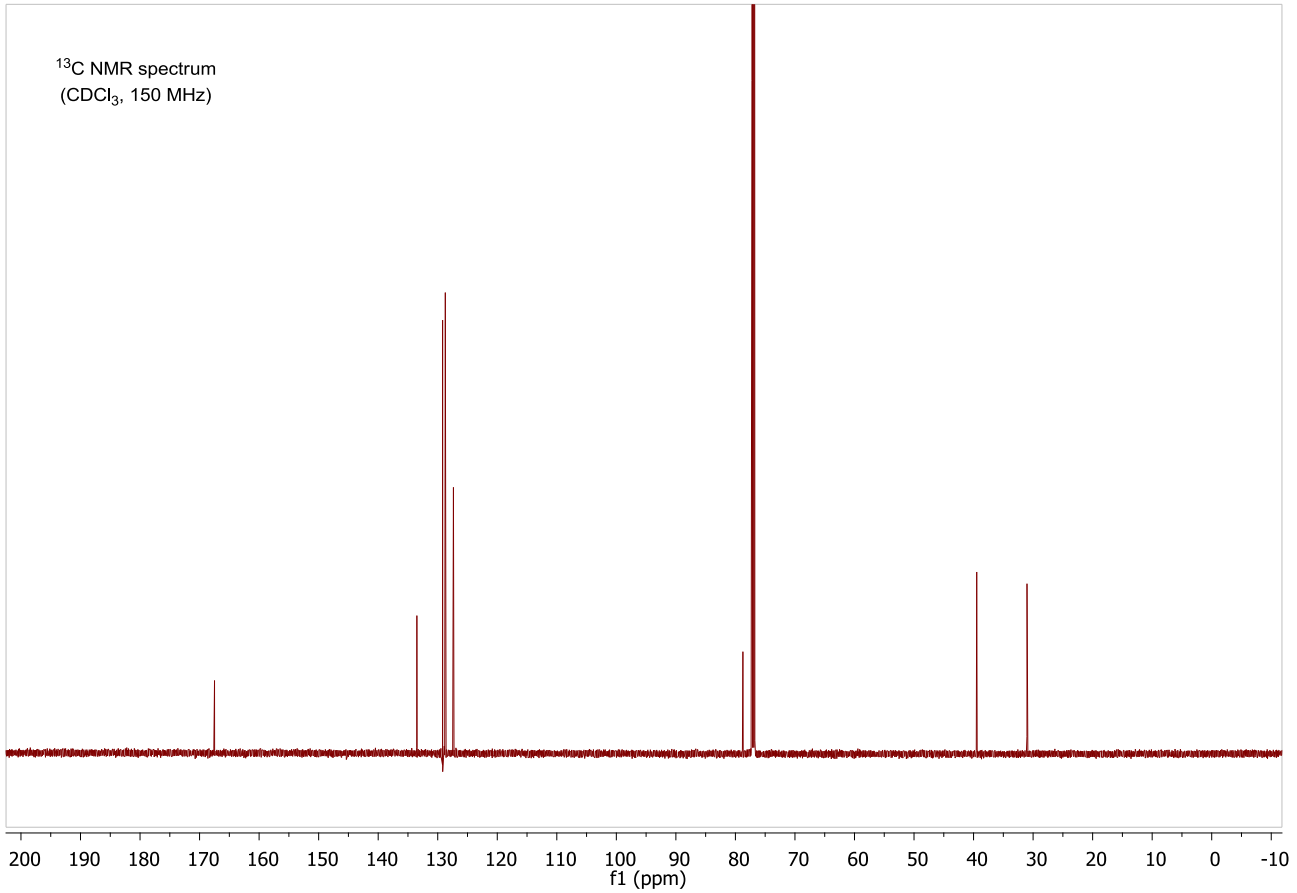


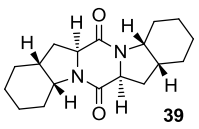


31

^{1}H NMR spectrum
($CDCl_3$, 600 MHz)

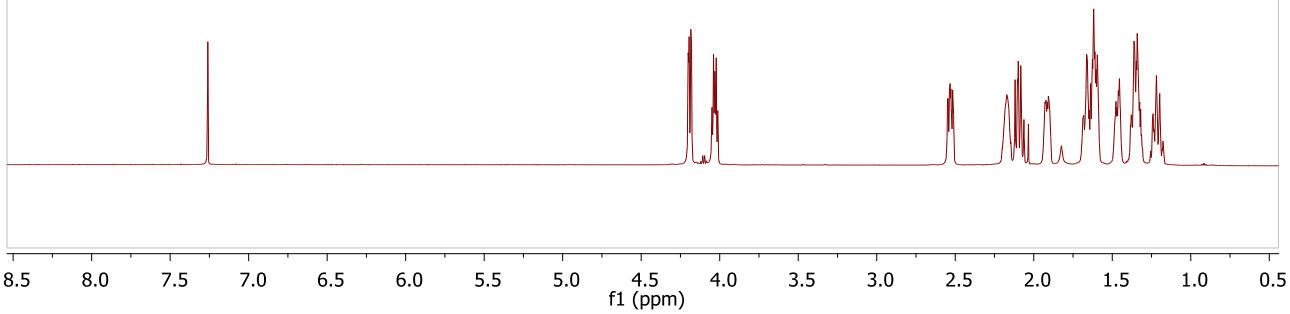
^{13}C NMR spectrum
($CDCl_3$, 150 MHz)



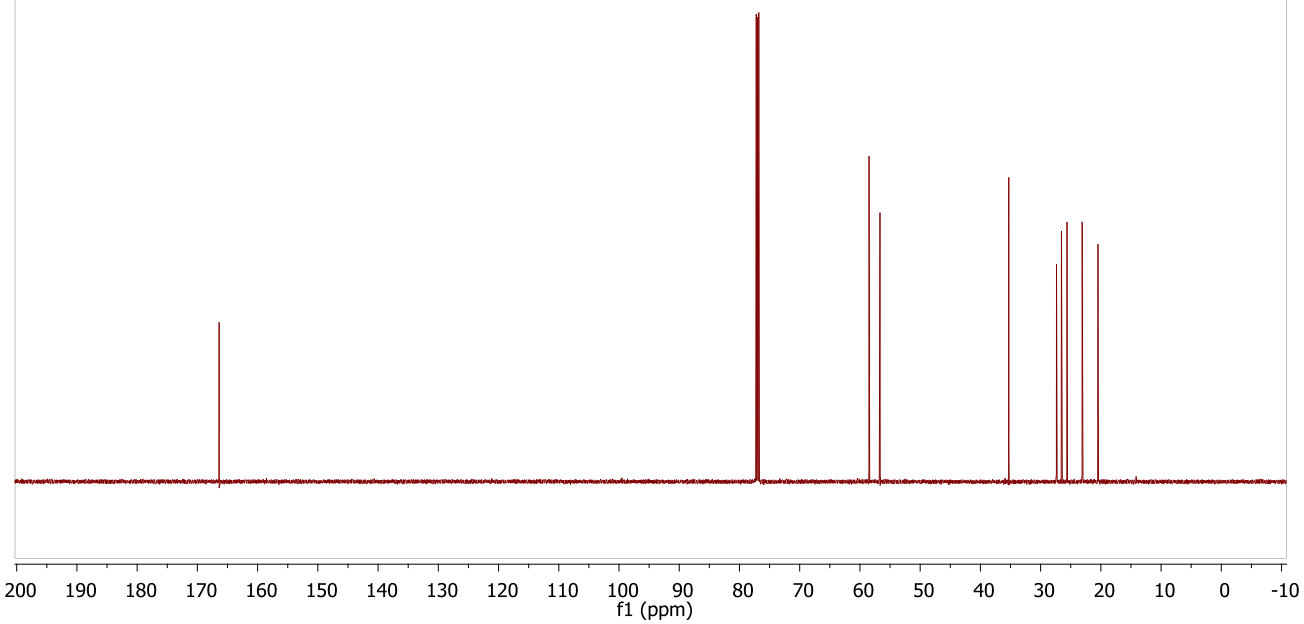


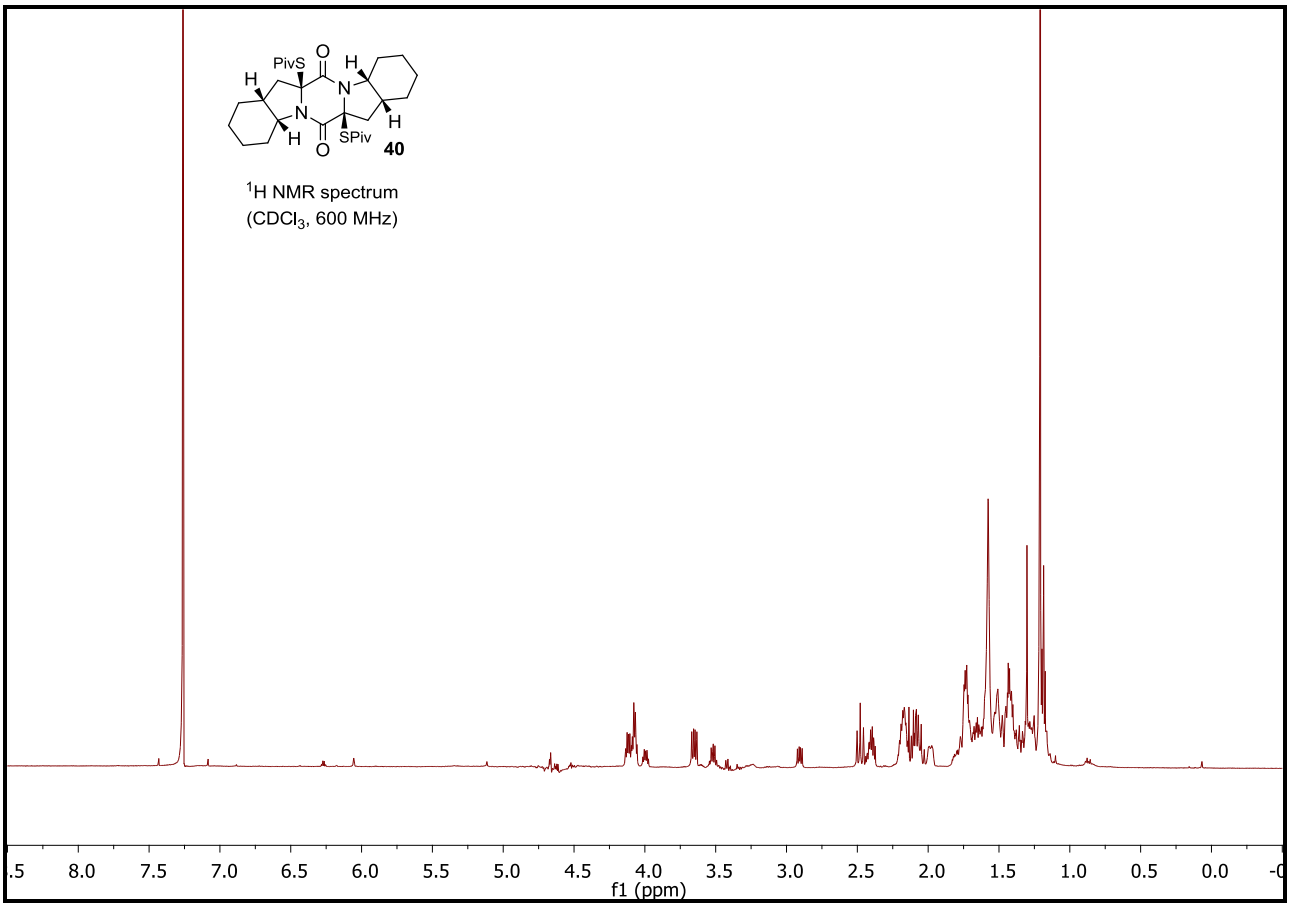
39

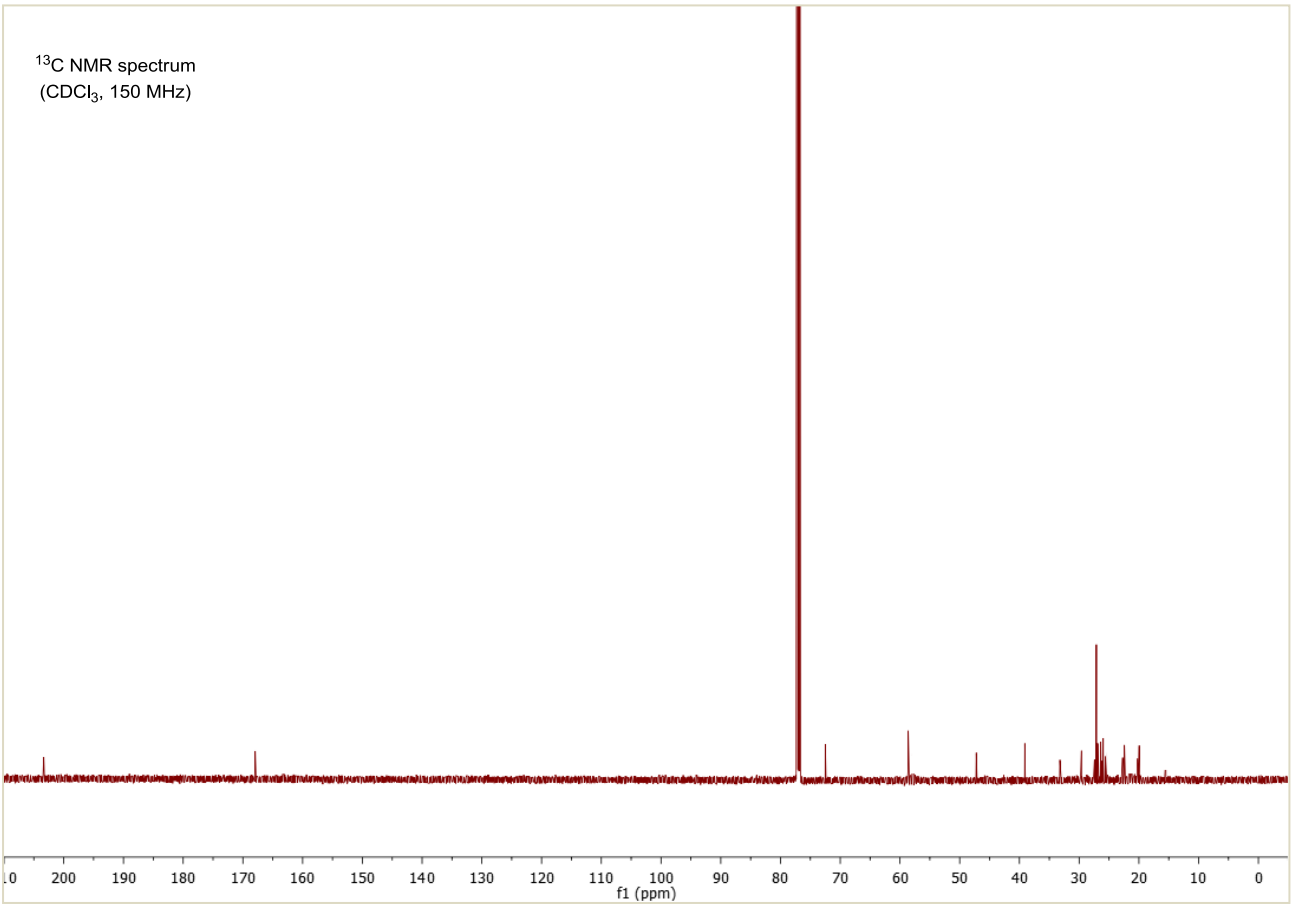
^{1}H NMR spectrum
($CDCl_3$, 600 MHz)

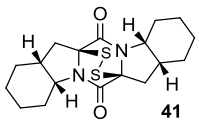


^{13}C NMR spectrum
($CDCl_3$, 150 MHz)




PivS
H
O
H
N
N
H
H
O
SPiv
40
^{1}H NMR spectrum
(CDCl$_3$, 600 MHz)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

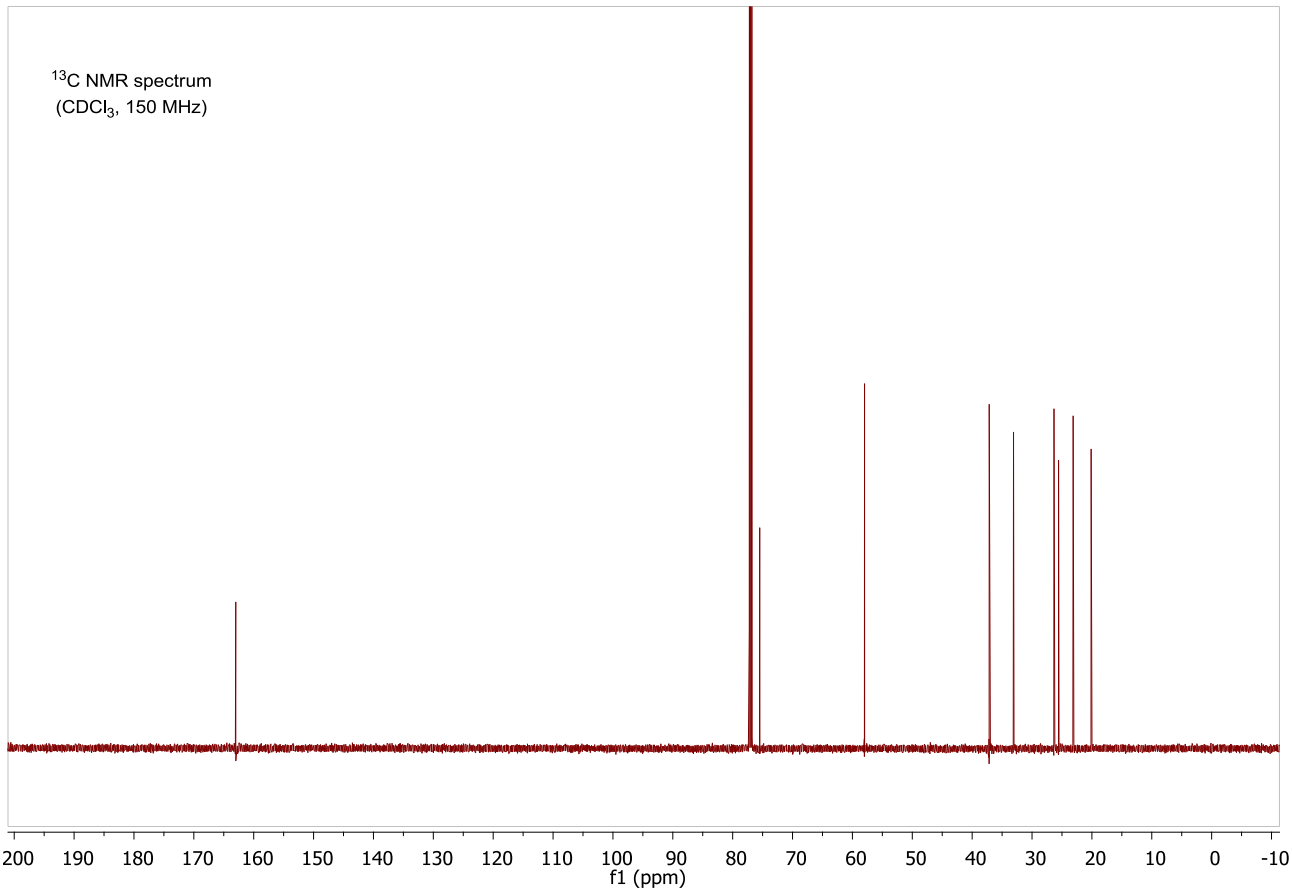

^{13}C NMR spectrum
(CDCl$_3$, 150 MHz)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

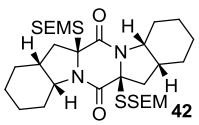


41

^{1}H NMR spectrum
($CDCl_3$, 600 MHz)

^{13}C NMR spectrum
($CDCl_3$, 150 MHz)

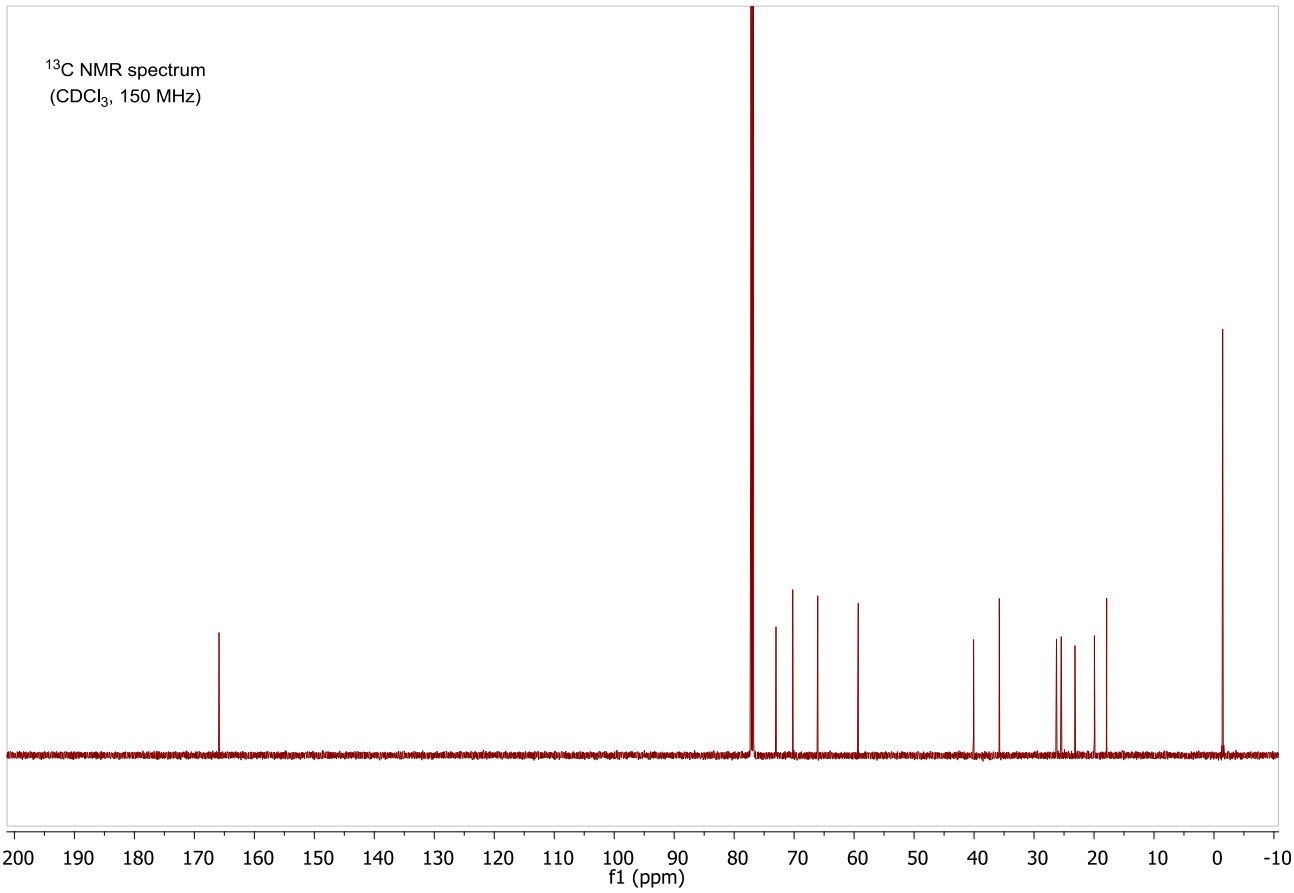


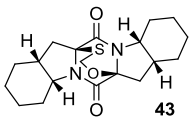


42

^{1}H NMR spectrum
($CDCl_3$, 600 MHz)

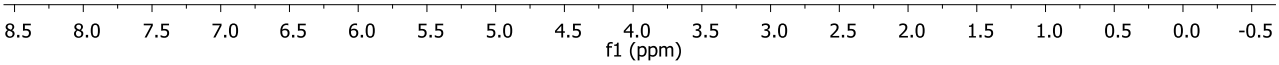
^{13}C NMR spectrum
($CDCl_3$, 150 MHz)



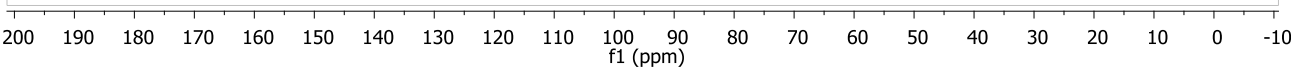


43

^{1}H NMR spectrum
($CDCl_3$, 600 MHz)



^{13}C NMR spectrum
($CDCl_3$, 150 MHz)



III. References

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