SUPPORTING INFORMATION

Synthesis of *NH*-Sulfoximines from Sulfides by Chemoselective One-Pot *N*- and *O*-Transfers

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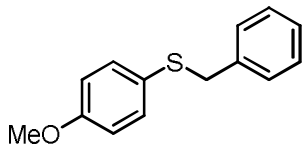
General (Standard techniques)

Reagent grade solvents were used without further purification or drying. Flash column chromatography was performed using 230-400 mesh silica with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on pre-coated, aluminium-backed silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance (254 nm), aqueous potassium permanganate stain or iodine impregnated silica (generally selective for NH sulfoximines). Infrared spectra (ν_{max}, FTIR ATR) were recorded in reciprocal centimeters (cm^{-1}). Nuclear magnetic resonance spectra were recorded on 400 and 500 MHz spectrometers. Chemical shifts for ^{1}H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform, δ = 7.27 ppm). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, app = apparent and br = broad), coupling constant in Hz, integration]. ^{13}C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard ($^{13}CDCl_3$: 77.0 ppm). The high resolution mass spectrometry (HRMS) analyses were performed using a Bruker microTOF QII mass spectrometer equipped with an electrospray ion source (ESI) operated in positive ion mode. The sample solutions (CH_3OH or CH_3OH + 0.1%v/v HCOOH) were introduced by continuous infusion at a flow rate of 180 mL min^{-1} with the aid of a syringe pump. The instrument was operated with end-plate offset and capillary voltages set to –500 V and –4500 V respectively. The nebulizer pressure was 0.4 bar (N_2), and the drying gas (N_2) flow rate was 4.0 L min^{-1}. The capillary exit and skimmer 1 voltages were 90 V and 30 V, respectively. The drying gas temperature was set at 180 °C. The calibration was carried out with sodium formate: a solution made up of 10 μl of 98% formic acid, 10 μl of sodium hydroxide (1.0 M), 490 μl of i-propanol and 490 μl of deionized water. The software used for the simulations was Bruker Daltonics DataAnalysis (version 4.0).

Reagents: Sulfides **1a-g, 1i, 1l, 1n, 1o, 1p, 1q**, sulfilimine **4b**, $PhI(OAC)_2$, $NH_4CO_2NH_2$, ^{15}N-labeled NH_4OAc, amino acids methyl esters were commercially available (Sigma Aldrich, Merck, TCI-Europe, Alfa Aesar). All commercial reagents were used as supplied or purified by standard techniques when required.

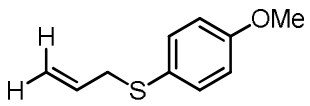
PREPARATION OF SULFIDES, AMINOACIDS AND DIPEPTIDES PRECURSORS

Benzyl(4-methoxyphenyl)sulfane (1h)



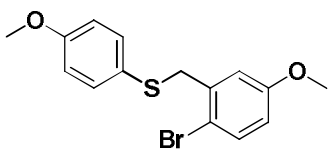
Prepared according to reported procedure.[1] Colorless oil, R_f = 0.5 (95% hexane/EtOAc); IR (film) ν_{max}: 2955, 1871, 1593, 1493, 1453, 1286, 1245, 1179, 1028, 814, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ): 7.29-7.20 (m, 7H), 6.79 (d, *J* = 8.9 Hz, 2H), 3.99 (s, 2H), 3.78 (s, 3H); ^{13}C {^1H} NMR (126 MHz, $CDCl_3$, δ): 159.2, 138.1, 134.1, 128.9, 128.3, 126.9, 126.1, 114.4, 55.3, 41.2; HRMS (ESI-TOF) *m/z*: calcd for $C_{14}H_{14}NaOS^+$ $[M+Na]^+$ 253.0658, found 253.0663.

Allyl(4-methoxyphenyl)sulfane (1k)



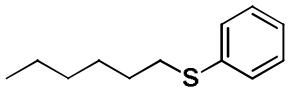
Prepared according to reported procedure.[1] Colorless oil, R_f = 0.5 (90% hexane/EtOAc); IR (film) ν_{max}: 3081, 2955, 2835, 2530, 2043, 1873, 1592, 1492, 1284, 1246, 1173, 1032, 918, 825 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ): 7.34 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 5.88-5.80 (m, 1H), 5.01-4.97 (m, 2H), 3.79 (s, 3H), 3.44-3.42 (m, 2H); ^{13}C {^1H} NMR (126 MHz, $CDCl_3$, δ): 159.0, 134.0, 133.9, 125.8, 117.2, 114.4, 55.3, 39.3; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{10}H_{12}OS$ 181.0682, found 181.0679.

(2-Bromo-5-methoxybenzyl)(4-methoxyphenyl)sulfane (1j)



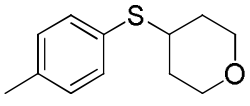
Prepared according to reported procedure.[1] Colorless oil (184 mg, 96%). R_f 0.36 (5% EtOAc:hexane). ^1H NMR (500 MHz, $CDCl_3$, δ): 7.41 (d, *J* = 7.4 Hz, 1H), 7.30-7.27 (m, 2H), 6.81 (d, *J* = 7.4 Hz, 2H), 6.66 (d, *J* = 7.4 Hz, 1H), 6.61 (s, 1H), 4.04 (s, 2H), 3.78 (s, 3H), 3.66, (s, 3H); ^{13}C {^1H} NMR (126 MHz, $CDCl_3$, δ): 159.5, 158.6, 138.2, 134.8, 133.4, 125.4, 115.9, 114.8, 114.7, 114.4, 55.3_5, 55.3_2, 41.8; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{15}H_{15}BrNaO_2S$ 360.9868, found 360.9870

n-Hexyl(phenyl)sulfane (1m)



To a precooled (0°C) solution of diphenyldisulfide (218 mg, 1.0 mmol) in THF (5.0 mL) was added a 1.6M hexane solution of *n*-hexyllithium (0.62 mL, 1.0 mmol) and the reaction was stirred at 0°C for 30 min. Water (5 mL) was added and the product was extracted with diethyl ether (3 x 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 5% EtOAc:Hexane) afforded the sulfide **1m** as a colorless oil (184 mg, 96%). R_f 0.36 (5% EtOAc:hexane). ^1H NMR (500 MHz, $CDCl_3$, δ): 7.34-7.31 (m, 2H) 7.30-7.25 (m, 2H), 6.83 (t, *J* = 7.4 Hz, 1H), 2.92 (t, *J* = 7.4 Hz, 2H), 1.65 (*quintet*, *J* = 7.4 Hz, 2H), 1.44 (*quintet*, *J* = 7.4 Hz, 2H), 1.35-1.25 (m, 4H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C {^1H} NMR (126 MHz, $CDCl_3$, δ): 137.2, 129.0, 128.9, 125.8, 33.8, 31.5, 29.3, 28.7, 22.7, 14.2; Analytical data in agreement with those reported in the literature.[2]

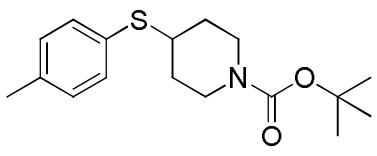
4-[(4-Methylphenyl)sulfanyl]oxane (1r)



4-Methylbenzene-1-thiol (298 mg, 2.4 mmol) was added to a stirred solution of sodium hydride (80 mg, 2.0 mmol) in DMF (3.3 mL) and the reaction was stirred at 25 °C for 30 min. 4-Bromooxane (225 µL, 2.0 mmol) was added and the reaction was heated to 80 °C for 1 h. Water (20 mL) was added and the product was extracted with diethyl ether (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 10% EtOAc:Pentane) afforded the sulfide **1r** as a colorless oil (186 mg, 45%). R_f 0.36 (10% EtOAc:pentane). IR (film)/cm^{-1} 2947, 2920, 2843, 1491, 1442, 1384, 1299, 1232, 1210, 1131, 1085, 1018, 1006. ^1H NMR (400 MHz, $CDCl_3$, δ): 7.36–7.33 (m, 2 H, Ar-H), 7.14–7.11 (m, 2 H, Ar-H), 3.97 (dt, *J* = 11.6, 3.9 Hz, 2 H, 2 × OC(*H*)H), 3.42 (td, *J* = 11.6, 2.4 Hz, 2 H, 2 × OC(H)*H*), 3.19 (tt, *J* = 10.7, 4.0 Hz, 1 H, SCH), 2.34 (s, 3 H, Ar-CH_3), 1.92–1.85 (m, 2 H, 2 × CHC(*H*)H), 1.72–1.60 (m, 2

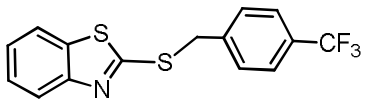
H, 2 × CHC(H)*H*). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, δ): 137.6 (Ar-C_q), 133.5 (2 × Ar-C), 129.8 (Ar-C_q), 129.7 (2 × Ar-C), 67.4 (2 × OCH_2), 43.9 (SCH), 33.2 (2 × $CHCH_2$), 21.1 (Ar-CH_3). HRMS (ESI) m/z Calcd. for $C_{12}H_{17}OS$ $[M+H]^+$: 209.0995; Found: 209.0997.

***tert*-Butyl 4-[(4-methylphenyl)sulfanyl]piperidine-1-carboxylate (1s)**



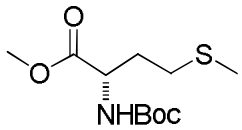
4-Methylbenzene-1-thiol (298 mg, 2.4 mmol) was added to a stirred solution of sodium hydride (80 mg, 2.0 mmol) in DMF (3.3 mL) and the reaction was stirred at 25 °C for 30 min. *tert*-Butyl 4-bromopiperidine-1-carboxylate (394 µL, 2.0 mmol) was added and the reaction was heated to 80 °C for 1 h. Water (20 mL) was added and the product was extracted with diethyl ether (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 10% EtOAc:Pentane) afforded sulfide **1s** as a white solid (186 mg, 45%). R_f 0.41 (10% EtOAc:pentane). IR(film)/cm^{-1} 2974, 2923, 2854, 1689 (C=O), 1492, 1446, 1418, 1364, 1342, 1275, 1262, 1246, 1207, 1160, 1111. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.35–7.32 (m, 2 H, Ar-H), 7.14–7.11 (m, 2 H, Ar-H), 3.97 (m, 2 H, 2 × NC(*H*)H), 3.13 (tt, *J* = 10.3, 3.9 Hz, 1 H, SCH), 2.92–2.86 (m, 2 H, 2 × NC(H)*H*), 2.34 (s, 3 H, Ar-CH_3), 1.94–1.84 (m, 2 H, 2 × CHC(*H*)H), 1.57–1.46 (m, 2 H, 2 × CHC(H)*H*), 1.45 (s, 9 H, $C(CH_3)$). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, δ): 154.7 (C=O), 137.6 (Ar-C_q), 133.5 (2 × Ar-C), 129.9 (Ar-C_q), 129.7 (2 × Ar-C), 79.5 ($C(CH_3)_3$), 45.0 (SCH), 43.2 (2 × NCH_2), 32.1 (2 × $CHCH_2$), 28.4 ($C(CH_3)_3$), 21.1 (Ar-CH_3). HRMS (ASAP) m/z Calcd. for $C_{13}H_{16}O_2S$ [M–*t*Bu]$^+$: 250.0902; Found: 250.0901.

2-[(4-(Trifluoromethyl)benzyl)thio]benzo[d]thiazole (1t)



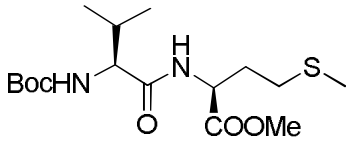
Prepared according to reported procedure.[1] White solid, clean product, 100%; mp = 89-91 °C; IR (KBr) ν_{max}: 3435, 2926, 1615, 1457, 1428, 1333, 1120, 1070, 1019, 840, 759 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.91 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.60-7.57 (m, 4H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 4.64 (s, 2H); ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 165.6, 153.1, 140.9, 135.5, 130.0 (q, $J_{Cq\text{-}F}$ = 32.4 Hz), 129.6, 126.3, 125.7 (q, $J_{CH\text{-}F}$ = 3.8 Hz), 124.6, 124.4 (q, J_{CF} = 273.0 Hz), 121.8, 121.2, 37.0; HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{10}F_3NNaS_2^+$ $[M+Na]^+$ 348.0099, found 348.0102.

***N*-(*tert*-Butoxycarbonyl)-L-methionine methyl ester**



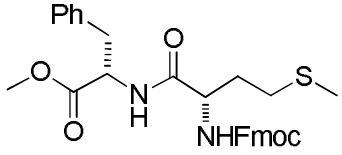
To a solution of L-methionine methyl ester hydrochloride (500 mg, 2.51 mmol) in methanol (2 mL) was added triethylamine (1.05 mL, 7.53 mmol), Boc_2O (602 mg, 2.76 mmol) and the reaction was stirred at 25 °C for 16 hours. The solvent was removed in vacuo, and the crude mixture was washed with acidic water solution (50% v/v HCl, 20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure, affording the sulfide as a colorless oil (581 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 5.13 (br s, d, *J* = 8.1 Hz, 1H), 4.43-4.40 (m, 1H), 3.74 (s, 3H), 2.52 (t, *J* = 7.5 Hz, 2H), 2.15-2.08 (m, 4H), 1.96-1.87 (m, 1H), 1.43 (s, 9H). Analytical data in agreement with those reported in the literature.[3]

***N*-Boc-L-Valinyl-L-Methionine methyl ester**



Prepared according to reported procedure starting from L-methionine methyl ester hydrochloride and N-Boc-L-valine.[3] White solid, R_f = 0.7 (100% EtOAc); mp = 96-100 °C; IR (film) ν_{max}: 3328, 3273, 2930, 2855, 2119, 1748, 1687, 1651, 1516, 1367, 1302, 1248, 1168, 1019 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, δ): 6.55 (br s, 1H), 5.02 (br s, 1H), 4.73-4.69 (m, 1H), 3.90 (dd, *J* = 8.6, 6.3 Hz, 1H), 3.75 (s, 3H), 2.51 (t, *J* = 7.6 Hz, 2H), 2.21-2.16 (m, 2H), 2.09 (s, 3H), 2.03-1.96 (m, 1H), 1.44 (s, 9H), 0.95 (dd, *J* = 19.2, 6.8 Hz, 6H); ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 172.2, 171.6, 155.9, 80.2, 60.2, 52.7, 51.6, 31.7, 30.9, 30.0, 28.4, 19.4, 18.0, 15.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{16}H_{30}N_2NaO_5S^+$ $[M+Na]^+$ 385.1768, found 385.1772.

***N*-Fmoc-L-Methionyl-L-phenylalanine methyl ester**



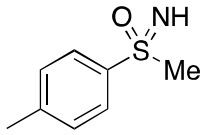
Prepared according to reported procedure starting from L-phenylalanine methyl ester hydrochloride and N-Fmoc-L-methionine.[4] White solid, R_f = 0.6 (50%, hexane/EtOAc), mp = 140-143 °C; IR (film) ν_{max}: 3295, 2926, 1736, 1695, 1539, 1446, 1348, 1282, 1257, 1083, 1036, 912, 756, 738 cm^{-1}; ^1H NMR (500 MHz, CD_3OD, δ): 7.80 (d, *J* = 7.6 Hz, 2H), 7.66 (d, *J* = 6.6 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.24-7.13 (m, 5H), 4.65-4.62 (m, 1H), 4.41-4.32 (m, 2H), 4.24-4.20 (m, 2H), 4.12 (q, *J* = 7.0 Hz, 2H), 3.13 (dd, *J* = 13.8, 5.9 Hz, 1H), 3.01 (dd, *J* = 14.0, 8.3 Hz, 1H), 2.51-2.41 (m, 2H), 2.06 (s, 3H), 2.00-1.89 (m, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.12-1.10 (m, 1H); ^{13}C {^1H} NMR (126 MHz, CD_3OD, δ): 178.7, 174.2, 172.7, 158.3_0, 158.2_9, 142.6_2, 142.6_0, 137.9, 130.3, 129.5, 128.8_1, 128.7_9,128.1_8, 128.1_7, 127.9, 126.2_1, 126.2_0, 120.9, 67.9, 62.4, 55.3, 55.2, 48.4, 38.3, 34.8, 32.8, 31.0, 15.2, 14.4; HRMS (ESI-TOF) *m/z*: calcd for $C_{31}H_{34}N_2NaO_5S^+$ $[M+Na]^+$ 569.2081, found 569.2079.

PREPARATION OF SULFOXIMINES

General Procedure A for the preparation of NH Sulfoximines

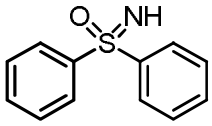
The sulfide **1** (0.5 mmol), (diacetoxyiodo)benzene (1.25 mmol, 2.5 equiv) and ammonium carbamate (2.0 equiv) were added to a flask containing a stirrer bar. MeOH (1 mL, 0.5 M) was added and the reaction was stirred at 25 °C for 3 h. The solvent was removed under reduced pressure. Purification by flash chromatography afforded the sulfoximine product.

Imino(methyl)(*p*-tolyl)-λ^6-sulfanone (2a)



Prepared according to **General Procedure A** using *p*-tolylmethyl sulfide **1a** (84 mg, 0.5 mmol) and purified by flash column chromatography (SiO_2, dry loaded, EtOAc) to afford the title sulfoximine as an off-white solid, 49 mg (96%). R_f = 0.18 (EtOAc); m.p. = 69-70 ºC; IR (film) ν_{max} (cm^{-1}): 3273, 2924, 1597, 1408, 1216, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, δ): 7.91–7.88 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 3.10 (s, 3H), 2.45 (s, 4H, C*H*$_3$, N*H*); ^{13}C {^1H} NMR (101 MHz, $CDCl_3$, δ): 143.9, 140.5, 129.9, 127.7, 46.3, 21.5; HRMS: (ESI-TOF) *m/z*: calcd for $C_8H_{12}NOS$ $[M+H]^+$ 170.0640, found 170.0640. Analytical data in agreement with those reported in the literature.[5]

Iminodiphenyl-λ^6-sulfanone (2b)



Prepared according to **General Procedure A** using diphenyl sulfide **1b** (76 mg, 0.5 mmol). Purification by flash column chromatography (EtOAc) afforded sulfoximine **2b** as a pale yellow solid (105 mg, 97%). R_f = 0.44 (60% EtOAc/pentane); mp = 103-104 °C; IR (film) ν_{max}: 3267, 3062, 1581, 1313, 1475, 1446, 1222, 1127, 1094, 1065, 956 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, δ): 8.09-7.96 (m, 4H), 7.54-7.40 (m, 6H), 3.08 (br s, 1H); ^{13}C {^1H} NMR (101 MHz, $CDCl_3$, δ): 143.2, 132.6, 129.1, 127.9; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{12}NOS$ 218.0640, found 218.0639.

Mechanistic study (see Scheme 3 of the manuscript)

<u>From diphenyl sulfoxide:</u>

Prepared according to General Procedure A starting from diphenyl sulfoxide **3b** (101 mg, 0.5 mmol). Purification by flash column chromatography (2:1 Et_2O:pentane) to afforded the sulfoximine **2b** as a white solid (102 mg, 94%).

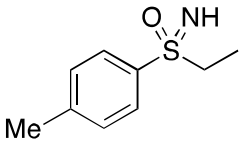
<u>From diphenyl sulfilimine, under standard conditions</u>

Prepared according to General Procedure A using *S*,*S*-diphenylsulfilimine monohydrate **4b** (110 mg, 0.5 mmol). Purification by flash column chromatography (2:1 Et_2O:pentane) to afforded the sulfoximine **2b** as a white solid (94 mg, 87%).

<u>From diphenyl sulfilimine, without N-source</u>

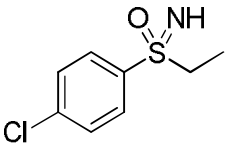
Prepared according to General Procedure A using *S*,*S*-diphenylsulfilimine monohydrate **4b** (110 mg, 0.5 mmol), without the addition of ammonium carbamate. Purification by flash column chromatography (2:3 EtOAc:pentane) afford sulfoximine **2b** as a white solid (98 mg, 90%).

(Phenyl)(ethyl)imino-λ⁶-sulfanone (2c)



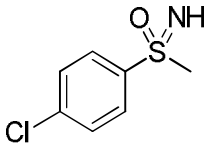
Prepared according to **General Procedure A** using ethyl *p*-tolyl sulfide **1c** (76 mg, 0.5 mmol). Purification by flash column chromatography (EtOAc) afforded sulfoximine **2c** as a pale yellow oil (82 mg, 89%). R_f = 0.24 (EtOAc). IR(film)/cm^{-1} 3271, 3059, 2977, 2938, 2873, 1649, 1596, 1454, 1409, 1209, 1096, 1053, 969, 816, 715. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88–7.80 (m, 2 H, Ar-H), 7.36–7.32 (m, 2 H, Ar-H), 3.15 (q, *J* = 7.4 Hz, 2 H, CH_2), 2.62 (br s, 1 H, NH), 2.44 (s, 3 H, CH_3), 1.25 (t, *J* = 7.4 Hz, 3 H, CH_3). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, δ): 143.9 (Ar-C_q), 138.4 (Ar-C_q), 129.8 (2 × Ar-C), 128.6 (2 × Ar-C), 51.9 (CH_2), 21.5 (Ar-CH_3), 7.9 (CH_3). HRMS (ESI) m/z Calcd. for $C_9H_{14}NOS$ [M+H]$^+$: 184.0796; Found: 184.0791. Compound previously reported with limited data.[6]

(4-Chlorophenyl)(ethyl)imino-λ⁶-sulfanone (2d)



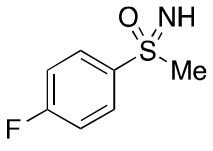
Prepared according to **General Procedure A** using ethyl 4-chlorophenyl sulfide **1d** (74 μL, 0.5 mmol) and purified by flash column chromatography (SiO_2, EtOAc) to afford sulfoximine **2d** as a colorless oil (80 mg, 78%). R_f = 0.36 (EtOAc). IR(film)/cm^{-1} 3263, 3085, 2979, 2959, 1648, 1579, 1471, 1392, 1237, 1210, 1083, 1053, 966. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.93–7.88 (m, 2 H, 2 × Ar-H), 7.56–7.51 (m, 2 H, 2 × Ar-H), 3.24–3.10 (m, 2 H, CH_2), 2.72 (bs, 1 H, NH), 1.27 (t, *J* = 7.4 Hz, 3 H, CH_3). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 139.9 (Ar-C_q), 139.8 (Ar-C_q), 130.1 (2 × Ar-C), 129.4 (2 × Ar-C), 51.9 (CH_2), 7.8 (CH_3). HRMS (ESI) m/z Calcd. for $C_8H_{11}NOS^{35}Cl$ [M+H]$^+$: 204.0250; Found: 204.0259. The observed data (^{1}H and ^{13}C) was consistent with that previously reported in the literature.[7]

(4-Chlorophenyl)(imino)methyl-λ⁶-sulfanone (2e)



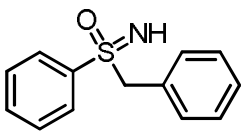
Prepared according to **General Procedure A** using methyl 4-chlorophenyl sulfide **1e** (65 μL, 0.5 mmol) and purified by flash column chromatography (SiO_2, 1:5 EtOAc:pentane) to afford sulfoximine **2e** as a colorless oil (76 mg, 80%). R_f = 0.21 (80% EtOAc: Pentane). IR(film)/cm^{-1} 3263, 3088, 3016, 2926, 1649 (w), 1578, 1470, 1392, 1321, 1218, 1112, 1082, 1023, 997. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.98–7.94 (m, 2 H, 2 × Ar-H), 7.55–7.52 (m, 2 H, 2 × Ar-H), 3.11 (s, 3 H, CH_3), 2.71 (bs, 1 H, NH). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.1 (Ar-C_q), 139.8 (Ar-C_q), 129.5 (2 × Ar-C), 129.2 (2 × Ar-C), 46.2 (CH_3). HRMS (ESI) m/z Calcd. for $C_7H_9NOS^{35}Cl$ [M+H]$^+$: 190.0093; Found: 190.0096. The observed data (^{1}H and ^{13}C) was consistent with that previously reported in the literature.[8]

(4-Fluorophenyl)(imino)methyl-λ⁶-sulfanone (2f)



Prepared according to **General Procedure A** using 4-fluorothioanisole **1f** (61 μL, 0.5 mmol) and purified by flash column chromatography (SiO_2, EtOAc) to afford sulfoximine **2f** as a beige crystalline solid (77 mg, 89%). R_f = 0.20 (EtOAc). IR(film)/cm^{-1} 3288, 3100, 3069, 2997, 2921, 1584, 1492, 1401, 1321, 1215, 1161, 1095, 1079, 1020, 999.^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.06–8.00 (m, 2 H, 2 × Ar-H), 7.26–7.17 (m, 2 H, 2 × Ar-H), 3.11 (s, 3 H, CH_3), 2.88 (br s, 1 H, NH). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, δ): 165.5 (d, $J_{C\text{-}F}$ = 255.3 Hz, Ar-CF), 139.5 (d, $J_{C\text{-}F}$ = 3.0 Hz, Ar-C_q), 130.5 (d, $J_{C\text{-}F}$ = 9.5 Hz, 2 × Ar-C), 116.4 (d, $J_{C\text{-}F}$ = 22.5 Hz, 2 × Ar-C), 46.4 (CH_3). ^{19}F NMR (377 MHz, $CDCl_3$) δ -105.1. HRMS (ESI) m/z Calcd. for C_7H_9NOSF [M+H]$^+$: 174.0389; Found: 174.0391. The observed data (^{1}H and ^{13}C) was consistent with that previously reported in the literature.[9]

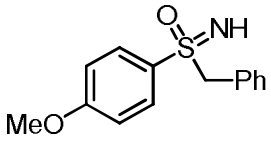
(Benzyl)(imino)(phenyl)-λ⁶sulfanone (2g)



Prepared according to **General Procedure A** using benzyl(phenyl)sulfide **1g** (100 mg, 0.5 mmol) and purified by flash column chromatography (SiO_2, EtOAc) to afford sulfoximine **2g** as a beige crystalline solid (105 mg, 93%). R_f = 0.5 (30% hexane/EtOAc); mp = 107-109 °C; IR ν_{max}(cm^{-1}): 3445, 1637, 1445, 1217, 1110, 977, 756, 700, 534; ^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.76 (d, *J* = 7.8 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.35-7.24 (m, 3H), 7.11 (d, *J* = 7.5 Hz, 2H), 4.44 and 4.37 (2 x

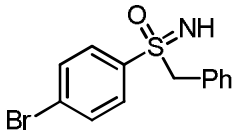
d, AB system, J = 13.4 Hz, 2H), 2.66 (s. br., 1H, NH). ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 139.8, 133.3, 131.1, 128.9, 128.8, 128.5, 128.3, 64.5. HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}NNaOS^+$ $[M+Na]^+$ 254.0610, found 254.0617.

(Benzyl)(imino)(4-methoxyphenyl)-λ^6-sulfanone (2h)



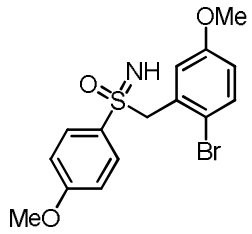
Prepared according to **General Procedure A** using benzyl(4-methoxyphenyl)sulfide **1h** (115 mg, 0.5 mmol) and purified by flash column chromatography (SiO_2, EtOAc) to afford sulfoximine **2h** as a yellow solid (111 mg, 85%). The solid was crystallized by Et_2O/hexane; mp = 94-98 °C; IR (film) ν_{max}: 2917, 1593, 1494, 1455, 1308, 1258, 1213, 1105, 1019, 828, 778, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ): 7.65 (d, J = 8.9 Hz, 2H), 7.35-7.26 (m, 3H), 7.11 (d, J = 7.1 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 4.37 and 4.29 (2 x d, AB system, J = 13.4 Hz, 2H), 3.86 (s, 3H); ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 163.5, 131.9, 131.1 (2C), 129.1, 128.8, 128.6, 114.1, 65.0, 55.8. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{14}H_{16}NO_2S$ 262.0896, found 262.0903.

(Benzyl)(4-bromophenyl)(imino)-λ^6-sulfanone (2i)



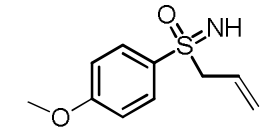
Prepared according to **General Procedure A** using benzyl(4-bromophenyl)sulfide **1i** (139 mg, 0.5 mmol) and purified by flash column chromatography (SiO_2, EtOAc) to afford sulfoximine **2i** as a yellow solid (117 mg, 76%). R_f = 0.7 (50%, EtOAc/hexane); mp = 130-131 °C; IR (film) ν_{max}: 3436, 1570, 1492, 1453, 1385, 1227, 1123, 1066, 991, 813, 770, 736, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ): 7.60-7.57 (m, 4H), 7.36-7.26 (m, 3H), 7.11 (d, J = 7.2 Hz, 2H), 4.37 and 4.30 (2 x d, AB system, J = 13.5 Hz, 2H), 2.35 (s. br. 1H, NH). ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 139.5, 132.1, 131.0, 130.5, 128.9, 128.6, 128.4, 128.3, 64.6. HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{12}BrNNaOS^+$ $[M+Na]^+$ 331.9715, found 331.9706.

(2-Bromo-5-methoxybenzyl)(4-methoxyphenyl)(imino)-λ^6-sulfanone (2j)



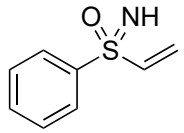
Prepared according to **General Procedure A** using (4-methoxyphenyl)(2-bromo-5-methoxybenzyl) sulfide **1j** (169 mg, 0.5 mmol) and ammonium carbamate (96 mg, 1.25 mmol, 2.5 equiv) and purified by flash column chromatography (SiO_2, ether) to afford sulfoximine **2j** as a colorless oil (100 mg, 54%). R_f = 0.3 (40% EtOAc/hexane); IR (film) ν_{max}: 3292, 2935, 1594, 1495, 1242, 1108, 1018, 834 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, δ): 7.68 (d, J = 9.0 Hz, 2H), 7.34 (d, J = 8.8 Hz, 1H), 6.96-6.88 (m, 3H), 6.74 (dd, J = 8.8, 3.1 Hz, 1H), 4.67 and 4.57 (2 x d, AB system, J = 13.6 Hz, 2H), 3.86 (s, 3H), 3.76 (s, 3H). ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 163.7, 158.6, 133.4, 131.3, 129.8, 117.8, 116.9, 116.5, 114.0, 63.7, 55.6, 55.5. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{16}BrNNaO_3S^+$ $[M+Na]^+$ 391.9926, found 393.9903.

Imino(phenyl)(allyl)-λ^6-sulfanone (2k)



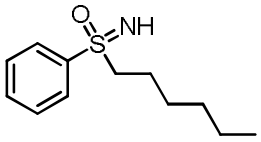
Prepared according to **General Procedure A** using allyl phenyl sulfide **1k** (75 mg, 0.5 mmol) and ammonium carbamate (96 mg, 1.25 mmol, 2.5 equiv) and purified by flash column chromatography (SiO_2, ether) to afford sulfoximine **2k** as a colorless oil (90 mg, 99%).R_f = 0.4 (90% EtOAc/hexane); IR (film) ν_{max}: 3273, 2918, 1594, 1496, 1311, 1259, 1218, 1100, 1018, 991, 834, 802 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ): 7.86 (d, J = 9.0 Hz, 2H), 6.99 (d, J = 9.0 Hz, 2H), 5.88-5.79 (m, 1H), 5.34-5.31 (m, 1H), 5.15-5.11 (m, 1H), 3.88 (s, 3H), 3.89-3.77 (m, 2H); ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 163.5, 132.3, 131.1, 125.8, 124.4, 114.3, 62.8, 55.8. HRMS (ESI-TOF) *m/z*: calcd for $C_{10}H_{13}NNaO_2S^+$ $[M+Na]^+$ 234.0559, found 234.0569.

Imino(phenyl)(vinyl)-λ^6-sulfanone (2l)



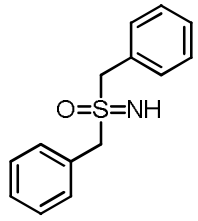
Prepared according to General Procedure A using phenyl vinyl sulfide **1l** (65 μL, 0.5 mmol) and ammonium carbamate (96 mg, 1.25 mmol, 2.5 equiv) and purified by flash column chromatography (SiO_2, ether) to afford sulfoximine **2l** as a colorless oil (12 mg, 14%). R_f = 0.13 (1:1 pentane:EtOAc). IR (film)/cm^{-1} 3265, 3062, 1639, 1583, 1476, 1446, 1255, 1218, 1128, 1095, 1070, 972, 760, 731, 691. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.01–7.97 (m, 2 H), 7.64–7.58 (m, 1 H), 7.57–7.52 (m, 2 H), 6.75 (dd, *J* = 16.4, 9.5 Hz, 1 H, alkene CH), 6.42 (d, *J* = 16.4 Hz, 1 H, alkene CH), 5.98 (d, *J* = 9.5 Hz, 1 H, alkene CH), 2.87 (br s, 1 H, NH). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, δ): 141.8 (C_q), 140.6 (SCH), 133.0 (Ar-C) 129.3 (2 × Ar-C), 128.2 (2 × Ar-C), 126.7 (=CH_2). The observed data (^{1}H and ^{13}C) was consistent with that previously reported in the literature.[7]

Imino(phenyl)(hexyl)-λ^6-sulfanone (2m)



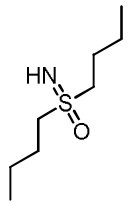
Prepared according to **General Procedure A** using phenyl hexyl sulfide **1m** (97 mg, 0.5 mmol) and ammonium carbamate (96 mg, 1.25 mmol, 2.5 equiv) and purified by flash column chromatography (SiO_2, ether) to afford sulfoximine **2k** as a colorless oil (106 mg, 95%). The product was washed with Et_2O; IR (film) ν_{max}: 3272, 2927, 1445, 1223, 1110, 991, 752, 689 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.97-7.95 (m, 2H), 7.62-7.59 (m, 1H), 7.56-7.52 (m, 2H), 3.17-3.07 (m, 2H), 1.78-1.61 (m, 2H), 1.35-1.19 (m, 6H), 0.84 (t, *J* = 7.0 Hz, 3H); ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 142.1, 133.0, 129.1, 128.4, 57.5, 31.2, 27.9, 23.0, 22.3, 13.9. HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{12}H_{20}NOS^+$ 226.1260, found 226.1263.

Dibenzyl(imino)-λ^6-sulfanone (2n)



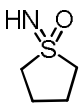
Prepared according to **General Procedure A** using dibenzyl sulfide **1n** (107 mg, 0.5 mmol) and ammonium carbamate (96 mg, 1.25 mmol, 2.5 equiv) and purified by flash column chromatography (SiO_2, ether) to afford sulfoximine **2n** as a white solid (106 mg, 86%). R_f = 0.24 (50% EtOAc/pentane); mp = 173-174 °C; IR (film) ν_{max}: 3246, 3064, 3030, 2978, 2919, 1490, 1454, 1418, 1257, 1247, 1156, 1150, 1072, 1026, 759, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.41 (s, 10H), 4,27 (d, *J* = 13.1 Hz, 2H), 4.17 (d, *J* = 13.1 Hz, 2H), 2.53 (br s, 1H). ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 131.1, 129.0, 128.9, 127.8, 60.5. HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{14}H_{16}NOS^+$ 246.0953, found 246.0958. The observed data (^{1}H and ^{13}C) was consistent with that previously reported in the literature.[6]

Iminodibutyl-λ^6-sulfanone (2o)



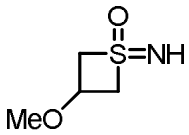
Prepared according to **General Procedure A** using dibutyl sulfide **1o** (73 mg, 0.5 mmol) and ammonium carbamate (96 mg, 1.25 mmol, 2.5 equiv) and purified by flash column chromatography (SiO_2, ether) to afford sulfoximine **2n** as a colorless oil (88 mg, 99%). R_f = 0.4 (70% Hex/EtOAc); IR (film) ν_{max}: 3272, 2960, 1724, 1466, 1380, 1242, 1101, 1016, 807, 729 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$, δ): 3.13-3.05 (m, 2H), 2.55 (br s, 1H), 1.84 (dt, *J* = 15.7, 7.9 Hz, 2H), 1.52-1.44 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, δ): 54.7, 24.5, 21.9, 13.7; HRMS (ESI-TOF) *m/z*: calcd for $C_8H_{19}NNaOS^+$ [M+Na]$^+$ 200.1080, found 200.187.

1-Iminotetrahydro-1*H*-1λ^6-thiophene 1-oxide (2p)



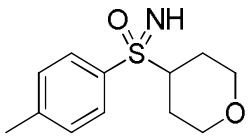
Prepared according to **General Procedure A** using tetrahydrothiophene **1p** (44 mg, 0.5 mmol) and ammonium carbamate (96 mg, 1.25 mmol, 2.5 equiv) and purified by flash column chromatography (SiO_2, ether) to afford sulfoximine **2p** as a colorless oil (56 mg, 99%). R_f = 0.36 (10% MeOH/CH_2Cl_2); IR (film) ν_{max}: 3401, 3259, 2953, 1650, 1449, 1416, 1275, 1192, 1140, 1077, 992, 895, 718, 664 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, δ): 3.13-3.02 (m, 4H), 2.27-2.13 (m, 5H, 2 x CH_2 overlapping NH). ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, δ): 55.4, 24.0. HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_4H_{10}NOS^+$ 120.0483, found 120.0476. The observed data (^{1}H and ^{13}C) was consistent with that previously reported in the literature.[7]

1-Imino-3-methoxy-1λ⁶-thietane 1-oxide (2q)



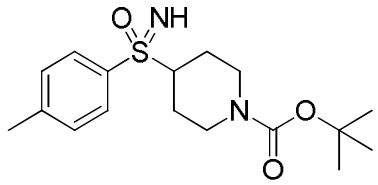
Prepared according to **General Procedure A** using 3-methoxythietane **1q** (52 mg, 0.5 mmol) and ammonium carbamate (96 mg, 1.25 mmol, 2.5 equiv) and purified by flash column chromatography (SiO_2, ether) to afford sulfoximine **2q** as a colorless oil (inseparable mixture of diastereoisomers dr = 3:2, 56 mg, 85%). R_f = 0.3 (100% EtOAc); IR (film) ν_{max}: 3271, 2937, 1633, 1462, 1385, 1241, 1216, 1145, 1084, 1021, 960, 731 cm^{-1}; ^1H NMR (500 MHz, 3:2 mixture of diasteroisomers A and B, $CDCl_3$, δ): 4.35-4.23 (m, 3H, diastereoisomers), 4.09-4.06 (m, 2H, diastereoisomers A and B), 3.33 (s, 3H, diastereoisomer A), 3.34 (s, 3H, diastereoisomer B), 3.12 (br s, 1H); ^{13}C {^1H} NMR (126 MHz, $CDCl_3$, δ): 72.1 (A), 71.8 (B), 62.0 (A), 61.8 (B), 57.1 (A/B). HRMS (ESI-TOF) *m/z*: calcd for $C_4H_9NNaO_2S^+$ $[M+Na]^+$ 158.0246, found 158.0255.

[(4-Methylphenyl)(oxan-4-yl)imino-λ⁶-sulfanyl]one (2r)



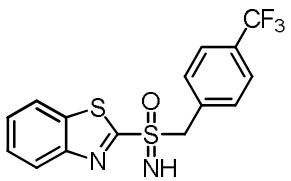
Prepared according to **General Procedure A** using 4-[(4-methylphenyl)sulfanyl]oxane **1r** (104 mg, 0.5 mmol) and purified by flash column chromatography (SiO_2, EtOAc) to afford sulfoximine **2r** as a white solid (91.2 mg, 76%). R_f 0.18 (EtOAc). IR (film)/cm^{-1} 3261, 2945, 2913, 2854, 1597, 1492, 1443, 1391, 1269, 1234, 1202, 1174, 1123, 1104, 1082, 1027, 1017, 979. ^1H NMR (400 MHz, $CDCl_3$, δ): 7.83–7.77 (m, 2 H, Ar-H), 7.38–7.32 (m, 2 H, Ar-H), 4.04 (td, *J* = 11.9, 3.7 Hz, 2 H, 2 × OC(*H*)H), 3.32 (tdd, *J* = 11.9, 6.7, 2.1 Hz, 2 H, 2 × OC(H)*H*), 3.15 (tt, *J* = 12.2, 3.8 Hz, 1 H, SCH), 2.65 (bs, 1 H, NH), 2.45 (s, 3 H, Ar-CH_3), 2.03 (dtd, *J* = 13.0, 4.1, 2.1 Hz, 1 H, CHC(*H*)H), 1.88 (dtd, *J* = 12.4, 4.1, 2.1 Hz, 1 H, CHC(*H*)H), 1.79–1.64 (m, 2 H, 2 × CHC(H)*H*). ^{13}C {^1H} NMR (101 MHz, $CDCl_3$, δ): 144.3 (Ar-C_q), 136.3 (Ar-C_q), 129.9 (2 × Ar-C), 129.7 (2 × Ar-C), 66.9 (OCH_2), 66.8 (OCH_2), 61.6 (SCH), 26.6 ($CHCH_2$), 26.1 ($CHCH_2$), 21.7 (Ar-CH_3). HRMS (ESI) m/z Calcd. for $C_{12}H_{18}NO_2S^+$ $[M+H]^+$: 240.1058; Found: 240.1060.

***tert*-Butyl 4-[(4-methylphenyl)oxo-λ⁶-sulfanyl]piperidine-1-carboxylate (2s)**



Prepared according to **General Procedure A** using *tert*-butyl 4-[(4-methylphenyl)sulfanyl]piperidine-1-carboxylate **1s** (154 mg, 0.5 mmol) and purified by flash column chromatography (SiO_2, EtOAc) to afford sulfoximine **2s** as a white solid (122 mg, 72%). R_f 0.31 (EtOAc). IR(film)/cm^{-1} 32771, 2974, 2931, 1686 (s, C=O), 1596, 1476, 1451, 1419, 1365, 1348, 1279, 1252, 1206, 1159, 1116, 1061, 1011, 977. ^1H NMR (400 MHz, $CDCl_3$, δ): 7.82–7.77 (m, 2 H, Ar-H), 7.38–7.33 (m, 2 H, Ar-H), 4.23 (bs, 2 H, NC(*H*)H), 3.04 (tt, *J* = 12.1, 3,4 Hz, 1 H, SCH), 2.64 (bs, 3 H, NC(H)*H* + NH), 2.46 (s, 3 H, Ar-CH_3), 2.10 (d, *J* = 12.1 Hz, 1 H, CHC(*H*)H), 1.97 (d, *J* = 12.1 Hz, 1 H, CHC(*H*)H), 1.63–1.48 (m, 2 H, CHC(H)*H*), 1.43 (s, *J* = 2.3 Hz, 9 H, $C(CH_3)_3$). ^{13}C {^1H} NMR (101 MHz, $CDCl_3$, δ): 154.4 (C=O), 144.3 (Ar-C_q), 136.4 (Ar-C_q), 129.8 (2 × Ar-C), 129.5 (2 × Ar-C), 80.0 ($C(CH_3)_3$), 62.6 (SCH), 42.8 (2 × NCH_2), 28.4 ($C(CH_3)_3$), 25.8 ($CHCH_2$), 25.3 ($CHCH_2$), 21.6 (Ar-CH_3). HRMS (ESI) m/z Calcd. for $C_{17}H_{27}N_2O_3S^+$ $[M+H]^+$: 339.1742; Found: 339.1759.

2-(*S*-(4-(Trifluoromethyl)benzyl)sulfonimidoyl)benzo[d]thiazole (2t)



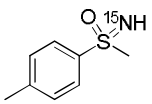
Prepared according to **General Procedure A** using 2-[(4-(trifluoromethyl)benzyl)thio]benzo[d]thiazole **1t** (162 mg, 0.5 mmol) and purified by crystallization with Et_2O to afford sulfoximine **2t** as a white solid (122 mg, 83%). IR (film) ν_{max}: 3246, 2917, 1466, 1419, 1335, 1254, 1117, 1069, 852, 761 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ): 8.23 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 8.3, 1H), 7.59-7.55 (m, 3H), 7.44 (d, *J* = 8.1 Hz, 2H), 4.87 and 4.74 (2 x d, AB system, *J* = 13.6 Hz, 2H), 3.44 (s, br. 1H, NH). ^{13}C {^1H} NMR (126 MHz, $CDCl_3$, δ): 168.4, 152.8, 137.6, 131.7, 131.3 (q, J_{C-F} = 32 Hz), 131.1, 127.8, 127.6, 125.7 (q, J_{C-F} = 3.6 Hz), 125.3, 123.7 (q, J_{C-F} = 273 Hz), 122.3, 62.0. ^{19}F NMR (470 MHz, $CDCl_3$ δ): -62.9; HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{11}F_3N_2NaOS_2^+$ $[M+Na]^+$ 379.0157, found 379.0163.

PREPARATION OF ^{15}N-LABELED SULFOXIMINES

General Procedure B for the preparation of ^{15}N-labeled sulfoximines

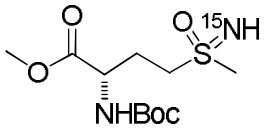
The sulfide **1a** (0.5 mmol), (diacetoxyiodo)benzene (1.25 mmol, 2.5 equiv) and ammonium acetate (up to 8.0 equiv) were added to a flask containing a stirrer bar. MeOH (1 mL, 0.5 M) was added and the reaction was stirred at 25 °C for 3 h. The solvent was removed under reduced pressure. Purification by flash chromatography afforded the sulfoximine product.

^{15}N-Labeled imino(methyl)(*p*-tolyl)-λ^6-sulfanone (2aa)



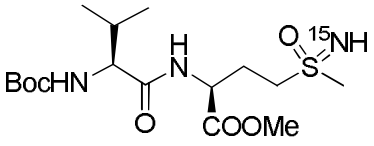
Prepared according to **General Procedure B** using *p*-tolylmethyl sulfide (84 mg, 0.5 mmol) and ^{15}N-ammonium acetate (1 mmol), and purified by flash column chromatography (SiO_2, dry loaded, EtOAc) to afford the title sulfoximine as an off-white solid, 49 mg (96%). R_f = 0.18 (EtOAc); m.p. = 69-70 ºC; IR (film) ν_{max} (cm^{-1}): 3273, 2924, 1597, 1408, 1216, 1093 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.84 (d, , 2H), 7.30 (d, J = 8.0 Hz, 2H), 3.05 (d, $J_{C\text{-}N}$ = 2.0 Hz, 3H), 2.41 (s, 3H, C*H*$_3$, N*H*); ^{13}C NMR (101 MHz, $CDCl_3$, δ): 144.0, 140.6, 130.0, 127.8, 46.3 (d, $J_{C\text{-}N}$ = 7.5 Hz), 21.6; HRMS: (ESI-TOF) *m/z*: calcd for $C_8H_{12}{}^{15}NOS^+$ $[M+H]^+$ 171.0604, found 171.0603.

^{15}N-Labeled methyl 2-[(tert-butoxycarbonyl)amino]-4-(S-methylsulfonimidoyl)butanoate (*^{15}HN=S(O)R$_2$, 5a, 1:1 mixture of diastereomers)*



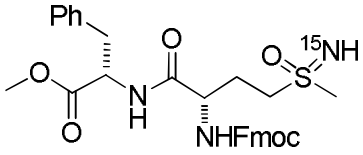
Prepared according to **General Procedure B** using *N*-Boc-L-methionine methyl ester (131 mg, 0.50 mmol) and ^{15}N-ammonium acetate (1 mmol), and purified by washing with Et_2O/MeOH (1:1, 10 mL) to afford the title sulfoximine as a white solid, 130 mg (88%). IR (KBr) ν_{max}: 3419, 2981, 2528, 1689, 1441, 1207, 1166, 1024, 973 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, inseparable *1:1 mixture of diastereoisomers*, δ): 5.3-5.33 (m, 1H), 4.42-4.41 (m, 1H), 3.76-3.75 (m, 3H, $J_{C\text{-}N}$ = 2 Hz, CH_3-S(O)=NH), 3.25-3.10 (m, 2H), 2.99 (s, 3H), 2.44-2.33 (m, 1H), 2.21-2.08 (m, 1H), 1.43 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$, δ): 171.8, 155.4, 80.5, 53.3, 52.7, 52.0, 43.2, 43.1, 28.2, 26.4, 25.9; HRMS (ESI-TOF) *m/z*: calcd for $C_{11}H_{22}{}^{15}NNNaO_5S^+$ $[M+Na]^+$ 318.1117, found 318.1106.

^{15}N-Labeled *N*-Boc-L-valinyl-L-methionine methyl ester sulfoximine (5b, *^{15}HN=S(O)R$_2$, 1:1 mixture of diastereomers*)



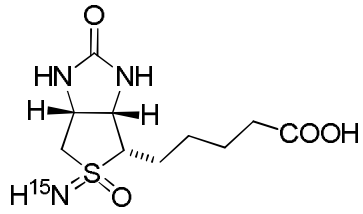
Prepared according to **General Procedure B** using *N*-Boc-L-Valinyl-L-Methionine methyl ester (108 mg, 0.30 mmol) and ^{15}N-ammonium acetate (2.4 mmol), and purified by chromatography on silica gel (90%, CH_2Cl_2/MeOH) to afford the title sulfoximine as a white solid, 100 mg (85%). White solid, R_f = 0.7 (90%, CH_2Cl_2/MeOH); ^{1}H NMR (500 MHz, CD_3OD, *1:1 mixture of diastereoisomers*, δ): 4.65-4.58 (m, 1H), 3.89-3.81 (m, 1H), 3.75-3.74 (m, 3H, $J_{C\text{-}N}$ = 2 Hz CH_3-S(O)=NH), 3.33-3.27 (m, 2H), 3.03 (s, 3H), 2.45-2.32 (m, 1H), 2.23-2.11 (m, 1H), 2.05-1.98 (m, 2H), 1.45 (s, 9H), 0.97 (dd, J = 11.9, 6.8 Hz, 6H). ^{13}C {^{1}H} NMR (126 MHz, CD_3OD, *mixture of diastereoisomers*, δ): 174.8, 172.6, 158.0, 157.9, 80.6, 61.8, 54.8, 53.9, 52.9$_5$, 52.9$_2$, 52.0, 51.9, 42.2$_6$, 42.2$_3$, 38.2, 38.1, 31.9, 31.7, 28.7$_7$, 28.7$_5$, 26.7, 19.7, 19.6, 18.8; HRMS (ESI-TOF) *m/z*: calcd for $C_{16}H_{31}N_2{}^{15}NNaO_6S^+$ $[M+Na]^+$ 417.1802, found 417.1799.

^{15}N-Labeled *N*-Fmoc-L-methionyl-L-phenylalanine methyl ester sulfoximine (5c, *^{15}HN=S(O)R$_2$, 1:1 mixture of diastereomers*)



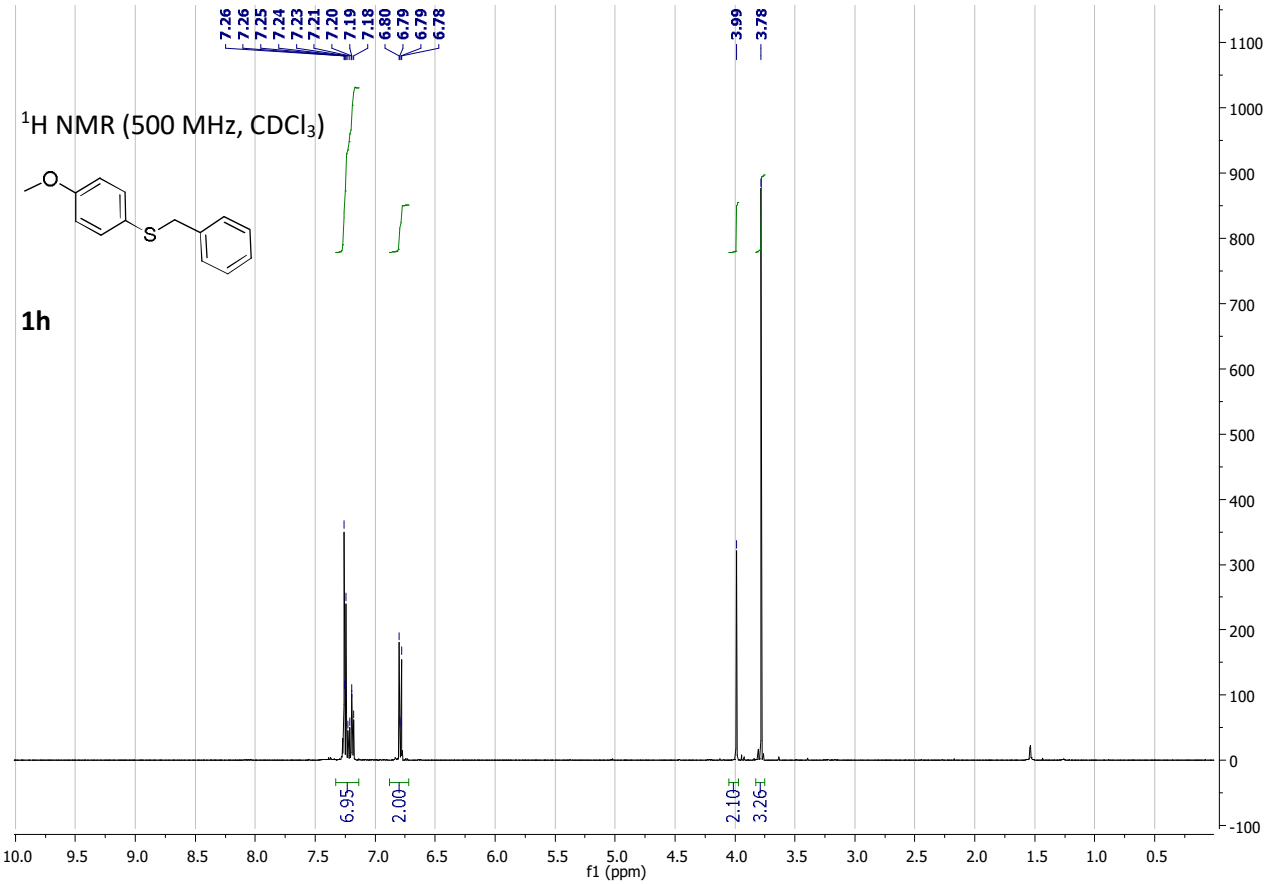
Prepared according to **General Procedure B** using *N*-Fmoc-L-methionyl-L-phenylalanine methyl ester (160 mg, 0.30 mmol) and ^{15}N-ammonium acetate (2.4 mmol), and purified by chromatography on silica gel (95%, CH_2Cl_2/MeOH) to afford the title sulfoximine as a white solid, 132 mg (78%). White solid, R_f = 0.5 (95% CH_2Cl_2/MeOH); ^{1}H NMR (500 MHz, CD_3OD, 1:1 *mixture of diastereoisomers*, δ): 7.80 (d, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 7.7 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.25-7.16 (m, 4H), 4.65 (dd, *J* = 8.0, 6.2 Hz, 1H), 4.38-4.37 (m, 2H), 4.29-4.26 (m, 1H), 4.20 (t, *J* = 6.7 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.23-3.19 (m, 1H), 3.14 (dd, *J* = 13.9, 5.8 Hz, 1H), 3.04-2.98 (m, 4H, *CH$_3$ 1° diast.*), 2.62 (s, 3H, *CH$_3$ 2° diast.*), 2.21-2.07 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, CD_3OD, *mixture of diastereoisomers*, δ): 173.2, 172.8$_8$, 172.8$_6$, 158.2, 145.3, 145.1, 142.6$_2$, 142.6$_1$, 137.9, 130.3, 129.5, 128.8$_4$, 128.8$_1$, 128.2$_5$, 128.2$_0$, 127.9, 126.1$_8$, 126.1$_9$, 121.0, 120.9, 68.0, 62.5, 55.4, 54.4$_7$, 54,4$_5$, 53.7$_7$, 53.7$_4$, 49.3, 42.2, 38.2, 26.9$_7$, 26.9$_5$, 14.4; HRMS (ESI-TOF) *m/z*: calcd for $C_{31}H_{35}{}^{15}N N_2NaO_6S^+$ $[M+Na]^+$ 601.2115, found 601.2098.

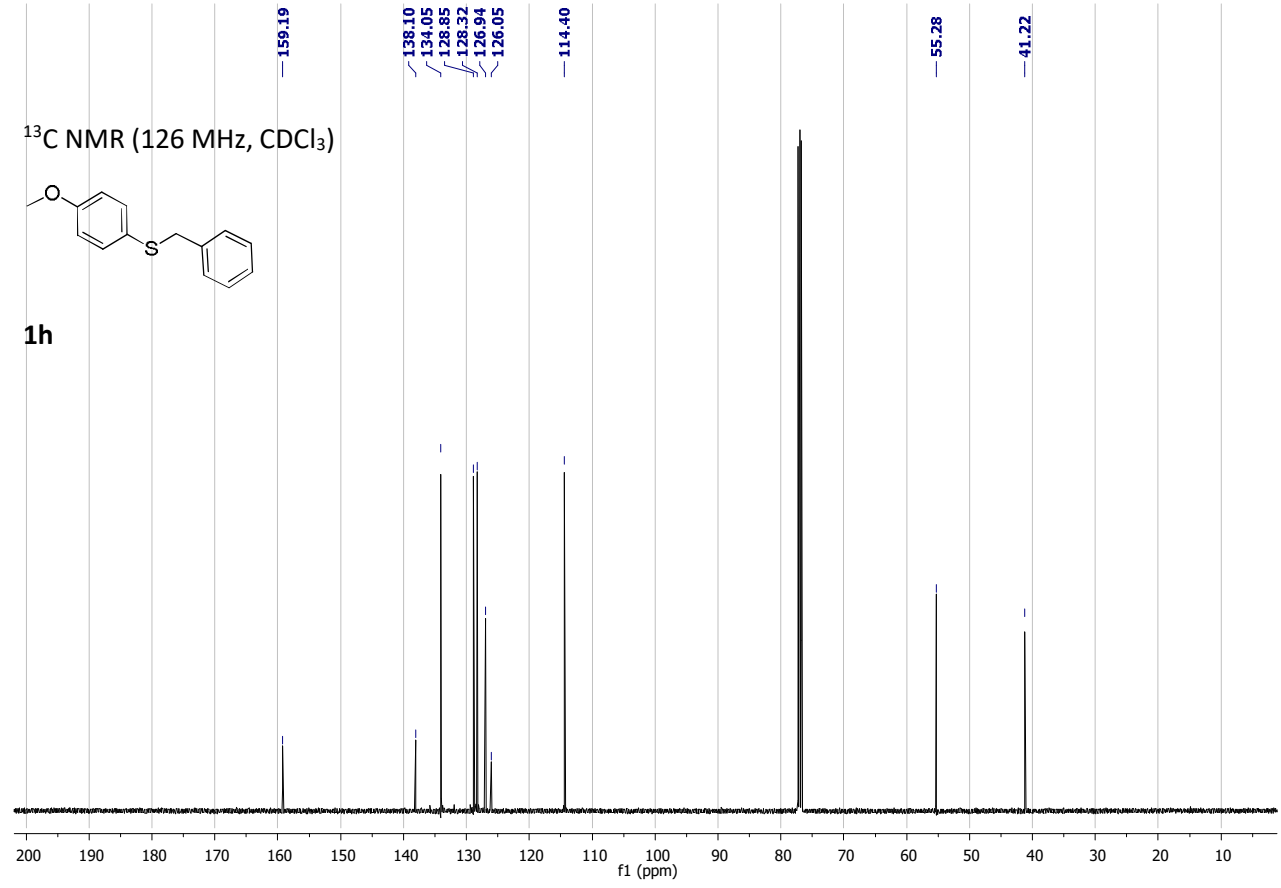
^{15}N-Labeled biotin sulfoximine (5d, *^{15}HN=S(O)R$_2$, 3:1 mixture of diastereomers*)

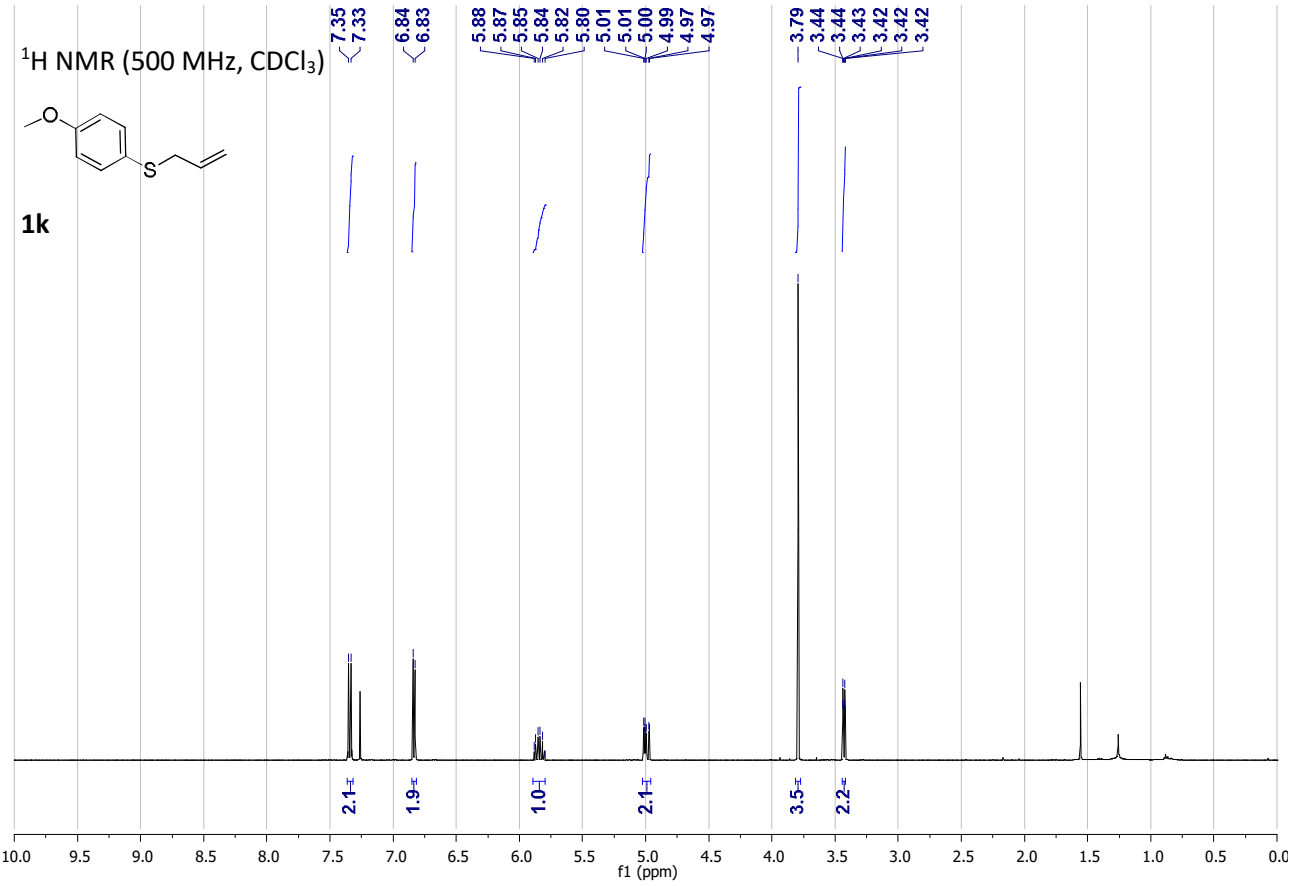


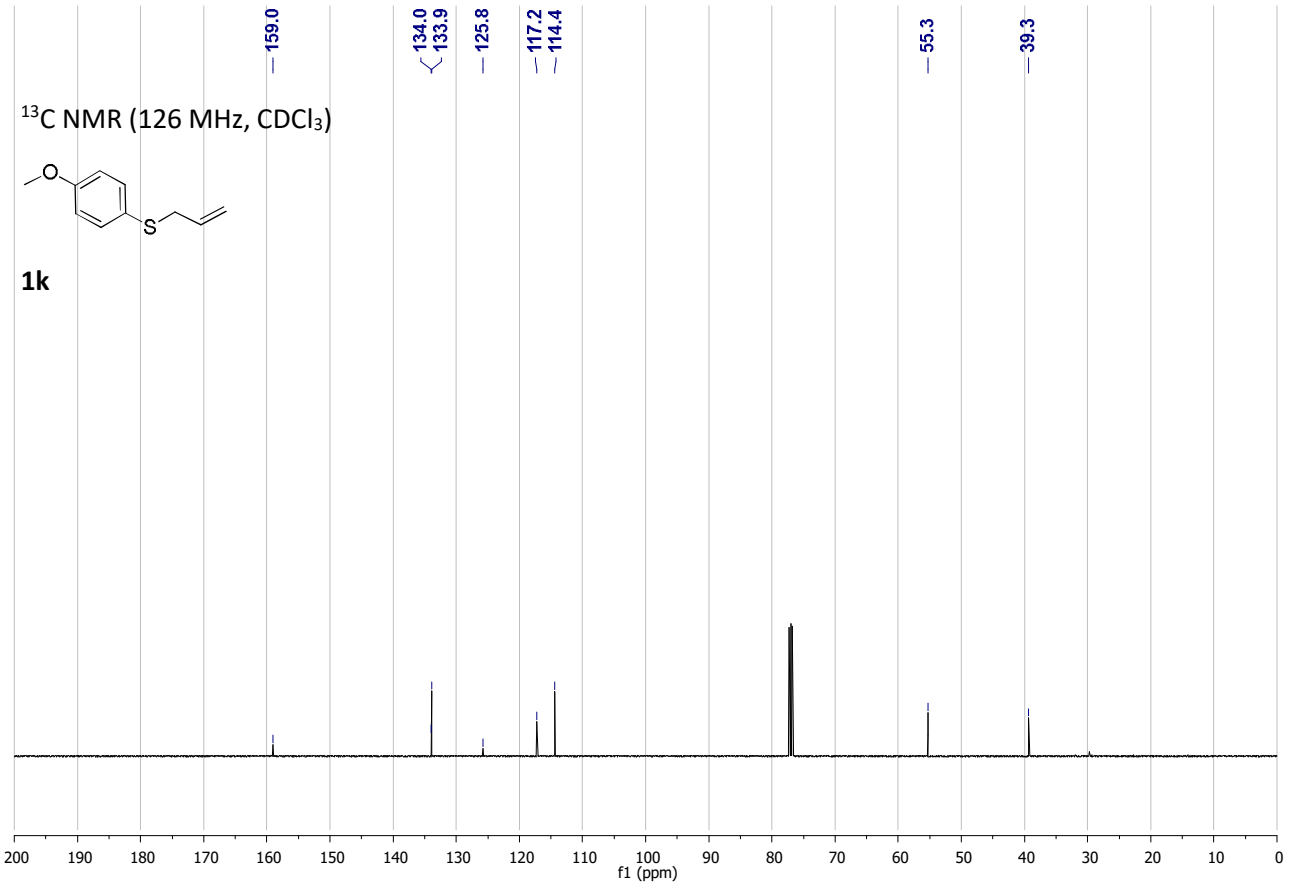
Prepared according to **General Procedure B** using Biotin (74 mg, 0.30 mmol) and ^{15}N-ammonium acetate (2.4 mmol), and purified by washing with Et_2O (10 mL) to afford the title sulfoximine as a white solid, 62 mg (75%).The product was washed with Et_2O; White solid; mp = 188-192 °C (the product decomposes); IR (KBr) ν_{max}: 3788, 3306, 2944, 2866, 2502, 1694, 1651, 1489, 1436, 1316, 1266, 1233, 1184, 989 cm^{-1}; ^{1}H NMR (500 MHz, 3:1 *mixture of diastereoisomers,* DMSO, δ): 6.62 (br s, 1H, *minor*), 6.51 (br s, 1H, *major* and *minor*), 6.45 (br s, 1H, *major*), 4.40-4.30 (m, 2H, *major* and *minor*), 3.21 (dd, *J* = 6.98, 13.23 Hz, 1H), 3.08 (dd, *J* = 13.1, 6.5 Hz, 1H), 3.02 (d, *J*= 13.6 Hz, 1H), 2.22 (t, *J* = 7.4 Hz, 2H, *major* and *minor*), 1.75-1.68 (m, 1H), 1.65-1.58 (m, 1H), 1.57-1.50 (m, 2H), 1.44-1.38 (m, 2H); ^{13}C NMR (126 MHz, DMSO, selected data for major isomer, δ): 174.4, 161.9, 62.6, 57.3, 54.5, 49.7, 33.4, 25.8, 24.5, 21.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{10}H_{17}{}^{15}NN_2NaO_4S^+$ $[M+Na]^+$ 299.0802, found 299.0812.

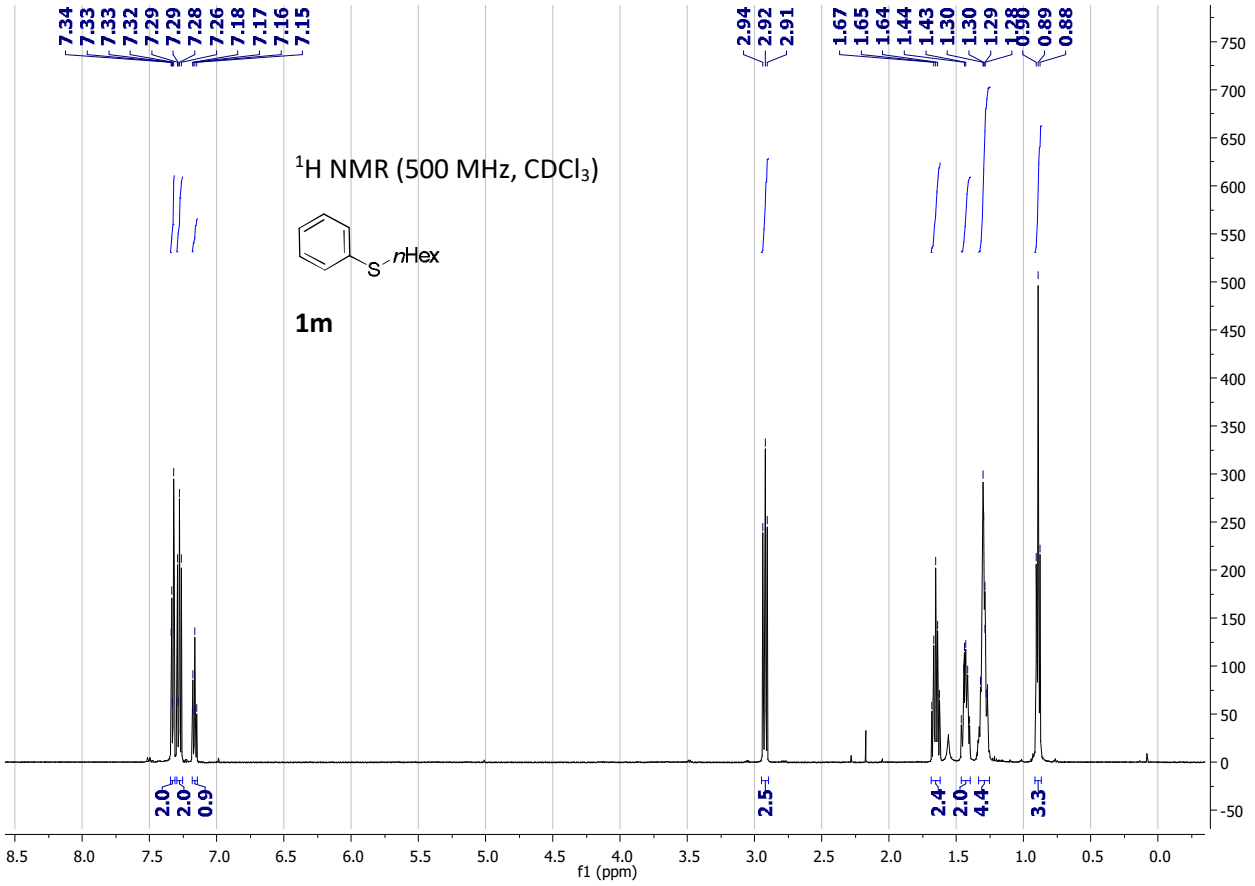
^{1}H and ^{13}C NMR spectra of sulfides

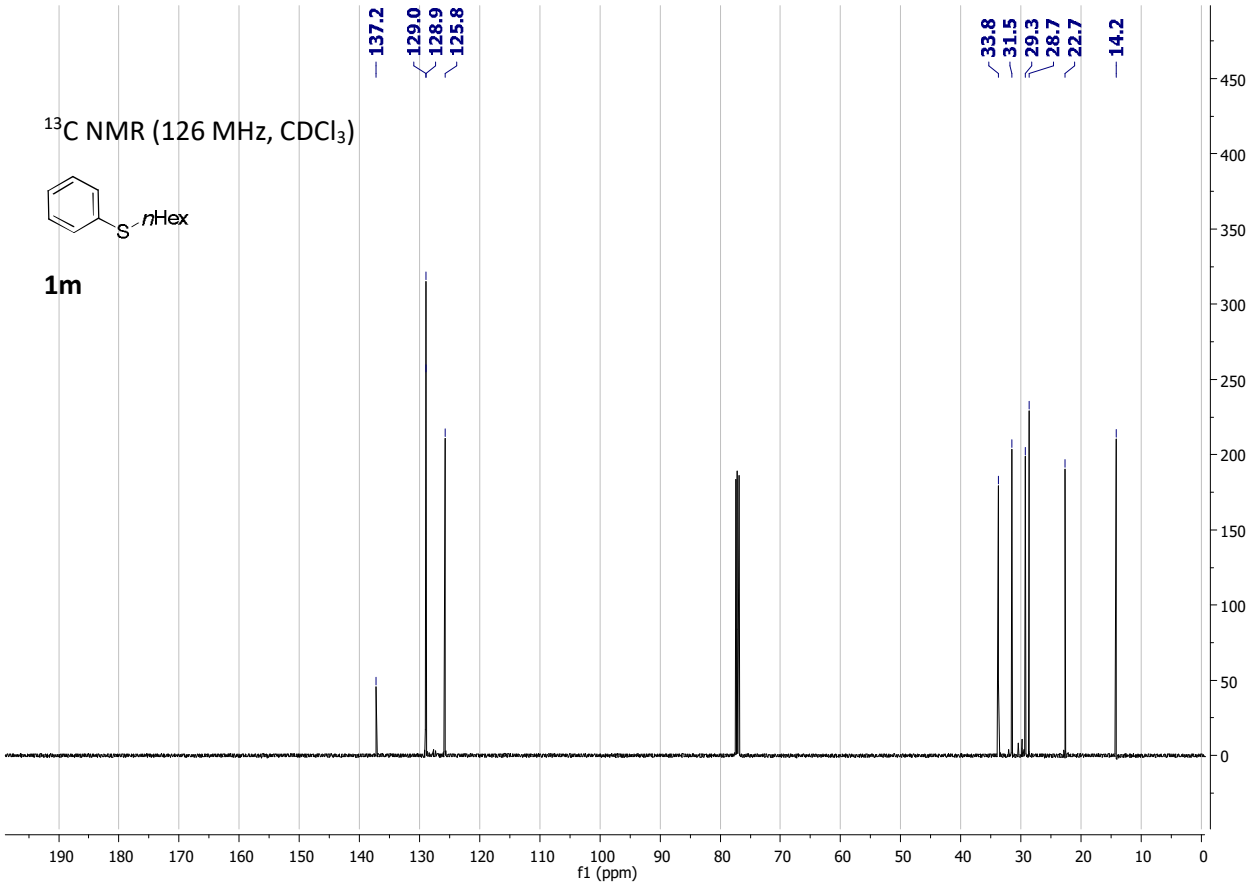

7.26
7.26
7.25
7.24
7.23
7.21
7.20
7.19
7.18
6.80
6.79
6.79
6.78
3.99
3.78
1H NMR (500 MHz, CDCl3)
1h
6.95
2.00
2.10
3.26
f1 (ppm)

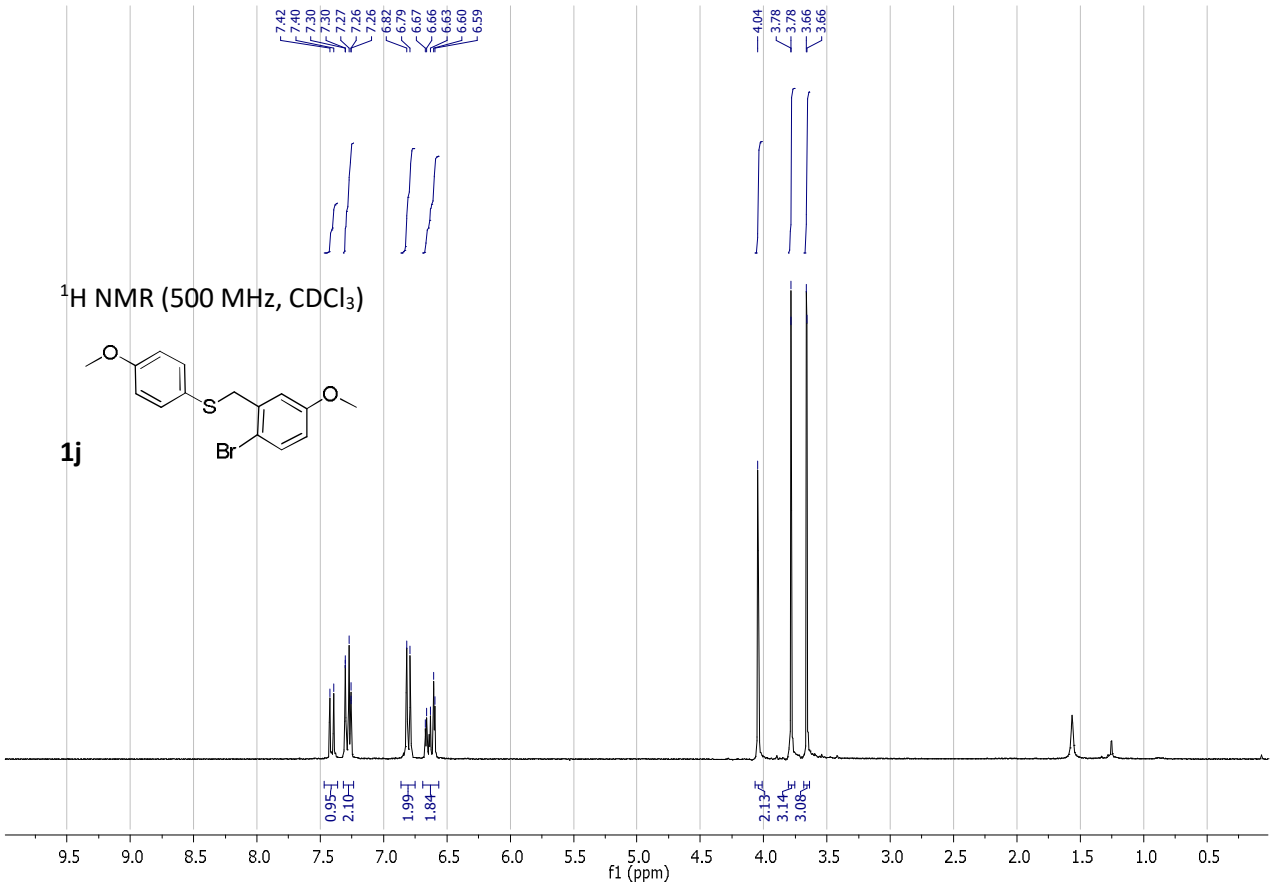

159.19
138.10
134.05
128.85
128.32
126.94
126.05
114.40
55.28
41.22
13C NMR (126 MHz, CDCl3)
1h
f1 (ppm)


^{1}H NMR (500 MHz, $CDCl_3$)
1k
7.35
7.33
6.84
6.83
5.88
5.87
5.85
5.84
5.82
5.80
5.01
5.01
5.00
4.99
4.97
4.97
3.79
3.44
3.44
3.43
3.42
3.42
3.42
2.1
1.9
1.0
2.1
3.5
2.2
f1 (ppm)


^{13}C NMR (126 MHz, $CDCl_3$)
1k
159.0
134.0
133.9
125.8
117.2
114.4
55.3
39.3
f1 (ppm)

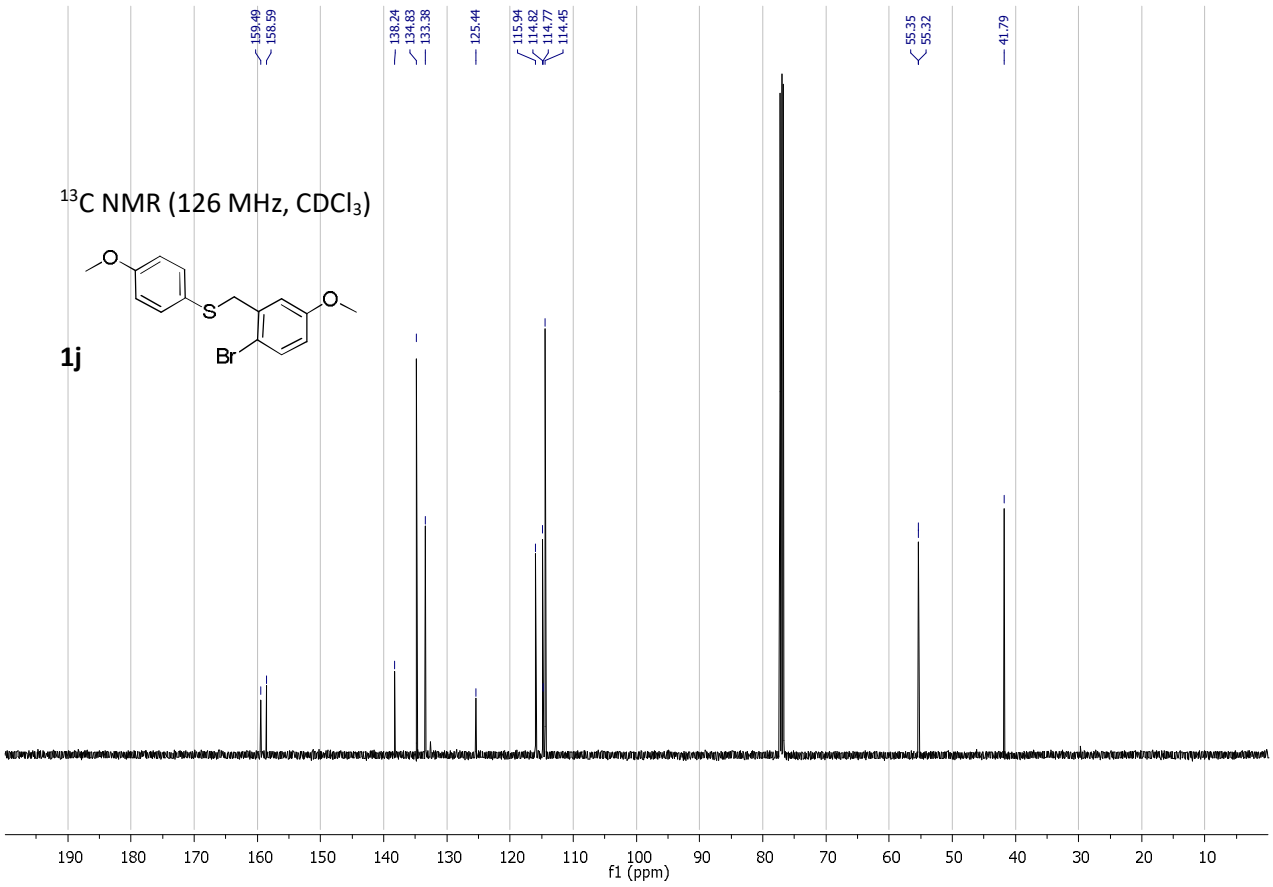

7.34
7.33
7.33
7.32
7.29
7.29
7.28
7.26
7.18
7.17
7.16
7.15
2.94
2.92
2.91
1.67
1.65
1.64
1.44
1.43
1.30
1.29
1.28
0.90
0.89
0.88
^{1}H NMR (500 MHz, $CDCl_3$)
nHex
1m
2.0
2.0
0.9
2.5
2.4
2.0
4.4
3.3
f1 (ppm)


137.2
129.0
128.9
125.8
33.8
31.5
29.3
28.7
22.7
14.2
^{13}C NMR (126 MHz, $CDCl_3$)
nHex
1m
f1 (ppm)



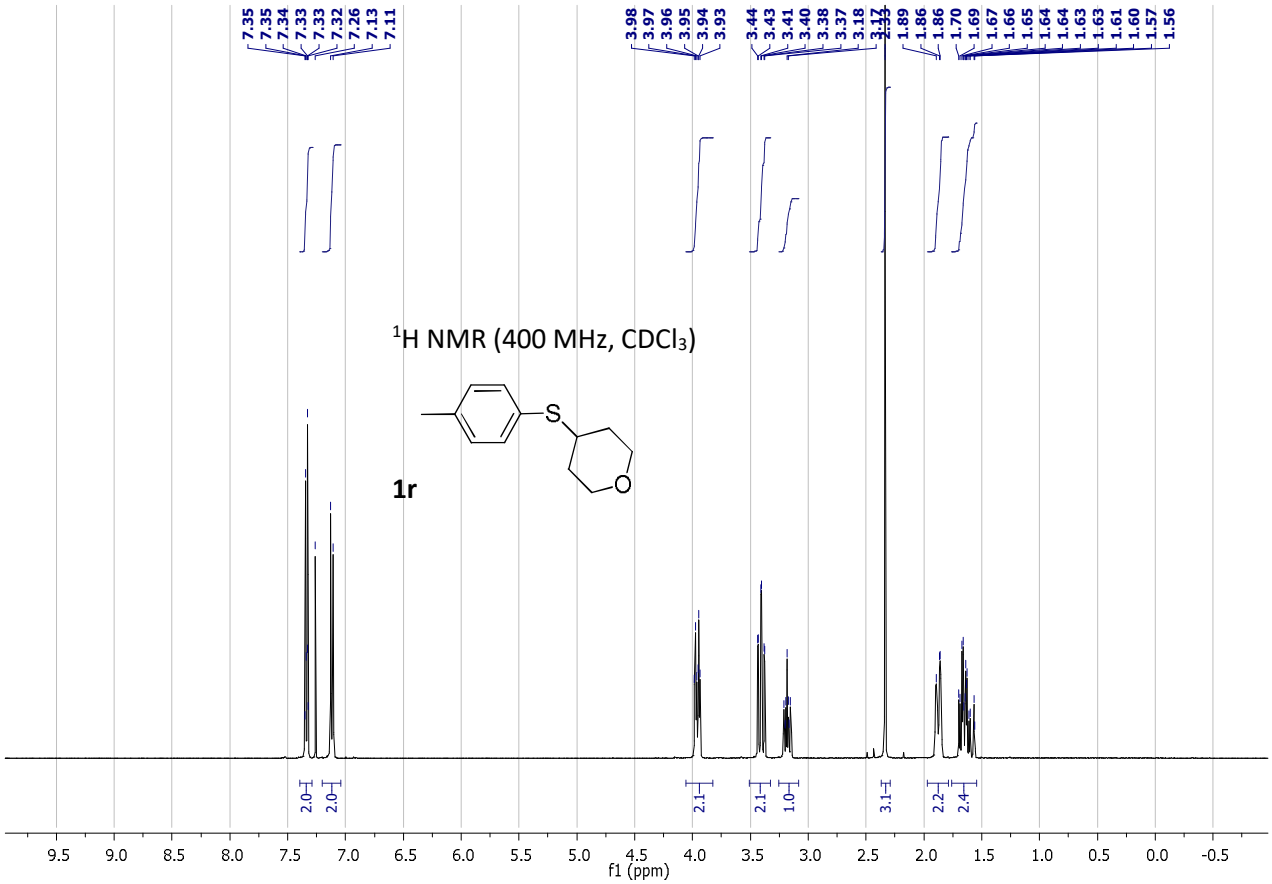
^{1}H NMR (500 MHz, $CDCl_3$)

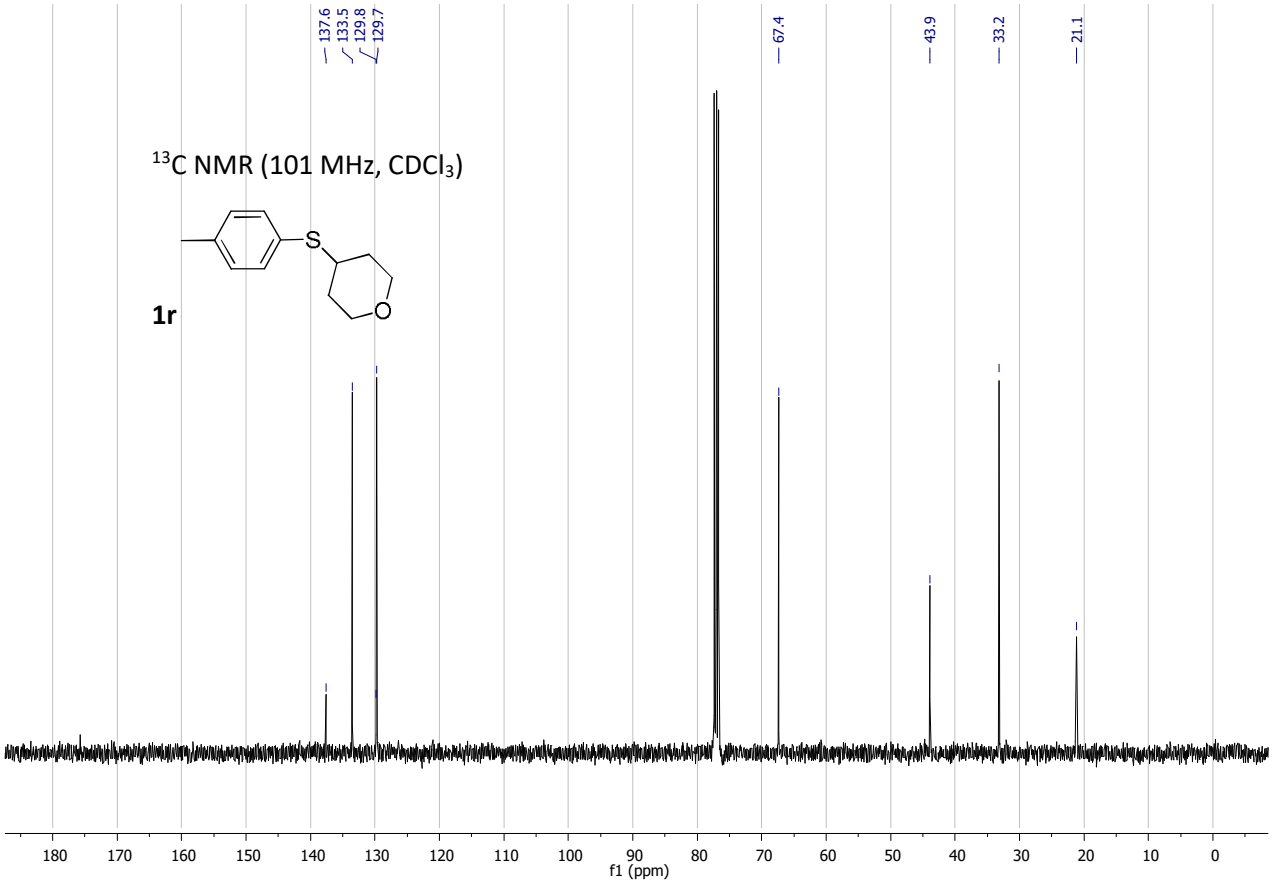
1j

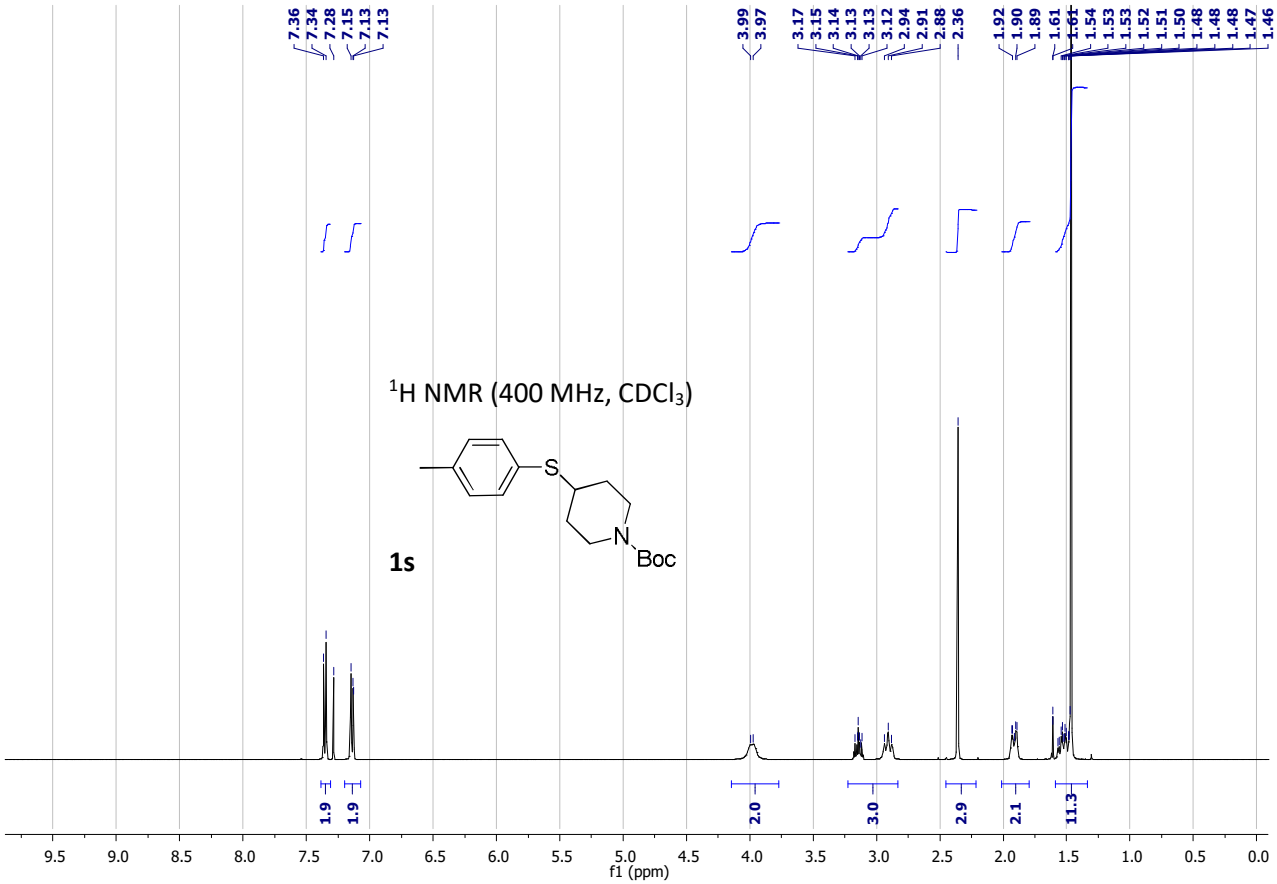


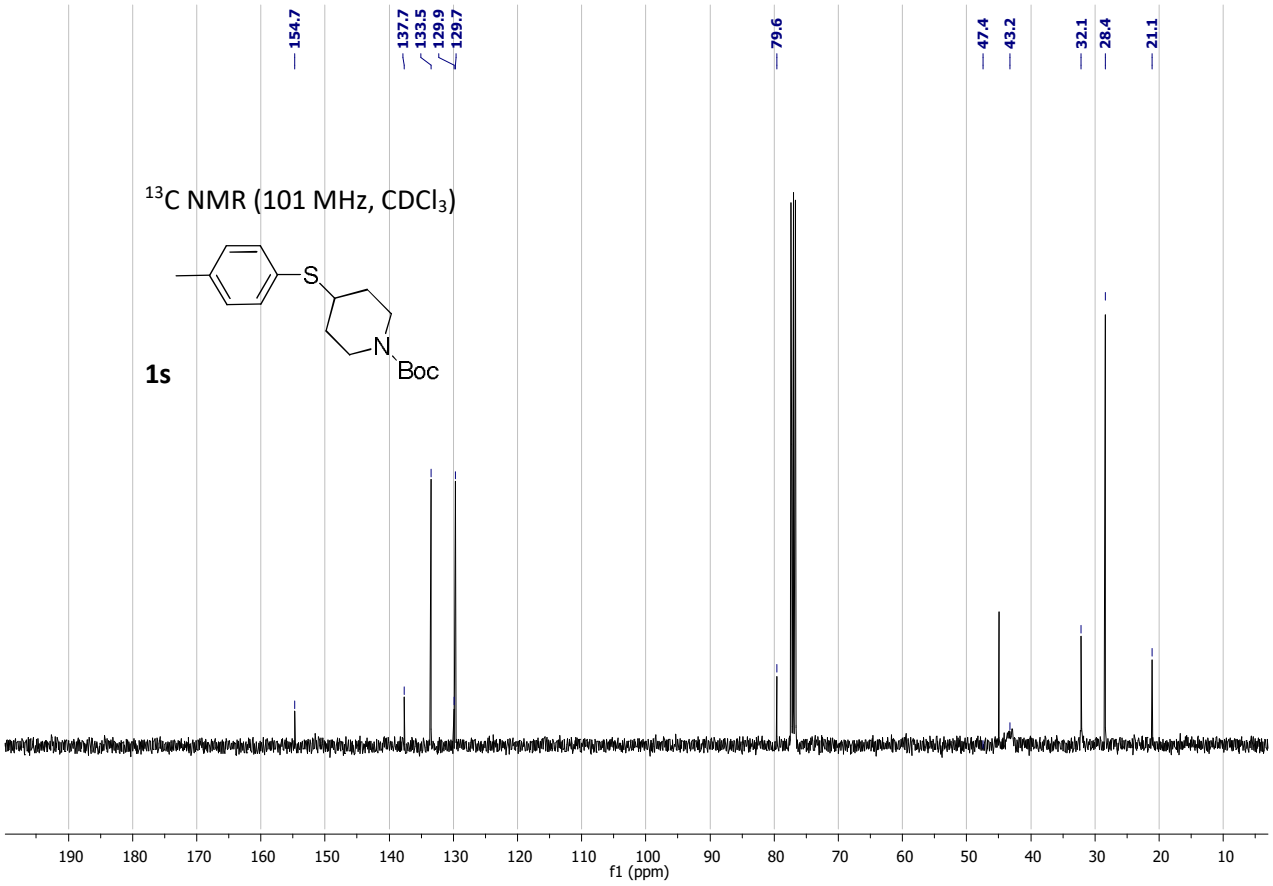
^{13}C NMR (126 MHz, $CDCl_3$)

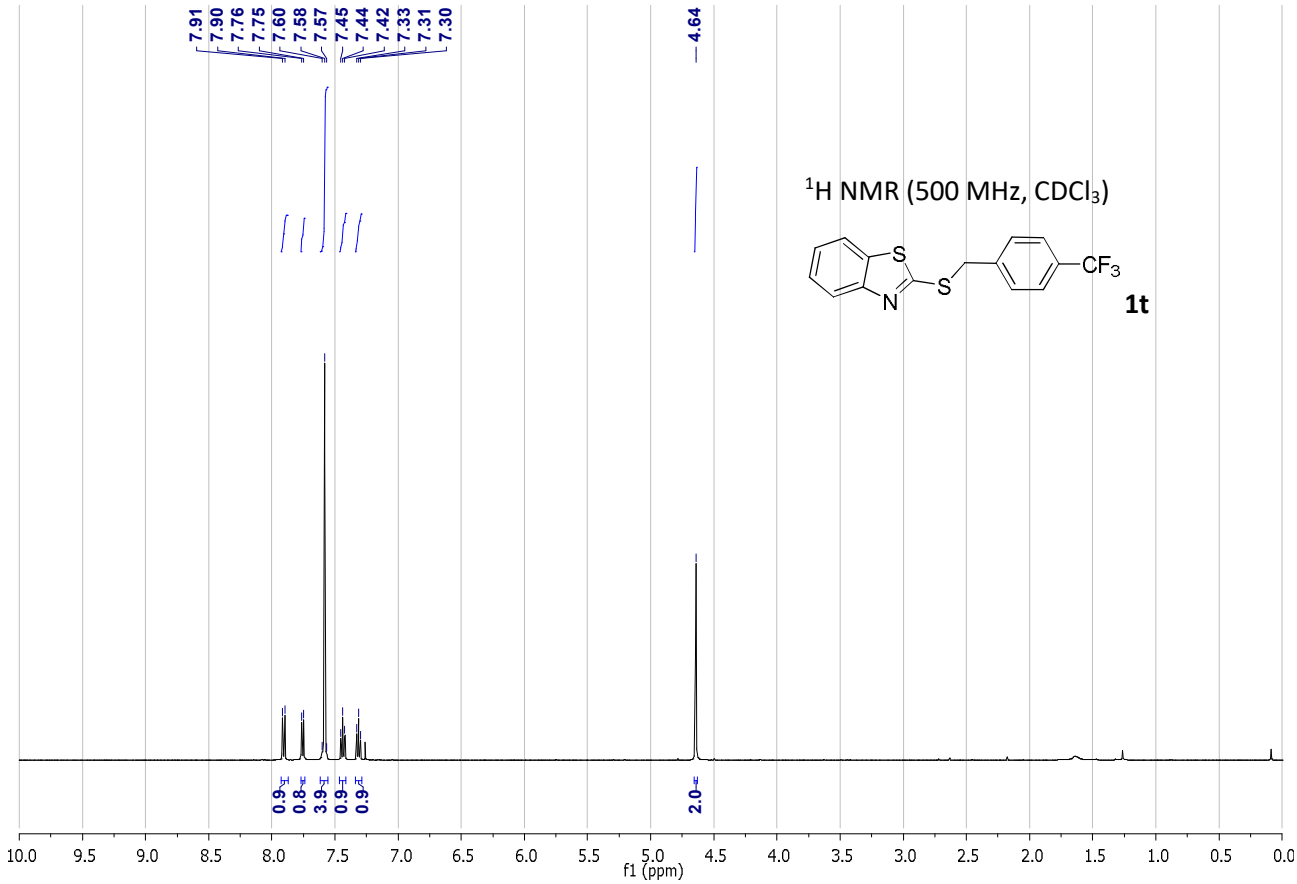
1j

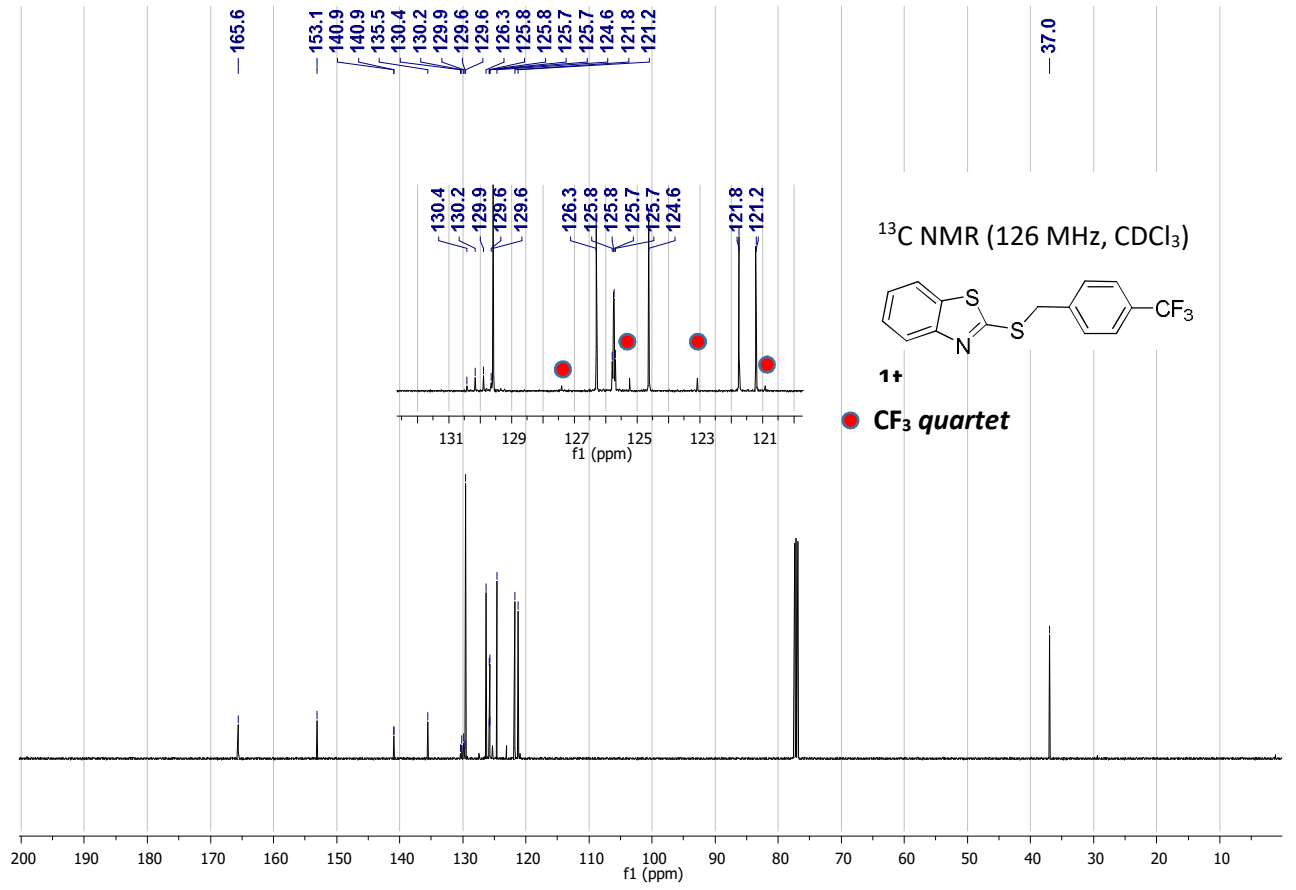

7.35
7.35
7.34
7.33
7.33
7.32
7.26
7.13
7.11
3.98
3.97
3.96
3.95
3.94
3.93
3.44
3.43
3.41
3.40
3.38
3.37
3.18
3.17
3.13
1.89
1.86
1.86
1.70
1.69
1.67
1.66
1.65
1.64
1.64
1.63
1.63
1.61
1.60
1.57
1.56
^{1}H NMR (400 MHz, $CDCl_3$)
S
O
1r
2.0
2.0
2.1
2.1
1.0
3.1
2.2
2.4
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


137.6
133.5
129.8
129.7
67.4
43.9
33.2
21.1
^{13}C NMR (101 MHz, $CDCl_3$)
S
O
1r
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

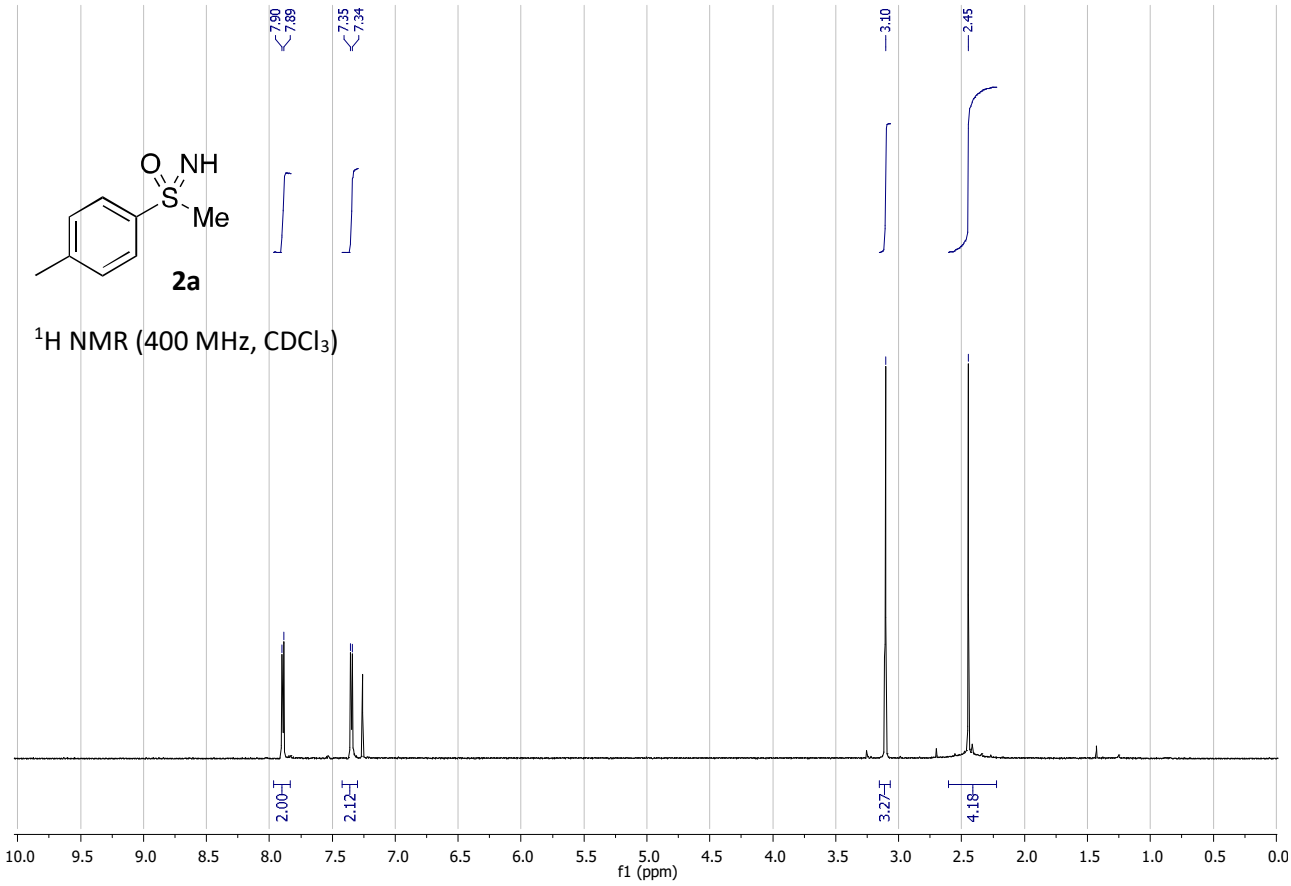

7.36
7.34
7.28
7.15
7.13
7.13
3.99
3.97
3.17
3.15
3.14
3.13
3.13
3.12
2.94
2.91
2.88
2.36
1.92
1.90
1.89
1.61
1.61
1.54
1.53
1.53
1.52
1.51
1.50
1.48
1.48
1.48
1.47
1.46
1H NMR (400 MHz, CDCl3)
S
N
Boc
1s
1.9
1.9
2.0
3.0
2.9
2.1
11.3
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

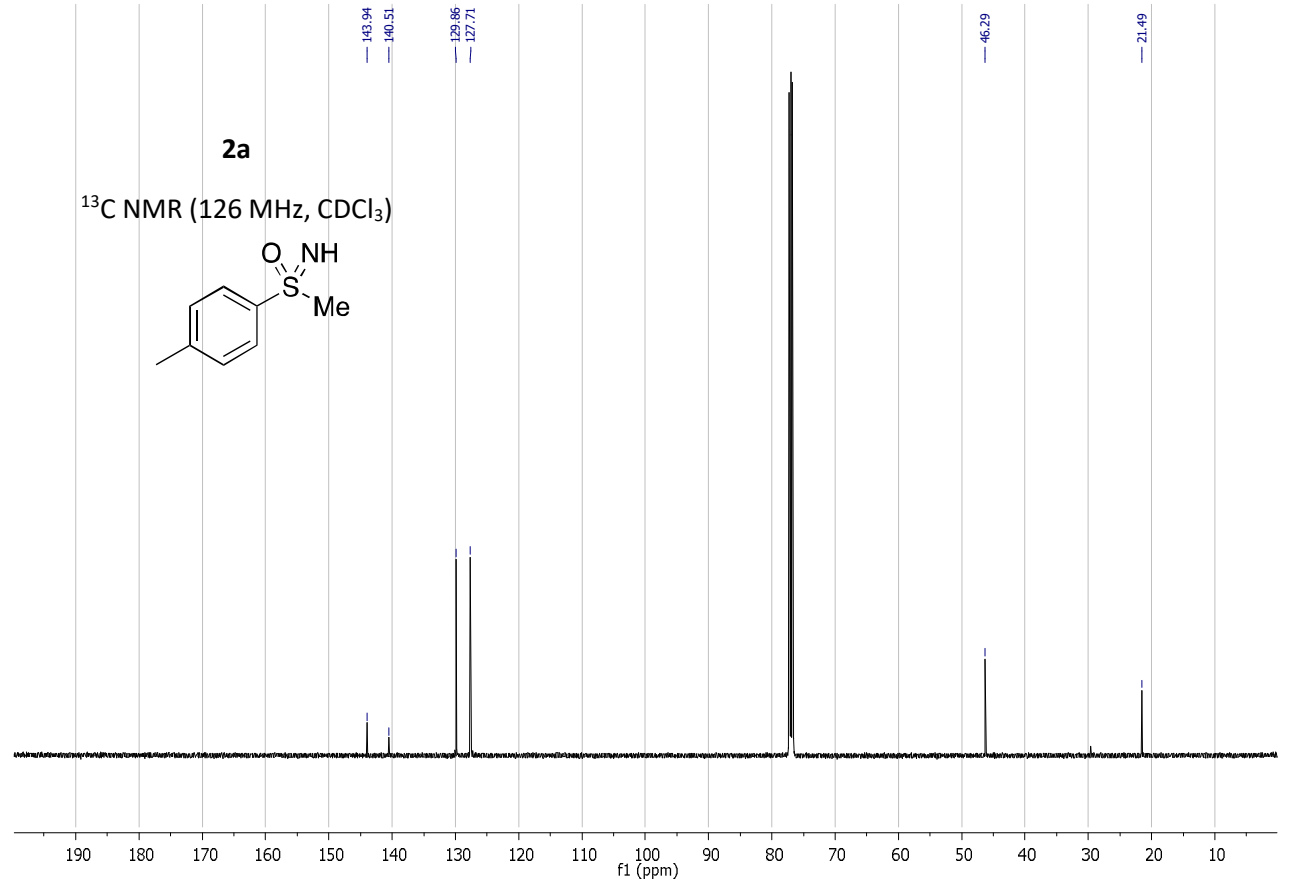

154.7
137.7
133.5
129.9
129.7
79.6
47.4
43.2
32.1
28.4
21.1
13C NMR (101 MHz, CDCl3)
S
N
Boc
1s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

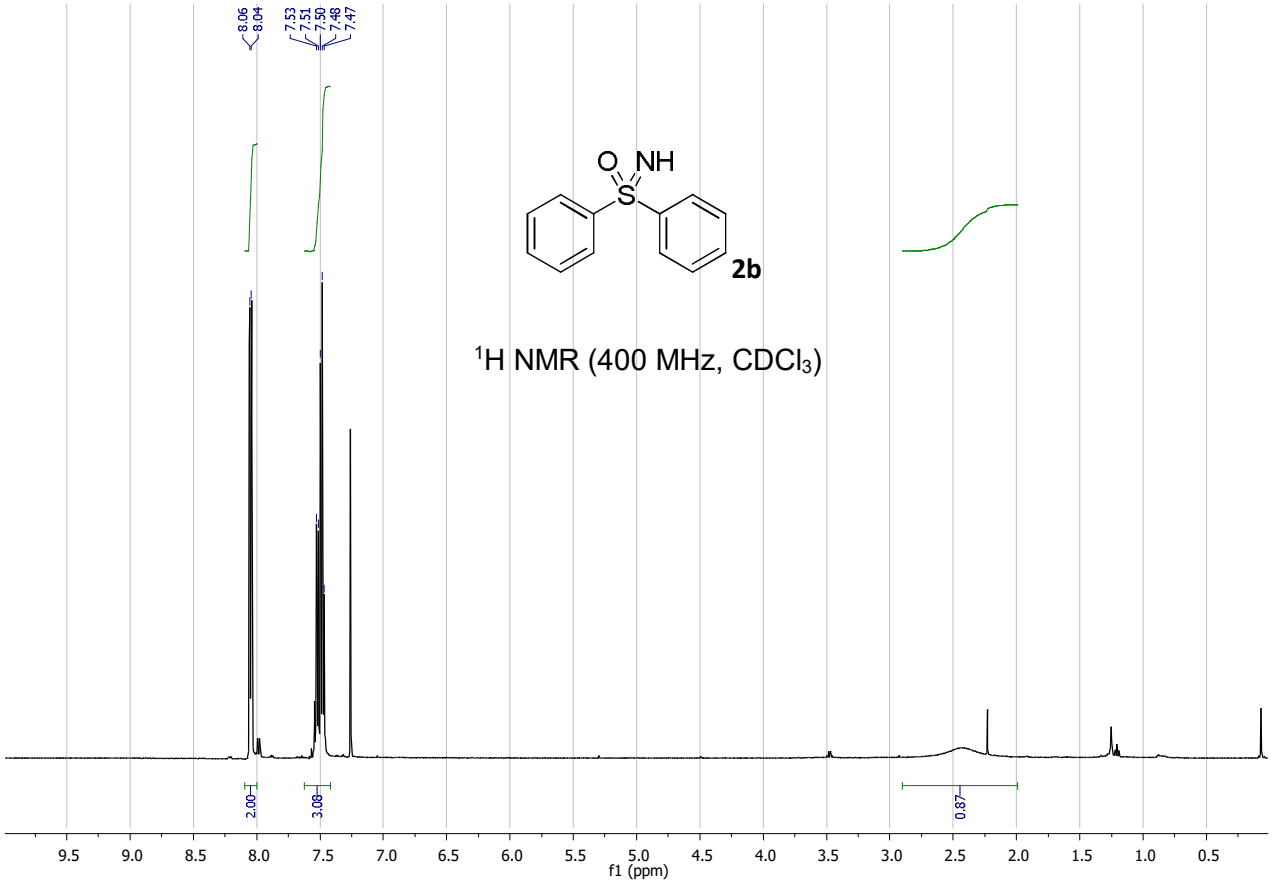

7.91
7.90
7.76
7.75
7.60
7.58
7.57
7.45
7.44
7.42
7.33
7.31
7.30
4.64
0.9
0.8
3.9
0.9
0.9
2.0
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
^{1}H NMR (500 MHz, $CDCl_3$)
S
N
S
CF_3
1t


165.6
153.1
140.9
140.9
135.5
130.4
130.2
129.9
129.6
129.6
126.3
125.8
125.8
125.7
125.7
124.6
121.8
121.2
37.0
130.4
130.2
129.9
129.6
129.6
126.3
125.8
125.8
125.7
125.7
124.6
121.8
121.2
131 129 127 125 123 121
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)
^{13}C NMR (126 MHz, $CDCl_3$)
S
N
S
CF_3
1t
CF_3 *quartet*

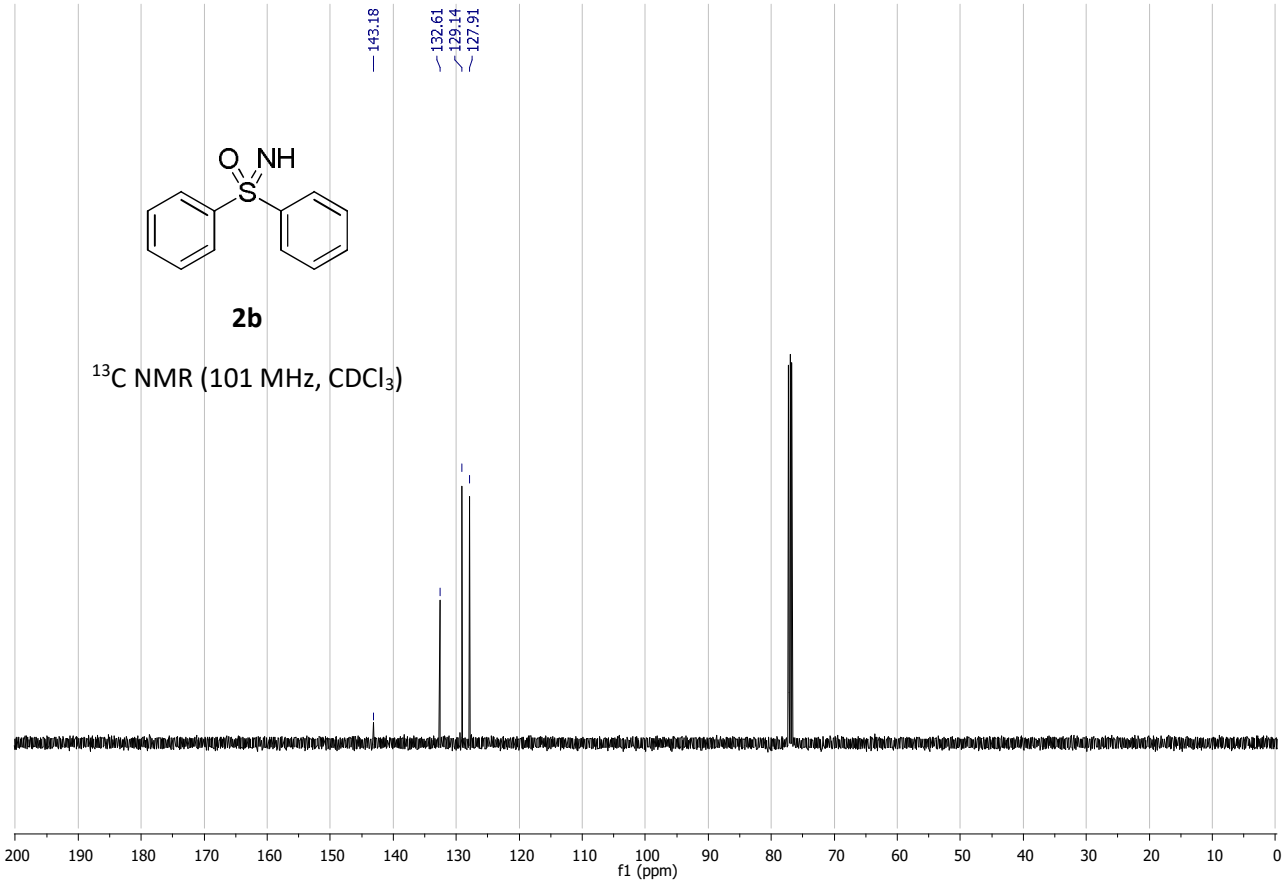
^{1}H and ^{13}C NMR spectra of sulfoximines


7.90
7.89
7.35
7.34
3.10
2.45
O NH
S
Me
2a
^{1}H NMR (400 MHz, $CDCl_3$)
2.00
2.12
3.27
4.18
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

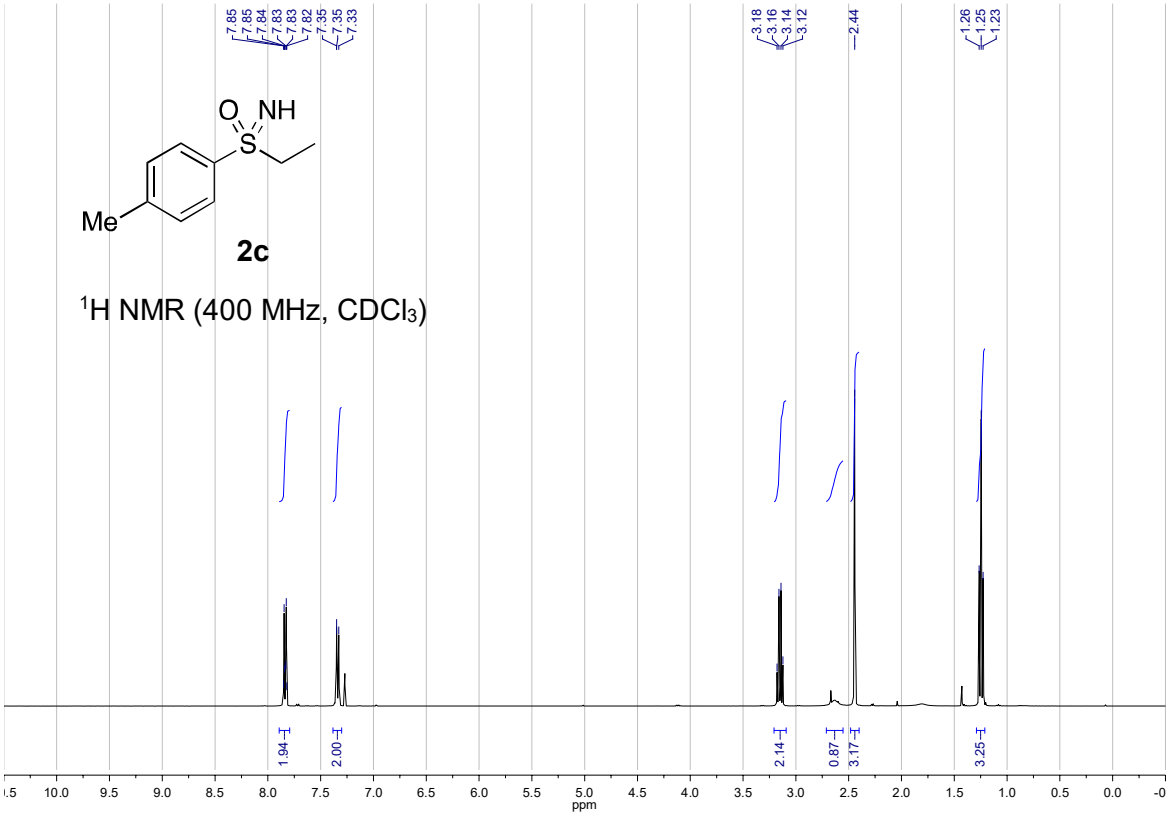

143.94
140.51
129.86
127.71
46.29
21.49
2a
^{13}C NMR (126 MHz, $CDCl_3$)
O NH
S
Me
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



^{1}H NMR (400 MHz, $CDCl_3$)

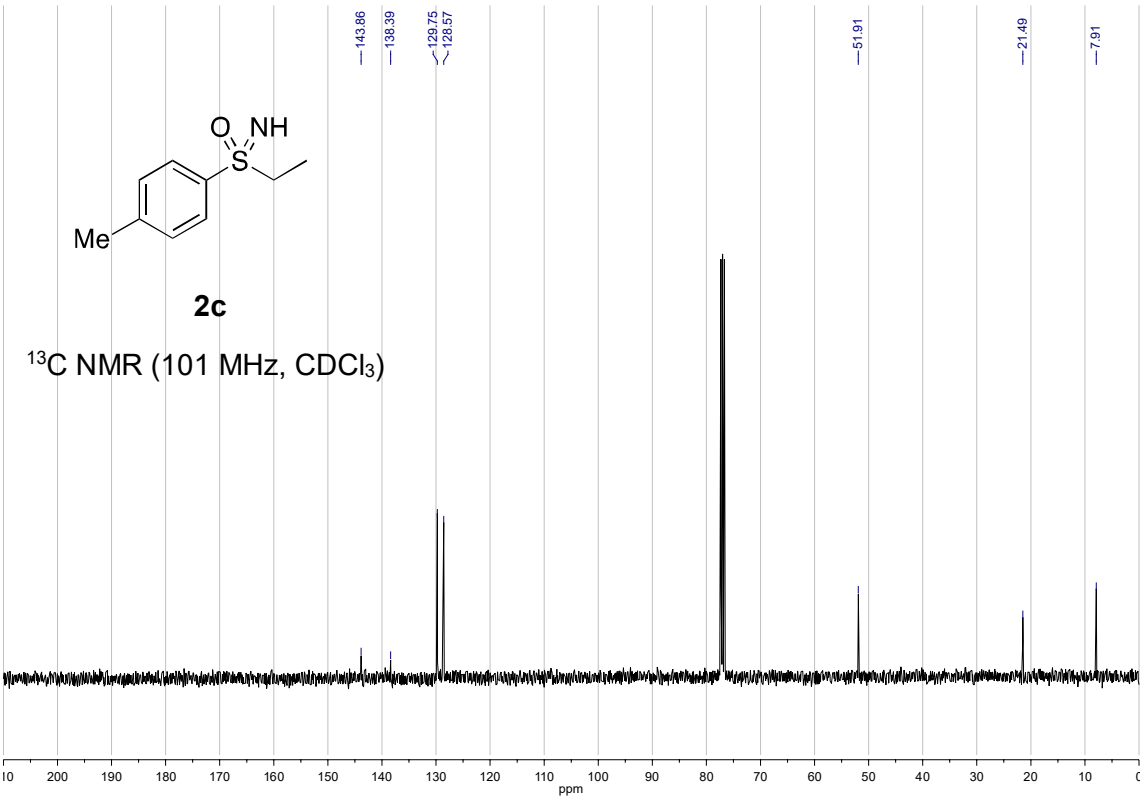


^{13}C NMR (101 MHz, $CDCl_3$)



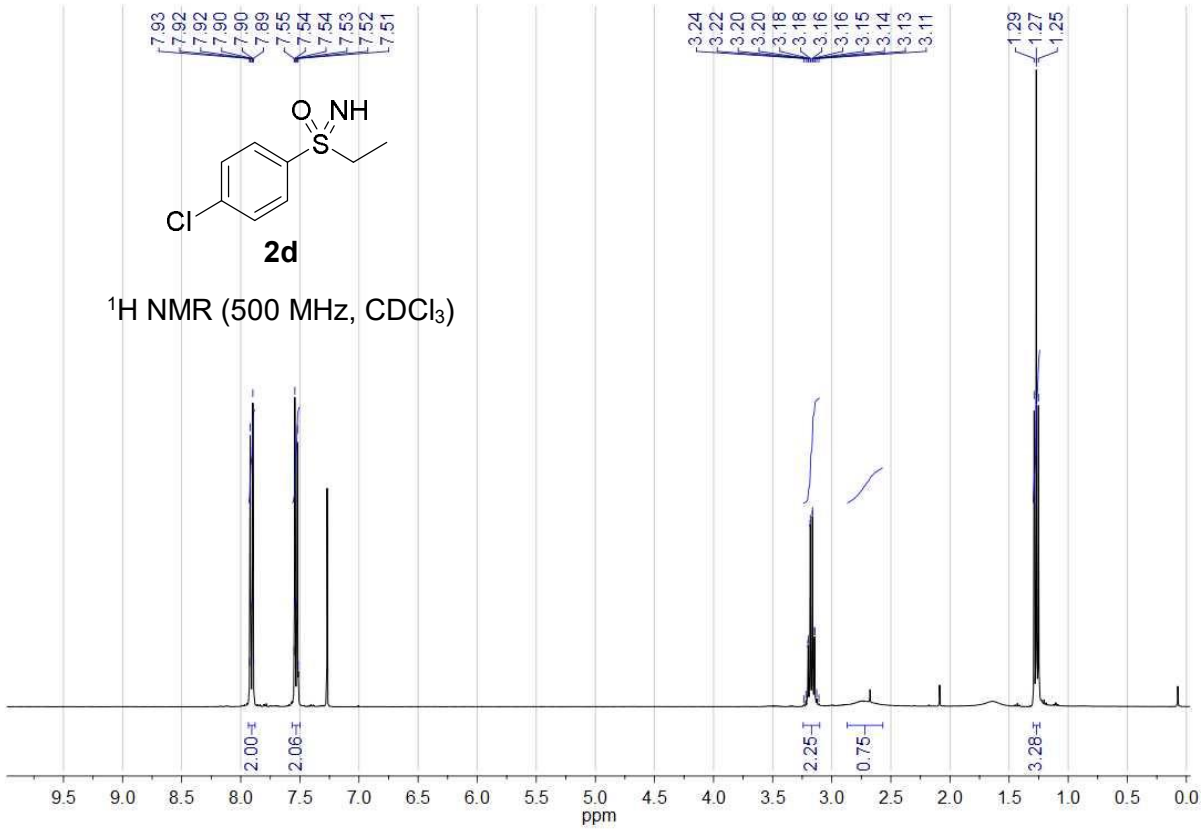
2c

^{1}H NMR (400 MHz, $CDCl_3$)



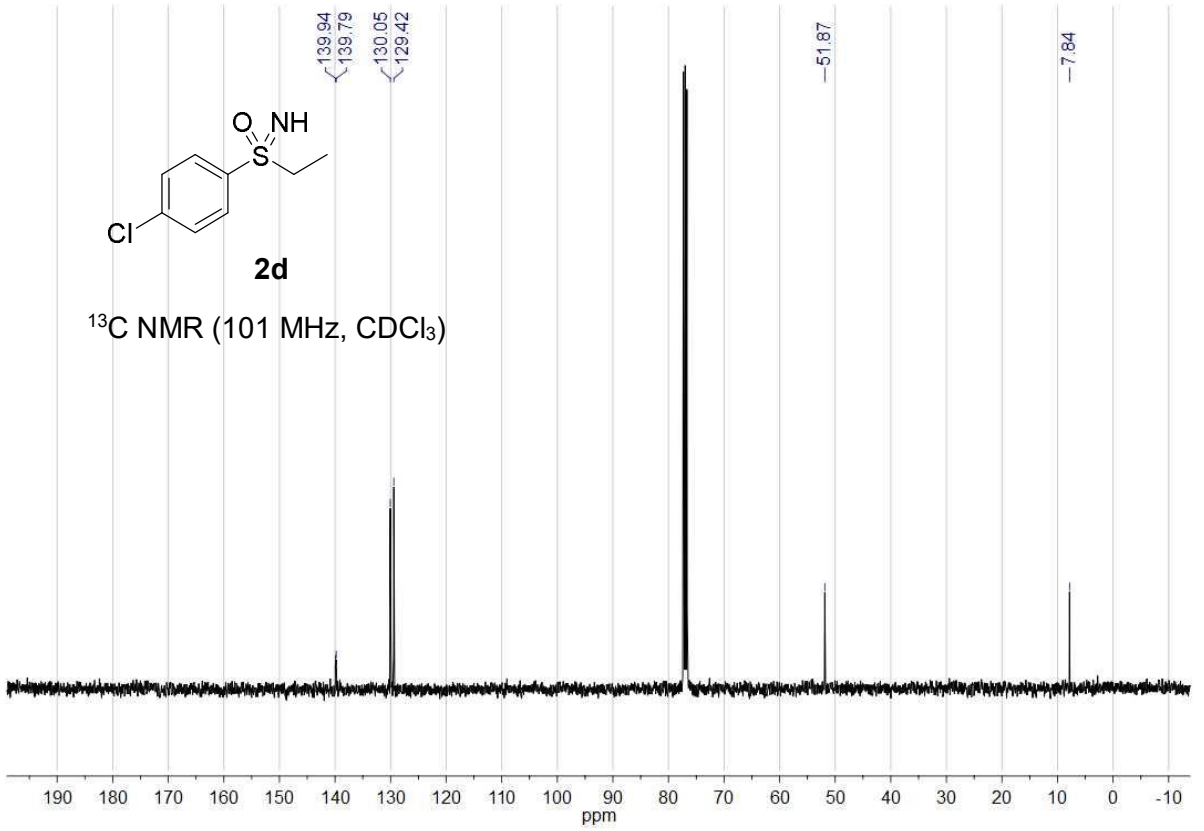
2c

^{13}C NMR (101 MHz, $CDCl_3$)



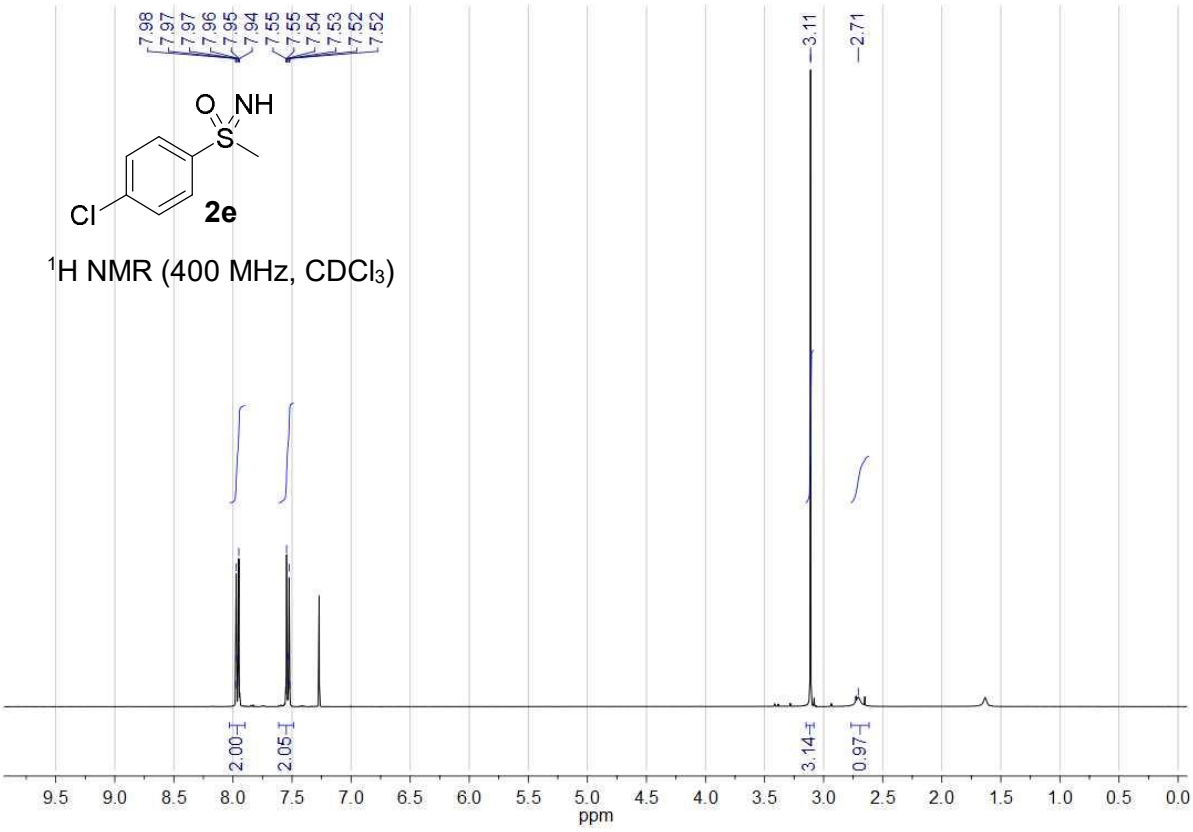
2d

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

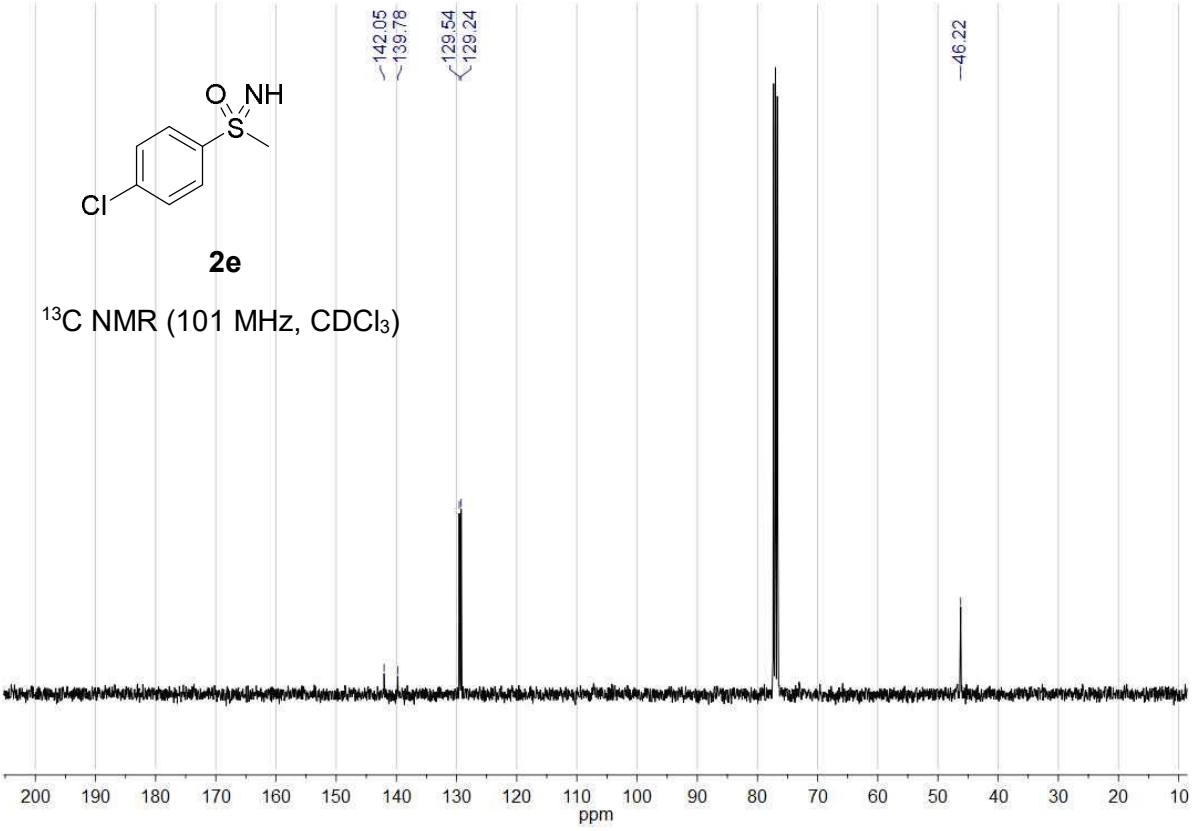


2d

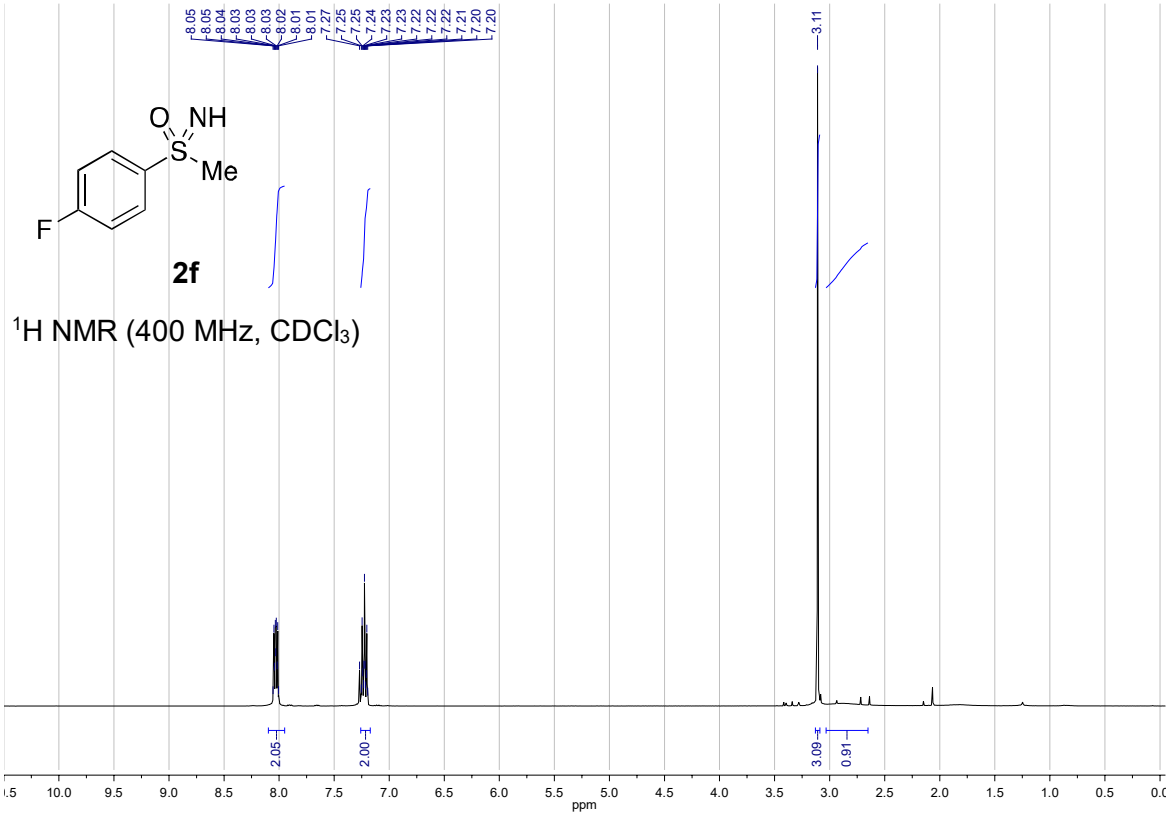
^{13}C NMR (101 MHz, $CDCl_3$)

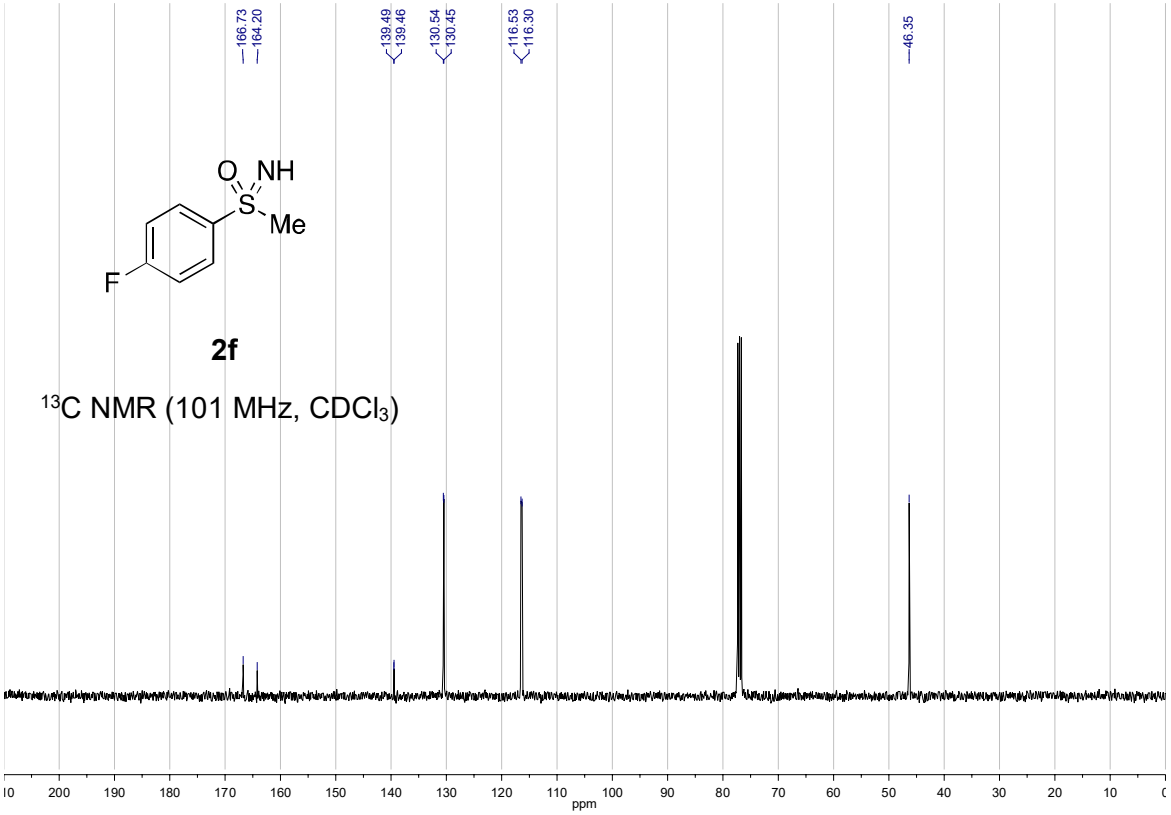


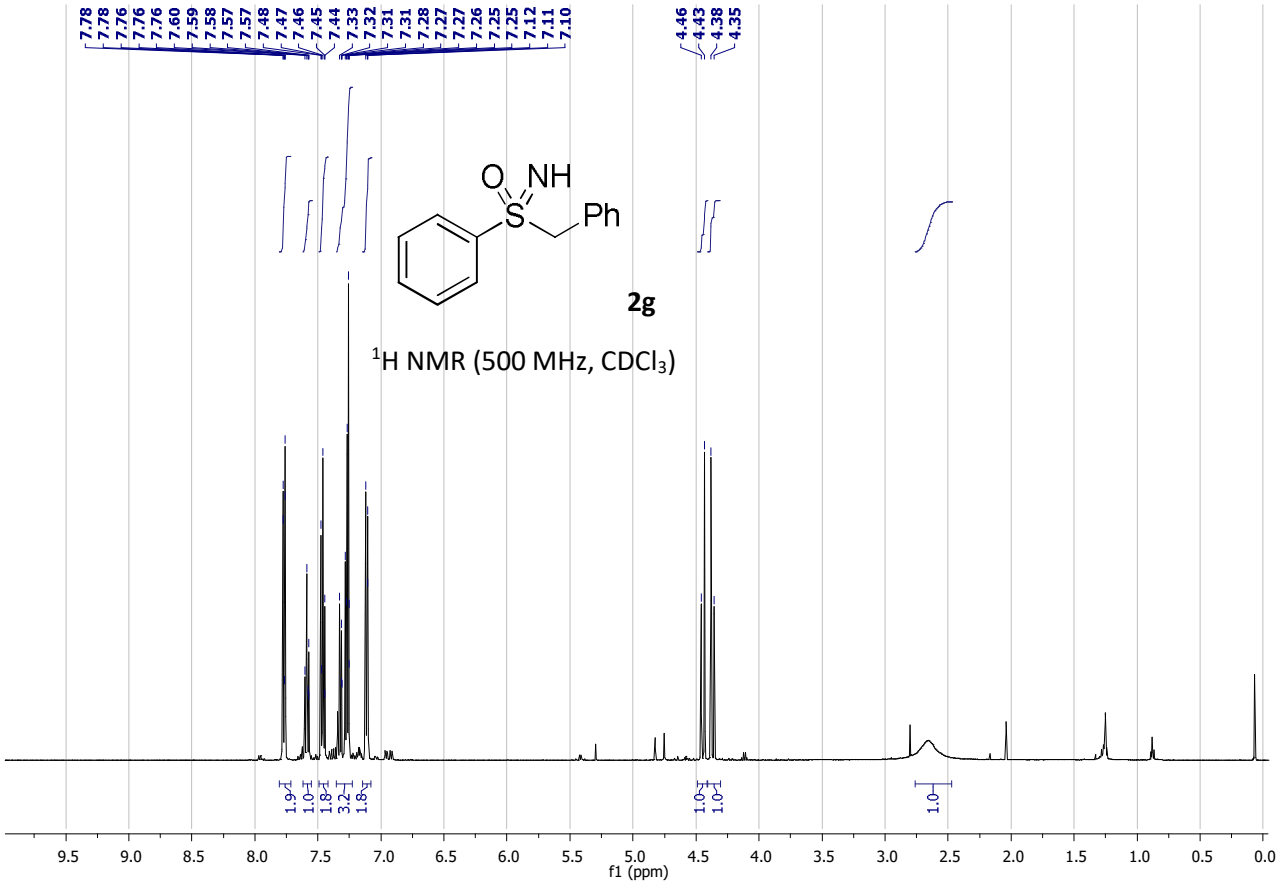
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

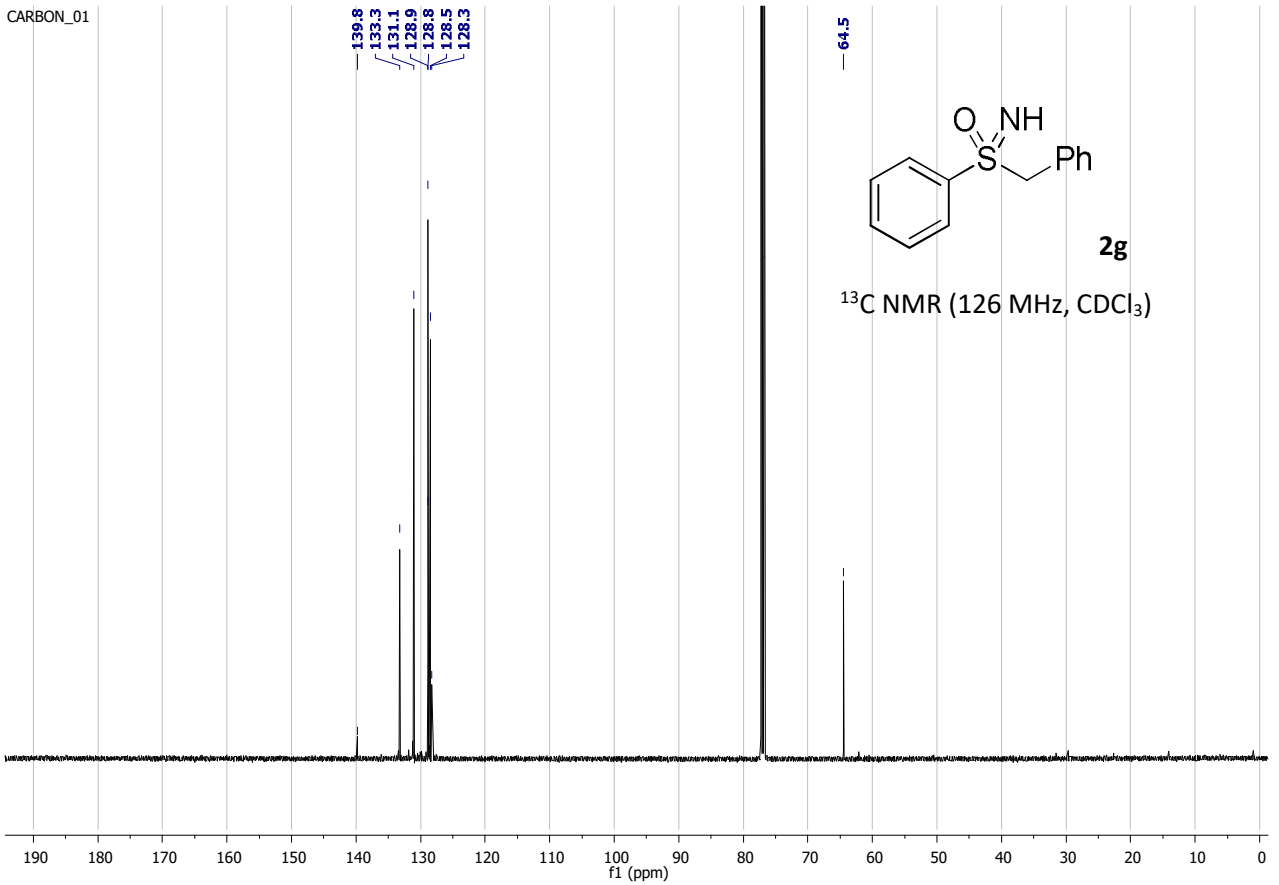

O
NH
S
Me
F
2f
^{1}H NMR (400 MHz, $CDCl_3$)
8.05
8.05
8.04
8.03
8.03
8.03
8.02
8.01
8.01
7.27
7.25
7.25
7.24
7.23
7.23
7.22
7.22
7.22
7.21
7.20
7.20
3.11
2.05
2.00
3.09
0.91
ppm


O
NH
S
Me
F
2f
^{13}C NMR (101 MHz, $CDCl_3$)
166.73
164.20
139.49
139.46
130.54
130.45
116.53
116.30
46.35
ppm



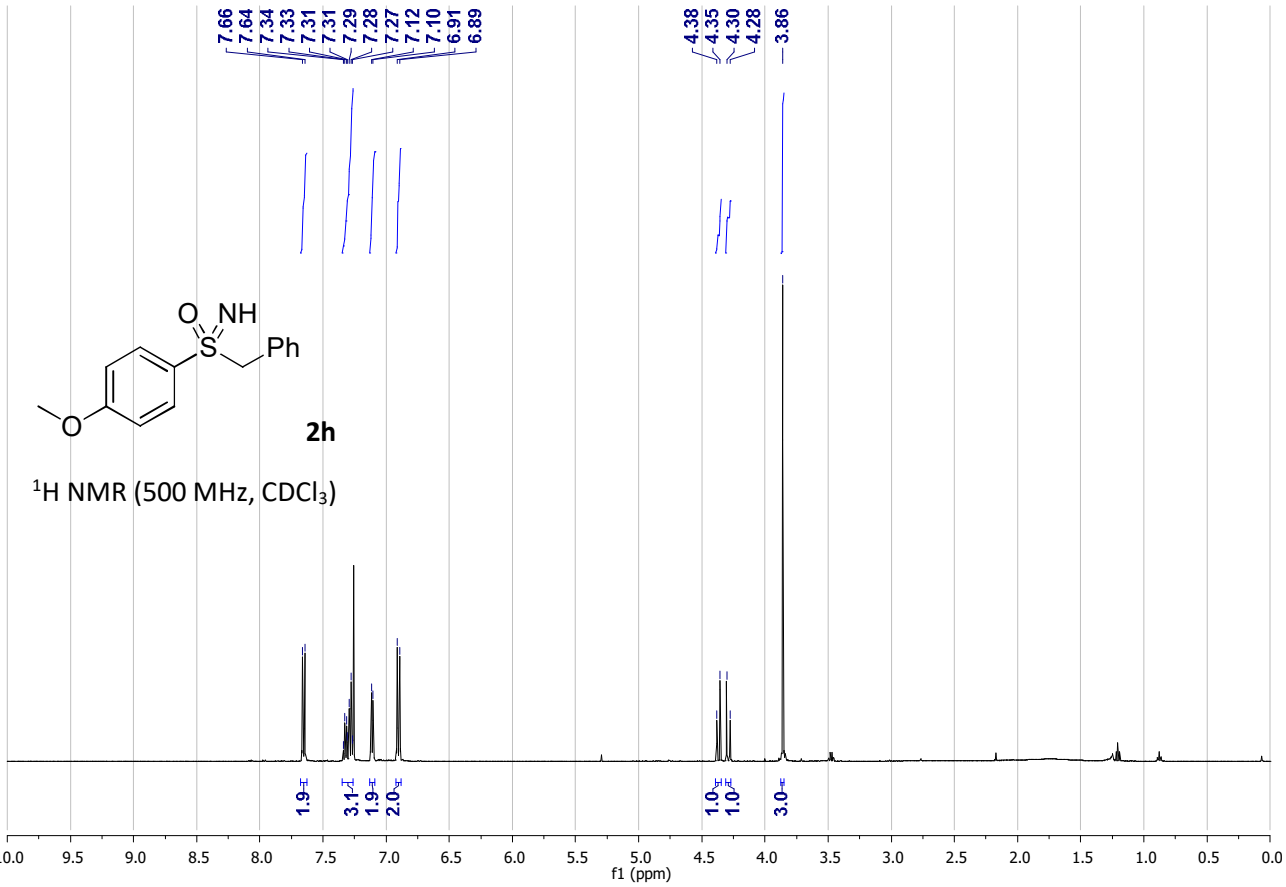
2g

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



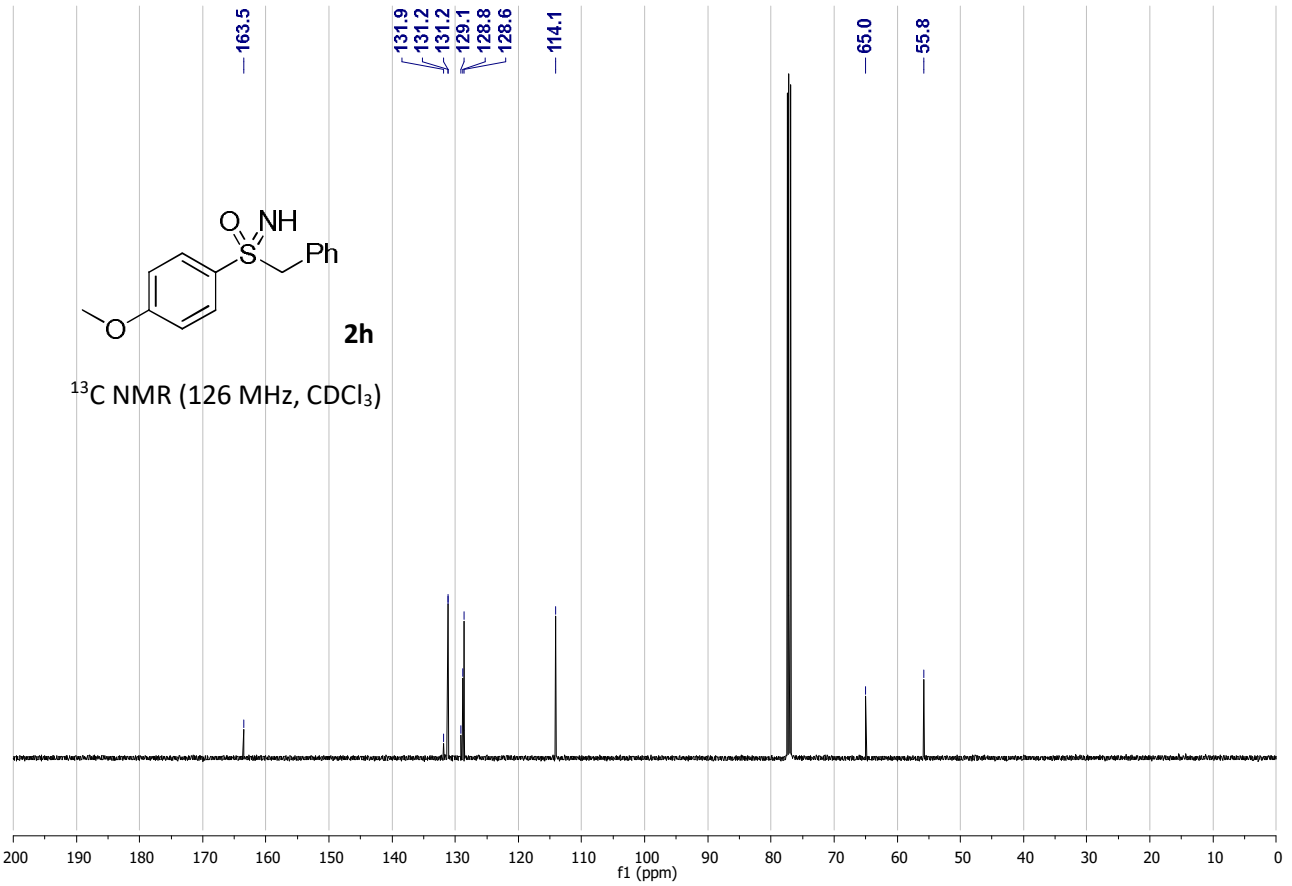
2g

^{13}C NMR (126 MHz, $CDCl_3$)



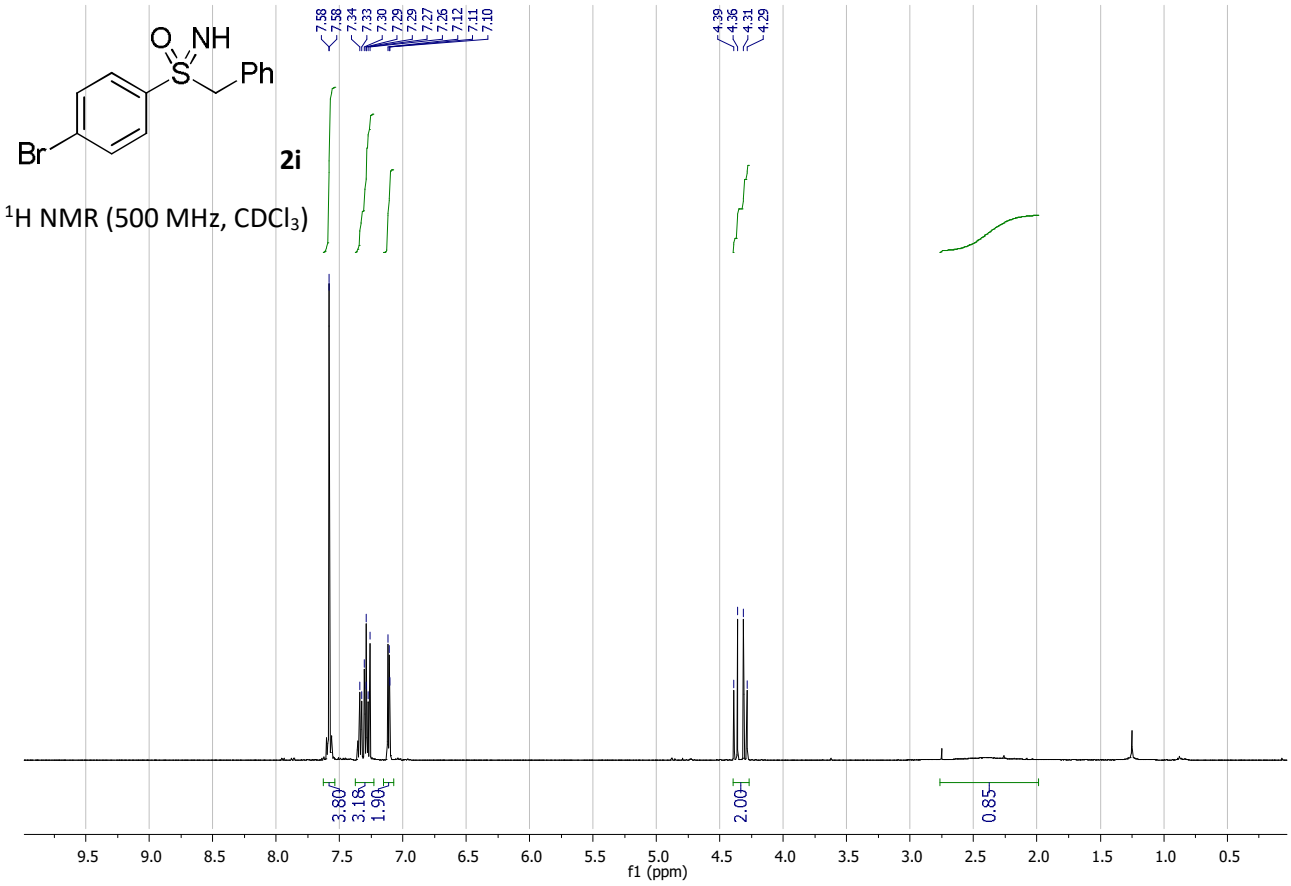
2h

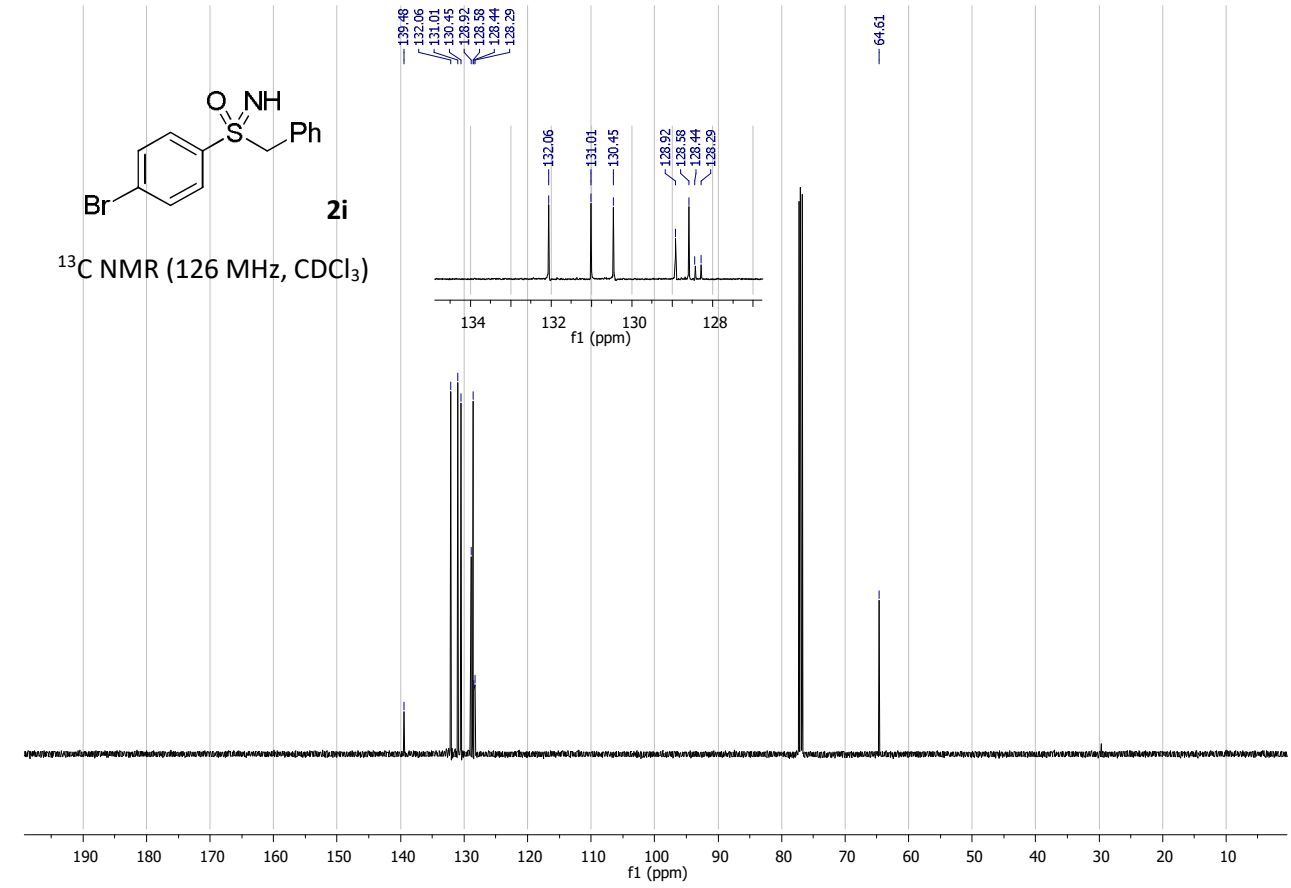
^{1}H NMR (500 MHz, $CDCl_3$)

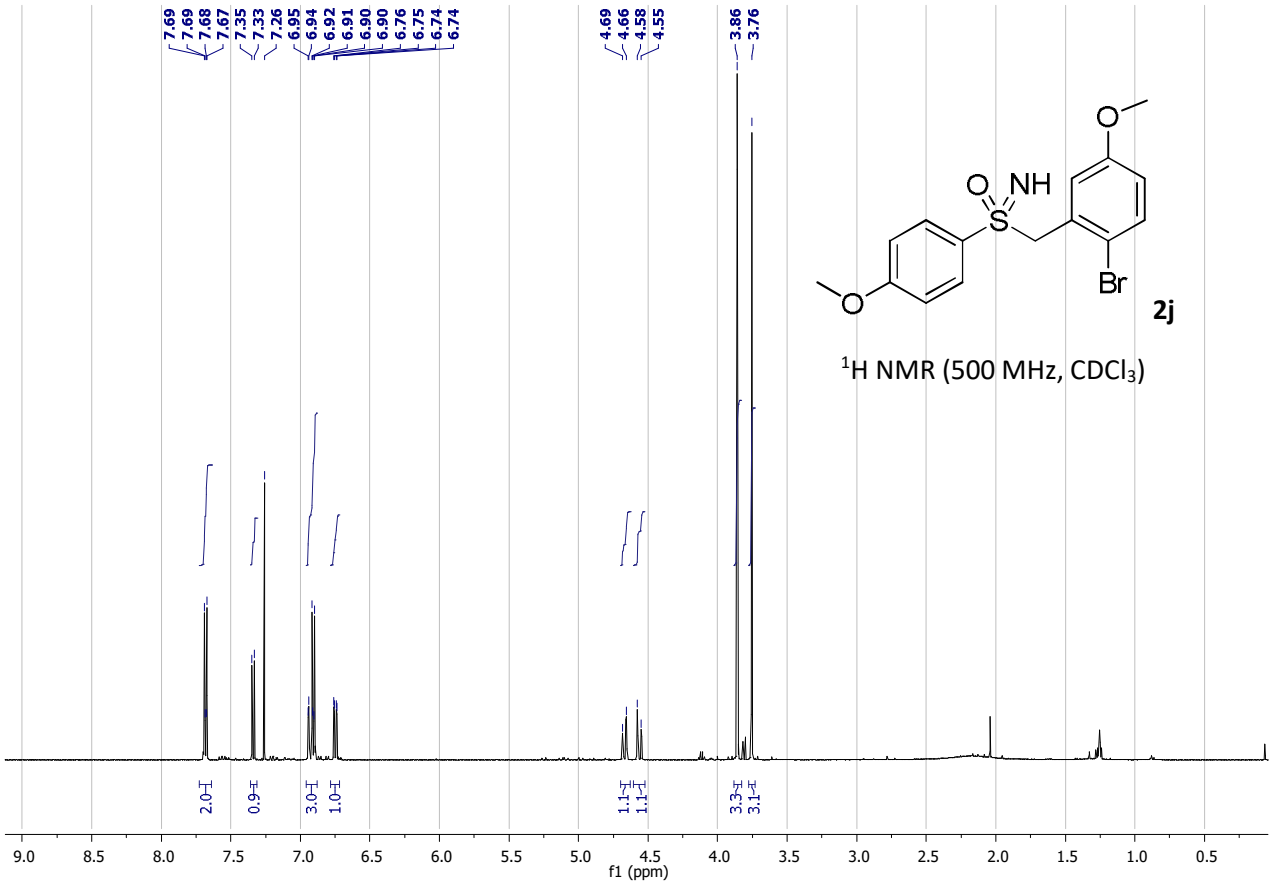


2h

^{13}C NMR (126 MHz, $CDCl_3$)

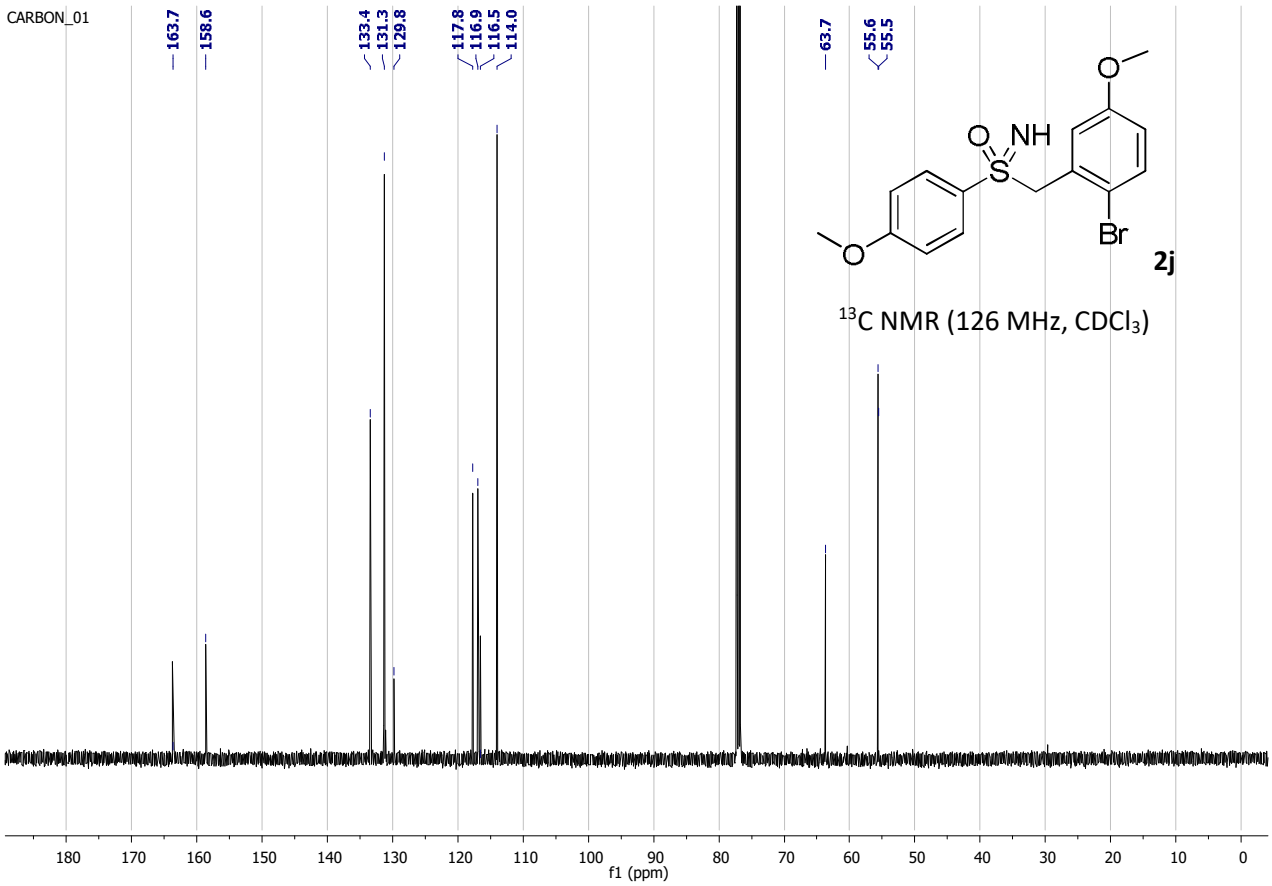

O
NH
S
Ph
Br
2i
^{1}H NMR (500 MHz, $CDCl_3$)
7.58
7.58
7.34
7.33
7.30
7.29
7.29
7.27
7.26
7.12
7.11
7.10
4.39
4.36
4.31
4.29
3.80
3.18
1.90
2.00
0.85
f1 (ppm)


O
NH
S
Ph
Br
2i
^{13}C NMR (126 MHz, $CDCl_3$)
139.48
132.06
131.01
130.45
128.92
128.58
128.44
128.29
64.61
f1 (ppm)



2j

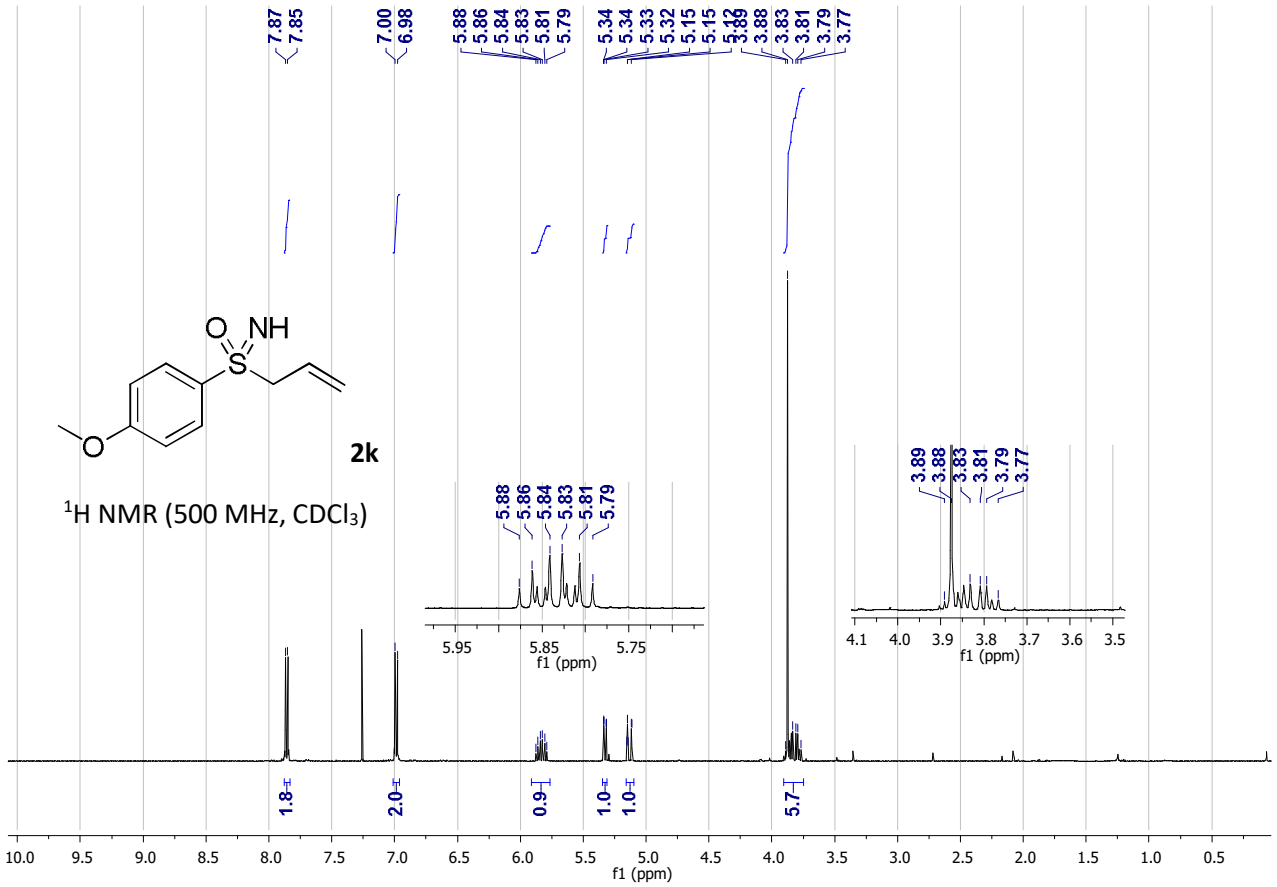
^{1}H NMR (500 MHz, $CDCl_3$)

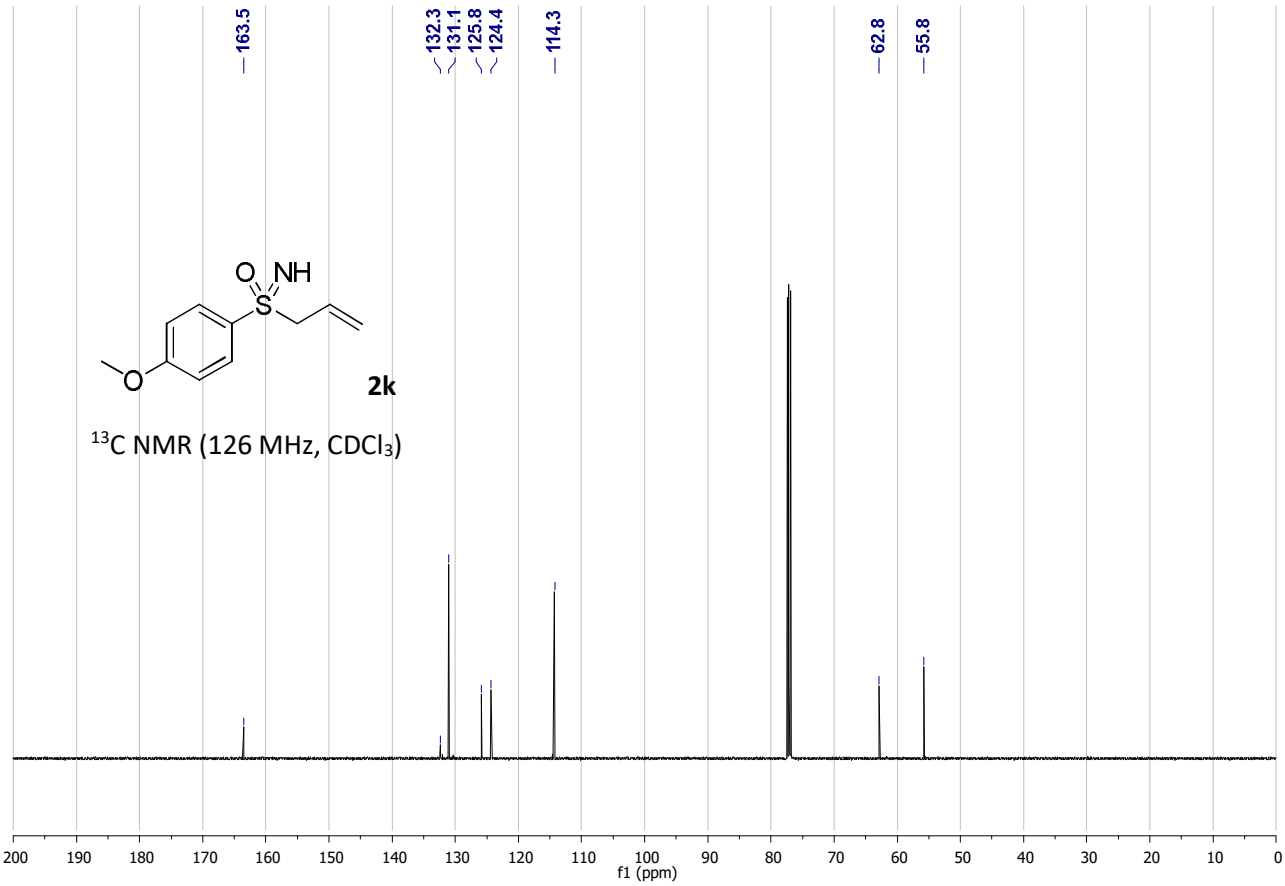


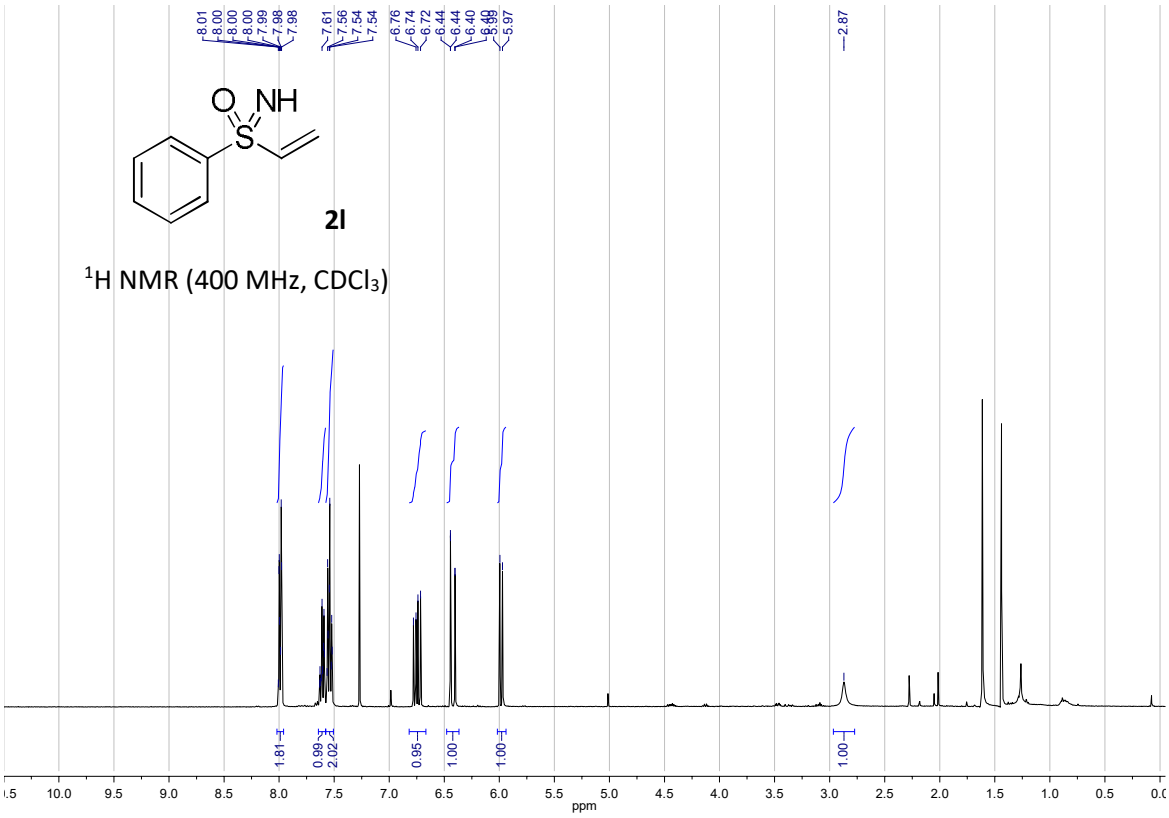
2j

^{13}C NMR (126 MHz, $CDCl_3$)

2i

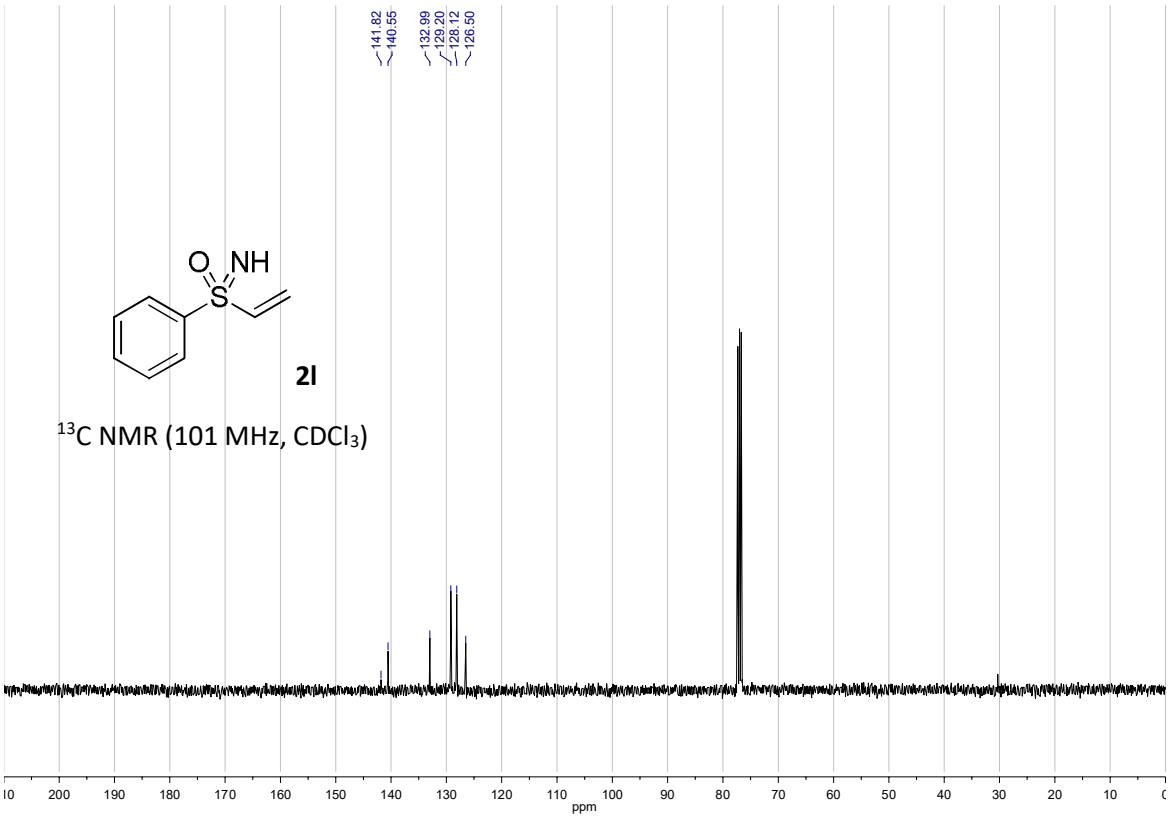

7.87
7.85
7.00
6.98
5.88
5.86
5.84
5.83
5.81
5.79
5.34
5.34
5.33
5.32
5.15
5.15
3.89
3.88
3.83
3.81
3.79
3.77
O
NH
S
O
2k
1H NMR (500 MHz, CDCl3)
5.95
5.85
5.75
f1 (ppm)
4.1
4.0
3.9
3.8
3.7
3.6
3.5
f1 (ppm)
1.8
2.0
0.9
1.0
1.0
5.7
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


163.5
132.3
131.1
125.8
124.4
114.3
62.8
55.8
O
NH
S
O
2k
13C NMR (126 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



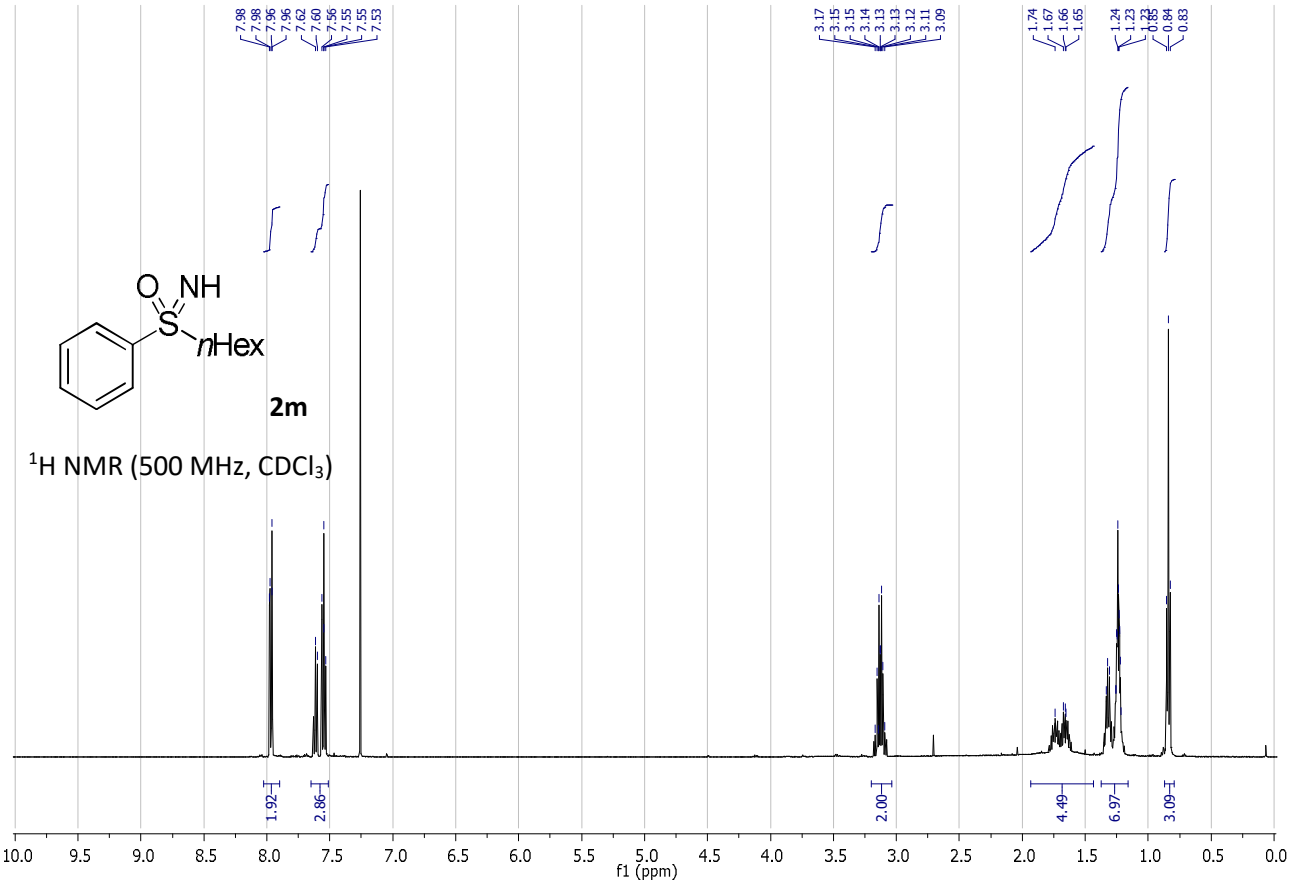
2l

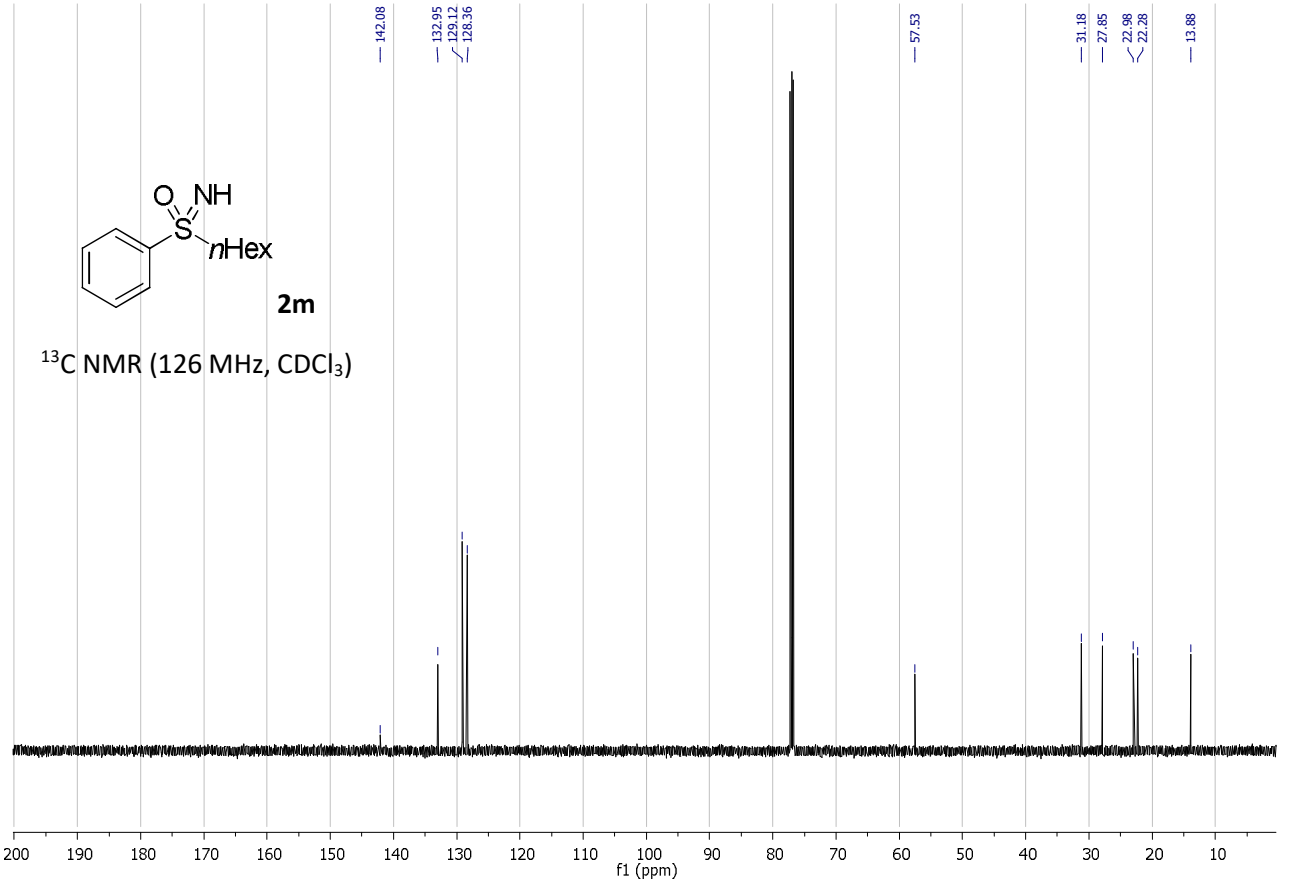
^{1}H NMR (400 MHz, $CDCl_3$)

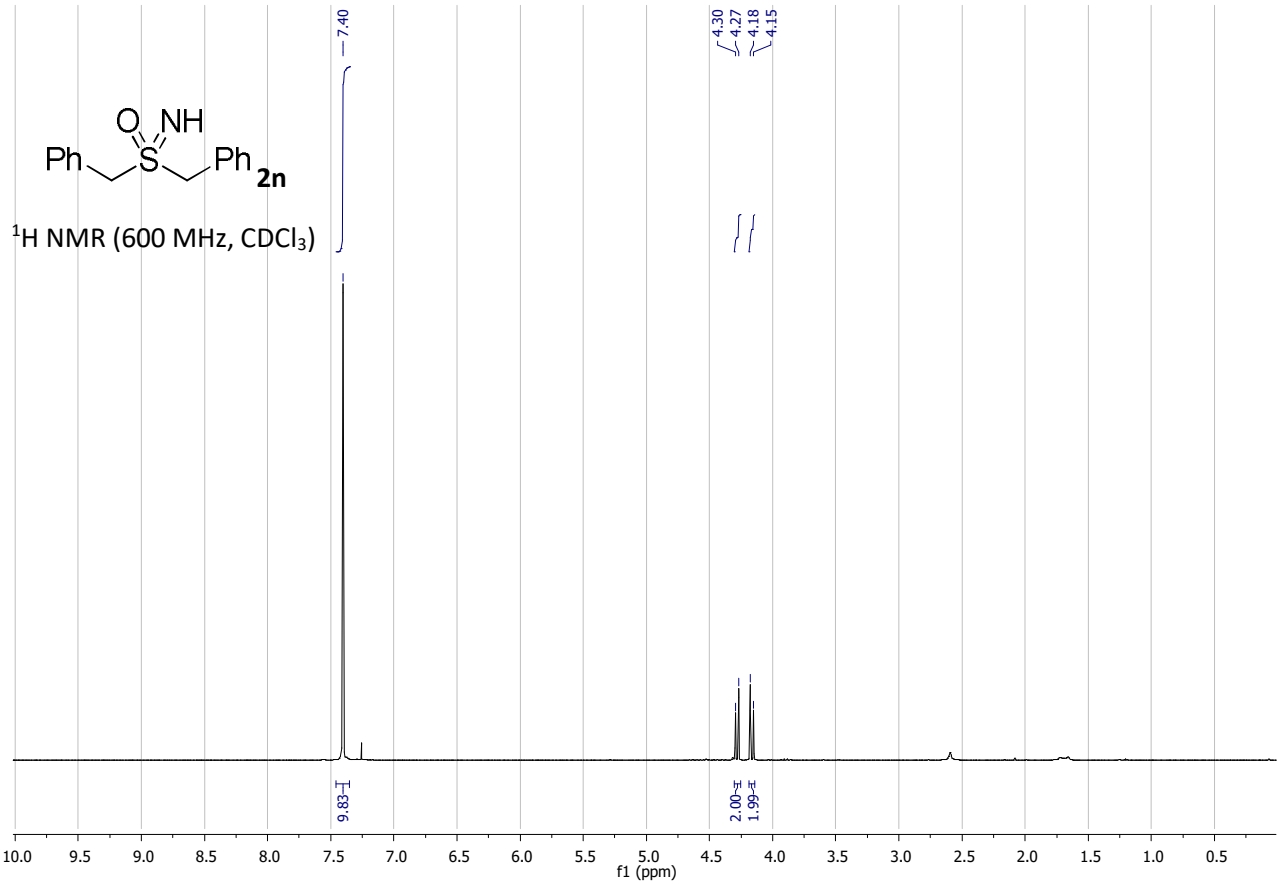


2l

^{13}C NMR (101 MHz, $CDCl_3$)

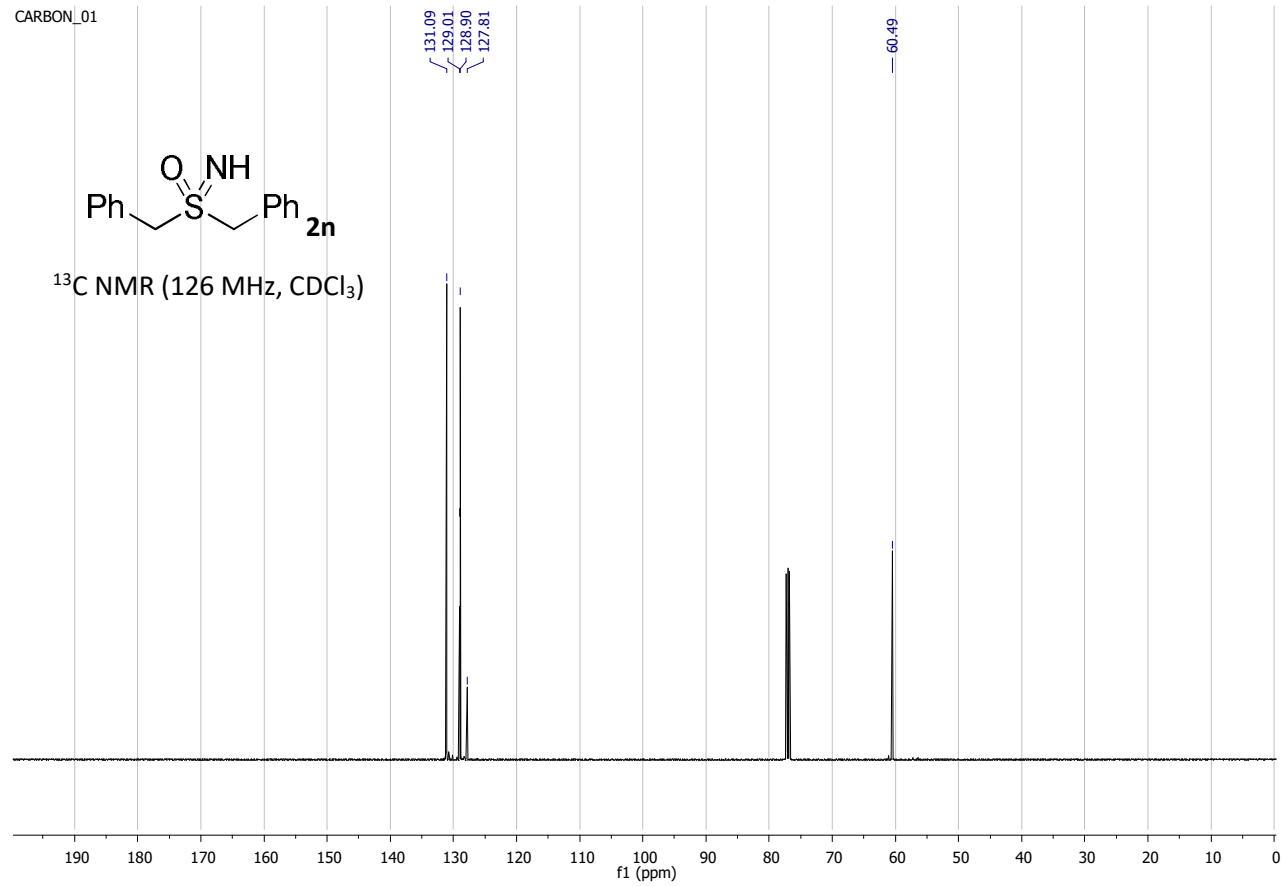

O NH
S
nHex
2m
1H NMR (500 MHz, CDCl3)
f1 (ppm)


O NH
S
nHex
2m
13C NMR (126 MHz, CDCl3)
f1 (ppm)



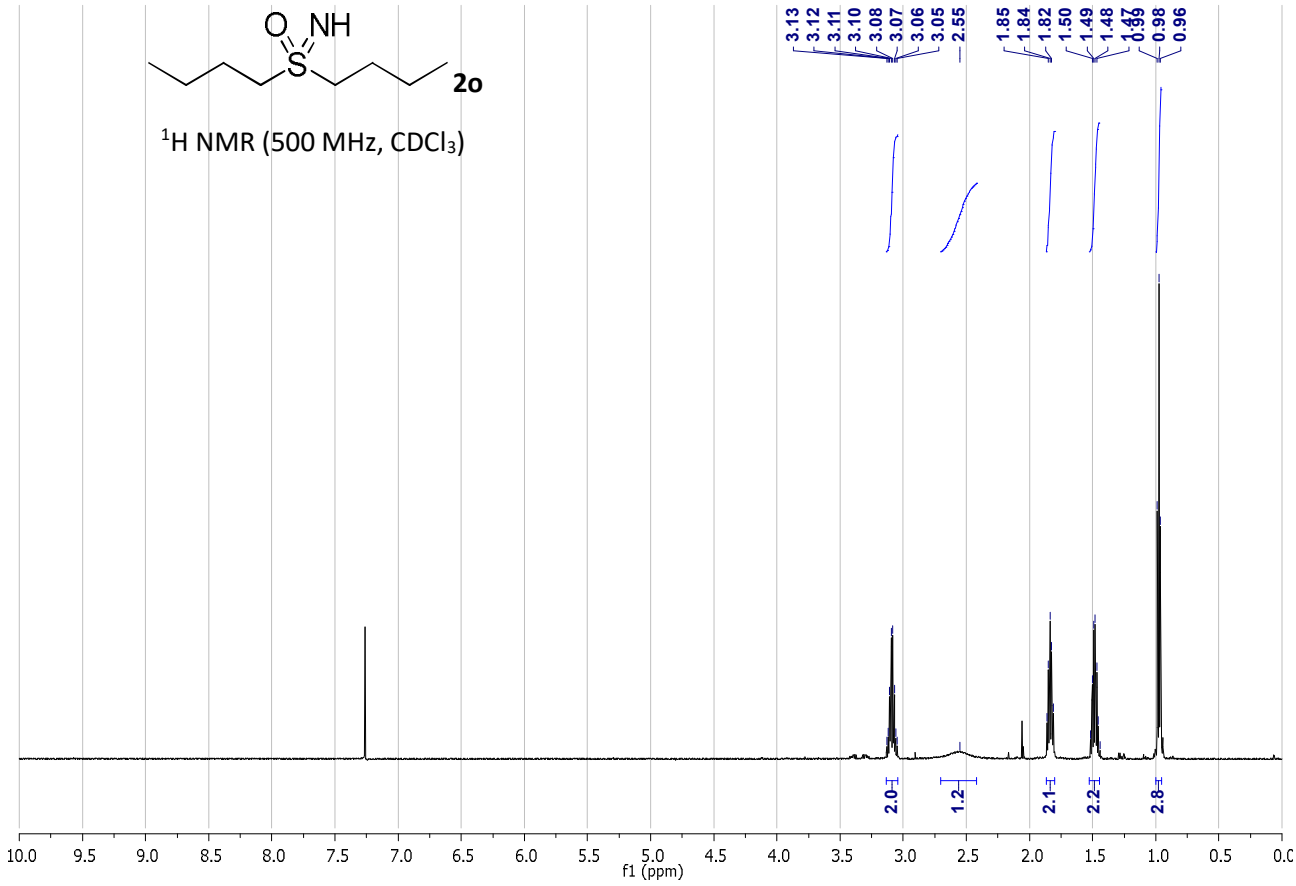
2n

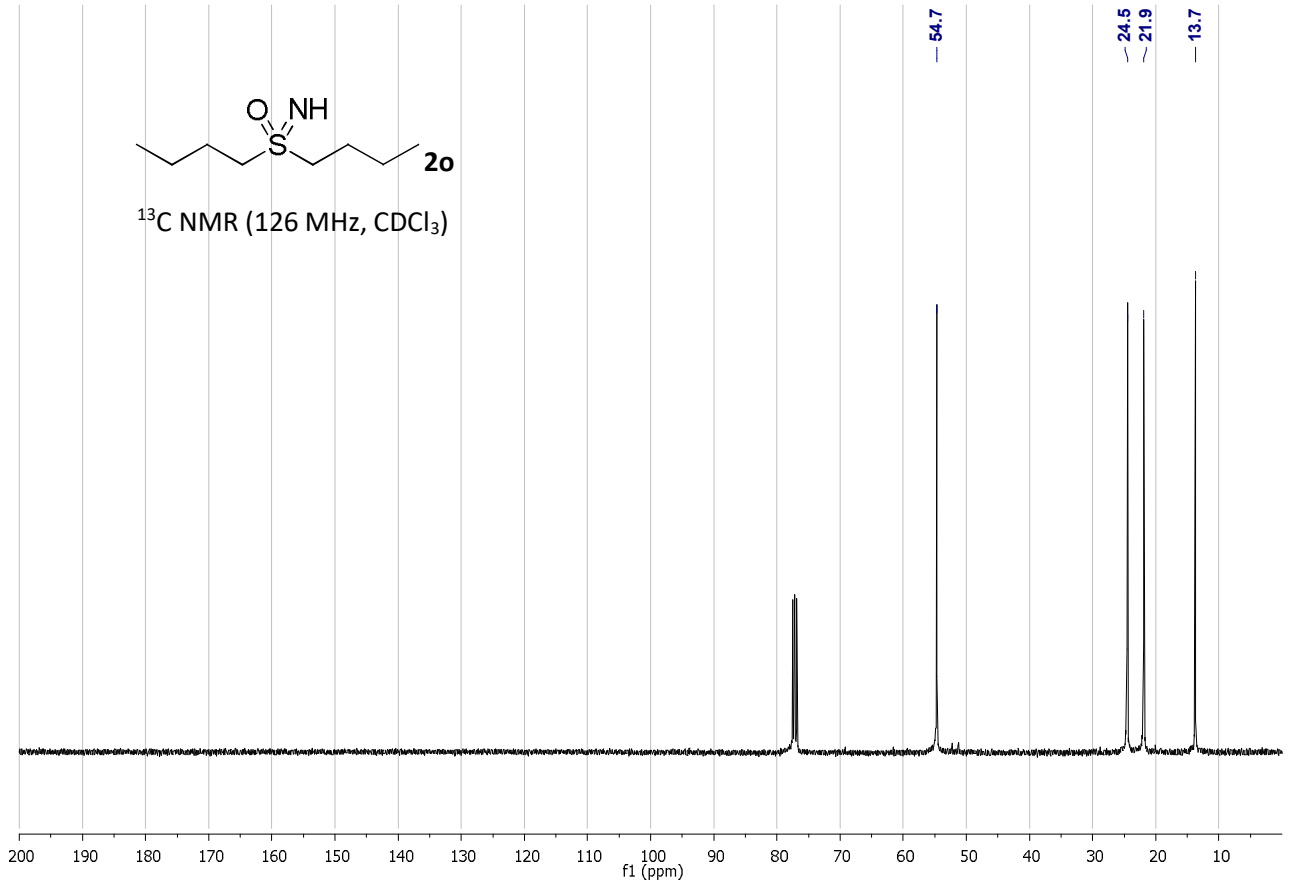
^{1}H NMR (600 MHz, $CDCl_3$)

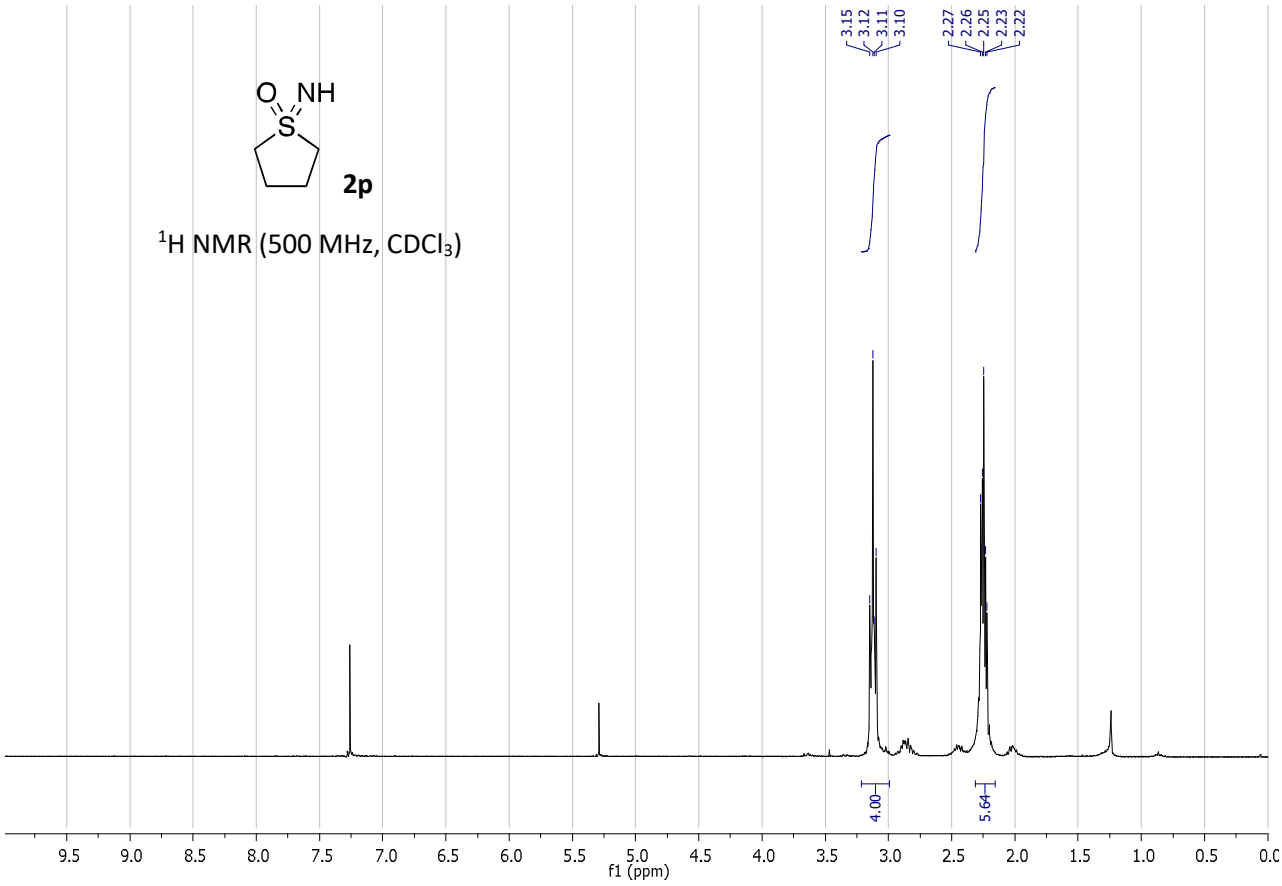


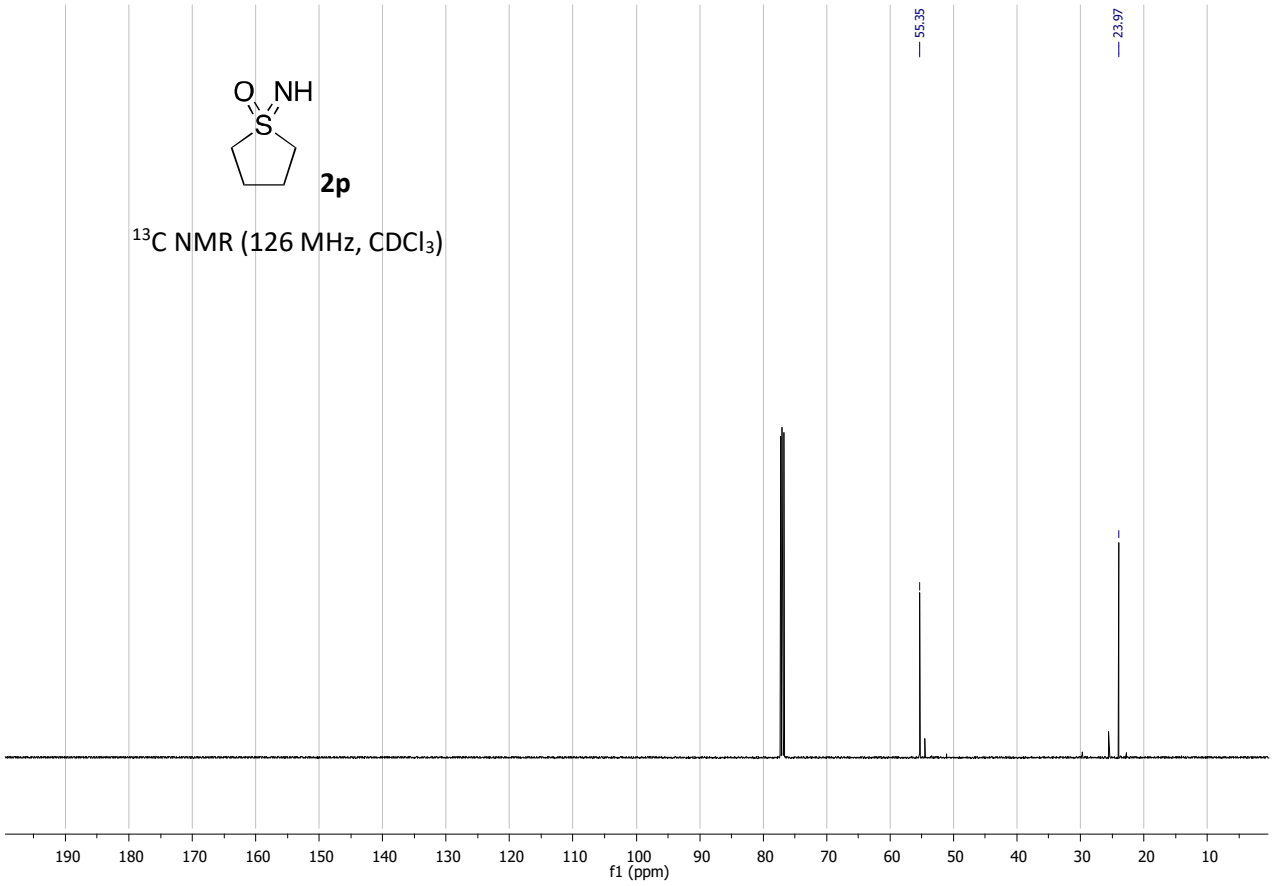
2n

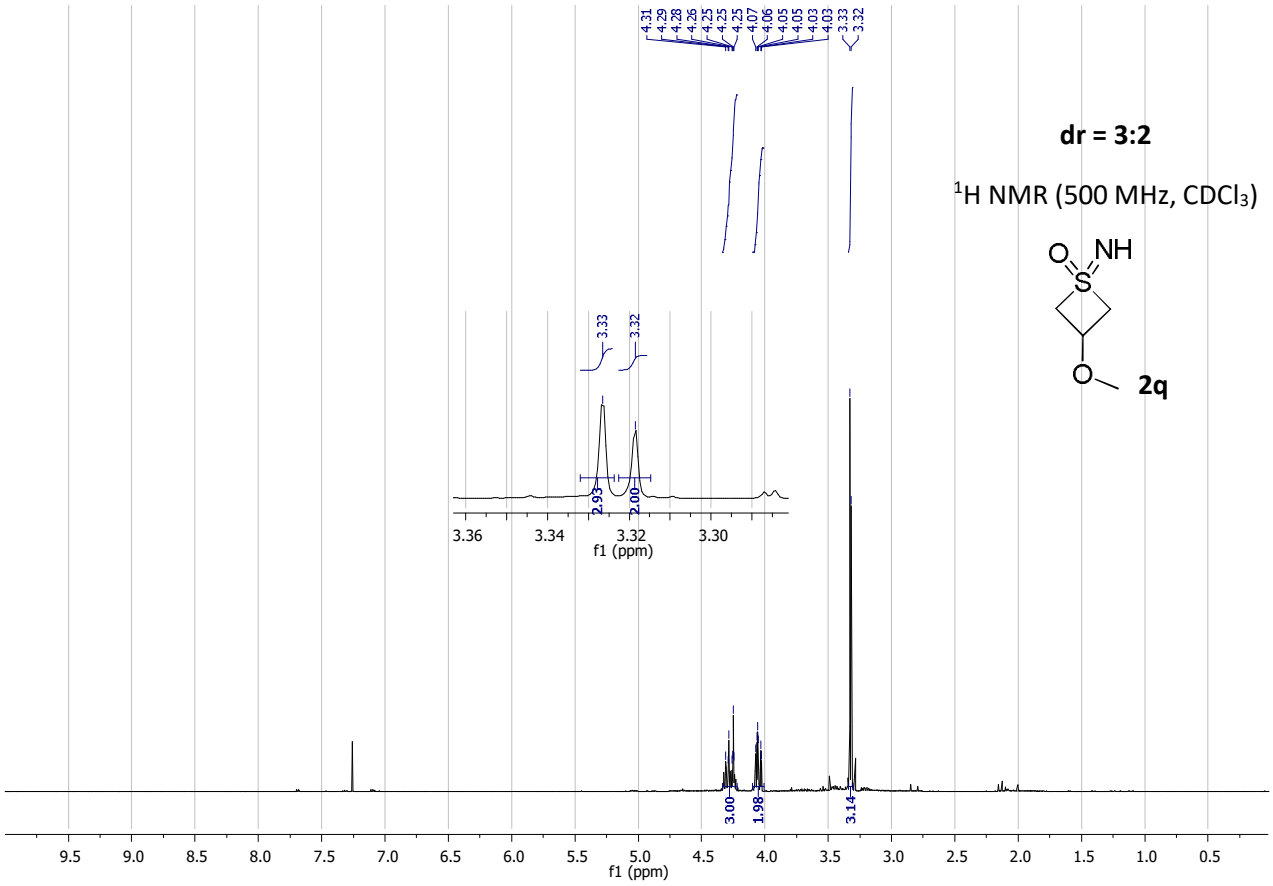
^{13}C NMR (126 MHz, $CDCl_3$)

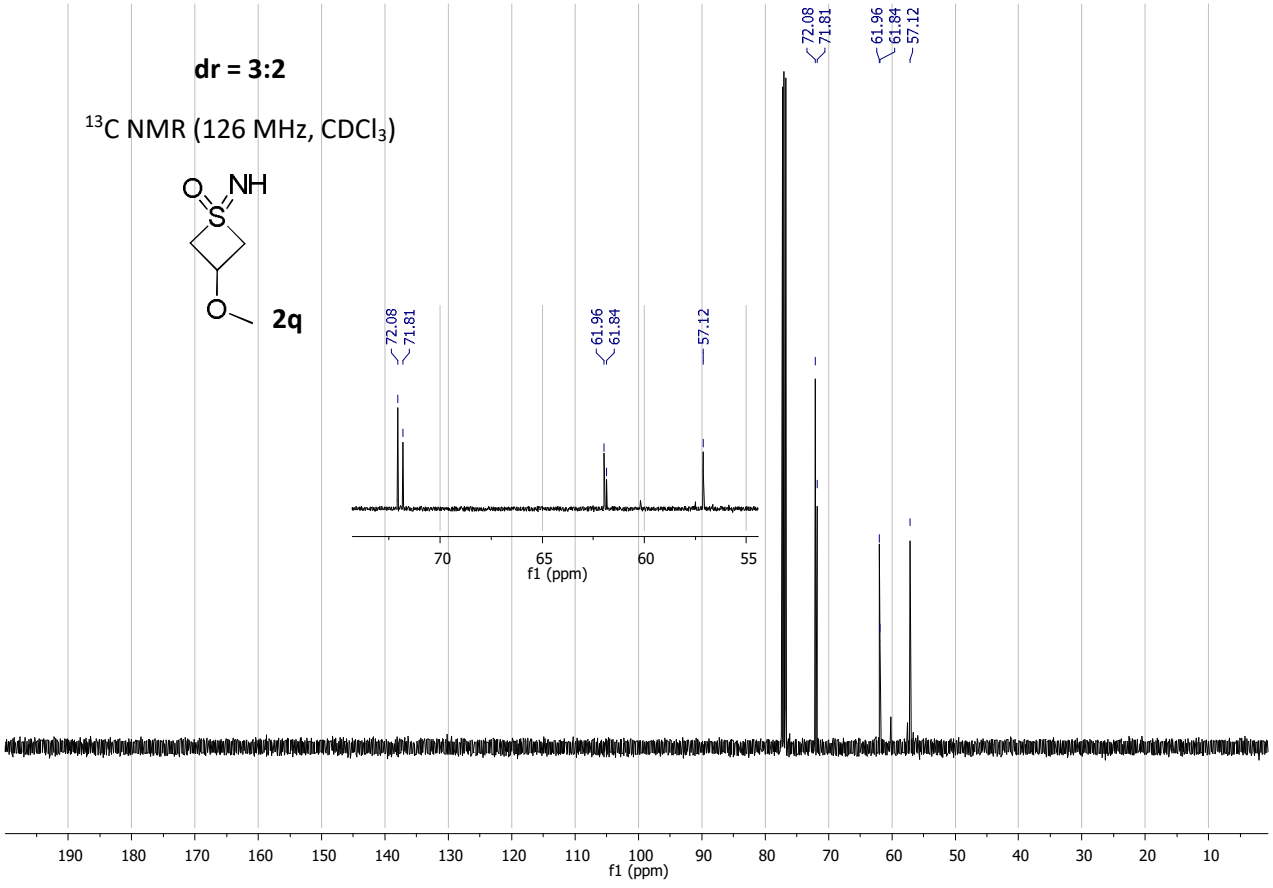

O NH
S
2o
^{1}H NMR (500 MHz, CDCl$_3$)
3.13
3.12
3.11
3.10
3.08
3.07
3.06
3.05
2.55
1.85
1.84
1.82
1.50
1.49
1.48
0.98
0.96
2.0
1.2
2.1
2.2
2.8
f1 (ppm)

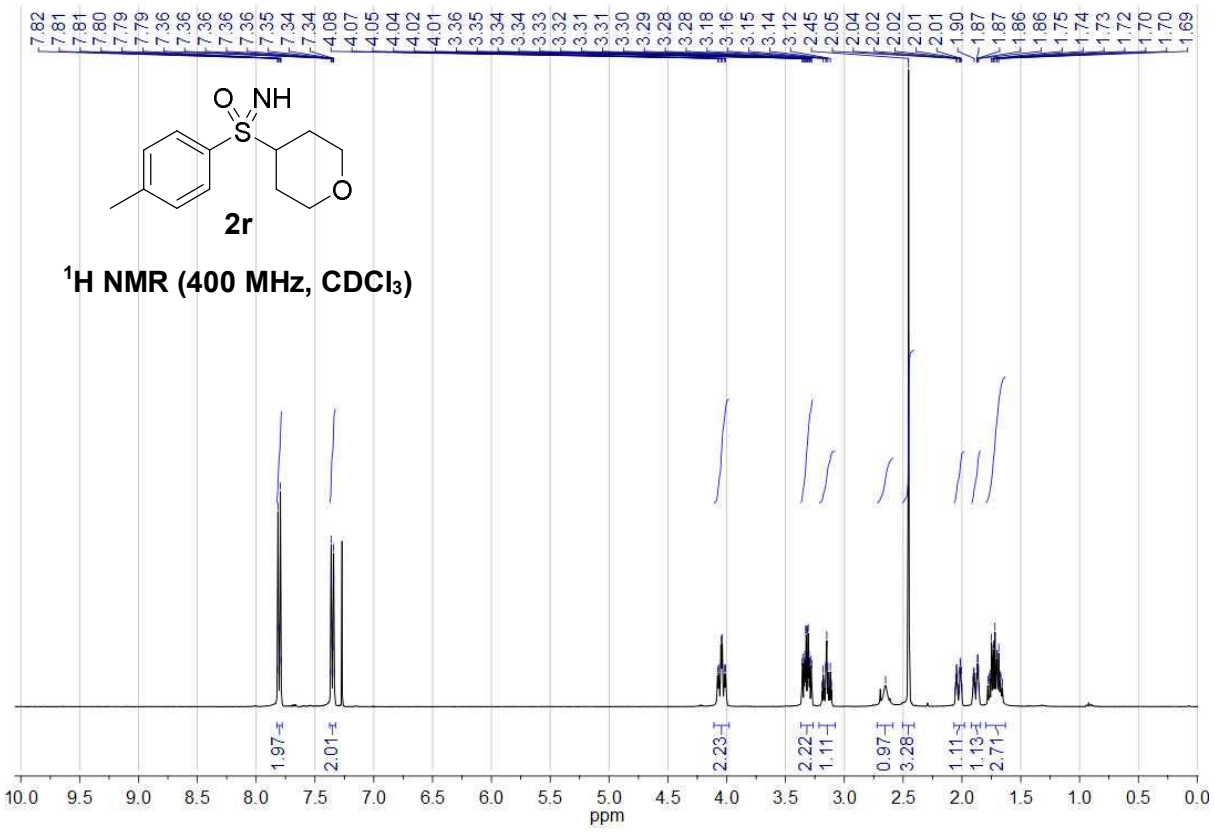

O NH
S
2o
^{13}C NMR (126 MHz, CDCl$_3$)
54.7
24.5
21.9
13.7
f1 (ppm)

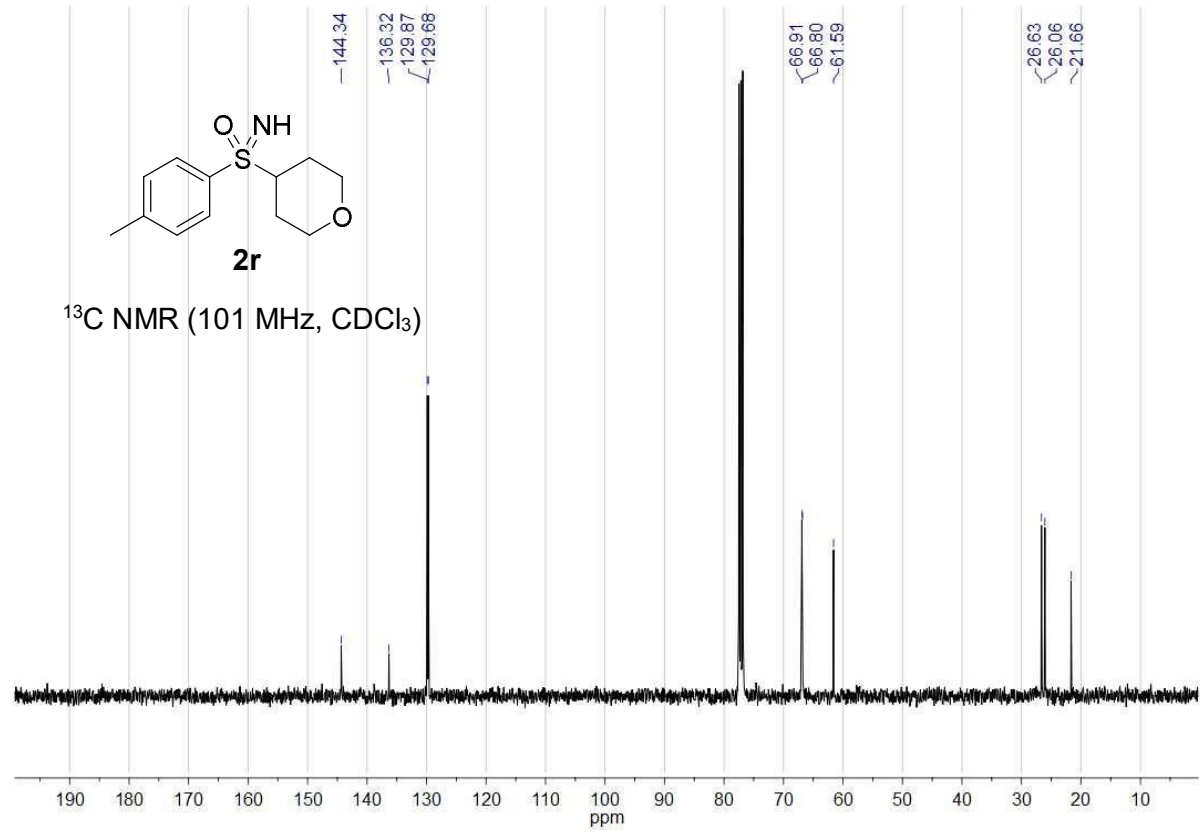

O NH
S
2p
^{1}H NMR (500 MHz, $CDCl_3$)
3.15
3.12
3.11
3.10
2.27
2.26
2.25
2.23
2.22
4.00
5.64
f1 (ppm)

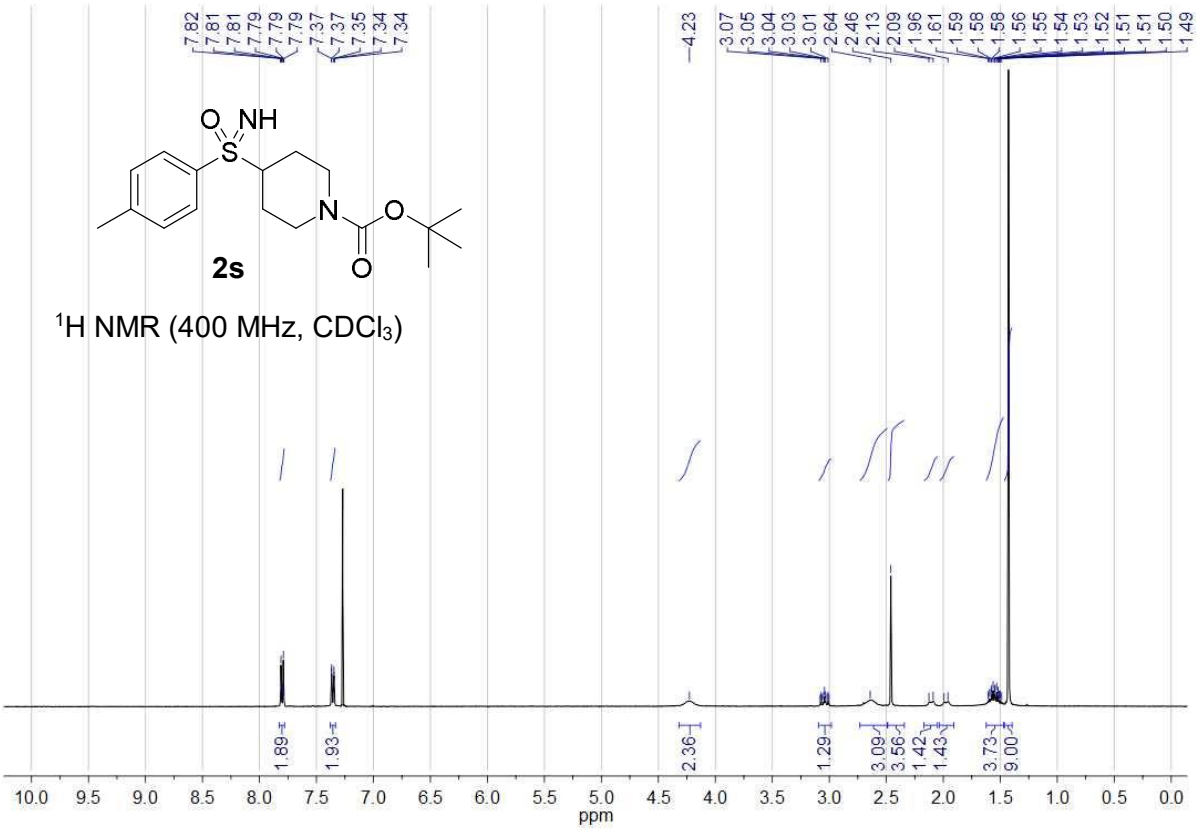

O NH
S
2p
^{13}C NMR (126 MHz, $CDCl_3$)
55.35
23.97
f1 (ppm)


dr = 3:2
^{1}H NMR (500 MHz, $CDCl_3$)
NH
O
S
O
2q
4.31
4.29
4.28
4.26
4.25
4.25
4.25
4.07
4.06
4.05
4.05
4.03
4.03
3.33
3.32
3.33
3.32
2.93
2.00
3.36
3.34
3.32
3.30
f1 (ppm)
3.00
1.98
3.14
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


dr = 3:2
^{13}C NMR (126 MHz, $CDCl_3$)
NH
O
S
O
2q
72.08
71.81
61.96
61.84
57.12
72.08
71.81
61.96
61.84
57.12
70
65
60
55
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

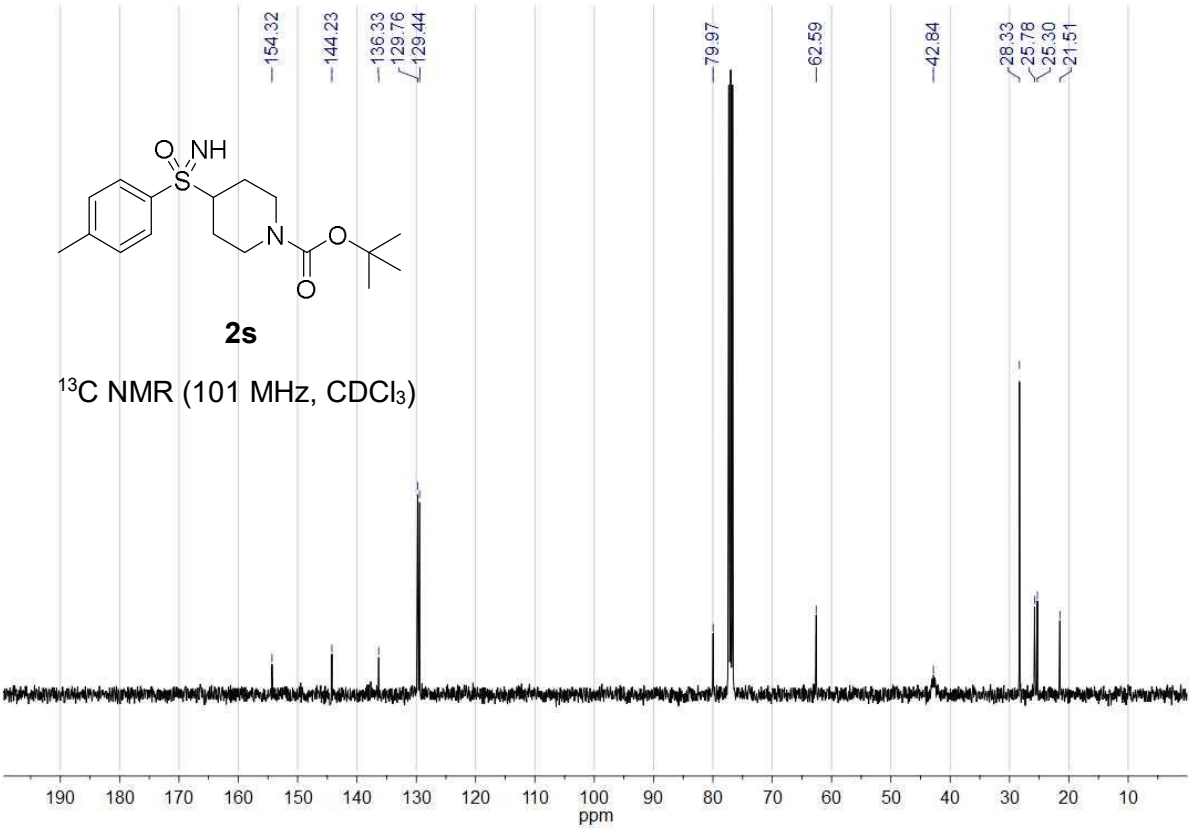

O
NH
S
O
2r
1H NMR (400 MHz, CDCl3)
ppm


O
NH
S
O
2r
13C NMR (101 MHz, CDCl3)
ppm



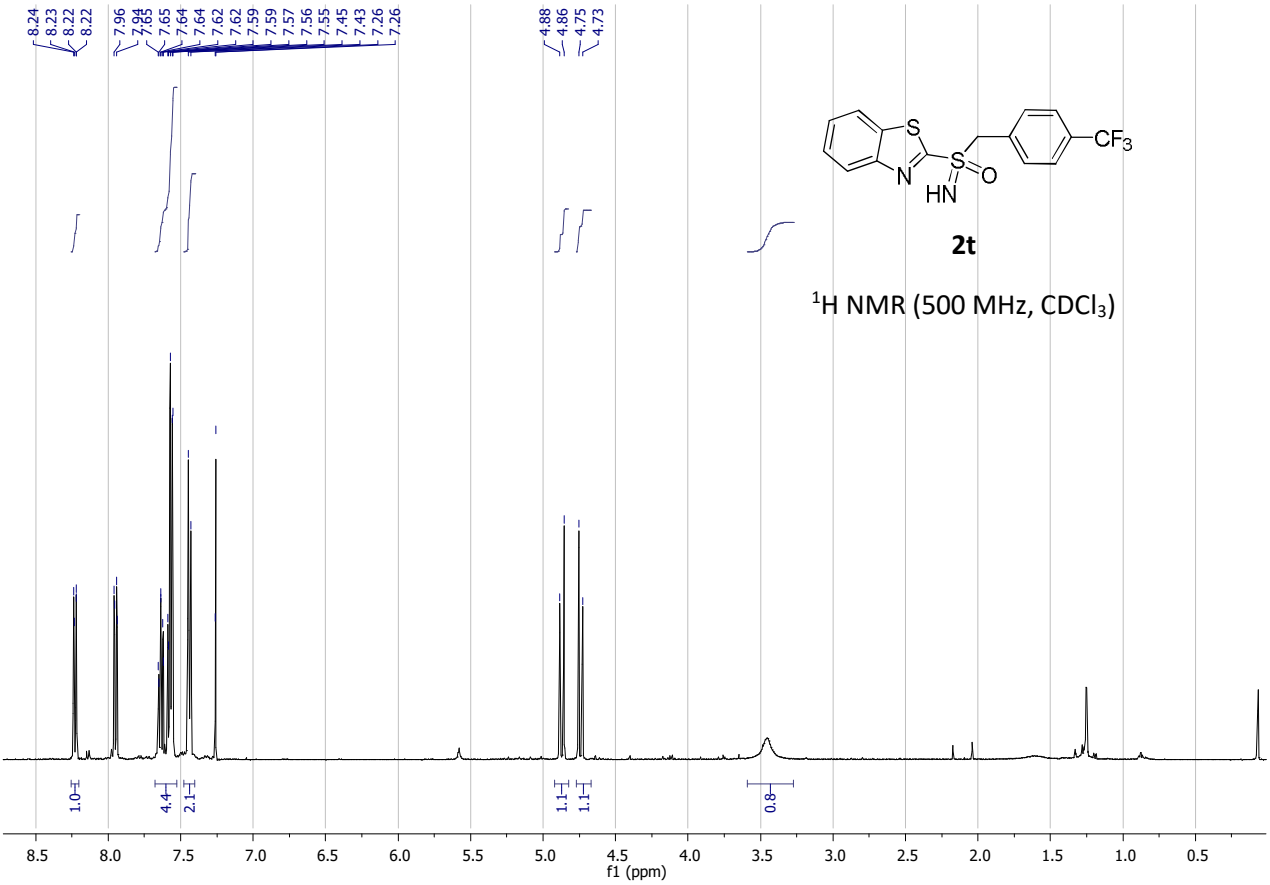
2s

^{1}H NMR (400 MHz, $CDCl_3$)



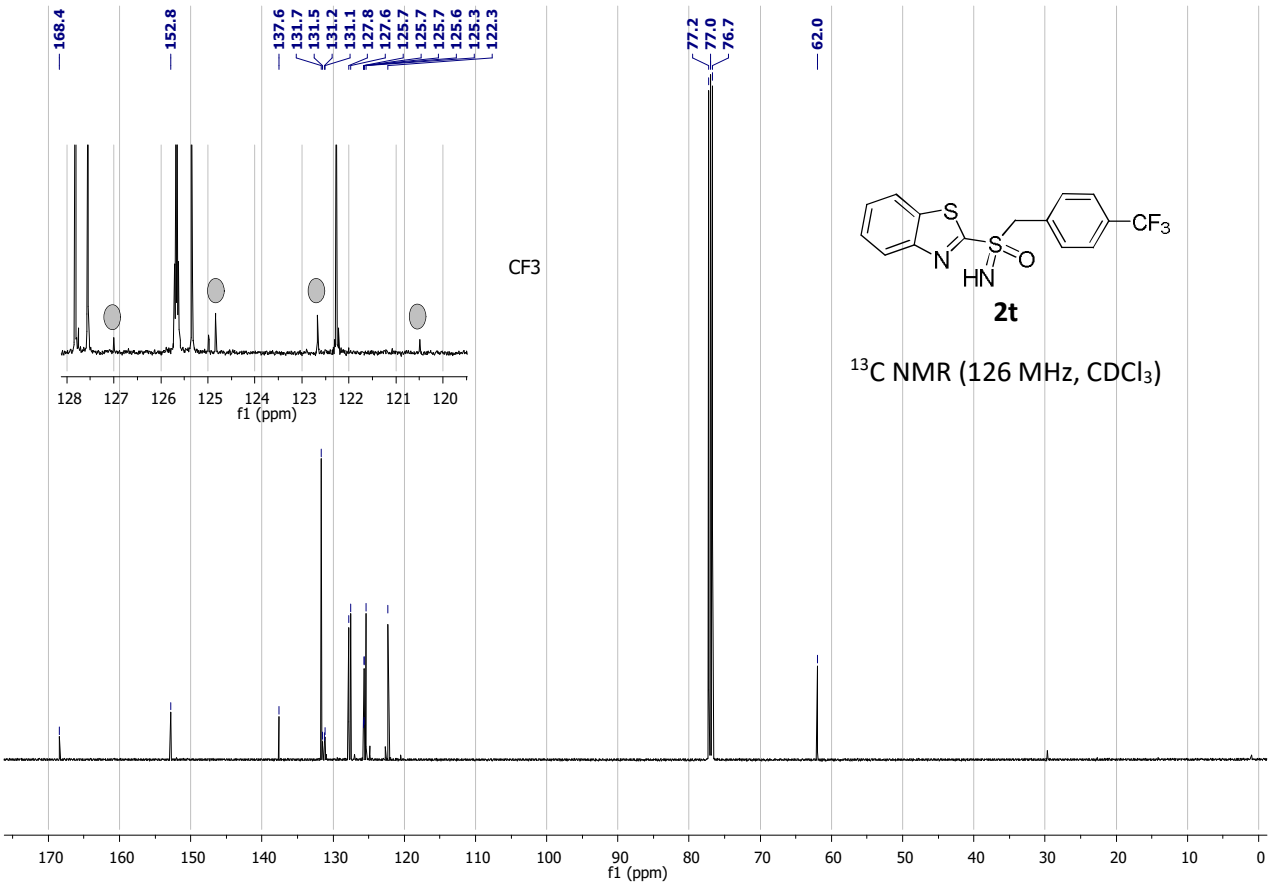
2s

^{13}C NMR (101 MHz, $CDCl_3$)



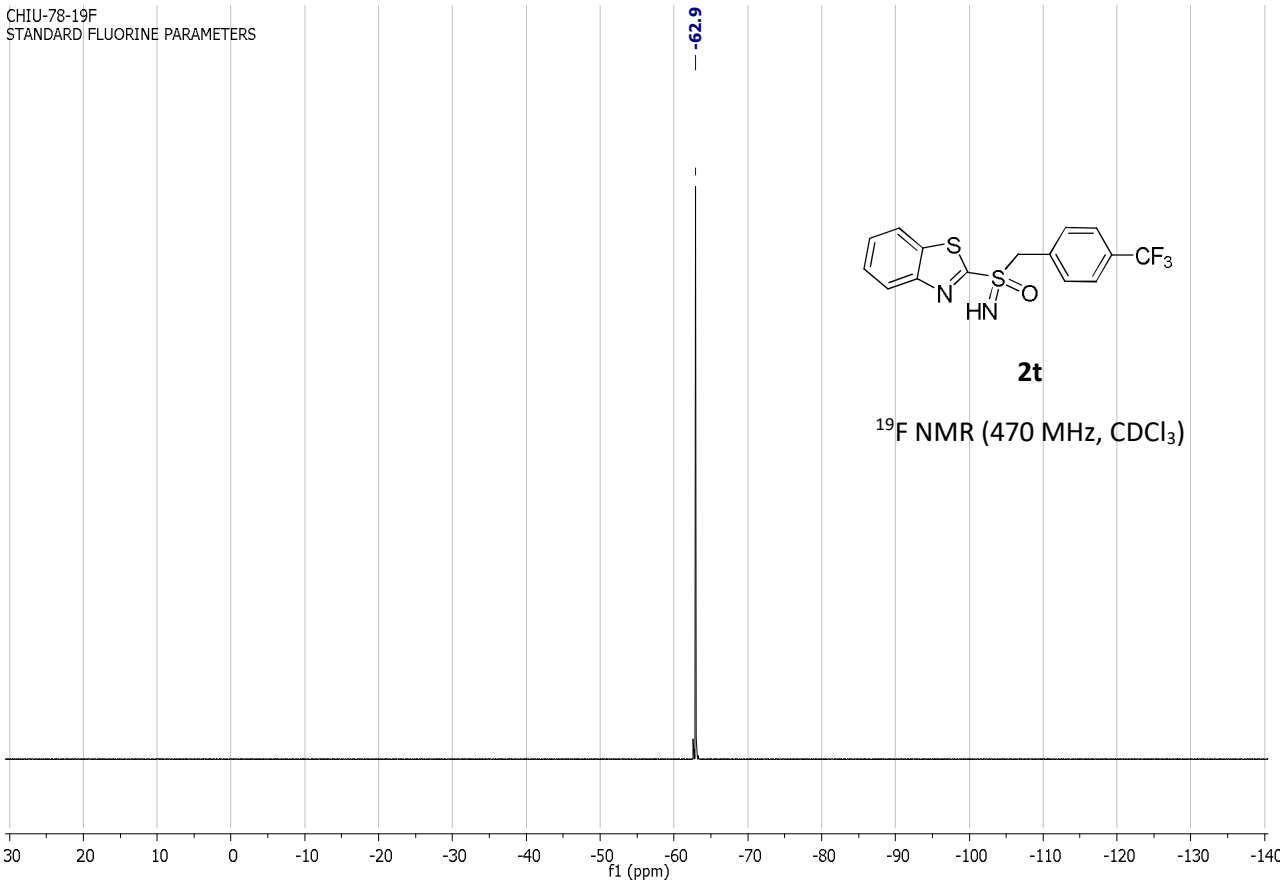
2t

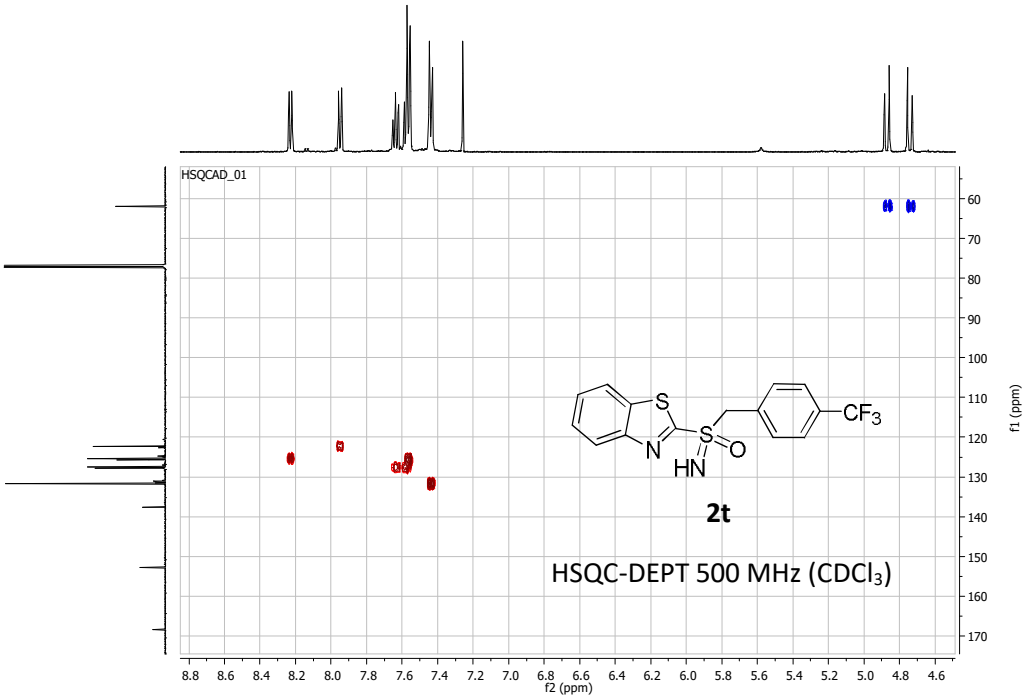
^{1}H NMR (500 MHz, $CDCl_3$)

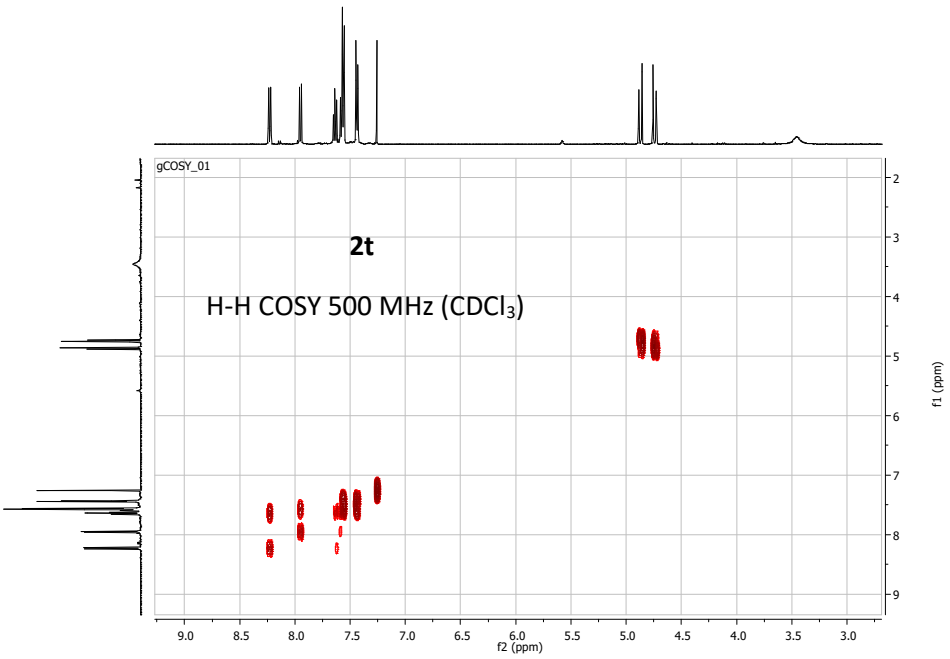


2t

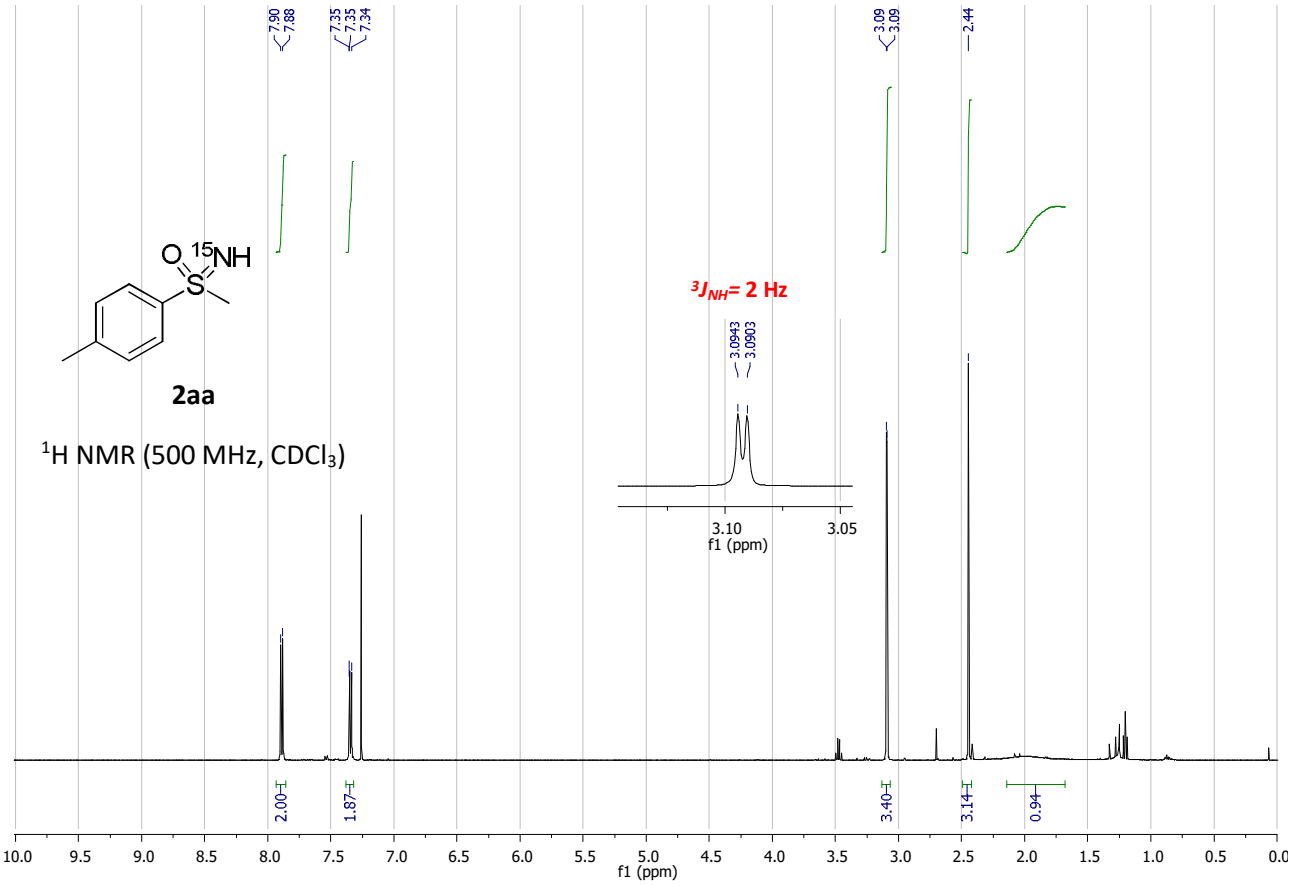
^{13}C NMR (126 MHz, $CDCl_3$)

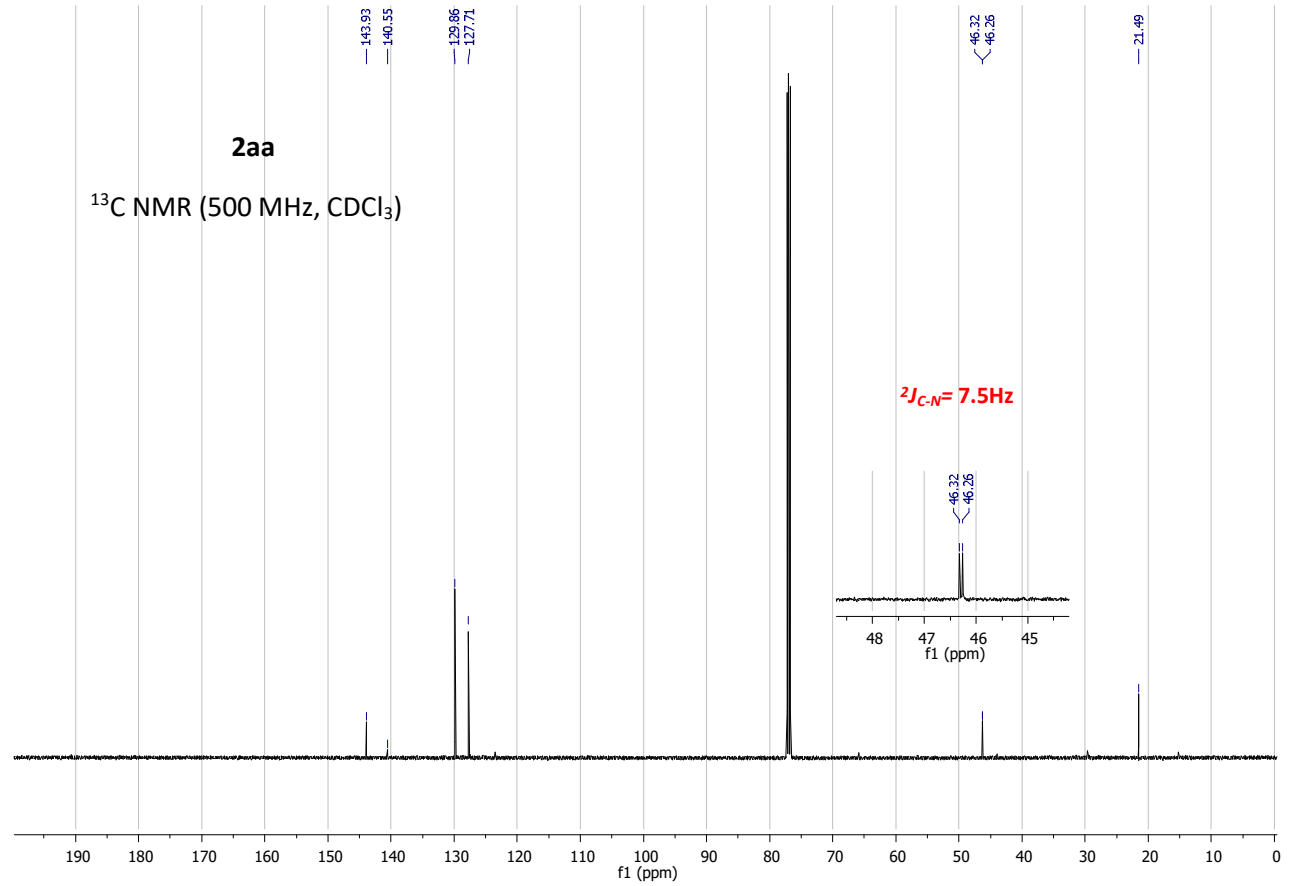

CHIU-78-19F
STANDARD FLUORINE PARAMETERS
-62.9
f1 (ppm)
2t
^{19}F NMR (470 MHz, $CDCl_3$)


HSQCAD_01
f2 (ppm)
f1 (ppm)
2t
HSQC-DEPT 500 MHz ($CDCl_3$)


gCOSY_01
2t
H-H COSY 500 MHz (CDCl3)
f2 (ppm)
f1 (ppm)

^{1}H ,^{13}C NMR, HSQC-DEPT and HRMS spectra of ^{15}N-labeled sulfoximines


7.90
7.88
7.35
7.35
7.34
3.09
3.09
2.44
O
15NH
S
2aa
1H NMR (500 MHz, CDCl3)
3JNH= 2 Hz
3.0943
3.0903
3.10
3.05
f1 (ppm)
2.00
1.87
3.40
3.14
0.94
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


143.93
140.55
129.86
127.71
46.32
46.26
21.49
2aa
13C NMR (500 MHz, CDCl3)
2JC-N= 7.5Hz
46.32
46.26
48
47
46
45
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

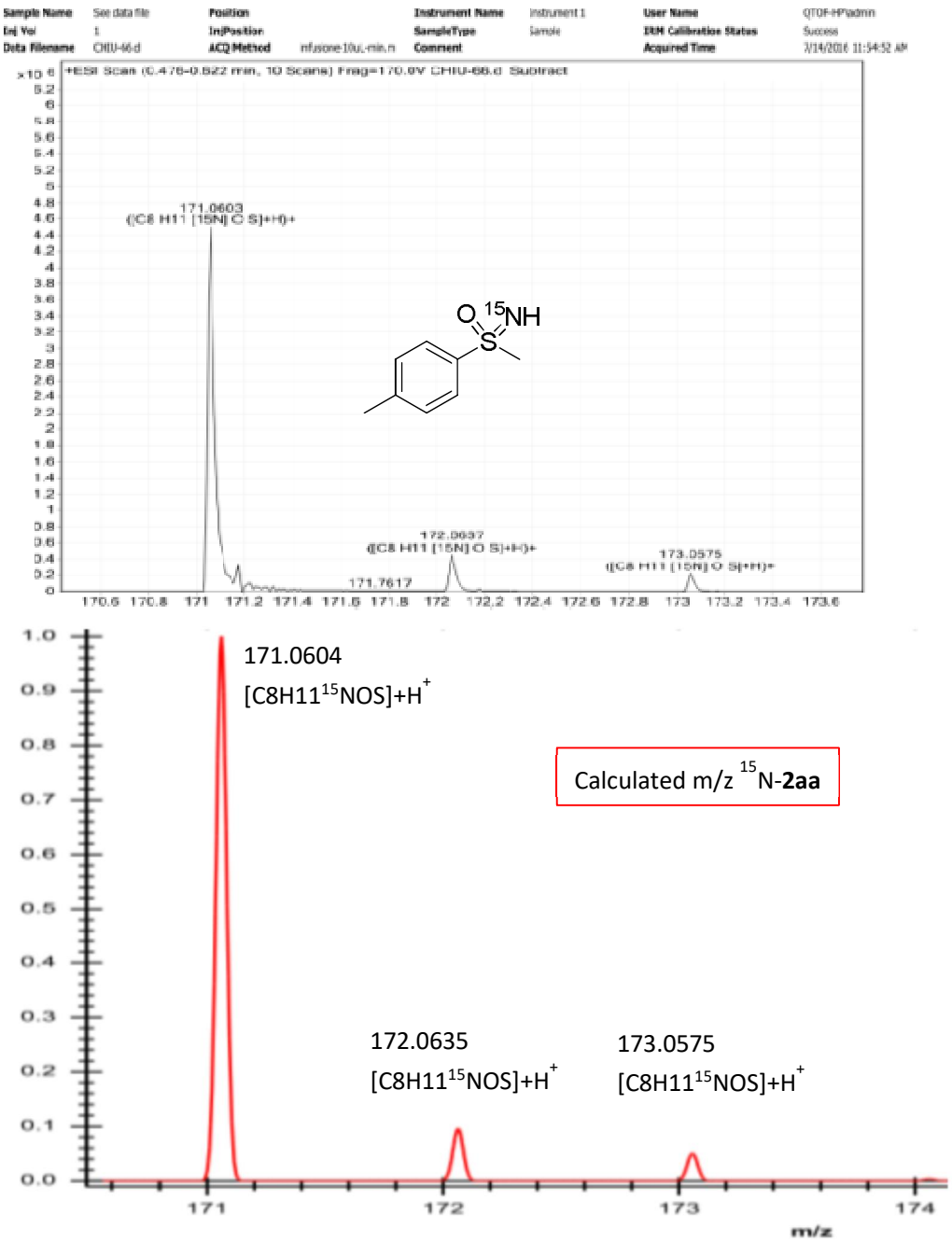
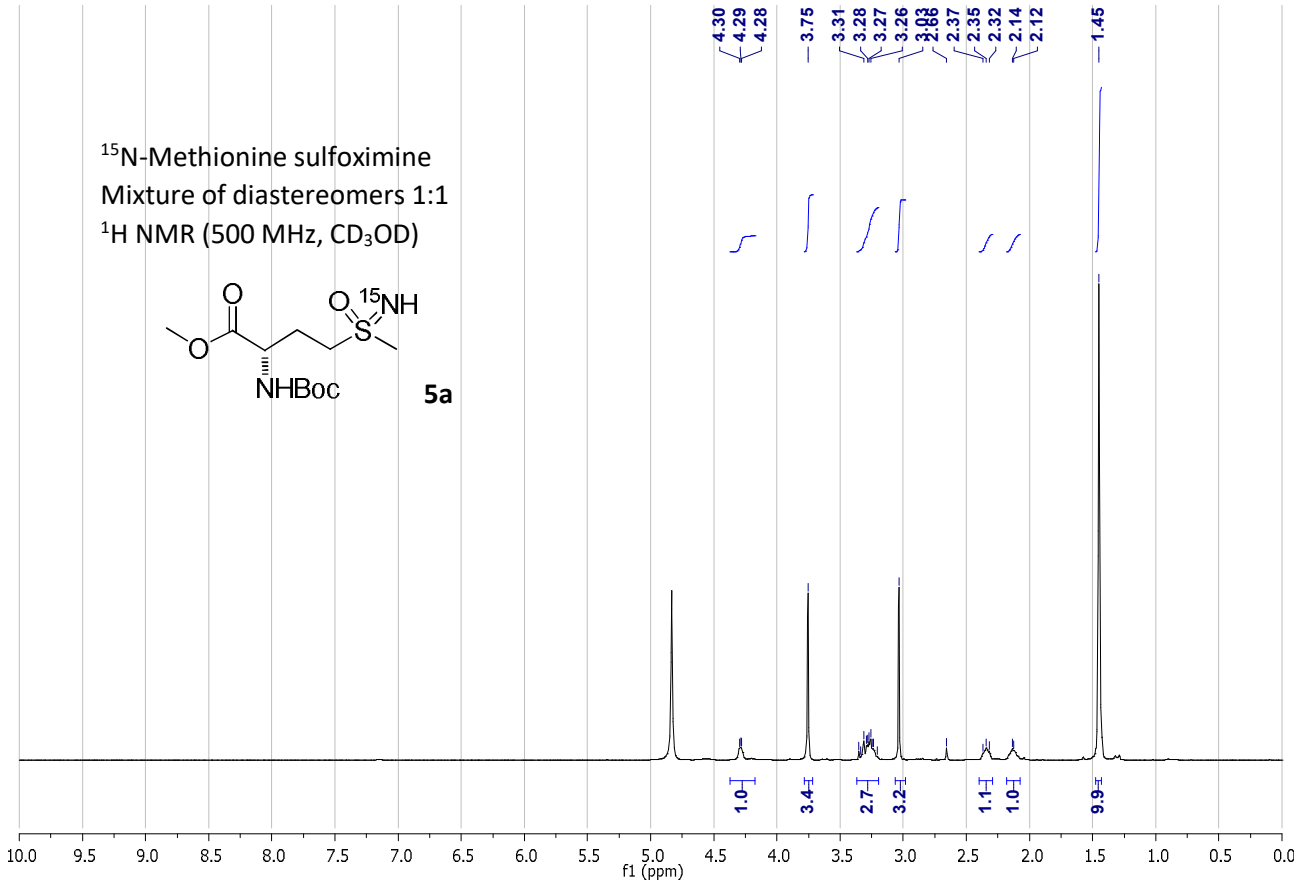
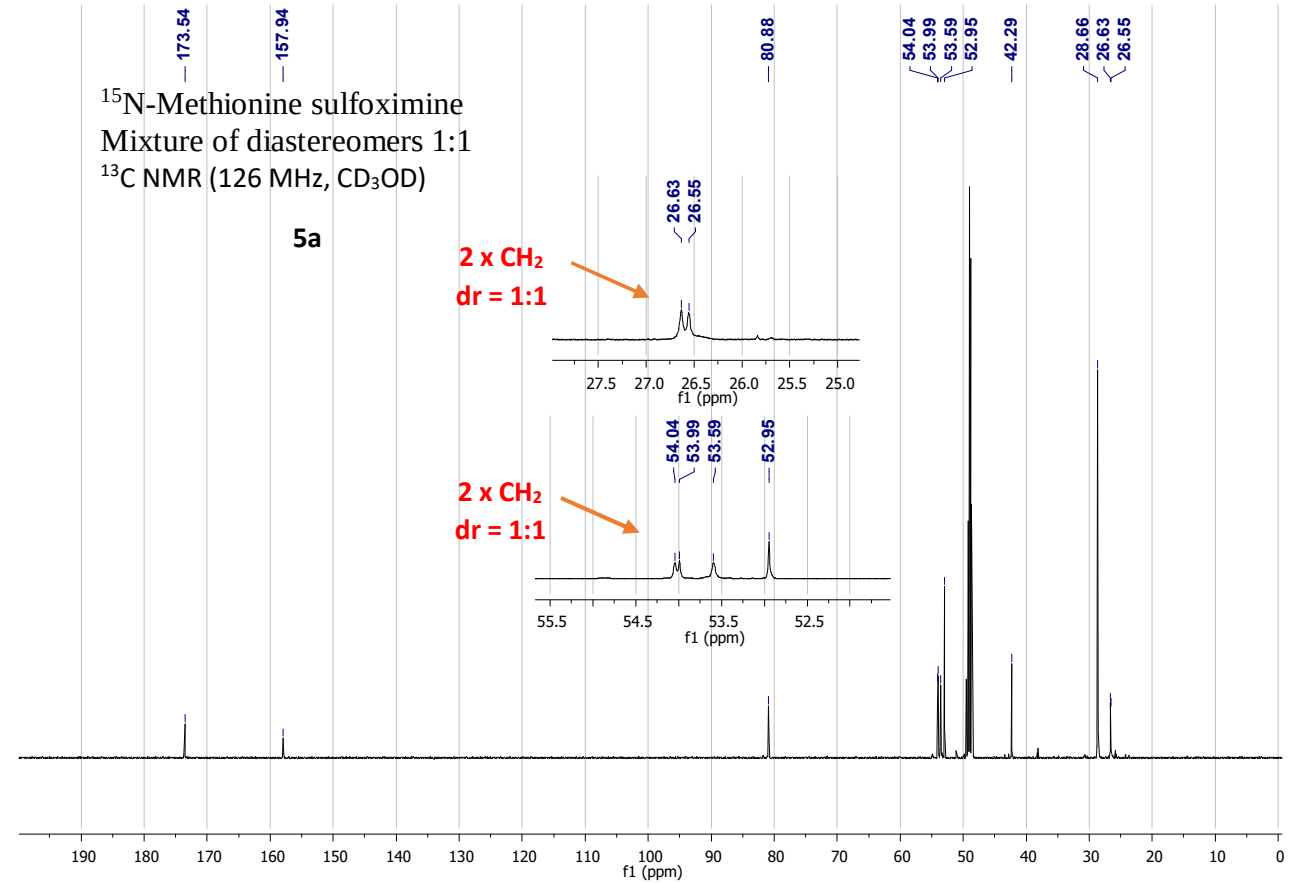
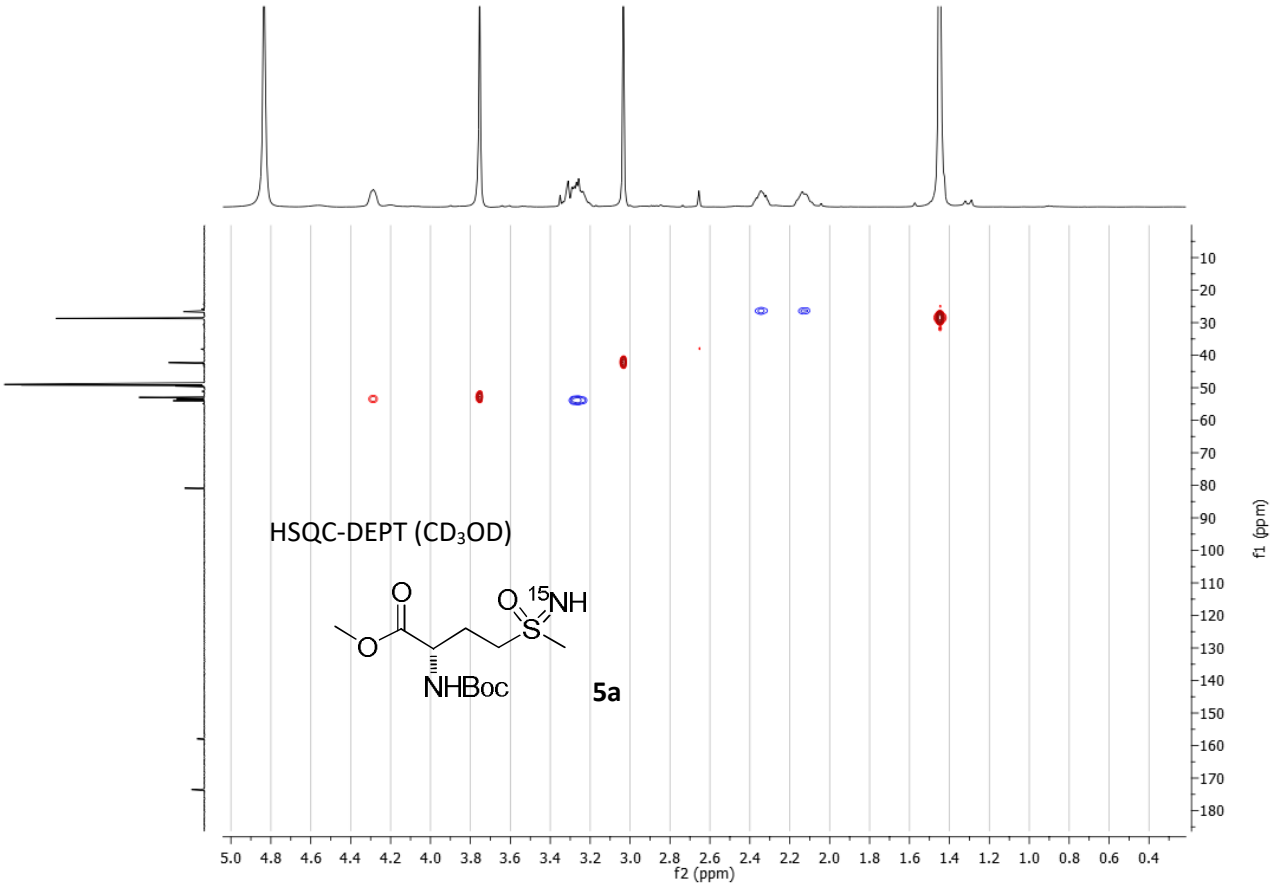


Figure 1. Expanded experimental HRMS (ESI+) of protonated adduct [M+H$^+$] of ^{15}N-**2aa.** In red: the calculated isotopic patterns of [^{15}N-**2aa**+H]$^+$ (exact mass = 171.0604 da).


^{15}N-Methionine sulfoximine
Mixture of diastereomers 1:1
^{1}H NMR (500 MHz, CD_3OD)
5a
f1 (ppm)


^{15}N-Methionine sulfoximine
Mixture of diastereomers 1:1
^{13}C NMR (126 MHz, CD_3OD)
5a
2 x CH_2
dr = 1:1
2 x CH_2
dr = 1:1
f1 (ppm)



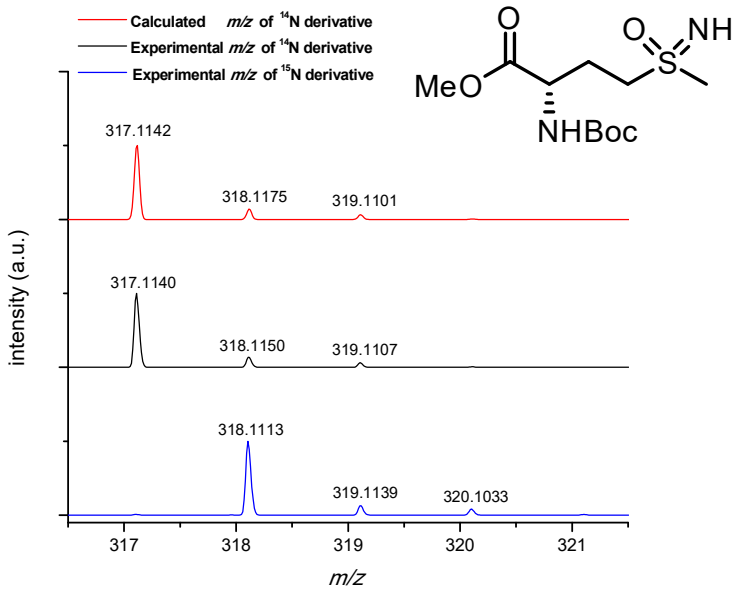
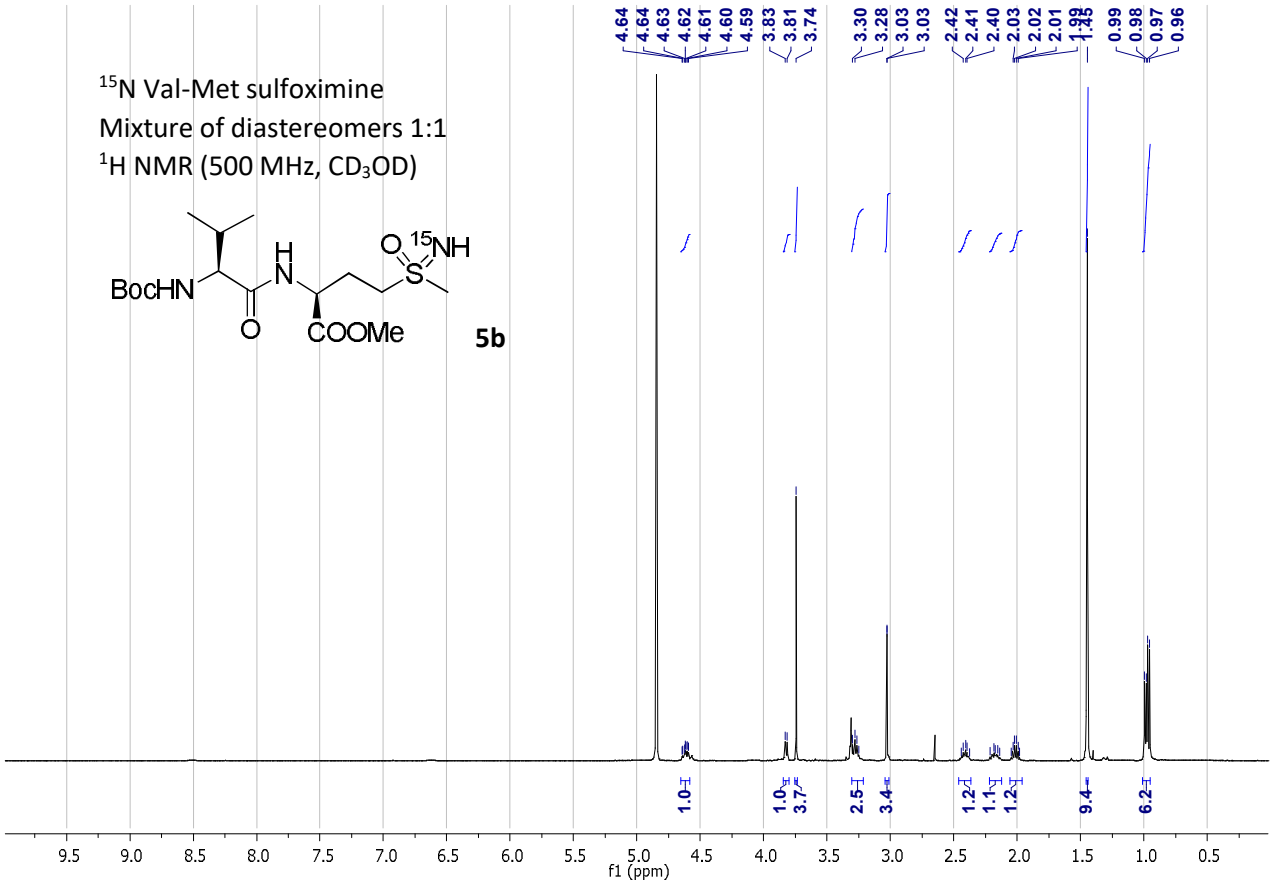
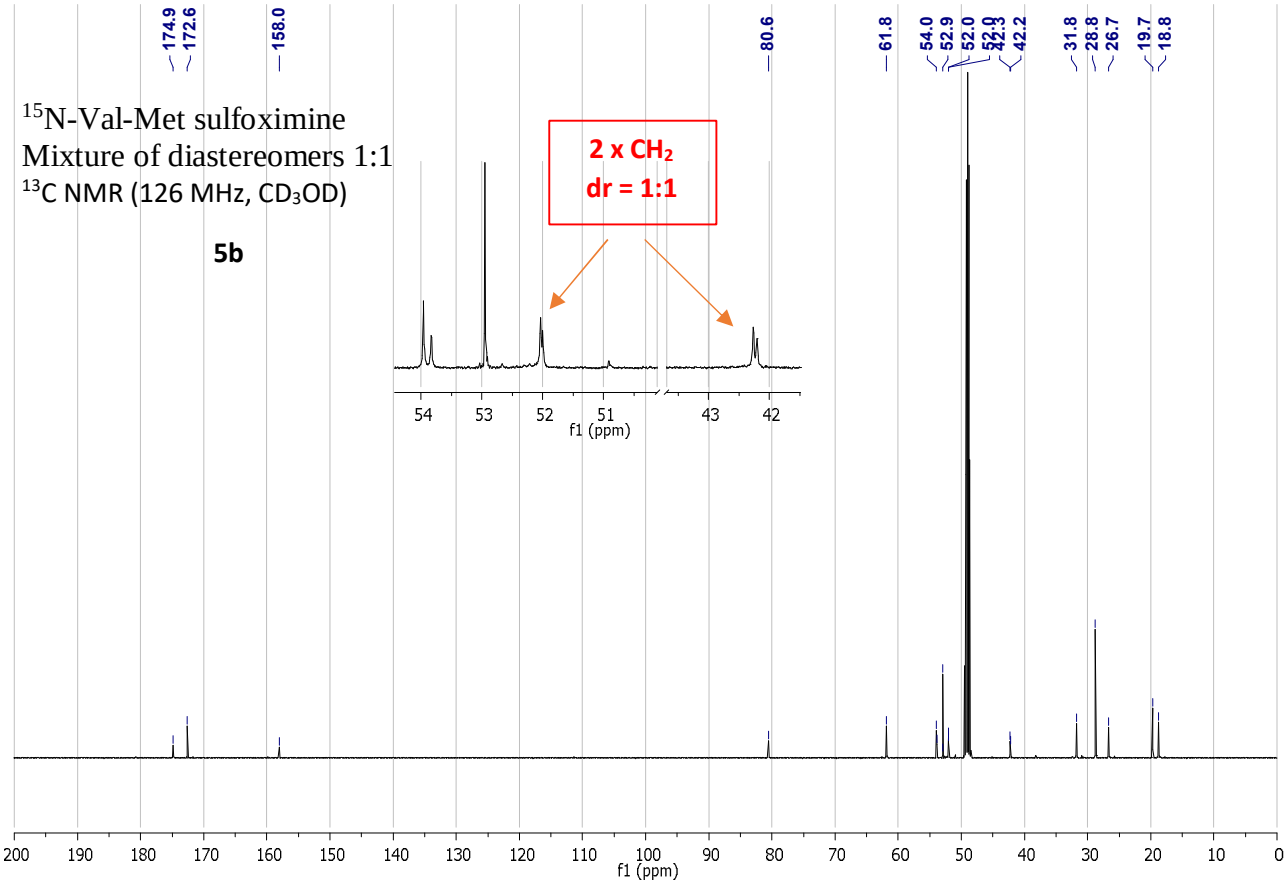


Figure 2. Expanded experimental HRMS (ESI+) of sodium adduct [M+Na$^+$] of ^{14}N-**5a** and ^{15}N-**5a** (exact mass = 318.1117 da). In red: the calculated isotopic patterns of [^{14}N-**5a**+Na]$^+$ (exact mass = 317.1142 da).


^{15}N Val-Met sulfoximine
Mixture of diastereomers 1:1
^{1}H NMR (500 MHz, CD_3OD)
BocHN
H
N
O
COOMe
O
^{15}NH
S
5b
4.64
4.64
4.63
4.62
4.61
4.60
4.59
3.83
3.81
3.74
3.30
3.28
3.03
3.03
2.42
2.41
2.40
2.03
2.02
2.01
1.99
1.45
0.99
0.98
0.97
0.96
1.0
1.0
3.7
2.5
3.4
1.2
1.1
1.2
9.4
6.2
f1 (ppm)


^{15}N-Val-Met sulfoximine
Mixture of diastereomers 1:1
^{13}C NMR (126 MHz, CD_3OD)
5b
2 x CH_2
dr = 1:1
174.9
172.6
158.0
80.6
61.8
54.0
52.9
52.0
42.3
42.2
31.8
28.8
26.7
19.7
18.8
f1 (ppm)

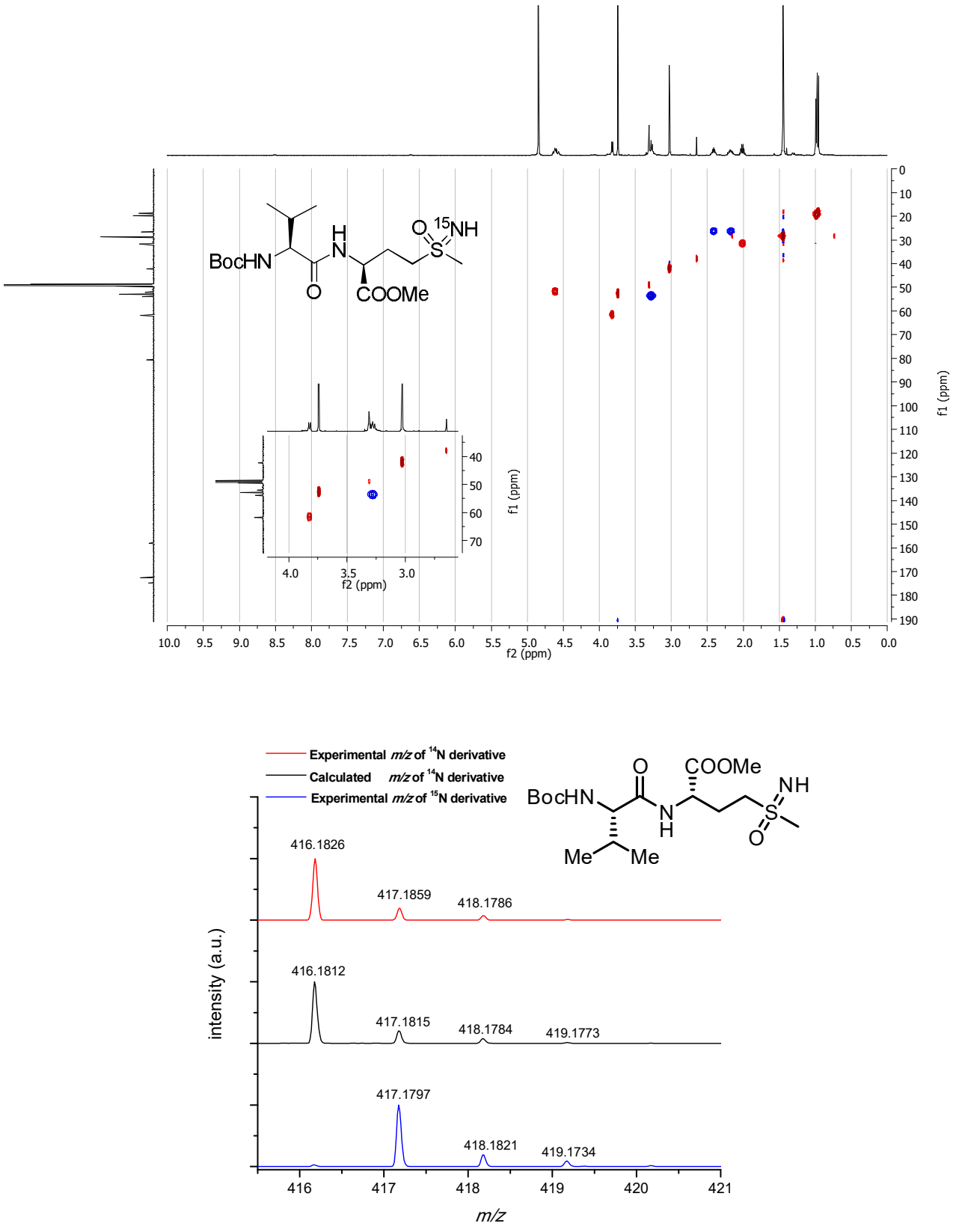
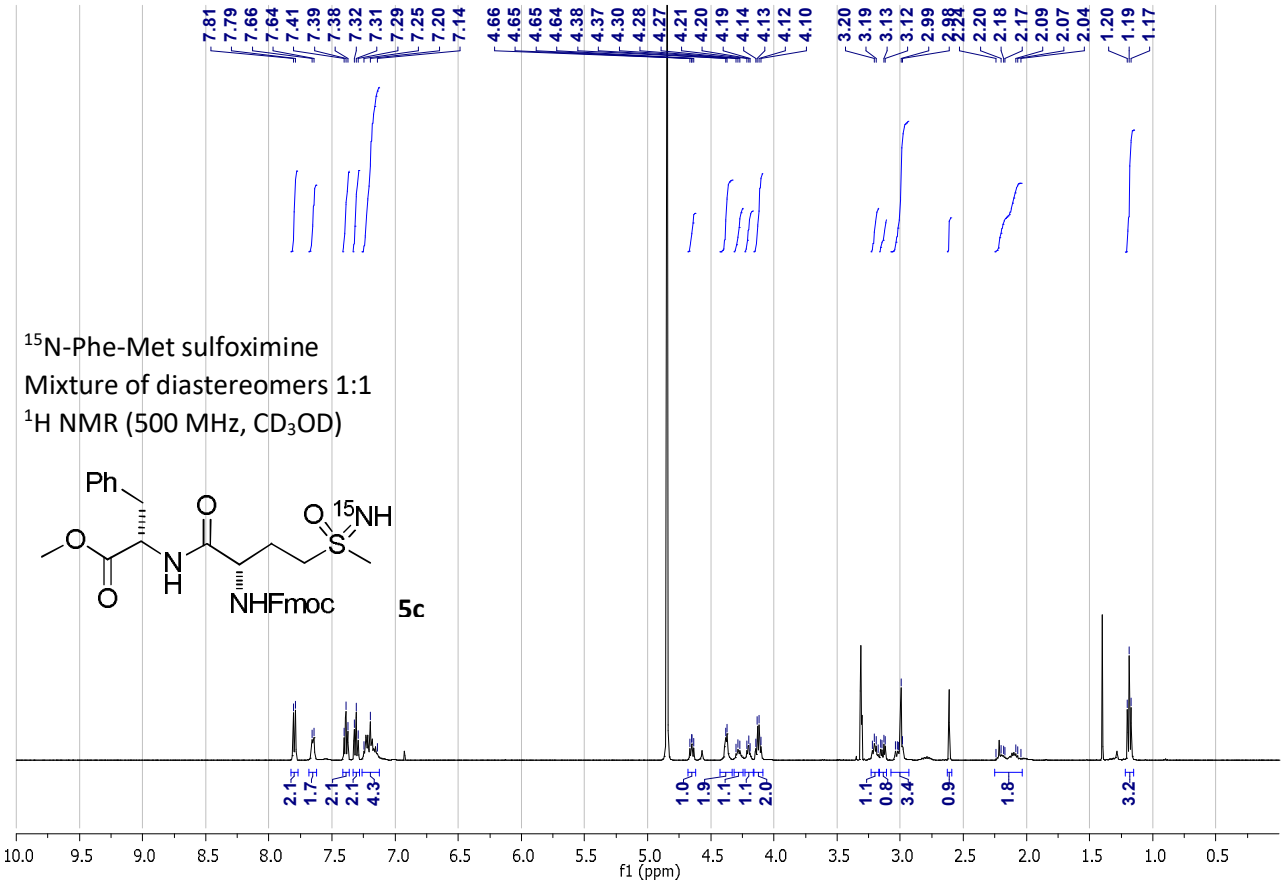
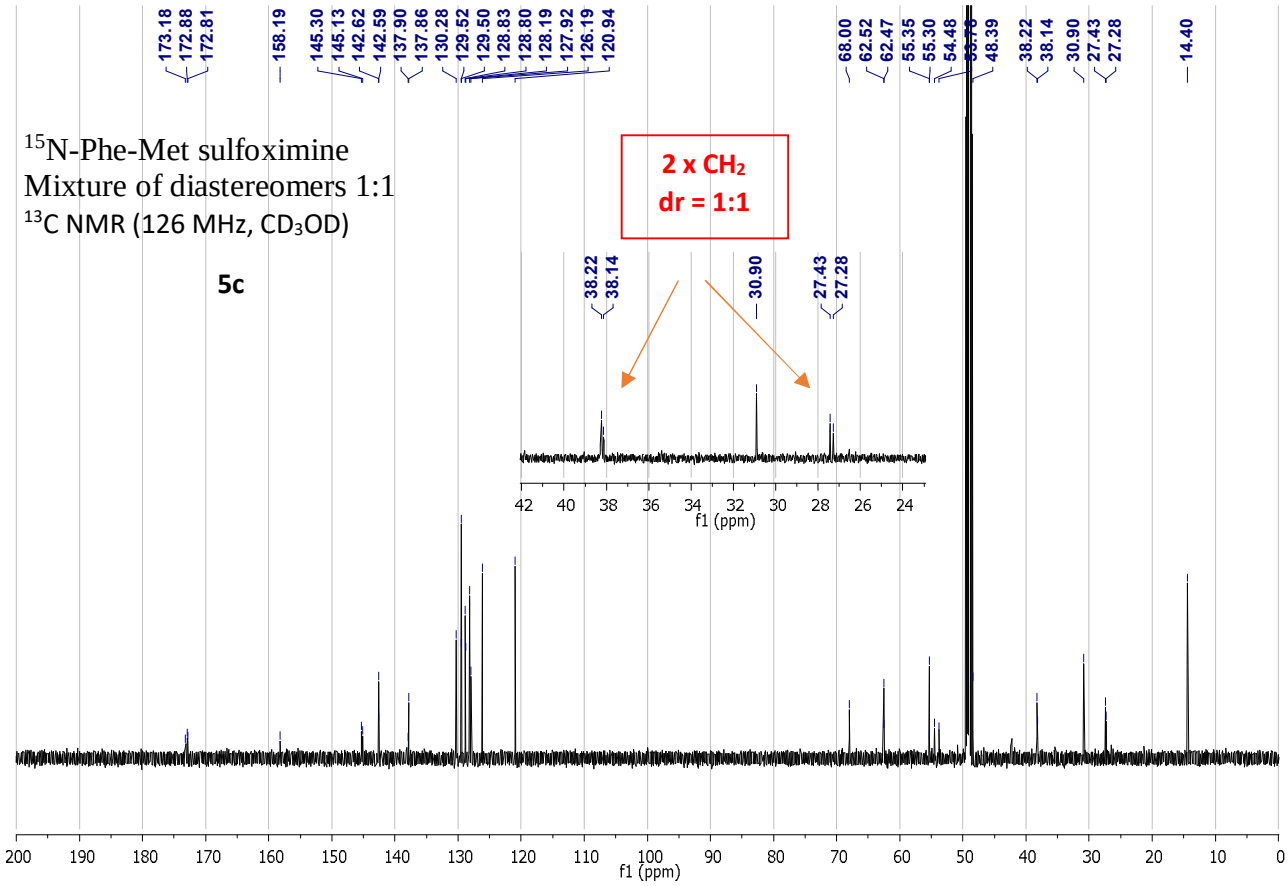
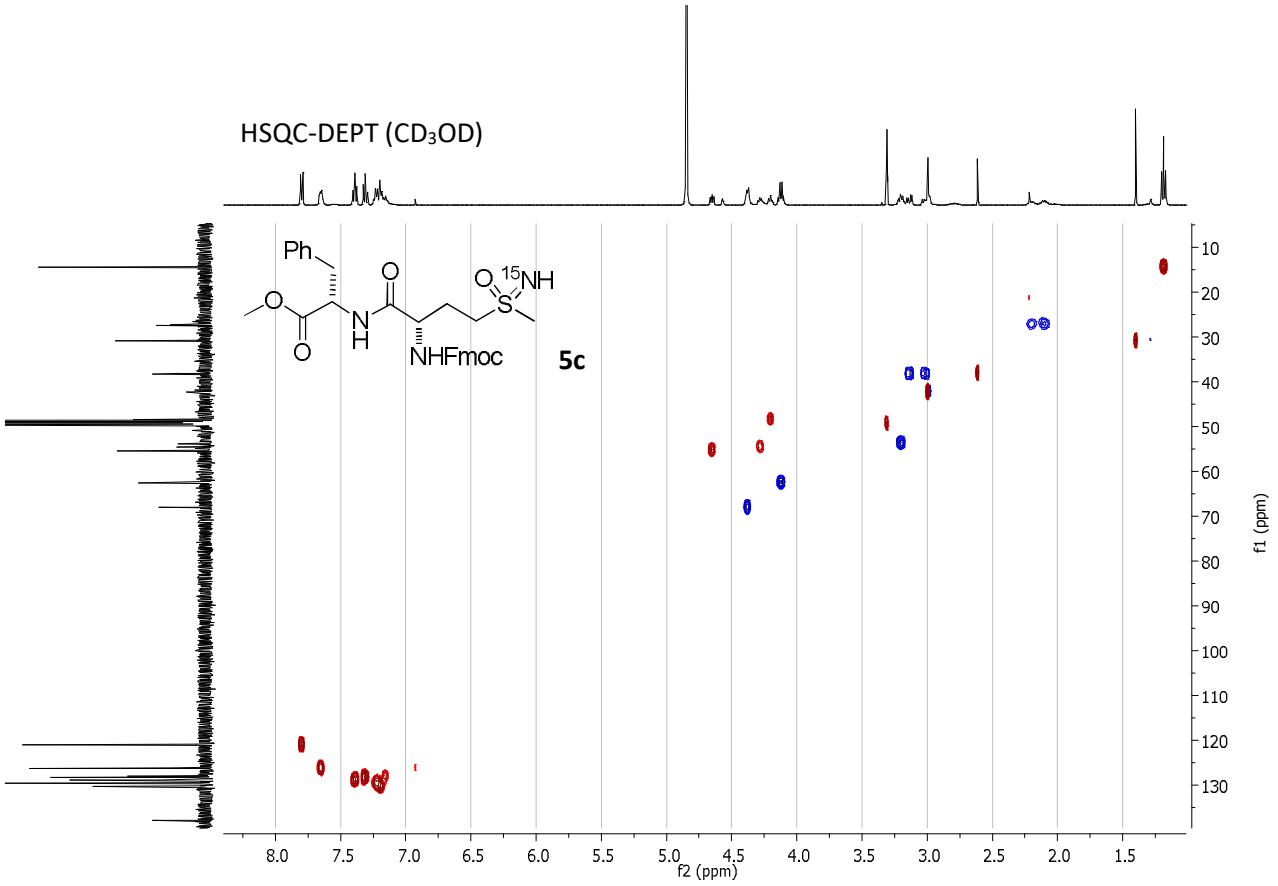


Figure 4. Expanded experimental HRMS (ESI+) of sodium adduct [M+Na$^+$] of ^{14}N-**5b** and ^{15}N-**5b** (exact mass = 417.1802 da). In red: the calculated isotopic patterns of [^{14}N-**5b** +Na]$^+$ (exact mass = 416.1826 da).


7.81 7.79 7.66 7.64 7.41 7.39 7.38 7.32 7.31 7.29 7.25 7.20 7.14
4.66 4.65 4.65 4.64 4.38 4.37 4.30 4.28 4.27 4.21 4.20 4.19 4.14 4.13 4.12 4.10
3.20 3.19 3.13 3.12 2.99 2.20 2.18 2.17 2.09 2.07 2.04
1.20 1.19 1.17
2.1 1.7 2.1 2.1 4.3
1.0 1.9 1.1 1.1 2.0
1.1 0.8 3.4 0.9 1.8 3.2
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
15N-Phe-Met sulfoximine
Mixture of diastereomers 1:1
1H NMR (500 MHz, CD3OD)
Ph
O
O
N
H
O
O
15NH
S
NHFmoc
5c


173.18 172.88 172.81
158.19
145.30 145.13 142.62 142.59 137.90 137.86 130.28 129.52 129.50 128.83 128.80 128.19 127.92 126.19 120.94
68.00 62.52 62.47 55.35 55.30 54.48 53.70 48.39
38.22 38.14 30.90 27.43 27.28
14.40
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
15N-Phe-Met sulfoximine
Mixture of diastereomers 1:1
13C NMR (126 MHz, CD3OD)
5c
2 x CH2
dr = 1:1
38.22 38.14
30.90
27.43 27.28
42 40 38 36 34 32 30 28 26 24
f1 (ppm)



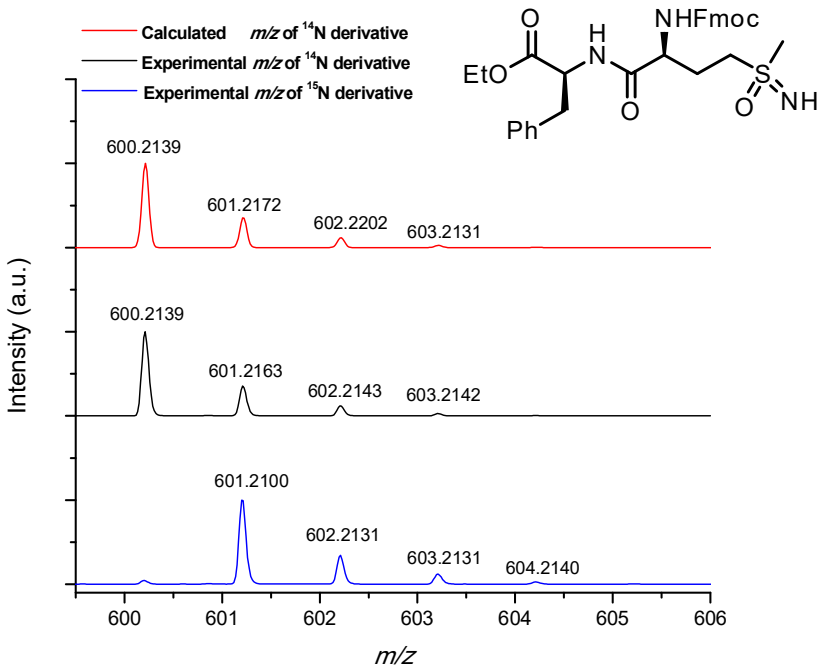
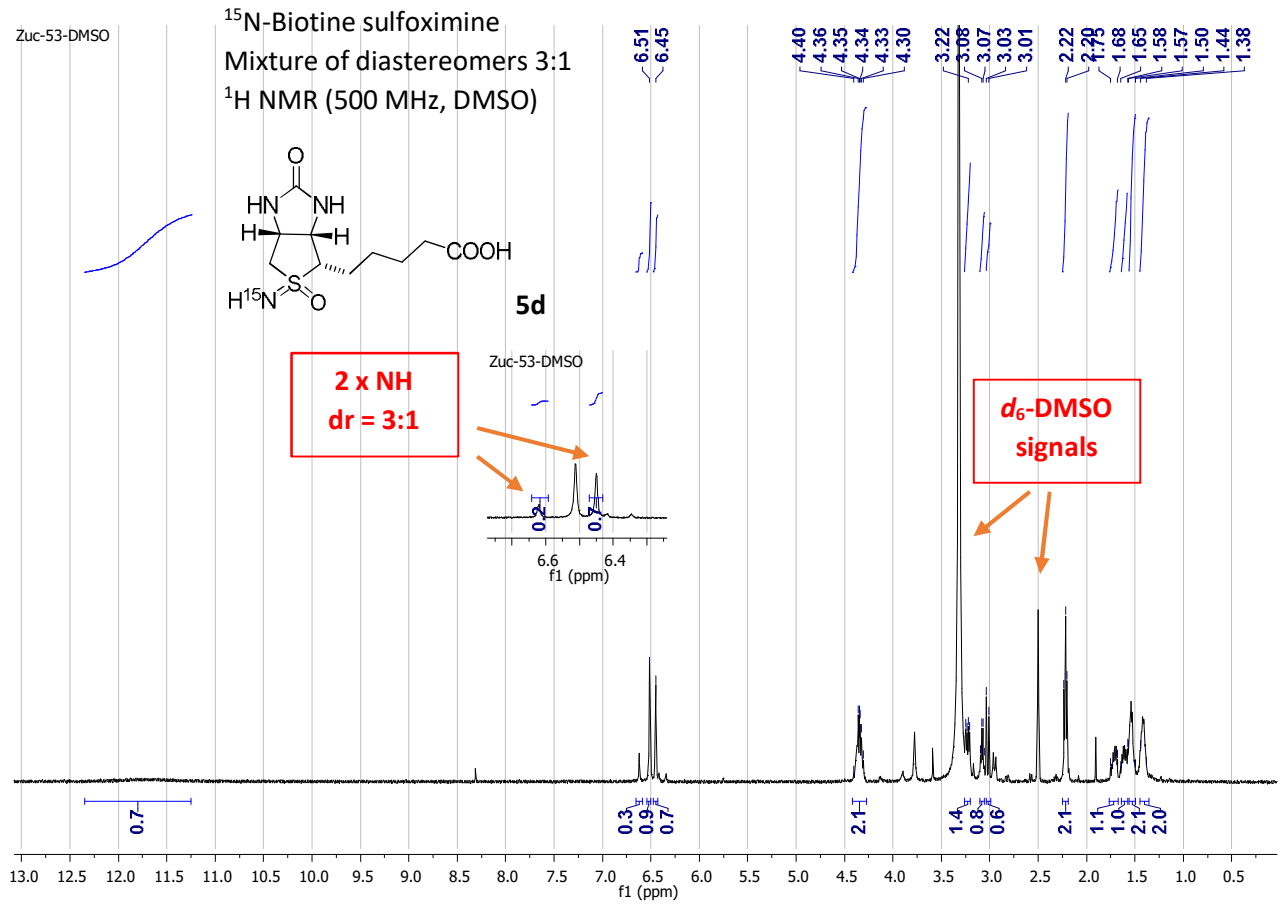
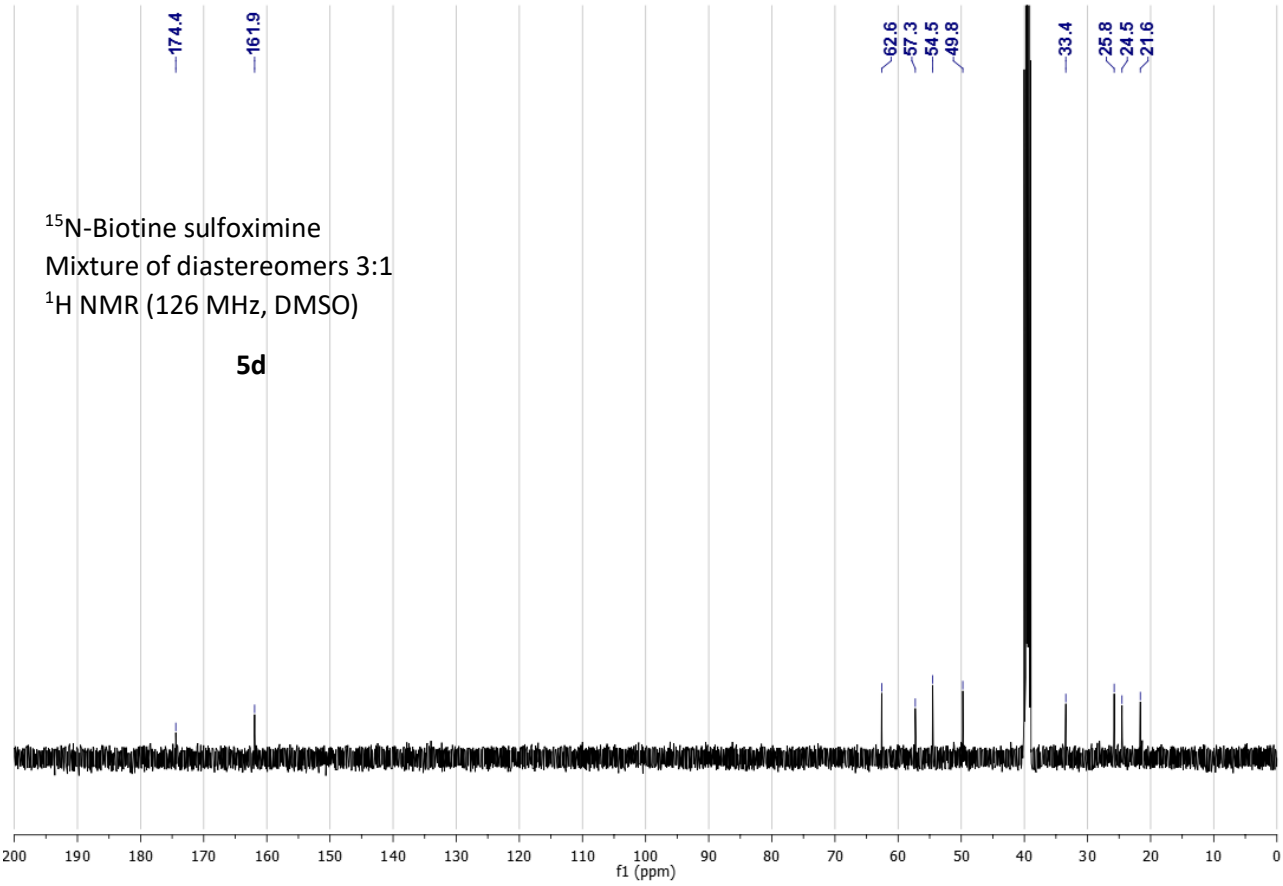
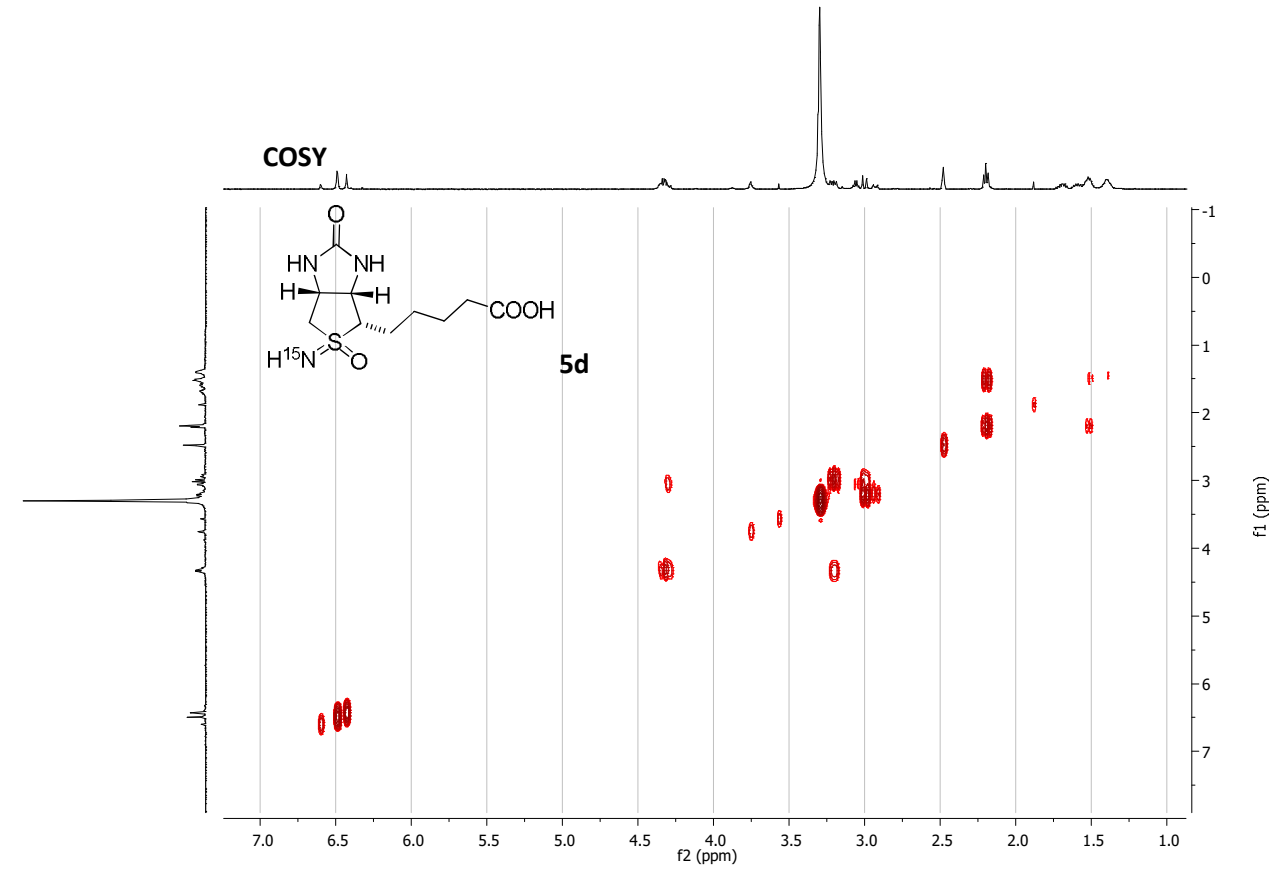
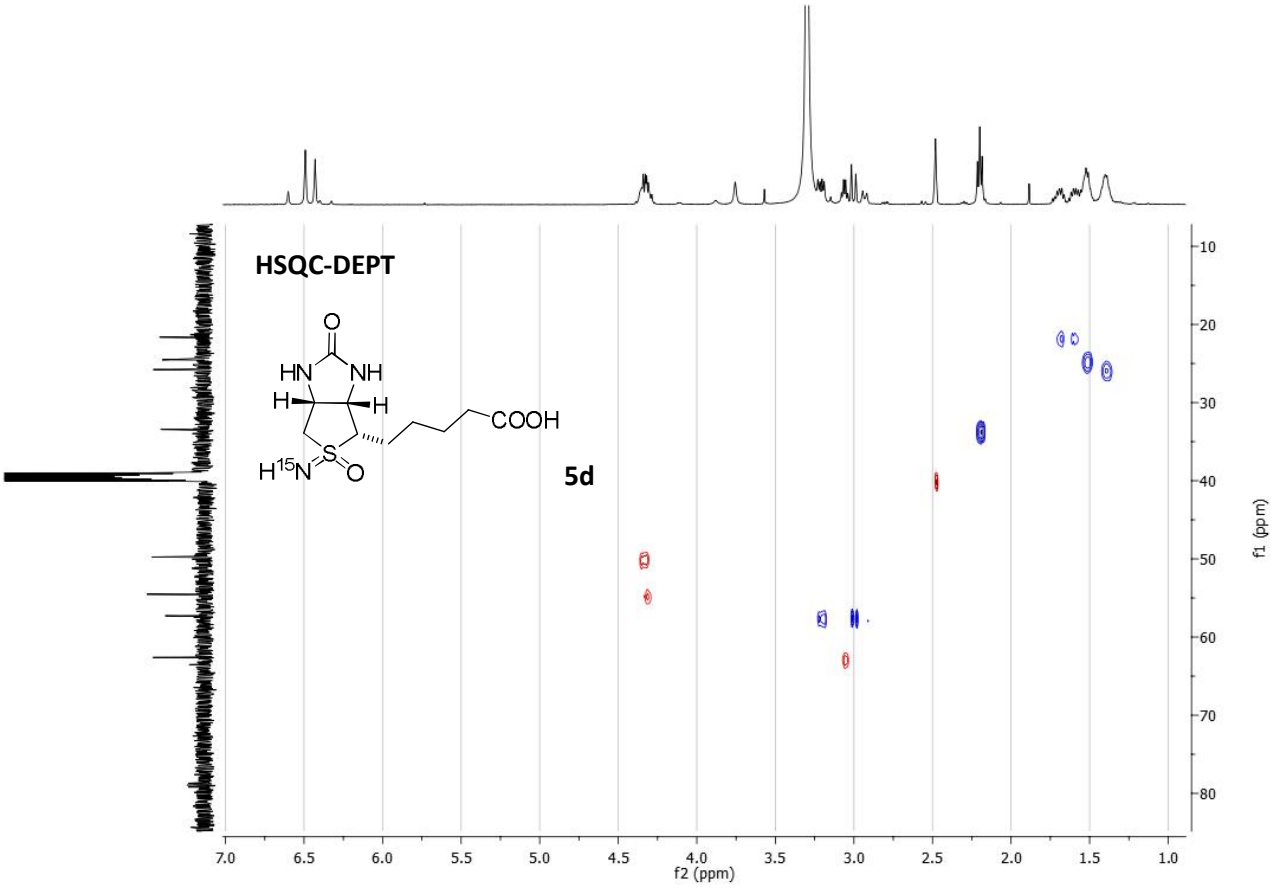


Figure 3. Expanded experimental HRMS (ESI+) of sodium adduct $[M+Na]^+$ of ^{14}N-**5c** and ^{15}N-**5c** (exact mass = 601.2115 da). In red: the calculated isotopic patterns of $[^{14}$N-**5c** $+Na]^+$ (exact mass = 600.2139 da).


Zuc-53-DMSO
15N-Biotine sulfoximine
Mixture of diastereomers 3:1
1H NMR (500 MHz, DMSO)
5d
2 x NH
dr = 3:1
d6-DMSO
signals
f1 (ppm)


15N-Biotine sulfoximine
Mixture of diastereomers 3:1
1H NMR (126 MHz, DMSO)
5d
f1 (ppm)


COSY
HN
NH
H
H
COOH
H15N
S
O
5d
f2 (ppm)
f1 (ppm)


HSQC-DEPT
HN
NH
H
H
COOH
H15N
S
O
5d
f2 (ppm)
f1 (ppm)

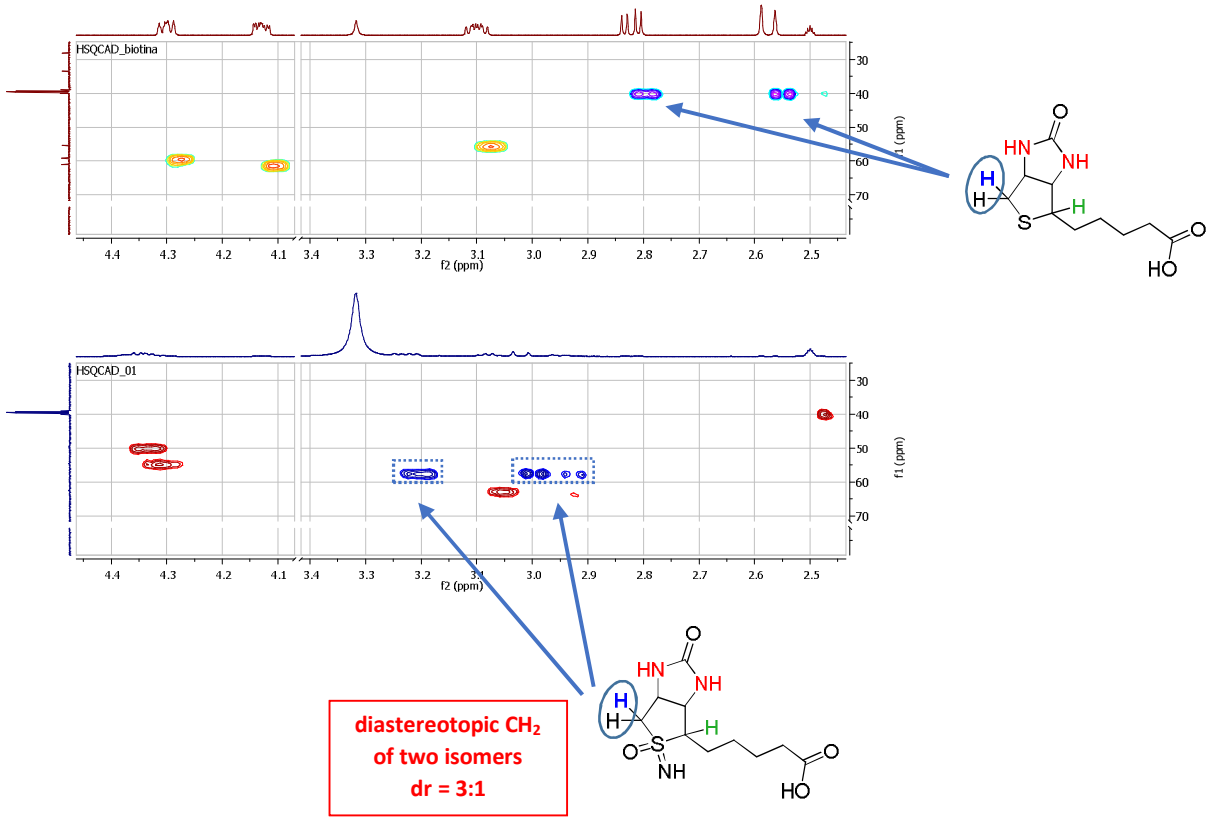


Figure 6. Compared expanded HSQC of ^{14}N-**5d** and Biotin. In dashed blue line: deshielded CH_2 protons of **5d**.

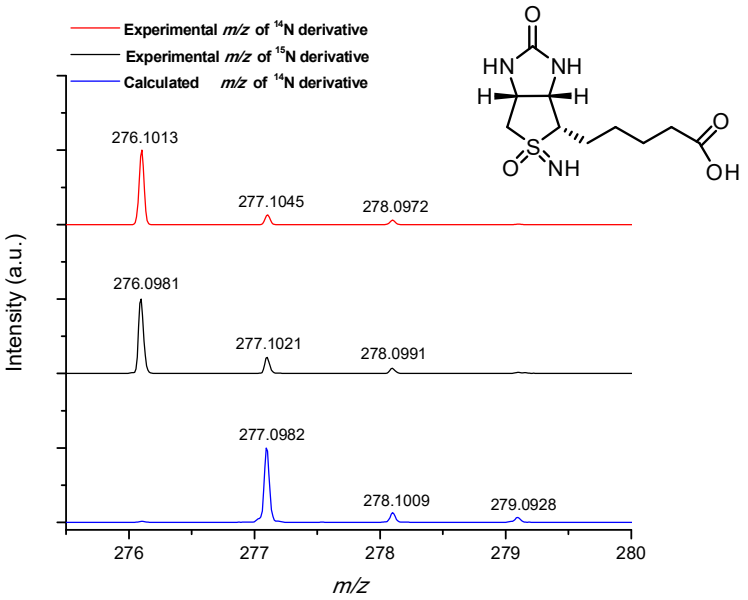


Figure 6. Expanded experimental HRMS (ESI+) of proton adduct [M+H$^+$] of ^{14}N-**5d** and ^{15}N-**5d** (exact mass = 277.0988 da). In red: the calculated isotopic patterns of [^{14}N-**5d** +H]$^+$ (exact mass = 276.1013 da).

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