Direct Arylation of Strong Aliphatic C–H Bonds

Ian B. Perry, Thomas F. Brewer, Patrick J. Sarver, Danielle M. Schultz, Daniel A. DiRocco, and David W. C. MacMillan*

Merck Center for Catalysis at Princeton University, Princeton, New Jersey 08544, USA and Department of Process Chemistry, Merck & Co., Inc., Rahway, NJ, 07065, USA

Supplementary Information

Table of Contents

1) General Information

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego[1]. All solvents were purified according to the method of Grubbs[2]. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished by flash chromatography on Silicycle F60 silica gel according to the method of Still[3]. Thin-layer chromatography (TLC) was performed on Analtech 250 micron silica gel plates. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and peaks are reported in terms of frequency of absorption (cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-II 500 (500 and 125 MHz) instrument, and are internally referenced to residual protic solvent signals (note: $CDCl_3$ referenced at δ 7.26 and 77.16 ppm respectively. Acetone-d6, referenced to δ 2.05 and 29.84 ppm respectively. MeOD, referenced to δ 3.31 and 49.00 ppm respectively. Benzene-d6, referenced to δ 7.16 and 128.06 ppm respectively. CD_2Cl_2 referenced to δ 5.32 and 53.84 ppm respectively, MeCN-d3 referenced to δ 1.94 and 118.26 ppm respectively). ^{19}F NMR spectra were taken on a Varian Inova 400 (400 MHz) instrument or a Bruker NB300 NanoBay (300 MHz) instrument. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. Quantitative ^{13}C NMR were taken with a relaxation delay of 30s. High-resolution mass spectra were obtained at Princeton University mass spectrometry facilities. Gas chromatography (GC) was performed on an Agilent 6850 Series chromatograph with splitless capillary injection and FID detection. Nickel(II) bromide•DME was purchased from Strem Chemicals. Sodium tungstate dihydrate and tetrabutylammonium bromide were purchased from Oakwood Chemical. 7-Azabicyclo[2.2.1]heptane hydrochloride and *N*-Boc-nortropinone were purchased from Combi-Blocks. 5-bromo-2-(trifluoromethyl)pyrimidine was purchased from Astatech. Spiro[3.3]heptan-2-one was purchased from Synthonix. Cyclopentane and acetonitrile were purchased from Acros Organics and stored over molecular sieves under an inert atmosphere. 4-chlorotetrahydro-2*H*-pyran was purchased from TCI America. All reagents not specified above were purchased at the highest available purity from Sigma Aldrich.

2) Synthesis of Catalysts

2.1) Preparation of Tetrabutylammonium Decatungstate (TBADT)

To a 2 L beaker wrapped in aluminum foil for insulation and equipped with a 4" Teflon stir bar was added tetrabutylammonium bromide (4.80 g, 14.9 mmol, 0.49 equiv.) and deionized water (1600 mL). In a separate 4 L beaker wrapped in aluminum foil for insulation and equipped with a 4" Teflon stir bar was added $Na_2WO_4 \cdot 2H_2O$ (10 g, 30.3 mmol, 1.00 equiv.) and deionized water (1600 mL). Both solutions were rapidly stirred and heated to 90 °C. When both solutions reached 90 °C, aqueous HCl was added to each solution until pH stabilized at 2. At this point, the acidified solutions were combined in the 4 L beaker, and the resultant suspension was stirred at 90 °C for an additional 30 minutes. The reaction mixture was cooled to room temperature, then filtered through a pad of silica gel. The solids were washed with water and left to dry under vacuum. When the silica-supported solids were dry, the receiving flask was exchanged, and the pad was washed with 3 x 200 mL acetonitrile. The filtrate was collected and solvent was removed. The crude residue was thoroughly dried under vacuum, dissolved in minimal hot acetonitrile, then placed in the freezer at –20 °C for 12 hours. The solids were collected on a filter, washed with minimal cold acetonitrile, then dried under vacuum. The filtrate was reconcentrated, dissolved in minimal hot acetonitrile, and crystallized again to afford a second crop of photocatalyst. Isolated as pale yellow crystals, 1^{st} crop (6.41 g, 1.934 mmol, 64%), 2^{nd} crop (2.36 g, 0.711 mmol, 87% combined yield). UV-Vis and CV characterization is consistent with literature data[4].

2.2) Preparation of $NiBr_2$•dtbbpy

To a 500 mL round-bottom flask equipped with a Teflon stir bar was added nickel(II) bromide ethylene glycol dimethyl ether adduct ($NiBr_2$•DME, 1.54 g, 5.0 mmol, 1.0 equiv.) and 4,4'-di-*tert*-butyl-2,2'-dipyridyl (dtbbpy, 1.35 g, 5.03 mmol, 1.005 equiv.). The vessel was sealed and purged with nitrogen for 10 minutes. 250 mL dry MeCN was added to the reaction mixture, which was stirred at 65 °C for 1 hour. The transparent green solution was removed from stirring and solvent was removed. The residue was dried under vacuum for 12 hours at 65 °C to ensure complete removal of DME. The solids were suspended in pentane, sonicated, and isolated on a medium porosity glass frit, washed with pentane, and

dried under high vacuum. The complex was isolated as a green solid (2.24 g, 4.59 mmol, 92% yield). Other methods of pre-complexation afford similar yields of product, although the presence of DME in the reaction mixture affords DME-functionalized products and reduces the yield to a small extent.

3) Standard Reaction Setup

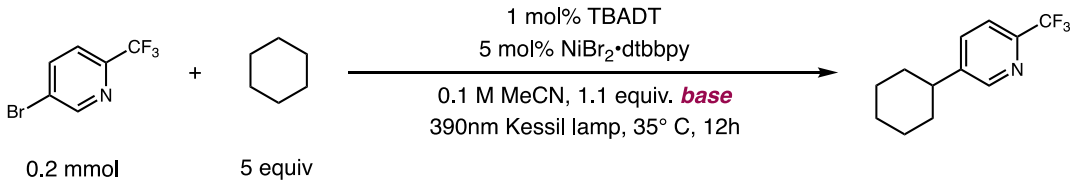
For reactions setup according to general procedure A, the reaction mixture is irradiated with two 34W Kessil PR160-390 lamps from 5 cm away. Regular fans are employed to maintain the temperature at 35 °C. If necessary, a water bath (shown below) can be used to provide additional evaporative cooling. The light, reaction vessel, stir plate, and fans are all placed behind UV-light-shielding 6 mm amber acryllic or 5 mm thick black hardboard (Thorlabs, Newton, NJ, USA) for the duration of the reaction.

Figure S1: Example reaction setup

4) Reaction Optimization

To an oven-dried 8-mL vial equipped with a stir bar and septum cap was added tetrabutylammonium decatungstate (6.6 mg, 2.0 μmol, 0.01 equiv.), 5-bromo-2-

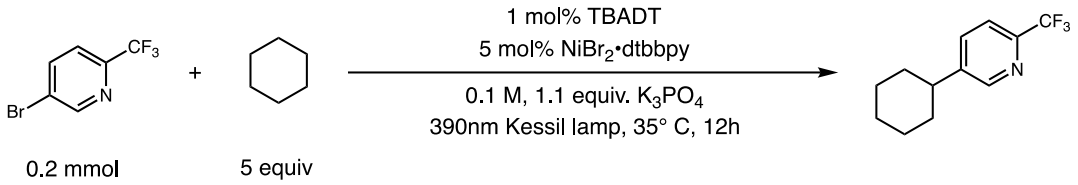
(trifluoromethyl)pyridine (45.2 mg, 0.2 mmol, 1.0 equiv.) and base (0.22 mmol, 1.1 equiv.). To a separate oven-dried 8-mL vial was added nickel(II) salt (5.0 μmol, 0.05 equiv.), and bipyridyl ligand (5.0 μmol, 0.05 equiv.). Solvent (2.0 mL) was added and the solution was sonicated under nitrogen for 2 minutes to allow for complete complexation. The solution of ligated-nickel was transferred to the reaction vessel, and the reaction mixture was sparged with nitrogen for 10 minutes at 0 °C (ice water bath). To the sparged reaction mixture was added cyclohexane (84.0 mg, 108.0 μL, 1.0 mmol, 5.0 equiv., sparged with nitrogen separately before addition). The reaction vial was then sealed with parafilm and placed 5 cm away from 34W 390 nm LEDs with adequate fans to keep the reaction mixture at 35 °C. After 8 hours, the reaction was quenched via exposure to air for 15 minutes. Mesitylene (27.8 μL, 0.2 mmol, 1 equiv.) was added to the reaction mixture, which was stirred for an additional 5 minutes. An aliquot (approximately 0.1 mL) was passed through a plug of celite into an NMR tube, followed by 0.7 mL DMSO-d_6, which was subsequently submitted for ^{1}H NMR analysis.



base	yield
K_3PO_4	**70%**
Na_3PO_4	**61%**
K_2HPO_4	**18%**
K_2CO_3	**55%**
Na_2CO_3	**59%**
LiOH	**27%**

Yields determined by ^{1}H NMR against mesitylene

Figure S2: Evaluation of base for decatungstate C–H arylation



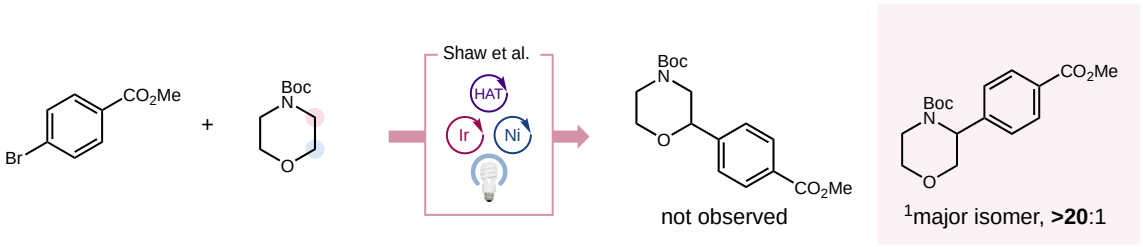
solvent	yield
acetonitrile	**72%**
propionitrile	**37%**
pivalonitrile	**42%**
benzonitrile	**39%**
dimethylsulfoxide	**0%**
acetone	**52%**
dichloromethane	**0%**
nitromethane	**0%**

Yields determined by ^{1}H NMR against mesitylene

Figure S3: Evaluation of solvent for decatungstate C–H arylation

4.1) Procedure for Quinuclidine-mediated Triple Catalytic C–H Arylation

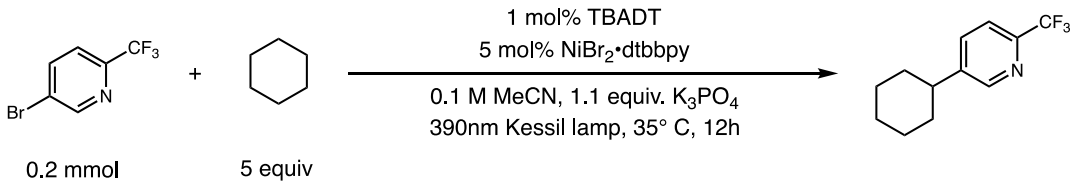
Adapted from Shaw *et al.*[5]: To an oven-dried 8-mL vial equipped with a stir bar was added N-Boc-morpholine (94 mg, 0.25 mmol, 2.0 equiv.). The vial was sealed with a cap equipped with a Teflon-lined septum and sparged with nitrogen. Methyl-4-bromobenzoate (54 mg, 0.25 mmol, 1 equiv.), $NiBr_2$•$3H_2O$ (0.59 mg, 2.5 µmol, 1.0 mol%), 4,7-dimethoxy-1,10-phenanthroline (0.60 mg, 2.5 µmol, 1.0 mol%) and [Ir(dF(CF_3)ppy)$_2$dtbbpy]•PF_6 (2.8 mg, 2.5 µmol, 1.0 mol%) were added as a stock solution in dry DMSO (1 mL, 0.25M). 3-acetoxyquinuclidine (46 mg, 1.1 equiv.) and water (45 µL, 2.5 mmol, 10 equiv.) were added to the reaction vessel via syringe, and the reaction mixture was deoxygenated via two cycles of freeze-pump-backfill-thaw. The reaction vessel was sealed with parafilm, stirred and irradiated using a 34 W Blue LED for 24 hours. The reaction mixture was then removed from irradiation and 1,3-benzodioxole (26 µL, 0.25 mmol) was added via microsyringe. The reaction mixture was diluted with EtOAc and brine and stirred vigorously at room temperature for 15 minutes. An aliquot of the organic phase was submitted for ^{1}H NMR analysis.



[1]product detection by [1]H NMR against 1,3-benzodioxole

Figure S4: Selectivity of quinuclidine-mediated triple catalytic arylation on morpholine. Conditions adapted from reference [5]. [1]Spectra matched literature precedents[6].

5) Control experiments



deviation from standard	**yield**
none	**70%**
without base	**0%**
without [Ni]	**0%**
without TBADT	**0%**
without light	**0%**
Kessil 40 W A160WE (blue LED)	**9%**
3 equiv. CyH	**61%**
1.5 equiv. CyH	**28%**

Yields determined by [1]H NMR against mesitylene

Figure S5: Control experiments for decatungstate C–H arylation

6.1) General Procedure A for TBADT-Mediated C–H Arylation

To an oven-dried 8-mL (0.1 M and 0.2 M reaction conditions) or 40-mL (0.04 M reaction conditions) vial equipped with a stir bar was added C–H nucleophile (if solid, 2.5 mmol, 5.0 equiv.) and anhydrous inorganic base (0.55 mmol, 1.1 equiv.). The vial was sealed with a cap equipped with a Teflon-lined septum and sparged with nitrogen. Aryl halide (0.5

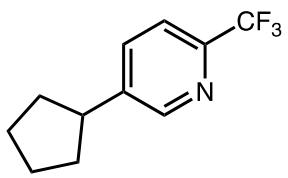
mmol, 1 equiv.), $NiBr_2$•dtbbpy (12 or 24 mg, 0.025 or 0.050 mmol, 5.0 or 10.0 mol%), and tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%) were added as a stock solution in dry acetonitrile (between 1.25 and 12.5 mL, 0.04 to 0.40 M). Subsequently, the reaction vessel was placed in an ice bath and deoxygenated by sparging with nitrogen for 10 minutes. C–H nucleophile (if liquid, 2.5 mmol, 5.0 equiv., deoxygenated in a separate vial) was added before sealing the reaction vessel with parafilm. The reaction mixture was stirred and irradiated using a 34 W 390 nm LED lamp (Kessil PR160-390, 5 cm away, with adequate fans and/or a water bath to keep the reaction at 35 °C) for 12 hours. In cases where multiple photocatalyst additions were required, a second portion of TBADT (17 mg, 0.005 mmol, 1.0 mol%) in 0.2 mL degassed acetonitrile was added, and the reaction was subjected once again to irradiation for 12 hours. This process can be repeated again if full conversion is not reached after a second addition. The reaction mixture was removed from light and quenched by stirring open to air for 15 minutes. The reaction mixture was diluted with ethyl acetate and passed through a pad of celite. The celite plug was washed thoroughly with additional ethyl acetate. Solvent was removed from the filtrate, and the residue was purified by flash chromatography on silica gel, reverse-phase chromatography on C18 silica gel and/or preparative thin-layer chromatography to afford the desired product.

6.2) General Procedure B for TBADT-mediated C–H Arylation

To an oven-dried 40-mL vial equipped with a cross-shaped stir bar was added C–H nucleophile (if solid, 2.5 mmol, 5.0 equiv.) anhydrous inorganic base (0.55 mmol, 1.1 equiv.). The vial was sealed with a cap equipped with a Teflon-lined septum and purged with nitrogen. Aryl halide (0.5 mmol, 1 equiv.), $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), and tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%) were added as a stock solution in dry acetonitrile (12.5 mL, 0.04 M). Subsequently, the reaction vessel was placed in an ice bath and deoxygenated by sparging with nitrogen for 10 minutes. C–H nucleophile (if liquid, 2.5 mmol, 5.0 equiv., deoxygenated in a separate vial) was added before sealing the reaction vessel with parafilm. The reaction mixture was stirred and irradiated using an integrated photoreactor (365 nm, stirred at 1000 rpm, maximum fans) for 18 hours. In cases where multiple photocatalyst additions were

required, a second portion of TBADT (17 mg, 0.005 mmol, 1.0 mol%) in 0.2 mL degassed acetonitrile was added, and the reaction was subjected once again to irradiation for 18 hours in the integrated photoreactor. This process can be repeated again if full conversion is not reached after a second addition. At this point, the reaction mixture was removed from light and quenched by stirring open to air for 15 minutes. The reaction mixture was diluted with ethyl acetate and passed through a pad of celite. The celite plug was washed thoroughly with additional ethyl acetate. Solvent was removed from the filtrate, and the residue was purified by flash chromatography and/or preparative thin-layer chromatography on silica gel to afford the desired product.

7) Alkylation of 5-bromo-2-(trifluoromethyl)pyridine



5-cyclopentyl-2-(trifluoromethyl)pyridine (13)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), cyclopentane (175.3 mg, 233.4 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded the pure product as a colorless solid (61 mg, 0.283 mmol, 57% yield).

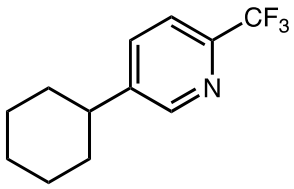
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.1 Hz, 1H), *7*.70 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 3.08 (p, *J* = 17.3, 9.7, 7.6 Hz, 1H), 2.23 – 2.08 (m, 2H), 1.85 (dddd, *J* = 13.7, 10.4, 6.8, 4.1 Hz, 2H), 1.78 – 1.69 (m, 2H), 1.65 – 1.57 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.4, 145.6 (q, *J* = 34.5 Hz), 145.1, 135.4, 121.7 (q, *J* = 273.7 Hz), 120.1 (q, *J* = 2.7 Hz), 43.2, 34.4, 25.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.68

IR (film) ν_{max} 2955, 2873, 1595, 1405, 1336, 1172, 1130, 1086, 1025 cm^{-1}

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{13}F_3N$ ($[M+H]^+$) 215.0922, found 215.0921.



5-cyclohexyl-2-(trifluoromethyl)pyridine (14)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded the pure product as a colorless solid (76 mg, 0.330 mmol, 66% yield).

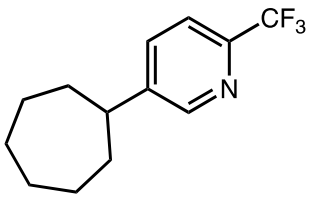
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.1 Hz, 1H), 7.68 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 2.63 (qd, *J* = 8.6, 7.2, 2.9 Hz, 1H), 1.97 – 1.83 (m, 4H), 1.83 – 1.74 (m, 1H), 1.50 – 1.36 (m, 4H), 1.35 – 1.19 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 146.2, 145.8 (q, *J* = 34.5 Hz), 135.2, 121.7 (q, *J* = 273.4 Hz), 120.2 (d, *J* = 2.7 Hz), 41.9, 33.9, 26.5, 25.8

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.67

IR (film) ν_{max} 2930, 2857, 1449, 1407, 1335, 1258, 1228, 1171, 1132, 1119, 1084, 1027 cm^{-1}

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3N$ ($[M+H]^+$) 229.1078, found 229.1077.



5-cycloheptyl-2-(trifluoromethyl)pyridine (15)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), cycloheptane (245.5 mg, 302.7 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded the pure product as a colorless solid (79 mg, 0.325 mmol, 65% yield).

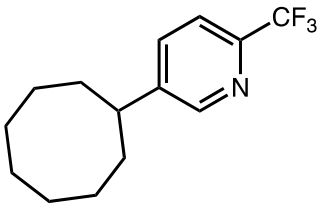
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 2.1 Hz, 1H), 7.66 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 2.78 (tt, *J* = 10.6, 3.6 Hz, 1H), 1.96 – 1.87 (m, 2H), 1.83 (ddq, *J* = 13.3, 6.8, 3.3 Hz, 2H), 1.76 – 1.53 (m, 8H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 148.1, 145.6 (q, *J* = 34.6 Hz), 135.1, 121.7 (q, *J* = 273.6 Hz), 120.2 (q, *J* = 2.7 Hz), 44.3, 36.4, 27.7, 27.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.65

IR (film) ν_{max} 2924, 2857, 1461, 1404, 1335, 1242, 1173, 1129, 1085, 1025 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{17}F_3N$ ($[M+H]^+$) 243.1235, found 243.1233.



5-cyclooctyl-2-(trifluoromethyl)pyridine (16)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025

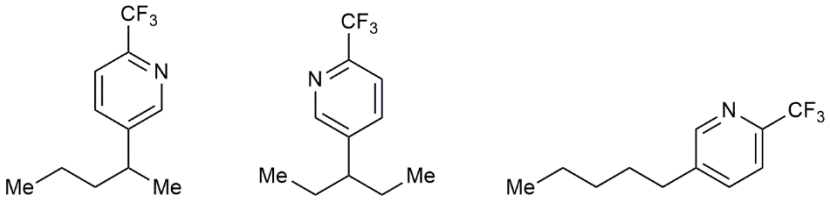
mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), cyclooctane (281 mg, 336 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded the pure product as a colorless solid (90 mg, 0.350 mmol, 70% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 2.0 Hz, 1H), 7.66 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 2.89 (td, *J* = 9.5, 3.7 Hz, 1H), 1.88 – 1.73 (m, 6H), 1.64 (m, *J* = 40.4, 6.8, 5.9 Hz, 8H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 148.5, 145.7 (q = 34.6), 135.4, 121.7 (q, *J* = 273.7 Hz), 120.2 (q, *J* = 2.8 Hz), 42.0, 34.1, 26.7, 26.2, 25.7.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.64

IR (film) ν_{max} 2921, 2855, 1471, 1447, 1405, 1335, 1216, 1170, 1131, 1085, 1023 cm^{-1}.
HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{19}F_3N$ ($[M+H]^+$) 257.1391, found 257.1387.



(±)-5-(pentan-2-yl)-2-(trifluoromethyl)pyridine (major, left, 17), 5-(pentan-3-yl)-2-(trifluoromethyl)pyridine (minor 1, center, SI-17a), and 5-pentyl-2-(trifluoromethyl)pyridine (minor 2, right, SI-17b)

Prepared following general procedure A outlined above, including a second addition of tetrabutylammonium decatungstate at 12 hours and a total reaction time of 24 hours and with the modification that the reaction concentration was 0.4 M, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (34 mg, 0.010 mmol, 2.0 mol%, divided over two addtions), MeCN (1.25 mL), 5-bromo-2-(trifluoromethyl)pyridine

(113.0 mg, 0.5 mmol, 1.0 equiv.), *n*-pentane (180 mg, 288 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0–20% EtOAc in hexanes) afforded the desired product as a mixture of regioisomers; colorless oil (6.0 (major):1.6 (minor 1):1.0 (minor 2) r.r., 70% selectivity, 53 mg, 49% yield). The presence of three regioisomers was confirmed by GCMS and quantitative ^{13}C NMR.

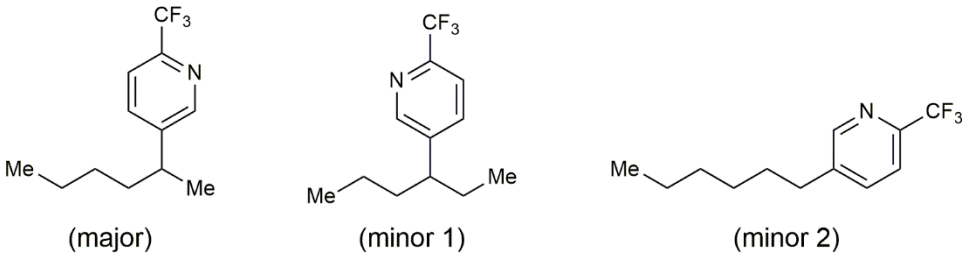
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J* = 2.1 Hz, 1H (major), 1H (minor 2)), 8.51 (d, *J* = 1.5 Hz, 1H (minor 1)), 7.66 (dd, *J* = 8.1, 2.2 Hz, 1H (major), 1H (minor 2)), 7.64 – 7.58 (m, 1H (major), 2H (minor 1), 1H (minor 2)), 2.83 (h, *J* = 7.1 Hz, 1H (major)), 2.73 – 2.64 (t, 7.7 Hz, 2H (minor 2)), 2.46 (tt, *J* = 9.1, 5.4 Hz, 1H (minor 1)), 1.77 (dqd, *J* = 14.8, 7.4, 5.4 Hz, 2H (minor 1)), 1.70 – 1.55 (m, 2H (major), 2H (minor 1), 2H (minor 2)), 1.38 – 1.13 (m, 5H (major), 4H (minor 2)), 0.88 (t, *J* = 7.3 Hz, 3H (major), 3H (minor 2)), 0.79 (t, *J* = 7.4 Hz, 6 H (minor 1)).

Quantitative ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.3 (1C (minor 1), 1C (minor 2)), 149.6 (1C (major)), 146.9 – 145.6 (2C (major), 1C (minor 1), 1C (minor 2)), 144.6 (1C (minor 1)), 141.6 (1C (minor 2)), 137.0 (1C (minor 2)), 136.2 (1C (minor 1)), 135.5 (1C (major)), 120.8 (q, *J* = 274.9 Hz, 1C (major), 1C (minor 1), 1C (minor 2)), 120.3 (1C (major), 1C (minor 1), 1C (minor 2)), 47.1 (1C (minor 1)), 40.2 (1C (major)), 37.3 (1C (major)), 33.0 (1C (minor 2)), 31.4 (1C (minor 2)), 30.7 (1C (minor 2)), 29.0 (2C (minor 1)), 22.5 (1C (minor 2)), 21.9 (1C (major)), 20.7 (1C (major)), 14.1 (1C (major), 1C (minor 2)), 12.1 (2C (minor 1)).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.70 (m).

IR (film) ν_{max} 2962, 2930, 2876, 1337, 1260, 1172, 1132, 1087, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{15}F_3N^+$ ($[M+H]^+$) 218.1151, found 218.1150.



(±)-5-(hexan-2-yl)-2-(trifluoromethyl)pyridine (major, left, SI-1a), (±)-5-(hexan-3-yl)-2-(trifluoromethyl)pyridine (minor 1, center, SI-1b), and 5-hexyl-2-(trifluoromethyl)pyridine (minor 2, right, SI-1c)

Prepared following general procedure A outlined above, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), *n*-hexane (215 mg, 326 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0–20% EtOAc in hexanes) afforded the desired product as a mixture of regioisomers; colorless oil (5.6 (major):2.8 (minor 1):1.0 (minor 2), 60% selective, 56 mg, 0.242 mmol, 48% yield). The presence of three regioisomers was confirmed by GCMS and quantitative ^{13}C NMR.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (s, 1H (major), 1H (minor 2)), 8.51 (s, 1H (minor 1)), 7.66 (dd, *J* = 8.1, 2.0 Hz, 1H (major), 1H (minor 2)), 7.61 (d, *J* = 8.8 Hz, 1H (major), 2H (minor 1), 1H (minor 2)), 2.80 (h, *J* = 7.1 Hz, 1H (major)), 2.68 (t, *J* = 7.8 Hz, 2H (minor 2)), 2.56 (tt, *J* = 9.3, 5.4 Hz, 1H (minor 1)), 1.83 – 1.47 (m, 2H (major), 4H (minor 1), 2H (minor 2)), 1.46 – 1.04 (m, 7H (major), 2H (minor 1), 6H (minor 2)), 0.86 (m, 3H (major), 3H (minor 1), 3H (minor 2)), 0.78 (t, *J* = 7.4 Hz, 3H (minor 1)).

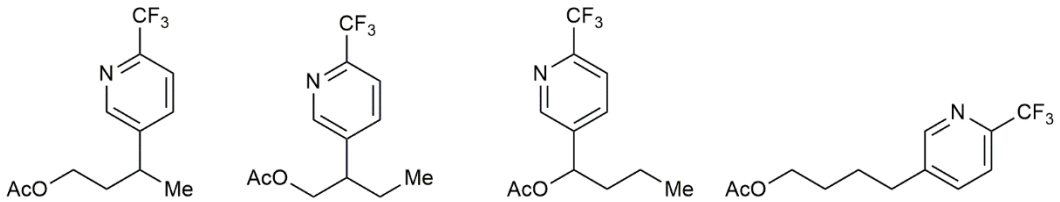
Quantitative ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.2 (1C (minor 1)), 149.6 (1C (major), 1C (minor 2)), 146.7 – 145.6 (m, 2C (major), 1C (minor 1), 1C (minor 2)), 144.8 (1C (minor 1)), 141.6 (1C (minor 2)), 137.0 (1C (minor 2)), 136.1 (1C (minor 1)), 135.5 (1C (major)), 121.9 (q, *J* = 273.4 Hz, 1C (major), 1C (minor 1), 1C (minor 2)), 120.4 (1C (major), 1C (minor 1), 1C (minor 2)), 45.1 (1C (minor 1)), 38.3 (1C (minor 1)), 37.8 (1C (major)), 37.6 (1C (major)), 33.0 (1C (minor 2)), 31.7 (1C (minor 2)), 31.0 (1C (minor 2)), 29.8 (1C (major)), 29.4 (1C (minor 1)), 28.9 (1C (minor 2)), 22.8 (1C (major)), 22.7 (1C

(minor 2)), 22.0 (1C (major)), 20.7 (1C (minor 1)), 14.2 (1C (minor 2)), 14.1 (1C (minor 1)), 14.1 (1C (major)), 12.1 (1C (minor 1)).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.70.

IR (film) ν_{max} 2962, 2930, 2861, 1336, 1261, 1172, 1132, 1086, 1025 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{17}F_3N^+$ ($[M+H]^+$) 232.1308, found 232.1306.



(±)-3-(6-(trifluoromethyl)pyridin-3-yl)butyl acetate (major, left, 18), (±)-2-(6-(trifluoromethyl)pyridin-3-yl)butyl acetate (minor 1, center-left, SI-18a), (±)-1-(6-(trifluoromethyl)pyridin-3-yl)butyl acetate (minor 2, center-right, SI-18b), and 4-(6-(trifluoromethyl)pyridin-3-yl)butyl acetate (minor 3, right, SI-18c)

Prepared following general procedure A outlined above, with the modification that the reaction concentration was 0.4 M, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (1.25 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), butyl acetate (290 mg, 329 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high performance silica gel, gradient 0–20% EtOAc in hexanes) afforded a mixture of major and minor 3 as a clear oil (44 mg, 7.3:1 major:minor 3 by ^{1}H NMR, 0.168 mmol, 34% yield), pure minor 1 as a clear oil (19 mg, 0.073 mmol, 15% yield), and pure minor 2 as a clear oil (10 mg, 0.034 mmol, 7% yield).

<u>18 (major regioisomer) and SI-18c (minor regioisomer 3):</u>

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.2 Hz, 1H (major), 1H (minor 3)), 7.69 (dd, *J* = 8.1, 2.2 Hz, 1H (major), 1H (minor 3)), 7.63 (d, *J* = 8.0 Hz, 1H (major), 1H (minor

3)), 4.13 – 4.00 (m, 1H (major), 2H (minor 3)), 3.95 (dt, *J* = 11.3, 6.6 Hz, 1H (major)), 2.99 (h, *J* = 7.1 Hz, 1H (major)), 2.74 (t, *J* = 7.2 Hz, 2H (minor 3)), 2.05 (d, *J* = 1.6 Hz, 3H (minor 3)), 2.01 – 1.94 (m, 5H (major)), 1.70 (m, 4H (minor 3)), 1.38 – 1.28 (d, *J* = 7.1 Hz, 3H (major)).

Quantitative ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3 (1C (minor 3)), 171.1 (1C (major)), 150.3 (1C (minor 3)), 149.5 (1C (major)), 147.2 – 145.7 (m, 1C (major), 1C (minor 3)), 145.1 (1C (major)), 140.8 (1C (minor 3)), 137.1 (1C (minor 3)), 135.6 (1C (major)), 125.4 – 117.6 (m, 1C (major), 1C (minor 3)), 120.5 (q, *J* = 2.8 Hz, 1C (major)), 120.3 (q, *J* = 2.7 Hz, 1C (minor 3)), 64.0 (1C (minor 3)), 62.3 (1C (major)), 36.4 (1C (major)), 34.5 (1C (major)), 32.6 (1C (minor 3)), 28.2 (1C (minor 3)), 27.4 (1C (minor 3)), 21.9 (1C (major)), 21.1 (1C (minor 3)), 21.0 (1C (major)).

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.73 (s, 3F (minor 3)), -67.77 (s, 3F (major)).

IR (film) ν_{max} 2969, 1739, 1340, 1241, 1174, 1137, 1087, 1045, 1025 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3NO_2^+$ ($[M+H]^+$) 262.1049, found 262.1053.

SI-18a, minor regioisomer 1:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.1 Hz, 1H), 7.70 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 4.28 (dd, *J* = 11.1, 5.6 Hz, 1H), 4.22 (dd, *J* = 11.1, 7.9 Hz, 1H), 2.97 (tt, *J* = 8.4, 5.7 Hz, 1H), 1.99 (s, 3H), 1.91 – 1.79 (m, 1H), 1.67 (ddq, *J* = 14.5, 9.2, 7.4 Hz, 1H), 0.87 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.95, 150.33, 146.95 (q, *J* = 34.7 Hz), 140.99, 136.39, 121.68 (q, *J* = 273.7 Hz), 120.46 (q, *J* = 2.8 Hz), 67.19, 44.26, 25.20, 20.95, 11.83.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.79.

IR (film) ν_{max} 2968, 1741, 1337, 1232, 1174, 1137, 1086, 1042, 1028 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3NO_2^+$ ($[M+H]^+$) 262.1049, found 262.1044.

SI-18b, minor regioisomer 2:

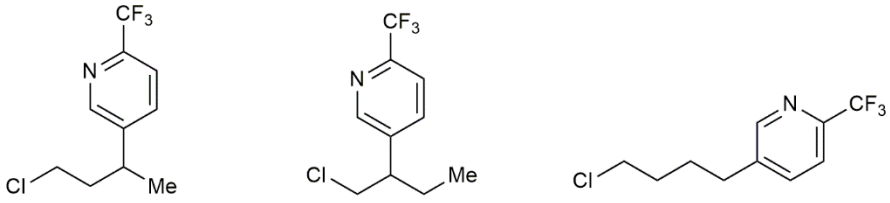
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, *J* = 2.1 Hz, 1H), 7.81 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 5.80 (dd, *J* = 8.0, 6.1 Hz, 1H), 2.10 (s, 3H), 1.99 – 1.89 (m, 1H), 1.76 (ddt, *J* = 13.9, 10.1, 5.9 Hz, 1H), 1.44 – 1.26 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 148.6, 147.6 (q, *J* = 35.3, 34.7 Hz), 139.8, 135.6, 121.6 (q, *J* = 273.7 Hz), 120.4 (q, *J* = 2.8 Hz), 73.2, 38.3, 21.2, 18.7, 13.8.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.92.

IR (film) ν_{max} 2963, 1740, 1337, 1237, 1176, 1140, 1087, 1027 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3NO_2^+$ ($[M+H]^+$) 262.1049, found 262.1047.



(major) (minor 1) (minor 2)

(±)-5-(4-chlorobutan-2-yl)-2-(trifluoromethyl)pyridine (major, left, 19), (±)-5-(1-chlorobutan-2-yl)-2-(trifluoromethyl)pyridine (minor 1, center, SI-19a), and 5-(4-chlorobutyl)-2-(trifluoromethyl)pyridine (minor 2, right, SI-19b)

Prepared following general procedure A outlined above, with the modification that the reaction concentration was 0.4 M, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (1.25 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 1-chlorobutane (231 mg, 261 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high performance silica gel, gradient 0–20%

EtOAc in hexanes) afforded 90% pure major product (42 mg, 0.159 mmol, 31% yield, contaminated with an unidentified isomeric product, 90% pure by ^{19}F NMR) and a mixture of major, minor 1, and minor 2 (15 mg, 27% major (0.017 mmol), 37% minor 1 (0.023 mmol), and 36% minor 2 (0.023 mmol), ratios determined by ^{1}H NMR, 13% yield). Pure fractions of both minor isomers were separately analyzed to confirm the assigned structures.

19, major regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.2 Hz, 1H), 7.71 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.64 (dd, *J* = 8.1, 0.8 Hz, 1H), 3.51 (dt, *J* = 11.1, 6.1 Hz, 1H), 3.32 (ddd, *J* = 11.1, 7.9, 5.9 Hz, 1H), 3.17 (h, *J* = 6.9 Hz, 1H), 2.16 – 2.00 (m, 2H), 1.35 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.5, 146.7 (q, *J* = 34.8 Hz), 144.4, 135.8, 121.7 (q, *J* = 273.8 Hz), 120.6 (q, *J* = 2.8 Hz), 42.6, 40.2, 34.5, 21.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.79.

IR (film) ν_{max} 2968, 1338, 1176, 1134, 1087, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{12}ClF_3N^+$ ($[M+H]^+$) 238.0605, found 238.0601.

SI-19a, minor regioisomer 1:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.1 Hz, 1H), 7.80 – 7.74 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 4.02 (tt, *J* = 8.7, 4.5 Hz, 1H), 3.17 (dd, *J* = 14.4, 4.6 Hz, 1H), 3.05 (dd, *J* = 14.4, 8.7 Hz, 1H), 1.89 (dqd, *J* = 14.6, 7.3, 4.3 Hz, 1H), 1.77 (ddq, *J* = 14.5, 8.5, 7.3 Hz, 1H), 1.10 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.0, 146.9 (q, *J* = 34.8 Hz), 138.4, 136.9, 121.7 (q, *J* = 273.9 Hz), 120.2 (q, *J* = 2.7 Hz), 64.4, 41.4, 31.4, 11.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.82.

IR (film) ν_{max} 2930, 1337, 1179, 1136, 1087, 1029 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{12}ClF_3N^+$ ($[M+H]^+$) 238.0605, found 238.0602.

SI-19b, minor regioisomer 2:

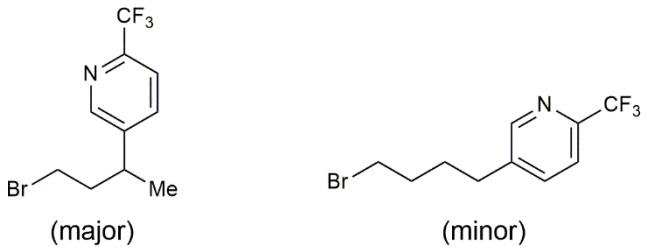
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 2.0 Hz, 1H), 7.69 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.62 (dd, *J* = 8.0, 0.8 Hz, 1H), 3.61 – 3.53 (m, 2H), 2.78 – 2.70 (m, 2H), 1.88 – 1.78 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.3, 146.3 (q, *J* = 34.6 Hz), 140.6, 137.1, 121.8 (q, *J* = 273.7 Hz), 120.4 (q, *J* = 2.7 Hz), 44.6, 32.2, 31.9, 28.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.75.

IR (film) ν_{max} 2939, 1338, 1176, 1136, 1087, 1028 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{12}ClF_3N^+$ ($[M+H]^+$) 238.0605, found 238.0601.



(±)-5-(4-bromobutan-2-yl)-2-(trifluoromethyl)pyridine (major, left, 20) and 5-(4-bromobutyl)-2-(trifluoromethyl)pyridine (minor, right, SI-20)

Prepared following general procedure A outlined above, with the modification that the reaction concentration was 0.4 M, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (1.25 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 1-bromobutane (343 mg, 268 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.).

Purification by column chromatography (high performance silica gel, gradient 0–20% EtOAc in hexanes) afforded pure major product as a clear oil (53 mg, 0.188 mmol, 38% yield) and impure minor product. Preparative TLC of the impure minor product (5% EtOAc/toluene) afforded impure minor product as a white solid (5 mg, 85% pure, 0.015 mmol, 3% yield).

20, major regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 2.1 Hz, 1H), 7.72 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 3.37 (dt, *J* = 10.5, 6.2 Hz, 1H), 3.23 – 3.09 (m, 2H), 2.16 (dq, *J* = 8.5, 6.5 Hz, 2H), 1.35 (dd, *J* = 7.0, 0.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.5, 146.7 (q, *J* = 35.0 Hz), 144.3, 135.9, 121.7 (q, *J* = 273.8 Hz), 120.6 (q, *J* = 2.8 Hz), 40.3, 35.7, 31.1, 21.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.78.

IR (film) ν_{max} 2968, 1339, 1176, 1136, 1087, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{12}BrF_3N^+$ ($[M+H]^+$) 282.0100, found 282.0096.

SI-20, minor regioisomer:

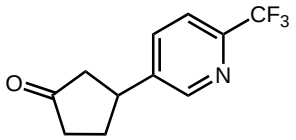
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 – 8.55 (m, 1H), 7.69 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 3.44 (t, *J* = 6.4 Hz, 2H), 2.74 (t, *J* = 7.7 Hz, 2H), 1.92 (dq, *J* = 9.0, 6.1 Hz, 2H), 1.83 (dq, *J* = 9.5, 7.0 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.2, 146.3 (q, *J* = 34.7 Hz), 140.6, 137.1, 121.8 (q, *J* = 273.9 Hz), 120.4 (q, *J* = 2.7 Hz), 33.2, 32.1, 32.1, 29.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.75.

IR (film) ν_{max} 2926, 2855, 1337, 1176, 1137, 1087, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{12}BrF_3N^+$ ($[M+H]^+$) 282.0100, found 282.0093.



(±)-3-(6-(trifluoromethyl)pyridin-3-yl)cyclopentan-1-one (21)

Prepared following general procedure A outlined above using $NiBr_2$•(4-4′-dimethoxy-2-2′-bipyridine) (22 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1 mol%), 5-bromo-2-(trifluoromethyl)pyridine (113 mg, 0.5 mmol, 1.0 equiv.), cyclopentanone (210 mg, 221 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (177 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5.0 mL). The reaction mixture was stirred and irradiated using an integrated photoreactor (365 nm, stirred at 1000 rpm, maximum fans) for 12 hours. Purification by column chromatography (silica gel, 15-40% ethyl acetate in hexanes) followed by purification by preparative thin-layer chromatography (25% acetone in hexanes) yielded the pure product as a pale yellow solid (58 mg, 0.253 mmol, 51% yield).

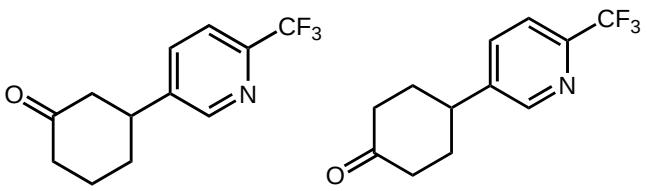
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 2.1 Hz, 1H), 7.75 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 3.53 (tt, *J* = 11.3, 6.8 Hz, 1H), 2.75 (dd, *J* = 18.0, 7.7 Hz, 1H), 2.58 – 2.48 (m, 2H), 2.43 – 2.29 (m, 2H), 2.09 – 1.97 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 216.2, 149.2, 147.0 (q, *J* = 34.8 Hz), 141.8, 135.4, 121.6 (q, *J* = 274.7 Hz), 120.6 (q, *J* = 2.6 Hz), 45.1, 39.8, 38.7, 30.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.83.

IR (film) ν_{max} 2939, 1741, 1406, 1335, 1172, 1127, 1085 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{11}F_3NO^+$ ($[M+H]^+$) 230.0787, found 230.0790.



(±)-3-(6-(trifluoromethyl)pyridin-3-yl)cyclohexan-1-one (22, major isomer, left) and 4-(6-(trifluoromethyl)pyridin-3-yl)cyclohexan-1-one (SI-22, minor isomer, right)

Prepared following the general procedure outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), cyclohexanone (245 mg, 259 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high-performance silica gel, gradient 25% to 40% EtOAc in hexanes) yielded the pure major regioisomer as a colorless solid (46 mg, 0.189 mmol, 38% yield) and the pure minor regioisomer as a colorless solid (33 mg, 0.136 mmol, 27% yield).

22, major regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 2.2 Hz, 1H), 7.72 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 3.15 (tt, *J* = 11.9, 3.9 Hz, 1H), 2.63 (ddt, *J* = 13.9, 4.2, 2.0 Hz, 1H), 2.58 – 2.48 (m, 2H), 2.41 (ddd, *J* = 14.3, 12.1, 6.2 Hz, 1H), 2.20 (ddt, *J* = 13.2, 6.7, 3.3 Hz, 1H), 2.13 (dddd, *J* = 13.0, 5.1, 3.4, 1.7 Hz, 1H), 1.95 – 1.78 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 209.1, 148.9, 146.8 (q, *J* = 34.8 Hz), 142.6, 135.2, 121.5 (q, *J* = 273.8 Hz), 120.5 (q, *J* = 2.7 Hz), 48.0, 42.0, 40.9, 32.2, 25.2.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.83

IR (film) ν_{max} 3058, 2946, 1711, 1447, 1410, 1337, 1279, 1242, 1225, 1198, 1170, 1124, 1083, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{13}F_3NO$ ($[M+H]^+$) 243.0871, found 243.0867.

SI-22, minor regioisomer:

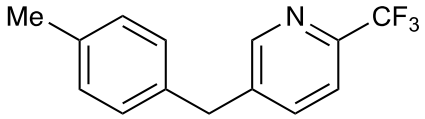
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, *J* = 2.2 Hz, 1H), 7.73 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 3.17 (tt, *J* = 12.2, 3.4 Hz, 1H), 2.55 (dd, *J* = 8.9, 4.3 Hz, 4H), 2.30 – 2.22 (m, 2H), 2.03 – 1.93 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 209.5, 149.1, 146.7 (q, *J* = 34.8 Hz), 143.3, 135.1, 123.7 (q, *J* = 273.8 Hz), 120.4 (q, *J* = 2.8 Hz), 40.9, 40.1, 33.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.82

IR (film) ν_{max} 2937, 2873, 1703, 1598, 1583, 1450, 1418, 1336, 1248, 1200, 1170, 1132, 1084, 1027 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{13}F_3NO$ ($[M+H]^+$) 243.0871, found 243.0867.



5-(4-methylbenzyl)-2-(trifluoromethyl)pyridine (23)

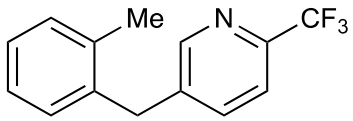
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), *p*-xylene (265 mg, 308 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 10% EtOAc in hexanes) yielded the pure product as a colorless solid (86 mg, 0.342 mmol, 69% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 2.1 Hz, 1H), 7.62 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.58 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 2H), 7.09 – 7.04 (m, 2H), 4.02 (s, 2H), 2.33 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 146.1 (q, *J* = 34.6 Hz), 140.2, 137.4, 136.5, 135.6, 129.6, 128.7, 121.7 (q, *J* = 273.9 Hz), 120.3 (q, *J* = 2.8 Hz), 38.4, 21.0.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.73

IR (film) ν_{max} 2924, 1514, 1399, 1335, 1251, 1174, 1128, 1083, 1027 cm^{-1}.
HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{13}F_3N$ ($[M+H]^+$) 251.0922, found 251.0917.



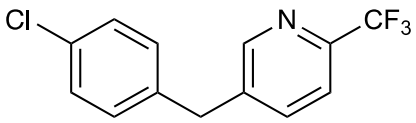
5-(2-methylbenzyl)-2-(trifluoromethyl)pyridine (24)
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), *o*-xylene (265 mg, 301 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 10% EtOAc in hexanes) yielded the pure product as a colorless liquid (90 mg, 0.358 mmol, 72% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.0 Hz, 1H), 7.74 – 7.44 (m, 2H), 7.24 – 7.16 (m, 3H), 7.12 – 7.07 (m, 1H), 4.06 (s, 2H), 2.23 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 150.4, 146.1 (q, *J* = 34.7 Hz), 139.3, 137.1, 136.5, 136.4, 130.7, 129.9, 127.3, 126.4, 121.7 (q, *J* = 273.8 Hz), 120.2 (q, *J* = 2.7 Hz), 36.5, 19.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.74

IR (film) ν_{max} 3021, 2926, 1596, 1580, 1494, 1462, 1399, 1335, 1251, 1171, 1127, 1083, 1026 cm^{-1}.
HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{13}F_3N$ ($[M+H]^+$) 251.0922, found 251.0918.



5-(4-chlorobenzyl)-2-(trifluoromethyl)pyridine (25)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 4-chlorotoluene (316 mg, 296 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 10% EtOAc in hexanes) yielded the pure product as a colorless liquid (84 mg, 0.309 mmol, 62% yield).

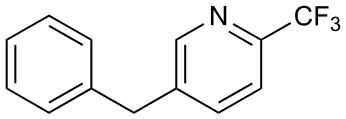
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 1.7 Hz, 1H), 7.60 (d, *J* = 1.5 Hz, 2H), 7.34 – 7.27 (m, 2H), 7.13 – 7.08 (m, 2H), 4.03 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 146.5 (q, *J* = 34.7 Hz), 139.4, 137.4, 137.1, 132.8, 130.2, 129.1, 121.6 (q, *J* = 273.9 Hz), 120.4 (q, *J* = 2.7 Hz), 38.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.78.

IR (film) ν_{max} 3026, 1492, 1435, 1399, 1334, 1251, 1174, 1128, 1083, 1027, 1015 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{10}ClF_3N$ ($[M+H]^+$) 271.0376, found 271.0371.



5-benzyl-2-(trifluoromethyl)pyridine (SI-2)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), toluene (230 mg, 266 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 10% EtOAc in

hexanes) yielded the pure product as a colorless liquid (55 mg, 0.232 mmol, 46% yield).

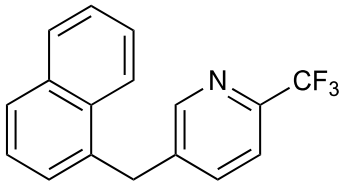
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 2.0 Hz, 1H), 7.63 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 8.2, 6.8 Hz, 2H), 7.28 – 7.25 (m, 1H), 7.20 – 7.15 (m, 2H), 4.06 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 146.2 (q, *J* = 34.6 Hz), 139.9, 138.6, 137.5, 128.9, 128.9, 126.9, 121.6 (q, *J* = 273.8 Hz), 120.4 – 120.0 (m), 38.8.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.75.

IR (film) ν_{max} 3028, 2970, 1496, 1454, 1400, 1365, 1334, 1229, 1216, 1174, 1126, 1083, 1027 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{11}F_3N$ ($[M+H]^+$) 237.0765, found 237.0764.



5-(naphthalen-1-ylmethyl)-2-(trifluoromethyl)pyridine (SI-3)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 1-methylnaphthalene (355 mg, 355 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 10% EtOAc in hexanes) yielded the pure product as a colorless liquid (75 mg, 0.261 mmol, 52% yield).

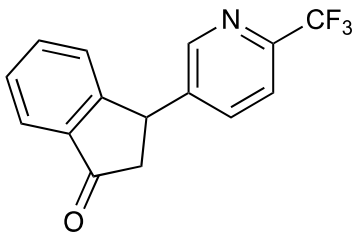
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 1.9 Hz, 1H), 7.93 – 7.78 (m, 3H), 7.57 – 7.43 (m, 5H), 7.32 (d, *J* = 7.0 Hz, 1H), 4.52 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 150.2, 146.2 (q, *J* = 34.6 Hz), 139.6, 137.2, 134.1, 134.1, 131.6, 129.0, 128.1, 127.6, 126.5, 125.9, 125.6, 123.6, 121.6 (q, *J* = 273.8 Hz), 120.3 (q, *J* = 2.7 Hz), 36.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.75

IR (film) ν_{max} 3018, 2970, 1597, 1510, 1435, 1400, 1334, 1216, 1169, 1127, 1084, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{13}F_3N$ ($[M+H]^+$) 287.0922, found 287.0922.



(±)-3-(6-(trifluoromethyl)pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-one (SI-4)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), indanone (330 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 10% EtOAc in hexanes) yielded the pure product as a colorless solid (78 mg, 0.281 mmol, 56% yield).

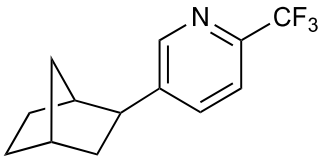
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 2.2 Hz, 1H), 7.86 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.70 – 7.60 (m, 2H), 7.55 – 7.46 (m, 2H), 7.25 (dd, *J* = 7.8, 1.0 Hz, 1H), 4.72 (dd, *J* = 8.3, 3.9 Hz, 1H), 3.31 (dd, *J* = 19.2, 8.3 Hz, 1H), 2.65 (dd, *J* = 19.1, 3.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 204.2, 155.6, 149.6, 147.2 (q, *J* = 34.9 Hz), 142.6, 136.8, 136.1, 135.6, 128.7, 126.6, 124.0, 121.4 (q, *J* = 273.9 Hz), 120.8 (q, *J* = 2.8 Hz), 46.1, 41.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.86

IR (film) ν_{max} 3056, 3020, 1715, 1599, 1461, 1413, 1340, 1267, 1201, 1162, 1132, 1083, 1017 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{11}F_3NO$ ($[M+H]^+$) 277.0715, found 277.0707.



(±)-bicyclo[2.2.1]heptan-2-yl)-2-(trifluoromethyl)pyridine (26)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), norbornane (240 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded the pure product as a colorless solid (74 mg, 0.325 mmol, 61% yield).

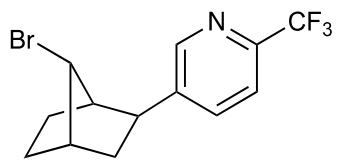
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 2.1 Hz, 1H), 7.70 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 2.85 (dd, *J*= 9.2, 5.5 Hz, 1H), 2.48 – 2.39 (m, 2H), 1.88 (ddd, *J* = 11.7, 9.1, 2.4 Hz, 1H), 1.71 – 1.61 (m, 3H), 1.51 (dp, *J* = 10.0, 2.0 Hz, 1H), 1.43 (tt, *J* = 10.2, 2.6 Hz, 1H), 1.37 – 1.27 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.6, 146.0, 145.4 (q, *J* = 34.6 Hz), 135.2, 122.8 (q, *J* = 273.4), 120.0 (q, *J* = 2.8 Hz), 44.9, 42.6, 38.9, 36.9, 36.1, 30.4, 28.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.66

IR (film) ν_{max} 2953, 2876, 1478, 1456, 1395, 1335, 1250, 1175, 1125, 1084, 1024 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{15}F_3N$ ($[M+H]^+$) 241.1078, found 241.1076.



(±)-7-*anti*-bromobicyclo[2.2.1]heptan-2-*exo*-yl-2-(trifluoromethyl)pyridine (27)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 7-bromobicyclo[2.2.1]heptane (438 mg, 317 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 1% to 10% EtOAc in hexanes) yielded the pure product as a colorless solid (107 mg, 0.334 mmol, 67% yield).

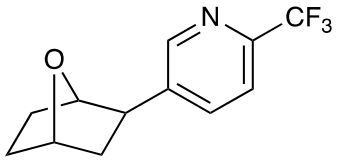
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.2 Hz, 1H), 7.69 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 4.11 (t, *J* = 1.6 Hz, 1H), 3.05 (dd, *J* = 10.3, 5.7 Hz, 1H), 2.54 (d, *J* = 4.2 Hz, 1H), 2.51 (t, *J* = 4.4 Hz, 1H), 2.22 (tt, *J* = 11.2, 4.0 Hz, 1H), 2.11 (tdd, *J* = 8.4, 5.3, 3.4 Hz, 1H), 2.05 (dd, *J* = 13.0, 10.3 Hz, 1H), 1.79 (ddt, *J* = 12.9, 5.7, 3.8 Hz, 1H), 1.56 – 1.43 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.4, 146.1 (q, *J* = 34.8 Hz), 143.8, 135.0, 121.6 (q, *J* = 273.7 Hz), 120.2 (q, *J* = 2.7 Hz), 55.1, 48.2, 43.4, 43.1, 36.2, 28.2, 26.6

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.76

IR (film) ν_{max} 2968, 2917, 2880, 1470, 1458, 1394, 1340, 1273, 1244, 1211, 1193, 1170, 1126, 1084, 1024, 1003 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{14}BrF_3N$ ($[M+H]^+$) 319.0184, found 319.0179.



(±)-7-oxabicyclo[2.2.1]heptan-2-*exo*-yl)-2-(trifluoromethyl)pyridine (28)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 7-oxabicyclo[2.2.1]heptane (245 mg, 253 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 1% to 20% EtOAc in hexanes) yielded the pure product as a colorless solid (48 mg, 0.197 mmol, 40% yield).

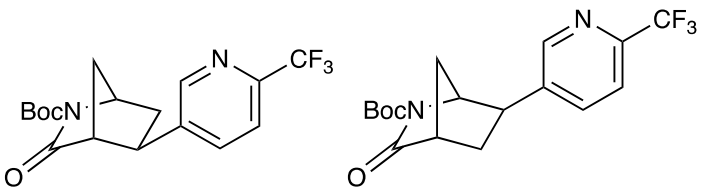
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 2.1 Hz, 1H), 7.88 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 1H), 4.77 (s, 1H), 4.52 – 4.39 (m, 1H), 2.99 (dd, *J* = 9.0, 4.6 Hz, 1H), 2.14 (dd, *J* = 12.4, 8.9 Hz, 1H), 1.81 (pt, *J* = 7.2, 3.6 Hz, 2H), 1.72 (dtd, *J* = 12.2, 5.0, 2.0 Hz, 1H), 1.66 – 1.55 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 146.2 (q, *J* = 34.6 Hz), 145.2, 135.7, 121.7 (q, *J* = 273.7 Hz), 120.4 (q, *J* = 2.9 Hz), 82.3, 76.4, 46.2, 41.9, 30.2, 29.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.72

IR (film) ν_{max} 2959, 2880, 1575, 1464, 1451, 1412, 1329, 1278, 1203, 1171, 1126, 1085, 1050, 1029 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{13}F_3NO$ ($[M+H]^+$) 243.0871, found 243.0868.



(±)-*tert*-butyl-3-oxo-5-(6-(trifluoromethyl)pyridin-3-*exo*-yl)-2-azabicyclo[2.2.1]heptane-2-carboxylate (29, major isomer, left) and (±)-*tert*-butyl-3-oxo-6-(6-(trifluoromethyl)pyridin-3-*exo*-yl)-2-azabicyclo[2.2.1]heptane-2-carboxylate (SI-29, minor isomer, right)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), *tert*-butyl-3-oxo-2-azabicyclo[2.2.1]heptane-2-carboxylate (synthesized according to literature procedures[7], 528 mg, 2.5 mmol, 5.0 equiv.), and Na_3PO_4 (90 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high performance silica gel, slow gradient 0% to 40% EtOAc in hexanes) yielded the pure minor regioisomer as a colorless solid (30 mg, 0.084 mmol, 17% yield) and the crude major regioisomer, which coeluted with solvent-coupled arene. Purification of the major product-containing mixture by preparative TLC (100% CH_2Cl_2, solvent-coupled product elutes first) gave the pure major regioisomer as a colorless solid (77 mg, 0.216 mmol, 43% yield).

29, major regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 2.2 Hz, 1H), 7.76 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 4.57 (s, 1H), 3.56 – 3.40 (m, 1H), 3.04 (dd, *J* = 4.1, 1.9 Hz, 1H), 2.38 (ddd, *J* = 13.4, 8.9, 2.2 Hz, 1H), 2.21 (dt, *J* = 13.5, 4.8 Hz, 1H), 2.00 (dt, *J* = 10.7, 2.0 Hz, 1H), 1.66 (dt, *J* = 10.7, 1.6 Hz, 1H), 1.56 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 149.4, 149.1, 146.81 (q, *J* = 35.0 Hz), 140.0, 135.9, 123.6 (q, *J* = 273.9 Hz), 120.4 (q, *J* = 2.7 Hz), 83.5, 63.4, 46.7, 44.4, 34.8, 30.3, 28.2.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.86

IR (film) ν_{max} 2981, 1786, 1709, 1395, 1369, 1340, 1304, 1253, 1172, 1136, 1087, 1025 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{19}F_3N_2NaO_3$ ($[M+Na]^+$) 356.1348, found 356.1347.

SI-29, minor regioisomer:

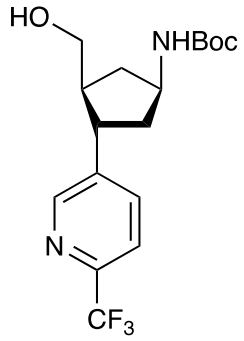
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 2.2 Hz, 1H), 7.72 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 4.71 (s, 1H), 3.51 (dd,*J* = 9.1, 5.3 Hz, 1H), 3.05 (d, *J* = 1.8 Hz, 1H), 2.50 (ddd, *J* = 12.1, 9.1, 2.4 Hz, 1H), 2.14 – 2.01 (m, 2H), 1.76 (d, *J* = 10.7, 1.5 Hz, 1H), 1.55 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 149.2, 149.0, 146.8 (q, *J* = 35.0 Hz), 141.1, 135.6, 123.6 (q, *J* = 273.9 Hz), 120.4 (q, *J* = 2.8 Hz), 83.3, 59.2, 52.4, 39.2, 36.9, 35.6, 28.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.86

IR (film) ν_{max} 2982, 1783, 1710, 1341, 1308, 1257, 1132, 1087, 1022, 1001 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{19}F_3N_2NaO_3$ ($[M+Na]^+$) 356.1348, found 356.1341.



(±)-*tert*-butyl ((1R,3R,4R)-3-(hydroxymethyl)-4-(6-(trifluoromethyl)pyridin-3-yl)cyclopentyl)carbamate (30)

To an 8 mL vial equipped with a teflon stir bar and (±)-*tert*-butyl-3-oxo-5-(6-(trifluoromethyl)pyridin-3-*exo*-yl)-2-azabicyclo[2.2.1]heptane-2-carboxylate (**29**) (as prepared above, 35.6 mg, 0.1 mmol, 1.0 equiv.) was added 4 mL anhydrous methanol under nitrogen flow. The reaction mixture was stirred and cooled to 0 °C. Sodium borohydride (7.6 mg, 0.2 mmol, 2 equiv.) was added as a single portion against nitrogen flow. The vial was sealed, pierced with a needle, and allowed to warm to room temperature over the course of 1h. The crude residue was diluted with EtOAc (10 mL), washed with water (3 x 10 mL), then brine (1 x 10 mL). The organic phase was isolated and dried over anhydrous $MgSO_4$, then filtered and concentrated. The crude residue was purified by preparative TLC (75% EtOAc/hexanes), and the pure product was isolated as a colorless solid (34 mg, 0.094 mmol, 94% yield).

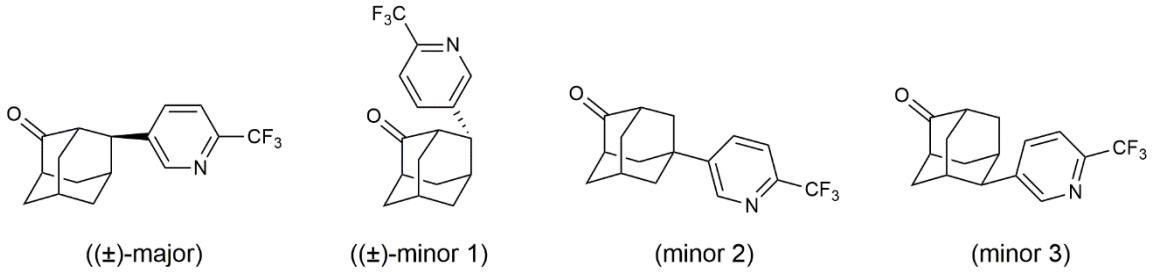
^{1}H NMR (500 MHz, $CDCl_3$) δ (d, *J* = 2.1 Hz, 1H), 7.74 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 5.18 (s, 1H), 4.23 (s, 1H), 3.65 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.59 (dd, *J*= 10.5, 4.2 Hz, 1H), 3.24 (q, *J* = 9.3 Hz, 1H), 2.47 – 2.35 (m, 1H), 2.26 – 2.16 (m, 1H), 2.09 (qd, *J* = 16.1, 14.5, 5.8 Hz, 3H), 1.57 (ddd, *J* = 12.8, 7.4, 4.9 Hz, 1H), 1.50 – 1.40 (m, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 149.7, 146.3 (q, *J* = 34.8 Hz), 143.4, 135.9, 121.6 (q, *J* = 273.8 Hz), 120.4 (q, *J* = 2.9 Hz), 79.3, 62.9, 51.1, 48.4, 42.4, 42.3, 36.2, 28.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.73

IR (film) ν_{max} 3314, 3057, 2976, 2940, 1701, 1534, 1390, 1365, 1337, 1246, 1171, 1130, 1087, 1032, 1002 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{24}F_3N_2O_3$ ($[M+H]^+$) 360.1661, found 360.1658.



(±)-(1R,3S,4S,5S,7R)-4-(6-(trifluoromethyl)pyridin-3-yl)adamantan-2-one (major, left, 31), (±)- (1R,3S,4R,5S,7R)-4-(6-(trifluoromethyl)pyridin-3-yl)adamantan-2-one (minor 1, center-left, SI-31a), (1R,3S,5s,7s)-5-(6-(trifluoromethyl)pyridin-3-yl)adamantan-2-one (minor 2, center-right, SI-31b), and (1r,3r,5R,7S)-6-(6-(trifluoromethyl)pyridin-3-yl)adamantan-2-one (minor 2, right, SI-31c). Prepared following general procedure A outlined above, with the modification that the reaction was run for 18 hours, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 2-adamantanone (376 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high performance silica gel, gradient 0–30% EtOAc in hexanes) afforded pure major product (42 mg, 0.142 mmol, 28% yield), pure minor diastereomer 1 (14 mg, 0.047 mmol, 9% yield), pure minor regioisomer 2 (10 mg, 0.037 mmol, 7% yield), and impure minor regioisomer 3. Minor regioisomer 3 was repurified by reverse-phase chromatography (C-18 silica gel, 20–100% acetonitrile) to afford impure minor regiosiomer 3 (5 mg, 0.017 mmol, 3% yield).

<u>31, major regioisomer and diastereomer</u>:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (d, *J* = 2.2 Hz, 1H), 7.82 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.69 (d, *J* = 8.2 Hz, 1H), 3.32 (s, 1H), 3.12 (s, 1H), 2.72 (t, *J* = 3.2 Hz, 1H), 2.70 – 2.64 (m, 1H), 2.29 (dt, *J* = 13.1, 2.9 Hz, 1H), 2.18 – 1.95 (m, 6H), 1.89 – 1.78 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 215.8, 149.3, 146.3 (q, *J* = 34.8 Hz), 139.9, 136.1, 121.7 (q, *J* = 273.9 Hz), 120.4 (q, *J* = 2.7 Hz), 49.2, 46.0, 46.0, 38.9, 38.6, 33.3, 30.6, 29.8, 27.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.83.

IR (film) ν_{max} 2925, 2860, 1715, 1339, 1172, 1134, 1087, 1055, 1023 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{17}F_3NO^+$ ($[M+H]^+$) 296.1257, found 262.1253.

SI-31a, major regioisomer, minor diastereomer 1:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, *J* = 2.2 Hz, 1H), 7.82 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 3.63 (s, 1H), 3.04 (s, 1H), 2.58 (s, 1H), 2.38 – 2.30 (m, 2H), 2.27 – 2.16 (m, 5H), 2.11 – 2.04 (m, 1H), 1.91 (dq, *J* = 13.6, 2.7 Hz, 1H), 1.79 (dt, *J* = 13.6, 2.8 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 217.9, 149.8, 146.1 (q, *J* = 34.8 Hz), 142.5, 135.7, 121.7 (q, *J* = 273.8 Hz), 120.2 (q, *J* = 2.8 Hz), 50.8, 49.4, 46.7, 41.1, 40.1, 37.9, 34.2, 32.6, 27.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.82.

IR (film) ν_{max} 2922, 2860, 1714, 1339, 1174, 1132, 1086, 1064, 1055, 1032, 1023 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{17}F_3NO^+$ ($[M+H]^+$) 296.1257, found 262.1256.

SI-31b, minor regioisomer 2:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (d, *J* = 2.3 Hz, 1H), 7.82 (dd, *J* = 8.3, 2.4 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 2.75-2.68 (m, 2H), 2.37-2.33 (m, 1H), 2.33 – 2.27 (m, 2H), 2.27 – 2.19 (m, 4H), 2.16 – 2.07 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 216.5, 147.6, 146.4, 146.4 (q, *J* = 34.7 Hz), 134.0, 121.7 (q, *J* = 273.8 Hz), 120.3 (q, *J* = 2.7 Hz), 46.4, 43.9, 41.6, 38.3, 35.6, 28.0.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.82.

IR (film) ν_{max} 2929, 2861, 1721, 1338, 1178, 1131, 1089, 1062, 1037, 1015 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{17}F_3NO^+$ ($[M+H]^+$) 296.1257, found 262.1256.

SI-31c, minor regioisomer 3:

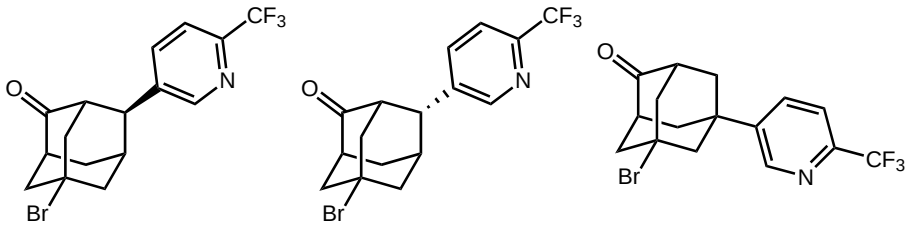
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, *J* = 2.2 Hz, 1H), 7.91 – 7.86 (m, 1H), 7.71 (d, *J* = 8.3 Hz, 1H), 3.34 (s, 1H), 2.70 (s, 1H), 2.65 (s, 2H), 2.48 (s, 1H), 2.33 – 2.26 (m, 4H), 2.13 – 2.09 (m, 2H), 1.92 (d, *J* = 13.0 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 216.7, 149.3, 146.1 (q, *J* = 34.7 Hz), 141.3, 135.8, 121.8 (q, *J* = 273.5 Hz), 120.3 (q, *J* = 2.7 Hz), 46.2, 45.9, 44.2, 40.0, 33.7, 30.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.78.

IR (film) ν_{max} 2927, 2860, 1720, 1337, 1175, 1133, 1087, 1042, 1022 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{17}F_3NO^+$ ($[M+H]^+$) 296.1257, found 262.1257.



major minor minor

(±)-(1S,3S,4S,5R,7S)-7-bromo-4-(6-(trifluoromethyl)pyridin-3-yl)adamantan-2-one (32), (±)-(1S,3S,4R,5R,7S)-7-bromo-4-(6-(trifluoromethyl)pyridin-3-yl)adamantan-2-one (SI-32a), and 5-bromo-7-(6-(trifluoromethyl)pyridin-3-yl)adamantan-2-one (SI-32b)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 5-bromo-2-(trifluoromethyl)pyridine (113 mg, 0.5 mmol, 1.0 equiv.), 5-bromo-2-adamantanone (573 mg, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by column chromatography (silica gel, 5–25% ethyl

acetate in hexanes) followed by purification by reverse-phase column chromatrography (SilaSep™ C18 silica flash cartridge, 10 to 100% MeCN in H_2O with 0.1% formic acid) yielded the pure major product as a white solid (54 mg, 0.144 mmol, 29% yield), pure product SI-31A as a white solid (10 mg, 0.027 mmol, 5%) and pure product SI-31B as a white solid (35 mg, 0.094 mmol, 19% yield), giving 53% overall yield (1.8:1 r.r. and 5.4:1 d.r. for secondary coupled product).

32, major regioisomer and diastereomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 3.33 (s, 1H), 3.17 (s, 1H), 2.89 (s, 1H), 2.76 (s, 1H), 2.67 (d, *J* = 12.8 Hz, 1H), 2.61 – 2.52 (m, 2H), 2.51 – 2.42 (m, 3H), 2.28 (ddd, *J* = 13.4, 3.1 Hz, 3.1 Hz, 1H), 2.17 (br d, *J* = 13.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 212.0, 149.0, 146.8 (q, *J* = 35.0 Hz), 138.4, 135.8, 121.6 (q, *J* = 274.0 Hz), 120.7 (q, *J* = 2.7 Hz), 58.3, 51.3, 48.7, 48.0, 44.5, 43.4, 42.2, 36.8, 33.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.88.

IR (film) ν_{max} 2941, 2866, 1724, 1340, 1136, 1087 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{16}BrF_3NO^+$ ($[M+H]^+$) 374.0362, found 374.0357.

SI-32a, major regioisomer, minor diastereomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 3.68 (s, 1H), 3.06 (br s, 1H), 2.90 – 2.84 (m, 1H), 2.83 – 2.75 (m, 3H), 2.71 – 2.66 (m, 1H), 2.64 – 2.58 (m, 2H), 2.53 (br s, 1H), 1.91 (dq, *J* = 13.9, 2.7 Hz, 1H), 1.86 – 1.80 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 214.1, 149.6, 146.6 (q, *J* = 34.9 Hz), 140.7, 135.7, 121.2 (q, *J* = 274.7 Hz), 120.3 (q, *J* = 2.4 Hz), 57.6, 51.0, 50.4, 49.6, 49.4, 48.9, 48.7, 37.5, 31.2.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.90.

IR (film) ν_{max} 2940, 2867, 1727, 1342, 1138, 1088 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{16}BrF_3NO^+$ ($[M+H]^+$) 374.0362, found 374.0368.

SI-32b, minor regioisomer:

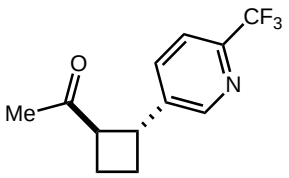
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (d, *J* = 1.5 Hz, 1H), 7.84 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 1H), 2.83 – 2.68 (m, 6H), 2.58 (br d, *J* = 12.0 Hz, 2H), 2.35 (d, *J* = 13.0 Hz, 2H), 2.28 (br d, *J* = 13.2 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 212.7, 147.3, 147.0 (q, *J* = 34.9 Hz), 144.2, 134.0, 121.6 (q, *J* = 274.7 Hz), 120.5 (q, *J* = 2.3 Hz), 57.9, 52.4, 48.2, 48.0, 42.4, 39.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.90.

IR (film) ν_{max} 2941, 2865, 2344, 1728, 1339, 1136, 1091 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{16}BrF_3NO^+$ ($[M+H]^+$) 374.0362, found 374.0366.



(±)-1-(*trans*-2-(6-(trifluoromethyl)pyridin-3-yl)cyclobutyl)ethan-1-one (33)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025

mmol, 5.0 mol%), tetrabutylammonium decatungstate (8.3 mg, 0.0025 mmol, 0.5 mol%), 5-bromo-2-(trifluoromethyl)pyridine (113 mg, 0.5 mmol, 1.0 equiv.), cyclobutyl methyl ketone (245 mg, 272 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (177 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5.0 mL). A total of 2 additional portions of 0.5 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by column chromatography (silica gel, 0–20% ethyl acetate in hexanes) followed by purification by reverse-phase column chromatrography (SilaSep™ C18 silica flash cartridge, 15 to 100% MeCN in H_2O with 0.1% formic acid) followed by extraction from basified fractions (pH to ~8 with $NaHCO_3$) with ethyl acetate yielded the pure product as a colorless oil (51 mg, 0.210 mmol, 42% yield).

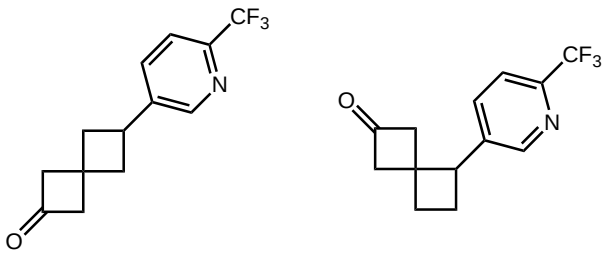
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.1 Hz, 1H), 7.73 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 3.86 (q, *J* = 9.3 Hz, 1H), 3.36 – 3.25 (m, 1H), 2.36 – 2.26 (m, 2H), 2.24 – 2.14 (m, 2H), 2.09 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.9, 148.8, 146.5 (q, *J* = 34.7 Hz), 142.4, 135.6, 121.8 (q, *J* = 273.8 Hz), 120.3 (q, *J* = 2.8 Hz), 53.4, 38.8, 27.6, 24.1, 22.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.77.

IR (film) ν_{max} 2954, 1706, 1335, 1170, 1129, 1087 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{13}F_3NO^+$ ($[M+H]^+$) 244.0944, found 244.0941.



major minor

6-(6-(trifluoromethyl)pyridin-3-yl)spiro[3.3]heptan-2-one (major, left, 34) and (±)-5-(6-(trifluoromethyl)pyridin-3-yl)spiro[3.3]heptan-2-one (minor, right, SI-34)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (4.2 mg, 0.0013 mmol, 0.25 mol%), 5-bromo-2-(trifluoromethyl)pyridine (113 mg, 0.5 mmol, 1.0 equiv.), spiro[3.3]heptan-2-one (275 mg, 262 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (177 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5.0 mL). A total of 2 additional portions of 0.25 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by column chromatography (silica gel, 0–20% ethyl acetate in hexanes) followed by purification by reverse-phase column chromatrography (SilaSep™ C18 silica flash cartridge, 15 to 100% MeCN in H_2O with 0.1% formic acid) followed by extraction from basified fractions (pH to ~8 with $NaHCO_3$) with ethyl acetate yielded the pure product as a mixture of regioisomers; colorless oil (40 mg, 0.157 mmol, 31% yield, 8.8:1 A:B).

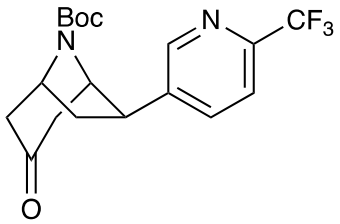
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (s, 1H(**A**) + 1H(**B**)), 7.84 – 7.57 (m, 2H(**A**) + 2H(**B**)), 3.79 (t, *J* = 8.5 Hz, 1H(**A**)), 3.66 (p, *J* = 9.1 Hz, 1H(**B**)), 3.29 (s, 2H(**B**)), 3.21 – 3.06 (m, 2H(**A**) + 2H(**B**)), 2.81 (dd, *J* = 17.9, 4.0 Hz, 1H(**A**)), 2.68 (d, *J* = 16.9 Hz, 1H(**A**) + 1H(**B**)), 2.52 – 2.27 (m, 3H(**A**) + 3H(**B**)), 2.25 – 2.17 (m, 1H(**A**)).

^{13}C NMR (126 MHz, $CDCl_3$) δ 206.5 (**B**), 205.0 (**A**), 149.4 (**A**), 148.8 (**B**), 148.2 (**B**), 147.0 (q, *J* = 34.9 Hz, **A**), 146.3 (q, *J* = 34.4 Hz, (**B**)), 139.5 (**A**), 136.2 (**A**), 135.1 (**B**), 122.9 (q, *J* = 273.5 Hz, (**B**)), 121.7 (q, *J* = 273.9 Hz, (**A**)), 120.5 (q, *J* = 2.8 Hz, (**A**)), 120.3 (q, *J* = 2.7 Hz, (**B**)), 59.4 (**B**), 58.2 (**B**), 58.0 (**A**), 54.1 (**A**), 45.5 (**A**), 41.0 (**B**), 38.3 (**B**), 32.5 (**B**), 31.9 (**A**), 29.8 (**B**), 21.9 (**A**).

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.72 (**B**), -67.79 (**A**).

IR (film) ν_{max} 2952, 1780, 1381, 1337, 1172, 1130, 1084 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{13}F_3NO^+$ ($[M+H]^+$) 256.0944, found 256.0945.



(±)-*tert*-butyl-3-oxo-6-(6-(trifluoromethyl)pyridin-3-*exo*-yl)-8-azabicyclo[3.2.1]octane-8-carboxylate (35)

Prepared following general procedure B outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (3 x 17 mg, 0.005 mmol, 3 x 1.0 mol%), MeCN (12.5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), *N*-Boc-nortropinone (563 mg, 2.5 mmol, 5.0 equiv.), and Na_3PO_4 (90 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 25% to 50% EtOAc in hexanes) yielded the product with a minor impurtity (~5%). Preparative TLC (25% EtOAc/toluene) afforded pure product (mixture of rotamers) as a colorless solid (112 mg, 0.302 mmol, 61% yield).

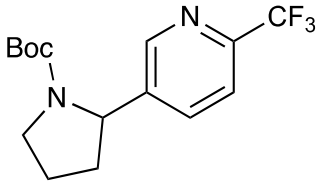
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 4.70 (d, *J* = 62.7 Hz, 1H), 4.46 (d, *J* = 68.9 Hz, 1H), 3.24 (d, *J* = 8.4 Hz, 1H), 2.86 (d, *J* = 14.7 Hz, 1H), 2.70 (d, *J* = 15.6 Hz, 1H), 2.57 (d, *J* = 16.6 Hz, 1H), 2.46 (dt, *J* = 15.9, 1.8 Hz, 1H), 2.34 (d, *J* = 11.7 Hz, 1H), 2.13 (s, 1H), 1.49 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 206.8, 153.2, 148.6, 146.8 (q, *J* = 34.5 Hz), 144.3 (q, *J* = 16.1 Hz), 135.0, 121.5 (q, *J* = 273.9 Hz), 120.7, 81.3, 60.3 (m, *J* = 84.4 Hz), 53.9 (m, *J* = 57.2 Hz), 48.6 (m, *J* = 57.0 Hz), 48.1 (m, *J* = 43.8 Hz), 45.3 (m, *J* = 124.6 Hz), 39.9 (m, *J* = 105.5 Hz), 28.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.84

IR (film) ν_{max} 2977, 1691, 1478, 1457, 1389, 1368, 1337, 1312, 1253, 1165, 1135, 1068, 1027, 1005 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{22}F_3N_2O_3$ ($[M+H]^+$) 370.1504, found 370.1498.



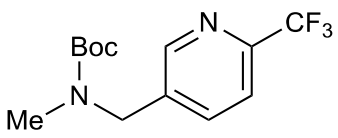
(±)-*tert*-butyl 2-(6-(trifluoromethyl)pyridin-3-yl)pyrrolidine-1-carboxylate (36)

Prepared following general procedure A outlined above using one light and $NiBr_2$•dtbbpy (24 mg, 0.050 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (12.5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), *N*-Boc-pyrrolidine (428 mg, 438 µL, 2.5 mmol, 5.0 equiv.), and Na_3PO_4 (90 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high performance silica gel, gradient 0% to 30% EtOAc in hexanes) yielded the pure product (mixture of rotamers) as a colorless solid (83 mg, 0.262 mmol, 53% yield). The spectroscopic properties of this compound are consistent with data reported in the literature[8].

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.1 Hz, 1H), 7.67 (q, *J* = 7.7, 7.2 Hz, 2H), 5.17 – 4.77 (m, 1H), 3.89 – 3.37 (m, 3H), 2.43 (dd, *J* = 14.8, 7.7 Hz, 1H), 1.94 (q, *J* = 6.5 Hz, 2H), 1.85 (dd, *J* = 12.7, 6.3 Hz, 1H), 1.35 (m, *J* = 125.7 Hz, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 154.3 (m, *J* = 46.9 Hz), 147.9 (m, *J* = 40.8 Hz), 146.8 (q, *J* = 35.1 Hz), 143.3 (m, *J* = 127.1 Hz), 134.3 (m, *J* = 27.2 Hz), 121.6 (q, *J* = 273.7 Hz), 120.1 (m, *J* = 18.3 Hz), 80.1, 58.8 (m, *J* = 40.2 Hz), 47.3 (m, *J* = 26.3 Hz), 35.9, 34.6, 28.3 (m, *J* = 34.7 Hz), 23.5 (m, *J* = 45.3 Hz).

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{20}F_3N_2O_2$ ($[M+H]^+$) 316.1399, found 316.1397.



***tert*-butyl methyl((6-(trifluoromethyl)pyridin-3-yl)methyl)carbamate (37)**

Prepared following general procedure A outlined above using one light and $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), *tert*-butyl *N*,*N*-dimethylcarbamate (363 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 20% to 40% EtOAc in hexanes) yielded the pure product as a colorless liquid (98 mg, 0.338 mmol, 68% yield).

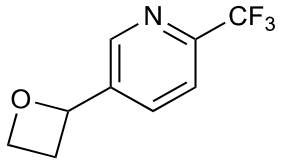
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 2.1 Hz, 1H), 7.84 – 7.69 (m, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 4.51 (s, 2H), 2.87 (d, *J* = 24.9 Hz, 3H), 1.48 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 147.3 (q, *J* = 34.6 Hz), 137.1, 136.6, 136.0, 123.7 (q, *J* = 273.9 Hz), 120.4, 80.4, 49.8 (d, *J* = 87.2 Hz), 34.4, 28.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.84

IR (film) ν_{max} 2978, 2932, 1690, 1481, 1454, 1390, 1367, 1333, 1299, 1132, 1083, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{18}F_3N_2O_2$ ($[M+H]^+$) 290.1242, found 290.1238.



(±)-5-(oxetan-2-yl)-2-(trifluoromethyl)pyridine (38)

Prepared following general procedure A outlined above using one light and $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), oxetane (145 mg, 163 μL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 20% EtOAc in hexanes) yielded the pure product as a colorless liquid (55 mg, 0.271 mmol, 54% yield).

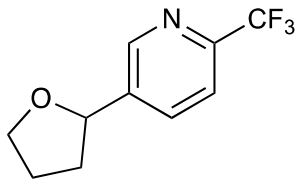
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 5.92 (t, *J* = 7.5 Hz, 1H), 4.89 (q, *J* = 7.9 Hz, 1H), 4.71 (dt, *J* = 9.1, 5.9 Hz, 1H), 3.23 – 3.08 (m, 1H), 2.65 (dq, *J* = 10.9, 7.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6 (q, *J* = 34.7 Hz), 147.2, 142.2, 134.1, 121.5 (q, *J* = 274.0 Hz), 120.4 (q, *J* = 2.7 Hz), 79.9, 68.8, 30.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.83

IR (film) ν_{max} 2891, 1402, 1331, 1233, 1172, 1128, 1084, 1029, 1011 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_9H_9F_3NO$ ($[M+H]^+$) 203.0558, found 203.0554.



(±)-5-(tetrahydrofuran-2-yl)-2-(trifluoromethyl)pyridine (39)

Prepared following general procedure A outlined above using one light and $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), tetrahydrofuran (180 mg, 203 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 20% EtOAc in hexanes) yielded the pure product as a colorless liquid (60 mg, 0.276 mmol, 55% yield).

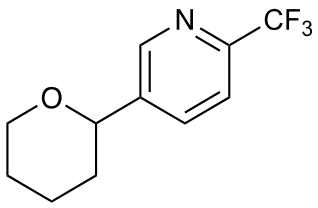
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 2.0 Hz, 1H), 7.84 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 4.99 (t, *J* = 7.2 Hz, 1H), 4.11 (q, *J* = 7.3 Hz, 1H), 3.97 (q, *J* = 7.4 Hz, 1H), 2.43 (dq, *J* = 13.1, 6.8 Hz, 1H), 2.04 (qq, *J* = 12.5, 5.8 Hz, 2H), 1.78 (dq, *J* = 12.3, 7.8 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 147.7, 147.0 (q, *J* = 34.6 Hz), 142.3, 134.3, 121.6 (q, *J* = 273.9 Hz), 120.1 (q, *J* = 2.8 Hz), 77.9, 69.0, 34.6, 25.9 .

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.78

IR (film) ν_{max} 2979, 2876, 1399, 1331, 1248, 1171, 1129, 1084, 1064, 1022 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{11}F_3NO$ ($[M+H]^+$) 217.0715, found 217.0711.



(±)-5-(tetrahydro-2*H*-pyran-2-yl)-2-(trifluoromethyl)pyridine (40)

Prepared following general procedure A outlined above using one light and $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), tetrahydropyran (215 mg, 245 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 30% EtOAc in hexanes) yielded the pure product as a colorless liquid (60 mg, 0.259 mmol, 52% yield).

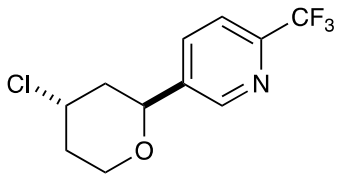
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 2.0 Hz, 1H), 7.87 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 4.45 (dd, *J* = 11.3, 2.3 Hz, 1H), 4.16 (dd, *J* = 11.4, 3.8 Hz, 1H), 3.62 (tt, *J* = 13.4, 5.1 Hz, 1H), 2.06 – 1.82 (m, 2H), 1.76 – 1.46 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.0 (q, *J* = 34.6 Hz), 142.0, 134.5, 121.6 (q, *J* = 274.1 Hz), 120.2 (q, *J* = 2.7 Hz), 77.0, 69.0, 34.1, 25.5, 23.7

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.78

IR (film) ν_{max} 3035, 2949, 2855, 1440, 1399, 1335, 1298, 1203, 1171, 1127, 1116, 1082, 1048, 1026, 1002 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{13}F_3NO$ ($[M+H]^+$) 231.0871, found 231.0871.



(±)-5-(trans-4-chlorotetrahydro-2*H*-pyran-2-yl)-2-(trifluoromethyl)pyridine (41)

Prepared following general procedure A outlined above, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 4-chlorotetrahydro-2H-pyran (301 mg, 271 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0–20% EtOAc in hexanes) afforded pure major product (66 mg, 0.248 mmol, 50% yield)

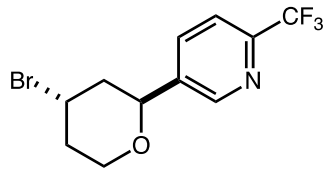
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 2.0 Hz, 1H), 7.87 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 5.01 (dd, *J* = 11.3, 2.2 Hz, 1H), 4.68 (p, *J* = 3.3 Hz, 1H), 4.16 (td, *J* = 12.0, 2.1 Hz, 1H), 4.05 (ddt, *J* = 12.0, 5.2, 1.3 Hz, 1H), 2.26 – 2.13 (m, 2H), 2.01 (ddd, *J* = 14.3, 11.2, 3.2 Hz, 1H), 1.97 – 1.89 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.9, 147.5 (q, *J* = 34.8 Hz), 140.9, 134.8, 121.7 (q, *J* = 273.9 Hz), 120.3 (q, *J* = 2.8 Hz), 71.1, 62.9, 55.7, 41.4, 33.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.84.

IR (film) ν_{max} 2962, 2925, 2869, 1336, 1268, 1247, 1178, 1136, 1108, 1087, 1075, 1043, 1028, 1013 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{12}ClF_3NO^+$ ($[M+H]^+$) 266.0554, found 266.0559.



(±)-5-(trans-4-bromotetrahydro-2*H*-pyran-2-yl)-2-(trifluoromethyl)pyridine (42)
Prepared following general procedure A outlined above using one light and $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 4-bromotetrahydropyran (413 mg, 281 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 20% EtOAc in hexanes) yielded the pure product as a colorless solid (108 mg, 0.348 mmol, 70% yield).

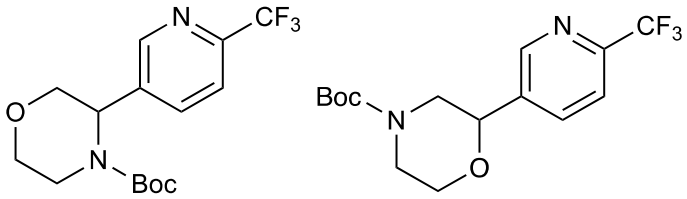
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 2.0 Hz, 1H), 7.86 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.66 (dd, *J* = 8.2, 0.8 Hz, 1H), 5.03 (dd, *J* = 11.1, 2.1 Hz, 1H), 4.80 (s, 1H), 4.16 (td, 1H), 4.06 (ddt, 1H), 2.29 – 2.20 (m, 2H), 2.09 – 1.97 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.3 (q, *J* = 34.8 Hz), 140.6, 134.7, 121.5 (q, *J* = 273.9 Hz), 120.2 (q, *J* = 2.7 Hz), 71.6, 63.4, 48.9, 41.6, 33.5.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.83

IR (film) ν_{max} 2958, 2870, 1582, 1466, 1425, 1406, 1336, 1252, 1241, 1215, 1181, 1145, 1128, 1083, 1070, 1051, 1023, 1008 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{12}BrF_3NO$ ($[M+H]^+$) 308.9976, found 308.9973.



(±)-*tert*-butyl 3-(6-(trifluoromethyl)pyridin-3-yl)morpholine-4-carboxylate (43, major isomer, left) and (±)-*tert*-butyl 2-(6-(trifluoromethyl)pyridin-3-yl)morpholine-4-carboxylate (SI-43, minor isomer, right)

Prepared following general procedure A outlined above using one light and $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), *N*-Boc-morpholine (prepared according to literature procedures[9], 468 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 20% to 40% EtOAc in hexanes) yielded the pure major product (62 mg, 0.187 mmol, 37% yield) and pure minor product (18 mg, 0.054 mmol, 11% yield, mixture of rotamers) as colorless solids.

43, major regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 4.55 (d, *J* = 9.2 Hz, 1H), 4.42 – 3.80 (m, 3H), 3.70 (t, *J* = 10.8 Hz, 1H), 3.06 (s, 1H), 2.78 (s, 1H), 1.48 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 148.0, 147.8 (q, *J* = 35.1 Hz), 138.1, 135.1, 121.5 (q, *J* = 274.1 Hz), 120.3 (q, *J* = 3.1 Hz), 80.6, 75.0, 66.8, 49.6 (m, *J* = 167.4 Hz), 43.3 (d, *J* = 147.4 Hz), 28.38.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.89

IR (film) ν_{max} 2976, 2927, 2858, 1685, 1446, 1392, 1423, 1365, 1339, 1248, 1236, 1169, 1120, 1085, 1024, 1014 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{20}F_3N_2O_3$ ($[M+H]^+$) 332.1348, found 332.1342.

SI-43, minor regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 – 8.83 (m, 1H), 8.07 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 5.18 (s, 1H), 4.31 (d, *J* = 12.1 Hz, 1H), 3.93 (ddd, *J* = 12.2, 7.8, 3.6 Hz, 2H), 3.83 (m, *J* = 13.8 Hz, 1H), 3.63 (td, *J* = 11.8, 3.0 Hz, 1H), 3.03 (td, *J* = 13.0, 3.7 Hz, 1H), 1.48 (s, 9H).

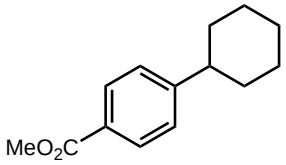
^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4, 149.9, 147.1 (q, *J* = 34.7 Hz), 138.5, 136.9, 121.5 (q, *J* = 274.0 Hz), 120.1 (q, *J* = 2.8 Hz), 81.2, 68.5, 67.0, 51.0, 39.7, 28.3.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.90

IR (film) ν_{max} 2961, 2867, 1689, 1455, 1408, 1367, 1337, 1297, 1217, 1166, 1138, 1113, 1084, 1027, 1009 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{20}F_3N_2O_3$ ($[M+H]^+$) 332.1348, found 332.1349.

8) Arylation of cyclohexane



methyl 4-cyclohexylbenzoate (SI-44)

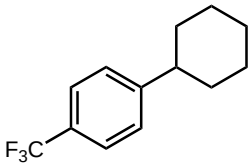
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), methyl 4-bromobenzoate (108.0 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by column chromatography (silica gel, 1% EtOAc in hexanes) yielded the pure product as a colorless oil (74 mg, 0.339 mmol, 68% yield).

^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 3.86 (s, 3H), 2.61 (tt, *J* = 11.5, 3.1 Hz, 1H), 1.90 – 1.79 (m, 4H), 1.78 – 1.69 (m, 1H), 1.54 – 1.36 (m, 4H), 1.29 (tdd, *J* = 12.8, 9.3, 5.9 Hz, 1H).

^{13}C NMR (126 MHz, $(CD_3)_2CO$) δ 167.2, 154.3, 130.3, 128.8, 127.8, 52.1, 45.4, 34.8, 27.4, 26.7.

IR (film) ν_{max} 2926, 2851, 1715, 1608, 1571, 1448, 1436, 1416 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{19}O_2^+$ ($[M+H]^+$) 219.1380, found 219.1381.



1-cyclohexyl-4-(trifluoromethyl)benzene (SI-45)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-bromobenzotrifluoride (70 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatography (hexanes) yielded the pure product as a colorless oil (80 mg, 0.350 mmol, 70% yield).

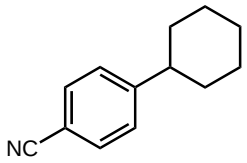
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.63 – 2.51 (m, 1H), 1.87 (dtt, *J* = 8.5, 5.6, 3.0 Hz, 4H), 1.80 – 1.73 (m, 1H), 1.48 – 1.35 (m, 4H), 1.31 – 1.24 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.0, 128.1 (q, *J* = 32.3 Hz), 127.1, 125.2 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 271.7 Hz), 44.5, 34.2, 26.7, 26.0.

^{19}F NMR (470 MHz, $CDCl_3$) δ -62.26.

IR (film) ν_{max} 2927, 2854, 1619, 1450, 1419, 1323, 1119 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{13}H_{15}F_3^+$ ($[M]^{\bullet+}$) 228.1120, found 228.1121.



4-cyclohexylbenzonitrile (SI-46)

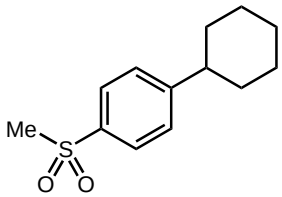
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-bromobenzonitrile (91.0 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatography (8% EtOAc in hexanes) yielded the pure product as a colorless oil (59 mg, 0.318 mmol, 64% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 2.60 – 2.49 (m, 1H), 1.91 – 1.81 (m, 4H), 1.80 – 1.72 (m, 1H), 1.46 – 1.33 (m, 4H), 1.29 – 1.20 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.6, 132.3, 127.8, 119.4, 109.7, 44.9, 34.1, 26.7, 26.1.

IR (film) ν_{max} 2925, 2852, 2226, 1607, 1504, 1448, 1416 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{16}N^+$ ($[M+H]^+$) 186.1277, found 186.1277.



1-cyclohexyl-4-(methylsulfonyl)benzene (SI-47)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0

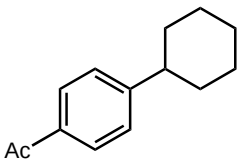
mol%), 1-bromo-4-(methylsulfonyl)benzene (118.0 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatrography (silica gel, 35% EtOAc in hexanes) yielded the pure product as a white solid (72 mg, 0.302 mmol, 60% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 3.03 (s, 3H), 2.59 (tt, *J* = 11.2, 2.6 Hz, 1H), 1.93 – 1.81 (m, 4H), 1.80 – 1.73 (m, 1H), 1.48 – 1.34 (m, 4H), 1.30 – 1.24 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.6, 138.0, 127.9, 127.6, 44.8, 44.7, 34.2, 26.7, 26.0.

IR (film) ν_{max} 3016, 2922, 2850, 1597, 1451, 1408, 1303, 1142 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{19}O_2S^+$ ($[M+H]^+$) 239.1100, found 239.1098.



4′-cyclohexyl acetophenone (SI-48)

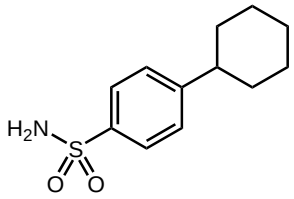
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4′-cyclohexyl acetophenone (99.5 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by column chromatography (silica gel, 0-5% EtOAc in hexanes) followed by preparative thin-layer chromatography (5% EtOAc in hexanes) yielded the pure product as a white solid (70 mg, 0.346 mmol, 69% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 2.57 (s, 3H), 1.94 – 1.81 (m, 4H), 1.80 – 1.71 (m, 1H), 1.49 – 1.33 (m, 4H), 1.27 (dtt, *J* = 12.9, 9.3, 4.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 153.9, 135.1, 128.6, 127.1, 44.8, 34.2, 26.8, 26.7, 26.1.

IR (film) ν_{max} 3004, 2925, 2850, 1672, 1606, 1449, 1416, 1363, 1270 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{19}O^+$ ($[M+H]^+$) 203.1430, found 203.1429.



4-cyclohexylbenzenesulfonamide (SI-49)

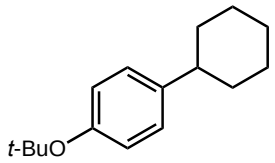
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-bromobenzenesulfonamide (118.0 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by column chromatography (silica gel, 30% EtOAc in hexanes) yielded the pure product as a white solid (76 mg, 0.318 mmol, 63% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 2.61 (tt, *J* = 11.7, 2.9 Hz, 1H), 1.93 – 1.81 (m, 4H), 1.81 – 1.74 (m, 1H), 1.55 – 1.40 (m, 4H), 1.37 – 1.25 (m, 1H).

^{13}C NMR (126 MHz, CD_3OD) δ 152.6, 141.0, 127.0, 125.9, 44.5, 34.0, 26.4, 25.7.

IR (film) ν_{max} 2924, 2851, 2509, 2405, 1600, 1450, 1413, 1317, 1145 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{18}NO_2S^+$ ($[M+H]^+$) 240.1053, found 240.1053.



1-(*tert*-butoxy)-4-cyclohexylbenzene (SI-50)

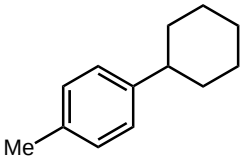
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-(*tert*-butoxy)-bromobenzene (115 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by preparative thin-layer chromatography (7.5% EtOAc in hexanes) yielded the pure product as a pale yellow oil (69 mg, 0.297 mmol, 59% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 2.46 (tt, *J* = 8.4, 4.7 Hz, 1H), 1.92 – 1.79 (m, 4H), 1.77 – 1.70 (m, 1H), 1.46 – 1.30 (m, 13H), 1.28 – 1.22 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.2, 143.1, 127.1, 124.1, 78.1, 44.0, 34.8, 29.0, 27.1, 26.3.

IR (film) ν_{max} 2977, 2925, 2852, 1607, 1507, 1449, 1389, 1365, 1235, 1166 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{16}H_{24}O^+$ ($[M]^{\bullet+}$) 232.1822, found 232.1821.



1-cyclohexyl-4-methylbenzene (SI-51)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-bromotoluene (86 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5

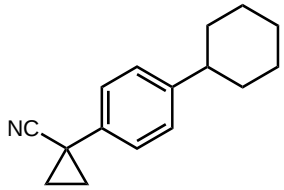
mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by preparative thin-layer chromatography (hexanes) yielded the pure product as a colorless oil (45 mg, 0.258 mmol, 52% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (s, 4H), 2.49 (tt, *J* = 11.3, 3.6 Hz, 1H), 2.35 (s, 3H), 1.94 – 1.82 (m, 4H), 1.81 – 1.74 (m, 1H), 1.49 – 1.36 (m, 4H), 1.33 – 1.25 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 135.3, 129.1, 126.8, 44.3, 34.7, 27.1, 26.3, 21.1.

IR (film) ν_{max} 3018, 2922, 2851, 1515, 1447 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{13}H_{18}^+$ ($[M]^{\bullet+}$) 174.1403, found 174.1405.



1-(4-cyclohexylphenyl)cyclopropane-1-carbonitrile (SI-52)

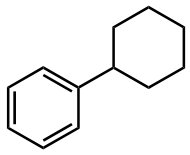
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 1-(4-bromophenyl)cyclopropanecarbonitrile (111 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by preparative thin-layer chromatography (10% EtOAc in hexanes) yielded the pure product as a colorless oil (60 mg, 0.266 mmol, 53% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.15 (m, 4H), 2.55 – 2.44 (m, 1H), 1.92 – 1.79 (m, 4H), 1.79 – 1.72 (m, 1H), 1.69 (q, *J* = 5.0 Hz, 2H), 1.46 – 1.32 (m, 6H), 1.30 – 1.23 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.8, 133.4, 127.5, 125.9, 122.9, 44.3, 34.5, 26.9, 26.2, 18.1, 13.6.

IR (film) ν_{max} 2923, 2851, 2234, 1515, 1448, 1429 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{20}N^+$ ($[M+H]^+$) 226.1590, found 226.1592.



cyclohexylbenzene (SI-53)

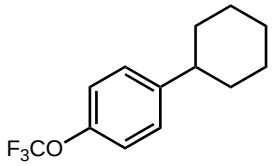
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), bromobenzene (53 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by preparative thin-layer chromatography (hexanes) yielded the pure product as a colorless oil (48 mg, 0.300 mmol, 60% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 7.24 (t, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 6.9 Hz, 2H), 7.12 (tt, *J* = 7.1, 1.5 Hz, 1H), 2.53 – 2.43 (m, 1H), 1.90 – 1.79 (m, 5H), 1.79 – 1.72 (m, 1H), 1.51 – 1.36 (m, 4H), 1.35 – 1.23 (m, 1H).

^{13}C NMR (126 MHz, CD_3OD) δ 149.2, 129.3, 127.8, 126.8, 46.1, 35.7, 28.0, 27.3.

IR (film) ν_{max} 3027, 2922, 2851, 1602, 1493, 1447 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{12}H_{16}^+$ ($[M]^{\bullet+}$) 160.1247, found 160.1248.



1-cyclohexyl-4-(trifluoromethoxy)benzene (SI-54)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-(trifluoromethoxy)-bromobenzene (74 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by preparative thin-layer chromatography (hexanes) yielded the pure product as a colorless oil (76 mg, 0.311 mmol, 62% yield).

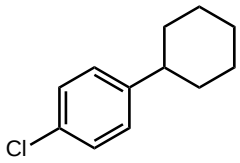
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 2.51 (tt, *J* = 11.9, 3.3 Hz, 1H), 1.86 (tt, *J* = 8.7, 2.5 Hz, 4H), 1.80 – 1.72 (m, 1H), 1.48 – 1.33 (m, 4H), 1.31 – 1.21 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.4 (q, *J* = 1.7 Hz), 146.9, 128.1, 120.9, 120.7 (q, *J* = 256.4 Hz), 44.1, 34.6, 26.9, 26.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.91.

IR (film) ν_{max} 2926, 2854, 1510, 1450, 1253, 1217, 1156 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{13}H_{15}F_3O^+$ ($[M]^{\bullet+}$) 244.1070, found 244.1069.



1-chloro-4-cyclohexylbenzene (SI-55)

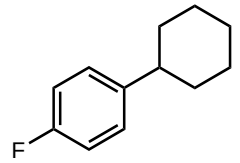
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 1-bromo-4-chlorobenzene (96 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 1 additional portion of 1.0 mol% tetrabutylammonium decatungstate was added with 12 hours of additional irradiation. Purification by preparative thin-layer chromatography (hexanes) yielded the pure product as a colorless oil (49 mg, 0.252 mmol, 50% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 2.50 (tt, *J* = 8.7, 2.8 Hz, 1H), 1.94 – 1.82 (m, 4H), 1.82 – 1.74 (m, 1H), 1.47 – 1.35 (m, 4H), 1.33 – 1.25 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.6, 131.4, 128.5, 128.3, 44.1, 34.6, 26.9, 26.2.

IR (film) ν_{max} 2923, 2851, 1492, 1448, 1409 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{12}H_{15}Cl^+$ ($[M]^{\bullet+}$) 194.0857, found 194.0859.



1-cyclohexyl-4-fluorobenzene (SI-5)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 1-bromo-4-fluorobenzene (87 mg, 55 μL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5

mL). A total of 1 additional portion of 1.0 mol% tetrabutylammonium decatungstate was added with 12 hours of additional irradiation. Purification by preparative thin-layer chromatography (cyclohexane) yielded the pure product as a colorless oil (49 mg, 0.275 mmol, 55% yield). The spectroscopic properties of this compound are consistent with data reported in the literature[10].

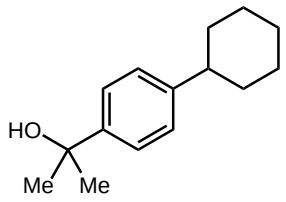
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 – 7.11 (m, 2H), 7.00 – 6.93 (m, 2H), 2.55 – 2.40 (m, 1H), 1.92 – 1.79 (m, 4H), 1.79 – 1.71 (m, 1H), 1.45 – 1.31 (m, 4H), 1.29 – 1.19 (m, 1H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 161.3 (d, *J* = 242.9 Hz), 143.9 (d, *J* = 3.1 Hz), 128.2 (d, *J* = 7.7 Hz), 115.0 (d, *J* = 20.8 Hz), 44.0, 34.8, 27.0, 26.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -118.04 (tt, *J* = 8.7, 5.5 Hz).

IR (film) ν_{max} 2924, 2852, 1604, 1509, 1449, 1223 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{12}H_{15}F^+$ ($[M]^{\bullet+}$) 178.1152, found 178.1150.



2-(4-cyclohexylphenyl)propan-2-ol (SI-56)

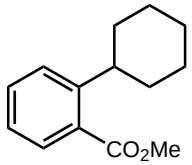
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 2-(4-bromophenyl)propan-2-ol (108 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 1 additional portion of 1.0 mol% tetrabutylammonium decatungstate was added with 12 hours of additional irradiation. Purification by column chromatography (silica gel, dichloromethane) followed by preparative thin-layer chromatography (25% EtOAc in hexanes) yielded the pure product as a white solid (60 mg, 0.275 mmol, 55% yield).

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.39 (d, *J* = 8.3 Hz, 2H), 7.17 (d, *J* = 8.3 Hz, 2H), 2.55 – 2.42 (m, 1H), 1.89 – 1.78 (m, 4H), 1.77 – 1.69 (m, 2H), 1.53 (s, 5H), 1.46 – 1.33 (m, 4H), 1.31 – 1.21 (m, 1H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 147.2, 146.9, 126.9, 124.7, 72.5, 44.5, 34.9, 32.0, 27.3, 26.6.

IR (film) ν_{max} 3377, 2974, 2923, 2851, 1509, 1448, 1410, 1362 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{15}H_{22}O^+$ ($[M]^{\bullet+}$) 218.1665, found 218.1662.



methyl 2-cyclohexylbenzoate (SI-57)

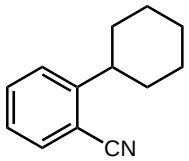
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), methyl-2-bromobenzoate (107.5 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL) using only one LED lamp. A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by preparative thin-layer chromatography (10% EtOAc in hexanes) yielded the pure product as a colorless oil (49 mg, 0.224 mmol, 45% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.1 Hz, 1H), 3.90 (s, 3H), 3.37 – 3.25 (m, 1H), 1.92 – 1.72 (m, 5H), 1.50 – 1.36 (m, 4H), 1.31 – 1.22 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 148.8, 131.8, 130.1, 130.0, 127.0, 125.5, 52.1, 40.4, 34.5, 27.1, 26.4.

IR (film) ν_{max} 2924, 2851, 1721, 1601, 1575, 1432, 1447, 1250 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{19}O_2^+$ ($[M+H]^+$) 219.1380, found 219.1380.



2-cyclohexylbenzonitrile (SI-58)

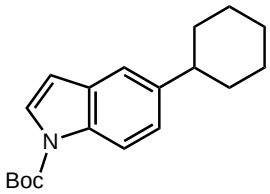
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 2-bromobenzonitrile (91.0 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatography (2.5% EtOAc in hexanes) yielded the pure product as a colorless oil (66 mg, 0.356 mmol, 71% yield).

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.61 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.55 (td, *J* = 7.7, 1.4 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.28 (td, *J* = 7.6, 1.2 Hz, 1H), 3.02 – 2.90 (m, 1H), 1.96 – 1.82 (m, 4H), 1.82 – 1.74 (m, 1H), 1.54 – 1.39 (m, 4H), 1.33 – 1.24 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.6, 133.0, 133.0, 126.7, 126.4, 118.4, 111.9, 42.9, 33.8, 26.7, 26.1.

IR (film) ν_{max} 2926, 2853, 2222, 1599, 1482, 1447 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{16}N^+$ ($[M+H]^+$) 186.1277, found 186.1276.



***N*-Boc-5-cyclohexylindole (SI-59)**

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05

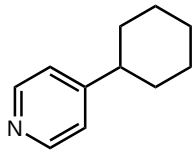
mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), *N*-Boc-5-bromoindole (148 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by preparative thin-layer chromatography (20% toluene in hexanes) followed by reverse-phase column chromatrography (SilaSep™ C18 silica flash cartridge, 40–100% MeCN in H_2O) yielded the pure product as an orange oil (57 mg, 0.190 mmol, 38% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.57 (br s, 1H), 7.39 (s, 1H), 7.18 (dd, *J* = 8.5, 1.7 Hz, 1H), 6.52 (d, *J* = 3.7 Hz, 1H), 2.59 (tt, *J* = 11.6, 3.3 Hz, 1H), 1.92 (d, *J* = 12.2 Hz, 2H), 1.89 – 1.82 (m, 2H), 1.80 – 1.73 (m, 1H), 1.67 (s, 9H), 1.54 – 1.37 (m, 4H), 1.33 – 1.24 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.0, 142.8, 133.7, 130.8, 126.0, 123.7, 118.7, 115.0, 107.4, 83.6, 44.7, 35.1, 28.4, 27.2, 26.4.

IR (film) ν_{max} 2978, 2923, 2851, 1729, 1470, 1446, 1361, 1336 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{19}H_{25}NO_2^+$ ($[M]^{\bullet+}$) 299.1880, found 299.1880.



4-cyclohexylpyridine (SI-60)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-bromopyridine•HCl (97 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (223 mg, 1.05 mmol, 2.1 equiv.), and MeCN (2.5 mL). A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. After quenching the reaction mixture by exposure to air, the acetonitrile solvent was removed by rotary evaporation. The crude reaction mixture

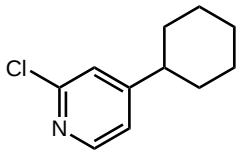
was partitioned between 40% aqueous K_2CO_3 (4 mL) and EtOAc (4 mL). The organic layer was collected, and the aqueous layer was further extracted with EtOAc (3 x 4 mL). The combined organic layers were concentrated by rotary evaporation, and purification by reverse-phase column chromatrography (SilaSep™ C18 silica flash cartridge, 5 to 40% MeCN in H_2O with 0.1% formic acid) followed by extraction from basified fractions (pH to ~10 with K_2CO_3) with dichloromethane yielded the pure product as a dark yellow oil (20 mg, 0.124 mmol, 25% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (d, *J* = 5.4 Hz, 2H), 7.16 – 7.10 (m, 2H), 2.54 – 2.45 (m, 1H), 1.92 – 1.80 (m, 4H), 1.80 – 1.73 (m, 1H), 1.46 – 1.33 (m, 4H), 1.30 – 1.22 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.0, 149.6, 122.6, 44.0, 33.6, 26.7, 26.1.

IR (film) ν_{max} 3023, 2924, 2852, 1596, 1557, 1448, 1410 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{16}N^+$ ($[M+H]^+$) 162.1277, found 162.1277.



2-chloro-4-cyclohexylpyridine (SI-61)

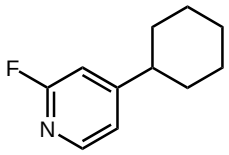
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 2-chloro-4-bromopyridine (55 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 1 additional portion of 1.0 mol% tetrabutylammonium decatungstate was added with 12 hours of additional irradiation. Purification by preparative thin-layer chromatography (15% EtOAc in hexanes) yielded the pure product as a colorless oil (48 mg, 0.245 mmol, 49% yield).

^{1}H NMR (500 MHz, C_6D_6) δ 8.05 (d, *J* = 5.1 Hz, 1H), 6.90 – 6.82 (m, 1H), 6.43 (dd, *J* = 5.1, 1.5 Hz, 1H), 1.93 (tt, *J* = 11.9, 3.4 Hz, 1H), 1.62 – 1.50 (m, 3H), 1.47 – 1.39 (m, 2H), 1.13 – 0.87 (m, 5H).

^{13}C NMR (126 MHz, C_6D_6) δ 159.5, 152.4, 149.9, 122.9, 121.2, 43.5, 33.2, 26.6, 26.0.

IR (film) ν_{max} 3049, 2926, 2853, 1589, 1543, 1461, 1447, 1396, 1357 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{15}ClN^+$ ($[M+H]^+$) 196.0888, found 196.0889.



4-cyclohexyl-2-fluoropyridine (SI-62)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-bromo-2-fluoropyridine (51 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatography (7.5% EtOAc in hexanes) yielded the pure product as a colorless oil (57 mg, 0.318 mmol, 64% yield).

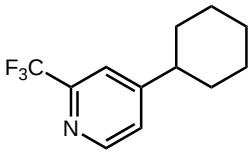
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 5.2 Hz, 1H), 7.00 (dt, *J* = 5.2, 1.8 Hz, 1H), 6.74 (s, 1H), 2.59 – 2.48 (m, 1H), 1.93 – 1.80 (m, 4H), 1.80 – 1.72 (m, 1H), 1.45 – 1.32 (m, 5H), 1.29 – 1.19 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3 (d, *J* = 238.0 Hz), 162.9 (d, *J* = 7.4 Hz), 147.4 (d, *J* = 15.3 Hz), 120.3 (d, *J* = 3.7 Hz), 107.6 (d, *J* = 36.7 Hz), 43.9 (d, *J* = 2.8 Hz), 33.5, 26.5, 26.0.

^{19}F NMR (470 MHz, $CDCl_3$) δ -69.13.

IR (film) ν_{max} 2927, 2854, 1609, 1564, 1556, 1480, 1449, 1409, 1368 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{15}FN^+$ ($[M+H]^+$) 180.1183, found 180.1182.



4-cyclohexyl-2-(trifluoromethyl)pyridine (SI-63)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 4-bromo-2-(trifluoromethyl)pyridine (66 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatography (10% EtOAc in hexanes) yielded the pure product as a colorless oil (68 mg, 0.318 mmol, 59% yield).

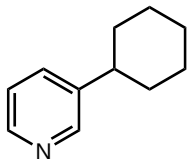
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 5.0 Hz, 1H), 7.51 (s, 1H), 7.31 (d, *J* = 4.9 Hz, 1H), 2.59 (tt, *J* = 11.3, 3.4 Hz, 1H), 1.94 – 1.84 (m, 4H), 1.82 – 1.75 (m, 1H), 1.49 – 1.35 (m, 4H), 1.31 – 1.23 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 150.1, 148.4 (q, *J* = 33.9 Hz), 125.1, 121.9 (q, *J* = 274.3 Hz), 119.3 (q, *J* = 2.8 Hz), 44.1, 33.6, 26.5, 25.9.

^{19}F NMR (470 MHz, $CDCl_3$) δ -67.93.

IR (film) ν_{max} 2929, 2856, 1607, 1563, 1450, 1428, 1331, 1136 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3N^+$ ($[M+H]^+$) 230.1151, found 230.1149.



3-cyclohexylpyridine (SI-64)

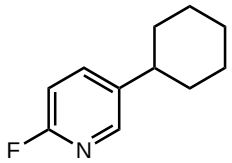
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (50.0 mg, 0.015 mmol, 3.0 mol%), 3-bromopyridine (48 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (159 mg, 0.75 mmol, 1.5 equiv.), and MeCN (2 mL). After quenching the reaction mixture by exposure to air, the acetonitrile solvent was removed by rotary evaporation. The crude reaction mixture was partitioned between 40% aqueous K_2CO_3 (4 mL) and EtOAc (4 mL). The organic layer was collected, and the aqueous layer was further extracted with EtOAc (3 x 4 mL). The combined organic layers were concentrated by rotary evaporation, and purification by reverse-phase column chromatrography (SilaSep™ C18 silica flash cartridge, 5 to 40% MeCN in H_2O with 0.1% formic acid) followed by extraction from basified fractions (pH to ~10 with K_2CO_3) with dichloromethane yielded the pure product as a pale yellow oil which smells of bananas (22 mg, 0.136 mmol, 27% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, *J* = 23.4 Hz, 2H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.24 (dd, *J* = 7.9, 4.8 Hz, 1H), 2.61 – 2.47 (m, 1H), 1.92 – 1.80 (m, 4H), 1.80 – 1.74 (m, 1H), 1.48 – 1.35 (m, 4H), 1.31 – 1.24 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6, 147.0, 143.3, 134.7, 123.63 42.2, 34.2, 26.8, 26.1.

IR (film) ν_{max} 2923, 1851, 1574, 1479, 1448, 1422 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{16}N^+$ ($[M+H]^+$) 162.1277, found 162.1277.



5-cyclohexyl-2-fluoropyridine (SI-65)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 5-bromo-2-fluoropyridine (51 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5

mL). A total of 1 additional portion of 1.0 mol% tetrabutylammonium decatungstate was added with 12 hours of additional irradiation. Purification by preparative thin-layer chromatography (7.5% EtOAc in hexanes) yielded the pure product as a colorless oil (49 mg, 0.273 mmol, 55% yield).

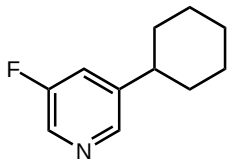
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 2.5 Hz, 1H), 7.60 (td, *J* = 8.1, 2.6 Hz, 1H), 6.84 (dd, *J* = 8.4, 3.0 Hz, 1H), 2.53 (ddq, *J* = 11.5, 8.5, 2.7 Hz, 1H), 1.91 – 1.79 (m, 4H), 1.79 – 1.71 (m, 1H), 1.38 (tt, *J* = 13.8, 7.6 Hz, 4H), 1.25 (ddt, *J* = 12.9, 6.6, 3.2 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 162.3 (d, *J* = 236.3 Hz), 146.0 (d, *J* = 14.1 Hz), 140.7 (d, *J* = 4.5 Hz), 139.5 (d, *J* = 7.6 Hz), 109.1 (d, *J* = 37.2 Hz), 41.3 (d, *J* = 1.4 Hz), 34.4, 26.8, 26.0.

^{19}F NMR (470 MHz, $CDCl_3$) δ -72.51 (d, *J* = 6.4 Hz).

IR (film) ν_{max} 2925, 2853, 1592, 1483, 1449, 1400, 1355, 1247 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{15}FN^+$ ($[M+H]^+$) 180.1183, found 180.1185.



3-cyclohexyl-5-fluoropyridine (SI-66)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (50.0 mg, 0.015 mmol, 3.0 mol%), 3-bromo-5-fluoropyridine (88 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (159 mg, 0.75 mmol, 1.5 equiv.), and MeCN (2 mL). Purification by preparative thin-layer chromatography (15% EtOAc in hexanes) yielded the pure product as a colorless oil (40 mg, 0.223 mmol, 45% yield).

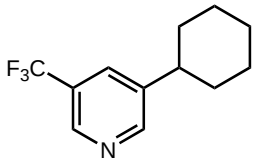
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 3.7 Hz, 2H), 7.23 (dt, *J* = 9.9, 2.0 Hz, 1H), 2.57 (tt, *J* = 8.3, 3.5 Hz, 1H), 1.93 – 1.80 (m, 4H), 1.79 – 1.73 (m, 1H), 1.46 – 1.34 (m, 4H), 1.30 – 1.20 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.9 (d, *J* = 255.9 Hz), 145.1 (d, *J* = 2.4 Hz), 144.9 (d, *J* = 3.6 Hz), 135.5 (d, *J* = 23.2 Hz), 121.0 (d, *J* = 17.6 Hz), 41.7, 34.1, 26.7, 26.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -127.70 (d, *J* = 9.9 Hz).

IR (film) ν_{max} 2926, 2853, 1600, 1578, 1448, 1429, 1369 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{15}FN^+$ ($[M+H]^+$) 180.1183, found 180.1182.



3-cyclohexyl-5-(trifluoromethyl)pyridine (SI-67)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 3-bromo-5-(trifluoromethyl)pyridine (113 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatography (15% EtOAc in hexanes) yielded the pure product as a colorless oil (60 mg, 0.262 mmol, 52% yield).

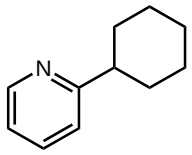
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 25.7 Hz, 2H), 7.73 (s, 1H), 2.62 (tt, *J* = 11.6, 3.3 Hz, 1H), 1.95 – 1.82 (m, 4H), 1.82 – 1.74 (m, 1H), 1.51 – 1.36 (m, 4H), 1.32 – 1.25 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.4, 144.2 (q, *J* = 4.2 Hz), 143.3, 131.2 (q, *J* = 3.6 Hz), 126.5 (q, *J* = 32.3 Hz), 123.8 (q, *J* = 272.6 Hz), 41.9, 34.1, 26.7, 25.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.39.

IR (film) ν_{max} 2928, 2855, 1580, 1452, 1336, 1125 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3N^+$ ($[M+H]^+$) 230.1151, found 230.1150.



2-cyclohexylpyridine (SI-68)

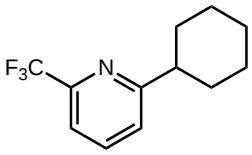
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (24.0 mg, 0.05 mmol, 10.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 2-bromopyridine (48 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). A total of 1 additional portion of 1.0 mol% tetrabutylammonium decatungstate was added with 12 hours of additional irradiation. After quenching the reaction mixture by exposure to air, the acetonitrile solvent was removed by rotary evaporation. The crude reaction mixture was partitioned between 40% aqueous K_2CO_3 (4 mL) and EtOAc (4 mL). The organic layer was collected, and the aqueous layer was further extracted with EtOAc (3 x 4 mL). The combined organic layers were concentrated by rotary evaporation, and purification by reverse-phase column chromatrography (SilaSep™ C18 silica flash cartridge, 5 to 40% MeCN in H_2O with 0.1% formic acid) followed by extraction from basified fractions (pH to ~10 with K_2CO_3) with dichloromethane yielded the pure product as a pale yellow oil which smells of green peppers (32 mg, 0.198 mmol, 40% yield). The spectroscopic properties of this compound are consistent with data reported in the literature[11].

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 – 8.49 (m, 1H), 7.59 (td, *J* = 7.7, 1.9 Hz, 1H), 7.14 (d, *J* = 7.9 Hz, 1H), 7.08 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 2.69 (tt, *J* = 11.9, 3.5 Hz, 1H), 2.00 – 1.92 (m, 2H), 1.89 – 1.81 (m, 2H), 1.78 – 1.70 (m, 1H), 1.52 (qd, *J* = 12.4, 3.1 Hz, 2H), 1.41 (qt, *J* = 12.9, 3.2 Hz, 2H), 1.33 – 1.25 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 149.1, 136.6, 121.2, 121.2, 46.7, 33.1, 26.7, 26.2.

IR (film) ν_{max} 3007, 2923, 2851, 1588, 1569, 1471, 1449, 1433 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{16}N^+$ ($[M+H]^+$) 162.1277, found 162.1276.



2-cyclohexyl-6-(trifluoromethyl)pyridine (SI-69)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 2-bromo-6-(trifluoromethyl)pyridine (113 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). A total of 1 additional portion of 1.0 mol% tetrabutylammonium decatungstate was added with 12 hours of additional irradiation. Purification by preparative thin-layer chromatography (20% toluene in hexanes) yielded the pure product as a colorless oil (36 mg, 0.198 mmol, 31% yield).

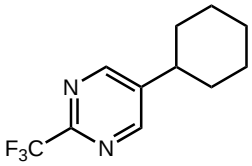
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (t, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 2.80 (tt, *J* = 11.9, 3.4 Hz, 1H), 2.00 – 1.94 (m, 2H), 1.90 – 1.81 (m, 2H), 1.79 – 1.72 (m, 1H), 1.52 (qd, *J* = 12.3, 2.9 Hz, 2H), 1.42 (qt, *J* = 12.8, 3.1 Hz, 2H), 1.33 – 1.25 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 147.6 (q, *J* = 34.0 Hz), 137.6, 123.7 (q, *J* = 1.1 Hz), 121.8 (q, *J* = 274.1 Hz), 117.7 (q, *J* = 2.9 Hz), 46.4, 32.9, 26.5, 26.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.03.

IR (film) ν_{max} 2930, 2855, 1598, 1463, 1341, 1184, 1141, 1111 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3N^+$ ($[M+H]^+$) 230.1151, found 230.1148.



5-cyclohexyl-2-(trifluoromethyl)pyrimidine (SI-70)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 5-bromo-2-(trifluoromethyl)pyrimidine (113 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatography (10% EtOAc in hexanes) yielded the pure product as a colorless oil (63 mg, 0.273 mmol, 55% yield).

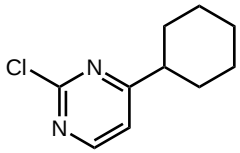
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 2H), 2.64 (tt, *J* = 12.0, 3.4 Hz, 1H), 1.98 – 1.86 (m, 4H), 1.84 – 1.74 (m, 1H), 1.52 – 1.37 (m, 4H), 1.35 – 1.24 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.6, 154.9 (q, *J* = 36.7 Hz), 142.6, 119.8 (q, *J* = 275.1 Hz), 40.0, 33.7, 26.4, 25.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -70.16.

IR (film) ν_{max} 2930, 2857, 1563, 1450, 1350, 1192, 1145, 1113 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{11}H_{14}F_3N_2^+$ ($[M+H]^+$) 231.1104, found 231.1100.



2-chloro-4-cyclohexylpyrimidine (SI-71)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0

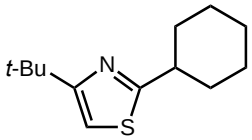
mol%), 4-bromo-2-chloropyrimidine (113 mg, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (5 mL). Purification by preparative thin-layer chromatography (15% EtOAc in hexanes) yielded the pure product as a pale yellow oil (50 mg, 0.254 mmol, 51% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, *J* = 5.1 Hz, 1H), 7.10 (d, *J* = 5.1 Hz, 1H), 2.67 (tt, *J* = 11.9, 3.4 Hz, 1H), 2.00 – 1.91 (m, 2H), 1.86 (dt, *J* = 13.1, 3.4 Hz, 2H), 1.79 – 1.71 (m, 1H), 1.49 (qd, *J* = 12.4, 3.1 Hz, 2H), 1.38 (qt, *J* = 12.7, 3.2 Hz, 2H), 1.26 (qt, *J* = 12.9, 3.4 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.7, 161.3, 159.4, 117.2, 46.0, 32.0, 26.2, 25.8.

IR (film) ν_{max} 2927, 2854, 1569, 1535, 1448, 1430, 1366, 1338 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{14}ClN_2^+$ ($[M+H]^+$) 197.0840, found 197.0839.



4-(*tert*-butyl)-2-cyclohexylthiazole (SI-72)

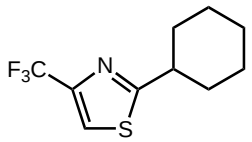
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 2-bromo-4-(tert-butyl)thiazole (110 mg, 80 μL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 μL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). Purification by preparative thin-layer chromatography (50% CH_2Cl_2 in hexanes) yielded the pure product as a pale yellow oil (60 mg, 0.269 mmol, 54% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71 (s, 1H), 3.00 (tt, *J* = 11.3, 2.7 Hz, 1H), 2.21 – 2.06 (m, 2H), 1.89 – 1.78 (m, 2H), 1.77 – 1.68 (m, 1H), 1.52 – 1.19 (m, 14H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 165.9, 108.5, 42.8, 34.8, 34.2, 30.2, 26.3, 26.0.

IR (film) ν_{max} 2926, 2854, 1513, 1449, 1389, 1361 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{22}NS^+$ ($[M+H]^+$) 224.1468, found 224.1465.



2-cyclohexyl-4-(trifluoromethyl)thiazole (SI-73)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12.0 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17.0 mg, 0.005 mmol, 1.0 mol%), 2-bromo-4-(trifluoromethyl)thiazole (116 mg, 61 µL, 0.5 mmol, 1.0 equiv.), cyclohexane (210.4 mg, 270.1 µL, 2.5 mmol, 5.0 equiv.), K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.), and MeCN (2.5 mL). Purification by preparative thin-layer chromatography (5% EtOAc in cyclohexane) yielded the pure product as a pale yellow oil (60 mg, 0.255 mmol, 51% yield).

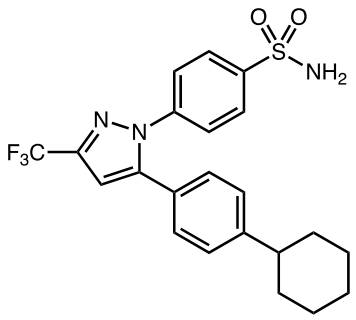
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (s, 1H), 3.04 (tt, *J* = 11.7, 3.6 Hz, 1H), 2.23 – 2.11 (m, 2H), 1.92 – 1.82 (m, 2H), 1.79 – 1.71 (m, 1H), 1.52 (qd, *J* = 12.3, 3.1 Hz, 2H), 1.41 (qt, *J* = 12.7, 3.2 Hz, 2H), 1.33 – 1.25 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 179.8, 144.2 (q, *J* = 36.7 Hz), 120.6 (q, *J* = 270.3 Hz), 119.5 (q, *J* = 3.6 Hz), 42.8, 33.8, 26.1, 25.8.

^{19}F NMR (282 MHz, $CDCl_3$) δ -63.88.

IR (film) ν_{max} 2929, 2856, 1533, 1483, 1450, 1359 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{13}F_3NS^+$ ($[M+H]^+$) 236.0715, found 236.0717.



4-(5-(4-cyclohexylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (75a)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (9.7 mg, 0.02 mmol, 10.0 mol%), tetrabutylammonium decatungstate (6.6 mg, 0.002 mmol, 1.0 mol%), 4-(5-(4-bromophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (prepared according to literature precedent[12], 89 mg, 0.2 mmol, 1.0 equiv.), cyclohexane (84 mg, 108 μL, 1.0 mmol, 5.0 equiv.), K_3PO_4 (47 mg, 0.22 mmol, 1.1 equiv.), and MeCN (1.0 mL). It should be noted that the aryl bromide starting material was recrystallized (toluene/hexane) and extensively dried under high vacuum prior to use; small amounts of solvent or other impurities are highly detrimental to this reaction. A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by preparative thin-layer chromatography (30% acetone in hexanes) yielded the pure product as a white solid (60 mg, 0.133 mmol, 67% yield).

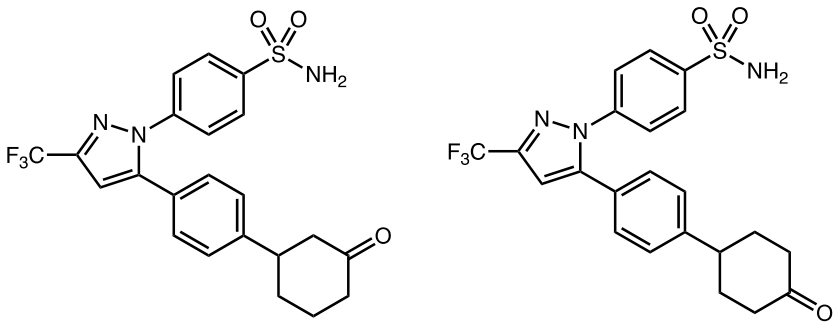
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.86 (m, 2H), 7.53 – 7.44 (m, 2H), 7.24 – 7.17 (m, 2H), 7.17 – 7.10 (m, 2H), 6.74 (s, 1H), 4.94 (s, 2H), 2.58 – 2.45 (m, 1H), 1.95 – 1.80 (m, 4H), 1.80 – 1.73 (m, 1H), 1.48 – 1.33 (m, 4H), 1.32 – 1.20 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.0, 145.4, 144.2 (q, J = 38.7 Hz), 142.8, 141.3, 128.9, 127.7, 127.7, 126.1, 125.6, 121.2 (q, J = 269.1 Hz), 106.6 (q, J = 2.1 Hz), 44.5, 34.4, 26.9, 26.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.47.

IR (film) ν_{max} 3269, 2927, 2853, 1596, 1498, 1471, 1450, 1409, 1339, 1162 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{23}F_3N_3O_2S^+$ ($[M+H]^+$) 450.1458, found 450.1456.



major minor

4-(5-(4-(3-oxocyclohexyl)phenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (major regioisomer, left, 75b) and 4-(5-(4-(4-oxocyclohexyl)phenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (minor regioisomer, right, SI-75b)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (9.7 mg, 0.02 mmol, 10.0 mol%), tetrabutylammonium decatungstate (6.6 mg, 0.002 mmol, 1.0 mol%), 4-(5-(4-bromophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (prepared according to literature precedent[12], 89 mg, 0.2 mmol, 1.0 equiv.), cyclohexanone (98 mg, 104 μL, 1.0 mmol, 5.0 equiv.), K_3PO_4 (47 mg, 0.22 mmol, 1.1 equiv.), and MeCN (1.0 mL). It should be noted that the aryl bromide starting material was recrystallized (toluene/hexane) and extensively dried under high vacuum prior to use; small amounts of solvent or other impurities are highly detrimental to this reaction. A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by column chromatography (silica gel, 15-40% acetone in hexanes) followed by preparative chiral SFC (Chiralpak AD-H 2 x 25 cm, 30% MeOH/CO_2, 100 bar, 60 mL/min) yielded the pure minor regioisomer as a white solid (23 mg, 0.050 mmol, 25% yield) and the pure major regioisomer as a white solid (33 mg, 0.071 mmol, 36% yield), giving 60% overall yield (1.43:1 r.r.).

4-(5-(4-(3-oxocyclohexyl)phenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.29 – 7.18 (m, 4H), 6.79 (s, 1H), 5.16 (s, 2H), 3.11 – 2.95 (m, 1H), 2.57 – 2.46 (m, 2H), 2.44 – 2.31 (m, 2H), 2.19 – 2.01 (m, 2H), 1.90 – 1.71 (m, 2H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 210.7, 146.6, 145.4, 144.1 (q, *J* = 38.4 Hz), 142.8, 142.1, 129.5, 127.8, 127.7, 127.2, 125.9, 121.6 (q, *J* = 268.9 Hz), 106.8 (q, *J* = 1.9 Hz), 48.8, 44.7, 41.4, 32.9, 25.8.

^{19}F NMR (376 MHz, CD_2Cl_2) δ -62.80.

IR (film) ν_{max} 3259, 2946, 1703, 1596, 1472, 1341, 1235, 1161, 1134 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{21}F_3N_3O_3S^+$ ($[M+H]^+$) 464.1250, found 464.1246.

4-(5-(4-(4-oxocyclohexyl)phenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide

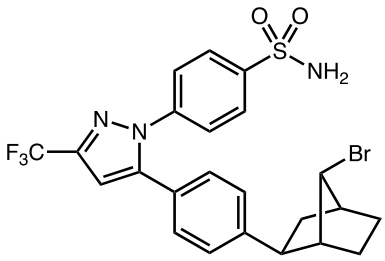
^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.91 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 6.78 (s, 1H), 4.91 (s, 2H), 3.06 (tt, *J* = 12.2, 3.4 Hz, 1H), 2.58 – 2.38 (m, 4H), 2.26 – 2.16 (m, 2H), 1.98 – 1.85 (m, 2H).

^{13}C NMR (126 MHz, CD_2Cl_2) δ 210.4, 147.2, 145.5, 144.1 (q, *J* = 38.3 Hz), 142.9, 142.0, 129.4, 127.9, 127.8, 127.2, 125.9, 121.6 (q, *J* = 269.0 Hz), 106.8 (q, *J* = 2.0 Hz), 42.8, 41.5, 34.2.

^{19}F NMR (376 MHz, CD_2Cl_2) δ -63.28.

IR (film) ν_{max} 3259, 2942, 1705, 1596, 1472, 1340, 1235, 1161, 1134 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{21}F_3N_3O_3S^+$ ($[M+H]^+$) 464.1250, found 464.1249.



(±)-4-(5-(4-((7-*anti*-bromobicyclo[2.2.1]heptan-2-*exo*-yl)phenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (75c)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (9.7 mg, 0.02 mmol, 10.0 mol%), tetrabutylammonium decatungstate (6.6 mg, 0.002 mmol, 1.0 mol%), 4-(5-(4-bromophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (prepared according to literature precedent[12], 89 mg, 0.2 mmol, 1.0 equiv.), 7-bromobicyclo[2.2.1]heptane (175 mg, 127 μL, 1.0 mmol, 5.0 equiv.), K_3PO_4 (47 mg, 0.22 mmol, 1.1 equiv.), and MeCN (1.0 mL). It should be noted that the aryl bromide starting material was recrystallized (toluene/hexane) and extensively dried under high vacuum prior to use; small amounts of solvent or other impurities are highly detrimental to this reaction. A total of 2 additional portions of 1.0 mol% tetrabutylammonium decatungstate were added with 12 hours of irradiation each. Purification by column chromatography (silica gel, 10–30% acetone in hexanes) yielded the pure product as a white solid (72 mg, 0.133 mmol, 67% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.22 – 7.13 (m, 4H), 6.75 (s, 1H), 5.15 (s, 2H), 4.15 (s, 1H), 2.95 (dd, *J* = 10.5, 5.7 Hz, 1H), 2.57 – 2.39 (m, 2H), 2.21 – 2.01 (m, 2H), 1.96 (t, *J* = 11.5 Hz, 1H), 1.82 – 1.73 (m, 1H), 1.51 – 1.39 (m, 2H).

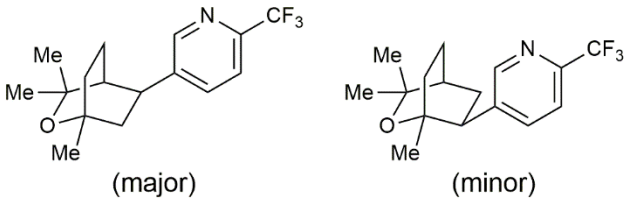
^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 145.0, 144.2 (q, *J* = 38.6 Hz), 142.6, 141.6, 129.0, 127.7, 127.7, 126.3, 125.7, 121.1 (q, *J* = 269.3 Hz), 106.6, 56.4, 48.6, 45.4, 43.5, 36.5, 28.3, 26.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.41.

IR (film) ν_{max} 3269, 2965, 1596, 1498, 1471, 1409, 1340, 1162 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{23}H_{22}BrF_3N_3O_2S^+$ ($[M+H]^+$) 540.0563, found 540.0564.

9) Arylation of abundant natural products



(±)-2-(trifluoromethyl)-5-((1R,4S)-1,3,3-trimethyl-2-oxabicyclo[2.2.2]octan-5-yl)pyridine (left, major, 76) and (±)-2-(trifluoromethyl)-5-((1R,4S,6S)-1,3,3-trimethyl-2-oxabicyclo[2.2.2]octan-6-yl)pyridine (right, minor, SI-76)

Prepared following general procedure A outlined above, except for the modification that the reaction was stirred for 18 hours, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), eucalyptol (386 mg, 418 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high performance silica gel, gradient 0–20% EtOAc in hexanes) afforded pure major product as a clear oil (64 mg, 0.214 mmol, 43% yield) and impure minor product. Preparative TLC of the impure minor product (15% EtOAc/toluene) afforded pure minor product as a clear oil that became a white solid upon standing (18 mg, 0.060 mmol, 12% yield).

76, major regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 2.2 Hz, 1H), 7.74 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.69 – 7.63 (m, 1H), 3.75 – 3.66 (m, 1H), 2.14 (ddd, *J* = 14.3, 11.3, 3.1 Hz, 1H), 1.87 – 1.71 (m, 3H), 1.60 – 1.54 (m, 1H), 1.54 – 1.45 (m, 1H), 1.43 (m, 4H), 1.35 (s, 3H), 1.21 – 1.16 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.2, 146.0 (q, *J* = 34.6 Hz), 143.8, 136.3, 121.8 (q, *J* = 273.6 Hz), 120.1 (q, *J* = 2.9 Hz), 74.1, 70.5, 39.60, 36.4, 35.1, 31.5, 29.1, 29.0, 27.5, 15.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.68.

IR (film) ν_{max} 2971, 2931, 1342, 1174, 1137, 1089, 1027, 985 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{21}F_3NO^+$ ($[M+H]^+$) 300.1570, found 300.1570.

SI-76, minor regioisomer:

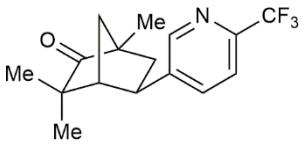
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 2.1 Hz, 1H), 7.75 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 3.15 (ddd, *J* = 11.5, 6.9, 2.1 Hz, 1H), 2.54 (ddt, *J* = 15.3, 12.1, 3.4 Hz, 1H), 2.26 – 2.13 (m, 1H), 1.77 – 1.56 (m, 5H), 1.34 (s, 3H), 1.33 (s, 3H), 0.82 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.1, 146.4 (q, *J* = 34.6 Hz), 142.6, 137.4, 121.8 (q, *J* = 273.7 Hz), 120.2 (q, *J* = 2.7 Hz), 74.0, 72.9, 46.7, 33.7, 31.4, 29.1, 29.0, 26.7, 26.0, 23.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.74.

IR (film) ν_{max} 2927, 1339, 1175, 1136, 1087, 1066, 987 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{21}F_3NO^+$ ($[M+H]^+$) 300.1570, found 300.1570.



(1S,4R,5R)-1,3,3-trimethyl-5-(6-(trifluoromethyl)pyridin-3-yl)bicyclo[2.2.2]octan-2-one (77)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025

mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), L-fenchone (381 mg, 401 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high performance silica gel, gradient 0–20% EtOAc in hexanes) afforded pure product as a white solid (58 mg, 0.195 mmol, 39% yield).

5.0 mmol scale procedure: To a 40 mL vial equipped with a cross stir bar was added $NiBr_2$•dtbbpy (122 mg, 0.25 mmol, 5.0 mol%), tetrabutylammonium decatungstate (166 mg, 0.05 mmol, 1.0 mol%), MeCN (12.5 mL, 0.4 M), 5-bromo-2-(trifluoromethyl)pyridine (1.130 g, 5.0 mmol, 1.0 equiv.), L-fenchone (3.81 g, 4.015 ml, 25.0 mmol, 5.0 equiv.), and K_3PO_4 (1.17 g, 5.50 mmol, 1.1 equiv.). The reaction mixture was irradiated using an integrated photoreactor for 24 hours (365 nm LEDs, 100% LED intensity, 1000 rpm stirring, maximum fan speed). The reaction mixture was stirred open to air for 15 minutes, diluted with EtOAc, and filtered through a plug of celite. The filtrate was collected, solvent was removed, and the crude residue was dried under vacuum for 12 hours. Purification by silica gel chromatography (0–20% EtOAc/hexanes) afforded pure product as a white solid (615 mg, 2.069 mmol, 41% yield).

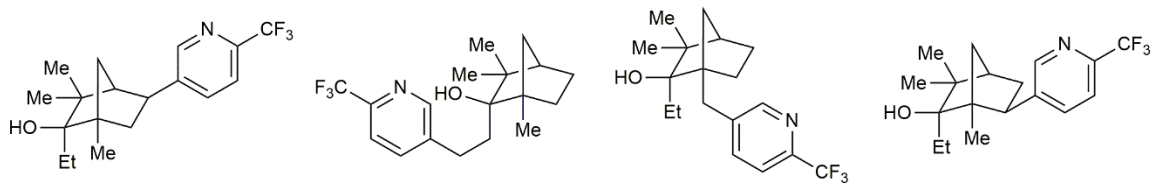
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, *J* = 2.2 Hz, 1H), 7.75 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 3.53 (dd, *J* = 9.5, 4.4 Hz, 1H), 2.40 (d, *J* = 1.6 Hz, 1H), 2.05 (ddd, *J* = 13.7, 9.1, 2.2 Hz, 1H), 1.91 – 1.70 (m, 3H), 1.23 (s, 3H), 1.21 (s, 3H), 1.15 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 221.5, 149.6, 146.0 (q, *J* = 34.9 Hz), 144.2, 135.6, 121.6 (q, *J* = 273.8 Hz), 120.1 (q, *J* = 2.7 Hz), 54.8, 50.9, 47.9, 39.3, 38.9, 38.2, 23.7, 21.6, 14.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.74.

IR (film) ν_{max} 2968, 1739, 1340, 1173, 1136, 1087, 1024 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{19}F_3NO^+$ ([M+H]$^+$) 298.1413, found 298.1414.



(major) (minor 1) (minor 2) (minor 3)

(1S,2R,4S)-2-ethyl-3,3,4-trimethyl-5-(6-(trifluoromethyl)pyridin-3-yl)bicyclo[2.2.1]heptan-2-ol (major, left, 78)

Prepared following general procedure A outlined above, except for the modification that the reaction was stirred for 18 hours, using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 2-ethylfenchol (456 mg, 477 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (high performance silica gel, gradient 0–30% EtOAc in hexanes) afforded the desired product as a mixture of regioisomers (16.7 (major):2.8 (minor 1):2.0 (minor 2):1.0 (minor 3) r.r., 74% selective, 85 mg, 52% yield). The presence of four isomers was confirmed by ^{1}H, ^{13}C, and ^{19}F NMR. A small amount of material was repurified by preparative chiral SFC (Chiralpak AD-H 2 x 25 cm, 30% MeOH/CO_2, 100 bar, 60 mL/min) to enable NMR analysis of the major isomer.

78, major regioisomer:

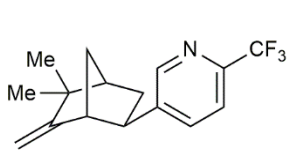
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 2.2 Hz, 1H), 7.69 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 3.42 (dd, *J* = 9.3, 5.8 Hz, 1H), 2.67 (ddd, *J* = 12.4, 9.2, 2.7 Hz, 1H), 1.81 (s, 1H), 1.72 – 1.62 (m, 2H), 1.59 (m, 1H), 1.32 – 1.29 (m, 1H), 1.16 (m, 7H), 1.06 (s, 3H), 1.02 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.9, 146.4, 145.4 (q, *J* = 34.6 Hz), 135.45, 121.91 (q, *J* = 273.6 Hz), 120.1 (q, *J* = 2.7 Hz), 80.4, 56.0, 54.0, 45.6, 39.8, 39.1, 38.7, 28.0, 27.6, 22.6, 18.0, 9.5.

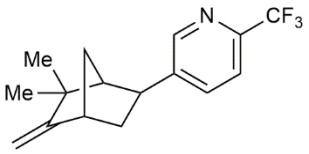
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.64.

IR (film) ν_{max} 3465, 2938, 1463, 1339, 1259, 1173, 1136, 1086, 1026, 976 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{25}F_3NO^+$ ($[M+H]^+$) 328.1883, found 328.1877.



(major)



(minor)

(±)-5-((1R,2R,4S)-5,5-dimethyl-6-methylenebicyclo[2.2.1]heptan-2-yl)-2-(trifluoromethyl)pyridine (major, left 79) and 5-((1S,2S,4S)-6,6-dimethyl-5-methylenebicyclo[2.2.1]heptan-2-yl)-2-(trifluoromethyl)pyridine (minor, right, SI-79)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), 2-ethylfenchol (456 mg, 477 µL, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, 5% Et_2O in pentane) afforded a mixture of product regioisomers (1.4:1 r.r., 98 mg, 0.348 mmol, 70% yield). A small amount of material was repurified by preparative chiral SFC (Chiralpak AD-H 2 x 25 cm, 10% MeOH/CO_2, 100 bar, 70 mL/min) to enable NMR analysis of each isomer.

<u>79, major regioisomer:</u>

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.2 Hz, 1H), 7.70 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 4.89 (s, 1H), 4.66 (s, 1H), 2.98 – 2.91 (m, 1H), 2.85 (d, *J* = 1.8

Hz, 1H), 2.35 (ddd, *J* = 13.1, 8.9, 2.7 Hz, 1H), 2.11 (dd, *J* = 3.7, 1.8 Hz, 1H), 1.79 (m, 1H), 1.56 – 1.49 (m, 2H), 1.16 (s, 3H), 1.10 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 149.6, 145.8 (q, *J* = 34.6 Hz), 145.2, 135.3, 121.9 (q, *J* = 274.0 Hz), 120.2 (q, *J* = 2.7 Hz), 101.2, 53.1, 48.9, 44.1, 41.7, 35.4, 33.6, 29.5, 26.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.69.

IR (film) ν_{max} 2962, 2925, 1657, 1461, 1340, 1260, 1172, 1134, 1086, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{19}F_3N^+$ ($[M+H]^+$) 282.1464, found 282.1460.

SI-79, minor regioisomer:

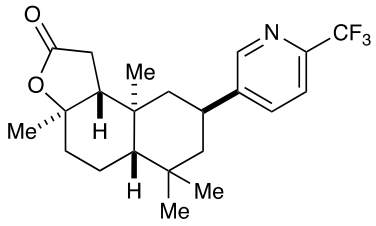
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.2 Hz, 1H), 7.70 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 4.85 (s, 1H), 4.63 (s, 1H), 3.41 (t, *J* = 7.0 Hz, 1H), 2.90 – 2.81 (m, 1H), 2.12 (s, 1H), 1.94 – 1.84 (m, 2H), 1.75 (dp, *J* = 10.5, 1.7 Hz, 1H), 1.43 (dt, *J* = 10.4, 1.5 Hz, 1H), 1.24 (s, 3H), 1.13 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.21, 150.01, 145.77, 145.55 (q, *J* = 34.6 Hz), 135.67, 121.87 (q, *J* = 273.7 Hz), 120.06 (q, *J* = 2.8 Hz), 101.02, 54.22, 47.34, 42.65, 38.32, 36.98, 34.49, 29.67, 25.78.

^{19}F NMR (376 MHz, $CDCl_3$) δ -67.66.

IR (film) ν_{max} 2959, 2924, 2854, 1662, 1462, 1341, 1260, 1175, 1138, 1088, 1026 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{19}F_3N^+$ ($[M+H]^+$) 282.1464, found 282.1459.



(3a*R*,5a*S*,8*S*,9a*S*,9b*R*)-3a,6,6,9a-tetramethyl-8-(6-(trifluoromethyl)pyridin-3-yl)decahydronaphtho[2,1-*b*]furan-2(1*H*)-one (80a)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 5-bromo-2-(trifluoromethyl)pyridine (113.0 mg, 0.5 mmol, 1.0 equiv.), sclareolide (626 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 25% to 50% EtOAc in hexanes) yielded the product with a minor impurtity (~5%). Preparative TLC (25% EtOAc/toluene) afforded pure product as a colorless solid (80 mg, 0.202 mmol, 41% yield).

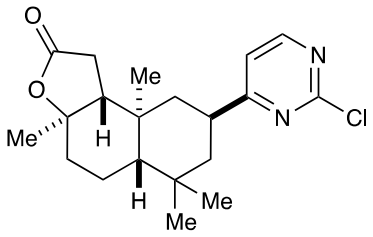
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.2 Hz, 1H), 7.70 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 3.10 (tt, *J* = 12.8, 3.5 Hz, 1H), 2.43 (dd, *J* = 16.2, 14.7 Hz, 1H), 2.22 (dd, *J* = 16.2, 6.5 Hz, 1H), 2.14 (dt, *J* = 12.0, 3.3 Hz, 1H), 2.06 (dd, *J* = 14.7, 6.4 Hz, 1H), 1.98 (dq, *J* = 14.2, 3.2 Hz, 1H), 1.75 (td, *J* = 12.5, 4.2 Hz, 1H), 1.70 – 1.56 (m, 3H), 1.50 – 1.40 (m, 2H), 1.38 (s, 3H), 1.28 (t, *J* = 12.7 Hz, 1H), 1.20 (dd, *J* = 12.6, 2.8 Hz, 1H), 1.08 (s, 3H), 0.99 (d, *J* = 1.7 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 149.4, 146.3 (q, *J* = 34.8 Hz), 144.6, 135.5, 121.6 (q, *J* = 273.9 Hz), 120.3 (q, *J* = 2.7 Hz), 86.0, 58.9, 56.3, 49.3, 46.6, 38.6, 36.9, 34.1, 33.4, 33.0, 28.6, 21.7, 21.3, 20.4, 15.8.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.73

IR (film) ν_{max} 2940, 1769, 1451, 1385, 1366, 1337, 1243, 1221, 1172, 1127, 1084, 1024, 1011 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{29}F_3NO_3$ ($[M+H]^+$) 395.2072, found 395.2070.



(3a*R*,5a*S*,8*S*,9a*S*,9b*R*)-8-(2-chloropyrimidin-4-yl)-3a,6,6,9a-tetramethyldecahydronaphtho[2,1-*b*]furan-2(1*H*)-one (80b)

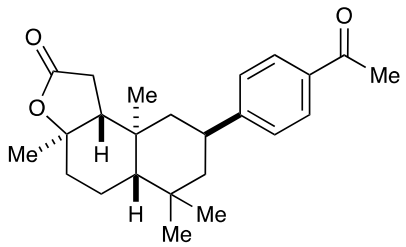
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 4-bromo-2-chloropyrimidine (97.0 mg, 0.5 mmol, 1.0 equiv.), sclareolide (626 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 30% to 50% EtOAc in hexanes) yielded the product with a minor impurtity (~5%). Preparative TLC (50% EtOAc/hexanes) afforded pure product as a colorless solid (62 mg, 0.171 mmol, 34% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, *J* = 5.1 Hz, 1H), 7.12 (d, *J* = 5.1 Hz, 1H), 3.11 (tt, *J* = 12.7, 3.5 Hz, 1H), 2.43 (dd, *J* = 16.1, 14.7 Hz, 1H), 2.25 (dd, *J* = 16.2, 6.5 Hz, 1H), 2.13 (dt, *J* = 12.0, 3.4 Hz, 1H), 2.06 (dd, *J* = 14.8, 6.5 Hz, 1H), 1.96 (dt, *J* = 14.3, 3.5 Hz, 1H), 1.78 – 1.64 (m, 3H), 1.56 – 1.39 (m, 3H), 1.37 (d, *J* = 5.0 Hz, 3H), 1.21 (dd, *J* = 12.6, 2.7 Hz, 1H), 1.04 (s, 3H), 0.97 (d, *J* = 12.0 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 176.2, 161.3, 159.5, 117.5, 86.0, 58.8, 56.1, 47.1, 44.3, 38.6, 37.9, 36.6, 33.9, 33.0, 28.6, 21.7, 21.4, 20.4, 15.8.

IR (film) ν_{max} 2932, 1768, 1571, 1538, 1431, 1365, 1337, 1286, 1223, 1205, 1162, 1119, 1097, 1034, 1008 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{28}ClN_2O_2$ ($[M+H]^+$) 362.1761, found 362.1756.



(3a*R*,5a*S*,8*S*,9a*S*,9b*R*)-8-(4-acetylphenyl)-3a,6,6,9a-tetramethyldecahydronaphtho[2,1-*b*]furan-2(1*H*)-one (80c)

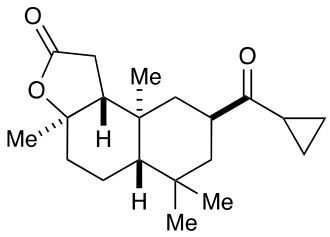
Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), 4'-bromoacetophenone (100 mg, 0.5 mmol, 1.0 equiv.), sclareolide (626 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 40% EtOAc in hexanes) yielded the crude product, which co-eluted with solvent-coupled product. Preparative TLC (30% EtOAc/cyclohexane) afforded pure product as a colorless solid (80 mg, 0.217 mmol, 43% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 3.05 (tt, *J* = 12.7, 3.5 Hz, 1H), 2.59 (d, *J* = 1.1 Hz, 3H), 2.42 (dd, *J* = 16.2, 14.8 Hz, 1H), 2.23 (dd, *J* = 16.2, 6.5 Hz, 1H), 2.18 – 2.11 (m, 1H), 2.05 (dd, *J* = 14.7, 6.5 Hz, 1H), 2.00 – 1.93 (m, 1H), 1.75 (td, *J* = 12.5, 4.1 Hz, 1H), 1.68 – 1.54 (m, 3H), 1.43 (t, *J* = 13.0 Hz, 2H), 1.37 (s, 3H), 1.31 – 1.24 (m, 1H), 1.19 (dd, *J* = 12.6, 2.6 Hz, 1H), 1.06 (s, 3H), 0.97 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 176.4, 151.9, 135.4, 128.7, 127.3, 86.2, 59.0, 56.4, 49.6, 46.8, 38.7, 36.9, 35.8, 34.1, 33.1, 28.7, 26.6, 21.7, 21.4, 20.5, 15.8.

IR (film) ν_{max} 2937, 1756, 1678, 1605, 1420, 1361, 1268, 1217, 1196, 1172, 1119, 1091, 1036, 1011 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{24}H_{33}O_3$ ($[M+H]^+$) 368.2351, found 368.2352.



(3a*R*,5a*S*,8*S*,9a*S*,9b*R*)-8-(cyclopropanecarbonyl)-3a,6,6,9a-tetramethyldecahydronaphtho[2,1-*b*]furan-2(1*H*)-one (80d)

Prepared following general procedure A outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (17 mg, 0.005 mmol, 1.0 mol%), MeCN (5 mL), cyclopropanecarbonyl chloride (52.3 mg, 45.5 µL, 0.5 mmol, 1.0 equiv.), sclareolide (626 mg, 2.5 mmol, 5.0 equiv.), and K_3PO_4 (117 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 0% to 40% EtOAc in hexanes) yielded the pure product as a colorless solid (50 mg, 0.157 mmol, 31% yield).

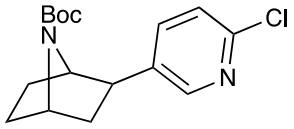
^{1}H NMR (500 MHz, $CDCl_3$) δ 2.93 (tt, *J* = 12.6, 3.4 Hz, 1H), 2.42 (dd, *J* = 16.2, 14.6 Hz, 1H), 2.29 (dd, *J* = 16.2, 6.5 Hz, 1H), 2.09 (dt, *J* = 12.0, 3.4 Hz, 1H), 2.03 – 1.88 (m, 3H), 1.76 – 1.66 (m, 2H), 1.62 (dt, *J* = 12.8, 2.6 Hz, 1H), 1.44 – 1.37 (m, 1H), 1.34 (s, 3H), 1.31 – 1.23 (m, 1H), 1.18 (t, *J* = 12.7 Hz, 1H), 1.10 – 1.05 (m, 1H), 1.00 (dt, *J* = 8.2, 2.9 Hz, 2H), 0.98 (s, 3H), 0.96 (s, 3H), 0.92 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 213.1, 176.4, 86.1, 58.8, 56.2, 43.9, 43.7, 40.8, 38.5, 36.2, 33.6, 33.0, 28.6, 21.6, 21.3, 20.4, 19.3, 15.7, 11.2, 11.0.

IR (film) ν_{max} 2929, 2843, 1766, 1696, 1448, 1426, 1286, 1245, 1224, 1195, 1177, 1157, 1120, 1067, 1023 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{31}O_3$ ($[M+H]^+$) 318.2195, found 318.2195.

10) Synthesis of (±)-N-Boc-epibatidine and analogues

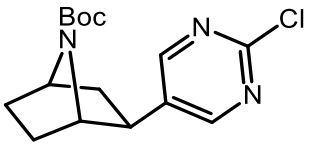


(±)-*tert*-butyl-2-(6-chloropyridin-3-*exo*-yl)-7-azabicyclo[2.2.1]heptane-7-carboxylate [(±)-*N*-Boc-epibatidine (82a)]

Prepared following general procedure B outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetra-*n*-butylammonium decatungstate (3 x 17 mg, 0.005 mmol, 3 x 1.0 mol%), MeCN (12.5 mL), 5-bromo-2-chloropyridine (98.0 mg, 0.51 mmol, 1.0 equiv.), *N*-Boc-7-Azabicyclo[2.2.1]heptane (466 mg, 2.4 mmol, 5.0 equiv.), and Na_3PO_4 (85 mg, 0.52 mmol, 1.1 equiv). Purification by column chromatography (silica gel, gradient 0% to 80% EtOAc in hexanes) yielded the pure product as a colorless oil (44 mg, 0.142 mmol, 28% yield). The spectroscopic properties of this compound are consistent with data reported in the literature[13].

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 4.39 (bs, 1H), 4.18 (bs, 1H), 2.88 (dd, *J* = 8.9, 4.8 Hz, 1H), 2.01 (dd, *J* = 12.3, 9.1 Hz, 1H), 1.93 – 1.77 (m, 3H), 1.63 – 1.53 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 149.3, 148.7, 140.1, 137.3, 124.1, 79.9, 61.9, 55.9, 45.0, 40.4, 20.9, 28.8, 28.3.



(±)-*tert*-butyl-2-(2-chloropyrimidin-5-*exo*-yl)-7-azabicyclo[2.2.1]heptane-7-carboxylate (82b)

Prepared following general procedure B outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (4 x 17 mg, 0.005 mmol, 4 x 1.0 mol%), MeCN (12.5 mL), 5-bromo-2-chloropyrimidine (99.0 mg, 0.51 mmol, 1.0 equiv.),

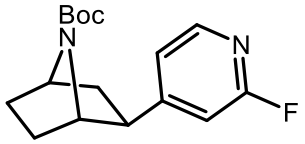
N-Boc-7-Azabicyclo[2.2.1]heptane (505 mg, 2.5 mmol, 5.0 equiv.), and Na_3PO_4 (92 mg, 0.56 mmol, 1.1 equiv). Purification by prep-TLC, eluting with 100% DCM yielded the pure product as a colorless oil (34 mg, 0.110 mmol, 21% yield). *Exo*-assignment was made based on analogy to literature precedents[13].

^{1}H NMR (500 MHz, CD_3CN) δ 8.57 (s, 1H), 4.42 (s, 1H), 4.20 (s, 1H), 2.87 (dd, *J* = 9.0, 4.7 Hz, 1H), 2.05 (dd, *J* = 12.4, 8.8 Hz, 1H), 1.89 – 1.85 (m, 3H), 1.65 – 1.55 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 158.4, 155.2, 137.3, 80.3, 61.8, 56.1, 43.0, 40.1, 29.7, 28.7, 28.3.

IR (film) ν_{max} 2978, 2252, 1689, 1613, 1456, 1367, 1152, 1098, 903, 726, 649 cm^{-1}.

HRMS (ESI+) m/z calcd. for $C_{15}H_{20}ClN_3O_2$ ($[M+H]^+$) 310.1322, found 310.1319.



(±)-*tert*-butyl-2-(2-fluoropyridin-4-yl)-7-azabicyclo[2.2.1]heptane-7-carboxylate (82c)

Prepared following general procedure B outlined above using $NiBr_2$•dtbbpy (13 mg, 0.026 mmol, 5.0 mol%), tetrabutylammonium decatungstate (3 x 17 mg, 0.005 mmol, 3 x 1.0 mol%), MeCN (12.5 mL), 4-bromo-2-fluoropyridine (91.0 mg, 0.51 mmol, 1.0 equiv.), *N*-Boc-7-Azabicyclo[2.2.1]heptane (510 mg, 2.5 mmol, 5.0 equiv.), and Na_3PO_4 (93 mg, 0.56 mmol, 1.1 equiv). Purification by column chromatography (silica gel, gradient 0% to 90% EtOAc in hexanes) yielded the pure product (mixture of rotamers) as a colorless oil (56 mg, 0.192 mmol, 37% yield). *Exo*-assignment was made based on analogy to literature precedents[13].

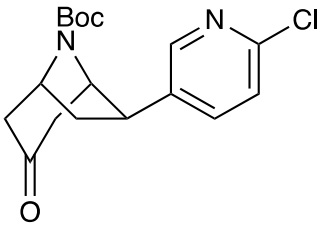
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 5.2 Hz, 1H), 7.11 (d, *J* = 4.6 Hz, 1H), 6.87 (s, 1H), 4.41 (bs, 1H), 4.28 (bs, 1H), 2.91 (dd, *J* = 8.6, 4.8 Hz, 1H), 2.02 (dd, *J* = 12.2, 9.1 Hz, 1H), 1.92 – 1.82 (m, 3H), 1.63 – 1.54 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.1 (d, *J* = 238.2 Hz), 160.3 (d, *J* = 7.7 Hz), 154.9, 147.4 (d, *J* = 15.3 Hz), 120.3 (d, *J* = 3.7 Hz), 107.7 (d, *J* = 37.3 Hz), 79.9, 61.2, 55.8, 47.4, 39.7, 29.7, 28.7, 28.3.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.65 (s)

IR (film) ν_{max} 2977, 2250, 1688, 1612, 1413, 1367, 1317, 1148, 1097, 905, 727, 647cm^{-1}.

HRMS (ESI+) m/z calcd. for $C_{16}H_{21}FN_2O_2$ ($[M+H]^+$) 293.1665, found 293.1676



(±)-*tert*-butyl-3-oxo-6-(6-chloropyridin-3-*exo*-yl)-8-azabicyclo[3.2.1]octane-8-carboxylate (83a)

Prepared following general procedure B outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (3 x 17 mg, 0.005 mmol, 3 x 1.0 mol%), MeCN (12.5 mL), 5-bromo-2-chloropyridine (96.0 mg, 0.5 mmol, 1.0 equiv.), *N*-Boc-nortropinone (563 mg, 2.5 mmol, 5.0 equiv.), and Na_3PO_4 (90 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 20% to 40% EtOAc in hexanes) yielded the pure product (mixture of rotamers) as a colorless solid (55 mg, 0.163 mmol, 33% yield).

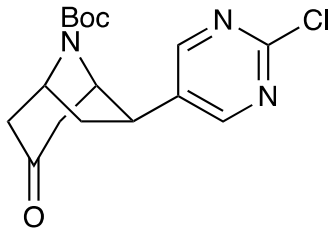
^{1}H NMR (500 MHz, CD_3CN) δ 8.24 (d, *J* = 2.5 Hz, 1H), 7.63 (dd, *J* = 8.3, 2.6 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 4.63 (s, 1H), 4.33 (d, *J* = 12.3 Hz, 1H), 3.27 (t, *J* = 7.7 Hz, 1H),

2.50 (d, *J* = 16.1 Hz, 1H), 2.36 (d, *J* = 15.9 Hz, 1H), 2.25 (t, *J* = 11.5 Hz, 1H), 2.10 (d, *J* = 13.0 Hz, 1H), 1.50 (d, *J* = 26.7 Hz, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 206.9, 153.1, 149.9, 148.0, 140.1 (m, *J* = 22.2 Hz), 136.6, 124.6 (m, *J* = 4.3 Hz), 81.2, 60.4 (m, *J* = 83.7 Hz), 53.9 (m, *J* = 68.1 Hz), 48.6 (m, *J* = 59.2 Hz), 48.1 (m, *J* = 37.9 Hz), 44.8 (m, *J* = 126.1 Hz), 39.9 (m, *J* = 109.8 Hz), 28.4

IR (film) ν_{max} 3088, 2926, 2967, 1715, 1690, 1454, 1348, 1337, 1326, 1254, 1196, 1163, 1105, 1085, 1066, 1005 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{22}ClN_2O_3$ ($[M+H]^+$) 336.1241, found 336.1227.



(±)-*tert*-butyl-3-oxo-6-(2-chloropyrimidin-5-*exo*-yl)-8-azabicyclo[3.2.1]octane-8-carboxylate (83b)

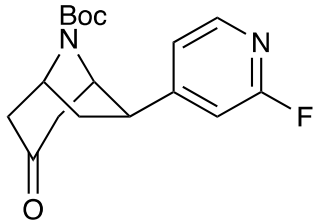
Prepared following general procedure B outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (3 x 17 mg, 0.005 mmol, 3 x 1.0 mol%), MeCN (12.5 mL), 5-bromo-2-chloropyrimidine (97.0 mg, 0.5 mmol, 1.0 equiv.), *N*-Boc-nortropinone (563 mg, 2.5 mmol, 5.0 equiv.), and Na_3PO_4 (90 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 25% to 40% EtOAc in hexanes) yielded the pure product (mixture of rotamers) as a colorless solid (63 mg, 0.187 mmol, 37% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (s, 2H), 4.70 (d, *J* = 56.2 Hz, 1H), 4.43 (d, *J* = 58.3 Hz, 1H), 3.16 (dd, *J* = 9.6, 4.9 Hz, 1H), 2.86 (d, *J* = 15.9 Hz, 1H), 2.70 (d, *J* = 14.2 Hz, 1H), 2.55 (d, *J* = 16.3 Hz, 1H), 2.45 (dt, *J* = 15.9, 1.9 Hz, 1H), 2.33 (dd, *J* = 13.9, 9.5 Hz, 1H), 2.10 (s, 1H), 1.54 – 1.49 (m, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 206.4, 160.0, 157.8, 153.0, 137.4 (m, *J* = 21.6 Hz), 81.5, 60.2 (m, *J* = 77.5 Hz), 53.8 (m, *J* = 43.7 Hz), 48.5 (m, *J* = 21.7 Hz), 47.9, 42.9 (m, *J* = 105.5 Hz), 39.6 (m, *J* = 79.6 Hz), 28.4.

IR (film) ν_{max} 2979, 2929, 1696, 1546, 1450, 1408, 1381, 1343, 1250, 1226, 1156, 1106, 1066, 1006 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{21}ClN_3O_3$ ($[M+H]^+$) 337.1193, found 337.1196.



(±)-*tert*-butyl-3-oxo-6-(2-fluoropyridin-4-*exo*-yl)-8-azabicyclo[3.2.1]octane-8-carboxylate (83c)

Prepared following general procedure B outlined above using $NiBr_2$•dtbbpy (12 mg, 0.025 mmol, 5.0 mol%), tetrabutylammonium decatungstate (2 x 17 mg, 0.005 mmol, 2 x 1.0 mol%), MeCN (12.5 mL), 4-bromo-2-fluoropyridine (88.0 mg, 51.4 µL, 0.5 mmol, 1.0 equiv.), *N*-Boc-nortropinone (563 mg, 2.5 mmol, 5.0 equiv.), and Na_3PO_4 (90 mg, 0.55 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, gradient 20% to 40% EtOAc in hexanes) yielded the pure product (mixture of rotamers) as a colorless solid (70 mg, 0.219 mmol, 44% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 5.1 Hz, 1H), 7.01 (s, 1H), 6.76 (s, 1H), 4.68 (d, *J* = 73.1 Hz, 1H), 4.47 (d, *J* = 67.9 Hz, 1H), 3.16 (q, *J* = 7.9, 7.3 Hz, 1H), 2.84 (t, *J* = 14.3 Hz, 1H), 2.75 – 2.60 (m, 1H), 2.53 (dd, *J* = 16.0, 5.7 Hz, 1H), 2.44 (dt, *J* = 16.0, 1.8 Hz, 1H), 2.39 – 2.22 (m, 1H), 2.11 (dd, *J* = 14.4, 7.0 Hz, 1H), 1.54 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 206.8, 164.2 (d, *J* = 239.1 Hz), 160.0 (d, *J* = 22.5 Hz), 153.1 (d, *J* = 25.9 Hz), 148.2 (d, *J* = 15.4 Hz), 119.6 (d, *J* = 3.9 Hz), 107.3 (d, *J* = 37.2 Hz), 81.2, 59.8 (d, *J* = 84.8 Hz), 53.8 (d, *J* = 76.6 Hz), 48.7 (d, *J* = 64.4 Hz), 48.2 (d, *J* = 29.7 Hz), 47.3 (d, *J* = 125.9 Hz), 39.4 (d, *J* = 115.9 Hz), 28.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.51 (d, *J* = 34.6 Hz)

IR (film) ν_{max} 2970, 1718, 1689, 1612, 1414, 1389, 1367, 1217, 1203, 1162, 1143, 1106, 1069, 1005 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{22}FN_2O_3$ ($[M+H]^+$) 320.1536, found 320.1531.

11) Selectivity Guide

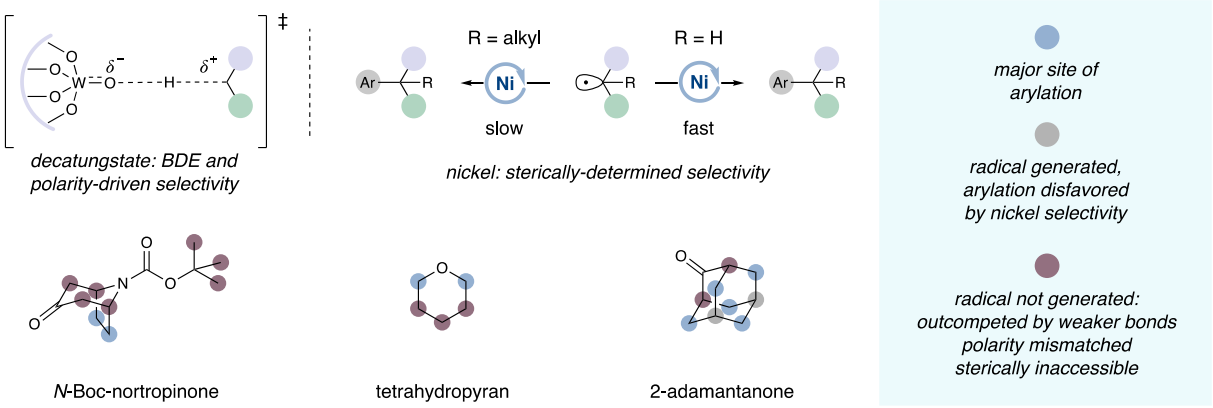


Figure S6: A graphical guide to predicting arylation selectivities.

12) Cyclic Voltammogram of Catalysts

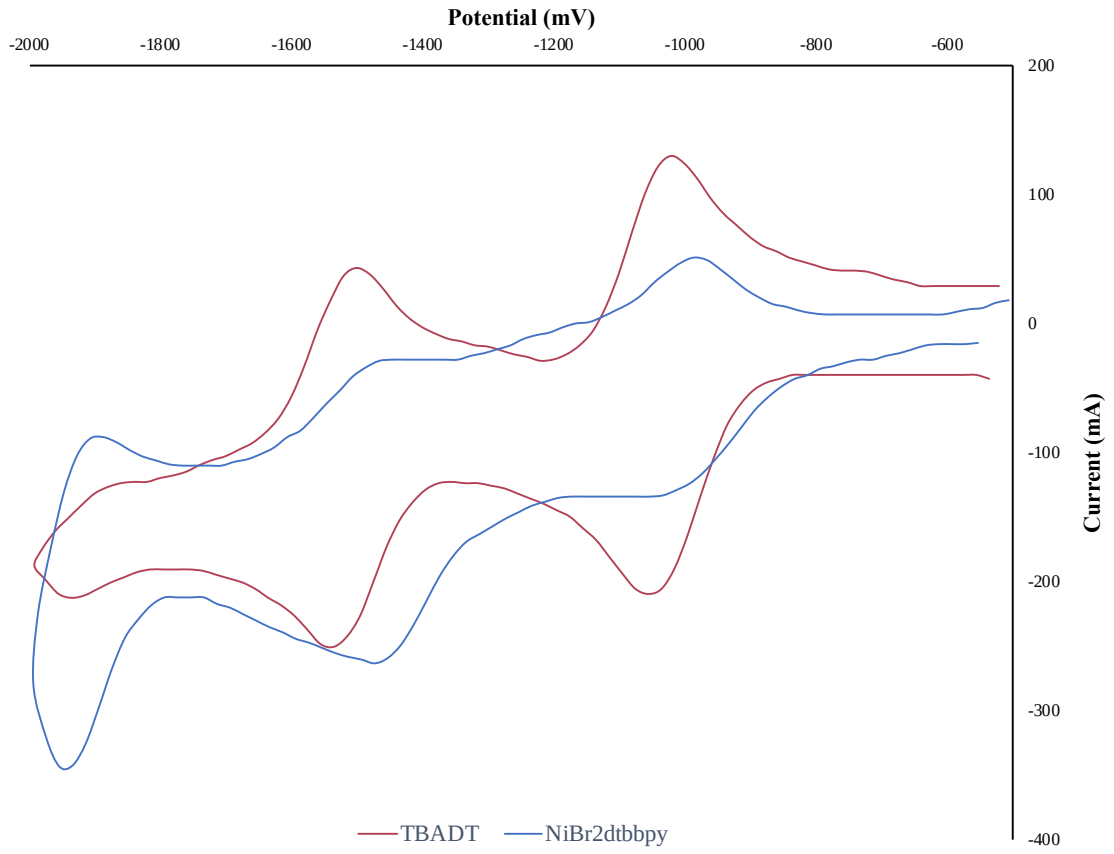
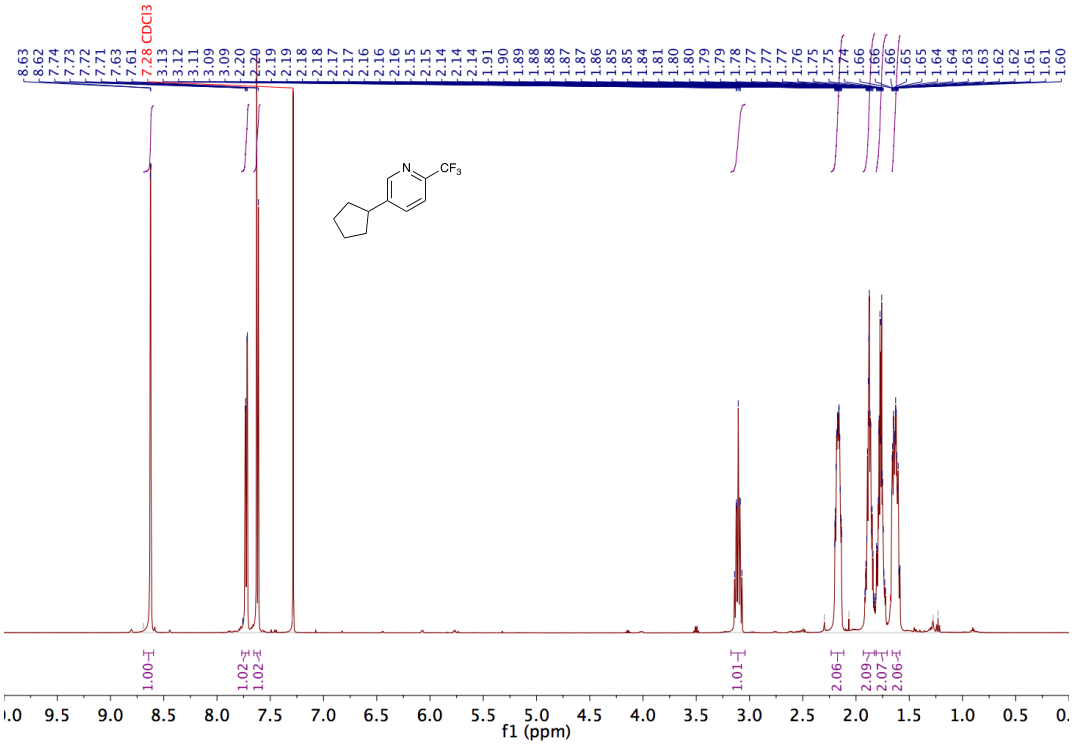


Figure S7 – Cyclic voltammogram of TBADT and $NiBr_2$•dtbbpy (taken separately and overlayed). $E_{1/2}^{ox}$ ($[W_{10}O_{32}]^{6-}/[W_{10}O_{32}]^{5-}$) = –1.52 V versus Ag/Ag^+ in MeCN. E_p ([Ni(II)Br_2•dtbbpy]/[Ni(0)]) = –1.47 V versus Ag/Ag^+ in MeCN. General procedure: A 10 mM solution of catalyst was prepared in MeCN with 0.5 M tetrabutylammonium hexafluorophosphate electrolyte. Scan rate was set at 0.2V/s. Reference electrode was Ag wire in 0.1 M $AgNO_3$.

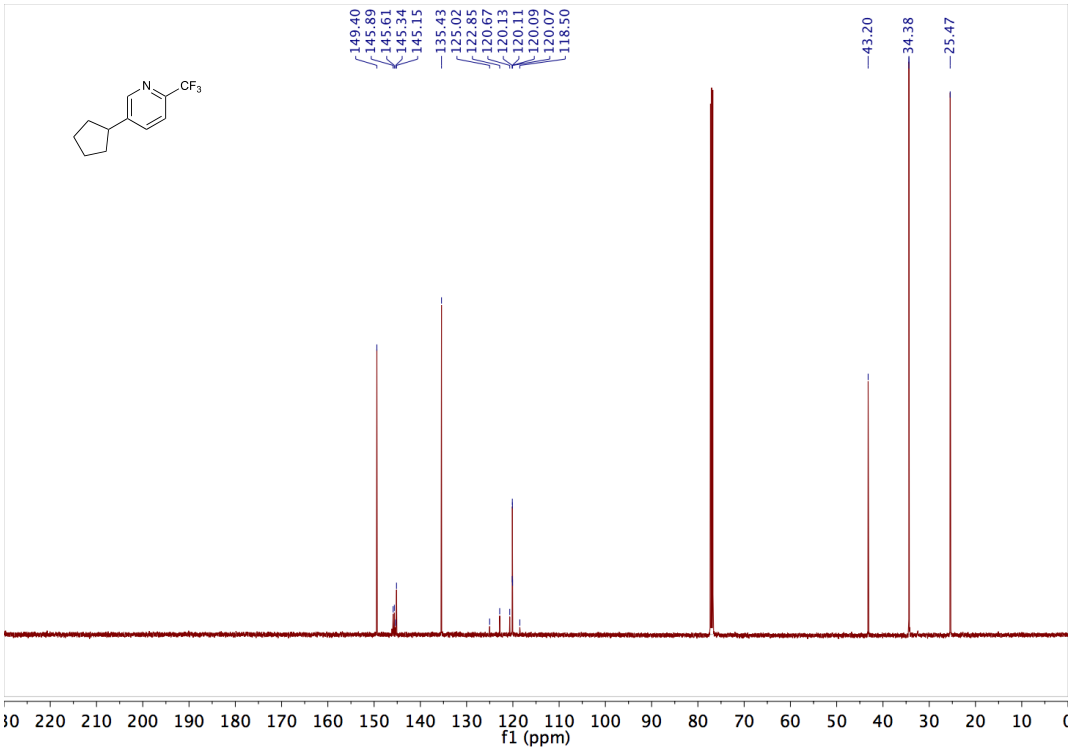
13) References Cited

1. Perrin, D. D. & Armarego, W. L. F. *Purification of Laboratory Chemicals*. Ed 3 edn, (Pergamon Press, 1988).
2. Pangborn, A. B., Giardello, M. A., Grubbs, R. H., Rosen, R. K. & Timmers, F. J. Safe and convenient procedure for solvent purification. *Organometallics* **15**, 1518-1520 (1996).
3. Still, W. C., Kahn, M. & Mitra, A. J. Rapid chromatographic technique for preparative separations with moderate resolution. *J. Org. Chem.* **43**, 2923-2925 (1978).
4. Yamase, T., Takabayashi, N. & Kaji, M. Solution photochemistry of tetrakis(tetrabutylammonium) decatungstate(VI) and catalytic hydrogen evolution from alcohols. *J. Chem. Soc., Dalton Trans.* **0**, 793-799 (1984).
5. Shaw, M. H., Shurtleff, V. W., Terrett, J. A., Cuthbertson, J. D. & MacMillan, D. W. C. Native functionality in triple catalytic cross-coupling: sp3 C–H bonds as latent nucleophiles. *Science* **352**, 1304-1308 (2016).
6. Charrier, J.-D., Young, S. C., Davis, C. J. & Studley, J. Compounds useful as inhibitors of ATR kinase. US patent 8,765,751 B2 (2014).
7. Brea, R. J., Amorín, M., Castedo, L. & Granja, J. R. Methyl-blocked dimeric α,γ-peptide nanotube segments: formation of a peptide heterodimer through backbone–backbone interactions. *Angew. Chem. Int. Ed.* **44**, 5710-5713 (2005).
8. Zuo, Z. *et al.* Merging photoredox with nickel catalysis: coupling of α-carboxyl sp^3-carbons with aryl halides. *Science* **345**, 437-440 (2014).
9. Mojtahedi, M. M., Niknedjad, N. & Veisi, H. A mild a green method for the N-Boc protection of amines without assistant of catalyst under solvent-free conditions. *Lett. Org. Chem.* **10**, 121-125 (2013).
10. Li, Z., Sun, H.-M. & Shen, Q. Iron-mediated inter- and intramolecular reductive cross-coupling of unactivated alkyl chlorides with aryl bromides. *Org. Biomol. Chem.* **14**, 3314-3321 (2016).
11. Li, Z., Liu, L., Sun, H.-M., Shen, Q. & Zhang, Y. Alkyl Grignard cross-coupling of aryl phosphates catalyzed by new, highly active ionic iron(II) complexes containing a phosphine ligand and an imidazolium cation. *Dalton Trans.* **45**, 17739-17747 (2016).
12. Prabhakaran, J. & al, e. Synthesis of [11C]celecoxib: a potential PET probe for imaging COX-2 expression. *J. Label. Compd. Radiopharm.* **48**, 887-895 (2005).
13. Fletcher, S. R. & al, e. Total synthesis and determination of absolute configuration of epibatidine. *J. Org. Chem.* **59**, 1771-1778 (1994).

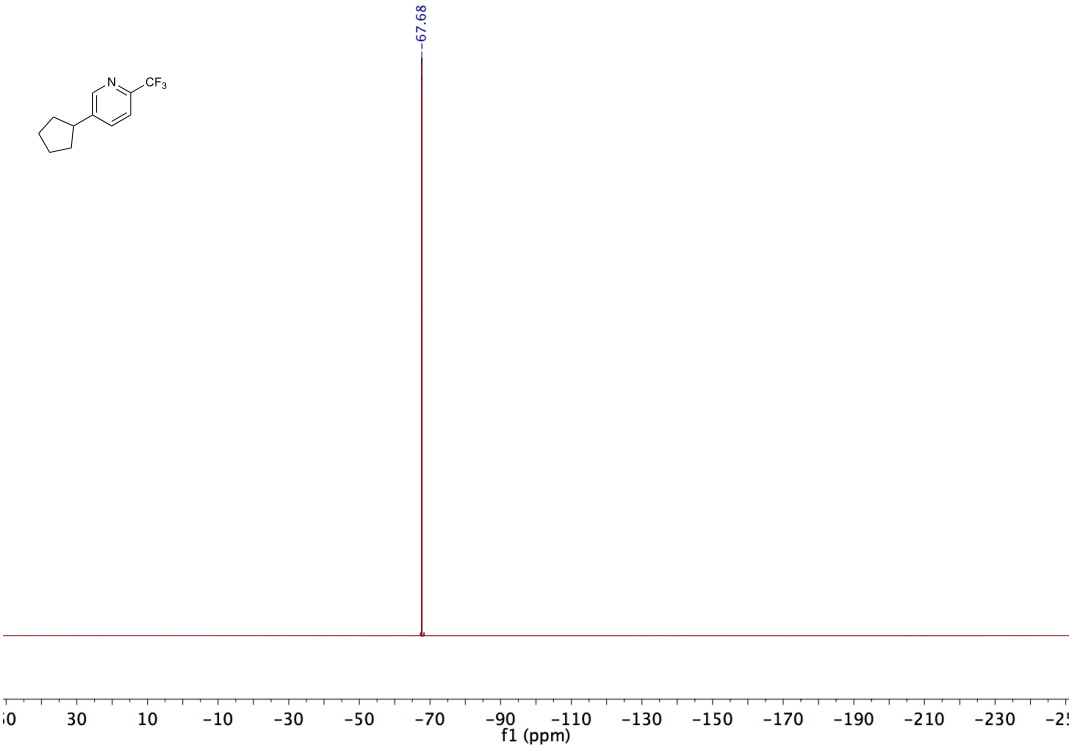
14) Spectral Data



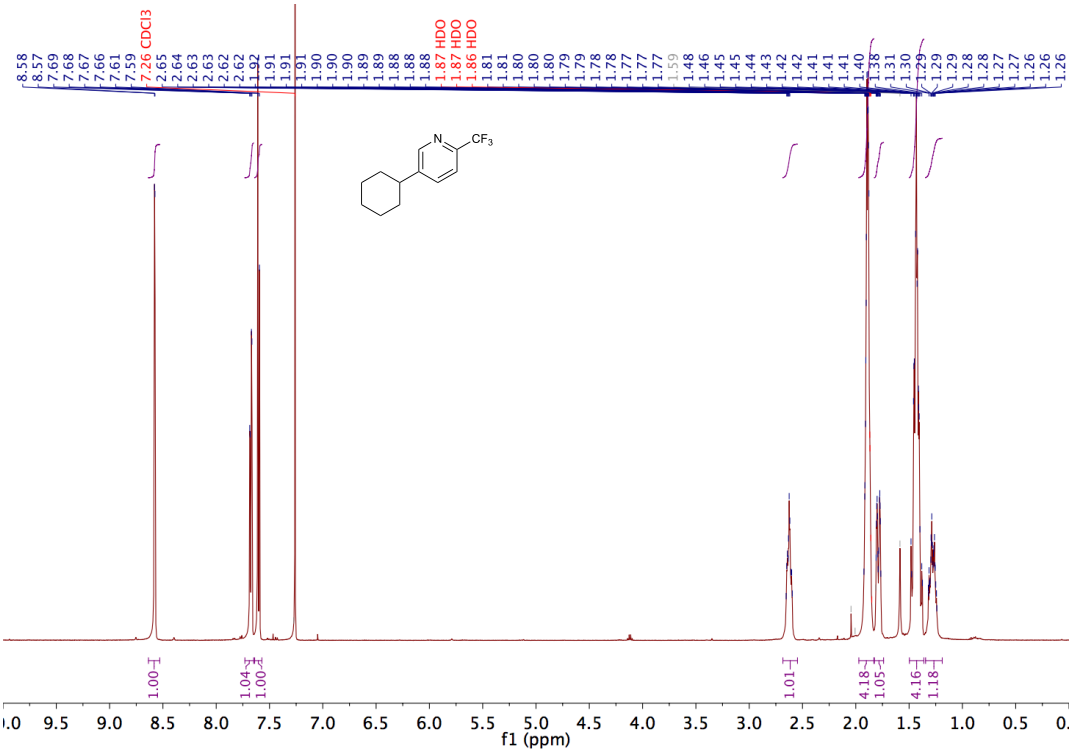
^{1}H NMR (500 MHz, $CDCl_3$) - (13)



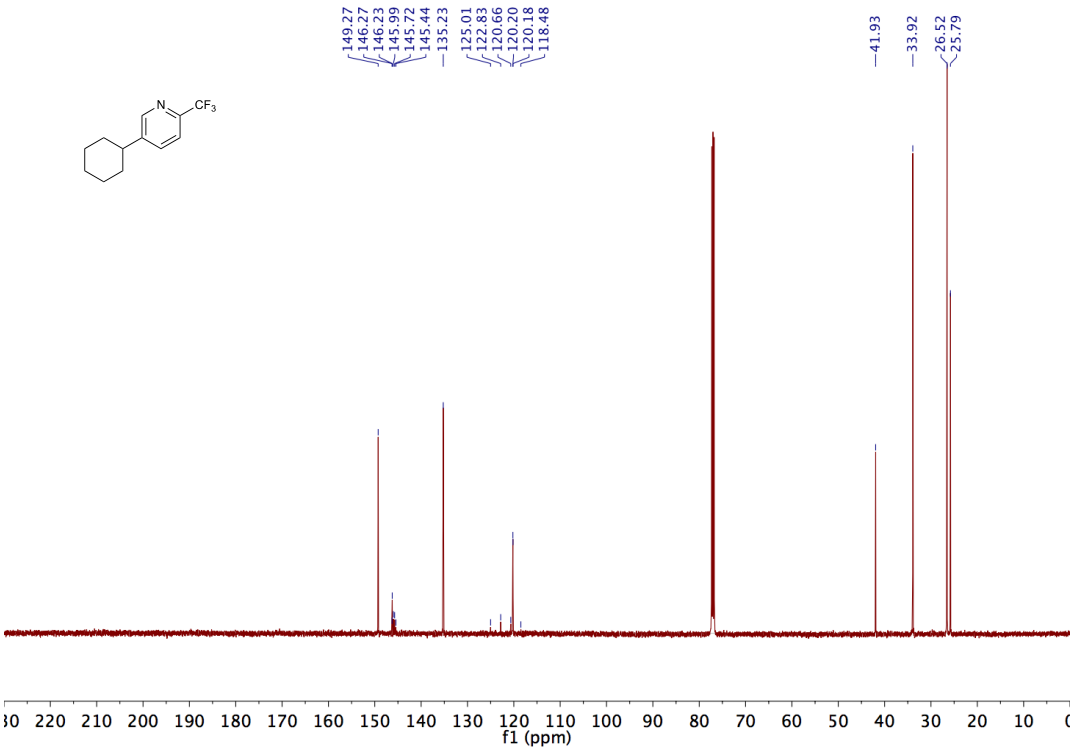
^{13}C NMR (126 MHz, $CDCl_3$) - (13)



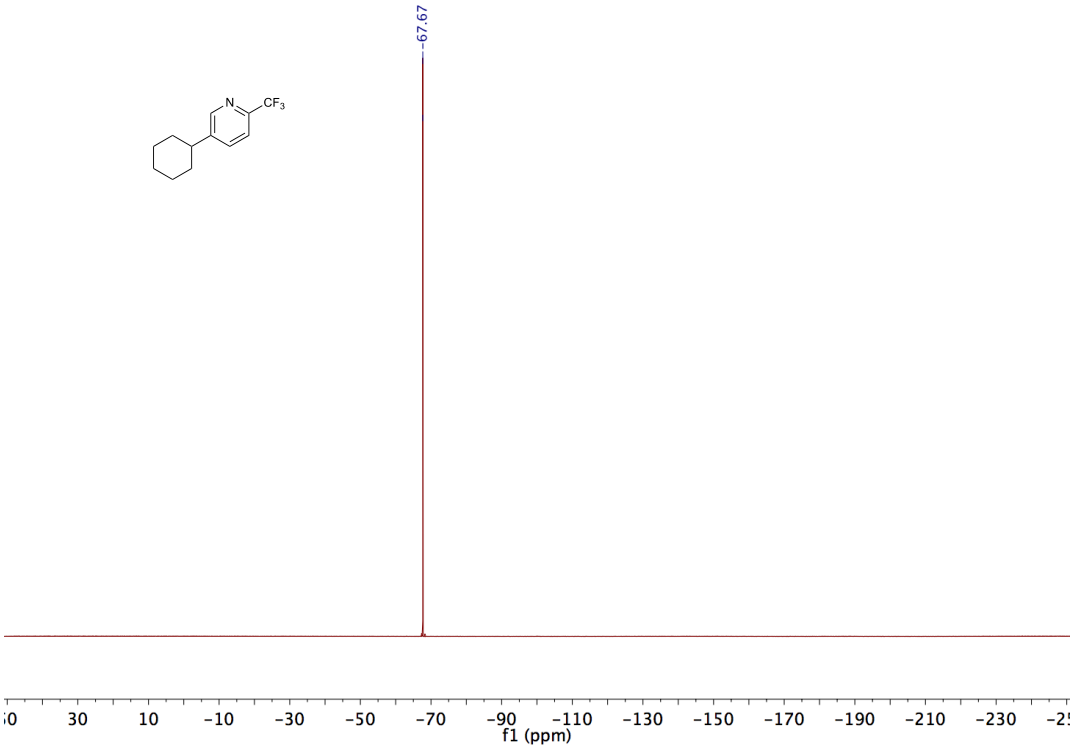
^{19}F NMR (376 MHz, $CDCl_3$) - (13)



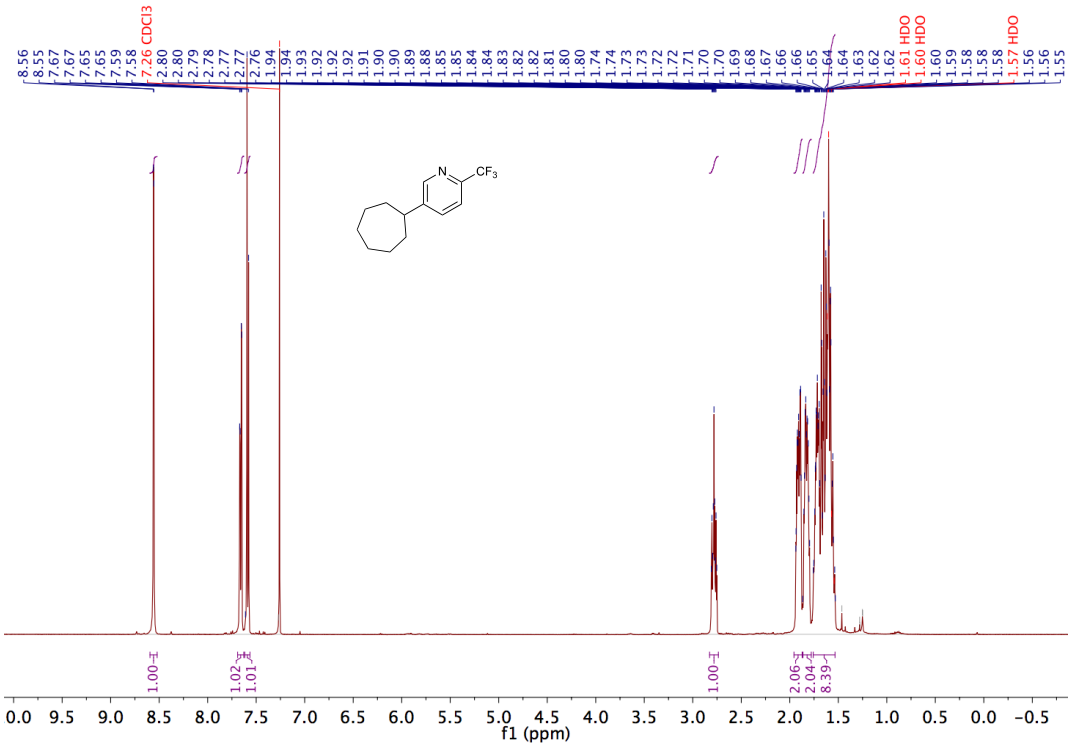
^{1}H NMR (500 MHz, $CDCl_3$) - (14)



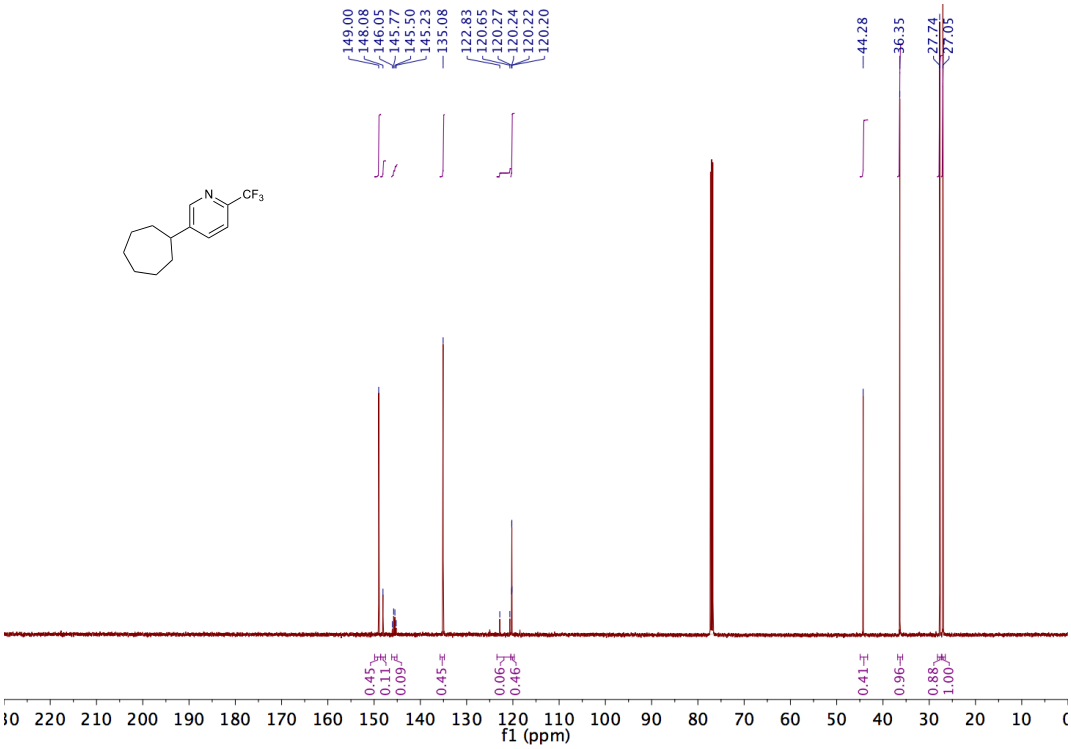
^{13}C NMR (126 MHz, $CDCl_3$) - (14)



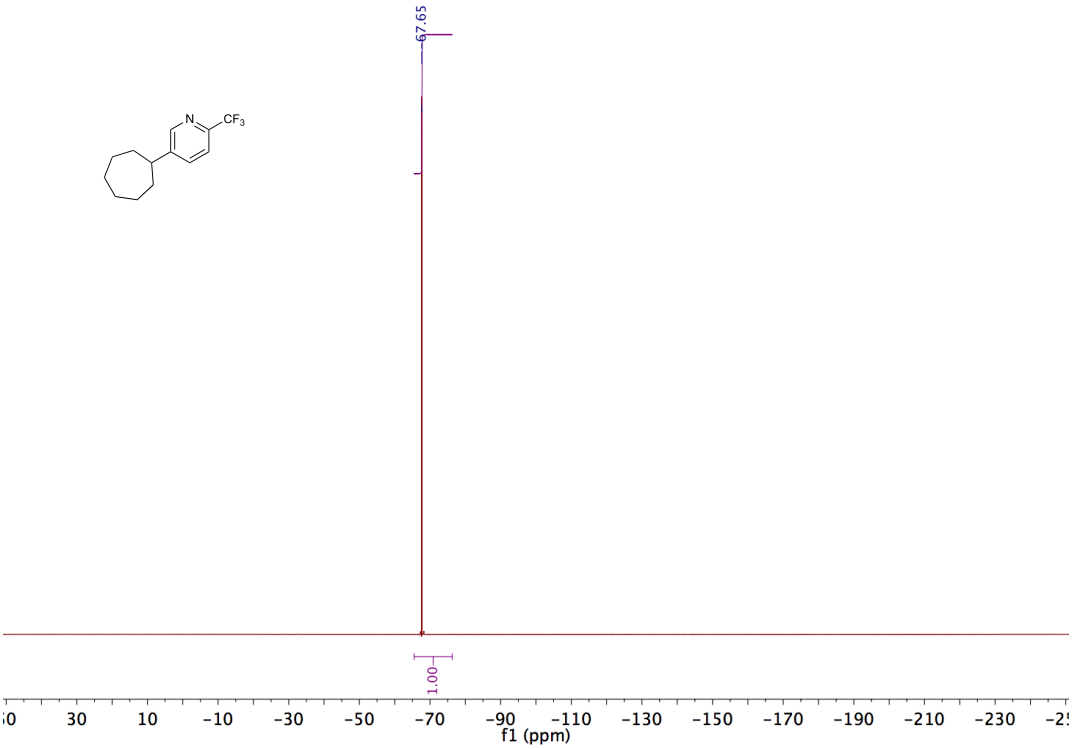
^{19}F NMR (376 MHz, $CDCl_3$) – (14)



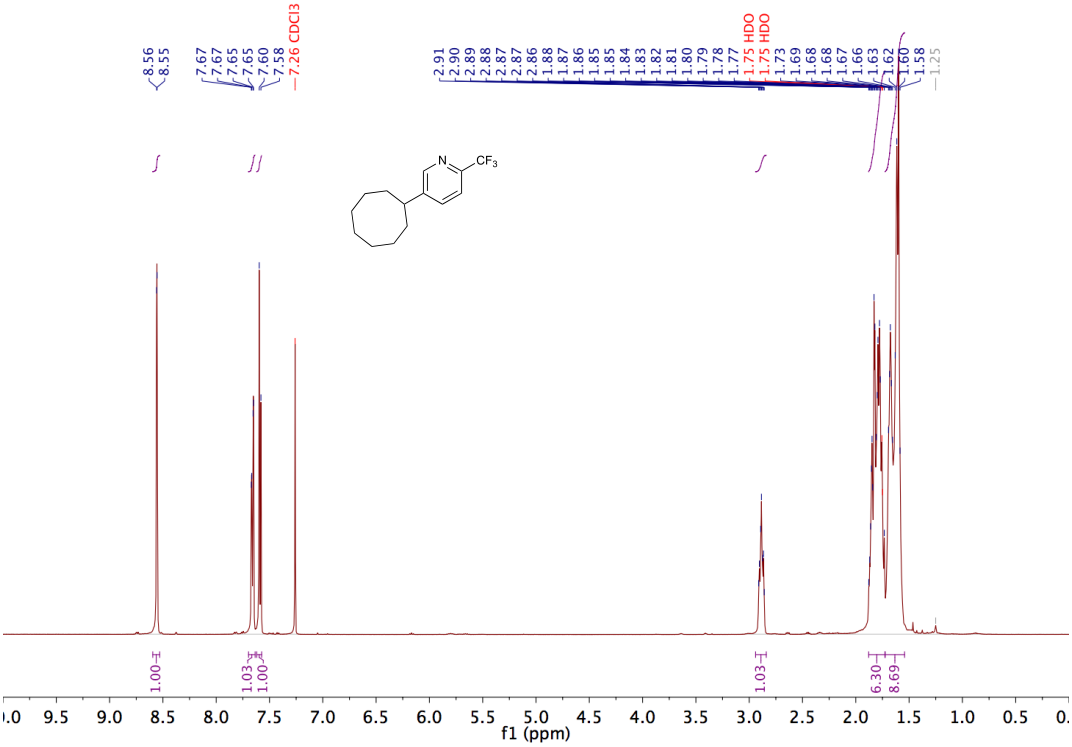
^{1}H NMR (500 MHz, $CDCl_3$) - (15)



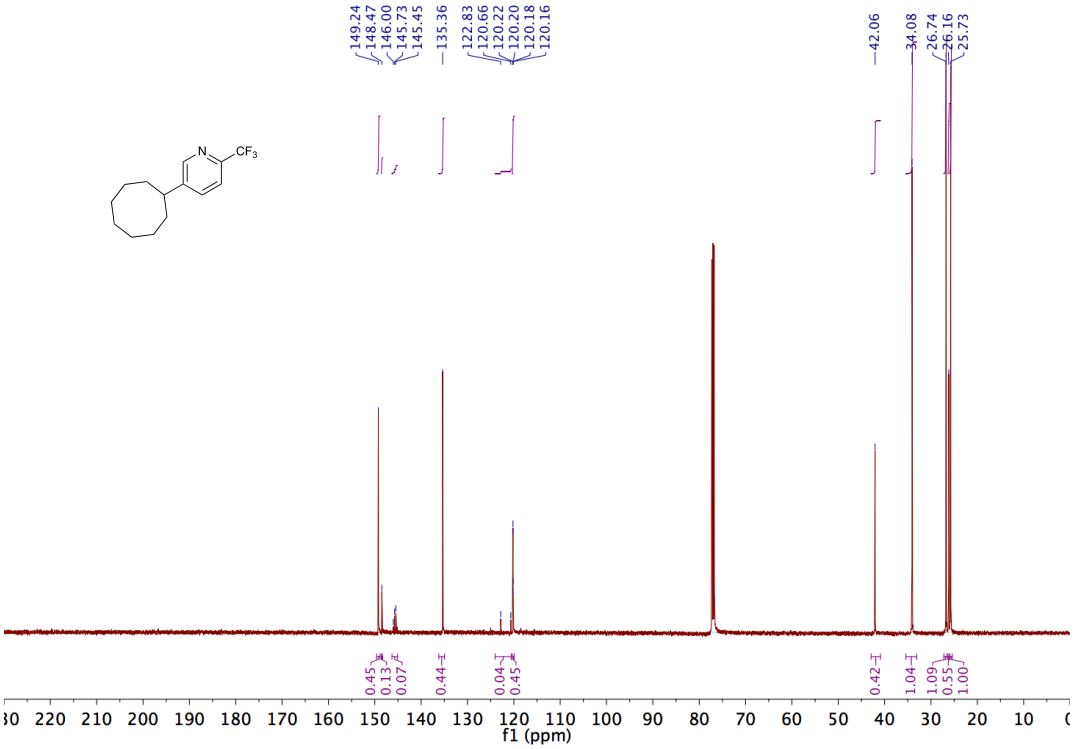
^{13}C NMR (126 MHz, $CDCl_3$) - (15)



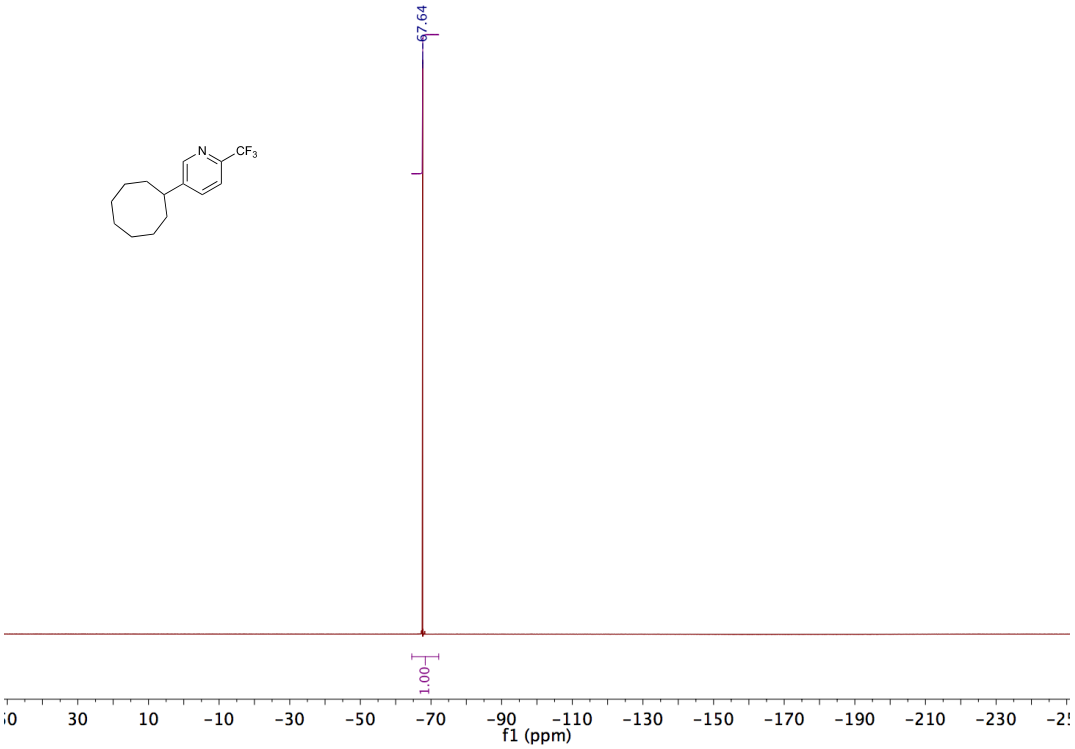
^{19}F NMR (376 MHz, $CDCl_3$) - (15)



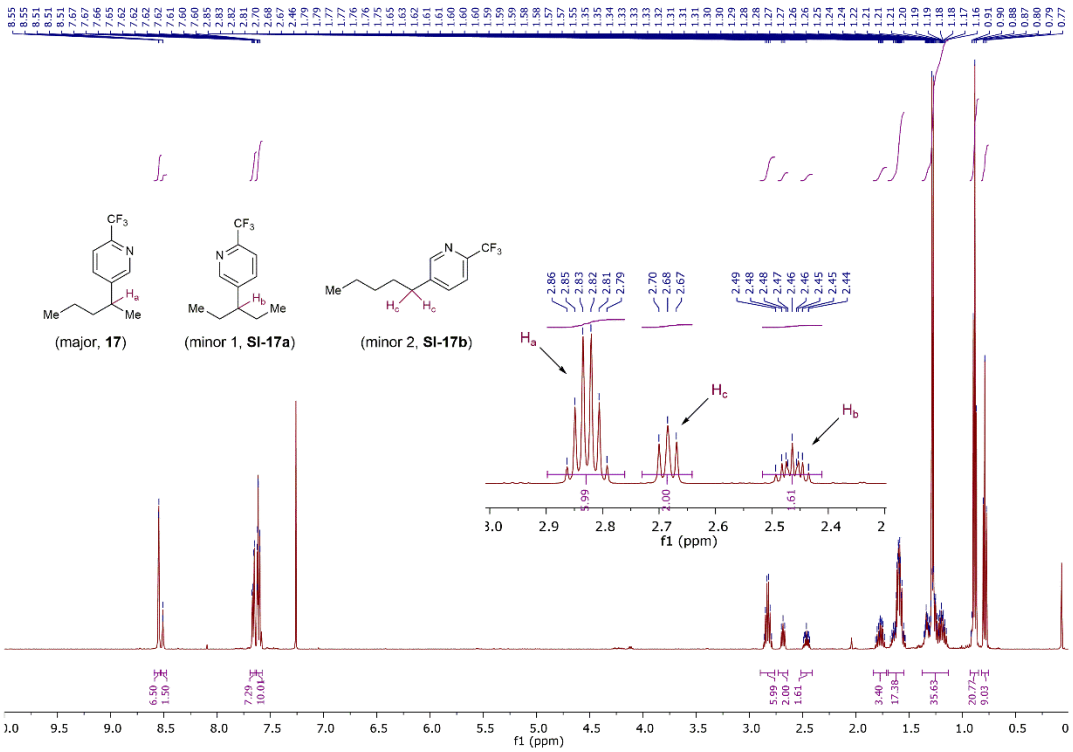
^{1}H NMR (500 MHz, $CDCl_3$) – (16)



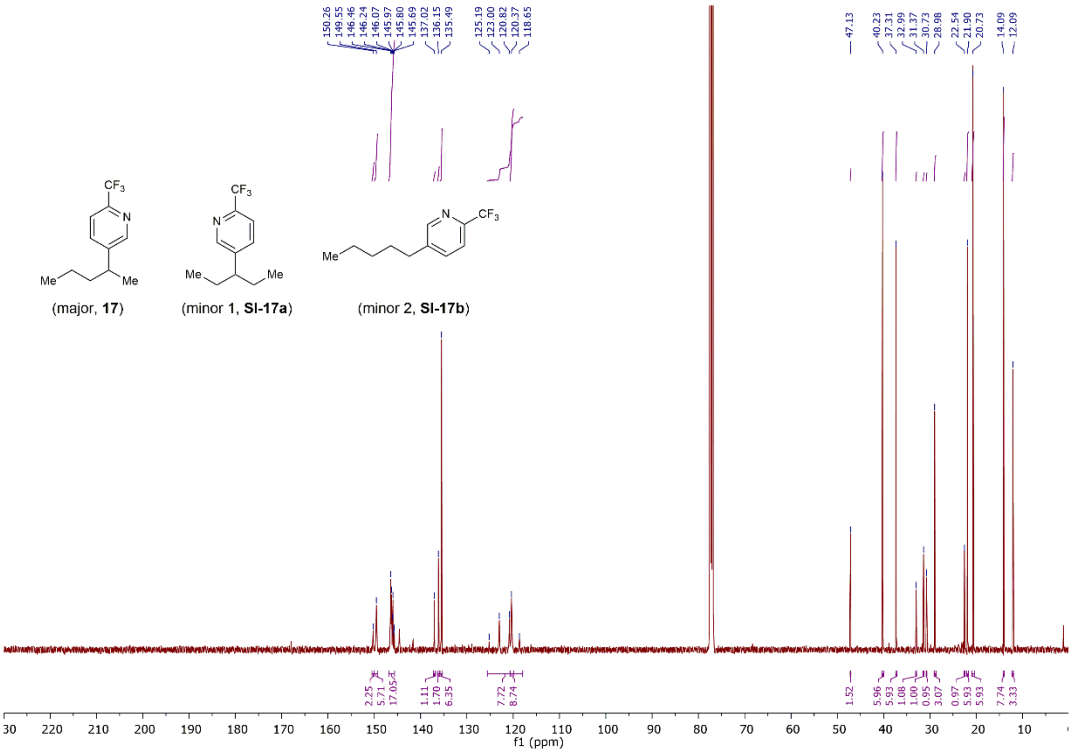
^{13}C NMR (126 MHz, $CDCl_3$) - (16)



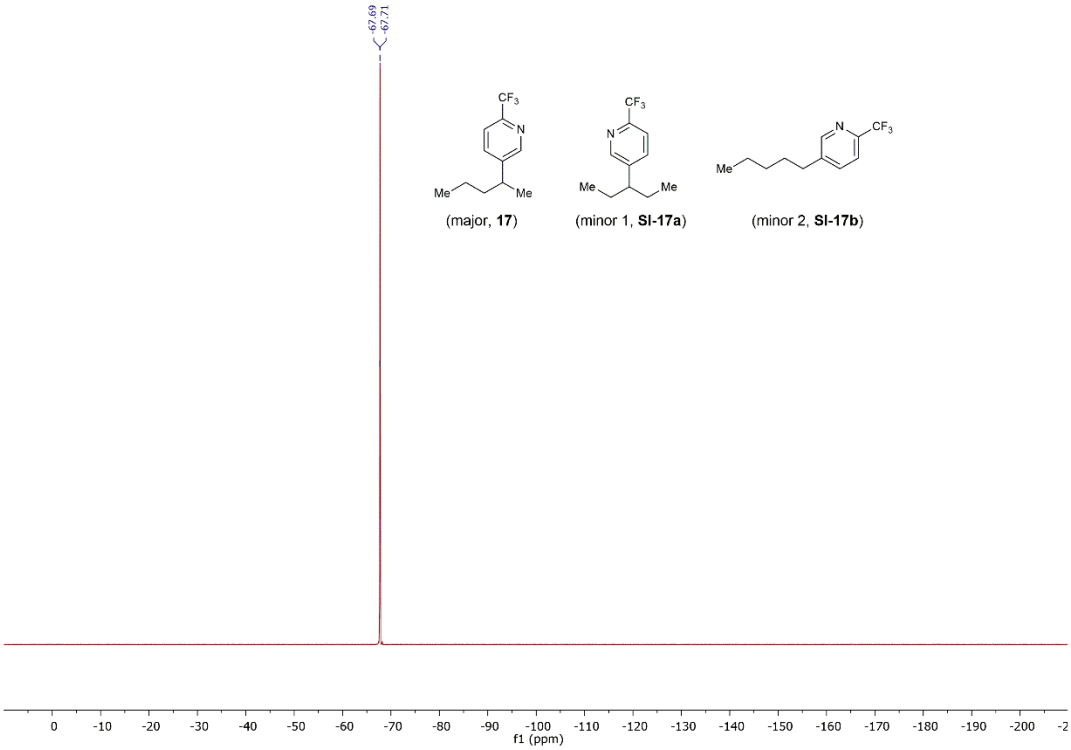
^{19}F NMR (376 MHz, $CDCl_3$) - (16)



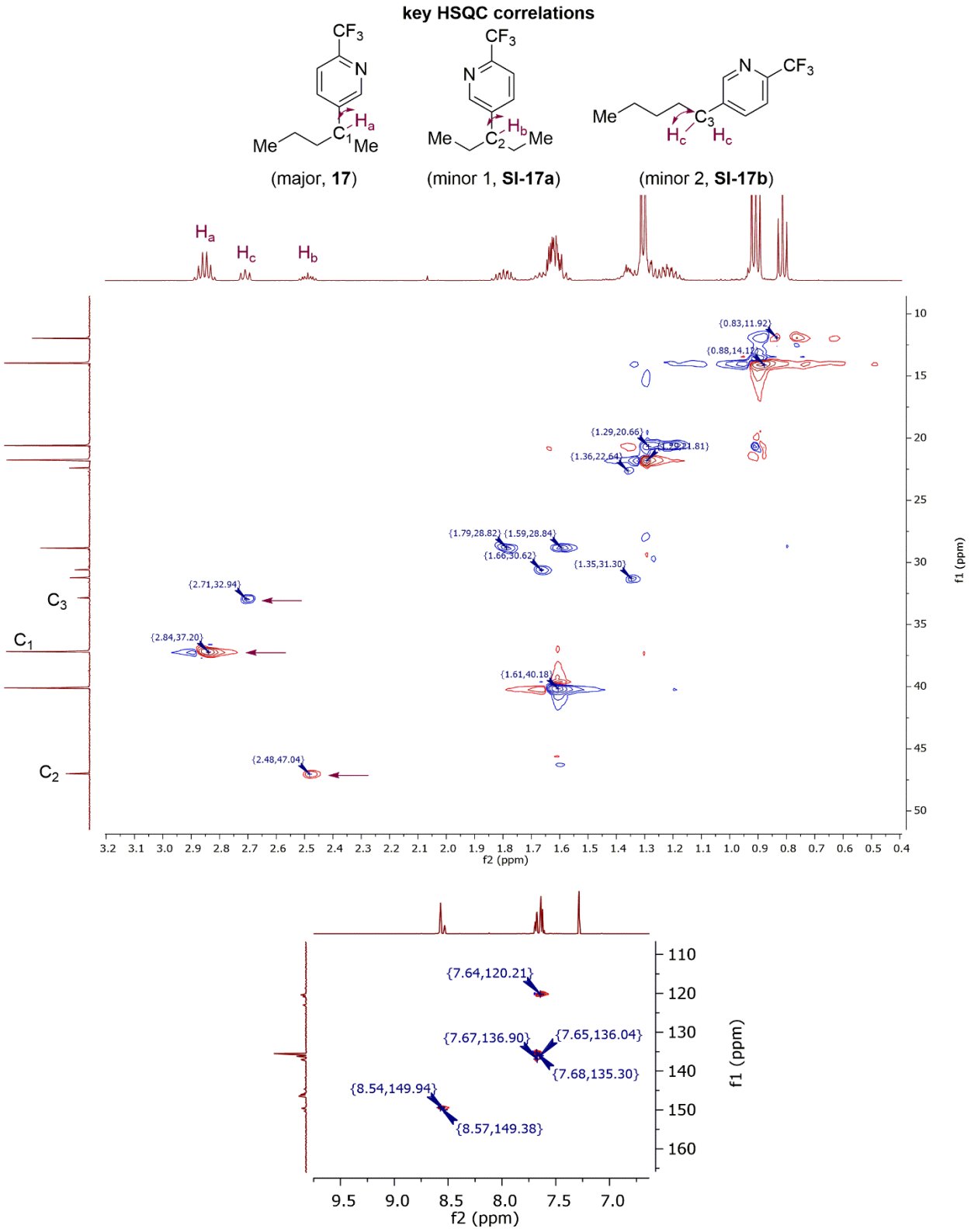
^{1}H NMR (500 MHz, $CDCl_3$) - (17, SI-17a, and SI-17b, isolated mixture from silica chraomatography)



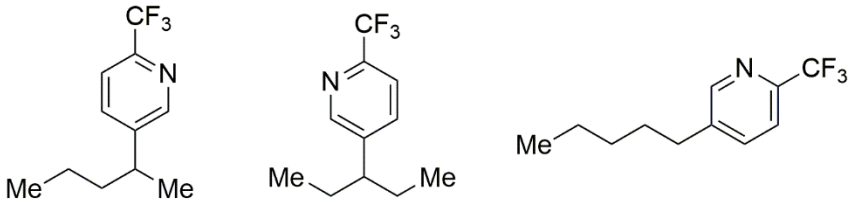
Quantitative ^{13}C NMR (126 MHz, $CDCl_3$) - (17, SI-17a, and SI-17b, isolated mixture from silica chromatography)



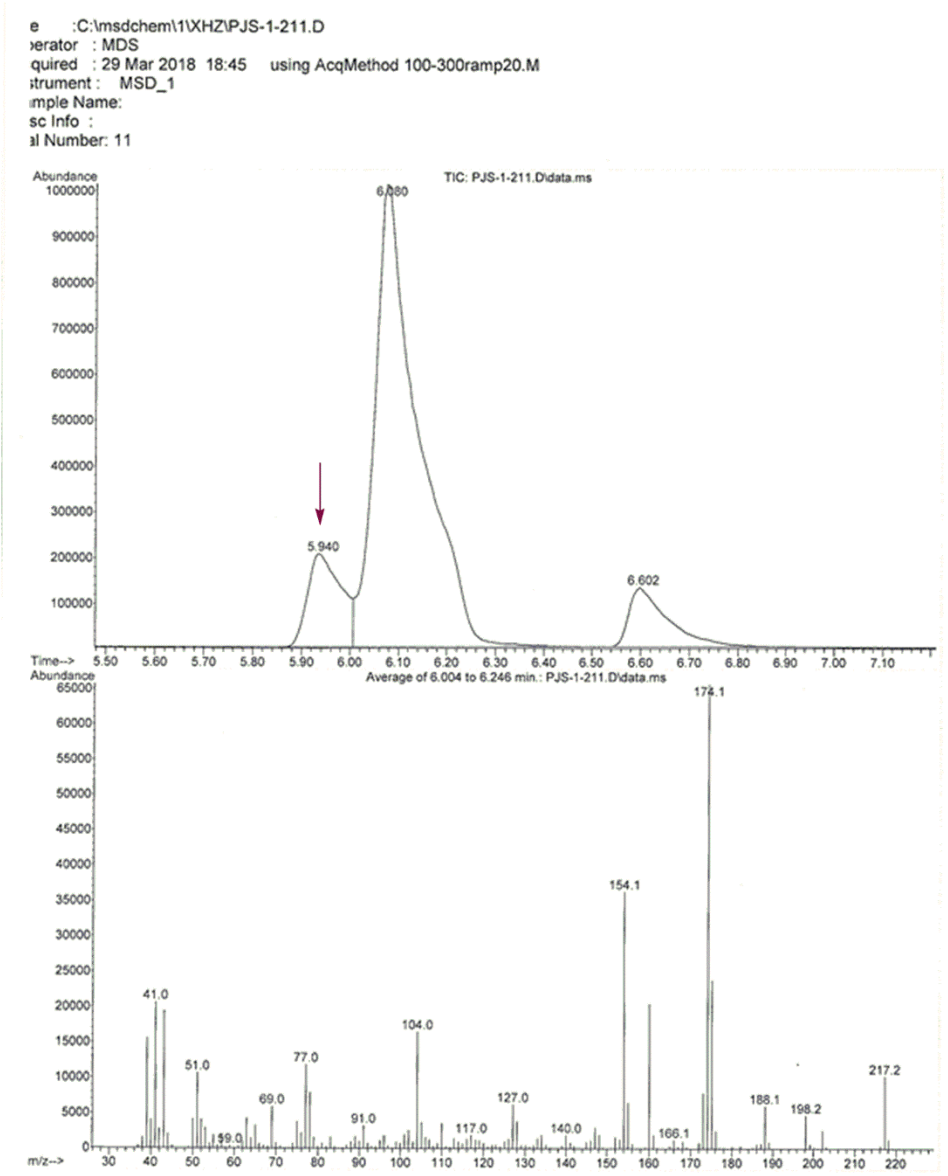
^{19}F NMR (376 MHz, $CDCl_3$) - (**17**, **SI-17a**, and **SI-17a**, isolated mixture from silica chromatography)



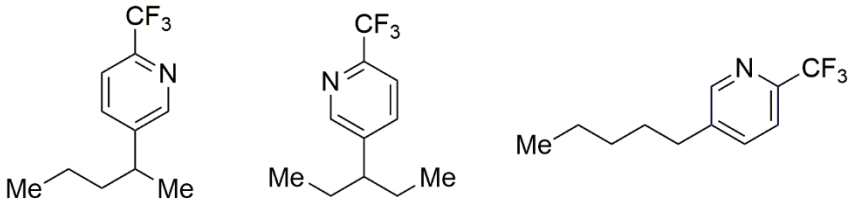
HSQC - (**17**, **SI-17a**, and **SI-17a**, isolated mixture from silica chromatography)



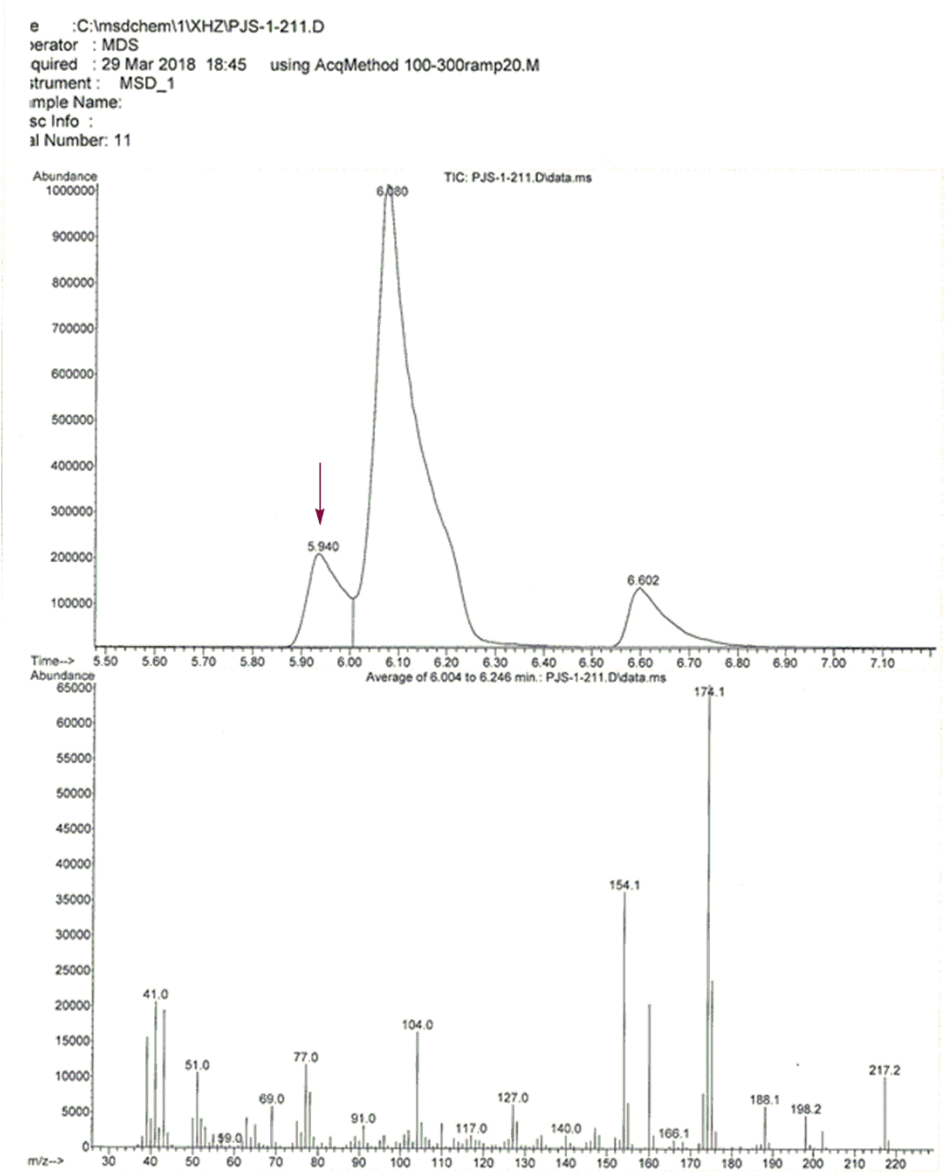
(major, **17**) (minor 1, **SI-17a**) (minor 2, **SI-17b**)



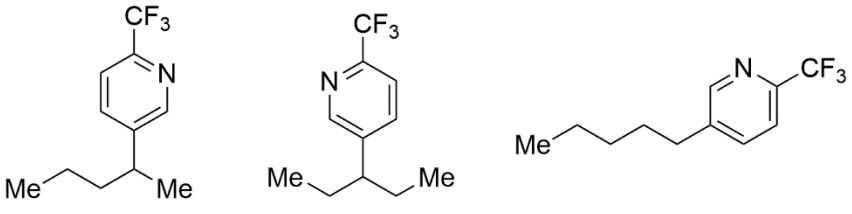
GCMS - (**17**, **SI-17a**, and **SI-17a**, isolated mixture from silica chromatography)



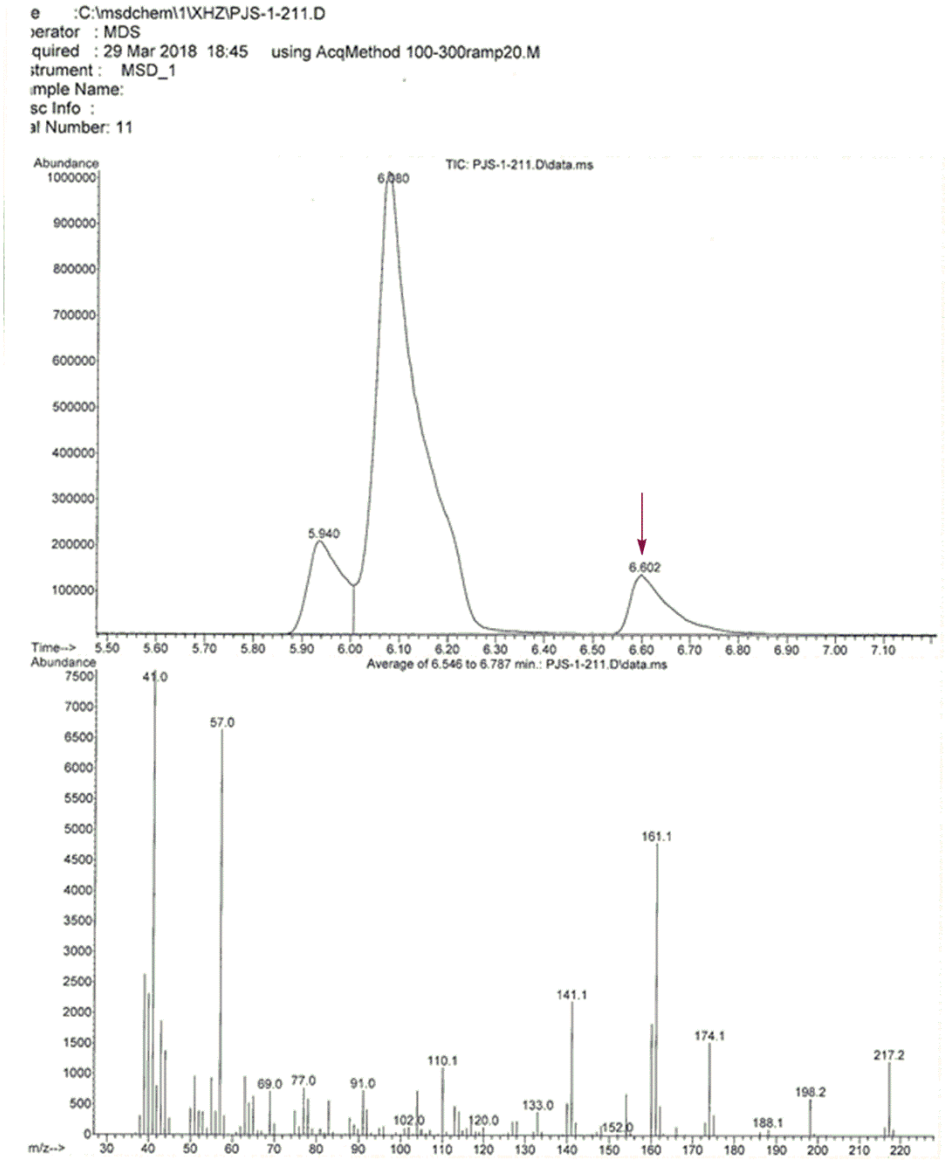
(major, **17**) (minor 1, **SI-17a**) (minor 2, **SI-17b**)



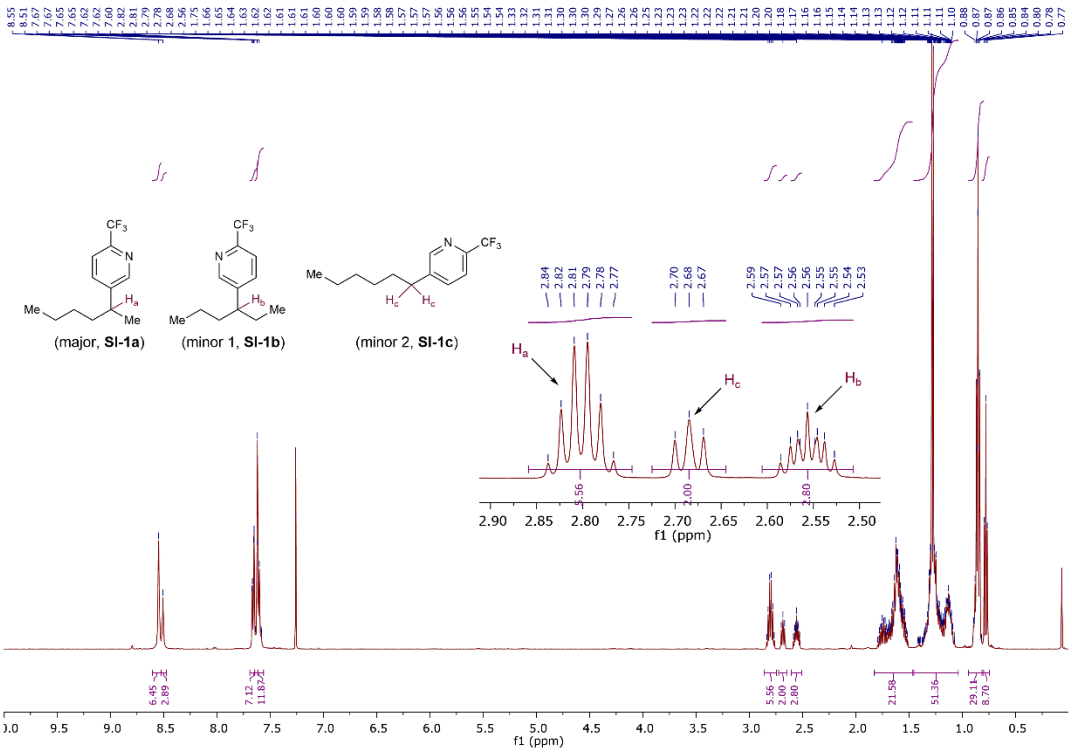
GCMS - (**17**, **SI-17a**, and **SI-17a**, isolated mixture from silica chromatography)



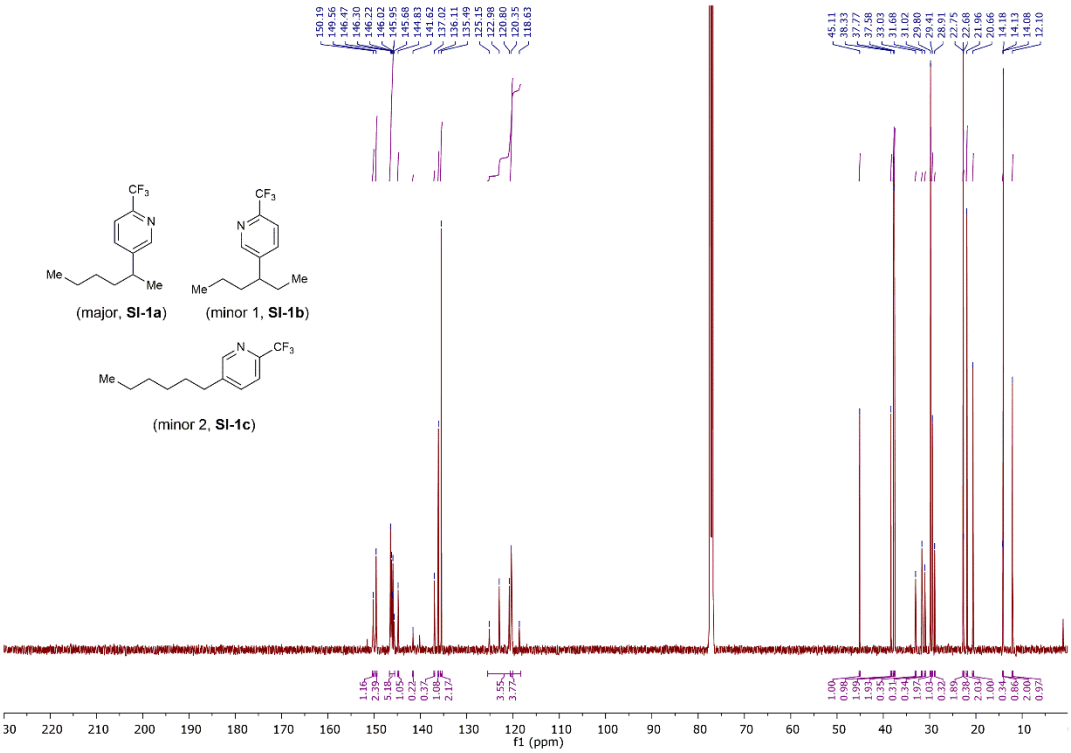
(major, **17**) (minor 1, **SI-17a**) (minor 2, **SI-17b**)



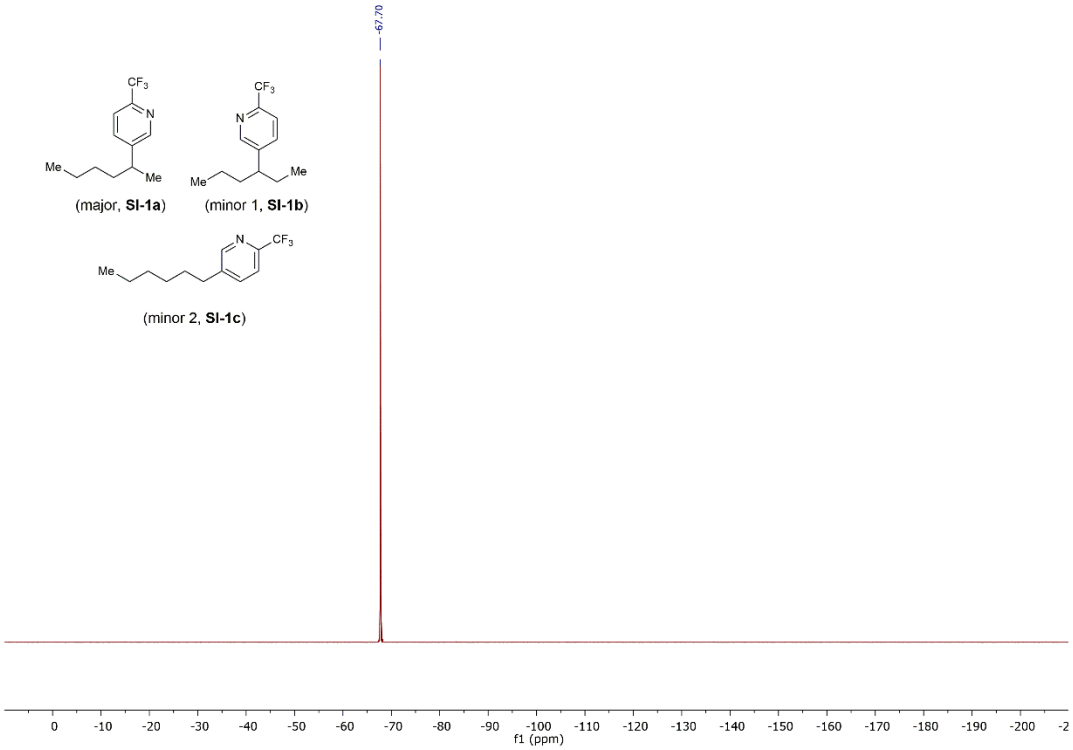
GCMS - (**17**, **SI-17a**, and **SI-17a**, isolated mixture from silica chromatography y)



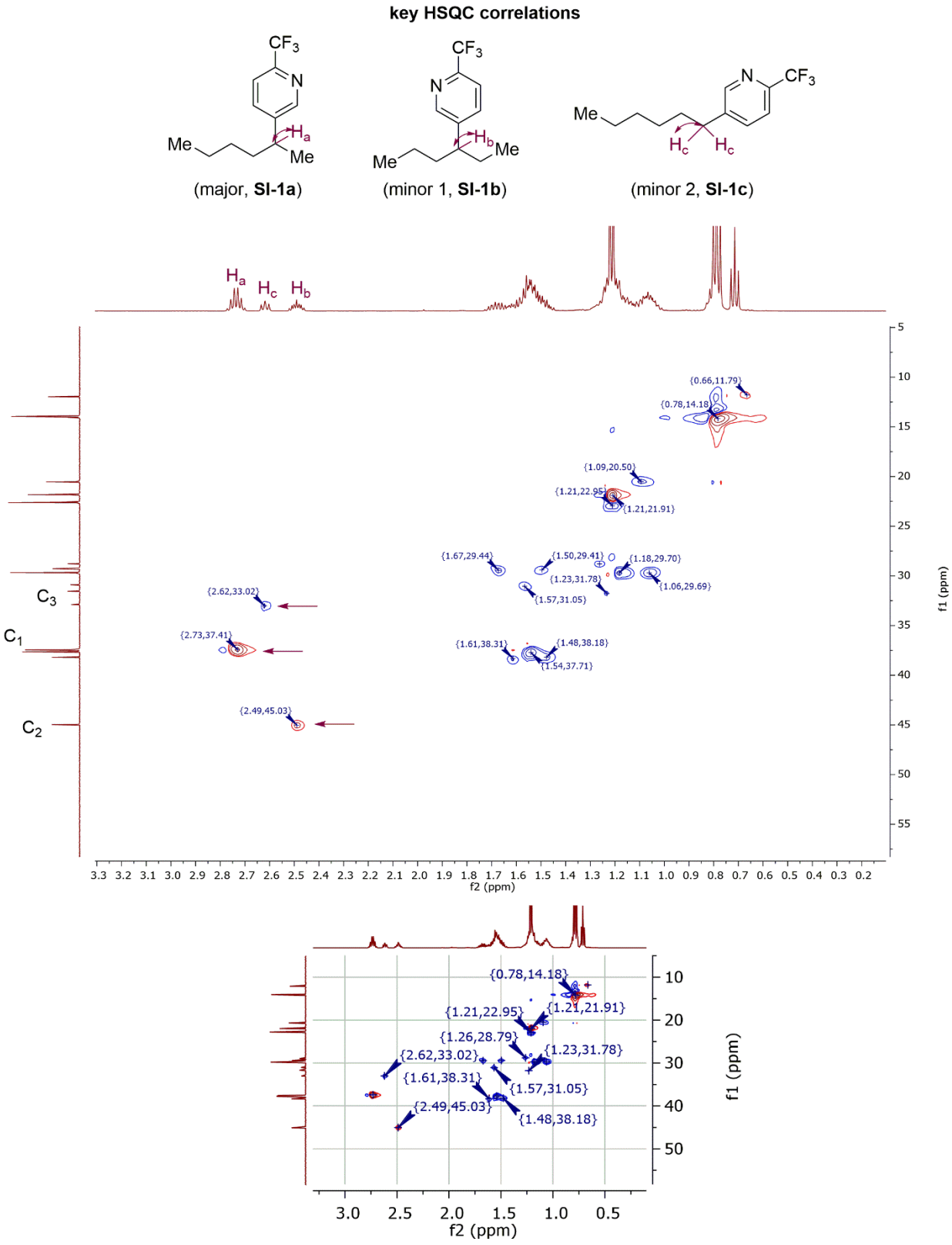
^{1}H NMR (500 MHz, $CDCl_3$) - (**SI-1a**, **SI-1b**, and **SI-1c**, isolated mixture from silica chromatography)



Quantitative ^{13}C NMR (126 MHz, $CDCl_3$) - (**SI-1a**, **SI-1b**, and **SI-1c**, isolated mixture from silica chromatography)

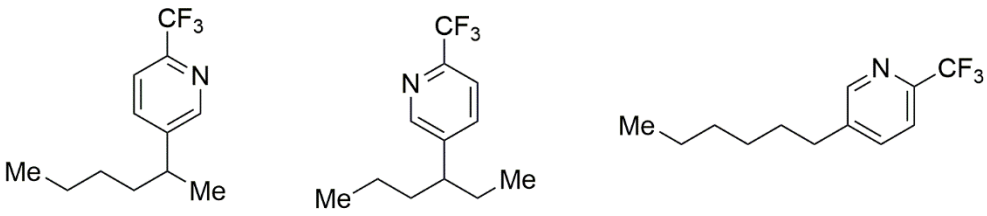


^{19}F NMR (376 MHz, $CDCl_3$) - (**SI-1a**, **SI-1b**, and **SI-1c**, isolated mixture from silica chromatography)

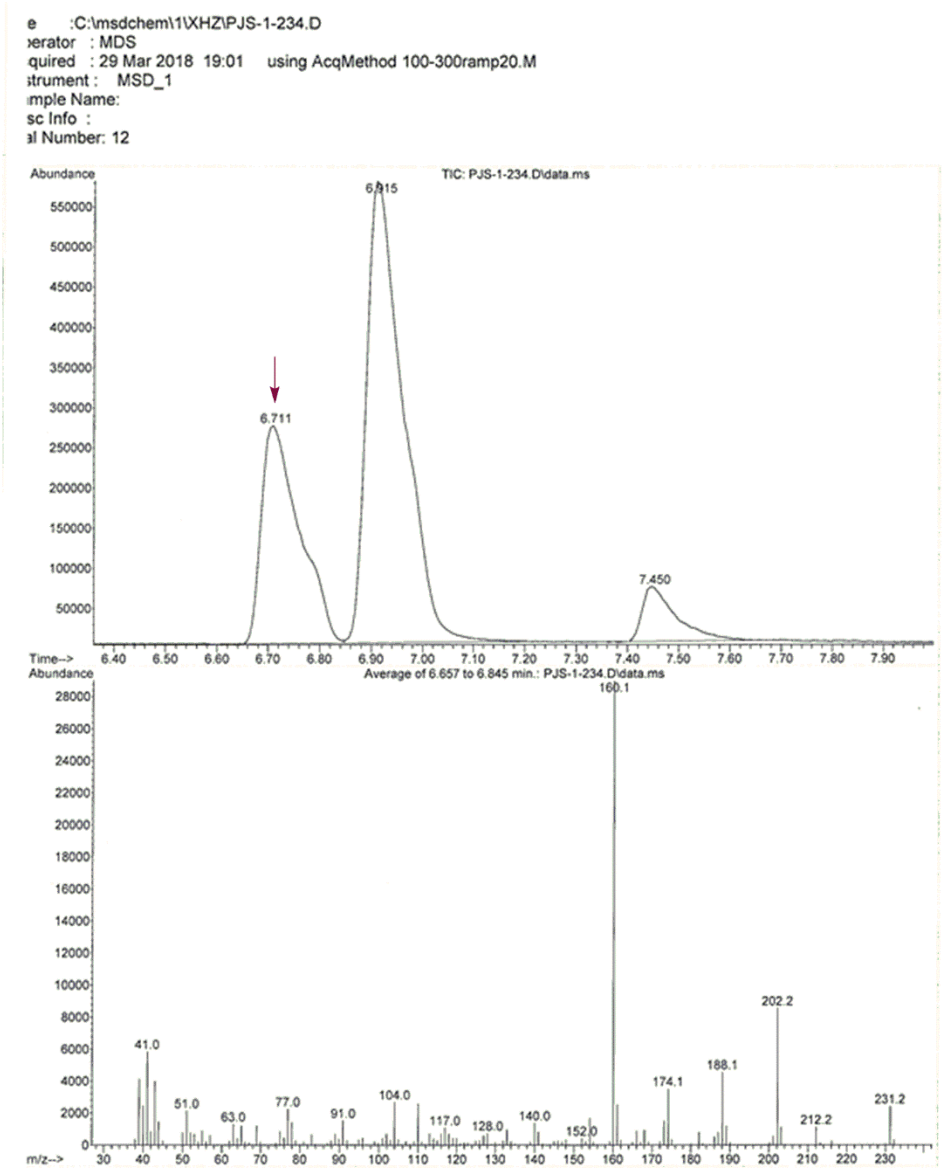


HSQC - (**SI-1a**, **SI-1b**, and **SI-1c**, isolated mixture from silica chromatography)

GCMS

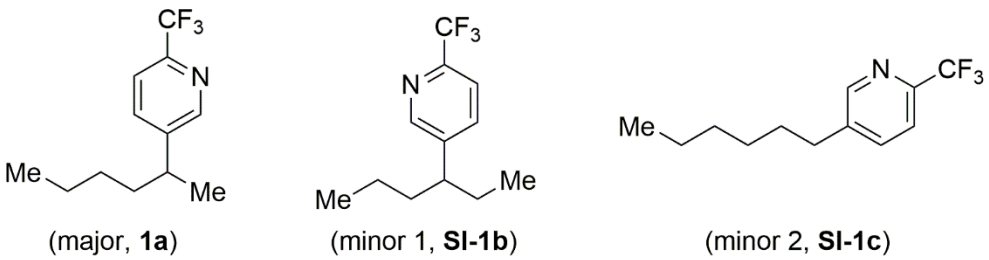


(major, **SI-1a**) (minor 1, **SI-1b**) (minor 2, **SI-1c**)

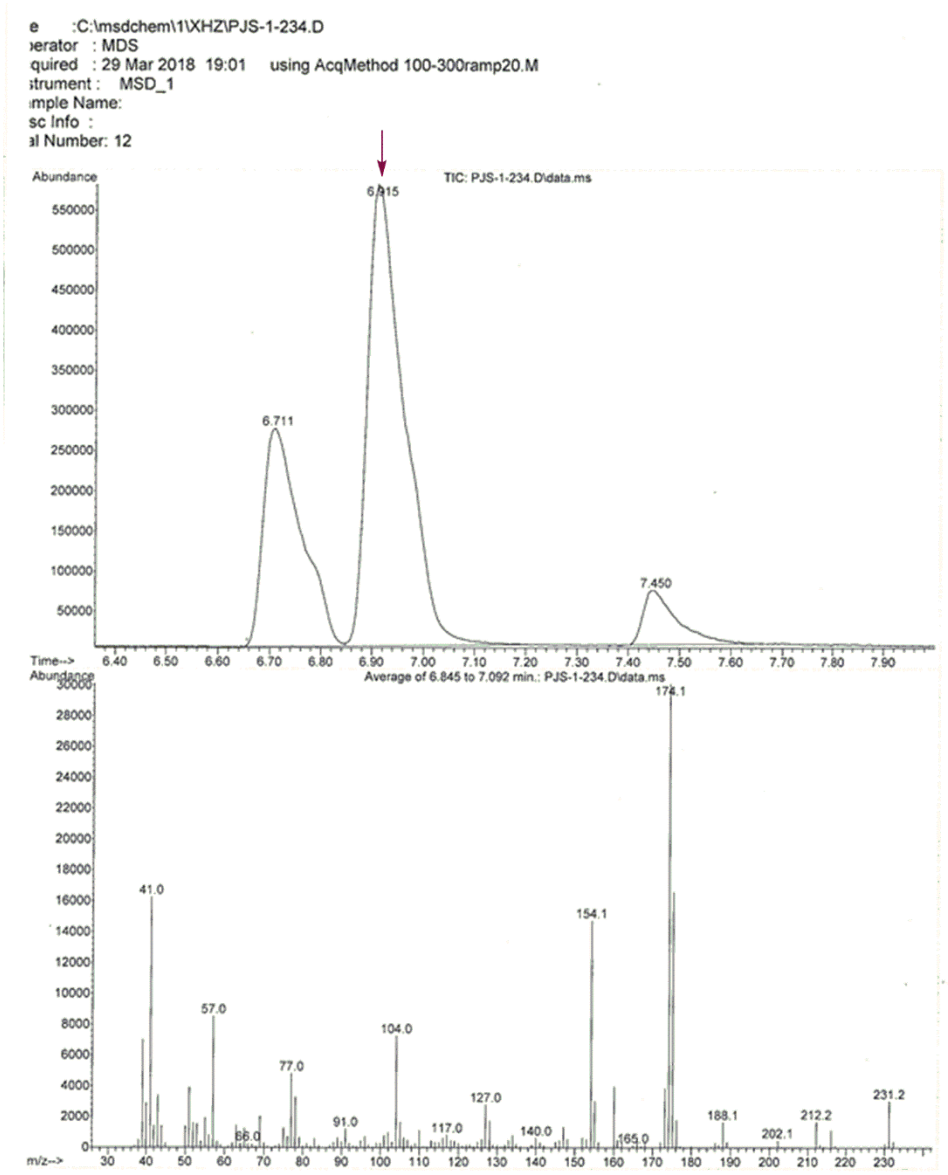


GCMS - (**SI-1a**, **SI-1b**, and **SI-1c**, isolated mixture from silica chromatography)

GCMS

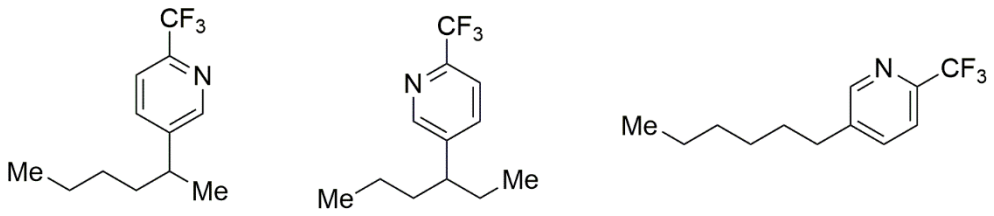


(major, **1a**) (minor 1, **SI-1b**) (minor 2, **SI-1c**)

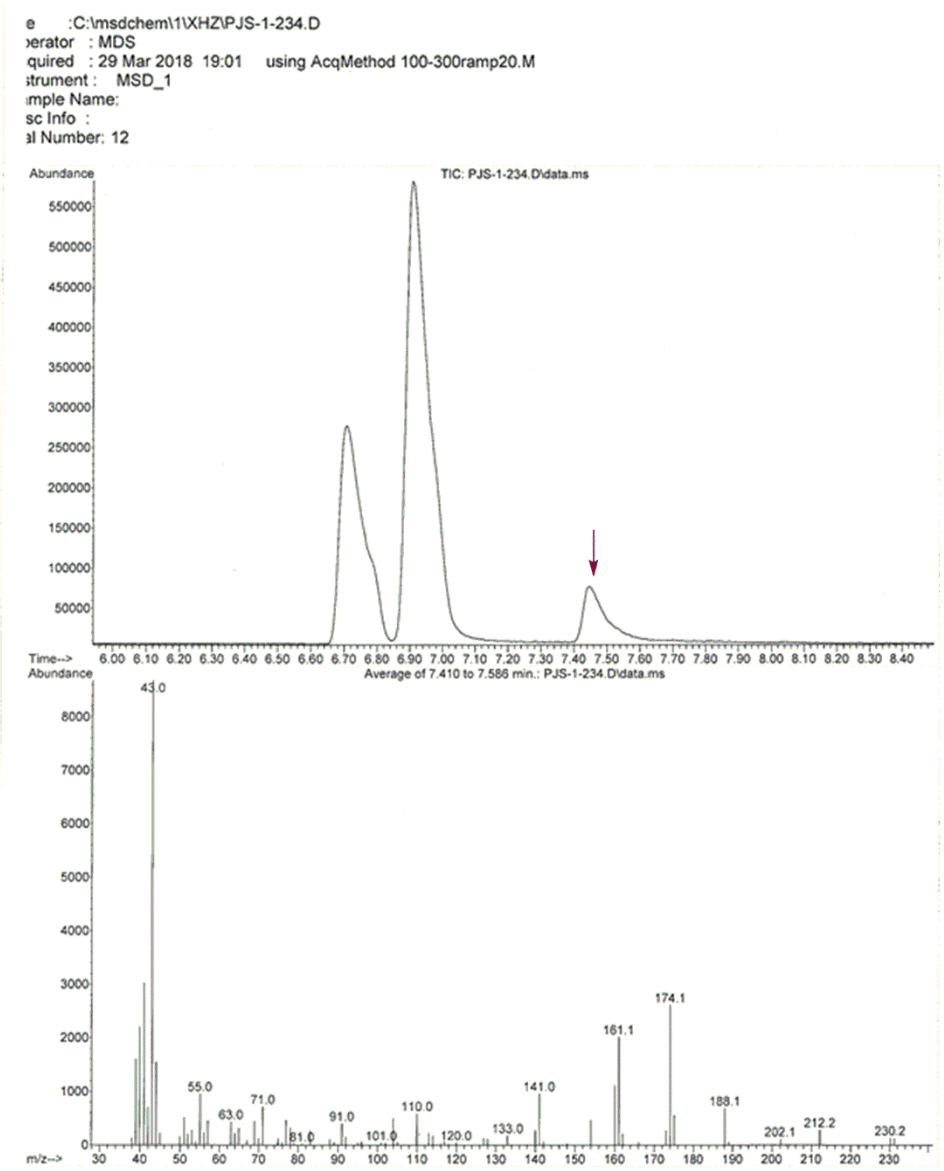


GCMS - (**SI-1a**, **SI-1b**, and **SI-1c**, isolated mixture from silica chromatography)

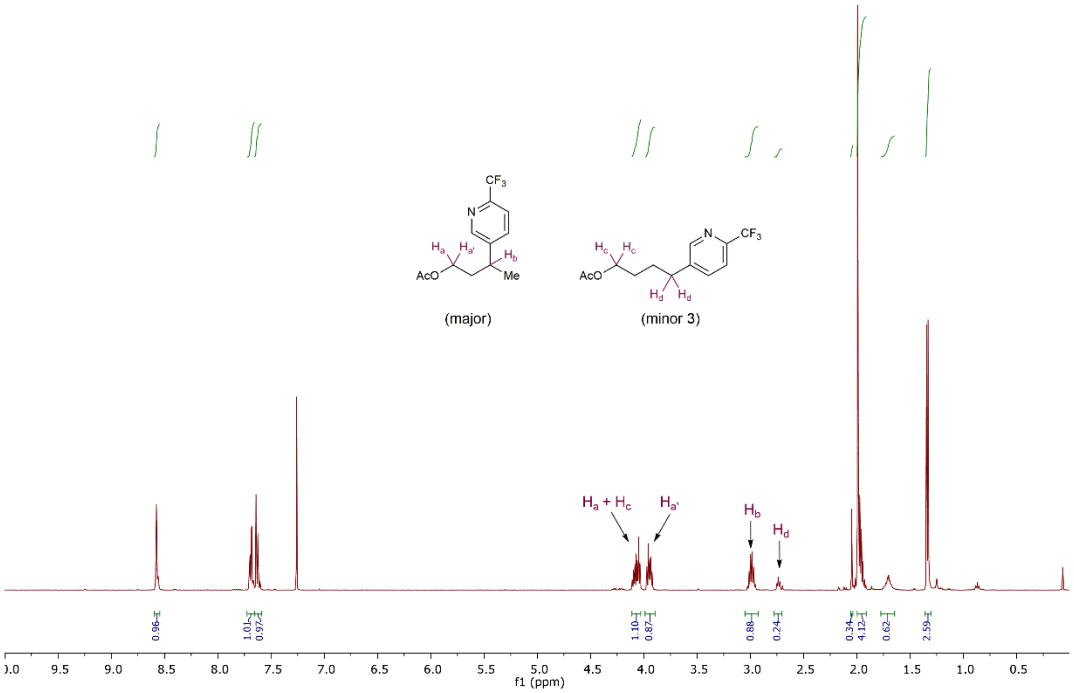
GCMS



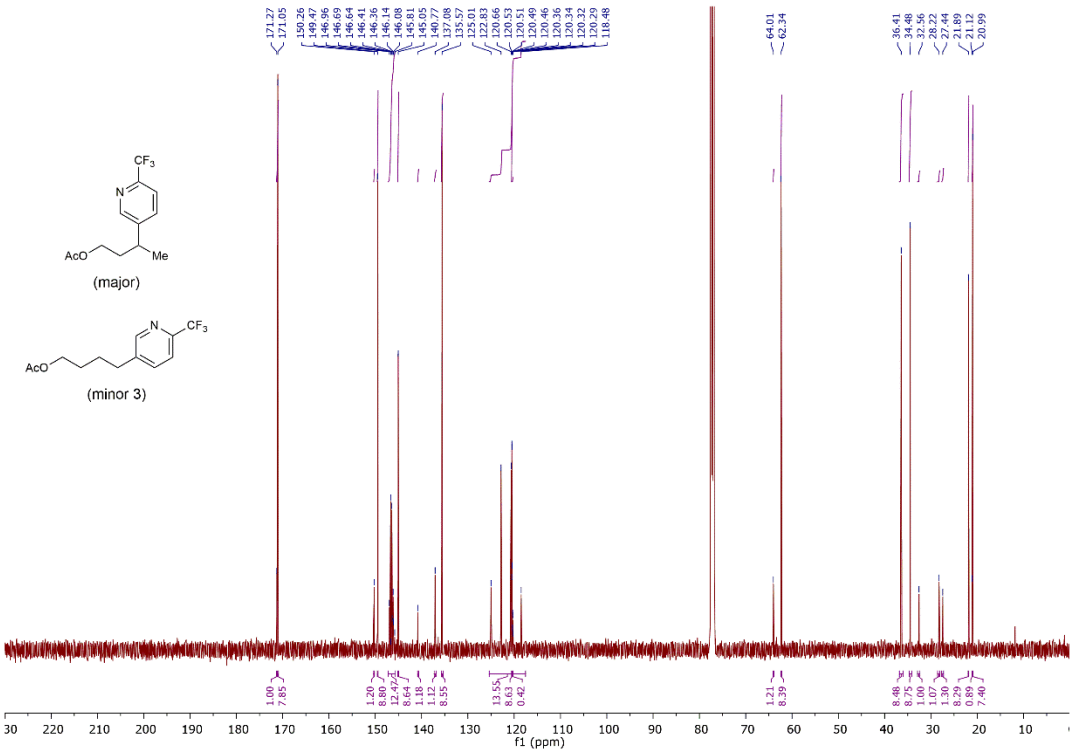
(major, **SI-1a**) (minor 1, **SI-1b**) (minor 2, **SI-1c**)



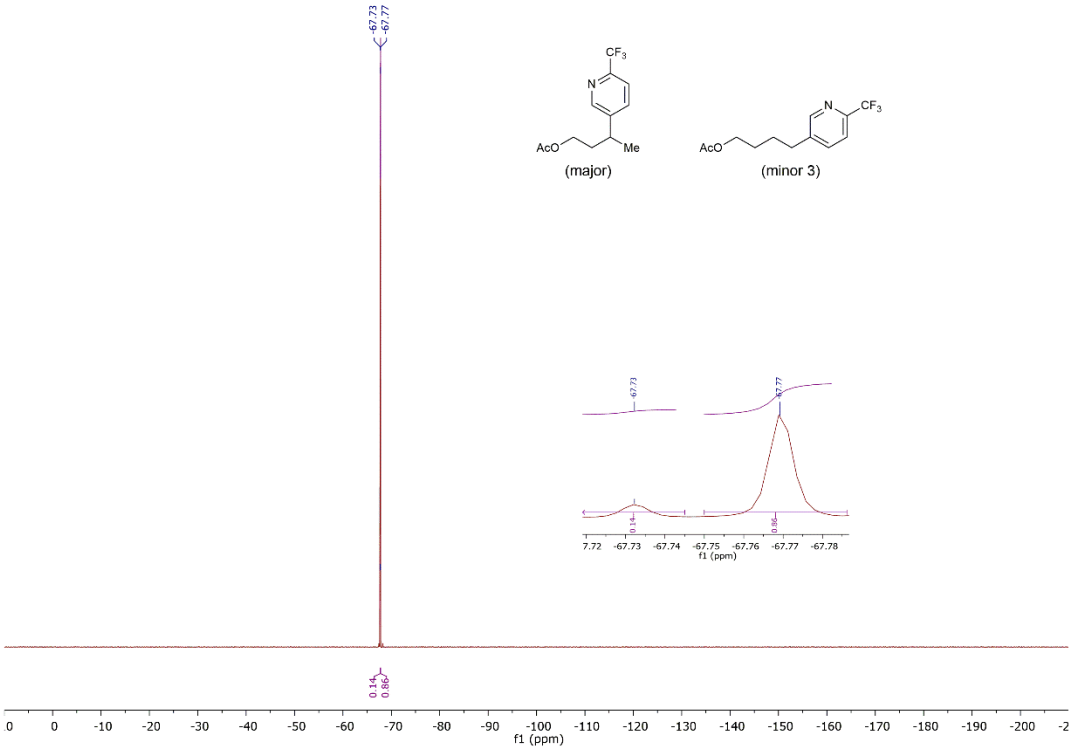
GCMS - (**SI-1a**, **SI-1b**, and **SI-1c**, isolated mixture from silica chromatography)



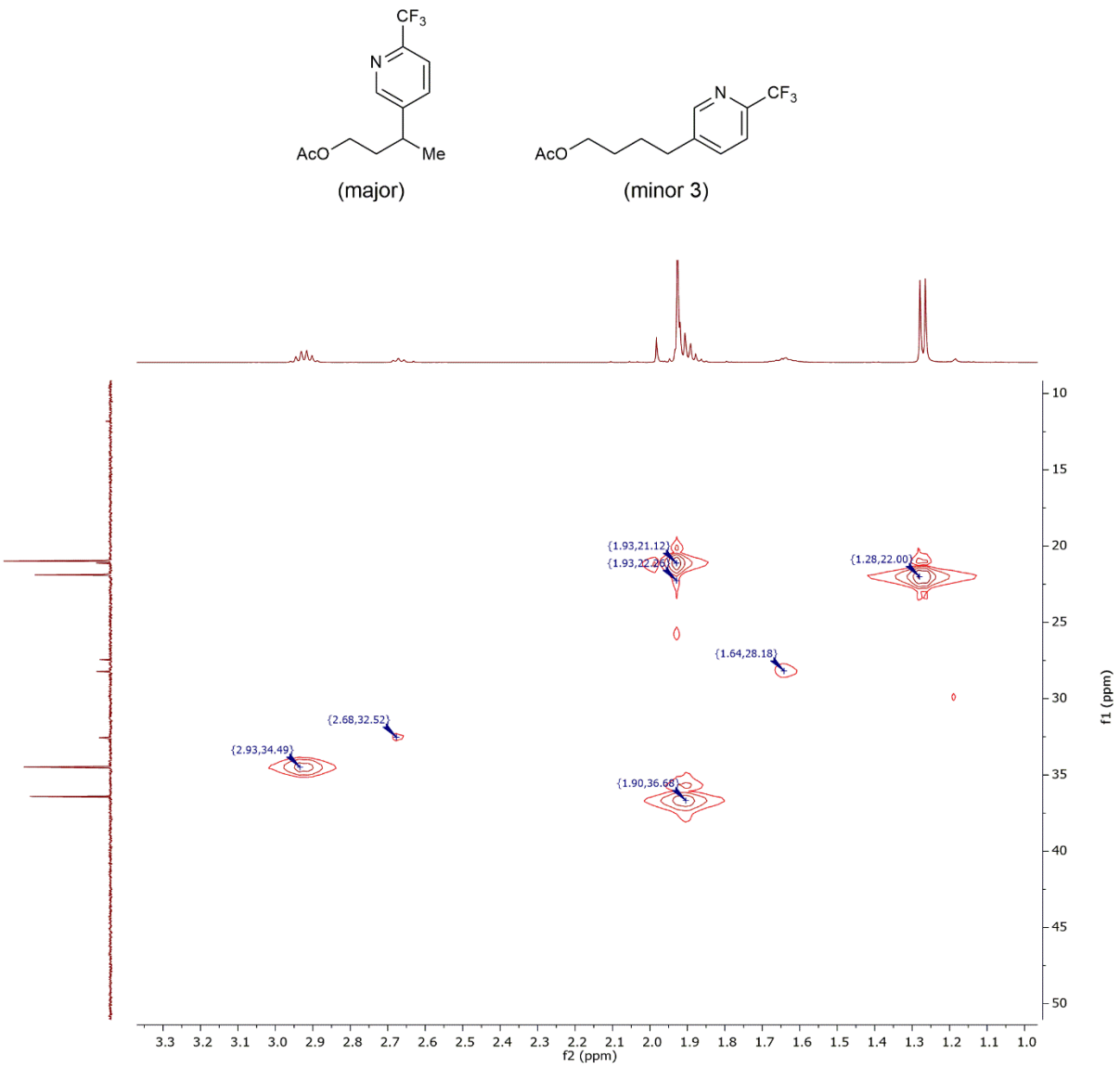
^{1}H NMR (500 MHz, $CDCl_3$) - (18 and SI-18c, isolated mixture from silica chromatography)



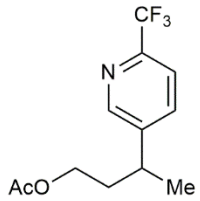
13C NMR (126 MHz, CDCl3) - (18 and SI-18c, isolated mixture from silica chromatography)



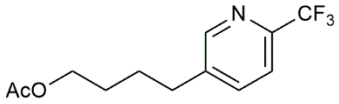
^{19}F NMR (282 MHz, $CDCl_3$) - (**18** and **SI-18c**, isolated mixture from silica chromatography)



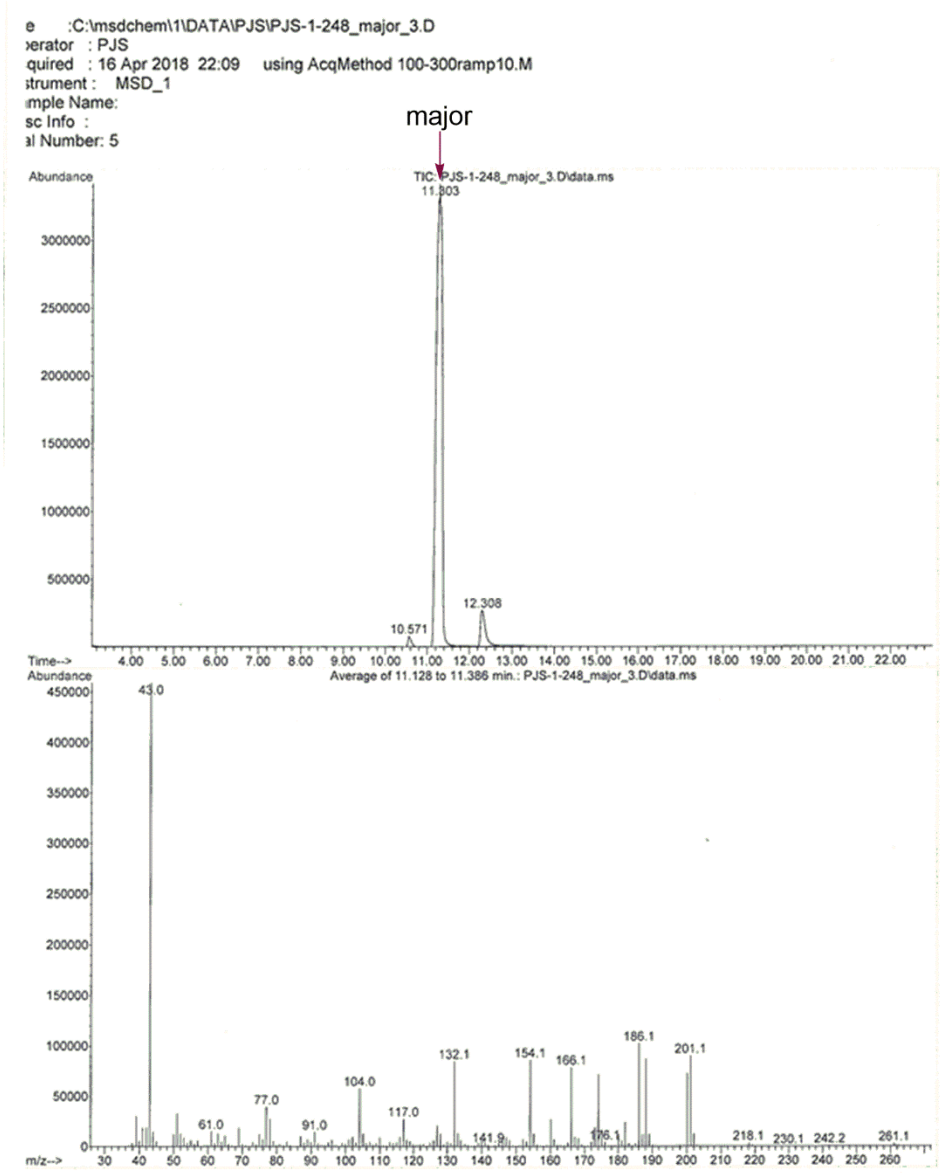
HSQC - (**18** and **SI-18c**, isolated mixture from silica chromatography)



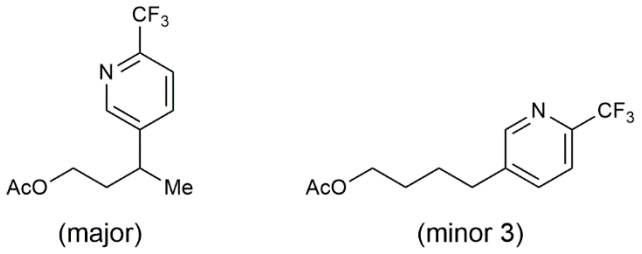
(major)

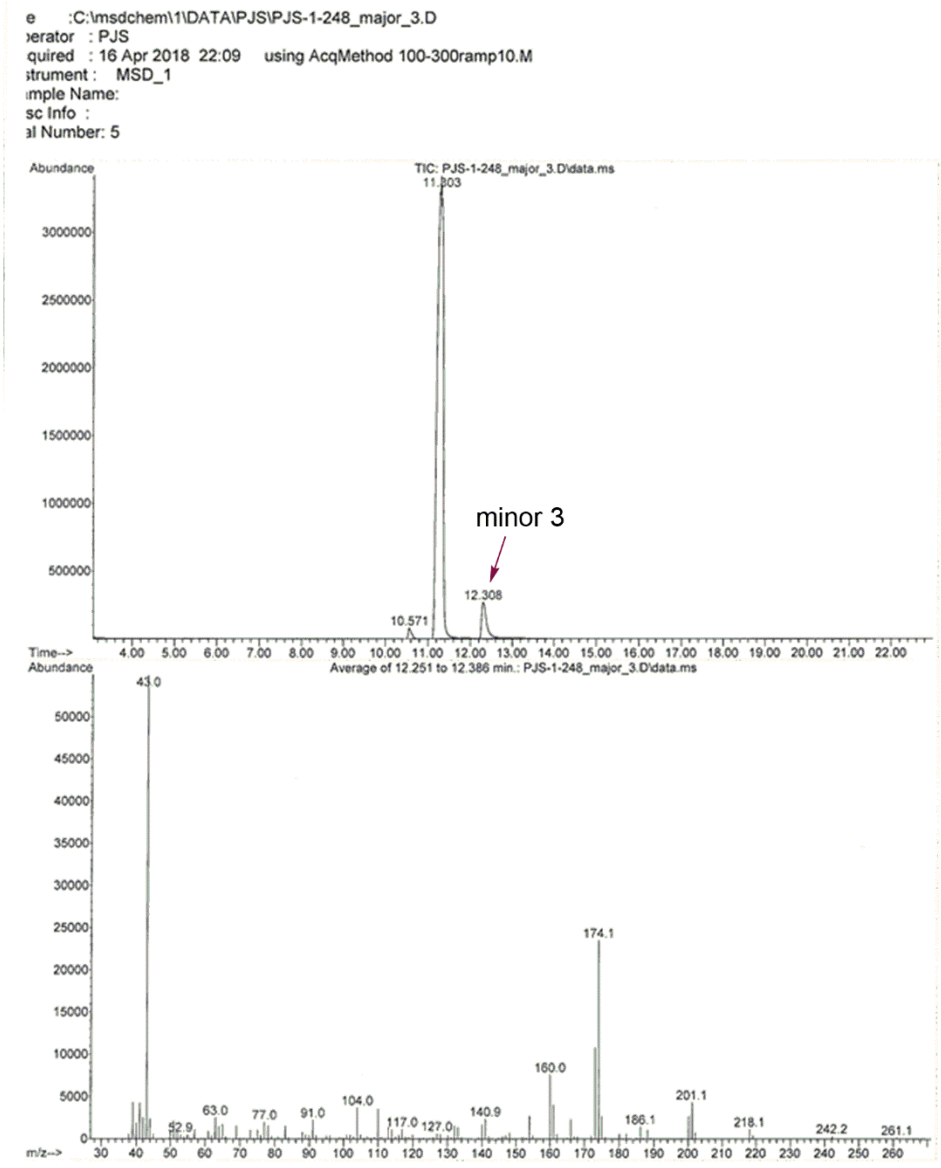


(minor 3)

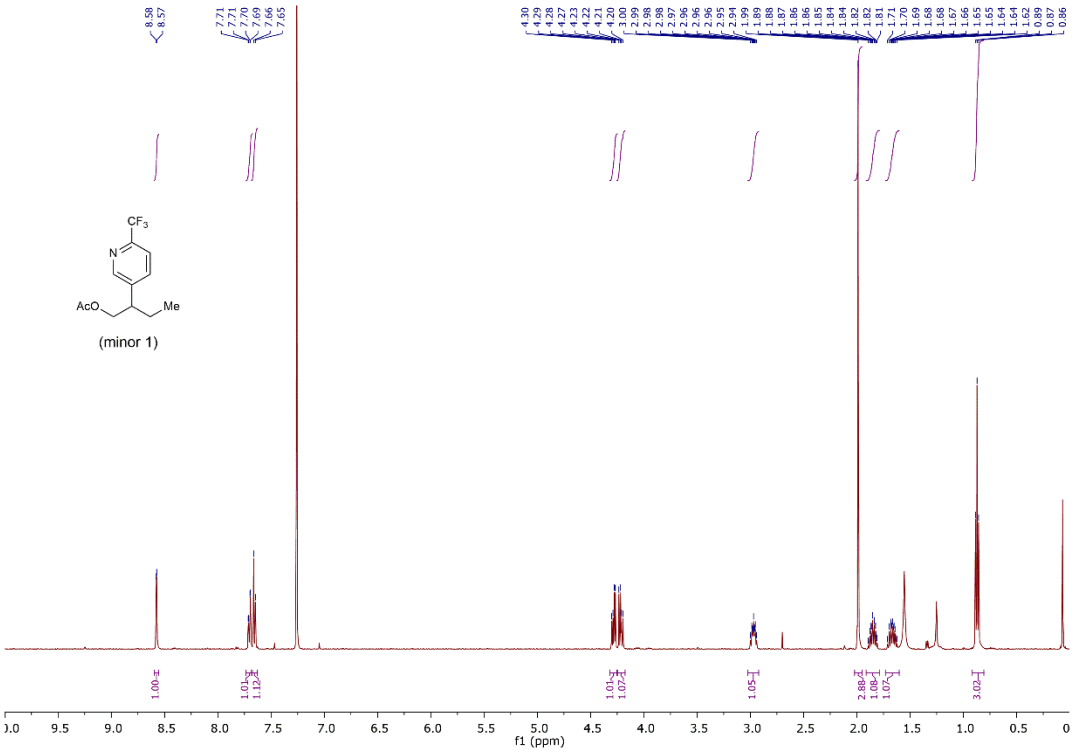


GCMS - (**18** and **SI-18c**, isolated mixture from silica chromatography)

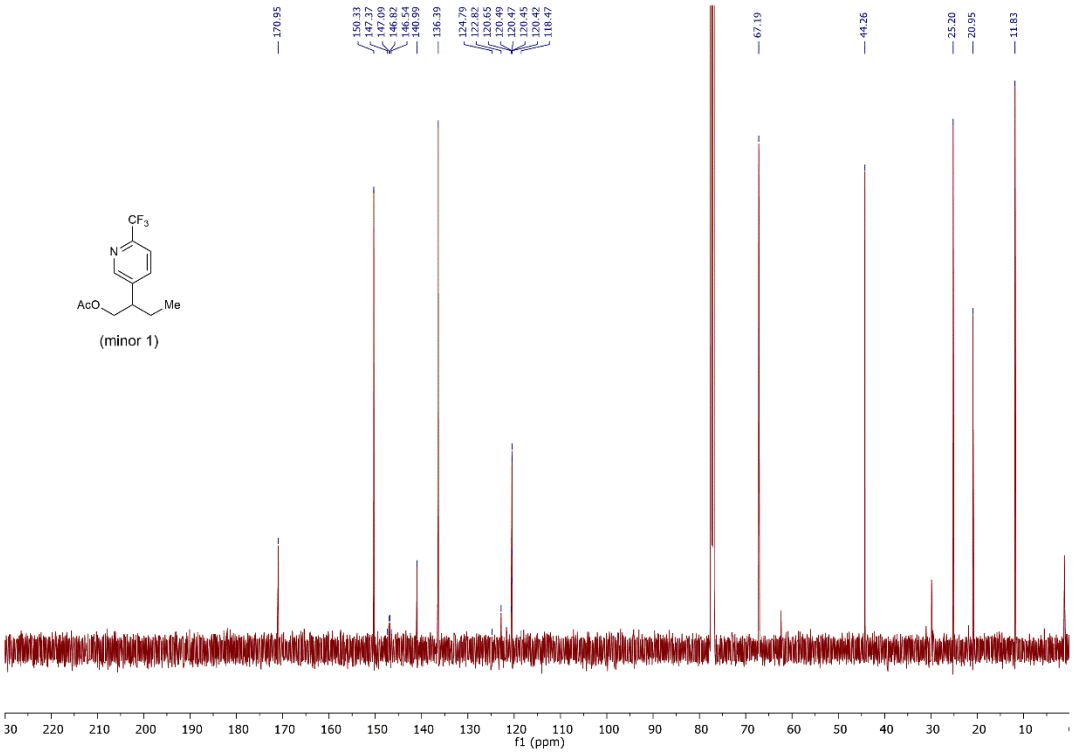




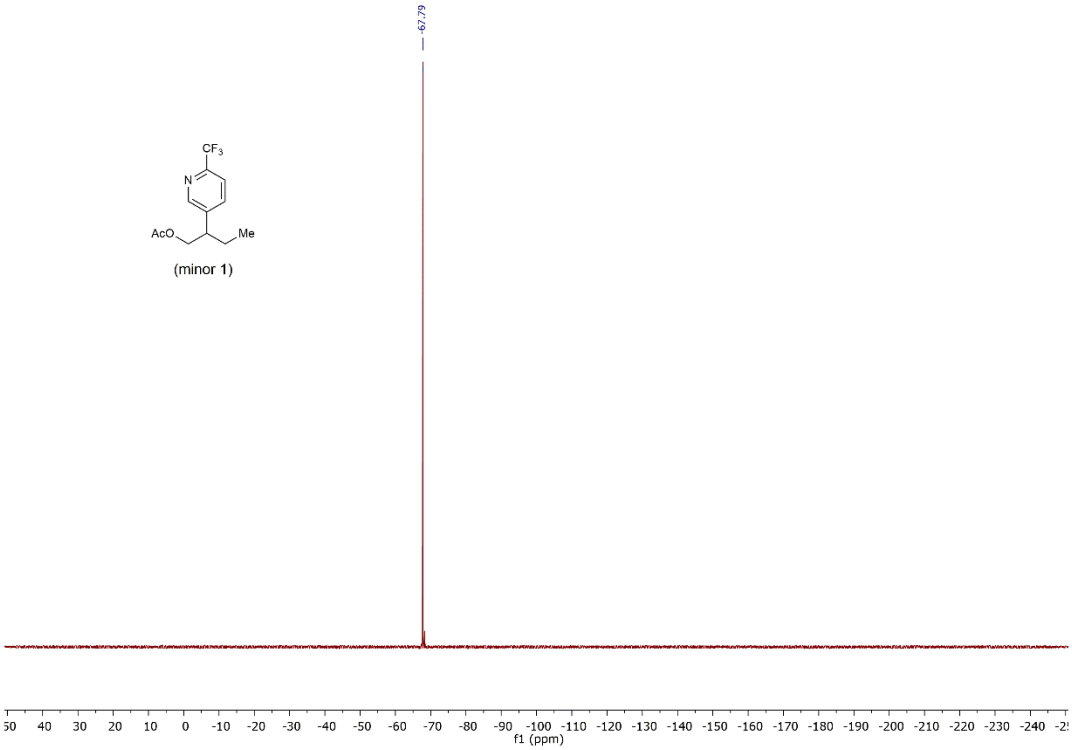
GCMS - (**18** and **SI-18c**, isolated mixture from silica chromatography)



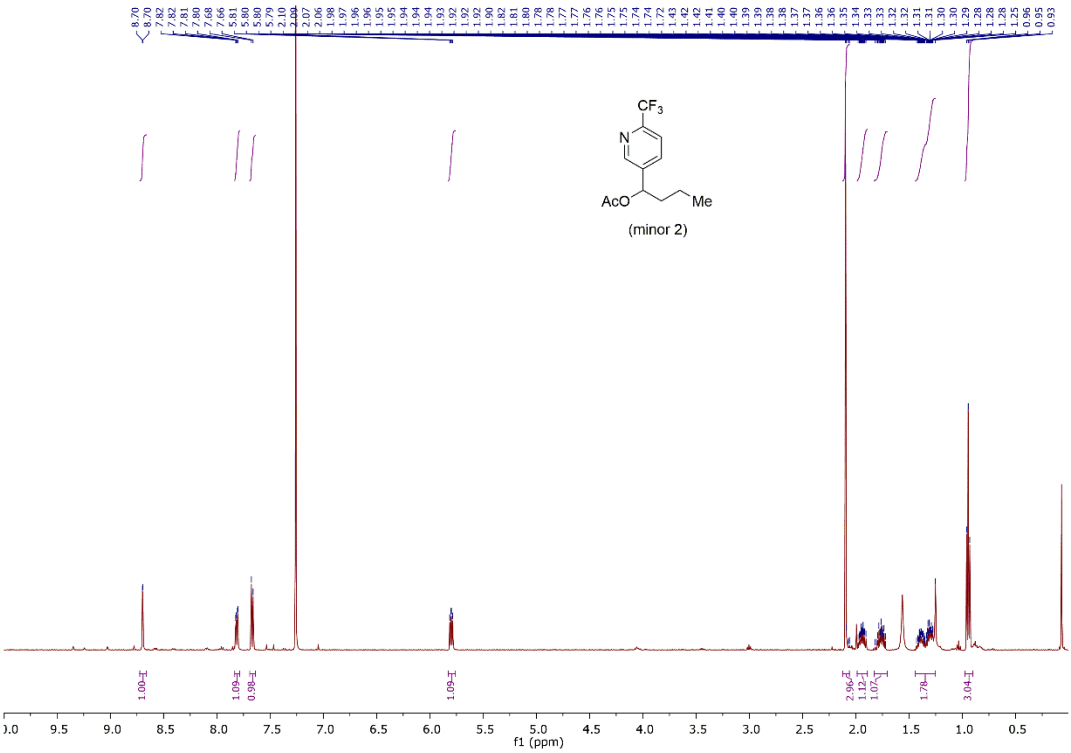
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-18a)



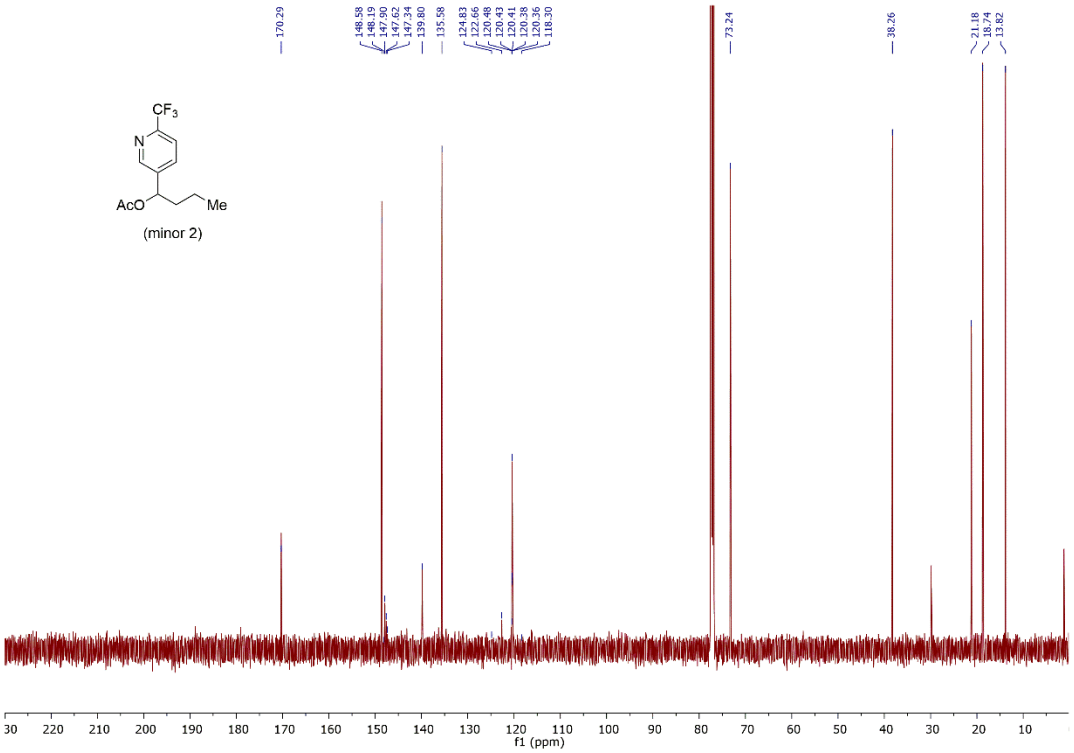
13C NMR (126 MHz, CDCl3) - (SI-18a)



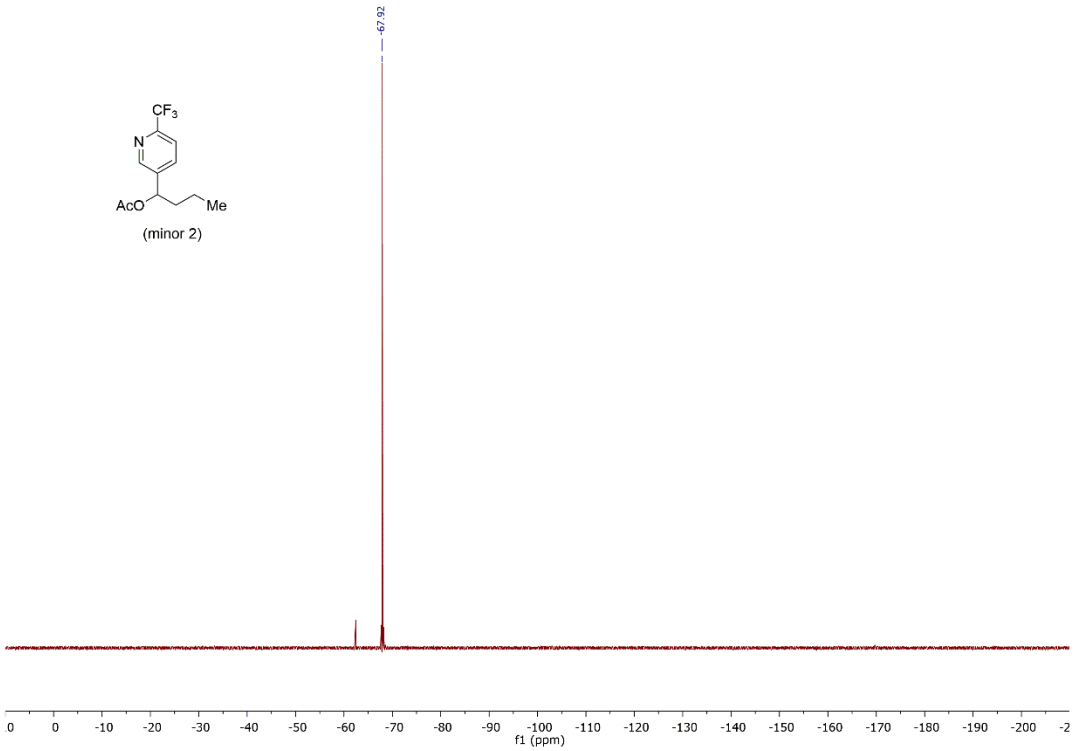
^{19}F NMR (282 MHz, $CDCl_3$) - (SI-18a)



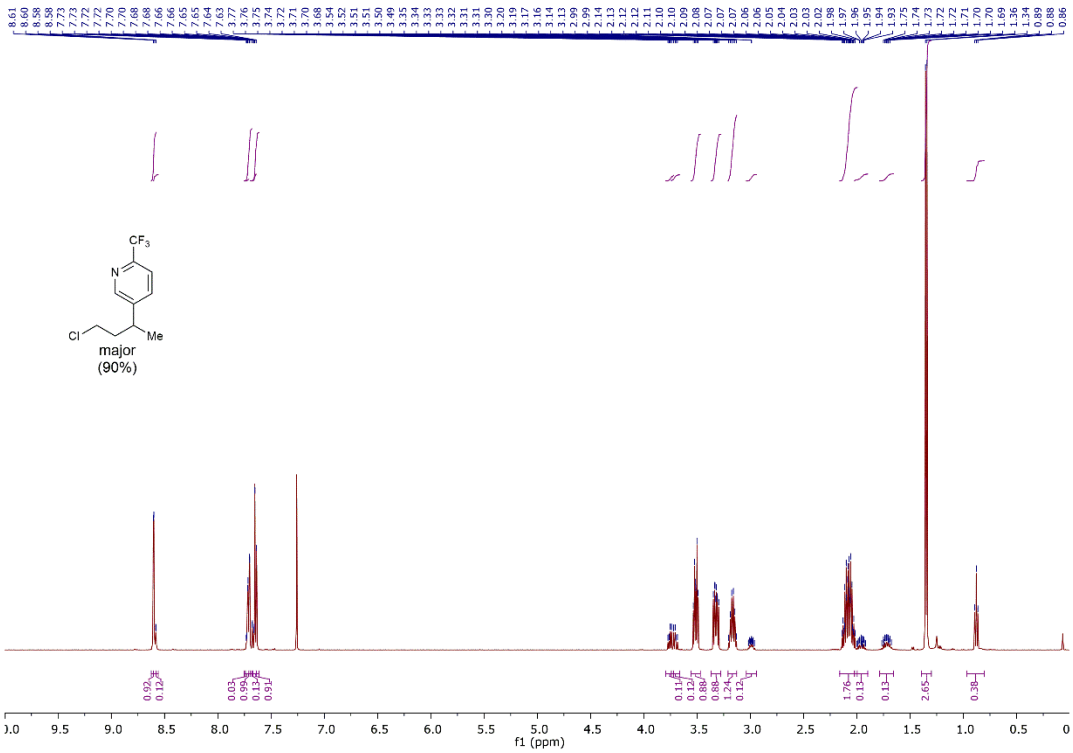
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-18b)



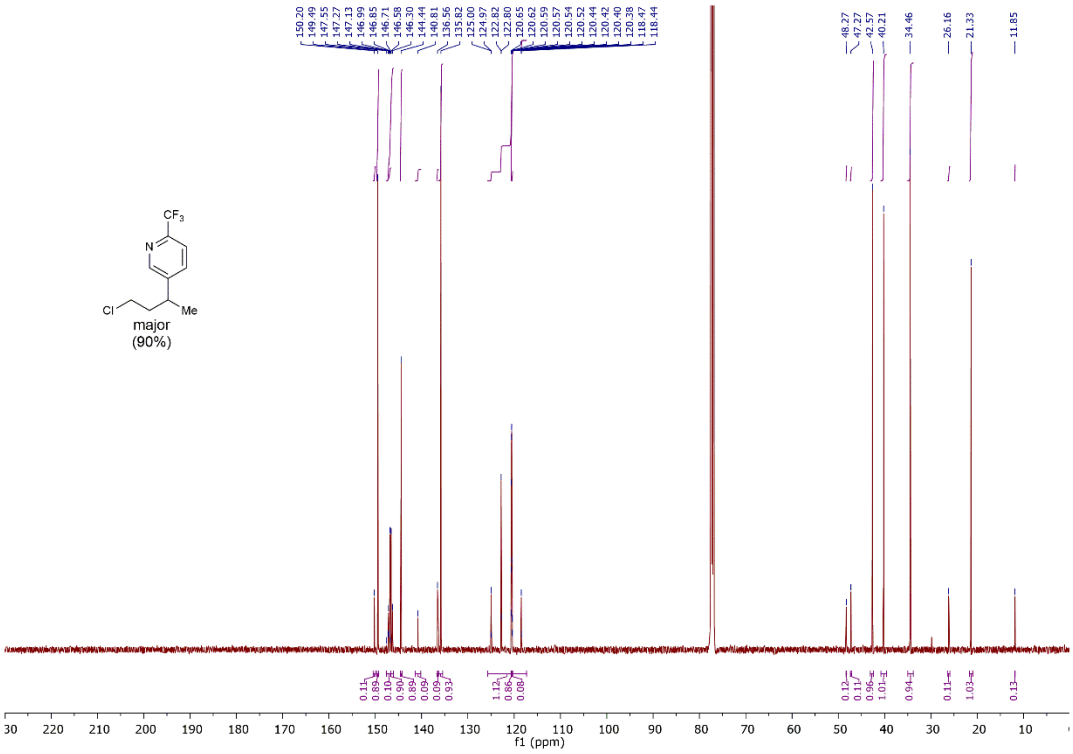
13C NMR (126 MHz, CDCl3) - (SI-18b)



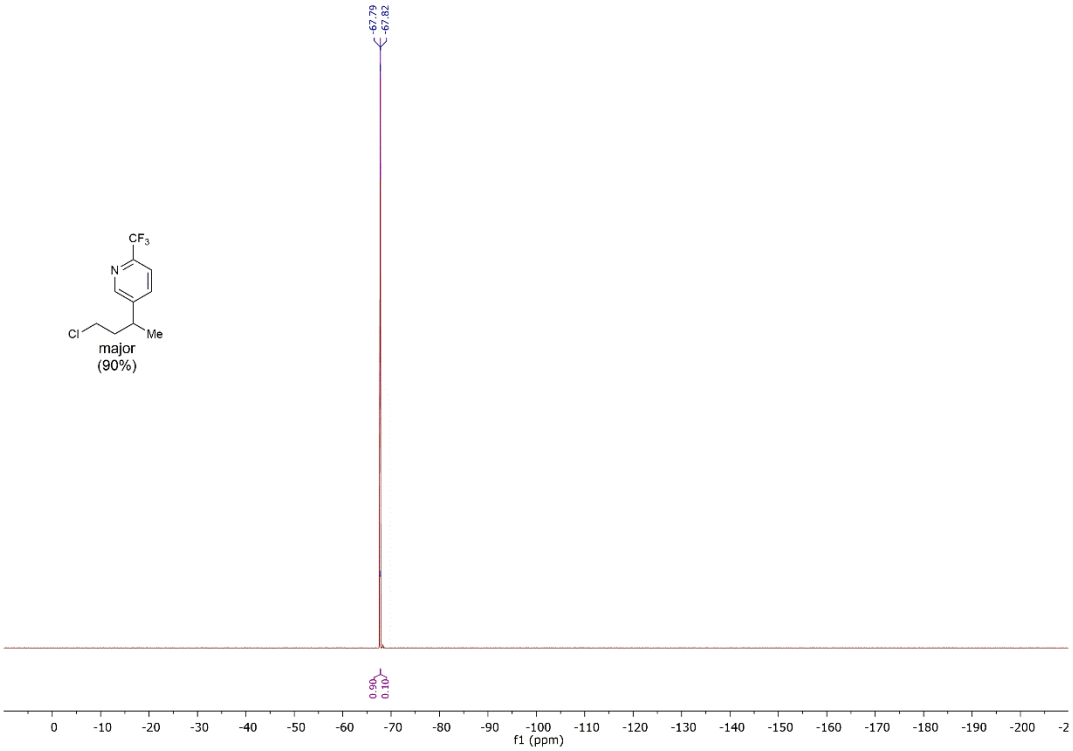
^{19}F NMR (282 MHz, $CDCl_3$) - (SI-18b)



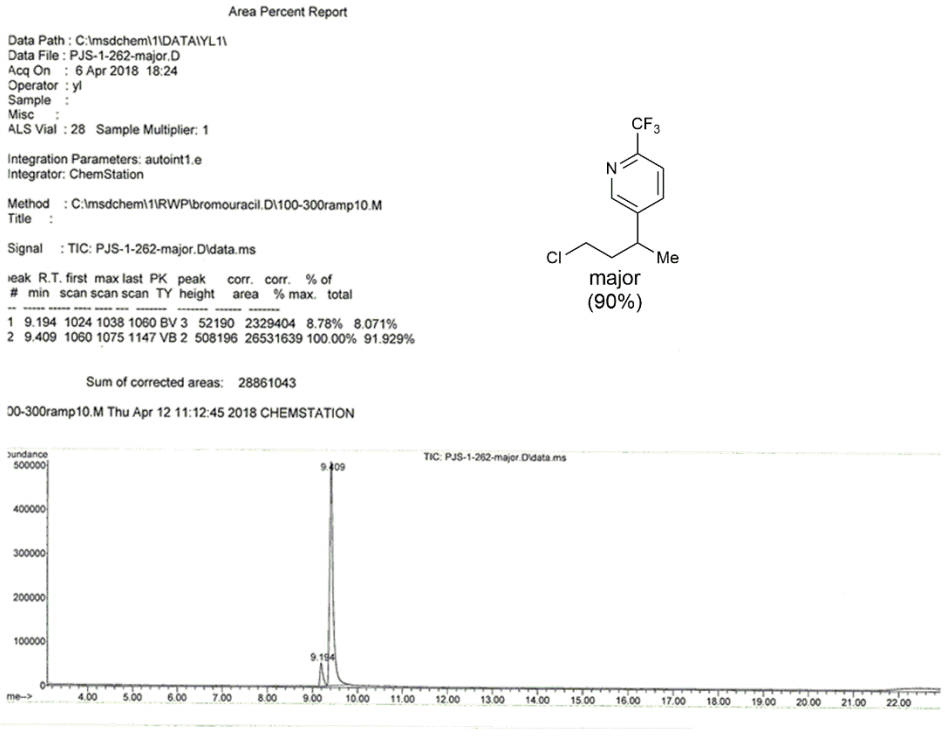
^{1}H NMR (500 MHz, $CDCl_3$) - (**19** and unidentified isomer)



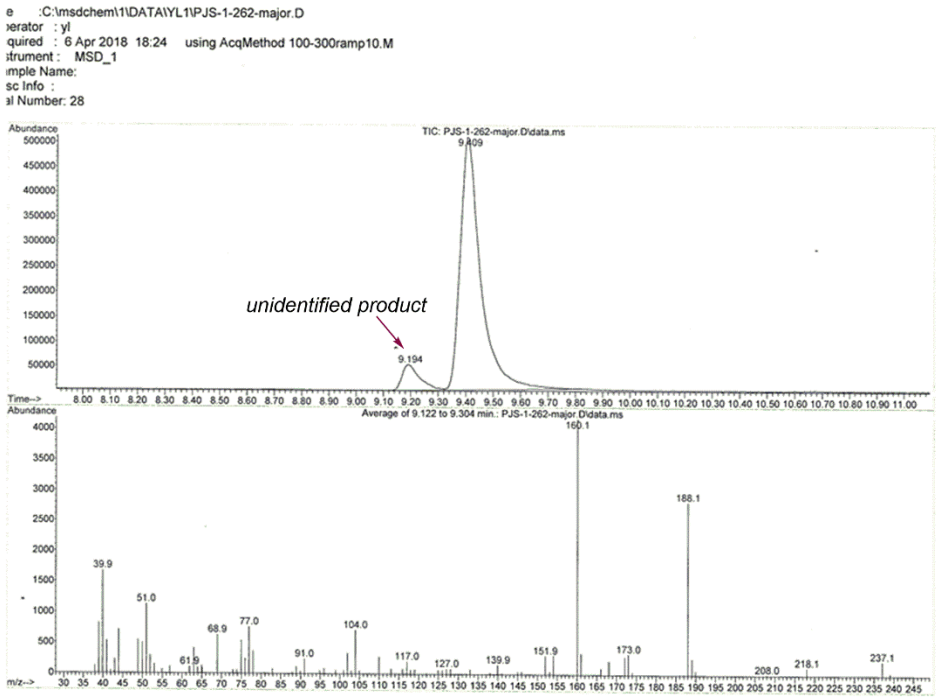
Quantitative ^{13}C NMR (126 MHz, CDCl$_3$) - (**19** and unidentified isomer)



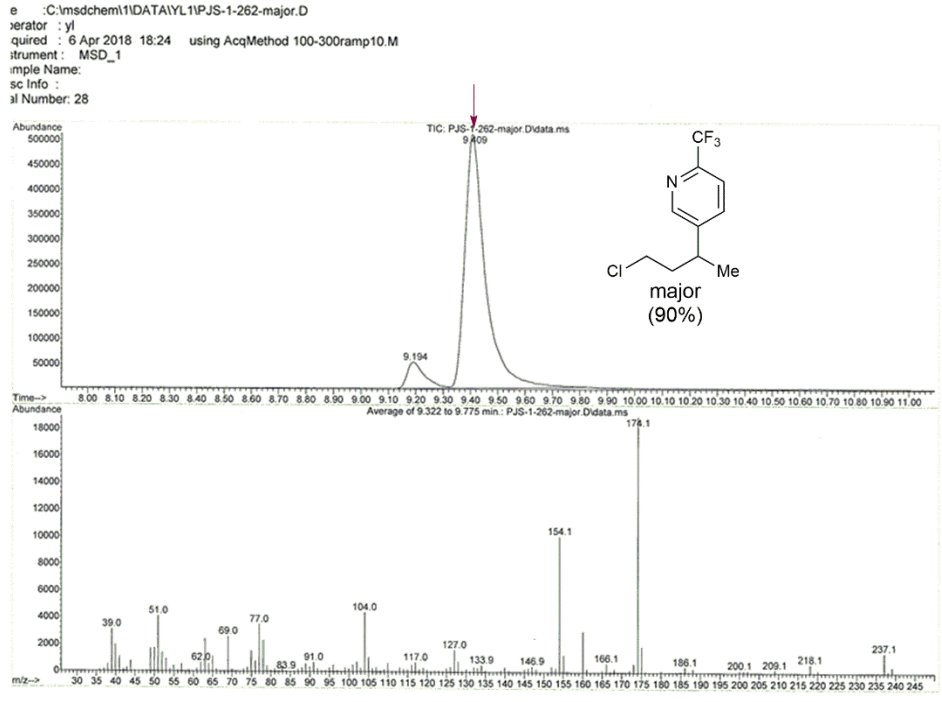
^{19}F NMR (376 MHz, CDCl$_3$) - (**19** and unidentified isomer)



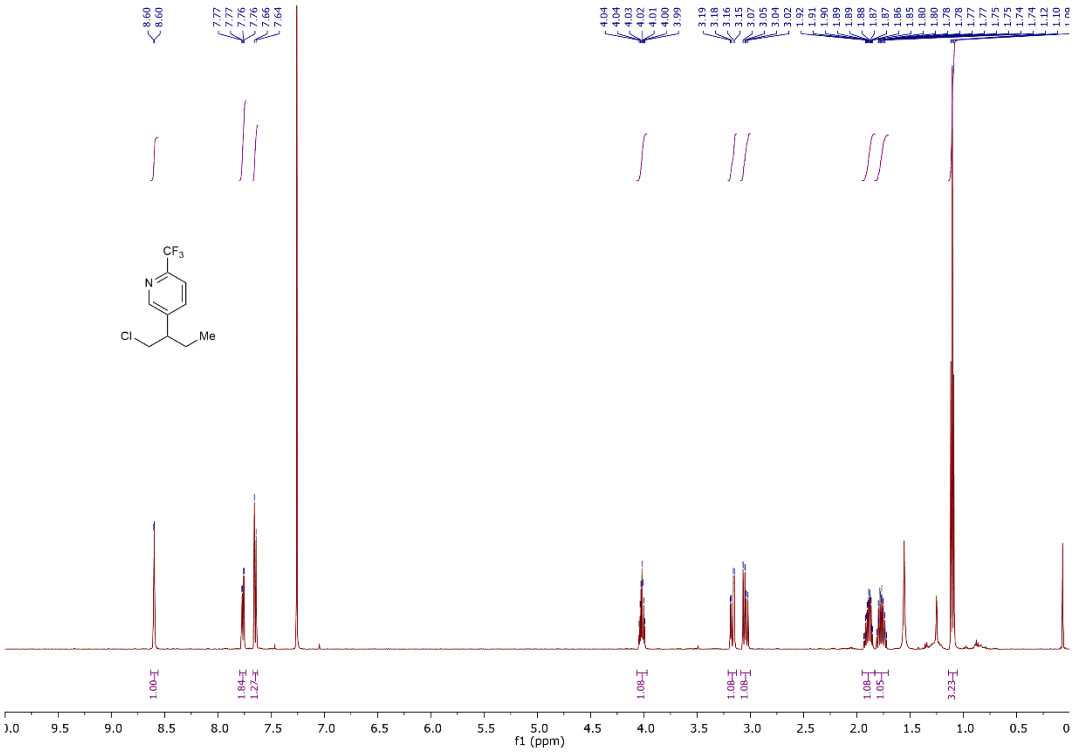
GCMS – (**19** and unidentified isomer)



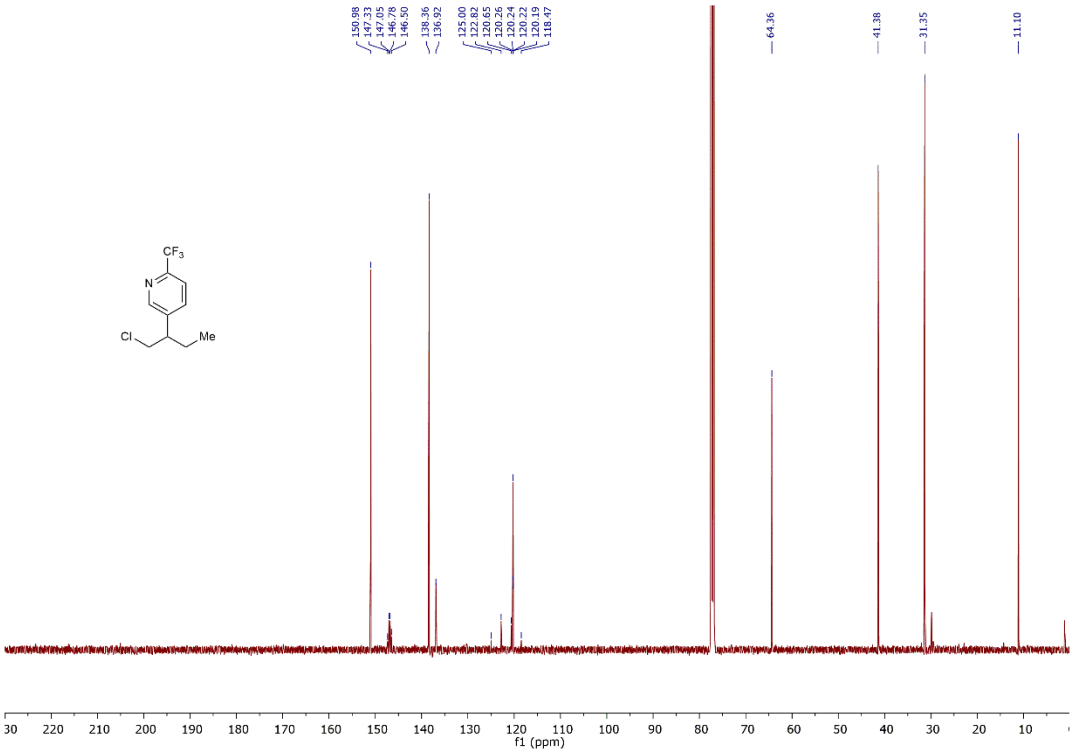
GCMS – (**19** and unidentified isomer)



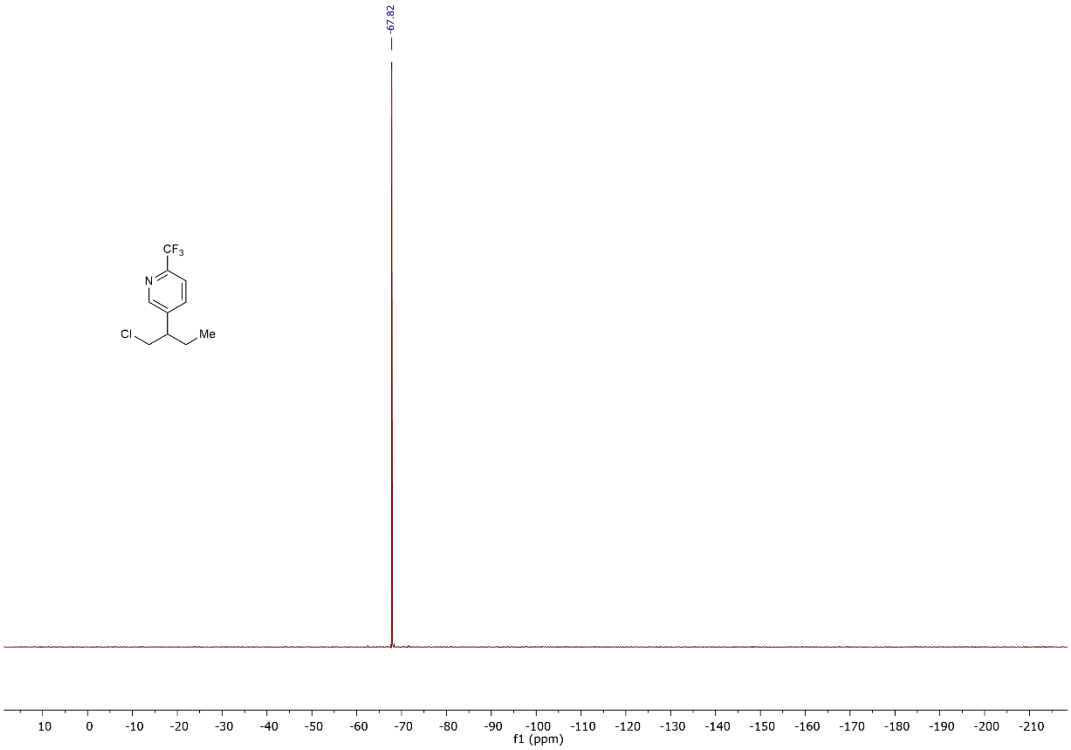
GCMS – (**19** and unidentified isomer)



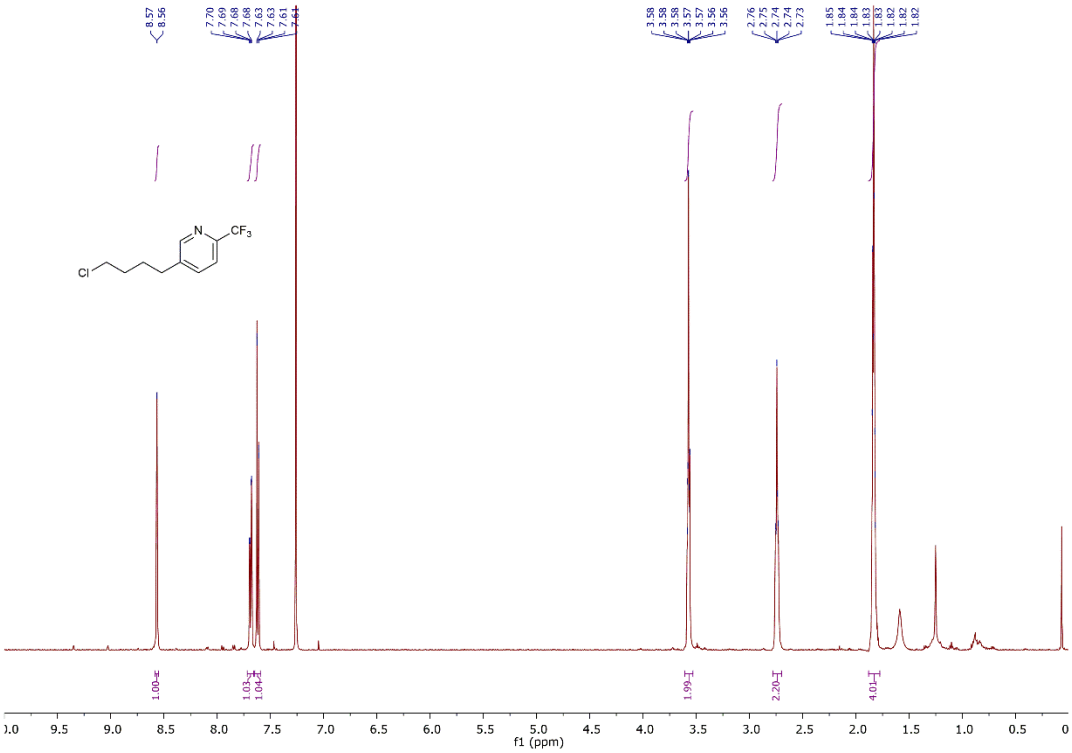
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-19a)



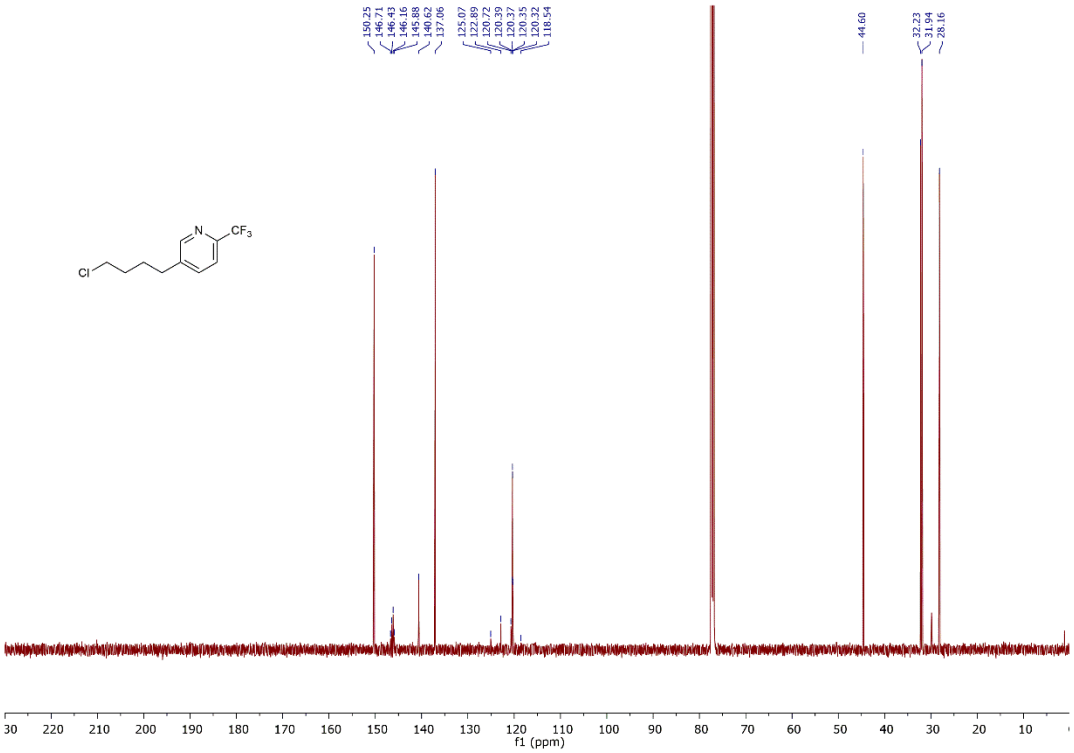
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-19a)



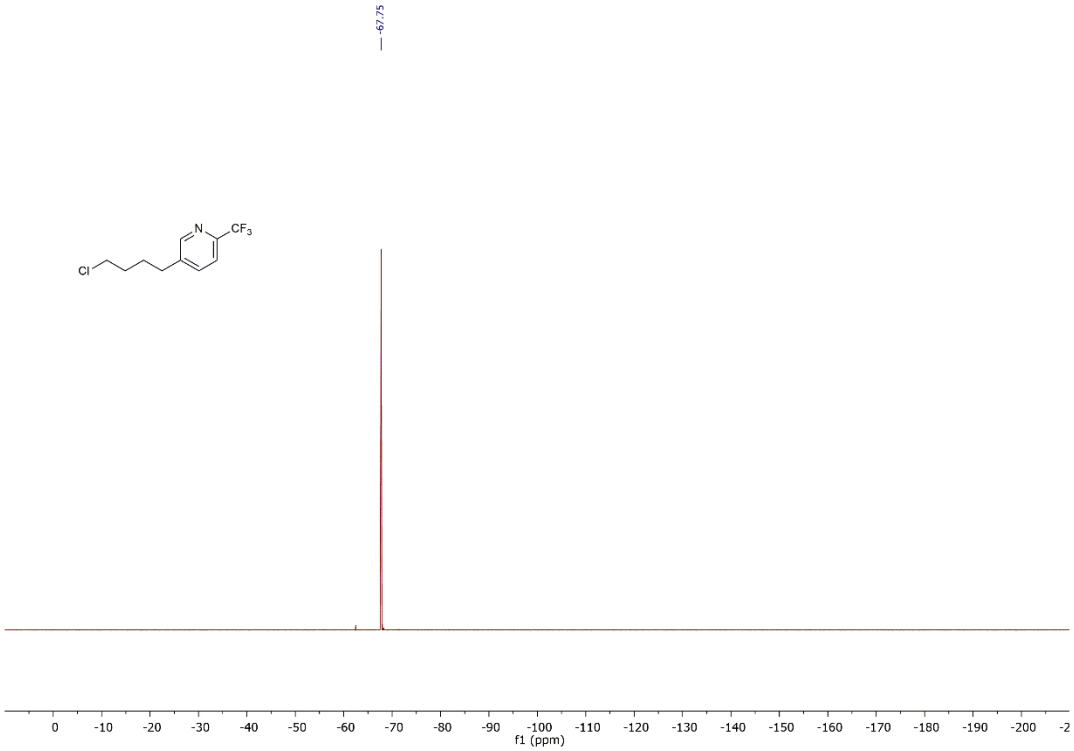
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-19a)



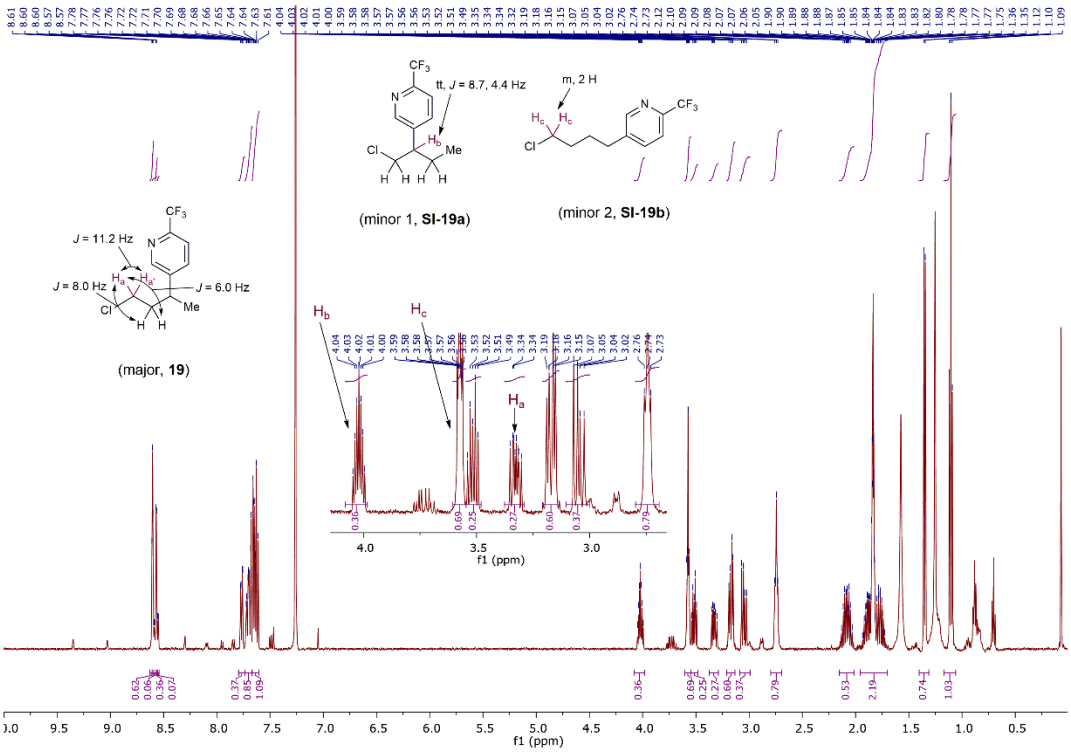
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-19b)



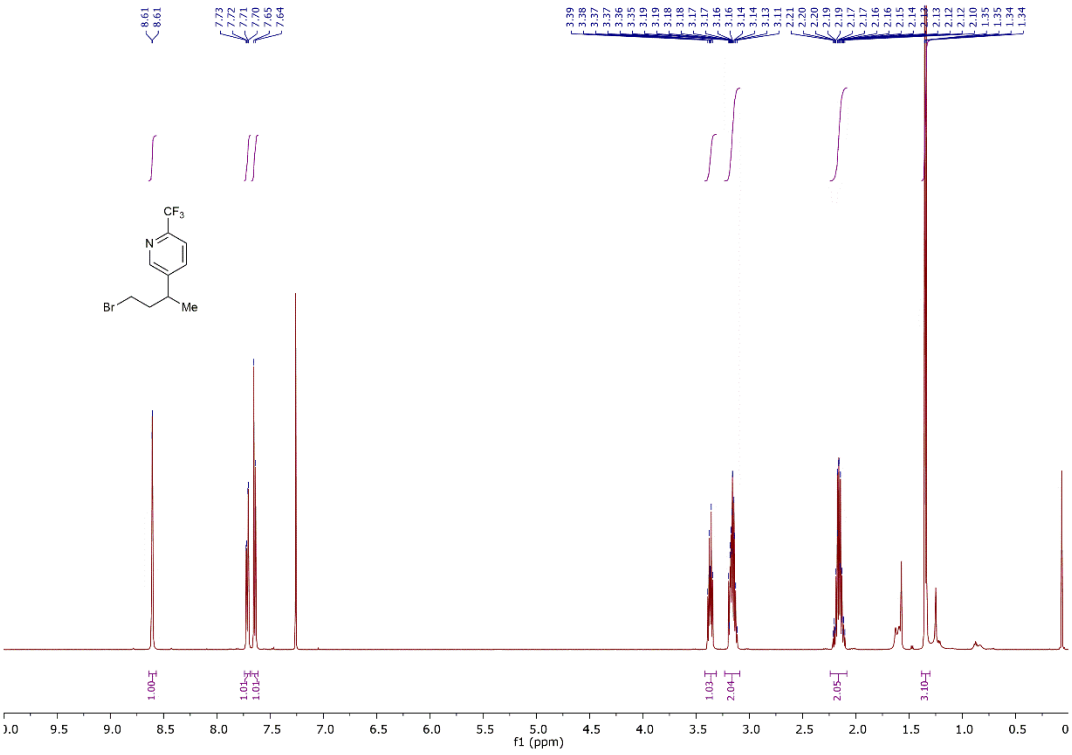
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-19b)



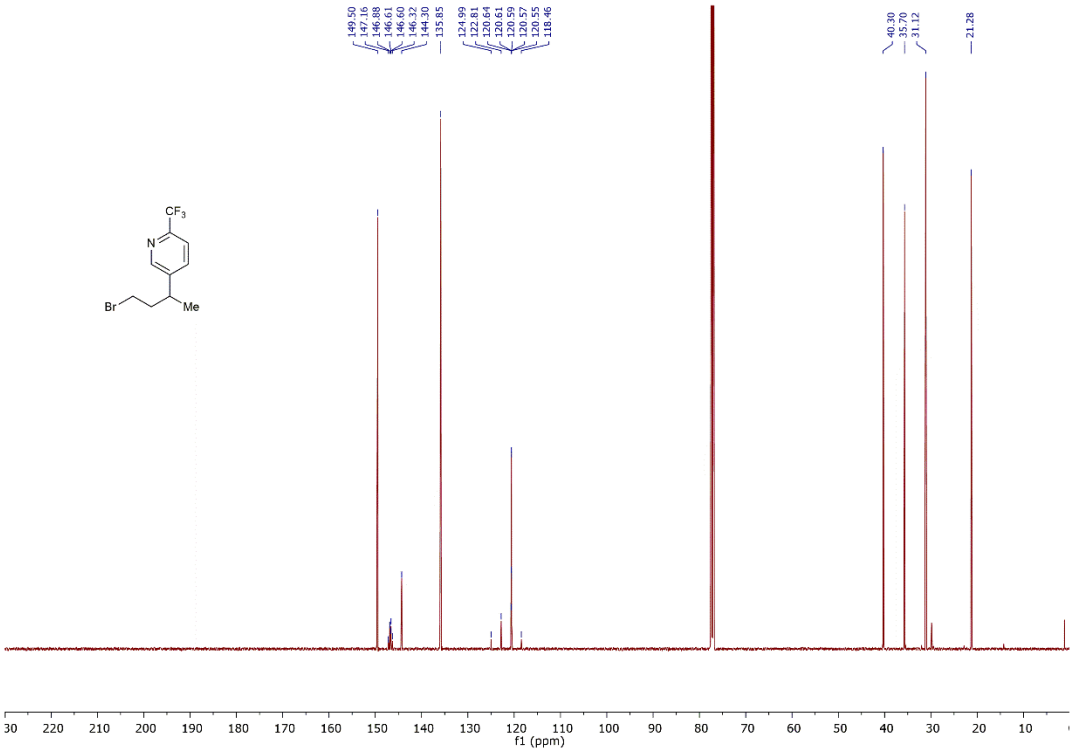
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-19b)



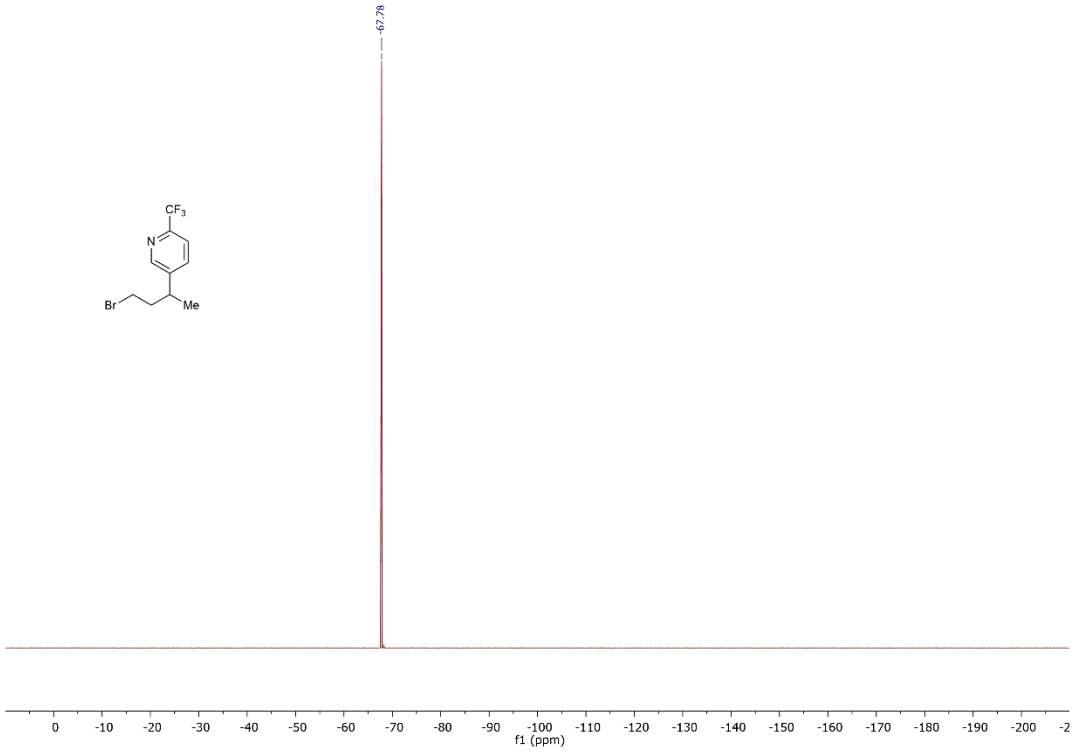
^{1}H NMR (500 MHz, $CDCl_3$) - (19, SI-19a, and SI-19b, isolated mixture from silica chroamtography)



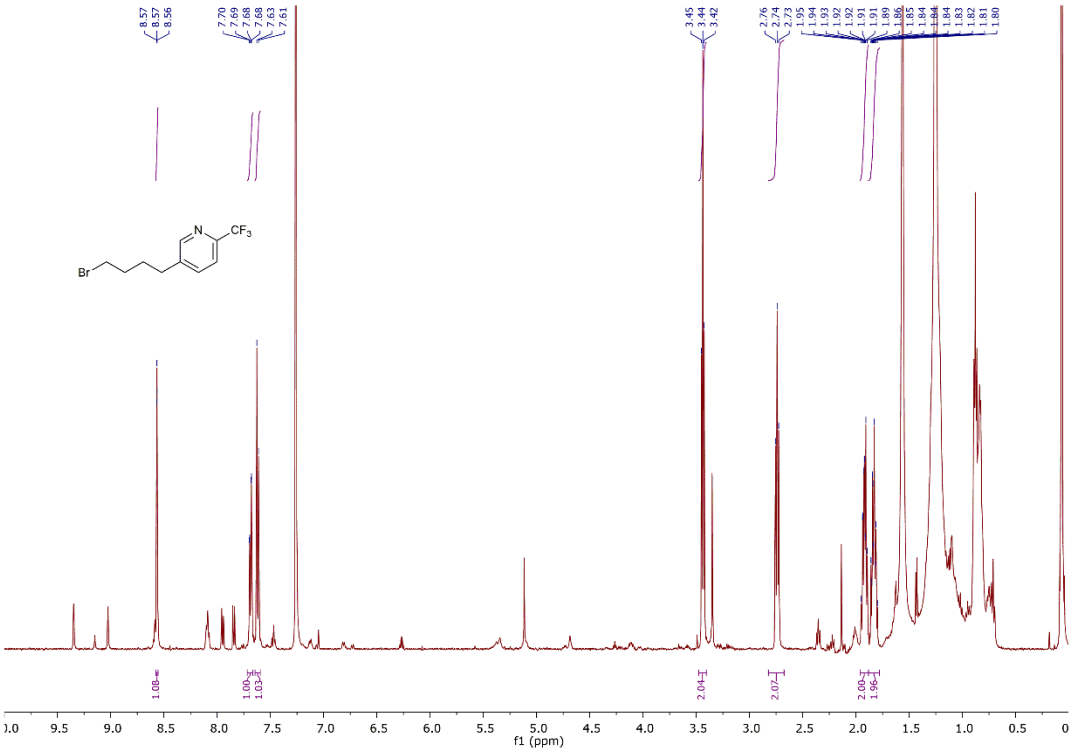
^{1}H NMR (500 MHz, $CDCl_3$) - (20)



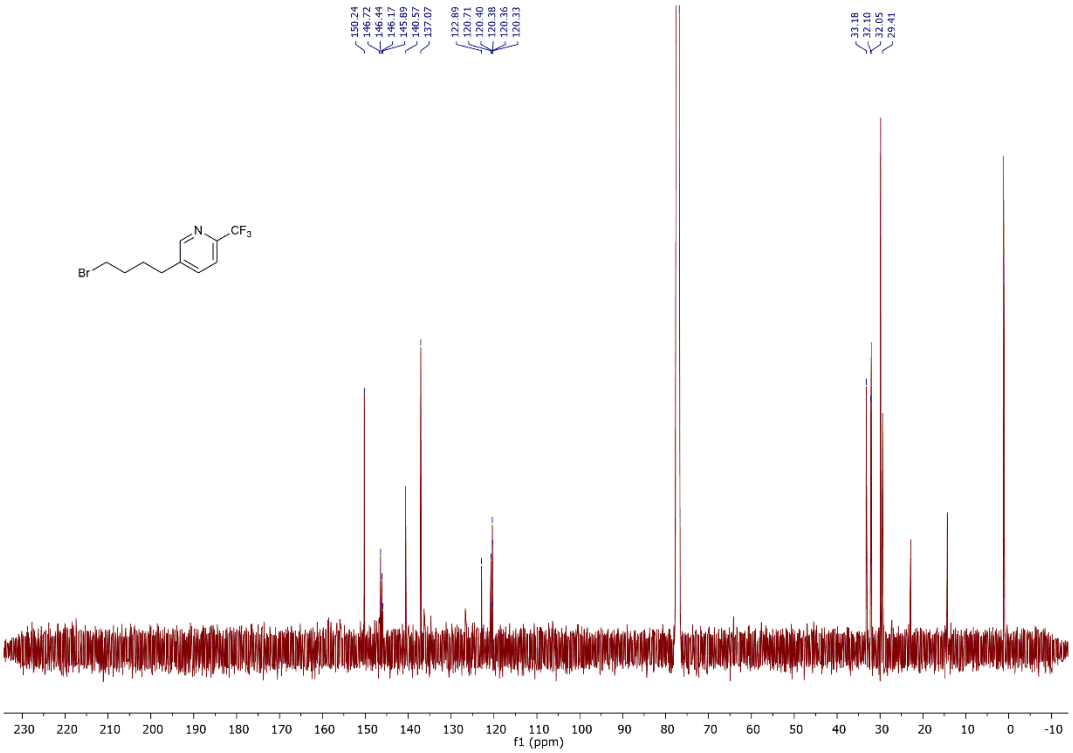
^{13}C NMR (126 MHz, $CDCl_3$) - (20)



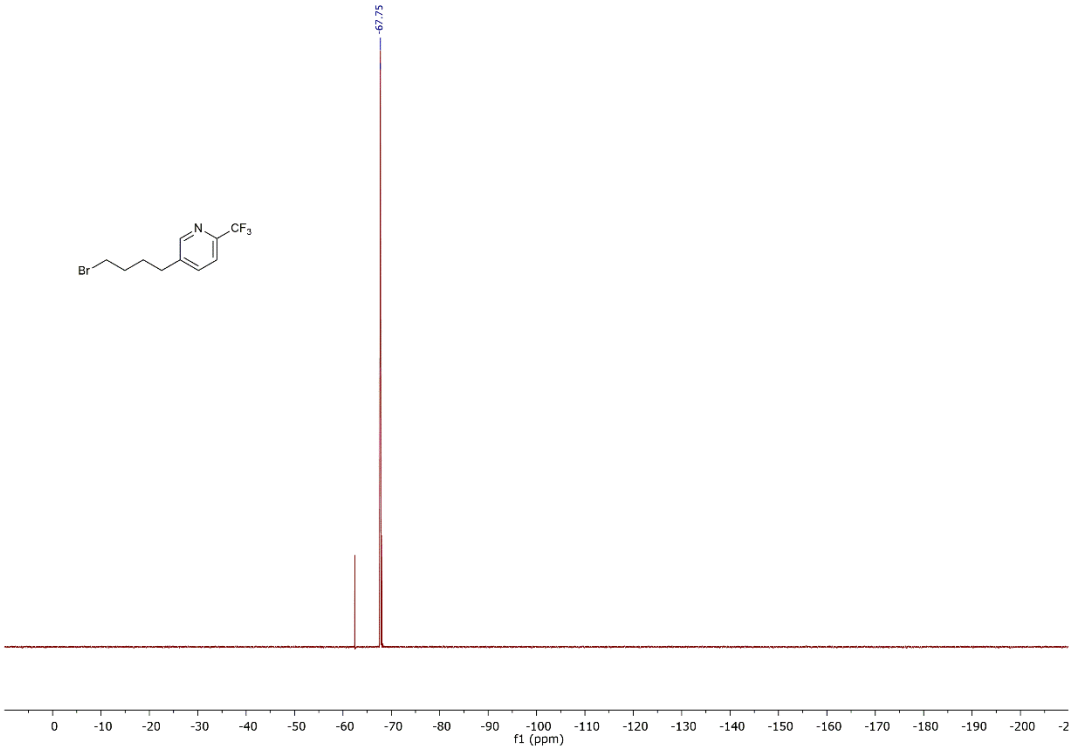
^{19}F NMR (376 MHz, $CDCl_3$) - (20)



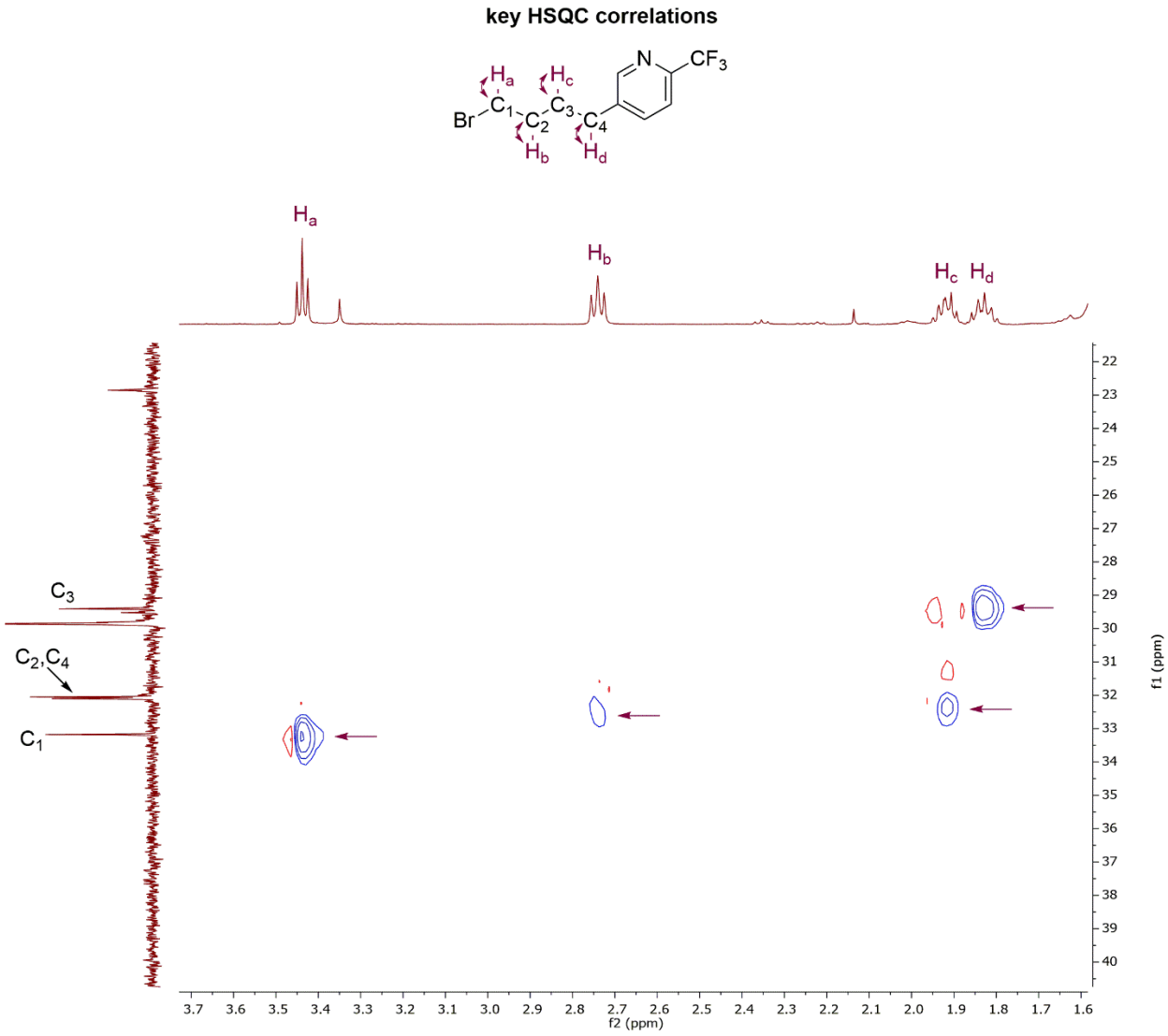
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-20)



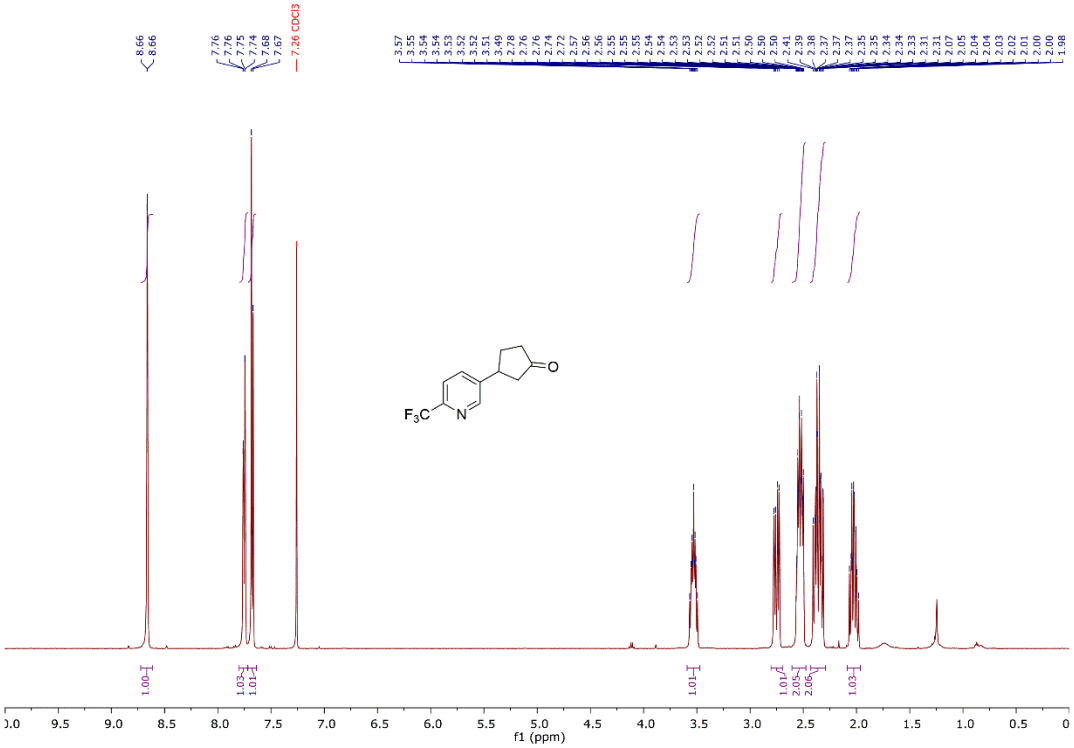
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-20)



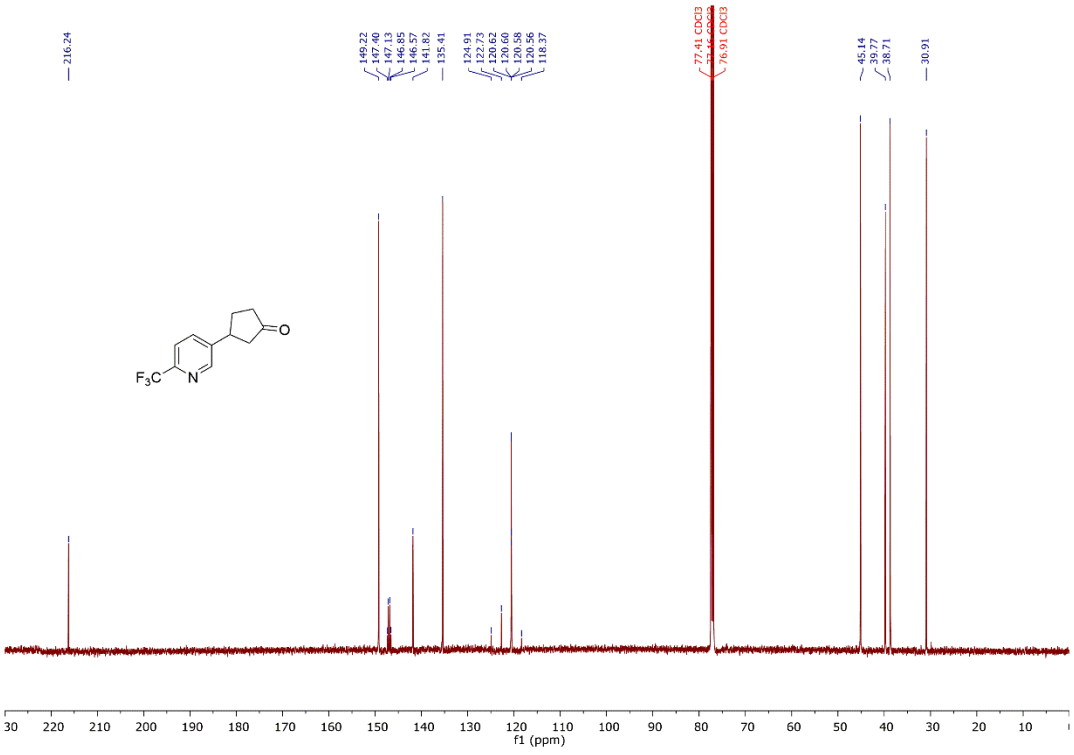
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-20)


key HSQC correlations
Ha
Hc
N
CF3
Br
C1
C2
C3
C4
Hb
Hd
Ha
Hb
Hc Hd
C3
C2,C4
C1
3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6
f2 (ppm)
22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40
f1 (ppm)

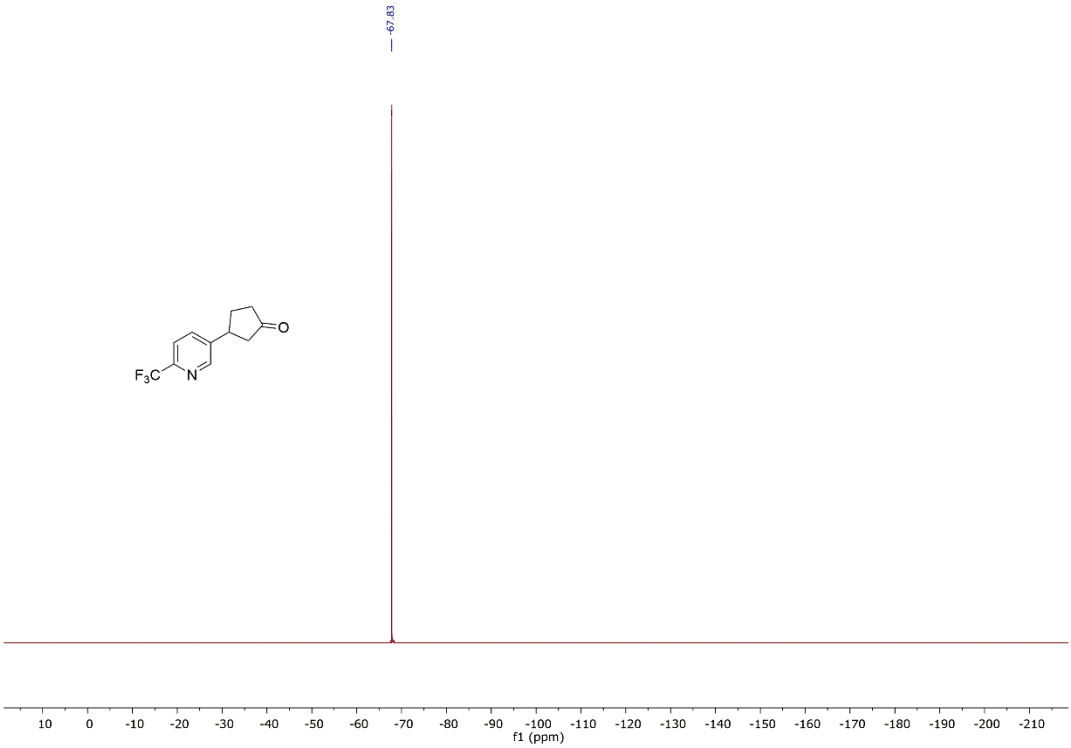
HSQC - (SI-20)



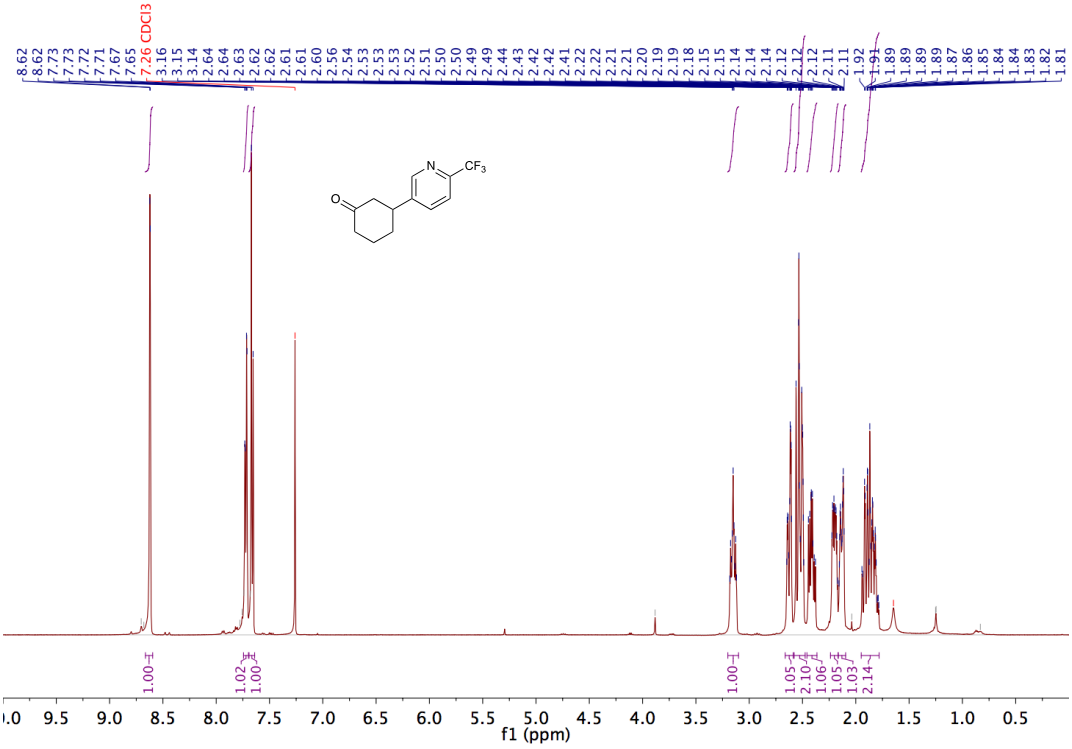
^{1}H NMR (500 MHz, $CDCl_3$) - (21)



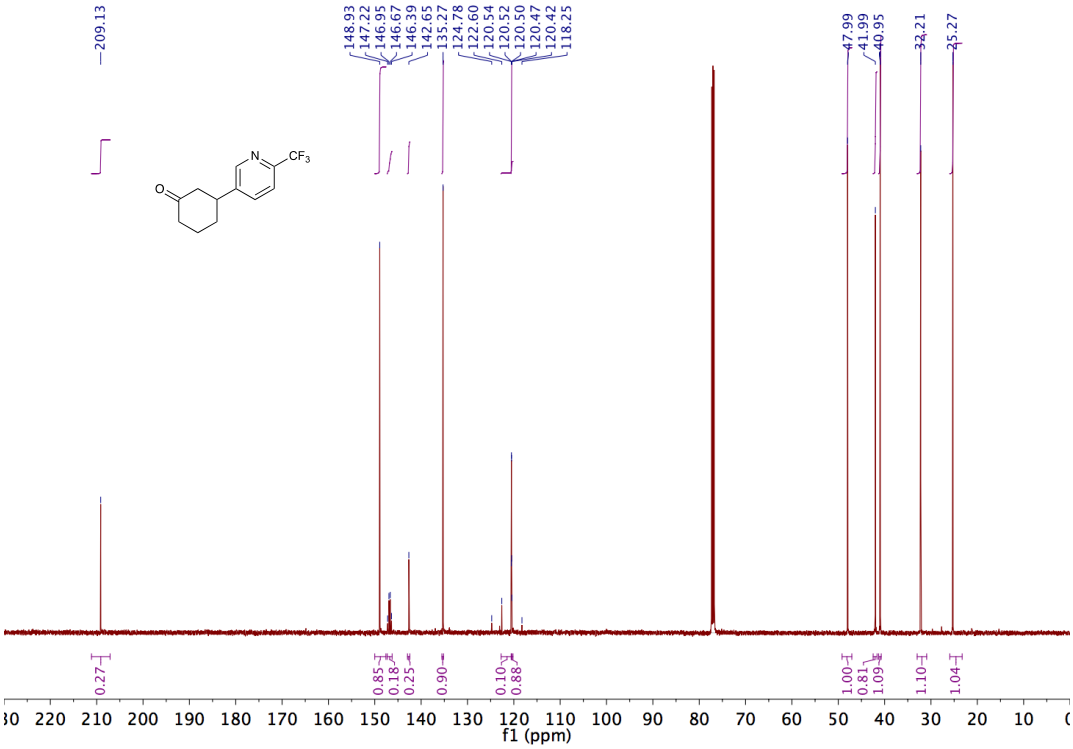
^{13}C NMR (126 MHz, $CDCl_3$) - (21)



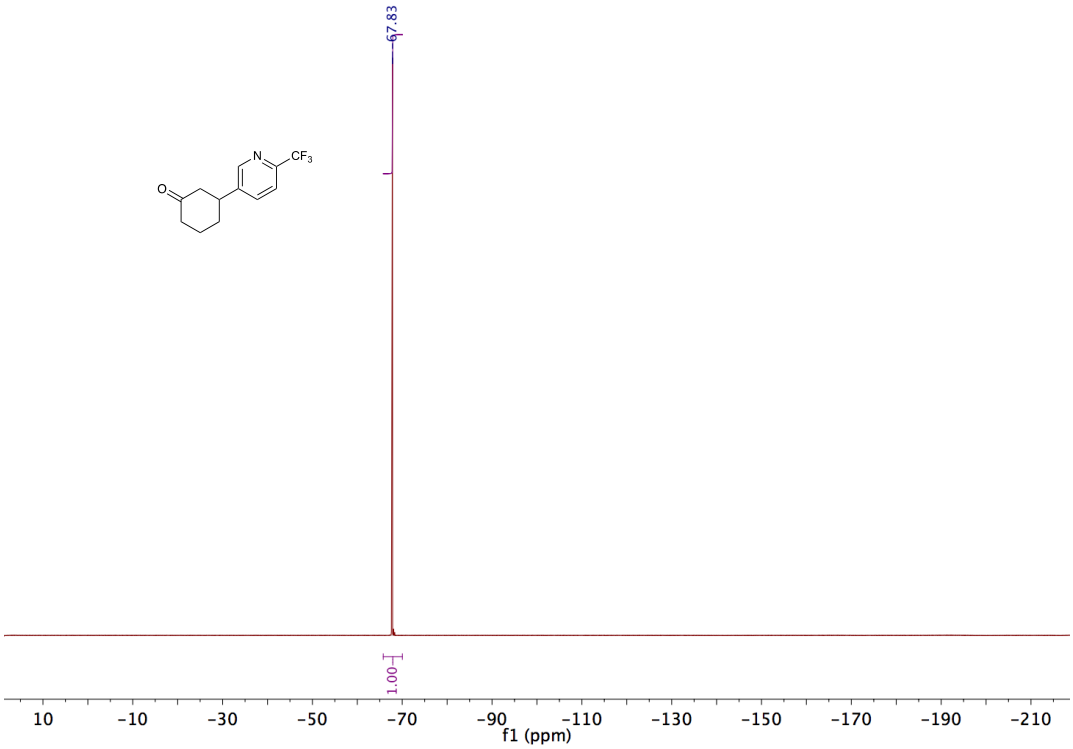
^{19}F NMR (376 MHz, $CDCl_3$) - (21)



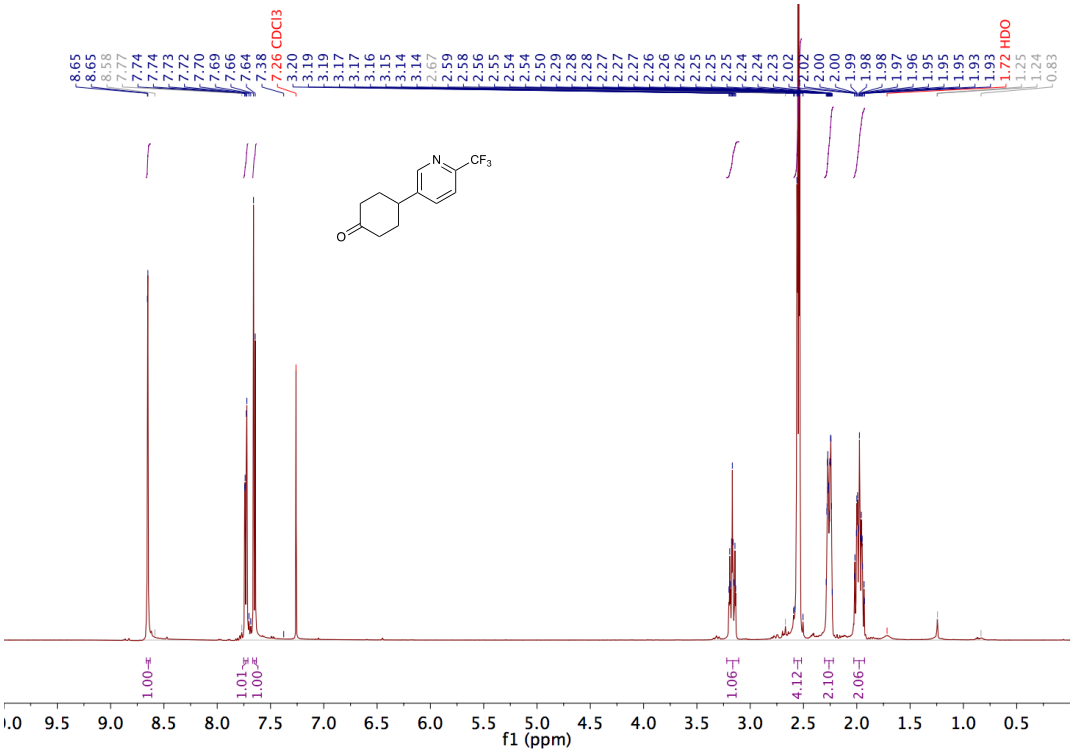
^{1}H NMR (500 MHz, $CDCl_3$) - (22)



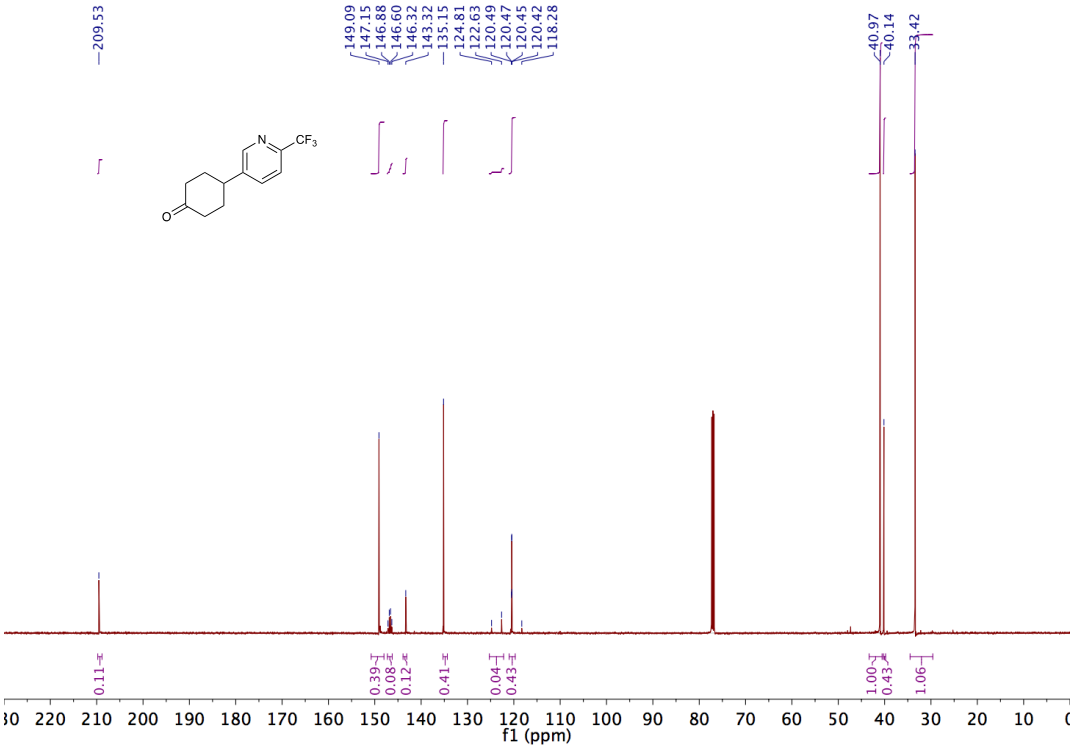
^{13}C NMR (126 MHz, $CDCl_3$) - (22)



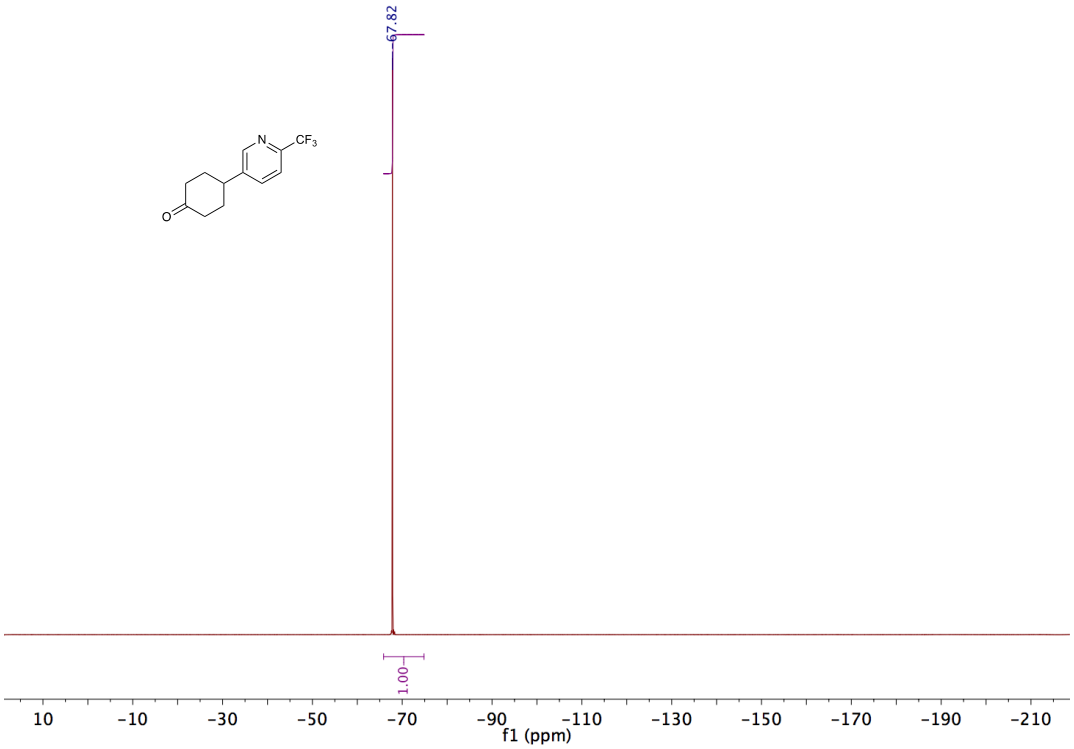
^{19}F NMR (376 MHz, $CDCl_3$) - (22)



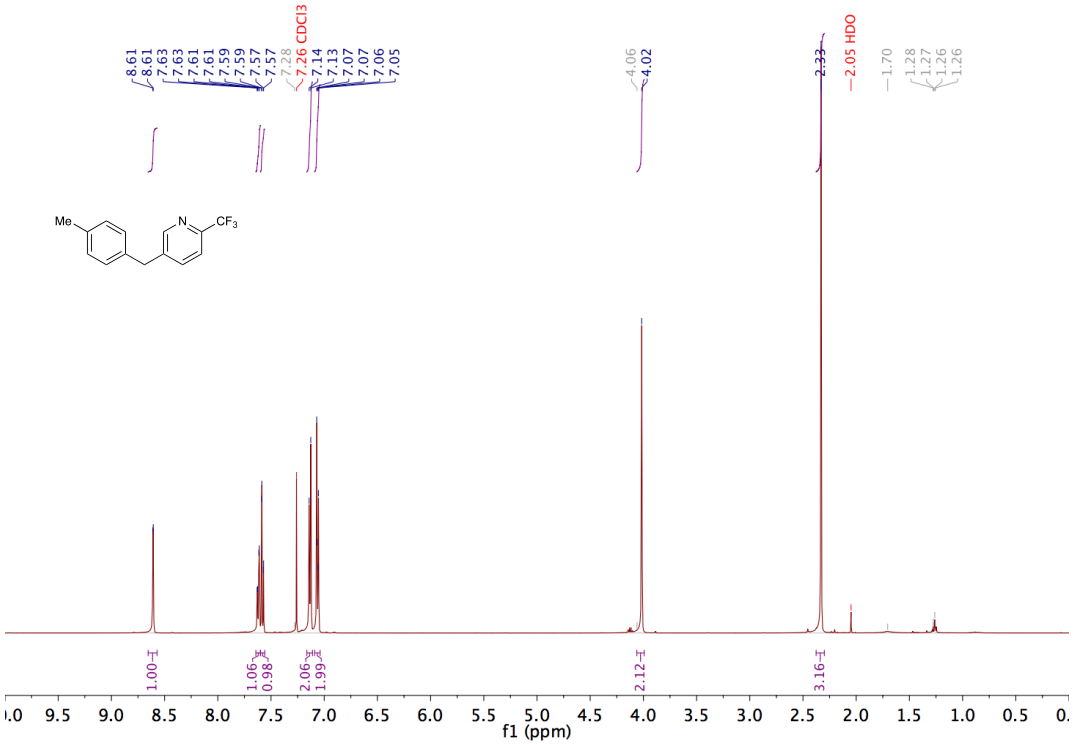
^{1}H NMR (500 MHz, $CDCl_3$) – (SI-22)



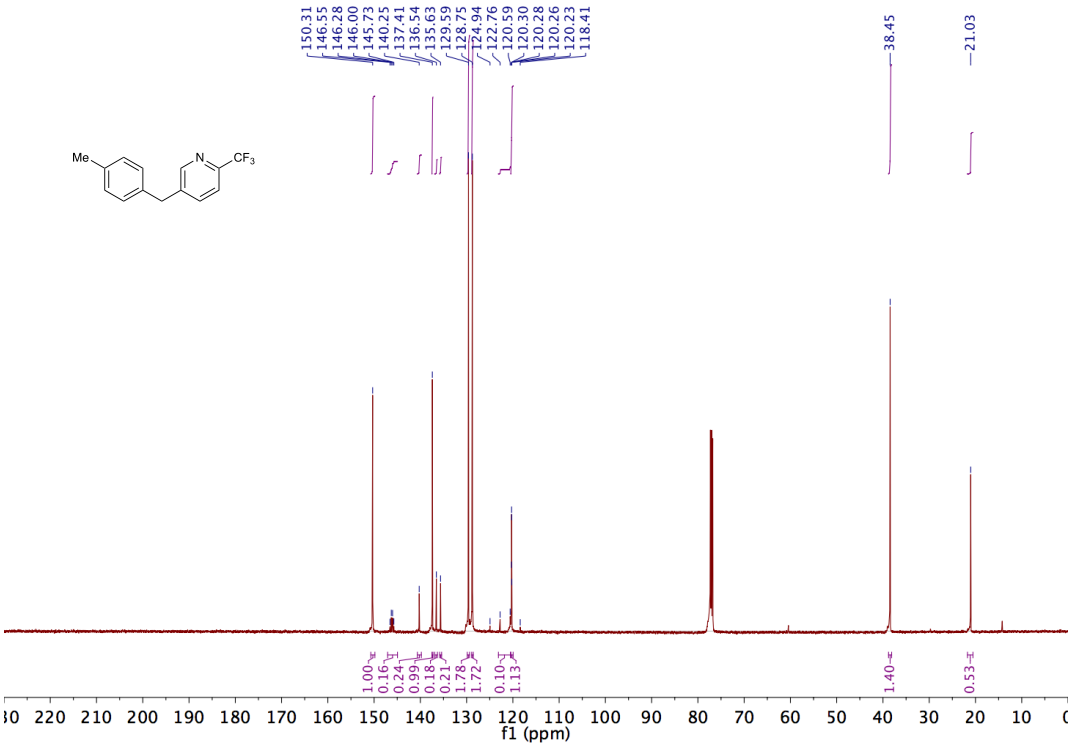
^{13}C NMR (126 MHz, $CDCl_3$) – (SI-22)



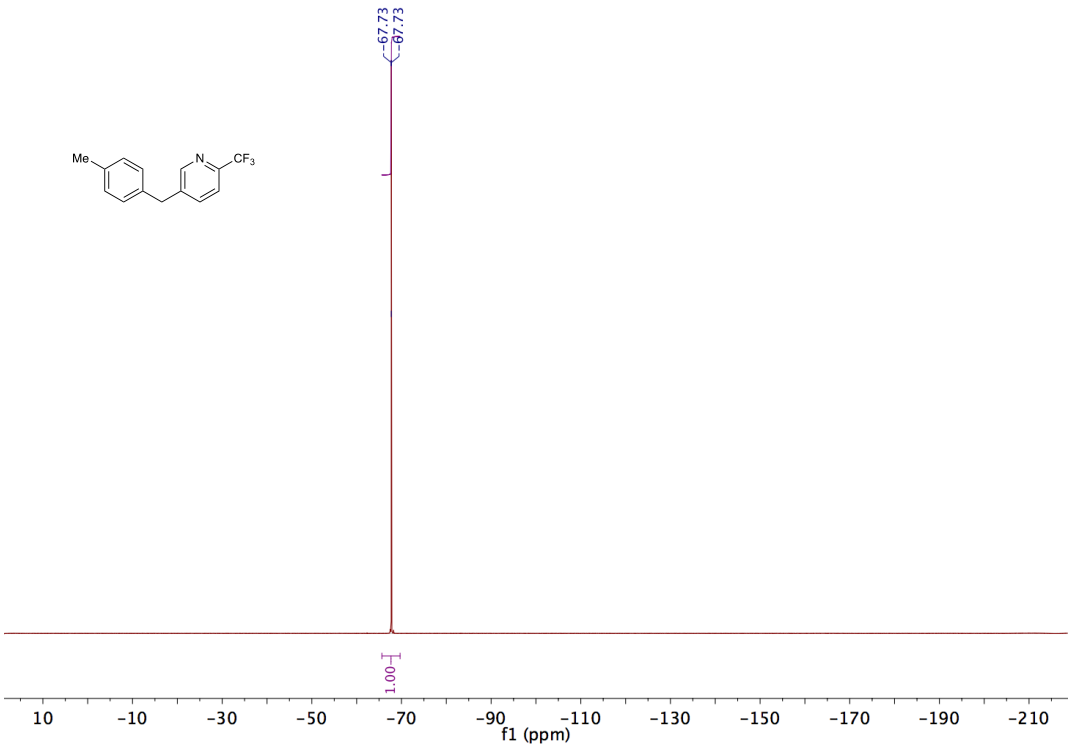
^{19}F NMR (376 MHz, $CDCl_3$) – (SI-22)



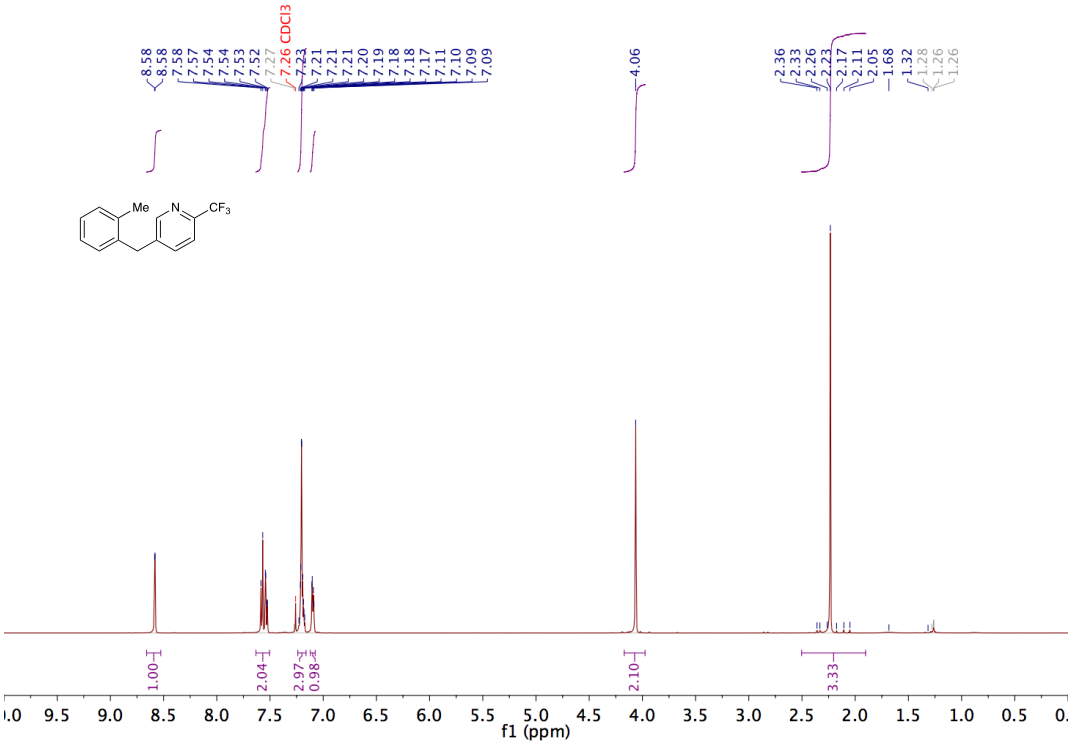
^{1}H NMR (500 MHz, $CDCl_3$) - (23)



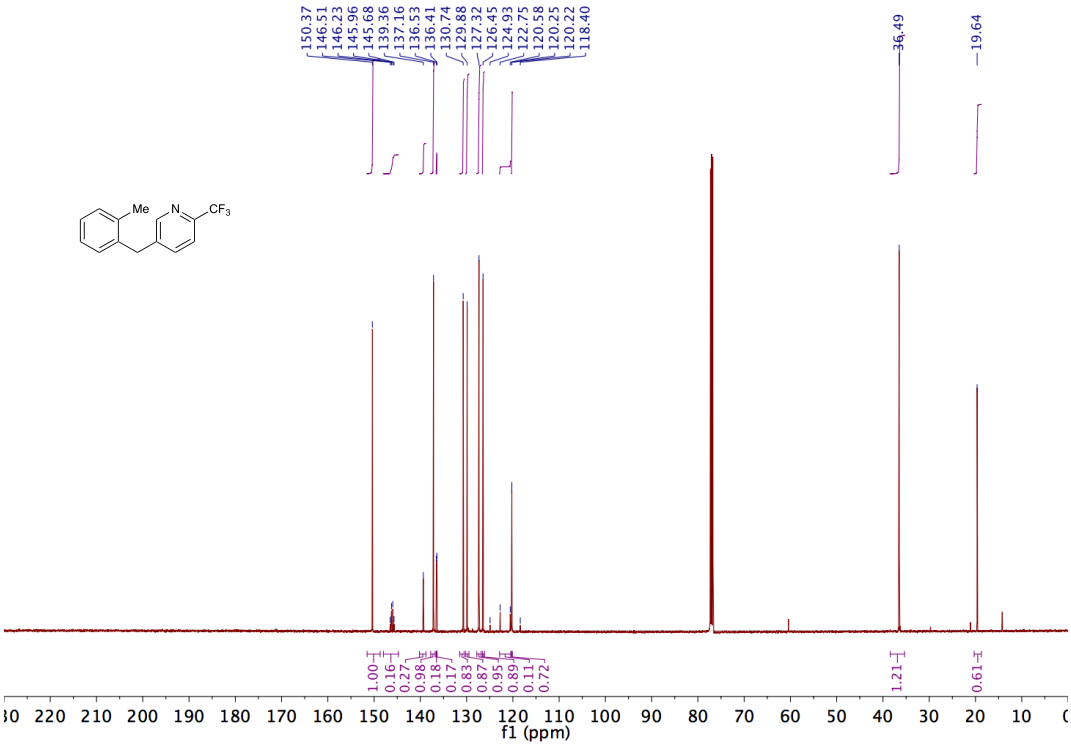
^{13}C NMR (126 MHz, $CDCl_3$) - (23)



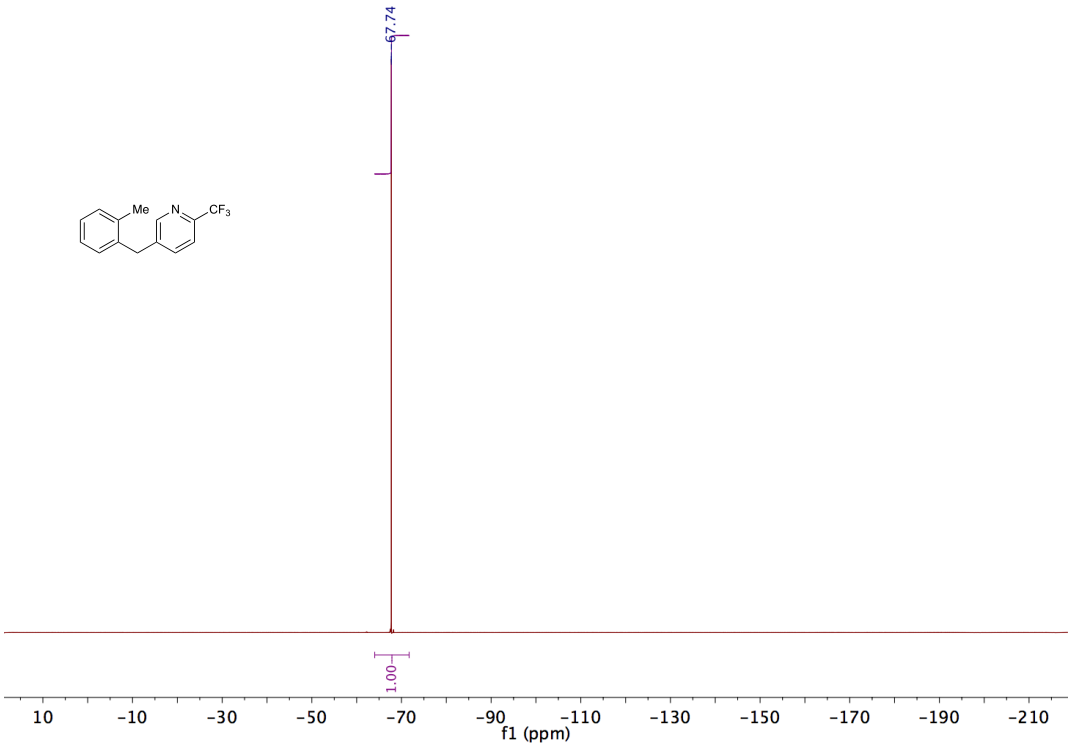
^{19}F NMR (376 MHz, $CDCl_3$) - (23)



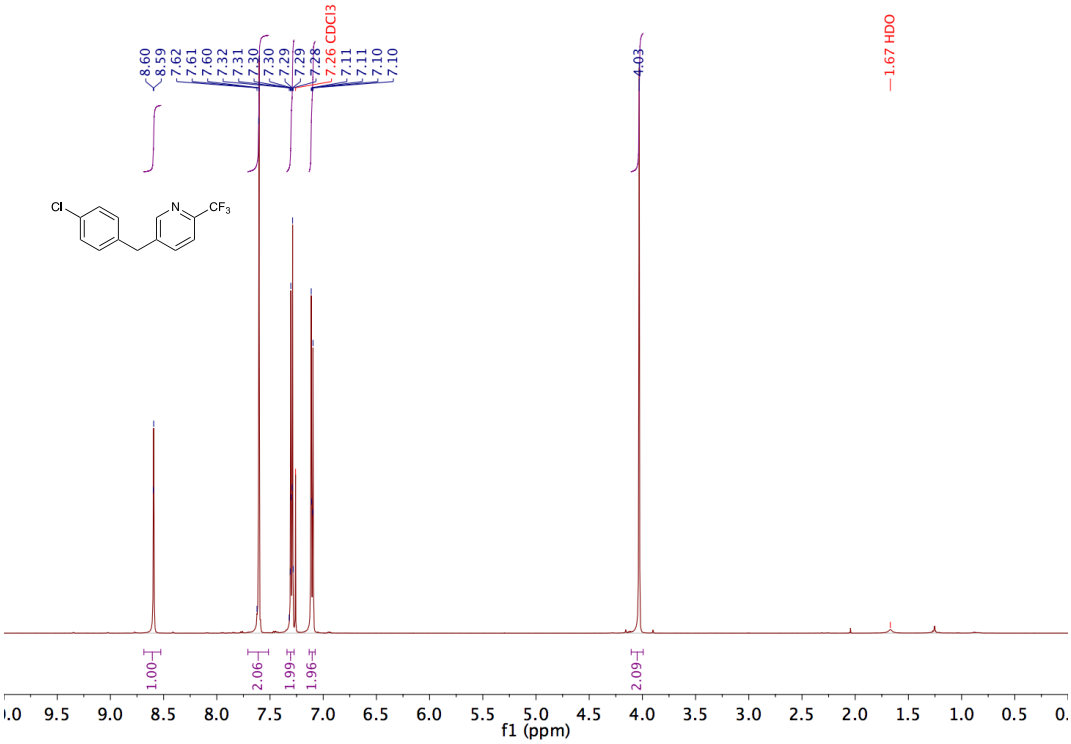
^{1}H NMR (500 MHz, $CDCl_3$) - (24)



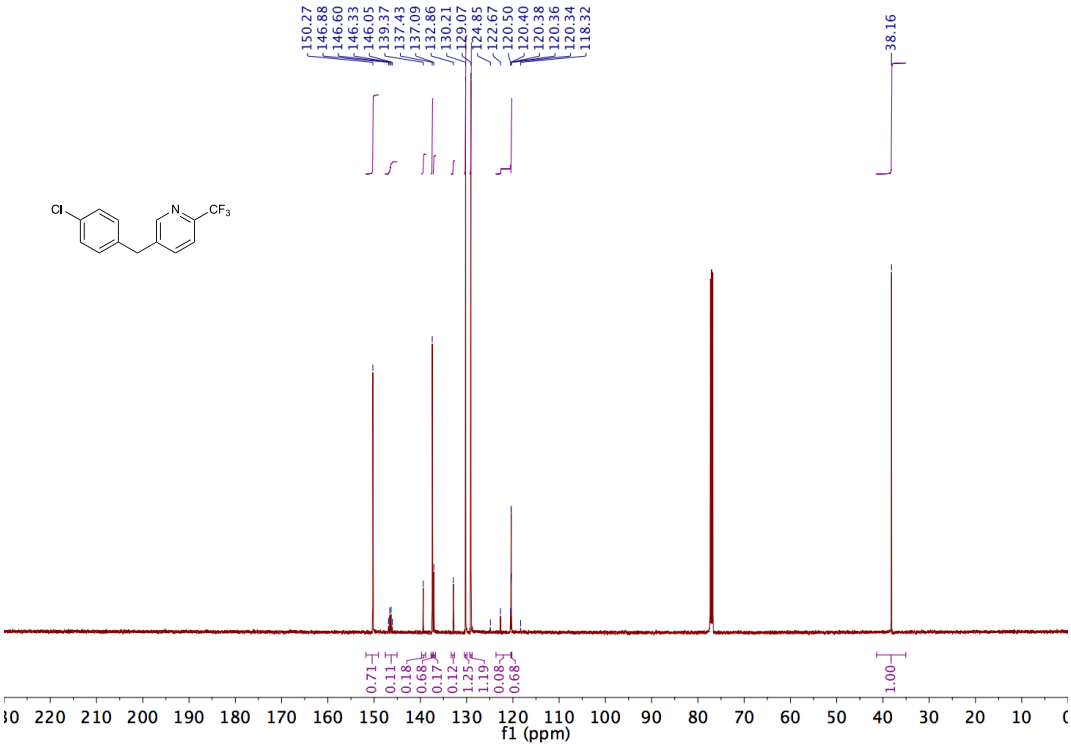
^{13}C NMR (126 MHz, $CDCl_3$) - (24)



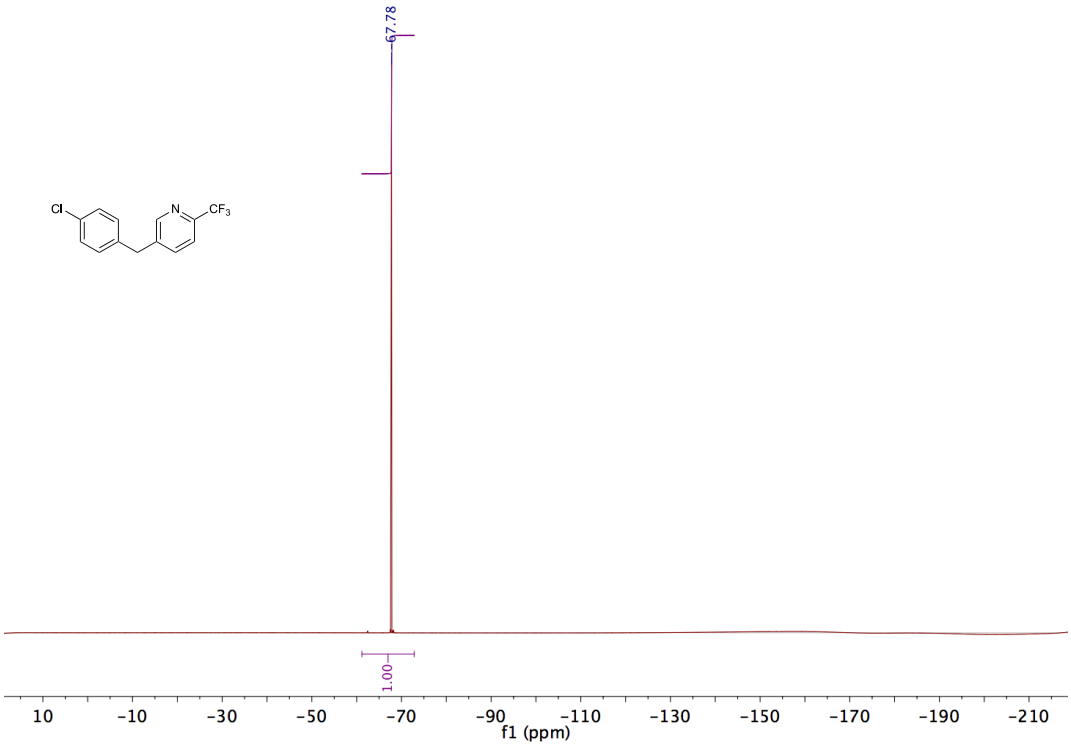
^{19}F NMR (376 MHz, $CDCl_3$) - (24)



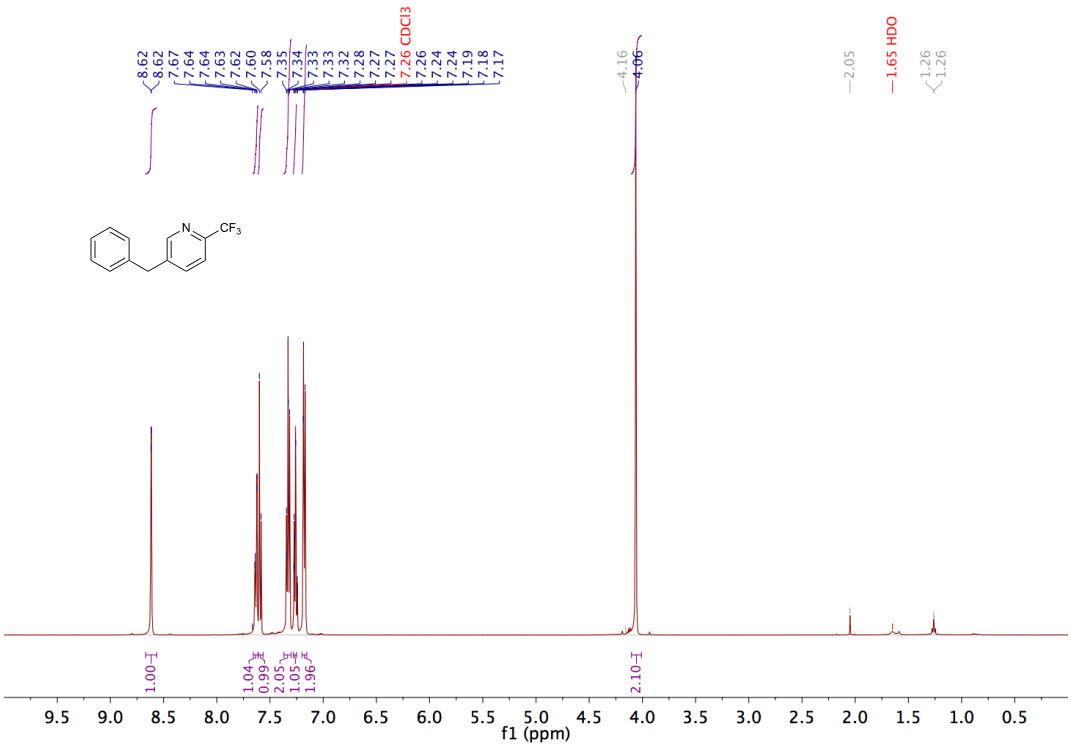
^{1}H NMR (500 MHz, $CDCl_3$) – (25)



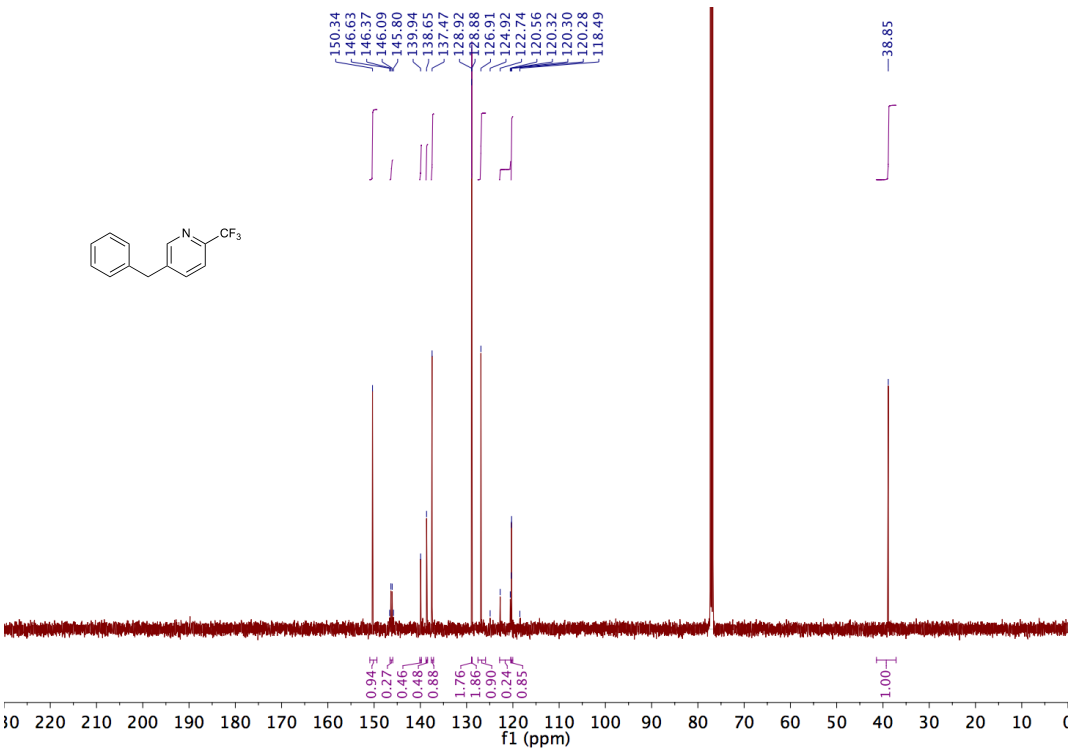
^{13}C NMR (126 MHz, $CDCl_3$) – (25)



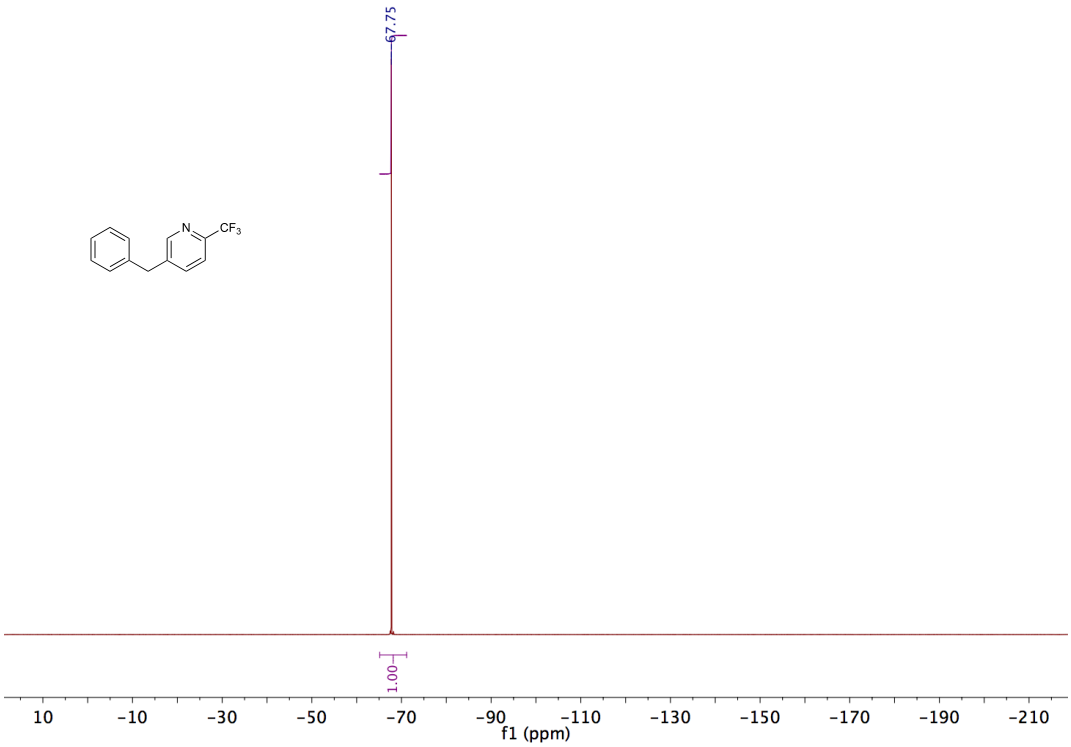
^{19}F NMR (376 MHz, $CDCl_3$) – (25)



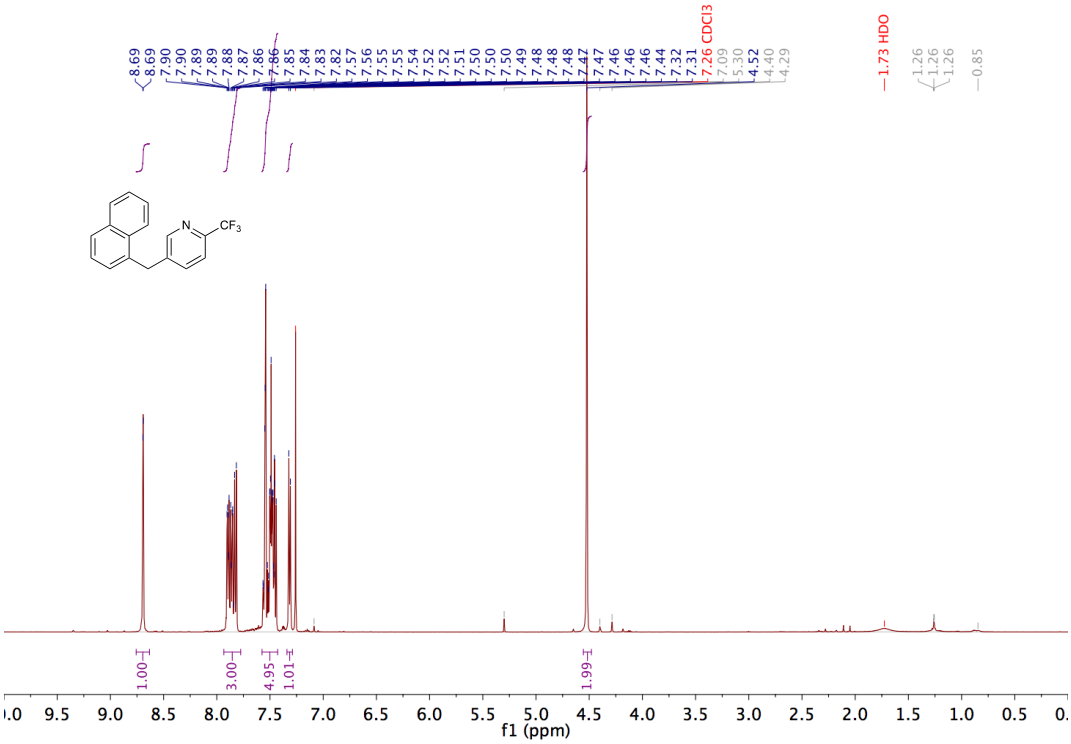
^{1}H NMR (500 MHz, $CDCl_3$) – (SI-2)



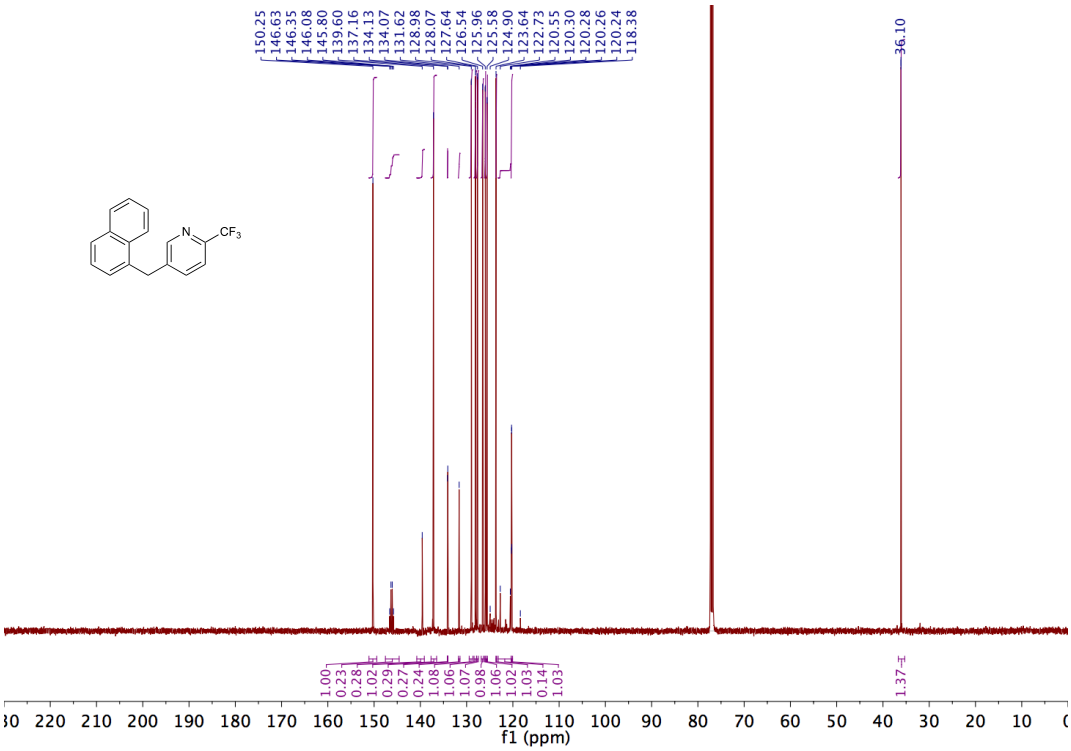
^{13}C NMR (126 MHz, $CDCl_3$) – (SI-2)



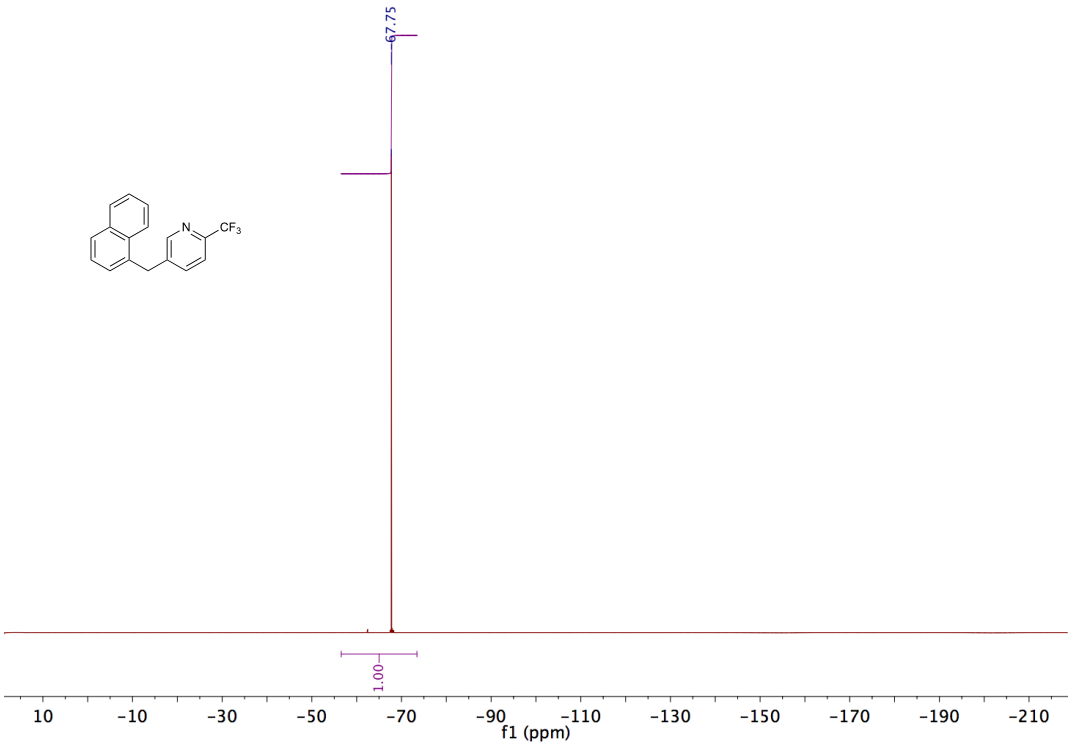
^{19}F NMR (376 MHz, $CDCl_3$) – (SI-2)



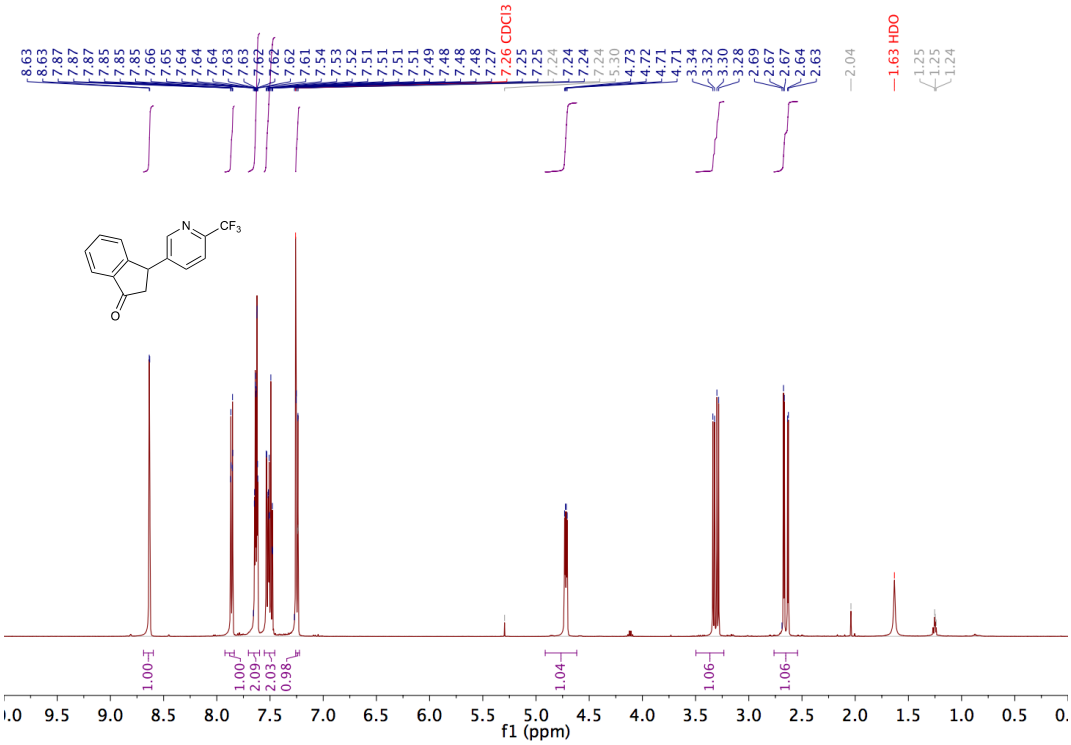
^{1}H NMR (500 MHz, $CDCl_3$) – (SI-3)



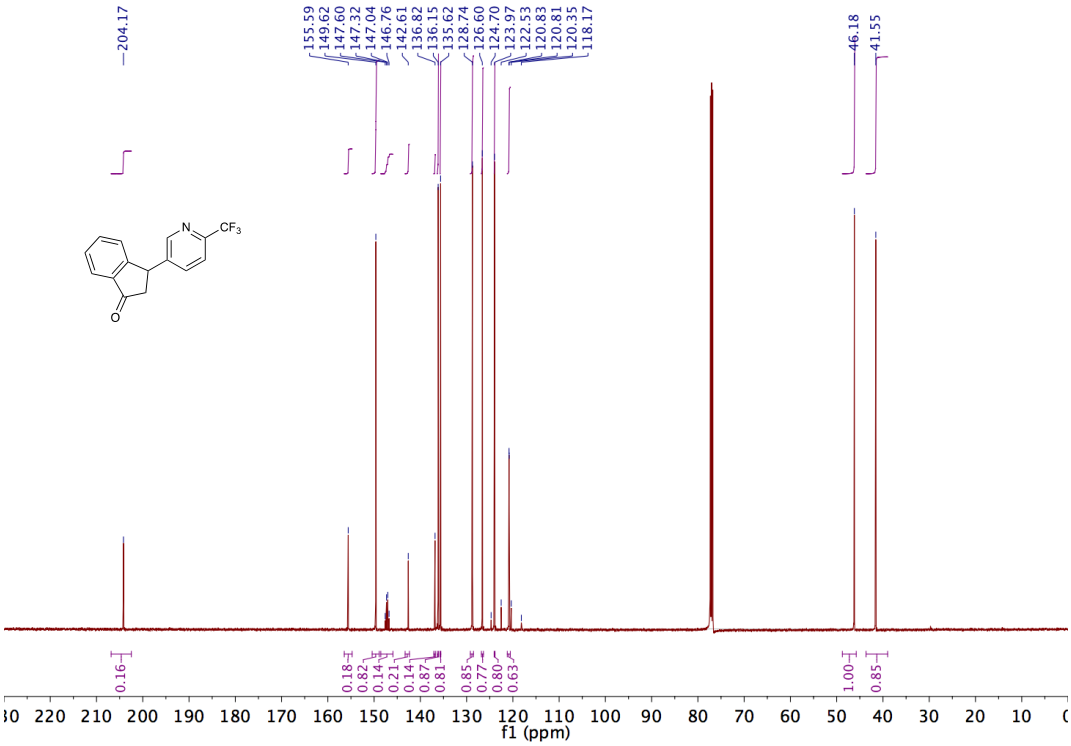
^{13}C NMR (126 MHz, $CDCl_3$) – (SI-3)



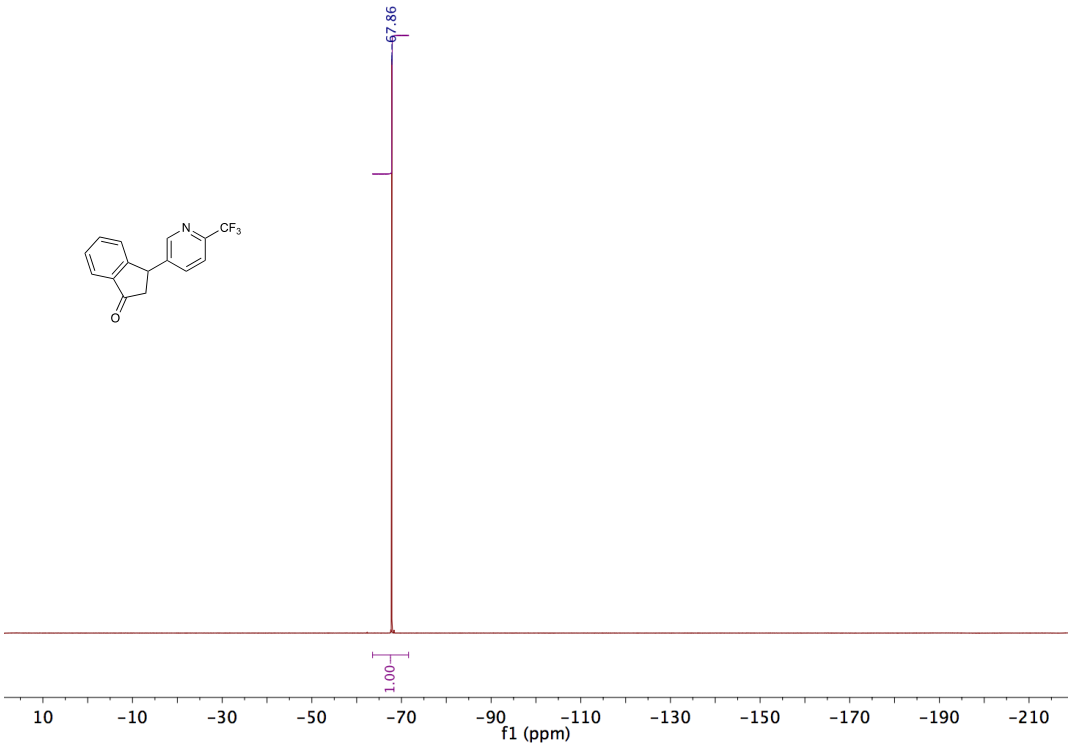
^{19}F NMR (376 MHz, $CDCl_3$) – (SI-3)



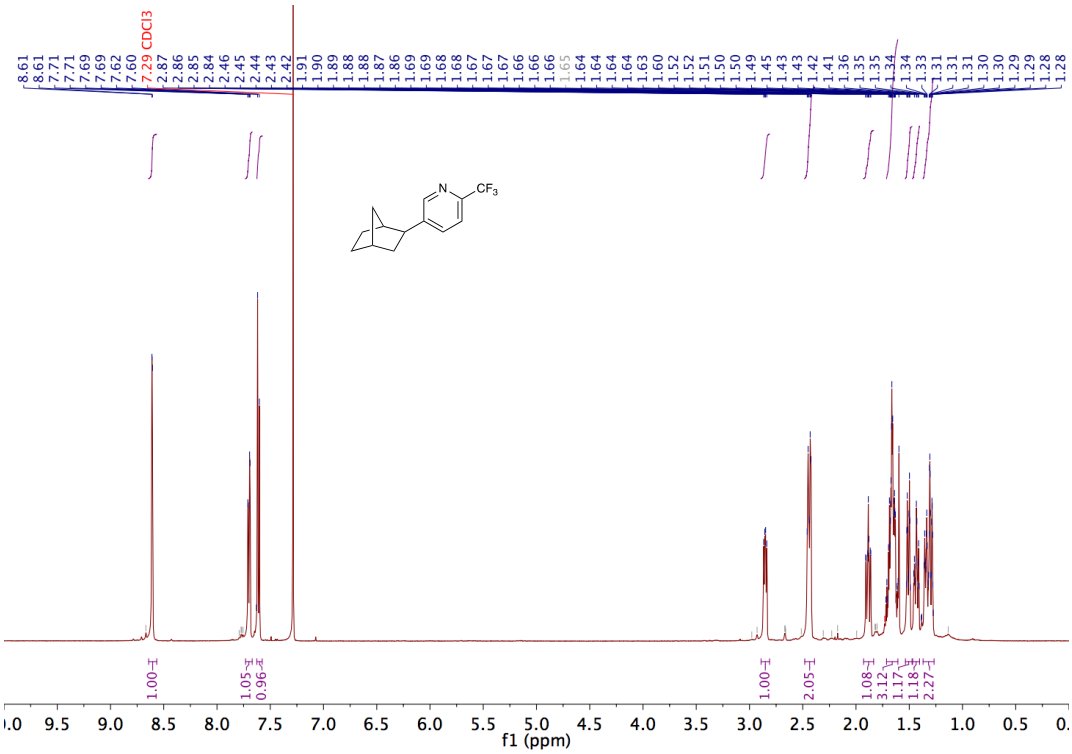
^{1}H NMR (500 MHz, $CDCl_3$) – (SI-4)



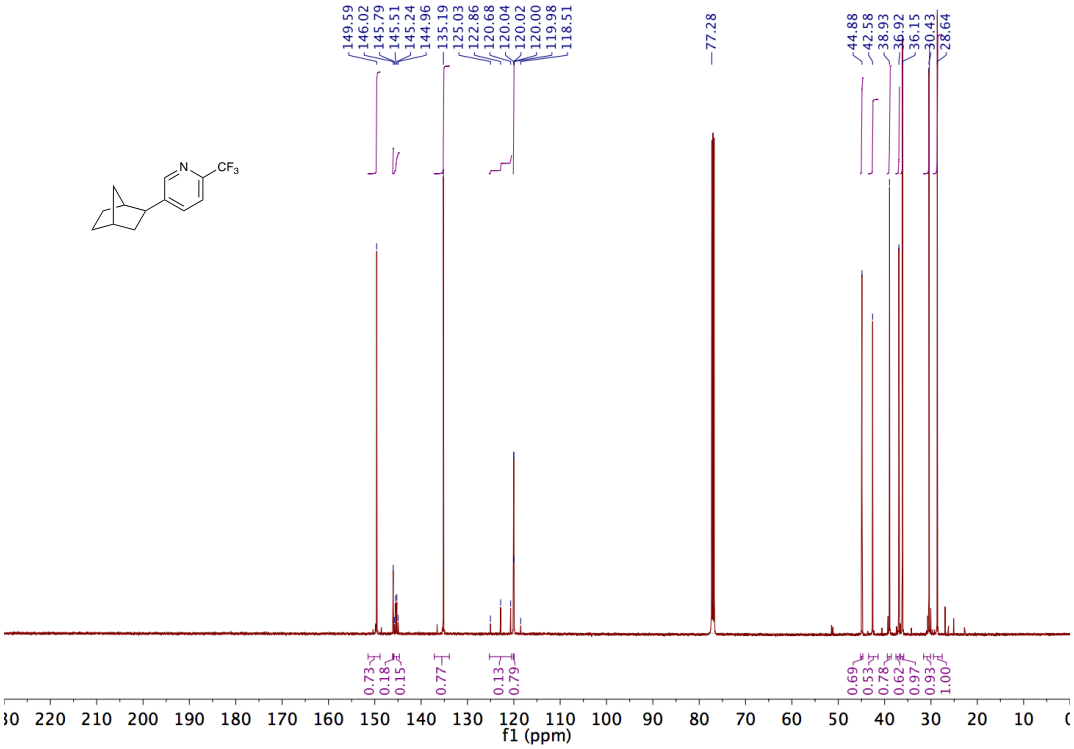
^{13}C NMR (126 MHz, $CDCl_3$) – (SI-4)



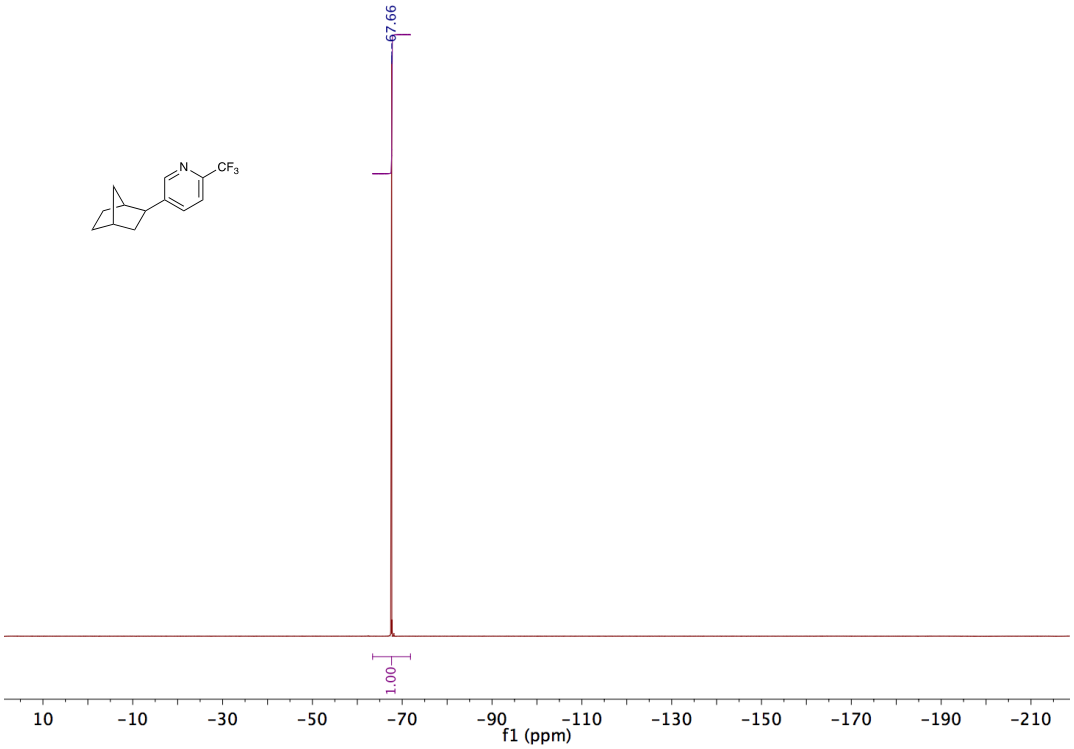
^{19}F NMR (376 MHz, $CDCl_3$) – (SI-4)



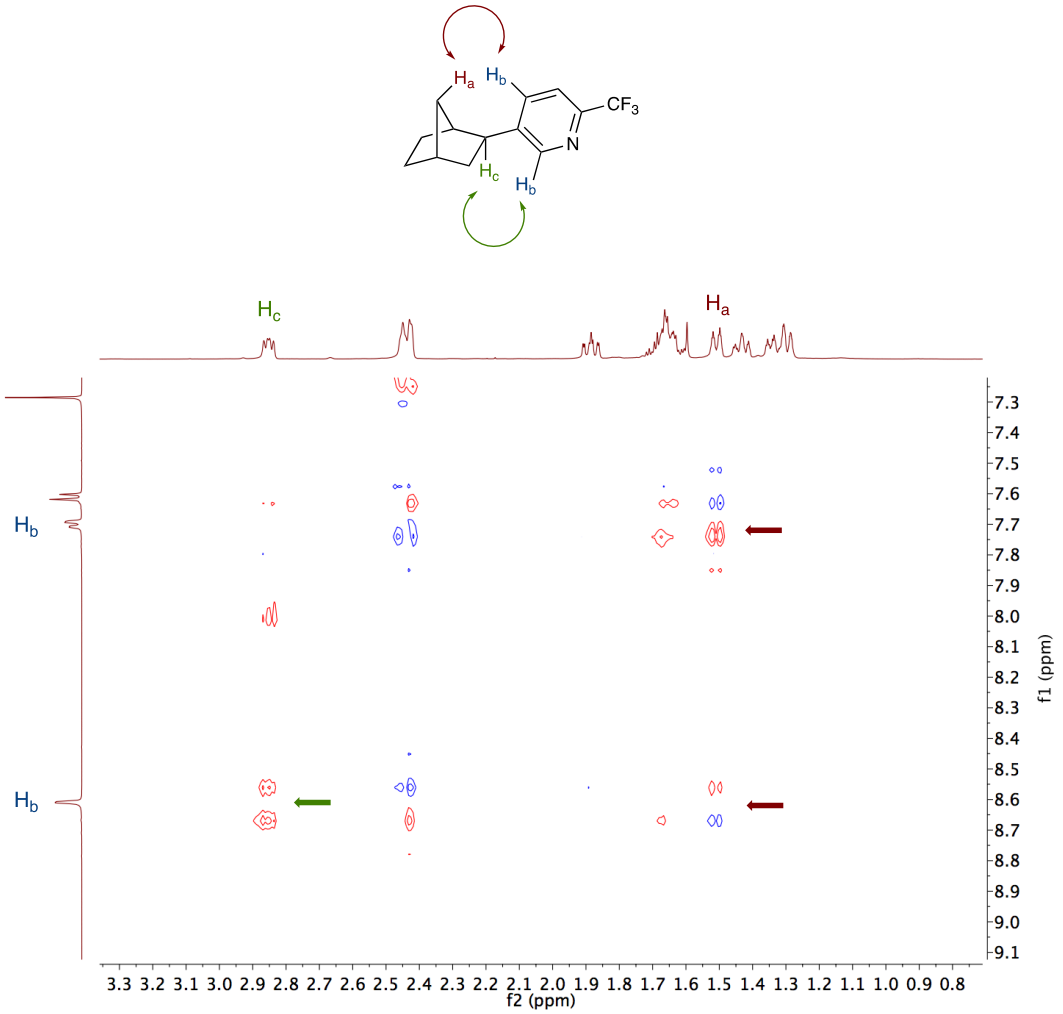
^{1}H NMR (500 MHz, $CDCl_3$) – (26)



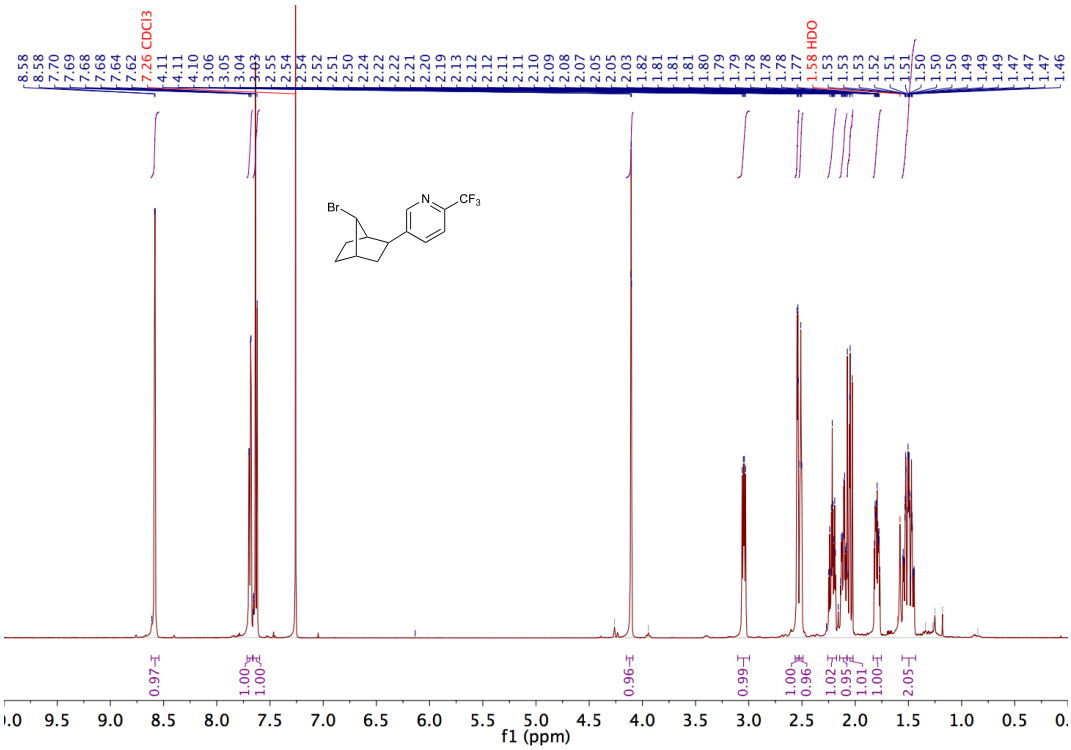
^{13}C NMR (126 MHz, $CDCl_3$) – (26)



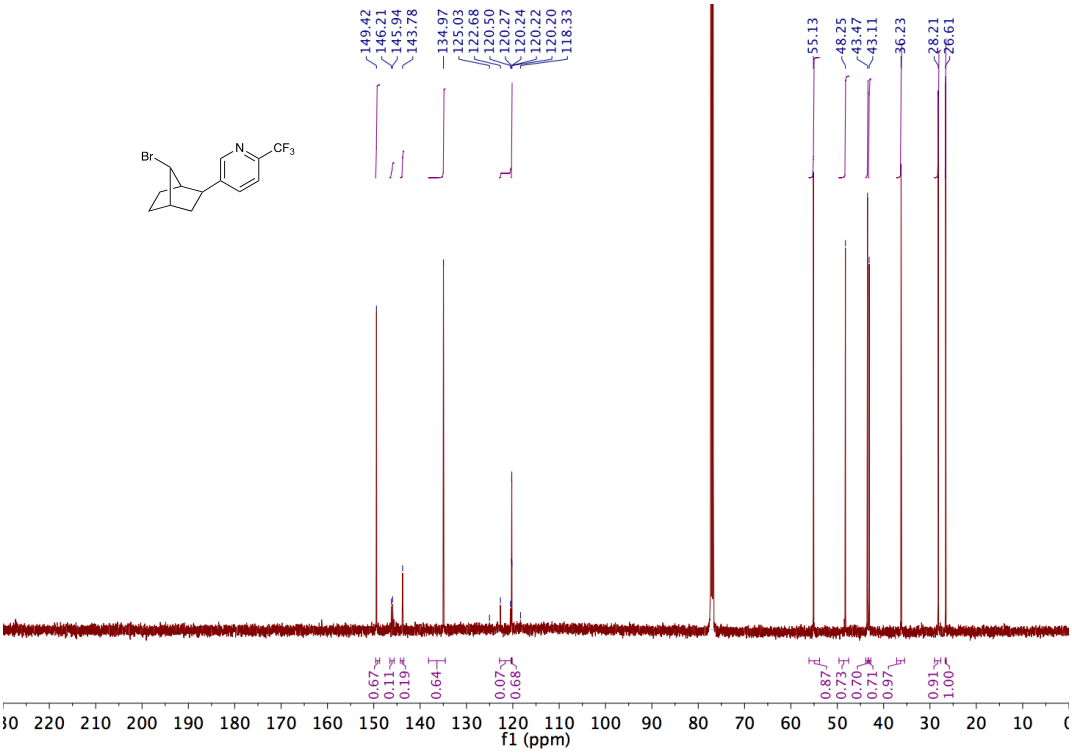
^{19}F NMR (376 MHz, $CDCl_3$) – (26)



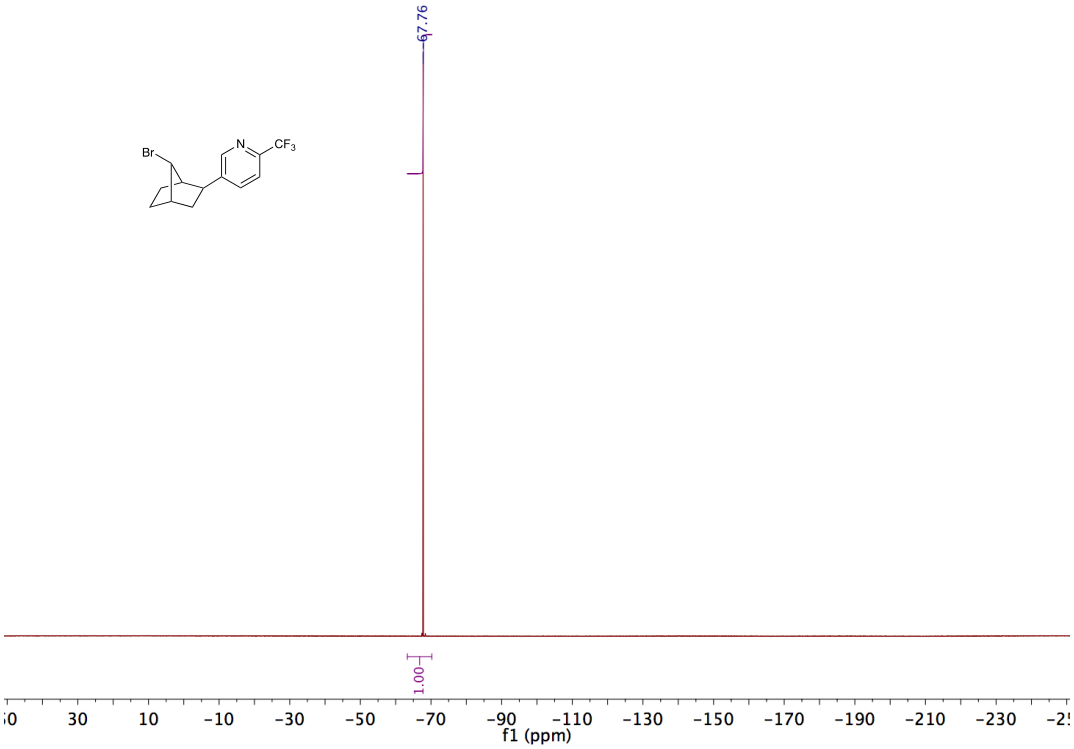
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (26)



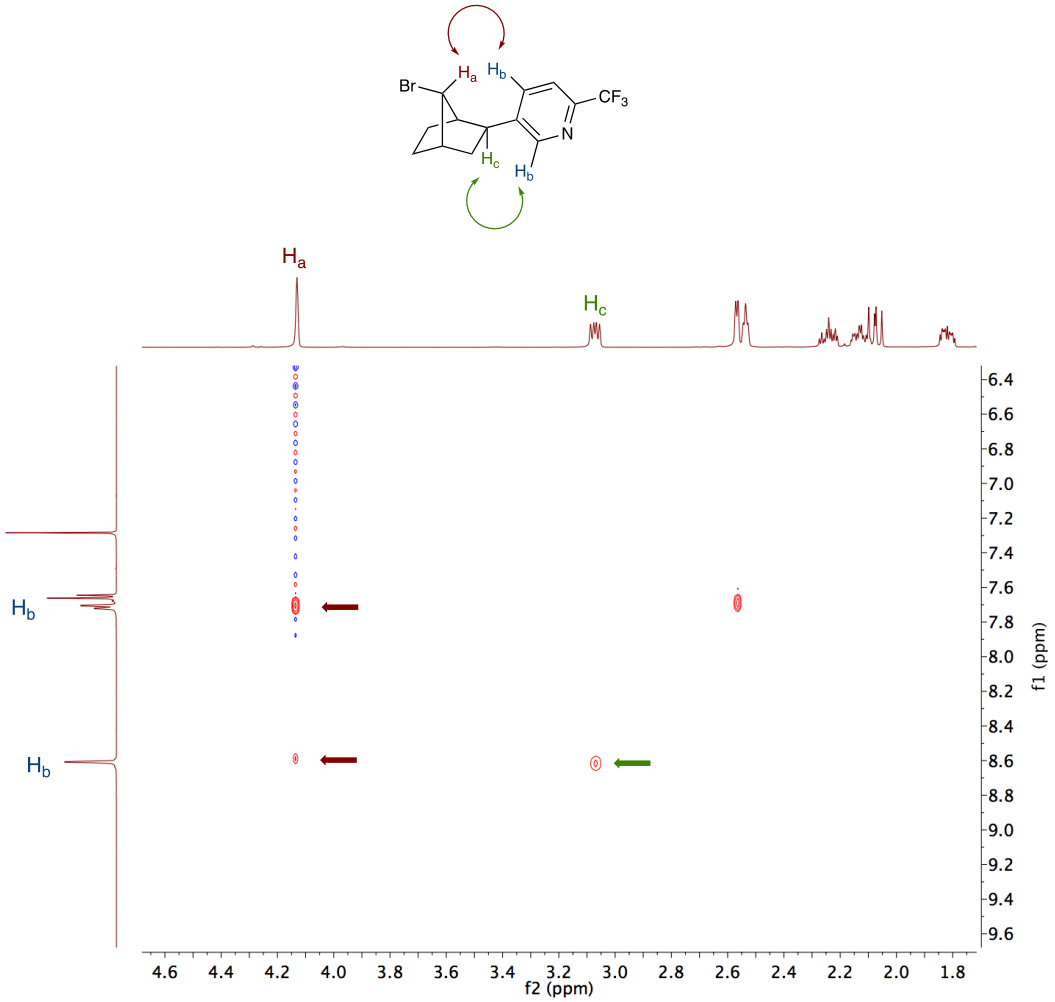
^{1}H NMR (500 MHz, $CDCl_3$) – (27)



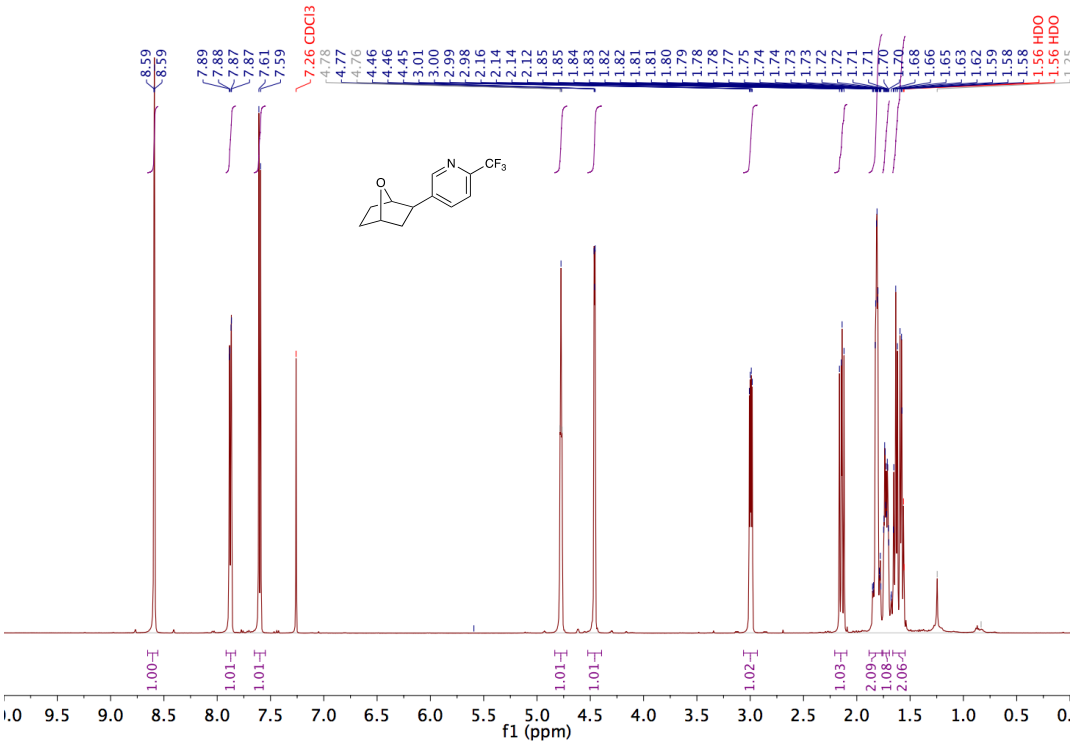
^{13}C NMR (126 MHz, $CDCl_3$) – (27)



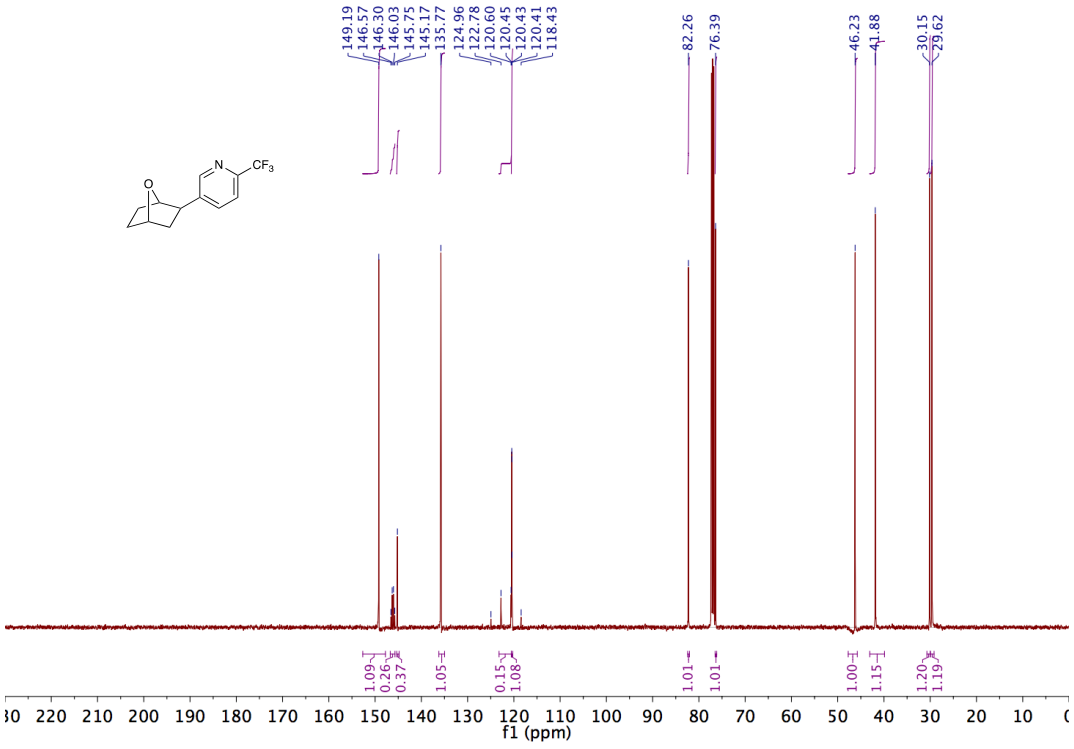
^{19}F NMR (376 MHz, $CDCl_3$) – (27)



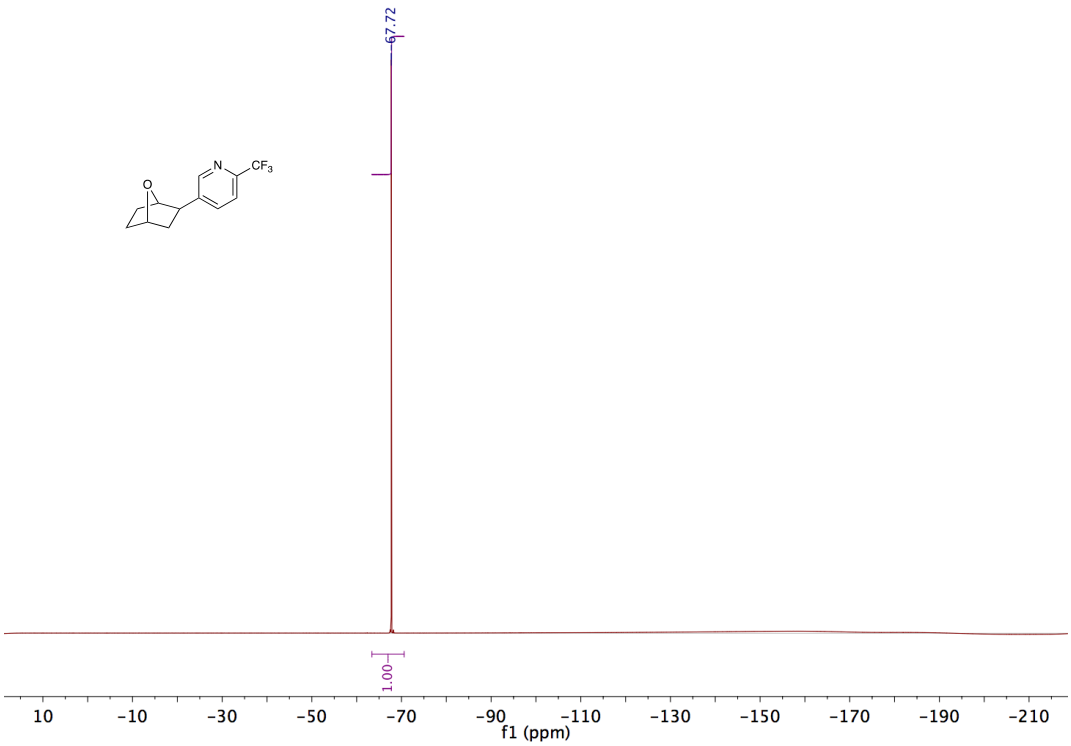
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (27)



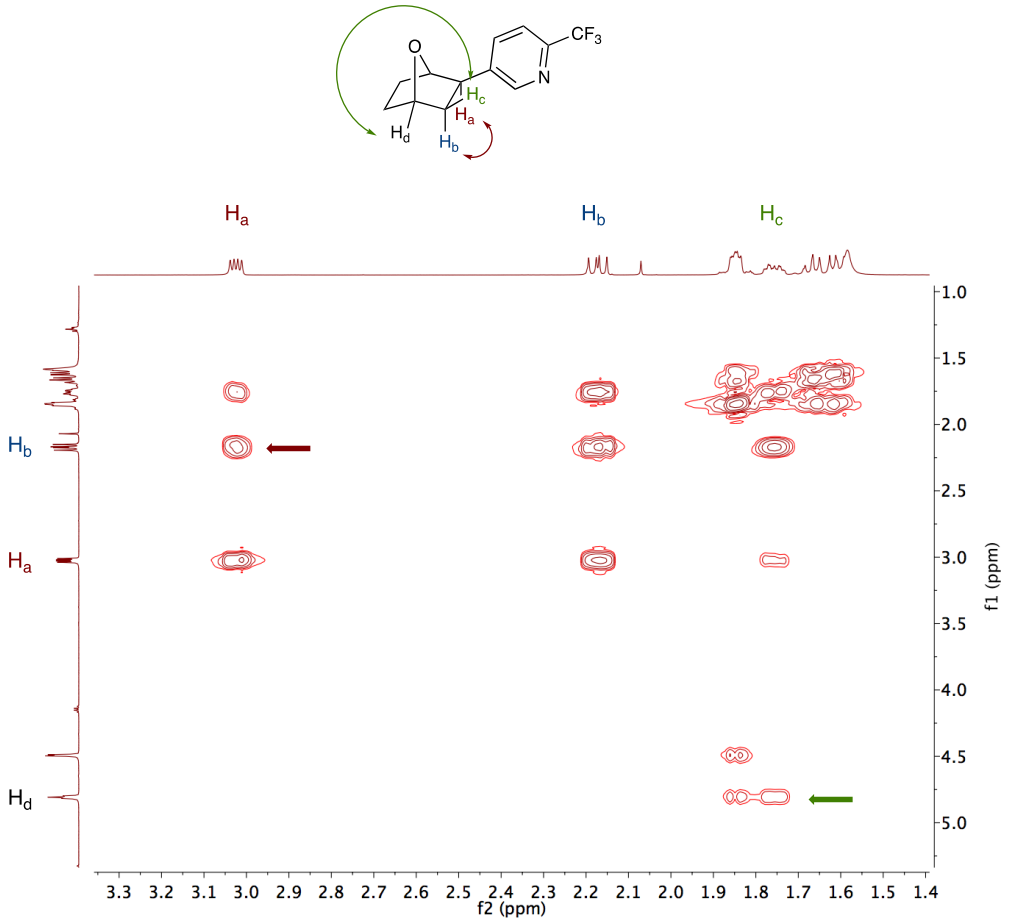
^{1}H NMR (500 MHz, $CDCl_3$) – (28)



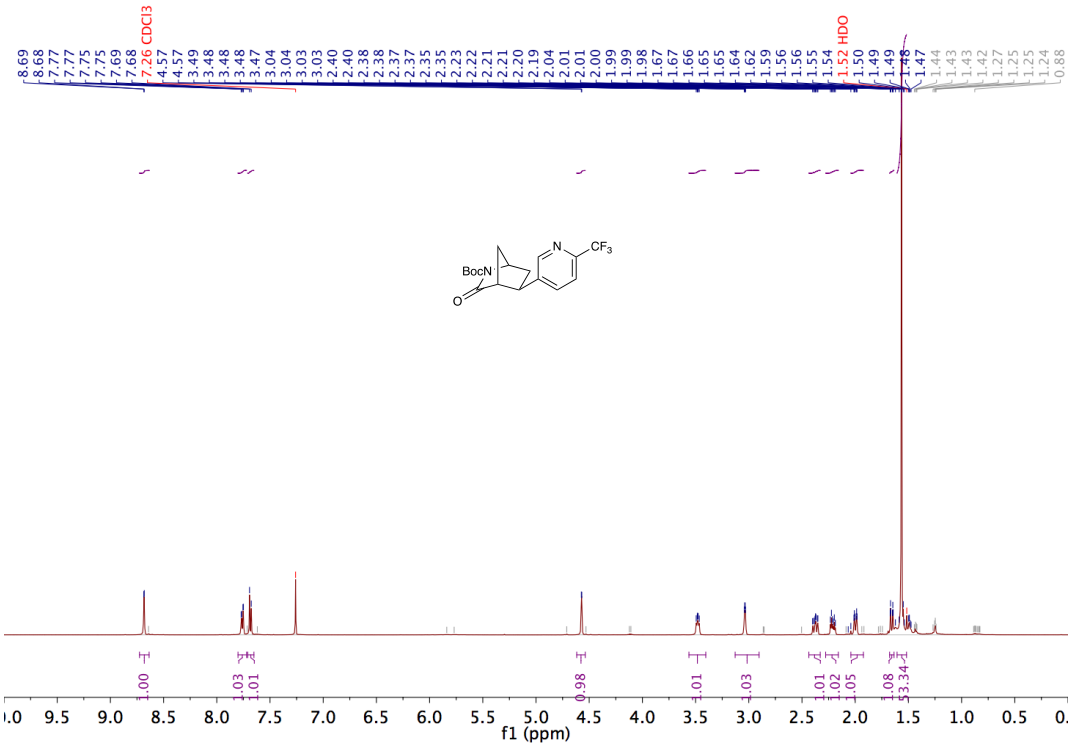
^{13}C NMR (126 MHz, $CDCl_3$) – (28)



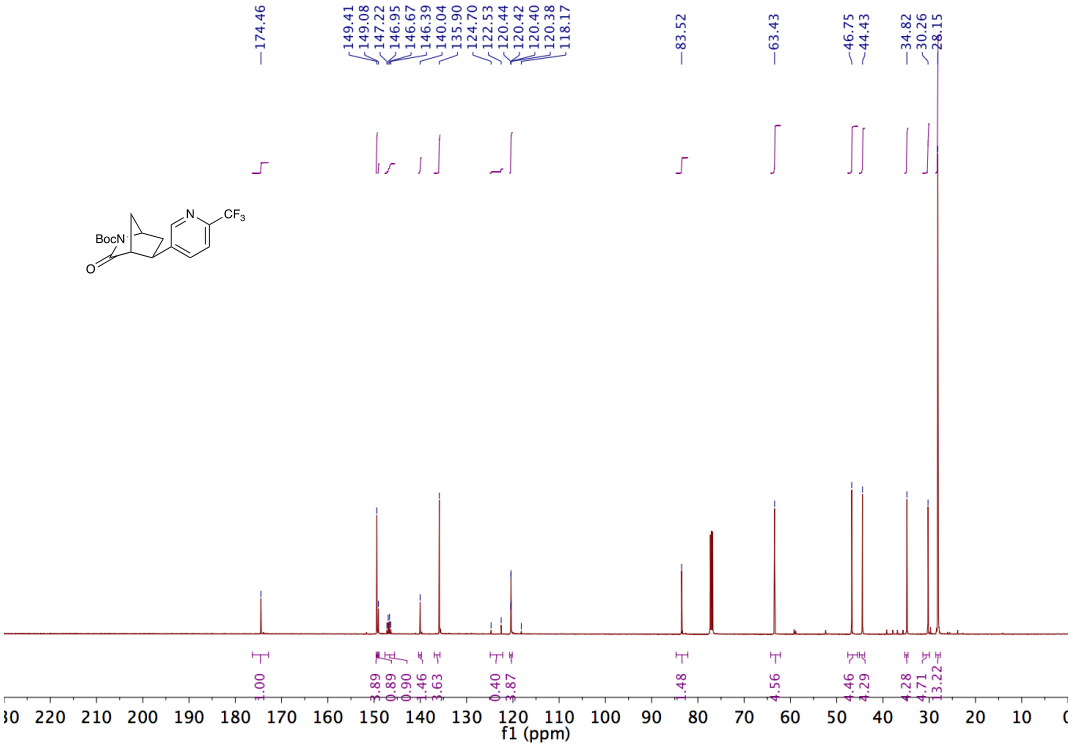
^{19}F NMR (376 MHz, $CDCl_3$) – (28)



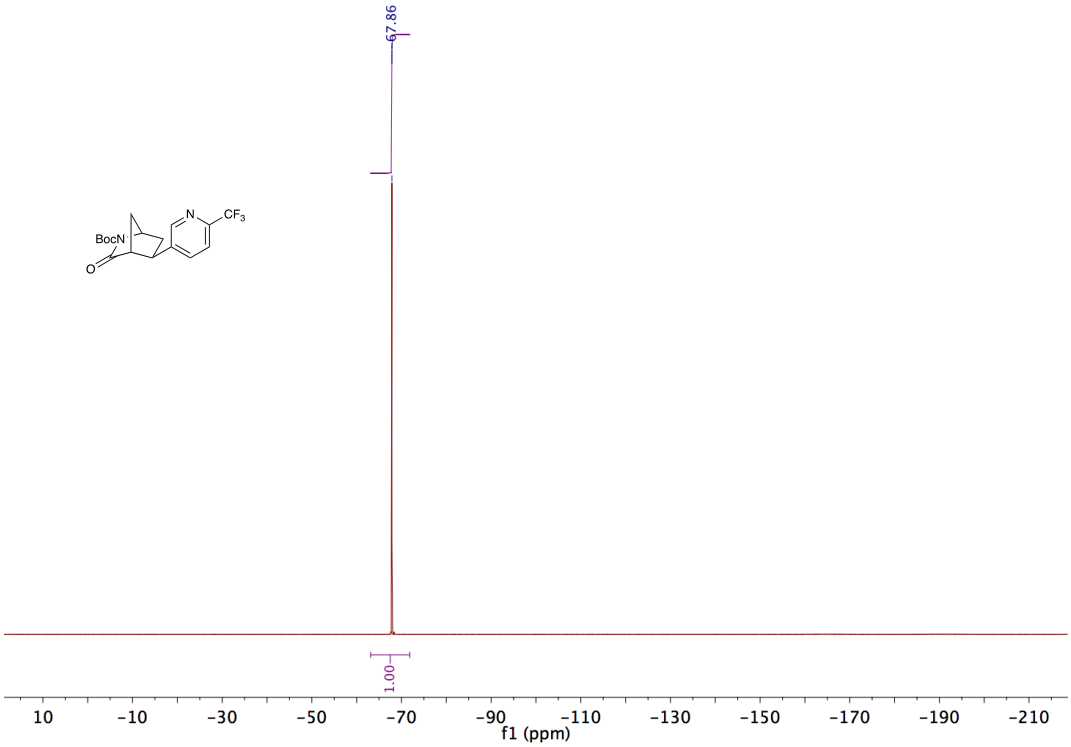
COSY(500 MHz, $CDCl_3$) – (28)



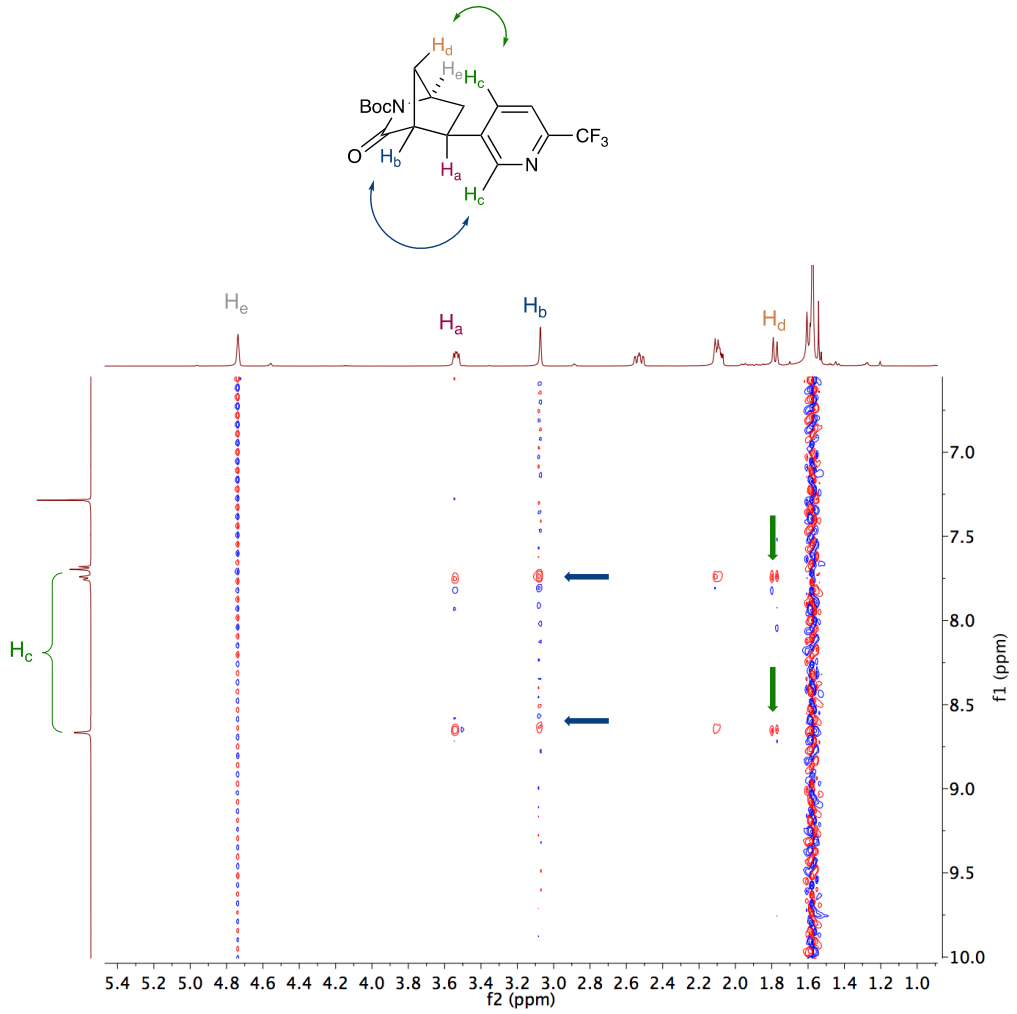
^{1}H NMR (500 MHz, $CDCl_3$) – (29)



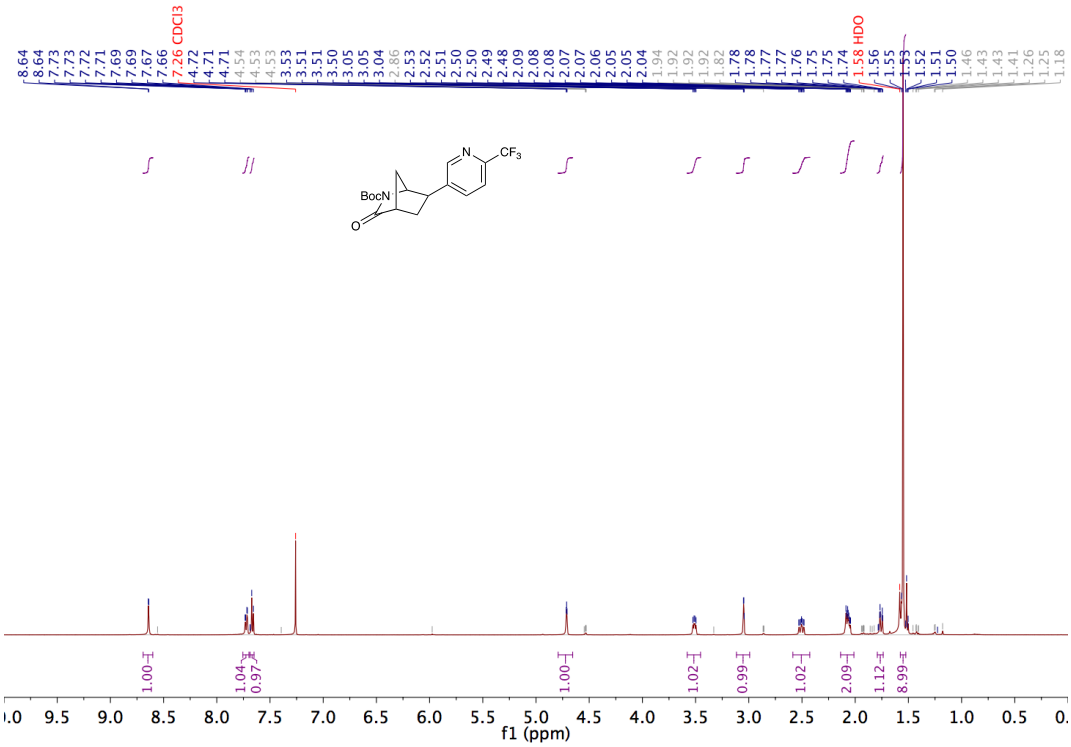
^{13}C NMR (126 MHz, $CDCl_3$) – (29)



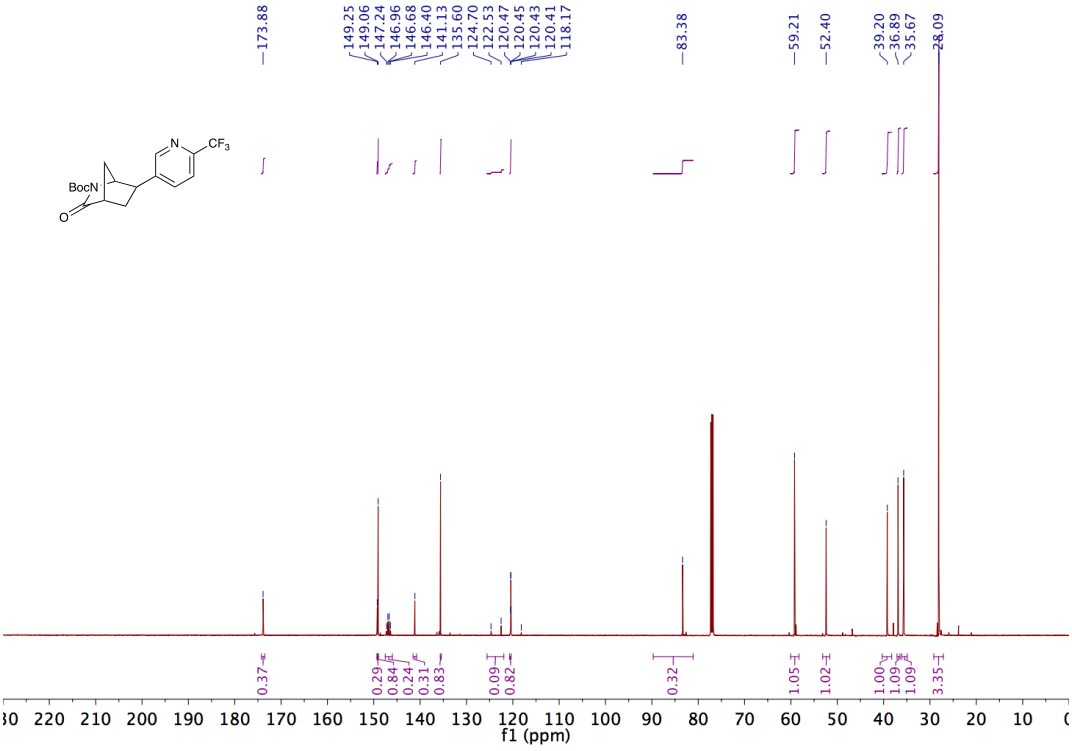
^{19}F NMR (376 MHz, $CDCl_3$) – (29)



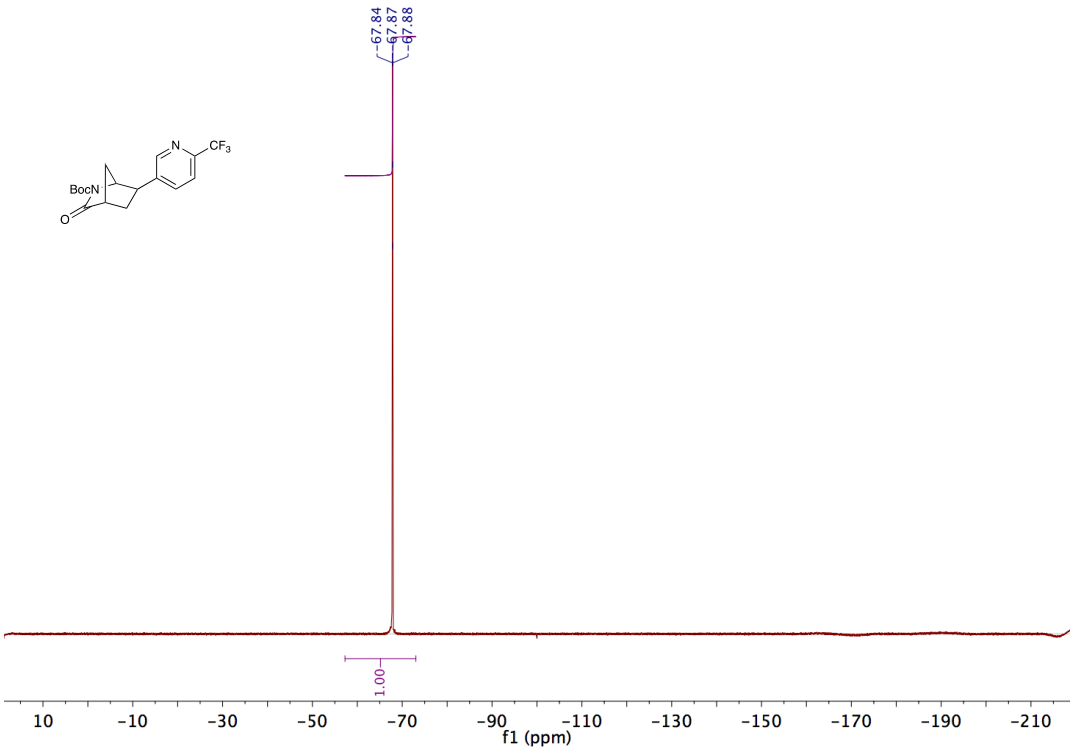
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (29)



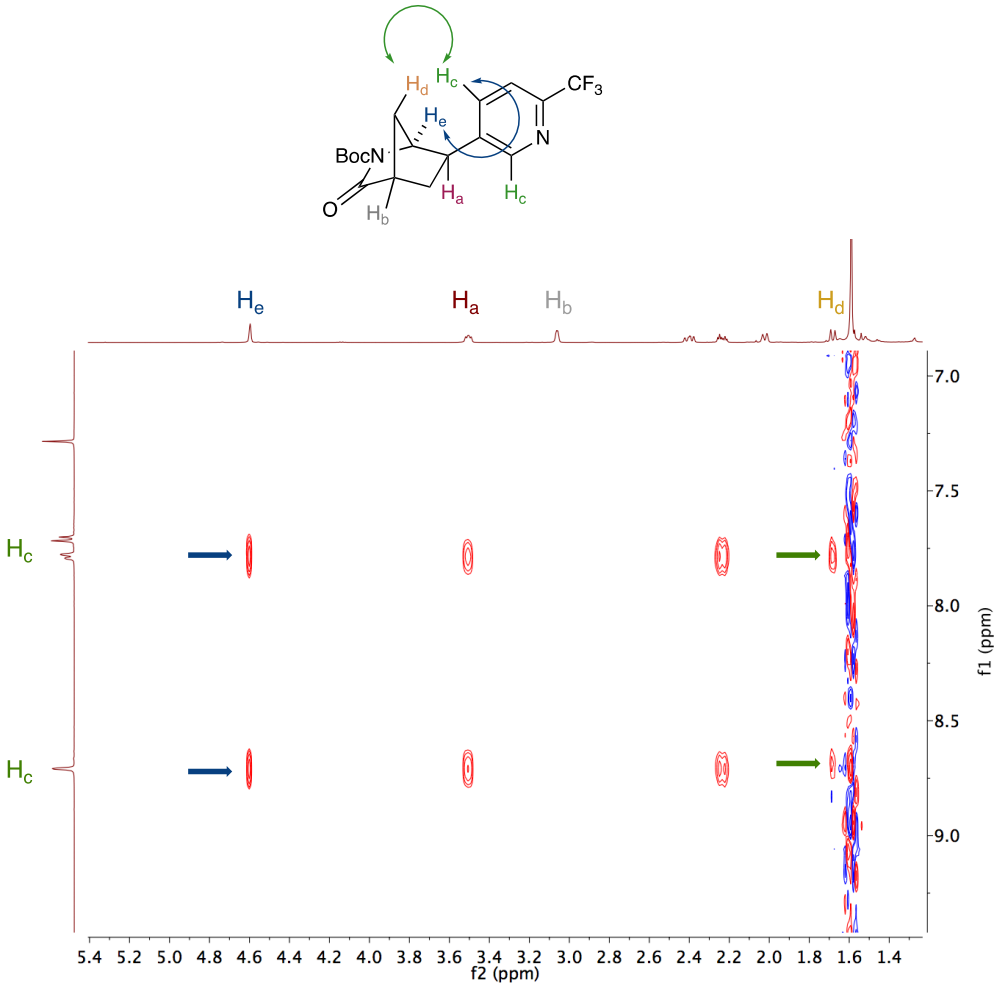
^{1}H NMR (500 MHz, $CDCl_3$) – (SI-29)



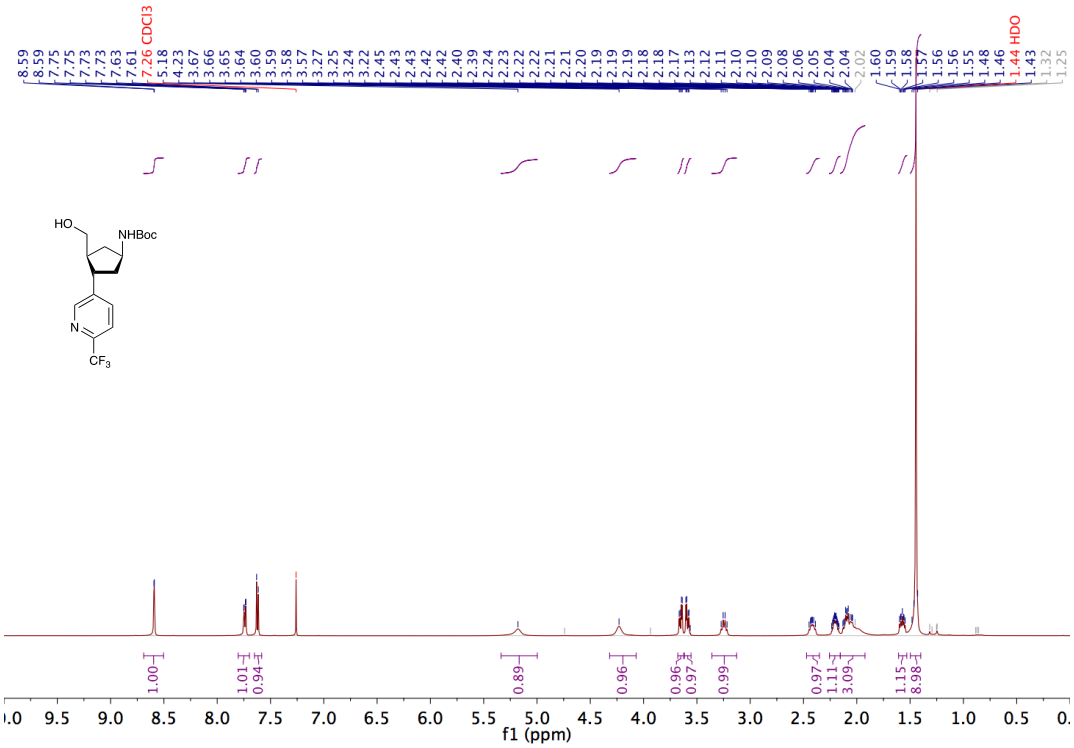
^{13}C NMR (126 MHz, $CDCl_3$) – (SI-29)



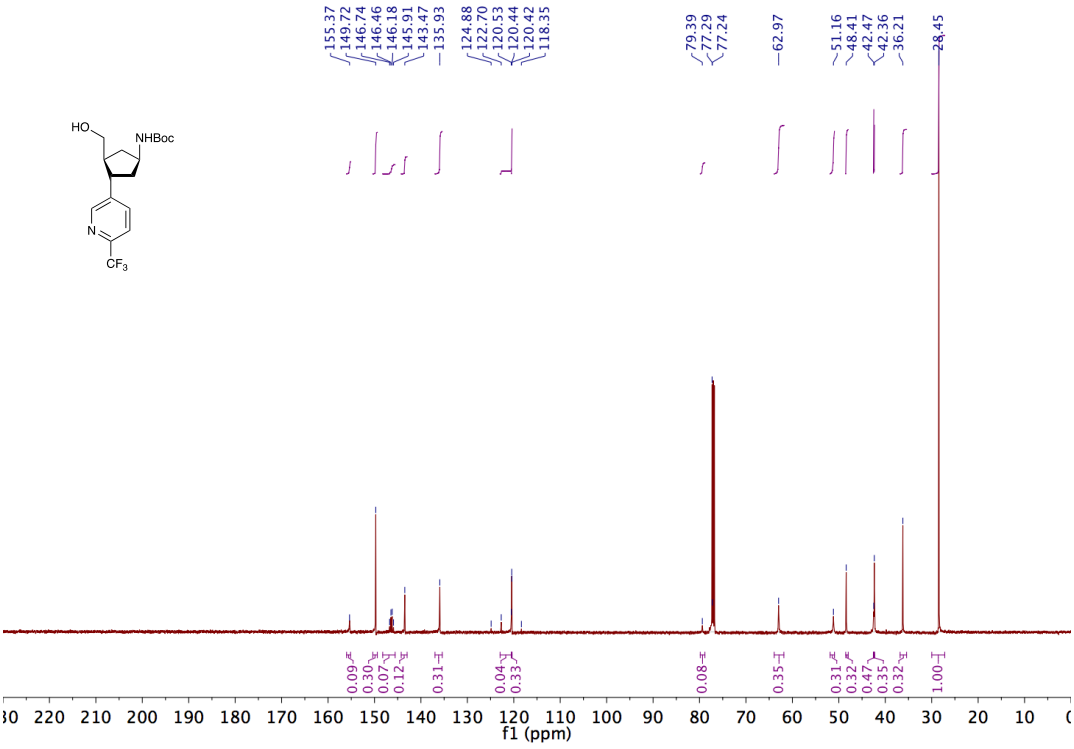
^{19}F NMR (376 MHz, $CDCl_3$) – (SI-29)



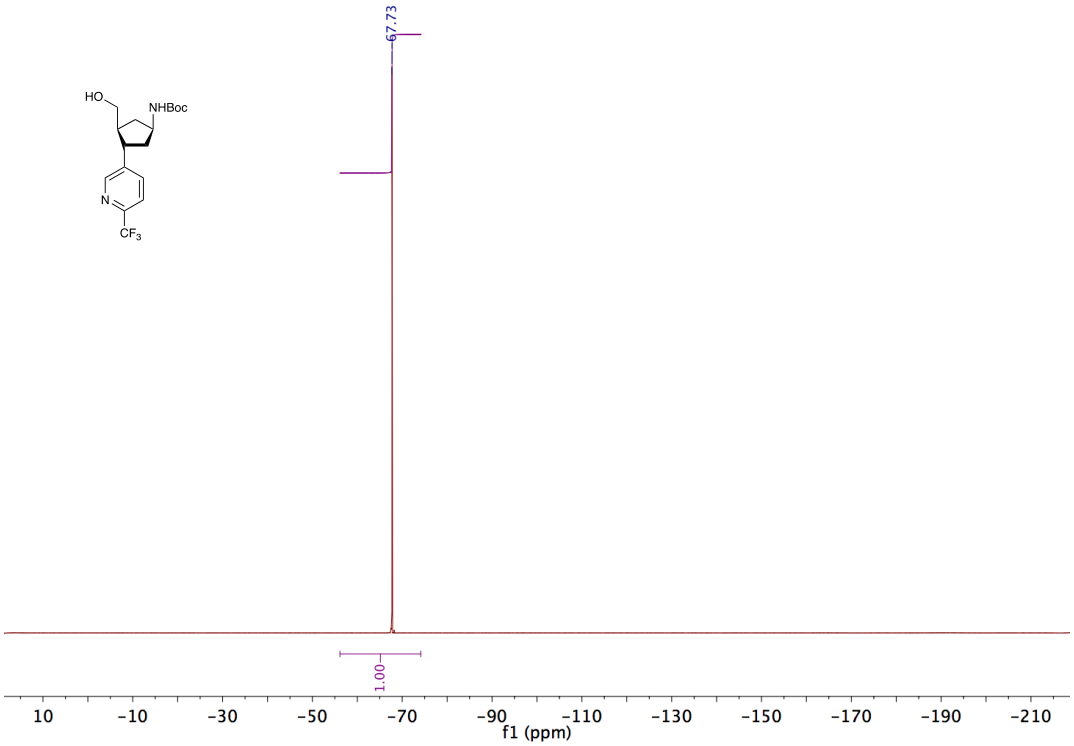
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (SI-29)



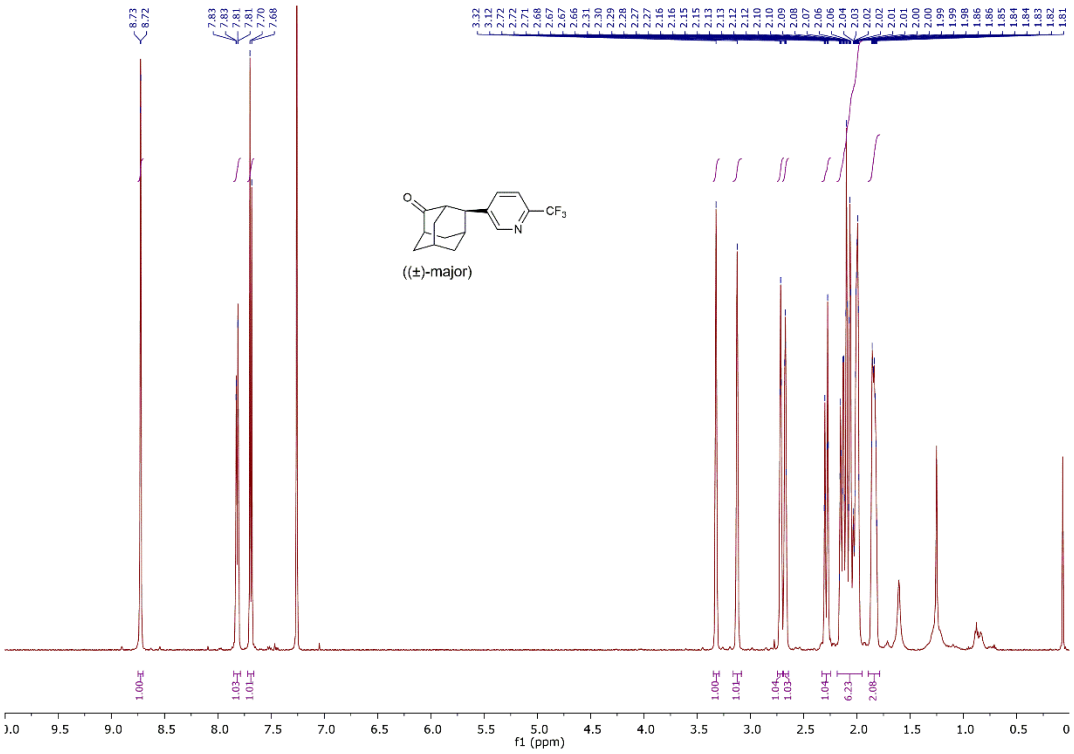
^{1}H NMR (500 MHz, $CDCl_3$) – (30)



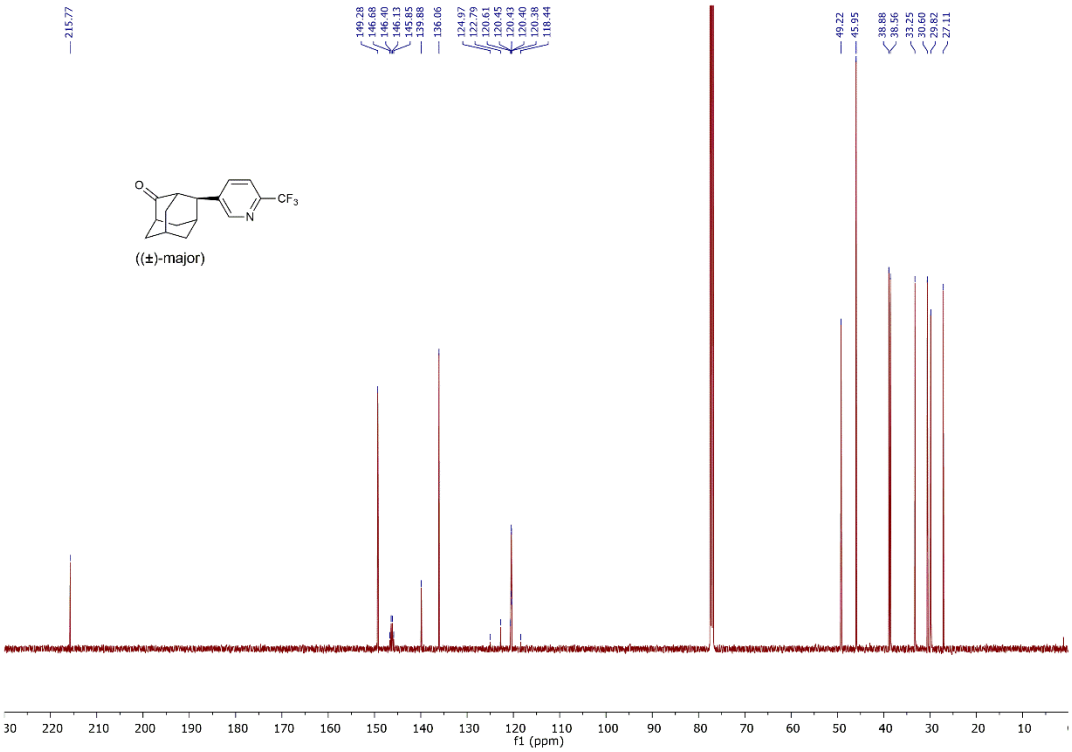
^{13}C NMR (126 MHz, $CDCl_3$) – (30)



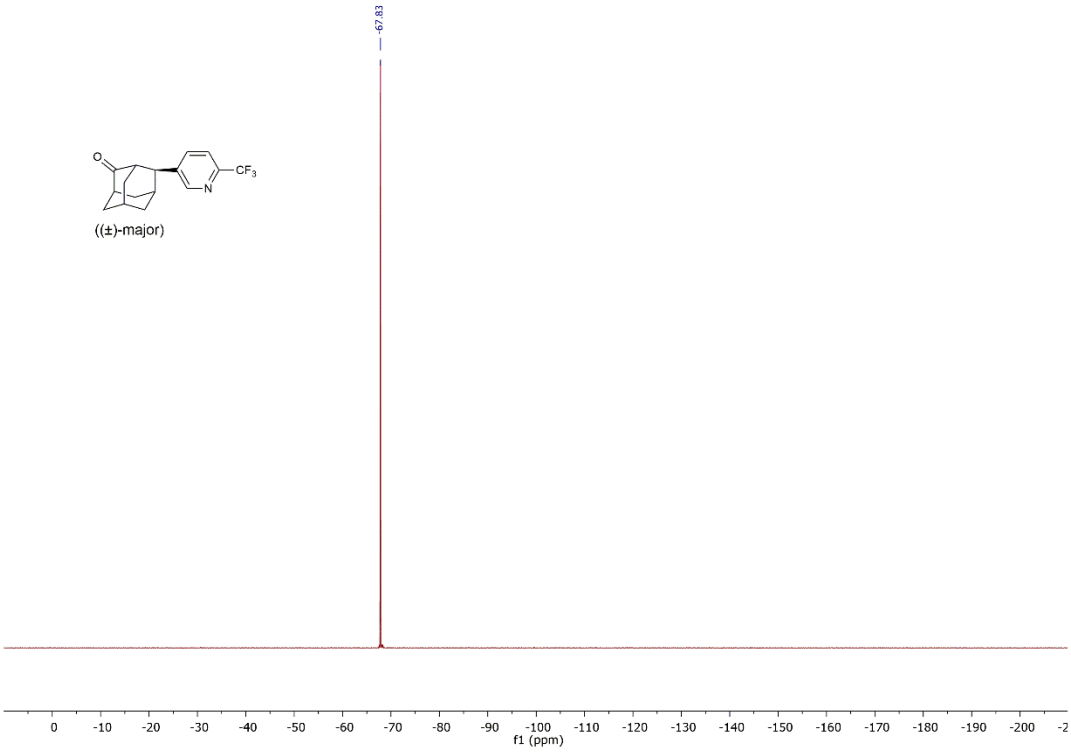
^{19}F NMR (376 MHz, CDCl$_3$) – (30)



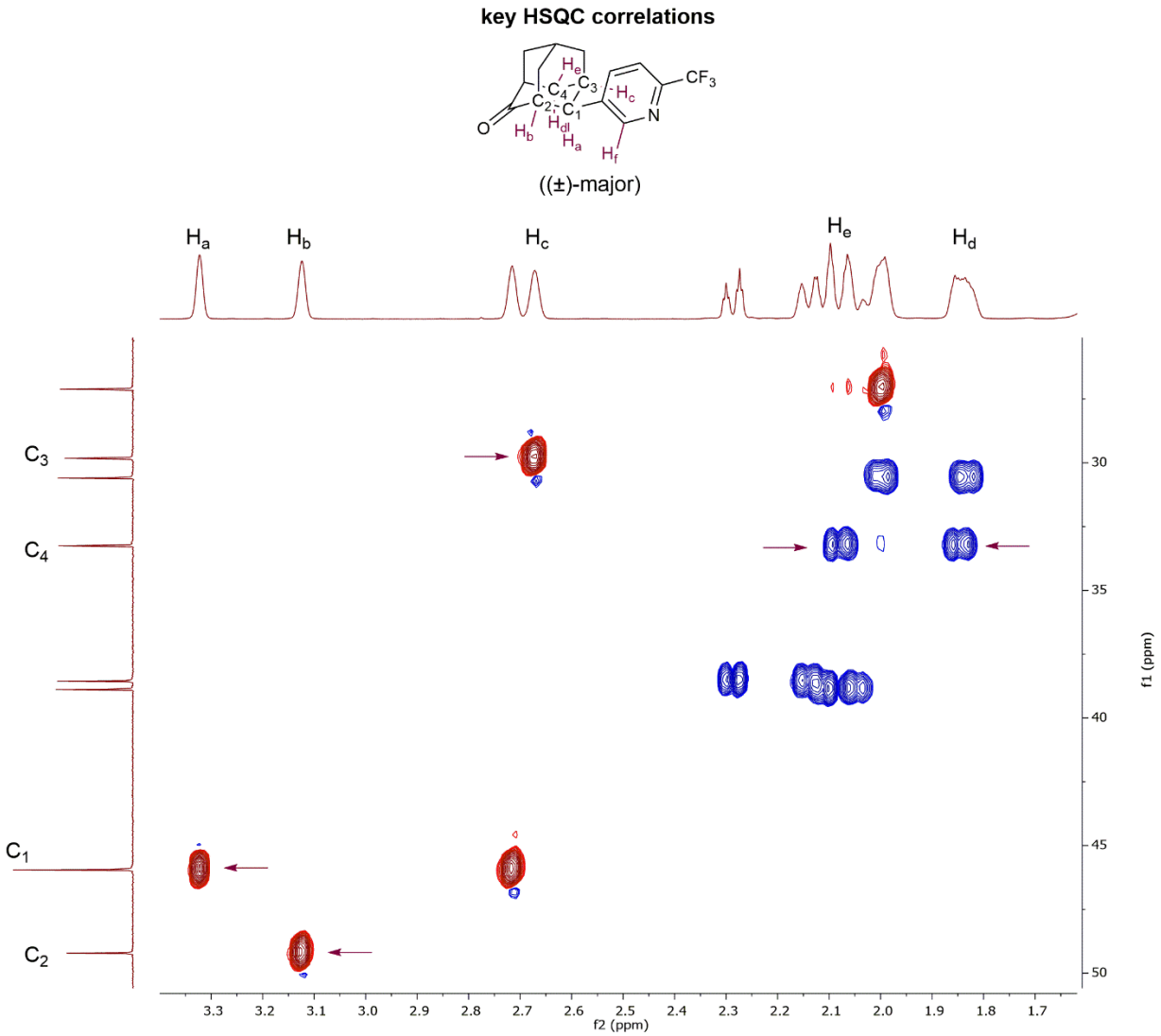
^{1}H NMR (500 MHz, CDCl$_3$) - (31)



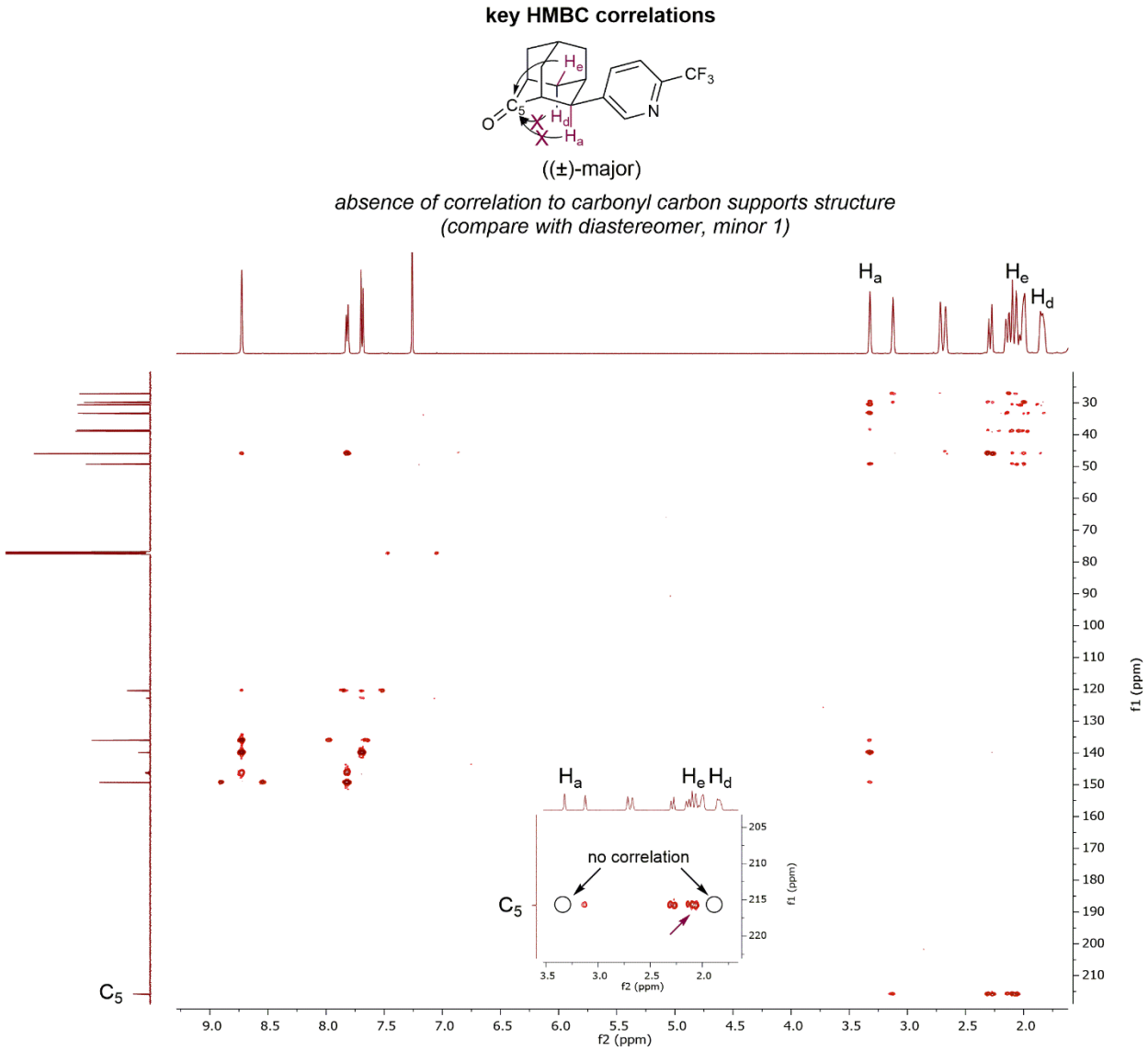
^{13}C NMR (126 MHz, $CDCl_3$) - (31)



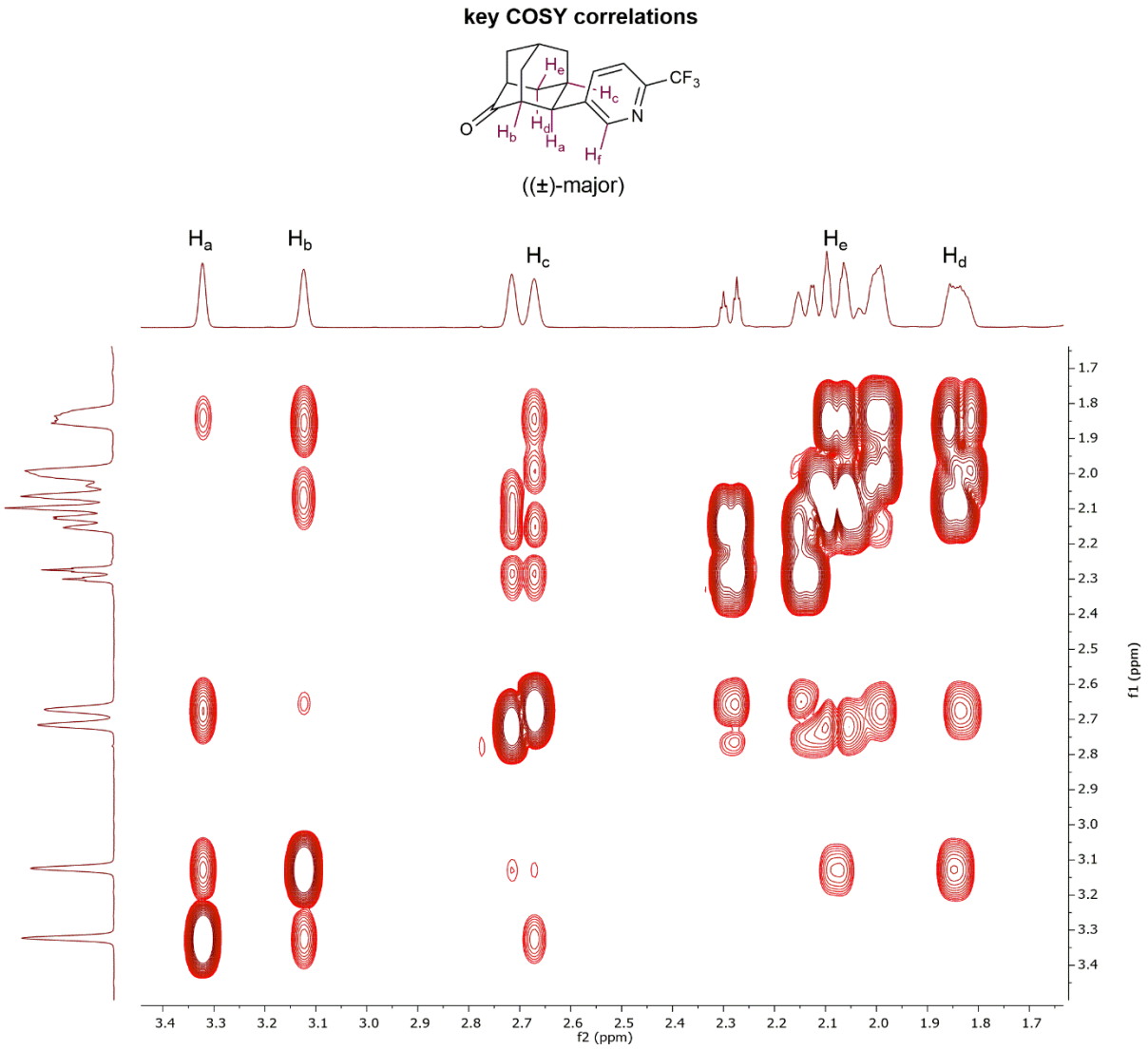
^{19}F NMR (376 MHz, CDCl3) - (31)


key HSQC correlations
((±)-major)
Ha
Hb
Hc
He
Hd
C3
C4
C1
C2
f2 (ppm)
f1 (ppm)

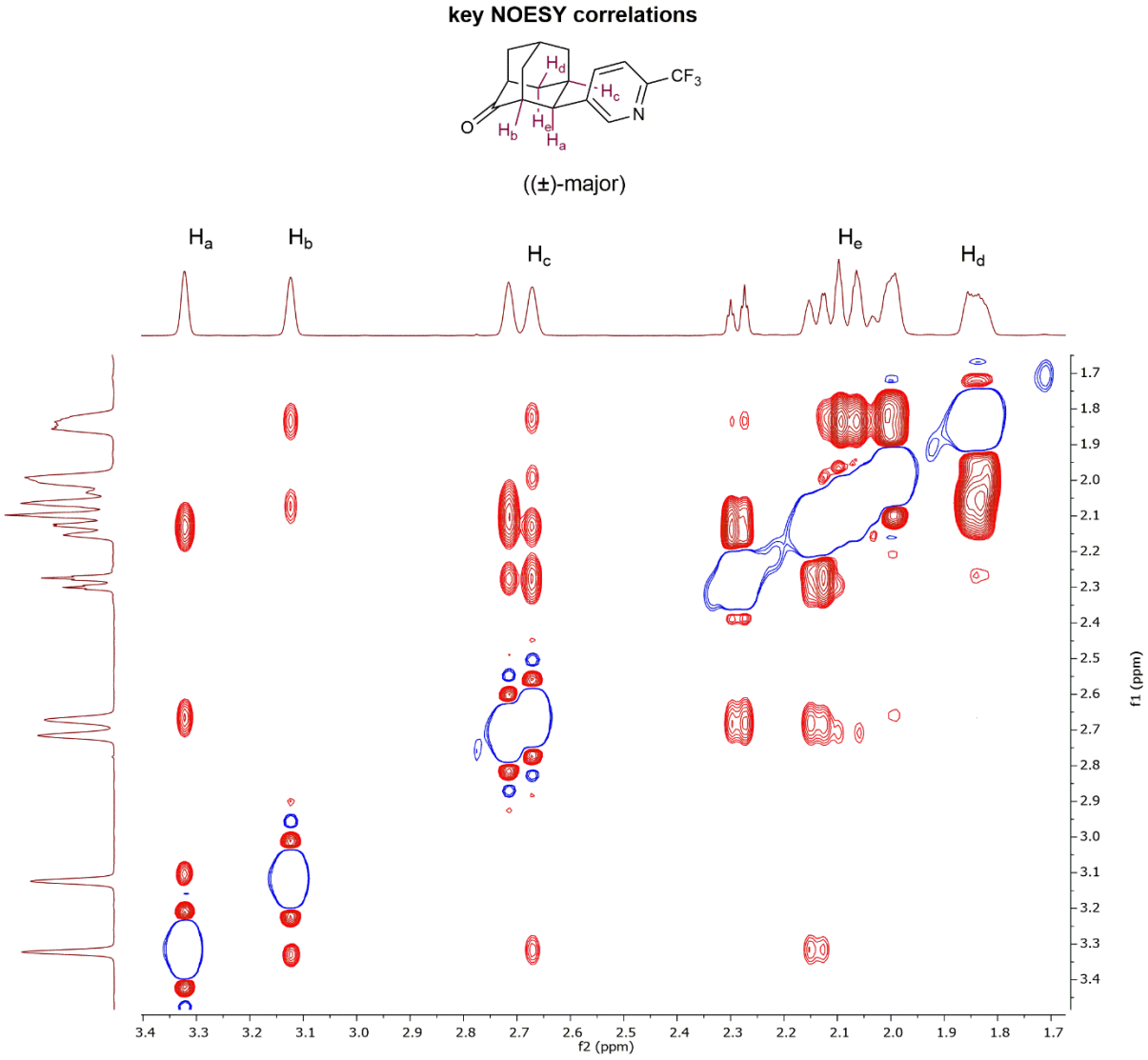
HSQC - (31)


key HMBC correlations
H_e
CF_3
C_5
O
H_d
N
H_a
((±)-major)
absence of correlation to carbonyl carbon supports structure
(compare with diastereomer, minor 1)
H_a
H_e
H_d
C_5
f2 (ppm)
f1 (ppm)
H_a
H_e H_d
no correlation
C_5

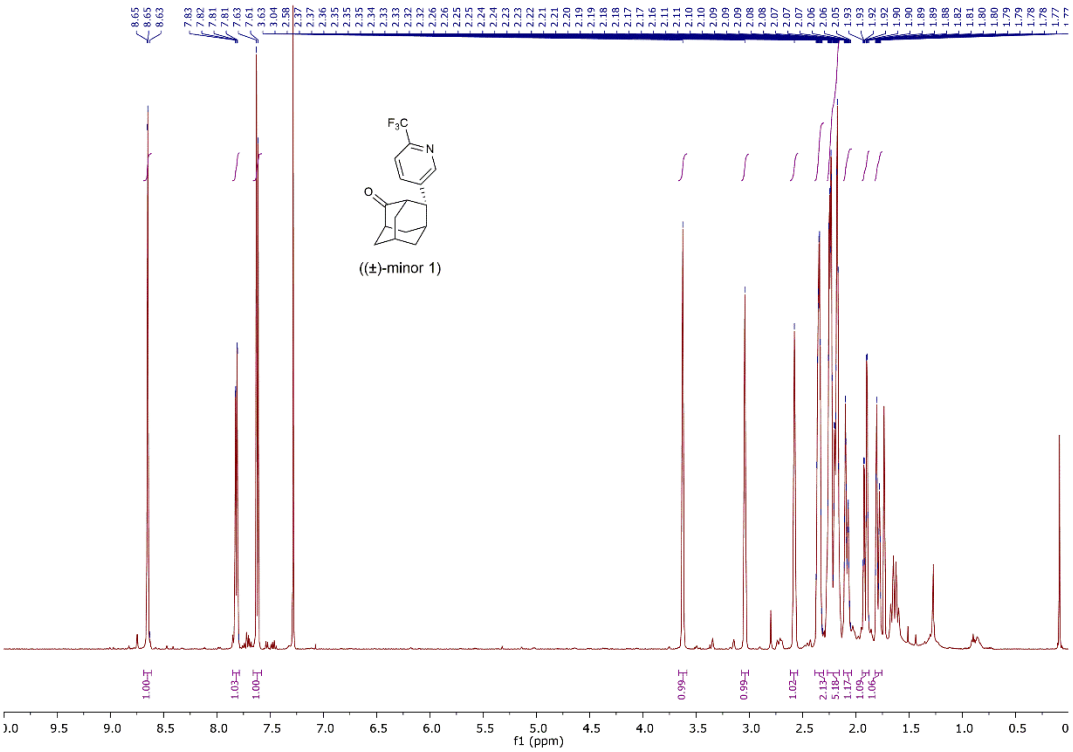
HMBC - (31)



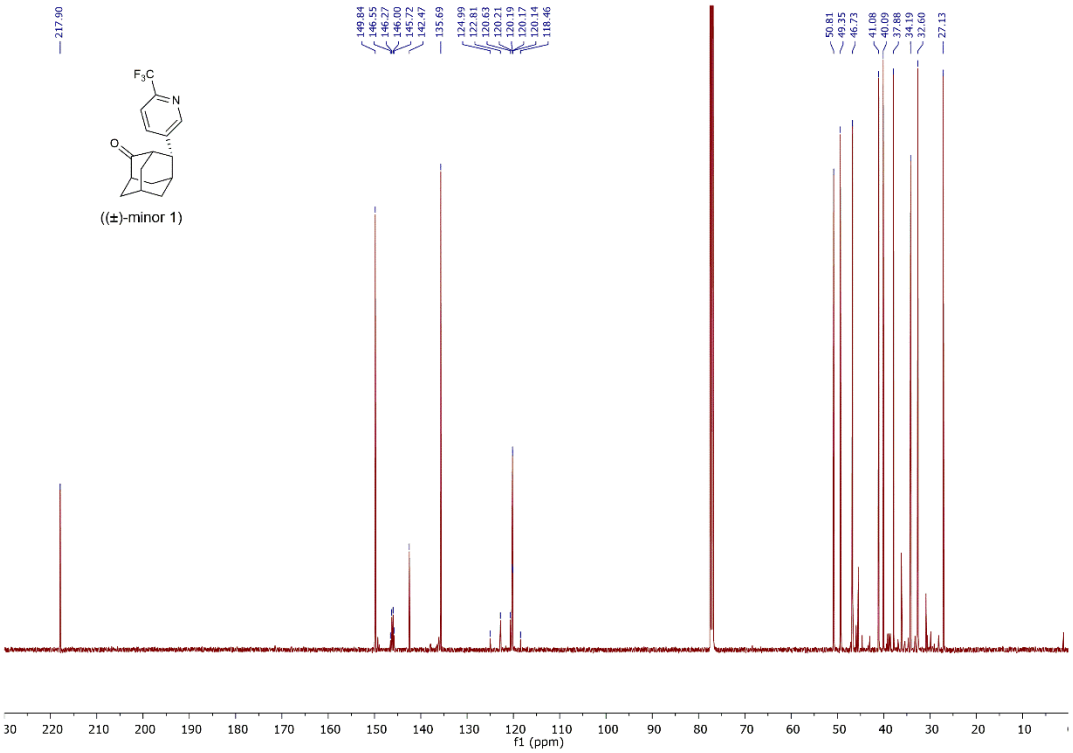
COSY - (31)


key NOESY correlations
Hd
Hc
CF3
N
O
Hb
He
Ha
((±)-major)
Ha
Hb
Hc
He
Hd
f2 (ppm)
f1 (ppm)

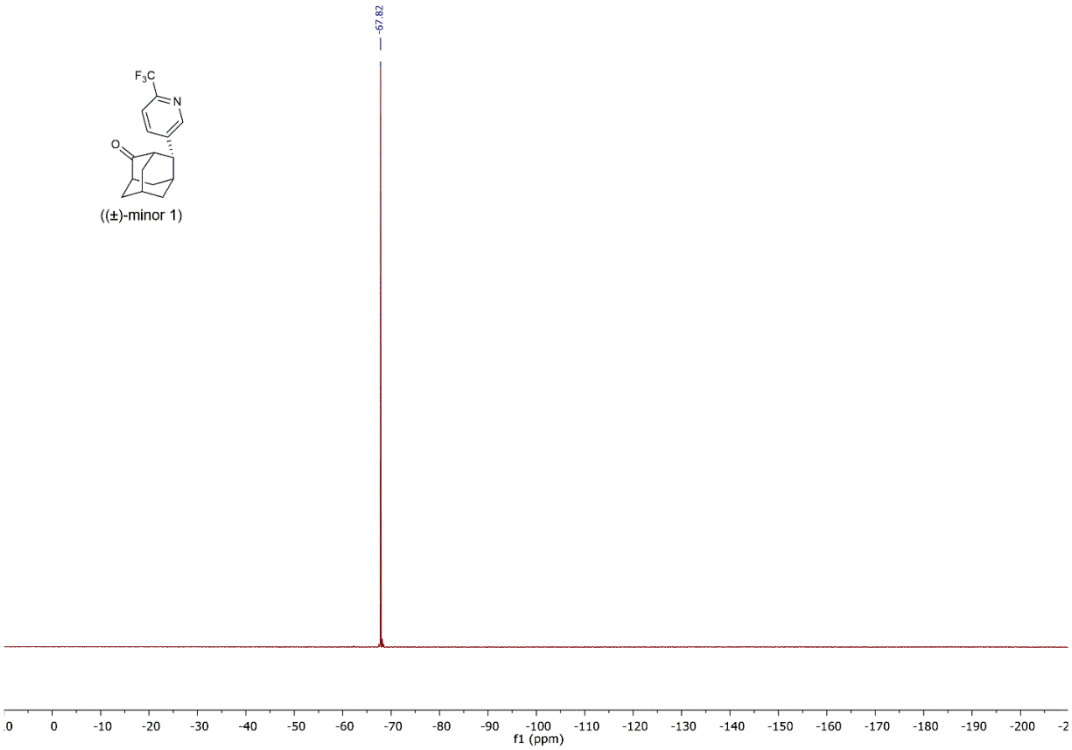
NOESY - (31)



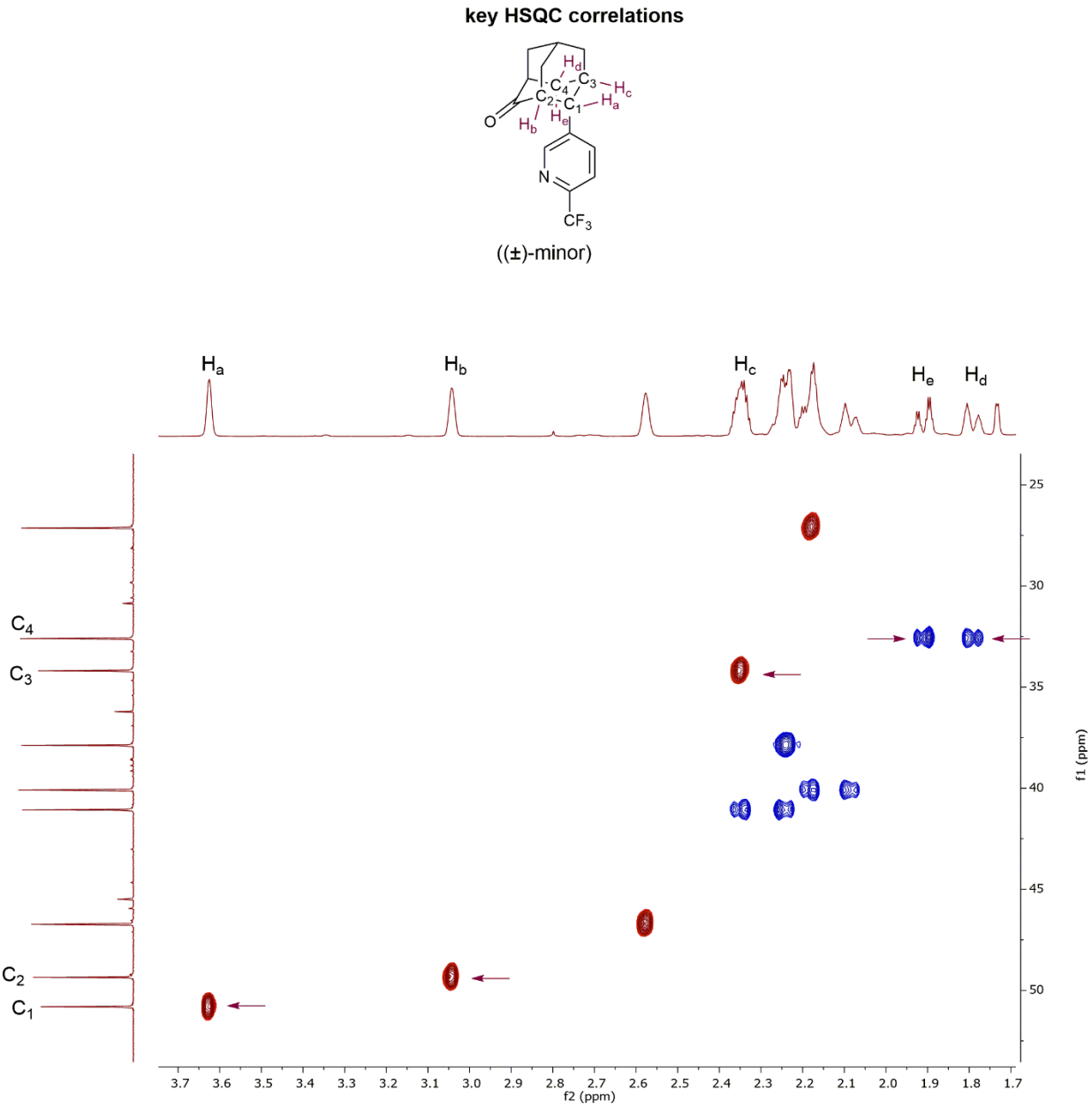
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-31a)



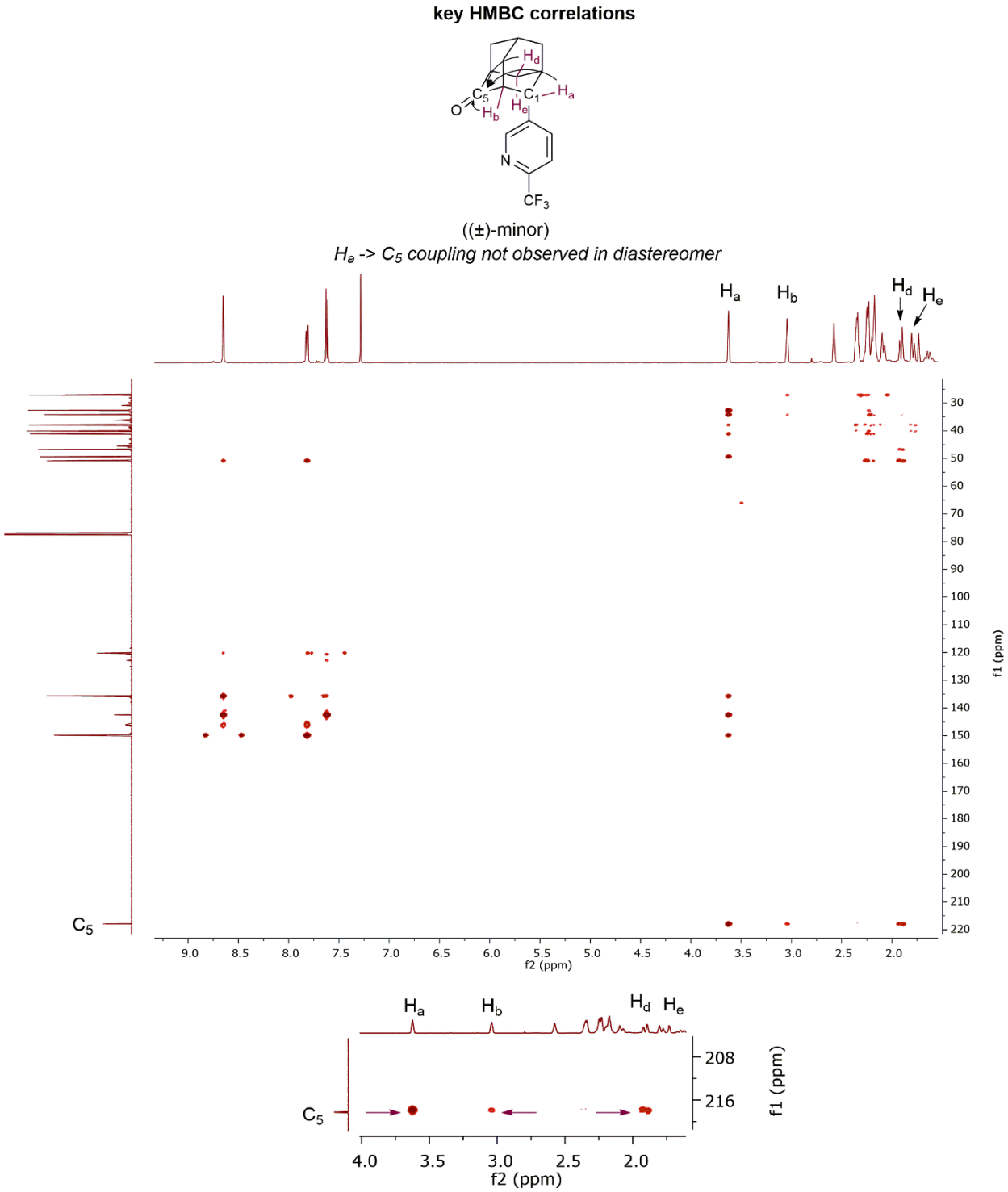
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-31a)



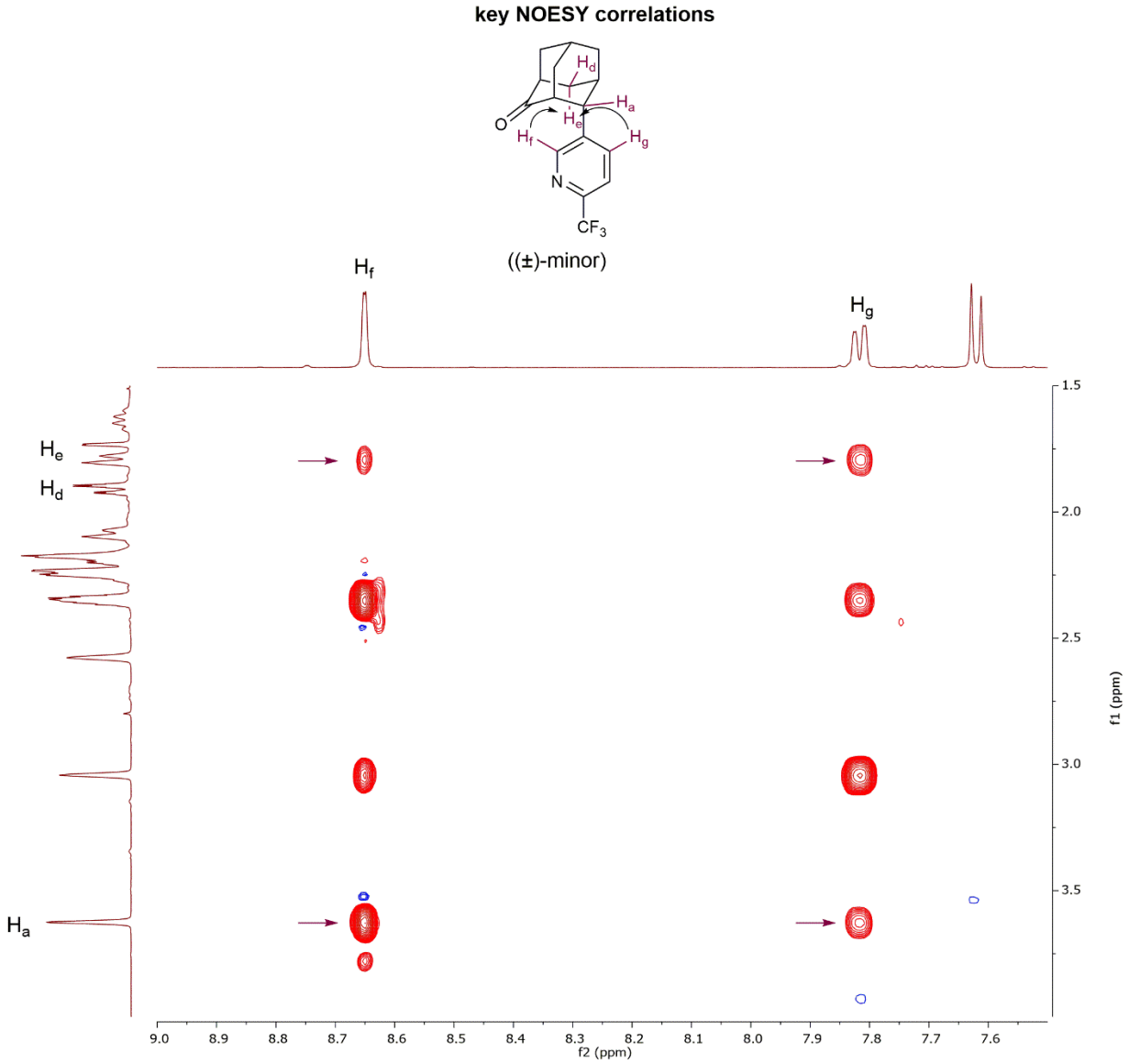
^{19}F NMR (282 MHz, $CDCl_3$) - (SI-31a)


key HSQC correlations
((±)-minor)
Ha
Hb
Hc
He
Hd
C4
C3
C2
C1
f2 (ppm)
f1 (ppm)

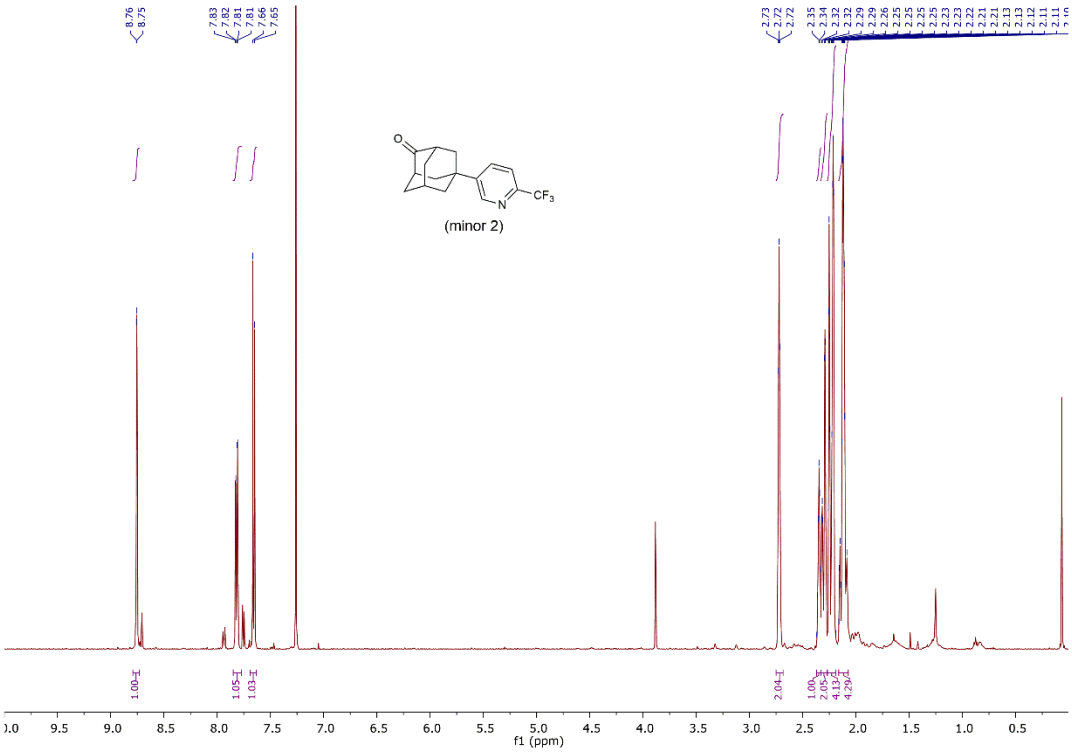
HSQC - (SI-31a)


key HMBC correlations
Hd
C5
C1
Ha
O
Hb
He
N
CF3
((±)-minor)
Ha -> C5 coupling not observed in diastereomer
Ha
Hb
Hd
He
C5
f2 (ppm)
f1 (ppm)
208
216

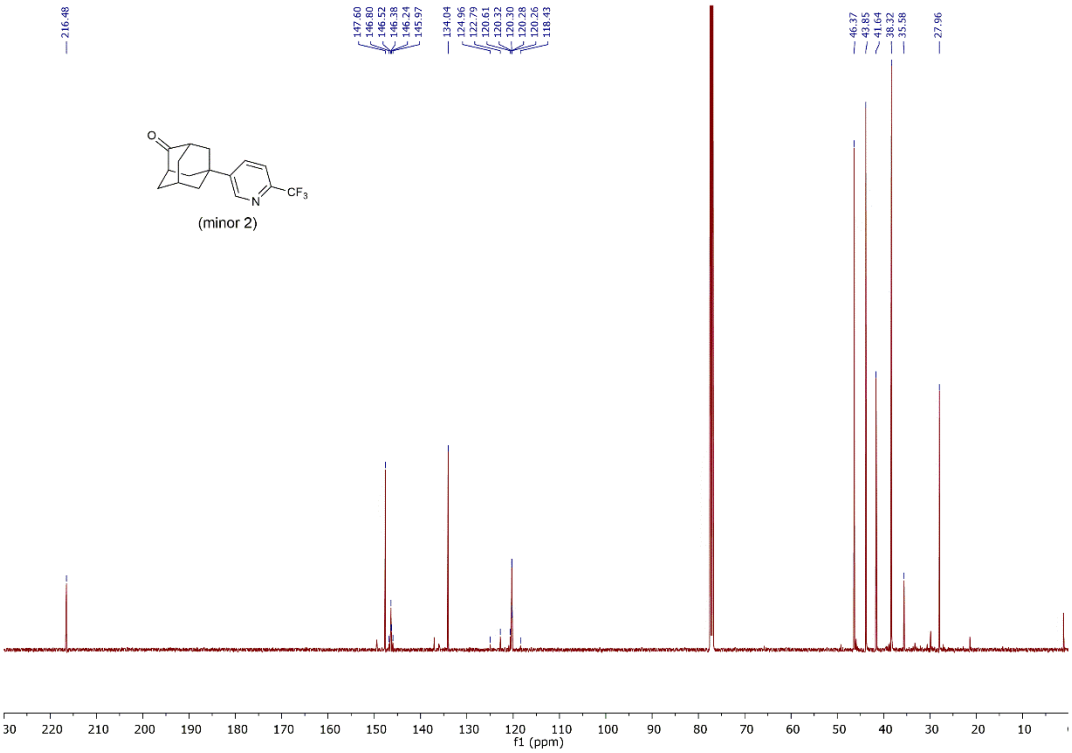
HMBC - (SI-31a)


key NOESY correlations
Hd
Ha
He
O
Hf
Hg
N
CF3
((±)-minor)
Hf
Hg
He
Hd
Ha
1.5
2.0
2.5
3.0
3.5
f1 (ppm)
9.0
8.9
8.8
8.7
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
f2 (ppm)

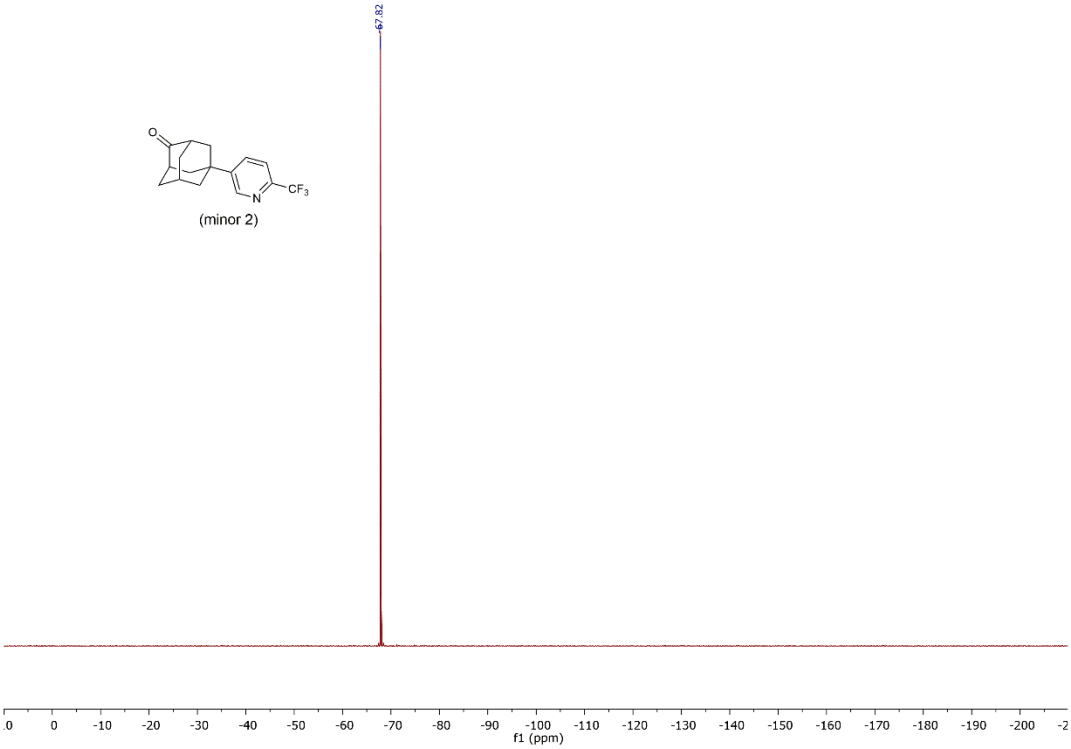
NOESY - (SI-31a)



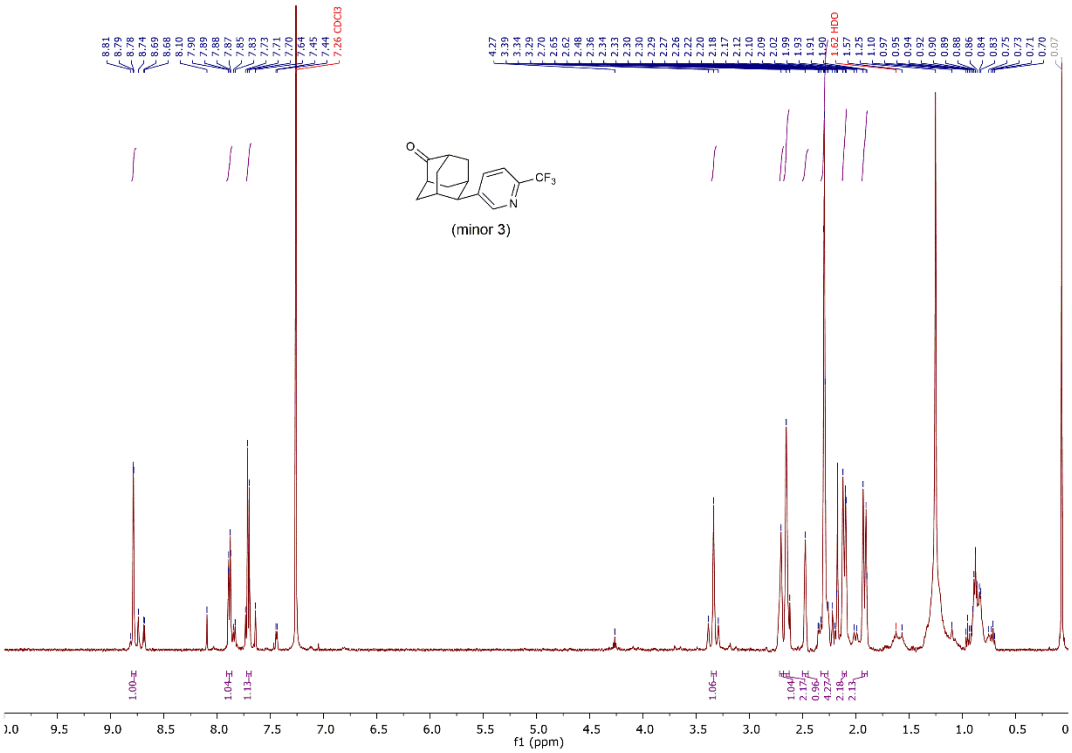
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-31b)



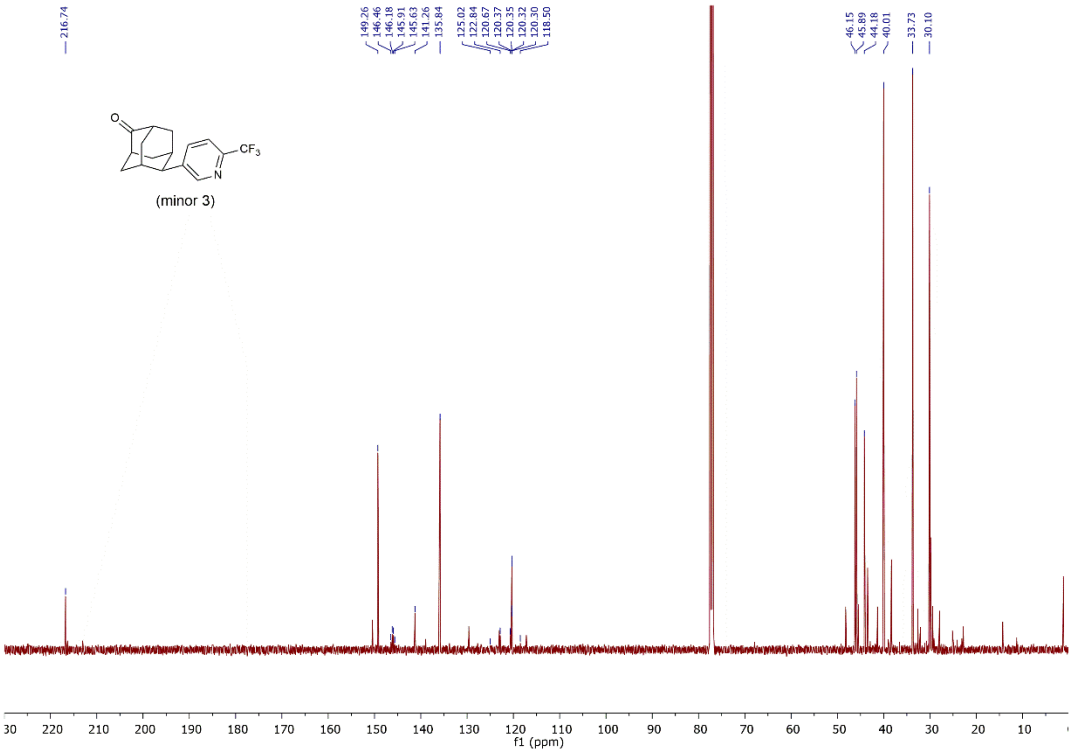
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-31b)



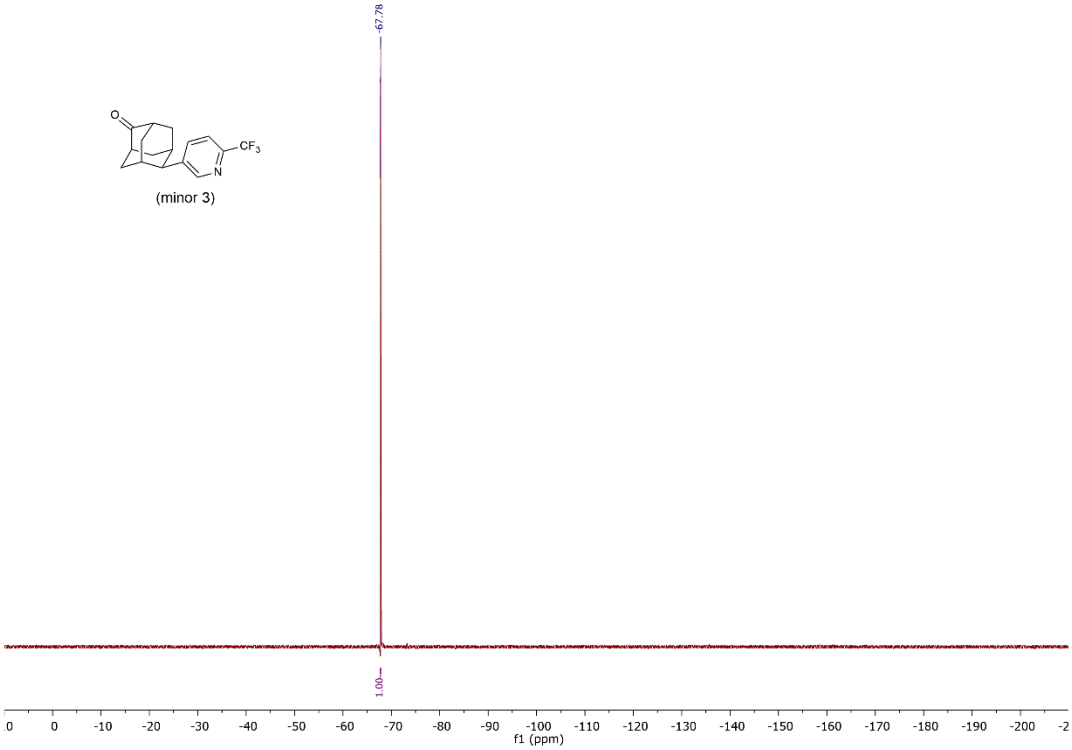
^{19}F NMR (282 MHz, $CDCl_3$) - (SI-31b)



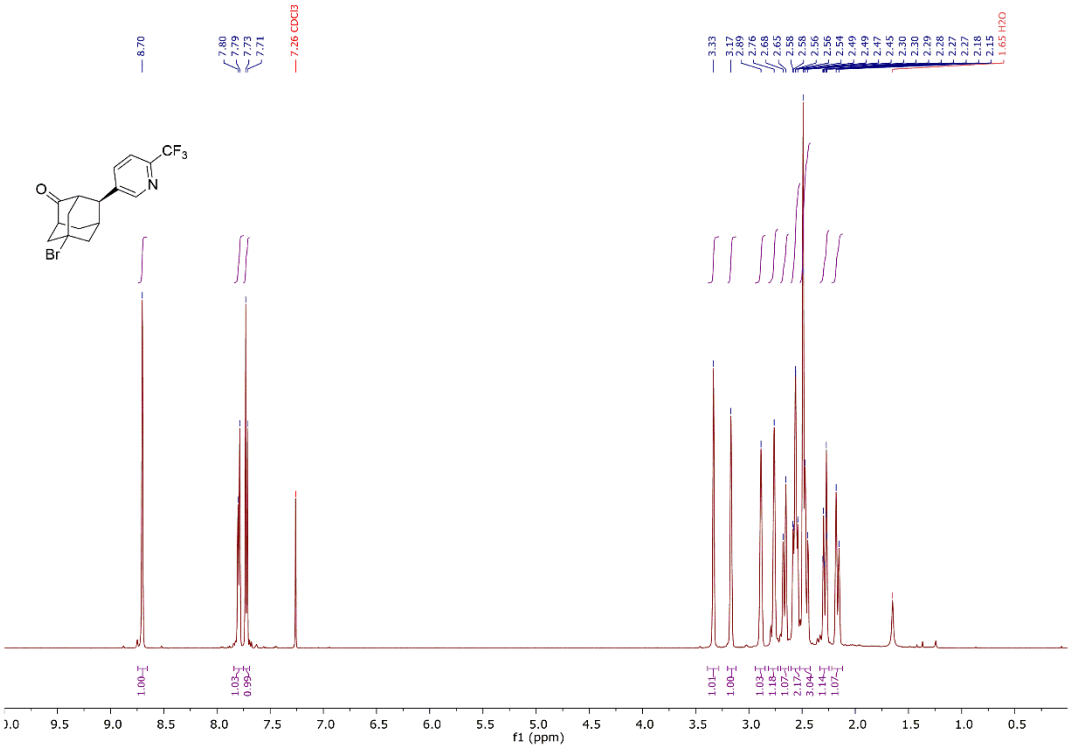
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-31c)



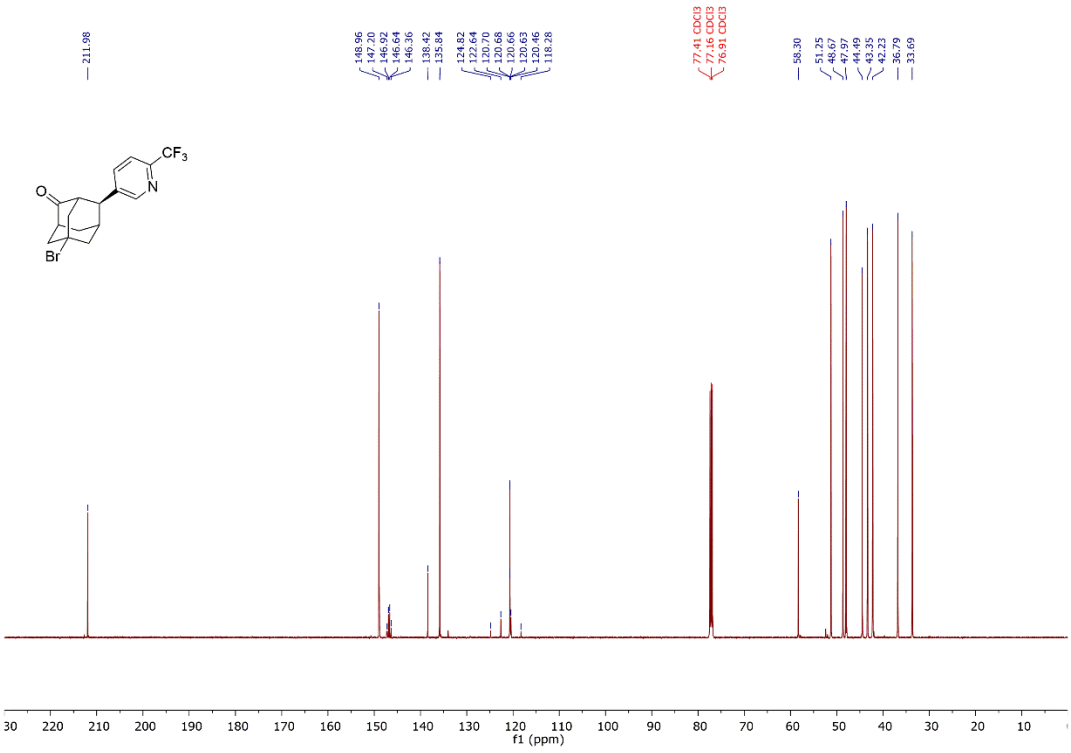
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-31c)



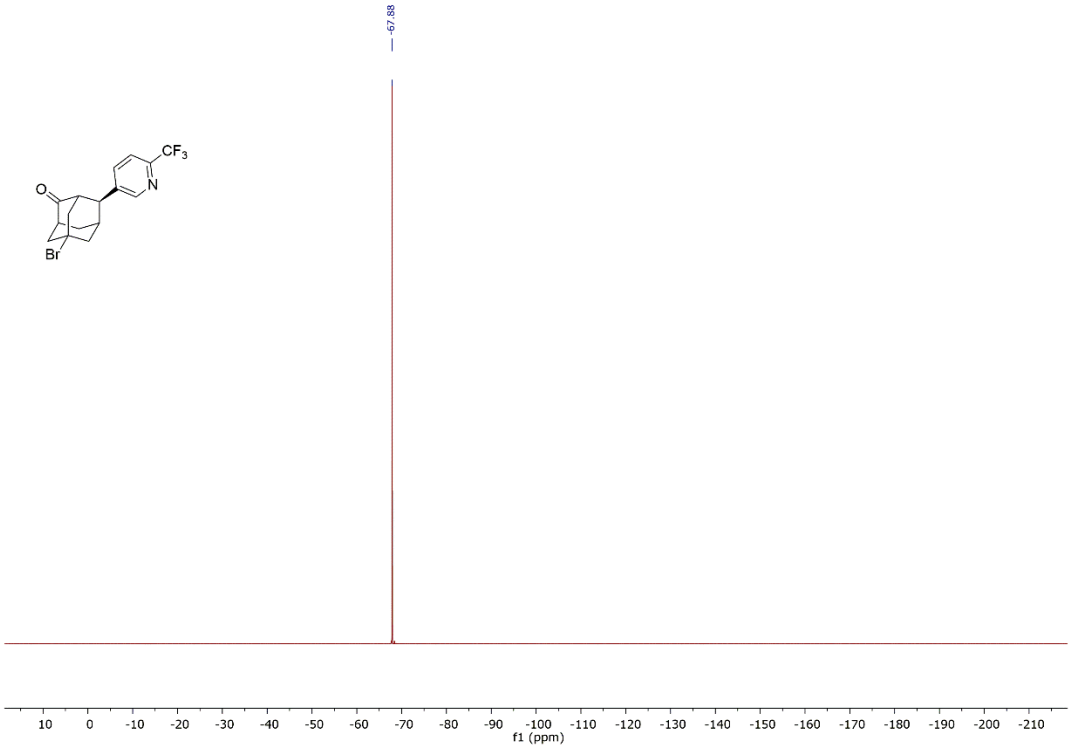
^{19}F NMR (282 MHz, $CDCl_3$) - (SI-31c)



^{1}H NMR (500 MHz, $CDCl_3$) – (32)

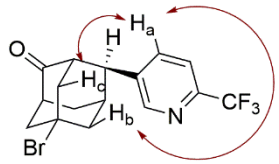


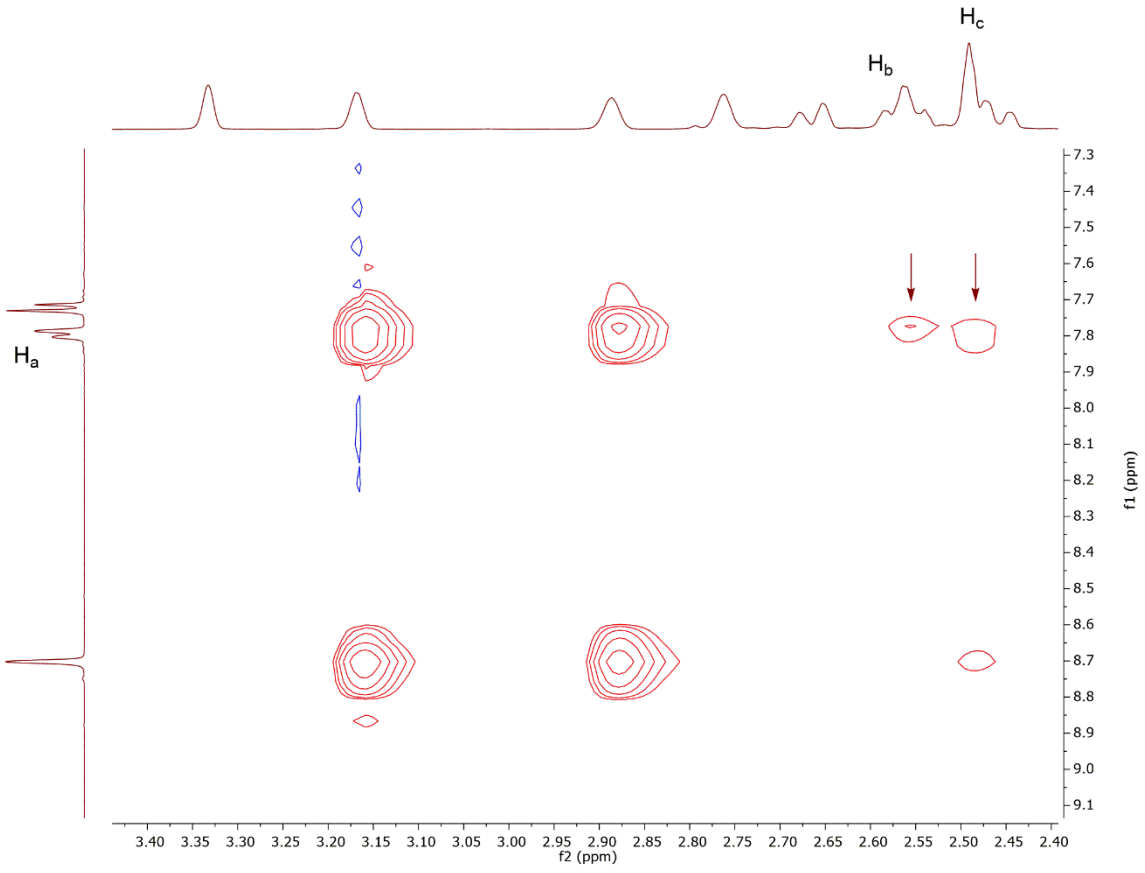
^{13}C NMR (126 MHz, $CDCl_3$) – (32)



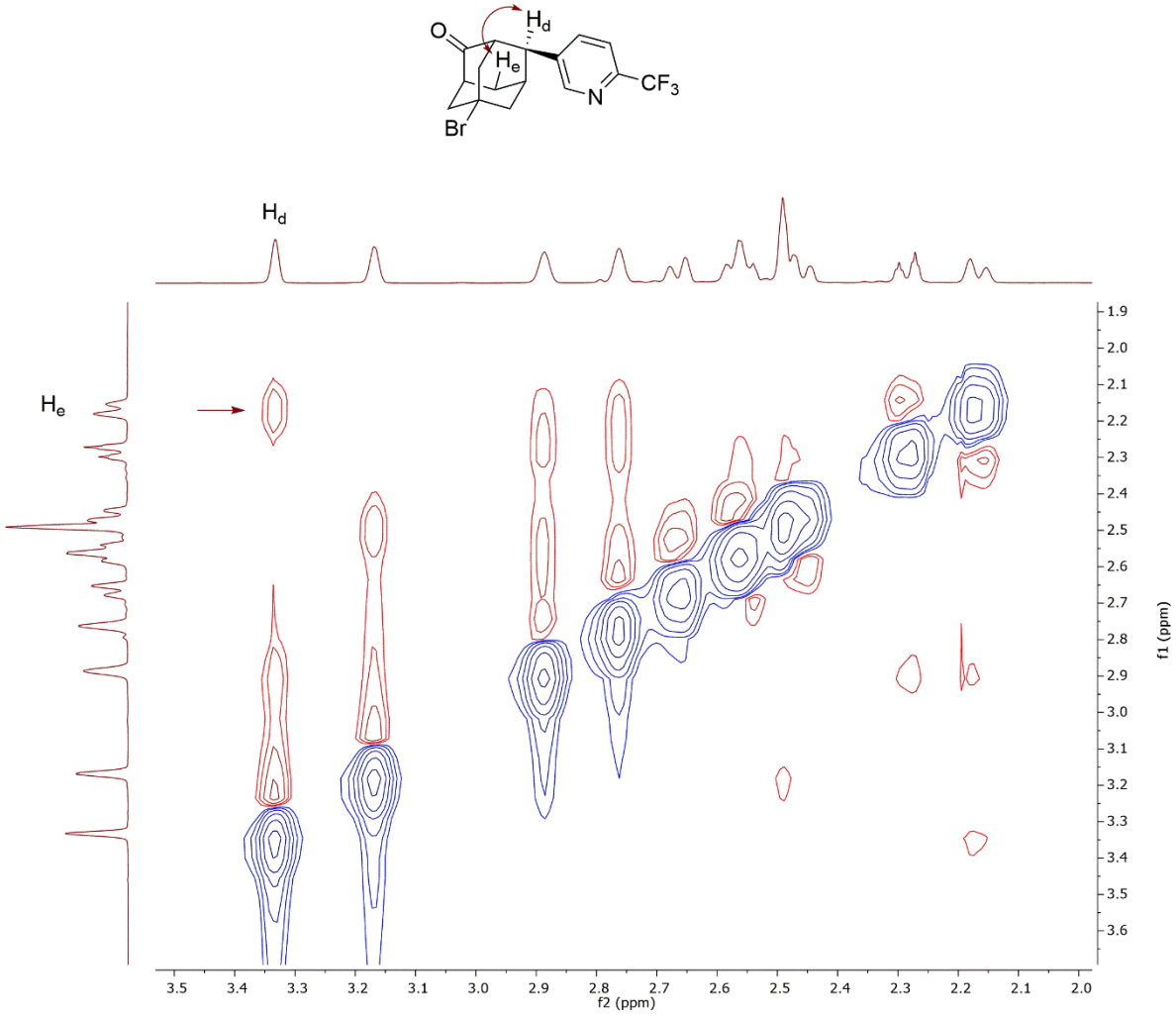
^{19}F NMR (376 MHz, $CDCl_3$) – (32)

Key NOESY correlations

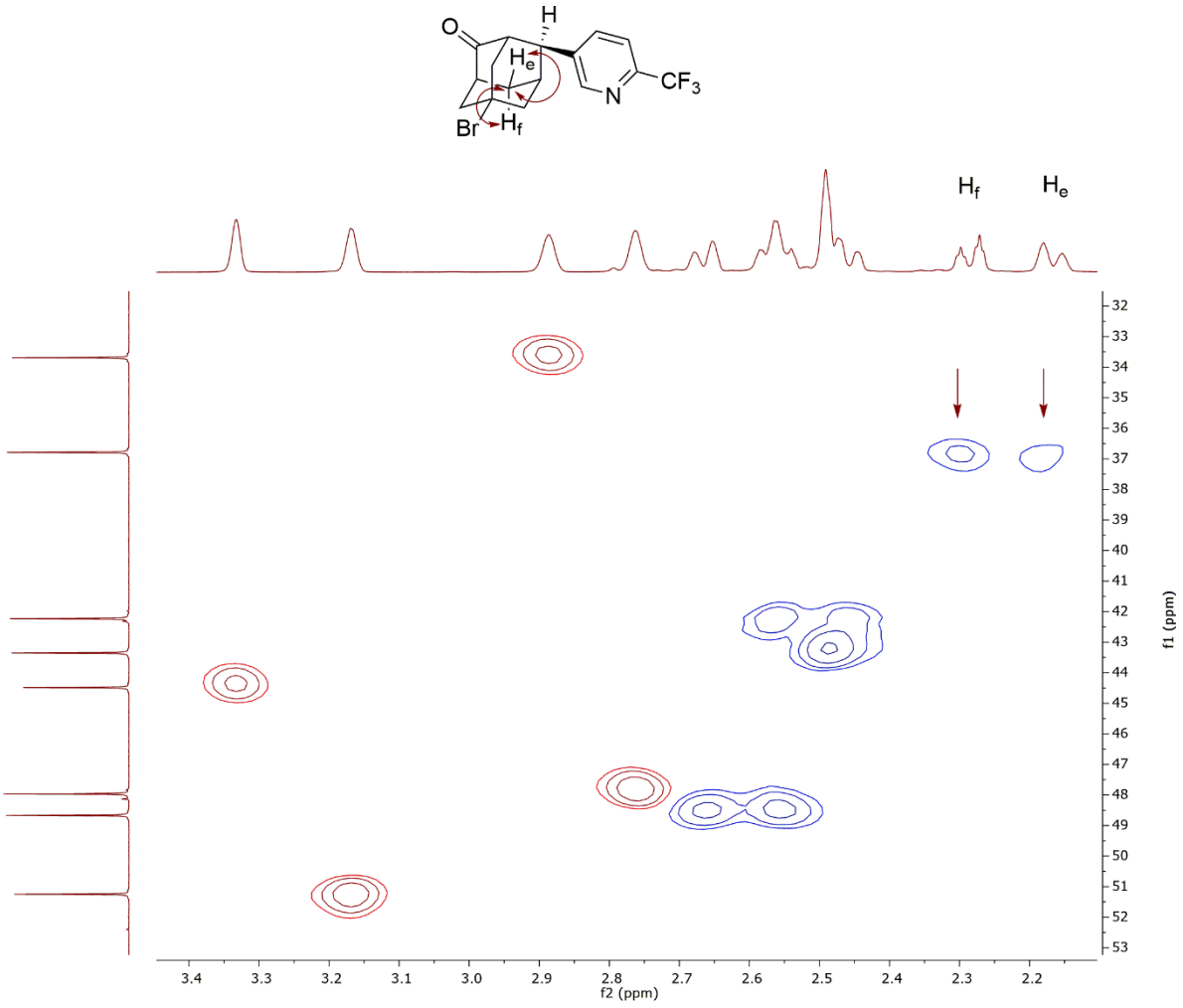




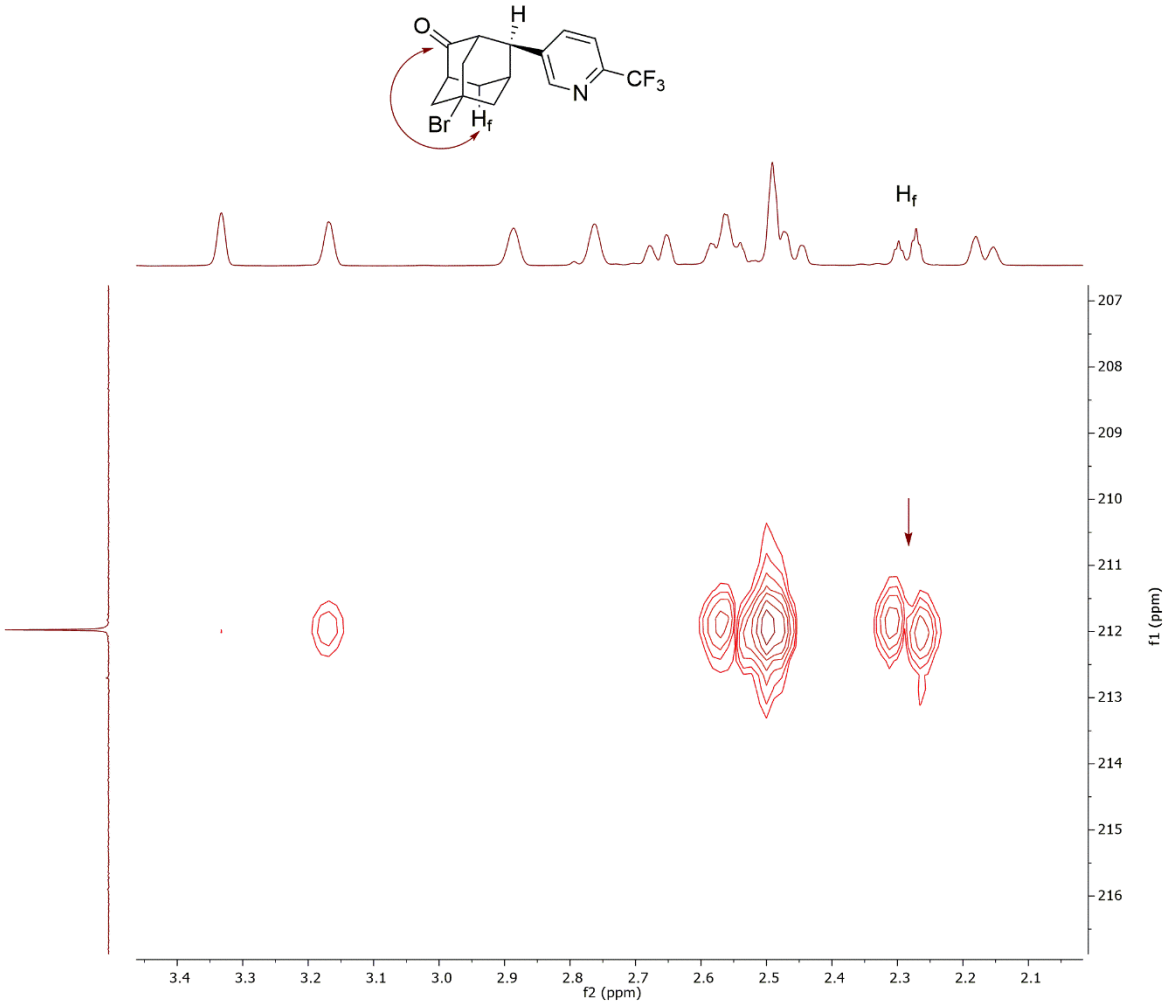
Key NOESY correlations

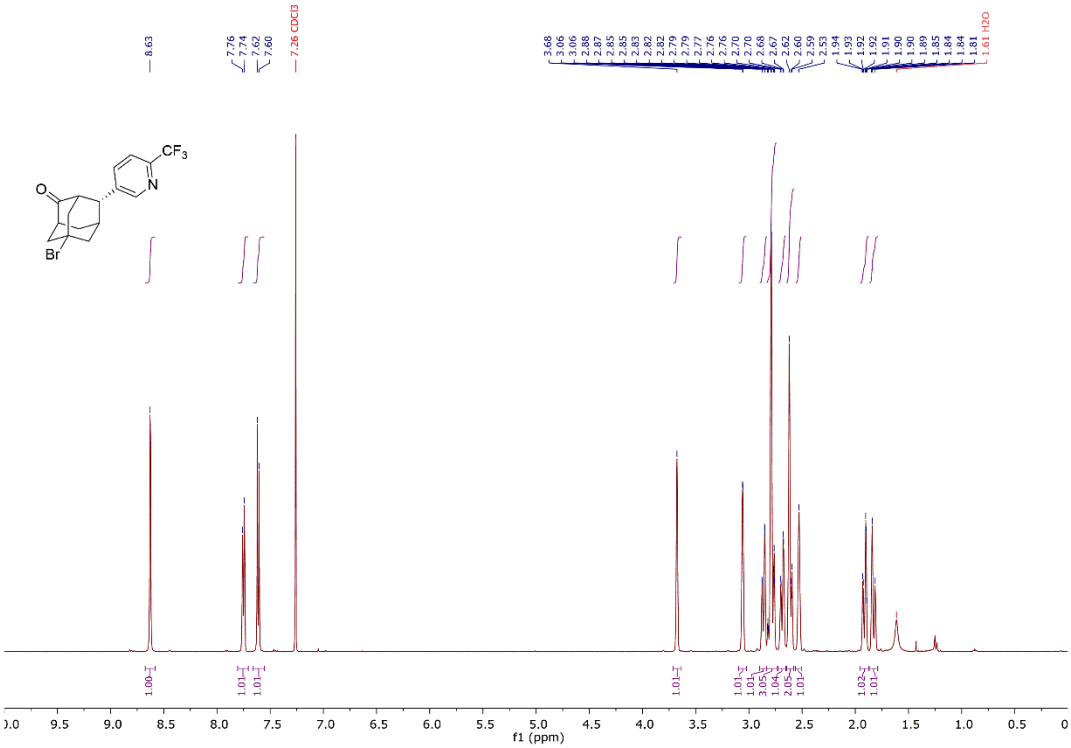


Key HSQC correlations

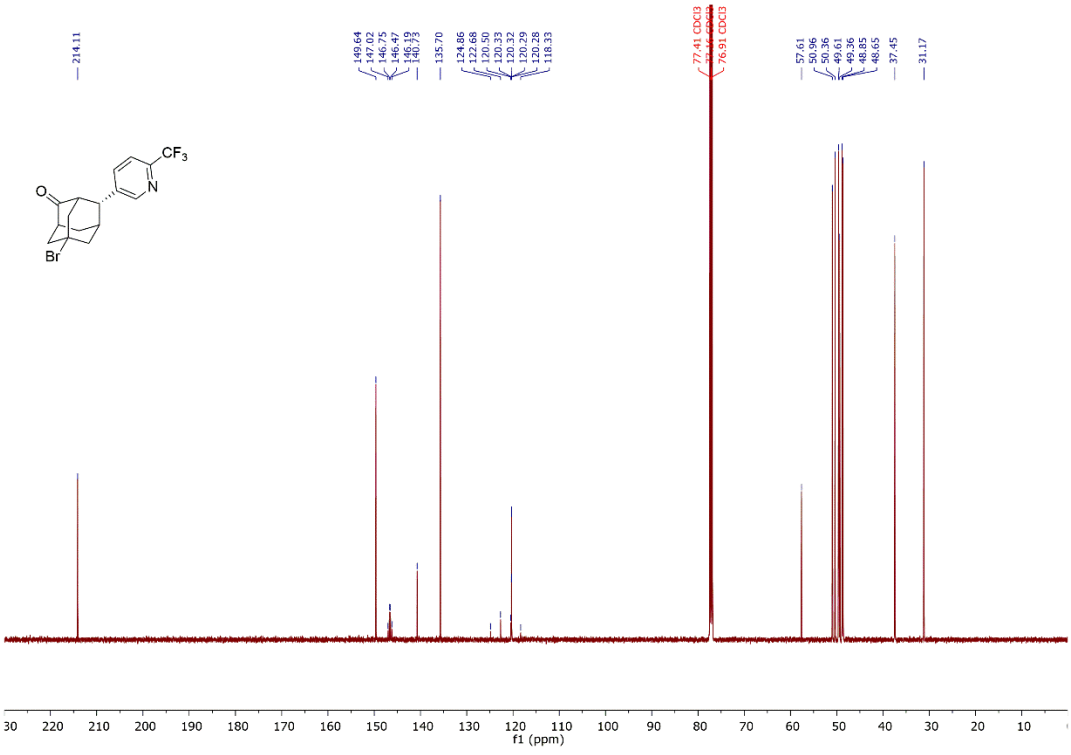


Key HMBC correlations

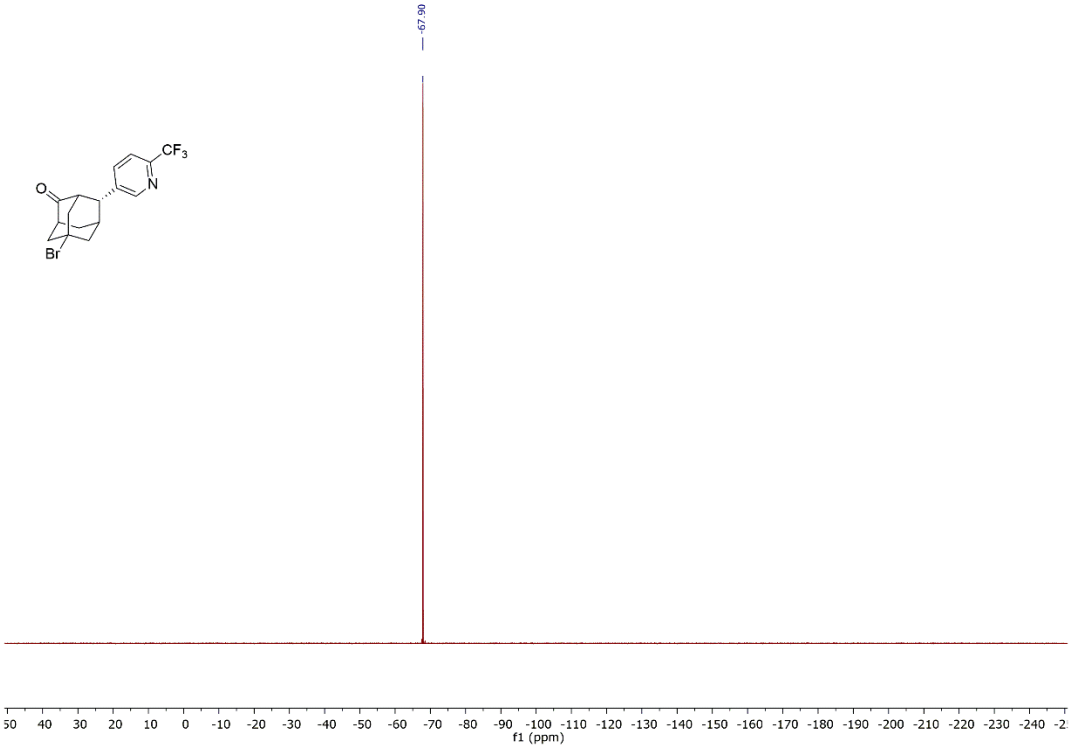




^{1}H NMR (500 MHz, $CDCl_3$) – (SI-32a)

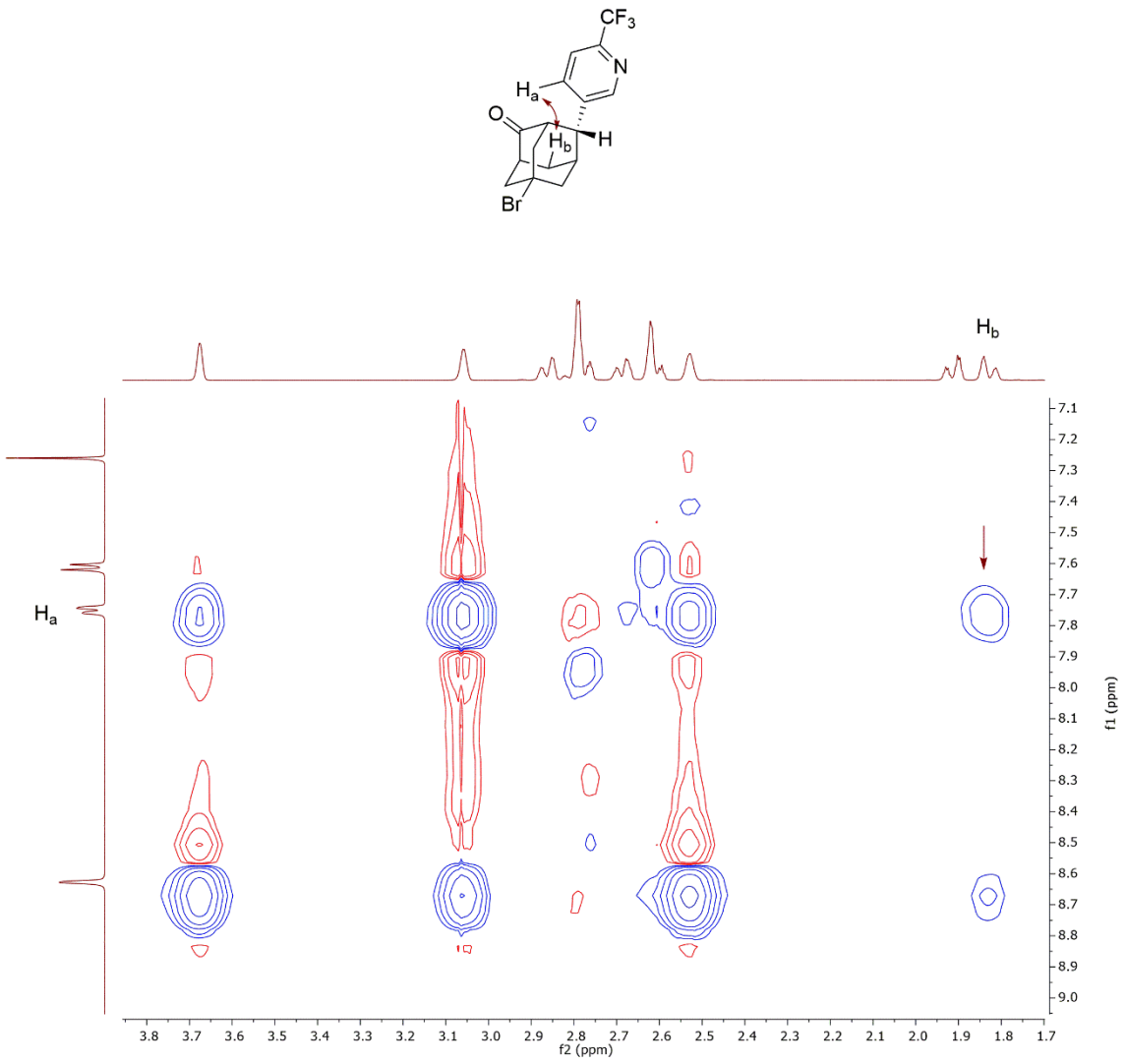


^{13}C NMR (126 MHz, $CDCl_3$) – (SI-32a)

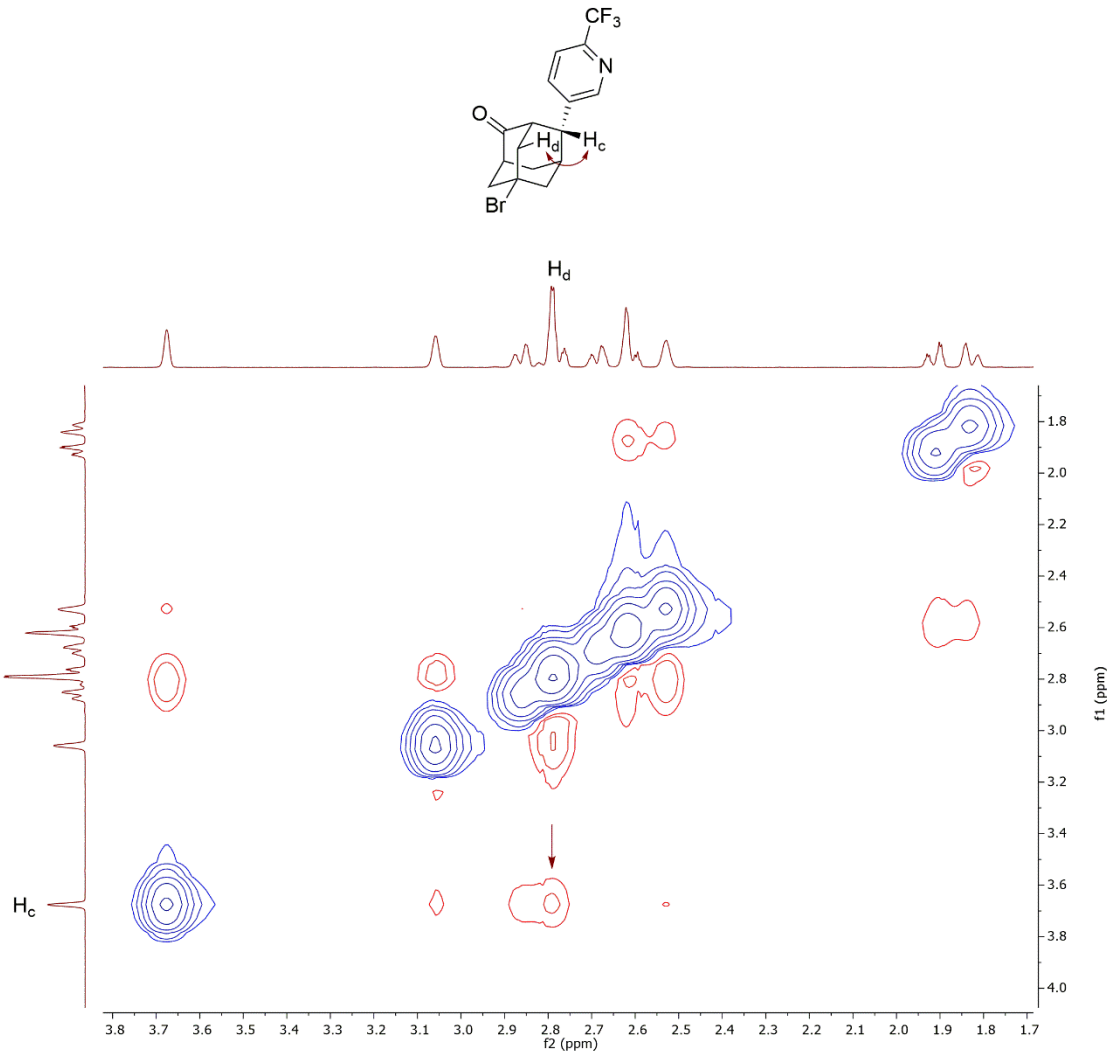


^{19}F NMR (282 MHz, $CDCl_3$) – (SI-32a)

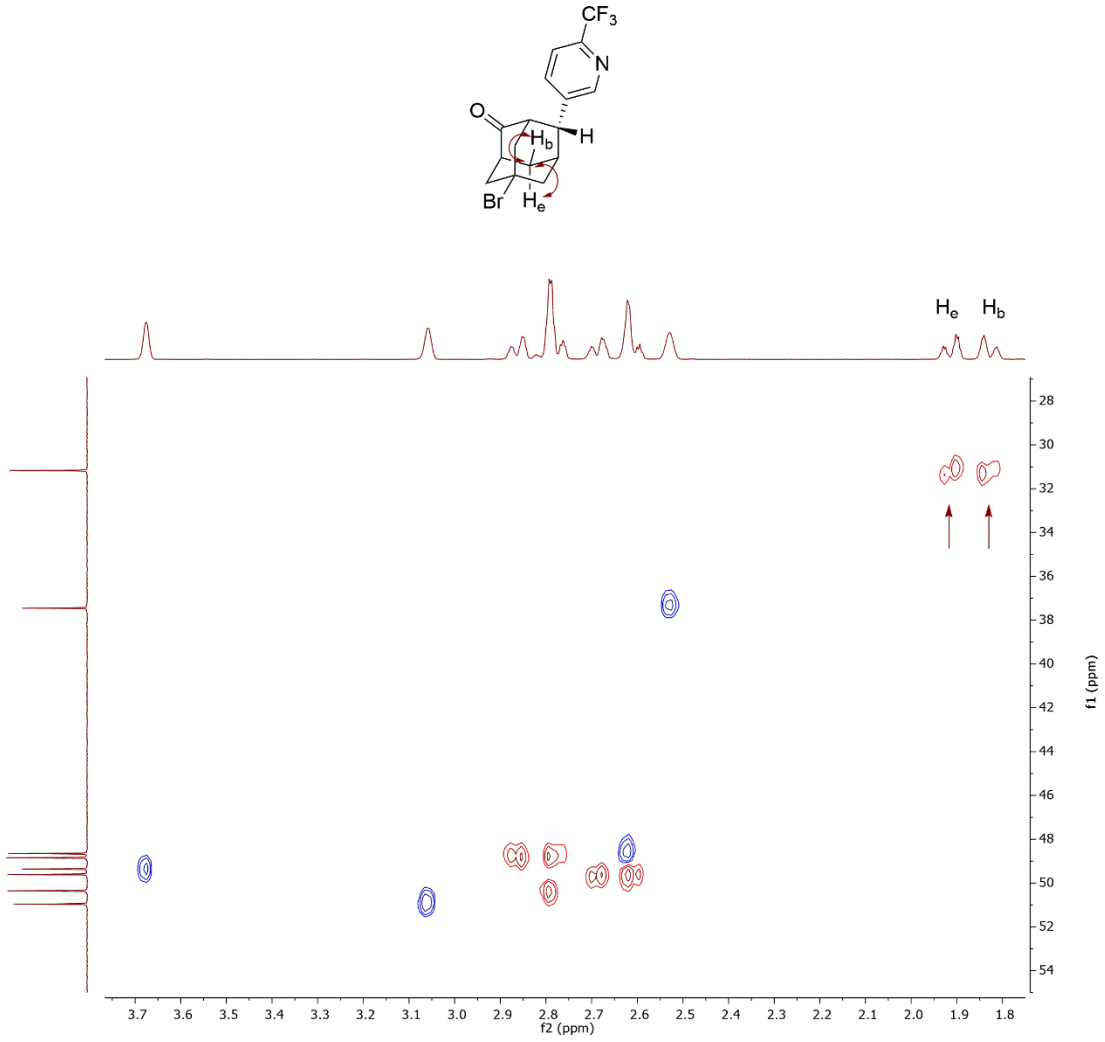
Key NOESY correlations



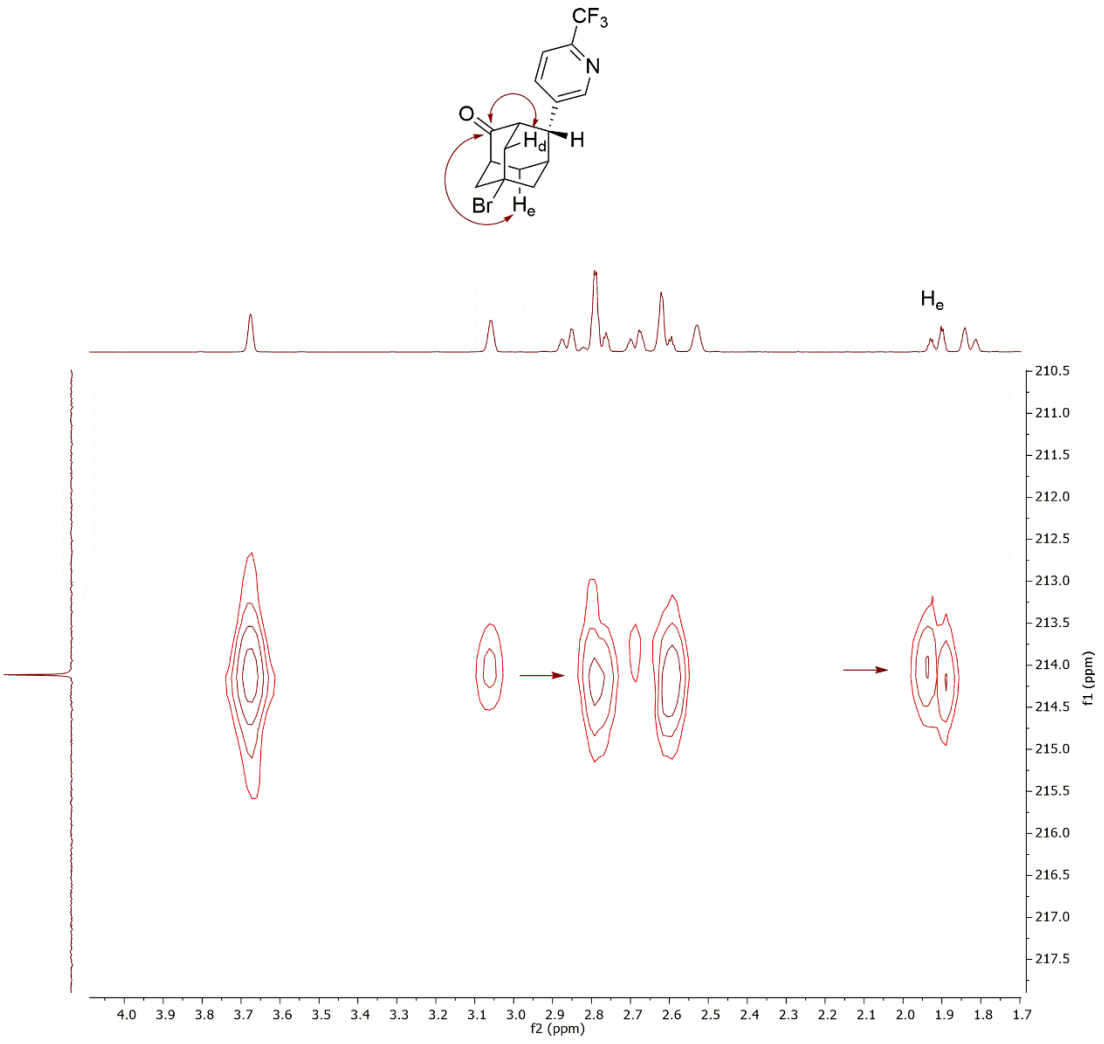
Key NOESY correlations

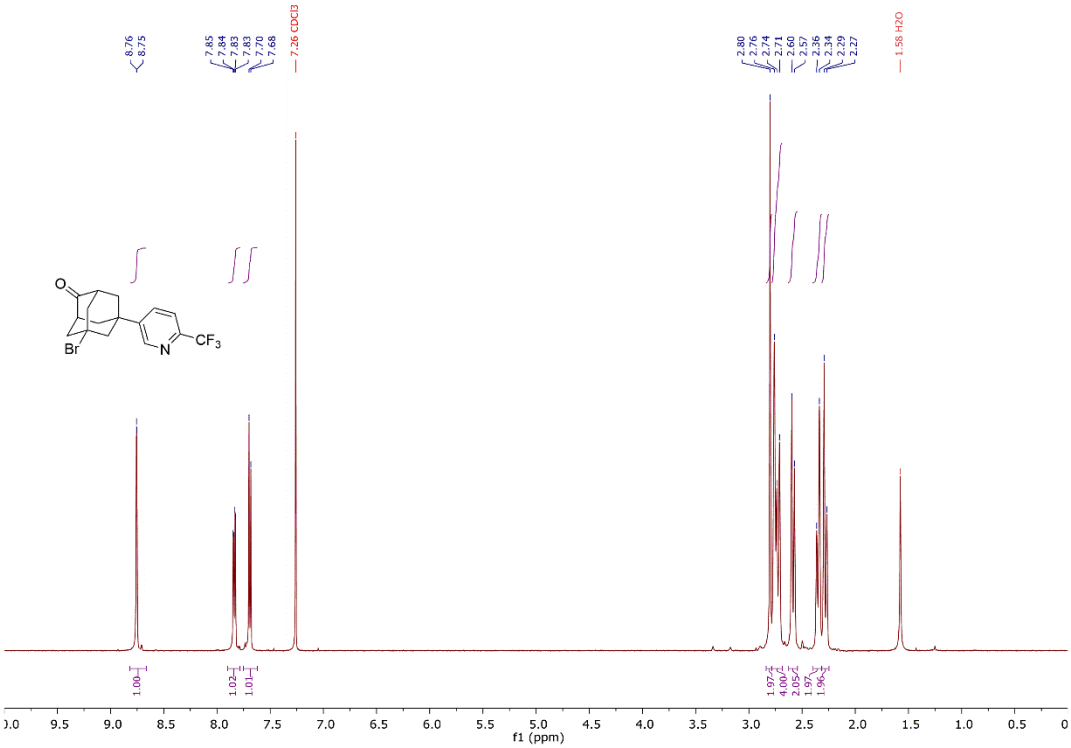


Key HSQC correlations

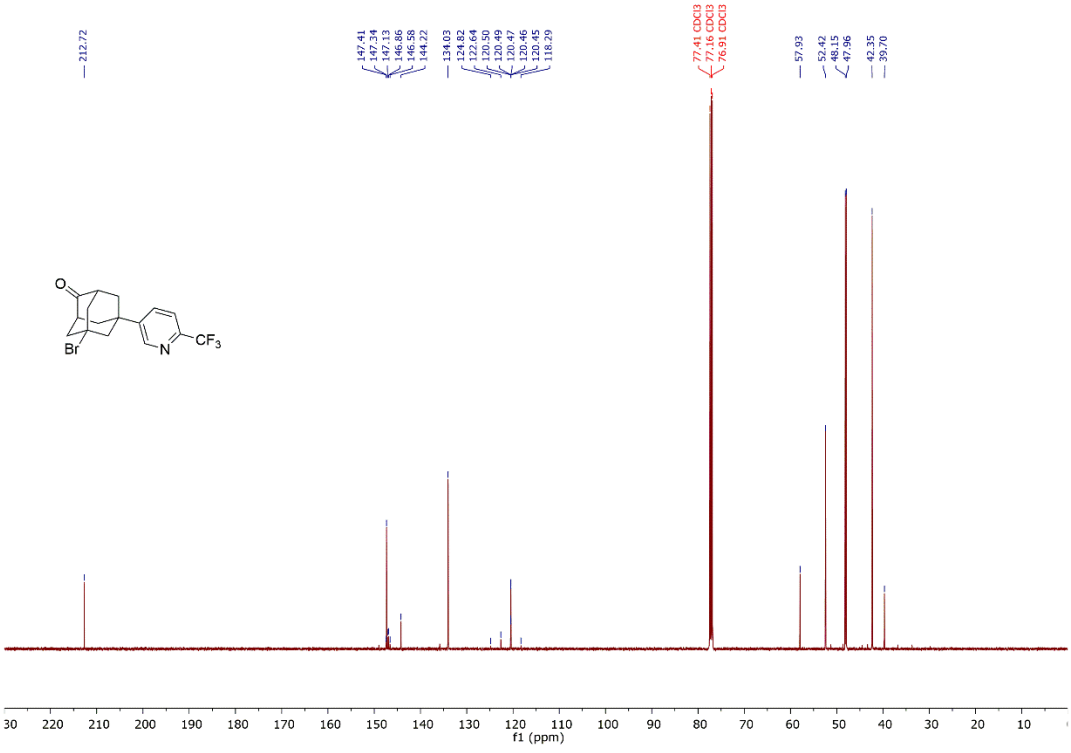


Key HMBC correlations

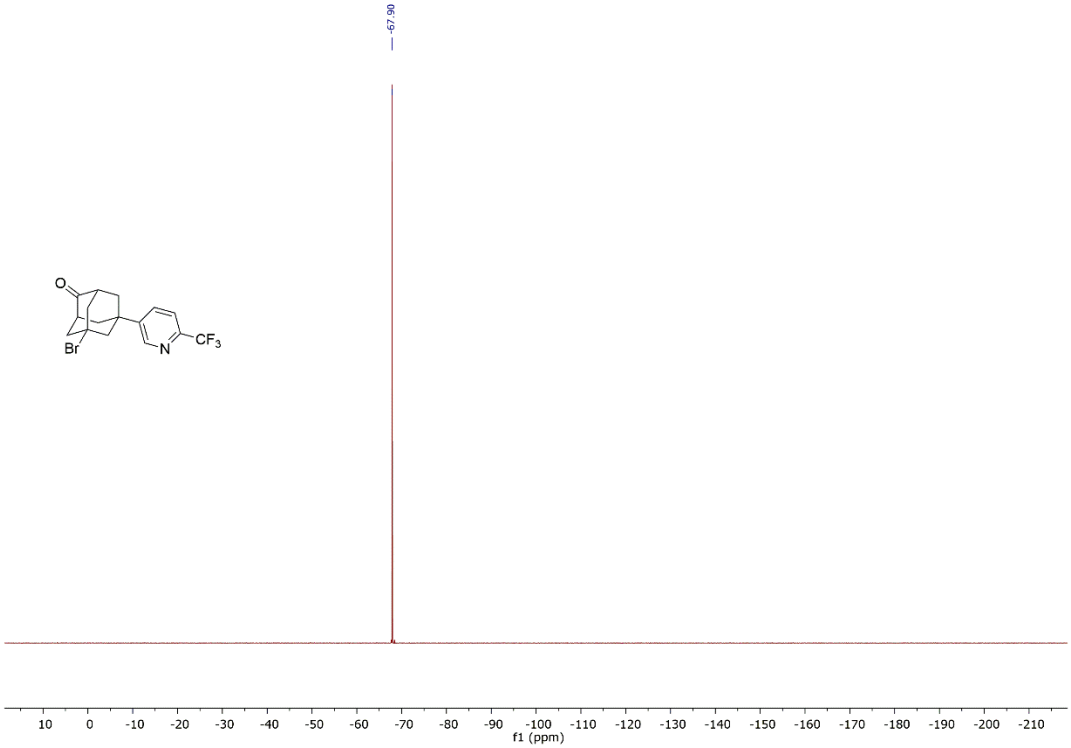




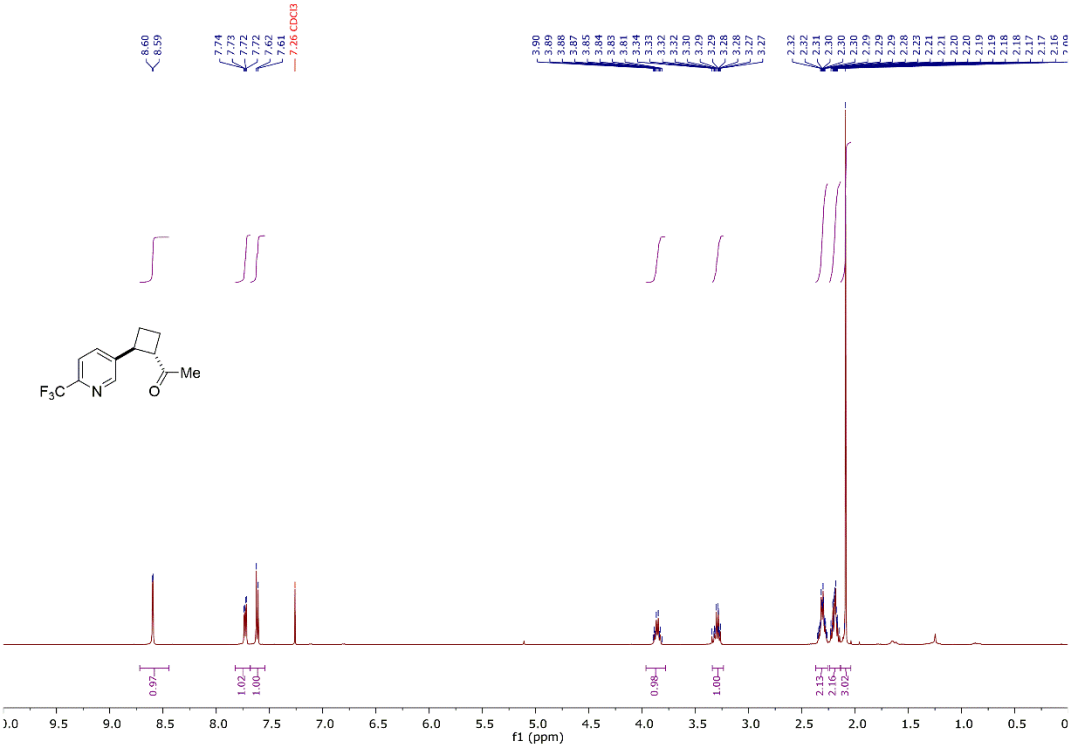
^{1}H NMR (500 MHz, $CDCl_3$) – (SI-32b)



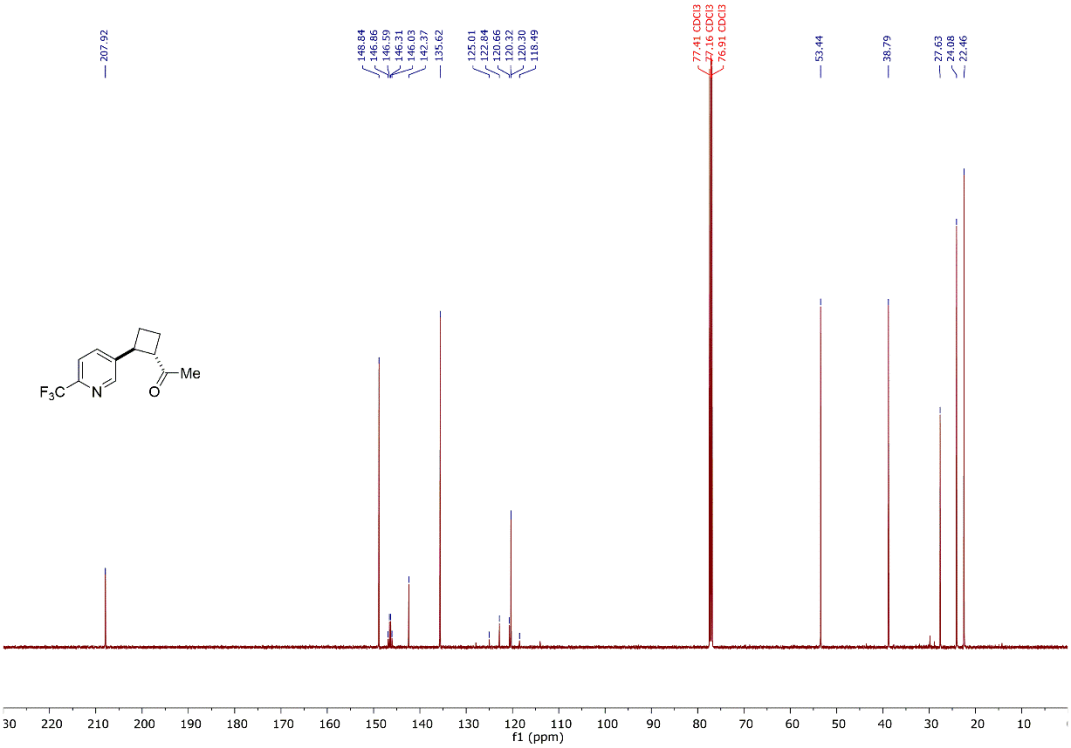
^{13}C NMR (126 MHz, $CDCl_3$) – (SI-32b)



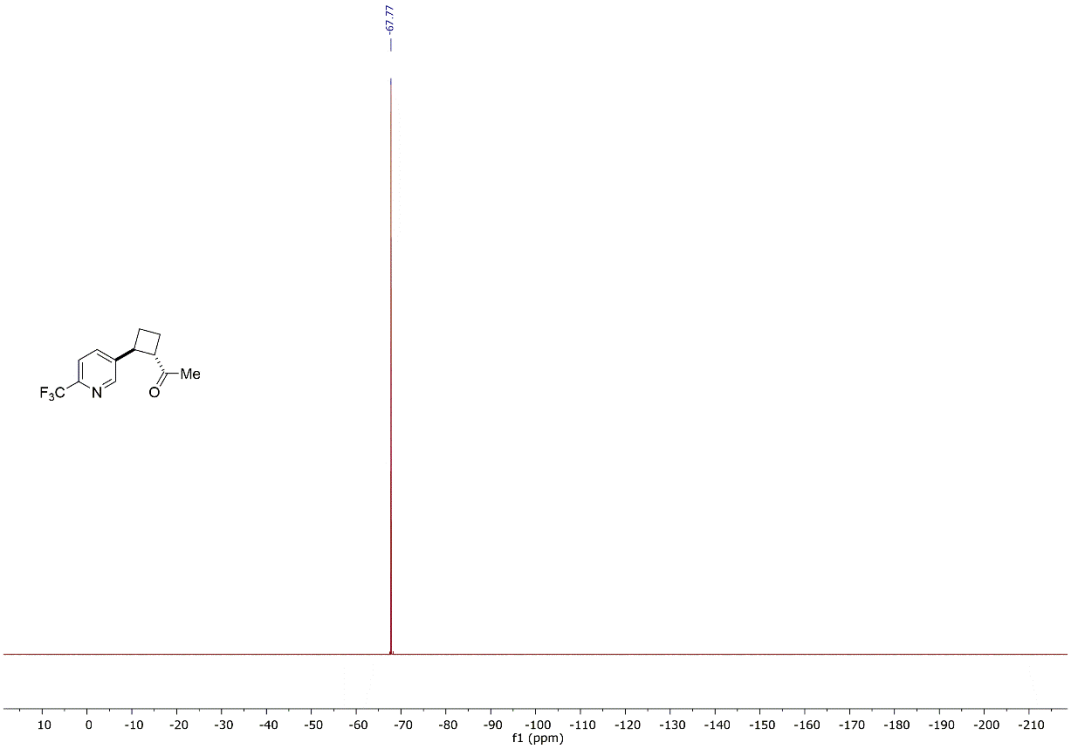
^{19}F NMR (376 MHz, $CDCl_3$) – (SI-32b)



^{1}H NMR (500 MHz, $CDCl_3$) - (33)

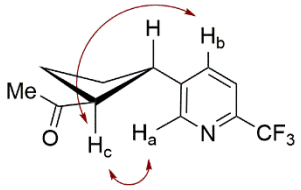


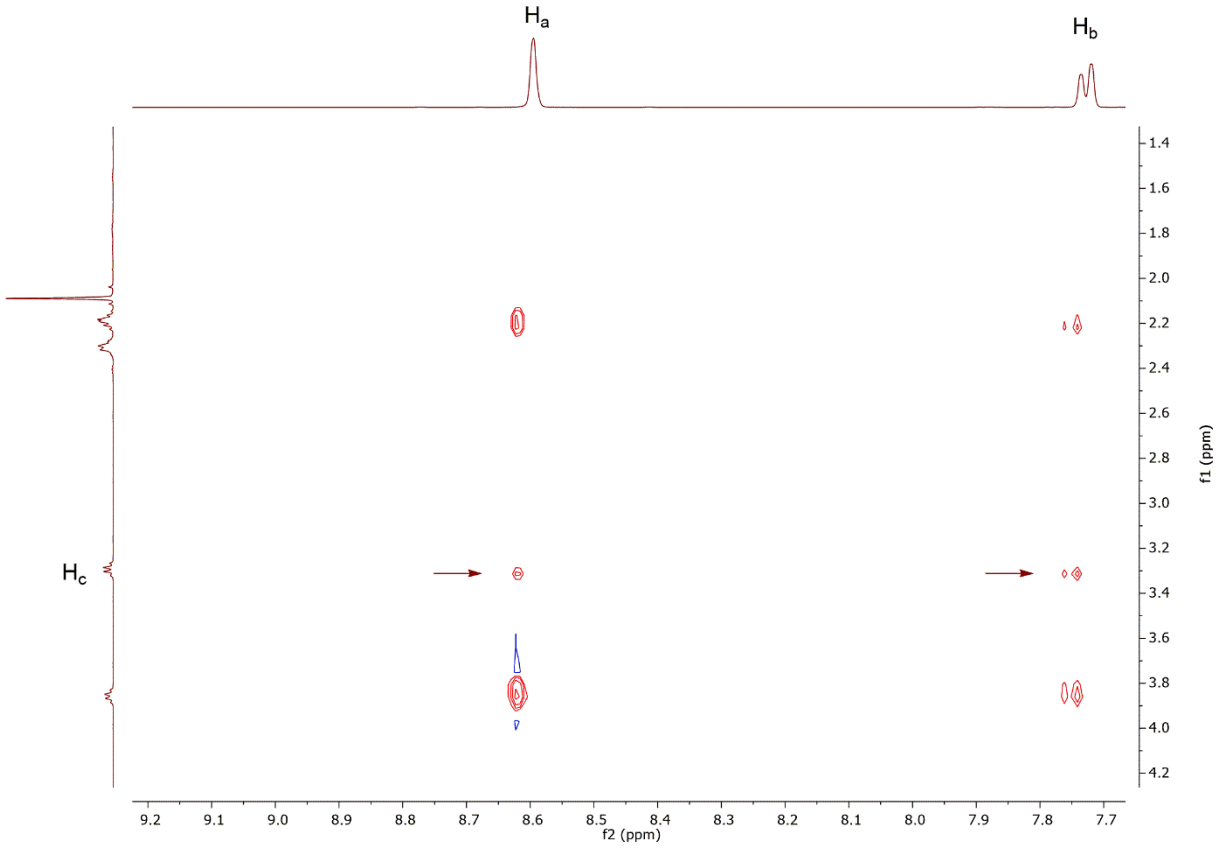
^{13}C NMR (126 MHz, $CDCl_3$) - (33)

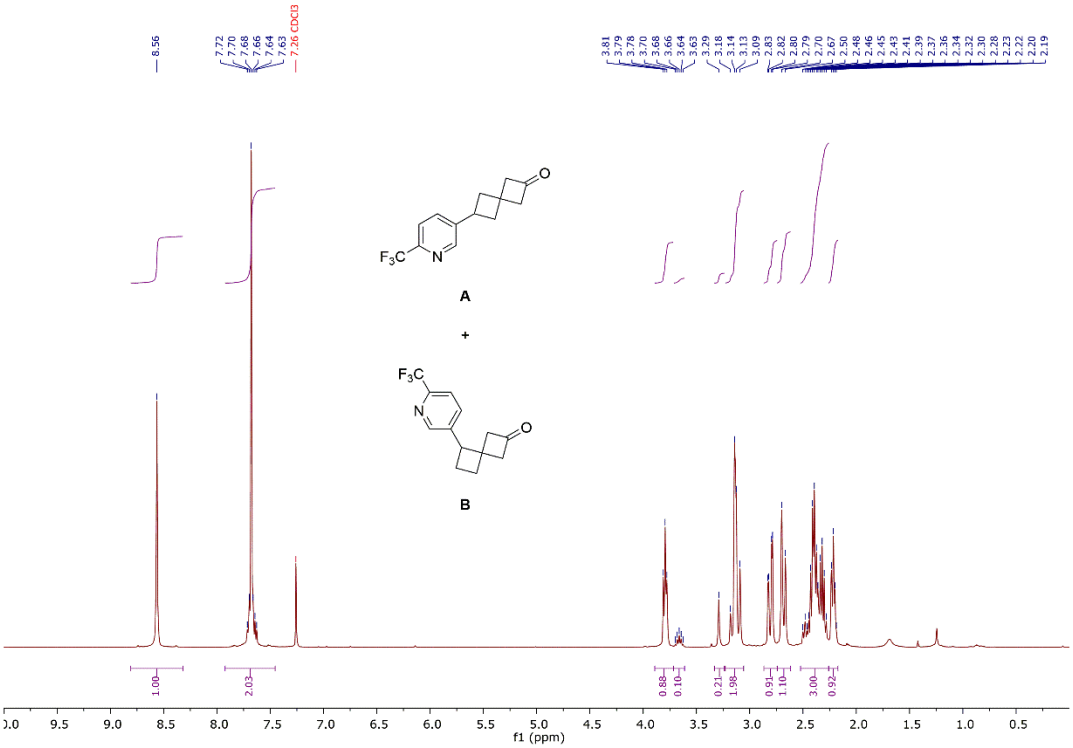


^{19}F NMR (376 MHz, $CDCl_3$) - (33)

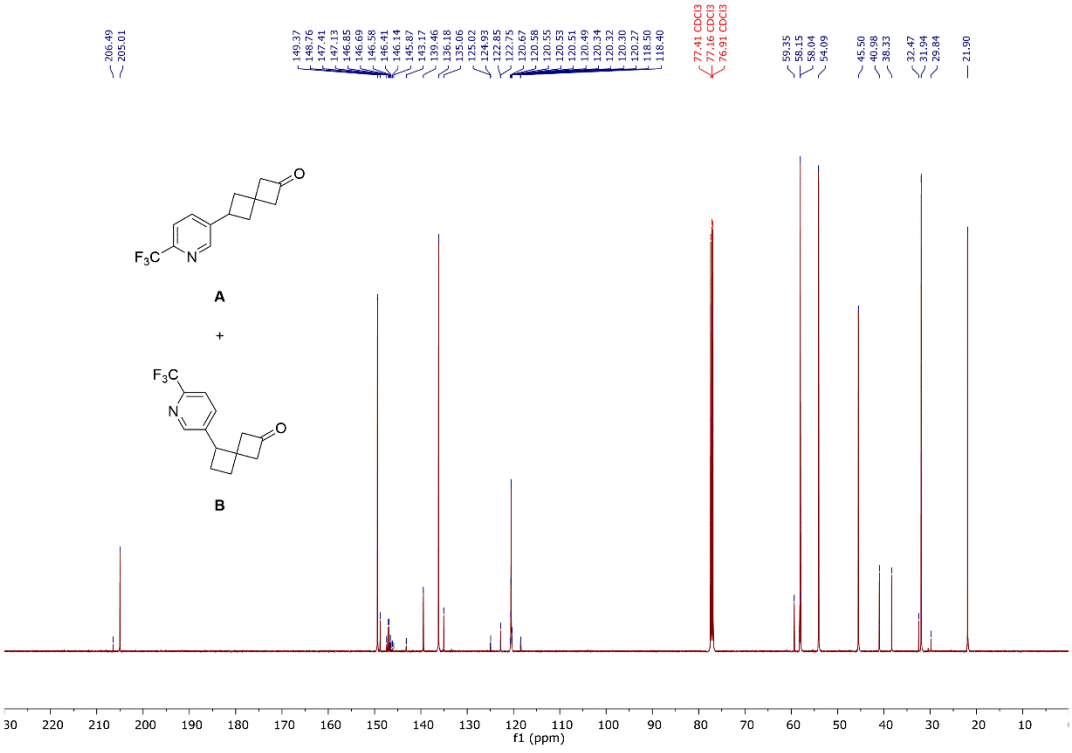
Key NOESY correlations



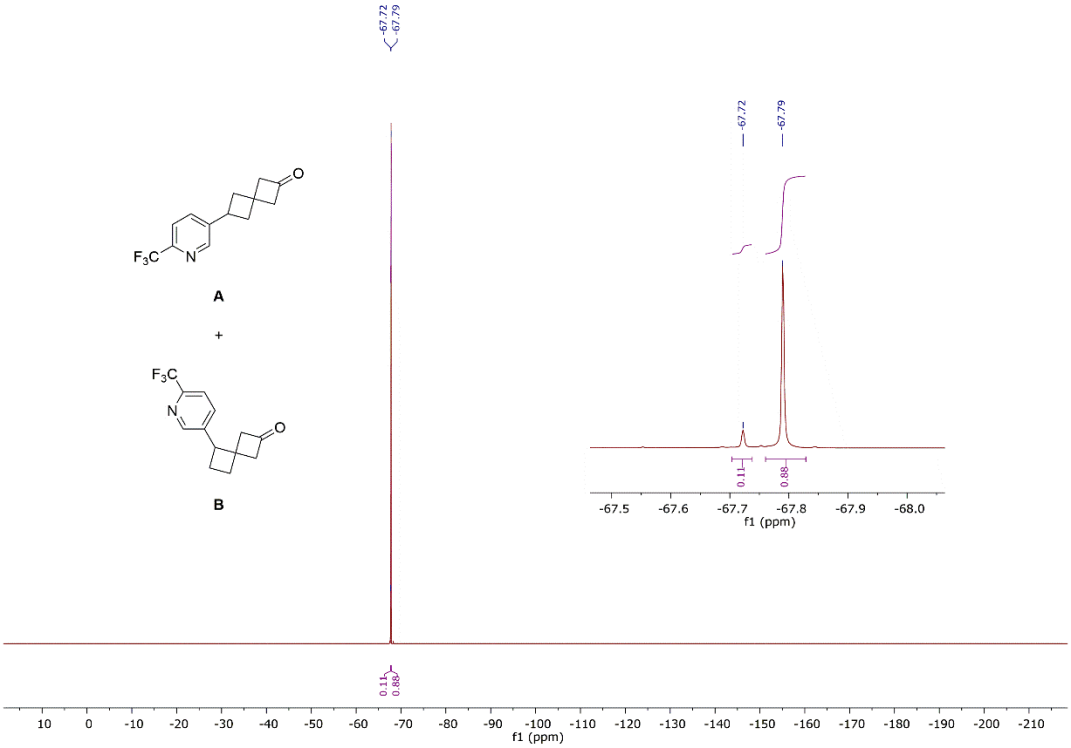




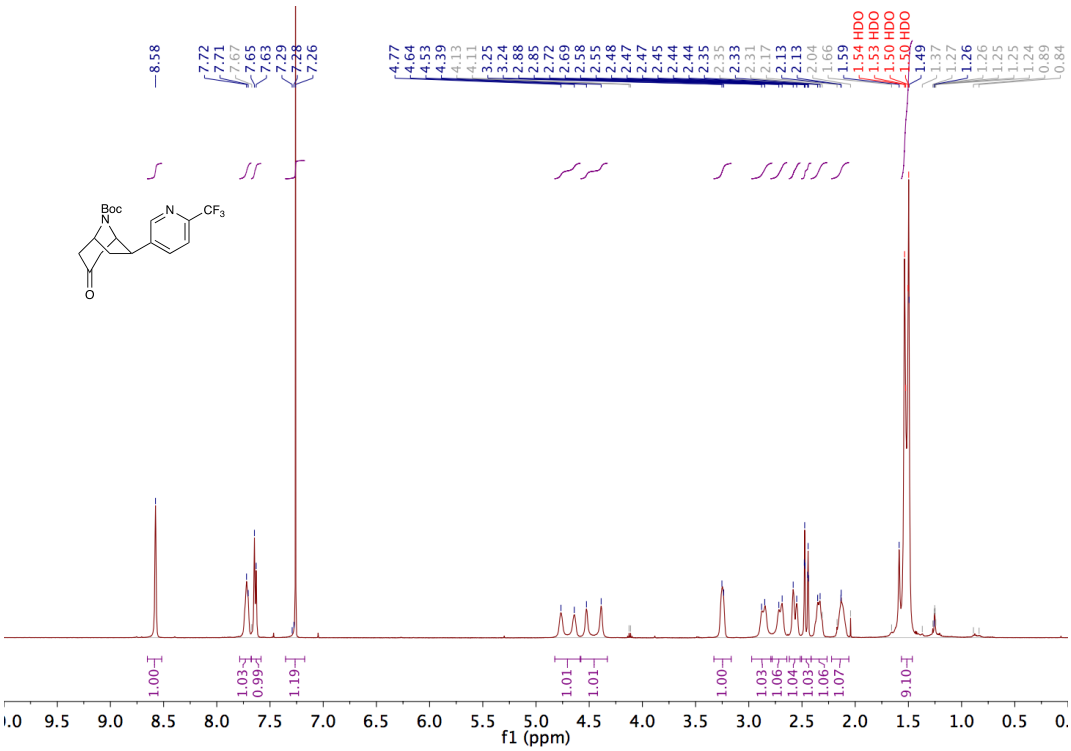
^{1}H NMR (500 MHz, $CDCl_3$) - (34 and SI-34)



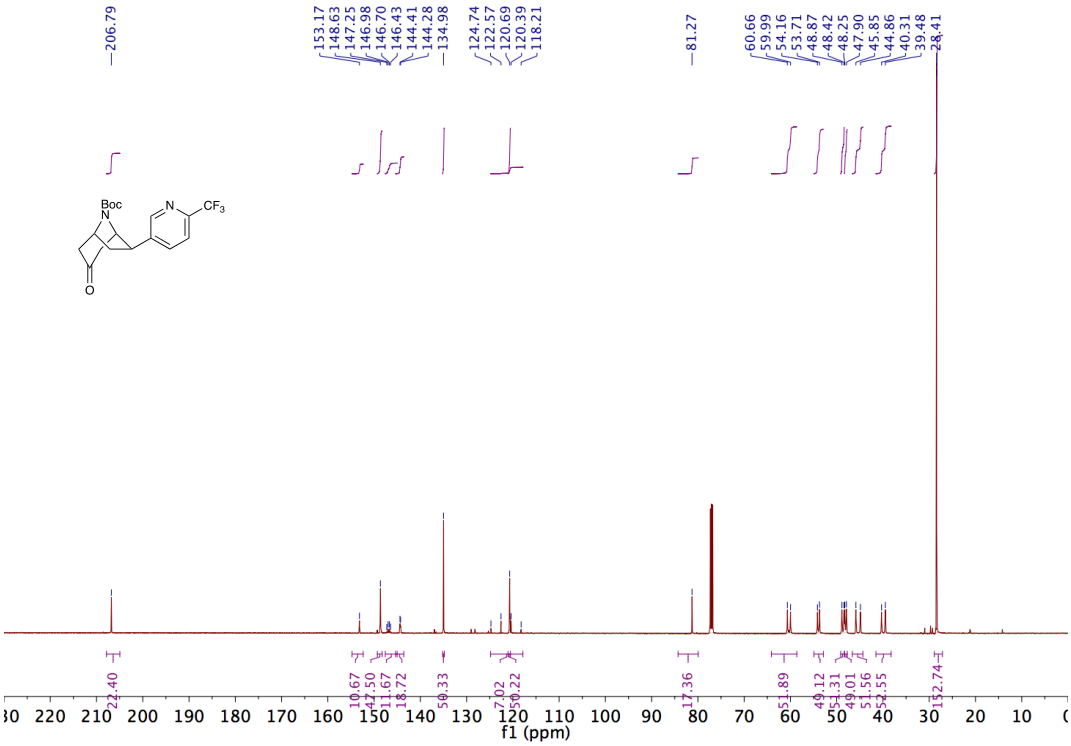
^{13}C NMR (126 MHz, $CDCl_3$) - (34 and SI-34)



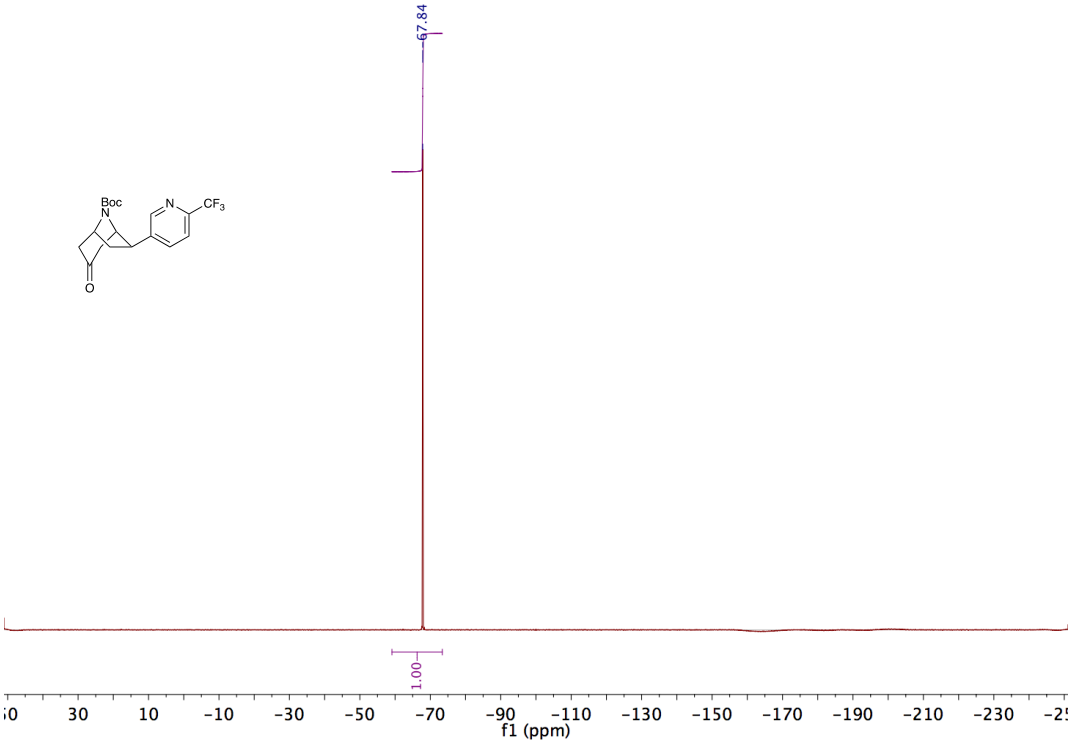
^{19}F NMR (376 MHz, $CDCl_3$) - (34 and SI-34)



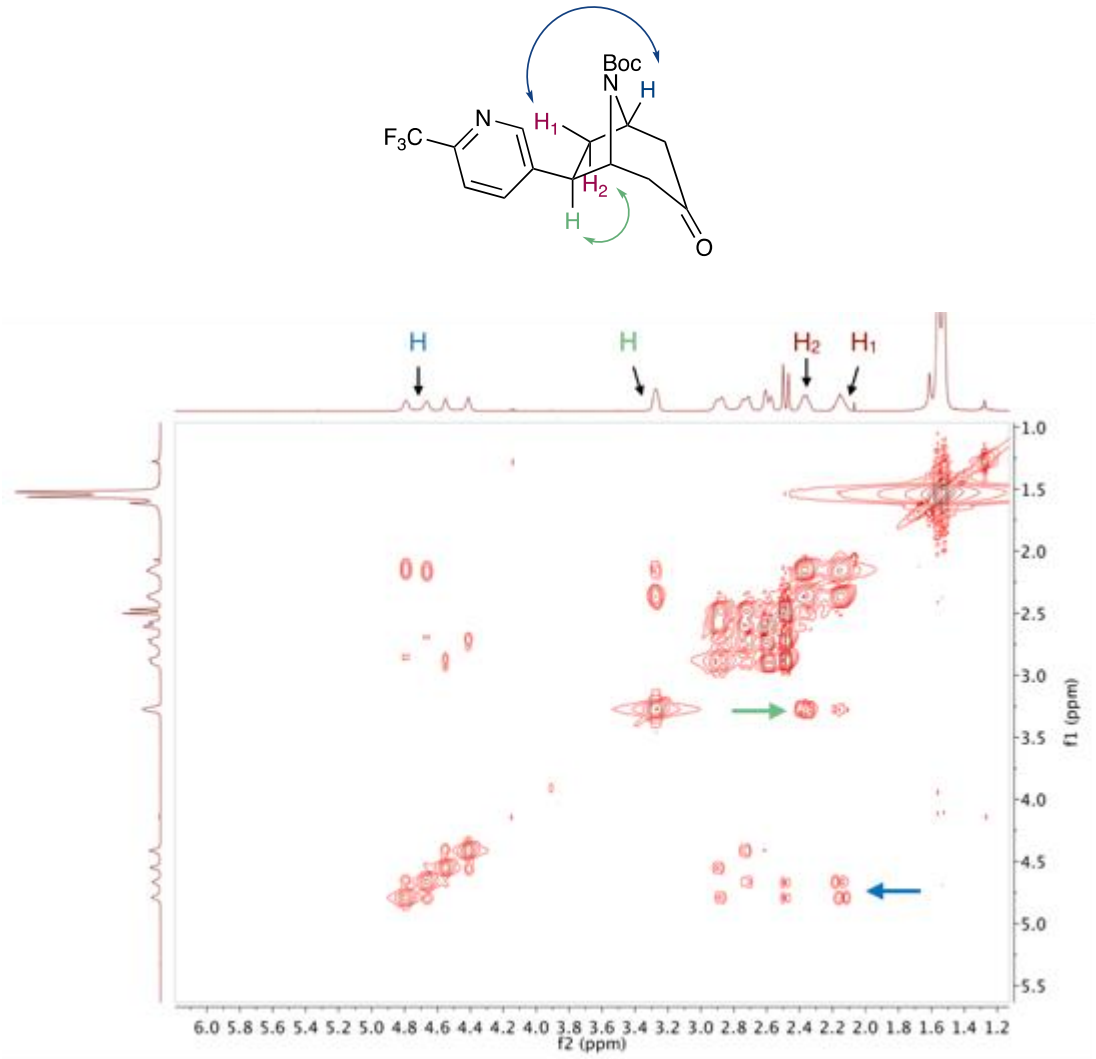
^{1}H NMR (500 MHz, $CDCl_3$) – (35)



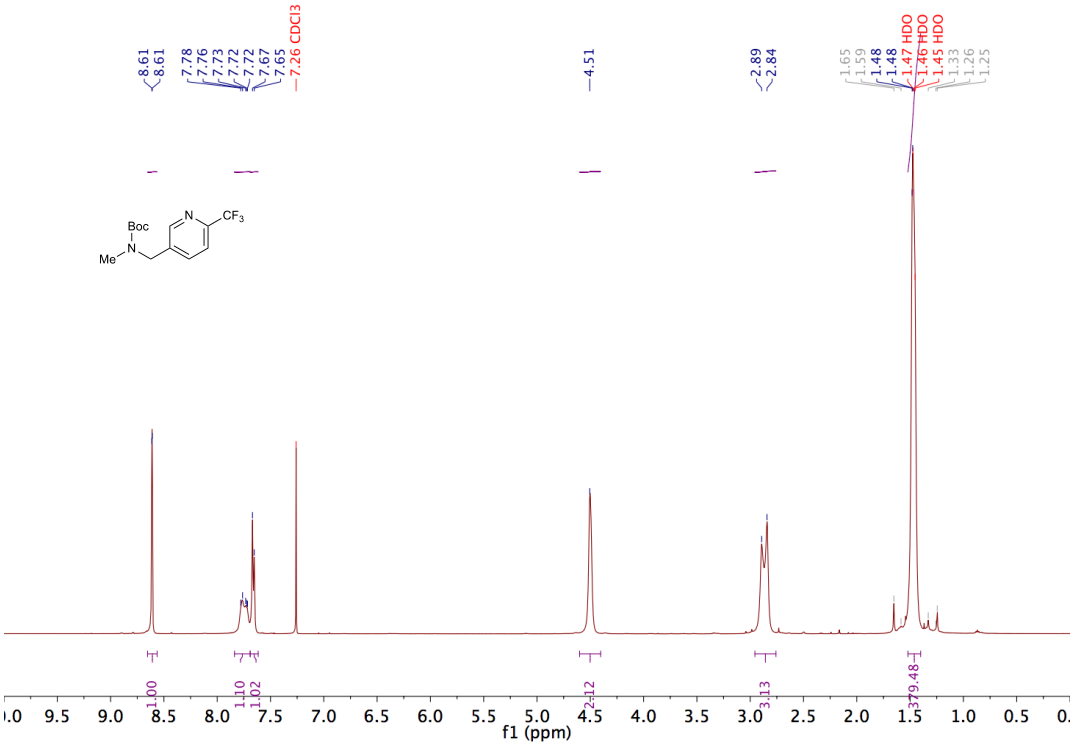
^{13}C NMR (126 MHz, $CDCl_3$) – (35)



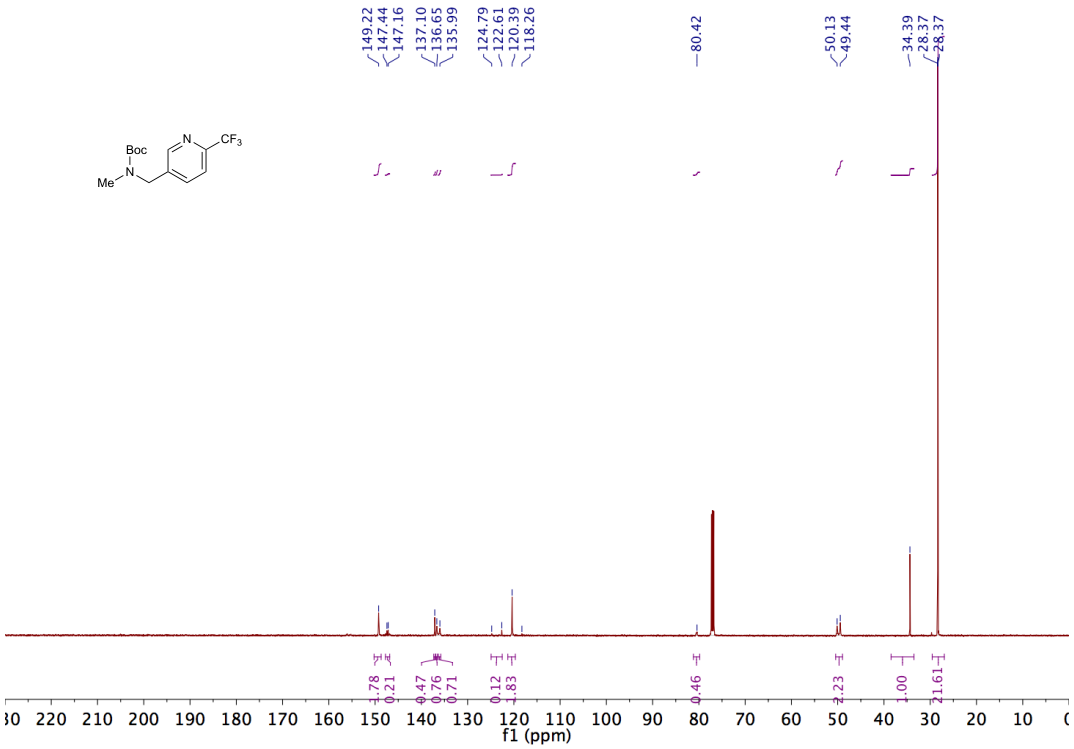
^{19}F NMR (376 MHz, $CDCl_3$) – (35)



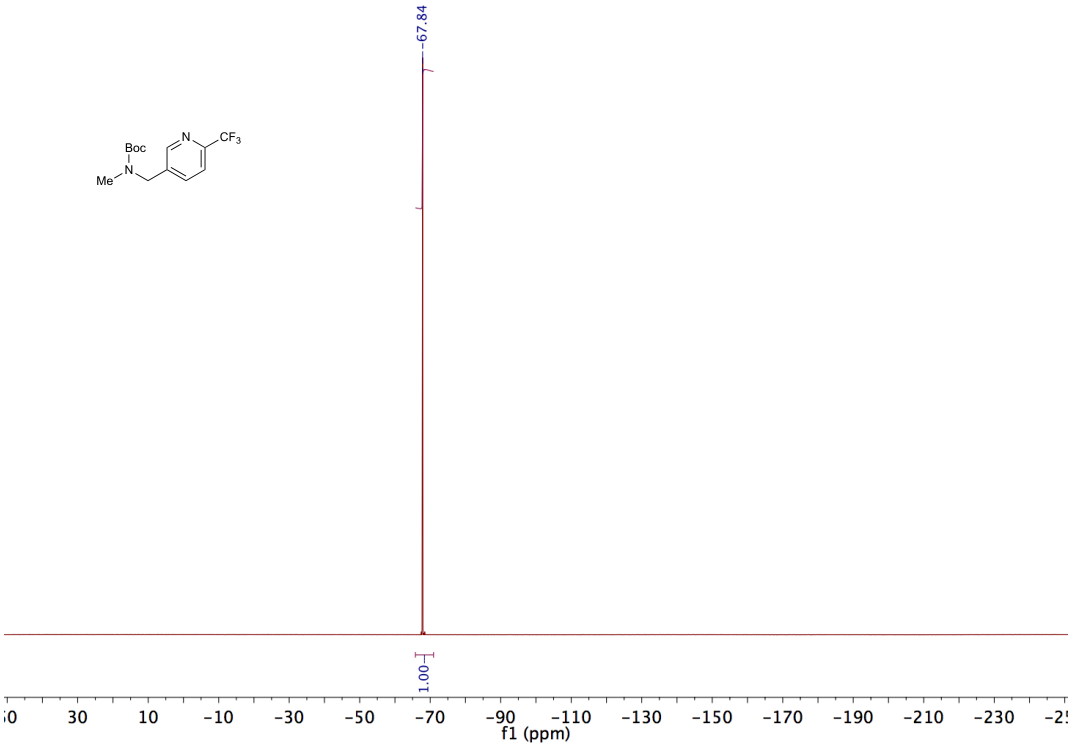
^{1}H NMR – COSY (500 MHz, $CDCl_3$) – (35)



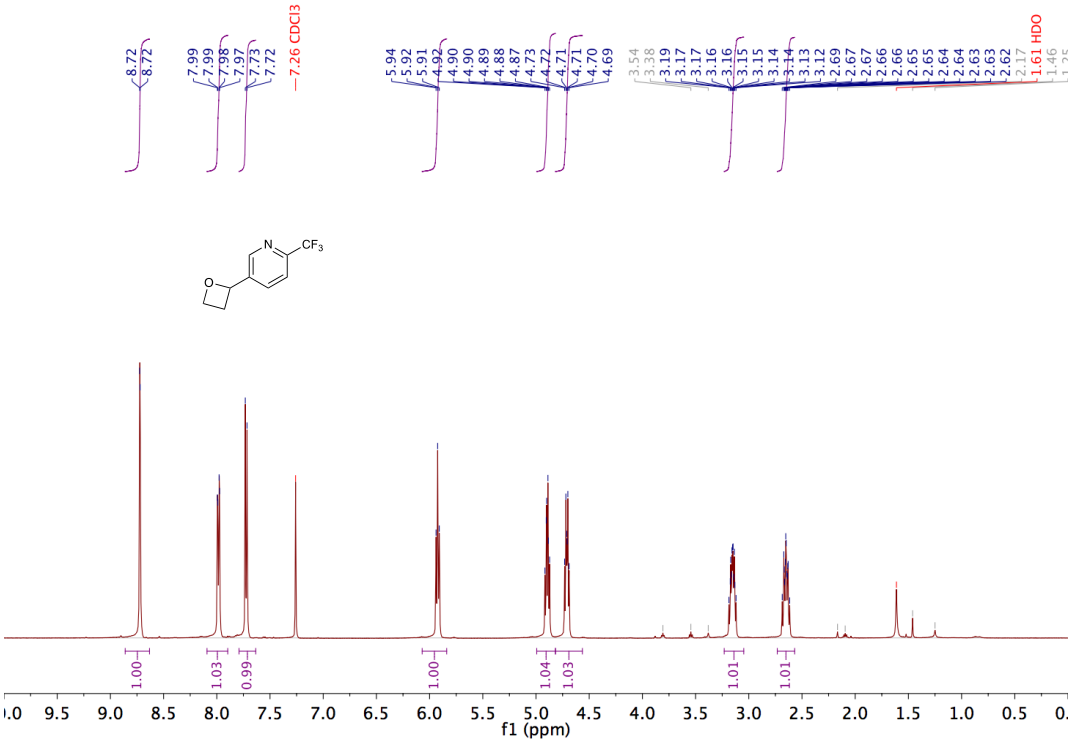
^{1}H NMR (500 MHz, $CDCl_3$) – (37)



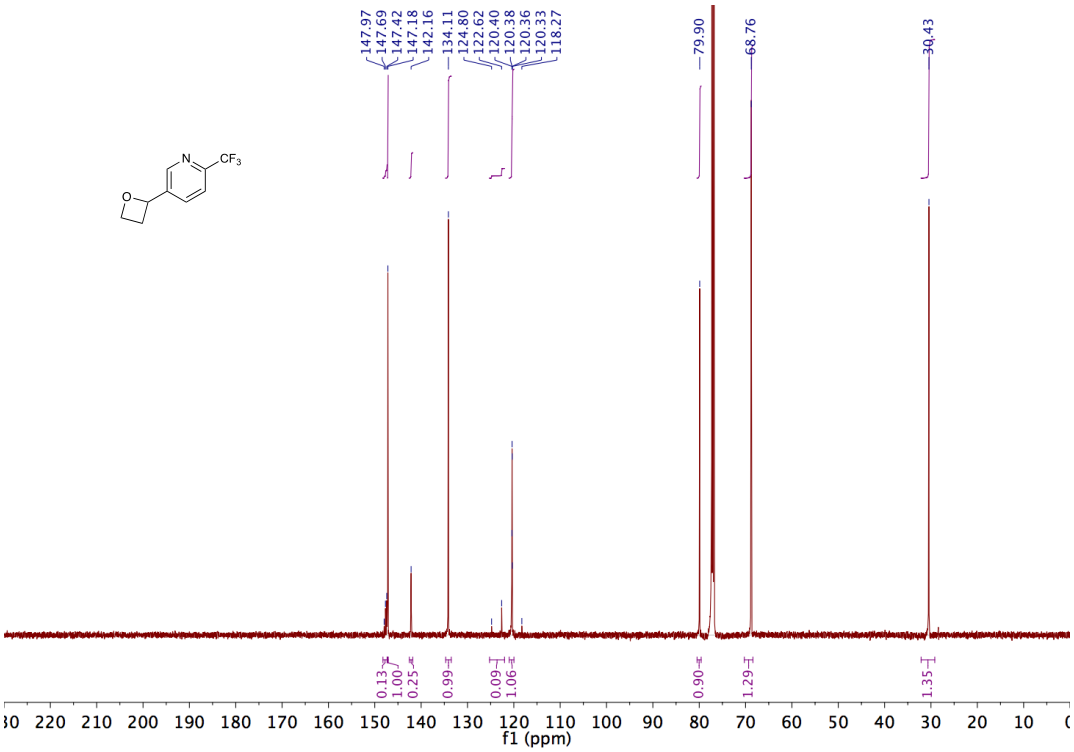
^{13}C NMR (126 MHz, $CDCl_3$) – (37)



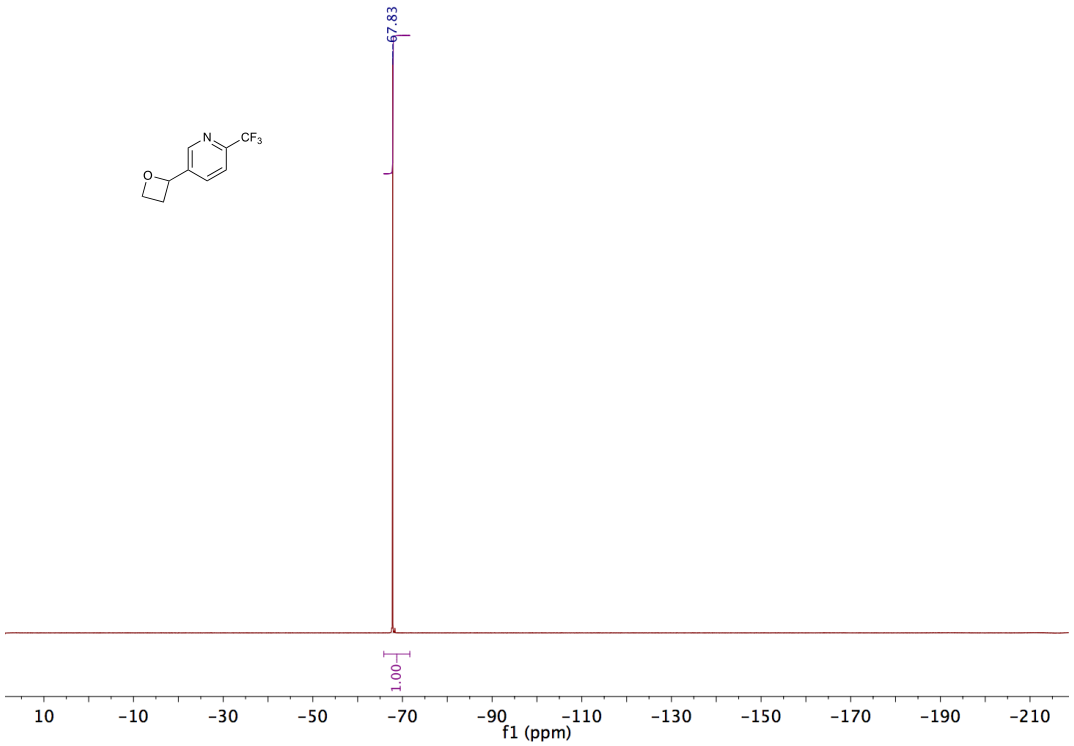
^{19}F NMR (376 MHz, $CDCl_3$) – (37)



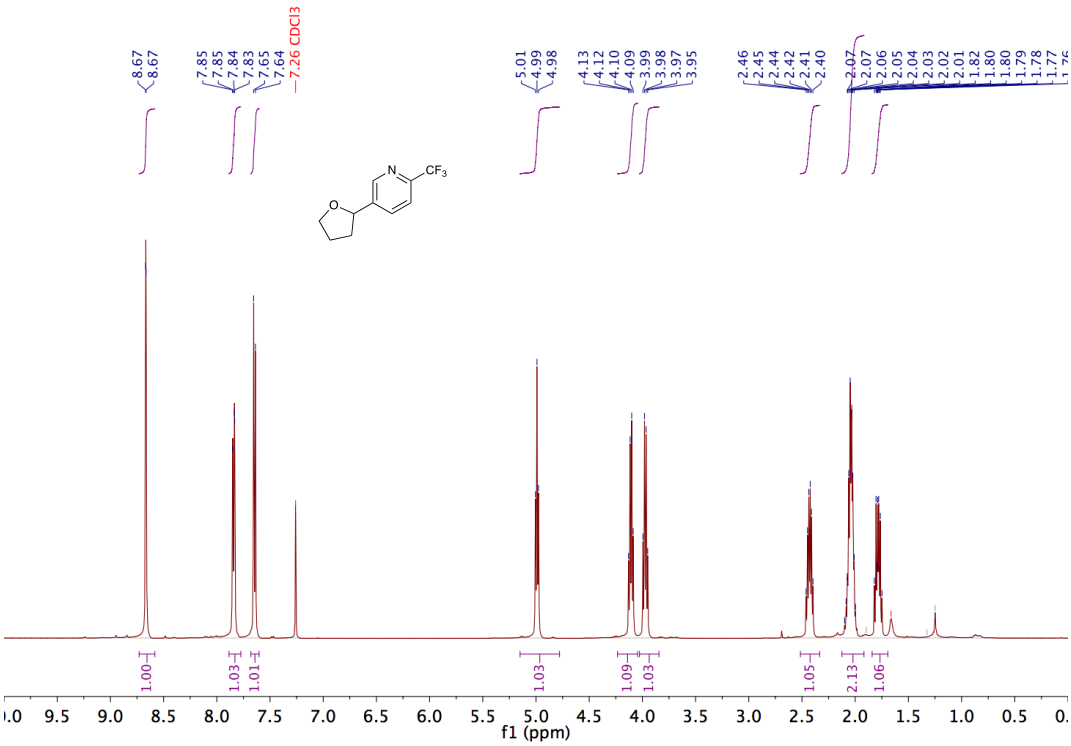
^{1}H NMR (500 MHz, $CDCl_3$) – (38)



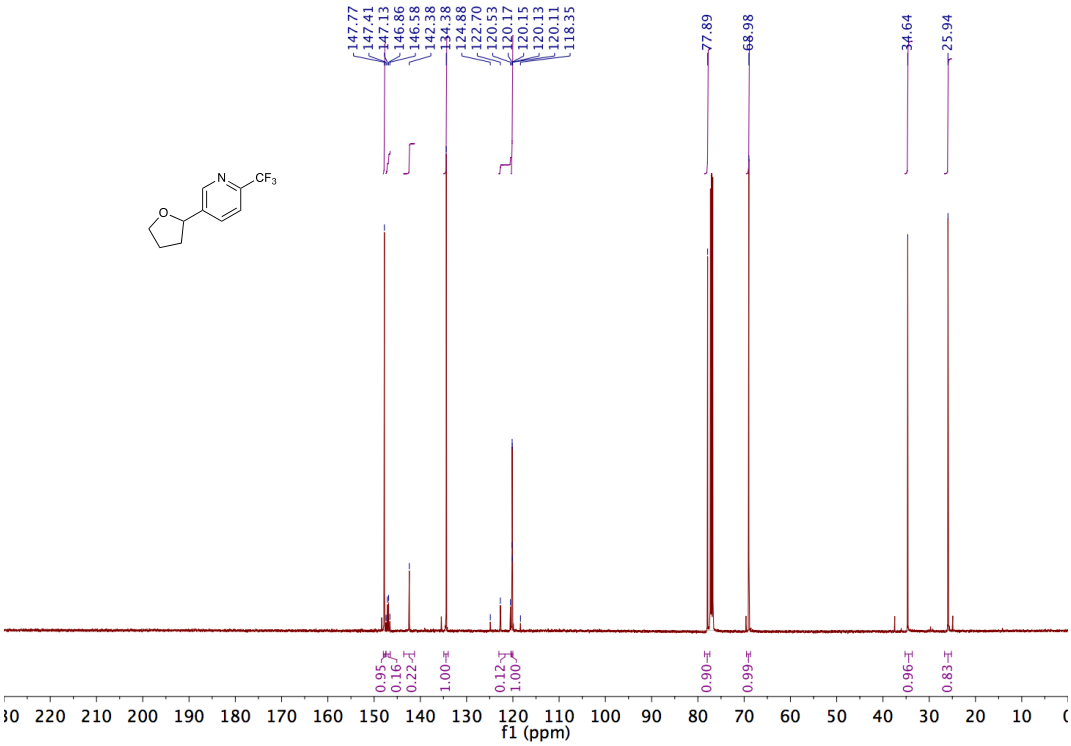
^{13}C NMR (126 MHz, $CDCl_3$) – (38)



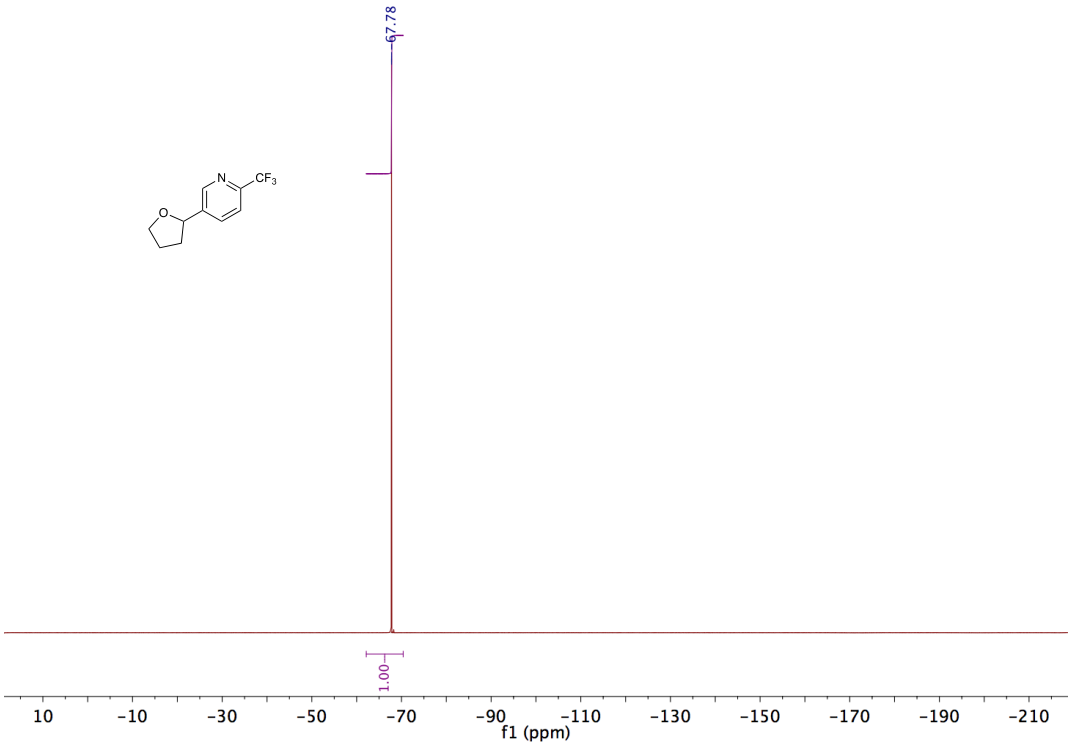
^{19}F NMR (376 MHz, $CDCl_3$) – (38)



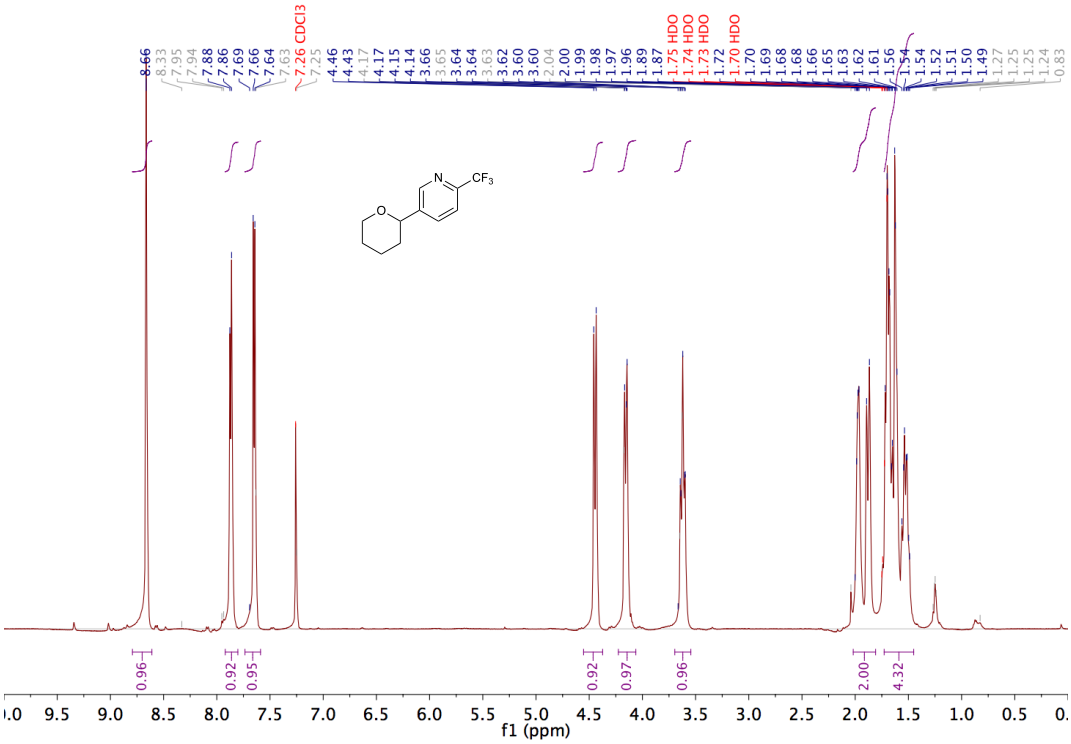
^{1}H NMR (500 MHz, $CDCl_3$) – (39)



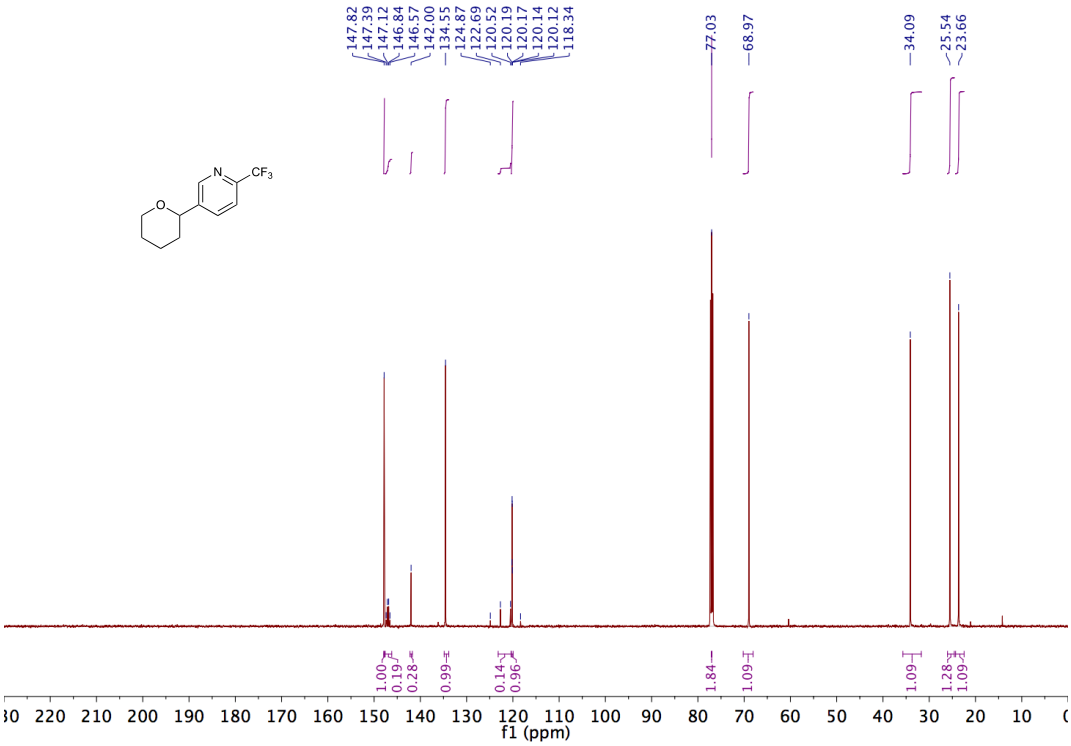
^{13}C NMR (126 MHz, $CDCl_3$) – (39)



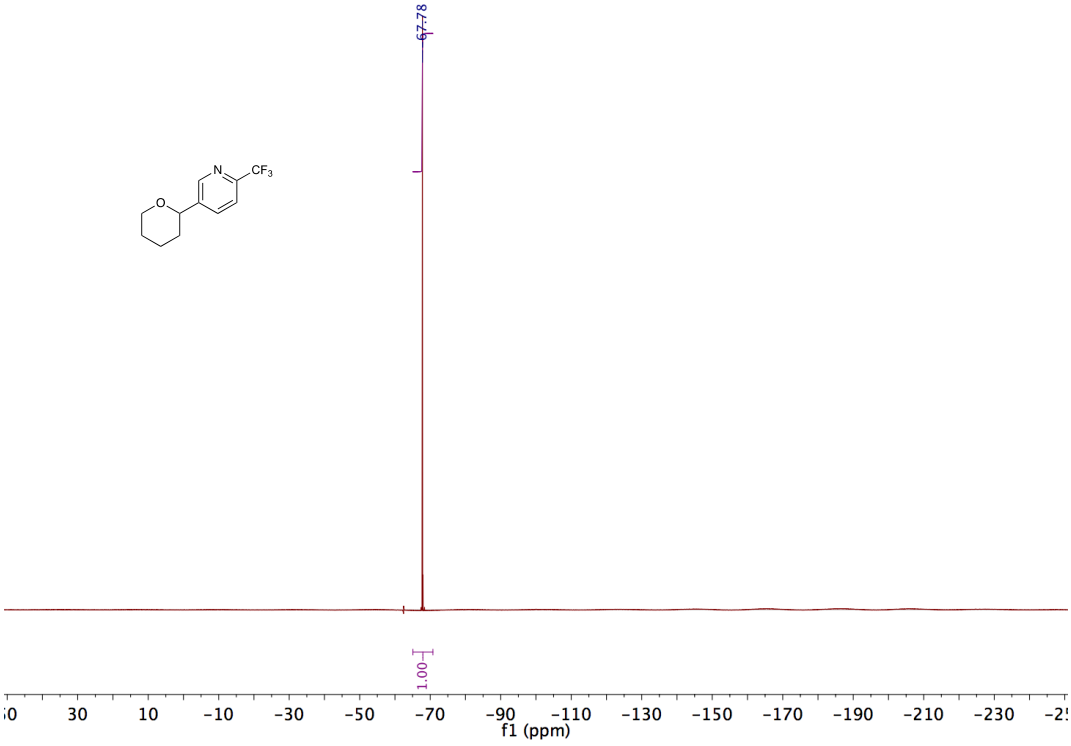
^{19}F NMR (376 MHz, $CDCl_3$) – (39)



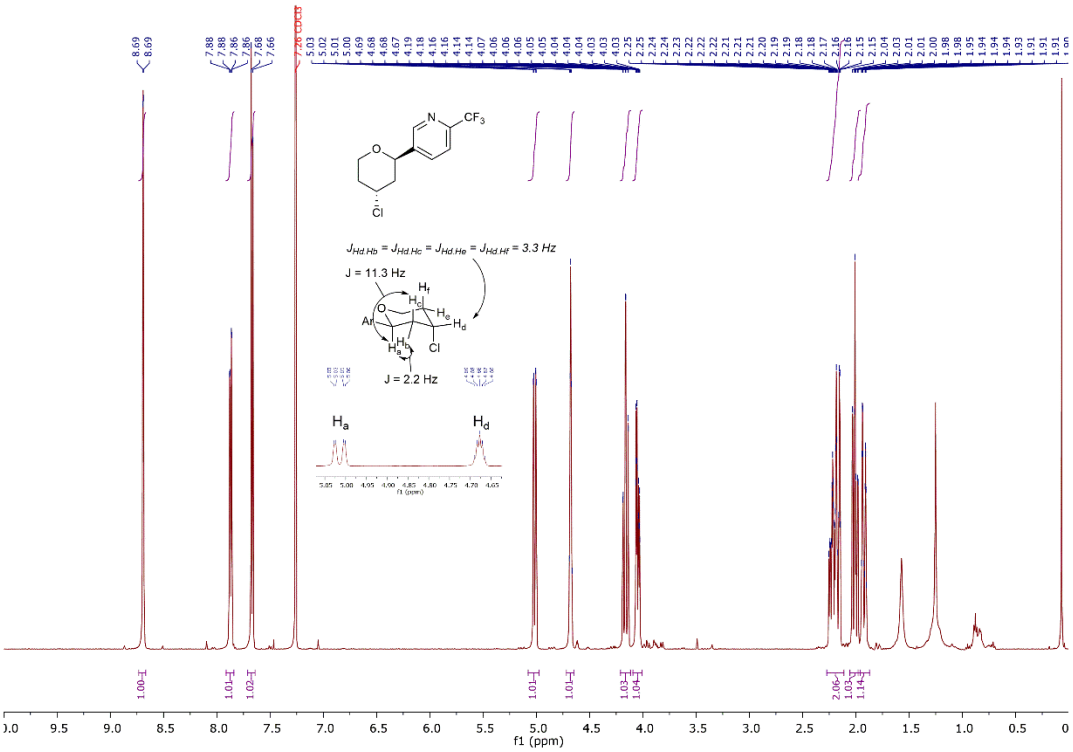
^{1}H NMR (500 MHz, $CDCl_3$) – (40)



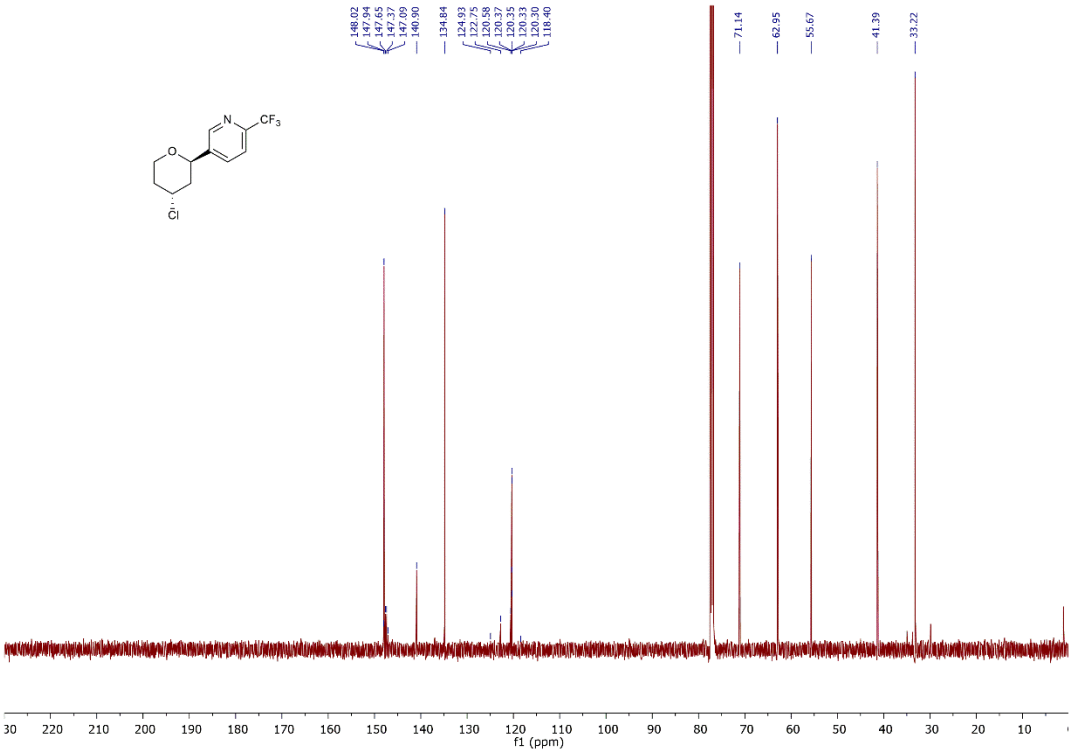
^{13}C NMR (126 MHz, $CDCl_3$) – (40)



^{19}F NMR (376 MHz, $CDCl_3$) – (40)

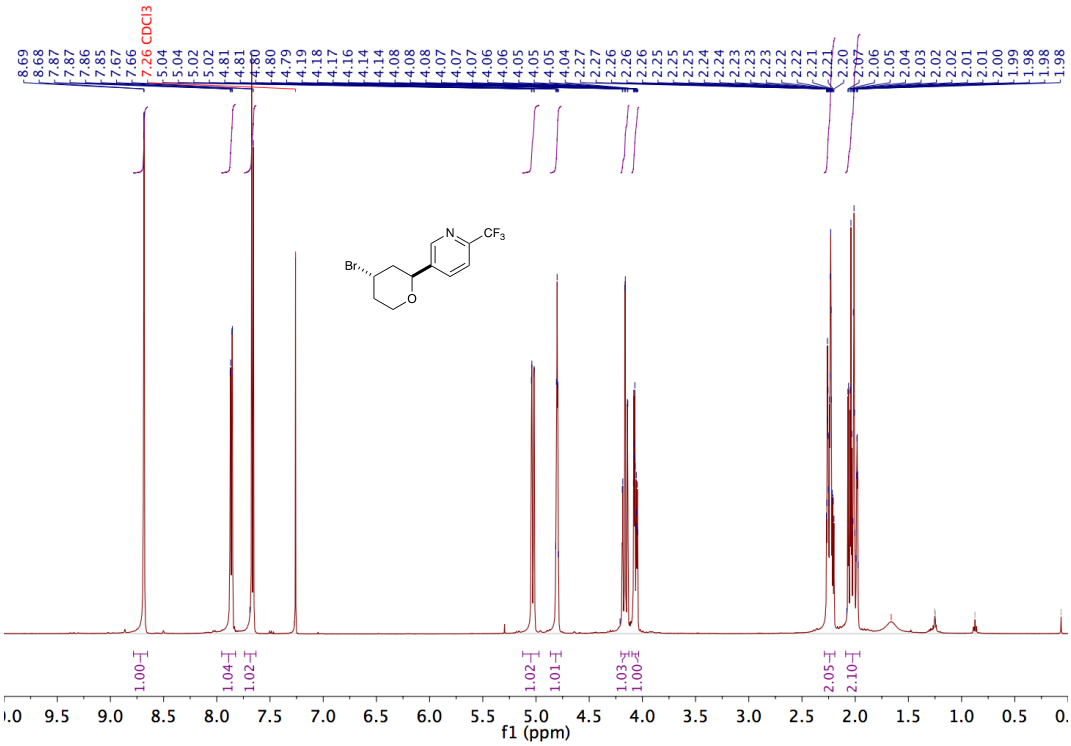


^{1}H NMR (500 MHz, $CDCl_3$) - (41)

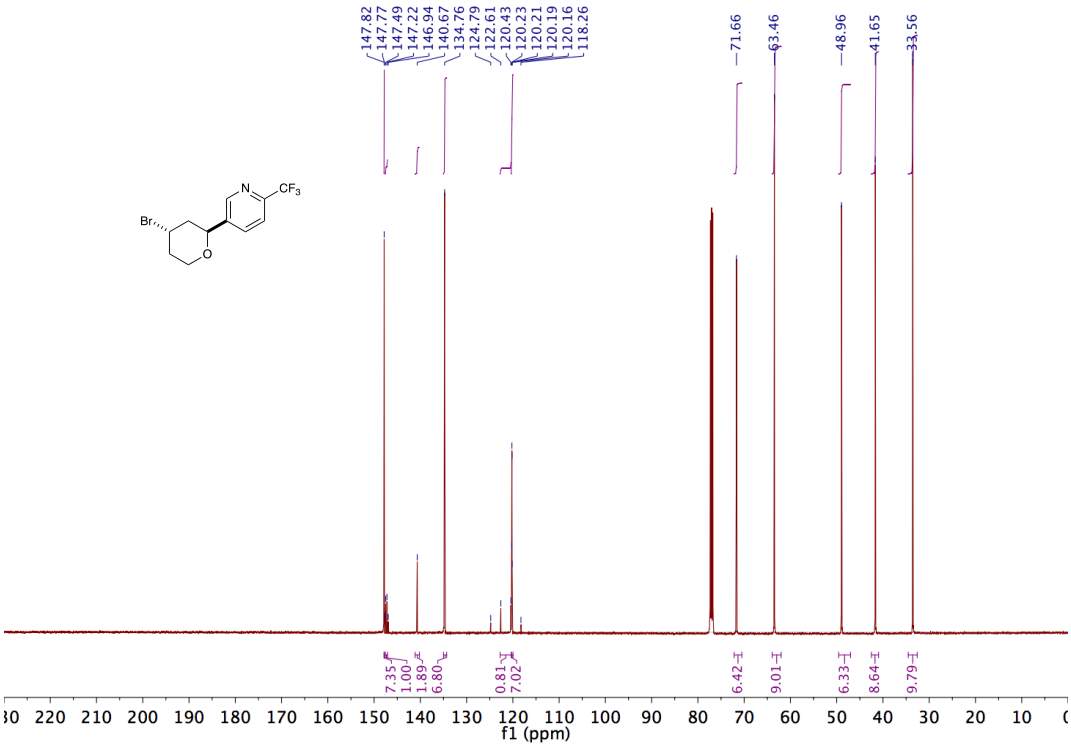


^{13}C NMR (126 MHz, $CDCl_3$) - (41)

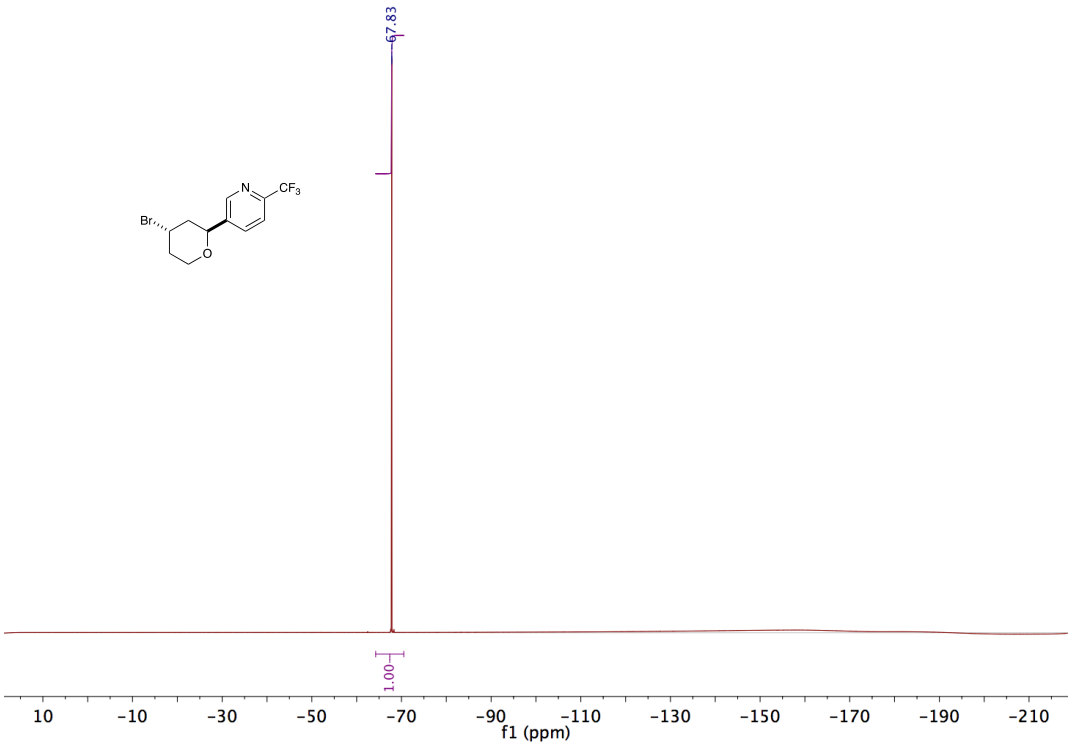
^{19}F NMR (376 MHz, $CDCl_3$) - (41)



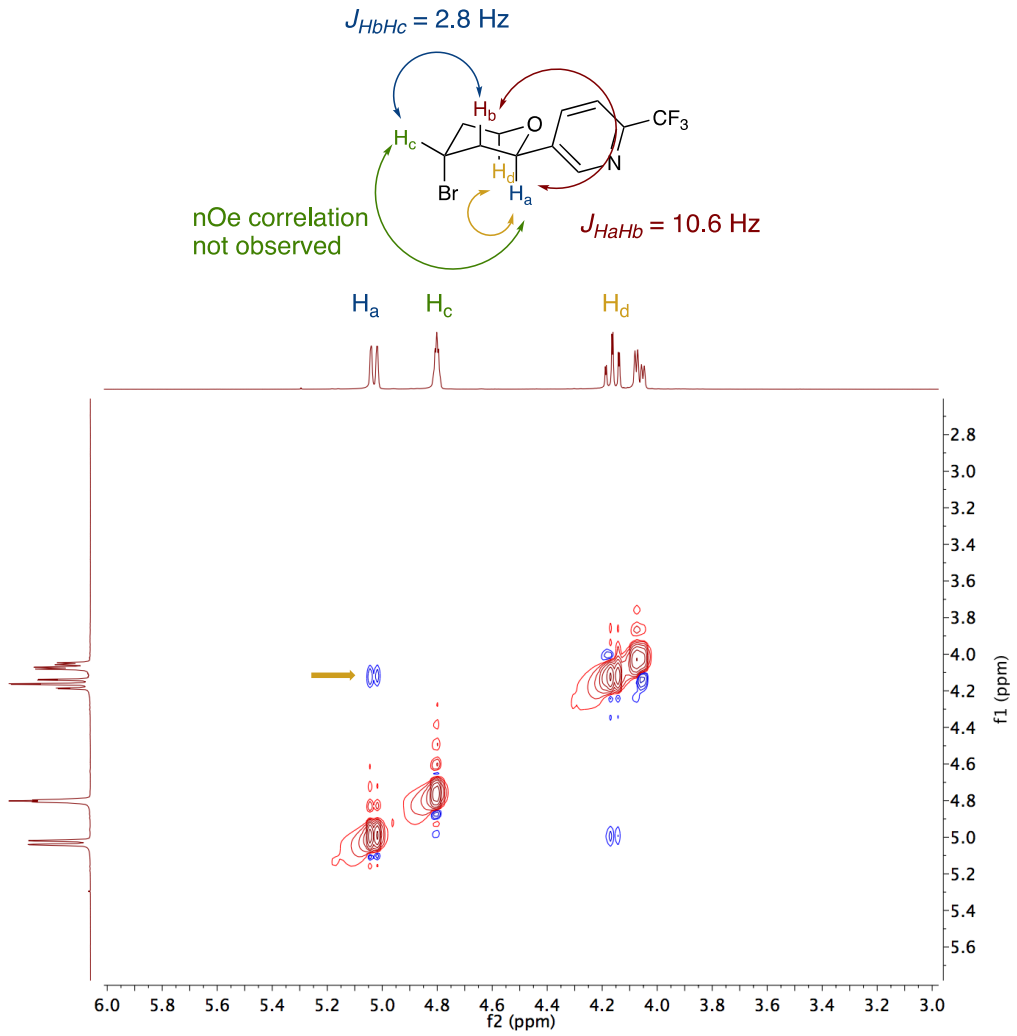
^{1}H NMR (500 MHz, $CDCl_3$) – (42)



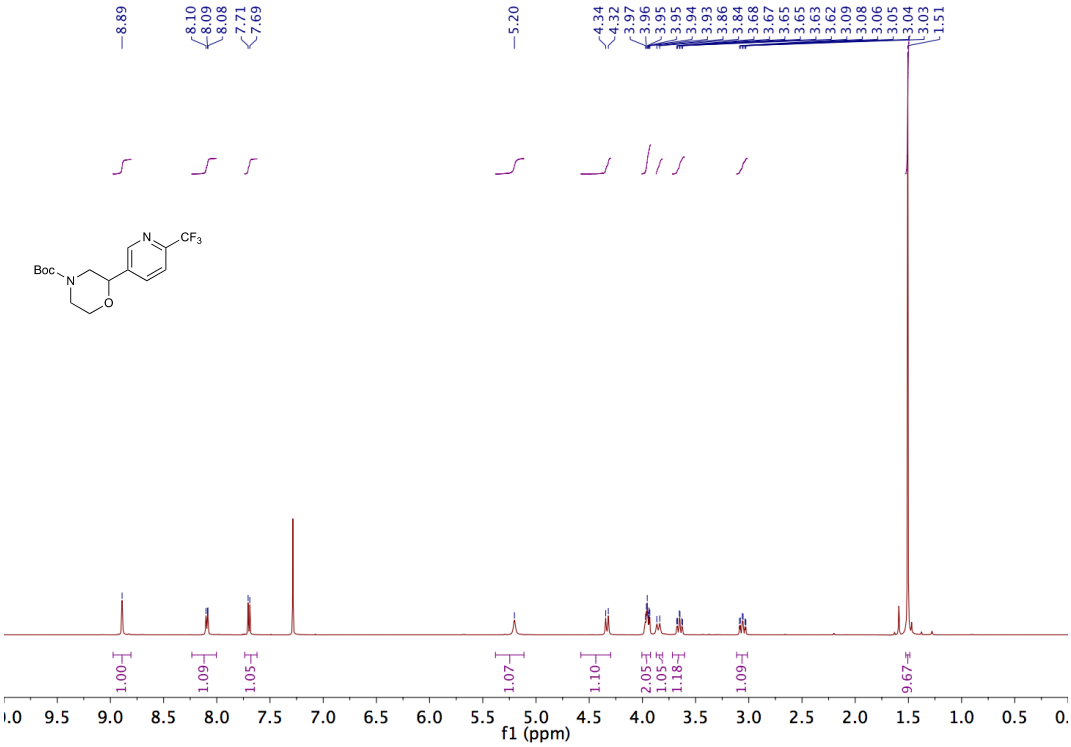
^{13}C NMR (126 MHz, $CDCl_3$) – (42)



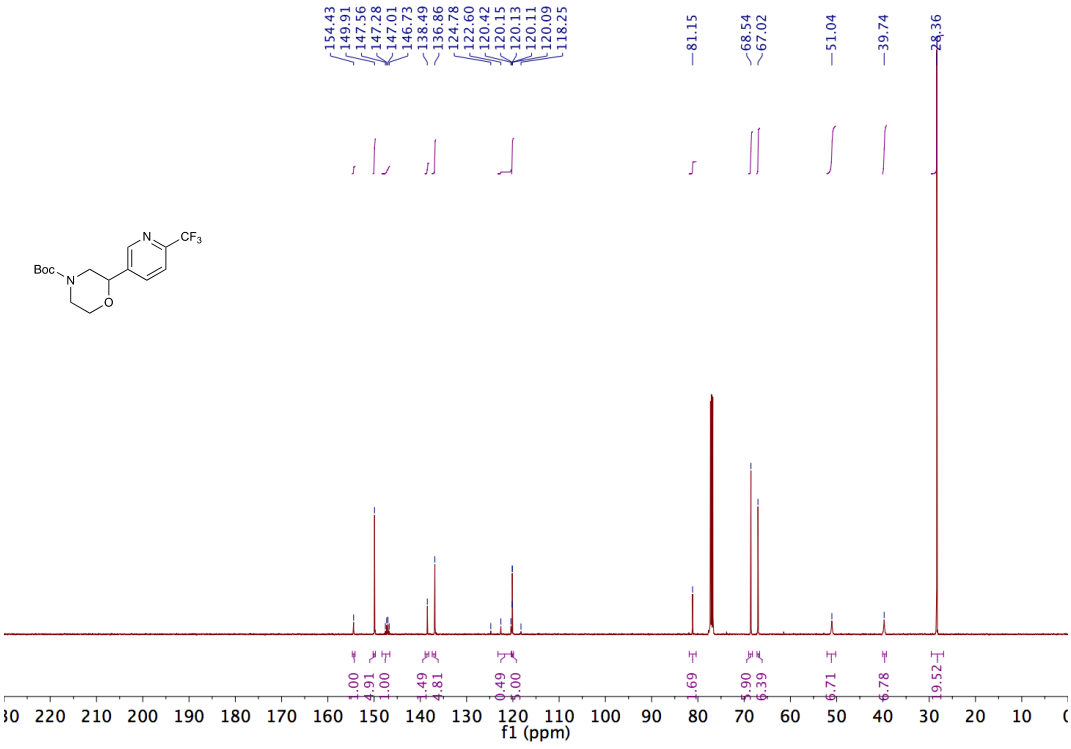
^{19}F NMR (376 MHz, $CDCl_3$) – (42)



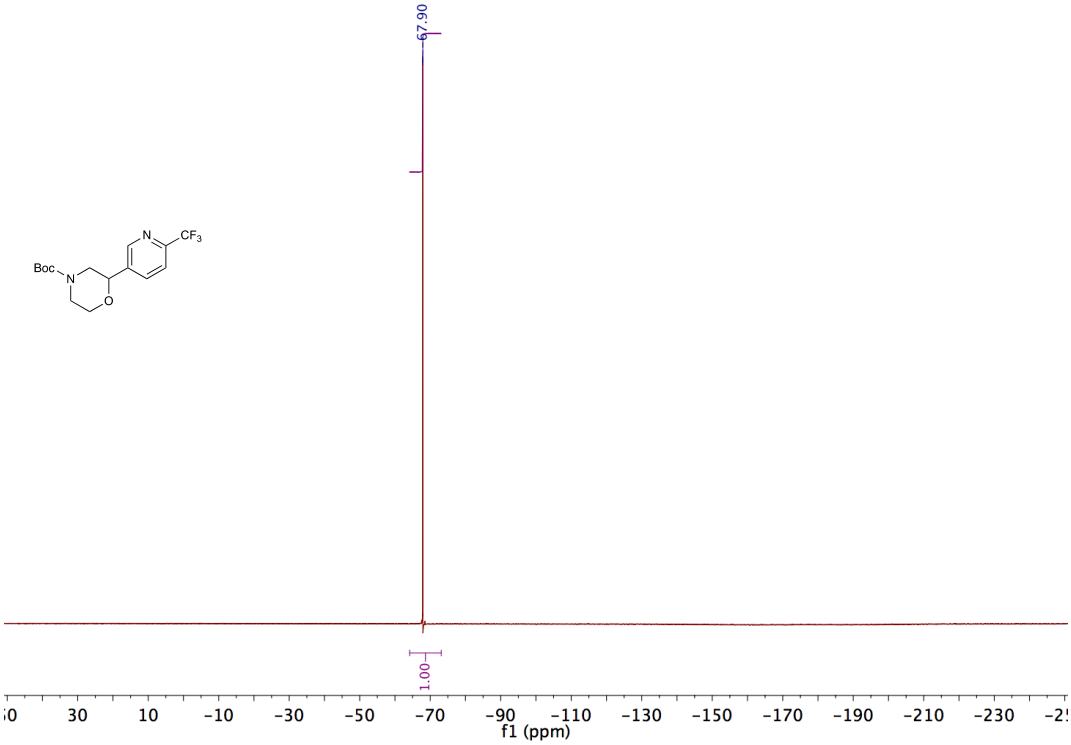
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (42)



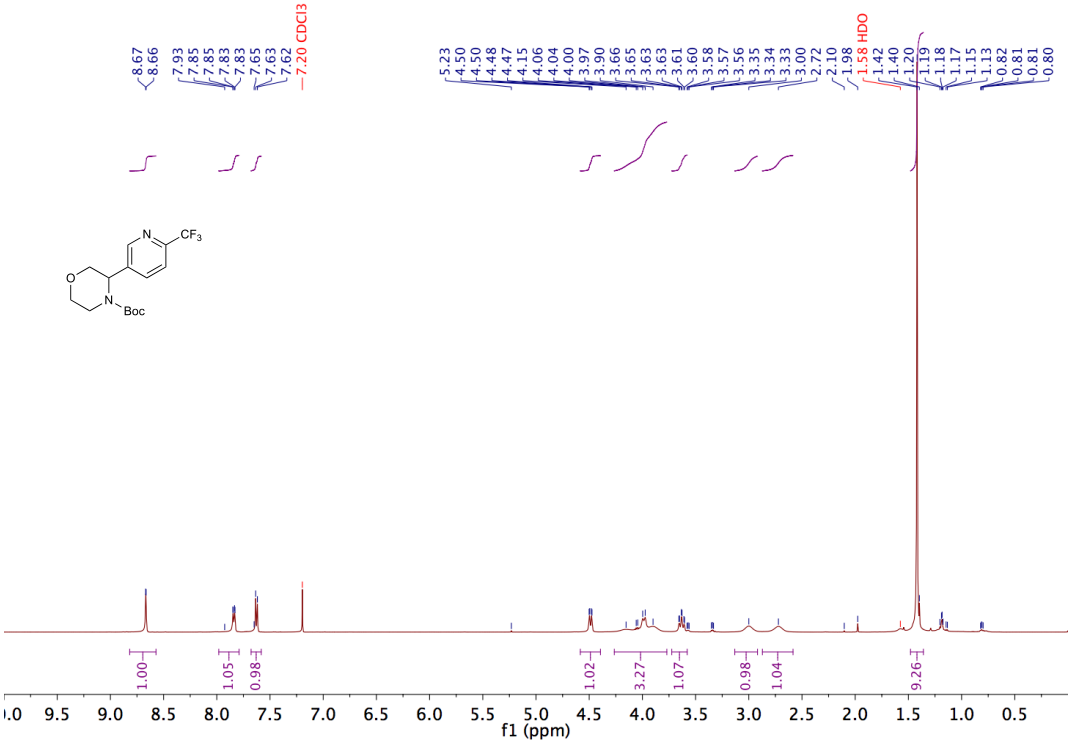
^{1}H NMR (500 MHz, $CDCl_3$) – (43)



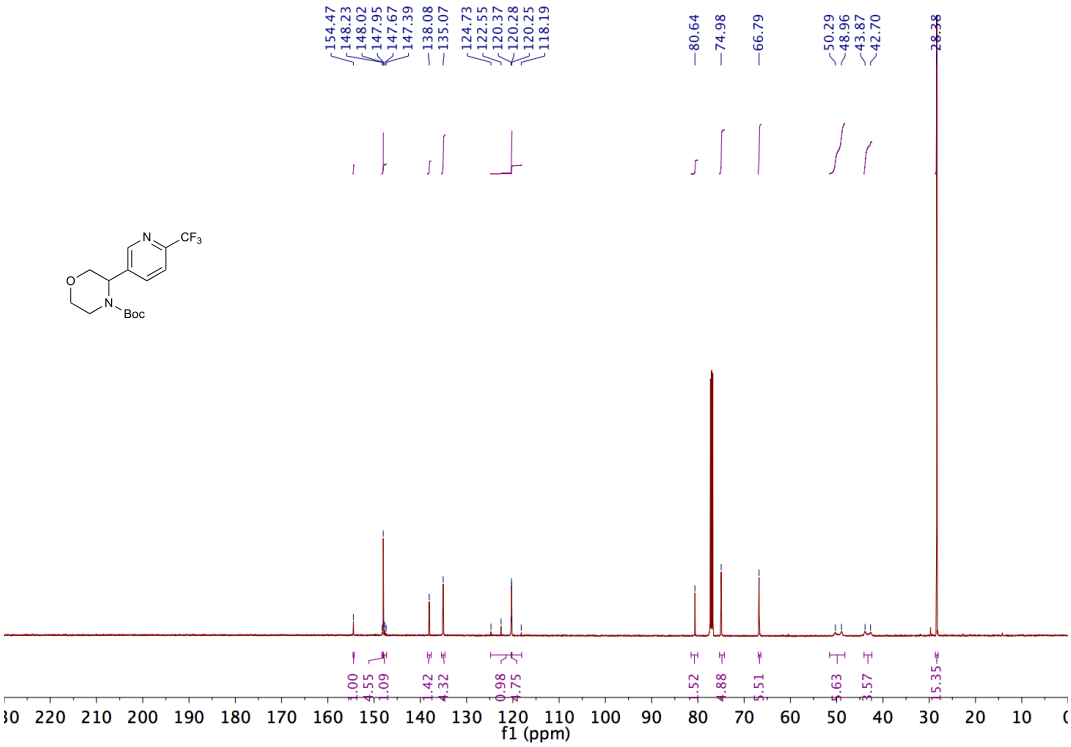
^{13}C NMR (126 MHz, $CDCl_3$) – (43)



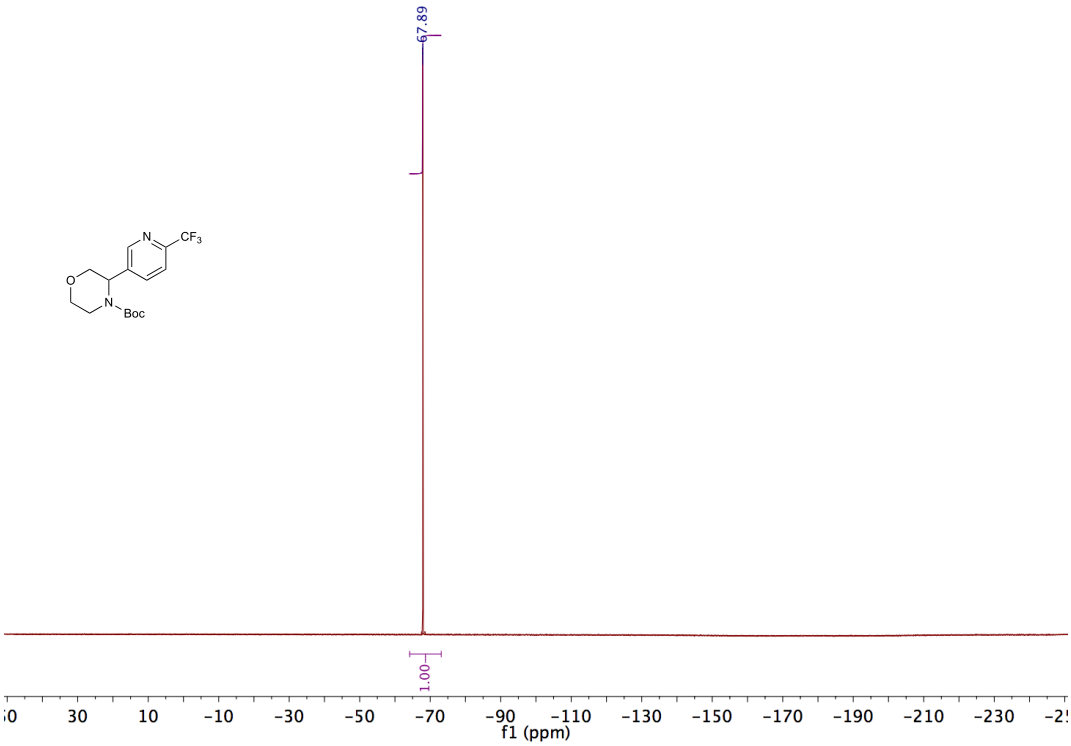
^{19}F NMR (376 MHz, $CDCl_3$) – (43)



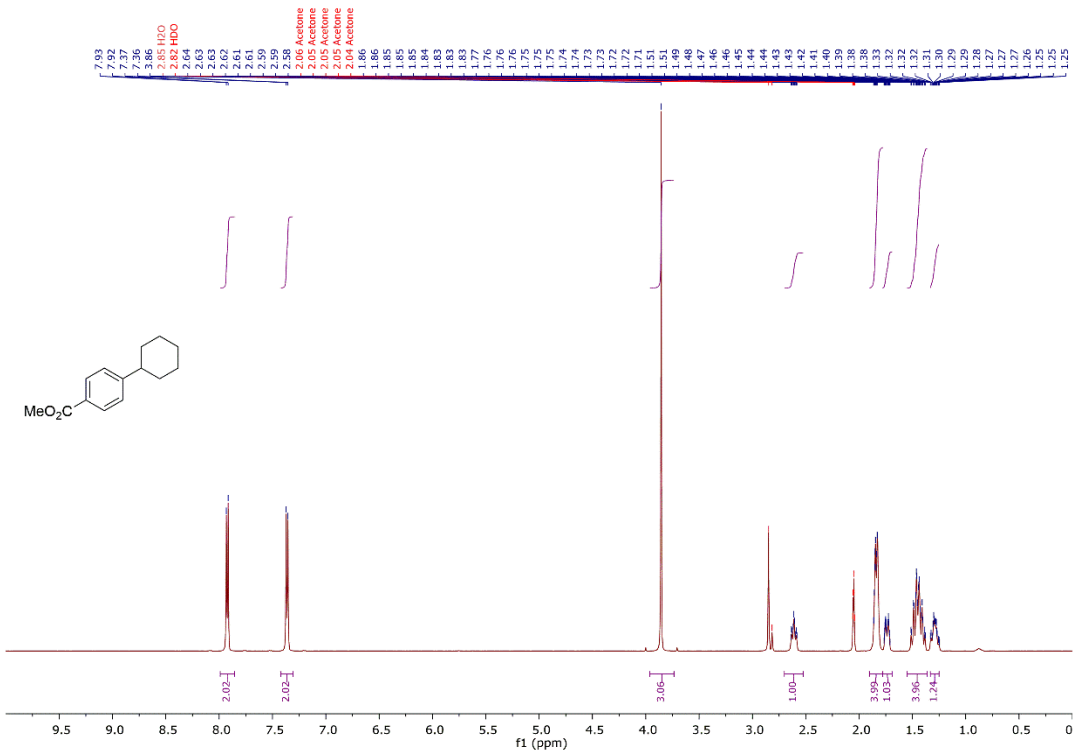
^{1}H NMR (500 MHz, $CDCl_3$) – (SI-43)



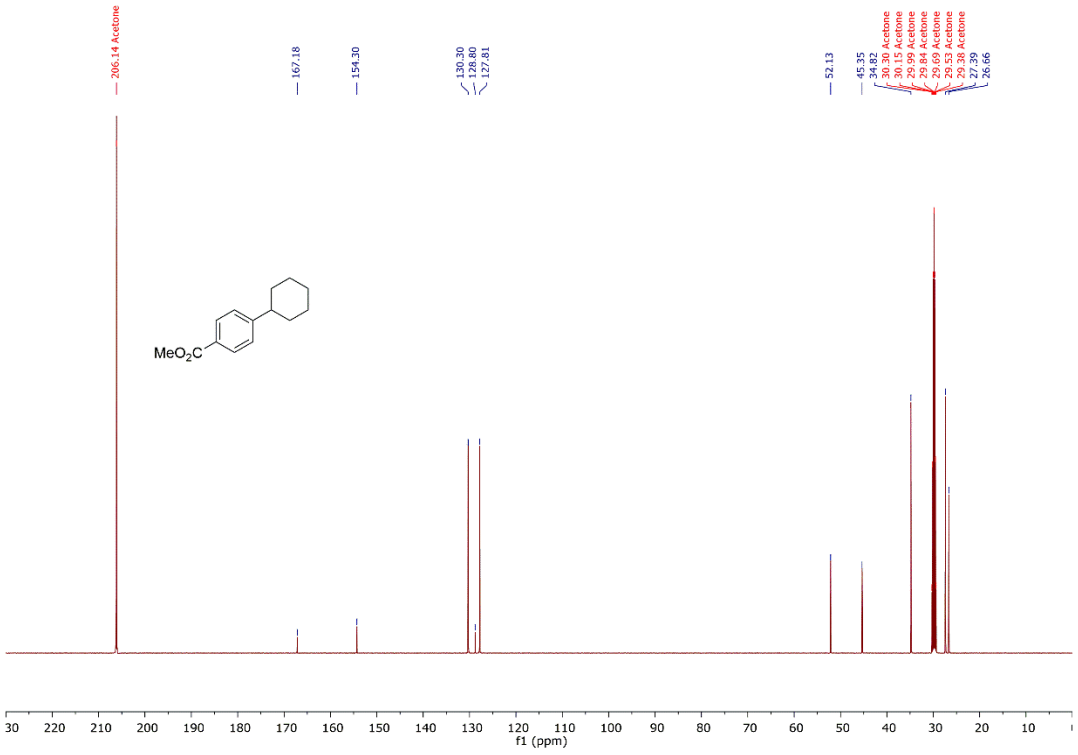
^{13}C NMR (126 MHz, $CDCl_3$) – (SI-43)



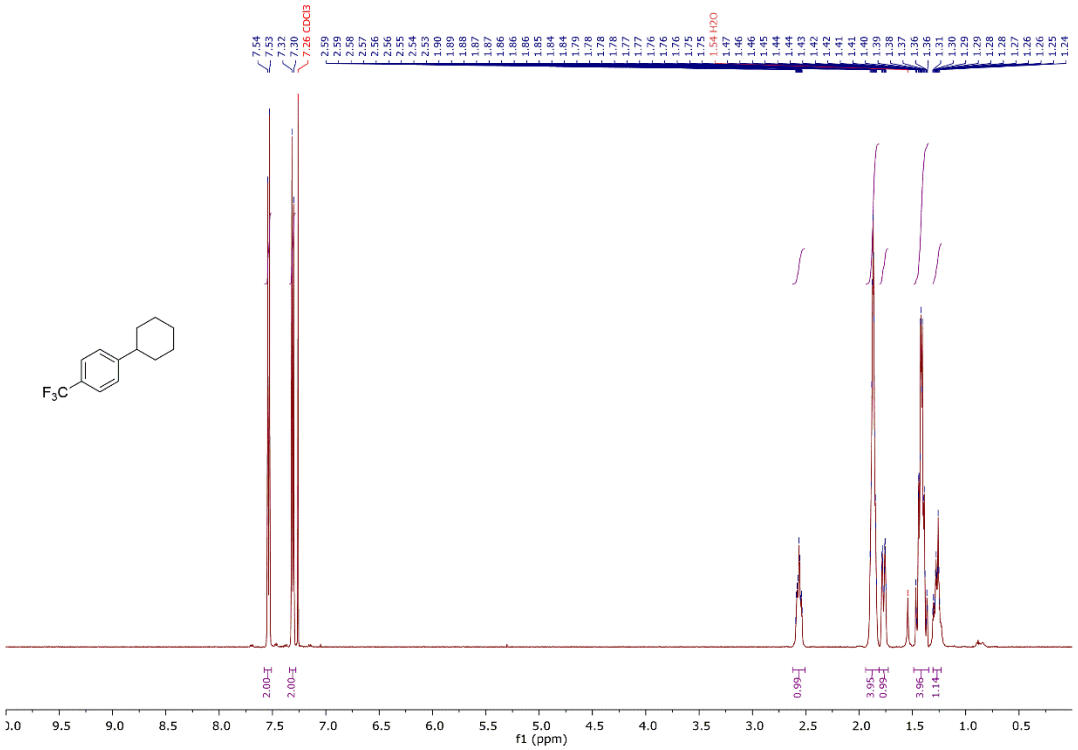
^{19}F NMR (376 MHz, $CDCl_3$) – (SI-43)



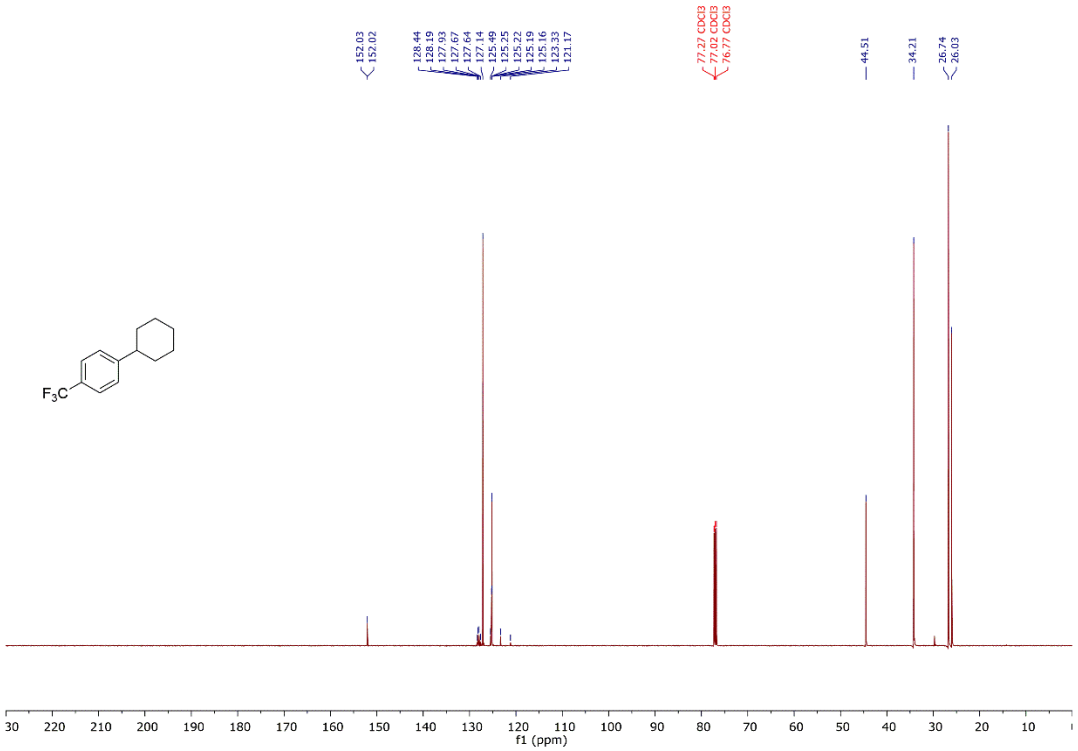
^{1}H NMR (500 MHz, $(CD_3)_2CO$) - (SI-44)



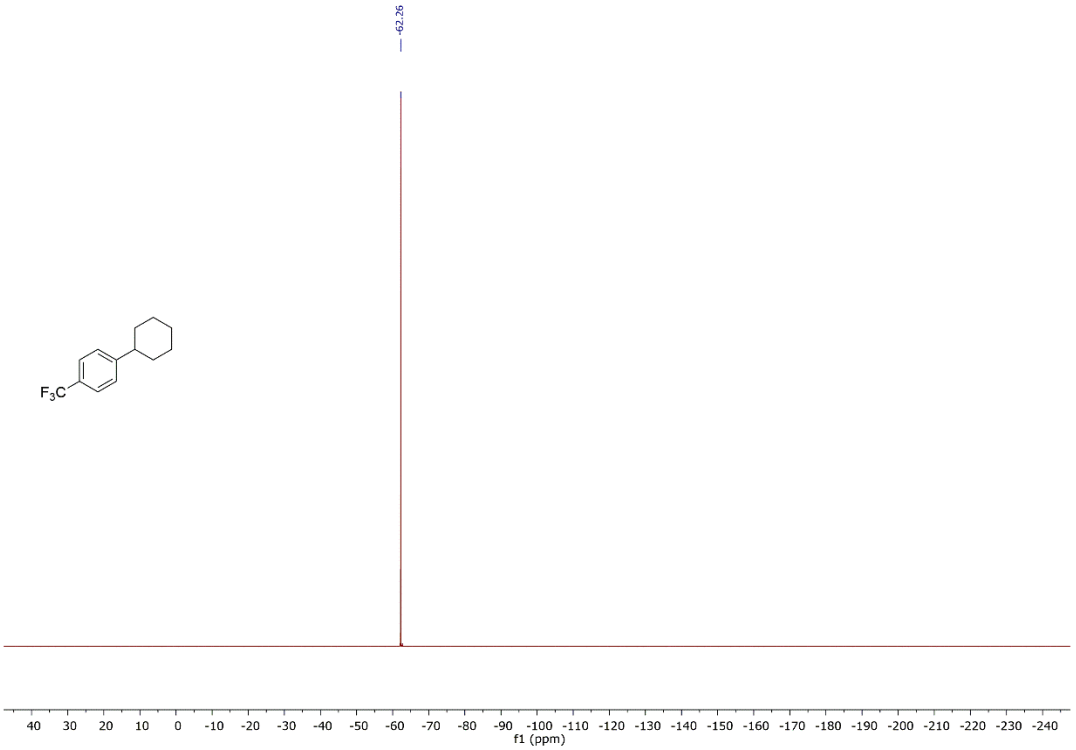
^{13}C NMR (126 MHz, $(CD_3)_2CO$) - (SI-44)



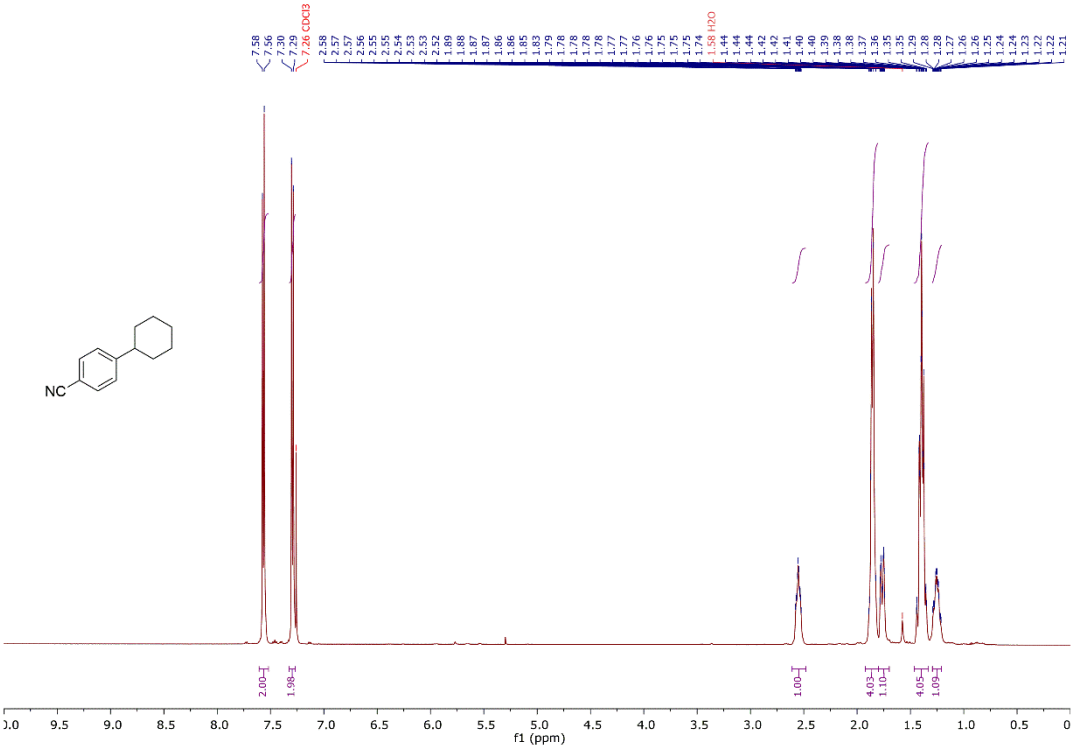
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-45)



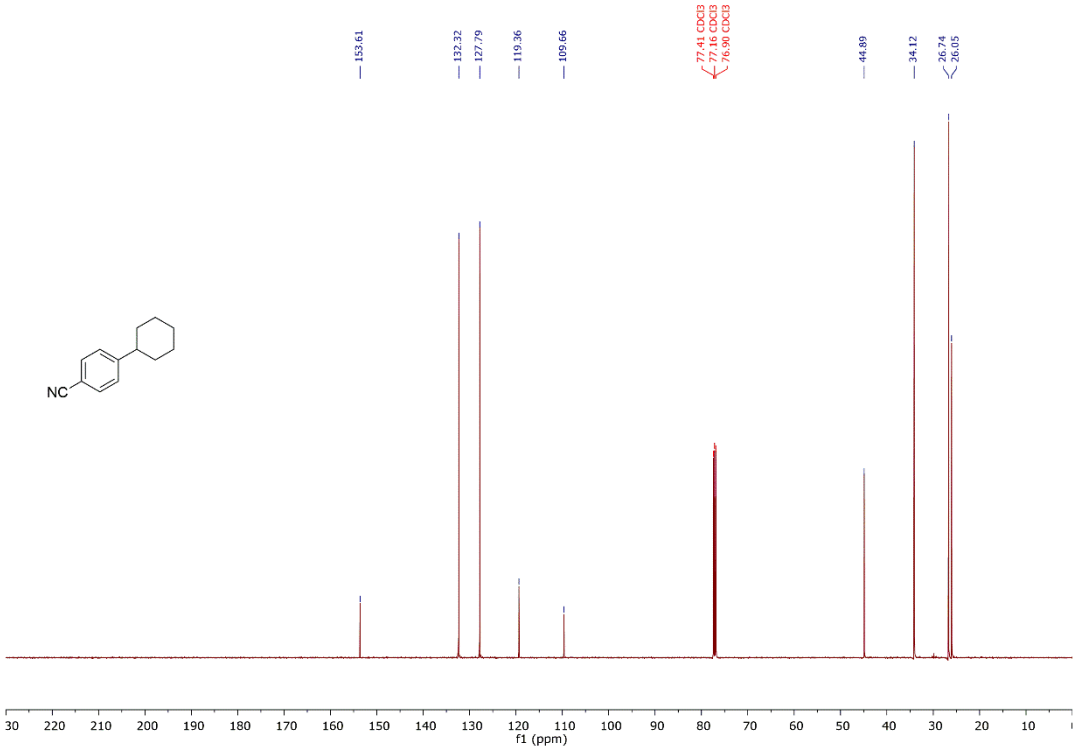
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-45)



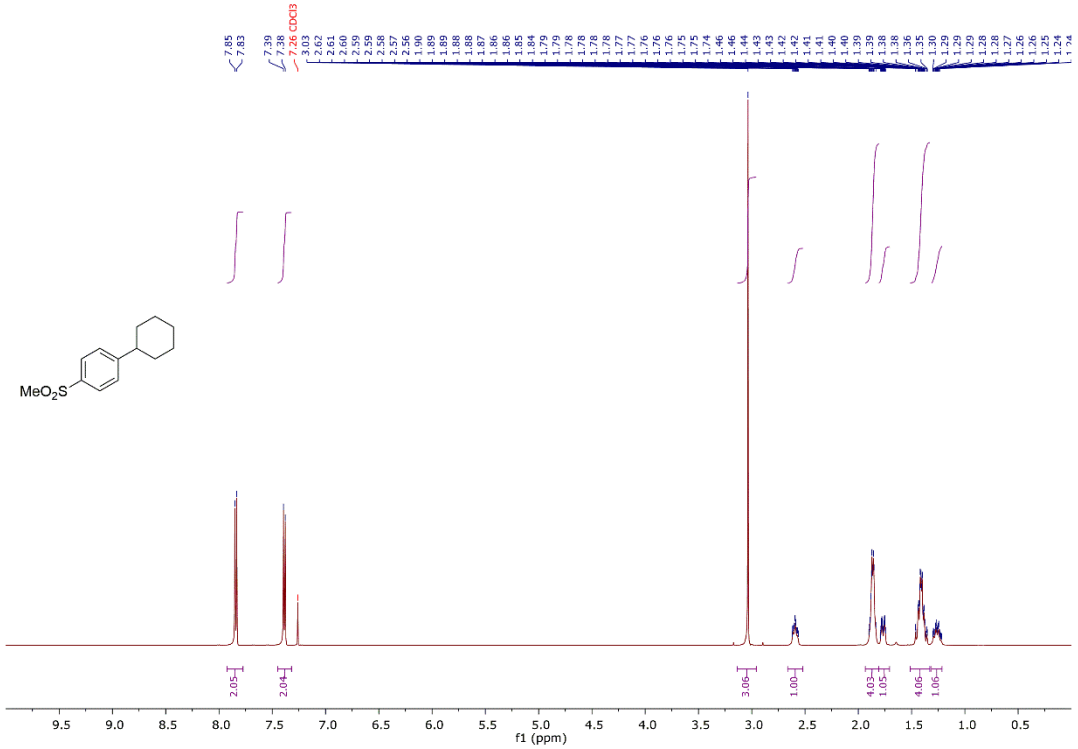
^{19}F NMR (470 MHz, $CDCl_3$) - (SI-45)



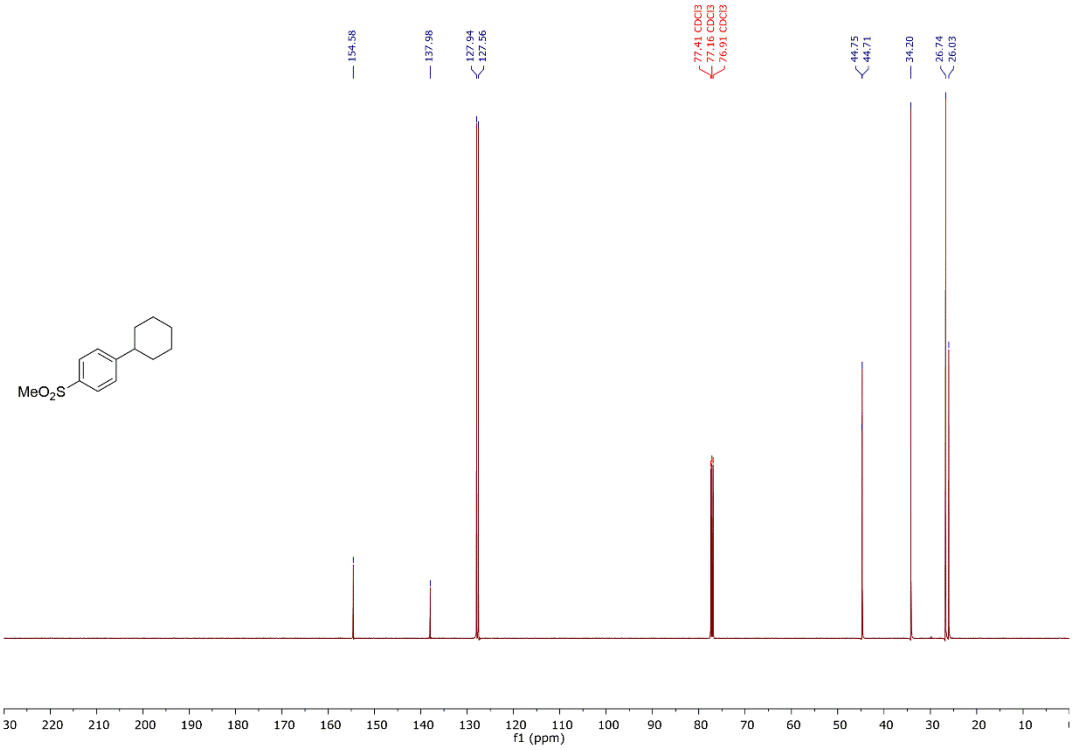
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-46)



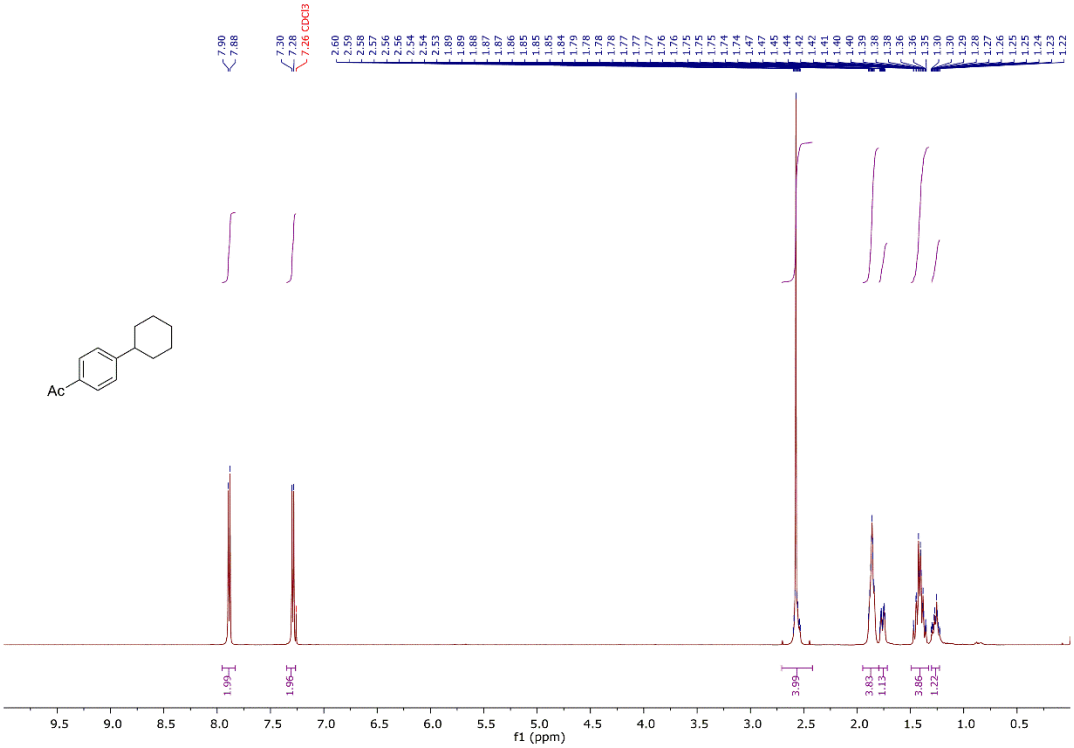
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-46)



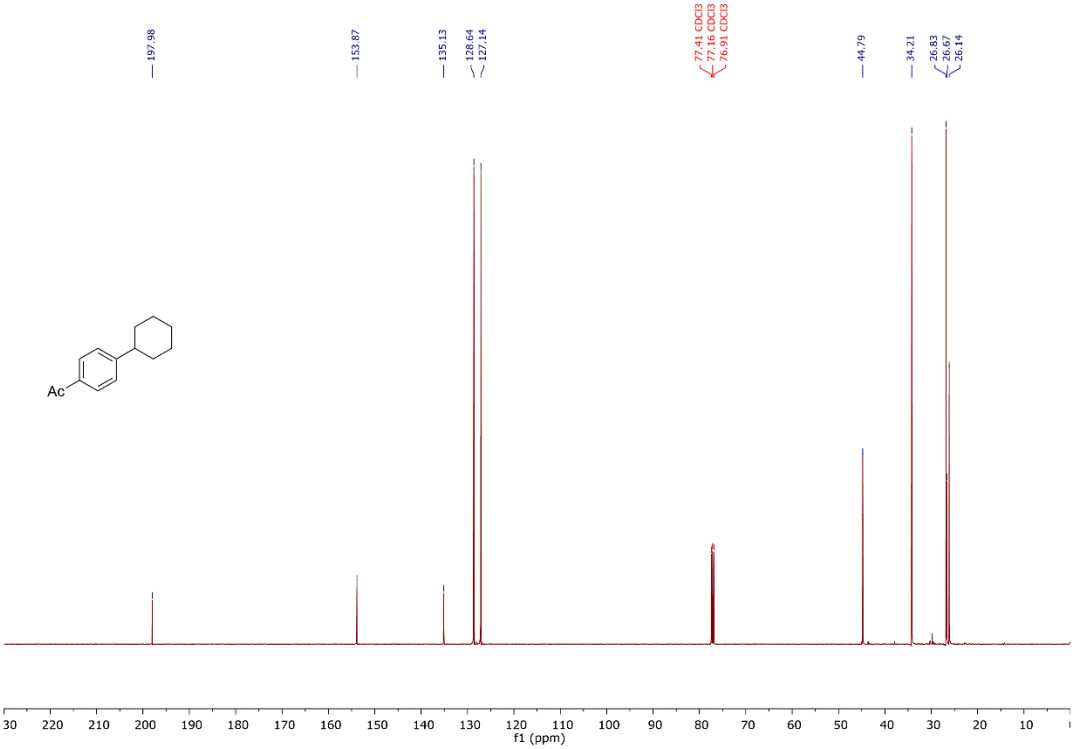
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-47)



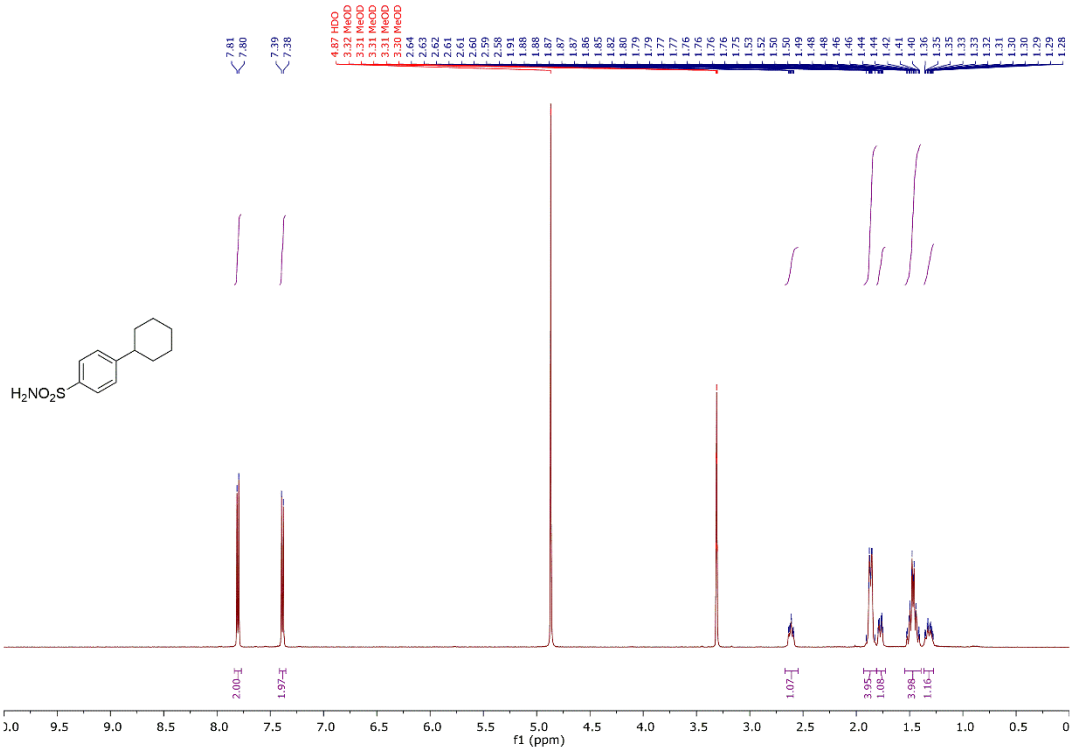
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-47)



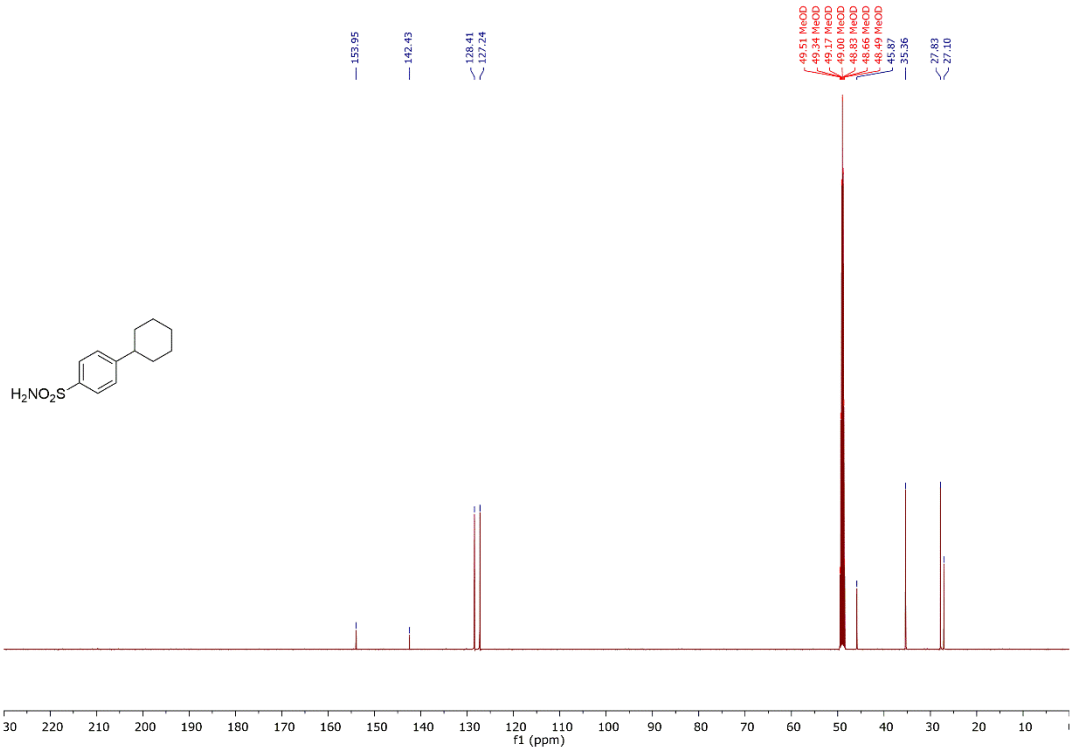
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-48)



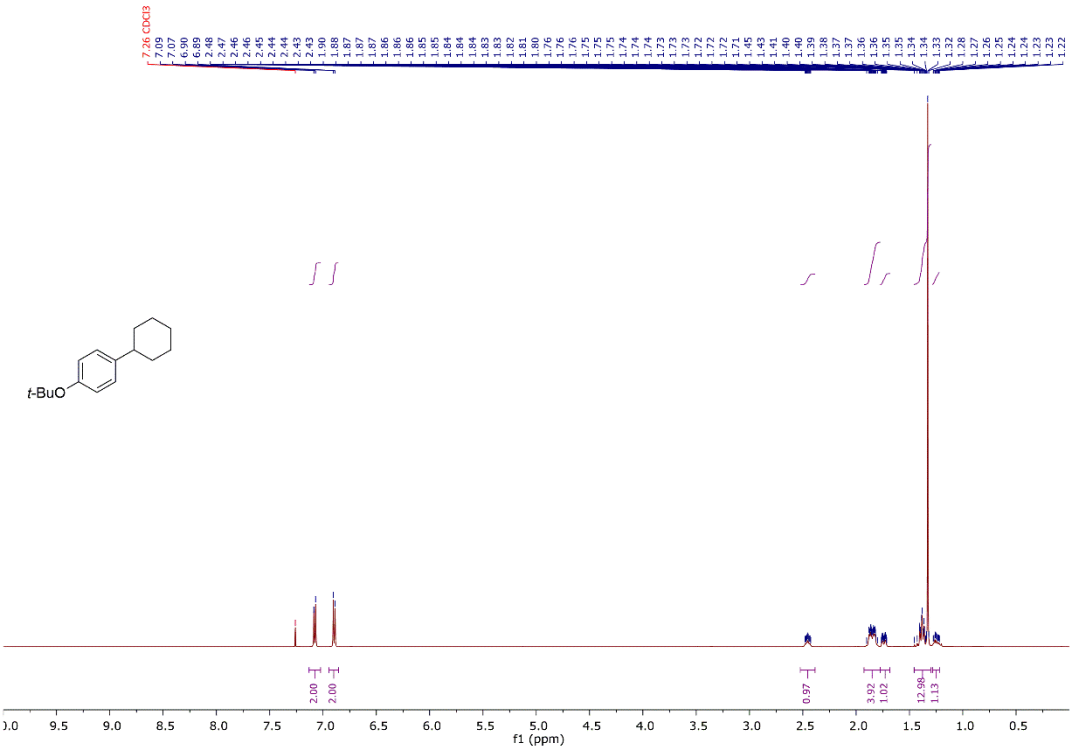
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-48)



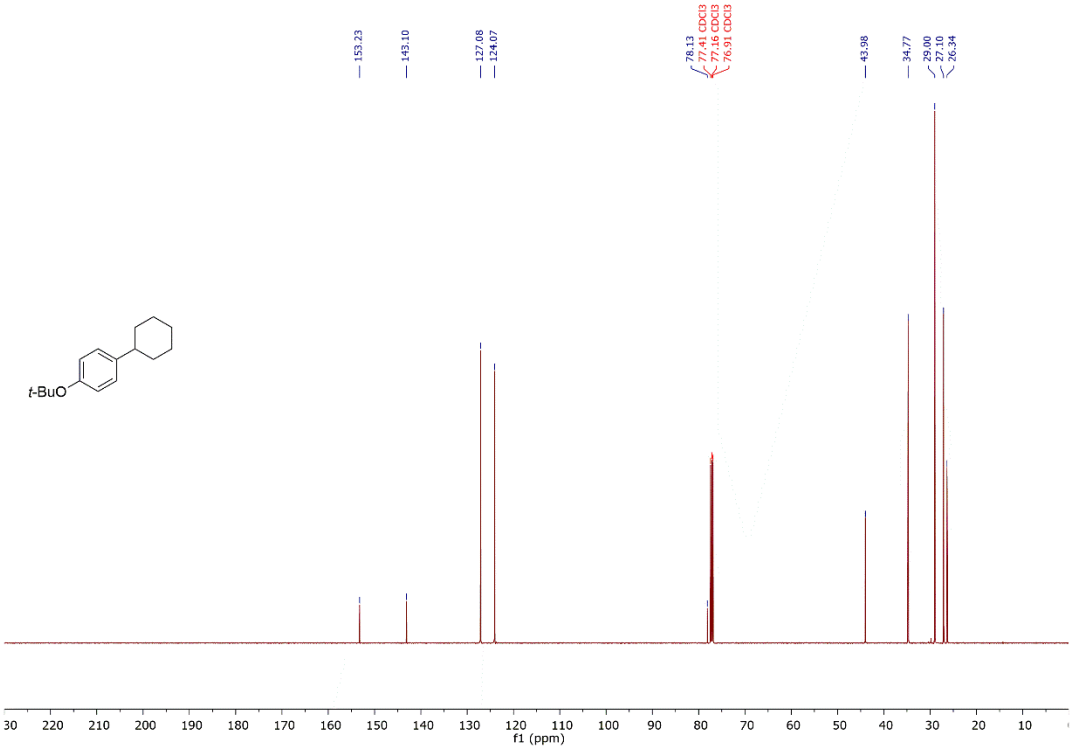
^{1}H NMR (500 MHz, CD_3OD) - (SI-49)



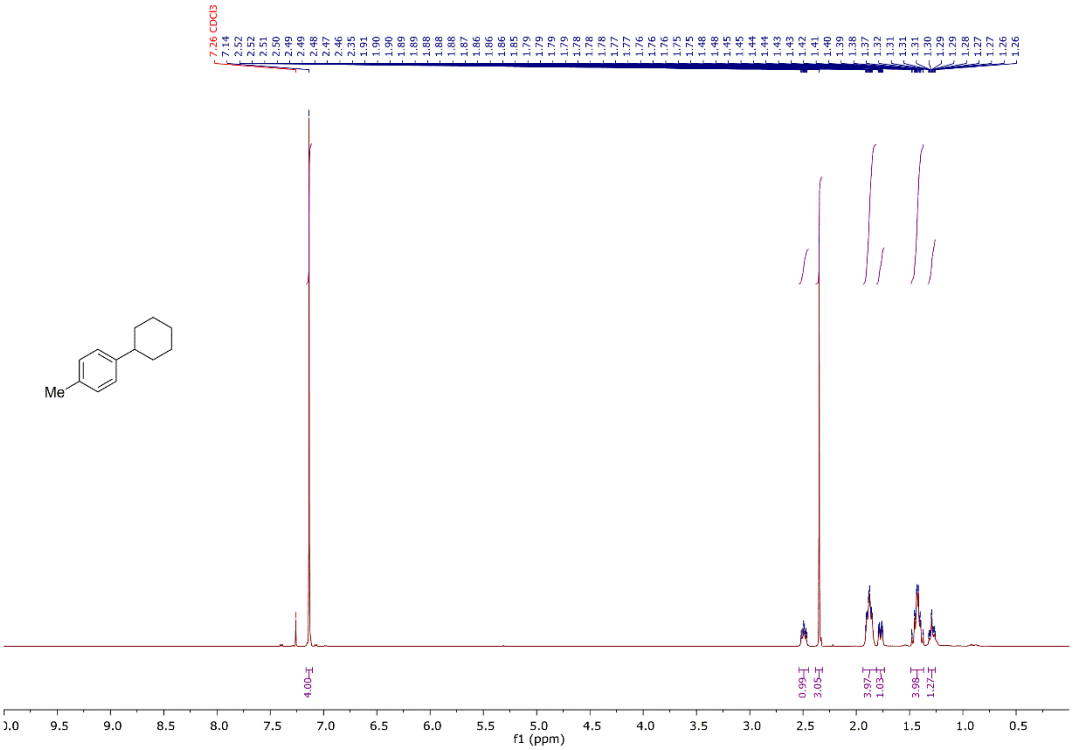
^{13}C NMR (126 MHz, CD_3OD) - (SI-49)



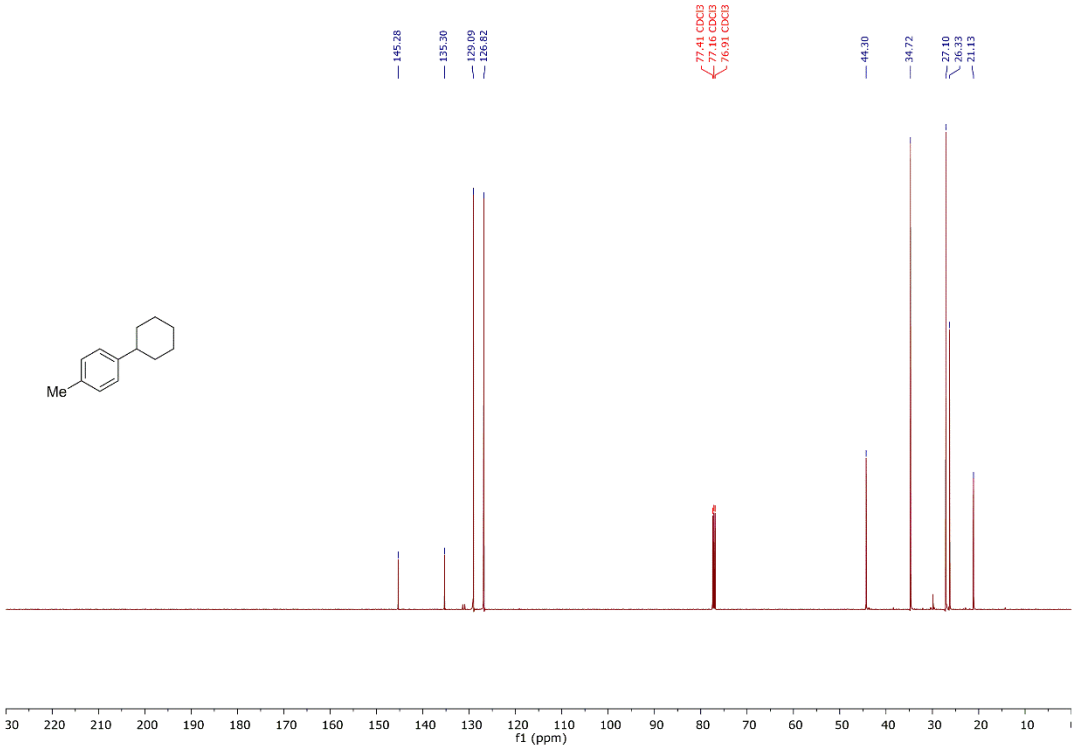
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-50)



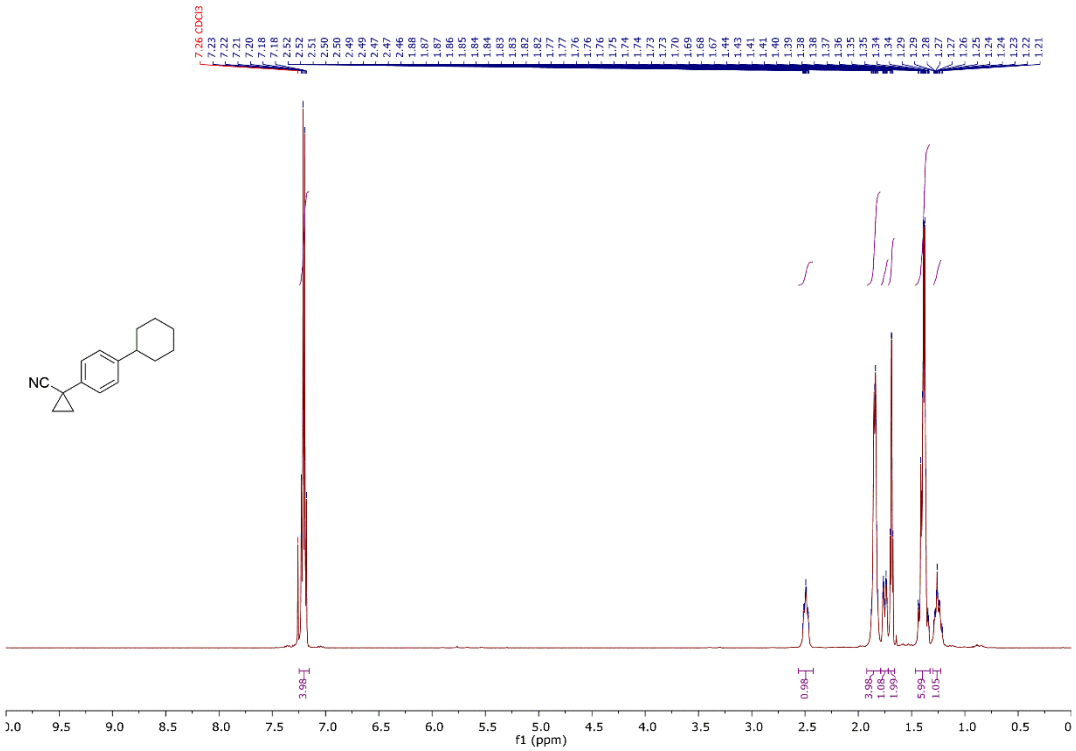
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-50)



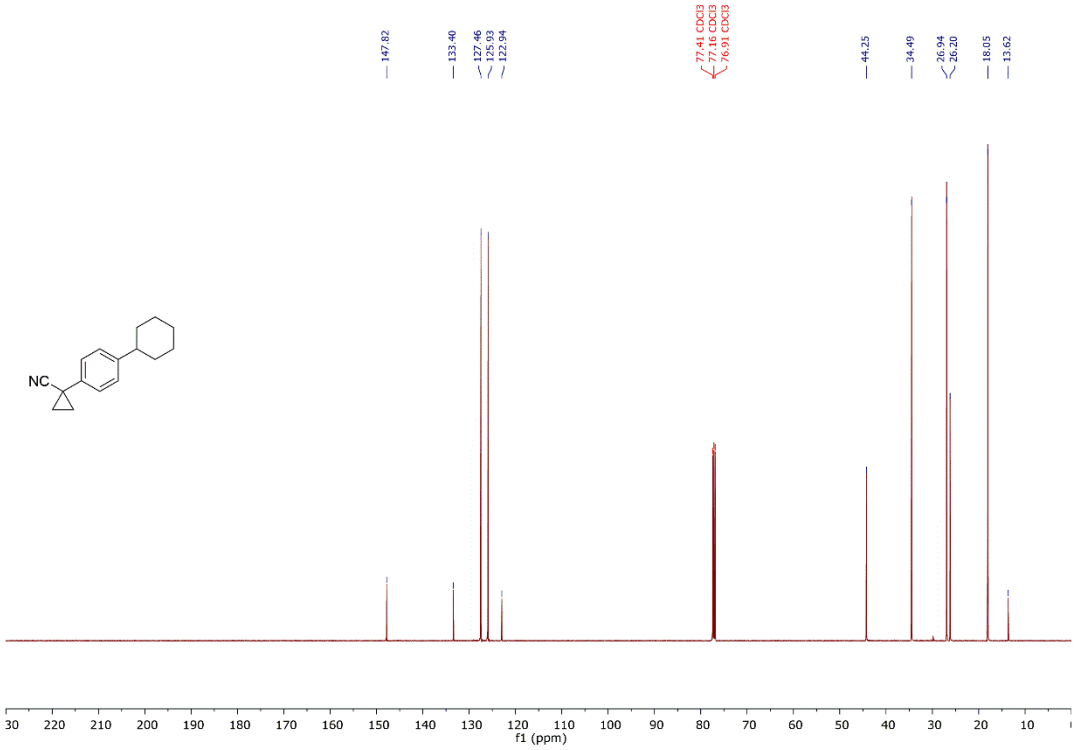
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-51)



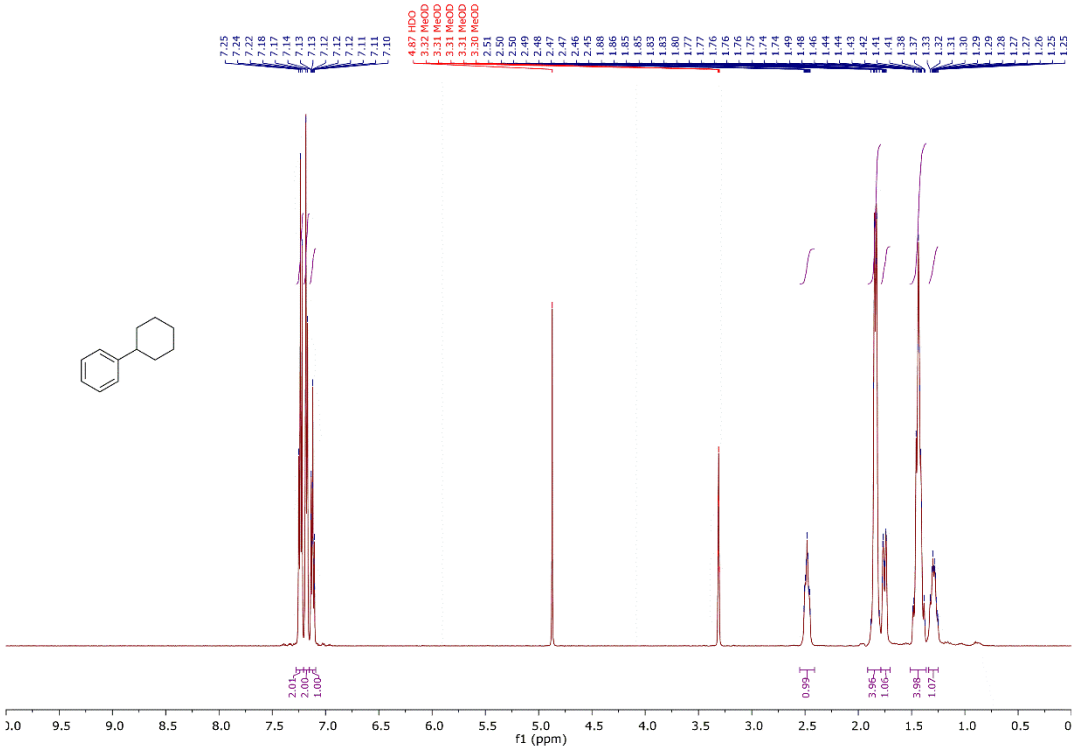
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-51)



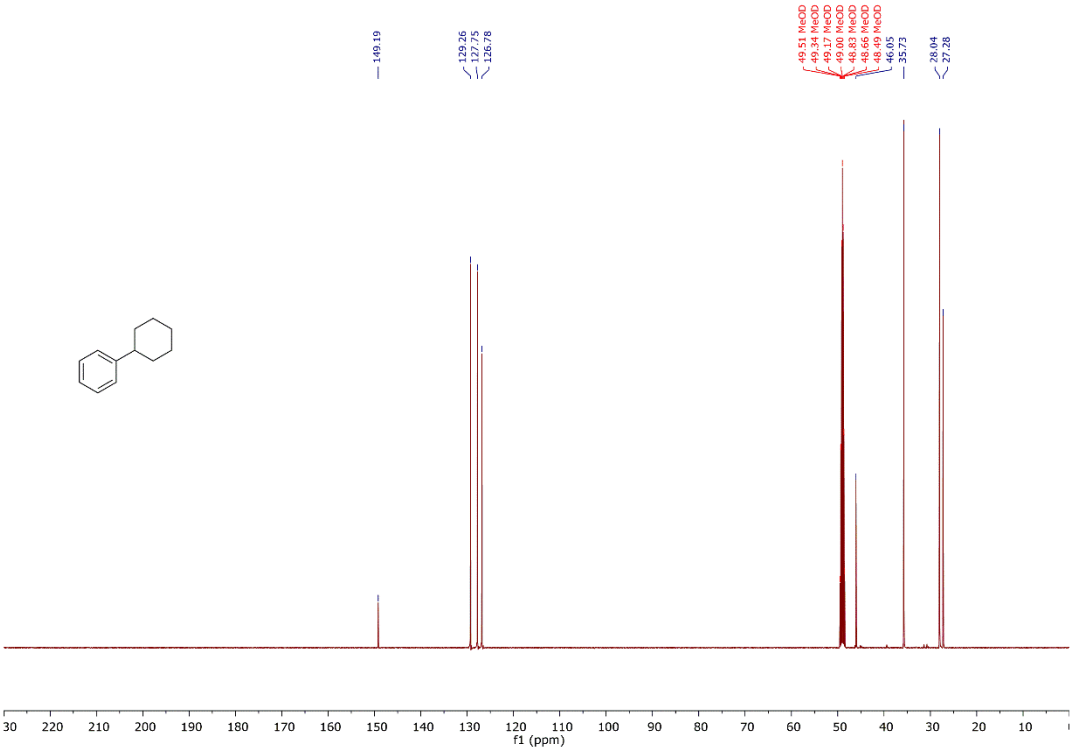
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-52)



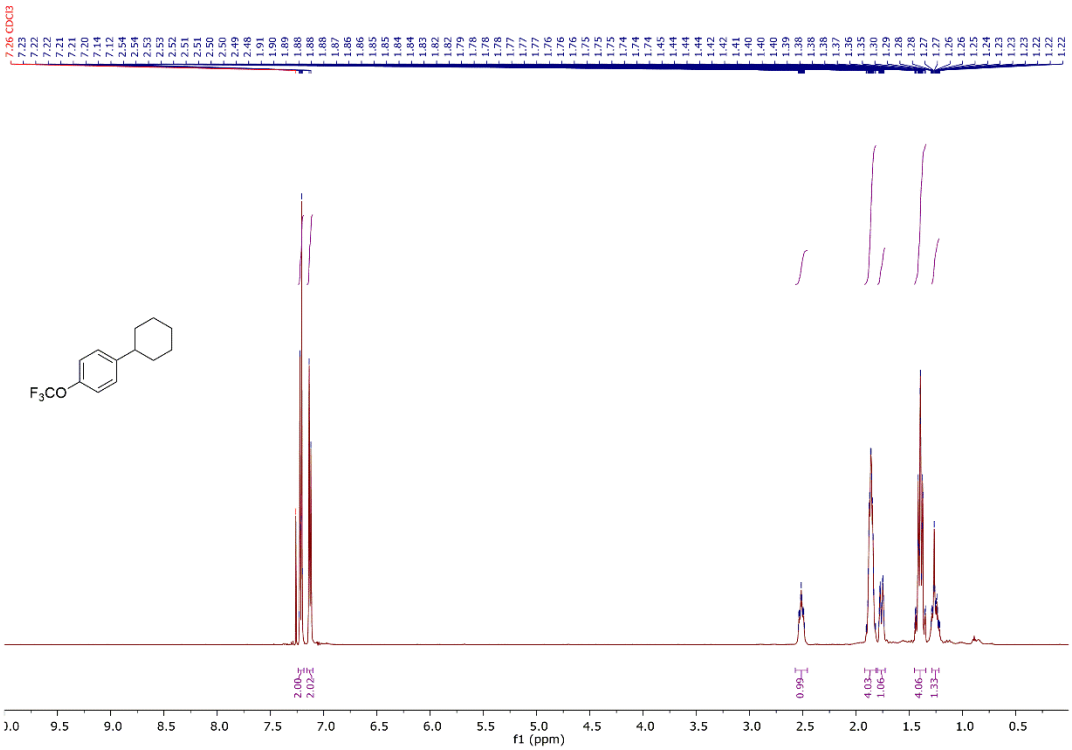
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-52)



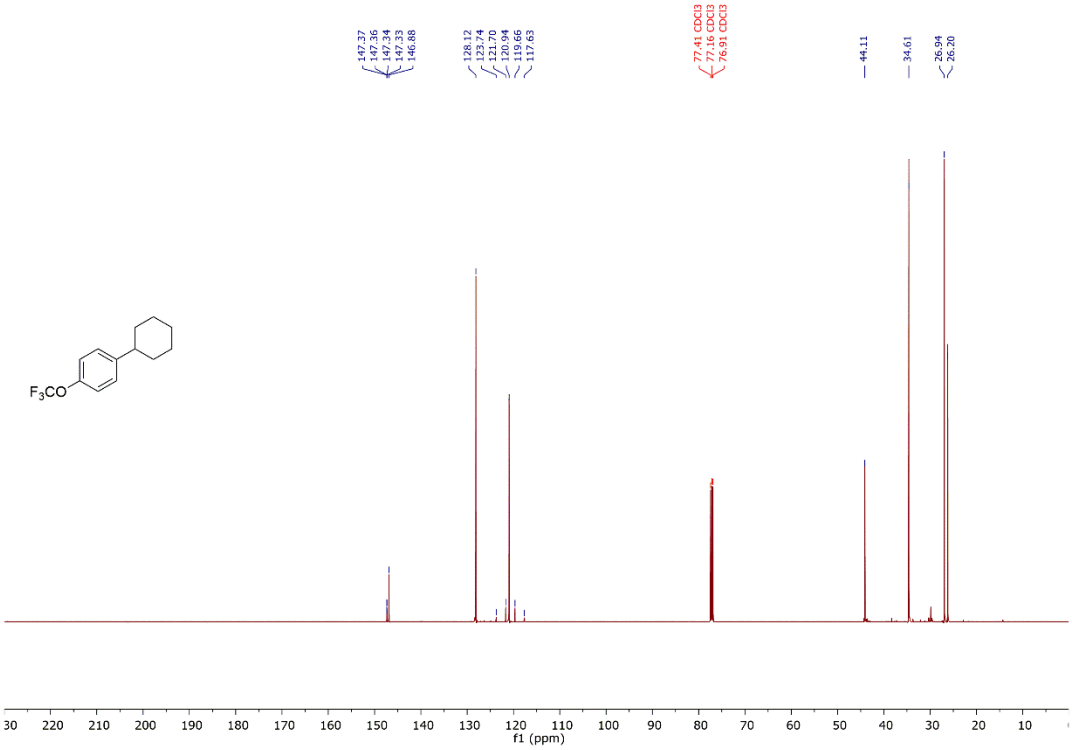
^{1}H NMR (500 MHz, CD_3OD) - (SI-53)



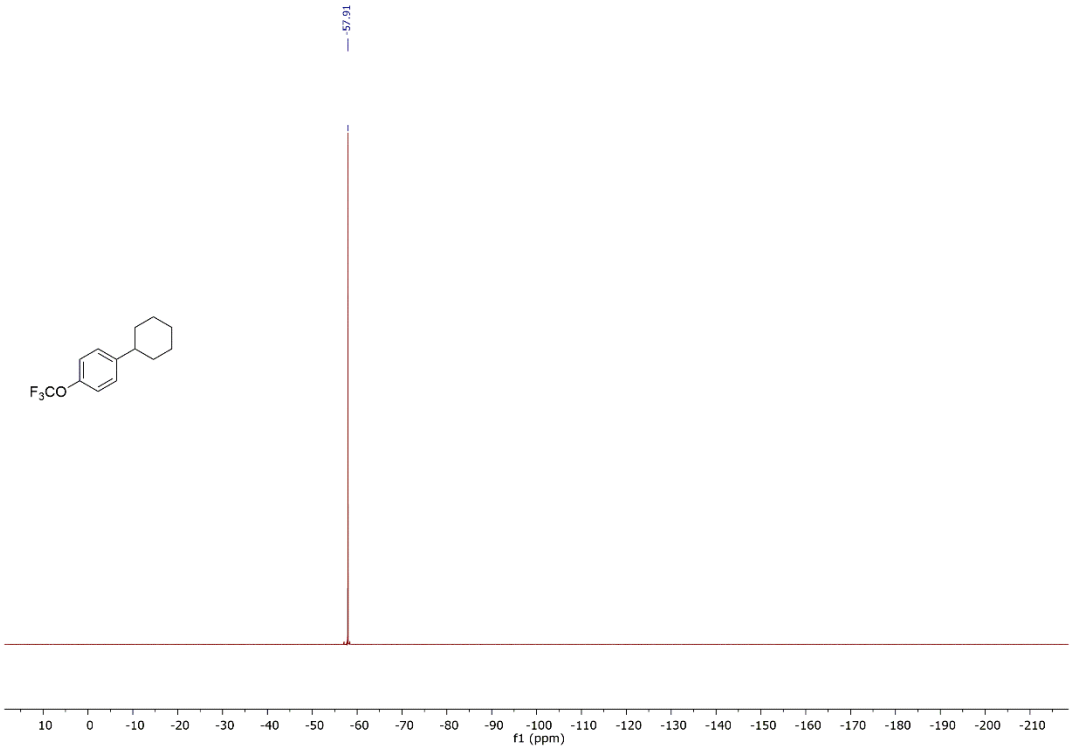
^{13}C NMR (126 MHz, CD_3OD) - (SI-53)



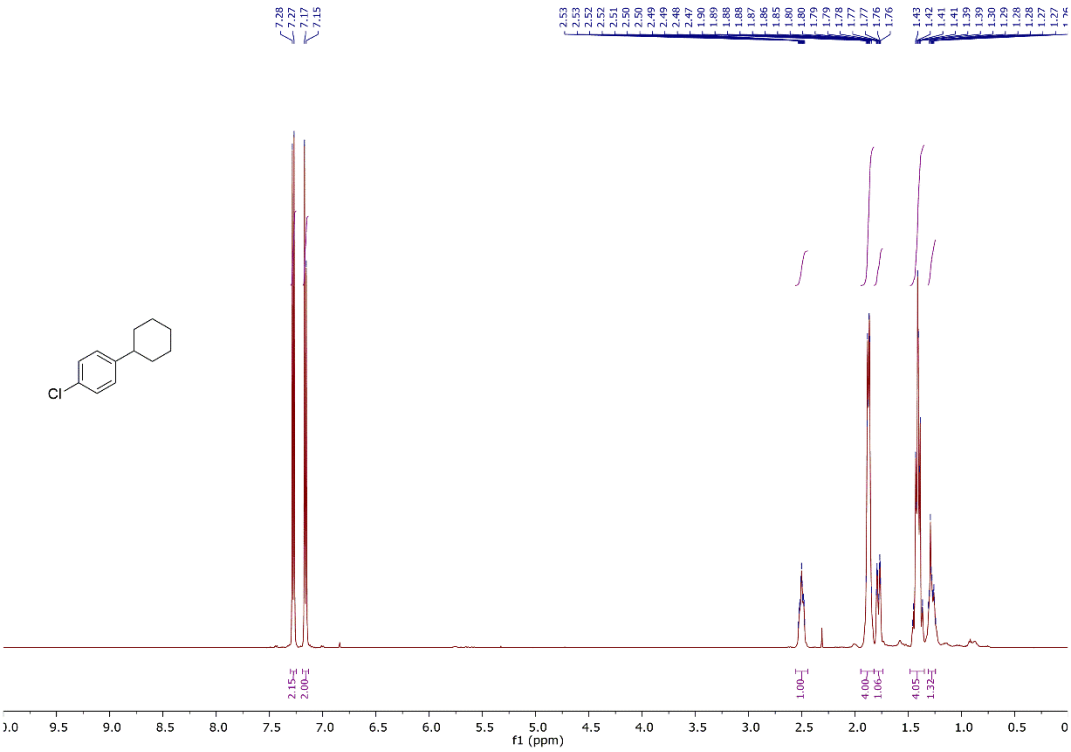
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-54)



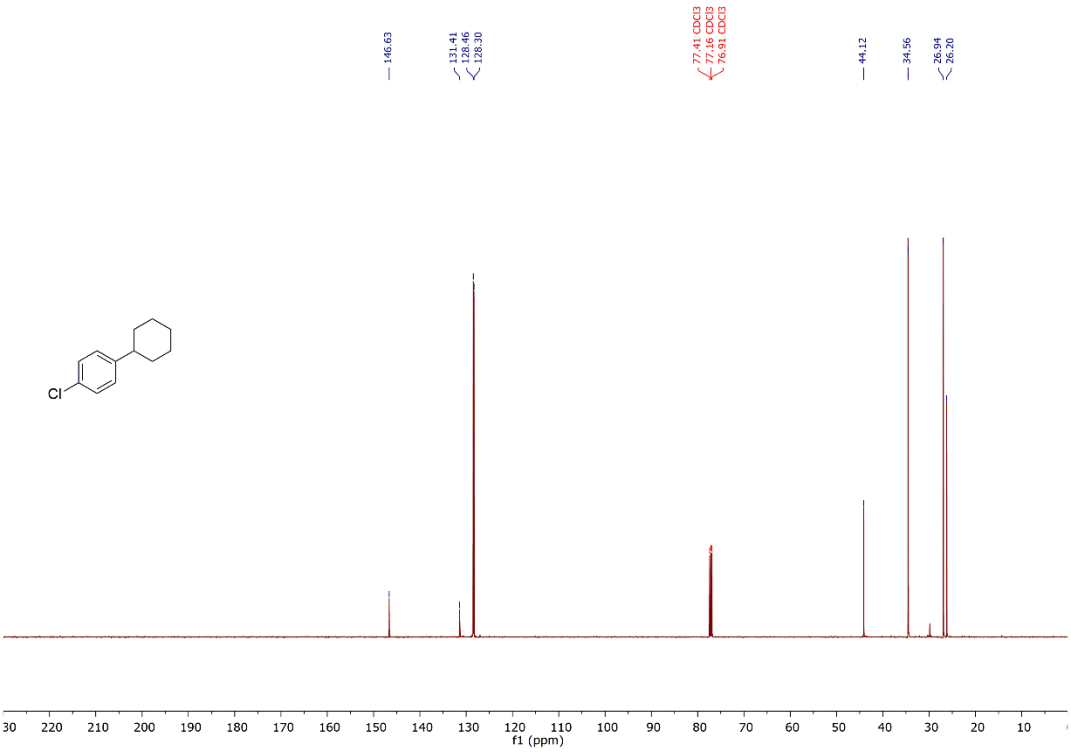
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-54)



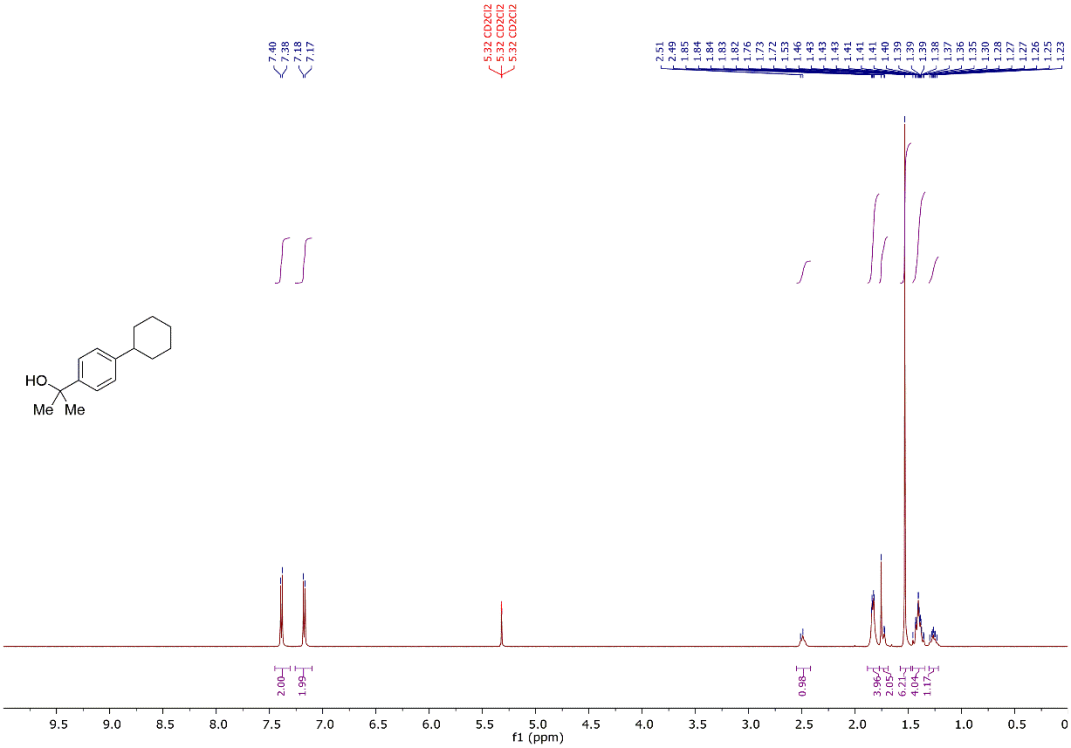
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-54)



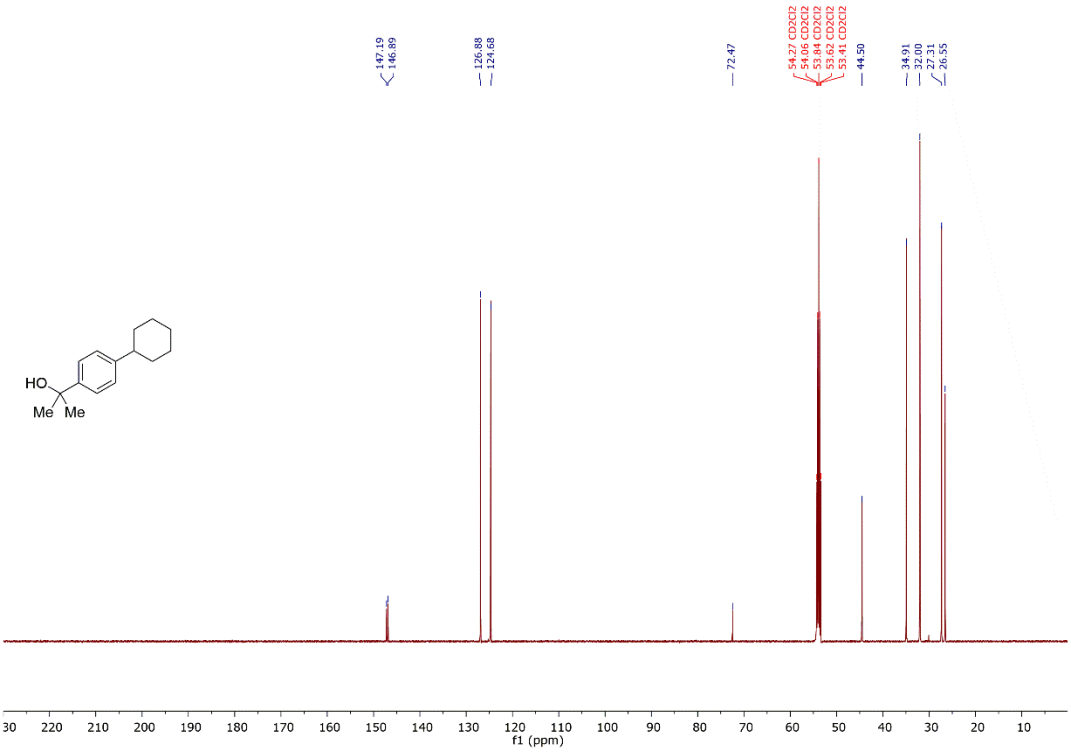
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-55)



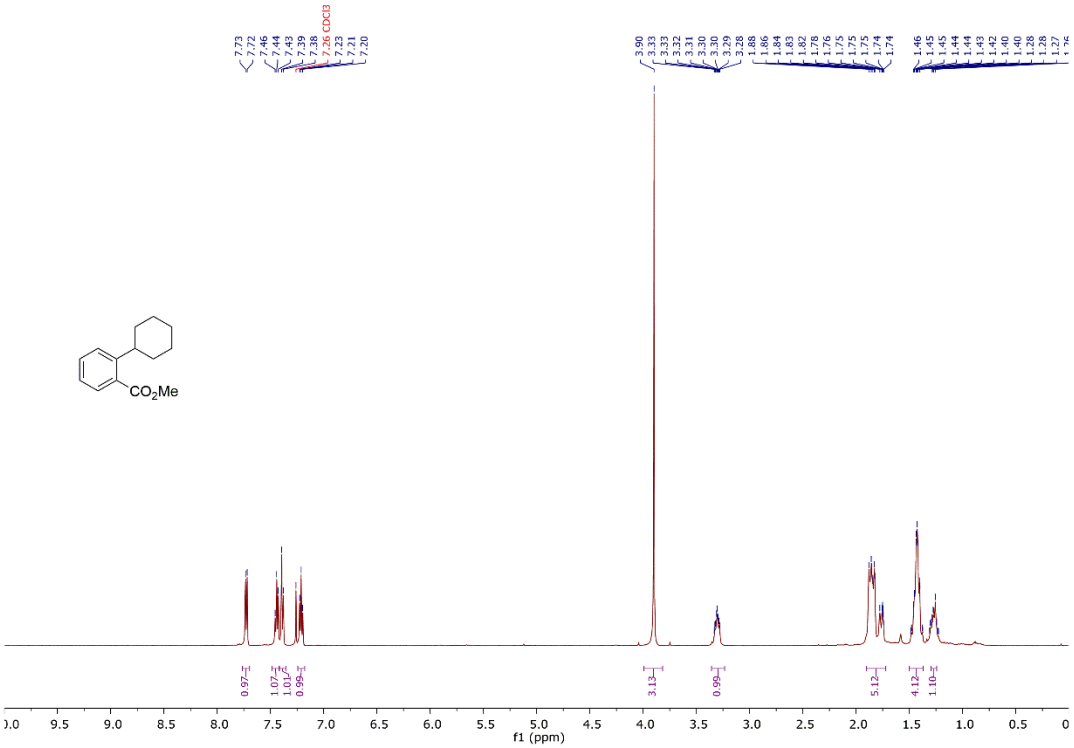
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-55)



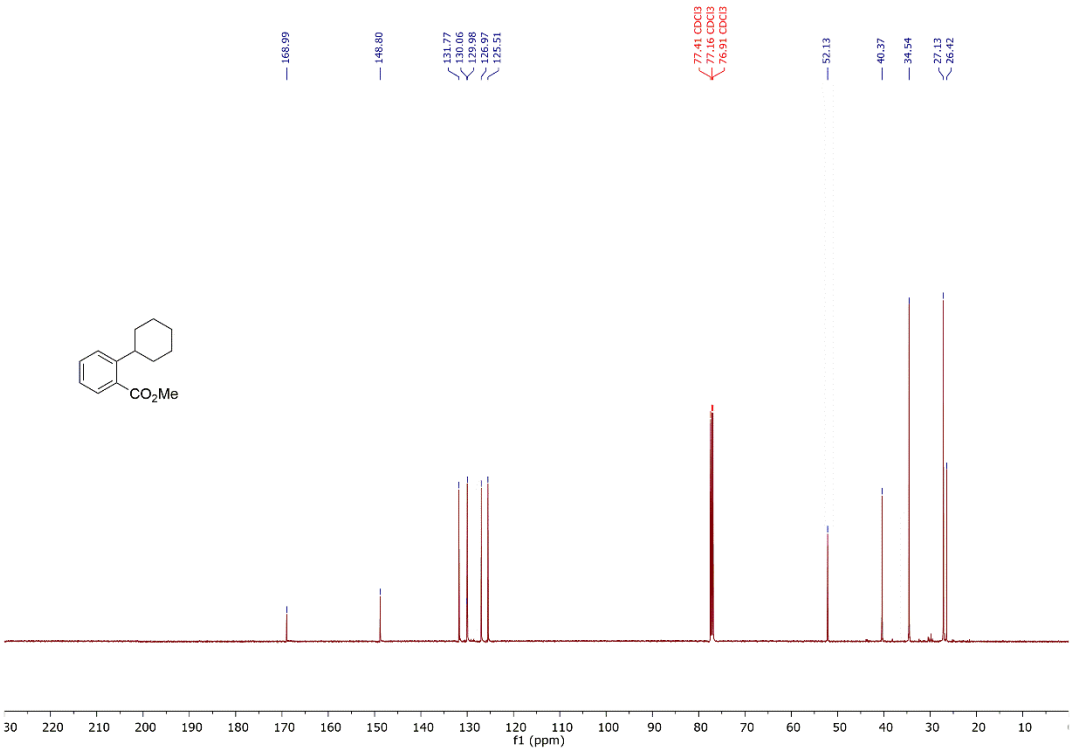
^{1}H NMR (500 MHz, CD_2Cl_2) - (SI-56)



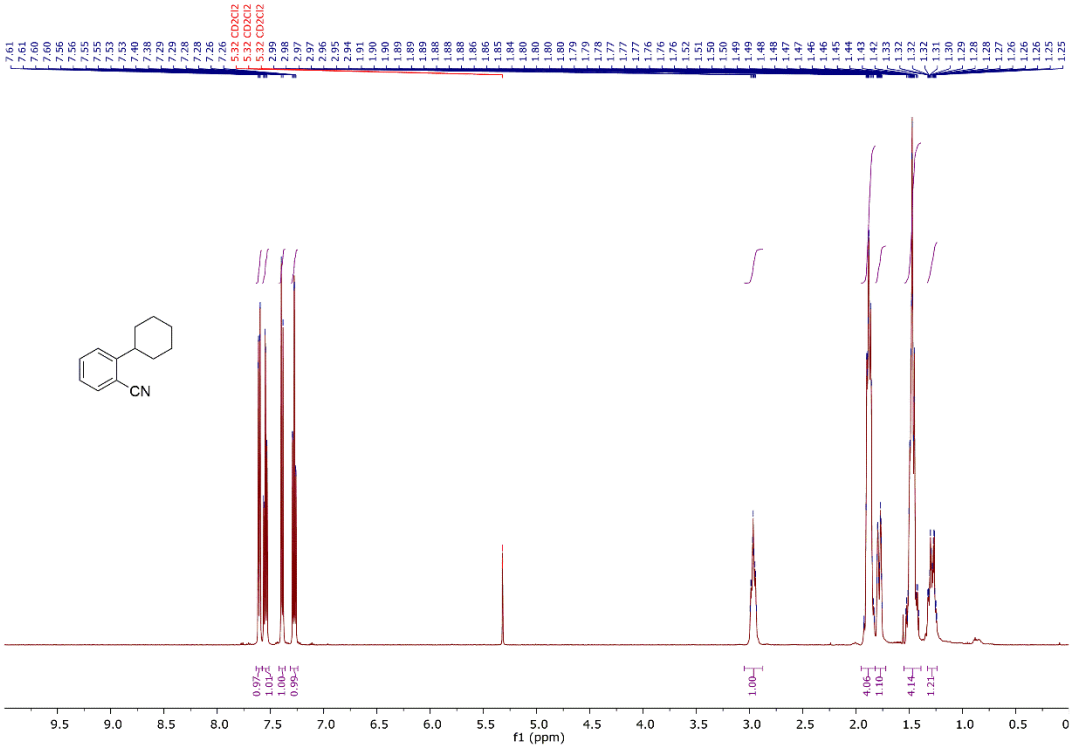
^{13}C NMR (126 MHz, CD_2Cl_2) - (SI-56)



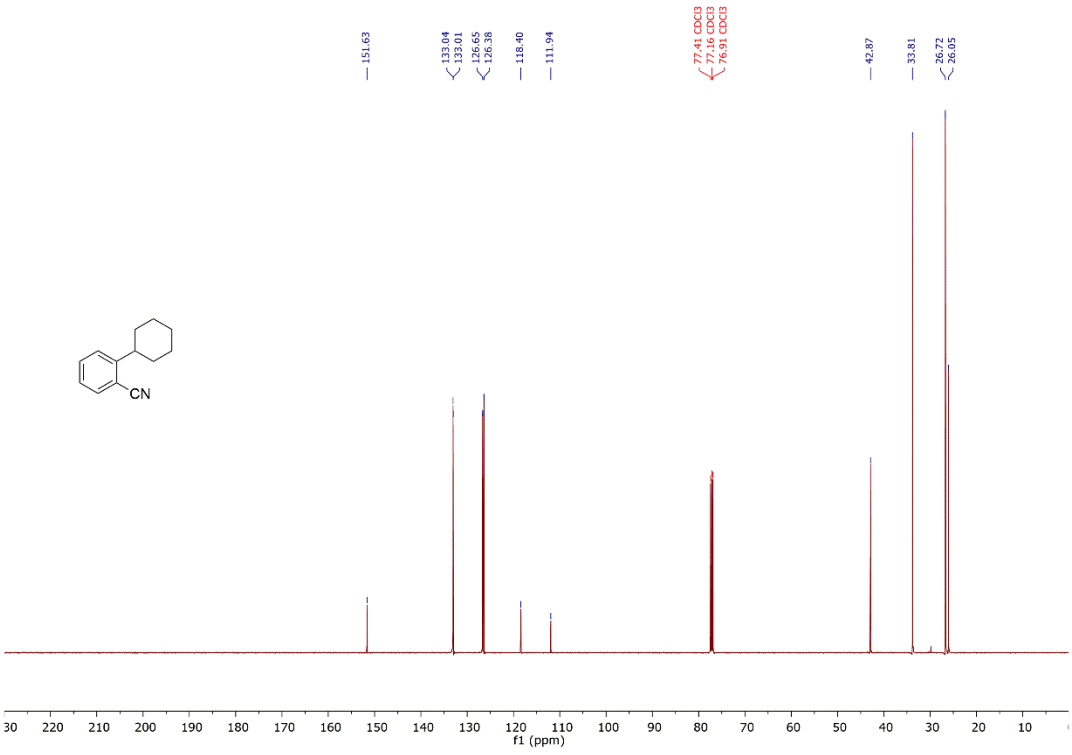
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-57)



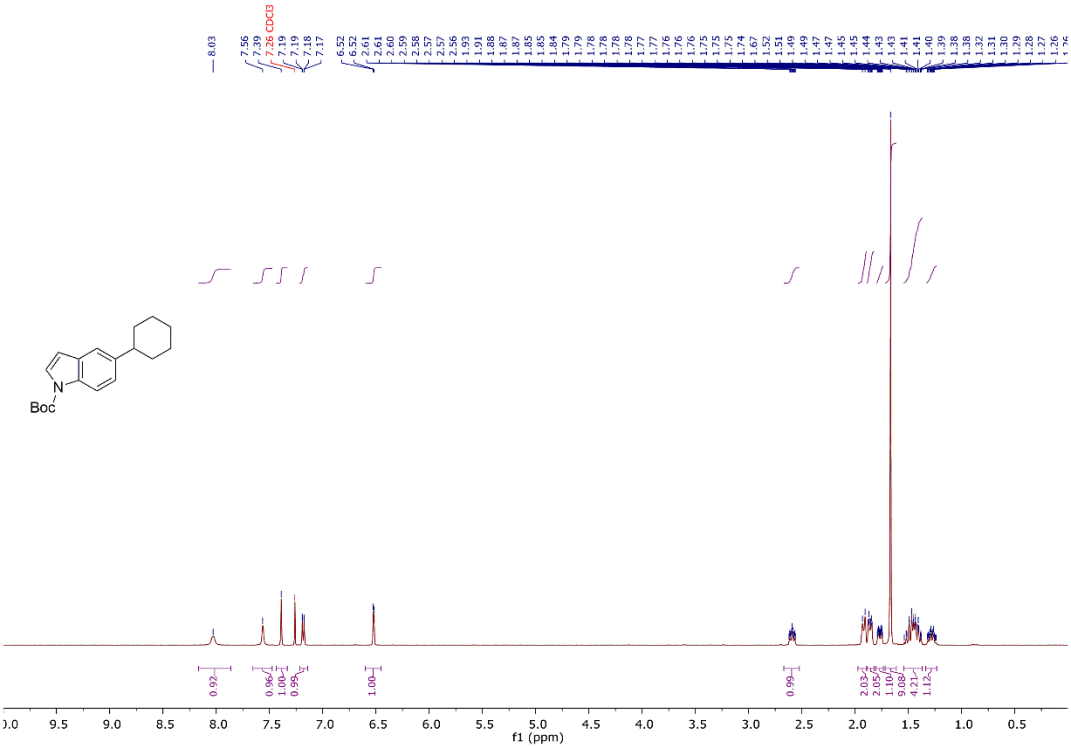
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-57)



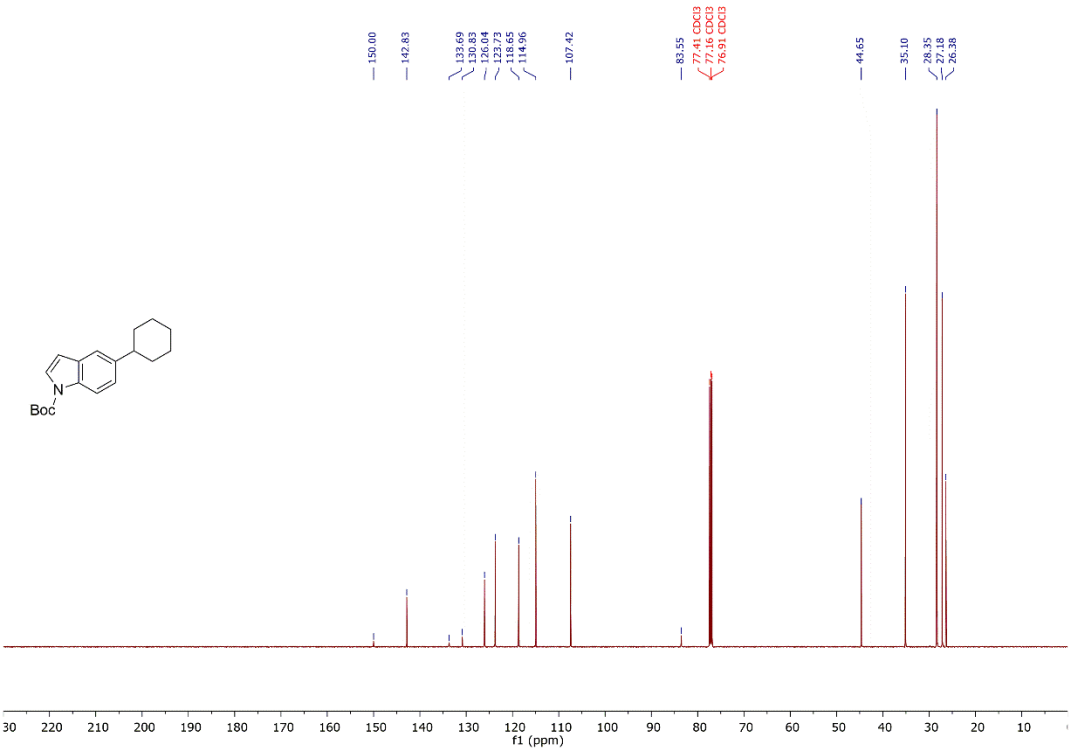
^{1}H NMR (500 MHz, CD_2Cl_2) - (SI-58)



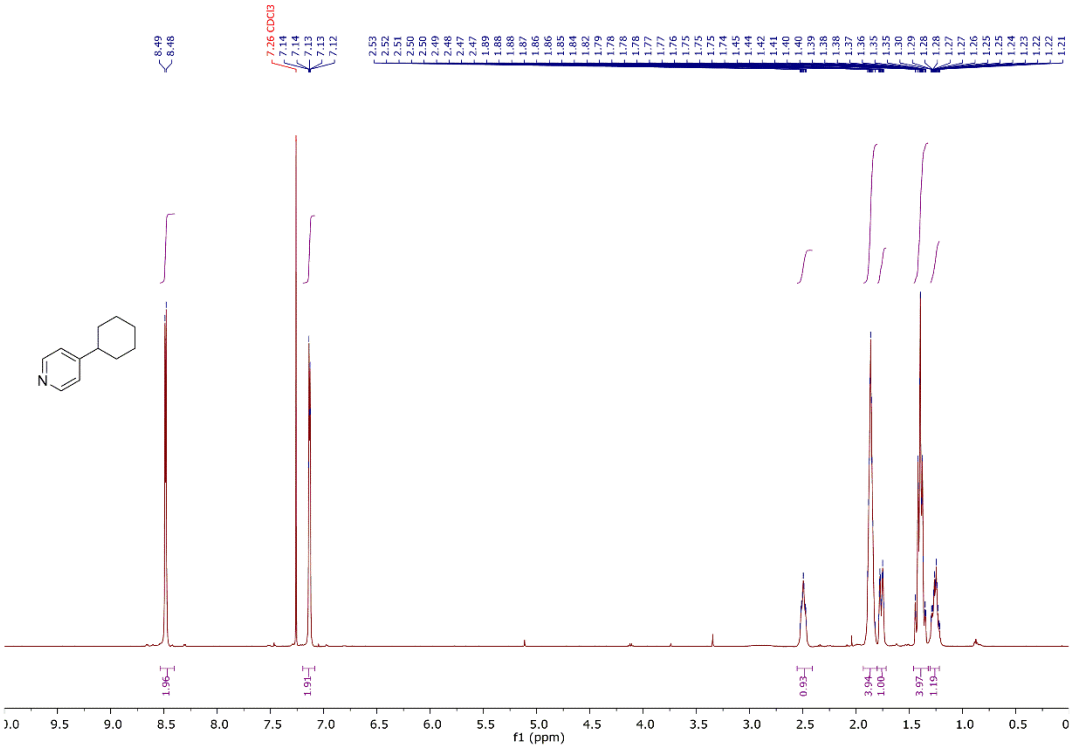
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-58)



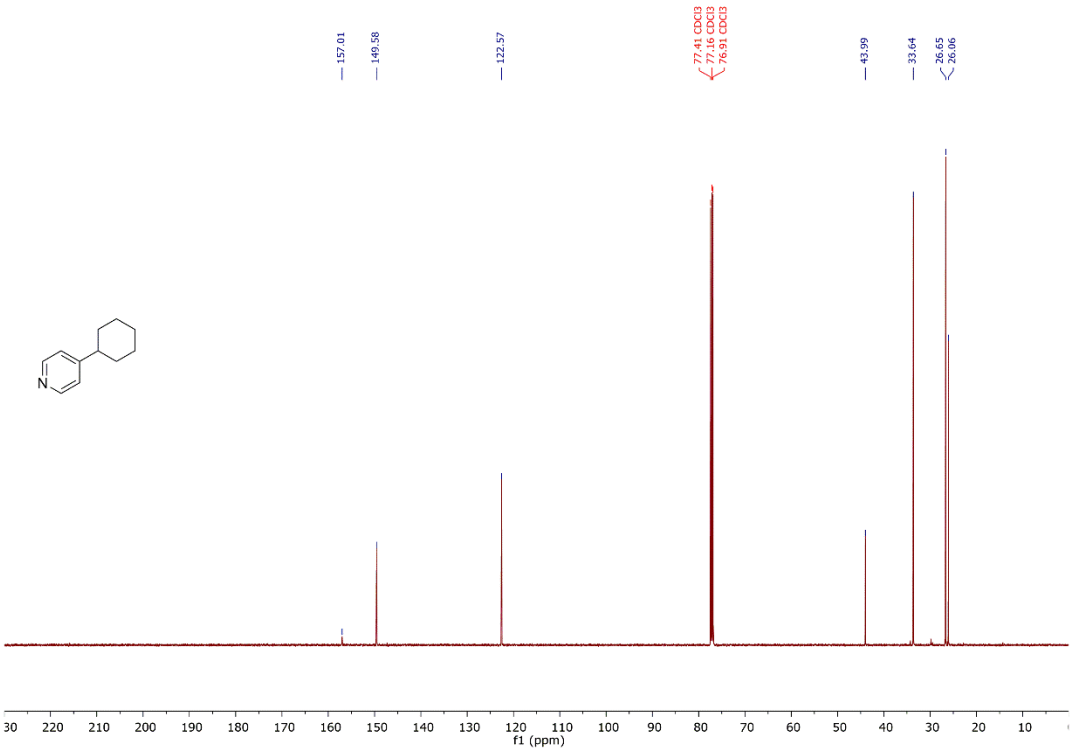
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-59)



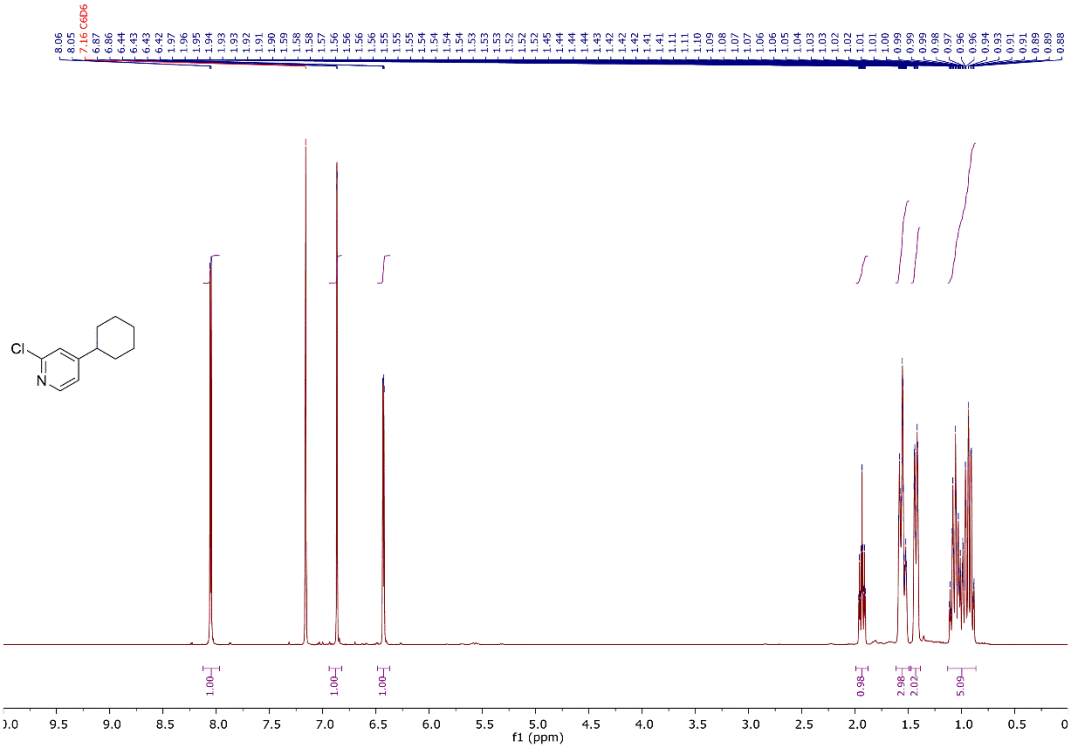
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-59)



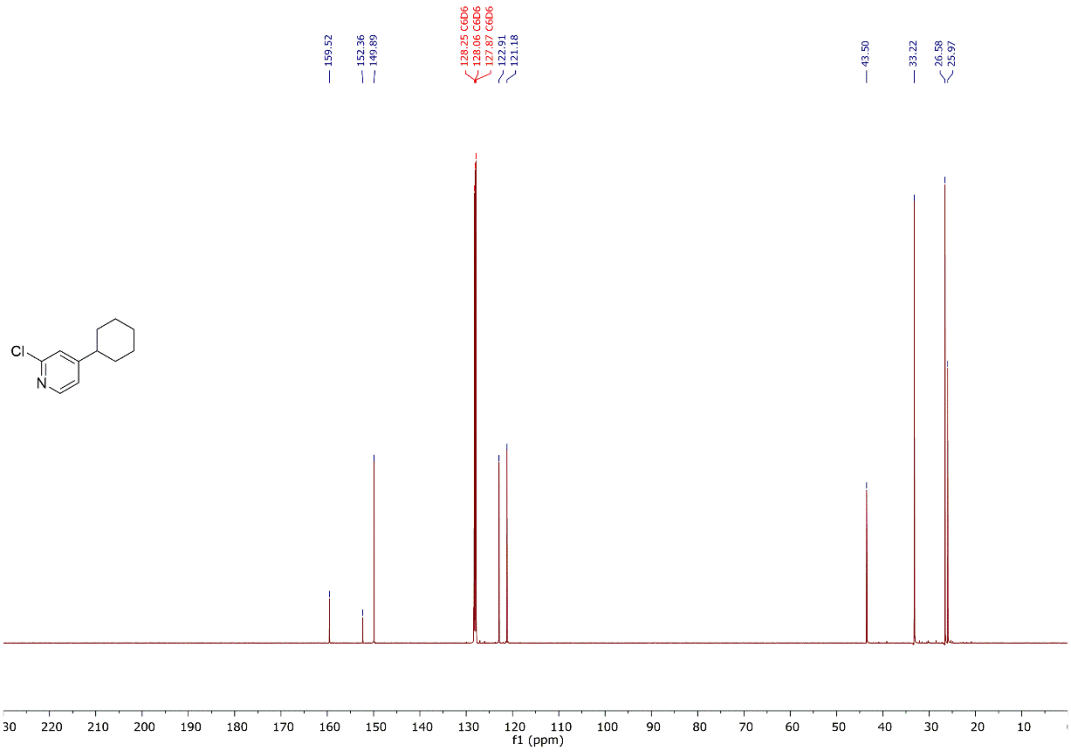
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-60)



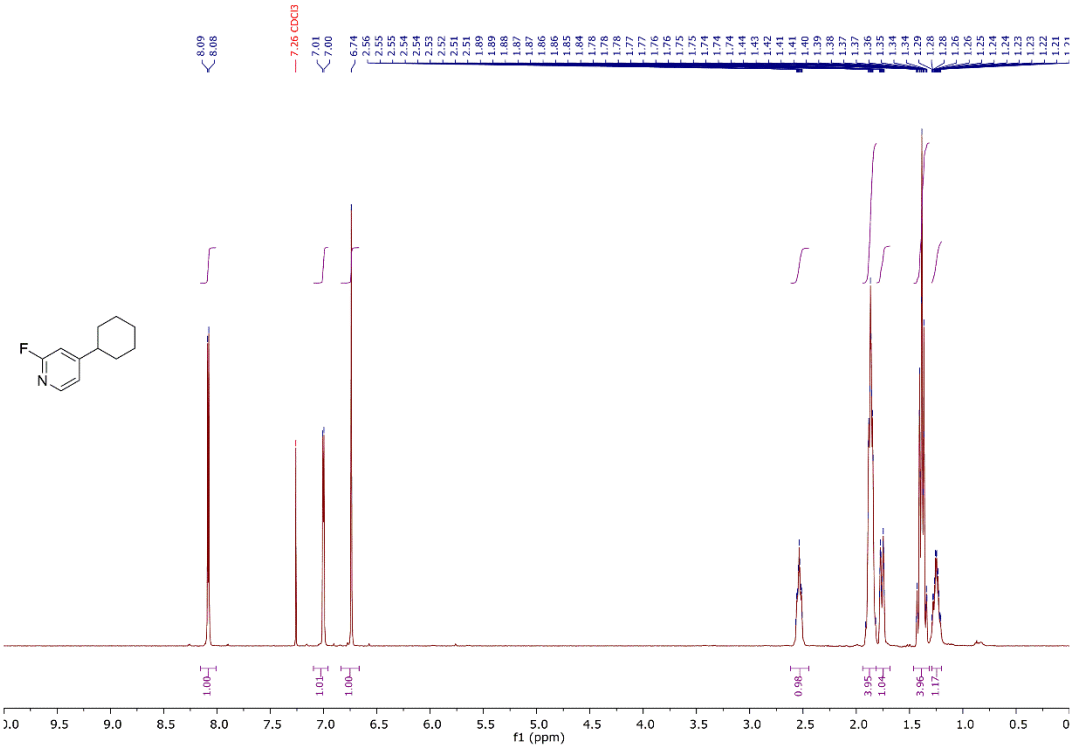
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-60)



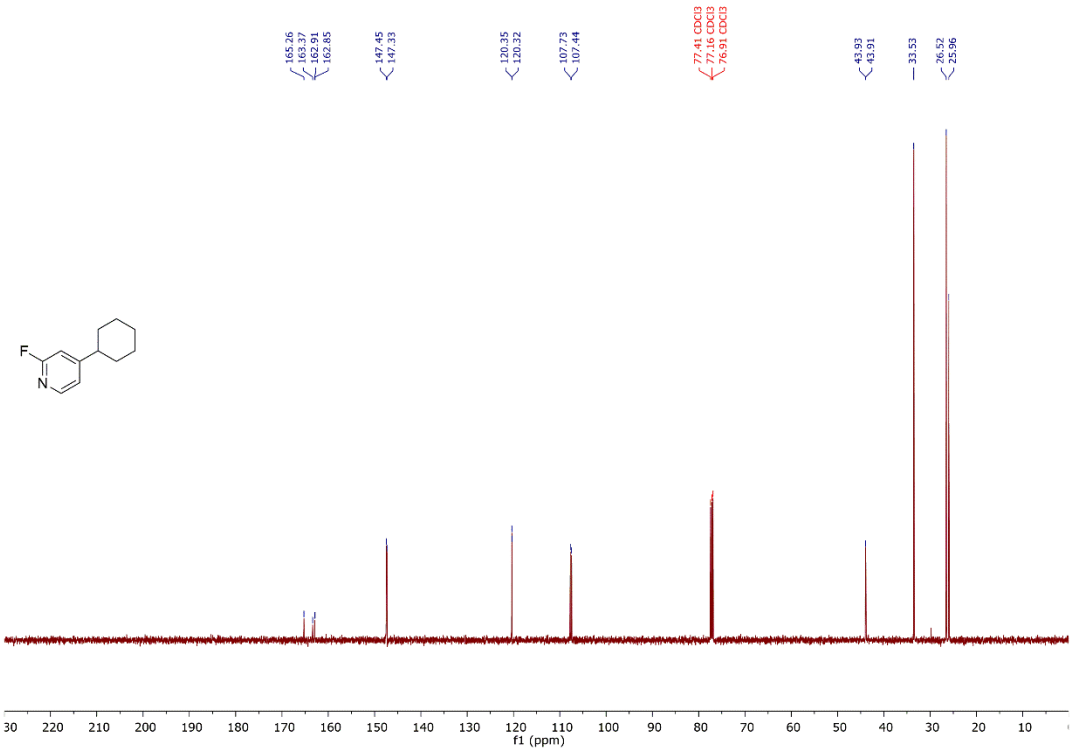
^{1}H NMR (500 MHz, C_6D_6) - (SI-61)



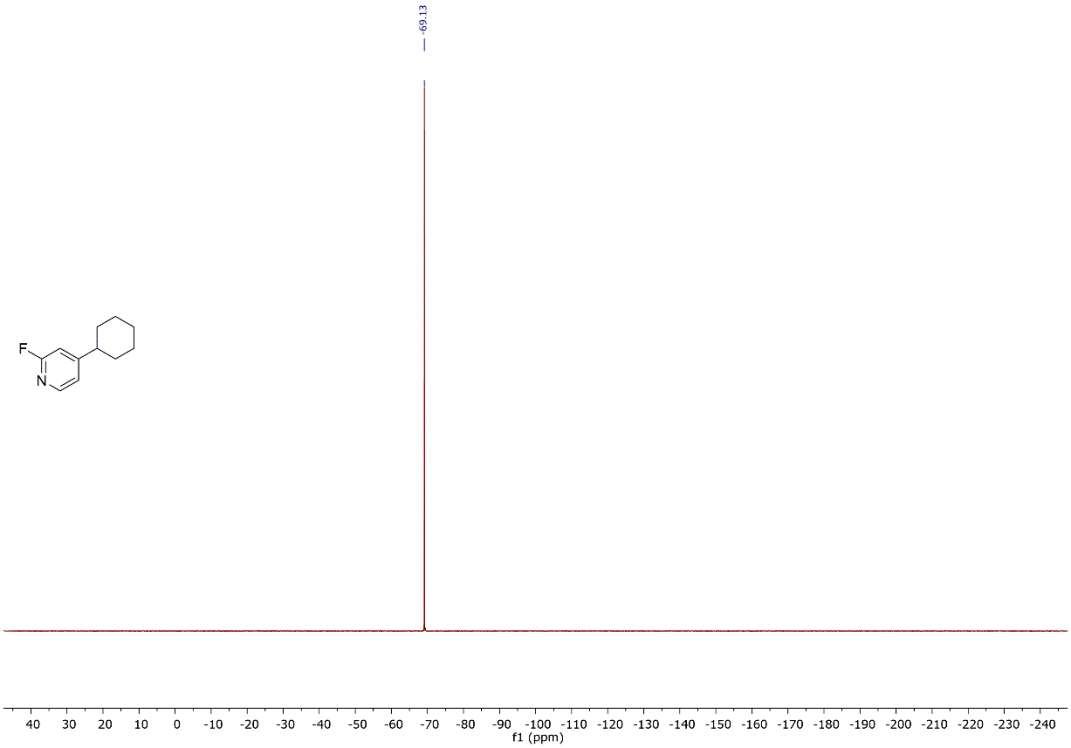
^{13}C NMR (126 MHz, C_6D_6) - (SI-61)



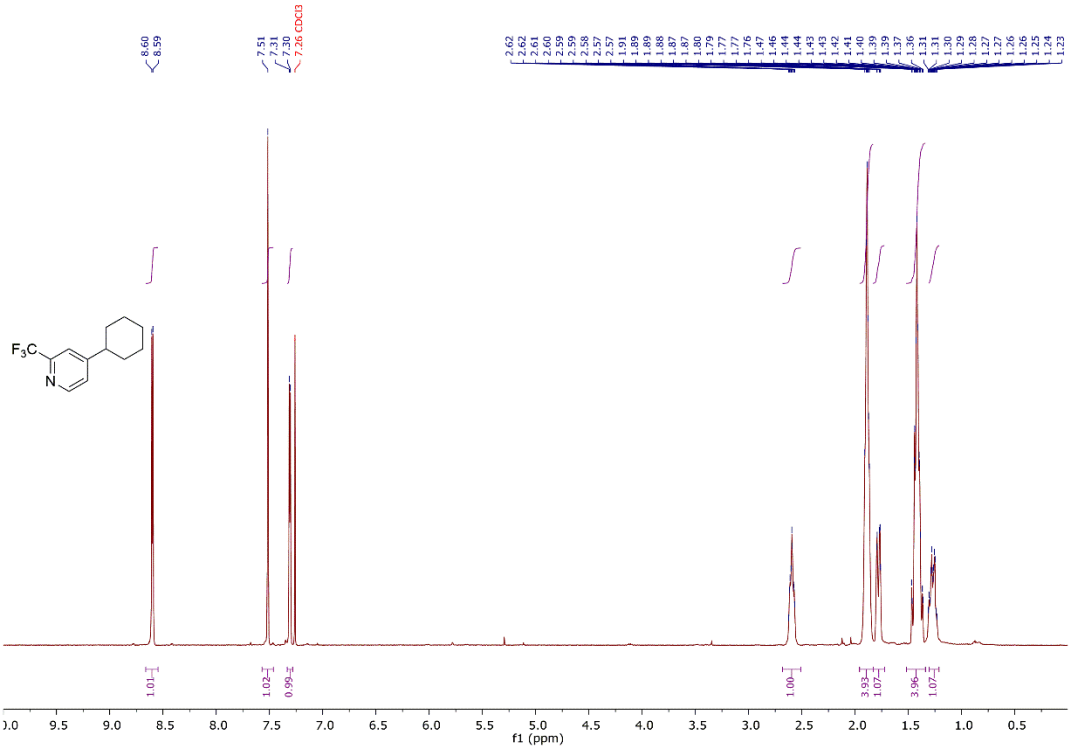
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-62)



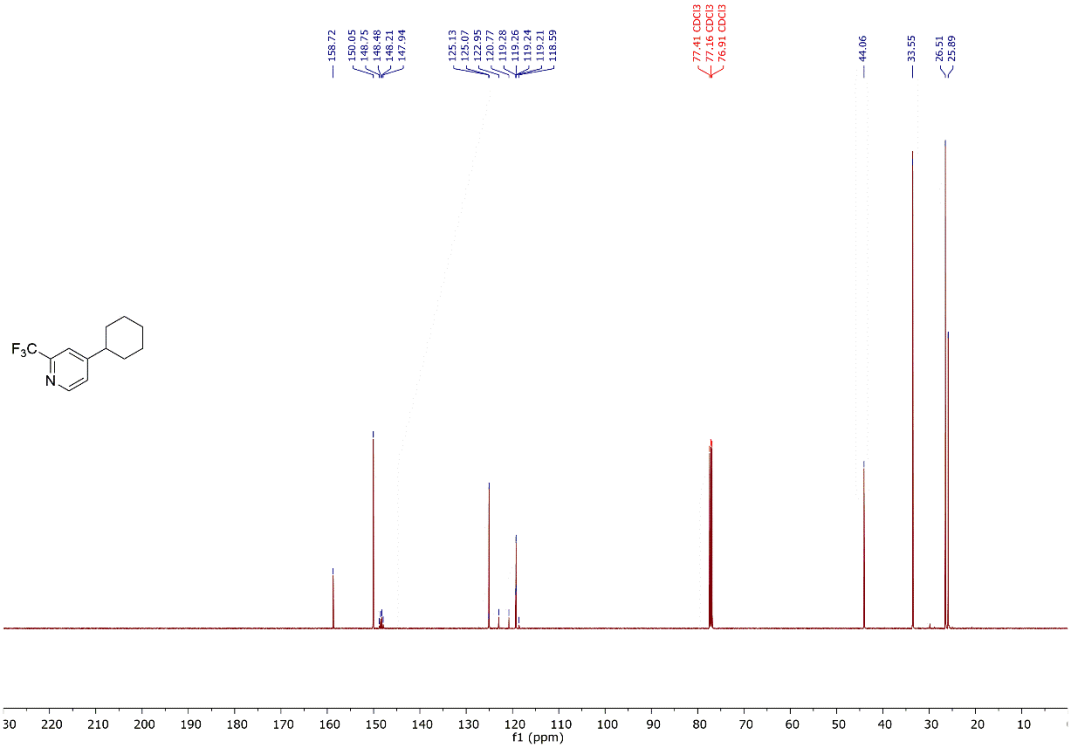
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-62)



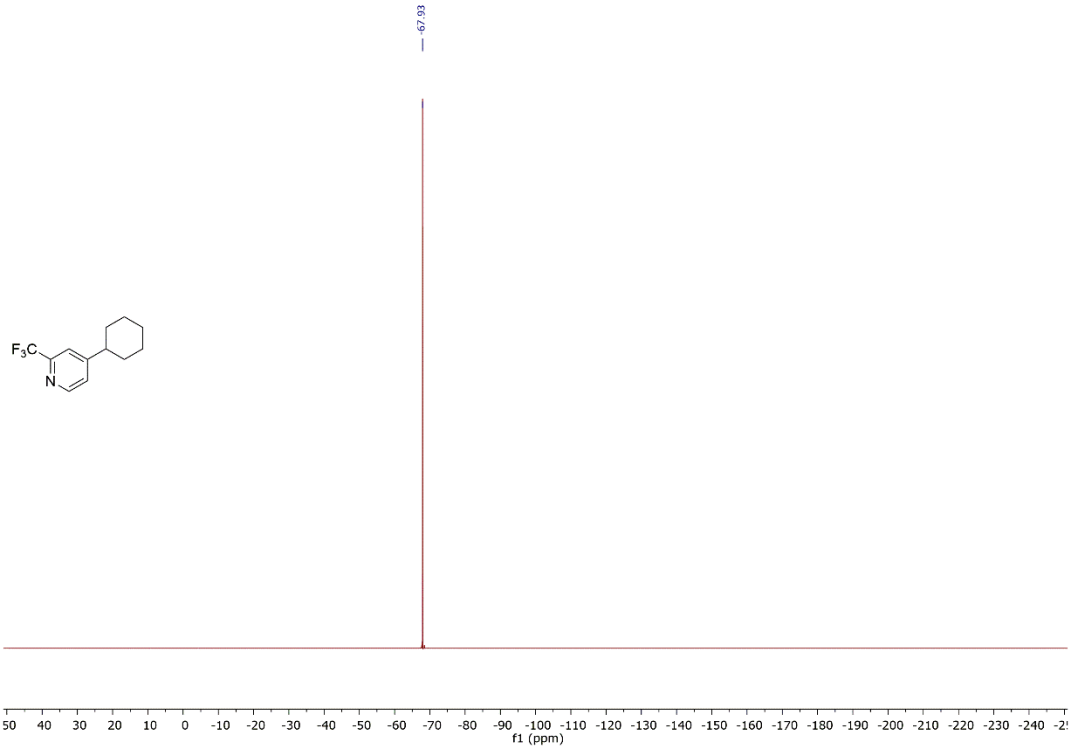
^{19}F NMR (470 MHz, $CDCl_3$) - (SI-62)



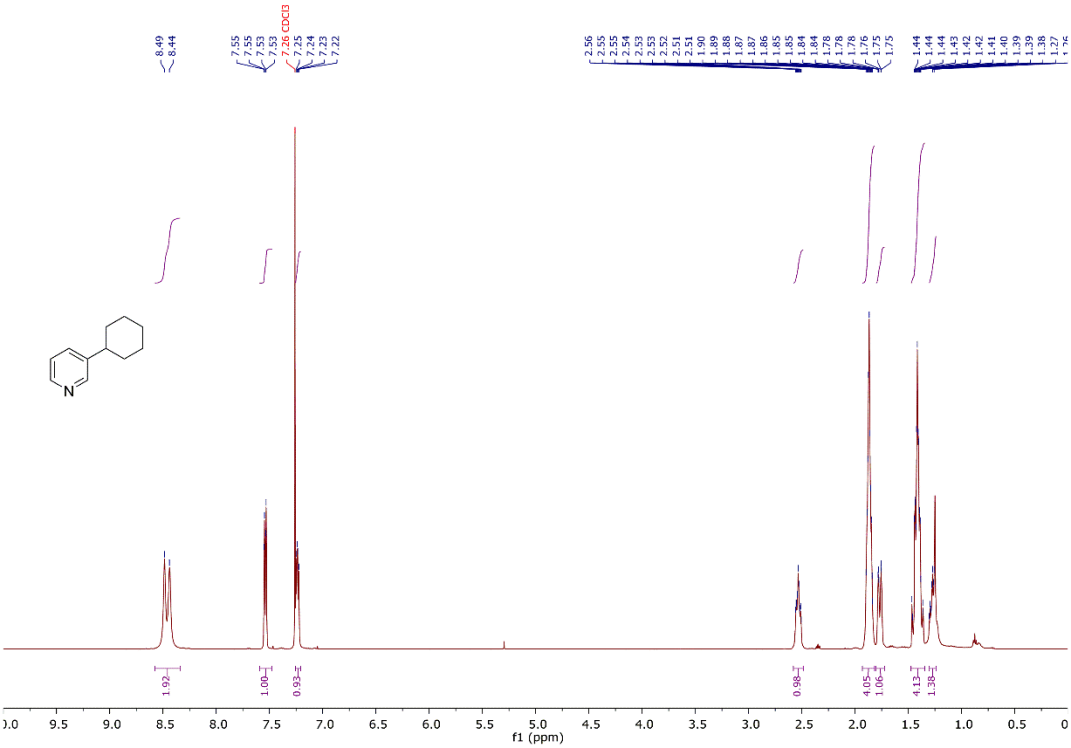
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-63)



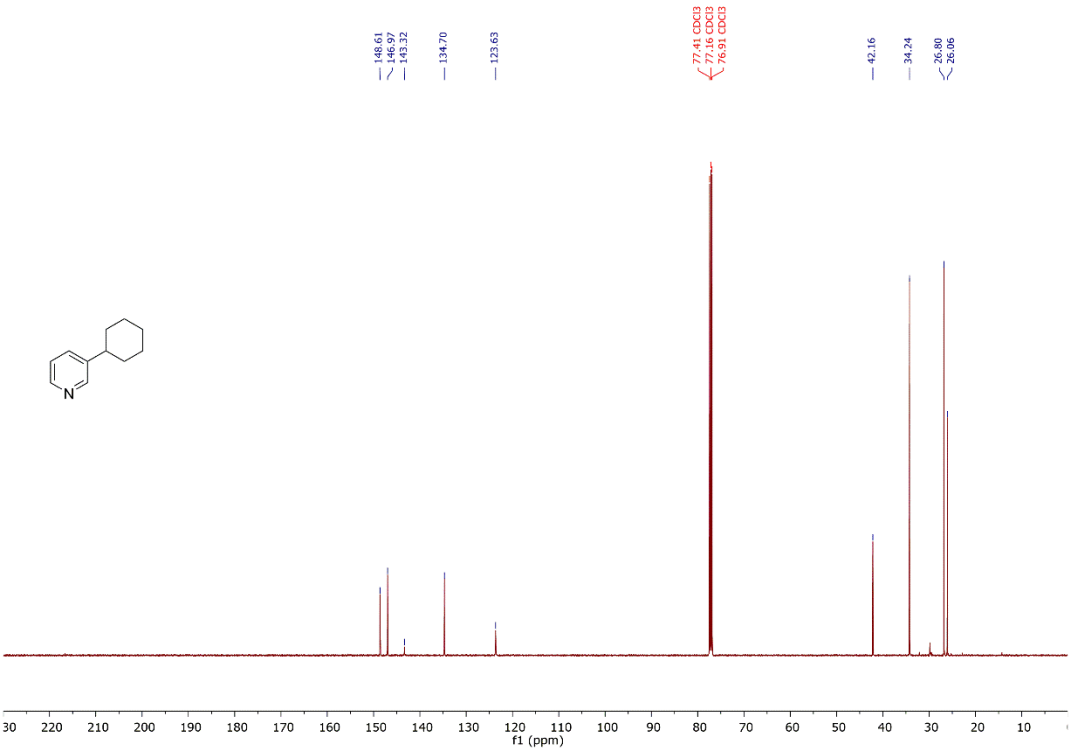
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-63)



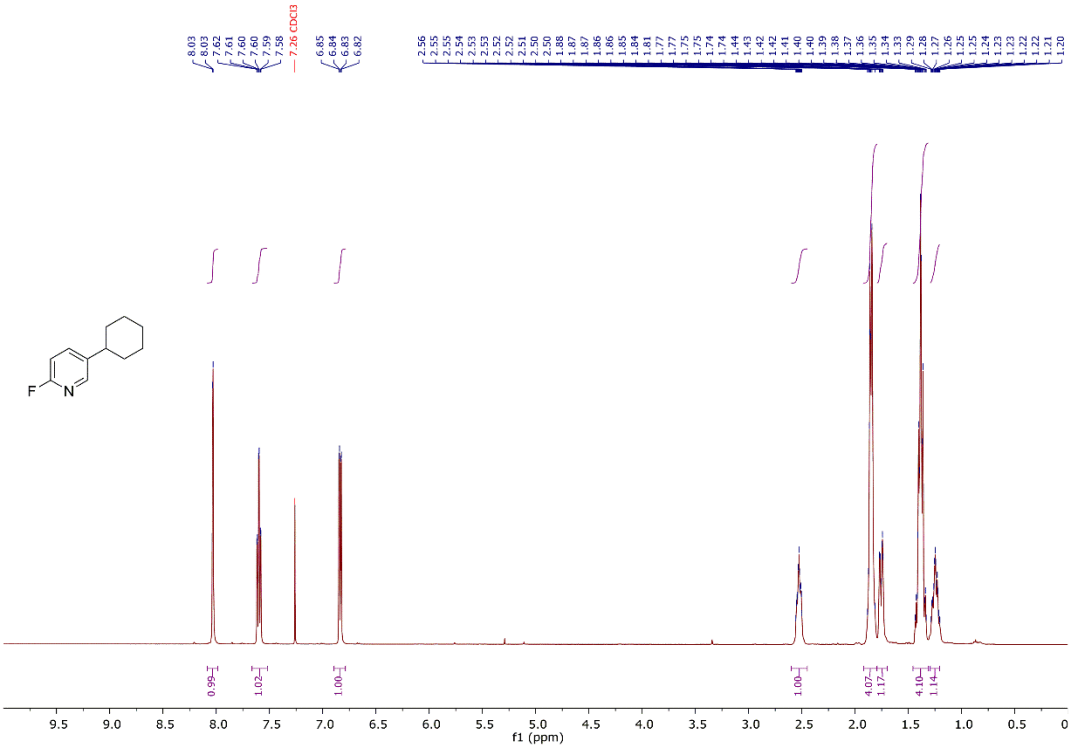
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-63)



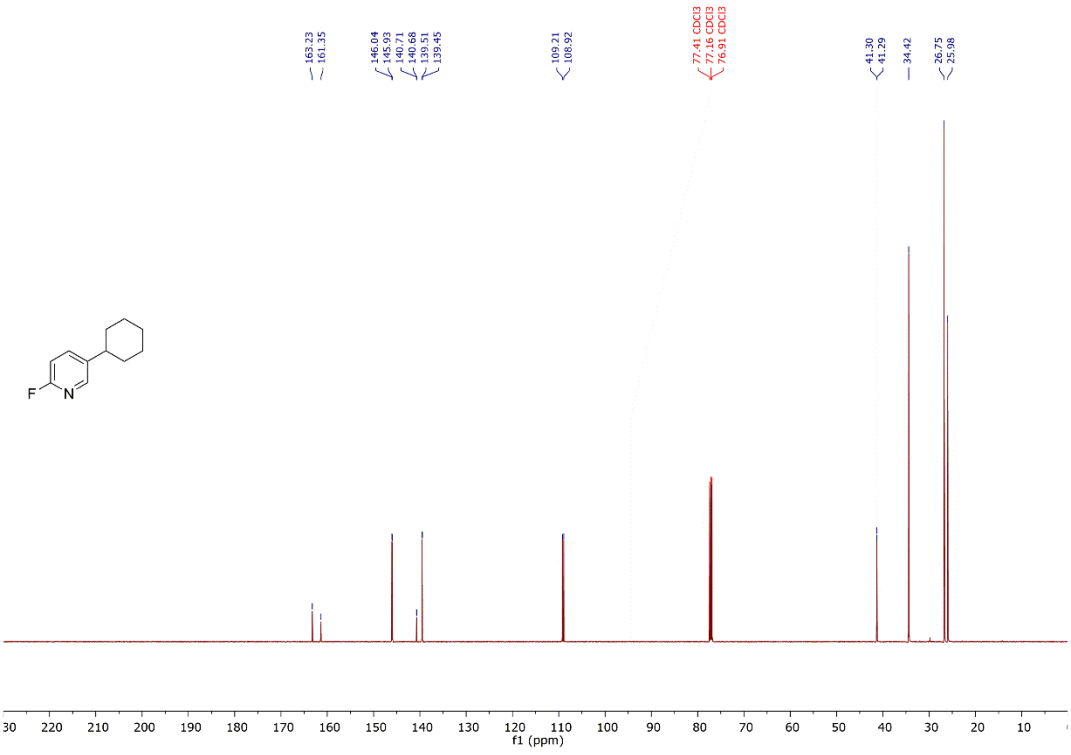
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-64)



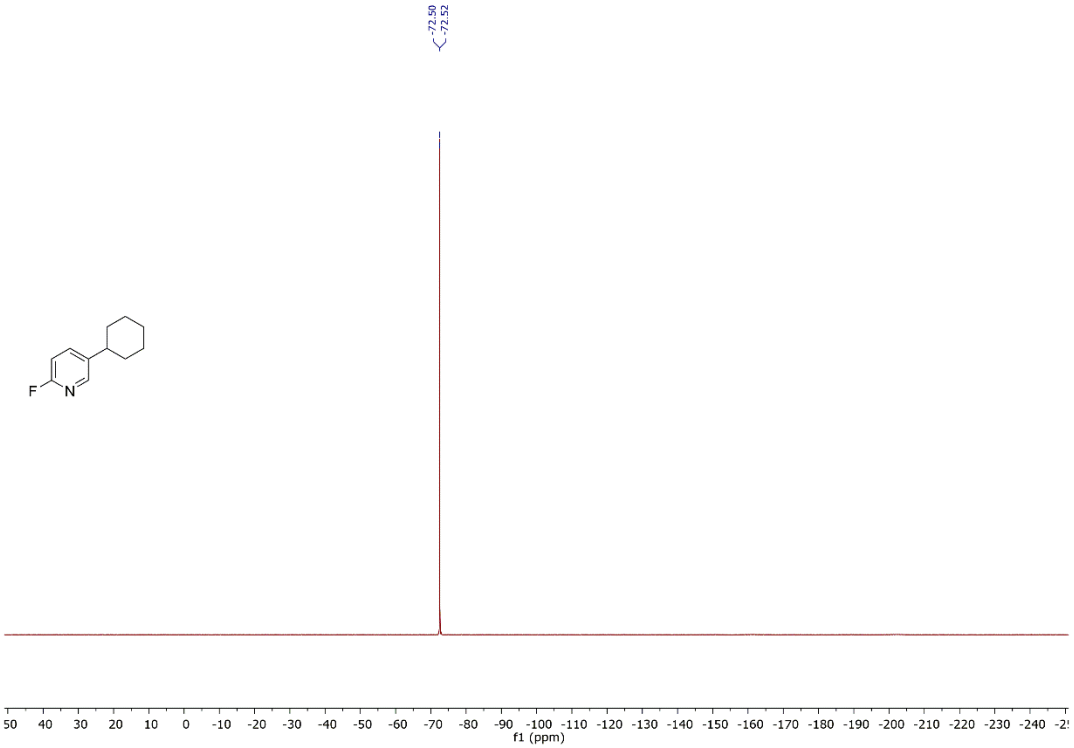
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-64)



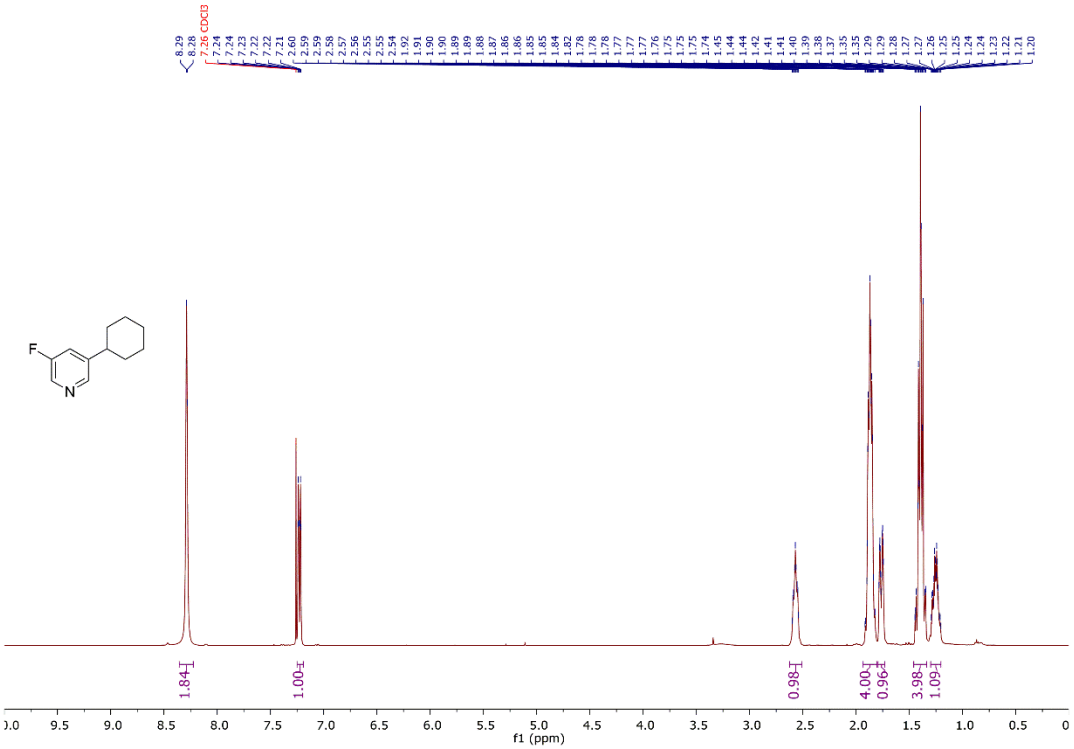
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-65)



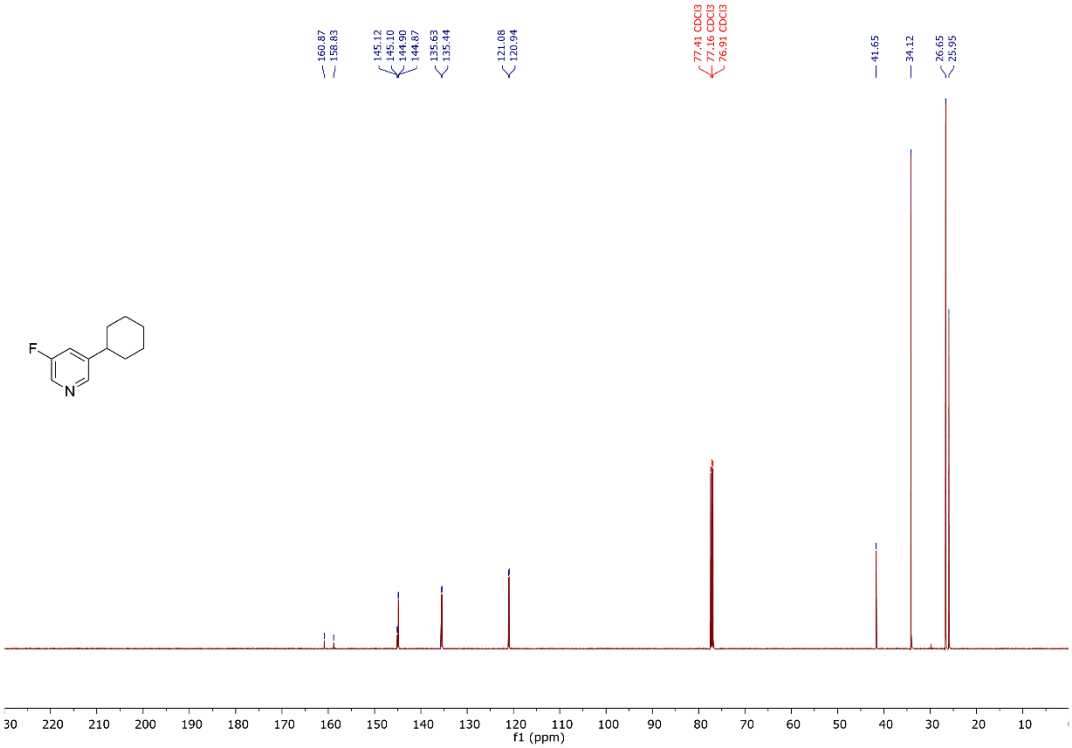
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-65)



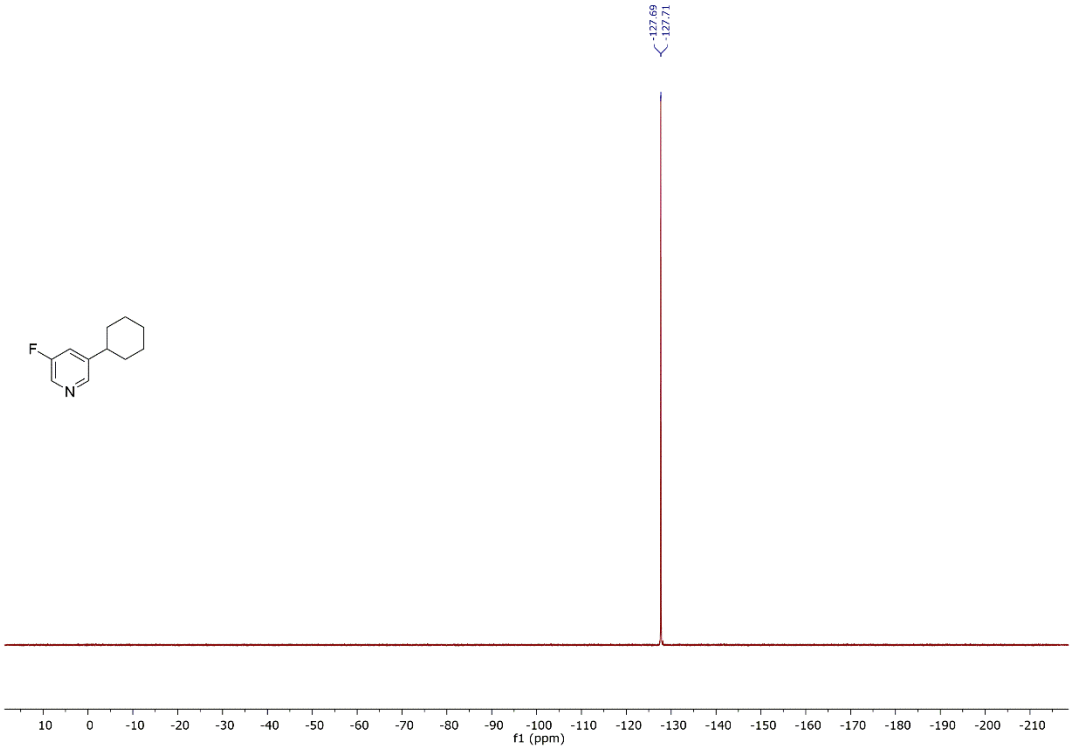
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-65)



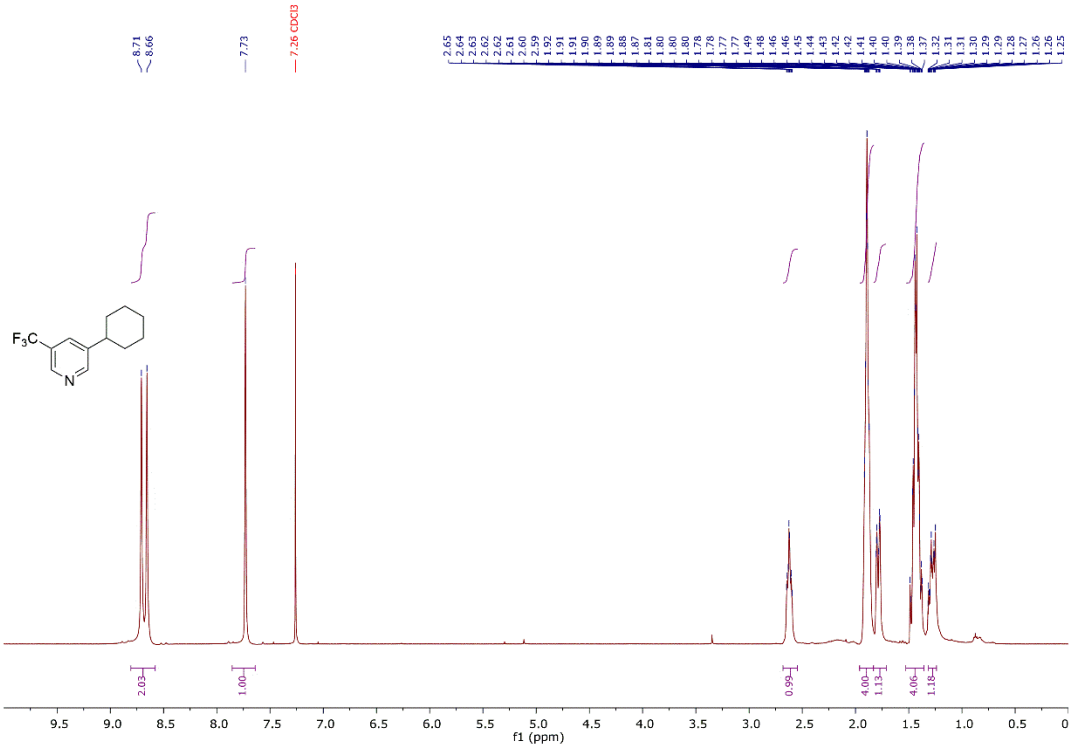
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-66)



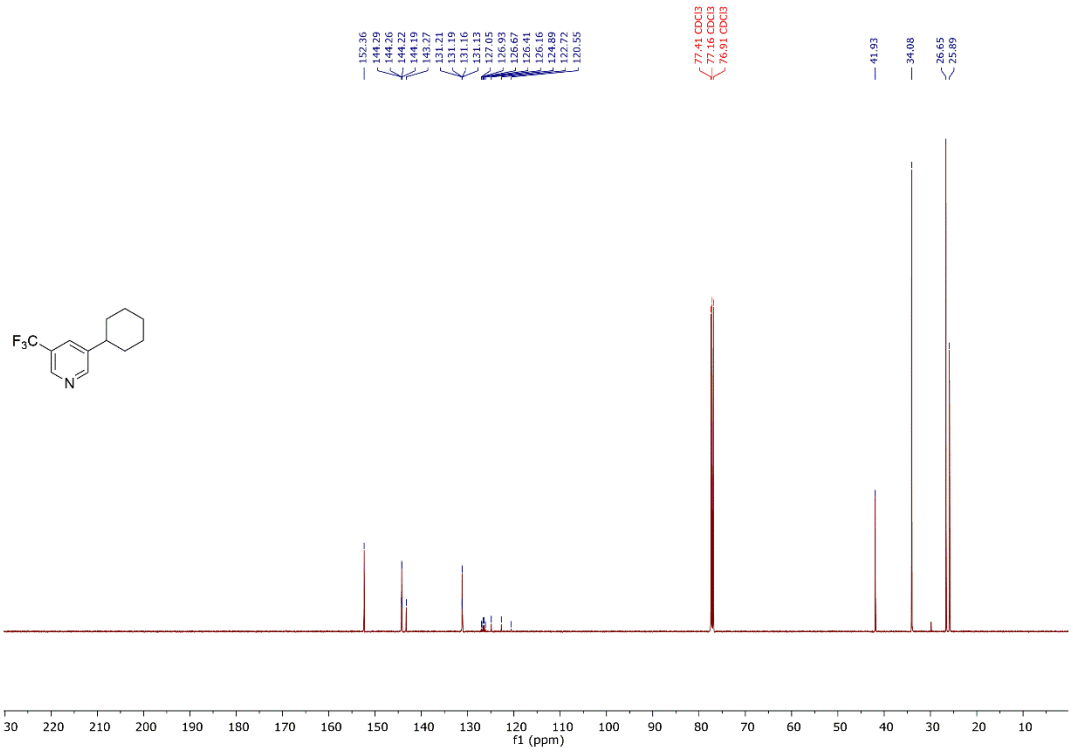
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-66)



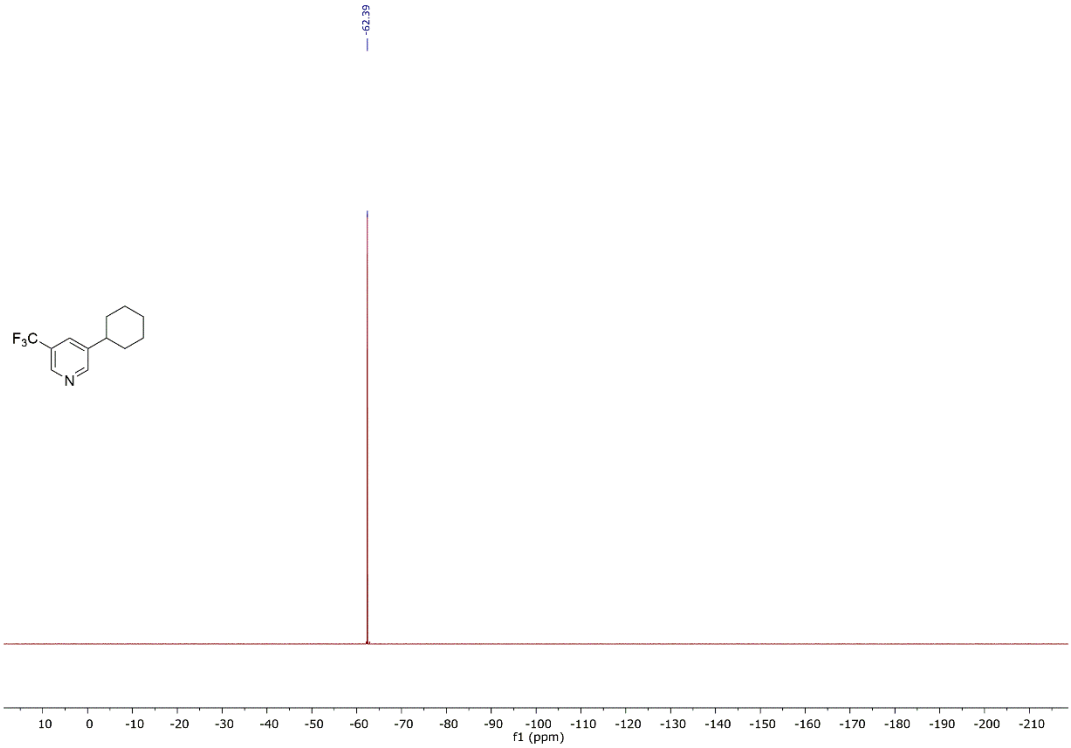
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-66)



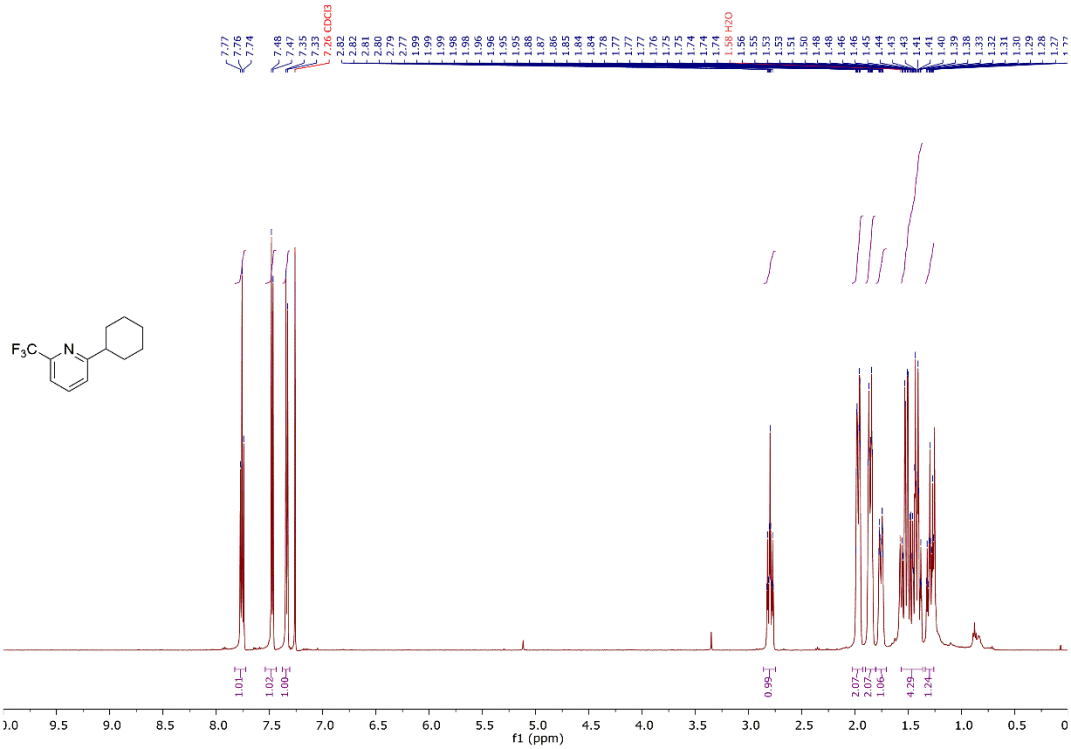
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-67)



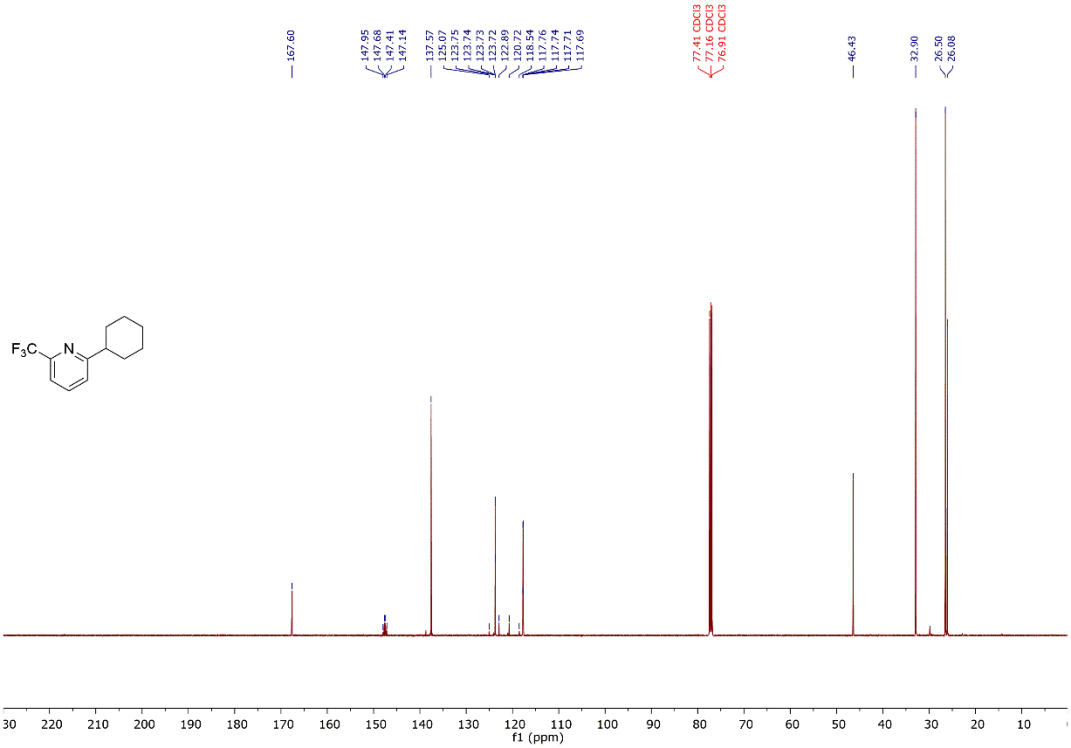
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-67)



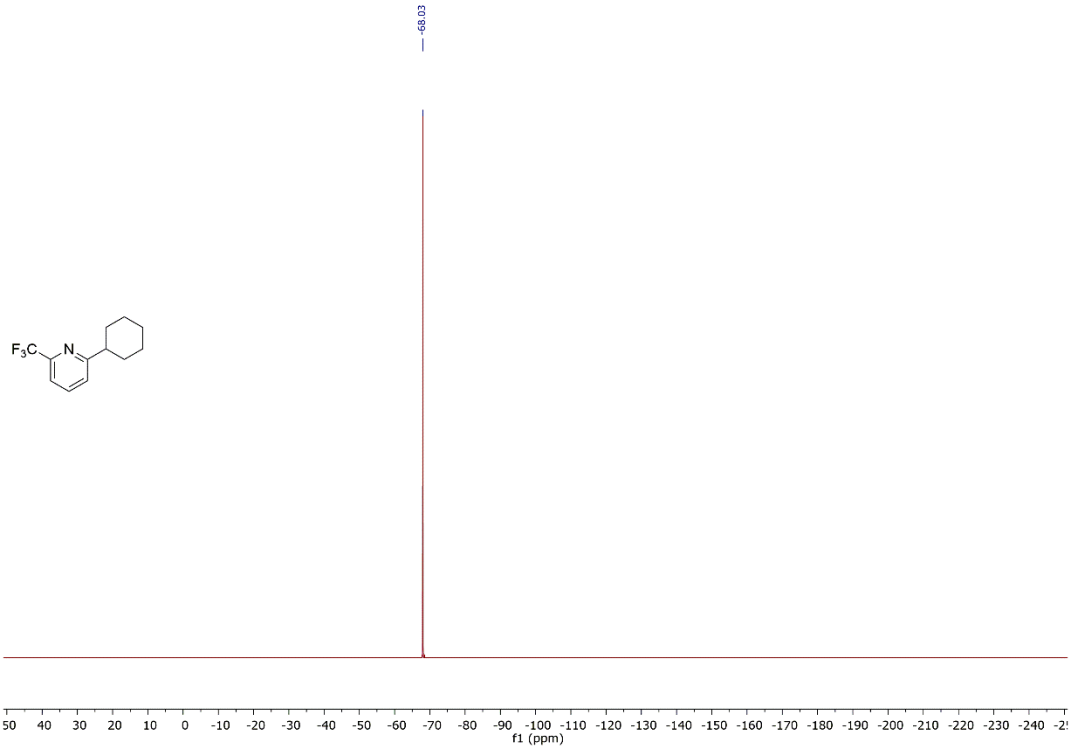
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-67)



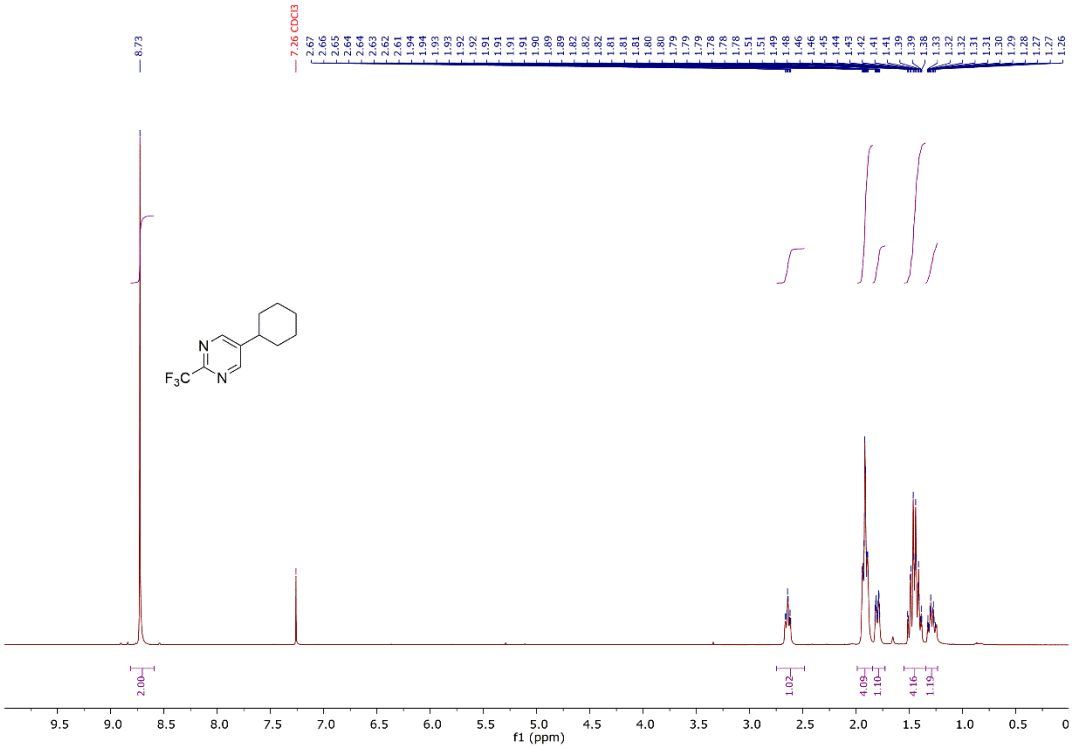
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-69)



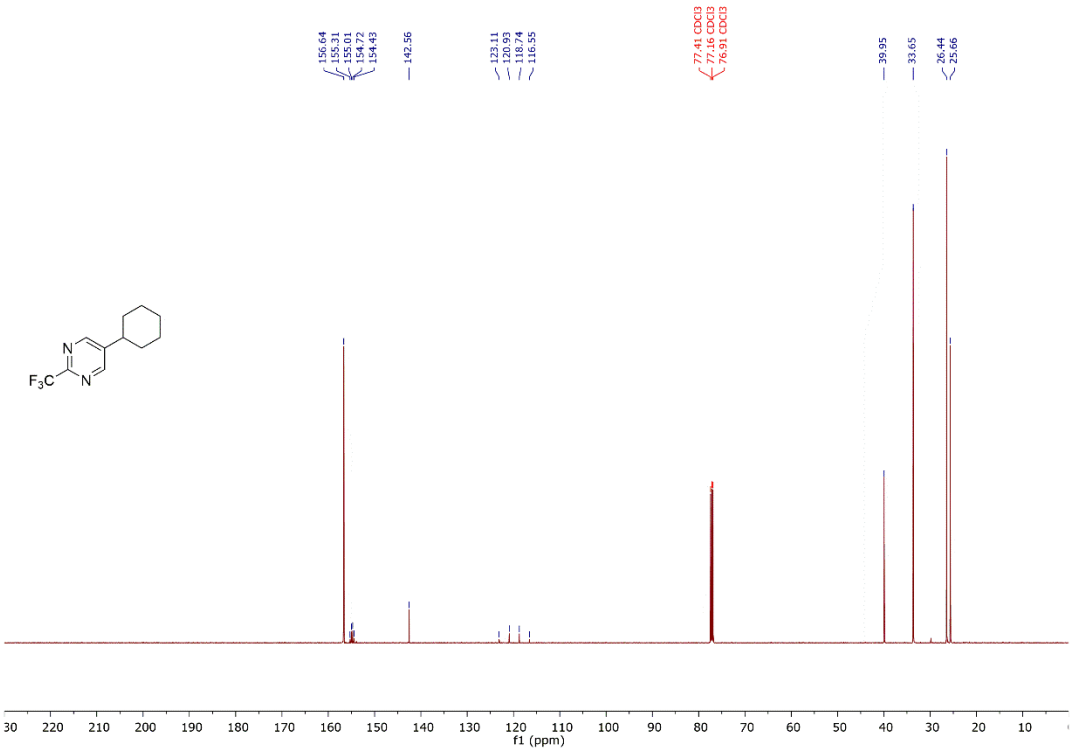
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-69)



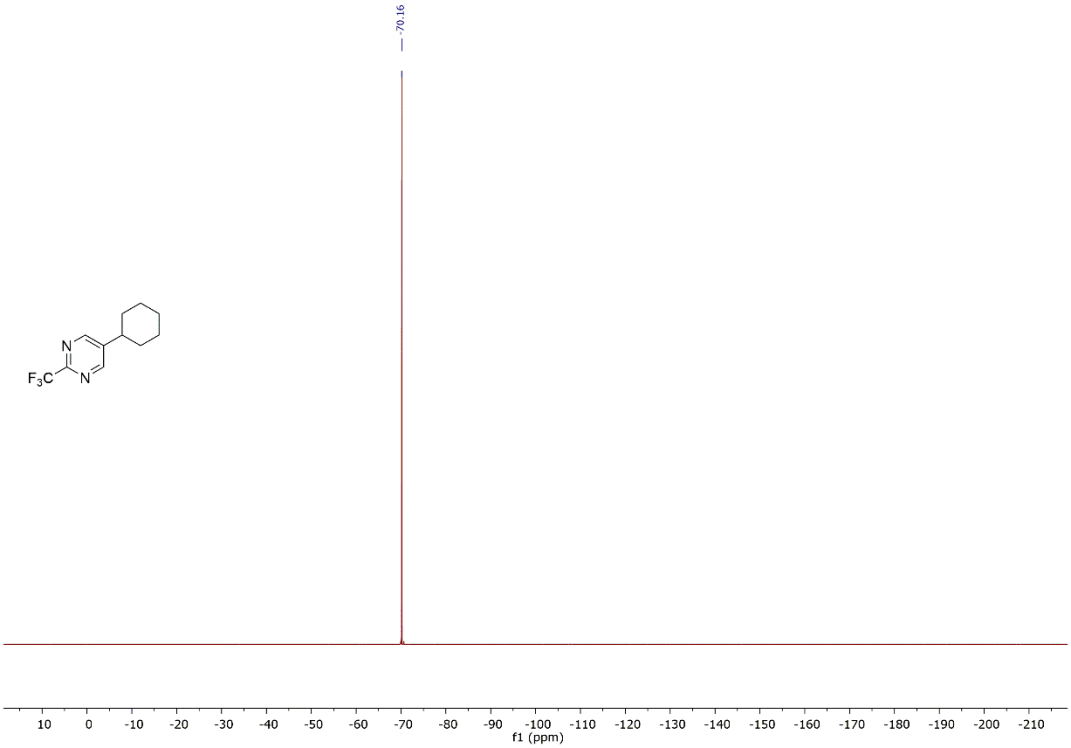
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-69)



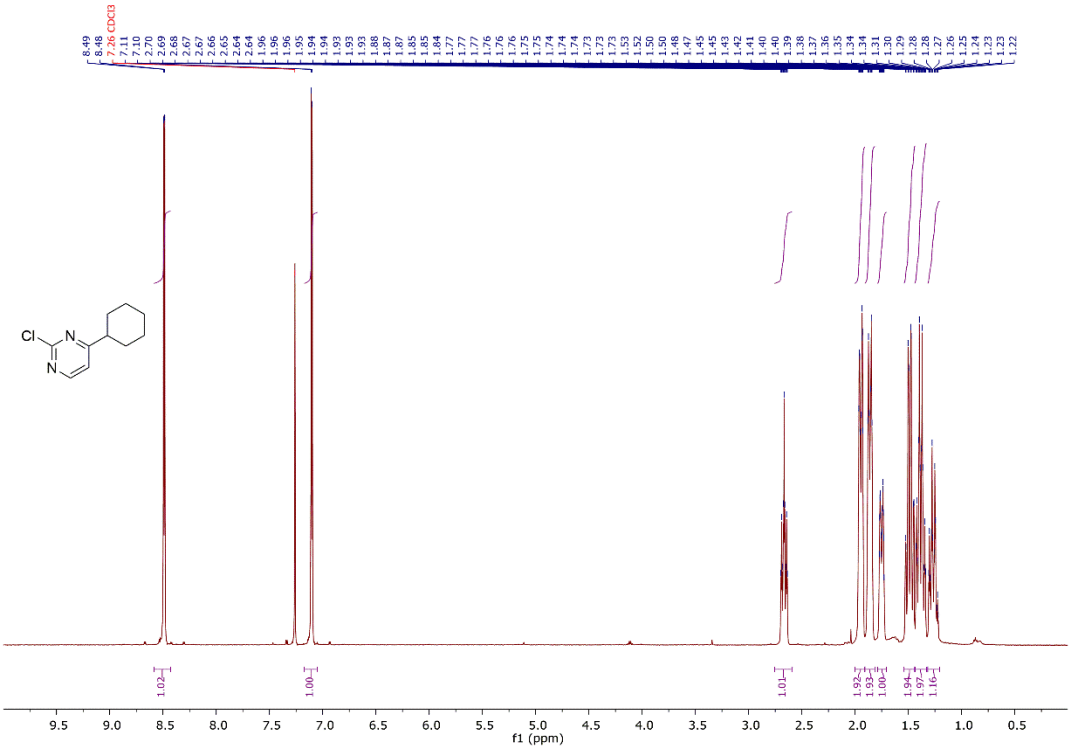
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-70)



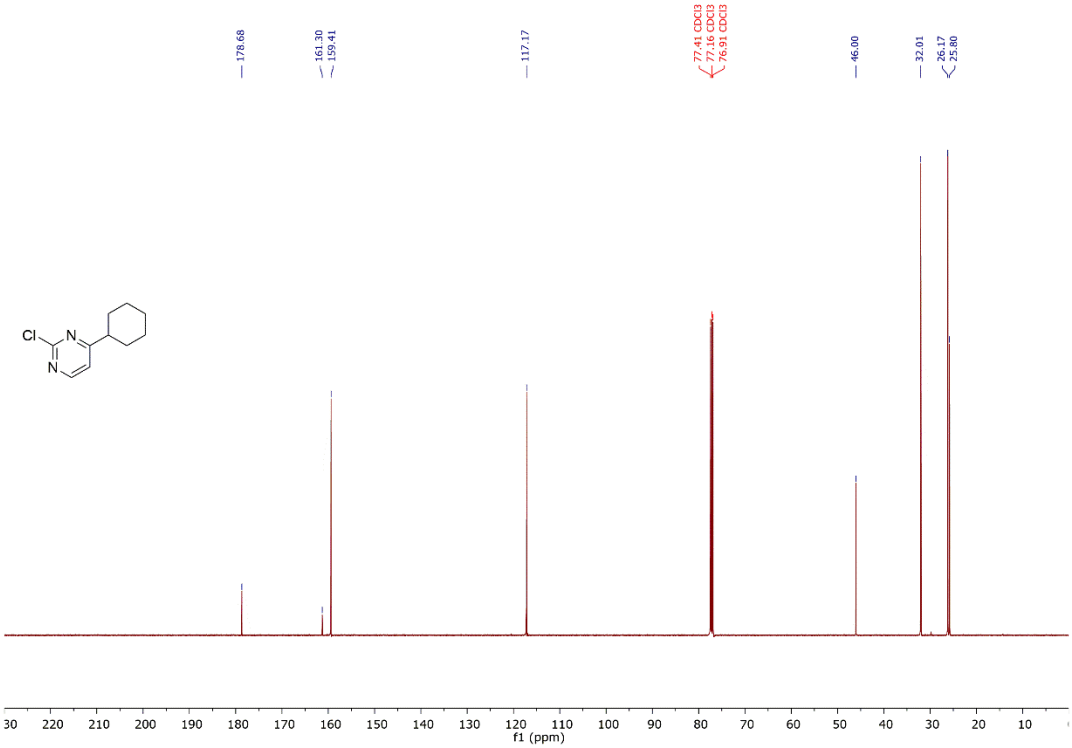
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-70)



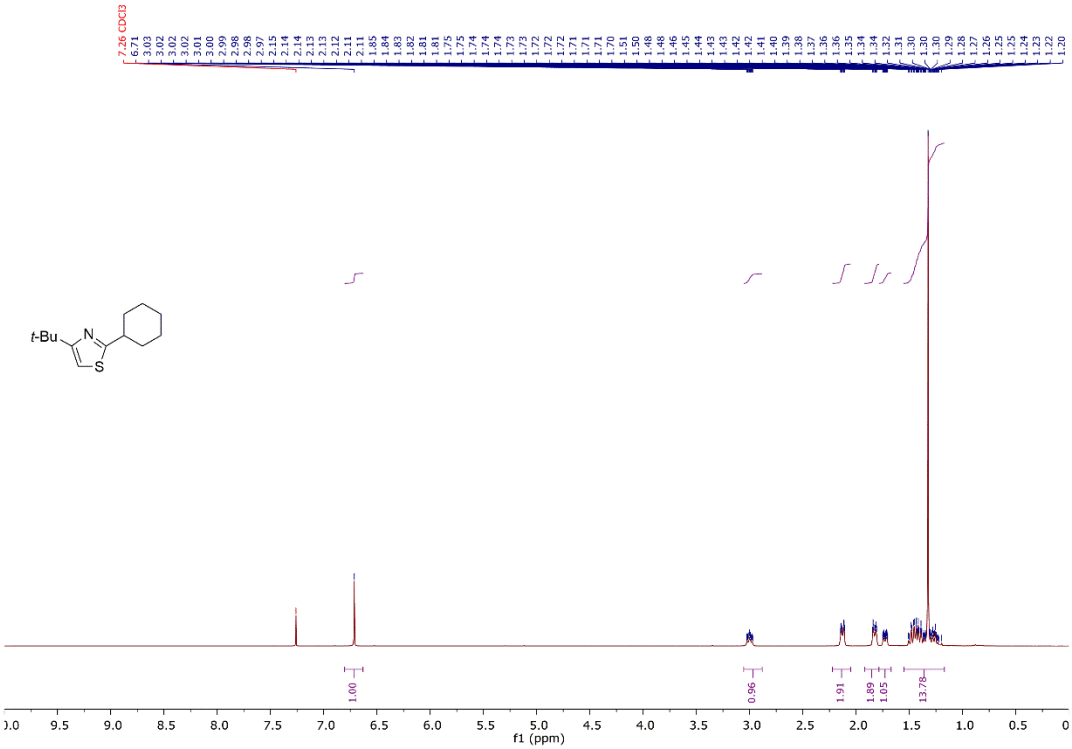
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-70)



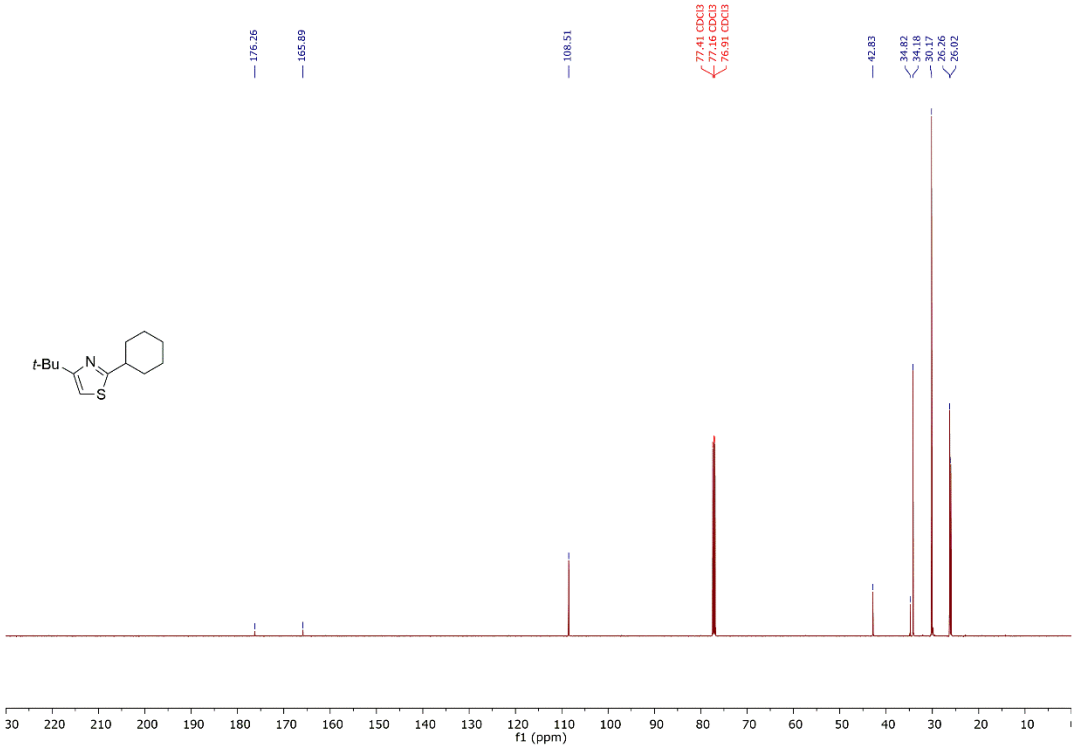
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-71)



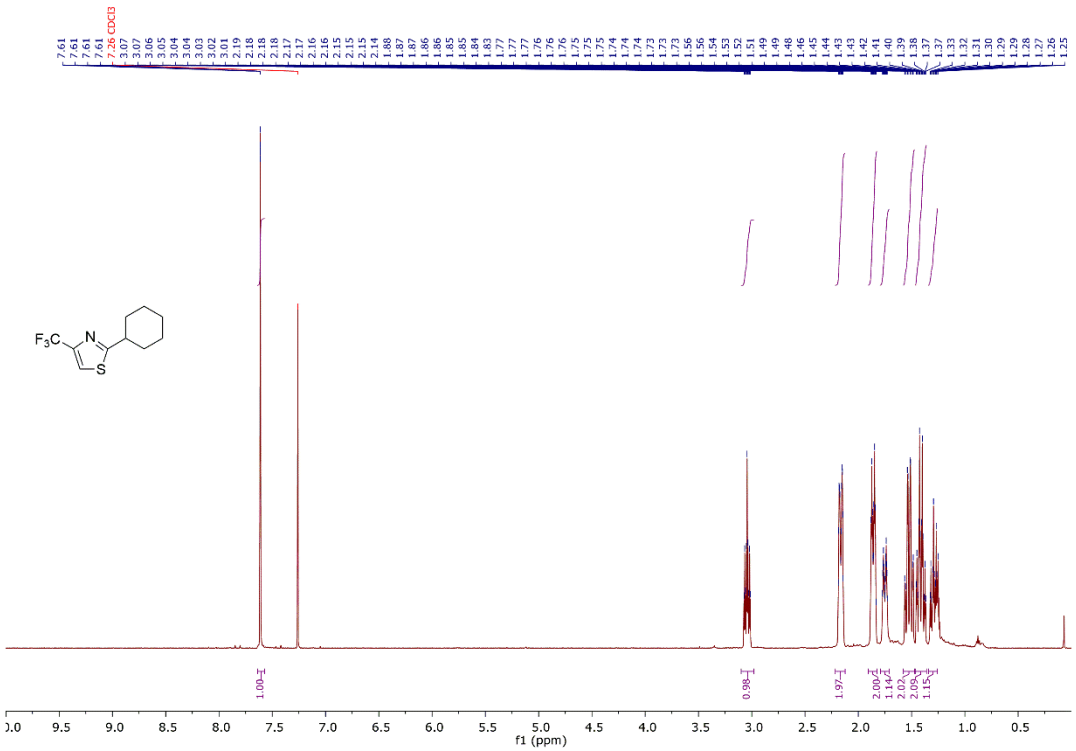
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-71)



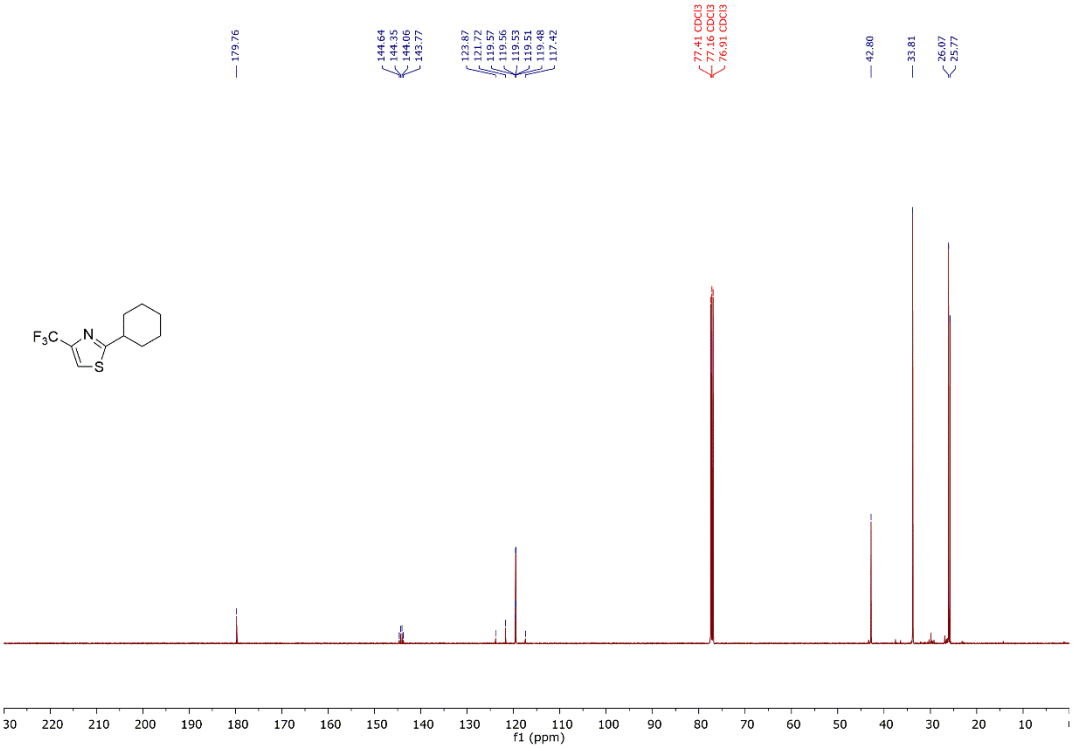
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-72)



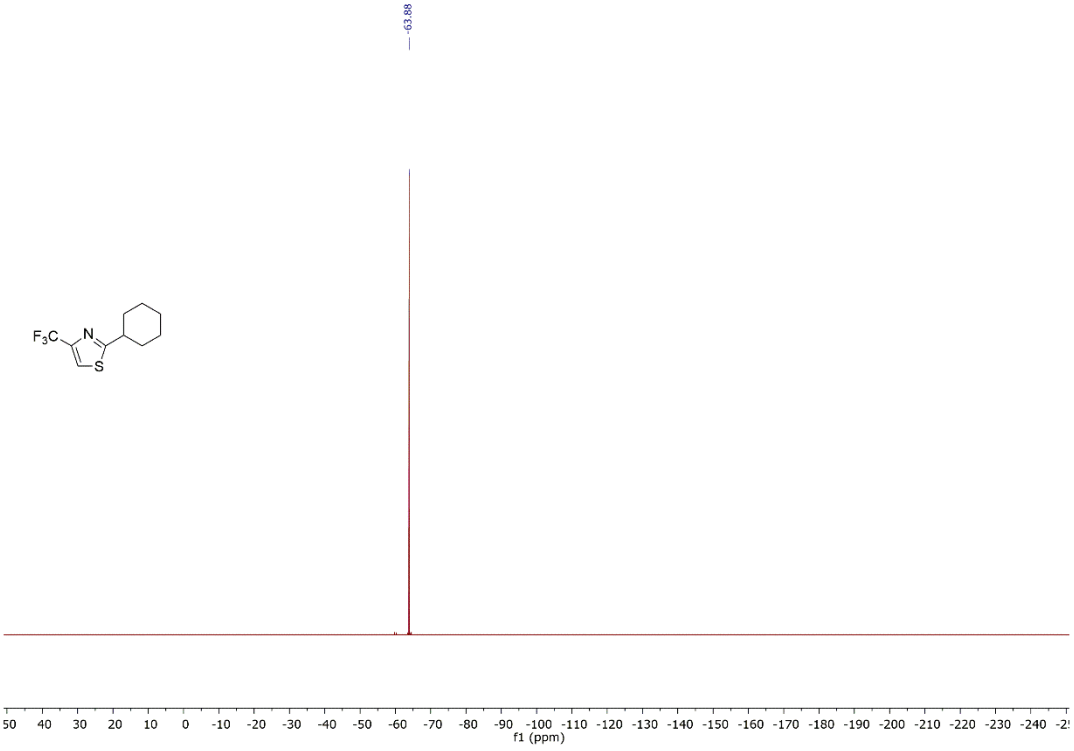
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-72)



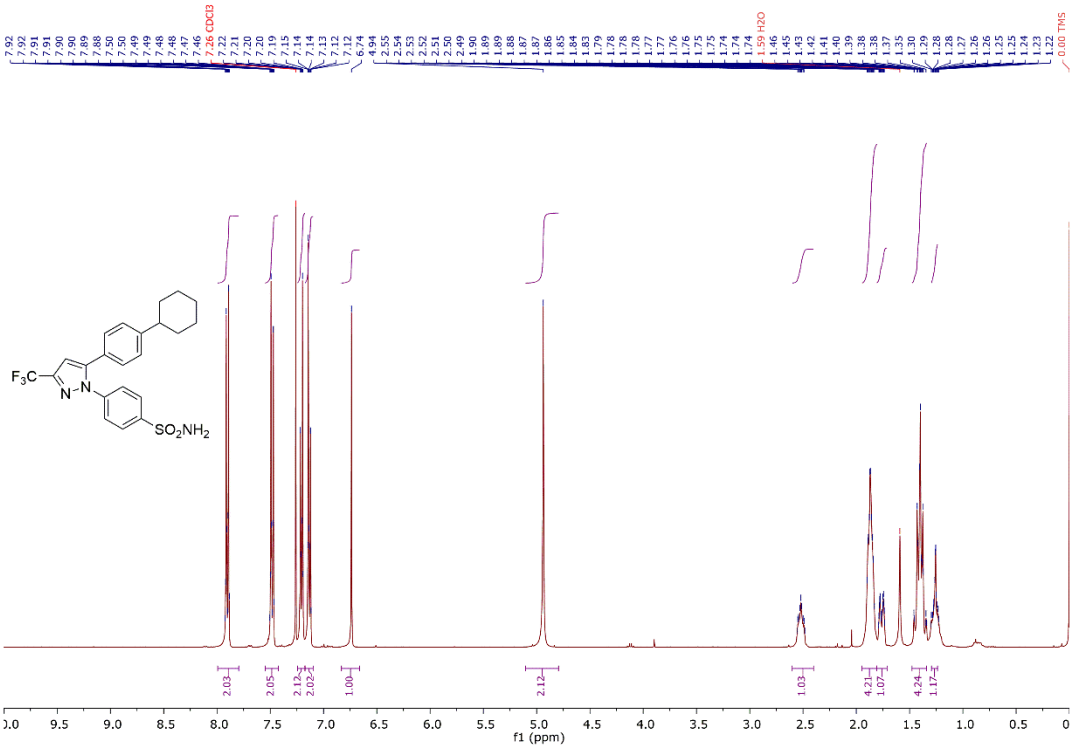
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-73)



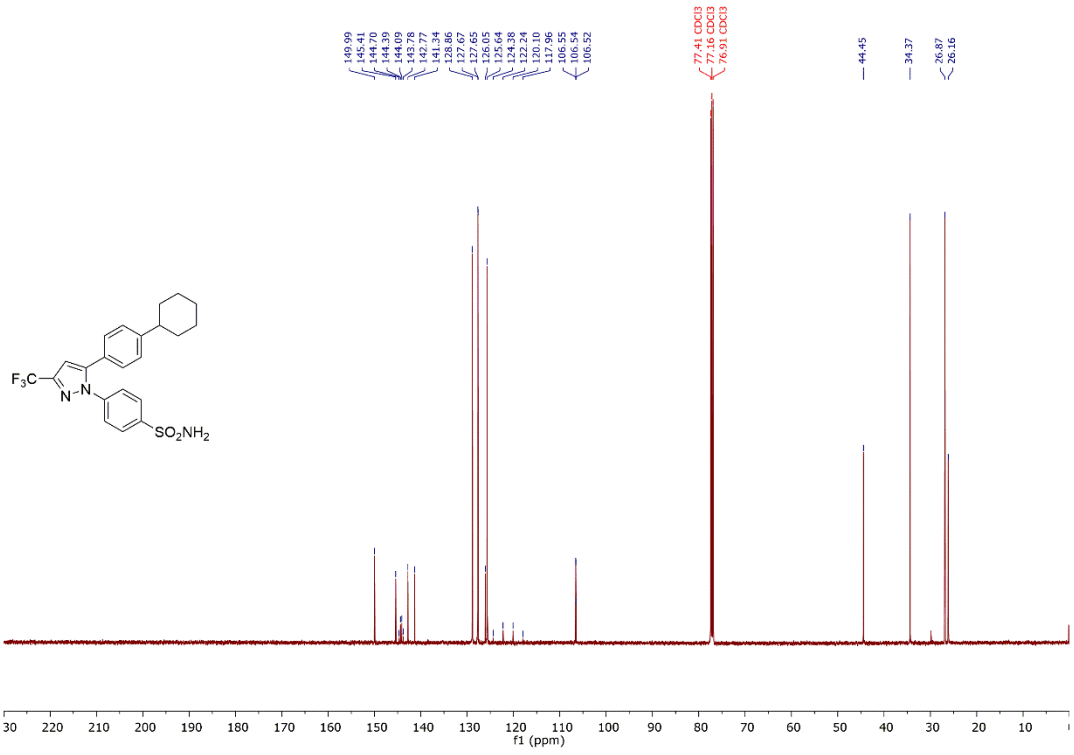
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-73)



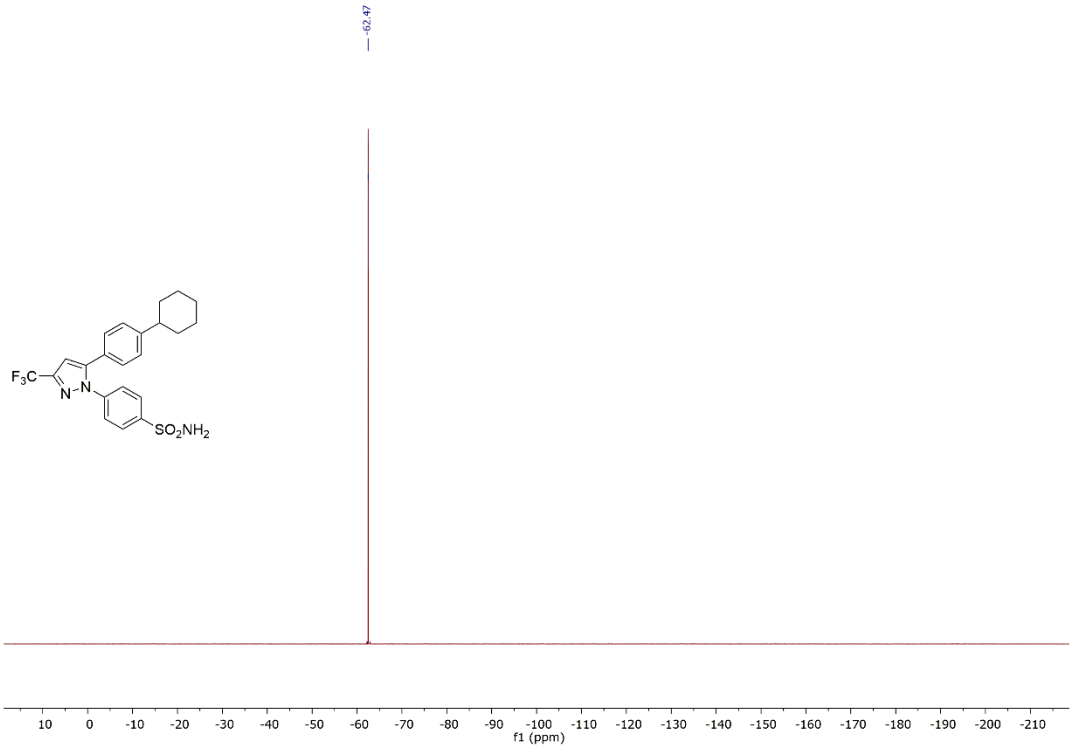
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-73)



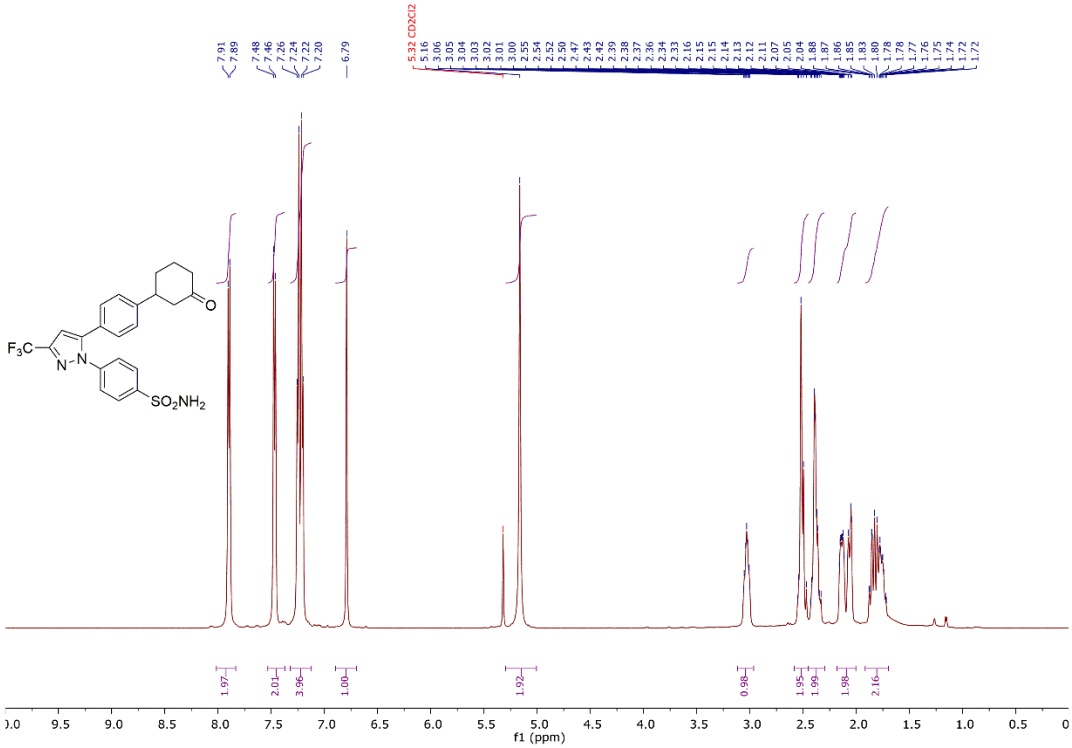
^{1}H NMR (500 MHz, $CDCl_3$) - (75a)



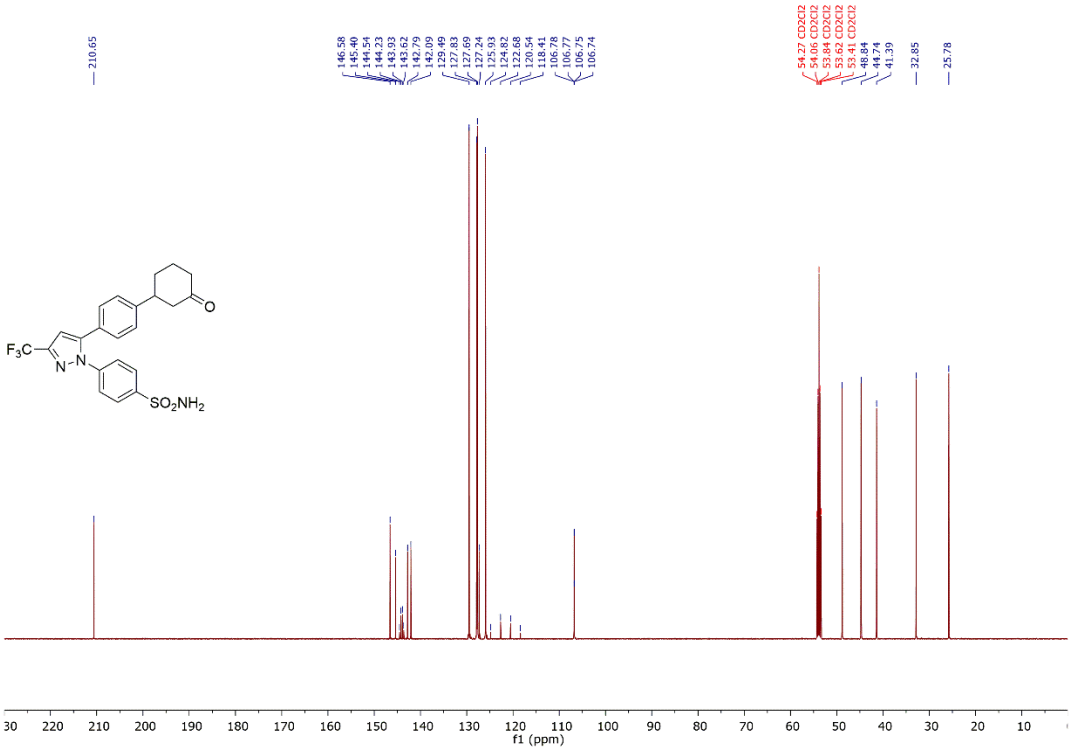
^{13}C NMR (126 MHz, $CDCl_3$) - (75a)



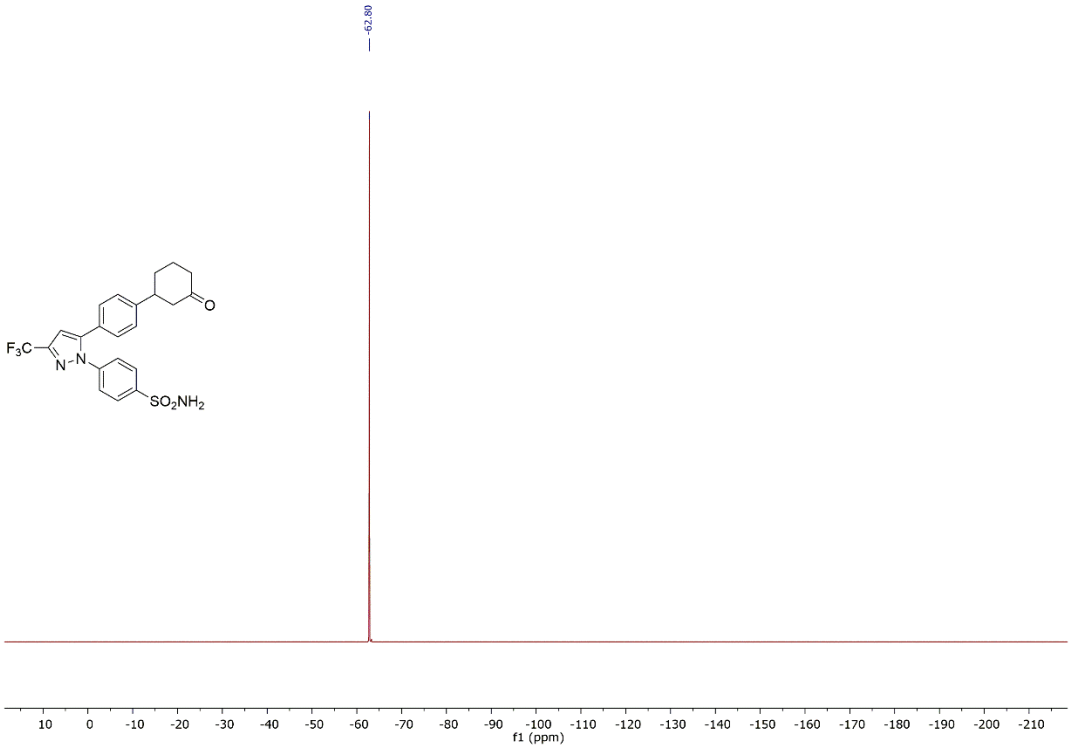
^{19}F NMR (376 MHz, $CDCl_3$) - (75a)



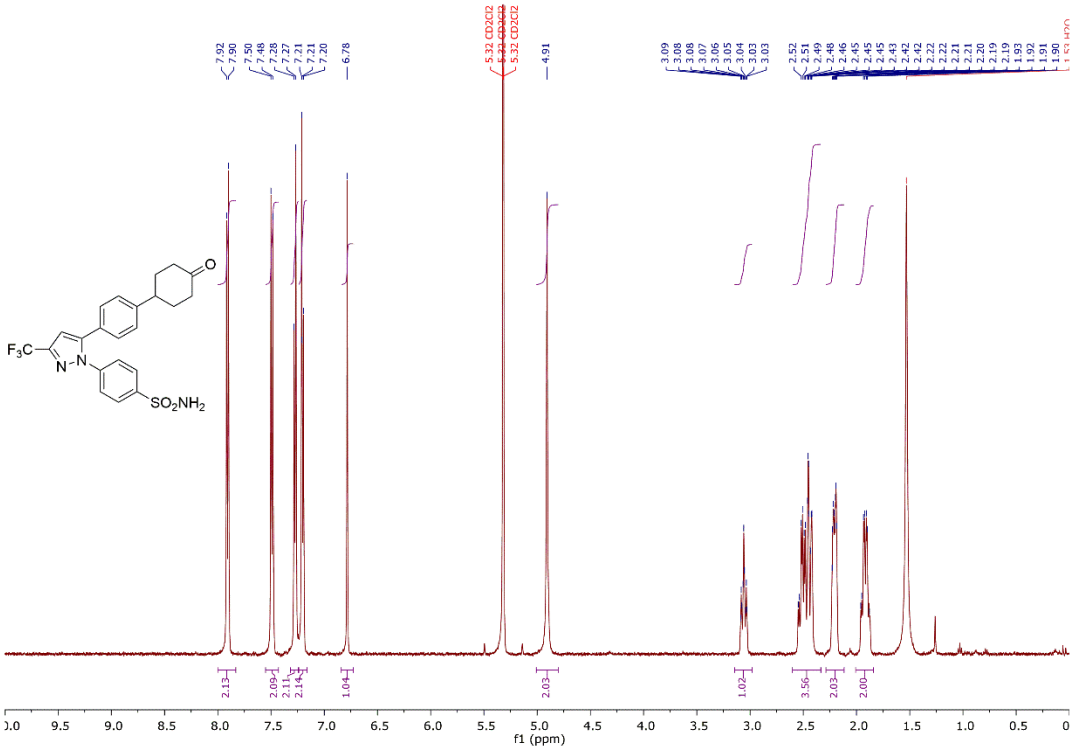
^{1}H NMR (500 MHz, CD_2Cl_2) - (75b)



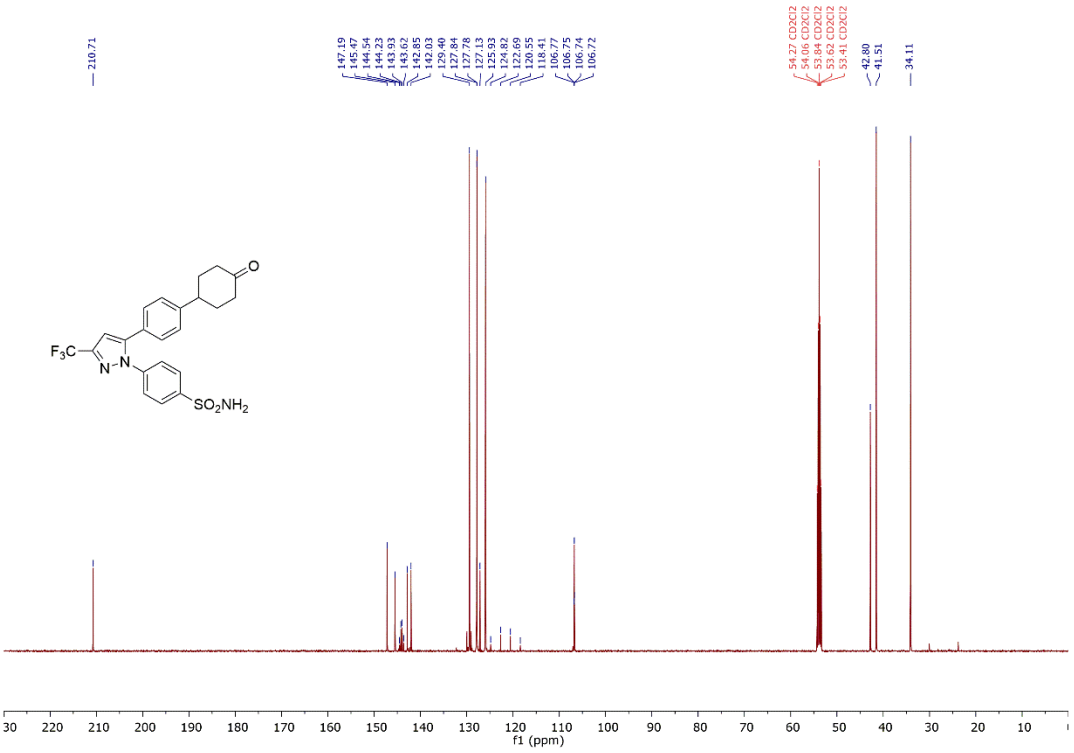
^{13}C NMR (126 MHz, CD_2Cl_2) - (75b)



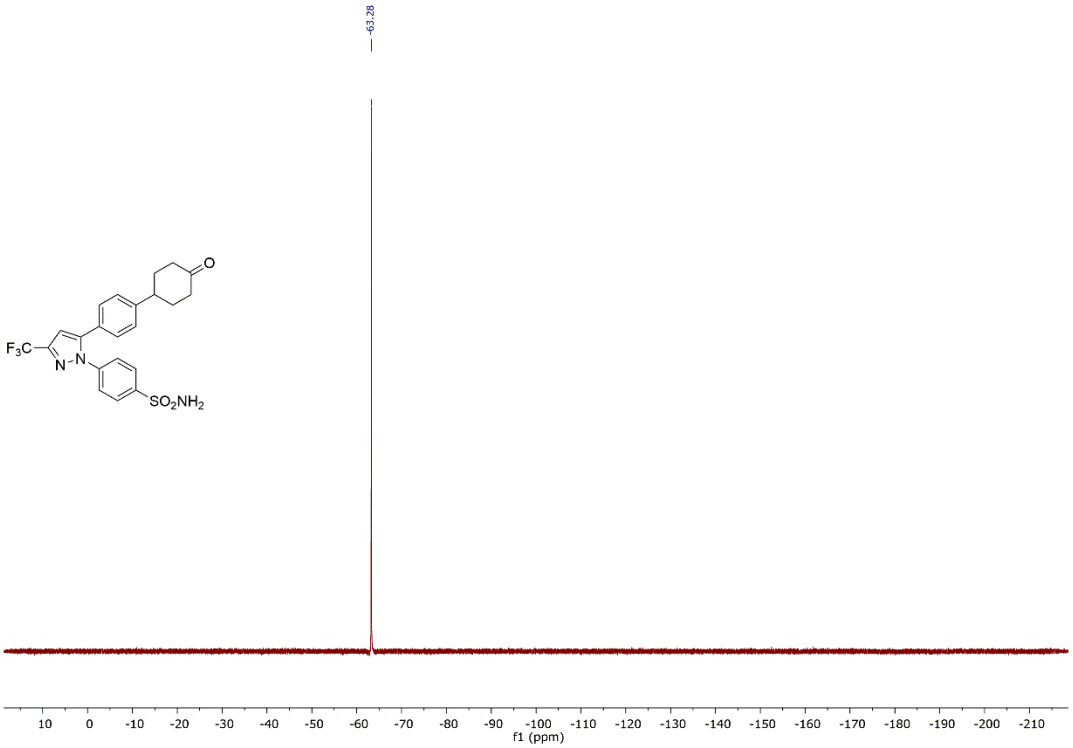
^{19}F NMR (376 MHz, CD_2Cl_2) - (75b)



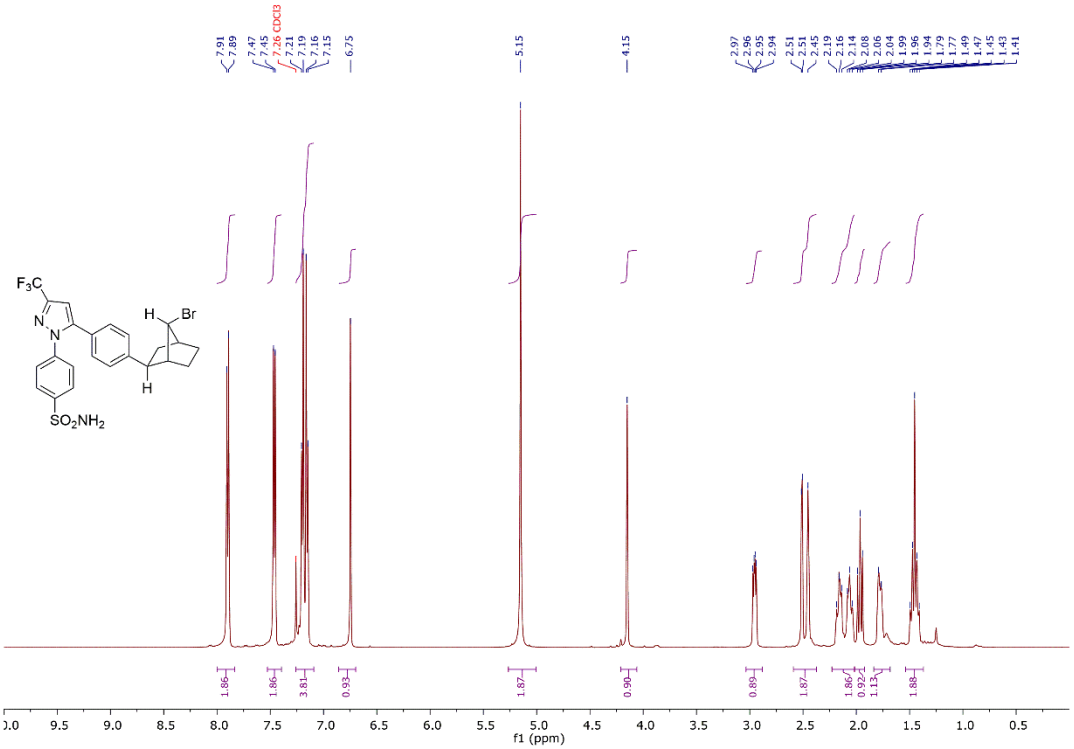
^{1}H NMR (500 MHz, CD_2Cl_2) - (SI-75b)



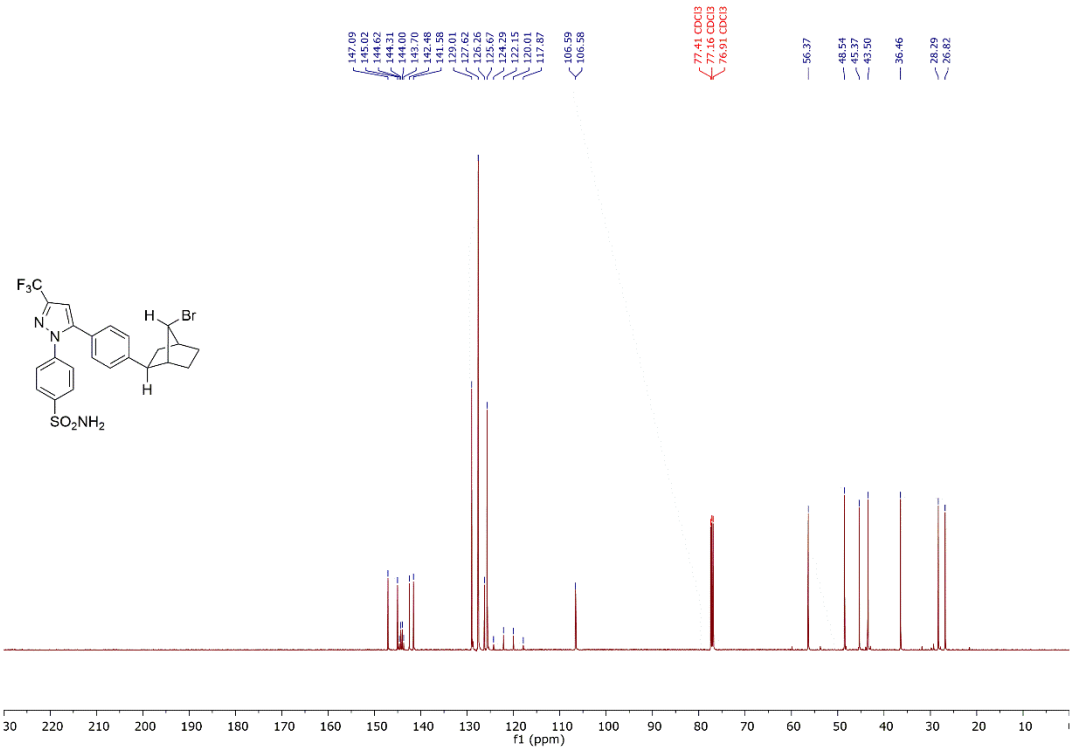
^{13}C NMR (126 MHz, CD_2Cl_2) - (SI-75b)



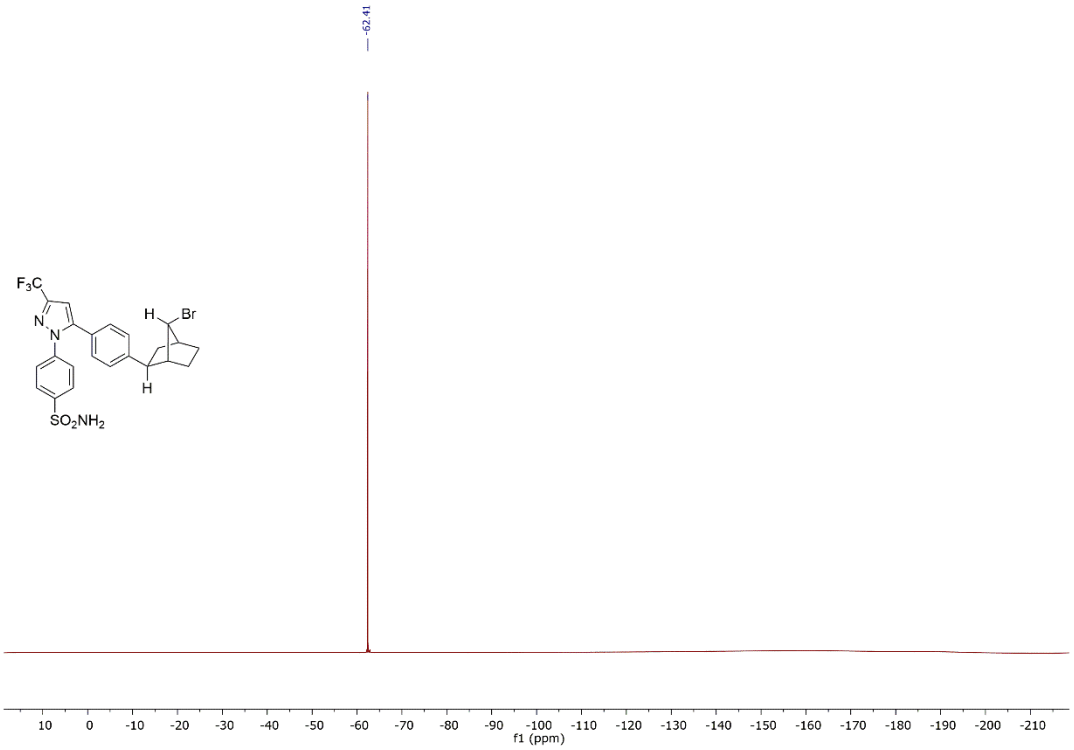
^{19}F NMR (376 MHz, CD_2Cl_2) - (SI-75b)



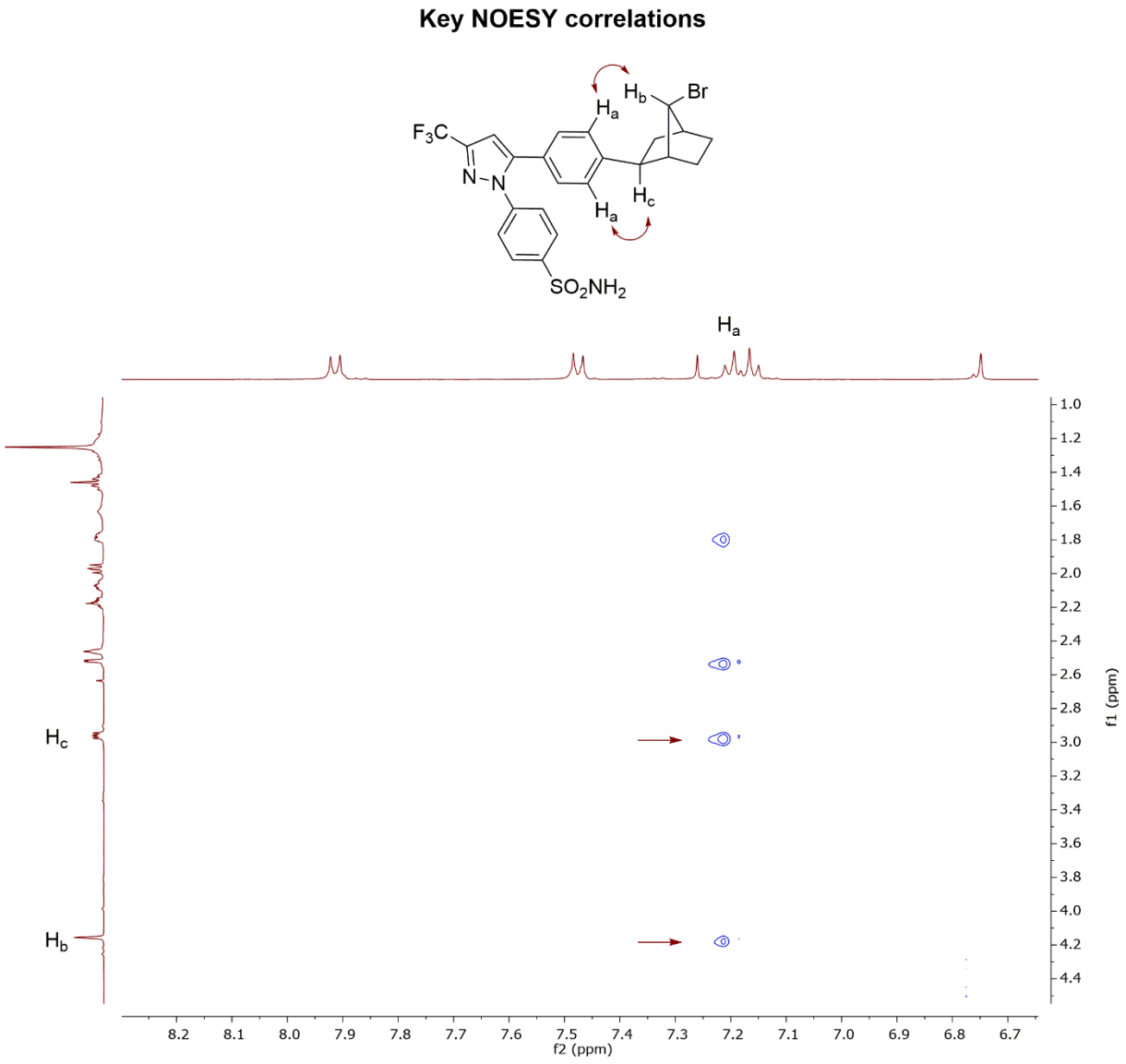
^{1}H NMR (500 MHz, $CDCl_3$) - (75c)



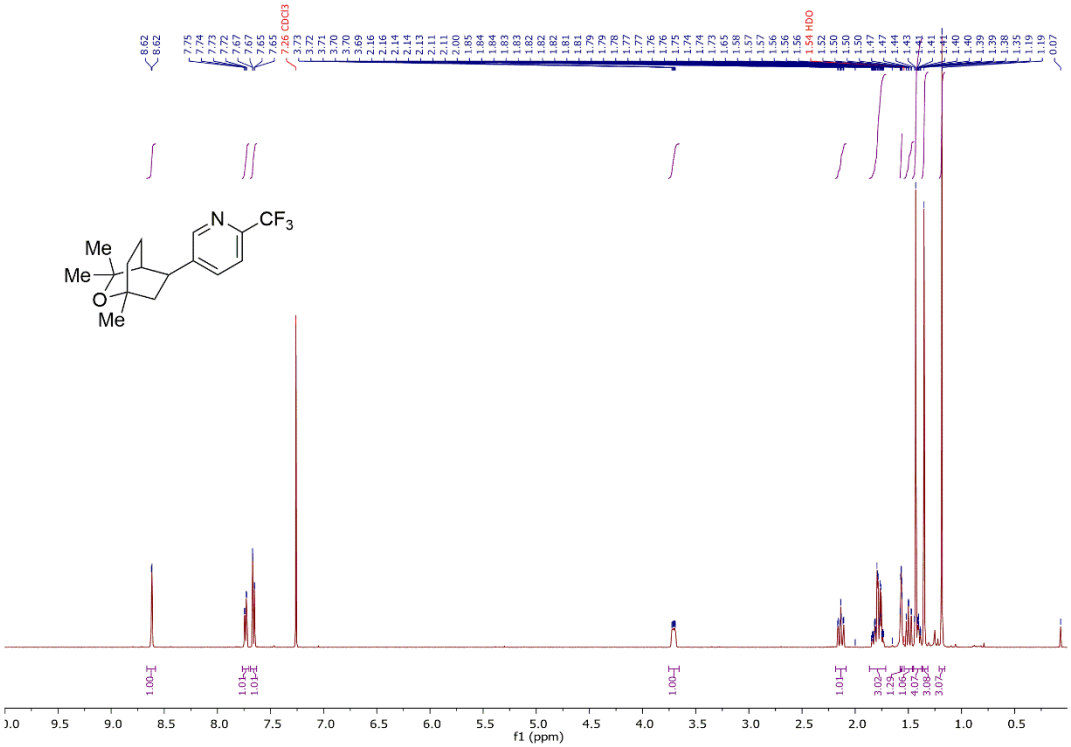
^{13}C NMR (126 MHz, $CDCl_3$) - (75c)



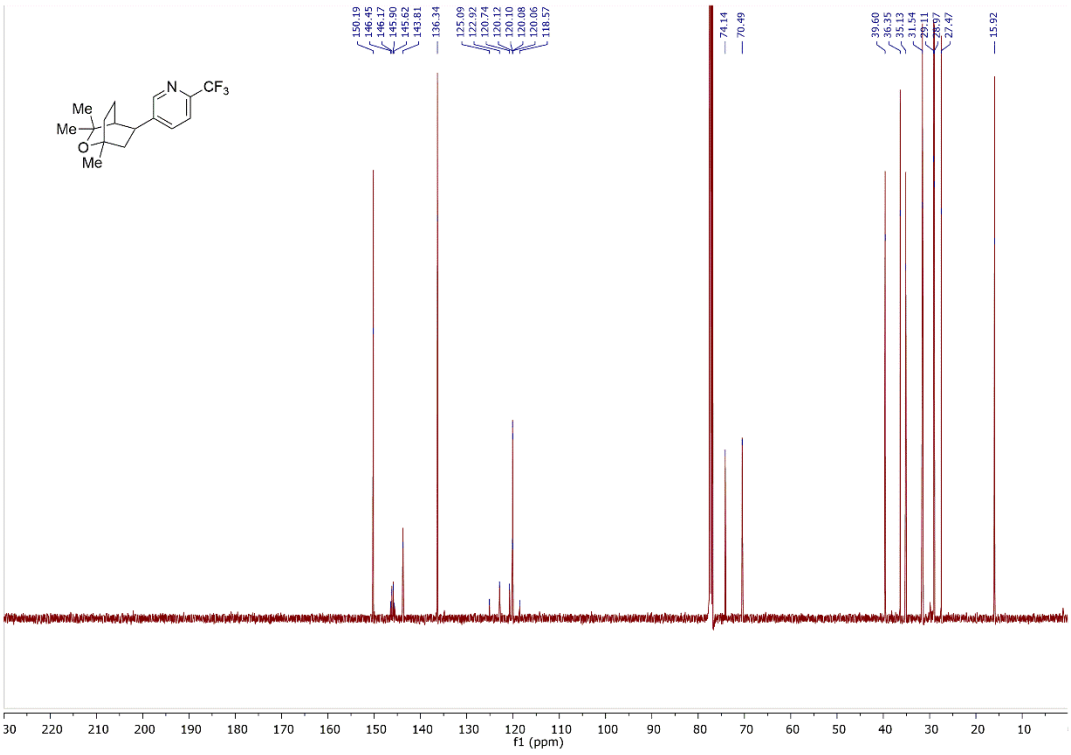
^{19}F NMR (376 MHz, $CDCl_3$) - (75c)


Key NOESY correlations
Hb
Br
Ha
F3C
N
N
Hc
Ha
SO2NH2
Ha
Hc
Hb
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
f2 (ppm)
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0
4.2
4.4
f1 (ppm)

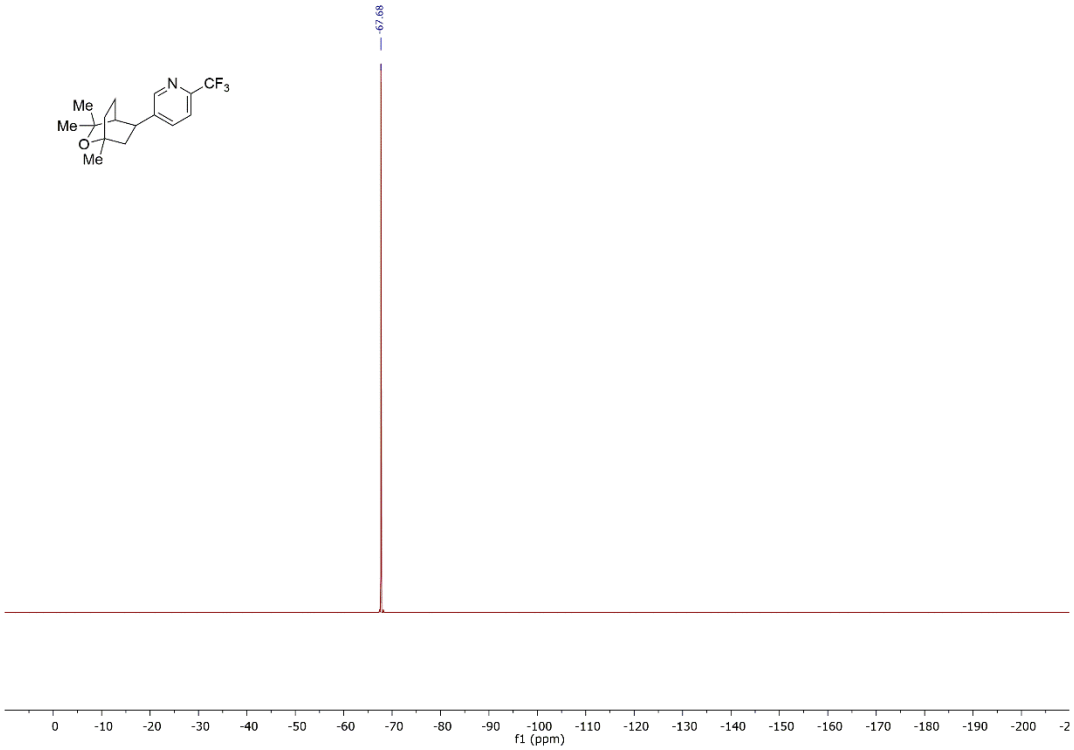
(75c)



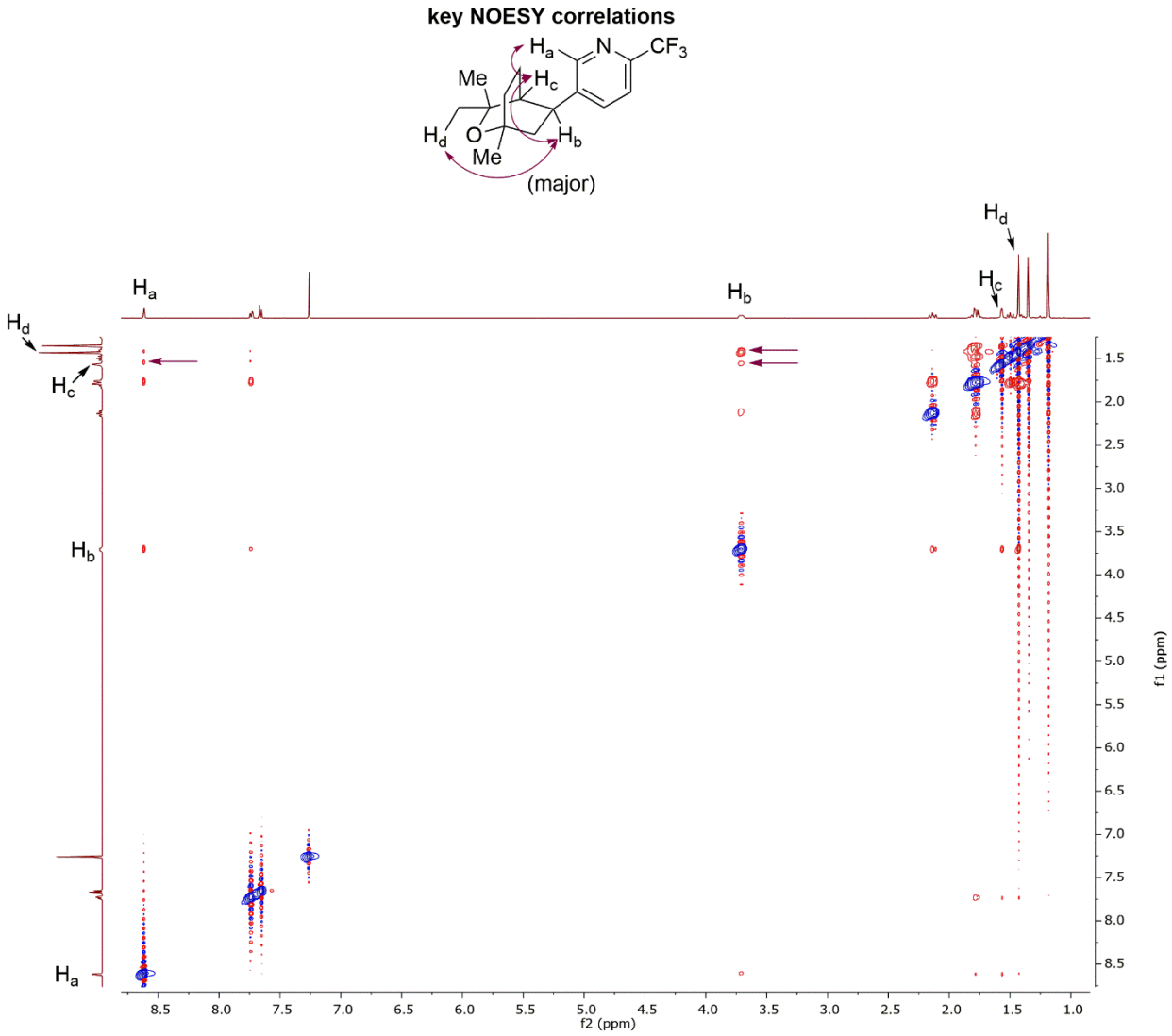
^{1}H NMR (500 MHz, $CDCl_3$) - 76



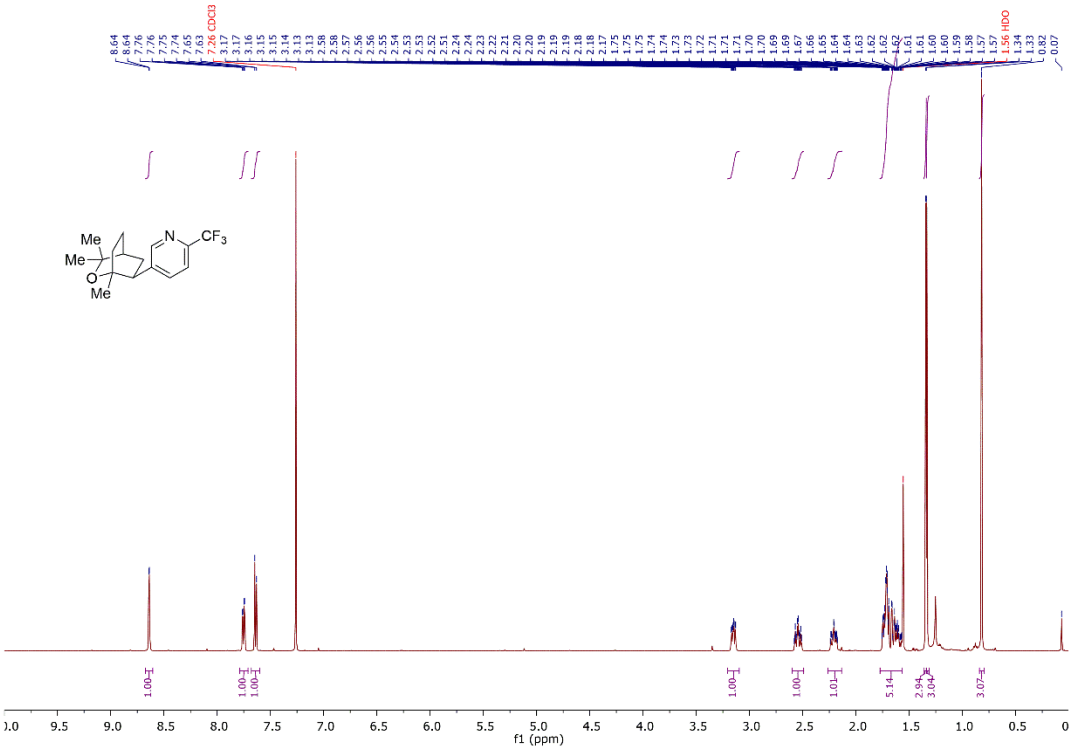
^{13}C NMR (126 MHz, $CDCl_3$) – (76)



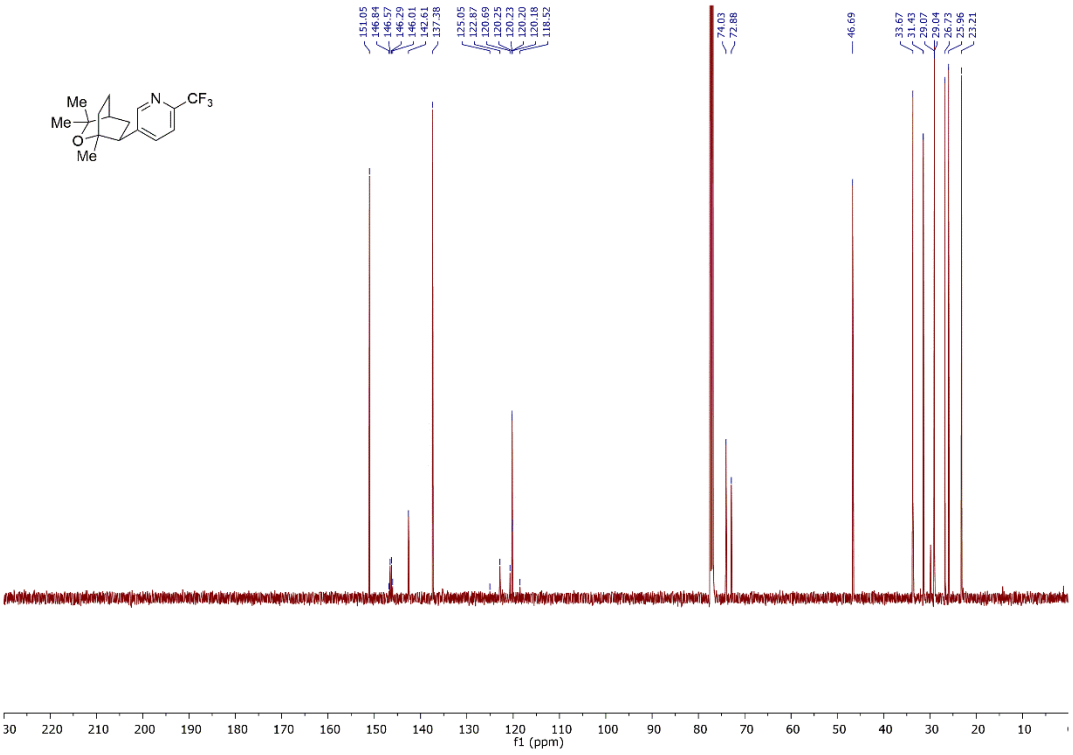
^{19}F NMR (376 MHz, $CDCl_3$) - (76)


key NOESY correlations
Ha
N
CF3
Me
Hc
Hd
O
Hb
Me
(major)
Ha
Hb
Hc
Hd
f2 (ppm)
f1 (ppm)

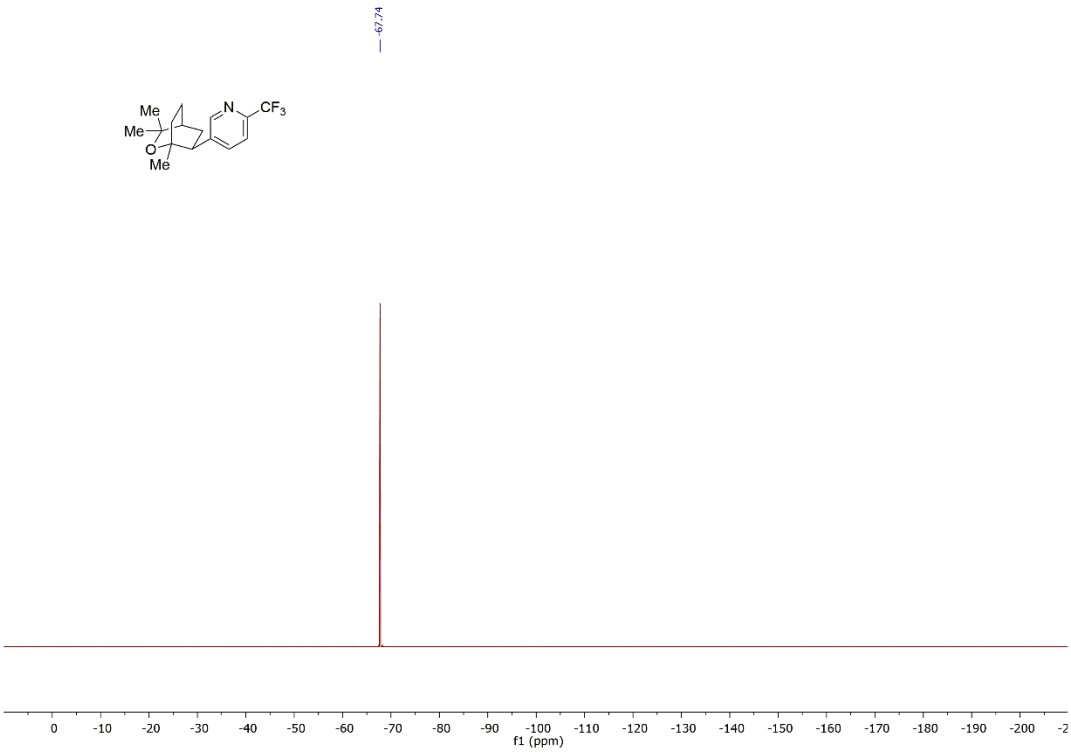
NOESY - (76)



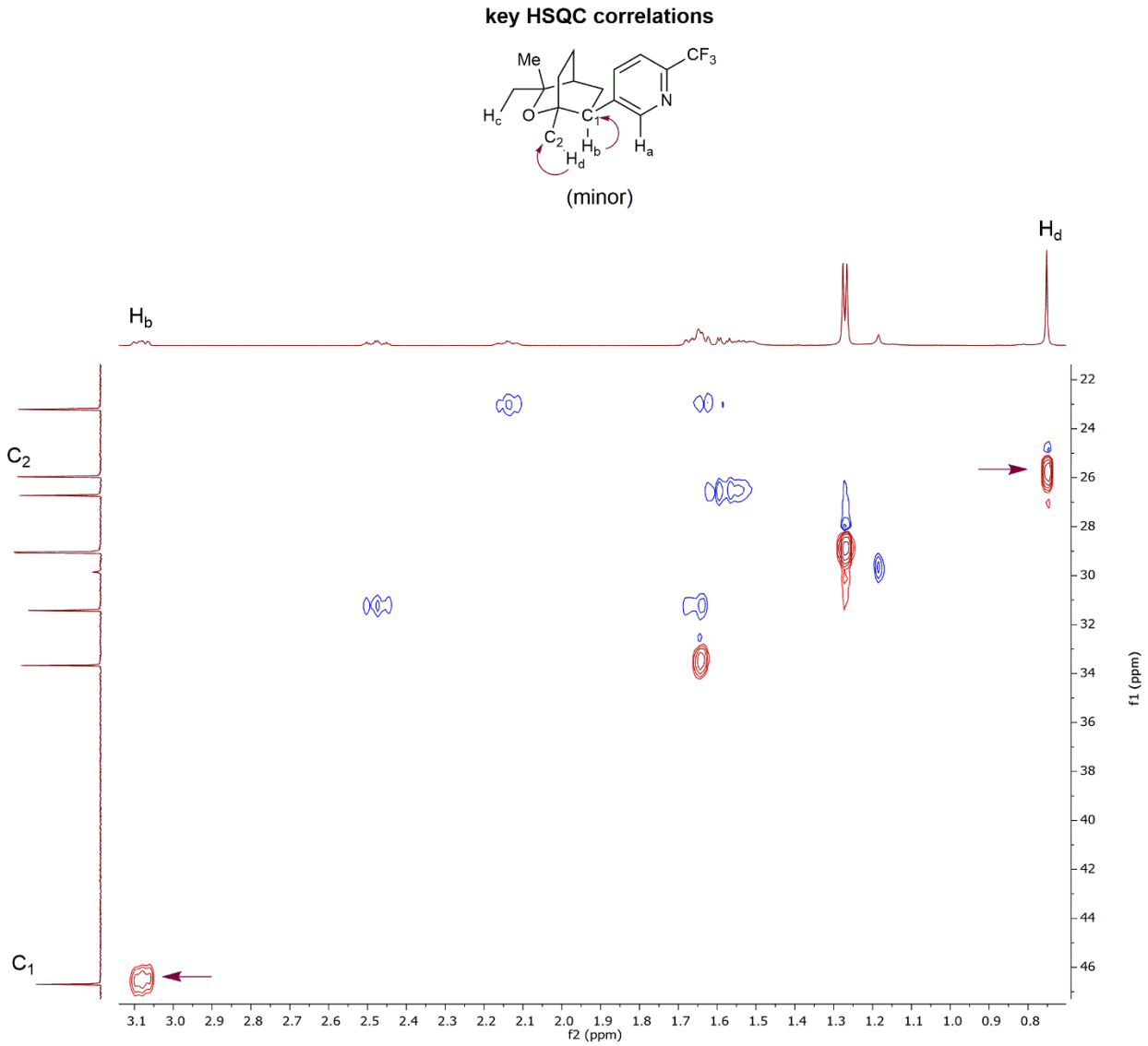
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-76)



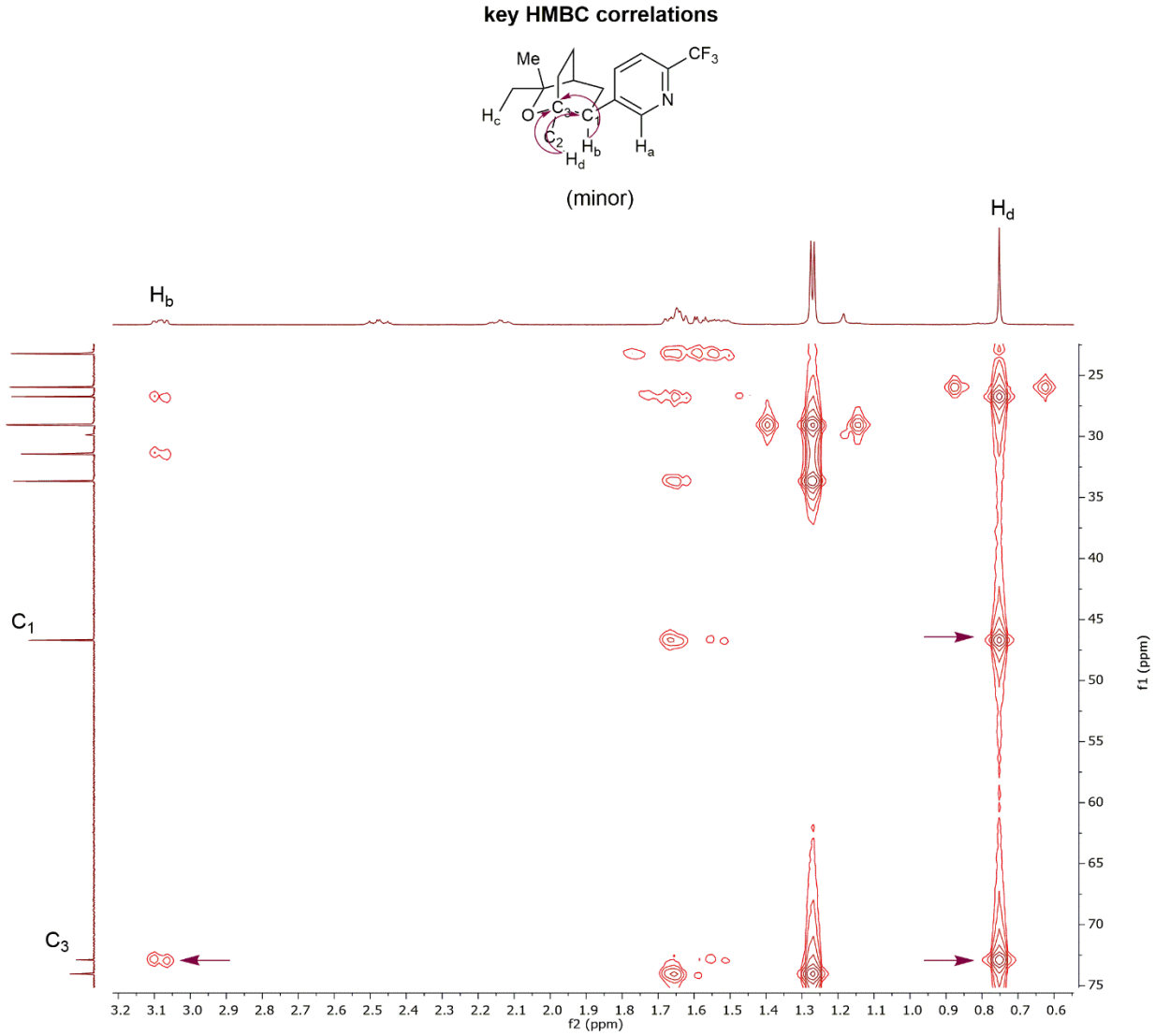
^{13}C NMR (126 MHz, $CDCl_3$) - (SI-76)



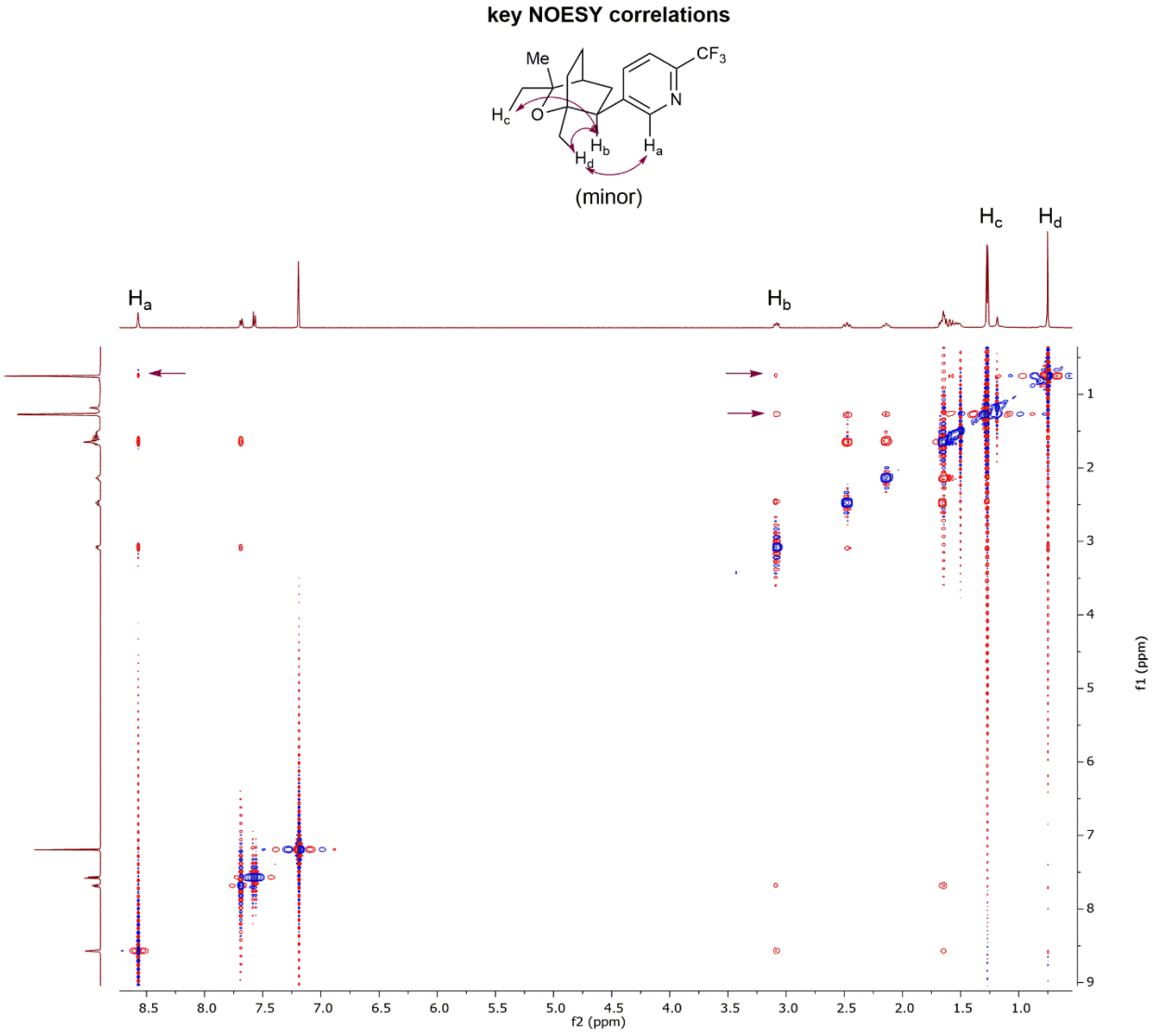
^{19}F NMR (376 MHz, $CDCl_3$) - (SI-76)


key HSQC correlations
Me
CF3
Hc
O
C1
N
C2
Hb
Ha
Hd
(minor)
Hd
Hb
C2
C1
f2 (ppm)
f1 (ppm)

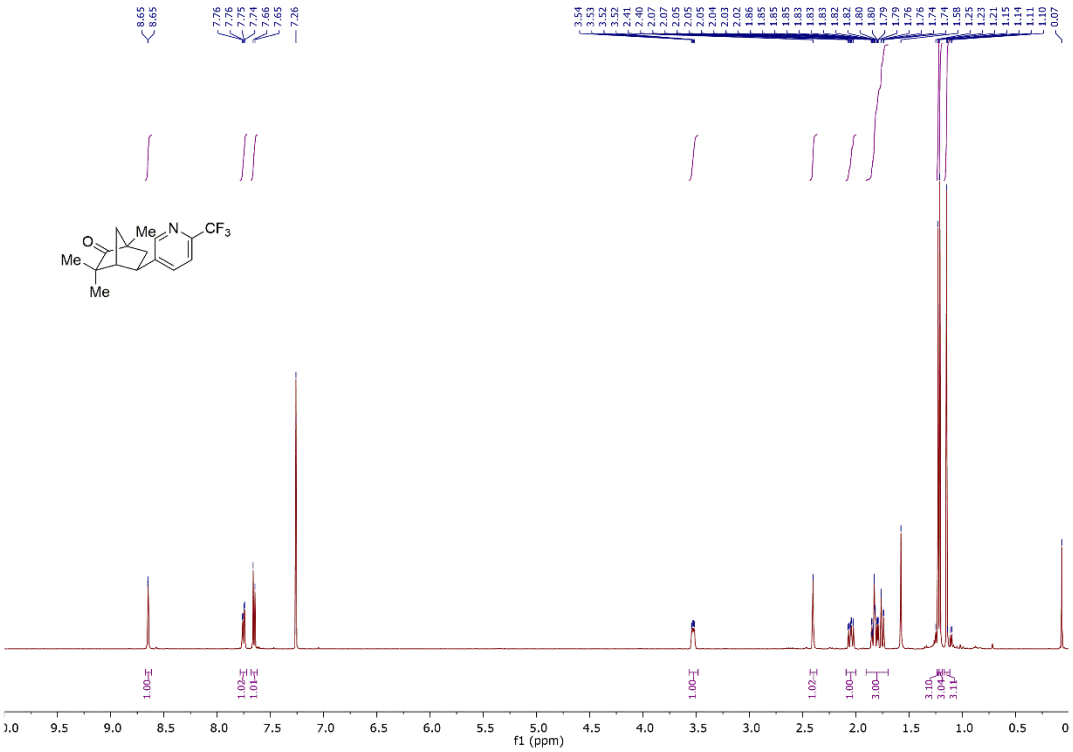
HSQC - (SI-76)


key HMBC correlations
Me
CF3
Hc
O
C3
C1
N
C2
Hb
Ha
Hd
(minor)
Hd
Hb
C1
C3
3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6
f2 (ppm)
25 30 35 40 45 50 55 60 65 70 75
f1 (ppm)

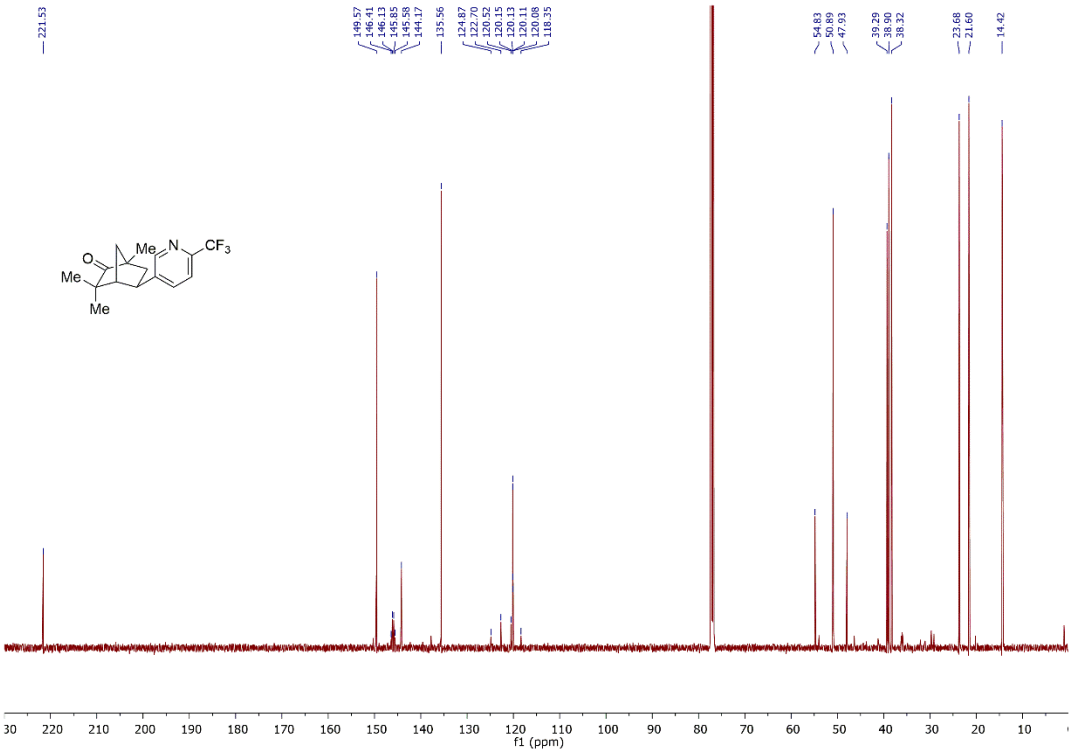
HMBC - (SI-76)


key NOESY correlations
Me
CF3
N
O
Hc
Hb
Ha
Hd
(minor)
Hc
Hd
Ha
Hb
f2 (ppm)
f1 (ppm)

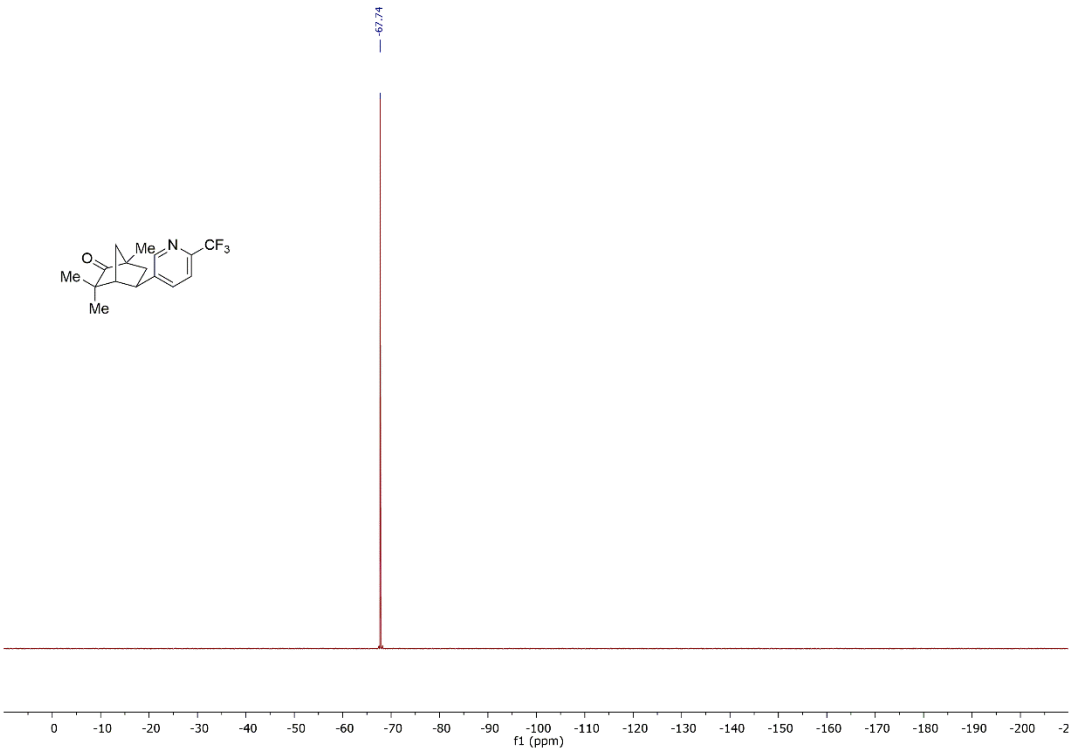
NOESY - (SI-76)



^{1}H NMR (500 MHz, $CDCl_3$) – (77)

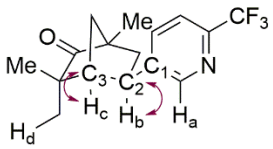


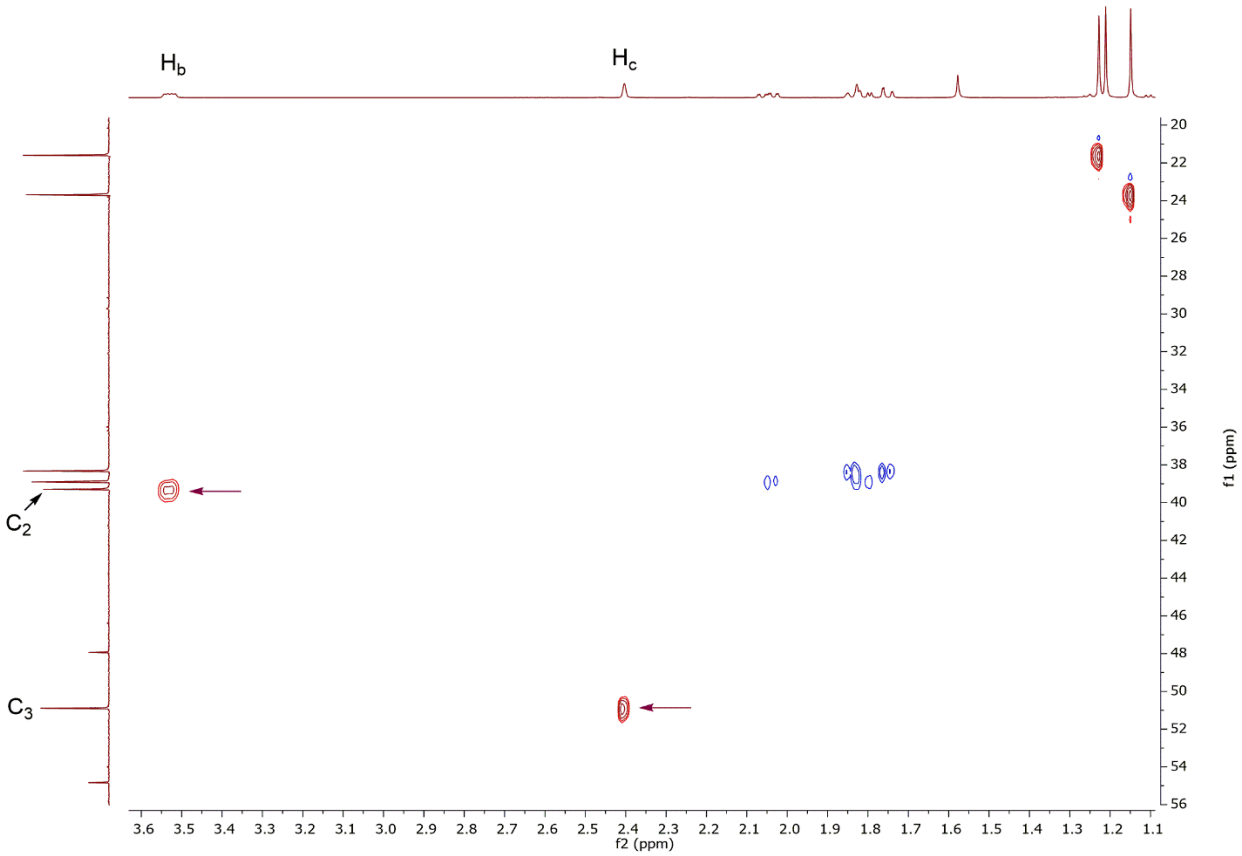
^{13}C NMR (126 MHz, $CDCl_3$) - (77)



^{19}F NMR (376 MHz, $CDCl_3$) - (77)

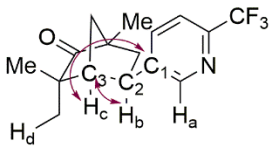
key HSQC correlations

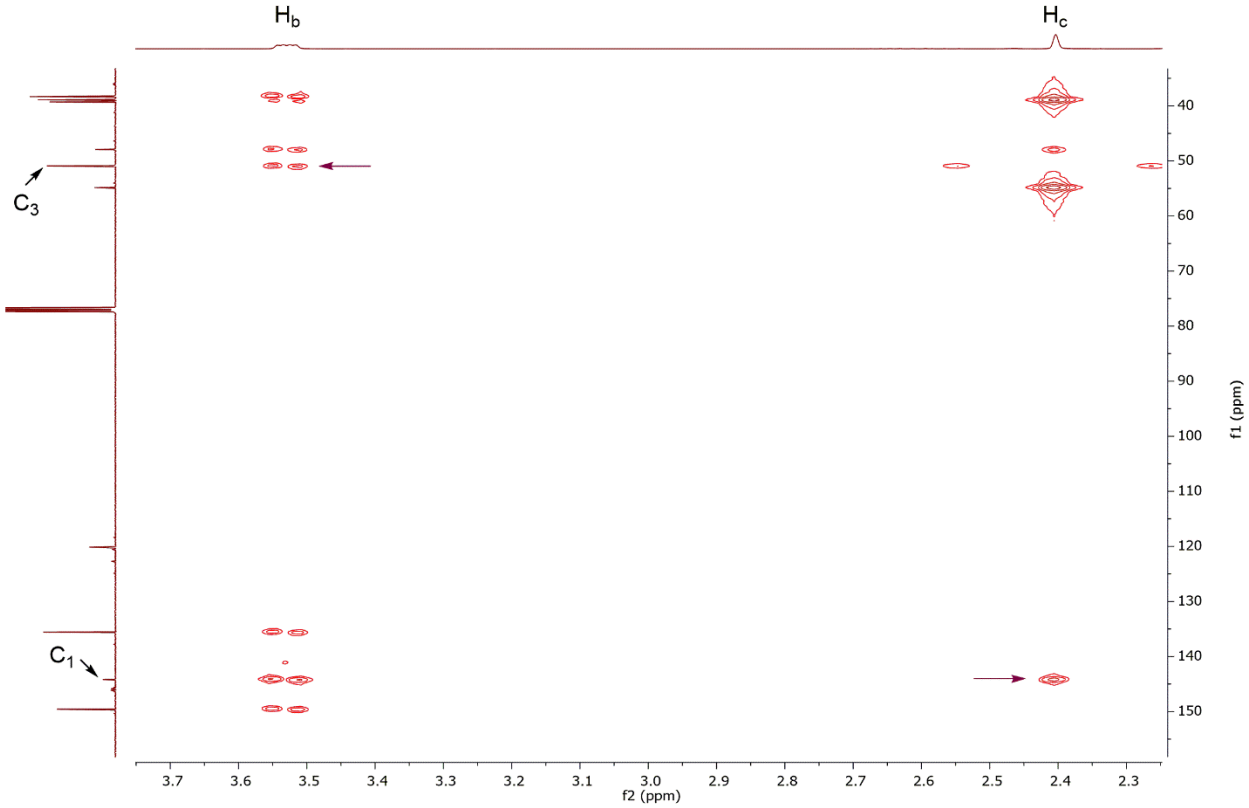




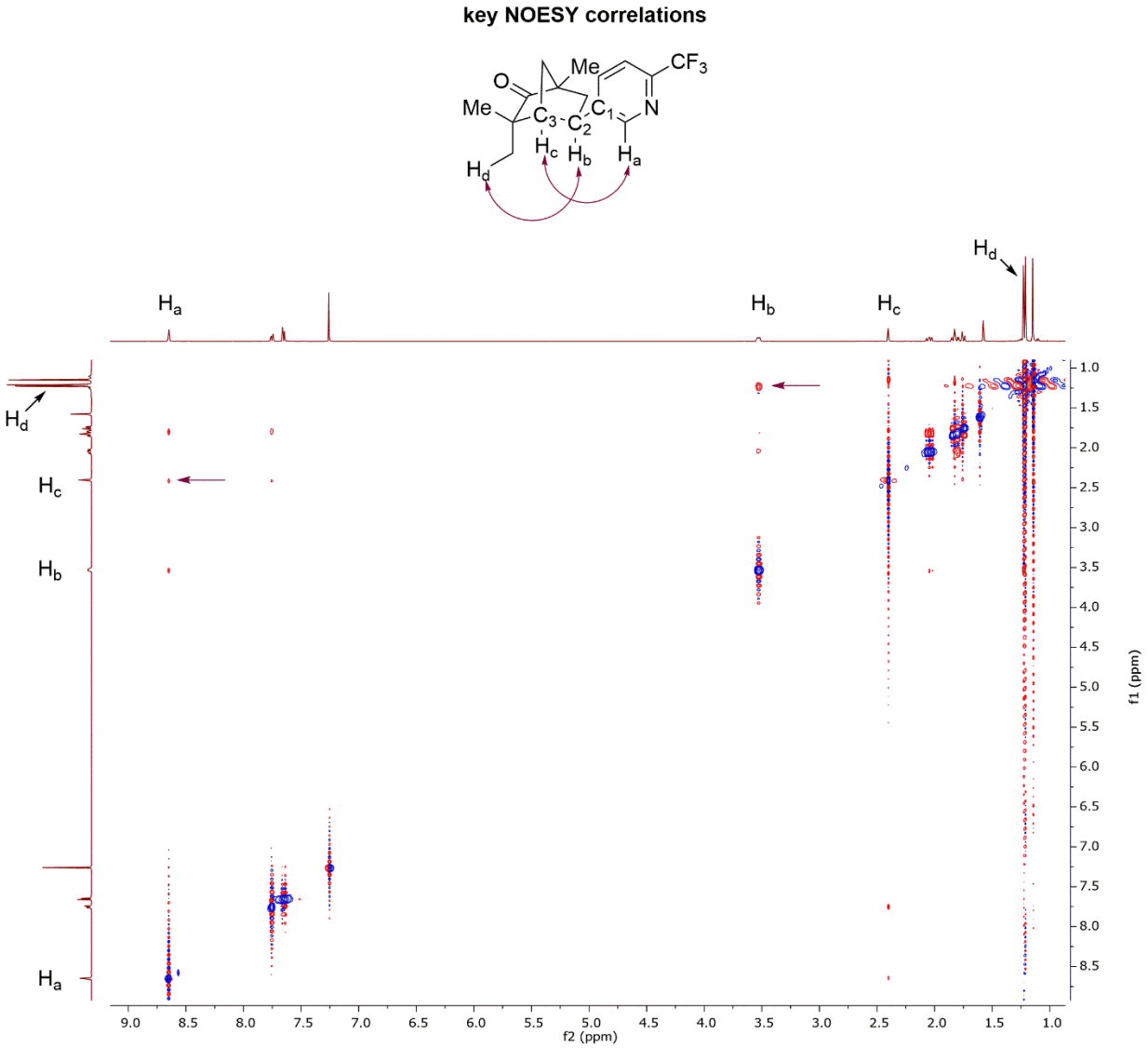
HSQC - (77)

key HMBC correlations

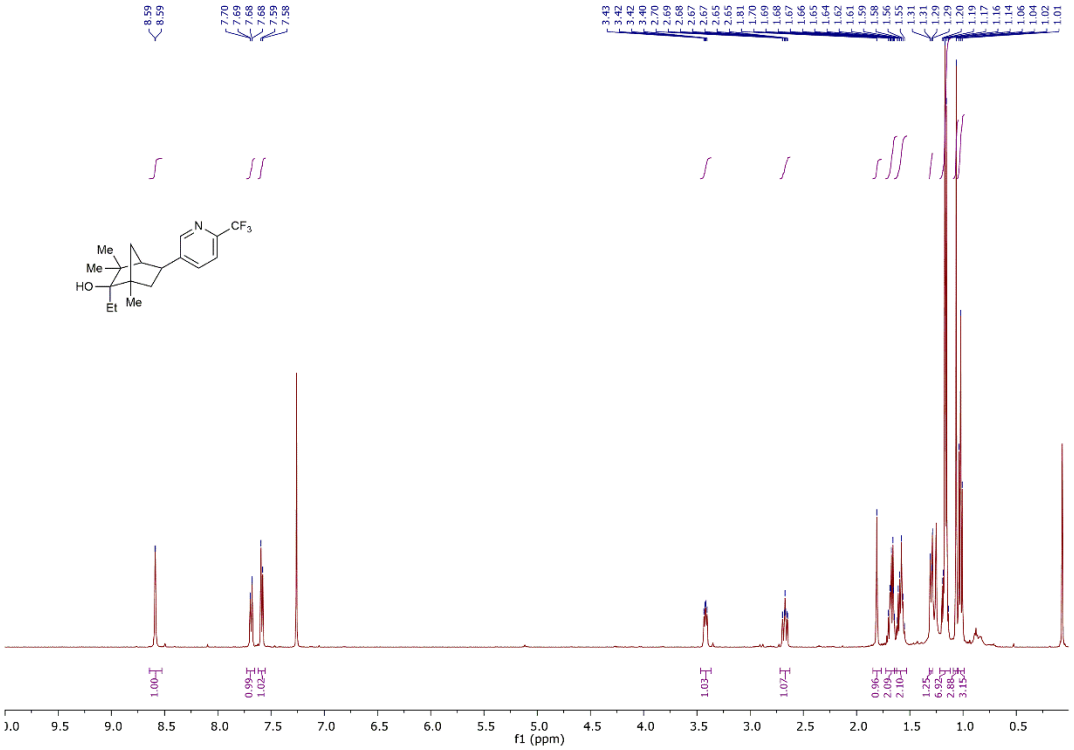




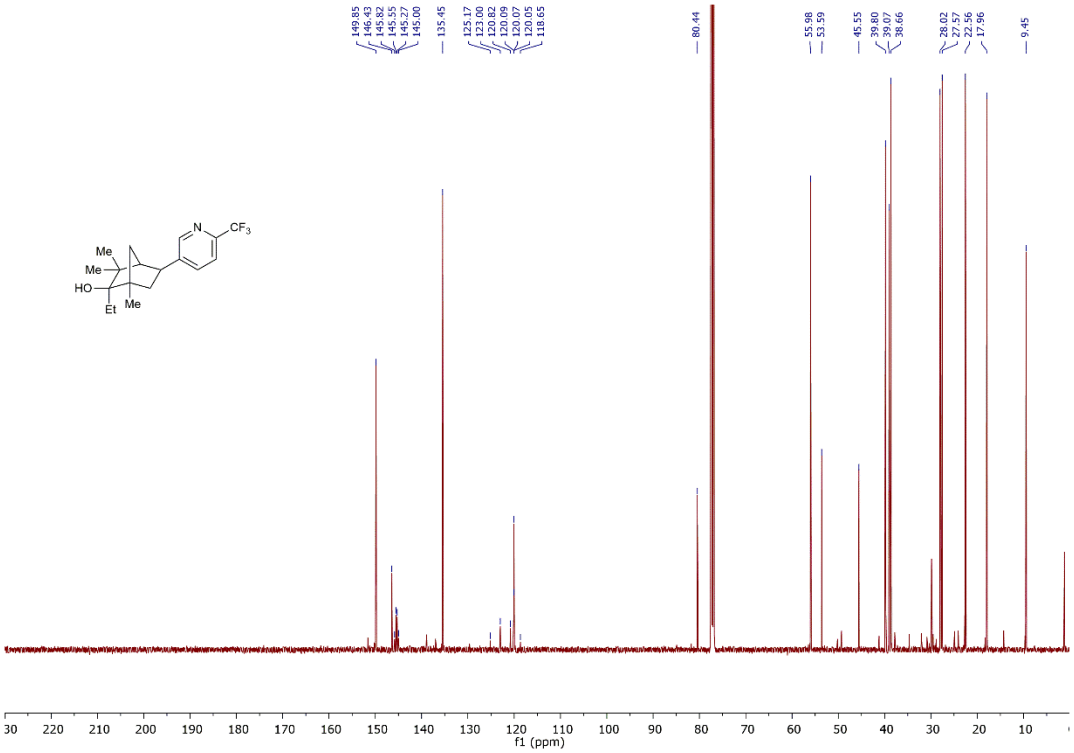
HMBC - (77)


key NOESY correlations
O
Me
CF3
Me
C3
C2
C1
N
Hc
Hb
Ha
Hd
Ha
Hb
Hc
Hd
Hd
Hc
Hb
Ha
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
f1 (ppm)

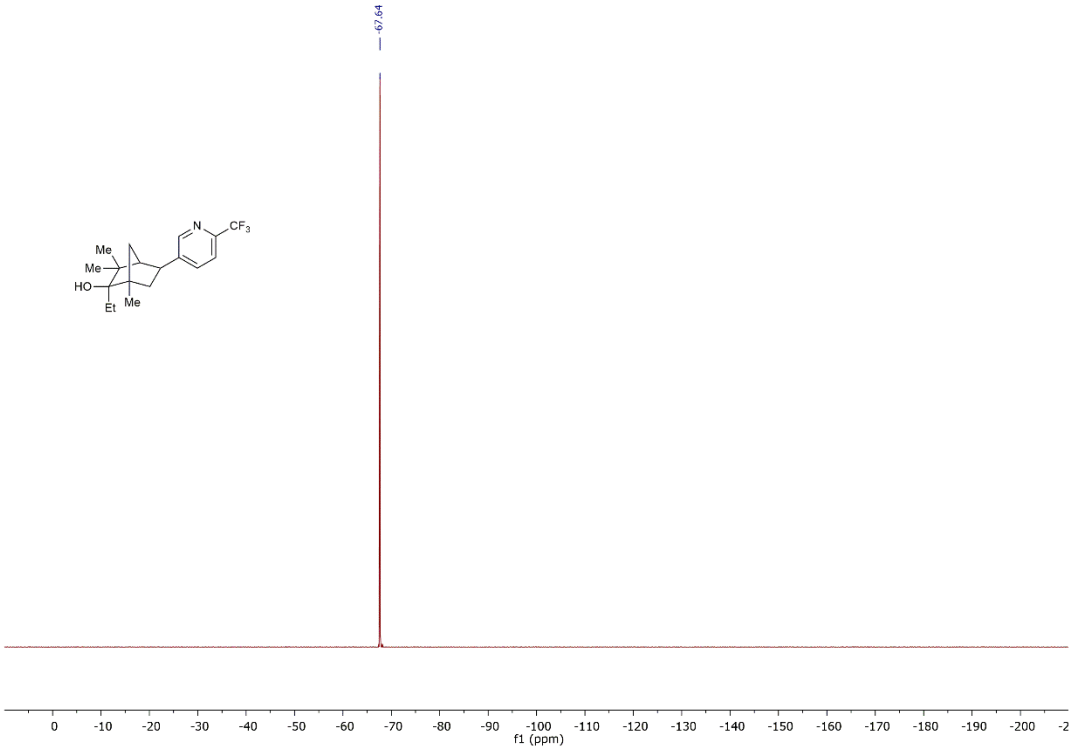
NOESY - (77)



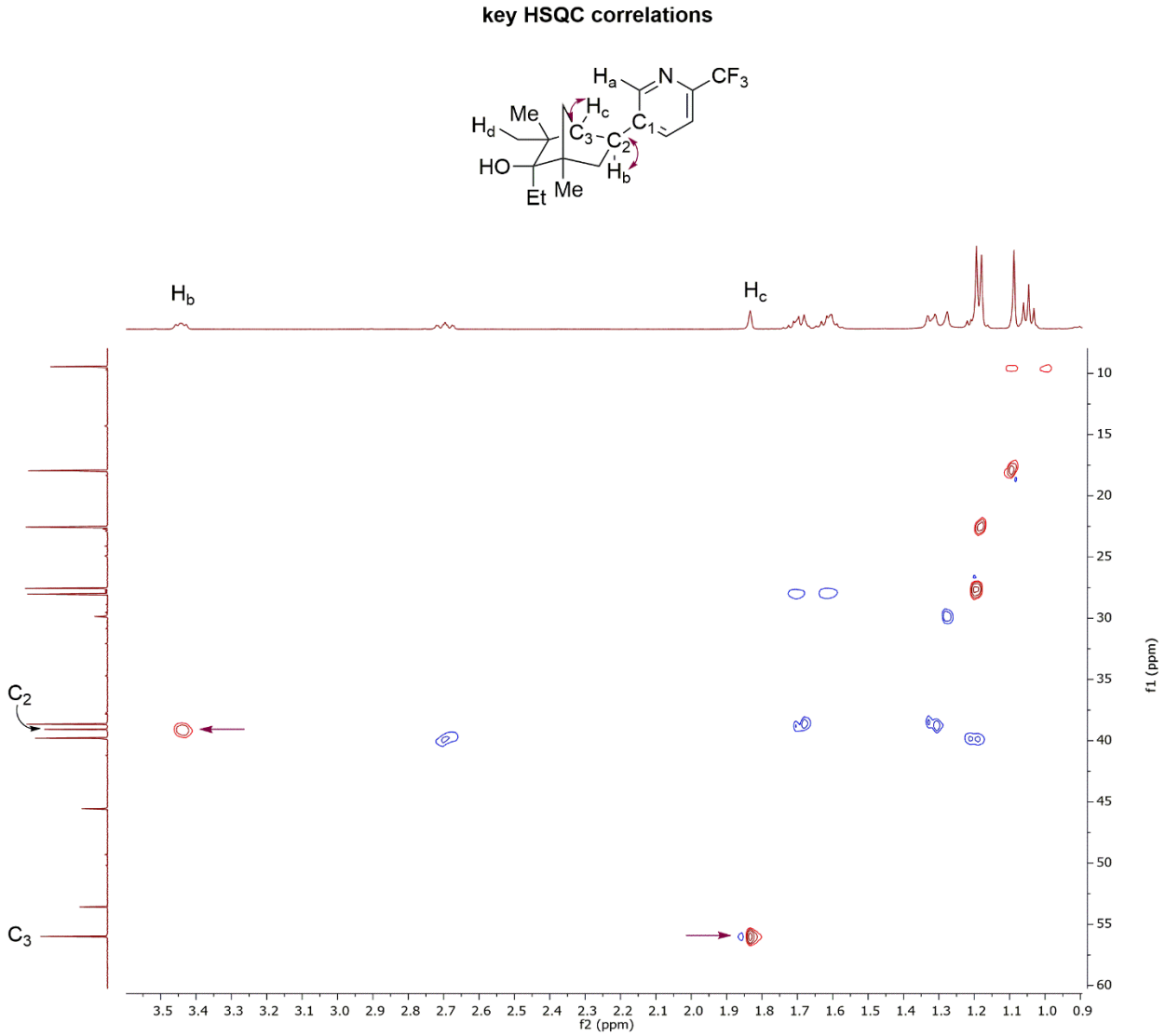
^{1}H NMR (500 MHz, $CDCl_3$) - (78)



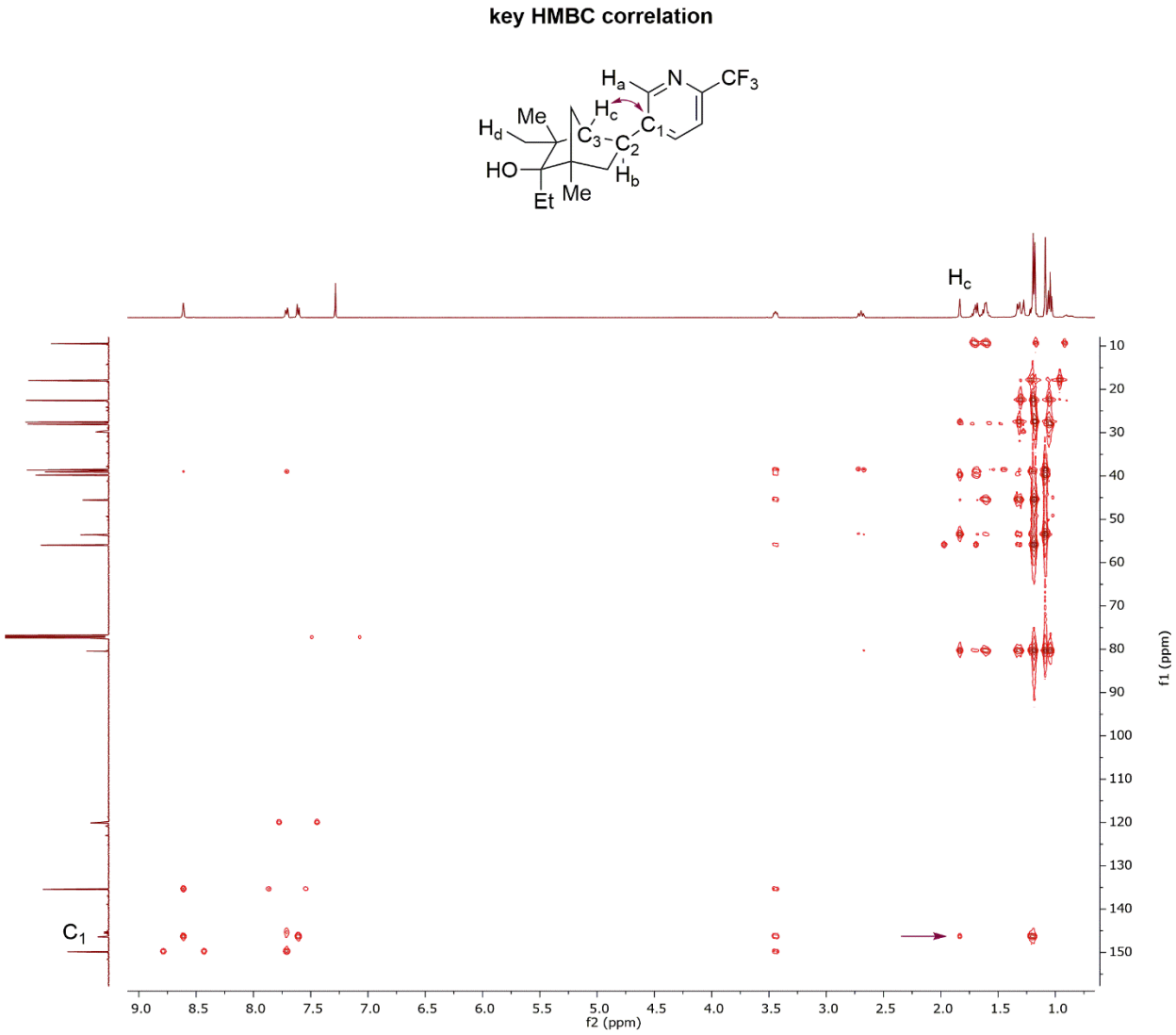
^{13}C NMR (126 MHz, $CDCl_3$) - (78)



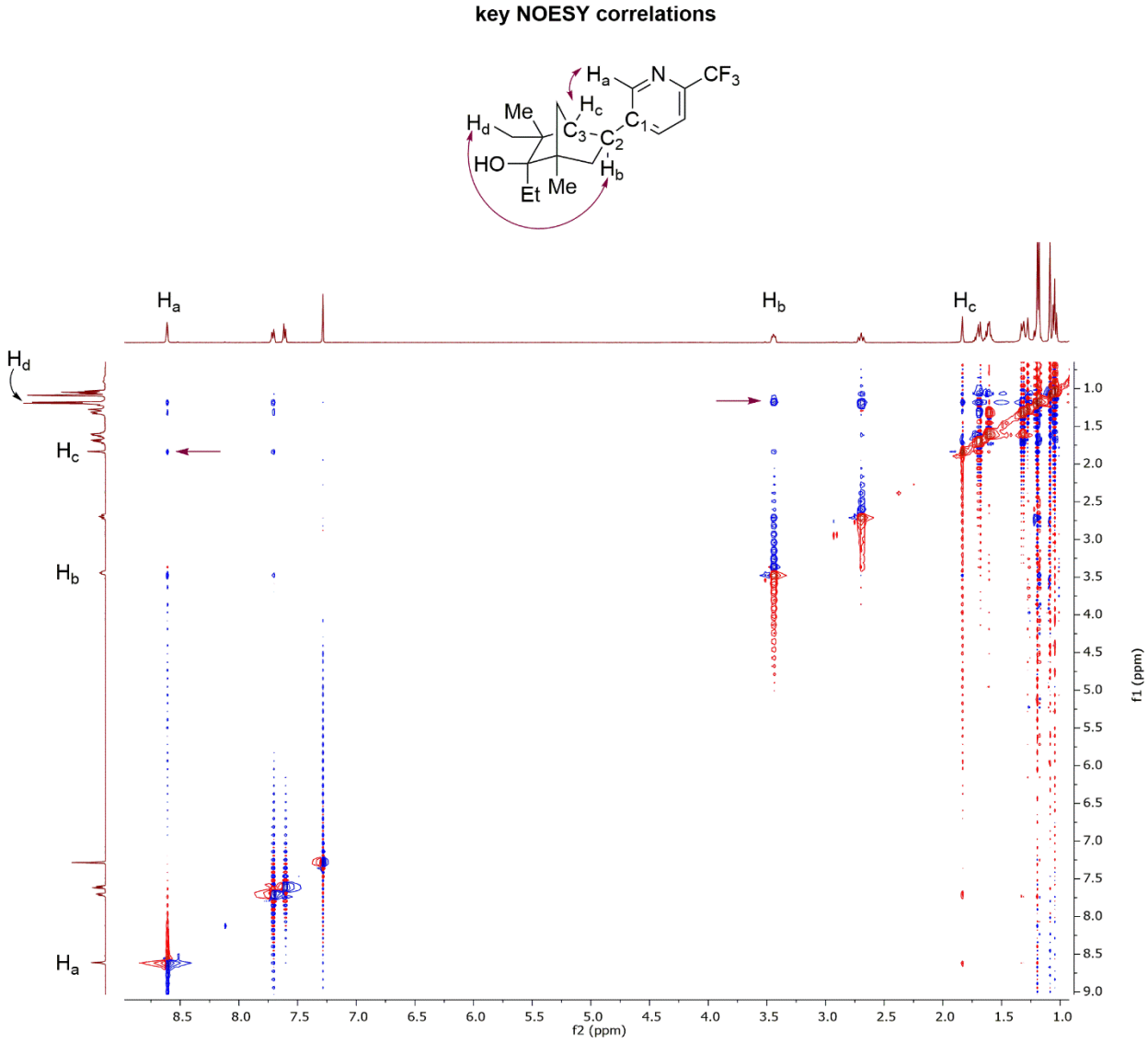
^{19}F NMR (376 MHz, $CDCl_3$) - (78)


key HSQC correlations
Ha
N
CF3
Hc
Me
Hd
C1
C3
C2
HO
Hb
Et
Me
Hb
Hc
C2
C3
f2 (ppm)
f1 (ppm)

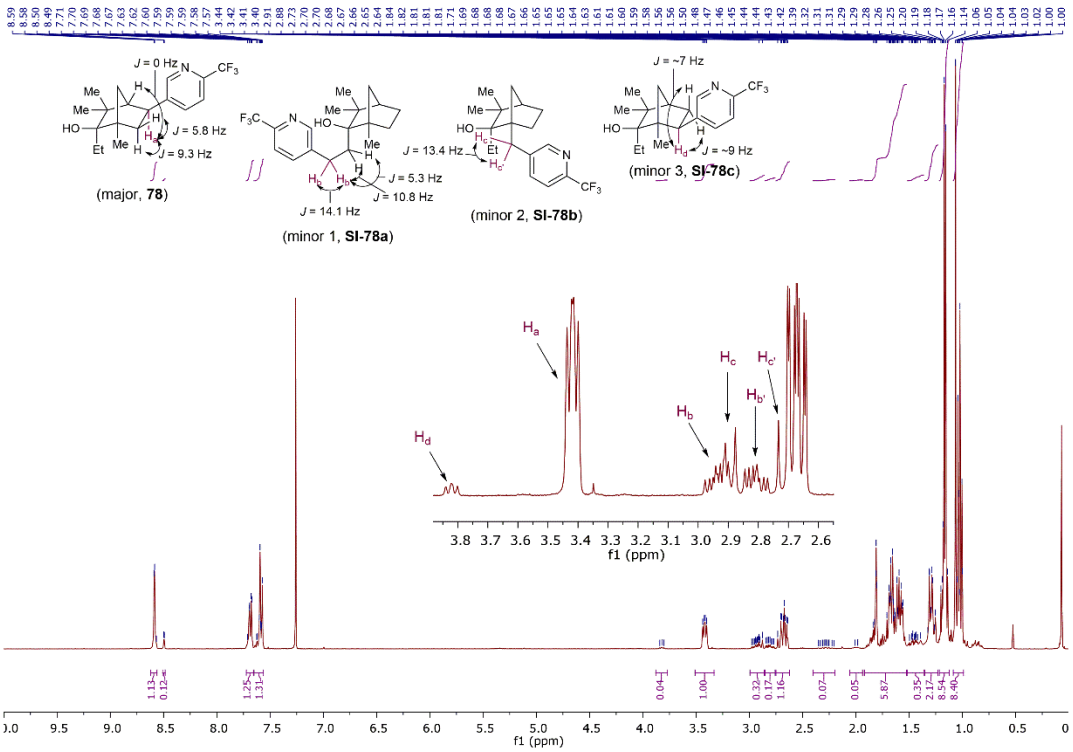
HSQC - (78)


key HMBC correlation
Ha
N
CF3
Hc
C1
Hd
Me
C3
C2
HO
Hb
Et
Me
Hc
C1
f2 (ppm)
f1 (ppm)

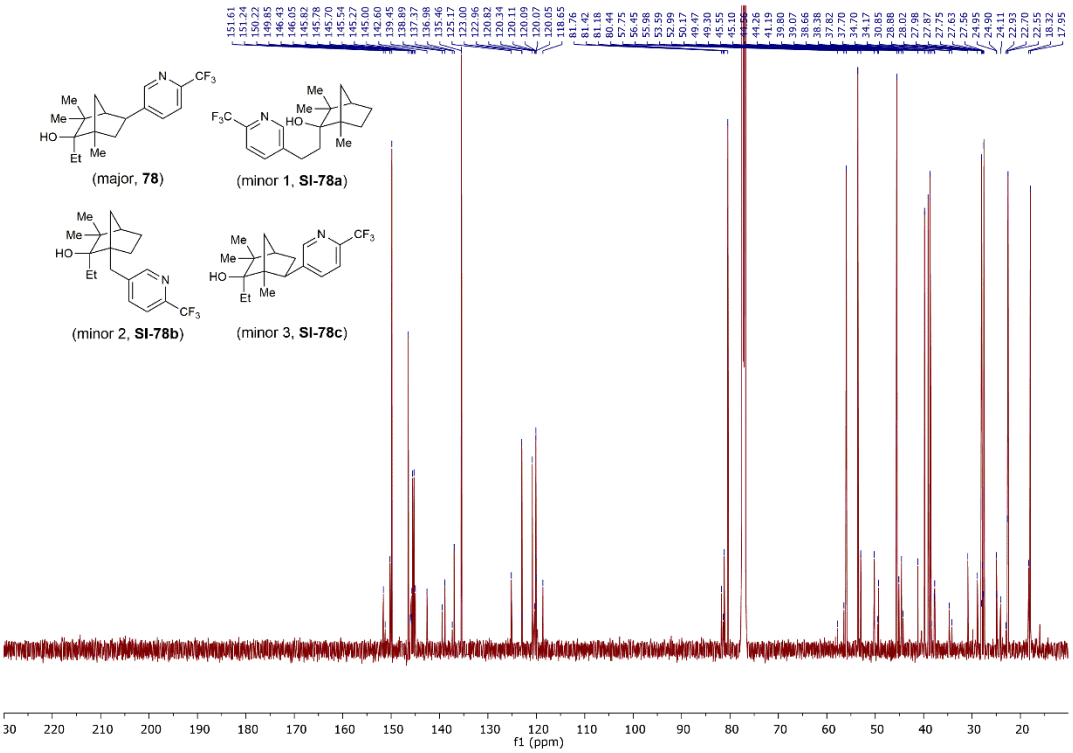
HMBC - (78)


key NOESY correlations
Ha
N
CF3
Hc
Me
Hd
C3
C2
C1
HO
Hb
Et
Me
Ha
Hb
Hc
Hd
Hc
Hb
Ha
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
f1 (ppm)

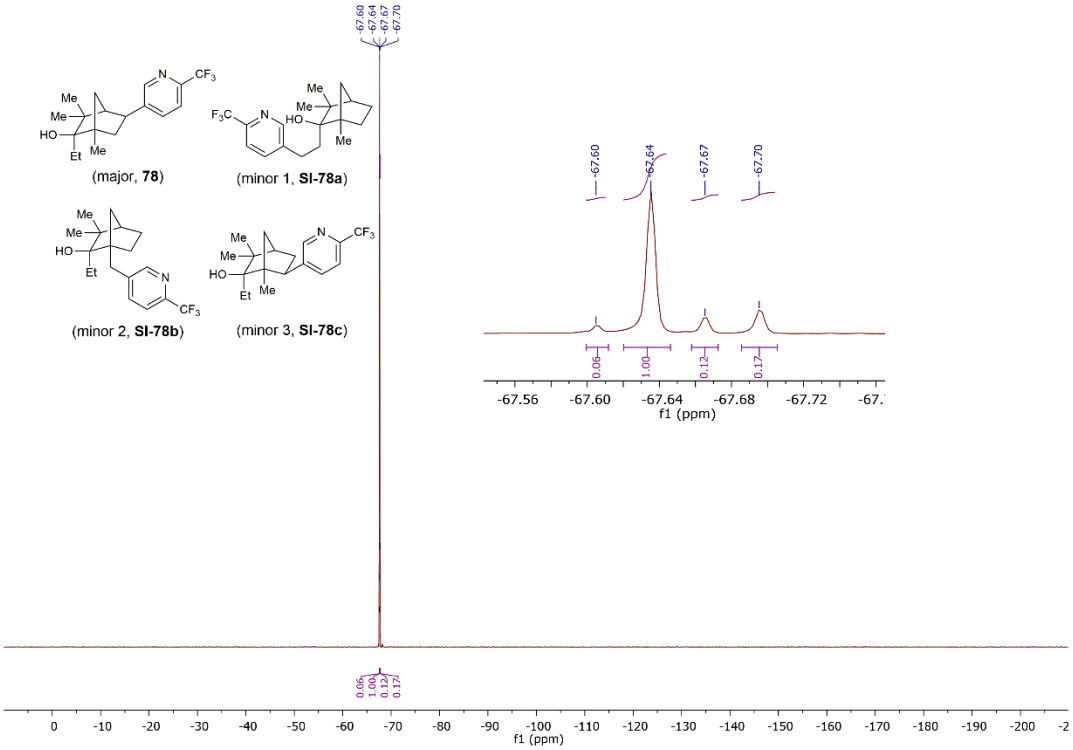
NOESY - (78)



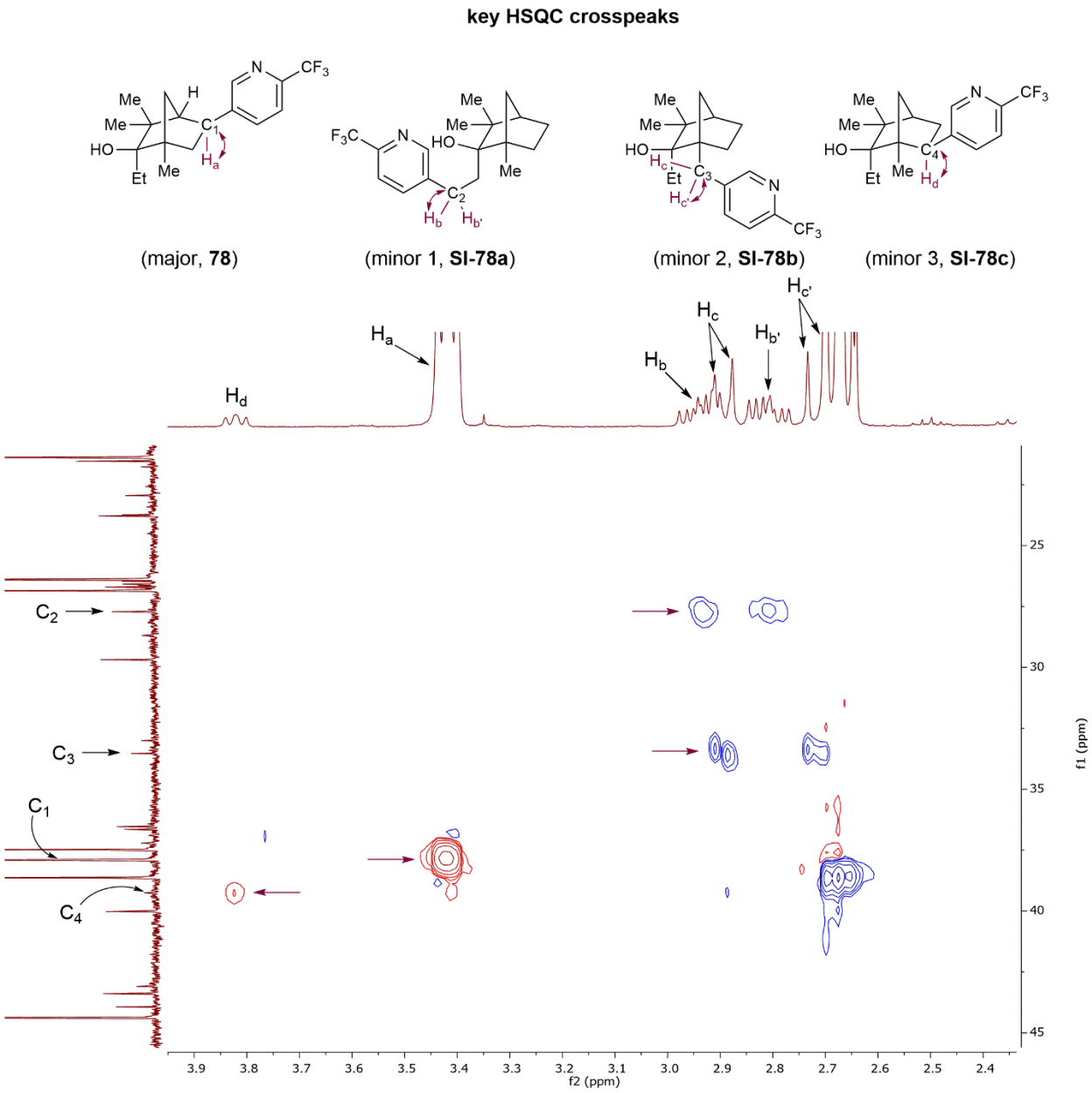
^{1}H NMR (400 MHz, $CDCl_3$) - (**78**, **SI-78a**, **SI-78b**, and **SI-78c**, isolated mixture from silica chromatography)



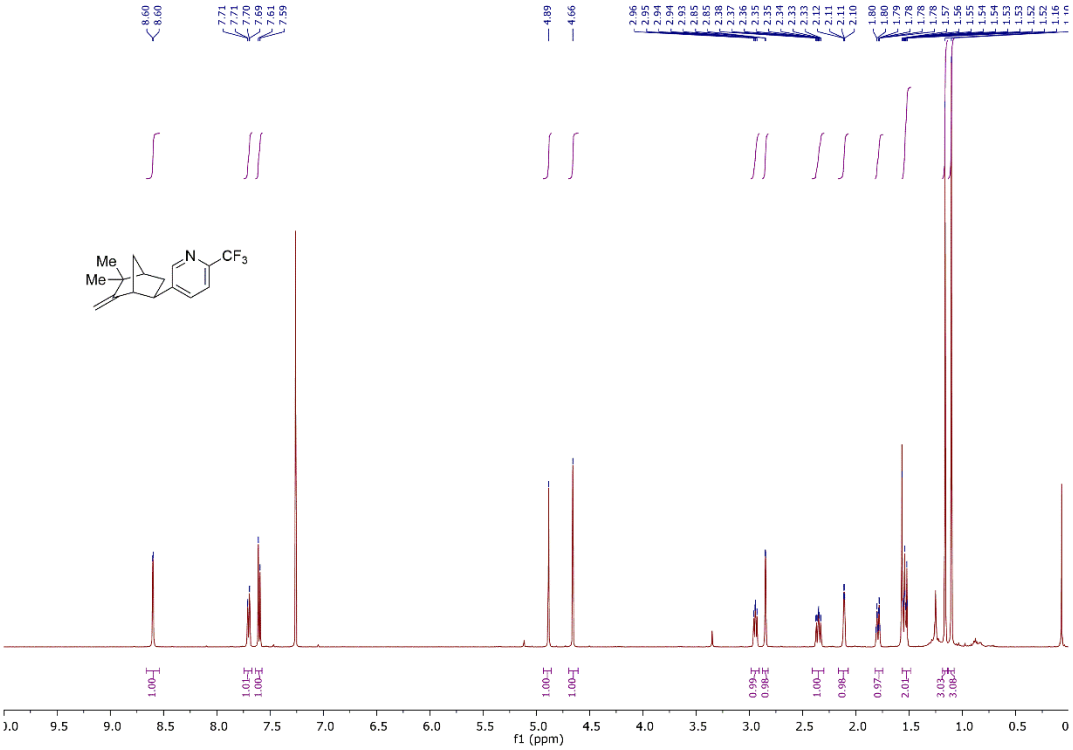
^{13}C NMR (126 MHz, $CDCl_3$) - (**78**, **SI-78a**, **SI-78b**, and **SI-78c**, isolated mixture from silica chromatography)



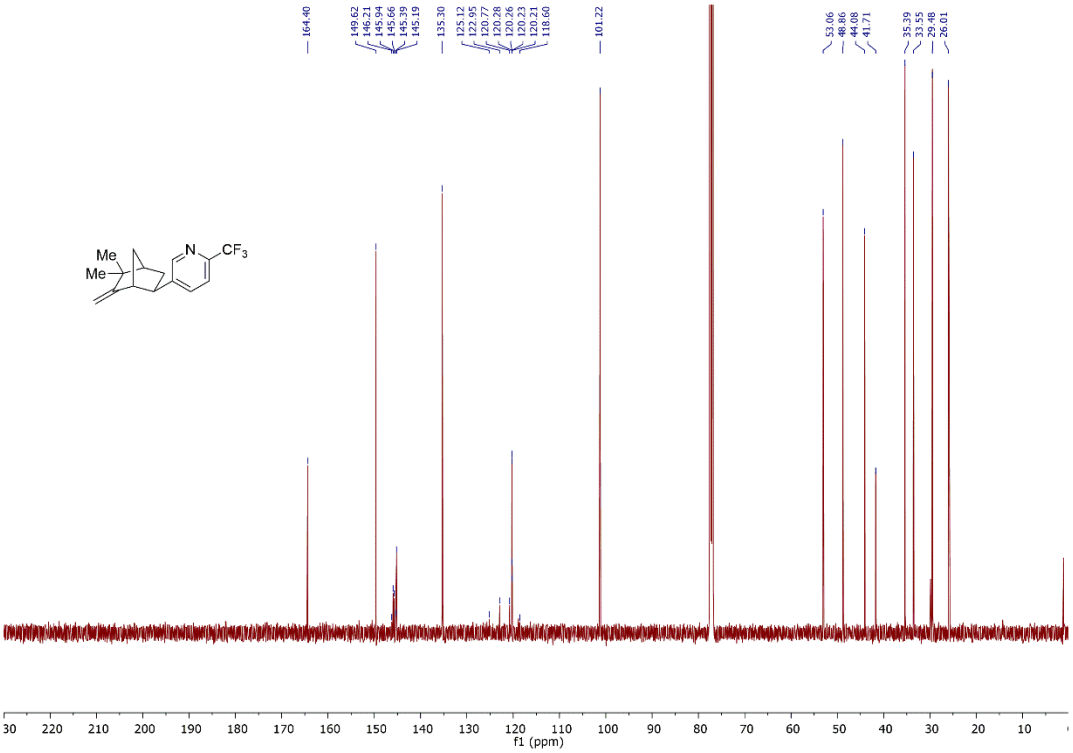
^{19}F NMR (376 MHz, $CDCl_3$) - (**78**, **SI-78a**, **SI-78b**, and **SI-78c**, isolated mixture from silica chromatography)



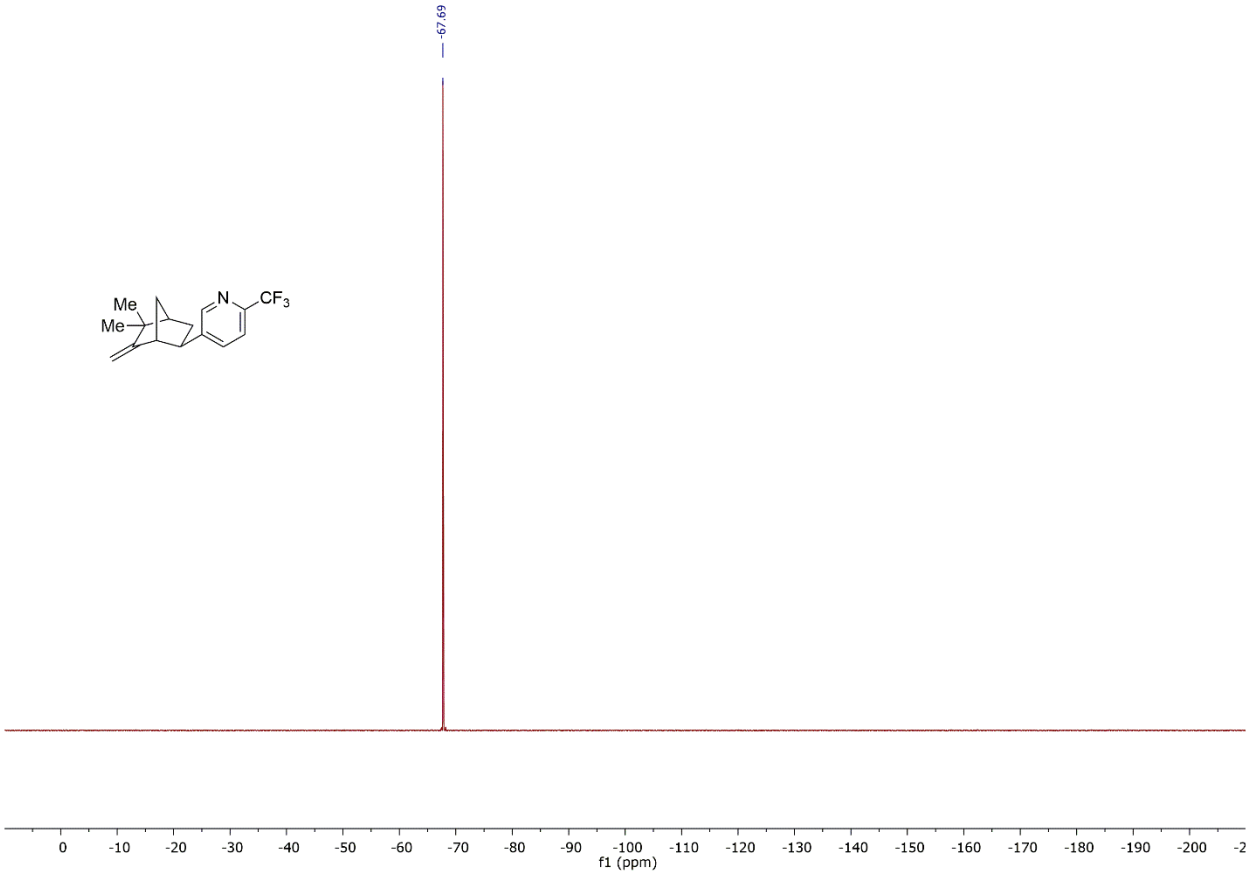
HSQC - (**78**, **SI-78a**, **SI-78b**, and **SI-78c**, isolated mixture from silica chromatography)



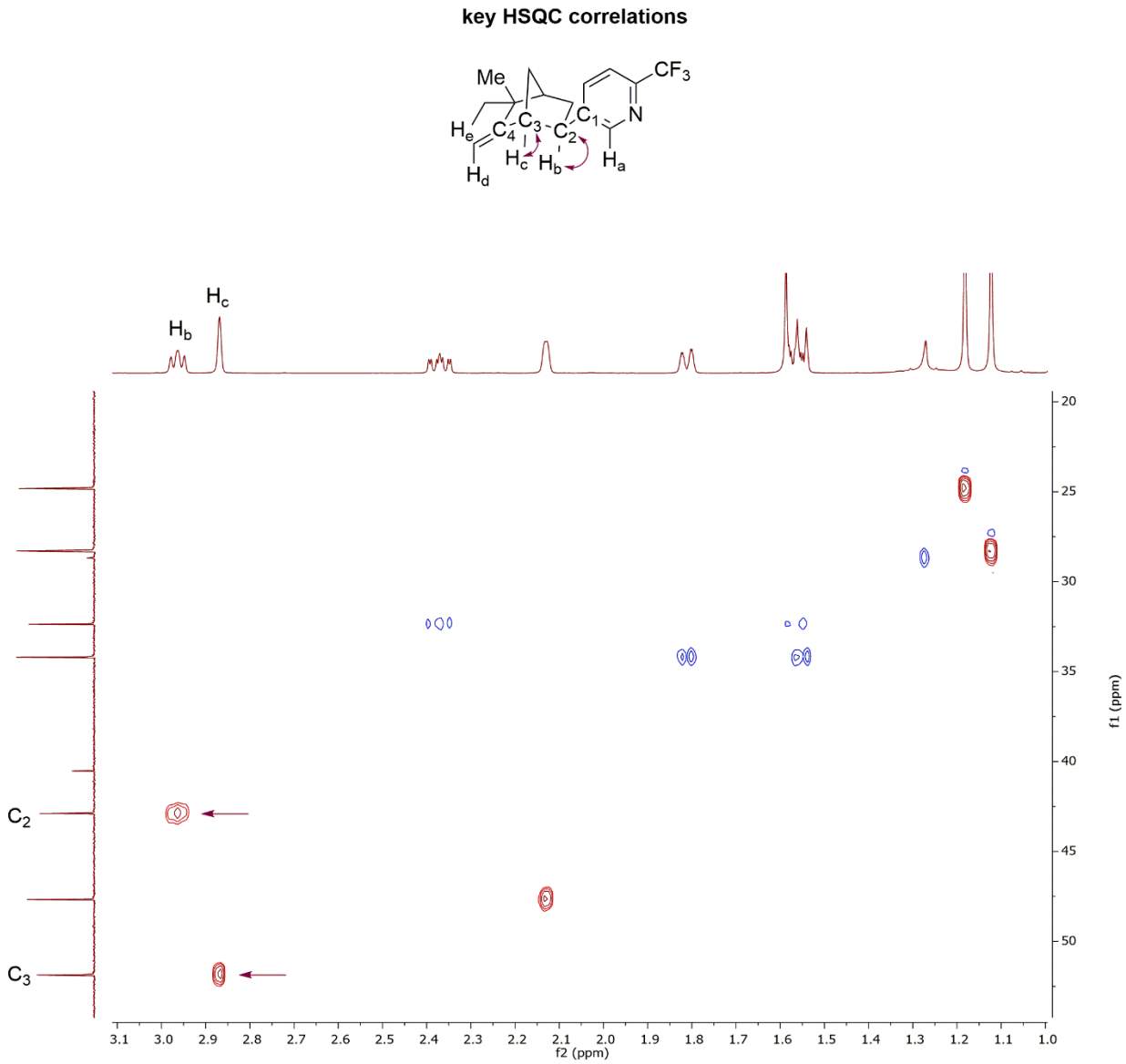
^{1}H NMR (500 MHz, $CDCl_3$) - (79)



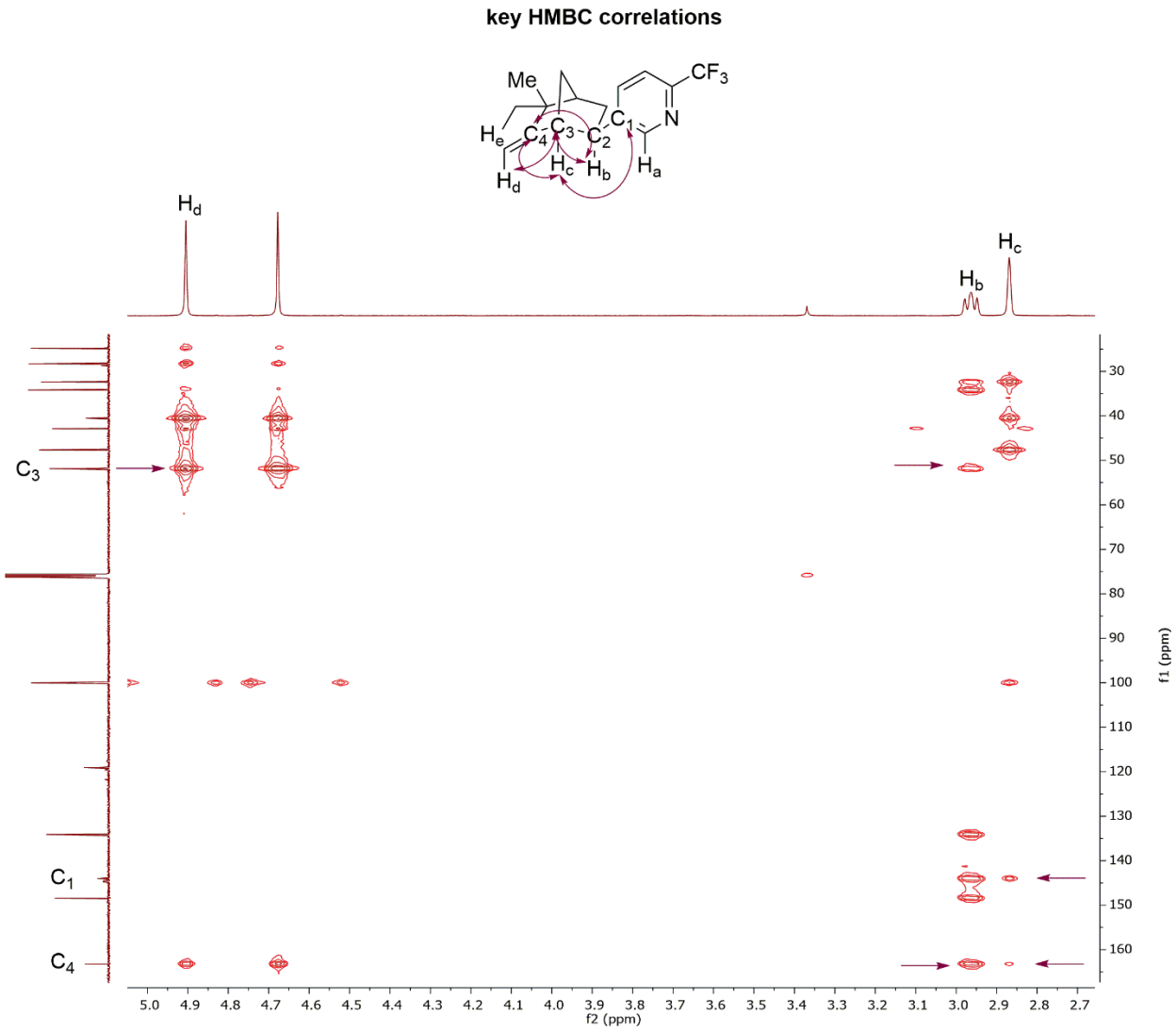
^{13}C NMR (126 MHz, $CDCl_3$) – (79)



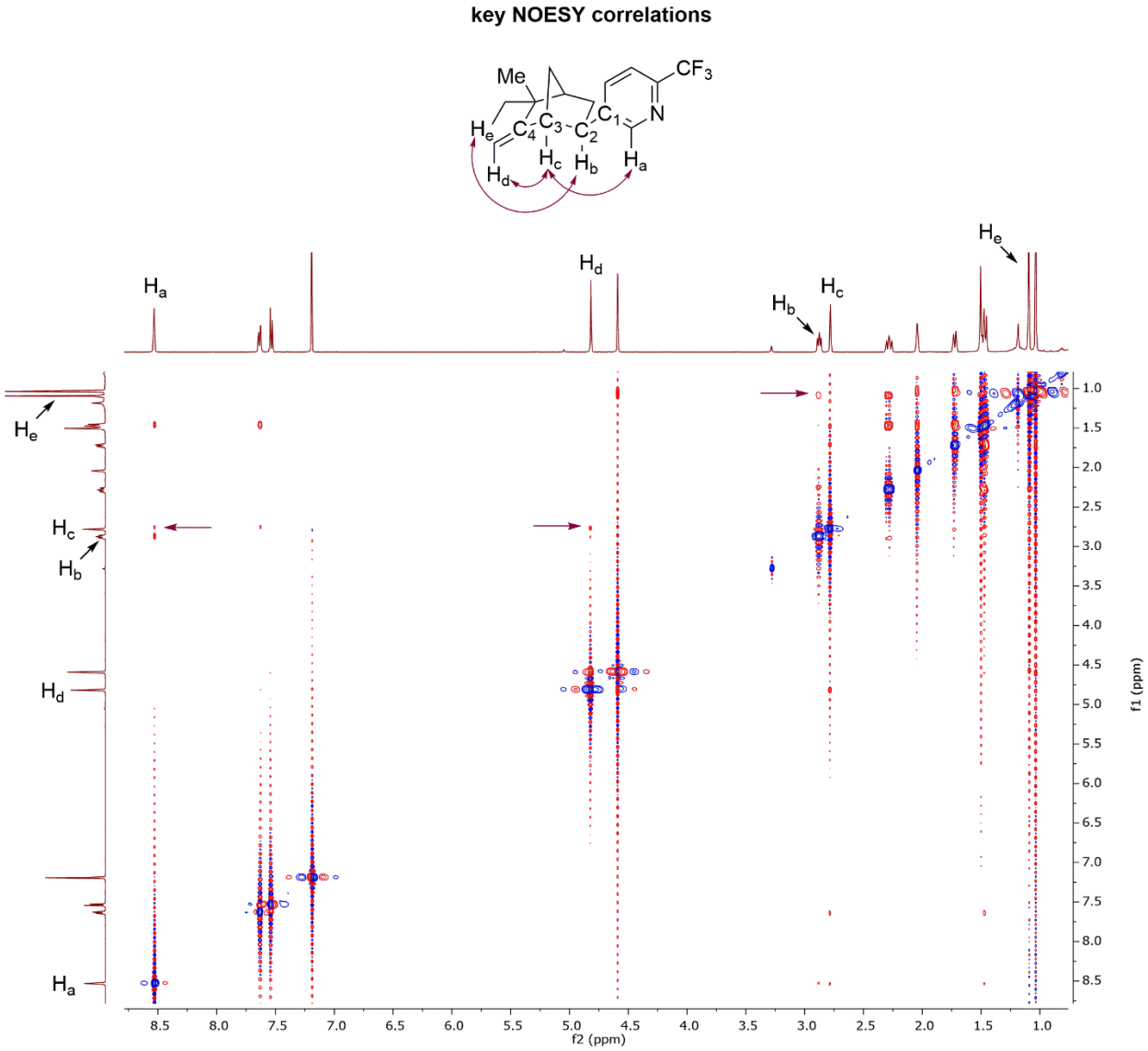
^{19}F NMR (376 MHz, CDCl3) - (79)


key HSQC correlations
Me
CF3
He
C4
C3
C2
C1
N
Hc
Hb
Ha
Hd
Hc
Hb
C2
C3
3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0
f2 (ppm)
20 25 30 35 40 45 50
f1 (ppm)

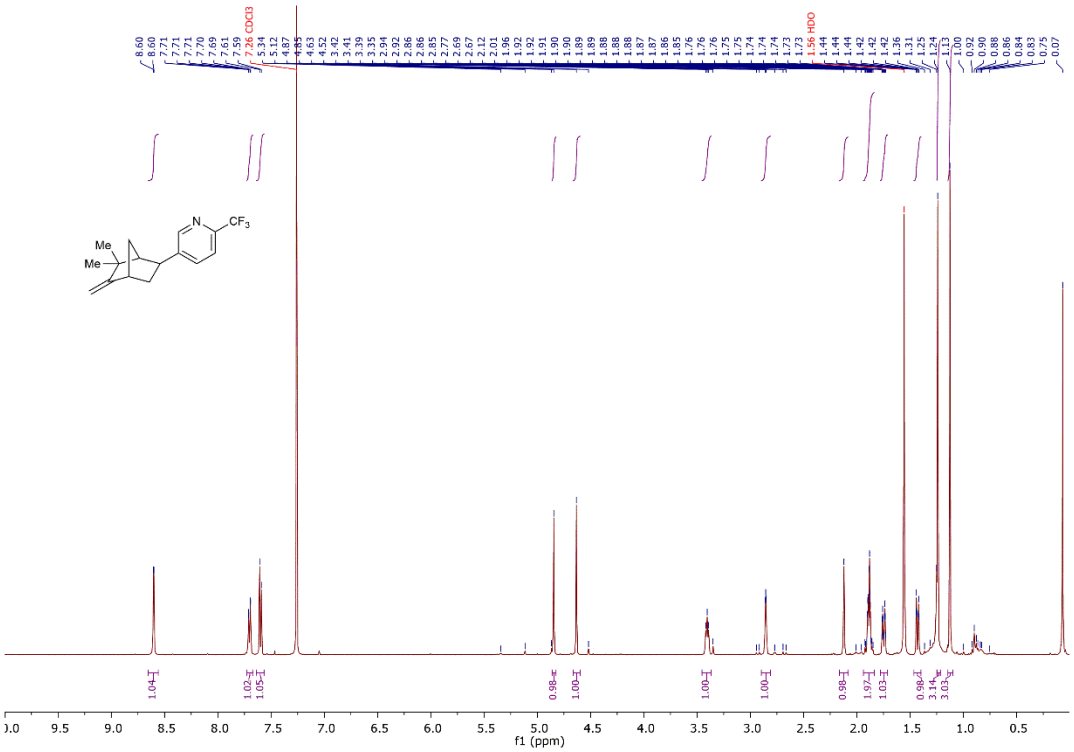
HSQC - (79)


key HMBC correlations
Me
CF3
He
C4
C3
C2
C1
N
Hc
Hb
Ha
Hd
Hd
Hb
Hc
C3
C1
C4
5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7
f2 (ppm)
30 40 50 60 70 80 90 100 110 120 130 140 150 160
f1 (ppm)

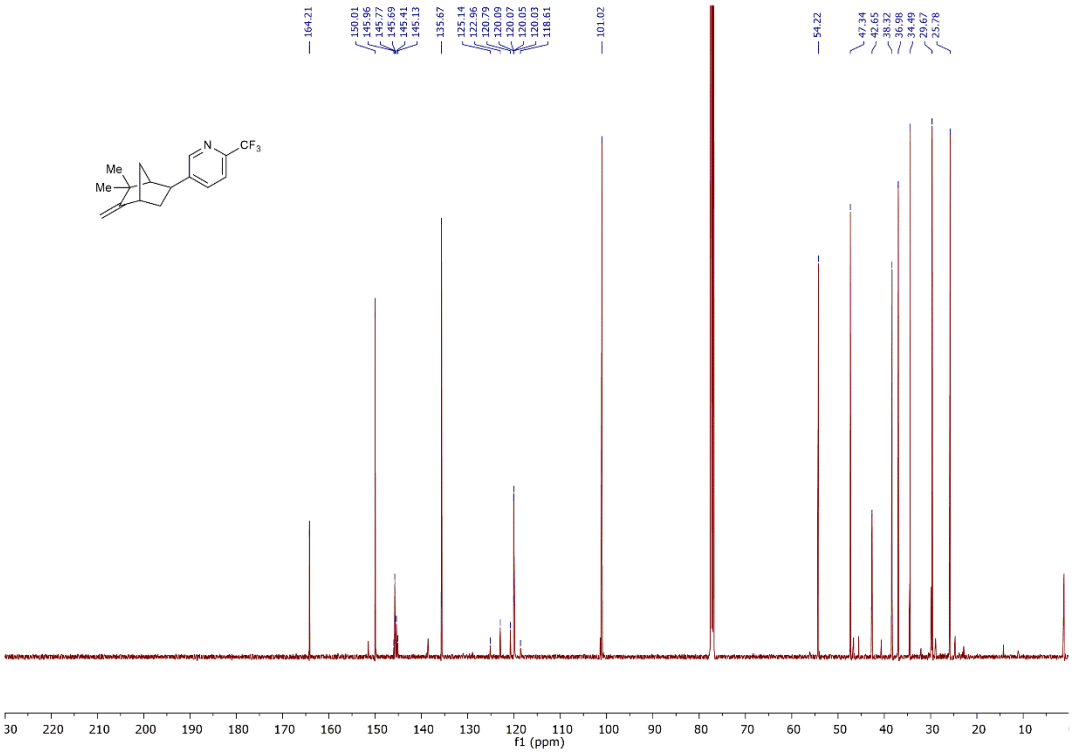
HMBC - (79)


key NOESY correlations
Me
CF3
He
C4
C3
C2
C1
N
Hc
Hb
Ha
Hd
Ha
Hd
Hb
Hc
He
He
Hc
Hb
Hd
Ha
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
f1 (ppm)

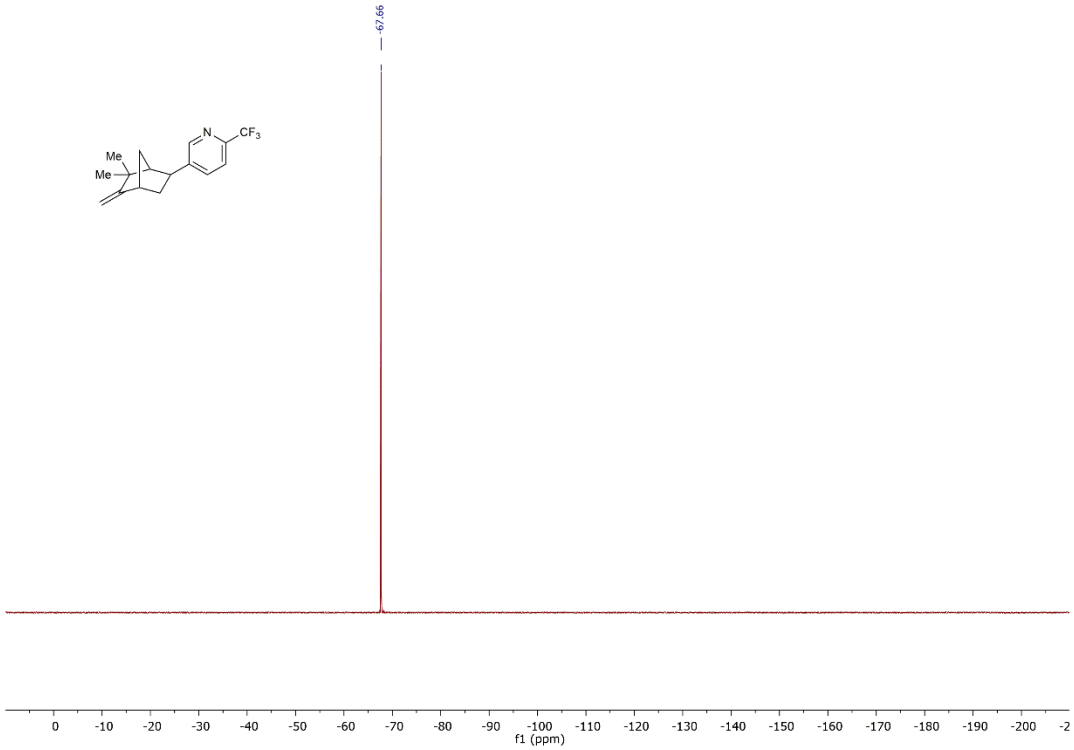
NOESY - (79)



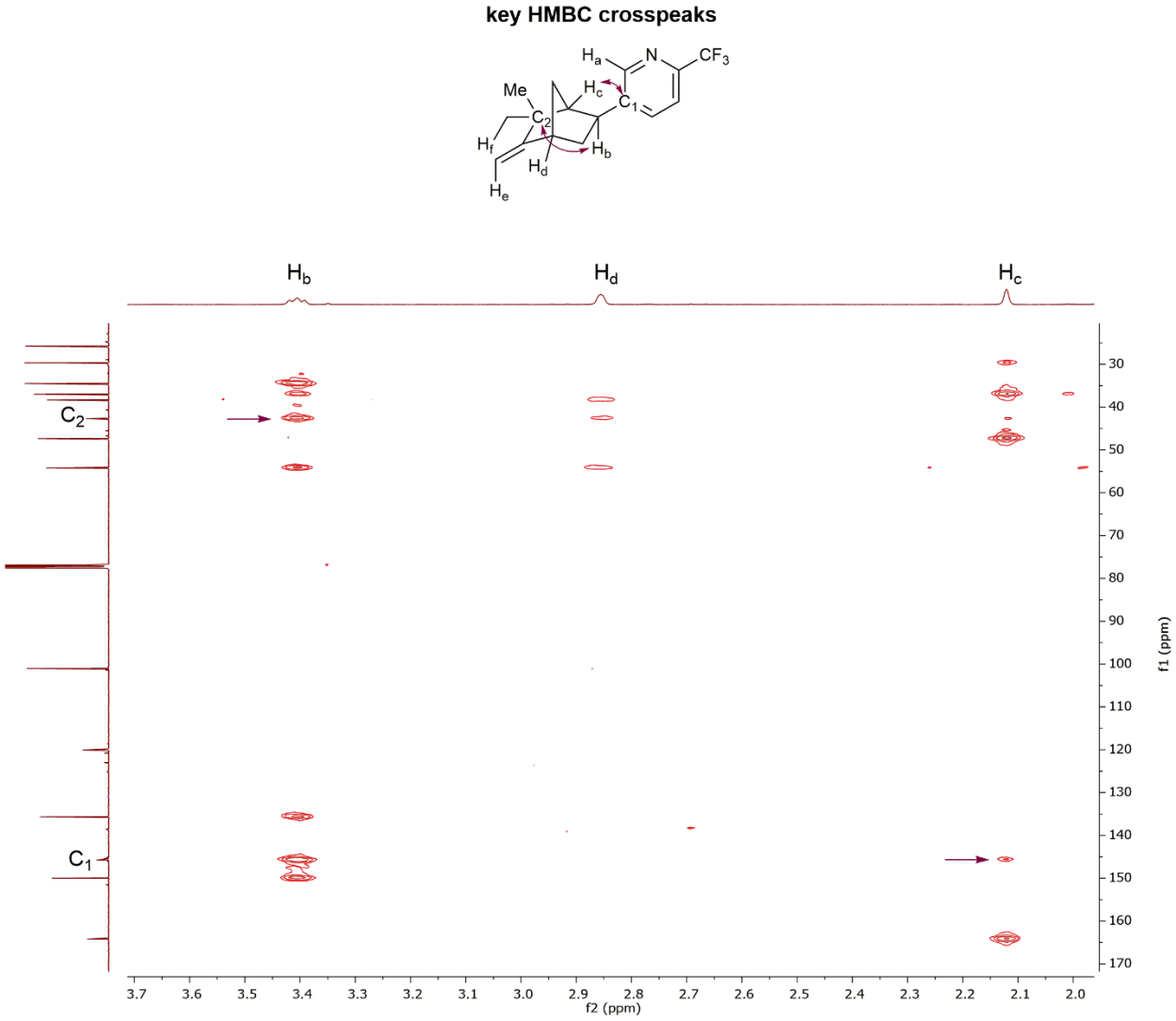
^{1}H NMR (500 MHz, $CDCl_3$) - (SI-79)



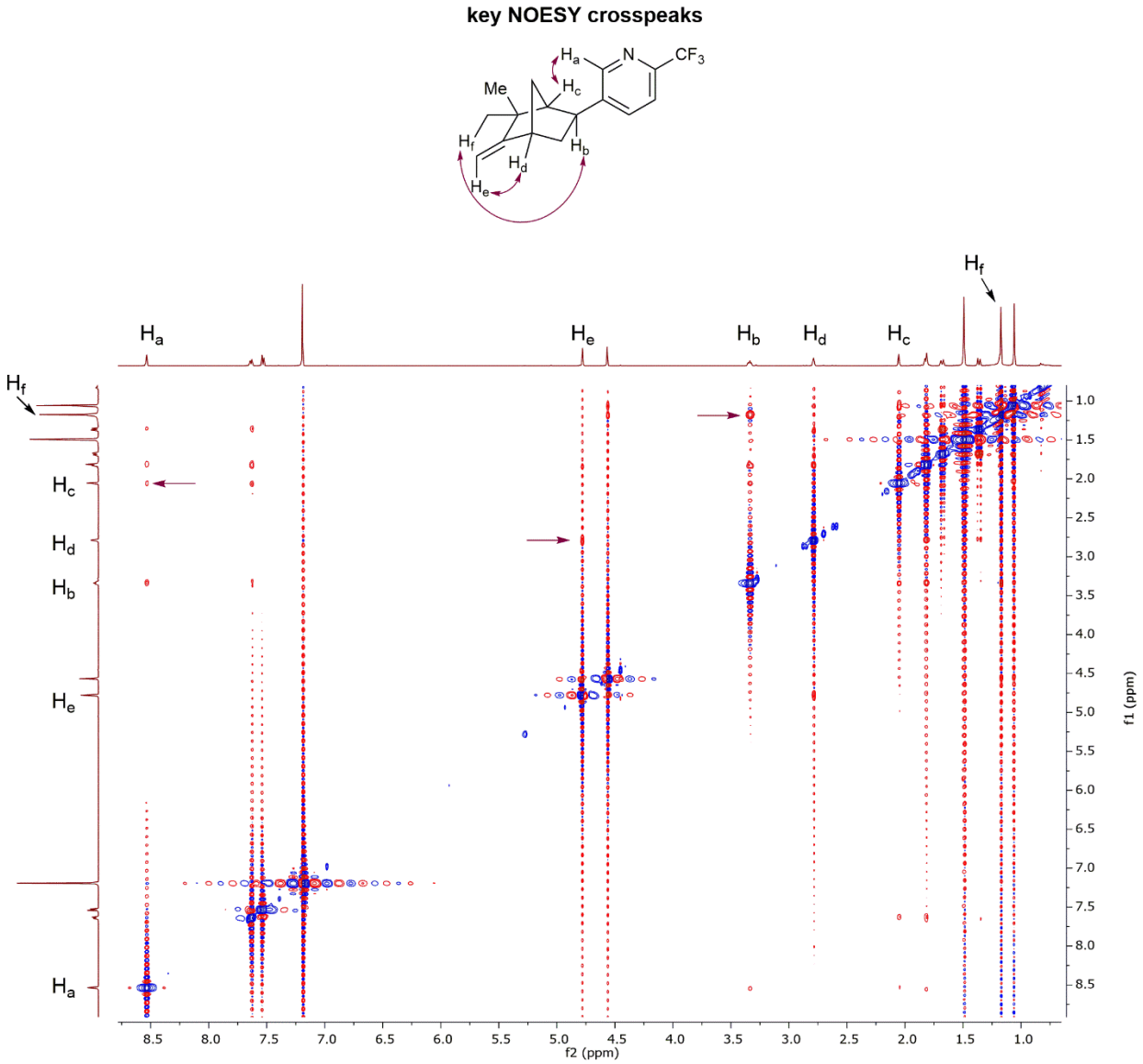
^{13}C NMR (126 MHz, $CDCl_3$) – (SI-79)



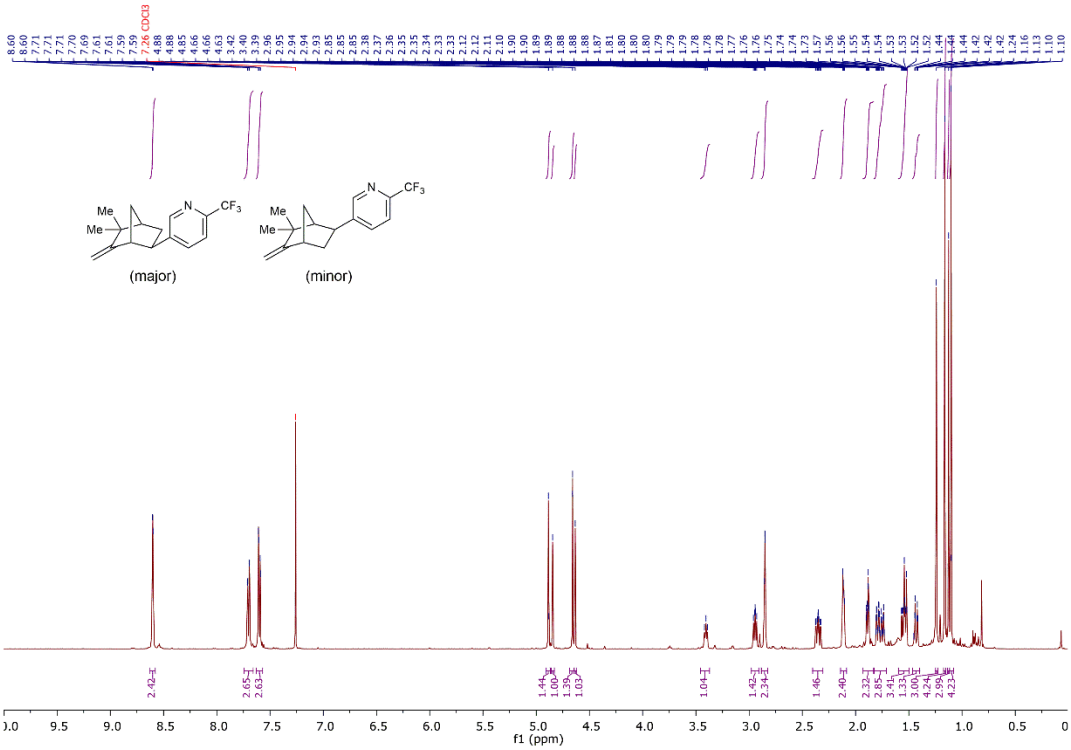
^{19}F NMR (376 MHz, CDCl3) - (SI-79)


key HMBC crosspeaks
Ha
N
CF3
Me
Hc
C1
C2
Hf
Hb
Hd
He
Hb
Hd
Hc
C2
C1
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
f2 (ppm)
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
f1 (ppm)

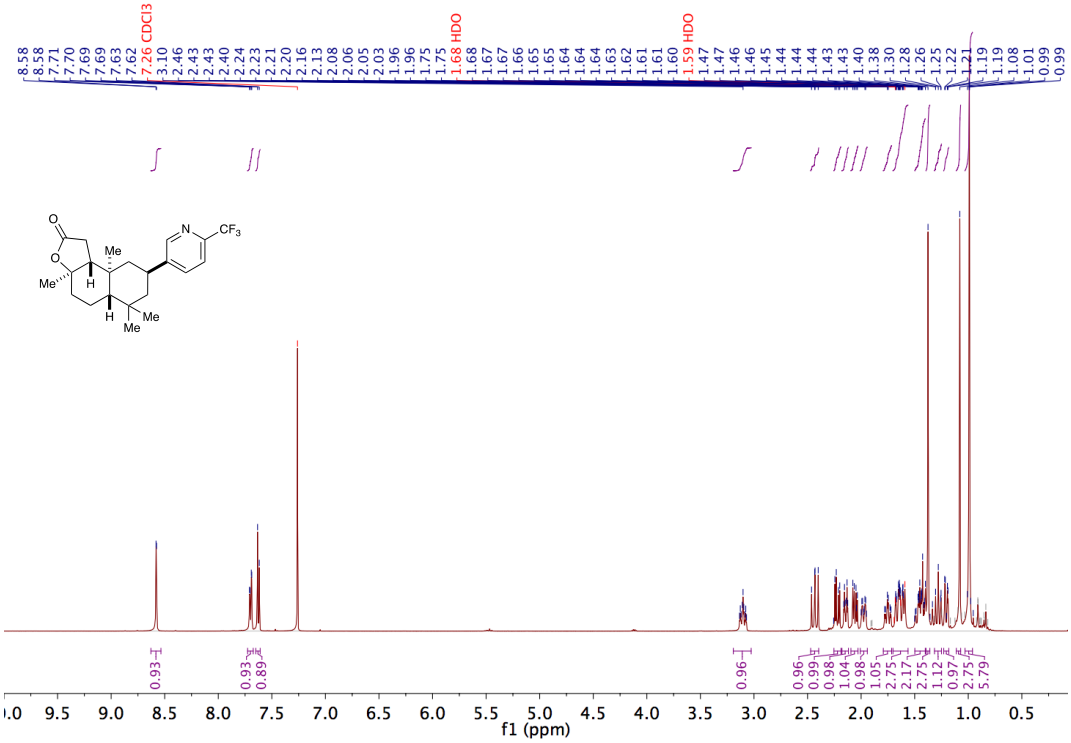
HMBC - (SI-79)


key NOESY crosspeaks
Ha
N
CF3
Me
Hc
Hf
Hb
Hd
He
Ha
He
Hb
Hd
Hc
Hf
Hf
Hc
Hd
Hb
He
Ha
f2 (ppm)
f1 (ppm)

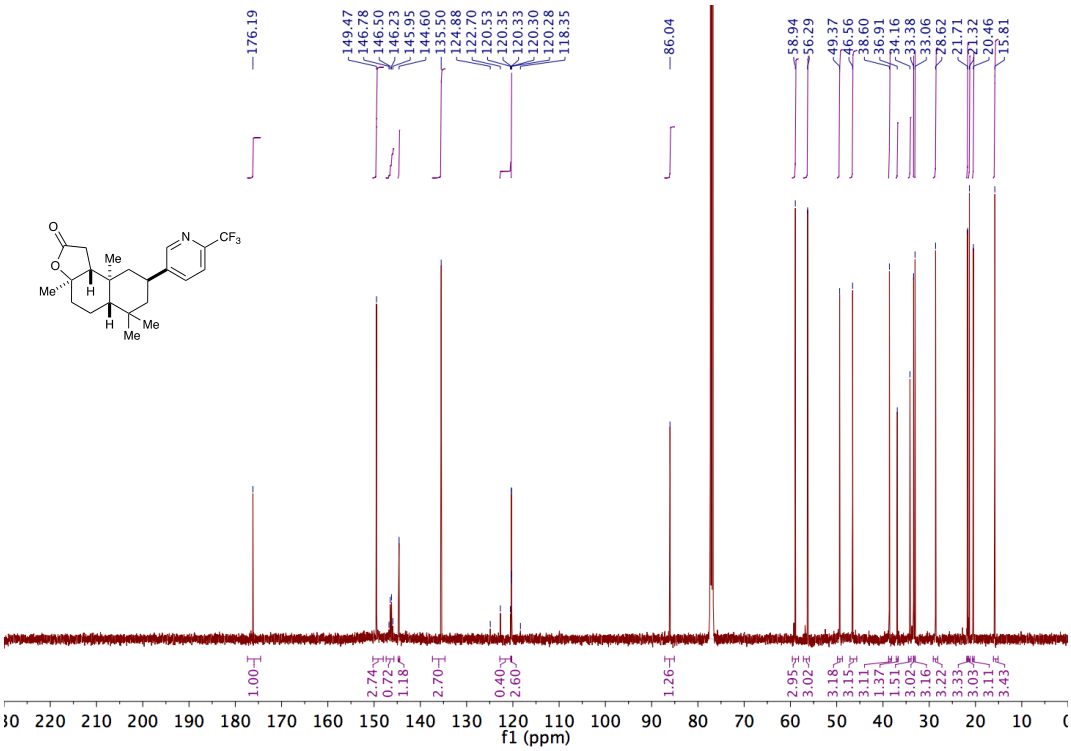
NOESY - (SI-79)



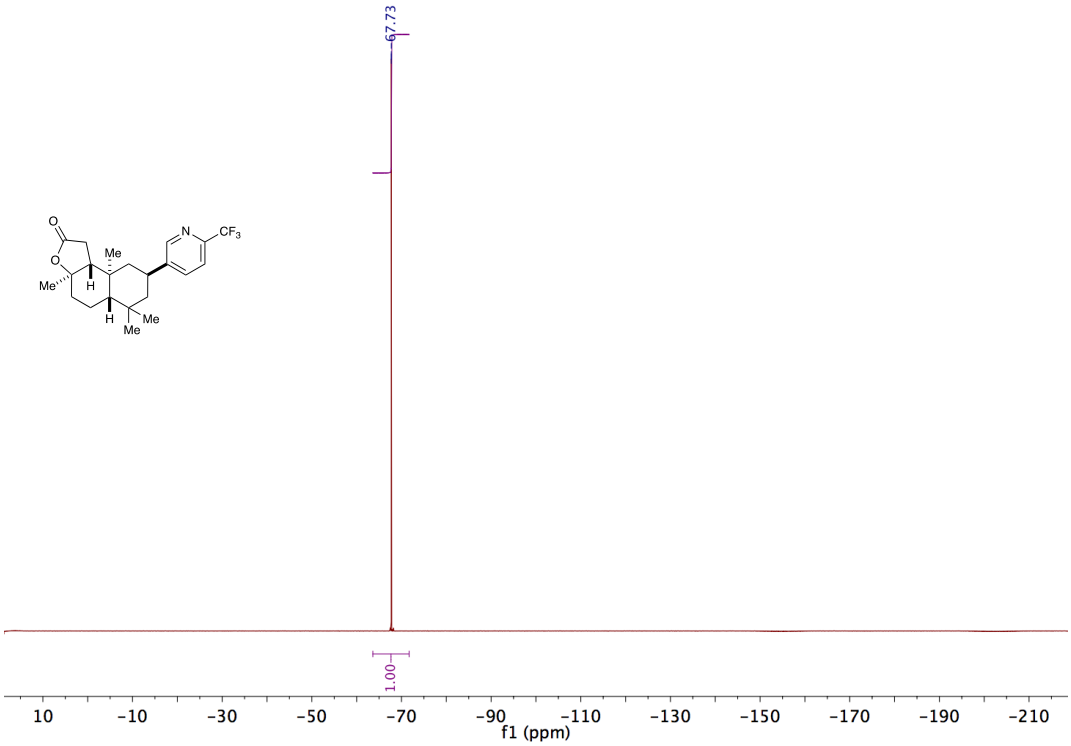
^{1}H NMR (500 MHz, $CDCl_3$) - (**79** and **SI-79**, isolated mixture from silica chromatography)



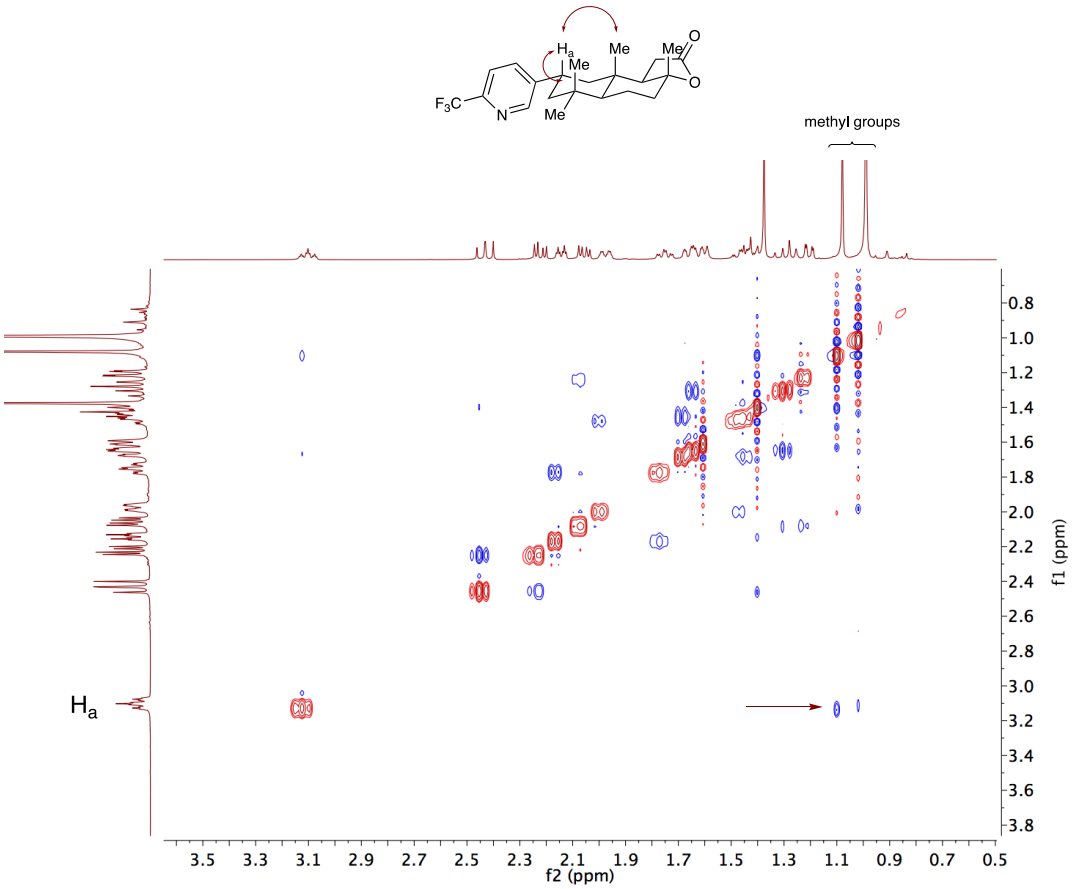
^{1}H NMR (500 MHz, $CDCl_3$) – (80a)



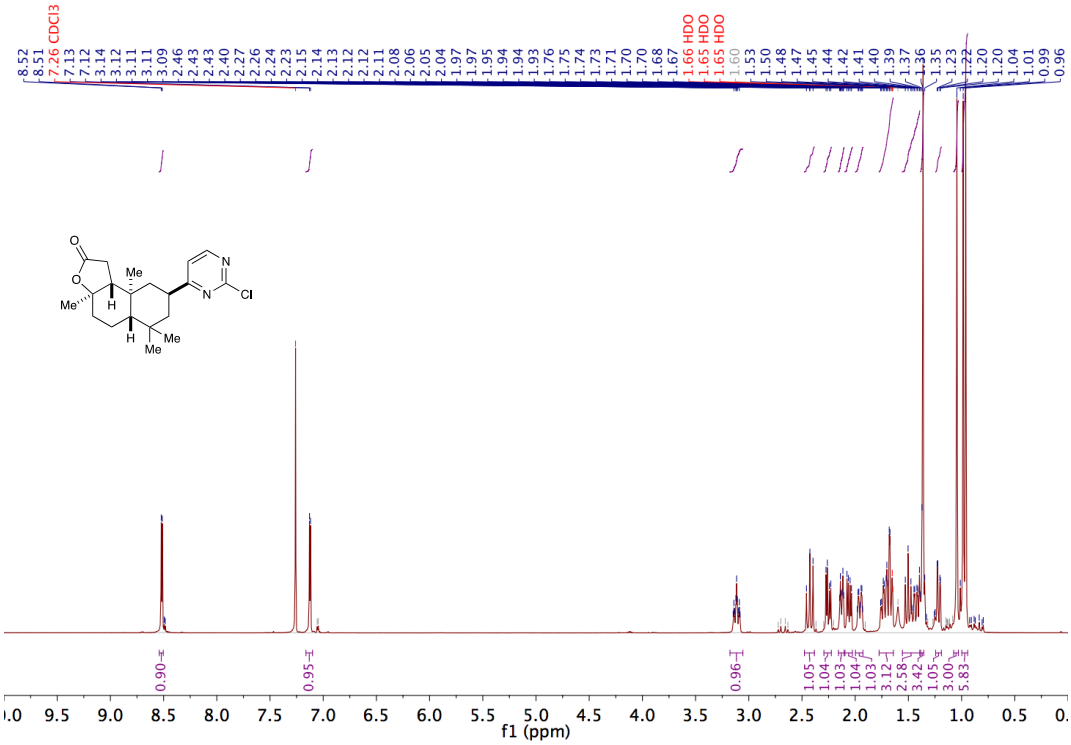
^{13}C NMR (126 MHz, $CDCl_3$) – (80a)



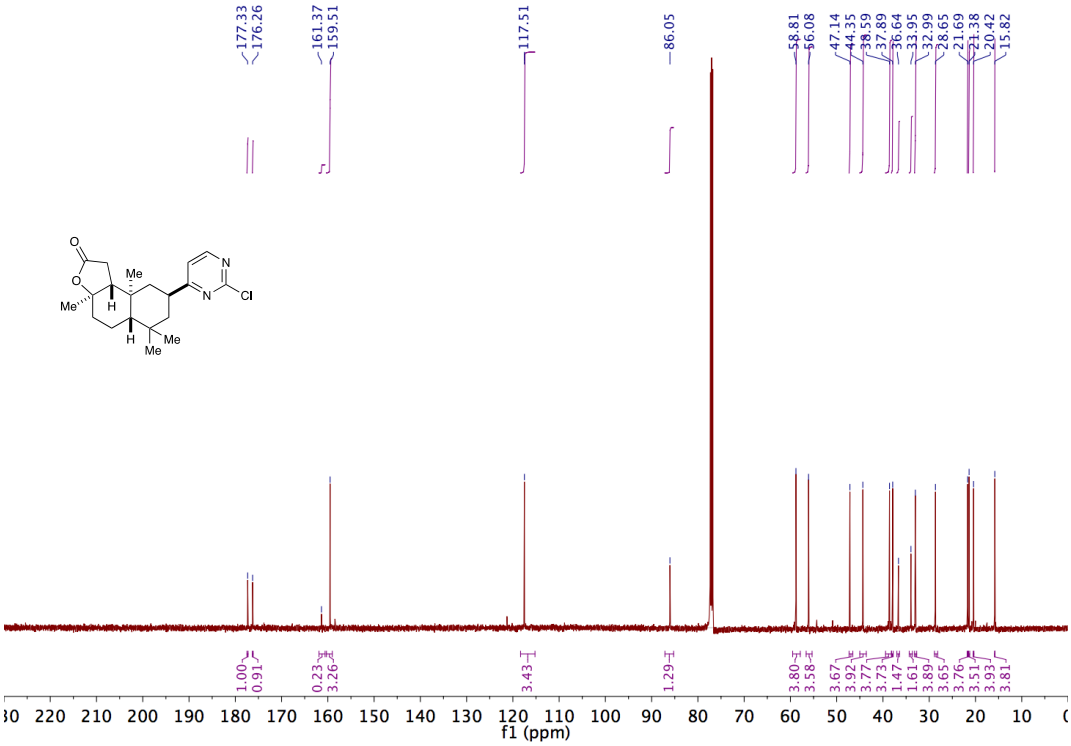
^{19}F NMR (376 MHz, $CDCl_3$) – (80a)



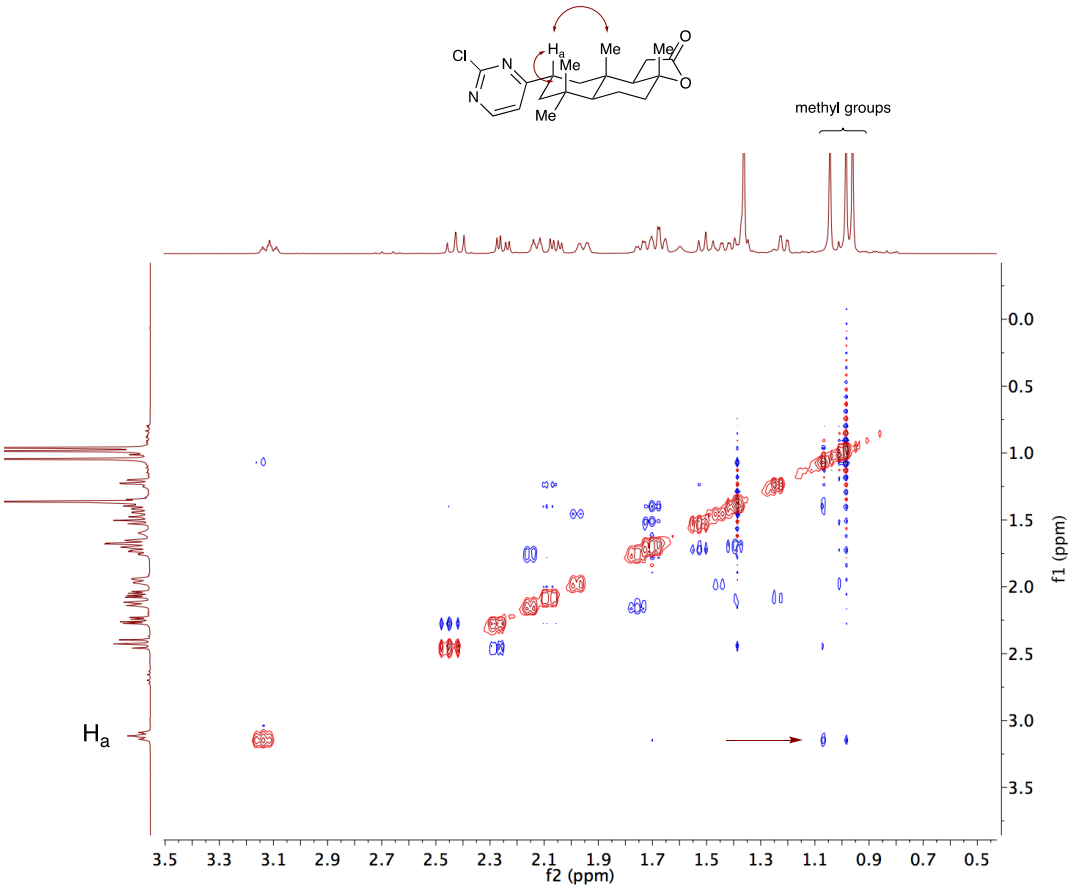
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (80a)



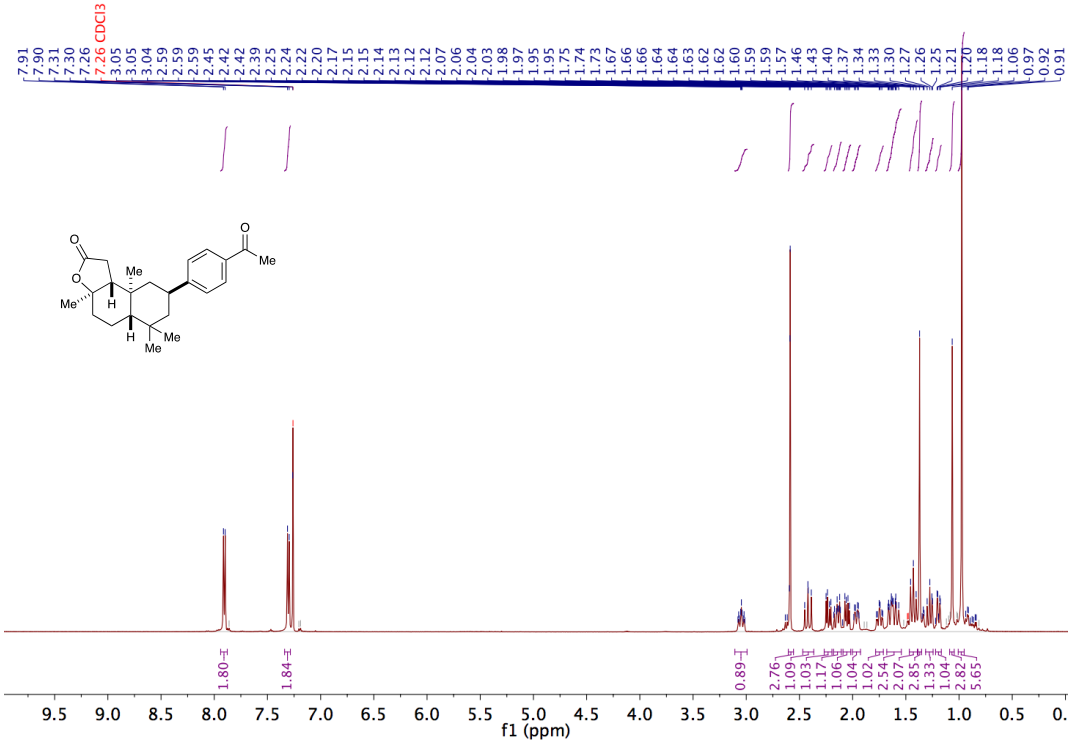
^{1}H NMR (500 MHz, $CDCl_3$) – (80b)



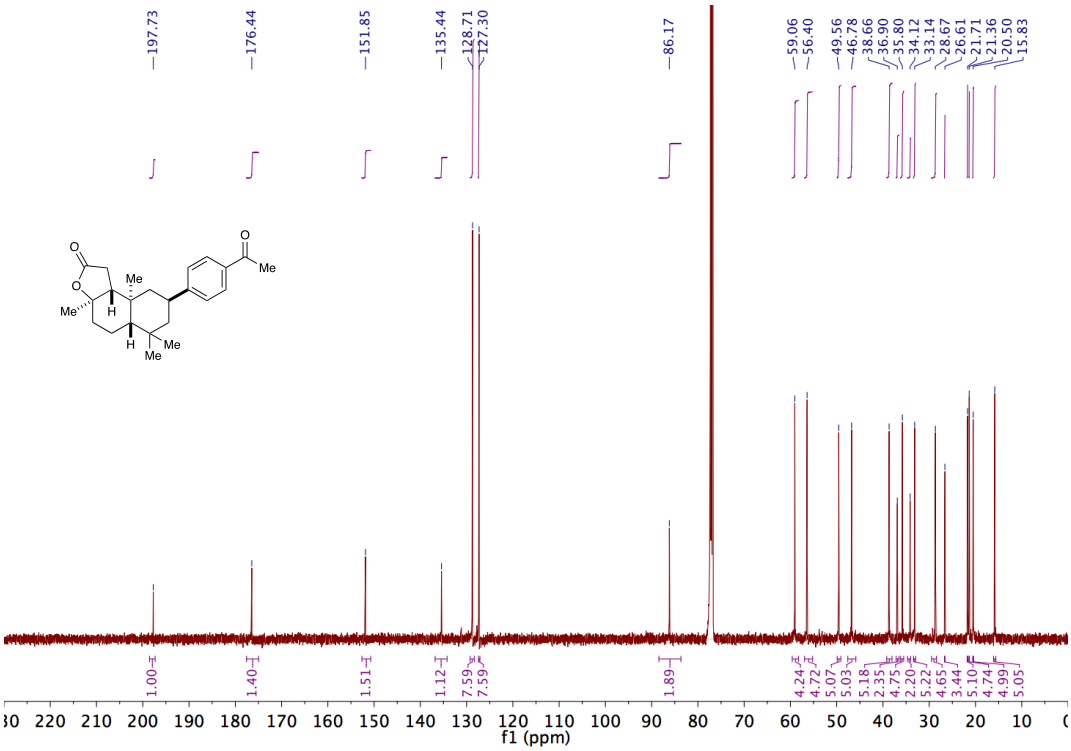
^{13}C NMR (126 MHz, $CDCl_3$) –(80b)



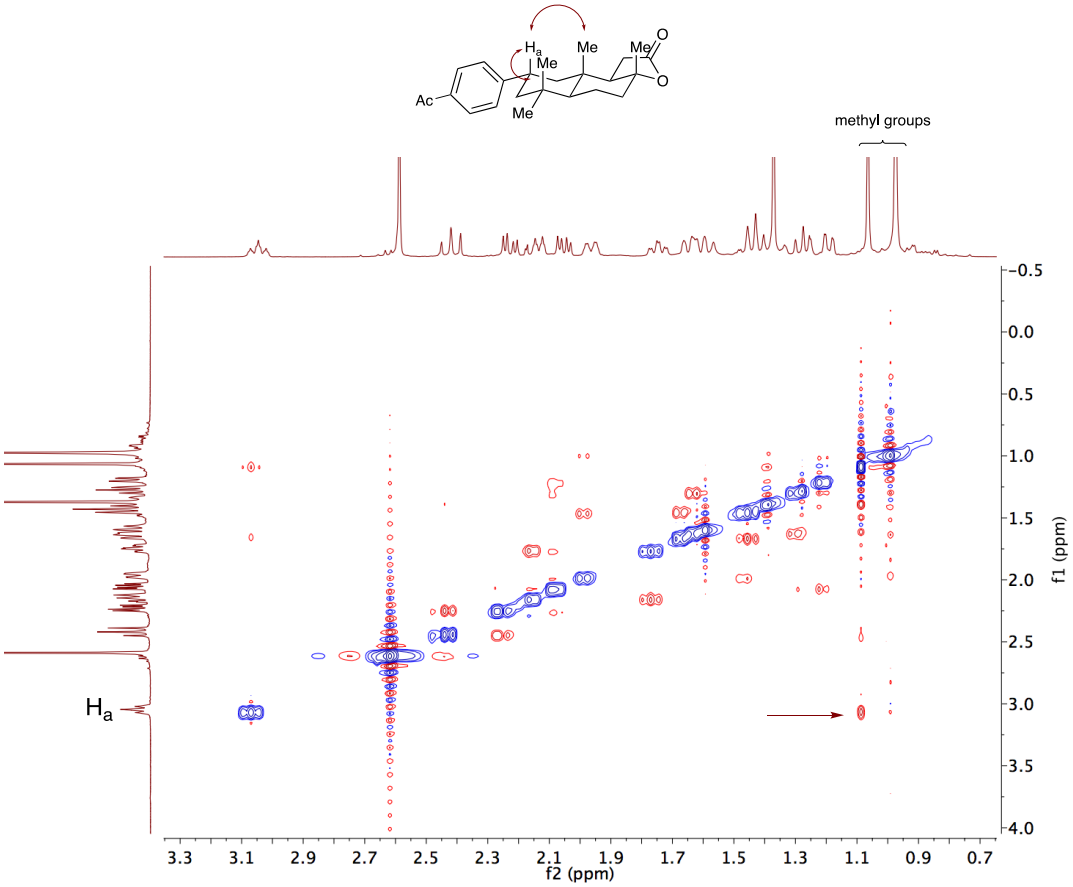
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (80b)



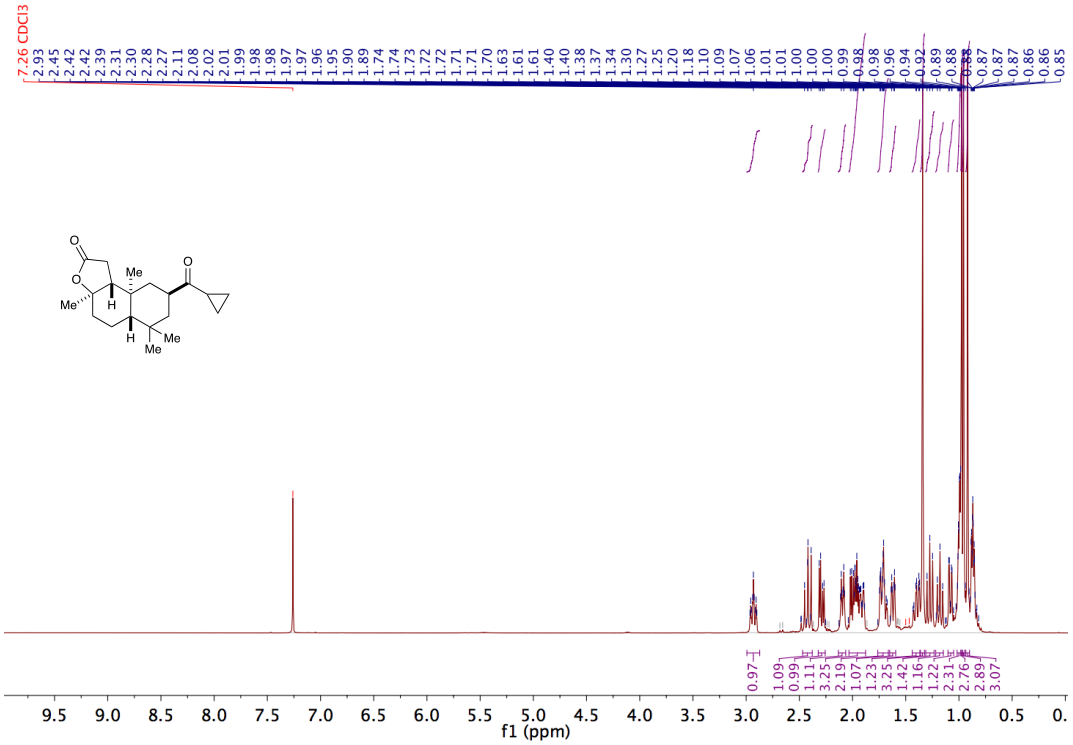
^{1}H NMR (500 MHz, $CDCl_3$) – (80c)



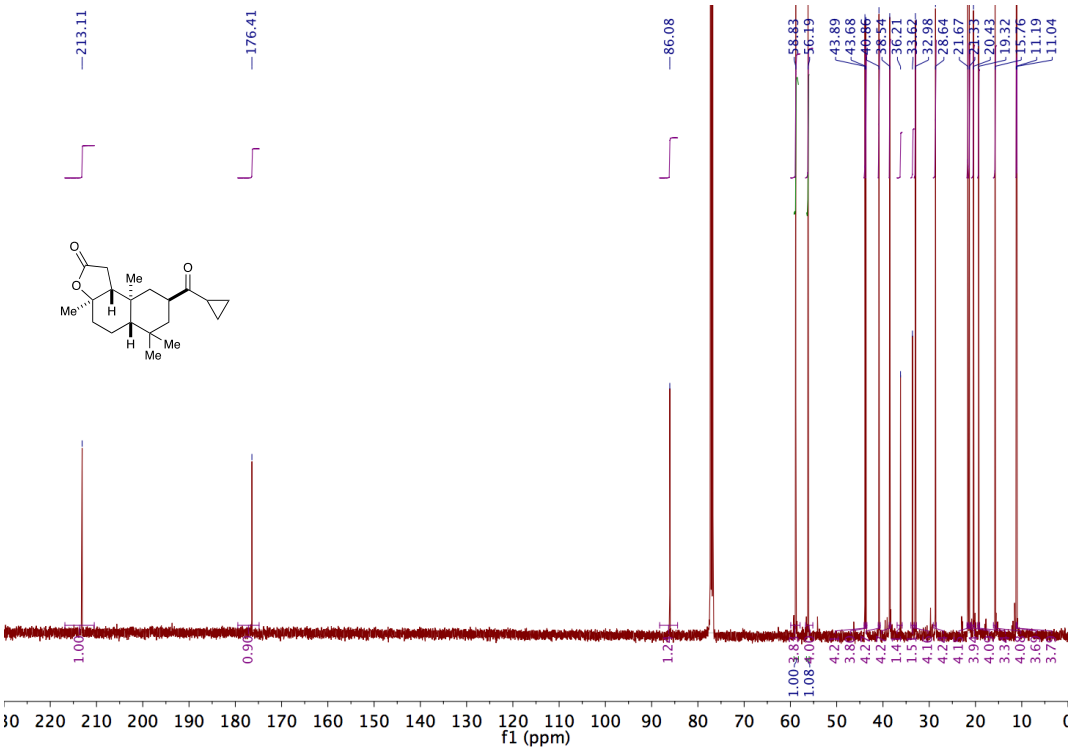
^{13}C NMR (126 MHz, $CDCl_3$) – (80c)



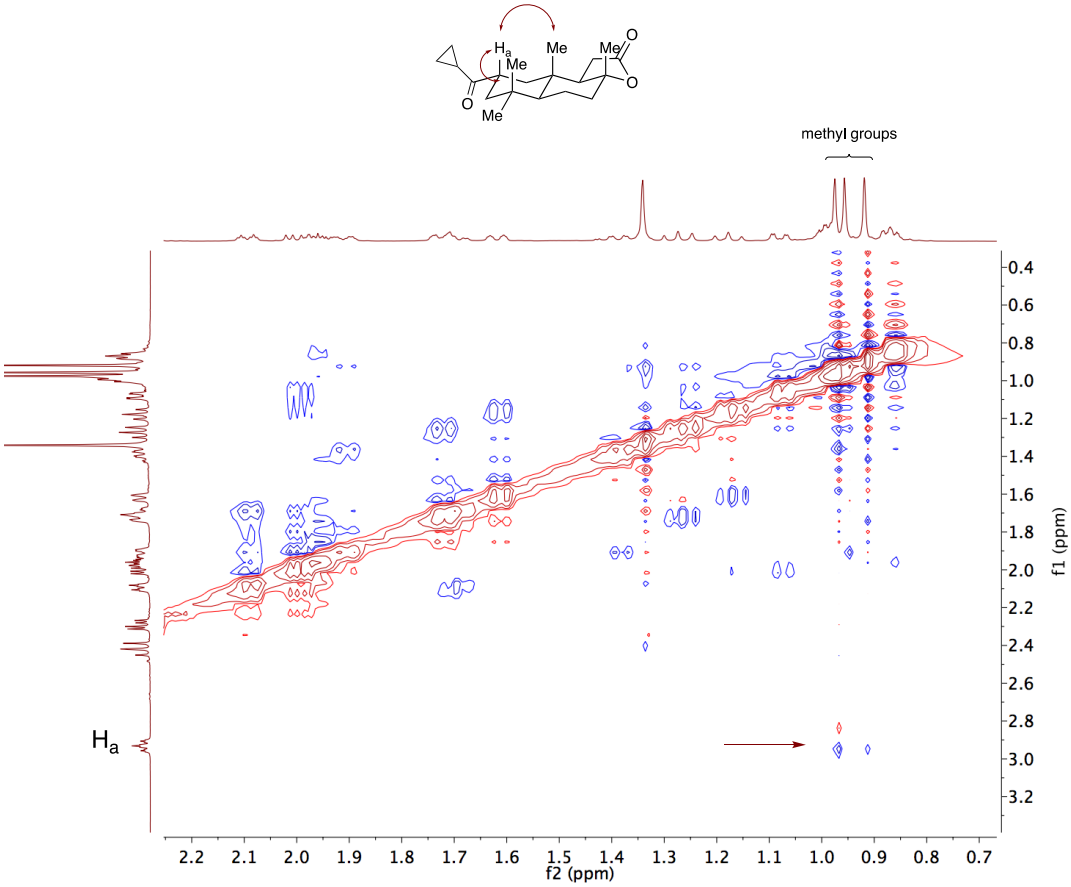
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (80c)



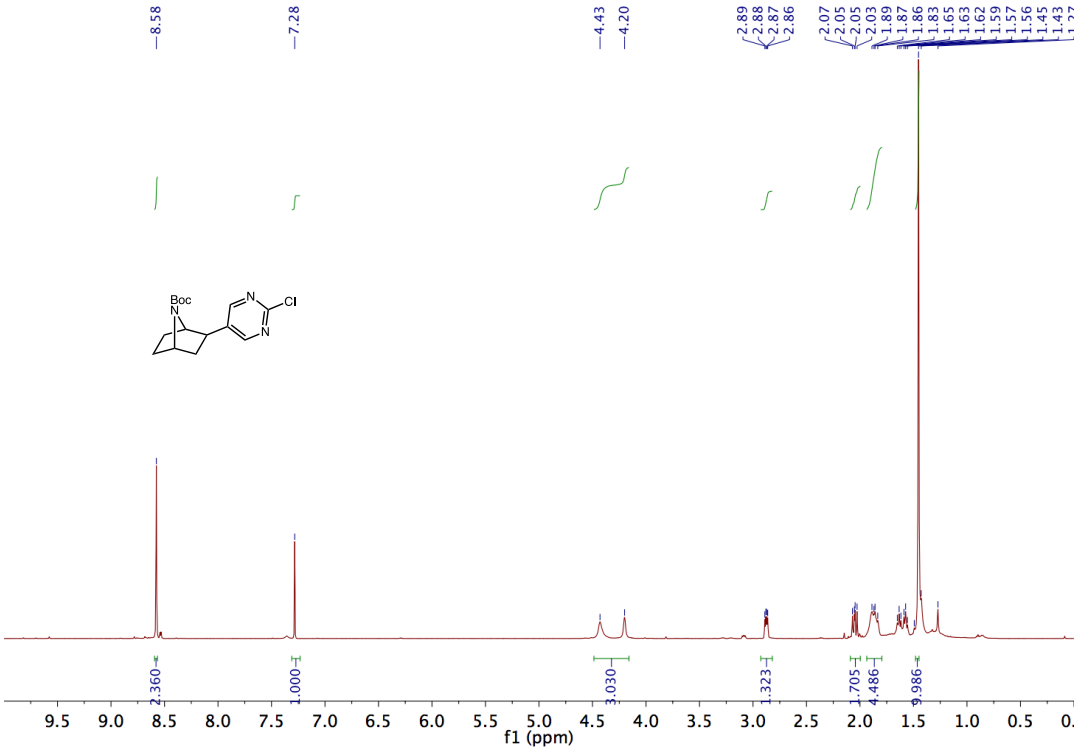
^{1}H NMR (500 MHz, $CDCl_3$) – (80d)



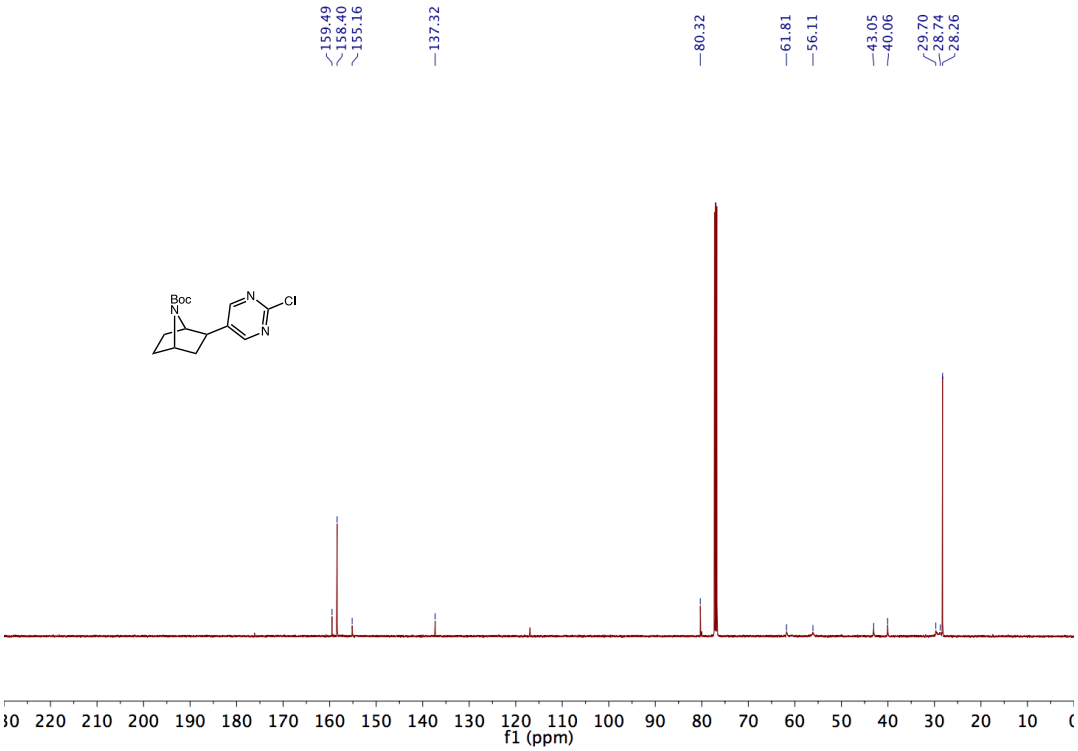
^{13}C NMR (126 MHz, $CDCl_3$) – (80d)



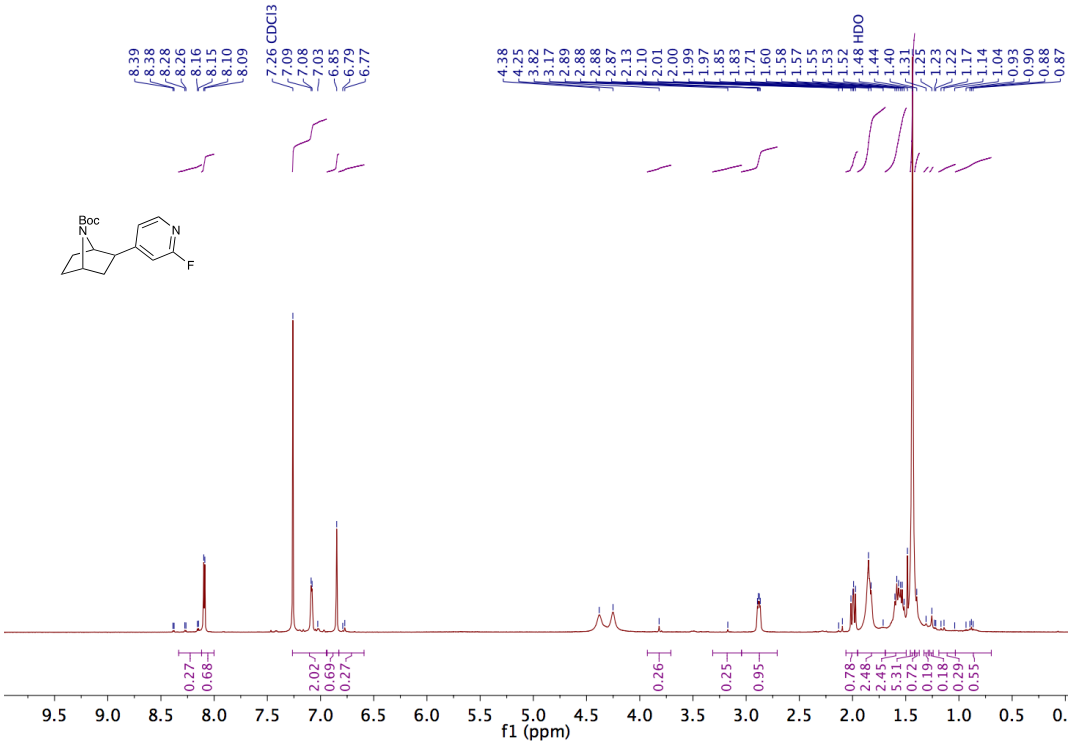
^{1}H NMR – NOESY (500 MHz, $CDCl_3$) – (80d)



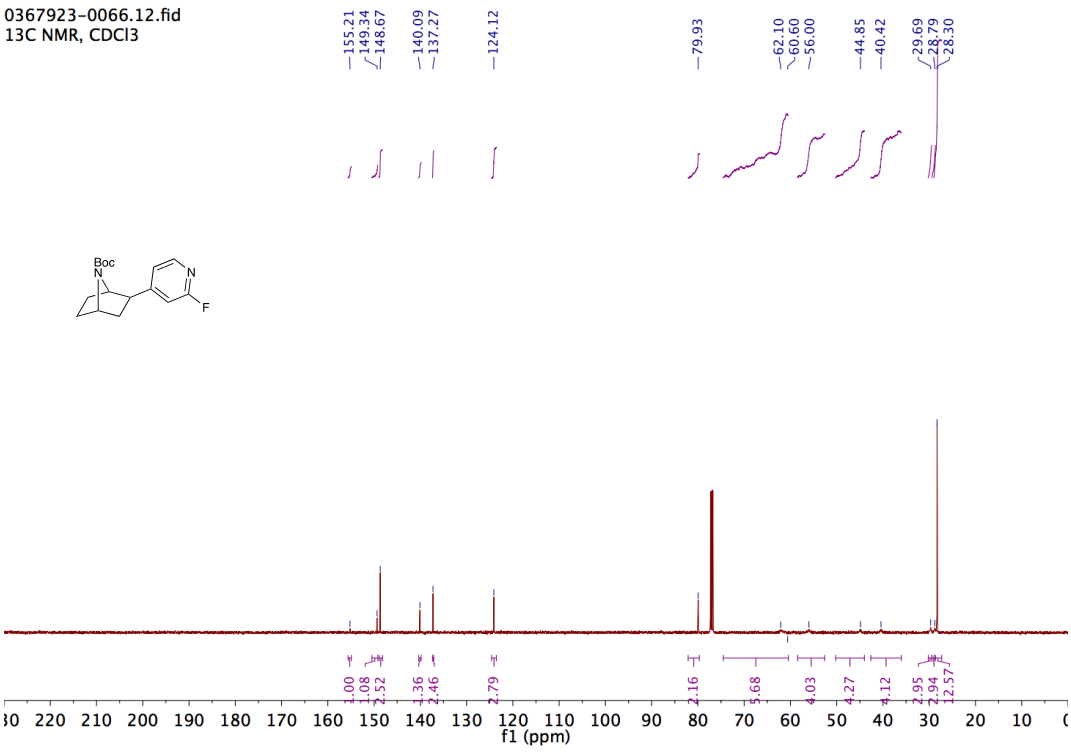
^{1}H NMR (500 MHz, $CDCl_3$) – (82b)



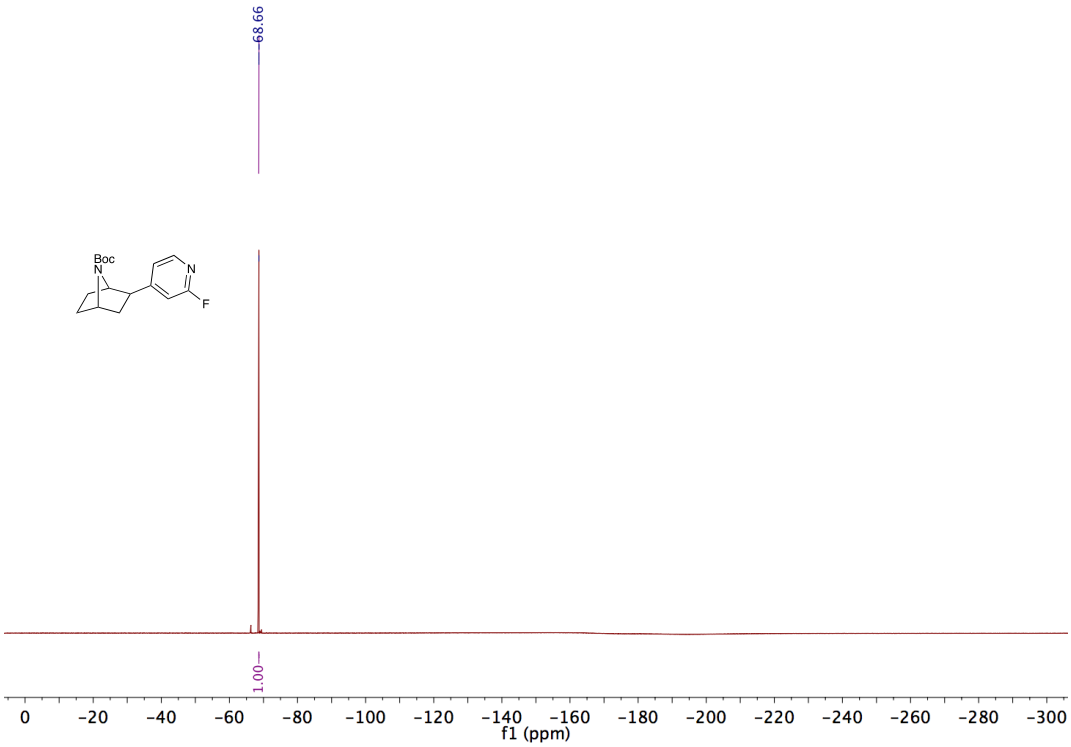
^{13}C NMR (126 MHz, $CDCl_3$) – (82b)



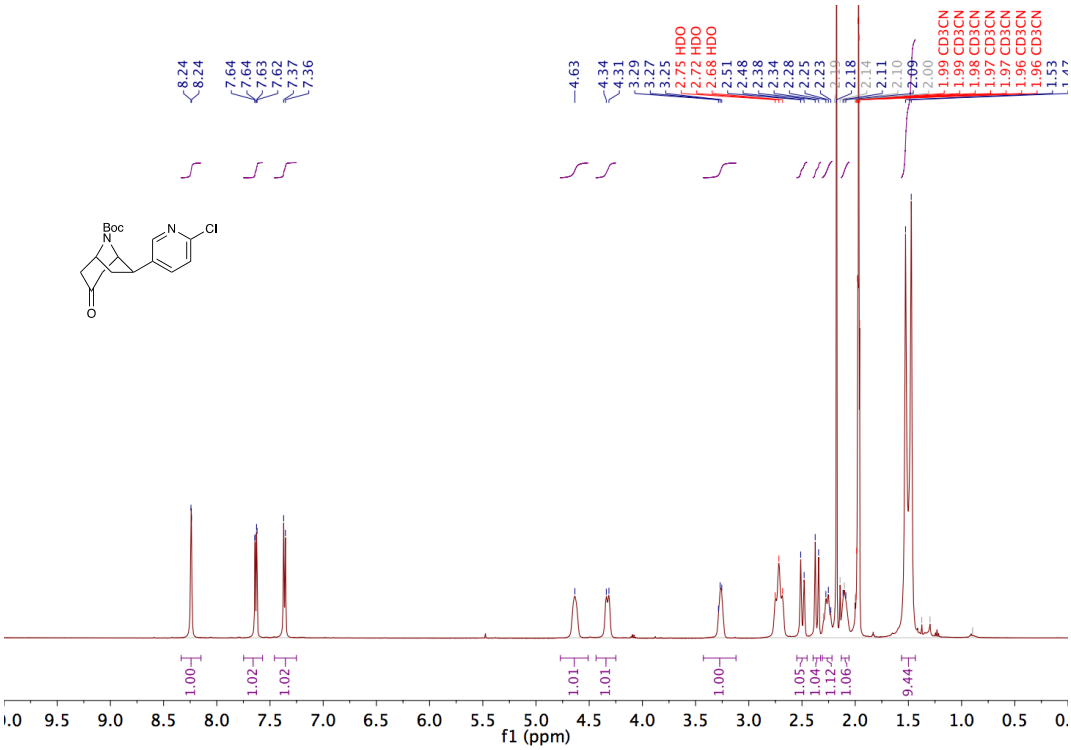
^{1}H NMR – (500 MHz, $CDCl_3$) – (82c)



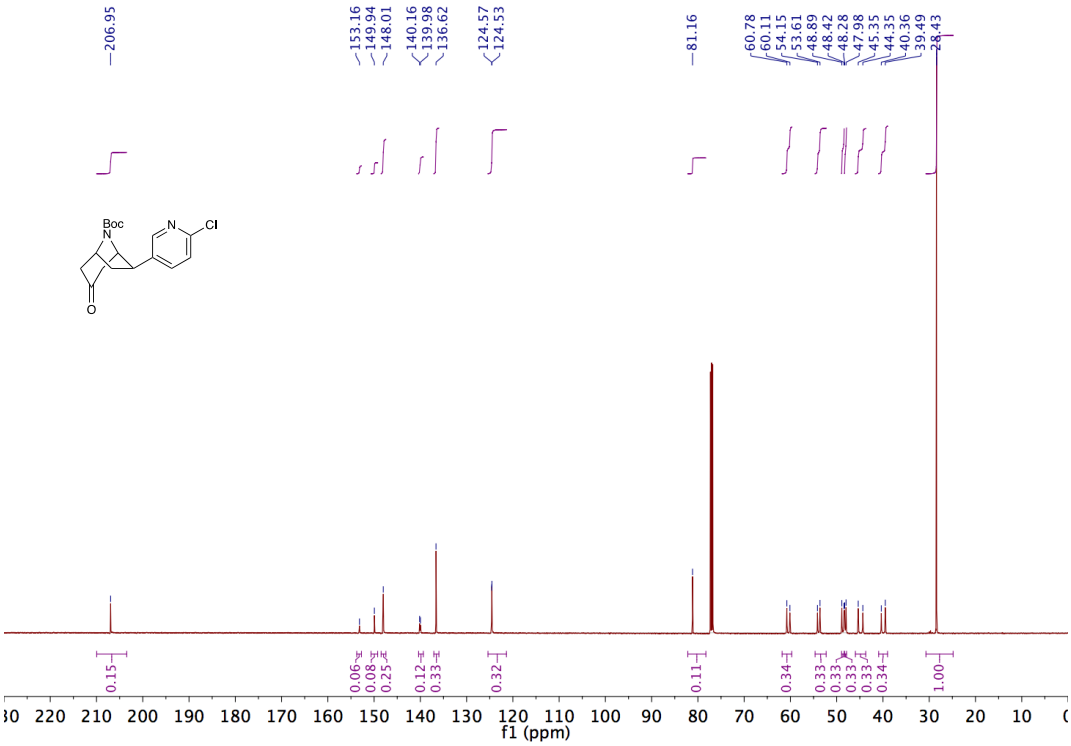
^{13}C NMR (126 MHz, $CDCl_3$) – (82c)



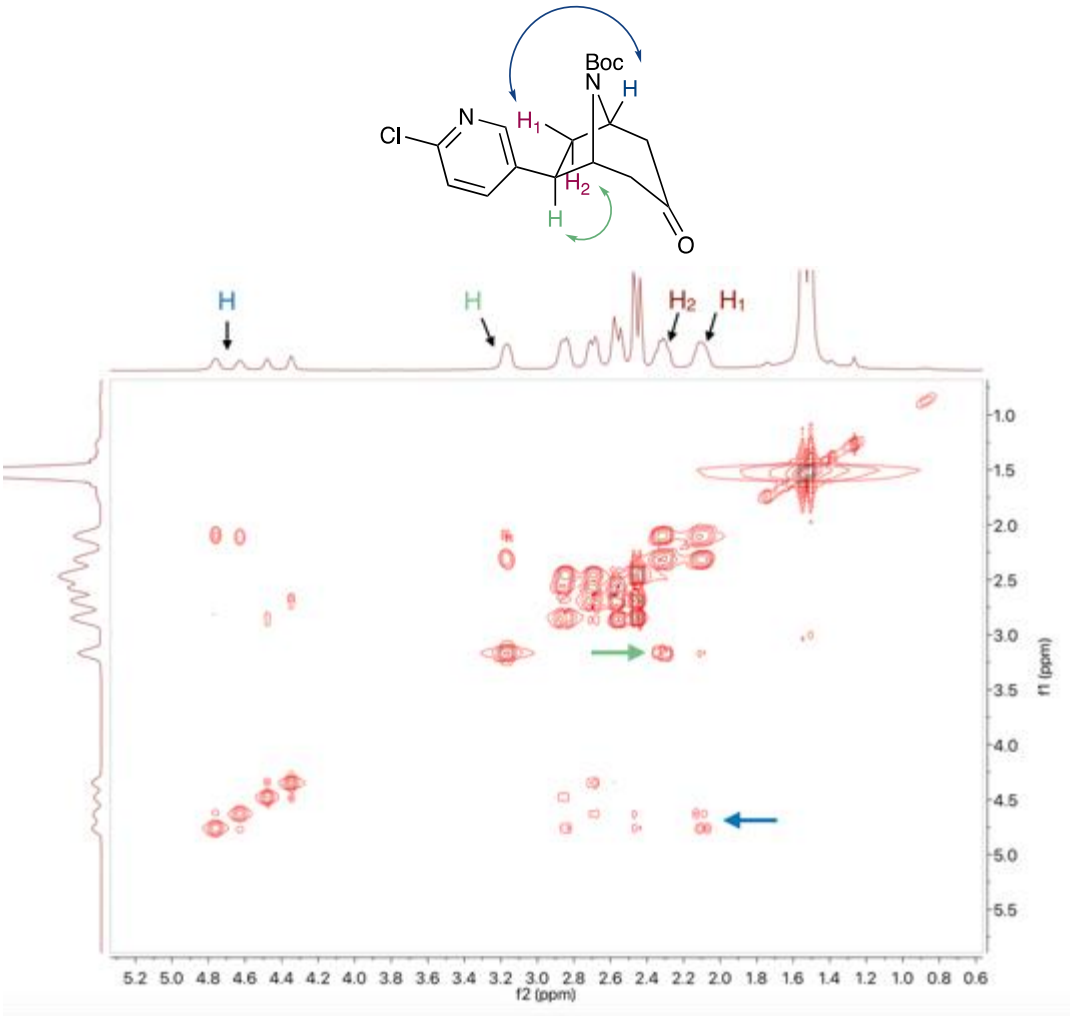
^{19}F NMR (376 MHz, $CDCl_3$) – (82c)



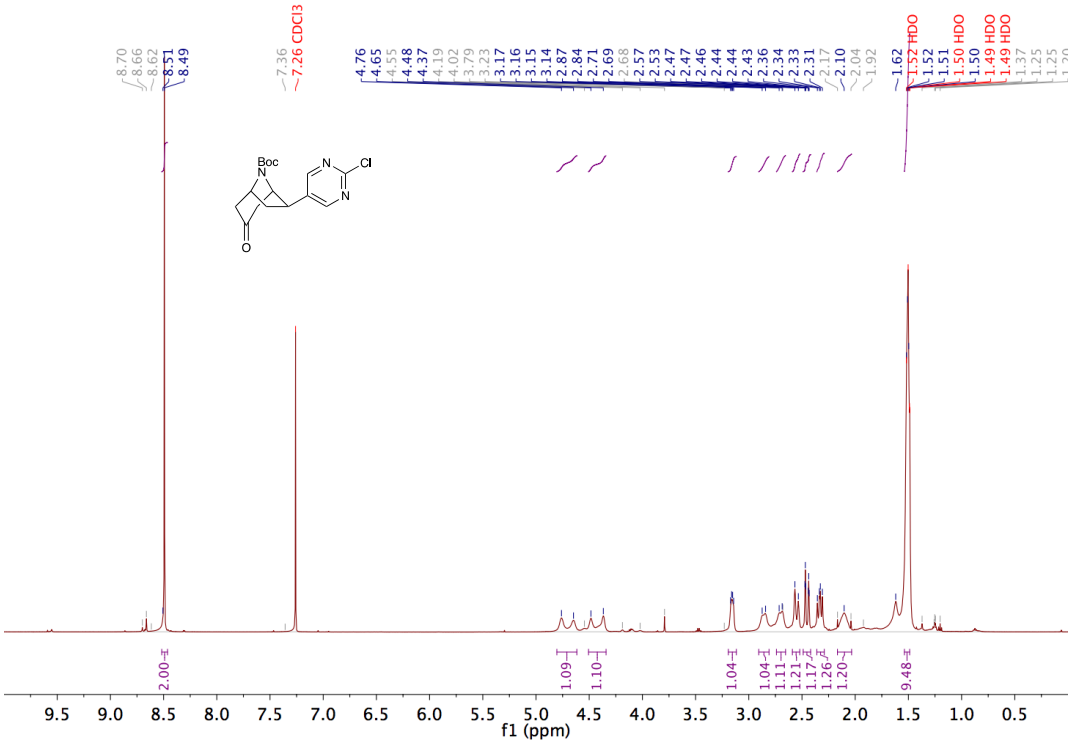
^{1}H NMR (500 MHz, CD_3CN) – (83a)



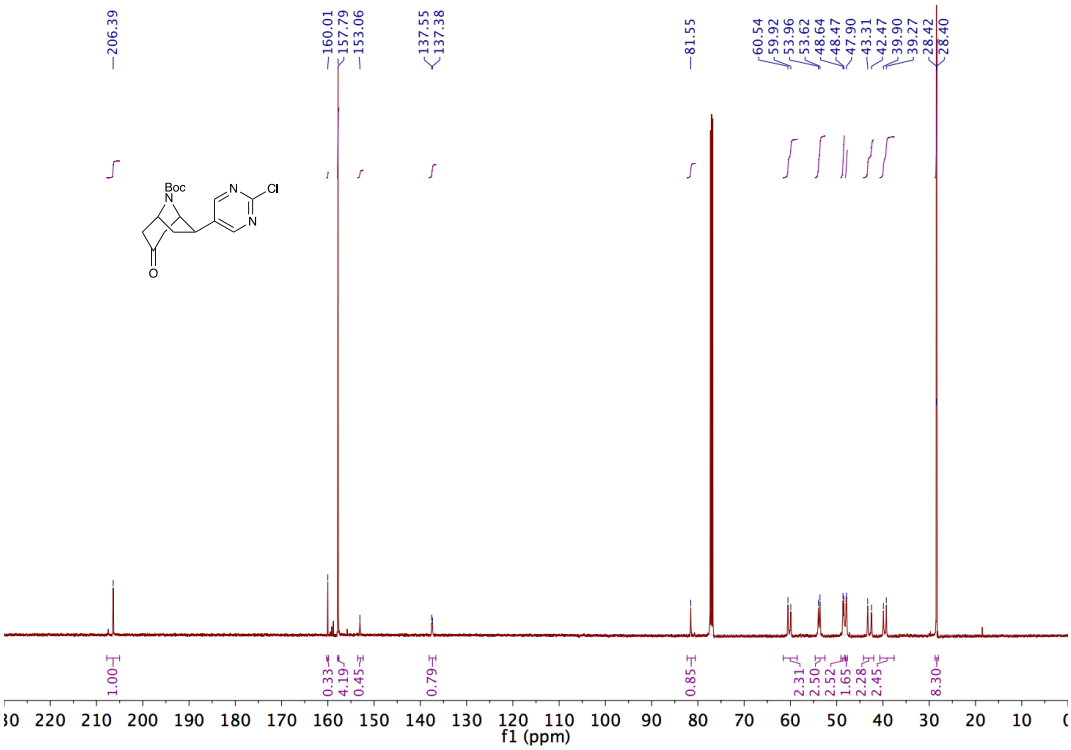
^{13}C NMR (126 MHz, $CDCl_3$) – (83a)



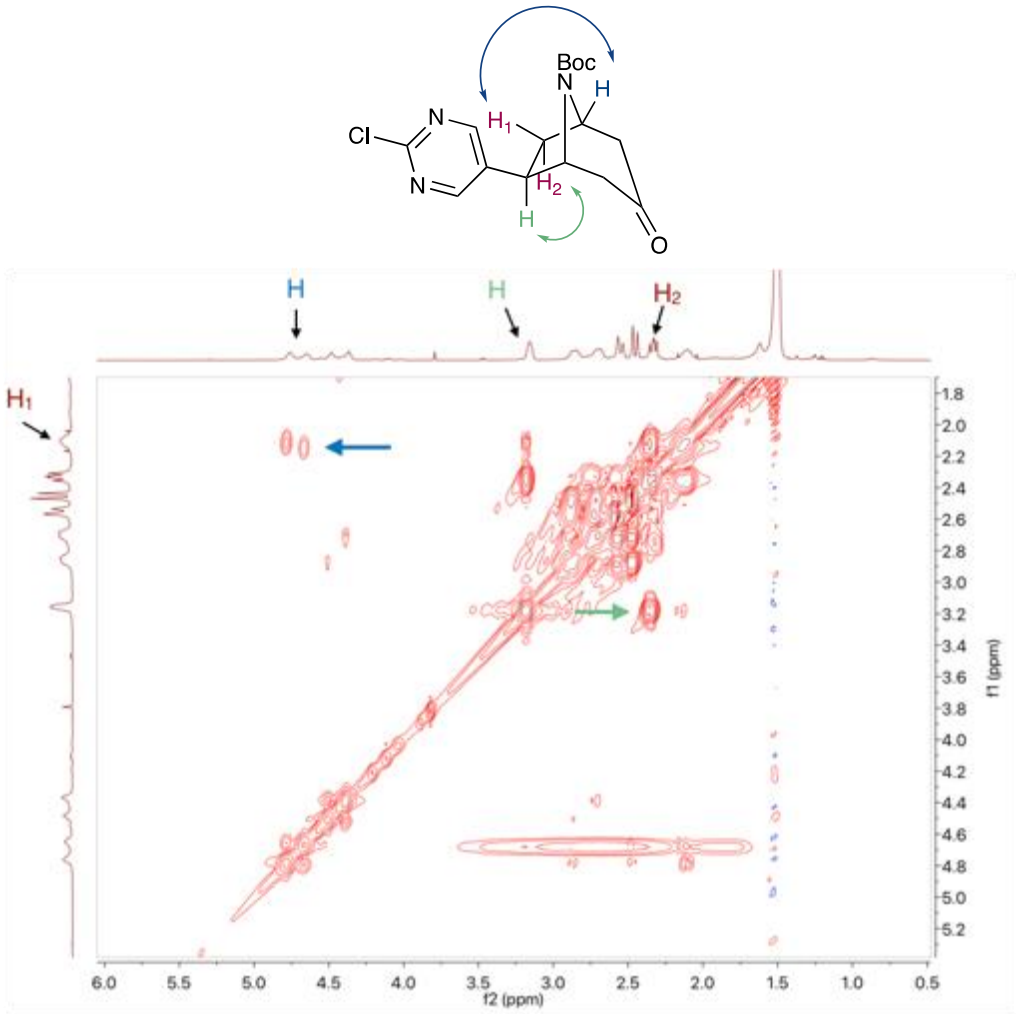
^{1}H NMR – COSY (500 MHz, $CDCl_3$) – (83a)



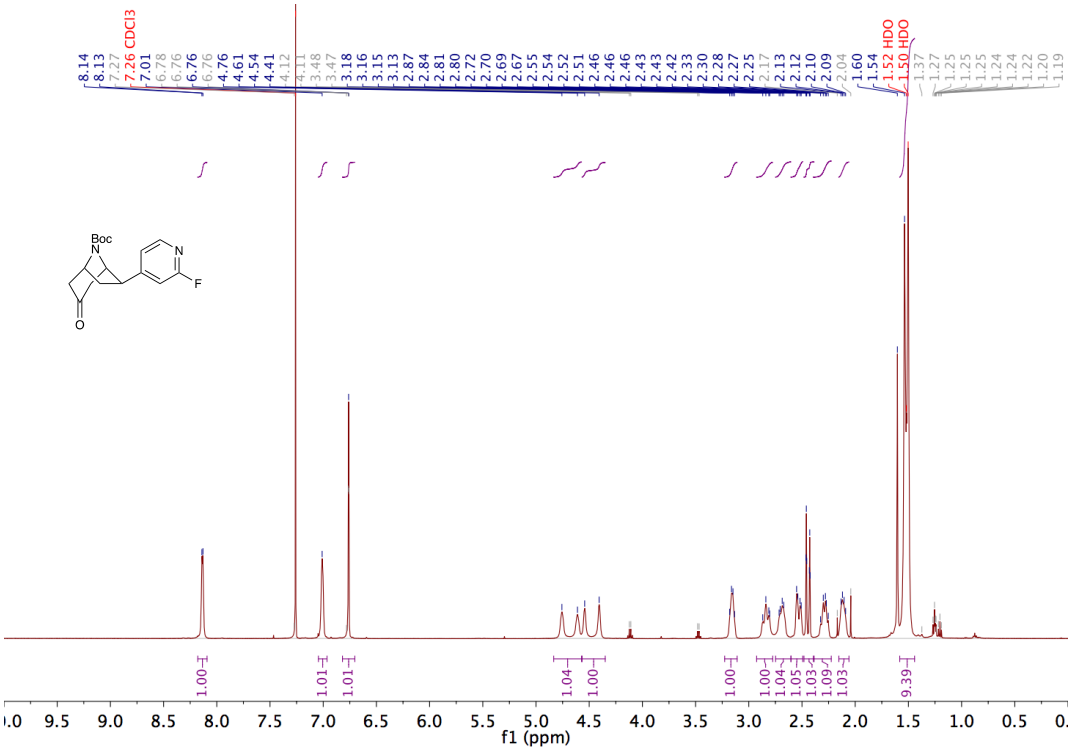
^{1}H NMR (500 MHz, $CDCl_3$) – (83b)



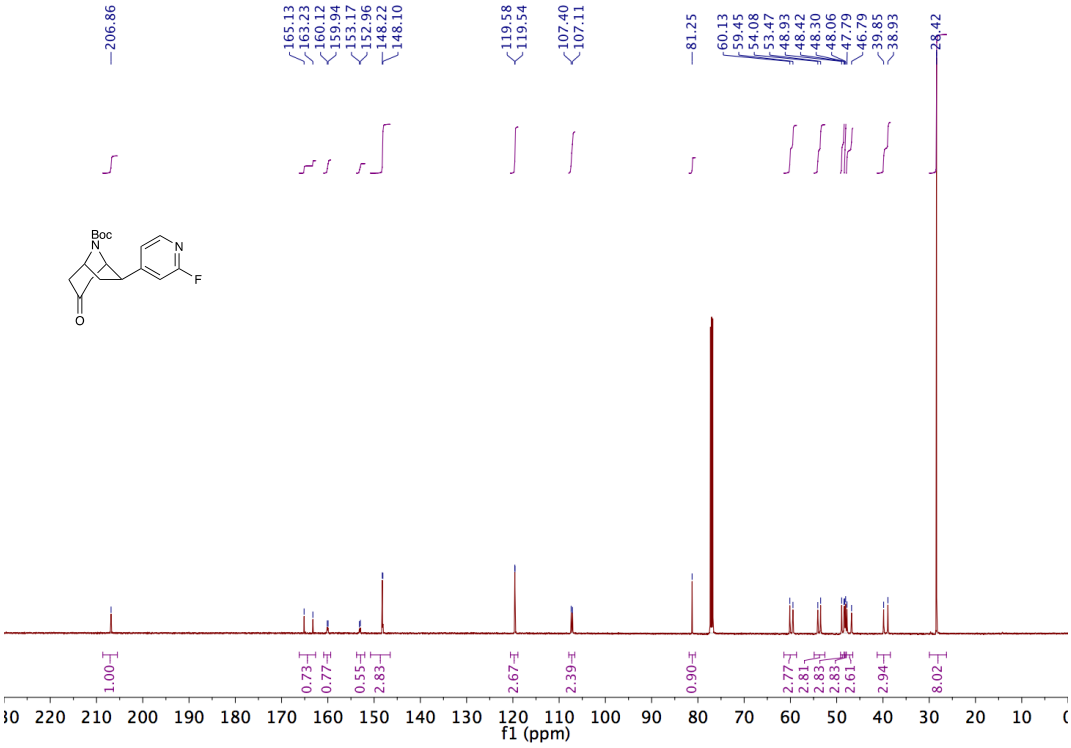
^{13}C NMR (126 MHz, $CDCl_3$) – (83b)



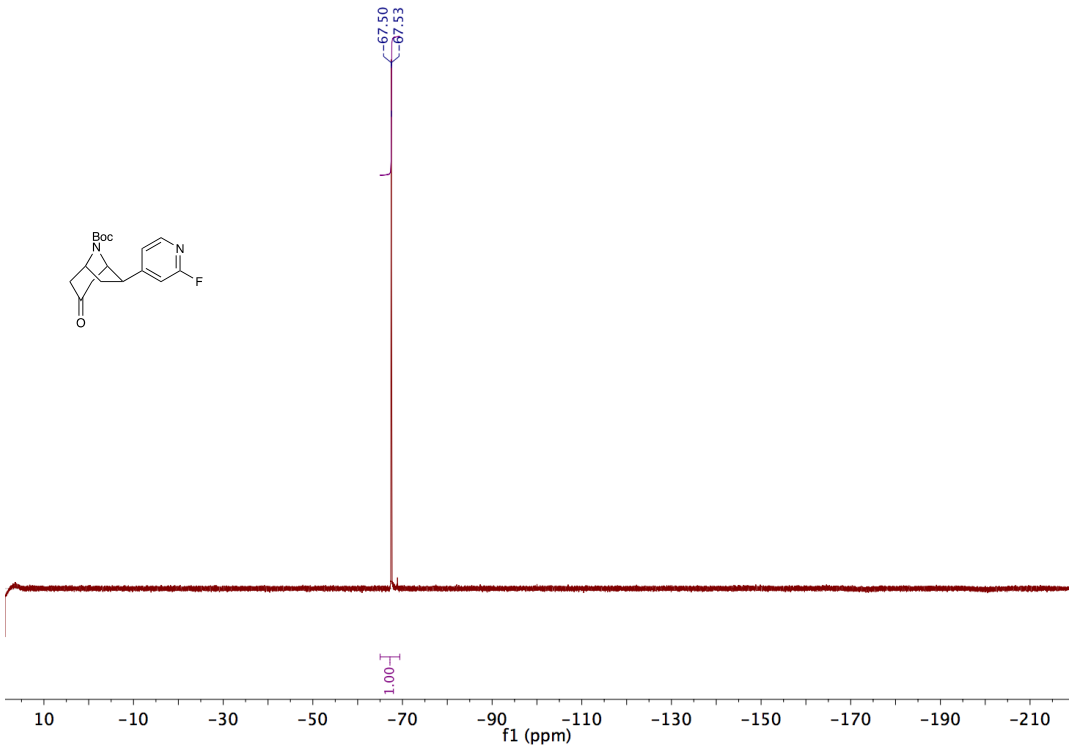
^{1}H NMR – COSY (500 MHz, $CDCl_3$) – (83b)



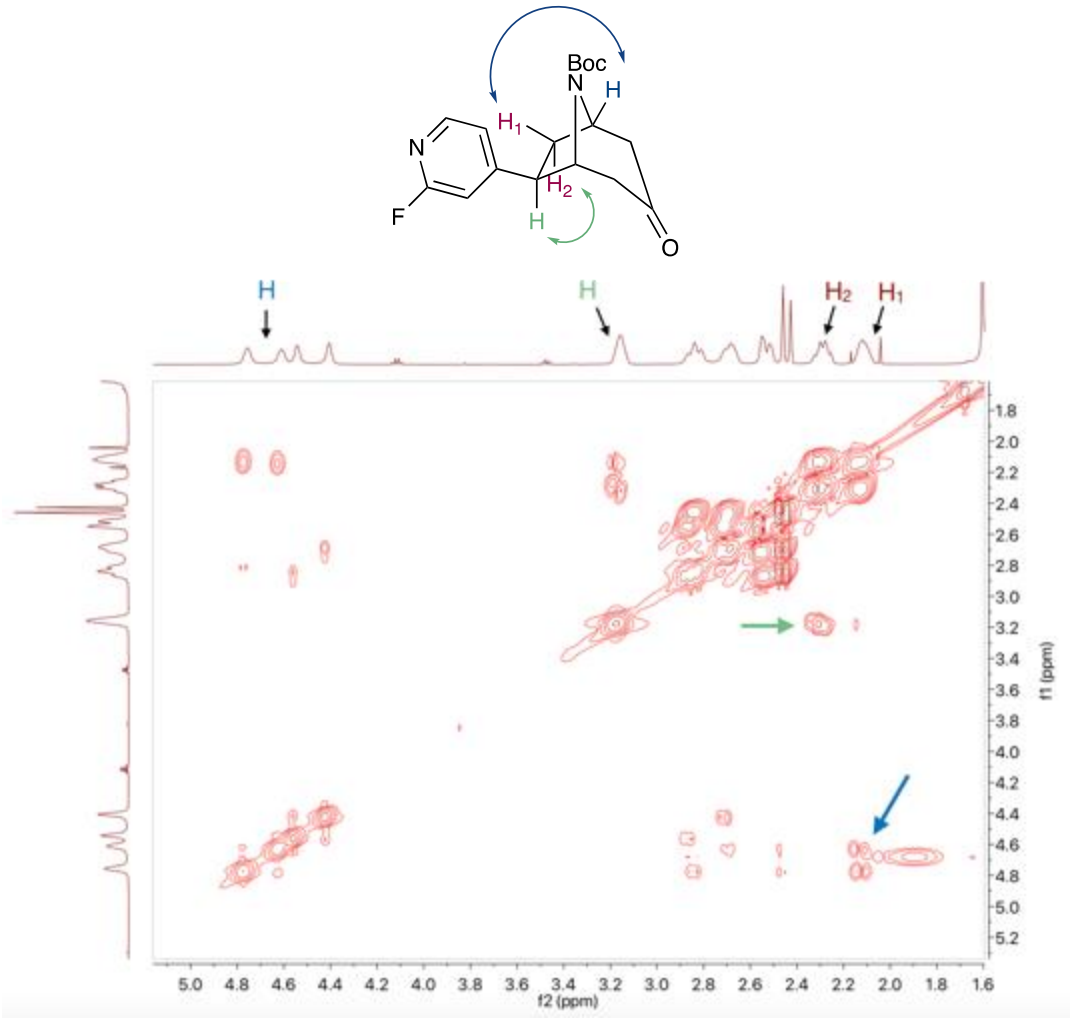
^{1}H NMR (500 MHz, $CDCl_3$) – (83c)



^{13}C NMR (126 MHz, $CDCl_3$) – (83c)



^{19}F NMR (376 MHz, $CDCl_3$) – (83c)



^{1}H NMR – COSY (500 MHz, $CDCl_3$) – (83c)