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SUPPORTING INFORMATION

Mechanistic Investigation of the NH-Sulfoximination of Sulfide. Evidence for λ^6-sulfanenitrile intermediates

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Table of Contents

GENERAL

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) or aqueous potassium permanganate stain. 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** = 7.26 ppm; methanol, **δ** = 3.34 ppm). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and bs = broad signal), 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 (chloroform, **δ** = 77.0 ppm; methanol, **δ** = 47.7 ppm). The high-resolution mass spectrometry (HRMS) analyses were performed using a Xevo G2-XS QTof WATERS mass spectrometer equipped with an electrospray ion source (ESI) operated in positive ion mode.

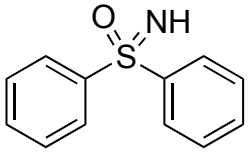
Reagents: Sulfides, $PhI(OAc)_2$, $NH_4CO_2NH_2$ and ammonium-^{15}N acetate were commercially available (Sigma Aldrich, Fischer, Alfa Aesar). All commercial reagents were used as supplied or purified by standard techniques when required.

PREPARATION OF SULFOXIMINES

General procedure A for the preparation of NH Sulfoximines

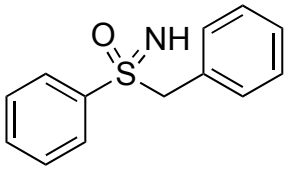
To a flask containing a stirrer bar was added successively, sulfide (1 equiv.), ammonium carbamate (1.5 equiv.) and then MeOH (0.5 M). PIDA (2.1 equiv.) was added in one portion and the reaction was stirred at 20 °C for 30 min (open flask to the atmosphere). The solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica gel.

Iminodiphenyl-λ^6-sulfanone (4a)



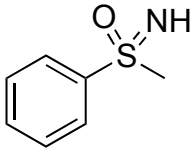
Prepared according to General Procedure **A** using diphenyl sulfide (186 mg, 1.0 mmol) and purified by flash chromatography (EtOAc/Pentane 1/1) to afford sulfoximine **4a** as a white solid (208 mg, 96%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 8.03-8.00 (m, 4H), 7.50-7.41 (m, 6H), 3.08 (bs, 1H, NH); **^{13}C NMR (101 MHz, $CDCl_3$, δ):** 143.4, 132.5, 129.1, 127.9; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_{12}H_{12}NOS^+$ $[M+H]^+$ 218.0640, found 218.0643. **FT-IR (cm^{-1})**: 3263, 1445, 1222, 1127, 1094, 958, 720, 683.

Benzyl(imino)(phenyl)-λ^6-sulfanone (4b)



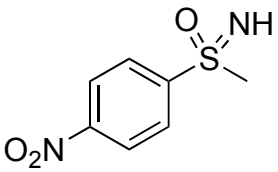
Prepared according to General Procedure **A** using phenyl benzyl sulfide (50 mg, 0.25 mmol) and purified by flash column chromatography (EtOAc/Pentane 1/1) to afford sulfoximine **4b** as a white solid (53 mg, 92%). **^{1}H NMR (400 MHz, $CDCl_3$, δ):** 7.77-7.75 (m, 2H), 7.60-7.56 (m, 1H), 7.47-7.43 (m, 2H), 7.35-7.25 (m, 3H), 7.1-7.10 (m, 2H), 4.39 and 4.30 (AB system, J_{AB} = 13.3 Hz, 2H, CH_2), 2.78 (bs, 1H, NH); **^{13}C NMR (101 MHz, $CDCl_3$, δ):** 140.6, 133.2, 131.2, 129.00, 128.97, 128.9, 128.8, 128.6, 64.83; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_{13}H_{14}NOS^+$ $[M+H]^+$ 232.0796 , found 232.0799. **FT-IR (cm^{-1})**: 3442, 1442, 1219, 1111, 977, 702.

Imino(methyl)(phenyl)-λ^6-sulfanone (4c)



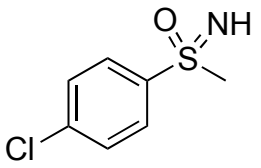
Prepared according to General Procedure **A** using methyl phenyl sulfide (50 mg, 0.4 mmol) and purified by flash column chromatography (EtOAc/MeOH 9/1) to afford sulfoximine **4c** as a colorless oil (58 mg, 94%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 8.01-7.98 (m, 2H), 7.62-7.59 (m, 1H), 7.56-7.52 (m, 2H), 3.09(s, 3H), 2.69 (bs, 1H, NH); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 143.6, 133.2, 129.4, 127.8, 46.3; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_7H_{10}NOS^+$ $[M+H]^+$ 156.0483 found 156.0486. **FT-IR (cm^{-1})**: 3263, 1214, 1095, 1008, 992, 739, 687.

Imino(methyl)(4-nitrophenyl)-λ^6-sulfanone (4d)



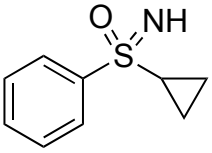
Prepared according to General Procedure **A** using methyl 4-nitrophenyl sulfide (93 mg, 0.55 mmol) and purified by flash column chromatography (EtOAc/Pentane 2/1) to afford sulfoximine **4d** as a white solid (105 mg, 96%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 8.39 (d, *J* = 8.8 Hz, 2H), 8.21 (d, *J* = 8.8 Hz, d), 3.15 (s, 3H), 2.88 (bs, 1H, NH); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 150.6, 149.6, 129.3, 124.6, 46.1; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_7H_9N_2O_3S^+$ $[M+H]^+$ 201,0334, found 201.0335. **MP**: 146-147°C. **FT-IR (cm^{-1}):** 3098, 1522, 1345, 1225, 996, 942, 853, 735.

(4-Chlorophenyl)(imino)(methyl)-λ^6-sulfanone (4e)



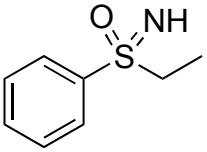
Prepared according to General Procedure **A** using methyl 4-chlorophenyl sulfide (64 mg, 0.4 mmol) and purified by flash column chromatography (EtOAc/Pentane 2/1) to afford sulfoximine **4e** as a colorless oil (65 mg, 86 %). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 7.94 (d, *J* = 8.6 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, d), 3.09 (s, 3H), 2.76 (bs, 1H, NH); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 142.2, 139.9, 129.7, 129.4, 46.3; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_7H_9ClNOS^+$ $[M+H]^+$190.0093, found 190.0098. **FT-IR (cm^{-1})**: 3266, 1217, 1082, 996, 826, 759.

(phenyl)(cyclopropyl)(imino)-λ^6-sulfanone (4f)



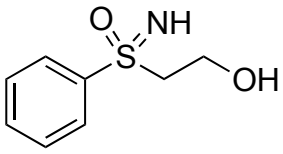
Prepared according to General Procedure **A** using phenyl cyclopropyl sulfide (75.12 mg, 0.5 mmol) and purified by flash column chromatography (EtOAc/Pentane 1/1) to afford sulfoximine **4f** as a pale yellow oil (90.6 mg, 91%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 7.88-7.85 (m, 2H), 7.53-7.49 (m, 1H), 7.45-7.42 (m, 2H), 2.75 (bs, 1H, NH), 2.48-2.42 (m, 1H), 1.30-1.24 (m, 1H), 1.12-1.05 (m, 1H), 0.98-0.91 (m, 1H), 0.85-0.78 (m, 1H); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 143.1, 132.8, 129.1, 127.8, 34.2, 5.9, 5.6; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_9H_{12}NOS^+$ $[M+H]^+$ 182.0640, found 182.0643. **FT-IR (cm^{-1})**: 3266, 1445, 1220, 1093, 971, 882, 715, 688.

(phenyl)(ethyl)(imino)-λ^6-sulfanone (4g)



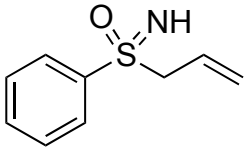
Prepared according to General Procedure **A** using phenyl ethyl sulfide (69.1 mg, 0.5 mmol) and purified by flash column chromatography (EtOAc/Pentane 1/1) to afford the title sulfoximine as a pale yellow oil (84.6 mg, 87%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 7.94-7.92 (m, 2H), 7.61-7.57 (m, 1H), 7.54-7.50 (m, 2H), 3.14 (q, *J* = 7.4 Hz, 2H), 2.59 (bs, 1H, NH), 1.22 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 141.3, 133.0, 129.1, 128.5, 51.8, 7.8; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_8H_{12}NOS^+$ $[M+H]^+$ 170.0640, found 170.0645. **FT-IR (cm^{-1})**: 3266, 1445, 1207, 1094, 964, 760, 718, 689

(2-Hydroxyethyl)(imino)(phenyl)-λ⁶- sulfanone (4h)



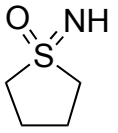
Prepared according to General Procedure **A** using 2-hydroxyethyl phenyl sulfide (154 mg, 1.0 mmol) and purified by flash column chromatography (EtOAc/MeOH 9/1) to afford sulfoximine **4h** as a colorless oil (150 mg, 81%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 8.00-7.98 (m, 2H), 7.66 (m, 1H), 7.58 (m, 2H), 4.07 (ddd, *J* = 12.8, 5.5 and 4.4 Hz, 1H), 3.83 (ddd, *J* = 12.8, 6.7 and 3.6 Hz, 1H), 3,31 (m, 2H); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 141.97, 133.7, 129.6, 128.5, 58.4, 56.6; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_8H_{12}NO_2S^+$ $[M+H]^+$ 186.0589, found 186.0592. **FT-IR (cm^{-1})**: 3252, 1209, 1094, 1028, 1011, 985, 687.

allyl(imino)(phenyl)-λ⁶-sulfanone (4i)



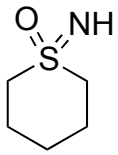
Prepared according to General Procedure **A** using allyl phenyl sulfide (75 mg, 0.5 mmol) and purified by flash column chromatography (EtOAc/Pentane 3/2) to afford sulfoximine **4i** as a colorless oil (82 mg, 91%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 7.94-7.92 (m, 2H), 7.62-7.58 (m, 1H), 7.54-7.50 (m, 2H), 5.82 (ddt, *J* = 17.1, 10.1 and 7.4 Hz, 1H), 5.31 (d, *J* = 10.1 Hz, 1H), 5.12 (dd, *J* = 17.1 and 0.9 Hz, 1H), 3.83 (part of an ABX system, *J* = 13.6 and 7.4 Hz, 2H), 2.86 (bs, 1H, NH); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 140.99, 133.2, 129.1, 128.8, 125.5, 124.5, 62.6; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_9H_{12}NOS^+$ $[M+H]^+$ 182.0640, found 182.0643. **FT-IR (cm^{-1})**: 3267, 1217, 979, 931, 751, 688.

1-iminotetrahydro-1H-1λ⁶-thiophene 1-oxide (4j)



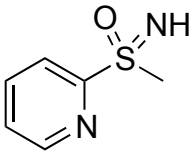
Prepared according to General Procedure **A** using tetrahydrothiophene (44 mg, 0.5 mmol) and purified by flash column chromatography (DCM/MeOH 9/1) to afford sulfoximine **4j** as a colorless oil (55.3 mg, 93%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 3.14-3.08 (m, 4H), 2.66 (bs, 1H, NH), 2.21 (m, 4H); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 56.3, 24.0; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_4H_{10}NOS^+$ $[M+H]^+$ 120.0483, found 120.0483. **FT-IR (cm^{-1})**: 3259, 1196, 1139, 1094, 1075, 986, 721.

1-iminohexahydro-1λ⁶-thiopyran-1-oxide (4k)



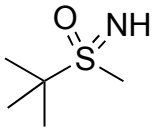
Prepared according to General Procedure **A** using pentamethylene sulfide (51.1 mg, 0.5 mmol) and purified by flash column chromatography (DCM/MeOH 98/2) to afford sulfoximine **4k** as an off-yellow solid (60.2 mg, 90%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 3.02-2.99 (m, 4H), 2.57 (bs, 1H, NH), 2.04-1.98 (m, 4H), 1.60-1.55 (m, 2H); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 54.3, 24.2, 24.1; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_5H_{12}NOS^+$ $[M+H]^+$ 134.0640, found 134.0641. **FT-IR (cm^{-1})**: 3258, 2929, 1441, 1221, 1186, 1117, 1079, 986, 828.

Imino(methyl)(pyridin-2-yl)-λ^6-sulfanone (4l)



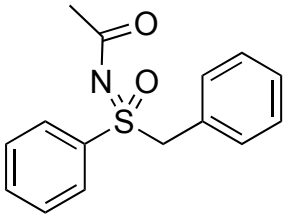
Prepared according to General Procedure **A** using 2-(methylthio)pyridine (62.6 mg, 0.5 mmol) and purified by flash column chromatography (EtOAc/Pentane 7/3) to afford sulfoximine **4l** as a yellowish oil (43.8 mg, 57%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 8.72 (d, *J* = 3.5 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.96-7.92 (m, 1H), 7.52-7.49 (m, 1H), 3.25 (s, 3H), 2.79 (bs, 1H, NH); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 160.5, 150.0, 138.3, 126.7, 121.0, 42.3; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_6H_9N_2OS^+$ $[M+H]^+$ 157.0436, found 157.0437. **FT-IR (cm^{-1})**: 3262, 1425, 1217, 1187, 989, 754.

***tert*-Butyl(Imino)(methyl)-λ^6-sulfanone (4m)**



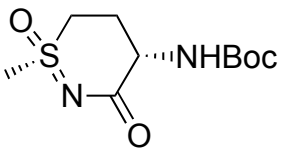
Prepared according to General Procedure **A** using *tert*-Butyl methyl sulfide (52 mg, 0.5 mmol) and purified by flash column chromatography (EtOAc/MeOH 9/1) to afford sulfoximine **4m** as a colorless solid (59 mg, 86%). **^{1}H NMR (400 MHz, $CDCl_3$, δ)**: 2.87 (s, 3H), 2.25 (bs, 1H, NH), 1.45 (s, 9H); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 60.3, 36.3, 24.0; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_5H_{13}NONaS^+$ $[M+Na]^+$ 158.0616, found 158.0615. **MP**: 124-125°C. **FT-IR(cm^{-1})**: 3297, 1189, 1083, 1026, 990, 932, 750.

N-(benzyl(oxo)(phenyl)-λ6-sulfaneylidene)acetamide (5b)



^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.64-7.58 (m, 3H), 7.46-7.402 (m, 2H), 7.31-7.26 (m, 1H), 7.22-7.18 (m, 2H), 6.95-6.93 (m, 2H), 4.81 and 4.76 (AB system, J_{AB} = 13.7 Hz, 2H, CH_2), 2.17 (s, 3H); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: 180.8, 135.4, 133.9, 131.3, 129.2, 129.1, 128.6 (2C), 127.4, 61.9, 27.1; **HRMS (ESI–QTOF)** *m/z* : calcd for $C_{15}H_{16}NO_2S^+$ $[M+H]^+$ 274.0902, found 274.0903.

Tert-Butyl(1-methyl-1-oxido-3-oxo-3,4,5,6-tetrahydro-1λ^6,2-thiazin-4-yl) carbamate (9)



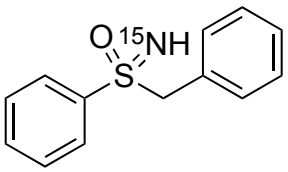
Prepared according to General Procedure **A** using N-Boc-*L*-Methionine (125 mg, 0.5 mmol). Cristallisation of the crude using slow evaporation of a dichloromethane solution afford colourless cristals of sulfoximine **9** (28 mg, 20%). **^{1}H NMR (500 MHz, $CDCl_3$, δ)**: Major diastereoisomer 5.81 (bs, 0.85H), 4.22-4.18 (m, 0.85H), 3.82-3.78 (m, 0.85H), 3.59-3.53 (m, 0.85H), 3.24 (s, 2.55H), 2.96-2.93 (m, 0.85H), 2.09-2.00 (m, 0.85H), 1.44 (s, 7.65). Minor diastereoisomer 5.30-5.26 (m, 0.15H), 4.45 (bs, 0.15H), 3.16-3.10 (m, 0.15H), 3.00 (s, 0.45H), 2.65 (m, 0.15H), 2.47-2.40 (m, 0.15H), 2.22-2.13 (m, 0.15H), 1.44 (s, 1.35); **^{13}C NMR (101 MHz, $CDCl_3$, δ)**: Major diastereoisomer 172.4, 155.8, 80.4, 52.9, 50.6, 43.8, 28.4, 26.9. Minor diastereoisomer 172.0, 155.6, 80.7, 53.4, 50.1, 43.3, 28.4, 26.6; **HRMS (ESI–QTOF)** *m/z*: calcd for $C_{10}H_{18}N_2O_4SNa^+$ $[M+Na]^+$ 285.0885, found 285.0886.

PREPARATION OF ^{15}N-LABELLED SULFOXIMINES

General procedure B for the preparation of ^{15}N-labeled Sulfoximines

To a flask containing a stirrer bar was added successively, sulfide (1 equiv.), ^{15}N-ammonium acetate (2 equiv.) and then MeOH (0.5 M). PIDA (2.1 equiv.) was added in one portion and the reaction was stirred at 20 °C for 3 hours (open flask to the atmosphere). The solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica gel.

^{15}N-labeled Benzyl(imino)(phenyl)-λ^6-sulfanone (^{15}N-4b)



Prepared according to General Procedure **B** using phenyl benzyl sulfide (100 mg, 0.5 mmol) and purified by flash column chromatography (EtOAc/Pentane 1/1) to afford sulfoximine **^{15}N-4b** as a white solid (74 mg, 32%). **^{1}H NMR (500 MHz, CD_3OD, δ):** 7.73-7.71 (m, 2H), 7.68-7.65 (m, 1H), 7.52-7.49 (m, 2H), 7.33-7.30 (m, 1H), 7.25-7.22 (m, 2H), 7.08-7.07 (m, 1H), 4.55 and 4.53 (AB system, J_{AB} = 13.7 Hz, 2H, CH_2); **^{13}C NMR (125 MHz, CD_3OD, δ):** 138.8 (d, $^2J_{C\text{-}N}$ = 2.9 Hz), 133.3, 130.9, 129.2, 128.9, 128.7, 128.4, 128.0, 63.46 (d, $^2J_{C\text{-}N}$ = 3.7 Hz); **^{15}N NMR (50.7 MHz, CD_3OD, δ):** 83.9 (s, ^{15}NH); **HRMS (ESI–QTOF)** *m/z*: calcd for $C_{13}H_{14}{}^{15}NOS^+$ $[M+H]^+$ 232.0766 , found 233.0768.

^{1}H NMR SPECTRA FOR MECHANISTIC INVESTIGATION

In this paragraph, NMR results that allowed the identification of intermediates **7b** and **8b** will be discussed.

Initially, intermediates **CD_3-7b** and **8b** were observed in ^{1}H NMR at 5°C after 5 min of reaction in CD_3OD using ammonium carbamate (Figure 1 – bottom). Indeed, new AX and AB systems were observed in addition to the AB system of sulfoximine **4b**. Nevertheless, attributing those signals with their respective structure was complicated but it was postulated that intermediate **CD_3-7b** was predominant due to large presence of CD_3OD in NMR tube. This hypothesis was comforted by the fact that when using ammonium-^{15}N acetate as ammonia source, the second AB system was then predominant (Figure 1 – top). It showed that this signal was very sensible to the amount of free-acetate in the tube. Therefore, it was postulated that the AX system corresponded to intermediate **CD_3-7b** and the AB system to intermediate **8b**.

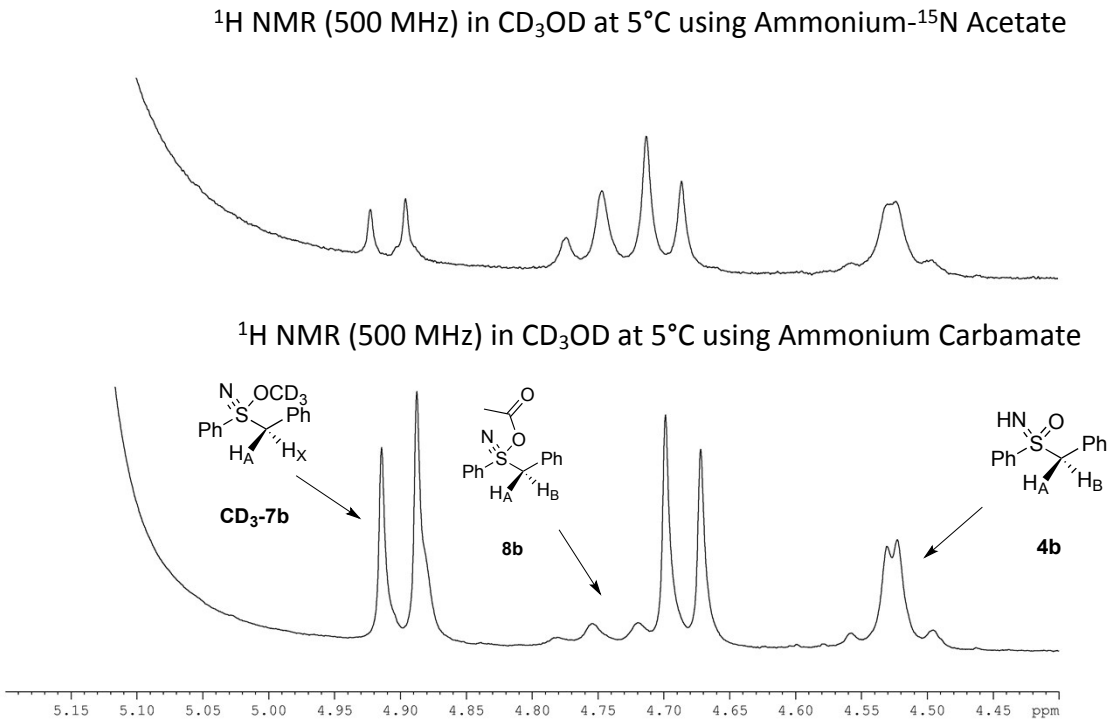


Figure 1 - ^{1}H NMR (500 MHz, CD_3OD) spectrum at 5°C after 5 min depending on ammonia source

To confirm this hypothesis, several ^{1}H, ^{15}N and ^{13}C NMR experiments were conducted at 5°C. However, those intermediates were only visible in ^{1}H NMR because of their short lifetime (< 10 min). Therefore, ^{1}H, ^{15}N and ^{13}C NMR experiments were conducted at –30 °C on the crude reaction in order to identify and characterize the chemical species involved (intermediates stable over 6 h at this temperature).

According to General Procedure **B** with extra one equiv. ammonium carbamate and after 2 minutes of reaction, a NMR tube was prepared and cooled in a nitrogen bath and then NMR experiments started. Beside formation of sulfoximine **^{15}N-4b**, the previous intermediates were clearly observed, notably in the benzylic area:

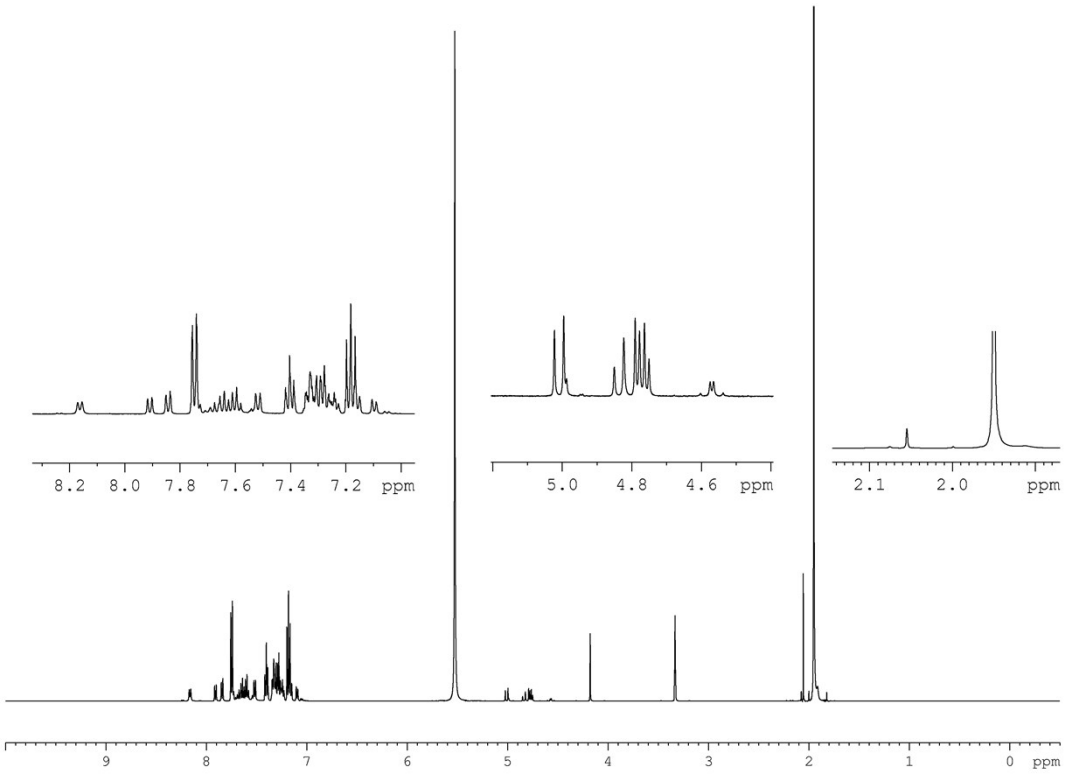


Figure 2 - ^{1}H NMR (500 MHz, CD_3OD) at –30 °C after 2 min (full spectrum)

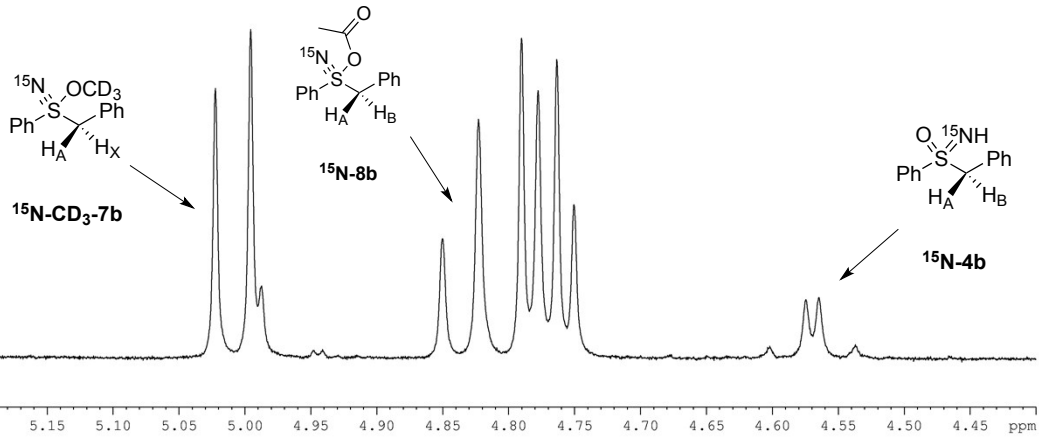
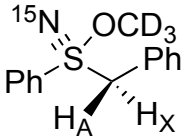
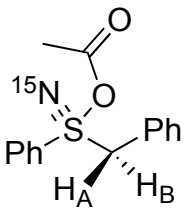


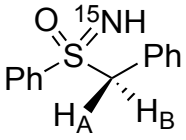
Figure 3 - ^{1}H NMR (500 MHz, CD_3OD) at –30 °C after 2 min (enlargement of the benzylic positions)



^{15}N-CD$_3$-7b 5.00 and 4.78 ppm (AX system, d, *J*= 13.4 Hz, 2H)



^{15}N-8b 4.83 and 4.77 ppm (AB system, J_{AB} = 13.7 Hz, 2H)



^{15}N-4b 4.58 and 4.56 ppm (AB system, J_{AB} = 13.8 Hz, 2H)

*Figure 4: Description of AX and AB systems of **^{15}N-CD$_3$-7b**, **^{15}N-8b** and **^{15}N-4b** in Methanol-d$_4$*

Species **^{15}N-CD$_3$-7b** and **^{15}N-8b** were also characterized by ^{15}N and ^{13}C NMR experiments at –30 °C (Figure 5 and Figure 7). Figure 6 displays the ^{15}N NMR spectrum of isolated sulfoximine **^{15}N-4b**.

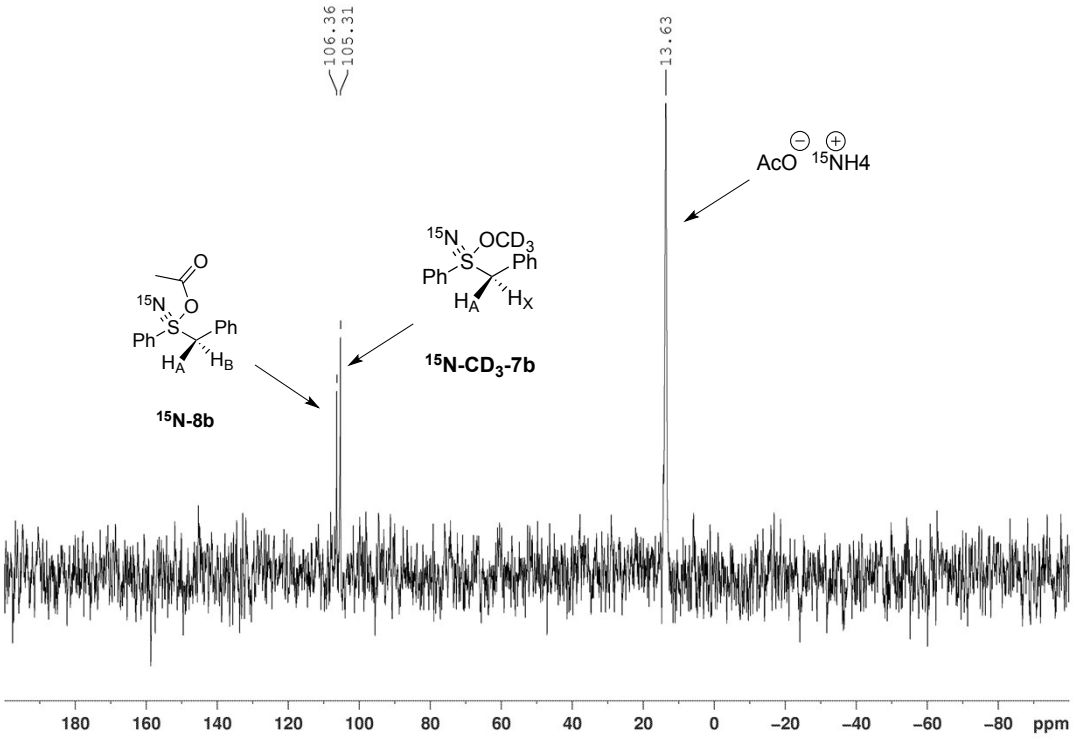


Figure 5 - ^{15}N NMR (50.7 MHz, CD$_3$OD) at –30 °C

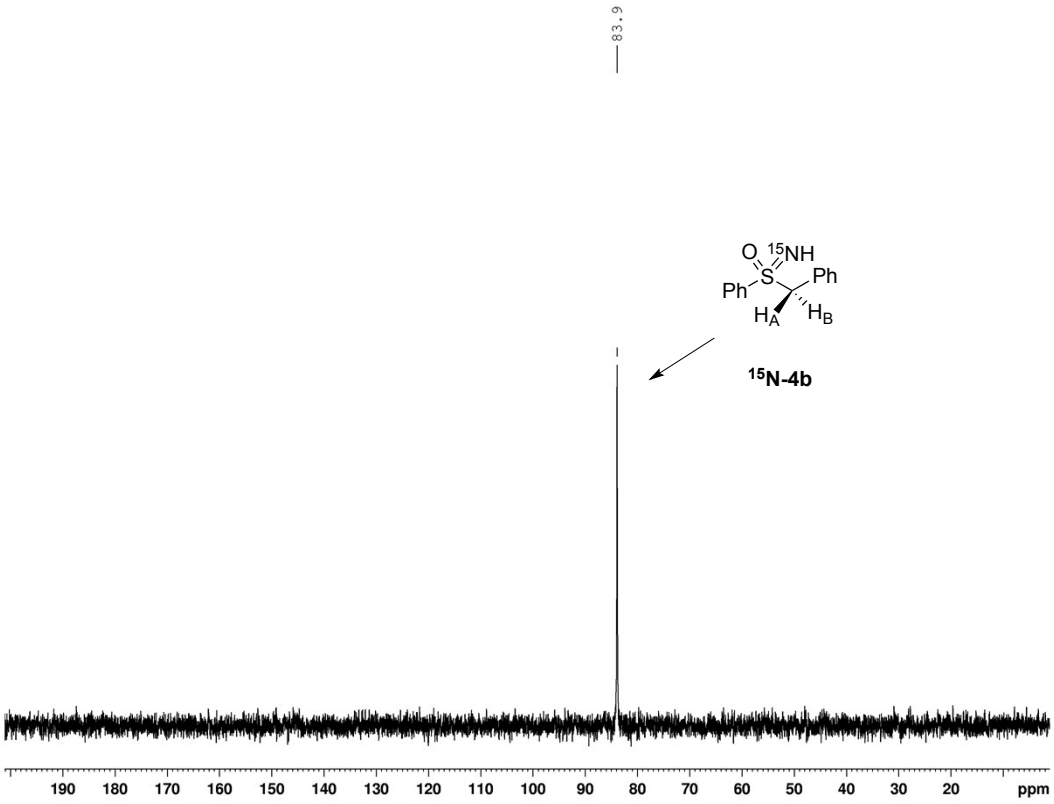


*Figure 6 - ^{15}N NMR (50.7 MHz, CD_3OD) of sulfoximine **^{15}N-4b** at room temperature*

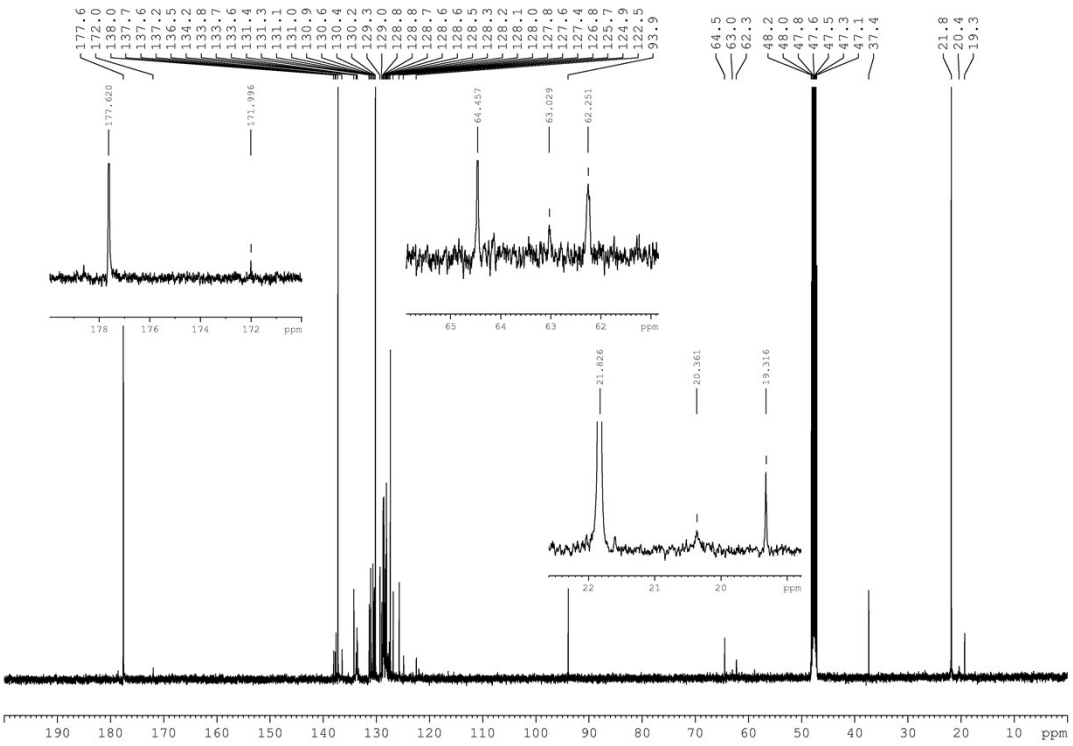


Figure 7 - ^{13}C NMR (125 MHz, CD_3OD) at –30 °C

As expected, beside the ^{15}N ammonium acetate (**δ** = 13.6 ppm) and sulfoximine **^{15}N-4b** (δ = 83.9 ppm, not seen due to low concentration), two signals were observed in ^{15}N NMR at 106.4 and 105.3 ppm corresponding to intermediates **^{15}N-CD$_3$-7b** and **^{15}N-8b**. ^{13}C NMR experiment of the crude showed the presence of two signals close to the CH_2 of sulfoximine **^{15}N-4b** (δ = 63.0 ppm) at 64.5 and 62.3 ppm. Moreover, new OAc signals (δ = 172.0 and 19.3 ppm) were observed closed to the strong signals dispatched by PIDA (δ = 177.6 and 21.8 ppm).

Furthermore, thanks to HSQC experiments (Figure 7 and Figure 8), we were able to assign each CH_2 signals to their corresponding ^{15}N and ^{13}C shifts. Thus, the ^{15}N chemical shifts for **^{15}N-CD$_3$-7b** and **^{15}N-8b** are 105.3 and 106.4 ppm respectively and ^{13}C chemical shifts for **^{15}N-CD$_3$-7b** and **^{15}N-8b** are 64.5 and 62.3 ppm respectively.

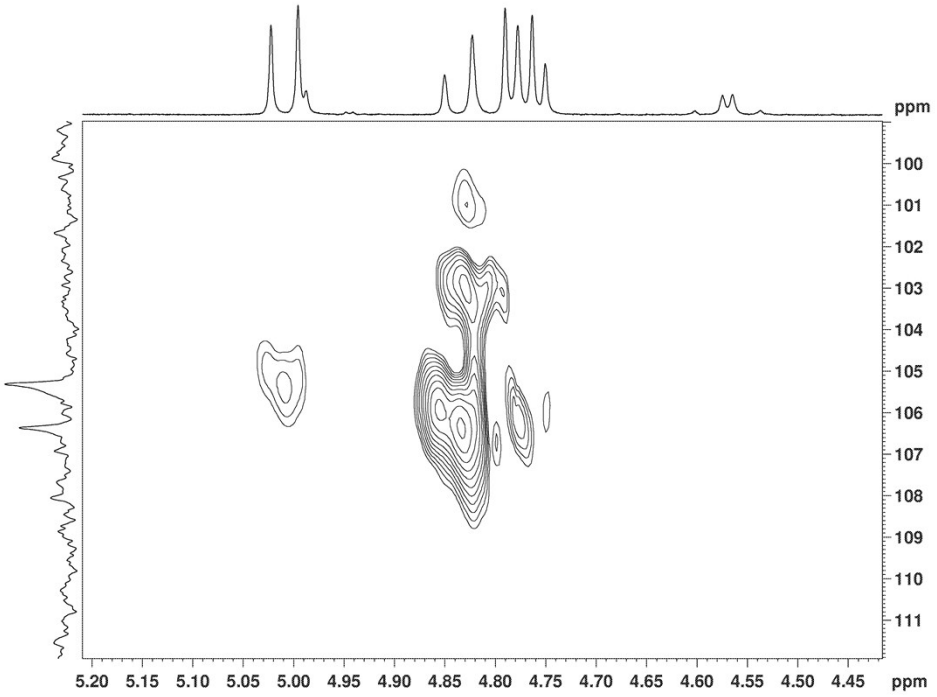


Figure 8 - HSQC (^{1}H NMR - ^{15}N NMR, CD$_3$OD) at –30 °C

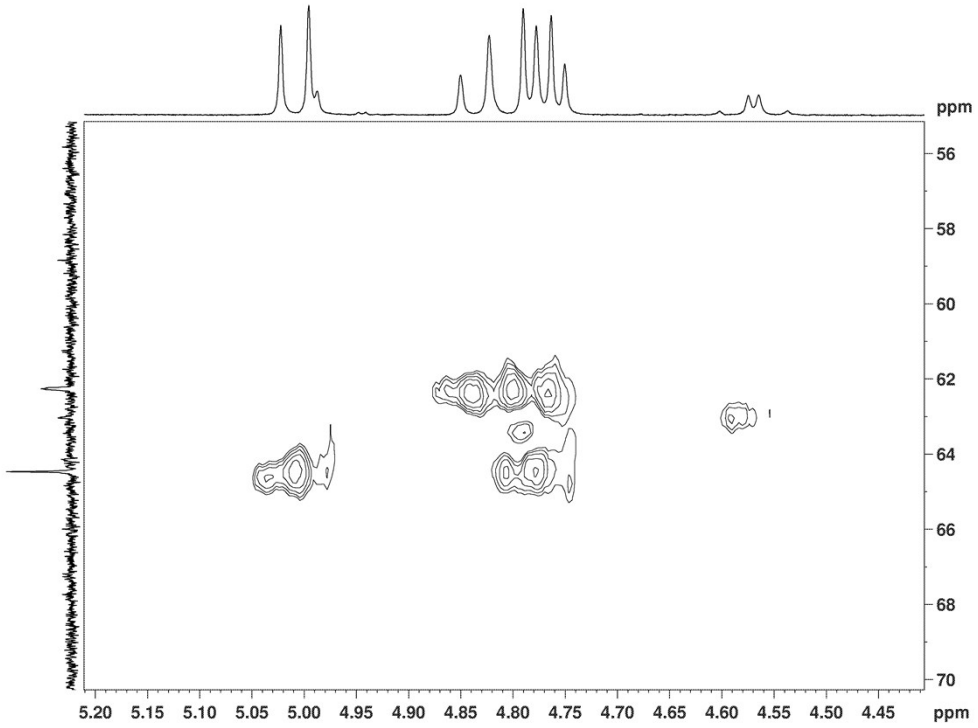


Figure 9 - HSQC (^{1}H NMR - ^{13}C NMR, CD_3OD) at –30 °C

Finally, evidence of acetate within the crude was demonstrated with a HMBC experiment (Figure 10). This acetate originates from intermediate **^{15}N-8b**.

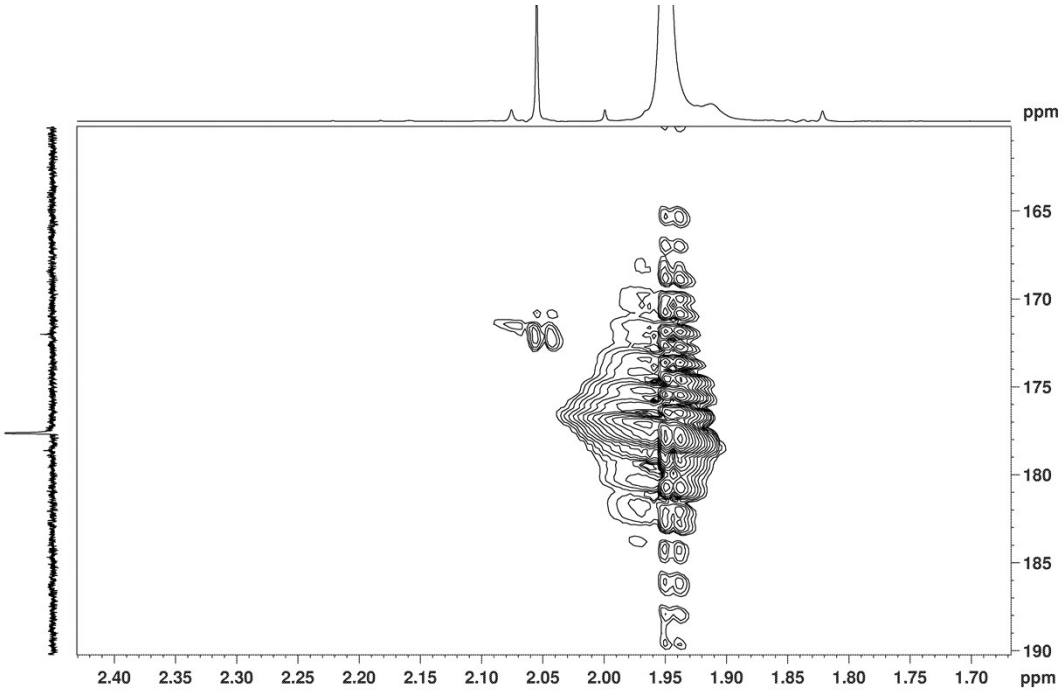


Figure 10 - HMBC (^{1}H NMR - ^{13}C NMR, CD_3OD) at –30 °C

	^{1}H NMR (δ, ppm)	^{13}C NMR (δ, ppm)	^{15}N NMR (δ, ppm)
^{15}N-CD$_3$-7b	5.00 and 4.78 (AX system, d, *J*= 13.4 Hz, 2H)	64.5 (CH_2)	105.3
^{15}N-8b	4.83 and 4.77 (AB system, J_{AB} = 13.7 Hz, 2H)	172.0 (CO) 62.3 (CH_2) 19.3 (CH_3)	106.4
^{15}N-4b	4.58 and 4.56 (AB system, J_{AB} = 13.8 Hz, 2H)	63.0 (CH_2)	83.9

*Figure 11 – Description of **^{15}N-CD$_3$-7b**, **^{15}N-8b** and **^{15}N-4b** in Methanol-d4 at -30 °C*

In addition to these observations, the formation of CD_3-methyl acetate was also observed but the residual CH_3 of the OCD_3 was not seen (Figure 12).

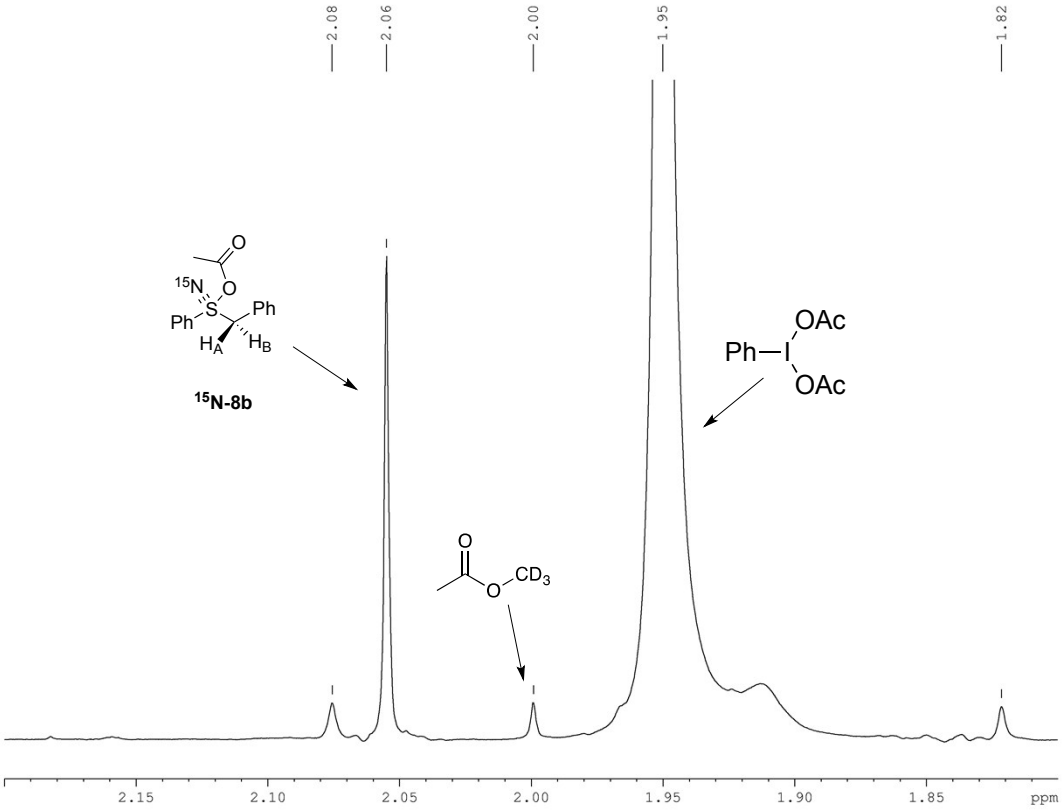


Figure 12 – Evidence of CD_3-methyl acetate formation

The formation of **6**, resulting from a PIDA-MeOH exchange was also observed in ^{1}H NMR when the reaction was performed at room temperature in Methanol-d4 (Figure 13).

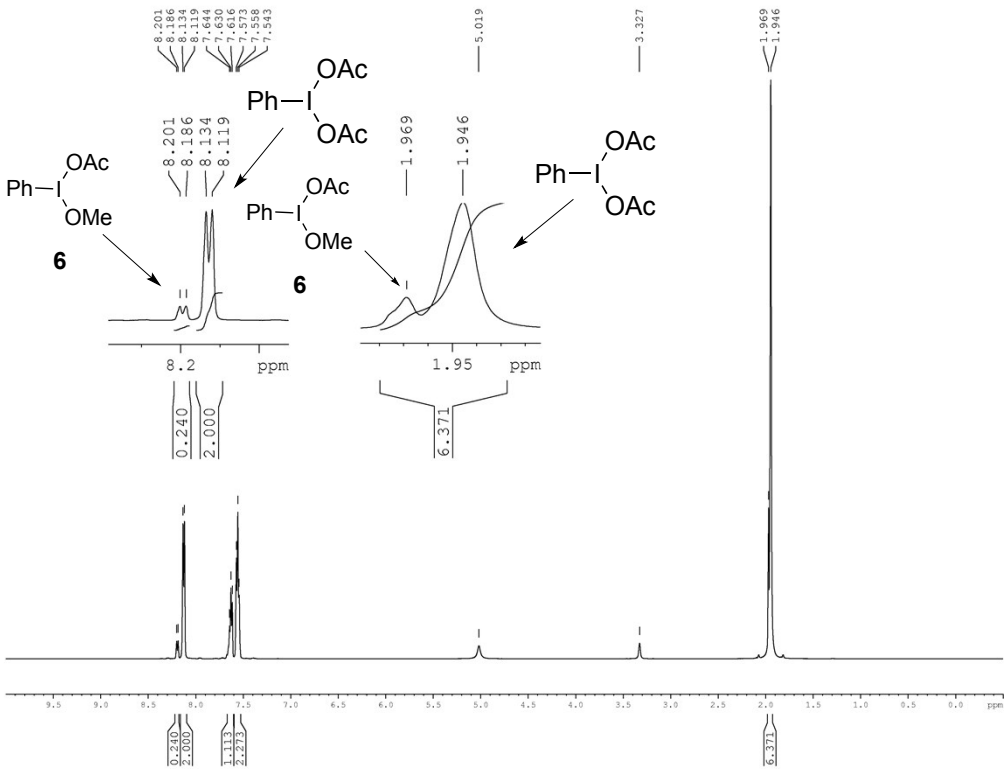


Figure 13 – Evidence for a PIDA-MeOH exchange (^{1}H NMR, 500 MHz, CD_3OD, 20 °C)

Moreover, when performed in Acetonitrile-d3 in presence of ethanol, the formation of ethyl acetate was observed in ^{1}H NMR during the reaction (Figure 14).

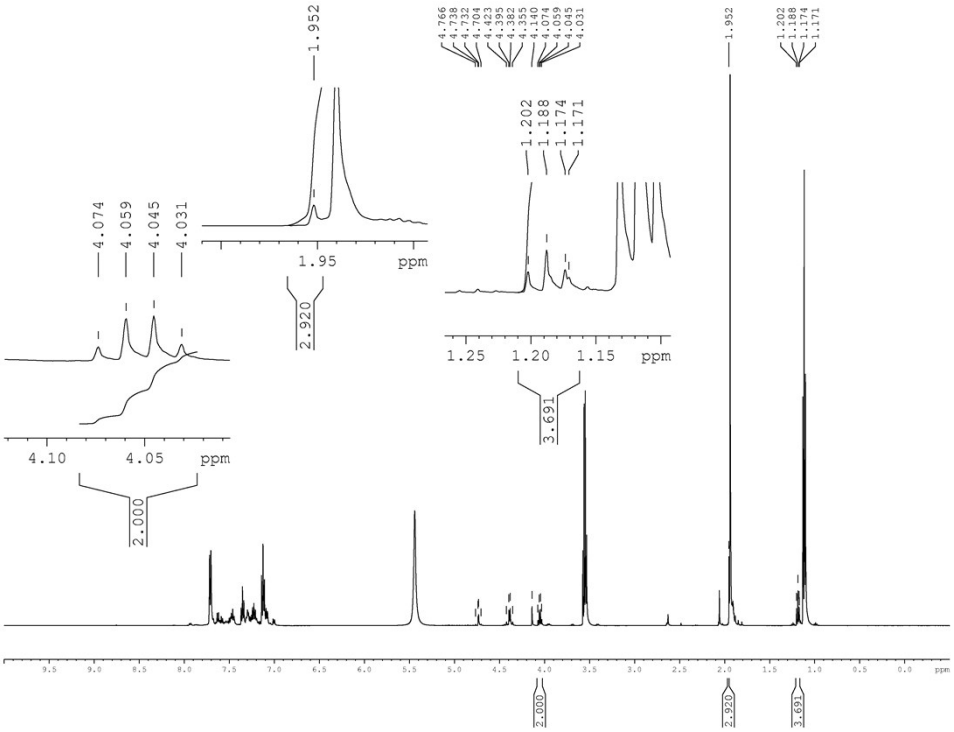
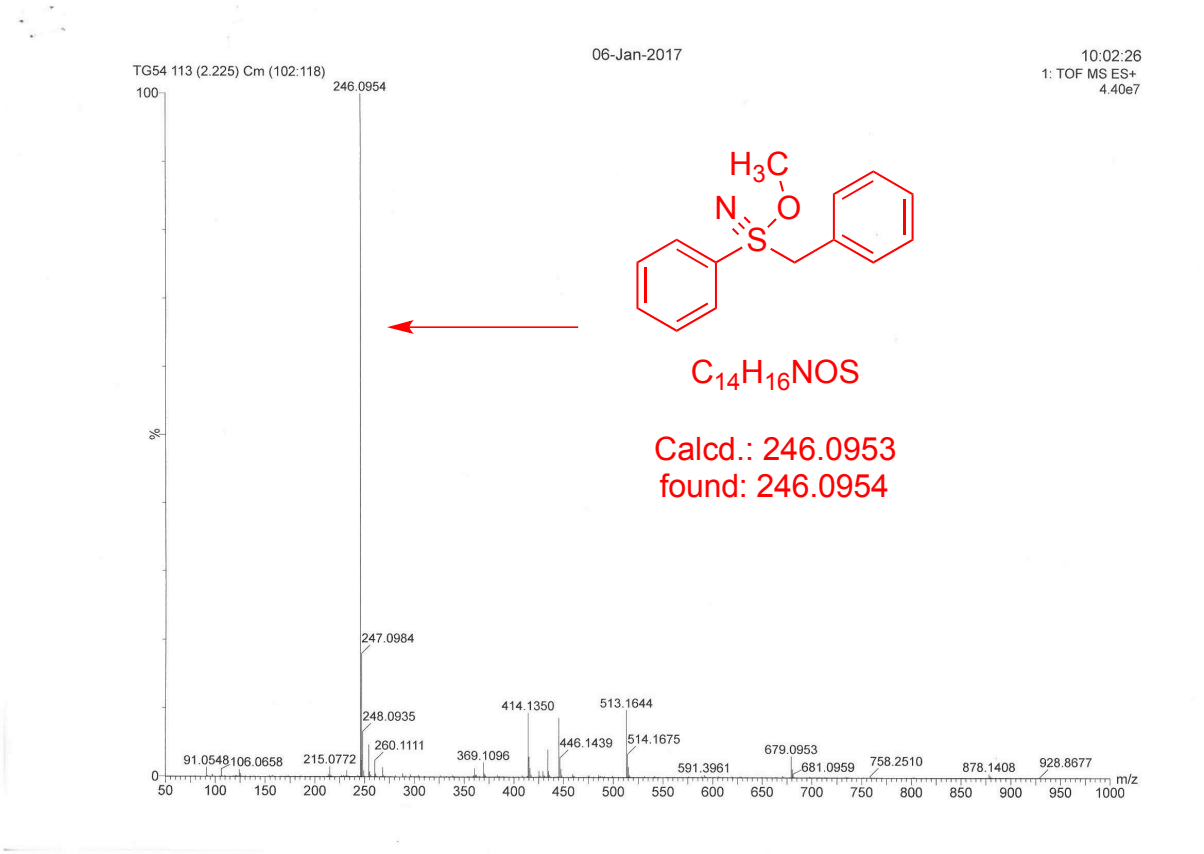


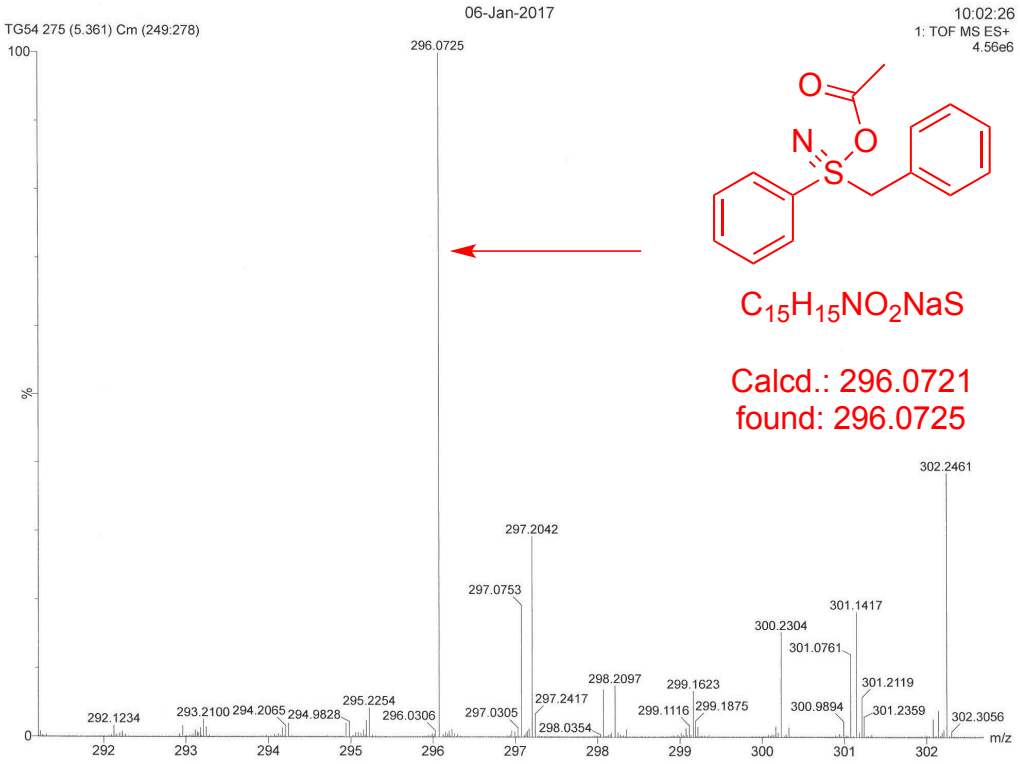
Figure 14 – Evidence for ethyl acetate formation (^{1}H NMR, 500 MHz, CD_3CN + EtOH, 20 °C)

HRMS SPECTRA FOR MECHANISTIC INVESTIGATION

In this paragraph, we detail the three HRMS experiment that we have conducted in order to confirm the structure of our proposed intermediates **7b** and **8b**.

The first experiment was achieved according to General Procedure **A** using phenyl benzyl sulfide (100.2 mg, 0.5 mmol). One minute after the addition of PIDA into the flask, a drop of the reaction mixture was collected in order to prepare the HRMS sample. This drop was diluted into 1 mL of analytical grade Methanol and was filtered through a 0.2 µm syringe filter. Then, 0.2 µL of this solution were diluted into 1 mL of analytical grade Methanol. This sample was then directly injected into the Xevo G2-XS QTof WATERS mass spectrometer equipped with an electrospray ion source (ESI) operated in positive ion mode (infusion). This experiment revealed that intermediates **7b** and **8b** are present in solution as well as sulfoximine **4b**.




06-Jan-2017
10:02:26
TG54 275 (5.361) Cm (249:278)
1: TOF MS ES+
4.56e6
296.0725
297.2042
297.0753
302.2461
301.1417
300.2304
301.0761
298.2097
299.1623
301.2119
297.2417
299.1116
299.1875
300.9894
301.2359
292.1234
293.2100
294.2065
294.9828
295.2254
296.0306
297.0305
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%
m/z
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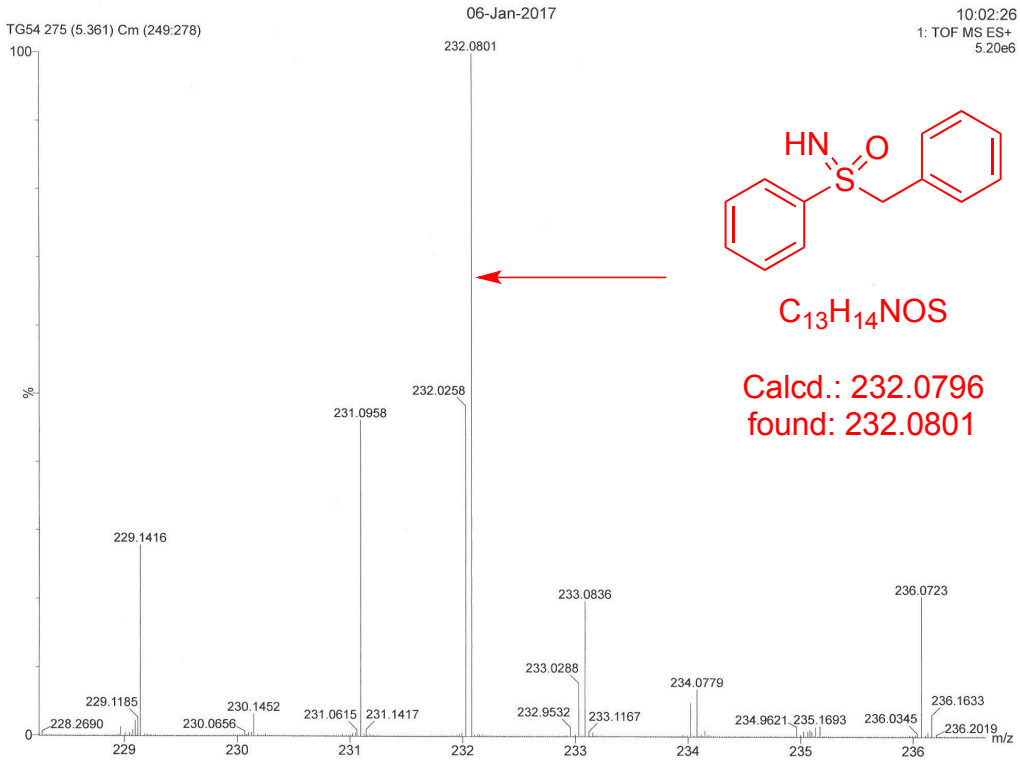
N
O
S
C15H15NO2NaS
Calcd.: 296.0721
found: 296.0725


06-Jan-2017
10:02:26
TG54 275 (5.361) Cm (249:278)
1: TOF MS ES+
5.20e6
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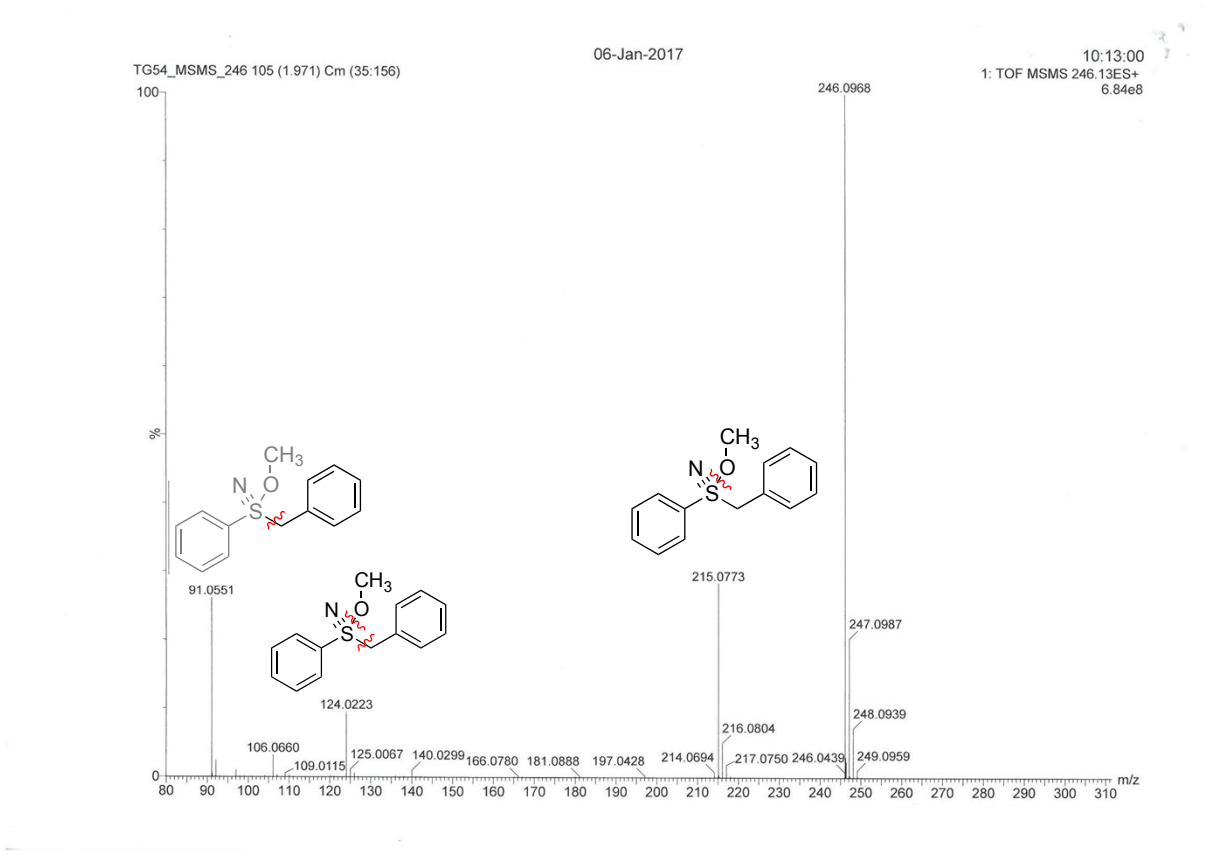
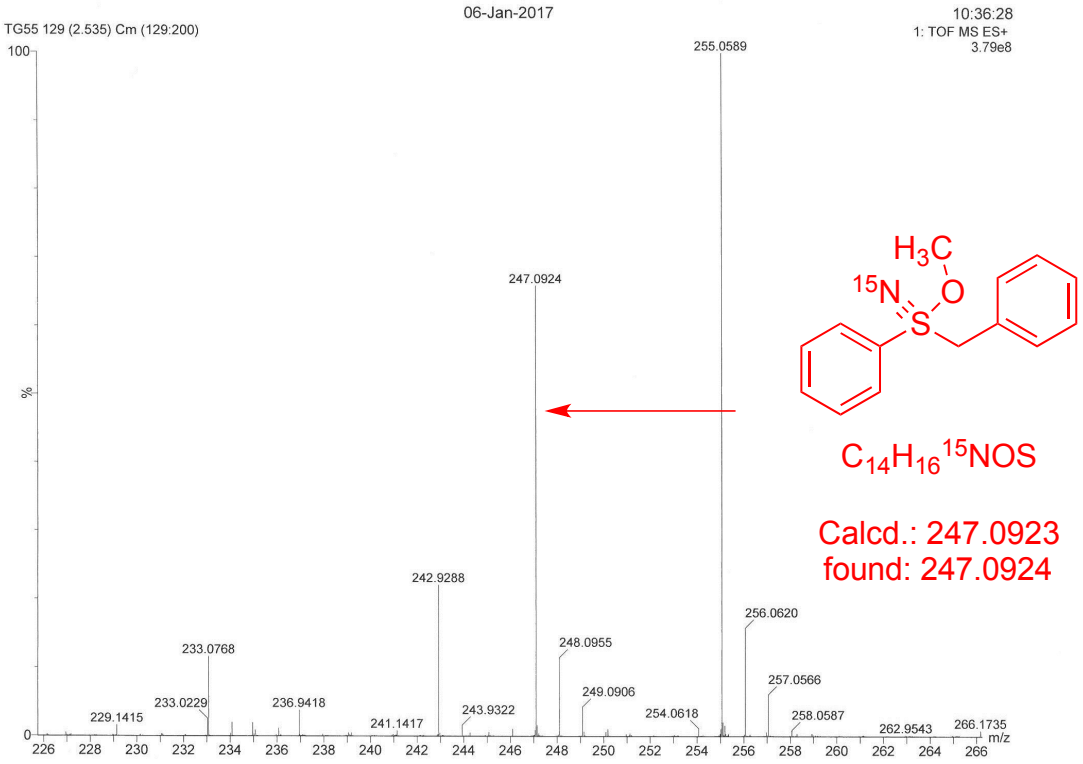
232.0258
231.0958
229.1416
233.0836
236.0723
233.0288
234.0779
236.1633
229.1185
230.1452
232.9532
233.1167
231.0615
231.1417
234.9621
235.1693
236.0345
236.2019
228.2690
230.0656
%
m/z
HN
O
S
C13H14NOS
Calcd.: 232.0796
found: 232.0801

Intermediate **7b** (m/z= 246) was confirmed and characterised by MS/MS experiment (spectrum below).



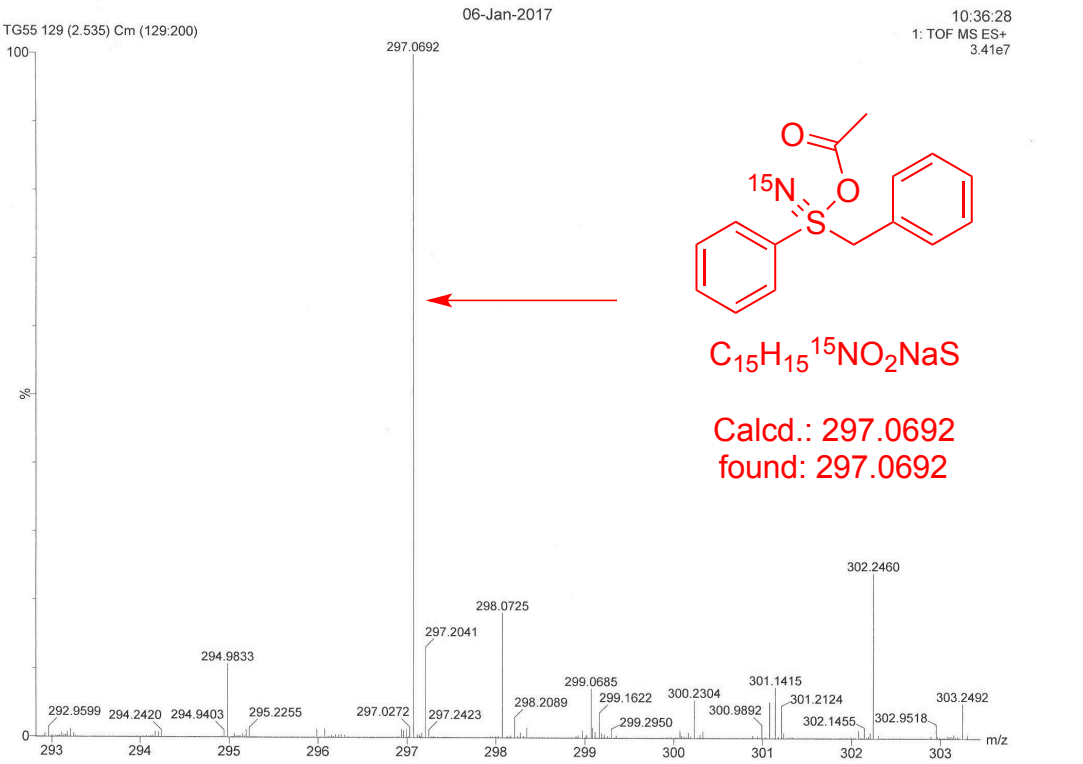
Unfortunately, due to presence of other peaks in the fragmentation window for intermediate **8b** (m/z= 296) and sulfoximine **4b** (m/z= 232), it was not possible to carry out MS/MS experiment on these two compounds.

The second experiment was conducted according to General Procedure **B** using phenyl benzyl sulfide (100.2 mg, 0.5 mmol). One minute after addition of PIDA into the flask, a drop of the reaction mixture was collected in order to prepare the HRMS sample. This sample was then directly injected into the mass spectrometer (infusion). This experiment confirmed the identification of the compounds observed during the first experiment: all the m/z were shifted from one unit due to the ^{15}N labelling.



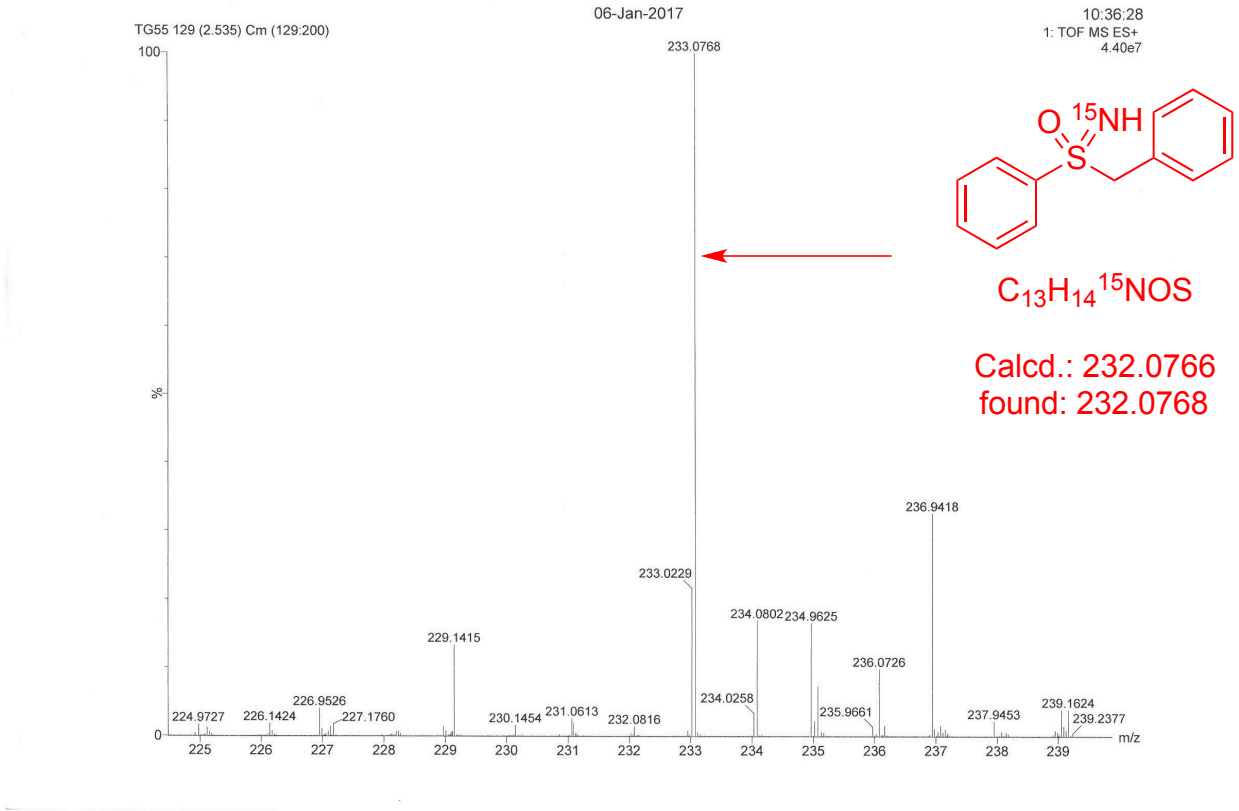
$C_{14}H_{16}{}^{15}NOS$

Calcd.: 247.0923
found: 247.0924

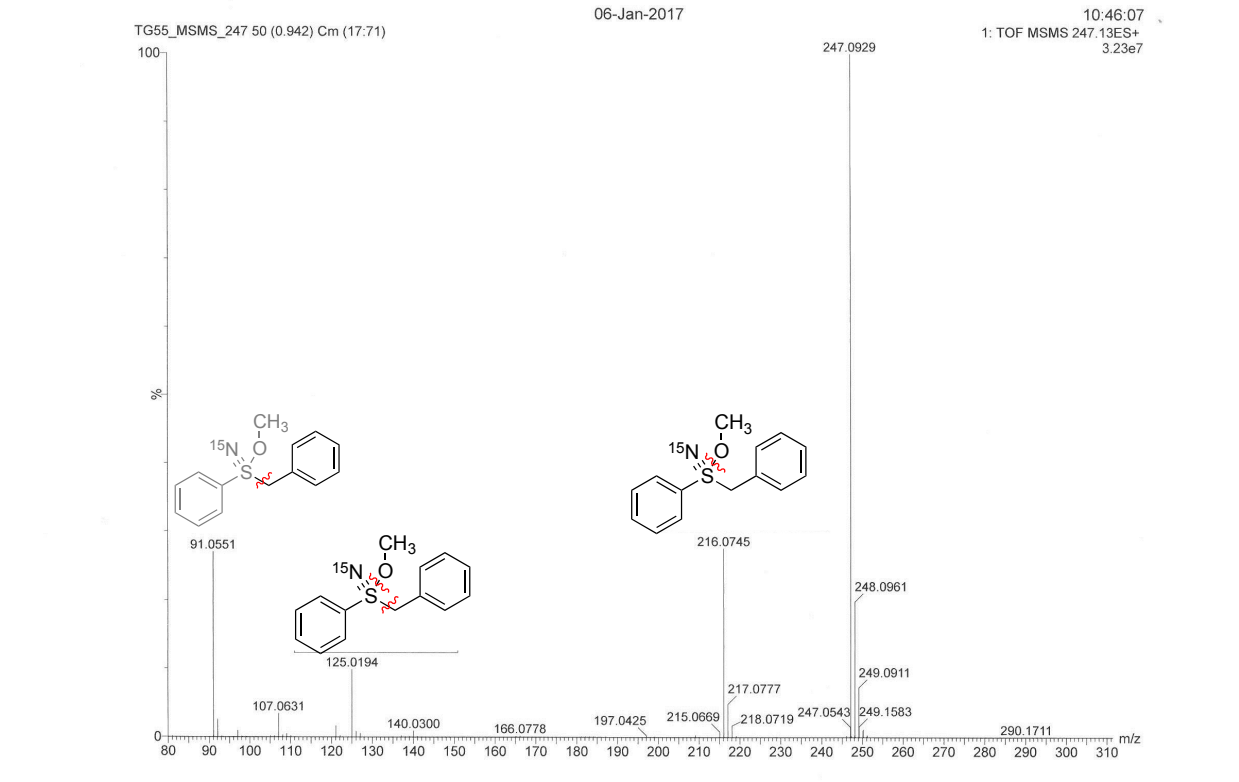


$C_{15}H_{15}{}^{15}NO_2NaS$

Calcd.: 297.0692
found: 297.0692

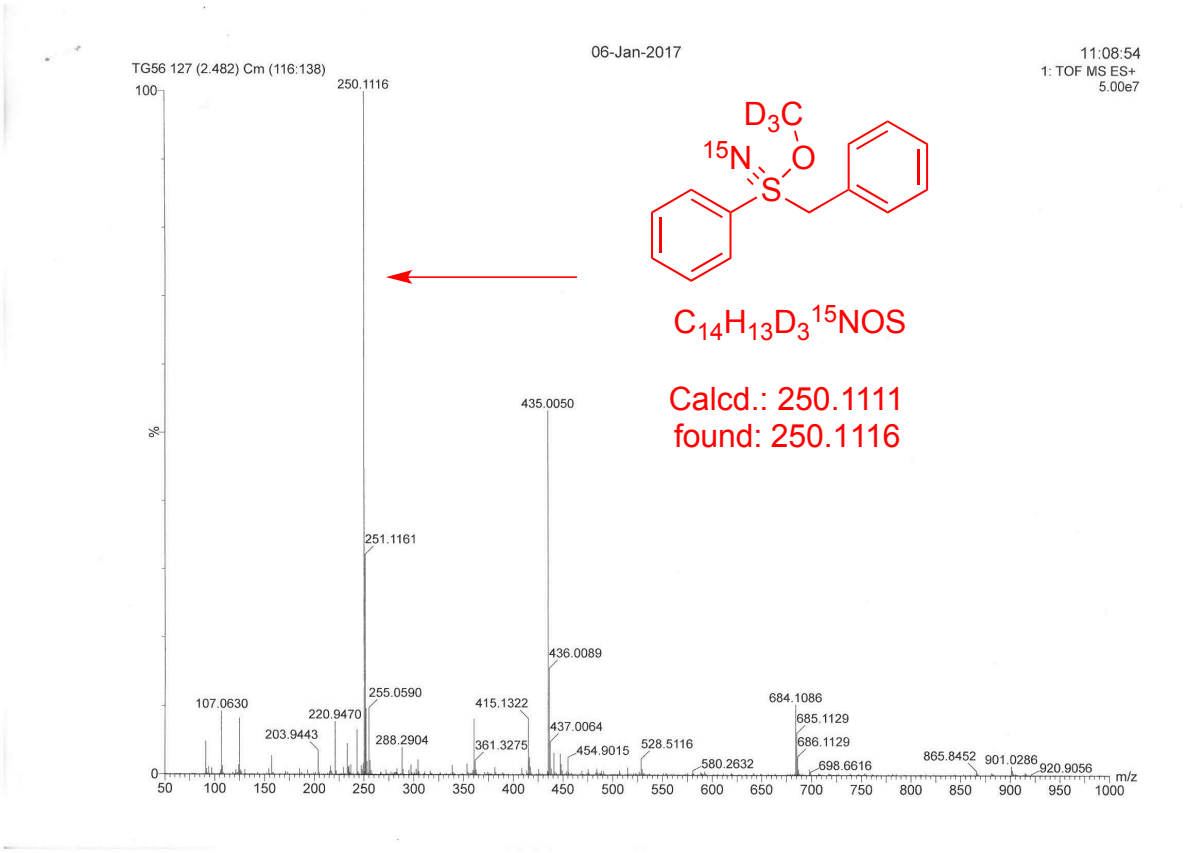


MS/MS spectrum of intermediate **^{15}N-7b** (m/z= 247) was also obtained.

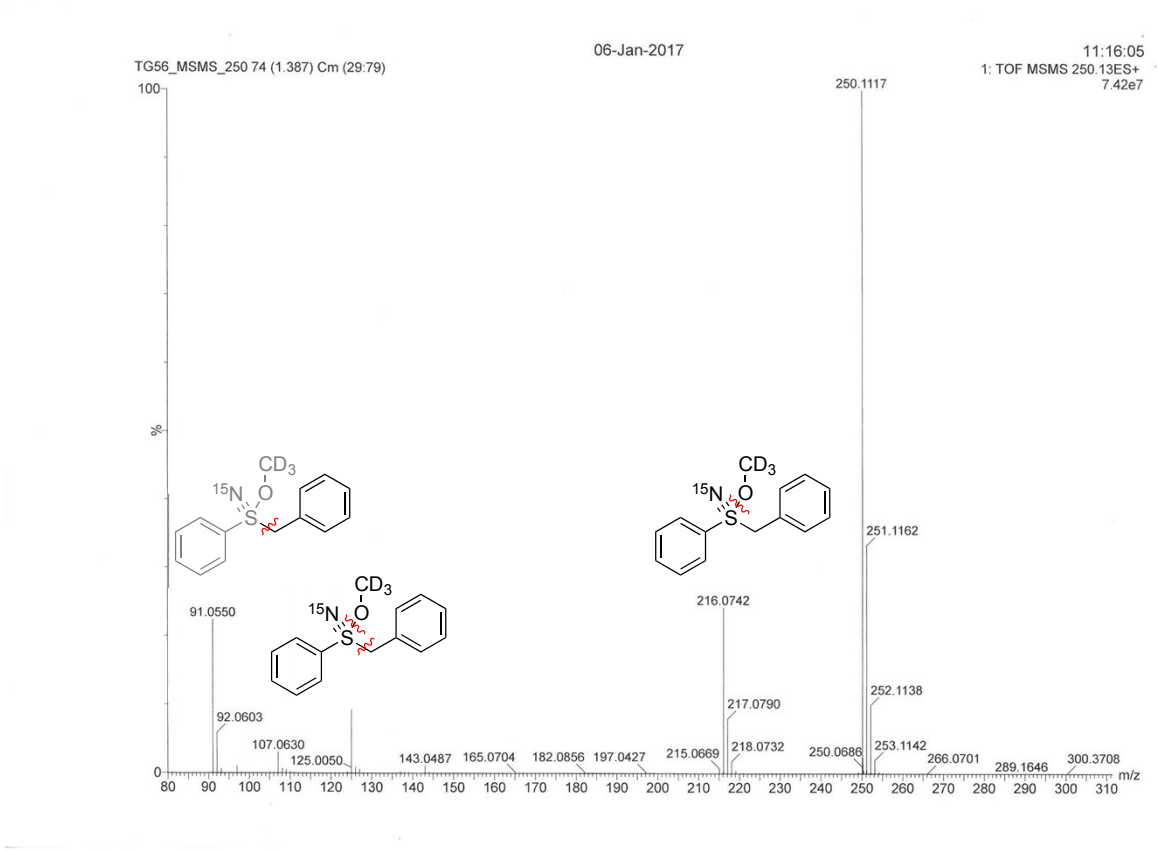


Presence of other peaks in the fragmentation window for intermediate **^{15}N-8b** (m/z= 297) and sulfoximine **^{15}N-4b** (m/z= 233), did not allow us to conduct MS/MS experiment with those compounds.

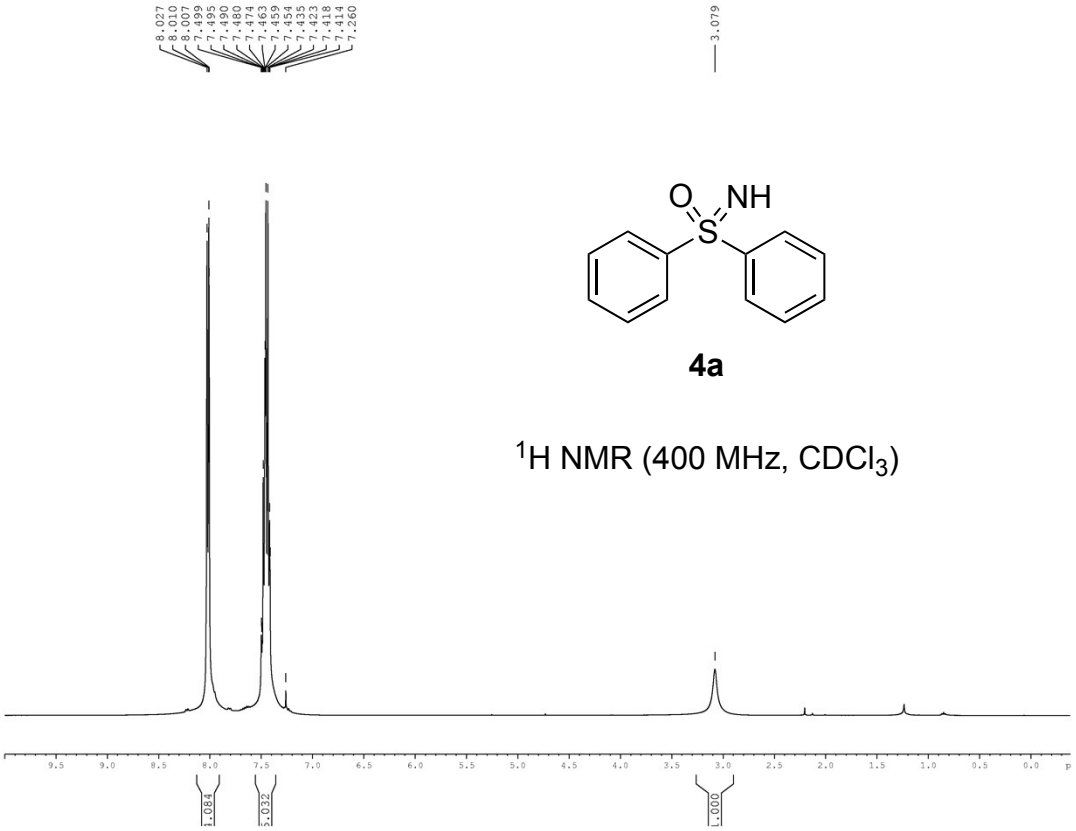
Finally, a third experiment was conducted according to General Procedure **B** using phenyl benzyl sulfide (100.2 mg, 0.5 mmol) in methanol-d^4. One minute after addition of PIDA into the flask, a drop the reaction mixture was collected in order to prepare the HRMS sample. This sample was then directly injected into the mass spectrometer (infusion). This experiment confirmed the nature of intermediate **7b** with a shift of 3 units as expected.



MS/MS experiment (spectrum below) of intermediate **^{15}N-CD$_3$-7b** (m/z= 250).

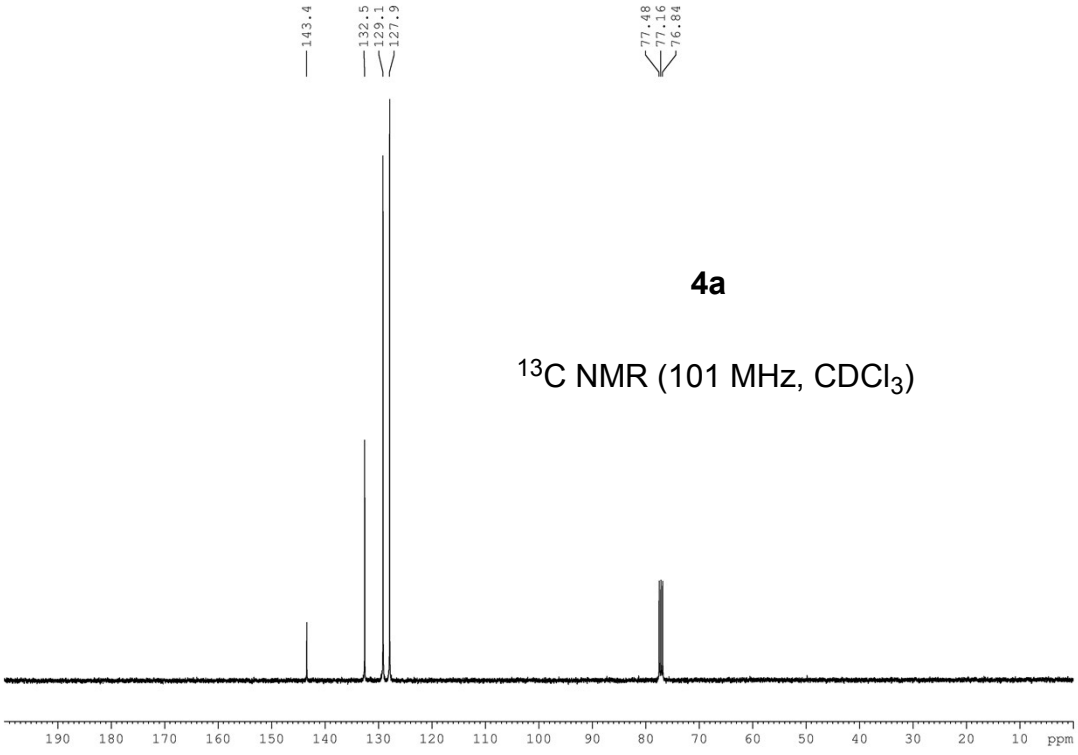


^{1}H AND ^{13}C NMR SPECTRA FOR SULFOXIMINES



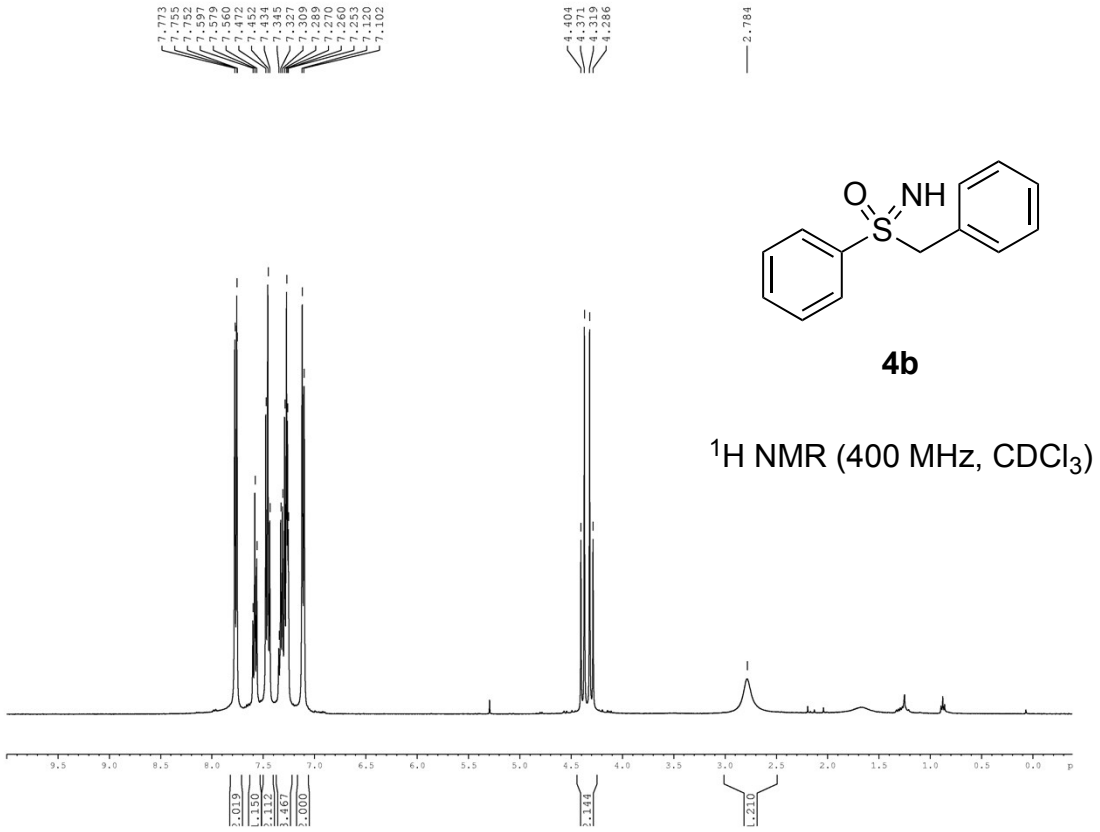
4a

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



4a

^{13}C NMR (101 MHz, $CDCl_3$)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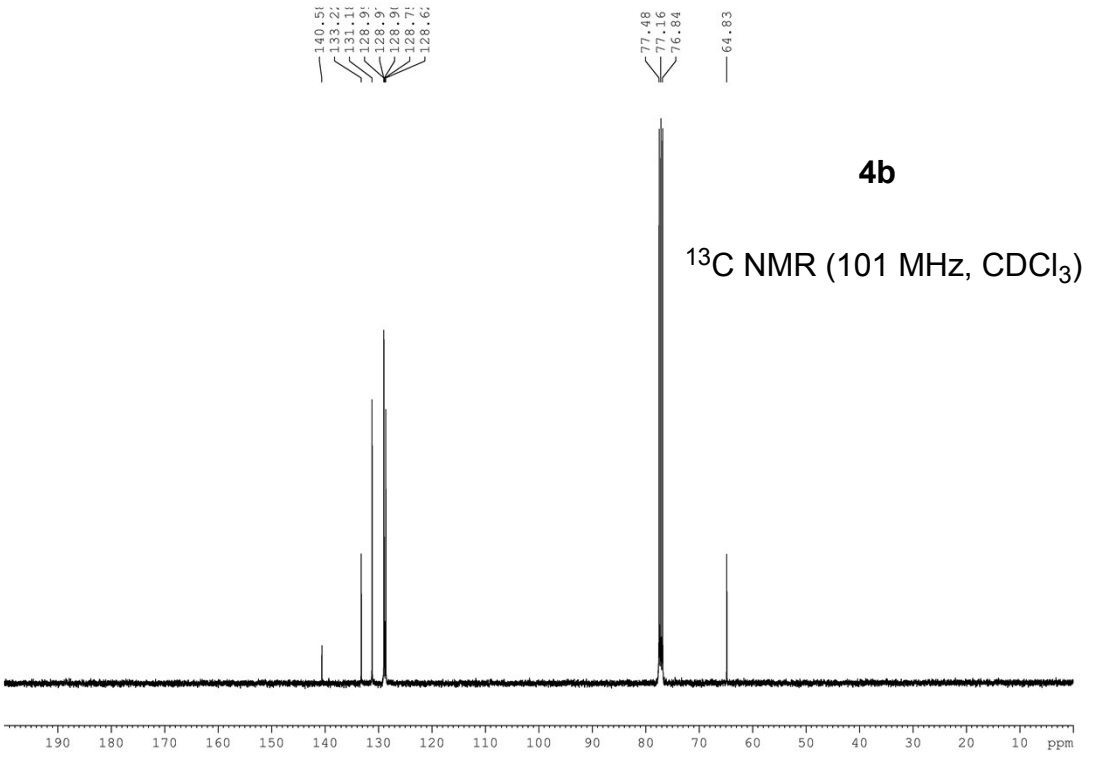
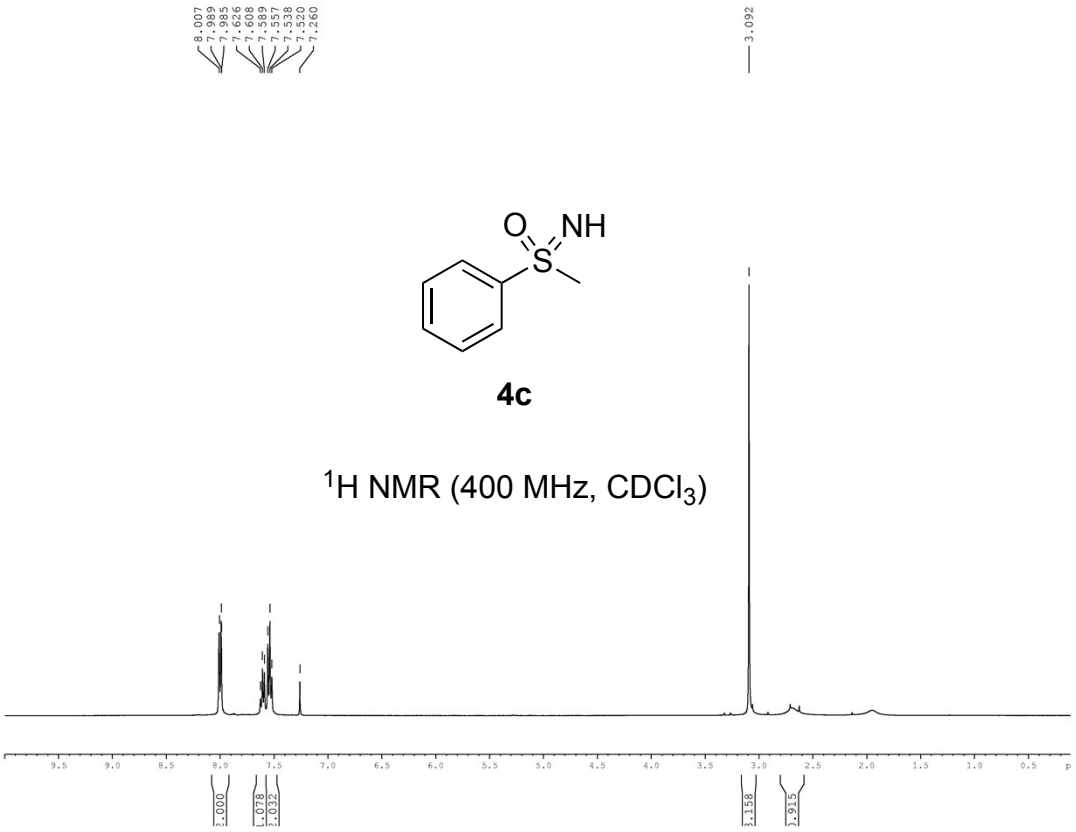
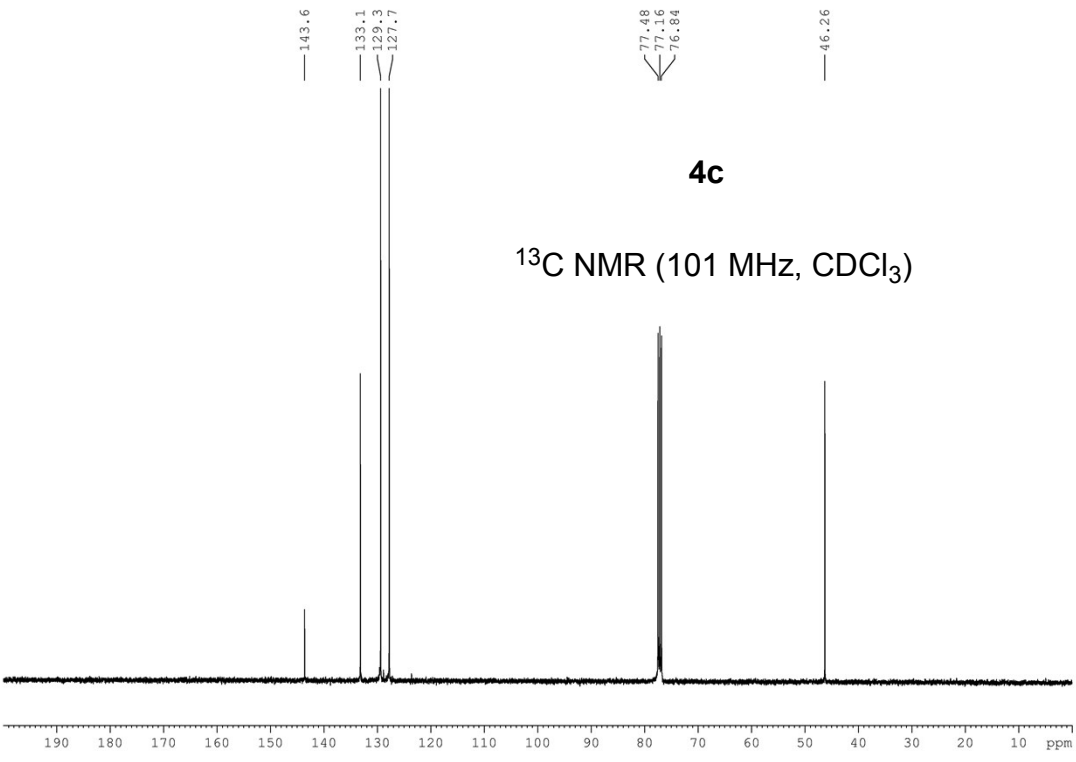
7.755
7.752
7.597
7.579
7.560
7.472
7.452
7.434
7.345
7.327
7.309
7.289
7.270
7.260
7.253
7.120
7.102
4.404
4.371
4.319
4.286
2.784
O
NH
S
4b
1H NMR (400 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 p
2.019
1.150
1.112
3.467
2.000
2.144
3.210


140.5
133.2
131.1
128.9
128.9
128.9
128.7
128.6
77.48
77.16
76.84
64.83
4b
13C NMR (101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



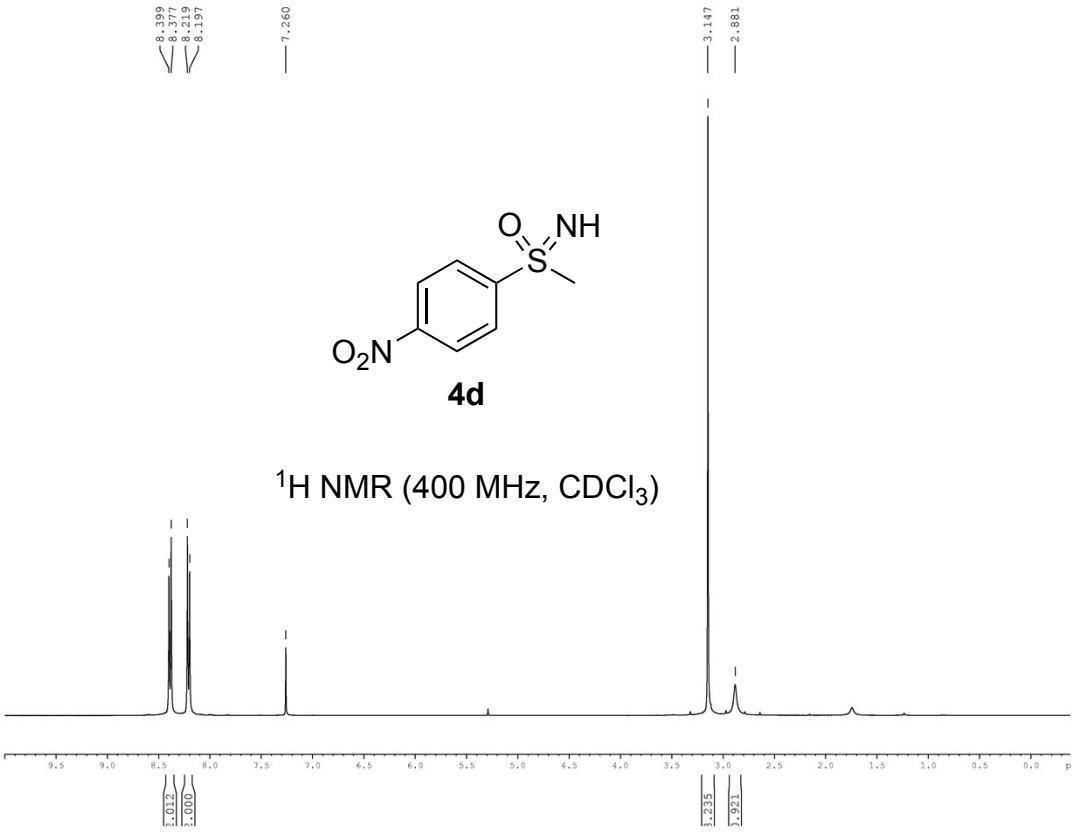
4c

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



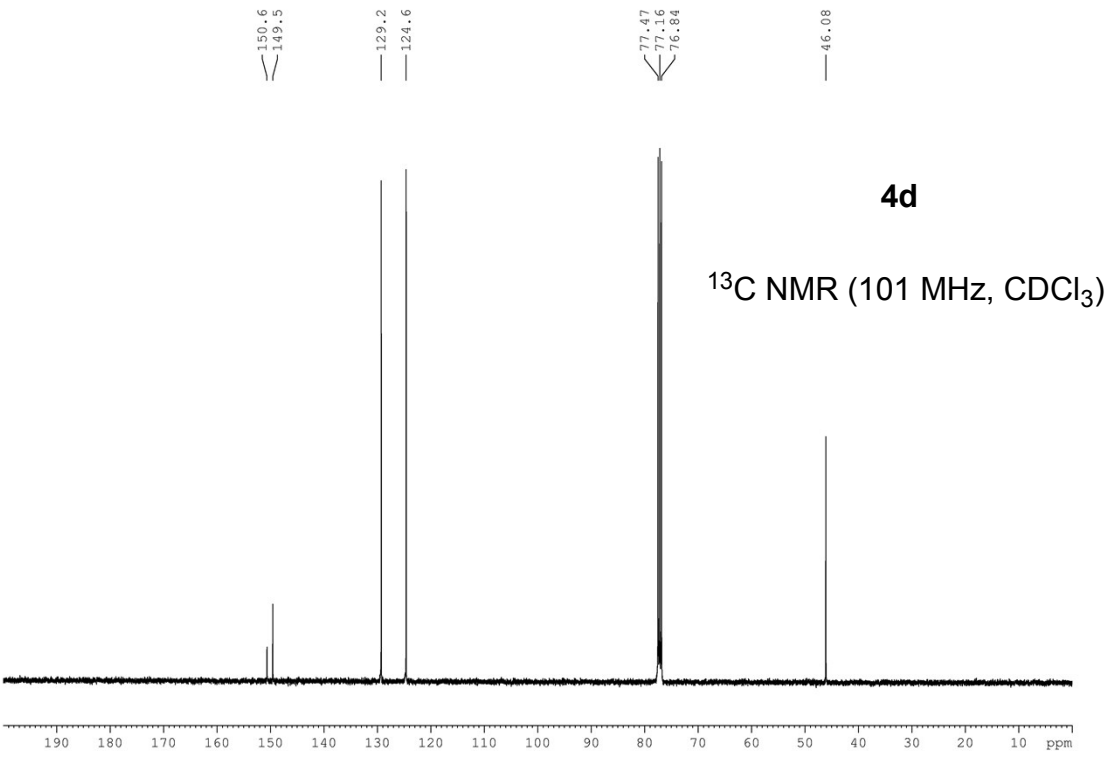
4c

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



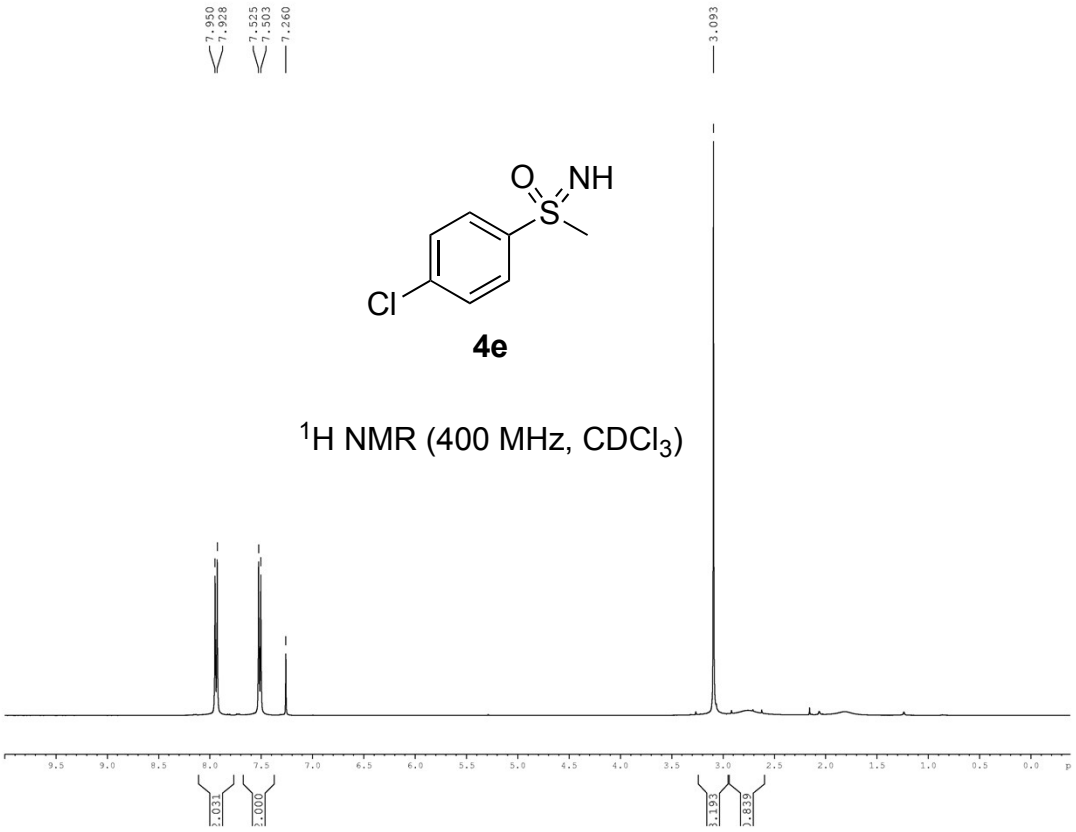
4d

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



4d

^{13}C NMR (101 MHz, $CDCl_3$)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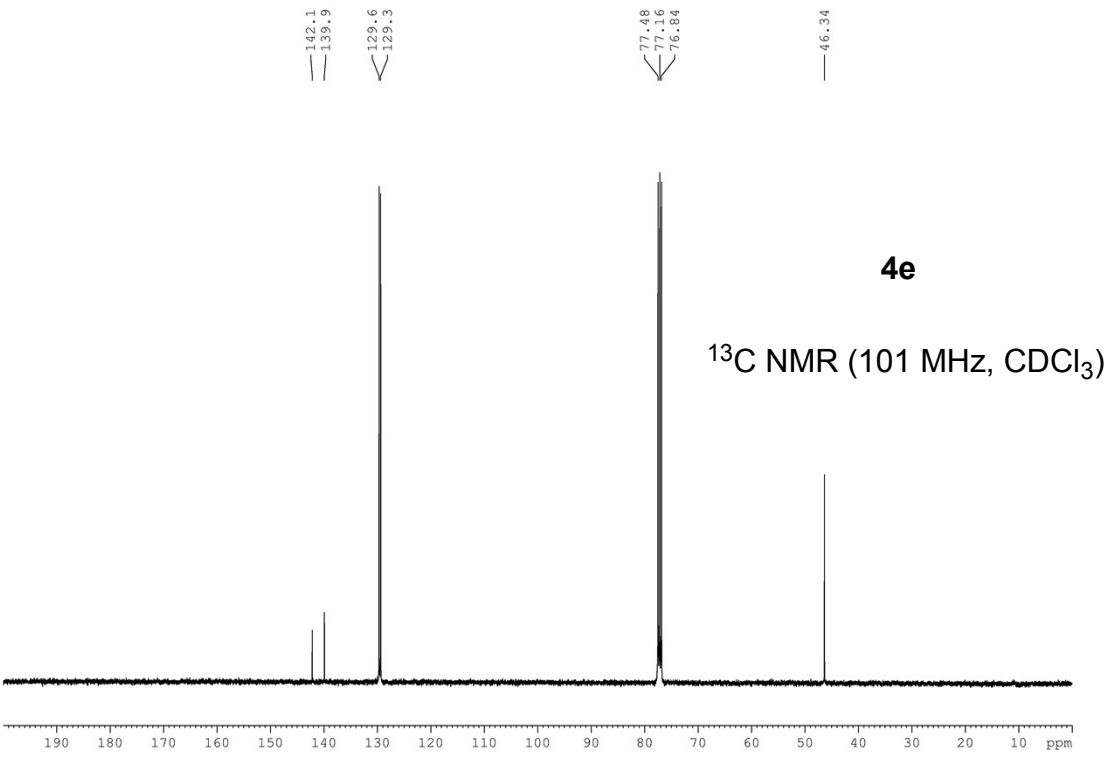
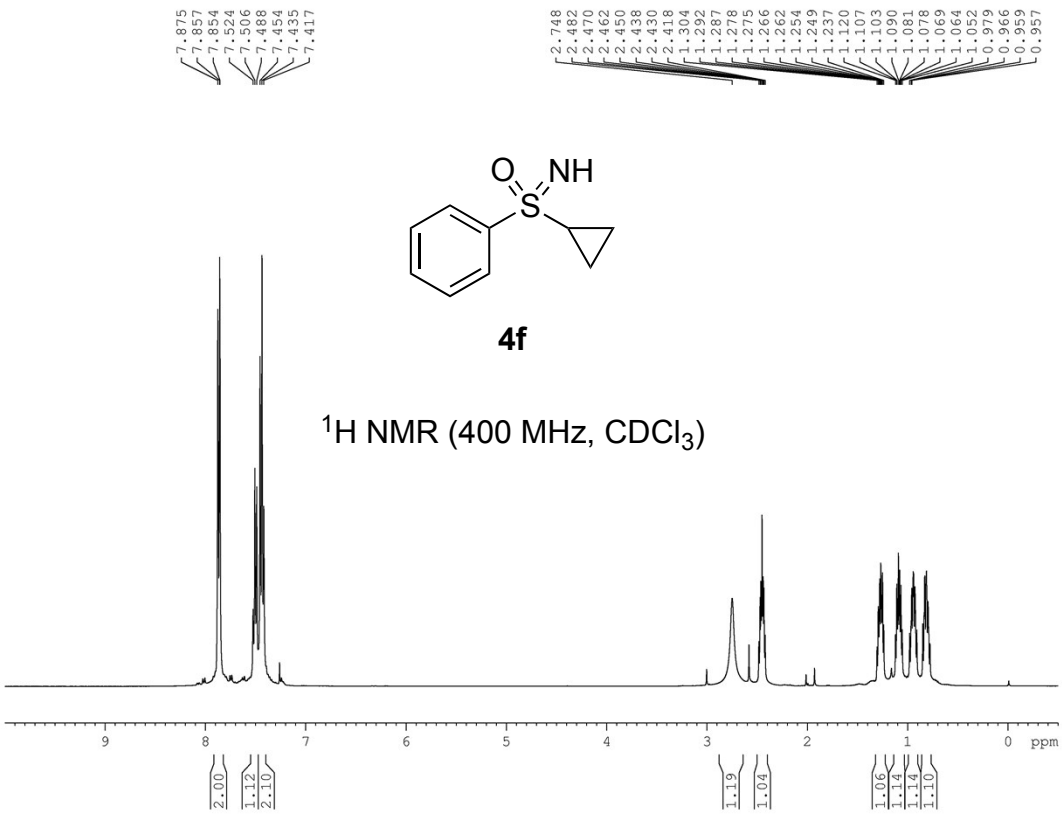
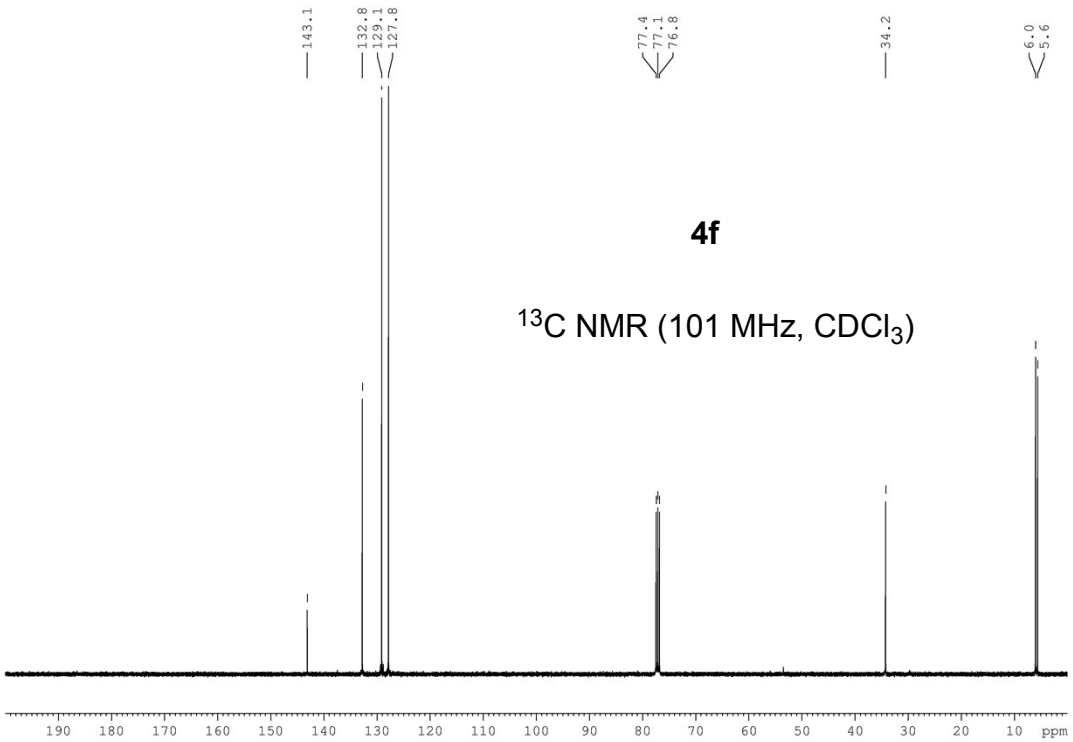
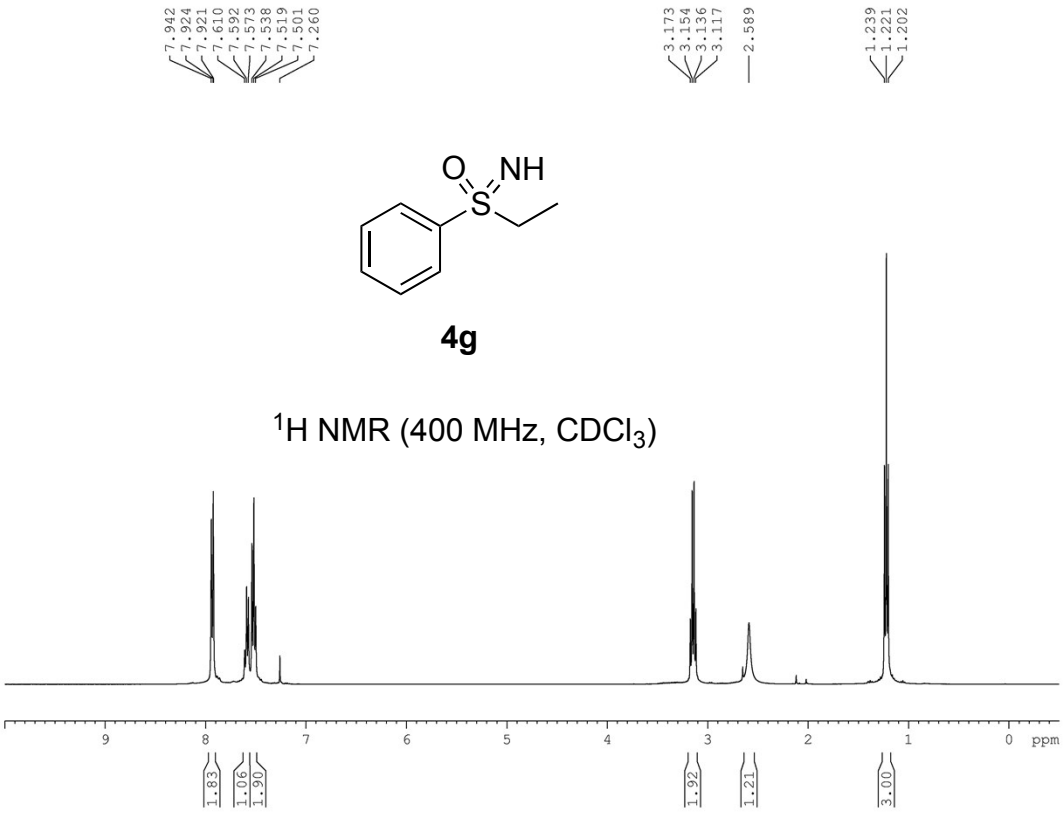
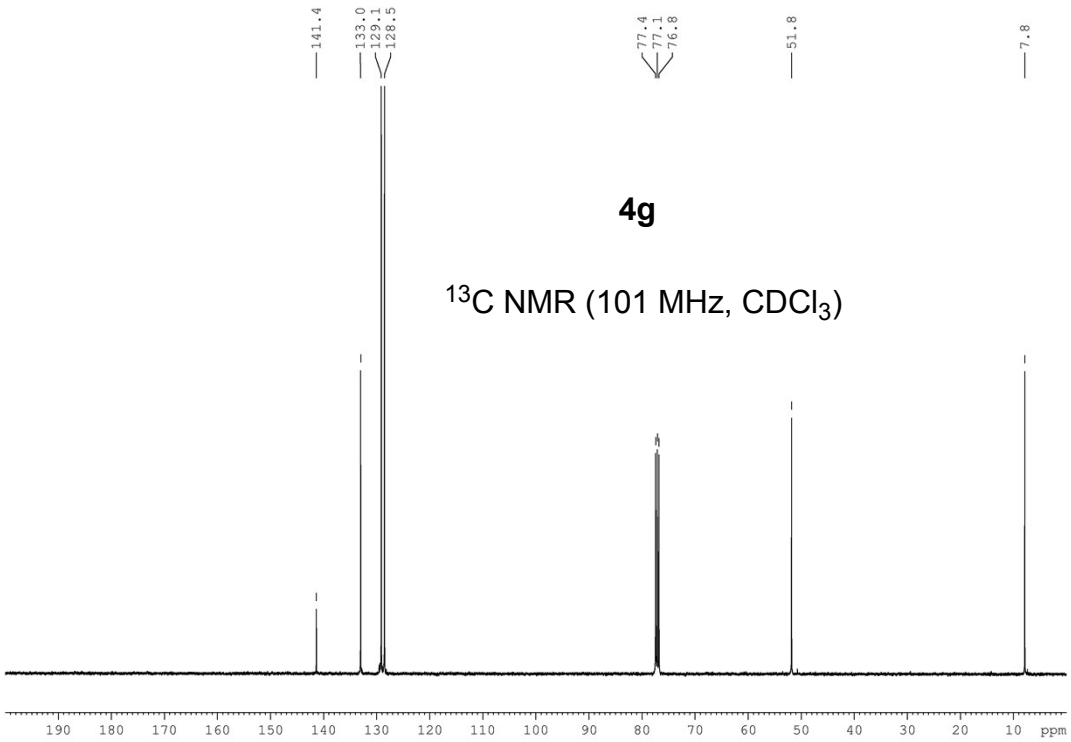
7.928
7.525
7.503
7.260
3.093
O
NH
S
Cl
4e
1H NMR (400 MHz, CDCl3)
2.031
2.000
3.193
2.839

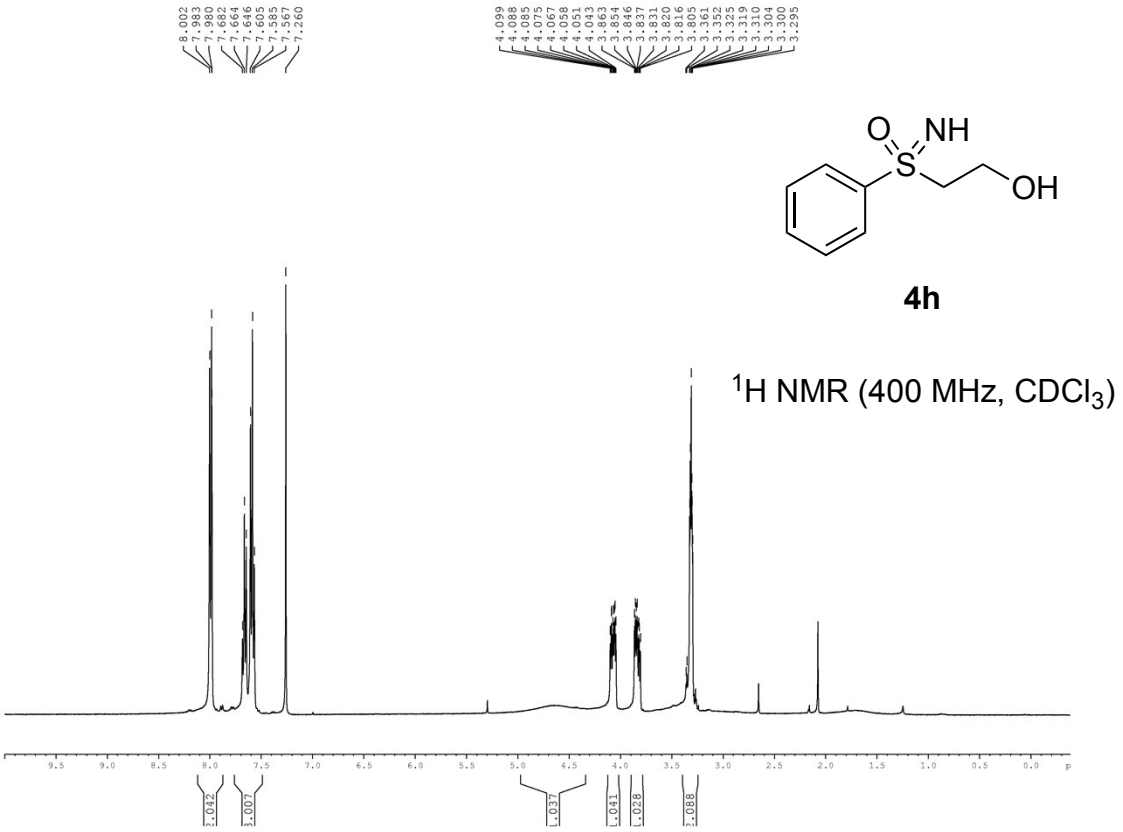

142.1
139.9
129.6
129.3
77.48
77.16
76.84
46.34
4e
13C NMR (101 MHz, CDCl3)
ppm

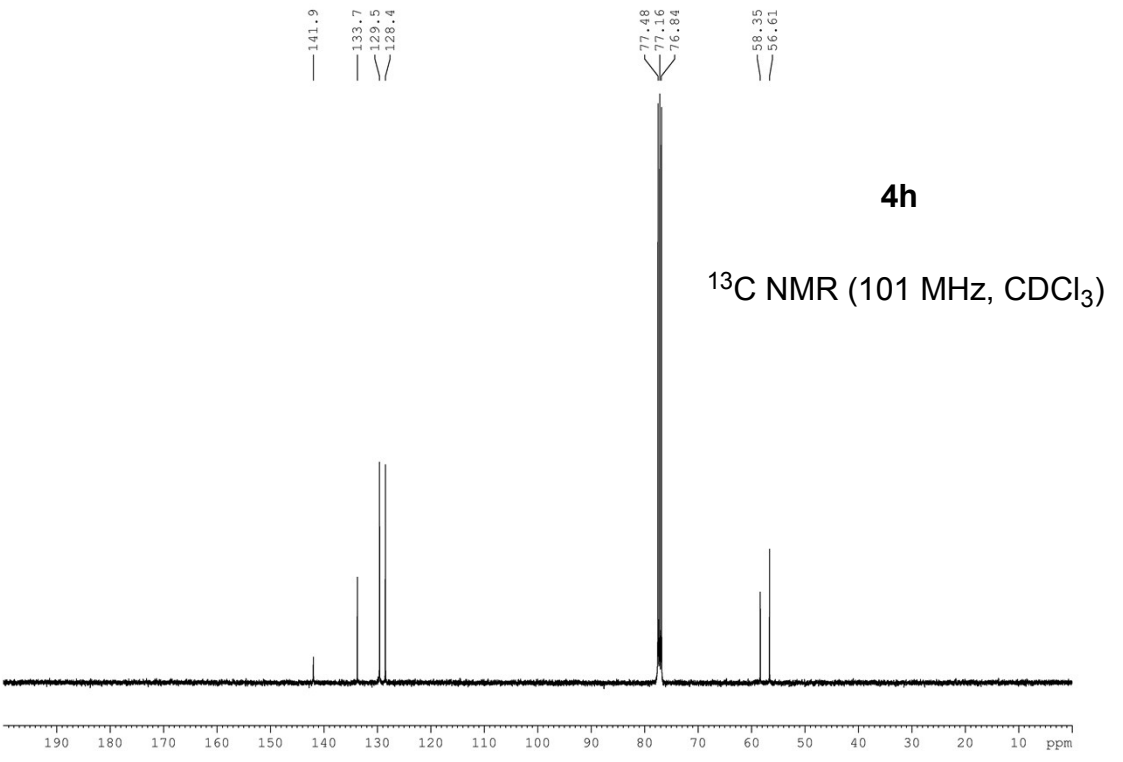

7.875
7.857
7.854
7.524
7.506
7.488
7.454
7.435
7.417
2.748
2.482
2.470
2.462
2.450
2.438
2.430
2.418
1.304
1.292
1.287
1.278
1.275
1.266
1.262
1.254
1.249
1.237
1.120
1.107
1.103
1.090
1.081
1.078
1.069
1.064
1.052
0.979
0.966
0.959
0.957
O
NH
S
4f
^{1}H NMR (400 MHz, $CDCl_3$)
9
8
7
6
5
4
3
2
1
0
ppm
2.00
1.12
2.10
1.19
1.04
1.06
1.14
1.14
1.14
1.10

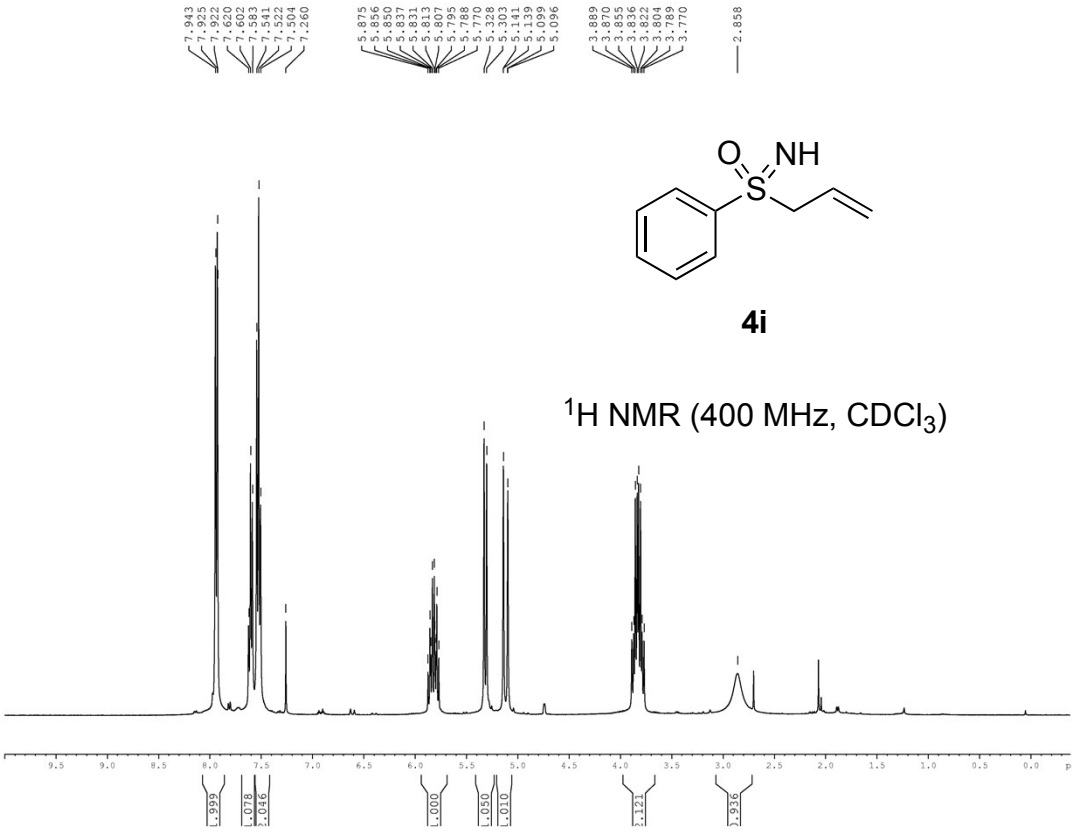

143.1
132.8
129.1
127.8
77.4
77.1
76.8
34.2
6.0
5.6
4f
^{13}C NMR (101 MHz, $CDCl_3$)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

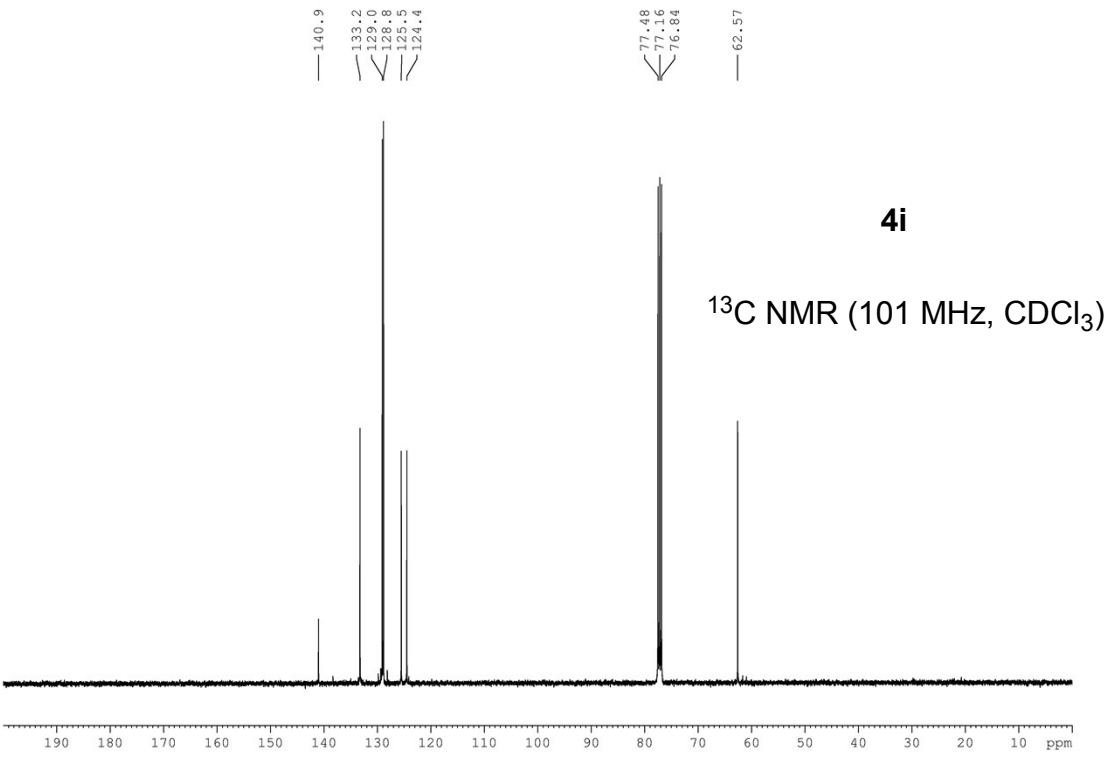

7.942
7.924
7.921
7.610
7.592
7.573
7.538
7.519
7.501
7.260
3.173
3.154
3.136
3.117
2.589
1.239
1.221
1.202
O
NH
S
4g
1H NMR (400 MHz, CDCl3)
9
8
7
6
5
4
3
2
1
0
ppm
1.83
1.06
1.90
1.92
1.21
3.00

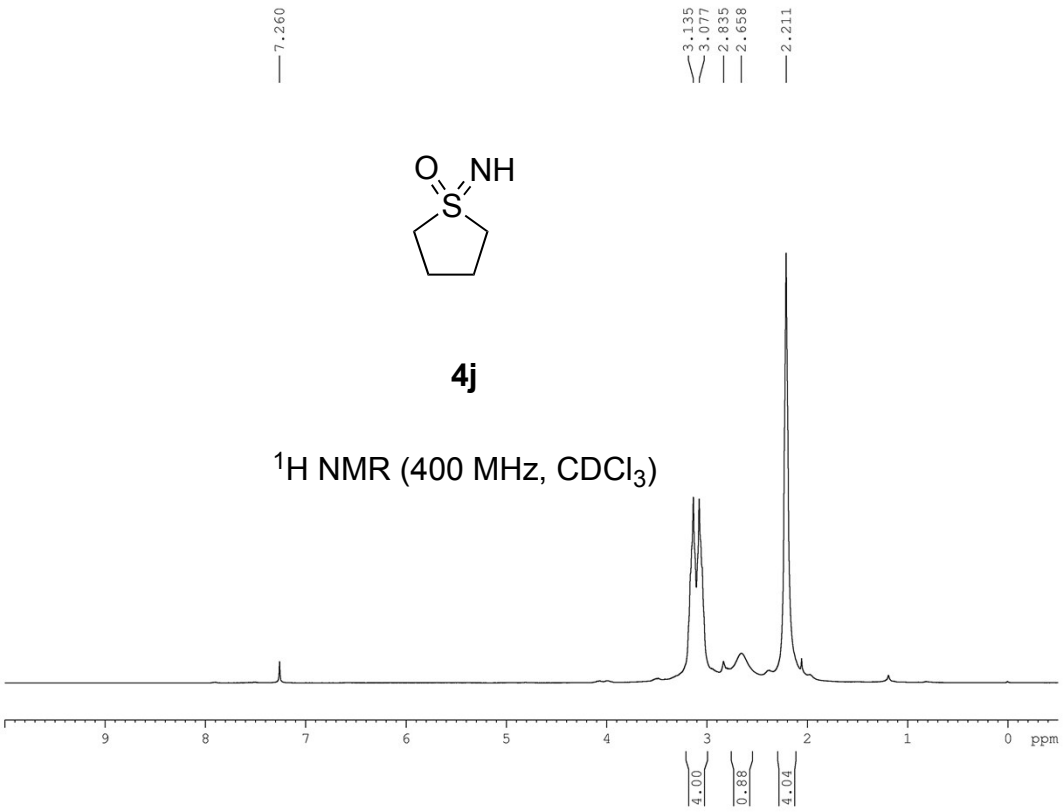

141.4
133.0
129.1
128.5
77.4
77.1
76.8
51.8
7.8
4g
13C NMR (101 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


8.002
7.983
7.980
7.682
7.664
7.646
7.605
7.585
7.567
7.260
4.099
4.088
4.085
4.075
4.067
4.058
4.051
4.043
3.863
3.854
3.846
3.837
3.831
3.820
3.816
3.805
3.361
3.352
3.325
3.319
3.310
3.304
3.300
3.295
O
NH
S
OH
4h
1H NMR (400 MHz, CDCl3)
1.042
1.007
1.037
1.041
1.028
2.088


141.9
133.7
129.5
128.4
77.48
77.16
76.84
58.35
56.61
4h
13C NMR (101 MHz, CDCl3)
ppm

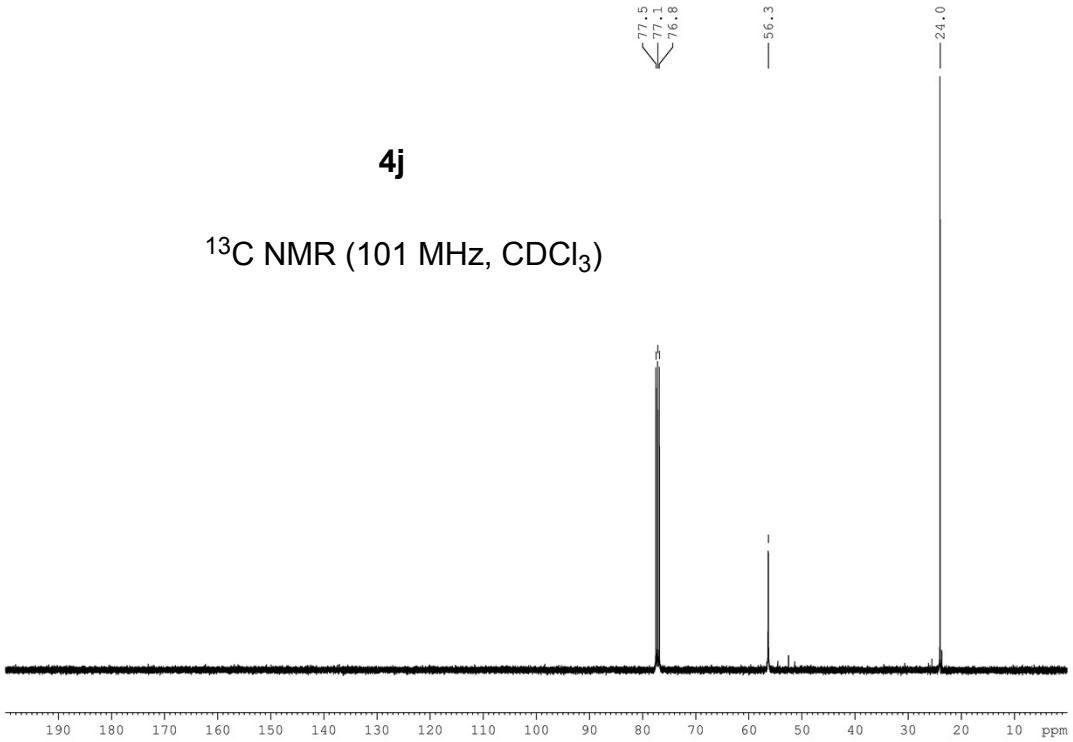

7.943
7.935
7.922
7.620
7.602
7.583
7.541
7.522
7.504
7.260
5.875
5.856
5.850
5.837
5.831
5.813
5.807
5.795
5.788
5.770
5.328
5.303
5.141
5.139
5.099
5.096
3.889
3.870
3.855
3.836
3.822
3.804
3.789
3.770
2.858
O
NH
S
4i
1H NMR (400 MHz, CDCl3)
1.999
1.078
1.046
1.000
1.050
1.010
2.121
1.936


140.9
133.2
129.0
128.8
125.5
124.4
77.48
77.16
76.84
62.57
4i
13C NMR (101 MHz, CDCl3)
ppm



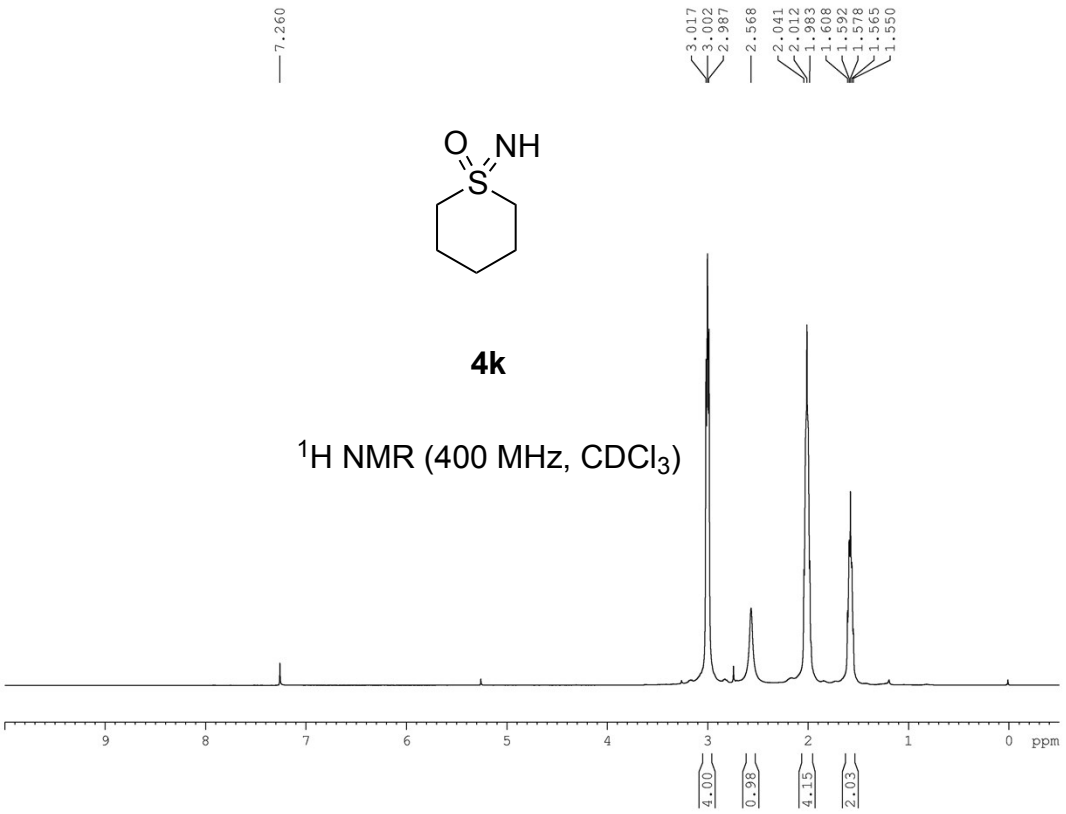
4j

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



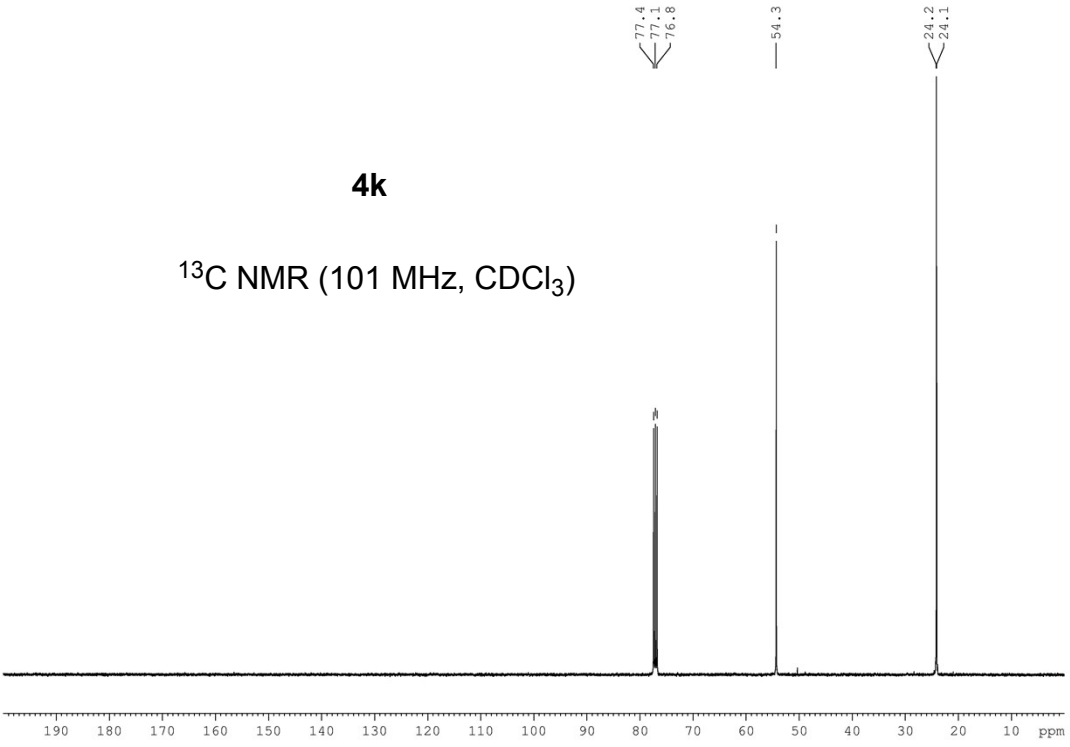
4j

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



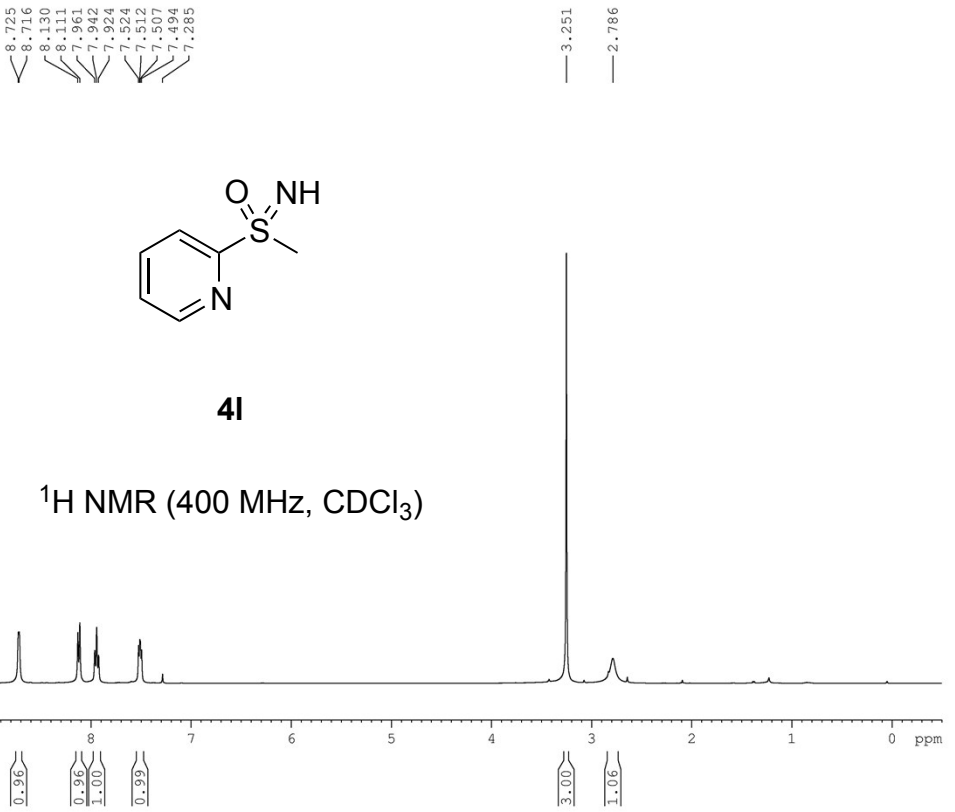
4k

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



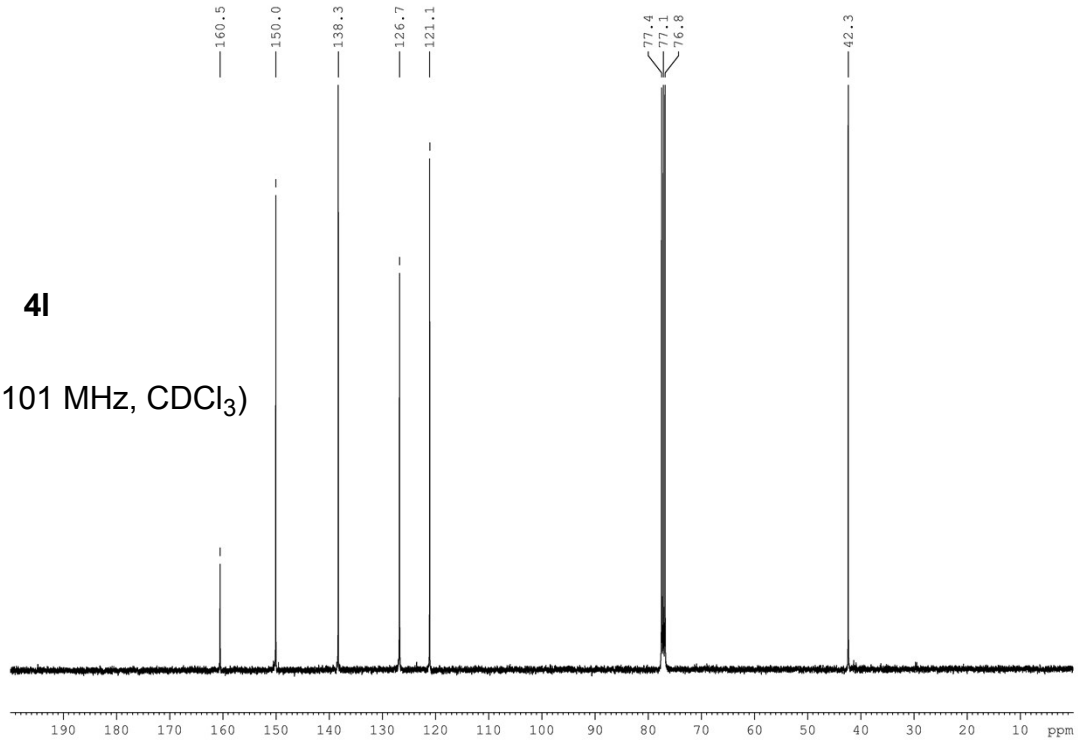
4k

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



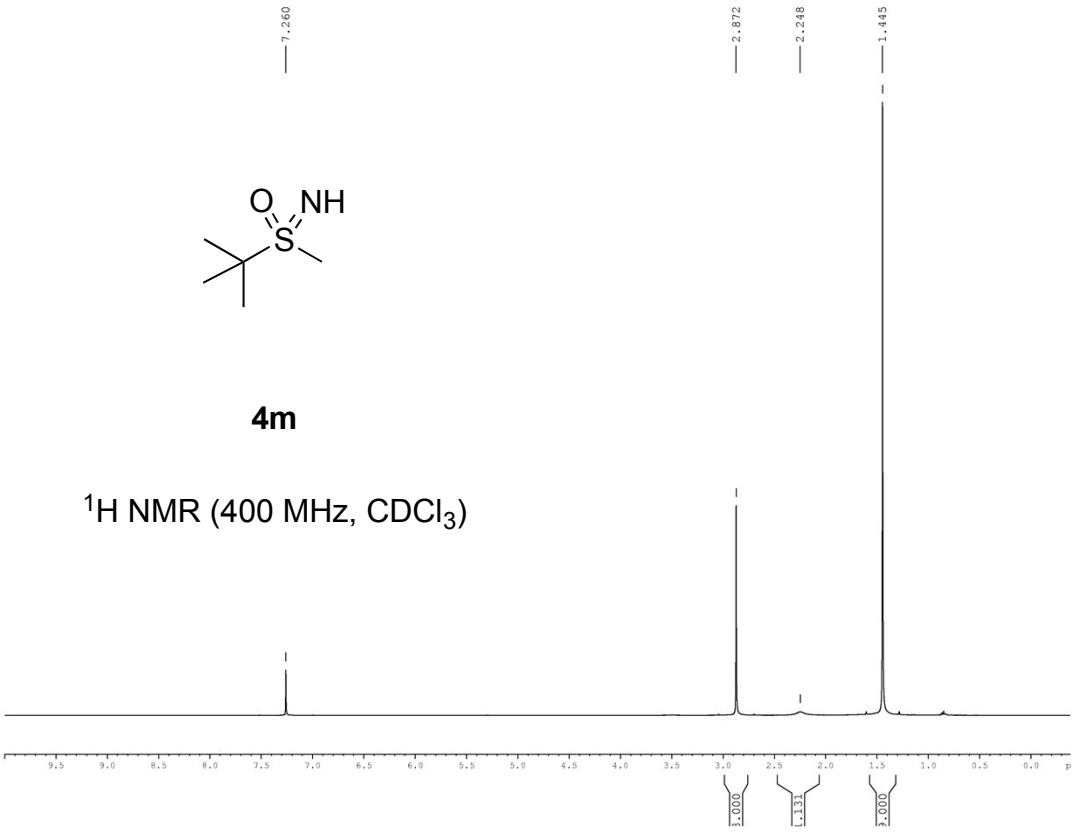
4l

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



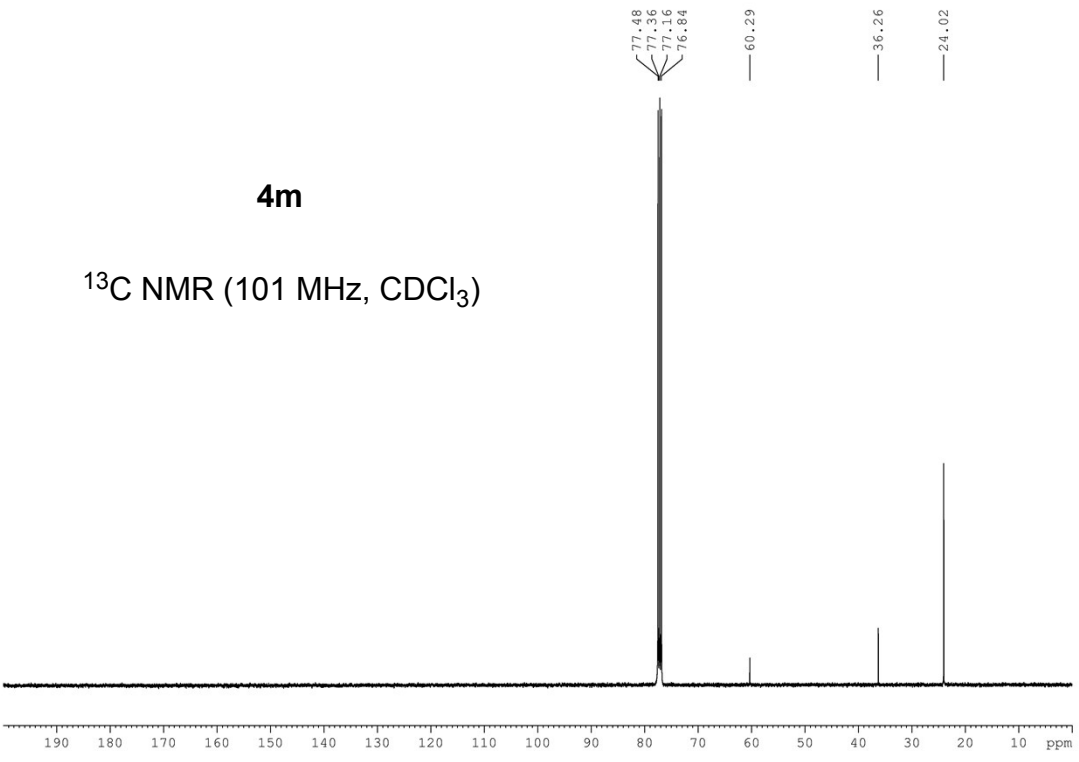
4l

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



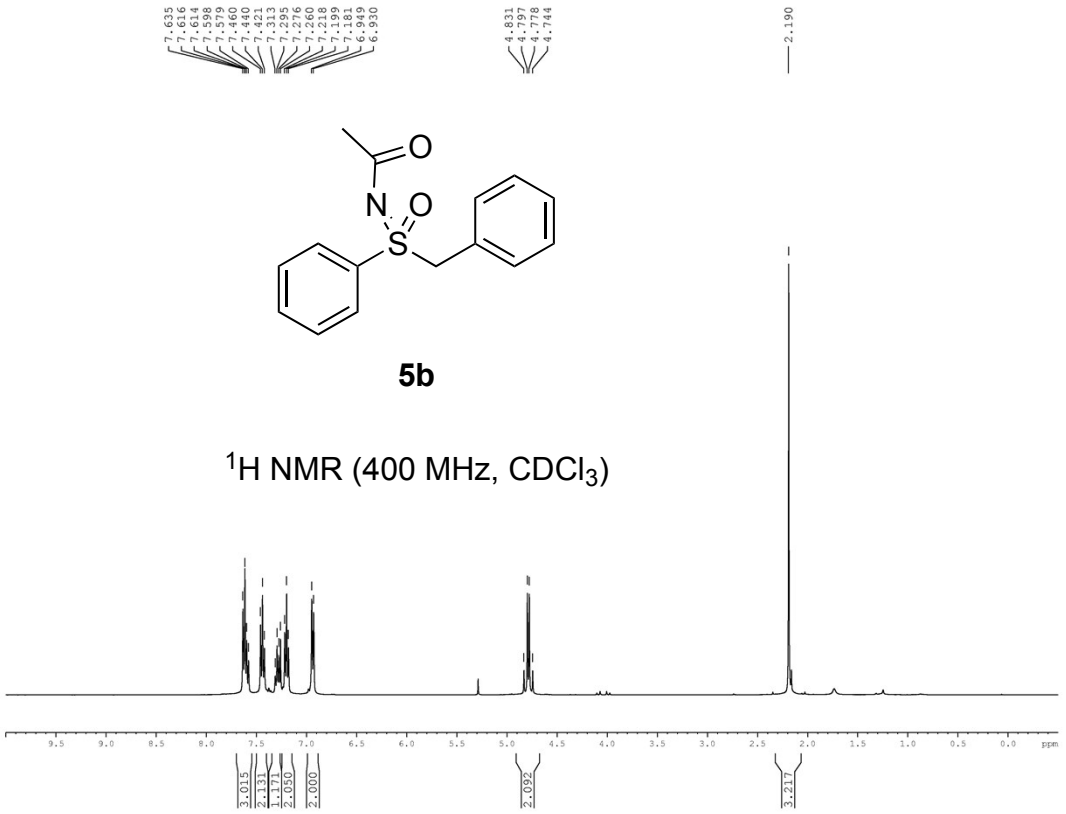
4m

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



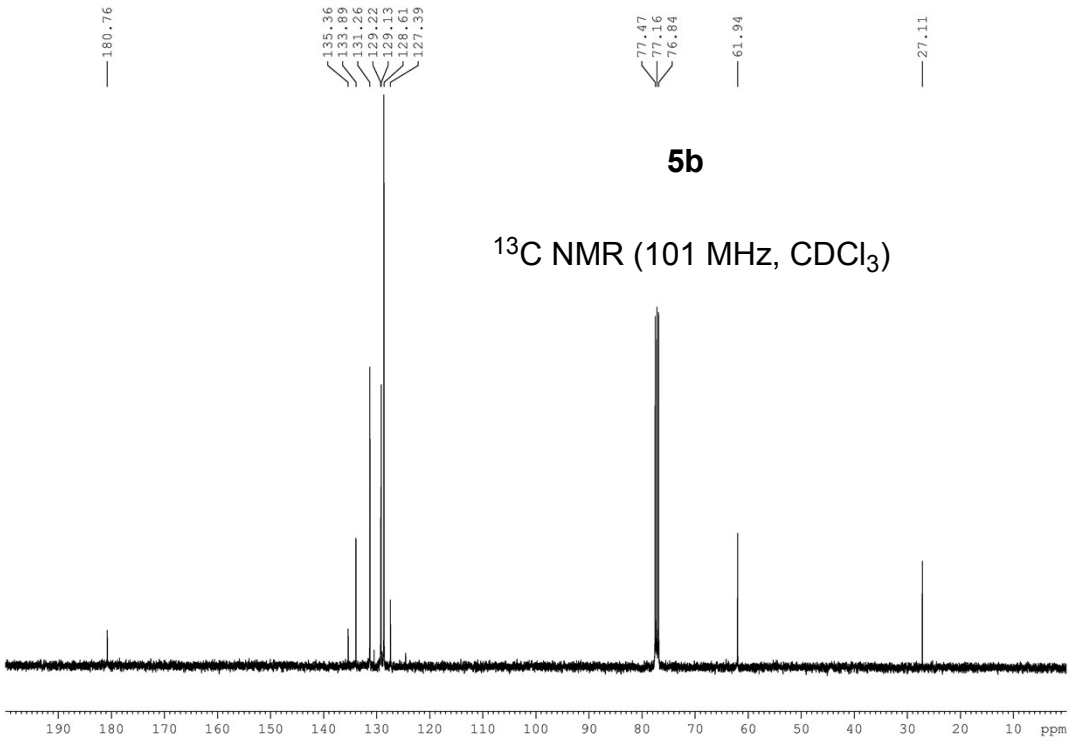
4m

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



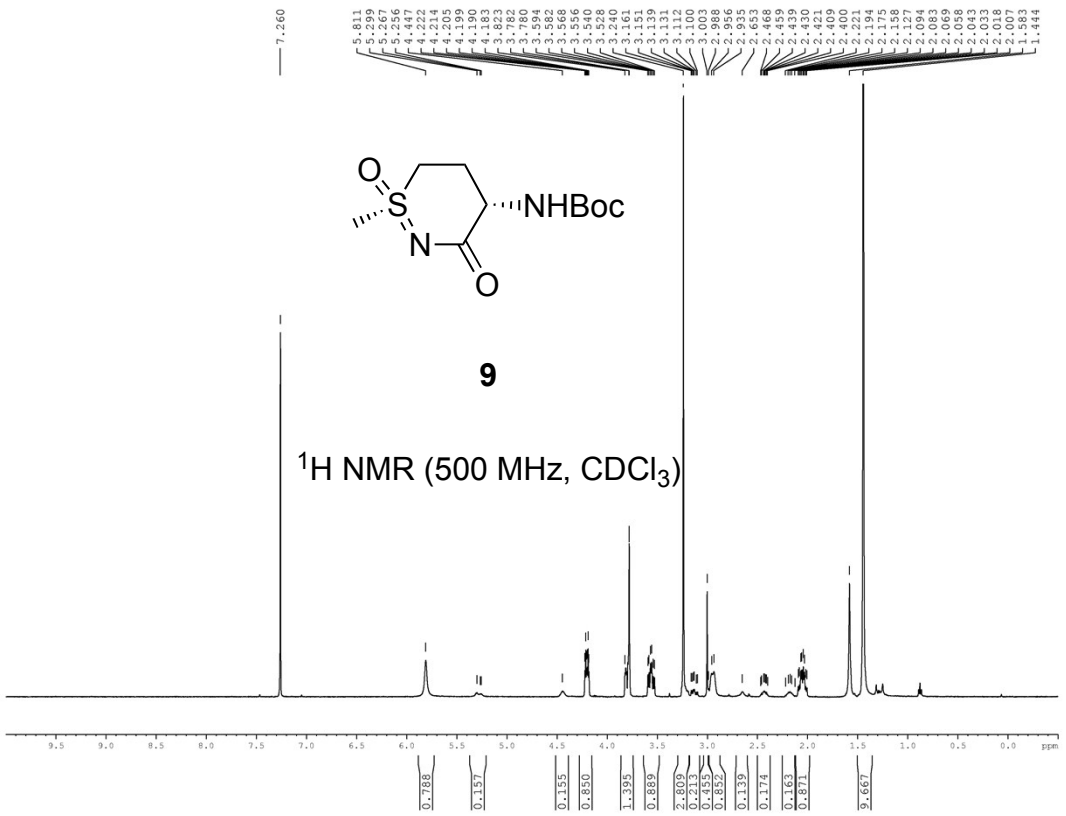
5b

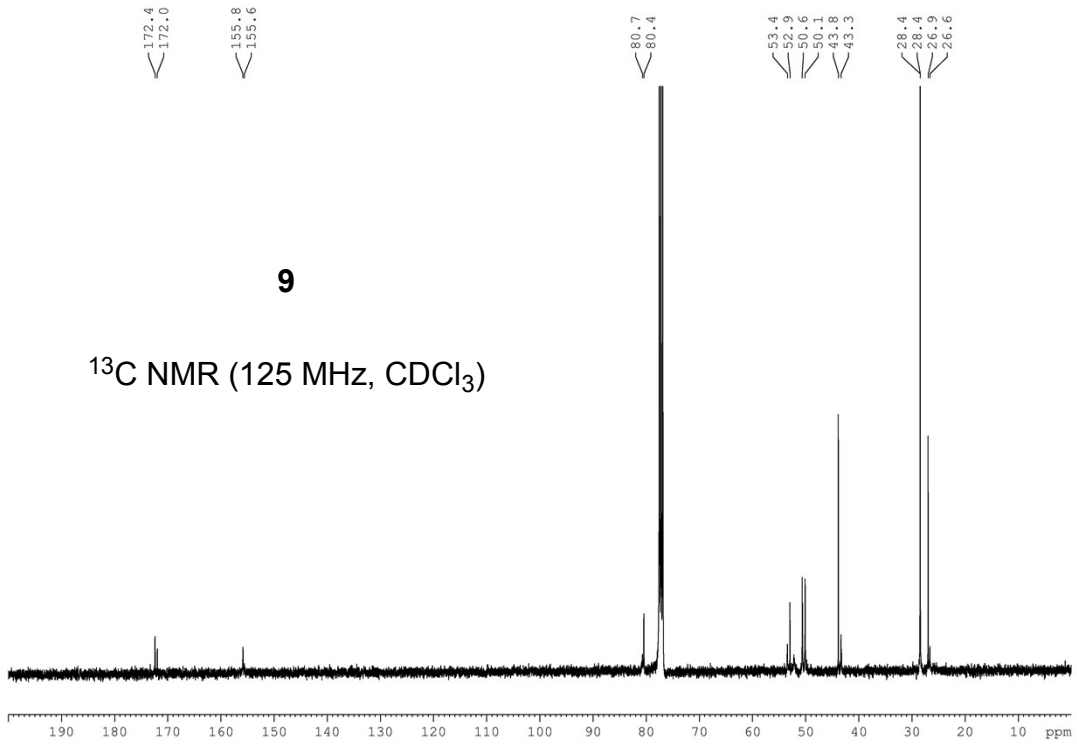
^{1}H NMR (400 MHz, $CDCl_3$)



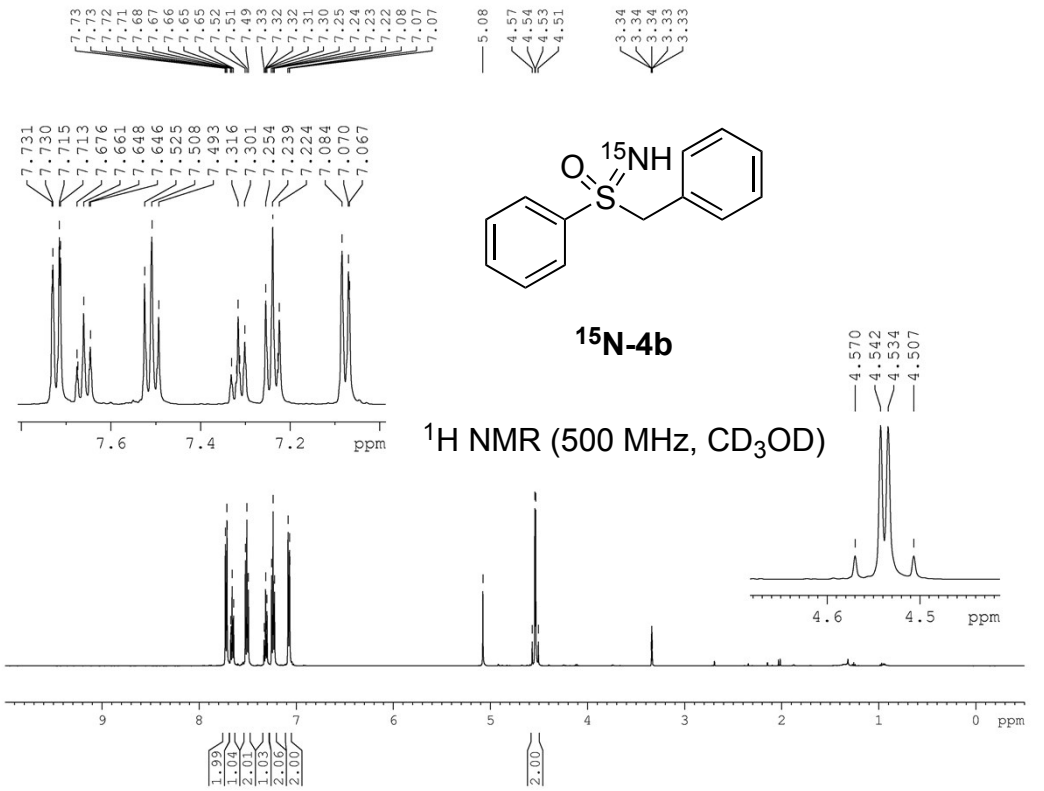
5b

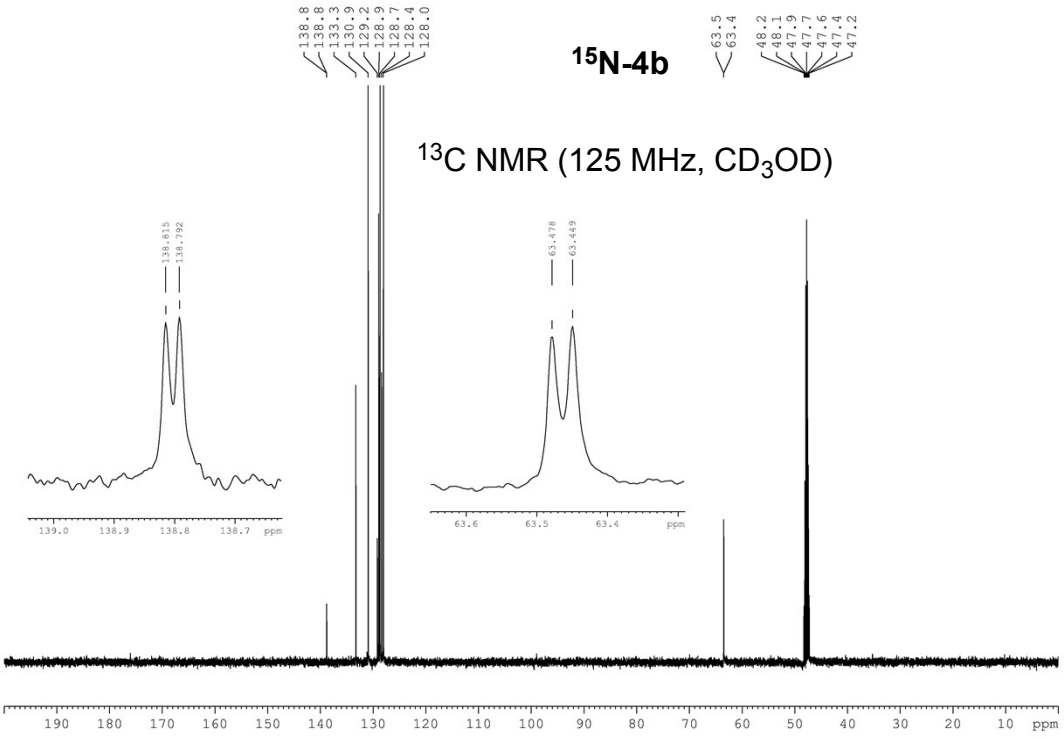
^{13}C NMR (101 MHz, $CDCl_3$)


NHBoc
9
1H NMR (500 MHz, CDCl3)


9
13C NMR (125 MHz, CDCl3)

NMR SPECTRA FOR ^{15}N-LABELLED SULFOXIMINES



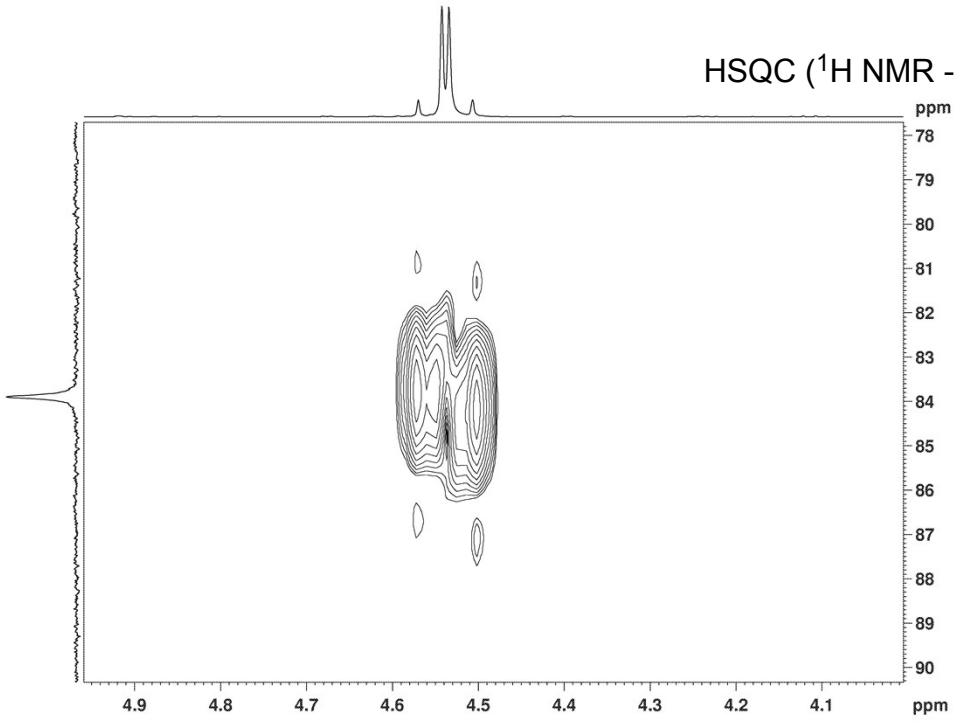


^{15}N-4b

^{15}N NMR (50.7 MHz, CD_3OD)

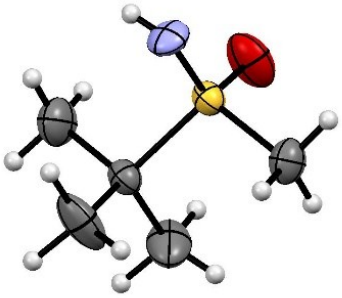
^{15}N-4b

HSQC (^{1}H NMR - ^{15}N NMR)



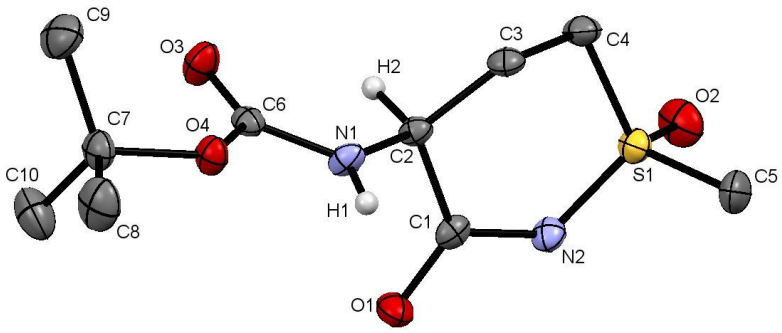
X-RAY CRYSTAL DATA

X-Ray Crystal Structure of 4m



Single crystals of allenyl sulfone **4m** suitable for X–ray crystallographic analysis were obtained by slow evaporation of ethyl acetate solution. X–ray diffraction experiments for monocrystal of **4m** were performed at 150 K with graphite–monochromatized Mo K_α radiation (λ = 0.71073 Å) on a Bruker–Nonius Kappa CCD area detector diffractometer. Formula $C_5H_{13}NOS$, formula weight 135.22, crystal system monoclinic, space group $P2_1/m$, a = 6.2849(4) Å, b = 8.8158(5) Å, c = 6.6483(4) Å, β = 96.781(3)°, V = 365.78(4) Å^3, Z = 2, calculated density = 1.228 g/cm^3, μ = 0.355 mm^{-1}, R_{int} = 0.0183, R[$F^2>2\sigma(F^2)$] = 0.0303, wR(F^2) = 0.0874, GOF = 1.140, $2\vartheta_{max}$ = 60.88°, 83 parameters, number of independent reflections : 1169, final difference map within 0.538 and -0.282 eÅ^{-3}. Selected bond lengths (Å), angles (deg) : N1-S1 1.558(11), O1-S1 1.400(10), S1-N1-H1 109(3), O1-S1-N1 120.20(15). Program(s) used to solve structure: SHELXS–97. Program(s) used to refine structure: SHELXL–2014. Software used to prepare material for publication: SHELXTL–2014.
CCDC **1522510** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

X-Ray Crystal Structure of 9



Single crystals of pyrroline **9** suitable for X–ray crystallographic analysis were obtained by slow evaporation of dichloromethane solution. X–ray diffraction experiments for monocrystal of **9** were performed at 150 K with graphite–monochromatized Mo K_{α} radiation (λ = 0.71073 Å) on a Bruker–Nonius Kappa CCD area detector diffractometer. Formula $C_{10}H_{18}N_2O_4S$, formula weight 262.32, crystal system monoclinic, space group $P2_12_12_1$, a = 6.7140(3) Å, b = 6.7632(3) Å, c = 27.8703(12) Å, $\alpha = \beta = \gamma = 90°$, V = 1265.54(10) Å^3, Z = 2, calculated density = 1.377 g/cm^3, μ = 0.262 mm^{-1}, R_{int} = 0.0298, R[$F^2>2\sigma(F^2)$] = 0.0314, wR(F^2) = 0.0731, GOF = 1.038, $2\vartheta_{max}$ = 58.26°, 162 parameters, number of independent reflections : 3007, Flack parameter 0.02(3), final difference map within 0.280 and -0.311 eÅ^{-3}. Selected bond lengths (Å), angles (deg) and torsion angles (deg) : N2-S1 1.560(2), O2-S1 1.4389(17), O2-S1-N2 113.81(11), N2-S1-C4-C3 35.93(18), C4-S1-N2-C1 -10.8(2). Program(s) used to solve structure: SHELXS–97. Program(s) used to refine structure: SHELXL–2014. Software used to prepare material for publication: SHELXTL–2014. CCDC **1522511** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.