

Supporting Information for:

Ni-Catalyzed Carboxylation of Aziridines en Route to β -Amino Acids

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1 Synthesis of Starting Materials

1.1 General Remarks

Reagents. Commercially available materials were used as received without further purification. NiCl₂glyme (98% purity), Manganese powder (≥ 99.9 trace metal basis), 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU, H₂O $\leq 0.03\%$), Chloramine-T trihydrate and Trimethylphenylammonium tribromide were purchased from Aldrich. 6,6'-dimethyl-2,2'-bipyridine was purchased from Fluorochem. 4-Toluenesulfonyl chloride, anhydrous MeOH (99.8% purity), anhydrous *N,N*-Dimethylacetamide (DMA, 99.5% purity) and anhydrous *N*-Methyl-2-Pyrrolidone (NMP, 99.5% purity) were purchased from Acros.

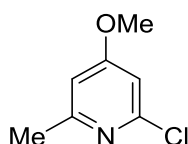
Analytical methods. ¹H, ¹³C NMR and ¹⁹F spectra were recorded on Bruker 300 MHz, Bruker 400 MHz and Bruker 500 MHz at 20 °C. All ¹H NMR spectra are reported in parts per million (ppm) downfield of TMS and were calibrated using the residual solvent peak of CHCl₃ (7.26 ppm), unless otherwise indicated. All ¹³C NMR spectra are reported in ppm relative to TMS, were calibrated using the signal of CDCl₃ (77.16 ppm). Coupling constants, *J*, are reported in Hertz. Melting points were measured using open glass capillaries in a Büchi B540 apparatus. Flash chromatography was performed with EM Science silica gel 60 (230-400 mesh). Thin layer chromatography was used to monitor reaction progress and analyze fractions from column chromatography. To this purpose, TLC Silica gel 60 F254 aluminium sheets from Merck were used and visualization was achieved using UV irradiation and/or staining with KMnO₄ or Bromocresol green solution. MALDI-TOF mass spectra were collected on a Bruker Autoflex MALDI-TOF mass spectrometer. Samples were prepared by the dried-droplet protocol, from solutions containing the charge-transfer matrix pyrene or trans-2-[3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) in THF.

1.2 Synthesis of L1 and LNiCl₂ complexes

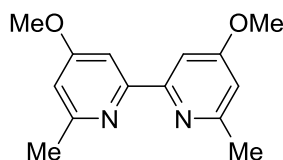
L3 (HETCAT) and **L5** (Aldrich) are commercially available and were used as received. **L2**¹, **L4**², **L5NiCl₂**³ and **L5₂Ni**⁴ were present in-house having been synthesized according to the described procedures.

Synthesis of 4,4'-dimethoxy-6,6'-dimethyl-2,2'-bipyridine (**L1**)

This ligand can be accessed via two routes depending on the quantity required. For synthesis of small quantities, a reductive cross-coupling of 2-chloro-4-methoxy-6-methylpyridine can be carried out.⁵ The low efficiency of this reaction and the high cost of the starting pyridine precursor, however, meant an alternative route was selected for gram scale synthesis.

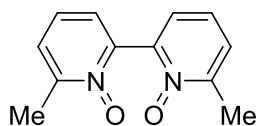


2-Chloro-4-methoxy-6-methylpyridine: To 2,6-chloro-4-methoxy-pyridine (1.0 g, 5.6 mmol) and Fe(acac)₃ (0.10 g, 0.28 mmol, 0.05 equiv.) in THF: NMP (25 ml: 6.0 ml) at 0 °C was added MeMgBr (3.0 M in Et₂O, 2.4 ml., 7.3 mmol) drop wise. The reaction was stirred for 30 minutes at this temperature before being quenched with NH₄Cl (sat.). The mixture was diluted with H₂O and extracted with EtOAc (3 × 25 ml). The combined organic layers were then washed with brine, dried (MgSO₄), filtered and reduced *in vacuo* to give 2-chloro-4-methoxy-6-methylpyridine (0.78 g, 88%) which was used in the next step without further purification. ¹H NMR (300 MHz, CDCl₃) δ 6.66 (d, *J* = 1.9 Hz, 1H), 6.59 (d, *J* = 2.1 Hz, 1H), 3.82 (s, 3H), 2.46 (s, 2H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 167.7, 160.2, 151.7, 108.9, 106.8, 55.6, 24.5 ppm.

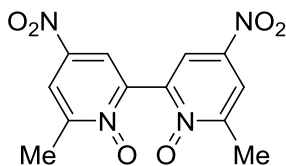


4,4'-Dimethoxy-6,6'-dimethyl-2,2'-bipyridine (L1**):** Following a modified literature procedure⁵, Ni(PPh₃)₂Cl₂ (0.65 g, 1.0 mmol, 0.20 equiv.), Zn powder (0.55 g, 8.4 mmol, 1.7 equiv.) and Bu₄Ni (1.8 g, 4.9 mmol, 1.0 equiv.) were stirred in THF (0.25 M, 20 ml) for 30 minutes at room temperature. 2-chloro-4-methoxy-6-methylpyridine (0.78 g, 4.9 mmol) was then added as a solution in THF (20 ml) and the mixture was heated to 50 °C for 20 h. After allowing to cool to room temperature, the reaction mixture was poured into 2.0 M aqueous NH₃ solution (170 ml) and CH₂Cl₂

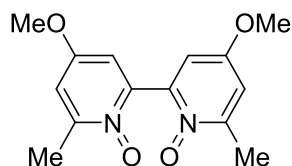
(280 ml) and stirred for 30 minutes. The resultant precipitate was removed by filtration, the phases were separated and the organic layer was dried (MgSO₄), filtered and reduced *in vacuo*. Purification by column chromatography (EtOAc) gave **L1** (0.30 g, 50%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, *J* = 2.4 Hz, 2H), 6.69 (d, *J* = 2.4 Hz, 2H), 3.93 (s, 6H), 2.58 (s, 6H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 159.3, 157.5, 109.9, 104.3, 55.4, 24.7 ppm. Spectroscopic data matched those previously reported in the literature.⁶



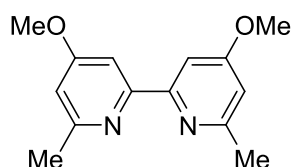
6,6'-Dimethyl-[2,2'-bipyridine] 1,1'-dioxide: Following literature procedure,⁷ to 6,6'-dimethyl-2,2'-bipyridine (6.0 g, 33 mmol) in CHCl₃ (0.50 M) was added *m*CPBA (15 g, 2.6 equiv., 85 mmol) as a solution in CHCl₃. The use of excess *m*CPBA ensured complete consumption of the intermediate mono-*N*-oxide. After stirring for 48 h, the solvent was evaporated and the crude purified by flash chromatography (hexane: EtOAc) gave 6,6'-dimethyl-[2,2'-bipyridine] 1,1'-dioxide (4.4 g, 62%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.34 (m, 4H), 7.29 – 7.21 (m, 2H), 2.58 (s, 6H) ppm. Spectroscopic data matched those previously reported in the literature.⁸



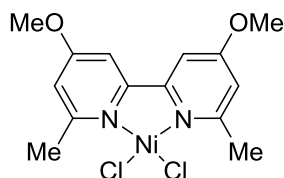
6,6'-Dimethyl-4,4'-dinitro-[2,2'-bipyridine] 1,1'-dioxide: Following literature procedure⁷, to 6,6'-dimethyl-[2,2'-bipyridine] 1,1'-dioxide (4.4 g, 20 mmol) dissolved in conc. H₂SO₄ (16 ml) and cooled to 0 °C was added fuming HNO₃ (13 ml) drop wise. The mixture was warmed to room temperature and then heated to 100 °C for 6 h. After cooling to 0 °C, crushed ice (100 g) was added and the resultant precipitate filtered, washed with H₂O (50 ml) and dried under air current. This solid was then dissolved in CHCl₃ and neutralized with solid NaOH (~30 g) to pH~6. The resultant orange solid was then filtered and washed with H₂O and CH₂Cl₂ giving 6,6'-dimethyl-4,4'-dinitro-[2,2'-bipyridine] 1,1'-dioxide (5.8 g, 92%) which was used without further purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.60 (dd, *J* = 3.4, 0.8 Hz, 2H), 8.53 (dd, *J* = 3.3, 0.7 Hz, 2H), 2.48 (s, 6H) ppm. Spectroscopic data matched those previously reported in the literature.⁷



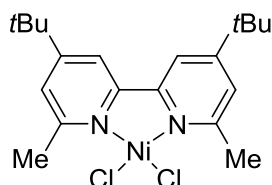
4,4'-Dimethoxy-6,6'-dimethyl-[2,2'-bipyridine] 1,1'-dioxide: Following literature procedure adapted to our substrate⁹, to 6,6'-dimethyl-4,4'-dinitro-[2,2'-bipyridine] 1,1'-dioxide (5.8 g, 19 mmol) dissolved in dry MeOH (190 ml) was added NaOMe (25% solution in MeOH, 3.5 equiv., 15 ml) drop wise. The mixture was then heated to 80 °C for 90 minutes. After allowing to cool to room temperature, the solution was neutralized with HCl (conc.) and the precipitate filtered off. The collected filtrate was concentrated *in vacuo* giving 4,4'-dimethoxy-6,6'-dimethyl-[2,2'-bipyridine] 1,1'-dioxide (4.1 g, 79%) as an orange solid which was used without and further purification.¹H NMR (400 MHz, CDCl₃) δ 6.93 (d, *J* = 3.5 Hz, 2H), 6.88 (d, *J* = 3.4 Hz, 2H), 3.83 (s, 6H), 2.54 (s, 6H) ppm. Spectroscopic data matched those previously reported in the literature.⁶



4,4'-Dimethoxy-6,6'-dimethyl-2,2'-bipyridine (L1): Following literature procedure⁹, to 4,4'-dimethoxy-6,6'-dimethyl-[2,2'-bipyridine] 1,1'-dioxide (4.1 g, 15 mmol) dissolved in dry CHCl₃ was added PCl₃ (26.0 ml, 20.0 equiv.) drop-wise before being heated to reflux for 3 h. After allowing to cool to room temperature, the reaction mixture was poured onto ice (~500 g) and the chloroform was removed *in vacuo*. The resultant aqueous solution was basified with solid NaOH until pH~10 and then extracted with CHCl₃ (4 × 200 ml). The collected organic layers were dried (MgSO₄), filtered and evaporated. The resultant pale brown solid was carefully washed with cold EtOH to give 4,4'-dimethoxy-6,6'-dimethyl-2,2'-bipyridine (3.4 g, 92%) as a white powder. ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, *J* = 2.4 Hz, 2H), 6.69 (d, *J* = 2.4 Hz, 2H), 3.93 (s, 6H), 2.58 (s, 6H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 159.3, 157.5, 109.9, 104.3, 55.4, 24.7 ppm. Spectroscopic data matched those previously reported in the literature.⁶



(4,4'-MeO-6,6'-Me-bpy)NiCl₂ (Ni-1): **L1** (0.30 g, 1.2 mmol) and NiCl₂ (0.15 g, 1.2 mmol) were dissolved in THF (0.10 M, 12 ml) and refluxed for 24 h. After this time, the reaction mixture was cooled to RT and filtered. The collected solid was then dissolved in CH₂Cl₂, precipitated with hexane, filtered again and dried *in vacuo* to give **Ni-1** (0.44 g, 98%) as a purple solid. Note: This complex is highly hygroscopic and should be stored under inert atmosphere. ¹H NMR (500 MHz, CDCl₃, paramagnetic) δ 79.2 (s, 2H), 59.9 (s, 2H), 47.8 (s, br, 6H), 12.6 (s, 6H) ppm.



(4,4'-tBu-6,6'-Me-bpy)NiCl₂ (Ni-2): **L2** (0.15 g, 0.52 mmol) and NiCl₂ (64 mg, 0.50 mmol) were dissolved in THF (0.10 M, 5.0 ml) and refluxed for 24 h. After this time, the reaction mixture was cooled to room temperature and filtered. The collected solid was then dissolved in CH₂Cl₂, precipitated with hexane, filtered again and dried *in vacuo* to give **Ni-2** (0.20 g, 94%) as a purple solid. Note: This complex is highly hygroscopic and should be stored under inert atmosphere. ¹H NMR (500 MHz, CDCl₃, paramagnetic) δ 76.9 (s, 2H), 60.6 (s, 2H), 31.1 (s, br, 6H), 1.9 (s, 18H) ppm.

1.3 Synthesis of Aziridines

General procedure 1 (GP1): Synthesis of (enantiopure) aziridines from amino alcohols.

Following a literature procedure,¹⁰ tosyl chloride (2.2 equiv.) was added portion wise at RT to a stirred mixture of the amino alcohol (1.0 equiv.) and K₂CO₃ (4.0 equiv.) in CH₃CN (0.50 M). After 6 h, the solid was filtered off and washed with EtOAc. The filtrate was concentrated *in vacuo* and purified by column chromatography on silica gel (hexane: EtOAc) to afford the pure *N*-tosyl aziridines.

General procedure 2 (GP2): Alternative synthesis of aziridines from amino alcohols.

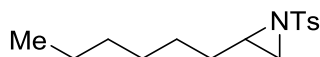
Following a literature procedure,¹⁰ tosyl chloride (2.5 equiv.) was added portion wise at RT under vigorous stirring to a mixture of KOH (35 equiv.), the amino alcohol (1.0 equiv.), water (0.50 M) and CH₂Cl₂ (0.50 M). After 30 min, ice and water were added and diluted with CH₂Cl₂. The organic layer was separated and washed with water, dried (MgSO₄), filtered and concentrated *in vacuo*. Flash column chromatography on silica gel (hexane: EtOAc) afforded the pure *N*-tosyl aziridines.

General procedure 3 (GP3): Synthesis of racemic aziridines from alkenes.

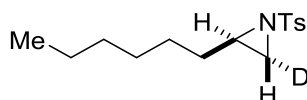
Following a literature procedure,^{11,12} to a mixture of Chloramine-T trihydrate (1.1 equiv.) and alkene (1.0 equiv.) in CH₃CN (25 mL) at ambient temperature was added PhNMe₃Br₃ (0.10 equiv.). The reaction was stirred vigorously for 16 h, the solid was filtered off and the filtrate was concentrated *in vacuo*. Flash column chromatography (hexane: EtOAc) afforded the pure *N*-tosyl aziridines.

General procedure 4 (GP4): Base cyclisation of aziridines containing uncyclized reaction intermediates.

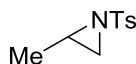
Note: In certain cases, cyclization to the aziridine was less favourable and trace uncyclized intermediates often co-eluted with the aziridine. A subsequent base cyclisation was performed to obtain high purity aziridine in these cases. The resulting material isolated from **GP1-3** was dissolved in CH₃CN (5-10 ml), K₂CO₃ (1.0 equiv.) was added and the mixture was stirred vigorously at 45 °C for 3 h. The mixture was cooled to RT, filtered and concentrated *in vacuo*. The material was then dissolved in CH₂Cl₂ (~1 mL) and filtered through a short plug of silica gel (3 × 4 cm) eluting with hexane: EtOAc (1:1).



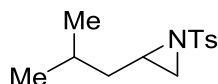
2-Hexyl-1-tosylaziridine (1a): Following **GP3** with 1-octene (15 mL, 100 mmol), purification by column chromatography on silica gel (hexane: EtOAc 95:5) afforded **1a** as a colorless oil (19 g, 68%). ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 7.7 Hz, 2H), 2.71 (tt, J = 7.3, 4.8 Hz, 1H), 2.63 (d, J = 7.0 Hz, 1H), 2.44 (s, 3H), 2.05 (d, J = 4.6 Hz, 1H), 1.57 – 1.47 (m, 1H), 1.39 – 1.10 (m, 9H), 0.85 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ 144.5, 135.4, 129.7, 128.1, 40.6, 33.9, 31.7, 31.4, 28.8, 26.8, 22.6, 21.7, 14.2 ppm. Spectroscopic data for **1a** match those previously reported in the literature.¹³



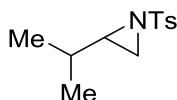
trans-2-Hexyl-1-tosylaziridine-3-d (1a-d₁): Following **GP3** with (*E*)-oct-1-ene-1-d (0.56 g, 5.0 mmol), which was synthesized using a literature procedure¹⁴, purification by column chromatography on silica gel (hexane: EtOAc 95:5) afforded **1a-d₁** as a colorless oil (0.30 g, 21%). ^1H NMR (400 MHz, CDCl_3) δ 7.87 – 7.79 (m, 2H), 7.37 – 7.30 (m, 2H), 2.71 (dt, J = 7.6, 4.8 Hz, 1H), 2.44 (s, 3H), 2.05 (d, J = 4.7 Hz, 1H), 1.55 – 1.49 (m, 1H), 1.39 – 1.09 (m, 9H), 0.85 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 144.5, 135.4, 129.8, 128.2, 40.6, 33.68 (t, J = 25.5 Hz), 31.8, 31.4, 28.8, 26.9, 22.6, 21.8, 14.2 ppm. Spectroscopic data for **1a-d₁** match with the non-deuterated analogue **1a**.



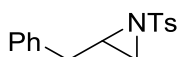
2-Methyl-1-tosylaziridine (1b): Following **GP1** with (\pm)-2-amino-1-propanol (1.5 g, 20 mmol), purification by column chromatography on silica gel (hexane: EtOAc 8:2) afforded **1b** as a white solid (0.93 g, 22%). ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 2.90 – 2.76 (m, 1H), 2.61 (d, J = 7.0 Hz, 1H), 2.44 (s, 3H), 2.02 (d, J = 4.6 Hz, 1H), 1.25 (d, J = 5.6 Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 144.5, 135.6, 129.8, 128.0, 36.0, 34.9, 21.8, 16.9 ppm. LRMS (ESI): 234 ($\text{M}+\text{Na}$)⁺, 212 ($\text{M}+\text{H}$)⁺. Spectroscopic data for **1b** match those previously reported in the literature.¹⁵



2-Isobutyl-1-tosylaziridine (1d): Following **GP1** with (±)-leucinol (1.2 g, 10 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **1d** as a white solid (1.2 g, 48%). ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 2.78 (tdd, *J* = 7.0, 5.9, 4.6 Hz, 1H), 2.62 (d, *J* = 7.0 Hz, 1H), 2.44 (s, 3H), 2.02 (d, *J* = 4.6 Hz, 1H), 1.67 – 1.55 (m, 1H), 1.40 – 1.26 (m, 2H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 144.5, 135.4, 129.8, 128.1, 40.6, 39.2, 34.2, 26.9, 22.9, 22.06, 21.8 ppm. LRMS (ESI): 253, 238, 224, 212, 155, 139, 98, 91. Spectroscopic data for **1d** match those previously reported in the literature.¹⁶

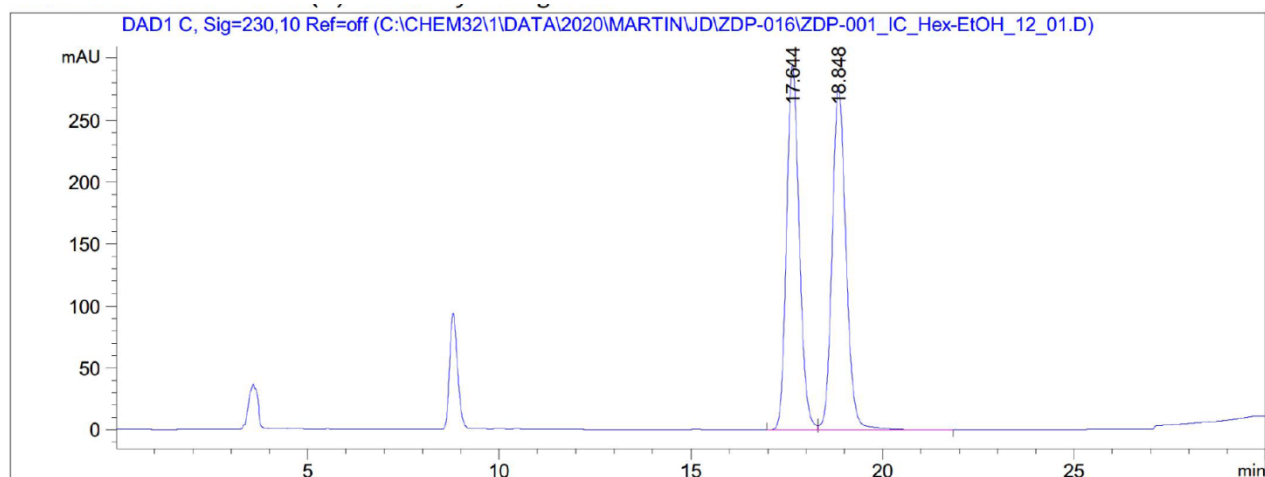


2-Isopropyl-1-tosylaziridine (1e): Following **GP1** with (±)-valinol (1.0 g, 10 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **1e** as a white solid (1.6 g, 56%). ¹H NMR (400 MHz, CDCl₃) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 2.61 (d, *J* = 7.0 Hz, 1H), 2.51 (ddd, *J* = 7.7, 7.0, 4.6 Hz, 1H), 2.43 (s, 3H), 2.10 (d, *J* = 4.6 Hz, 1H), 1.42 (dp, *J* = 7.5, 6.7 Hz, 1H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.80 (d, *J* = 6.7 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.6, 135.3, 129.7, 128.2, 46.4, 32.9, 30.3, 21.8, 19.7, 19.2. LRMS (ESI): 239, 224, 155, 146, 139, 91, 84. Spectroscopic data for **1e** match those previously reported in the literature.¹⁷



(±)-2-Benzyl-1-tosylaziridine (1f): Following **GP3** with allylbenzene (0.59 g, 5.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 → 5:1) afforded **1f** as a white solid (0.67 g, 47%). ¹H NMR (400 MHz, CDCl₃) δ 7.71 – 7.67 (m, 2H), 7.24 – 7.20 (m, 2H), 7.18 – 7.13 (m, 3H), 7.07 – 7.02 (m, 2H), 2.95 (tdd, *J* = 7.0, 5.2, 4.5 Hz, 1H), 2.81 (dd, *J* = 14.5, 5.2 Hz, 1H), 2.73 – 2.66 (m, 2H), 2.42 (s, 3H), 2.16 (d, *J* = 4.5 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 144.4, 137.1, 135.0, 129.7, 128.9, 128.6, 128.0, 126.6, 41.3, 37.6, 33.0, 21.7 ppm. LRMS (ESI): 287, 172, 155, 132, 117, 105, 91, 77. Spectroscopic data for **1f** match those previously reported in the literature.¹⁸

HPLC: *rac* (CHIRALPAK[®] IC, hexane/ EtOH = 88:12, 1 mL/min, 220 nm, *t_R* = 17.644; 18.848).

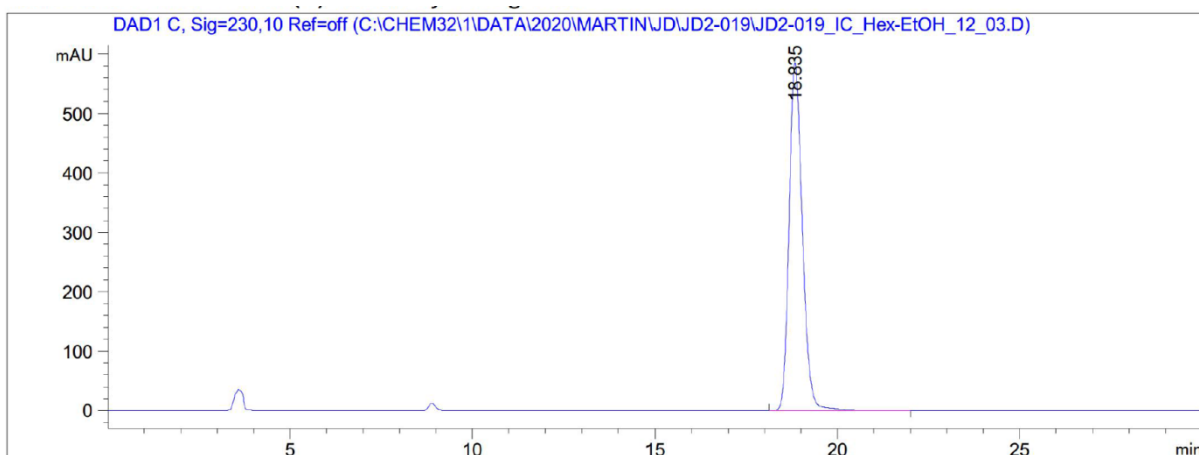


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Totals : 1.38108e4 571.37994

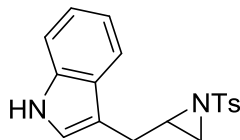


(S)-2-benzyl-1-tosylaziridine ((S)-1f): Following **GP1** with (–)-2-amino-3-phenyl-1-propanol (0.60 g, 4.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1→5:1) afforded **(S)-1f** as a white solid (0.72 g, 63%). ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 7.20 – 7.10 (m, 3H), 7.09 – 7.00 (m, 2H), 2.95 (tt, *J* = 7.0, 5.0 Hz, 1H), 2.81 (dd, *J* = 14.5, 5.2 Hz, 1H), 2.74 – 2.64 (m, 2H), 2.42 (s, 3H), 2.16 (d, *J* = 4.5 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 144.4, 137.1, 135.0, 129.7, 128.9, 128.6, 128.0, 126.6, 41.3, 37.6, 33.0, 21.7 ppm. Spectroscopic data for **(S)-1f** match those previously reported in the literature.¹⁸ HPLC: >99% *ee* (CHIRALPAK[®] IC, hexane/*i*-PrOH = 85/15, 1 mL/min, 220 nm, *t*_R = 18.835).

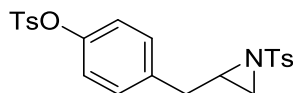


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.835	BB	0.3884	1.47844e4	585.94495	100.0000

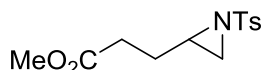
Totals : 1.47844e4 585.94495



3-((1-Tosylaziridin-2-yl)methyl)-1H-indole (1g): Following literature procedure¹⁹ with tryptophanol (0.48 g, 2.5 mmol), purification by column chromatography (hexane: EtOAc 8:2→6:4) afforded **1g** as a pale yellow solid (0.17 g, 20%). ¹H NMR (400 MHz, CDCl₃) δ 7.95 (s, br, 1H), 7.69 – 7.62 (m, 2H), 7.46 (dq, *J* = 7.9, 0.9 Hz, 2H), 7.31 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.18 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.17 – 7.09 (m, 1H), 7.07 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 6.99 (d, *J* = 2.3 Hz, 1H), 3.11 – 3.05 (m, 1H), 3.01 (ddd, *J* = 15.1, 5.1, 0.9 Hz, 1H), 2.85 (ddd, *J* = 15.0, 6.8, 0.9 Hz, 1H), 2.71 (d, *J* = 6.7 Hz, 1H), 2.39 (s, 3H), 2.20 (d, *J* = 4.5 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 144.3, 136.2, 134.9, 129.5, 127.9, 127.3, 122.4, 122.2, 119.6, 118.7, 111.4, 111.2, 40.8, 33.5, 27.3, 21.8. LRMS: 349 (M+Na)⁺, 327 (M+H)⁺. Spectroscopic data for **1g** match those previously reported in the literature.¹⁹

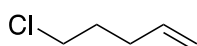


4-((1-Tosylaziridin-2-yl)methyl)phenyl 4-methylbenzenesulfonate (1h): Following **GP1** using L-tyrosinol hydrochloride (0.20 g, 1.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 →6:4) afforded **1h** as a colorless oil (0.15 g, 32%). ¹H NMR (400 MHz, CDCl₃) δ 7.72 – 7.61 (m, 4H), 7.31 (d, *J* = 7.7 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 2H), 6.99 – 6.91 (m, 2H), 6.80 – 6.71 (m, 2H), 2.93 – 2.78 (m, 2H), 2.70 (d, *J* = 6.7 Hz, 1H), 2.56 (dd, *J* = 14.3, 7.4 Hz, 1H), 2.45 (d, *J* = 3.1 Hz, 6H), 2.12 (d, *J* = 4.3 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 148.5, 145.5, 144.9, 136.3, 134.9, 132.6, 130.0, 129.9, 129.8, 128.6, 128.0, 122.4, 41.0, 37.0, 32.9, 21.9, 21.8 ppm. HRMS calcd. for (C₂₃H₂₃NNaO₅S₂) [M+Na]⁺: 480.0910 found 480.0909. This compound is reported in literature, but no spectroscopic data is provided.^{10, 20}

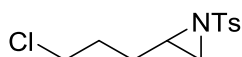


Methyl 3-(1-tosylaziridin-2-yl) propanoate (1i): Following **GP3** with methyl-4-pentanoate (0.23 g, 2.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 →7:3) afforded

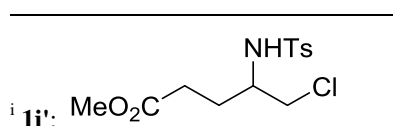
1i along with uncyclized intermediate **1i'**. This mixture was submitted to a base cyclisation step (**GP4**) to afford **1i** (0.15 g, 22%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.83 – 7.78 (m, 2H), 7.38 – 7.30 (m, 2H), 3.65 (s, 3H), 2.82 (ddt, $J = 7.9, 6.9, 4.6$ Hz, 1H), 2.65 (d, $J = 7.0$ Hz, 1H), 2.45 (s, 3H), 2.36 – 2.19 (m, 2H), 2.11 (d, $J = 4.5$ Hz, 1H), 1.99 (dtd, $J = 14.3, 7.7, 4.6$ Hz, 1H), 1.55 (dtd, $J = 14.0, 7.7, 6.1$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 172.8, 144.6, 134.8, 129.7, 128.0, 51.6, 39.1, 33.9, 30.8, 26.4, 21.6 ppm. IR (neat, cm^{-1}): 2999, 2953, 1732, 1597, 1494, 1438, 1365, 1320, 1206, 1156, 1091. HRMS calcd. for $(\text{C}_{13}\text{H}_{17}\text{NNaO}_4\text{S})$ $[\text{M}+\text{Na}]^+$: 306.0770 found 306.0770.

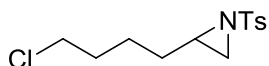


5-Chloropent-1-ene (S1): Following literature procedure²¹, pent-4-en-1-ol (10 g, 0.12 mol) was dissolved in the mixture of CH_2Cl_2 (30 ml) and pyridine (1.0 ml). The mixture was cooled to 10 °C, and SOCl_2 (15 g, 0.13 mol) was added drop wise with stirring. Vigorous gas evolution occurred. The reaction was stirred overnight at RT and poured over ice. The organic phase was separated and washed additionally with NaHCO_3 (sat.) and brine, dried (MgSO_4) and distilled under atmospheric pressure. The target product **S1** (B.P. = 104 – 105 °C) was obtained as a colorless liquid (1.5 g, 12%) and used in the next synthetic step without any further purification. ^1H NMR (400 MHz, CDCl_3) δ 5.78 (ddt, $J = 16.9, 10.2, 6.7$ Hz, 1H), 5.11 – 4.99 (m, 2H), 3.55 (t, $J = 6.6$ Hz, 2H), 2.26 – 2.17 (m, 2H), 1.92 – 1.82 (m, 2H). Spectroscopic data for **S1** match those previously reported in the literature.²²

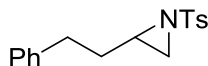


2-(3-Chloropropyl)-1-tosylaziridine (1j): Following **GP3** with **S1** (0.28 g, 2.7 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 → 5:1) afforded **1j** as a colorless oil (0.26 g, 36%). ^1H NMR (400 MHz, CDCl_3) δ 7.85 – 7.80 (m, 2H), 7.37 – 7.33 (m, 2H), 3.54 – 3.45 (m, 2H), 2.79 – 2.72 (m, 1H), 2.64 (d, $J = 7.0$ Hz, 1H), 2.45 (s, 3H), 2.09 (d, $J = 4.5$ Hz, 1H), 1.90 – 1.81 (m, 1H), 1.80 – 1.73 (m, 2H), 1.46 – 1.37 (m, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 144.8, 135.2, 129.9, 128.1, 44.1, 39.3, 34.0, 29.9, 28.7, 21.8 ppm. IR (neat, cm^{-1}): 2999, 2957, 2871, 1597, 1446, 1402, 1319, 1305, 1291, 1235, 1156, 1090, 929, 875, 815, 712, 690, 659, 567, 549. HRMS calcd. for $(\text{C}_{12}\text{H}_{16}\text{ClNNaO}_2\text{S})$ $[\text{M}+\text{H}]^+$: 296.0482 found 296.0479.





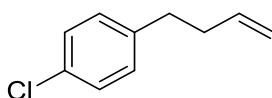
2-(4-Chlorobutyl)-1-tosylaziridine (1k): Following **GP3** with 6-chloro-1-hexene (0.66 mL, 5.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **1k** as a colorless oil (1.4 g, 91%). ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 3.42 (td, *J* = 6.6, 1.0 Hz, 2H), 2.71 (tt, *J* = 6.9, 4.5 Hz, 1H), 2.64 (d, *J* = 7.0 Hz, 1H), 2.44 (s, 3H), 2.07 (d, *J* = 4.5 Hz, 1H), 1.84 – 1.54 (m, 3H), 1.48 – 1.22 (m, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 144.7, 135.2, 129.8, 128.1, 44.7, 40.1, 33.8, 31.9, 30.7, 24.3, 21.8 ppm. LRMS: 287 (M⁺), 252, 238, 210, 184, 172, 155, 132, 91. Spectroscopic data for **1k** match those previously reported in the literature.¹¹



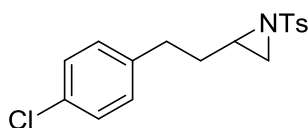
2-Phenethyl-1-tosylaziridine (1l): Following **GP3** with 4-phenyl-1-butene (4.5 mL, 30 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **1l** as a colorless solid (5.7 g, 63%). ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.32 (m, 2H), 7.30 – 7.24 (m, 2H), 7.21 – 7.16 (m, 1H), 7.14 – 7.10 (m, 2H), 2.78 (tt, *J* = 7.7, 4.7 Hz, 1H), 2.67 – 2.54 (m, 3H), 2.45 (s, 3H), 2.06 (d, *J* = 4.6 Hz, 1H), 1.93 – 1.83 (m, 1H), 1.73 – 1.62 (m, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 144.6, 140.8, 135.2, 129.8, 128.6, 128.4, 128.1, 126.2, 39.9, 34.0, 33.3, 33.1, 21.8 ppm. LRMS (ESI): 301 (M⁺), 260, 184, 155, 117, 91, 77. Spectroscopic data for **1l** match those previously reported in the literature.¹³

General procedure 5 (GP5): Synthesis of propenylated and butenylated arenes (S2-4).

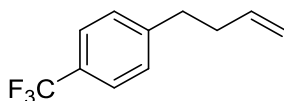
To a flame-dried 250 mL round-bottom flask was added aryl or benzyl bromide (1.0 equiv.) and anhydrous THF (0.50 M). The reaction flask was cooled to 0 °C while under an atmosphere of nitrogen and allylmagnesium bromide was added drop wise (1.0 M in Et₂O, 1.1 equiv.). The reaction was stirred for 2 h at 0 °C and then allowed to warm to RT before being quenched with H₂O. The layers were separated and the aqueous layer was extracted with Et₂O (3 times). The combined organic fractions were washed with Na₂SO₄ (sat.), brine and dried (MgSO₄). Purification of the crude reaction mixture by column chromatography was carried out when necessary.



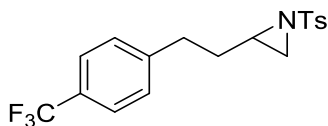
1-(But-3-en-1-yl)-4-chlorobenzene (S2): Following **GP5** with 4-chlorobenzyl bromide (3.1 g, 15 mmol, 1.0 equiv.), purification by column chromatography on silica gel (hexane: EtOAc 95:5) afforded **S2** (1.9 g, 76%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.26 – 7.22 (m, 2H), 7.13 – 7.09 (m, 2H), 5.82 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.08 – 4.94 (m, 2H), 2.68 (dd, J = 8.8, 6.7 Hz, 2H), 2.35 (qq, J = 7.8, 6.5, 1.4, 0.6 Hz, 2H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 140.4, 137.8, 131.7, 129.9, 128.5, 115.4, 35.5, 34.8 ppm. Spectroscopic data for **S2** match those previously reported in the literature.²³



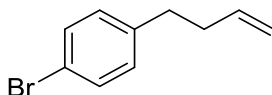
2-(4-Chlorophenethyl)-1-tosylaziridine (1m): Following **GP3** with **S2** (2.0 g, 12 mmol) purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **1m** as a white solid (1.05 g, 26%). M.P: 46 - 48 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 7.9 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H), 2.86 (ddt, J = 7.8, 7.0, 4.6 Hz, 1H), 2.77 – 2.61 (m, 3H), 2.55 (s, 3H), 2.15 (d, J = 2.5 Hz, 1H), 1.97 (dddd, J = 13.6, 8.7, 7.5, 4.8 Hz, 1H), 1.73 (dtd, J = 14.2, 8.1, 6.3 Hz, 1H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ 144.7, 139.2, 135.1, 132.0, 129.8, 129.8, 128.6, 128.1, 39.5, 34.1, 33.1, 32.4, 21.7 ppm. IR (neat, cm^{-1}): 2926, 2862, 1597, 1492, 1452, 1405, 1320, 1305, 1231, 1157, 1090, 1015. HRMS calcd. for $(\text{C}_{17}\text{H}_{18}\text{ClNNaO}_2\text{S})$ $[\text{M}+\text{Na}]^+$: 358.0639 found 358.0633.



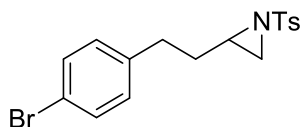
1-(But-3-en-1-yl)-4-trifluoromethylbenzene (S3): Following **GP5**, 4-trifluoromethylbenzyl bromide (1.5 ml, 10 mmol, 1.0 equiv.) afforded **S3** (1.4 g, 68%) as a colourless oil. In this case, no purification was carried out. ^1H NMR (400 MHz, CDCl_3) δ 7.53 (d, J = 7.8 Hz, 2H), 7.29 (d, J = 7.9 Hz, 2H), 5.83 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.10 – 4.97 (m, 2H), 2.77 (dd, J = 8.7, 6.8 Hz, 2H), 2.39 (tdt, J = 7.8, 6.6, 1.4 Hz, 2H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 146.1, 137.5, 128.9, 128.4 (q, J = 32.0 Hz), 125.9, 124.5 (q, J = 271.0 Hz), 125.4 (q, J = 3.8 Hz), 115.6, 35.3, 35.2 ppm. ^{19}F NMR (376 MHz, CDCl_3) δ -62.02. Spectroscopic data for **S3** match those previously reported in the literature.²⁴



1-Tosyl-2-(4-(trifluoromethyl)phenethyl) aziridine (1n): Following **GP3** with **S3** (1.4 g, 7.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **1n** as a white solid (0.95 g, 37%). M.P: 80 - 83 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.88 – 7.76 (m, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.38 – 7.31 (m, 2H), 7.24 (d, J = 8.0 Hz, 2H), 2.77 (ddt, J = 8.0, 6.9, 4.6 Hz, 1H), 2.72 – 2.66 (m, 2H), 2.61 (d, J = 6.9 Hz, 1H), 2.45 (s, 3H), 2.06 (d, J = 4.5 Hz, 1H), 1.94 (dddd, J = 13.2, 8.7, 7.6, 4.6 Hz, 1H), 1.65 (dtd, J = 14.4, 8.1, 6.6 Hz, 1H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ 144.9 (q, J = 1.1 Hz), 144.8, 134.9, 129.8, 128.8, 128.5 (q, J = 32.3 Hz), 128.1, δ 125.4 (q, J = 3.9 Hz), 124.3 (d, J = 269.4 Hz), 39.3, 34.1, 32.9, 32.8, 21.7 ppm. ^{19}F NMR (376 MHz, CDCl_3) δ -62.45. IR (neat, cm^{-1}): 3067, 2936, 1615, 1456, 1415, 1317, 1234, 1154, 1115, 1093, 1063, 1017. HRMS calcd. for ($\text{C}_{18}\text{H}_{18}\text{F}_3\text{NNaO}_2\text{S}$) [$\text{M}+\text{Na}$] $^+$: 392.0903 found 392.0892.



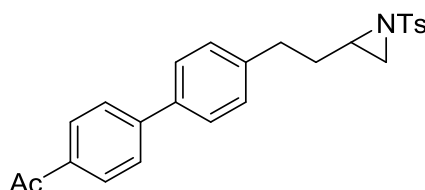
1-(But-3-en-1-yl)-4-chlorobenzene (S4): Following **GP5**, 4-bromobenzyl bromide (6.8 g, 27 mmol, 1.0 equiv.) gave **S4** (5.4 g, 89%) as a colourless oil. In this case, no purification was carried out. ^1H NMR (300 MHz, CDCl_3) δ 7.45 – 7.32 (m, 2H), 7.11 – 6.95 (m, 2H), 5.82 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.10 – 4.93 (m, 2H), 2.66 (dd, J = 8.8, 6.6 Hz, 2H), 2.42 – 2.27 (m, 2H) ppm. Spectroscopic data for **S4** match those previously reported in the literature.²⁴



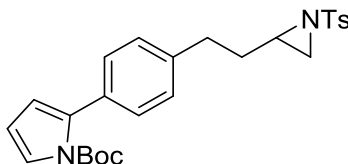
2-(4-Bromophenethyl)-1-tosylaziridine (S5): Following **GP3** with **S4** (3.2 g, 15 mmol, 1.0 equiv.), purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **S5** (2.5 g, 44%) as a white solid. M.P. = 46 – 49 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.86 – 7.78 (m, 2H), 7.40 – 7.36 (m, 2H), 7.38 – 7.31 (m, 2H), 7.04 – 6.96 (m, 2H), 2.75 (ddt, J = 7.9, 7.0, 4.7 Hz, 1H), 2.62 – 2.54 (m, 3H), 2.45 (s, 3H), 2.04 (d, J = 4.6 Hz, 1H), 1.87 (dddd, J = 13.6, 8.7, 7.5, 4.7 Hz, 1H), 1.62 (dtd, J = 14.3, 8.1, 6.4 Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 144.7, 139.8, 135.1, 131.7, 130.3, 129.8, 128.2, 120.1, 39.5, 34.1, 33.1, 32.6, 21.8 ppm. IR (neat, cm^{-1}): 3274, 3055, 2956, 2931, 2892, 1596, 1488, 1450, 1399, 1317, 1291, 1223, 1151, 1112, 1088, 1007. HRMS calcd. for ($\text{C}_{17}\text{H}_{18}\text{BrNNaO}_2\text{S}$) [$\text{M}+\text{Na}$] $^+$: 402.0134 found 402.0122.

General procedure 6 (GP6): Cross-coupling of **S5** with aryl-boronic acids

A flame dried Schlenk flask was charged with **S5**, boronic acid (1.3 equiv.), PdCl₂(dppf) (2.0 mol%) and Na₂CO₃ (aq. 1.0 M) under a flow of argon. Then a mixture of PhMe:EtOH:H₂O (3:2:1, 0.08 M), degassed in advance, was added into the flask. The resulting reaction was heated to 80 °C and stirred at this temperature overnight (the reaction progress can be monitored by TLC). Upon completion, the reaction was cooled to RT and diluted with H₂O. The organic phase was separated and the aqueous phase was extracted with EtOAc. The combined organic fractions were dried (MgSO₄) and concentrated *in vacuo*. The crude was purified by column chromatography on silica gel (hexane: EtOAc 2:1 → 1:1) to afford the product. If necessary, the product can be washed with Et₂O for additional purification.

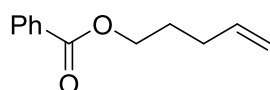


1-(4'-(2-(1-Tosylaziridin-2-yl)ethyl)-[1,1'-biphenyl]-4-yl) ethan-1-one (1o): Following **GP6** with (4-acetylphenyl)boronic acid (0.49 g, 1.5 equiv.), **S5** (0.76 g, 2.0 mmol, 1.0 equiv.) afforded **1o** as a white solid (0.72 g, 86%) after purification by column chromatography on silica gel (hexane: EtOAc 9:1). M.P. = 126 – 127 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (d, *J* = 8.5 Hz, 2H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 2.87 – 2.76 (m, 1H), 2.68 (m, 2H), 2.67 – 2.64 (m, 4H), 2.45 (s, 3H), 2.08 (d, *J* = 4.6 Hz, 1H), 1.94 (dddd, *J* = 13.6, 8.7, 7.5, 4.8 Hz, 1H), 1.70 (dtd, *J* = 14.2, 8.1, 6.4 Hz, 1H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ 197.9, 145.6, 144.7, 141.1, 137.9, 135.9, 135.2, 129.8, 129.2, 129.1, 128.2, 127.5, 127.2, 39.7, 34.2, 33.2, 32.8, 26.8, 21.8 ppm. IR (neat, cm⁻¹): 3004, 2925, 1672, 1601, 1527, 1493, 1446, 1421, 1398, 1360, 1336, 1308, 1264, 1234, 1160, 1088. HRMS calcd. for (C₂₅H₂₅NO₃S) [M+Na]⁺: 442.1447 found 442.1463.

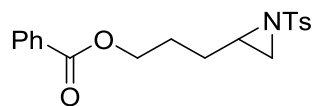


tert-Butyl 2-(4-(2-(1-tosylaziridin-2-yl)ethyl)phenyl)-1H-pyrrole-1-carboxylate (1p): Following **GP6** with *N*-Boc-2-pyrroleboronic acid (0.82 g, 1.3 equiv.), **S5** (1.1 g, 2.9 mmol, 1.0 equiv.) afforded **1p** as a yellow viscous oil (0.55 g, 39%) after purification by column chromatography on silica gel (hexane: EtOAc 8:2). ¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* =

7.9 Hz, 2H), 7.33 (dd, $J = 3.3, 1.8$ Hz, 1H), 7.25 (d, $J = 8.2$ Hz, 2H), 7.09 (d, $J = 8.2$ Hz, 2H), 6.21 (t, $J = 3.3$ Hz, 1H), 6.15 (dd, $J = 3.3, 1.8$ Hz, 1H), 2.79 (ddt, $J = 7.8, 6.9, 4.7$ Hz, 1H), 2.66 – 2.58 (m, 3H), 2.45 (s, 3H), 2.09 (d, $J = 4.6$ Hz, 1H), 1.91 (dddd, $J = 13.5, 8.6, 7.5, 4.8$ Hz, 1H), 1.67 (dtd, $J = 14.5, 8.0, 6.9$ Hz, 1H), 1.36 (s, 9H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 149.5, 144.7, 139.8, 135.2, 135.0, 132.4, 129.8, 129.4, 128.2, 127.7, 122.6, 114.4, 110.7, 83.6, 39.9, 34.1, 33.3, 32.9, 27.8, 21.8 ppm. IR (neat, cm^{-1}): 2979, 2931, 1734, 1597, 1515, 1474, 1456, 1393, 1370, 1309, 1255, 1144, 1091. HRMS calcd. for $(\text{C}_{26}\text{H}_{30}\text{N}_2\text{NaO}_4\text{S}) [\text{M}+\text{Na}]^+$: 489.1818 found 489.1822.

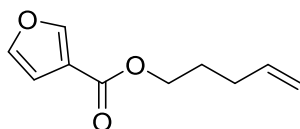


Pent-4-en-1-yl benzoate (S6): To a 100 mL round-bottomed flask under nitrogen, pent-4-en-1-ol (2.9 mL, 1.0 equiv., 28 mmol) and Et_3N (7.8 mL, 2.0 equiv., 56 mmol) were dissolved in CH_2Cl_2 (20 mL). To this solution cooled to 0 °C, benzoyl chloride (3.9 g, 3.3 mL, 28 mmol) was added drop wise over 10 min. The reaction mixture was stirred for an additional 50 min at 0 °C and at room temperature for 3 h. The reaction mixture was quenched with HCl (1.0 M, 50 mL), the layers were separated and the aqueous layer was extracted with Et_2O (30 mL). The combined organic layers were washed with aqueous NaHCO_3 (50 mL), dried (MgSO_4) and filtered. After evaporation of the solvent under reduced pressure, purification by column chromatography on silica gel, eluting with hexane: Et_2O (98:2) gave **S6** (4.6 g, 87 %). ^1H NMR (400 MHz, CDCl_3) δ 8.09 – 7.99 (m, 2H), 7.62 – 7.49 (m, 1H), 7.48 – 7.38 (m, 2H), 5.85 (ddt, $J = 16.9, 10.2, 6.6$ Hz, 1H), 5.07 (dq, $J = 17.1, 1.7$ Hz, 1H), 5.04 – 4.99 (m, 1H), 4.34 (t, $J = 6.6$ Hz, 2H), 2.27 – 2.17 (m, 2H), 1.93 – 1.80 (m, 2H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 166.7, 137.6, 132.9, 130.5, 130.3, 129.6, 128.4, 115.5, 64.4, 30.3, 28.0 ppm. Spectroscopic data for **S6** match those previously reported in the literature.²⁵

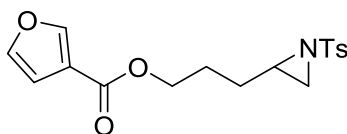


3-(1-Tosylaziridin-2-yl) propyl benzoate (1q): Following **GP3** with **S6** (0.57 g, 3.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **1q** as a white solid (0.44 g, 41%). ^1H NMR (400 MHz, CDCl_3) δ 8.04 – 7.97 (m, 2H), 7.87 – 7.73 (m, 2H), 7.61 – 7.52 (m, 1H), 7.49 – 7.39 (m, 2H), 7.33 (d, $J = 7.9$ Hz, 1H), 4.26 (td, $J = 6.3, 2.2$ Hz, 2H), 2.86 – 2.76 (m, 1H), 2.67 (d, $J = 6.9$ Hz, 1H), 2.42 (s, 3H), 2.11 (d, $J = 4.5$ Hz, 1H), 1.86 – 1.68 (m, 3H), 1.53 – 1.40 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.6, 144.7, 135.2, 133.1, 130.3, 129.8, 129.7,

128.5, 128.2, 64.1, 39.7, 34.0, 28.1, 26.3, 21.7. LRMS (ESI): 359, 254, 237, 204, 155, 105, 91. Spectroscopic data for **1q** match those previously reported in the literature.¹¹



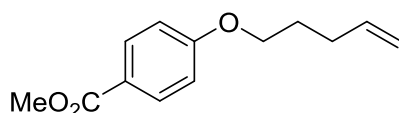
Pent-4-en-1-yl furan-3-carboxylate (S7): Following literature procedure,²⁶ a round-bottom flask was flame dried and charged with furan-3-carboxylic acid (0.56 g, 5.0 mmol), CH₂Cl₂ (25 ml), DMAP (61 mg, 0.50 mmol) and pent-4-en-1-ol (0.43 g, 5.0 mmol). A solution of DCC (1.0 g, 5.0 mmol) in CH₂Cl₂ (1.0 M, 5.0 ml) was then added and reaction was stirred at RT overnight. The resulting mixture was filtered through a pad of silica gel eluted with hexane: EtOAc (95:5) and the filtrate was concentrated *in vacuo* to afford **S7** as a colorless liquid (0.79 g, 88%). ¹H NMR (400 MHz, CDCl₃) δ 8.01 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.42 (t, *J* = 1.7 Hz, 1H), 6.74 (dd, *J* = 1.9, 0.8 Hz, 1H), 5.83 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.09 – 4.98 (m, 2H), 4.26 (t, *J* = 6.6 Hz, 2H), 2.22 – 2.14 (m, 2H), 1.87 – 1.78 (m, 2H) ppm. Spectroscopic data for **S7** match those previously reported in the literature.²⁶



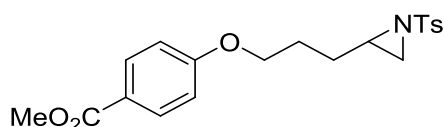
3-(1-Tosylaziridin-2-yl) propyl furan-3-carboxylate (1r): Following **GP3** with **S7** (0.80 g, 4.4 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 → 8:2) afforded **1r** as a colorless oil (0.53 g, 34%). ¹H NMR (400 MHz, CDCl₃) δ 7.98 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.85 – 7.80 (m, 2H), 7.42 (t, *J* = 1.7 Hz, 1H), 7.36 – 7.31 (m, 2H), 6.72 (dd, *J* = 1.9, 0.8 Hz, 1H), 4.24 – 4.14 (m, 2H), 2.83 – 2.77 (m, 1H), 2.65 (d, *J* = 6.9 Hz, 1H), 2.43 (s, 3H), 2.09 (d, *J* = 4.6 Hz, 1H), 1.79 – 1.66 (m, 3H), 1.47 – 1.39 (m, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 163.1, 147.8, 144.8, 143.9, 135.1, 129.8, 128.1, 119.4, 109.9, 63.7, 39.7, 34.0, 28.2, 26.2, 21.8 ppm. IR (neat, cm⁻¹): 3149, 2957, 1718, 1597, 1578, 1507, 1452, 1404, 1304, 1234, 1155, 1076, 1007, 970, 942, 898, 873, 815, 762, 712, 691, 660, 603, 568, 550. HRMS calcd. for (C₁₇H₁₉NNaO₅S) [M+H]⁺: 372.0876 found 372.0871.

General procedure 7 (GP7): Synthesis of pentenylated phenols (S8-11).

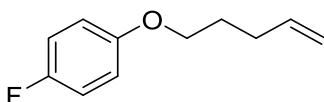
To the phenol (1.1 equiv.) and K_2CO_3 (2.0 equiv.) in CH_3CN (1.0 M) was added 5-bromopent-1-ene (1.0 equiv.). The reaction mixture was heated to 80 °C for 16 h and then allowed to cool to RT. The mixture was diluted with Et_2O (25 ml) and filtered, washing with Et_2O until all product had eluted. Purification was carried out by column chromatography (hexane: $EtOAc$ 95:5).



Methyl 4-(pent-4-en-1-yloxy) benzoate (S8): Following **GP7**, methyl 4-hydroxybenzoate (2.43 g, 1.1 equiv.) afforded **S8** (2.9 g, 87%) as an oil. 1H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.94 (m, 2H), 6.94 – 6.86 (m, 2H), 5.85 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H), 5.07 (dq, J = 17.1, 1.7 Hz, 1H), 5.01 (ddt, J = 10.2, 2.0, 1.2 Hz, 1H), 4.02 (t, J = 6.4 Hz, 2H), 3.88 (s, 3H), 2.30 – 2.19 (m, 2H), 1.96 – 1.85 (m, 2H) ppm. Spectroscopic data for **S8** match those previously reported in the literature.²⁷

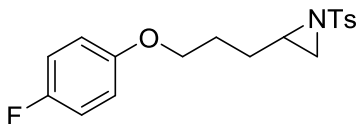


Methyl 4-(3-(1-tosylaziridin-2-yl)propoxy) benzoate (1s): Following **GP3** with **S8** (0.44 g, 2.0 mmol), purification by column chromatography on silica gel (hexane: $EtOAc$ 9:1 → 8:2) afforded **1s** as a white solid (0.21 g, 27%). M.P: 67 - 69 °C. 1H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.95 (m, 2H), 7.83 – 7.78 (m, 2H), 7.33 – 7.29 (m, 2H), 6.87 – 6.83 (m, 2H), 3.97 (td, J = 6.2, 2.3 Hz, 2H), 3.88 (s, 3H), 2.83 (ddt, J = 8.1, 6.9, 4.5 Hz, 1H), 2.65 (d, J = 6.9 Hz, 1H), 2.42 (s, 3H), 2.09 (d, J = 4.6 Hz, 1H), 1.88 (dddd, J = 13.3, 8.9, 6.3, 4.4 Hz, 1H), 1.85 – 1.76 (m, 2H), 1.53 – 1.42 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 162.7, 144.7, 135.2, 131.7, 129.8, 128.1, 122.7, 114.2, 67.1, 52.0, 39.8, 34.0, 28.0, 26.6, 21.8 ppm. IR (neat, cm^{-1}): 2953, 2923, 2880, 1700, 1611, 1513, 1442, 1397, 1318, 1292, 1269, 1218, 1193, 1173, 1154, 1118, 1098, 1029, 1005. HRMS calcd. for $(C_{20}H_{23}NNaO_5S) [M+Na]^+$: 412.1189 found 412.1180.

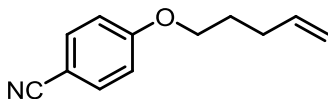


1-Fluoro-4-(pent-4-en-1-yloxy) benzene (S9): Following **GP7**, 4-fluorophenol (1.8 g, 1.1 equiv.) gave **S9** (2.0 g, 74%) as a colorless oil. 1H NMR (400 MHz, $CDCl_3$) δ 7.01 – 6.91 (m, 2H), 6.87 – 6.78 (m, 2H), 5.85 (ddtd, J = 16.9, 10.1, 6.7, 0.9 Hz, 1H), 5.06 (dp, J = 17.2, 1.7 Hz, 1H), 5.00 (ddt,

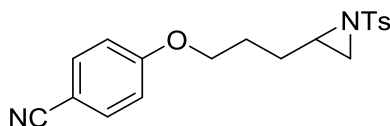
$J = 10.2, 2.0, 1.2$ Hz, 1H), 3.93 (t, $J = 6.4$ Hz, 2H), 2.29 – 2.19 (m, 2H), 1.93 – 1.81 (m, 2H) ppm. ^{19}F NMR (376 MHz, CDCl_3) δ -124.10 ppm. Spectroscopic data for **S9** match those previously reported in the literature.²⁸



2-(3-(4-Fluorophenoxy)propyl)-1-tosylaziridine (1t): Following **GP3** with **S9** (0.90 g, 5.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 \rightarrow 8:2) afforded **1t** as a colorless oil (0.37 g, 41%). M.P: 55 – 57 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.84 – 7.77 (m, 2H), 7.34 – 7.30 (m, 2H), 7.01 – 6.90 (m, 2H), 6.85 – 6.73 (m, 2H), 3.94 – 3.79 (m, 2H), 2.82 (ddt, $J = 8.1, 7.0, 4.5$ Hz, 1H), 2.64 (d, $J = 7.0$ Hz, 1H), 2.43 (s, 3H), 2.09 (d, $J = 4.6$ Hz, 1H), 1.91 – 1.80 (m, 1H), 1.82 – 1.71 (m, 2H), 1.54 – 1.41 (m, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 158.5, 156.1, 155.1 (d, $J = 2.2$ Hz), 144.7, 135.2, 128.9 (d, $J = 172.8$ Hz), 115.9 (d, $J = 23.0$ Hz), 115.5 (d, $J = 8.0$ Hz), 67.5, 39.9, 34.0, 28.1, 26.7, 21.7. ^{19}F NMR (376 MHz, CDCl_3) δ -124.19 (tt, $J = 8.3, 4.3$ Hz) ppm. IR (neat, cm^{-1}): 3071, 3055, 2953, 2932, 2879, 1595, 1504, 1474, 1392, 1318, 1293, 1245, 1200, 1154, 1095, 1028. HRMS calcd. for ($\text{C}_{18}\text{H}_{21}\text{FNO}_3\text{S}$) $[\text{M}+\text{H}]^+$: 350.1221 found 350.1225.

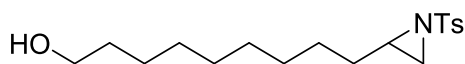


4-(Pent-4-en-1-yloxy) benzonitrile (S10): Following **GP7**, 4-hydroxybenzonitrile (1.2 g, 10 mmol), gave **S10** as a colorless oil (1.9 g, 99%). ^1H NMR (400 MHz, CDCl_3) δ 7.61 – 7.53 (m, 2H), 6.97 – 6.89 (m, 2H), 5.84 (ddt, $J = 16.9, 10.2, 6.7$ Hz, 1H), 5.06 (dq, $J = 17.0, 1.6$ Hz, 1H), 5.02 (ddt, $J = 10.2, 1.8, 1.2$ Hz, 1H), 4.01 (t, $J = 6.4$ Hz, 2H), 2.29 – 2.19 (m, 2H), 1.91 (tt, $J = 7.0, 6.4$ Hz, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ 162.5, 137.5, 134.1, 119.4, 115.7, 115.3, 103.9, 67.7, 30.1, 28.2 ppm. Spectroscopic data for **S10** match those previously reported in the literature.²⁹

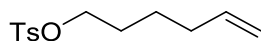


4-(3-(1-Tosylaziridin-2-yl)propoxy) benzonitrile (1u): Following **GP3** with **S10** (0.94 g, 5.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 \rightarrow 6:4) gave **1u** as a white solid (0.93 g, 52%). M.P: 63 – 65 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, $J = 8.3$ Hz, 2H), 7.59 (d, $J = 8.9$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 6.93 (d, $J = 8.9$ Hz, 2H), 4.02 (t, $J = 6.0$ Hz, 2H),

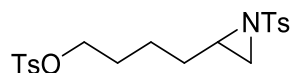
2.87 (ddt, $J = 8.7, 7.0, 4.3$ Hz, 1H), 2.65 (d, $J = 7.0$ Hz, 1H), 2.45 (s, 3H), 2.10 (d, $J = 4.5$ Hz, 1H), 1.99 – 1.79 (m, 3H), 1.55 – 1.42 (m, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 162.3, 144.8, 135.1, 134.1, 129.8, 128.1, 119.4, 115.3, 104.0, 67.2, 39.6, 34.1, 28.0, 26.5, 21.8 ppm. IR (neat, cm^{-1}): 2915, 2223, 1604, 1573, 1506, 1476, 1403, 1304, 1259, 1157, 1087, 1019. HRMS calcd. for $(\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_5\text{S})$ $[\text{M}+\text{H}]^+$: 357.1267 found 357.1260.



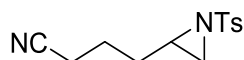
9-(1-Tosylaziridin-2-yl) nonan-1-ol (1v): Following literature procedure³⁰ with 10-undecen-1-ol (4.0 ml, 20 mmol, 2.0 equiv.), **1v** was isolated with trace uncyclized intermediate after purification by column chromatography on silica gel (CH_2Cl_2 : Et_2O 2:1). This mixture was submitted to a base cyclization (**GP4**) to give **1v** in >98% purity (2.5 g, 74%). ^1H NMR (400 MHz, CDCl_3) δ 7.86 – 7.79 (m, 2H), 7.37 – 7.29 (m, 2H), 3.63 (t, $J = 6.6$ Hz, 2H), 2.72 (tt, $J = 7.3, 4.8$ Hz, 1H), 2.63 (d, $J = 7.0$ Hz, 1H), 2.44 (s, 3H), 2.05 (d, $J = 4.6$ Hz, 1H), 1.61 – 1.47 (m, 4H), 1.41 – 1.13 (m, 12H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 144.5, 135.4, 129.8, 128.1, 63.2, 40.6, 34.0, 32.9, 31.4, 29.5, 29.5, 29.4, 29.1, 26.9, 25.8, 21.8 ppm. LRMS (ESI): 701 (2M+Na), 679 (2M+H), 362 (M+Na), 340 (M+H). Spectroscopic data for **1v** match those previously reported in the literature.³⁰



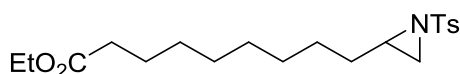
Hex-5-en-1-yl 4-methylbenzenesulfonate (S11): A solution of hex-5-en-1-ol (3.6 ml, 30 mmol, 1.0 equiv.) in CH_2Cl_2 (60 mL) was cooled down to 0 °C. Et_3N (5.0 mL, 36 mmol, 1.2 equiv) and *p*-toluenesulfonyl chloride (5.7 g, 30 mmol, 1.0 equiv) were added subsequently. After addition, the reaction mixture was warmed to RT and stirred for 5 h. A aqueous solution of NaHCO_3 (sat.) was then added and the aqueous phase was extracted with EtOAc (3×60 ml). The combined organic phases were washed with brine (30 ml), dried (MgSO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane: EtOAc 96:4 → 92:8) gave (6.4 g, 83%) as a colorless liquid. ^1H NMR (400 MHz, CDCl_3): δ 7.81 – 7.77 (m, 2H), 7.37 – 7.31 (m, 2H), 5.72 (ddt, $J = 17.0, 10.2, 6.7$ Hz, 1H), 4.99 – 4.91 (m, 2H), 4.03 (t, $J = 6.4$ Hz, 2H), 2.45 (s, 3H), 2.00 (m, 2H), 1.65 (m, 2H), 1.46 – 1.36 (m, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3): δ 144.8, 138.0, 133.4, 130.0, 128.0, 115.2, 100.1, 70.6, 33.0, 28.4, 24.7, 21.8 ppm. Spectroscopic data for **S11** match those previously reported in the literature.³¹



4-(1-Tosylaziridin-2-yl) butyl 4-methylbenzenesulfonate (1w): Following **GP3** with **S11** (0.64 g, 2.5 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 → 8:2) afforded **1w** as a colorless oil (0.57 g, 55%). ^1H NMR (400 MHz, CDCl_3) δ 7.84 – 7.76 (m, 2H), 7.80 – 7.73 (m, 2H), 7.38 – 7.33 (m, 2H), 7.36 – 7.30 (m, 2H), 3.91 (td, J = 6.4, 1.1 Hz, 2H), 2.67 (tt, J = 7.1, 4.5 Hz, 1H), 2.59 (d, J = 7.0 Hz, 1H), 2.45 (s, 6H), 2.01 (d, J = 4.5 Hz, 1H), 1.65 – 1.51 (m, 3H), 1.37 – 1.18 (m, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ 144.9, 144.8, 135.1, 133.2, 130.0, 129.8, 128.1, 128.0, 70.2, 39.8, 33.8, 30.7, 28.2, 22.9, 21.8 ppm. IR (neat, cm^{-1}): 2927, 2867, 1597, 1495, 1455, 1354, 1320, 1232, 1174, 1157, 1094, 1019. HRMS calcd. for $(\text{C}_{20}\text{H}_{25}\text{NNaO}_5\text{S}_2)$ $[\text{M}+\text{Na}]^+$: 446.1066 found 446.1060.

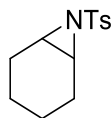


4-(1-Tosylaziridin-2-yl) butanenitrile (1x): Following **GP3** but keeping the reaction scale to 1.0 mmol, hex-5-enenitrile (3×0.12 mL, 3×1 mmol) afforded **1x** as a yellow oil (0.20 g, 25%) after purification of the combined reactions by column chromatography on silica gel (hexane: EtOAc 8:2 → 6:4). ^1H NMR (400 MHz, CDCl_3) δ 7.83 – 7.77 (m, 2H), 7.38 – 7.31 (m, 2H), 2.73 (ddt, J = 8.5, 7.0, 4.2 Hz, 1H), 2.61 (d, J = 7.0 Hz, 1H), 2.44 (s, 3H), 2.36 (td, J = 7.1, 2.5 Hz, 2H), 2.07 (d, J = 4.5 Hz, 1H), 1.89 (dddd, J = 14.3, 8.4, 6.5, 3.9 Hz, 1H), 1.67 (dq, J = 8.9, 7.1, 1.9 Hz, 2H), 1.42 – 1.28 (m, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 145.0, 134.8, 129.9, 128.1, 119.2, 38.7, 33.8, 30.0, 23.0, 21.7, 16.5 ppm. IR (neat, cm^{-1}): 2941, 2246, 1597, 1455, 1404, 1319, 1291, 1233, 1157, 1091. HRMS calcd. for $(\text{C}_{13}\text{H}_{16}\text{N}_2\text{NaO}_2\text{S})$ $[\text{M}+\text{Na}]^+$: 287.0825 found 287.0820.

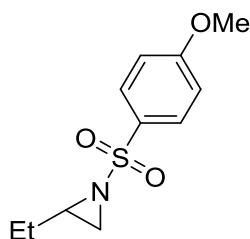


Ethyl 9-(1-tosylaziridin-2-yl) nonanoate (1y): Following **GP3** with ethyl undec-10-enoate (1.2 mL, 5.0 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 → 8:2) afforded **1y** as a colourless oil (1.2 g, 63%). ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 7.9 Hz, 2H), 4.22 (q, J = 7.1 Hz, 2H), 2.81 (tt, J = 7.3, 4.8 Hz, 1H), 2.73 (d, J = 7.0 Hz, 1H), 2.54 (s, 3H), 2.37 (t, J = 7.5 Hz, 2H), 2.15 (d, J = 4.6 Hz, 1H), 1.75 – 1.58 (m, 3H), 1.47 – 1.24 (m, 14H). ^{13}C NMR (101 MHz, CDCl_3) δ 174.0, 144.5, 135.4, 129.8, 128.2, 60.3, 40.6, 34.5, 33.9, 31.4, 29.3, 29.2, 29.2, 29.1, 26.9, 25.1, 21.8, 14.4. IR (neat, cm^{-1}): 2928, 2855, 1731, 1597, 1457, 1373,

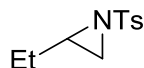
1323, 1305, 1232, 1184, 1158, 1090, 1033. HRMS calcd. for (C₂₀H₃₁NNaO₄S) [M+Na]⁺: 404.1866 found 404.1859.



7-Tosyl-7-azabicyclo[4.1.0]heptane (1z) Following **GP3** with cyclohexene (4.1 ml, 40 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1) afforded **1z** as a white solid (2.5 g, 25%). ¹H NMR (500 MHz, CDCl₃) δ 7.84 – 7.79 (m, 2H), 7.35 – 7.29 (m, 2H), 2.97 (p, *J* = 1.6 Hz, 2H), 2.44 (s, 3H), 1.83 – 1.73 (m, 4H), 1.45 – 1.33 (m, 2H), 1.27 – 1.16 (m, 2H) ppm. LRMS: 251, 223, 210, 197, 155, 96, 91. ¹³C NMR (101 MHz, CDCl₃) δ 144.1, 136.1, 129.7, 127.8, 39.9, 22.9, 21.8, 19.6 ppm. Spectroscopic data for **1z** match those previously reported in the literature.¹⁹

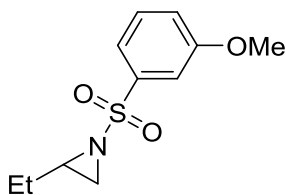


2-Ethyl-1-((4-methoxyphenyl)sulfonyl) aziridine (1aa): Following **GP1** but with 4-methoxybenzenesulfonyl chloride (6.7 g, 2.2 equiv., 33 mmol) instead of TsCl, (±)-2-amino-1-butanol (1.4 mL, 15 mmol) afforded **1aa** as a white solid (1.4 g, 39%) after purification by column chromatography on silica gel (hexane: EtOAc 3:1). M.P. = 59 – 61 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 8.9 Hz, 2H), 7.00 (d, *J* = 8.9 Hz, 2H), 3.88 (s, 3H), 2.67 (tt, *J* = 7.4, 4.7 Hz, 1H), 2.61 (d, *J* = 6.7 Hz, 1H), 2.06 (d, *J* = 4.5 Hz, 1H), 1.64 – 1.56 (m, 1H), 1.30 – 1.38 (m, 1H), 0.84 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 163.7, 130.3, 129.9, 114.3, 55.8, 41.8, 33.7, 24.6, 11.0. IR (neat, cm⁻¹): 3098, 3995, 2980, 2969, 2931, 2873, 2849, 1592, 1578, 1501, 1462, 1445, 1320, 1304, 1258, 1229, 1154, 1143, 1098, 1020. HRMS calcd. for (C₁₁H₁₅NNaO₂S) [M+Na]⁺: 264.0665 found 264.0663.

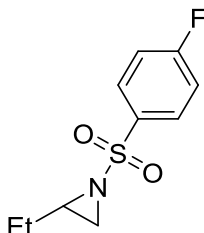


2-Ethyl-1-tosylaziridine (1ab): Following **GP2**, (±)-2-amino-1-butanol (8.7 g, 98 mmol) afforded **1ab** as a colourless oil (18 g, 81%) after purification by column chromatography on silica gel (hexane: EtOAc 9:1). ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 2.69 (tt, *J* = 7.2, 4.7 Hz, 1H), 2.62 (d, *J* = 7.0 Hz, 1H), 2.44 (s, 3H), 2.07 (d, *J* = 4.6 Hz, 1H), 1.67 – 1.52 (m, 1H), 1.30 – 1.38 (m, 1H), 0.83 (t, *J* = 7.5 Hz, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃)

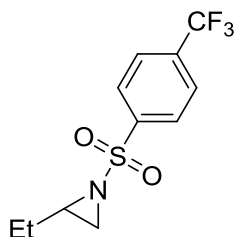
δ 144.5, 135.3, 129.7, 128.1, 41.8, 33.7, 24.6, 21.7, 11.0 ppm. Spectroscopic data for **1ab** match those previously reported in the literature.³²



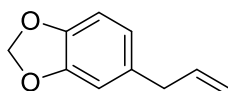
2-Ethyl-1-((3-methoxyphenyl)sulfonyl) aziridine (1ac): Following **GP1** but with 3-methoxybenzenesulfonyl chloride (3.6 g, 2.2 equiv., 18 mmol) instead of TsCl, (\pm)-2-amino-1-butanol (0.76 mL, 8.0 mmol) afforded **1ac** as a colourless oil (0.84 g, 44%) after purification by column chromatography on silica gel (hexane: EtOAc 3:1). ¹H NMR (500 MHz, CDCl₃) δ 7.50 (ddd, J = 7.7, 1.7, 1.0 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.13 (ddd, J = 8.3, 2.7, 1.1 Hz, 1H), 3.85 (s, 3H), 2.71 (tt, J = 7.1, 4.8 Hz, 1H), 2.63 (d, J = 7.0 Hz, 1H), 2.08 (d, J = 4.7 Hz, 1H), 1.60 (dq, J = 14.8, 7.5, 4.9 Hz, 1H), 1.35 (dp, J = 14.8, 7.4 Hz, 1H), 0.83 (t, J = 7.4 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ 159.9, 139.3, 130.1, 120.2, 120.1, 112.6, 55.8, 41.9, 33.8, 24.5, 10.9 ppm. IR (neat, cm⁻¹): 3074, 2968, 2938, 2879, 2839, 1598, 1483, 1464, 1433, 1311, 1287, 1241, 1152, 1099, 1031. HRMS calcd. for (C₁₁H₁₅NNaO₂S) [M+Na]⁺: 264.0665 found 264. 0668.



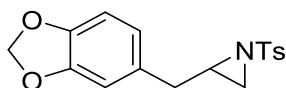
2-Ethyl-1-((4-fluorophenyl)sulfonyl) aziridine (1ad): Following **GP1** but with 4-fluorobenzenesulfonyl chloride (13 g, 66 mmol) instead of TsCl, (\pm)-2-amino-1-butanol (2.8 mL, 30 mmol) afforded **1ad** as a colourless oil (2.5 g, 36%) after purification by column chromatography on silica gel (hexane: EtOAc 9:1). ¹H NMR (400 MHz, CDCl₃) δ 7.99 – 7.94 (m, 2H), 7.24 – 7.19 (m, 2H), 2.72 (tt, J = 7.3, 4.7 Hz, 1H), 2.65 (d, J = 7.0 Hz, 1H), 2.10 (d, J = 4.6 Hz, 1H), 1.62 (dq, J = 14.8, 7.4, 5.0 Hz, 1H), 1.34 (dq, J = 14.7, 7.4 Hz, 1H), 0.83 (t, J = 7.5 Hz, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) 165.8 (d, J = 255.8 Hz), 134.5 (d, J = 3.3 Hz), 130.9 (d, J = 9.5 Hz), 116.4 (d, J = 22.7 Hz), 42.1, 33.9, 24.6, 10.9 ppm. ¹⁹F NMR (376 MHz, CDCl₃) δ -103.63 (tt, J = 8.2, 5.0 Hz) ppm. IR (neat, cm⁻¹): 3106, 3075, 2970, 2937, 2880, 1591, 1493, 1461, 1405, 1323, 1291, 1230, 1166, 1152, 1096, 1085, 1026. 920. HRMS calcd. for (C₁₀H₁₂FNNaO₂S) [M+Na]⁺: 252.0465 found 252.0461.



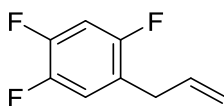
2-Ethyl-1-((4-(trifluoromethyl)phenyl)sulfonyl) aziridine (1ae): Following **GP1** but with a 3 h reaction time and using 4-trifluoromethyl benzenesulfonyl chloride (0.65 g, 2.6 mmol) instead of TsCl, (±)-2-amino-1-butanol (0.11 mL, 1.2 mmol) afforded **1ae** as a colorless oil (0.56 g, 80%) after purification by column chromatography on silica gel (hexane: EtOAc 9:1). ^1H NMR (400 MHz, CDCl_3) δ 8.14 – 8.06 (m, 2H), 7.86 – 7.77 (m, 2H), 2.82 (tt, $J = 7.2, 4.8$ Hz, 1H), 2.70 (d, $J = 7.0$ Hz, 1H), 2.14 (d, $J = 4.7$ Hz, 1H), 1.64 (dtd, $J = 14.8, 7.4, 4.9$ Hz, 1H), 1.40 (dp, $J = 14.7, 7.4$ Hz, 1H), 0.87 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 142.1 (q, $J = 1.0$ Hz), 135.3 (q, $J = 33.0$ Hz), 128.6, 126.3 (q, $J = 3.7$ Hz), 123.3 (q, $J = 273.0$ Hz), 42.4, 34.2, 24.5, 10.9. ^{19}F NMR (376 MHz, CDCl_3) δ -62.92. IR (neat, cm^{-1}): 2972, 2938, 1461, 1404, 1319, 1233, 1162, 1129, 1106, 1087, 1061, 1016. HRMS calcd. for $(\text{C}_{11}\text{H}_{12}\text{F}_3\text{NNaOS})$ $[\text{M}+\text{Na}]^+$: 302.0433 found 302.0434.



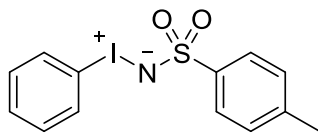
5-Allylbenzo[d][1,3]dioxole (S12): 5-bromobenzo[d][1,3]dioxole (6.0 g, 30 mmol) was dissolved in dry THF (20 ml) and Mg stirrings (1.1 g, 45 mmol) were added. Formation of the organomagnesium compound was promoted by addition of catalytic amount of I_2 at room temperature (caution! reaction is very exothermic; condenser is required). After reaction completion, the resulting solution was added drop wise to a solution of allyl bromide (2.6 ml, 30 mmol) in dry THF (20 ml). After addition, the reaction was stirred at RT for 1 hour. Then reaction mixture was quenched with aqueous NH_4Cl (sat.), the layers were separated and the organic phase was washed with water. After drying (MgSO_4) and concentrating *in vacuo*, the crude material was purified by column chromatography on silica gel (pure pentane) to afford **S12** (4.3 g, 88%) as a colorless liquid. ^1H NMR (400 MHz, CDCl_3) δ 6.75 (d, $J = 7.9$ Hz, 1H), 6.70 (d, $J = 1.4$ Hz, 1H), 6.67 – 6.63 (m, 1H), 5.98 – 5.94 (m, 1H), 5.93 (s, 2H), 5.11 – 5.04 (m, 2H), 3.34 – 3.29 (m, 2H) ppm. Spectroscopic data for **S12** match those previously reported in the literature.³³



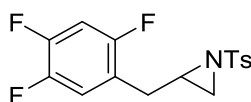
2-(Benzo[d][1,3]dioxol-5-ylmethyl)-1-tosylaziridine (1af): Following **GP3** with **S12** (4.3 g, 27 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 → 5:1) afforded **1af** as a white solid (2.9 g, 32%). ¹H NMR (400 MHz, CDCl₃) δ 7.71 – 7.65 (m, 2H), 7.25 – 7.21 (m, 2H), 6.60 – 6.56 (m, 1H), 6.50 – 6.46 (m, 2H), 5.90 (q, *J* = 1.4 Hz, 1H), 2.91 – 2.83 (m, 1H), 2.76 (dd, *J* = 14.5, 4.8 Hz, 1H), 2.72 (d, *J* = 6.9 Hz, 1H), 2.52 (dd, *J* = 14.5, 7.5 Hz, 1H), 2.43 (s, 3H), 2.15 (d, *J* = 4.5 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 147.6, 146.4, 144.5, 135.0, 130.9, 129.6, 128.1, 121.9, 109.3, 108.3, 101.0, 41.6, 37.3, 32.9, 21.7 ppm. LRMS (ESI): 331, 176, 161, 148, 135, 119, 105, 91, 77. Spectroscopic data for **1af** match those previously reported in the literature.³⁴



1-Allyl-2,4,5-trifluorobenzene (S13): Following a modified literature procedure,³⁴ an oven dried RBF was charged with 1-bromo-2,4,5-trifluorobenzene (4.4 g, 20 mmol) and dry THF (5.0 ml) under Ar atmosphere. The solution was cooled to –10 °C in an ice/ salt bath and then *i*PrMgCl·LiCl (1.2 M in THF, 21 mmol) was added drop wise to reaction mixture. After stirring at 0 °C for 1 h, allyl bromide (1.8 ml, 21 mmol) was added drop wise. The obtained mixture was stirred at 0 °C for 1 h and then allowed to warm to RT and stirred overnight. The reaction was quenched with water and acidified to pH = 1 with aqueous HCl (2.0 M). The layers were separated and the aqueous phase was extracted with EtOAc. The combined organic fractions were washed with brine, dried (MgSO₄), filtered and concentrated *in vacuo*. The crude mixture was purified by flushing through a plug of silica gel using pentane as eluent to afford **S13** as a colorless liquid (2.9 g, 85%). ¹H NMR (400 MHz, CDCl₃) δ 7.00 (ddd, *J* = 10.8, 8.8, 6.8 Hz, 1H), 6.89 (ddd, *J* = 10.2, 9.1, 6.6 Hz, 1H), 5.89 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H), 5.13 (dq, *J* = 10.1, 1.4 Hz, 1H), 5.09 (dq, *J* = 16.9, 1.6, 0.5 Hz, 1H), 3.36 – 3.32 (m, 2H) ppm.



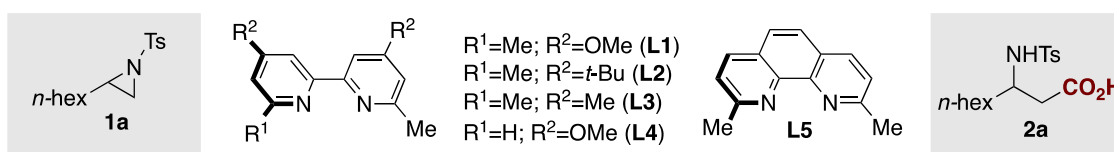
(Tosylimino) phenyliodinane (S14): Following literature procedure,³⁵ toluenesulfonamide (2.8 g, 16 mmol) and KOH (2.3 g, 41 mmol) were dissolved in MeOH (60 ml). The resulting solution was cooled to $-10\text{ }^{\circ}\text{C}$ in an ice/ salt bath and (diacetoxy) iodosobenzene (5.3 g, 17 mmol) was added portion wise. The reaction was stirred for 30 minutes at $-10\text{ }^{\circ}\text{C}$ and then an additional 3 h at RT. Ice cold water (100 ml) was then added and resulting mixture was cooled to $0\text{ }^{\circ}\text{C}$. The formed precipitate was collected by filtration and washed with cold MeOH (20 ml) and EtOAc (100 ml) to afford **S14** (3.2 g, 53%) as a white solid. ^1H NMR (400 MHz, DMSO- d_6) δ 7.71 – 7.67 (m, 2H), 7.49 – 7.41 (m, 3H), 7.29 (t, $J = 7.7\text{ Hz}$, 2H), 7.09 – 7.03 (m, 2H), 2.27 (s, 3H) ppm. Spectroscopic data for **S14** match those previously reported in the literature.³⁵



1-Tosyl-2-(2,4,5-trifluorobenzyl) aziridine (1ag): An oven dried Schlenk flask was charged with anhydrous $\text{Cu}(\text{OTf})_2$ (0.27 mg, 0.74 mmol) and a solution of 1-allyl-2,4,5-trifluorobenzene (**S13**) (1.3 g, 3.0 equiv., 7.5 mmol) in dry CH_3CN (8.0 ml). **S14** (0.93 g, 1.0 equiv., 2.5 mmol) was then added into the reaction solution in one portion under a flow of Ar and the resulting mixture was stirred at RT for 2 hours. The reaction mixture was then diluted with EtOAc (10 ml) and filtered through a pad of silica gel followed by elution with additional EtOAc (20 ml). The obtained solution was concentrated *in vacuo*, and the crude material was purified by column chromatography on silica gel (hexane: EtOAc 9:1 \rightarrow 5:1) to afford **1ag** as a white solid (0.53 g, 42%). ^1H NMR (400 MHz, CDCl_3) δ 7.65 – 7.61 (m, 2H), 7.22 – 7.18 (m, 2H), 6.79 – 6.66 (m, 2H), 3.07 – 3.01 (m, 1H), 2.87 – 2.79 (m, 2H), 2.42 (s, 3H), 2.28 (ddd, $J = 14.5, 8.3, 1.5\text{ Hz}$, 1H), 2.20 (d, $J = 4.2\text{ Hz}$, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 155.6 (ddd, $J = 244.5, 9.3, 2.7\text{ Hz}$), 149.2 (ddd, $J = 250.0, 14.5, 12.2\text{ Hz}$), 146.4 (ddd, $J = 244.8, 12.6, 3.7\text{ Hz}$), 145.0, 134.6, 129.7, 127.9, 120.8 (ddd, $J = 18.4, 5.7, 4.2\text{ Hz}$), 118.7 (ddd, $J = 19.2, 5.9, 1.4\text{ Hz}$), 105.2 (dd, $J = 28.2, 20.8\text{ Hz}$), 40.1, 32.8, 30.5, 21.6 ppm. ^{19}F (367 MHz, CDCl_3) δ (-119.9) – (-120.1) (m), -135.64 (dtd, $J = 21.9, 9.6, 3.4\text{ Hz}$), -142.54 (dddd, $J = 21.6, 15.2, 10.3, 6.5\text{ Hz}$) ppm. LRMS (ESI): 321, 176, 161, 148, 135, 119, 105, 91, 77. Spectroscopic data for **1ag** match those previously reported in the literature.³⁴

2 Optimization of the Reaction Conditions

The Ni-catalyzed carboxylation of aziridines was initially assessed with a batch of **1a** (95% purity) that contained minor impurities (see page S57 for the identity of these compounds), hoping that these might not interfere with productive formation of **2a**. After considerable optimization, it was revealed that the presence of MeOH and amide solvents (DMA, NMP, DMPU) with Mn as reducing agent was critical for success. Notably, (a) the utilization of alcohols other than MeOH resulted in traces, if any, of **2a** and (2) **L1**, **L2** and **L5** gave rise to **2a** in 50-60% yield whereas less electron-rich **L3** or less hindered **L4** resulted in complete loss of reactivity (Scheme S1), thus showing the importance of both MeOH and the ligand environment in this carboxylation reaction. Unfortunately, reproducibility issues came into play with different batches of **1a**, suggesting that the purity might be a critical factor for success. Gratifyingly, this was indeed the case and reproducible results were found for **1a** (>99% purity). In addition, we observed a similar trend to that shown for **1a** (95% purity) in terms of the ligand employed and the critical role found for MeOH. To this end, we continued the optimization with **1a** (>99% purity).



Scheme S1: Ligands employed in the catalytic carboxylation of **1a** (95% purity)

General procedure for the optimization of **2a** from aziridine **1a** (>99% purity):

To an oven dried Schlenk tube in the glove box was added Ni(II) pre-catalyst, ligand and manganese (Mn). A stirrer bar was added and the Schlenk was capped before being removed from the glove box. An atmosphere of CO₂ was then generated by 3 cycles between vacuum (<1 mbar pressure) and CO₂ line (1 bar). Under a flow of CO₂, dry DMPU (or other solvent) was added followed by **1a** (52 μ l, 1 equiv. 0.2 mmol) and finally MeOH (40 μ l, 5 equiv. 1.0 mmol). Note: between each addition, the Schlenk tube was agitated for ~10 s to ensure the components were well dissolved. The Schlenk tube was then tightly capped and stirred at 10 °C (or other specified temperature) for the noted time. The reaction was quenched by careful addition of HCl (1.0 M, 2.0 ml) at 10 °C, diluted with EtOAc and then stirred at RT. Trimethoxybenzene (11 mg, 0.33 equiv.) internal standard was added as a stock solution in EtOAc, the layers were separated and the aqueous layer was extracted with EtOAc (3 \times 5.0 ml). The combined organic layers were then washed twice with HCl (1.0 M, 15 ml), dried (MgSO₄), filtered and concentrated *in vacuo*. Quantification was carried out by integration of ¹H NMR against the TMB internal standard.

Table S1. Influence of the Ni(II) precatalyst and ligand on the carboxylation of **1a**.

Ni(II) precatalyst / L	Conv. (%)	2a (%)	TsNH ₂ (%)
NiCl ₂ ·glyme / L1	90, 84 ^a	73, 67 ^a	12, 17 ^a
NiCl ₂ ·glyme / L1 (10 mol%)	53	32	8
NiCl ₂ ·glyme / L1 (15 mol%)	92	61	11
(L1)NiCl ₂ / no L1	75	50	12
(L1)NiCl ₂ / L1 (10 mol%)	63	49	14
NiCl ₂ ·glyme / L2	99	47	46
(L2)NiCl ₂ / L2 (10 mol%)	42	42	39
NiCl ₂ ·glyme / L3	15	0	trace
NiCl ₂ ·glyme / L4	27	trace	8
NiCl ₂ ·glyme / L5	87	56	20

R¹=Me; R²=OMe (L1)
 R¹=Me; R²=*i*-Bu (L2)
 R¹=Me; R²=Me (L3)
 R¹=H; R²=OMe (L4)
 L5

^a NiCl₂ glyme (20 mol%), L1 (40 mol%).**Table S2.** Influence of the temperature, solvent and Mn equivalent.

T (°C)	solvent	Conv. (%)	2a (%)	TsNH ₂ (%)
10	DMPU	90, 89 ^a	73, 58 ^a	12, 10 ^a
15	DMPU	83	70	15
25	DMPU	86	53	20
10	DMA	82	62	15
10	NMP	90	67	17

^a Mn (2 equiv.)**Table S3.** Influence of the reaction time and CO₂ pressure.

CO ₂ (bar)	Conv. (%)	2a (%)	TsNH ₂ (%)
1.0	94	76	12
0.5	93	71	20
1.75	80	69	10
2.5	76	65	9
3.25	62	62	8
1.0	20 ^a	0 ^a	3 ^a
1.0	0 ^b	0 ^b	0 ^b

^a No MeOH ^b No NiCl₂·glyme or L1

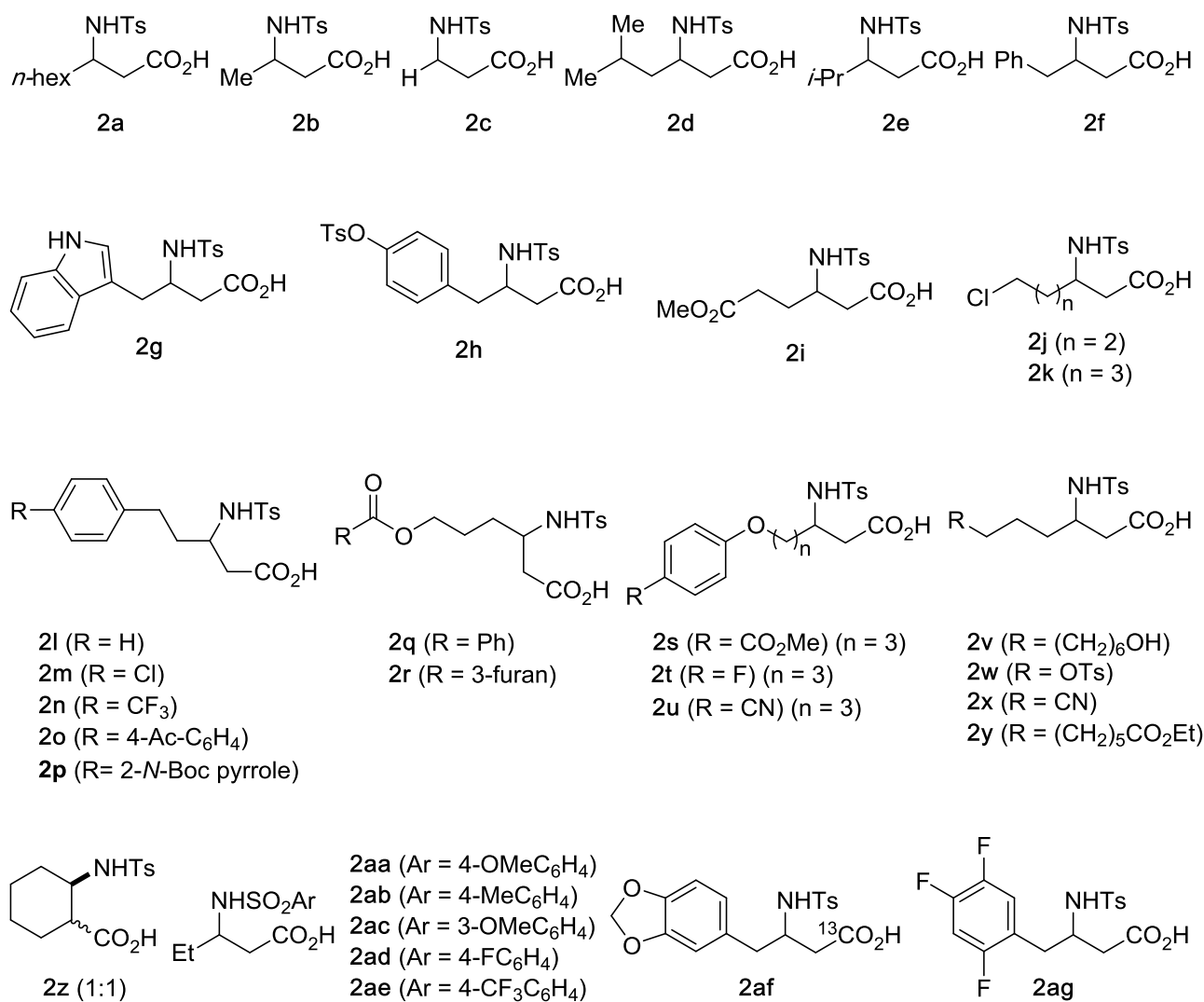
3 Ni-Catalyzed Reductive Carboxylation of Aziridines

3.1 Table 2 Substrate Scope

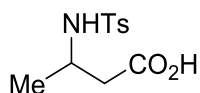
General procedure 8 (GP8): Ni-catalyzed coupling of aziridines with CO₂ (2a - 2ag)

To an oven dried Schlenk tube in the glove box was added NiCl₂glyme (4.4 mg, 0.020 mmol), **L1** (9.8 mg, 0.040 mmol), Mn (33 mg, 0.60 mmol) and the aziridine (1.0 equiv., 0.20 mmol) if solid. A stirrer bar was added and the Schlenk was capped before being removed from the glove box. An atmosphere of CO₂ was generated by 3 cycles between vacuum (< 1 mbar pressure) and CO₂ line (1 atm). Under a flow of CO₂, dry DMPU (0.40 M, 0.50 ml) was added followed by the aziridine (1.0 equiv. 0.20 mmol) if liquid and MeOH (40 µl, 1.0 mmol). Note: between each addition, the Schlenk tube was manually agitated for ~10 s. The Schlenk tube was then capped and stirred at 10 °C for the specified timeⁱⁱ. The reaction was quenched by addition of HCl (1.0 M, 2.0 ml) at 10 °C, diluted with EtOAc and then stirred at RT. The layers were separated and the aqueous layer extracted with EtOAc (3 × 5 ml). The combined organic layers were washed twice with HCl (1.0 M, 15 ml), dried (MgSO₄), filtered and concentrated *in vacuo*. Purification was carried out by column chromatography on silica gel. The crude reaction mixture was dissolved in CH₂Cl₂: Et₃N (1.0 ml:0.2 ml) and loaded onto a short plug of silica equilibrated with hexane: EtOAc (1:1). A second wash of the flask was performed using CH₂Cl₂: Et₃N (1.0 ml:0.2 ml) and a third with CH₂Cl₂ (1.0 ml). The impurities of the reaction were removed by flushing through hexane: EtOAc (1:1, 100 ml) and the product was eluted with EtOAc: AcOH (98:2).

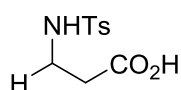
ⁱⁱ Although high yields and conversions can be obtained after 48 h, the inability to monitor the progress of these pressurized reactions meant that they were generally run for 72 h to ensure complete consumption of the aziridine and the maximum possible yield. In certain cases, the reaction stalled with significant aziridine remaining and prolonged reaction times did not lead to more acid being generated.



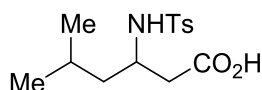
3-((4-Methylphenyl)sulfonamido) nonanoic acid (2a): Following **GP8** with a reaction time of 3 days, **1a** (52 μ l, 0.20 mmol) gave **2a** (45 mg, 69%) as a white solid. In a scale up experiment **1a** (0.13 ml, 0.50 mmol) gave **2a** (0.12 g, 73%) giving an average yield of 71%. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 5.39 (d, J = 9.1 Hz, 1H), 3.57 – 3.48 (m, 1H), 2.57 – 2.50 (m, 2H), 2.44 (s, 3H), 1.54 – 1.43 (m, 2H), 1.29 – 1.05 (m, 8H), 0.86 (t, J = 7.2 Hz, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 143.6, 138.0, 129.8, 127.2, 50.7, 39.0, 34.7, 31.7, 28.8, 25.8, 22.6, 21.6, 14.2 ppm. LRMS (ESI): 653 (2M–H), 440 (M+TFA⁺), 326 (M–H). Spectroscopic data for **2a** match those previously reported in the literature.³⁶



3-((4-Methylphenyl)sulfonamido) butanoic acid (2b): Following **GP8** with a reaction time of 3 days, **1b** (42 mg, 0.20 mmol) gave **2b** (34 mg, 66%) as a white solid. In a separate independent experiment **2b** (33 mg, 64%) was isolated giving an average yield of 65%. ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, J = 8.3 Hz, 2H), 7.32 – 7.29 (m, 2H), 5.38 (d, J = 8.5 Hz, 1H), 3.77 – 3.66 (m, 1H), 2.51 (d, J = 5.3 Hz, 2H), 2.42 (s, 3H), 1.16 (d, J = 6.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.0, 143.7, 137.9, 129.9, 127.2, 46.4, 40.6, 21.7, 21.0 ppm. Spectroscopic data for **2b** match those previously reported in the literature.³⁷



3-((4-Methylphenyl)sulfonamido) propanoic acid (2c): Following **GP8** with a reaction time of 2 days,ⁱⁱⁱ *N*-tosylaziridine (40 mg, 0.20 mmol) gave **2c** (20 mg, 41%) as a white solid. In a separate independent experiment **2c** (19 mg, 39%) was isolated giving an average yield of 40%. ^1H NMR (400 MHz, CDCl_3) δ 7.75 (d, J = 8.3 Hz, 2H), 7.34 – 7.29 (m, 2H), 5.81 (t, J = 6.7 Hz, 1H), 3.23 – 3.15 (m, 2H), 2.62 (t, J = 5.7 Hz, 2H), 2.43 (s, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.0, 143.8, 137.0, 130.0, 127.2, 38.4, 34.0, 21.7 ppm. LRMS (ESI): 485 (2M–H), 278 (M+Cl), 242 (M–H). Spectroscopic data for **2c** match those previously reported in the literature.³⁷

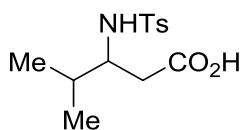


5-Methyl-3-((4-methylphenyl)sulfonamido) hexanoic acid (2d): Following **GP8** with a reaction time of 5 days,^{iv} **1d** (46 μl , 0.20 mmol) gave **2d** (43 mg, 72%) as a white solid. In a separate independent experiment **2d** (49 mg, 82%) was isolated giving an average yield of 77%. ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, J = 8.3 Hz, 2H), 7.32 – 7.27 (m, 2H), 5.43 (d, J = 9.1 Hz, 1H), 3.57 (tq, J = 10.0, 5.1 Hz, 1H), 2.47 (d, J = 5.0 Hz, 2H), 2.42 (s, 3H), 1.59 – 1.47 (m, 1H), 1.41 (ddd, J = 14.4, 8.9, 5.6 Hz, 1H), 1.30 – 1.22 (m, 2H), 0.80 (d, J = 6.6 Hz, 3H), 0.69 (d, J = 6.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.7, 143.7, 138.0, 129.9, 127.2, 48.7, 43.9, 39.1, 24.6, 22.8, 21.8, 21.7

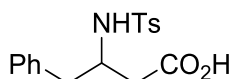
ⁱⁱⁱ The reaction was complete after 48 h due to the reduced steric environment of the aziridine. Although most by-products generated in this reaction are volatile and hence not observed, the large amount of TsNH_2 (45%) generated suggests β -hydride and deamination pathways are more prevalent.

^{iv} The steric hindrance of the *i*Bu group reduces the rate of the reaction but complete conversion is reached if a longer reaction time is used. Conversely, the reaction is more selective for the desired β -amino acid with the highest yield (80–83% by ^1H NMR) observed of all aziridines tested and only trace amounts of TsNH_2 (5–10%) generated.

ppm. LRMS (ESI): 597 (2M-H), 298 (M-H). Spectroscopic data for **2d** match those previously reported in the literature.³⁸

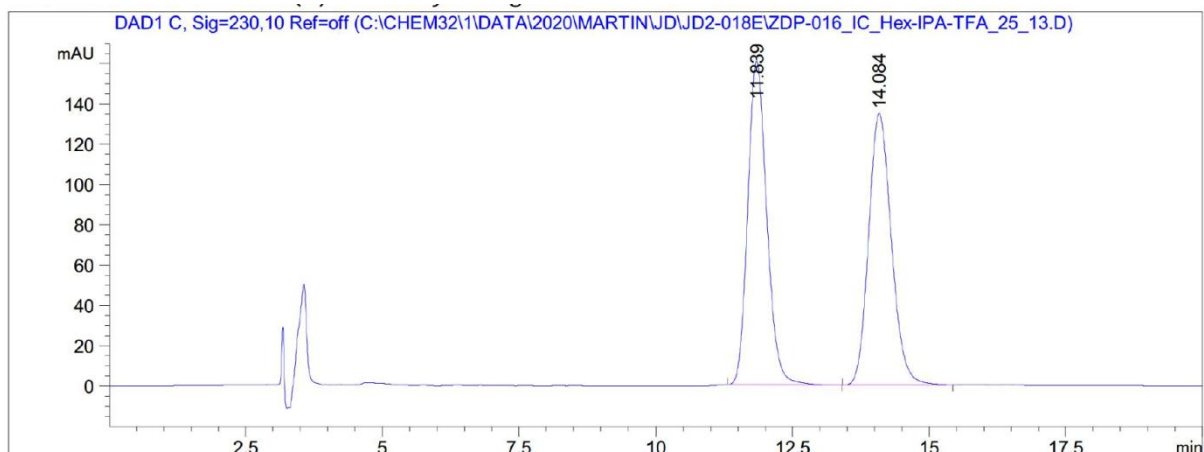


4-Methyl-3-((4-methylphenyl)sulfonamido) pentanoic acid (2e): Following **GP8** with a reaction time of 7 days,^v **1e** (48 mg, 0.20 mmol) gave **2e** (24 mg, 42%) as a white solid. In a separate independent experiment **2e** (23 mg, 40%) was isolated giving an average yield of 41%. ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.33 (d, *J* = 9.2 Hz, 1H), 3.40 – 3.28 (m, 1H), 2.50 (dd, *J* = 16.2, 5.1 Hz, 1H), 2.45 – 2.38 (m, 4H), 1.83 (hept, *J* = 6.8 Hz, 1H), 0.83 (dd, *J* = 6.8, 5.8 Hz, 6H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 176.8, 143.6, 137.9, 129.8, 127.3, 56.2, 36.4, 31.7, 21.7, 19.1, 18.7 ppm. LRMS (ESI): 569 (2M-H), 284 (M-H). Spectroscopic data for **2e** match those previously reported in the literature.³⁹



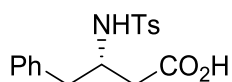
3-((4-Methylphenyl)sulfonamido)-4-phenyl butanoic acid (2f): Following **GP8** with a reaction time of 3 days and the temperature maintained at 10 – 13 °C for the duration, **1f** (0.29 g, 1.0 mmol) gave **2f** (0.21 g, 63%) as a white solid. In a separate independent experiment **2f** (0.20 g, 60%) was isolated giving an average yield of 62%. Note: when performing the reaction on larger scale, it is important to ensure efficient stirring due to the non-homogenous nature of the reaction. M.P. = 103 – 106 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.24 – 7.18 (m, 5H), 7.04 – 7.00 (m, 2H), 5.58 (d, *J* = 8.5 Hz, 1H), 3.84 – 3.68 (m, 1H), 2.87 (dd, *J* = 13.7, 7.6 Hz, 1H), 2.79 (dd, *J* = 13.7, 6.7 Hz, 1H), 2.56 (d, *J* = 5.3 Hz, 2H), 2.40 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 176.4, 143.6, 137.3, 136.9, 129.8, 129.4, 128.8, 127.1, 127.0, 51.9, 40.7, 37.9, 21.6 ppm. LRMS (ESI): 334 (M+H)⁺, 356 (M+Na)⁺. Spectroscopic data for **2f** match those previously reported in the literature.³⁷ HPLC: *rac* (CHIRALPAK[®] IC, hexane/ *i*-PrOH/ TFA = 75:25:0.1, 1 mL/min, 220 nm, *t*_R = 11.839; 14.084).

^v After 3 days with this hindered substrate, 27% of **2f** was observed by ¹H NMR and 66% **1f** remained. After 7 days, 41% of **2f** was observed by and 45% **1f** remained. After 10 days, 42% of **2f** was observed and 50% **1f** still remained suggesting the reaction had stalled and the maximum amount of **2f** had been reached. Other reaction variables were modified to try and improve the yield such as increasing the [Ni] to 20 mol%, switching to less hindered **L4** and increasing the temperature but without success.

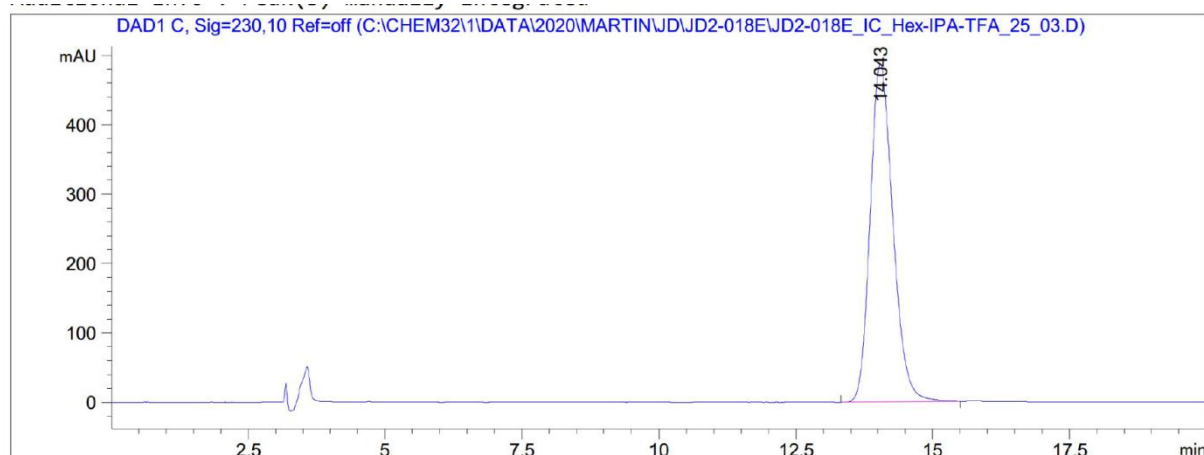


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.839	BB	0.3728	3899.17773	160.85664	49.9536
2	14.084	BB	0.4482	3906.41431	134.74947	50.0464

Totals : 7805.59204 295.60611

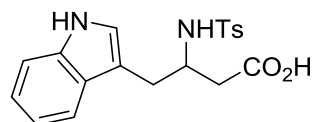


(S)-3-((4-Methylphenyl)sulfonamido)-4-phenyl butanoic acid (7): Following **GP8** with a reaction time of 3 days, **(S)-1f** (57 mg, 0.20 mmol) gave **7** (47 mg, 70%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.24 – 7.18 (m, 5H), 7.04 – 7.00 (m, 2H), 5.58 (d, *J* = 8.5 Hz, 1H), 3.84 – 3.68 (m, 1H), 2.87 (dd, *J* = 13.7, 7.6 Hz, 1H), 2.79 (dd, *J* = 13.7, 6.7 Hz, 1H), 2.56 (d, *J* = 5.3 Hz, 2H), 2.40 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 176.4, 143.6, 137.3, 136.9, 129.8, 129.4, 128.8, 127.1, 127.0, 51.9, 40.7, 37.9, 21.6 ppm. Spectroscopic data for **7** match those previously reported in the literature.³⁷ HPLC: *rac* (CHIRALPAK[®] IC, hexane/ *i*-PrOH/ TFA = 75:25:0.1, 1 mL/min, 220 nm, *t_R* = 14.043).

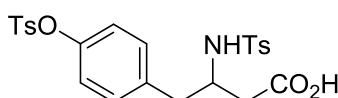


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.043	BB	0.4473	1.40904e4	487.42010	100.0000

Totals : 1.40904e4 487.42010



4-(1H-Indol-3-yl)-3-((4-methylphenyl)sulfonamido) butanoic acid (2g): Following **GP8** with a reaction time of 6 days,^{vi} **1g** (65 mg, 0.20 mmol) gave **2g** (39 mg, 52%) as a pink solid. In a separate independent experiment **2g** (40 mg, 54%) was isolated giving an average yield of 53%. M.P: 178-180 °C. ¹H NMR (400 MHz, MeOD)^{vii} δ 7.40 – 7.36 (m, 2H), 7.34 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.24 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.04 (ddd, *J* = 8.1, 7.0, 1.0 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.93 (s, 1H), 6.89 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 3.82 (tt, *J* = 7.7, 5.4 Hz, 1H), 2.94 (dd, *J* = 14.4, 5.7 Hz, 1H), 2.74 (dd, *J* = 14.3, 7.9 Hz, 1H), 2.60 (dd, *J* = 15.9, 5.1 Hz, 1H), 2.48 (dd, *J* = 15.9, 7.7 Hz, 1H), 2.27 (s, 3H). ¹³C NMR (101 MHz, MeOD) δ 144.0, 138.7, 138.1, 130.1, 128.5, 127.6, 124.5, 122.2, 119.6, 119.3, 112.2, 111.5, 52.6, 41.3, 31.7, 21.5. IR (neat, cm⁻¹): 3410, 3276, 3055, 2922, 1707, 1598, 1457, 1419, 1317, 1290, 1150, 1088, 1019. HRMS calcd. for (C₁₉H₁₉N₂O₄S) [M-H]⁻: 371.1071 found 371.1073.



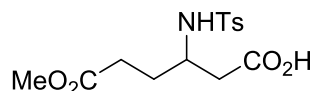
3-((4-Methylphenyl)sulfonamido)-4-(4-(tosyloxy)phenyl) butanoic acid (2h): Following **GP8** with a reaction time of 7 days,^{viii} **1h** (92 mg, 0.20 mmol) gave **2h** (44 mg, 44%) as a white solid. In a separate independent experiment **2h** (38 mg, 38%) was isolated giving an average yield of 41%. ¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.1 Hz, 2H), 6.79 (d, *J* = 8.1 Hz, 2H), 5.62 (d, *J* = 8.8 Hz, 1H), 3.69 (h, *J* = 7.1 Hz, 1H), 2.82 (dd, *J* = 13.8, 7.0 Hz, 1H), 2.74 (dd, *J* = 13.9, 7.3 Hz, 1H), 2.60 – 2.44 (m, 2H), 2.44 (s, 3H), 2.40 (s, 3H) ppm. ¹³C NMR (101 MHz, CD₂Cl₂) δ 176.2, 148.9, 146.2, 144.2, 137.6, 136.5, 132.6, 130.8, 130.3, 130.1, 128.8, 127.2, 122.8, 52.1, 40.3, 38.5, 21.8, 21.6. ppm

^{vi} A shorter reaction time was not attempted in this case but trace **1g** was observed in the crude ¹H NMR suggesting that the prolonged reaction time was necessary. The free indole may coordinate to Ni and slow the rate of reaction.

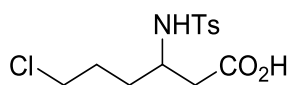
^{vii} The NH indole and NHTs signals were not observed in MeOD.

^{viii} After a 4 day reaction, 28% of **2h** was observed by ¹H NMR and 27% **1h** remained. Therefore, a prolonged reaction time was used to maximize the yield. Many trace by-products were observed in this reaction but were not identified.

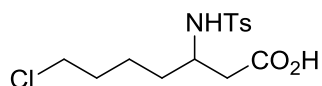
IR (neat, cm^{-1}): 3590, 3366, 3290, 3239, 2929, 1728, 1701, 1598, 1502, 1416, 1374, 1318, 1300, 1199, 1175, 1152, 1093, 1071, 1019. HRMS calcd. for $(\text{C}_{24}\text{H}_{24}\text{NO}_7\text{S}_2)$ $[\text{M}-\text{H}]^-$: 502.1000 found 502.0986.



6-Methoxy-3-((4-methylphenyl)sulfonamido)-6-oxo hexanoic acid (2i): Following **GP8** with a reaction time of 3 days, **1i** (57 mg, 0.20 mmol) gave **2i** (37 mg, 56%) as a white solid. In a separate independent experiment **2i** (33 mg, 50%) was isolated giving an average yield of 53%. M.P.: 108 – 108 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.77 – 7.71 (m, 2H), 7.30 (d, J = 8.0 Hz, 2H), 5.69 (d, J = 9.3 Hz, 1H), 3.63 (s, 3H), 3.57 (tq, J = 9.5, 5.0 Hz, 1H), 2.45 (dd, J = 7.5, 4.9 Hz, 2H), 2.42 (s, 3H), 2.32 (t, J = 7.1 Hz, 2H), 1.91 – 1.76 (m, 2H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 174.0, 143.8, 137.8, 129.9, 127.1, 52.0, 50.1, 38.7, 30.4, 29.4, 21.7 ppm. IR (neat, cm^{-1}): 3289, 2964, 2931, 1711, 1598, 1436, 1417, 1342, 1327, 1255, 1232, 1192, 1157, 1080. HRMS calcd. for $(\text{C}_{14}\text{H}_{18}\text{NO}_6\text{S})$ $[\text{M}-\text{H}]^-$: 328.0860 found 328.0860.

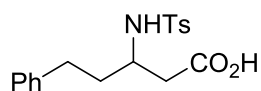


6-Chloro-3-((4-methylphenyl)sulfonamido) hexanoic acid (2j): Following **GP8** with a reaction time of 3 days, **1j** (55 mg, 0.20 mmol) gave **2j** (33 mg, 52%) as a white solid. In a separate independent experiment **2j** (38 mg, 58%) was isolated giving an average yield of 55%. M.P. = 118 – 121 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.78 – 7.73 (m, 2H), 7.34 – 7.29 (m, 2H), 5.42 (d, J = 9.5 Hz, 1H), 3.58 – 3.50 (m, 1H), 3.49 – 3.39 (m, 2H), 2.46 (d, J = 4.9 Hz, 2H), 2.43 (s, 3H), 1.84 – 1.62 (m, 4H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.0, 143.9, 137.8, 130.0, 127.1, 49.9, 44.4, 38.6, 31.9, 28.9, 21.7 ppm. IR (neat, cm^{-1}): 3337, 3294, 3067, 2948, 2924, 2867, 2690, 2590, 1691, 1597, 1494, 1448, 1424, 1327, 1307, 1156, 1086, 1023, 984, 938, 903, 815, 729, 663, 580, 545, 514. HRMS calcd. for $(\text{C}_{13}\text{H}_{17}\text{ClNO}_4\text{S})$ $[\text{M}-\text{H}]^-$: 318.0572 found 318.0571.

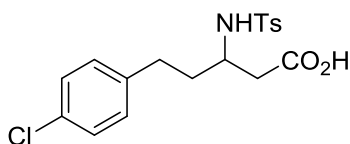


7-Chloro-3-((4-methylphenyl)sulfonamido) heptanoic acid (2k): Following **GP8** with a reaction time of 3 days, **1k** (57 mg, 0.20 mmol) gave **2k** (48 mg, 72%) as a white solid. In a separate independent experiment **2k** (45 mg, 67%) was isolated giving an average yield of 70%. M.P. = 78 – 80 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.02 (s, br, 1H), 7.75 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.0 Hz,

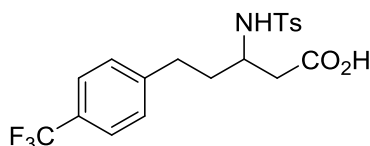
2H), 5.56 (d, $J = 9.1$ Hz, 1H), 3.51 (q, $J = 7.0, 6.5$ Hz, 1H), 3.37 (t, $J = 6.6$ Hz, 2H), 2.56 – 2.45 (m, 2H), 2.41 (s, 3H), 1.59 (p, $J = 7.1$ Hz, 2H), 1.55 – 1.45 (m, 2H), 1.44 – 1.29 (m, 1H), 1.29 – 1.15 (m, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.4, 143.8, 137.8, 129.9, 127.2, 50.3, 44.7, 38.9, 33.9, 31.9, 23.2, 21.7 ppm. IR (neat, cm^{-1}): 3271, 2926, 2867, 1707, 1598, 1414, 1320, 1304, 1152, 1088. HRMS calcd. for $(\text{C}_{14}\text{H}_{19}\text{ClNO}_4\text{S}) [\text{M}-\text{H}]^-$: 332.0729 found 332.0736.



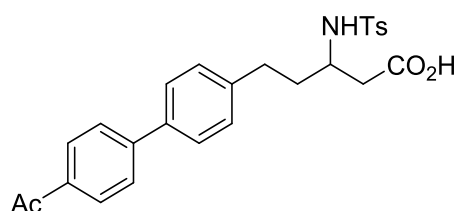
3-((4-Methylphenyl)sulfonamido)-5-phenyl pentanoic acid (2l): Following **GP8** with a reaction time of 3 days, **1l** (60 mg, 0.20 mmol) gave **2l** (48 mg, 69%) as a white solid. In a separate independent experiment **2l** (47 mg, 67%) was isolated giving an average yield of 68%. ^1H NMR (500 MHz, CDCl_3) δ 7.79 – 7.73 (m, 2H), 7.32 – 7.27 (m, 2H), 7.25 – 7.21 (m, 2H), 7.19 – 7.15 (m, 1H), 7.05 – 6.99 (m, 2H), 5.64 (d, $J = 8.7$ Hz, 1H), 3.69 – 3.46 (m, 1H), 2.60 (ddd, $J = 14.0, 9.5, 6.2$ Hz, 1H), 2.49 (d, $J = 5.1$ Hz, 2H), 2.50 – 2.43 (m, 1H), 2.42 (s, 3H), 1.90 – 1.74 (m, 2H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.6, 143.8, 141.0, 138.0, 130.0, 128.7, 128.5, 127.3, 126.3, 50.3, 38.8, 36.4, 32.2, 21.8 ppm. LRMS (ESI): 693 (2M-H), 346 (M-H). Spectroscopic data for **2l** match those previously reported in the literature.⁴⁰



5-(4-Chlorophenyl)-3-((4-methylphenyl)sulfonamido) pentanoic acid (2m): Following **GP8** with a reaction time of 3 days, **1m** (67 mg, 0.20 mmol) gave **2m** (40 mg, 52%) as a white solid. In a separate independent experiment **2m** (38 mg, 50%) was isolated giving an average yield of 51%. M.P. = 150 – 152 °C. ^1H NMR (400 MHz, MeOD) δ 7.76 – 7.69 (m, 2H), 7.39 – 7.31 (m, 2H), 7.22 – 7.12 (m, 2H), 7.03 – 6.95 (m, 2H), 3.61 – 3.49 (m, 1H), 2.55 (ddd, $J = 13.8, 9.8, 5.6$ Hz, 1H), 2.42 (s, 3H), 2.45 – 2.34 (m, 3H), 1.76 (dddd, $J = 14.3, 9.8, 6.4, 4.6$ Hz, 1H), 1.62 (dddd, $J = 13.9, 9.8, 8.4, 5.6$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, MeOD) δ 174.4, 144.7, 141.5, 140.0, 132.6, 130.9, 130.8, 129.3, 128.1, 51.5, 41.0, 37.4, 32.1, 21.5 ppm. IR (neat, cm^{-1}): 3310, 2922, 1695, 1491, 1466, 1444, 1408, 1322, 1305, 1285, 1206, 1151, 1089, 1013. HRMS calcd. for $(\text{C}_{18}\text{H}_{19}\text{ClNO}_4\text{S}) [\text{M}-\text{H}]^-$: 380.0729 found 380.0725.



3-((4-Methylphenyl)sulfonamido)-5-(4-(trifluoromethyl)phenyl) pentanoic acid (2n): Following **GP8** with a reaction time of 3 days, **1n** (74 mg, 0.20 mmol) gave **2n** (48 mg, 58%) as a white solid. In a separate independent experiment **2n** (45 mg, 54%) was isolated giving an average yield of 56%. M.P. = 194 – 196 °C. ^1H NMR (400 MHz, MeOD)^{ix} δ 7.79 – 7.72 (m, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 3.65 – 3.54 (m, 1H), 2.69 (ddd, J = 14.8, 9.8, 5.5 Hz, 1H), 2.54 (ddd, J = 14.0, 9.7, 6.5 Hz, 1H), 2.44 (s, 3H), 2.39 (d, J = 1.5 Hz, 1H), 2.38 (d, J = 3.1 Hz, 1H), 1.84 (dddd, J = 14.2, 9.8, 6.5, 4.5 Hz, 1H), 1.69 (dddd, J = 14.0, 9.8, 8.5, 5.6 Hz, 1H) ppm. ^{13}C NMR (101 MHz, MeOD) δ 173.0, 146.0, 143.3, 138.7, 129.4, 128.6, 127.8 (q, J = 32.0 Hz), 126.7, 125.8, 124.8 (q, J = 3.8 Hz), 124.5 (q, J = 270.8 Hz), 123.1, 50.1, 39.6, 35.8, 31.1, 20.1 ppm. ^{19}F NMR (376 MHz, MeOD, decoupled) δ -63.84 ppm. IR (neat, cm^{-1}): 3312, 2927, 1687, 1616, 1467, 1445, 1417, 1320, 1284, 1208, 1151, 1114, 1093, 1066, 1017. HRMS calcd. for ($\text{C}_{19}\text{H}_{19}\text{F}_3\text{NO}_4\text{S}$) $[\text{M}-\text{H}]^-$: 414.0992 found 414.0991.



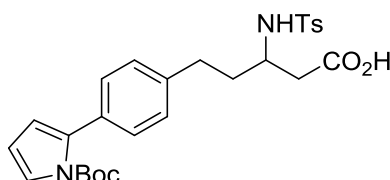
5-(4'-Acetyl-[1,1'-biphenyl]-4-yl)-3-((4-methylphenyl)sulfonamido) pentanoic acid (2o): Following **GP8** with a reaction time of 5 days,^x **1o** (84 mg, 0.20 mmol) gave **2o** (45 mg, 48%) as a white solid. In a separate independent experiment **2o** (48 mg, 52%) was isolated giving an average yield of 50%. M.P. = 180 – 182 °C. ^1H NMR (400 MHz, DMSO)^{xi} δ 8.02 (d, J = 8.2 Hz, 2H), 7.79 (d, J = 8.3 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 7.9 Hz, 2H), 7.11 (d, J = 7.8 Hz, 2H), 3.56 – 3.43 (m, 1H), 2.60 (s, 3H), 2.39 (s, 3H), 2.36 – 2.26 (m, 3H), 1.75 – 1.49 (m, 2H) ppm. ^1H NMR (400 MHz, CDCl_3) δ 8.06 – 7.97 (m, 2H), 7.80 – 7.73 (m, 2H), 7.67 – 7.63 (m, 2H), 7.54 – 7.48 (m, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.18 – 7.12 (m, 2H), 5.50 (d, J = 9.4 Hz, 1H), 3.65 – 3.53 (m, 1H), 2.69 (ddd, J = 15.2, 9.5, 5.9 Hz, 1H), 2.64 (s, 3H), 2.61 – 2.51 (m, 1H), 2.49 (d,

^{ix} The NH signal was not observed in MeOD.

^x After a 3 day reaction, 47% **2o** was observed by ^1H NMR and 15% **1o** remained. Therefore, a prolonged reaction time was used to maximize the yield. The high molecular weight allowed the accurate quantification of by-products with 26% terminal olefin and 40% TsNH_2 observed along with other trace by-products.

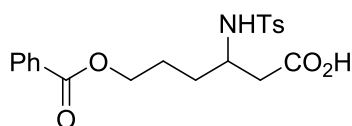
^{xi} The NH signal was not observed and the α -carboxylic acid protons were obscured by the $\text{DMSO}-d_6$ solvent peak. The solubility of **2o** in CDCl_3 is very low by the ^1H NMR has been included for clarity.

$J = 4.8$ Hz, 2H), 2.42 (s, 3H), 1.98 – 1.77 (m, 2H) ppm. ^{13}C NMR (101 MHz, DMSO) δ 197.4, 172.0, 144.4, 142.5, 141.8, 138.9, 136.3, 135.4, 129.6, 128.9, 128.9, 126.8, 126.6, 126.5, 50.2, 35.8, 30.6, 26.7, 21.0 ppm. IR (neat, cm^{-1}): 3248, 2957, 2916, 1722, 1645, 1600, 1451, 1427, 1399, 1362, 1327, 1280, 1244, 1152, 1092, 1073. HRMS calcd. for $(\text{C}_{26}\text{H}_{26}\text{NO}_5\text{S})$ $[\text{M}-\text{H}]^-$: 464.1537 found 414.1530.



5-(4-(1-(*tert*-Butoxycarbonyl)-1*H*-pyrrol-2-yl)phenyl)-3-((4-methylphenyl)sulfonamido)

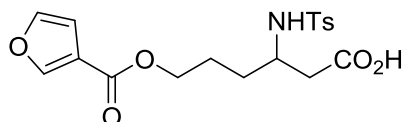
pentanoic acid (2p): Following **GP8** with a reaction time of 6 days,^{xii} **1p** (93 mg, 0.20 mmol) gave **2p** (63 mg, 61%) as a purple oil. In a separate independent experiment **2p** (52 mg, 51%) was isolated giving an average yield of 56%. ^1H NMR (400 MHz, CDCl_3) δ 7.78 (d, $J = 8.3$ Hz, 2H), 7.33 (dd, $J = 3.3, 1.8$ Hz, 1H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.21 (d, $J = 8.1$ Hz, 2H), 7.00 (d, $J = 8.1$ Hz, 2H), 6.21 (t, $J = 3.3$ Hz, 1H), 6.15 (dd, $J = 3.3, 1.8$ Hz, 1H), 5.61 (d, $J = 9.2$ Hz, 1H), 3.65 – 3.52 (m, 1H), 2.63 (ddd, $J = 15.1, 9.6, 6.0$ Hz, 1H), 2.55 – 2.42 (m, 3H), 2.42 (s, 3H), 1.94 – 1.75 (m, 2H), 1.37 (s, 9H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.3, 149.5, 143.7, 139.8, 137.9, 135.0, 132.3, 129.9, 129.3, 127.6, 127.2, 122.6, 114.4, 110.7, 83.7, 50.2, 38.7, 36.3, 27.8, 21.7 ppm. IR (neat, cm^{-1}): 3275, 2890, 2930, 1709, 1394, 1370, 1310, 1256, 1144, 1092, 1074. HRMS calcd. for $(\text{C}_{27}\text{H}_{31}\text{N}_2\text{O}_6\text{S})$ $[\text{M}-\text{H}]^-$: 511.1908 found 511.1888.



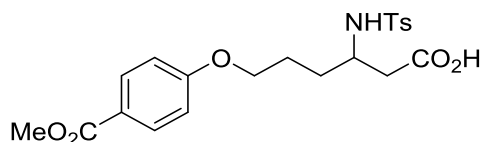
6-(Benzoyloxy)-3-((4-methylphenyl)sulfonamido) hexanoic acid (2q): Following **GP8** with a reaction time of 3 days, **1q** (72 mg, 0.20 mmol) gave **2q** (51 mg, 62%) as a white solid. In a separate independent experiment **2q** (56 mg, 69%) was isolated giving an average yield of 66%. M.P. = 122–124 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.02 – 7.94 (m, 2H), 7.75 (d, $J = 8.3$ Hz, 2H), 7.59 – 7.50 (m, 1H), 7.46 – 7.38 (m, 2H), 7.25 (d, $J = 8.3$ Hz, 2H), 6.46 (s, br, 1H), 5.71 (d, $J = 4.7$ Hz, 1H), 4.25 – 4.08 (m, 2H), 3.60 (s, br, 1H), 2.49 (d, $J = 4.4$ Hz, 1H), 2.34 (s, 3H), 1.80 – 1.56 (m, 4H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 175.5, 166.8, 143.8, 137.8, 133.1, 130.2, 129.9, 129.7, 128.5, 127.1,

^{xii} After a 3 day reaction, 40% of **2p** was observed by ^1H NMR and 31% **1p** remained. Therefore, a prolonged reaction time was used to reach completion.

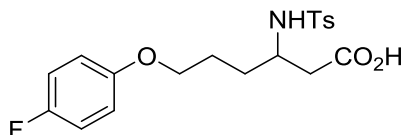
64.3, 50.3, 38.9, 31.1, 25.3, 21.6 ppm. IR (neat, cm^{-1}): 3301, 3212, 2963, 2934, 1727, 1687, 1587, 1492, 1464, 1451, 1423, 1395, 1317, 1301, 1283, 1212, 1156, 1141, 1121, 1089, 1060, 1037. HRMS calcd. for ($\text{C}_{20}\text{H}_{22}\text{NO}_6\text{S}$) [$\text{M}-\text{H}$] $^-$: 404.1173 found 404.1164.



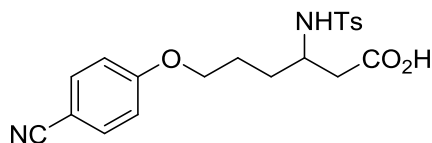
6-((Furan-3-carbonyl)oxy)-3-((4-methylphenyl)sulfonamido) hexanoic acid (2r): Following **GP8** with a reaction time of 3 days, **1r** (70 mg, 0.20 mmol) gave **2r** (49 mg, 62%) as a pale-yellow oil. In a separate independent experiment **2r** (54 mg, 68 %) was isolated giving an average yield of 65%. ^1H NMR (400 MHz, CDCl_3) δ 7.97 (dd, $J = 1.6, 0.8$ Hz, 1H), 7.77 – 7.72 (m, 2H), 7.41 (t, $J = 1.7$ Hz, 1H), 7.30 – 7.25 (m, 2H), 6.70 (dd, $J = 1.9, 0.8$ Hz, 1H), 5.62 (d, $J = 9.2$ Hz, 1H), 4.17 – 4.06 (m, 2H), 3.63 – 3.53 (m, 1H), 2.47 (d, $J = 5.1$ Hz, 2H), 2.38 (s, 3H), 1.78 – 1.52 (m, 4H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.0, 163.3, 147.9, 143.9, 143.8, 137.8, 129.9, 127.1, 119.4, 109.9, 63.8, 50.2, 38.7, 31.1, 25.2, 21.6 ppm. IR (neat, cm^{-1}): 3270, 2958, 1708, 1598, 1406, 1305, 1152, 1090, 968, 873, 814, 765, 707, 663, 575, 548. HRMS calcd. for ($\text{C}_{18}\text{H}_{20}\text{NO}_7\text{S}$) [$\text{M}-\text{H}$] $^-$: 394.0966 found 394.0983.



6-(4-(Methoxycarbonyl)phenoxy)-3-((4-methylphenyl)sulfonamido) hexanoic acid (2s): Following **GP8** with a reaction time of 3 days, **1s** (78 mg, 0.20 mmol) gave **2s** (41 mg, 47%) as a white solid. In a separate independent experiment **2s** (43 mg, 48%) was isolated giving an average yield of 48%. M.P: 122–124 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.01 – 7.92 (m, 2H), 7.79 – 7.71 (m, 2H), 7.27 (d, $J = 7.5$ Hz, 2H), 6.87 – 6.79 (m, 2H), 5.53 (d, $J = 8.0$ Hz, 1H), 3.92 – 3.83 (m, 5H), 3.59 (s, br, 1H), 2.50 (dd, $J = 5.0, 2.2$ Hz, 2H), 2.38 (s, 3H), 1.85 – 1.64 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 176.0, 167.1, 162.7, 143.8, 137.9, 131.7, 129.9, 127.2, 122.8, 114.2, 67.3, 52.1, 50.2, 38.7, 31.3, 25.6, 21.7. IR (neat, cm^{-1}): 3187, 2955, 2874, 1713, 1607, 1511, 1434, 1280, 1259, 1193, 1153, 1091, 1935. HRMS calcd. for ($\text{C}_{21}\text{H}_{24}\text{NO}_7\text{S}$) [$\text{M}-\text{H}$] $^-$: 434.1279 found 434.1286.



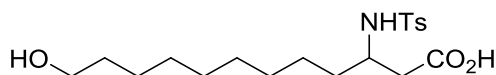
6-(4-Fluorophenoxy)-3-((4-methylphenyl)sulfonamido) hexanoic acid (2t): Following **GP8** with a reaction time of 3 days, **1t** (70 mg, 0.20 mmol) gave **2t** (49 mg, 62%) as a white solid. In a separate independent experiment **2t** (52 mg, 66%) was isolated giving an average yield of 64%. M.P: 93–94 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.92 (s, 1H), 7.75 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 6.99 – 6.89 (m, 2H), 6.75 (m, 2H), 5.62 (d, J = 9.0 Hz, 1H), 3.78 (t, J = 5.1 Hz, 2H), 3.58 (m, 1H), 2.59 – 2.43 (m, 2H), 2.39 (s, 3H), 1.79 – 1.58 (m, 4H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.5, 157.4 (d, J = 238.3 Hz), 154.9 (d, J = 2.1 Hz), 143.8, 137.8, 129.9, 127.2, 115.9 (d, J = 23.0 Hz), 115.5 (d, J = 7.9 Hz), 67.8, 50.3, 38.9, 31.3, 25.7, 21.6 ppm. ^{19}F NMR (376 MHz, CDCl_3) δ -123.99 (tt, J = 8.4, 4.3 Hz) ppm. IR (neat, cm^{-1}): 3325, 3288, 2926, 2872, 1696, 1598, 1506, 1465, 1435, 1419, 1332, 1295, 1256, 1155, 1092, 1038. HRMS calcd. for $(\text{C}_{19}\text{H}_{21}\text{FNO}_5\text{S})$ $[\text{M}-\text{H}]^-$: 394.1130 found 392.1138.



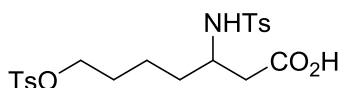
6-(4-Cyanophenoxy)-3-((4-methylphenyl)sulfonamido) hexanoic acid (2u): Following **GP8** with a reaction time of 6 days,^{xiii} **1u** (71 mg, 0.20 mmol) gave **2u** (32 mg, 40%) as a white solid. In a separate independent experiment **2u** (34 mg, 42%) was isolated giving an average yield of 41%. M.P: 150–152 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.75 (d, J = 8.2 Hz, 2H), 7.56 (m, 2H), 7.29 (d, J = 8.1 Hz, 2H), 6.90 – 6.85 (m, 2H), 5.44 (d, J = 9.3 Hz, 1H), 3.93 – 3.89 (m, 2H), 3.59 (m, 1H), 2.48 (d, J = 1.6 Hz, 1H), 2.46 (d, J = 2.4 Hz, 1H), 2.40 (s, 3H), 1.83 (m, 1H), 1.72 (m, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3)^{xiv} δ 175.3, 162.2, 143.9, 137.9, 134.2, 130.0, 127.2, 119.3, 115.3, 104.2, 67.5, 50.2, 38.4, 31.3, 25.6, 21.7 ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 174.4, 163.9, 144.7, 139.9, 135.1, 130.7, 128.0, 116.5, 104.5, 68.8, 51.5, 41.2, 32.2, 26.2, 21.4. IR (neat, cm^{-1}): 3265, 2921, 2215, 1712, 1605, 1574, 1508, 1450, 1404, 1302, 1259, 1172, 1152, 1095, 1022. HRMS calcd. for $(\text{C}_{20}\text{H}_{21}\text{N}_2\text{O}_5\text{S})$ $[\text{M}-\text{H}]^-$: 401.1177 found 401.1183

^{xiii} After a 3 day reaction, 34% of **2u** was observed by ^1H NMR and 25% **1u** remained. Therefore, a prolonged reaction time was used to maximize the yield.

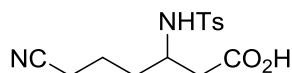
^{xiv} The solubility of **2u** in CDCl_3 is low so the ^{13}C NMR in CD_3OD has also been provided.



12-Hydroxy-3-((4-methylphenyl)sulfonamido) dodecanoic acid (2v): Following **GP8** with a reaction time of 6 days,^{xv} **1v** (62 μ l, 0.20 mmol) gave **2v** (49 mg, 64%) as a white solid. In a separate independent experiment **2v** (50 mg, 65%) was isolated giving an average yield of 65%. M.P.: 85–86 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.78 – 7.71 (m, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.50 (d, J = 9.0 Hz, 1H), 5.38 (s, br, 2H), 3.63 (t, J = 6.6 Hz, 2H), 3.57 – 3.44 (m, 1H), 2.52 – 2.35 (m, 5H), 1.60 – 1.48 (m, 2H), 1.46 (q, J = 7.1 Hz, 2H), 1.37 – 1.04 (m, 13H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 175.5, 143.5, 138.1, 129.8, 127.2, 63.1, 50.6, 38.8, 34.6, 32.5, 29.3, 29.2, 29.1, 28.9, 25.7, 25.6, 21.7 ppm. IR (neat, cm⁻¹): 3467, 3310, 2918, 2854, 1707, 1430, 1333, 1298, 1258, 1157, 1136, 1094, 1040, 1004. HRMS calcd. for (C₁₉H₃₀NO₅S) [M–H][–]: 384.1850 found 384.1842.



33-((4-Methylphenyl)sulfonamido)-7-(tosyloxy) heptanoic acid (2w): Following **GP8** with a reaction time of 3 days, **1w** (85 mg, 0.20 mmol) gave **2w** (40 mg, 43%) as a colourless oil. In a separate independent experiment **2w** (36 mg, 38%) was isolated giving an average yield of 41%. ¹H NMR (400 MHz, CDCl₃) δ 7.80 – 7.74 (m, 2H), 7.74 – 7.69 (m, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 6.75 (s, br, 1H), 5.47 (d, J = 9.1 Hz, 1H), 3.96 – 3.83 (m, 2H), 3.46 (tq, J = 9.9, 5.6 Hz, 1H), 2.51 – 2.39 (m, 7H), 1.56 – 1.38 (m, 4H), 1.37 – 1.21 (m, 1H), 1.23 – 1.08 (m, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 176.0, 145.0, 143.8, 137.8, 133.1, 130.0, 129.9, 128.0, 127.1, 70.2, 50.4, 38.7, 33.9, 28.3, 21.8, 21.8, 21.6 ppm. IR (neat, cm⁻¹): 3278, 2926, 1709, 1598, 1422, 1326, 1173, 1154, 1092. HRMS calcd. for (C₂₁H₂₆NO₇S₂) [M–H][–]: 468.1156 found 468.1157.

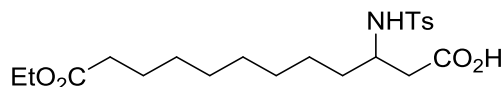


6-Cyano-3-((4-methylphenyl)sulfonamido) hexanoic acid (2x): Following **GP8** with a reaction time of 6 days,^{xvi} **1x** (53 mg, 0.20 mmol) gave **2x** (31 mg, 50%) as a white solid. In a separate independent experiment **2x** (35 mg, 55%) was isolated giving an average yield of 53%. M.P.: 90–92 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, J = 7.9 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H), 6.61 (s, br, 1H), 5.72 (d, J = 9.3 Hz, 1H), 3.58 – 3.48 (m, 1H), 2.45 – 2.39 (m, 5H), 2.32 – 2.24 (m, 2H), 1.75 – 1.48

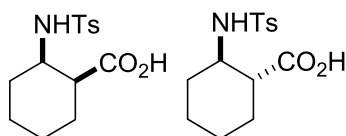
^{xv} In this case a shorter reaction was not carried out but trace **1v** (7%) observed in the crude ¹H NMR suggested that the prolonged reaction time was necessary.

^{xvi} A shorter reaction was not carried out but trace **1x** (3%) observed in the crude ¹H NMR suggested that the prolonged reaction time was necessary. In this case, the cyano group may coordinate to Ni and slow the reaction.

(m, 4H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 175.5, 144.1, 137.7, 130.1, 127.1, 119.4, 49.7, 38.7, 33.4, 21.9, 21.7, 16.7 ppm. IR (neat, cm^{-1}): 3302, 2947, 2924, 2244, 1704, 1597, 1426, 1350, 1324, 1206, 1154, 1090, 1070, 1013. HRMS calcd. for $(\text{C}_{14}\text{H}_{17}\text{N}_2\text{O}_4\text{S}) [\text{M}-\text{H}]^-$: 309.0915 found 309.0916.



12-Ethoxy-3-((4-methylphenyl)sulfonamido)-12-oxo dodecanoic acid (2y): Following **GP8** with a reaction time of 3 days, **1y** (70 μl , 0.20 mmol) gave **2y** (59 mg, 69%) as a white solid. In a separate independent experiment **2y** (60 mg, 70%) was isolated giving an average yield of 70%. M.P.: 106 – 109 $^{\circ}\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.80 – 7.71 (m, 2H), 7.29 (d, J = 8.3 Hz, 2H), 5.38 (d, J = 7.8 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.56 – 3.43 (m, 1H), 2.47 (dd, J = 5.2, 3.1 Hz, 2H), 2.41 (s, 3H), 2.27 (t, J = 7.5 Hz, 2H), 1.58 (apparent p, J = 7.5 Hz, 2H), 1.46 (d, J = 7.2 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.30 – 1.06 (m, 10H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 176.26, 174.2, 143.6, 138.0, 129.8, 127.2, 60.4, 50.5, 38.8, 34.6, 34.5, 29.2, 29.1, 29.1, 29.0, 25.8, 25.0, 21.6, 14.4 ppm. IR (neat, cm^{-1}): 3271, 2937, 2859, 1703, 1597, 1451, 1422, 1329, 1290, 1258, 1188, 1156, 1093, 1004. HRMS calcd. for $(\text{C}_{21}\text{H}_{32}\text{NO}_6\text{S}) [\text{M}-\text{H}]^-$: 426.1956 found 426.1961.

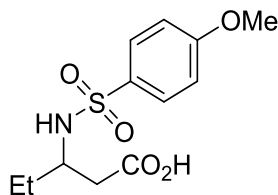


2-((4-Methylphenyl)sulfonamido)cyclohexane-1-carboxylic acid (2z): Following **GP8** with a reaction time of 10 days^{xvii}, **1z** (50 mg, 0.20 mmol) gave **2z** (25 mg, 42%, d.r. 1:0.9 *cis:trans*) as a white solid. In a separate independent experiment **1z** (56 mg, 0.22 mmol) gave **2z** (25 mg, 38%) was isolated giving an average yield of 40%. ^1H NMR (400 MHz, CDCl_3 , diastereomers) δ 7.79 – 7.72 (m, 2H), 7.33 – 7.24 (m, 2H), 5.89 (d, J = 9.4 Hz, 0.55H), 5.17 (d, J = 8.0 Hz, 0.45H), 3.48 – 3.30 (m, 1H), 2.75 (q, J = 4.7 Hz, 0.55H), 2.42 (s, 1.65H), 2.40 (s, 1.35H), 2.32 (ddd, J = 11.3, 10.2, 3.8 Hz, 0.45H), 2.10 – 2.01 (m, 0.55H), 2.01 – 1.92 (m, 1H), 1.83 – 1.71 (m, 0.55H), 1.71 – 1.61 (m, 1.45H), 1.60 – 1.41 (m, 2H), 1.37 – 1.14 (m, 2.45H). ^{13}C NMR (101 MHz, CDCl_3 , diastereomers)^{xviii} δ 178.8^m, 178.5^M, 143.5^m, 143.5^M, 138.4^M, 138.0^m, 129.9^M, 129.7^m, 127.3^m, 127.0^M, 54.0^m, 52.5^M, 49.6^m, 45.1^M, 33.2^m, 29.9^M, 28.7^m, 27.4^M, 24.4^m, 24.1^M, 24.1^m, 22.2^M, 21.7^m, 21.7^M. LRMS (ESI):

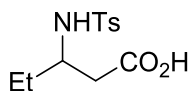
^{xvii} After a 7 day reaction, ~30% of **2z** was observed by ^1H NMR and 40% **1z** remained. After a 10 day reaction, ~40% of **2z** was observed and 25% **1z** remained. A 14 day reaction was also performed; no crude NMR was taken but the isolated yield of **2z** was again 42%. Other reaction variables were modified to improve the yield such as switching to less hindered **L4** and increasing the temperature but without success.

^{xviii} Major (M) and minor (m) isomers have been assigned.

594 (2M–H), 410 (M+TFA⁺), 296 (M–H). Spectroscopic data for **2z** match those previously reported in the literature.⁴¹

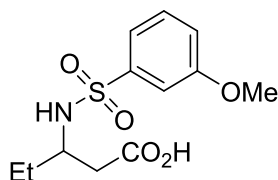


3-((4-Methoxyphenyl)sulfonamido) pentanoic acid (2aa): Following **GP8** with a reaction time of 5 days,^{xix} **1aa** (40 μ l, 0.20 mmol) gave **2aa** (38 mg, 66%) as a white solid. In a separate independent experiment **2aa** (41 mg, 73%) was isolated giving an average yield of 70%. M.P.: 104–106 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.58 (s, 1H), 7.93 – 7.74 (m, 2H), 7.09 – 6.83 (m, 2H), 5.42 (d, J = 8.2 Hz, 1H), 3.85 (s, 3H), 3.56 – 3.33 (m, 1H), 2.47 (m, 2H), 1.53 (p, J = 7.2 Hz, 2H), 0.80 (t, J = 7.2 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ 176.7, 163.0, 132.5, 129.3, 114.4, 55.7, 52.1, 38.6, 27.8, 10.4 ppm. IR (neat, cm⁻¹): 3278, 2974, 2918, 1709, 1596, 1579, 1497, 1455, 1433, 1412, 1314, 1299, 1284, 1260, 1192, 1144, 1121, 1096, 1073, 1038, 1016. HRMS calcd. for (C₁₂H₁₆NO₅S) [M–H][–]: 286.0755 found 286.0757.

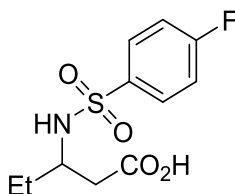


3-((4-Methylphenyl)sulfonamido) pentanoic acid (2ab): Following **GP8** with a reaction time of 3 days, **1ab** (39 μ l, 0.20 mmol) gave **2ab** (39 mg, 73%) as a white solid. In a separate independent experiment **2ab** (41 mg, 77%) was isolated giving an average yield of 75%. ¹H NMR (500 MHz, CDCl₃) δ 7.75 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 5.41 (s, br, 1H), 3.46 (s, br, 1H), 2.56 – 2.41 (m, 2H), 2.41 (s, 3H), 1.52 (m, 2H), 0.79 (t, J = 7.4 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ 176.8, 143.6, 138.0, 129.8, 127.2, 52.1, 38.6, 27.7, 21.6, 10.4 ppm. LRMS (ESI): 541 (2M–H), 270 (M–H). Spectroscopic data for **2ab** match those previously reported in the literature.⁴⁰

^{xix} After a 3 day reaction, ~67% of **2aa** was observed by ¹H NMR and 18% **1aa** remained. Therefore, a prolonged reaction time was used to reach completion.

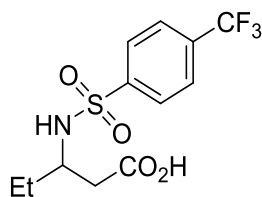


3-((3-Methoxyphenyl)sulfonamido) pentanoic acid (2ac): Following **GP8** with a reaction time of 5 days,^{xx} **1ac** (48 mg, 0.20 mmol) gave **2ac** (33 mg, 57%) as a white solid. In a separate independent experiment **2ac** (34 mg, 59%) was isolated giving an average yield of 58%. M.P.: 89 – 91 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.35 (s, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.09 (dd, *J* = 8.5, 2.6 Hz, 1H), 5.45 (d, *J* = 9.0 Hz, 1H), 3.84 (s, 3H), 3.50 (q, *J* = 7.0 Hz, 1H), 2.54 – 2.41 (m, 2H), 1.54 (p, *J* = 7.3 Hz, 2H), 0.81 (t, *J* = 7.4 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ 176.7, 160.1, 142.1, 130.3, 119.3, 119.3, 111.8, 55.8, 52.2, 38.5, 27.8, 10.4 ppm. IR (neat, cm⁻¹): 3230, 2975, 2945, 1704, 1595, 1581, 1475, 1427, 1333, 1283, 1237, 1155, 1035. HRMS calcd. for (C₁₂H₁₆NO₅S) [M–H][–]: 286.0755 found 286.0754.

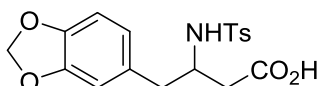


3-((4-Fluorophenyl)sulfonamido) pentanoic acid (2ad): Following **GP8** with a reaction time of 3 days, **1ad** (36 μl, 0.20 mmol) gave **2ad** (25 mg, 45%) as a white solid. In a separate independent experiment **2ad** (26 mg, 47%) was isolated giving an average yield of 46%. M.P.: 97 – 99 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.00 – 7.83 (m, 2H), 7.22 – 7.12 (m, 2H), 5.50 (d, *J* = 9.0 Hz, 1H), 3.59 – 3.38 (m, 1H), 2.50 (d, *J* = 5.4 Hz, 2H), 1.54 (p, *J* = 7.3 Hz, 2H), 0.79 (t, *J* = 7.4 Hz, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 176.6, 165.2 (d, *J* = 254.7 Hz), 137.1 (d, *J* = 3.3 Hz), 129.9 (d, *J* = 9.2 Hz), 116.4 (d, *J* = 22.5 Hz), 52.3, 38.7, 27.9, 10.4. ¹⁹F NMR (376 MHz, CDCl₃) δ -105.31 (tt, *J* = 8.6, 4.9 Hz) ppm. IR (neat, cm⁻¹): 3206, 2980, 2960, 2925, 1695, 1593, 1496, 1451, 1430, 1407, 1332, 1289, 1238, 1152, 1117, 1091, 1070, 1034, 1011. HRMS calcd. for (C₁₁H₁₃FO₄S) [M–H][–]: 274.0555 found 274.0544.

^{xx} A shorter reaction was not carried out but trace **1ac** (10%) observed in the crude NMR suggested that the prolonged reaction time was necessary.



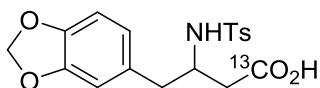
3-((4-(Trifluoromethyl)phenyl)sulfonamido) pentanoic acid (2ae): Following **GP8** with a reaction time of 5 days,^{xxi} **1ae** (43 μ l, 0.20 mmol) gave **2ae** (14 mg, 22%) as a white solid. In a separate independent experiment **2ae** (15 mg, 23%) was isolated giving an average yield of 23%. M.P.: 100–102 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.01 (d, J = 8.1 Hz, 2H), 7.77 (d, J = 8.2 Hz, 2H), 6.25 (s, br, 1H), 5.48 (d, J = 9.1 Hz, 1H), 3.60 – 3.47 (m, 1H), 2.52 (d, J = 5.2 Hz, 2H), 1.57 (p, J = 7.3 Hz, 2H), 0.81 (t, J = 7.4 Hz, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 176.4, 144.7, 134.51 (q, J = 33.1 Hz), 127.7, 126.39 (q, J = 3.8 Hz), 123.36 (q, J = 273.1 Hz), 52.5, 38.5, 28.0, 10.5 ppm. ¹⁹F NMR (376 MHz, CDCl₃) δ -63.2. IR (neat, cm⁻¹): 3300, 2968, 2918, 1699, 1422, 1406, 1320, 1292, 1160, 1127, 1109, 1093, 1061, 1026. HRMS calcd. for (C₁₂H₁₃F₃NO₄S) [M–H][–]: 324.0523 found 324.0522.



4-(Benzo[d][1,3]dioxol-5-yl)-3-((4-methylphenyl)sulfonamido) butanoic acid (2af): Following **GP8** with a reaction time of 5 days,^{xxii} **1af** (66 mg, 0.20 mmol) gave **2af** (45 mg, 60%) as a colorless solid. In a separate independent experiment **2af** (48 mg, 64%) was isolated giving an average yield of 62%. M.P. = 113 – 116 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.64 – 7.59 (m, 2H), 7.25 – 7.21 (m, 2H), 6.64 (d, J = 7.8 Hz, 1H), 6.50 – 6.42 (m, 2H), 5.93 – 5.90 (m, 2H), 5.40 – 5.10 (br. s., 1H), 3.72 – 3.62 (s, 1H), 2.78 (dd, J = 13.8, 7.1 Hz, 1H), 2.68 (dd, J = 13.8, 7.2 Hz, 1H), 2.58 (dd, J = 5.3, 2.6 Hz, 2H), 2.41 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 175.7, 148.0, 146.7, 143.6, 137.2, 130.5, 129.7, 127.2, 122.5, 109.5, 108.5, 101.1, 52.0, 40.4, 38.0, 21.7 ppm. IR (neat, cm⁻¹): 3315, 2917, 2635, 1710, 1599, 1501, 1491, 1445, 1407, 1326, 1293, 1248, 1232, 1192, 1157, 1088, 1065, 1031, 927, 859, 806, 665, 583, 569, 546. HRMS calcd. for (C₁₈H₁₉NNaO₆S) [M+Na]⁺: 400.0831 found 400.0821.

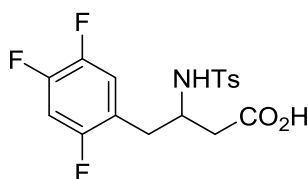
^{xxi} After a 3 day reaction, 16% of **2ae** was observed by ¹H NMR and 12% **1ae** remained.

^{xxii} A shorter reaction was not carried out but trace **1af** (5%) observed in the crude NMR suggested that the prolonged reaction time was necessary. 25% TsNH₂ was also observed.



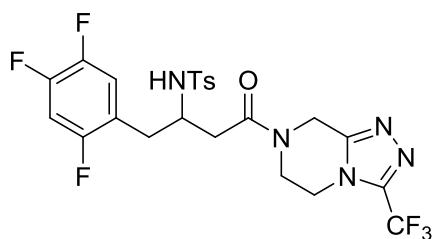
4-(Benzo[d][1,3]dioxol-5-yl)-3-((4-methylphenyl)sulfonamido) butanoic-1-¹³C acid (2af-¹³C):

Following a modified **GP8**, to **1af** (66 mg, 0.20 mmol) and other solid reagents in a Schlenk tube under a flow of N₂ was added dry DMPU (0.50 ml, 0.40 M), MeOH (40 µl, 5.0 equiv.) and then frozen with liquid nitrogen. 3 × vacuum (<1 mbar)/ ¹³CO₂ cycles were then performed using the head-space volume between the gas canister and valve filled with ¹³CO₂ for each addition. The Schlenk tube was then sealed, warmed to 10 °C and stirred for 5 days, giving **2af-¹³C** (47 mg, 63%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 9.42 (s, br, 1H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.62 (d, *J* = 7.8 Hz, 1H), 6.50 – 6.42 (m, 2H), 5.96 – 5.86 (m, 2H), 5.46 (s, br, 1H), 3.76 – 3.61 (m, 1H), 2.76 (dd, *J* = 13.9, 7.0 Hz, 1H), 2.67 (dd, *J* = 13.9, 7.3 Hz, 1H), 2.63 – 2.49 (m, 2H), 2.40 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 176.6 (¹³C), 147.9, 146.6, 143.6, 137.2, 130.5, 129.7, 127.1, 122.5, 109.5, 108.4, 101.1, 52.0, 40.4, 38.6, 38.0, 21.6 ppm. Spectroscopic data for **2af-¹³C** match that of the non-labelled analogue.



3-((4-Methylphenyl)sulfonamido)-4-(2,4,5-trifluorophenyl) butanoic acid (2ag): Following **GP8** with a reaction time of 5 days,^{xxiii} **1ag** (68 mg, 0.20 mmol) gave **2ag** (29 mg, 37%) as a white solid. In a separate independent experiment **2ag** (30 mg, 39%) was isolated giving an average yield of 38%. M.P. = 142 – 145 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.57 – 7.52 (m, 2H), 7.21 – 7.16 (m, 2H), 6.83 – 6.67 (m, 2H), 5.48 (d, *J* = 9.4 Hz, 1H), 3.77 – 3.67 (m, 1H), 2.88 – 2.71 (m, 3H), 2.63 (dd, *J* = 17.1, 4.0 Hz, 1H), 2.41 (s, 3H) ppm. ¹³C NMR (101 MHz, DMSO-*d*₆) δ 171.6, 142.3, 138.3, 129.3, 126.0, 121.6 (d, *J* = 18.6 Hz), 119.4 (dd, *J* = 19.4, 6.1 Hz), 105.4 (dd, *J* = 29.0, 20.9 Hz), 50.7, 40.8, 33.0, 20.9. ¹⁹F (367 MHz, DMSO-*d*₆) δ -118.7 (ddt, *J* = 15.8, 10.1, 5.0 Hz), -137.2 (dtd, *J* = 23.5, 10.9, 10.2, 3.6 Hz), -144.2 (dddd, *J* = 22.5, 15.4, 11.2, 6.9 Hz) ppm. IR (neat, cm⁻¹): 3241, 3058, 2926, 2698, 2590, 1696, 1633, 1599, 1518, 1424, 1328, 1241, 1218, 1200, 1155, 1097, 1083, 1068, 964, 917, 880, 845, 835, 813, 755, 708, 654, 586, 547, 514, 483. HRMS calcd. for (C₁₇H₁₅F₃NO₄S) [M-H]⁻: 386.0679 found 386.0676.

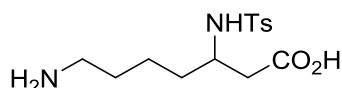
^{xxiii} After a 5 day reaction: 15% **1ag** was observed in the crude NMR along with 20% TsNH₂. Accurate quantification of **2ag** was not possible because of its' low solubility in CDCl₃. Increasing the reaction time to 7 days did not improve the yield in this case.



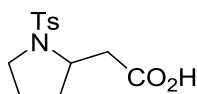
4-Methyl-N-(4-oxo-4-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)-1-(2,4,5-trifluorophenyl)butan-2-yl) benzenesulfonamide (3): Formally following literature procedure,³⁴ to a solution of 3-(trifluoromethyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-7-ium chloride (15 mg, 0.080 mmol), EDC.HCl (28 mg, 0.14 mmol) and DMAP (35 mg, 0.29 mmol) in CH₂Cl₂ (2.0 ml) was added drop wise a solution of **2ag** (28 mg, 0.070 mmol) in CH₂Cl₂ (2.0 ml) and the resulting mixture was stirred at room temperature overnight. The reaction was quenched with 4.0 M HCl and acidified to pH = 1. The aqueous phase was extracted with CH₂Cl₂. The combined organic fractions were dried (MgSO₄), filtered and concentrated. The crude material was purified by column chromatography on silica gel (CH₂Cl₂: MeOH 99:1 → 97:3) to afford **3** as a white solid (30 mg, 74%). The product appears as a mixture of rotamers (~1:1) at RT. M.P. = 204 – 207 °C. ¹H NMR (400 MHz, CD₃CN) δ 7.47 – 7.39 (m, 2H), 7.20 – 7.14 (m, 2H), 7.01 – 6.89 (m, 1H), 6.88 – 6.75 (m, 1H), 5.95 – 5.85 (m, 1H), 4.89 – 4.75 (m, 2H), 4.03 – 3.70 (m, 3H), 2.84 – 2.59 (m, 4H), 2.35 (s, 3H) ppm. ¹H NMR (500 MHz, DMSO-*d*₆, T = 115 °C)^{xxiv} δ 7.52 – 7.43 (m, 2H), 7.33 (s, br, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.15 (ddd, *J* = 11.4, 9.2, 6.9 Hz, 1H), 7.09 (ddd, *J* = 10.9, 9.6, 6.8 Hz, 1H), 4.84 (s, 2H), 4.17 (m, 2H), 3.92 (t, *J* = 5.5 Hz, 2H), 3.86 (m, 1H), 2.83 (dd, *J* = 14.0, 5.1 Hz, 1H), 2.75 – 2.67 (m, 2H), 2.64 (dd, *J* = 15.5, 6.9 Hz, 1H), 2.34 (s, 3H) ppm. ¹³C NMR (126 MHz, DMSO-*d*₆, T = 115 °C) δ 168.5, 155.3 (ddd, *J* = 243.5, 9.9, 2.4 Hz), 150.2, 147.6 (ddd, *J* = 247.1, 14.3, 12.7 Hz), 145.1 (ddd, *J* = 241.6, 12.3, 3.4 Hz), 142.1 (q, *J* = 39.6 Hz), 141.7, 138.3, 128.5, 125.5, 121.4 (ddd, *J* = 18.2, 5.8, 4.1 Hz), 118.7 (dd, *J* = 19.3, 6.2 Hz), 118.0 (q, *J* = 270.0 Hz), 104.6 (dd, *J* = 29.1, 21.1 Hz), 50.8, 42.9, 38.2 (2C), 32.9 (2C), 20.1. ¹⁹F NMR (471 MHz, DMSO-*d*₆, T = 95 °C) δ -61.7, -118.34 (d, *J* = 15.3 Hz), -137.21 (dd, *J* = 22.1, 3.0 Hz), -144.12 (dd, *J* = 21.9, 16.0 Hz). IR (neat, cm⁻¹): 3157, 3057, 2927, 1626, 1515, 1477, 1445, 1425, 1336, 1272, 1236, 1201, 1162, 1136, 1095, 1073, 1034, 1016, 984, 969, 940, 854, 810, 709, 671, 575, 547. HRMS calcd. for (C₂₃H₂₀F₆N₅O₃S) [M-H]⁻: 560.1197 found 560.1184.

^{xxiv} The presence of rotamers of **3** at RT resulted in complicated NMR spectrum, particularly for the ¹³C in which ¹³C-¹⁹F couplings' make analysis challenging. Therefore, variable temperature NMR was carried out in DMSO-*d*₆ with complete resolution of the rotamers observed at 115 °C.

3.2 Modification of β -Amino Acid Products



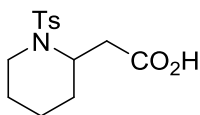
7-Amino-3-((4-methylphenyl)sulfonamido) heptanoic acid (4): To **2k** (36 mg, 1.0 equiv, 1.1 mmol) in a Schlenk tube was added 5.0 M NH_4OH solution (0.44 ml, 20 equiv., 2.2 mmol) under Ar atmosphere. The tube was sealed and the reaction was heated to reflux for 4 h. After this time, the solvent was removed *in vacuo* and the product purified by column chromatography on silica gel, eluting with CHCl_3 : MeOH: NH_4OH (80:15:2 \rightarrow 70:30:4) to give **4** (26 mg, 70%) as a white solid. M.P. = 212 – 214 °C (decomposition at 220 °C). ^1H NMR (400 MHz, MeOD)^{xxv} δ 7.72 – 7.65 (m, 2H), 7.32 – 7.27 (m, 2H), 3.56 – 3.41 (m, 1H), 3.28 (s, 1H), 2.76 (td, J = 7.5, 1.4 Hz, 2H), 2.35 (s, 3H), 2.16 (m, 2H), 1.60 – 1.43 (m, 3H), 1.43 – 1.20 (m, 3H) ppm. ^{13}C NMR (101 MHz, MeOD)^{xxvi} δ 144.6, 140.2, 130.8, 130.8, 128.0, 52.4, 40.5, 35.3, 27.9, 23.5, 21.5 ppm. ^{13}C NMR (101 MHz, D_2O) δ 177.4, 144.9, 136.5, 130.1, 126.7, 51.0, 41.9, 39.2, 33.6, 26.2, 21.8, 20.7. IR (neat, cm^{-1}): 3327, 2918, 2861, 1634, 1557, 1396, 1315, 1229, 1155, 1093. HRMS calcd. for ($\text{C}_{14}\text{H}_{21}\text{N}_2\text{O}_4\text{S}$) [$\text{M}-\text{H}$] $^-$: 313.1228 found 313.1226.



2-(1-Tosylpyrrolidin-2-yl) acetic acid (5): NaH (60% in mineral oil, 9.5 mg, 0.23 mmol) was added in one portion to a solution of **2j** (33 mg, 0.11 mmol) in dry DMF (1.0 ml) and the resulting mixture was stirred at RT for 2 hours. The reaction mixture was diluted then with EtOAc (10 ml) and washed with 1 M HCl (2 \times 10 ml). The organic phase was dried (MgSO_4), concentrated *in vacuo*, and crude was washed several times with pentane to remove traces of mineral oil. Final product **5** was obtained as a white solid (24 mg, 81%). M.P. = 111 – 114 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.76 – 7.71 (m, 2H), 7.36 – 7.30 (m, 2H), 3.94 (ddt, J = 10.7, 7.4, 3.9 Hz, 1H), 3.50 – 3.42 (m, 1H), 3.19 – 3.09 (m, 2H), 2.57 (dd, J = 16.4, 10.0 Hz, 1H), 2.44 (s, 3H), 1.86 – 1.75 (m, 2H), 1.74 – 1.64 (m, 1H), 1.59 – 1.48 (m, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 175.7, 143.8, 134.2, 129.9, 127.8, 56.5, 49.4, 41.1, 31.9, 23.9, 21.7. IR (neat, cm^{-1}): 3059, 2987, 2952, 2880, 2735, 2663, 1701, 1598, 1440, 1399, 1340, 1320, 1238, 1208, 1197, 1159, 1119, 1092, 1041, 988, 928, 821, 808, 709, 678, 659, 609, 583, 549. HRMS calcd. for ($\text{C}_{13}\text{H}_{16}\text{NO}_4\text{S}$) [$\text{M}-\text{H}$] $^-$: 282.0805 found 282.0802.

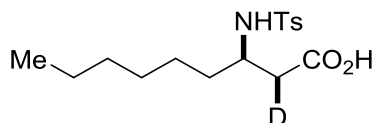
^{xxv} The NH_2 and NHTs signals were not observed in the ^1H spectra when taken in CD_3OD .

^{xxvi} The carboxylic acid peak was not observed in the ^{13}C spectra when taken in CD_3OD . Therefore, the ^{13}C spectrum in D_2O is also reported.

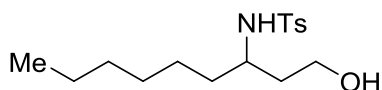


2-(1-Tosylpiperidin-2-yl) acetic acid (6): To **2k** (44 mg, 1.0 equiv., 0.13 mmol) in dry DMF (1.0 ml) at 0 °C was added NaH (60% dispersion in mineral oil, 7.0 mg, 2.2 equiv. 0.29 mmol). The reaction mixture was warmed to RT and stirred overnight. After this time, the reaction was diluted with EtOAc and washed with 1.0 M HCl (2 times). The conversion was essentially quantitative and was purified by titration with pentane to remove any grease, giving **6** (24 mg, 88%) as a white solid. M.P. = 107 – 109 °C. ¹H NMR (400 MHz, CDCl₃) δ 10.04 (s, 1H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.54 (m, 1H), 3.82 (dd, *J* = 13.9, 4.4 Hz, 1H), 2.94 (td, *J* = 13.3, 2.5 Hz, 1H), 2.70 (dd, *J* = 15.3, 9.4 Hz, 1H), 2.54 (dd, *J* = 15.3, 5.4 Hz, 1H), 2.43 (s, 3H), 1.68 – 1.32 (m, 6H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 176.9, 143.4, 138.1, 129.9, 127.1, 49.5, 41.1, 34.8, 27.8, 24.7, 21.6, 18.4 ppm. IR (neat, cm⁻¹): 2930, 2860, 1698, 1596, 1474, 1428, 1406, 1337, 1292, 1228, 1190, 1152, 1091, 1034. HRMS calcd. for (C₁₄H₁₈NO₄S) [M-H]⁻: 296.0962 found 296.0970.

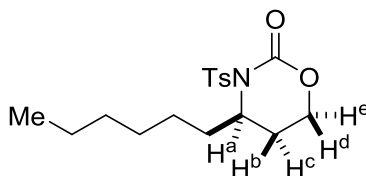
3.3 Synthesis of Deuterium-labeled β-Amino Acid and Subsequent Modification



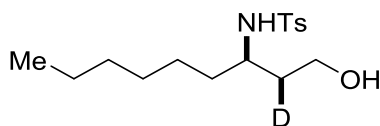
(2S,3R)-3-((4-Methylphenyl)sulfonamido) nonanoic-2-*d* acid (8). Following **GP8** with a reaction time of 3 days, **1a-d_I** (51 μl, 0.20 mmol) gave **8** (43 mg, 66%, d.r 4:1 (major shown)) as a white solid. ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 5.48 – 5.36 (m, 1H), 3.50 (p, *J* = 7.0 Hz, 1H), 2.47 (m, 1H), 2.48 (d, *J* = 4.5 Hz)^m & 2.46 (d, *J* = 5.8 Hz)^M (1H), 2.41 (s, 3H), 1.63 – 1.36 (m, 2H), 1.24 – 0.98 (m, 8H), 0.83 (t, *J* = 7.2 Hz, 3H). Note: NMR was also taken in CD₂Cl₂ which gave better but not perfect resolution of the isotopic doublets. ¹H NMR (500 MHz, CD₂Cl₂) δ 9.24 (s, br, 1H), 7.79 – 7.70 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.39 – 5.14 (m, 1H), 3.50 (q, *J* = 6.6 Hz, 1H), 2.49 (d, *J* = 4.6 Hz, 0.3H), 2.45 (d, *J* = 5.9 Hz, 0.8H), 2.42 (s, 3H), 1.45 (q, *J* = 7.0 Hz, 1H), 1.25 – 1.01 (m, 8H), 0.84 (t, *J* = 7.2 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ 176.7, 143.6, 138.0, 129.8, 127.2, 50.5, 38.8 (t, *J* = 18.0 Hz), 34.7, 31.7, 28.8, 25.8, 22.6, 21.6, 14.1 ppm. ¹³C NMR (101 MHz, CD₂Cl₂) δ 176.9, 144.1, 138.3, 130.1, 127.4, 50.9, 39.3, 39.1, 38.9, 35.0, 35.0, 32.0, 3.1, 26.0, 22.9, 21.7, 14.2. To confirm the presence of isomers in the isolated **8** and to determine their relative conformation, **2a** and **8** were converted to the cyclic carbamate derivatives.



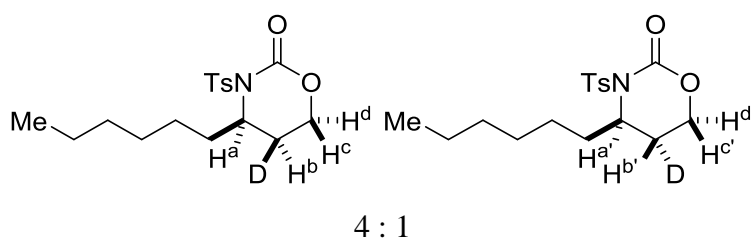
N-(1-Hydroxynonan-3-yl)-4-methylbenzenesulfonamide (S15): To a slurry of LiAlH_4 (34 mg, 6.6 equiv.) in dry THF (1.0 ml) cooled to 0 °C was added **2a** (45 mg) as a solution in THF (2.0 ml) drop wise. The mixture was then allowed to warm to RT and stirred for 2 h. After this time, the reaction was quenched by careful addition of H_2O (~5 drops) and stirred until it turned white. CH_2Cl_2 (10 ml) was added and the mixture was filtered, washing with CH_2Cl_2 (2×5.0 ml). This gave **S15** (41 mg, 95%) which was used in the following step without further purification. ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, $J = 7.9$ Hz, 2H), 7.30 (d, $J = 7.9$ Hz, 2H), 4.79 (d, $J = 8.4$ Hz, 1H), 3.92 – 3.81 (m, 1H), 3.68 – 3.58 (m, 1H), 3.43 – 3.34 (m, 1H), 2.42 (s, 3H), 1.75 (ddt, $J = 14.1, 9.2, 4.0$ Hz, 1H), 1.47 – 1.35 (m, 1H), 1.37 – 1.26 (m, 2H), 1.16 (q, $J = 6.8$ Hz, 2H), 1.10 – 0.88 (m, 6H), 0.82 (t, $J = 7.2$ Hz, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 143.5, 138.1, 129.8, 127.2, 59.0, 51.6, 37.6, 35.8, 31.7, 29.0, 25.5, 22.5, 21.6, 14.2 ppm.



4-Hexyl-3-tosyl-1,3-oxazinan-2-one (S16): Following a modified literature procedure,⁴² to **S15** (41 mg, 0.13 mmol, 1.0 equiv.) and pyridine (0.42 ml, 5.2 mmol, 40 equiv.) in dry CH_2Cl_2 (10 ml) cooled to 0 °C was added triphosgene (0.22 g, 0.65 mmol, 5.0 equiv.) as a solution in CH_2Cl_2 (6.0 ml). After stirring for an hour at this temperature, the solution was warmed to RT and stirred overnight. The solution was again cooled to 0 °C, quenched with NH_4Cl (sat.) and diluted with EtOAc (20 ml). The layers were separated and the aqueous layer was extracted with EtOAc (2×10 ml). The combined organic fractions were dried (MgSO_4), filtered and concentrated under reduced pressure. Purification by column chromatography gave **S16** (16 mg, 36%) as a white solid. M.P. = 80–82 °C. ^1H NMR (500 MHz, CD_2Cl_2) δ 7.88 – 7.81 (m, 2H), 7.36 – 7.31 (m, 2H), 4.61 – 4.54 (m, H^a), 4.37 (td, $J = 11.6, 3.8$ Hz, H^d), 4.27 (dddd, $J = 11.3, 5.2, 2.8, 1.1$ Hz, H^e), 2.44 (s, 3H), 2.12 (ddtd, $J = 14.8, 11.5, 5.2, 0.9$ Hz, H^c), 2.04 (ddt, $J = 14.6, 3.9, 3.0$ Hz, H^b), 1.99 – 1.90 (m, 1H), 1.73 – 1.62 (m, 1H), 1.42 – 1.24 (m, 8H), 0.91 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (126 MHz, CD_2Cl_2) δ 148.9, 145.4, 136.7, 129.7, 129.2, 65.2, 55.7, 34.4, 32.1, 29.3, 26.1, 25.7, 23.0, 21.8, 14.2. IR (neat, cm^{-1}): 2925, 2858, 1708, 1597, 1490, 1458, 1411, 1368, 1340, 1265, 1168, 1144, 1087, 1020. HRMS calcd. for $(\text{C}_{17}\text{H}_{26}\text{NO}_4\text{S})$ $[\text{M}+\text{H}]^+$: 340.1577 found 340.1572. Note: As for **2a-d**, better resolution was obtained in CD_2Cl_2 and allowed quantification of the isotopic ratio in the case of **9-d**.



***N*-((2*S*,3*R*)-1-Hydroxynonan-3-yl-2-d)-4-methylbenzenesulfonamide (S17):** Following the above procedure for the synthesis of **S15**, **8** (43 mg) gave **S17** (38 mg, 93%) which was used in the following step without further purification. ^1H NMR (400 MHz, CDCl_3) δ 7.79 – 7.73 (m, 2H), 7.32 – 7.27 (m, 2H), 3.87 – 3.80 (m, 1H), 3.62 (dd, $J = 11.4, 4.9$ Hz, 1H), 3.36 (tq, $J = 6.5, 2.8$ Hz, 1H), 2.41 (s, 3H), 1.76 – 1.65 (m, 1H), 1.36 – 1.23 (m, 2H), 1.15 (q, $J = 6.8$ Hz, 2H), 1.09 – 0.91 (m, 6H), 0.81 (t, $J = 7.2$ Hz, 3H) ppm.

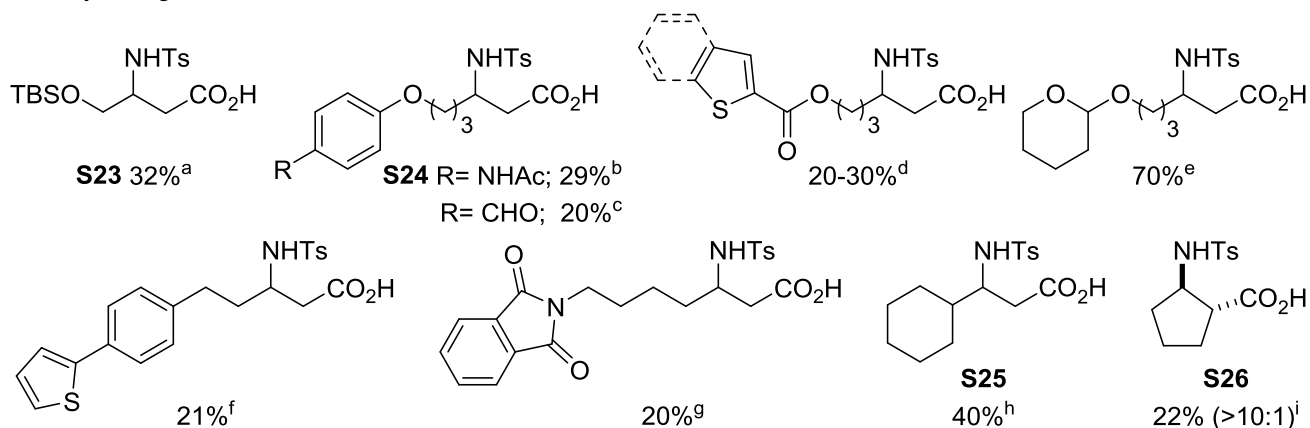


(4*R*,5*S*)-4-Hexyl-3-tosyl-1,3-oxazinan-2-one-5-d (9): Following the above procedure for the synthesis of **S16**, **S17** (38 mg) gave **9** (15 mg, 37%, 4:1 d.r) as a white solid. ^1H NMR (500 MHz, CD_2Cl_2) δ 7.87 – 7.83 (m, 2H), 7.36 – 7.32 (m, 2H), 4.59 – 4.53 (m, $\text{H}^{a/a'}$), 4.37 (t, $J = 11.7$ Hz, H^c) & 4.37 (dd, $J = 11.3, 3.3$ Hz, $\text{H}^{c'}$), 4.26 (ddd, $J = 11.3, 5.3, 1.1$ Hz, H^d) & 4.26 (m, $\text{H}^{d'}$), 2.44 (s, 3H), 2.10 (dt, $J = 11.5, 5.3$ Hz, 0.8H^b), 2.03 (dt, $J = 4.1, 2.6$ Hz, $0.2\text{H}^{b'}$), 2.00 – 1.90 (m, 1H), 1.73 – 1.64 (m, 1H), 1.43 – 1.24 (m, 9H), 0.94 – 0.87 (m, 3H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2 , diastereomers)^{xxvii} δ 149.0^M & 148.9^m, 145.4, 136.7, 129.7, 129.2, 65.2, 55.6^M & 55.6^m, 34.4^M & 34.3^m, 32.1, 29.3, 26.1^m & 26.1^M, 25.42 (t, $J = 20.0$ Hz)^{M&m}, 23.0, 21.8, 14.2 ppm. Based on the closest available literature,⁴³ **9** has been assigned as a 4:1 *cis:trans* mixture of isomers.

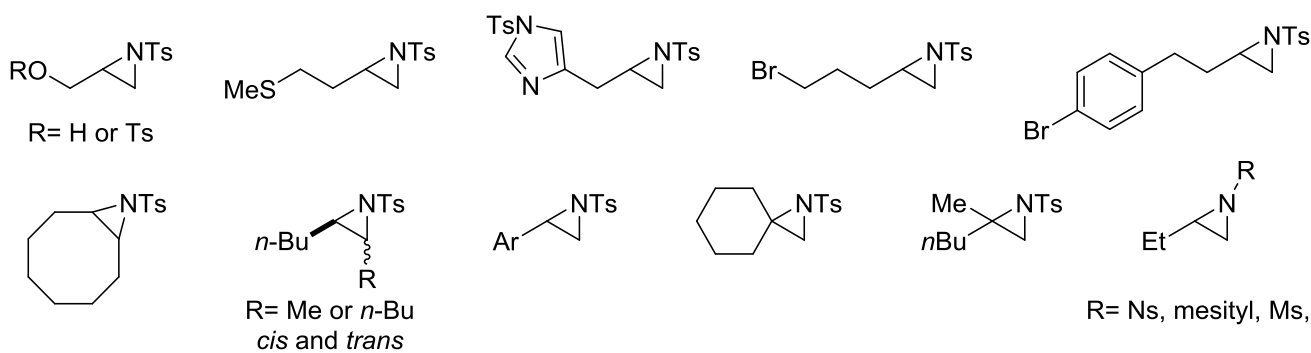
^{xxvii} The major (M) and minor (m) isomers have been assigned where the resolution was sufficient to detect separate peaks.

3.4 Low Yielding and Unsuccessful Aziridines

Low yielding reactions:

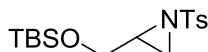


Unsuccessful aziridines:



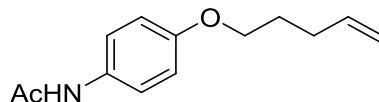
Scheme S2: ^a 5 day reaction, isolated yield. ^b 6 day reaction, isolated yield. ^c ¹H NMR yield against internal standard. 45% of olefins were also detected. ^d ¹H NMR yield against internal standard. In this case the product was unstable to isolation. ^e ¹H NMR yield against internal standard. Quench and work-up carried out with NH₄Cl instead of HCl. In this case, the product proved unstable to isolation. ^f 3 day reaction. 21% of product was detected by ¹H NMR and 45% of the aziridine remained. 7 day reaction: 15% of the product and 35% of the aziridine was observed ^g ¹H NMR yield against internal standard. In this case the product was unstable to isolation. ^h 5 day reaction, isolated yield. ⁱ 10 day reaction, isolated yield. Unlike with **2z**, the *trans* product was generated in high selectivity. The *cis*-cyclic carbamate was detected suggesting at a competing pathway with *cis*-intermediates.

3.4.1 Characterisation of Low Yielding Aziridines and Isolated β -Amino Acids

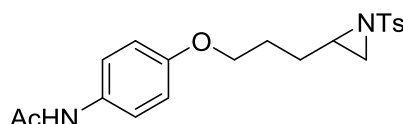


2-(((tert-Butyldimethylsilyl)oxy)methyl)-1-tosylaziridine (S18): Following **GP3** with (allyloxy)(tert-butyl)dimethylsilane (1.7 g, 10 mmol), purification by column chromatography on silica gel (hexane: EtOAc 9:1 \rightarrow 5:1) afforded **S18** as a colorless oil (1.2 g, 36%). ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.80 (m, 2H), 7.35 – 7.30 (m, 2H), 3.69 (dd, *J* = 11.6, 4.0 Hz, 1H), 3.59 (dd, *J* = 11.6, 5.3 Hz, 1H), 2.96 – 2.88 (m, 1H), 2.64 (d, *J* = 7.1 Hz, 1H), 2.44 (s, 3H), 2.20 (d, *J* = 4.5 Hz,

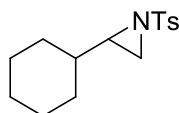
1H), 0.81 (s, 9H), -0.03 (s, 3H), -0.04 (s, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 144.6, 135.3, 129.8, 128.2, 62.5, 40.9, 30.7, 25.9, 21.8, 18.4, -5.3, -5.4. Spectroscopic data for **S18** match those previously reported in the literature.⁴⁴



N-(4-(Pent-4-en-1-yloxy)phenyl) acetamide (S19): Following **GP6**, *N*-(4-hydroxyphenyl)acetamide (2.4 g, 16 mmol) gave **S19** as a colourless oil (2.4 g, 73%). ^1H NMR (400 MHz, CDCl_3) δ 7.41 – 7.32 (m, 2H), 7.09 (s, br, 1H), 6.91 – 6.80 (m, 2H), 5.85 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.06 (dq, J = 17.1, 1.7 Hz, 1H), 4.99 (ddt, J = 10.2, 2.3, 1.3 Hz, 1H), 3.94 (t, J = 6.5 Hz, 2H), 2.28 – 2.17 (m, 2H), 2.15 (s, 3H), 1.87 (dq, J = 7.8, 6.5 Hz, 2H), 1.62 – 1.56 (m, 2H). Spectroscopic data for **S19** match those previously reported in the literature.⁴⁵

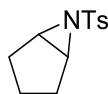


N-(4-(3-(1-Tosylaziridin-2-yl)propoxy)phenyl) acetamide (S20): Following **GP3** with **S19** (1.8 g, 8.0 mmol), purification by column chromatography (hexane: EtOAc 8:2 \rightarrow 6:4) gave **S20** as a viscous oil (1.3 g, 43%). ^1H NMR (400 MHz, CDCl_3) δ 7.81 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 9.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.17 (s, 1H), 6.79 (d, J = 9.0 Hz, 2H), 3.92 – 3.81 (m, 2H), 2.86 – 2.76 (m, 1H), 2.64 (d, J = 7.0 Hz, 1H), 2.43 (s, 3H), 2.14 (s, 3H), 2.09 (d, J = 4.6 Hz, 1H), 1.90 – 1.77 (m, 1H), 1.80 – 1.68 (m, 2H), 1.52 – 1.42 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.1, 155.4, 144.4, 134.8, 130.9, 129.5, 127.8, 121.7, 114.5, 66.8, 39.7, 33.7, 27.8, 26.4, 24.1, 21.4. IR (neat, cm^{-1}): 3306, 3064, 2928, 1661, 1599, 1538, 1509, 1473, 1410, 1371, 1317, 1234, 1156, 1092, 1018. HRMS calcd. for ($\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_4\text{S}$) $[\text{M}+\text{H}]^+$: 389.1530 found 389.1532.

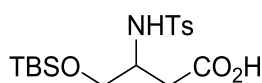


2-Cyclohexyl-1-tosylaziridine (S21): Following **GP3** with vinylcyclohexane (0.79 g, 4.8 mmol), purification by column chromatography (hexane: EtOAc 9:1) gave **S21** as a white solid (0.51 g, 38%). ^1H NMR (400 MHz, CDCl_3) δ 7.83 – 7.78 (m, 2H), 7.32 (d, J = 8.1 Hz, 2H), 2.59 (d, J = 7.0 Hz, 1H), 2.53 (td, J = 7.2, 4.5 Hz, 1H), 2.44 (s, 3H), 2.09 (d, J = 4.6 Hz, 1H), 1.73 – 1.55 (m, 4H), 1.49 (dtd, J = 12.4, 3.5, 1.7 Hz, 1H), 1.24 – 0.84 (m, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 144.5, 135.2, 129.7, 128.2, 45.3, 39.5, 32.8, 30.3, 29.7, 26.1, 25.7, 25.5, 21.8, 21.0. LRMS (ESI): 279 (M^+),

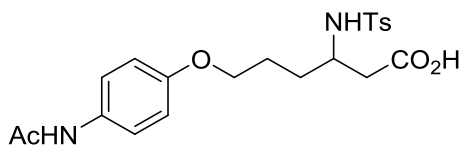
252, 238, 210, 184, 155, 132, 91. Spectroscopic data for **S21** match those previously reported in the literature.¹¹



6-Tosyl-6-azabicyclo[3.1.0] hexane (S22): Following **GP3**, cyclopentene (1.8 ml, 20 mmol) gave **S22** as a white solid (4.2 g, 88%). ¹H NMR (400 MHz, CDCl₃) δ 7.83 – 7.78 (m, 2H), 7.36 – 7.28 (m, 2H), 3.33 (d, *J* = 1.4 Hz, 2H), 2.44 (s, 3H), 1.99 – 1.88 (m, 2H), 1.67 – 1.51 (m, 3H), 1.48 – 1.33 (m, 1H). Spectroscopic data for **S22** match those previously reported in the literature.⁴⁶



4-((tert-Butyldimethylsilyl)oxy)-3-((4-methylphenyl)sulfonamido) butanoic acid (S23): Following **GP8** with a reaction time of 6 days^{xxviii} and quenching the reaction with NH₄Cl (sat.) instead of HCl, **S18** (68 mg, 0.20 mmol) gave **S23** (24 mg, 32%) as a white solid. In a separate independent experiment **S23** (25 mg, 32%) was isolated giving an average yield of 32%. ¹H NMR (400 MHz, CDCl₃) δ 7.79 – 7.72 (m, 2H), 7.33 – 7.26 (m, 2H), 5.30 (d, *J* = 8.5 Hz, 1H), 3.70 – 3.59 (m, 1H), 3.55 (dd, *J* = 10.1, 4.0 Hz, 1H), 3.49 (dd, *J* = 10.1, 5.5 Hz, 1H), 2.64 (dd, *J* = 16.6, 4.9 Hz, 1H), 2.50 (dd, *J* = 16.6, 7.0 Hz, 1H), 2.42 (s, 3H), 0.83 (s, 9H), -0.02 (s, 3H), -0.03 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 175.6, 143.7, 137.8, 129.9, 127.2, 64.0, 51.6, 35.7, 25.9, 21.6, 18.3, -5.5, -5.5. IR (neat, cm⁻¹): 3259, 2928, 2857, 1777, 1598, 1540, 1452, 1408, 1320, 1252, 1156, 1091. HRMS calcd. for (C₁₇H₂₈NO₅SSi) [M-H]⁻: 386.1463 found 386.1475.

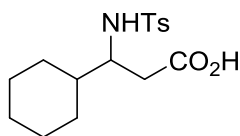


6-(4-Acetamidophenoxy)-3-((4-methylphenyl)sulfonamido) hexanoic acid (S24): Following **GP8** with a reaction time of 6 days,^{xxix} **S20** (78 mg, 0.20 mmol) gave **S24** (27 mg, 31%) as a white solid. In a separate independent experiment **S24** (23.5 mg, 27%) was isolated giving an average yield of 29%. M.P. = 112 – 116 °C. ¹H NMR (400 MHz, MeOD) δ 7.77 – 7.71 (m, 2H), 7.44 – 7.35 (m, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 6.82 – 6.74 (m, 2H), 3.75 (t, *J* = 6.0 Hz, 2H), 3.64 – 3.52 (m, 1H), 2.45 –

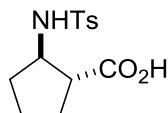
^{xxviii} Crude NMR was not taken in this case due to the instability of the **S23**. A long reaction time was used as it was proposed that the presence of the bulky TBS group would likely inhibit the reaction.

^{xxix} In this case, accurate quantification by NMR was not possible due to the poor solubility of **S24** in CDCl₃. After the 6 day reaction, however, a small amount of **S20** remained suggesting the long reaction time was necessary.

2.29 (m, 5H), 2.09 (s, 3H), 1.68 (m, 2H), 1.62 – 1.44 (m, 2H). ^{13}C NMR (101 MHz, MeOD) δ 174.5, 171.4, 157.1, 144.7, 139.9, 132.8, 130.7, 128.0, 123.0, 115.6, 68.5, 51.7, 41.4, 32.3, 26.5, 23.6, 21.4. IR (neat, cm^{-1}): 3273, 2925, 1711, 1660, 1600, 1541, 1509, 1411, 1303, 1240, 1152, 1090, 1024. HRMS calcd. for ($\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}_6\text{S}$) $[\text{M}-\text{H}]^-$: 433.1439 found 433.1434.



3-Cyclohexyl-3-((4-methylphenyl)sulfonamido) propanoic acid (S25): Following **GP8** with a reaction time of 5 days,^{xxx} **S21** (56 mg, 0.20 mmol) gave **S25** (24 mg, 37%) as a white solid. In a separate independent experiment **S25** (28 mg, 43%) was isolated giving an average yield of 40%. M.P. = 112 – 116 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.75 (d, J = 7.8 Hz, 2H), 7.29 (d, J = 7.8 Hz, 2H), 5.33 (d, J = 9.4 Hz, 1H), 3.39 – 3.29 (m, 1H), 2.55 – 2.34 (m, 5H), 1.83 – 1.40 (m, 6H), 1.20 – 1.02 (m, 3H), 0.83 (dq, J = 46.2, 12.0 Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 176.3, 143.6, 138.1, 129.8, 127.2, 55.4, 41.3, 35.9, 29.6, 29.3, 26.2, 26.1, 26.0, 21.7. IR (neat, cm^{-1}): 3273, 2930, 2848, 1700, 1597, 1445, 1403, 1319, 1249, 1230, 1158, 1091, 1068, 1048. HRMS calcd. for ($\text{C}_{16}\text{H}_{22}\text{NO}_4\text{S}$) $[\text{M}-\text{H}]^-$: 324.1275 found 324.1280.



(trans)-2-((4-Methylphenyl)sulfonamido)cyclopentane-1-carboxylic acid (S26): Following **GP8** with a reaction time of 10 days^{xxxi}, **S22** (48 mg, 0.20 mmol) gave **S26** (13 mg, 22%, >10:1 *trans:cis*) as a white solid. In a separate independent experiment with a reaction time of 7 days, **S26** (9 mg, 27%) was isolated. ^1H NMR (400 MHz, CDCl_3 , diastereomers) δ 7.79 – 7.73 (m, 2H), 7.30 (d, J = 8.1 Hz, 2H), 5.27 (d, J = 8.3 Hz, 0.08H), 5.14 (d, J = 6.4 Hz, 0.92H), 3.78 (p, J = 7.1 Hz, 1H), 2.83 (dt, J = 12.1, 6.2 Hz, 0.08H), 2.72 (dt, J = 9.3, 7.4 Hz, 0.92H), 2.41 (s, 3H), 2.09 – 1.90 (m, 1H), 1.80 (tdd, J = 15.4, 8.0, 5.9 Hz, 1H), 1.75 – 1.57 (m, 1H), 1.46 (dq, J = 12.9, 7.9 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3 , major diastereomer) δ 179.3, 143.8, 137.1, 129.9, 127.4, 57.7, 50.8, 33.6, 28.3, 23.1, 21.7. LRMS (ESI): 565 (2M-H), 396 (M+TFA), 282 (M-H). Spectroscopic data for **S26** match those previously reported in the literature.⁴¹

^{xxx} After a 5 day reaction, **S21** (41%) was detected by ^1H NMR of the crude reaction mixture. Longer reaction times did not lead to better conversions suggesting the reaction had stalled. Other reaction variables such as increasing the temperature and changing the ligand were modified to try and improve the yield but without success.

^{xxxi} After a 7 day reaction, 17% of **S26** was detected by ^1H NMR and 50% **S22** still remained. After a 10 day reaction, 25% of **S26** was detected by ^1H NMR and 35% **S22** still remained.

4 Mechanistic Investigation

4.1 Impurities in Aziridine Synthesis and Poisoning Experiments

In the synthesis of aziridines from terminal olefins and Chloramine-T as reported by Sharpless¹² minor side-products are generated which have similar elution times to the desired aziridine and care must be taken during the purification to successfully remove these impurities. For substrate **1a**, a column of approximately 6 g of silica per mmol and keeping the eluent polarity at 95:5 hexane:EtOAc was sufficient to mostly remove these impurities but some mixed fractions were obtained. The first fractions before **1a** eluted pure contained an impurity in ~10% (Figure S1) which was identified as 1-bromooctan-2-ol (**S27**)^{xxxii} by independent synthesis of this compound from 1-octene following literature procedure.⁴⁷ This impurity comes from the use of commercially available Chloramine.T trihydrate resulting in nucleophilic ring opening of the bromonium intermediate by H₂O. The last fractions with **1a** contained many impurities (Figure S2) with the major impurity being *N*-(1-bromooctan-2-yl)-4-methylbenzenesulfonamide (**S28**)^{xxxiii} which was verified by independent synthesis of this compound from **1a** following literature procedure.⁴⁸ The opposite regioisomer of **S28** and *N*-(1-chlorooctan-2-yl)-4-methylbenzenesulfonamide (**S29**)^{xxxiv} were also identified as minor impurities (Figure S3).

^{xxxii} **1-Bromooctan-2-ol (S27)**. Colourless oil. ¹H NMR (400 MHz, CDCl₃) δ 3.78 (tdd, *J* = 7.1, 5.6, 3.2 Hz, 1H), 3.55 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.38 (dd, *J* = 10.3, 7.1 Hz, 1H), 2.08 (s, br, 1H), 1.62 – 1.22 (m, 10H), 0.95 – 0.81 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 71.2, 40.8, 35.3, 31.8, 29.3, 25.7, 22.7, 14.2. GC-MS (ESI): 207/ 209 (M–H), 123/ 125 (M–(CH₂)₅CH₃), 115 (M–CH₂Br). Spectroscopic data for **S27** match those previously reported in the literature.⁵⁴

^{xxxiii} ***N*-(1-Bromooctan-2-yl)-4-methylbenzenesulfonamide (S28)**. White solid. ¹H NMR (400 MHz, CDCl₃) δ 7.80 – 7.74 (m, 2H), 7.34 – 7.29 (m, 2H), 4.67 (d, *J* = 8.7 Hz, 1H), 3.46 – 3.26 (m, 3H), 2.43 (s, 3H), 1.58 – 1.35 (m, 2H), 1.31 – 1.03 (m, 8H), 0.85 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 143.8, 138.0, 129.9, 127.2, 53.3, 38.5, 33.7, 31.7, 28.8, 25.4, 22.6, 21.7, 14.2. GC-MS (ESI): 361 (M+), 276/ 278 (M–(CH₂)₅CH₃), 268 (M–CH₂Br), 155 (Ts), 91 (Tolyl). Spectroscopic data for **S28** match those previously reported in the literature.⁵⁵

^{xxxiv} ***N*-(1-Chlorooctan-2-yl)-4-methylbenzenesulfonamide (S29)**. White solid. ¹H NMR (400 MHz, CDCl₃) δ 7.79 – 7.74 (m, 2H), 7.34 – 7.28 (m, 2H), 4.69 (d, *J* = 8.2 Hz, 1H), 3.55 – 3.40 (m, 3H), 2.43 (s, 3H), 1.56 – 1.39 (m, 2H), 1.23 – 1.04 (m, 8H), 0.85 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 143.8, 138.0, 129.9, 127.2, 53.9, 48.3, 32.6, 31.7, 28.9, 25.5, 22.6, 21.7, 14.2. GC-MS (ESI): 317 (M+), 268 (M–CH₂Cl), 232 (M–(CH₂)₅CH₃), 155 (Ts), 91 (Tolyl); Spectroscopic data for **S29** match those previously reported in the literature.⁵⁶

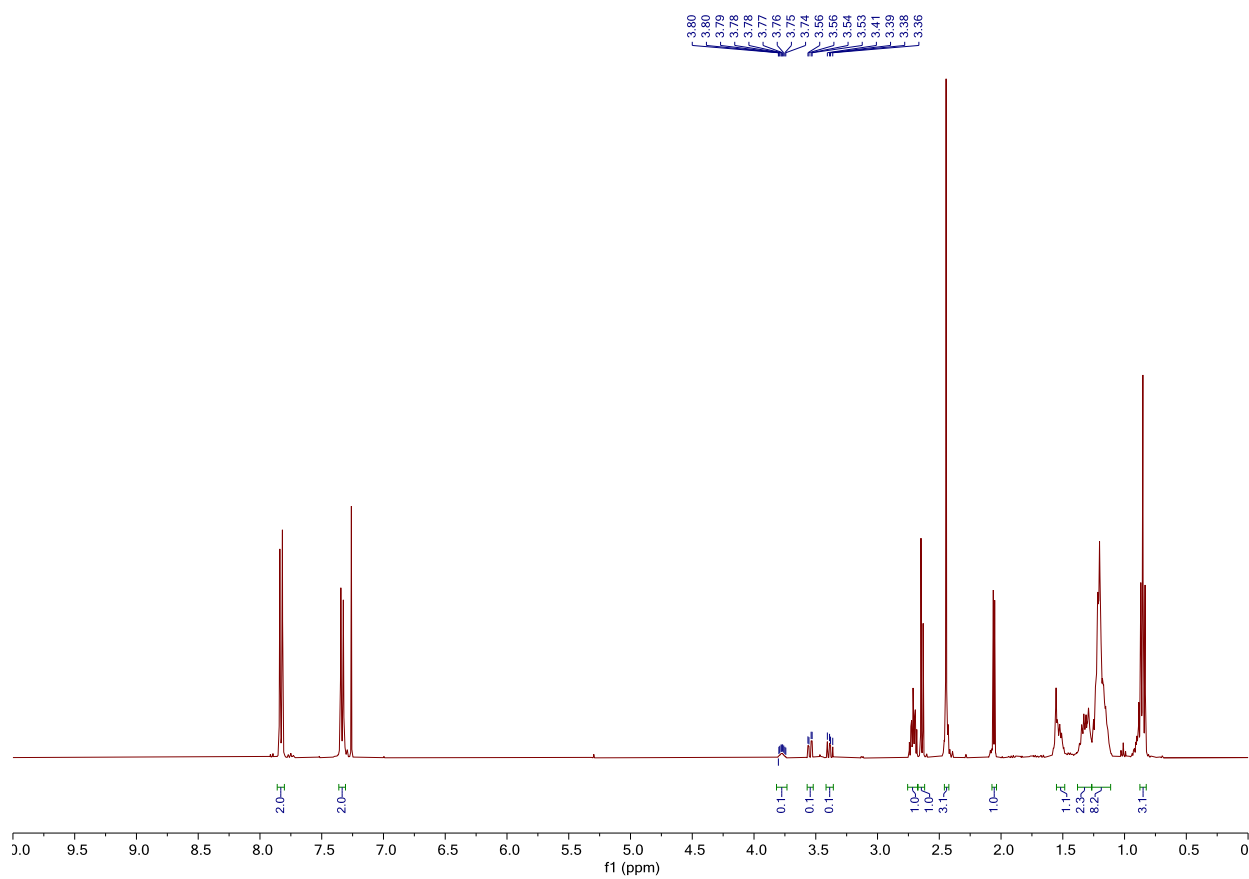


Figure S1: ^1H (CDCl_3 , 400 MHz)

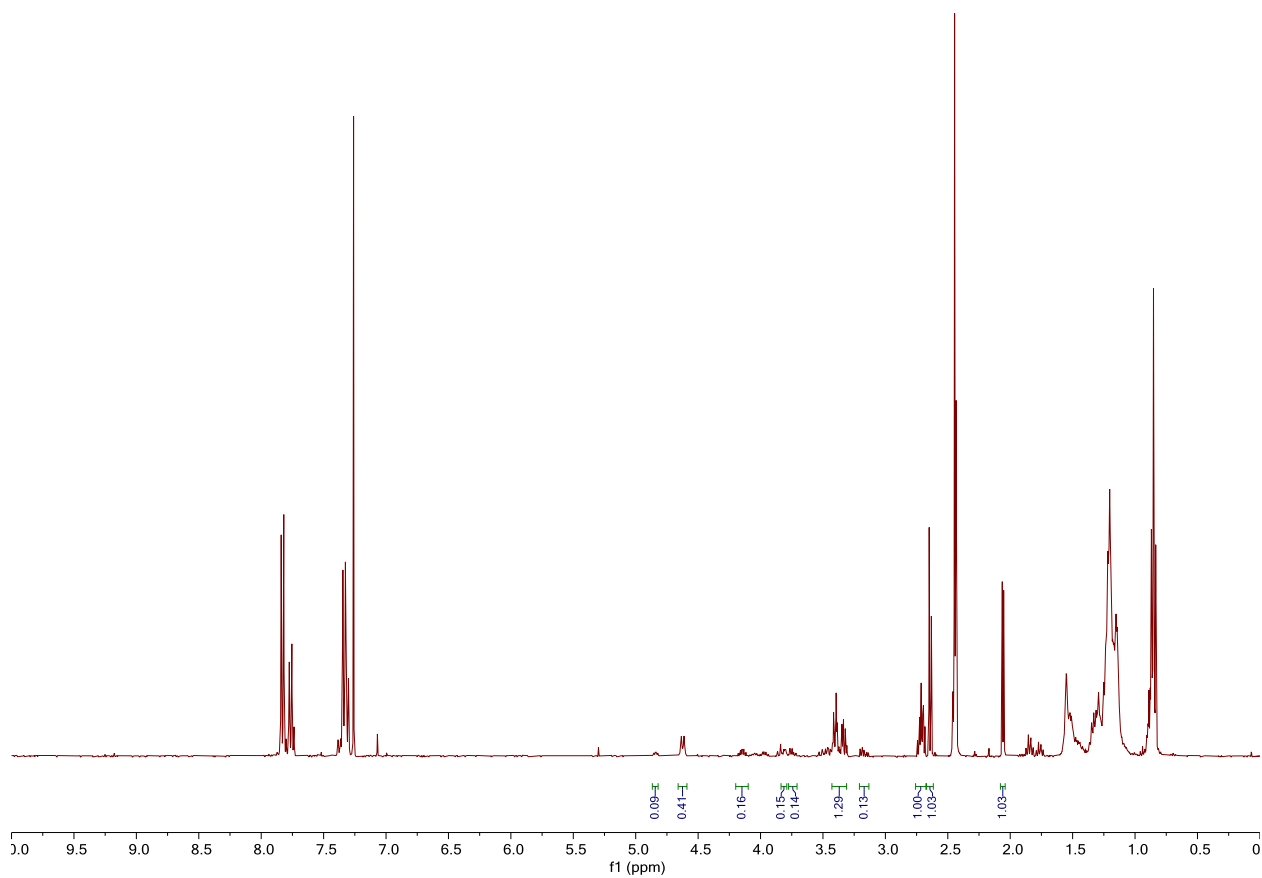


Figure S2: ^1H (CDCl_3 , 400 MHz)

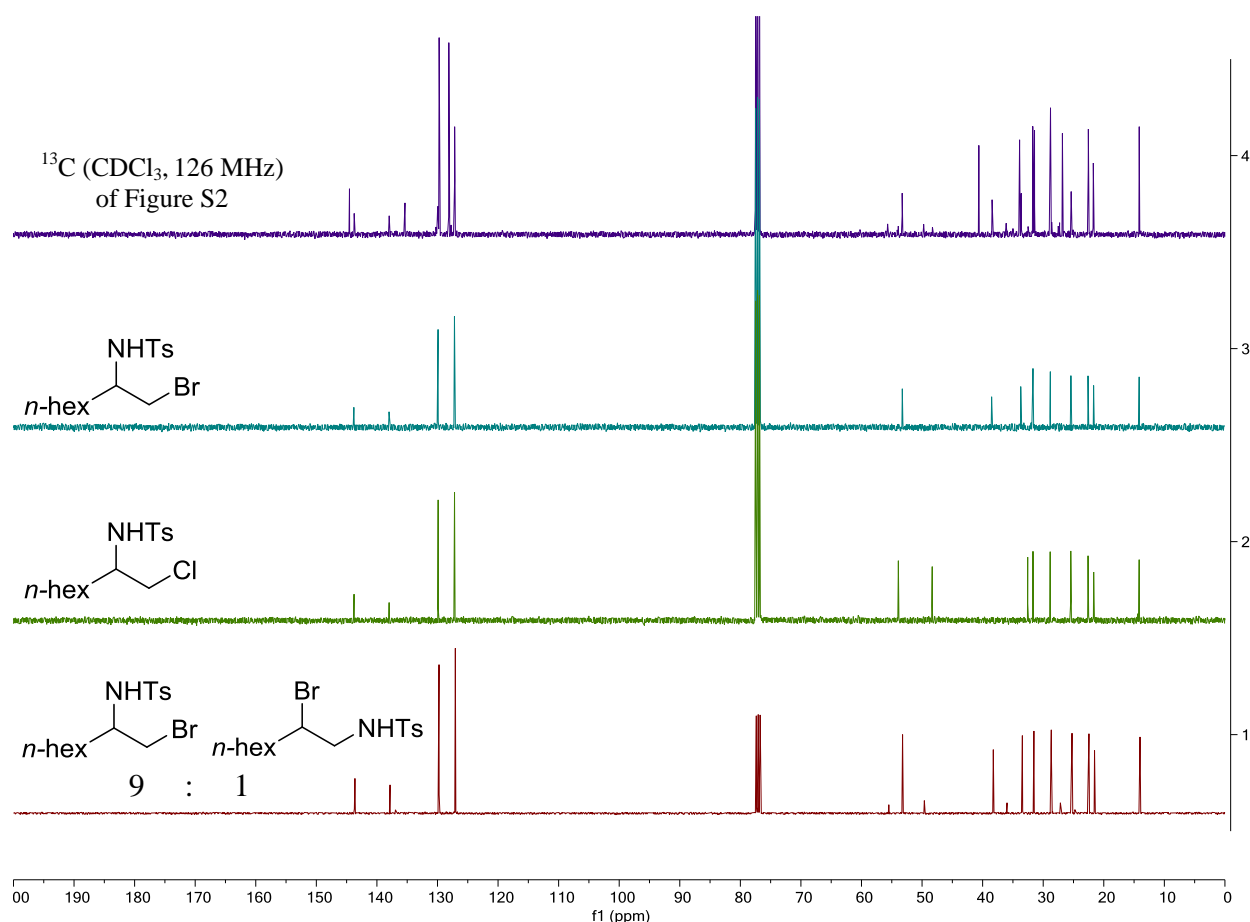


Figure S3

As mentioned during the optimization studies (see §2), it was realized that the presence of even trace amounts (2-5%) of these impurities in the batch of **1a** significantly influenced the reaction outcome. Side-reactions were more prevalent resulting in quicker consumption of the aziridine and a lower yield of the desired β -amino acid (**2a**) overall. To study this under a controlled setting, poisoning experiments were conducted with the independently synthesized **S27**, **S28** and **S29**, introducing them into back into the reaction in increasing amounts. The addition of **S27** to the reaction decreased the yield of **2a** with 56% observed when 10% **S27** was present as well as over twice as much TsNH₂ (Table S4) suggesting β -hydride and deamination pathways were promoted.

The addition of **S28** had a similar influence on the reaction outcome (Table S5) with less **2a** and more TsNH₂ generated as the loading of **S28** was increased. Importantly, when **S28** was used in place of **1a**, the major product was TsNH₂ and only small amounts of **2a** were generated. In contrast, addition of **S29** did not result in a clear trend besides a small drop in conversion and yield of **2a** (Table S6). When **S29** was used in place of **1a**, a small amount of **2a** was again generated but the conversion was low and ~10% of **1a** was also detected. The presence of **1a** in the crude reaction

mixture, along with the tolerance of the alkyl chloride in substrates **1j-k**, suggests that **2a** may be generated via the aziridine formed *in situ*.

Table S4

$ \begin{array}{c} \text{Ts} \\ \\ \text{N} \\ / \quad \backslash \\ \text{C} \quad \text{C} \\ \quad \\ n\text{-hex} \quad \text{Br} \\ \textbf{1a} \quad \textbf{S27} \end{array} + \begin{array}{c} \text{OH} \\ \\ n\text{-hex} \quad \text{Br} \\ \textbf{S27} \end{array} \xrightarrow[\text{MeOH (5 equiv.), DMPU (0.40M), CO}_2 \text{ (1 bar), 10 }^\circ\text{C, 48 h}]{\text{NiCl}_2\text{glyme (10 mol\%), L1 (20 mol\%), Mn (3 equiv.)}} \begin{array}{c} \text{NHTs} \\ \\ n\text{-hex} \quad \text{CO}_2\text{H} \\ \textbf{2a} \end{array} + \text{TsNH}_2 $			
S27 (mol%)	Conv. / % ^a	2a / % ^a	TsNH ₂ / % ^a
0	90	73	12
2.5	85	69	17
5.0	92	66	22
10	92	56	28
13 ^b	90	54	30

^a ¹H-NMR yields using trimethoxybenzene as internal standard. ^b The mixed fractions as shown in Figure S1 were used in place of pure **1a**.

Table S5

$ \begin{array}{c} \text{Ts} \\ \\ \text{N} \\ / \quad \backslash \\ \text{C} \quad \text{C} \\ \quad \\ n\text{-hex} \quad \text{Br} \\ \textbf{1a} \quad \textbf{S28} \end{array} + \begin{array}{c} \text{NHTs} \\ \\ n\text{-hex} \quad \text{Br} \\ \textbf{S28} \end{array} \xrightarrow[\text{MeOH (5 equiv.), DMPU (0.40M), CO}_2 \text{ (1 bar), 10 }^\circ\text{C, 48 h}]{\text{NiCl}_2\text{glyme (10 mol\%), L1 (20 mol\%), Mn (3 equiv.)}} \begin{array}{c} \text{NHTs} \\ \\ n\text{-hex} \quad \text{CO}_2\text{H} \\ \textbf{2a} \end{array} + \text{TsNH}_2 $			
S28 (mol%)	Conv. / % ^a	2a / % ^a	TsNH ₂ / % ^a
0	90	73	12
2.5	91	72	19
5.0	96	70	24
10	93	58	33
100 ^b	95	18	50

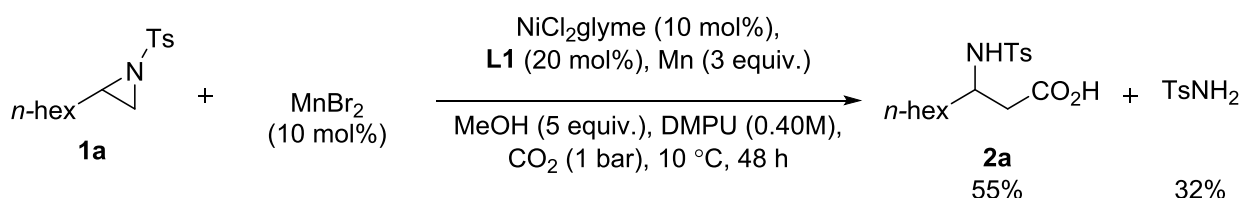
^a ¹H-NMR yields using trimethoxybenzene as internal standard. ^b 1 equiv. of **S28** was used in place of **1a**.

Table S6

$ \begin{array}{c} \text{Ts} \\ \\ \text{n-hex} \text{---} \text{N} \text{---} \\ \diagup \quad \diagdown \\ \text{1a} \end{array} + \begin{array}{c} \text{NHTs} \\ \\ \text{n-hex} \text{---} \text{CH} \text{---} \text{CH}_2 \text{---} \text{Cl} \\ \text{S29} \\ (2.5 \text{--} 10 \text{ mol}\%) \end{array} \xrightarrow[\text{MeOH (5 equiv.), DMPU (0.40M), CO}_2 \text{ (1 bar), 10 }^\circ\text{C, 48 h}]{\text{NiCl}_2\text{glyme (10 mol\%), L1 (20 mol\%), Mn (3 equiv.)}} \begin{array}{c} \text{NHTs} \\ \\ \text{n-hex} \text{---} \text{CH} \text{---} \text{CH}_2 \text{---} \text{CO}_2\text{H} \\ \text{2a} \end{array} + \text{TsNH}_2 $			
S29 (mol%)	Conv. / % ^a	Product / % ^a	TsNH ₂ / % ^a
0	90	73	12
2.5	78	63	13
5	84	67	14
10	84	65	14
100 ^a	30	12	5

^a ¹H-NMR yields using trimethoxybenzene as internal standard. Average of 2 independent runs ^b 1 equiv. of **S29** was used in place of **1a**.

It is not fully understood how these impurities influence the reaction but the use of nickel bromide pre-catalysts always resulted in worse results, suggesting that it is the presence of bromide in the reaction mixture that is detrimental. To test this theory, a reaction was performed with MnBr₂ added (Scheme S3) and a very similar result to that with 10 mol% of **S27/28** was obtained. Although it is possible that **S28** and **S29** are intermediates in the reaction, the small amount of **2a** observed when **S28/29** were subjected to the reaction conditions suggests this is unlikely.



Scheme S3

4.2 Electrochemical Studies

Cyclic voltammetry was conducted on a PARSTAT 2273 potentiometer (Princeton Applied Research) using a 3-electrode cell configuration. A glassy carbon working electrode was employed alongside a platinum flag counter electrode and a Ag/AgCl (KCl sat.) reference electrode. Tetrabutylammonium hexafluorophosphate (Bu_4NPF_6) was used as a supporting electrolyte (0.10 M). Ferrocene solutions (2.0 mM) were used as an internal standard to determine the precise potential scale in different solvents. The aziridine **1ab** was made up as a 5 mM solution in CH_3CN (dry). The Ni complexes: **L1NiCl₂** and **L5NiCl₂** were made up as 5 mM solutions in CH_3CN or DMA. Argon was passed through the samples for 10 minutes before taking any measurements and an Ar atmosphere was maintained for the duration to avoid the deleterious influence of oxygen reduction. Samples were examined at scan rates from 20 to 1000 mV s^{-1} depending on the substrate. In the situations where there is no apparent return oxidation peak, we have stated the $E_{\text{p}}^{\text{red}}$ (the potential corresponding to the maximum reductive current).

The reduction of aziridine **1ab** (Figure S4) showed an irreversible profile over all scan rates tested (20 to 1000 mV s^{-1}) suggesting a rapid fragmentation upon reduction of the tosyl moiety. An oxidation peak is then observed at 0.5 V which is likely the oxidation of one of the fragments generated (no peak is observed if first scanning in the forward direction, see Figure S5). The extremely difficult reduction (-2.4 V vs. Ag/AgCl at 100 mVs^{-1}) provides evidence against a single electron transfer type oxidative addition **1ab** into Ni(0) as this would be highly unfavorable. Furthermore, the addition of MeOH (5 equiv.) to **1ab** did not alter the reduction profile (Figure S5).

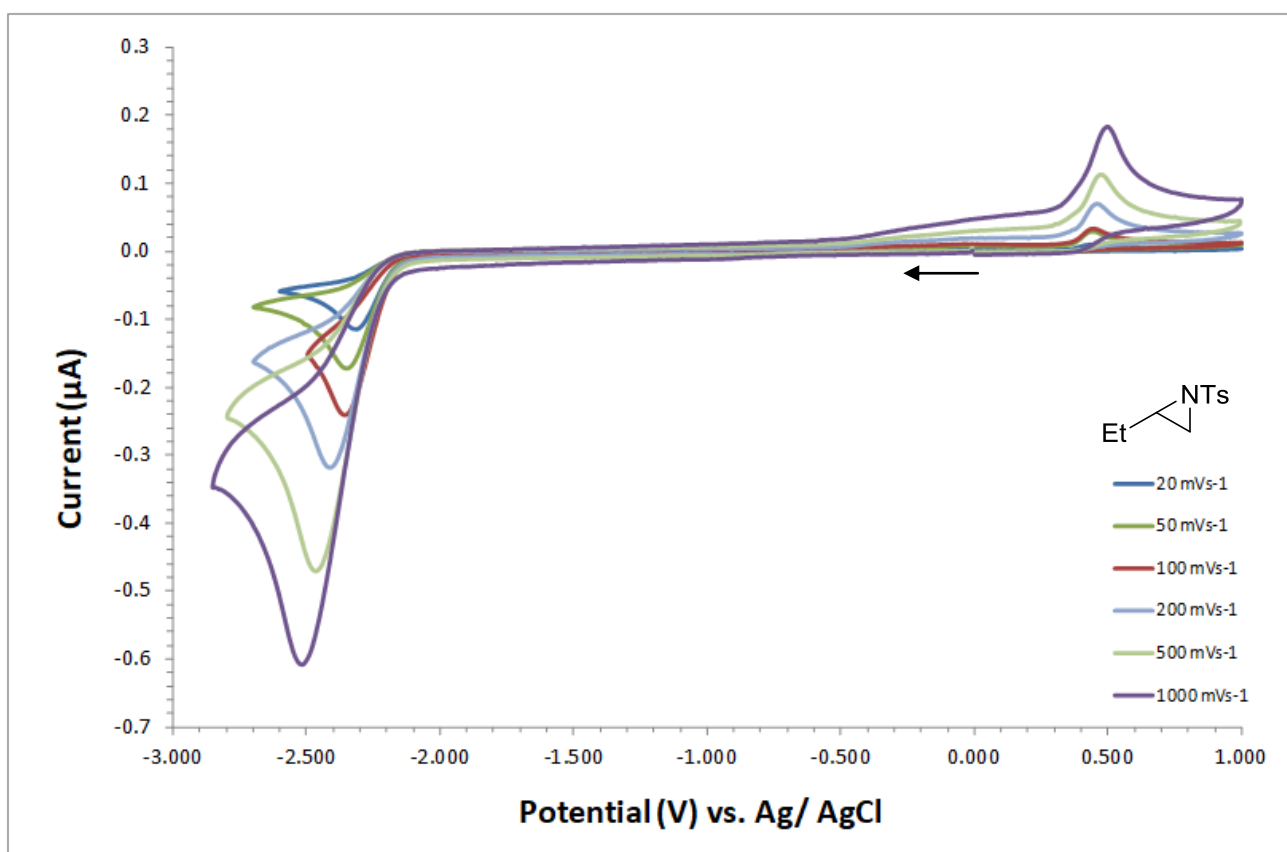


Figure S4: CV of **1ab** in MeCN at different scan rates

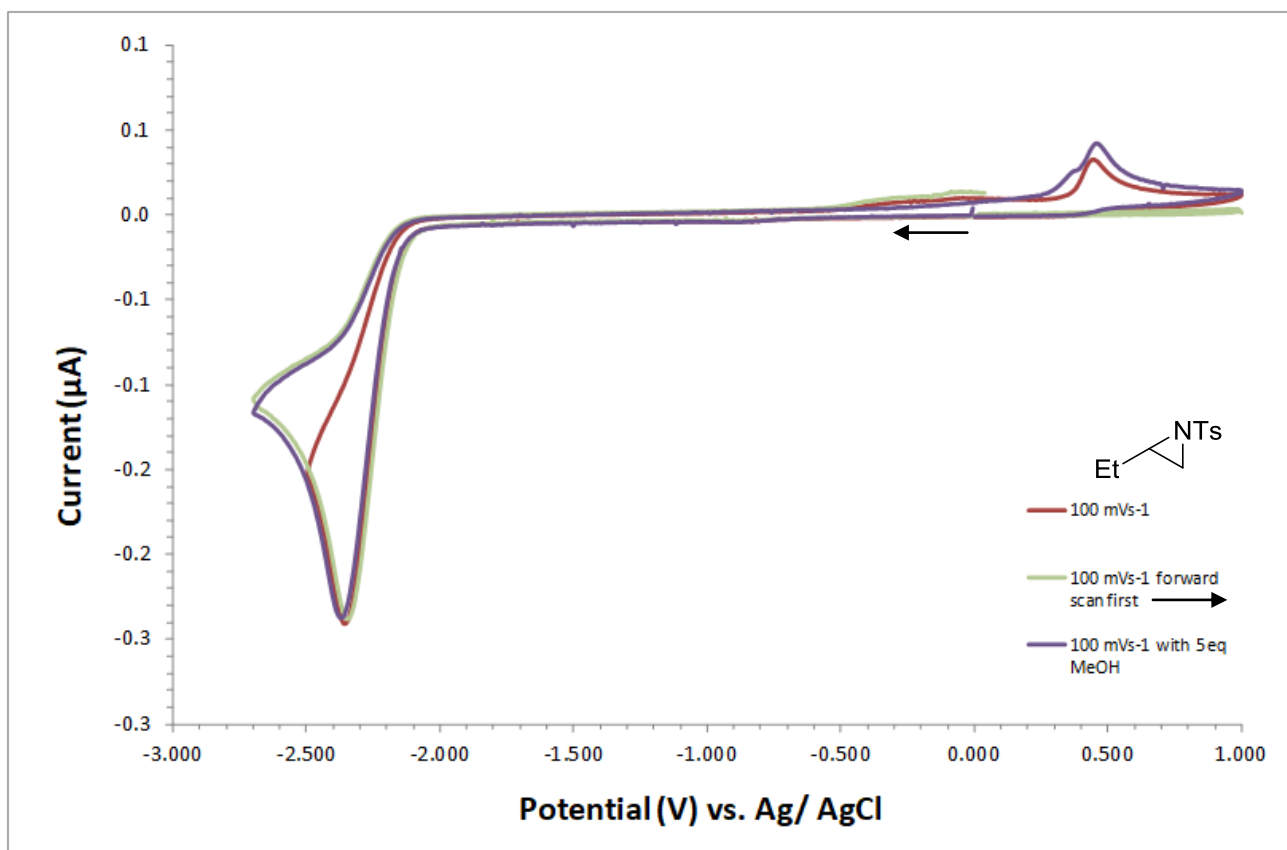


Figure S5: CV of **1ab** in MeCN. Backward and forward scans and addition of MeOH

The reduction profile of Ni(II) pre-catalysts (**L1NiCl₂** and **L5NiCl₂**) were also measured to investigate whether there was any correlation with the experimental results. The reduction of **L5NiCl₂** in CH₃CN shows 3 sequential reductions at -0.75, -1.1 and -1.8 V vs. Ag/ AgCl (Figure S6). The peak currents (E_p) and peak-peak separation (ΔE_p) were found to correlate linearly with the square root of the scan rate ($v^{1/2}$) and therefore are tentatively assigned as quasi-reversible freely diffusing reductions to Ni(I), Ni(0) and Ni(-I) respectively. These results also suggest that the formation of Ni(0) is possible with manganese as reductant (Mn/ Mn (II) = -1.4 V vs. Ag/ AgCl)^{xxxv} in agreement with the stoichiometric and catalytic experiments with (**L5**)₂Ni(0). The reduction of **L5NiCl₂** was also measured in DMA (Figure S7) to better represent the conditions under which the carboxylation of aziridines is performed. The reduction profiles observed are more complex in this solvent; the second reduction has very large ΔE_p which may be the result of interaction of DMA with the Ni-complex. The measured reductions (-0.75 V and -1.2 V vs. Ag/ AgCl), however, are very similar to that observed in CH₃CN.

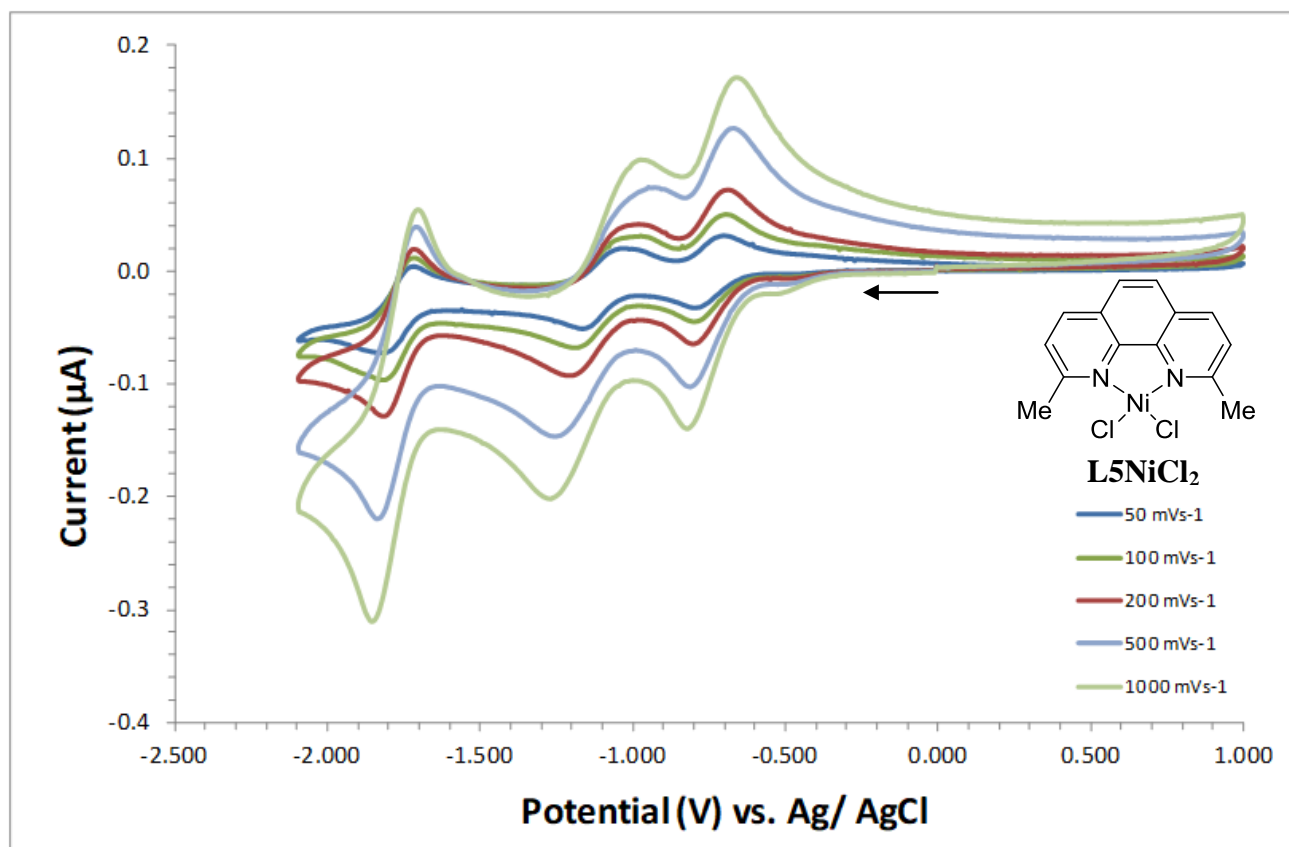


Figure S6: CV of **L5NiCl₂ in MeCN**

^{xxxv} A conversion factor of -0.2 V was used to convert the value from that vs. normal hydrogen electrode (NHE) to Ag/ AgCl reference electrode. See Bard, A. J.; Faulkner, L. R. *Electrochemical Methods :Fundamentals and Applications*; Wiley: New York, 1980.

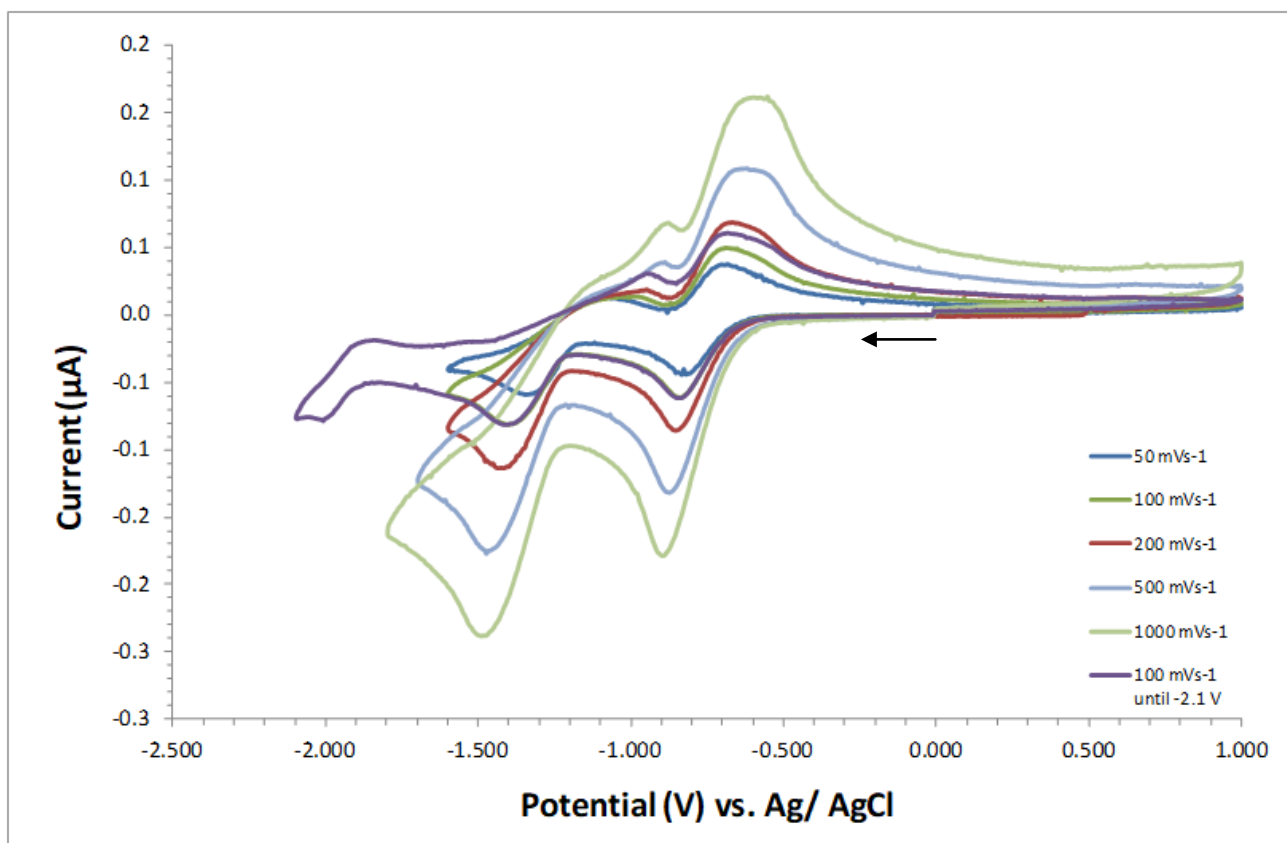


Figure S7: CV of $L5NiCl_2$ in DMA

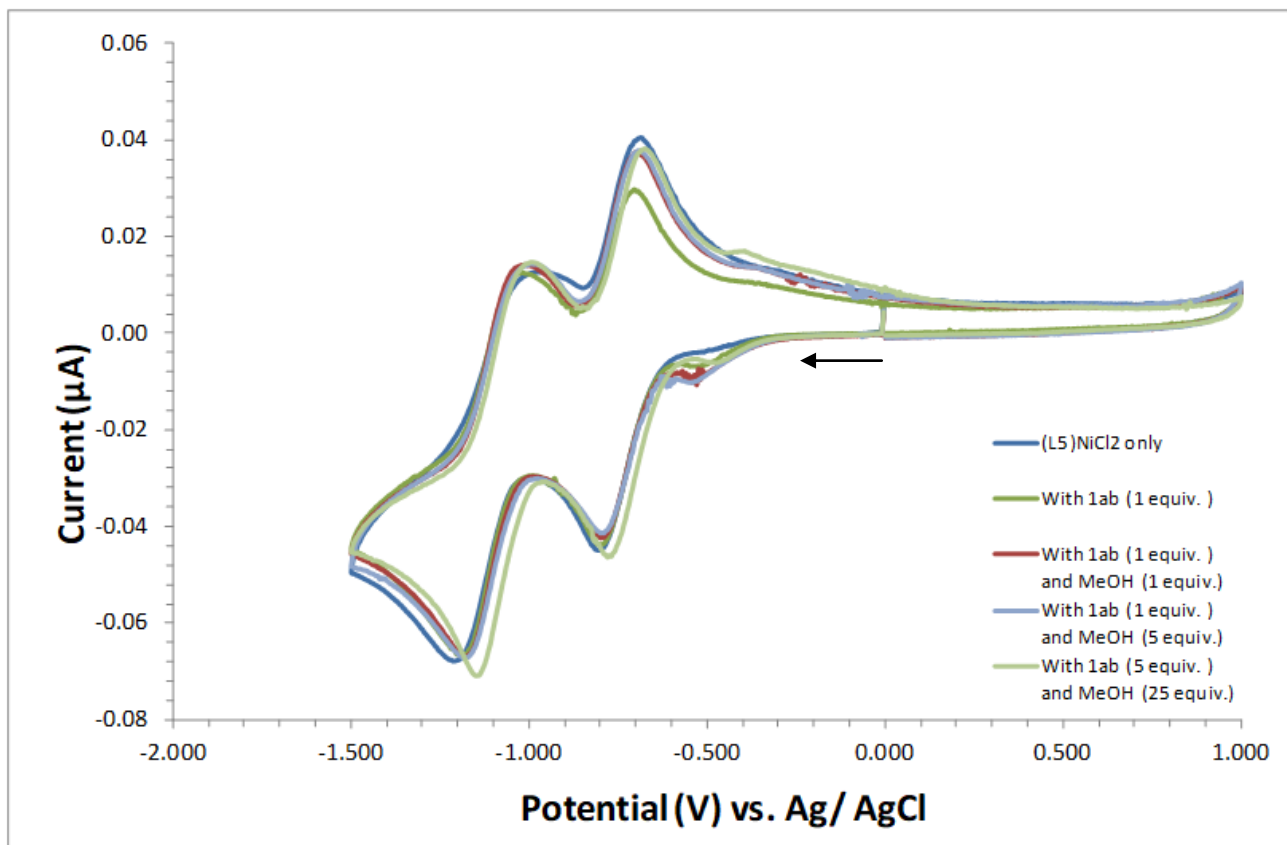


Figure S8: CV of $L5NiCl_2$ in MeCN with additions of **1ab** and MeOH

The cyclic voltammogram of **L1NiCl₂** was also measured and similarly shows a fairly complex reduction profile (Figure S9). In MeCN, 3 quasi-reversible reductions can be observed at -0.8, -1.2 and -1.9 V vs. Ag/ AgCl. Although slightly more difficult to reduce than **L5NiCl₂**, the first 2 reductions are within range of Mn and do not suggest at any difficulties in generating Ni(0). On the other hand, these investigations imply that more weakly reducing zinc (Zn/Zn (II) = -1.0 V vs. Ag/ AgCl)^{xxxv} would not be suitable and this is indeed observed experimentally.

After the lack of success in isolation of azanickelacyclobutanes (see §4.3.2) with hindered nitrogen ligands such as **L1** and **L5**, it was theorized that evidence may be gained by changes to the cyclic voltammogram of LNiCl₂ complexes upon the addition of aziridine and/or MeOH. However, absolutely no difference was observed (Figure S8 & Figure S10) even under conditions similar to that of the catalytic reaction (5 equiv. of **1ab** and 25 equiv. of MeOH respective to **L5NiCl₂**). On the other hand, it could be argued that this provides evidence for the oxidative addition of terminal aziridines into hindered Ni-complexes being very challenging.

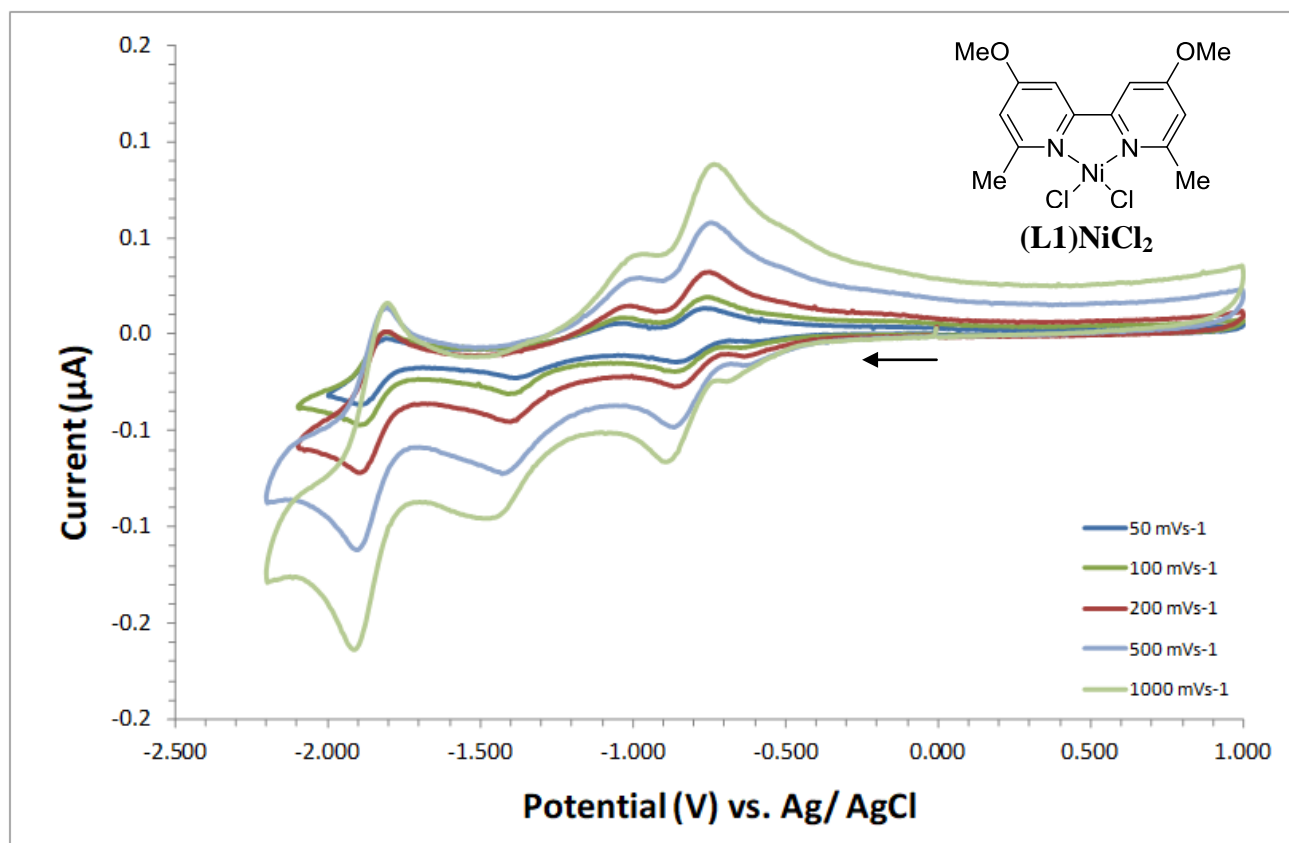


Figure S9: CV of **L1NiCl₂** in MeCN

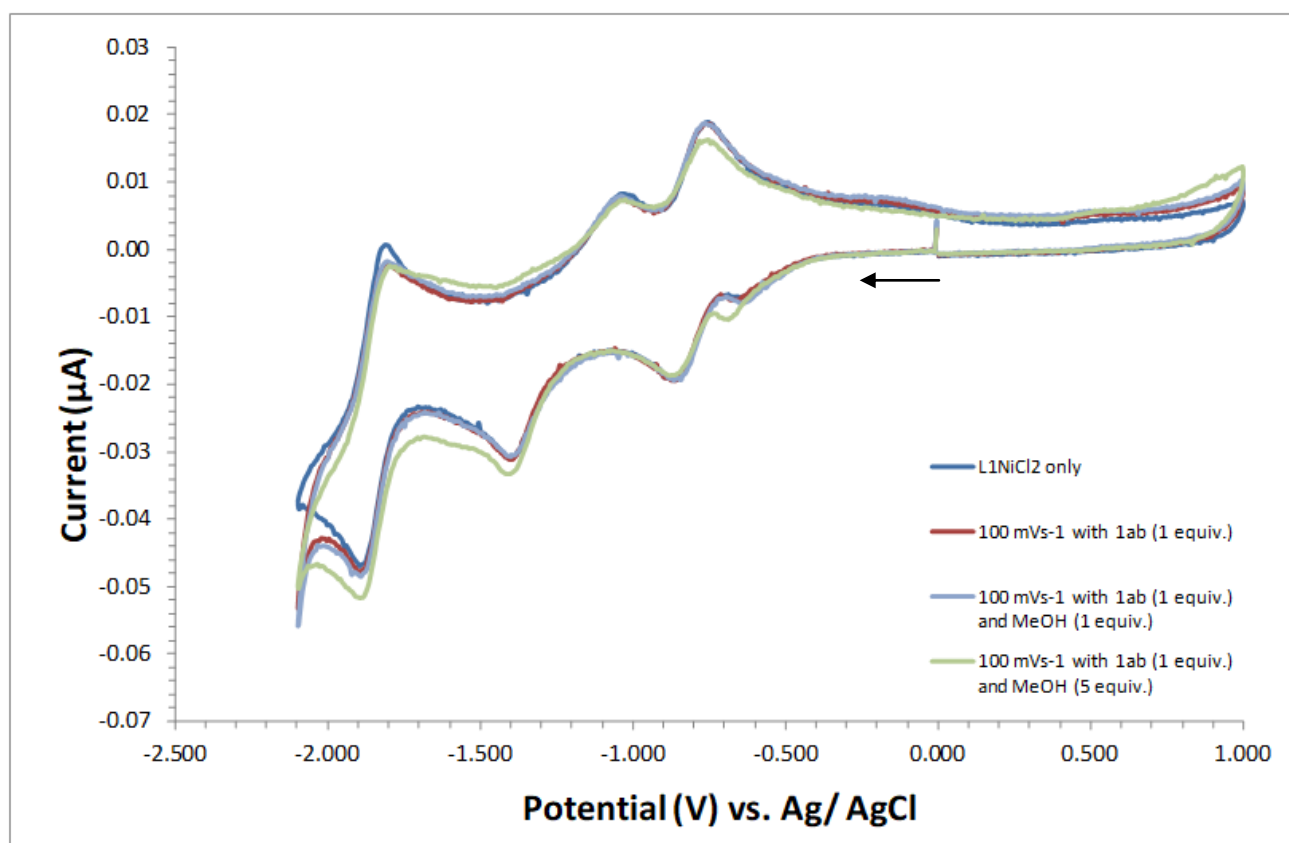


Figure S10: CV of **L1NiCl₂** in MeCN with additions of **1ab** and MeOH

4.3 Experiments with (L5)₂Ni(0)

4.3.1 Synthesis of (L5)₂Ni

Following a modified literature procedure:⁴ in the glovebox, Ni(COD)₂ (0.60 g, 2.2 mmol) and neocuproine (0.93 g, 4.5 mmol, 2.05 equiv.) were added to a 12 ml vial with a stirrer bar and charged with 6.0 mL of toluene. The reaction was left to stir for 16 h and the solvent was then removed to afford a brown solid. To the solid, 2.0 ml of toluene was added and stirred for 10 minutes followed by the addition of 5.0 ml of pentane. The solid was then filtered and washed with pentane (3 × 1 ml) to afford (L5)₂Ni as a dark brown solid (1.0 g, 99 % yield). ¹H NMR (500 MHz, C₆D₆) δ 9.00 (d, *J* = 7.3 Hz, 2H), 7.68 (d, *J* = 7.3 Hz, 2H), 7.32 (s, 2H), 2.24 (s, 6H). Spectroscopic data for this compound matches with that reported in the literature.^{49,50}

4.3.2 Stoichiometric Monitoring of Ni(0) Undergoing Oxidative Addition to Aziridine and MALDI-MS Identification of (L5)Ni(Aza-metallacycle)

In the glovebox, (L5)₂Ni (5.5 mg, 0.010 mmol) and **1ab** (6.7 mg, 0.030 mmol) were added to a 10 ml vial and dissolved in 1.0 ml THF-*d*₈. This solution was then added to a J-Young NMR tube and monitored by ¹H and paramagnetic ¹H NMR. After 7 h at 70 °C, a mixture of both diamagnetic (Figure S11) and paramagnetic species (Figure S12) had formed. Throughout the monitoring of this reaction, at no point were diamagnetic signals (δ = 12-0 ppm) corresponding to (L5)Ni^{II}(Aza-metallacycle) formed. However, analysis by MALDI-MS of the crude reaction mixture after 21.5 h (t₄) revealed the corresponding *m/z*-H signal of (L5)Ni^{II}(Aza-metallacycle) (Figure S13).⁵¹ These results suggest that if (L5)Ni^{II}(Aza-metallacycle) is formed in significant quantities, it may be as a paramagnetic species. Trace 1-butene was also detected after 7 h at 70 °C along with the formation of TsNH₂ with increasing amounts observed at 12.5 and 21.5 h.

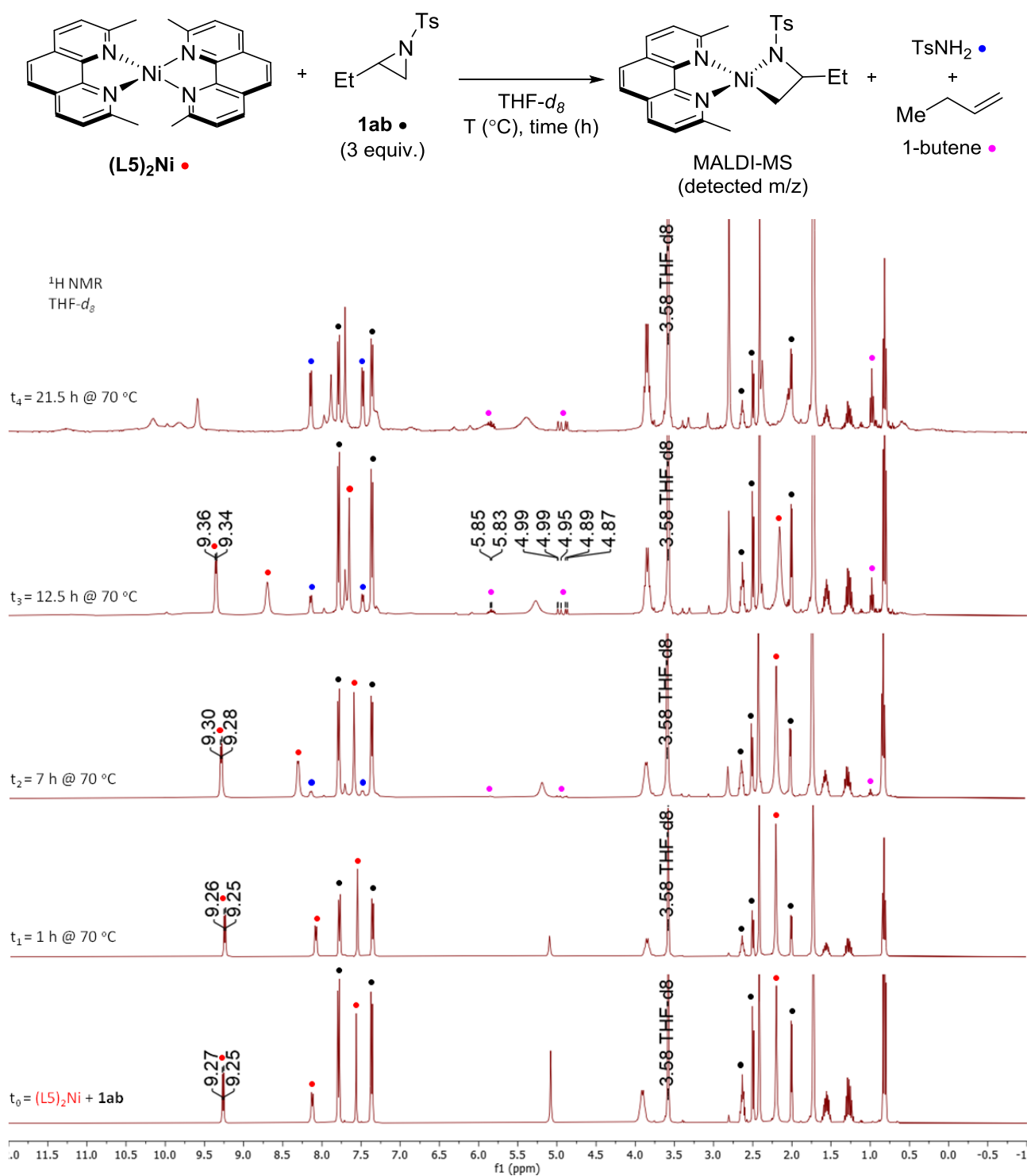


Figure S11: 1H NMR spectra from monitoring the reaction between $(L5)_2Ni$ (red) and **1ab** (black) in THF- d_8 forming a mixture of products.

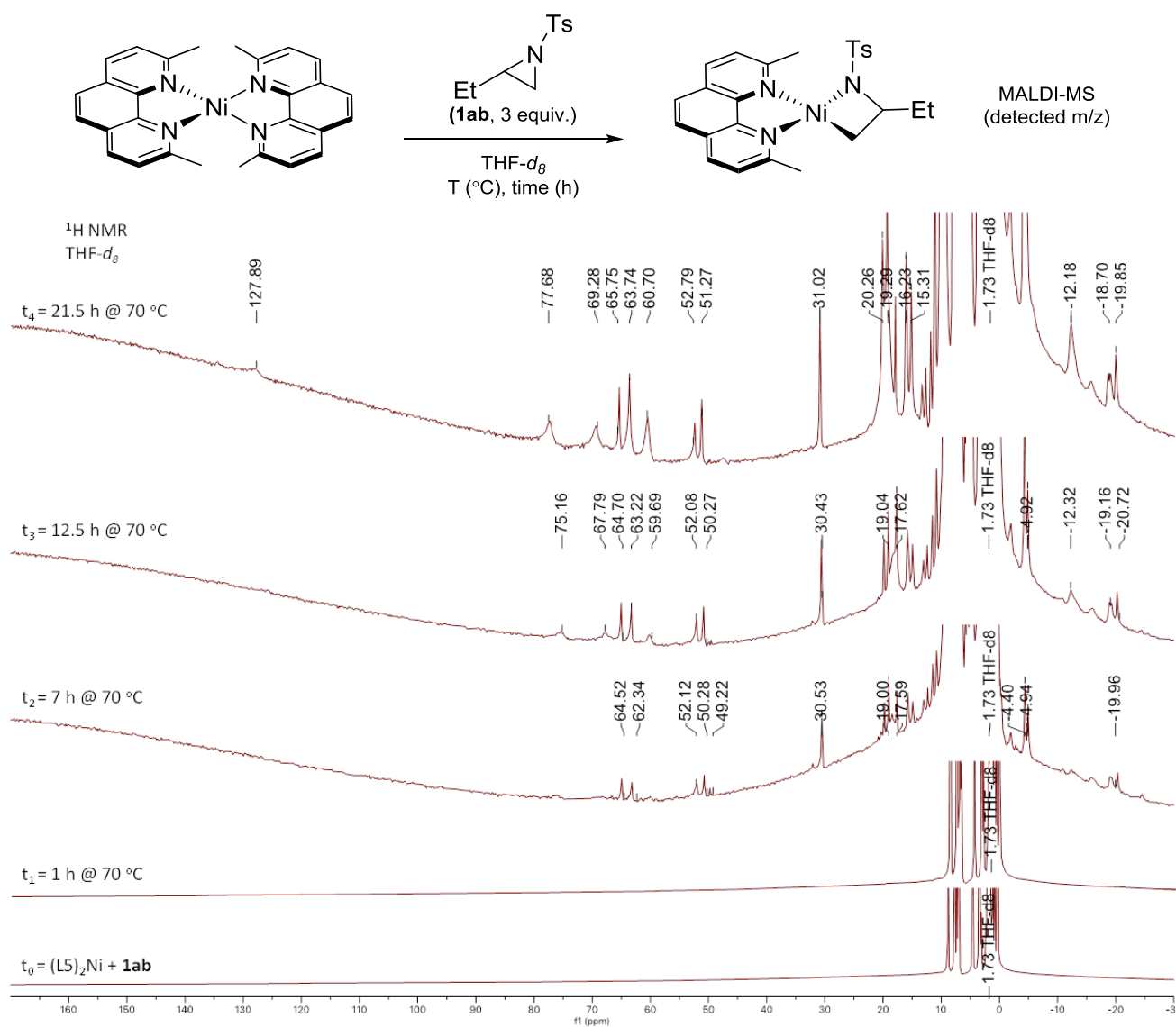


Figure S12: Paramagnetic 1H NMR spectra from monitoring the reaction between $(L5)_2Ni$ and **1ab** in THF- d_8 forming a mixture of products.

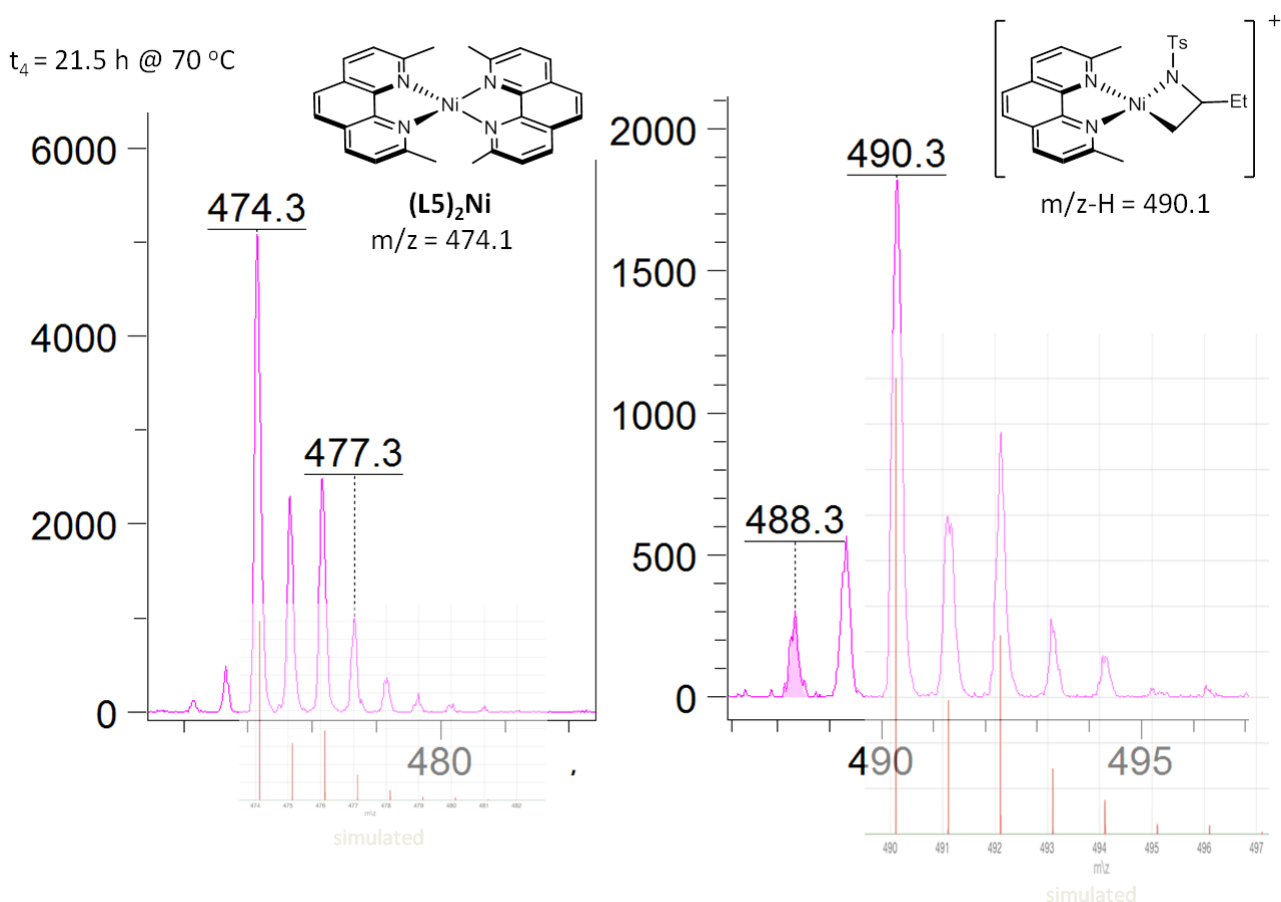


Figure S13: MALDI-MS of the crude reaction mixture after the final timepoint (t_4), identifying m/z -H signal of $(\text{L5})\text{Ni}^{\text{II}}(\text{Aza-metallacycle})$ - right

4.3.3 Stoichiometric Monitoring of $\text{Ni}(0)$ Undergoing Oxidative Addition to Aziridine with Clean Formation of Organic Products Originating from Deamination of the Aziridine

In the glovebox, $(\text{L5})_2\text{Ni}$ (4.2 mg, 0.010 mmol), **1ad** (5.7 mg, 0.030 mmol) and LiCl (2.3 mg, 0.050 mmol) were added to a 10 ml vial and dissolved in 1.0 ml $\text{THF-}d_8$. This solution was then added to a J-Young NMR tube and monitored by ^1H , paramagnetic ^1H and ^{19}F NMR. Again, after 3 h at 60°C , organic product 1-butene starts to be observed, followed by an increased amount after 18 h and full conversion of $(\text{L5})_2\text{Ni}$ (Figure S14). While monitoring this and similar reactions, at no point were we able to identify signals that could correspond to $(\text{L5})\text{Ni}^{\text{II}}(\text{Aza-metallacycle})$.

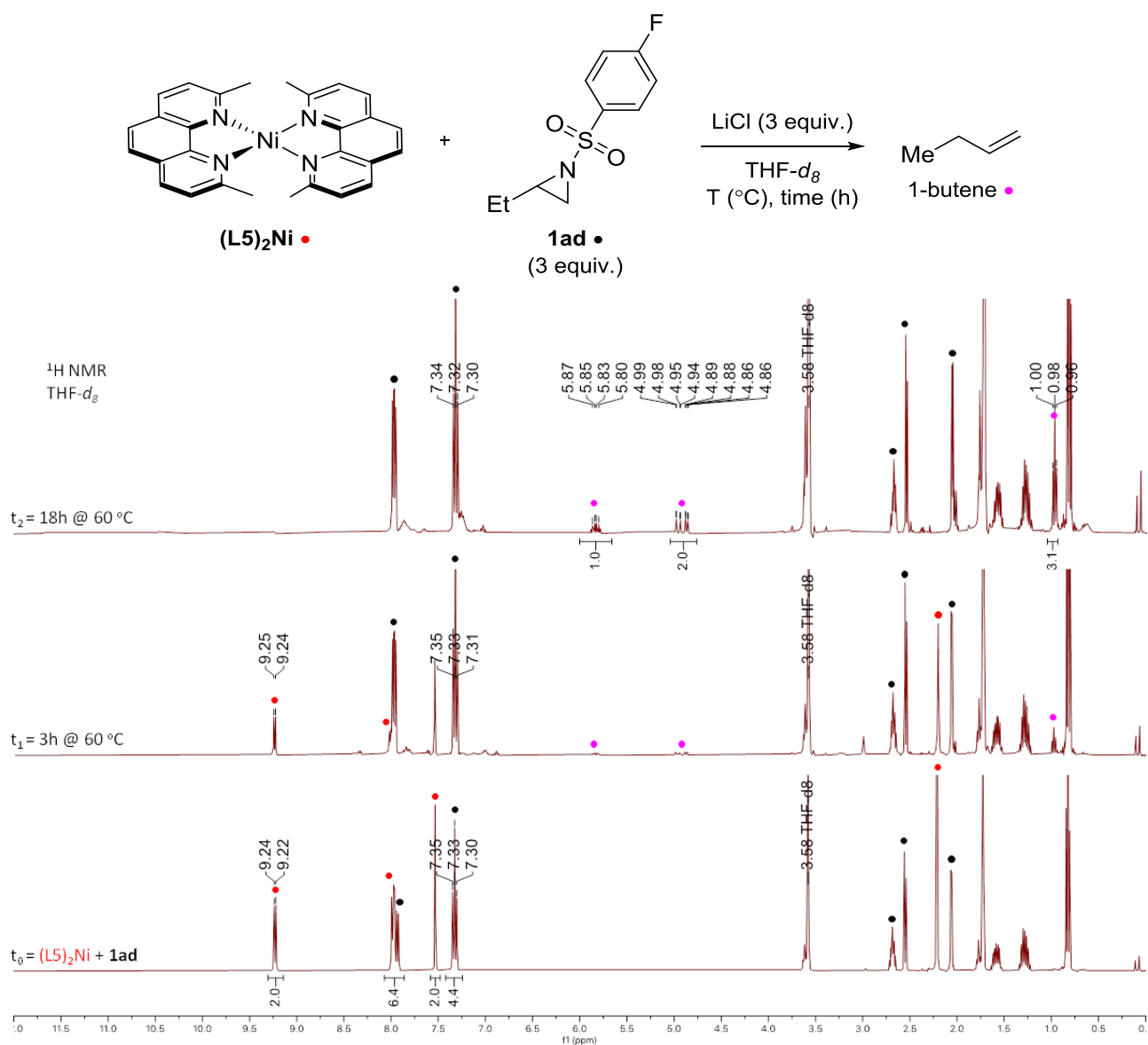
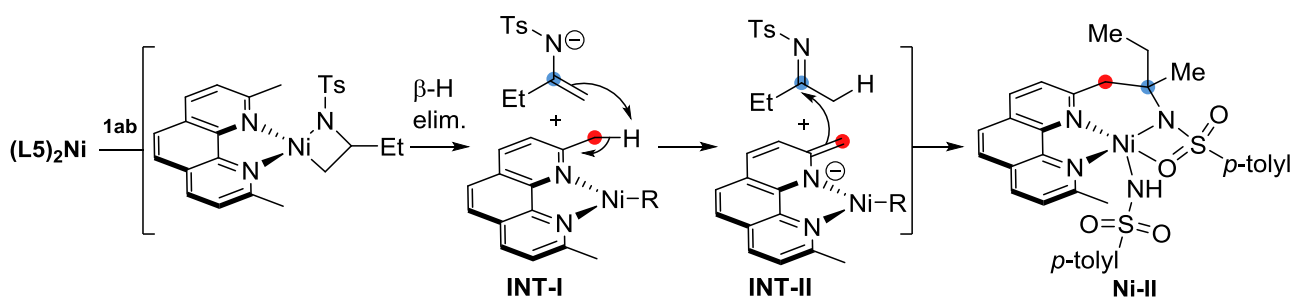


Figure S14: ^1H NMR spectra of monitoring the reaction between $(\text{L5})_2\text{Ni}$ (red) and 1a3 (black) with clean formation of 1-butene in $\text{THF-}d_8$.

4.3.4 Stoichiometric Monitoring of Ni(0) Undergoing Oxidative Addition to Aziridine and Single Crystal Identification of Complexes Originating from Ligand Activation

In the glovebox, (**L5**)₂Ni (6.9 mg, 0.010 mmol) and **1ab** (11 mg, 0.050 mmol) were added to a 10 ml vial and dissolved in 1 mL THF-*d*₈. This solution was then added to a J-Young NMR tube and monitored by ¹H and paramagnetic ¹H NMR. After 48 h at 50 °C a mixture of both diamagnetic (Figure S15) and paramagnetic species (Figure S16) had formed, with the identification of organic product 1-butene derived from deamination. Crystallization of the crude reaction mixture from THF/Pentane led to crystals of a nickel complex (**Ni-II**) that has undergone ligand activation shown below. The mechanism by which this complex is generated is very much uncertain, particularly as the formation of a quaternary carbon is required in the ligand activation. This suggests at the formation of an enamine intermediate via β-hydride elimination which acts as a base to deprotonate the *ortho*-Me of **L5** (Scheme S4). Finally, addition of **INT-II** to the imine forms the quaternary centre leading to **Ni-II**. Note: the nature of **INT-I** is uncertain so has been written with an ambiguous R group, but the presence of a ligated NHTs group in **Ni-II** suggests at the possibility of a nickel nitrene complex (e.g. **INT-III**, Scheme S5).



Scheme S4: Possible mechanism for the formation of **Ni-II**

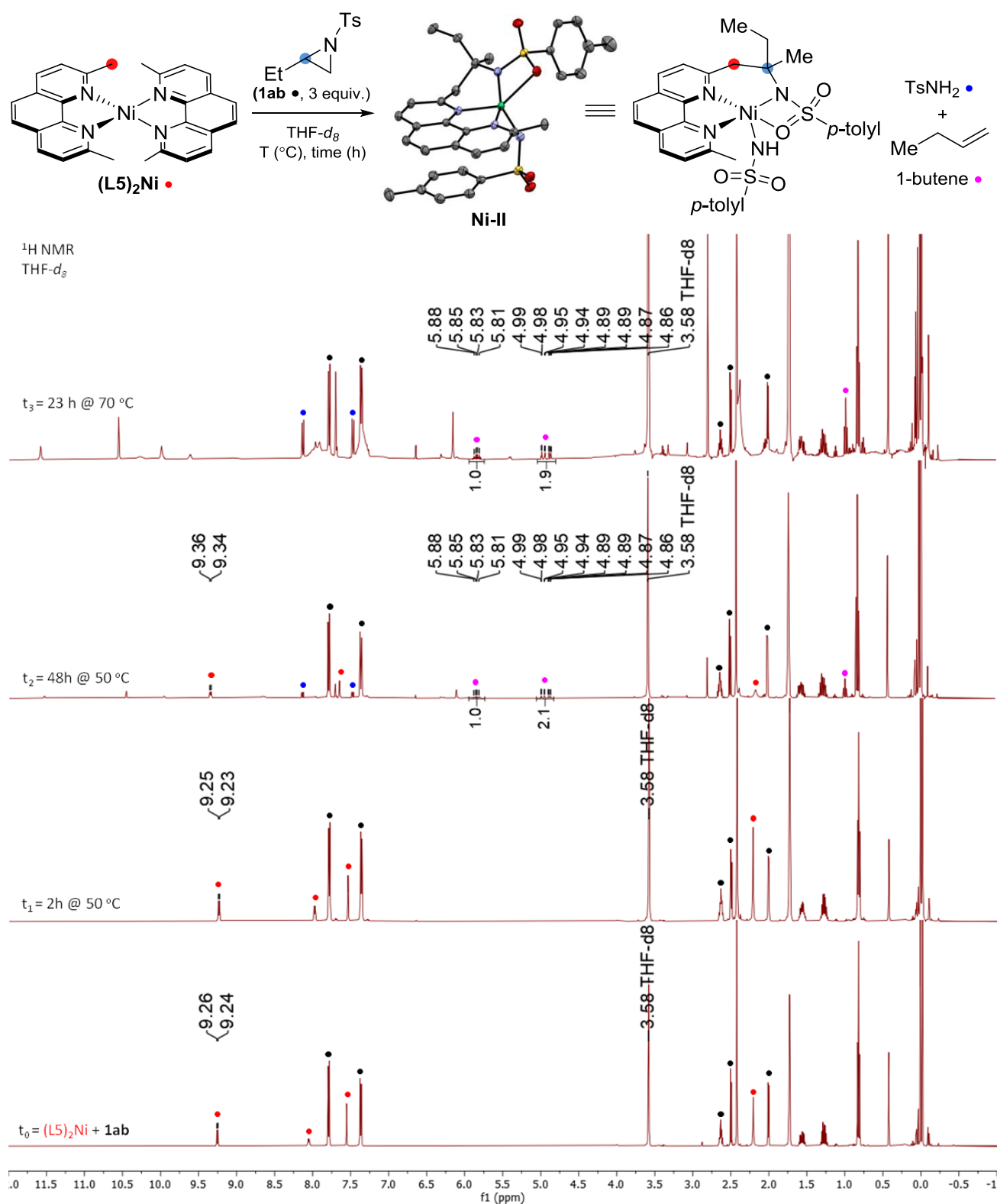


Figure S15: 1H NMR spectra of monitoring the reaction between $(L5)_2Ni$ (red) and **1ab** (black) in $THF-d_8$.

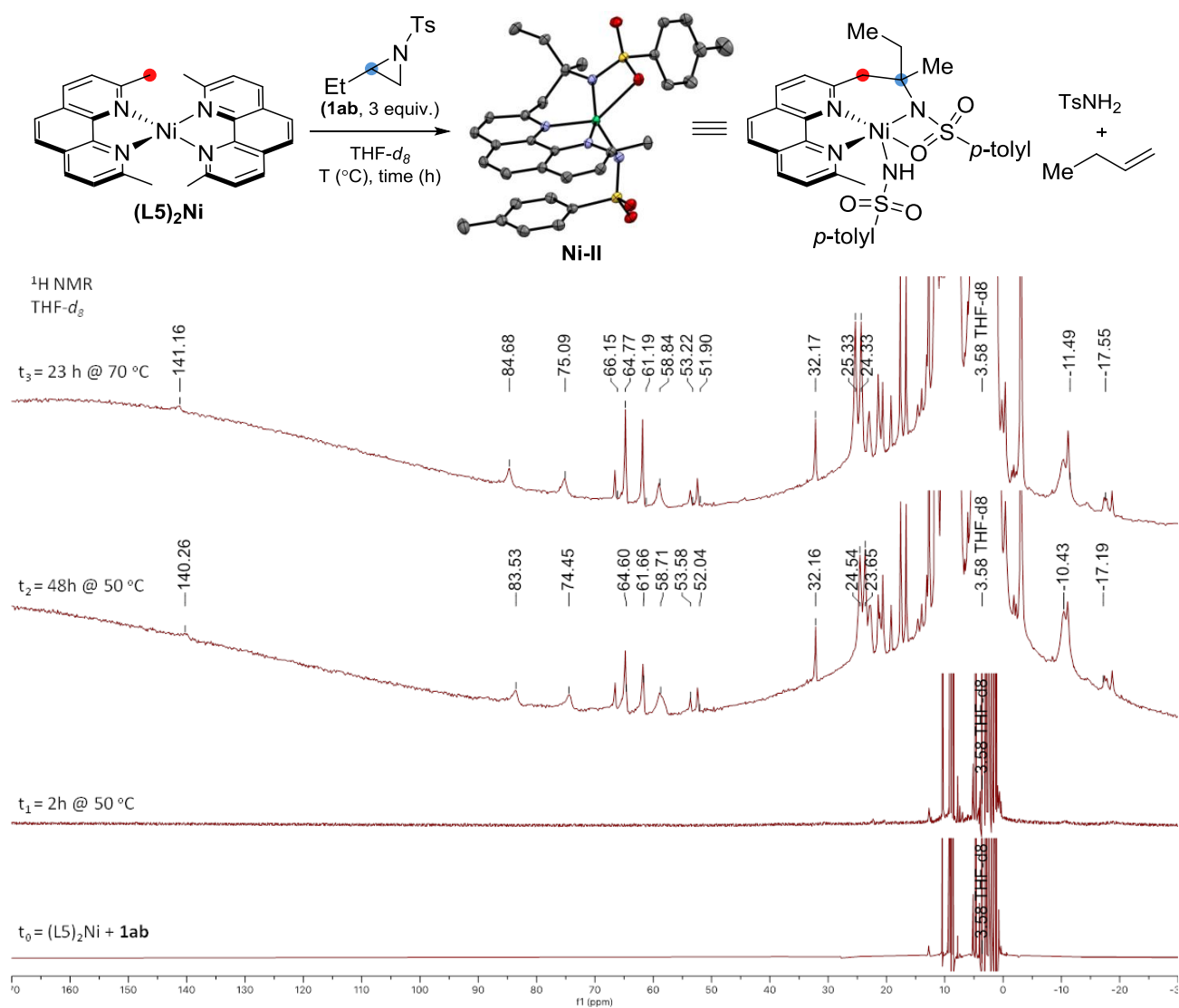


Figure S16: Paramagnetic 1H NMR spectra monitoring the reaction between $(L5)_2Ni$ and **1ab** in $THF-d_8$.

4.3.5 Isolating An Aziridine Derived Complex Post Oxidative Addition

In the glovebox, (**L5**)₂Ni (30.6 mg, 0.050 mmol) and **1ab** (37.0 mg, 0.16 mmol) were added to a 10 ml Schlenk flask and dissolved in 6.0 mL of THF with a stirrer bar. This stirred solution was then heated at 70 °C for 4 days where a gradual color change from brown to purple/ blue was observed. To this solution, Et₂O (8.0 ml) was added and a blue solid precipitated which was then filtered and washed with pentane (3 × 1 ml) to afford (L5)Ni(*N,N*-ditosyl-1-ethyl-diamine) **Ni-I** (12 mg, 29%) as a blue powder. ¹H NMR (400 MHz, Toluene-*d*₈) δ 78.15 (s, 1H), 62.11 (s, 1H), 59.25 (s, 1H), 22.90 (s, 7H), 15.00 (d, *J* = 325.3 Hz, 2H), -4.05 (s, 3H), -11.47 (s, 1H). ¹³C NMR is omitted due to paramagnetic line broadening. Although only a hypothesis, it is possible that a nickel nitrene species is generated from deamination of an azanickelacyclobutane intermediate, which then undergoes cycloaddition into another molecule of **1ab** to form diazanickelacyclopentene **Ni-I** (Scheme S5).

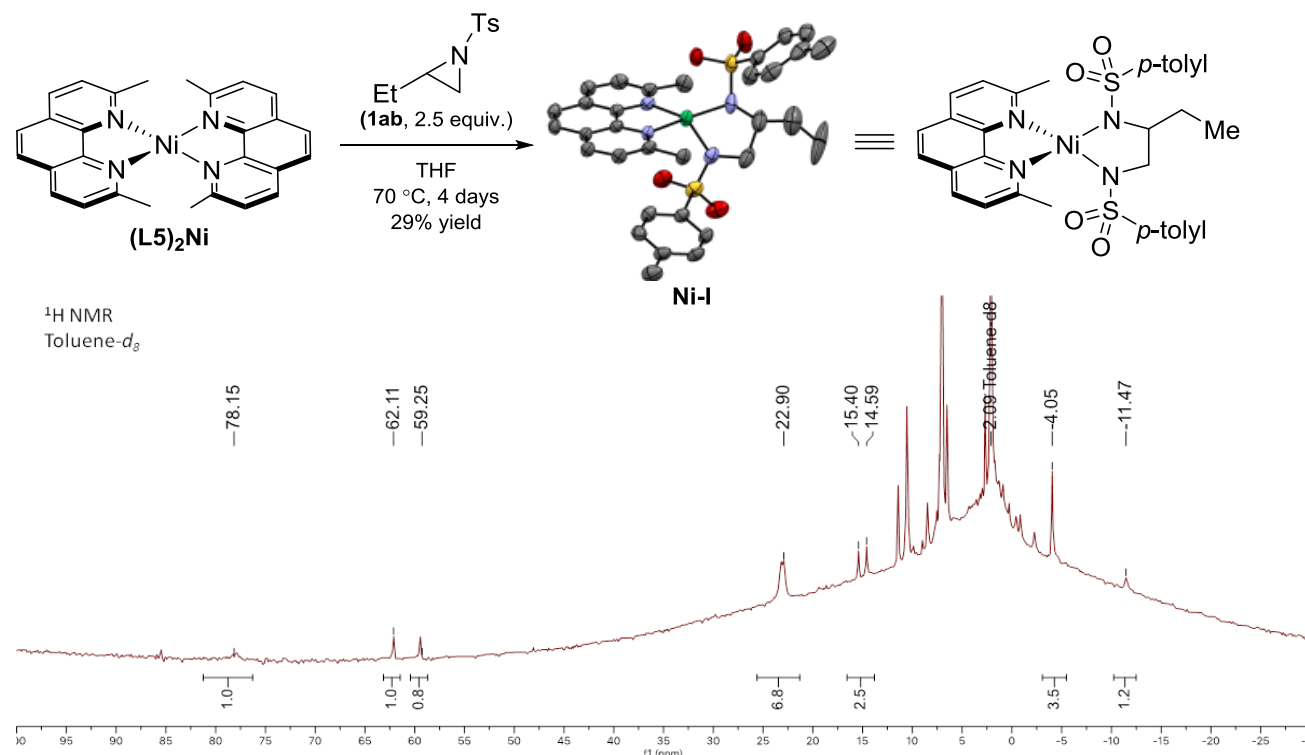
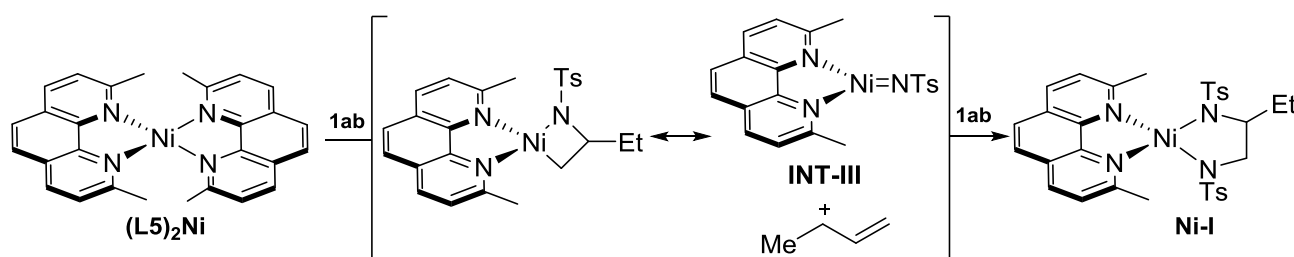


Figure S17: Paramagnetic ¹H NMR spectra of **Ni-I** in Toluene-*d*₈.



Scheme S5: Possible mechanism for the formation of **Ni-I**

4.3.6 Confirmation of (L5)₂Ni as a competent catalyst in the carboxylation of aziridines and quantification of by-products

The reaction was set up following **GP8** except that (L5)₂Ni (10 mol%) was used in place of NiCl₂glyme and **L1**. Also, special care was taken when removing the solvent after work-up with pressures no lower than 100 mbar employed to avoid removal of volatile compounds. Under these conditions, 47% of **21** was detected (Figure S18) which is in agreement to that with NiCl₂ (10 mol%) and **L5** (20 mol%).^{xxxvi} In addition, 25% of TsNH₂ was observed which is likely generated via 2 side reactions. Firstly, β-hydride elimination from a Ni(II)-**11** intermediate would give an iminium which after tautomerization and hydrolysis generates 4-phenylbutan-2-one and TsNH₂. Secondly, supported by isolation of Ni-NTs complexes in stoichiometric experiments (see §4.3.4 & 4.3.5), deamination of a Ni(II)-**11** intermediate generates 4-phenyl-1-butene and subsequently TsNH₂.

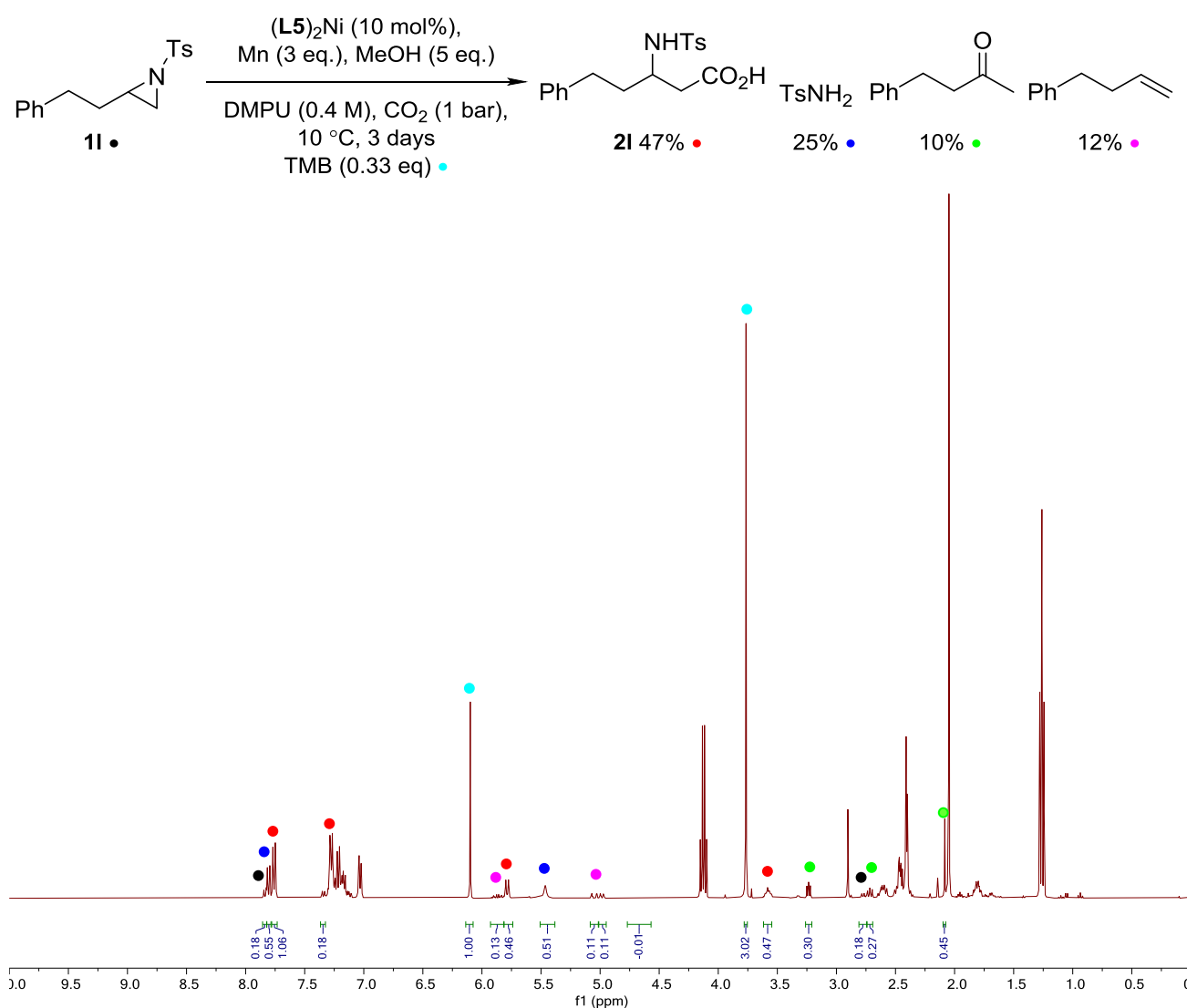
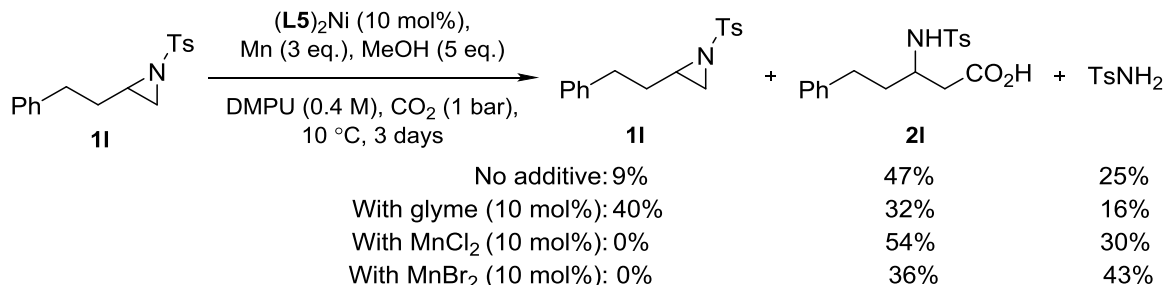


Figure S18: Crude ¹H NMR of the carboxylation of **11** employing catalytic (L5)₂Ni.

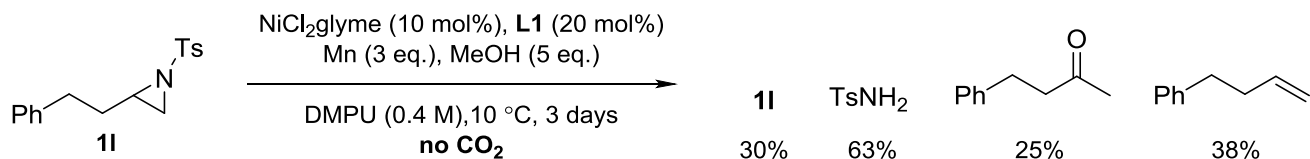
^{xxxvi} A 3 day reaction with **11** under the standard conditions but with **L5** (20 mol%) in place of **L1** gave 48% **21**, 28% TsNH₂, 10% 4-phenyl-1-butene and 7% 4-phenylbutan-2-one.

Addition of glyme (10 mol%) to the above reaction with **(L5)₂Ni** (10 mol%) resulted in a decrease in reaction rate and a lower yield of **2I** (Scheme S6) possibly a result of competitive ligation to Ni. In contrast, addition of MnCl₂ or MnBr₂ resulted in complete consumption of **1I** and a detrimental effect on the yield of **2I** in the case of MnBr₂, as observed in the previous poisoning experiments (§4.1).



Scheme S6

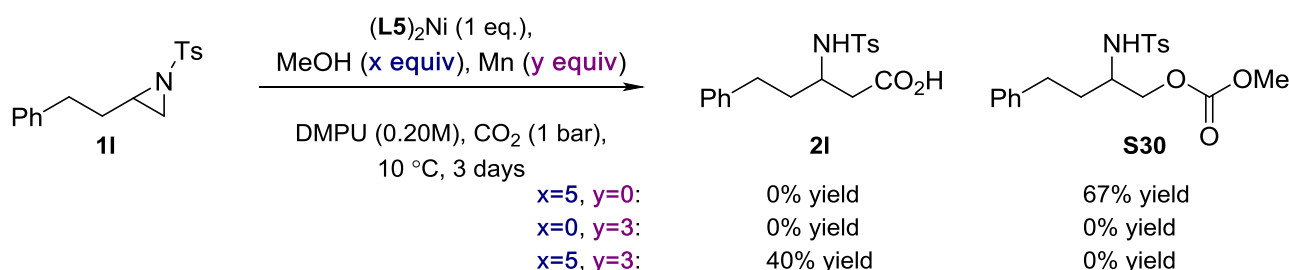
An experiment was also conducted under the standard reaction conditions (**GP8**) but without CO₂ atmosphere (Scheme S7). The aziridine **1I** was consumed with 4-phenylbutan-2-one (25%) and 4-phenyl-1-butene (38%) again observed. The quantification of these products agrees with the amount of TsNH₂ generated and provides further evidence for the 2 side reactions that compete with acid formation.



Scheme S7

4.3.7 Experiments with stoichiometric (L5)₂Ni and aziridine in the presence of Mn and/ or MeOH

Having established (L5)₂Ni as a competent catalyst in the aziridine carboxylation reaction, stoichiometric experiments were then carried out omitting certain components to probe the reaction mechanism. The reaction was set up following GP8 with the exception that (L5)₂Ni (1.0 equiv.) was used in place of NiCl₂glyme and L1 and the reaction was run under higher dilution (0.20 M) due to the poor solubility of (L5)₂Ni. The acid **2l** was only observed in the presence of both MeOH and Mn, suggesting at the intervention of Ni(I) species within the catalytic cycle (Scheme S8)⁵². Interestingly, when MeOH is present but not Mn, aliphatic carbamate **S30**^{xxxvii} is generated apparently via the oxazolidinone intermediate followed by ring opening with MeOH. Yet without Mn or MeOH, trace if any cyclic oxazolidinones are observed in the crude NMR. Note: it was also confirmed that **S30** is not a reaction intermediate as submitting it to the standard reaction conditions in place of the aziridine did not generate any **2l**.

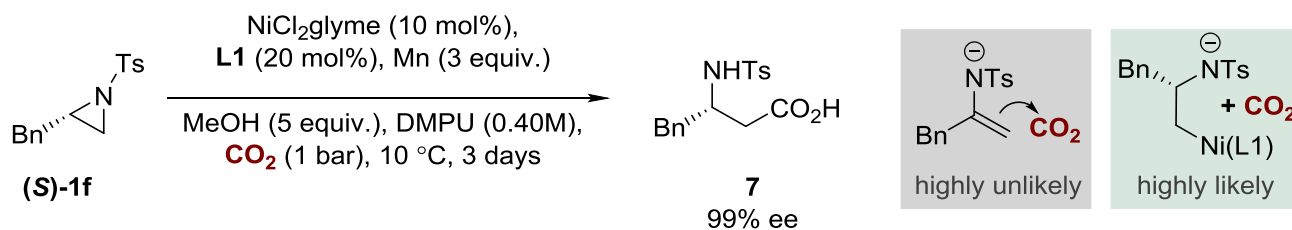


Scheme S8

4.3.8 Preservation of the chiral integrity with enantioenriched aziridines

It is plausible that the carboxylation event might occur via nucleophilic addition of in situ generated metalla-enamines onto CO₂. To probe this possibility, enantiopure (*S*)-**1f** was submitted to the reaction conditions and **7** was isolated with complete preservation of the chiral integrity at the *sp*³ C–N site (Scheme S9). Therefore, it is highly unlikely that the reaction proceeds via the formation of an enamine intermediate and instead we propose the insertion of CO₂ into the C–Ni bond, likely in oxidation state I (§4.3.7), to be the most plausible scenario.

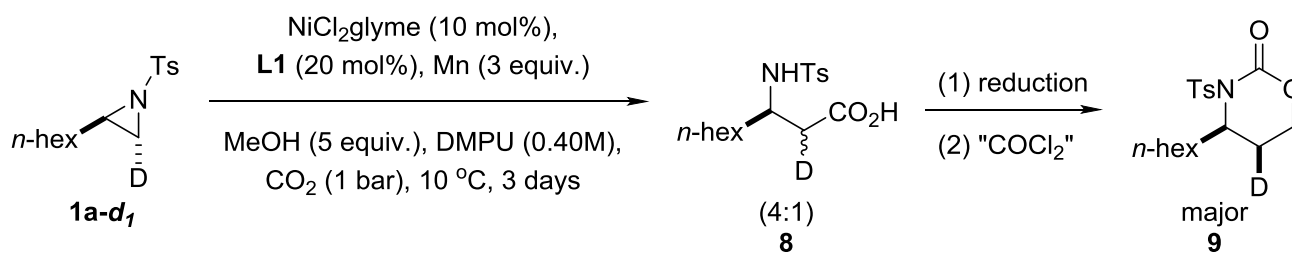
^{xxxvii} **Methyl (2-((4-methylphenyl)sulfonamido)-4-phenylbutyl) carbonate (S30)**. Colorless oil. ¹H NMR: ¹H NMR (400 MHz, CDCl₃) δ 7.79 – 7.71 (m, 2H), 7.32 – 7.25 (m, 2H), 7.25 – 7.21 (m, 2H), 7.19 – 7.13 (m, 1H), 7.07 – 7.00 (m, 2H), 5.18 (d, *J* = 8.6 Hz, 1H), 4.07 (dd, *J* = 11.1, 4.6 Hz, 1H), 3.99 (dd, *J* = 11.1, 4.5 Hz, 1H), 3.72 (s, 3H), 3.51 (tdt, *J* = 8.5, 5.6, 4.6 Hz, 1H), 2.60 (ddd, *J* = 13.9, 9.6, 6.2 Hz, 1H), 2.49 (ddd, *J* = 14.0, 9.7, 6.3 Hz, 1H), 2.42 (s, 3H), 1.89 – 1.67 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 155.5, 143.5, 140.8, 137.9, 129.8, 128.5, 128.4, 127.1, 126.13, 69.1, 55.0, 52.4, 33.7, 31.7, 21.6. IR (neat, cm⁻¹): 3281, 3027, 2956, 2862, 1748, 1599, 1495, 1442, 1385, 1326, 1261, 1154, 1090. HRMS calcd. for (C₁₉H₂₃NNaO₅S) [M+Na]⁺: 400.1189 found 400.1191.



Scheme S9

4.3.9 Stereochemical course of the reaction via isotope-labelling

Next, we turned our attention to studying the stereochemical course of the reaction (Scheme S10). We found that the carboxylation of *trans* **1a-d₁** followed by reduction and a cyclization event resulted in **9** with a 4:1 *cis/trans* ratio. It is possible that **8** could isomerise under the reaction conditions so it was resubmitted to the standard reaction conditions in place of the aziridine. However, no change in the *cis/trans* ratio was observed. While the identity of the major product might be explained via an S_N2 type insertion of Ni(0) into the aziridine backbone, the presence of the *trans* isomer, together with the lack of diastereocontrol in formation of **2z**, suggests that other conceivable pathways might come into play such as (1) single-electron transfer type oxidative addition or (2) homolytic cleavage/ recombination events of Ni-intermediates. The high reduction potential of **1ab** ($E_{\text{p}}^{\text{red}} = -2.4 \text{ V vs. Ag/AgCl in MeCN}$) argues against the former scenario, however (see §4.2).



Scheme S10

4.3.10 Influence of different reductants on product distribution

Finally, experiments were conducted with reductants other than Mn to investigate whether there was a correlation between the reductant strength and the experimental outcome. Intriguingly, the utilization of homogeneous reductants such as DMAP-OED or cobaltocene resulted in no conversion of **11** to **21** (Scheme S11). Instead, we again obtained substantial amounts of **S30** in the presence of MeOH. This was somewhat unexpected, particularly with Cp*₂Co which has a reduction potential very similar to that of Mn.⁵³ The formation of **S30** is sub-stoichiometric in DMAP-OED, suggesting its' role is to generate Ni(0) which then acts catalytically. This was confirmed by using (L5)₂Ni (10 mol%) without any reductant with **S30** (35%) observed in the presence of MeOH (Scheme S12). Again, without MeOH, only trace (<5%) of cyclic oxazolidinone product was observed. These results provide evidence for MeOH playing an important role in the oxidative addition of the aziridine to Ni(0), with neither β-amino acid nor carbamate observed without it. Conversely, the slow conversion of aziridine to **21** or **S30** suggests this is still challenging, which is supported by the inability to isolate (L)Ni-Azametallacycles and the electrochemical studies.

NiCl ₂ glyme (10 mol%), L1 (20 mol%), reductant (equiv.) MeOH (5 equiv.), DMPU (0.40M), CO ₂ (1 bar), 10 °C, 3 days				
11	→	11	21	S30
	Zn (3):	66%	5%	0%
	Cp₂Co (1.5):	65%	0%	10%
	DMAP-OED (1.5):	0%	0%	98%
	DMAP-OED (0.2):	43%	0%	56%
	Cp*₂Co (1.5):	trace	0%	80%
	Mn:	trace	75%	0%

Scheme S11

(L5)₂Ni (10 mol%), MeOH (x equiv.), DMPU (0.40M), CO ₂ (1 bar), 10 °C, 3 days				
11	→	11	21	S30
	x=5	56%	0%	35%
	x=0	75%	0%	-

Scheme S12

4.4 Mechanistic Hypothesis

Despite the complex mechanistic picture suggested by the evidence presented above, we have provided a mechanistic rationale for the Ni catalyzed reductive carboxylation of aziridines as well as other deleterious side reactions that occur. Firstly, the Ni(II) precatalyst is reduced by manganese (Mn) to Ni(0) complex **A** which can then undergo oxidative addition with the aziridine to give **B**. The stability of azanickelacyclobutane **B** is proposed to be low with hindered *ortho*-substituted bipyridine or phenanthroline ligands and could only be detected *in situ* by MALDI-MS (§4.3.2). Therefore, it is proposed that ring opened zwitterionic form **C** dominates and may be stabilized by complexation/ H-bonding with methanol. Note: evidence for complex **C** undergoing Ni–C bond homolysis/ radical rebound is provided by the *cis:trans* mixtures obtained with the deuterium labelled aziridine **1a-d_I** (§4.3.9) and with 2,3-substituted aziridine **1z**. Reduction of **C** to Ni(I) complex **D** is then required before CO₂ insertion which is supported by Mn, as well as MeOH, being necessary for acid formation in stoichiometric experiments with (L5)₂Ni (§4.3.7). Finally, reduction of complex **E** regenerates **A** and releases the manganese carboxylate.

Several deleterious side reactions can also take place. β-hydride elimination from **C** results in enamine **F** which undergoes tautomerization/ hydrolysis to generate the ketone and TsNH₂, both of which were detected in the crude reaction mixture (§4.3.6). Although nucleophilic addition of **F** to CO₂ would result in a β-amino acid, the preservation of the stereocenter of enantiopure aziridines disproves this as being a possible mechanism under the reaction conditions. On the other hand, **F** in combination with a Ni-nitrene species may be involved in the formation of Ni-II (§4.3.4), though whether this pathway occurs under the reaction conditions is unknown at present. Alternatively, deamination can occur to give the terminal olefin which was also detected in the crude reaction mixture (§4.3.6) and a Ni-nitrene species, which might also be an intermediate in the formation of Ni-I (§4.3.5). Finally, although not relevant under the reaction conditions, in the absence of Mn, nucleophilic addition of the *N*-tosylate to CO₂ followed by displacement of Ni generates cyclic carbamate **G**. In the presence of MeOH, this undergoes ring opening forming **H** which was isolated during stoichiometric experiments with (L5)₂Ni (§4.3.7) and when using reductants other than Mn (§4.3.10).

5 Crystallographic Data

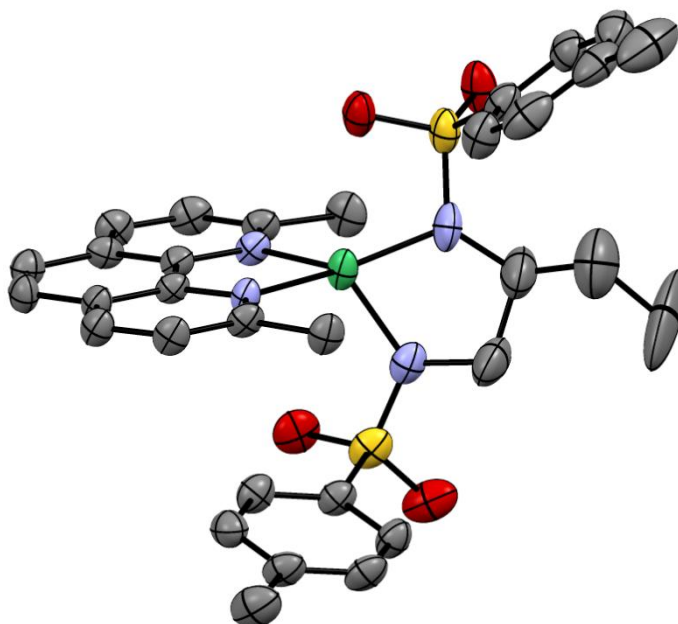


Figure S19: ORTEP Diagram **Ni-I**
CCSD deposition number 2049250

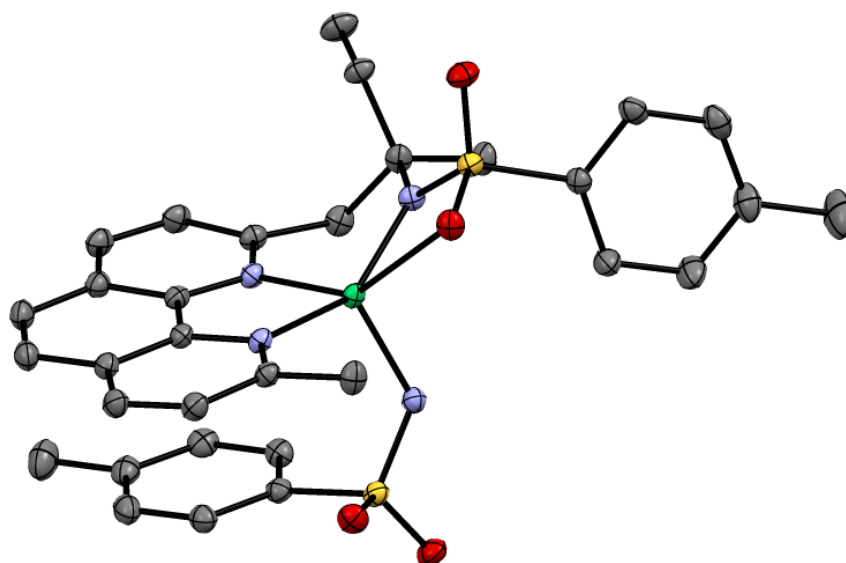


Figure S20: ORTEP Diagram of **Ni-II**
CCSD deposition number 2049249

Table 1. Crystal data and structure refinement for **Ni-I**

Identification code	mo_CSD0356A_0m	
Empirical formula	C ₃₆ H ₄₂ N ₄ Ni O ₅ S ₂	
Formula weight	733.56	
Temperature	100(2)K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 10.3280(8)Å	$\alpha = 107.062(2)^\circ$.
	b = 11.2508(8)Å	$\beta = 91.452(2)^\circ$.
	c = 15.8254(13)Å	$\gamma = 95.082(2)^\circ$.
Volume	1748.5(2) Å ³	
Z	2	
Density (calculated)	1.393 Mg/m ³	
Absorption coefficient	0.722 mm ⁻¹	
F(000)	772	
Crystal size	0.100 x 0.050 x 0.010 mm ³	
Theta range for data collection	1.979 to 24.782°.	
Index ranges	-12 ≤ h ≤ 8, -13 ≤ k ≤ 13, -18 ≤ l ≤ 18	
Reflections collected	17694	
Independent reflections	5870[R(int) = 0.0490]	
Completeness to theta = 24.782°	97.7%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.74 and 0.63	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	5870/ 0/ 438	
Goodness-of-fit on F ²	1.033	
Final R indices [I > 2σ(I)]	R1 = 0.0623, wR2 = 0.1579	
R indices (all data)	R1 = 0.1070, wR2 = 0.1824	
Largest diff. peak and hole	1.531 and -0.403 e.Å ⁻³	

Table 2. Bond lengths [\AA] and angles [$^\circ$] for **Ni-I**.

Bond lengths----

Ni1	N1	1.913(4)
Ni1	N2	1.968(4)
Ni1	N3	2.014(4)
Ni1	N4	2.019(4)
S1	O1	1.436(4)
S1	O2	1.451(4)
S1	N1	1.573(5)
S1	C5	1.769(5)
S2	O3	1.429(4)
S2	O4	1.447(4)
S2	N2	1.572(5)
S2	C12	1.784(5)
N1	C1	1.495(7)
N2	C2	1.459(7)
N3	C19	1.336(5)
N3	C23	1.367(6)
N4	C30	1.335(6)
N4	C27	1.351(6)
C1	C3	1.488(9)
C1	C2	1.517(9)
C3	C4	1.551(11)
C5	C6	1.366(7)
C5	C10	1.398(7)
C6	C7	1.396(8)
C7	C8	1.366(9)
C8	C9	1.392(9)
C8	C11	1.519(8)
C9	C10	1.386(8)
C12	C17	1.384(7)
C12	C13	1.398(7)
C13	C14	1.389(7)
C14	C15	1.392(8)
C15	C16	1.391(7)
C15	C18	1.502(7)
C16	C17	1.389(7)

C19	C20	1.400(7)
C19	C31	1.499(6)
C20	C21	1.376(7)
C21	C22	1.412(6)
C22	C23	1.392(6)
C22	C24	1.431(6)
C23	C27	1.438(6)
C24	C25	1.353(7)
C25	C26	1.437(7)
C26	C27	1.397(6)
C26	C28	1.401(6)
C28	C29	1.364(7)
C29	C30	1.406(7)
C30	C32	1.504(7)
O1S	C4S	1.383(10)
O1S	C1S	1.451(9)
C1S	C2S	1.456(12)
C2S	C3S	1.478(14)
C3S	C4S	1.409(13)

Angles-----

N1	Ni1	N2	83.04(19)
N1	Ni1	N3	128.73(17)
N2	Ni1	N3	116.21(17)
N1	Ni1	N4	139.71(18)
N2	Ni1	N4	108.33(16)
N3	Ni1	N4	81.81(15)
O1	S1	O2	116.4(2)
O1	S1	N1	114.8(2)
O2	S1	N1	103.5(2)
O1	S1	C5	106.6(2)
O2	S1	C5	107.6(2)
N1	S1	C5	107.5(2)
O3	S2	O4	117.4(2)
O3	S2	N2	112.5(2)
O4	S2	N2	107.5(2)
O3	S2	C12	106.5(2)
O4	S2	C12	104.8(2)

N2	S2	C12	107.5(2)
C1	N1	S1	123.2(4)
C1	N1	Ni1	114.5(4)
S1	N1	Ni1	110.6(2)
C2	N2	S2	118.1(4)
C2	N2	Ni1	112.4(4)
S2	N2	Ni1	123.9(3)
C19	N3	C23	118.5(4)
C19	N3	Ni1	128.6(3)
C23	N3	Ni1	112.9(3)
C30	N4	C27	119.2(4)
C30	N4	Ni1	128.0(3)
C27	N4	Ni1	112.8(3)
C3	C1	N1	114.8(6)
C3	C1	C2	111.1(6)
N1	C1	C2	105.1(5)
N2	C2	C1	107.2(5)
C1	C3	C4	111.4(7)
C6	C5	C10	120.4(5)
C6	C5	S1	120.7(4)
C10	C5	S1	118.8(4)
C5	C6	C7	119.3(5)
C8	C7	C6	121.4(6)
C7	C8	C9	119.1(5)
C7	C8	C11	121.6(7)
C9	C8	C11	119.3(6)
C10	C9	C8	120.3(6)
C9	C10	C5	119.4(6)
C17	C12	C13	119.8(5)
C17	C12	S2	119.8(4)
C13	C12	S2	120.3(4)
C14	C13	C12	118.8(5)
C13	C14	C15	122.1(5)
C16	C15	C14	118.1(5)
C16	C15	C18	120.7(5)
C14	C15	C18	121.2(5)
C17	C16	C15	120.7(5)
C12	C17	C16	120.6(5)

N3	C19	C20	121.0(4)
N3	C19	C31	118.0(4)
C20	C19	C31	120.9(4)
C21	C20	C19	120.8(4)
C20	C21	C22	119.1(5)
C23	C22	C21	116.8(4)
C23	C22	C24	118.9(4)
C21	C22	C24	124.3(4)
N3	C23	C22	123.8(4)
N3	C23	C27	115.7(4)
C22	C23	C27	120.5(4)
C25	C24	C22	121.2(5)
C24	C25	C26	120.8(4)
C27	C26	C28	116.2(5)
C27	C26	C25	119.3(4)
C28	C26	C25	124.4(4)
N4	C27	C26	123.8(4)
N4	C27	C23	116.8(4)
C26	C27	C23	119.4(4)
C29	C28	C26	119.9(5)
C28	C29	C30	120.6(4)
N4	C30	C29	120.1(5)
N4	C30	C32	117.7(4)
C29	C30	C32	122.2(4)
C4S	O1S	C1S	103.6(7)
O1S	C1S	C2S	104.9(7)
C1S	C2S	C3S	104.8(8)
C4S	C3S	C2S	104.5(8)
O1S	C4S	C3S	105.6(8)

Table 3. Torsion angles [°] for **Ni-I**.

O1	S1	N1	C1	38.8(5)
O2	S1	N1	C1	166.7(4)
C5	S1	N1	C1	-79.6(5)
O1	S1	N1	Ni1	-101.9(3)
O2	S1	N1	Ni1	25.9(3)
C5	S1	N1	Ni1	139.6(2)
O3	S2	N2	C2	-37.2(5)
O4	S2	N2	C2	-168.0(4)
C12	S2	N2	C2	79.6(5)
O3	S2	N2	Ni1	171.1(2)
O4	S2	N2	Ni1	40.4(3)
C12	S2	N2	Ni1	-72.0(3)
S1	N1	C1	C3	63.4(8)
Ni1	N1	C1	C3	-157.1(6)
S1	N1	C1	C2	-174.1(4)
Ni1	N1	C1	C2	-34.7(6)
S2	N2	C2	C1	168.1(4)
Ni1	N2	C2	C1	-37.1(6)
C3	C1	C2	N2	169.1(6)
N1	C1	C2	N2	44.4(7)
N1	C1	C3	C4	173.8(8)
C2	C1	C3	C4	54.7(10)
O1	S1	C5	C6	-1.9(5)
O2	S1	C5	C6	-127.4(5)
N1	S1	C5	C6	121.7(5)
O1	S1	C5	C10	179.8(4)
O2	S1	C5	C10	54.3(5)
N1	S1	C5	C10	-56.6(5)
C10	C5	C6	C7	1.0(8)
S1	C5	C6	C7	-177.2(4)
C5	C6	C7	C8	-0.3(9)
C6	C7	C8	C9	-0.9(9)
C6	C7	C8	C11	178.9(6)
C7	C8	C9	C10	1.3(9)
C11	C8	C9	C10	-178.5(5)
C8	C9	C10	C5	-0.5(9)

C6	C5	C10	C9	-0.6(8)
S1	C5	C10	C9	177.6(4)
O3	S2	C12	C17	-141.8(4)
O4	S2	C12	C17	-16.7(5)
N2	S2	C12	C17	97.5(4)
O3	S2	C12	C13	41.0(5)
O4	S2	C12	C13	166.1(4)
N2	S2	C12	C13	-79.7(5)
C17	C12	C13	C14	-0.7(8)
S2	C12	C13	C14	176.5(4)
C12	C13	C14	C15	0.9(8)
C13	C14	C15	C16	-0.7(8)
C13	C14	C15	C18	-179.5(5)
C14	C15	C16	C17	0.3(8)
C18	C15	C16	C17	179.1(5)
C13	C12	C17	C16	0.4(8)
S2	C12	C17	C16	-176.8(4)
C15	C16	C17	C12	-0.2(8)
C23	N3	C19	C20	-0.5(7)
Ni1	N3	C19	C20	179.3(4)
C23	N3	C19	C31	176.6(4)
Ni1	N3	C19	C31	-3.6(7)
N3	C19	C20	C21	0.4(8)
C31	C19	C20	C21	-176.6(5)
C19	C20	C21	C22	0.6(8)
C20	C21	C22	C23	-1.4(7)
C20	C21	C22	C24	179.3(5)
C19	N3	C23	C22	-0.3(7)
Ni1	N3	C23	C22	179.8(4)
C19	N3	C23	C27	180.0(4)
Ni1	N3	C23	C27	0.2(5)
C21	C22	C23	N3	1.3(7)
C24	C22	C23	N3	-179.3(5)
C21	C22	C23	C27	-179.1(4)
C24	C22	C23	C27	0.3(7)
C23	C22	C24	C25	-0.2(8)
C21	C22	C24	C25	179.1(5)
C22	C24	C25	C26	0.0(8)

C24	C25	C26	C27	0.1(7)
C24	C25	C26	C28	178.7(5)
C30	N4	C27	C26	-1.7(7)
Ni1	N4	C27	C26	-179.4(4)
C30	N4	C27	C23	178.3(4)
Ni1	N4	C27	C23	0.6(5)
C28	C26	C27	N4	1.3(7)
C25	C26	C27	N4	179.9(5)
C28	C26	C27	C23	-178.7(4)
C25	C26	C27	C23	-0.1(7)
N3	C23	C27	N4	-0.5(6)
C22	C23	C27	N4	179.9(4)
N3	C23	C27	C26	179.5(4)
C22	C23	C27	C26	-0.1(7)
C27	C26	C28	C29	-0.2(7)
C25	C26	C28	C29	-178.8(5)
C26	C28	C29	C30	-0.3(8)
C27	N4	C30	C29	1.2(7)
Ni1	N4	C30	C29	178.5(4)
C27	N4	C30	C32	-177.9(4)
Ni1	N4	C30	C32	-0.6(7)
C28	C29	C30	N4	-0.2(8)
C28	C29	C30	C32	178.8(5)
C4S	O1S	C1S	C2S	-32.2(9)
O1S	C1S	C2S	C3S	11.2(11)
C1S	C2S	C3S	C4S	13.3(12)
C1S	O1S	C4S	C3S	41.8(10)
C2S	C3S	C4S	O1S	-34.4(12)

Symmetry operations

-
- 1 'x, y, z'
2 '-x, -y, -z'

Table 1. Crystal data and structure refinement for **Ni-II**.

Identification code	CSD-3-22
Empirical formula	C32 H34 N4 Ni O4 S2
Formula weight	661.46

Temperature	100(2)K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 10.03268(11)Å	$\alpha = 89.2731(7)^\circ$.
	b = 11.52248(10)Å	$\beta = 71.8705(8)^\circ$.
	c = 14.40581(12)Å	$\gamma = 70.1261(9)^\circ$.
Volume	1480.30(3) Å ³	
Z	2	
Density (calculated)	1.484 Mg/m ³	
Absorption coefficient	0.842 mm ⁻¹	
F(000)	692	
Crystal size	0.300 x 0.200 x 0.050 mm ³	
Theta range for data collection	2.284 to 32.185°.	
Index ranges	-14<=h<=14,-17<=k<=17,-21<=l<=21	
Reflections collected	113880	
Independent reflections	10027[R(int) = 0.0364]	
Completeness to theta =32.185°	96.0%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00 and 0.60	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	10027/ 0/ 418	
Goodness-of-fit on F ²	1.048	
Final R indices [I>2sigma(I)]	R1 = 0.0301, wR2 = 0.0799	
R indices (all data)	R1 = 0.0329, wR2 = 0.0810	
Largest diff. peak and hole	0.545 and -0.567 e.Å ⁻³	

Table 2. Bond lengths [\AA] and angles [$^\circ$] for **Ni-II**.

Bond lengths----

C1	N2	1.3354(14)
C1	C2	1.4095(16)
C1	C13	1.4916(16)
N1	C12	1.3331(14)
N1	C9	1.3514(14)
N1	Ni1	1.9960(9)
S1	O2	1.4477(9)
S1	O1	1.4755(8)
S1	N3	1.5658(10)
S1	C20	1.7686(12)
S1	Ni1	2.7652(3)
O1	Ni1	2.3305(9)
Ni1	N4	1.9734(9)
Ni1	N3	1.9786(9)
Ni1	N2	2.0622(9)
C2	C3	1.3739(17)
C2	H2	0.9500
S2	O3	1.4445(9)
S2	O4	1.4550(9)
S2	N4	1.5814(10)
S2	C27	1.7809(12)
N2	C5	1.3650(14)
N3	C15	1.4825(14)
C3	C4	1.4113(16)
C3	H3	0.9500
C4	C5	1.4024(15)
C4	C6	1.4373(16)
N4	H4N	0.9062
C5	C9	1.4335(15)
C6	C7	1.3601(18)
C6	H6	0.9500
C7	C8	1.4333(17)
C7	H7	0.9500
C8	C9	1.4022(15)
C8	C10	1.4113(16)

C10	C11	1.3763(18)
C10	H10	0.9500
C11	C12	1.4082(16)
C11	H11	0.9500
C12	C14	1.5033(16)
C13	H13A	0.9800
C13	H13B	0.9800
C13	H13C	0.9800
C13	H13D	0.9800
C13	H13E	0.9800
C13	H13F	0.9800
C14	C15	1.5516(17)
C14	H14A	0.9900
C14	H14B	0.9900
C15	C16	1.505(3)
C15	C16'	1.515(9)
C15	C18	1.549(2)
C15	C18'	1.681(12)
C20	C21	1.3897(16)
C20	C25	1.3901(16)
C21	C22	1.3889(18)
C21	H21	0.9500
C22	C23	1.385(2)
C22	H22	0.9500
C23	C24	1.401(2)
C23	C26	1.5083(19)
C24	C25	1.3895(17)
C24	H24	0.9500
C25	H25	0.9500
C26	H26A	0.9800
C26	H26B	0.9800
C26	H26C	0.9800
C26	H26D	0.9800
C26	H26E	0.9800
C26	H26F	0.9800
C27	C28	1.3878(16)
C27	C32	1.3972(16)
C28	C29	1.3967(18)

C28	H28	0.9500
C29	C30	1.3937(19)
C29	H29	0.9500
C30	C31	1.3976(18)
C30	C33	1.5061(19)
C31	C32	1.3892(17)
C31	H31	0.9500
C32	H32	0.9500
C33	H33A	0.9800
C33	H33B	0.9800
C33	H33C	0.9800
C33	H33D	0.9800
C33	H33E	0.9800
C33	H33F	0.9800
C16	C17	1.517(3)
C16	H16A	0.9900
C16	H16B	0.9900
C17	H17A	0.9800
C17	H17B	0.9800
C17	H17C	0.9800
C18	H18A	0.9800
C18	H18B	0.9800
C18	H18C	0.9800
C16'	C17'	1.537(12)
C16'	H16D	0.9900
C16'	H16E	0.9900
C17'	H17D	0.9800
C17'	H17E	0.9800
C17'	H17F	0.9800
C18'	H18F	0.9800
C18'	H18D	0.9800
C18'	H18E	0.9800

Angles-----

N2	C1	C2	120.97(10)
N2	C1	C13	118.00(10)
C2	C1	C13	121.04(10)
C12	N1	C9	120.20(10)

C12	N1	Ni1	125.41(8)
C9	N1	Ni1	114.15(7)
O2	S1	O1	115.63(5)
O2	S1	N3	116.62(5)
O1	S1	N3	101.87(5)
O2	S1	C20	105.94(5)
O1	S1	C20	106.51(5)
N3	S1	C20	109.88(5)
O2	S1	Ni1	133.53(4)
O1	S1	Ni1	57.44(3)
N3	S1	Ni1	44.44(3)
C20	S1	Ni1	120.27(4)
S1	O1	Ni1	90.32(4)
N4	Ni1	N3	106.97(4)
N4	Ni1	N1	110.13(4)
N3	Ni1	N1	89.50(4)
N4	Ni1	N2	103.62(4)
N3	Ni1	N2	149.37(4)
N1	Ni1	N2	81.43(4)
N4	Ni1	O1	104.43(4)
N3	Ni1	O1	65.89(3)
N1	Ni1	O1	142.27(3)
N2	Ni1	O1	104.96(3)
N4	Ni1	S1	109.05(3)
N3	Ni1	S1	33.64(3)
N1	Ni1	S1	118.20(3)
N2	Ni1	S1	131.09(3)
O1	Ni1	S1	32.25(2)
C3	C2	C1	120.70(10)
C3	C2	H2	119.6
C1	C2	H2	119.6
O3	S2	O4	116.53(5)
O3	S2	N4	109.95(5)
O4	S2	N4	110.81(5)
O3	S2	C27	105.94(5)
O4	S2	C27	106.08(5)
N4	S2	C27	106.92(5)
C1	N2	C5	118.51(9)

C1	N2	Ni1	130.20(8)
C5	N2	Ni1	111.25(7)
C15	N3	S1	127.22(8)
C15	N3	Ni1	130.57(7)
S1	N3	Ni1	101.92(5)
C2	C3	C4	119.31(10)
C2	C3	H3	120.3
C4	C3	H3	120.3
C5	C4	C3	116.58(10)
C5	C4	C6	119.10(10)
C3	C4	C6	124.31(11)
S2	N4	Ni1	125.97(6)
S2	N4	H4N	108.2
Ni1	N4	H4N	113.7
N2	C5	C4	123.90(10)
N2	C5	C9	116.69(10)
C4	C5	C9	119.41(10)
C7	C6	C4	121.11(11)
C7	C6	H6	119.4
C4	C6	H6	119.4
C6	C7	C8	120.84(11)
C6	C7	H7	119.6
C8	C7	H7	119.6
C9	C8	C10	116.62(11)
C9	C8	C7	118.74(10)
C10	C8	C7	124.64(11)
N1	C9	C8	123.05(10)
N1	C9	C5	116.31(9)
C8	C9	C5	120.63(10)
C11	C10	C8	119.47(11)
C11	C10	H10	120.3
C8	C10	H10	120.3
C10	C11	C12	120.57(11)
C10	C11	H11	119.7
C12	C11	H11	119.7
N1	C12	C11	119.99(11)
N1	C12	C14	117.14(10)
C11	C12	C14	122.78(10)

C1 C13 H13A 109.5
 C1 C13 H13B 109.5
 H13A C13 H13B 109.5
 C1 C13 H13C 109.5
 H13A C13 H13C 109.5
 H13B C13 H13C 109.5
 C1 C13 H13D 109.5
 H13A C13 H13D 141.1
 H13B C13 H13D 56.3
 H13C C13 H13D 56.3
 C1 C13 H13E 109.5
 H13A C13 H13E 56.3
 H13B C13 H13E 141.1
 H13C C13 H13E 56.3
 H13D C13 H13E 109.5
 C1 C13 H13F 109.5
 H13A C13 H13F 56.3
 H13B C13 H13F 56.3
 H13C C13 H13F 141.1
 H13D C13 H13F 109.5
 H13E C13 H13F 109.5
 C12 C14 C15 116.37(9)
 C12 C14 H14A 108.2
 C15 C14 H14A 108.2
 C12 C14 H14B 108.2
 C15 C14 H14B 108.2
 H14A C14 H14B 107.3
 N3 C15 C16 112.81(12)
 N3 C15 C16' 117.3(3)
 N3 C15 C18 110.14(11)
 C16 C15 C18 112.21(14)
 N3 C15 C14 105.59(9)
 C16 C15 C14 110.64(14)
 C16' C15 C14 117.7(4)
 C18 C15 C14 104.95(12)
 N3 C15 C18' 103.5(4)
 C16' C15 C18' 101.5(5)
 C14 C15 C18' 110.2(5)

C21	C20	C25	120.76(11)
C21	C20	S1	119.23(9)
C25	C20	S1	119.92(9)
C22	C21	C20	119.69(12)
C22	C21	H21	120.2
C20	C21	H21	120.2
C23	C22	C21	120.76(12)
C23	C22	H22	119.6
C21	C22	H22	119.6
C22	C23	C24	118.77(12)
C22	C23	C26	120.37(14)
C24	C23	C26	120.86(14)
C25	C24	C23	121.25(12)
C25	C24	H24	119.4
C23	C24	H24	119.4
C24	C25	C20	118.77(12)
C24	C25	H25	120.6
C20	C25	H25	120.6
C23	C26	H26A	109.5
C23	C26	H26B	109.5
H26A	C26	H26B	109.5
C23	C26	H26C	109.5
H26A	C26	H26C	109.5
H26B	C26	H26C	109.5
C23	C26	H26D	109.5
H26A	C26	H26D	141.1
H26B	C26	H26D	56.3
H26C	C26	H26D	56.3
C23	C26	H26E	109.5
H26A	C26	H26E	56.3
H26B	C26	H26E	141.1
H26C	C26	H26E	56.3
H26D	C26	H26E	109.5
C23	C26	H26F	109.5
H26A	C26	H26F	56.3
H26B	C26	H26F	56.3
H26C	C26	H26F	141.1
H26D	C26	H26F	109.5

H26E	C26	H26F	109.5
C28	C27	C32	120.16(11)
C28	C27	S2	121.11(9)
C32	C27	S2	118.61(9)
C27	C28	C29	119.52(11)
C27	C28	H28	120.2
C29	C28	H28	120.2
C30	C29	C28	121.25(11)
C30	C29	H29	119.4
C28	C29	H29	119.4
C29	C30	C31	118.25(11)
C29	C30	C33	121.07(12)
C31	C30	C33	120.67(12)
C32	C31	C30	121.23(11)
C32	C31	H31	119.4
C30	C31	H31	119.4
C31	C32	C27	119.56(11)
C31	C32	H32	120.2
C27	C32	H32	120.2
C30	C33	H33A	109.5
C30	C33	H33B	109.5
H33A	C33	H33B	109.5
C30	C33	H33C	109.5
H33A	C33	H33C	109.5
H33B	C33	H33C	109.5
C30	C33	H33D	109.5
H33A	C33	H33D	141.1
H33B	C33	H33D	56.3
H33C	C33	H33D	56.3
C30	C33	H33E	109.5
H33A	C33	H33E	56.3
H33B	C33	H33E	141.1
H33C	C33	H33E	56.3
H33D	C33	H33E	109.5
C30	C33	H33F	109.5
H33A	C33	H33F	56.3
H33B	C33	H33F	56.3
H33C	C33	H33F	141.1

H33D C33 H33F 109.5
 H33E C33 H33F 109.5
 C15 C16 C17 116.92(16)
 C15 C16 H16A 108.1
 C17 C16 H16A 108.1
 C15 C16 H16B 108.1
 C17 C16 H16B 108.1
 H16A C16 H16B 107.3
 C16 C17 H17A 109.5
 C16 C17 H17B 109.5
 H17A C17 H17B 109.5
 C16 C17 H17C 109.5
 H17A C17 H17C 109.5
 H17B C17 H17C 109.5
 C15 C18 H18A 109.5
 C15 C18 H18B 109.5
 H18A C18 H18B 109.5
 C15 C18 H18C 109.5
 H18A C18 H18C 109.5
 H18B C18 H18C 109.5
 C15 C16' C17' 109.6(6)
 C15 C16' H16D 109.7
 C17' C16' H16D 109.7
 C15 C16' H16E 109.7
 C17' C16' H16E 109.7
 H16D C16' H16E 108.2
 C16' C17' H17D 109.5
 C16' C17' H17E 109.5
 H17D C17' H17E 109.5
 C16' C17' H17F 109.5
 H17D C17' H17F 109.5
 H17E C17' H17F 109.5
 C15 C18' H18F 109.5
 C15 C18' H18D 109.5
 H18F C18' H18D 109.5
 C15 C18' H18E 109.5
 H18F C18' H18E 109.5
 H18D C18' H18E 109.5

Table 3. Torsion angles [°] for **Ni-II**.

O2	S1	O1	Ni1	126.87(5)
N3	S1	O1	Ni1	-0.62(5)
C20	S1	O1	Ni1	-115.75(4)
N2	C1	C2	C3	-0.10(17)
C13	C1	C2	C3	-179.95(11)
C2	C1	N2	C5	1.37(16)
C13	C1	N2	C5	-178.77(10)
C2	C1	N2	Ni1	-175.96(8)
C13	C1	N2	Ni1	3.90(15)
O2	S1	N3	C15	48.21(11)
O1	S1	N3	C15	175.06(9)
C20	S1	N3	C15	-72.31(10)
Ni1	S1	N3	C15	174.32(12)
O2	S1	N3	Ni1	-126.11(5)
O1	S1	N3	Ni1	0.74(6)
C20	S1	N3	Ni1	113.37(5)
C1	C2	C3	C4	-1.55(17)
C2	C3	C4	C5	1.83(16)
C2	C3	C4	C6	-177.02(11)
O3	S2	N4	Ni1	-61.06(8)
O4	S2	N4	Ni1	168.68(6)
C27	S2	N4	Ni1	53.51(8)
C1	N2	C5	C4	-1.04(16)
Ni1	N2	C5	C4	176.78(9)
C1	N2	C5	C9	178.80(9)
Ni1	N2	C5	C9	-3.39(12)
C3	C4	C5	N2	-0.57(16)
C6	C4	C5	N2	178.34(10)
C3	C4	C5	C9	179.60(10)
C6	C4	C5	C9	-1.49(16)
C5	C4	C6	C7	-1.94(17)
C3	C4	C6	C7	176.89(12)
C4	C6	C7	C8	2.60(18)
C6	C7	C8	C9	0.21(17)
C6	C7	C8	C10	179.24(12)
C12	N1	C9	C8	2.02(16)

Ni1	N1	C9	C8	176.72(8)
C12	N1	C9	C5	-178.27(10)
Ni1	N1	C9	C5	-3.57(12)
C10	C8	C9	N1	-3.07(16)
C7	C8	C9	N1	176.05(10)
C10	C8	C9	C5	177.24(10)
C7	C8	C9	C5	-3.65(16)
N2	C5	C9	N1	4.73(14)
C4	C5	C9	N1	-175.43(10)
N2	C5	C9	C8	-175.55(10)
C4	C5	C9	C8	4.29(16)
C9	C8	C10	C11	1.27(17)
C7	C8	C10	C11	-177.79(11)
C8	C10	C11	C12	1.42(18)
C9	N1	C12	C11	0.86(16)
Ni1	N1	C12	C11	-173.20(8)
C9	N1	C12	C14	-175.75(10)
Ni1	N1	C12	C14	10.19(14)
C10	C11	C12	N1	-2.58(18)
C10	C11	C12	C14	173.83(11)
N1	C12	C14	C15	-63.37(14)
C11	C12	C14	C15	120.12(12)
S1	N3	C15	C16	-62.64(17)
Ni1	N3	C15	C16	110.04(15)
S1	N3	C15	C16'	43.0(4)
Ni1	N3	C15	C16'	-144.4(4)
S1	N3	C15	C18	63.60(15)
Ni1	N3	C15	C18	-123.73(13)
S1	N3	C15	C14	176.41(8)
Ni1	N3	C15	C14	-10.92(13)
S1	N3	C15	C18'	-67.8(5)
Ni1	N3	C15	C18'	104.9(5)
C12	C14	C15	N3	59.78(12)
C12	C14	C15	C16	-62.58(14)
C12	C14	C15	C16'	-167.0(4)
C12	C14	C15	C18	176.17(12)
C12	C14	C15	C18'	-51.3(4)
O2	S1	C20	C21	-5.30(11)

O1	S1	C20	C21	-128.92(9)
N3	S1	C20	C21	121.49(9)
Ni1	S1	C20	C21	169.57(8)
O2	S1	C20	C25	178.04(10)
O1	S1	C20	C25	54.41(11)
N3	S1	C20	C25	-55.18(11)
Ni1	S1	C20	C25	-7.10(11)
C25	C20	C21	C22	0.66(18)
S1	C20	C21	C22	-175.97(9)
C20	C21	C22	C23	-0.57(19)
C21	C22	C23	C24	0.1(2)
C21	C22	C23	C26	-179.90(14)
C22	C23	C24	C25	0.2(2)
C26	C23	C24	C25	-179.74(15)
C23	C24	C25	C20	-0.1(2)
C21	C20	C25	C24	-0.32(19)
S1	C20	C25	C24	176.30(10)
O3	S2	C27	C28	-7.69(11)
O4	S2	C27	C28	116.76(10)
N4	S2	C27	C28	-124.94(10)
O3	S2	C27	C32	168.42(9)
O4	S2	C27	C32	-67.12(10)
N4	S2	C27	C32	51.17(10)
C32	C27	C28	C29	-0.66(17)
S2	C27	C28	C29	175.39(9)
C27	C28	C29	C30	-0.53(18)
C28	C29	C30	C31	0.70(18)
C28	C29	C30	C33	-179.41(12)
C29	C30	C31	C32	0.33(18)
C33	C30	C31	C32	-179.56(12)
C30	C31	C32	C27	-1.50(18)
C28	C27	C32	C31	1.66(17)
S2	C27	C32	C31	-174.49(9)
N3	C15	C16	C17	-176.80(16)
C18	C15	C16	C17	58.1(2)
C14	C15	C16	C17	-58.8(2)
N3	C15	C16'	C17'	70.9(6)
C14	C15	C16'	C17'	-56.9(6)

C18' C15 C16' C17' -177.2(6)

Symmetry operations

1 'x, y, z'

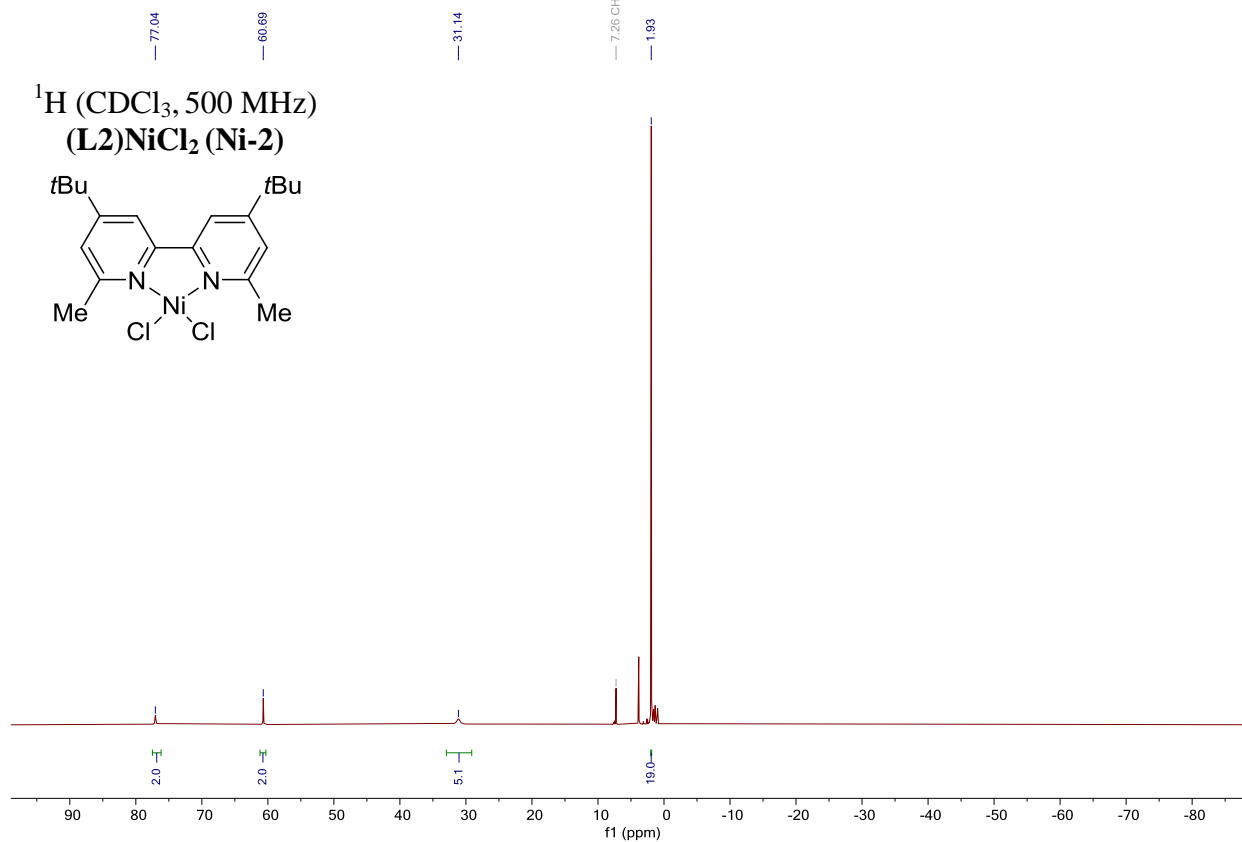
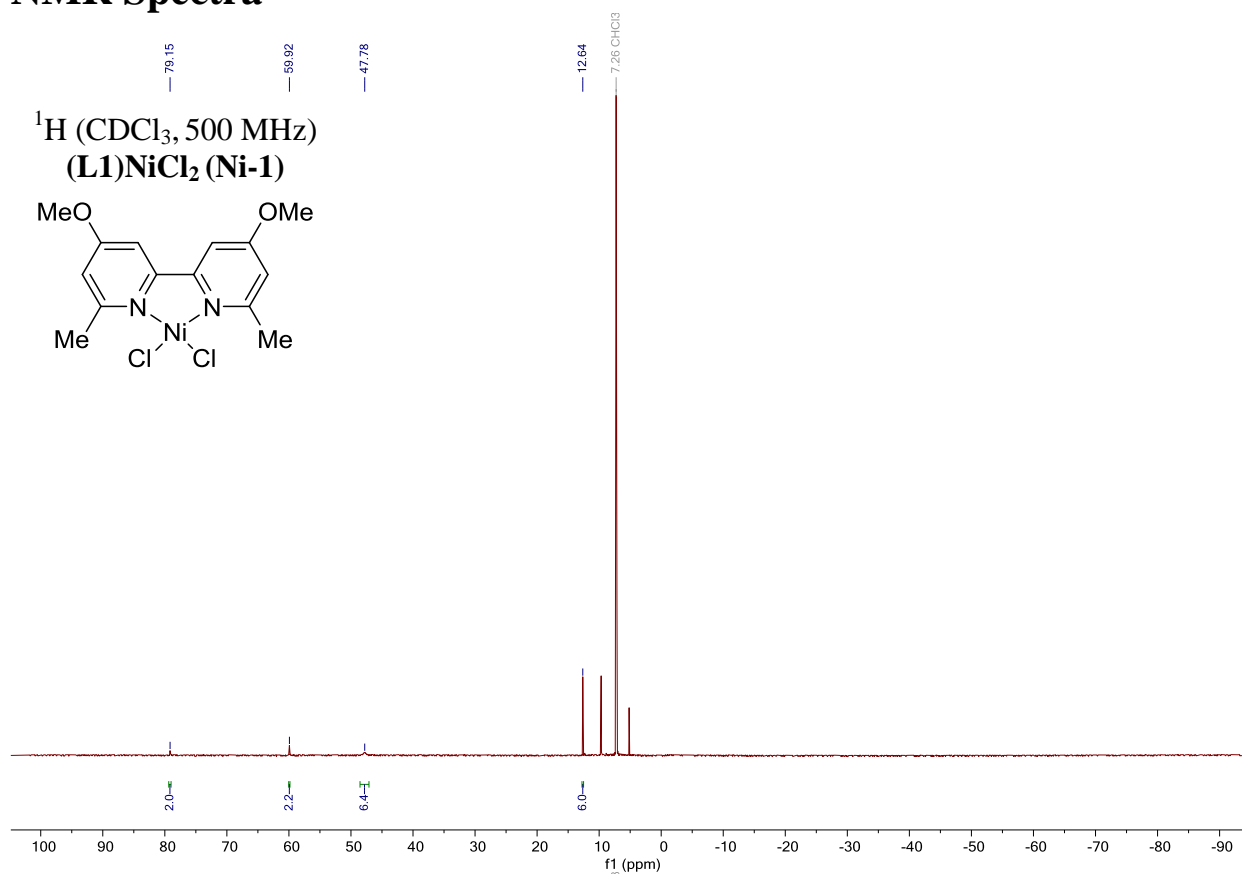
2 '-x, -y, -z'

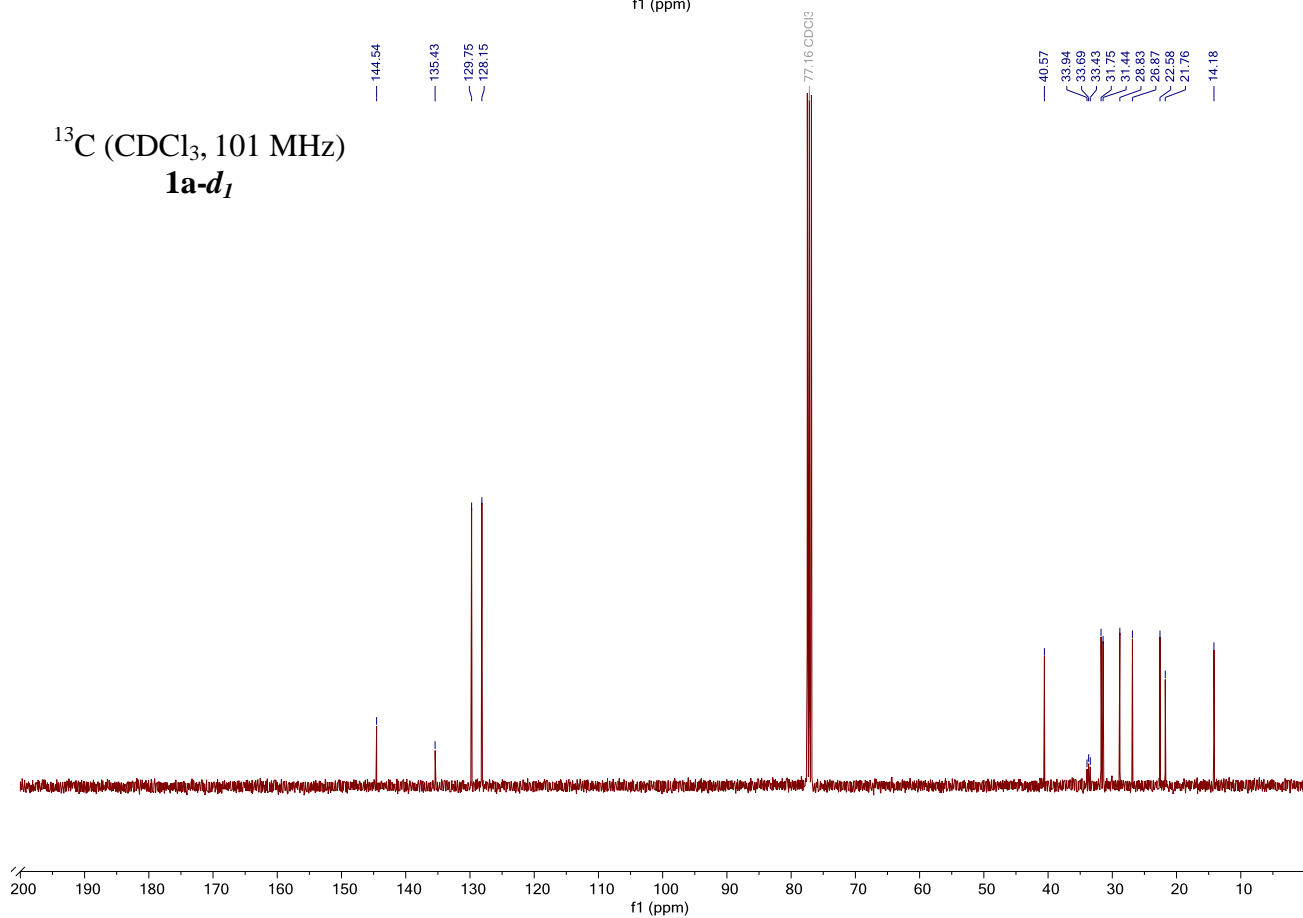
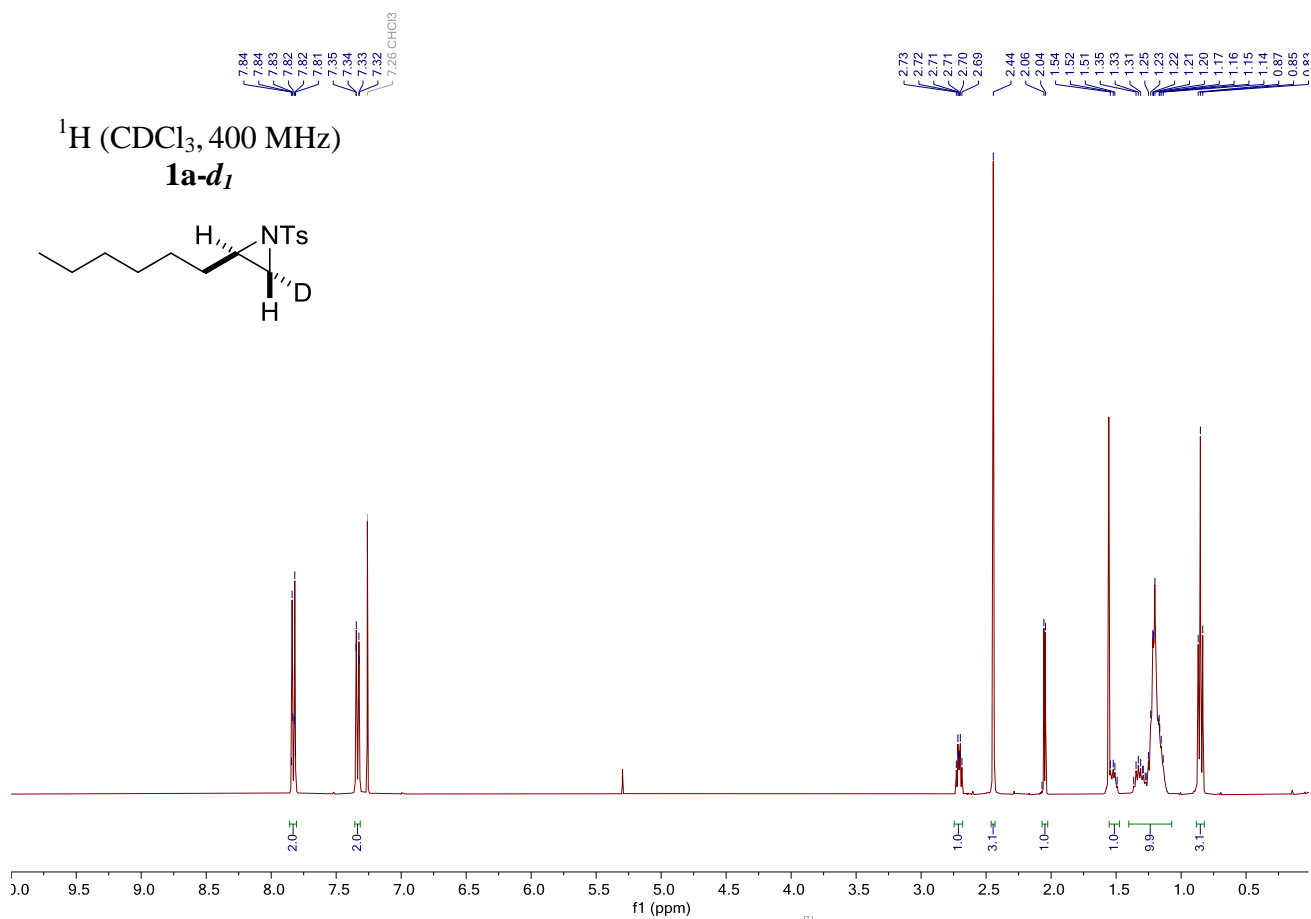
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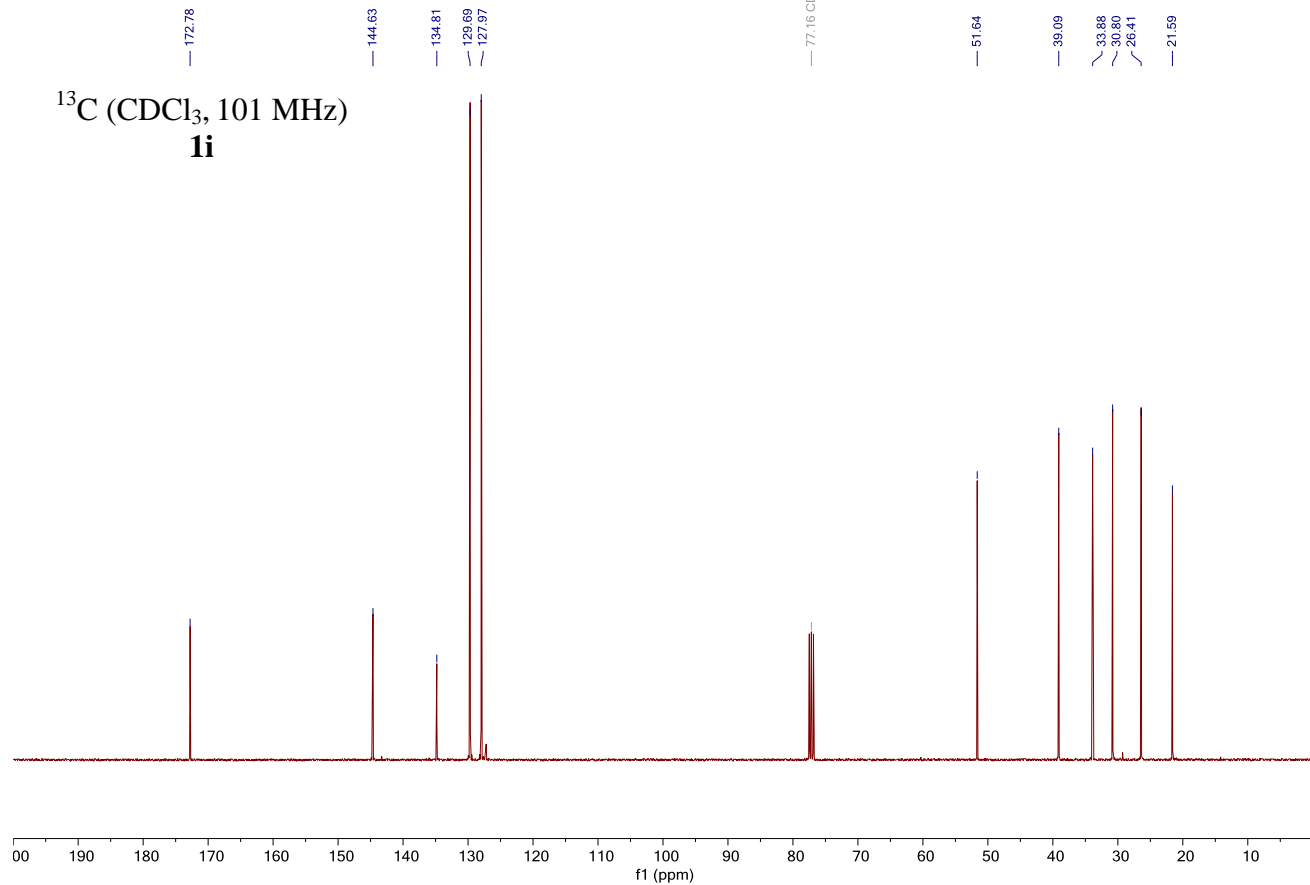
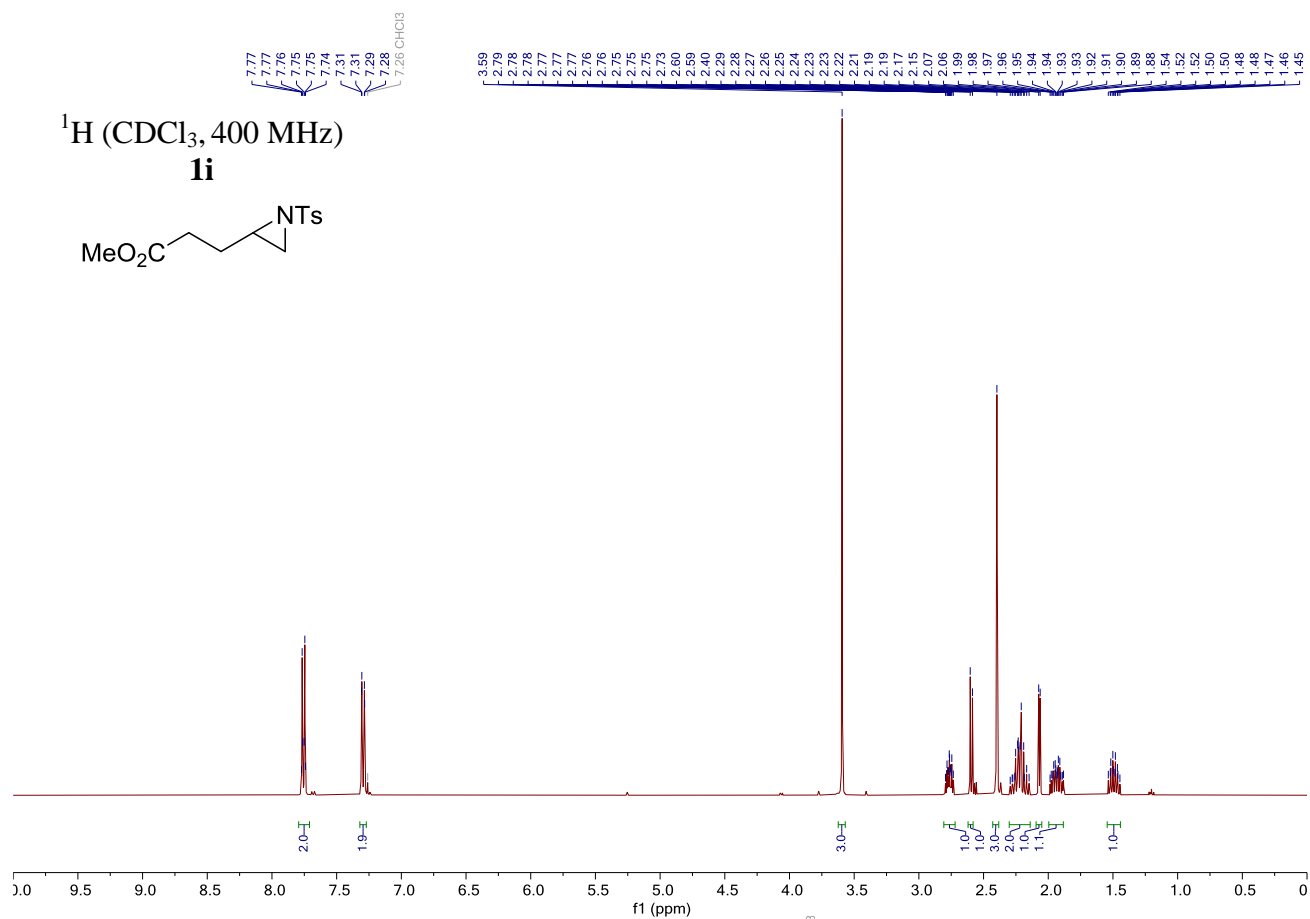
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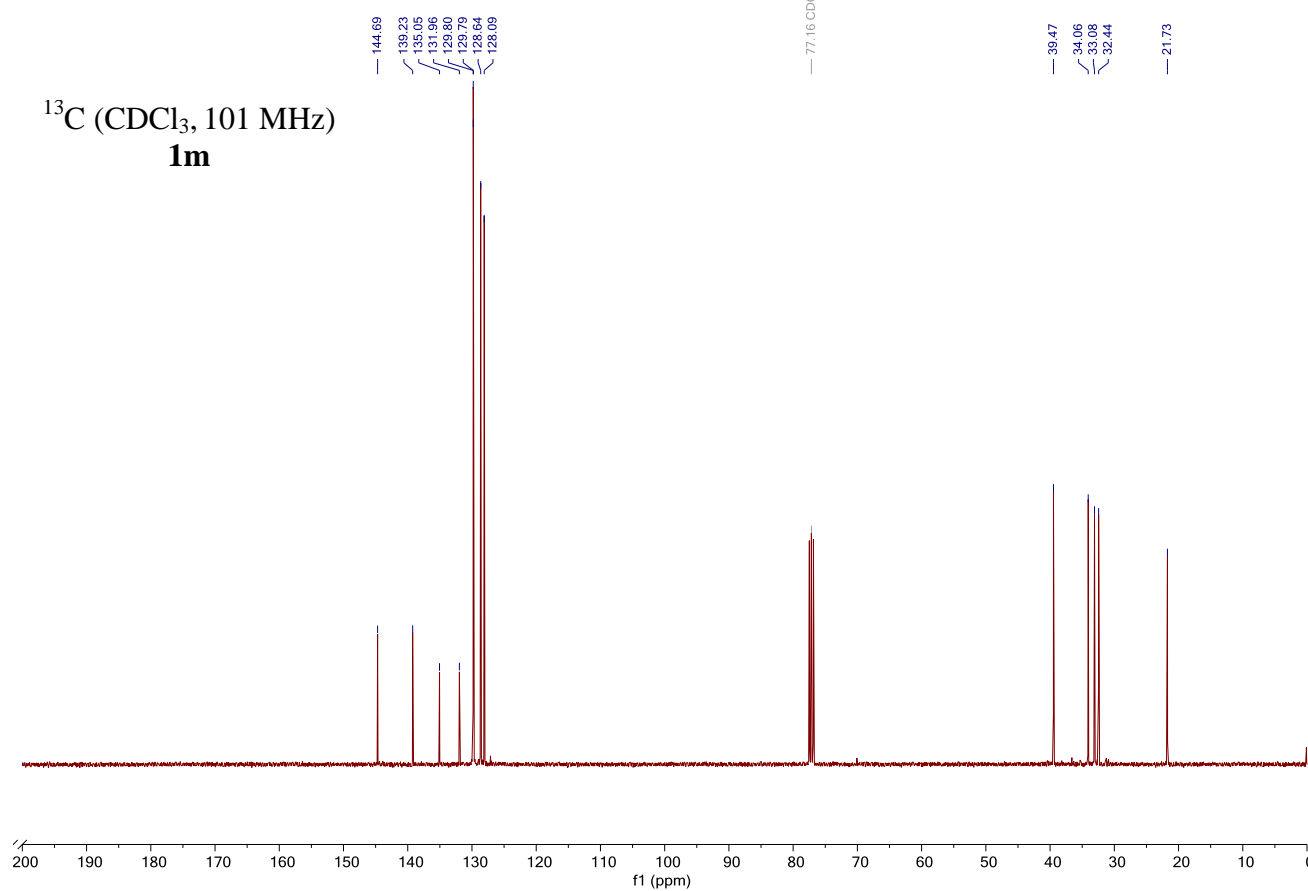
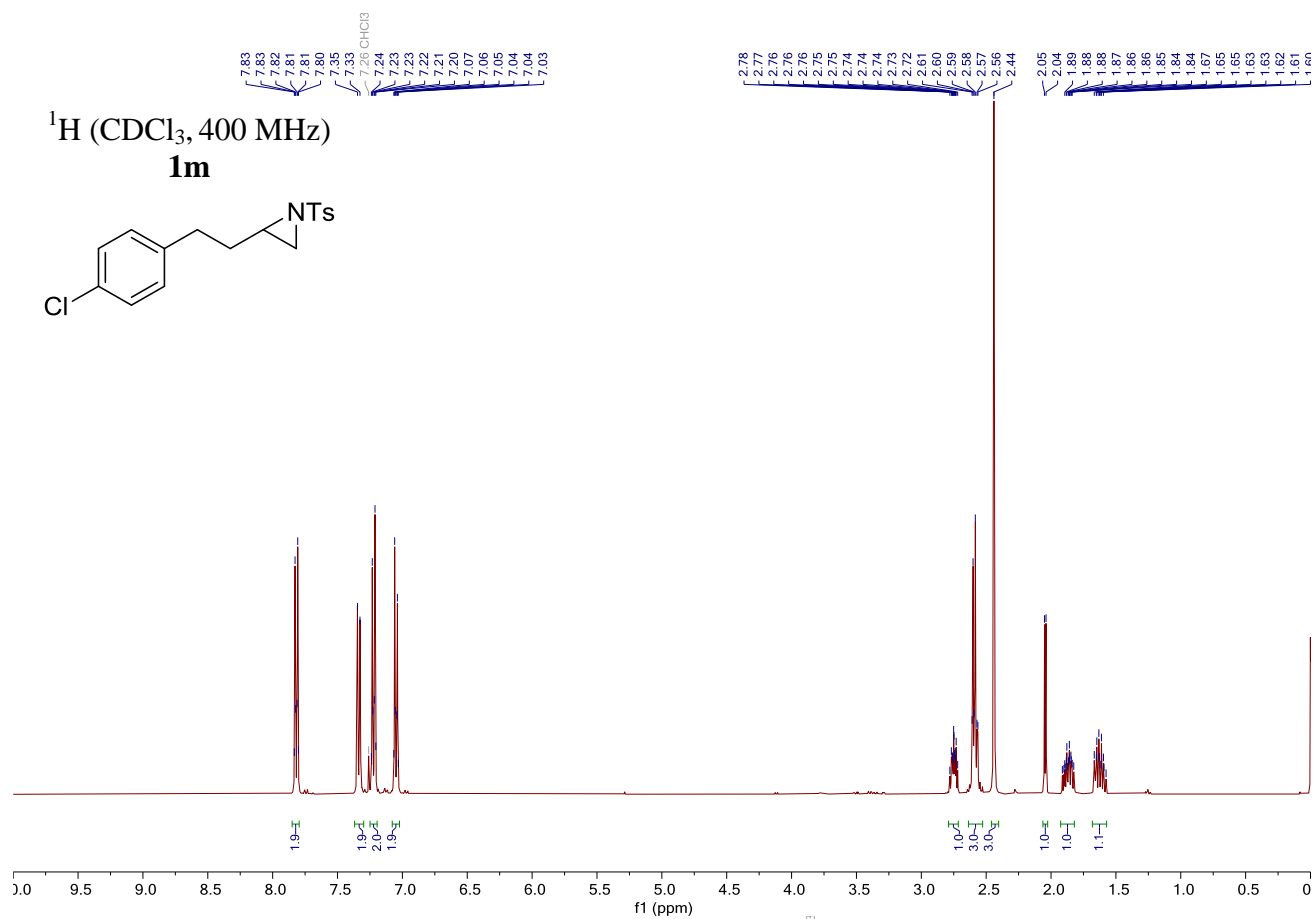
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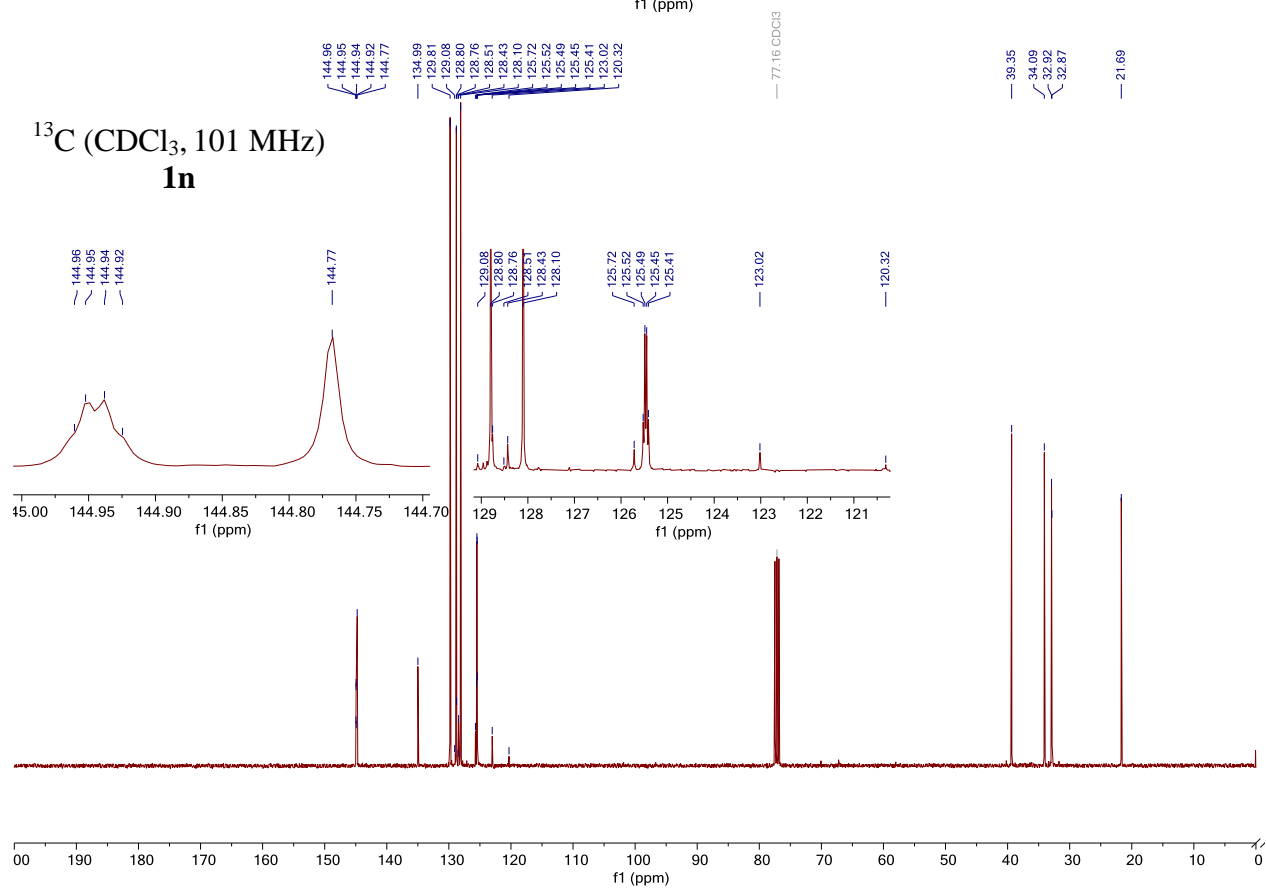
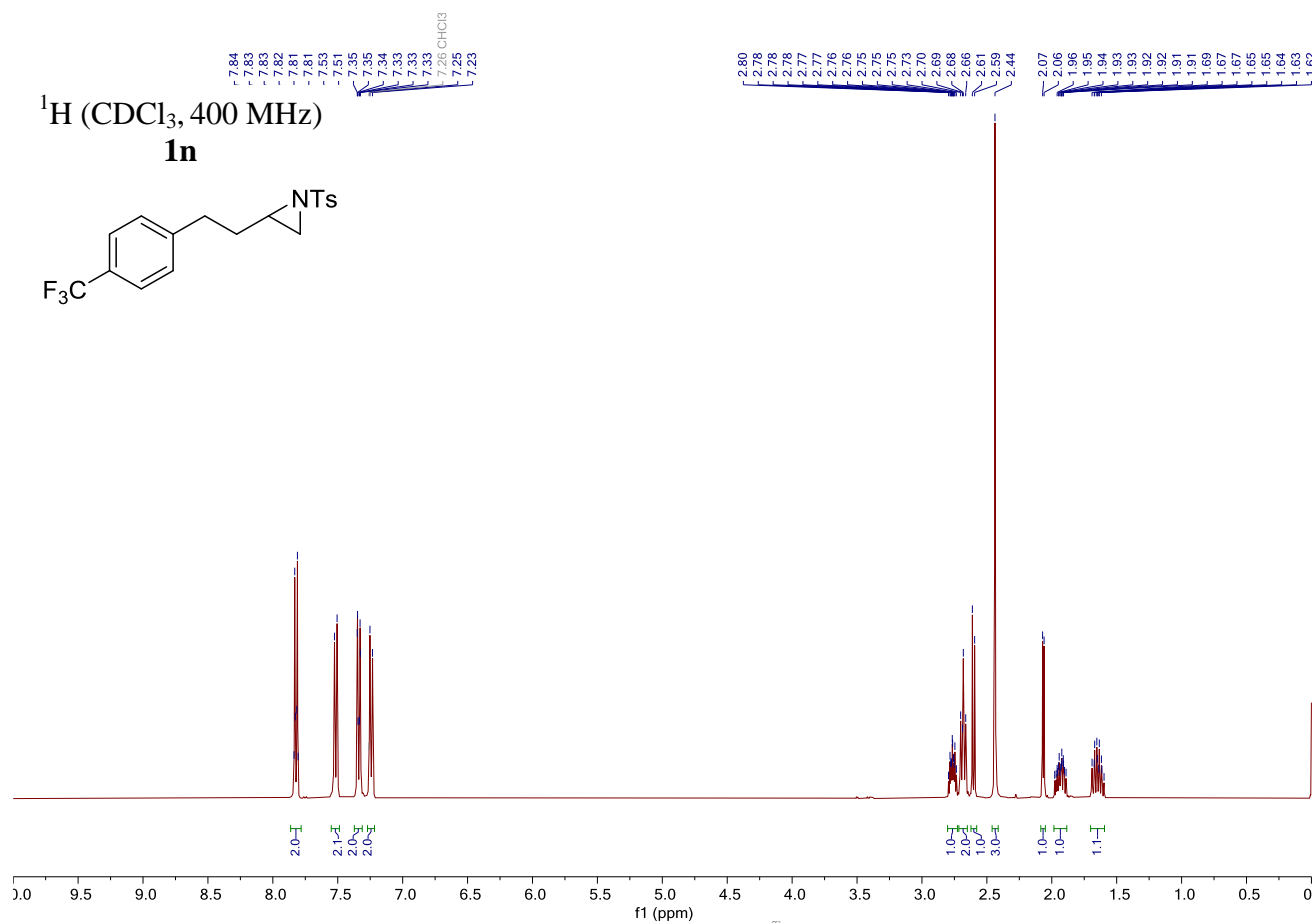
7 NMR Spectra

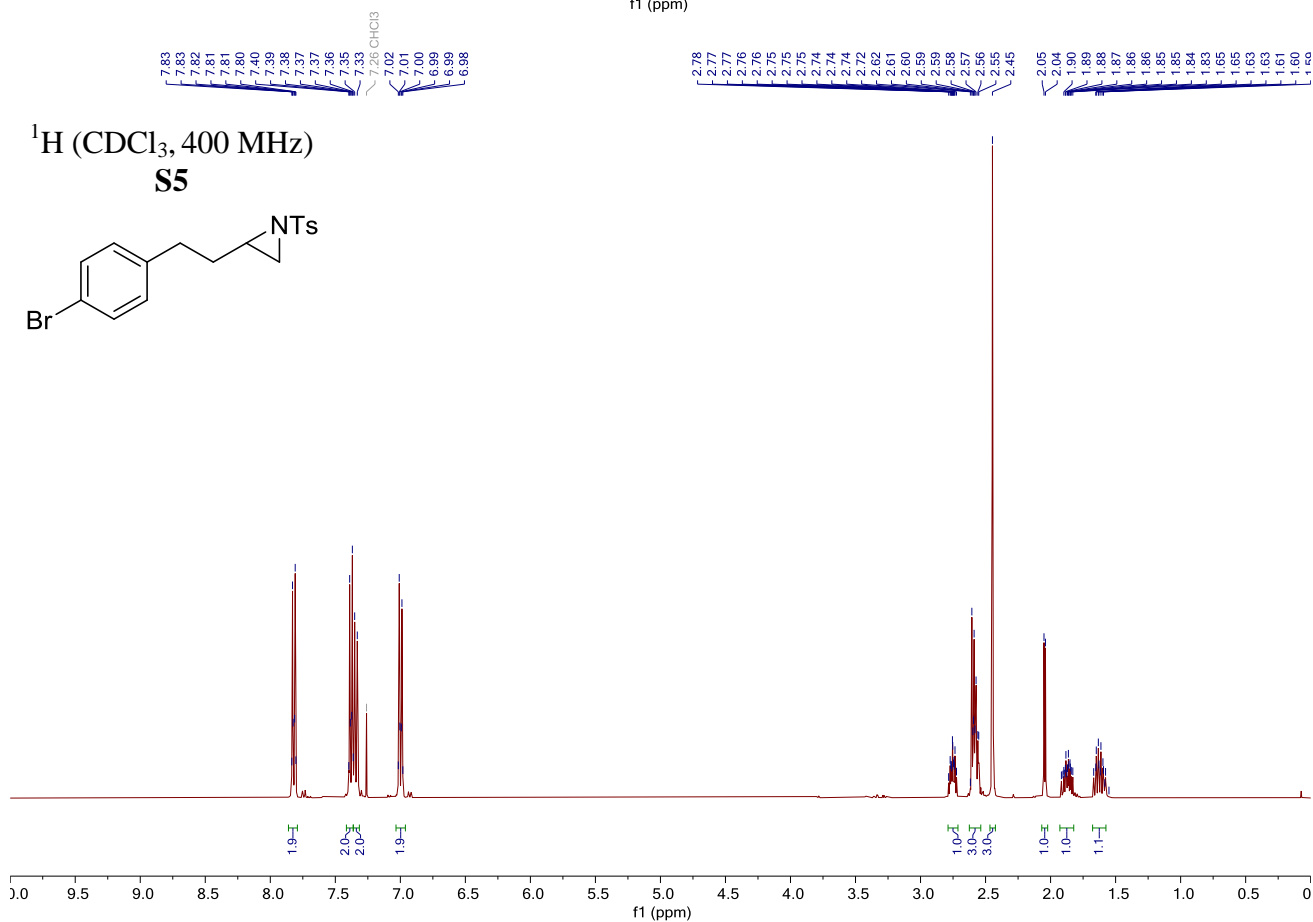
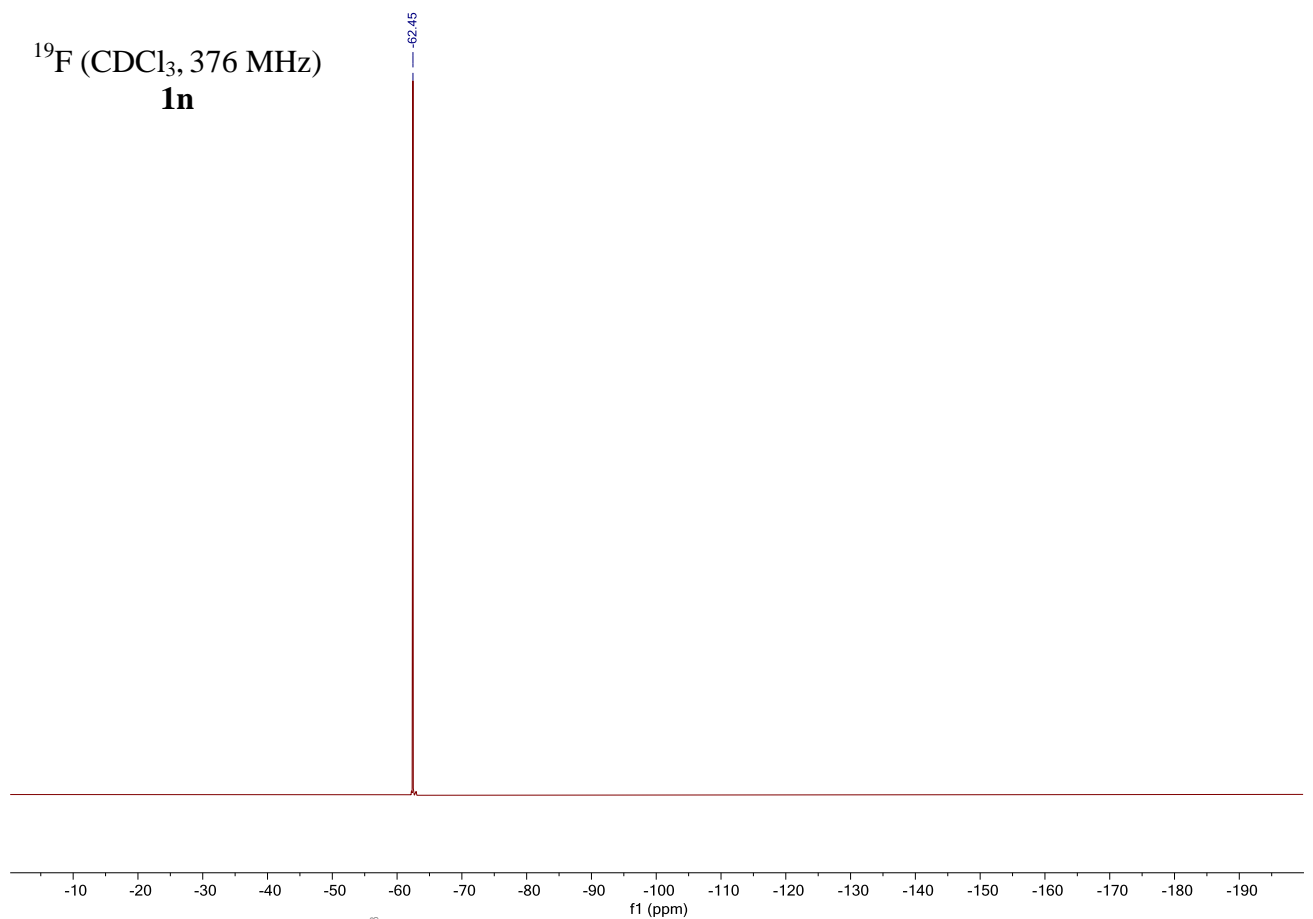


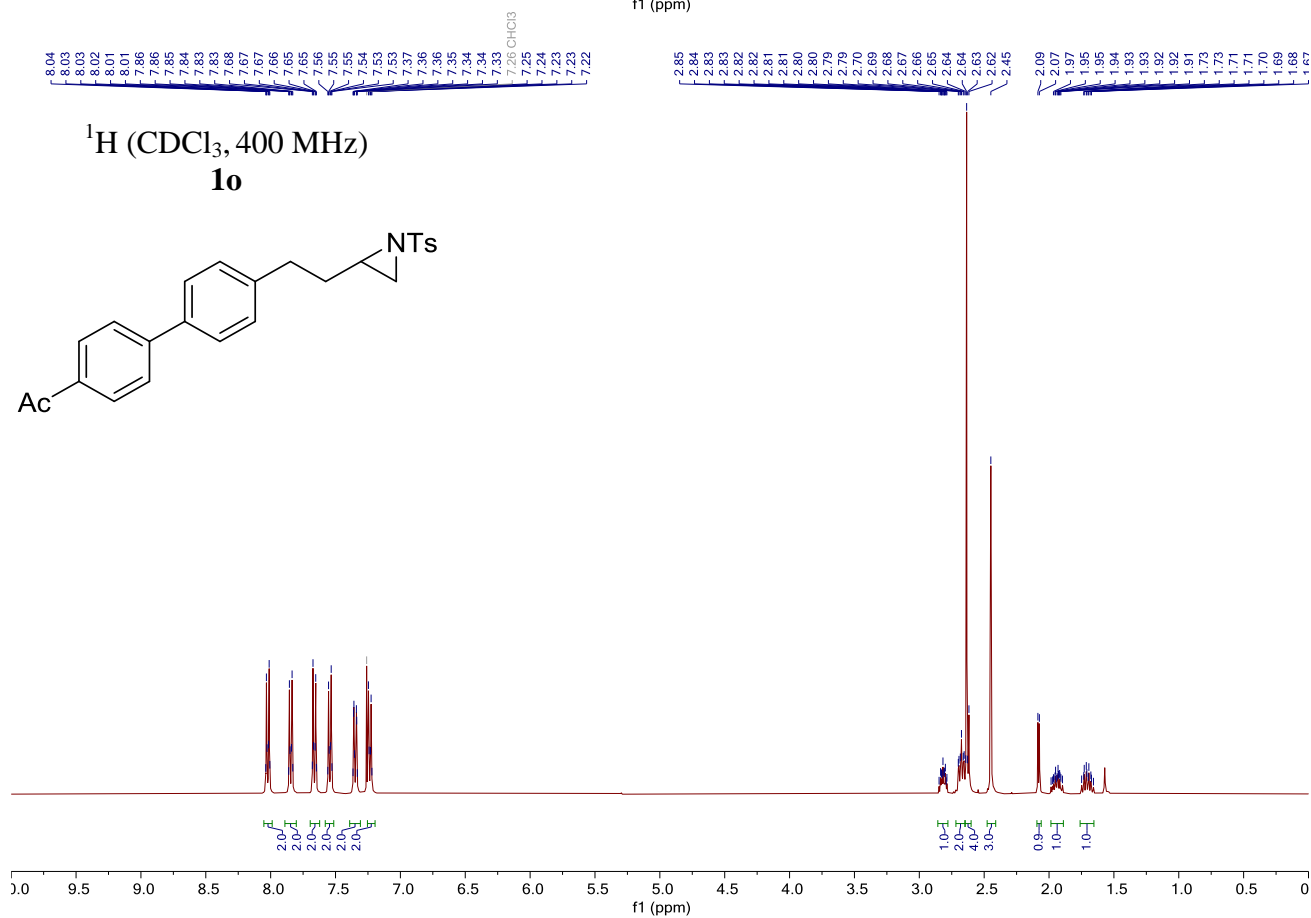
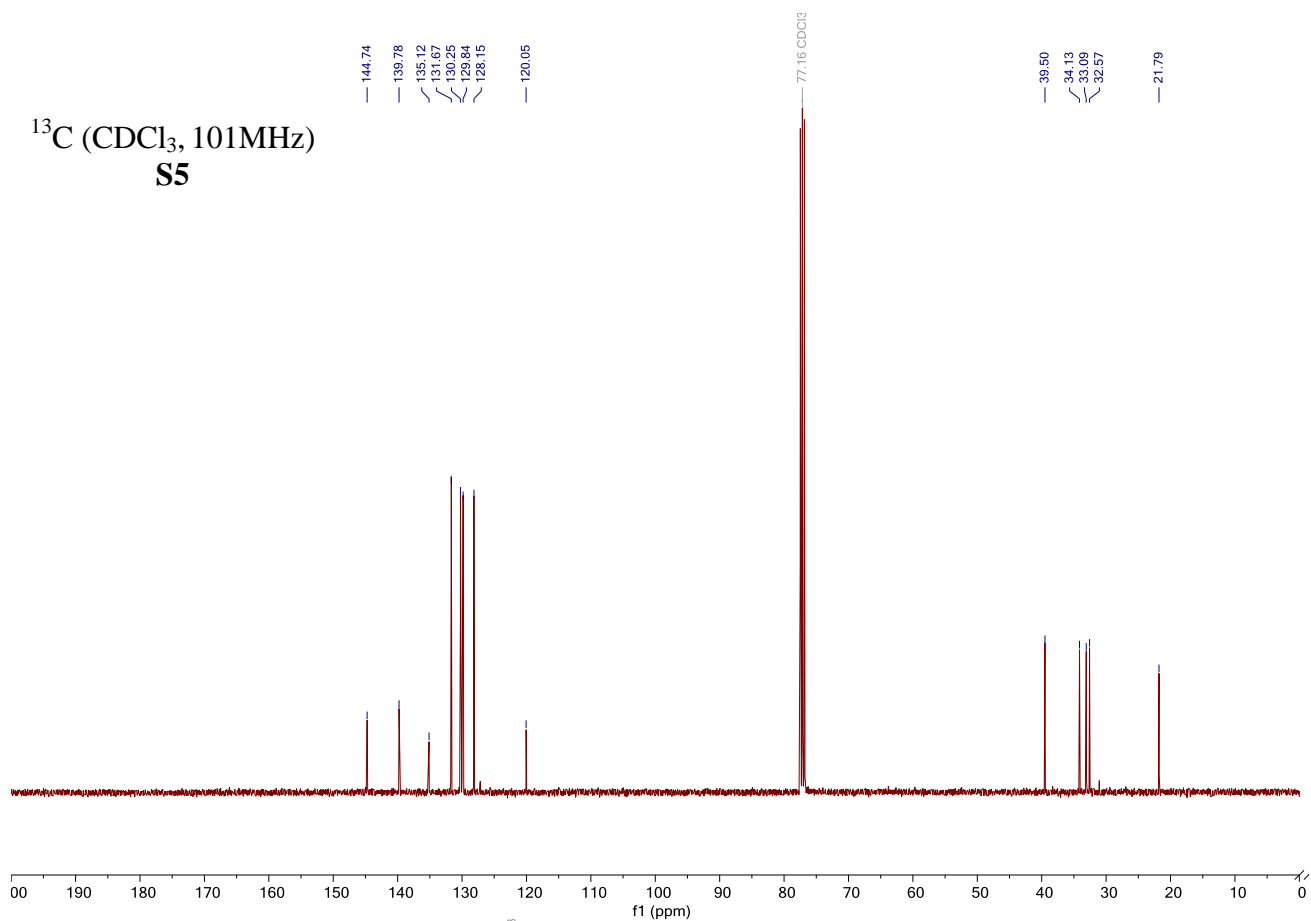


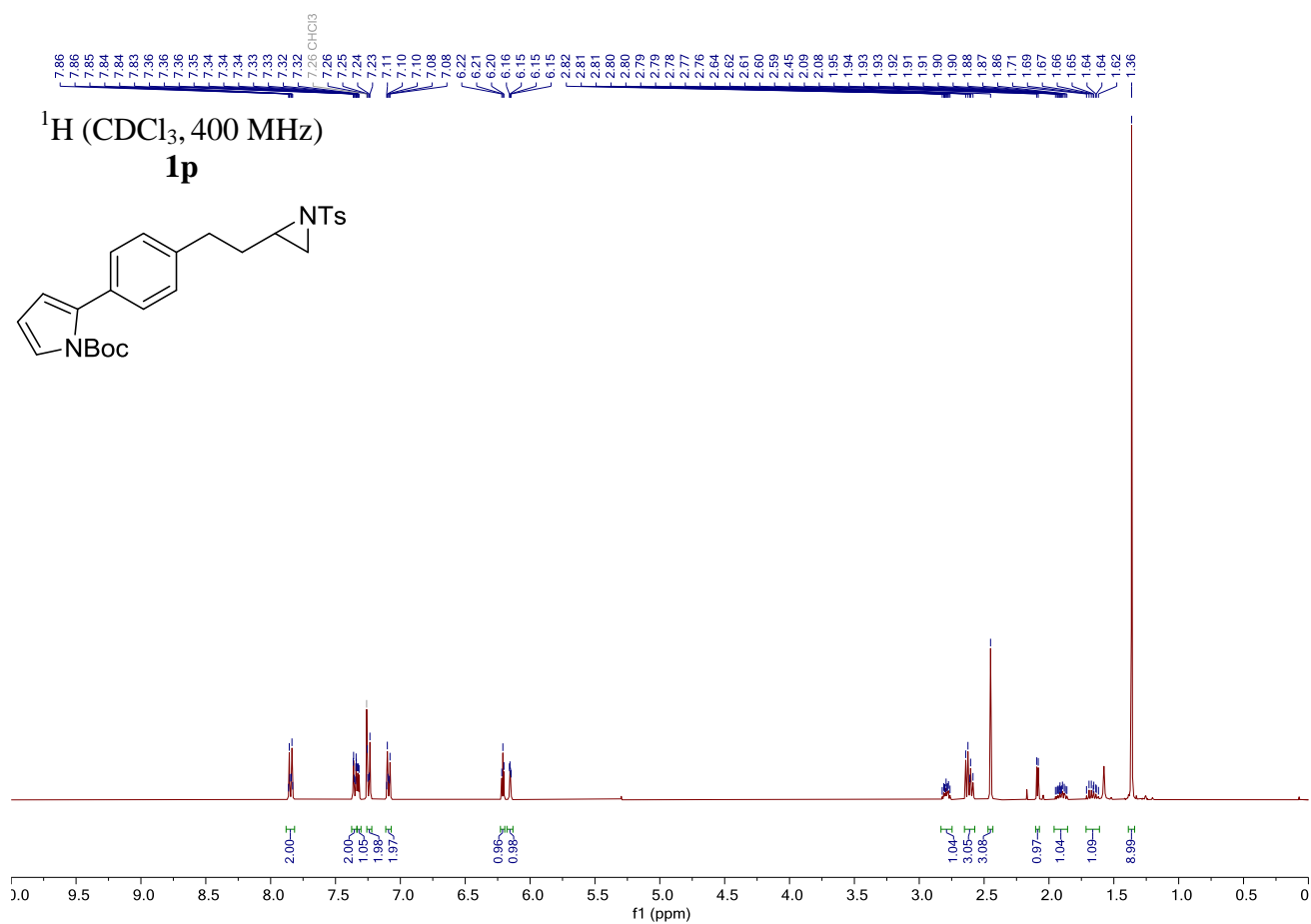
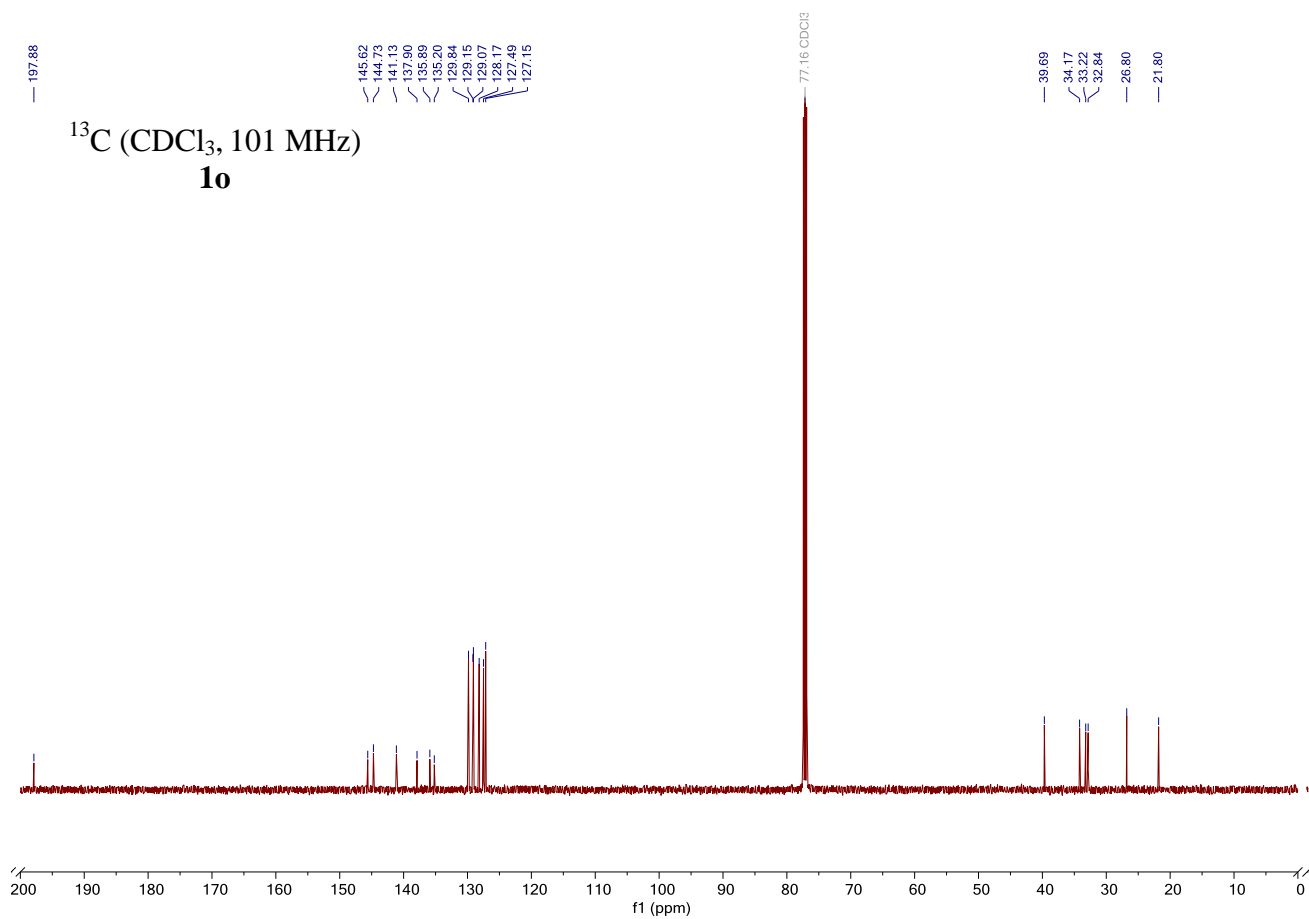


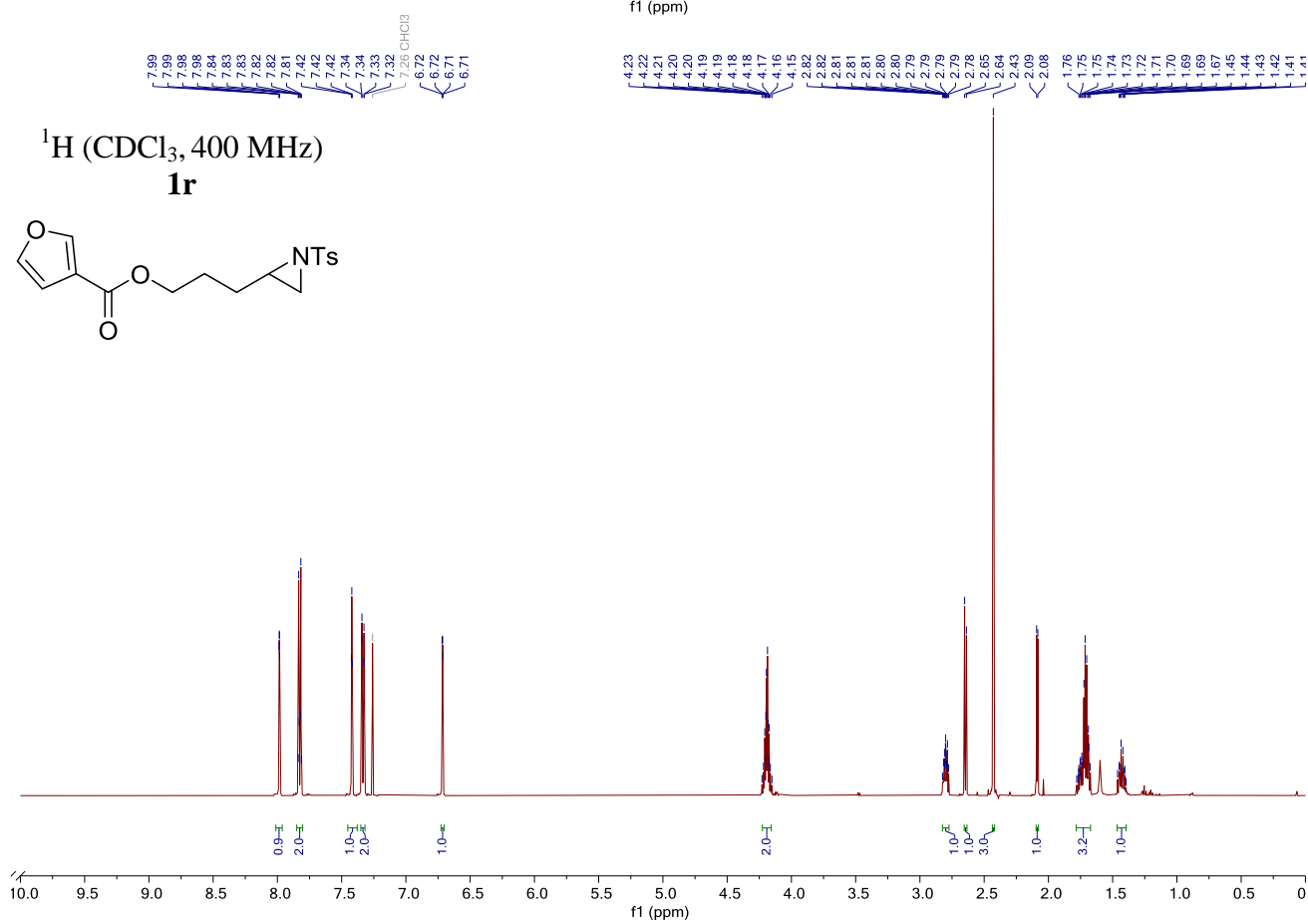
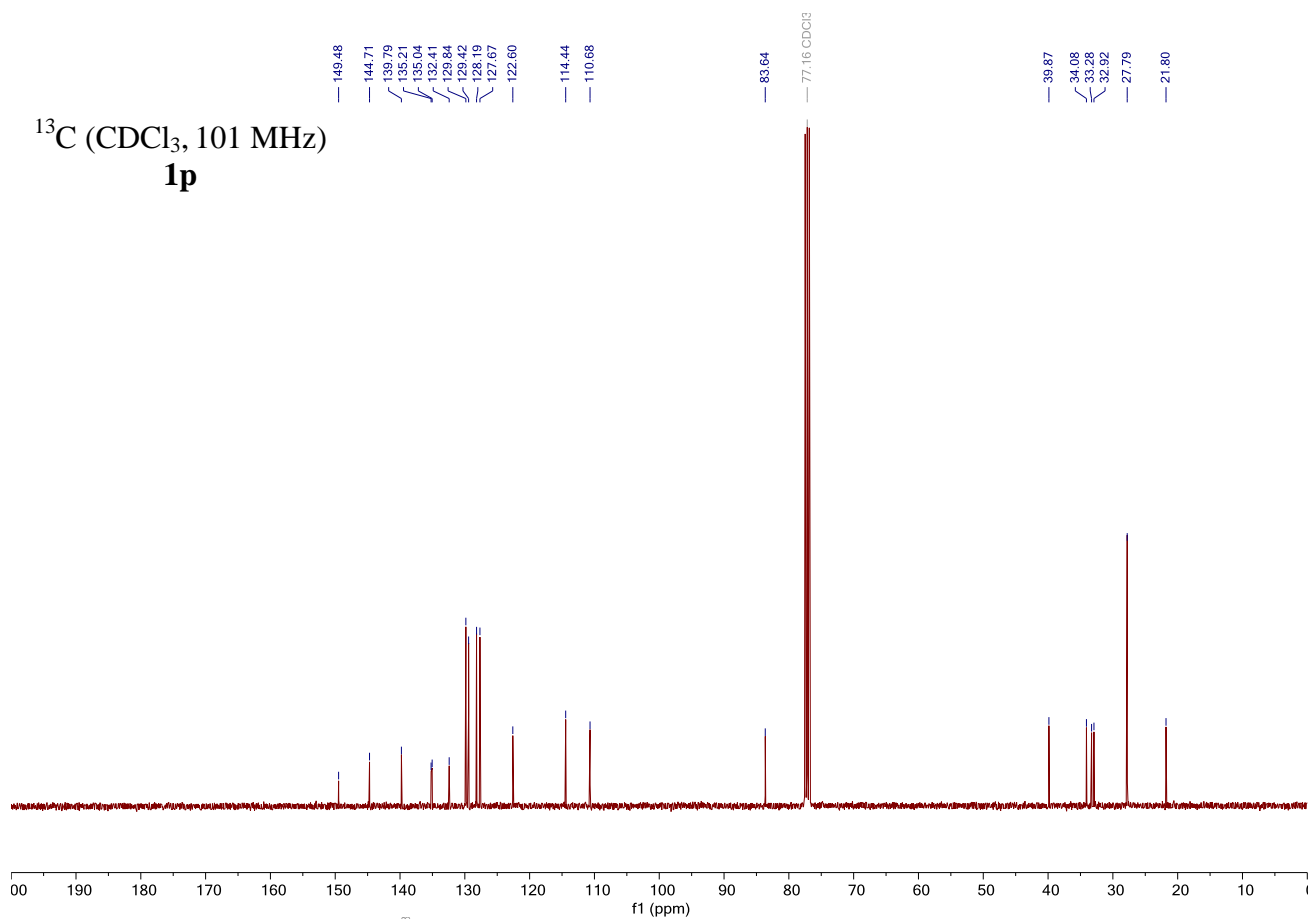


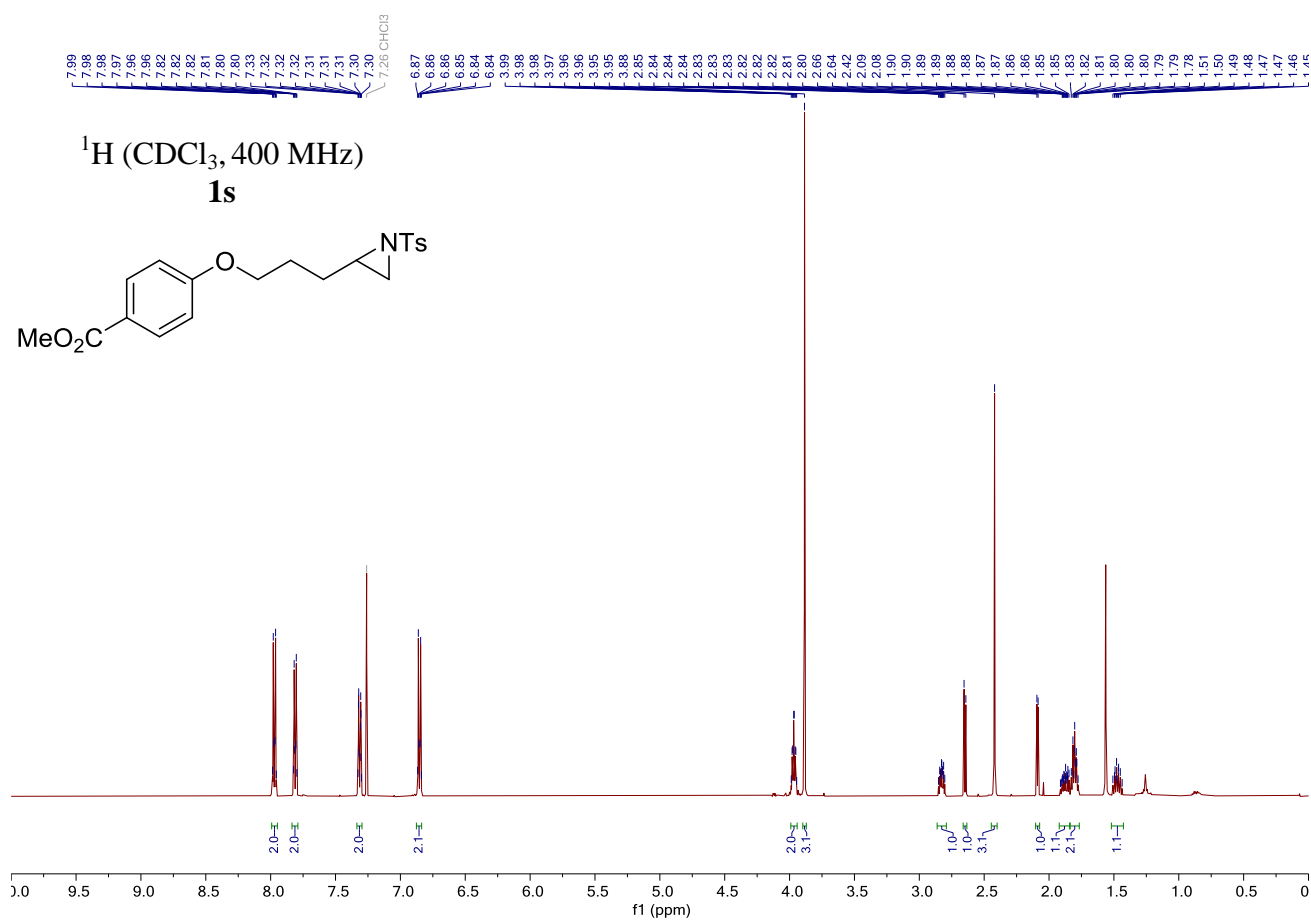
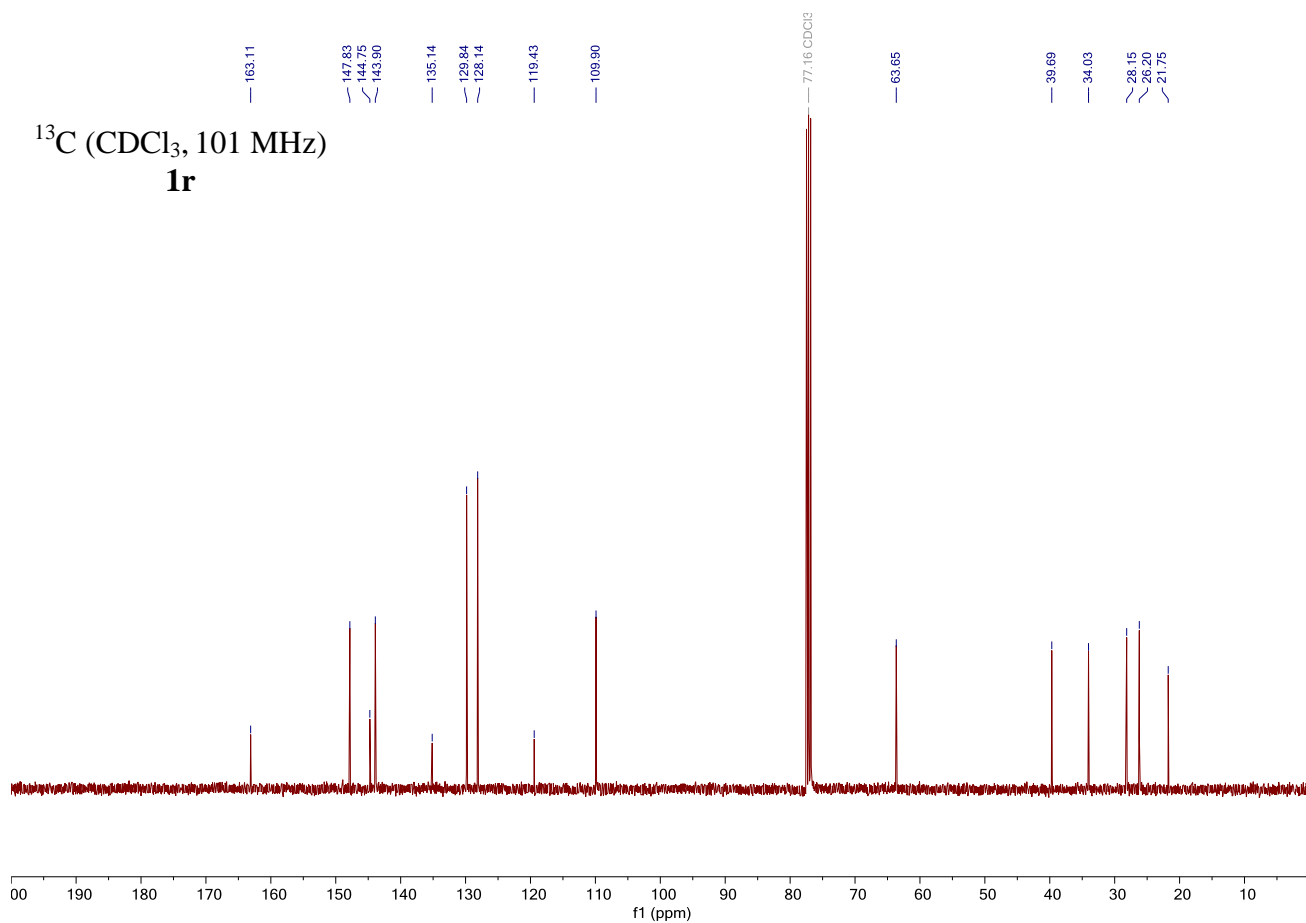


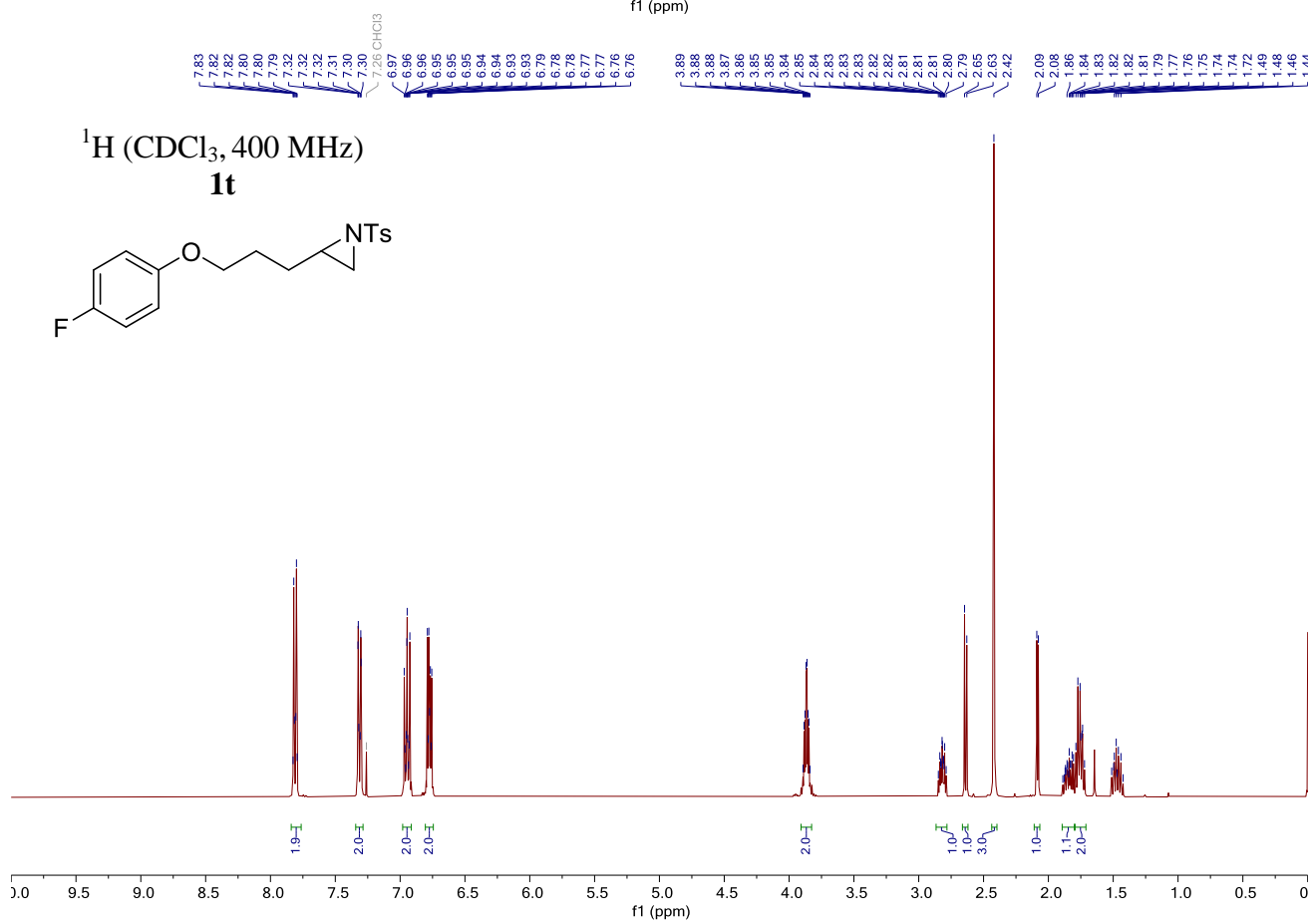
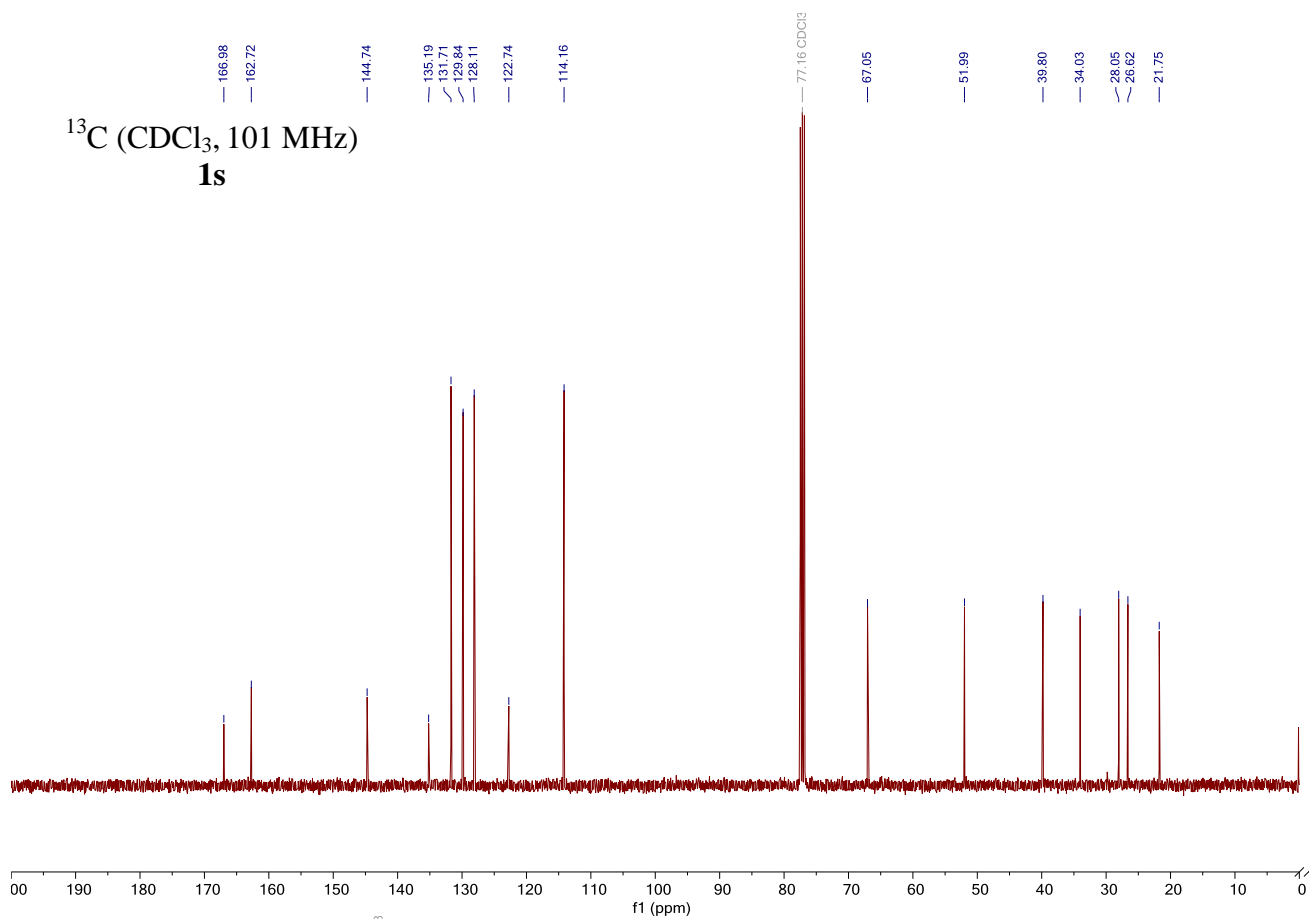


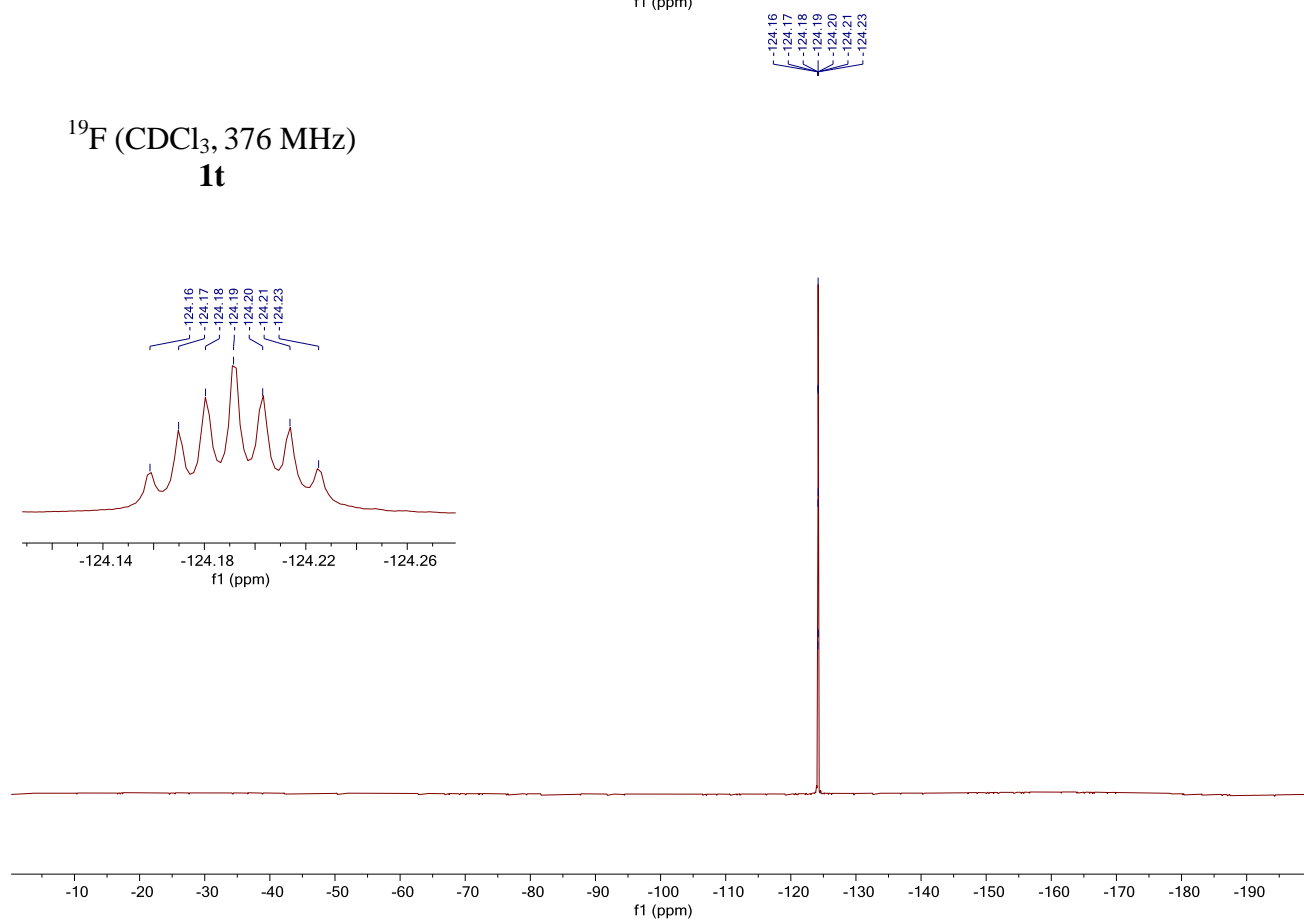
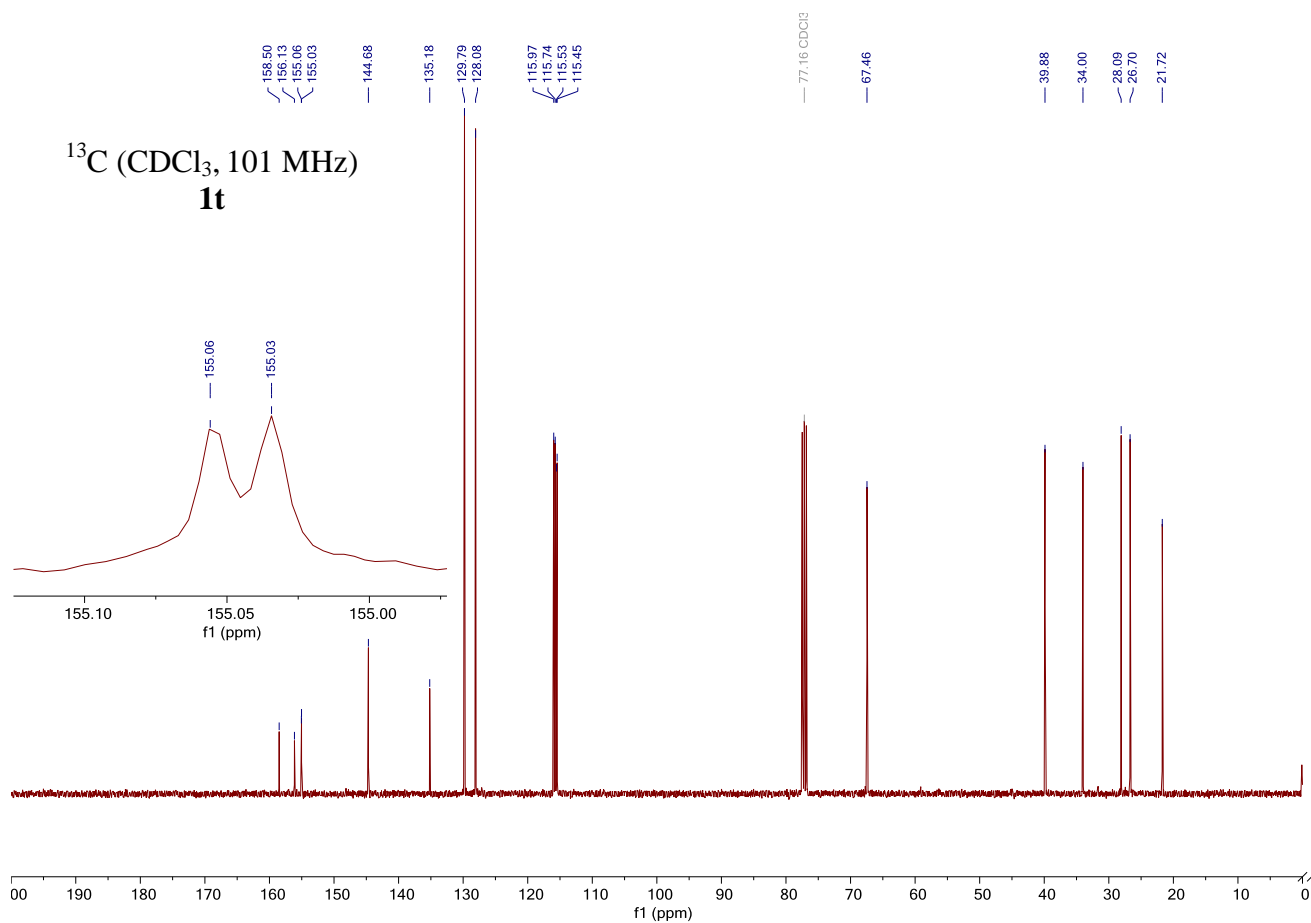


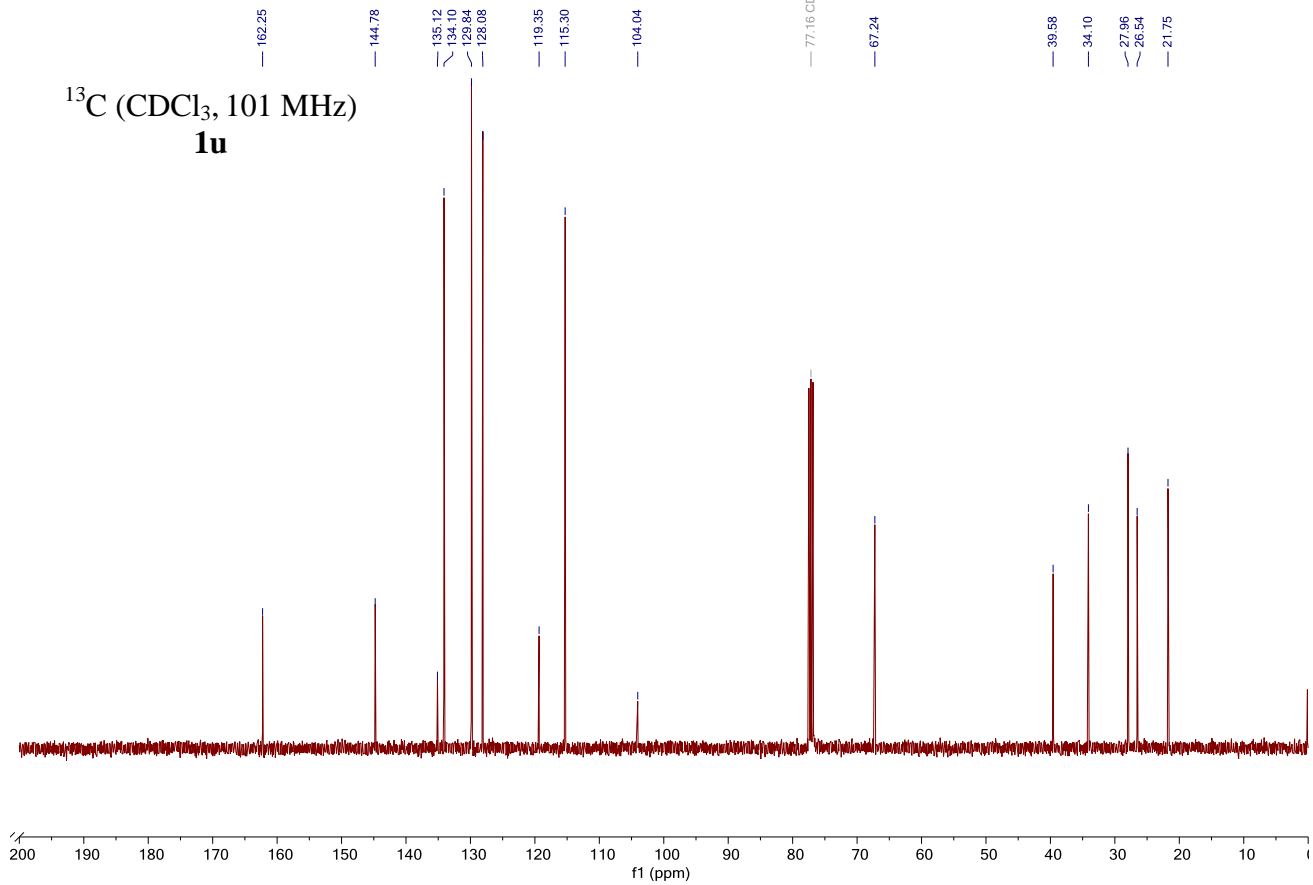
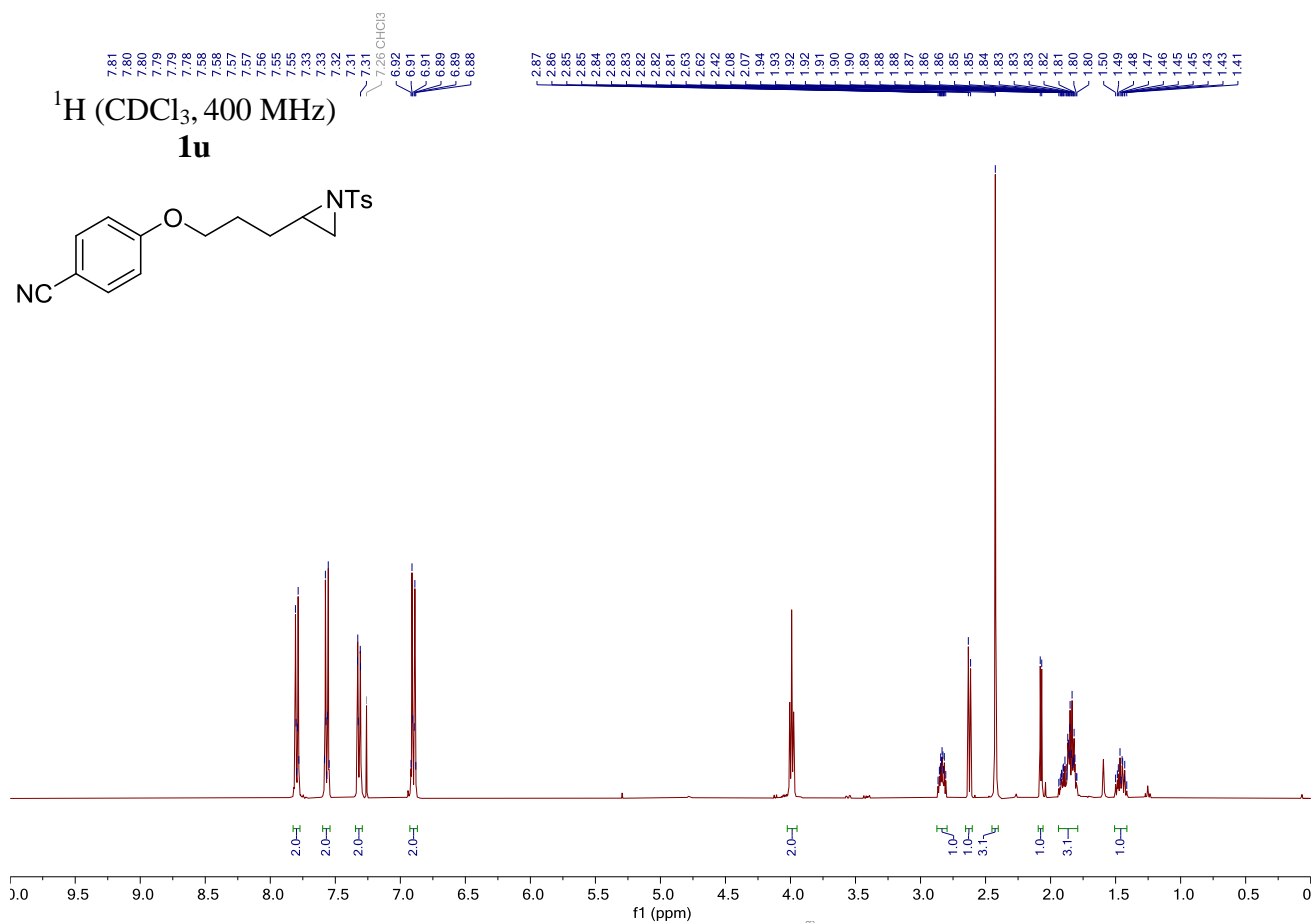


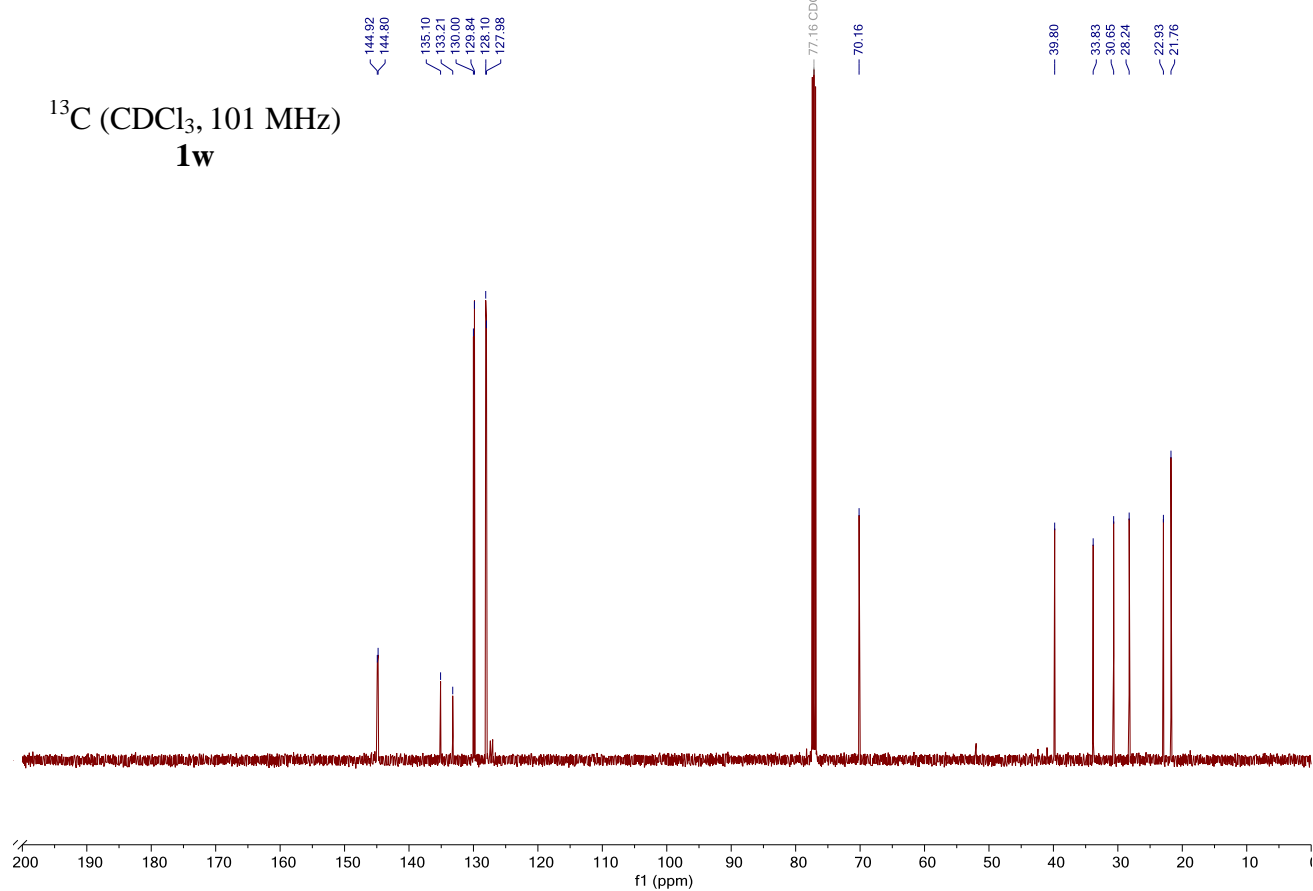
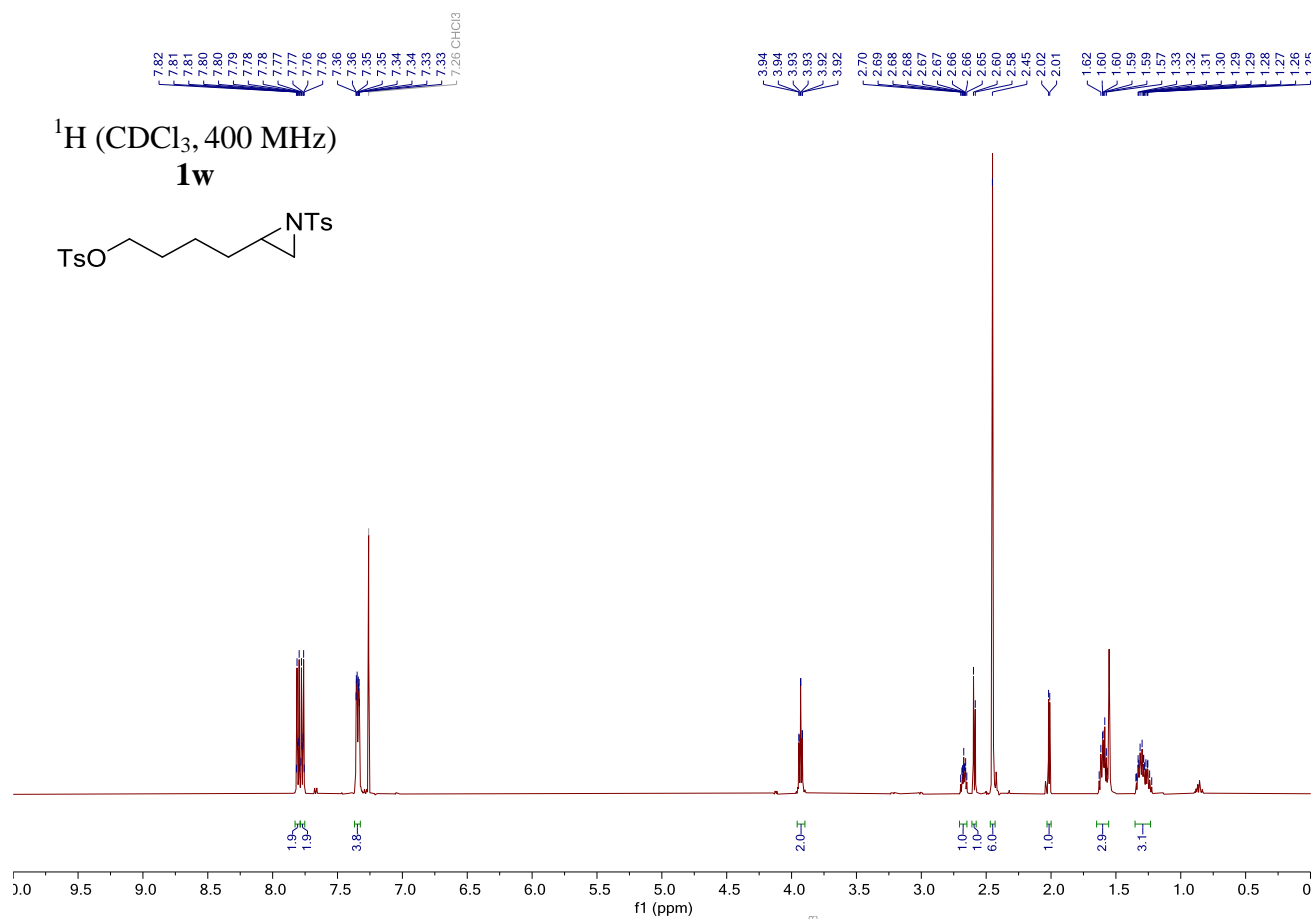


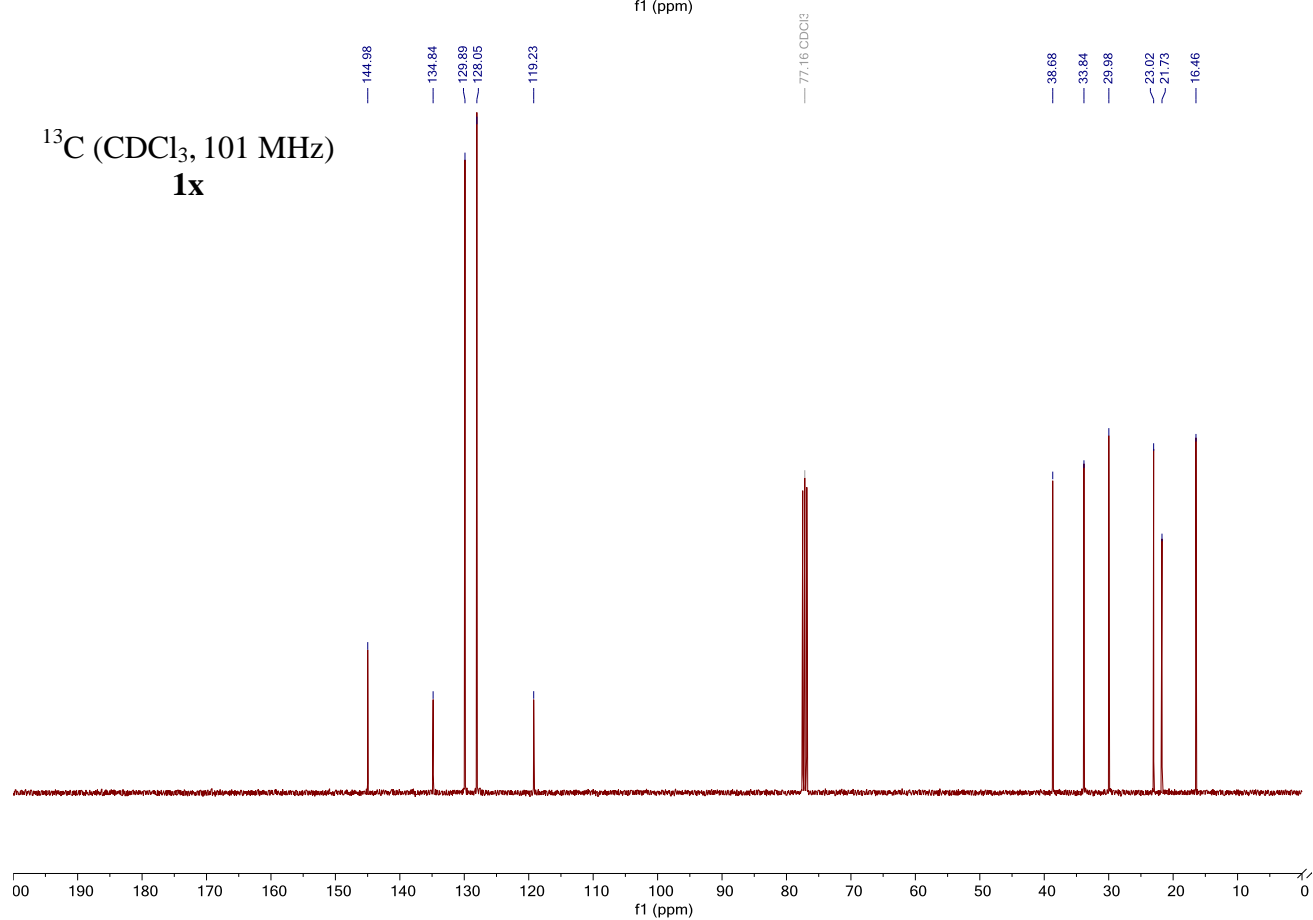
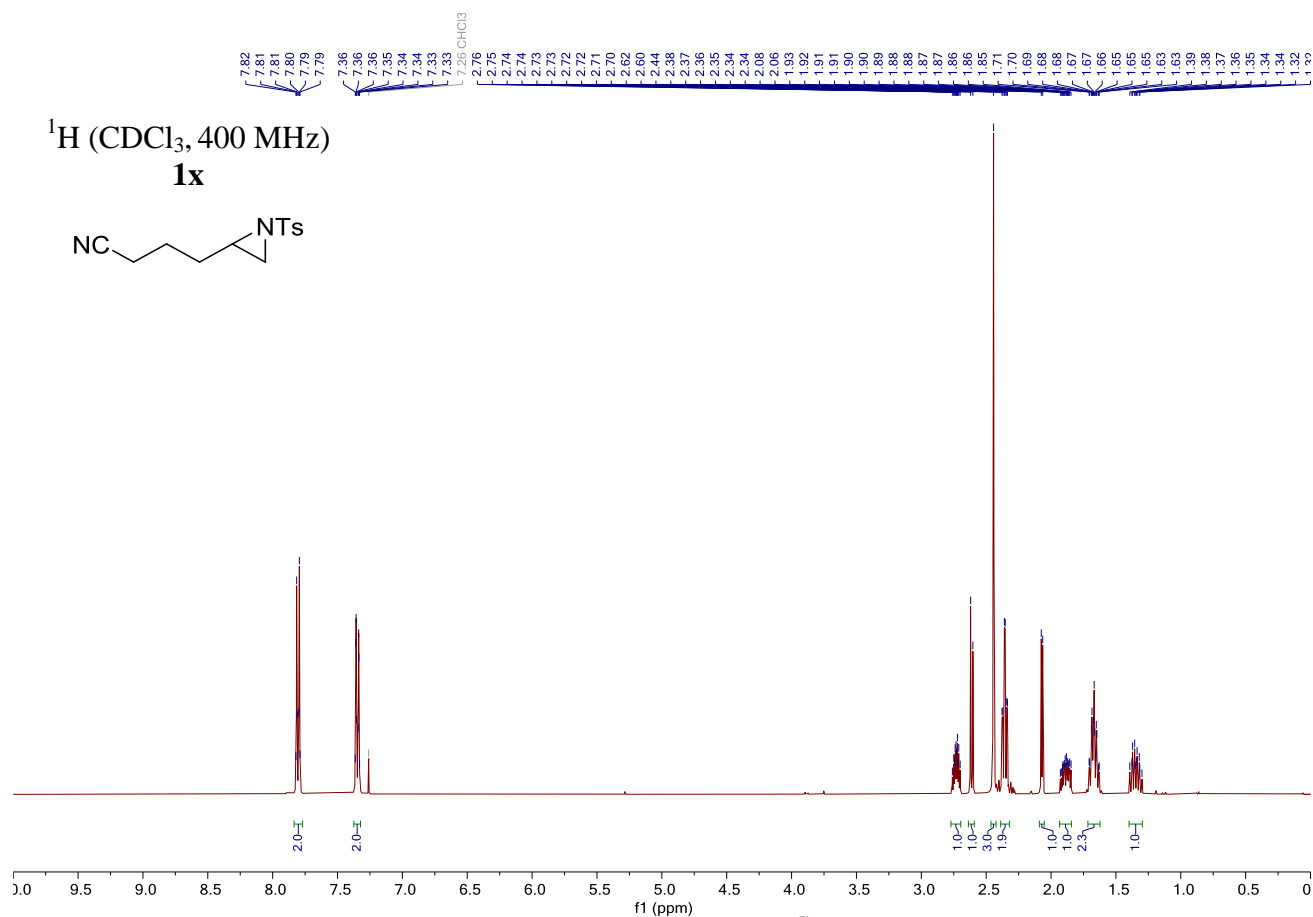


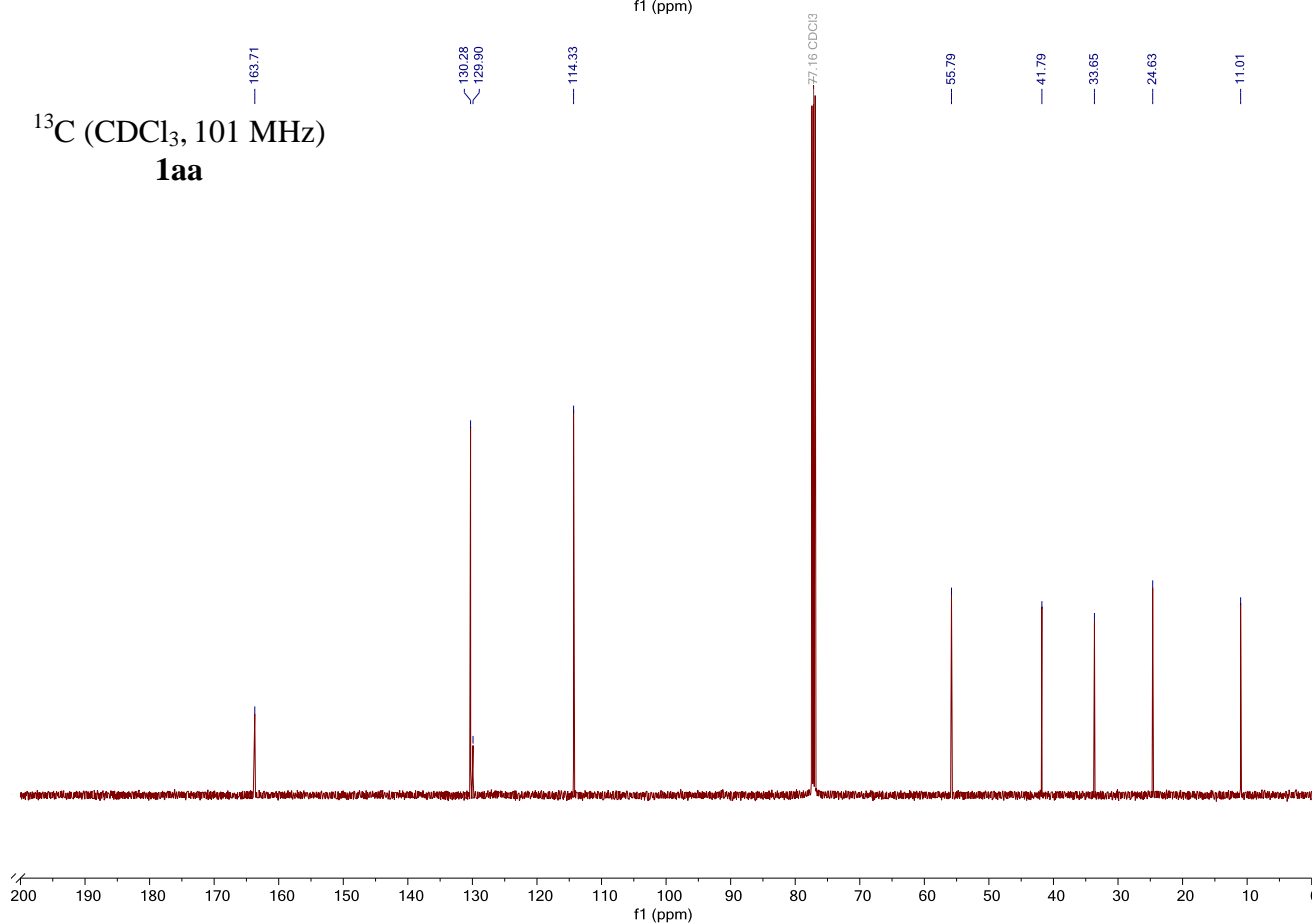
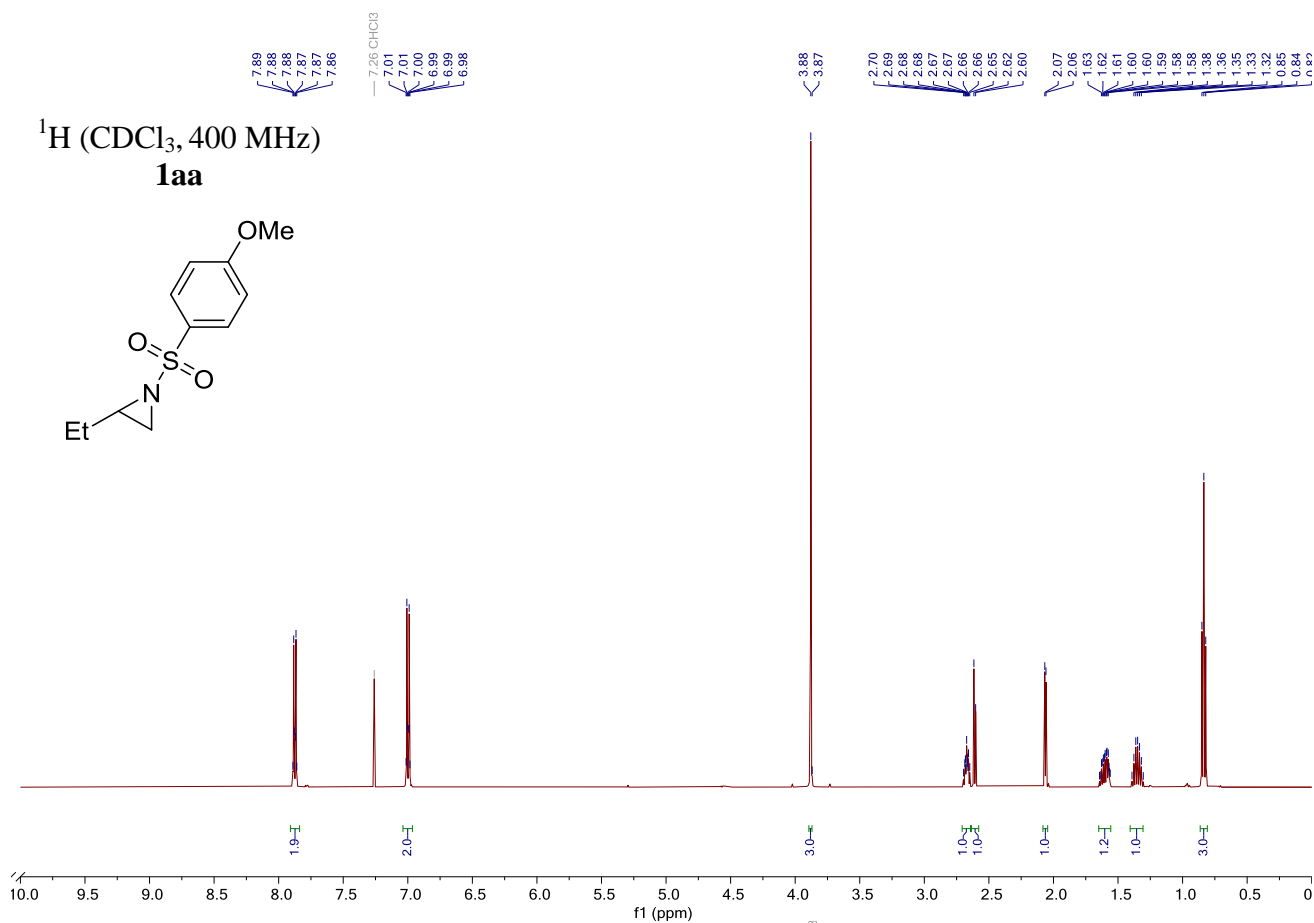


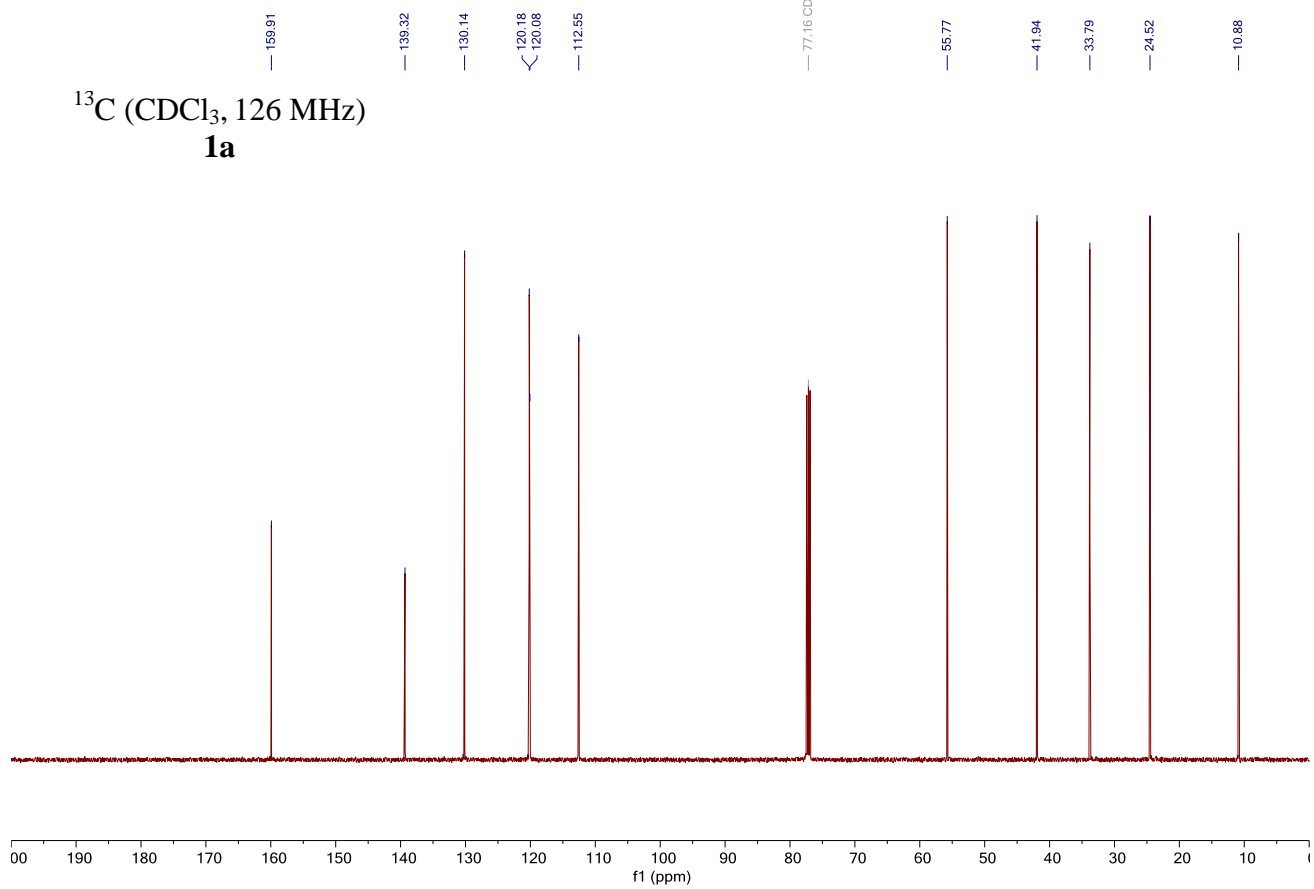
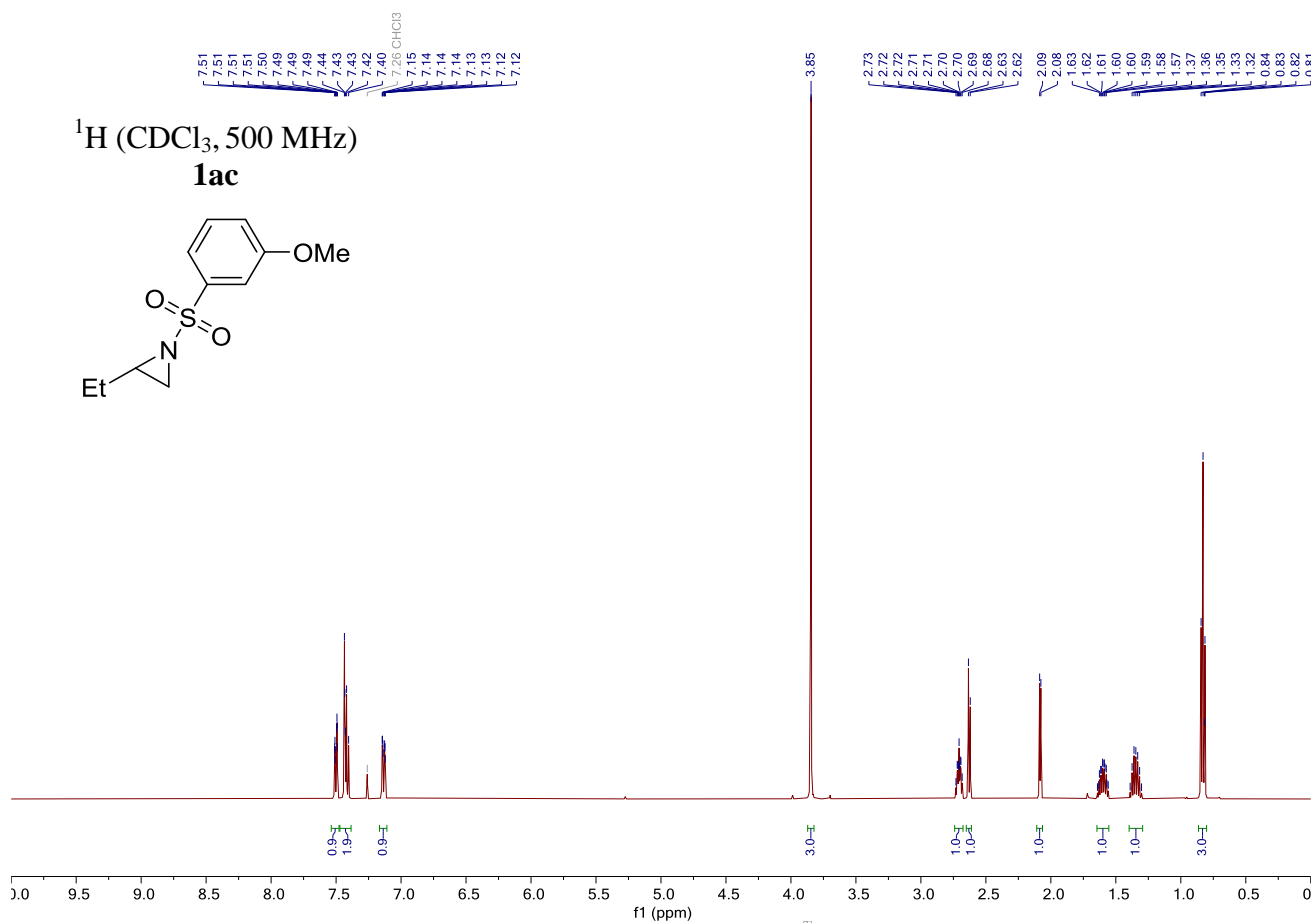


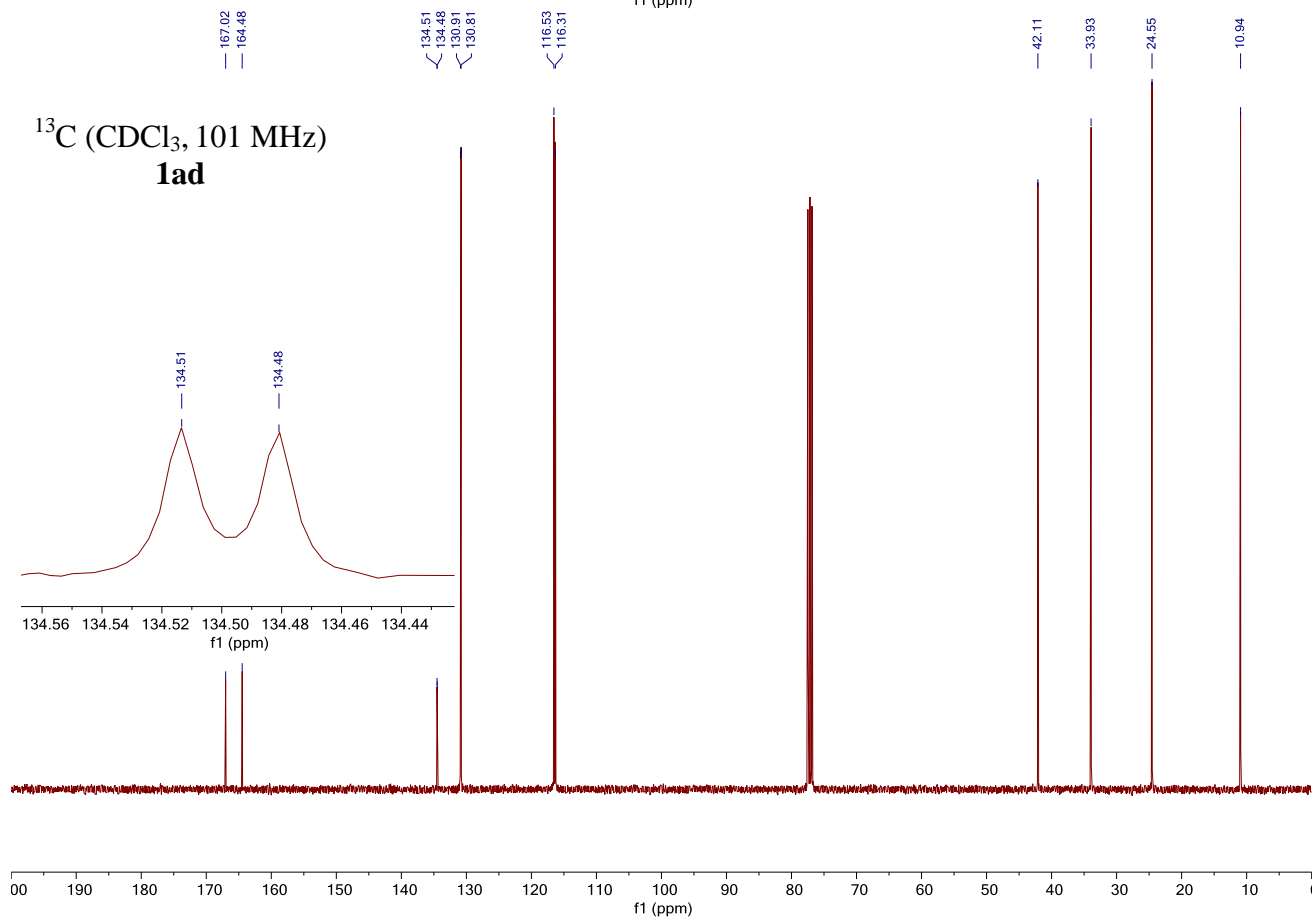
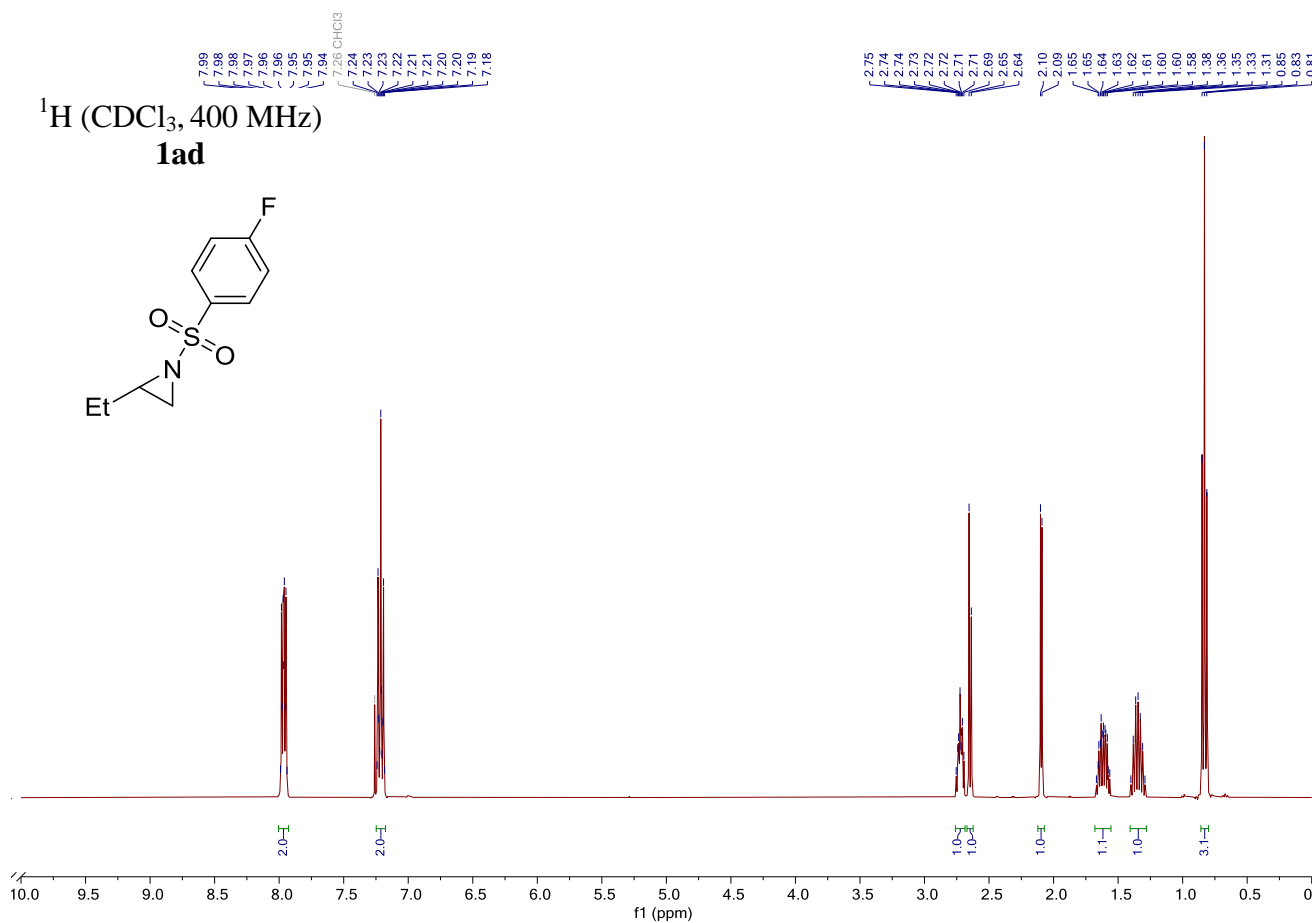


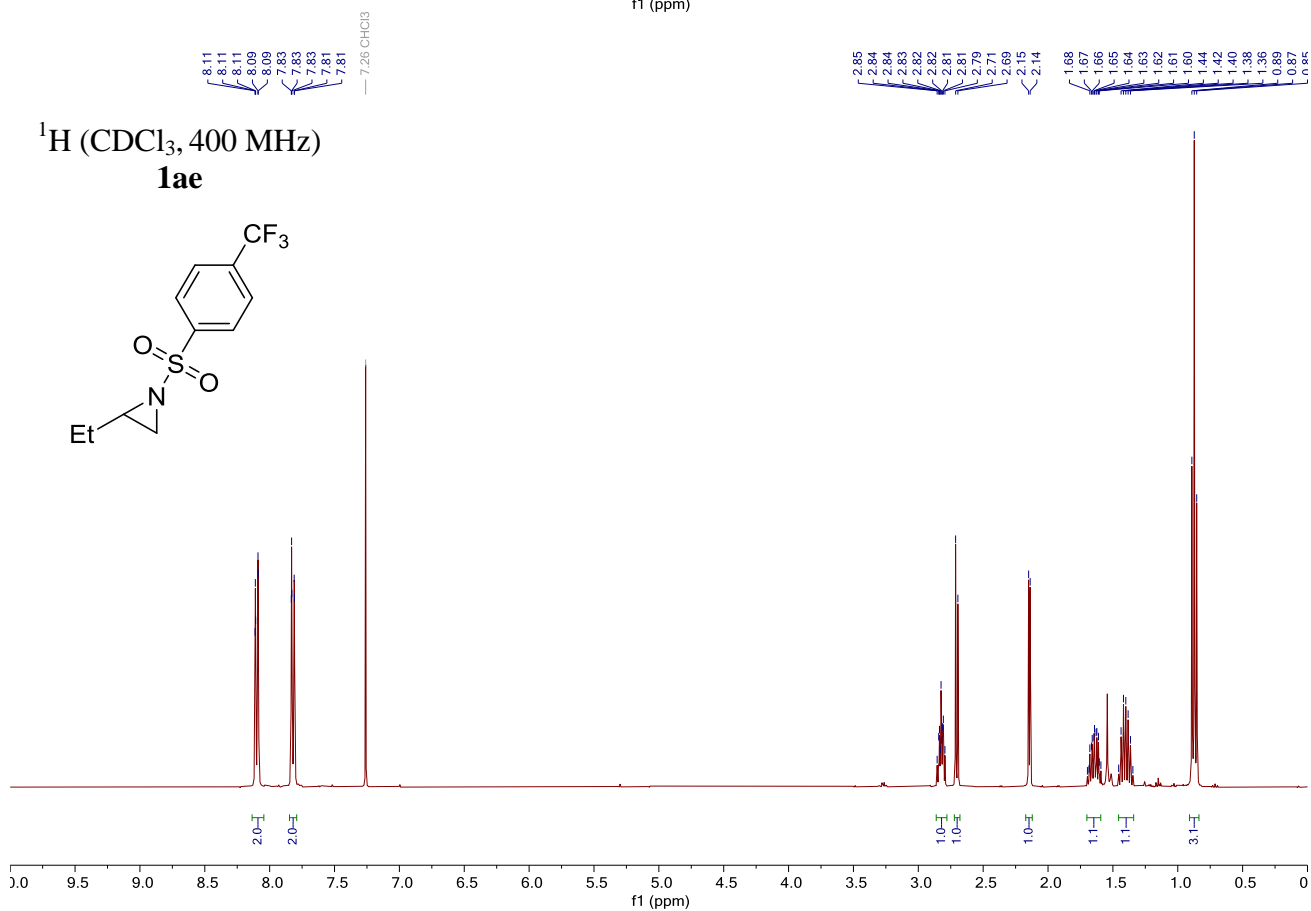
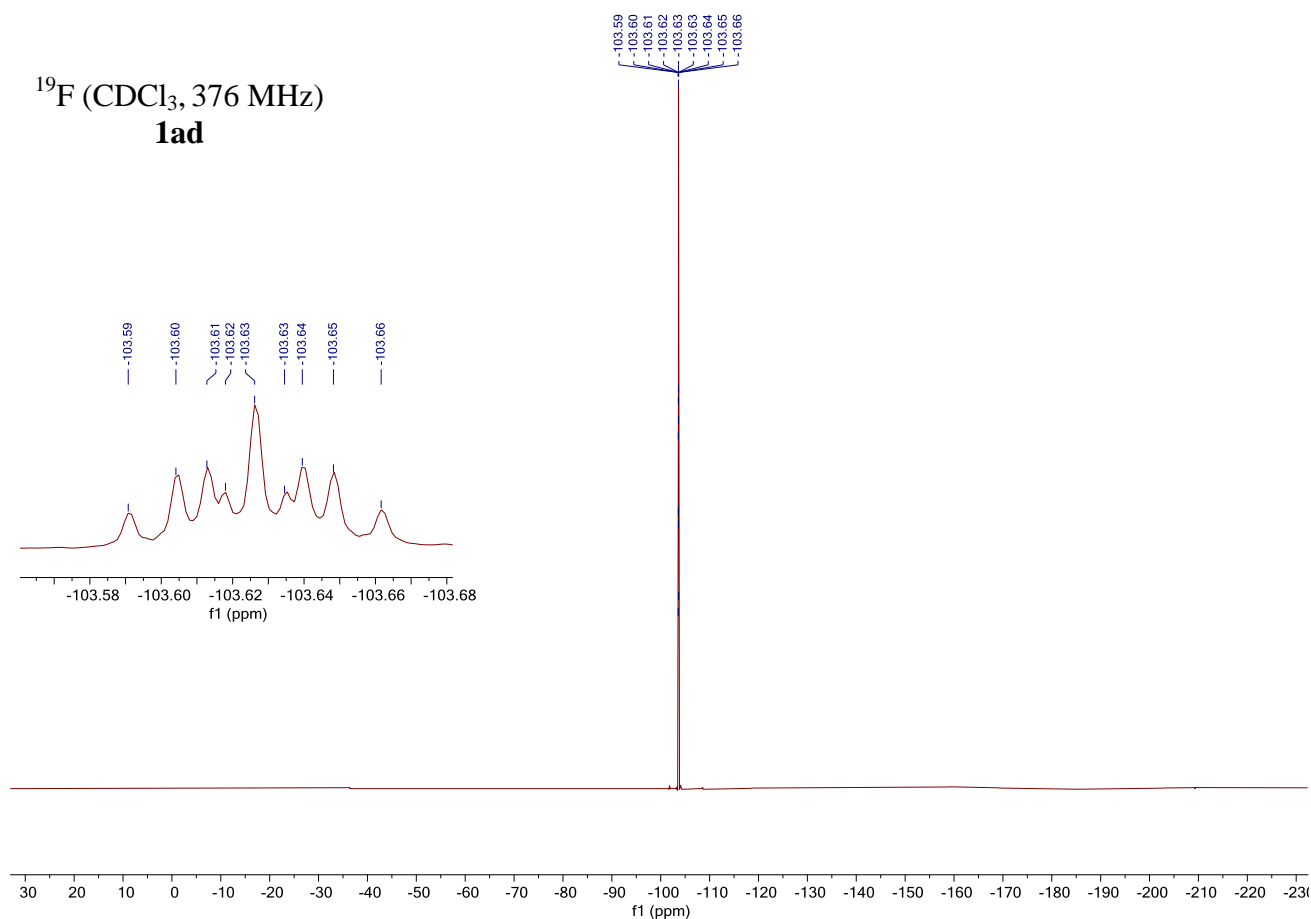


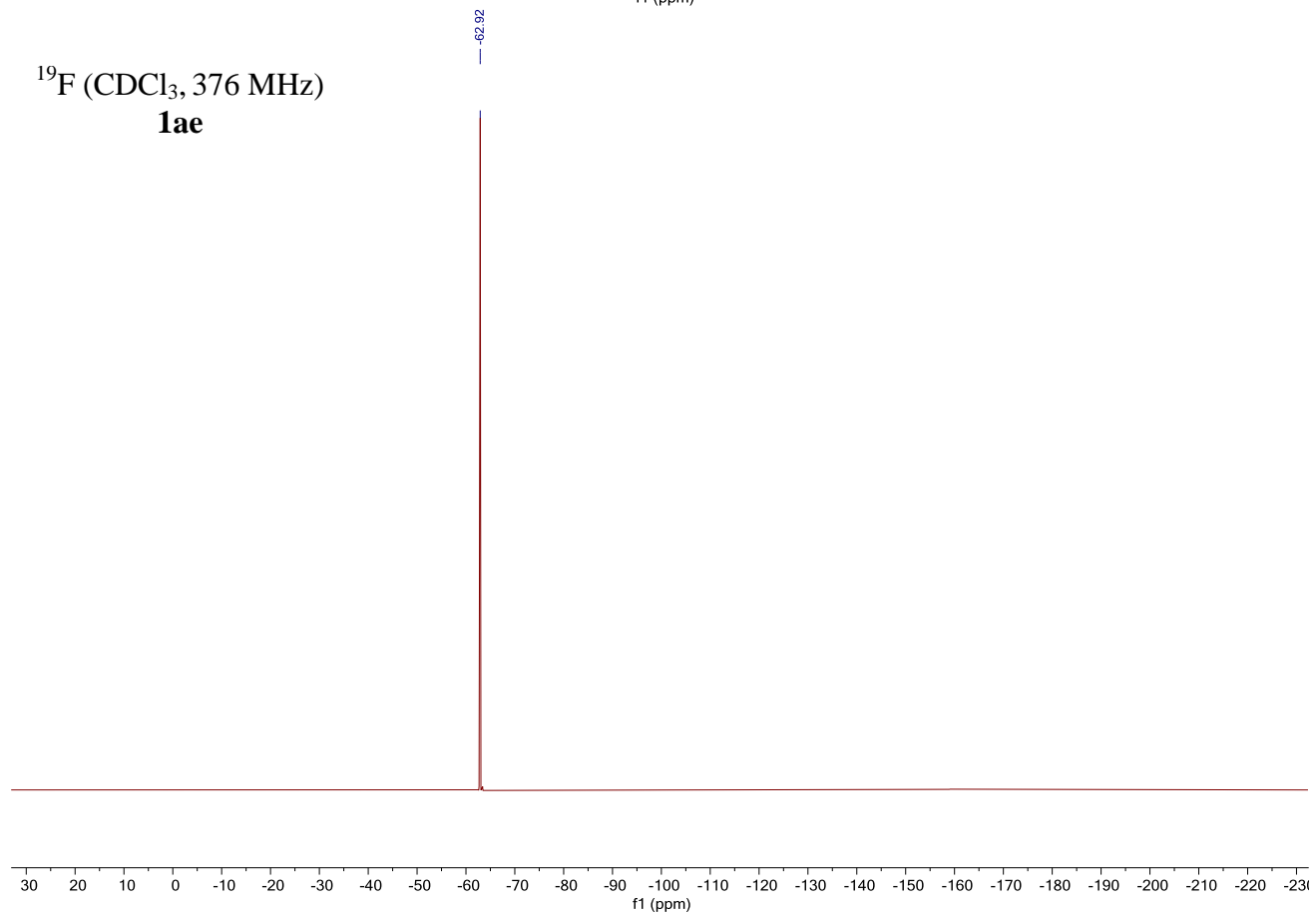
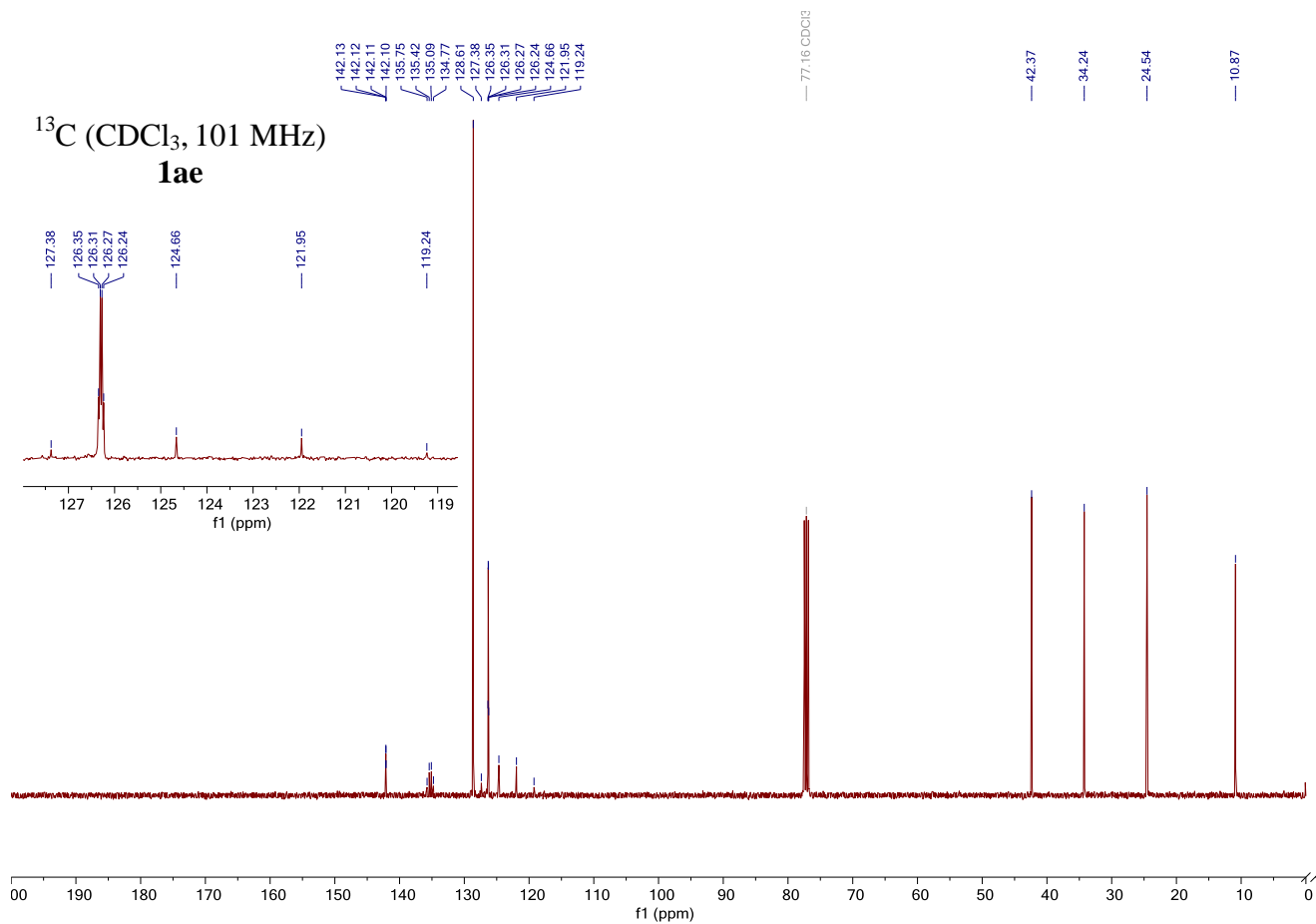


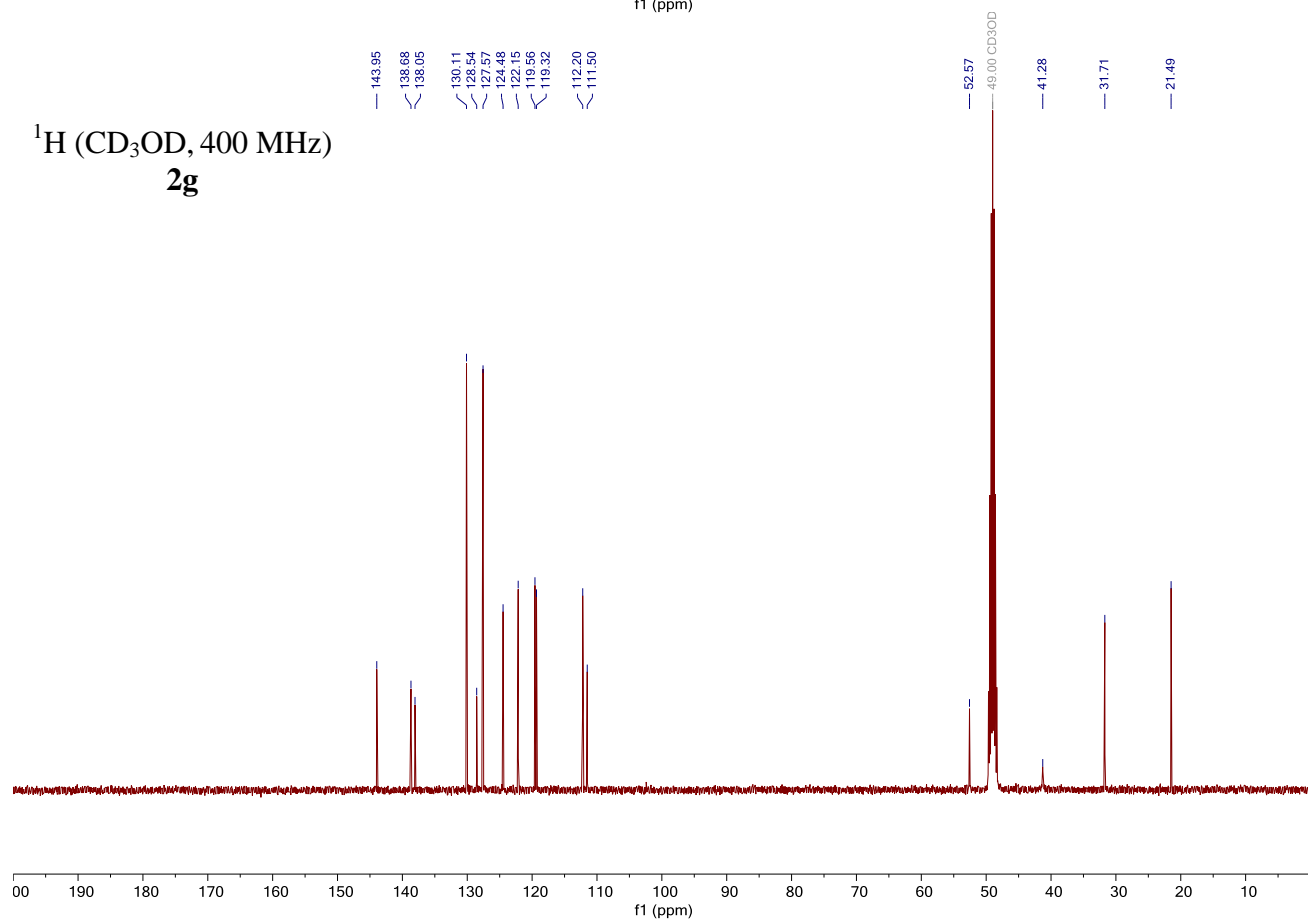
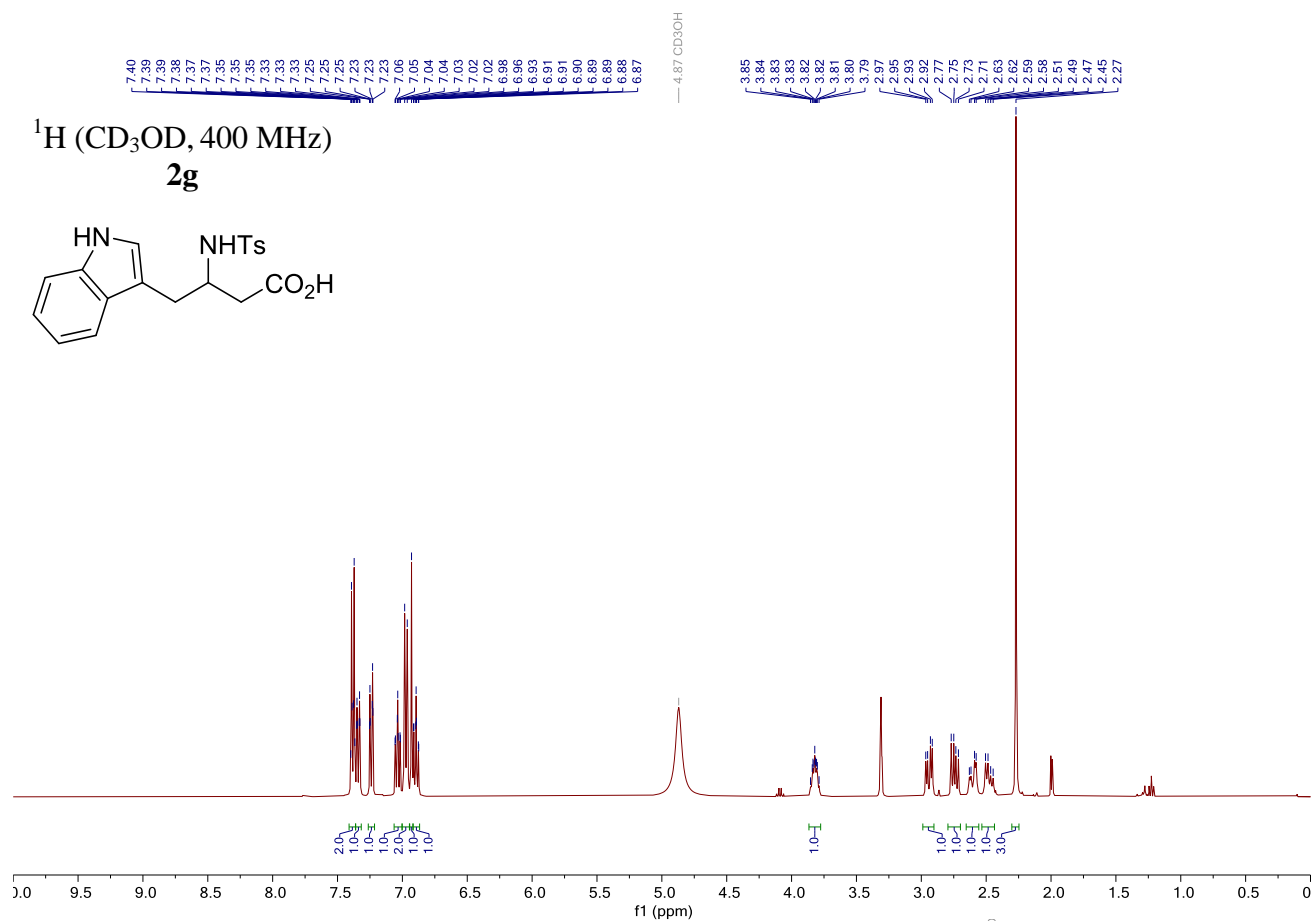


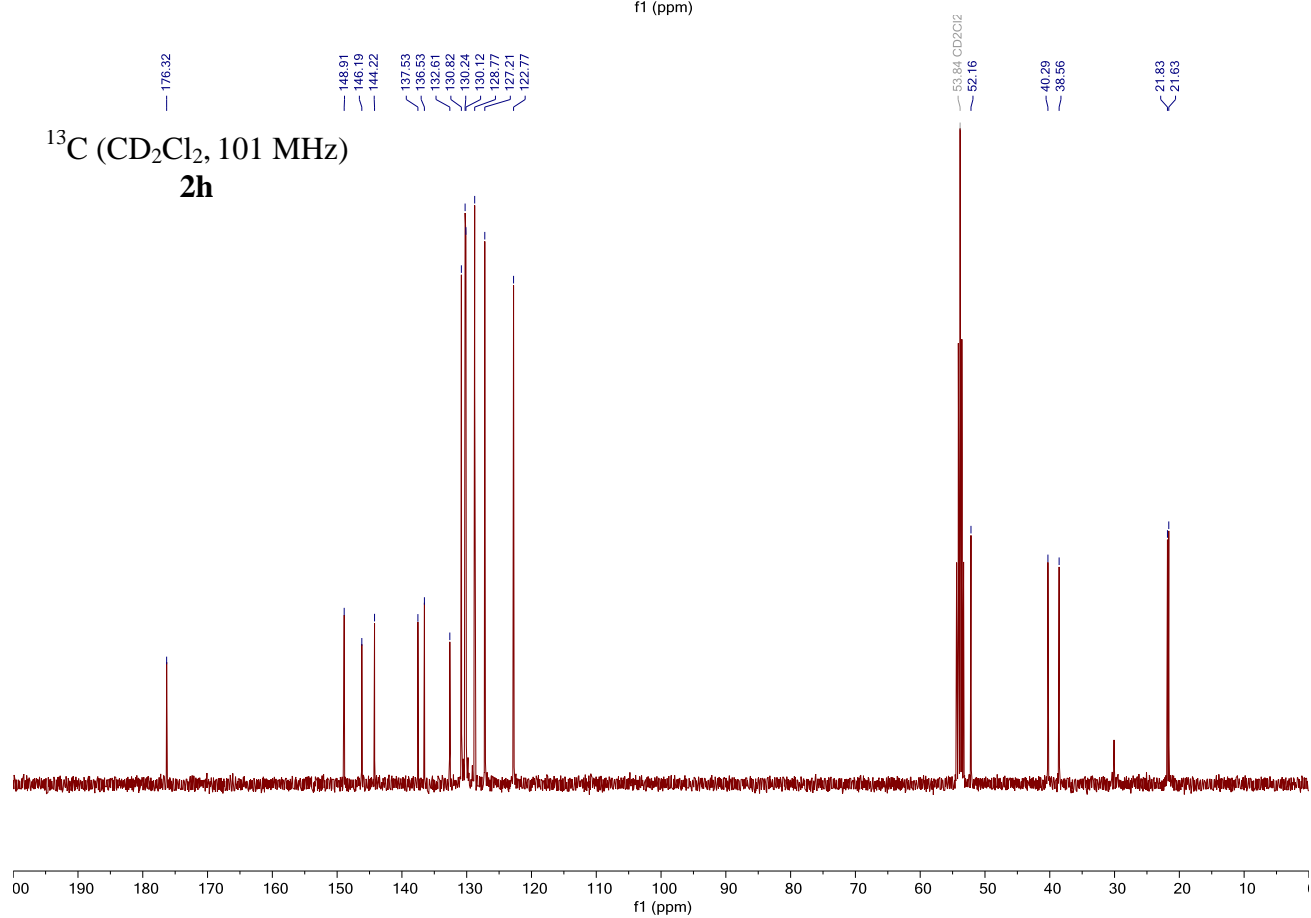
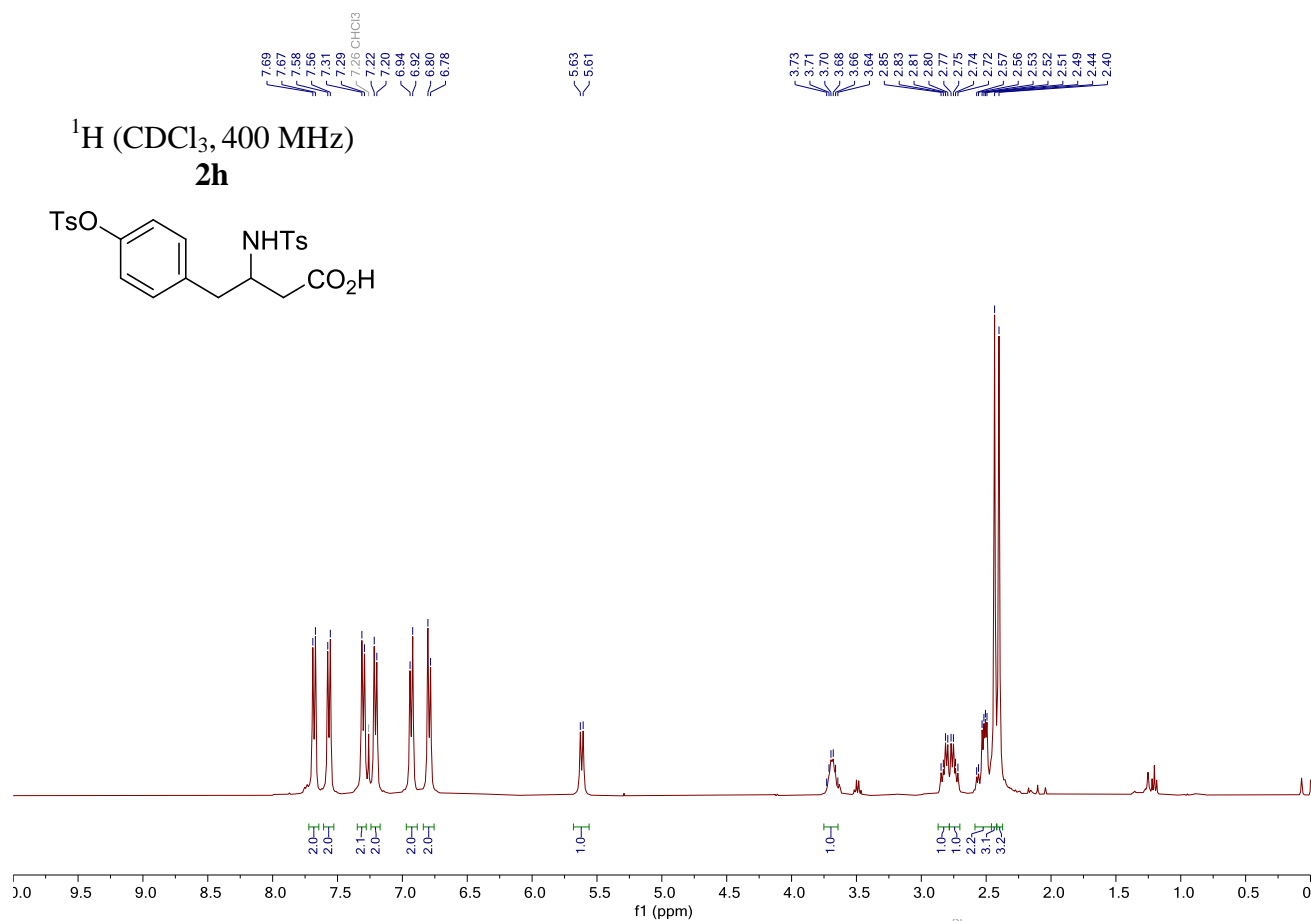


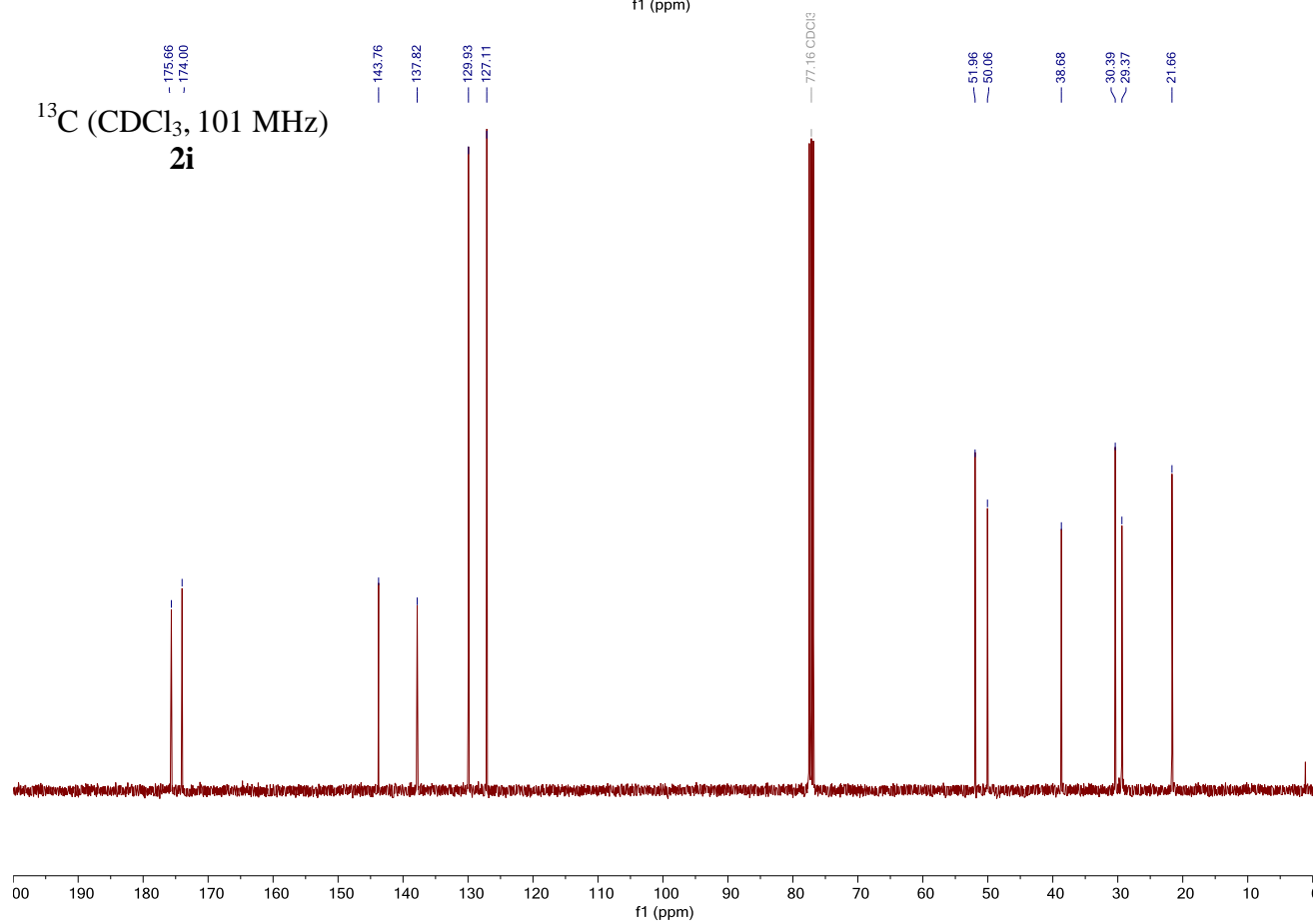
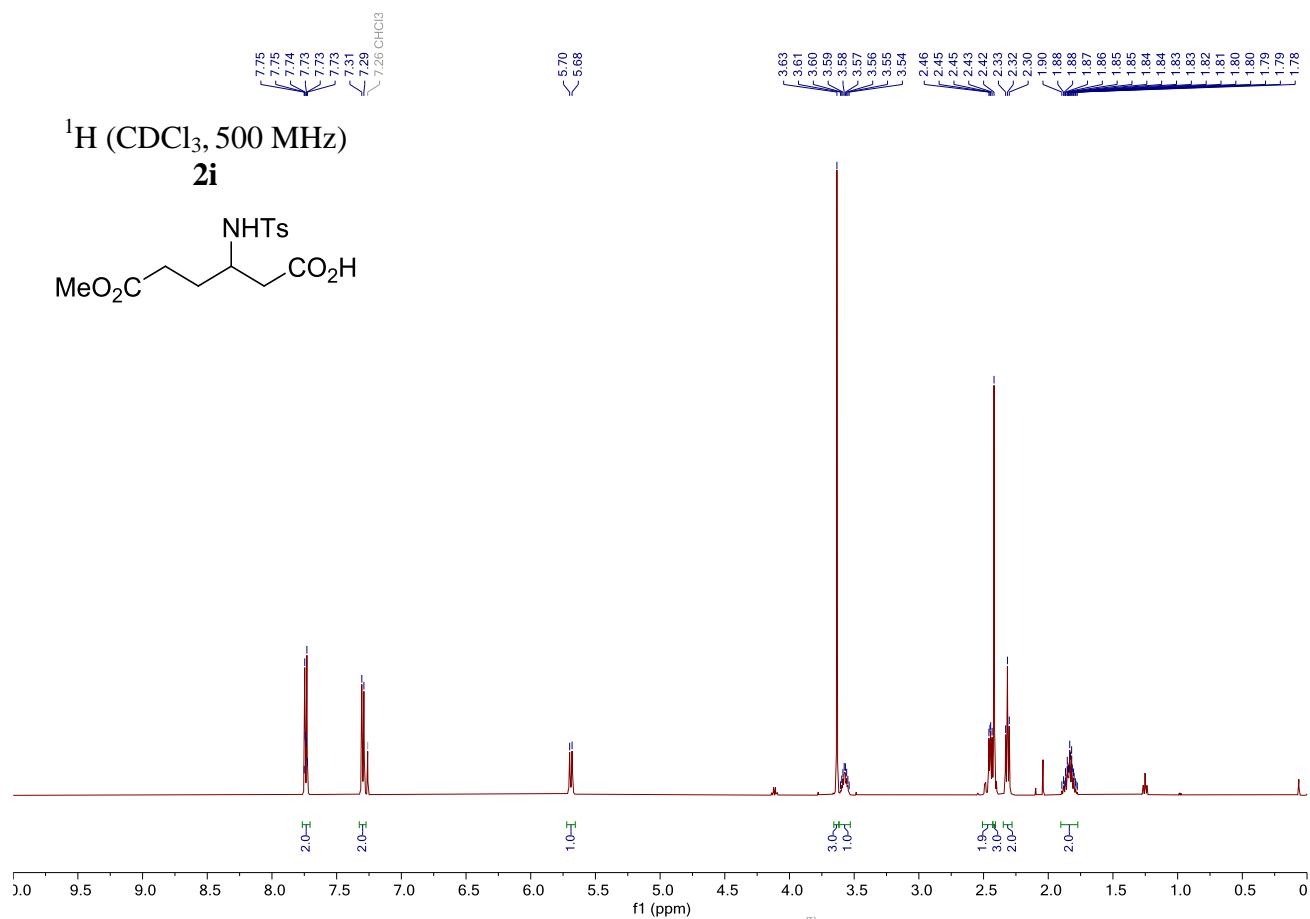


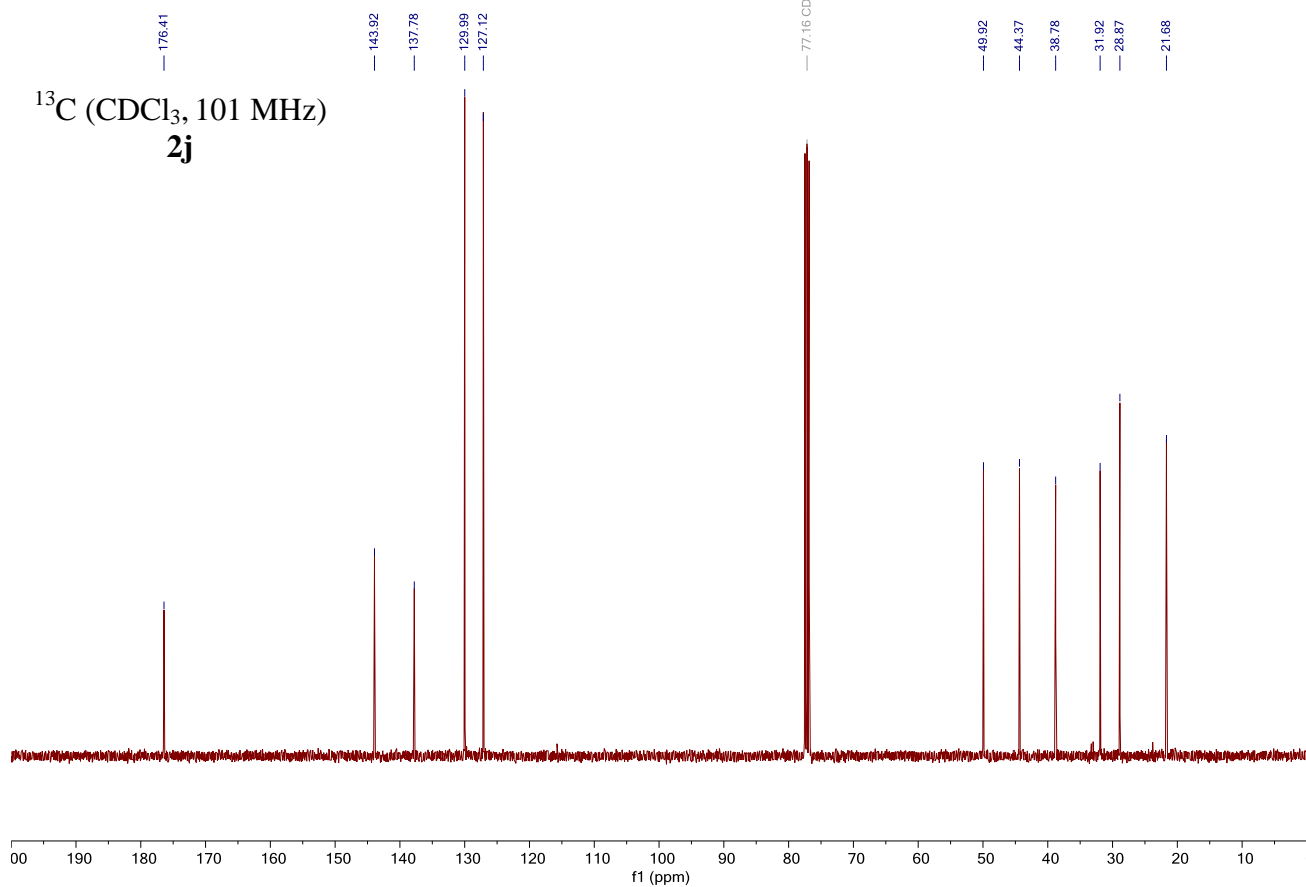
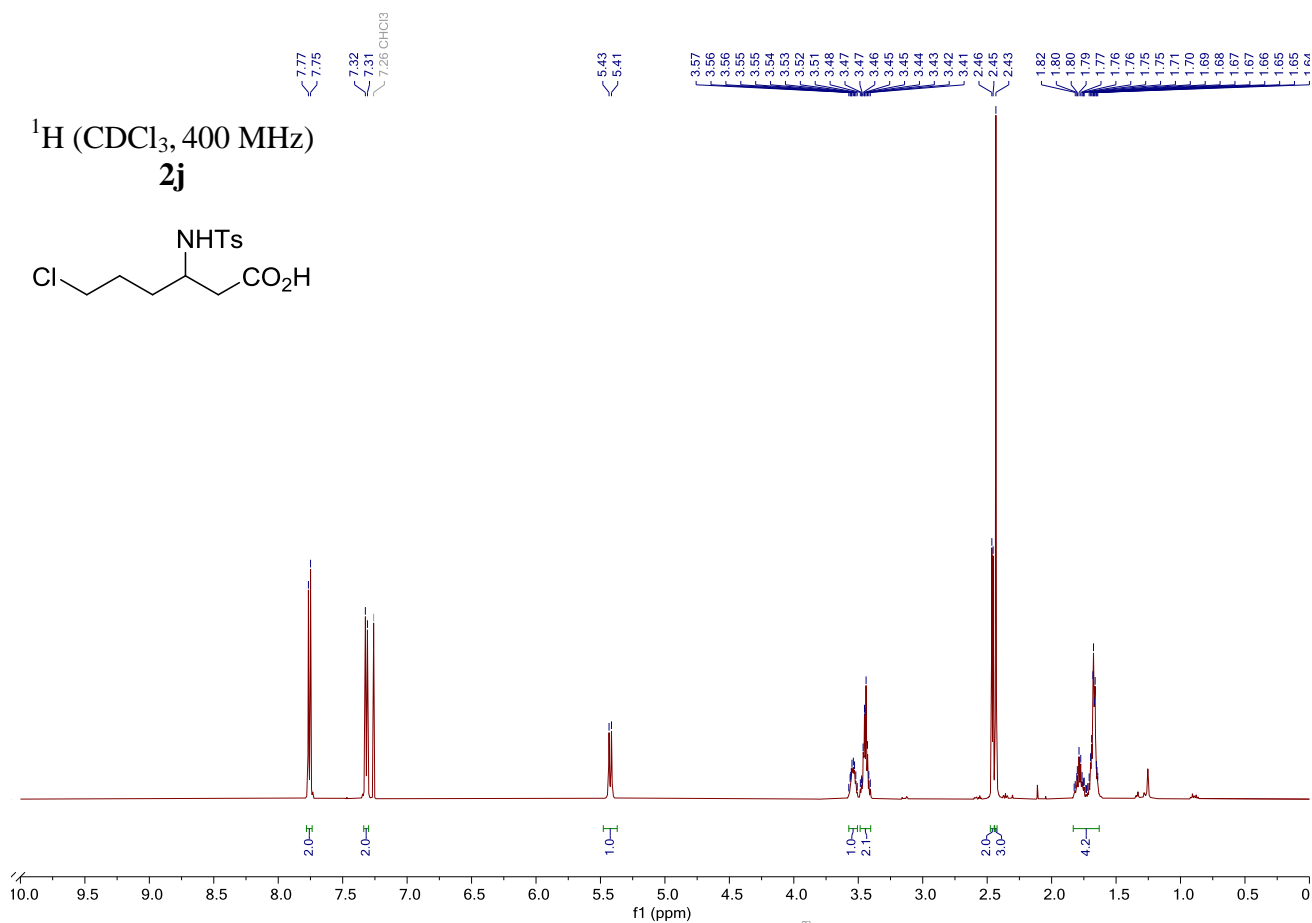


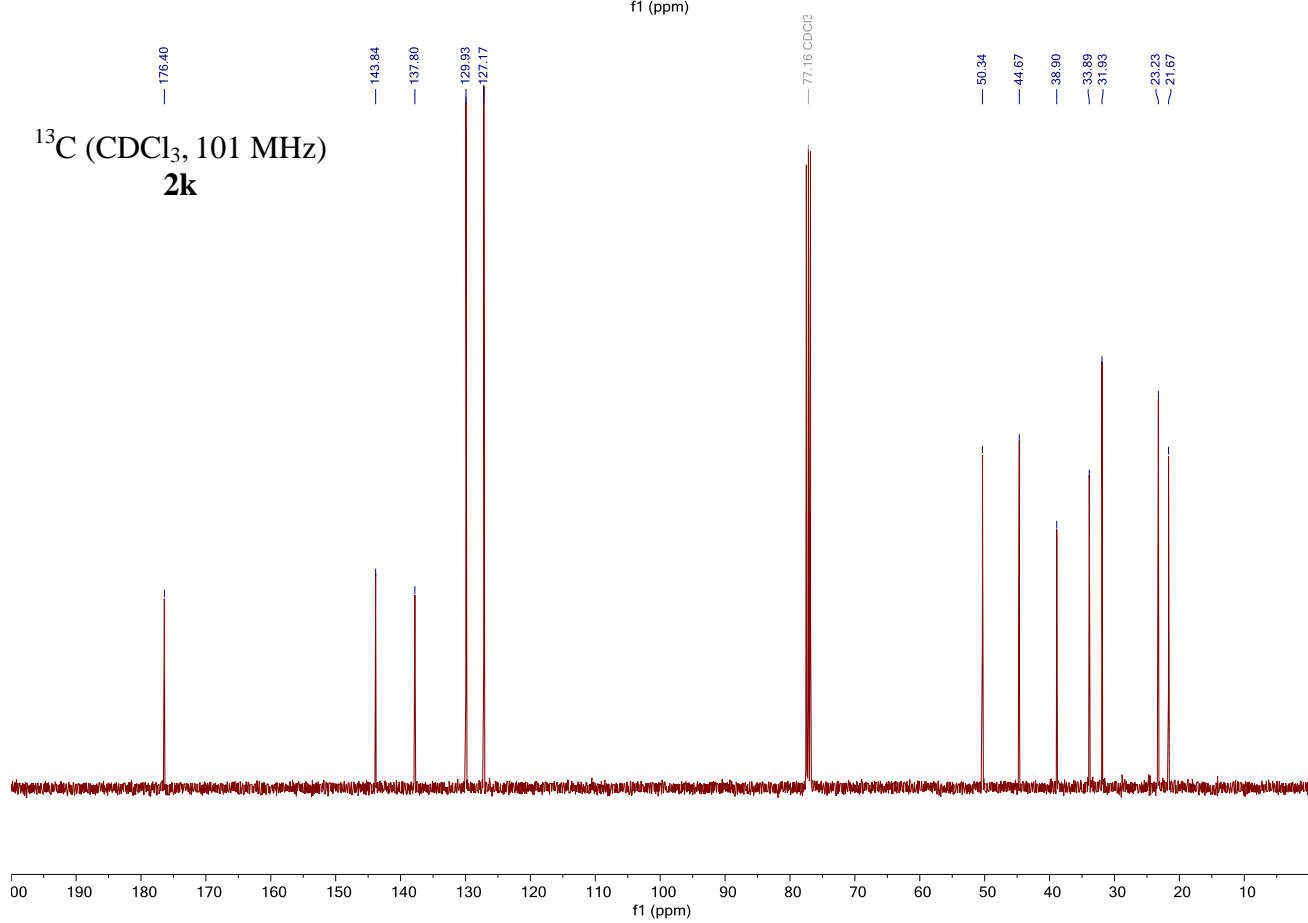
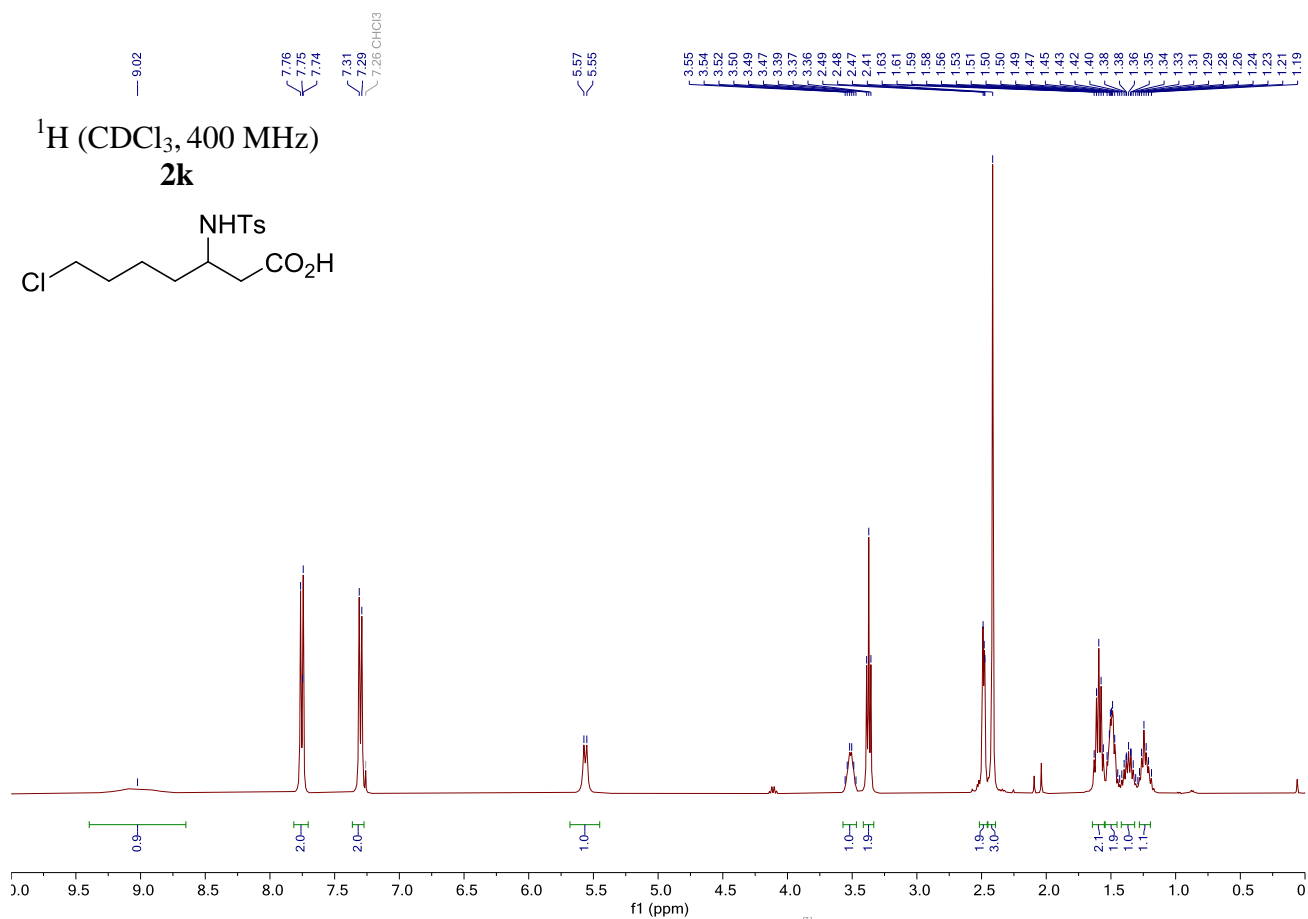


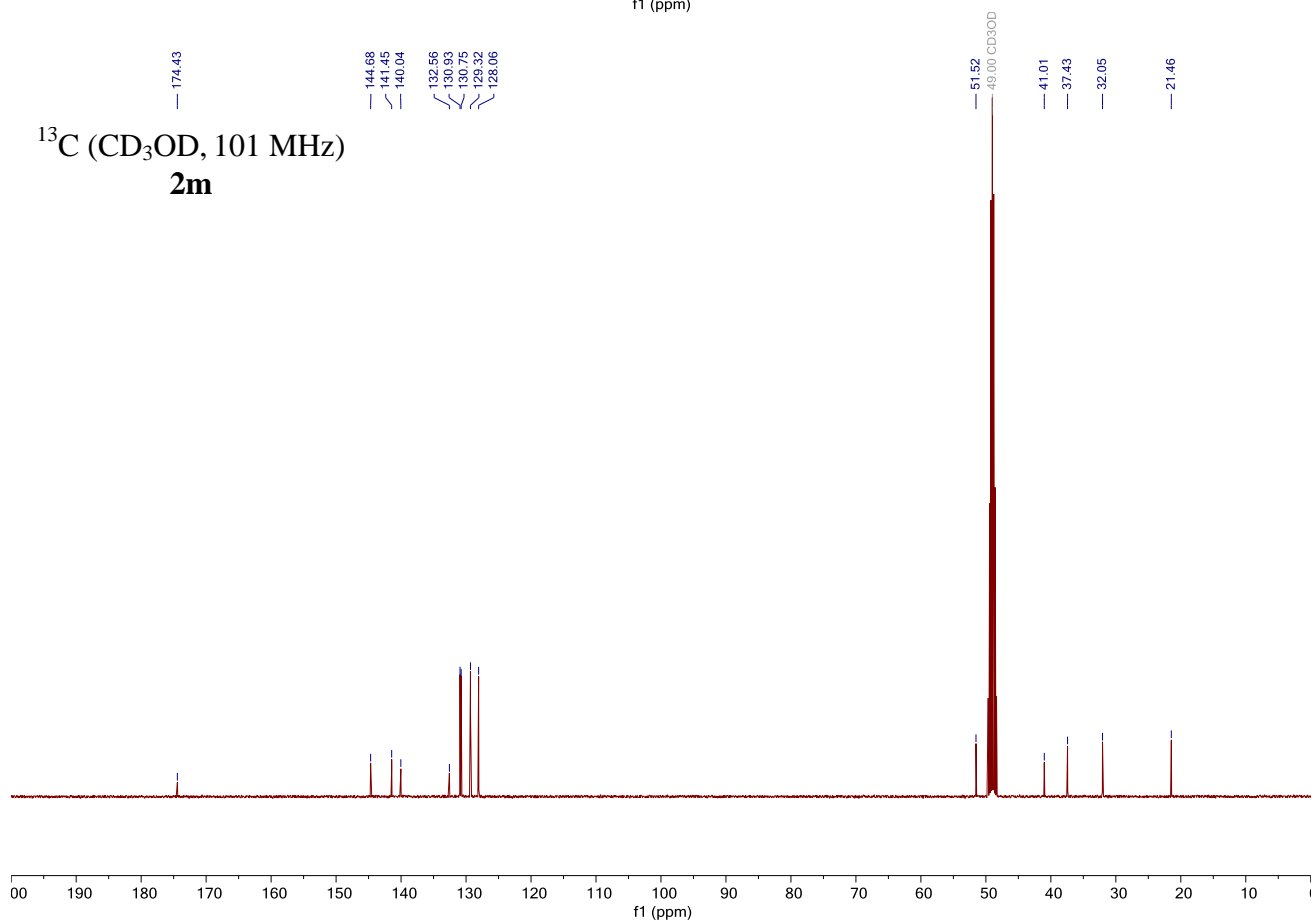
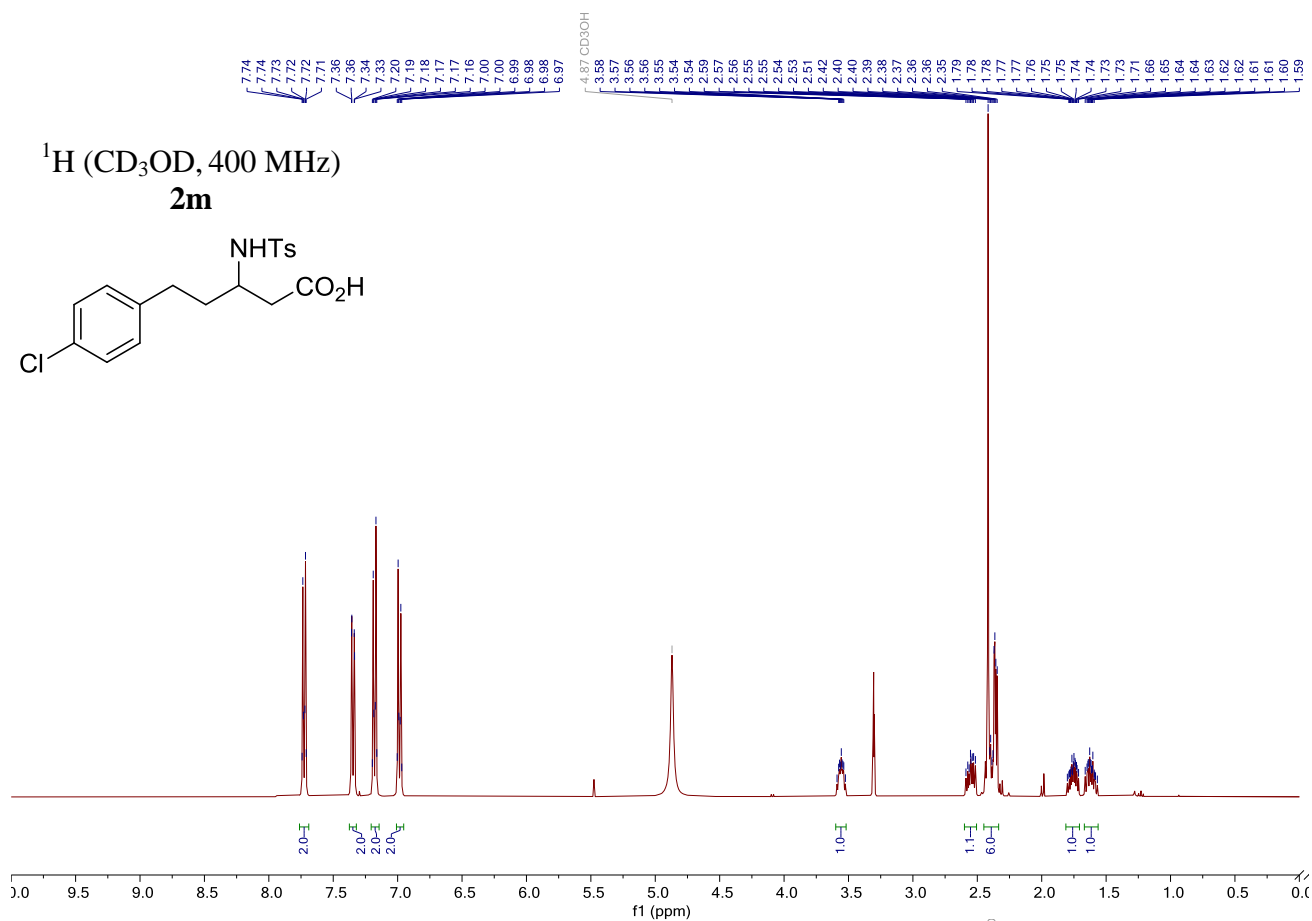


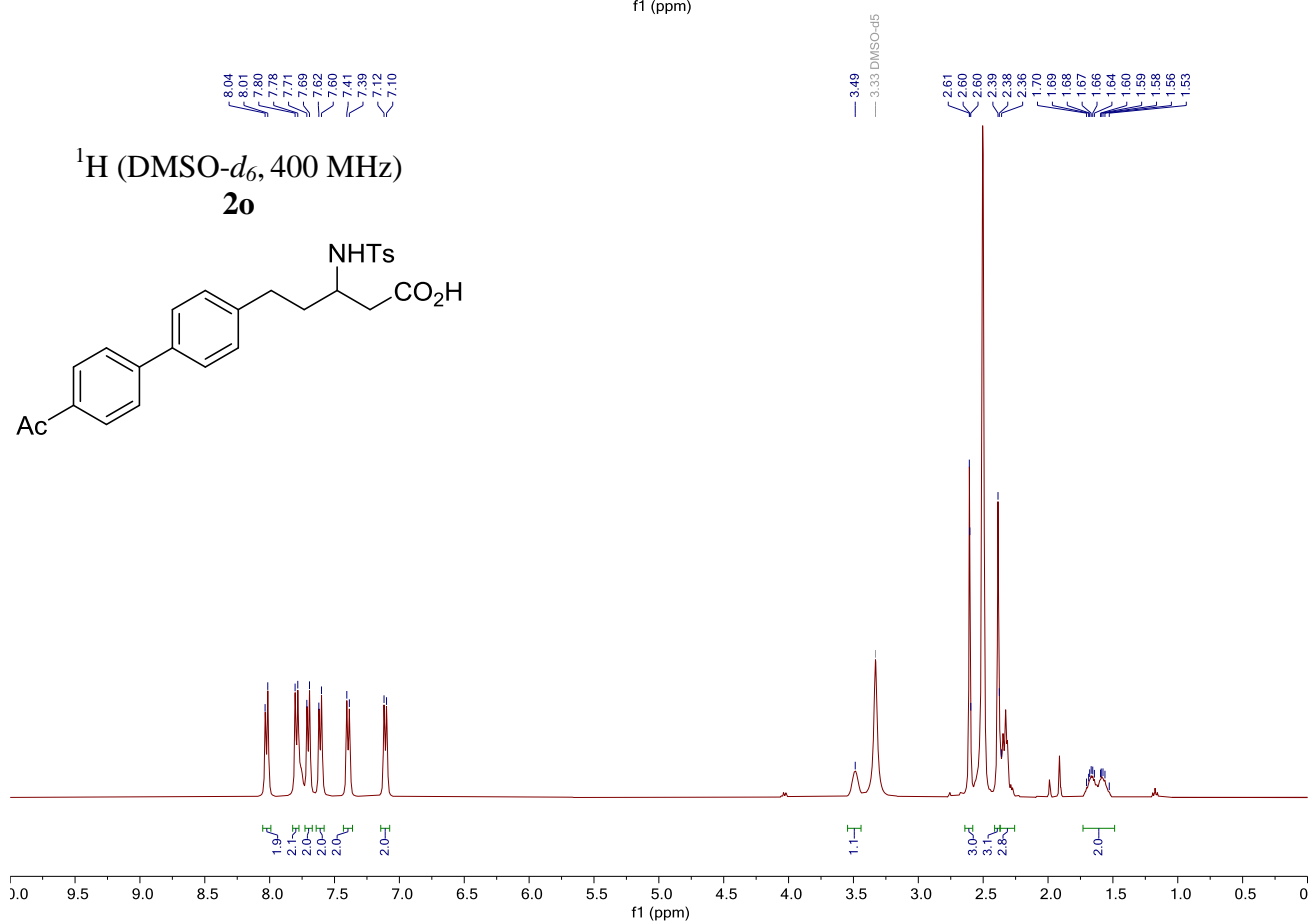
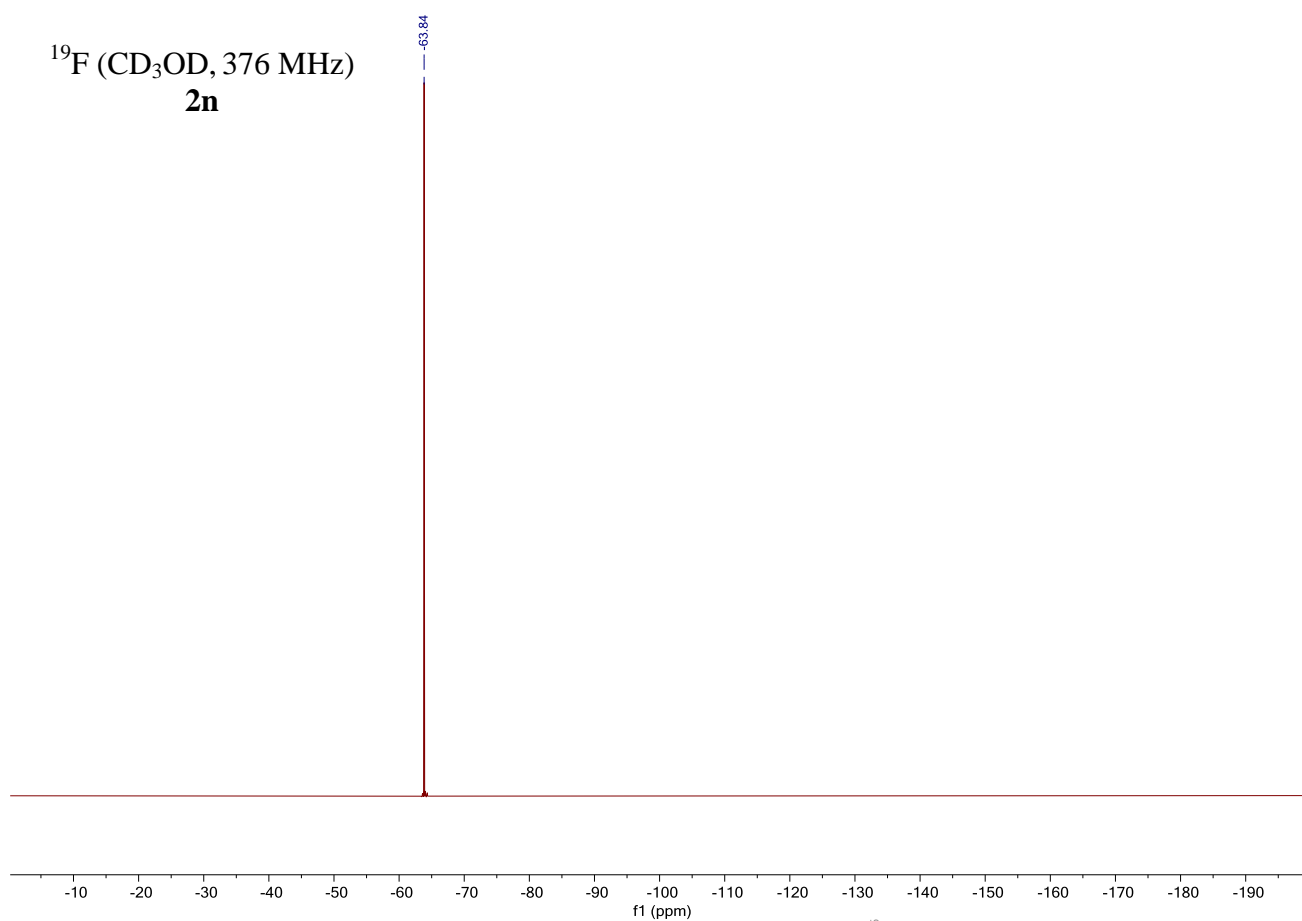


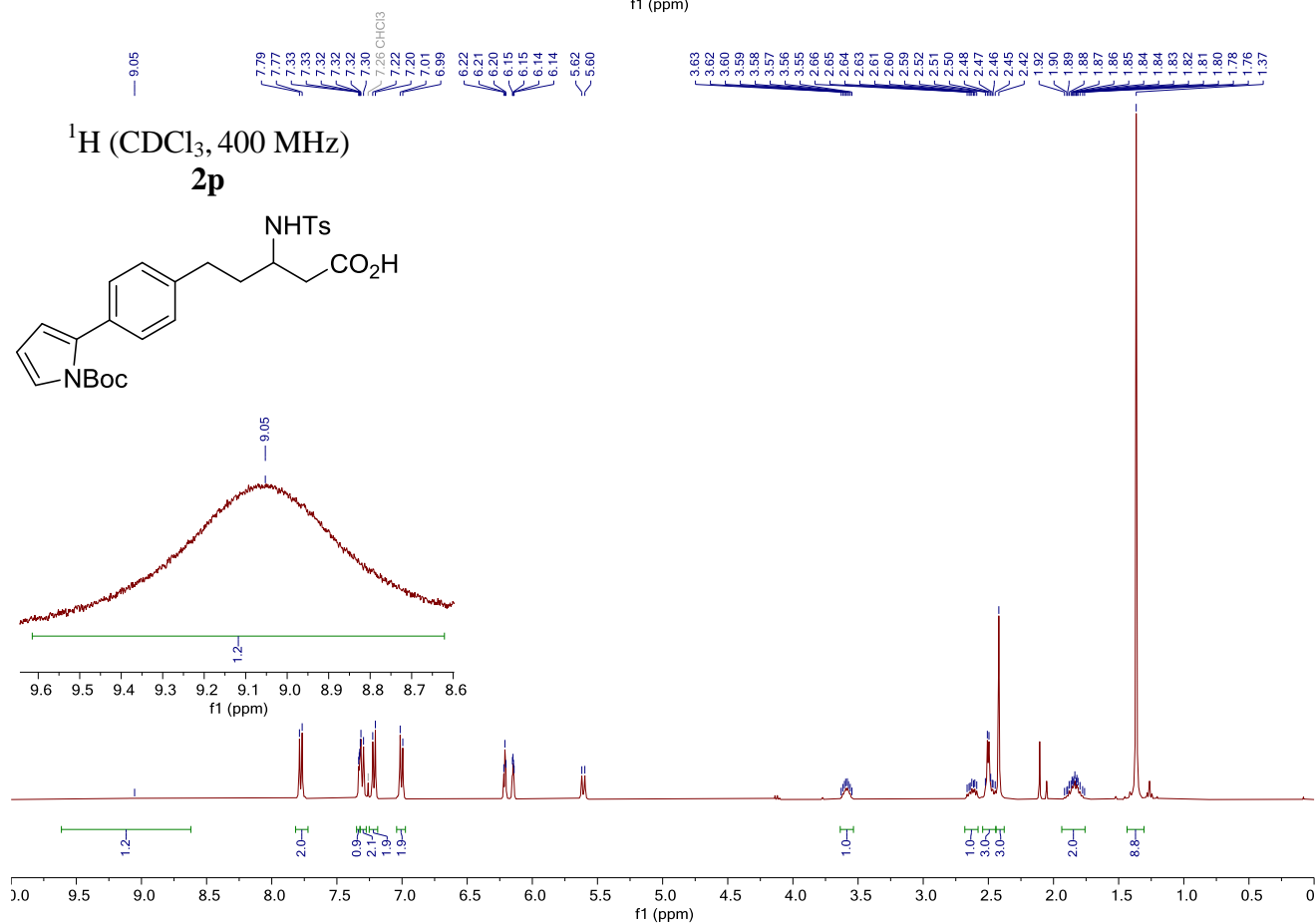
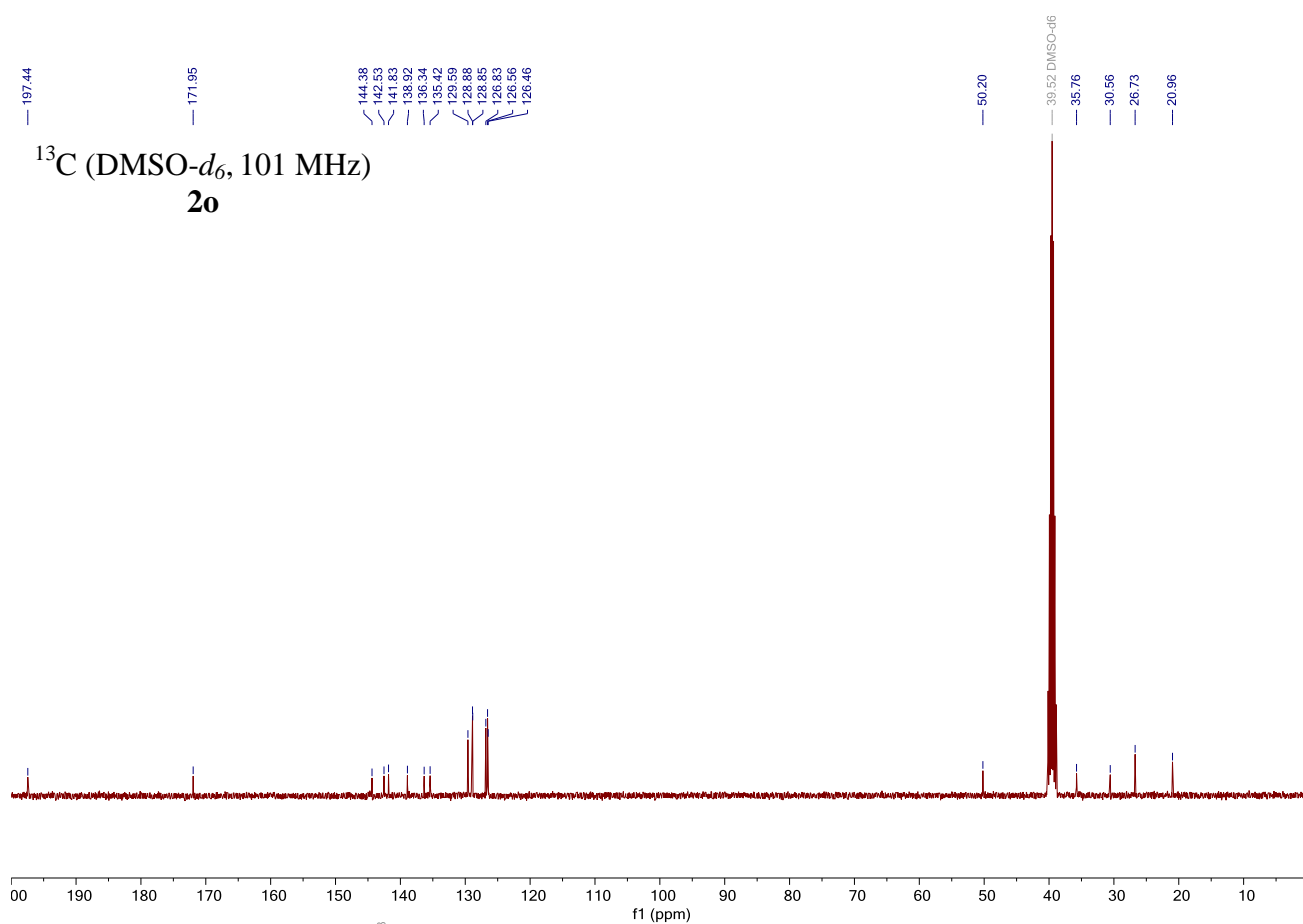


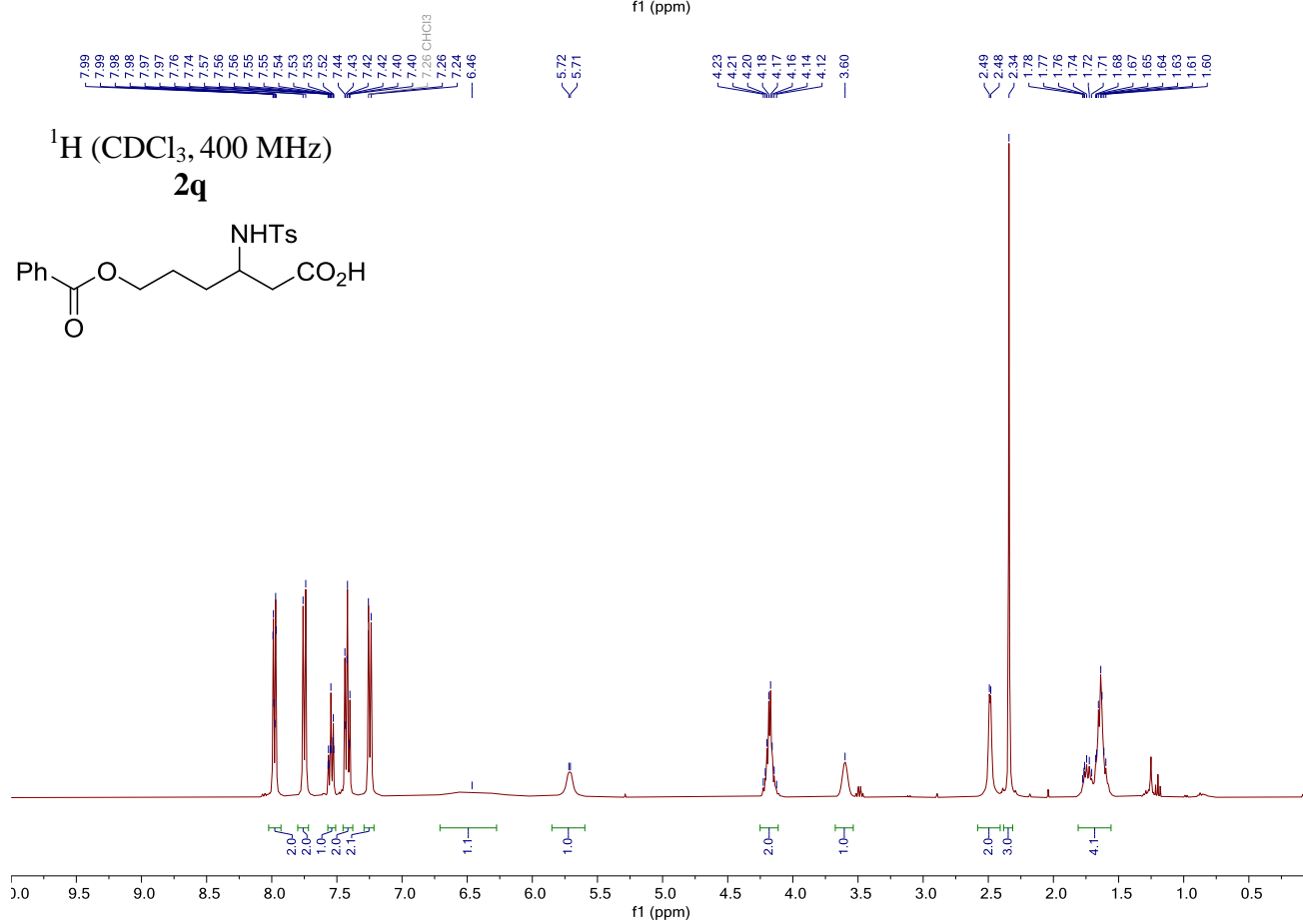
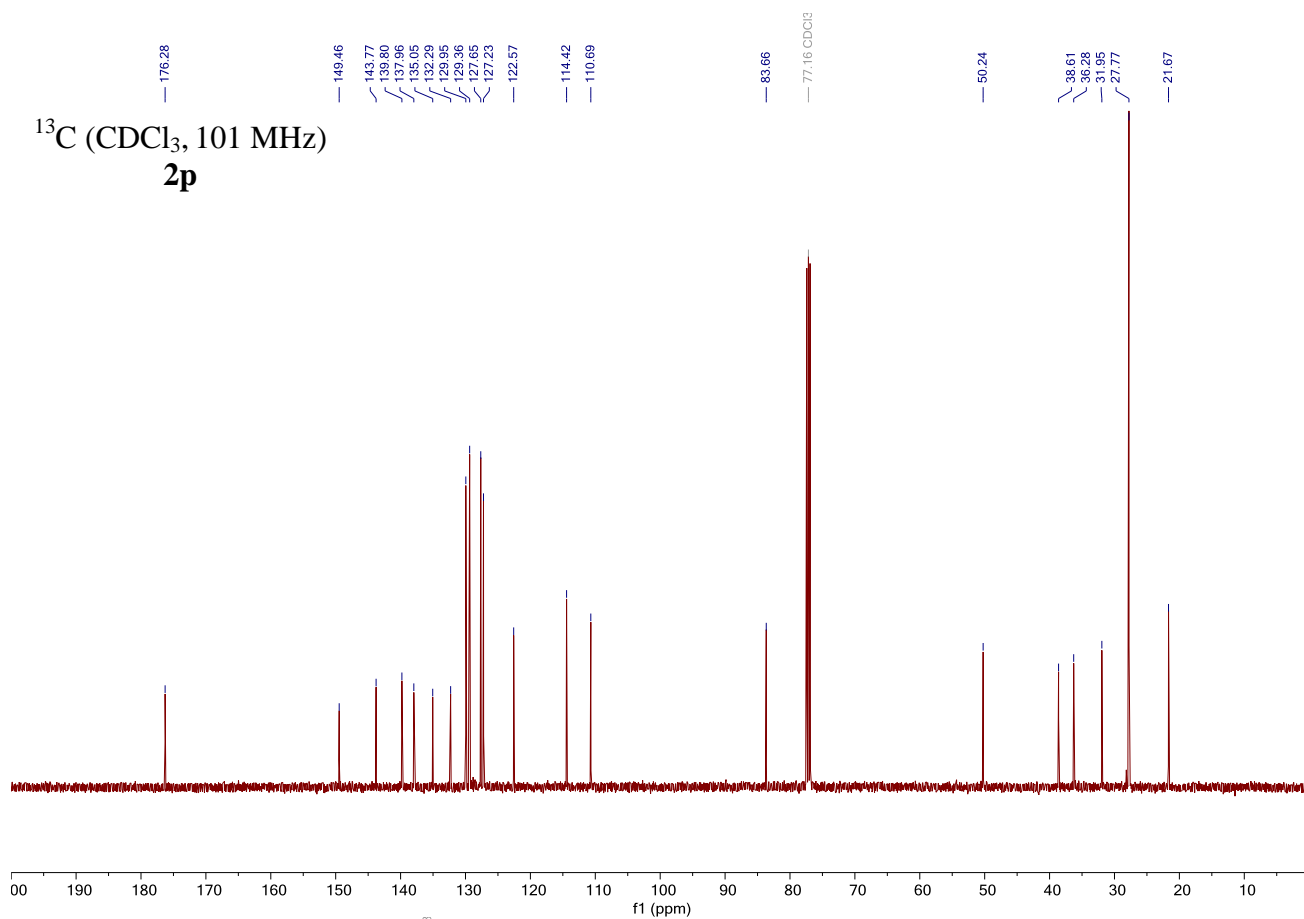


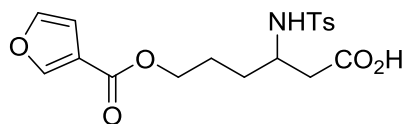
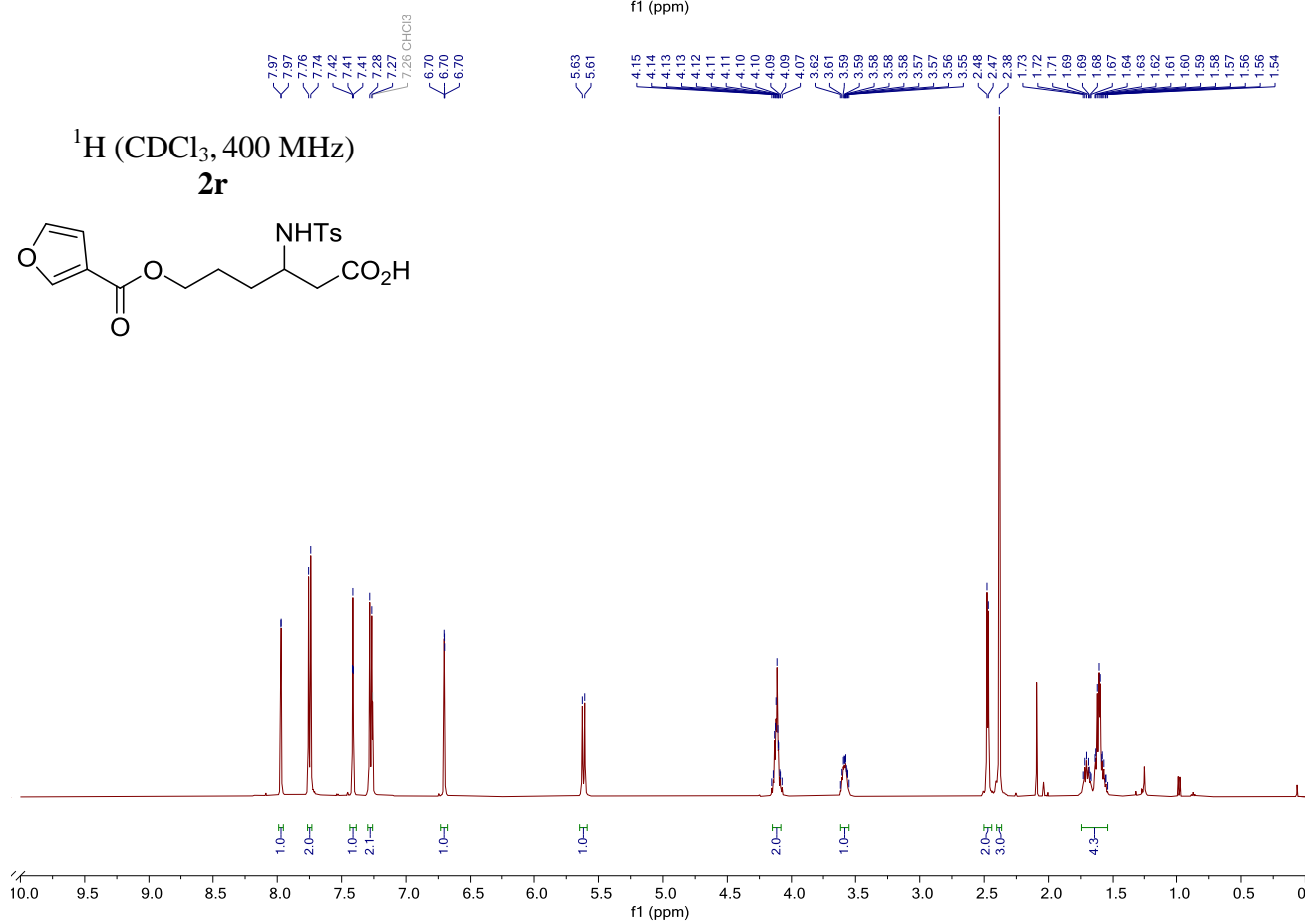
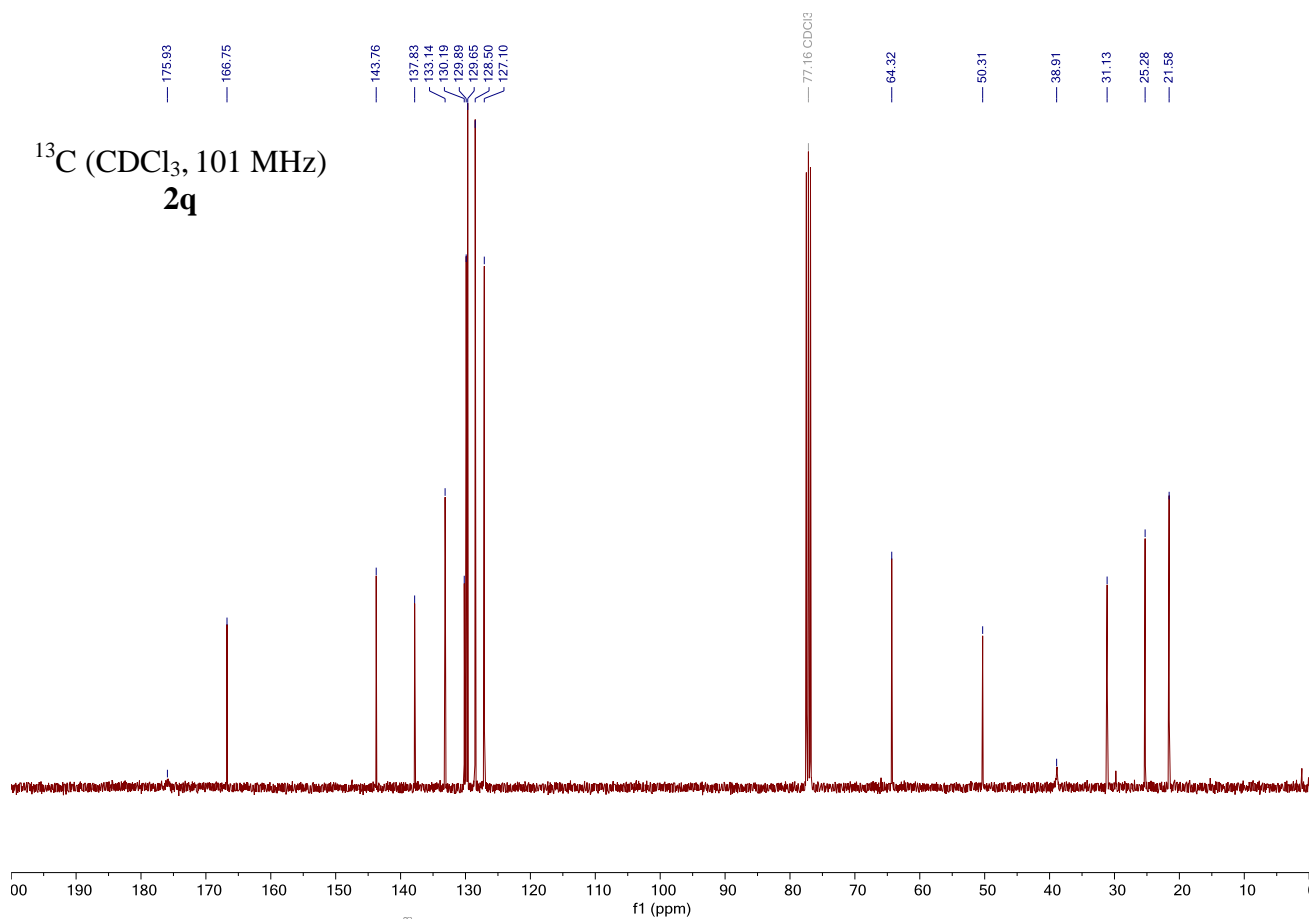


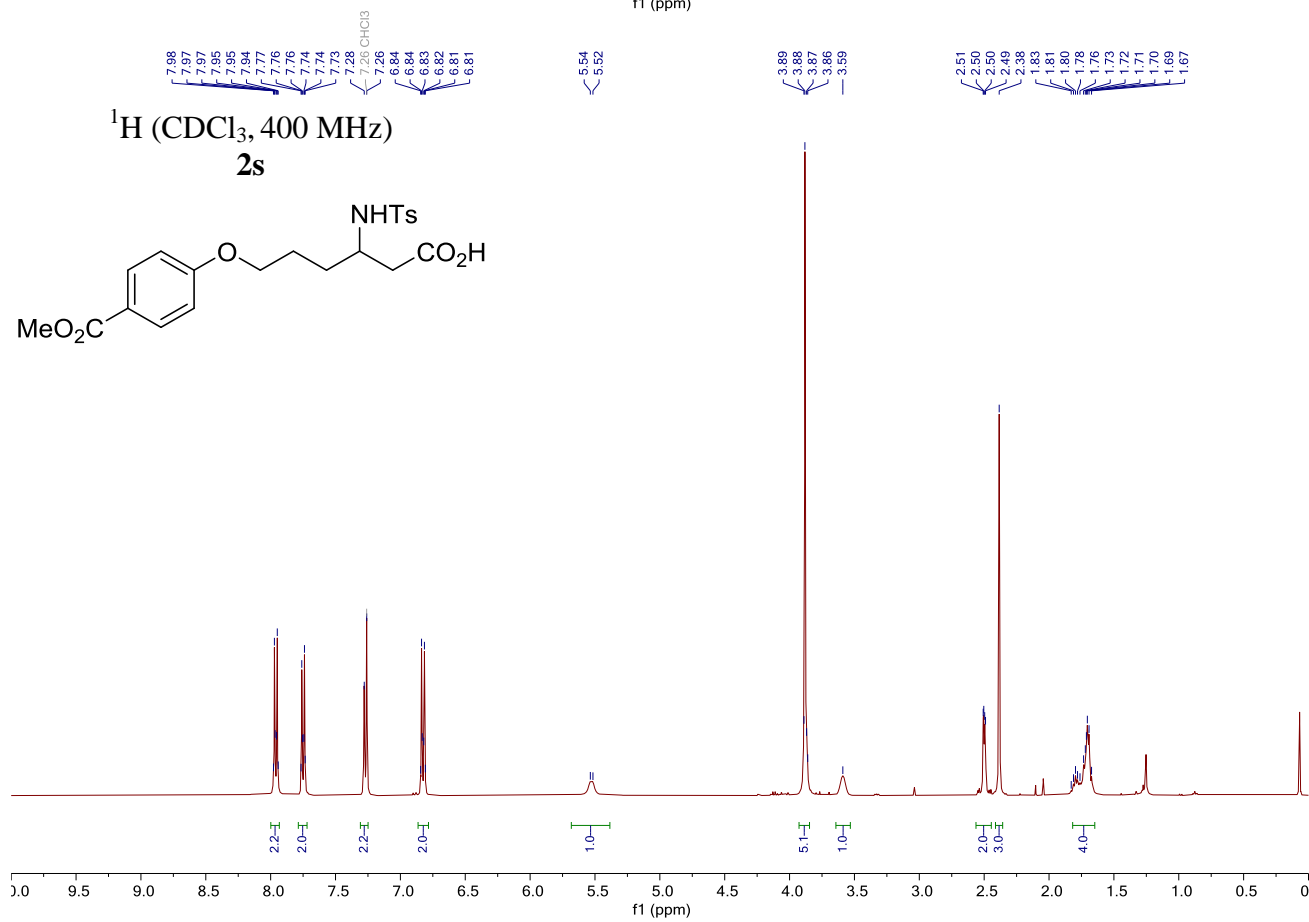
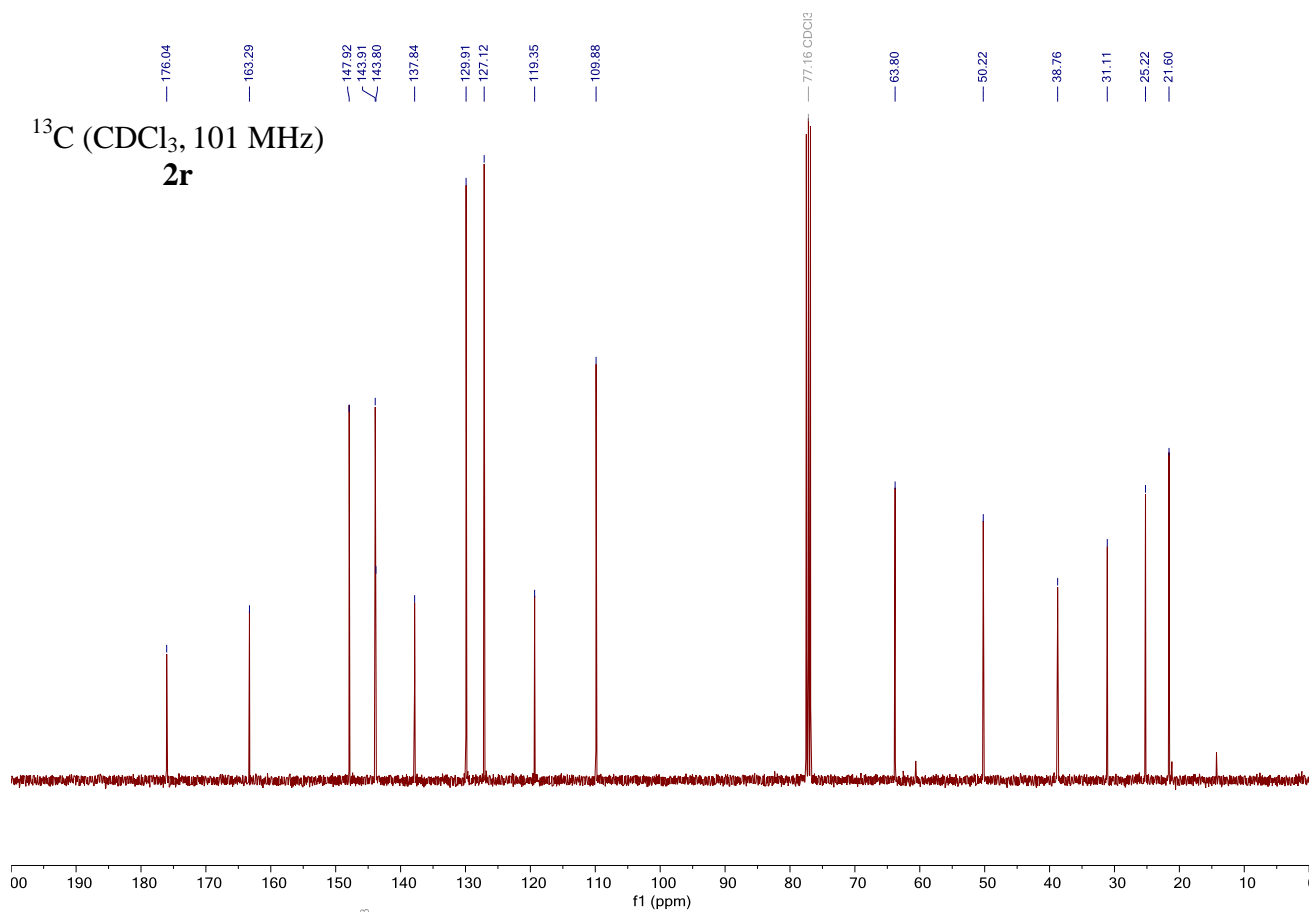


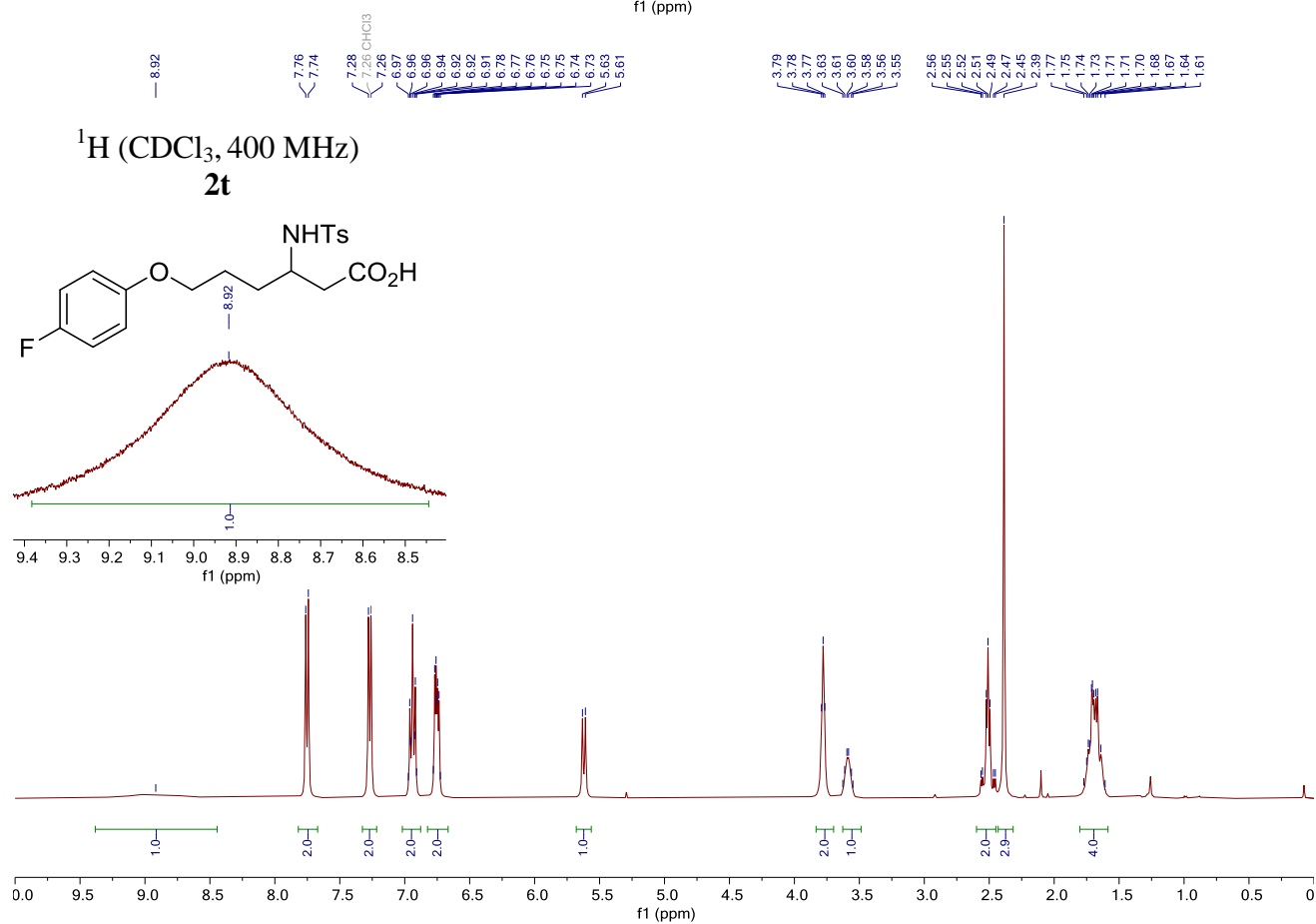
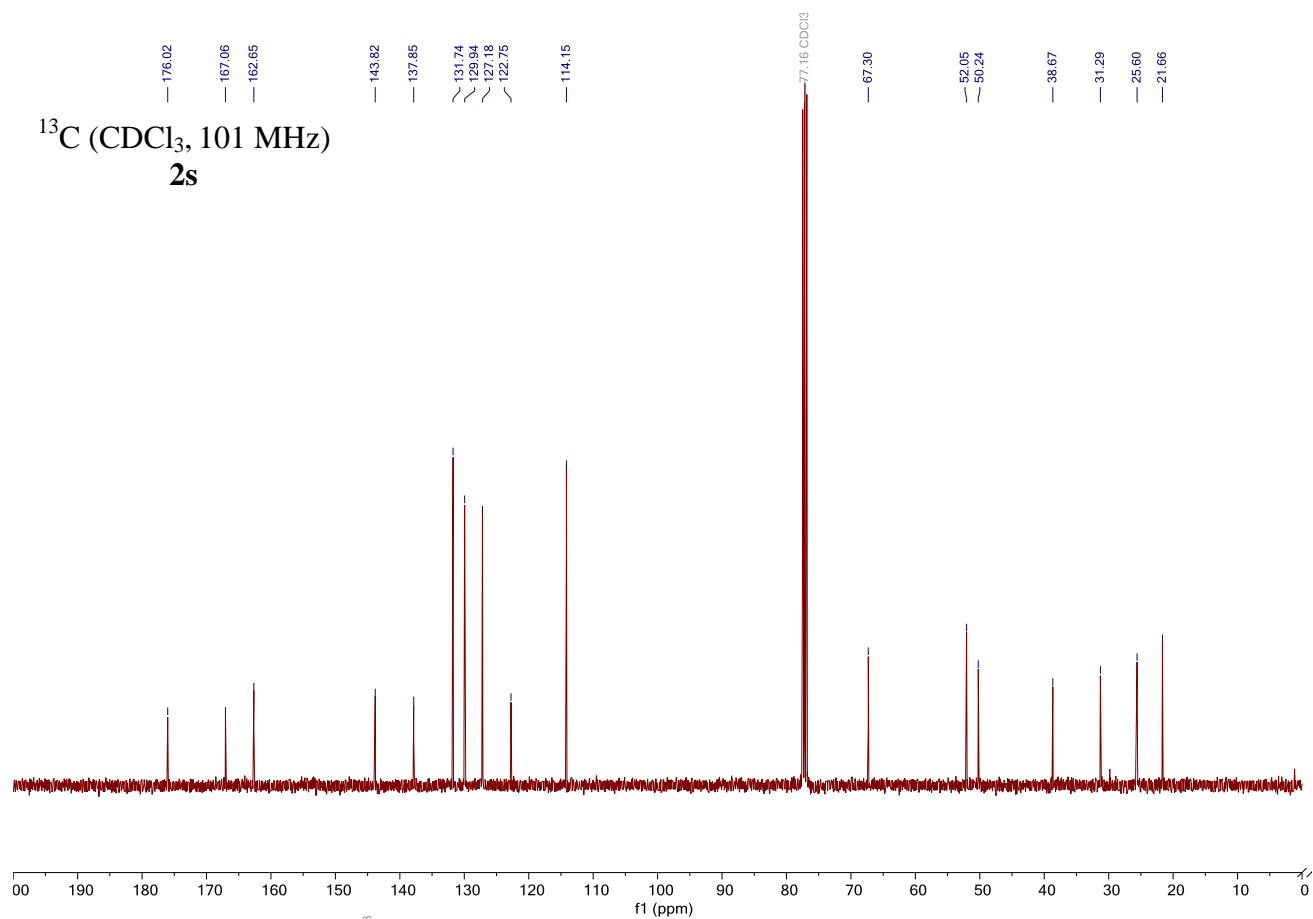


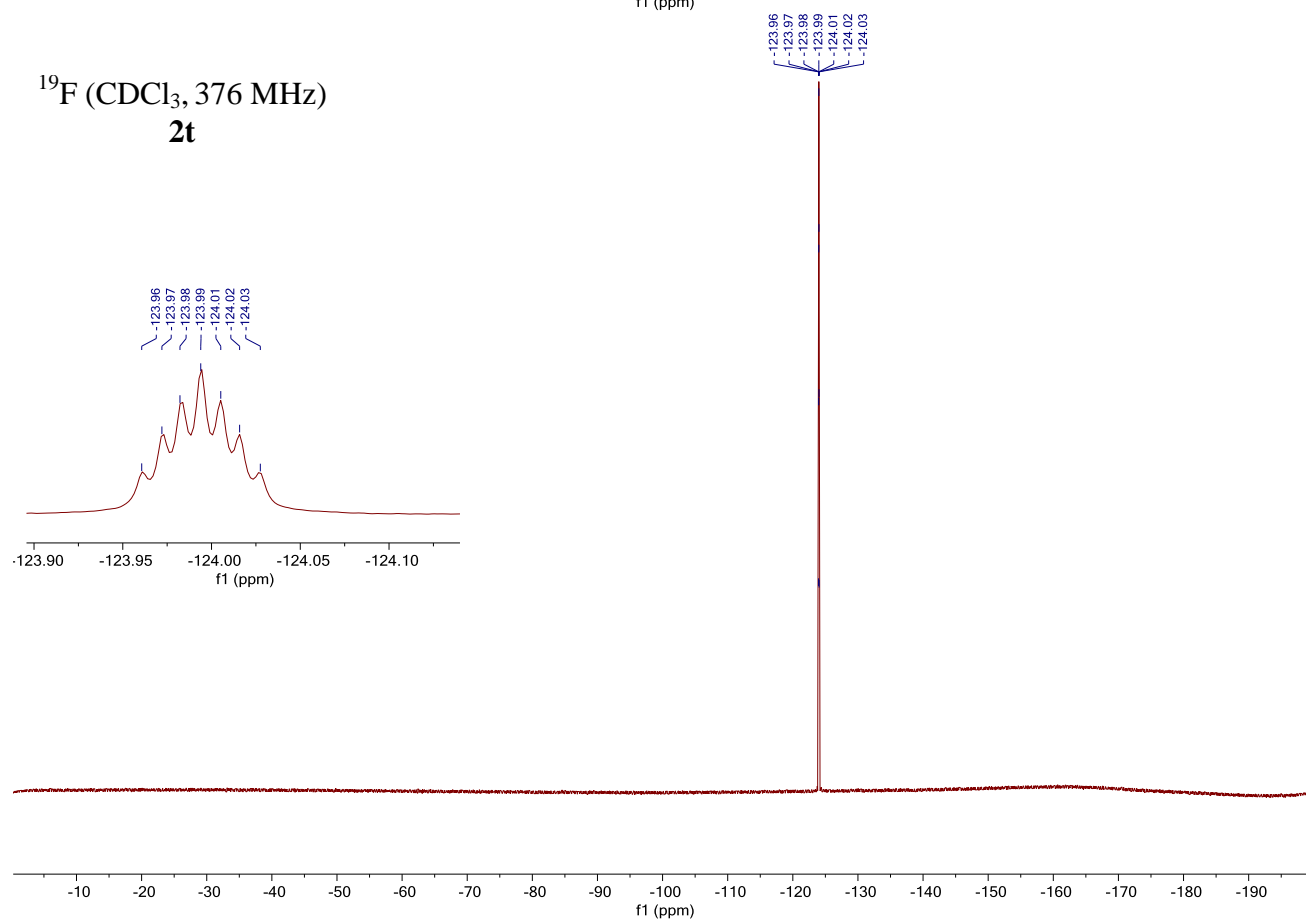
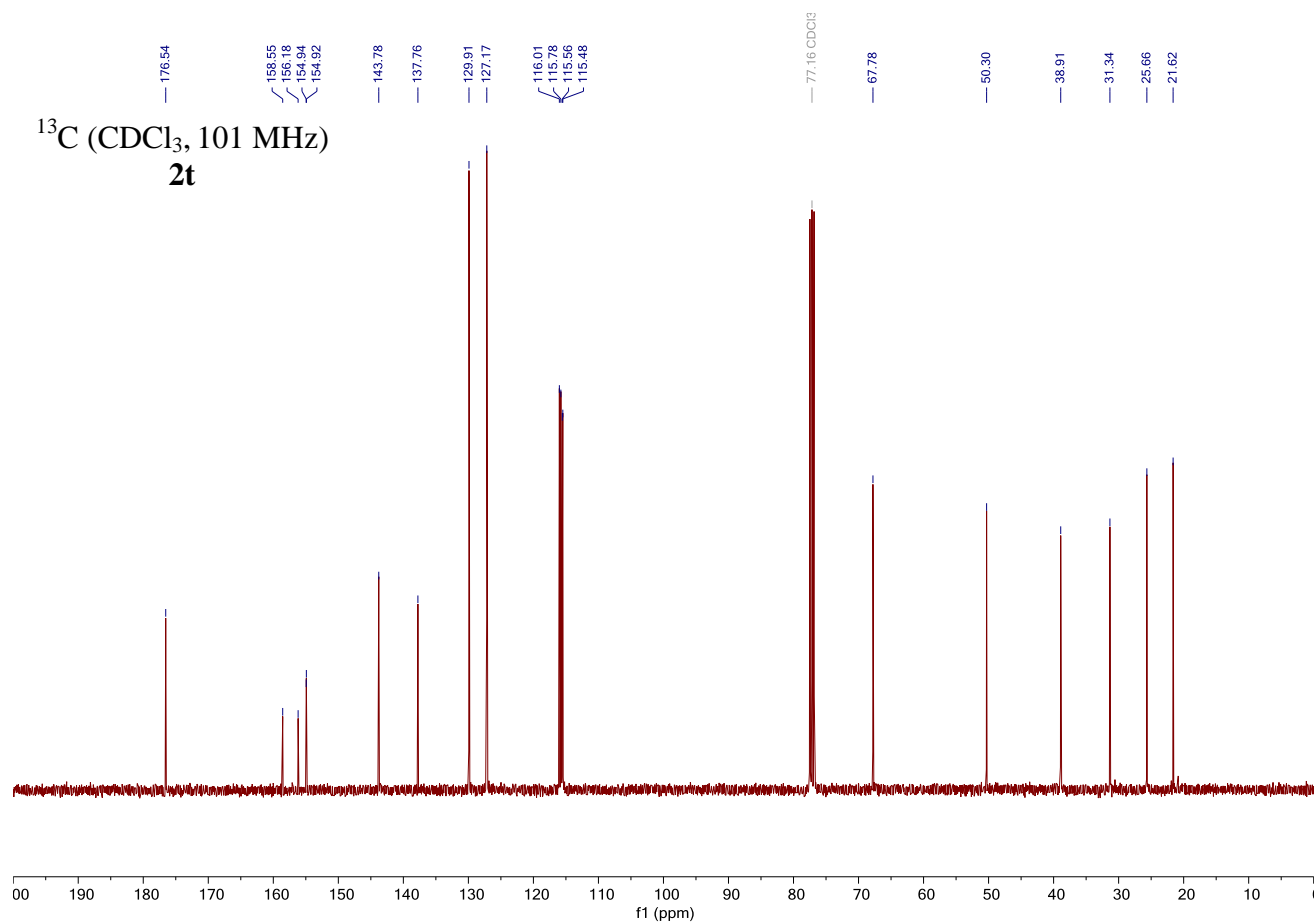


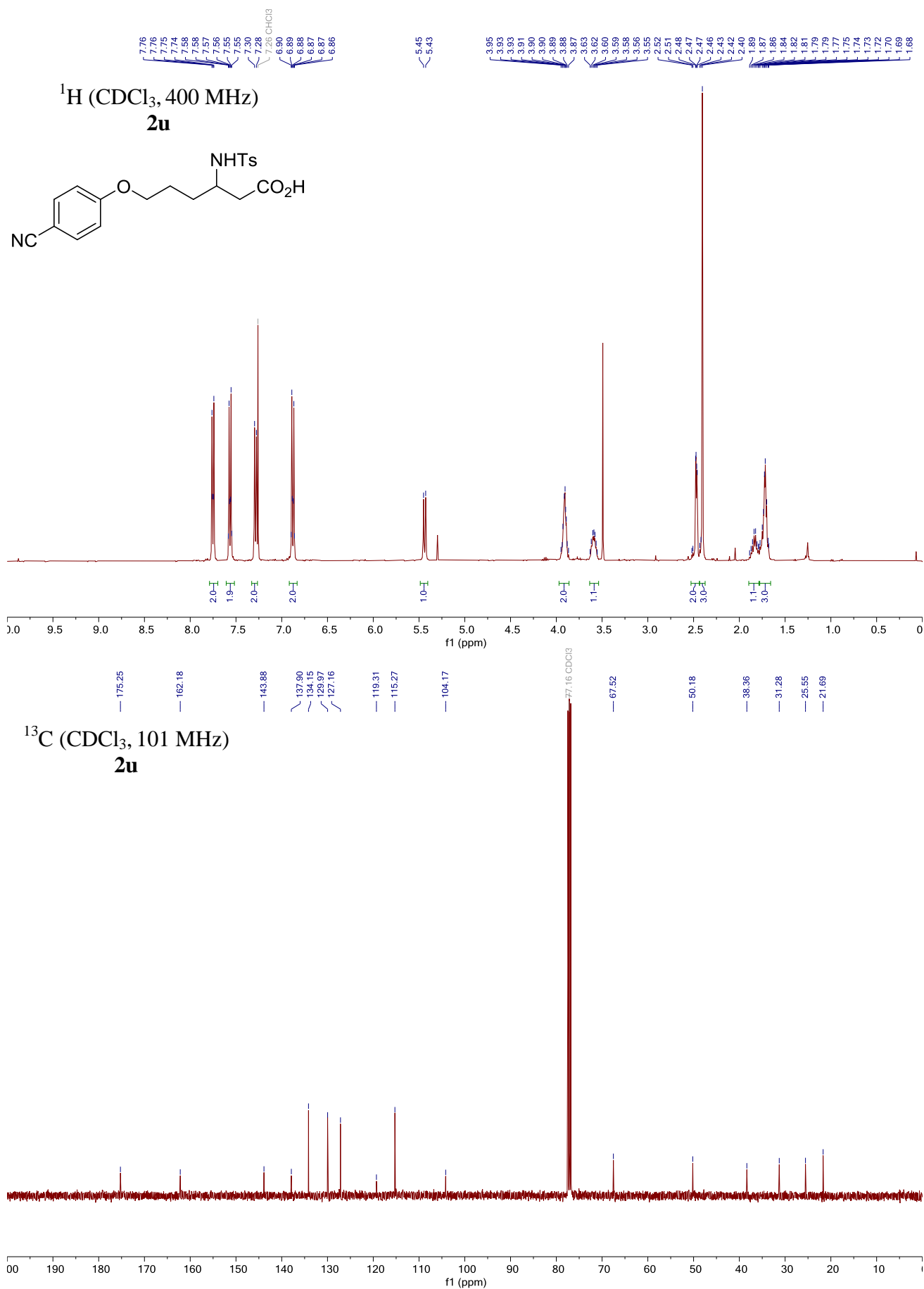


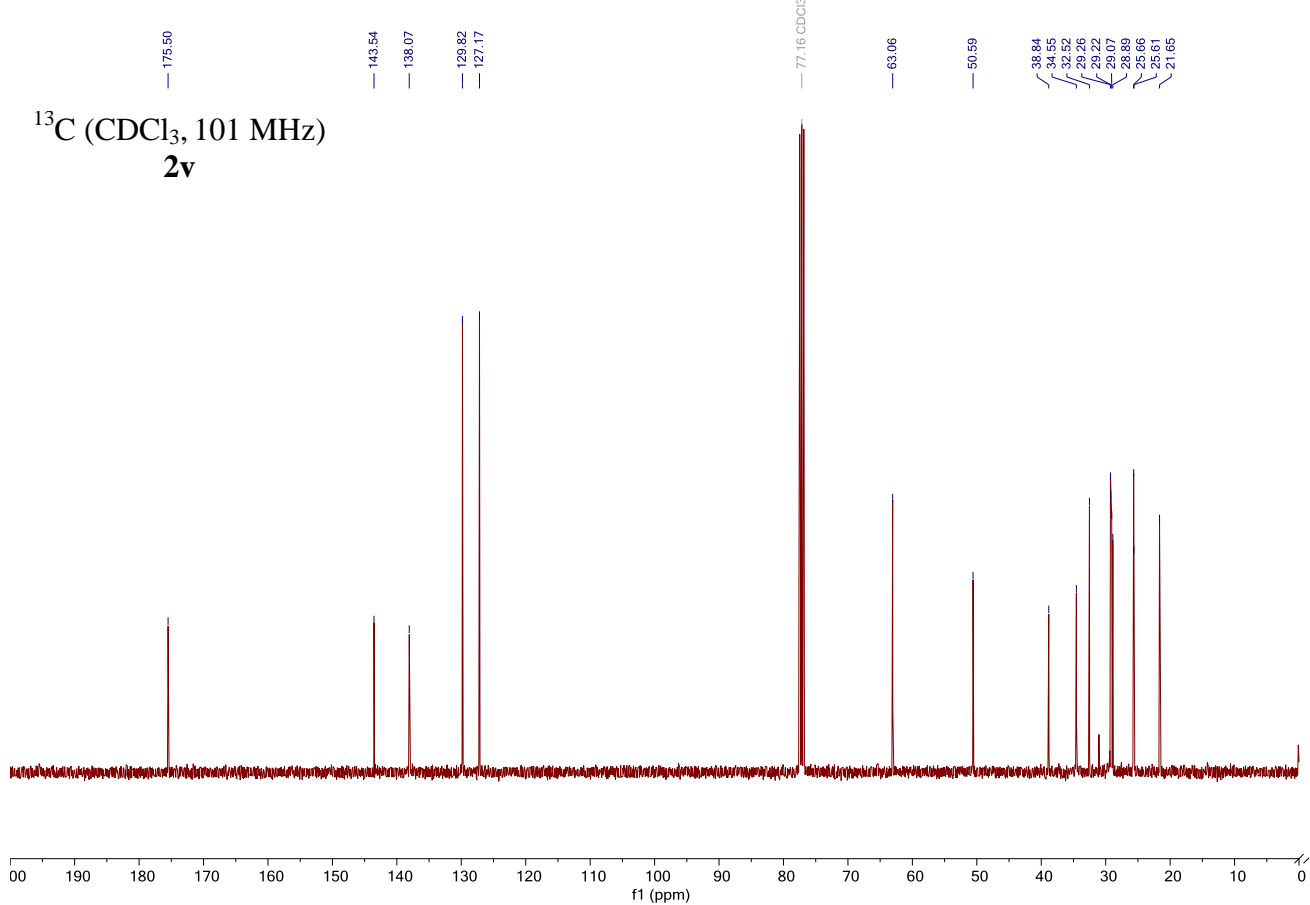
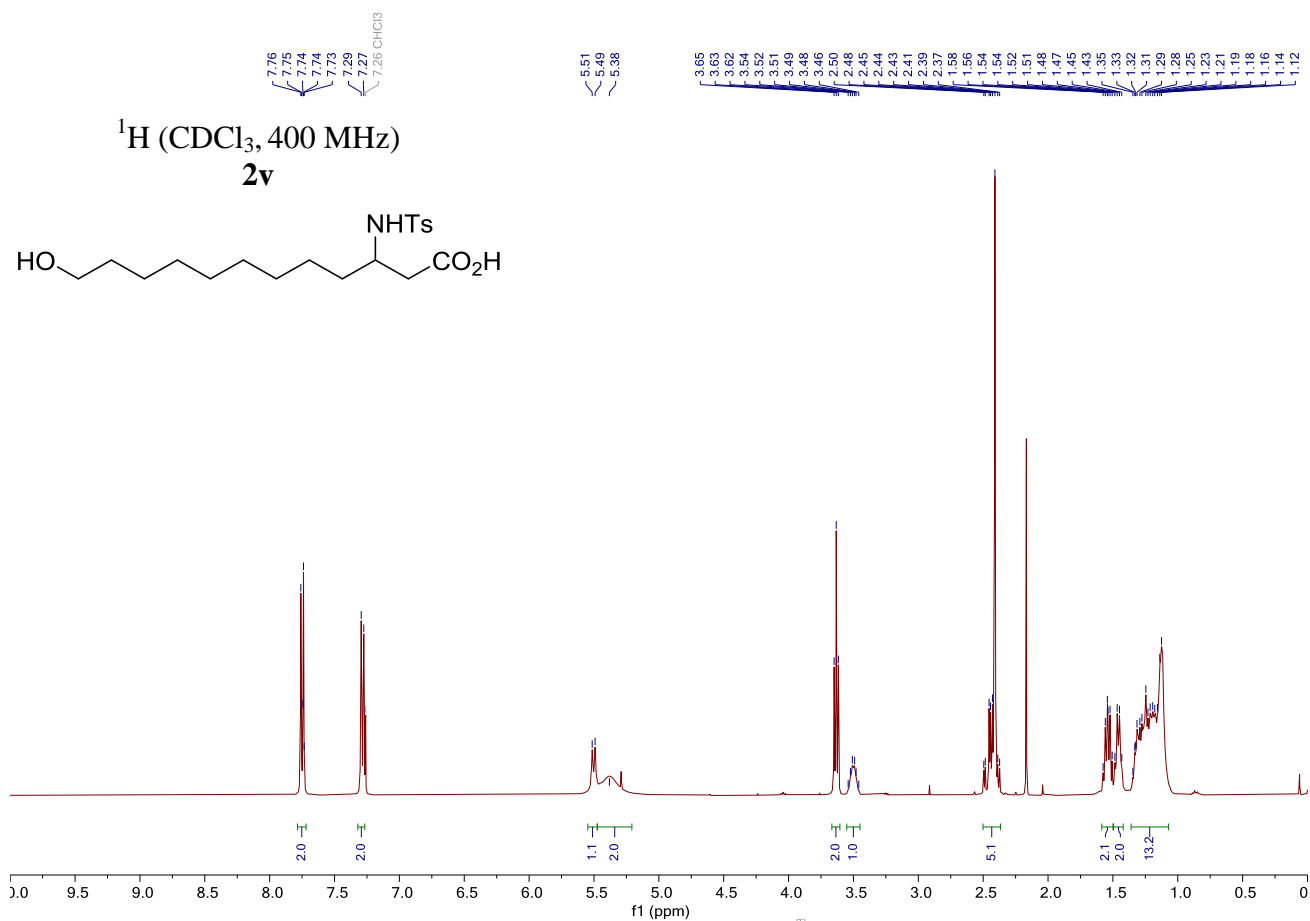


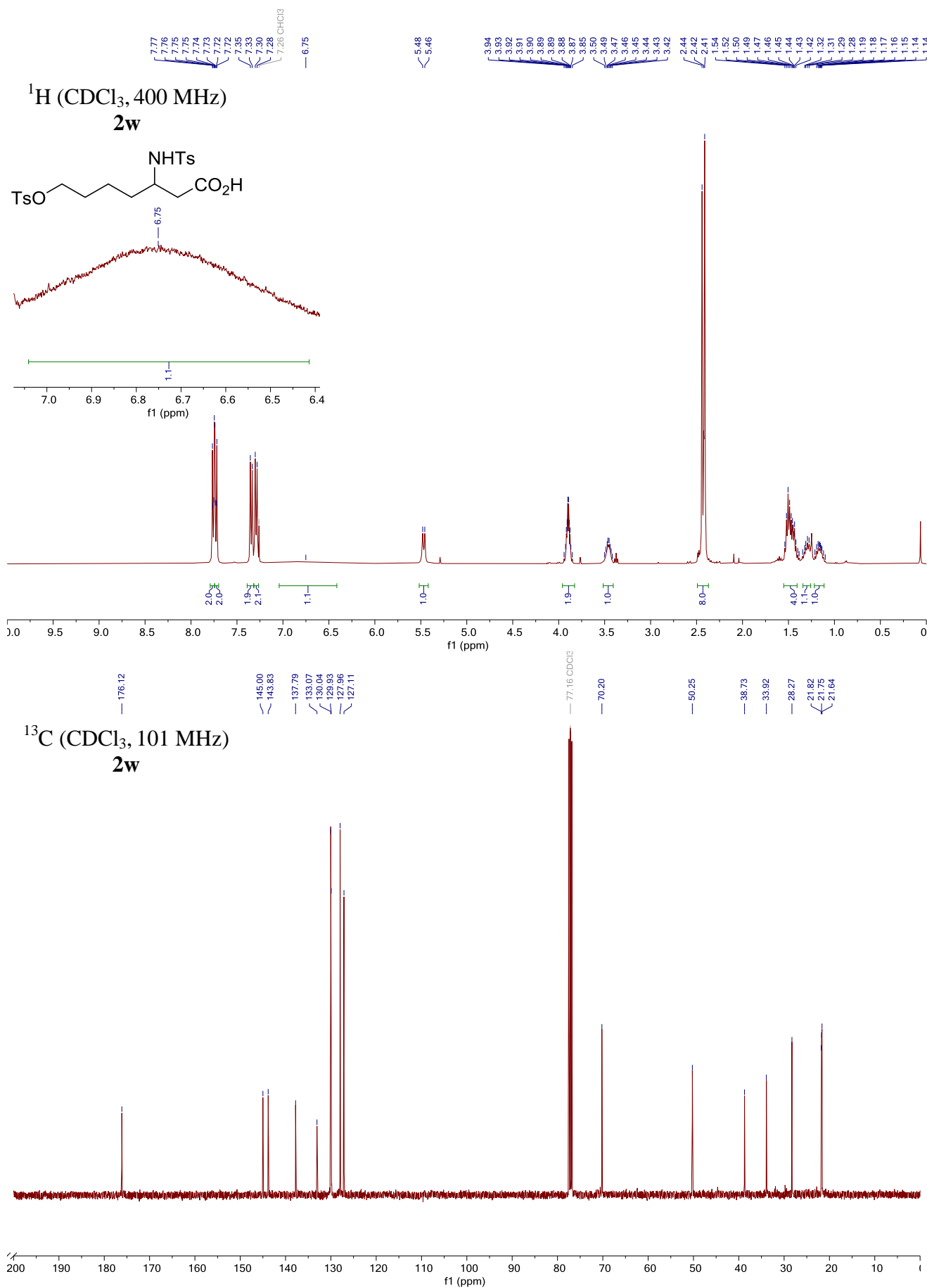


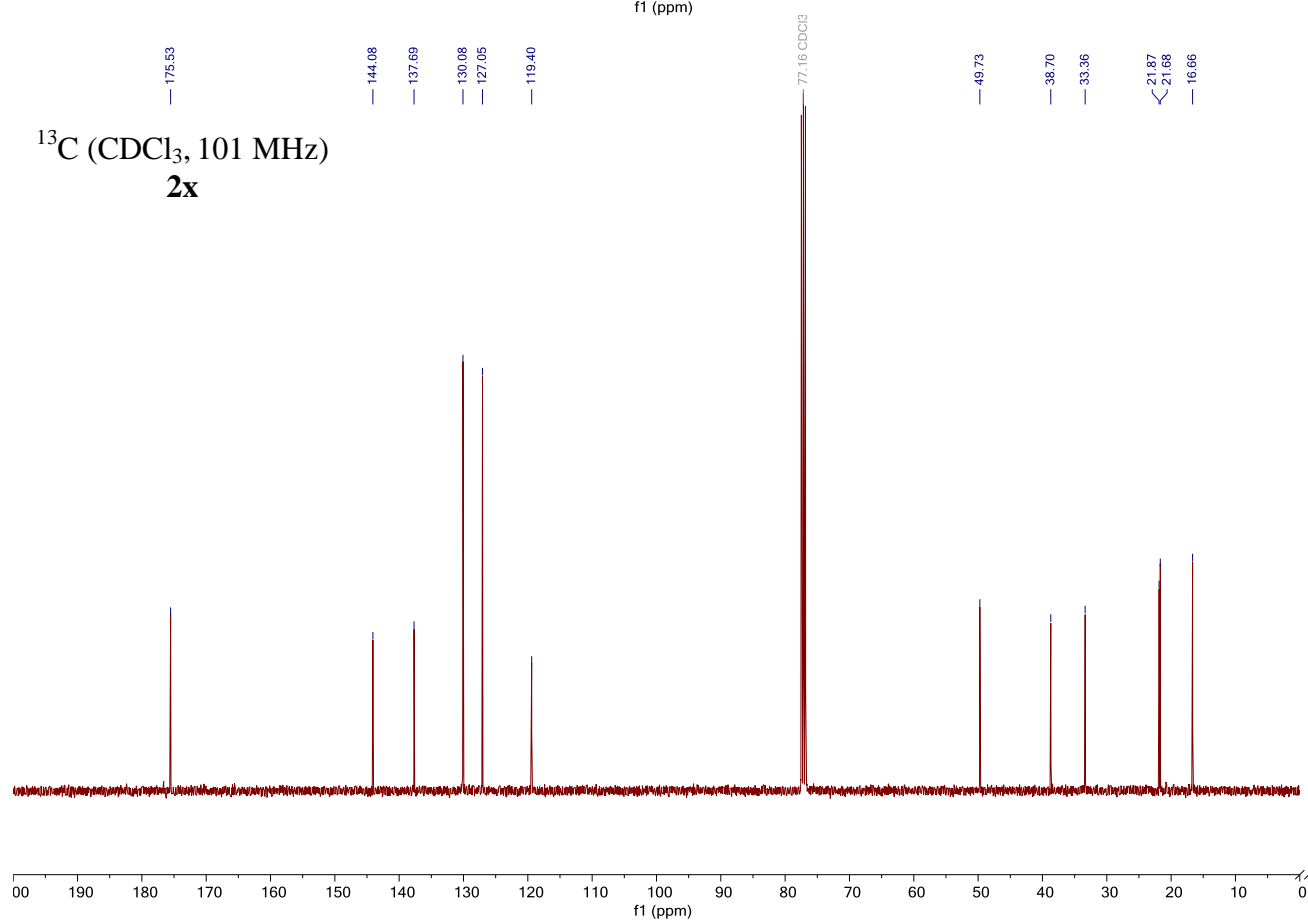
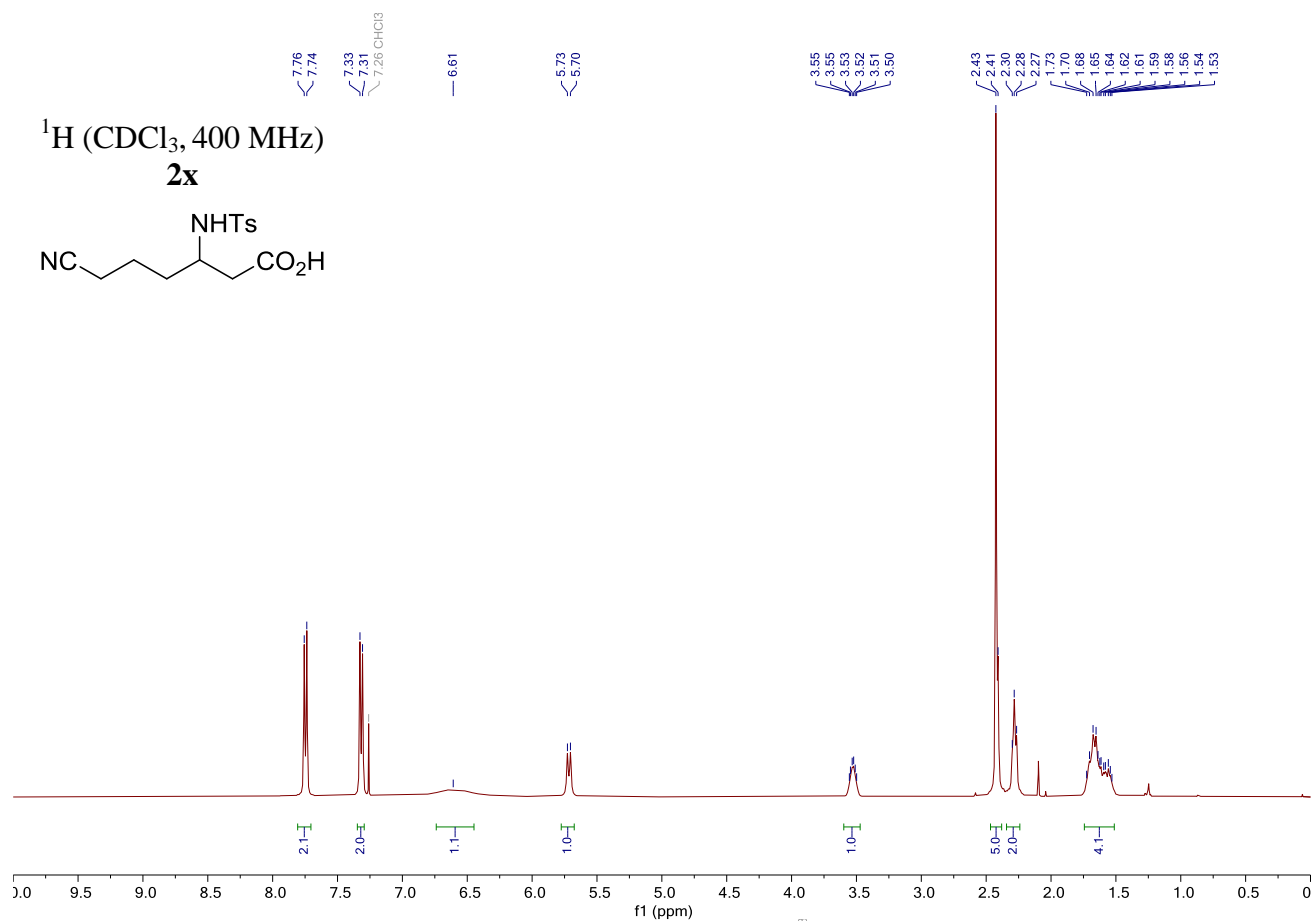


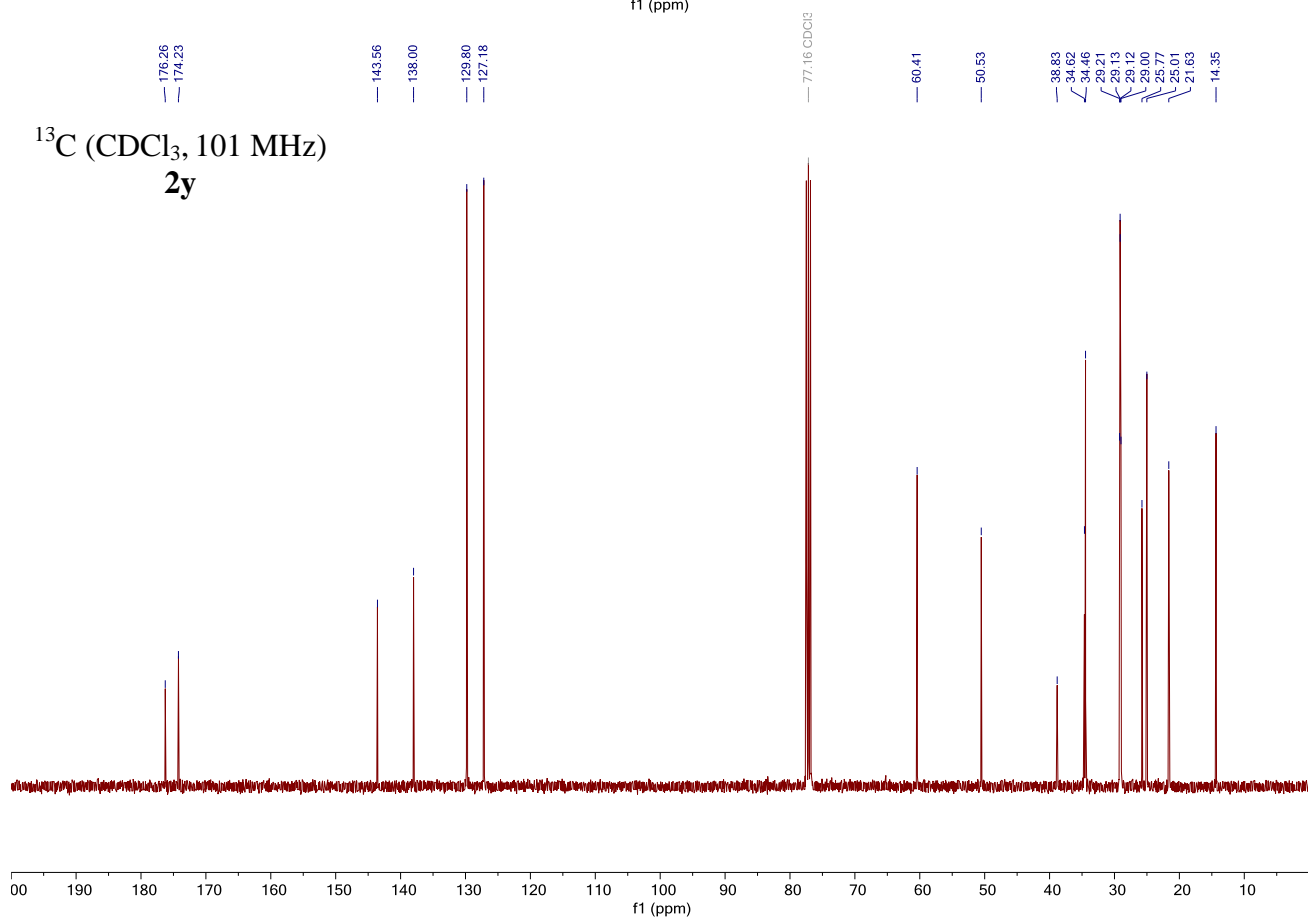
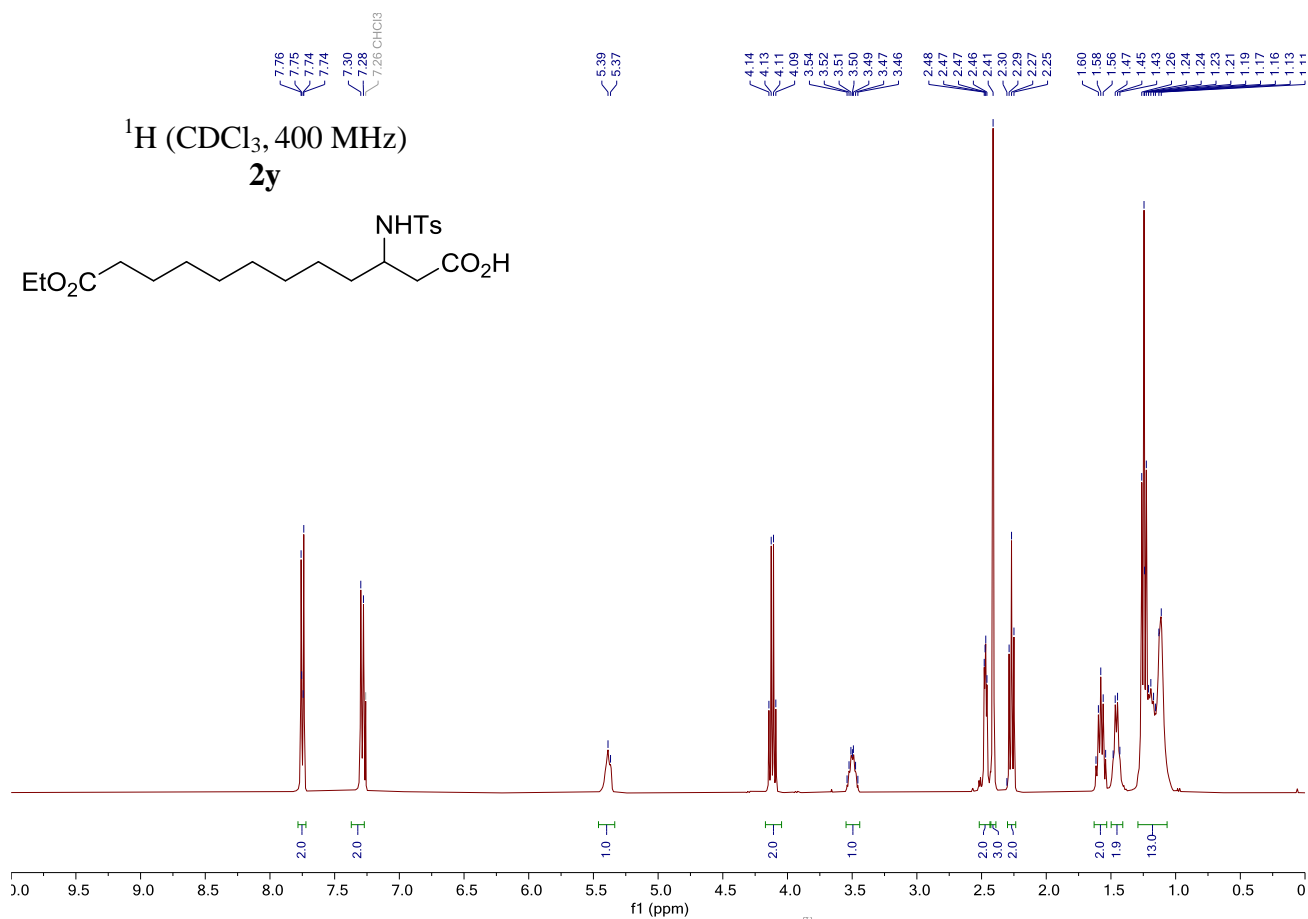


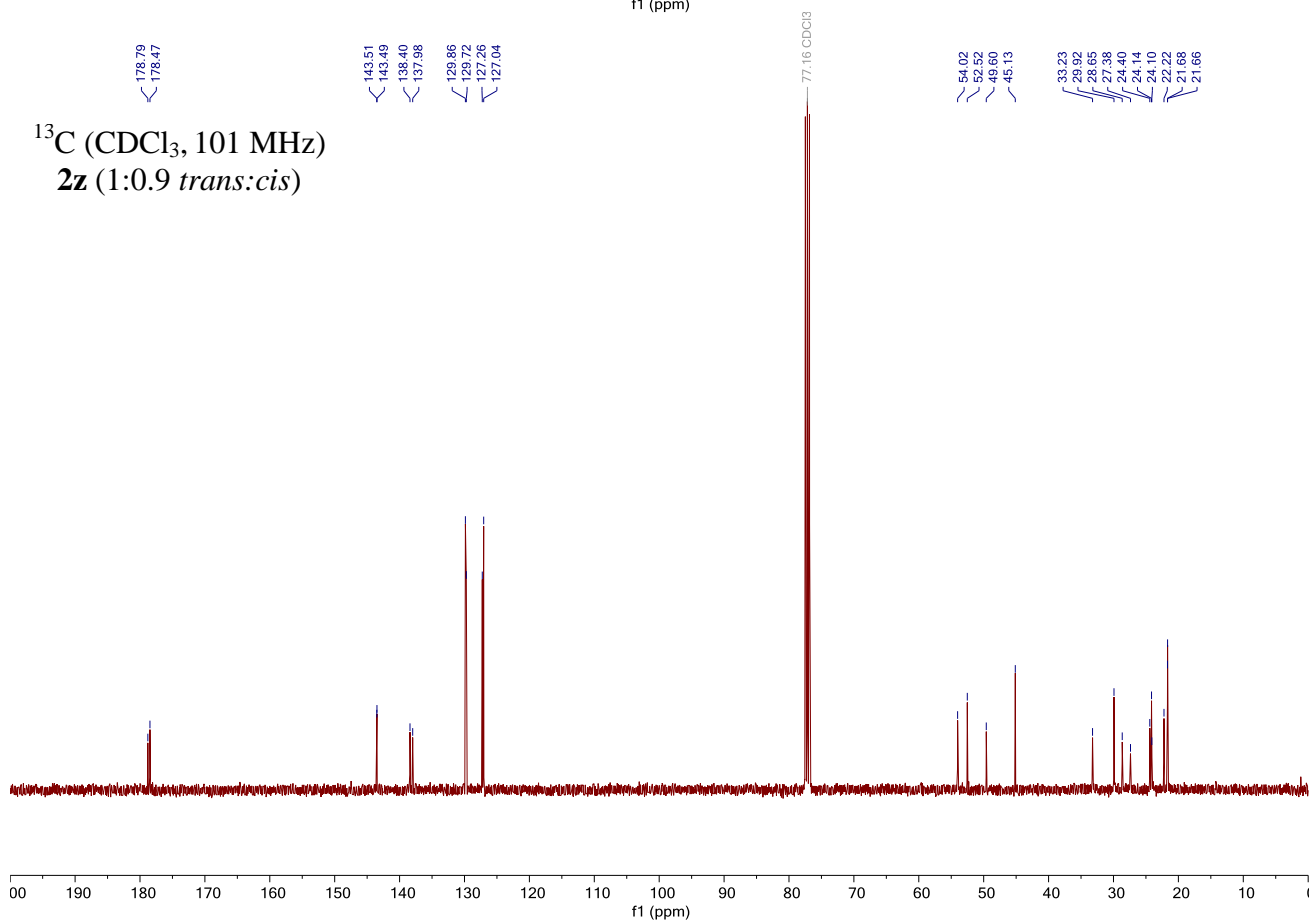
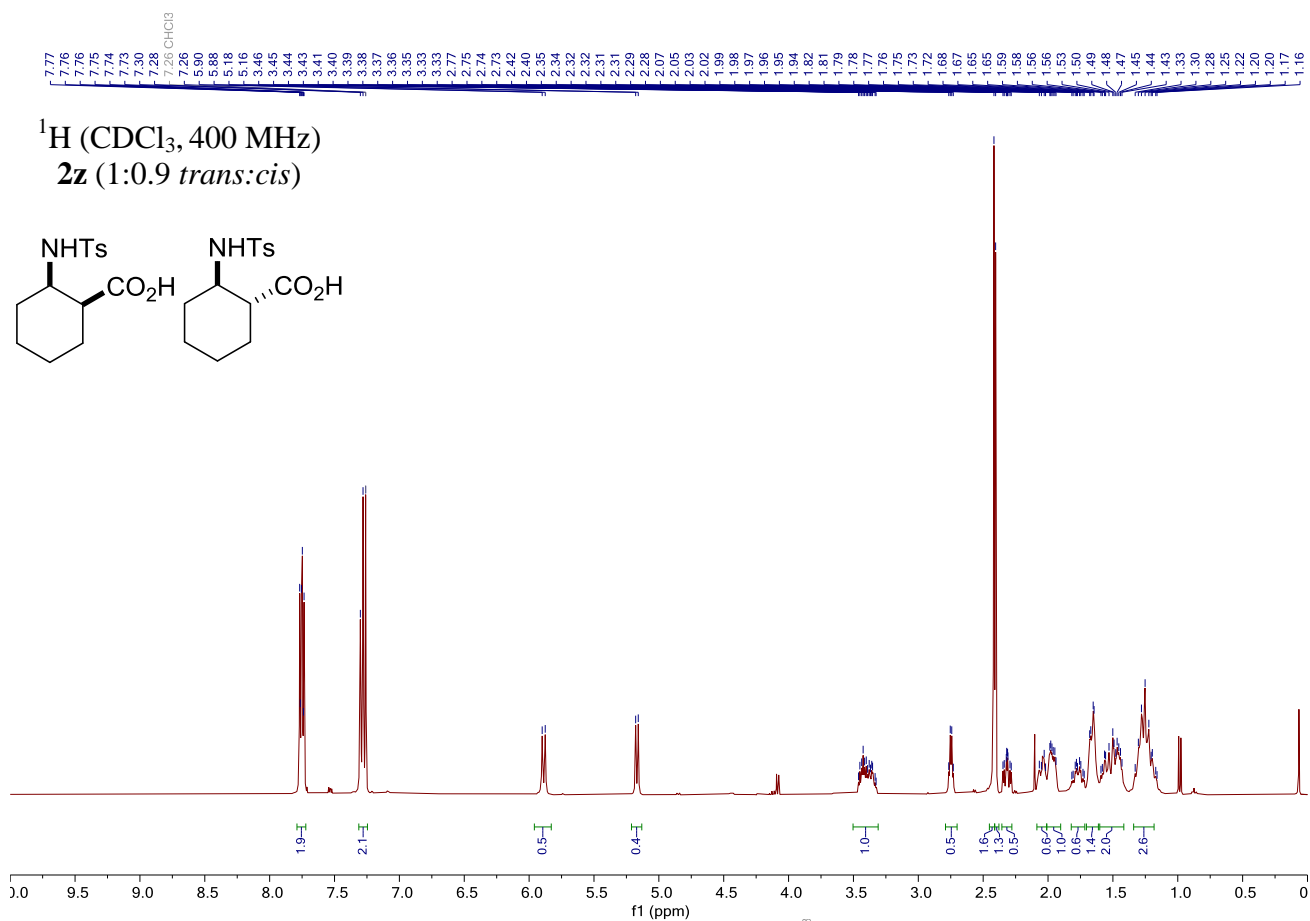


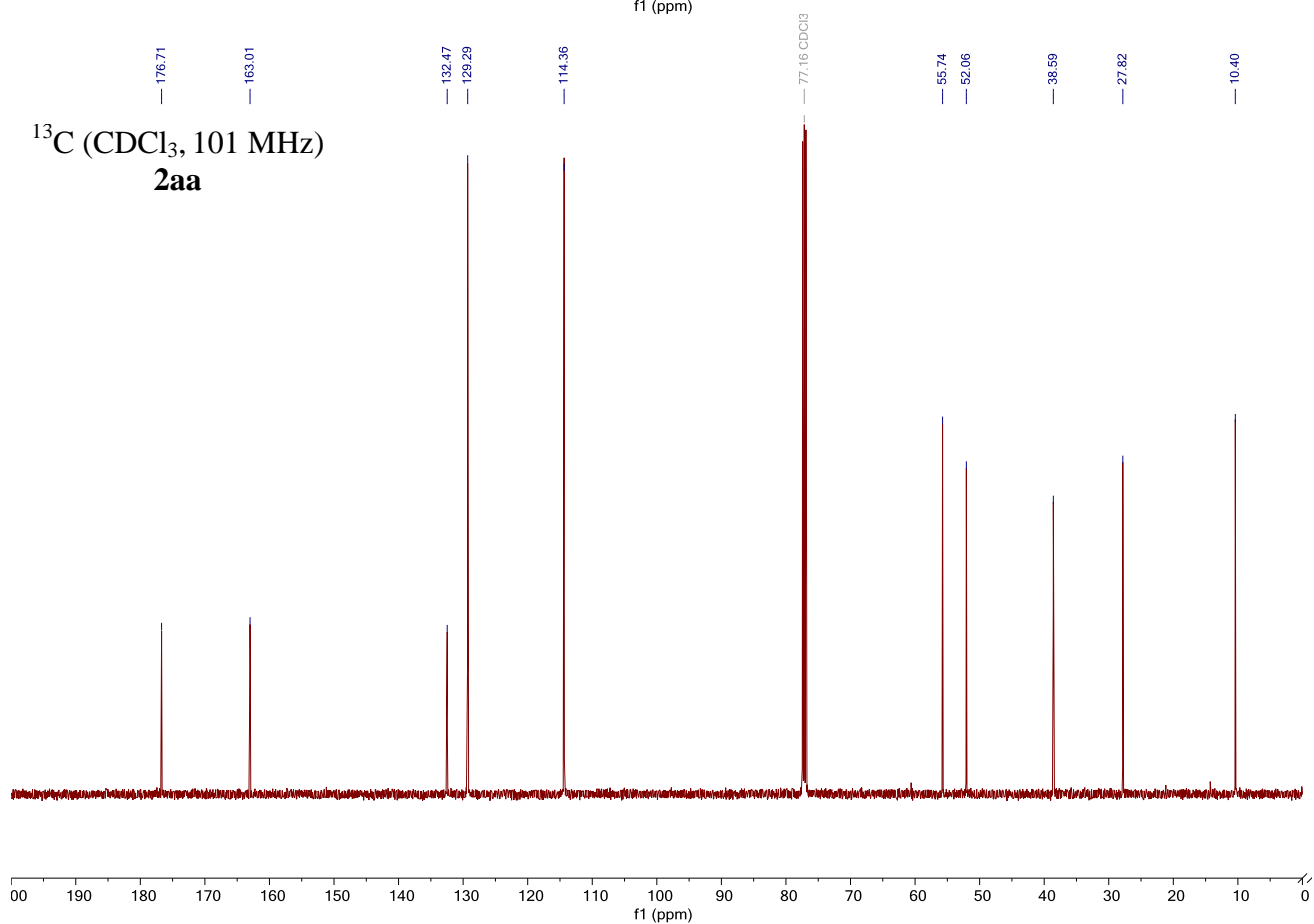
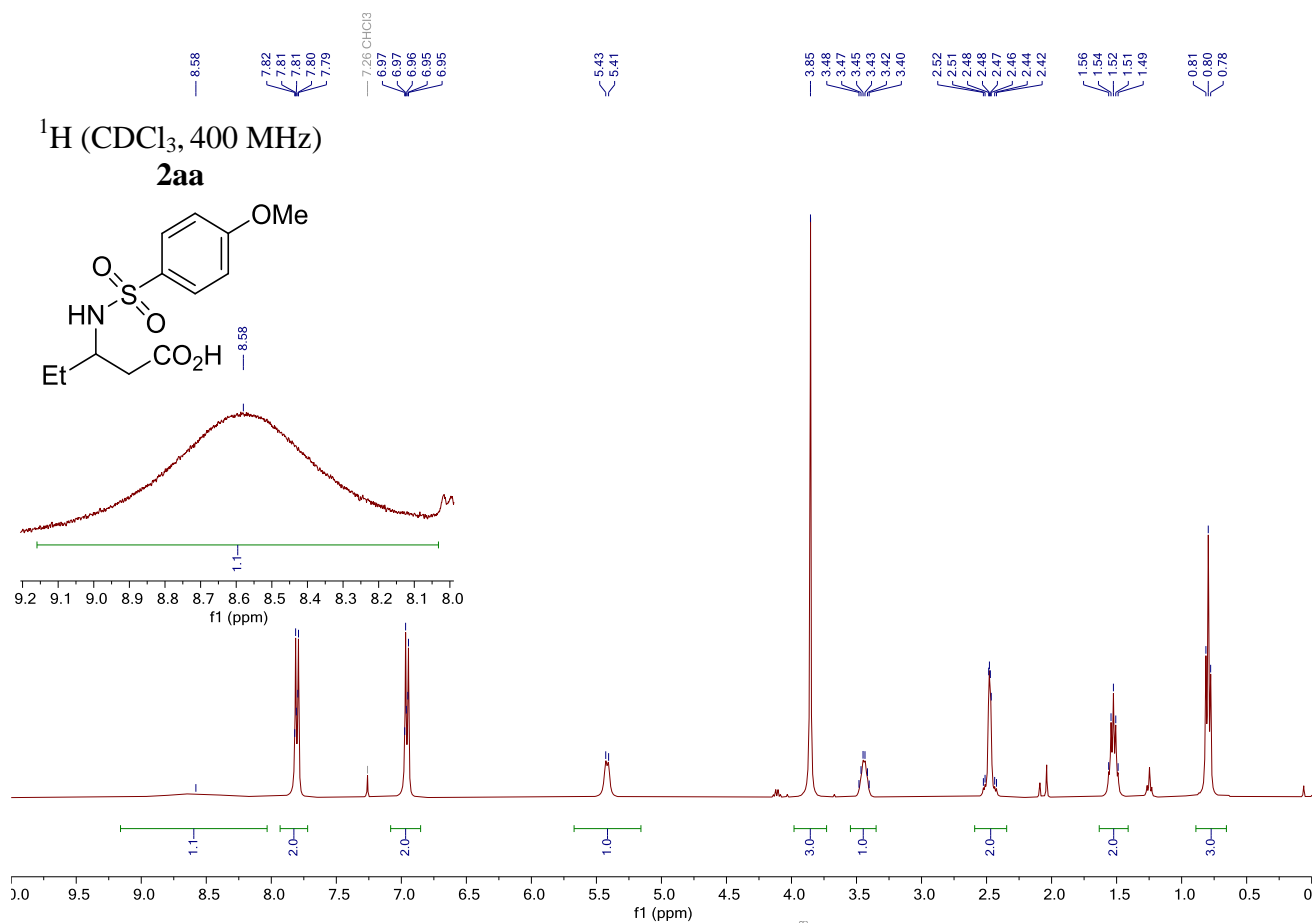


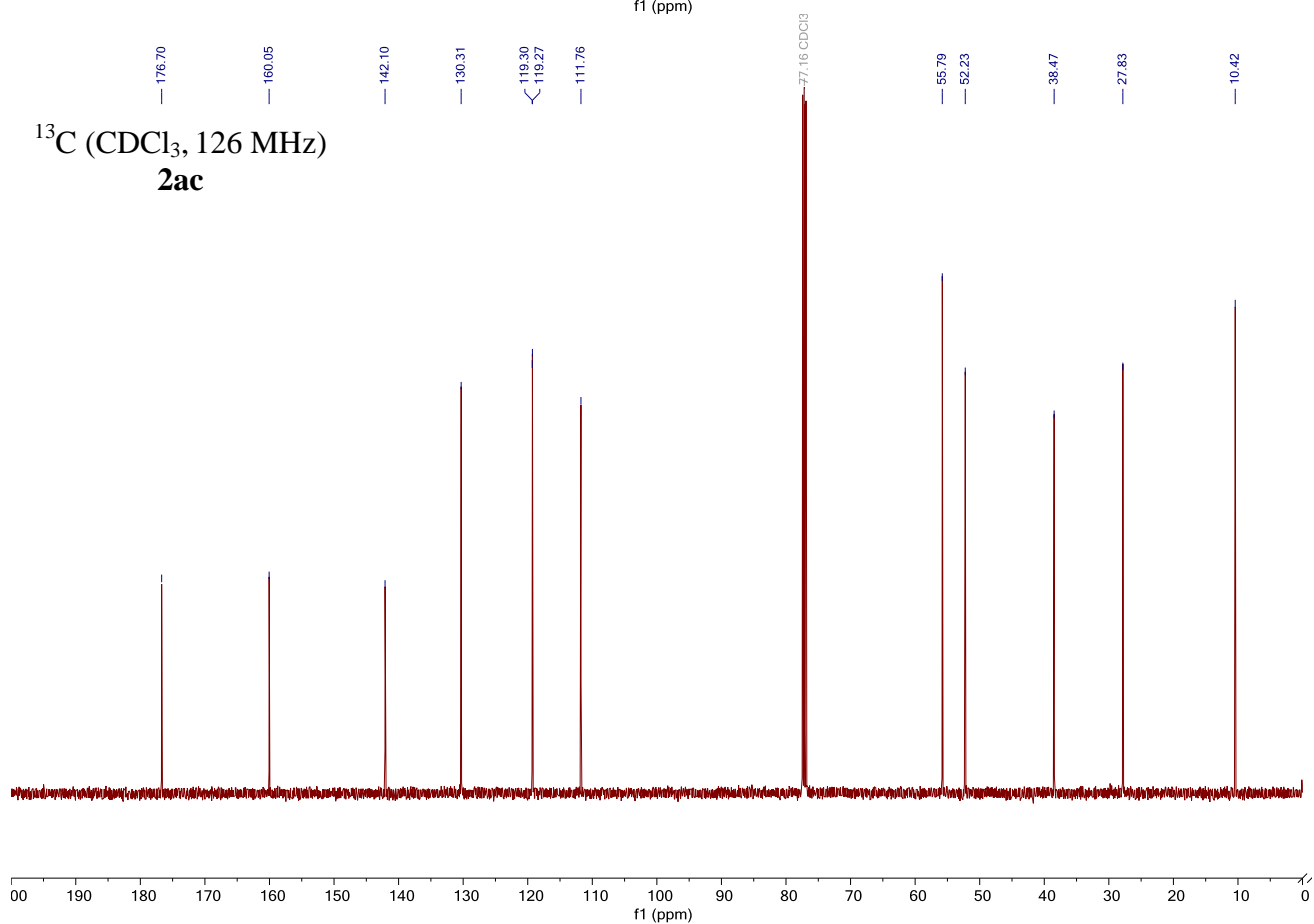
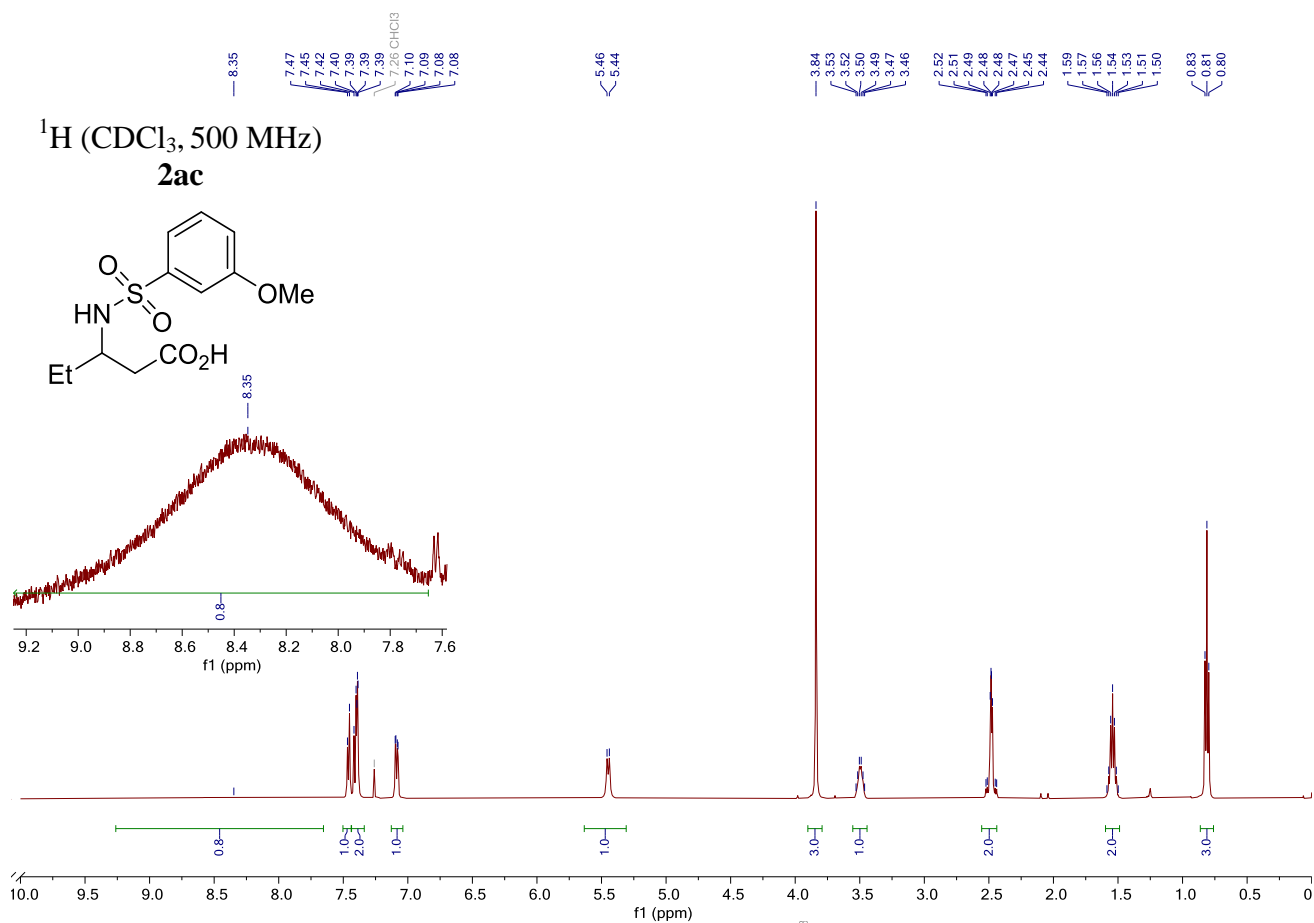


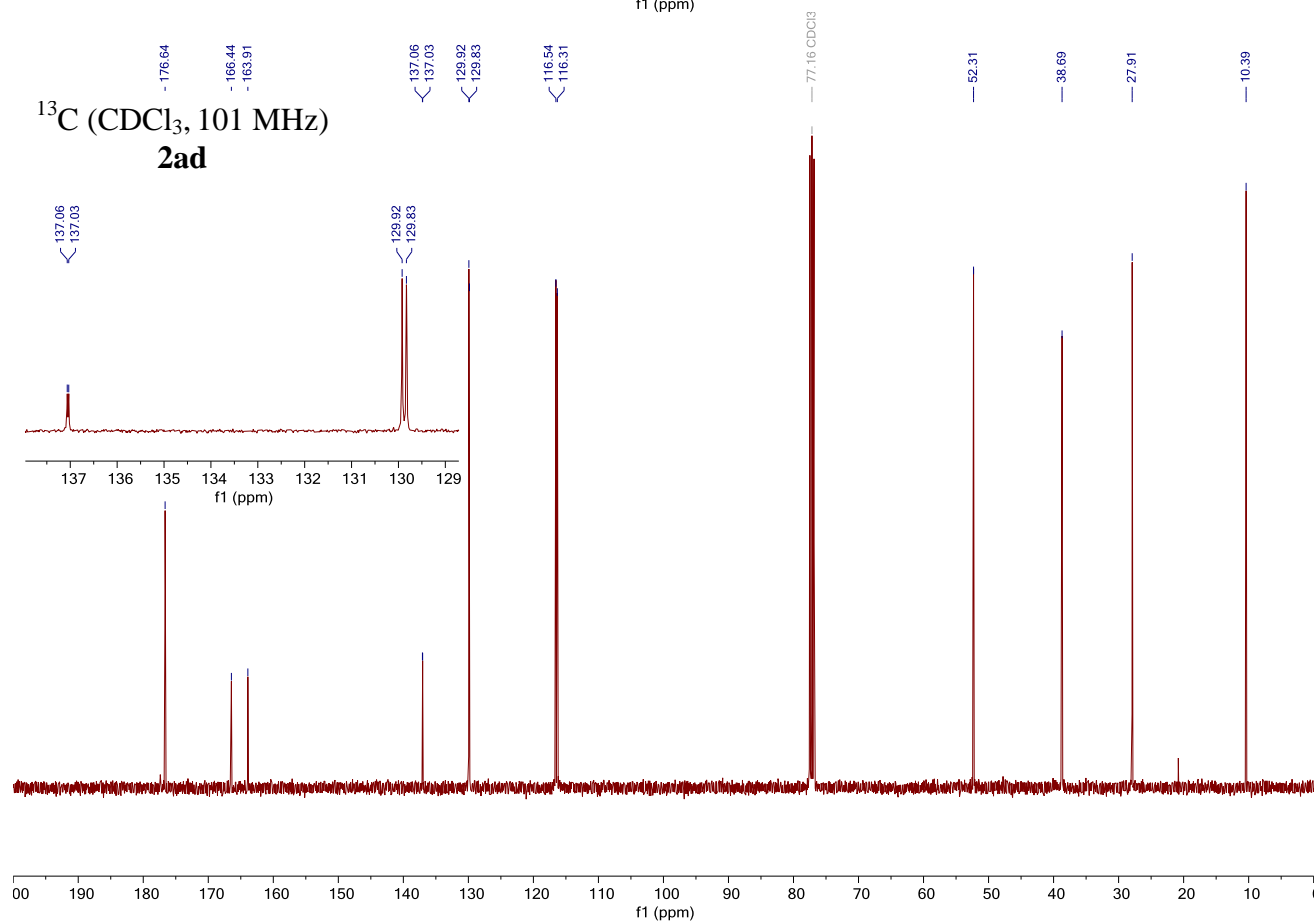
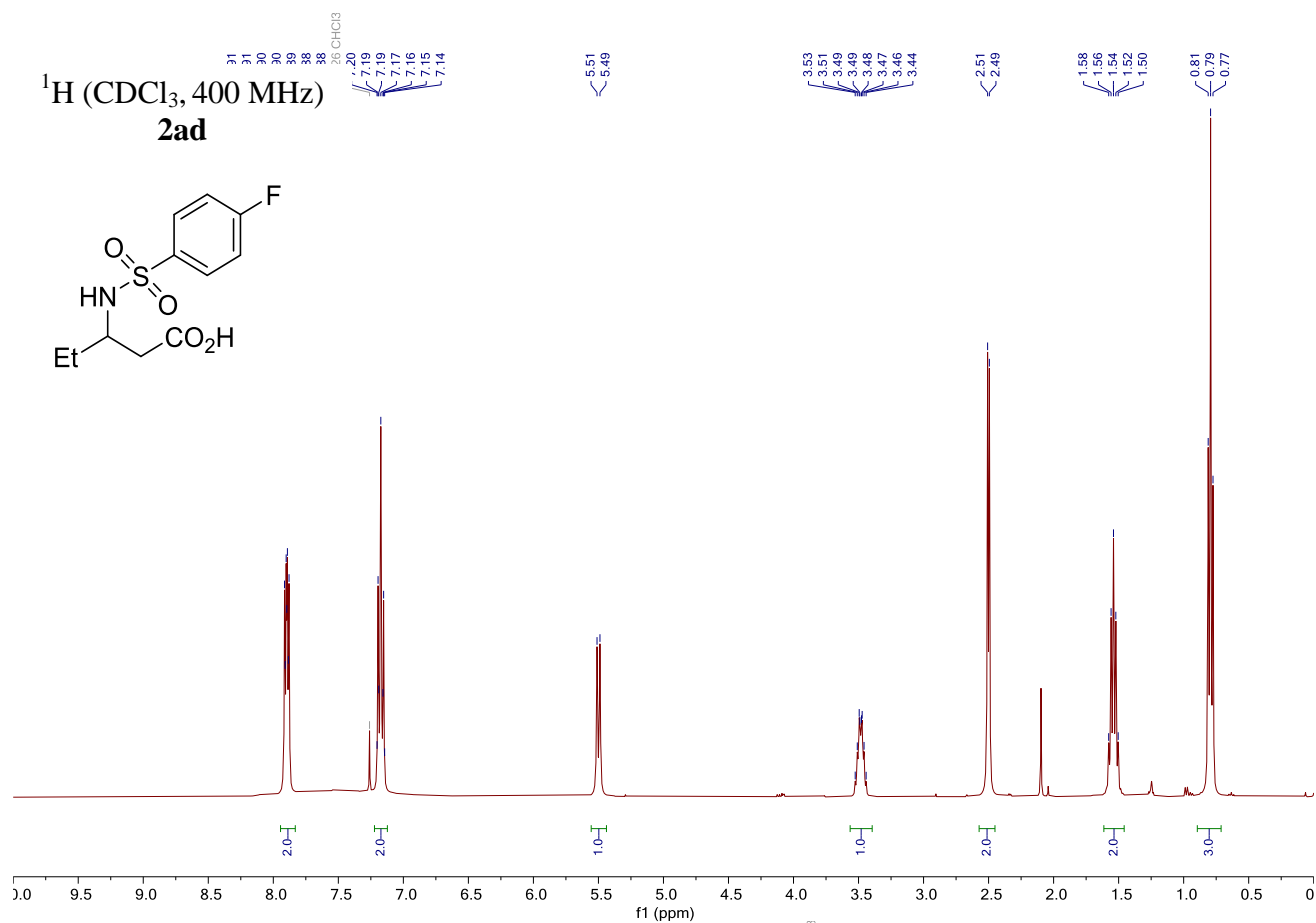


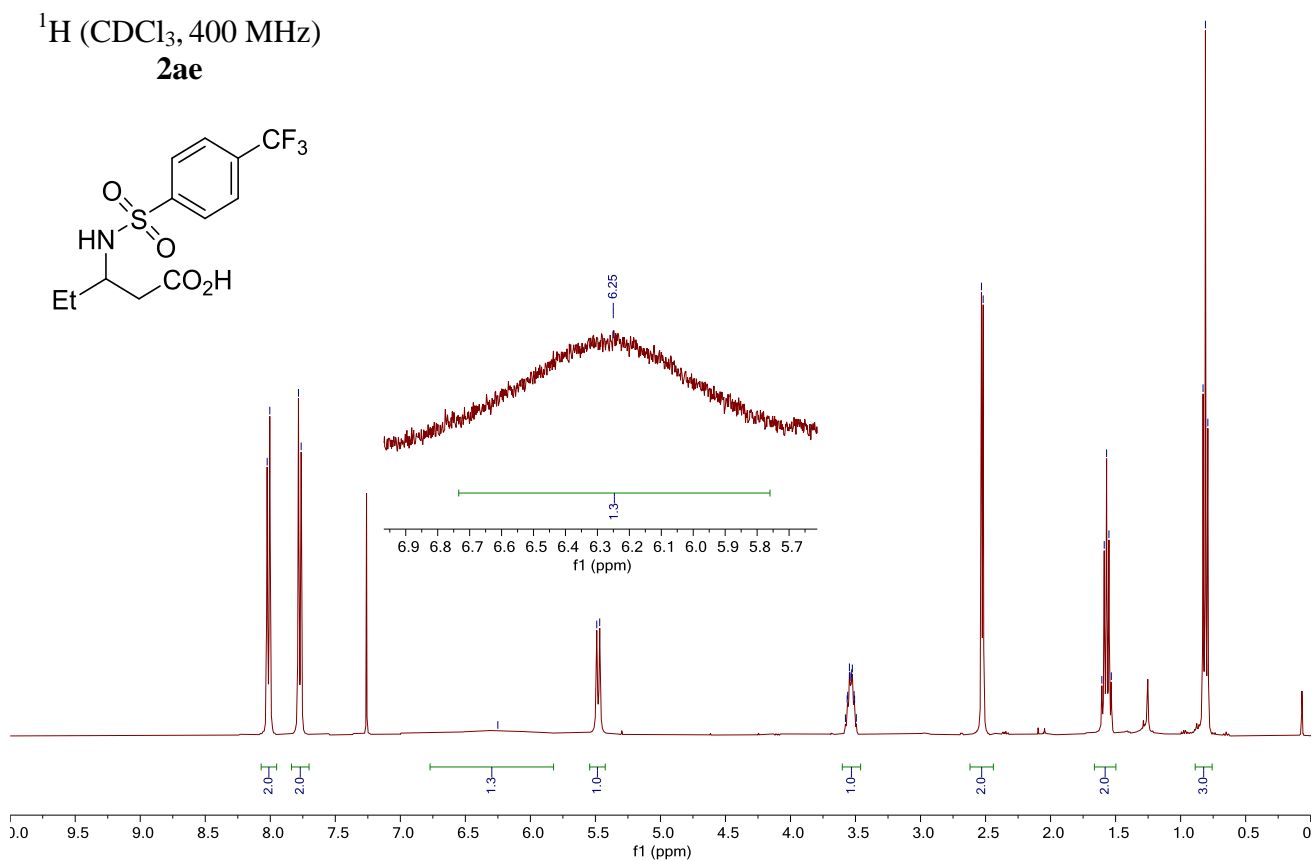
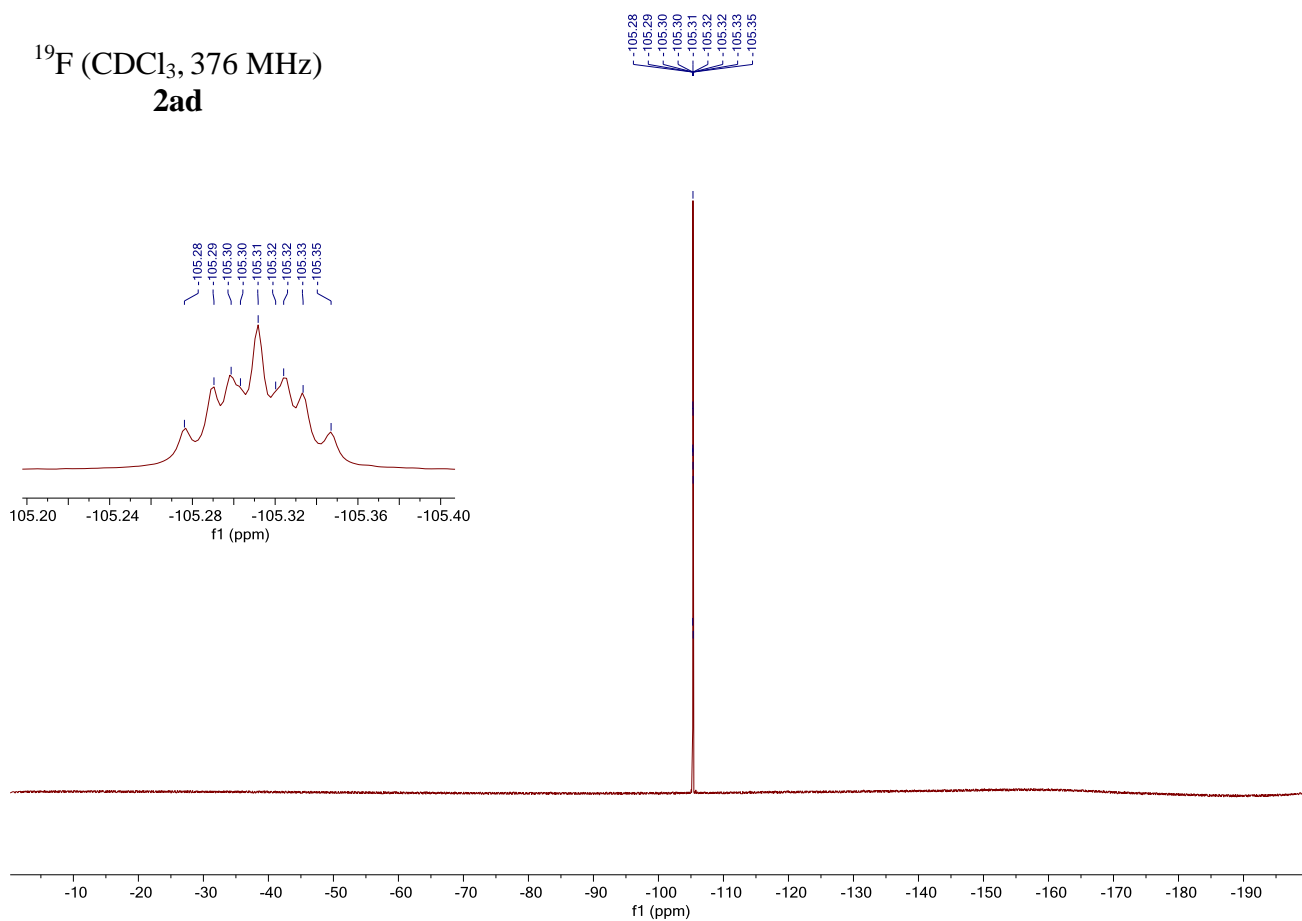


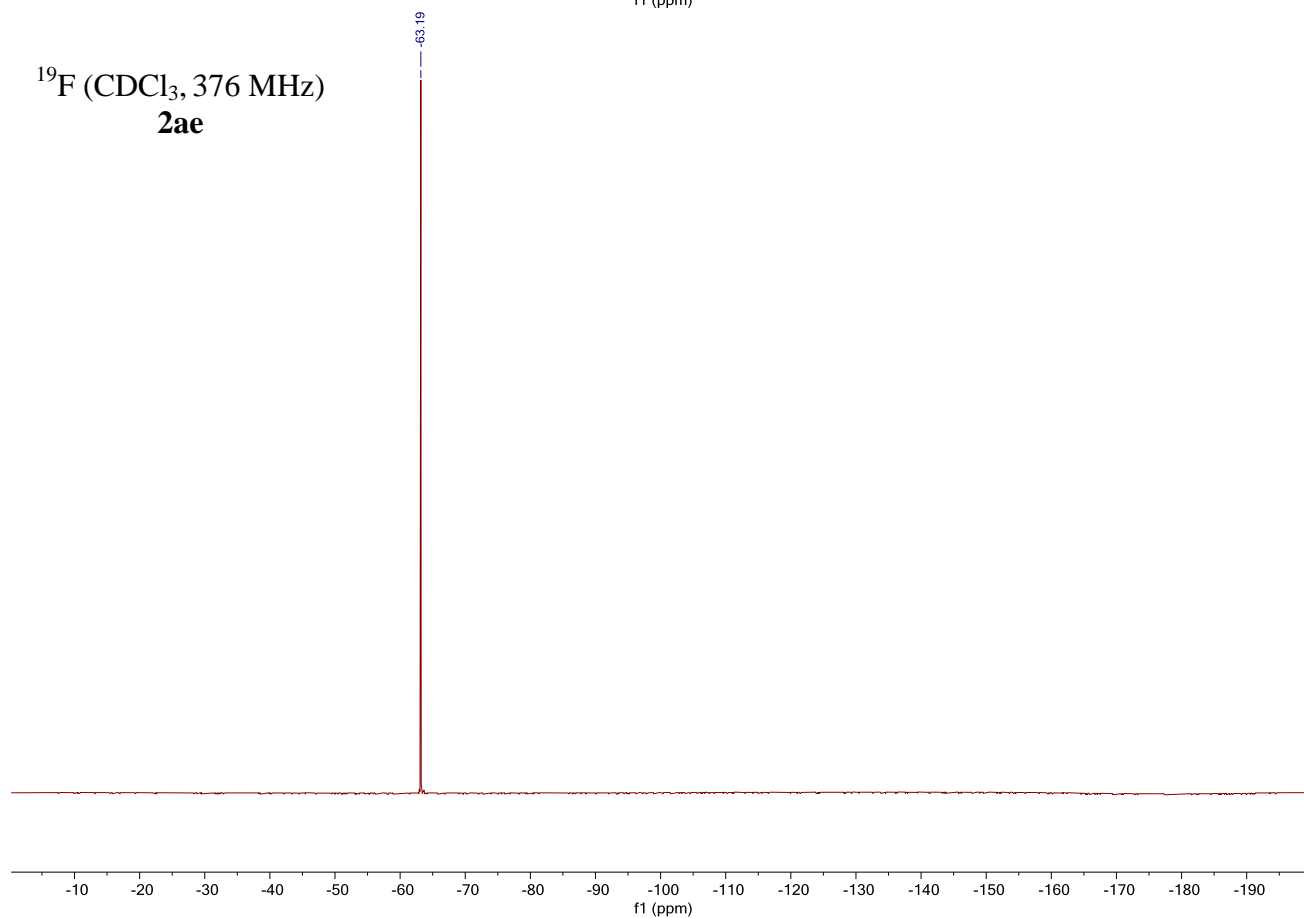
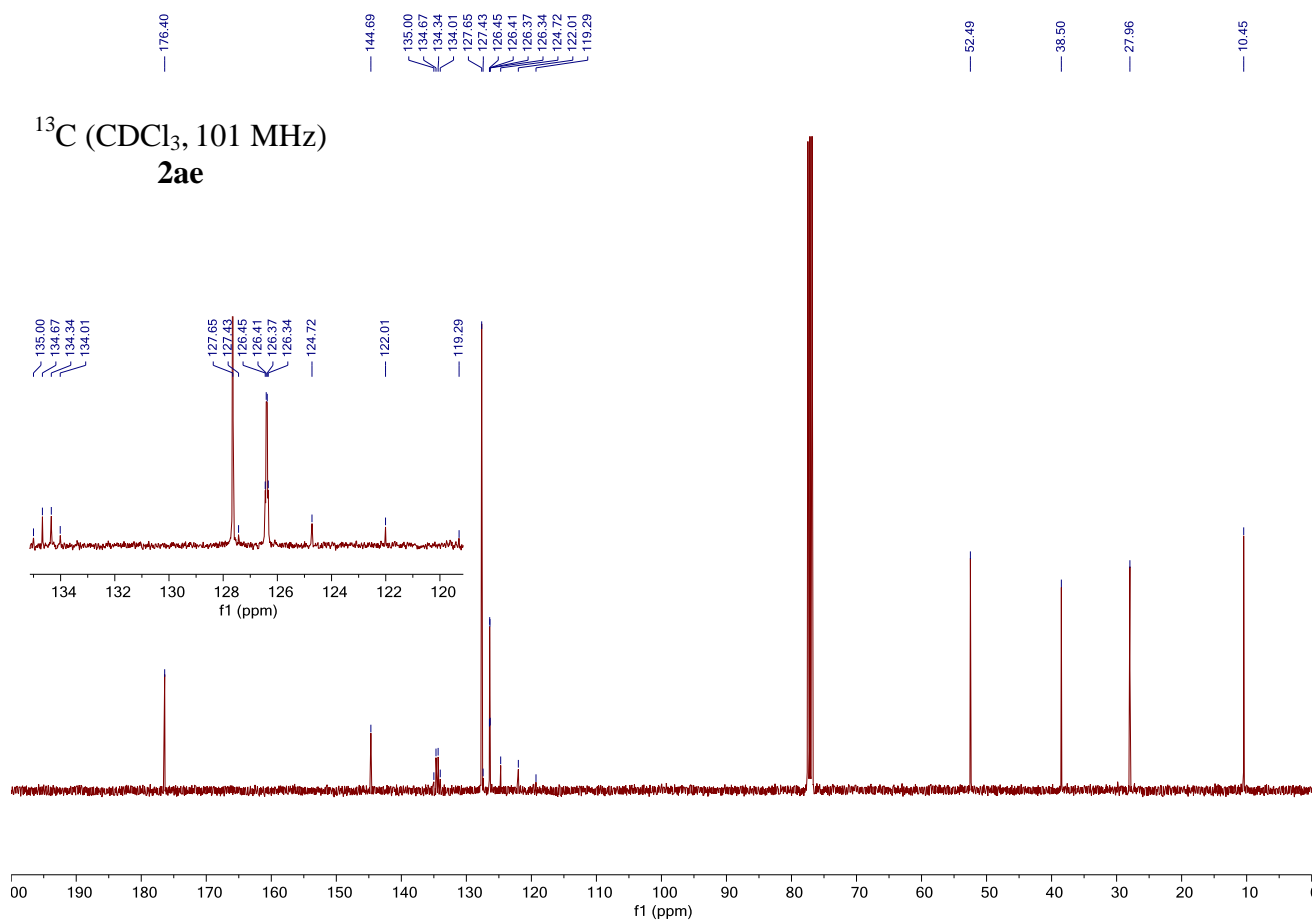


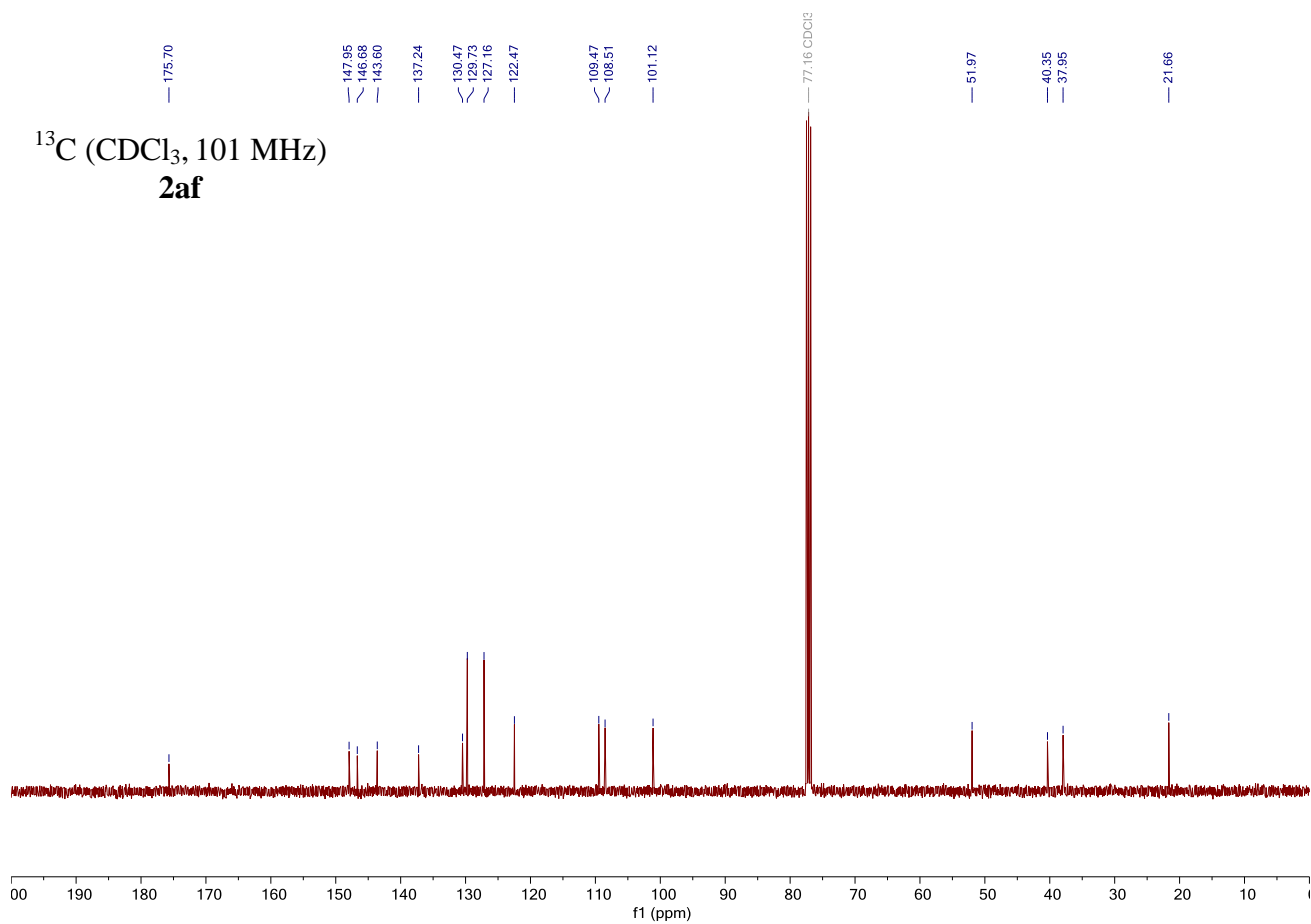
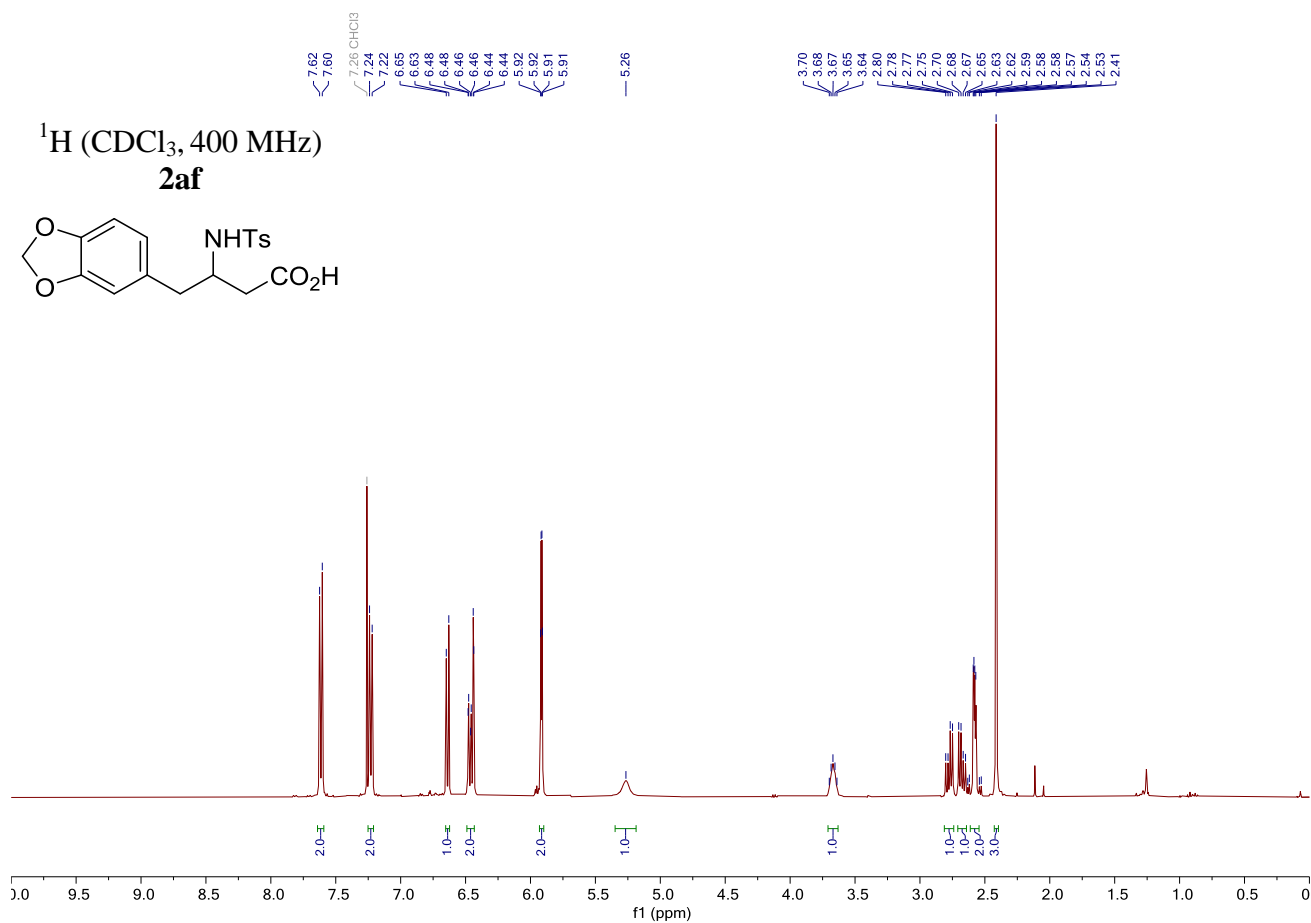


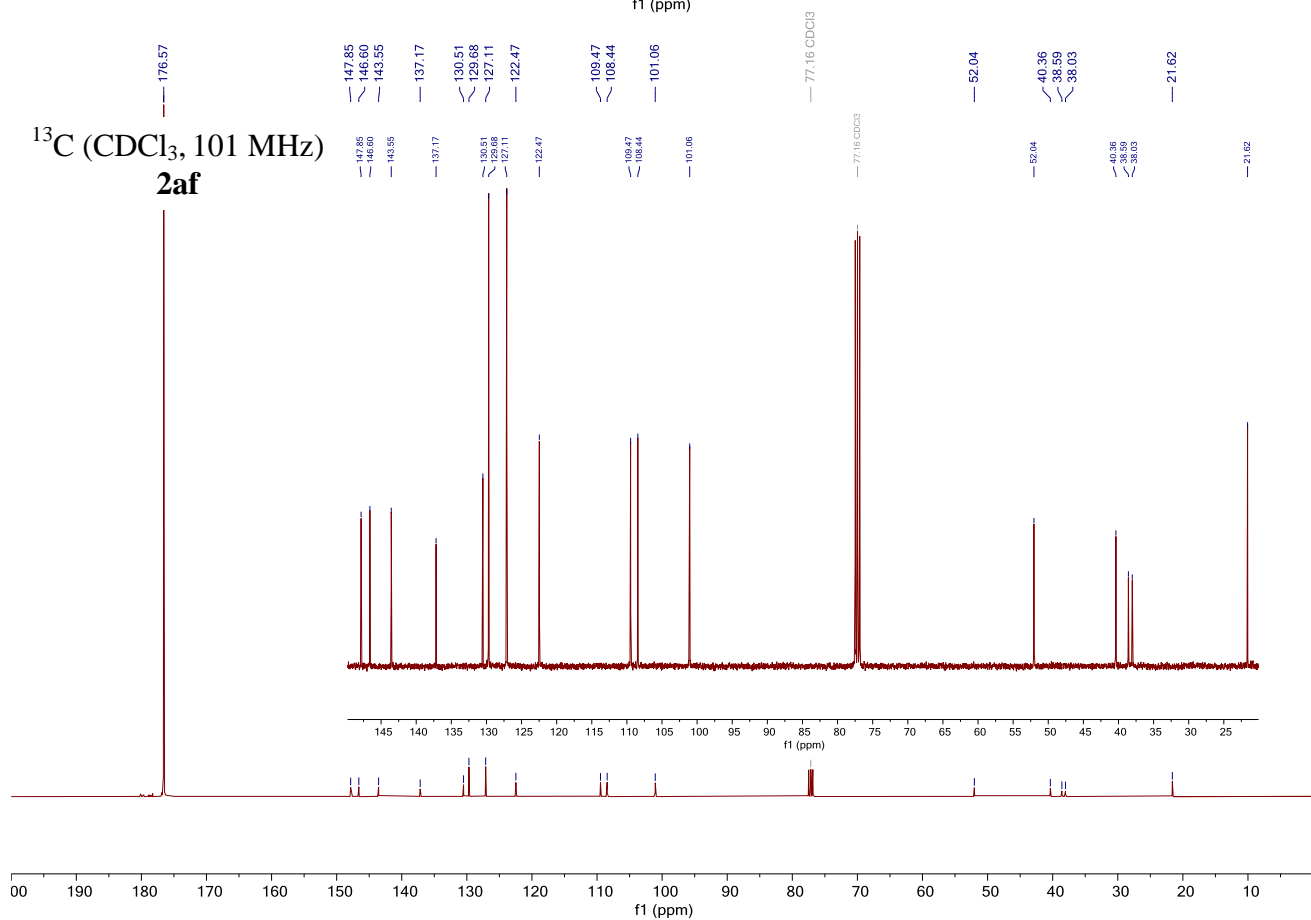
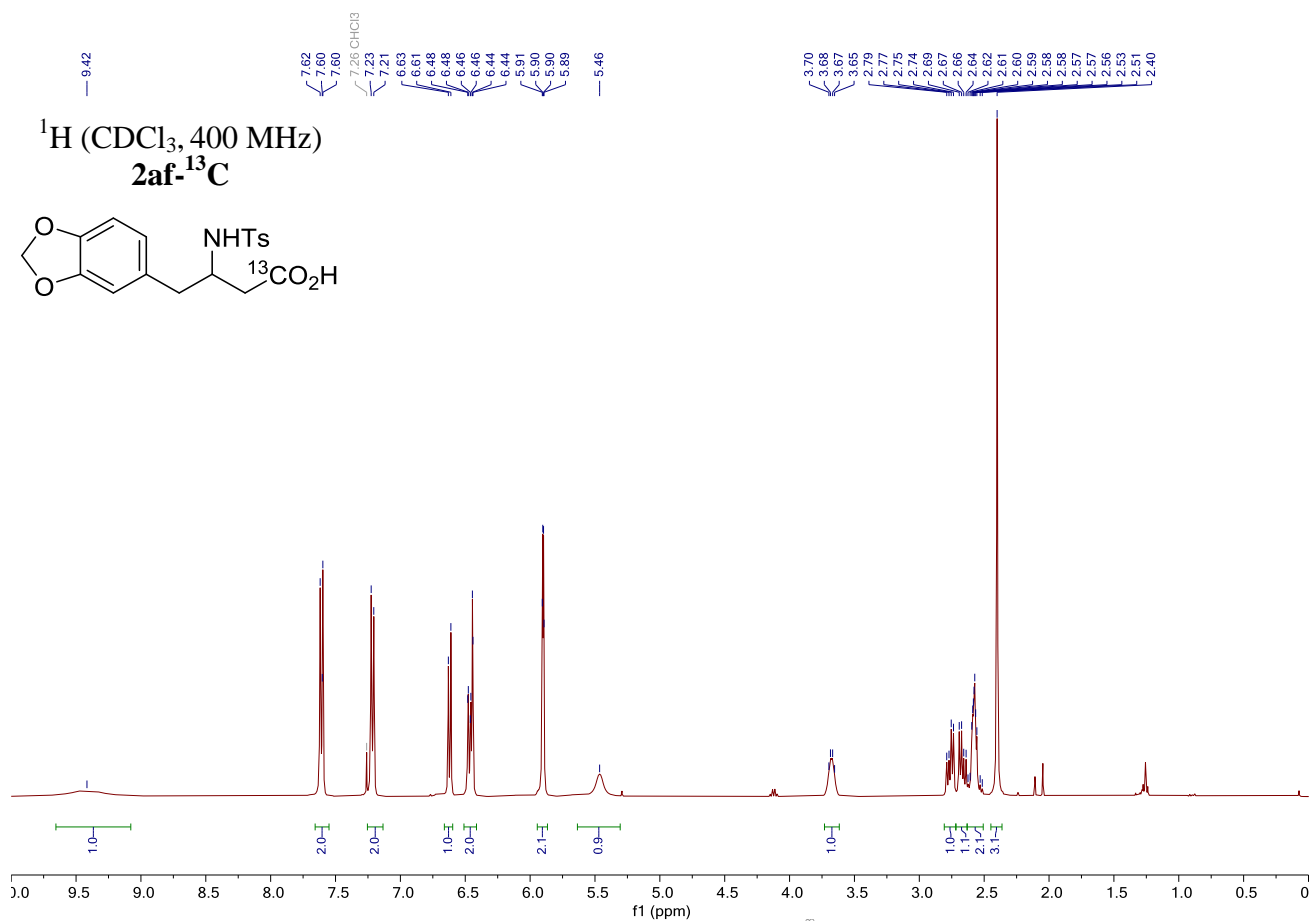


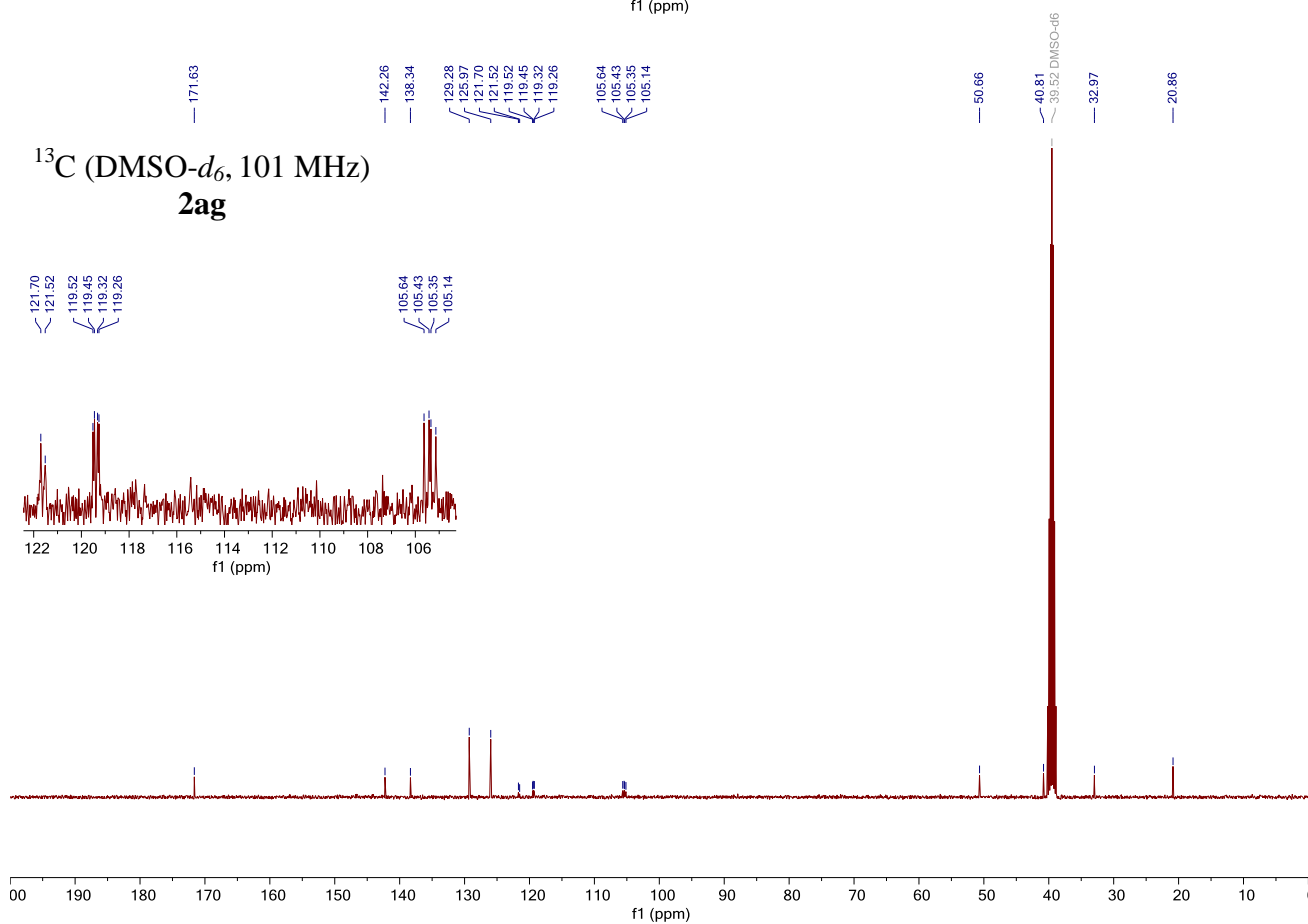
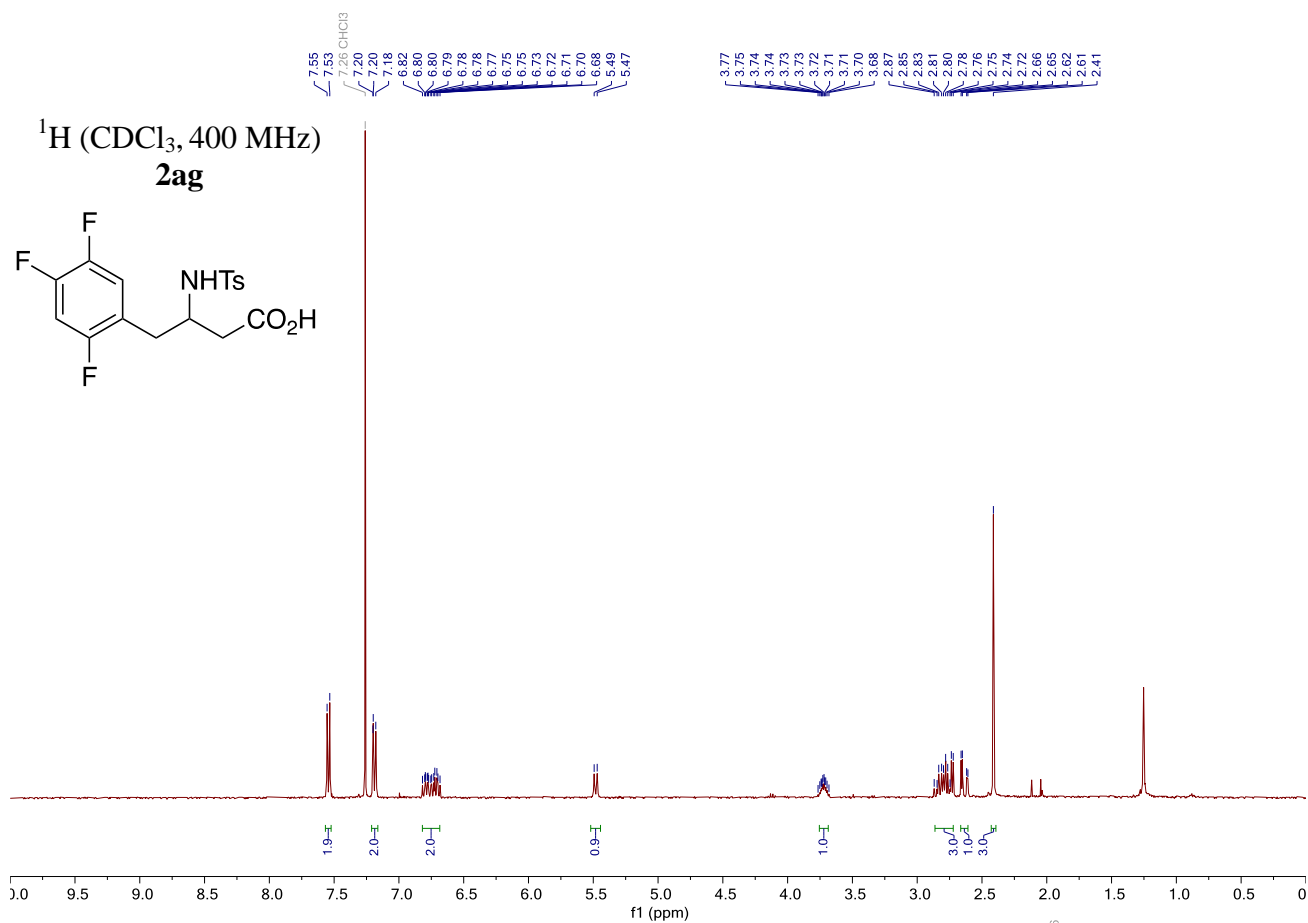




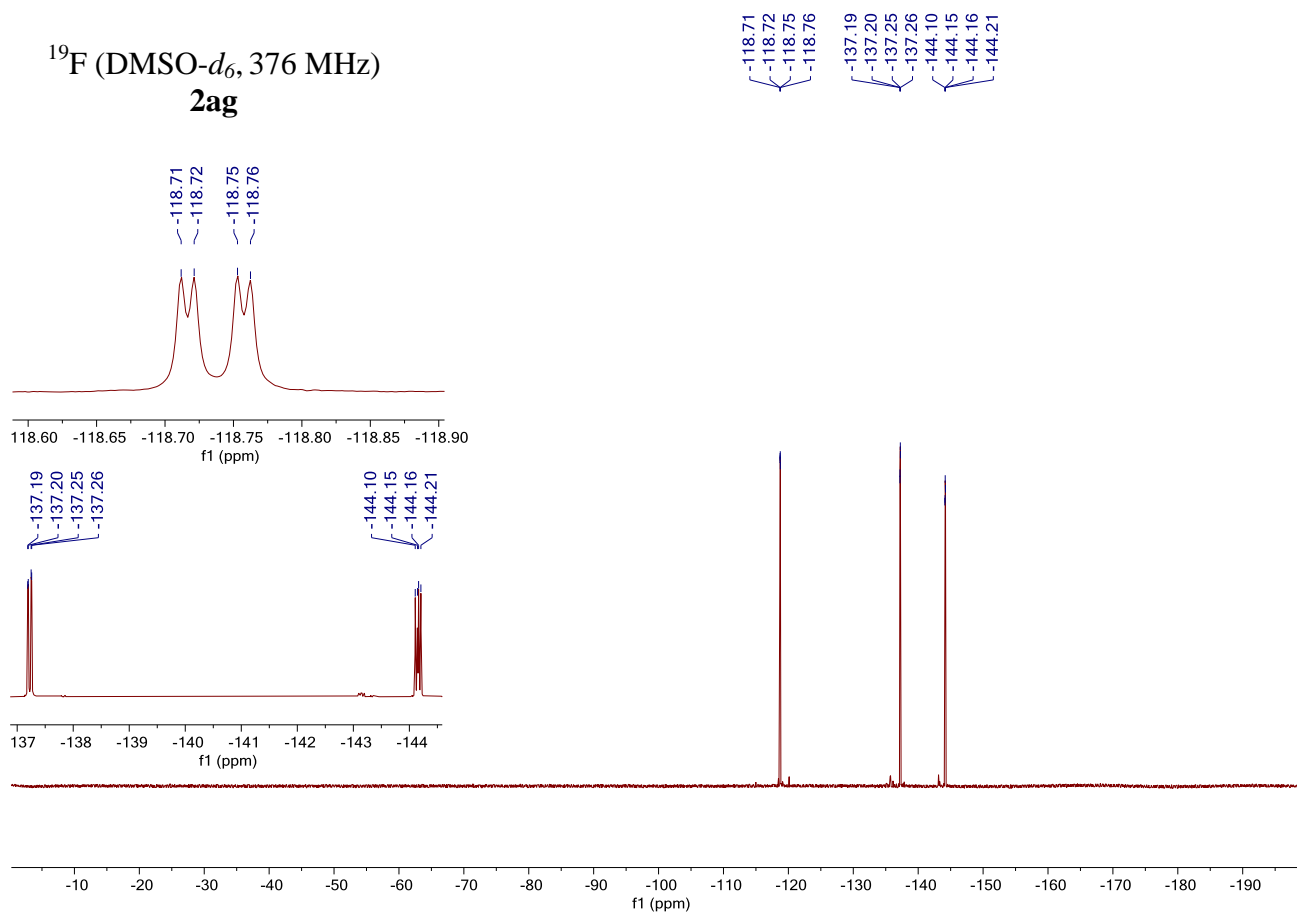




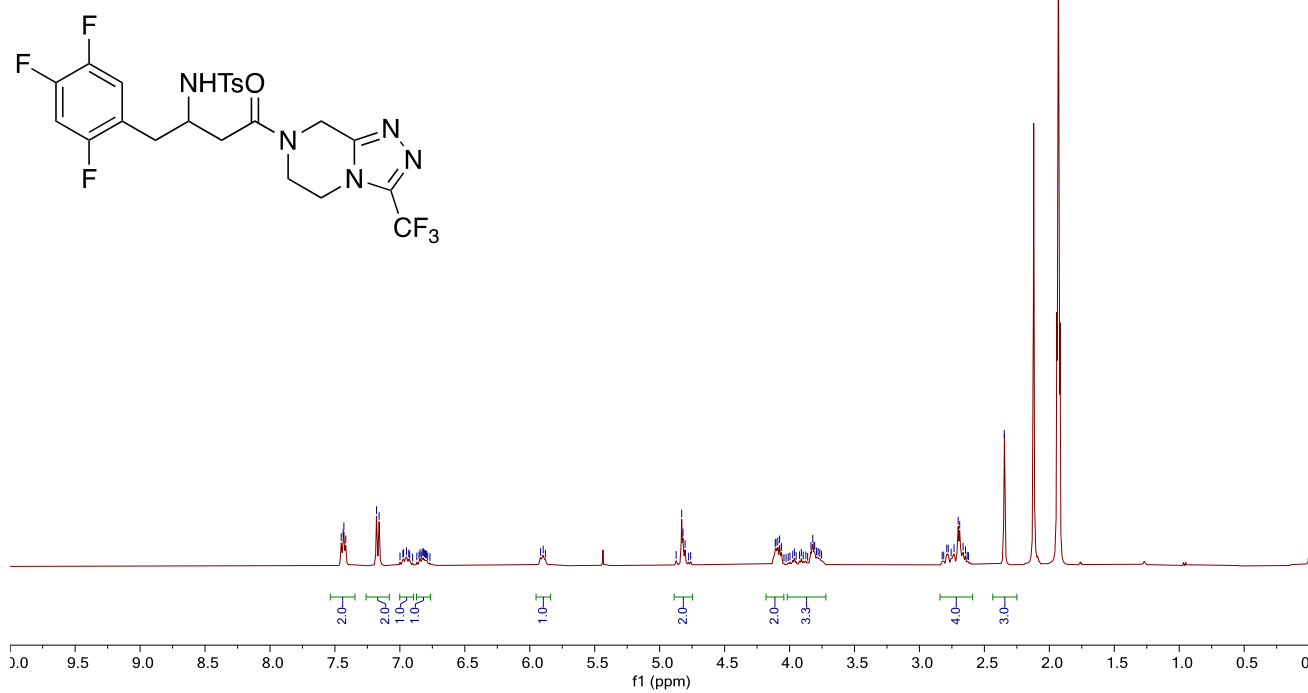


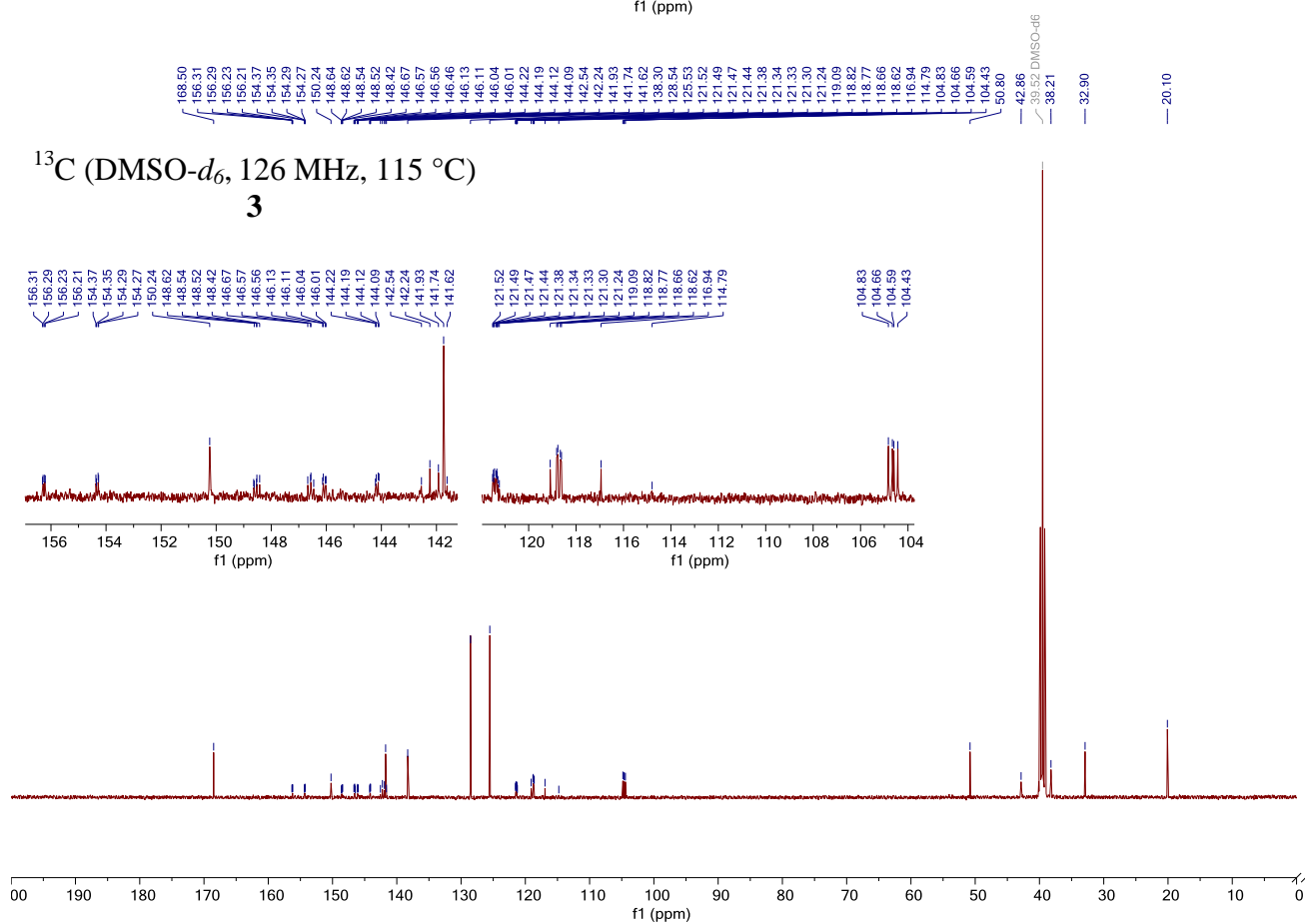
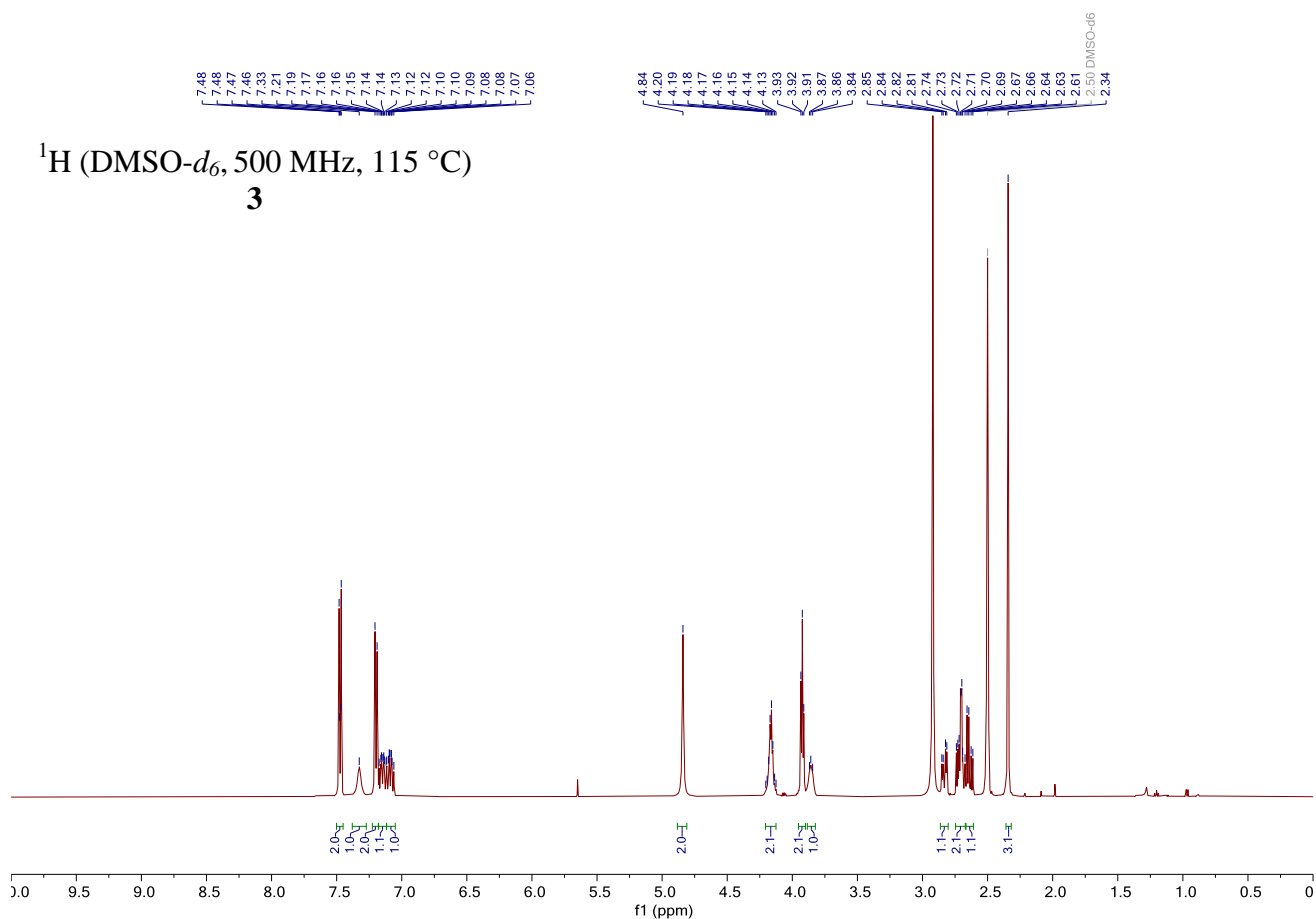


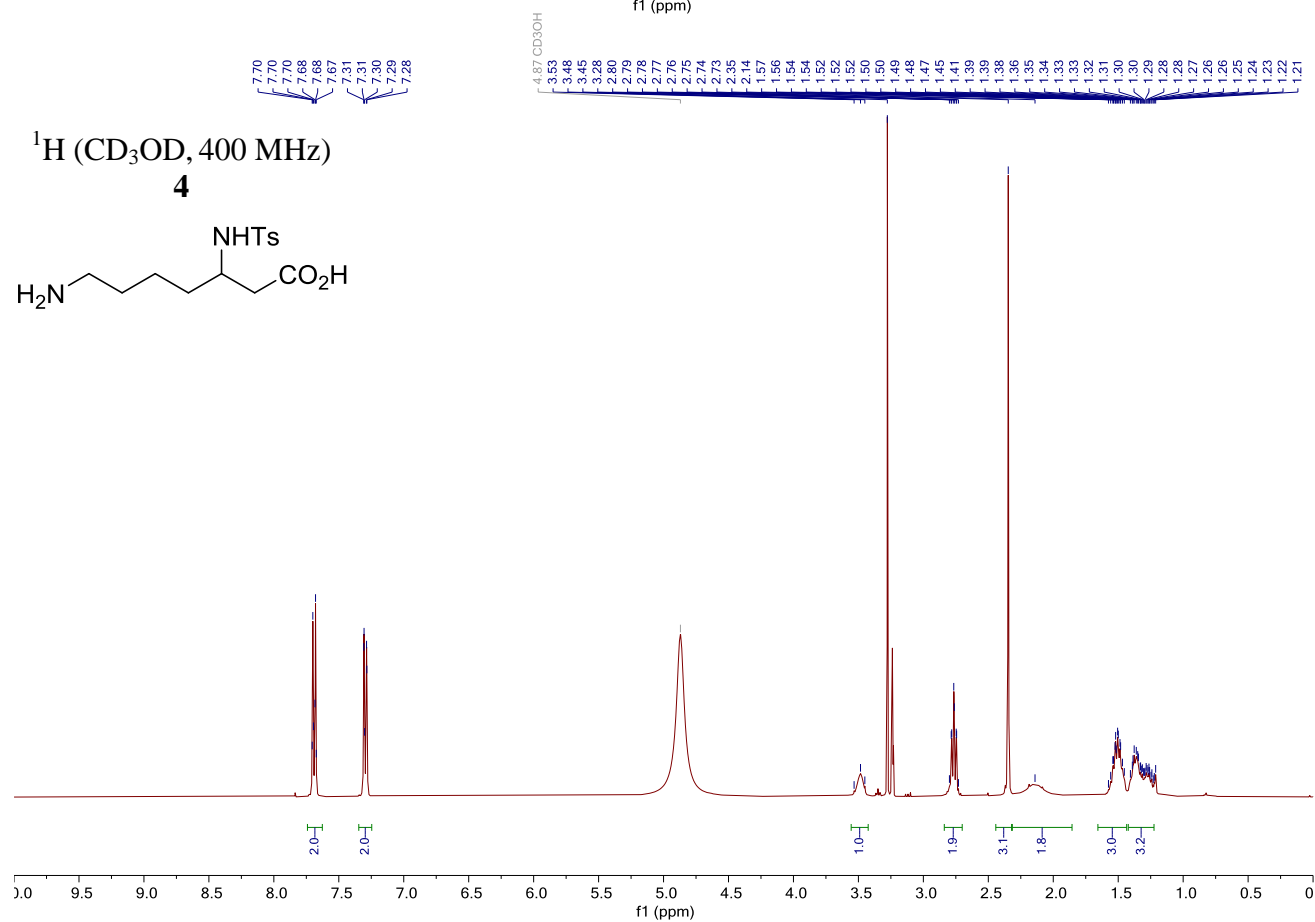
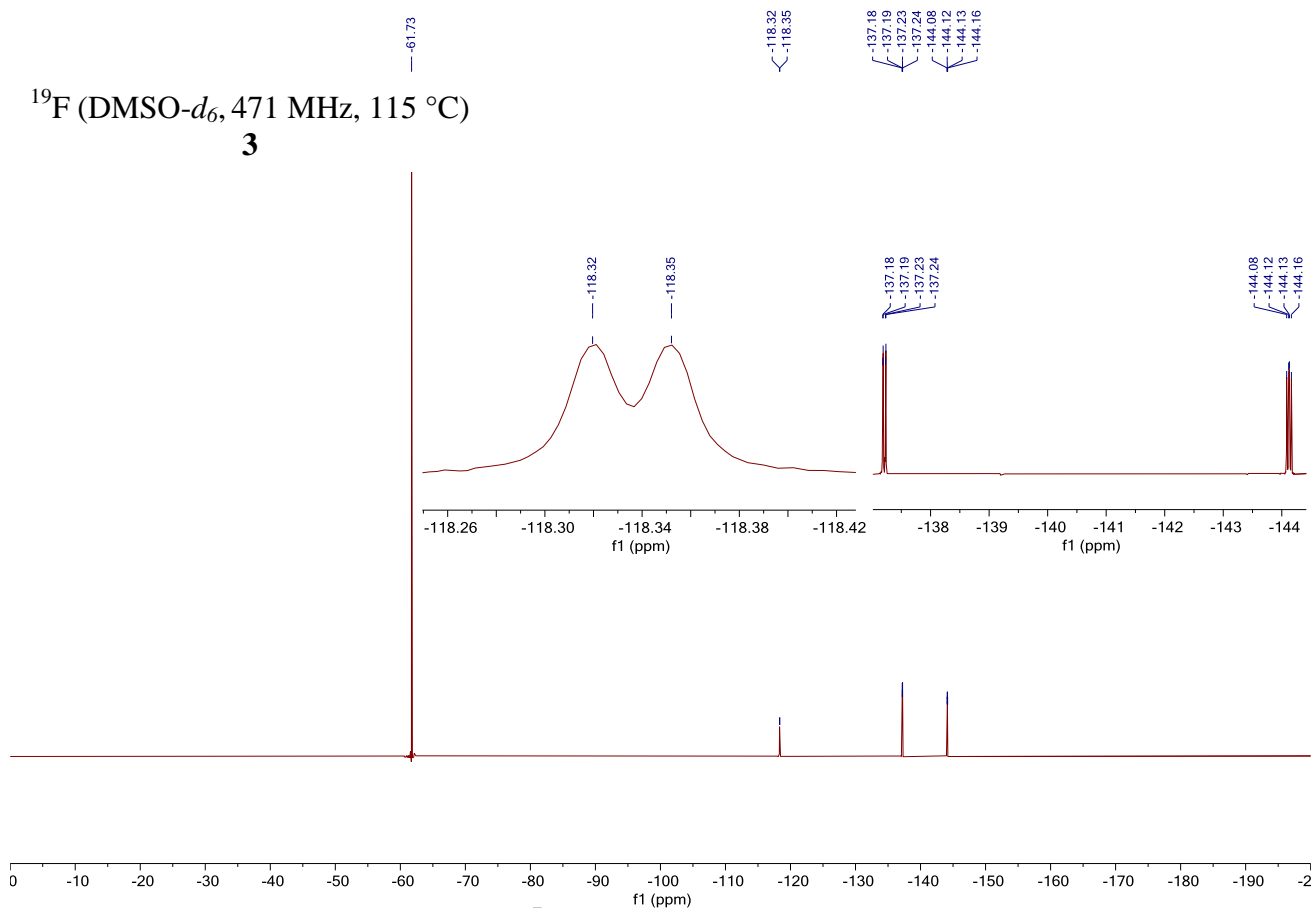
^{19}F (DMSO- d_6 , 376 MHz)
2ag

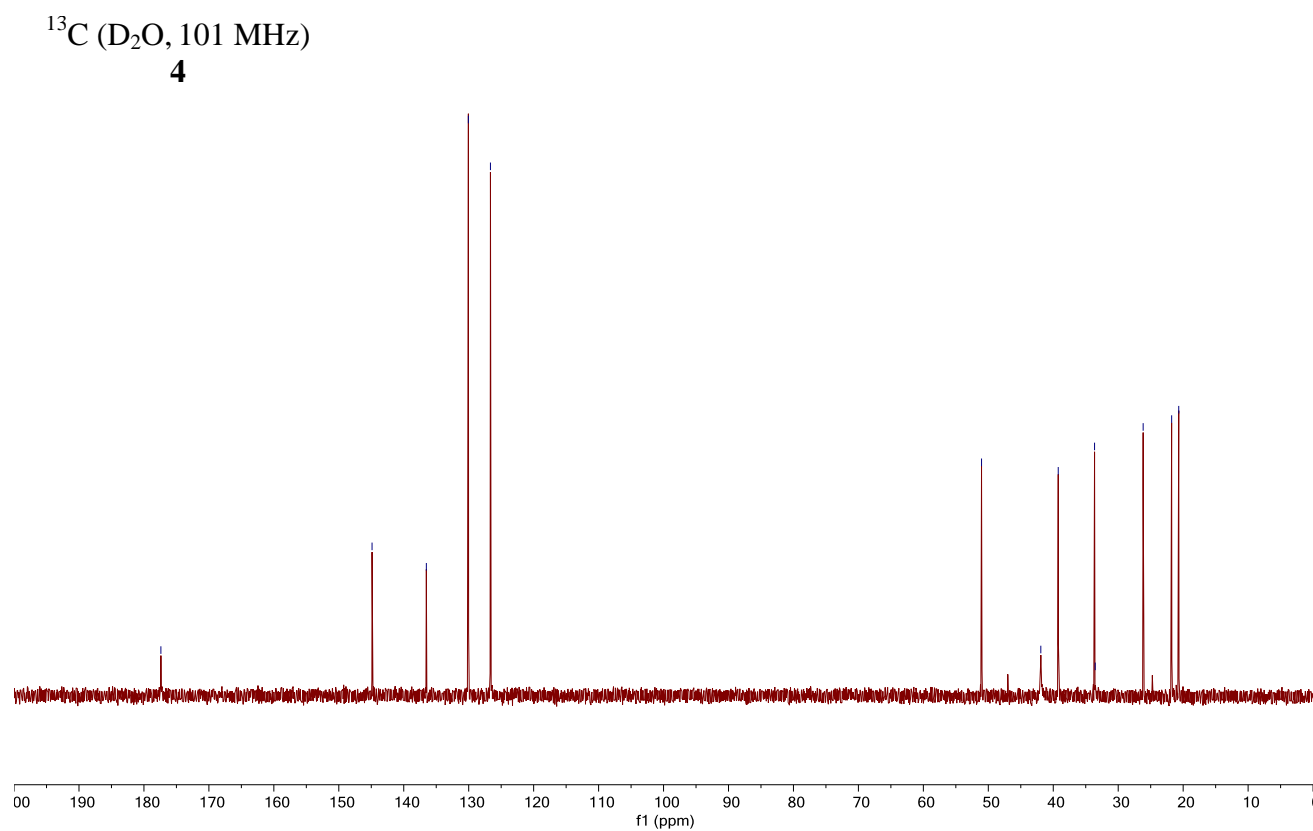
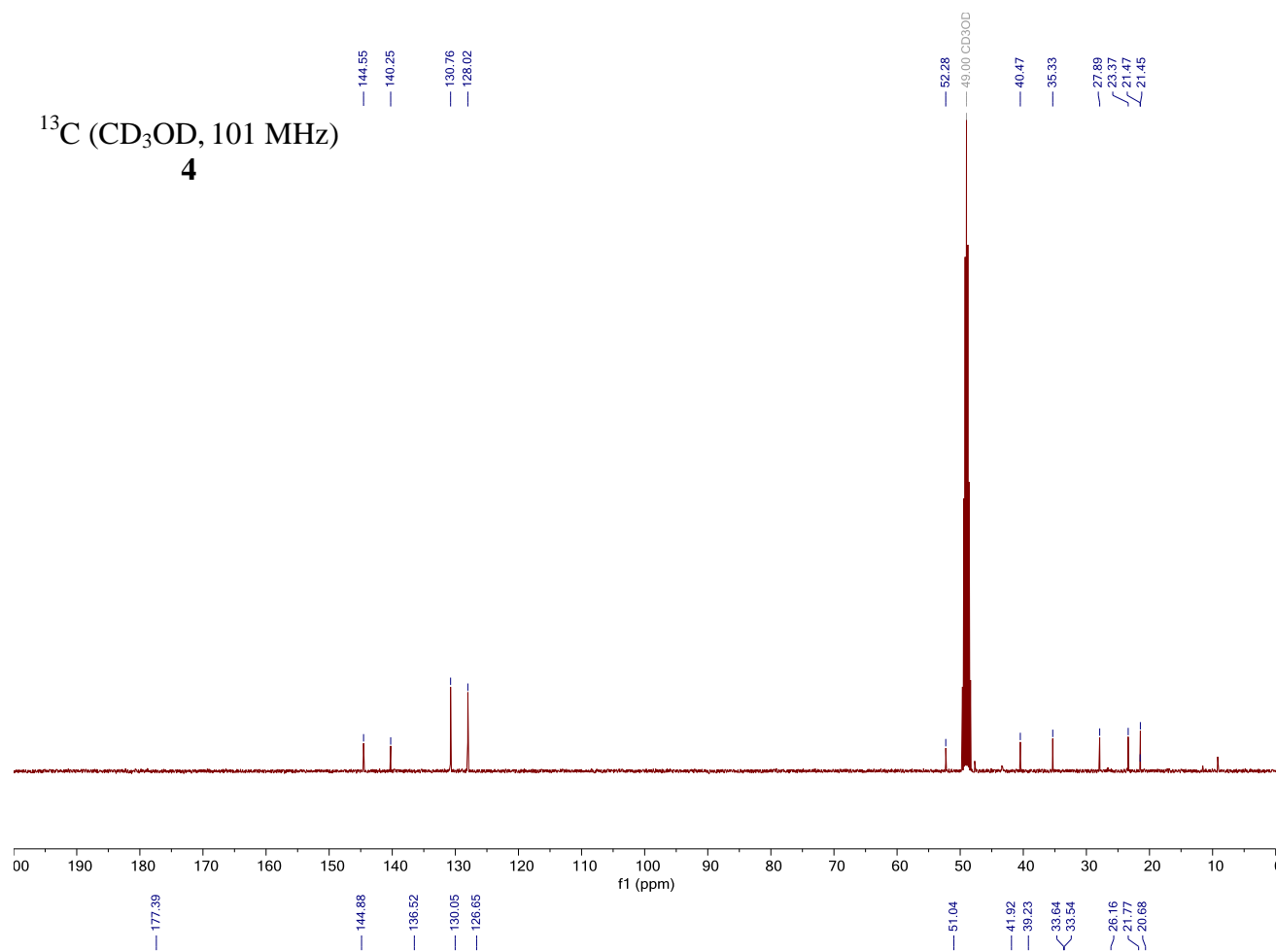


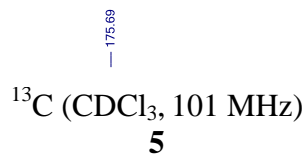
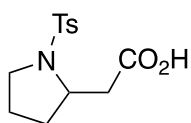
^1H (CD $_3$ CN, 400 MHz)
3

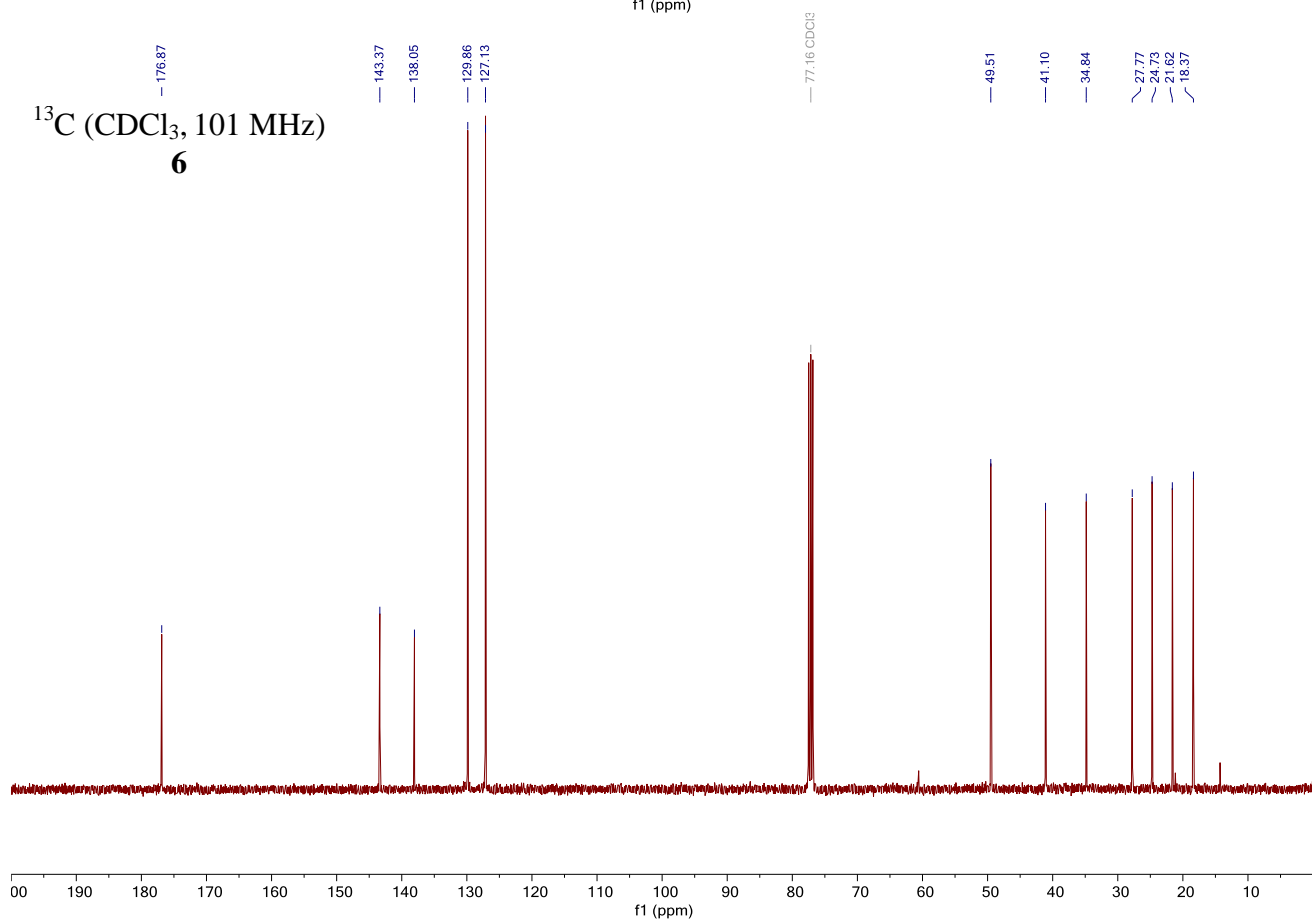
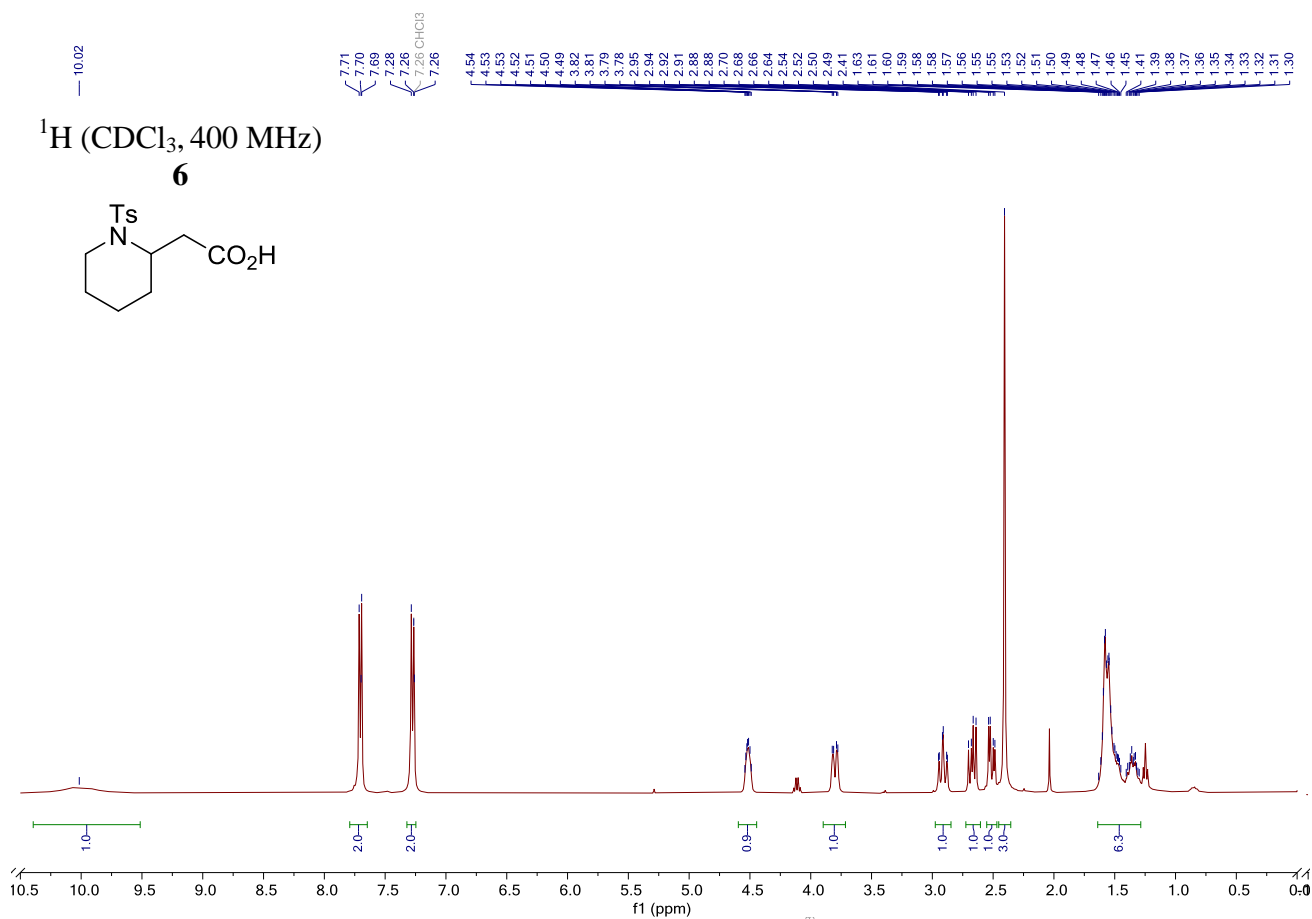


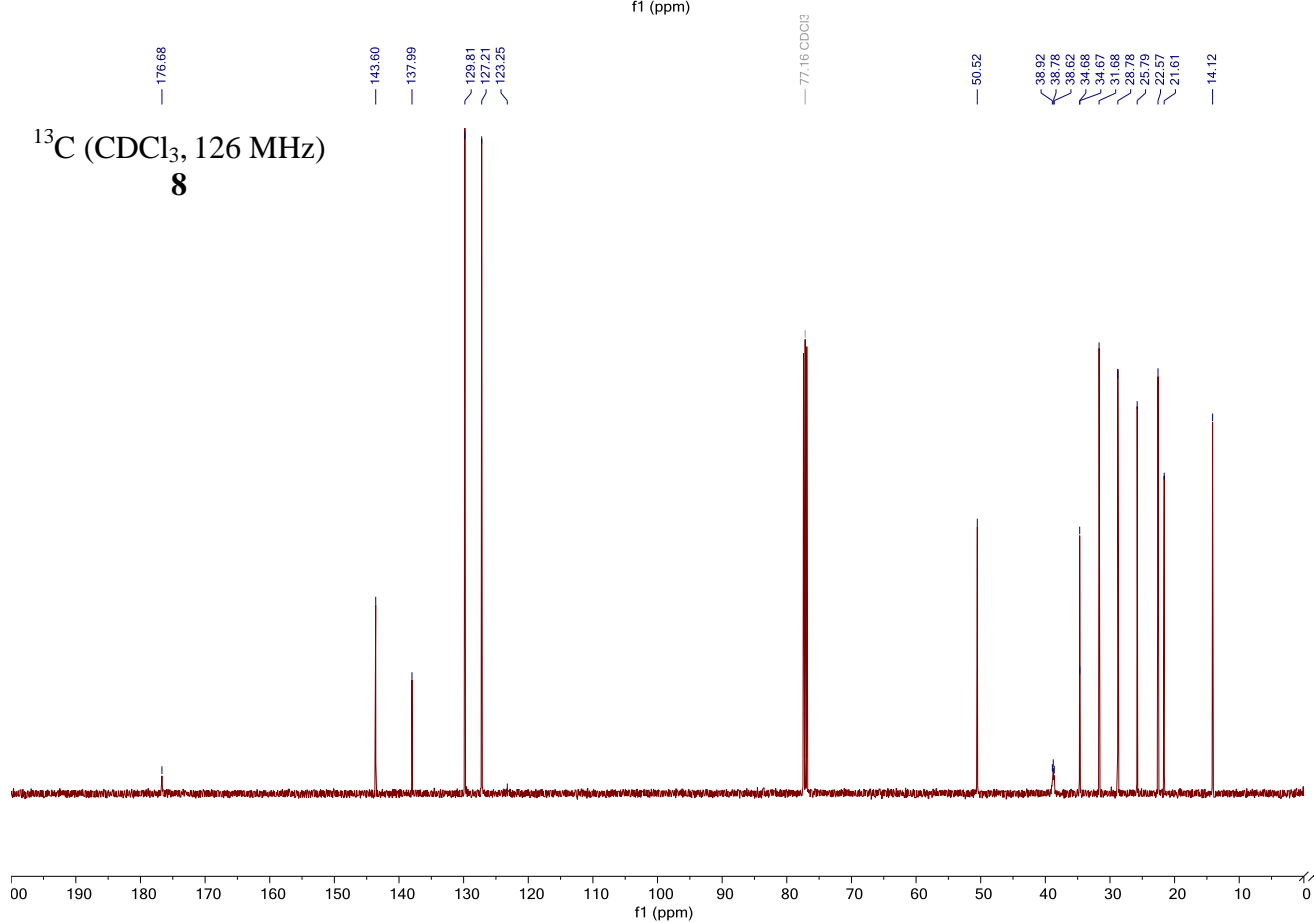
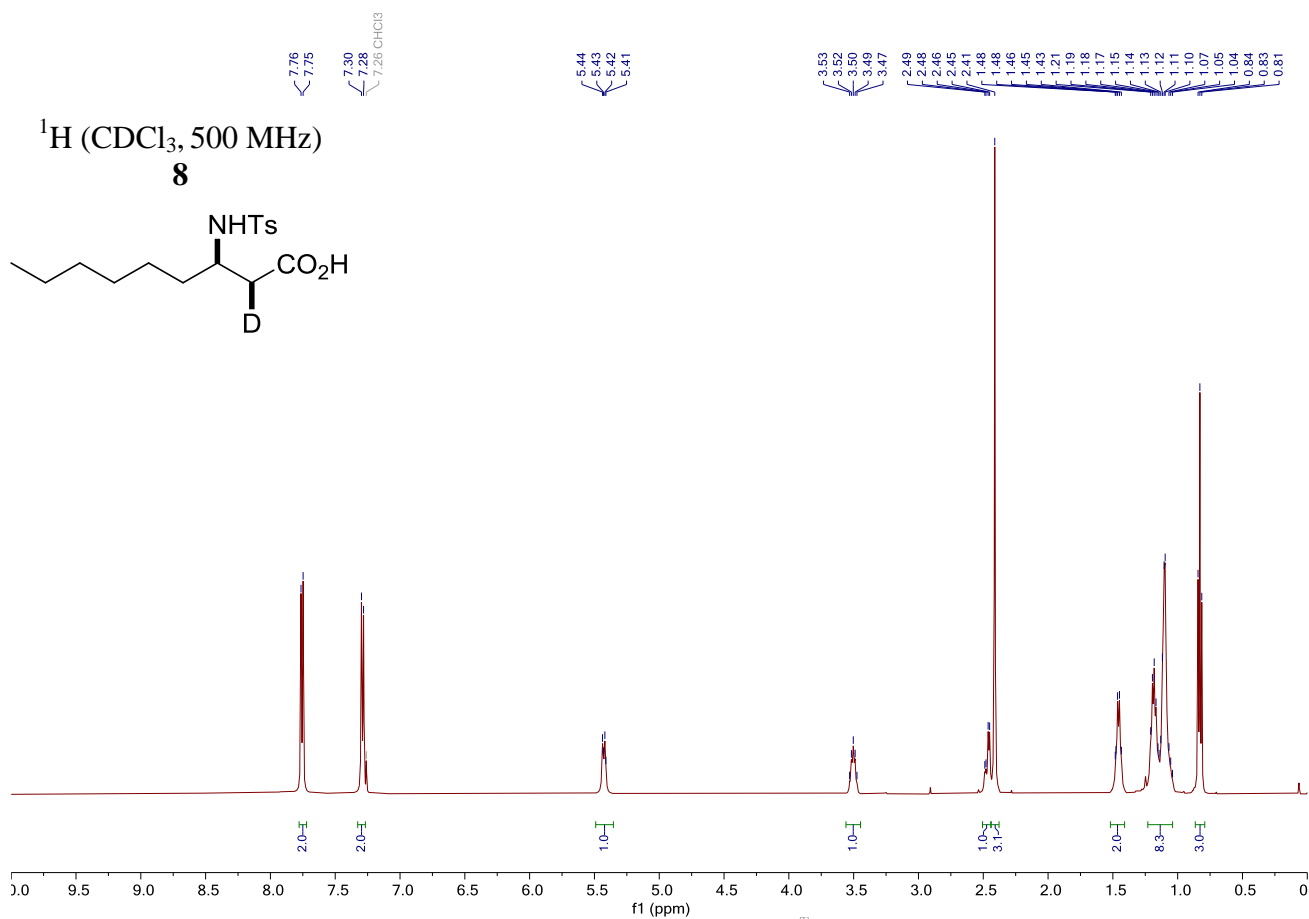


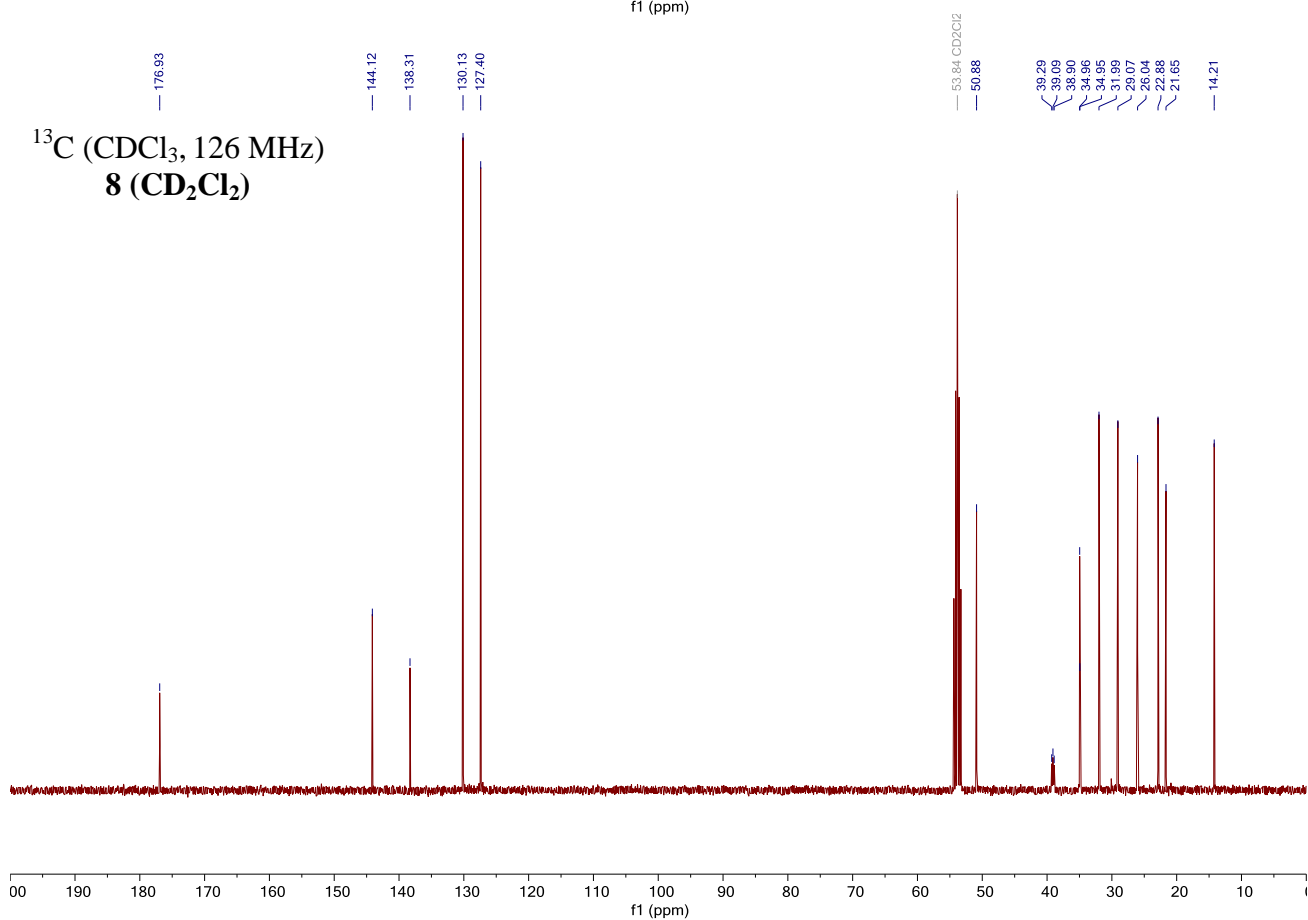
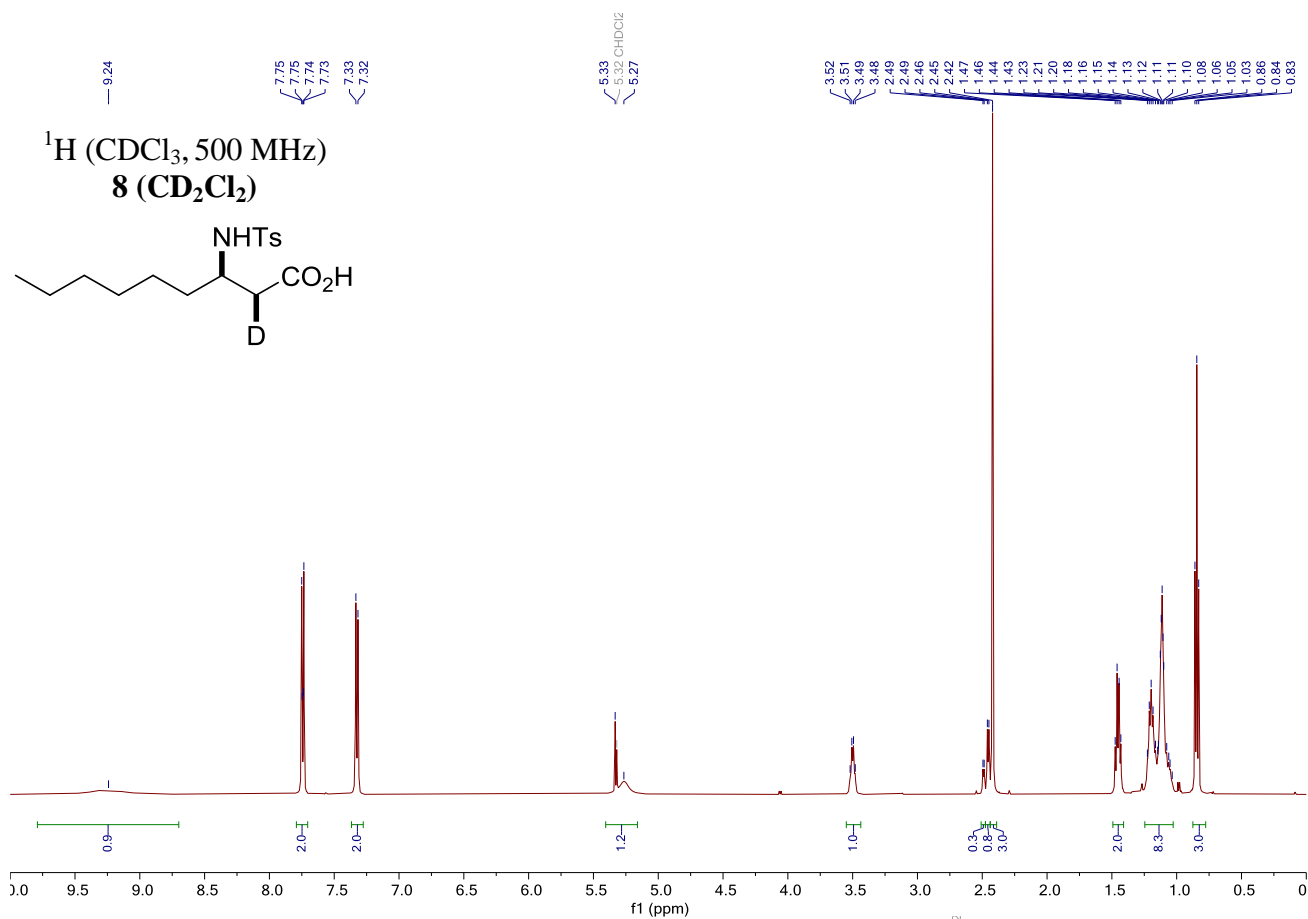


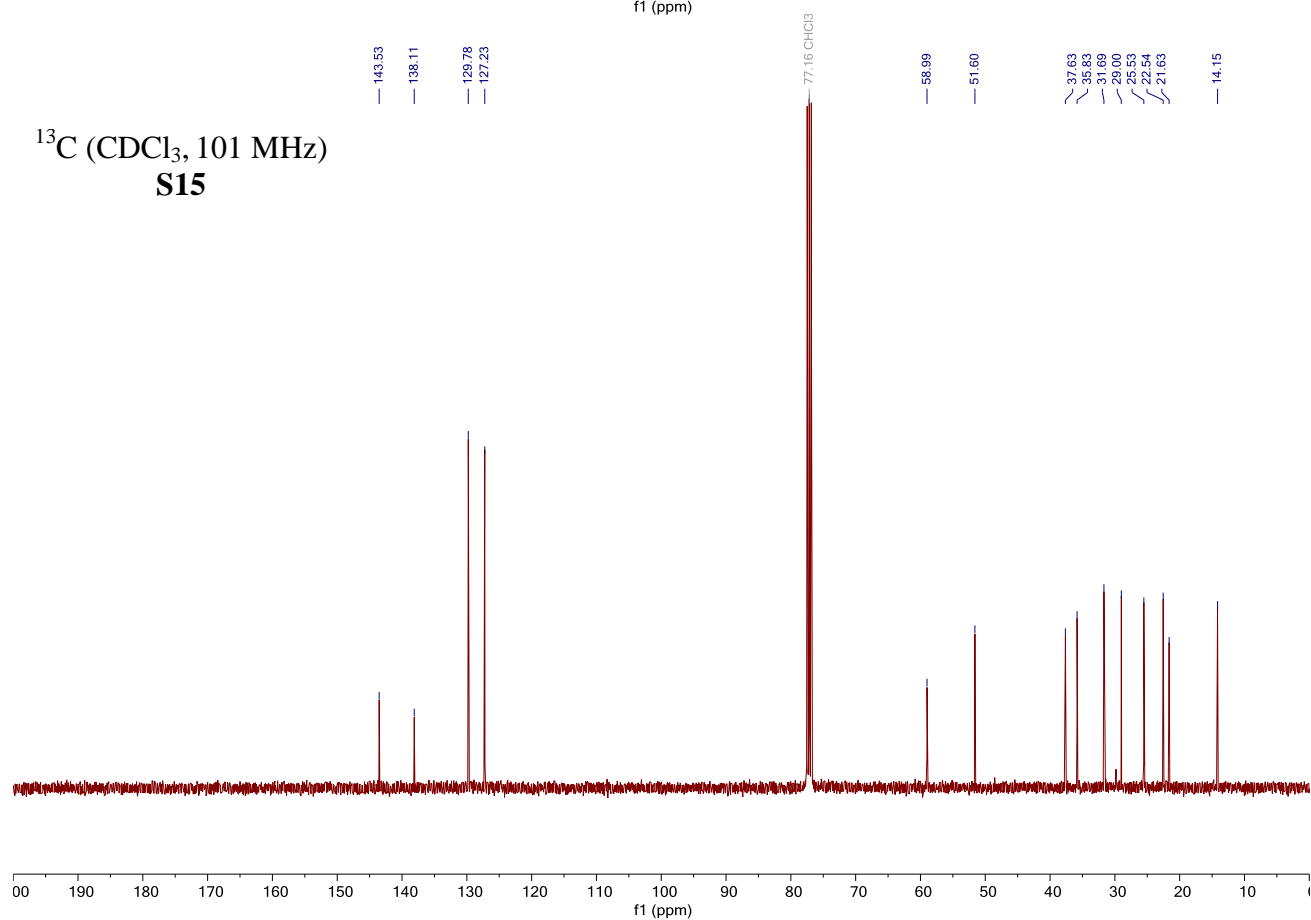
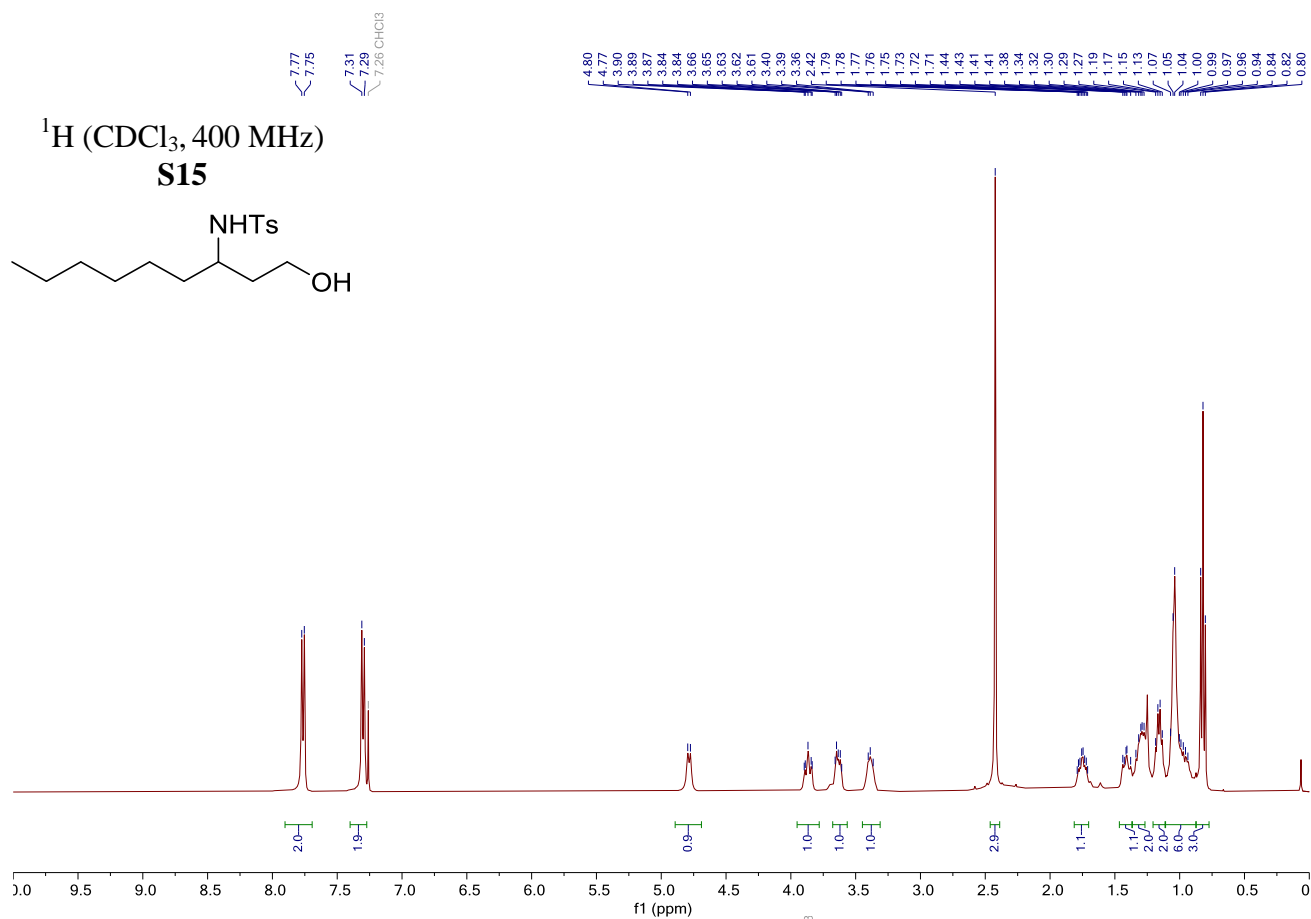


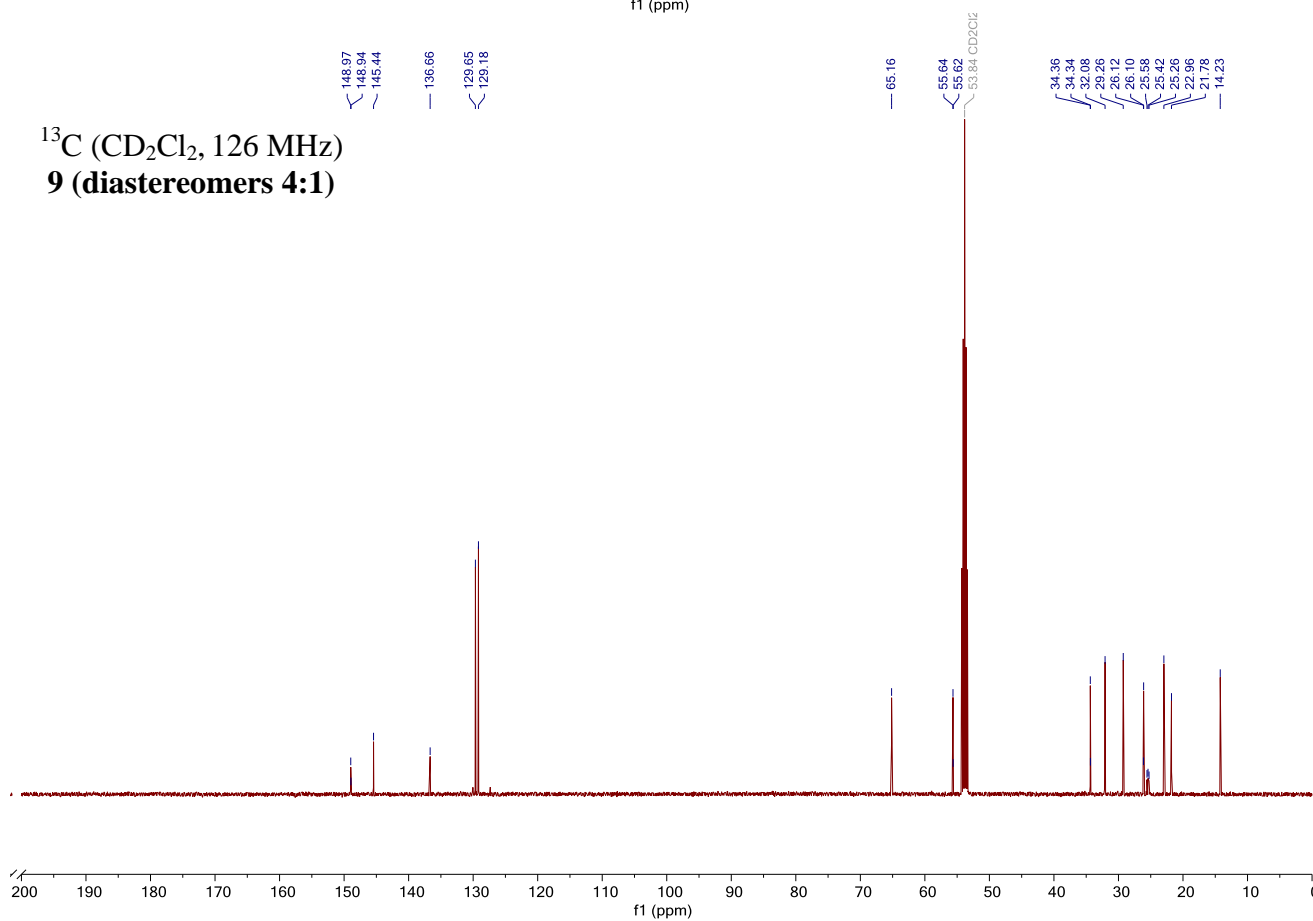
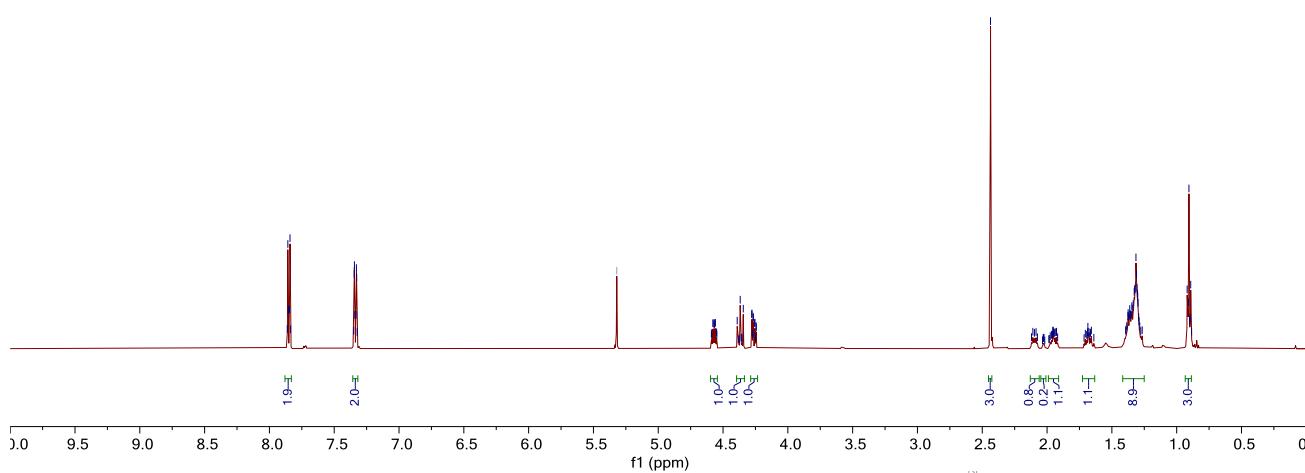
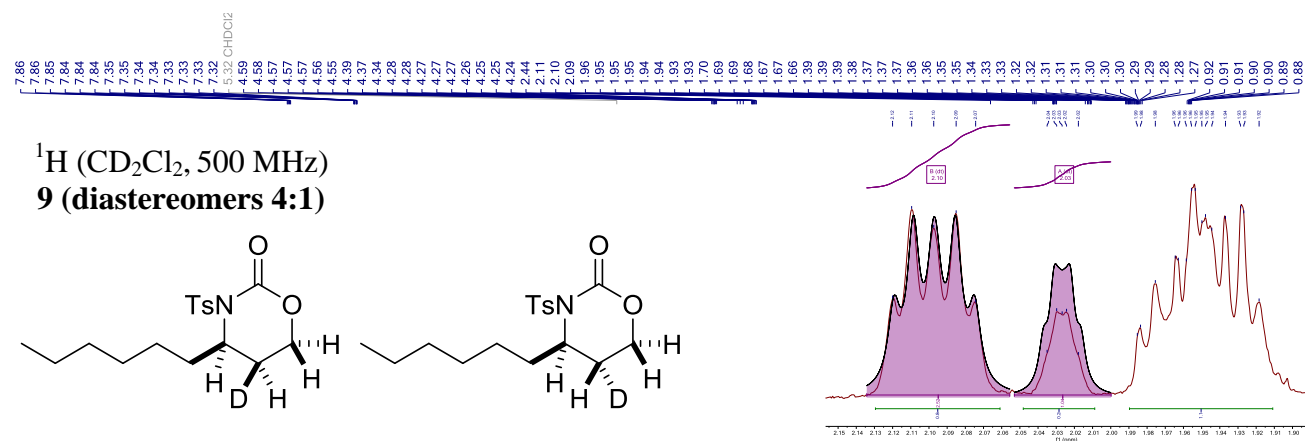


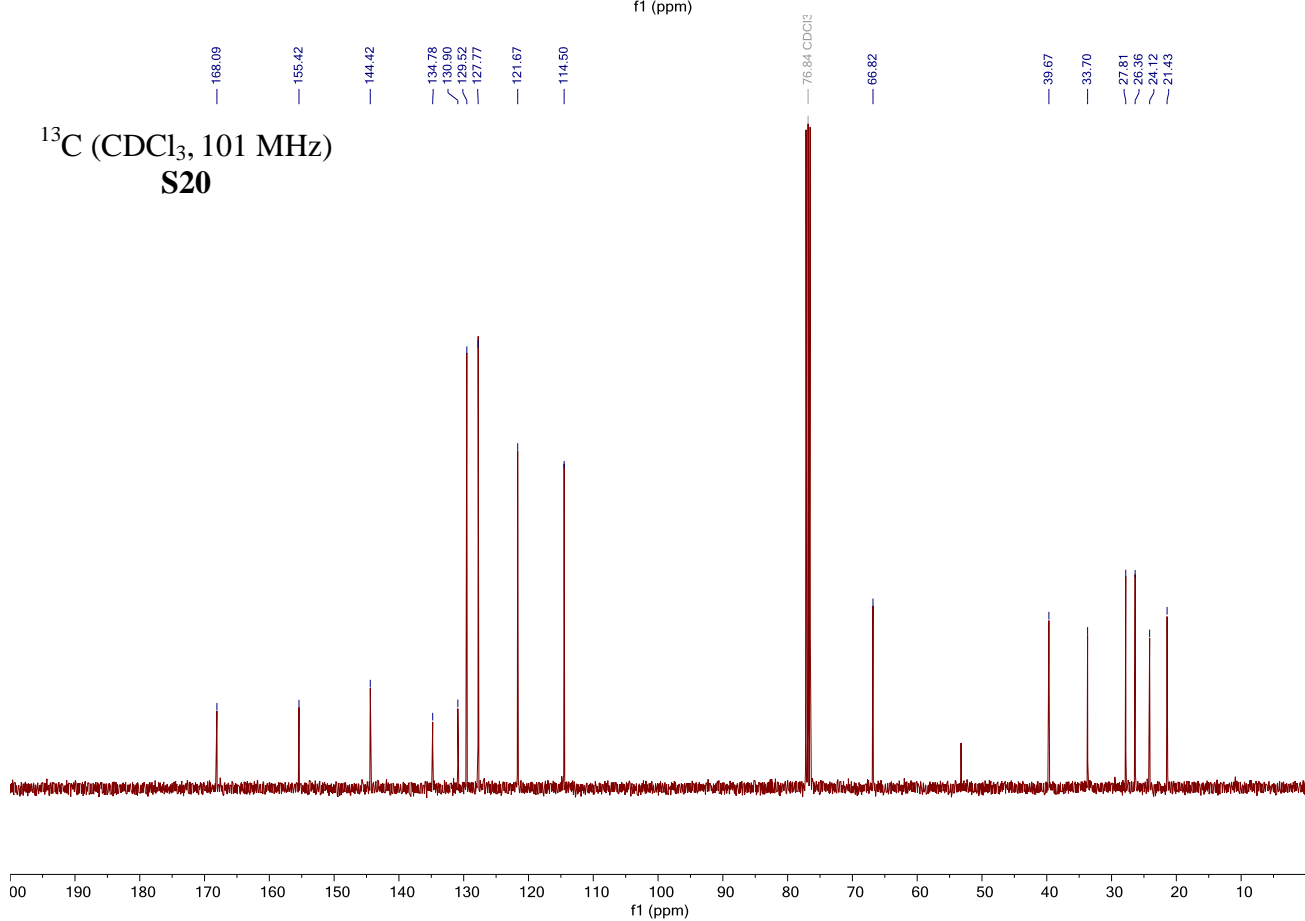
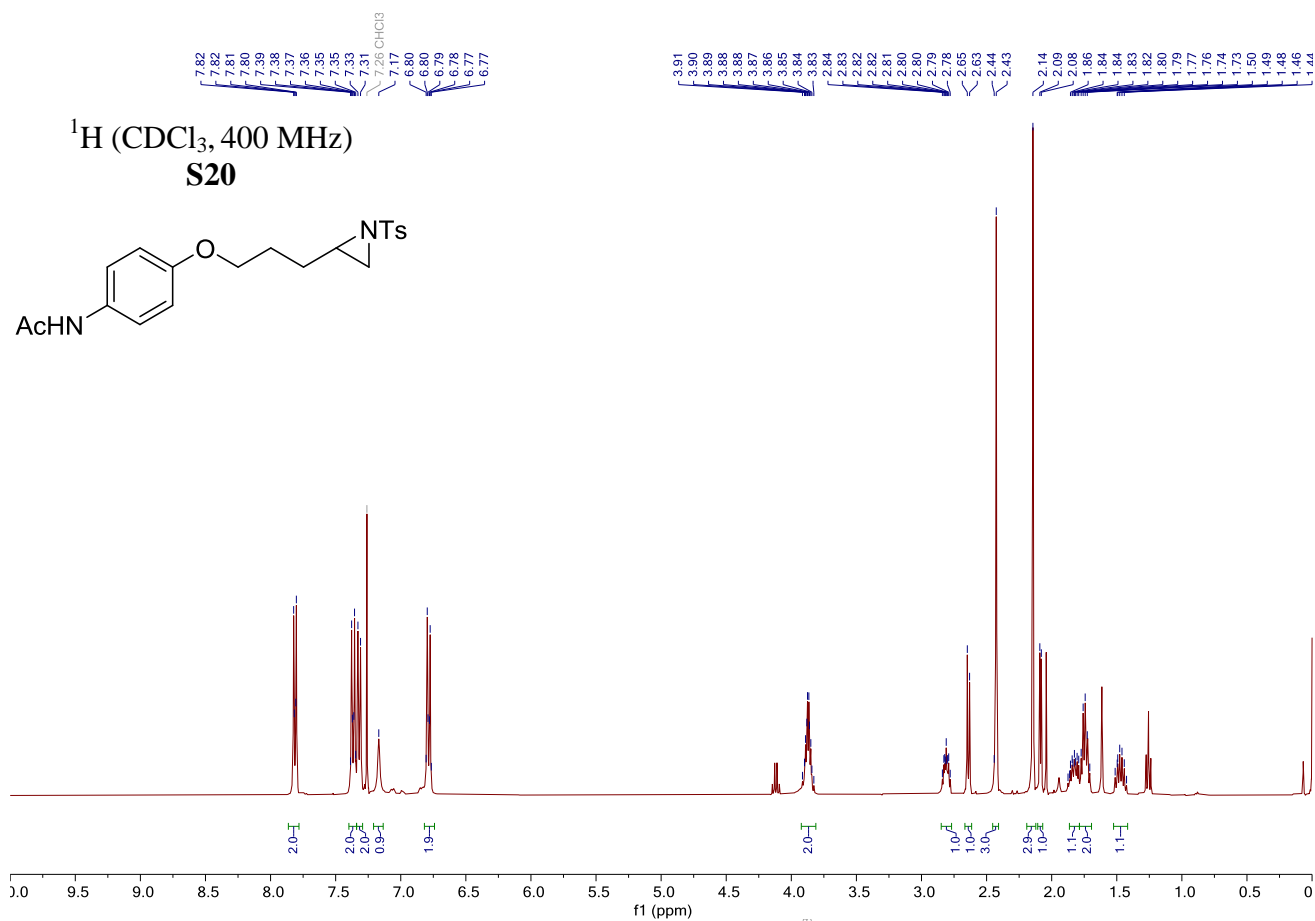






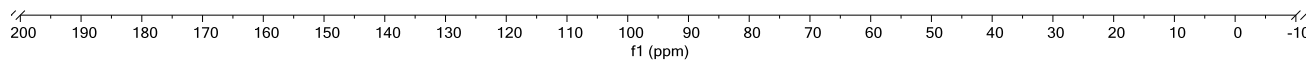


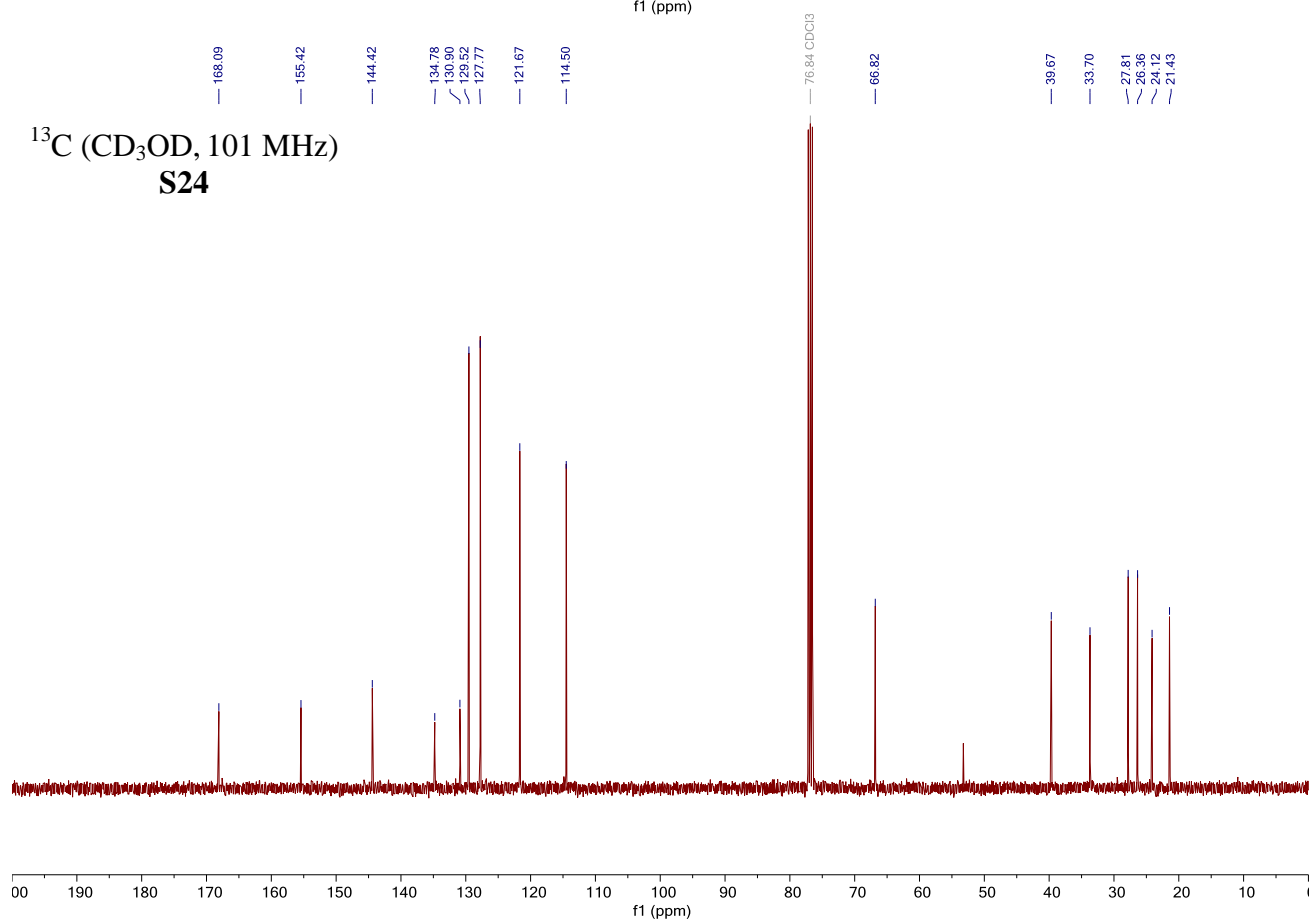
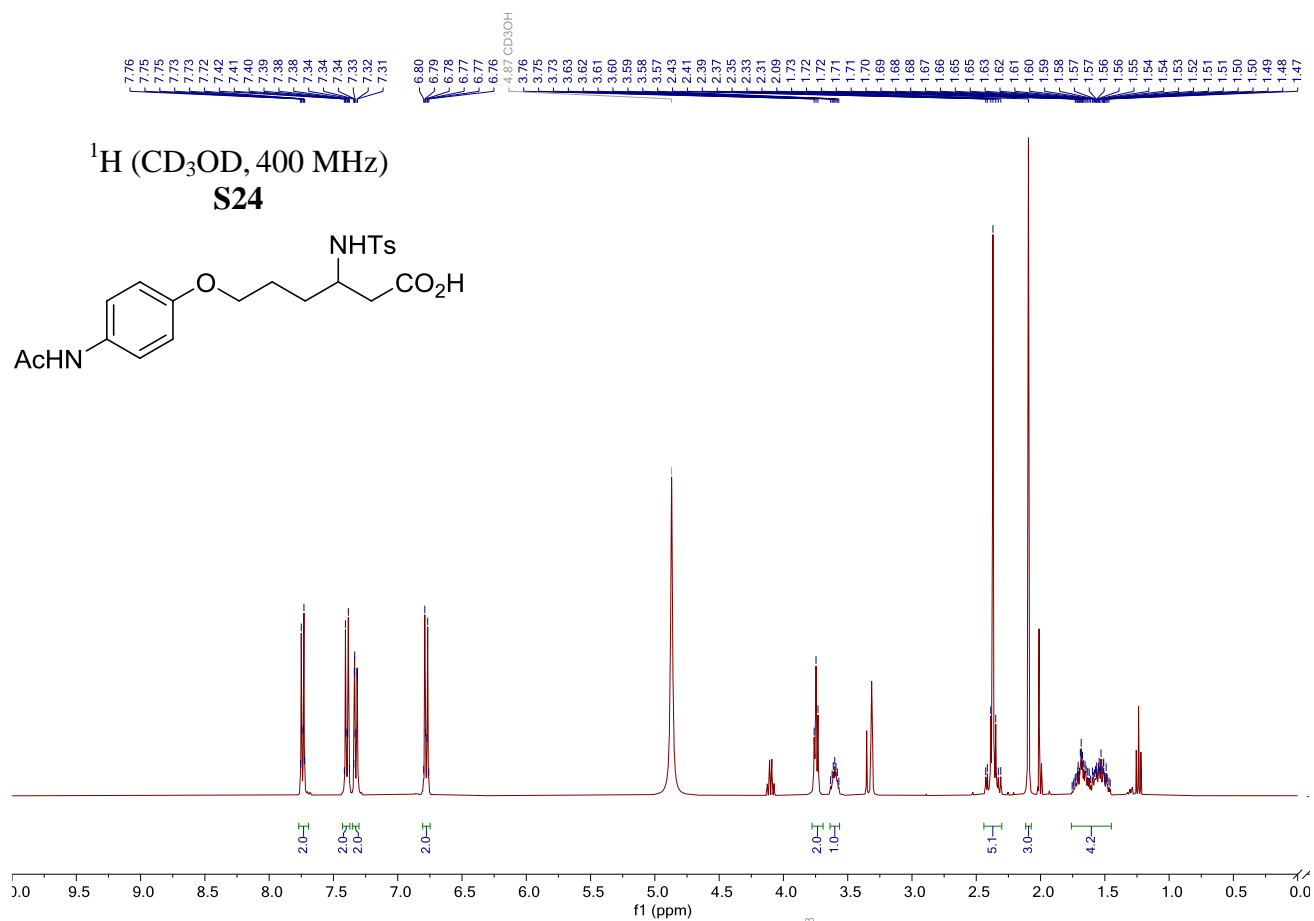




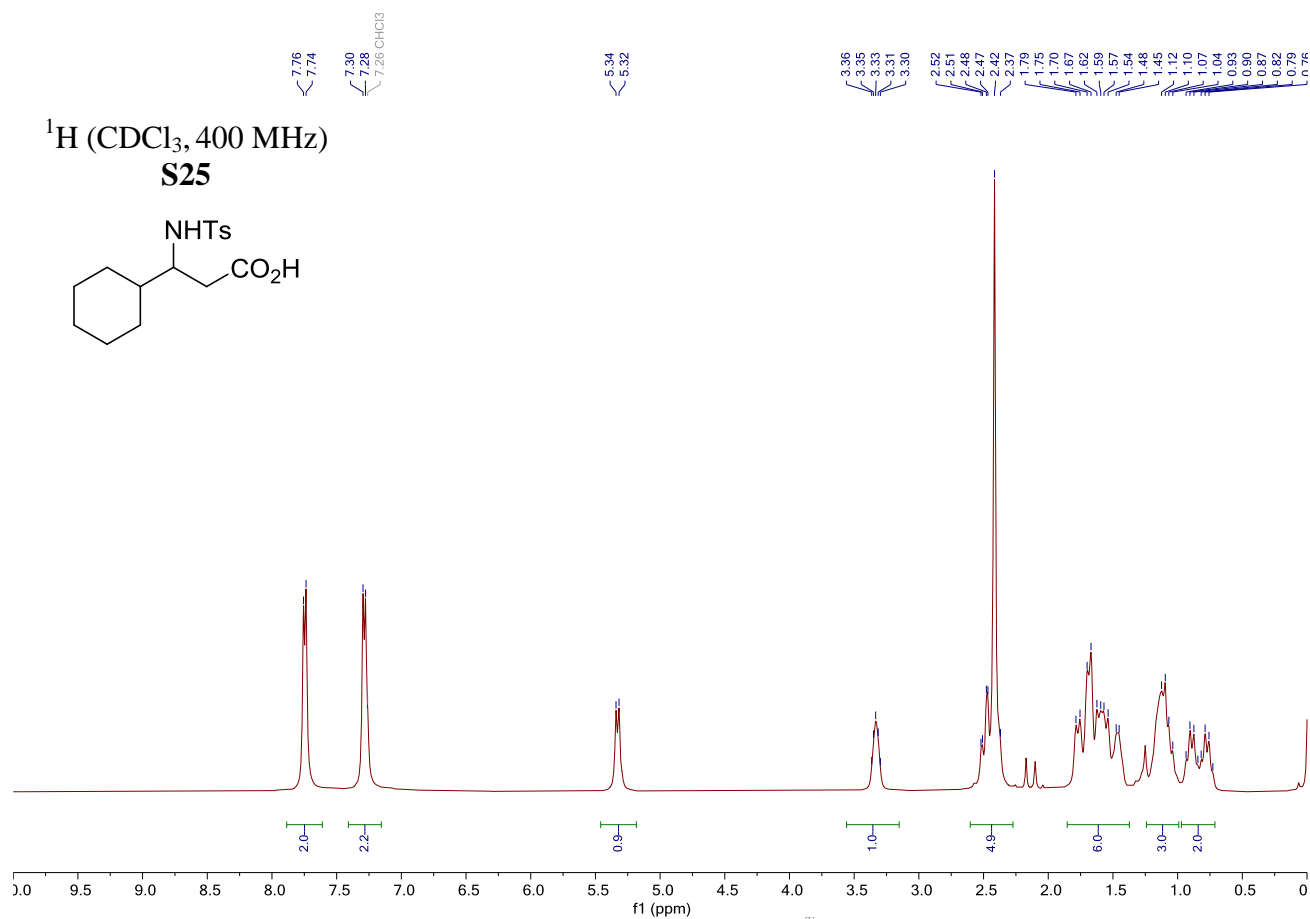
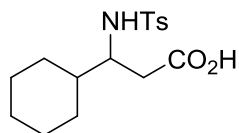
CC(C(=O)O)Nc1ccc(C)cc1

S23





^1H (CDCl₃, 400 MHz)
S25



^{13}C (CDCl₃, 101 MHz)
S25

