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Flavia Izzo,[a] Martina Schäfer,[b] Philip Lienau,[b] Ursula Ganzer,[b] Robert Stockman,*[a] and Ulrich Lücking*[b]

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Exploration of Novel Chemical Space: Synthesis and in vitro Evaluation of N-Functionalized Tertiary Sulfonimidamides

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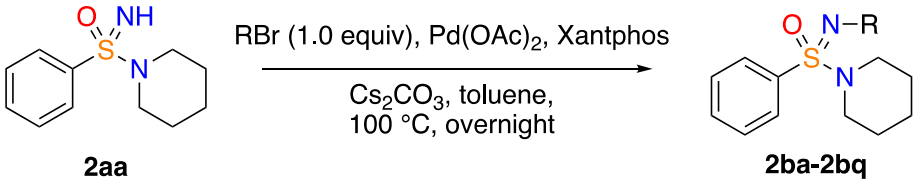
General methods and materials

Commercially available reagents and anhydrous solvents were purchased from Alfa Aesar, abcr, Acros Organics, Merck and Sigma-Aldrich, and were used without further purification. All reactions were carried out in microwave (MW) vials (Biotage®) and under Ar or O_2 atmosphere. Reactions were monitored by UPLC analysis with a Waters Acquity UPLC MS Single Quad system; column: Acquity UPLC BEH C18 1.7 μm, 50 × 2.1 mm; eluent A: H_2O + 0.2 vol% aq NH_3 (32%), eluent B: MeCN; gradient: 0–1.6 min 1–99% B, 1.6–2.0 min 99% B; flow: 0.8 mL/min; temperature: 60 °C; DAD scan: 210–400 nm. Flash chromatography was carried out using a Biotage® Isolera™ One system with 200–400 nm variable detector, using Biotage® SNAP KP-Sil and KP-NH cartridges. Preparative HPLC was carried out with a Waters AutoPurification MS Single Quad system; column: Waters XBridge C18 5 μm, 100 × 30 mm; eluent A: H_2O + 0.2 vol% aq NH_3 (32%), eluent B: MeCN; gradient: 0–0.50 min 5% B, flow: 25 mL/min; 0.51–5.50 min 10–100% B, flow: 70 mL/min; 5.51–6.50 min 100% B, flow: 70 mL/min; temperature: 25 °C; DAD scan: 210–400 nm. Analytical TLC was carried out on aluminum-backed plates coated with Merck Kieselgel 60 F254, with visualization under UV light at 254 nm and, where not possible, using $KMnO_4$ stain. NMR spectra were recorded on Bruker Avance III HD, Bruker AV400 or Bruker AV(III)400 spectrometers. ^{1}H NMR spectra were obtained at 400 MHz and referenced to the residual solvent signal (7.26 ppm for $CDCl_3$, 2.50 ppm for [D_6]DMSO). ^{13}C NMR spectra were obtained at 101 MHz and also referenced to the residual solvent signal (77.16 ppm for $CDCl_3$, 39.52 ppm for [D_6]DMSO). All spectra were obtained at ambient temperature (22 ± 1 °C). Data are reported as follows: chemical shift (δ) in ppm, multiplicity (standard abbreviations), coupling constant(s) (Hz), and integration. High-resolution mass spectra were recorded on a Xevo® G2-XS QTof (Waters) instrument or an OpenAccess Bruker micrOTOF spectrometer. Melting points were determined with a Büchi B-540 or Stuart Scientific SMP20 melting point apparatus. Solutions of compounds were dried by filtration through water-repellent filter paper (MACHEREY-NAGEL 617 WA, 125 mm diam). Petroleum ether (PE) refers to the fraction with a boiling range of 40–60 °C. Sulfonimidamide **2aa** was synthesized according to a reported procedure.[1]

N-Arylation of sulfonimidamide 2aa

General procedure A:

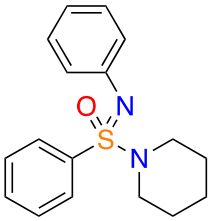


2aa
1.1 equiv

2ba-2bq

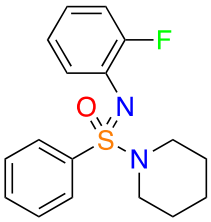
In a dry MW vial flushed with Ar, sulfonimidamide **2aa** (100 mg, 0.45 mmol, 1.1 equiv) and an aryl bromide (0.40 mmol, 1.0 equiv) were dissolved in toluene (6.8 mL). The mixture was then degassed for 10 min and $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 5 mol%), Xantphos (23 mg, 0.04 mmol, 10 mol%) and Cs_2CO_3 (200 mg, 0.60 mmol, 1.5 equiv) were added at RT. The reaction mixture was heated to 100 °C and stirred overnight. Once the starting material had been consumed (monitored by TLC), the mixture was cooled, diluted with methyl *tert*-butyl ether, filtered through a pad of Celite under reduced pressure and washed with methyl *tert*-butyl ether. Solvent was removed under reduced pressure and the crude product was purified by flash column chromatography.

1-(*N*,*S*-Diphenylsulfonimidoyl)piperidine (2ba)



Prepared according to general procedure **A**, from bromobenzene; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in PE) to give **2ba** as a white solid (104 mg, 86%): m.p. 118–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.96 (m, 2H), 7.62–7.52 (m, 3H), 7.27 (d, J = 6.1 Hz, 2H), 7.25 (d, J = 2.4 Hz, 2H), 6.98 (tt, J = 5.70, 2.91 Hz, 1H), 3.10–2.99 (m, 4H), 1.58–1.49 (m, 4H), 1.37 ppm (quin, J = 6.08 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 143.9, 136.6, 132.3, 129.9, 128.9, 127.9, 123.9, 121.8, 47.6, 25.4, 23.7 ppm; IR (KBr): ν = 3074, 2939, 2849, 1585, 1485, 1306, 1219, 931, 781, 694 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{17}H_{21}N_2OS$: 301.1375, found: 301.1378.

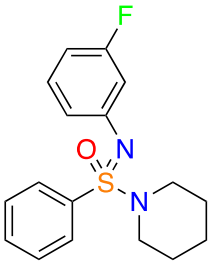
1-[*N*-(2-Fluorophenyl)-*S*-phenylsulfonimidoyl]piperidine (2bb)



Prepared according to general procedure **A**, from 1-bromo-2-fluorobenzene; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2bb** as a white solid (59 mg, 46%): m.p. 76–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–7.97 (m, 2H), 7.62–7.50 (m, 3H), 7.43 (td, J = 8.2, 1.8 Hz, 1H), 7.05 (ddd, J = 10.9, 7.9, 1.7 Hz, 1H), 6.98 (td, J = 7.6, 1.8 Hz, 1H), 6.95–6.88 (m, 1H), 3.04 (t, J = 5.5 Hz, 4H), 1.51 (qdd, J = 13.4, 6.8, 4.3 Hz, 4H), 1.39–1.30 ppm (m,

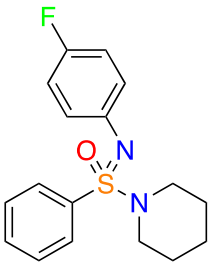
2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.9 (d, J = 244.2 Hz), 136.5, 132.5, 131.7 (d, J = 11.4 Hz), 129.0, 128.1, 125.6 (d, J = 1.9 Hz), 124.1 (d, J = 3.8 Hz), 122.7 (d, J = 7.3 Hz), 115.9 (d, J = 20.4 Hz), 47.6, 25.5, 23.7 ppm; IR (KBr): ν = 3076, 2935, 2849, 1603, 1495, 1315, 1227, 928, 750 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{17}H_{20}N_2OFS$: 319.1280, found: 319.1281.

1-[*N*-(3-Fluorophenyl)-*S*-phenylsulfonimidoyl]piperidine (2bc)



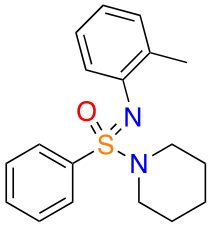
Prepared according to general procedure **A**, from 1-bromo-3-fluorobenzene; crude purified by flash column chromatography (KP-Sil, 0–20% EtOAc in hexane) to give **2bc** as a white solid (124 mg, 97%): m.p. 92–94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.93 (m, 2H), 7.63–7.49 (m, 3H), 7.16 (td, J = 8.1, 6.8 Hz, 1H), 7.01 (ddd, J = 7.9, 2.0, 1.0 Hz, 1H), 6.97 (dt, J = 11.1, 2.3 Hz, 1H), 6.66 (tdd, J = 8.4, 2.6, 0.9 Hz, 1H), 3.11–2.94 (m, 4H), 1.54 (m, 4H), 1.37 ppm (quin, J = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.4, 162.0, 145.6 (d, J = 10.5 Hz), 136.1, 132.4, 129.6 (d, J = 9.8 Hz), 128.8, 127.7, 119.4 (d, J = 2.6 Hz), 110.6 (d, J = 22.8 Hz), 108.4 (d, J = 21.3 Hz), 47.4, 25.3, 23.5 ppm; IR (KBr): ν = 3076, 2937, 2849, 1604, 1225, 1148, 1094 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{17}H_{20}N_2OFS$: 319.1280, found: 319.1281.

1-[*N*-(4-Fluorophenyl)-*S*-phenylsulfonimidoyl]piperidine (2bd)



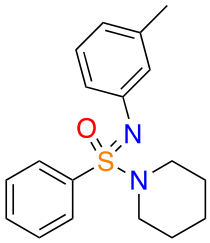
Prepared according to general procedure **A**, from 1-bromo-4-fluorobenzene; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2bd** as a white solid (91 mg, 72%): m.p. 83–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.94 (m, 2H), 7.58–7.51 (m, 3H), 7.21 (m, 2H), 6.95 (m, 2H), 3.01 (m, 4H), 1.59–1.44 (m, 4H), 1.37 ppm (quin, J = 5.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.6, 157.3, 136.4, 132.4, 128.9, 127.9, 124.8 (d, J = 7.7 Hz), 115.5 (d, J = 22.1 Hz), 47.6, 25.4, 23.7 ppm; IR (KBr): ν = 3053, 2939, 2847, 1499, 1207, 1016, 919 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{17}H_{20}N_2OFS$: 319.1280, found: 319.1281.

1-[*S*-Phenyl-*N*-(2-tolyl)sulfonimidoyl]piperidine (2be)



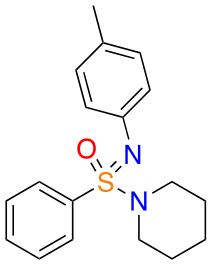
Prepared according to general procedure **A**, from 2-bromotoluene; crude purified by flash column chromatography (KP-Sil, 0–20% EtOAc in hexane) to give **2be** as a yellow oil (122 mg, 97%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.97 (m, 2H), 7.60–7.51 (m, 3H), 7.38 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.15 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.06 (td, *J* = 7.7, 1.7 Hz, 1H), 6.88 (td, *J* = 7.4, 1.3 Hz, 1H), 3.06 (ddd, *J* = 11.3, 7.0, 3.9 Hz, 2H), 2.96 (ddd, *J* = 11.4, 7.0, 3.9 Hz, 2H), 2.39 (s, 3H), 1.60–1.45 (m, 4H), 1.36 ppm (quin, *J* = 6.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.1, 137.1, 132.2, 132.0, 130.2, 128.7, 127.8, 126.2, 122.1, 121.5, 47.3, 25.3, 23.6, 18.8 ppm; IR (KBr): ν = 3063, 3015, 2935, 2849, 1596, 1487, 1313, 1290, 1269, 1227, 1121, 914 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{18}H_{23}N_2OS$: 315.1531, found: 315.1534.

1-[*S*-Phenyl-*N*-(3-tolyl)sulfonimidoyl]piperidine (2bf)



Prepared according to general procedure **A**, from 3-bromotoluene; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2bf** as a white solid (106 mg, 84%): m.p. 67–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.95 (m, 2H), 7.59–7.50 (m, 3H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.08–7.06 (m, 2H), 6.81–6.76 (m, 1H), 3.09–2.98 (m, 4H), 2.31 (s, 3H), 1.61–1.45 (m, 4H), 1.37 ppm (quin, *J* = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 143.5, 138.5, 136.5, 132.1, 128.7, 128.6, 127.8, 124.5, 122.6, 120.6, 47.4, 25.3, 23.6, 21.5 ppm; IR (KBr): ν = 3070, 2932, 2853, 1597, 1485, 1300, 1223, 1059, 926 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{18}H_{23}N_2OS$: 315.1531, found: 315.1535.

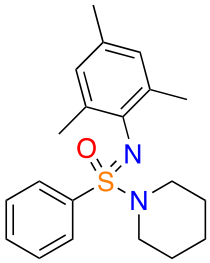
1-[*S*-Phenyl-*N*-(4-tolyl)sulfonimidoyl]piperidine (2bg)



Prepared according to general procedure **A**, from 4-bromotoluene; crude purified by flash column chromatography (KP-Sil, 0–20% EtOAc in hexane) to give **2bg** as a white solid (125 mg, 99%): m.p. 113–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.95 (m, 2H), 7.59–7.50 (m, 3H), 7.15–7.12 (m, 2H), 7.05–7.03 (m, 2H), 3.02 (qt, *J* = 11.2, 4.8 Hz, 4H), 2.28 (s, 3H), 1.60–1.45 (m, 4H), 1.36 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 140.8, 136.5, 132.1, 131.0,

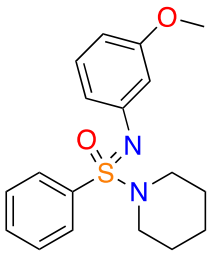
129.5, 128.7, 127.8, 123.5, 47.4, 25.3, 23.6, 20.8 ppm; IR (KBr): ν = 3026, 2935, 2847, 1506, 1310, 1221, 1055, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{18}H_{23}N_2OS$: 315.1531, found: 315.1530.

1-(*N*-Mesityl-*S*-phenylsulfonimidoyl)piperidine (2bh)



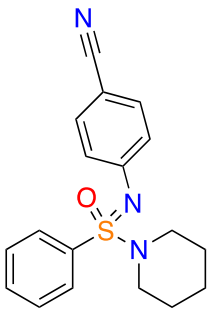
Prepared according to general procedure **A**, from 2-bromo-1,3,5-trimethylbenzene; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2bh** as a white solid (4 mg, 3%): m.p. 92–94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96–7.93 (m, 2H), 7.55–7.48 (m, 3H), 6.81 (s, 2H), 3.02 (t, *J* = 5.4 Hz, 4H), 2.32 (s, 6H), 2.22 (s, 3H), 1.58 (m, 4H), 1.41–1.35 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.6, 137.8, 133.2, 131.6, 128.9, 128.5, 127.6, 47.5, 25.5, 23.7, 20.7, 20.6 ppm; IR (KBr): ν = 3056, 2936, 1479, 1272, 1222, 1059, 903 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{20}H_{27}N_2OS$: 343.1839, found: 343.1849.

1-[*N*-(3-Methoxyphenyl)-*S*-phenylsulfonimidoyl]piperidine (2bi)



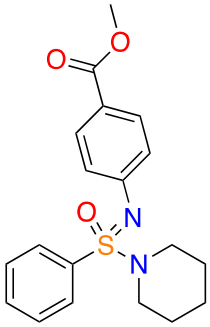
Prepared according to general procedure **A**, from 3-bromoanisole; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2bi** as a yellow solid (86 mg, 65%): m.p. 69–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.95 (m, 2H), 7.60–7.51 (m, 3H), 7.13 (t, *J* = 8.1 Hz, 1H), 6.86 (ddd, *J* = 7.9, 2.0, 1.0 Hz, 1H), 6.81 (t, *J* = 2.2 Hz, 1H), 6.54 (ddd, *J* = 8.2, 2.5, 0.9 Hz, 1H), 3.79 (s, 3H), 3.03 (qdd, *J* = 11.6, 6.5, 4.1 Hz, 4H), 1.60–1.50 (m, 4H), 1.36 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.1, 145.0, 136.5, 132.2, 129.4, 128.8, 127.8, 116.2, 109.2, 107.8, 55.2, 47.4, 25.3, 23.6 ppm; IR (KBr): ν = 3063, 2995, 2937, 2833, 1593, 1236, 1200, 1159, 916 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{18}H_{23}N_2O_2S$: 331.1480, found: 331.1480.

4-{[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}benzonitrile (2bj)



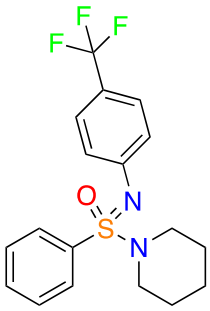
Prepared according to general procedure **A**, from 4-bromobenzonitrile; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2bj** as a white solid (115 mg, 88%): m.p. 136–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96–7.93 (m, 2H), 7.64–7.60 (m, 1H), 7.59–7.54 (m, 2H), 7.52–7.49 (m, 2H), 7.29–7.27 (m, 2H), 3.06 (ddd, *J* = 11.3, 7.1, 3.9 Hz, 2H), 2.97 (ddd, *J* = 11.4, 7.1, 3.8 Hz, 2H), 1.62–1.47 (m, 4H), 1.38 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 149.0, 135.6, 133.1, 132.8, 129.0, 127.7, 123.8, 119.8, 104.1, 47.3, 25.2, 23.4 ppm; IR (KBr): ν = 3057, 2941, 2849, 2226, 1599, 1497, 1227, 845, 741 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{18}H_{20}N_3OS$: 326.1327, found: 326.1325;

Methyl 4-{[oxo(phenyl)(piperidin-1-yl)-λ^{6}-sulfanylidene]amino}benzoate (2bk)



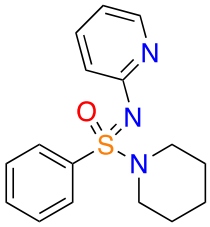
Prepared according to general procedure **A**, from methyl 4-bromobenzoate; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2bk** as a white solid (142 mg, 99%): m.p. 104–106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.95 (m, 2H), 7.94–7.90 (m, 2H), 7.62–7.52 (m, 3H), 7.28–7.25 (m, 2H), 3.88 (s, 3H), 3.06 (ddd, *J* = 11.2, 7.1, 3.9 Hz, 2H), 2.98 (ddd, *J* = 11.5, 7.1, 3.8 Hz, 2H), 1.60–1.45 (m, 4H), 1.36 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.3, 149.2, 136.0, 132.5, 130.7, 128.9, 127.8, 123.1, 51.8, 47.3, 25.2, 23.5 ppm; IR (KBr): ν = 2941, 2837, 1713, 1269, 1101, 916 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{19}H_{23}N_2O_3S$: 359.1429, found: 359.1427.

1-{*S*-Phenyl-*N*-[4-(trifluoromethyl)phenyl]sulfonimidoyl}piperidine (2bl)



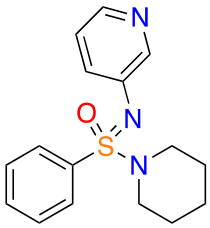
Prepared according to general procedure **A**, from 4-bromobenzotrifluoride; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2bl** as a white solid (149 mg, quantitative): m.p. 102–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.95 (m, 2H), 7.63–7.53 (m, 3H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 3.06 (ddd, *J* = 11.2, 7.1, 3.9 Hz, 2H), 2.98 (ddd, *J* = 11.4, 7.0, 3.9 Hz, 2H), 1.62–1.47 (m, 4H), 1.37 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 147.5, 135.9, 132.5, 128.9, 127.8, 126.1 (q, *J* = 3.7 Hz), 123.3, 47.4, 25.2, 23.5 ppm; IR (KBr): ν = 3065, 2939, 2851, 1610, 1512, 1308, 1229, 1101 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{18}H_{20}N_2OF_3S$: 369.1248, found: 369.1243.

2-{[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}pyridine (2bm)



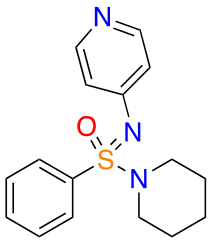
Prepared according to general procedure **A**, from 2-bromopyridine; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2bm** as a white solid (85 mg, 71%): m.p. 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (ddd, *J* = 5.0, 2.1, 0.9 Hz, 1H), 8.01–7.99 (m, 2H), 7.59–7.49 (m, 4H), 7.10 (m, 1H), 6.83 (ddd, *J* = 7.3, 4.9, 1.0 Hz, 1H), 3.10 (t, *J* = 5.5 Hz, 4H), 1.54 (m, 4H), 1.38 ppm (quin, *J* = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 157.3, 148.6, 137.5, 136.6, 132.3, 128.8, 127.9, 117.3, 116.8, 47.2, 25.3, 23.6 ppm; IR (KBr): ν = 2935, 2922, 2854, 2843, 1585, 1554, 1462, 1423, 1228, 1095, 980 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{16}H_{20}N_3OS$: 302.1327, found: 302.1330.

3-{[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}pyridine (2bn)



Prepared according to general procedure **A**, from 3-bromopyridine; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2bn** as a colorless oil (93 mg, 77%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 (dd, *J* = 2.7, 0.8 Hz, 1H), 8.20 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.99–7.96 (m, 2H), 7.63–7.54 (m, 4H), 7.15 (ddd, *J* = 8.2, 4.7, 0.9 Hz, 1H), 3.06 (ddd, *J* = 11.2, 7.1, 3.9 Hz, 2H), 2.98 (ddd, *J* = 11.6, 7.0, 3.9 Hz, 2H), 1.61–1.46 (m, 4H), 1.36 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.8, 132.5, 130.0, 128.9, 127.8, 123.5, 47.4, 25.2, 23.5 ppm; IR (KBr): ν = 3059, 3028, 2939, 2851, 1578, 1560, 1475, 1294, 1230, 1107, 1063, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{16}H_{20}N_3OS$: 302.1327, found: 302.1326.

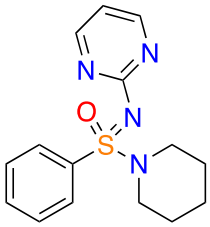
4-{[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}pyridine (2bo)



Prepared according to general procedure **A**, from 4-bromopyridine; crude purified by flash column chromatography (KP-Sil, 0–80% EtOAc in hexane) to give **2bo** as a colorless oil (87 mg, 72%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37–8.35 (m, 2H), 7.96–7.93 (m, 2H), 7.64–7.54 (m, 3H), 7.12–7.10 (m, 2H), 3.07 (ddd, *J* = 11.3, 7.2, 4.0 Hz, 2H), 2.97 (ddd, *J* = 11.6, 7.0, 3.9 Hz, 2H), 1.64–1.49 (m, 4H), 1.39 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.8, 150.3, 135.6, 132.7, 129.0, 127.7, 118.5, 47.3, 25.2, 23.4 ppm; IR (KBr): ν = 3059, 3016, 2937, 2849, 1587, 1315,

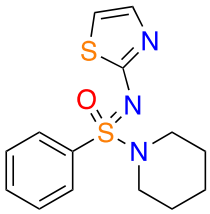
1298, 1230, 1209, 1103, 1016 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{16}H_{20}N_3OS$: 302.1327, found: 302.1327.

2-{[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}pyrimidine (2bp)



Prepared according to general procedure **A**, from 2-bromopyrimidine; crude purified by flash column chromatography (KP-NH, 0–50% EtOAc in hexane) to give **2bp** as a yellow solid (93 mg, 77%): m.p. 122–128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.45 (d, *J* = 4.8 Hz, 2H), 7.99–7.96 (m, 2H), 7.59–7.55 (m, 1H), 7.53–7.49 (m, 2H), 6.76 (t, *J* = 4.8 Hz, 1H), 3.22–3.13 (m, 4H), 1.61 (m, 4H), 1.43 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.2, 158.3, 136.7, 132.4, 128.8, 127.9, 113.8, 46.8, 25.3, 23.6 ppm; IR (KBr): ν = 3026, 2947, 2849, 1545, 1408, 1238, 926 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{15}H_{19}N_4OS$: 303.1280, found: 303.1280.

1-[*S*-Phenyl-*N*-(1,3-thiazol-2-yl)sulfonimidoyl]piperidine (2bq)



Prepared according to general procedure **A**, from 2-bromo-1,3-thiazole; crude purified by flash column chromatography (KP-NH, 0–40% EtOAc in hexane) to give **2bq** as a colorless oil (55 mg, 45%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01–7.98 (m, 2H), 7.63–7.59 (m, 1H), 7.57–7.53 (m, 2H), 7.34 (d, *J* = 3.8 Hz, 1H), 6.79 (d, *J* = 3.8 Hz, 1H), 3.12 (t, *J* = 5.5 Hz, 4H), 1.64–1.56 (m, 4H), 1.42 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.4, 139.1, 135.5, 132.9, 129.0, 127.8, 112.8, 47.2, 25.1, 23.5 ppm; IR (KBr): ν = 3067, 2937, 2849, 1439, 1223, 1140, 916 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{14}H_{18}N_3OS_2$: 308.0891, found: 308.0893.

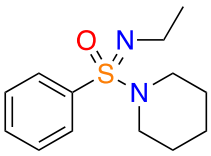
N-Alkylation of sulfonimidamide 2aa

General procedure B:[2]

2aa **2ca-2cr**

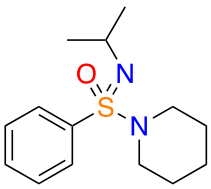
In a dry MW vial flushed with Ar, sulfonimidamide **2aa** (100 mg, 0.45 mmol, 1.0 equiv) and KOH (50 mg, 0.89 mmol, 2.0 equiv) were stirred in DMSO (0.7 mL) at RT for 15 min. Then, an alkyl bromide/iodide (0.67 mmol, 1.5 equiv) was added and the mixture was stirred at RT for 4–16 h. Once the starting material had been consumed (monitored by TLC), H_2O was added and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic phases were filtered through water-repellent filter paper. Solvent was removed under reduced pressure and the crude product was purified by flash column chromatography or preparative HPLC.

1-(*N*-Ethyl-*S*-phenylsulfonimidoyl)piperidine (2ca)



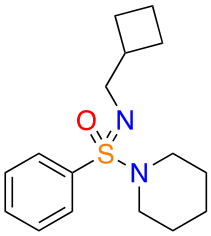
Prepared according to general procedure **B**, from bromoethane; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2ca** as a colorless oil (111 mg, 99%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.63 (m, 2H), 7.33–7.24 (m, 3H), 3.10 (dq, J = 12.3, 7.2 Hz, 1H), 2.93 (dq, J = 12.3, 7.2 Hz, 1H), 2.71 (qt, J = 11.7, 5.4 Hz, 4H), 1.39 (quin, J = 5.6 Hz, 4H), 1.17 (tt, J = 8.3, 4.7 Hz, 2H), 1.06 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.1, 131.8, 128.5, 127.7, 47.7, 36.8, 25.5, 23.7, 18.3 ppm; IR (KBr): ν = 3063, 2934, 2853, 1254, 1153, 914 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{13}H_{21}N_2OS$: 253.1375, found: 253.1379.

1-(*N*-Isopropyl-*S*-phenylsulfonimidoyl)piperidine (2cb)



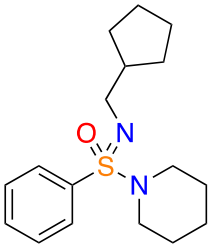
Prepared according to general procedure **B**, from 2-bromopropane; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2cb** as a colorless oil (46 mg, 38%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.83 (m, 2H), 7.53–7.44 (m, 3H), 3.77 (hept, J = 6.4 Hz, 1H), 2.96–2.87 (m, 4H), 1.60 (quin, J = 5.6 Hz, 4H), 1.40–1.34 (m, 2H), 1.25 ppm (dd, J = 13.1, 6.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.3, 131.6, 128.5, 127.8, 47.9, 44.5, 26.9, 26.0, 25.5, 23.7 ppm; IR (KBr): ν = 3064, 2933, 2854, 1444, 1263, 1145, 916 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{14}H_{23}N_2OS$: 267.1531, found: 267.1533.

1-[*N*-(Cyclobutylmethyl)-*S*-phenylsulfonimidoyl]piperidine (2cc)



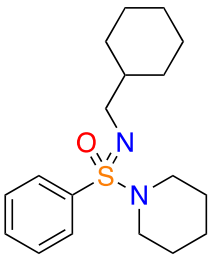
Prepared according to general procedure **B**, from (bromomethyl)cyclobutane; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in PE) to give **2cc** as a white solid (80 mg, 61%): m.p. 57–58 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.78–7.75 (m, 2H), 7.65–7.56 (m, 3H), 3.09 (dd, *J* = 12.2, 7.0 Hz, 1H), 2.97 (dd, *J* = 12.3, 6.7 Hz, 1H), 2.80 (t, *J* = 5.4 Hz, 4H), 2.46–2.44 (m, 1H), 2.03–1.94 (m, 2H), 1.87–1.67 (m, 4H), 1.50 (m, 4H), 1.31 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, [D$_6$]DMSO): δ = 135.8, 132.0, 128.8, 47.2, 46.6, 37.0, 25.3, 25.1, 23.2, 17.7 ppm; IR (KBr): ν = 3060, 2924, 2828, 1442, 1263, 1146, 913 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{16}H_{25}N_2OS$: 293.1682, found: 293.1692.

1-[*N*-(Cyclopentylmethyl)-*S*-phenylsulfonimidoyl]piperidine (2cd)



Prepared according to general procedure **B**, from(bromomethyl)cyclopentane; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2cd** as a colorless oil (40 mg, 29%): ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.78–7.76 (m, 2H), 7.65–7.56 (m, 3H), 3.00 (dd, *J* = 12.0, 6.9 Hz, 1H), 2.87 (dd, *J* = 12.0, 6.9 Hz, 1H), 2.80 (t, *J* = 5.4 Hz, 4H), 2.05 (hept, *J* = 7.3 Hz, 1H), 1.76–1.64 (m, 2H), 1.59–1.46 (m, 8H), 1.35–1.27 ppm (m, 4H); ^{13}C NMR (101 MHz, [D$_6$]DMSO): δ = 135.9, 132.0, 128.8, 127.4, 47.2, 46.0, 41.6, 30.1, 30.0, 25.1, 25.0, 24.9, 23.2 ppm; IR (KBr): ν = 3065, 2937, 2853, 1265, 1146, 916 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{17}H_{27}N_2OS$: 307.1844, found: 307.1844.

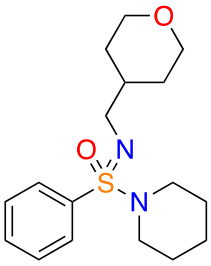
1-[*N*-(Cyclohexylmethyl)-*S*-phenylsulfonimidoyl]piperidine (2ce)



Prepared according to general procedure **B**, from (bromomethyl)cyclohexane; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in PE) to give **2ce** as a white solid (102 mg, 71%): m.p. 57–58 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.79–7.76 (m, 2H), 7.65–7.56 (m, 3H), 2.92 (dd, *J* = 11.9, 6.5 Hz, 1H), 2.81–2.76 (m, 5H), 1.86–1.75 (m, 2H), 1.71–1.61 (m, 3H), 1.53–1.47 (m, 4H), 1.45–1.37 (m, 1H), 1.34–1.28 (m, 2H), 1.24–1.11 (m, 3H), 0.94 ppm (qd, *J* = 12.3, 3.4 Hz, 2H); ^{13}C NMR (101 MHz, [D$_6$]DMSO): δ = 135.9, 132.0, 128.8, 127.4, 47.5, 47.1, 30.8,

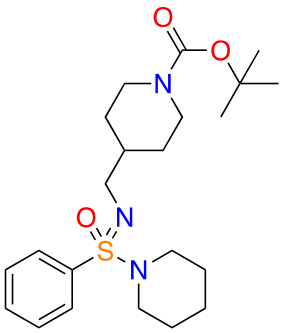
26.3, 25.6, 25.1, 23.2 ppm; IR (KBr): ν = 3060, 2923, 2832, 1442, 1265, 1156, 917 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{18}H_{29}N_2OS$: 321.1995, found: 321.2010.

1-[*S*-Phenyl-*N*-(tetrahydro-2*H*-pyran-4-ylmethyl)sulfonimidoyl]piperidine (2cf)



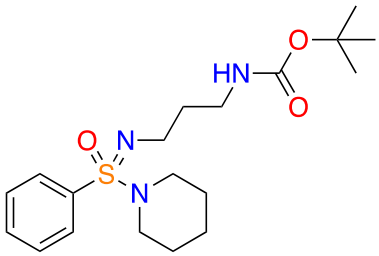
Prepared according to general procedure **B**, from 4-(bromomethyl)tetrahydro-2*H*-pyran; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2cf** as a colorless oil (86 mg, 60%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.83 (m, 2H), 7.55–7.45 (m, 3H), 3.99 (ddt, *J* = 10.9, 4.3, 1.8 Hz, 2H), 3.41 (tdd, *J* = 11.7, 4.7, 2.0 Hz, 2H), 3.17 (dd, *J* = 12.2, 6.1 Hz, 1H), 3.00–2.85 (m, 5H), 1.86–1.79 (m, 1H), 1.79–1.73 (m, 1H), 1.60 (quin, *J* = 5.6 Hz, 5H), 1.43–1.32 ppm (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.2, 131.8, 128.5, 127.8, 68.0, 47.8, 47.6, 37.6, 31.3, 31.2, 25.5, 23.7 ppm; IR (KBr): ν = 3063, 2918, 2833, 1257, 1153, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{17}H_{27}N_2O_2S$: 323.1793, found: 323.1793;

***tert*-Butyl 4-({[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}methyl)piperidine-1-carboxylate (2cg)**



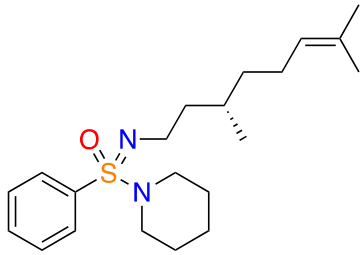
Prepared according to general procedure **B**, from *tert*-butyl 4-(bromomethyl)piperidine-1-carboxylate; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2cg** as a colorless oil (65 mg, 35%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.83 (m, 2H), 7.55–7.45 (m, 3H), 4.12 (brs, 2H), 3.17 (dd, *J* = 12.1, 6.5 Hz, 1H), 2.96–2.84 (m, 5H), 2.74–2.67 (m, 2H), 1.90–1.77 (m, 2H), 1.74–1.64 (m, 1H), 1.62–1.57 (m, 4H), 1.45 (s, 9H), 1.41–1.35 (m, 2H), 1.22–1.12 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.0, 136.2, 131.8, 128.6, 127.8, 79.1, 47.6, 47.5, 38.7, 30.3, 28.5, 25.5, 23.7 ppm; IR (KBr): ν = 3061, 2934, 2918, 2847, 2839, 1690, 1246, 1134, 922 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{22}H_{36}N_3O_3S$: 422.2477, found: 422.2474.

tert-Butyl 3-{[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}propylcarbamate (2ch)



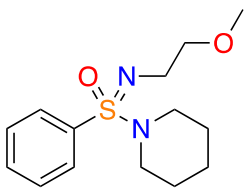
Prepared according to general procedure **B**, from *tert*-butyl 3-bromopropylcarbamate; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2ch** as a colorless oil (86 mg, 50%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.82 (m, 2H), 7.55–7.45 (m, 3H), 5.33 (brs, 1H), 3.38–3.24 (m, 3H), 3.12 (dt, J = 12.4, 6.1 Hz, 1H), 2.99–2.85 (m, 4H), 1.76 (m, 2H), 1.59 (quin, J = 5.6 Hz, 4H), 1.42–1.34 ppm (m, 11H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.0, 136.0, 131.9, 128.6, 78.6, 47.6, 39.9, 39.4, 31.5, 28.4, 25.5, 23.7 ppm; IR (KBr): ν = 3360, 3063, 2934, 2853, 1707, 1250, 1153, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{19}H_{32}N_3O_3S$: 382.2164, found: 382.2164.

1-{*N*-[(*S*)-3,7-Dimethyloct-6-en-1-yl]-*S*-phenylsulfonimidoyl}piperidine (2ci)



Prepared according to general procedure **B**, from (*S*)-8-bromo-2,6-dimethyloct-2-ene; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2ci**, a mixture of diastereoisomers, as a colorless oil (75 mg, 46%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.84 (m, 2H), 7.54–7.45 (m, 3H), 5.11 (tdt, J = 5.7, 2.8, 1.4 Hz, 1H), 3.26 (dddd, J = 23.4, 12.3, 8.9, 5.9 Hz, 1H), 3.10 (dddd, J = 25.2, 12.2, 8.9, 6.0 Hz, 1H), 2.91 (qt, J = 11.6, 5.4 Hz, 4H), 2.04–1.98 (m, 2H), 1.71–1.56 (m, 12H), 1.52–1.33 (m, 4H), 1.23–1.13 (m, 1H), 0.92 ppm (dd, J = 6.6, 2.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.3, 131.7, 131.0, 131.0, 128.5, 127.8, 125.1, 125.0, 47.7, 40.1, 40.0, 39.9, 37.2, 30.6, 30.4, 25.7, 25.6, 25.5, 23.8, 19.6, 17.7 ppm; IR (KBr): ν = 3065, 2918, 2851, 1445, 1263, 1151, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{21}H_{35}N_2OS$: 363.2470, found: 363.2469.

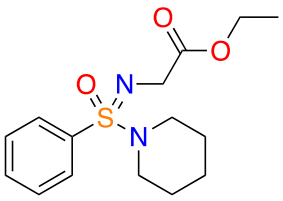
1-[*N*-(2-Methoxyethyl)-*S*-phenylsulfonimidoyl]piperidine (2cj)



Prepared according to general procedure **B**, from 1-bromo-2-methoxyethane; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in PE) to give **2cj** as a yellow oil (100 mg, 80%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.85 (m, 2H), 7.55–7.45 (m, 3H), 3.61–3.57 (m, 2H), 3.47–3.41 (m, 1H), 3.40 (s, 3H), 3.27 (dt, J = 12.6, 6.6 Hz, 1H), 2.95–2.91 (m, 4H), 1.60 (quin, J = 5.7 Hz, 4H), 1.40–1.34 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.1, 132.0, 128.7, 128.0,

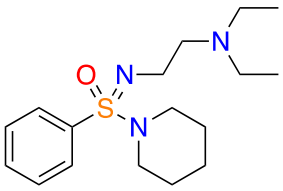
74.4, 59.0, 47.8, 41.7, 25.7, 23.9 ppm; IR (KBr): ν = 3063, 2933, 2852, 1445, 1291, 1156, 1118, 917 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{14}H_{23}N_2O_2S$: 283.1475, found: 283.1489.

Ethyl 2-{[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}acetate (2ck)



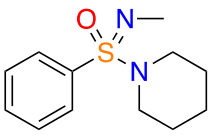
Prepared according to general procedure **B**, from ethyl bromoacetate; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in PE) to give **2ck** as a yellow oil (56 mg, 40%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.91 (m, 2H), 7.57–7.47 (m, 3H), 4.22 (tdd, *J* = 8.2, 6.7, 1.1 Hz, 2H), 4.00 (d, *J* = 17.6 Hz, 1H), 3.95 (d, *J* = 17.4 Hz, 1H), 3.01 (dt, *J* = 11.2, 5.5 Hz, 2H), 2.93 (dt, *J* = 11.6, 5.5 Hz, 2H), 1.62–1.56 (m, 4H), 1.39 (q, *J* = 6.2 Hz, 2H), 1.29 ppm (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.3, 135.7, 132.3, 128.8, 128.1, 60.9, 47.7, 43.8, 25.6, 23.8, 14.4 ppm; IR (neat): ν = 3061, 2935, 1747, 1295, 1156, 920 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{15}H_{23}N_2O_3S$: 311.1424, found: 311.1421.

***N*,*N*-Diethyl-2-{[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}ethanamine (2cl)**



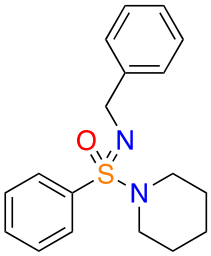
Prepared according to general procedure **B**, from *N*-(2-bromoethyl)-*N*,*N*-diethylamine; crude purified by preparative HPLC to give **2cl** as a colorless oil (20 mg, 13%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.84 (m, 2H), 7.54–7.45 (m, 3H), 3.40–3.33 (m, 1H), 3.20–3.13 (m, 1H), 2.97–2.87 (m, 4H), 2.74 (t, *J* = 8.0 Hz, 2H), 2.61 (q, *J* = 7.1 Hz, 4H), 1.60 (quin, *J* = 5.6 Hz, 4H), 1.38 (m, 2H), 1.06 ppm (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.1, 131.9, 128.6, 127.8, 55.3, 47.7, 40.3, 25.6, 23.7, 11.9 ppm; IR (KBr): ν = 3063, 2934, 2853, 1265, 1151, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{17}H_{30}N_3OS$: 324.2110, found: 324.2108.

1-(*N*-Methyl-*S*-phenylsulfonimidoyl)piperidine (2cm)



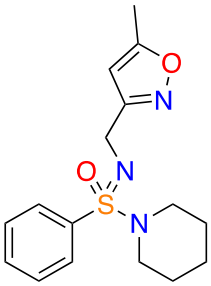
Prepared according to general procedure **B**, from methyl iodide (95 mg, 0.67 mmol, 1.5 equiv); crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2cm** as a white solid (63 mg, 59%): m.p. 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.83 (m, 2H), 7.55–7.45 (m, 3H), 2.98–2.85 (m, 4H), 2.85 (s, 3H), 1.61 (dt, *J* = 11.5, 5.6 Hz, 4H), 1.44–1.35 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.0, 131.9, 128.6, 127.7, 47.5, 27.9, 25.5, 23.7 ppm; IR (KBr): ν = 2970, 2935, 2812, 1265, 1149, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{12}H_{19}N_2OS$: 239.1218, found: 239.1218.

1-(*N*-Benzyl-*S*-phenylsulfonimidoyl)piperidine (2cn)



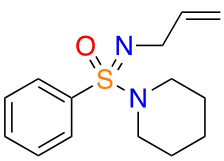
Prepared according to general procedure **B**, from benzyl bromide; crude purified by flash column chromatography (KP-Sil, 0–40% EtOAc in hexane) to give **2cn** as a colorless oil (80 mg, 57%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.69 (m, 2H), 7.34–7.26 (m, 5H), 7.13–7.09 (m, 2H), 7.03–6.98 (m, 1H), 4.28 (d, *J* = 14.8 Hz, 1H), 4.11 (d, *J* = 14.8 Hz, 1H), 2.77–2.64 (m, 4H), 1.38–1.30 (m, 4H), 1.17–1.12 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.8, 136.2, 132.0, 128.7, 128.3, 128.0, 127.6, 126.5, 47.8, 45.5, 25.6, 23.8 ppm; IR (KBr): ν = 3063, 2937, 1445, 1269, 1151, 924 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{18}H_{23}N_2OS$: 315.1531, found: 315.1534.

5-Methyl-3-({[oxo(phenyl)(piperidin-1-yl)-λ^{6}-sulfanylidene]amino}methyl)isoxazole (2co)



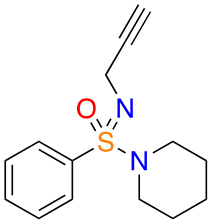
Prepared according to general procedure **B**, from 3-(bromomethyl)-5-methylisoxazole; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2co** as a colorless oil (88 mg, 62%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89–7.86 (m, 2H), 7.57–7.53 (m, 1H), 7.51–7.47 (m, 2H), 6.16 (s, 1H), 4.41 (d, *J* = 14.8 Hz, 1H), 4.33 (d, *J* = 14.9 Hz, 1H), 2.99–2.88 (m, 4H), 2.39 (s, 3H), 1.60 (quin, *J* = 5.5 Hz, 4H), 1.41–1.35 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.1, 164.7, 135.8, 132.3, 128.8, 128.0, 101.8, 47.8, 37.6, 25.6, 23.8, 12.4 ppm; IR (KBr): ν = 3063, 2935, 2849, 1607, 1445, 1283, 1263, 1148, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{16}H_{22}N_3O_2S$: 320.1433, found: 320.1434.

1-(*N*-Allyl-*S*-phenylsulfonimidoyl)piperidine (2cp)



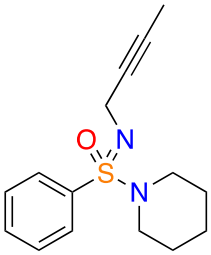
Prepared according to general procedure **B**, from allyl bromide; crude purified by flash column chromatography (KP-Sil, 0–30% EtOAc in hexane) to give **2cp** as a yellow oil (85 mg, 72%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.87 (m, 2H), 7.56–7.46 (m, 3H), 6.04 (ddt, *J* = 17.0, 10.4, 5.3 Hz, 1H), 5.36 (dq, *J* = 17.0, 1.8 Hz, 1H), 5.09 (dq, *J* = 10.1, 1.7 Hz, 1H), 3.89 (ddt, *J* = 15.5, 5.0, 1.8 Hz, 1H), 3.77 (ddt, *J* = 15.6, 5.7, 1.6 Hz, 1H), 2.98–2.88 (m, 4H), 1.60 (dt, *J* = 11.5, 5.6 Hz, 4H), 1.41–1.35 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.1, 136.3, 132.0, 128.7, 128.0, 114.3, 47.8, 44.5, 25.6, 23.8 ppm; IR (KBr): ν = 3067, 2935, 2833, 1445, 1269, 1153, 914 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{14}H_{21}N_2OS$: 265.1375, found: 265.1374.

1-[*S*-Phenyl-*N*-(prop-2-yn-1-yl)sulfonimidoyl]piperidine (2cq)



Prepared according to general procedure **B**, from propargyl bromide; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2cq** as a yellow oil (74 mg, 63%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.87 (m, 2H), 7.57–7.47 (m, 3H), 4.07–3.94 (m, 2H), 2.97 (ddt, *J* = 12.0, 10.1, 6.3 Hz, 4H), 2.22 (t, *J* = 2.5 Hz, 1H), 1.69–1.56 (m, 4H), 1.39 ppm (quin, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.4, 132.1, 128.6, 127.7, 83.2, 69.7, 47.7, 30.8, 25.4, 23.6 ppm; IR (KBr): ν = 3267, 2937, 2841, 1445, 1269, 1230, 1144, 916 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{14}H_{19}N_2OS$: 263.1218, found: 263.1219.

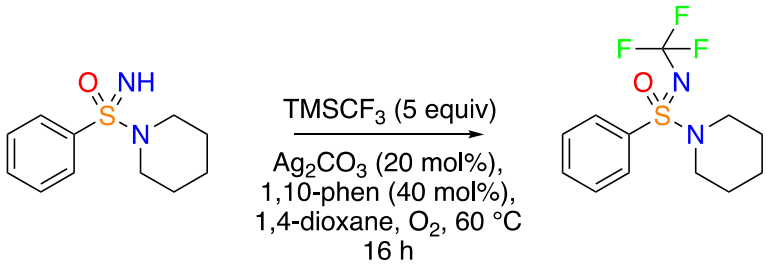
1-[*N*-(But-2-yn-1-yl)-*S*-phenylsulfonimidoyl]piperidine (2cr)



Prepared according to general procedure **B**, from 1-bromobut-2-yne; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in hexane) to give **2cr** as a yellow oil (87 mg, 71%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.87 (m, 2H), 7.56–7.46 (m, 3H), 3.96 (quin, *J* = 2.4 Hz, 2H), 2.97 (m, 4H), 1.83 (t, *J* = 2.5 Hz, 3H), 1.65–1.59 (m, 4H), 1.42–1.36 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.6, 132.0, 128.6, 127.8, 78.2, 47.8, 31.2, 25.5, 23.7, 3.8 ppm; IR (KBr): ν = 3063, 2937, 2851, 1672, 1445, 1230, 1149, 916 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{15}H_{21}N_2OS$: 277.1375, found: 277.1376.

N-Trifluoromethylation of sulfonimidamide 2aa[3]

1-[*S*-Phenyl-*N*-(trifluoromethyl)sulfonimidoyl]piperidine (2cs)

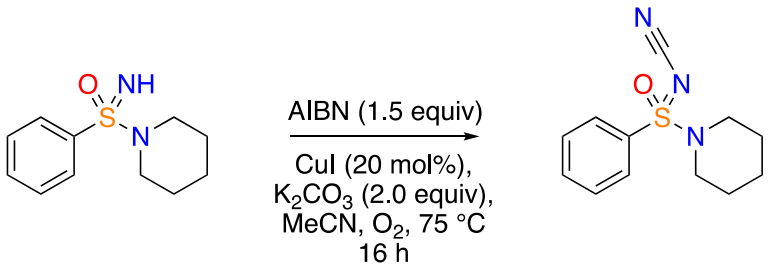


2aa **2cs**

In a MW vial charged with sulfonimidamide **2aa** (100 mg, 0.45 mmol, 1.0 equiv), $TMSCF_3$ (4.44 mL, 2.22 mmol, 5.0 equiv; 0.5 M solution in THF), Ag_2CO_3 (24 mg, 0.09 mmol, 0.2 equiv), 1,10-phenanthroline (32 mg, 0.18 mmol, 0.4 equiv) and 1,4-dioxane (8.9 mL) were added. Then, a balloon charged with O_2 was attached to the MW vial and the solution was degassed for 10 min. The mixture was stirred and heated in an oil bath at 60 °C for 16 h. Then, the solution was cooled, solvent removed in vacuo and the crude product purified by flash column chromatography (KP-Sil, 0–50% EtOAc in PE) to give **2cs** as a yellow oil (57 mg, 44%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89–7.86 (m, 2H), 7.65–7.60 (m, 1H), 7.57–7.53 (m, 2H), 3.11–3.00 (m, 4H), 1.68–1.62 (m, 4H), 1.48–1.42 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.6, 133.3, 129.2, 127.5, 121.6 (q, J = 255 Hz), 47.5, 25.3, 23.7 ppm; IR (neat): ν = 3069, 2944, 2856, 1256, 1077, 921 cm^{-1}; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{12}H_{16}N_2OF_3S$: 293.0930, found: 293.0935.

N-Cyanation of sulfonimidamide 2aa[4]

N-[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]cyanamide (2da)

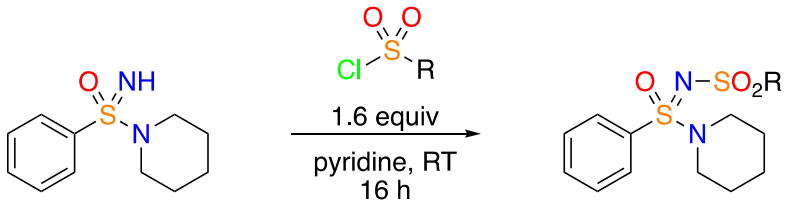


2aa **2da**

In a MW vial charged with sulfonimidamide **2aa** (100 mg, 0.45 mmol, 1.0 equiv), AIBN (108 mg, 0.66 mmol, 1.5 equiv), CuI (16 mg, 0.09 mmol, 0.2 equiv), K_2CO_3 (122 mg, 0.88 mmol, 2.0 equiv) and MeCN (6.7 mL) were added. Then, a balloon charged with O_2 was attached to the MW vial and the solution was degassed for 10 min. The mixture was stirred and heated in an oil bath at 75 °C for 16 h. Then, the solution was cooled, filtered and the solids washed with MeCN. The liquid phase was collected, solvent removed in vacuo and the crude product purified by flash column chromatography (KP-Sil, 0–100% EtOAc in PE) to give **2da** as a brown oil (47 mg, 43%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.84 (m, 2H), 7.72–7.67 (m, 1H), 7.62–7.57 (m, 2H), 3.14 (td, *J* = 5.6, 2.2 Hz, 4H), 1.77–1.63 (m, 4H), 1.54–1.46 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 134.4, 133.6, 129.7, 127.8, 111.2, 47.4, 25.1, 23.4 ppm; IR (neat): ν = 3063, 2924, 2853, 2151, 1268, 1200, 924 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{12}H_{16}N_3OS$: 250.1009, found: 250.1011.

N-Sulfonylation of sulfonimidamide 2aa

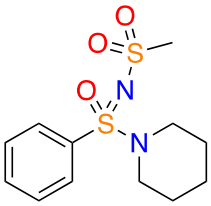
General procedure C:



2aa **2ea, 2eb**

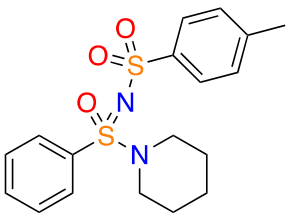
Sulfonimidamide **2aa** (100 mg, 0.45 mmol, 1.0 equiv) was dissolved in pyridine (3.0 mL) under Ar atmosphere; then, the appropriate sulfonyl chloride (0.71 mmol, 1.6 equiv) was added. The reaction mixture was stirred at RT overnight; then, the reaction was quenched with aqueous $NaHCO_3$ and diluted with EtOAc (3 mL). The mixture was transferred to a separating funnel, the aqueous layer was extracted with EtOAc (3 × 10 mL), and the combined organic phases were washed with brine (3 × 10 mL), then filtered through water-repellent filter paper. Solvent was removed in vacuo and the crude product purified (when needed).

N-[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]methanesulfonamide (2ea)



Prepared according to general procedure **C**, from methanesulfonyl chloride; crude purified by preparative HPLC to give **2ea** as a white solid (83 mg, 62%): m.p. 93–95 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.90 (m, 2H), 7.67–7.63 (m, 1H), 7.59–7.54 (m, 2H), 3.23 (ddd, J = 11.4, 7.1, 4.0 Hz, 2H), 3.18 (s, 3H), 3.10 (ddd, J = 11.5, 6.9, 3.9 Hz, 2H), 1.74–1.60 (m, 4H), 1.49 ppm (quin, J = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.1, 133.7, 129.4, 127.6, 47.2, 45.0, 25.1, 23.5 ppm; IR (KBr): ν = 2939, 2856, 1311, 1246, 1099, 918 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{12}H_{19}N_2O_3S_2$: 303.0837, found: 303.0838.

4-Methyl-*N*-[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]benzenesulfonamide (2eb)

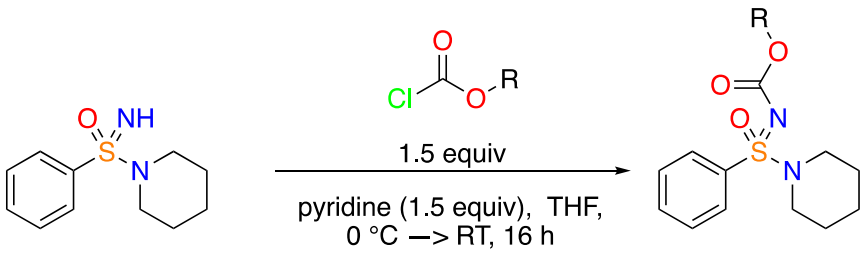


Prepared according to general procedure **C**, from *p*-toluenesulfonyl chloride; after workup, the ^{1}H NMR spectrum indicated clean formation of **2eb** as a yellow solid (97 mg, 58%): m.p. 124–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.84 (m, 4H), 7.63–7.59 (m, 1H), 7.54–7.49 (m, 2H), 7.26–7.24 (m, 2H), 3.24–3.18 (m, 2H), 3.11–3.05 (m, 2H), 2.39 (s, 3H), 1.69–1.59 (m, 4H), 1.47 ppm (quin, J = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.8, 141.0, 136.2, 133.5, 129.3, 129.2, 127.7, 126.9, 47.2, 25.1, 23.6, 21.7 ppm; IR (neat): ν = 3063, 2936, 2857, 1312, 1257, 1155, 1112,

1088, 922 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{18}H_{23}N_2O_3S_2$: 379.1145, found: 379.1151.

N-Alkoxycarbonylation of sulfonimidamide 2aa (carbamate formation)[5]

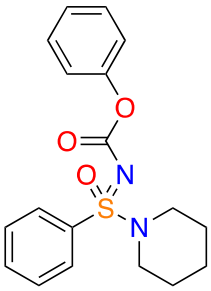
General procedure D:



2aa **2fa, 2fb**

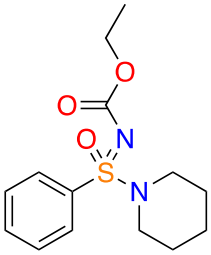
To a solution of sulfonimidamide **2aa** (100 mg, 0.45 mmol, 1.0 equiv) and pyridine (54 μL, 0.67 mmol, 1.5 equiv) in THF (0.9 mL) under Ar atmosphere at 0 °C, the corresponding chloroformate (0.67 mmol, 1.5 equiv) was added. As soon as the chloroformate was in solution, a white precipitate formed. The temperature was allowed to rise to RT and the mixture was stirred overnight. The reaction was quenched with H_2O and diluted with Et_2O (3 mL). The mixture was transferred to a separating funnel, the aqueous layer was extracted with Et_2O (3 × 10 mL), and the combined organic phases were washed with 1 M HCl (3 × 10 mL) and brine (3 × 10 mL), then filtered through water-repellent filter paper. Solvent was removed in vacuo and the crude product purified (when needed).

Phenyl [oxo(phenyl)(piperidin-1-yl)-λ⁶-sulfanylidene]carbamate (2fa)



Prepared according to general procedure **D**, from phenyl chloroformate; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in PE) to give **2fa** as a white solid (90 mg, 60%): m.p. 114–117 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.91 (m, 2H), 7.65–7.60 (m, 1H), 7.58–7.53 (m, 2H), 7.34–7.29 (m, 2H), 7.17–7.11 (m, 3H), 3.25–3.15 (m, 4H), 1.66 (quin, J = 5.6 Hz, 4H), 1.53–1.47 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.1, 151.8, 136.2, 133.4, 129.3, 129.2, 127.9, 125.3, 121.8, 46.7, 25.3, 23.7 ppm; IR (neat): ν = 3068, 2945, 2856, 1687, 1274, 1248, 1194, 877 cm^{-1}; HRMS (ESI-TOF) *m/z* [*M* + H]$^+$ calcd for $C_{18}H_{21}N_2O_3S$: 345.1267, found: 345.1275.

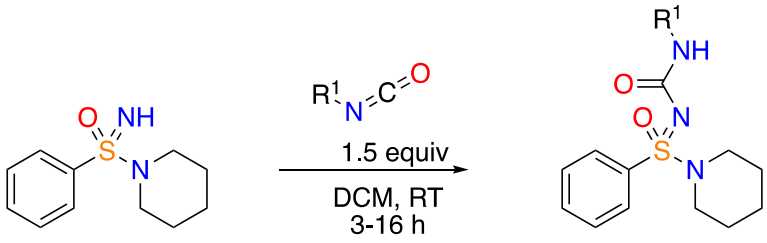
Ethyl [oxo(phenyl)(piperidin-1-yl)-λ⁶-sulfanylidene]carbamate (2fb)



Prepared according to general procedure **D**, from ethyl chloroformate; after workup, the ^{1}H NMR spectrum indicated clean formation of **2fb** as a yellow solid (90 mg, 69%): m.p. 75–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.86 (m, 2H), 7.62–7.58 (m, 1H), 7.56–7.51 (m, 2H), 4.11 (qd, *J* = 7.1, 1.6 Hz, 2H), 3.14 (td, *J* = 5.0, 3.0 Hz, 4H), 1.64 (quin, *J* = 5.7 Hz, 4H), 1.50–1.43 (m, 2H), 1.23 ppm (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 157.9, 136.4, 133.1, 129.2, 127.8, 62.0, 46.7, 25.3, 23.7, 14.5 ppm; IR (neat): ν = 2946, 1668, 1252, 885 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^{+}$ calcd for $C_{14}H_{21}N_2O_3S$: 297.1267, found: 297.1278.

N-Aminocarbonylation of sulfonimidamide 2aa (urea formation)[6]

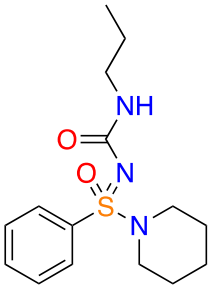
General procedure E:



2aa **2ga-2gf**

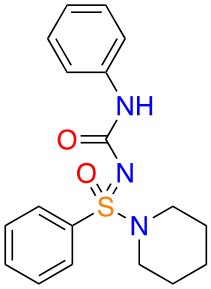
To a solution of sulfonimidamide **2aa** (100 mg, 0.45 mmol, 1.0 equiv) in anhydrous DCM (0.9 mL), the corresponding isocyanate (0.66 mmol, 1.5 equiv) was added dropwise at RT under Ar atmosphere. The reaction mixture was stirred until a precipitate formed (3–16 h) and starting material had been consumed (TLC analysis). Et_2O was added, and the precipitate was collected by filtration under reduced pressure and washed with Et_2O. The solid was purified by flash column chromatography (when needed).

1-[Oxo(phenyl)(piperidin-1-yl)-λ⁶-sulfanylidene]-3-propylurea (2ga)



Prepared according to general procedure **E**, from *n*-propyl isocyanate; crude purified by flash column chromatography (KP-Sil, 0–100% EtOAc in PE) to give **2ga** as a colorless oil (89 mg, 65%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dt, *J* = 8.4, 1.3 Hz, 2H), 7.59–7.55 (m, 1H), 7.51 (ddd, *J* = 8.3, 6.5, 1.2 Hz, 2H), 5.16 (brs, 1H), 3.17–3.06 (m, 6H), 1.63 (quin, *J* = 5.4 Hz, 4H), 1.55–1.42 (m, 4H), 0.92–0.88 ppm (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.4, 137.1, 132.7, 129.0, 127.7, 46.9, 42.4, 25.4, 23.7, 23.3, 11.5 ppm; IR (neat): ν = 3252, 2931, 2855, 1617, 1520, 1244, 931 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{15}H_{24}N_3O_2S$: 310.1584, found: 310.1602.

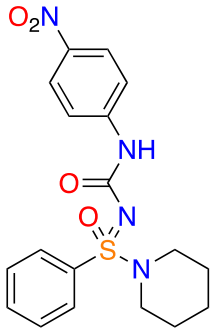
1-[Oxo(phenyl)(piperidin-1-yl)-λ⁶-sulfanylidene]-3-phenylurea (2gb)



Prepared according to general procedure **E**, from phenyl isocyanate; crude purified by flash column chromatography (KP-Sil, 0–50% EtOAc in PE) to give **2gb** as a white solid (120 mg, 79%): m.p. 187–189 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.90 (m, 2H), 7.63–7.58 (m, 1H), 7.57–

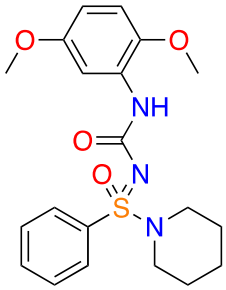
7.52 (m, 2H), 7.45–7.42 (m, 2H), 7.28–7.24 (m, 3H), 7.02–6.98 (m, 1H), 3.21–3.11 (m, 4H), 1.66 (quin, J = 5.6 Hz, 4H), 1.51–1.45 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 139.3, 136.9, 133.0, 129.2, 129.0, 127.8, 122.9, 46.3, 25.4, 23.7 ppm; IR (neat): ν = 3296, 2940, 2844, 1632, 1540, 1438, 1235, 939 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{18}H_{22}N_3O_2S$: 344.1438, found: 344.1427.

1-(4-Nitrophenyl)-3-[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]urea (2gc)



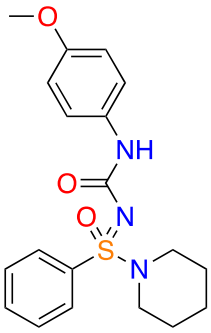
Prepared according to general procedure **E**, from 4-nitrophenyl isocyanate; after workup, the ^{1}H NMR spectrum indicated clean formation of **2gc** as a yellow solid (141 mg, 82%): m.p. >207 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16–8.12 (m, 2H), 7.92–7.89 (m, 2H), 7.66–7.55 (m, 5H), 7.30 (brs, 1H), 3.19–3.16 (m, 4H), 1.67 (quin, J = 5.9 Hz, 4H), 1.53–1.47 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.0, 145.5, 142.5, 136.3, 133.4, 129.4, 127.7, 125.2, 117.8, 46.8, 25.3, 23.7 ppm; IR (neat): ν = 3314, 2923, 1639, 1545, 1491, 1239, 1107, 931 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{18}H_{21}N_4O_4S$: 389.1278, found: 389.1297.

1-(2,5-Dimethoxyphenyl)-3-[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]urea (2gd)



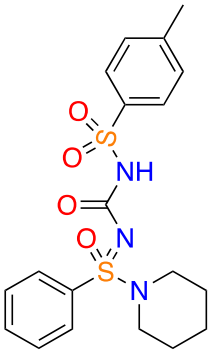
Prepared according to general procedure **E**, from 2,5-dimethoxyphenyl isocyanate; after workup, the ^{1}H NMR spectrum indicated clean formation of **2gd** as a white solid (133 mg, 75%): m.p. 128–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (brs, 1H), 7.93–7.90 (m, 2H), 7.62–7.52 (m, 4H), 6.74 (d, J = 8.9 Hz, 1H), 6.46 (dd, J = 8.8, 3.1 Hz, 1H), 3.82 (s, 3H), 3.73 (s, 3H), 3.20–3.10 (m, 4H), 1.68–1.64 (m, J = 5.7 Hz, 4H), 1.50–1.44 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.0, 154.1, 141.7, 136.6, 132.8, 129.8, 129.1, 127.7, 110.8, 107.3, 104.6, 56.3, 55.8, 46.7, 25.3, 23.6 ppm; IR (neat): ν = 3396, 2982, 2836, 1651, 1527, 1241, 1212, 1041, 934 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{20}H_{26}N_3O_4S$: 404.1639, found: 404.1656.

1-(4-Methoxyphenyl)-3-[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]urea (2ge)



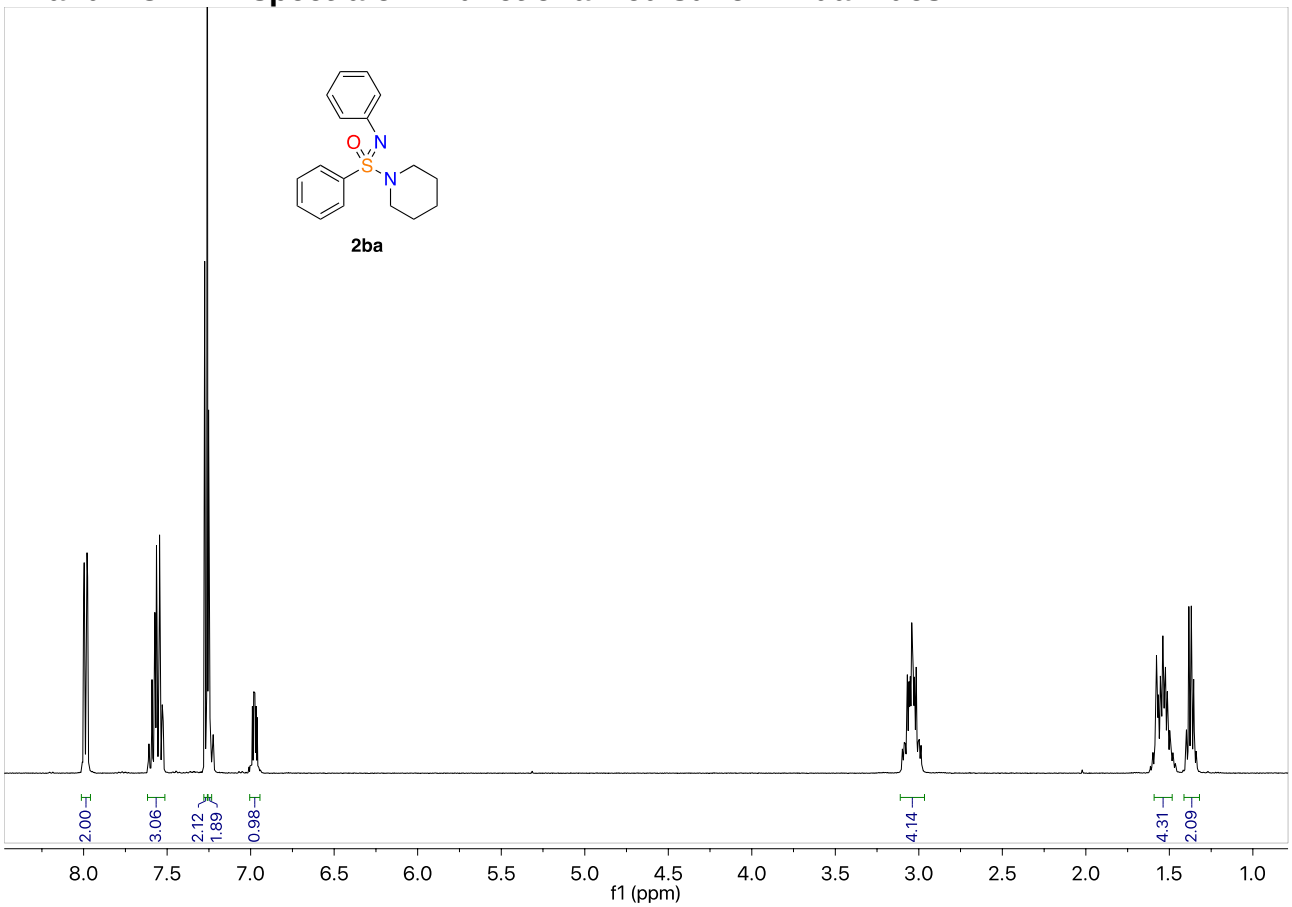
Prepared according to general procedure **E**, from 4-methoxyphenyl isocyanate; after workup, the ^{1}H NMR spectrum indicated clean formation of **2ge** as a white solid (134 mg, 82%): m.p. 205–207 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, J = 7.6 Hz, 2H), 7.62–7.58 (m, 1H), 7.55–7.51 (m, 2H), 7.35 (d, J = 8.6 Hz, 2H), 6.87 (brs, 1H), 6.83–6.79 (m, 2H), 3.76 (s, 3H), 3.21–3.11 (m, 4H), 1.65 (quin, J = 5.6 Hz, 4H), 1.50–1.45 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.0, 132.9, 129.2, 127.8, 120.6, 114.2, 55.7, 46.8, 25.4, 23.7 ppm; IR (neat): ν = 3310, 2942, 1629, 1507, 1185, 939 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{19}H_{24}N_3O_3S$: 374.1533, found: 374.1539.

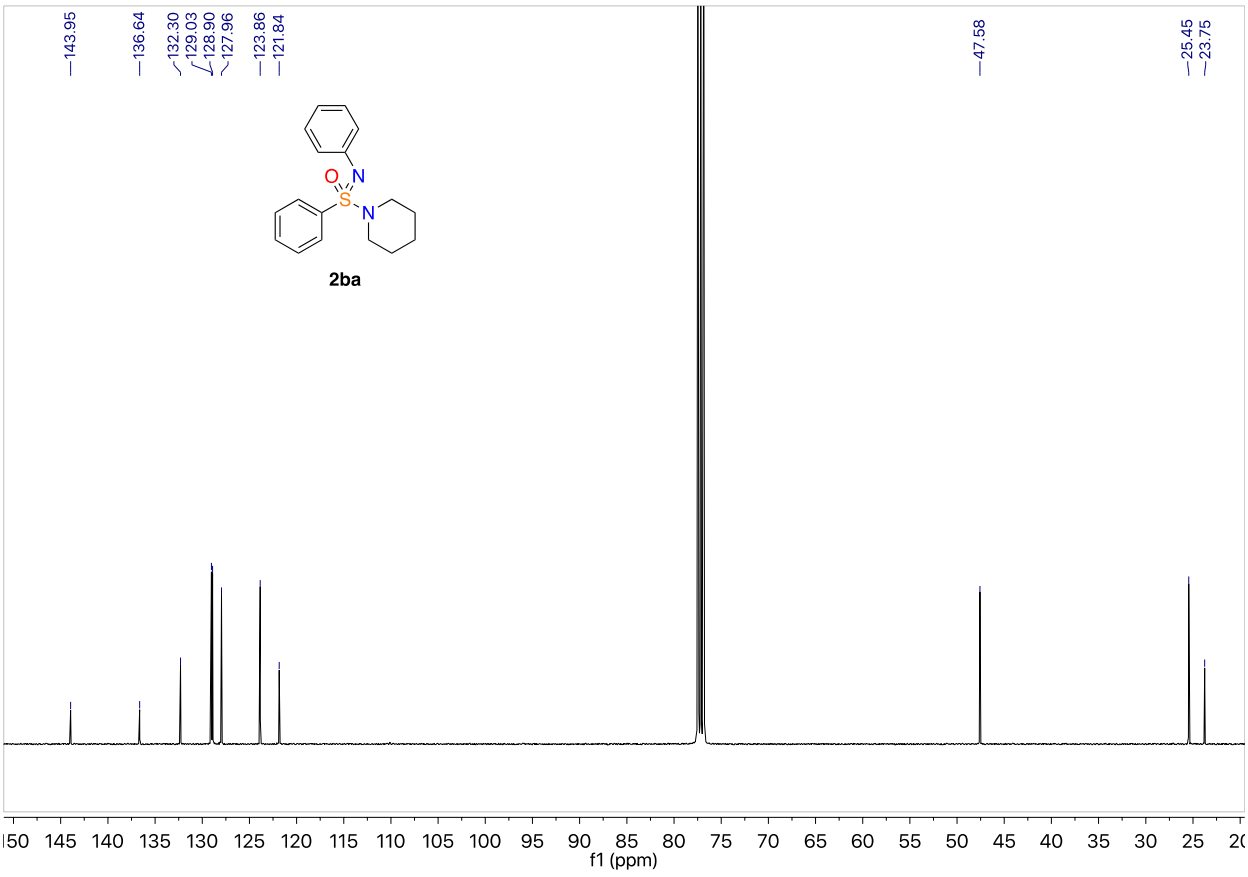
4-Methyl-*N*-{[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]carbamoyl}benzenesulfonamide (2gf)

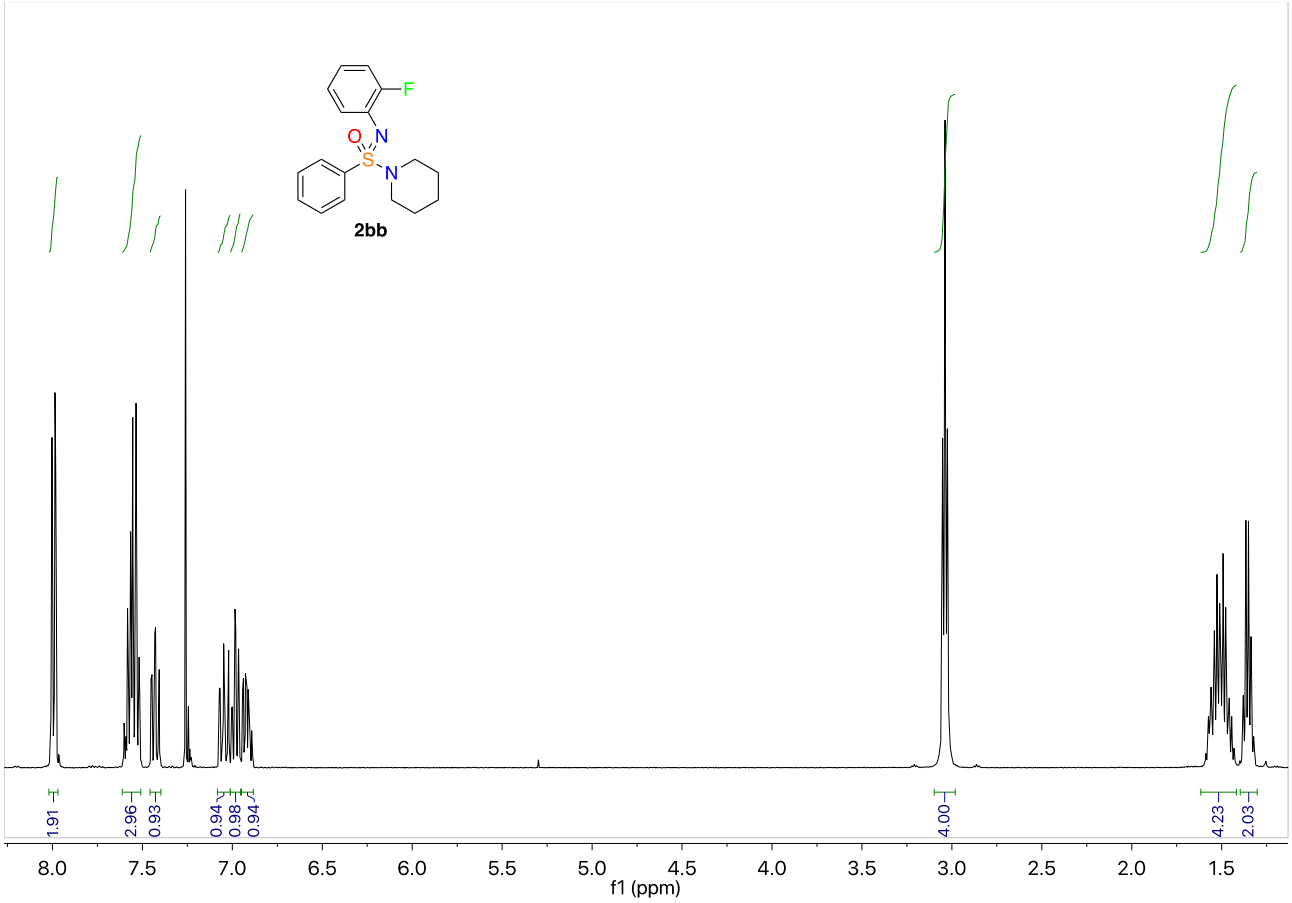


Prepared according to general procedure **E**, from 4-methylbenzenesulfonyl isocyanate; crude purified by flash column chromatography (KP-Sil, 0–100% EtOAc in PE) to give **2gf** as a colorless oil (92 mg, 49%): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, J = 8.1 Hz, 2H), 7.81–7.79 (m, 2H), 7.62–7.58 (m, 1H), 7.51 (t, J = 5.9 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 3.10–2.96 (m, 4H), 2.39 (s, 3H), 1.58–1.56 (m, 4H), 1.44–1.42 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 153.4, 144.3, 136.7, 135.6, 133.5, 129.5, 129.4, 128.2, 127.8, 46.6, 25.2, 23.6, 21.7 ppm; IR (neat): ν = 3244, 2940, 2854, 1674, 1329, 1253, 1153, 926 cm^{-1}; HRMS (ESI-TOF) *m*/*z* [*M* + H]$^+$ calcd for $C_{19}H_{24}N_3O_4S_2$: 422.1203, found: 422.1209.

^{1}H and ^{13}C NMR spectra of N-functionalized sulfonimidamides



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O
N
S
N
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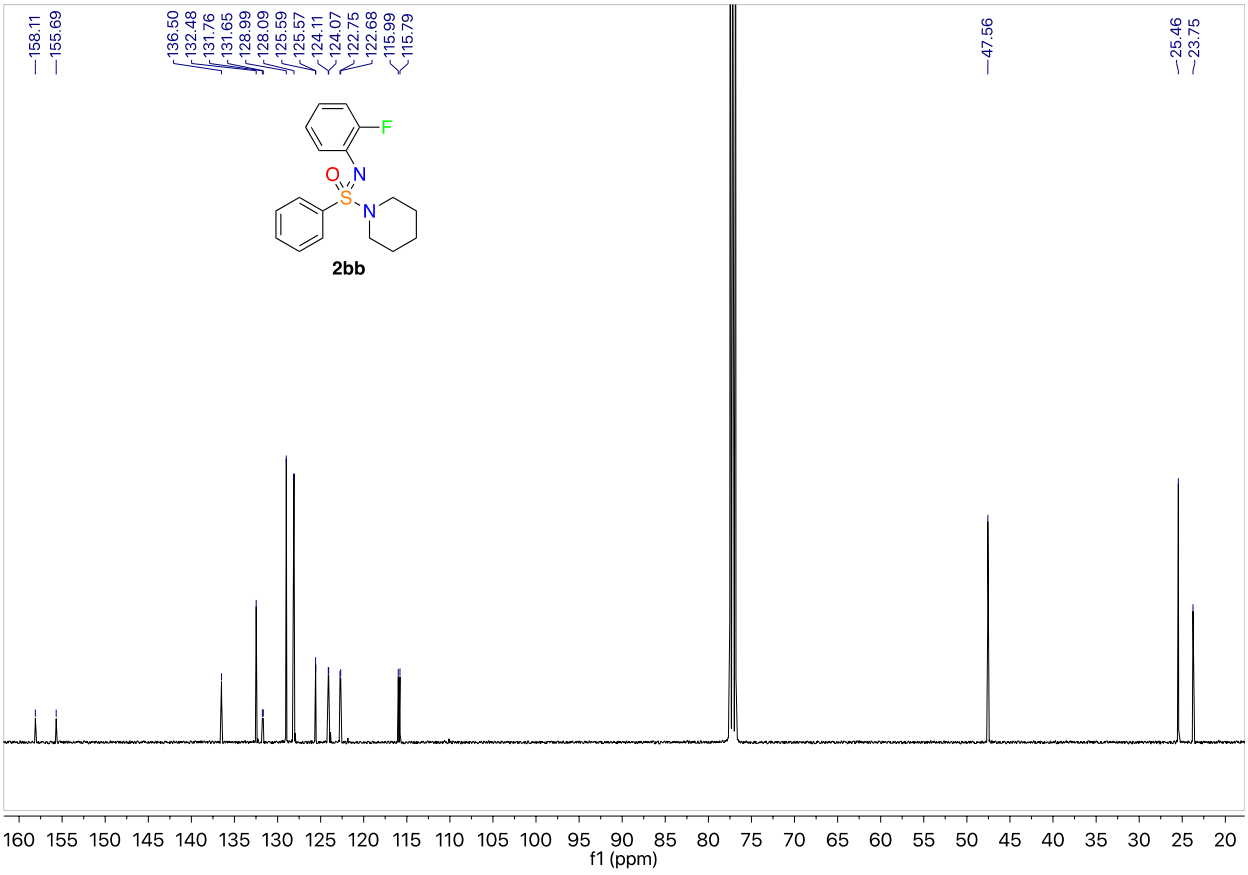
2.96
0.93
0.94
0.98
0.94
4.00
4.23
2.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)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122.68
115.99
115.79
47.56
25.46
23.75
F
O
N
S
N
2bb
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
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75
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45
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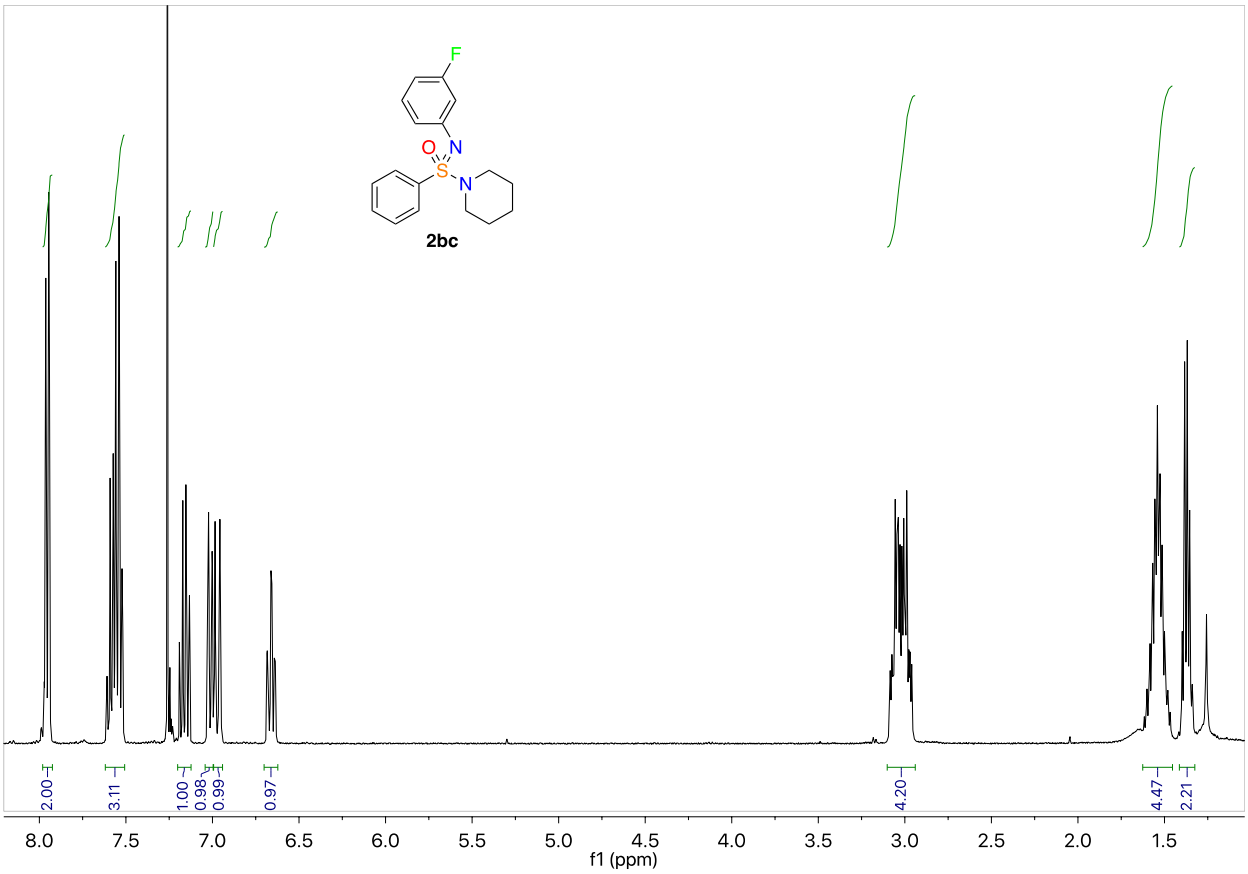
25
20
f1 (ppm)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S
N
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7.5
7.0
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4.0
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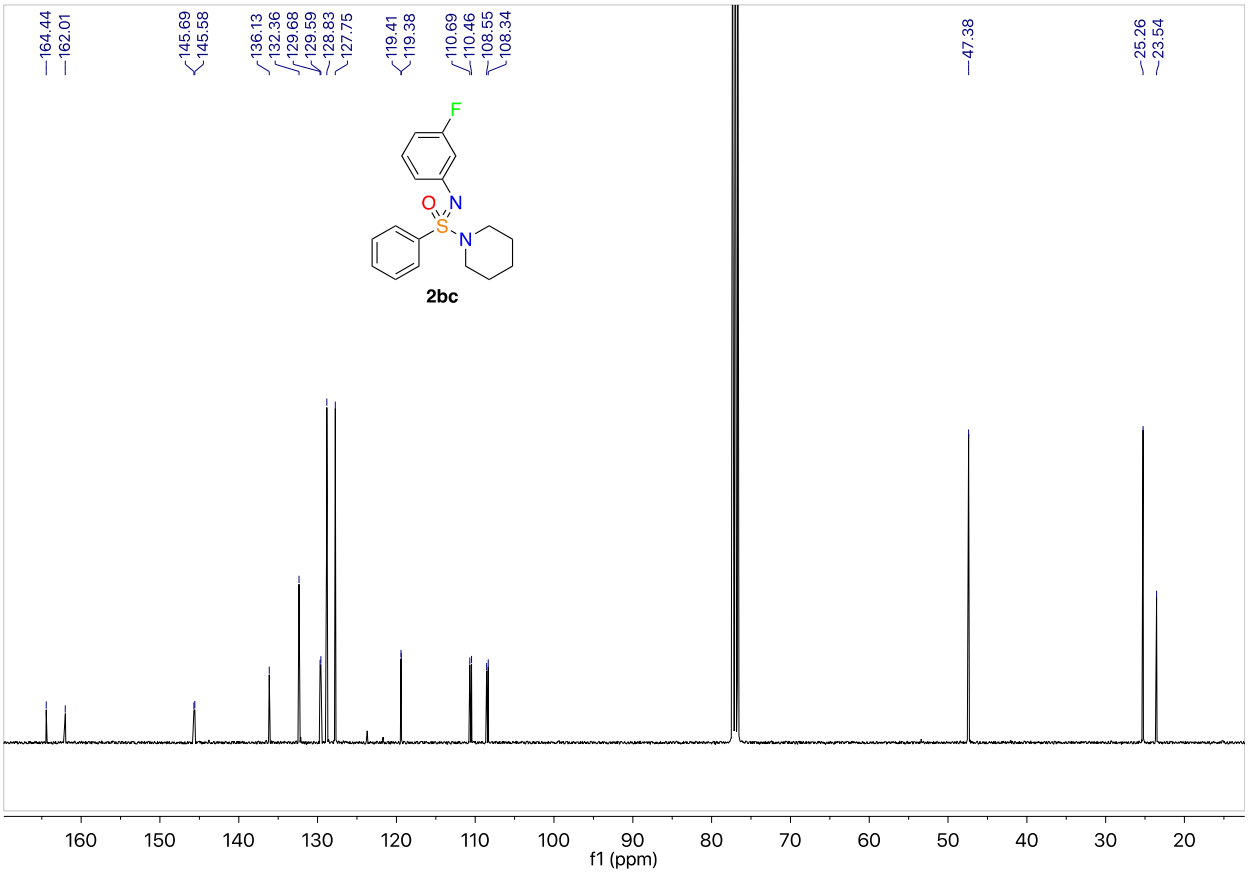
2.0
1.5
f1 (ppm)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80
70
60
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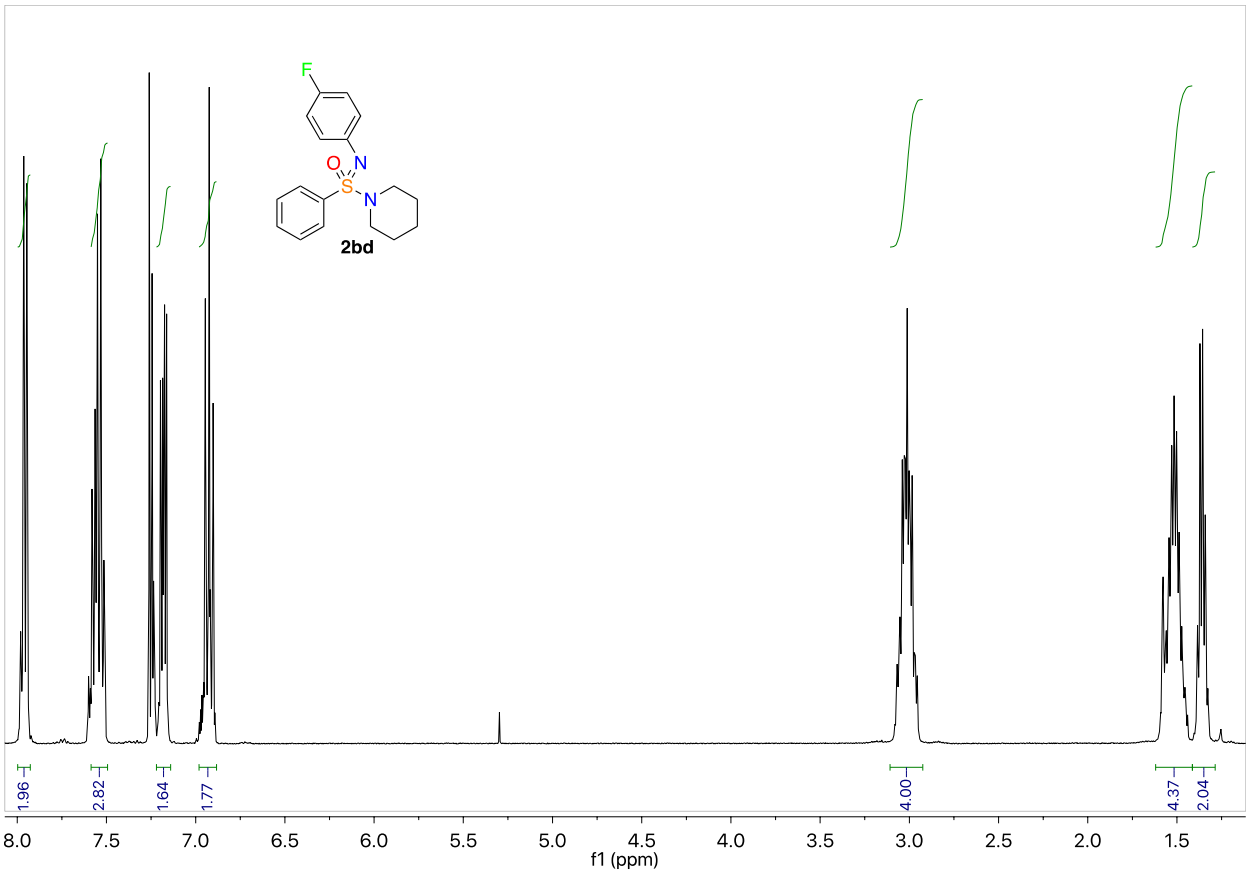
30
20
f1 (ppm)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S
N
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7.0
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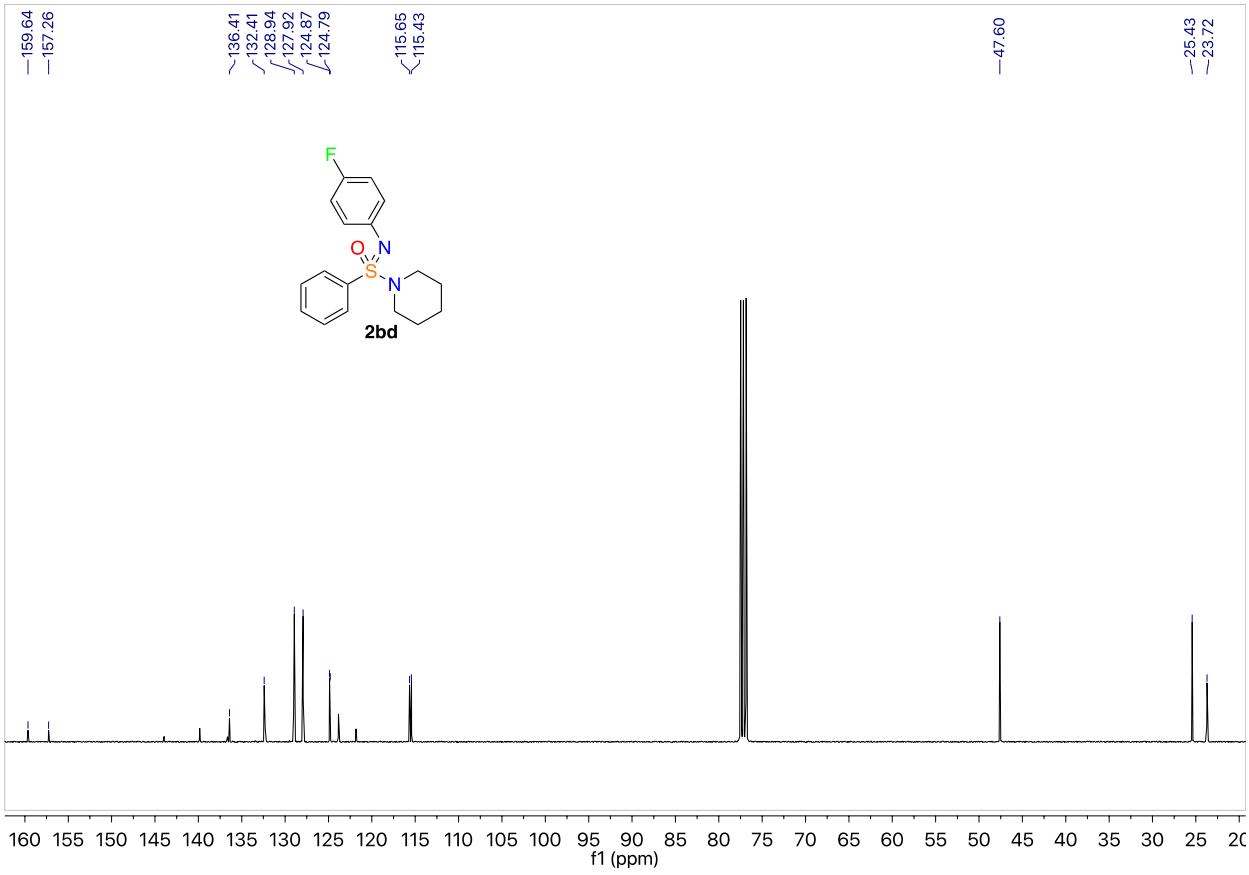
3.0
2.5
2.0
1.5
f1 (ppm)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55
50
45
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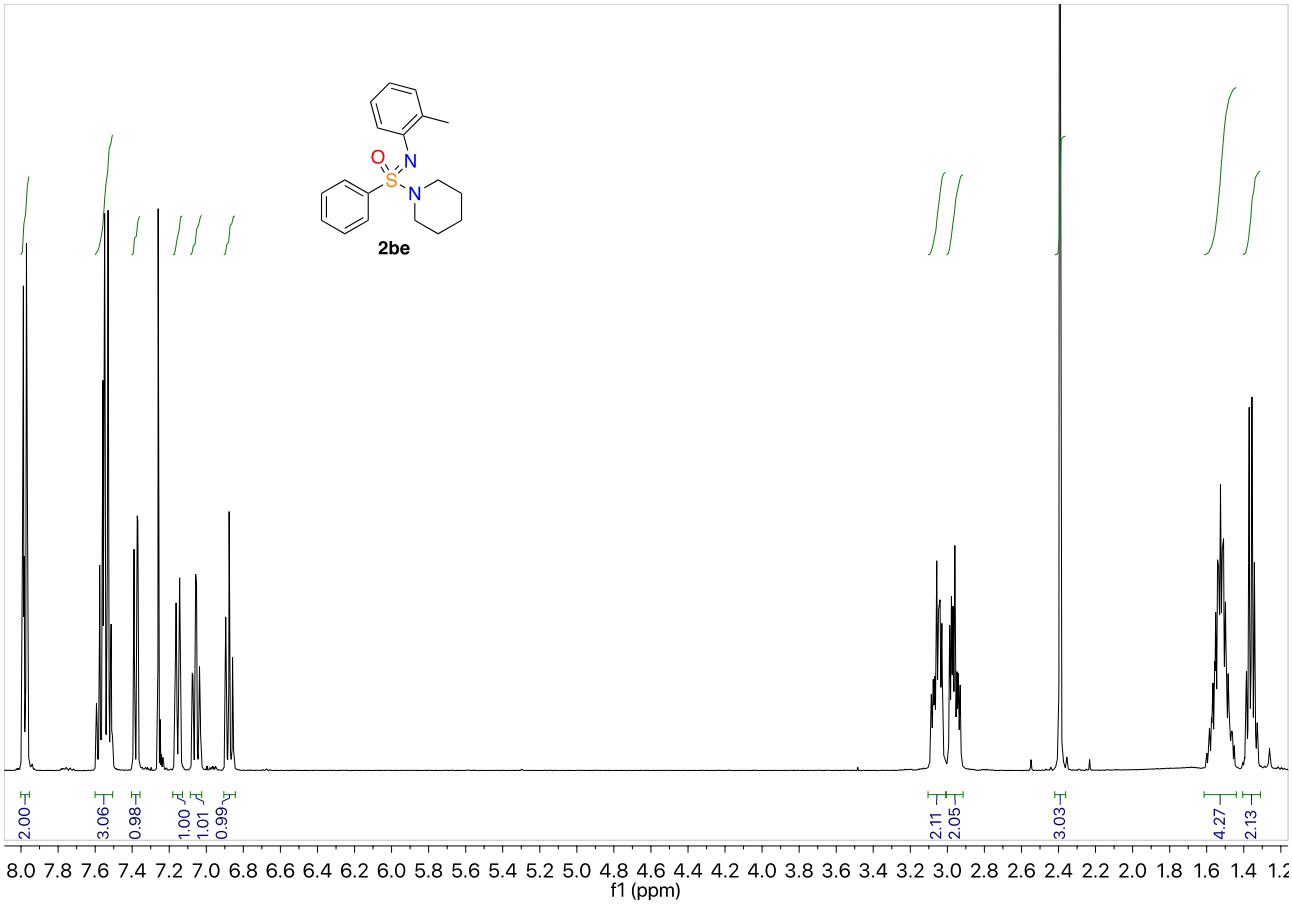
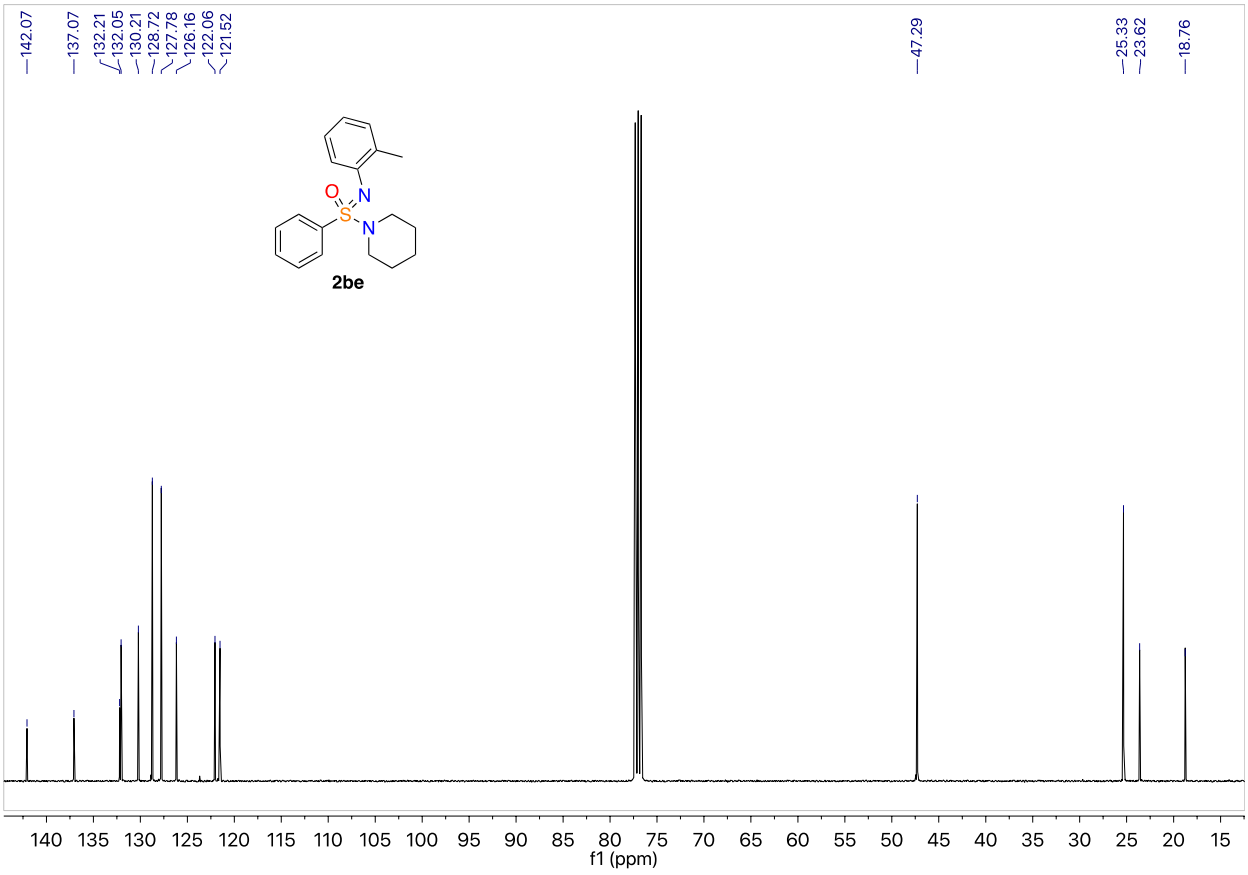
30
25
f1 (ppm)


2be
2.00
3.06
0.98
1.00
1.01
0.99
2.11
2.05
3.03
4.27
2.13
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)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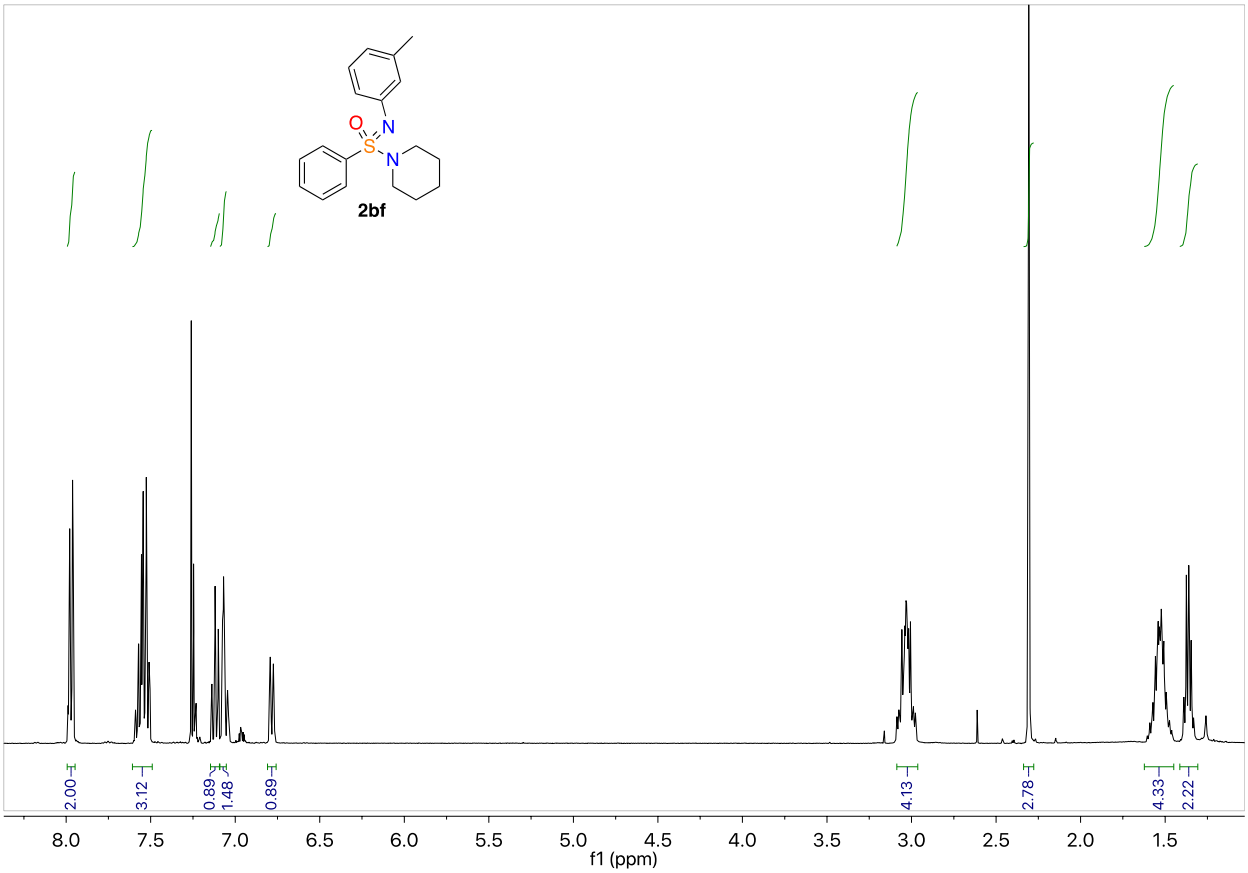
137.07
132.21
132.05
130.21
128.72
127.78
126.16
122.06
121.52
47.29
25.33
23.62
18.76
2be
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)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0.89
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7.0
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6.0
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5.0
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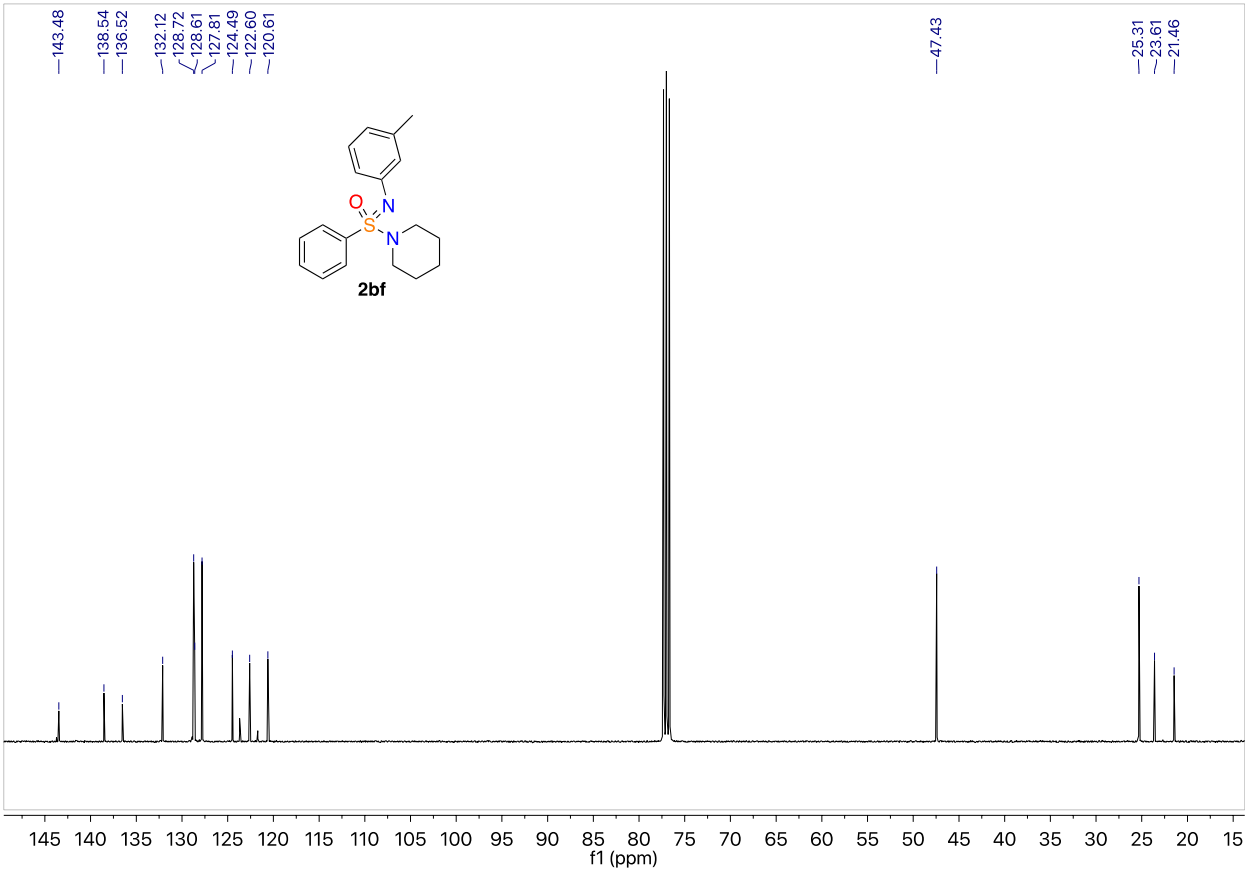
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)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45
40
35
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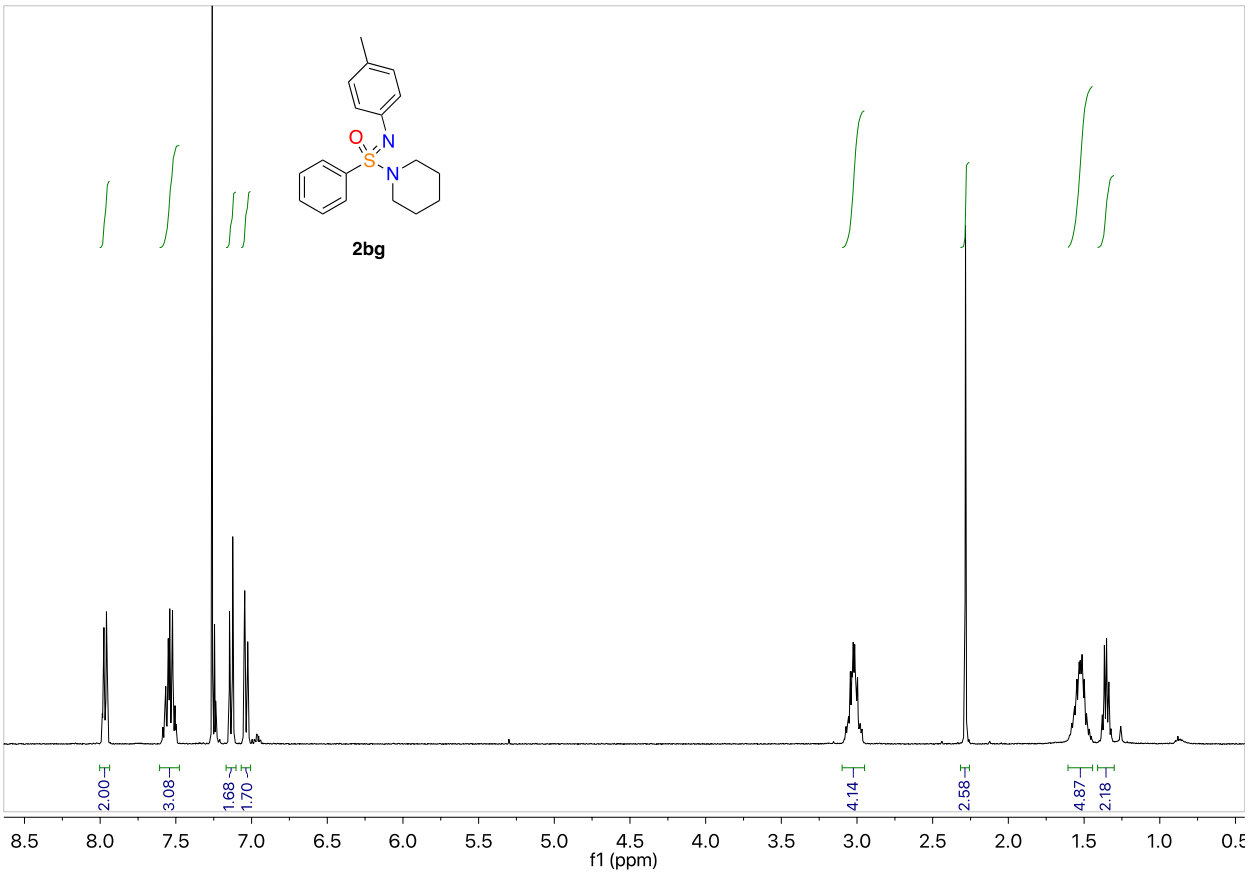
25
20
15
f1 (ppm)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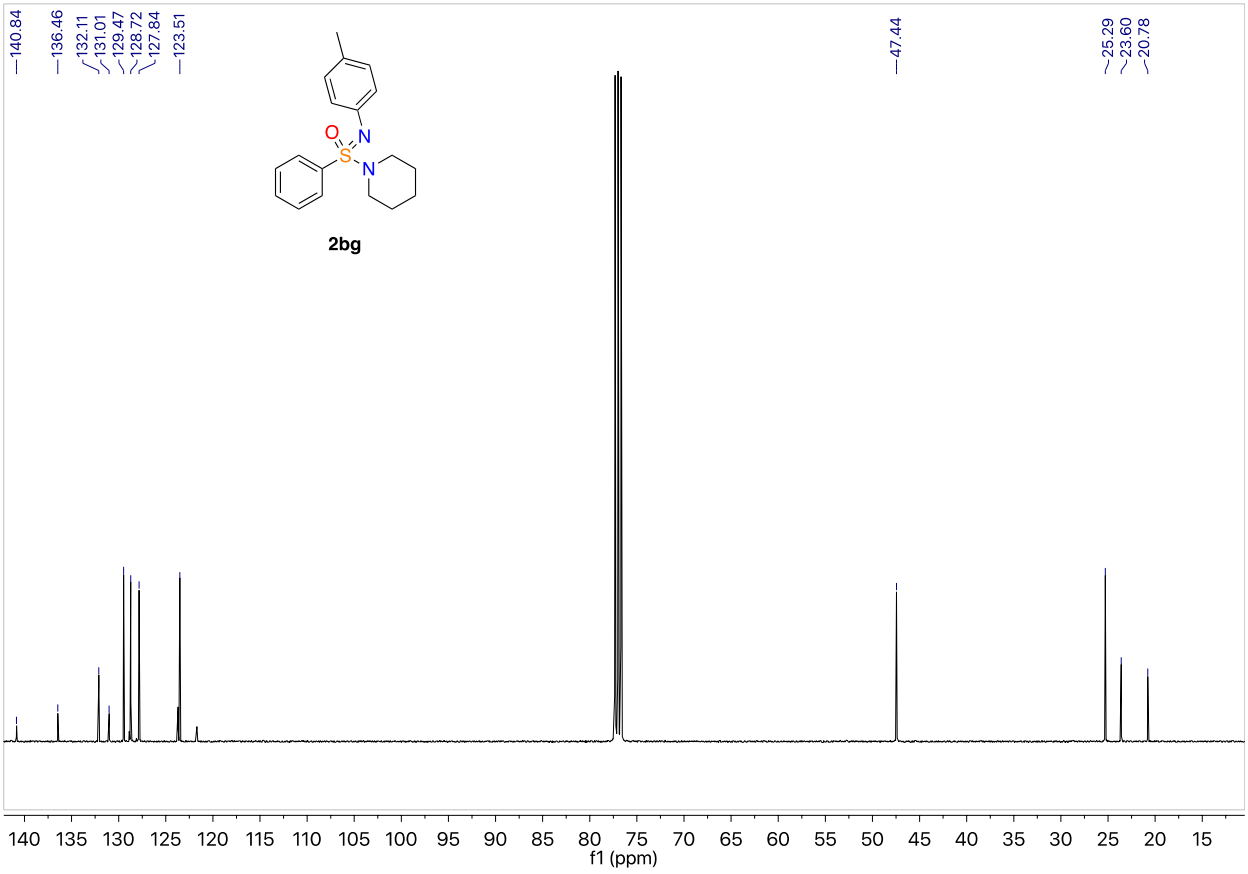
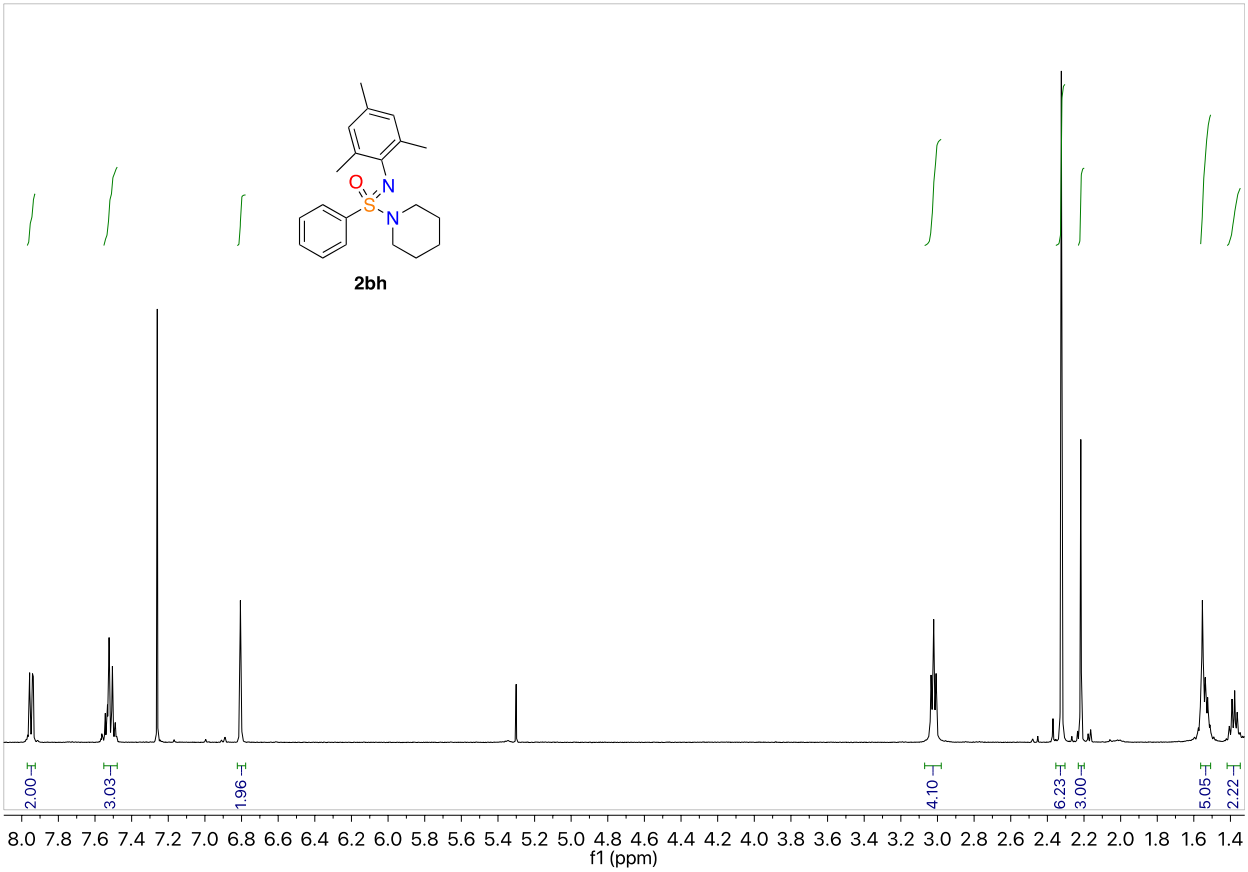
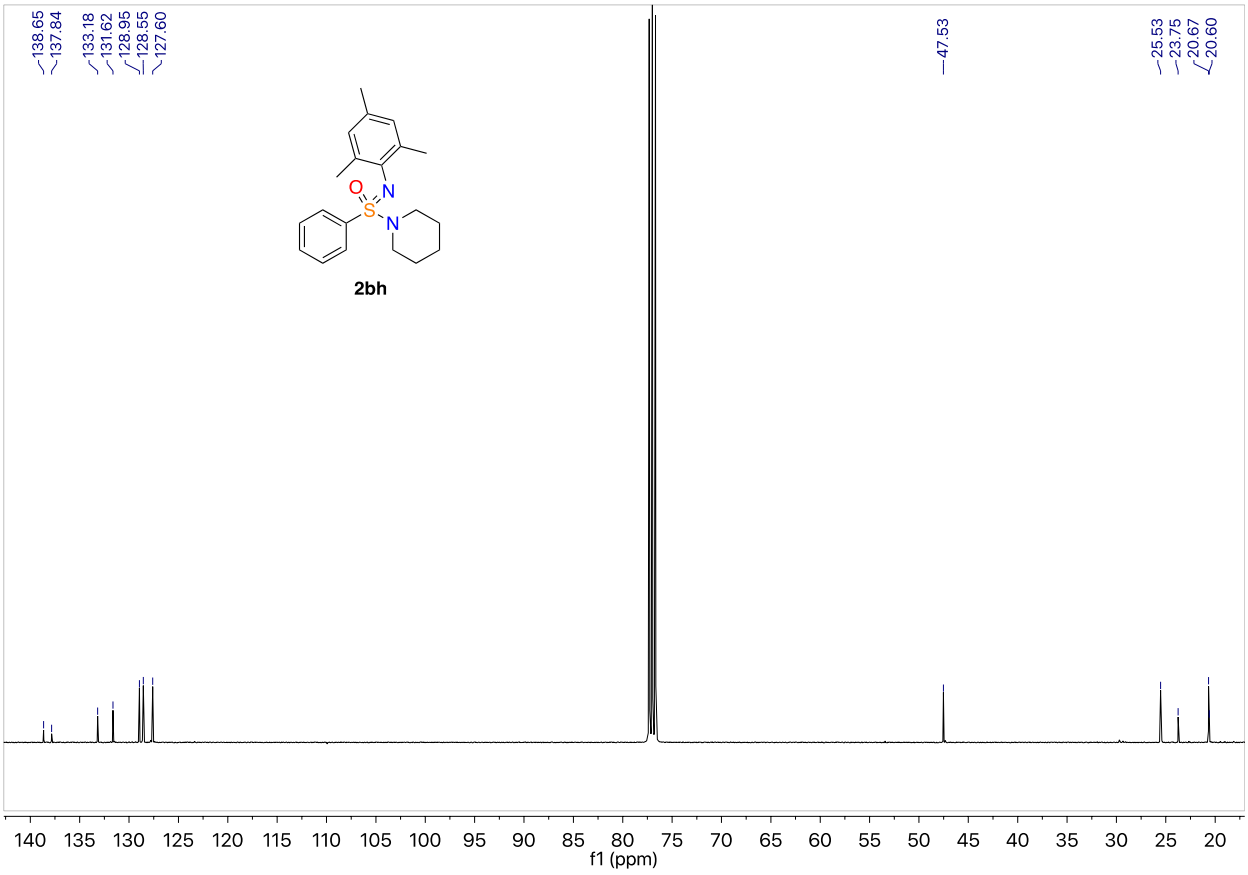
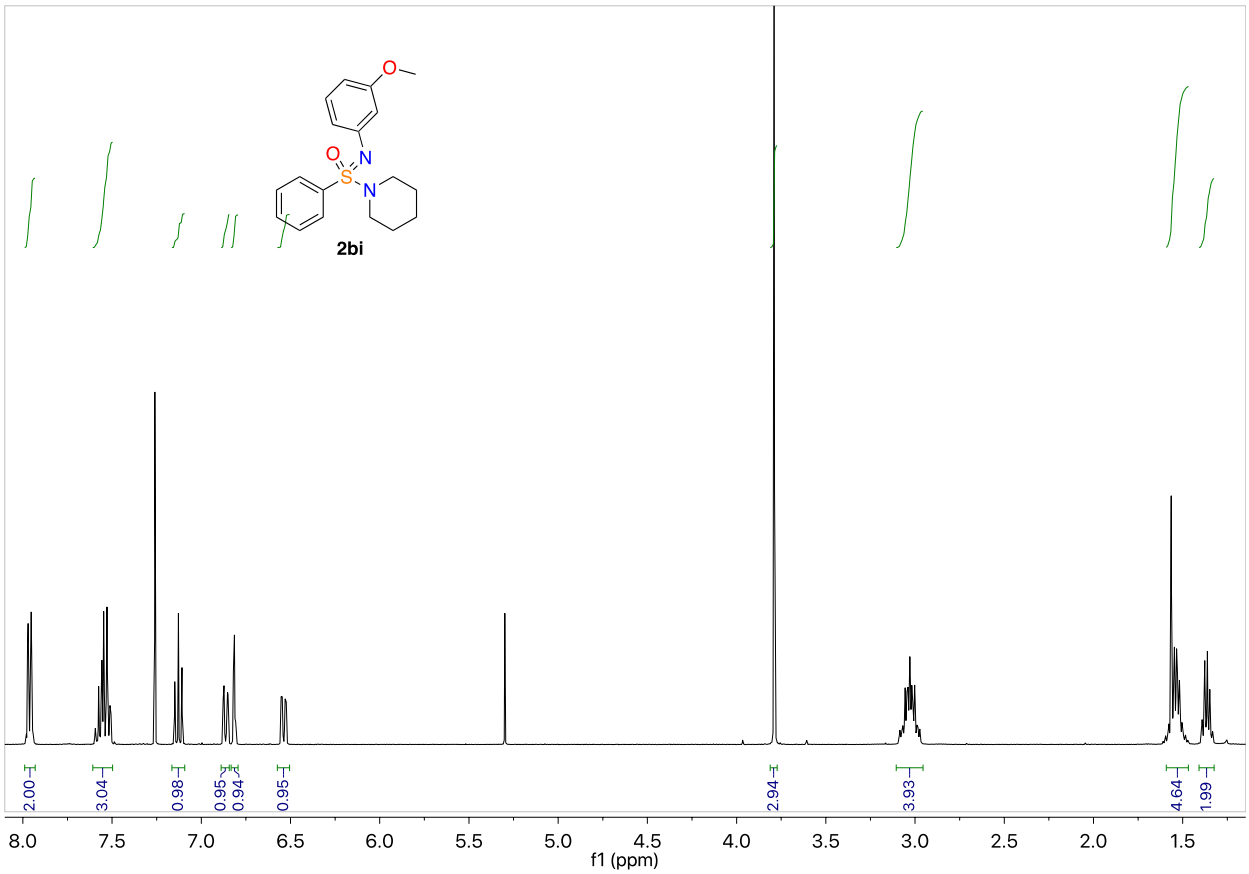
1.70
4.14
2.58
4.87
2.18
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


140.84
136.46
132.11
131.01
129.47
128.72
127.84
123.51
47.44
25.29
23.60
20.78
2bg
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)


2bh
2.00
3.03
1.96
4.10
6.23
3.00
5.05
2.22
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)


138.65
137.84
133.18
131.62
128.95
128.55
127.60
47.53
25.53
23.75
20.67
20.60
2bh
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)


2bi
2.00
3.04
0.98
0.95
0.94
0.95
2.94
3.93
4.64
1.99
8.0
7.5
7.0
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4.5
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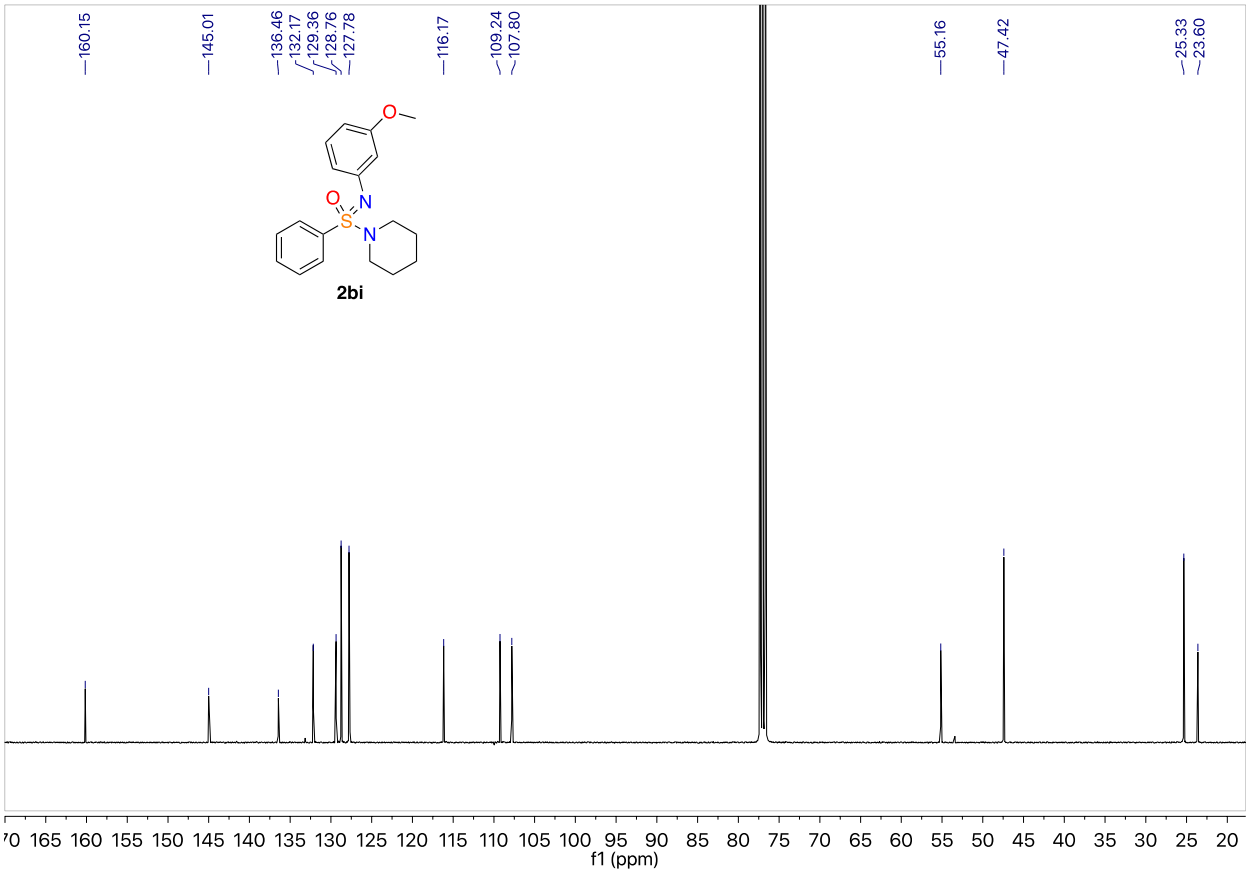
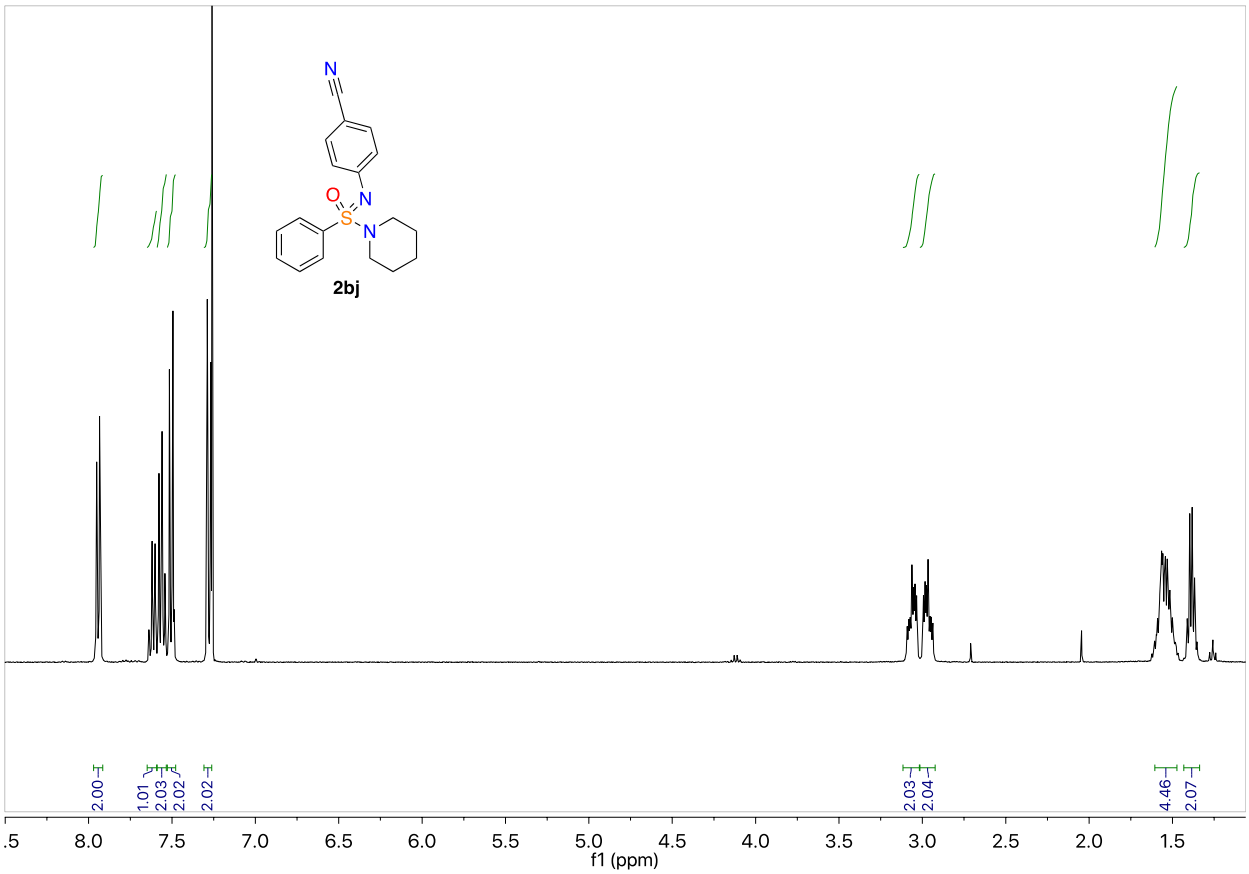
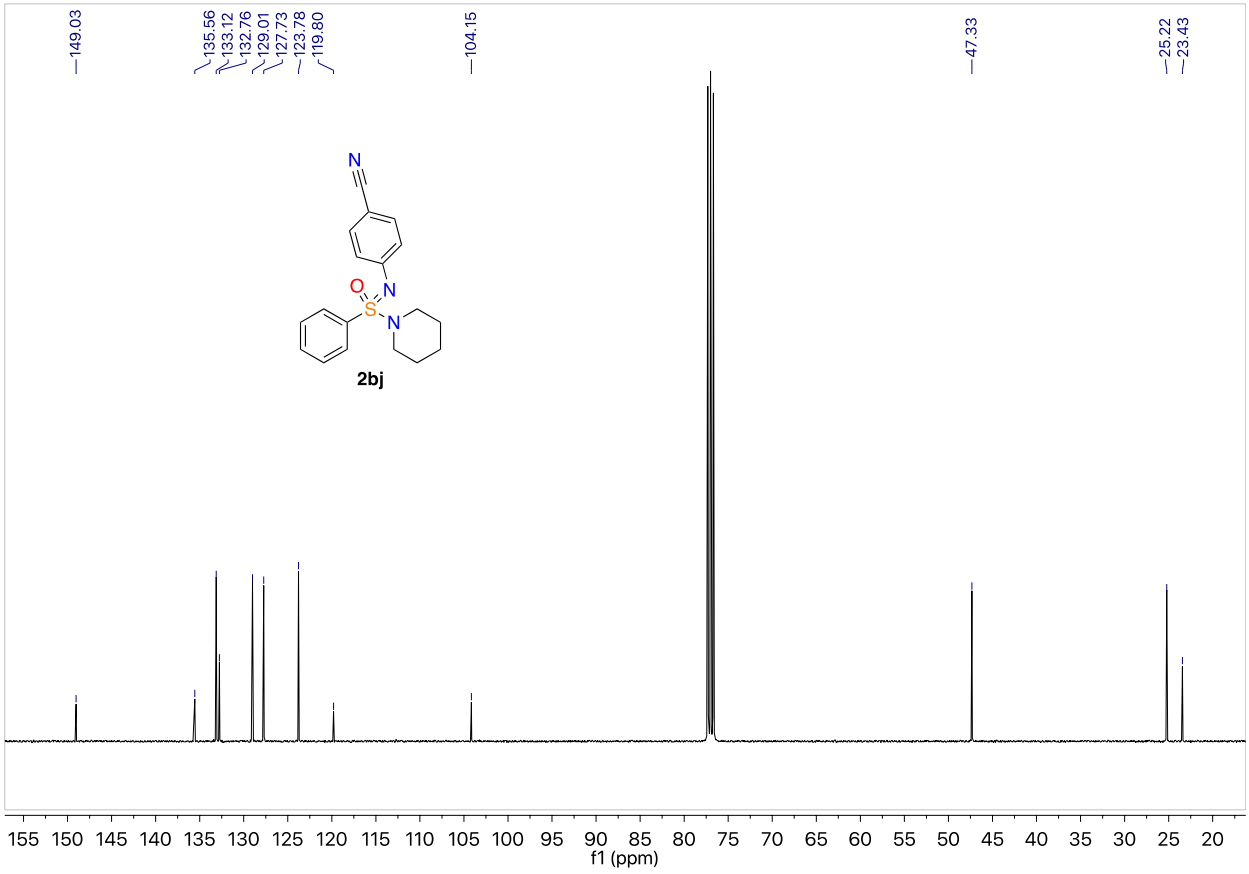
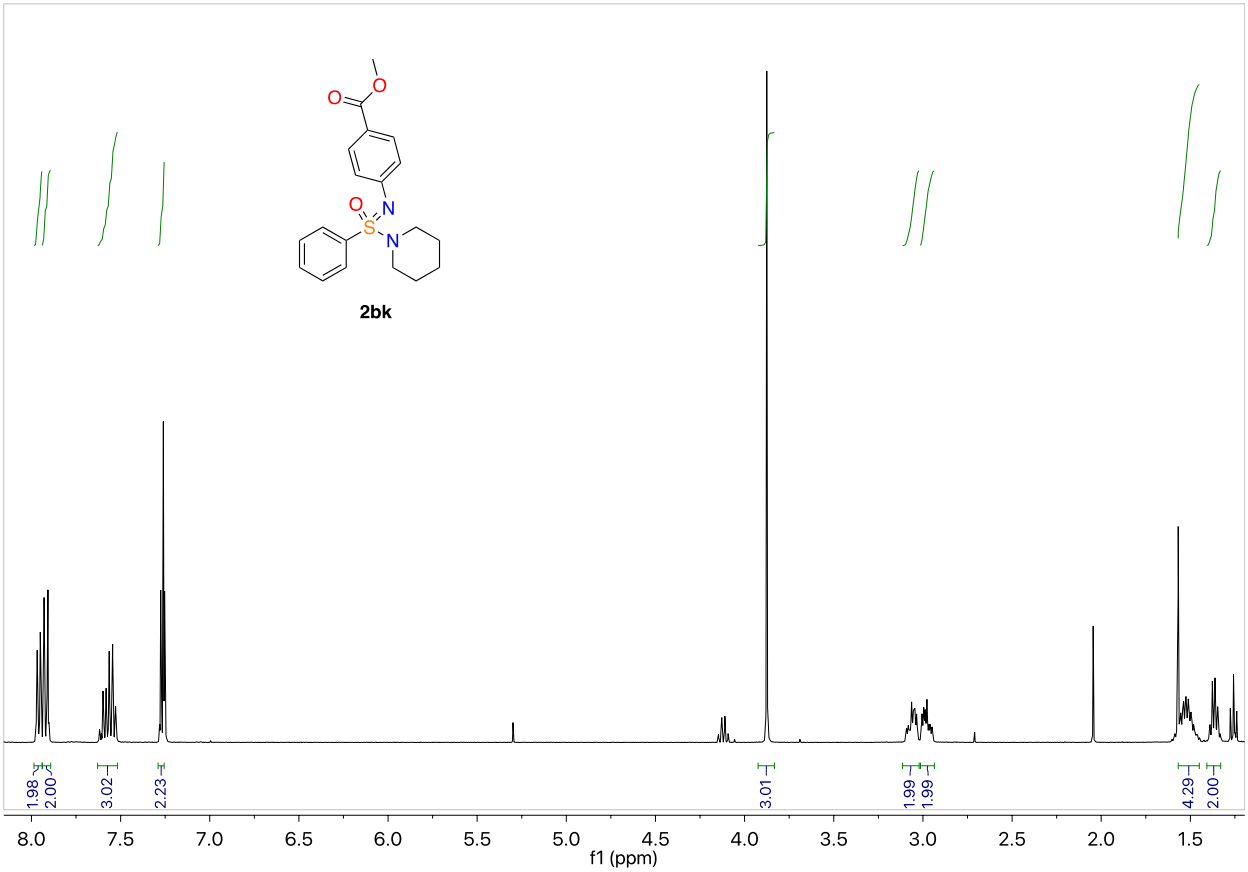
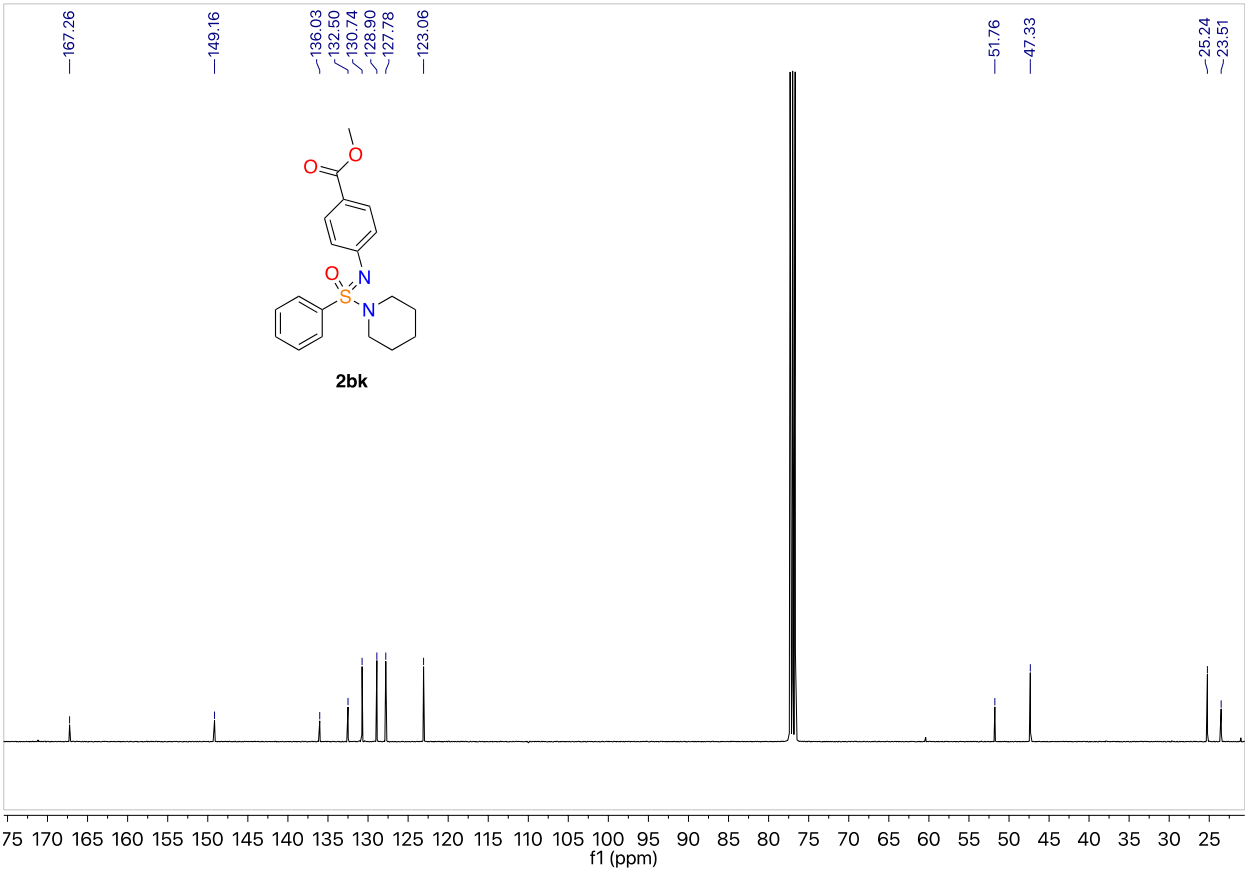
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

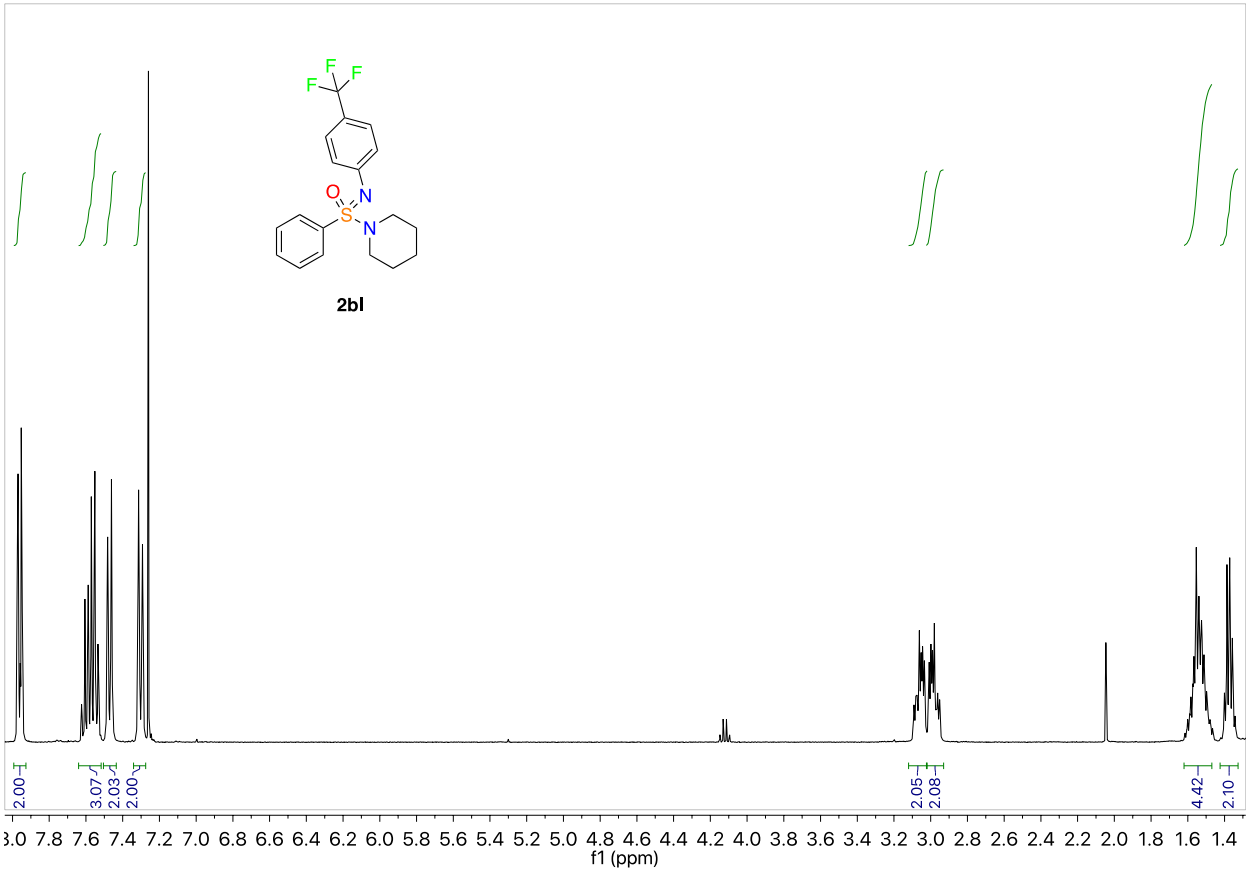

160.15
145.01
136.46
132.17
129.36
128.76
127.78
116.17
109.24
107.80
55.16
47.42
25.33
23.60
2bi
165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

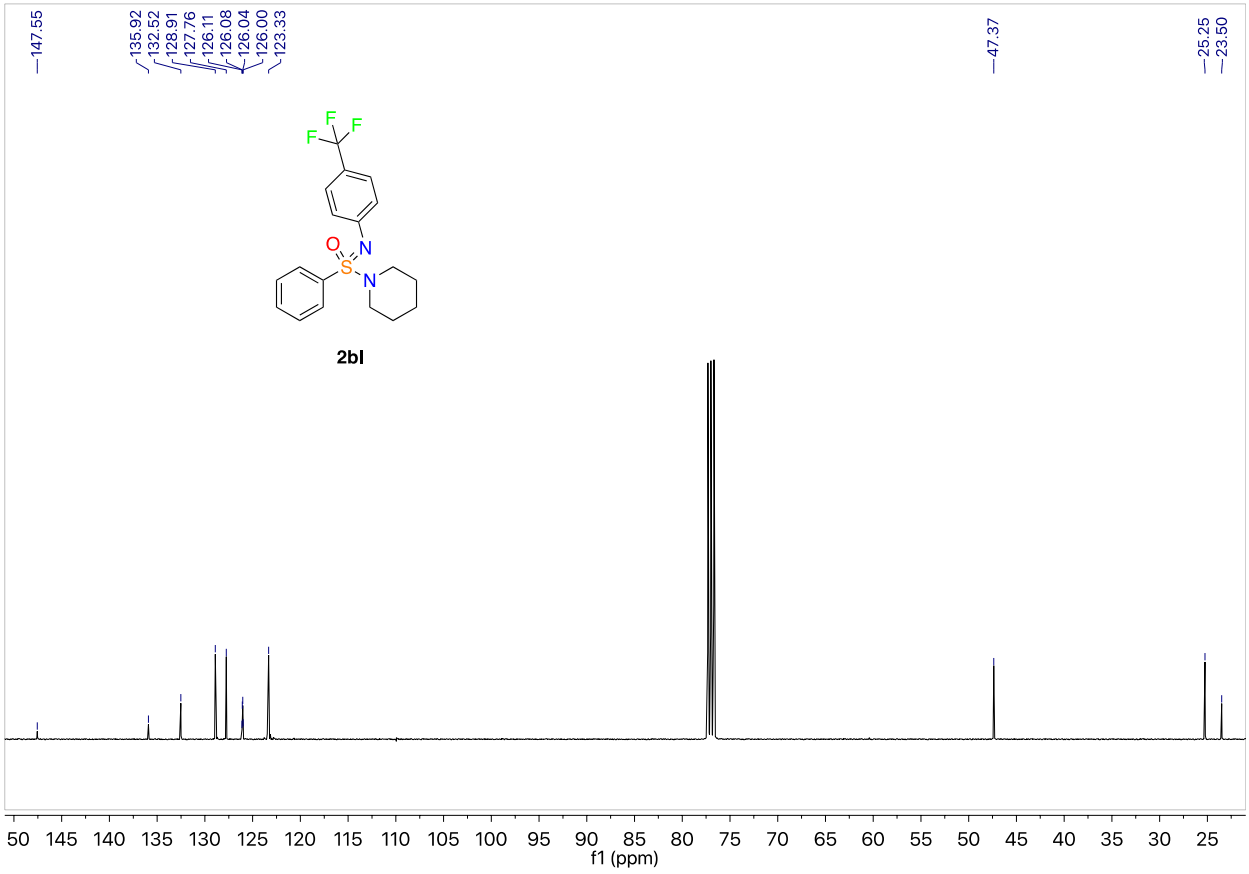

N
O
S
N
N
2bj
2.00
1.01
2.03
2.02
2.02
2.03
2.04
4.46
2.07
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

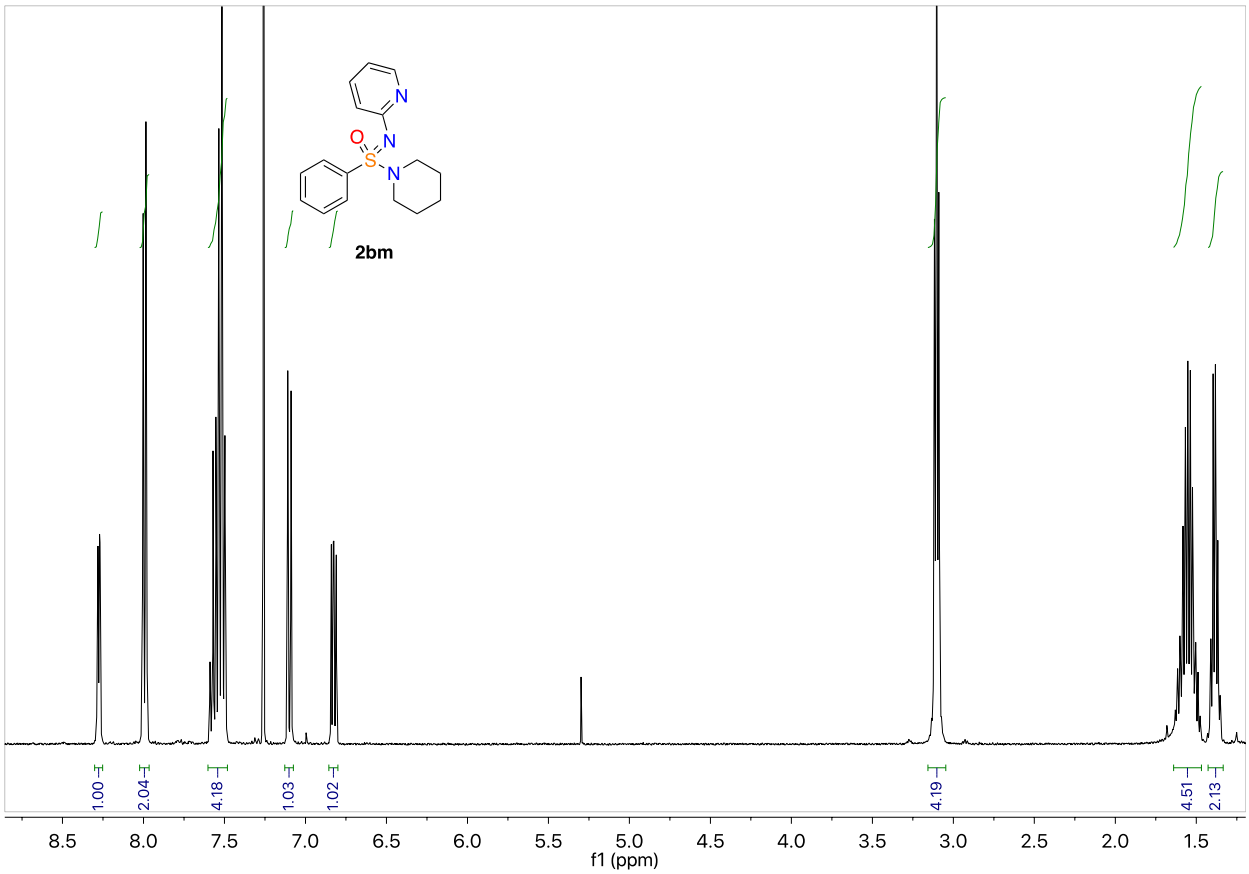

149.03
135.56
133.12
132.76
129.01
127.73
123.78
119.80
104.15
47.33
25.22
23.43
N
O
S
N
N
2bj
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
f1 (ppm)

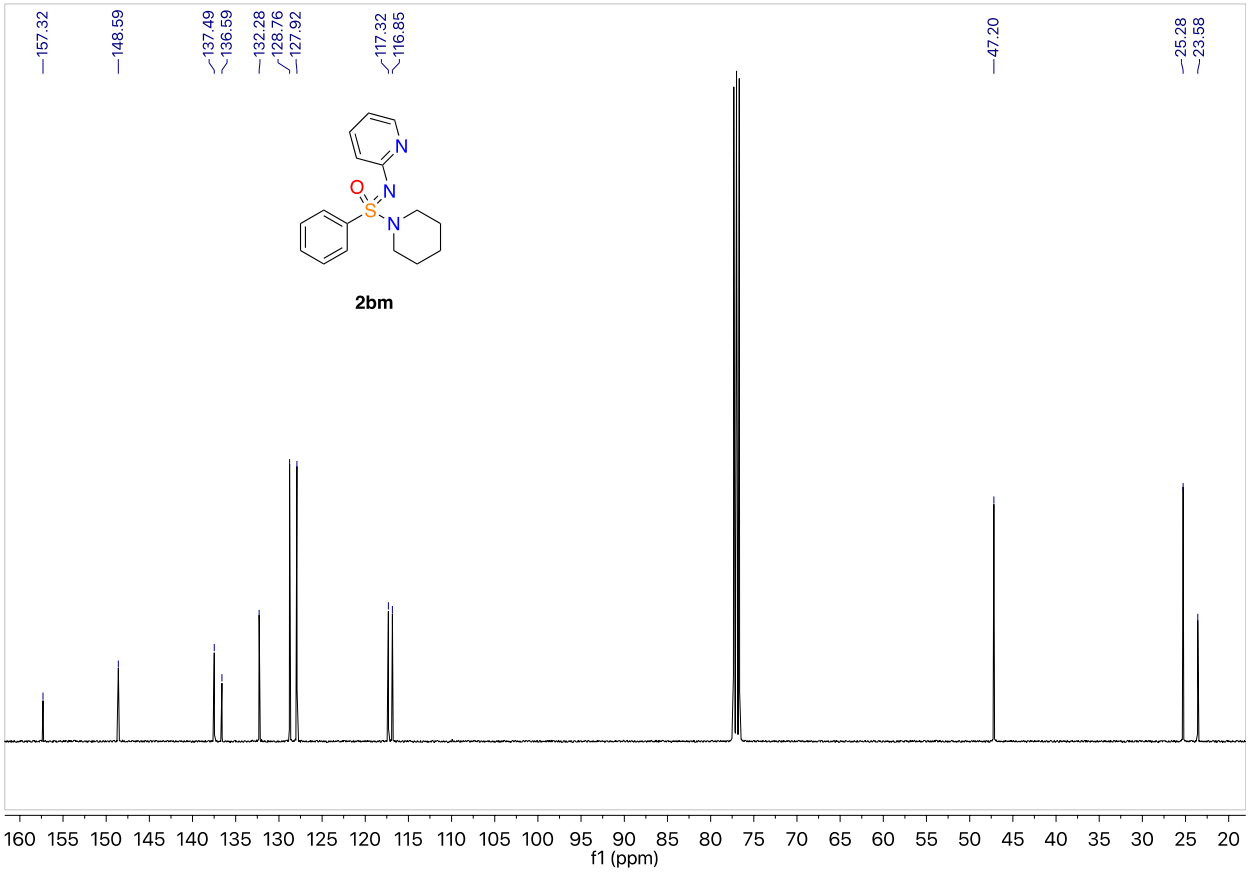

2bk
1.98
2.00
3.02
2.23
3.01
1.99
1.99
4.29
2.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)

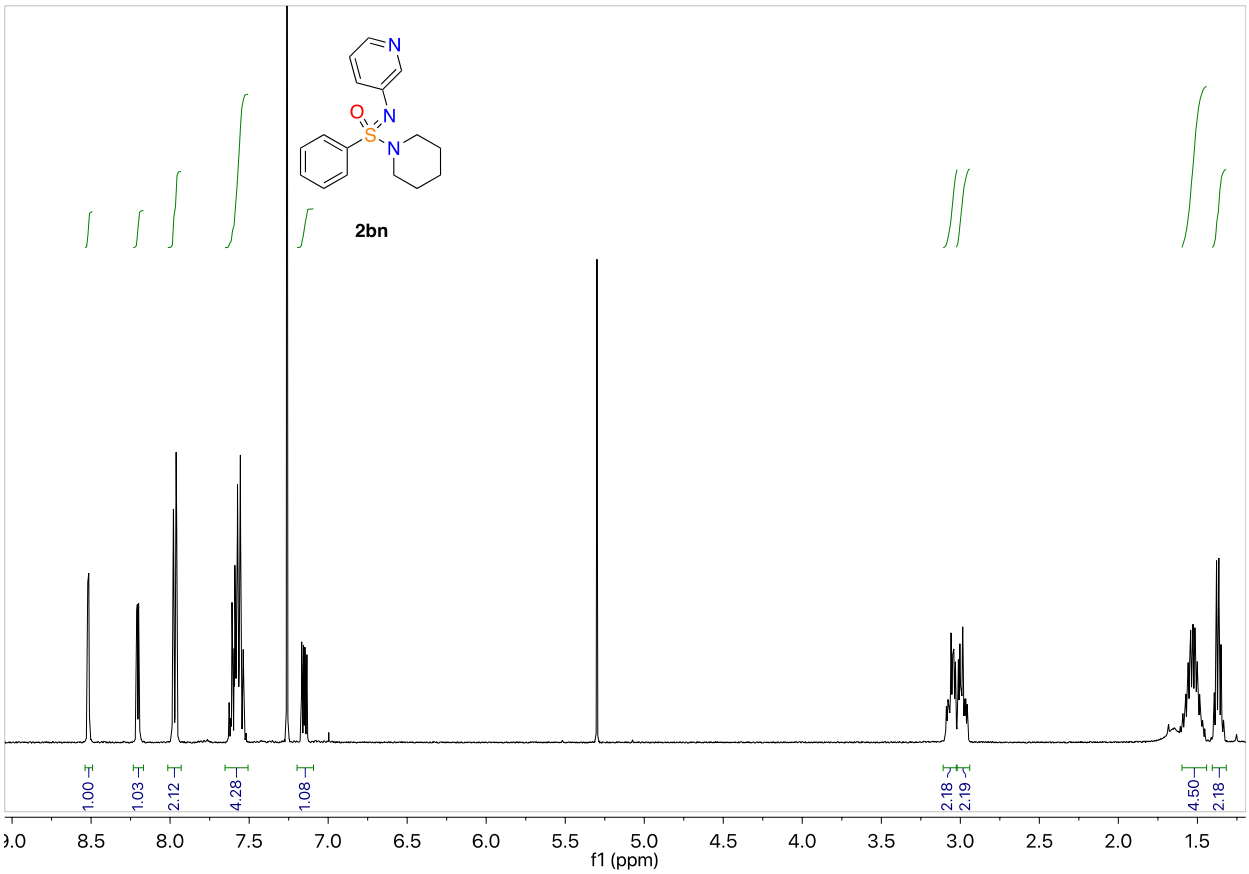

167.26
149.16
136.03
132.50
130.74
128.90
127.78
123.06
51.76
47.33
25.24
23.51
2bk
75 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

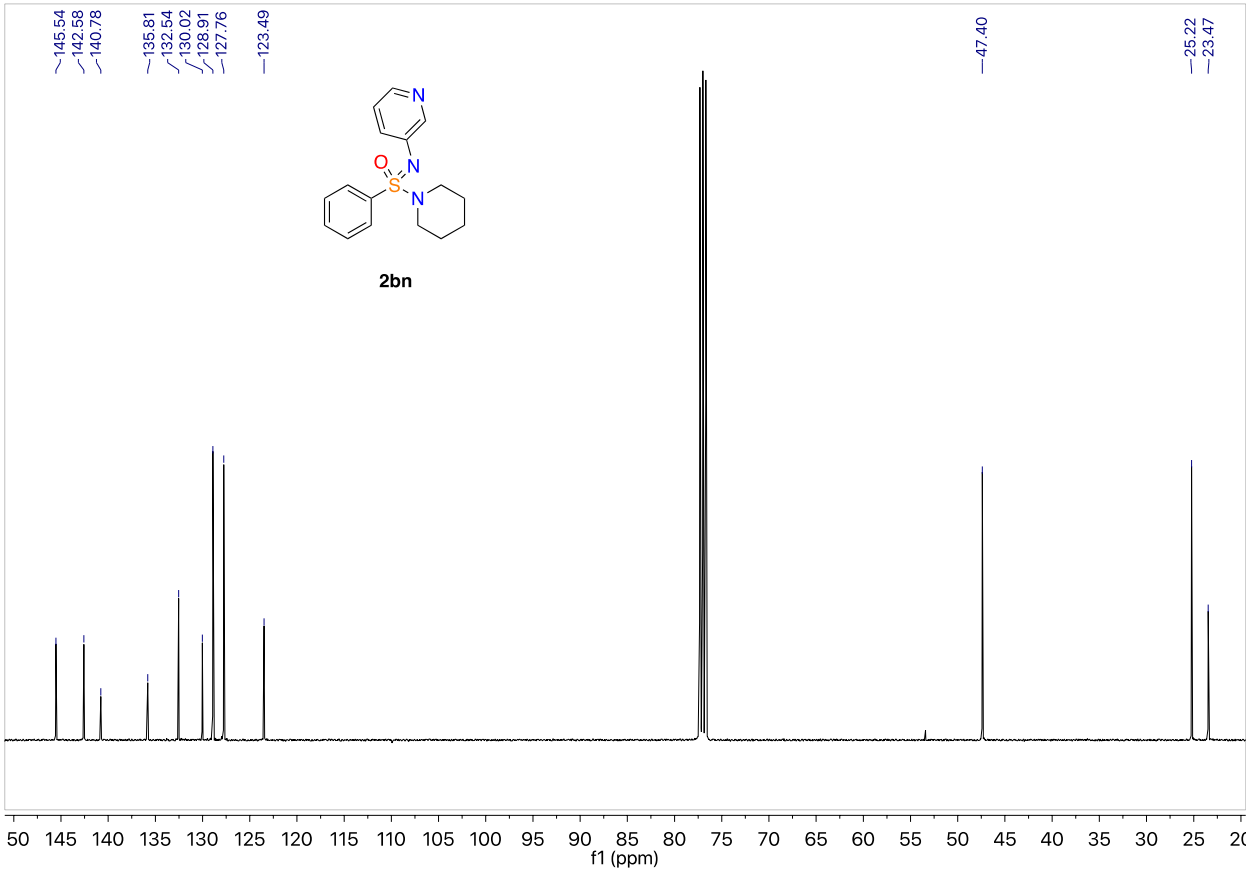

F
F
F
O
N
S
N
2bl
2.00
3.07
2.03
2.00
2.05
2.08
4.42
2.10
f1 (ppm)

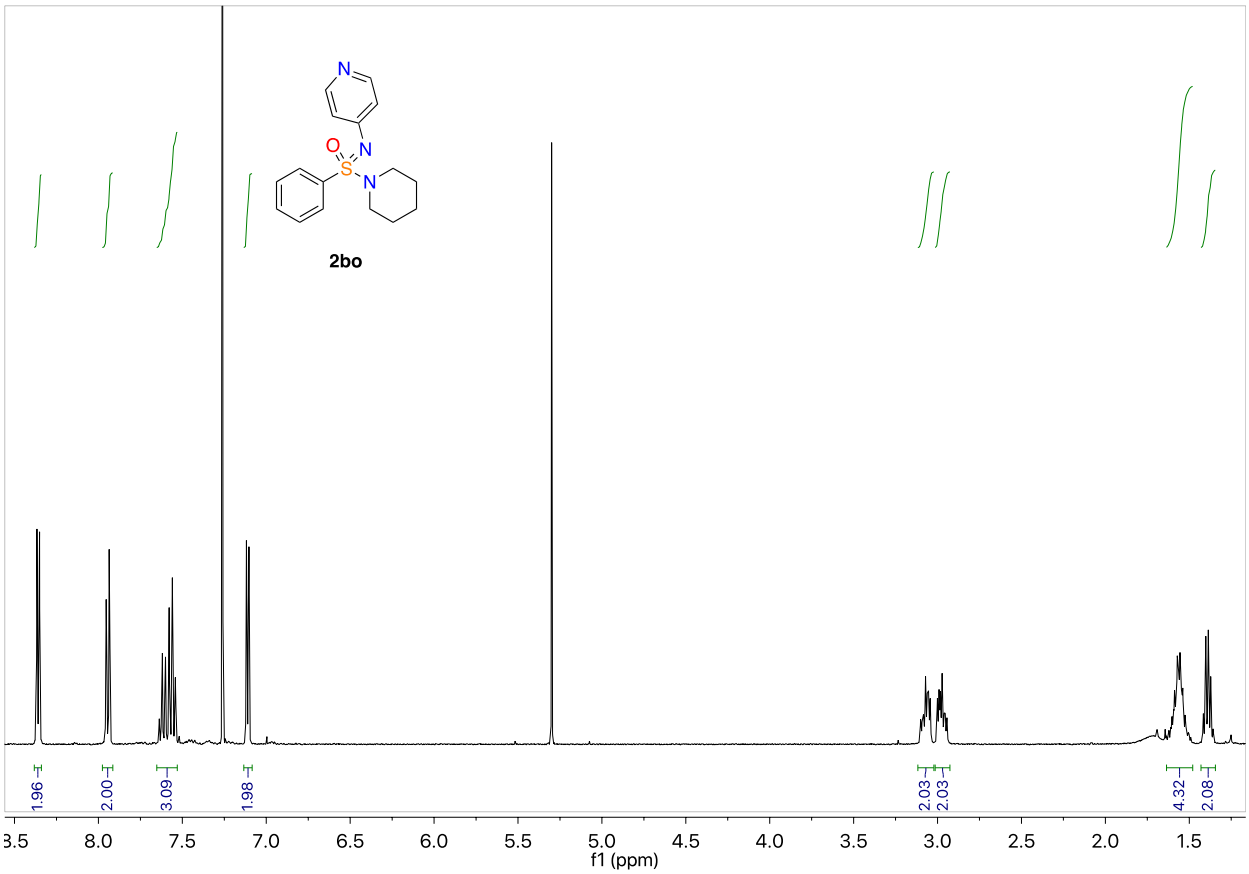

147.55
135.92
132.52
128.91
127.76
126.11
126.08
126.04
126.00
123.33
47.37
25.25
23.50
F
F
F
O
N
S
N
2bl
f1 (ppm)

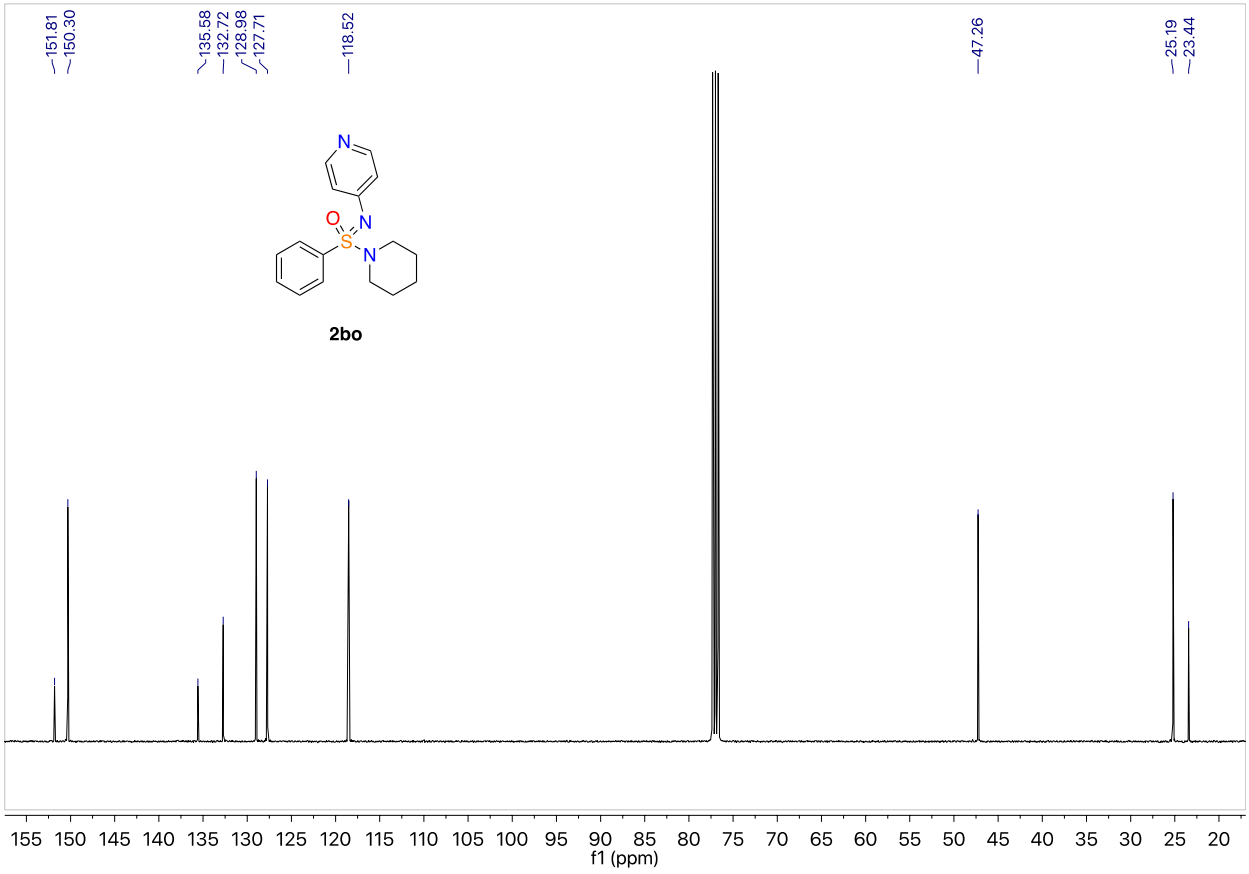

2bm
1.00
2.04
4.18
1.03
1.02
4.19
4.51
2.13
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)

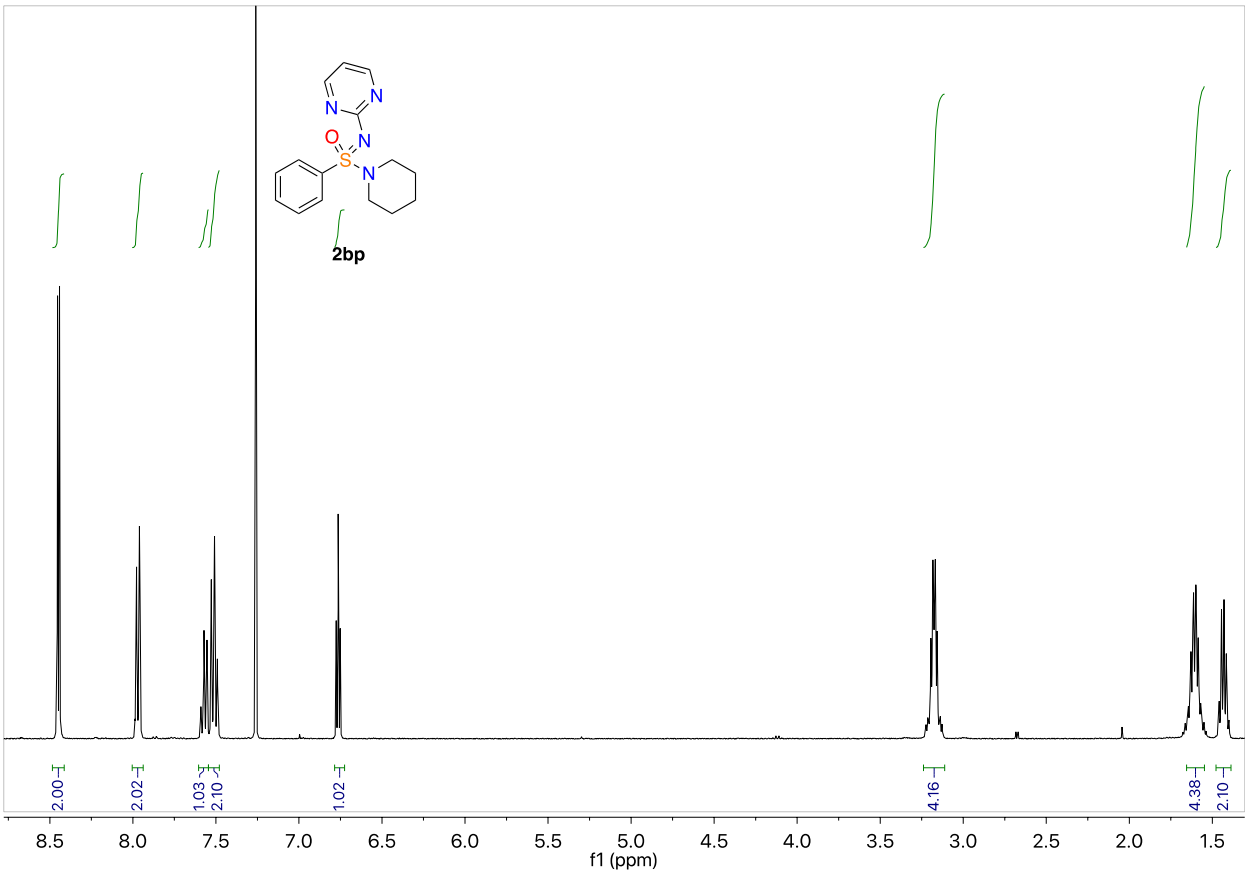

157.32
148.59
137.49
136.59
132.28
128.76
127.92
117.32
116.85
47.20
25.28
23.58
2bm
160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

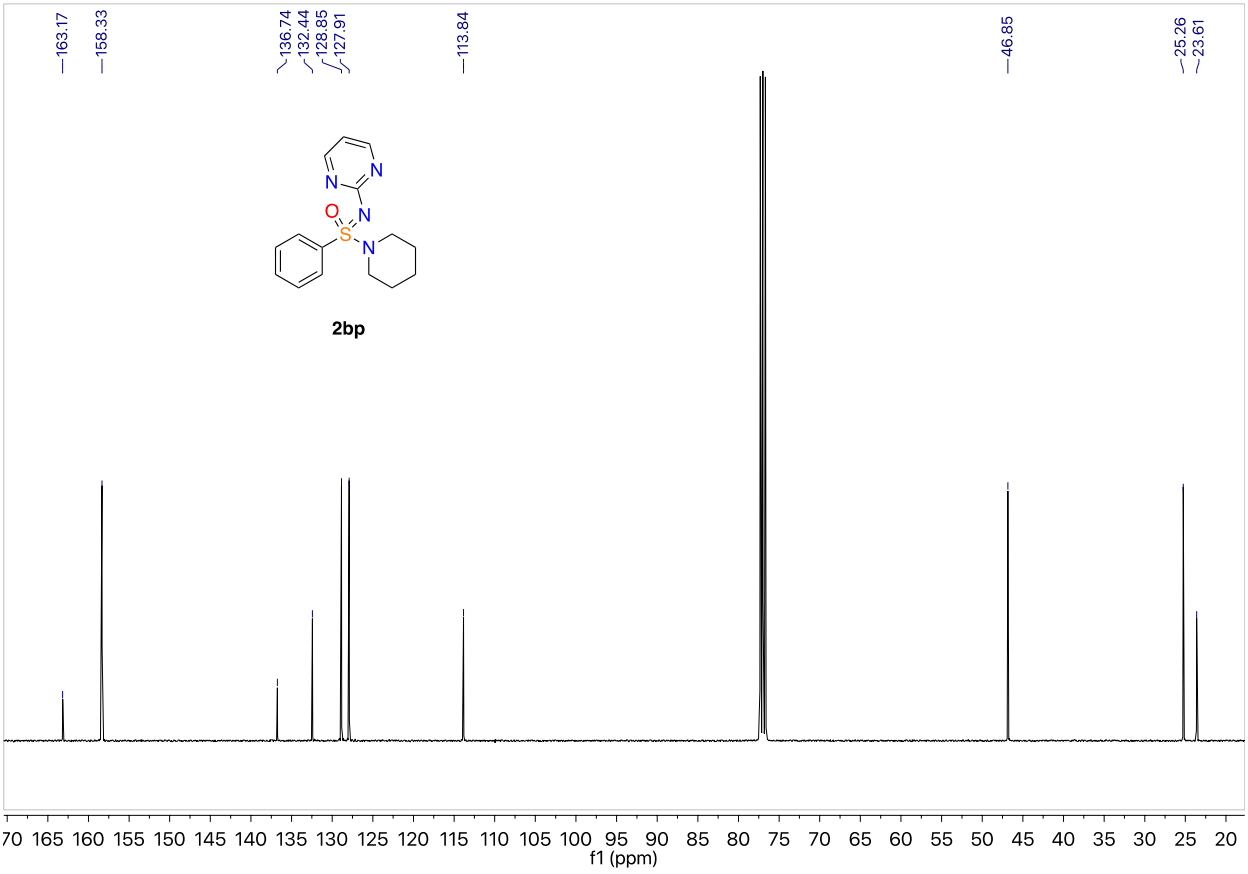

2bn
1.00
1.03
2.12
4.28
1.08
2.18
2.19
4.50
2.18
f1 (ppm)

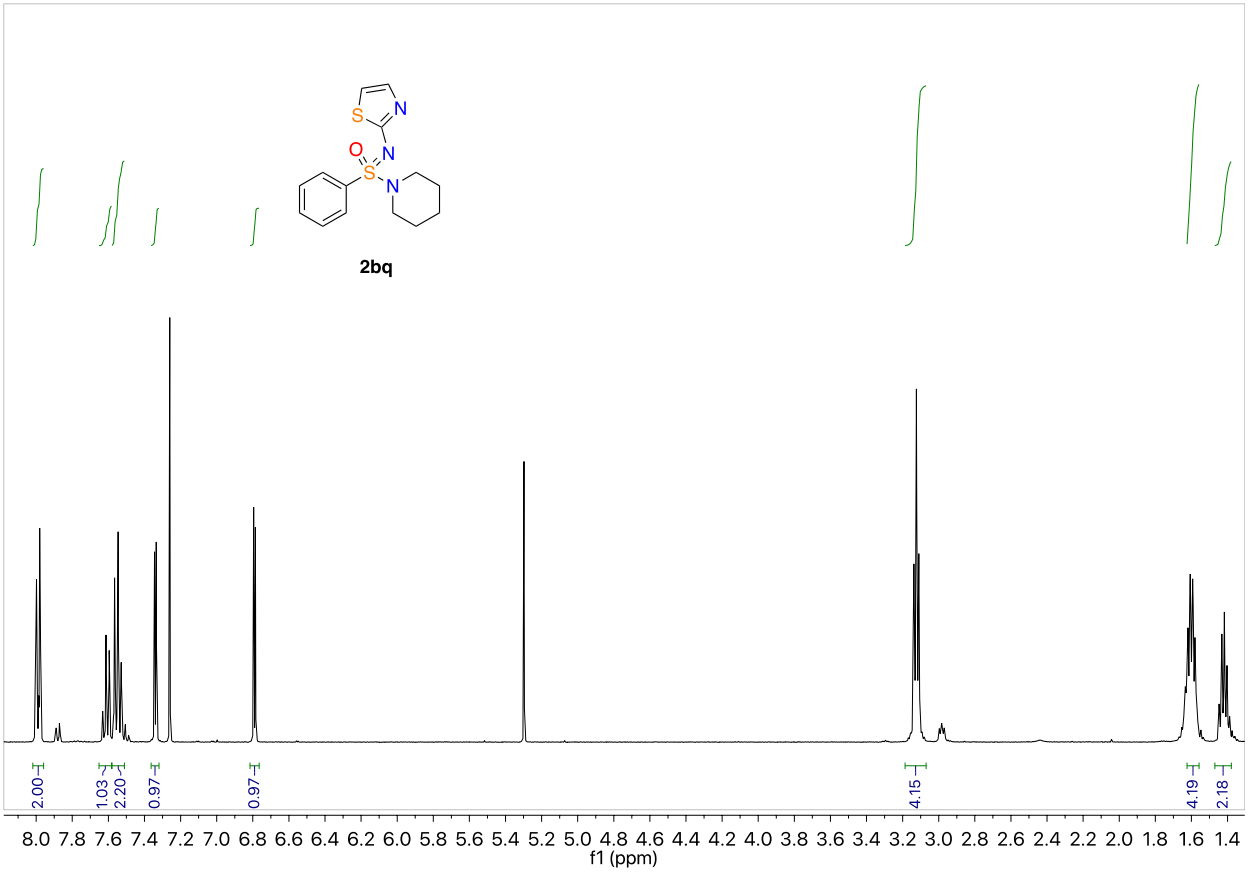

145.54
142.58
140.78
135.81
132.54
130.02
128.91
127.76
123.49
47.40
25.22
23.47
2bn
f1 (ppm)

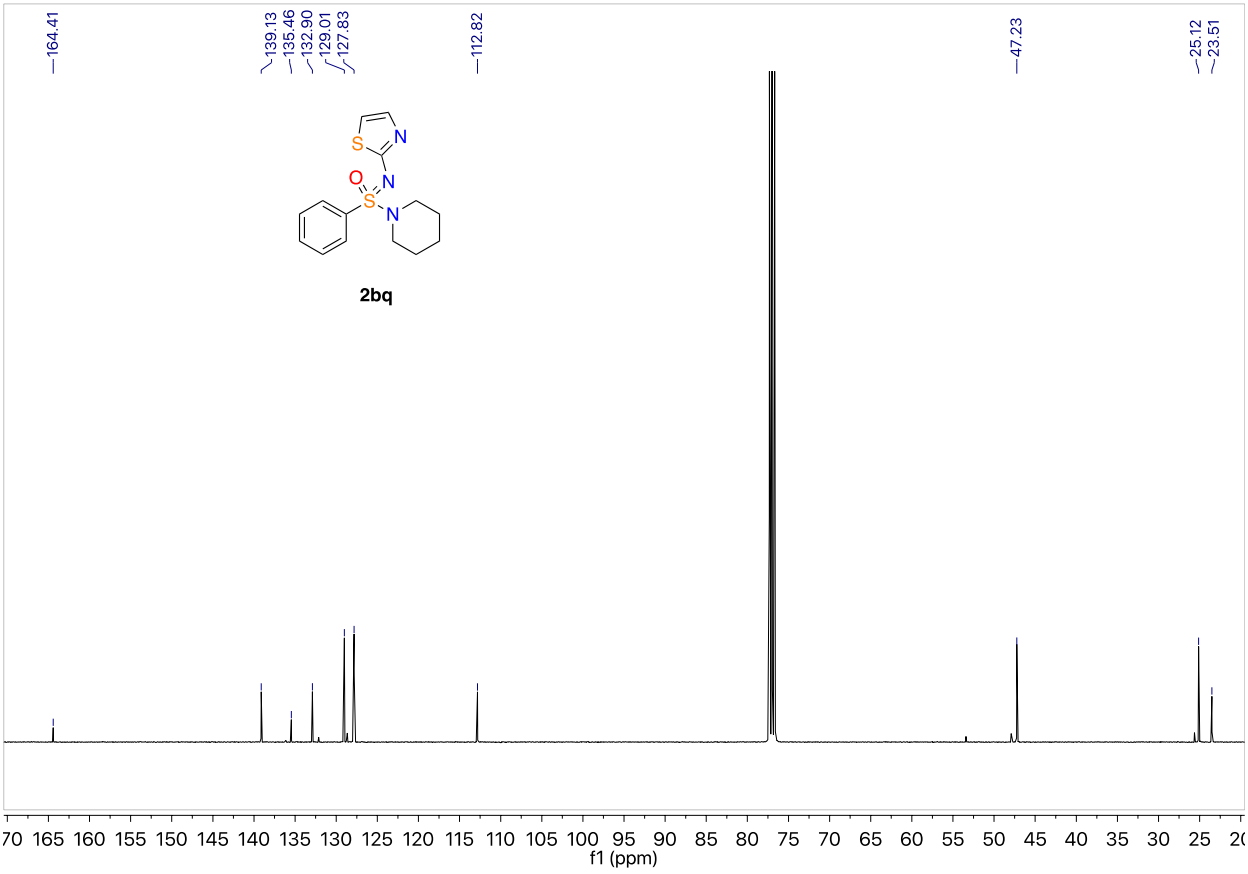

2bo
1.96
2.00
3.09
1.98
2.03
2.03
4.32
2.08
f1 (ppm)

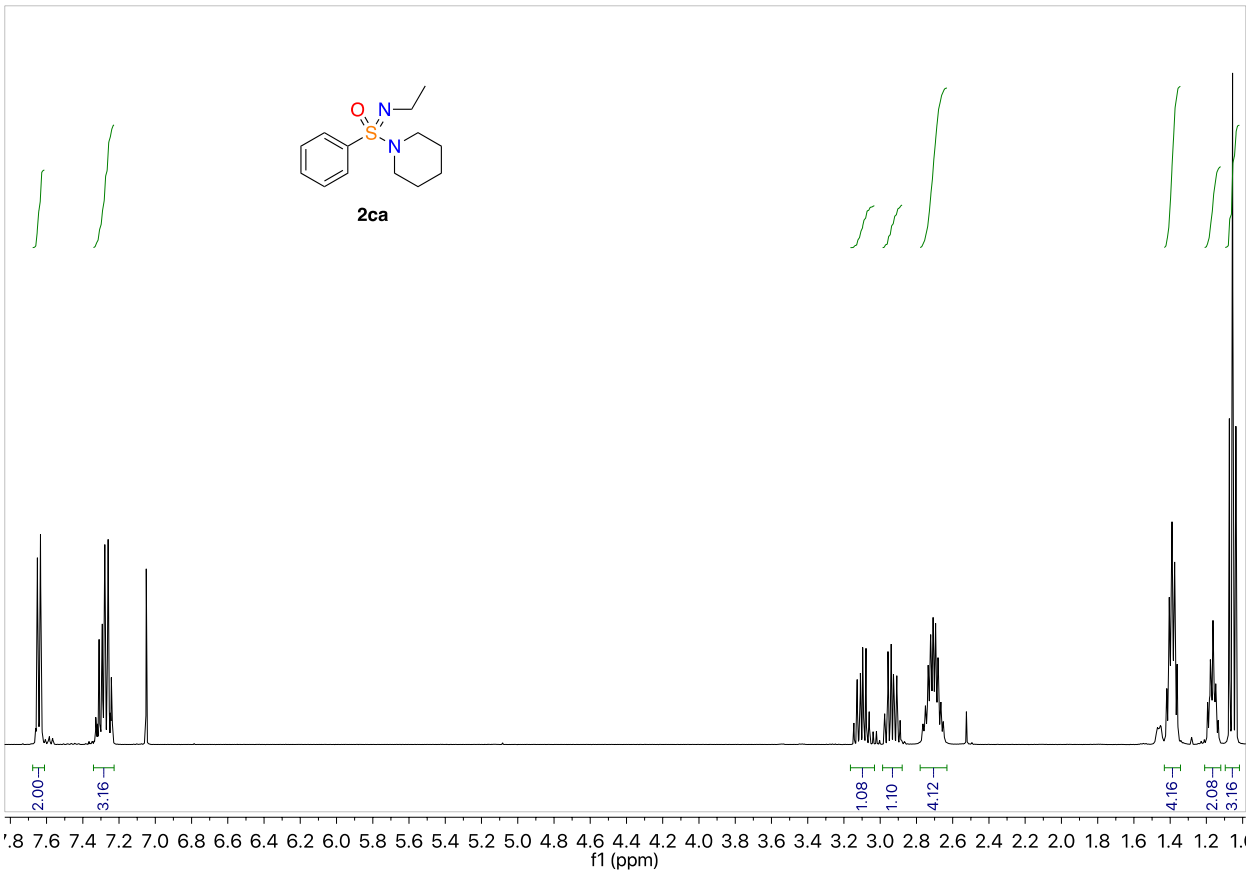

151.81
150.30
135.58
132.72
128.98
127.71
118.52
47.26
25.19
23.44
2bo
f1 (ppm)

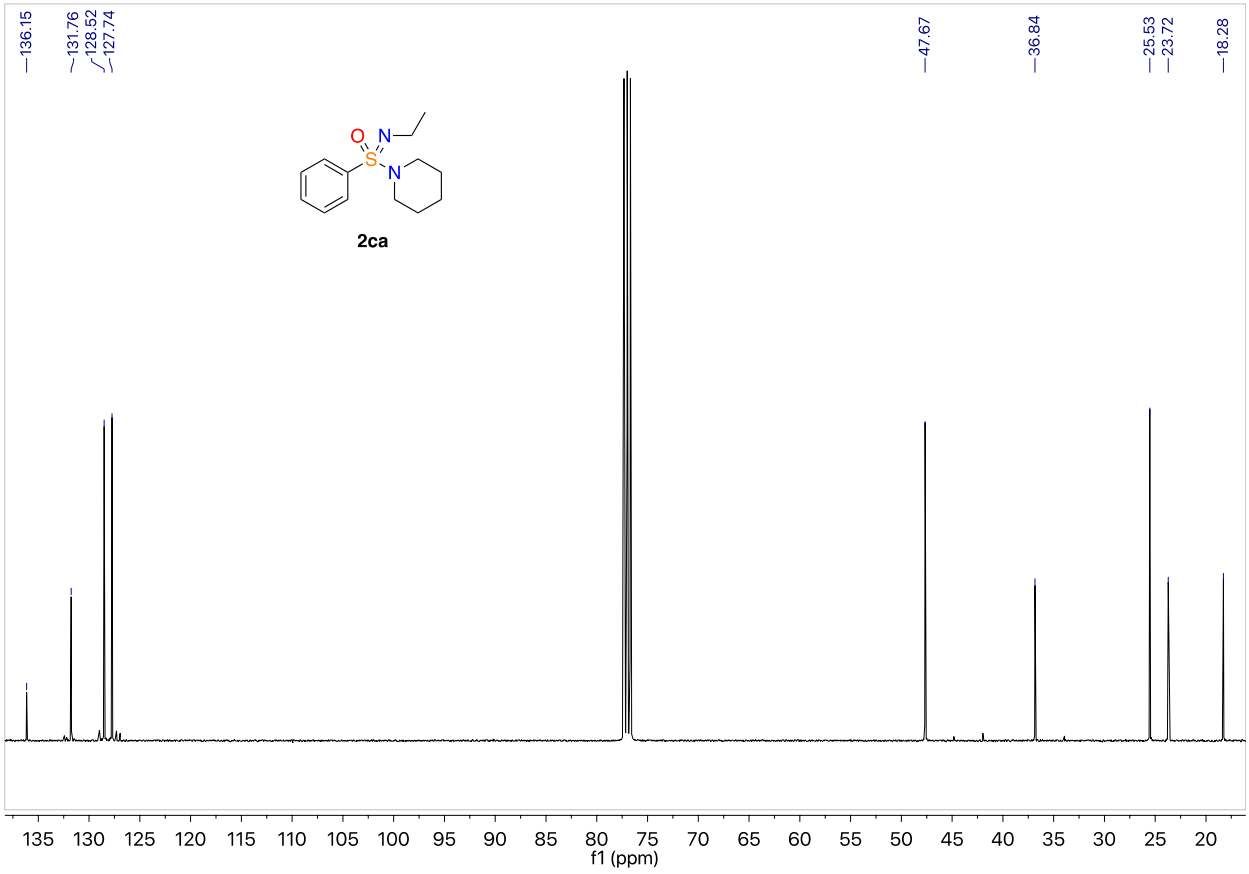

2bp
2.00
2.02
1.03
2.10
1.02
4.16
4.38
2.10
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

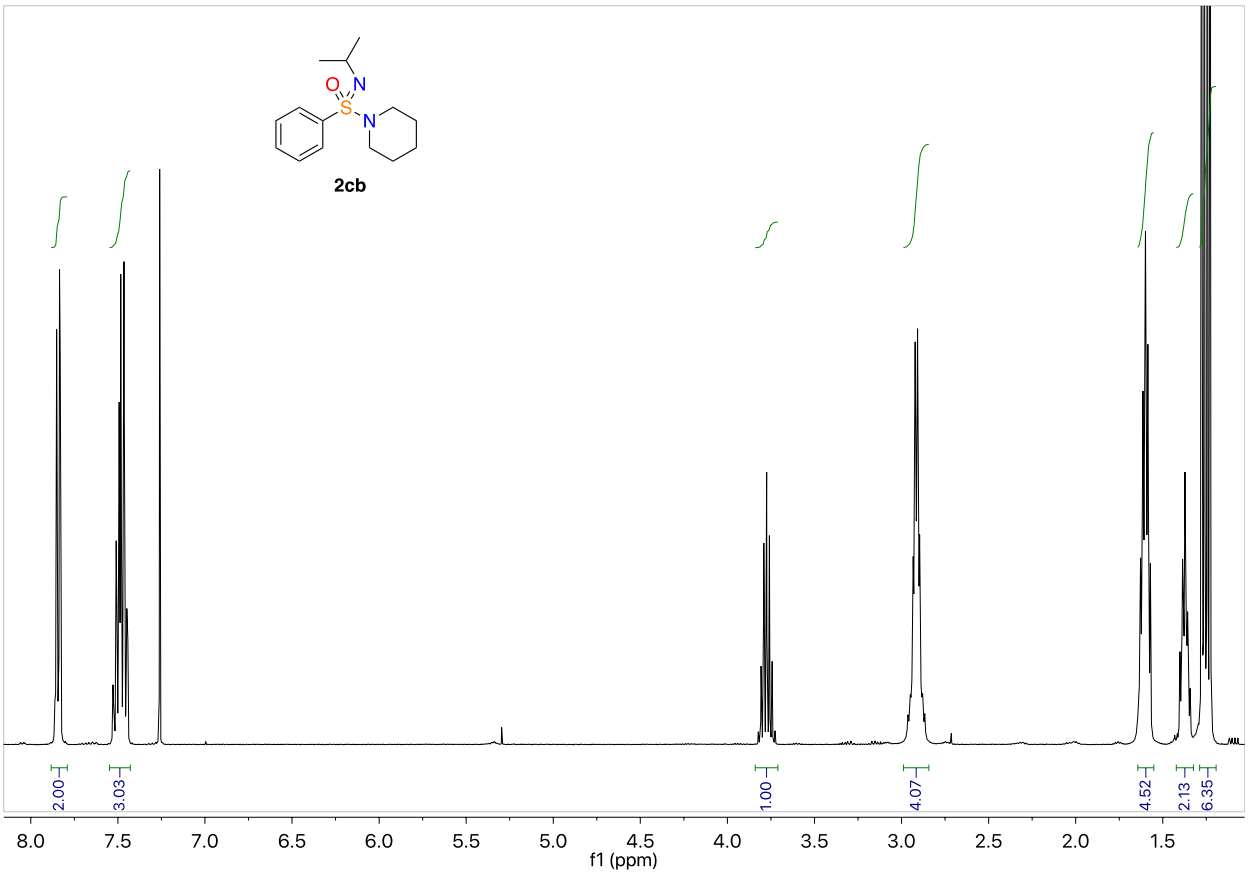

163.17
158.33
136.74
132.44
128.85
127.91
113.84
46.85
25.26
23.61
2bp
70 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)


2bq
2.00
1.03
2.20
0.97
0.97
4.15
4.19
2.18
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)


164.41
139.13
135.46
132.90
129.01
127.83
112.82
47.23
25.12
23.51
2bq
70 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)


2ca
2.00
3.16
1.08
1.10
4.12
4.16
2.08
3.16
f1 (ppm)


136.15
131.76
128.52
127.74
47.67
36.84
25.53
23.72
18.28
2ca
f1 (ppm)


2cb
2.00
3.03
1.00
4.07
4.52
2.13
6.35
8.0
7.5
7.0
6.5
6.0
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5.0
4.5
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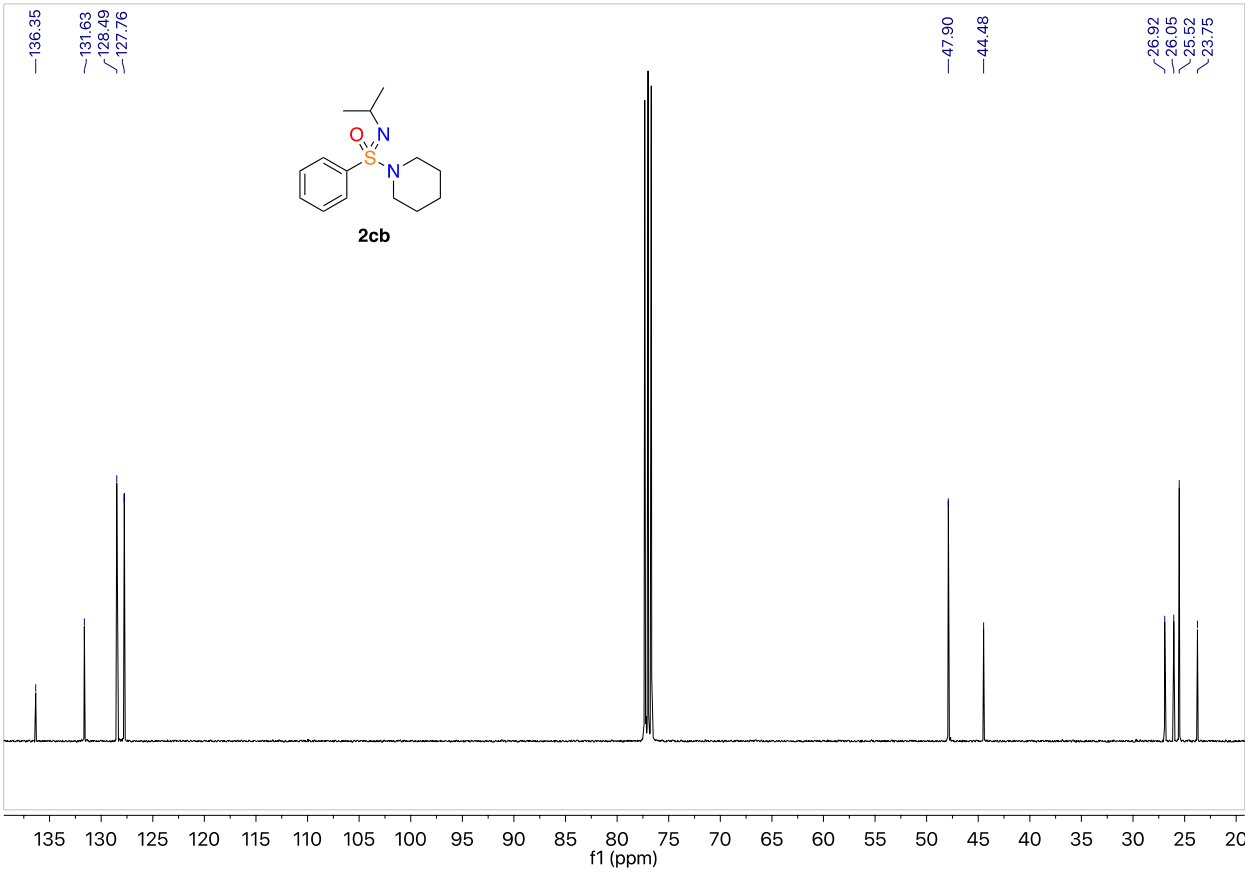
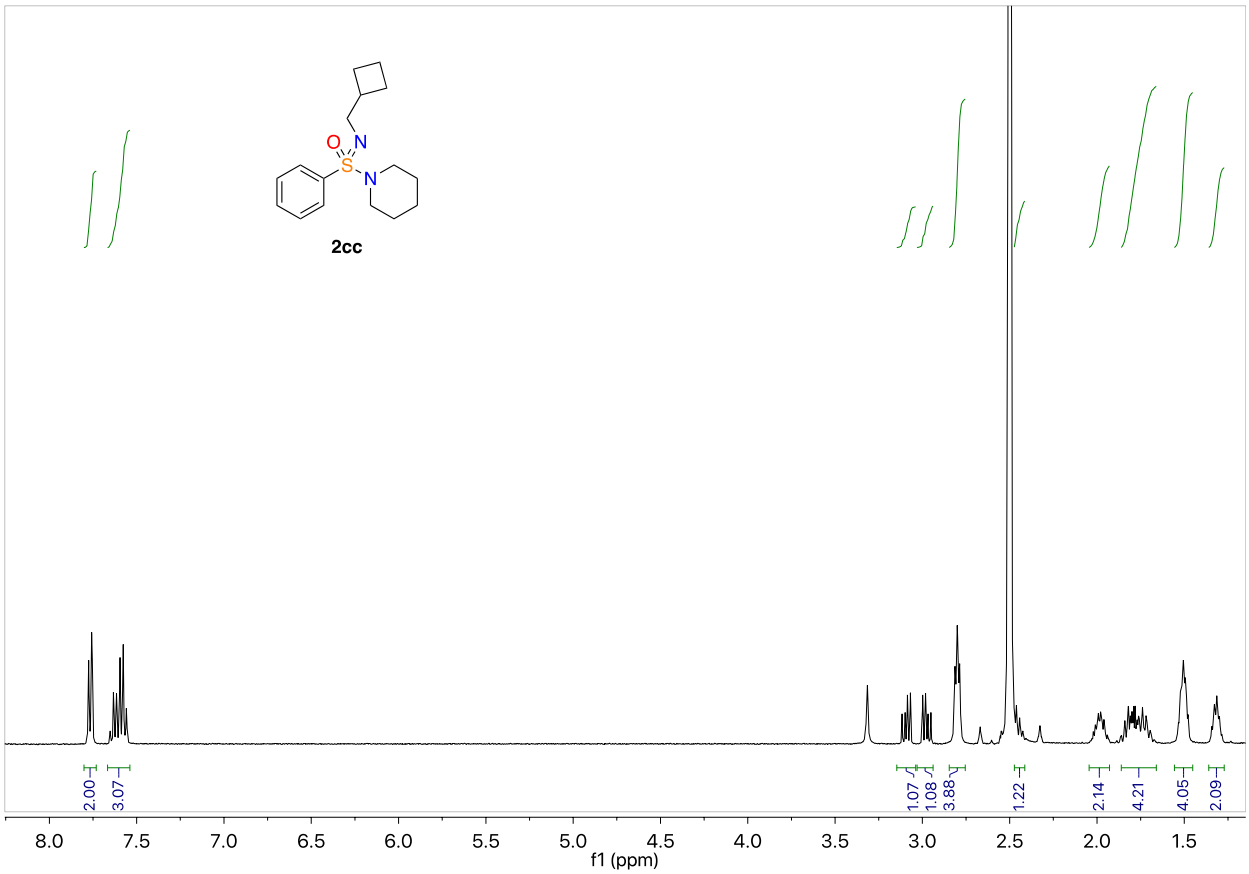
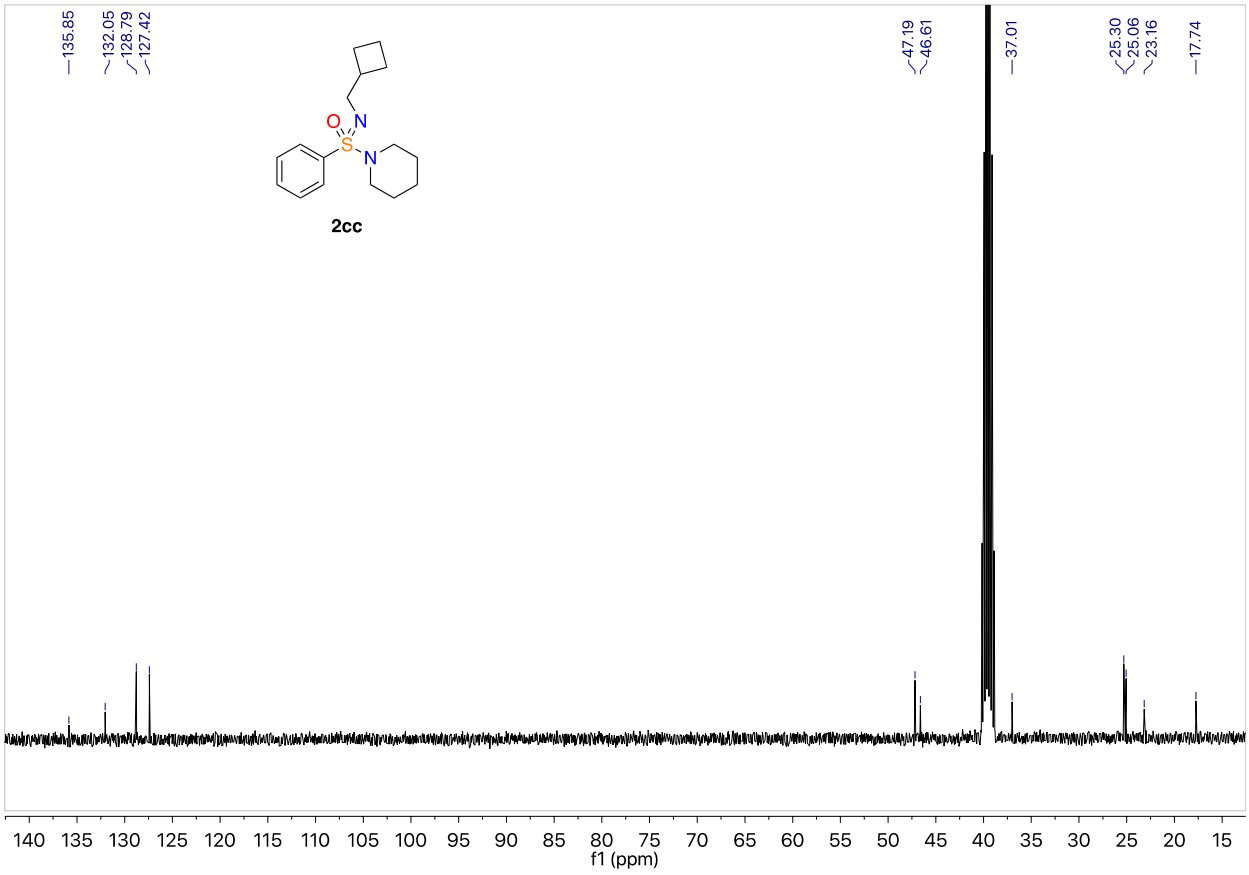
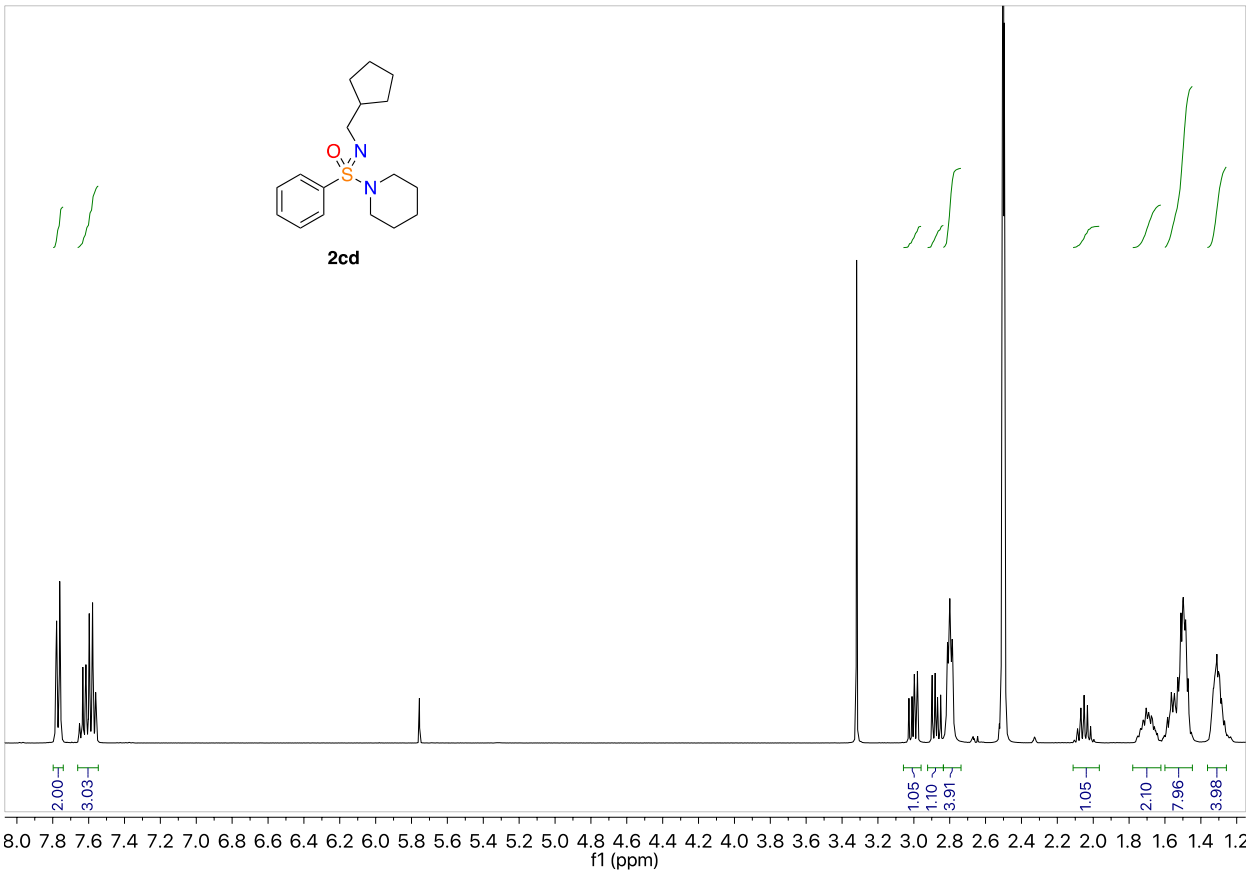
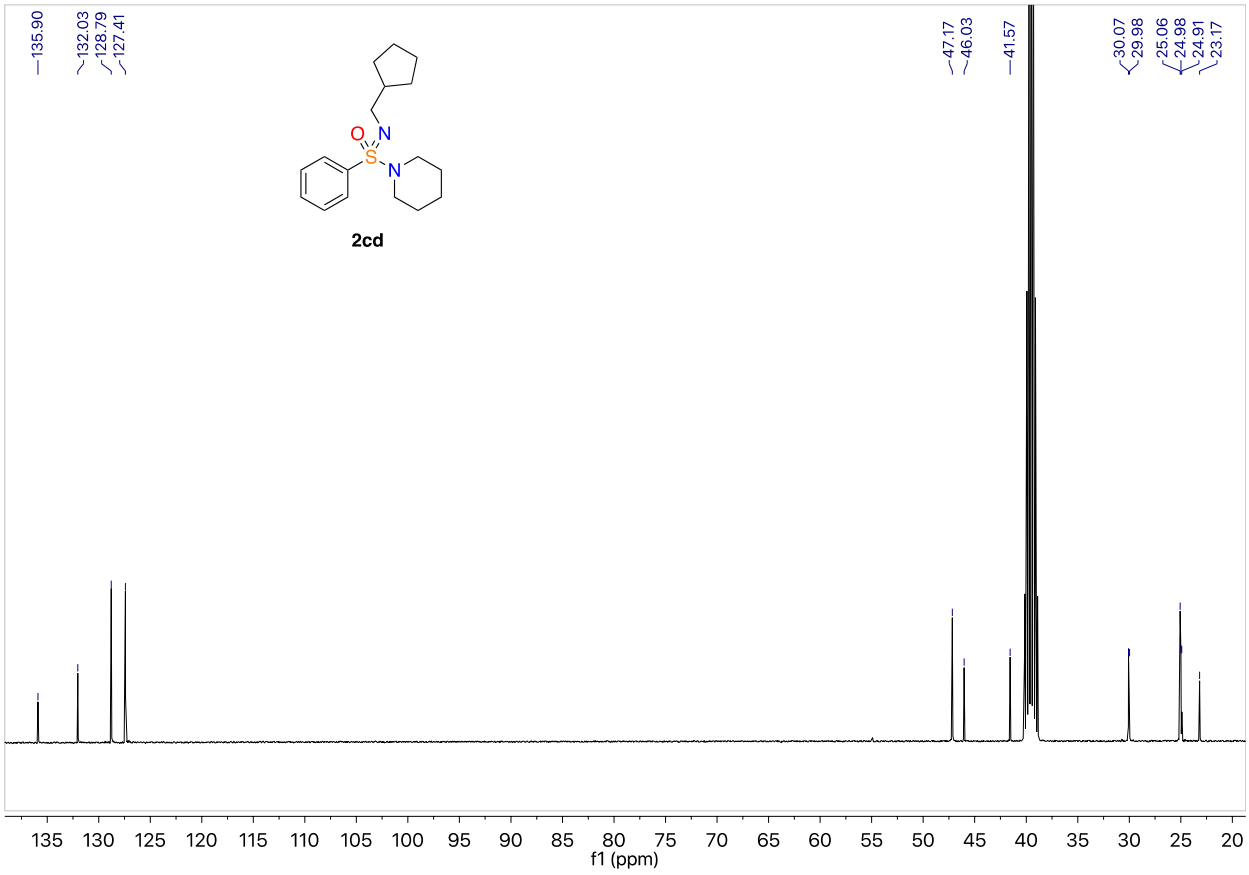
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

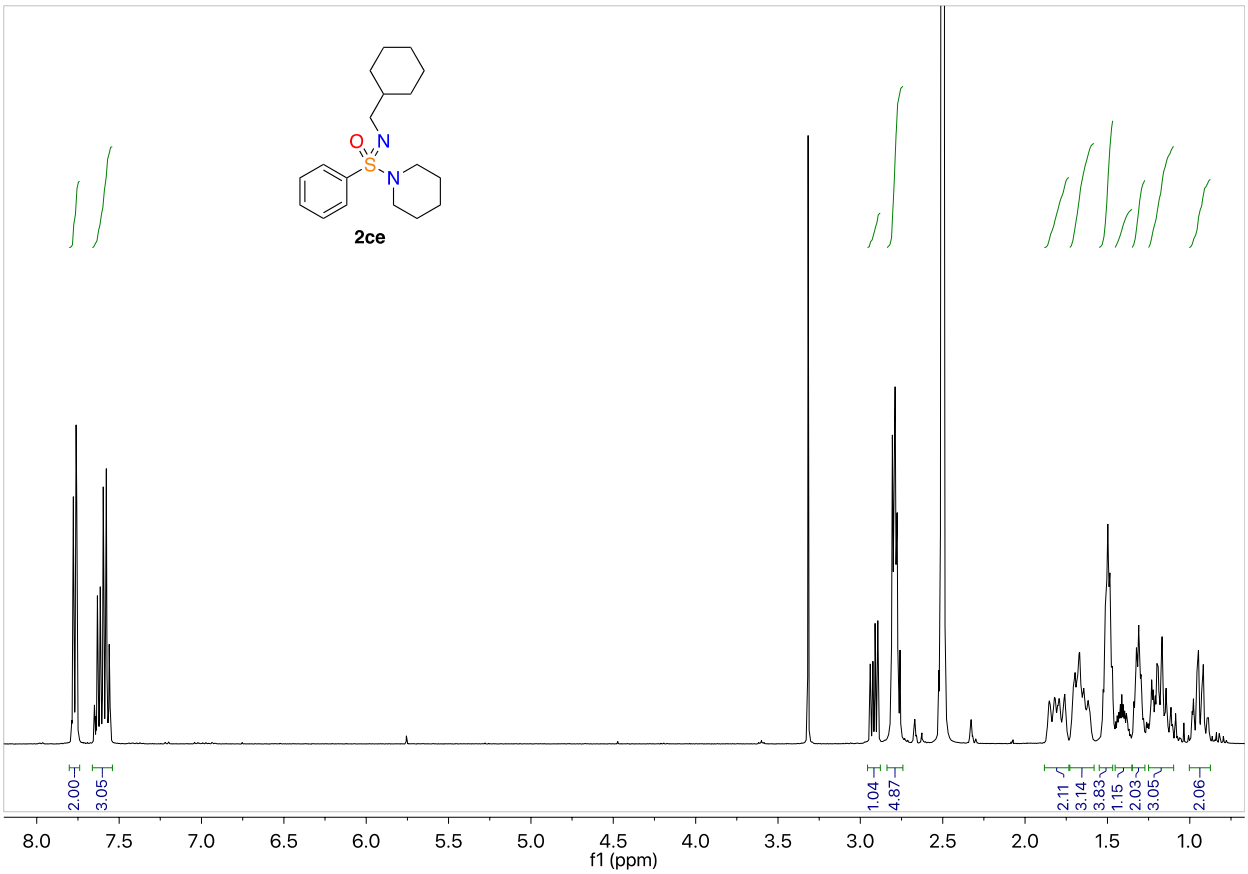

136.35
131.63
128.49
127.76
47.90
44.48
26.92
26.05
25.52
23.75
2cb
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
f1 (ppm)

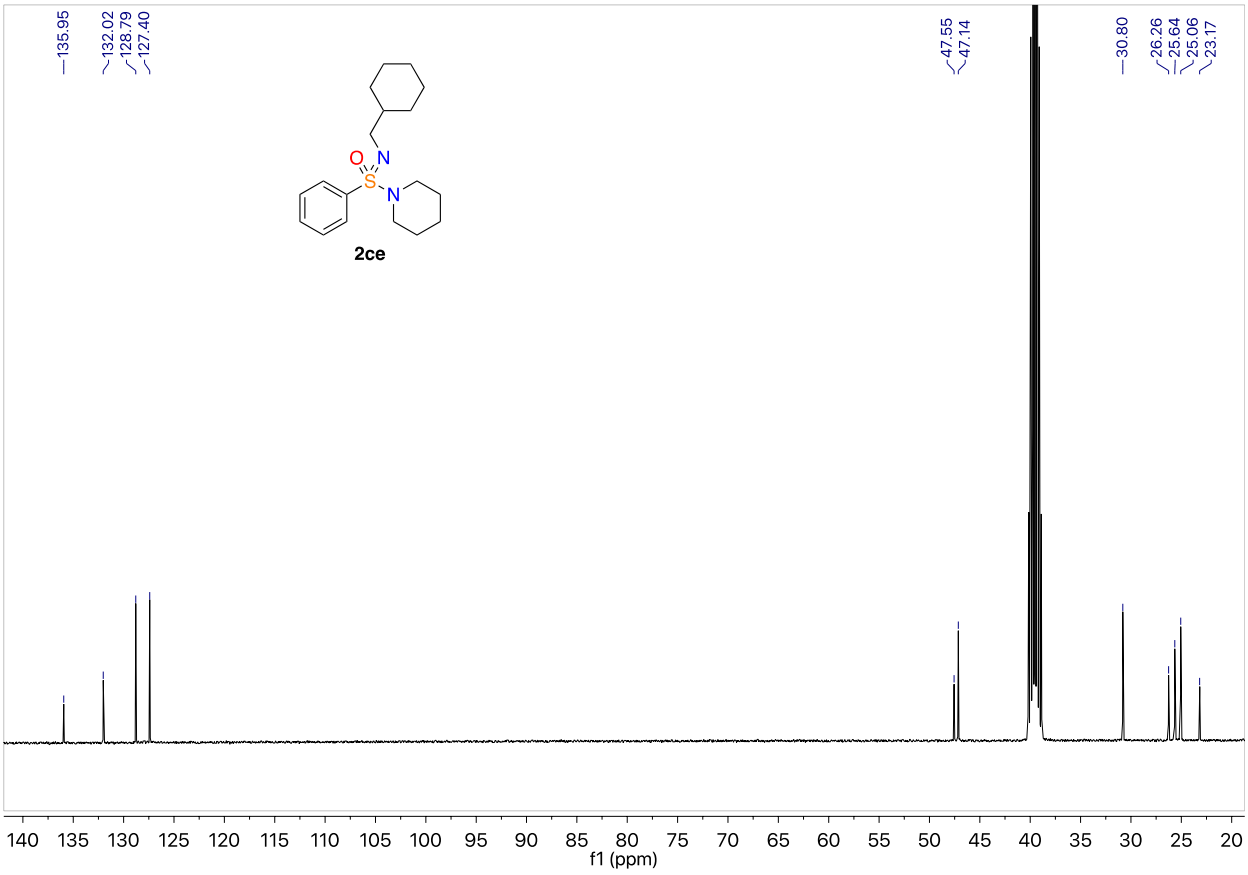

2cc
2.00
3.07
1.07
1.08
3.88
1.22
2.14
4.21
4.05
2.09
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)

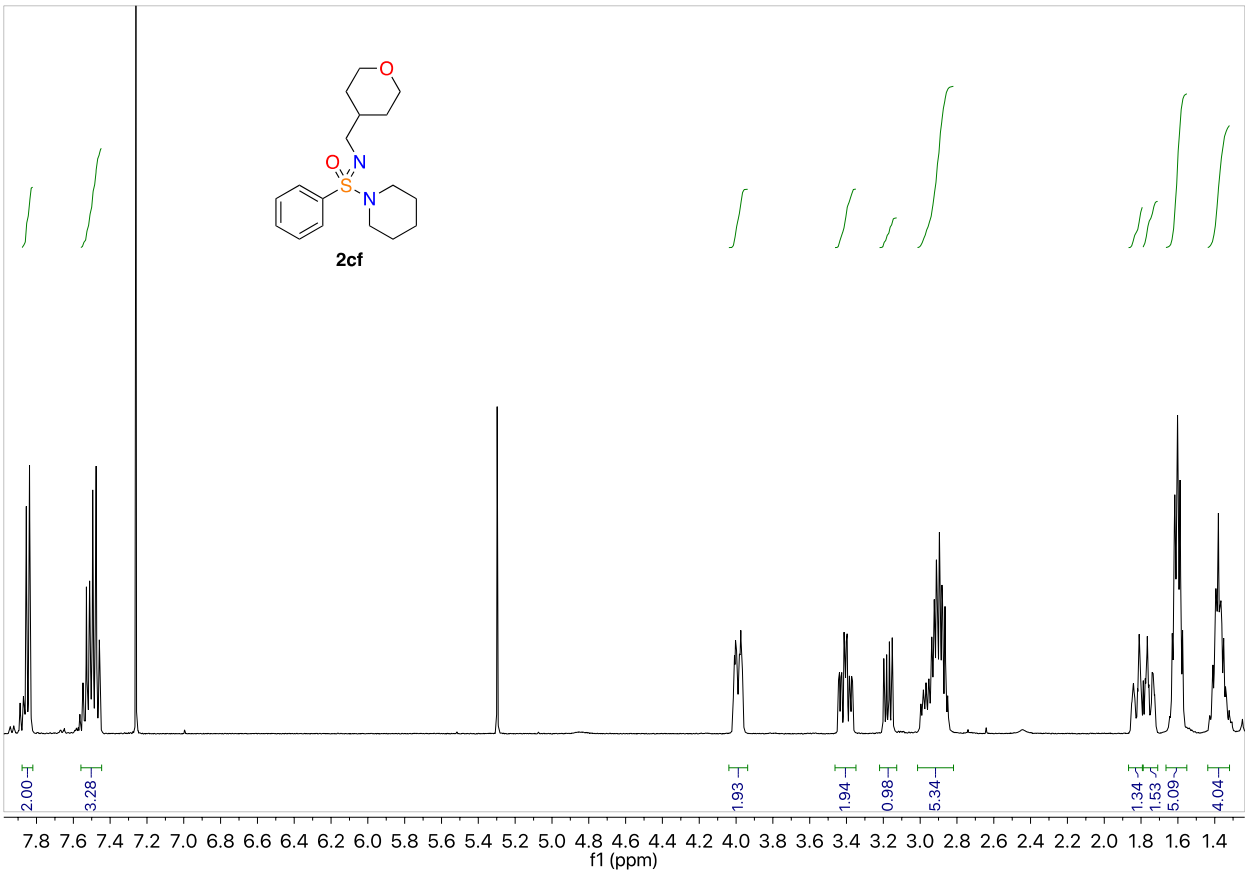

135.85
132.05
128.79
127.42
47.19
46.61
37.01
25.30
25.06
23.16
17.74
2cc
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)

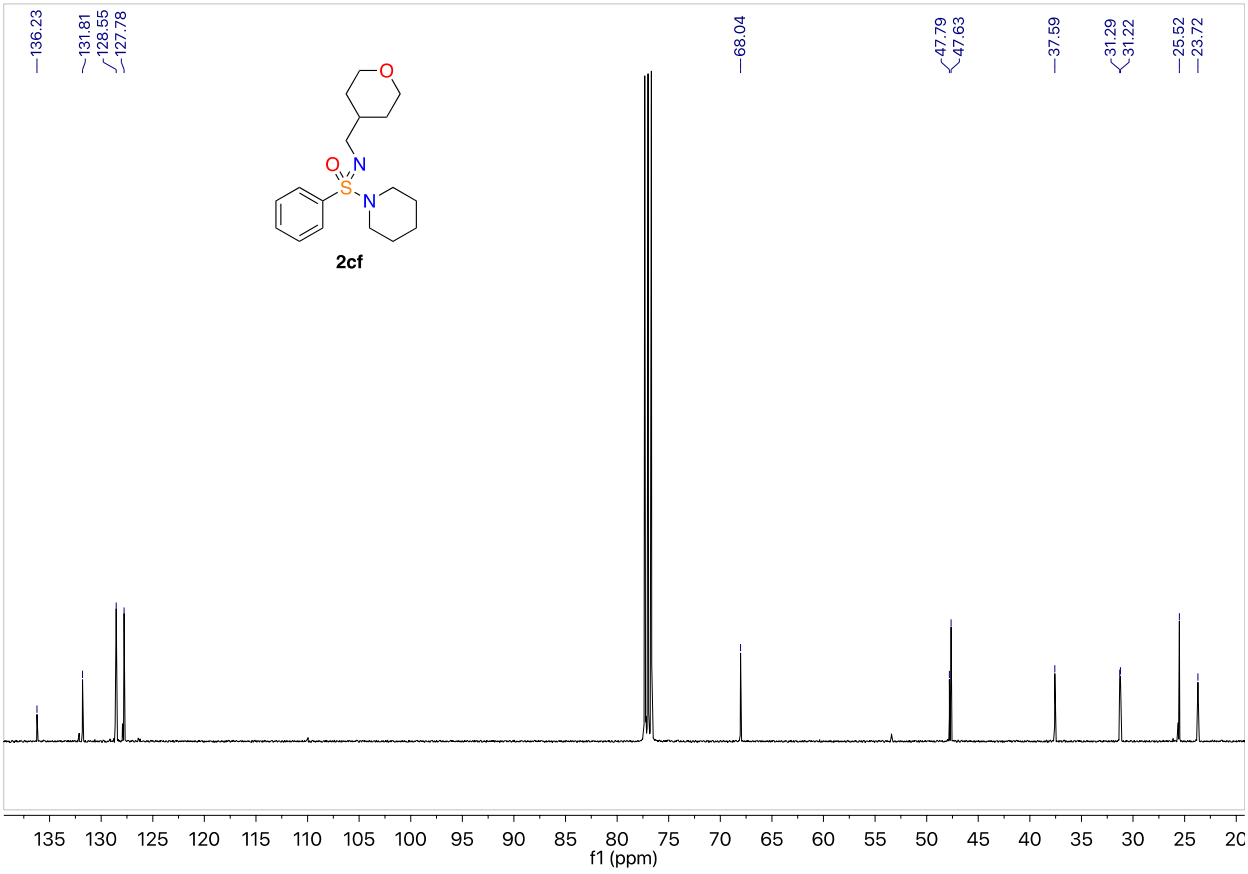

2cd
2.00
3.03
1.05
1.10
3.91
1.05
2.10
7.96
3.98
f1 (ppm)

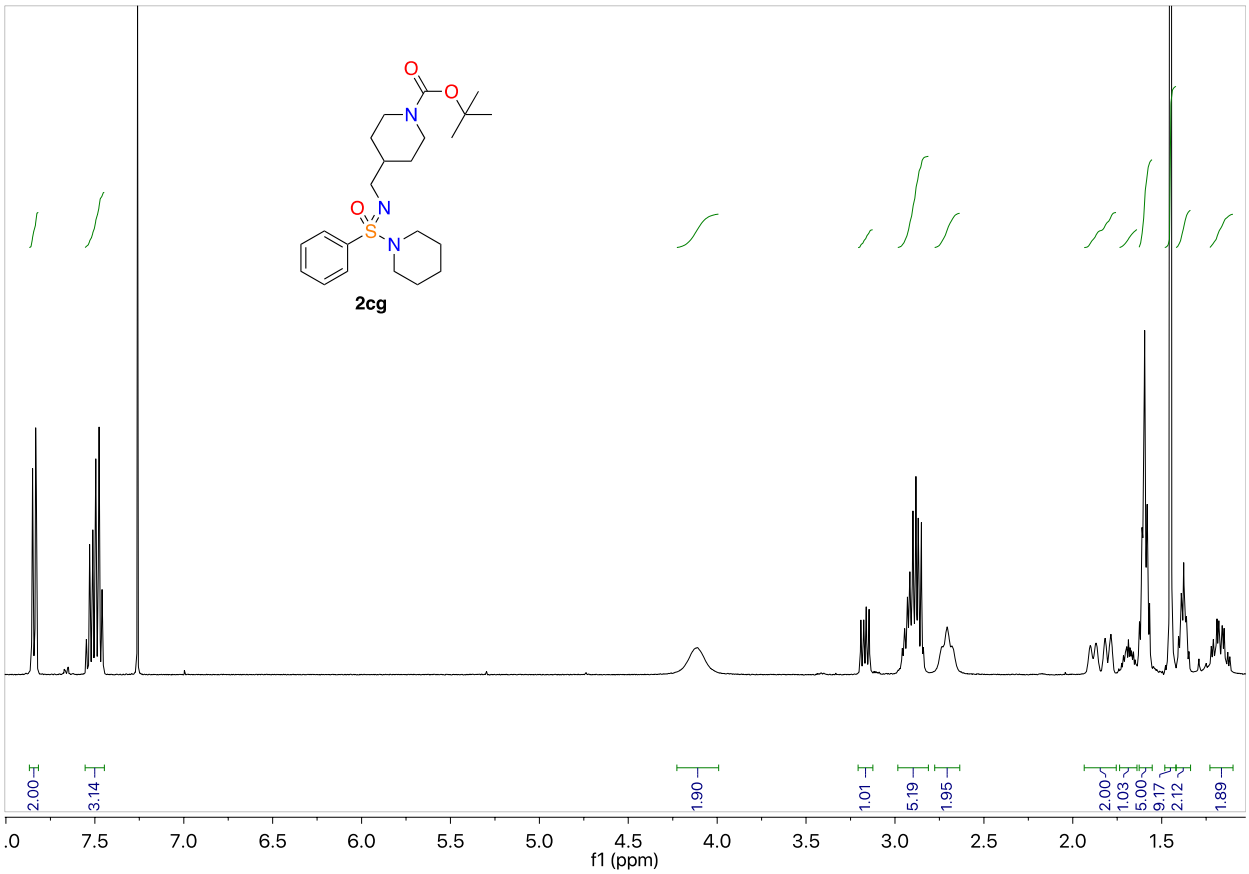

135.90
132.03
128.79
127.41
47.17
46.03
41.57
30.07
29.98
25.06
24.98
24.91
23.17
2cd
f1 (ppm)

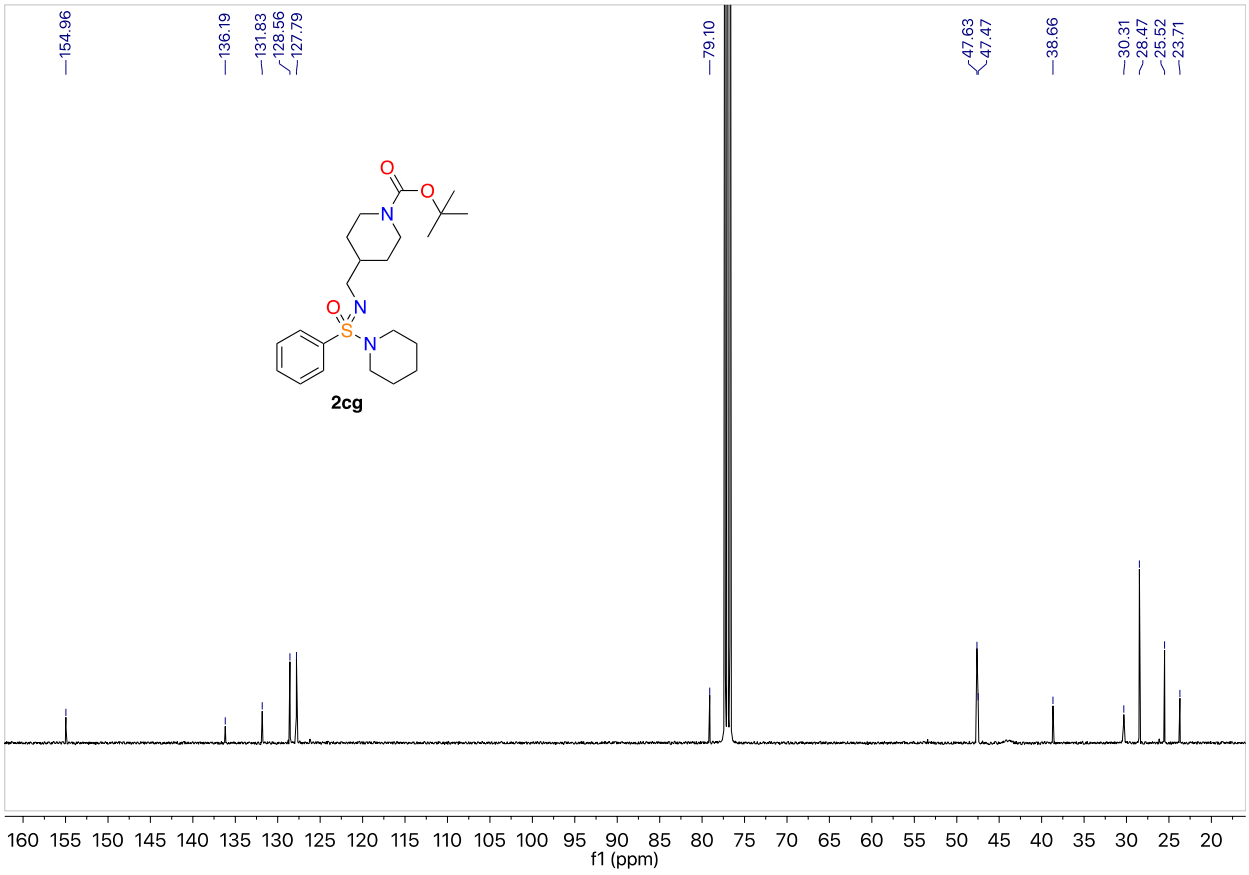

2ce
2.00
3.05
1.04
4.87
2.11
3.14
3.83
1.15
2.03
3.05
2.06
f1 (ppm)

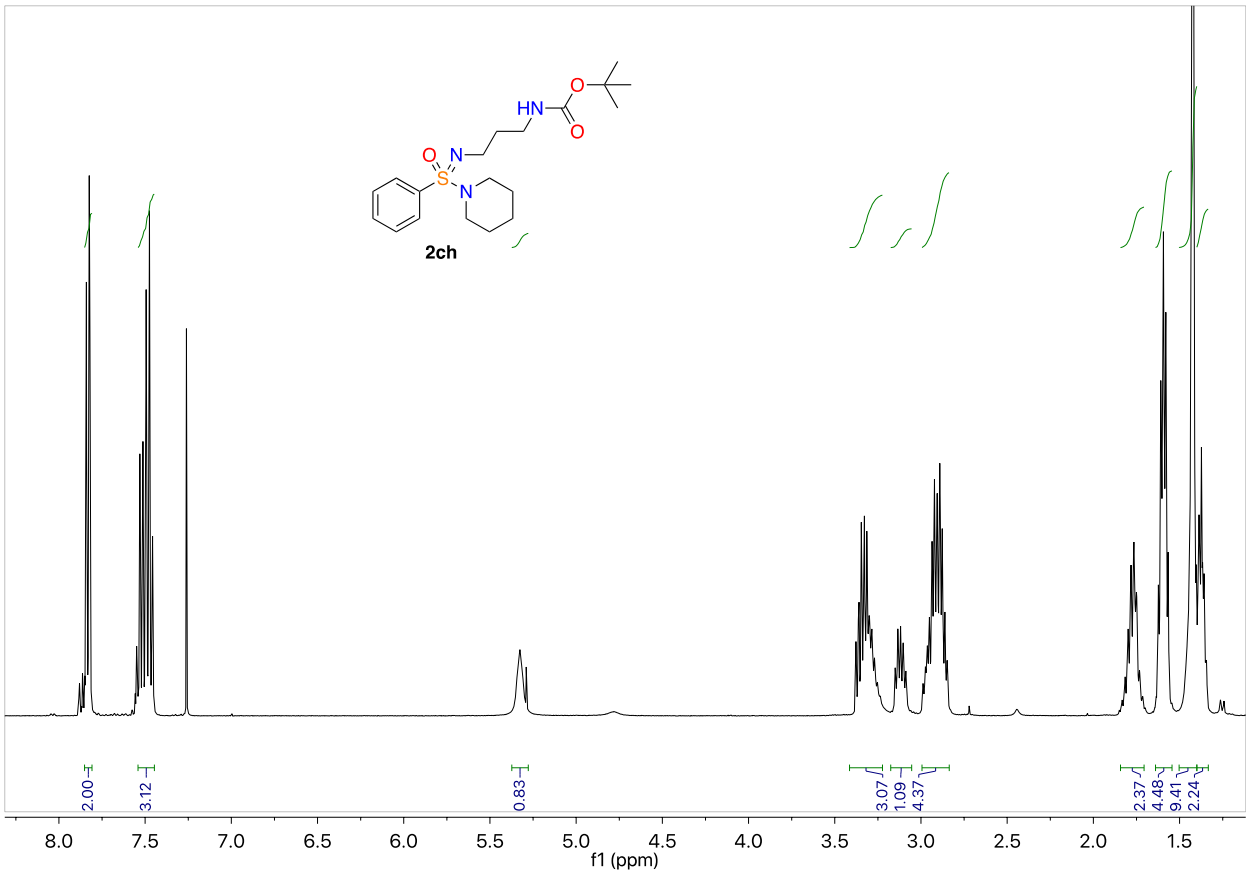

135.95
132.02
128.79
127.40
47.55
47.14
30.80
26.26
25.64
25.06
23.17
2ce
f1 (ppm)

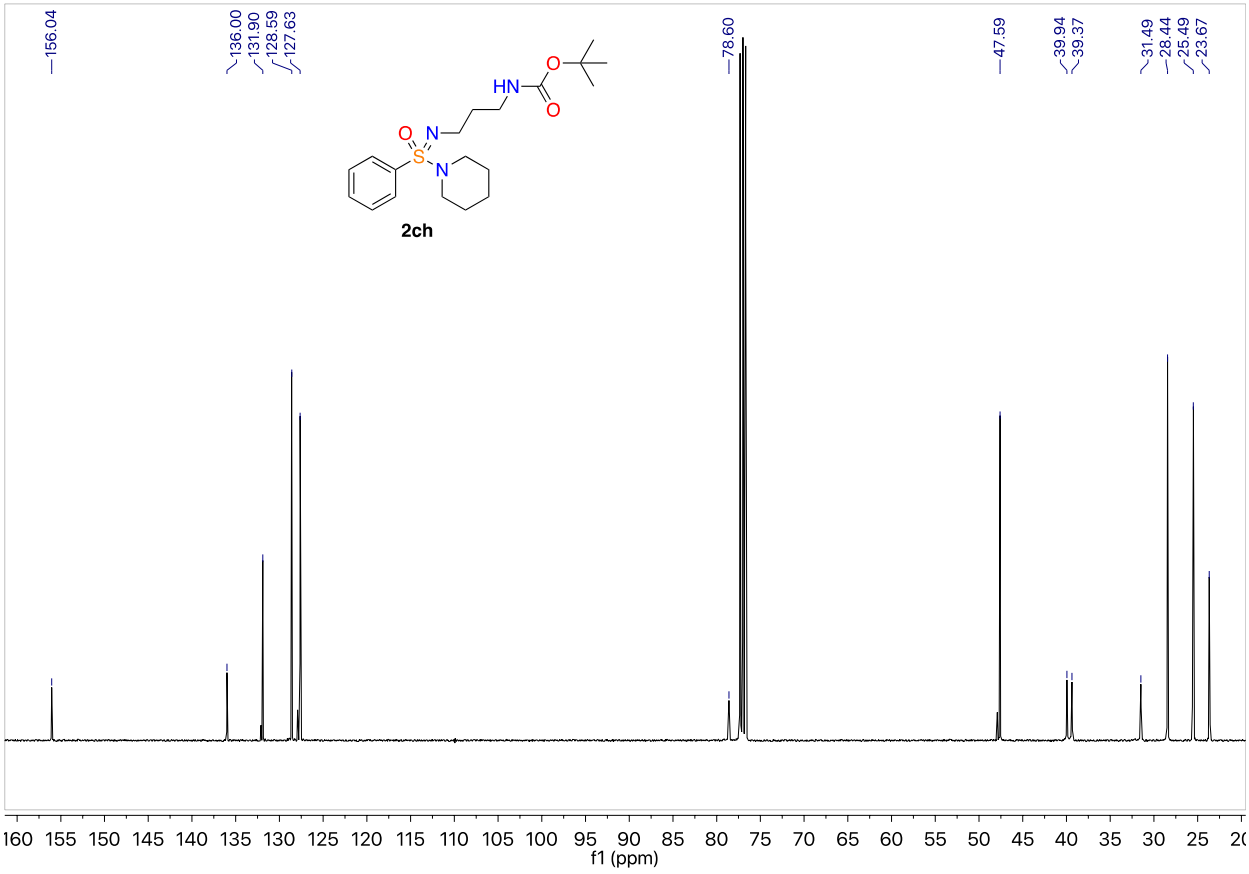

2cf
2.00
3.28
1.93
1.94
0.98
5.34
1.34
1.53
5.09
4.04
7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)

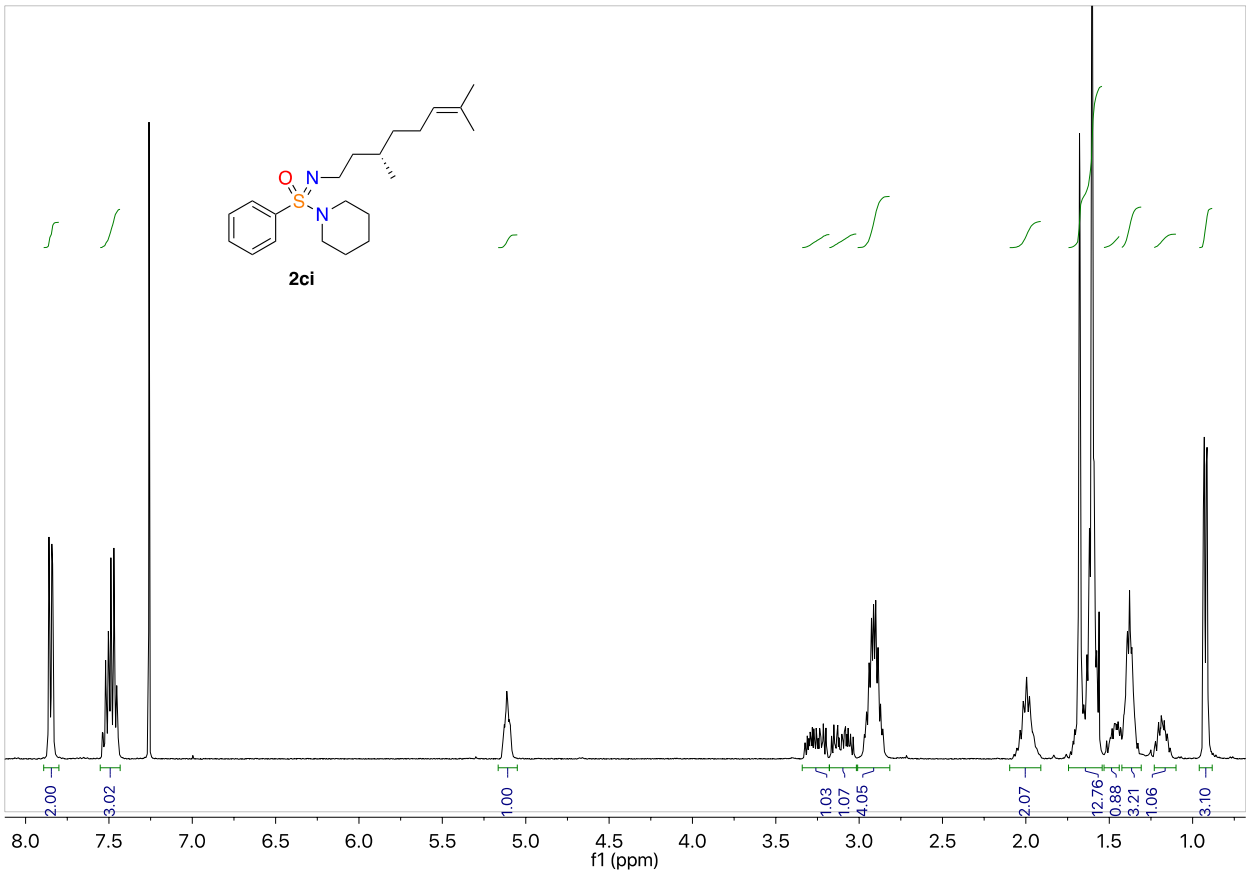

136.23
131.81
128.55
127.78
68.04
47.79
47.63
37.59
31.29
31.22
25.52
23.72
2cf
135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

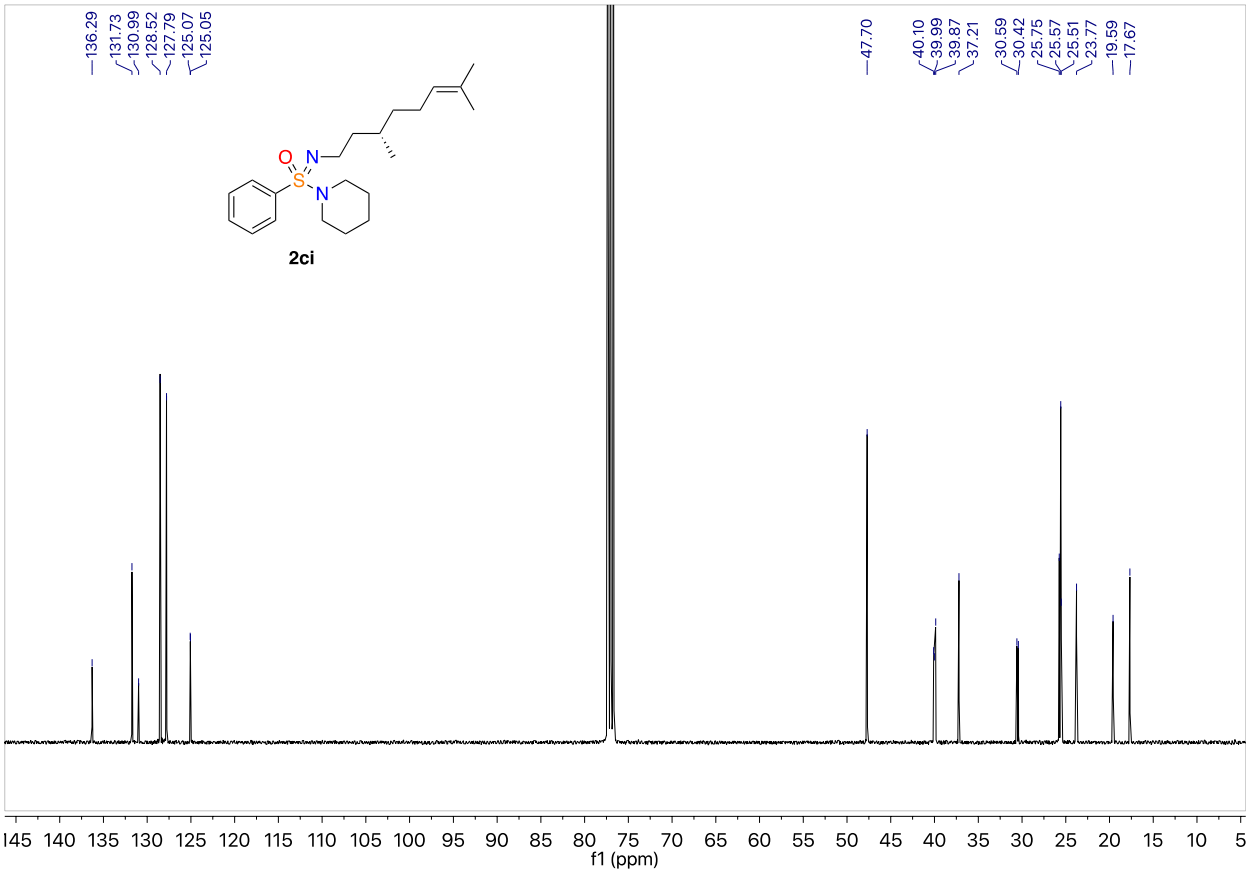

2cg
2.00
3.14
1.90
1.01
5.19
1.95
2.00
1.03
5.00
9.17
2.12
1.89
f1 (ppm)

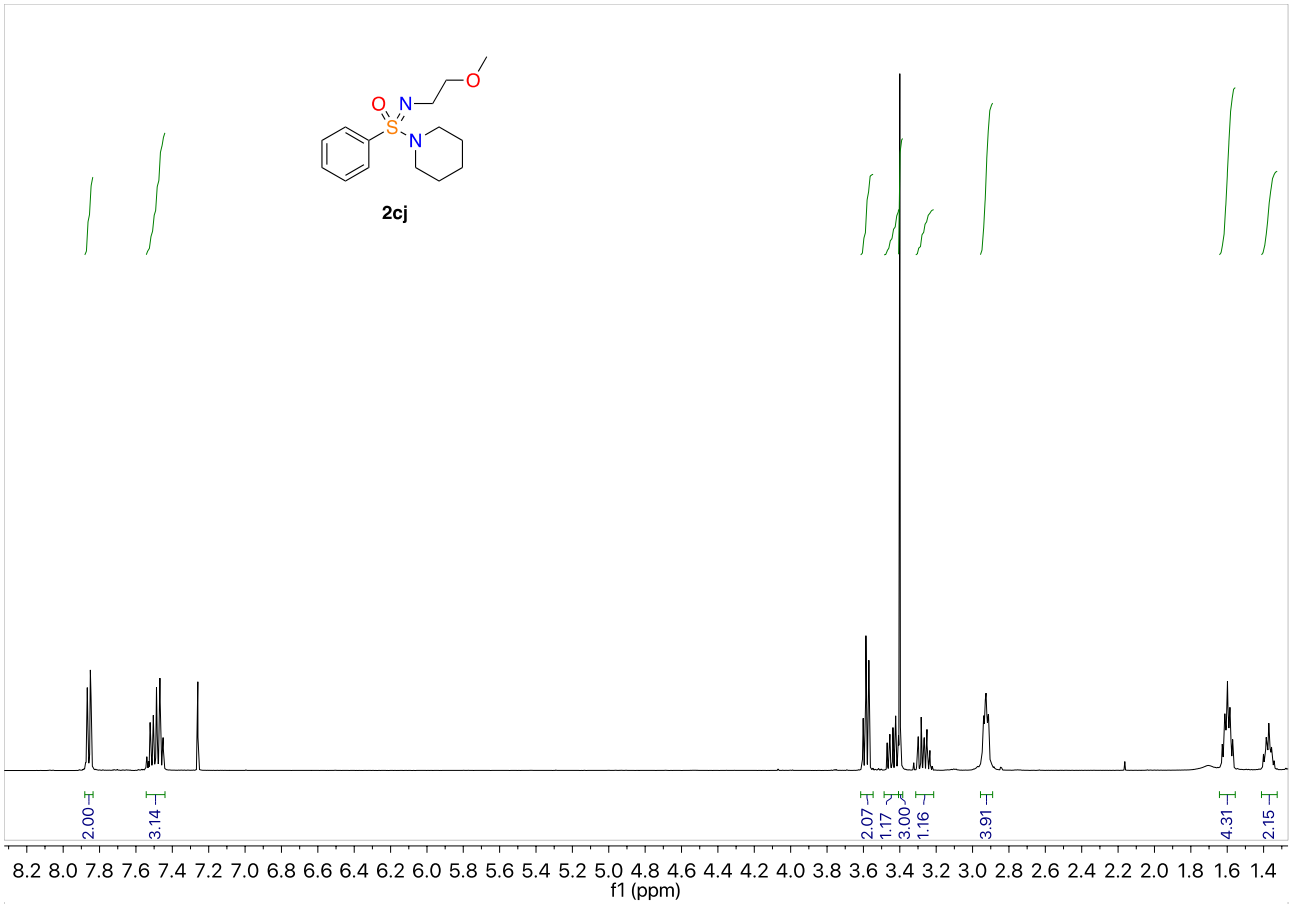

154.96
136.19
131.83
128.56
127.79
79.10
47.63
47.47
38.66
30.31
28.47
25.52
23.71
2cg
f1 (ppm)

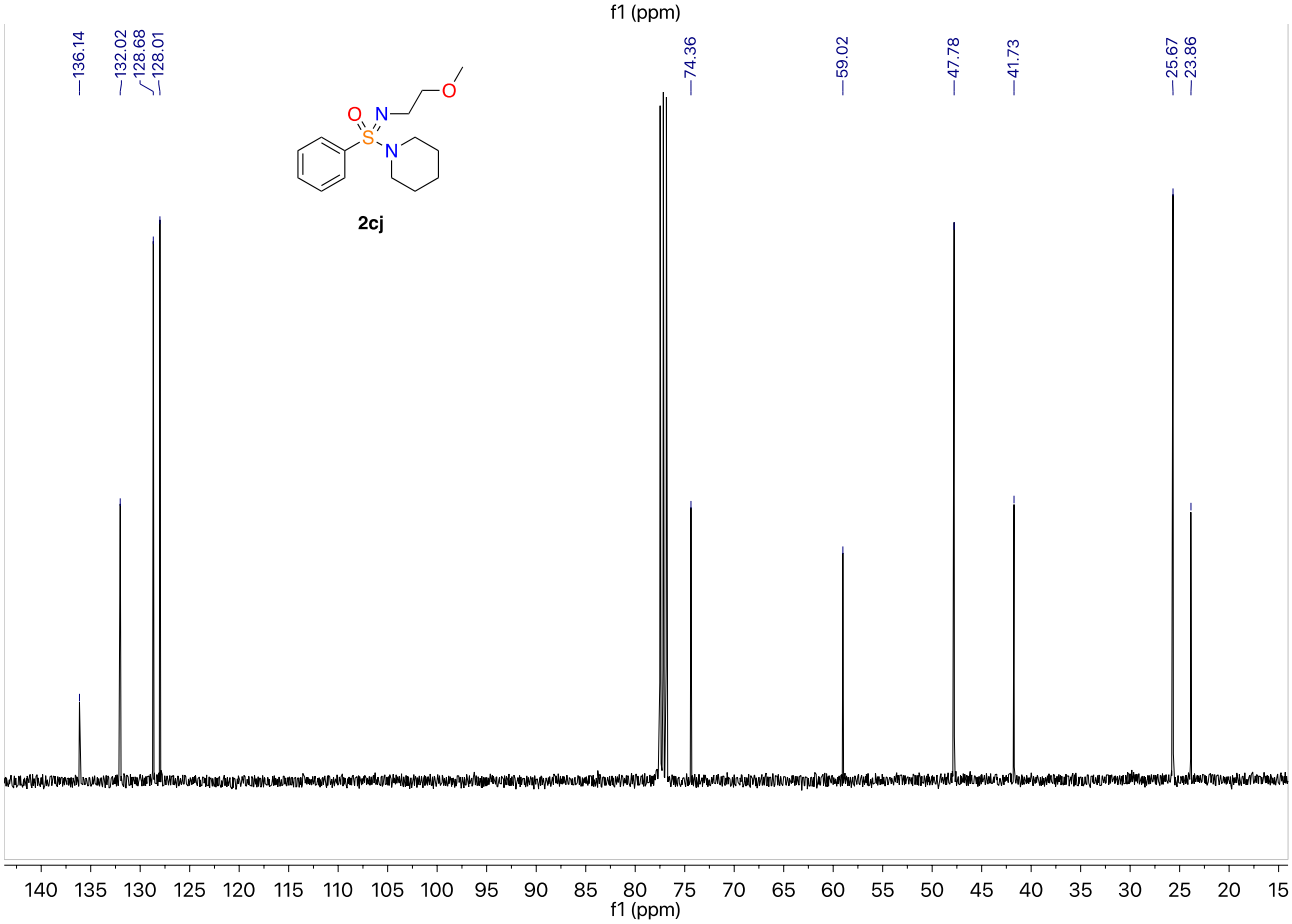

2ch
2.00
3.12
0.83
3.07
1.09
4.37
2.37
4.48
9.41
2.24
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

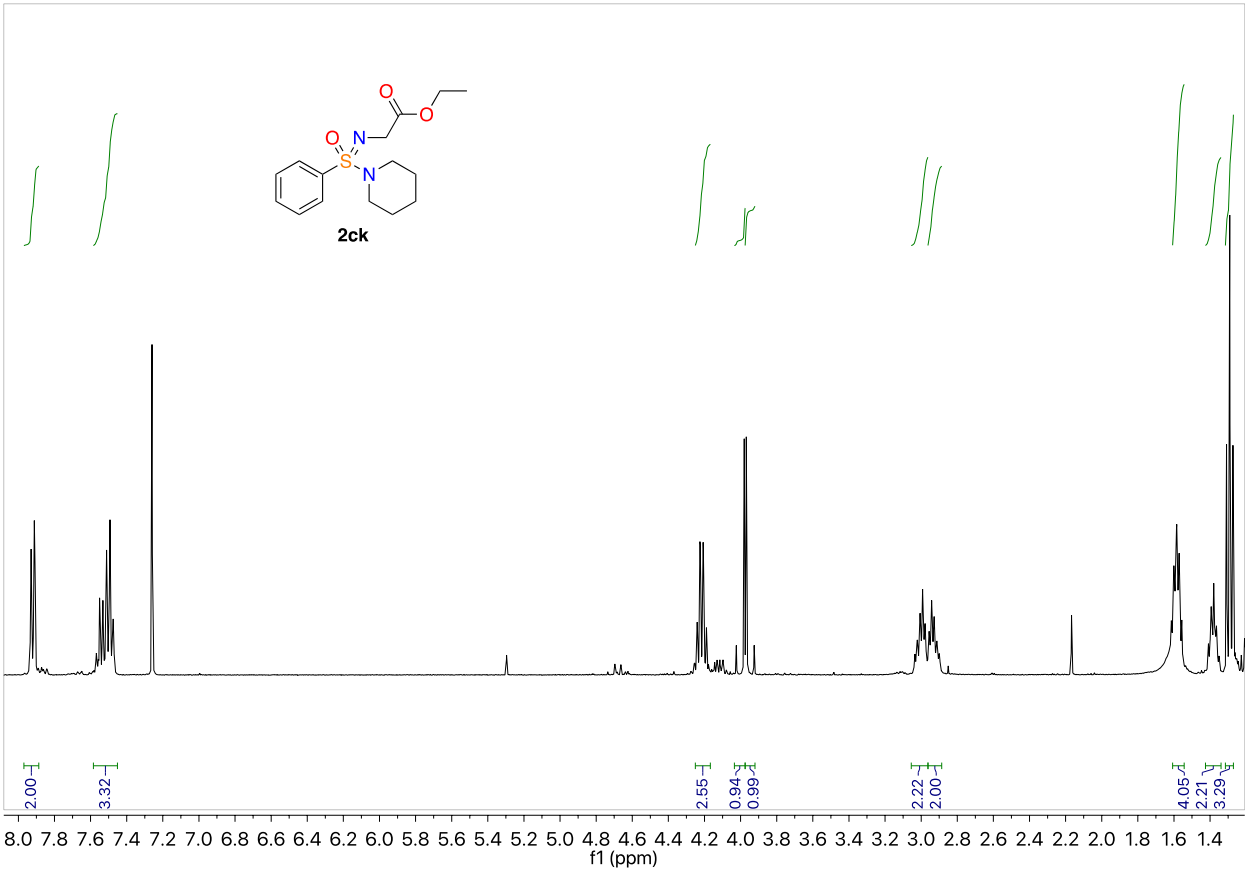

156.04
136.00
131.90
128.59
127.63
78.60
47.59
39.94
39.37
31.49
28.44
25.49
23.67
2ch
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
f1 (ppm)

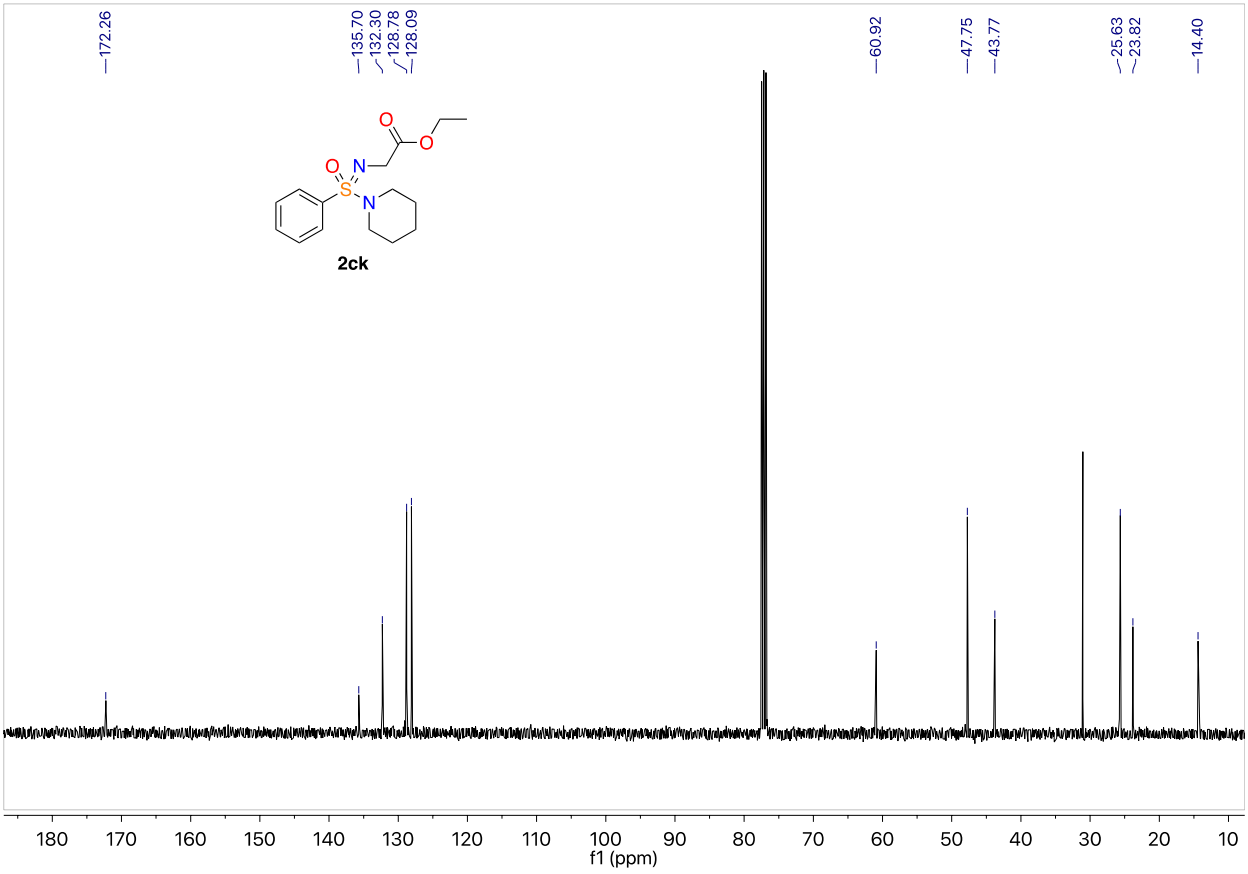

2ci
2.00
3.02
1.00
1.03
1.07
4.05
2.07
12.76
0.88
3.21
1.06
3.10
f1 (ppm)

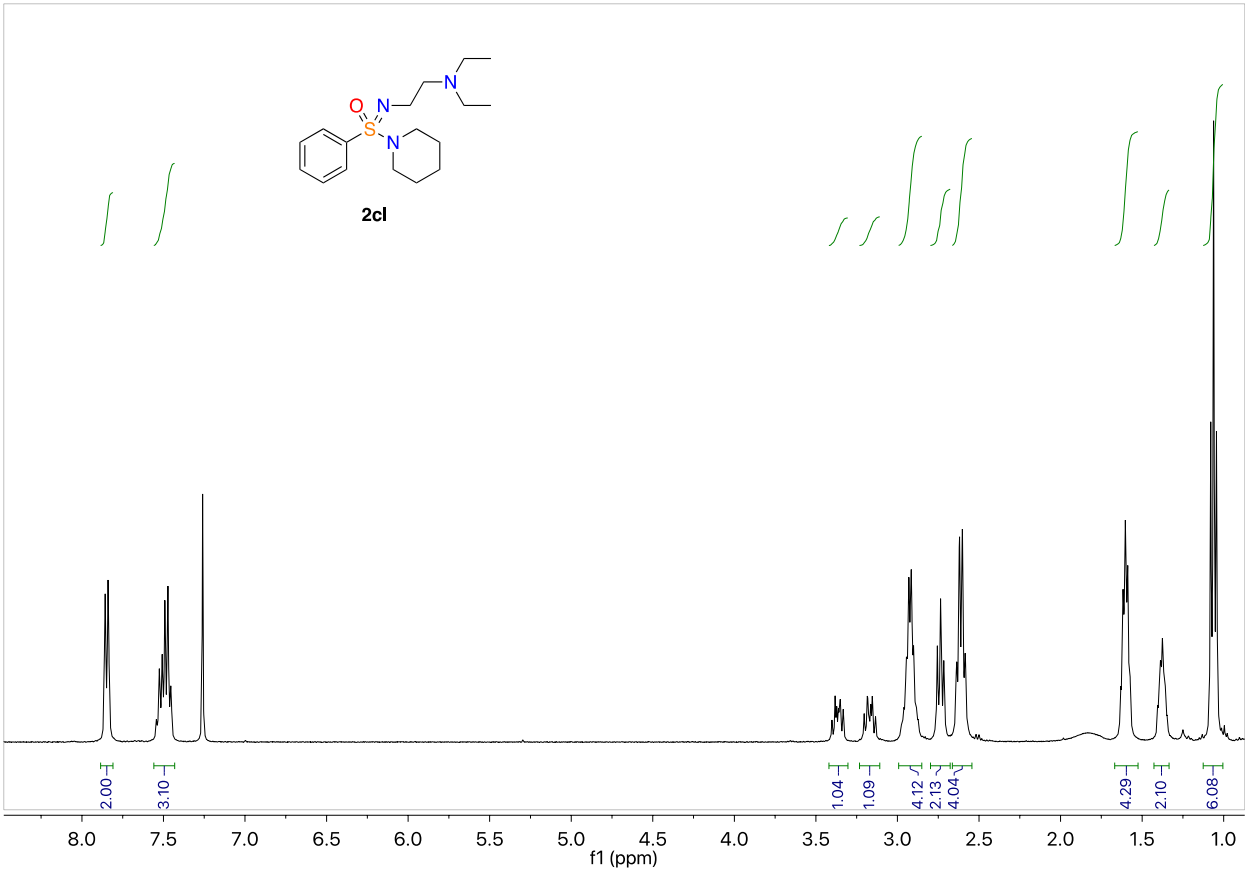

136.29
131.73
130.99
128.52
127.79
125.07
125.05
47.70
40.10
39.99
39.87
37.21
30.59
30.42
25.75
25.57
25.51
23.77
19.59
17.67
2ci
f1 (ppm)

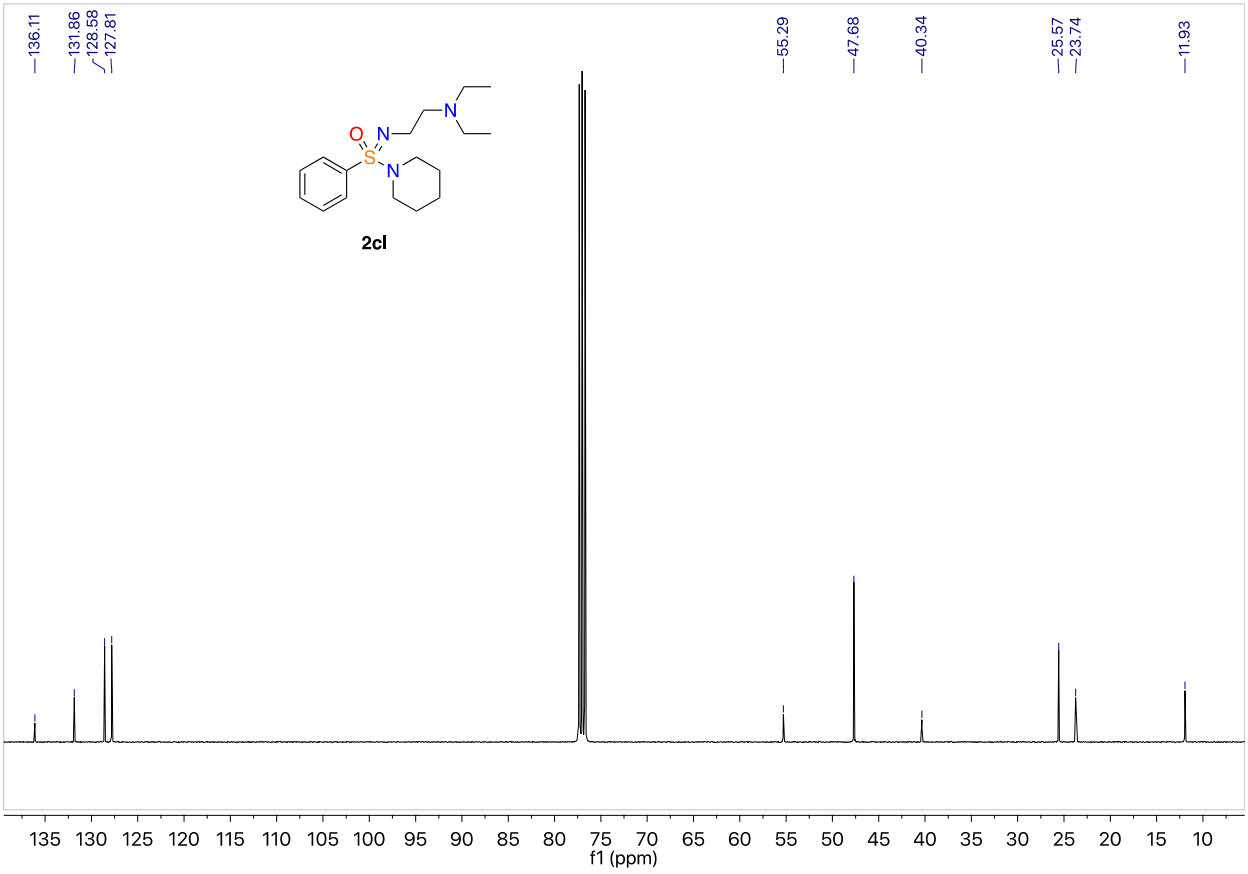

2cj
2.00
3.14
2.07
1.17
3.00
1.16
3.91
4.31
2.15
8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)

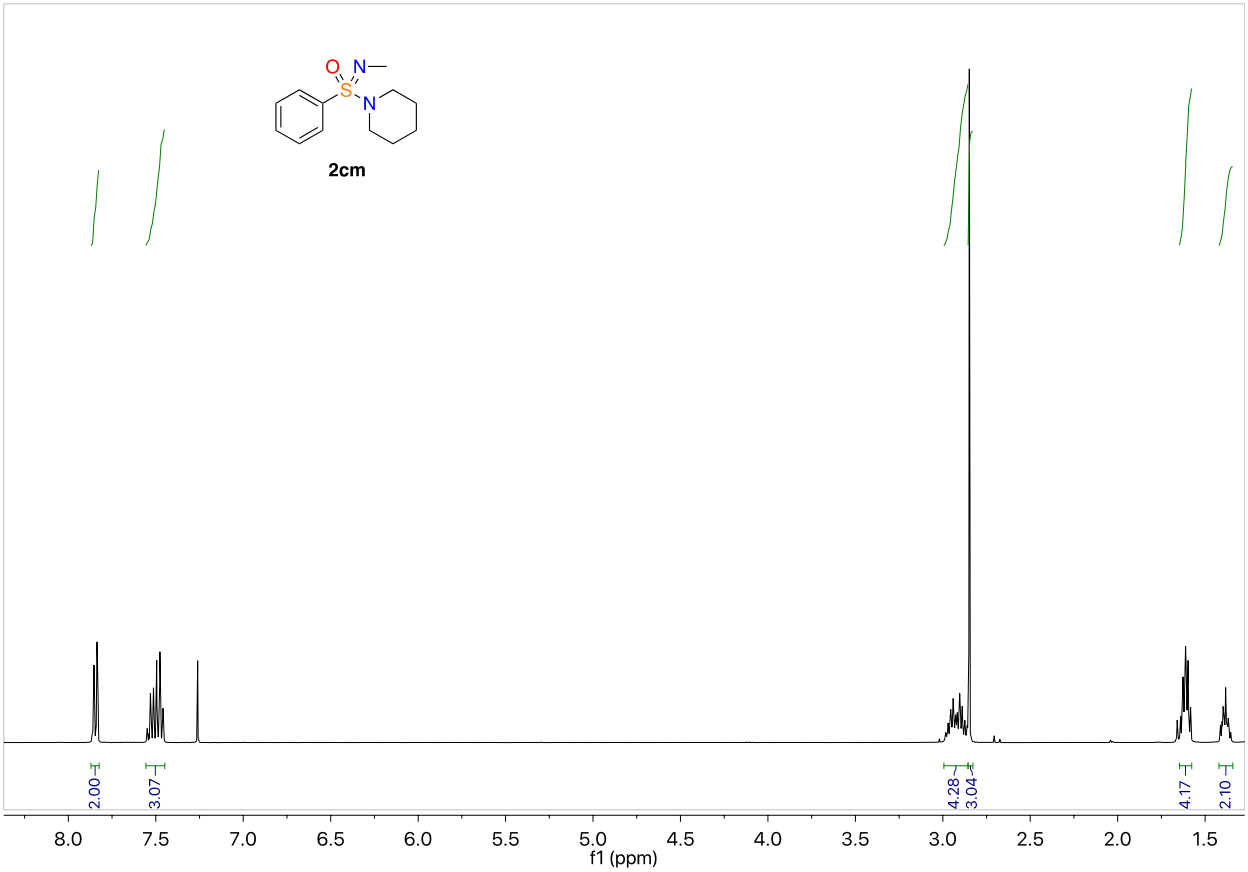

136.14
132.02
128.68
128.01
74.36
59.02
47.78
41.73
25.67
23.86
2cj
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)

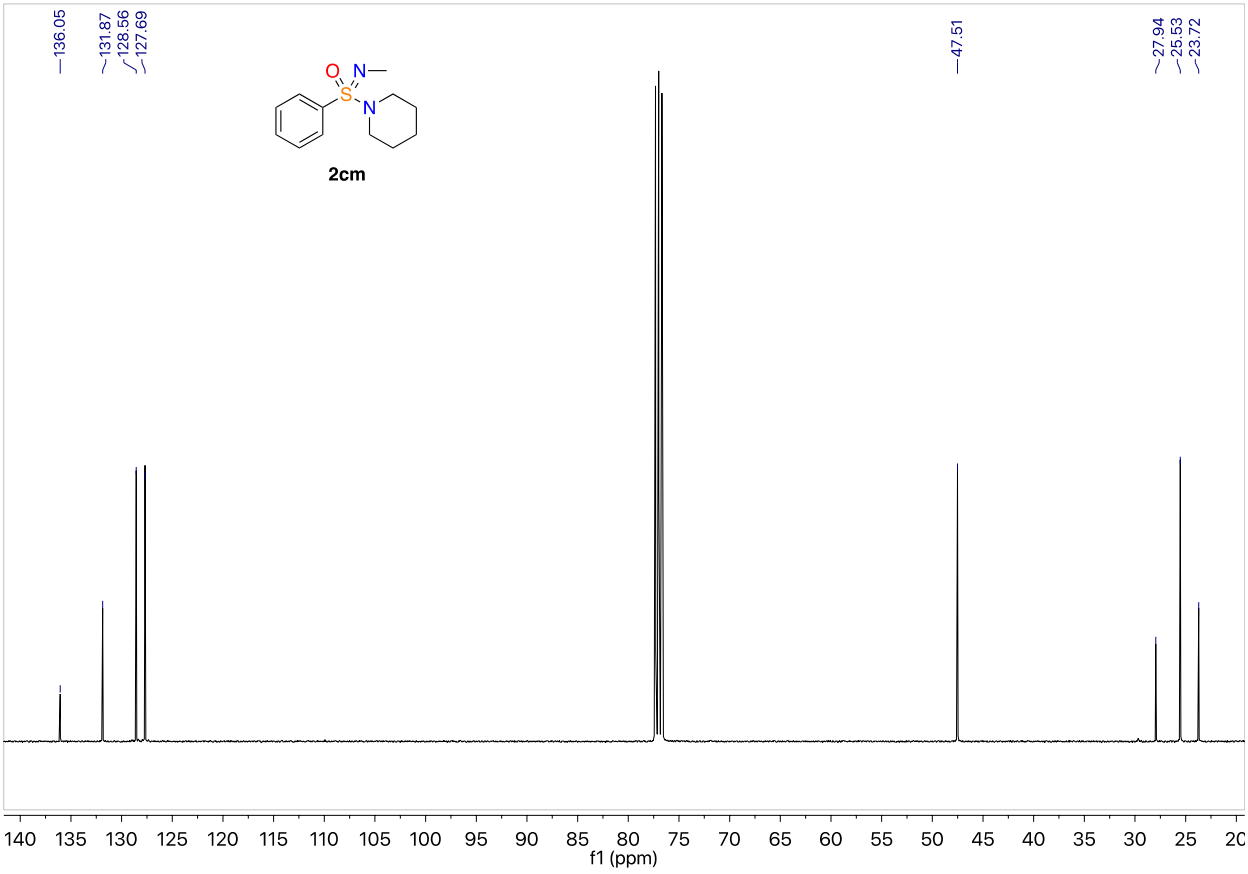

2ck
2.00
3.32
2.55
0.94
0.99
2.22
2.00
4.05
2.21
3.29
f1 (ppm)

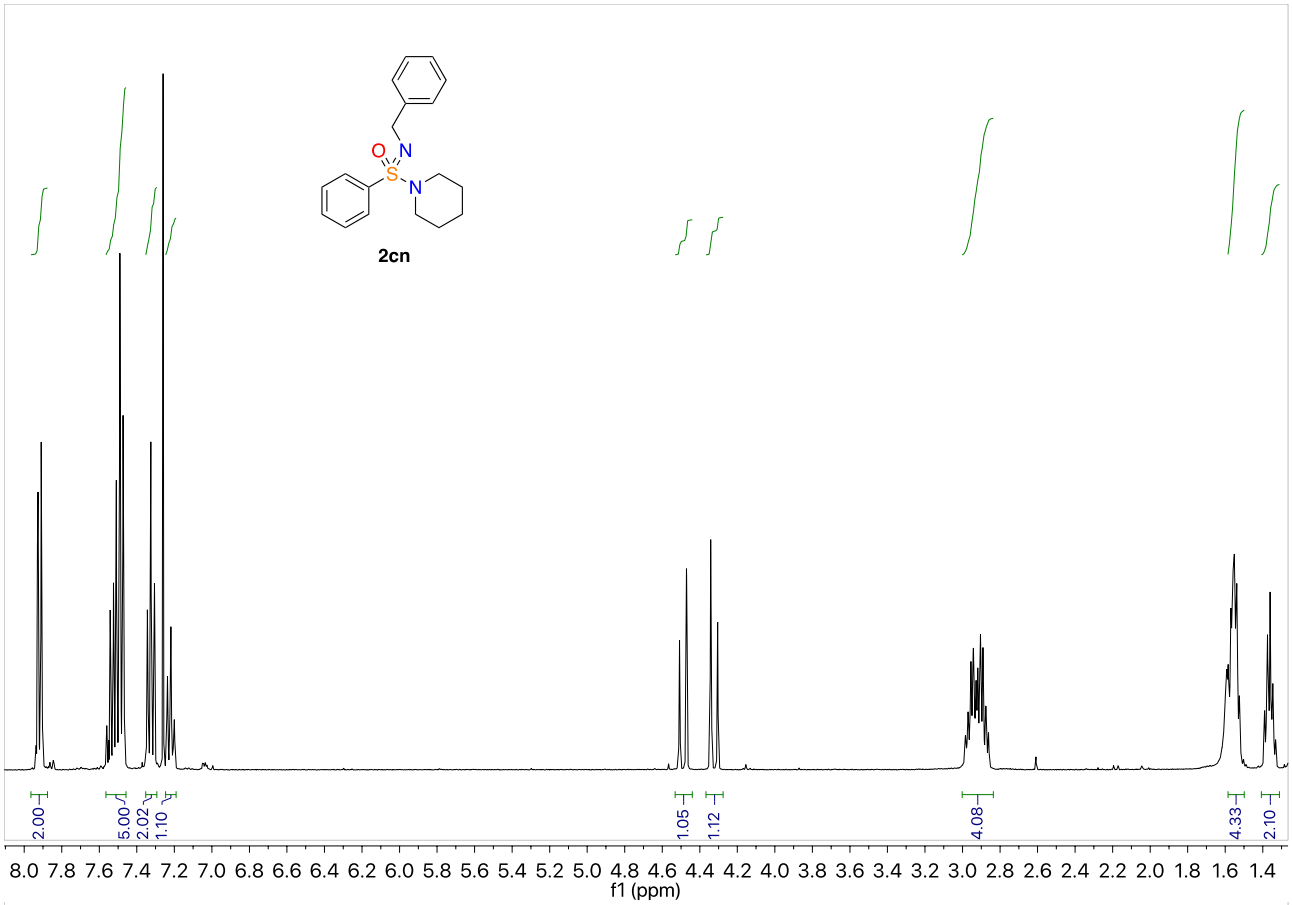

172.26
135.70
132.30
128.78
128.09
60.92
47.75
43.77
25.63
23.82
14.40
2ck
f1 (ppm)

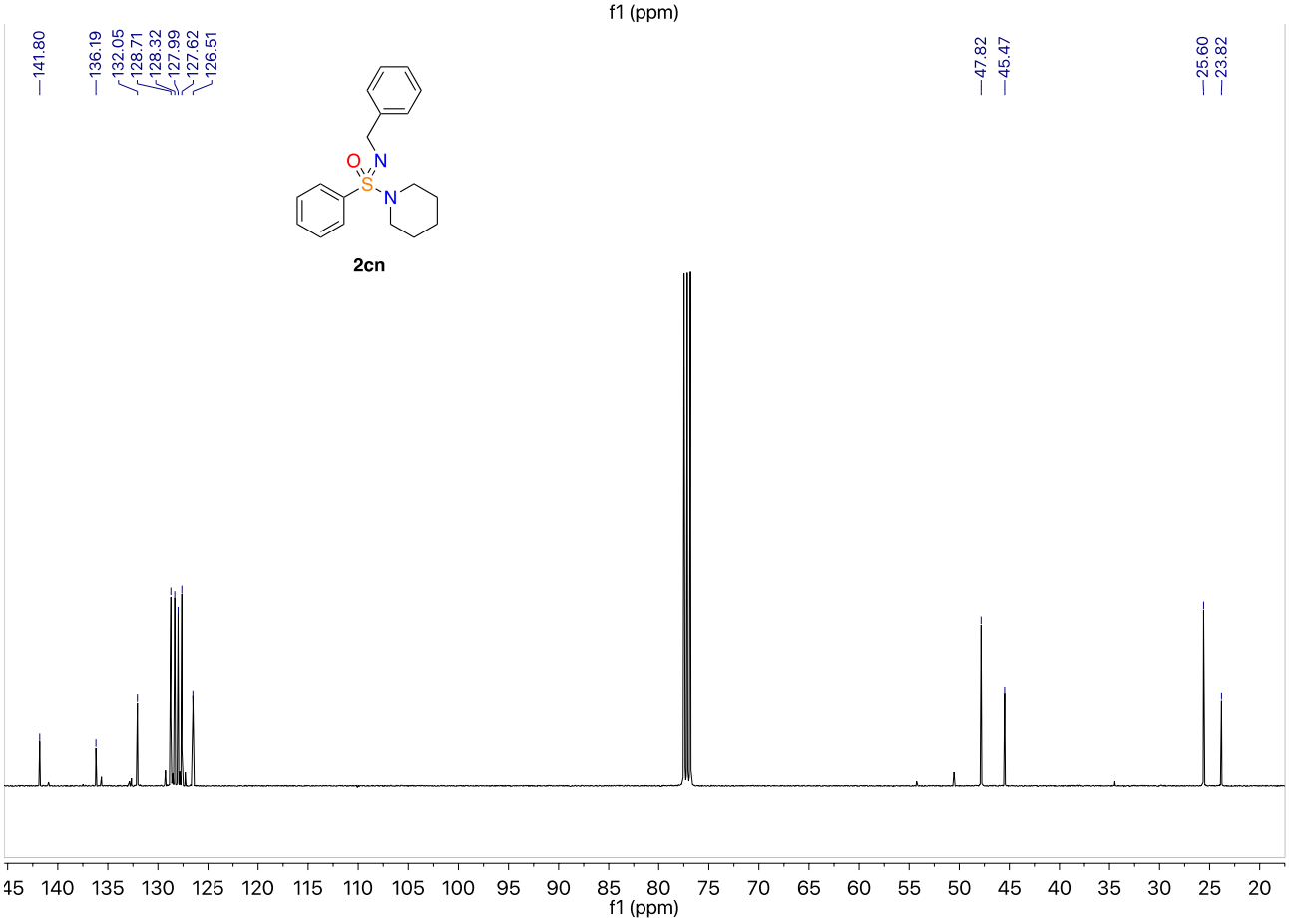

2cl
2.00
3.10
1.04
1.09
4.12
2.13
4.04
4.29
2.10
6.08
f1 (ppm)

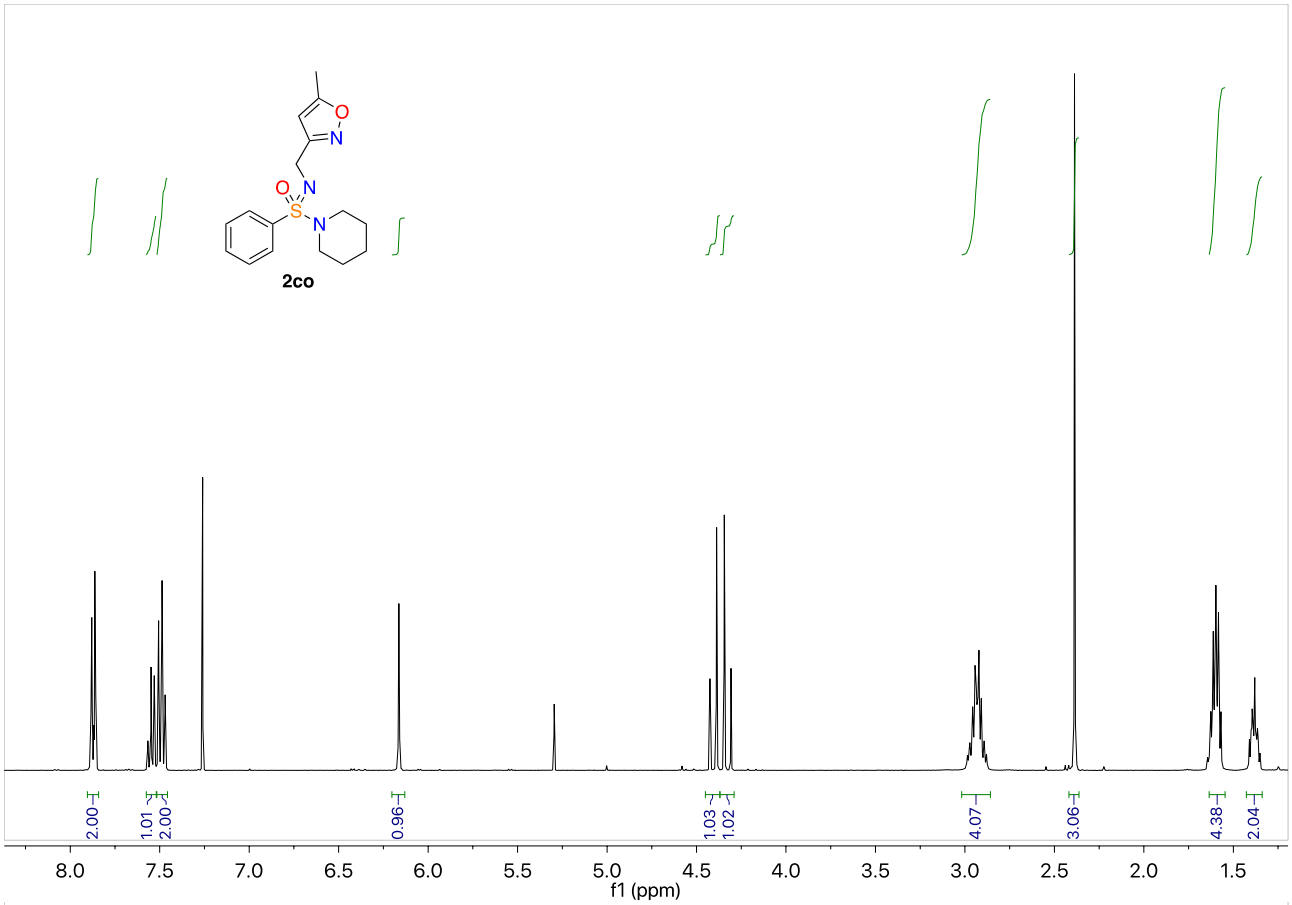

136.11
131.86
128.58
127.81
55.29
47.68
40.34
25.57
23.74
11.93
2cl
f1 (ppm)

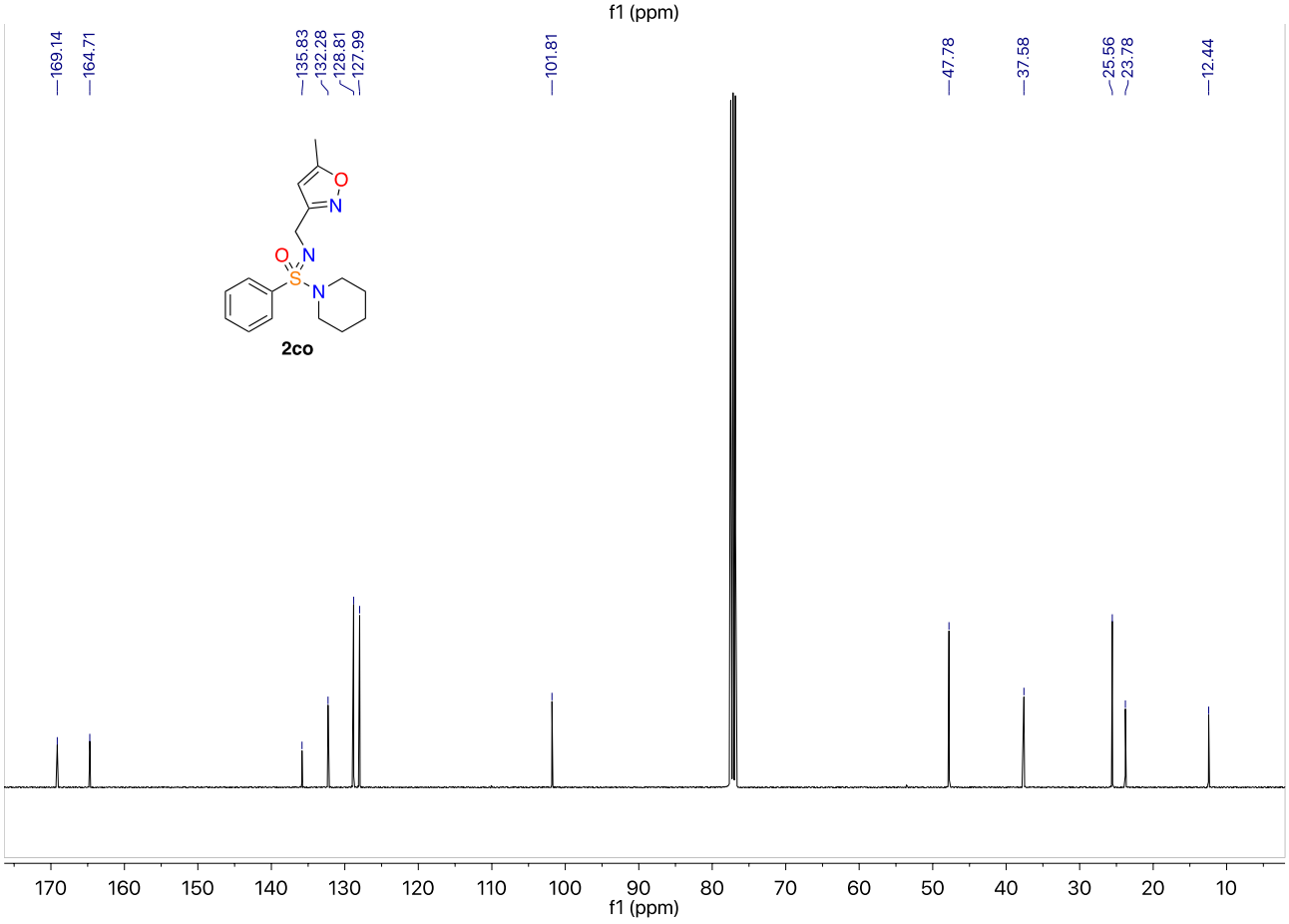

2cm
2.00
3.07
4.28
3.04
4.17
2.10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

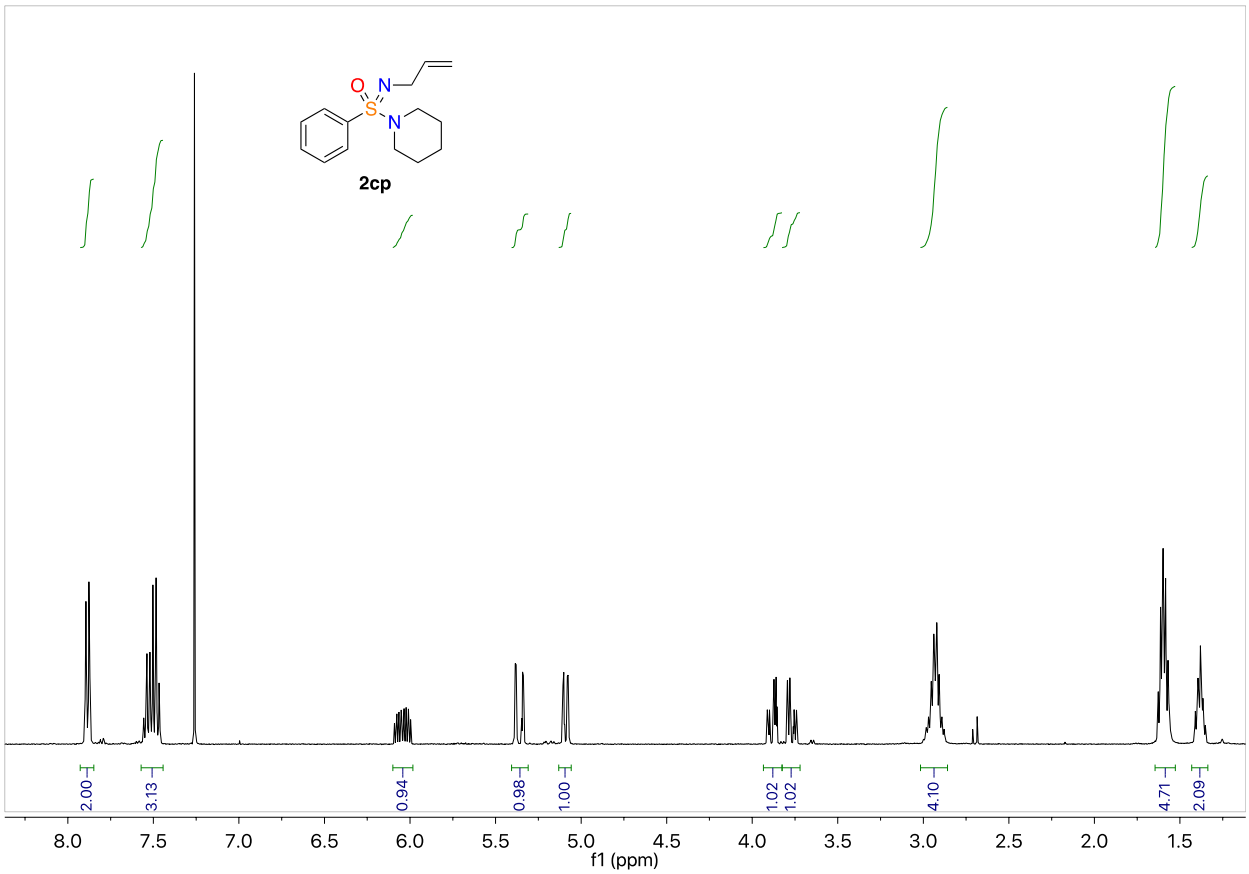

136.05
131.87
128.56
127.69
47.51
27.94
25.53
23.72
2cm
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
f1 (ppm)

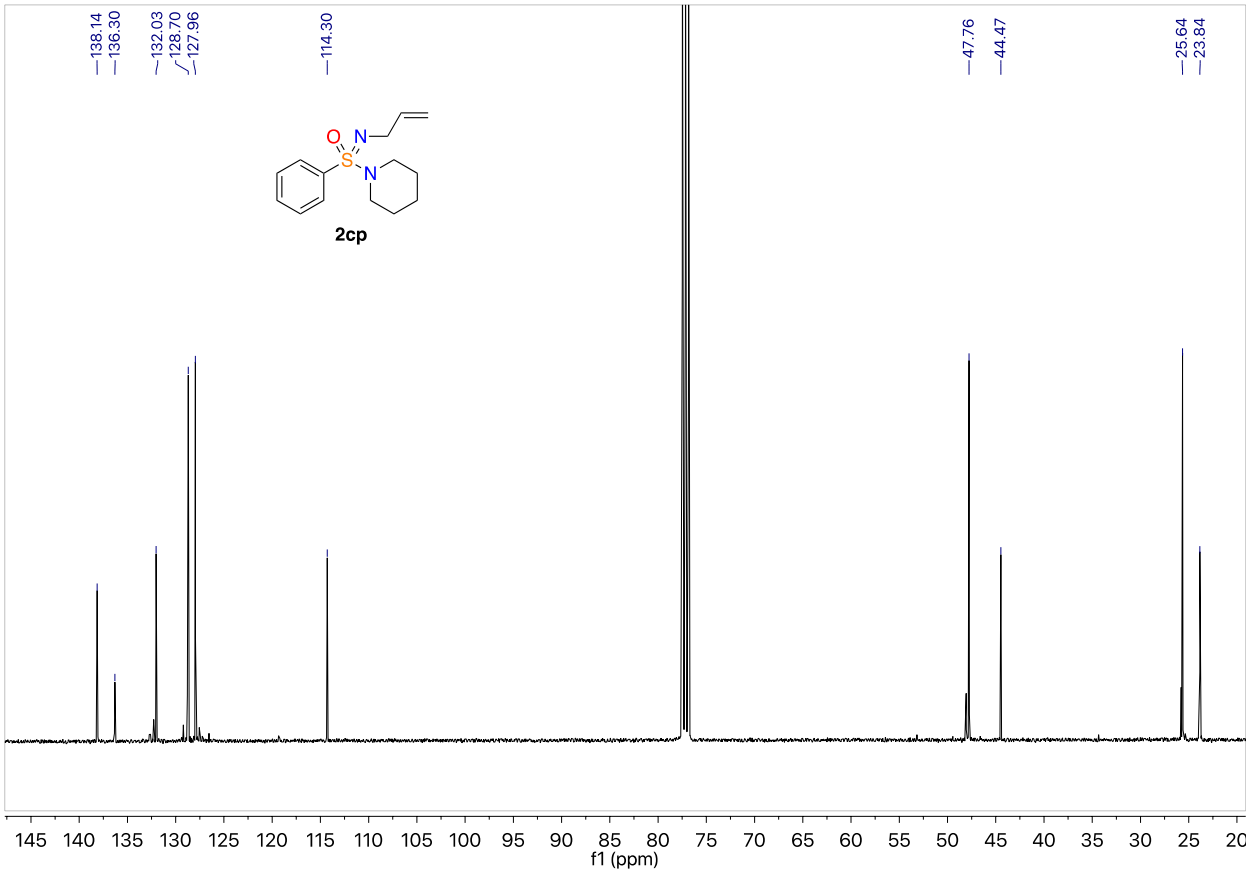

2cn
2.00
5.00
2.02
1.10
1.05
1.12
4.08
4.33
2.10
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)

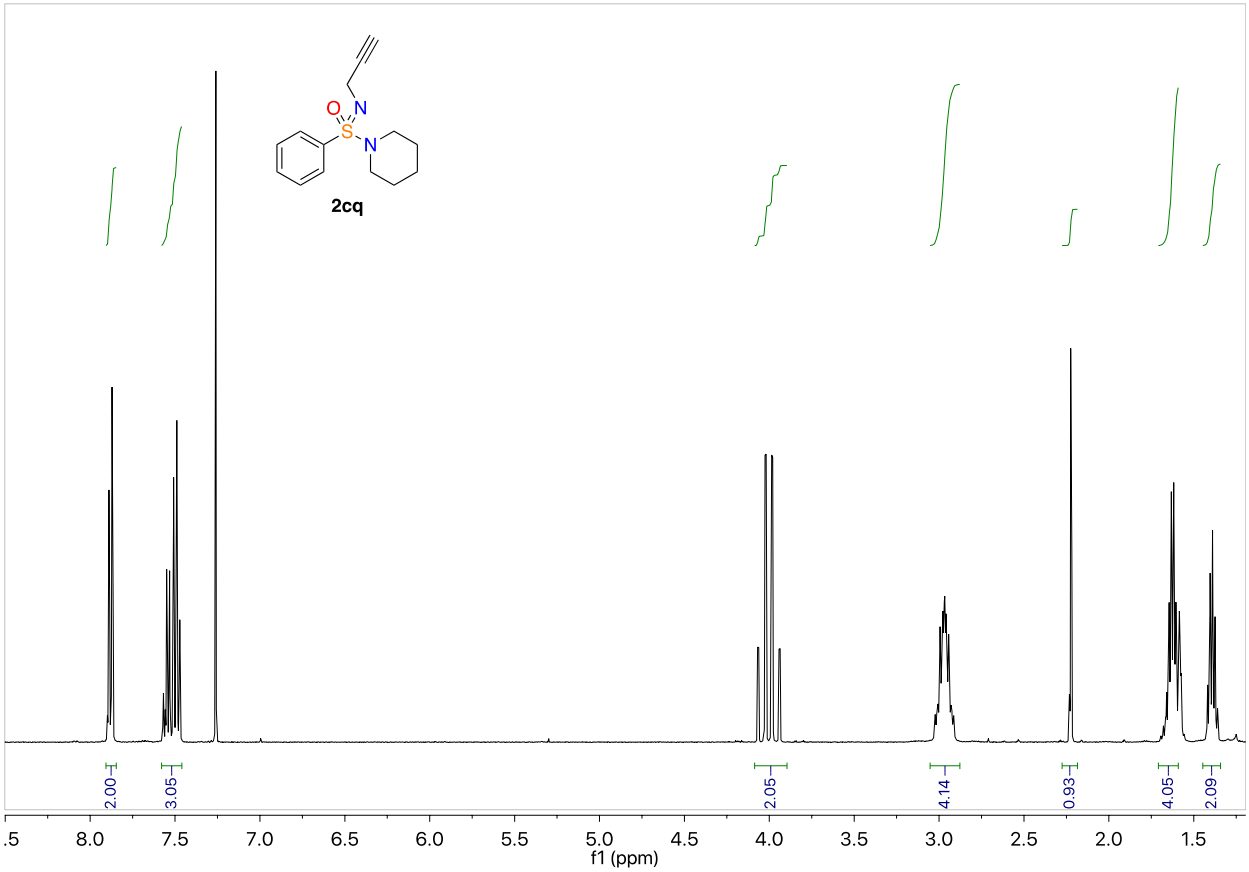

141.80
136.19
132.05
128.71
128.32
127.99
127.62
126.51
47.82
45.47
25.60
23.82
2cn
45 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

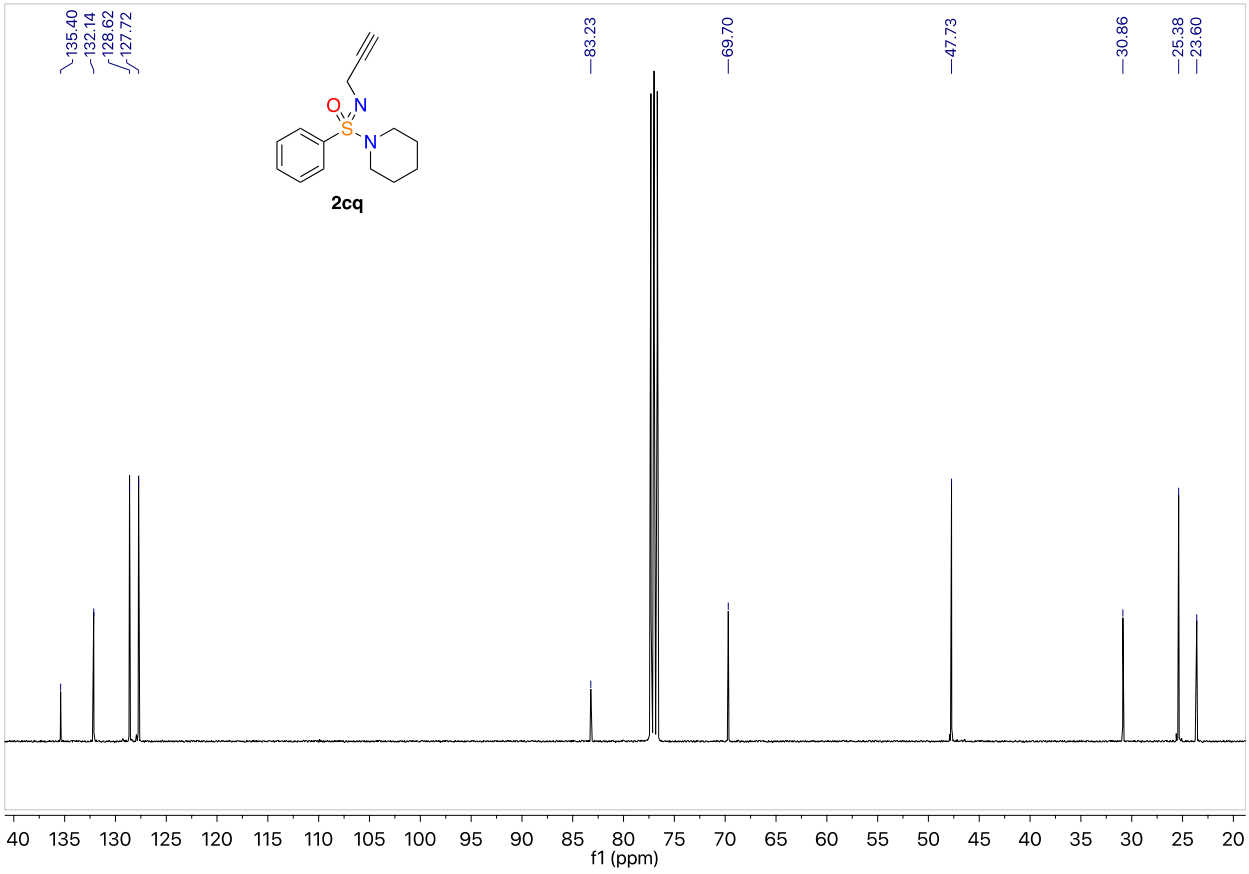

2co
2.00
1.01
2.00
0.96
1.03
1.02
4.07
3.06
4.38
2.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

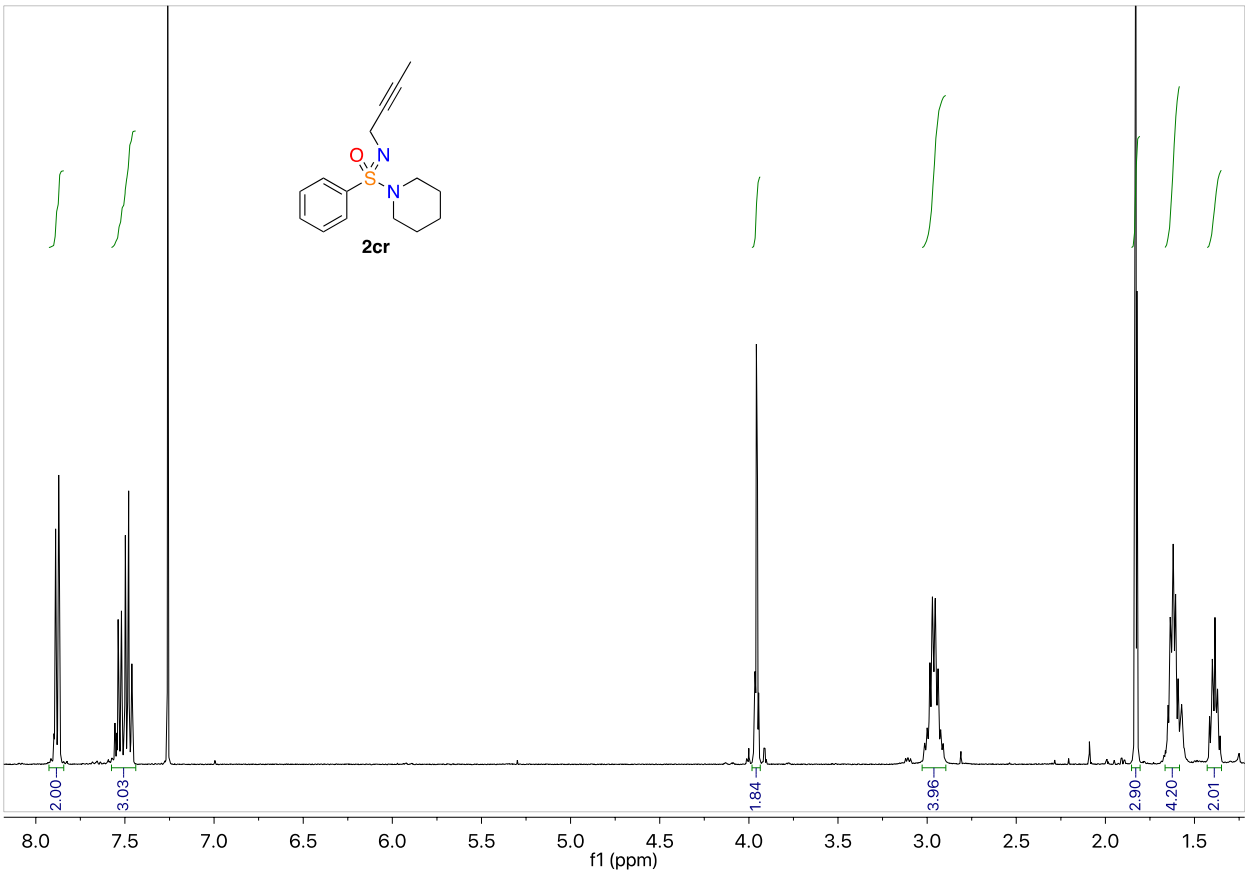

169.14
164.71
135.83
132.28
128.81
127.99
101.81
47.78
37.58
25.56
23.78
12.44
2co
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

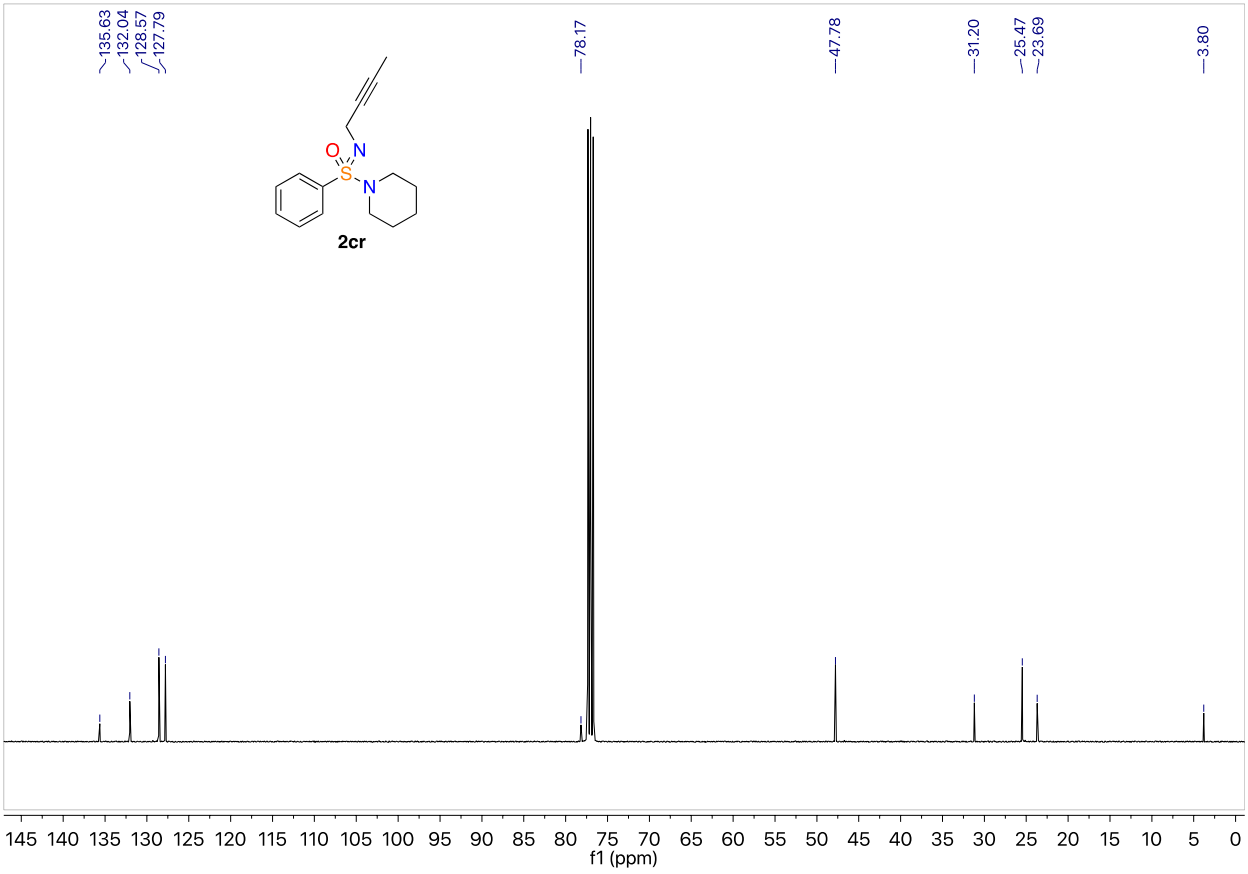

2cp
2.00
3.13
0.94
0.98
1.00
1.02
1.02
4.10
4.71
2.09
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)

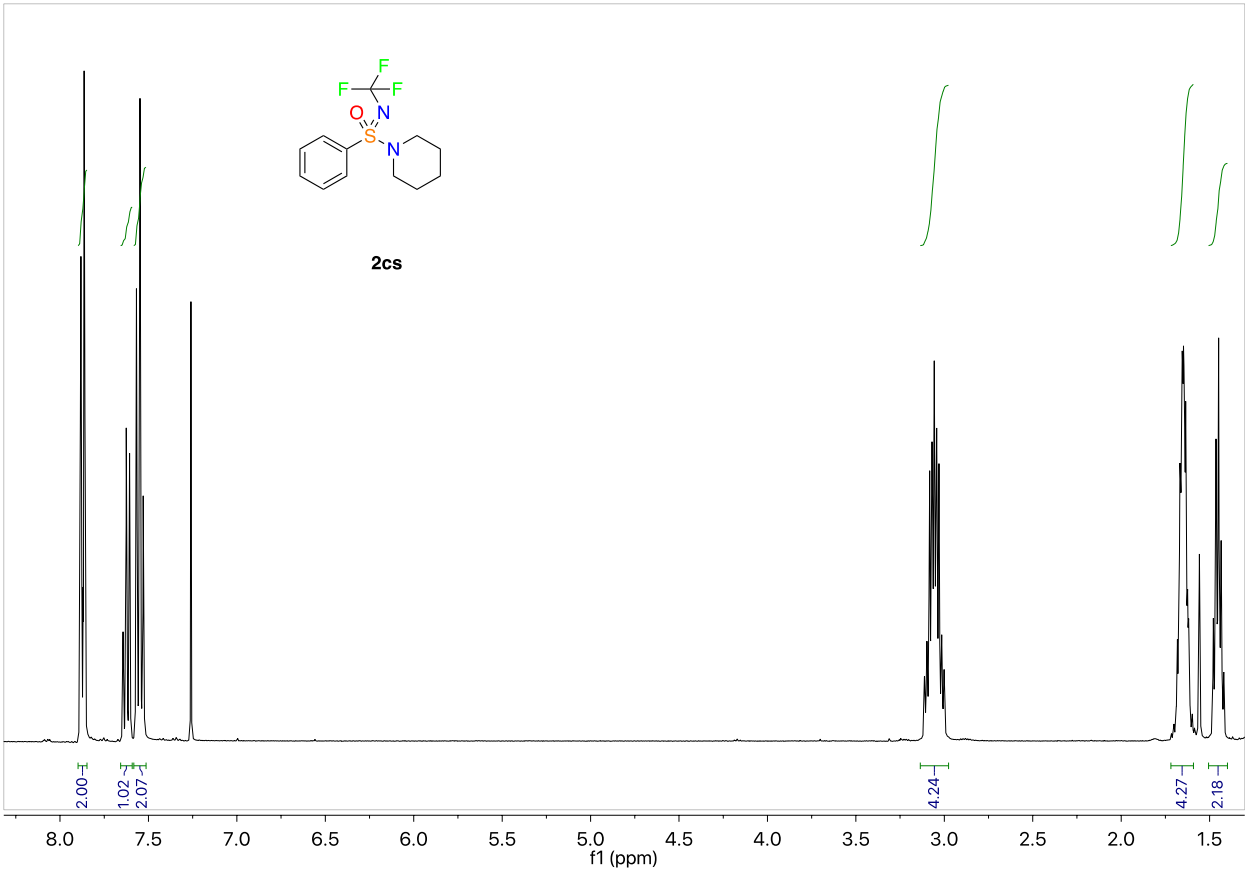

138.14
136.30
132.03
128.70
127.96
114.30
47.76
44.47
25.64
23.84
2cp
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

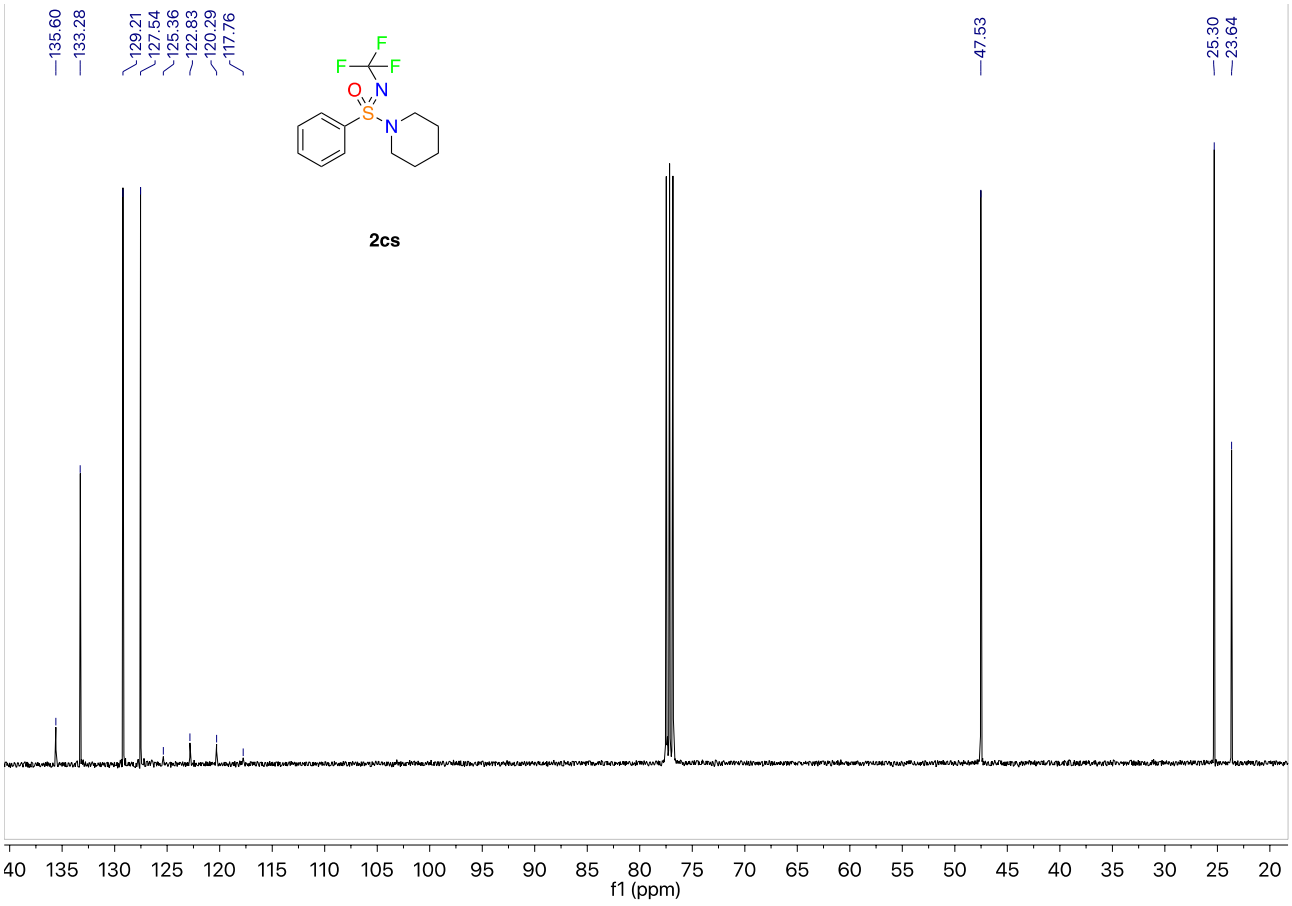

2cq
2.00
3.05
2.05
4.14
0.93
4.05
2.09
f1 (ppm)

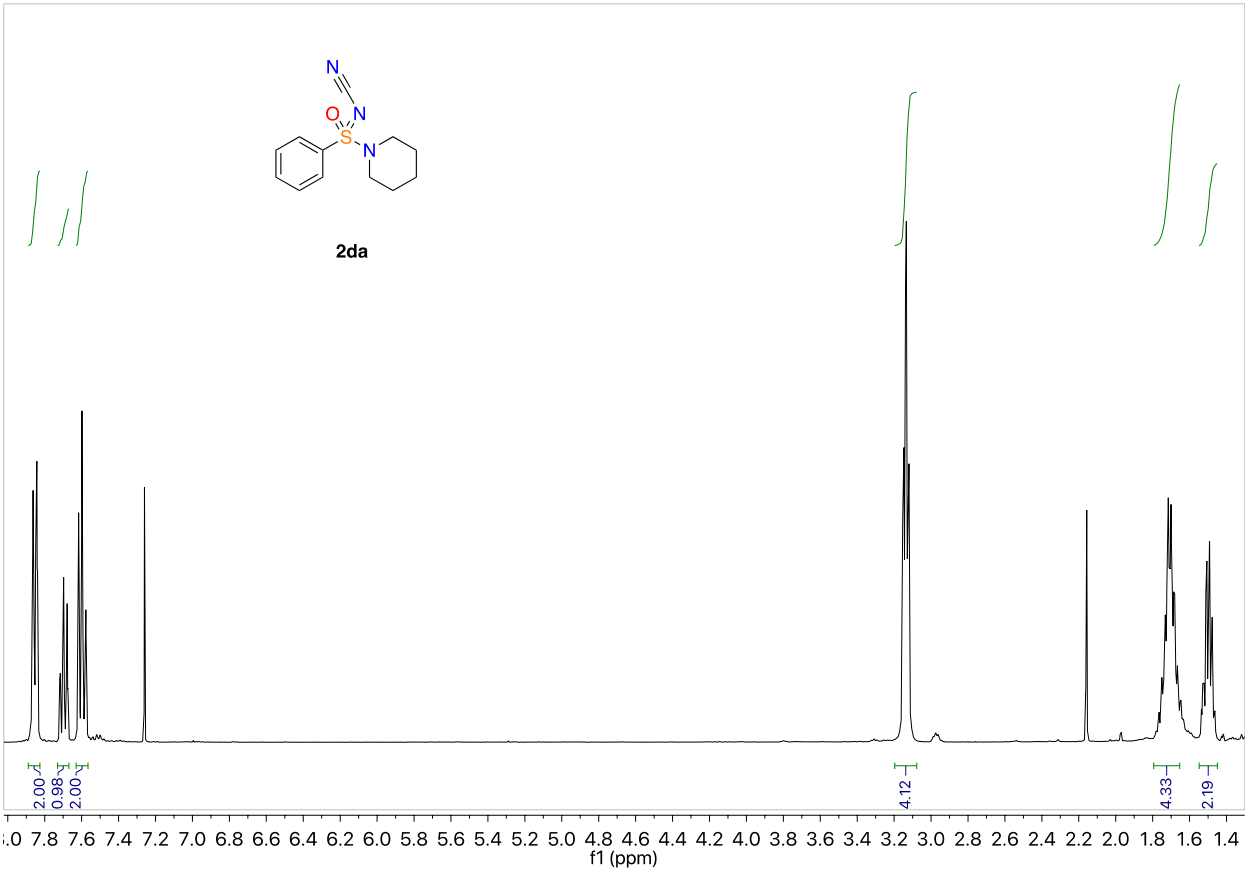

135.40
132.14
128.62
127.72
83.23
69.70
47.73
30.86
25.38
23.60
2cq
f1 (ppm)

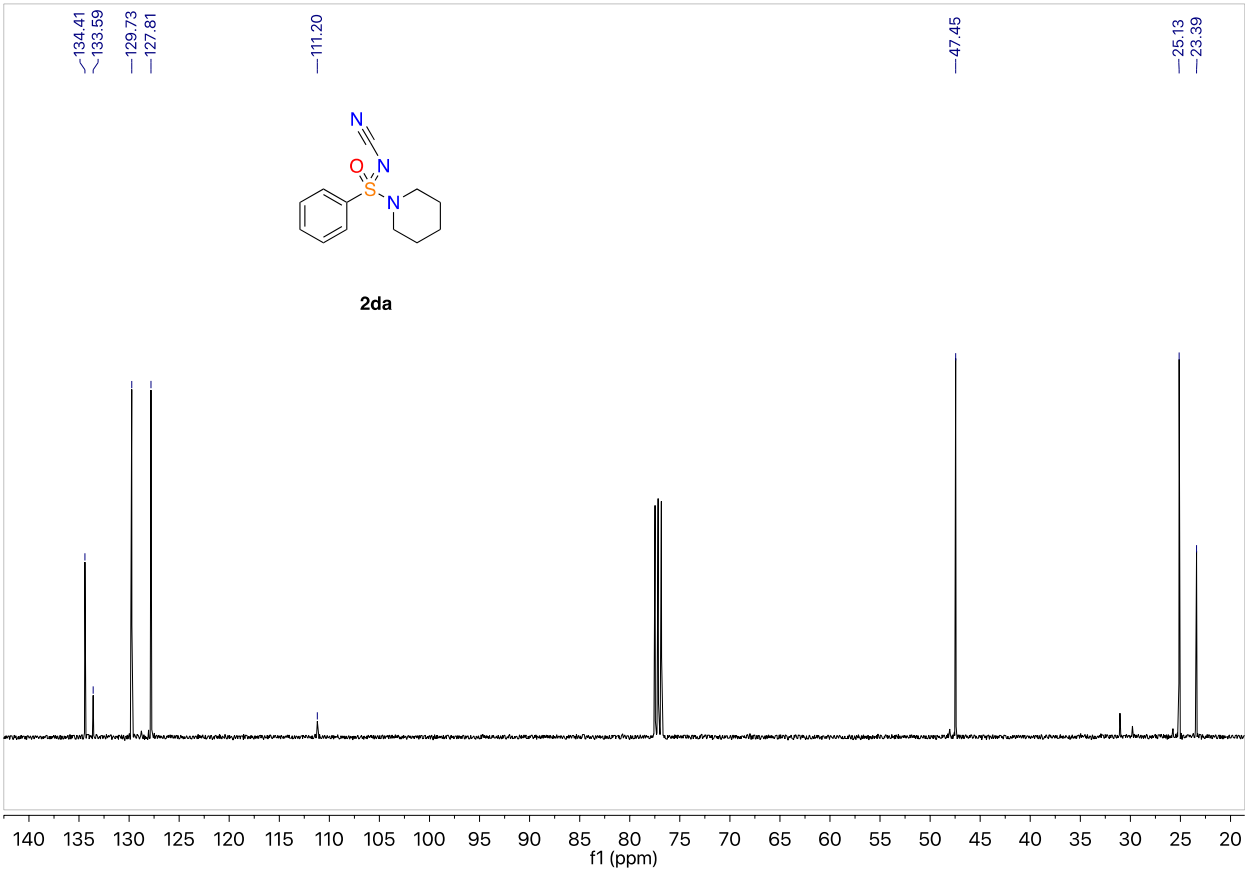

2cr
2.00
3.03
1.84
3.96
2.90
4.20
2.01
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)

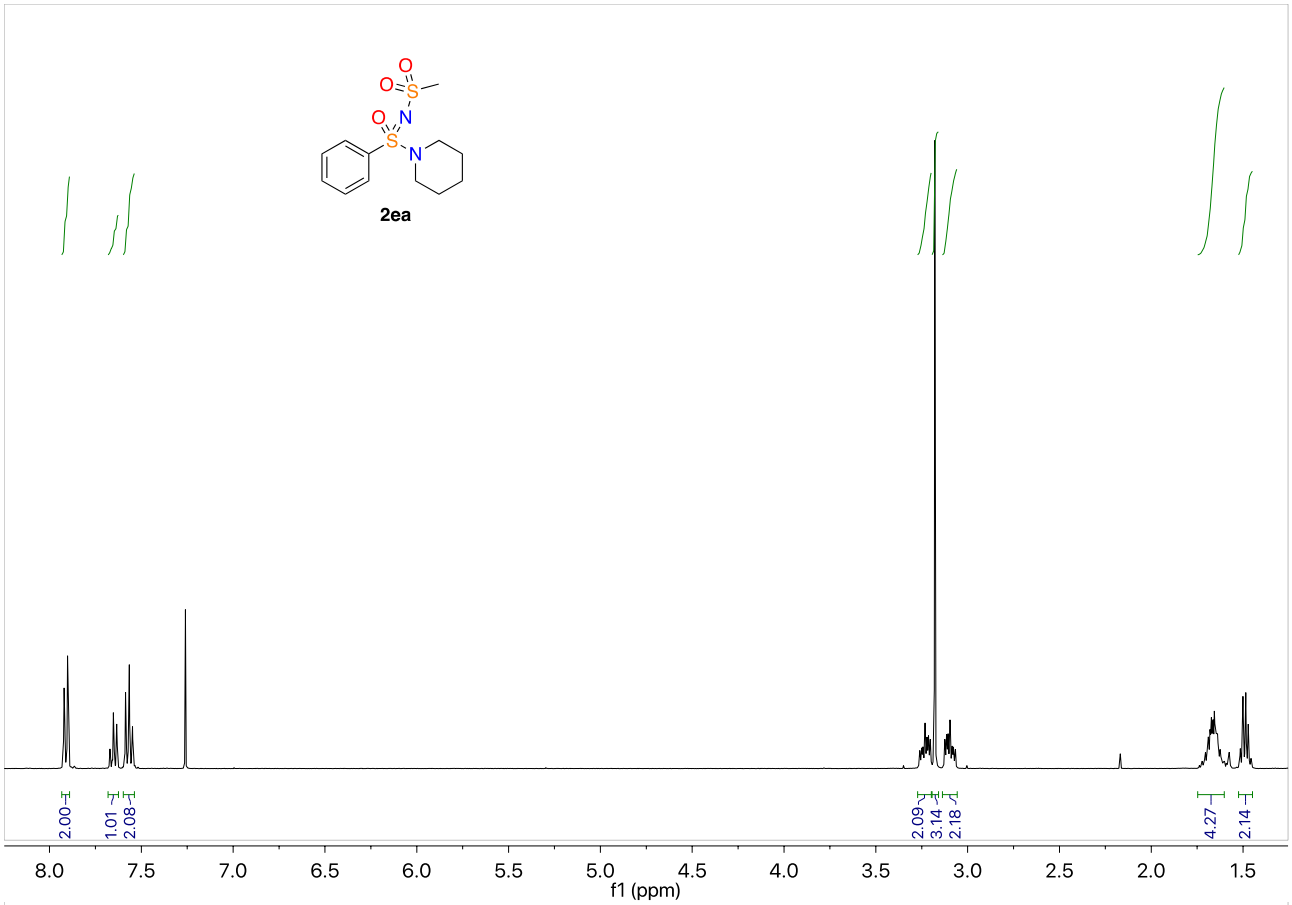

135.63
132.04
128.57
127.79
78.17
47.78
31.20
25.47
23.69
3.80
2cr
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

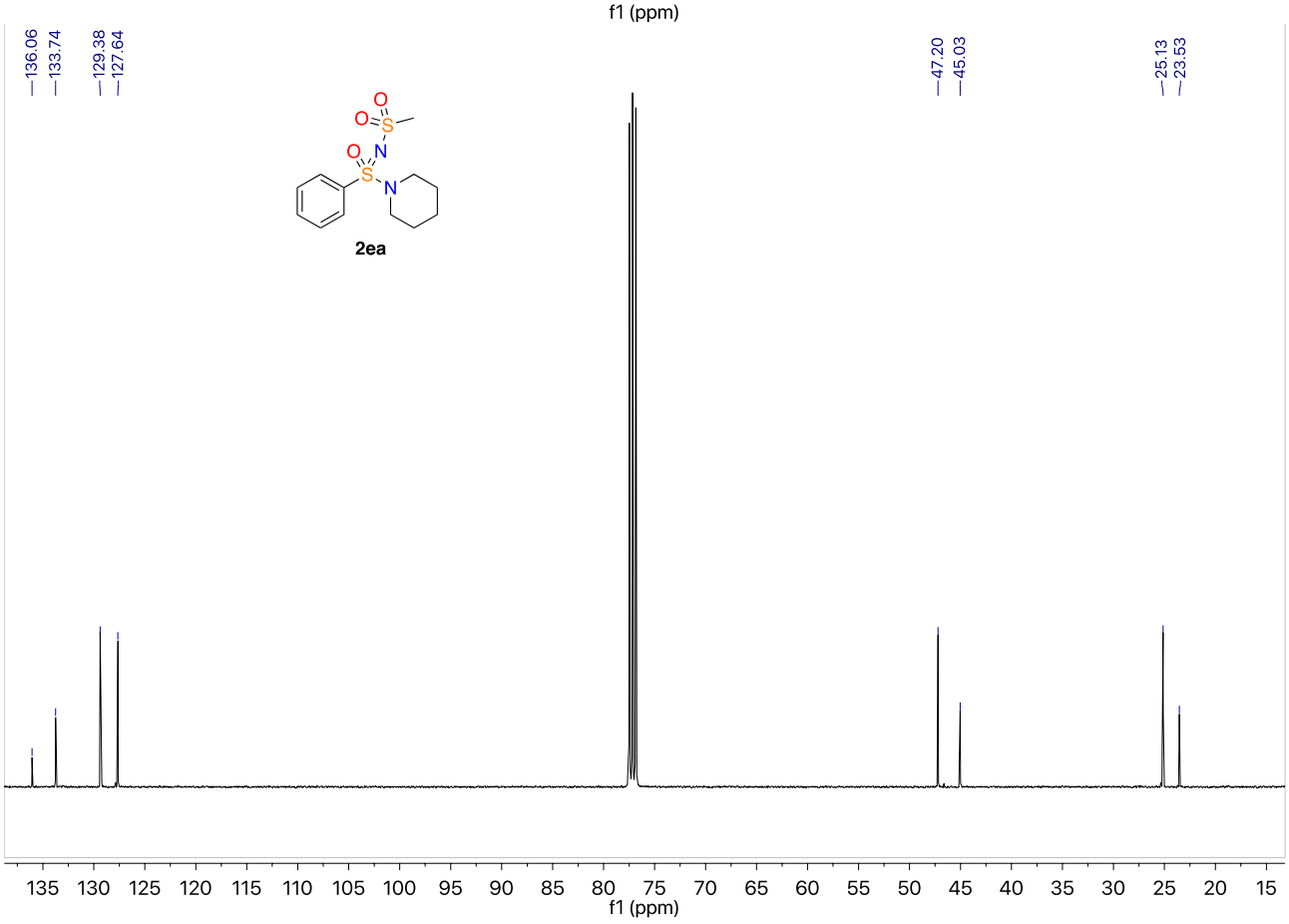

F
F
F
O
N
S
N
2cs
2.00
1.02
2.07
4.24
4.27
2.18
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

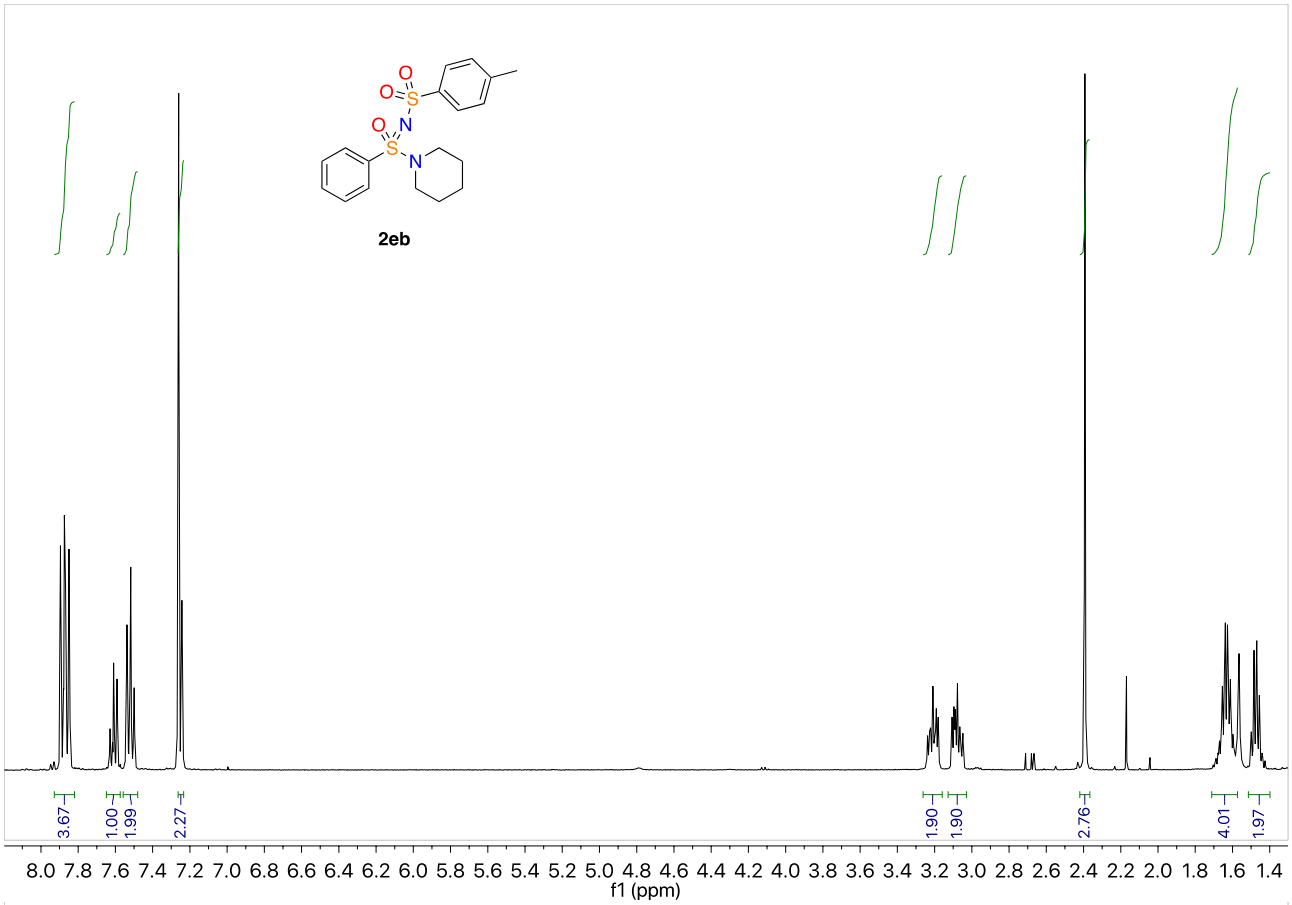

135.60
133.28
129.21
127.54
125.36
122.83
120.29
117.76
47.53
25.30
23.64
F
F
F
O
N
S
N
2cs
40
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
f1 (ppm)

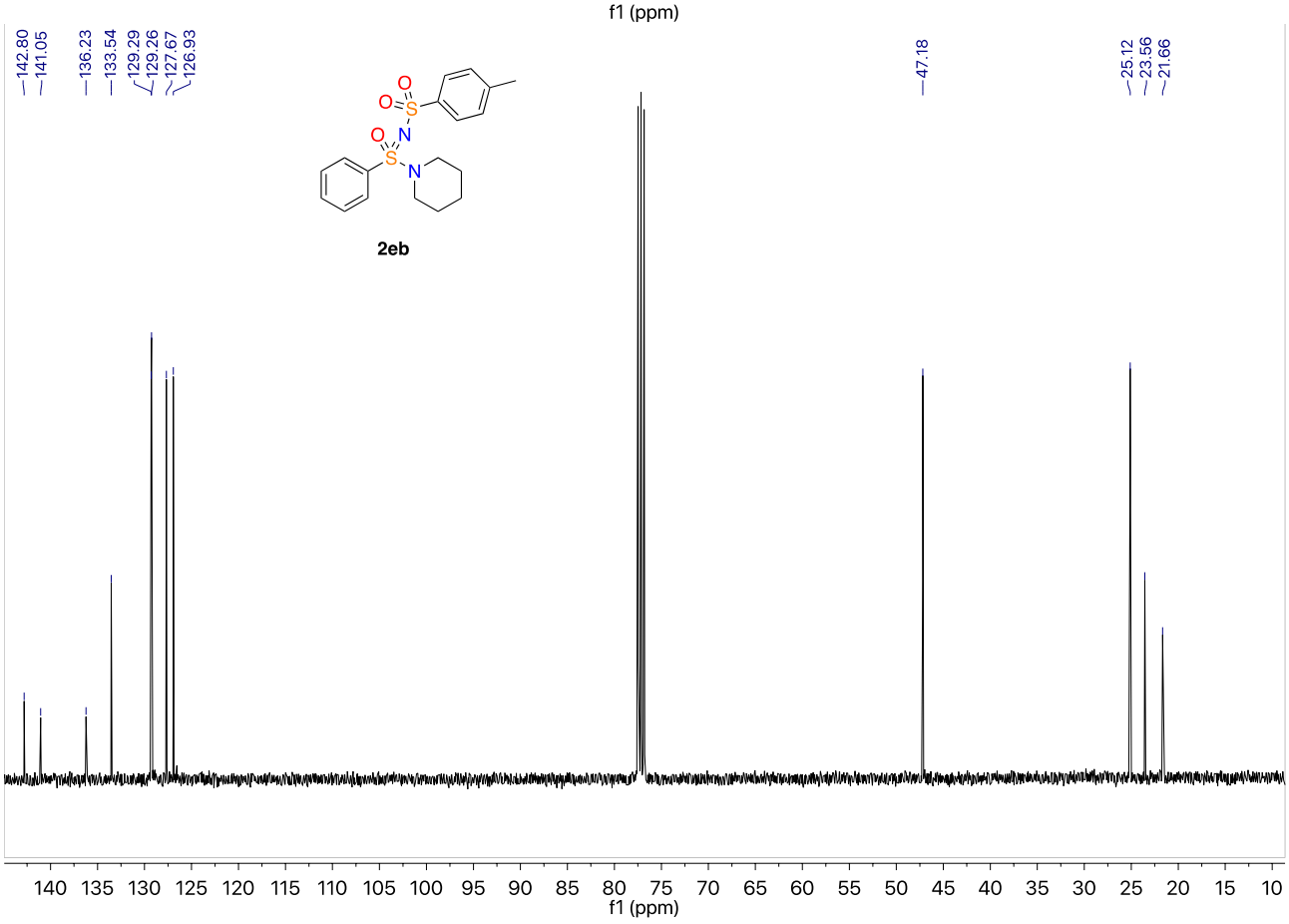

2da
2.00
0.98
2.00
4.12
4.33
2.19
f1 (ppm)

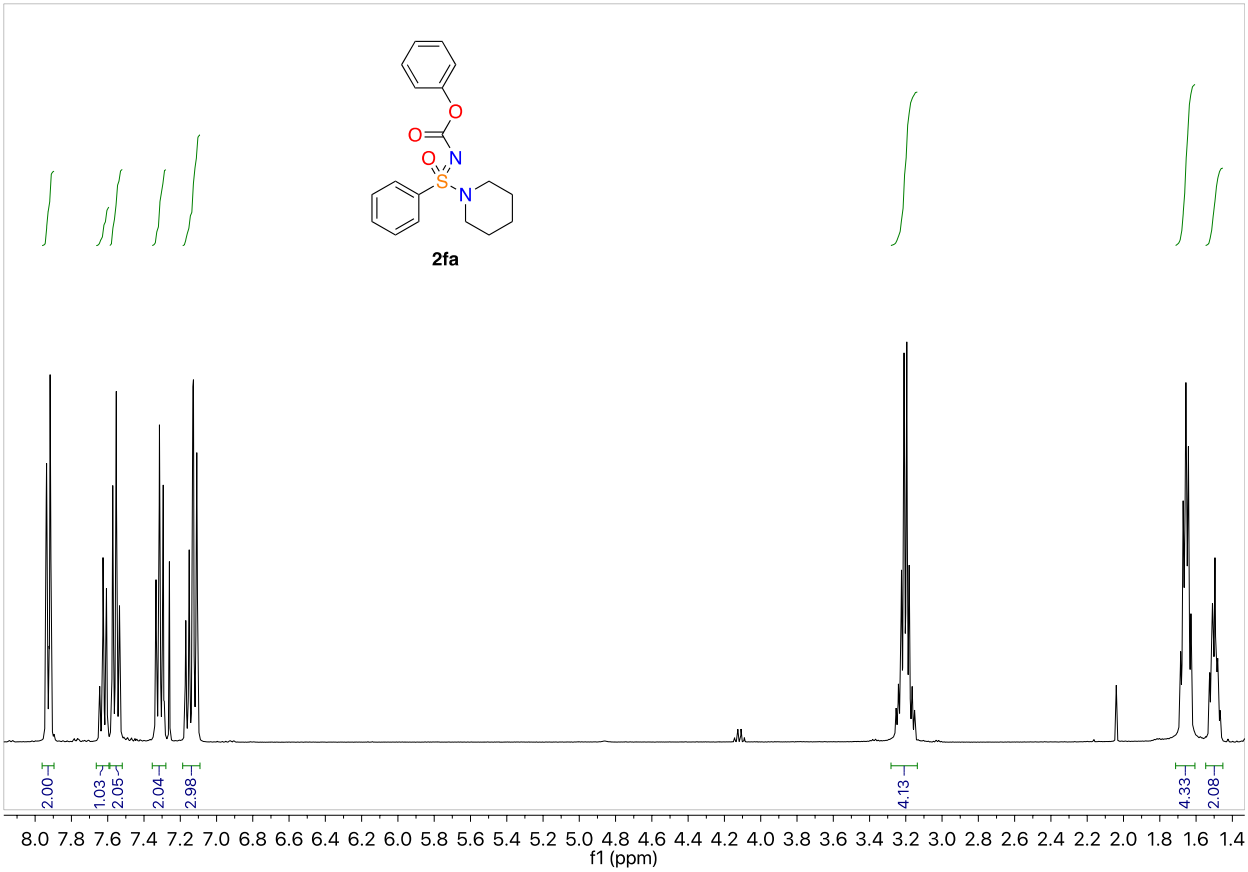

134.41
133.59
129.73
127.81
111.20
47.45
25.13
23.39
2da
f1 (ppm)

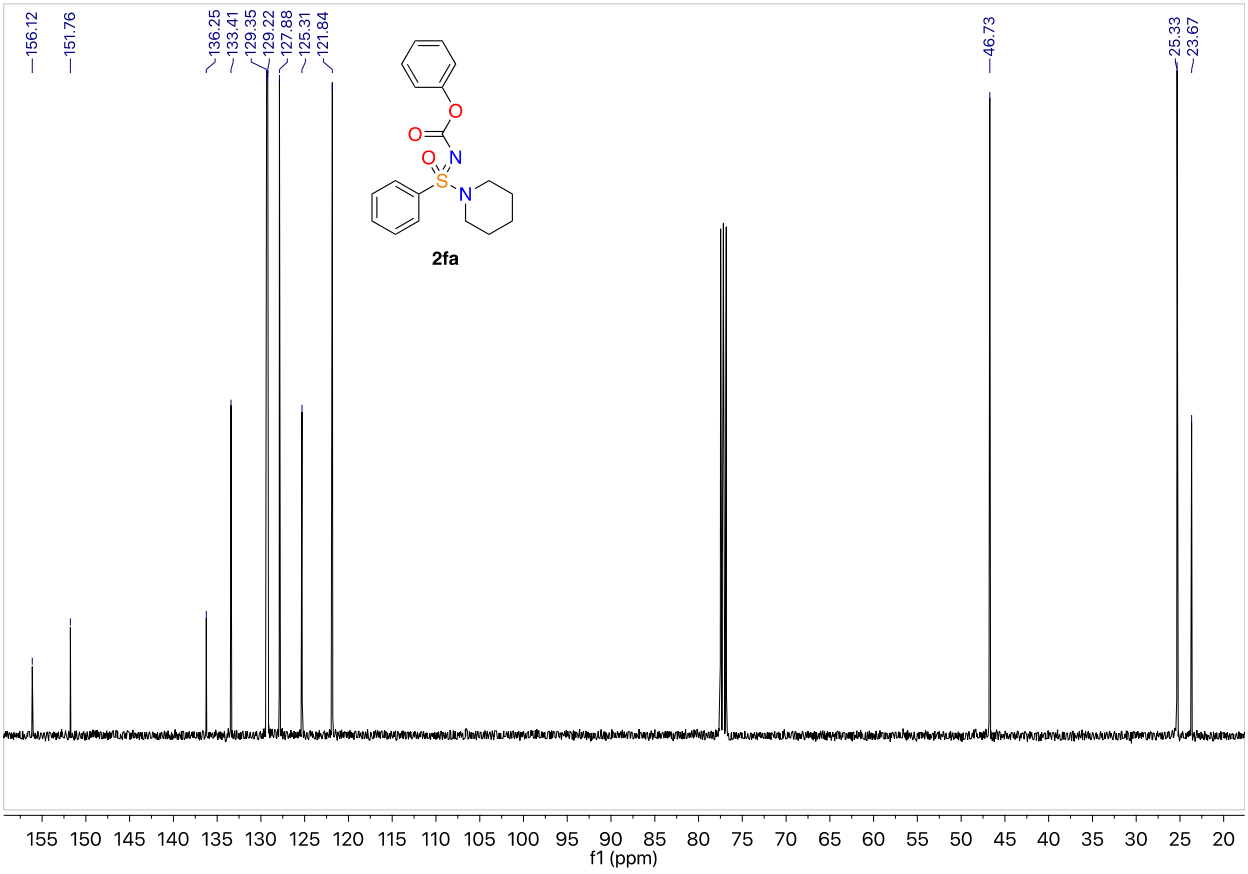

2ea
2.00
1.01
2.08
2.09
3.14
2.18
4.27
2.14
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

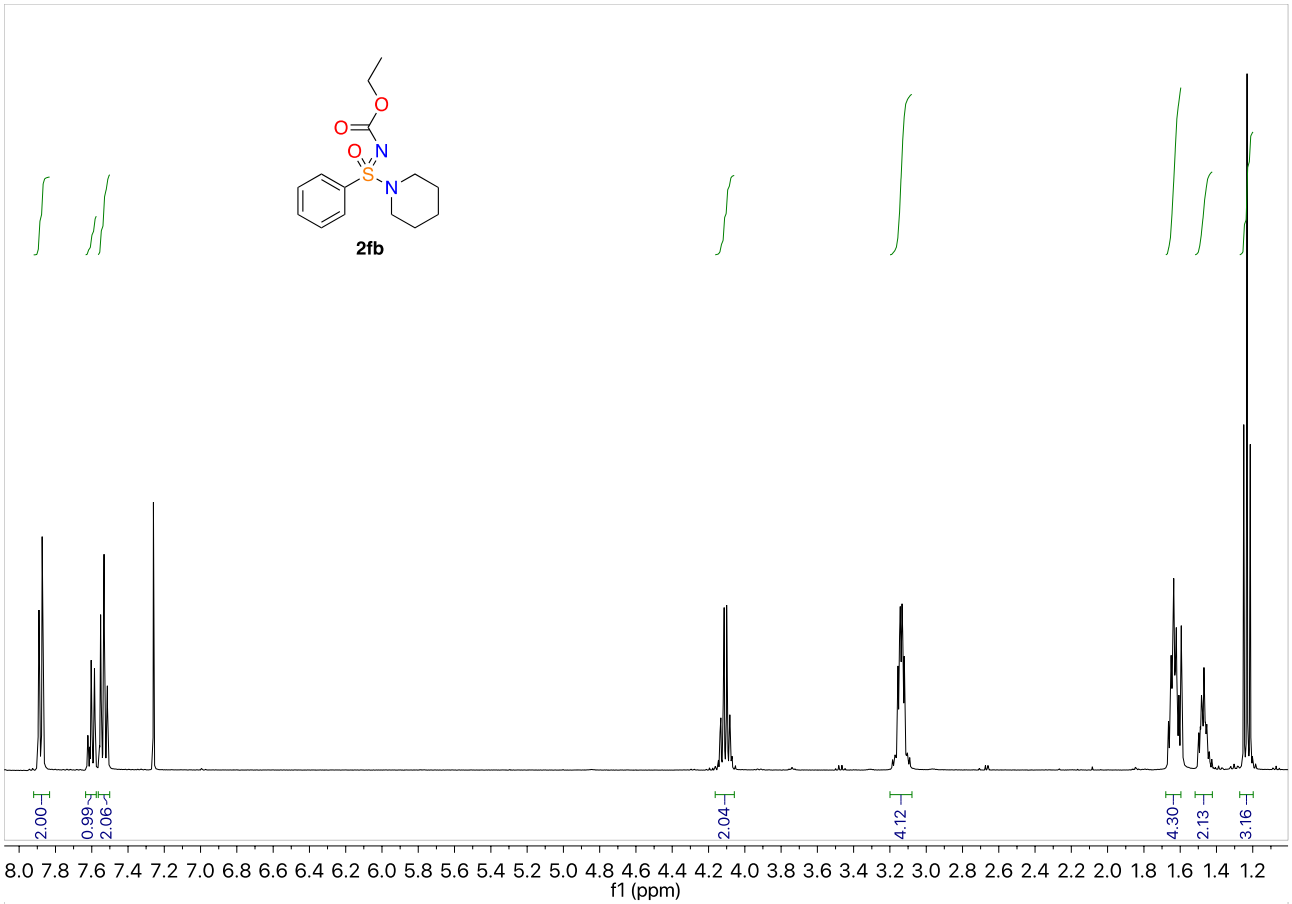

136.06
133.74
129.38
127.64
47.20
45.03
25.13
23.53
2ea
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
f1 (ppm)

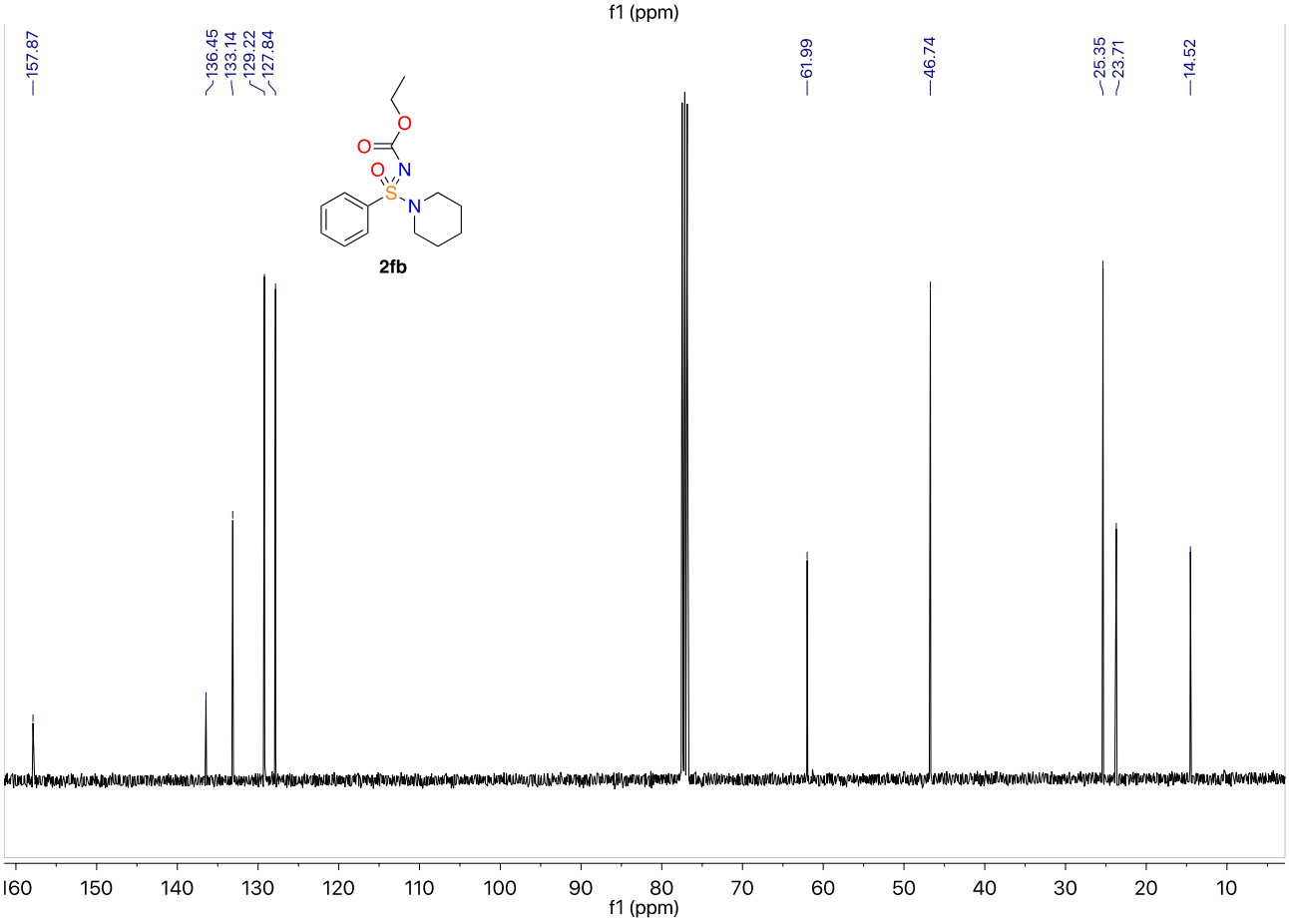

2eb
3.67
1.00
1.99
2.27
1.90
1.90
2.76
4.01
1.97
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)

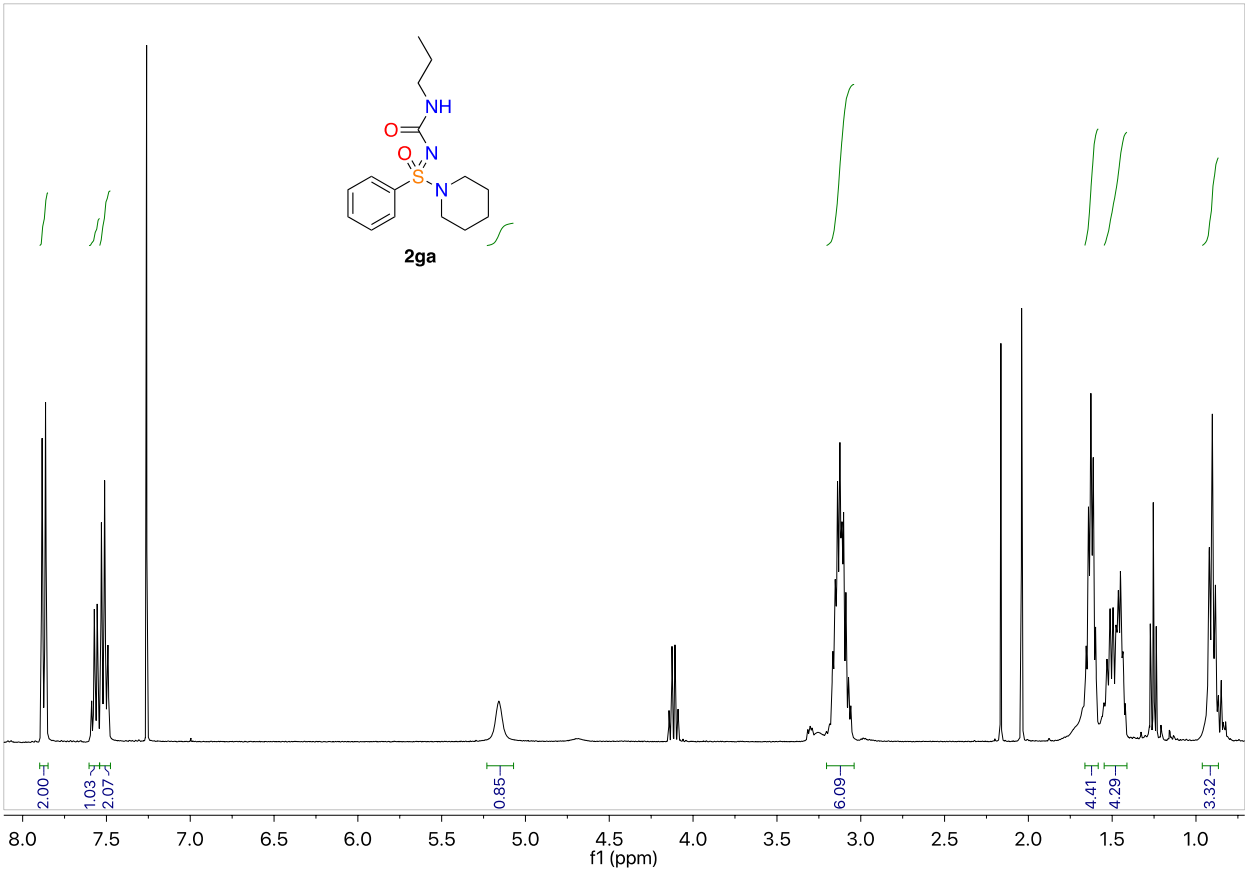

142.80
141.05
136.23
133.54
129.29
129.26
127.67
126.93
47.18
25.12
23.56
21.66
2eb
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10
f1 (ppm)


2fa
2.00
1.03
2.05
2.04
2.98
4.13
4.33
2.08
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)


156.12
151.76
136.25
133.41
129.35
129.22
127.88
125.31
121.84
46.73
25.33
23.67
2fa
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)


2fb
2.00
0.99
2.06
2.04
4.12
4.30
2.13
3.16
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)


157.87
136.45
133.14
129.22
127.84
61.99
46.74
25.35
23.71
14.52
2fb
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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N
S
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6.09
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4.29
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7.0
6.5
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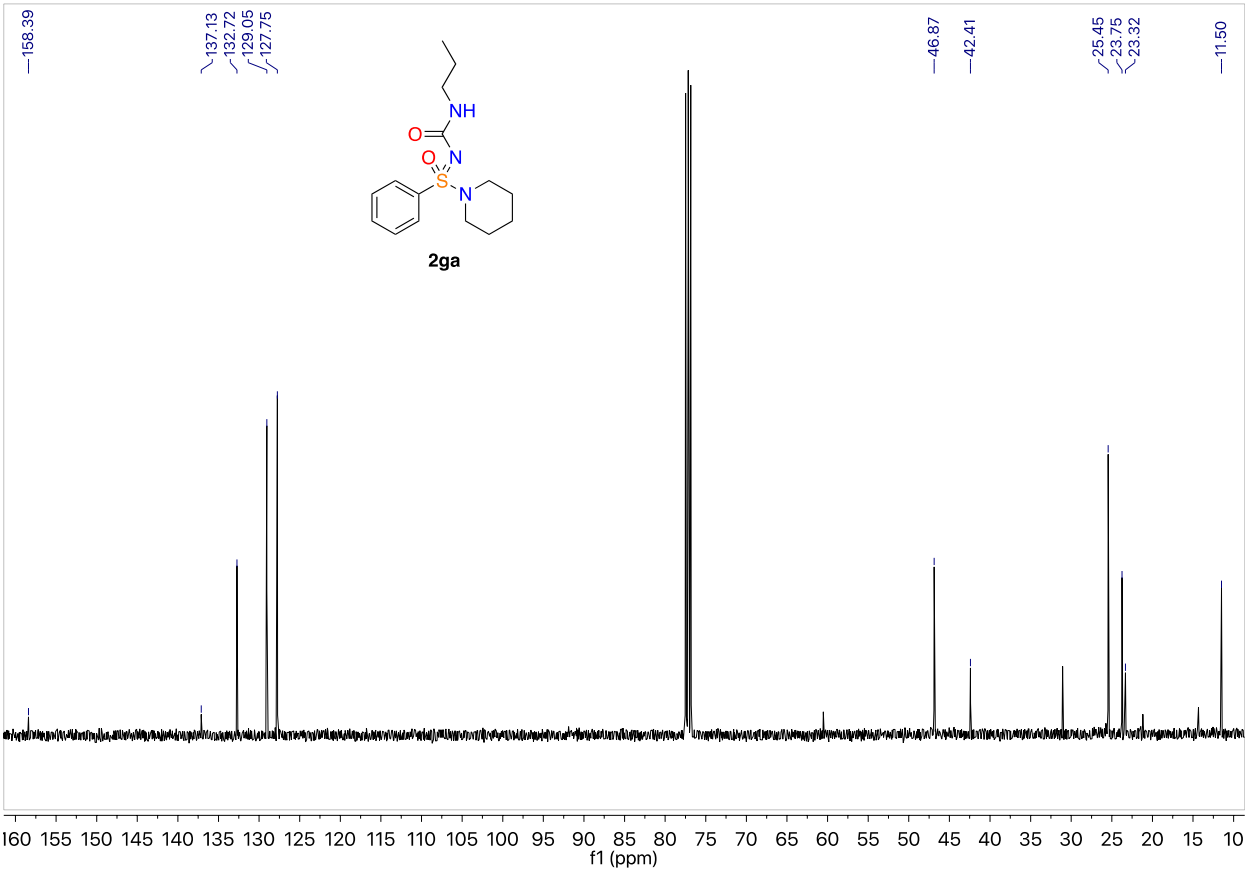
2.0
1.5
1.0
f1 (ppm)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42.41
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23.75
23.32
11.50
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N
S
N
2ga
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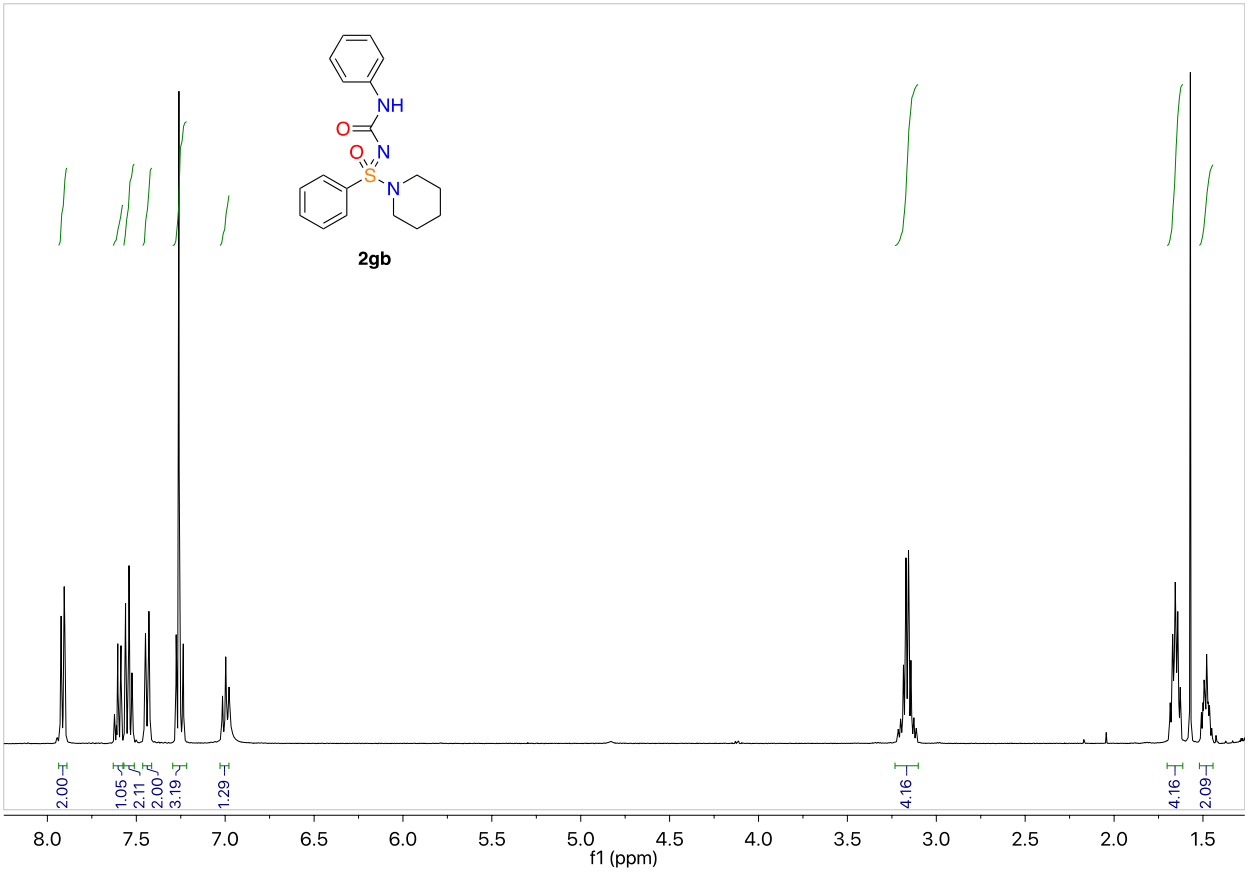
f1 (ppm)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2.09
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4.0
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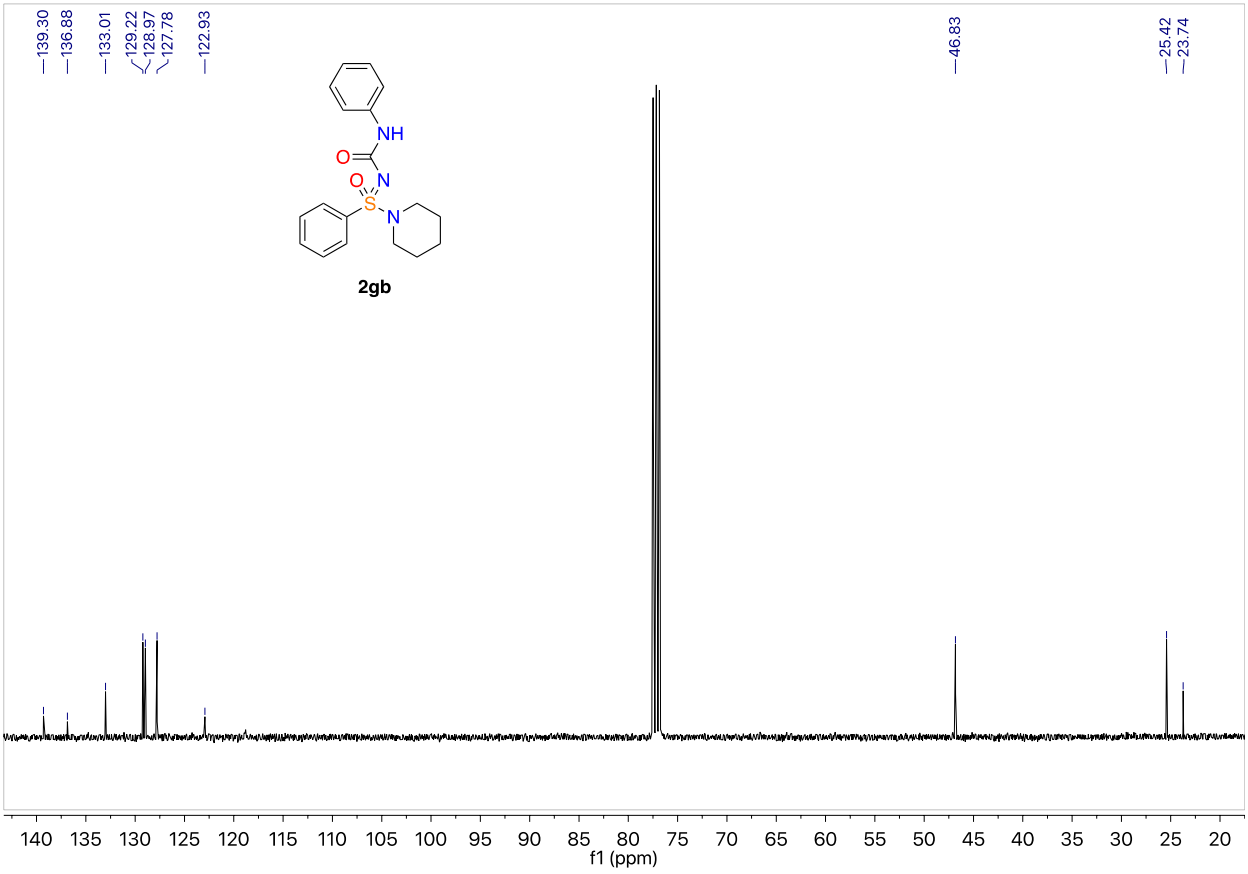
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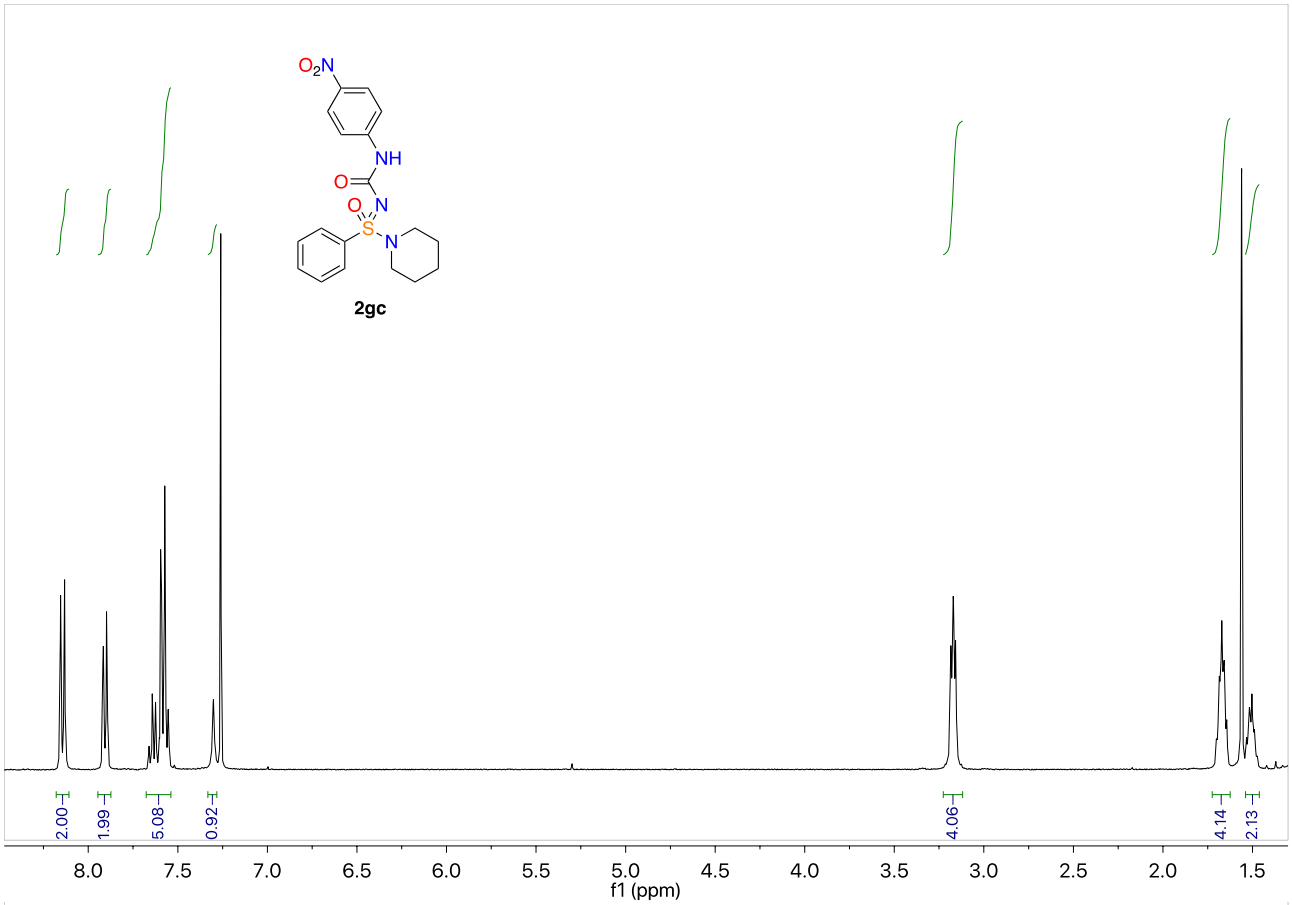
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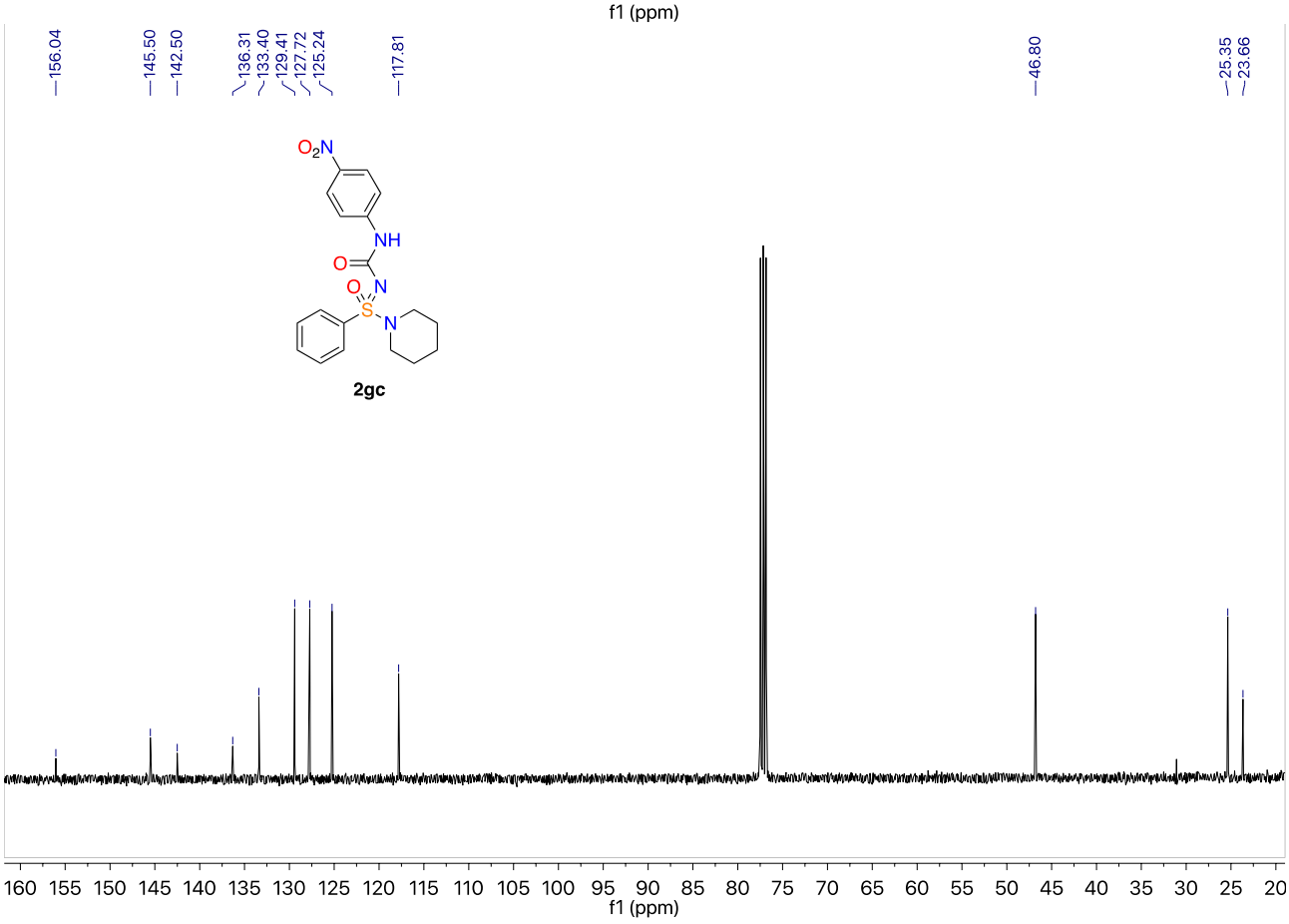
1.5
f1 (ppm)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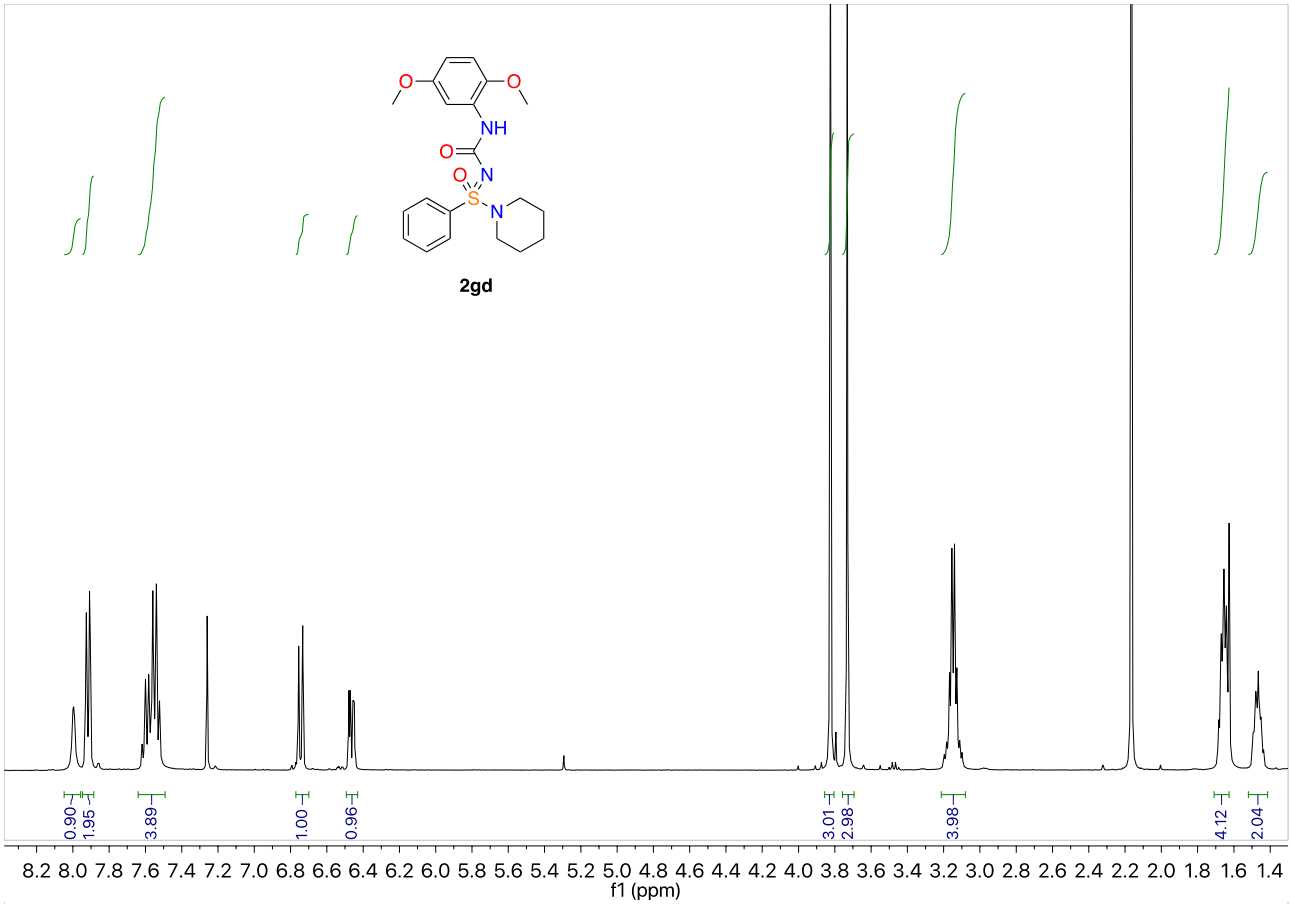
f1 (ppm)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2.98
3.98
4.12
2.04
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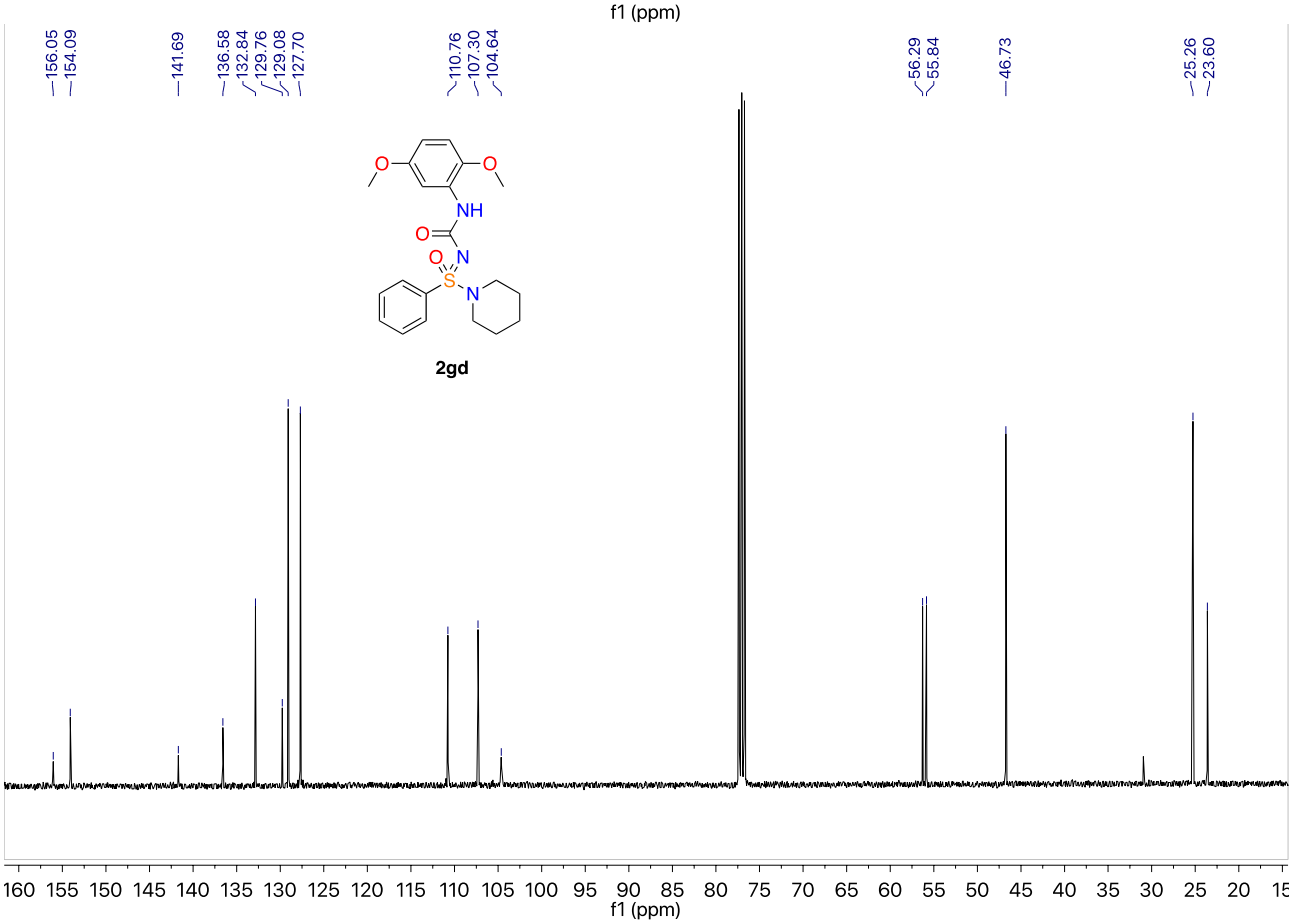
f1 (ppm)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25.26
23.60
2gd
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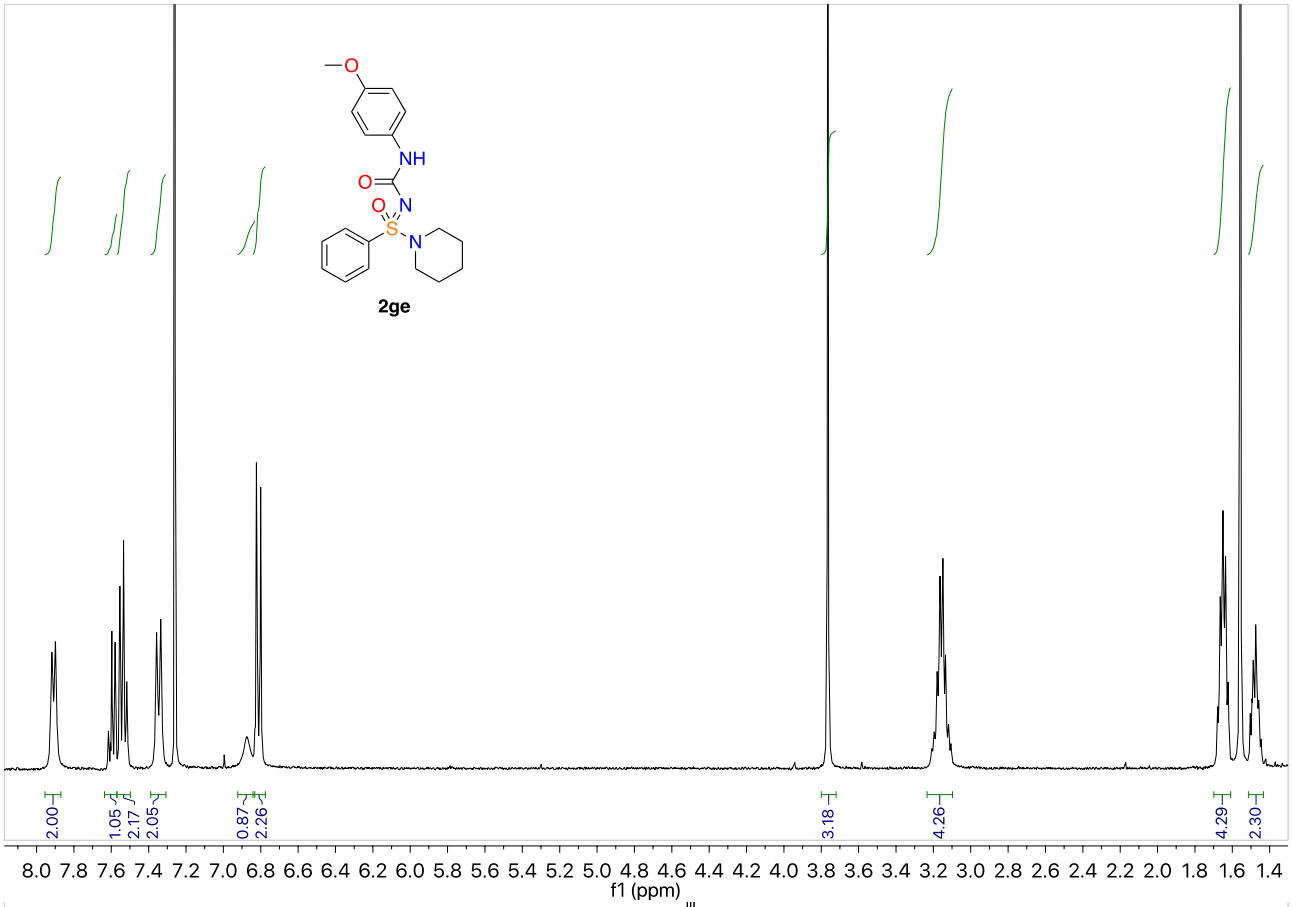
f1 (ppm)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3.18
4.26
4.29
2.30
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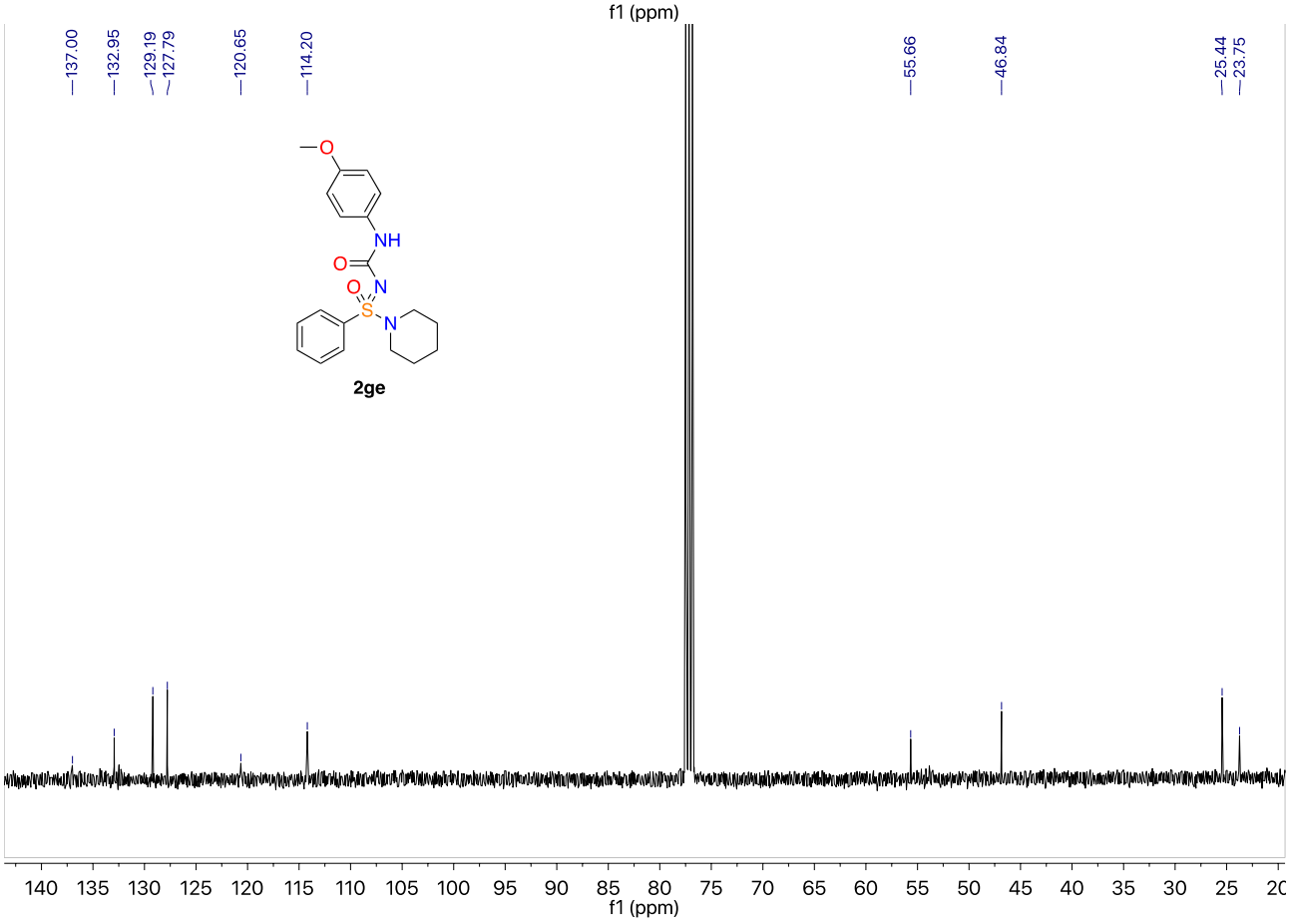
f1 (ppm)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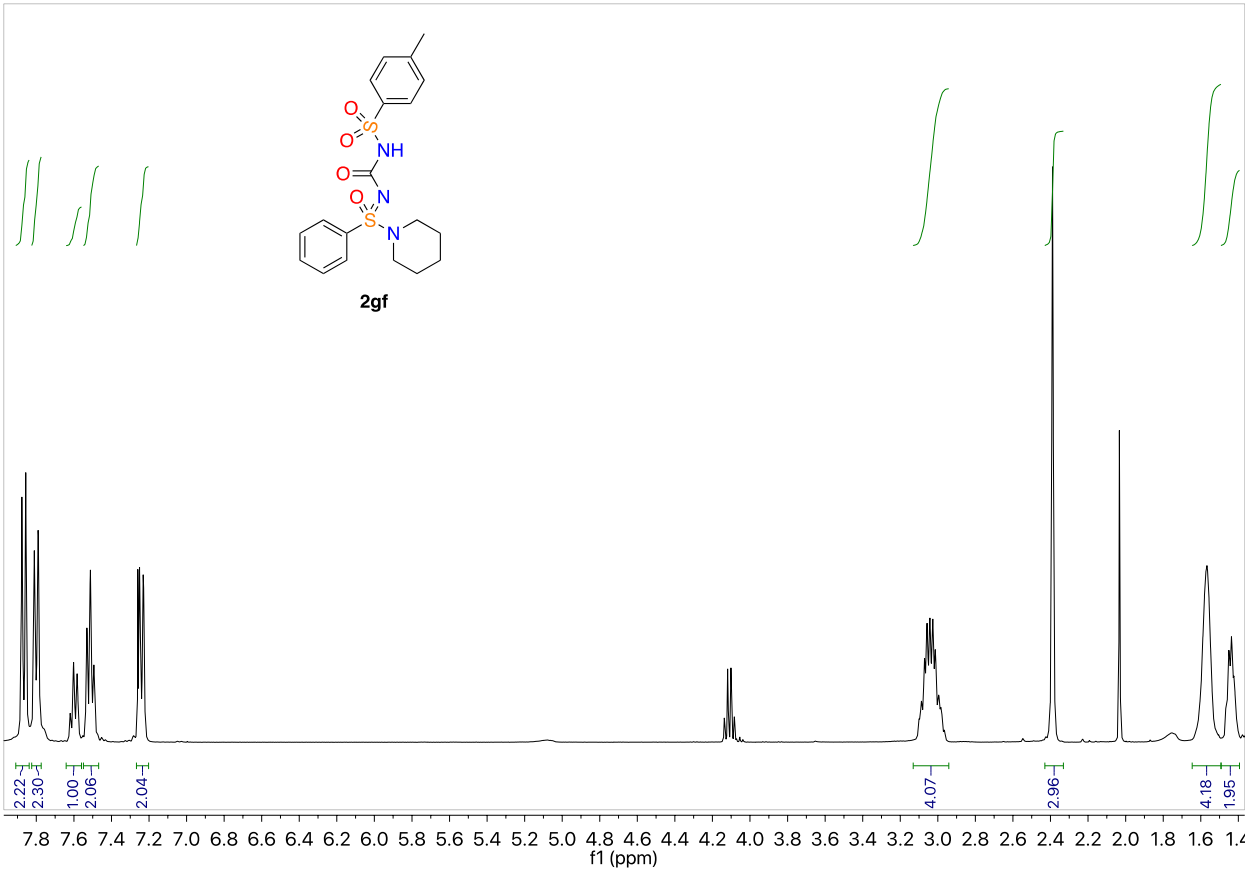
f1 (ppm)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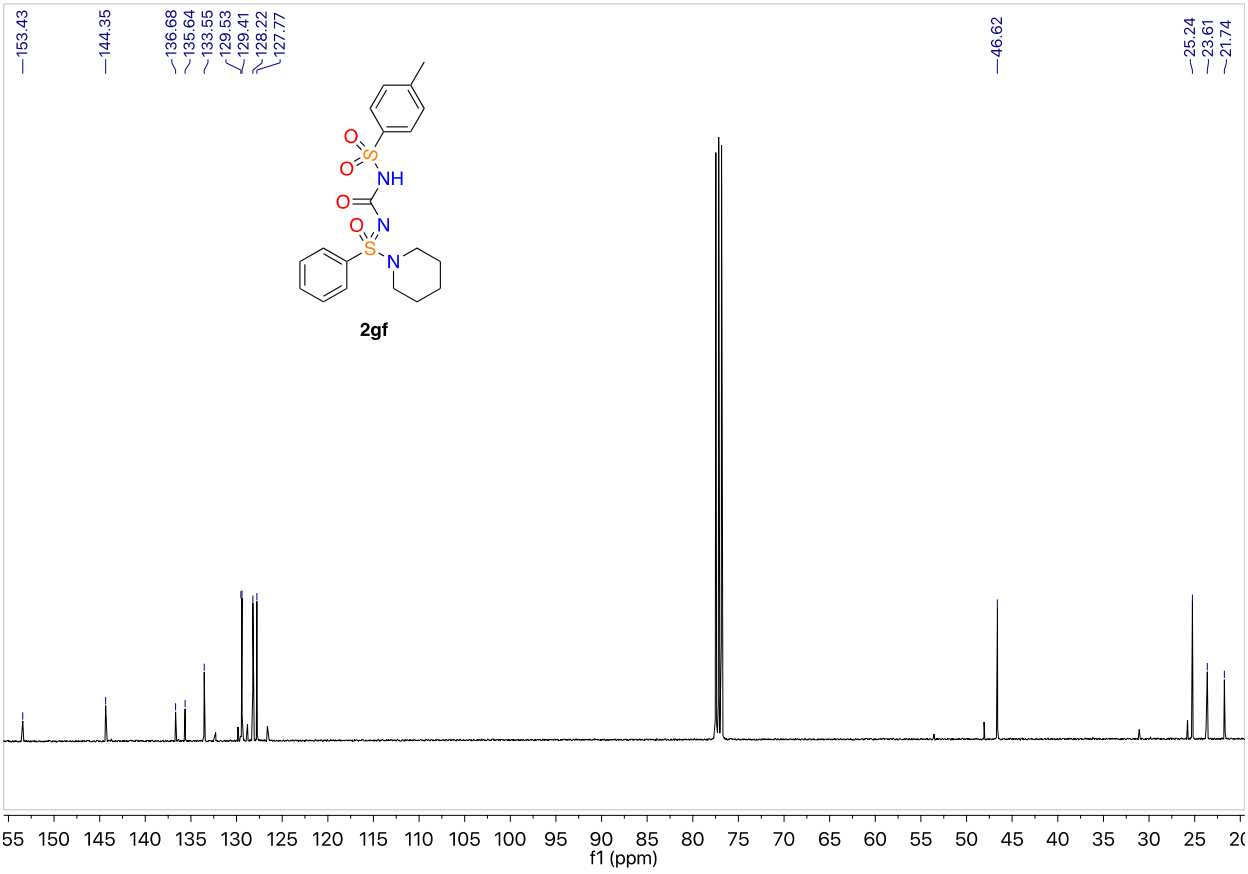
2.04
4.07
2.96
4.18
1.95
7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6
f1 (ppm)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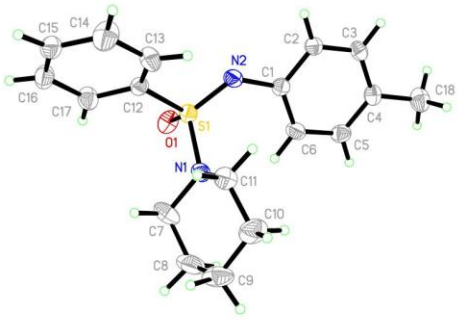
46.62
25.24
23.61
21.74
2gf
55 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

Small molecule X-ray structures of compounds 2bg, 2bj, 2bk and 2bm

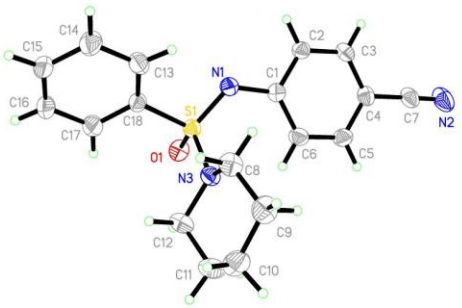
All data for compounds **2bg**, **2bj**, **2bk** and **2bm** were collected at 100 K on a Bruker Proteum X8 system equipped with a CCD area detector and Cu X-ray radiation (Cu Kα, λ = 1.54178 Å). X-ray data collection and processing of data were performed using the Proteum software package.[7] SHELXS was used for structure solution and SHELXL was used for full-matrix least-squares refinement on F^2[8] for all four X-ray structures. All non-hydrogen atoms were refined anisotropically. All carbon hydrogen atoms were placed in geometrically ideal positions using the riding model. Non-carbon hydrogen atoms were taken from the difference Fourier map. The isotropic temperature factors of all hydrogen atoms were 1.2 and 1.5 times the size of the temperature factors of the corresponding heavy atoms. The program XP in the Proteum software package was used for all molecular representations.

1-[*S*-Phenyl-*N*-(4-tolyl)sulfonimidoyl]piperidine (2bg)



Compound **2bg** was crystallized by slow evaporation of a DCM solution of the compound at RT. A single crystal with dimensions of 0.2 × 0.1 × 0.03 mm^3 was mounted on a CryoLoop using a protective oil. **2bg** crystallizes in the monoclinic space group *C2/c* with cell constants of *a* = 27.748(17) Å, *b* = 7.812(4) Å, *c* = 19.68(2) Å and β = 130.935(8)°. A total of 36030 reflections of which 2468 are unique (R_{int} = 0.0260) were collected. The final *R* values were R_1 = 0.0376, I > 2σ(I) and wR_2 = 0.1012 for all data. The crystallographic data for **2bg** have been deposited with the Cambridge Crystallographic Data Centre with deposition code CCDC 1841270.

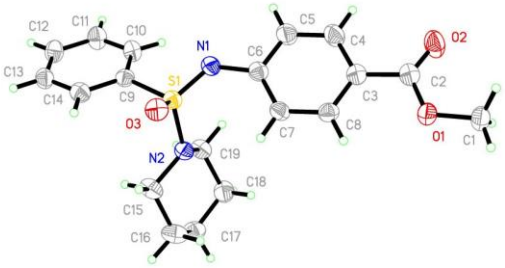
4-{[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}benzonitrile (2bj)



Compound **2bj** was crystallized by slow evaporation of a DCM solution of the compound at RT. A single crystal with dimensions of 0.72 × 0.15 × 0.03 mm^3 was mounted on a CryoLoop using a protective oil. **2bj** crystallizes in the monoclinic space group *C2/c* with cell constants of *a* = 27.3860(14) Å, *b* = 7.8635(4) Å, *c* = 19.710(1) Å and β = 129.787(1)°. A total of 31481 reflections

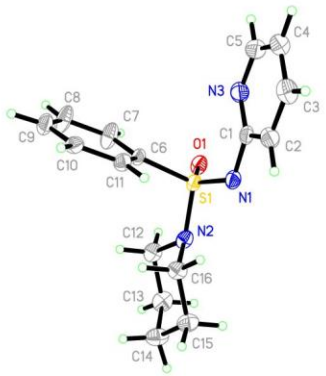
of which 2289 are unique (R_{int} = 0.0270) were collected. The final *R* values were R_1 = 0.0327, I > 2σ(I) and wR_2 = 0.0892 for all data. The crystallographic data for **2bj** have been deposited with the Cambridge Crystallographic Data Centre with deposition code CCDC 1841271.

Methyl 4-{[oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}benzoate (2bk)



Colorless needles of compound **2bk** were obtained by slow evaporation of a DCM solution of the compound at RT. A single crystal with dimensions of 0.17 × 0.10 × 0.02 mm^3 was mounted on a CryoLoop using a protective oil. **2bk** crystallizes in the monoclinic space group *P2(1)/c* with cell constants of *a* = 7.6392(3) Å, *b* = 10.0895(4) Å, *c* = 23.1311(9) Å and β = 91.384(2)°. A total of 35295 reflections of which 2677 are unique (R_{int} = 0.0383) were collected. The final *R* values were R_1 = 0.0335, I > 2σ(I) and wR_2 = 0.0929 for all data. The crystallographic data for **2bk** have been deposited with the Cambridge Crystallographic Data Centre with deposition code CCDC 1841273.

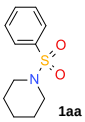
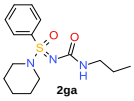
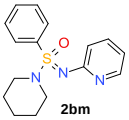
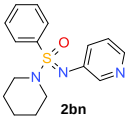
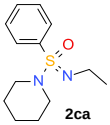
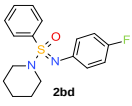
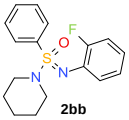
2-{[Oxo(phenyl)(piperidin-1-yl)-λ^6-sulfanylidene]amino}pyridine (2bm)



Colorless needles of compound **2bm** were obtained by slow evaporation of a DCM solution of the compound at RT. A single crystal with dimensions of 0.72 × 0.15 × 0.03 mm^3 was mounted on a CryoLoop using a protective oil. **2bm** crystallizes in the monoclinic space group *Cc* with cell constants of *a* = 8.3468(10) Å, *b* = 16.054(2) Å, *c* = 11.8711(15) Å and β = 108.625(3)°. A total of 44118 reflections of which 1195 are unique (R_{int} = 0.0358) were collected. The final *R* values were R_1 = 0.0231, I > 2σ(I) and wR_2 = 0.0633 for all data. The crystallographic data for **2bm** have been deposited with the Cambridge Crystallographic Data Centre with deposition code CCDC 1841272.

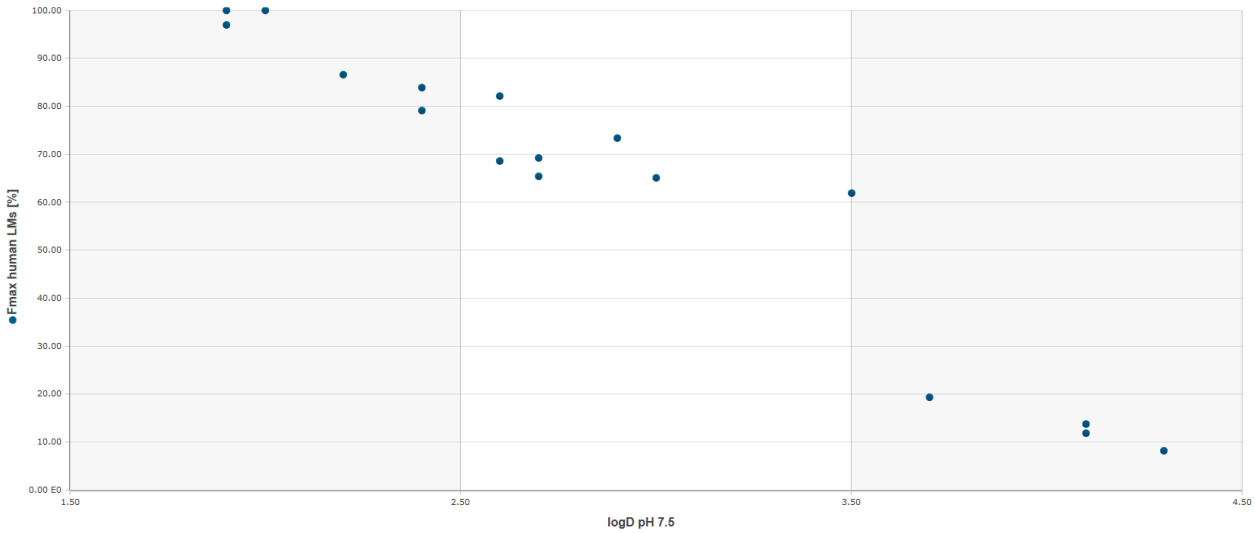
Comparison of the in vitro properties (additional examples)

Supporting Information Table 1. Comparison of the in vitro properties of sulfonamide **1aa** and the analogous =NH sulfonimidamide **2aa** with a structural variety of N-functionalized sulfonimidamides.

Compound	Recovery [%][a] (pH)	F_{max}[b] (h/r/m)-LMs [%]	F_{max}[b] rHep [%]	P_{app} A–B[c] [nm/s]	Efflux ratio[c]	log*D* pH 7.5[d]
 **1aa**	100 (1) 100 (7) 100 (10)	69 (h) 10 (r) 26 (m)	4.3	393	0.64	2.6
 **2aa**	100 (1) 100 (7) 100 (10)	97 (h) 30 (r) 79 (m)	14	378	0.59	1.9
 **2ga**	100 (1) 100 (7) 100 (10)	79 (h) 20 (r) 42 (m)	7.7	376	0.59	2.4
 **2bm**	100 (1) 100 (7) 100 (10)	65 (h) 6.2 (r) 36 (m)	6.2	447	0.53	2.7
 **2bn**	100 (1) 100 (7) 100 (10)	73 (h) 21 (r) 61 (m)	13	365	0.69	2.9
 **2ca**	100 (1) 100 (7) 100 (10)	65 (h) 26 (r) 28 (m)	11	297	0.65	3.0
 **2cb**	100 (1) 100 (7) 100 (10)	62 (h) 13 (r) 39 (m)	4.9	381	0.51	3.5
 **2bd**	100 (1) 100 (7) 100 (10)	14 (h) 5.4 (r) 16 (m)	3.6	386	0.42	4.1
 **2bb**	100 (1) 100 (7) 100 (10)	12 (h) 2.5 (r) 13 (m)	0.3	264	0.54	4.1

[a] Hydrolytic stability measured as recovery of test compound after 24 hours with stirring at pH 1 (HCl buffer), pH 7 (phosphate-buffered saline) and pH 10 (sodium borate buffer).[9] [b] Predicted hepatic metabolic first pass given as the maximum oral bioavailability F_{max} based on a metabolic stability assay using (i) pooled human liver microsomes (hLMs), (ii) pooled rat liver microsomes (rLMs), (iii) pooled mouse liver microsomes (mLMs) and (iv) freshly harvested rat hepatocytes (rHep).[10] [c] P_{app} A–B (apical to basolateral) and efflux ratio (ER) data were generated in a bidirectionally performed Caco2 permeability assay in a 24-well format; ER was calculated as P_{app} B–A/P_{app} A–B.[10] [d] Determined by reversed-phase HPLC.[11]

Correlation of predicted metabolic stabilities in human liver microsomes, given as F_{max}, with the corresponding log*D* values (all tested compounds)



References

1) F. Izzo, M. Schäfer, R. Stockman, U. Lücking, *Chem. Eur. J.* **2017**, *23*, 15189.
2) C. M. M. Hendriks, R. A. Bohmann, M. Bohlem, C. Bolm, *Adv. Synth. Catal.* **2014**, *356*, 1847.
3) F. Teng, J. Cheng, C. Bolm, *Org. Lett.* **2015**, *17*, 3166.
4) F. Teng, J.-T. Yu, Z. Zhou, H. Chu, J. Cheng, *J. Org. Chem.* **2015**, *80*, 2822.
5) M.-A. Virolleaud, V. Sridharan, D. Mailhol, D. Bonne, C. Bressy, G. Chouraqui, L. Commeiras, Y. Coquerel, J. Rodriguez, *Tetrahedron* **2009**, *65*, 9756.
6) M. Frings, I. Thomé, C. Bolm, *Beilstein J. Org. Chem.* **2012**, *8*, 1443.
7) PROTEUM2, Version 2009, Bruker, AXS Inc., Madison, Wisconsin, USA, **2009**.
8) G. M. Sheldrick, *Acta Crystallogr., Sect. A* **2008**, *64*, 112.
9) For the assay description, see: E. H. Kerns, L. Di, *Drug-like Properties: Concepts, Structure Design and Methods*, Elsevier Inc./Academic Press, Burlington, MA, USA, **2008**, pp. 353–356.
10) For the assay description, see U. Lücking, P. Wasnaire, A. Scholz, P. Lienau, G. Siemeister, C. Stegmann, U. Bömer, K. Zheng, P. Gao, G. Chen, J. Xi (Bayer Schering Pharma Aktiengesellschaft), WO 2015155197, **2015**.
11) For the assay description, see: D. J. Minick, J. H. Frenz, M. A. Patrick, D. A. Brent, *J. Med. Chem.* **1988**, *31*, 1023.