Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Alkylation of *N*H-Sulfoximines Under Mitsunobu-Type Conditions

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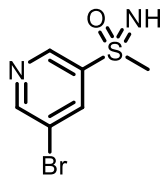
General Synthetic Methods

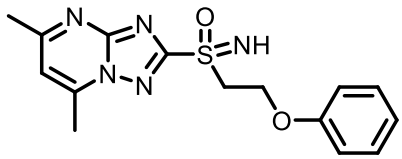
All reactions were carried out employing standard chemical techniques. Solvents used for extraction, washing, and chromatography were HPLC grade. All reagents were purchased from commercial sources and were used without further purification. Erythropoietin-mimetic **28** (CAS No. 866142-71-4) was purchased from Key Organics/BIONET. All NMR spectra were recorded on a 400 MHz Bruker AV-400 instrument. ^{1}H chemical shifts are reported as δ values in ppm relative to the residual solvent peak ($CDCl_3$= 7.26, CD_3OD = 3.31). Data are reported as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, ddd = doublet of doublet of doublets, td = triplet of doublets, m = multiplet), coupling constant, and integration. ^{13}C chemical shifts are reported as δ values in ppm relative to the residual solvent peak ($CDCl_3$ = 77.16, CD_3OD = 49.0). High resolution mass spectra were obtained on an Agilent 6540 UHD Q-TOF with ESI source. MS parameters were as follows: fragmentor: 150, capillary voltage: 3500 V, nebulizer pressure: 60 psig, drying gas flow: 13 L/min, drying gas temperature: 275° C. Samples were introduced via an Agilent 1290 UHPLC comprised of a G4220A binary pump, G4226A ALS, G1316C TCC, and G4212A DAD with ULD flow cell. UV absorption was observed at 215 nm and 254 nm with a 4 nm bandwidth. Column: Agilent Zorbax Extend C18, 1.8 um, 2.1 x 50 mm. Gradient conditions: 5% to 95% CH_3CN in H_2O (0.1% Formic Acid) over 1 min, hold at 95% CH_3CN for 0.1 min, 0.5 mL/min, 40° C. Automated flash column chromatography was performed on a Biotage Isolera 1 or a Teledyne ISCO CombiFlash system. RP-HPLC was performed on a Gilson preparative reversed-phase HPLC system comprised of a 333 aqueous pump with solvent-selection valve, 334 organic pump, GX-271 or GX-281 liquid hander, two column switching valves, and a 155 UV detector. Absorbance was monitored at 215 and 254 nm. Column: Phenomenex Axia-packed Gemini C18, 5 um. Mobile phase: CH_3CN in H_2O (0.1% TFA) or CH_3CN in H_2O (0.05% v/v NH_4OH) under the specified gradient, then hold 95% CH_3CN in 5% aqueous phase, 50 mL/min, 23**°** C. Melting points were recorded on an OptiMelt automated melting point system by Stanford Research Systems.

General Procedure A: Preparation of *N*H-Sulfoximines from Thioethers

Thioether (1 eq.) was added to a vial equipped with a stir bar, followed by MeOH (0.2 M). Ammonium carbonate (4.6 eq.) and (diacetoxyiodo)benzene (3 eq.) were then added sequentially. The vial was sealed and the resulting reaction mixture was stirred at r.t. for 1 h, after which time the reaction was quenched with the addition of sat. $NaHCO_3$ solution, and diluted with DCM. The aqueous layer was extracted with DCM, and combined organic extracts were dried over $MgSO_4$. Solvents were filtered and concentrated, and crude residue was purified by column chromatography to give the desired product.



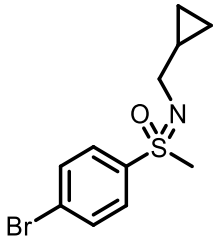
(5-bromopyridin-3-yl)(imino)(methyl)-λ^6-sulfanone (31). Followed General Procedure A with 3-bromo-5-(methylthio)pyridine (231 mg, 1.13 mmol) to give product as a tan solid after column chromatography (0-4% MeOH in DCM) (207 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 – 9.09 (m, 1H), 8.90 – 8.88 (m, 1H), 8.42 (t, *J* = 2.1 Hz, 1H), 3.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0, 147.0, 141.4, 138.1, 121.2, 46.6. HRMS (TOF, ES+) $C_6H_8BrN_2OS$ $[M+H]^+$ calc. mass 234.9535, found 234.9534. m.p. = 68-70 °C.



(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)(imino)(2-phenoxyethyl)-λ^6-sulfanone (29). Followed General Procedure A with 5,7-dimethyl-2-((2-phenoxyethyl)thio)-[1,2,4]triazolo[1,5-a]pyrimidine (**28**) (75 mg, 0.25 mmol) to give the product as a tan oil that solidified upon standing after column chromatography (0-5% MeOH in DCM) (47.2 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 2H), 6.95 (d, *J* = 1.0 Hz, 1H), 6.93 – 6.89 (m, 1H), 6.72 – 6.69 (m, 2H), 4.60 – 4.50 (m, 2H), 4.09 – 3.97 (m, 2H), 2.75 (d, *J* = 0.9 Hz, 3H), 2.72 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 166.8, 157.8, 155.4, 147.9, 129.6, 121.5, 114.5, 112.7, 61.8, 54.1, 25.4, 17.1. HRMS (TOF, ES+) $C_{15}H_{18}N_5O_2S$ $[M+H]^+$ calc. mass 332.1176, found 332.1175. m.p. = 53-55 °C.

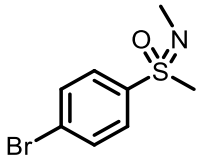
General Procedure B: Mitsunobu-Type Alkylation of *N*H-Sulfoximines

*N*H-sulfoximine (1 eq.) was added to a vial equipped with a stir bar, followed by dry toluene (0.2 M). Alcohol (2 eq.) was then added, followed by CMBP (2 eq.). The vial was sealed, and the solution was briefly stirred under vacuum and then purged with N_2 by bubbling for 3-5 min, after which time the vial was resealed and heated to 70 °C using a heating block equipped with a thermometer for 24 h. The reaction mixture was cooled to r.t. and diluted with MeOH. Solvents were concentrated, and crude residue was purified by column chromatography to give the desired product.

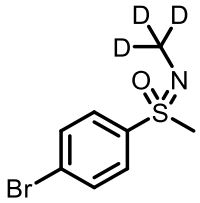


(4-bromophenyl)((cyclopropylmethyl)imino)(methyl)-λ^6-sulfanone (6). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ^6-sulfanone (**5**) (30.0 mg, 0.13 mmol) and cyclopropanemethanol to give product as a colorless oil after purification by column chromatography (3-100% EtOAc in hexanes) (27.1 mg, 73%). *On a 1 mmol scale (234 mg), 204 mg (71%) was obtained after column chromatography*. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.77 (m, 2H), 7.71 – 7.68 (m, 2H), 3.11 (s, 3H), 2.83 (dd, *J* = 12.8, 6.7 Hz, 1H), 2.68 (dd, *J* = 12.8, 6.8 Hz, 1H), 1.02 – 0.92 (m, 1H), 0.50 – 0.39 (m, 2H), 0.15 – 0.10 (m, 1H), 0.09 – 0.03 (m, 1H). ^{13}C

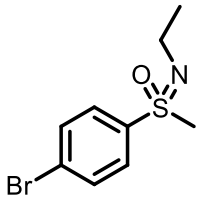
NMR (101 MHz, $CDCl_3$) δ 139.0, 132.9, 130.5, 128.2, 49.1, 45.5, 13.5, 4.3, 4.0. HRMS (TOF, ES+) $C_{11}H_{15}BrNOS$ $[M+H]^+$ calc. mass 288.0052, found 288.0049.



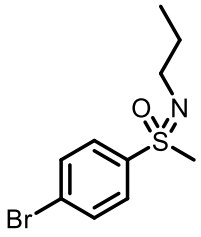
(4-bromophenyl)(methyl)(methylimino)-λ⁶-sulfanone (7). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.2 mg, 0.13 mmol) and anhydrous methanol to give the product as a clear residue after purification by column chromatography (50-100% EtOAc in hexanes) (25.2 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.74 (m, 2H), 7.74 – 7.68 (m, 2H), 3.10 (s, 3H), 2.64 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 133.0, 130.5, 128.5, 45.0, 29.5. HRMS (TOF, ES+) $C_8H_{11}BrNOS$ $[M+H]^+$ calc. 247.9739, found 247.9740.



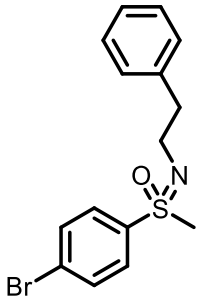
(4-bromophenyl)(methyl)((methyl-*d3*)imino)-λ⁶-sulfanone (8). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.1 mg, 0.13 mmol) and methanol-*d4* to give the product as a clear oil after purification by column chromatography (50-100% EtOAc in hexanes) (22.5 mg, 70%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.74 (m, 2H), 7.73 – 7.68 (m, 2H), 3.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 133.00, 130.5, 128.4, 45.1, 28.8 (pentet, $J_{C\text{-}D}$ = 21.0 Hz). Note: The ^{13}C peak for the CD_3 carbon should appear as a septet, but despite efforts to improve the signal to noise, the peak remained as a very shallow pentet. HRMS (TOF, ES+) $C_8H_8D_3BrNOS$ $[M+H]^+$ calc. 250.9928, found 250.9926.



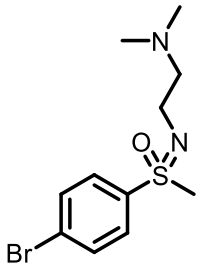
(4-bromophenyl)(ethylimino)(methyl)-λ⁶-sulfanone (9). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.2 mg, 0.13 mmol) and anhydrous ethanol to give the product as a gold oil after purification by column chromatography (50-100% EtOAc in hexanes) (21.8 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 2H), 7.73 – 7.67 (m, 2H), 3.10 (s, 3H), 3.01 (dq, *J* = 12.3, 7.2 Hz, 1H), 2.83 (dq, *J* = 12.3, 7.2 Hz, 1H), 1.18 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 132.9, 130.5, 128.3, 45.4, 38.6, 18.2. HRMS (TOF, ES+) $C_9H_{13}BrNOS$ $[M+H]^+$ calc. 261.9896, found 261.9895.



(4-bromophenyl)(methyl)(propylimino)-λ⁶-sulfanone (10). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.5 mg, 0.13 mmol) and 1-propanol to give the product as a gold oil after purification by column chromatography (0-100% EtOAc in hexanes) (24.1 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.73 (m, 2H), 7.71 – 7.65 (m, 2H), 3.08 (s, 3H), 2.89 (dt, *J* = 12.1, 7.2 Hz, 1H), 2.71 (dt, *J* = 12.1, 7.2 Hz, 1H), 1.55 (app. sextet, *J* = 7.3 Hz, 2H), 0.88 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 132.8, 130.4, 128.2, 45.8, 45.3, 26.0, 11.9. HRMS (TOF, ES+) $C_{10}H_{15}BrNOS$ $[M+H]^+$ calc. 276.0052, found 276.0054.

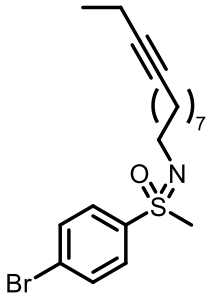


(4-bromophenyl)(methyl)(phenethylimino)-λ⁶-sulfanone (11). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.3 mg, 0.13 mmol) and 2-phenylethanol to afford the product as a gold oil after column chromatography (0-100% EtOAc in hexanes) (22.5 mg, 51%). ^{1}H NMR (400 MHz, MeOD-*d4*) δ 7.74 – 7.68 (m, 2H), 7.63 – 7.58 (m, 2H), 7.27 – 7.21 (m, 2H), 7.20 – 7.11 (m, 3H), 3.18 (ddd, *J* = 12.2, 7.6, 6.1 Hz, 1H), 3.10 (s, 3H), 2.98 – 2.89 (m, 1H), 2.85 – 2.73 (m, 2H). ^{13}C NMR (101 MHz, MeOD-*d4*) δ 141.4, 139.1, 139.1, 133.8, 131.6, 130.0, 129.3, 129.2, 127.2, 46.7, 44.4, 39.9. HRMS (TOF, ES+) $C_{15}H_{17}BrNOS$ $[M+H]^+$ calc. 338.0209, found 338.0208.

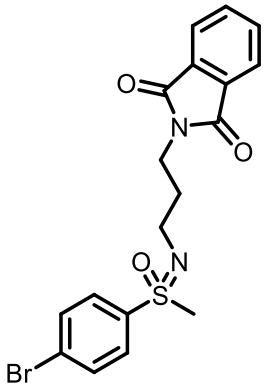


(4-bromophenyl)((2-(dimethylamino)ethyl)imino)(methyl)-λ⁶-sulfanone (12). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.0 mg, 0.13 mmol) and *N,N*-dimethylethanolamine to give the product as a clear oil after purification via RP-HPLC (13-50% MeCN in 0.05% aqueous NH_4OH) (8.9 mg, 23%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.72 – 7.66 (m, 2H), 3.09 (s, 3H), 3.07 (ddd, *J* = 12.4, 7.5, 6.4 Hz, 1H), 2.87 (ddd, *J* = 12.4, 7.7, 6.3 Hz, 1H), 2.54 – 2.41 (m, 2H), 2.22 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9,

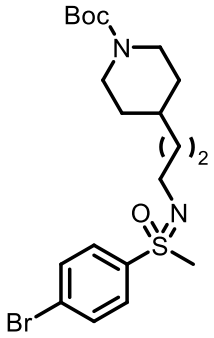
132.9, 130.4, 128.2, 61.8, 45.8, 45.4, 41.9. HRMS (TOF, ES+) $C_{11}H_{18}BrN_2OS$ $[M+H]^+$ calc. 305.0318, found 305.0318.



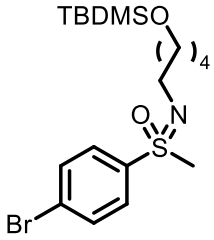
(4-bromophenyl)(dodec-9-yn-1-ylimino)(methyl)-λ⁶-sulfanone (13). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.3 mg, 0.13 mmol) and 9-dodecyn-1-ol to give the product as a gold oil after purification via column chromatography (0-65% EtOAc in hexanes) (20.5 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.73 (m, 2H), 7.72 – 7.66 (m, 2H), 3.08 (s, 3H), 2.92 (dt, *J* = 12.1, 7.2 Hz, 1H), 2.73 (dt, *J* = 12.1, 7.2 Hz, 1H), 2.18 – 2.06 (m, 4H), 1.58 – 1.49 (m, 2H), 1.48 – 1.39 (m, 2H), 1.38 – 1.20 (m, 8H), 1.09 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 132.9, 130.4, 128.2, 81.7, 79.7, 45.3, 43.9, 32.8, 29.4, 29.2, 29.2, 28.9, 27.3, 18.8, 14.5, 12.5. HRMS (TOF, ES+) $C_{19}H_{29}BrNOS$ $[M+H]^+$ calc. 398.1148, found 398.1137.



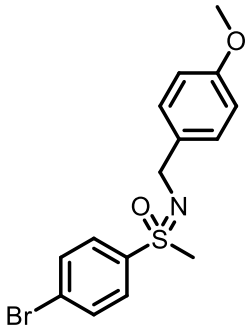
(4-bromophenyl)(methyl)(3-(*N*-phthalimido)propylimino)-λ⁶-sulfanone (14). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.4 mg, 0.13 mmol) and *N*-(3-hydroxypropyl)phthalimide to give the product as a clear residue after column chromatography (0-100% EtOAc in hexanes) (26.3 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 2H), 7.78 – 7.74 (m, 2H), 7.71 – 7.65 (m, 4H), 3.87 – 3.70 (m, 2H), 3.03 (s, 3H), 3.02 (dt, *J* = 12.4, 6.7 Hz, 1H), 2.84 (dt, *J* = 12.4, 6.6 Hz, 1H), 1.92 (app. quintet, *J* = 6.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 138.5, 133.9, 132.9, 132.3, 130.4, 128.4, 123.2, 45.0, 41.1, 36.4, 31.0. HRMS (TOF, ES+) $C_{18}H_{18}BrN_2O_3S$ $[M+H]^+$ calc. 421.0216, found 421.0215.



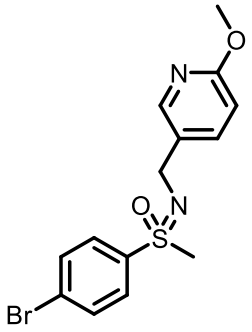
***tert*-butyl 4-(3-(((4-bromophenyl)(methyl)(oxo)-λ^6-sulfaneylidene)amino)propyl)piperidine-1-carboxylate (15).** Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ^6-sulfanone (**5**) (30.0 mg, 0.13 mmol) and N-(*tert*-butoxycarbonyl)-4-piperidinpropanol to afford the product as a gold oil after column chromatography (0-90% EtOAc in hexanes) (34.9 mg, 59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.71 – 7.65 (m, 2H), 4.02 (s, 2H), 3.06 (s, 3H), 2.90 (dt, *J* = 12.1, 7.1 Hz, 1H), 2.72 (dt, *J* = 12.1, 7.2 Hz, 1H), 2.60 (t, *J* = 12.1 Hz, 2H), 1.65 – 1.48 (m, 4H), 1.42 (s, 9H), 1.37 – 1.27 (m, 1H), 1.27 – 1.18 (m, 2H), 1.10 – 0.95 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0, 138.8, 132.8, 130.4, 128.2, 79.2, 45.2, 44.2 (bs), 44.1, 35.9, 34.1, 32.3, 29.9, 28.6. HRMS (TOF, ES+) $C_{20}H_{32}BrN_2O_3S$ $[M+H]^+$ calc. mass 459.1312, found 459.1306.



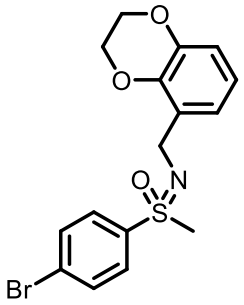
(4-bromophenyl)((5-((isopropyldimethylsilyl)oxy)pentyl)imino)(methyl)-λ^6-sulfanone (16). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ^6-sulfanone (**5**) (30.0 mg, 0.13 mmol) and 5-(*tert*-butyldimethlsilyoxy)-1-pentanol to afford the product as a gold oil after column chromatography (0-40% EtOAc in hexanes) (40.1 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.72 (m, 2H), 7.71 – 7.65 (m, 2H), 3.57 (t, *J* = 6.6 Hz, 2H), 3.07 (s, 3H), 2.93 (dt, *J* = 12.0, 7.1 Hz, 1H), 2.73 (dt, *J* = 12.0, 7.2 Hz, 1H), 1.61 – 1.43 (m, 4H), 1.39 – 1.28 (m, 2H), 0.88 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 132.8, 130.4, 128.2, 63.3, 45.3, 43.9, 32.6 (d, *J* = 9.2 Hz), 26.1, 23.5, 18.5, -5.1. HRMS (TOF, ES+) $C_{18}H_{33}BrNO_2SiS$ $[M+H]^+$ calc. mass 434.1179, found 434.1176.



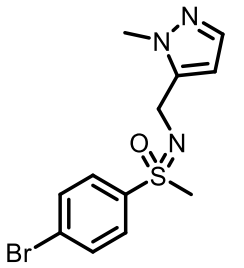
(4-bromophenyl)((4-methoxybenzyl)imino)(methyl)-λ⁶-sulfanone (17). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.0 mg, 0.13 mmol) and p-anisyl alcohol to afford the product as a gold oil after column chromatography (0-40% EtOAc in hexanes) (21.8 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.72 (m, 2H), 7.71 – 7.63 (m, 2H), 7.25 – 7.19 (m, 2H), 6.85 – 6.78 (m, 2H), 4.13 (d, *J* = 14.0 Hz, 1H), 3.90 (d, *J* = 13.9 Hz, 1H), 3.78 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 138.9, 133.1, 132.8, 130.4, 129.0, 128.2, 113.9, 55.4, 46.9, 45.5. HRMS (TOF, ES+) $C_{15}H_{17}BrNO_2S$ $[M+H]^+$ calc. mass 354.0158, found 354.0159.



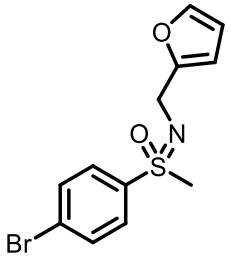
(4-bromophenyl)(((6-methoxypyridin-3-yl)methyl)imino)(methyl)-λ⁶-sulfanone (18). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ⁶-sulfanone (**5**) (30.0 mg, 0.13 mmol) and (6-methoxypyridin-3-yl)methanol to afford the product as a clear oil after column chromatography (0-100% EtOAc in hexanes) and RP-HPLC (5-45% MeCN in 0.1% aqueous TFA) (13.7 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 2.5, 0.8 Hz, 1H), 7.79 – 7.72 (m, 2H), 7.72 – 7.66 (m, 2H), 7.59 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.69 (dd, *J* = 8.5, 0.8 Hz, 1H), 4.10 (d, *J* = 14.1 Hz, 1H), 3.90 (s, 3H), 3.89 (d, *J* = 14.1 Hz, 1H), 3.13 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 145.8, 138.9, 138.6, 133.0, 130.4, 129.2, 128.5, 110.8, 53.6, 45.4, 44.5. HRMS (TOF, ES+) $C_{14}H_{16}BrN_2O_2S$ $[M+H]^+$ calc. mass 355.0110, found 355.0114.



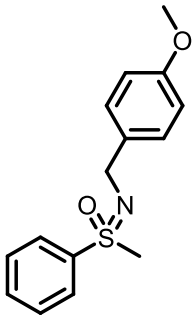
(4-bromophenyl)(((2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl)methyl)imino)(methyl)-λ^6-sulfanone (19). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ^6-sulfanone (**5**) (30.0 mg, 0.13 mmol) and (2,3-dihydrobenzo[*b*][1,4]dioxin-5-yl) to afford the product as a gold oil after column chromatography (0-80% EtOAc in hexanes) (25.0 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.73 (m, 2H), 7.69 – 7.62 (m, 2H), 7.03 (dd, *J* = 7.4, 1.8 Hz, 1H), 6.78 (t, *J* = 7.7 Hz, 1H), 6.73 (dd, *J* = 8.2, 1.8 Hz, 1H), 4.24 – 4.14 (m, 4H), 4.12 (d, *J* = 14.7 Hz, 1H), 4.01 (d, *J* = 14.8 Hz, 1H), 3.13 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 141.0, 138.9, 132.7, 130.5, 129.5, 128.1, 121.3, 120.8, 115.9, 64.3, 64.2, 45.6, 41.5. HRMS (TOF, ES+) $C_{16}H_{17}BrNO_3S$ $[M+H]^+$ calc. mass 382.0107, found 382.0106.



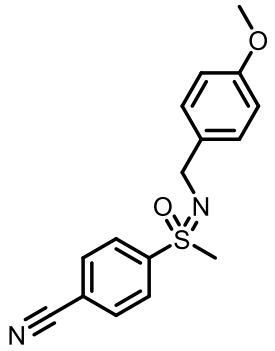
(4-bromophenyl)(((1-methyl-1H-pyrazol-5-yl)methyl)imino)(methyl)-λ^6-sulfanone (20). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ^6-sulfanone (**5**) (30.0 mg, 0.13 mmol) and (1-methyl-1H-pyrazol-5-yl)methanol to afford the product as a clear oil after column chromatography (100% EtOAc wash, then 0-2% (MeOH + 1% NH_4OH) in DCM) and RP-HPLC (5-45% MeCN in 0.1% aqueous TFA) (10.5 mg, 25%).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.65 (m, 4H), 7.31 (d, *J* = 1.8 Hz, 1H), 6.02 (d, *J* = 1.8 Hz, 1H), 4.15 (d, *J* = 14.7 Hz, 1H), 3.98 (d, *J* = 14.7 Hz, 1H), 3.87 (s, 3H), 3.10 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.2, 138.4, 138.0, 133.0, 130.2, 128.6, 105.4, 45.5, 38.0, 36.7. HRMS (TOF, ES+) $C_{12}H_{15}BrN_3OS$ $[M+H]^+$ calc. mass 328.0114, found 328.0114.



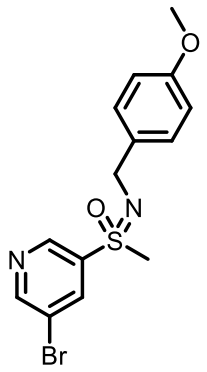
(4-bromophenyl)((furan-2-ylmethyl)imino)(methyl)-λ^6-sulfanone (21). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ^6-sulfanone (**5**) (30.0 mg, 0.13 mmol) and furfuryl alcohol to afford the product as a gold oil after column chromatography (0-70% EtOAc in hexanes) (11.2 mg, 28%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.73 (m, 2H), 7.72 – 7.62 (m, 2H), 7.29 (d, *J* = 1.0 Hz, 1H), 6.24 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.10 (d, *J* = 3.2 Hz, 1H), 4.15 (d, *J* = 14.9 Hz, 1H), 3.99 (d, *J* = 14.9 Hz, 1H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 141.9, 138.6, 132.9, 130.4, 128.4, 110.4, 106.8, 45.5, 40.3. HRMS (TOF, ES+) $C_{12}H_{13}BrNO_2S$ $[M+H]^+$ calc. mass 313.9845, found 313.9846.



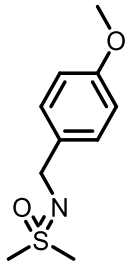
((4-methoxybenzyl)imino)(methyl)(phenyl)- λ^6-sulfanone (22). Followed General Procedure B with imino(methyl)(phenyl)- λ^6-sulfanone (30.0 mg, 0.193 mmol) and (4-methoxyphenyl)methanol to give product as a colorless oil after purification by column chromatography (0-100% EtOAc in hexanes) (26.4 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.89 (m, 2H), 7.64 – 7.59 (m, 1H), 7.58 – 7.53 (m, 2H), 7.26 – 7.22 (m, 2H), 6.85 – 6.79 (m, 2H), 4.14 (d, *J* = 14.0 Hz, 1H), 3.92 (d, *J* = 14.0 Hz, 1H), 3.77 (s, 3H), 3.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 139.3, 133.2, 133.0, 129.5, 128.9, 128.7, 113.8, 55.3, 46.8, 45.3. HRMS (TOF, ES+) $C_{15}H_{18}NO_2S$ $[M+H]^+$ calc. mass 276.1053, found 276.1053.



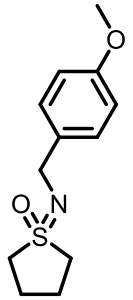
4-(N-(4-methoxybenzyl)-*S*-methylsulfonimidoyl)benzonitrile (23). Followed General Procedure B with 4-(*S*-methylsulfonimidoyl)benzonitrile (30.0 mg, 0.167 mmol) and (4-methoxyphenyl)methanol to give product as a colorless oil after purification by column chromatography (0-100% EtOAc in hexanes) (10.6 mg, 21%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.98 (m, 2H), 7.85 – 7.78 (m, 2H), 7.22 – 7.15 (m, 2H), 6.83 – 6.75 (m, 2H), 4.17 (d, *J* = 14.0 Hz, 1H), 3.93 (d, *J* = 14.0 Hz, 1H), 3.77 (s, 3H), 3.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 144.5, 133.3, 132.3, 129.4, 129.1, 117.4, 116.9, 113.9, 55.4, 46.8, 45.1. HRMS (TOF, ES+) $C_{16}H_{17}N_2O_2S$ $[M+H]^+$ calc. mass 301.1005, found 301.1003.



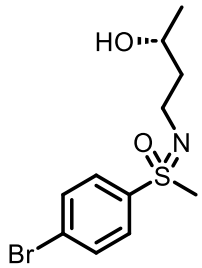
(5-bromopyridin-3-yl)((4-methoxybenzyl)imino)(methyl)- λ^6-sulfanone (24). Followed General Procedure B with (5-bromopyridin-3-yl)(imino)(methyl)- λ^6-sulfanone (**31**) (30.0 mg, 0.128 mmol) and (4-methoxyphenyl)methanol to give product as a colorless oil after purification by column chromatography (0-100% EtOAc in hexanes) (30.6 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (d, *J* = 2.0 Hz, 1H), 8.82 (d, *J* = 2.2 Hz, 1H), 8.20 (t, *J* = 2.1 Hz, 1H), 7.21 – 7.14 (m, 2H), 6.81 – 6.75 (m, 2H), 4.18 (d, *J* = 13.9 Hz, 1H), 3.98 (d, *J* = 13.9 Hz, 1H), 3.77 (s, 3H), 3.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 154.6, 147.6, 138.9, 138.0, 132.1, 129.2, 121.3, 113.9, 55.4, 47.0, 45.8. HRMS (TOF, ES+) $C_{14}H_{16}BrN_2O_2S$ $[M+H]^+$ calc. mass 355.0110, found 355.0103.



((4-methoxybenzyl)imino)dimethyl-λ^6-sulfanone (25). Followed General Procedure B with iminodimethyl-λ^6-sulfanone (30.0 mg, 0.322 mmol) and (4-methoxyphenyl)methanol to give product as a colorless oil after purification by RP-HPLC (5-95% MeCN in 0.05% aqueous NH_4OH) (20.8 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 6.88 – 6.83 (m, 2H), 4.22 (s, 2H), 3.78 (s, 3H), 2.97 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 133.4, 129.0, 114.0, 55.4, 46.5, 42.7. HRMS (TOF, ES+) $C_{10}H_{16}NO_2S$ $[M+H]^+$ calc. mass 214.0896, found 214.0893.

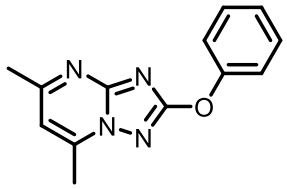


1-((4-methoxybenzyl)imino)tetrahydro-1H-1λ^6-thiophene 1-oxide (26). Followed General Procedure B with 1-iminotetrahydro-1H-1λ^6-thiophene 1-oxide (30.0 mg, 0.25 mmol) and (4-methoxyphenyl)methanol to give product as a colorless oil after purification by RP-HPLC (5-95% MeCN in 0.05% aqueous NH_4OH) (24.6 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H), 6.89 – 6.79 (m, 2H), 4.24 (s, 2H), 3.78 (s, 3H), 3.09 – 2.99 (m, 2H), 2.98 – 2.87 (m, 2H), 2.25 – 2.05 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 133.2, 129.2, 113.9, 55.4, 52.7, 47.8, 23.6. HRMS (TOF, ES+) $C_{12}H_{18}NO_2S$ $[M+H]^+$ calc. mass 240.1053, found 240.1053.



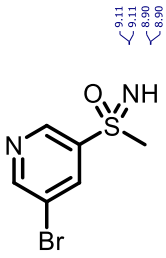
(4-bromophenyl)(((*R*)-3-hydroxybutyl)imino)(methyl)-λ^6-sulfanone (27). Followed General Procedure B with (4-bromophenyl)(imino)(methyl)-λ^6-sulfanone (**5**) (30.0 mg, 0.13 mmol) and (*R*)-(-)-1,3-butanediol to give a mixture of inseparable diastereomers as a clear oil after purification via RP-HPLC (18-51% MeCN in 0.05% aqueous NH_4OH) (13.5 mg, 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.74 – 7.68 (m, 2H), 4.05* (dqd, *J* = 9.0, 6.2, 2.9 Hz, 0.5 H), 3.99*

(m, 0.5 H), 3.33 (br. m, -O*H*, buried), 3.20* (ddd, *J* = 12.3, 5.4, 5.4 Hz, 0.5 H), 3.14* (ddd, *J* = 12.4, 9.0, 4.7 Hz, 0.5 H), 3.10* (s, 1.5 H), 3.09* (s. 1.5H), 2.97* (ddd, *J* = 12.3, 5.1, 5.1 Hz, 0.5 H), 2.87* (ddd, *J* = 12.4, 7.8, 5.1 Hz, 0.5 H), 1.70 – 1.52 (m, 2H), 1.19* (d, *J* = 6.2 Hz, 1.5 H), 1.18* (d, *J* = 6.2 Hz, 1.5H). *Denotes discernible diastereomeric signal. ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.1, 137.7, 133.1, 133.0, 130.4, 130.4, 128.7, 128.6, 68.6, 68.3, 45.2, 42.0, 41.9, 39.4, 39.4, 23.6, 23.5. Note: All diastereomeric ^{13}C NMR signals, except for the *S*-methyl peak, are shown as distinct peaks. HRMS (TOF, ES+) $C_{11}H_{17}BrNO_2S$ $[M+H]^+$ calc. 306.0158, found 306.0156.



5,7-dimethyl-2-phenoxy-[1,2,4]triazolo[1,5-*a*]pyrimidine (30). Followed General Procedure B with (5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)(imino)(2-phenoxyethyl)-λ^6-sulfanone (**29**) (30 mg, 0.091 mmol) and cyclopropanemethanol to give product as a tan solid after purification by column chromatography (3-100% EtOAc in hexanes) (10 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.37 (m, 4H), 7.23 – 7.19 (m, 1H), 6.76 (s, 1H), 2.71 (s, 3H), 2.61 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 164.2, 154.5, 154.1, 146.3, 129.6, 125.2, 120.3, 110.5, 25.0, 17.1. HRMS (TOF, ES+) $C_{13}H_{13}N_4O$ $[M+H]^+$ calc. mass 241.1084, found 241.1081. m.p. = 174-176 °C.

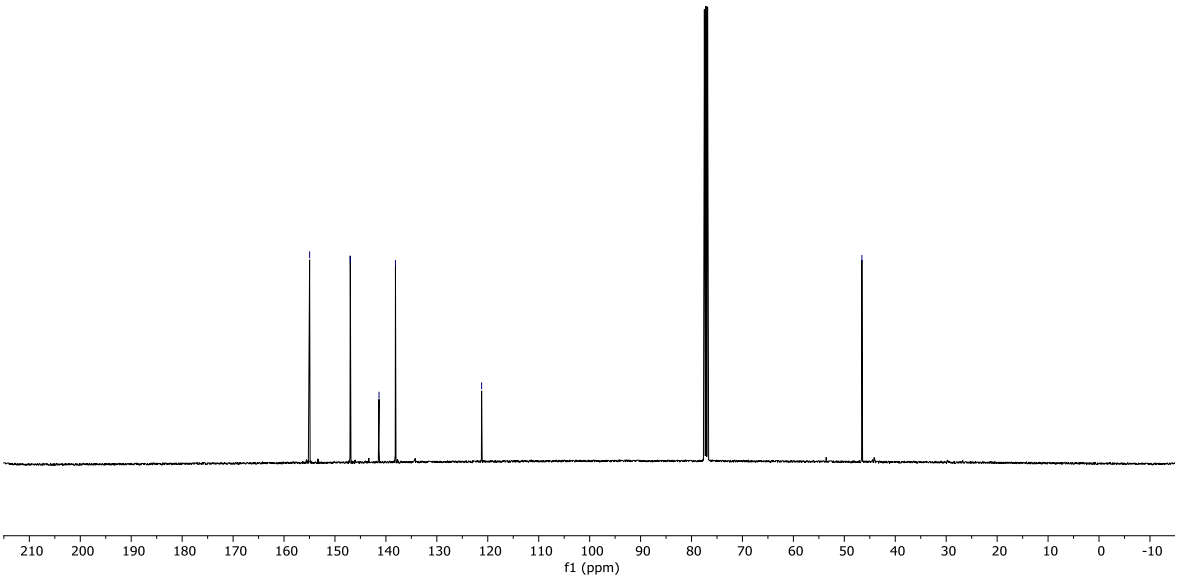
Copies of ^{1}H and ^{13}C NMR Spectra

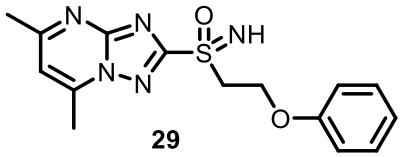


31

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

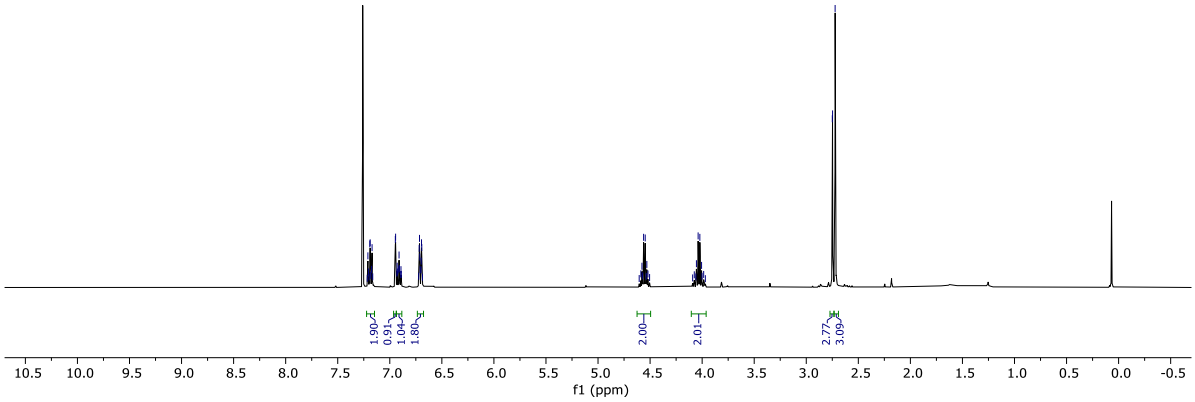
^{13}C NMR (101 MHz, $CDCl_3$)



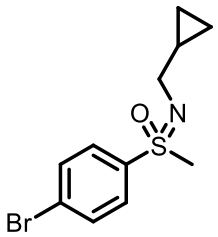


29

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

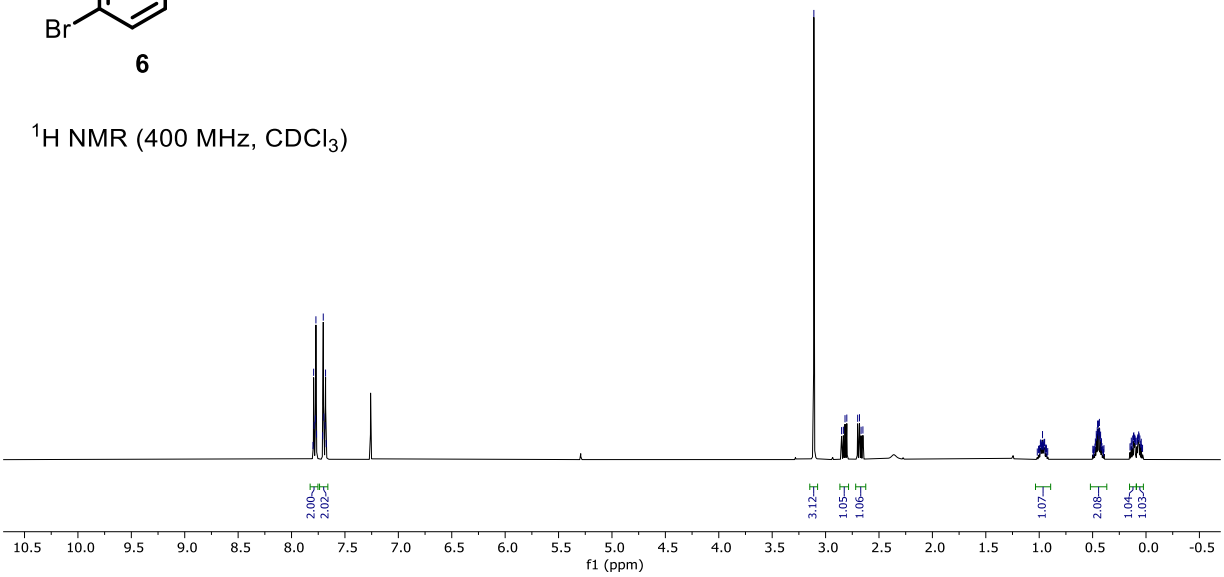


^{13}C NMR (101 MHz, $CDCl_3$)

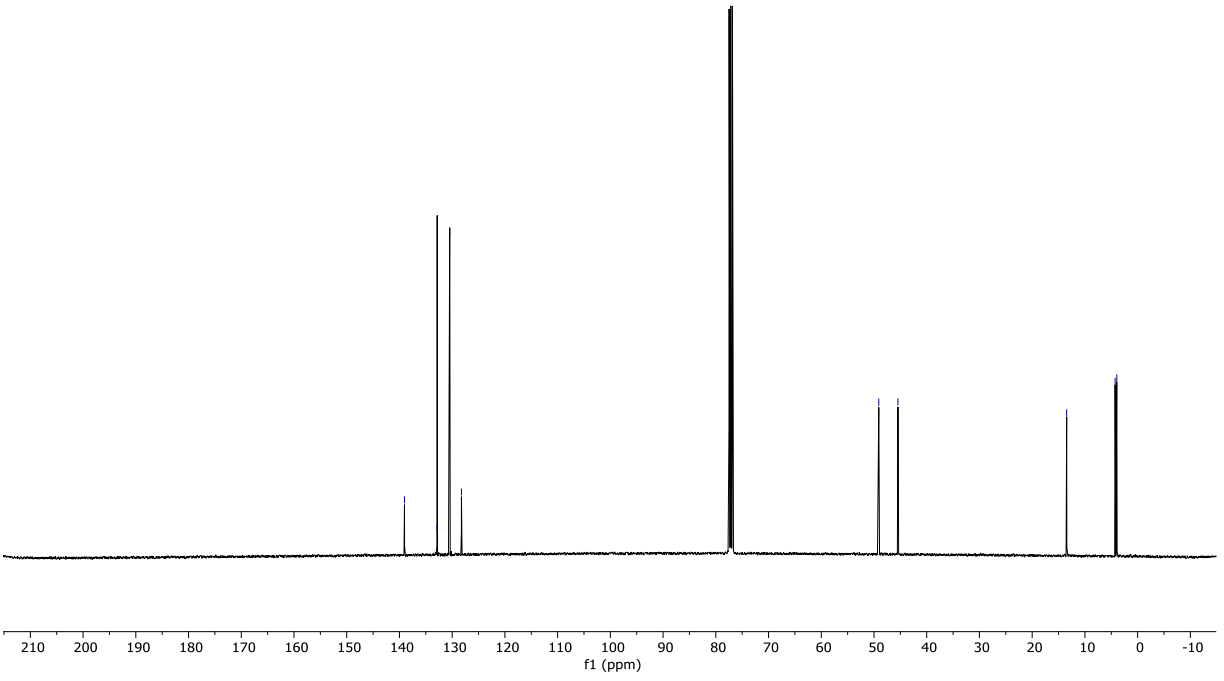


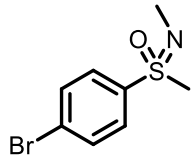
6

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



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

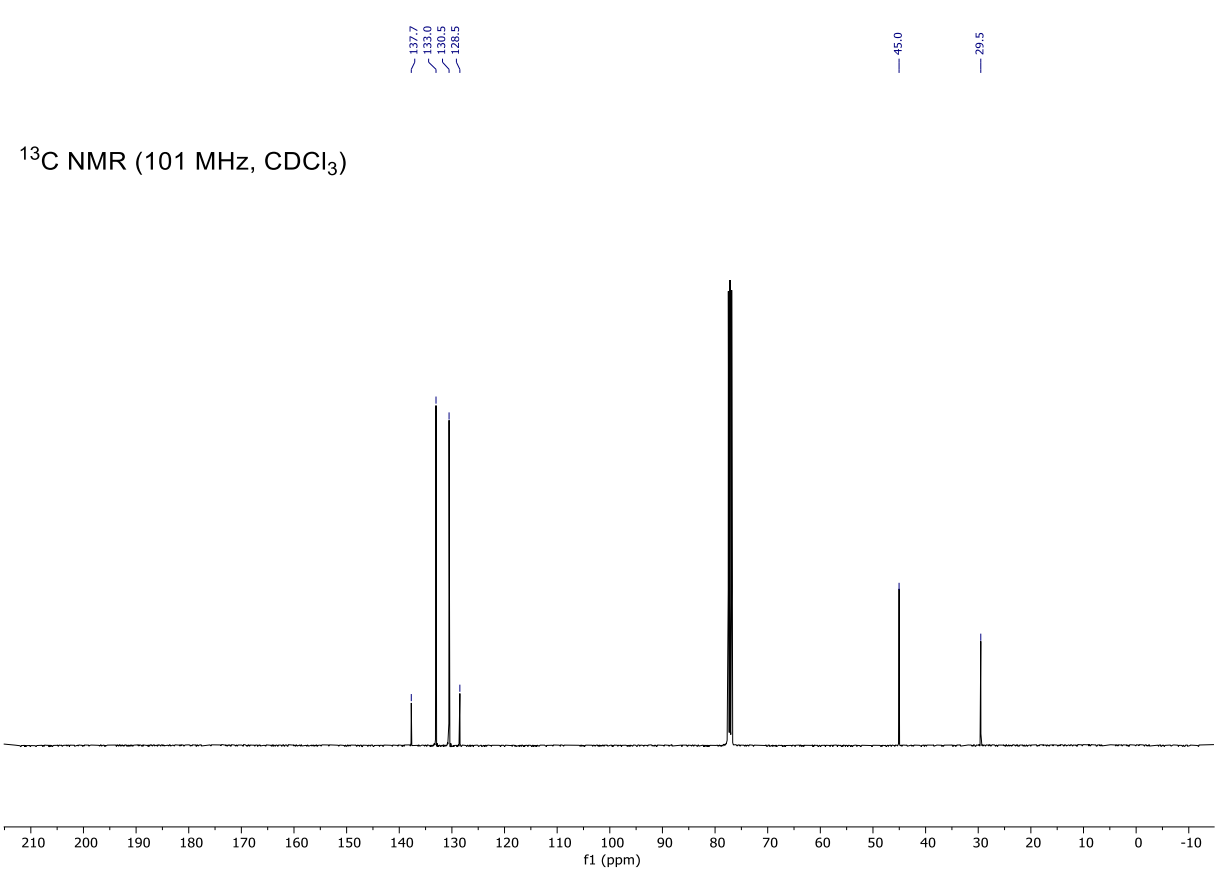


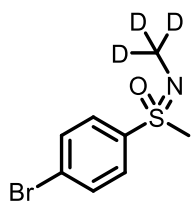


7

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

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

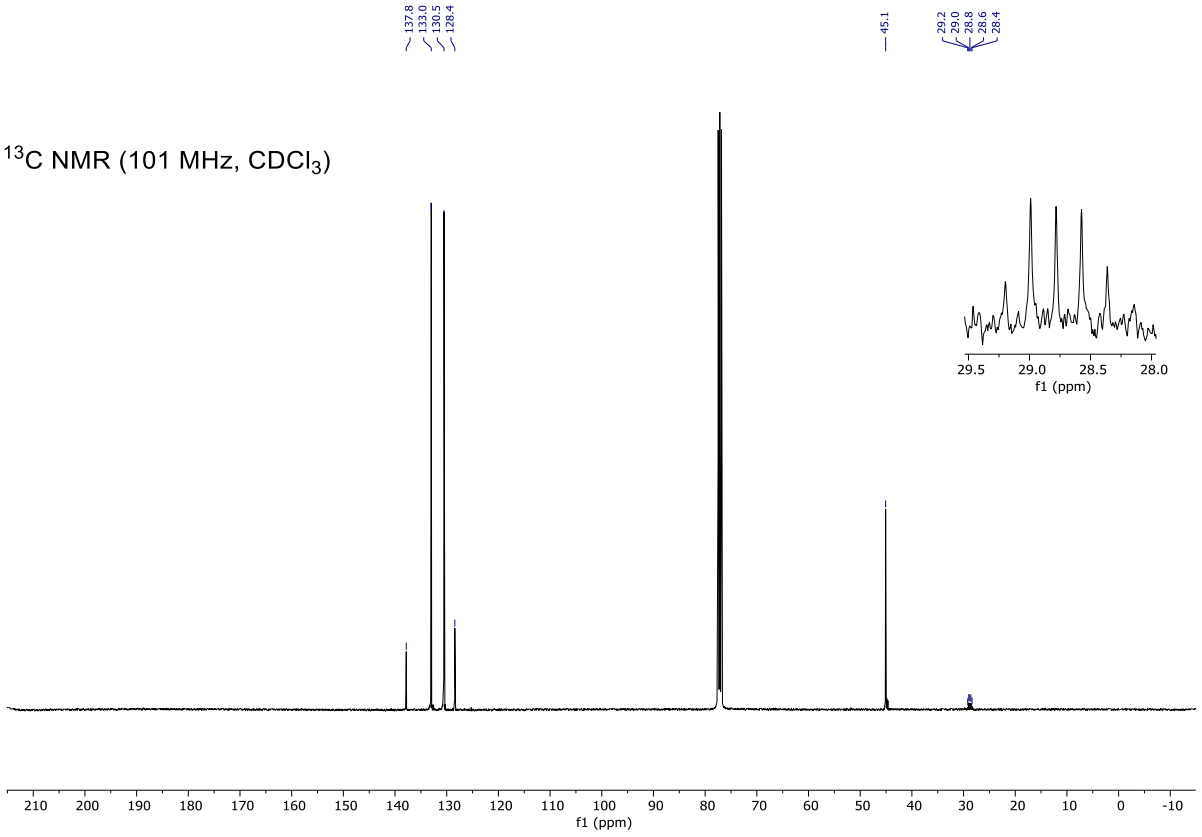


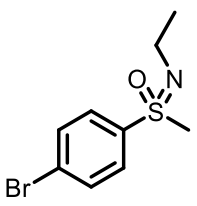


8

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

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

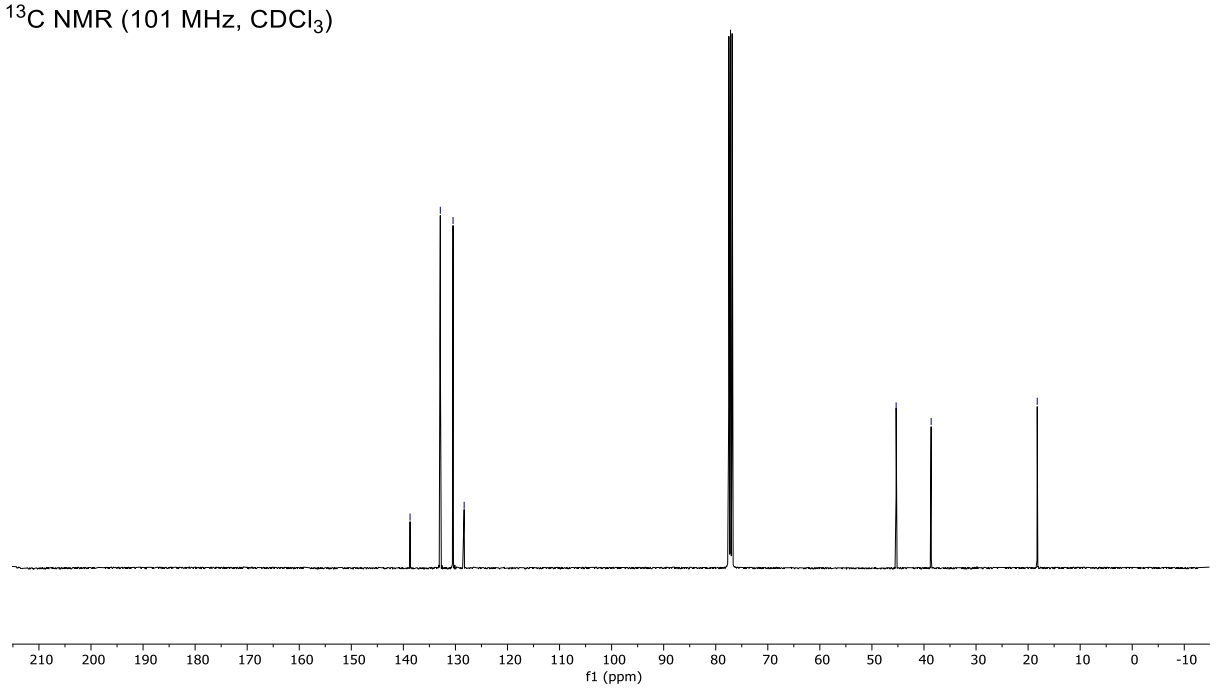


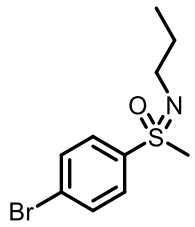


9

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

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

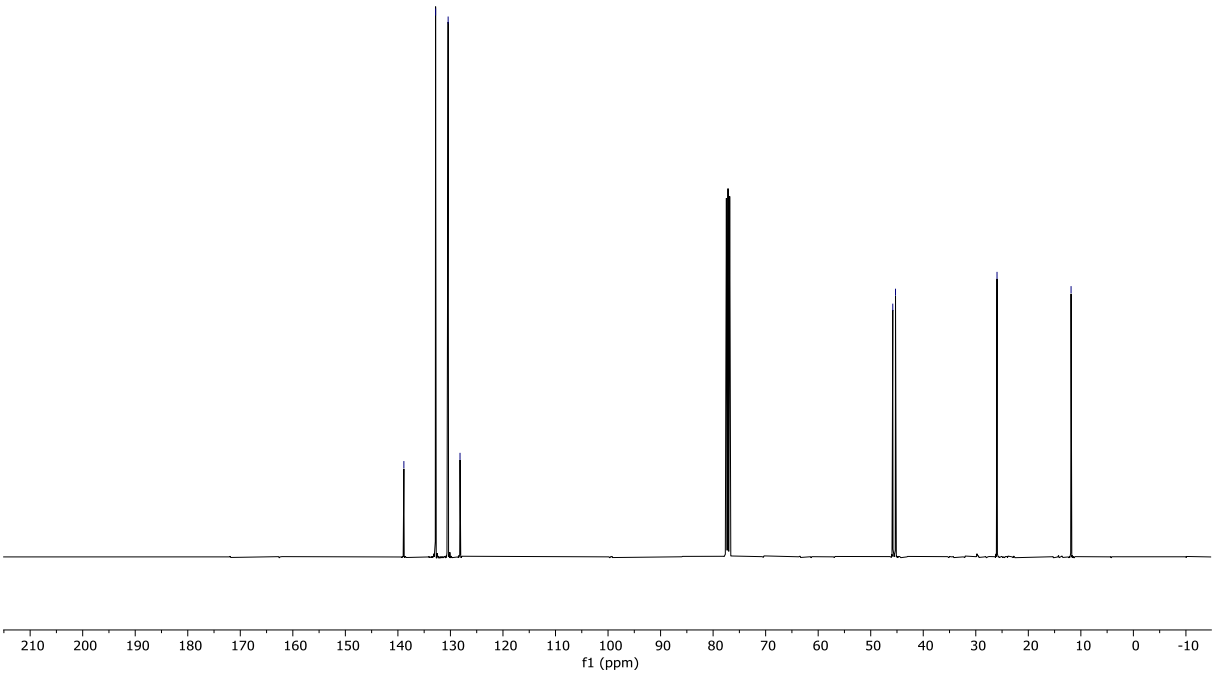


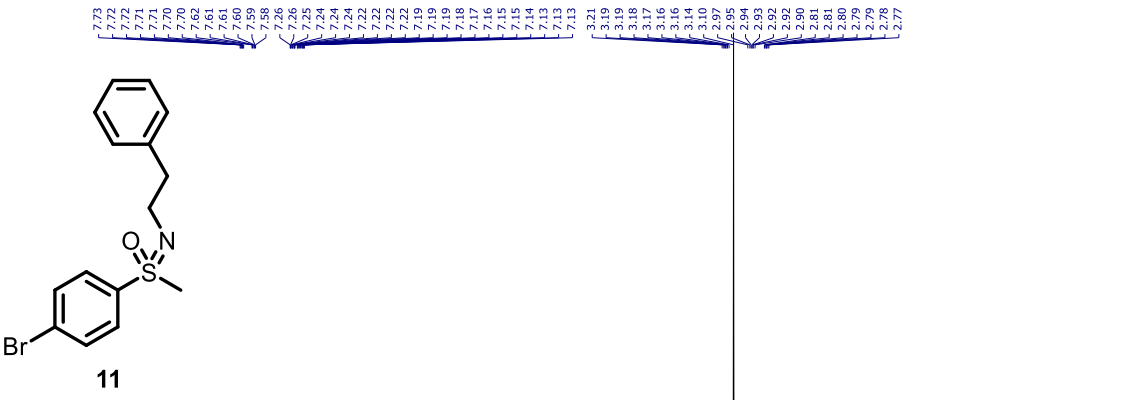


10

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

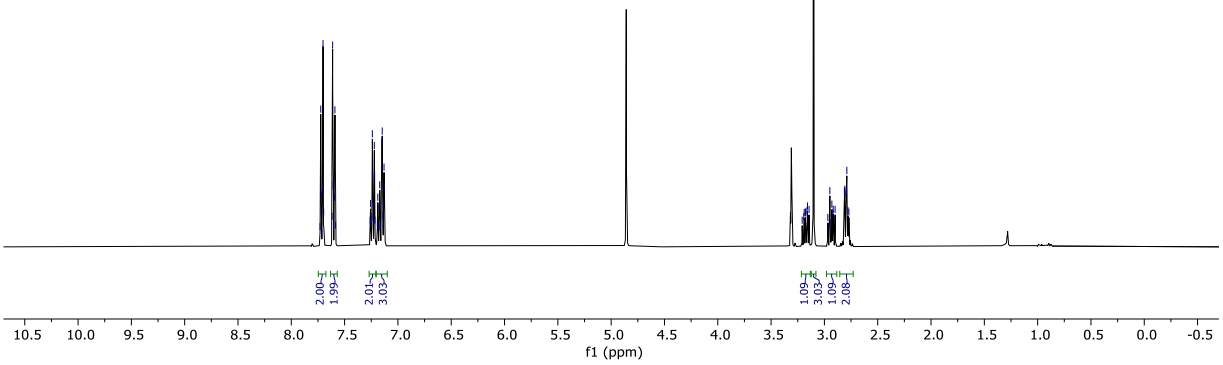
^{13}C NMR (101 MHz, $CDCl_3$)



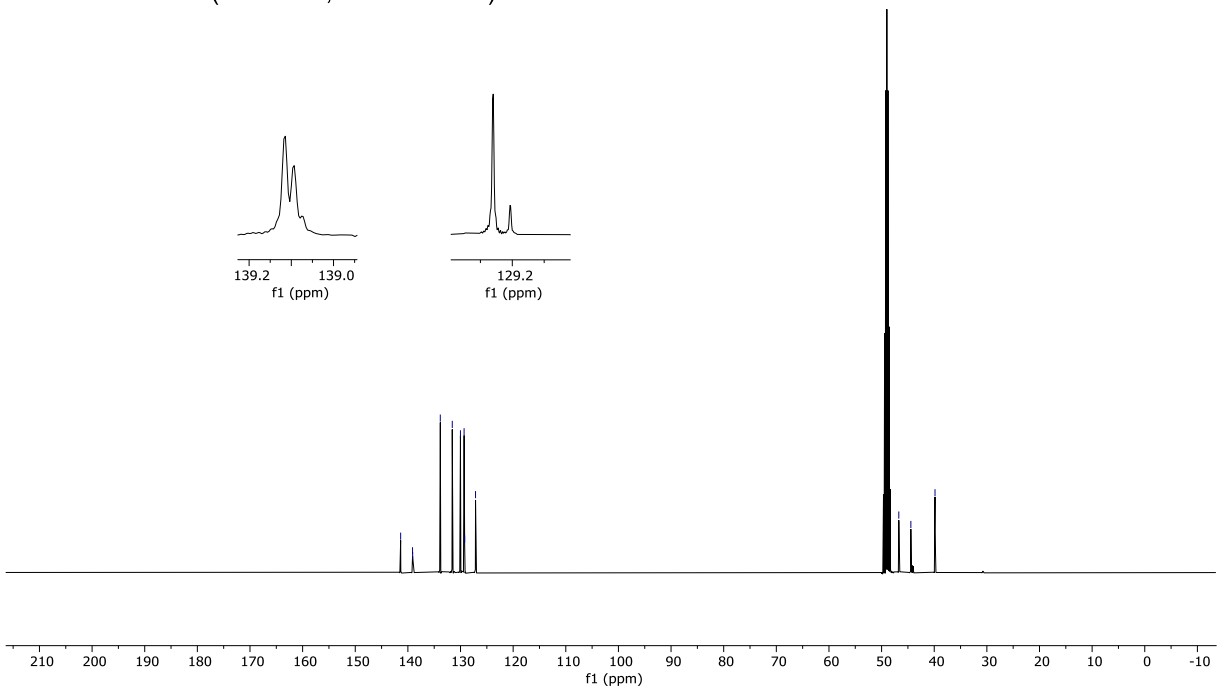


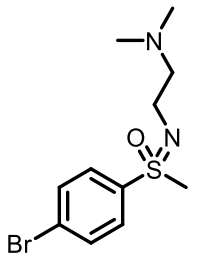
11

^{1}H NMR (400 MHz, methanol-*d*4)



^{13}C NMR (101 MHz, methanol-*d*4)

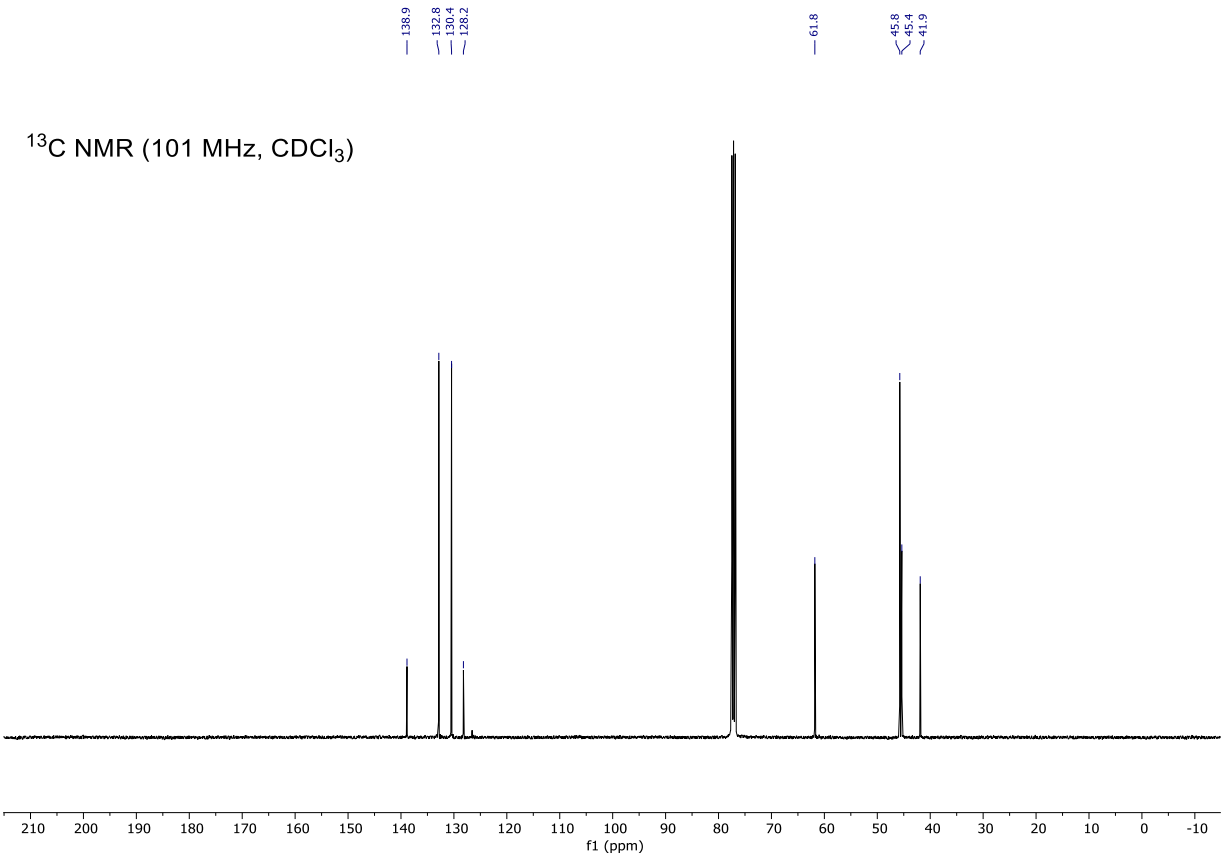


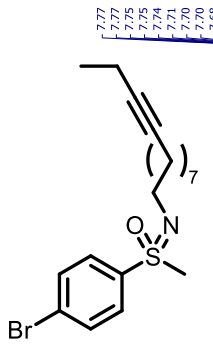


12

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

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

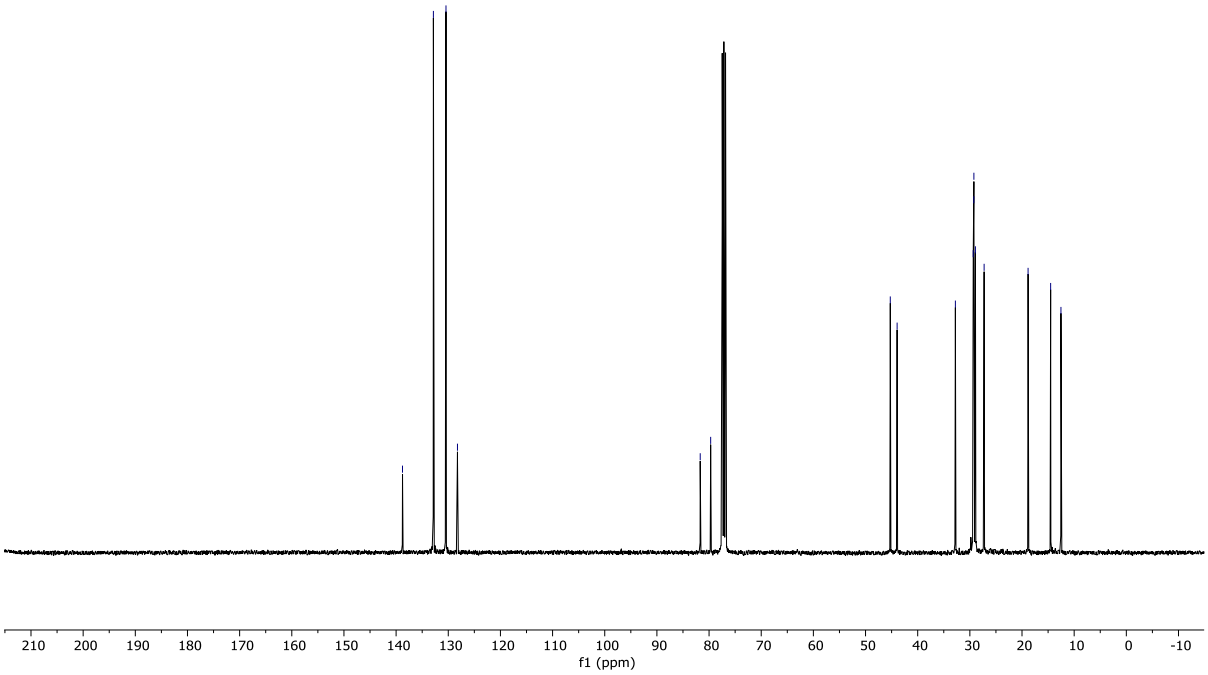


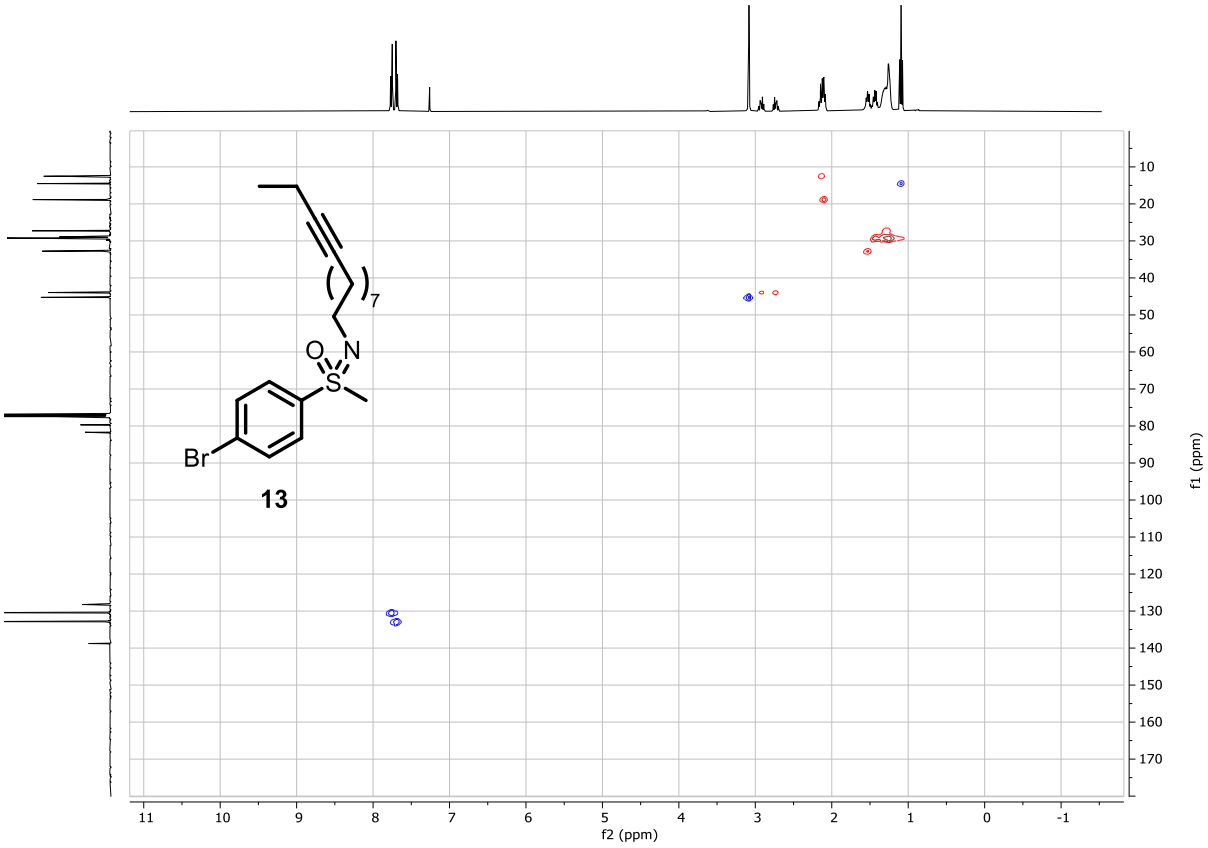


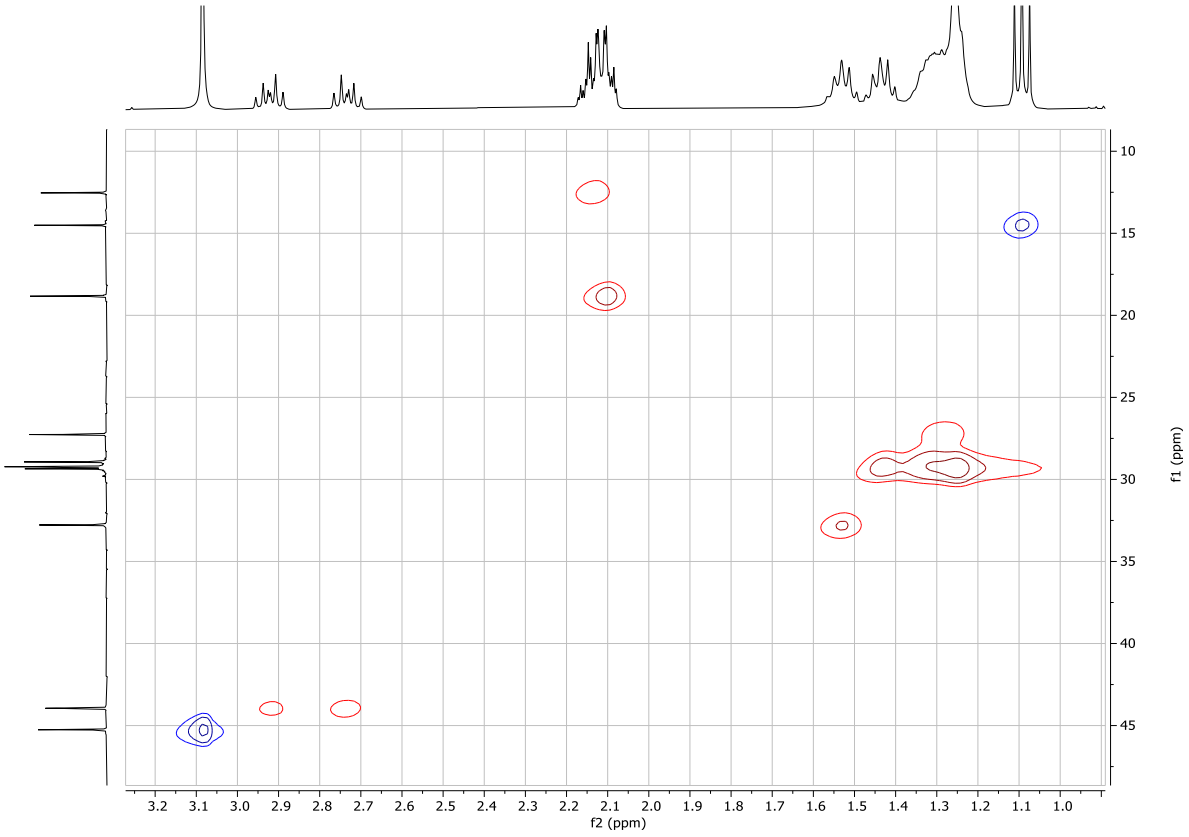
13

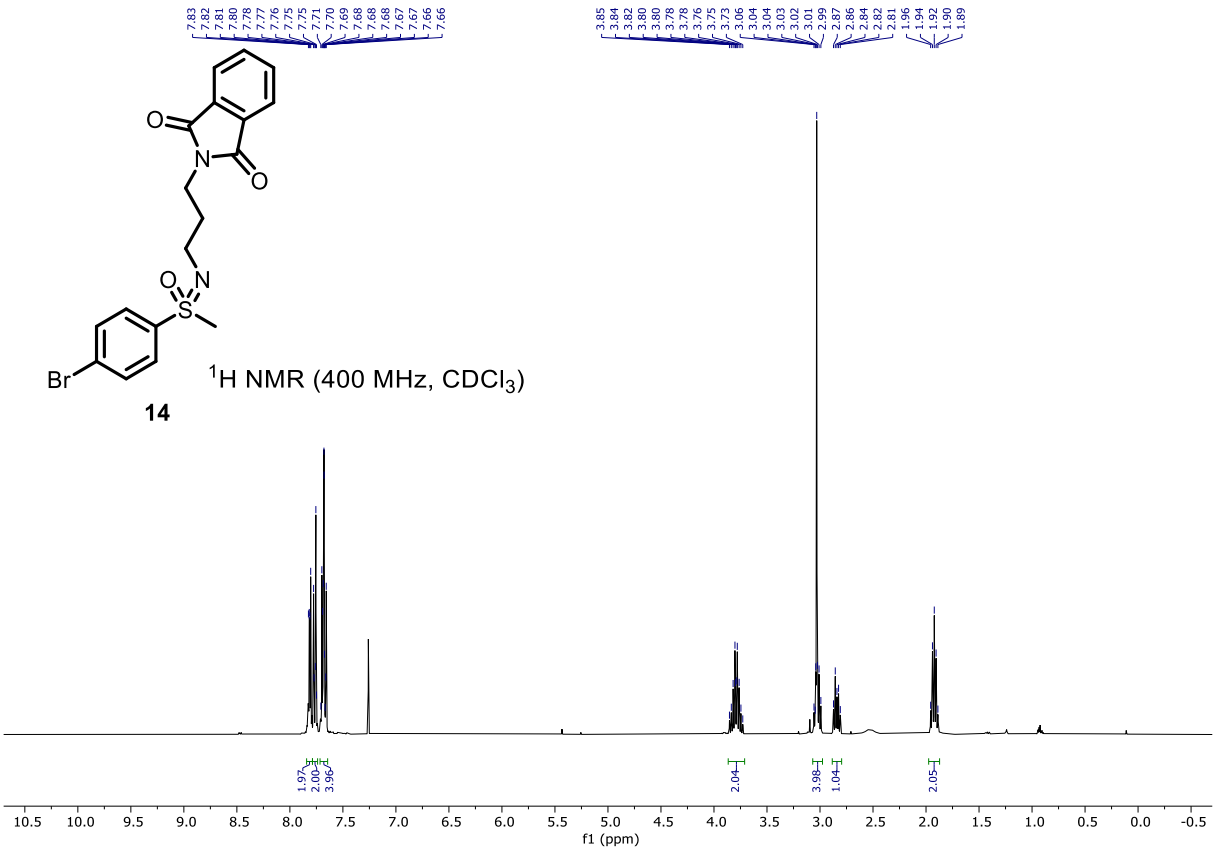
^{1}H NMR (400 MHz, $CDCl_3$)

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

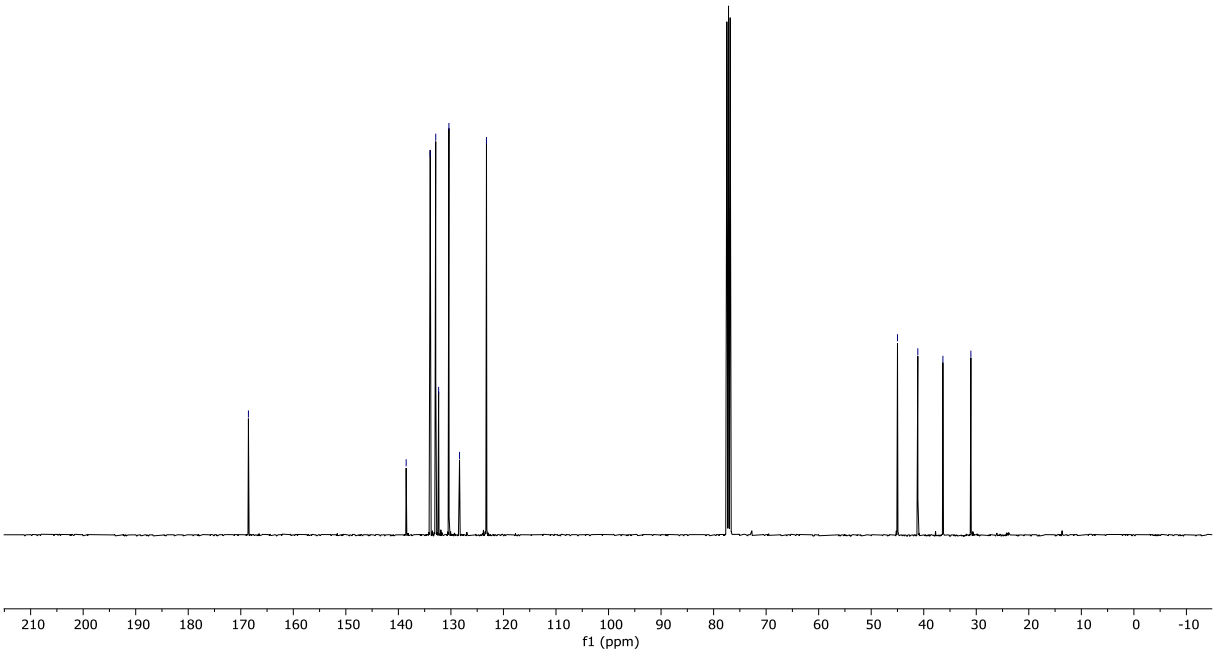


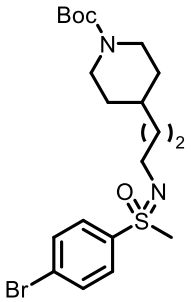

Br
13
f2 (ppm)
f1 (ppm)


f2 (ppm)
f1 (ppm)



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

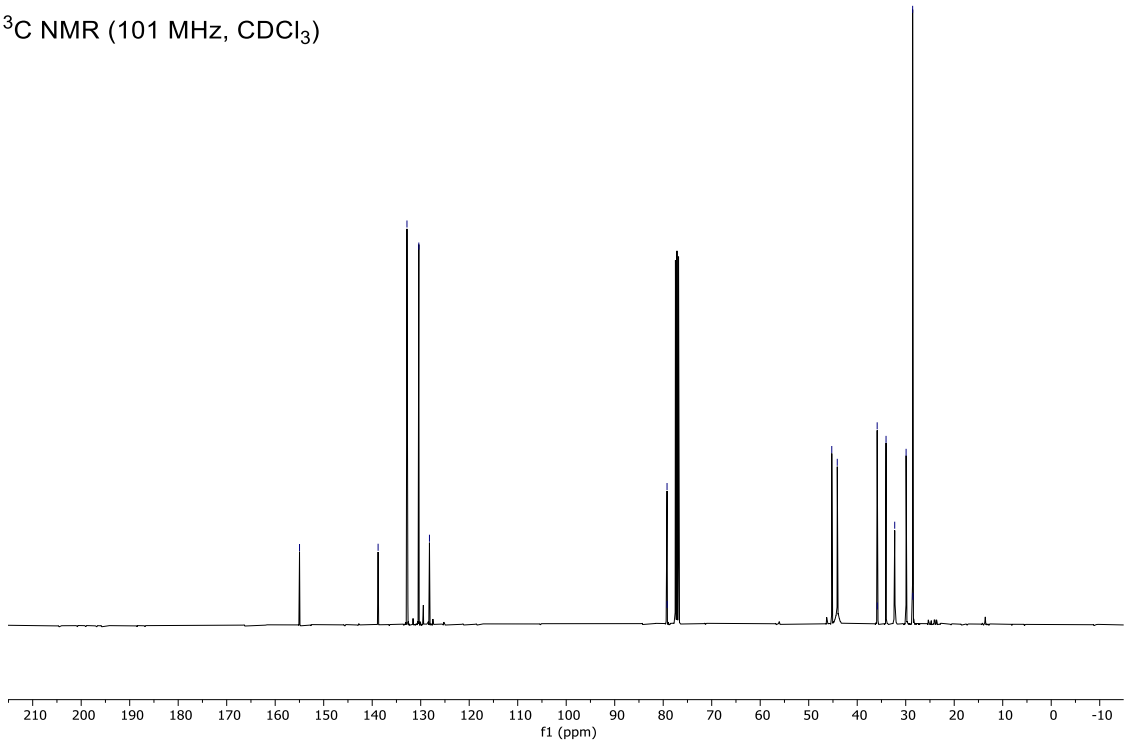


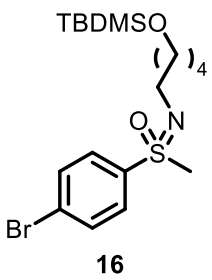


15

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

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

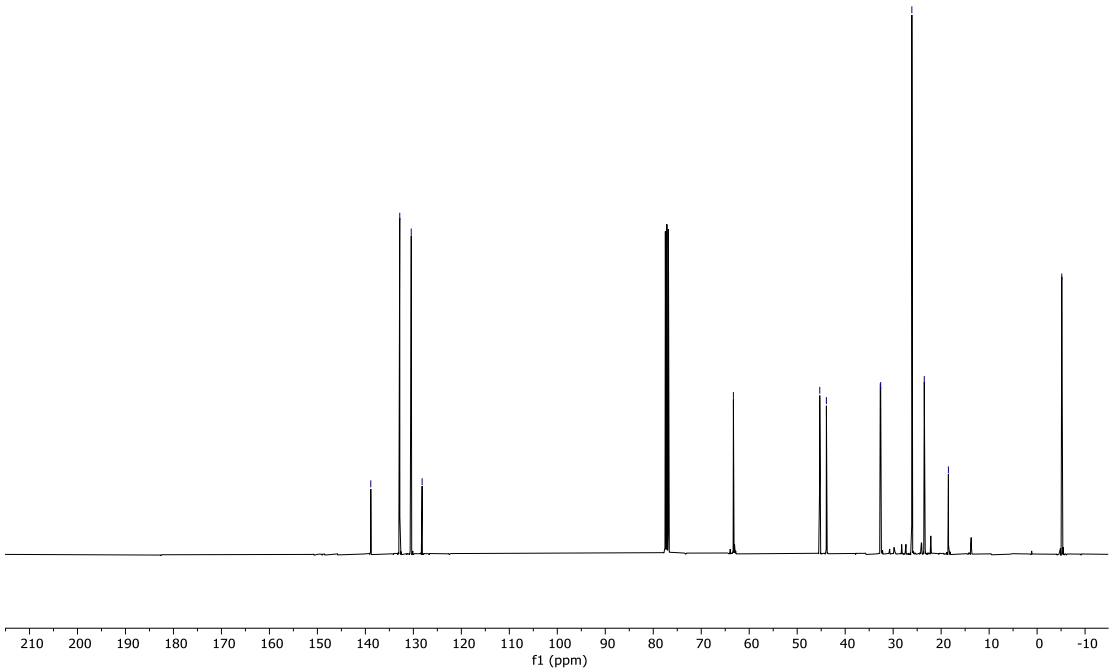


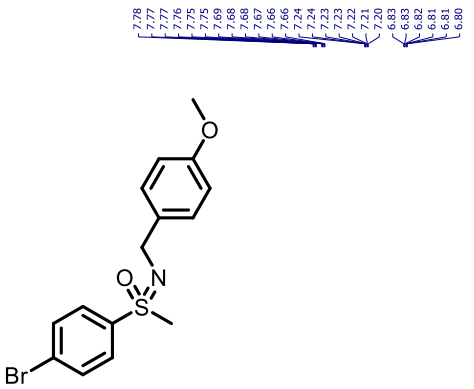


16

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

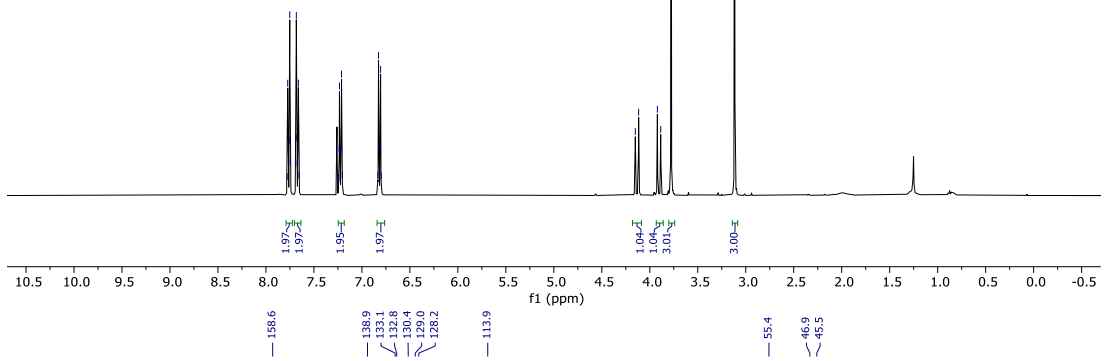
^{13}C NMR (101 MHz, $CDCl_3$)



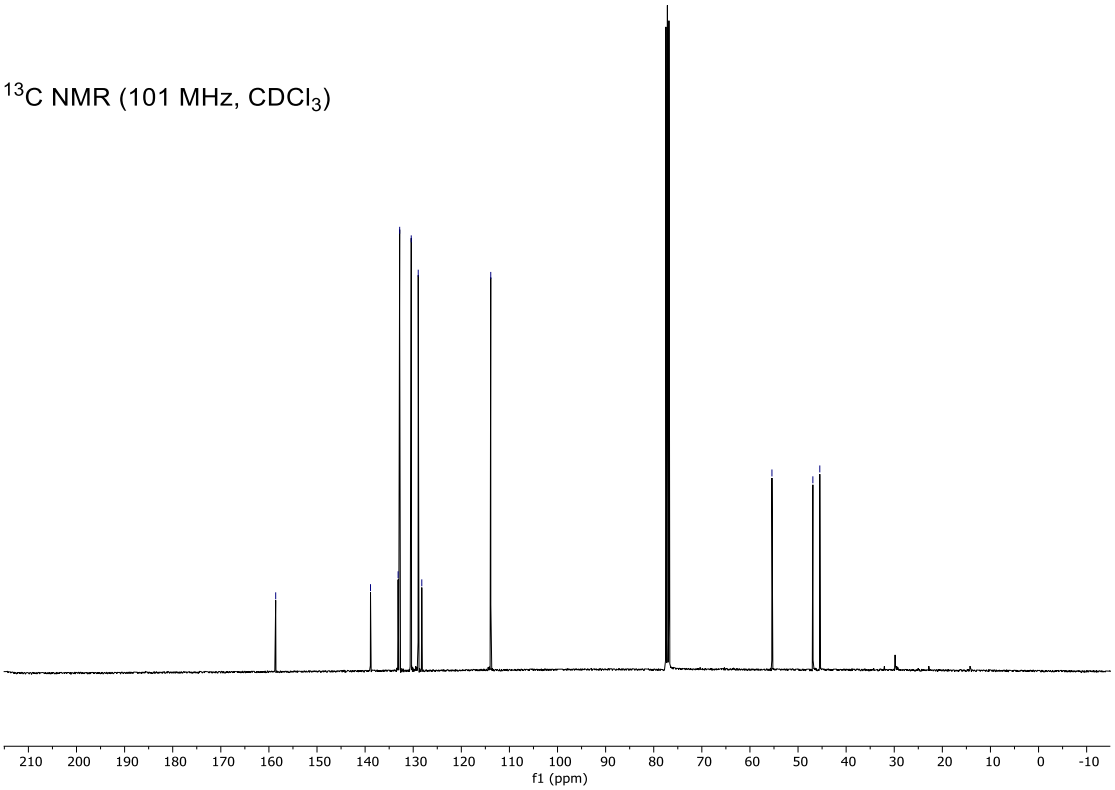


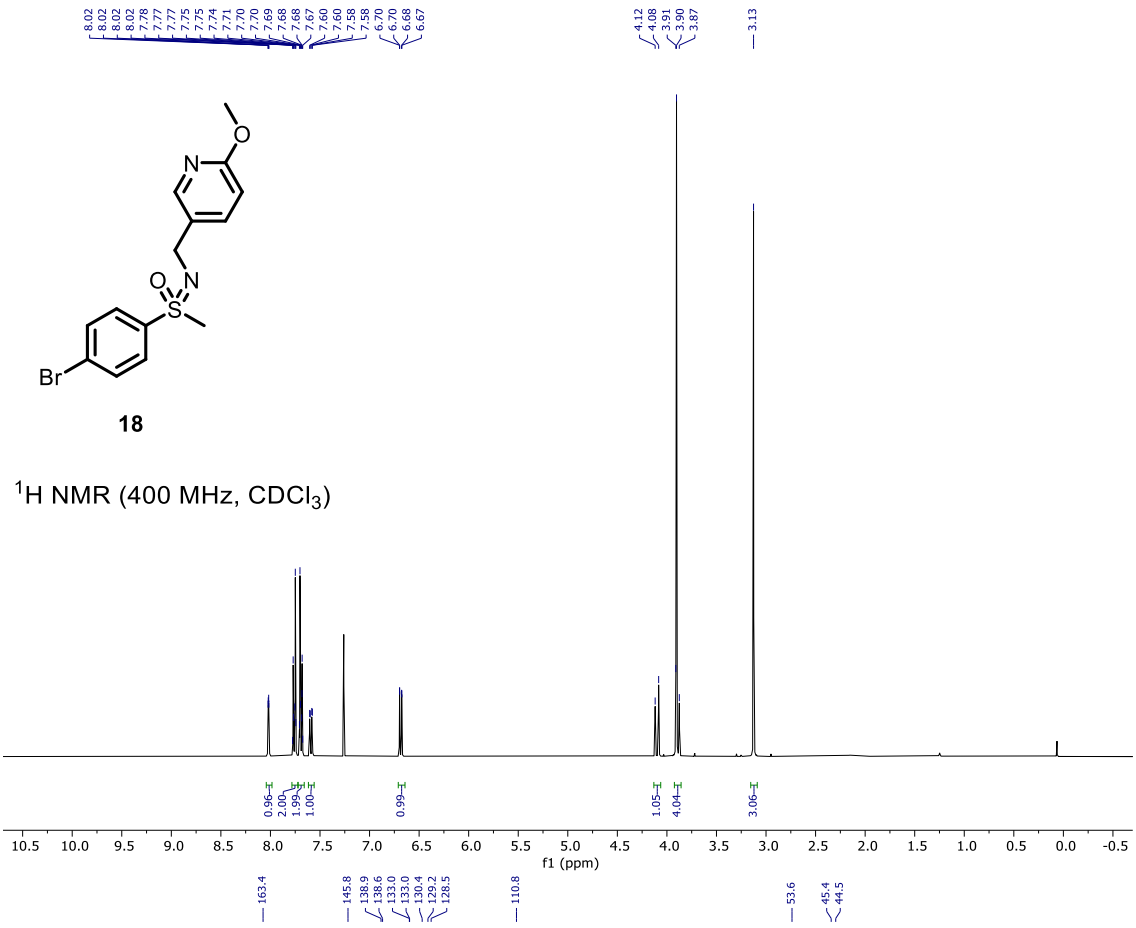
17

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



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

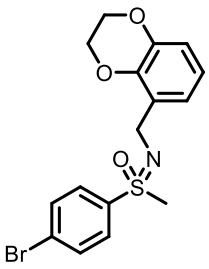




18

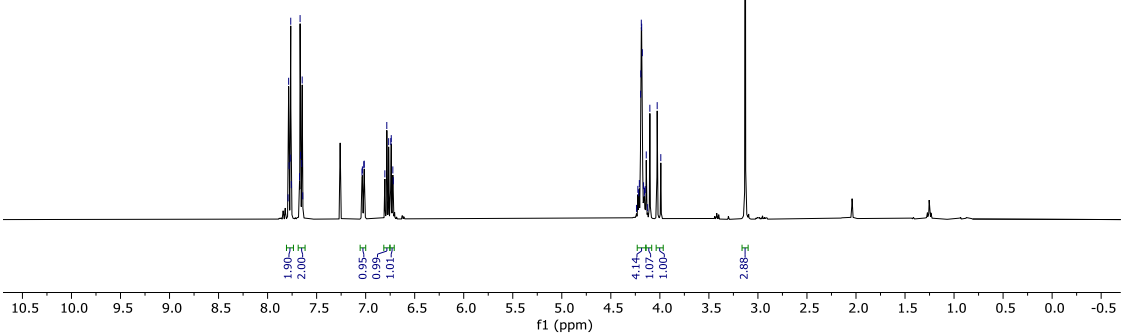
^{1}H NMR (400 MHz, $CDCl_3$)

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

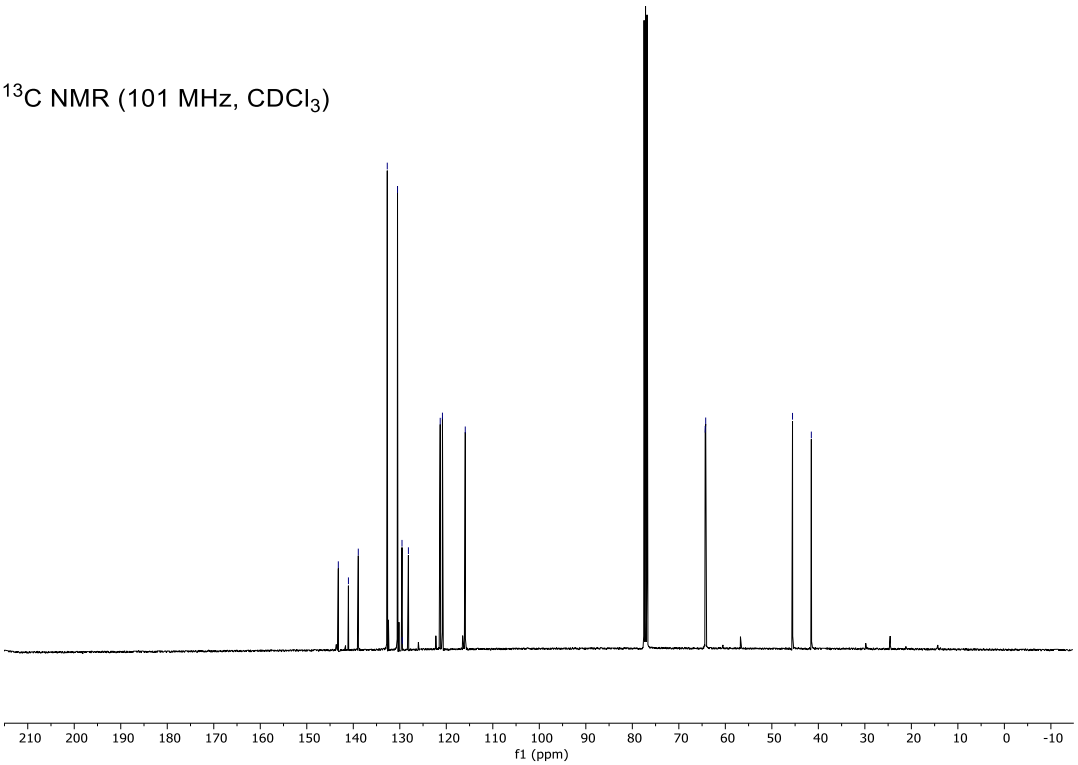


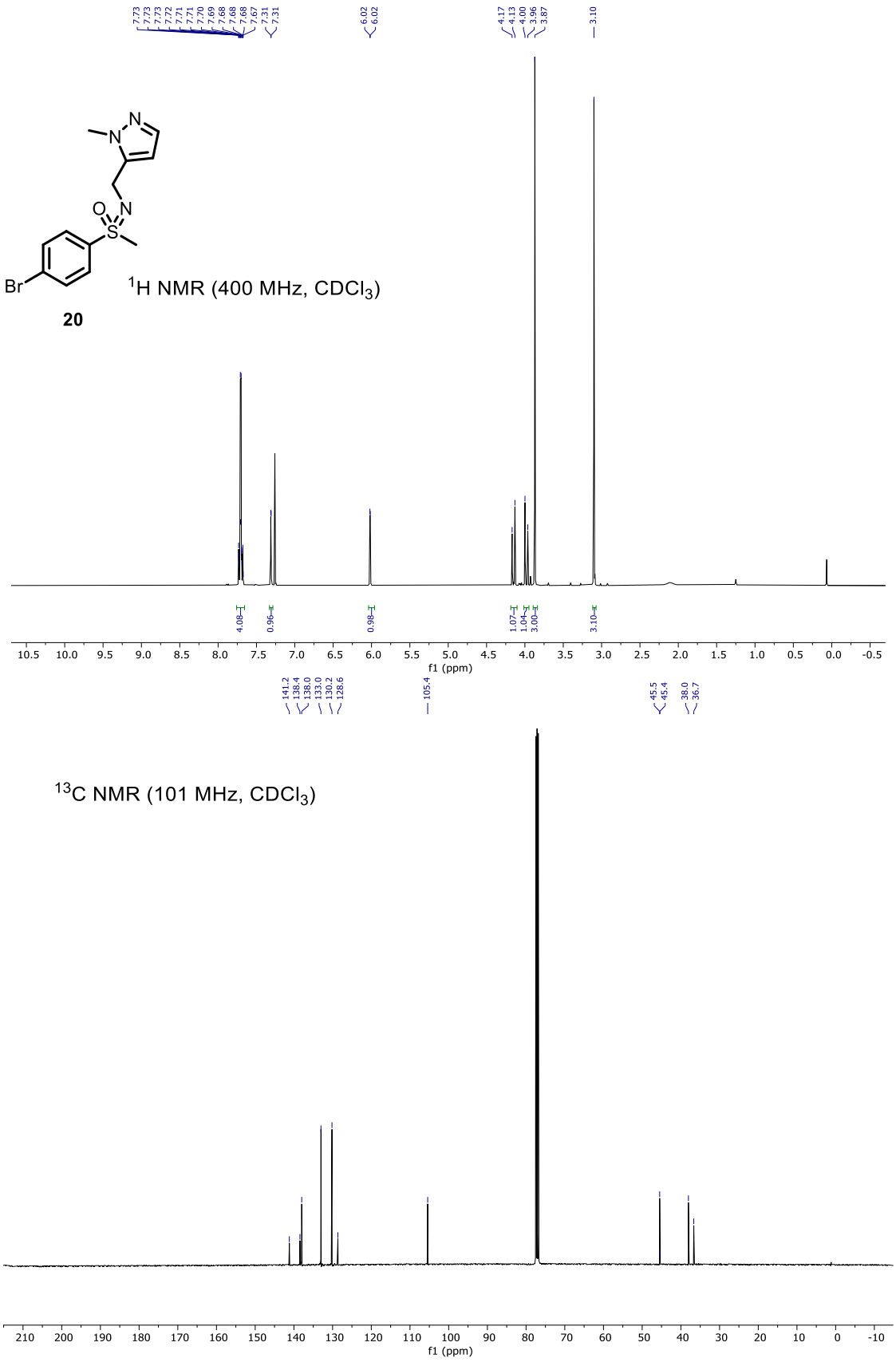
19

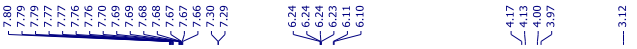
^{1}H NMR (400 MHz, $CDCl_3$)

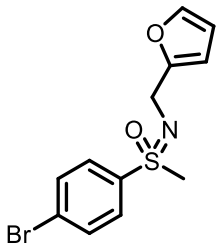


^{13}C NMR (101 MHz, $CDCl_3$)



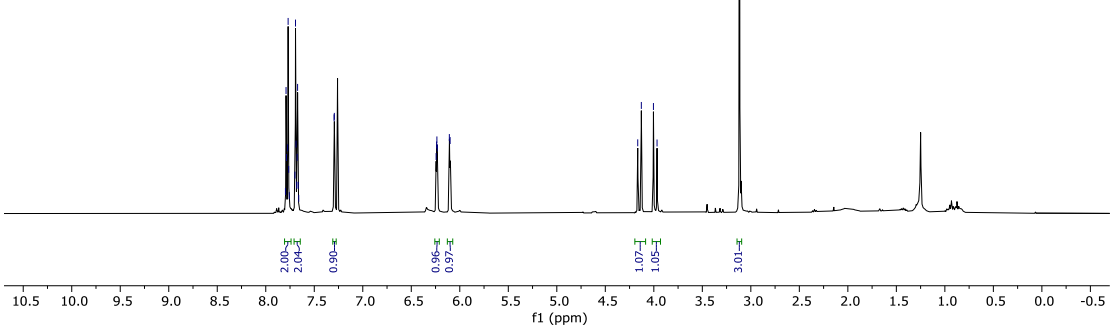

7.73
7.73
7.73
7.72
7.71
7.71
7.70
7.69
7.68
7.68
7.68
7.67
7.31
7.31
6.02
6.02
4.17
4.13
4.00
3.96
3.87
3.10
N
N
O
N
S
Br
20
^{1}H NMR (400 MHz, $CDCl_3$)
4.08
0.96
0.98
1.07
1.04
3.00
3.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
141.2
138.4
138.0
133.0
130.2
128.6
105.4
45.5
45.4
38.0
36.7
^{13}C NMR (101 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



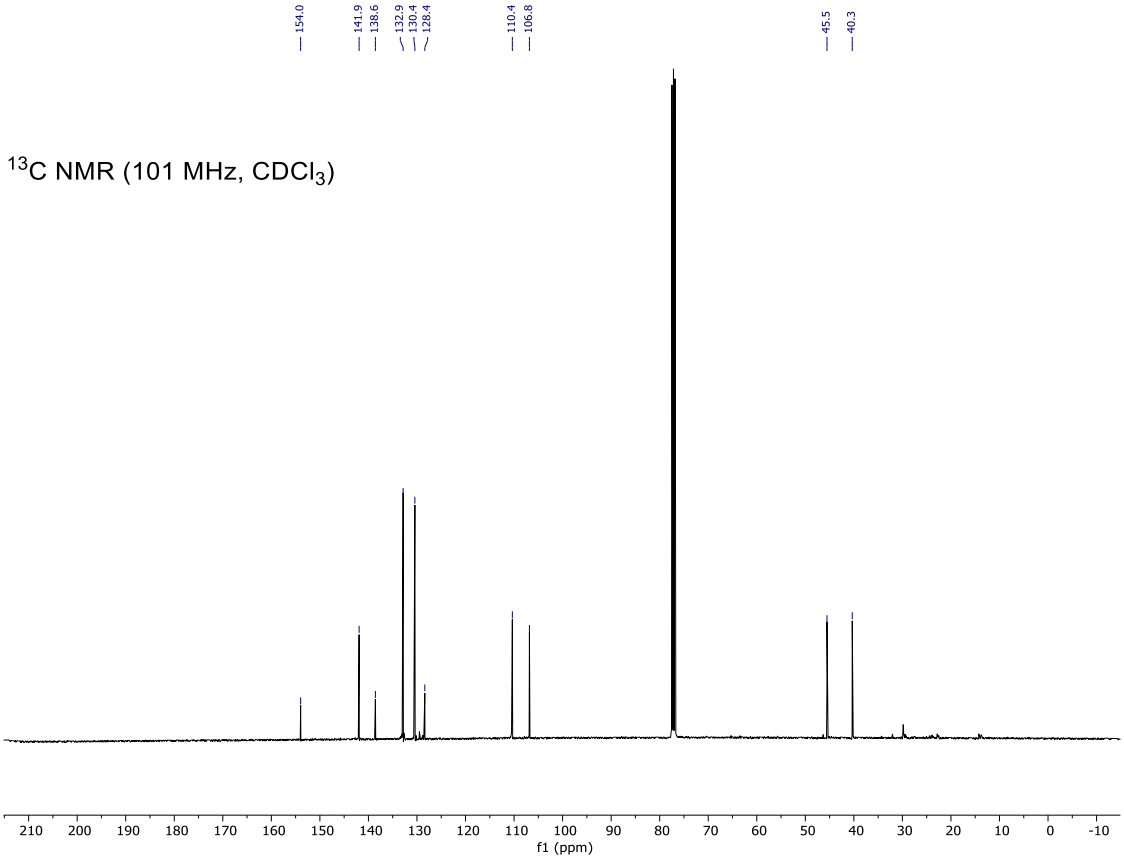


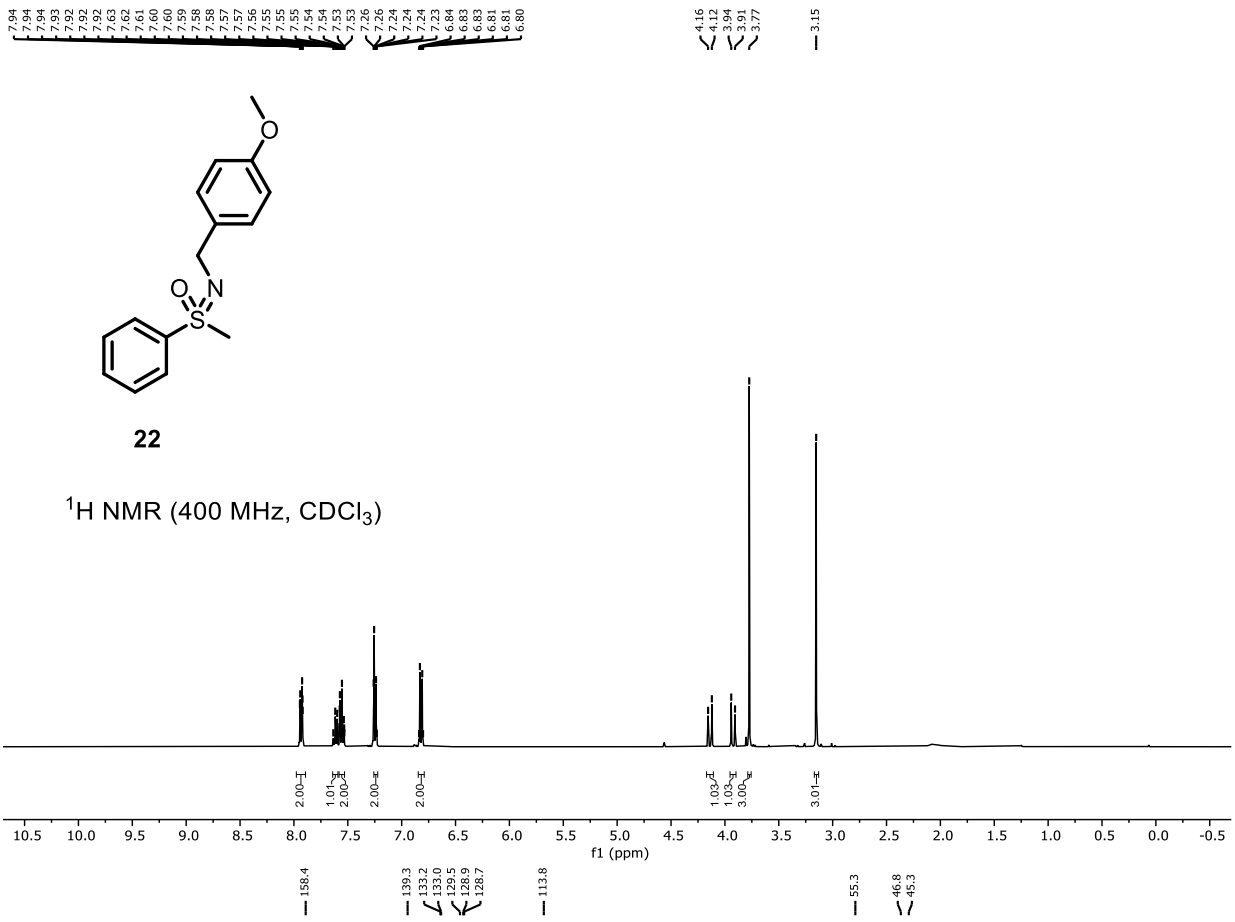
21

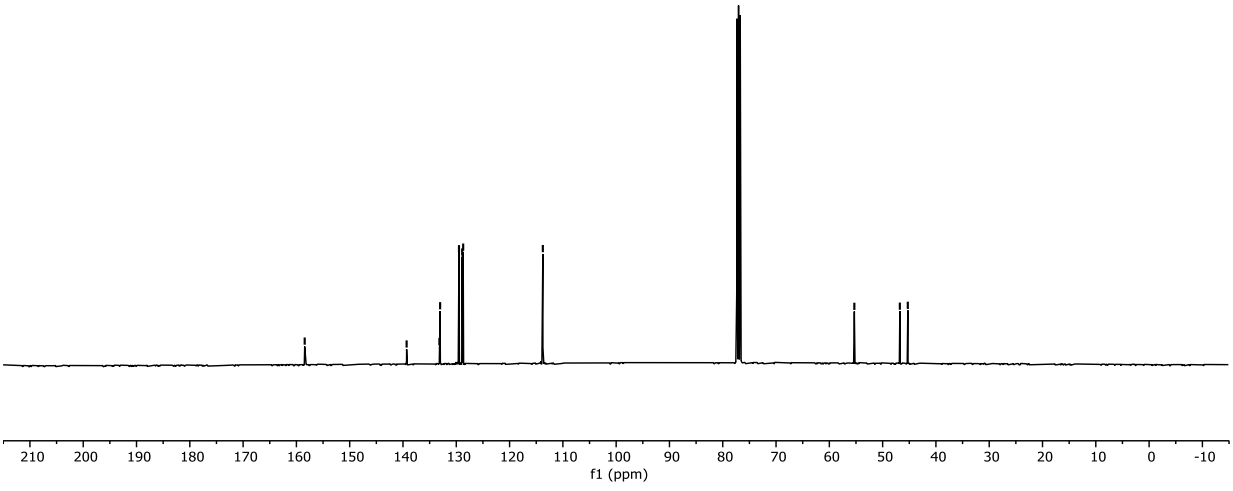
^{1}H NMR (400 MHz, $CDCl_3$)

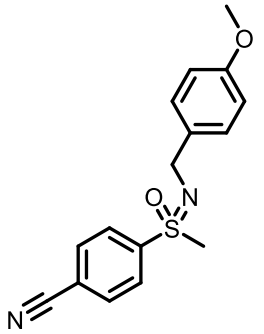


^{13}C NMR (101 MHz, $CDCl_3$)



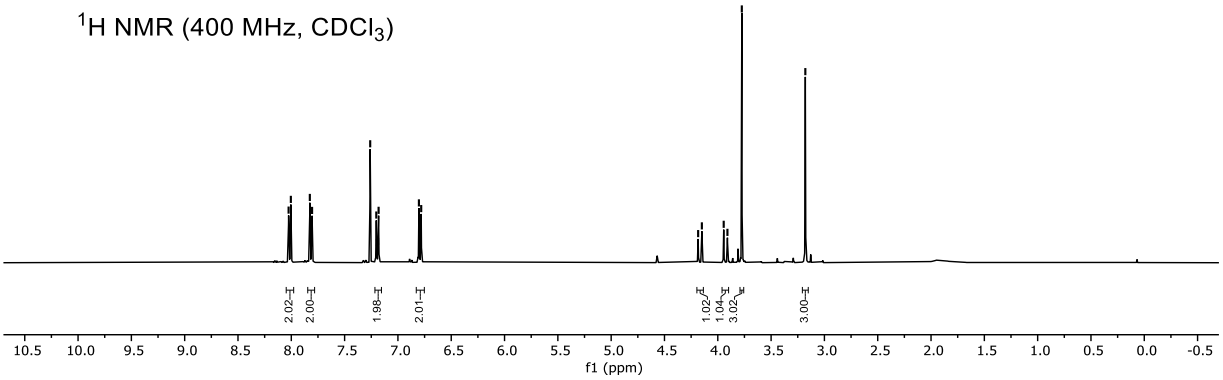

7.94
7.94
7.94
7.93
7.92
7.92
7.92
7.63
7.62
7.61
7.60
7.60
7.59
7.58
7.58
7.57
7.57
7.56
7.55
7.55
7.54
7.54
7.53
7.53
7.26
7.26
7.24
7.24
7.24
7.23
6.84
6.83
6.83
6.81
6.81
6.80
4.16
4.12
3.94
3.91
3.77
3.15
O
O
N
S
22
1H NMR (400 MHz, CDCl3)
2.00
1.01
2.00
2.00
2.00
1.03
1.03
3.00
3.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
158.4
139.3
133.2
133.0
129.5
128.9
128.7
113.8
55.3
46.8
45.3


13C NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

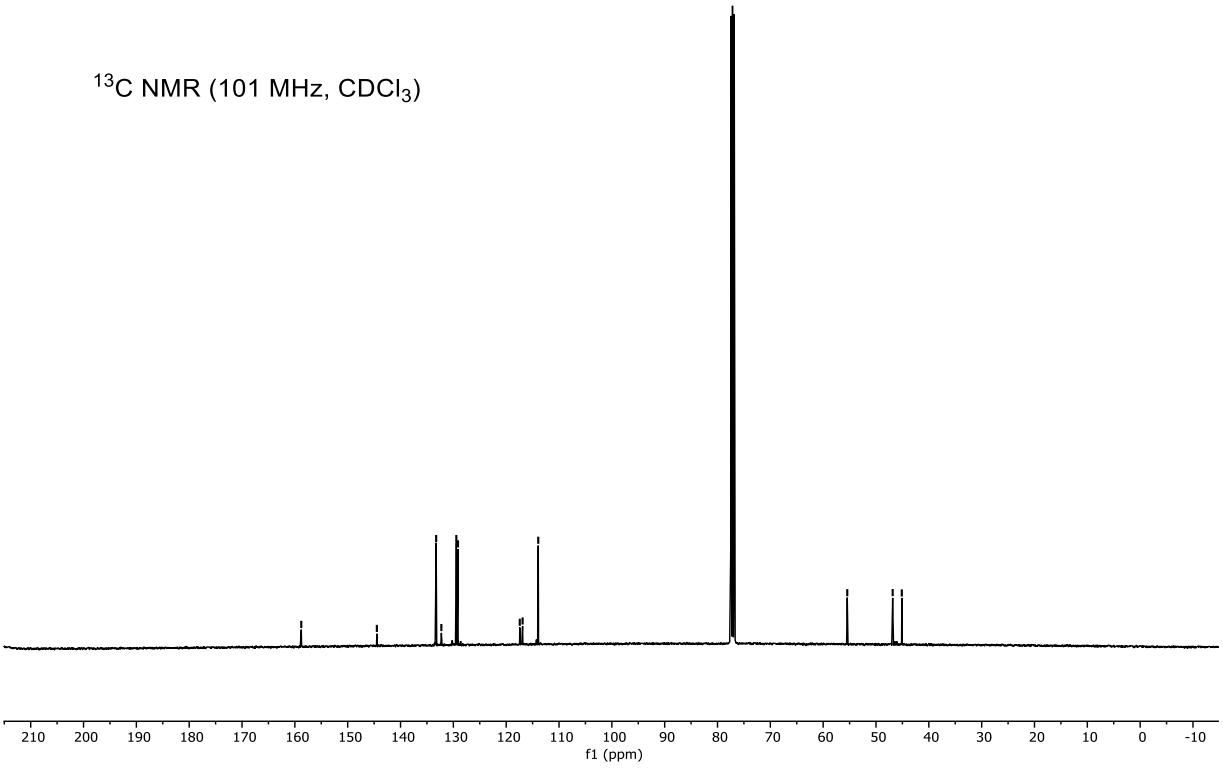


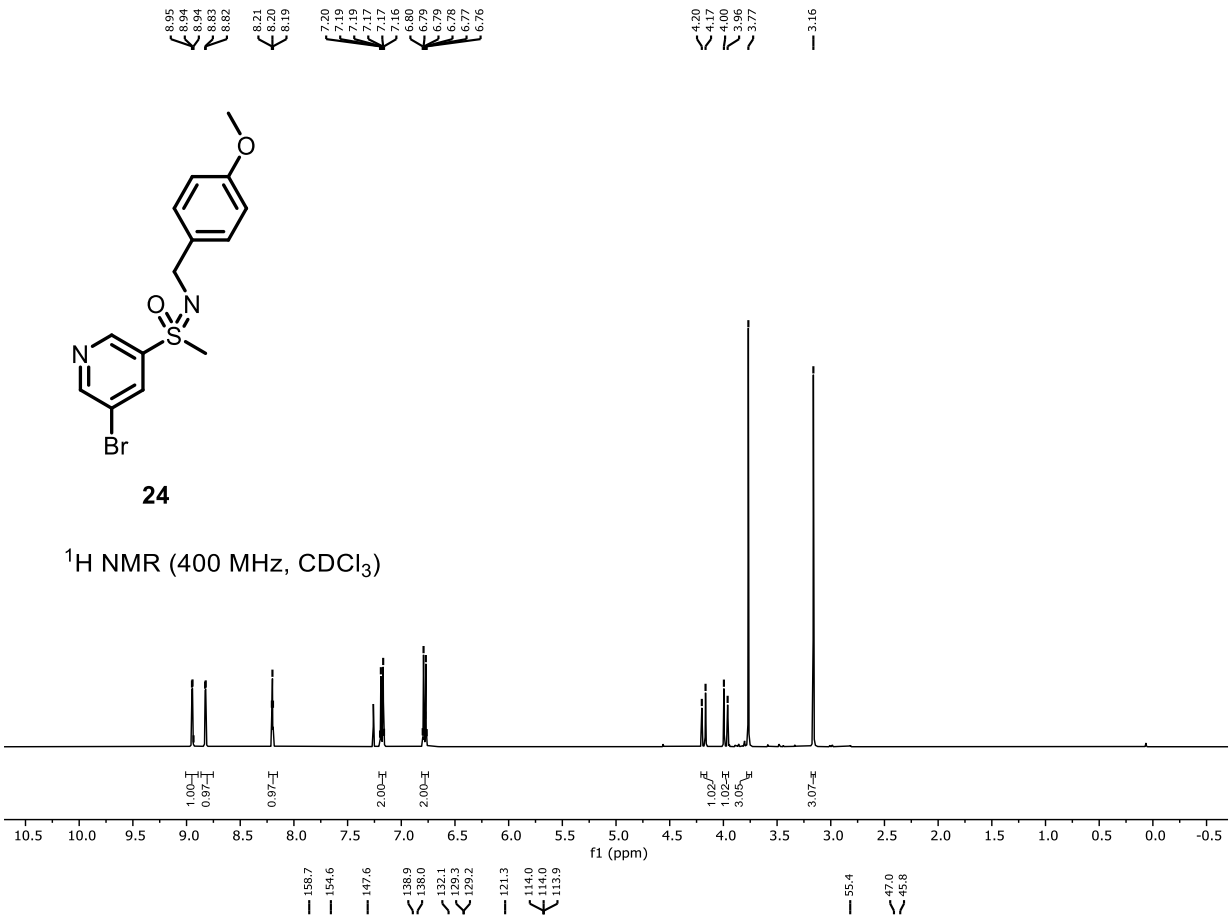
23

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



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

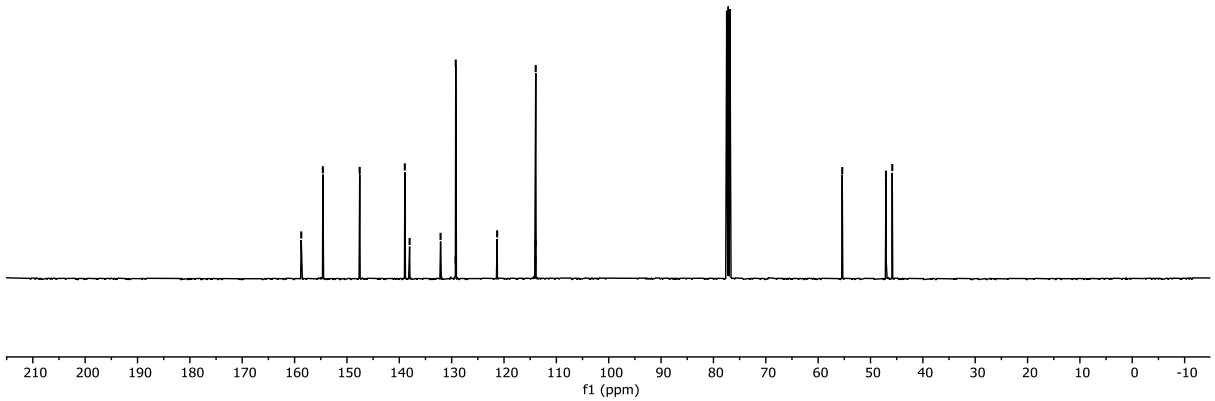


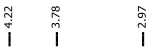


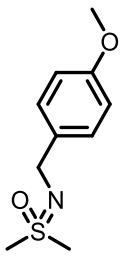
24

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

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

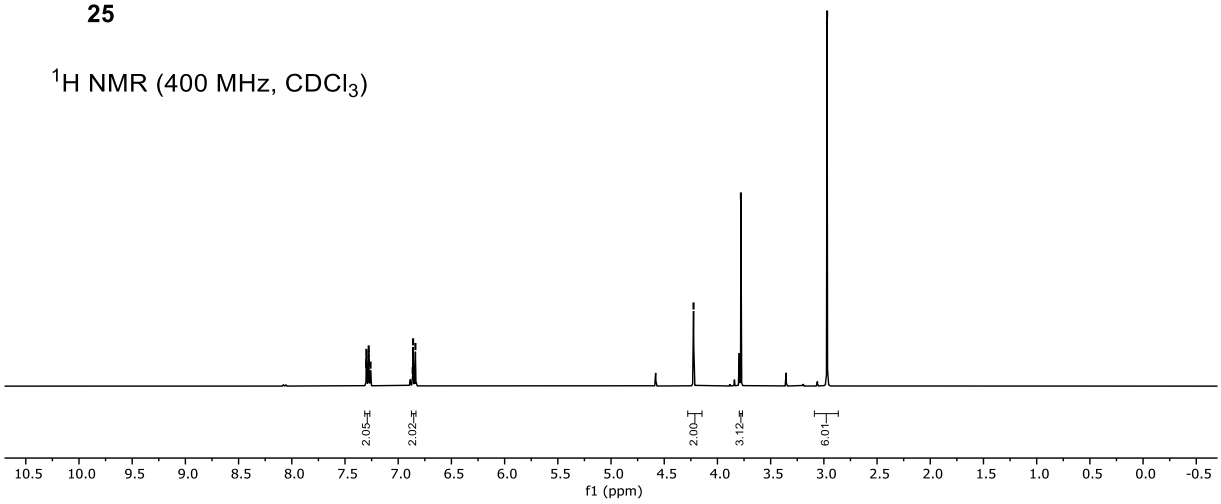




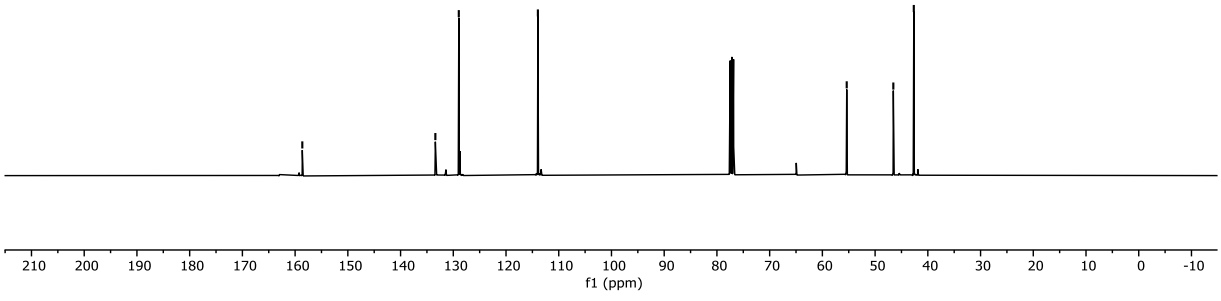


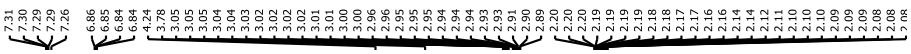
25

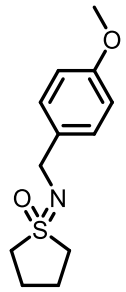
^{1}H NMR (400 MHz, $CDCl_3$)



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

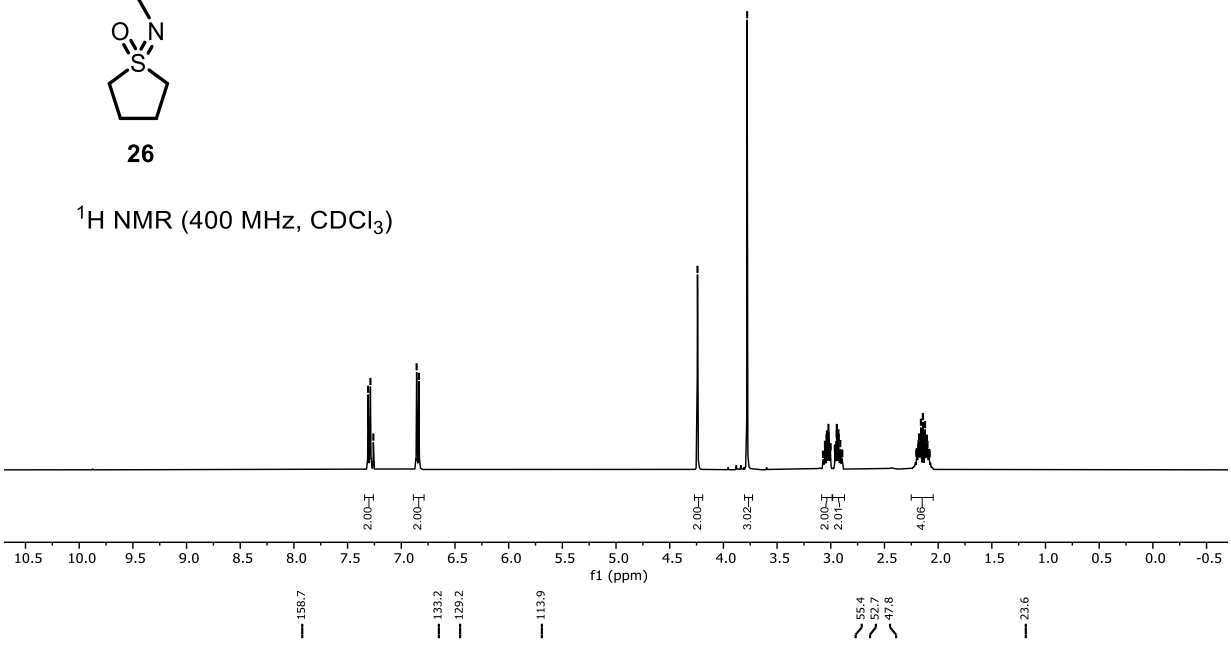




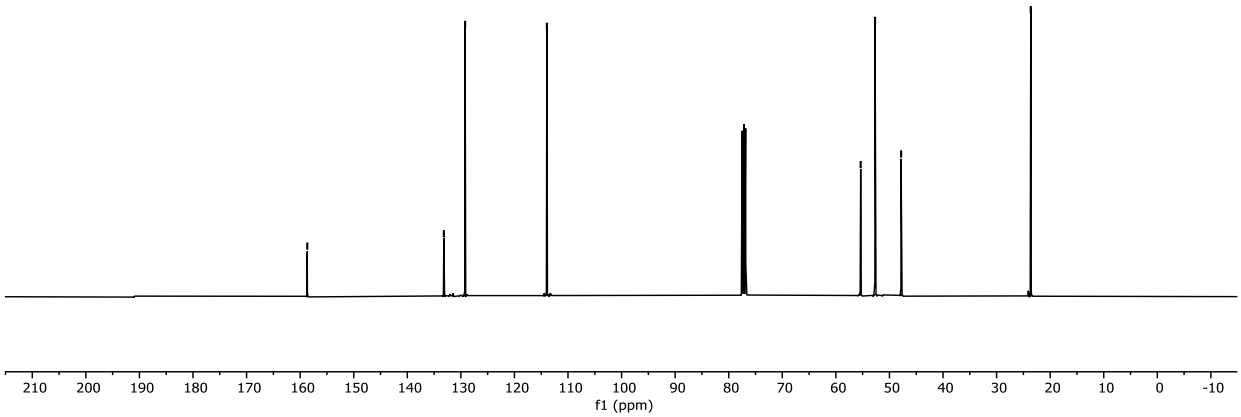


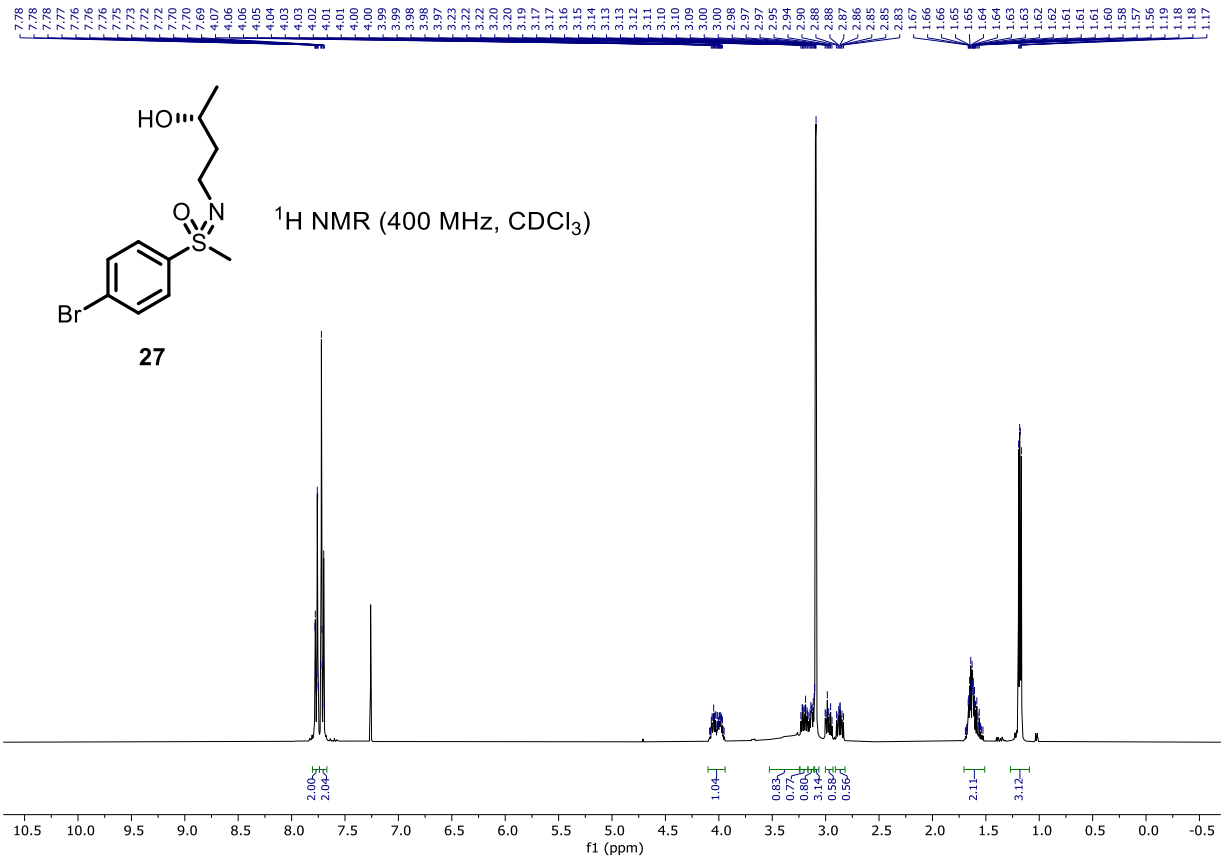
26

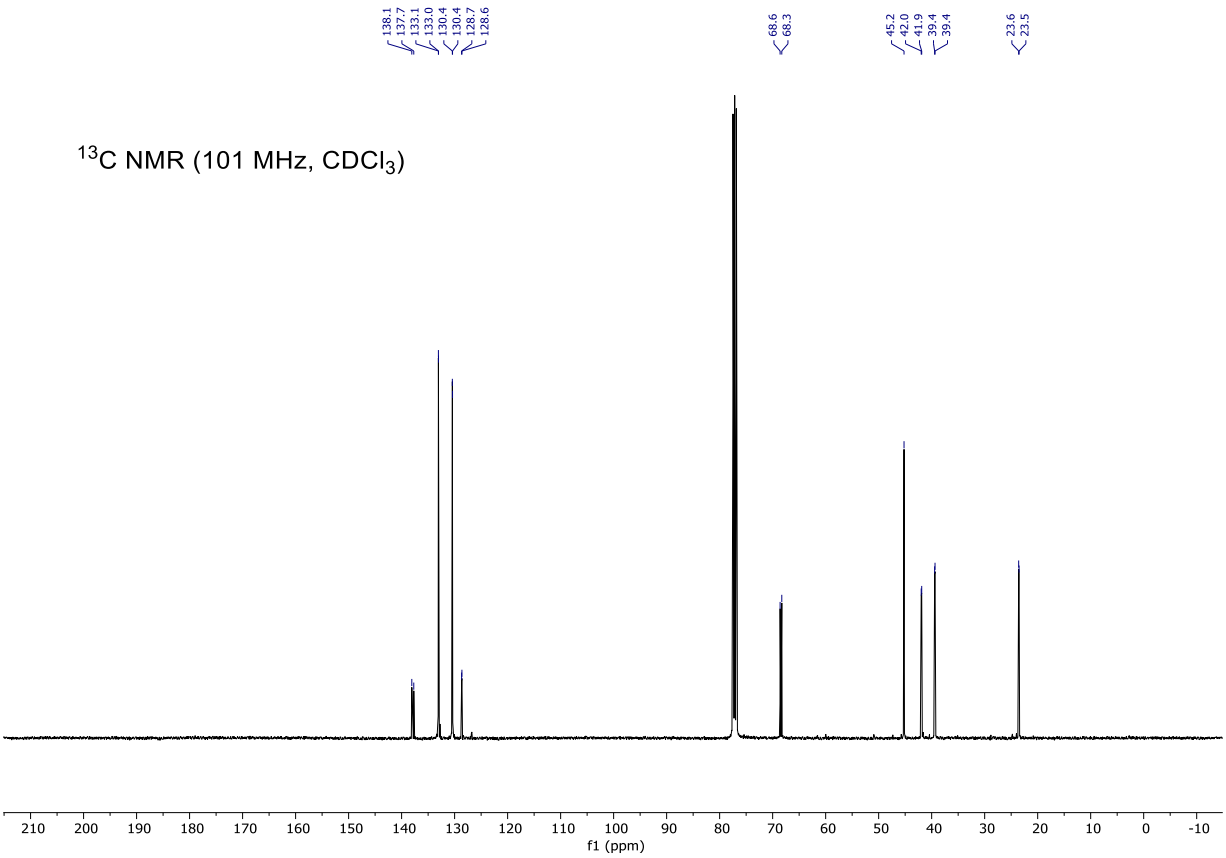
^{1}H NMR (400 MHz, $CDCl_3$)

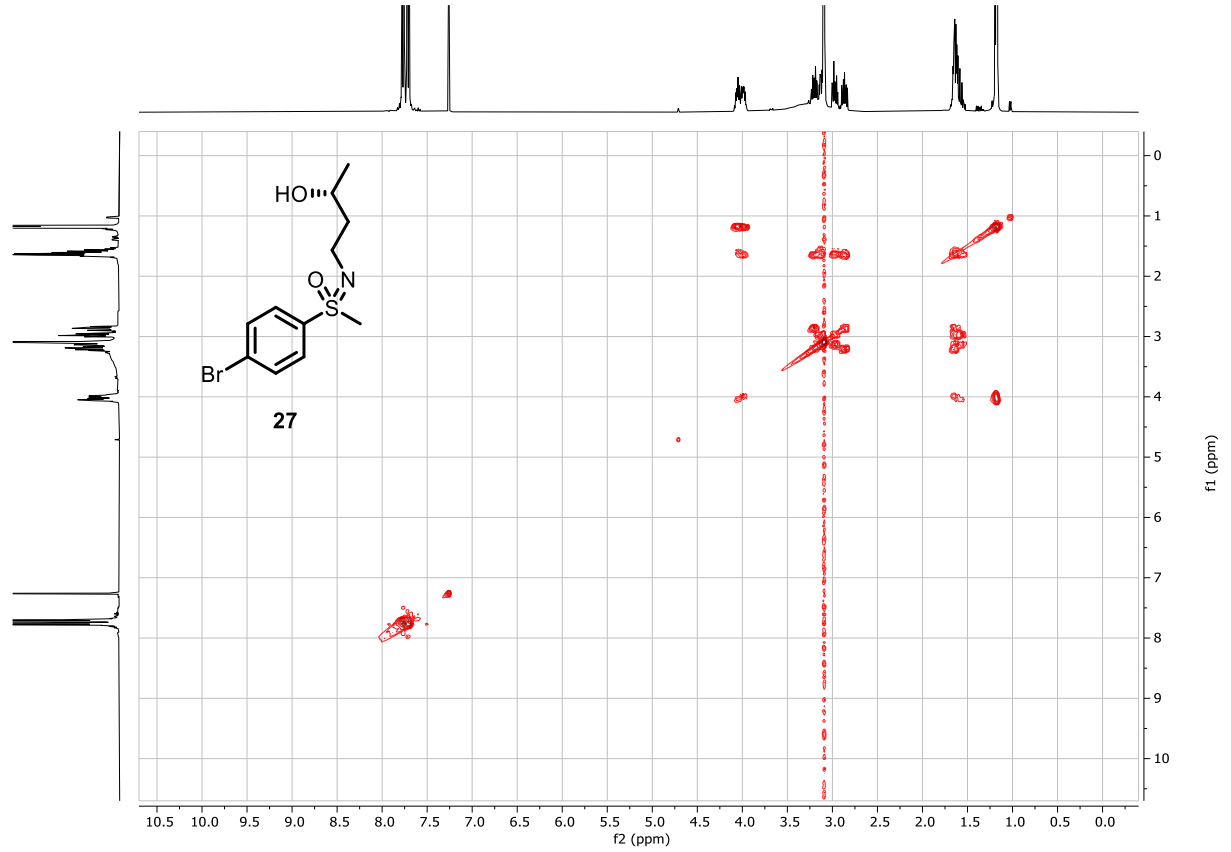


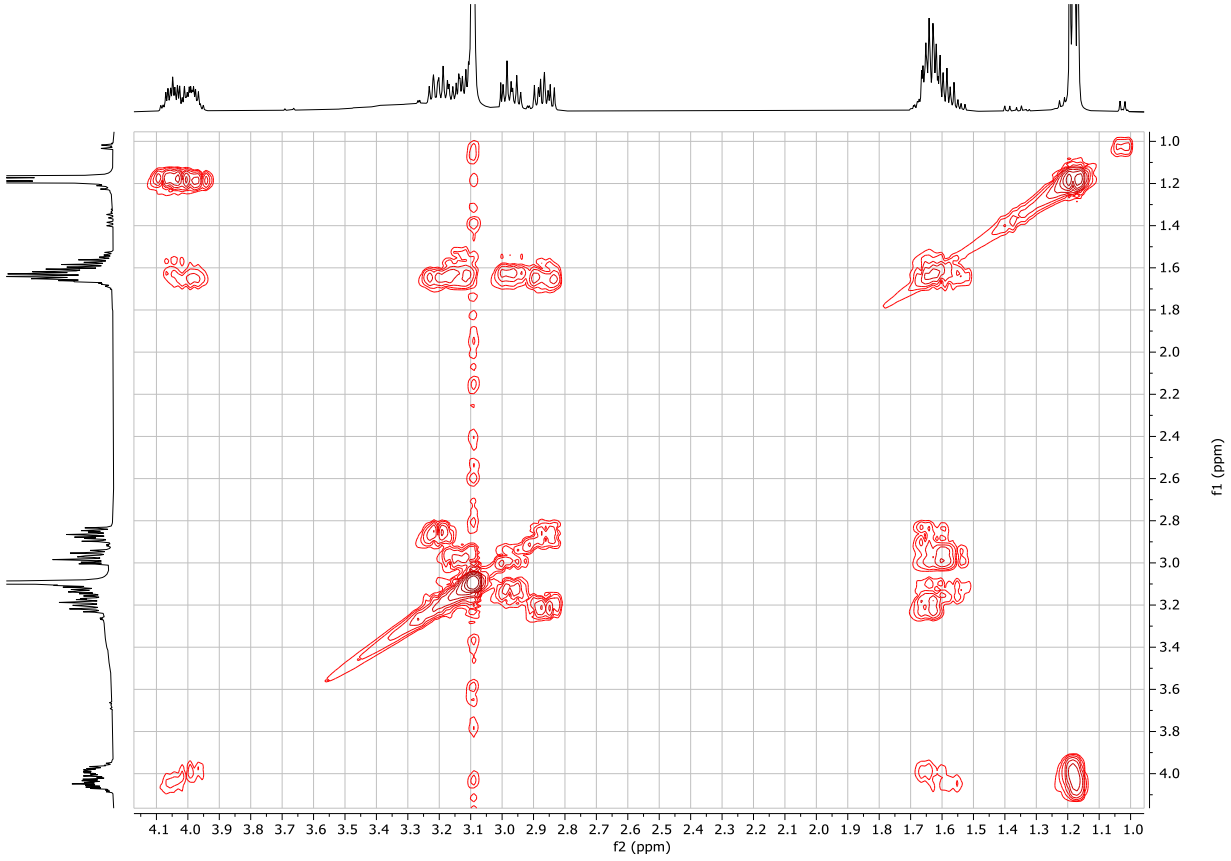
^{13}C NMR (101 MHz, $CDCl_3$)

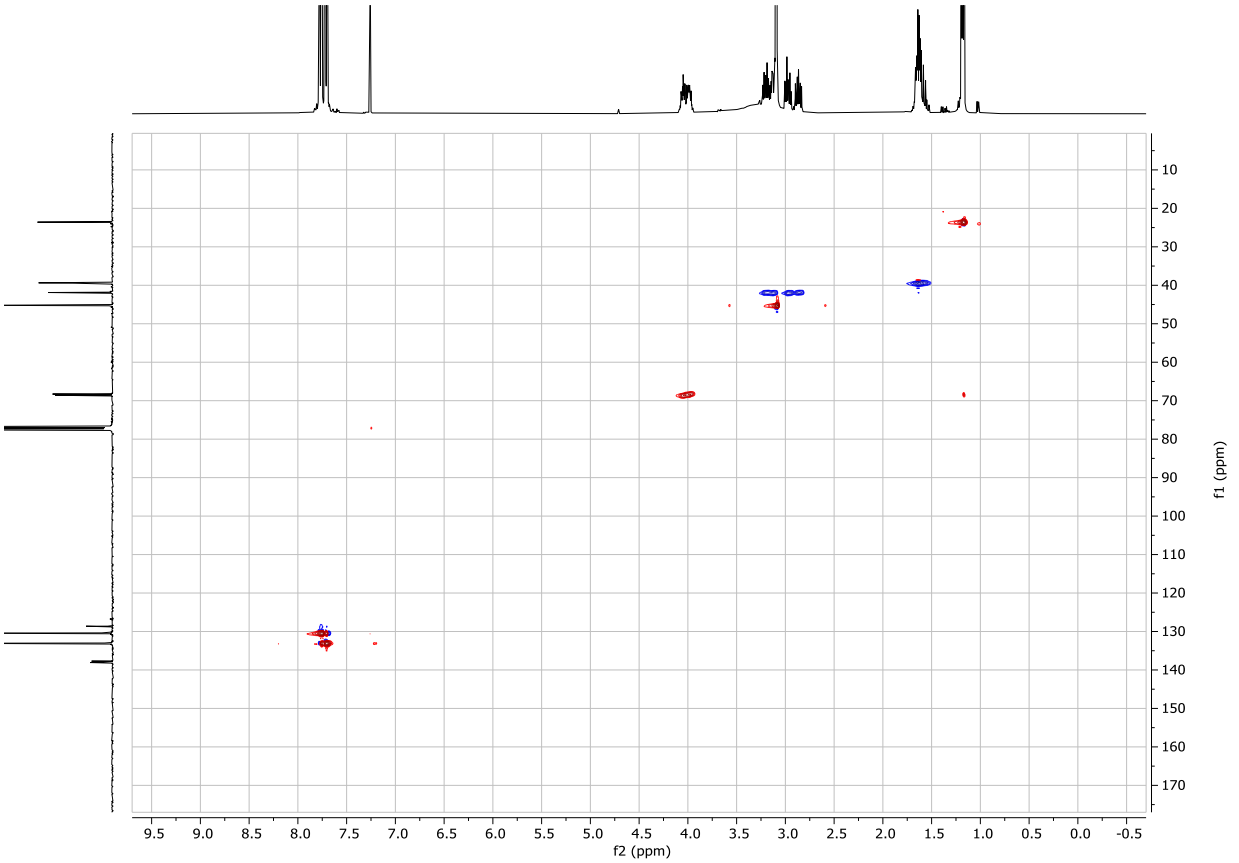


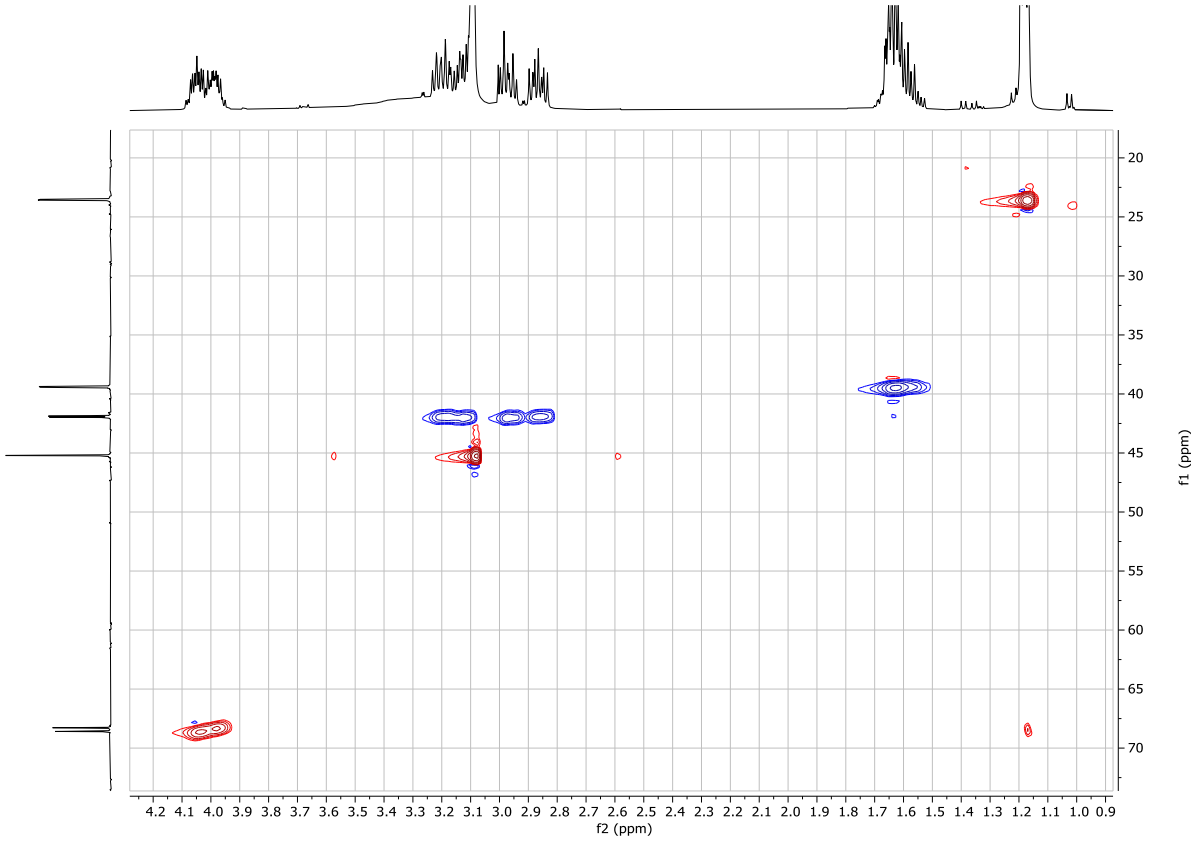

HO
O
N
S
Br
27
^{1}H NMR (400 MHz, $CDCl_3$)
f1 (ppm)

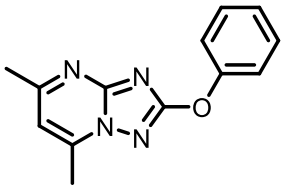

^{13}C NMR (101 MHz, $CDCl_3$)
f1 (ppm)


HO
O
N
S
Br
27
f2 (ppm)
f1 (ppm)


f2 (ppm)
f1 (ppm)

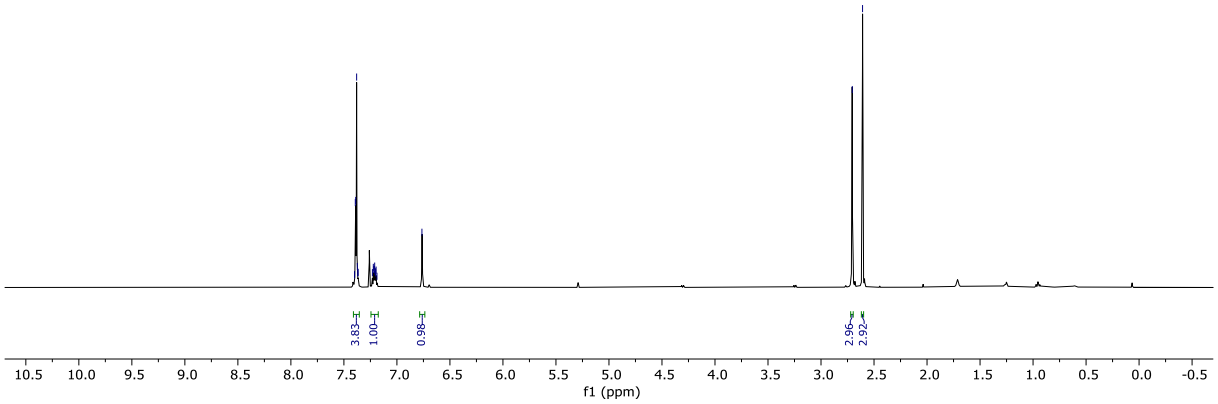

f1 (ppm)
f2 (ppm)


f1 (ppm)
f2 (ppm)



30

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



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