Metallaphotoredox-Catalyzed Cross-Electrophile C_{sp^3}–C_{sp^3} Coupling of Aliphatic Bromides

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Supporting Information

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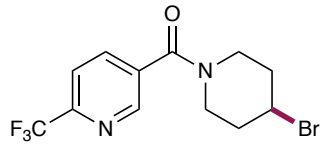
1) General Information

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ was prepared using literature procedures.[2] All solvents were purified according to the method of Grubbs.[3] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on silica gel (Fluka, 230–400 mesh) according to the method of Still.[4] Thin-layer chromatography (TLC) was performed on Silicycle 0.25 mm silica gel F-254 plates. Visualization of the developed chromatogram was performed by fluorescence quenching or $KMnO_4$ stain. ^1H NMR spectra were recorded on a Bruker UltraShield Plus Avance III 500 MHz and are internally referenced to residual protic $CDCl_3$ (δ 7.26 ppm). Data for ^1H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, br = broad), coupling constant (Hz), and integration. ^{13}C NMR spectra were recorded on a Bruker UltraShield Plus Avance III 500 MHz (125 MHz) and data are reported in terms of chemical shift relative to $CDCl_3$ (77.16 ppm). ^{19}F NMR spectra were recorded on a Bruker NanoBay 400 MHz (376 MHz). IR spectra were recorded on a Perkin Elmer Spectrum 100 FTIR spectrometer and are reported in wavenumbers (cm^{-1}). High Resolution Mass Spectra were obtained from the Princeton University Mass Spectral Facility.

2) Substrate Synthesis

(4-Bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (14)



4-bromopiperidin-1-ium bromide (6.4 g, 26.2 mmol, 1.0 equiv), HOBt hydrate (4.8 g, 31.4 mmol, 1.2 equiv), and 6-(trifluoromethyl)nicotinic acid (5 g, 26.2 mmol, 1.0 equiv) were added to a 100 mL round bottom flask (RBF) along with a stir bar. DCM (20 mL) was then added. In a separate flask, EDC•HCl (6 g, 31.4 mmol, 1.2 equiv) and triethylamine (10.6 g, 14.5 mL, 105 mmol, 4 equiv) were dissolved in 32 mL DCM. The EDC solution was then added to the suspension of amine and acid. The reaction was stirred for 8 hours, after which time it was washed with 1 M HCl followed by brine. The DCM layer was then dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by column chromatography (0 to 40% EtOAc in hexanes) yielded the desired product as a white solid (6 g, 17.8 mmol, 68% yield).

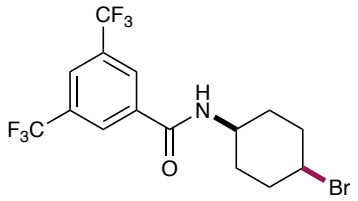
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.95 (s, 1H), 7.78 (s, 1H), 4.49 (s, 1H), 3.92 (s, 2H), 3.65 (s, 1H), 3.36 (s, 1H), 2.25-1.95 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.51, 149.07 (q, J = 34.3 Hz), 148.05, 136.56, 134.43, 121.24 (q, J = 274.4 Hz), 120.67 (q, J = 2.6 Hz), 48.08, 45.70, 40.31, 36.01, 34.99.

IR (film) ν_{max} 2944, 1637, 1443, 1335. 1141, 1084, 998, 857 cm^{-1}.

HRMS (ESI-TOF): m/z calcd. For $C_{12}H_{13}BrF_3N_2O$ ([M+H$^+$]) 337.01579, found 337.01575.

***cis*-*N*-(4-Bromocyclohexyl)-3,5-bis(trifluoromethyl)benzamide**



Step 1: *trans*-4-aminocyclohexanol (1 g, 8.7 mmol, 1.1 equiv) and triethylamine (0.9 g, 1.2 mL, 8.7 mmol, 1.1 equiv) were dissolved in 40 mL DCM. 3,5-bis(trifluoromethyl)benzoyl chloride (2.2 g, 1.43 mL, 7.9 mmol, 1 equiv) was then added slowly dropwise at 0 ºC. The reaction was warmed to room temperature and stirred for 2 hours. The reaction mixture was then washed with 1 M HCl followed by brine. The DCM layer was then dried with $MgSO_4$ and concentrated *in vacuo*. The crude alcohol was used in the next step.

Step 2: trans-*N*-(4-hydroxycyclohexyl)-3,5-bis(trifluoromethyl)benzamide (600 mg, 1.7 mmol, 1.0 equiv) and carbon tetrabromide (672 mg, 2.0 mmol, 1.2 equiv) were dissolved in 8.5 mL DCM and cooled to 0 ºC. Triphenylphosphine (532 mg, 2.0 mmol, 1.2 equiv) was then added portionwise over 30 minutes. The reaction was allowed to warm to room temperature and subsequently heated to 50 ºC. It was run at this temperature for 4 to 6 hours, monitored by LC-MS and TLC. Once starting material was fully consumed, the reaction was cooled to room temperature, diluted with ethyl acetate, and washed with saturated $Na_2S_2O_3$. The organic layer was then concentrated to obtain an orange-red oil. Purification by column chromatography (0 to 30% EtOAc in hexanes) gave the desired product as a white solid (230 mg, 0.55 mmol, 33% yield).

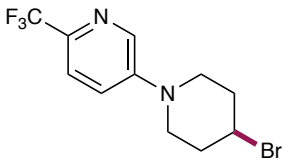
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (s, 2H), 8.01 (s, 1H), 6.29 (s, 1H), 4.27-3.98 (m, 2H), 2.81-2.59 (m, 1H), 2.30 (d, *J* = 16.6 Hz, 1H), 2.08 (d, *J* = 12.3 Hz, 1H), 1.96-1.89 (m, 1H), 1.89-1.75 (m, 2H), 1.55-1.45 (m, 1H), 1.40-1.35 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 163.75, 136.63, 132.40 (q, *J* = 33.9 Hz), 127.39, 125.42 (hept, *J* = 3.6 Hz), 124.09 (q, *J* = 271.99 Hz), 48.87, 47.88, 43.47, 36.91, 31.49, 23.89.

IR (film) ν_{max} 3284, 2945, 1643, 1551, 1278, 1180, 1134, 908, 792, 682 cm^{-1}.

HRMS (ESI-TOF): m/z calcd. For $C_{15}H_{15}BrF_6NO$ ($[M+H^+]$) 417.0163, found 417.0169.

5-(4-Bromopiperidin-1-yl)-2-(trifluoromethyl)pyridine



Step 1: (Procedure S1) 5-(4-hydroxypiperidin-1-yl)-2-(trifluoromethyl)pyridine was prepared via a recent C–N coupling reported by our group.[5] $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (15 mg, 13 μmol, 0.0002 equiv.), $NiCl_2•6H_2O$ (783 mg, 3.3 mmol, 0.05 equiv), DABCO (13.3 g, 119 mmol, 1.8 equiv.), piperidine-4-ol (10 g, 99 mmol, 1.5 equiv), and 5-bromo-2-(trifluoromethyl)pyridine (14.9 g, 66 mmol, 1 equiv) were weighed into a 250 mL RBF, and a stir bar was added. 60 mL DMA was then added and the reaction was capped with a septum and sparged with N_2 for 15 minutes, then sealed with parafilm. The vessel was then irradiated by blue LEDs and stirred for 3 hours, after which time the reaction was determined to be complete by LCMS. The reaction was diluted with ethyl acetate and washed several times with saturated LiCl. The organic layer was dried with $MgSO_4$, filtered, and concentrated to give a yellow solid (14.2 g, 57.7 mmol, 87% yield).
Step 2: (Procedure S2) Triphenylphosphine (5.33 g, 20.3 mmol, 1 equiv.) was dissolved in DCM (60 mL) and cooled to 0 ºC. Bromine (3.25 g, 1.05 mL, 20.3 mmol, 1 equiv) was then added slowly dropwise. To this solution was then slowly added a solution of crude 5-(4-hydroxypiperidin-1-yl)-2-(trifluoromethyl)pyridine (5 g, 20.3 mmol, 1 equiv.) and imidazole (1.4 g, 20.3 mmol, 1 equiv.) in DCM (40 mL). The reaction was then warmed to room temperature and run for 3 hours until complete. Once starting material was fully consumed, the reaction was cooled to room temperature, diluted with ethyl acetate, and washed with saturated $Na_2S_2O_3$. The organic layer was then concentrated to obtain an orange-red oil. Purification by column chromatography (0 to 20% EtOAc in hexanes) gave the desired product as a white solid (3.5 g, 11.3 mmol, 56% yield).

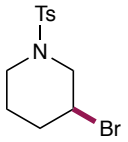
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, *J* = 2.8 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.20 (dd, *J* = 8.8, 2.7 Hz, 1H), 4.43 (tt, *J* = 7.5, 3.8 Hz, 1H), 3.72-3.54 (m, 2H), 3.43-3.25 (m, 2H), 2.36-2.24 (m, 2H), 2.21-2.10 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 148.12, 137.79 (q, *J* = 35.1 Hz), 137.78, 122.23 (q, *J* = 272.4 Hz), 121.26, 121.03 (q, *J* = 2.7 Hz), 48.66, 46.20, 34.92.

IR (film) ν_{max} 2832, 1586, 1571, 1341, 1242, 1177, 1116, 1091, 1001, 833 cm^{-1}.

HRMS (ESI-TOF): m/z calcd. For $C_{11}H_{13}BrF_3N_2$ ($[M+H^+]$) 309.0209, found 309.0204.

(±) 3-Bromo-1-tosylpiperidine



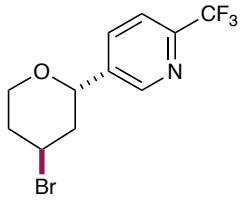
Step 1: Ethyl nipecotate (1 g, 0.99 mL, 6.4 mmol, 1 equiv.) and triethylamine (2.6 g, 3.6 mL, 25.4 mmol, 4 equiv.) were dissolved in isopropanol (10 mL). Tosyl chloride (1.21 g, 6.4 mmol, 1 equiv.) was then added and the reaction was stirred at room temperature for 2 hours. 1 M NaOH (aq.) was then added and the mixture stirred another hour. At this point, the mixture was acidified and subsequently extracted with DCM. The DCM layer was then dried with $MgSO_4$, filtered, and concentrated *in vacuo* to give a white solid (1.7 g, 6 mmol, 94% yield), which was used without purification.

Step 2: (Procedure S3) Following a recently reported procedure,[6] $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (39.6 mg, 35 μmol, 0.02 equiv.), 1-tosylpiperidine-3-carboxylic acid (500 mg, 1.8 mmol, 1 equiv.), and cesium carbonate (575 mg, 1.8 mmol, 1 equiv.) were weighed into a 40 mL vial. 35 mL of chlorobenzene was then added, followed by diethyl-2-bromomalonate (1.06 g, 752 μL, 4.4 mmol, 2.5 equiv.). The reaction mixture was then sparged with nitrogen for 15 minutes, then irradiated by blue LEDs for 4 hours. The reaction mixture was then filtered through silica and concentrated *in vacuo* to give an oil. Purification by column chromatography (0 to 20% EtOAc in hexanes) gave the desired product as a white solid (140 mg, 0.44 mmol, 25% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 9.7 Hz, 2H), 7.34 (d, *J* = 9.4 Hz, 2H), 4.14-4.03 (m, 1H), 4.00-3.91 (m, 1H), 3.66-3.56 (m, 1H), 2.62 (dd, *J* = 11.7, 10.0 Hz, 1H), 2.48 – 2.42 (m, 1H), 2.44 (s, 3H), 2.29-2.20 (m, 1H), 1.89-1.79 (m, 1H), 1.78-1.67 (m, 1H), 1.68-1.57 (m, 1H)

Data in agreement with literature values.[7]

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



Prepared from 4-bromotetrahydropyran via known literature procedure.[8]

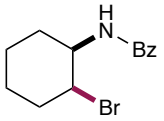
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 5.04 (d, *J* = 10.7 Hz, 1H), 4.81 (s, 1H), 4.17 (td, *J* = 11.9, 1.9 Hz, 1H), 4.07 (dd, *J* = 11.9, 4.9 Hz, 1H), 2.35-2.17 (m, 2H), 2.11-1.90 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 147.91, 147.30 (q, *J* = 35.2 Hz), 140.80, 134.88, 121.66 (q, *J* = 273.9 Hz), 120.33 (q, *J* = 7.9 Hz), 71.80, 63.60, 49.07, 41.80, 33.71.

IR (film) ν_{max} 2963, 2868, 1334, 1176, 1133, 1086, 1073, 1028, 847 cm^{-1}.

HRMS (ESI-TOF): m/z calcd. For $C_{11}H_{12}BrF_3NO$ ($[M+H^+]$) 310.00489, found 310.00459.

(±) *cis*-*N*-(2-Bromocyclohexyl)benzamide



Following Procedure S3, *trans*-2-benzamidocyclohexanecarboxylic acid was converted to the desired bromide. Purification via column chromatography gave both cis and trans diastereomers as white solids (separated, 2:1 ratio). The minor diastereomer (70 mg, 0.24 mmol, 23% yield) was determined to be *trans* by comparison to the literature.[9] We therefore conclude the major diastereomer (140 mg, 0.5 mmol, 47% yield) to be in the *cis* configuration. The *cis* compound was used in the methylation reaction, and characterization data for this diastereomer is given below.

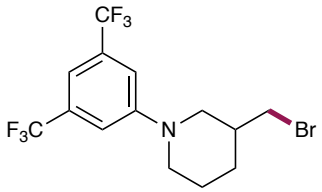
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.1 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 6.33 (d, *J* = 8.6 Hz, 1H) 4.79 (d, *J* = 2.8 Hz, 1H), 4.16-4.06 (m, 1H), 2.22 (dt, *J* = 15.0, 2.8 Hz, 1H), 2.06-1.95 (m, 1H), 1.87-1.71 (m, 4H), 1.63-1.57 (m, 1H), 1.52-1.41 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.42, 134.37, 131.64, 128.64, 126.96, 61.19, 50.68, 33.80, 27.86, 24.59, 19.79.

IR (film) ν_{max} 3342, 2944, 1638, 1527, 1489, 1447, 1315, 1243, 1100, 720, 692 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{17}BrNO$ ($[M+H]^+$) 282.0488, found 282.04871.

(±) 1-(3,5-Bis(trifluoromethyl)phenyl)-3-(bromomethyl)piperidine



Step 1: Following Procedure S1, 3-piperidinemethanol was coupled with 1-bromo-3,5-bis(trifluoromethyl)benzene to give 1-(3,5-bis(trifluoromethyl)phenyl)-3-(hydroxymethyl)piperidine as a yellow solid (2.06 g, 6.29 mmol, 92% crude yield).

Step 2: Following Procedure S2, the crude alcohol was converted to the bromide. Following purification by column chromatography (0 to 10% EtOAc in hexanes), 1-(3,5-bis(trifluoromethyl)phenyl)-3-(bromomethyl)piperidine was isolated as a white solid (630 mg, 1.62 mmol, 51% yield).

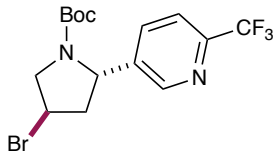
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (s, 3H), 3.85-3.74 (m, 1H), 3.65-3.56 (m, 1H), 3.46-3.33 (m, 2H), 2.98-2.87 (m, 1H), 2.84-2.75 (m, 1H), 2.11-2.03 (m, 1H), 2.00-1.92 (m, 1H), 1.88-1.79 (m, 1H), 1.76-1.63 (m, 1H), 1.43-1.31 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 151.93, 132.50 (q, J = 32.1 Hz), 123.89 (q, J = 272.1 Hz), 115.75 – 115.12 (m), 112.21 – 111.50 (m), 53.62, 49.41, 37.87, 36.09, 29.53, 24.09.

IR (film) ν_{max} 2939, 1618, 1479, 1399, 1275, 1171, 1126, 998, 963, 862, 682 cm^{-1}.

HRMS (ESI-TOF): m/z calcd. For $C_{14}H_{15}BrF_6N$ ($[M+H^+]$) 390.02866, found 390.02821.

(±) *N*-Boc-4-bromo-2-(6-(trifluoromethyl)pyridin-3-yl)pyrrolidine



Step 1: Following a recently published protocol from our group,[10] *N*-Boc-*trans*-4-hydroxyproline underwent coupling with 5-bromo-2-(trifluoromethyl)pyridine to give *N*-Boc-4-bromo-2-(6-(trifluoromethyl)pyridin-3-yl)pyrrolidine (2.15 g, 6.5 mmol, 73% yield, 2:1 d.r.).

Step 2: The mixture of alcohol diastereomers (200 mg, 0.6 mmol, 1 equiv.), carbon tetrabromide (259 mg, 0.8 mmol, 1.3 equiv.), and polymer-supported triphenylphosphine (3 mmol/g loading, 441 mg, 1.3 mmol, 2.2 equiv) were dissolved/suspended in chloroform (5 mL). The reaction was stirred at reflux for 6 hours, after which time it was cooled to room temperature, filtered, and concentrated. The crude mixture was then purified via column chromatography (7 to 60% EtOAc in hexanes) to give the two expected diastereomers, which were separated (major diastereomer (cis): 64 mg; minor diastereomer (trans): 32 mg; 40% combined yield).

Note: Characterization below is for the trans product, and this compound was used for subsequent reactions. Relative stereochemistry determined via NOESY (see S66).

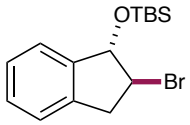
^{1}H NMR (500 MHz, Acetonitrile-d_3) rotameric mixture: δ 8.66 (s, 1H), 7.91 – 7.85 (m, 1H), 7.77 – 7.71 (m, 1H), 5.19 – 5.08 (m, 1H), 4.75 – 4.64 (m, 1H), 4.04 (s, 2H), 2.74 (dd, J = 14.3, 7.1 Hz, 1H), 2.42-2.23 (m, 1H), 1.41 (s, 4H), 1.15 (s, 5H).

^{13}C NMR (126 MHz, Acetonitrile-d_3) rotameric mixture, resonances for minor rotamer are enclosed in parenthesis (): δ (155.53), 154.97, 149.68, (149.44), 147.81 (q, J = 33.5 Hz), 144.06, (143.39), 136.47, (136.37), 122.89 (q, J = 272.9 Hz), 121.32, (80.95), 80.70, 58.94, (58.70), (58.37), 57.96, (48.78), 48.67, 47.16, (46.09), (28.49), 28.19.

IR (film) ν_{max} 2977, 1691, 1393, 1338, 1171, 1128, 1084, 1027, 850, 767 cm^{-1}.

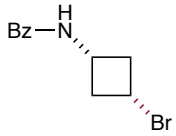
HRMS (ESI-TOF): m/z calcd. For $C_{15}H_{19}BrF_3N_2O_2$ ([M+H$^+$]) 395.05765, found 395.05843.

(±) *trans*-((2-Bromo-2,3-dihydro-1*H*-inden-1-yl)oxy)(*tert*-butyl)dimethylsilane



Prepared via a previously reported procedure, data matches that reported in the literature.[11]

***cis*-*N*-(3-Bromocyclobutyl)benzamide**



Step 1: *trans*-3-hydroxycyclobutanamine hydrochloride (1.66 g, 13.4 mmol, 1.1 equiv.) and triethylamine (3.71 g, 5.1 mL, 36.6 mmol, 3 equiv.) were dissolved in DCM (30 mL) and cooled to 0 ºC. Benzoyl chloride (1.7 g, 1.4 mL, 12.2 mmol, 1 equiv.) was then added slowly dropwise. The reaction was stirred at room temperature for 1 hour, then washed with 1 M HCl. The DCM layer was then dried with $MgSO_4$, filtered, and concentrated *in vacuo* to give a white solid which was used without further purification (1.7 g, 8.9 mmol, 73% yield).

Step 2: Following Procedure S2 (except using MeCN instead of DCM, and heating to 50 ºC), the crude alcohol was converted to the bromide. Purification by column chromatography gave the title compound as a 6:1 mixture of diastereomers (white solid, 700 mg, 2.8 mmol, 31% yield).

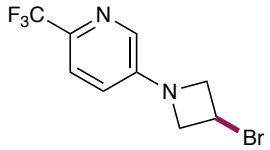
^{1}H NMR (500 MHz, $CDCl_3$) mixture of diastereomers, only major peaks reported: δ 7.75 (d, *J* = 7.7 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 6.31 (s, 1H), 4.96 (h, *J* = 7.2 Hz, 1H), 4.54 (tt, *J* = 7.5, 3.8 Hz, 1H), 2.95-2.84 (m, 2H), 2.84-2.71 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) mixture of diastereomer, only major peaks reported: δ 167.25, 134.26, 131.83, 128.78, 127.00, 44.48, 44.01, 42.22, 39.49.

IR (film) ν_{max} 3299, 3058, 1636, 1535, 1313, 1234, 1187, 691 cm^{-1}.

HRMS (ESI-TOF): m/z calcd. For $C_{11}H_{12}BrNNaO$ ([M+Na^+]) 275.99945, found 275.99926.

5-(3-Bromoazetidin-1-yl)-2-(trifluoromethyl)pyridine



Step 1: Following Procedure S1, 3-hydroxyazetidine hydrochloride was coupled with 5-bromo-2-(trifluoromethyl)pyridine to give the alcohol product as a yellow solid (1.77 g, 8.1 mmol, 92% yield).

Step 2: Following Procedure S2 (except using MeCN instead of DCM, and heating to 50 ºC), the crude alcohol was converted to the bromide. Purification by column chromatography gave the title compound as a white solid (1 g, 2.8 mmol, 31% yield).

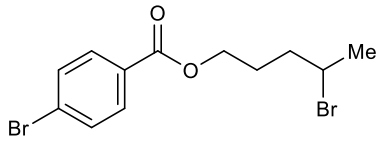
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 1H), 6.74 (d, *J* = 11.1 Hz, 1H), 4.81-4.69 (m, 1H), 4.62 (t, *J* = 7.9 Hz, 2H), 4.33-4.20 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 147.60, 137.64 (q, *J* = 35.0 Hz), 134.09, 122.31 (q, *J* = 272.5 Hz), 120.95 (q, *J* = 2.7 Hz), 117.70, 62.83, 33.50.

IR (film) ν_{max} 2854, 1593, 1360, 1343, 1141, 1114, 1093, 838, 711 cm^{-1}.

HRMS (ESI-TOF): m/z calcd. For $C_9H_9BrF_3N_2$ ($[M+H^+]$) 280.98957, found 280.98927.

(±) 4-Bromopentyl 4-bromobenzoate (51)



A round-bottom flask was charged with 4-bromobenzoic acid (2.07 g, 10.2 mmol 1.0 equiv) followed by the addition of DMF (25 mL). To this solution, cesium carbonate (5.02 g, 14.4 mmol, 1.5 equiv) and 1,4-dibromopentane (2.36 g, 1.4 mL, 10.2 mmol 1.0 equiv) was added. The mixture was stirred vigorously for 16 h at room temperature, then filtered, and concentrated. The residue was purified by flash chromatography (0-8% EtOAc/hexanes) provided the title compound (2.10 g, 58% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 4.37-4.30 (m, 2H), 4.21-4.13 (m, 1H), 2.10-1.84 (m, 4H), 1.75 (d, *J* = 6.6 Hz, 3H).

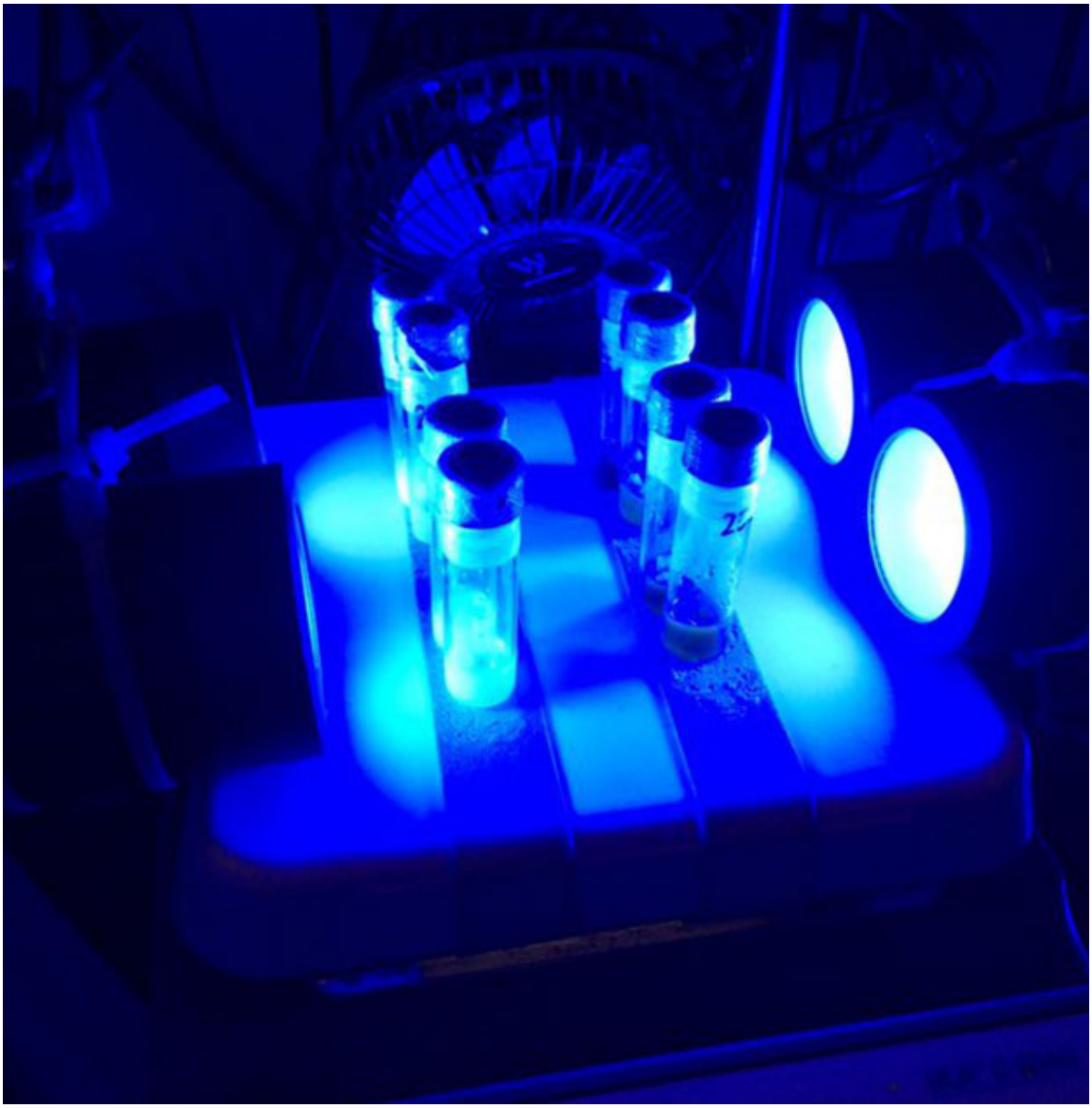
^{13}C NMR (125 MHz, $CDCl_3$) δ 165.95, 131.87, 131.22, 129.23, 128.22, 64.62, 50.86, 37.71, 27.25, 26.66.

IR (film) ν_{max} 2963, 1718, 1590, 1269, 1115, 1102, 1012, 848, 756 cm^{-1}.

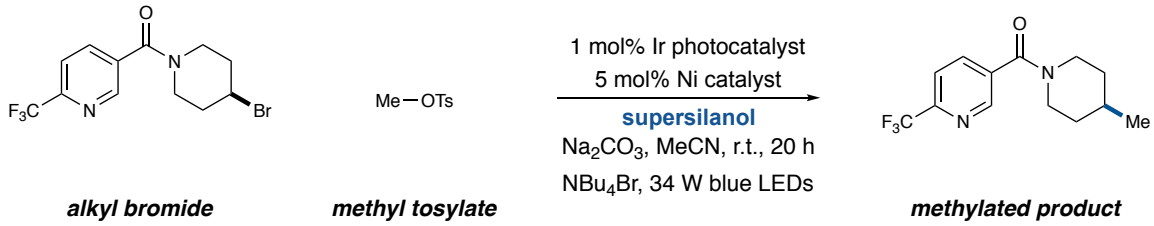
3) Procedure for Optimization Studies

To an 8 mL vial equipped with a stir bar was added photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (1.1 mg, 1 μmol, 0.01 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (33.7 mg, 0.1 mmol, 1.0 equiv.), tetrabutylammonium bromide (81 mg, 0.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol [super silanol] (39.7 mg, 0.15 mmol, 1.5 equiv.), and anhydrous sodium carbonate (21.2 mg, 0.2 mmol, 2.0 equiv.). The vial was sealed and placed under nitrogen before MeCN (0.5 mL) was added. To a separate vial was added $NiCl_2 \bullet 6H_2O$ (1.2 mg, 5 μmol, 0.05 equiv.) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (1.3 mg, 5 μmol, 0.05 equiv). The precatalyst vial was sealed, dissolved in MeCN (0.5 mL) and then sonicated until it became homogeneous. Subsequently, the precatalyst solution was syringed into the reaction vessel and the solution was degassed by sparging with nitrogen for 15 minutes. Methyl 4-methylbenzenesulfonate (30.2 μL, 0.2 mmol, 2.0 equiv) was then added before sealing with parafilm. The reaction was stirred and irradiated using 34 W blue LED lamps (6 cm away, with cooling fan to keep the reaction at room temperature) for 20 hours. The reaction was quenched by exposure to air. Methyl benzoate (internal standard, 12.6 μL, 0.1 mmol, 1.0 equiv.) was added then the reaction mixture was analyzed by UPLC.

4) Typical Reaction Set Up



5) Optimization Table and Control Experiments



alkyl bromide ***methyl tosylate*** ***methylated product***

entry	conditions	yield	alkyl dimer	dehalogenation
1	super silane	25%	3%	54%
2	LiOH	25%	4%	8%
3	DME	27%	2%	5%
4	no light	0%	0%	0%
5	no photocatalyst	0%	0%	0%
6	no Ni catalyst	trace	trace	12%
7	no NBu_4Br	27%	24%	10%
8	as above	70%	4%	6%

Figure S1: Optimization and Control Experiments. Reactions performed and analyzed as outlined above.

6) Procedure for Silanol-Mediated Reductive Coupling of Alkyl Halides

A) General Procedure for Coupling with Methyl Tosylate

To an 8 mL vial equipped with a stir bar was added photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), tetrabutylammonium bromide (403 mg, 1.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (198 mg, 0.75 mmol, 1.5 equiv.), and anhydrous sodium carbonate (106 mg, 1.00 mmol, 2.0 equiv.). The vial was sealed and placed under nitrogen before MeCN (4 mL) was added. To a separate vial was added $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.). The precatalyst vial was sealed, dissolved in MeCN (1 mL) and then sonicated until it became homogeneous. Subsequently, the precatalyst solution was syringed into the reaction vessel and the solution was degassed by sparging with nitrogen for 15 minutes. Methyl 4-methylbenzenesulfonate (186 mg, 151 μL, 1.00 mmol, 2.0 equiv) were then added before sealing with parafilm. The reaction was stirred and irradiated using 34 W blue LED lamps (6 cm away, with cooling fan to keep the reaction at room temperature) for 20 hours. The reaction was quenched by exposure to air. The reaction mixture was then added to a larger vial containing KF on Alumina (40 wt. % from Sigma-Aldrich, 2 grams) and rinsed with 2 mL MeCN. The suspension was then stirred, open to air, for approximately 30 minutes. Then the mixtures were filtered, and concentrated. The residue was purified by flash chromatography on silica gel to afford the desired product.

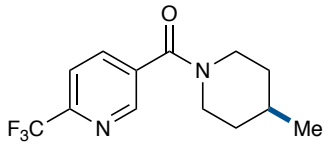
B) General Procedure for Coupling with Other Small Alkyl Halides

To an 8 mL vial equipped with a stir bar was added photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (135 mg, 0.40 mmol, 1.0 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (318 mg, 1.2 mmol, 3 equiv.), and anhydrous potassium phosphate (255 mg, 1.2 mmol, 3.0 equiv.). The vial was sealed and placed under nitrogen before MeCN (3 mL) was added. To a separate vial was added $NiCl_2 \bullet 6H_2O$ (4.8 mg, 20 μmol, 0.05 equiv.) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.4 mg, 20 μmol, 0.05 equiv.). The precatalyst vial was sealed, dissolved in MeCN (1 mL) and then sonicated until it became homogeneous. Subsequently, the precatalyst solution was syringed into the reaction vessel and the solution was degassed by sparging with nitrogen for 15 minutes. The appropriate small alkyl halide was then added (1.60 mmol, 4.0 equiv) was then added before sealing with parafilm. The reaction was stirred and irradiated using 34 W blue LED lamps (6 cm away, with cooling fan to keep the reaction at room temperature) for 20 hours. The reaction was quenched by exposure to air. The reaction mixture was then added to a larger vial containing KF on Alumina (40 wt. % from Sigma-Aldrich, 2 grams) and tetrabutylammonium bromide (500 mg, 1.55 mmol, 3.9 equiv.), and rinsed with 2 mL MeCN. The suspension was then stirred, open to air, for approximately 30 minutes. Then the mixtures were filtered, and concentrated. The residue was purified by flash chromatography on silica gel to afford the desired product.

Note: for each example, conditions may vary in stoichiometry of the small halide, super-silanol, and base, as well as the identity of the base (sometimes Na_2CO_3 is slightly better) and concentration. In particular, electron withdrawing groups (such as cyclic ethers or protected amines) on the bromide substrates tend to affect substrate reactivity and reaction stoichiometry. Also note that in the case of acyclic secondary halides, 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine [PyBox] is used in place of di-*tert*-butyl bipyridine as the ligand. See examples below for specific details.

7) Experimental Data

(4-Methylpiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (15)



Prepared following general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.8 mg, 20 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.4 mg, 20 μmol, 0.05 equiv.), tetrabutylammonium bromide (322 mg, 1.0 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (159 mg, 0.60 mmol, 1.5 equiv.), anhydrous sodium carbonate (85 mg, 0.80 mmol, 2.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (135 mg, 0.40 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (149 mg, 121 μL, 0.80 mmol, 2.0 equiv), and MeCN (4 mL). Purification by flash chromatography (0-25% EtOAc/hexanes) provided the title compound (78 mg, 72% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (d, *J* = 2.0 Hz, 1H), 7.91 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 4.66 (d, *J* = 13.2 Hz, 1H), 3.58 (d, *J* = 13.5 Hz, 1H), 3.06 (t, *J* = 12.5 Hz, 1H), 2.80 (t, *J* = 12.1 Hz, 1H), 1.79 (d, *J* = 13.6 Hz, 1H), 1.73-1.60 (m, 2H), 1.31-1.18 (m, 1H), 1.17-1.04 (m, 1H), 0.98 (d, *J* = 6.4 Hz, 3H).

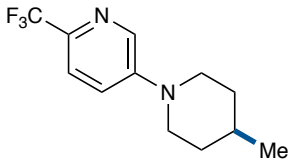
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.24, 148.75 (q, *J* = 35.1 Hz), 148.02, 136.37, 135.17, 121.13 (q, *J* = 274.6 Hz), 120.53 (q, *J* = 2.5 Hz), 48.25, 42.82, 34.79, 33.73, 31.11, 21.71.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.11.

IR (film) ν_{max} 2930, 1627, 1445, 1334, 1175, 1128, 1082, 1029, 969, 855, 738 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{13}H_{16}F_3N_2O$ ($[M+H]^+$) 273.12092, found 273.12136.

5-(4-Methylpiperidin-1-yl)-2-(trifluoromethyl)pyridine (16)



Prepared following general procedure A outlined above using Ir[dF(Me)ppy]$_2$(dtbbpy)PF_6 (5.1 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2$•DME (5.5 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), tetrabutylammonium bromide (403 mg, 1.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (198 mg, 0.75 mmol, 1.5 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), 5-(4-bromopiperidin-1-yl)-2-(trifluoromethyl)pyridine (155 mg, 0.50 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (186 mg, 151 μL, 1.0 mmol, 2.0 equiv), and MeCN (5 mL). Purification by flash chromatography (0-15% EtOAc/hexanes) provided the title compound (89 mg, 73% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 2.9 Hz, 1H), 7.47 (d, *J* = 8.9 Hz, 1H), 7.16 (dd, *J* = 8.8, 2.9 Hz, 1H), 3.79 (d, *J* = 12.4 Hz, 2H), 2.85 (td, *J* = 12.5, 2.7 Hz, 2H), 1.76 (d, *J* = 13.4 Hz, 2H), 1.64-1.53 (m, 1H), 1.40-1.23 (m, 2H), 0.98 (d, *J* = 6.6 Hz, 3H).

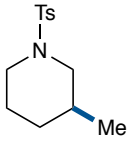
^{13}C NMR (125 MHz, $CDCl_3$) δ 148.62, 137.50, 136.75 (q, *J* = 34.8 Hz), 122.40 (q, *J* = 272.2 Hz), 120.93 (q, *J* = 2.6 Hz), 120.72, 48.12, 33.50, 30.71, 21.90.

^{19}F NMR (376 MHz, $CDCl_3$) δ -66.59.

IR (film) ν_{max} 2930, 1587, 1568, 1353, 1237, 1126, 1091, 909, 833, 731 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{16}F_3N_2$ ($[M+H]^+$) 245.12601, found 245.12611.

(±) 3-Methyl-1-tosylpiperidine (17)



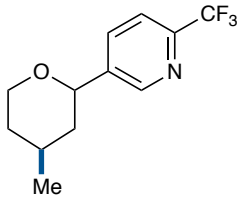
Prepared following general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.6 mg, 4.1 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.9 mg, 20 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.5 mg, 20 μmol, 0.05 equiv.), tetrabutylammonium bromide (329 mg, 1.0 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (162 mg, 0.61 mmol, 1.5 equiv.), anhydrous sodium carbonate (87 mg, 0.82 mmol, 2.0 equiv.), 3-bromo-1-tosylpiperidine (130 mg, 0.41 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (152 mg, 123 μL, 0.82 mmol, 2.0 equiv), and MeCN (4.1 mL). Purification by flash chromatography (0-25% EtOAc/hexanes) provided the title compound (72 mg, 70% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.74-3.55 (m, 2H), 2.43 (s, 3H), 2.20 (td, *J* = 11.4, 2.7 Hz, 1H), 1.86 (t, *J* = 10.7 Hz, 1H), 1.82-1.59 (m, 4H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.85-0.76 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.39, 133.42, 129.68, 127.82, 53.36, 46.59, 32.23, 30.83, 24.84, 21.68, 19.16.

Data in agreement with reported literature values.[12]

(±) 5-((4-Methyltetrahydro-2*H*-pyran-2-yl)-2-(trifluoromethyl)pyridine (18)



Prepared following general procedure A outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2$•$6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), tetrabutylammonium bromide (403 mg, 1.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (198 mg, 0.75 mmol, 1.5 equiv.), anhydrous sodium carbonate (106 mg, 1.00 mmol, 2.0 equiv.), *cis*-5-(4-bromotetrahydro-2*H*-pyran-2-yl)-2-(trifluoromethyl)pyridine (155 mg, 0.50 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (186 mg, 151 μL, 1.00 mmol, 2.0 equiv), and MeCN (5 mL). Purification by flash chromatography (0-15% EtOAc/hexanes) provided the title compound (86 mg, 70% yield, d.r. = 1.5:1) as a clear oil.

Note: The major diastereomer was assigned as *cis* by comparison to the nmr spectra of isomers of an analogous compound.[13]

^{1}H NMR (500 MHz, $CDCl_3$) minor diastereomer in brackets [ ]: δ 8.73-8.60 (m, 1H), 7.99-7.82 (m, 1H), 7.74-7.60 (m, 1H), [4.78 (dd, *J* = 9.9, 3.0 Hz, 0.4H)], 4.44 (dd, *J* = 11.5, 2.2 Hz, 0.6H), 4.18 (ddd, *J* = 11.5, 4.7, 1.6 Hz, 0.6H), [3.86 (dd, *J* = 3.3, 1.4 Hz, 0.4H)], [3.84 (d, *J* = 3.3 Hz, 0.4H)], 3.61 (ddd, *J* = 12.6, 11.6, 2.2 Hz, 0.6H), [2.19-2.07 (m, 0.4H)], 1.94-1.87 (m, 1H), [1.85-1.76 (m, 0.6H)], 1.70-1.62 (m, 1H), 1.42-1.29 (m, 1H), 1.26-1.11 (m, 2H), 1.00 (d, *J* = 6.5 Hz, 2H).

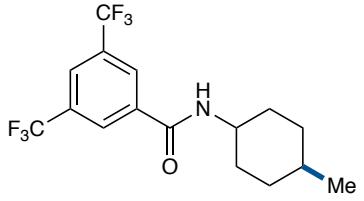
^{13}C NMR (125 MHz, $CDCl_3$) δ 148.21, 147.97, 147.14 (q, *J* = 34.6 Hz), 142.04, 141.90, 135.08, 134.67, 121.28 (q, *J* = 273.0 Hz), 120.31 (q, *J* = 2.8 Hz), 77.37, 71.59, 68.69, 63.29, 42.73, 39.09, 34.23, 31.74, 30.71, 25.28, 22.29, 18.42.

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

IR (film) ν_{max} 2928, 2850, 1334, 1172, 1136, 1083, 1027, 847 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{15}F_3NO$ ($[M+H]^+$) 246.11003, found 246.11001.

***N*-(4-Methylcyclohexyl)-3,5-bis(trifluoromethyl)benzamide (19)**



Prepared following general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.0 mg, 3.6 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.3 mg, 18 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (4.8 mg, 18 μmol, 0.05 equiv.), tetrabutylammonium bromide (289 mg, 0.90 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (142 mg, 0.54 mmol, 1.5 equiv.), anhydrous sodium carbonate (76 mg, 0.72 mmol, 2.0 equiv.), cis-*N*-(4-bromocyclohexyl)-3,5-bis(trifluoromethyl)benzamide (150 mg, 0.36 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (134 mg, 108 μL, 0.72 mmol, 2.0 equiv), and MeCN (3.6 mL). Purification by flash chromatography (0-20% EtOAc/hexanes) provided the title compound (80 mg, 63% yield, d.r. = 2.5:1) as a white solid.

Note: The major diastereomer was assigned as *trans* by comparison to the nmr spectra of isomers of an analogous compound.[14]

^{1}H NMR (500 MHz, $CDCl_3$) minor diastereomer in brackets [ ]: δ 8.18 (d, *J* = 1.9 Hz, 2H), 7.99 (d, *J* = 4.6 Hz, 1H), [6.22 (d, *J* = 7.5 Hz, 0.3H)], 6.02 (d, *J* = 8.1 Hz, 0.7H), [4.40-4.30 (m, 0.3H)], 3.99 (tdt, *J* = 11.9, 8.1, 4.0 Hz, 0.7H), 2.08 (d, *J* = 12.2 Hz, 1H), 1.88-1.65 (m, 3H), 1.63-1.54 (m, 2H), 1.52-1.39 (m, 1H), 1.21-1.09 (m, 1H), 0.98 (d, *J* = 6.5 Hz, 1H), 0.94 (d, *J* = 6.5 Hz, 2H), 0.92-0.81 (m, 1H).

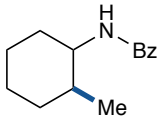
^{13}C NMR (125 MHz, $CDCl_3$) δ mixture of rotamers and diastereomers: δ 163.95, 163.80, 137.34, 137.21, 132.25 (q, *J* = 33.8 Hz), 127.33, 125.12 – 124.81 (m), 123.06 (q, *J* = 272.9 Hz), 49.78, 46.14, 41.98, 38.63, 34.28, 33.54, 32.96, 31.95, 30.78, 27.83, 24.91, 22.52, 21.45, 20.91.

^{19}F NMR (376 MHz, $CDCl_3$) δ minor diastereomer in brackets [ ]: δ [-62.85 (s, 0.27F)], -62.87 (s, 0.73F).

IR (film) ν_{max} 3288, 2931, 1643, 1551, 1278, 1181, 1136, 908 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{18}F_6NO$ ($[M+H]^+$) 354.12871, found 354.12817.

(±) *N*-((2*S*)-2-Methylcyclohexyl)benzamide (20)



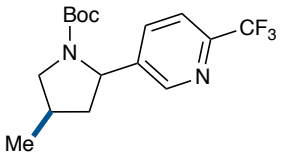
Prepared following general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.0 mg, 3.5 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.2 mg, 18 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (4.8 mg, 18 μmol, 0.05 equiv.), tetrabutylammonium bromide (286 mg, 0.89 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (141 mg, 0.53 mmol, 1.5 equiv.), anhydrous sodium carbonate (75 mg, 0.71 mmol, 2.0 equiv.), cis-*N*-(2-bromocyclohexyl)-benzamide (100 mg, 0.35 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (132 mg, 107 μL, 0.71 mmol, 2.0 equiv), and MeCN (3.5 mL). Purification by flash chromatography (0-20% EtOAc/hexanes) provided the title compound (59 mg, 77% yield, d.r. = 2.7:1) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) minor diastereomer in brackets [ ]: δ 7.78 – 7.74 (m, 2H), 7.52 – 7.47 (m, 1H), 7.46 – 7.41 (m, 2H), [6.12 (d, *J* = 4.3 Hz, 0.12H)], 5.82 (d, *J* = 8.9 Hz, 0.67H)], [4.28 (td, *J* = 9.5, 3.7 Hz, 0.25H)], 3.72 (qd, *J* = 10.8, 4.0 Hz, 0.78H), 2.12-2.01 (m, 0.83 H), [2.01-1.91 (m, 0.26H)], 1.83-1.67 (m, 2H), 1.66-1.59 (m, 1H), 1.52-1.10 (m, 5H), 0.99 (d, *J* = 6.5 Hz, 2.4H), [0.95 (d, *J* = 7.0 Hz, 0.8H)].

^{13}C NMR (125 MHz, $CDCl_3$) δ major diastereomer only: δ 167.10, 135.32, 131.38, 128.69, 126.92, 54.62, 38.96, 34.51, 33.97, 25.94, 25.63, 19.33.

The data for the major diastereomer are consistent with those in the literature for the *trans* compound.[15]

(±) *t*-Butyl-4-methyl-2-(6-(trifluoromethyl)pyridin-3-yl)pyrrolidine-1-carboxylate (21)



Prepared following general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.9 mg, 3.5 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.2 mg, 17.5 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (4.7 mg, 17.5 μmol, 0.05 equiv.), tetrabutylammonium bromide (282 mg, 0.88 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (139 mg, 0.53 mmol, 1.5 equiv.), anhydrous sodium carbonate (74 mg, 0.70 mmol, 2.0 equiv.), *trans*-*N*-Boc-4-bromo-2-(6-(trifluoromethyl)pyridin-3-yl)pyrrolidine (138 mg, 0.35 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (130 mg, 106 μL, 0.70 mmol, 2.0 equiv), and MeCN (3.5 mL). Purification by flash chromatography (0-20% EtOAc/hexanes) provided the title compound (82 mg, 71% yield, d.r. = 3:1) as a light yellow oil.

Note: The major diastereomer was assigned as *trans* by comparison to the nmr spectra of isomers of an analogous compound.[16] Furthermore, due to the nature of the spectra of this compound, purity is also demonstrated by UPLC trace (see below).

^{1}H NMR (500 MHz, DMSO-d_6) mixture of rotamers and diastereomers: δ 8.72-8.48 (m, 1H), 7.99-7.75 (m, 2H), 5.07-4.89 (m, 1H), 3.85-3.68 (m, 1H), 3.13-2.94 (m, 1H), 2.38-2.20 (m, 1H), 2.14-1.95 (m, 1H), 1.95-1.79 (m, 1H), 1.41-1.34 (m, 4H), 1.10 (s, 3H), 1.04 (s, 1H), 1.03-0.97 (m, 4H).

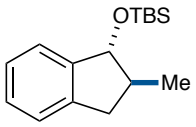
^{13}C NMR (125 MHz, DMSO-d_6) mixture of rotamers and diastereomers: δ 153.59, 153.08, 148.63 – 147.61 (m), 144.87, 144.49, 135.39, 135.16, 135.16, 134.90, 121.79 (q, *J* = 273.7 Hz), 120.64 – 120.11 (m), 78.92, 78.56, 78.50, 58.54, 58.14, 53.83, 53.52, 44.68, 42.30, 41.43, 32.31, 30.95, 30.58, 29.96, 28.10, 27.76, 17.31, 16.86, 16.38.

^{19}F NMR (376 MHz, DMSO-d_6) δ -66.16.

IR (film) ν_{max} 2969, 2930, 1692, 1391, 1338, 1161, 1134, 1085, 851 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{21}F_3N_2NaO_2$ ($[M+Na]^+$) 353.14473, found 353.14457.

(±) *tert*-Butyldimethyl((*trans*-2-methyl-2,3-dihydro-1*H*-inden-1-yl)oxy)silane (22)



Prepared following general procedure A outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2$•$6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), tetrabutylammonium bromide (403 mg, 1.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (198 mg, 0.75 mmol, 1.5 equiv.), anhydrous sodium carbonate (106 mg, 1.00 mmol, 2.0 equiv.), *trans*-((2-bromo-2,3-dihydro-1*H*-inden-1-yl)oxy)(*tert*-butyl)dimethylsilane (164 mg, 0.50 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (186 mg, 151 μL, 1.00 mmol, 2.0 equiv), and MeCN (5 mL). Purification by flash chromatography (0-10% EtOAc/hexanes) provided the title compound (55 mg, 42% yield, d.r.>20:1) as a clear oil.

Note: product could not be separated from a small amount of indanone. Relative stereochemistry by NOESY (see below).

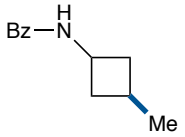
^{1}H NMR (500 MHz, $CDCl_3$) 7.29 – 7.25 (m, 1H), 7.23-7.14 (m, 3H), 4.75 (d, *J* = 7.1 Hz, 1H), 3.06 (dd, *J* = 15.4, 7.7 Hz, 1H), 2.44 (dd, *J* = 15.4, 9.1 Hz, 1H), 2.35-2.25 (m, 1H), 1.22 (d, *J* = 6.8 Hz, 3H), 0.97 (s, 9H), 0.20 (s, 3H), 0.17 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 145.99, 141.82, 127.59, 126.50, 124.67, 123.97, 83.09, 45.27, 37.89, 26.08, 18.29, 17.99, -3.91, -3.95.

IR (film) ν_{max} 2956, 2929, 2857, 1461, 1253, 1104, 1076, 864, 832, 773, 739 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{12}H_{17}OSi$ ($[M-C_4H_9]^+$) 205.10432, found 205.10432.

***N*-(3-Methylcyclobutyl)benzamide (23)**



Prepared following the general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), tetrabutylammonium bromide (403 mg, 1.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (198 mg, 0.75 mmol, 1.5 equiv.), anhydrous sodium carbonate (106 mg, 1.00 mmol, 2.0 equiv.), *N*-(3-bromocyclobutyl)benzamide (127 mg, 0.50 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (186 mg, 151 μL, 1.00 mmol, 2.0 equiv), and MeCN (10 mL). Purification by flash chromatography (20-25% EtOAc/hexanes) provided the title compound (64 mg, 68% yield, d.r. = 1.2:1) as a white solid.

Note: The major diastereomer was assigned as *cis* by comparison to the nmr spectra of isomers of an analogous compound.[17]

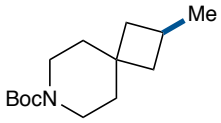
^{1}H NMR (500 MHz, $CDCl_3$) [mixture of diastereomers] δ 7.78-7.69 (m, 2H), 7.46-7.41 (m, 1H), 7.36 (t, *J* = 7.5 Hz, 2H), 6.69 (br, 0.44H), 6.60 (br, 0.53H), 4.67 (h, *J* = 7.8 Hz, 0.45H), 4.36 (h, *J* = 7.7 Hz, 0.58H), 2.57-2.51 (m, 1H), 2.35-2.27 (m, 0.48H), 2.18-2.09 (m, 1H), 2.09-1.98 (m, 1.51H), 1.54-1.48 (m, 1H), 1.14 (d, *J* = 7.0 Hz, 1.41H), 1.04 (d, *J* = 6.6 Hz, 1.72H).

^{13}C NMR (125 MHz, $CDCl_3$) [mixture of diastereomers] δ 166.92, 166.77, 134.74, 134.67, 131.30, 131.29, 128.46, 127.02, 127.02, 43.44, 41.53, 39.01, 36.98, 23.93, 23.89, 21.89, 21.21.

IR (film) ν_{max} 3315, 2954, 2930, 1630, 1536, 1297, 694 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{16}NO$ ($[M+H]^+$) 190.1226, found 190.1227.

***tert*-Butyl 2-methyl-7-azaspiro[3.5]nonane-7-carboxylate (24)**



Prepared following the general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), tetrabutylammonium bromide (403 mg, 1.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (198 mg, 0.75 mmol, 1.5 equiv.), anhydrous potassium phosphate (212 mg, 1.00 mmol, 2.0 equiv.), *tert*-butyl 2-bromo-7-azaspiro[3.5]nonane-7-carboxylate (152 mg, 0.50 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (186 mg, 151 μL, 1.00 mmol, 2.0 equiv), and MeCN (10 mL). Purification by flash chromatography (5-10% EtOAc/hexanes) provided the title compound (78 mg, 65% yield) as a pale yellow oil.

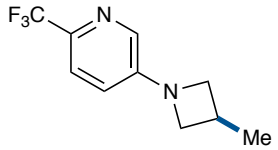
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.34-3.29 (m, 2H), 3.26-3.19 (m, 2H), 2.35-2.24 (m, 1H), 1.98-1.87 (m, 2H), 1.53-1.49 (m, 2H), 1.42 (s, 9H), 1.42-1.40 (m, 2H), 1.31 (ddd, J = 10.5, 8.5, 2.3 Hz, 2H), 1.04 (d, J = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.09, 79.16, 40.70, 39.84, 39.70, 36.50, 33.64, 28.56, 23.75, 23.00.

IR (film) ν_{max} 2918, 2847, 1692, 1417, 1365, 1240, 1147, 967, 769 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{25}NNaO_2$ ($[M+Na]^+$) 262.1778, found 262.1776.

5-(3-methylazetidin-1-yl)-2-(trifluoromethyl)pyridine (25)



Prepared following general procedure A outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (6.0 mg, 5.3 μmol, 0.01 equiv.), $NiCl_2$•$6H_2O$ (6.3 mg, 27 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (7.2 mg, 27 μmol, 0.05 equiv.), tetrabutylammonium bromide (430 mg, 1.33 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (212 mg, 0.80 mmol, 1.5 equiv.), anhydrous sodium carbonate (113 mg, 1.07 mmol, 2.0 equiv.), 5-(3-bromoazetidin-1-yl)-2-(trifluoromethyl)pyridine (150 mg, 0.53 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (199 mg, 161 μL, 1.07 mmol, 2.0 equiv), and MeCN (5.3 mL). Purification by flash chromatography (0-15% EtOAc/hexanes) provided the title compound (56 mg, 49% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 2.7 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 6.67 (dd, *J* = 8.5, 2.6 Hz, 1H), 4.12 (t, *J* = 7.6 Hz, 2H), 3.56 (dd, *J* = 7.1, 5.7 Hz, 2H), 2.93 (h, *J* = 6.6 Hz, 1H), 1.32 (d, *J* = 6.9 Hz, 3H).

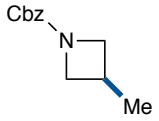
^{13}C NMR (125 MHz, $CDCl_3$) δ 148.60, 136.05 (q, *J* = 34.6 Hz), 133.68, 122.59 (q, *J* = 270.8 Hz), 120.84 (q, *J* = 2.7 Hz), 116.69, 58.83, 25.87, 19.87.

^{19}F NMR (282 MHz, $CDCl_3$) δ -66.31.

IR (film) ν_{max} 2965, 2855, 1590, 1385, 1343, 1278, 1125, 1093, 831 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{10}H_{12}F_3N_2$ ($[M+H]^+$) 217.09471, found 217.09476.

Benzyl 3-methylazetidine-1-carboxylate (26)



Prepared following the general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), tetrabutylammonium bromide (403 mg, 1.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (198 mg, 0.75 mmol, 1.5 equiv.), anhydrous potassium phosphate (212 mg, 1.00 mmol, 2.0 equiv.), benzyl 3-bromoazetidine-1-carboxylate (135 mg, 0.50 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (186 mg, 151 μL, 1.00 mmol, 2.0 equiv), and MeCN (10 mL). Purification by flash chromatography (25-30% EtOAc/hexanes) provided the title compound (65 mg, 63% yield) as a yellow oil.

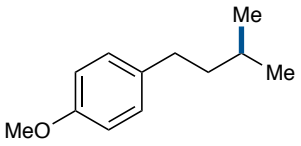
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.29 (m, 5H), 5.09 (s, 2H), 4.11 (t, *J* = 8.4 Hz, 2H), 3.57 (dd, *J* = 8.5, 5.5 Hz, 2H), 2.82-2.51 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 156.54, 136.93, 128.52, 128.02, 127.98, 66.52, 56.30, 24.27, 19.70.

IR (film) ν_{max} 2961, 2878, 1702, 1412, 1356, 1124, 1060, 767, 697 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{12}H_{16}NO_2$ ($[M+H]^+$) 206.1176, found 206.1172.

1-Isopentyl-4-methoxybenzene (27)



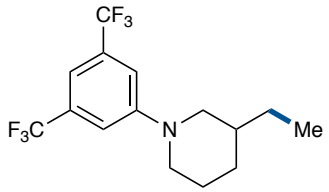
Prepared following the general procedure A outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), tetrabutylammonium bromide (403 mg, 1.25 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (198 mg, 0.75 mmol, 1.5 equiv.), anhydrous sodium carbonate (106 mg, 1.00 mmol, 2.0 equiv.), 1-(3-bromobutyl)-4-methoxybenzene[18] (122 mg, 0.50 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (186 mg, 151 μL, 1.00 mmol, 2.0 equiv), and MeCN (10 mL). This yielded an inseparable mixture of product and hydrodehalogenation byproduct, and the 62% yield was calculated from a calibrated GC assay after the addition of a standard (methyl benzoate).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 2.55 (t, *J* = 8.0 Hz, 2H), 1.59-1.44 (m, 2H), 0.92 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.67, 135.33, 129.32, 113.80, 55.40, 41.24, 32.97, 27.74, 22.70.

Spectroscopic data matches with previously reported data.[19]

(±) 1-(3,5-Bis(trifluoromethyl)phenyl)-3-ethylpiperidine (28)



Prepared following general procedure A outlined above using Ir[dF(Me)ppy]$_2$(dtbbpy)PF$_6$ (3.1 mg, 3.1 μmol, 0.01 equiv.), NiCl$_2$•6H$_2$O (3.7 mg, 15 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (4.1 mg, 15 μmol, 0.05 equiv.), tetrabutylammonium bromide (248 mg, 0.77 mmol, 2.5 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (122 mg, 0.46 mmol, 1.5 equiv.), anhydrous sodium carbonate (98 mg, 0.92 mmol, 3.0 equiv.), 1-(3,5-bis(trifluoromethyl)phenyl)-3-(bromomethyl)piperidine (120 mg, 0.31 mmol, 1.0 equiv.), methyl 4-methylbenzenesulfonate (115 mg, 93 μL, 0.62 mmol, 2.0 equiv), and MeCN (3.1 mL). Purification by flash chromatography (0-10% EtOAc/hexanes) provided the title compound (70 mg, 70% yield) as a white solid.

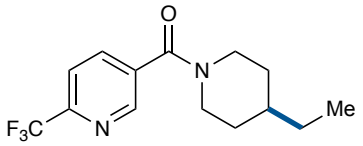
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.22 (s, 2H), 7.21 (s, 1H), 3.76-3.61 (m, 2H), 2.81 (td, *J* = 12.1, 3.0 Hz, 1H), 2.48 (t, *J* = 12.1 Hz, 1H), 1.96-1.86 (m, 1H), 1.86-1.77 (m, 1H), 1.68-1.59 (m, 1H), 1.55-1.49 (m, 1H), 1.43-1.20 (m, 2H), 1.09 (qd, *J* = 12.5, 3.9 Hz, 1H), 0.97 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 152.18, 132.32 (q, *J* = 32.5 Hz), 123.82 (q, *J* = 272.6 Hz), 114.98 – 114.83 (m), 111.14 (hept, *J* = 3.9 Hz), 54.96, 49.49, 37.43, 30.34, 26.97, 24.91, 11.49.

IR (film) ν_{max} 2935, 1618, 1480, 1400, 1275, 1172, 1128, 965, 864 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{18}F_6N$ ([M+H]$^+$) 326.1338, found 326.13381.

(4-Ethylpiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (29)



Prepared following general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.8 mg, 20 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.4 mg, 20 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (423 mg, 1.6 mmol, 4.0 equiv.), anhydrous potassium phosphate (255 mg, 1.20 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (135 mg, 0.40 mmol, 1.0 equiv.), bromoethane (305 mg, 209 μL, 2.80 mmol, 7.0 equiv), and MeCN (4 mL). Purification by flash chromatography (10-30% EtOAc/hexanes) provided the title compound (88 mg, 0.31 mmol, 77% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 2.0 Hz 1H), 7.92 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 4.71 (d, *J* = 12.6 Hz, 1H), 3.61 (d, *J* = 12.7 Hz, 1H), 3.07 (t, *J* = 12.6 Hz, 1H), 2.80 (t, *J* = 12.4 Hz, 1H), 1.87 (d, *J* = 12.5 Hz, 1H), 1.71 (d, *J* = 12.4 Hz, 1H), 1.55-1.41 (m, 1H), 1.37-1.28 (m, 2H), 1.27-1.03 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H).

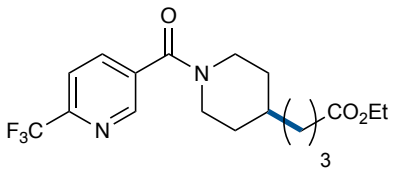
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.24, 148.82 (q, *J* = 35.1 Hz), 148.08, 136.42, 135.18, 120.99 (q, *J* = 274.4 Hz), 120.55 (q, *J* = 3.6 Hz), 48.36, 42.93, 37.84, 32.74, 31.61, 29.09, 11.30.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.12.

IR (film) ν_{max} 2930, 2857, 1632, 1444, 1334, 1283, 1175, 1125, 1082, 986, 856 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{14}H_{18}F_3N_2O$ ($[M+H]^+$) 287.13657, found 287.1362.

Ethyl 4-(1-(6-(trifluoromethyl)nicotinoyl)piperidin-4-yl)butanoate (30)



Prepared following general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.8 mg, 20 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.4 mg, 20 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (318 mg, 1.2 mmol, 3.0 equiv.), anhydrous potassium phosphate (255 mg, 1.20 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (135 mg, 0.40 mmol, 1.0 equiv.), ethyl 4-bromobutanoate (312 mg, 229 μL, 1.60 mmol, 4.0 equiv), and MeCN (4 mL). Purification by flash chromatography (10-40% EtOAc/hexanes) provided the title compound (105 mg, 0.28 mmol 71% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 1.9 Hz, 1H), 7.91 (dd, *J* = 8.1, 2.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 4.70 (d, *J* = 13.1 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.61 (d, *J* = 13.1 Hz, 1H), 3.07 (t, *J* = 12.8 Hz, 1H), 2.80 (t, *J* = 12.7 Hz, 1H), 2.30 (t, *J* = 7.4 Hz, 2H), 1.92-1.83 (m, 1H), 1.74-1.53 (m, 4H), 1.34 – 1.28 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 4H), 1.18-1.04 (m, 1H).

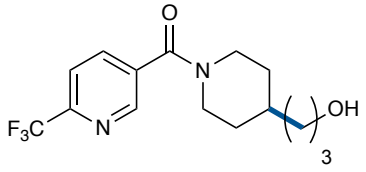
^{13}C NMR (125 MHz, $CDCl_3$) δ 173.62, 166.25, 148.85 (q, *J* = 35.3 Hz), 148.07, 136.42, 135.08, 121.30 (q, *J* = 274.3 Hz), 120.55 (q, *J* = 2.8 Hz), 60.48, 48.23, 42.81, 35.97, 35.77, 34.43, 32.93, 31.80, 22.15, 14.40.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.13.

IR (film) ν_{max} 2932, 1731, 1635, 1446, 1376, 1335, 1177, 1139, 1083, 856 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{18}H_{24}F_3N_2O_3$ ($[M+H]^+$) 373.17335, found 373.17301.

(4-(3-Hydroxypropyl)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (31)



Prepared following general procedure B outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (11.2 mg, 10.0 μmol, 0.02 equiv.), $NiCl_2$•$6H_2O$ (11.8 mg, 50 μmol, 0.10 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (13.4 mg, 50 μmol, 0.10 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.5 mmol, 3.0 equiv.), anhydrous potassium phosphate (212 mg, 1. 0 mmol, 2.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), 3-bromopropan-1-ol (347 mg, 226 μL, 2.50 mmol, 5.0 equiv), and MeCN (5 mL). Methyl benzoate (68.1 mg, 63.0 μL, 0.5 mmol, 1.0 equiv) was then added as the internal standard, and the yield was determined by UHPLC (55% yield). This compound could not be completely separated from the dimerized byproduct of the model substrate. This impurity is seen in the spectra.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 1.9 Hz, 1H), 7.91 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 4.73 (d, *J* = 13.0 Hz, 1H), 3.62 (m, 3H), 3.07 (t, *J* = 12.7 Hz, 1H), 2.79 (t, *J* = 12.2 Hz, 1H), 1.86 (d, *J* = 13.6 Hz, 1H), 1.70 (d, *J* = 14.0 Hz, 2H), 1.60-1.52 (m, 2H), 1.40 – 1.31 (m, 2H), 1.29-1.05 (m, 2H).

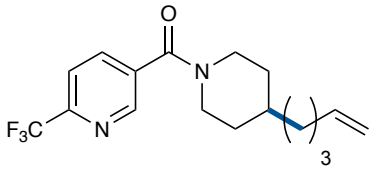
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.23, 148.78 (q, *J* = 35.2 Hz), 148.01, 136.40, 135.06, 121.27 (q, *J* = 274.2 Hz), 120.55 (q, *J* = 2.9 Hz), 62.94, 48.23, 42.81, 35.96, 33.01, 32.44, 31.87, 29.80.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.11.

IR (film) ν_{max} 3423, 2932, 2858, 1623, 1447, 1333, 1176, 1134, 1082, 856, 730 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{20}F_3N_2O_2$ ($[M+H]^+$) 317.14714, found 317.14686.

(4-(Pent-4-en-1-yl)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (32)



Prepared following general procedure B outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiCl_2$•$6H_2O$ (4.8 mg, 20 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.4 mg, 20 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (318 mg, 1.2 mmol, 3.0 equiv.), anhydrous potassium phosphate (170 mg, 0.80 mmol, 2.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (135 mg, 0.40 mmol, 1.0 equiv.), 5-bromopent-1-ene (298 mg, 237 μL, 2.0 mmol, 5.0 equiv), and MeCN (4 mL). Purification by flash chromatography (10-30% EtOAc/hexanes) provided the title compound (82 mg, 0.25 mmol 63% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 1.9 Hz, 1H), 7.92 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 5.80 (ddt, *J* = 16.9, 10.3, 6.7 Hz, 1H), 5.08-4.91 (m, 2H), 4.70 (d, *J* = 13.2 Hz, 1H), 3.61 (d, *J* = 13.5 Hz, 1H), 3.07 (t, *J* = 13.1 Hz, 1H), 2.80 (t, *J* = 12.7 Hz, 1H), 2.13-1.99 (m, 2H), 1.86 (d, *J* = 13.5 Hz, 1H), 1.70 (d, *J* = 13.4 Hz, 1H), 1.63-1.50 (m, 1H), 1.47 – 1.39 (m, 2H), 1.33-1.21 (m, 3H), 1.16-1.04 (m, 1H).

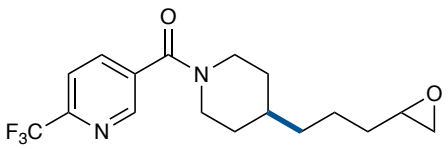
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.24, 148.83 (q, *J* = 35.2 Hz), 148.07, 138.74, 136.42, 135.15, 120.78 (q, *J* = 273.5 Hz), 120.55 (q, *J* = 2.6 Hz), 114.79, 48.32, 42.90, 36.07, 35.80, 33.94, 33.08, 31.93, 26.01.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.12.

IR (film) ν_{max} 2927, 2856, 1632, 1443, 1334, 1175, 1132, 1082, 855, 732 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{22}F_3N_2O$ ($[M+H]^+$) 327.16787, found 327.16805.

(±) (4-(3-(Oxiran-2-yl)propyl)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (33)



Prepared following general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.8 mg, 20 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.4 mg, 20 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (318 mg, 1.2 mmol, 3.0 equiv.), anhydrous potassium phosphate (170 mg, 0.80 mmol, 2.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (135 mg, 0.40 mmol, 1.0 equiv.), 2-(3-bromopropyl)oxirane (330 mg, 2.0 mmol, 5.0 equiv), and MeCN (4 mL). Purification by flash chromatography (10-50% EtOAc/hexanes) provided the title compound (60 mg, 0.18 mmol 44% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 2.0 Hz, 1H), 7.92 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.75 (dd, *J* = 8.0, 0.9 Hz, 1H), 4.71 (d, *J* = 13.2 Hz, 1H), 3.57 (d, *J* = 12.8 Hz, 1H), 3.08 (t, *J* = 12.9 Hz, 1H), 2.96-2.88 (m, 1H), 2.80 (t, *J* = 12.5 Hz, 1H), 2.76 (dd, *J* = 5.0, 3.9 Hz, 1H), 2.47 (dd, *J* = 5.0, 2.7 Hz, 1H), 1.87 (d, *J* = 13.6 Hz, 1H), 1.71 (d, *J* = 13.3 Hz, 1H), 1.64-1.53 (m, 2H), 1.53-1.43 (m, 3H), 1.39-1.30 (m, 2H), 1.29-1.19 (m, 1H), 1.18-1.05 (m, 1H).

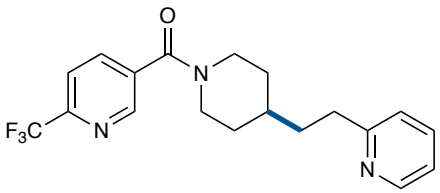
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.25, 148.86 (q, *J* = 35.0 Hz), 148.07, 136.43, 135.10, 121.31 (q, *J* = 275.4 Hz), 120.56 (q, *J* = 2.8 Hz), 52.33, 48.28, 47.19, 42.85, 36.13 (2C), 33.02, 32.70, 31.86, 23.29.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.12.

IR (film) ν_{max} 2928, 2858, 1631, 1444, 1333, 1175, 1130, 1082, 856, 718 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{22}F_3N_2O_2$ ($[M+H]^+$) 343.16279, found 343.16225.

(4-(2-(Pyridin-2-yl)ethyl)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (34)



Prepared following general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (4.8 mg, 20 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.4 mg, 20 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (318 mg, 1.2 mmol, 3.0 equiv.), anhydrous potassium phosphate (594 mg, 2.80 mmol, 7.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (135 mg, 0.40 mmol, 1.0 equiv.), 2-(2-bromoethyl)pyridin-1-ium bromide (534 mg, 2.0 mmol, 5.0 equiv), and MeCN (4 mL). Purification by reverse-phase chromatography (0-90% MeCN/water) provided the title compound (114 mg, 0.31 mmol 78% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 1.9 Hz, 1H), 8.53 (d, *J* = 4.0 Hz, 1H), 7.92 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.75 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.62 (td, *J* = 7.7, 1.9 Hz, 1H), 7.17-7.14 (m, 1H), 7.14-7.12 (m, 1H), 4.71 (d, *J* = 13.1 Hz, 1H), 3.62 (d, *J* = 13.5 Hz, 1H), 3.08 (t, *J* = 12.8 Hz, 1H), 2.88-2.75 (m, 3H), 1.93 (d, *J* = 13.6 Hz, 1H), 1.81-1.71 (m, 3H), 1.69-1.58 (m, 1H), 1.42-1.11 (m, 2H).

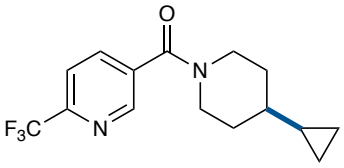
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.26, 161.69, 149.17, 148.85 (q, *J* = 35.2 Hz), 148.06, 136.86, 136.43, 135.07, 122.92, 121.41, 121.15 (q, *J* = 275.6 Hz), 120.55 (q, *J* = 2.7 Hz), 48.21, 42.79, 36.34, 35.86, 35.33, 32.94, 31.80.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.12.

IR (film) ν_{max} 2926, 2856, 1631, 1592, 1441, 1334, 1176, 1136, 1083, 857, 772 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{19}H_{21}F_3N_3O_2$ ($[M+H]^+$) 364.16312, found 364.16275.

(4-Cyclopropylpiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (35)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (463 mg, 1.75 mmol, 3.5 equiv.), anhydrous potassium phosphate (318 mg, 1.50 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), bromocyclopropane (484 mg, 320 μL, 4.00 mmol, 8.0 equiv), and MeCN (10 mL). Reaction time: 40 h. Purification by flash chromatography (50% EtOAc/hexanes) provided the title compound (59 mg, 40% yield) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 4.65 (d, *J* = 12.4 Hz, 1H), 3.60 (d, *J* = 12.8 Hz, 1H), 3.01 (t, *J* = 12.4 Hz, 1H), 2.77 (t, *J* = 12.1 Hz, 1H), 1.90 (d, *J* = 12.7 Hz, 1H), 1.74 (d, *J* = 12.4 Hz, 1H), 1.44-1.27 (m, 2H), 0.85-0.71 (m, 1H), 0.61-0.48 (m, 1H), 0.44-0.41 (m, 2H), 0.09-0.07 (m, 2H).

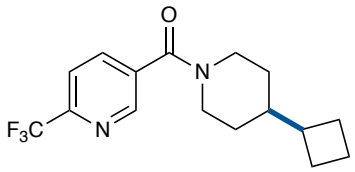
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.21, 148.73 (q, *J* = 35.0 Hz), 148.02, 136.36, 135.13, 121.27 (q, *J* = 274.2 Hz), 120.50 (q, *J* = 2.4 Hz), 48.19, 42.77, 41.49, 32.80, 31.65, 16.54, 3.34.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.12.

IR (film) ν_{max} 2931, 2859, 1631, 1444, 1334, 1130, 1082, 995, 854 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{18}F_3N_2O$ ($[M+H]^+$) 299.1366, found 299.1365.

(4-Cyclobutylpiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (36)



Prepared following the general procedure B outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2$•$6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.50 mmol, 3.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), bromocyclobutane (338 mg, 235 μL, 2.50 mmol, 5.0 equiv), and MeCN (10 mL). Reaction time: 40 h. Purification by flash chromatography (40-50% EtOAc/hexanes) provided the title compound (105 mg, 67% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.89 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 4.65 (d, *J* = 12.6 Hz, 1H), 3.57 (d, *J* = 12.9 Hz, 1H), 3.02 (t, *J* = 12.4 Hz, 1H), 2.76 (t, *J* = 12.2 Hz, 1H), 2.04-1.92 (m, 3H), 1.88-1.58 (m, 6H), 1.48-1.39 (m, 1H), 1.14-0.88 (m, 2H).

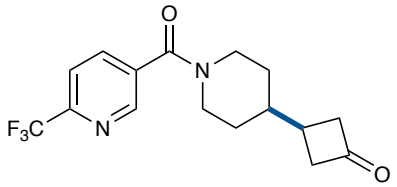
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.17, 148.66 (q, *J* = 35.1 Hz), 147.99, 136.31, 135.13, 121.25 (q, *J* = 274.3 Hz), 120.45 (q, *J* = 2.5 Hz), 48.15, 42.69, 42.62, 40.90, 29.90, 28.78, 26.41, 18.02.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.14

IR (film) ν_{max} 2936, 2857, 1633, 1444, 1334, 1131, 1083, 993, 857 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{19}F_3N_2NaO$ ($[M+Na]^+$) 335.1342, found 335.1341.

3-(1-(6-(Trifluoromethyl)nicotinoyl)piperidin-4-yl)cyclobutan-1-one (37)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.50 mmol, 3.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), 3-bromocyclobutanone (372 mg, 205 μL, 2.50 mmol, 5.0 equiv), and MeCN (10 mL). Reaction time: 40 h. Purification by flash chromatography (200% EtOAc/hexanes) provided the title compound (84 mg, 52% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.95-7.85 (m, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 4.75 (d, *J* = 11.8 Hz, 1H), 3.67 (d, *J* = 12.2 Hz, 1H), 3.16-3.05 (m, 3H), 2.80-2.71 (m, 3H), 2.19-2.11 (m, 1H), 1.91 (d, *J* = 11.9 Hz, 1H), 1.75 (d, *J* = 12.0 Hz, 1H), 1.61-1.54 (m, 1H), 1.33-1.13 (m, 2H).

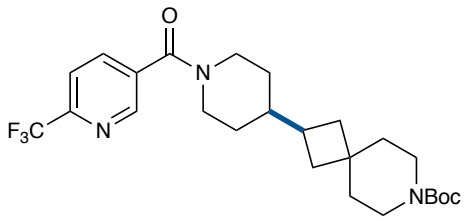
^{13}C NMR (125 MHz, $CDCl_3$) δ 206.52, 166.30, 148.88 (q, *J* = 35.1 Hz), 148.00, 136.41, 134.82, 121.22 (q, *J* = 274.3 Hz), 120.54 (q, *J* = 2.6 Hz), 50.77, 47.88, 42.47, 41.97, 30.87, 29.76, 29.24.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.11

IR (film) ν_{max} 3006, 1781, 1633, 1335, 1276, 1261, 1137, 1082, 750 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{16}H_{18}F_3N_2O_2$ ($[M+H]^+$) 327.1315, found 327.1316.

***tert*-Butyl 2-(1-(6-(trifluoromethyl)nicotinoyl)piperidin-4-yl)-7-azaspiro[3.5]nonane-7-carboxylate (38)**



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.50 mmol, 3.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), *tert*-butyl 2-bromo-7-azaspiro[3.5]nonane-7-carboxylate (456 mg, 1.50 mmol, 3.0 equiv), and MeCN (10 mL). Reaction time: 40 h. Purification by flash chromatography (60-70% EtOAc/hexanes) provided the title compound (170 mg, 71% yield) as a white foam.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.88 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 4.66 (d, *J* = 12.5 Hz, 1H), 3.58 (d, *J* = 12.8 Hz, 1H), 3.37-3.28 (m, 2H), 3.26-3.17 (m, 2H), 3.01 (t, *J* = 12.4 Hz, 1H), 2.74 (t, *J* = 12.1 Hz, 1H), 1.99-1.81 (m, 3H), 1.78 (d, *J* = 12.7 Hz, 1H), 1.62 (d, *J* = 12.5 Hz, 1H), 1.58-1.48 (m, 2H), 1.40 (s, 9H), 1.40-1.37 (m, 5H), 1.13-0.87 (m, 2H).

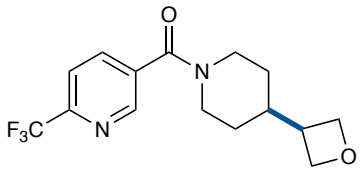
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.17, 154.99, 148.69 (q, *J* = 35.1 Hz), 147.96, 136.31, 135.05, 121.22 (q, *J* = 274.3 Hz), 120.46 (q, *J* = 2.6 Hz), 79.28, 48.08, 43.40, 42.63, 40.74, 39.64, 36.19, 35.99, 33.81, 33.69, 30.02, 28.90, 28.50.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.11

IR (film) ν_{max} 2926, 1689, 1637, 1427, 1335, 1275, 1139, 1083, 764 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{25}H_{34}F_3N_3NaO_3$ ($[M+Na]^+$) 504.2445, found 504.2443.

(4-(Oxetan-3-yl)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (39)



Prepared following general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.5 mmol, 3.0 equiv.), anhydrous potassium phosphate (212 mg, 1. 0 mmol, 2.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), 3-bromooxetane (274 mg, 166 μL, 2.0 mmol, 4.0 equiv), and MeCN (5 mL). Methyl benzoate (68.1 mg, 63.0 μL, 0.5 mmol, 1.0 equiv) was then added as the internal standard, and the yield was determined by UHPLC (50% yield). This compound could not be completely separated from the dimerized byproduct of the model substrate. This impurity is seen in the spectra.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 1.9 Hz, 1H), 7.90 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 4.79-4.65 (m, 3H), 4.51-4.35 (m, 2H), 3.63 (d, *J* = 13.1 Hz, 1H), 3.10 (t, *J* = 12.9 Hz, 1H), 2.88-2.70 (m, 2H), 2.05-1.92 (m, 1H), 1.76 (d, *J* = 13.8 Hz, 1H), 1.61 (d, *J* = 13.3 Hz, 1H), 1.22-0.92 (m, 2H).

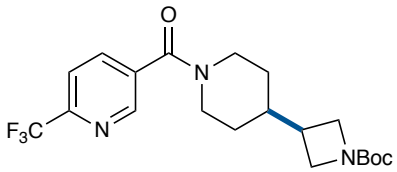
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.28, 148.84 (q, *J* = 35.2 Hz), 147.97, 136.41, 134.81, 120.91 (q, *J* = 274.3 Hz), 120.55 (d, *J* = 2.6 Hz), 75.56, 47.81, 42.39, 40.06, 39.85, 29.69, 28.60.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.13.

IR (film) ν_{max} 2932, 2867, 1629, 1444, 1333, 1175, 1130, 1082, 992, 978, 856, 730 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{18}F_3N_2O_2$ ($[M+H]^+$) 315.13149, found 315.13139.

***tert*-Butyl 3-(1-(6-(trifluoromethyl)nicotinoyl)piperidin-4-yl)azetidine-1-carboxylate (40)**



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.50 mmol, 3.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), *tert*-butyl 3-bromoazetidine-1-carboxylate (354 mg, 1.50 mmol, 3.0 equiv), and MeCN (10 mL). Reaction time: 40 h. Purification by flash chromatography (150% EtOAc/hexanes) provided the title compound (119 mg, 58% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.88 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 4.70 (d, *J* = 12.1 Hz, 1H), 4.00-3.78 (m, 2H), 3.67-3.52 (m, 3H), 3.05 (t, *J* = 12.3 Hz, 1H), 2.76 (t, *J* = 12.1 Hz, 1H), 2.28-2.21 (m, 1H), 1.78-1.61 (m, 3H), 1.38 (s, 9H), 1.16-0.97 (m, 2H).

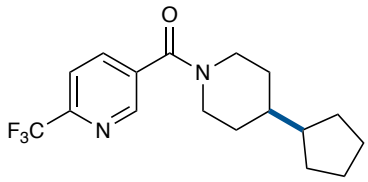
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.21, 156.28, 148.77 (q, *J* = 35.1 Hz), 147.94, 136.32, 134.78, 121.17 (q, *J* = 274.3 Hz), 120.46 (q, *J* = 2.7 Hz), 79.45, 52.44, 47.76, 42.33, 40.07, 33.71, 29.69, 28.61, 28.39.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.13

IR (film) ν_{max} 2935, 1692, 1631, 1334, 1133, 1082, 987, 856, 729 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{20}H_{26}F_3N_3NaO_3$ ($[M+Na]^+$) 436.1819, found 436.1814.

(4-Cyclopentylpiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (41)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (11.2 mg, 10.0 μmol, 0.02 equiv.), $NiCl_2 \bullet 6H_2O$ (11.8 mg, 50 μmol, 0.10 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (10.9 mg, 50 μmol, 0.10 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.50 mmol, 3.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), bromocyclopentane (373 mg, 268 μL, 2.50 mmol, 5.0 equiv), and MeCN (10 mL). Reaction time: 40 h. Purification by flash chromatography (30-40% EtOAc/hexanes) provided the title compound (73 mg, 45% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.94-7.85 (m, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 4.68 (d, *J* = 12.9 Hz, 1H), 3.59 (d, *J* = 13.0 Hz, 1H), 3.04 (t, *J* = 12.5 Hz, 1H), 2.76 (t, *J* = 11.7 Hz, 1H), 1.88 (d, *J* = 11.8 Hz, 1H), 1.81-1.69 (m, 3H), 1.62-1.47 (m, 5H), 1.37-1.25 (m, 2H), 1.16-1.09 (m, 3H).

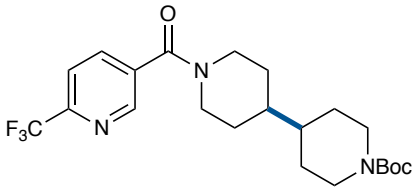
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.12, 148.70 (q, *J* = 35.1 Hz), 148.03, 136.35, 135.14, 121.27 (q, *J* = 274.3 Hz), 120.47 (q, *J* = 2.6 Hz), 48.34, 45.86, 42.90, 41.93, 32.14, 31.01, 30.47, 25.22.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.13

IR (film) ν_{max} 2947, 2865, 1635, 1445, 1335, 1136, 1081, 857 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{22}F_3N_2O$ ($[M+H]^+$) 327.1679, found 327.1676.

***tert*-Butyl 1'-(6-(trifluoromethyl)nicotinoyl)-[4,4'-bipiperidine]-1-carboxylate (42)**



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (6.7 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.50 mmol, 3.0 equiv.), anhydrous potassium phosphate (318 mg, 1.50 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), *tert*-butyl 4-bromopiperidine-1-carboxylate (396 mg, 1.50 mmol, 3.0 equiv), and MeCN (10 mL). Reaction time: 40 h. Purification by flash chromatography (100% EtOAc/hexanes) provided the title compound (125 mg, 57% yield) as a pale yellow foam.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.87 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 4.71 (d, *J* = 12.4 Hz, 1H), 4.08 (d, *J* = 10.5 Hz, 2H), 3.60 (d, *J* = 12.6 Hz, 1H), 3.02 (t, *J* = 12.5 Hz, 1H), 2.70 (t, *J* = 12.2 Hz, 1H), 2.59 (t, *J* = 12.1 Hz, 2H), 1.82 (d, *J* = 12.1 Hz, 1H), 1.73-1.53 (m, 3H), 1.39 (s, 9H), 1.36-1.31 (m, 1H), 1.26-1.08 (m, 5H).

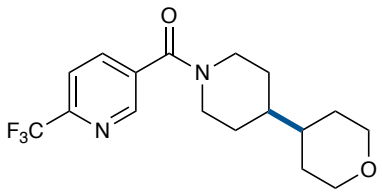
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.04, 154.77, 148.67 (q, *J* = 35.1 Hz), 147.95, 136.29, 134.91, 121.18 (q, *J* = 274.3 Hz), 120.42 (q, *J* = 2.7 Hz), 79.35, 48.23, 44.14, 42.81, 41.02, 40.84, 29.98, 29.15, 28.92, 28.44.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.12

IR (film) ν_{max} 2936, 2856, 1684, 1632, 1334, 1142, 1083, 919, 856, 730 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{22}H_{30}F_3N_3NaO_3$ ($[M+Na]^+$) 464.2132, found 464.2127.

(4-(Tetrahydro-2*H*-pyran-4-yl)piperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (43)



Prepared following general procedure B outlined above using Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (4.5 mg, 4.0 μmol, 0.01 equiv.), $NiCl_2$•$6H_2O$ (4.8 mg, 20 μmol, 0.05 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (5.4 mg, 20 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (318 mg, 1.2 mmol, 3.0 equiv.), anhydrous potassium phosphate (170 mg, 0.80 mmol, 2.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (135 mg, 0.40 mmol, 1.0 equiv.), 4-bromotetrahydro-2H-pyran (330 mg, 225 μL 2.0 mmol, 5.0 equiv), and MeCN (4 mL). Purification by flash chromatography (10-50% EtOAc/hexanes) provided the title compound (75 mg, 0.22 mmol 55% yield) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, *J* = 1.9 Hz, 1H), 7.93 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.75 (dd, *J* = 8.0, 0.8 Hz, 1H), 4.77 (d, *J* = 13.2 Hz, 1H), 4.00 (d, *J* = 11.3 Hz, 2H), 3.66 (d, *J* = 13.5 Hz, 1H), 3.36 (t, *J* = 11.1 Hz, 2H), 3.07 (t, *J* = 12.9 Hz, 1H), 2.76 (t, *J* = 12.6 Hz, 1H), 1.90 (d, *J* = 13.2 Hz, 1H), 1.74 (d, *J* = 13.2 Hz, 1H), 1.66 – 1.54 (m, 2H), 1.44-1.22 (m, 5H), 1.21-1.09 (m, 1H).

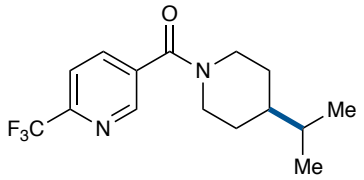
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.22, 148.92 (q, *J* = 35.1 Hz), 148.07, 136.49, 134.98, 120.57 (q, *J* = 2.7 Hz), 120.39 (q, *J* = 273.6 Hz), 68.26, 48.37, 42.96, 41.43, 39.98, 30.29, 30.02, 28.93.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.13.

IR (film) ν_{max} 2939, 2849, 1630, 1444, 1333, 1174, 1128, 1082, 1020, 857, 734, cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{17}H_{22}F_3N_2O_2$ ($[M+H]^+$) 343.16279, found 343.16303.

(4-Isopropylpiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (44)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (11.2 mg, 10.0 μmol, 0.02 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (5.4 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.50 mmol, 3.0 equiv.), anhydrous potassium phosphate (318 mg, 1.50 mmol, 3.0 equiv.), (4-bromopiperidin-1-yl)(6-(trifluoromethyl)pyridin-3-yl)methanone (169 mg, 0.50 mmol, 1.0 equiv.), 2-bromopropane (369 mg, 282 μL, 3.00 mmol, 6.0 equiv), and MeCN (10 mL). Reaction time: 40 h. Purification by flash chromatography (30-40% EtOAc/hexanes) provided the title compound (63 mg, 42% yield) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.91 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 4.74 (d, *J* = 12.8 Hz, 1H), 3.62 (d, *J* = 13.0 Hz, 1H), 3.04 (t, *J* = 12.7 Hz, 1H), 2.73 (t, *J* = 11.9 Hz, 1H), 1.82 (d, *J* = 10.4 Hz, 1H), 1.66 (d, *J* = 12.6 Hz, 1H), 1.47 (dq, *J* = 13.1, 6.6 Hz, 1H), 1.35-1.27 (m, 2H), 1.17-1.11 (m, 1H), 0.88 (d, *J* = 4.8 Hz, 6H).

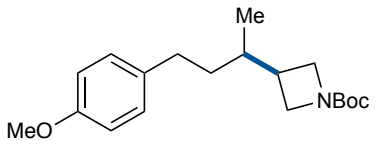
^{13}C NMR (125 MHz, $CDCl_3$) δ 166.12, 148.74 (q, *J* = 35.1 Hz), 148.05, 136.38, 135.12, 121.28 (q, *J* = 274.3 Hz), 120.48 (q, *J* = 2.6 Hz), 48.52, 43.08, 42.64, 32.38, 30.09, 28.96, 19.71.

^{19}F NMR (376 MHz, $CDCl_3$) δ -68.13

IR (film) ν_{max} 2955, 1633, 1444, 1334, 1128, 1083, 996, 855 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{15}H_{20}F_3N_2O$ ($[M+H]^+$) 301.1522, found 301.1523.

(±) *tert*-Butyl 3-(4-(4-methoxyphenyl)butan-2-yl)azetidine-1-carboxylate (45)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (5.4 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (265 mg, 1.00 mmol, 2.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), 1-(3-bromobutyl)-4-methoxybenzene (122 mg, 0.50 mmol, 1.0 equiv.), *tert*-butyl 3-bromoazetidine-1-carboxylate (236 mg, 1.00 mmol, 2.0 equiv), and MeCN (10 mL). Purification by flash chromatography (10-15% EtOAc/hexanes), followed by another flash chromatography (5-10% EtOAc/toluene) provided the title compound (79 mg, 50% yield) as a pale yellow oil.

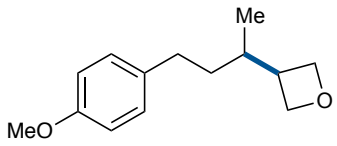
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.92 (td, *J* = 8.4, 3.2 Hz, 2H), 3.79 (s, 3H), 3.58 (dt, *J* = 8.5, 5.7 Hz, 2H), 2.64 (ddd, *J* = 14.7, 10.1, 5.1 Hz, 1H), 2.49-2.39 (m, 1H), 2.34-2.23 (m, 1H), 1.63-1.54 (m, 2H), 1.43 (s, 9H), 1.33-1.25 (m, 1H), 0.90 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.86, 156.50, 134.48, 129.25, 113.93, 79.28, 55.38, 53.36, 53.05, 36.71, 36.20, 35.21, 32.39, 28.55, 16.12.

IR (film) ν_{max} 2932, 1700, 1512, 1400, 1245, 1132, 1037 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{19}H_{29}NNaO_3$ ($[M+Na]^+$) 342.2040, found 342.2014.

(±) 3-(4-(4-Methoxyphenyl)butan-2-yl)oxetane (46)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (5.4 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (331 mg, 1.25 mmol, 2.5 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), 1-(3-bromobutyl)-4-methoxybenzene (122 mg, 0.50 mmol, 1.0 equiv.), 3-bromooxetane (171 mg, 95 μL, 1.25 mmol, 2.5 equiv), and MeCN (10 mL). Purification by flash chromatography (15-20% EtOAc/hexanes) provided the title compound (66 mg, 60% yield) as a colorless oil.

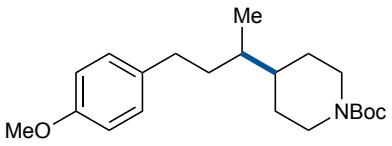
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 4.72 (dt, *J* = 7.9, 5.4 Hz, 2H), 4.44 (q, *J* = 5.9 Hz, 2H), 3.79 (s, 3H), 2.78 (dq, *J* = 14.9, 7.6 Hz, 1H), 2.63 (ddd, *J* = 14.9, 10.4, 5.1 Hz, 1H), 2.49-2.39 (m, 1H), 1.89-1.79 (m, 1H), 1.58-1.48 (m, 1H), 1.35-1.26 (m, 1H), 0.88 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.81, 134.42, 129.16, 113.86, 76.69, 76.40, 55.30, 41.48, 36.52, 36.36, 32.33, 16.19.

IR (film) ν_{max} 2929, 2862, 1511, 1242, 1035, 976, 823 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{14}H_{20}O_2$ (M^+) 220.1458, found 220.1458.

(±) *tert*-Butyl 4-(4-(4-methoxyphenyl)butan-2-yl)piperidine-1-carboxylate (47)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (5.4 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (265 mg, 1.00 mmol, 2.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), 1-(3-bromobutyl)-4-methoxybenzene (122 mg, 0.50 mmol, 1.0 equiv.), *tert*-butyl 4-bromopiperidine-1-carboxylate (264 mg, 1.00 mmol, 2.0 equiv), and MeCN (10 mL). Purification by flash chromatography (5-10% EtOAc/hexanes) provided the title compound (97 mg, 56% yield) as a colorless oil.

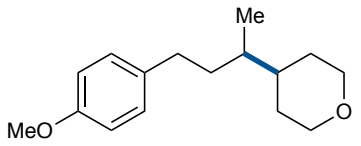
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 4.11 (brs, 2H), 3.79 (s, 3H), 2.70-2.40 (m, 4H), 1.67-1.50 (m, 4H), 1.45 (s, 9H), 1.41-1.31 (m, 3H), 1.22-1.15 (m, 1H), 0.90 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.70, 154.89, 134.90, 129.21, 113.78, 79.21, 55.29, 44.34, 41.26, 36.94, 36.17, 32.80, 29.65, 28.55, 28.07, 16.03.

IR (film) ν_{max} 2930, 1689, 1511, 1420, 1365, 1241, 1167, 1036, 823 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{21}H_{33}NNaO_3$ ($[M+Na]^+$) 370.2353, found 370.2346.

(±) 4-(4-(4-Methoxyphenyl)butan-2-yl)tetrahydro-2*H*-pyran (48)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (5.4 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (265 mg, 1.00 mmol, 2.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), 1-(3-bromobutyl)-4-methoxybenzene (122 mg, 0.50 mmol, 1.0 equiv.), 4-bromotetrahydro-2*H*-pyran (165 mg, 112 μL, 1.00 mmol, 2.0 equiv), and MeCN (10 mL). Purification by flash chromatography (5-10% EtOAc/hexanes) provided the title compound (72 mg, 58% yield) as a colorless oil.

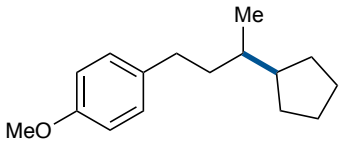
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 4.01-3.97 (m, 2H), 3.79 (s, 3H), 3.36 (t, *J* = 11.7 Hz, 2H), 2.72-2.57 (m, 1H), 2.51-2.45 (m, 1H), 1.75-1.63 (m, 1H), 1.51 (d, *J* = 11.0 Hz, 2H), 1.44-1.35 (m, 5H), 0.93 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.71, 134.97, 129.22, 113.79, 68.58, 68.55, 55.30, 40.22, 37.22, 35.96, 32.71, 30.68, 29.25, 15.94.

IR (film) ν_{max} 2933, 2838, 1511, 1242, 1094, 1036, 824 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{16}H_{24}O_2$ (M^+) 248.1771, found 248.1776.

(±) 1-(3-Cyclopentylbutyl)-4-methoxybenzene (49)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (5.4 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.5 mmol, 3.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), 1-(3-bromobutyl)-4-methoxybenzene (122 mg, 0.50 mmol, 1.0 equiv.), bromocyclopentane (224 mg, 161 μL, 1.50 mmol, 3.0 equiv), and MeCN (10 mL). This yielded an inseperable mixture of product and hydrodehalogenation byproduct, and the 58% yield was calculated from a calibrated GC assay after the addition of a standard (methyl benzoate).

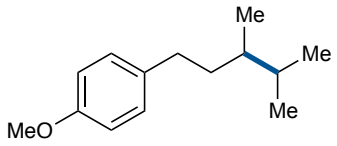
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 2.64 (ddd, *J* = 13.8, 10.8, 4.8 Hz, 1H), 2.45 (ddd, *J* = 13.8, 10.3, 6.3 Hz, 1H), 1.80-1.69 (m, 3H), 1.64-1.55 (m, 4H), 1.53-1.47 (m, 1H), 1.40-1.30 (m, 2H), 1.15-1.06 (m, 2H), 0.94 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.67, 135.52, 129.32, 113.81, 55.40, 46.40, 38.09, 37.96, 32.61, 30.85, 30.36, 25.60, 25.59, 17.85.

IR (film) ν_{max} 2948, 1511, 1245, 1040, 823 cm^{-1}.

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

(±) 1-(3,4-Dimethylpentyl)-4-methoxybenzene (50)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.6 mg, 5.0 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (5.9 mg, 25 μmol, 0.05 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (5.4 mg, 25 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (397 mg, 1.5 mmol, 3.0 equiv.), anhydrous sodium carbonate (159 mg, 1.50 mmol, 3.0 equiv.), 1-(3-bromobutyl)-4-methoxybenzene (122 mg, 0.50 mmol, 1.0 equiv.), 2-bromopropane (307 mg, 235 μL, 2.50 mmol, 5.0 equiv), and MeCN (10 mL). This yielded an inseperable mixture of product and hydrodehalogenation byproduct, and the 62% yield was calculated from a calibrated GC assay after the addition of a standard (methyl benzoate).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 2.61 (ddd, *J* = 15.6, 10.7, 4.8 Hz, 1H), 2.50-2.43 (m, 1H), 1.63-1.55 (m, 3H), 1.37-1.34 (m, 1H), 0.86 (d, *J* = 6.8 Hz, 6H), 0.81 (d, *J* = 6.8 Hz, 3H).

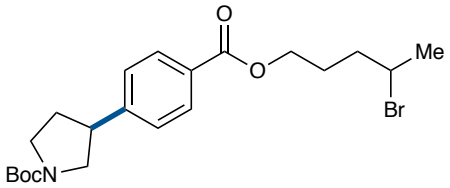
^{13}C NMR (125 MHz, $CDCl_3$) δ 157.69, 135.47, 129.32, 113.81, 55.40, 38.28, 36.57, 33.14, 32.11, 20.31, 18.12, 15.42.

IR (film) ν_{max} 2957, 1512, 1246, 1177, 1040, 822 cm^{-1}.

HRMS (EI-TOF) m/z calcd. for $C_{14}H_{22}O$ (M^+) 206.1665, found 206.1662.

Iterative Coupling Sequence

(±)-*tert*-Butyl 3-(4-(((4-bromopentyl)oxy)carbonyl)phenyl)pyrrolidine-1-carboxylate (52)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.4 mg, 3.0 μmol, 0.01 equiv.), $NiCl_2$•glyme (1.3 mg, 6 μmol, 0.02 equiv.), 4,4'-di-*tert*-butyl-2,2'-bipyridine (1.6 mg, 6 μmol, 0.02 equiv.), tris(trimethylsilyl)silane (82 mg, 102 μL, 0.33 mmol, 1.1 equiv.), 2,6-lutidine (129 mg, 140 μL, 1.20 mmol, 4.0 equiv.), 4-bromopentyl 4-bromobenzoate (105 mg, 0.30 mmol, 1.0 equiv.), *tert*-butyl 3-bromopyrrolidine-1-carboxylate (225 mg, 0.90 mmol, 3.0 equiv), and DME (4 mL). Light source: integrated photoreactor. Reaction time: 2 h. Purification by flash chromatography (10-15% EtOAc/hexanes) provided the title compound (80 mg, 61% yield, rotameric) as a colorless oil.

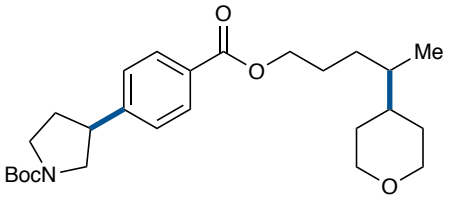
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.38-4.31 (m, 2H), 4.19 (h, *J* = 6.6 Hz, 1H), 3.86 (t, *J* = 5.5 Hz, 0.45H), 3.80 (t, *J* = 9.4 Hz, 0.51H), 3.65 (t, *J* = 8.8 Hz, 0.51H), 3.56 (t, *J* = 8.3 Hz, 0.47H), 3.49-3.24 (m, 3H), 2.33-2.23 (m, 1H), 2.06-1.86 (m, 5H), 1.74 (d, *J* = 6.7 Hz, 3H), 1.47 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) rotameric mixture: δ 166.46, 154.59, 154.58, 147.12, 147.08, 130.04, 128.92, 127.27, 79.55, 64.31, 52.38, 51.71, 50.98, 45.96, 45.68, 44.38, 43.46, 37.77, 33.36, 32.48, 28.68, 27.32, 26.67.

IR (film) ν_{max} 2972, 1717, 1693, 1402, 1274, 1112, 770 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{21}H_{30}BrNNaO_4$ ($[M+Na]^+$) 462.1250, found 462.1234.

(±) *tert*-Butyl 3-(4-(((4-(tetrahydro-2H-pyran-4-yl)pentyl)oxy)carbonyl)phenyl)pyrrolidine-1-carboxylate (53)



Prepared following the general procedure B outlined above using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 3.3 μmol, 0.01 equiv.), $NiCl_2 \bullet 6H_2O$ (3.9 mg, 17 μmol, 0.05 equiv.), 2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (3.6 mg, 17 μmol, 0.05 equiv.), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilan-2-ol (263 mg, 1.00 mmol, 3.0 equiv.), anhydrous sodium carbonate (105 mg, 1.00 mmol, 3.0 equiv.), *tert*-butyl 3-(4-(((4-bromopentyl)oxy)carbonyl)phenyl)pyrrolidine-1-carboxylate (146 mg, 0.33 mmol, 1.0 equiv.), 4-bromotetrahydro-2*H*-pyran (164 mg, 111 μL, 1.00 mmol, 3.0 equiv), and MeCN (6 mL). Purification by flash chromatography (30% EtOAc/hexanes) provided the title compound (74 mg, 50% yield, rotameric) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) [mixture of rotamers] δ 7.98 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 4.29 (t, *J* = 6.5 Hz, 2H), 4.02-3.95 (m, 2H), 3.86 (t, *J* = 6.5 Hz, 0.47H), 3.79 (t, *J* = 8.3 Hz, 0.52H), 3.64 (t, *J* = 8.5 Hz, 0.53H), 3.56 (t, *J* = 8.3 Hz, 0.49H), 3.43-3.28 (m, 5H), 2.34- 2.22 (m, 1H), 2.03-1.94 (m, 1H), 1.85-1.80 (m, 1H), 1.72-1.66 (m, 1H), 1.55-1.50 (m, 2H), 1.48 (s, 4.1H), 1.47 (s, 4.7H), 1.44-1.33 (m, 4H), 1.29-1.19 (m, 2H), 0.88 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) [mixture of rotamers] δ 166.53, 154.59, 154.56, 146.98, 146.92, 129.97, 129.13, 129.09, 127.22, 79.54, 79.51, 68.58, 68.56, 65.38, 52.37, 51.70, 45.95, 45.66, 44.36, 43.44, 40.13, 37.40, 33.31, 32.47, 30.72, 29.93, 29.31, 28.66, 26.54, 16.03.

IR (film) ν_{max} 2941, 1718, 1695, 1400, 1273, 1102, 880, 771 cm^{-1}.

HRMS (ESI-TOF) m/z calcd. for $C_{26}H_{39}NNaO_5$ ($[M+Na]^+$) 468.2720, found 468.2723.

8) References

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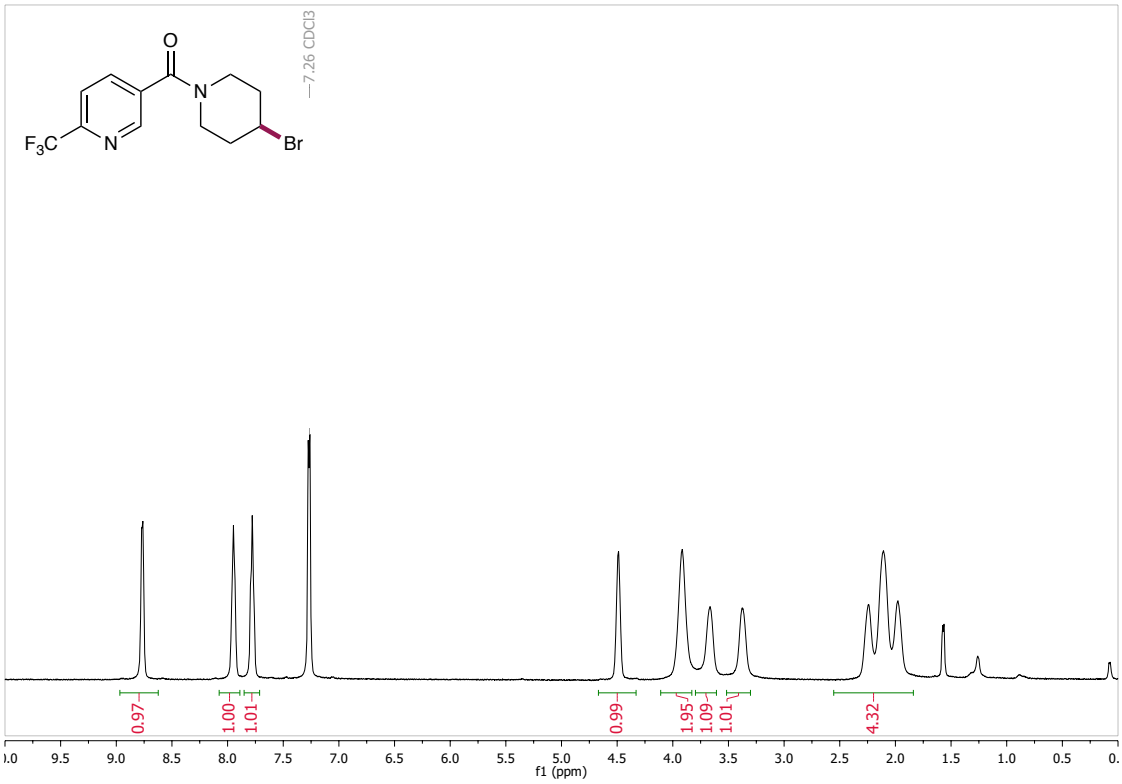
9) Spectra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N
F3C
N
Br
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1.00
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0.99
1.95
1.09
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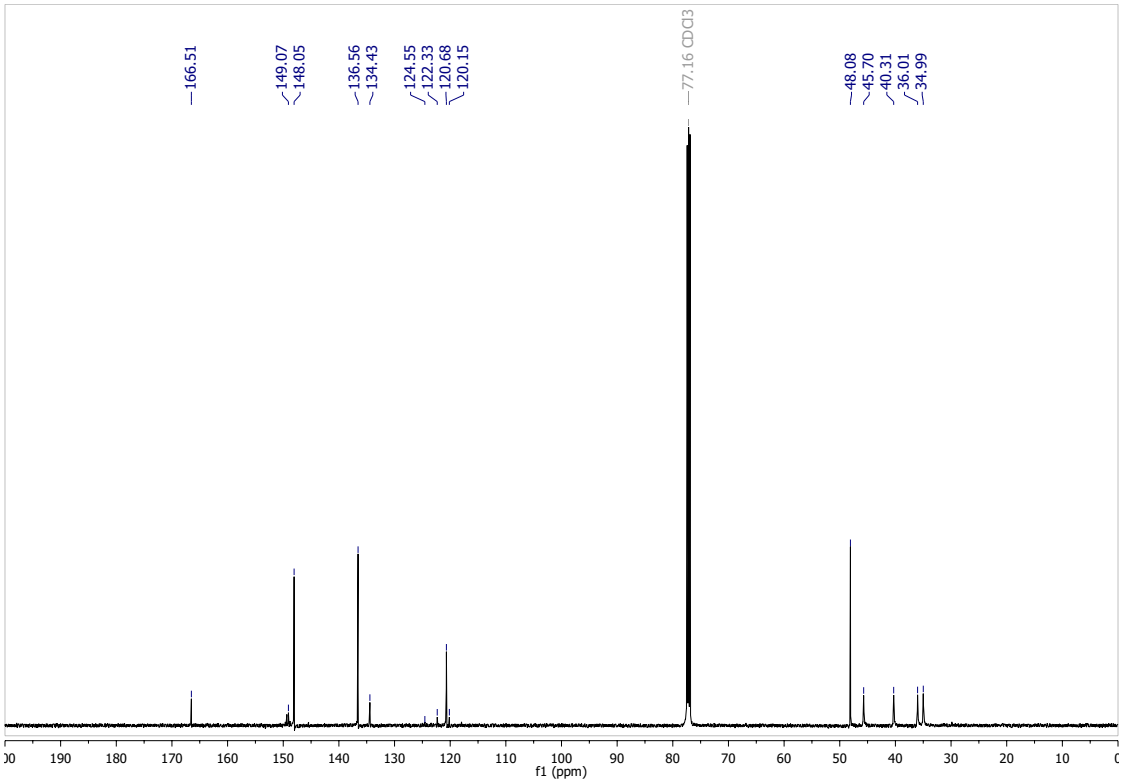
4.32
f1 (ppm)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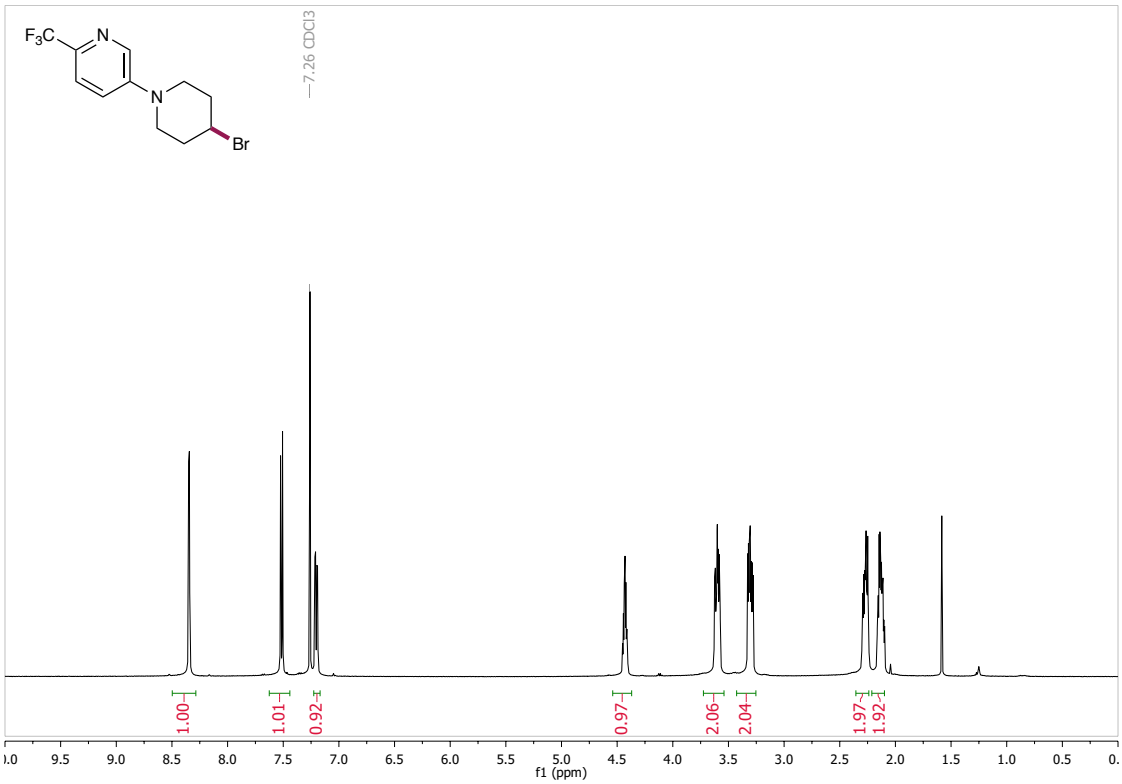
34.99
f1 (ppm)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N
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Br
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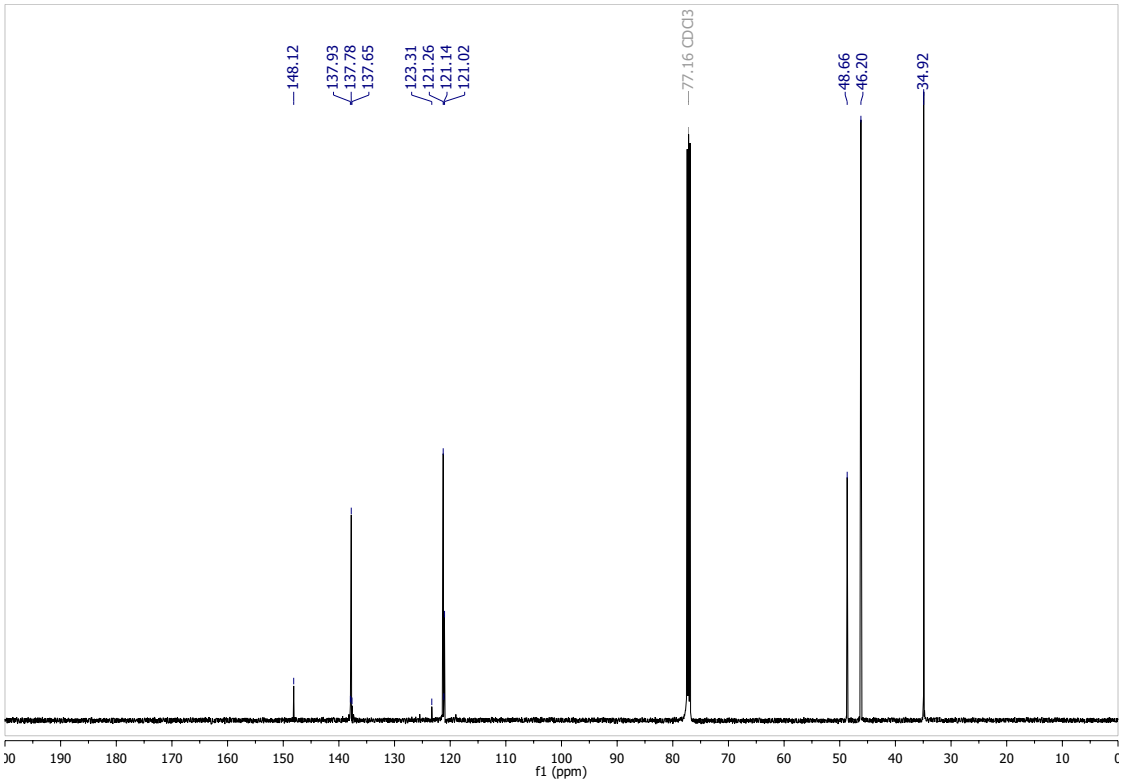
0.92
0.97
2.06
2.04
1.97
1.92
f1 (ppm)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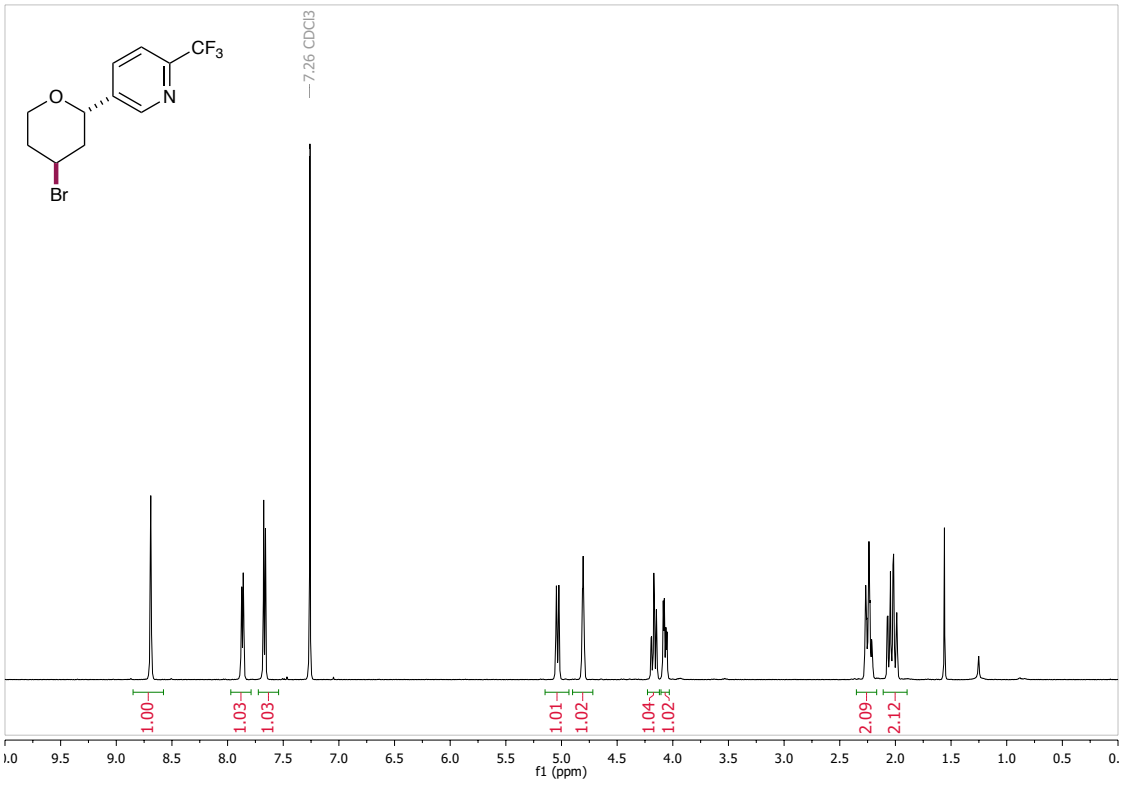
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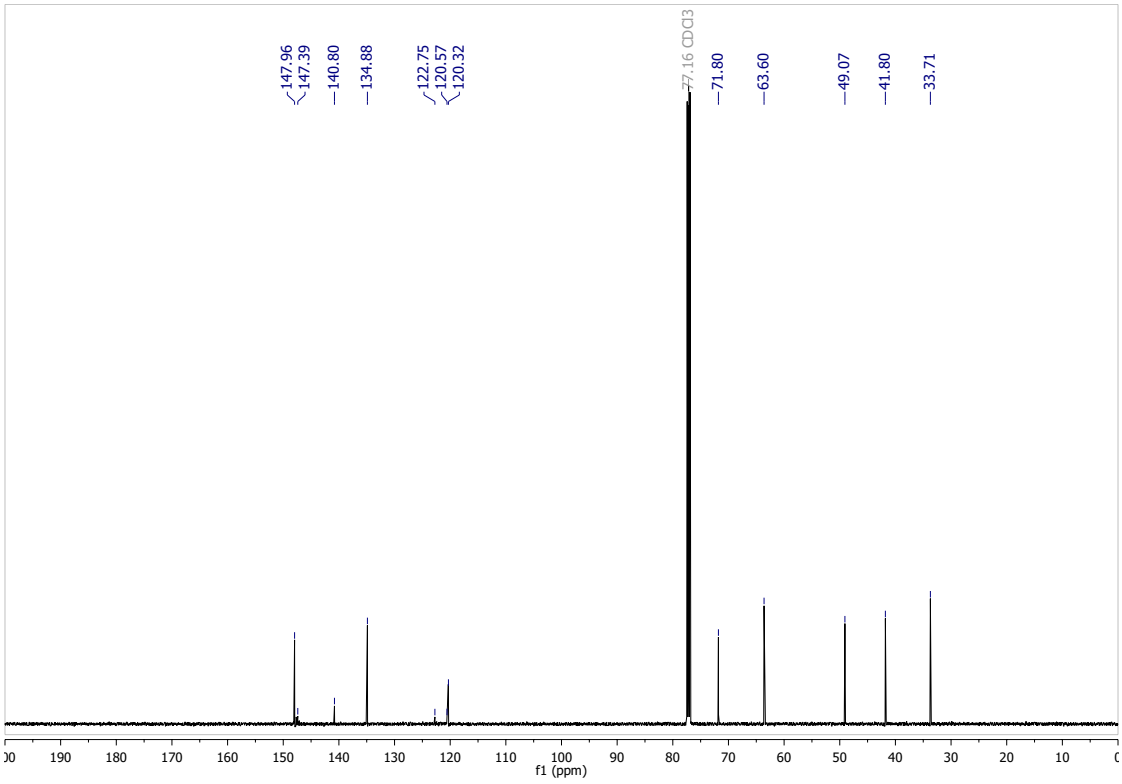
f1 (ppm)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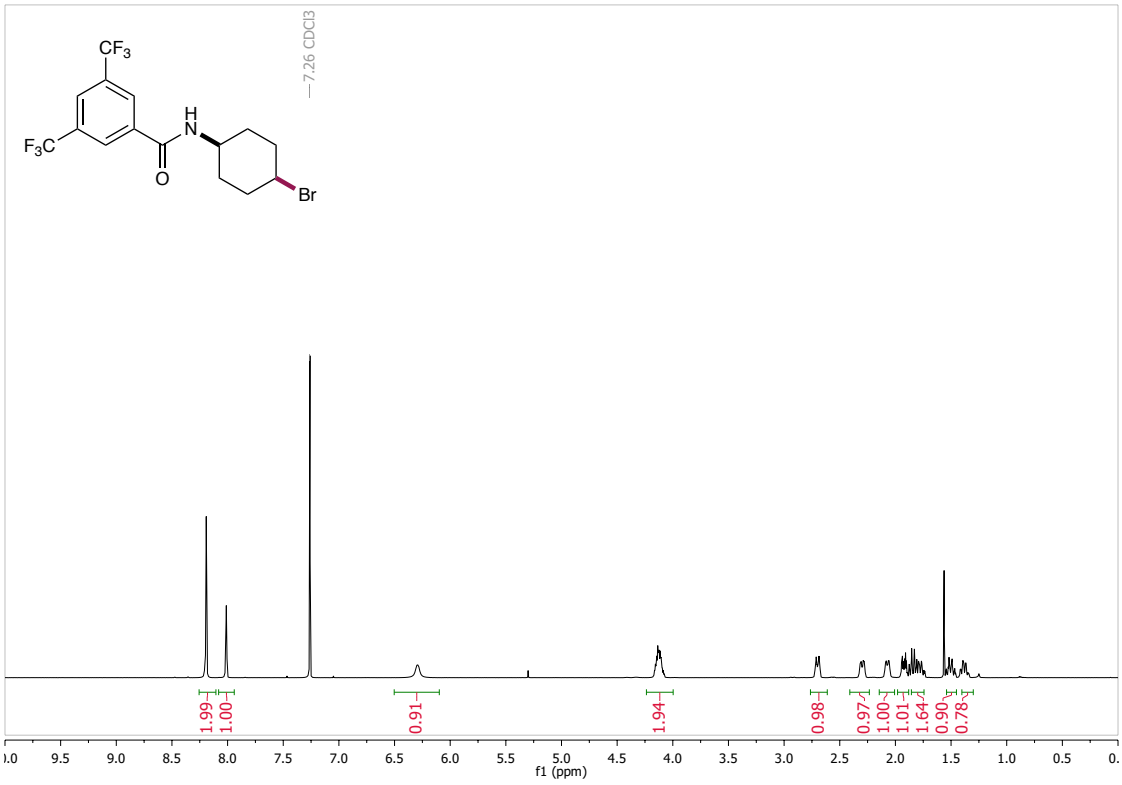
f1 (ppm)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H
N
O
Br
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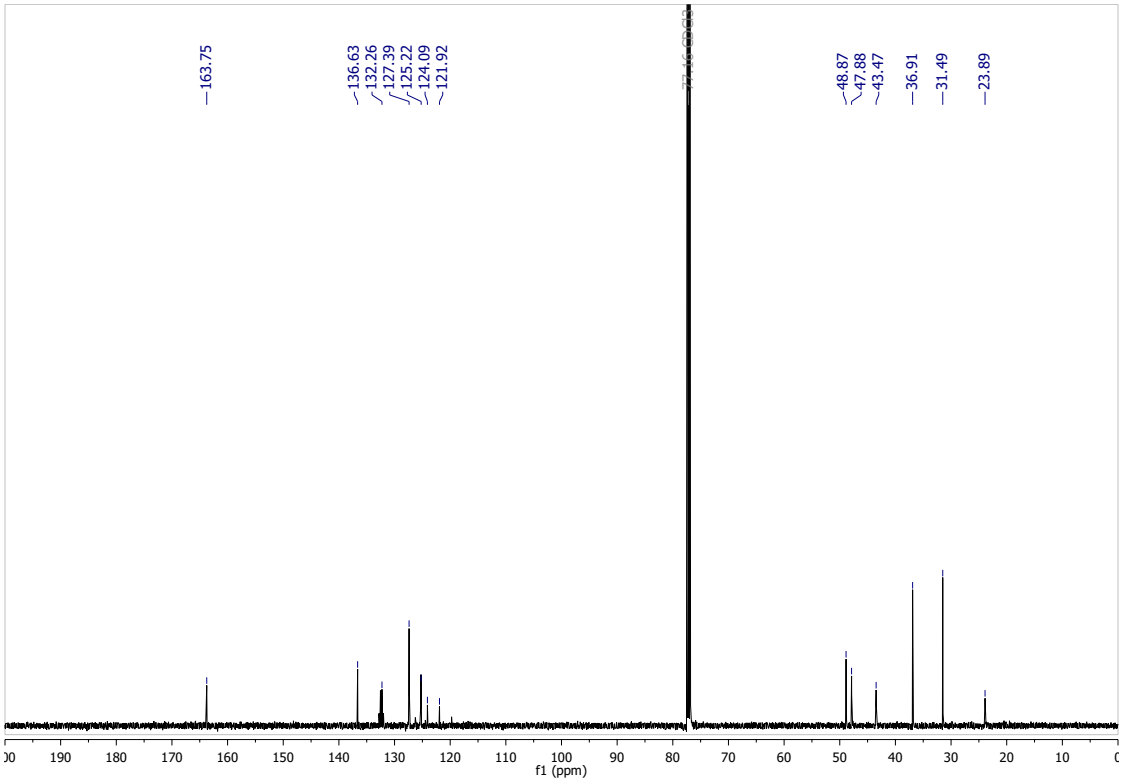
f1 (ppm)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136.63
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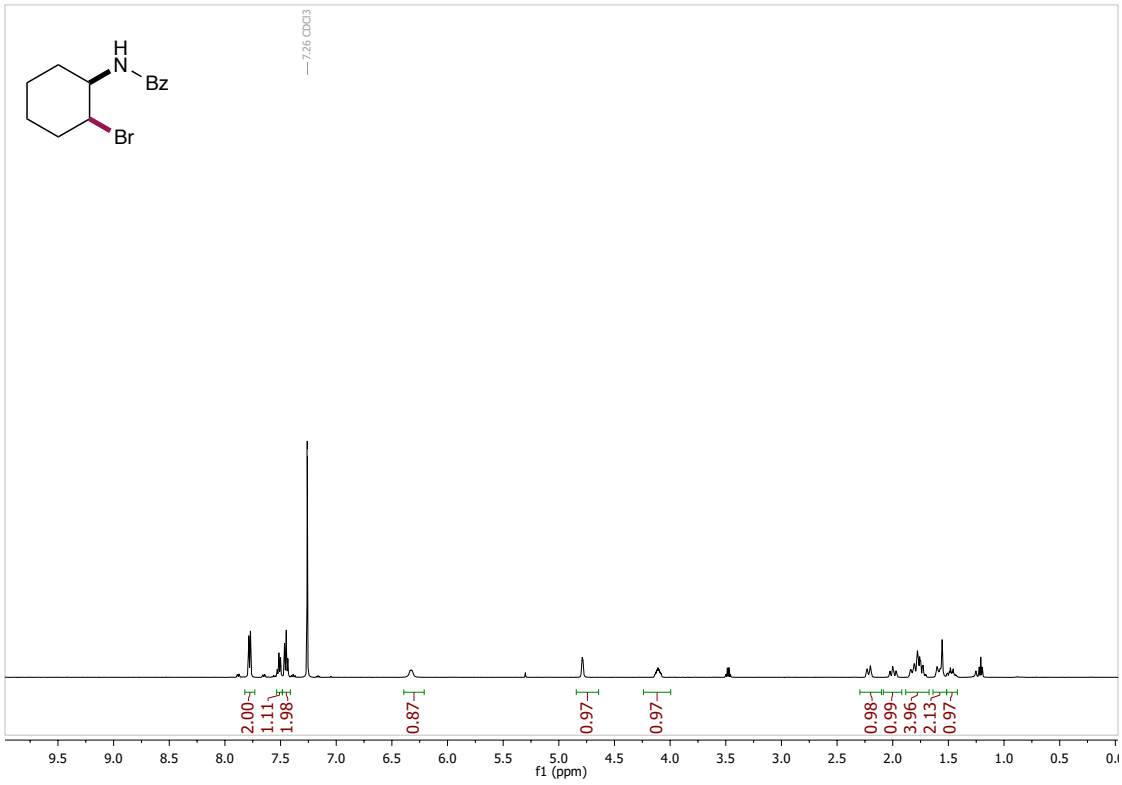
f1 (ppm)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N
Bz
Br
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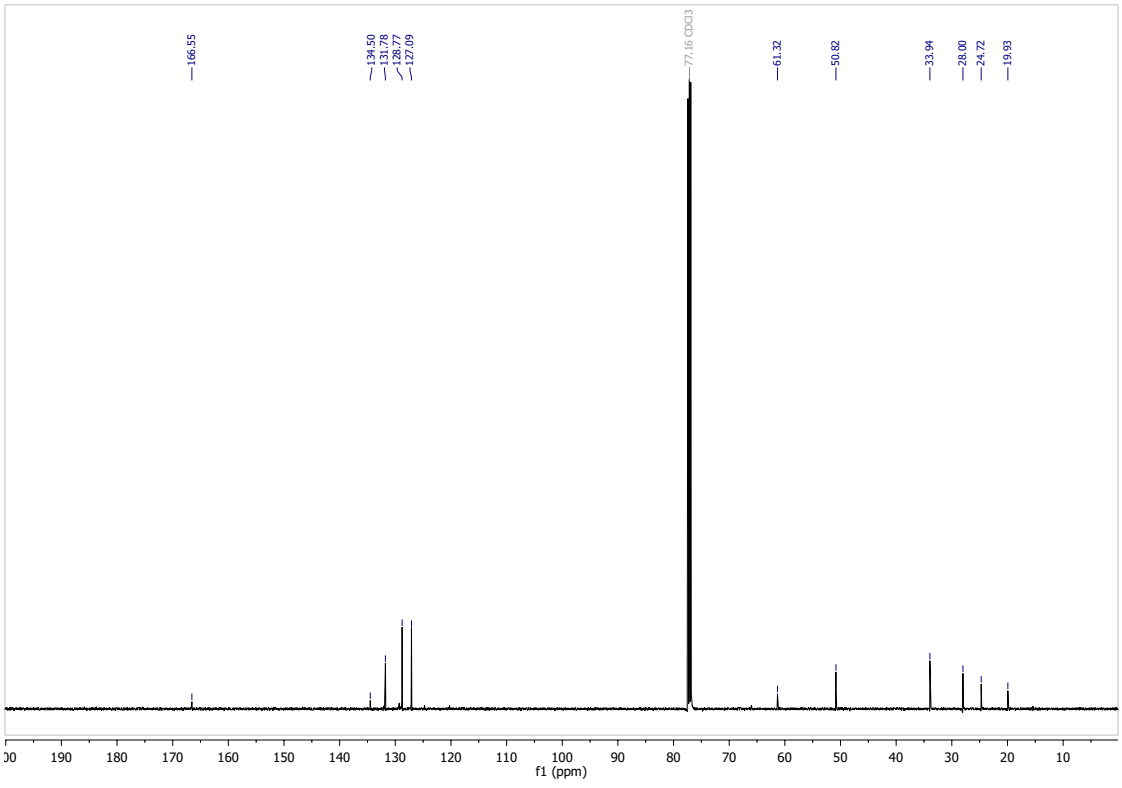
3.96
2.13
0.97
f1 (ppm)


166.55
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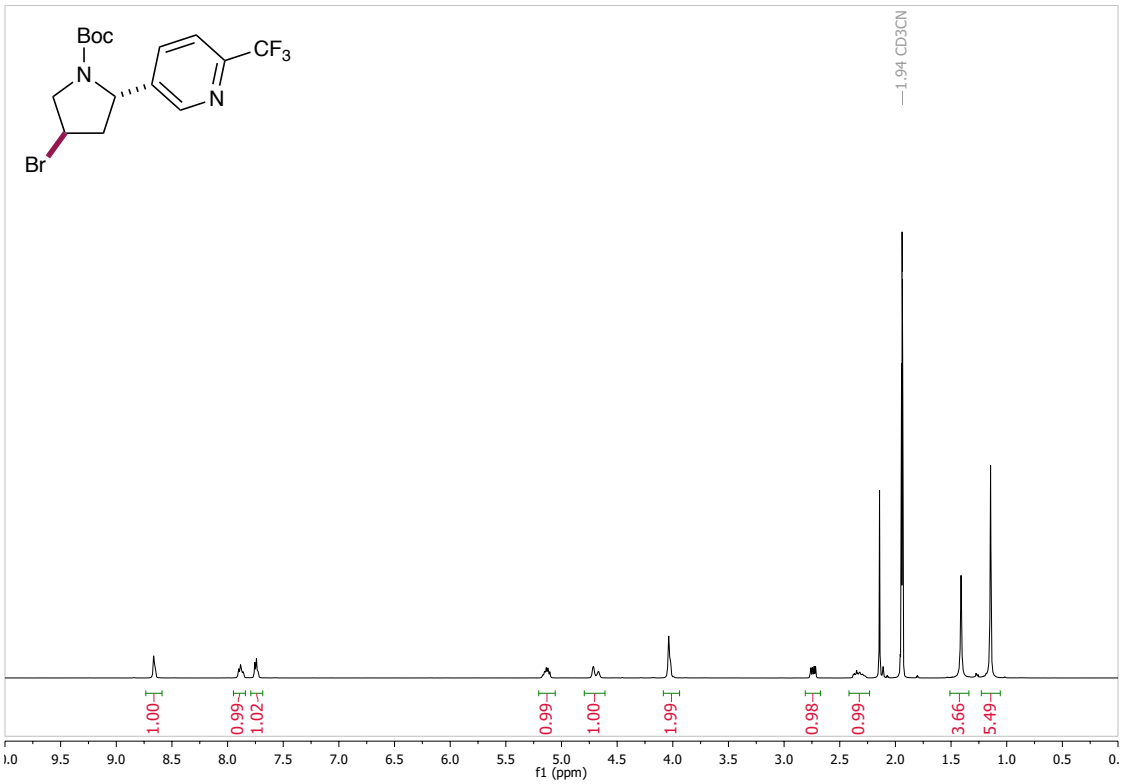
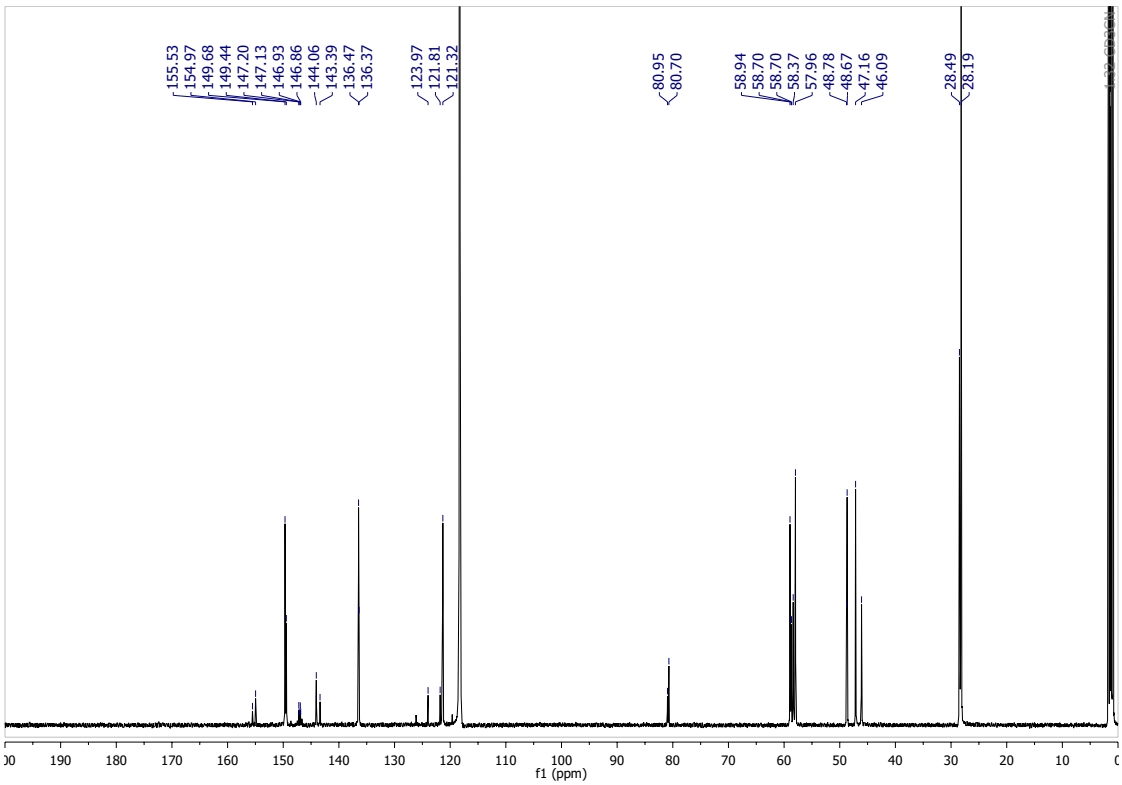
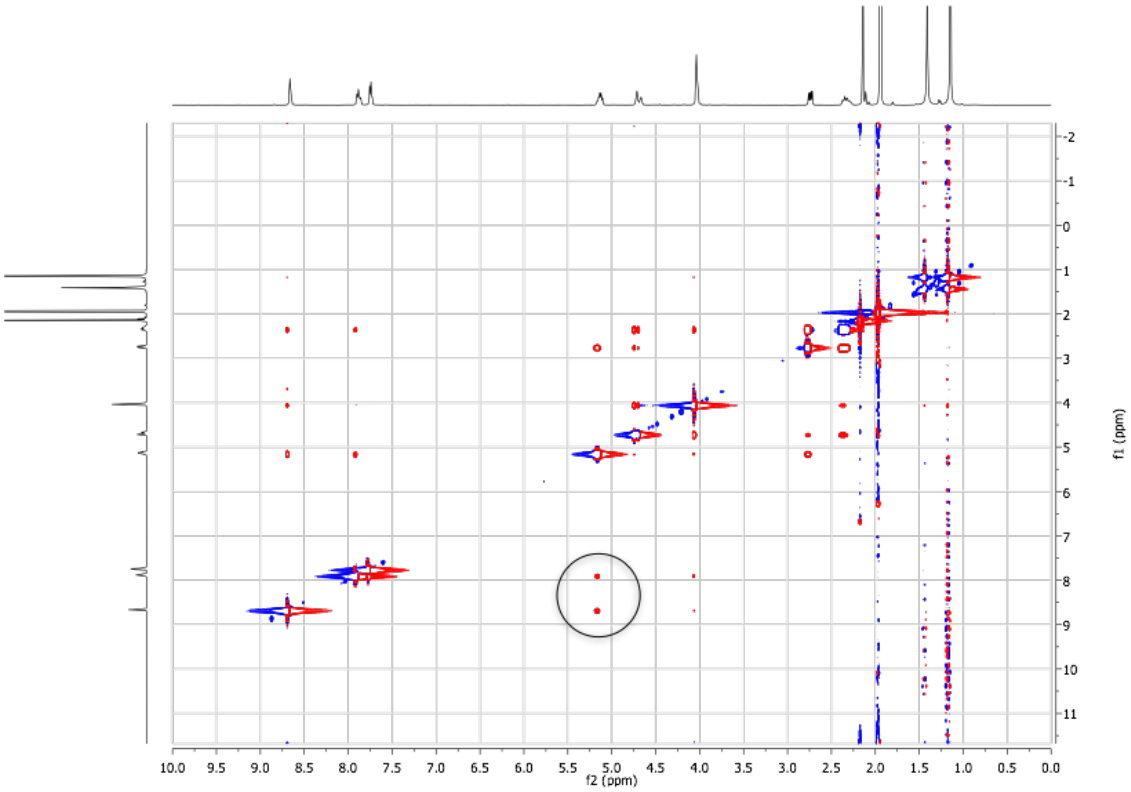
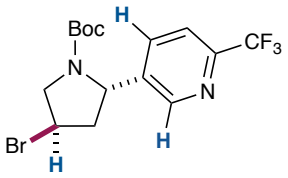
50.82
33.94
28.00
24.72
19.93
f1 (ppm)

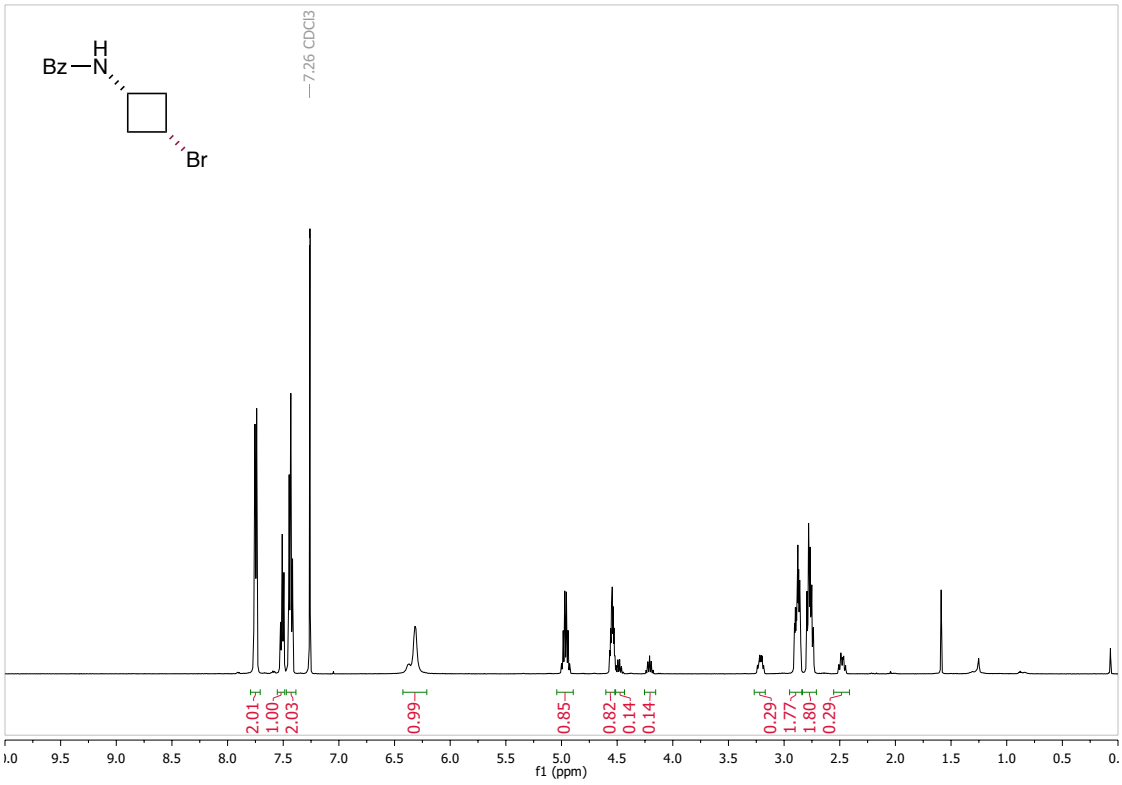

Boc
N
Br
CF3
N
1.94 CD3CN
1.00
0.99
1.02
0.99
1.00
1.99
0.98
0.99
3.66
5.49
f1 (ppm)

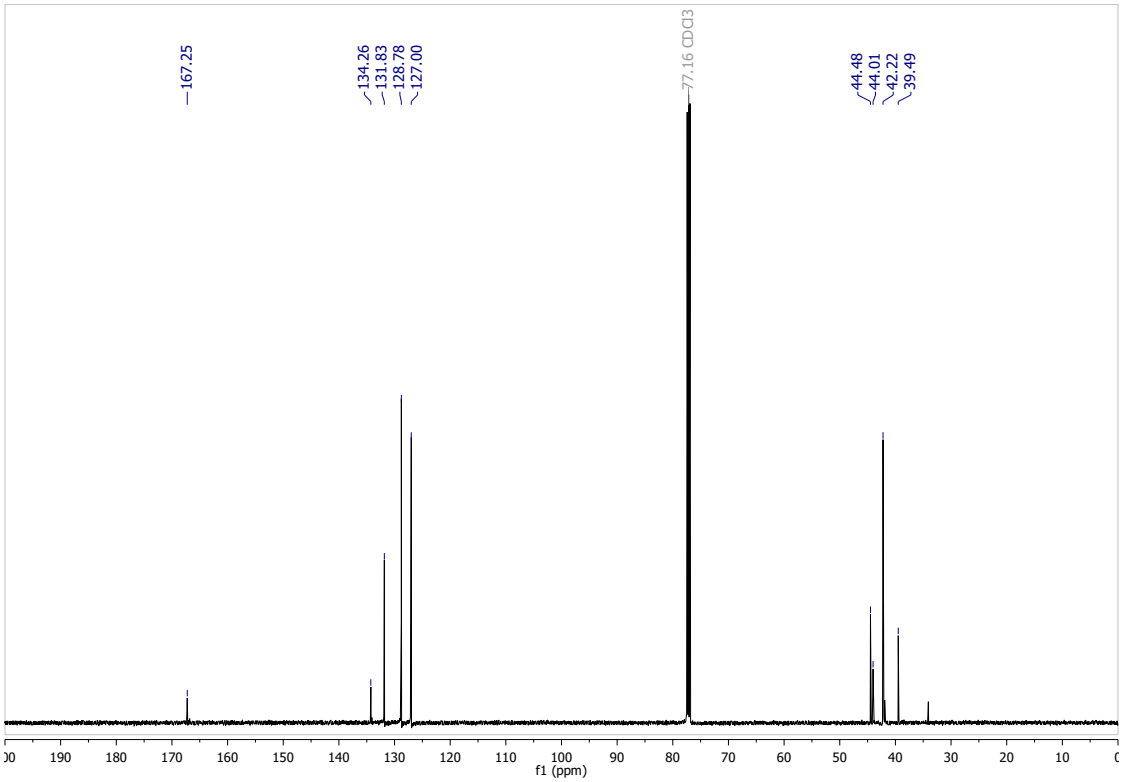

155.53
154.97
149.68
149.44
147.20
147.13
146.93
146.86
144.06
143.39
136.47
136.37
123.97
121.81
121.32
80.95
80.70
58.94
58.70
58.70
58.37
57.96
48.78
48.67
47.16
46.09
28.49
28.19
f1 (ppm)

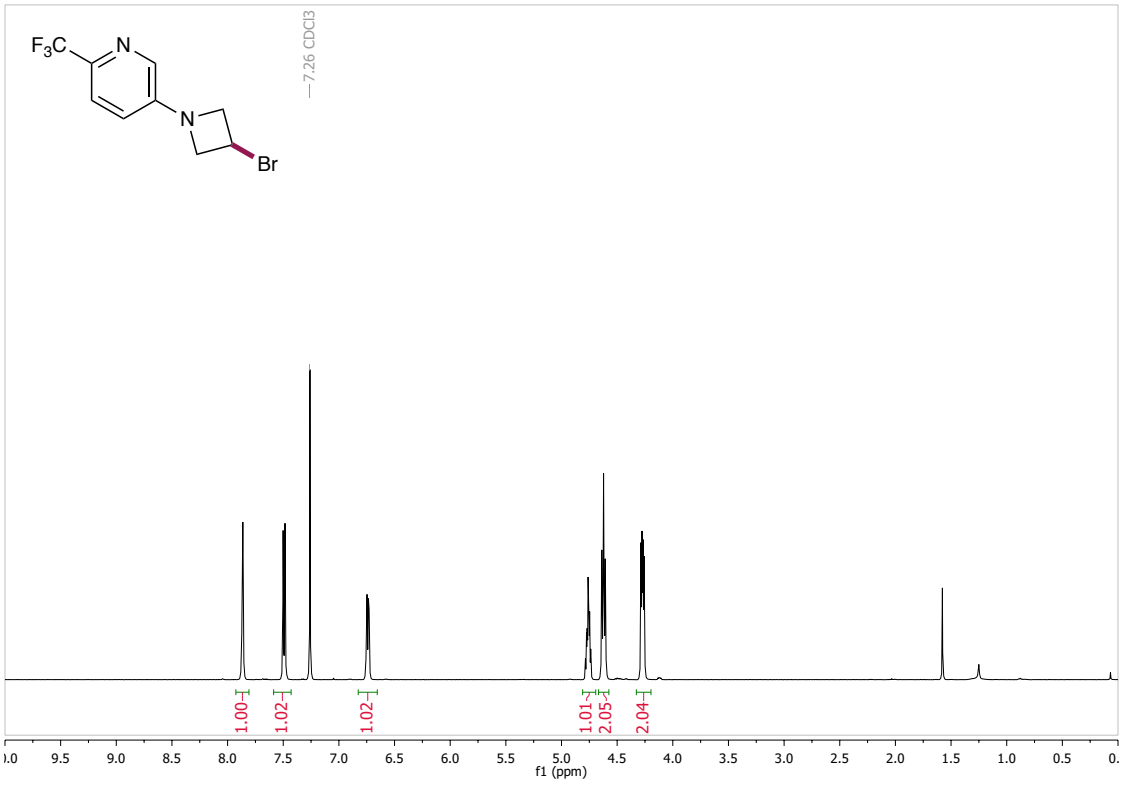


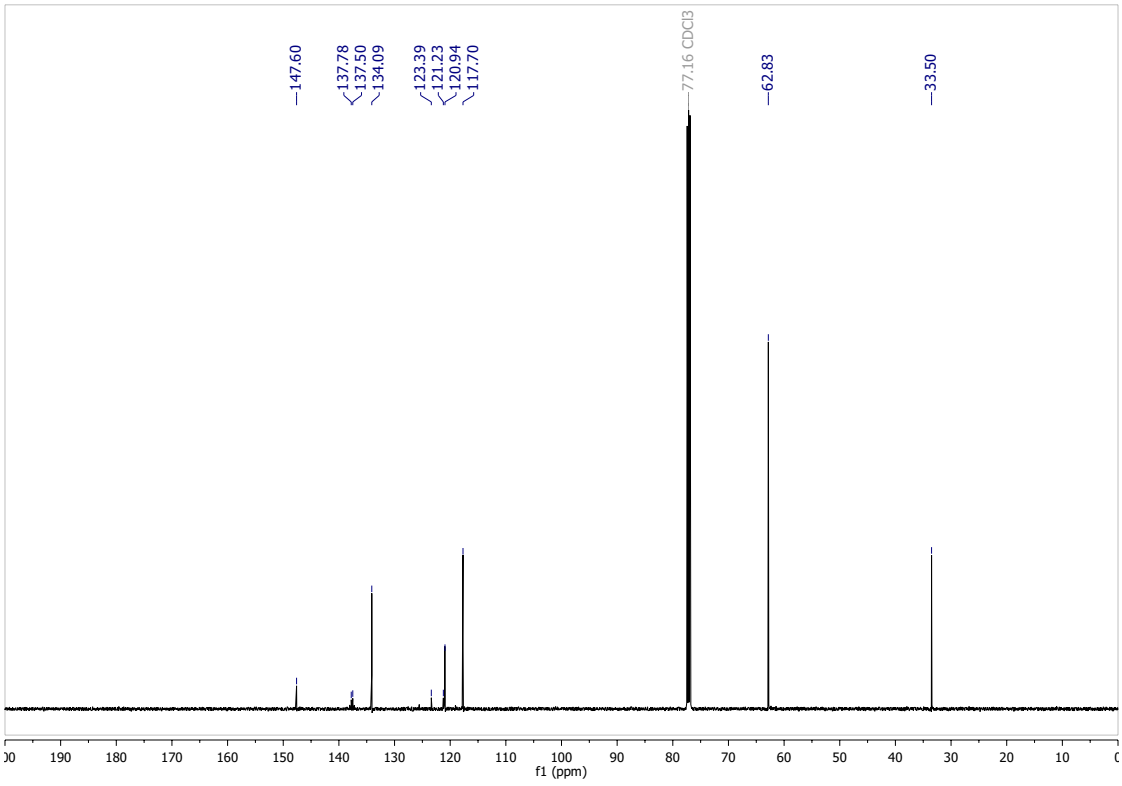


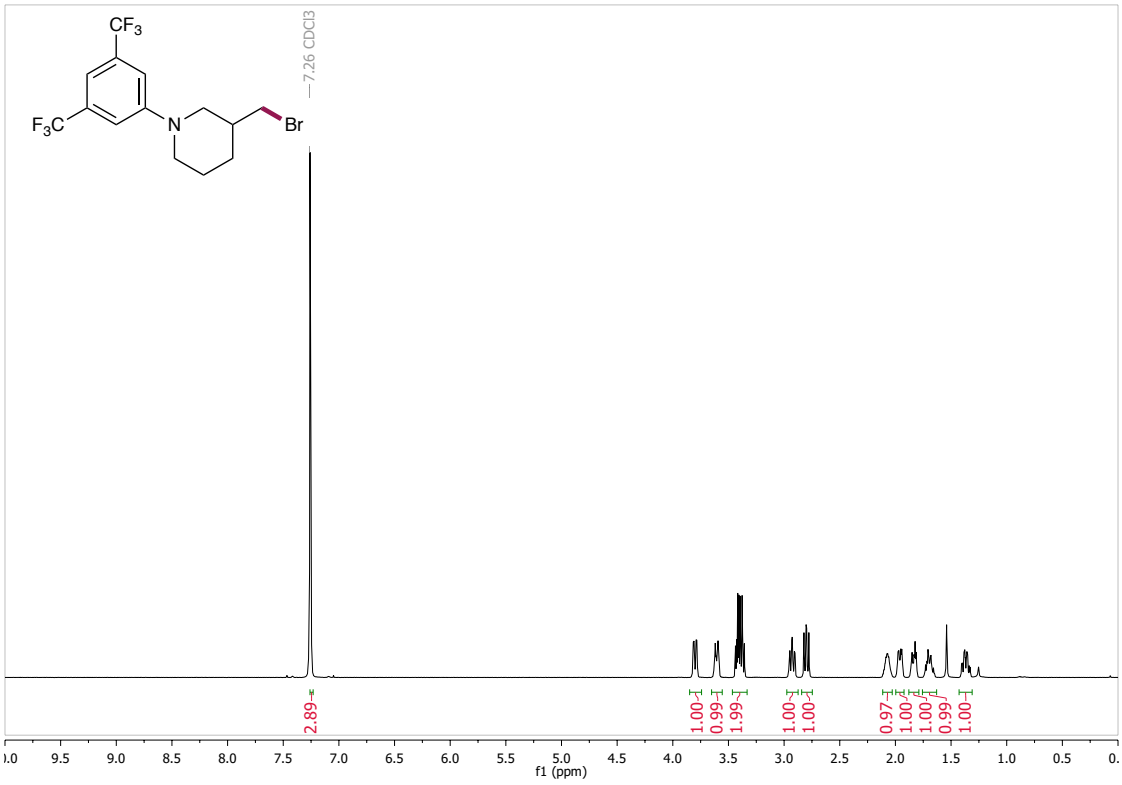
The protons highlighted in blue show a correlation in the NOESY spectrum (circled above), indicating a *trans* geometry, as shown.

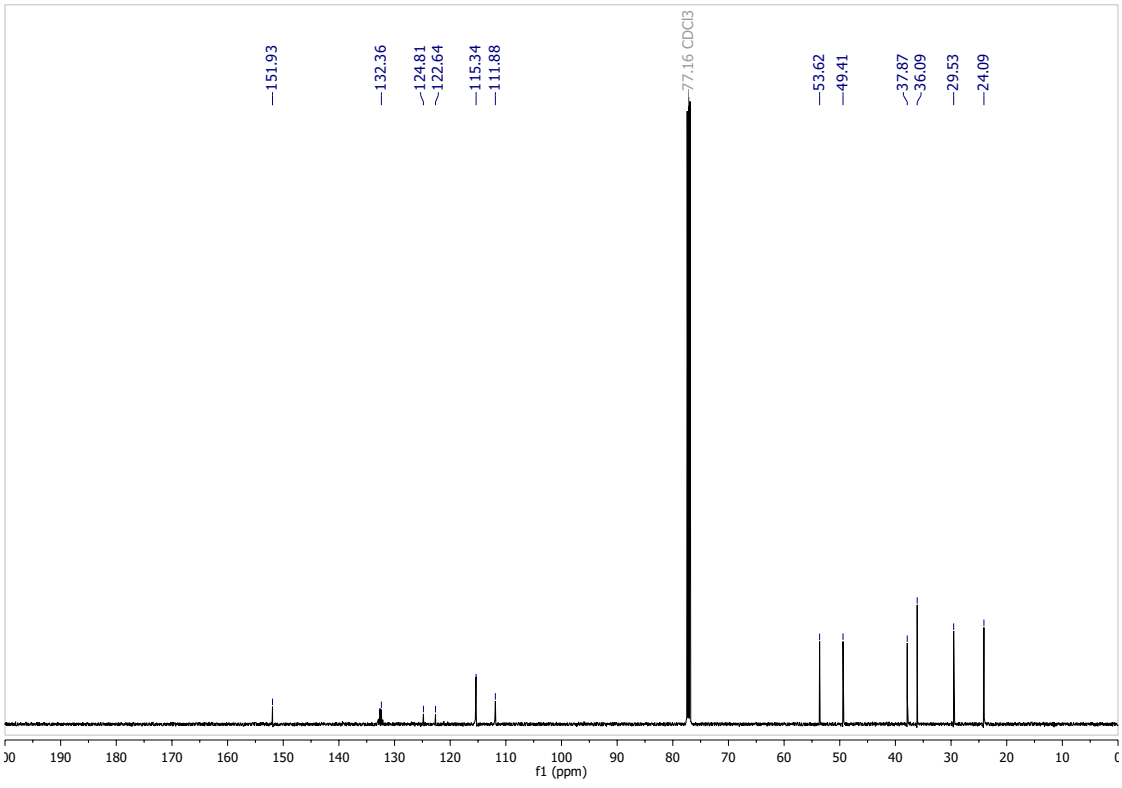

Bz
H
N
Br
7.26 CDCl3
2.01
1.00
2.03
0.99
0.85
0.82
0.14
0.14
0.29
1.77
1.80
0.29
f1 (ppm)

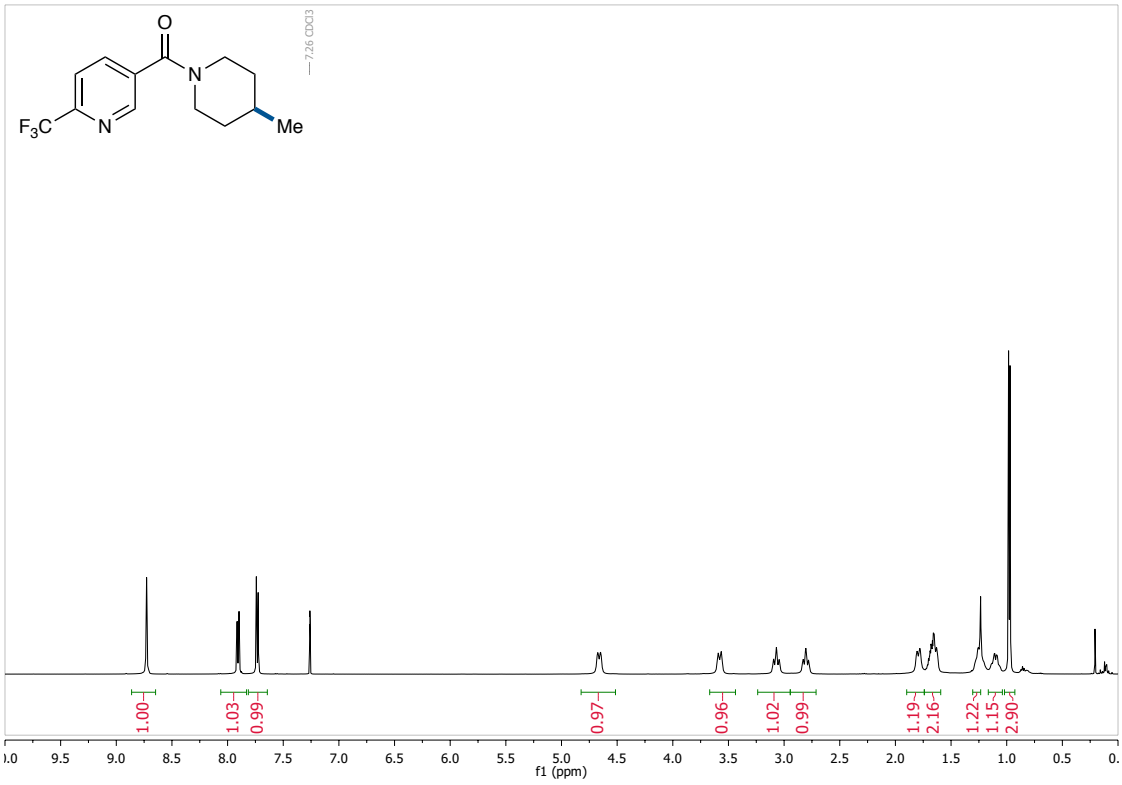

167.25
134.26
131.83
128.78
127.00
77.16 CDCl3
44.48
44.01
42.22
39.49
f1 (ppm)

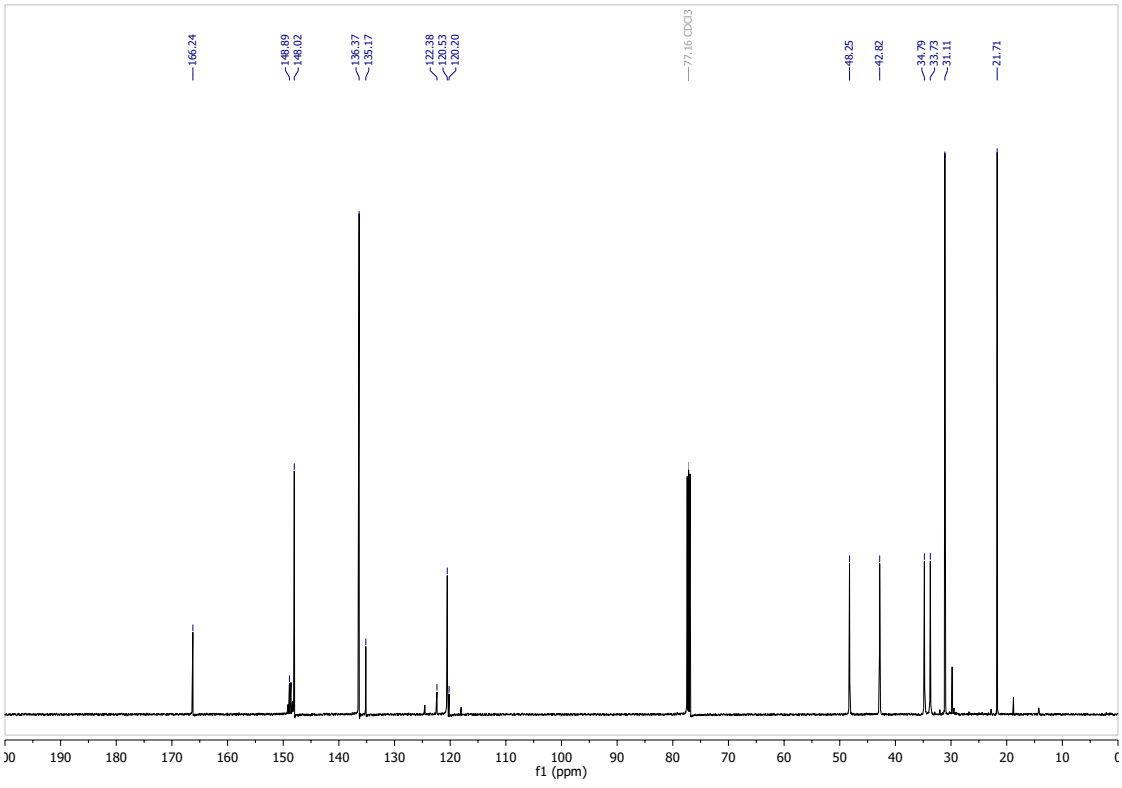

F3C
N
N
Br
7.26 CDCl3
1.00
1.02
1.02
1.01
2.05
2.04
f1 (ppm)

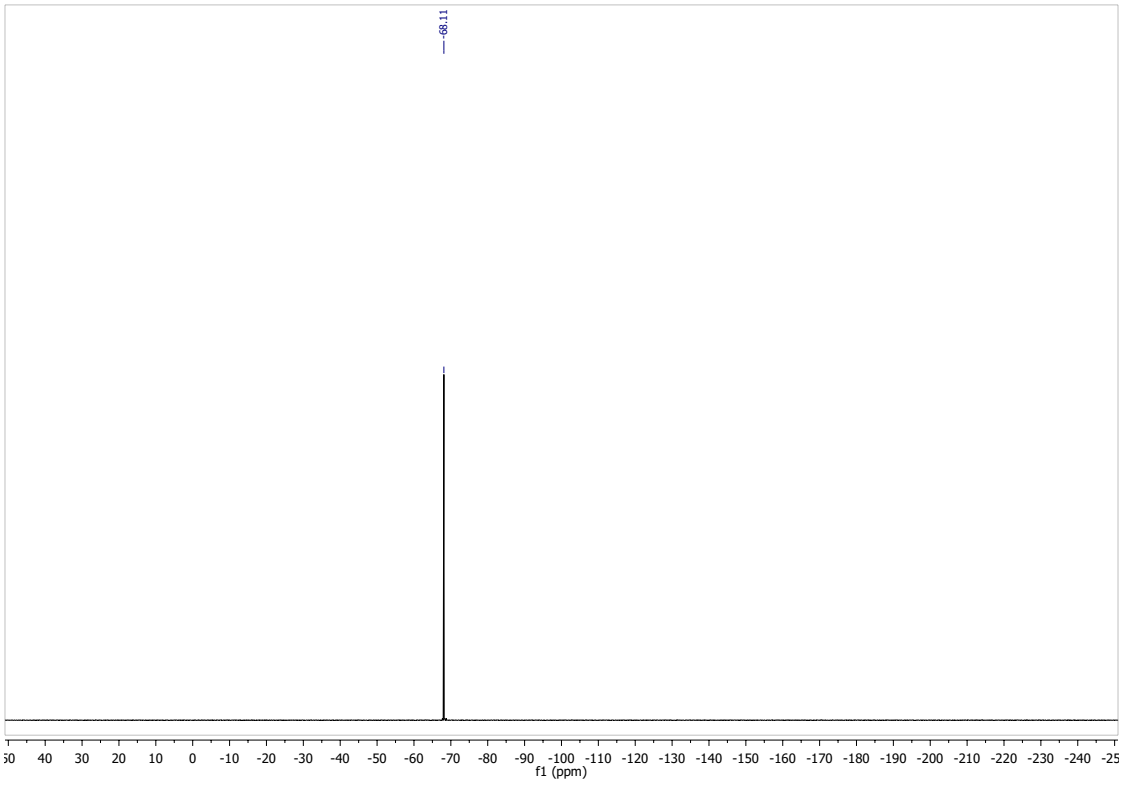

147.60
137.78
137.50
134.09
123.39
121.23
120.94
117.70
77.16 CDCl3
62.83
33.50
f1 (ppm)

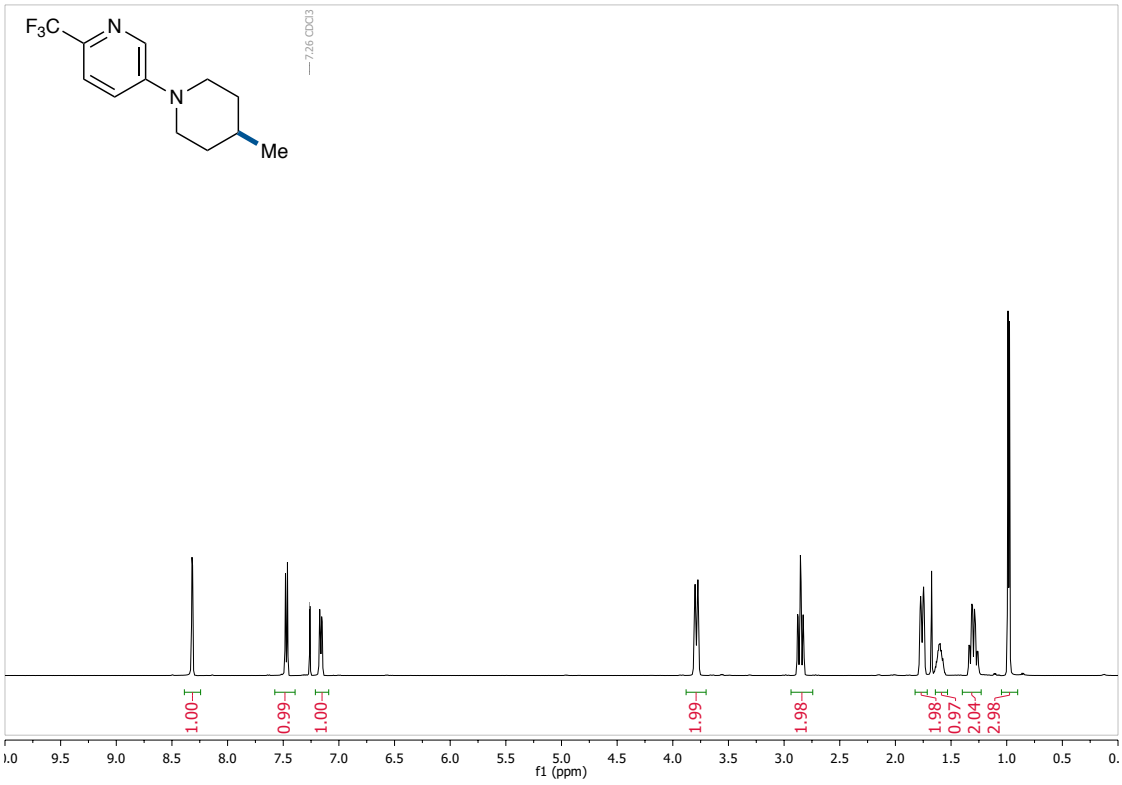

CF3
F3C
N
Br
7.26 CDCl3
2.89
1.00
0.99
1.99
1.00
1.00
0.97
1.00
1.00
0.99
1.00
f1 (ppm)

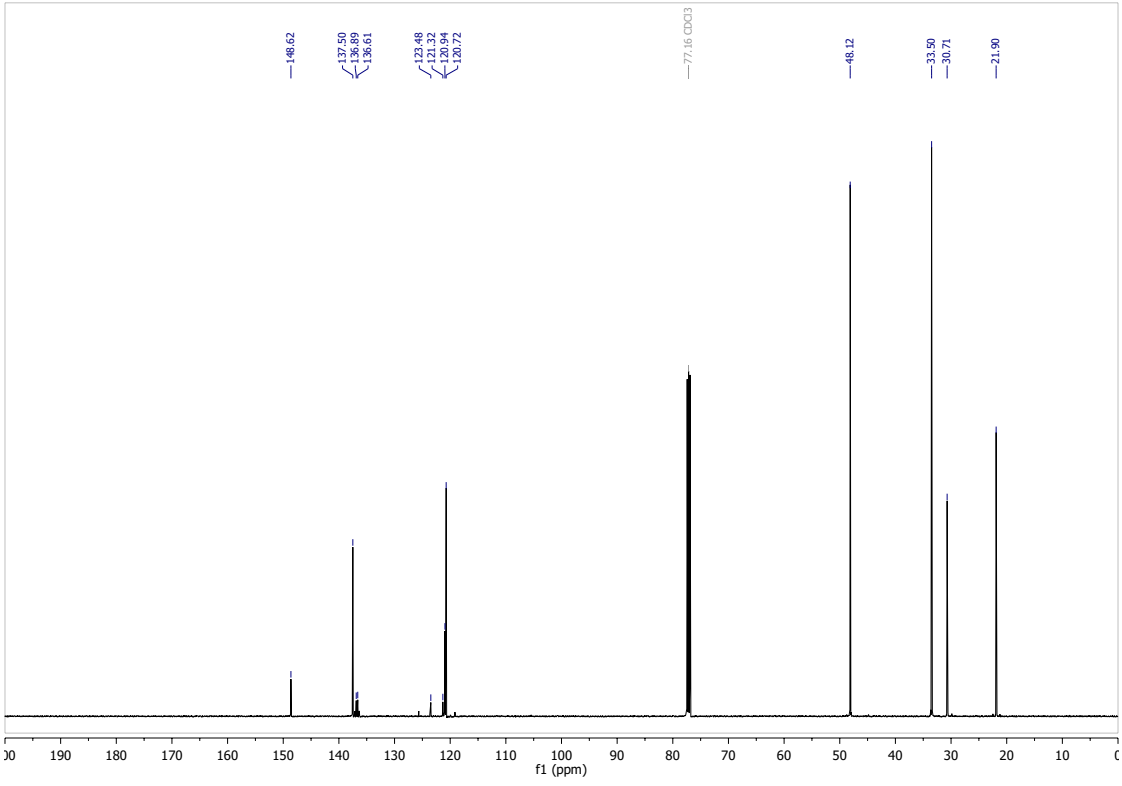

151.93
132.36
124.81
122.64
115.34
111.88
77.16 CDCl3
53.62
49.41
37.87
36.09
29.53
24.09
f1 (ppm)

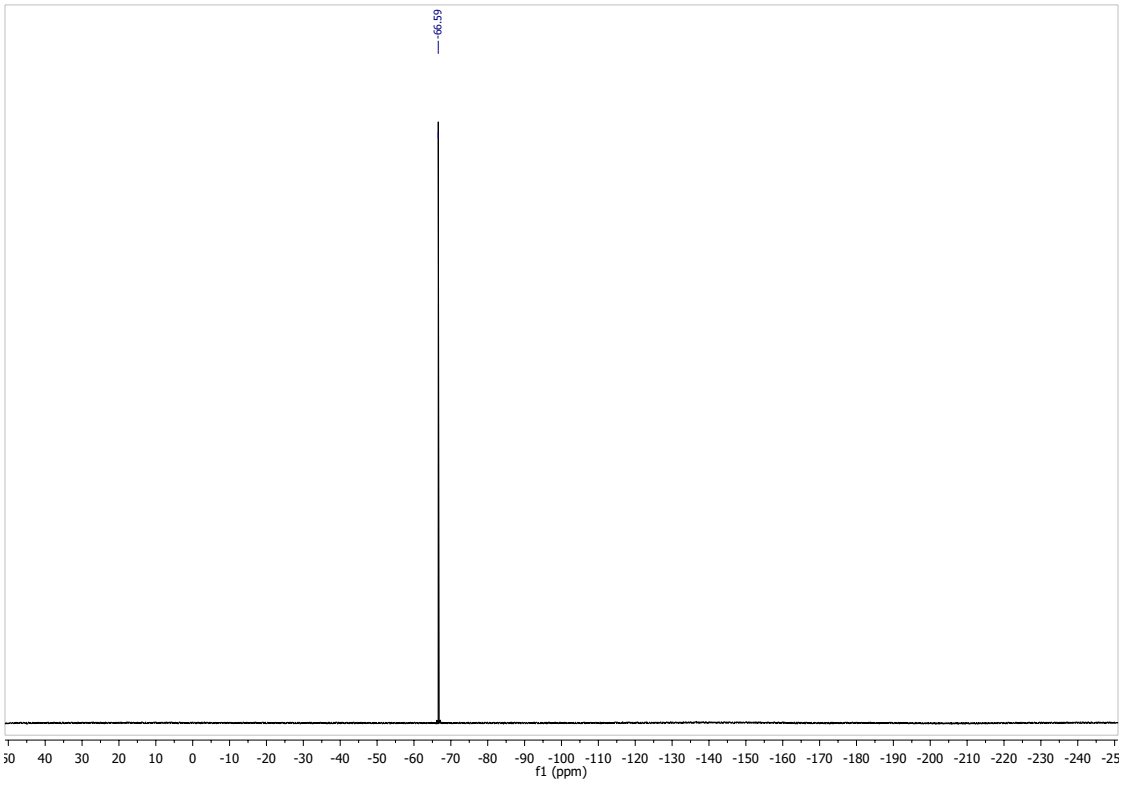

O
N
F3C
N
Me
7.26 CDCl3
1.00
1.03
0.99
0.97
0.96
1.02
0.99
1.19
2.16
1.22
1.15
2.90
f1 (ppm)

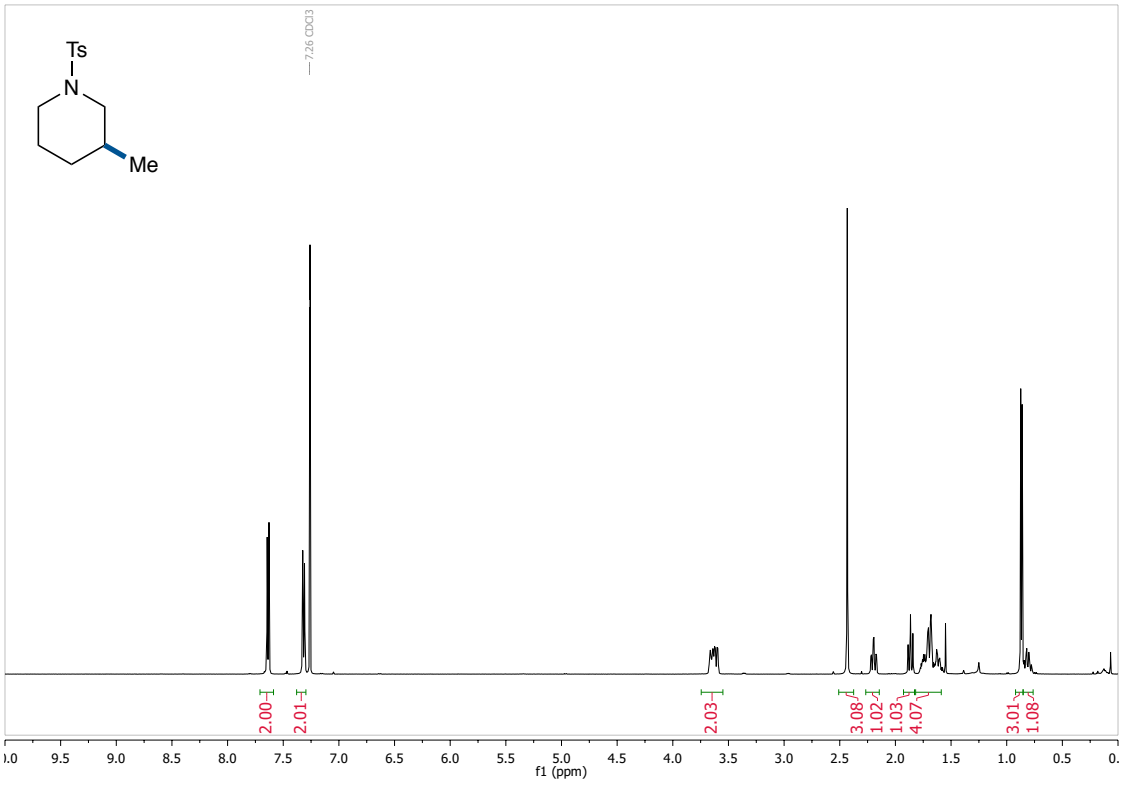

166.24
148.89
148.02
136.37
135.17
122.38
120.53
120.20
77.16 CDCl3
48.25
42.82
34.79
33.73
31.11
21.71
f1 (ppm)

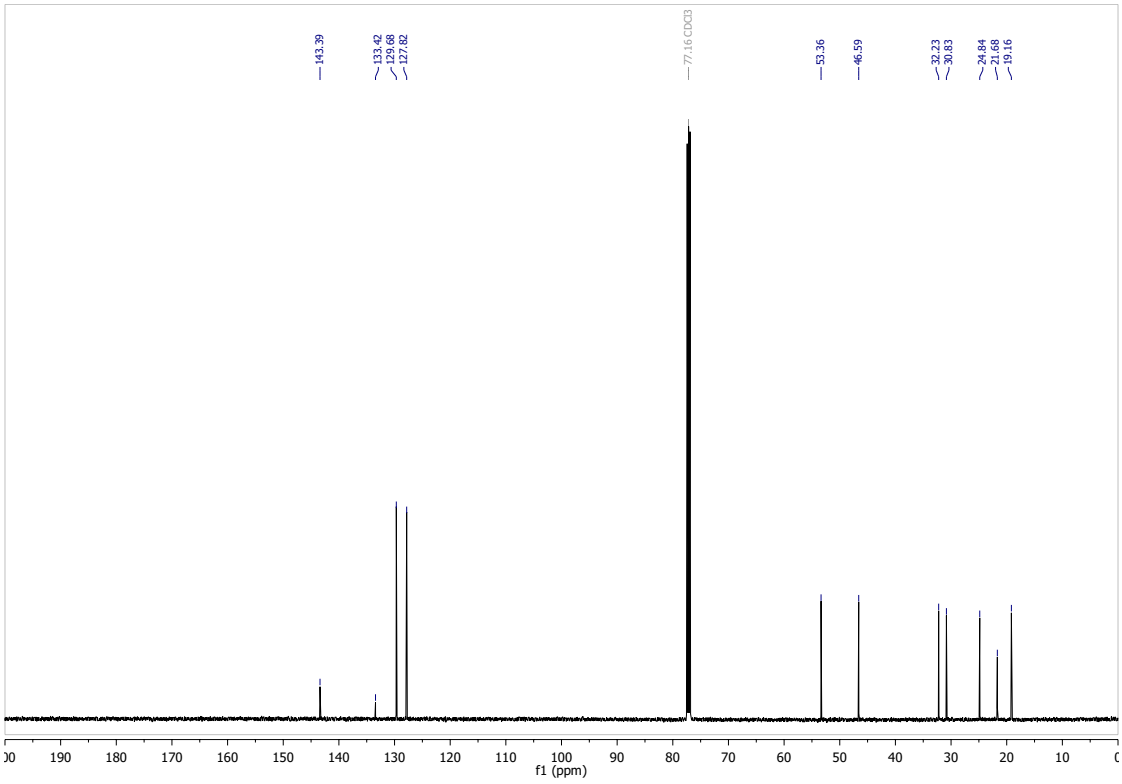

-68.11
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -25
f1 (ppm)

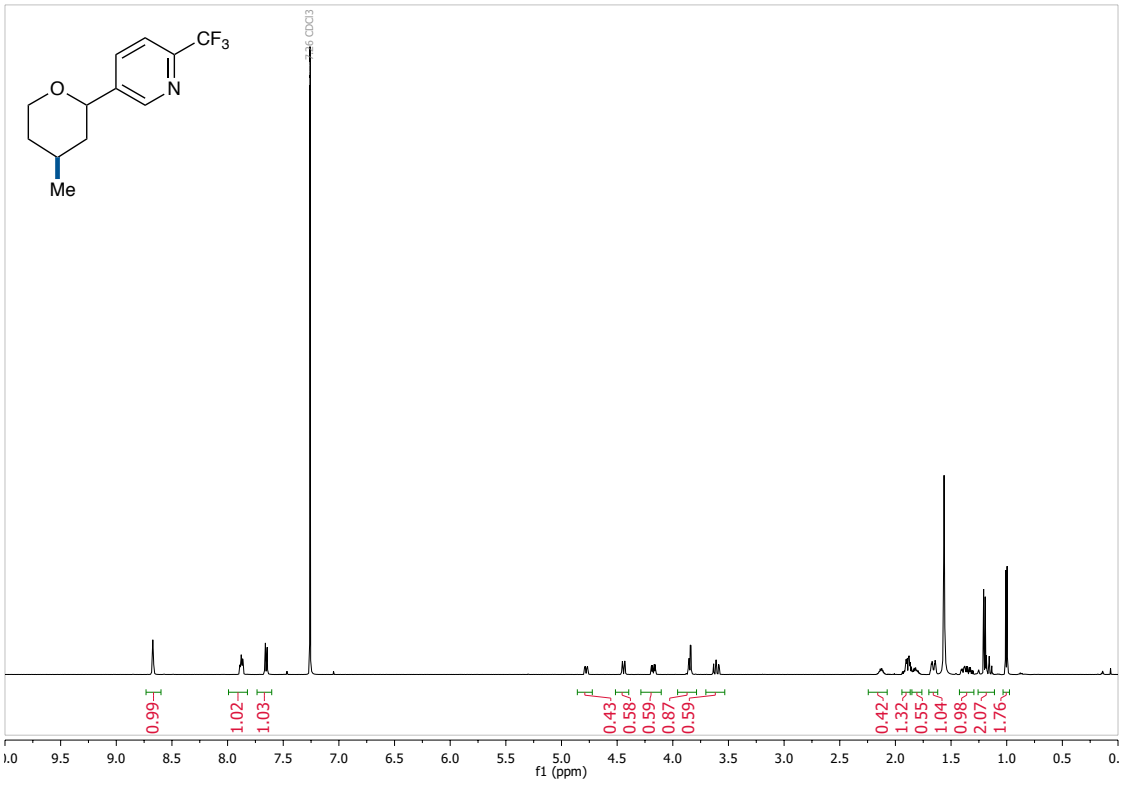

F3C
N
N
Me
7.26 CDCl3
1.00
0.99
1.00
1.99
1.98
1.98
0.97
2.04
2.98
f1 (ppm)

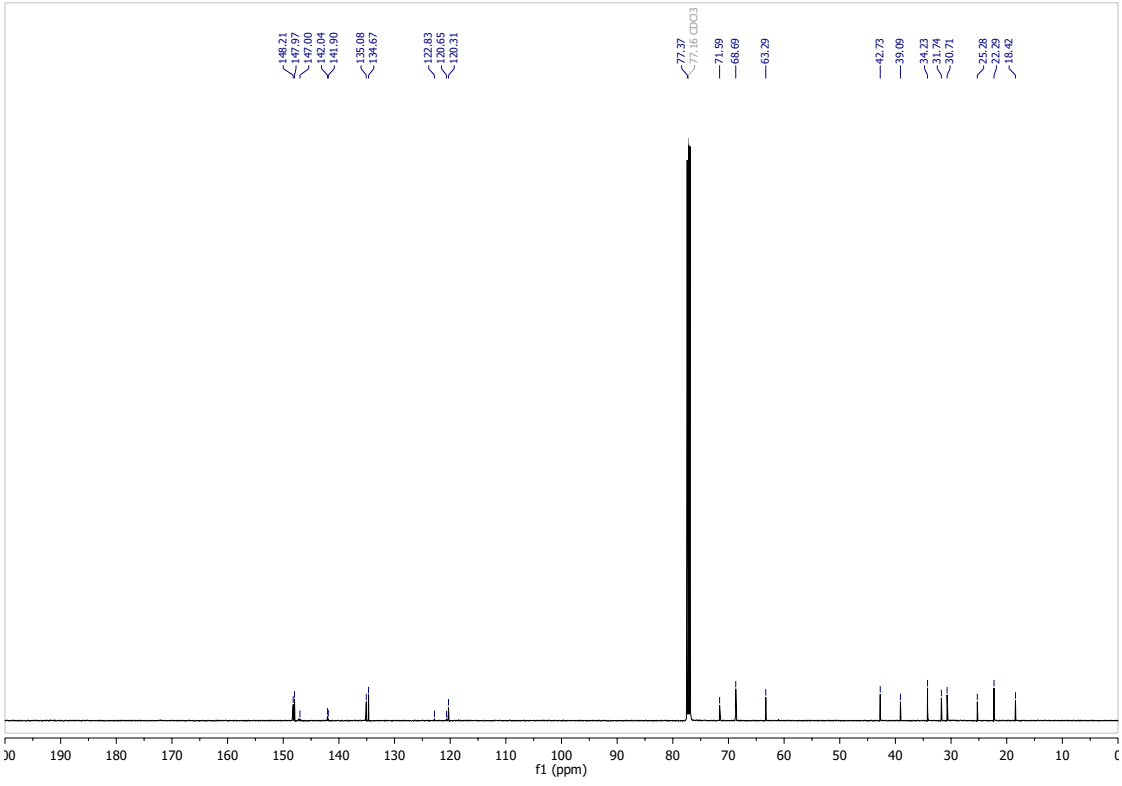

148.62
137.50
136.89
136.61
123.48
121.32
120.94
120.72
77.16 CDCl3
48.12
33.50
30.71
21.90
f1 (ppm)

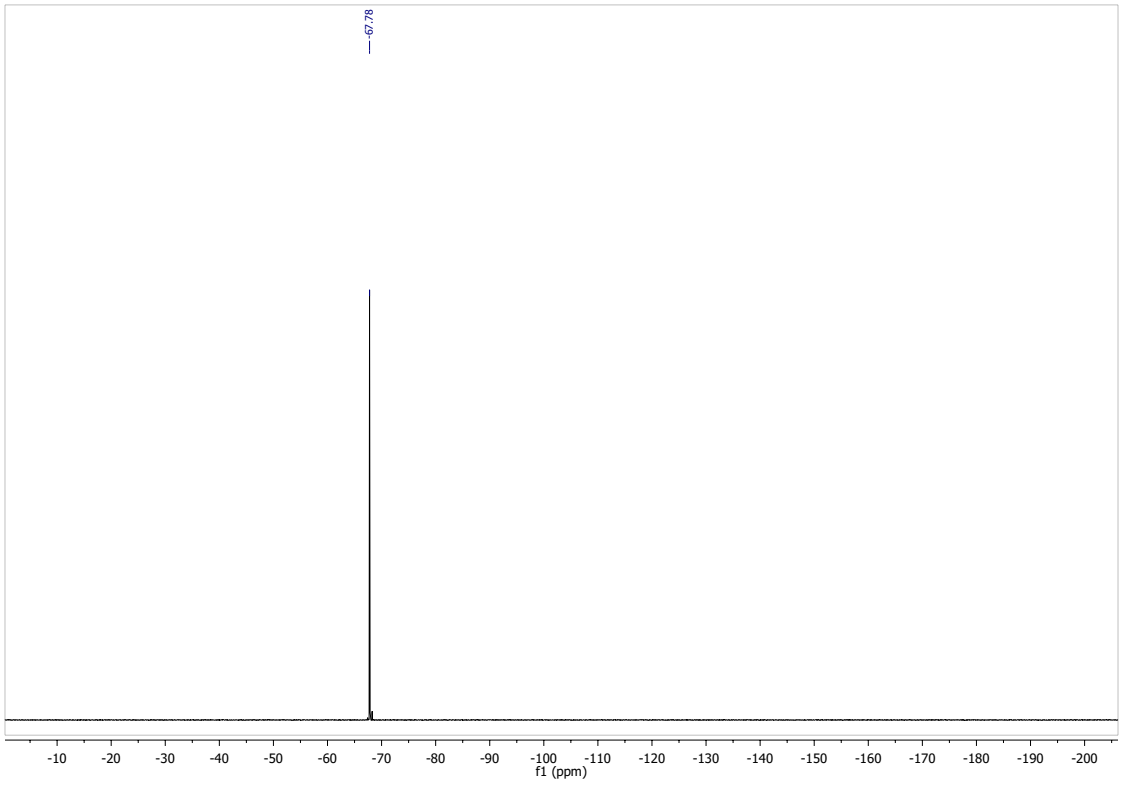

-66.59
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -25
f1 (ppm)

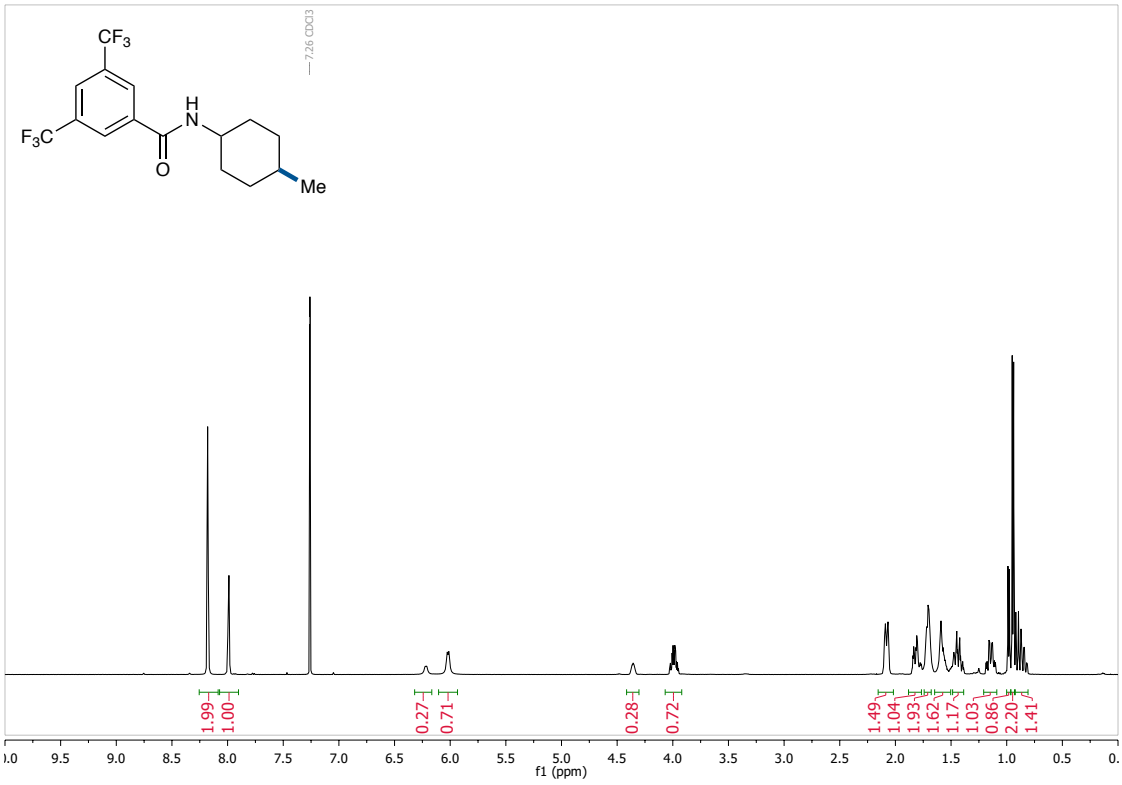

Ts
N
Me
7.26 CDCl3
2.00
2.01
2.03
3.08
1.02
1.03
4.07
3.01
1.08
f1 (ppm)

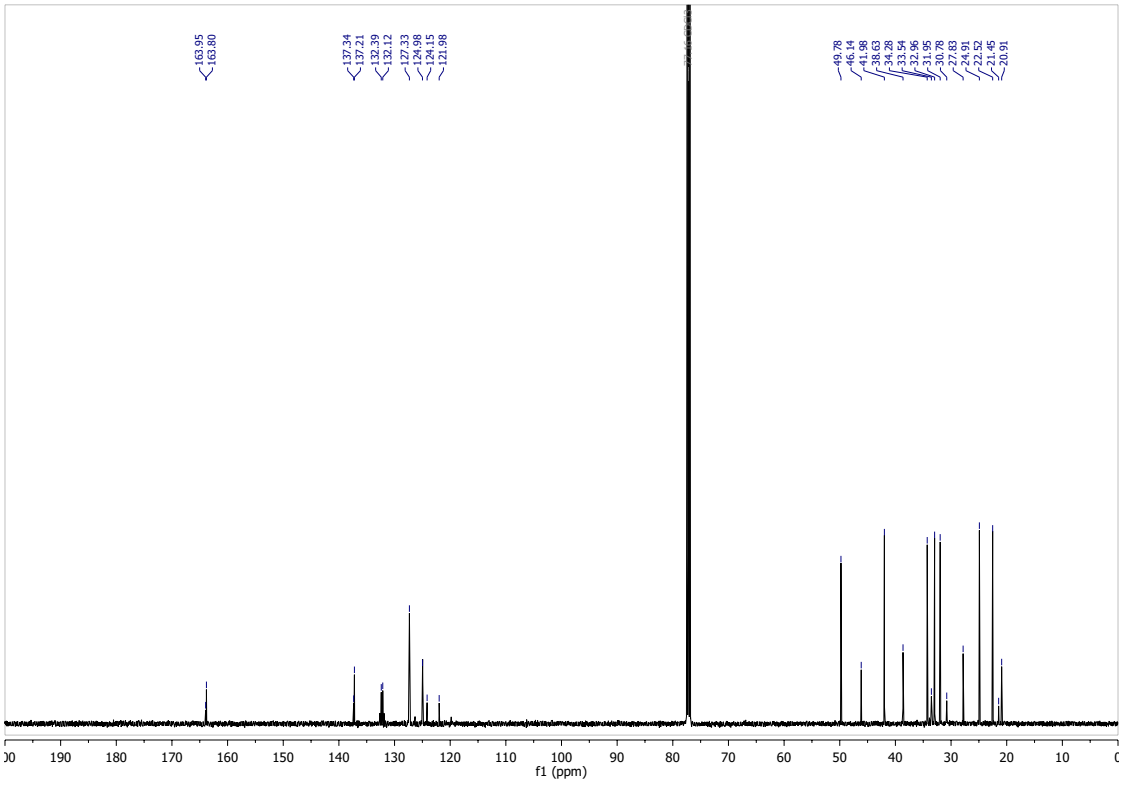

143.39
133.42
129.68
127.02
77.16 CDCl3
53.36
46.59
32.23
30.83
24.84
21.68
19.16
f1 (ppm)

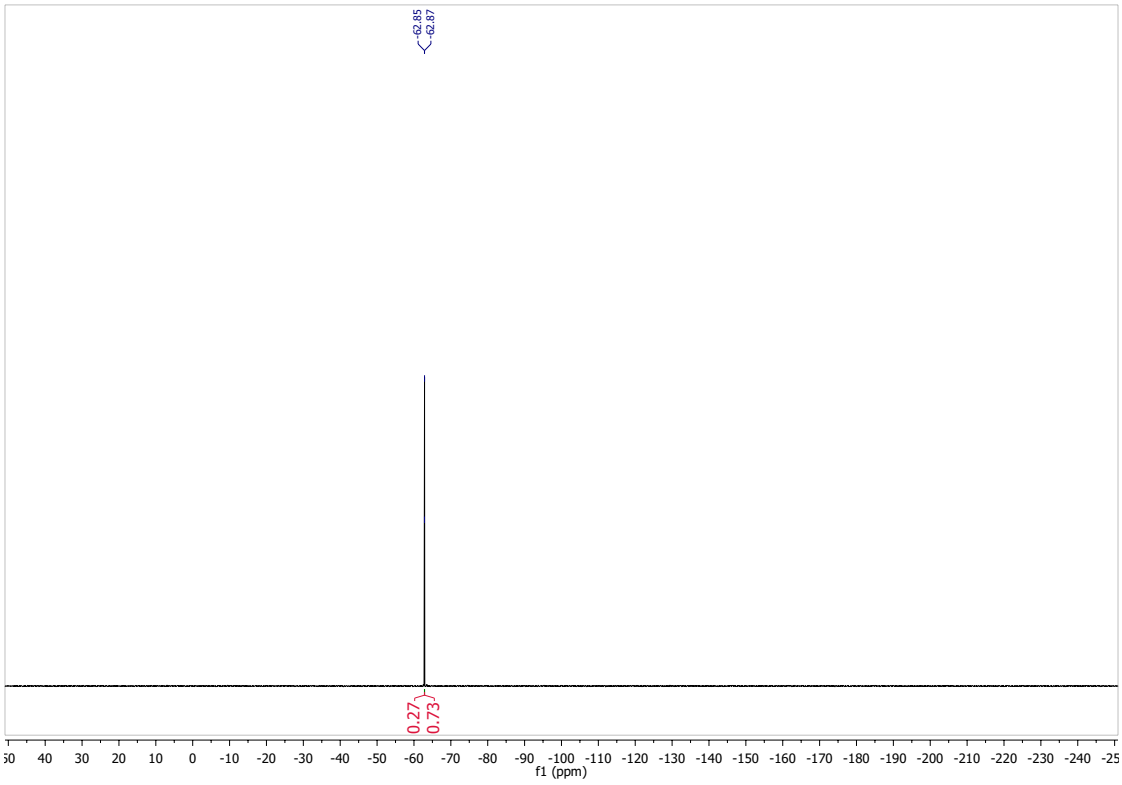

CF3
O
N
Me
7.26 CDCl3
0.99
1.02
1.03
0.43
0.58
0.59
0.87
0.59
0.42
1.32
0.55
1.04
0.98
2.07
1.76
f1 (ppm)

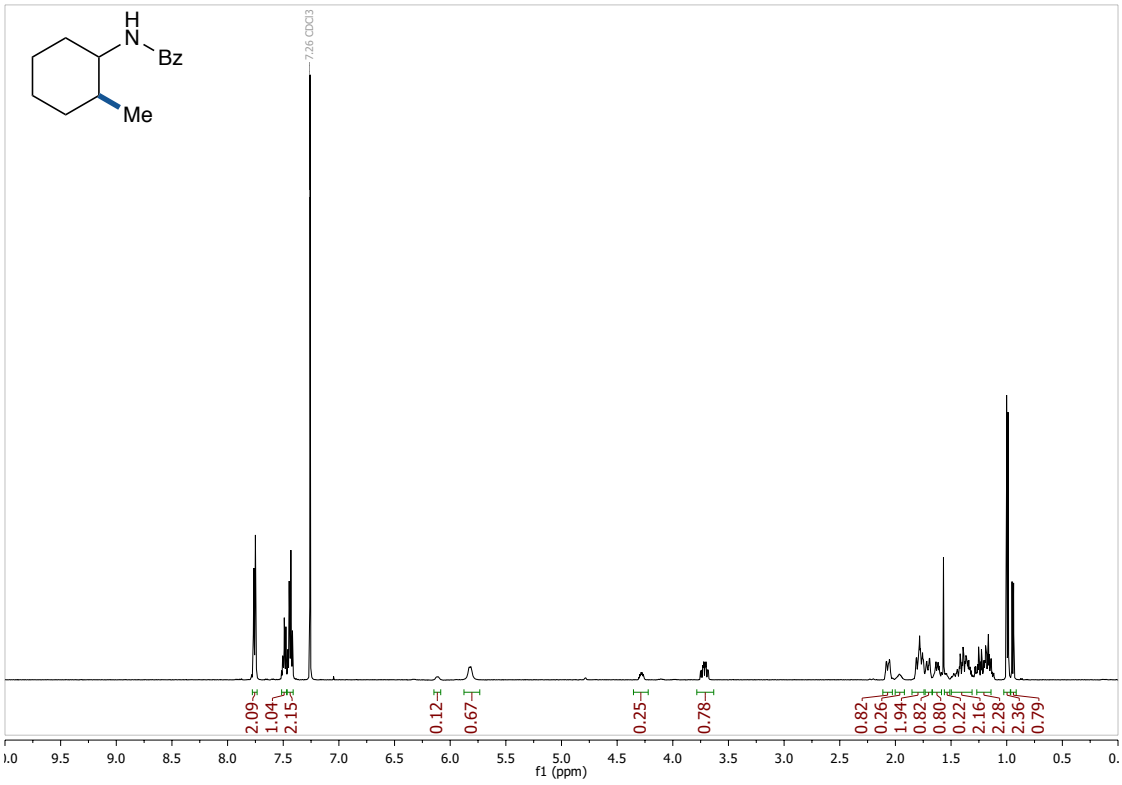

148.21
147.97
147.00
142.04
141.90
135.08
134.67
122.83
120.65
120.31
77.37
77.16 CDCl3
71.59
68.69
63.29
42.73
39.09
34.23
31.74
30.71
25.28
22.29
18.42
f1 (ppm)

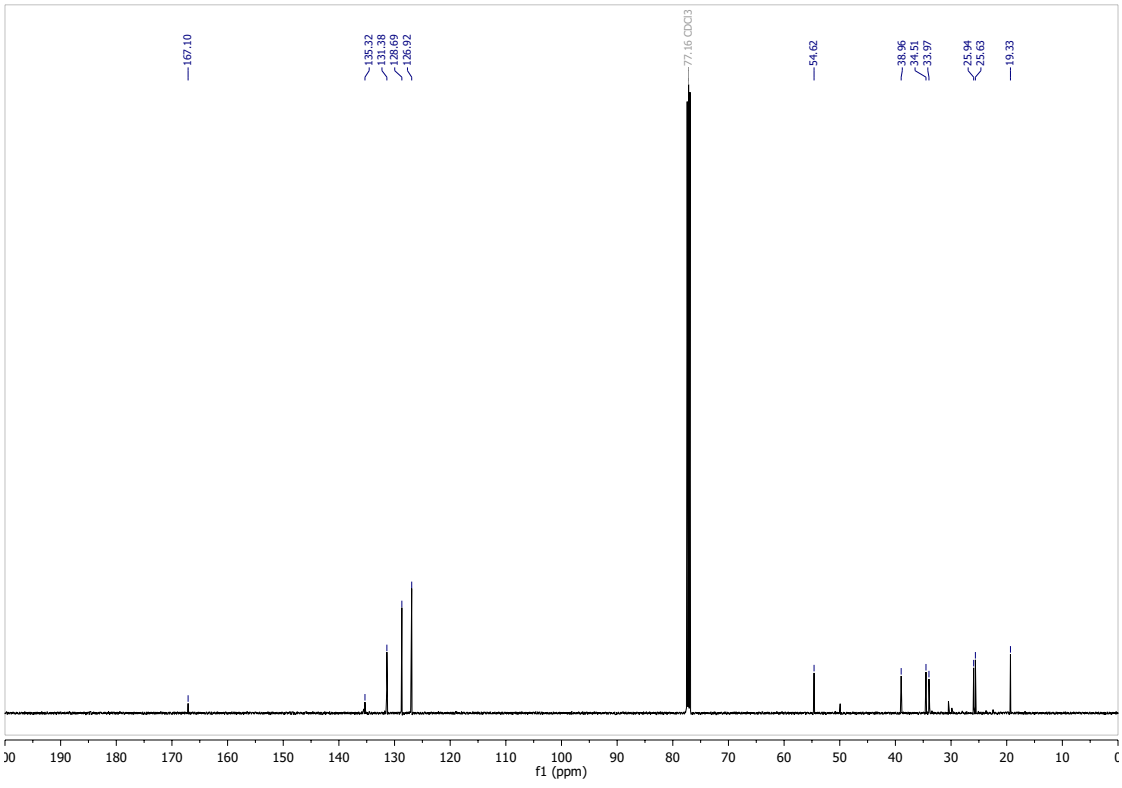

-67.78
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

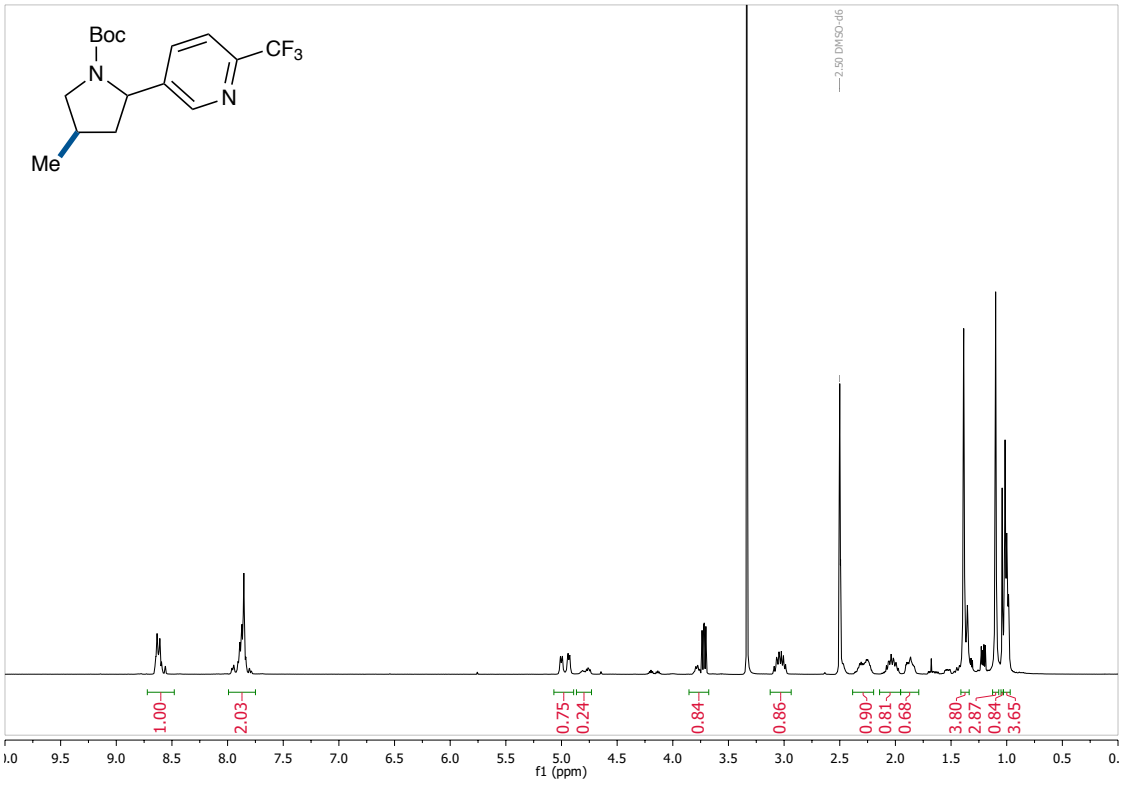

CF3
F3C
H
N
O
Me
7.26 CDCl3
1.99
1.00
0.27
0.71
0.28
0.72
1.49
1.04
1.93
1.62
1.17
1.03
0.86
2.20
1.41
f1 (ppm)

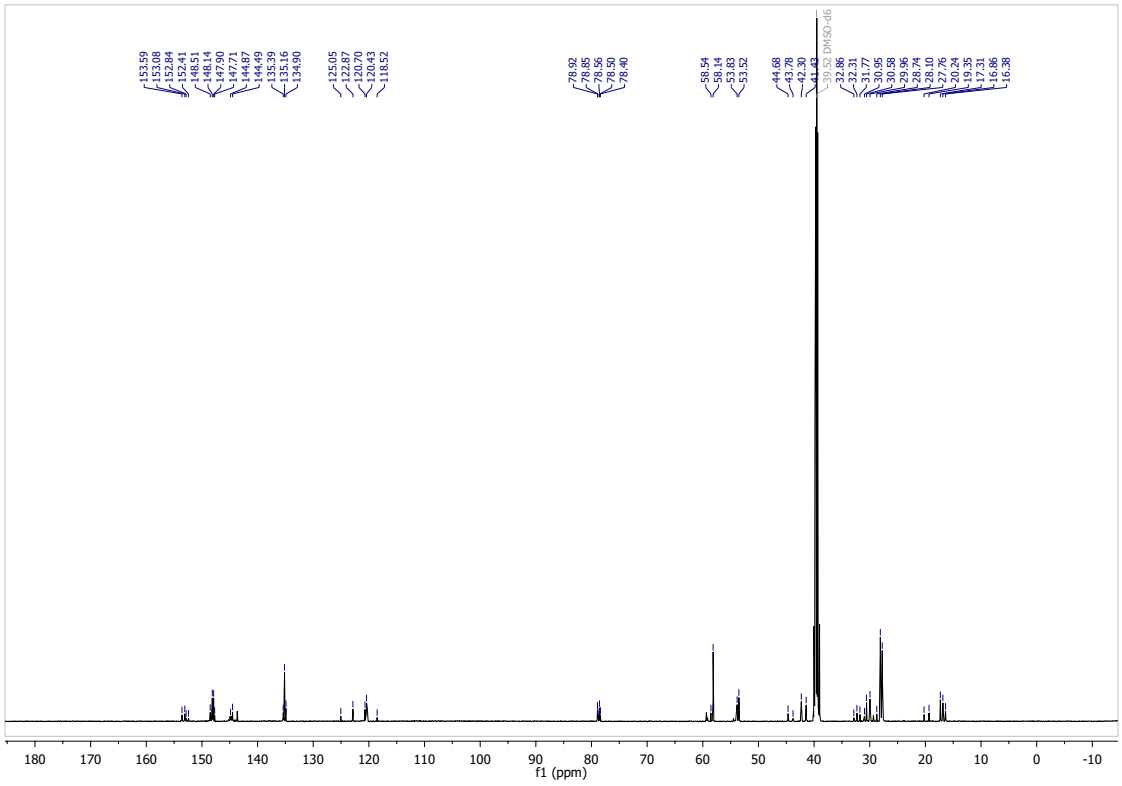

163.95
163.80
137.34
137.21
133.39
132.12
127.33
124.98
124.15
121.98
49.78
46.14
41.98
38.63
34.28
33.54
32.96
31.95
30.78
27.83
24.91
22.52
21.45
20.91
f1 (ppm)

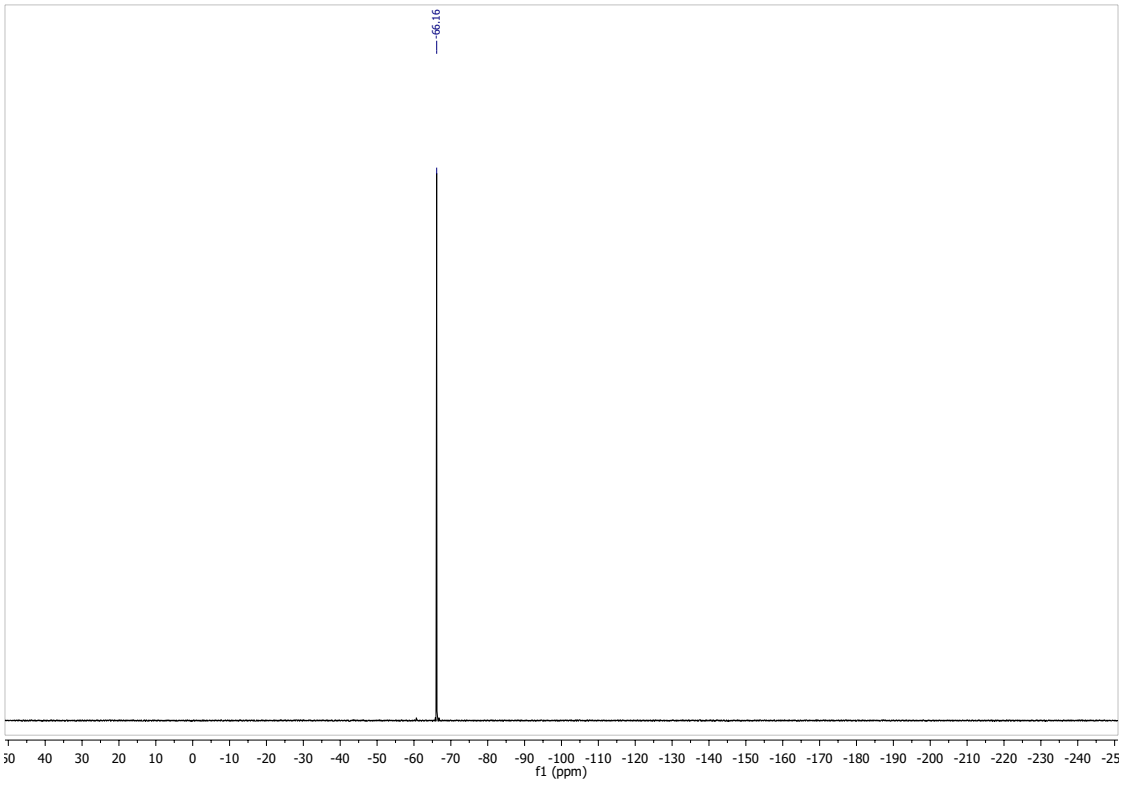

-62.85
-62.87
0.27
0.73
f1 (ppm)


H
N
Bz
Me
7.26 CDCl3
2.09
1.04
2.15
0.12
0.67
0.25
0.78
0.82
0.26
1.94
0.82
0.80
0.22
2.16
2.28
2.36
0.79
f1 (ppm)

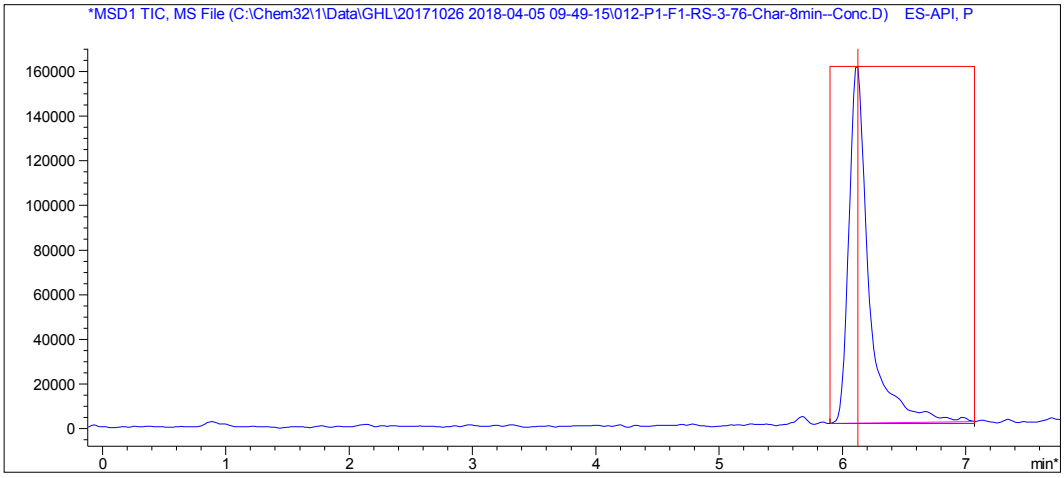

167.10
135.32
131.38
128.69
126.92
77.16 CDCl3
54.62
38.96
34.51
33.97
25.94
25.63
19.33
f1 (ppm)

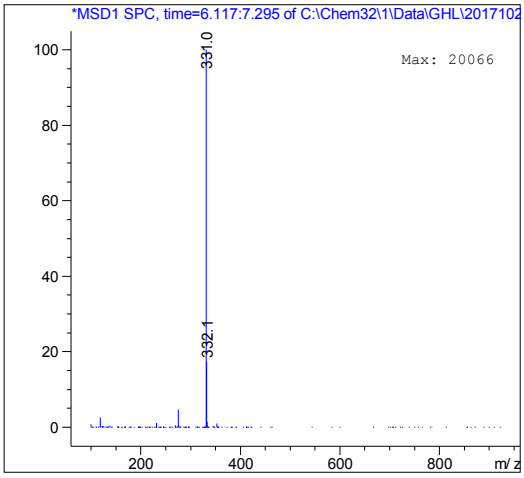

Boc
N
CF3
N
Me
2.50 DMSO-d6
1.00
2.03
0.75
0.24
0.84
0.86
0.90
0.81
0.68
3.80
2.87
0.84
3.65
f1 (ppm)

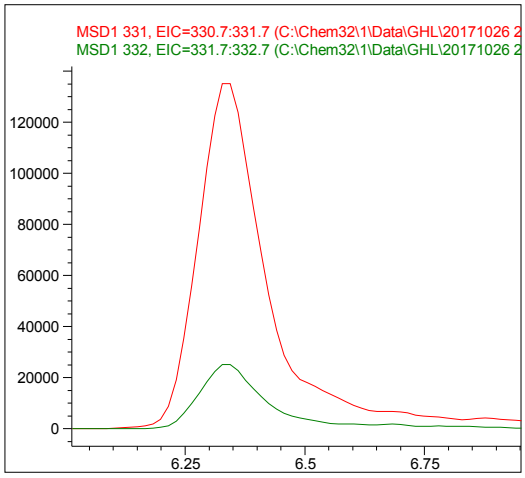

153.59
153.08
152.84
152.41
148.51
148.14
147.90
147.71
144.87
144.49
135.39
135.16
134.90
125.05
122.87
120.70
120.43
118.52
78.92
78.85
78.55
78.50
78.40
58.54
58.14
53.83
53.52
44.68
43.78
42.30
41.43
39.92 DMSO-d6
32.86
31.31
31.17
31.07
30.58
29.96
28.74
28.10
27.76
20.24
19.35
17.31
16.86
16.38
f1 (ppm)


-66.16
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -25
f1 (ppm)

MS Peak Purity Range Report
Data File C:\Chem32\...HL\20171026 2018-04-05 09-49-15\012-P1-F1-RS-3-76-Char-8min--Conc.D
Sample Name: RS-3-76-Char-8min--Conc



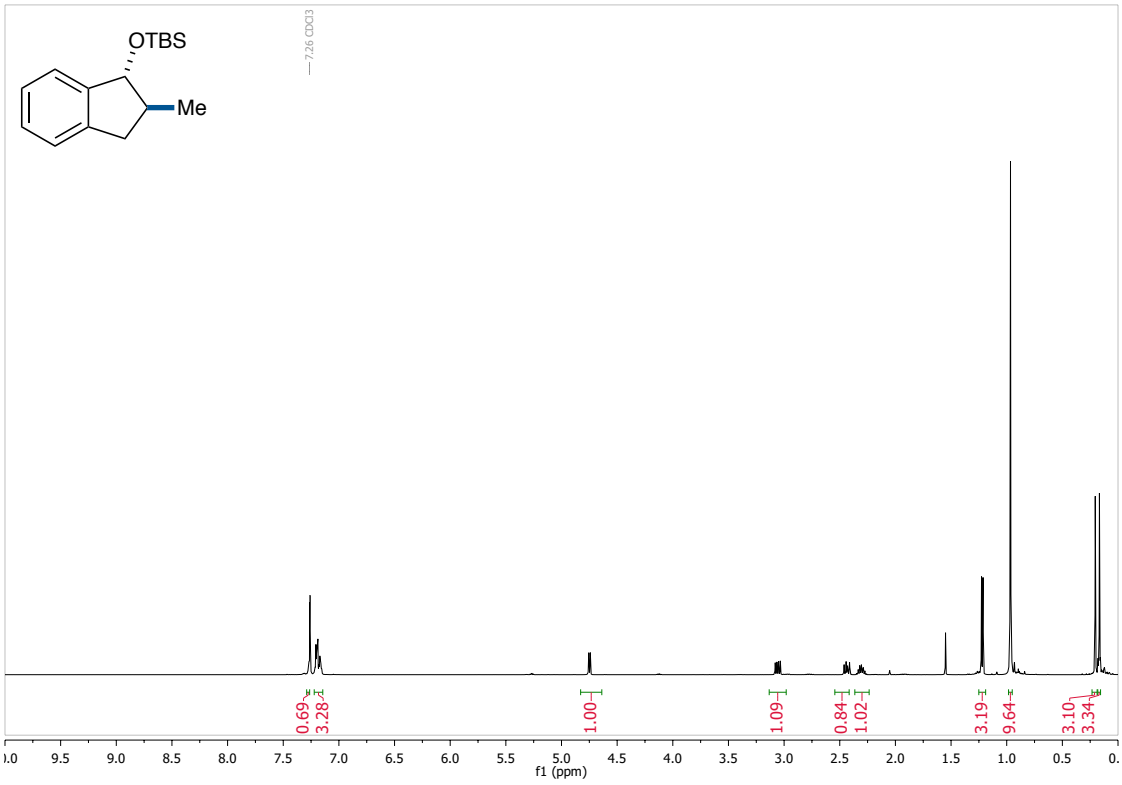


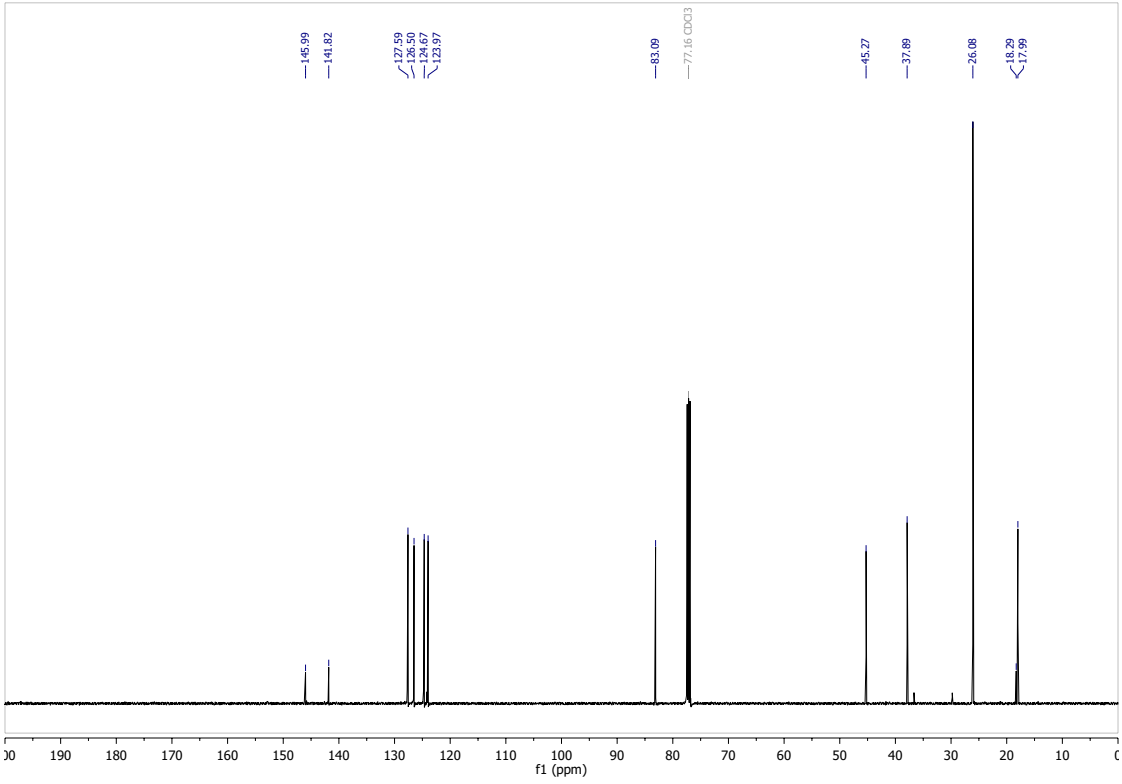


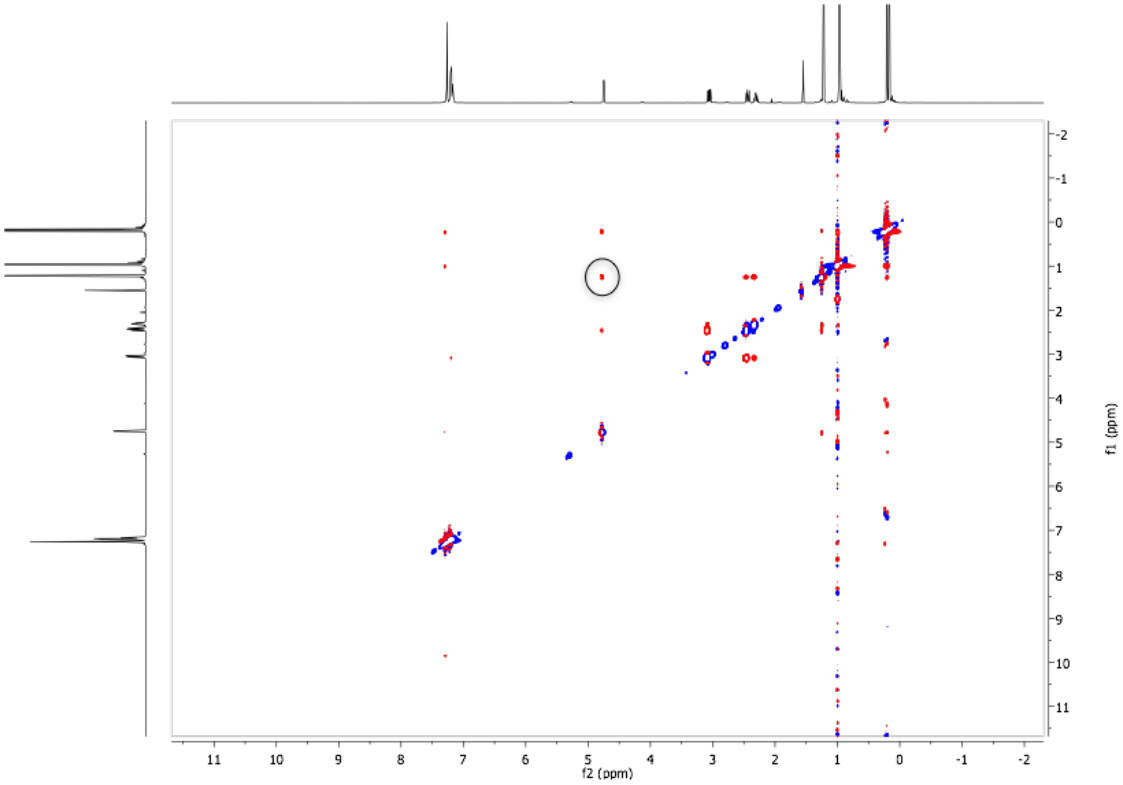
Peak #1 at 6.114 min (5.895 to 7.068 min)
-> The analysis found only one component, indicating a pure peak. <-

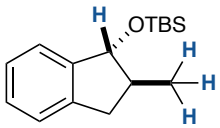
Component 1: Peak at Scan 387.5. Top ions are 331 332

*** End of Report ***

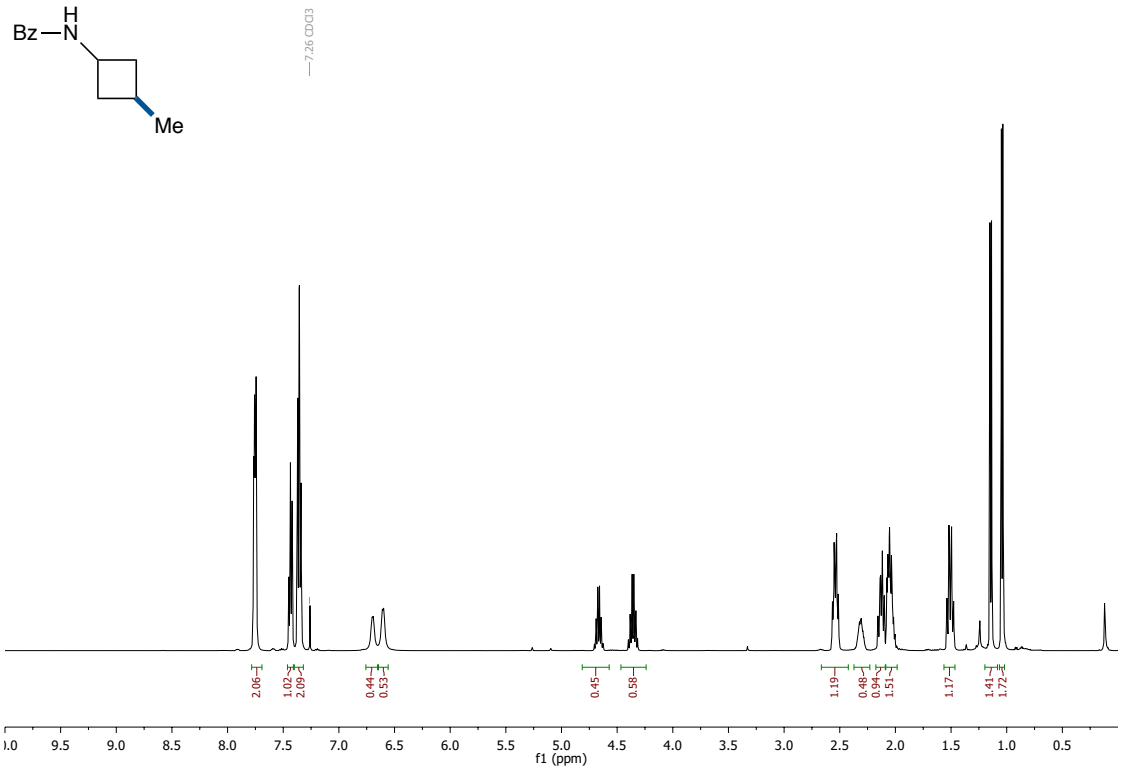

OTBS
Me
7.26 CDCl3
0.69
3.28
1.00
1.09
0.84
1.02
3.19
9.64
3.10
3.34
f1 (ppm)

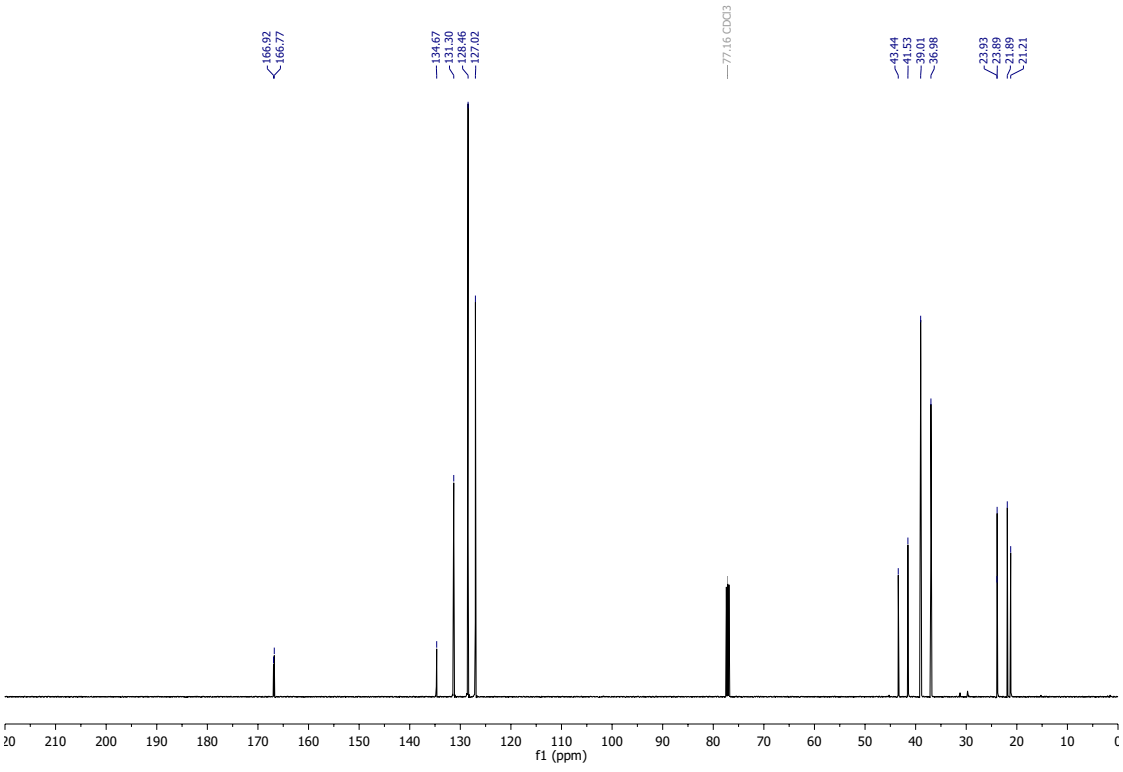

145.99
141.82
127.59
126.50
124.67
123.97
83.09
77.16 CDCl3
45.27
37.89
26.08
18.29
17.99
f1 (ppm)

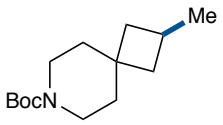




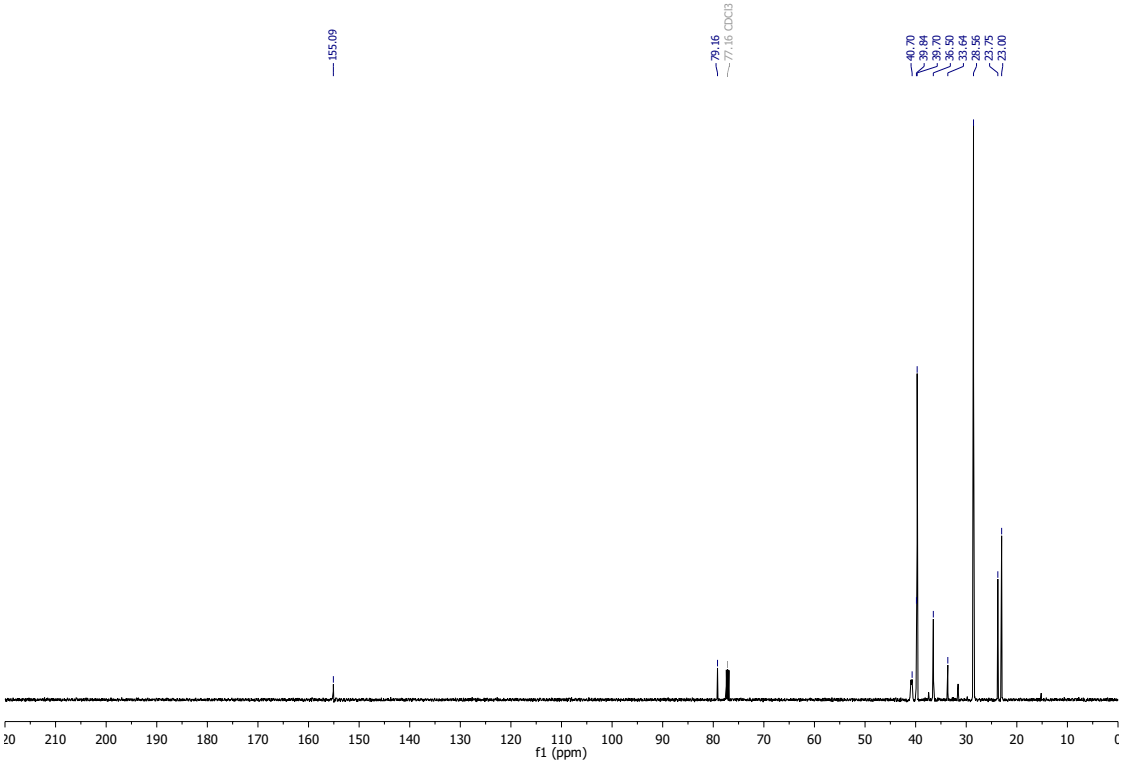
The highlighted protons show correlation in the NOESY spectrum (circled above), indicating the *trans* geometry.

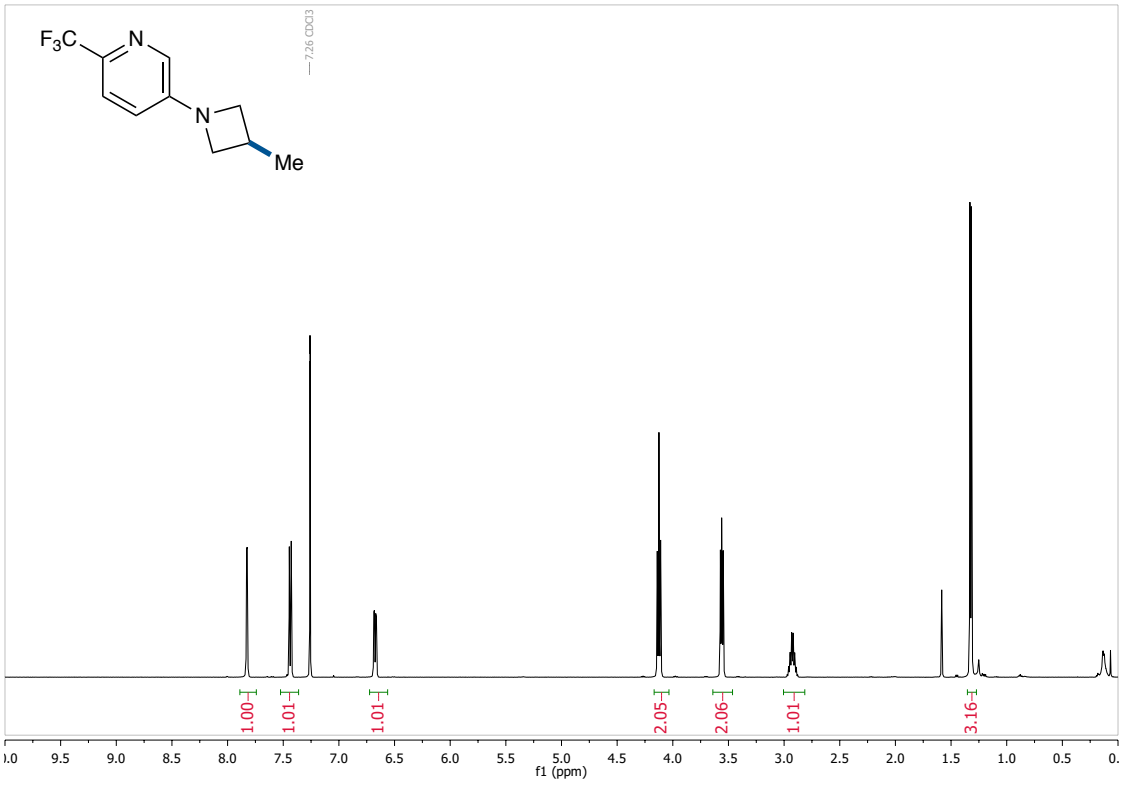

Bz—N
H
Me
7.26 CDCl3
2.06
1.02
2.09
0.44
0.53
0.45
0.58
1.19
0.48
0.94
1.51
1.17
1.41
1.72
f1 (ppm)

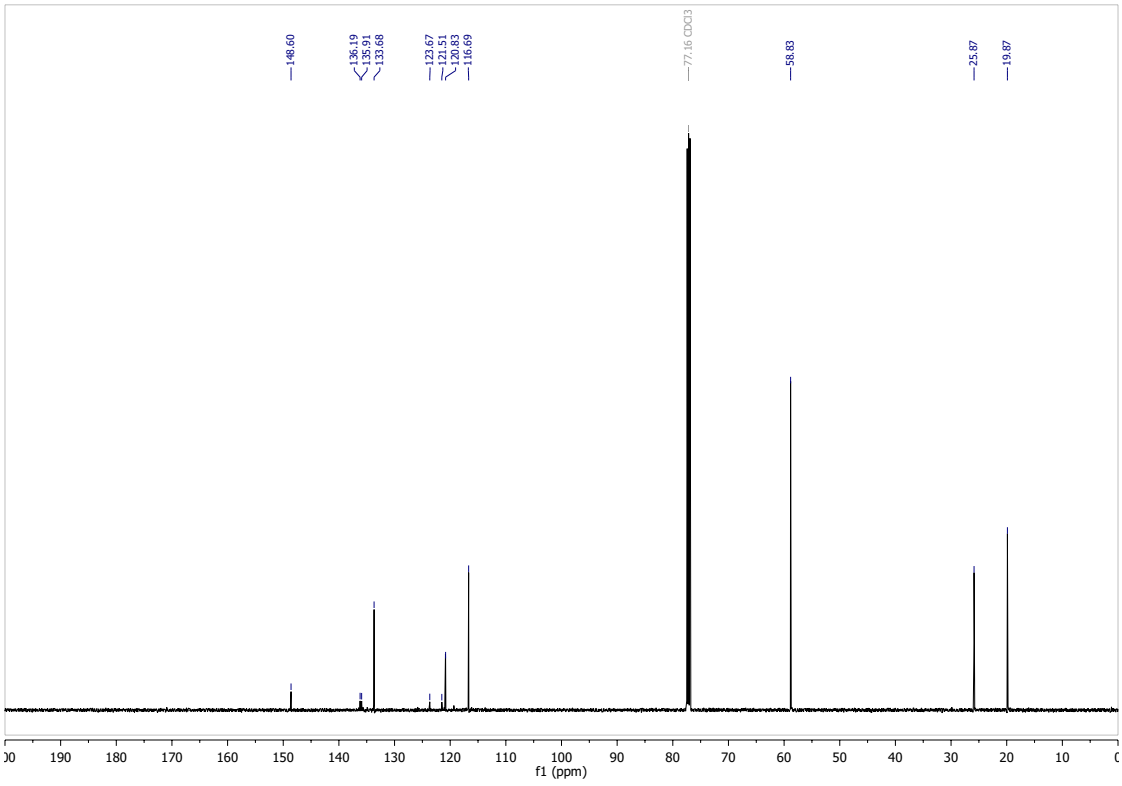

166.92
166.77
134.67
131.30
128.46
127.02
77.16 CDCl3
43.44
41.53
39.01
36.98
23.93
23.89
21.89
21.21
f1 (ppm)

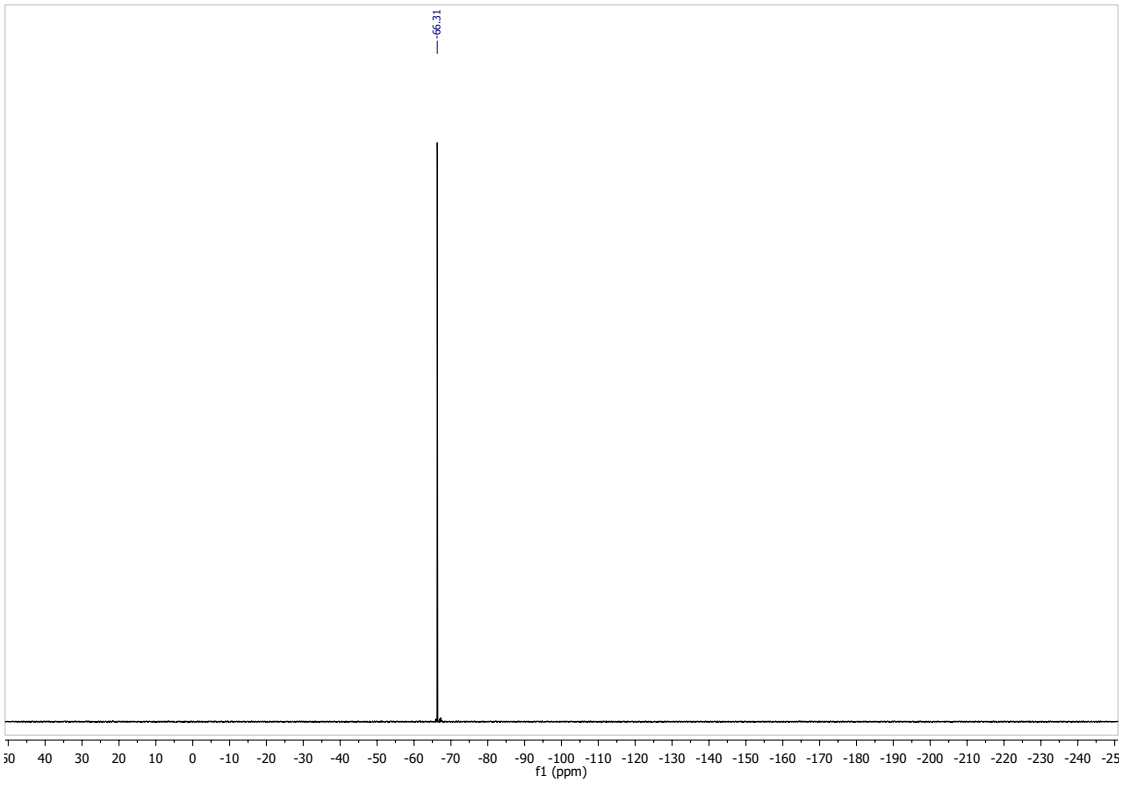

Me
BocN

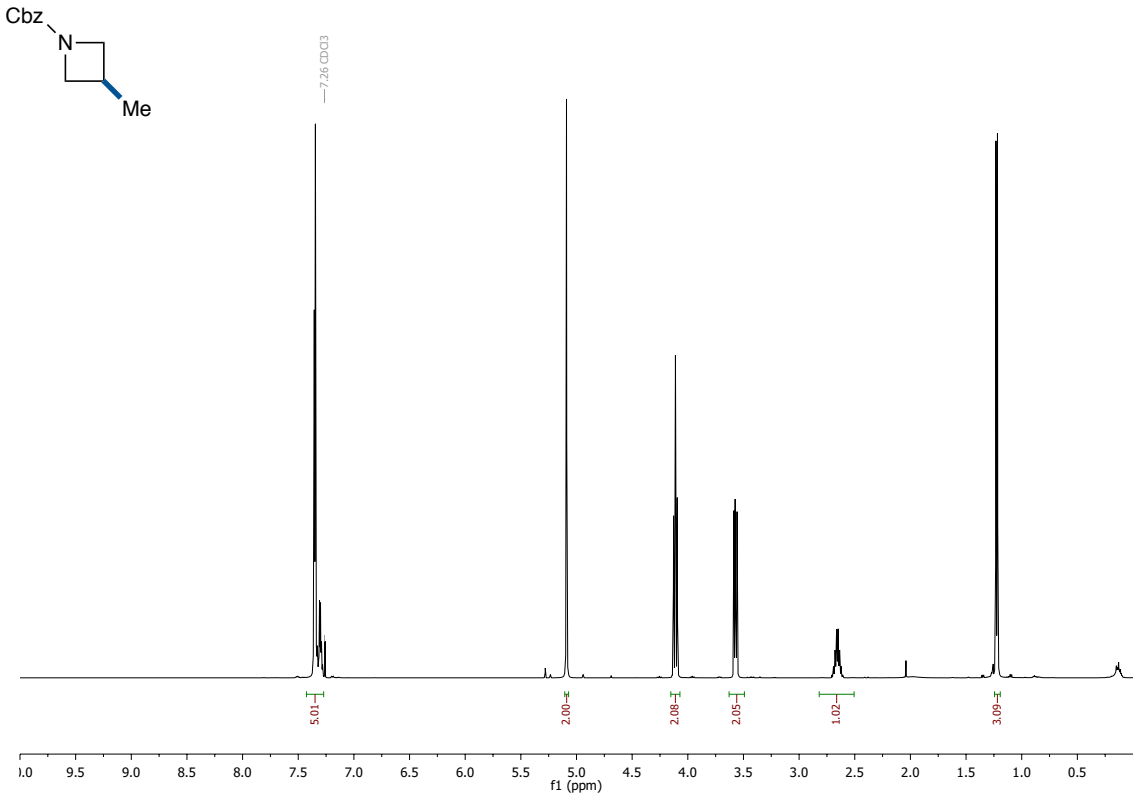
7.26 CDCl3
2.05
1.99
1.00
2.06
2.09
8.98
1.99
2.19
3.05
f1 (ppm)

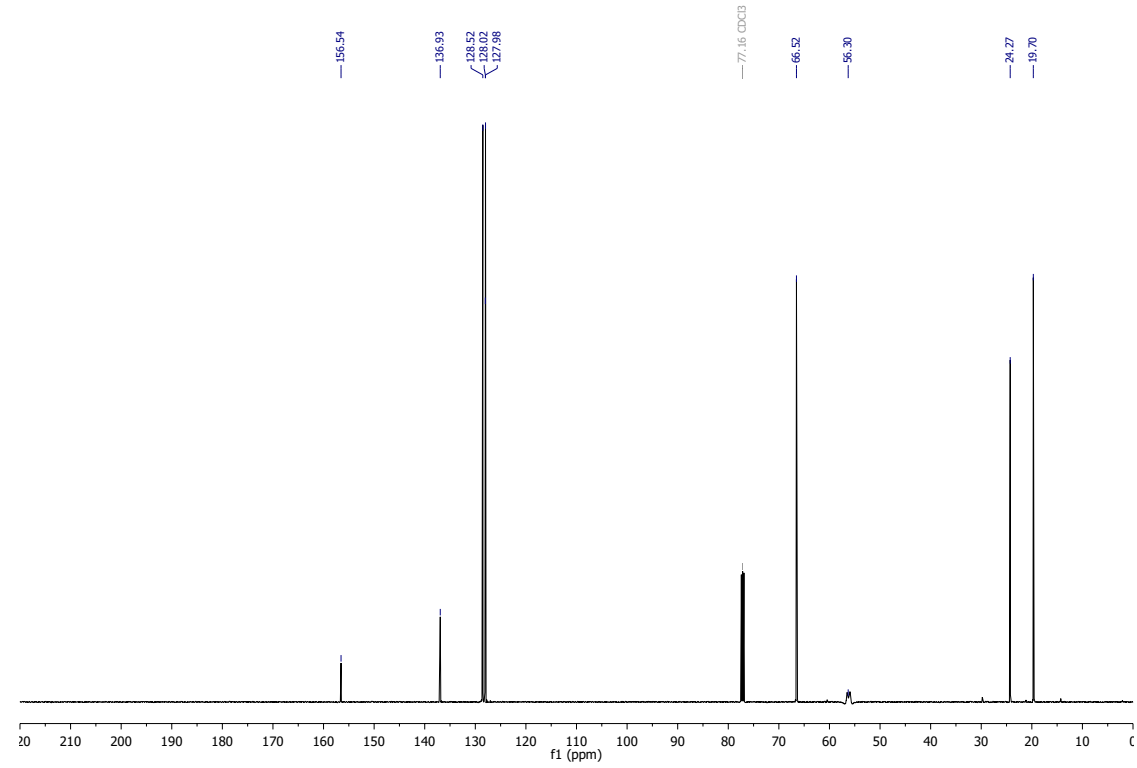

155.09
79.16
77.16 CDCl3
40.70
39.84
39.70
38.50
33.64
28.56
23.75
23.00
f1 (ppm)

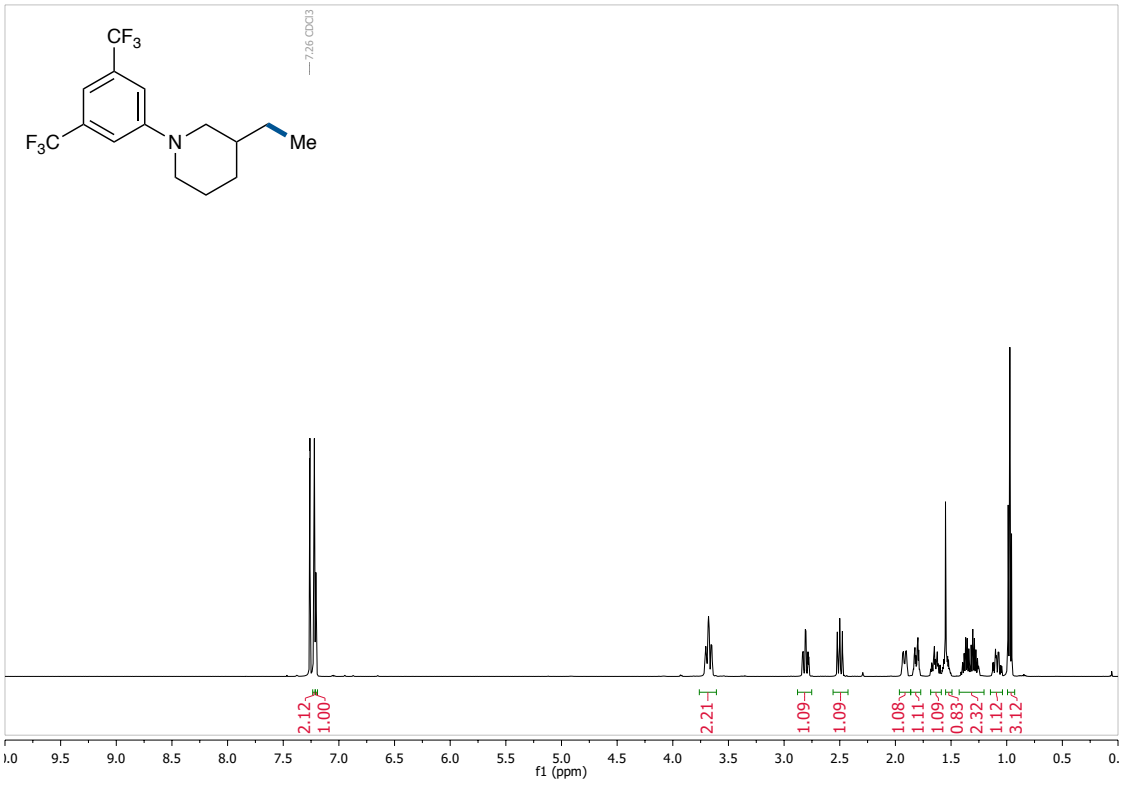

F3C
N
N
Me
7.26 CDCl3
1.00
1.01
1.01
2.05
2.06
1.01
3.16
f1 (ppm)

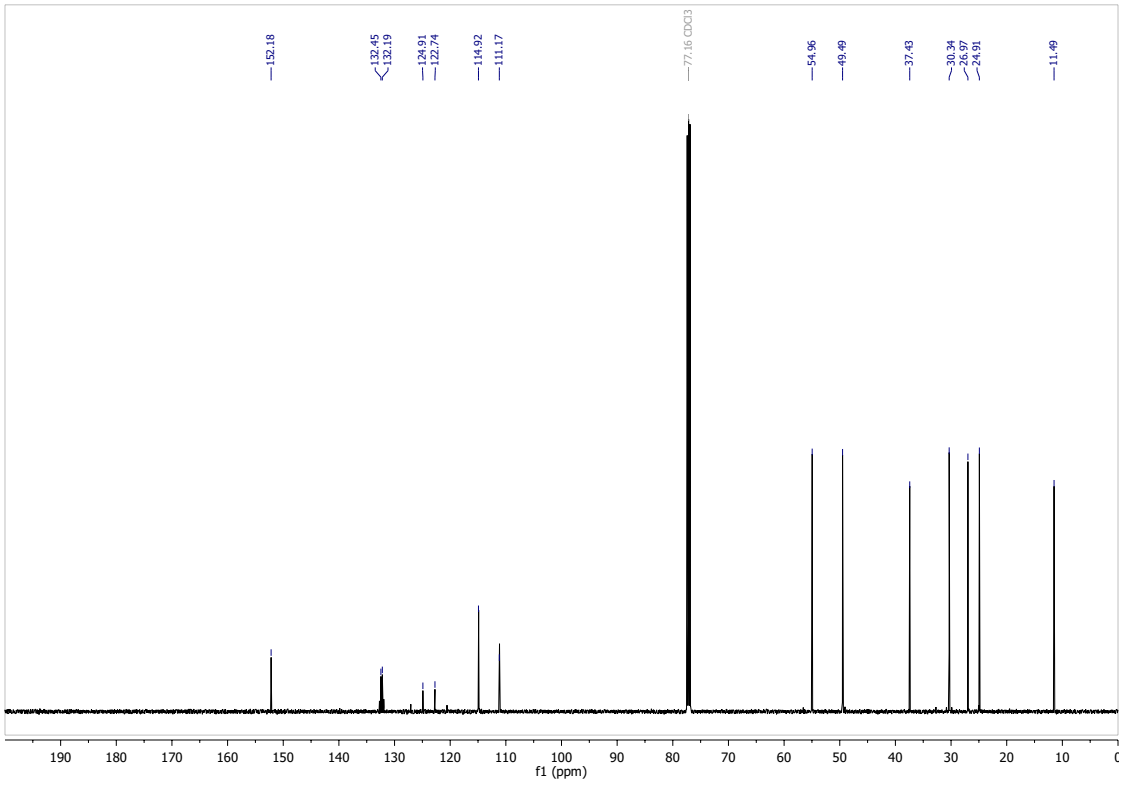

148.60
136.19
135.91
133.68
123.67
121.51
120.83
116.69
77.16 CDCl3
58.83
25.87
19.87
f1 (ppm)

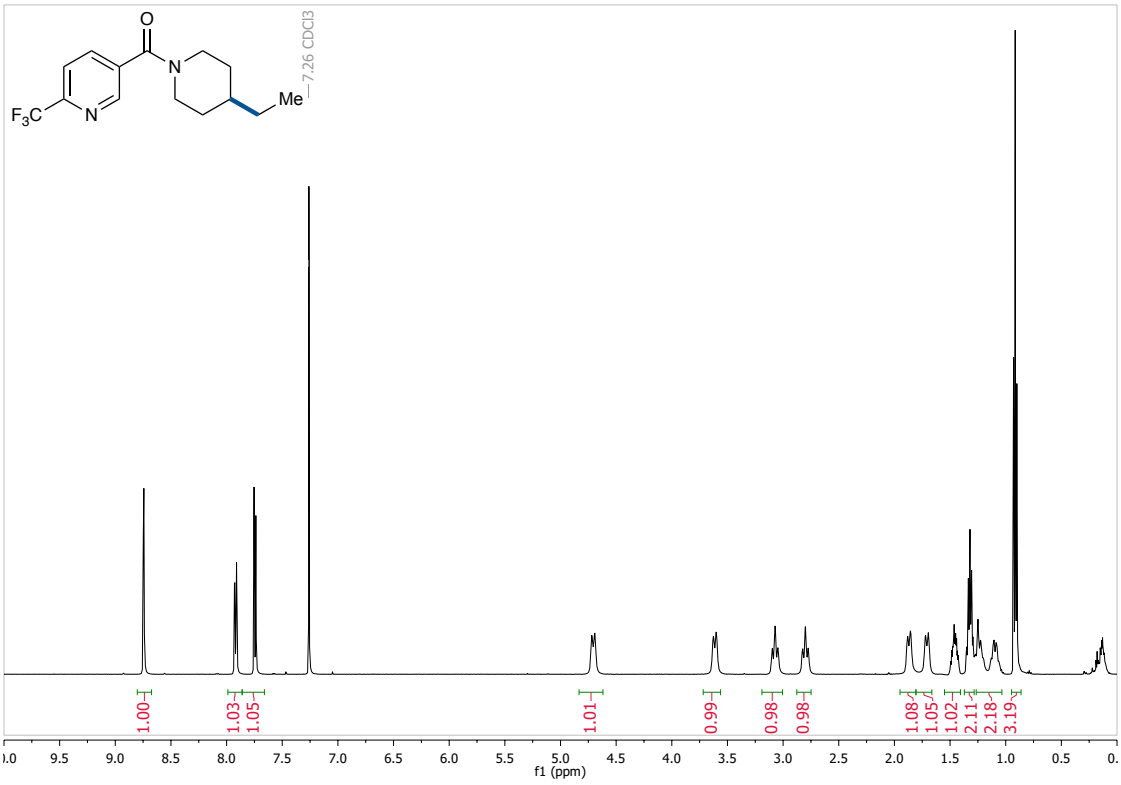

-66.31
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -25
f1 (ppm)

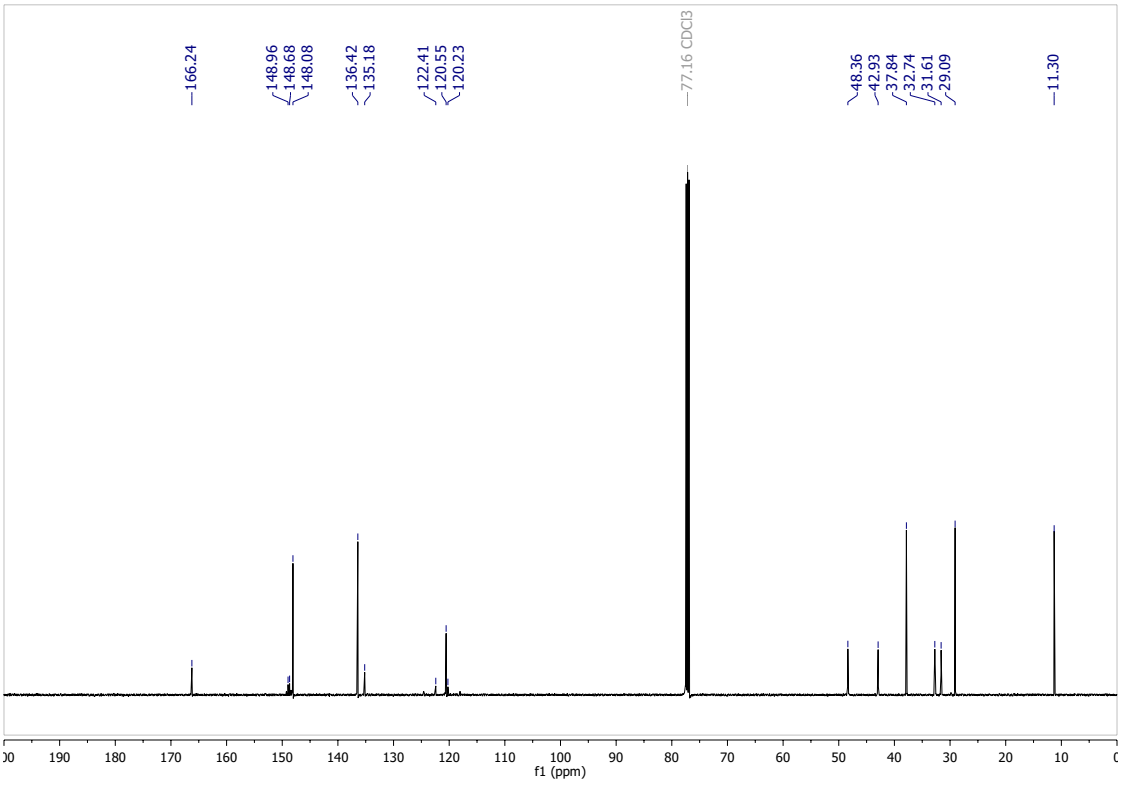

Cbz
N
Me
7.26 CDCl3
5.01
2.00
2.08
2.05
1.02
3.09
f1 (ppm)

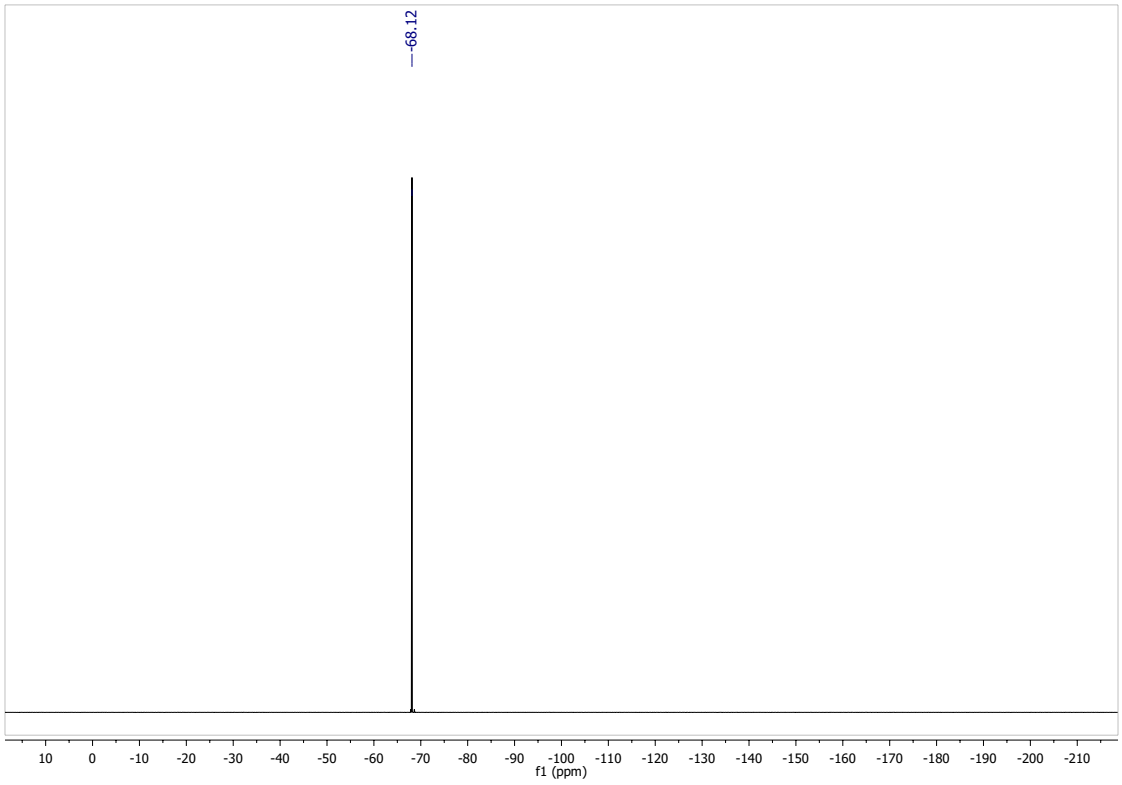

156.54
136.93
128.52
128.02
127.98
77.16 CDCl3
66.52
56.30
24.27
19.70
f1 (ppm)

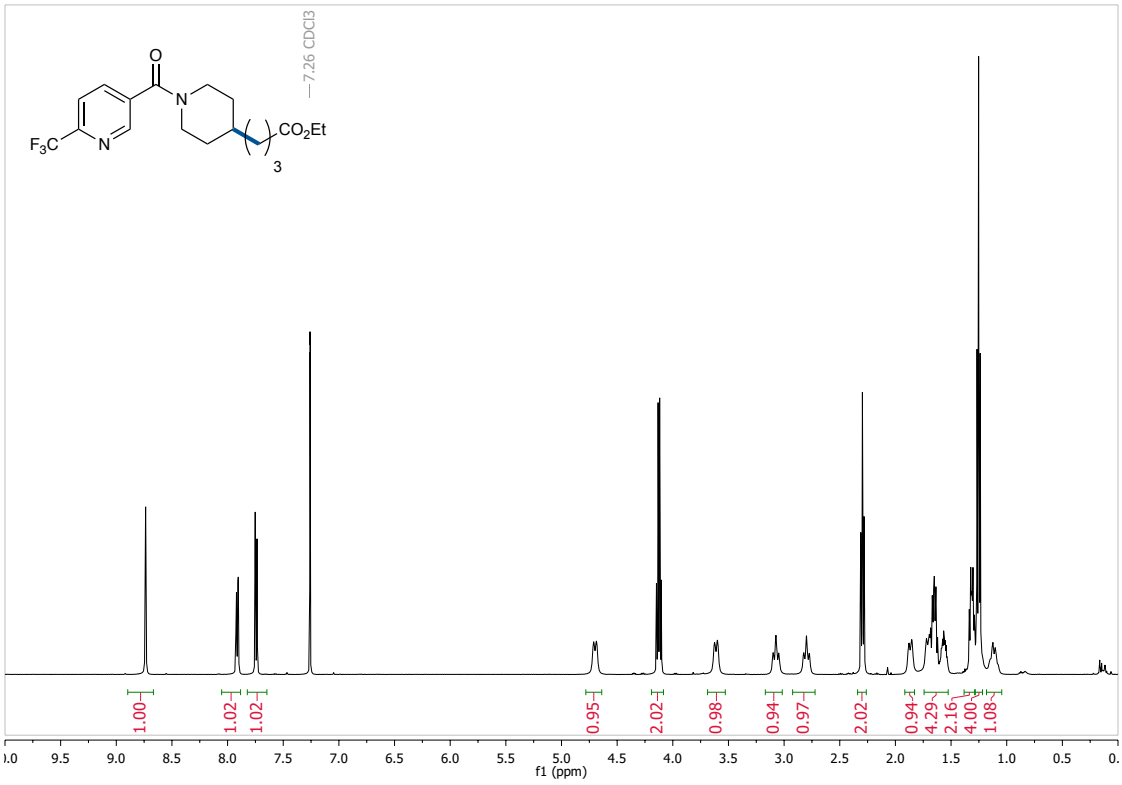

CF3
F3C
N
Me
7.26 CDCl3
2.12
1.00
2.21
1.09
1.09
1.08
1.11
1.09
0.83
2.32
1.12
3.12
f1 (ppm)

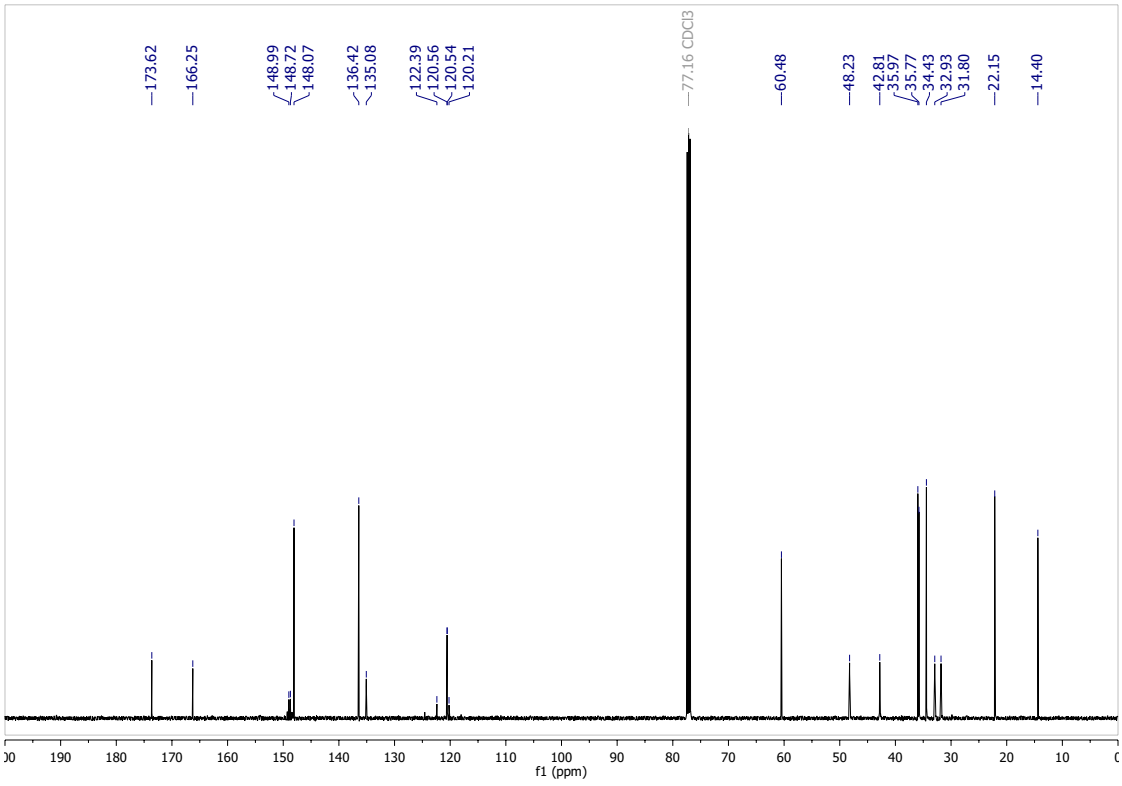

152.18
132.45
132.19
124.91
122.74
114.92
111.17
77.16 CDCl3
54.96
49.49
37.43
30.34
26.97
24.91
11.49
f1 (ppm)

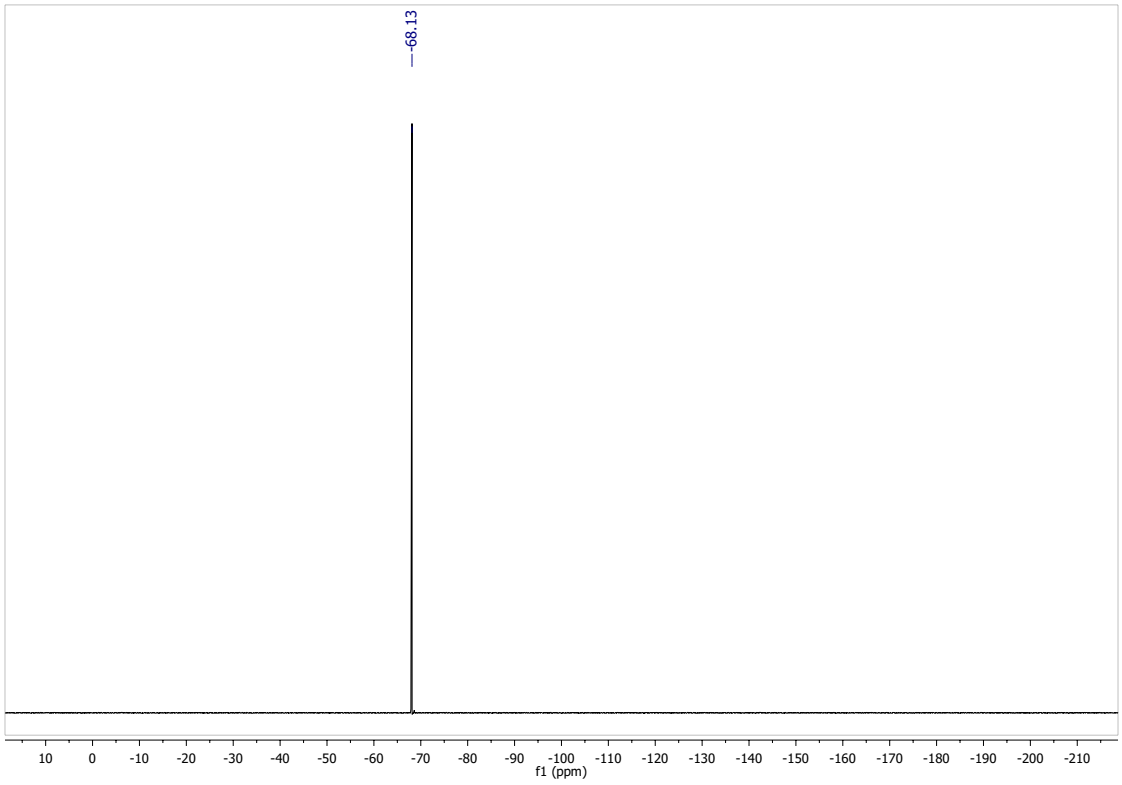

O
N
F3C
N
Me
7.26 CDCl3
1.00
1.03
1.05
1.01
0.99
0.98
0.98
1.08
1.05
1.02
2.11
2.18
3.19
f1 (ppm)

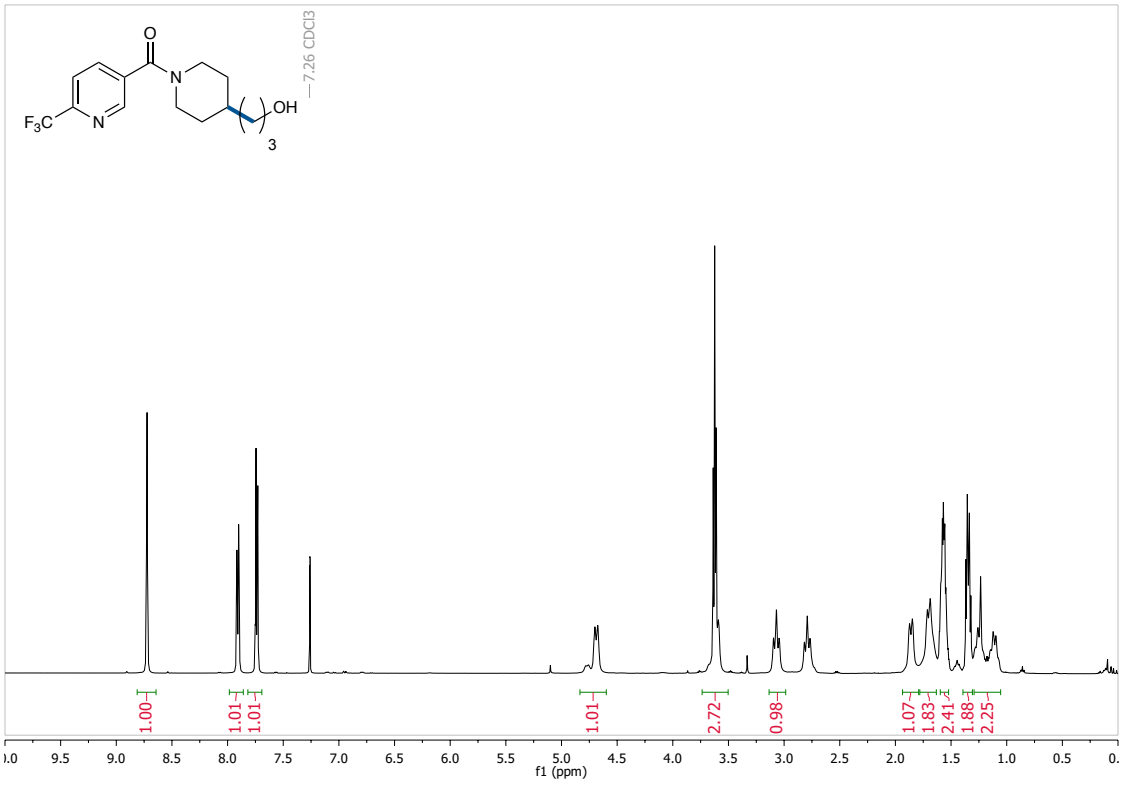

166.24
148.96
148.68
148.08
136.42
135.18
122.41
120.55
120.23
77.16 CDCl3
48.36
42.93
37.84
32.74
31.61
29.09
11.30
f1 (ppm)

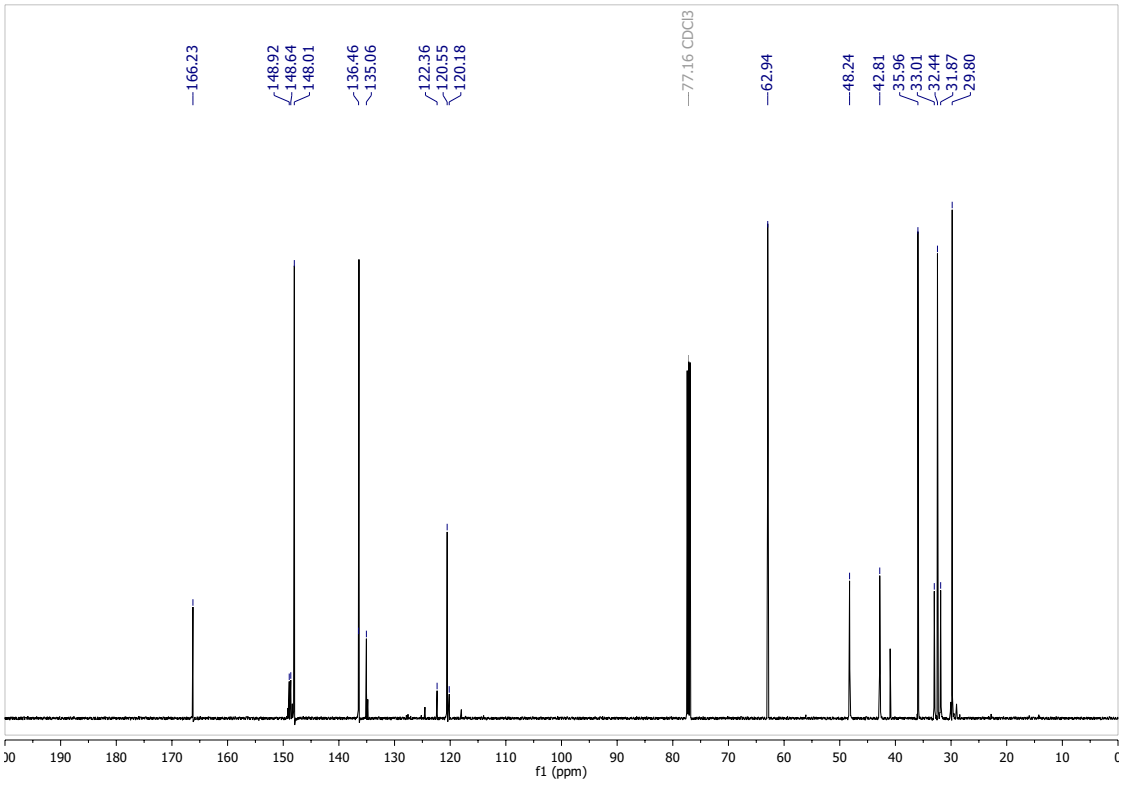

-68.12
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

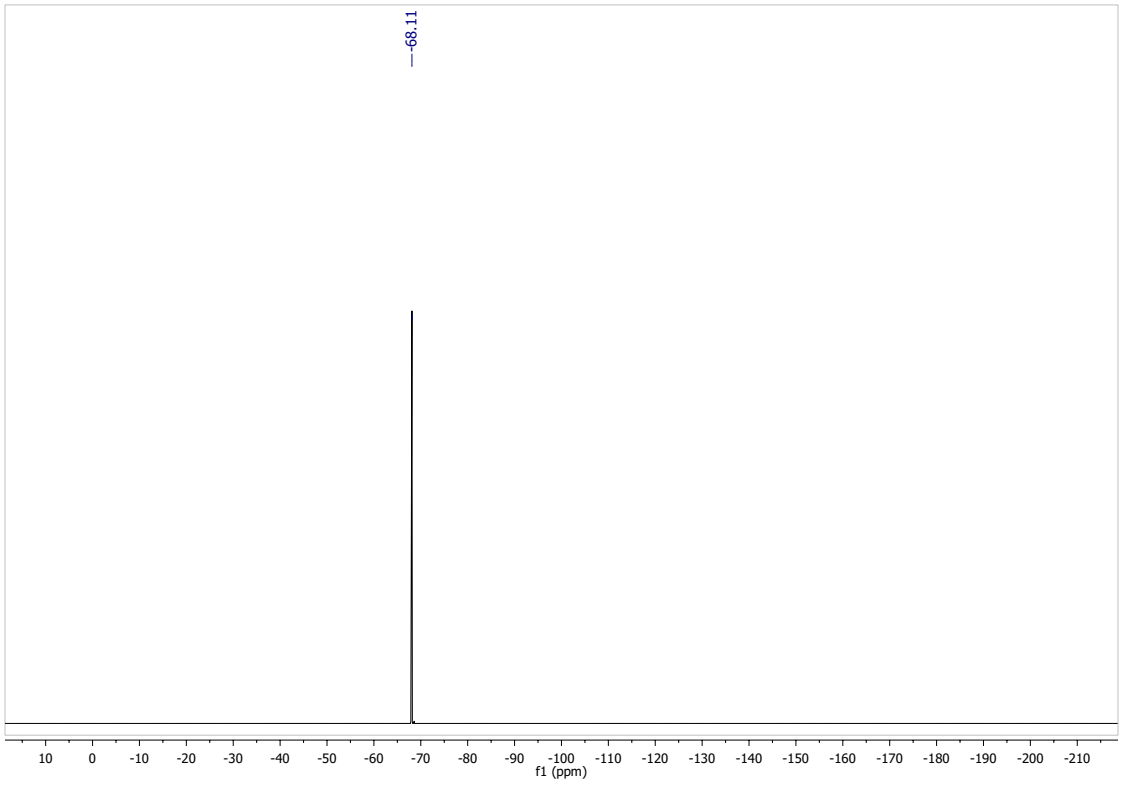

7.26 CDCl3
O
N
F3C
N
CO2Et
3
1.00
1.02
1.02
0.95
2.02
0.98
0.94
0.97
2.02
0.94
4.29
2.16
4.00
1.08
f1 (ppm)

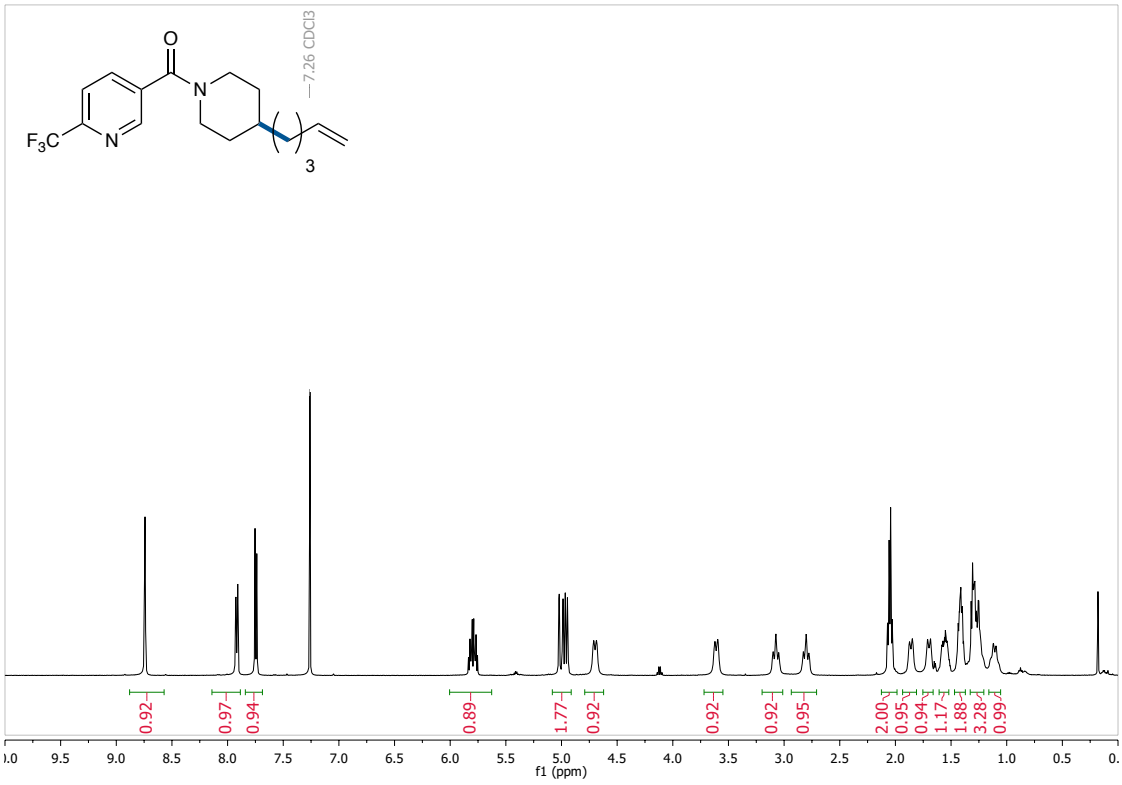

173.62
166.25
148.99
148.72
148.07
136.42
135.08
122.39
120.56
120.54
120.21
77.16 CDCl3
60.48
48.23
42.81
35.97
35.77
34.43
32.93
31.80
22.15
14.40
f1 (ppm)

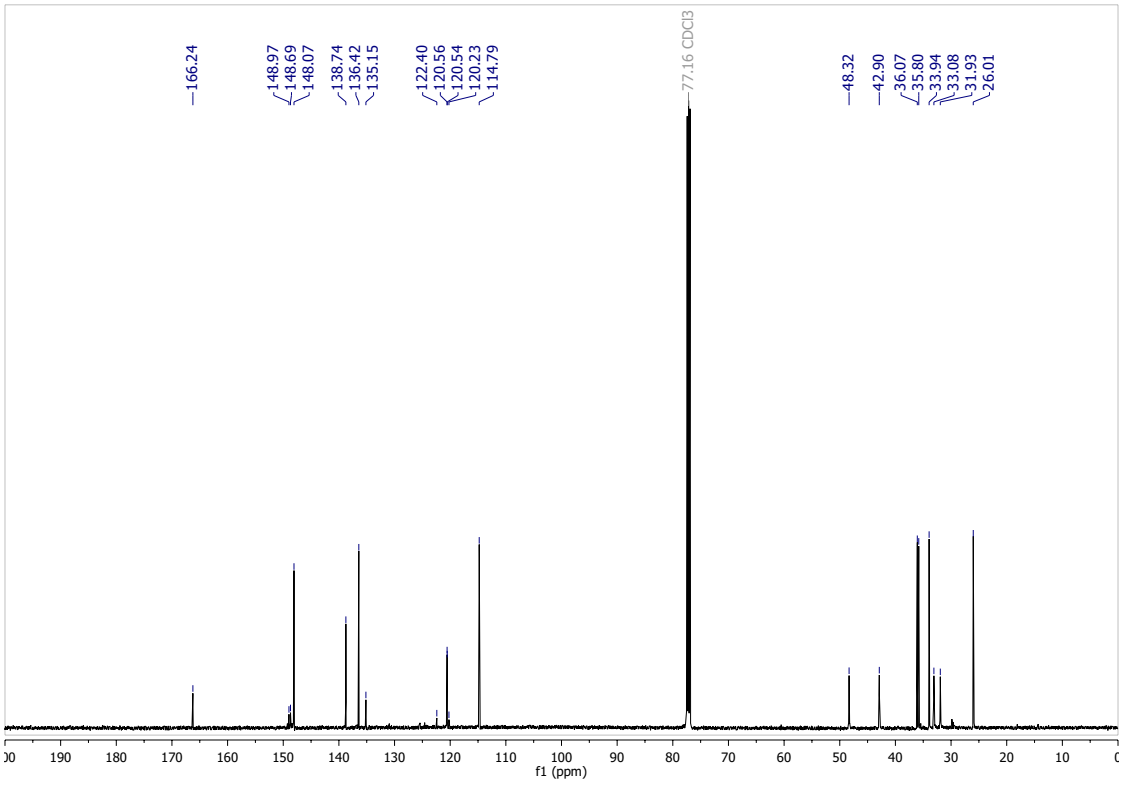

-68.13
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

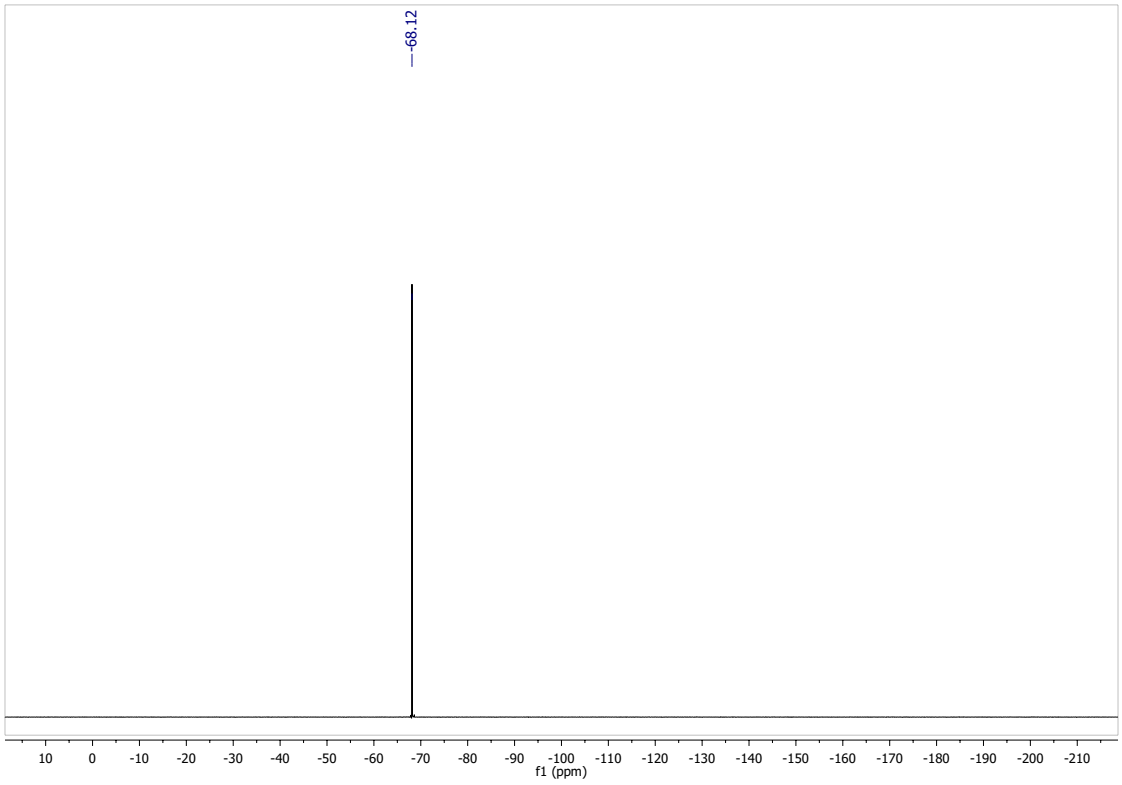

7.26 CDCl3
O
N
F3C
N
OH
3
1.00
1.01
1.01
1.01
2.72
0.98
1.07
1.83
2.41
1.88
2.25
f1 (ppm)

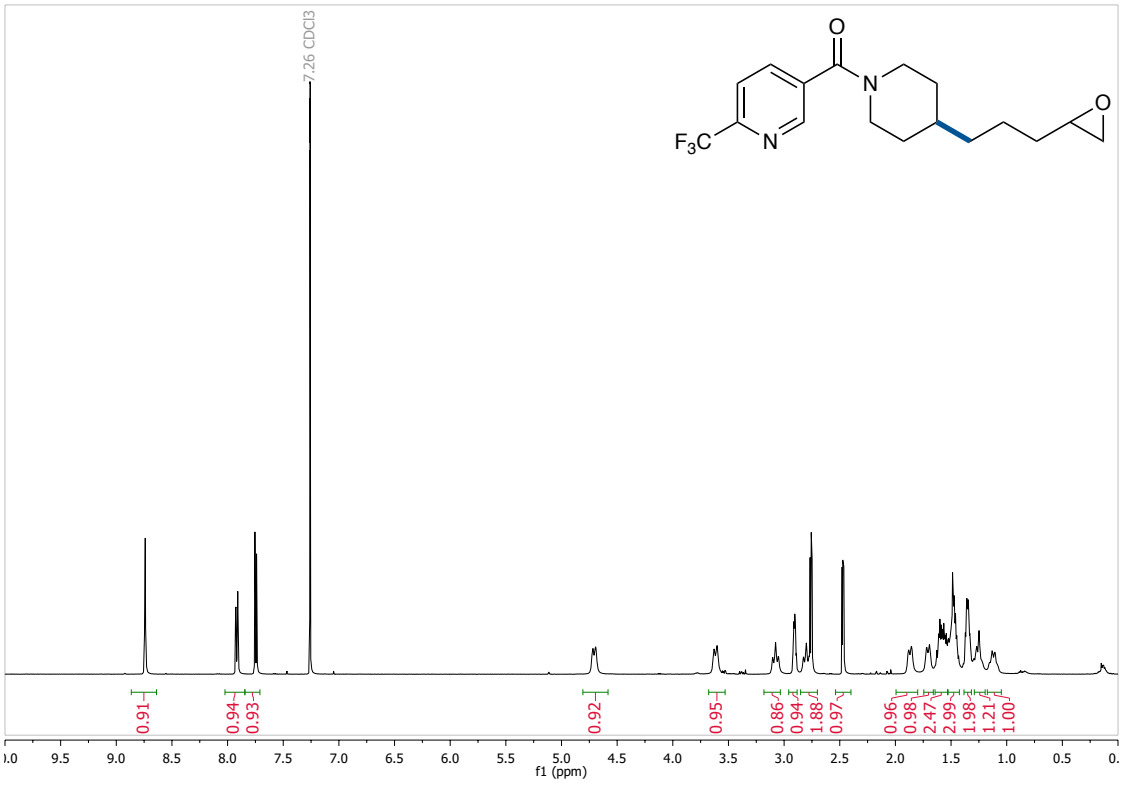

166.23
148.92
148.64
148.01
136.46
135.06
122.36
120.55
120.18
77.16 CDCl3
62.94
48.24
42.81
35.96
33.01
32.44
31.87
29.80
f1 (ppm)

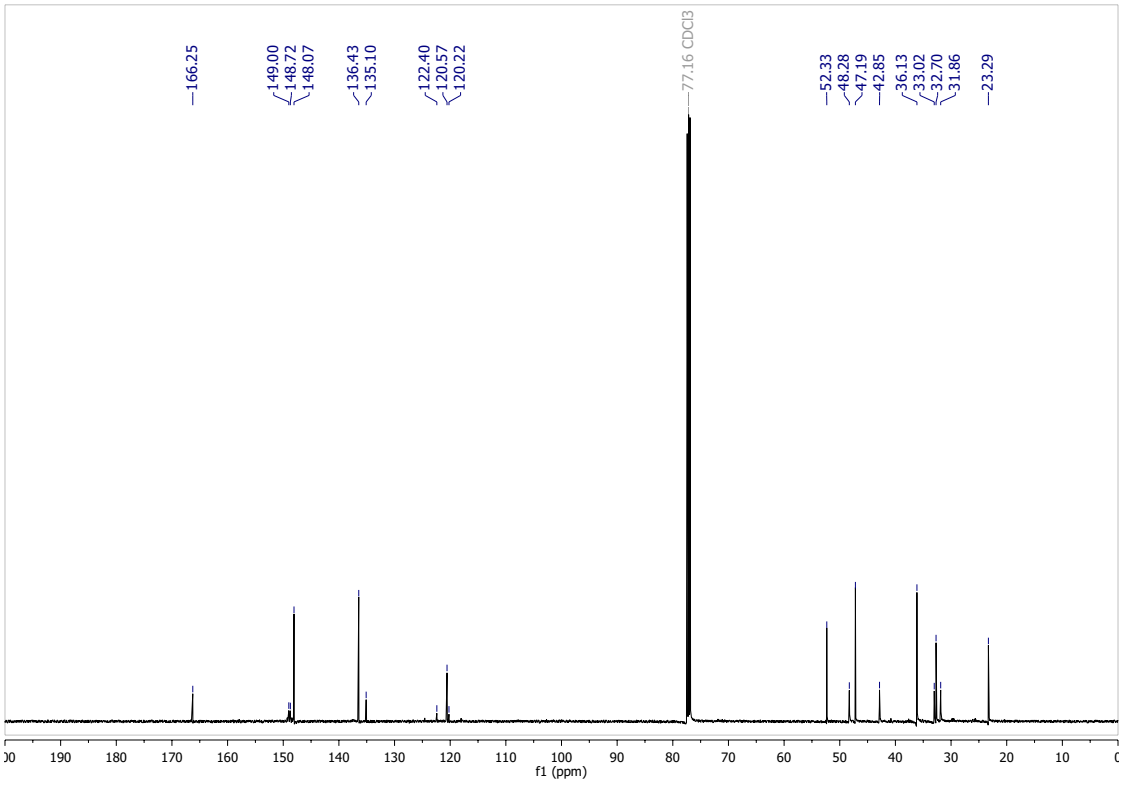

-68.11
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

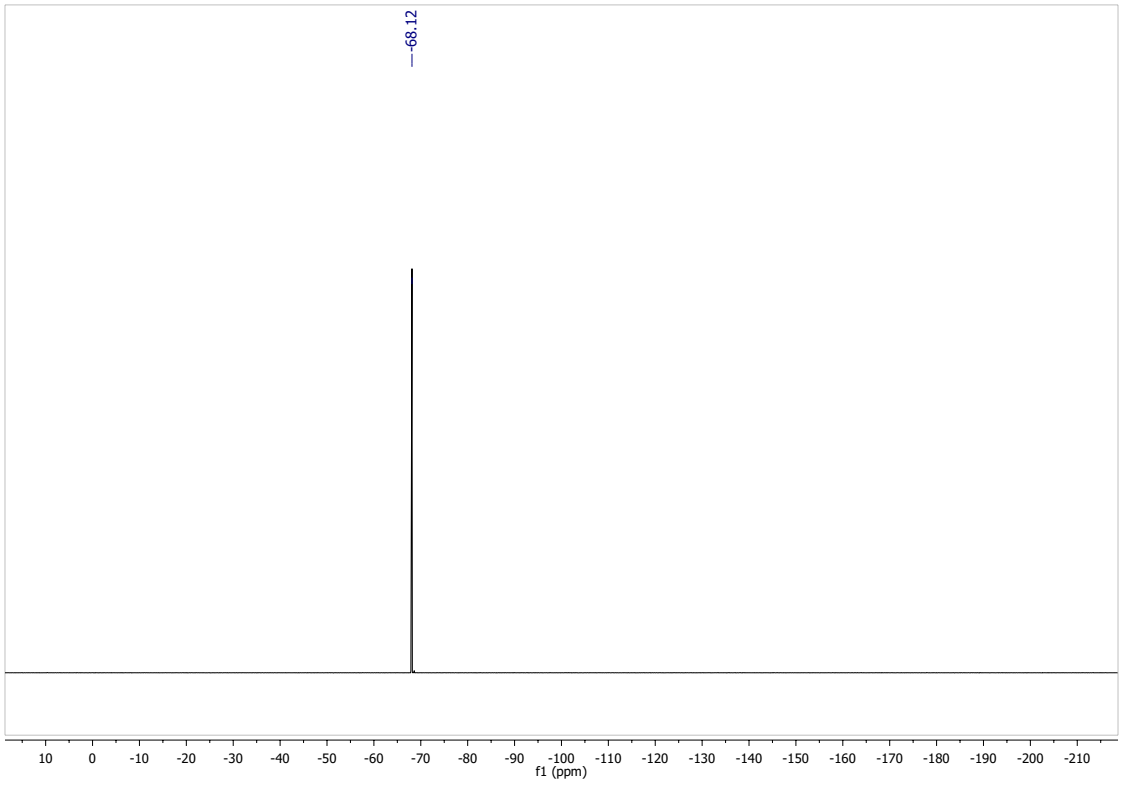

O
N
F3C
N
3
7.26 CDCl3
0.92
0.97
0.94
0.89
1.77
0.92
0.92
0.92
0.95
2.00
0.95
0.94
1.17
1.88
3.28
0.99
f1 (ppm)

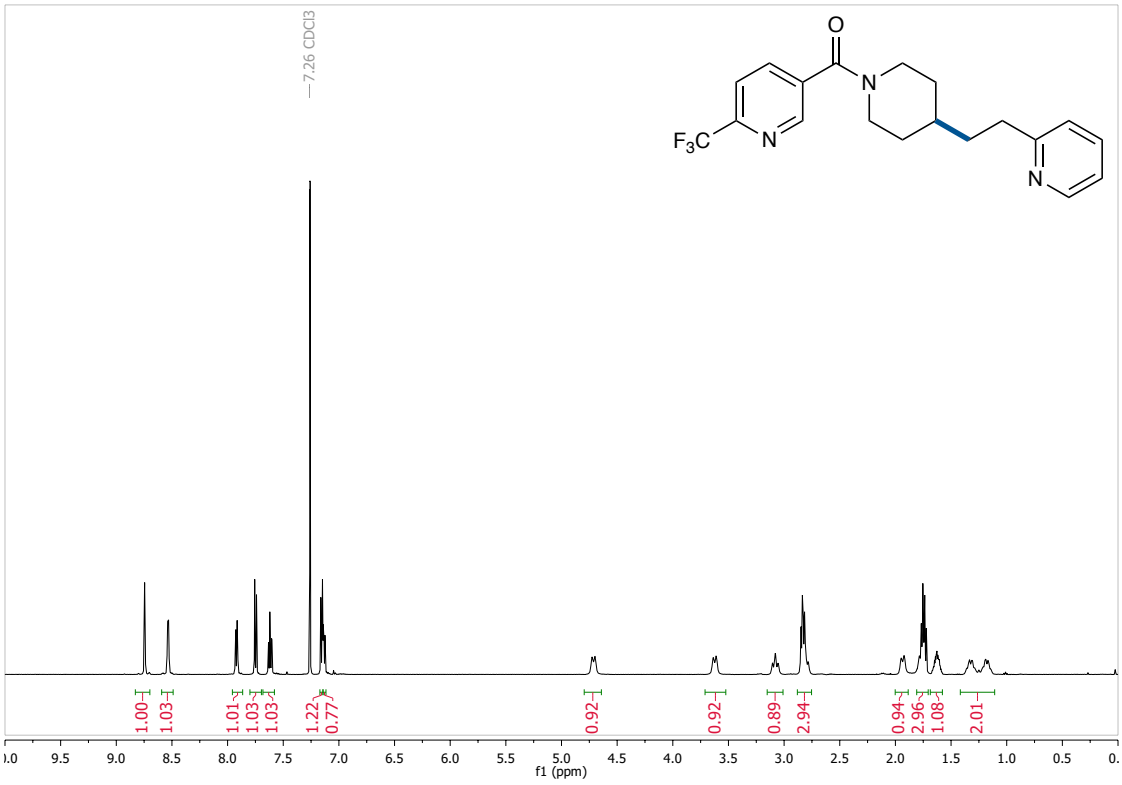

166.24
148.97
148.69
148.07
138.74
136.42
135.15
122.40
120.56
120.54
120.23
114.79
77.16 CDCl3
48.32
42.90
36.07
35.80
33.94
33.08
31.93
26.01
f1 (ppm)

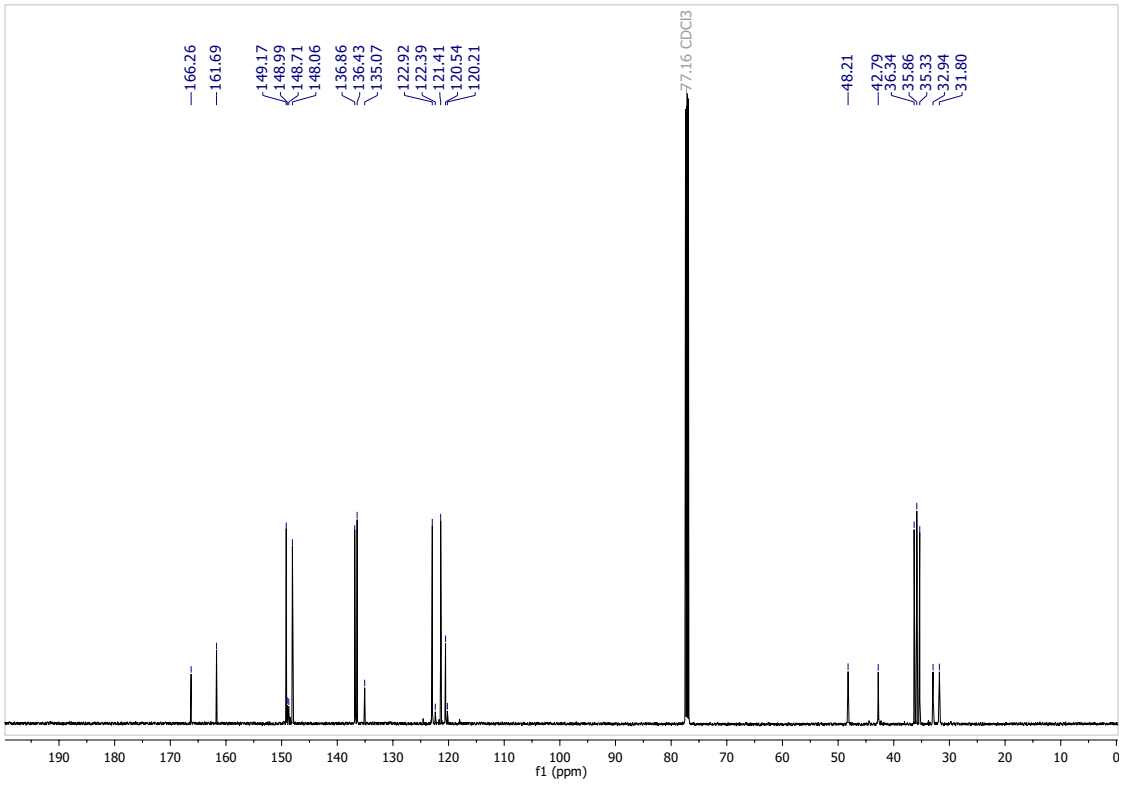

-68.12
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

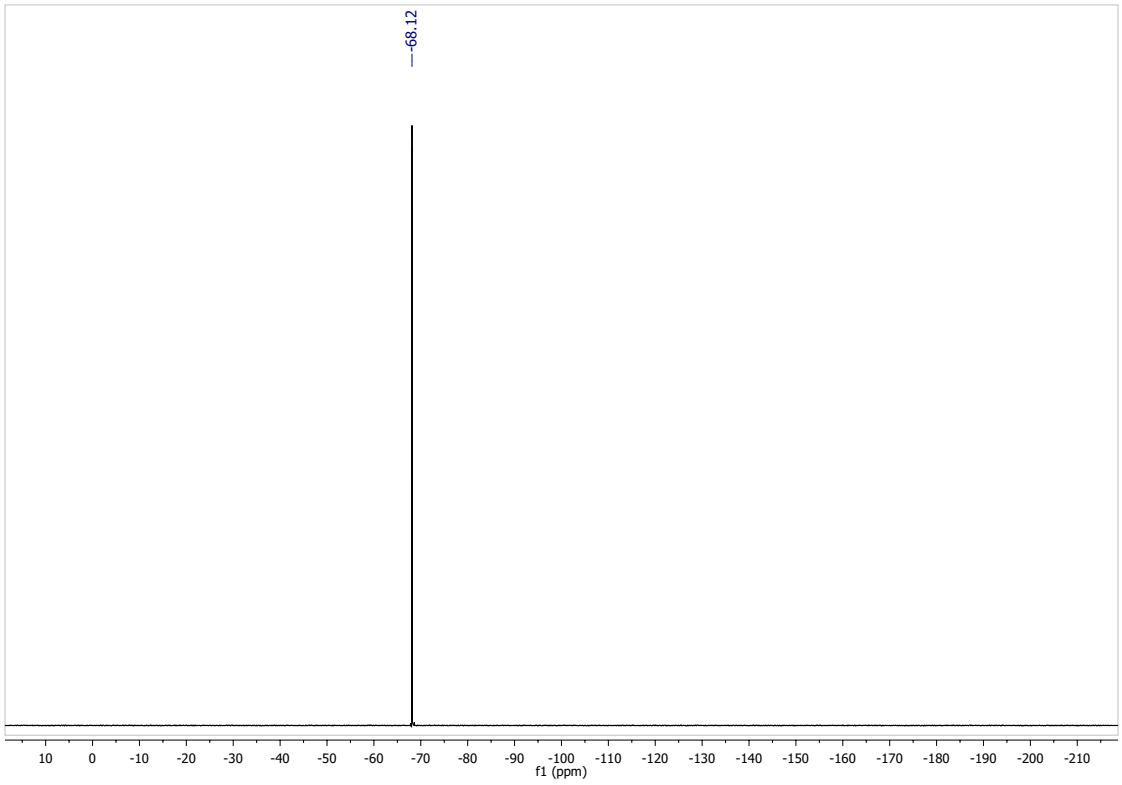

7.26 CDCl3
O
N
F3C
N
O
0.91
0.94
0.93
0.92
0.95
0.86
0.94
1.88
0.97
0.96
0.98
2.47
2.99
1.98
1.21
1.00
f1 (ppm)

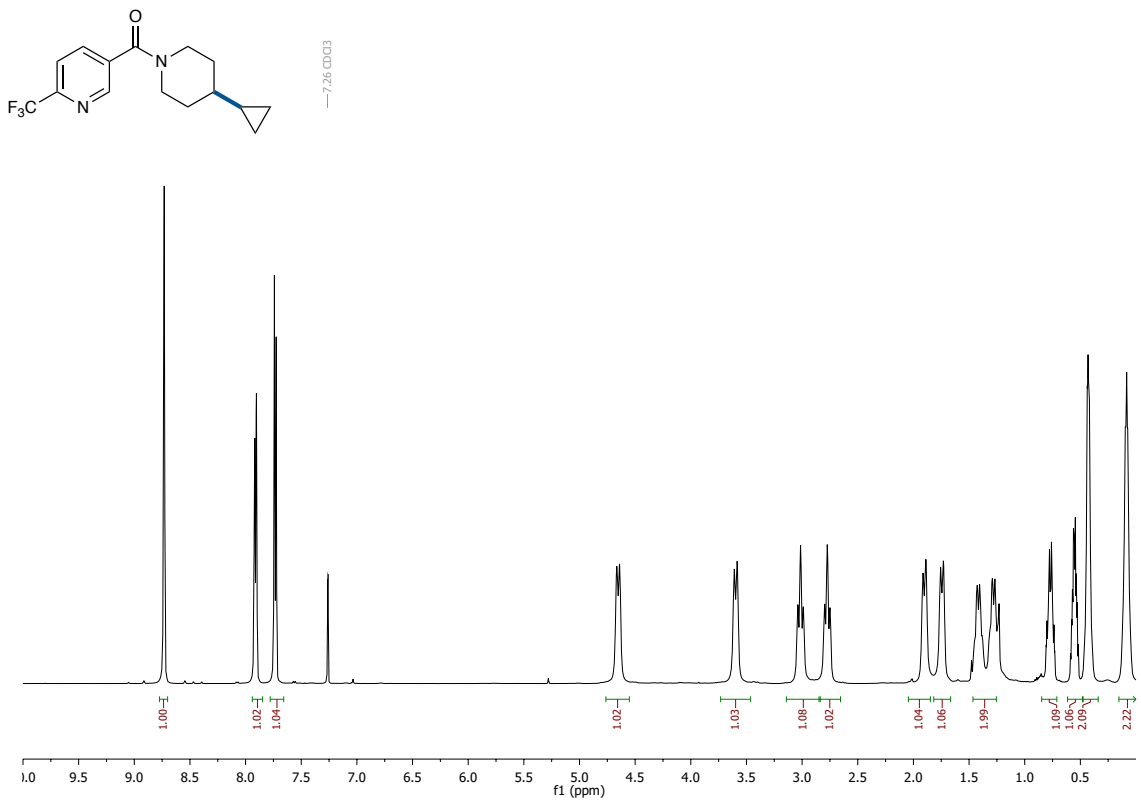

166.25
149.00
148.72
148.07
136.43
135.10
122.40
120.57
120.22
77.16 CDCl3
52.33
48.28
47.19
42.85
36.13
33.02
32.70
31.86
23.29
f1 (ppm)

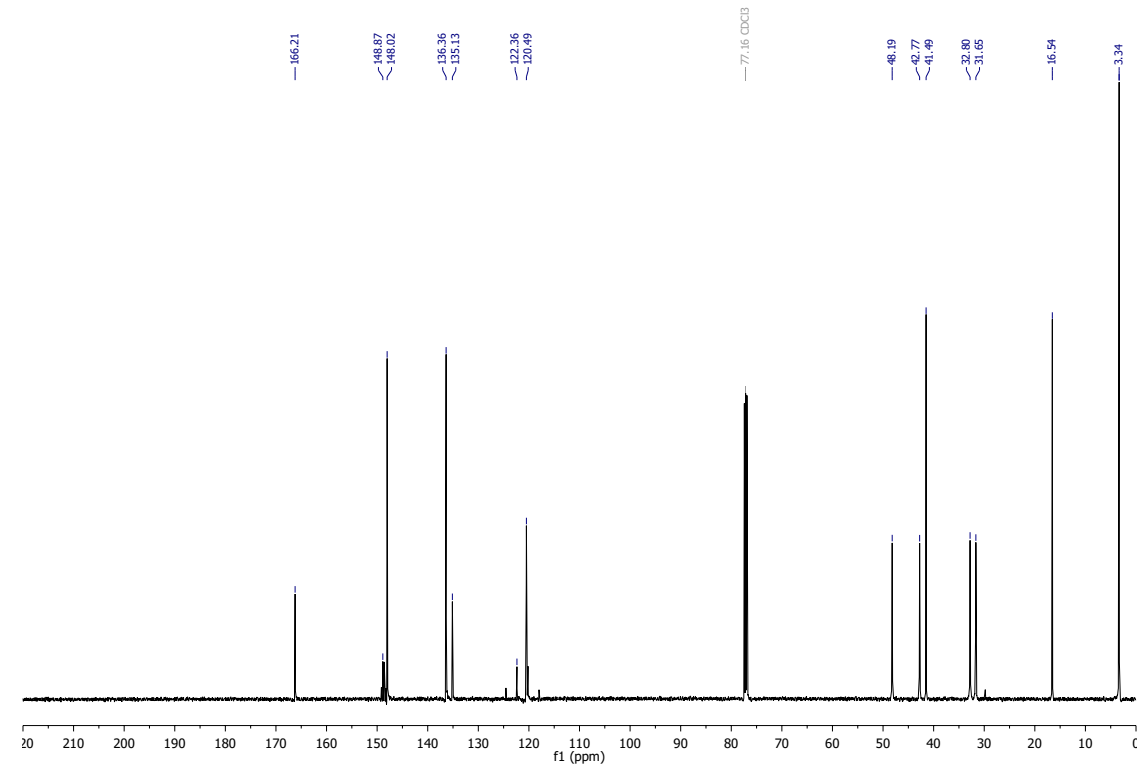

-68.12
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

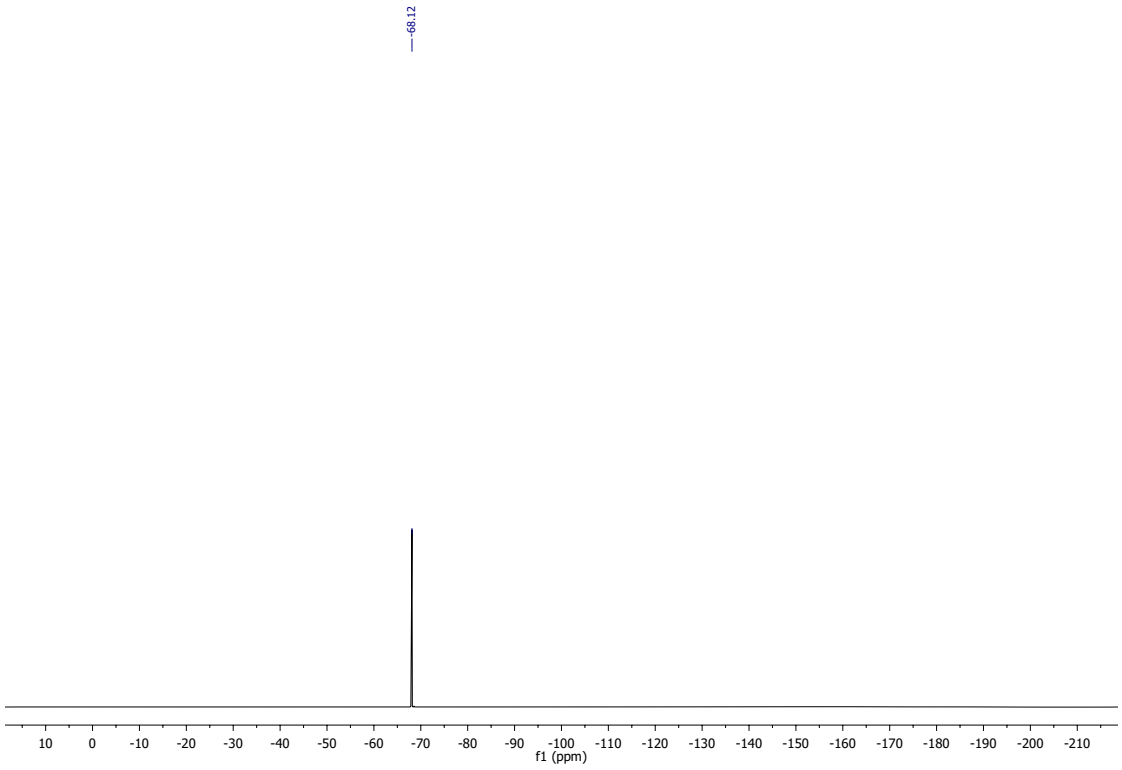

7.26 CDCl3
O
N
F3C
N
N
1.00
1.03
1.01
1.03
1.03
1.22
0.77
0.92
0.92
0.89
2.94
0.94
2.96
1.08
2.01
f1 (ppm)

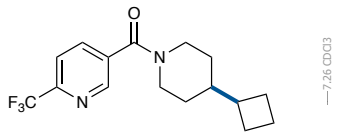

166.26
161.69
149.17
148.99
148.71
148.06
136.86
136.43
135.07
122.92
122.39
121.41
120.54
120.21
77.16 CDCl3
48.21
42.79
36.34
35.86
35.33
32.94
31.80
f1 (ppm)

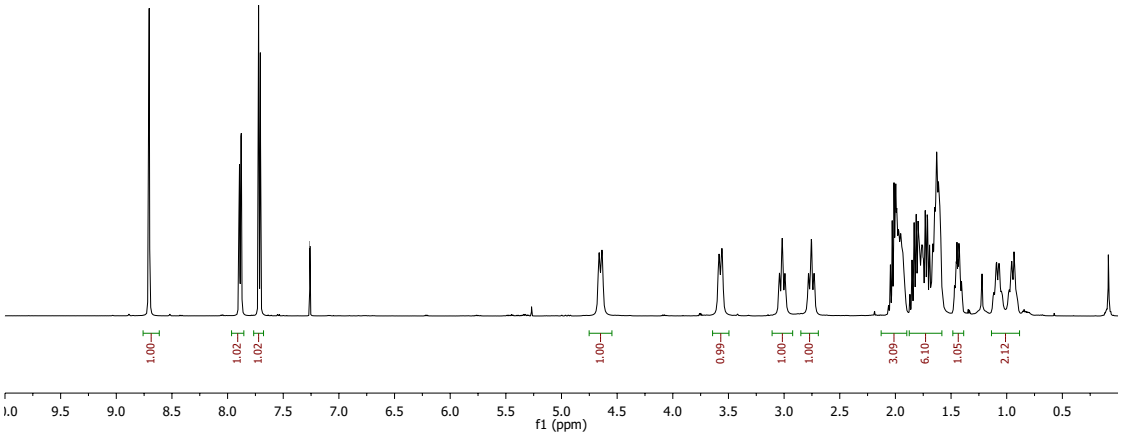

-68.12
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

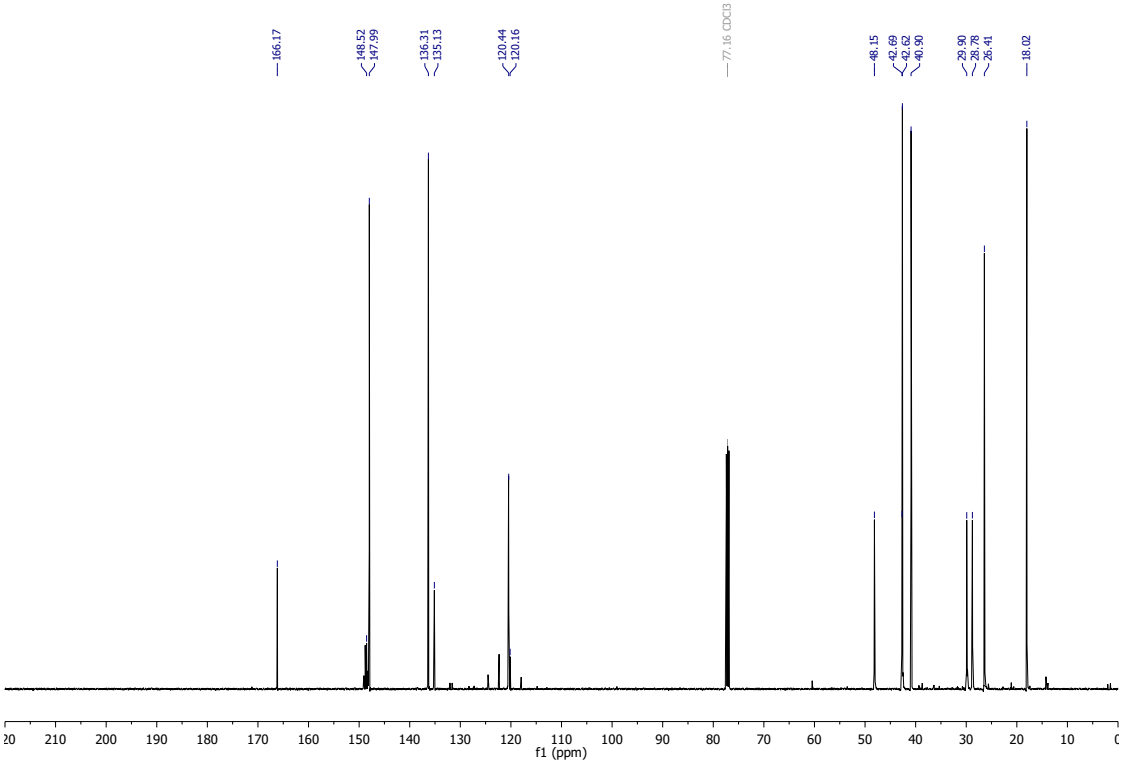

O
N
F3C
N
7.26 CDCl3
1.00
1.02
1.04
1.02
1.03
1.08
1.02
1.04
1.06
1.99
1.09
1.06
2.09
2.22
f1 (ppm)

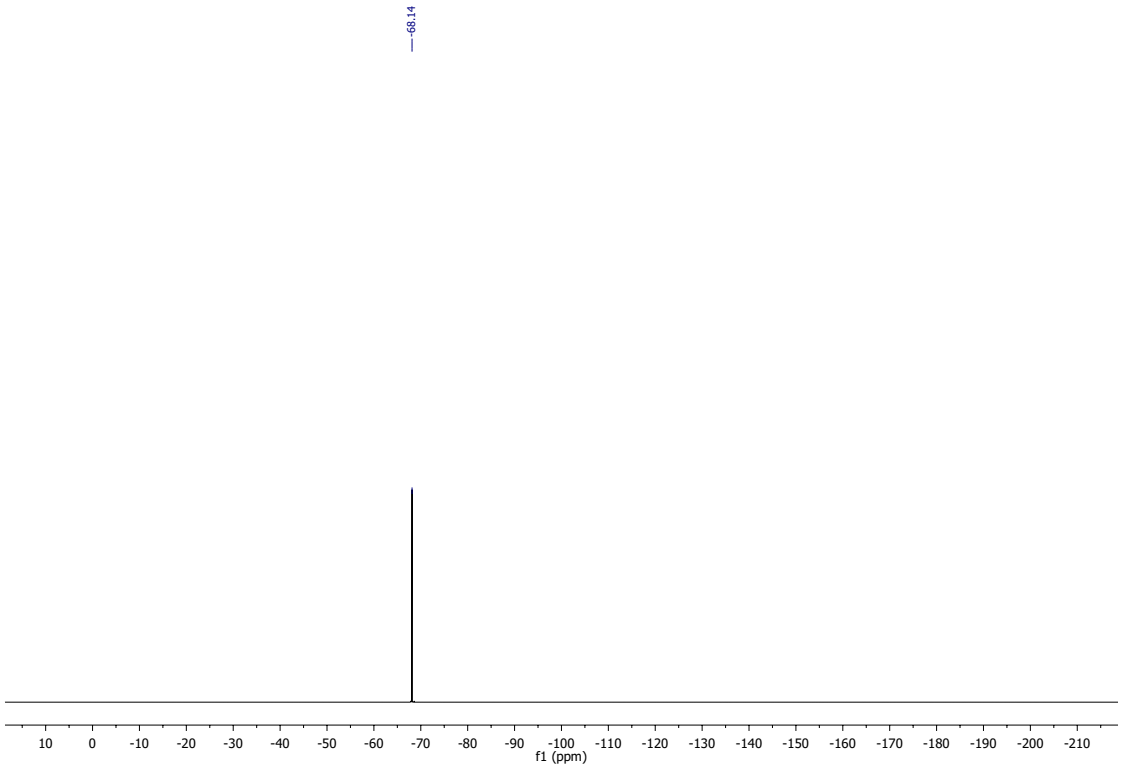

166.21
148.87
148.02
136.36
135.13
122.36
120.49
77.16 CDCl3
48.19
42.77
41.49
32.80
31.65
16.54
3.34
f1 (ppm)

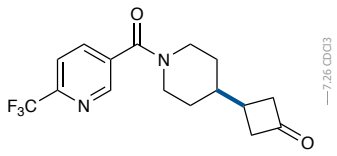

-68.12
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

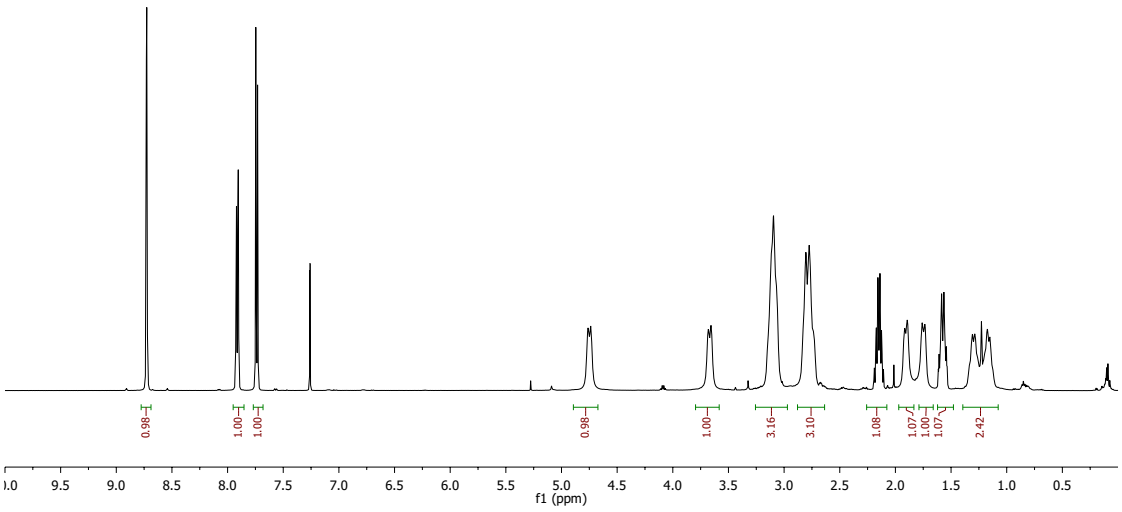

O
N
F3C
N

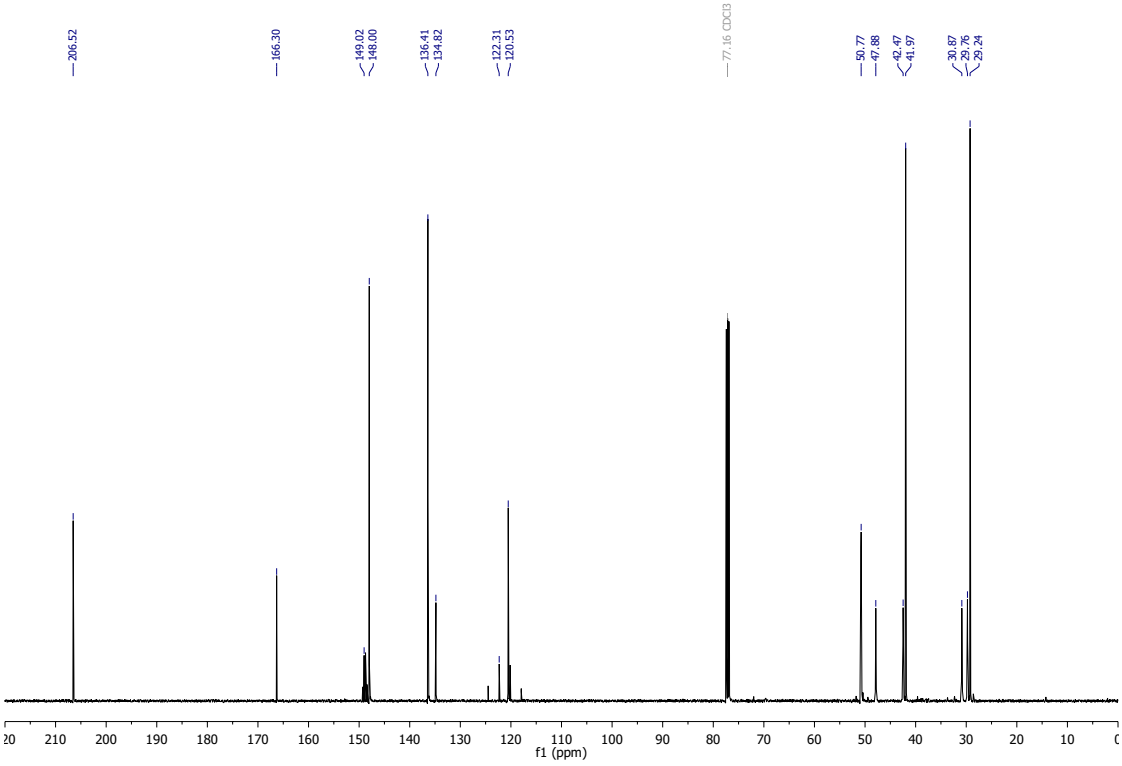

7.26 CDCl3
1.00
1.02
1.02
1.00
0.99
1.00
1.00
3.09
6.10
1.05
2.12
f1 (ppm)

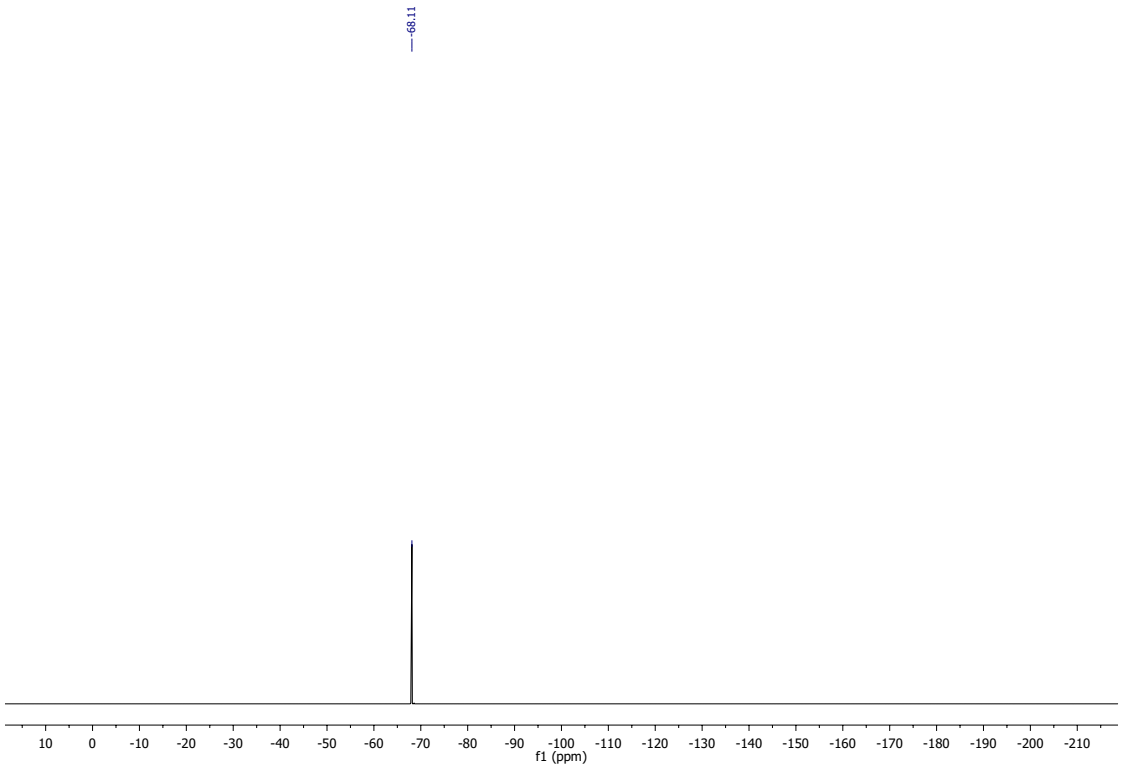

166.17
148.52
147.99
136.31
135.13
120.44
120.16
77.16 CDCl3
48.15
42.69
42.62
40.90
29.90
28.78
26.41
18.02
f1 (ppm)

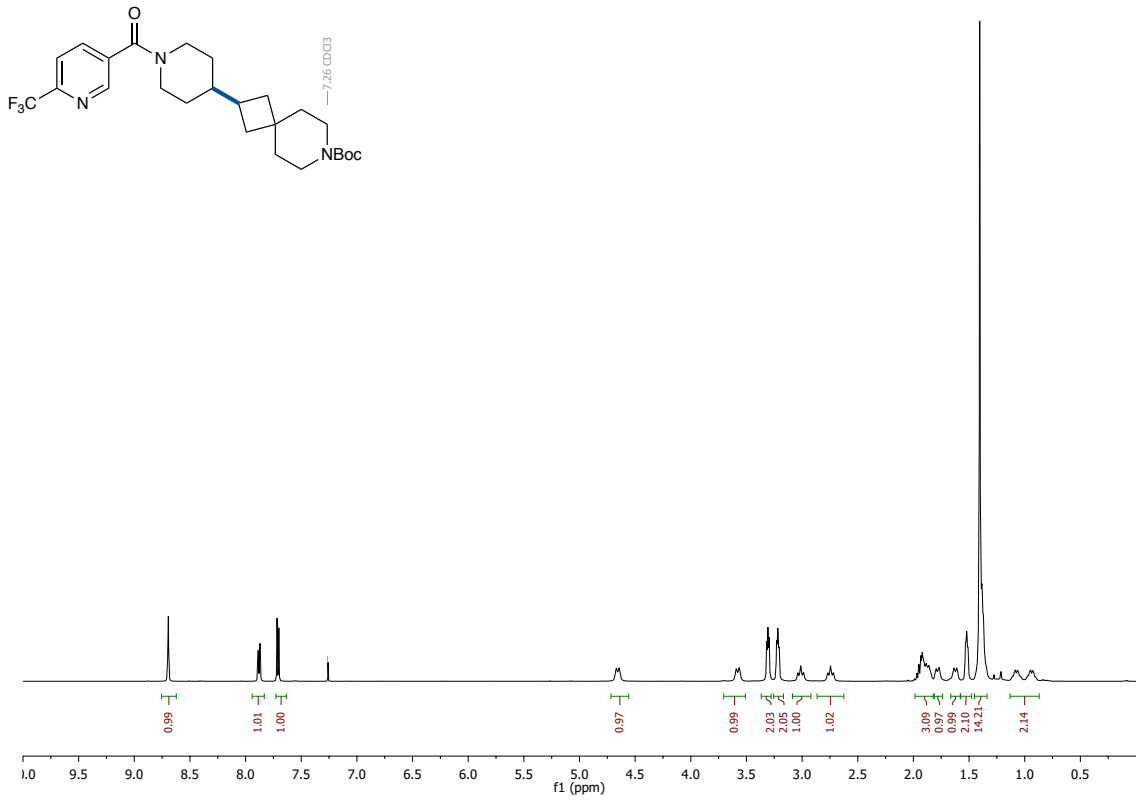

-68.14
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

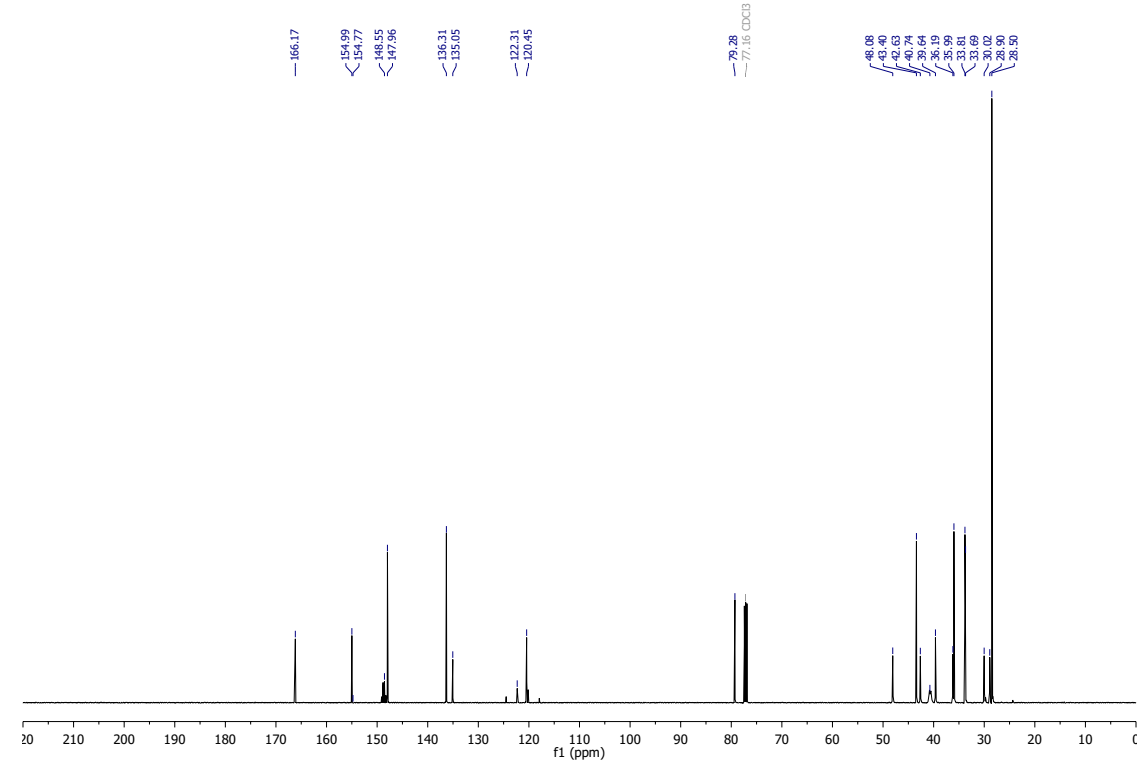

O
N
F3C
N
O

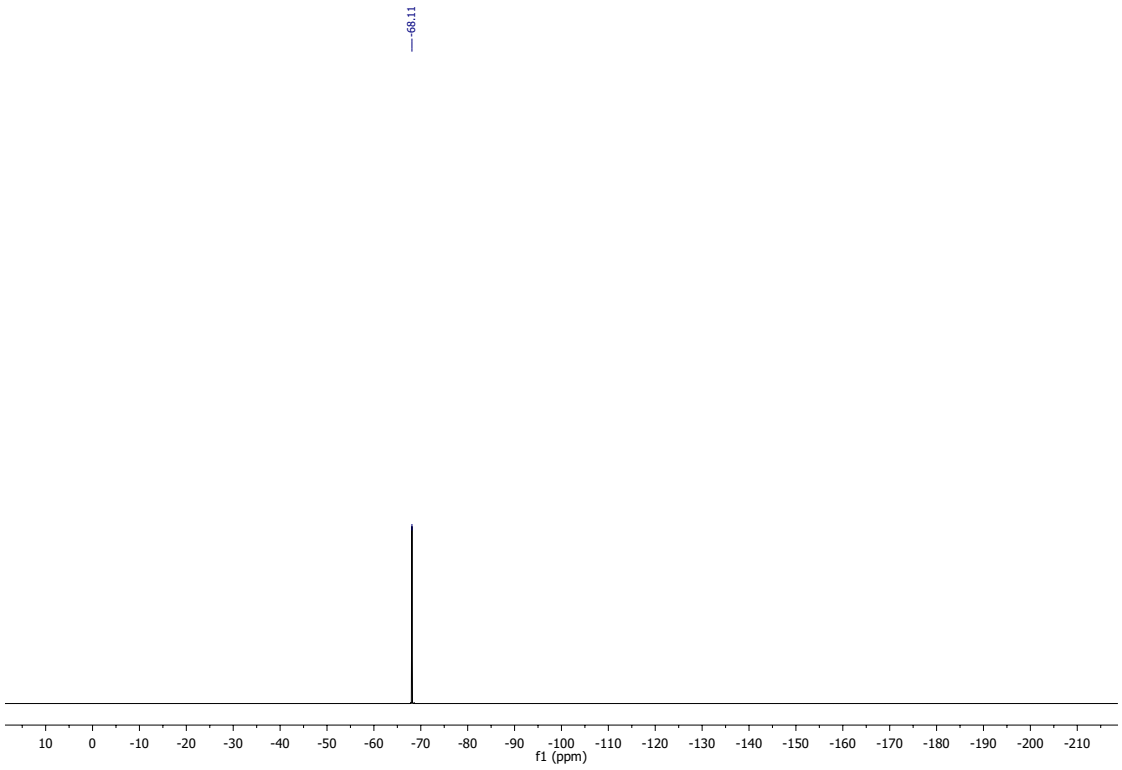

7.26 CDCl3
0.98
1.00
1.00
0.98
1.00
3.16
3.10
1.08
1.07
1.00
1.07
2.42
f1 (ppm)

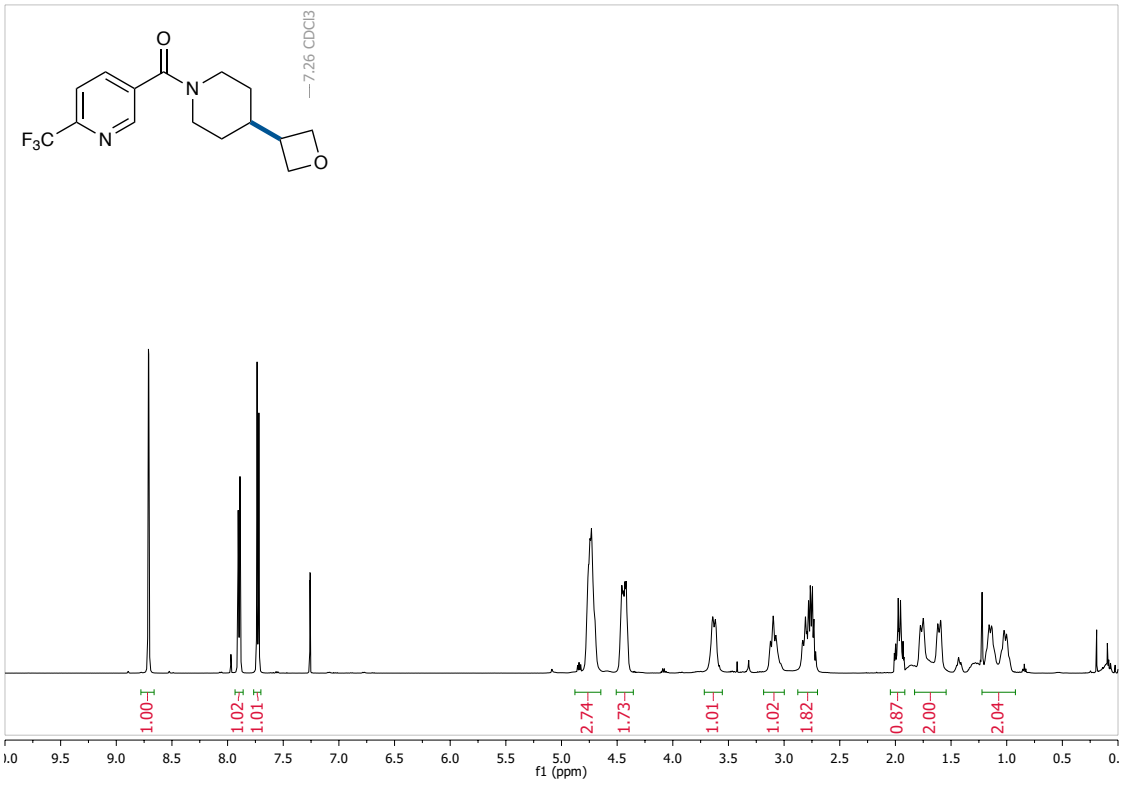

206.52
166.30
149.02
148.00
136.41
134.82
122.31
120.53
77.16 CDCl3
50.77
47.88
42.47
41.97
30.87
29.76
29.24
f1 (ppm)

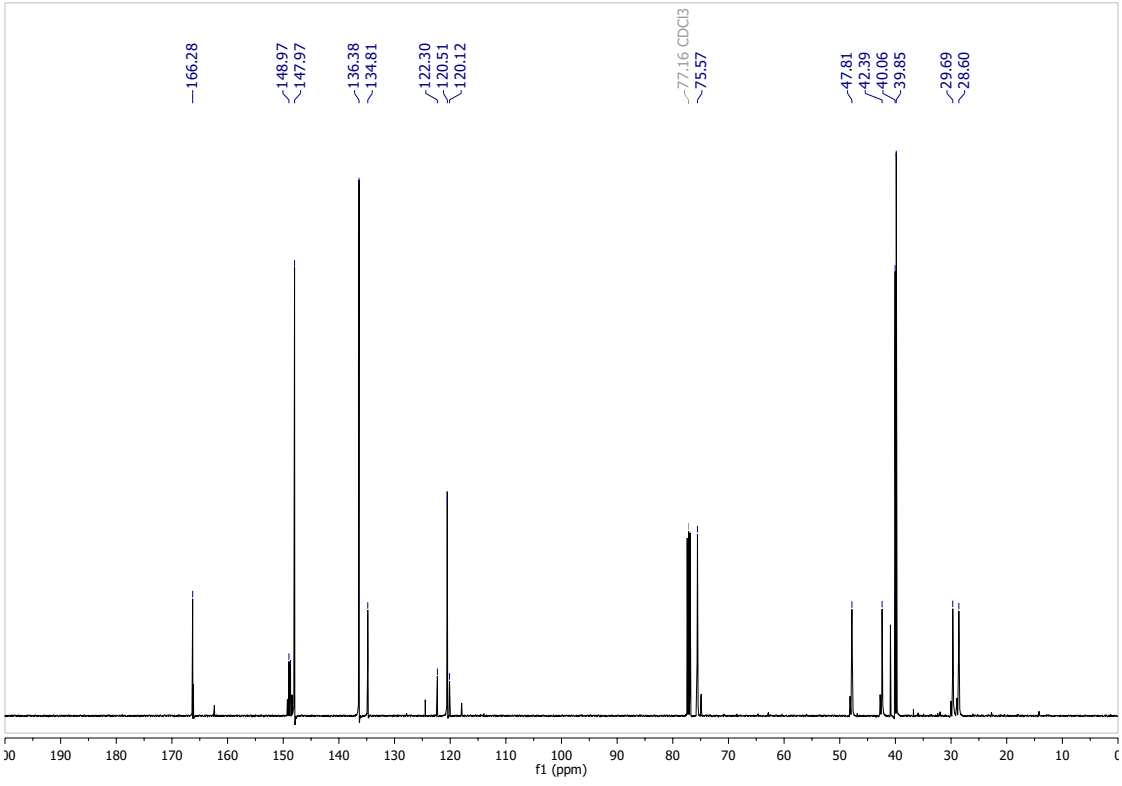

-68.11
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

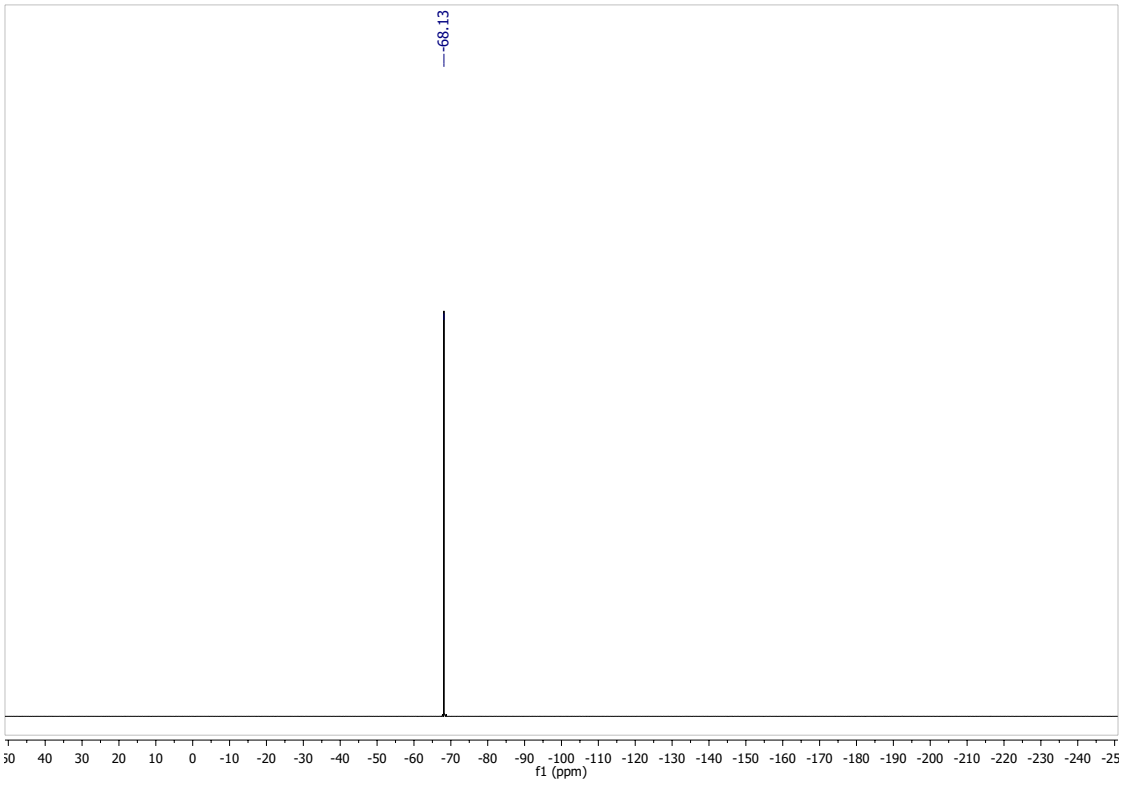

O
N
F3C
N
NBoc
7.26 CDCl3
0.99
1.01
1.00
0.97
0.99
2.03
2.05
1.00
1.02
3.09
0.97
0.99
2.10
14.21
2.14
f1 (ppm)

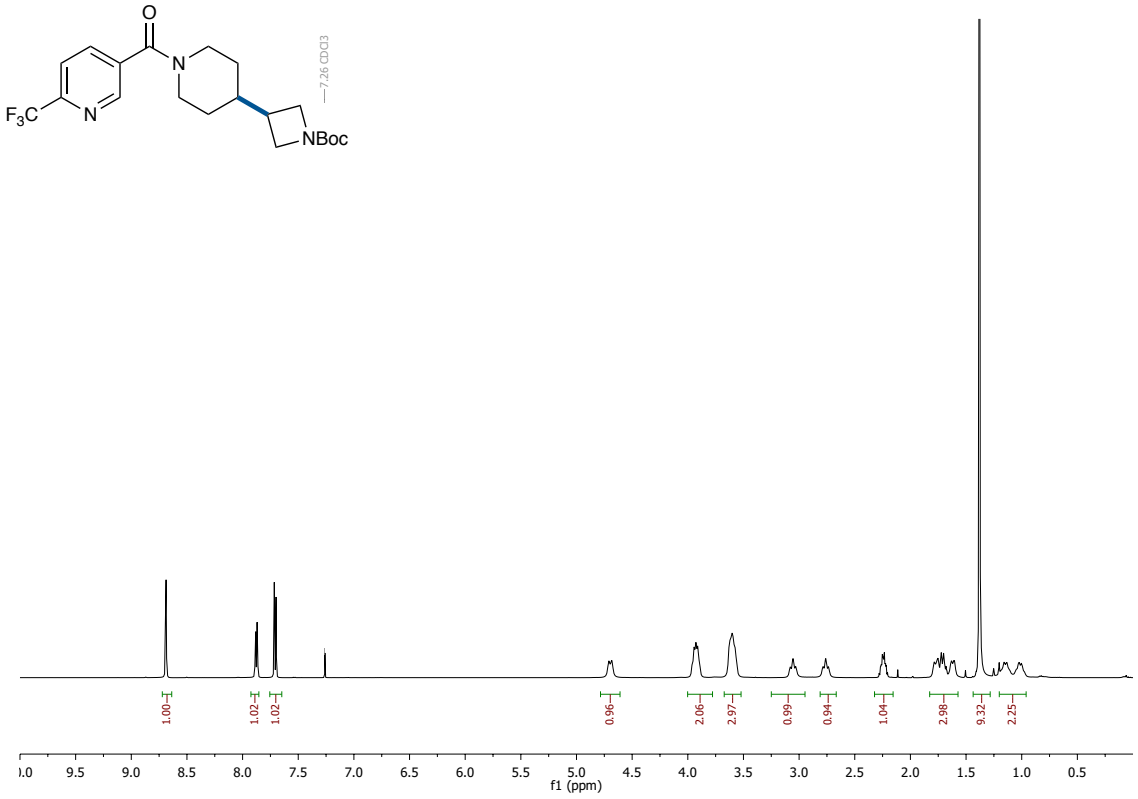

166.17
154.99
154.77
148.55
147.96
136.31
135.05
122.31
120.45
79.28
77.16 CDCl3
48.08
43.40
42.63
40.74
39.64
36.19
35.99
33.81
33.69
30.02
28.90
28.50
f1 (ppm)

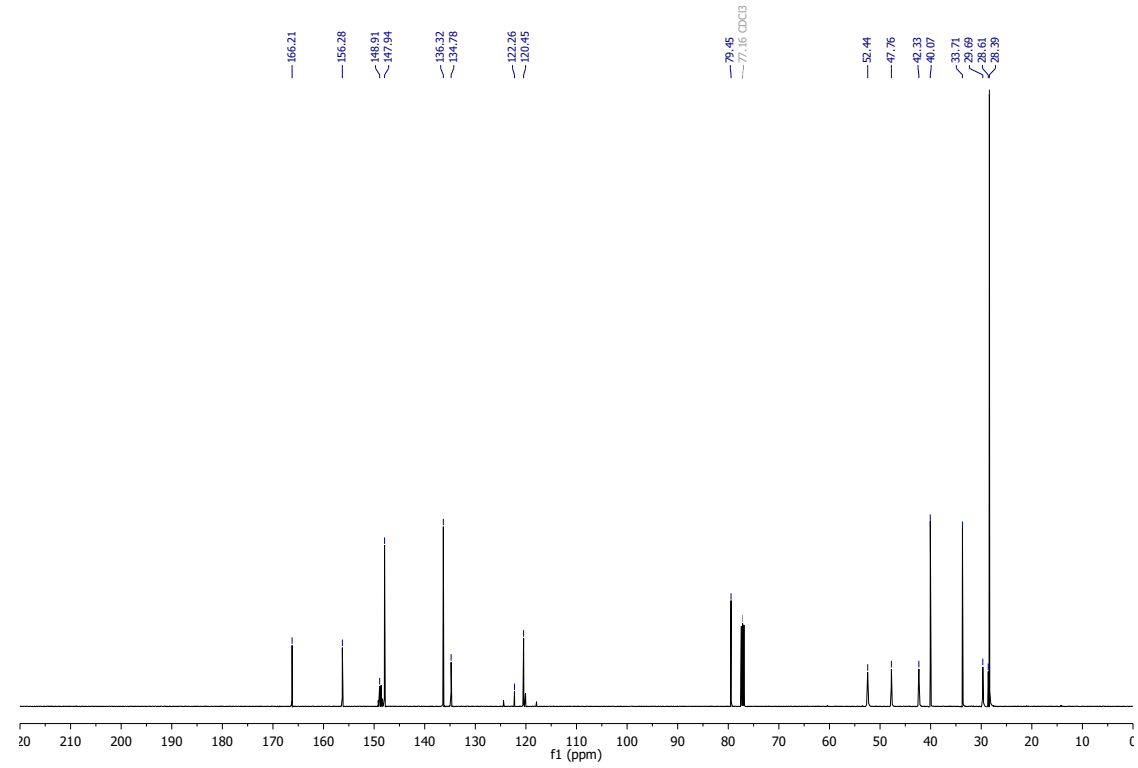

-68.11
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

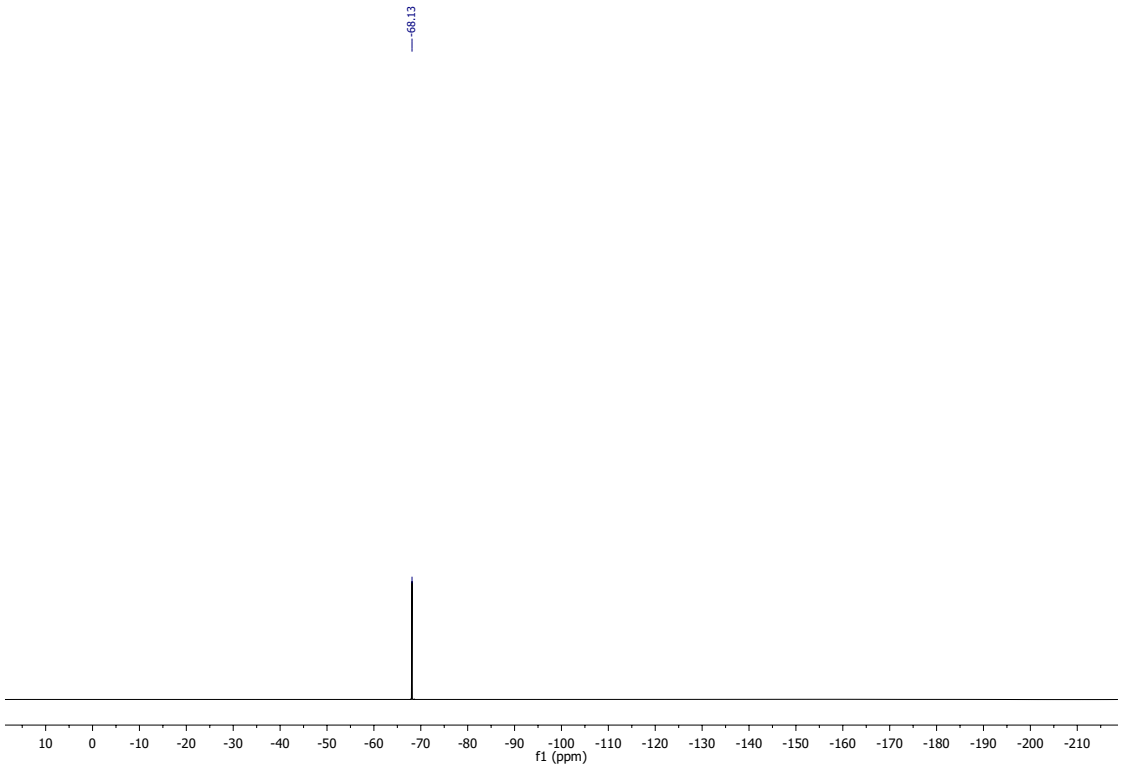

7.26 CDCl3
1.00
1.02
1.01
2.74
1.73
1.01
1.02
1.82
0.87
2.00
2.04
f1 (ppm)

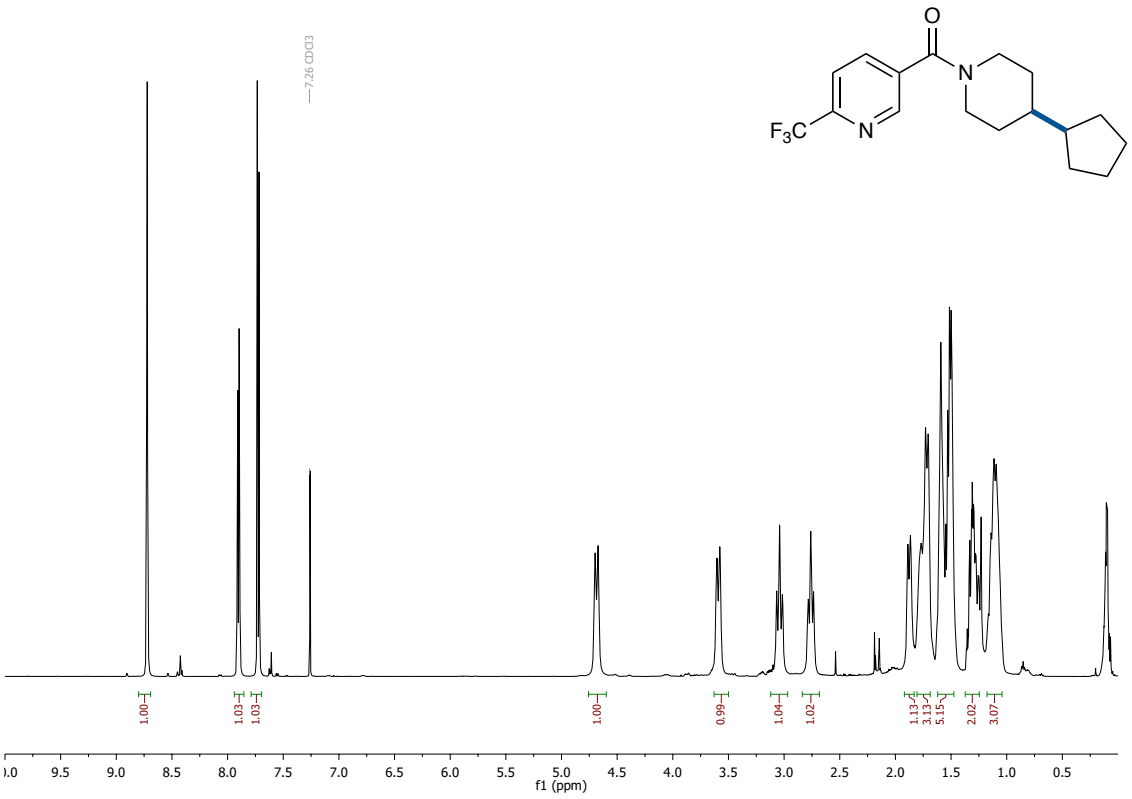

166.28
148.97
147.97
136.38
134.81
122.30
120.51
120.12
77.16 CDCl3
75.57
47.81
42.39
40.06
39.85
29.69
28.60
f1 (ppm)

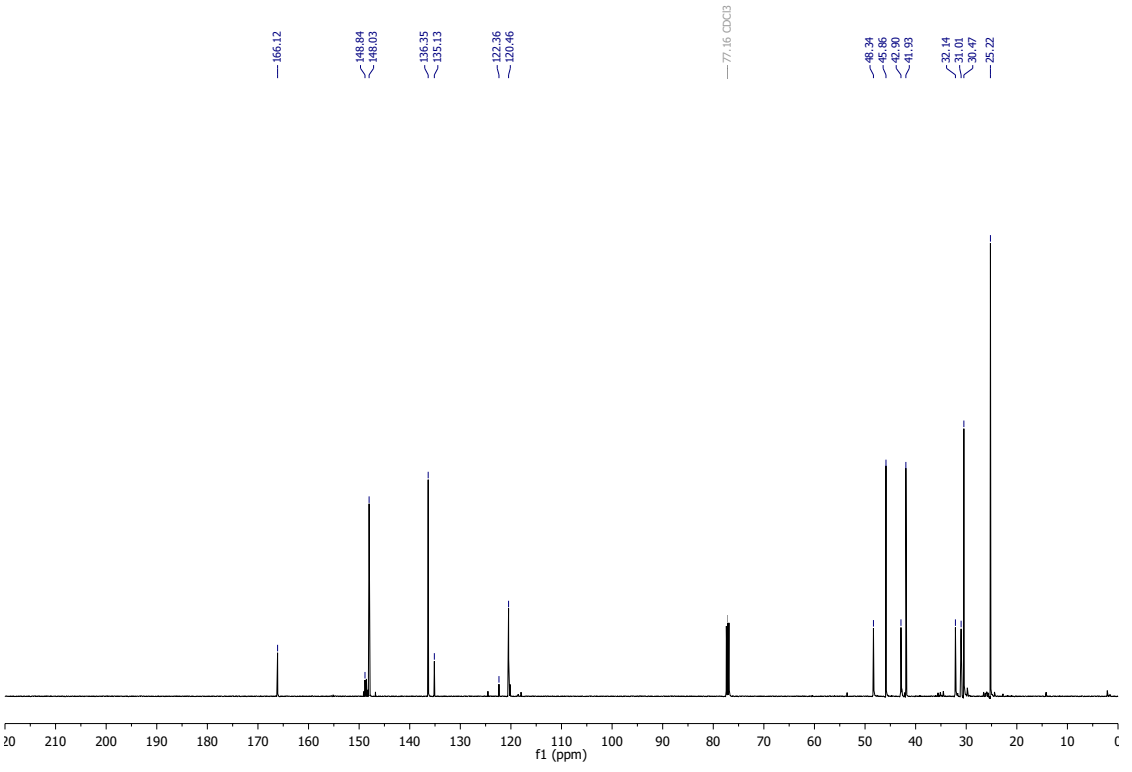

-68.13
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -25
f1 (ppm)

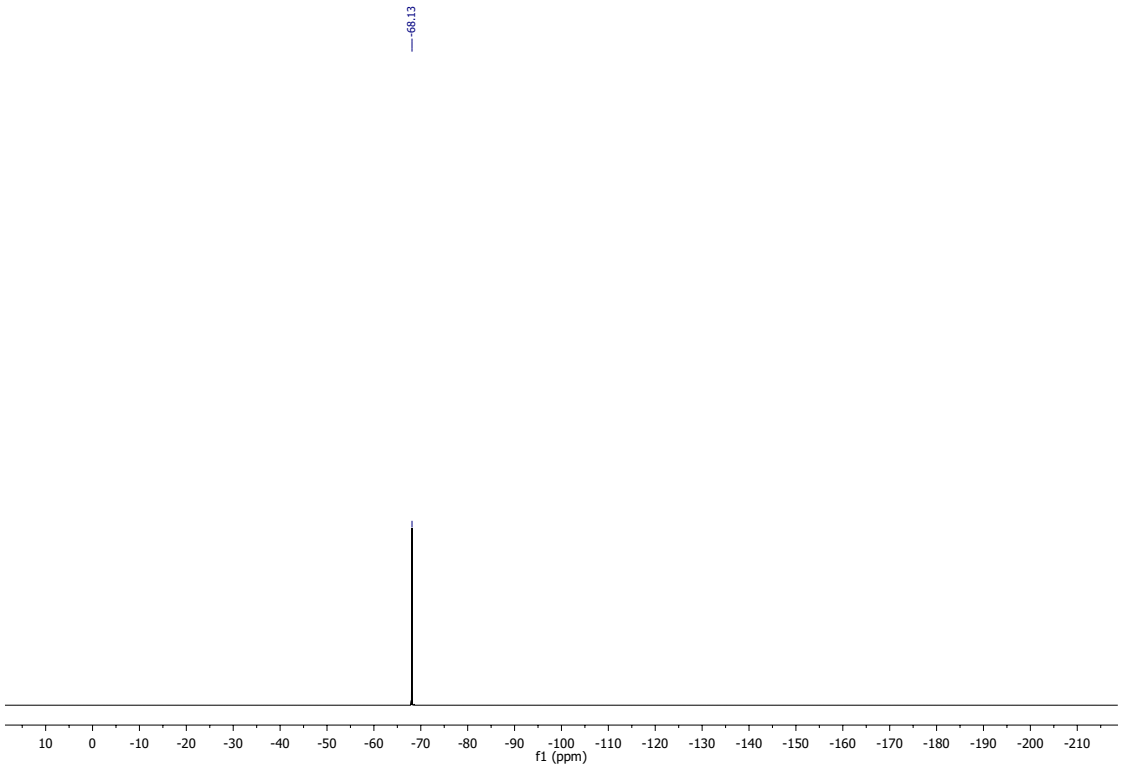

O
N
F3C
N
NBoc
7.26 CDCl3
1.00
1.02
1.02
0.96
2.06
2.97
0.99
0.94
1.04
2.98
9.32
2.25
f1 (ppm)


166.21
156.28
148.91
147.94
136.32
134.78
122.26
120.45
79.45
77.16 CDCl3
52.44
47.76
42.33
40.07
33.71
29.69
28.61
28.39
f1 (ppm)


-68.13
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


O
N
F3C
N
7.26 CDCl3
1.00
1.03
1.03
1.00
0.99
1.04
1.02
1.13
3.13
5.15
2.02
3.07
f1 (ppm)


166.12
148.84
148.03
136.35
135.13
122.36
120.46
77.16 CDCl3
48.34
45.86
42.90
41.93
32.14
31.01
30.47
25.22
f1 (ppm)


-68.13
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
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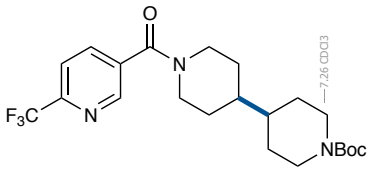
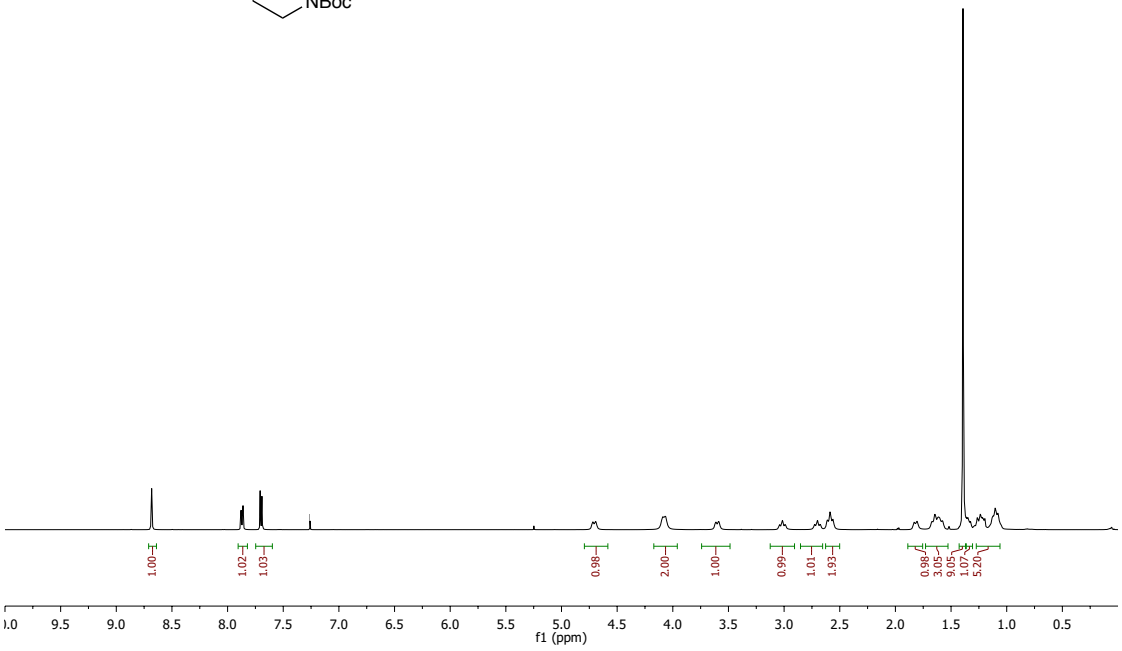
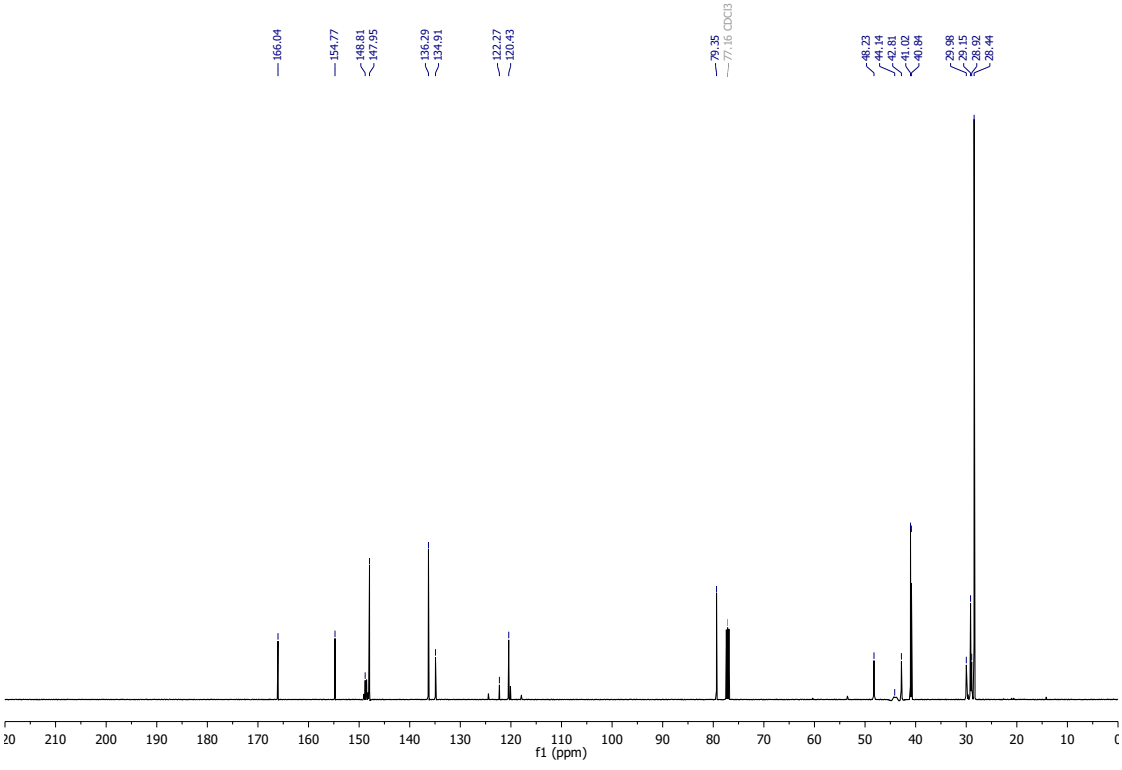
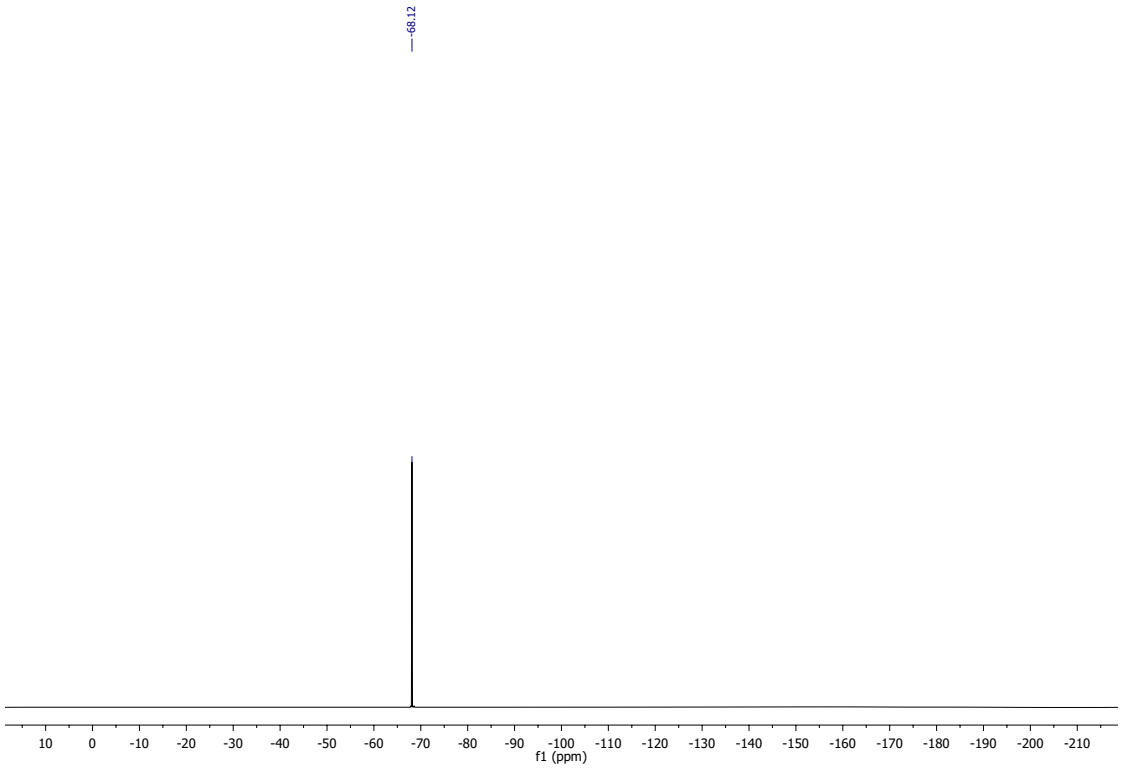
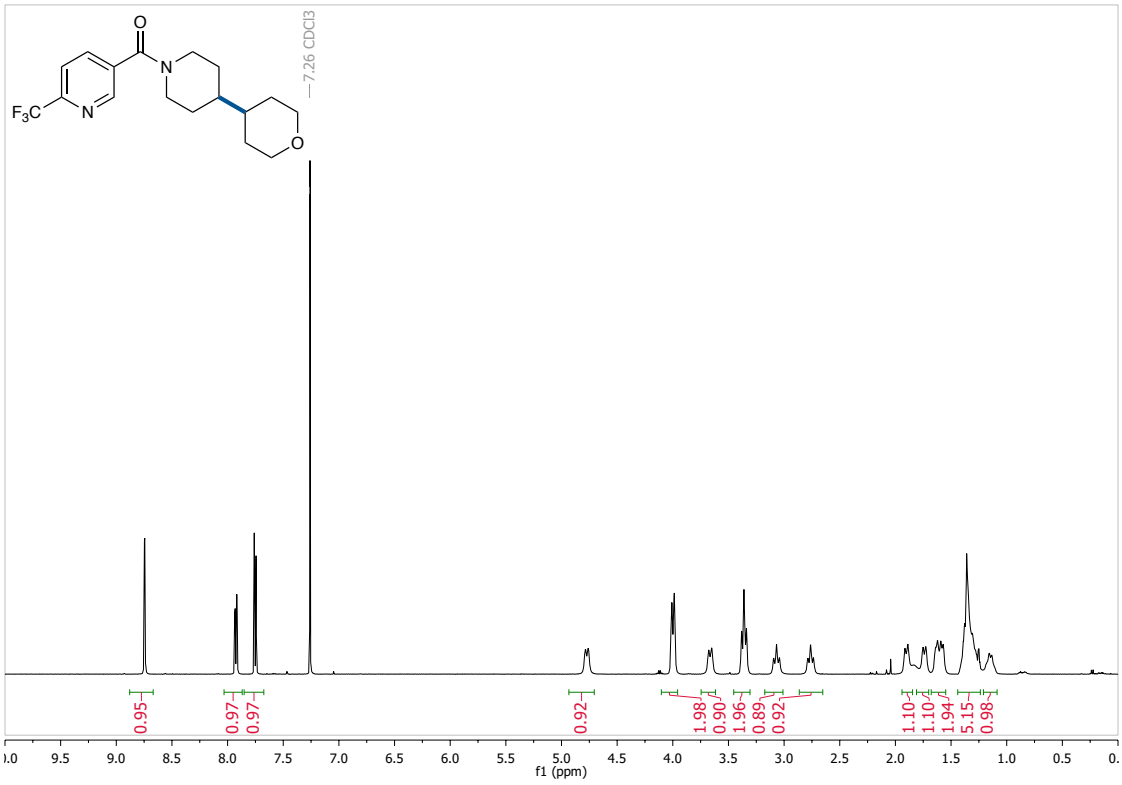
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

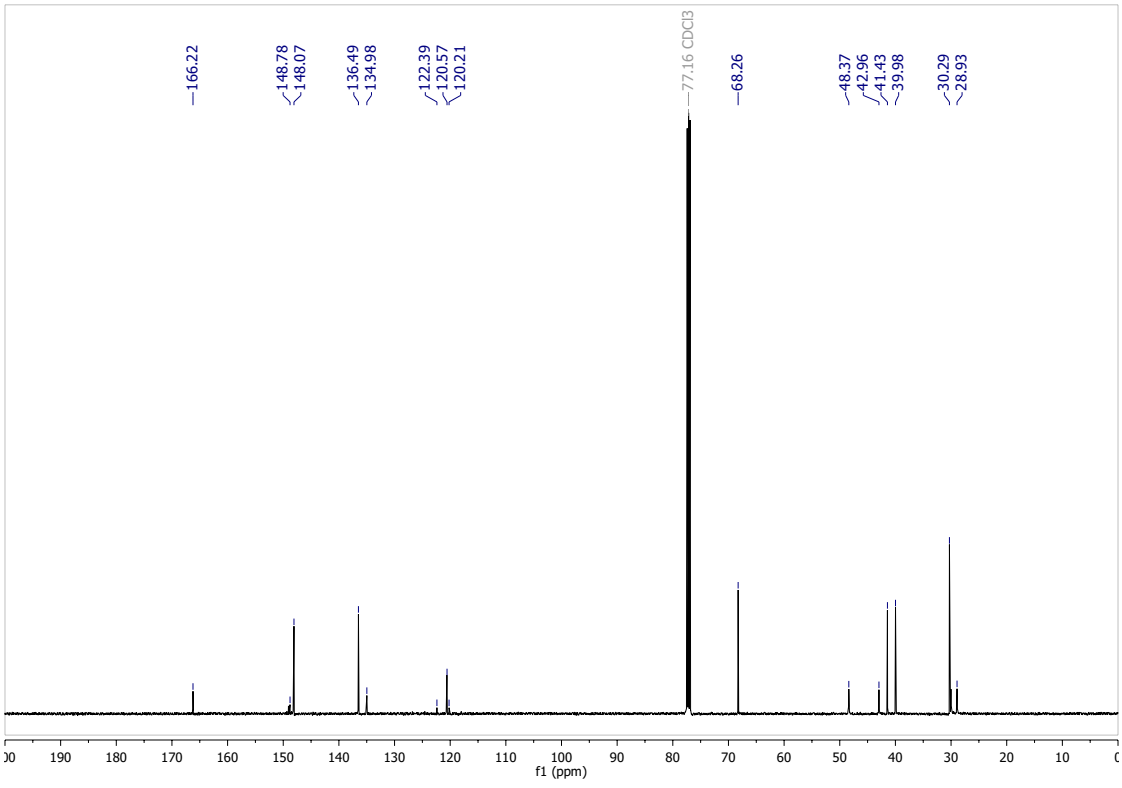

O
N
F3C
N
NBoc
7.26 CDCl3

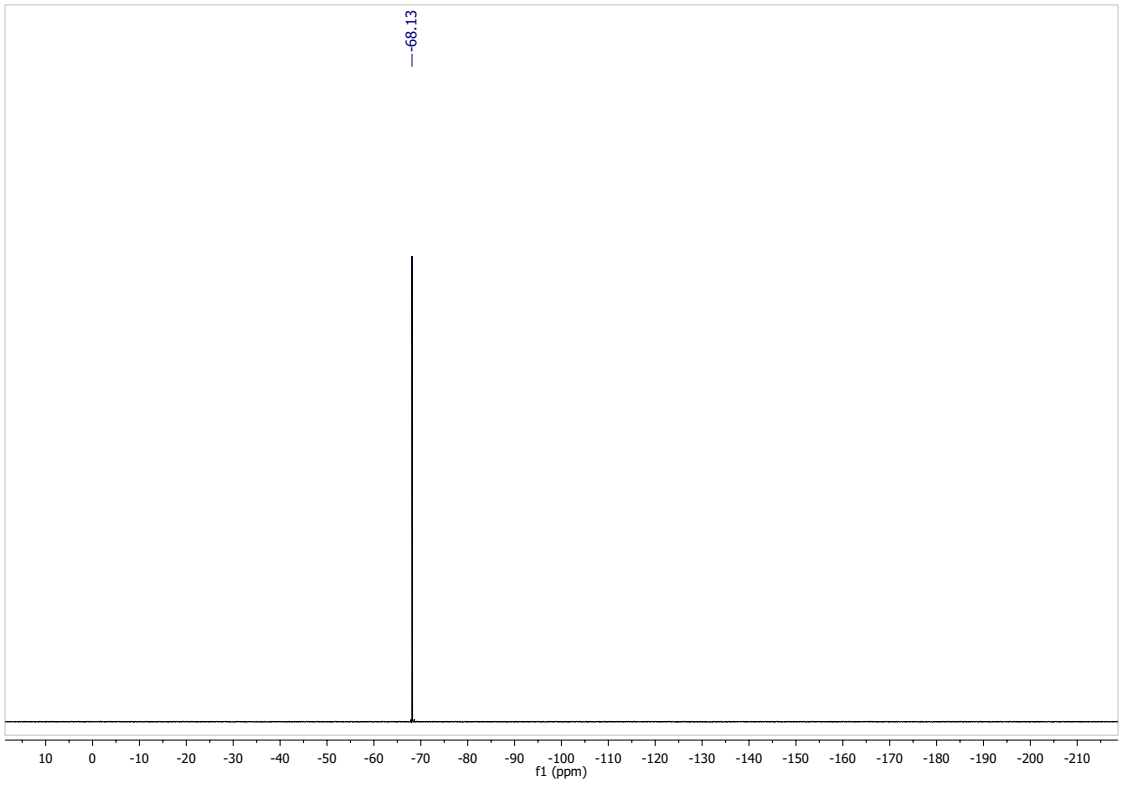

1.00
1.02
1.03
0.98
2.00
1.00
0.99
1.01
1.93
0.98
3.05
9.05
1.07
5.20
f1 (ppm)

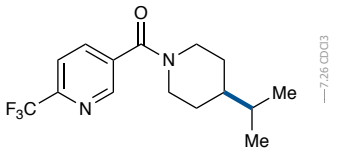

166.04
154.77
148.81
147.95
136.29
134.91
122.27
120.43
79.35
77.16 CDCl3
48.23
44.14
42.81
41.02
40.84
29.98
28.15
28.92
28.44
f1 (ppm)

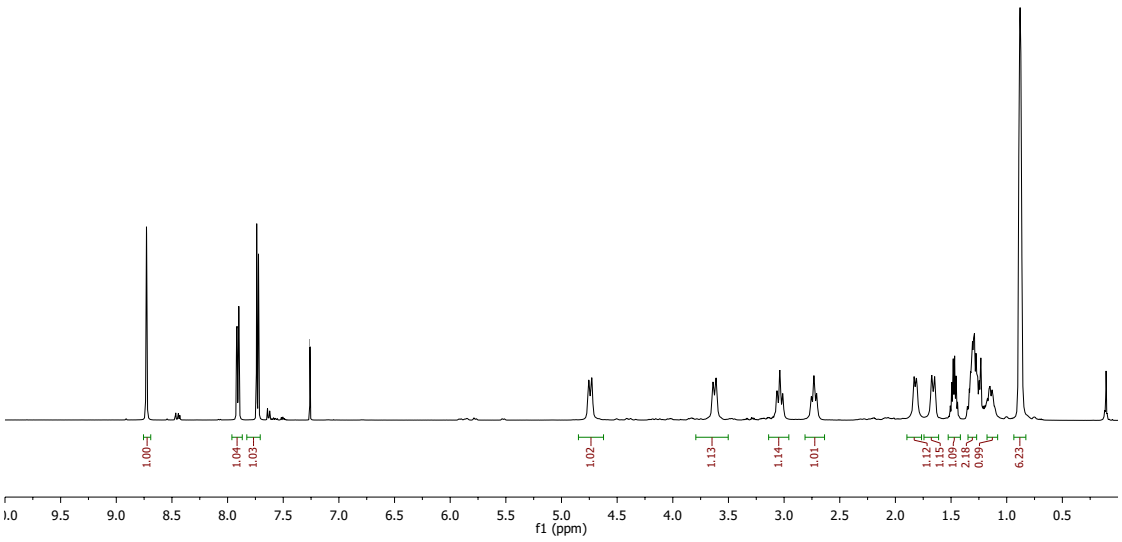

-68.12
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

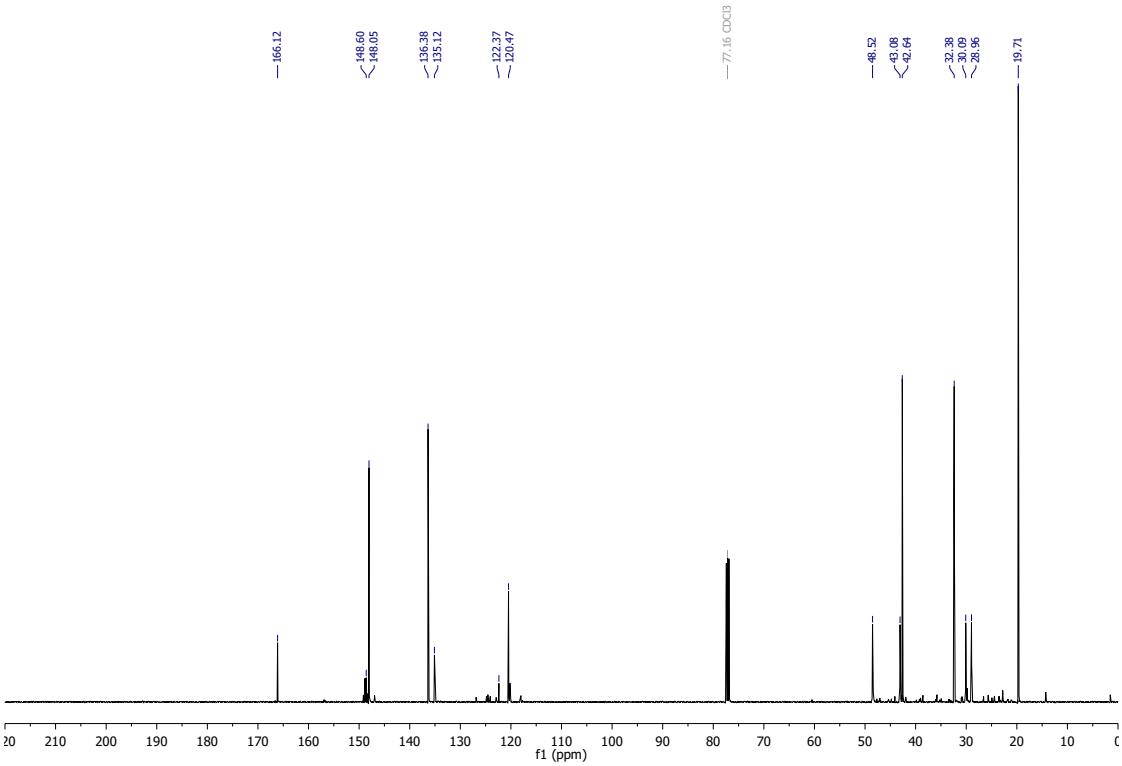

O
N
F3C
N
O
7.26 CDCl3
0.95
0.97
0.97
0.92
1.98
0.90
1.96
0.89
0.92
1.10
1.10
1.94
5.15
0.98
f1 (ppm)

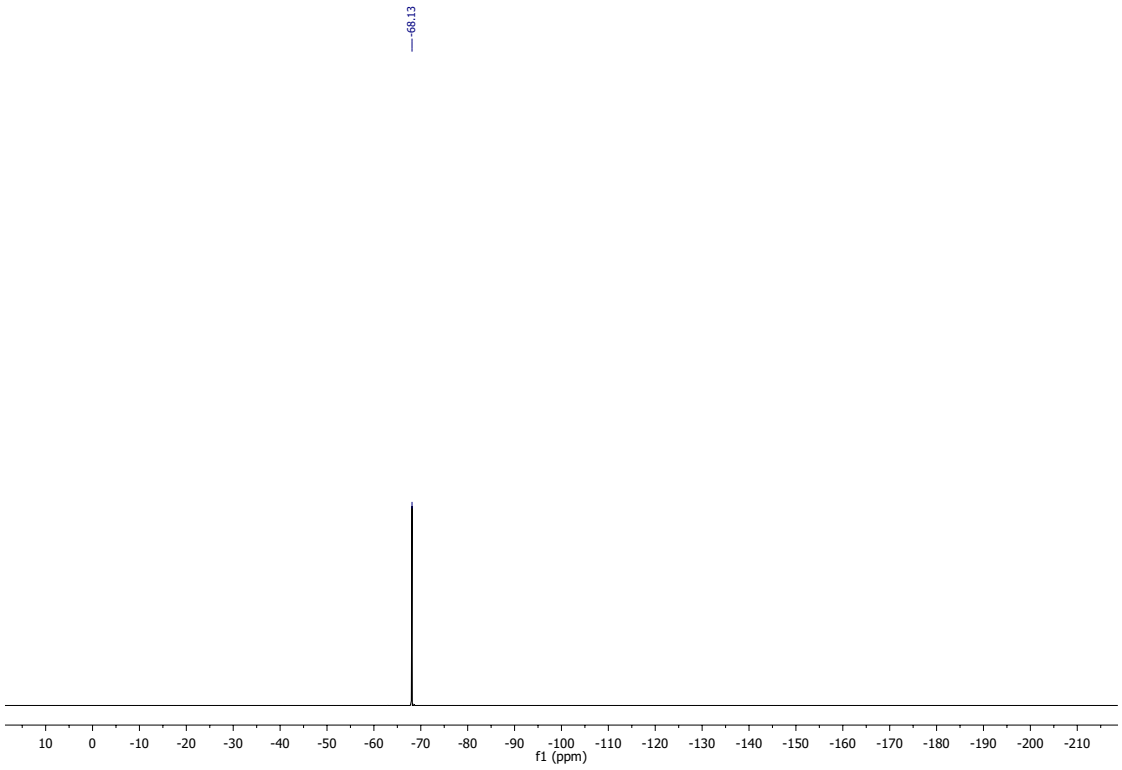

166.22
148.78
148.07
136.49
134.98
122.39
120.57
120.21
77.16 CDCl3
68.26
48.37
42.96
41.43
39.98
30.29
28.93
f1 (ppm)

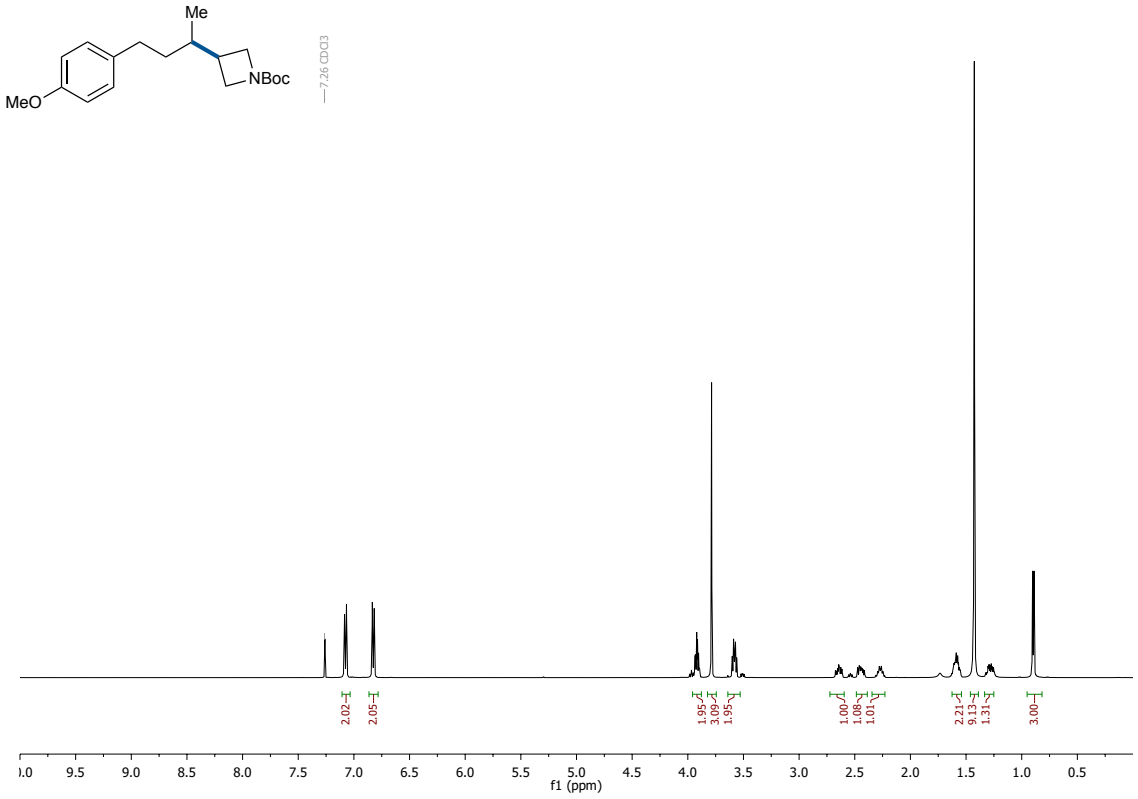

-68.13
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

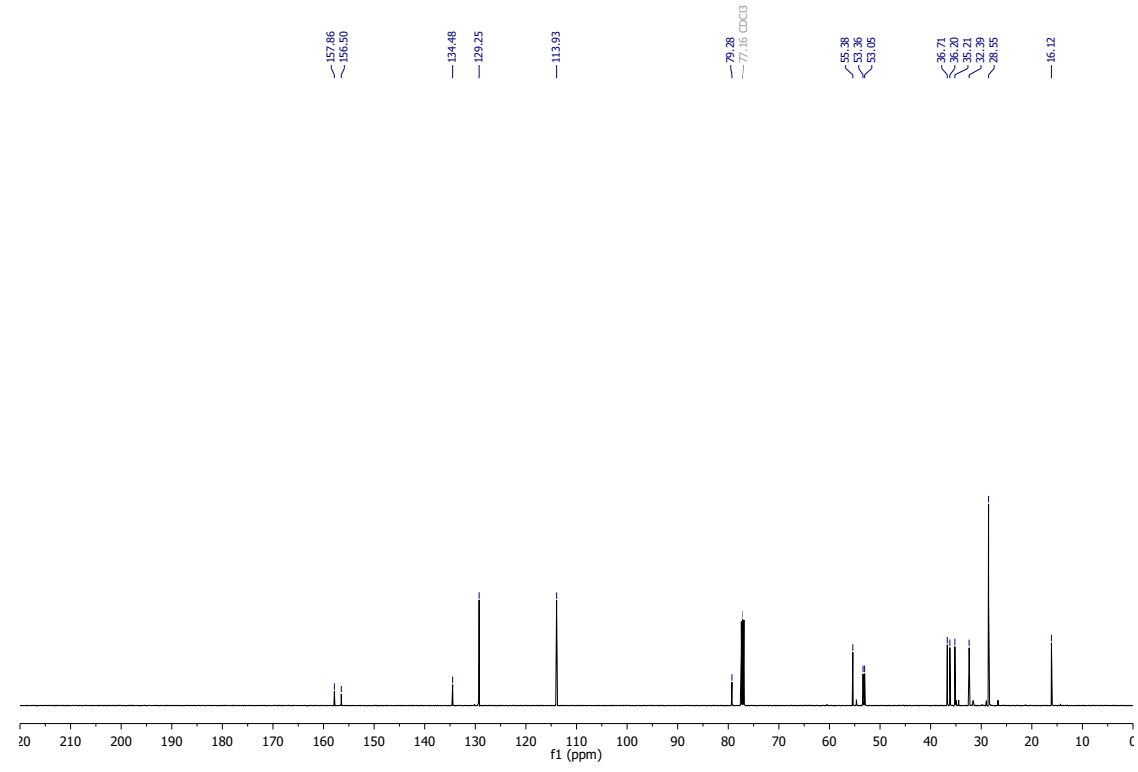

O
N
F3C
N
Me
Me

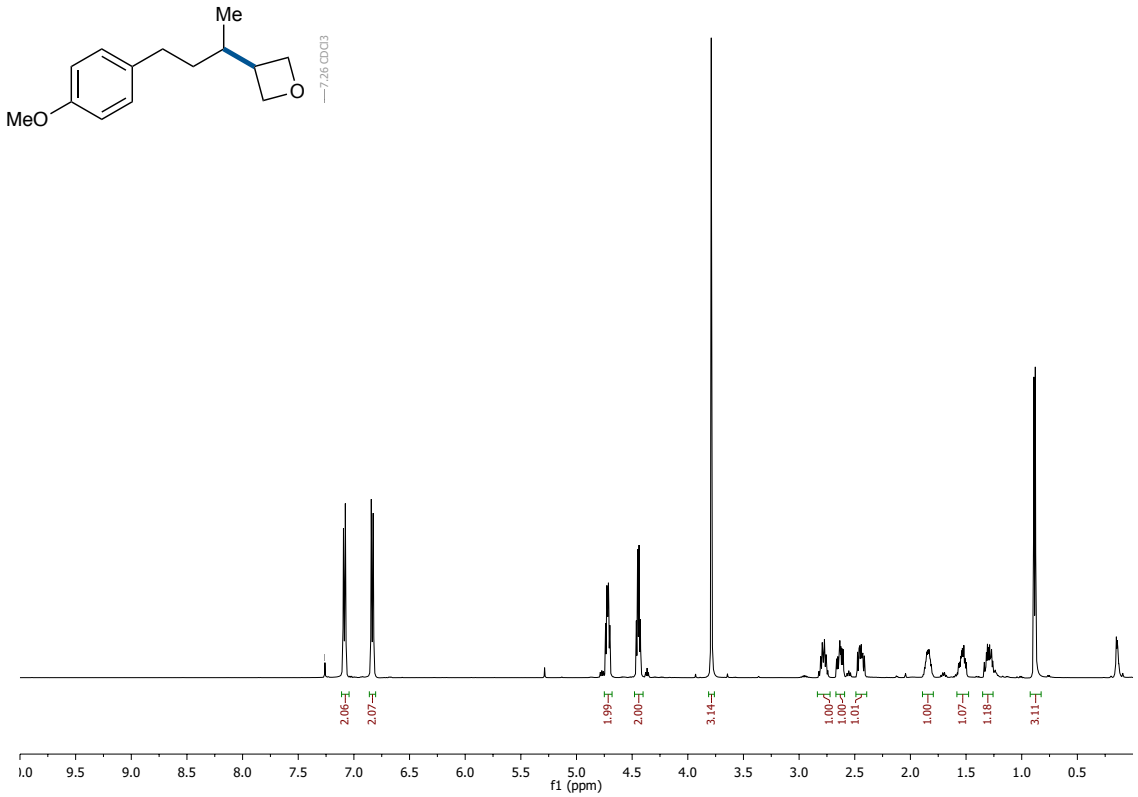

7.26 CDCl3
1.00
1.04
1.03
1.02
1.13
1.14
1.01
1.12
1.15
1.09
2.18
0.99
6.23
f1 (ppm)

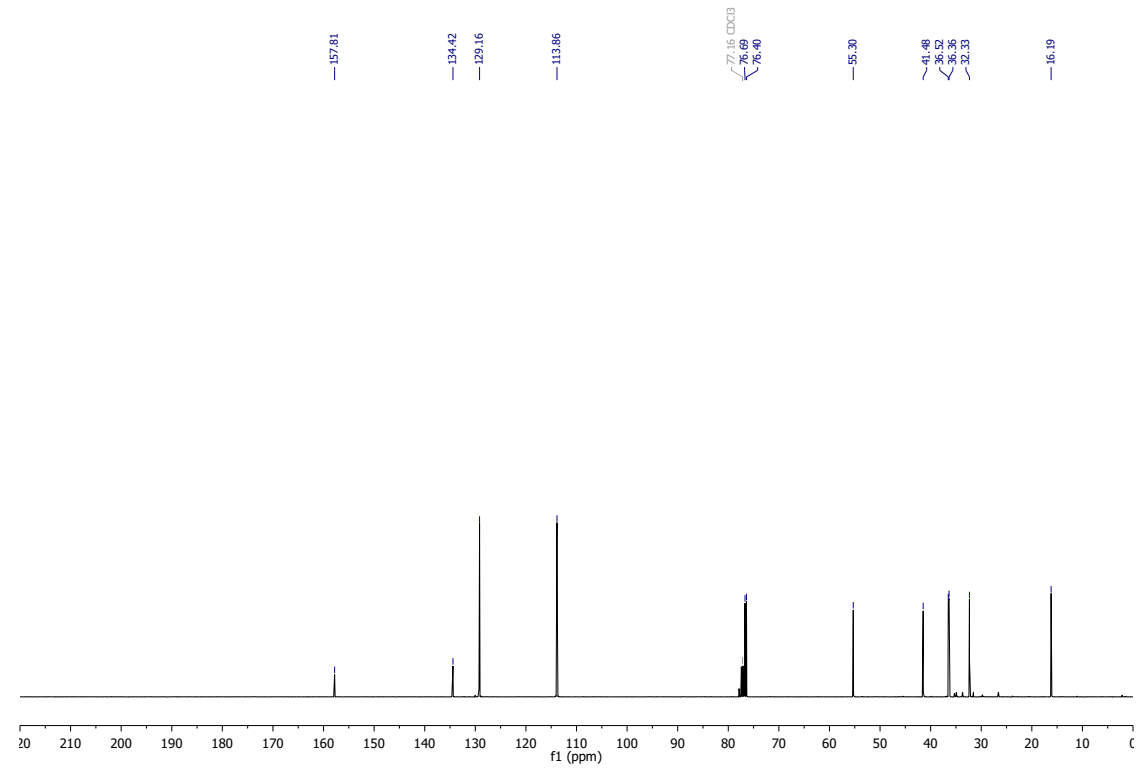

166.12
148.60
148.05
136.38
135.12
122.37
120.47
77.16 CDCl3
48.52
43.08
42.64
32.38
30.09
28.96
19.71
f1 (ppm)

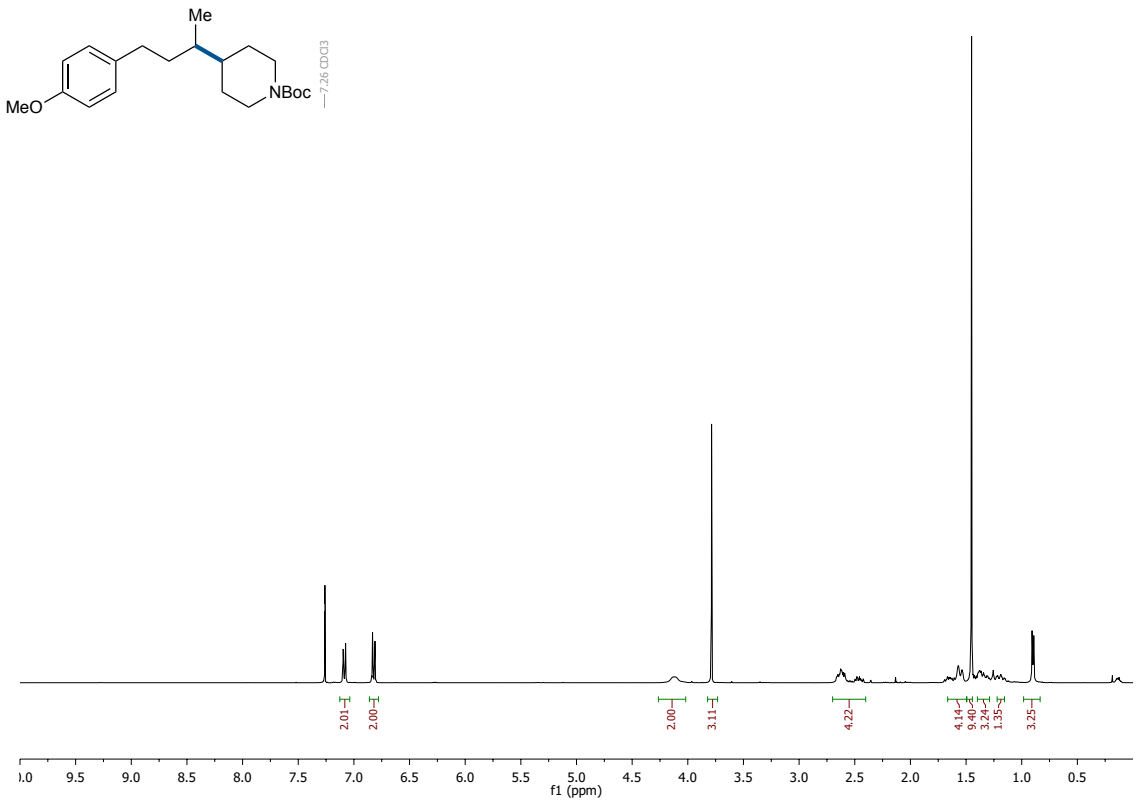

-68.13
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

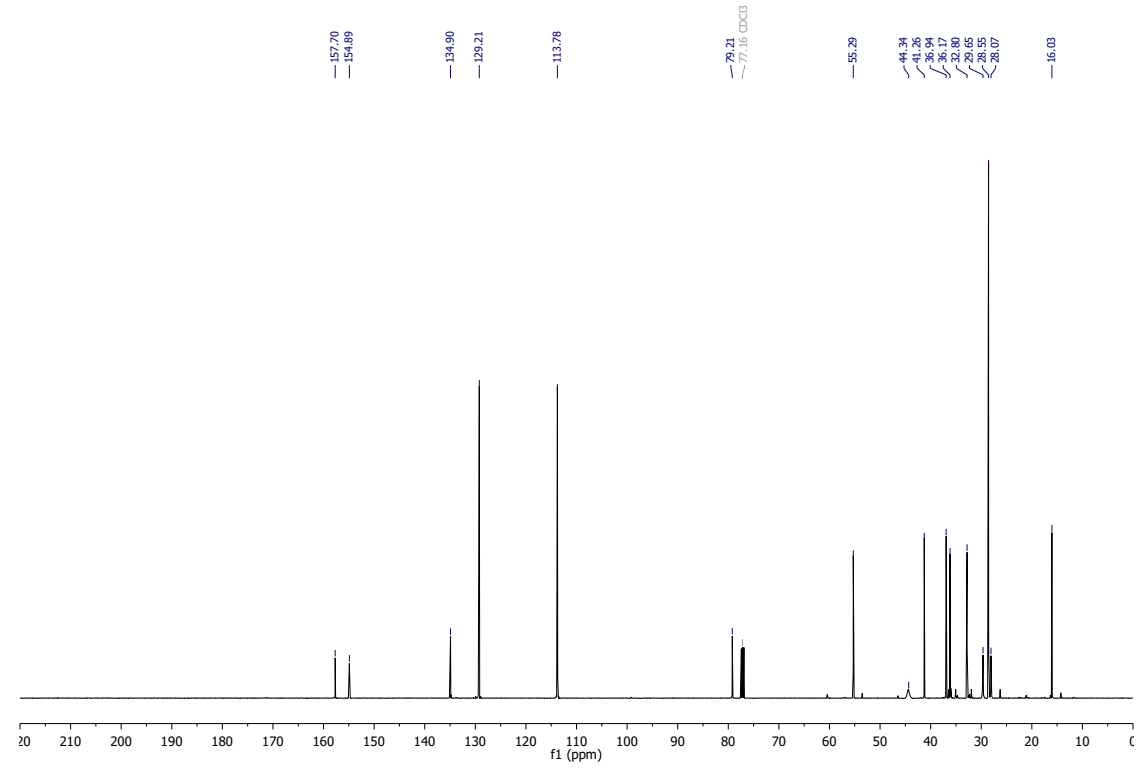

Me
NBoc
MeO
7.26 CDCl3
2.02
2.05
1.95
3.09
1.95
1.00
1.08
1.01
2.21
9.13
1.31
3.00
f1 (ppm)

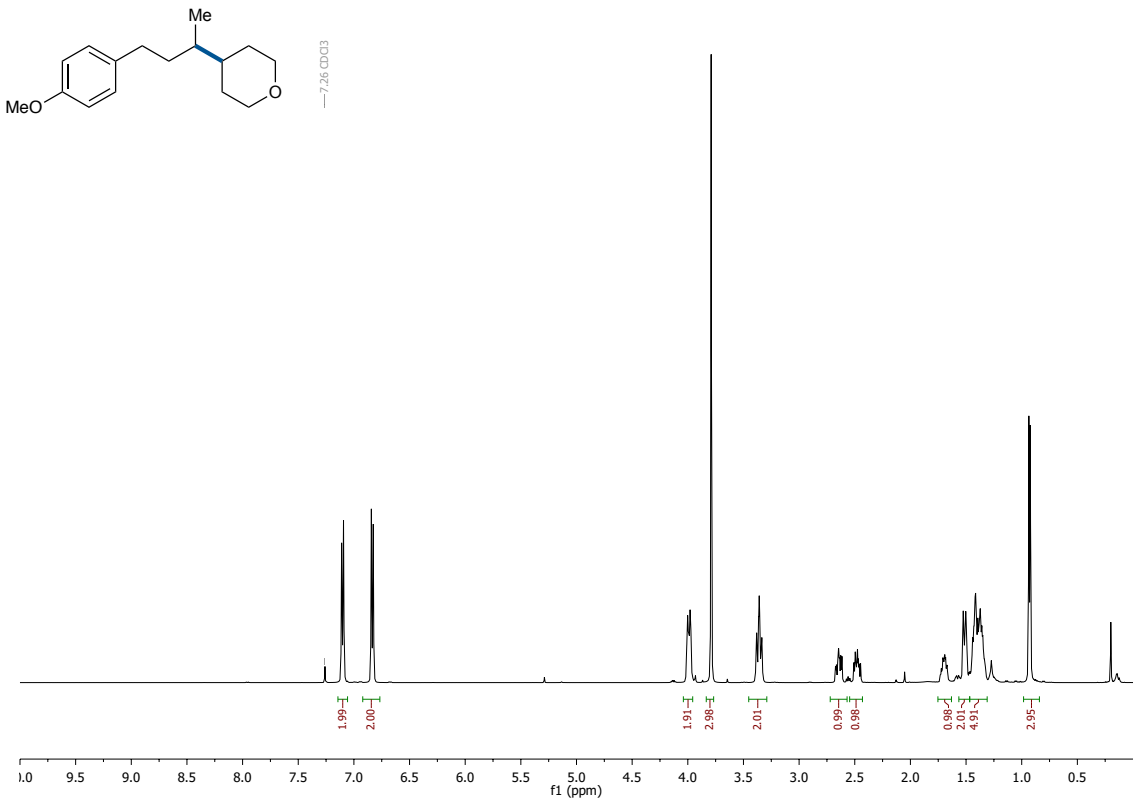

157.86
156.50
134.48
129.25
113.93
79.28
77.16 CDCl3
55.38
53.36
53.05
36.71
36.20
35.21
32.39
28.55
16.12
f1 (ppm)

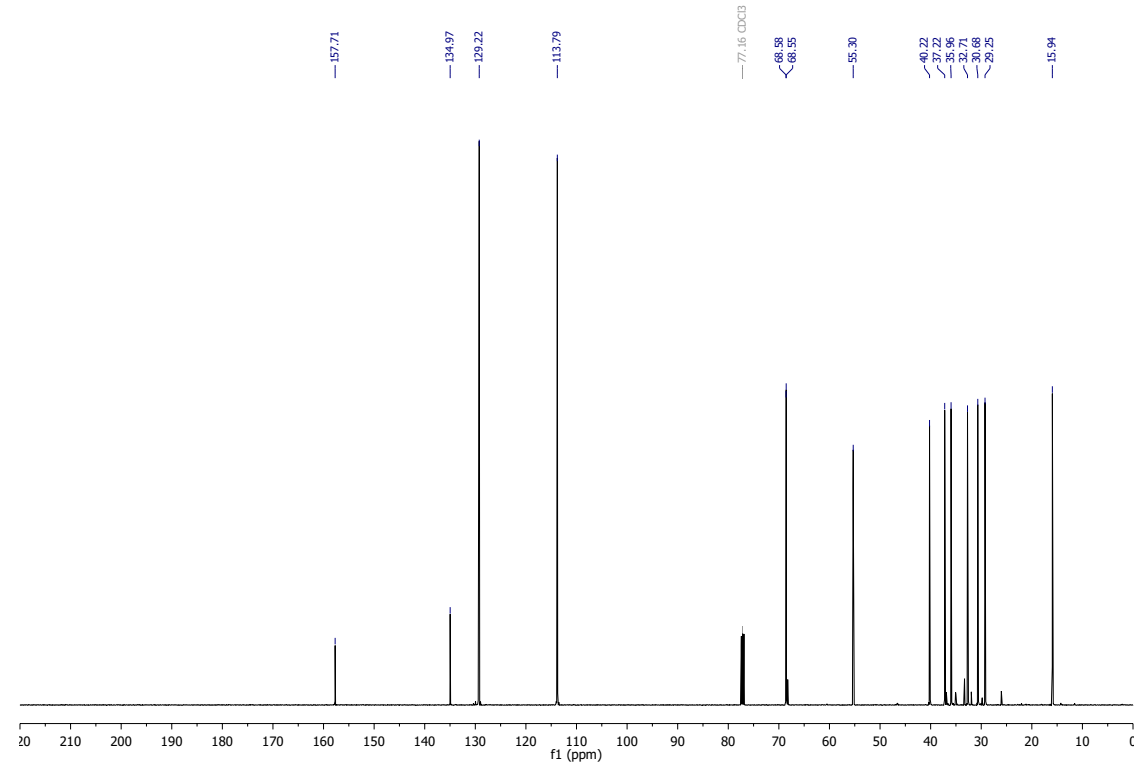

Me
MeO
O
7.26 CDCl3
2.06
2.07
1.99
2.00
3.14
1.00
1.00
1.01
1.00
1.07
1.18
3.11
f1 (ppm)

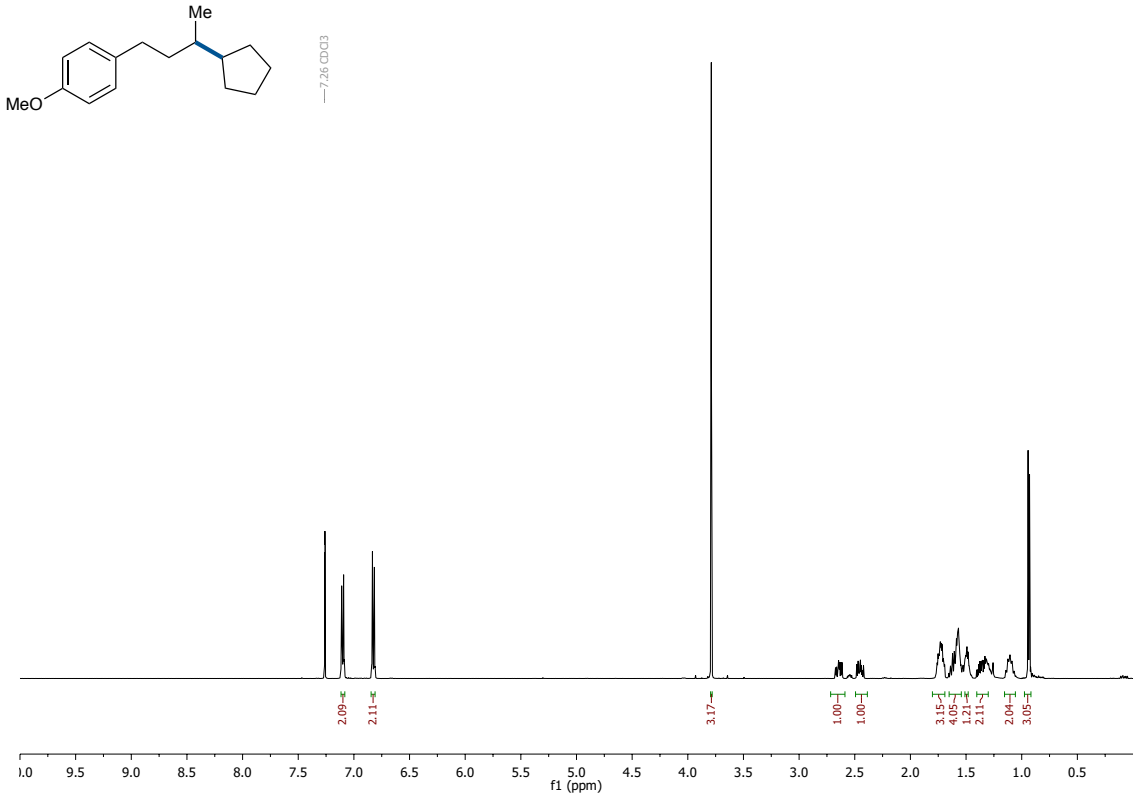

157.81
134.42
129.16
113.86
77.16 CDCl3
76.69
76.40
55.30
41.48
36.52
35.36
32.33
16.19
f1 (ppm)

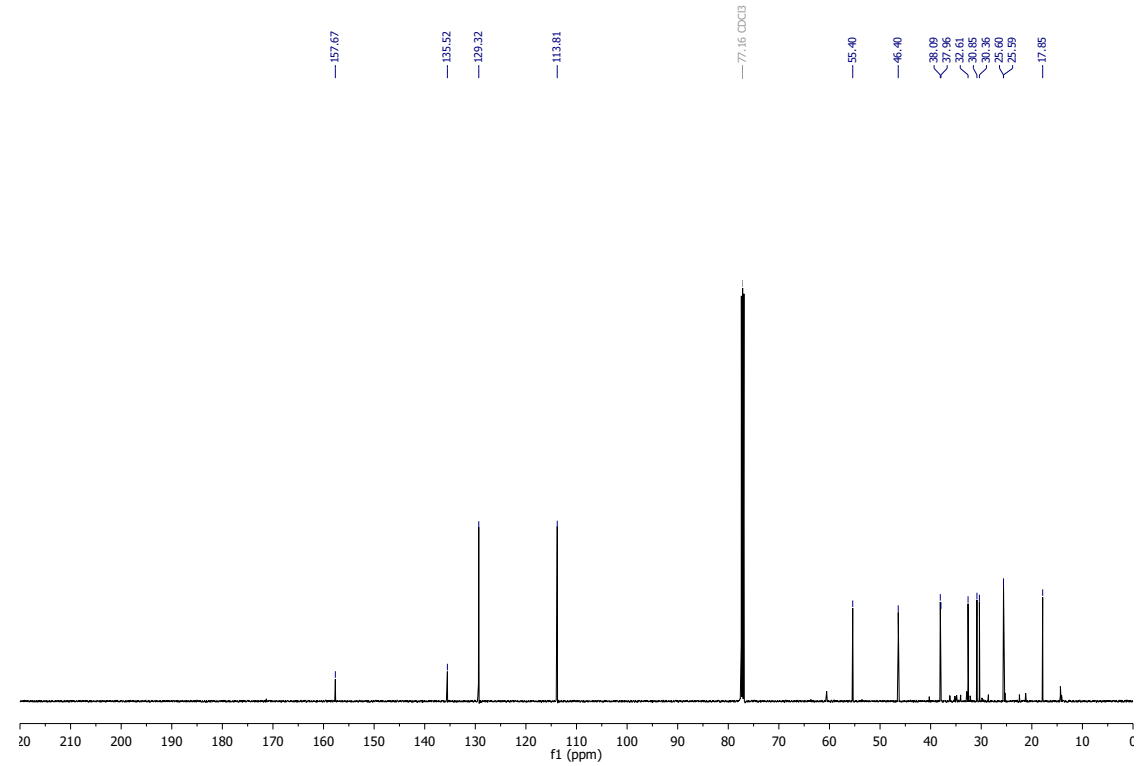

Me
MeO
NBoc
7.26 CDCl3
2.01
2.00
2.00
3.11
4.22
4.14
9.40
3.24
1.35
3.25
f1 (ppm)

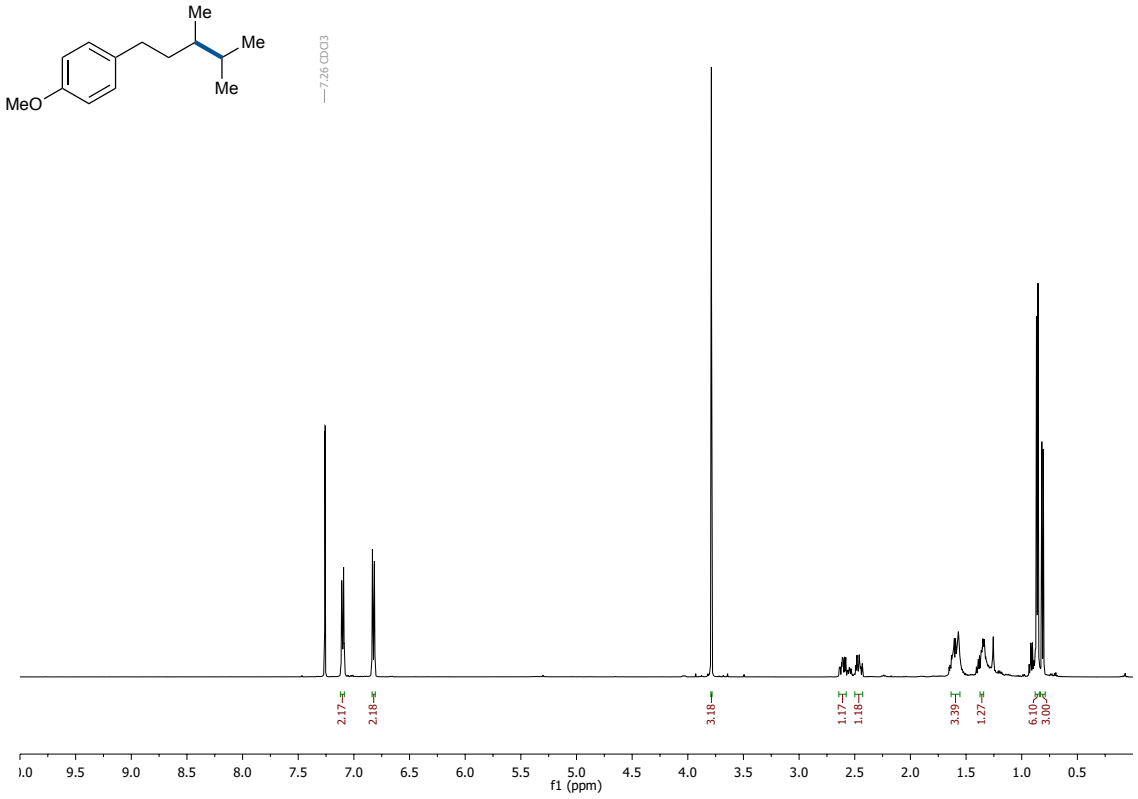

157.70
154.89
134.90
129.21
113.78
79.21
77.16 CDCl3
55.29
44.34
41.26
36.94
36.17
32.80
29.65
28.55
28.07
16.03
f1 (ppm)

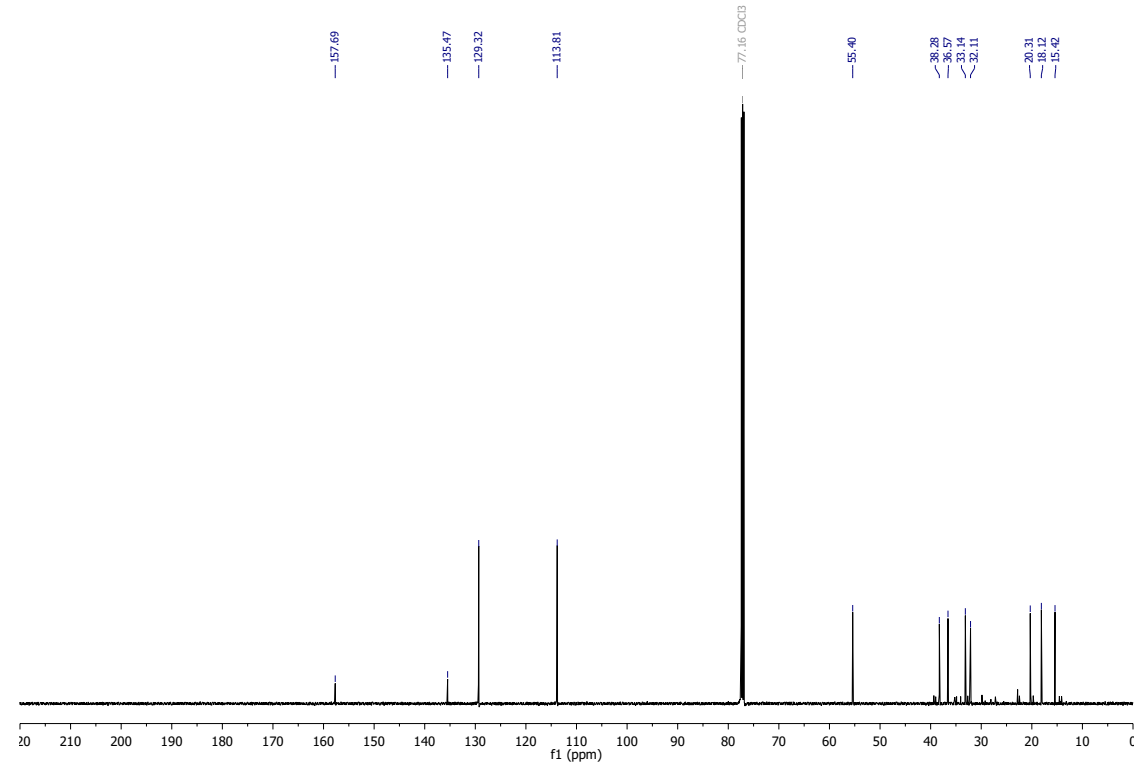

Me
MeO
O
7.26 CDCl3
1.99
2.00
1.91
2.98
2.01
0.99
0.98
0.98
2.01
4.91
2.95
f1 (ppm)

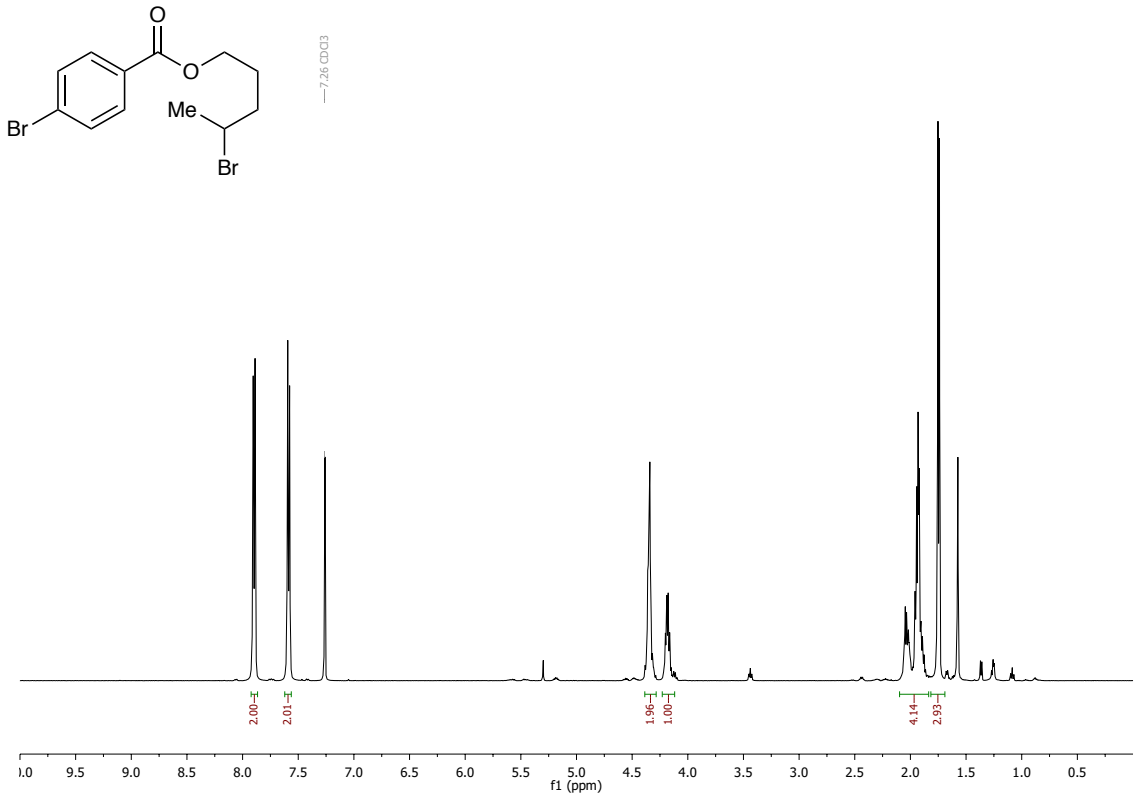

157.71
134.97
129.22
113.79
77.16 CDCl3
68.58
68.55
55.30
40.22
37.22
35.96
32.71
30.68
29.25
15.94
f1 (ppm)

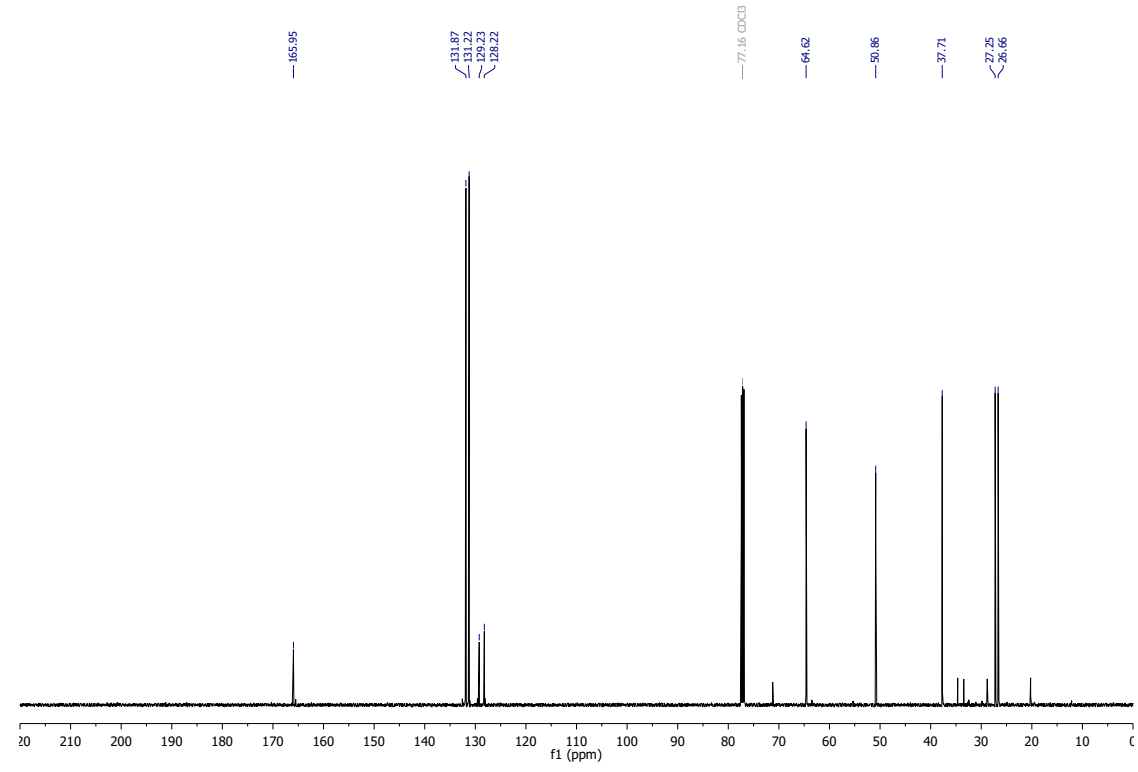

Me
MeO
7.26 CDCl3
2.09
2.11
3.17
1.00
1.00
3.15
4.05
1.21
2.11
2.04
3.05
f1 (ppm)

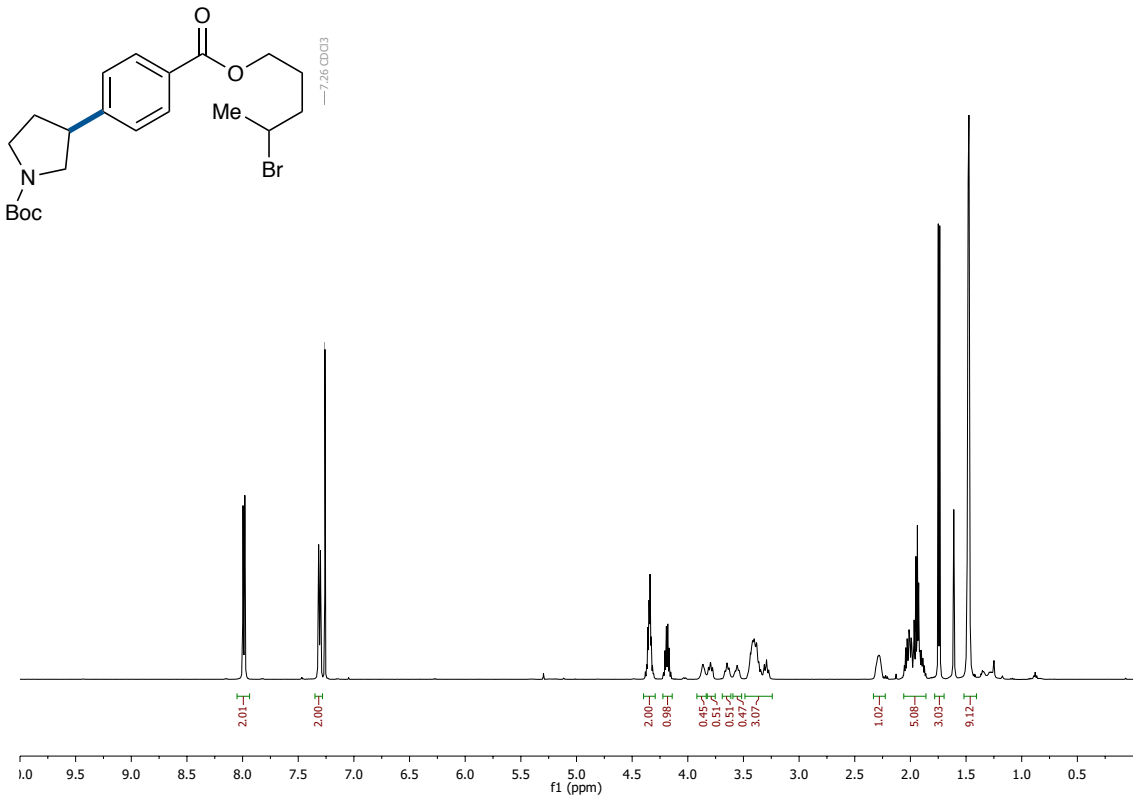

157.67
135.52
129.32
113.81
77.16 CDCl3
55.40
46.40
38.09
37.96
32.61
30.85
30.36
25.60
25.59
17.85
f1 (ppm)

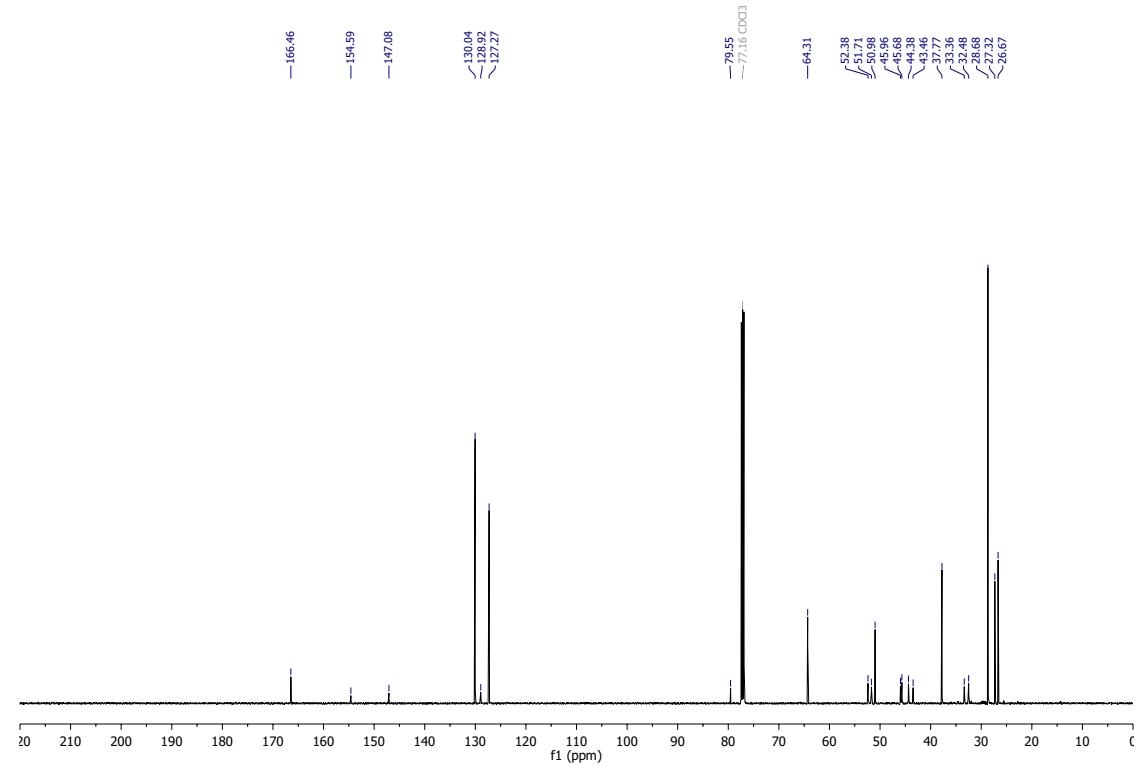

Me
Me
Me
MeO
7.26 CDCl3
2.17
2.18
3.18
1.17
1.18
3.39
1.27
6.10
3.00
f1 (ppm)

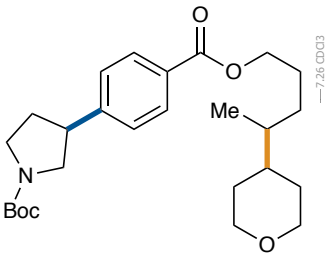

157.69
135.47
129.32
113.81
77.16 CDCl3
55.40
38.28
36.57
33.14
32.11
20.31
18.12
15.42
f1 (ppm)

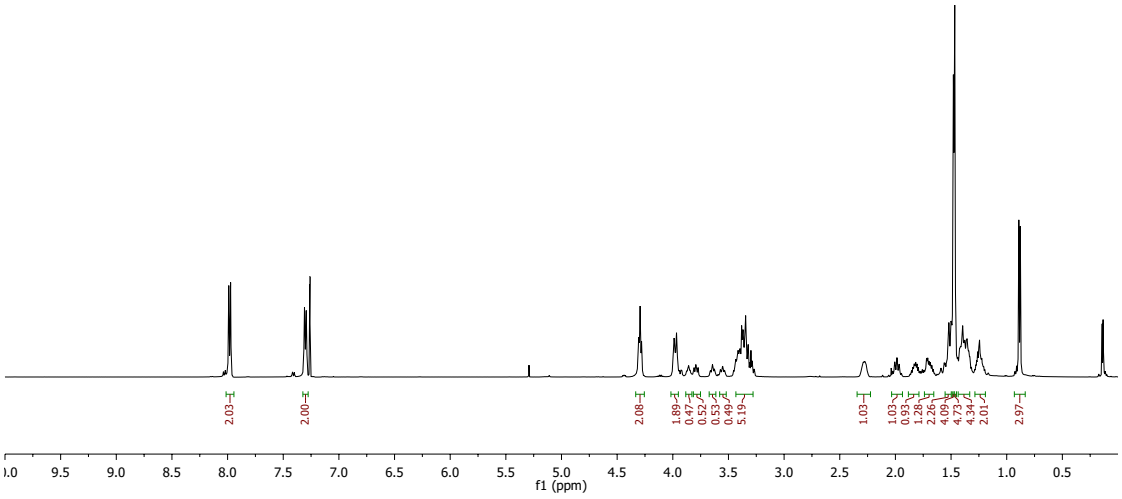

O
O
Me
Br
Br
7.26 CDCl3
2.00
2.01
1.96
1.00
4.14
2.93
f1 (ppm)

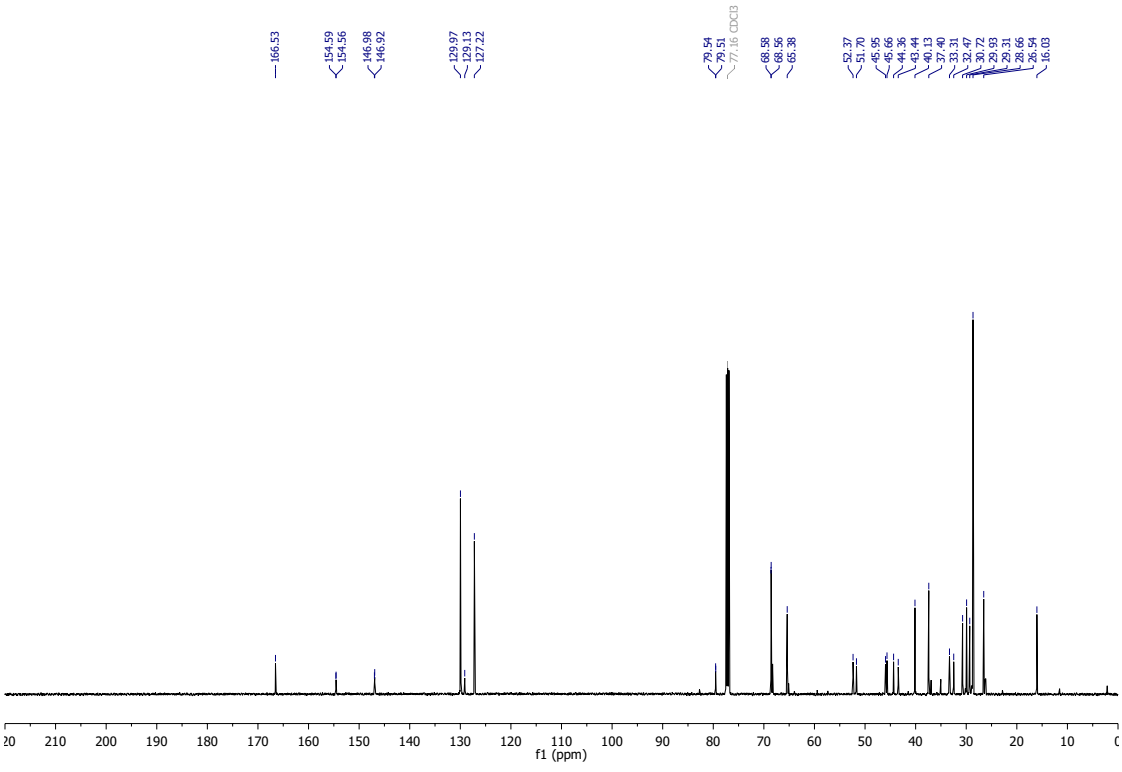

165.95
131.87
131.22
129.23
128.22
77.16 CDCl3
64.62
50.86
37.71
27.25
26.66
f1 (ppm)


O
O
Me
Br
N
Boc
7.26 CDCl3
2.01
2.00
2.00
0.98
0.45
0.51
0.51
0.47
3.07
1.02
5.08
3.03
9.12
f1 (ppm)


166.46
154.59
147.08
130.04
128.92
127.27
79.55
77.16 CDCl3
64.31
52.38
51.71
50.98
45.96
45.68
44.38
43.46
33.77
33.36
32.48
28.68
27.32
26.67
f1 (ppm)


O
O
Me
N
Boc
O
7.26 CDCl3


2.03
2.00
2.08
1.89
0.47
0.52
0.53
0.49
5.19
1.03
1.03
0.93
1.28
2.26
4.09
4.73
4.34
2.01
2.97
f1 (ppm)


166.53
154.59
154.56
146.98
146.92
129.97
129.13
127.22
79.54
79.51
77.16 CDCl3
68.58
68.56
65.38
52.37
51.70
45.95
45.66
44.36
43.44
40.13
37.40
33.31
32.47
30.72
29.93
29.31
28.66
26.54
16.03
f1 (ppm)