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Supplementary Materials for

Deconstructive fluorination of cyclic amines by carbon-carbon cleavage

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1. General Considerations

1.1. Solvents and Reagents

Tetrahydrofuran (THF) and triethylamine (Et_3N) were sparged with argon and dried by passing through alumina columns using argon in a Glass Contour solvent purification system. Dichloromethane (CH_2Cl_2) was freshly distilled over calcium hydride under a N_2 atmosphere prior to each use. N-Boc-piperidine (**1c**), N-methyl-2-pyrrolidinone (**1p**) and N-methyl-2-piperidinone (**1n**) were obtained from commercial vendors and used as received. Reagents for the fluorination reaction were purchased from commercial vendors as follows: Silver tetrafluoroborate ($AgBF_4$, 99%) was purchased from Oakwood Chemicals and stored in a glovebox. Selectfluor® was purchased from Matrix Scientific. Acetone (HPLC) was purchased from Fisher Scientific. Water (HPLC) was purchased from Fisher Scientific.

1.2. Experimental Procedures

Unless otherwise noted in the experimental procedures, reactions were carried out in flame or oven-dried glassware under a positive pressure of N_2 in anhydrous solvents using standard Schlenk techniques. Reaction temperatures above room temperature (22–23 °C) were controlled by an IKA® temperature modulator and monitored using liquid-in-glass thermometers. Reaction progress was monitored using a combination of LC/MS analysis (via a Shimadzu LCMS-2020 (UFLC) equipped with the LC-20AD solvent delivery system, a SPD-20AV prominence UV/Vis detector (SPD-M20A Photo Diode Array), and a Thermo Scientific Hypersil GOLD HPLC column (5 μm particle size, 4.6 × 50 mm)), and thin-layer chromatography (TLC) on SiliCycle Siliaplates (glass backed, extra hard layer, 60 Å, 250 μm thickness, F254 indicator). Flash column chromatography was performed with either glass columns using Silicycle silica gel (40–63 μm particle size) or with a Yamazen Smart Flash EPCLC W-Prep 2XY (dual channel) automated flash chromatography system on prefilled, premium, universal columns using ACS grade solvents. Preparative thin layer chromatography was performed on SiliCycle Siliaplates (glass backed, extra hard layer, 60 Å, 250 μm thickness, F254 indicator).

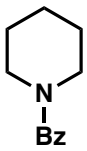
1.3. Analytical Instrumentation

^1H NMR and ^{13}C NMR data were recorded on Bruker AVQ-400, AVB-400, RDX-500, AV-600 and AV-700 spectrometers using $CDCl_3$ as solvents, typically at 20–23 °C. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (δ 7.26 for ^1H NMR, δ 77.16 for ^{13}C NMR in $CDCl_3$, δ 3.31 for ^1H NMR, δ 49.00 for ^{13}C NMR in CD_3OD). The ^{19}F NMR spectra were acquired on an AVQ-400 spectrometer and internally referenced to $CFCl_3$ (δ 0.00). Data for ^1H, ^{13}C and ^{19}F NMR spectroscopy are reported as follows; chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, hept = heptet, m = multiplet, br = broad), coupling constant (Hz), integration. Melting points were determined using a MEL-TEMP™ apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241

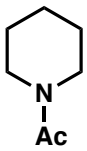
polarimeter. High-resolution mass spectra (HRMS) were obtained from the Catalysis Facility of the Lawrence Berkeley National Laboratory (supported by the Director, Office of Science, of the US Department of Energy under contract no. DE-AC02-05CH11231) using a PerkinElmer AxION 2 TOF-MS.

2. Experimental Procedures for Preparation of Starting Materials

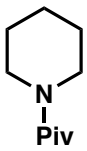
2.1. Preparation of *N*-Protected Cyclic Amines



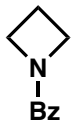
Phenyl(piperidin-1-yl)methanone (1a) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*44*).



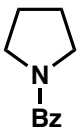
1-(Piperidin-1-yl)ethan-1-one (1b) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*45*).



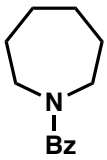
2,2-Dimethyl-1-(piperidin-1-yl)propan-1-one (1d) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*46*).



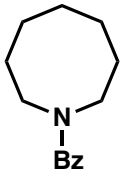
Azetidin-1-yl(phenyl)methanone (1e) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*44*).



Phenyl(pyrrolidin-1-yl)methanone (1f) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*44*).



Azepan-1-yl(phenyl)methanone (1g) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*47*).

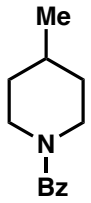


Azocan-1-yl(phenyl)methanone (1h): A 25 mL round-bottomed flask was charged with a solution of azocane (300 mg, 3.02 mmol) and Et_3N (0.57 mL, 4.1 mmol) in CH_2Cl_2 (5.0 mL) and cooled to 0 °C. Benzoyl chloride (0.320 mL, 2.75 mmol) was added dropwise over 5 min and the resulting mixture was warmed to room temperature. After 24 h, the reaction mixture was quenched with 1 M HCl aq. (5.0 mL) and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were washed with brine (2.0 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, 50% EtOAc/hexanes) to provide the title compound (400 mg, 66%) as a yellow oil.

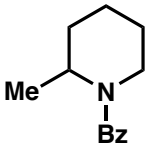
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.34 (m, 5H), 3.62 (t, *J* = 6.1 Hz, 2H), 3.31 (br, 2H), 1.86 (br, 2H), 1.61–1.59 (m, 8H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 137.7, 129.0, 128.5, 126.4, 51.2, 46.7, 27.0, 26.5, 26.4, 25.6, 24.2;

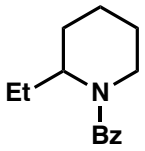
HRMS (ESI): Calc'd for $C_{14}H_{20}NO$ $[M+H]^+$: 218.1539, found: 218.1535.



(4-Methylpiperidin-1-yl)(phenyl)methanone (1i) was prepared from 4-methylpiperidine using a procedure analogous to that for the preparation of **1h**. Spectral data were in full agreement with the reported literature values (*48*).



(2-Methylpiperidin-1-yl)(phenyl)methanone (1j) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*49*).

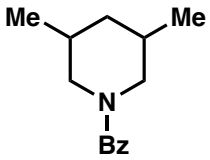


(2-Ethylpiperidin-1-yl)(phenyl)methanone (1k) was prepared from 2-ethylpiperidine using a procedure analogous to that used for the synthesis of **1h**. The title compound was obtained as a colorless oil (525 mg, 81%).

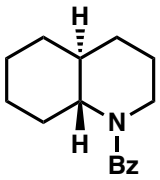
^{1}H NMR (600 MHz, $CDCl_3$, *ca.* 1:1 mixture of rotamers): δ 7.38–7.33 (m, 5H), 4.81 (br, 0.5H), 4.57 (br, 0.5H), 3.67 (br, 0.5H), 3.49 (br, 0.5H), 3.02 (br, 0.5H), 2.78 (br, 0.5H), 1.81–1.76 (m, 1H), 1.74–1.31 (m, 7H), 0.95 (br, 1.5H), 0.73 (br, 1.5H);

^{13}C NMR (151 MHz, $CDCl_3$, mixture of rotamers): δ 170.9, 137.3, 129.1, 128.5, 126.6, 56.1, 49.8, 43.3, 37.0, 28.8, 28.0, 26.4, 25.9, 22.8, 19.2, 10.8 (*One ^{13}C signal is overlapping with others due to amide rotation*);

HRMS (ESI): Calc'd for $C_{14}H_{20}NO$ $[M+H]^+$: 218.1538, found: 218.1540.



(3,5-Dimethylpiperidin-1-yl)(phenyl)methanone (1l) was prepared from 3,5-dimethylpiperidine **(**mixture of *cis* and *trans)* using a procedure analogous to that for the preparation of **1h**. Spectral data were in full agreement with the literature values (*50*).

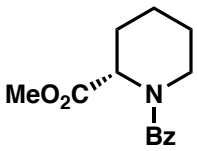


(Octahydroquinolin-1(2*H*)-yl)(phenyl)methanone (1m) was prepared from *trans*-decahydroquinoline using a procedure analogous to that used for the synthesis of **1h**. The title compound was obtained as a yellow oil (276 mg, 53%).

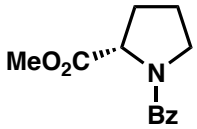
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (br, 5H), 3.50 (td, J = 10.7, 3.2 Hz, 1H), 2.43–2.28 (m, 2H), 2.29–2.24 (m, 1H), 1.79–1.52 (m, 7H), 1.49–1.16 (m, 4H), 1.13–1.03 (m, 1H);

^{13}C NMR (101 MHz, $CDCl_3$): 171.6, 137.8, 129.3, 128.4, 126.9, 61.3, 42.4, 38.2, 33.2, 30.5, 26.7, 26.3, 25.6, 23.7;

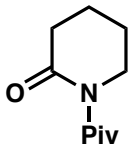
HRMS (ESI): Calc'd for $C_{16}H_{22}NO$ $[M+H]^+$: 244.1696, found: 244.1697.



Methyl (*S*)-1-Benzoylpiperidine-2-carboxylate (1n) was prepared from L-pipecolic acid methyl ester hydrochloride using a procedure analogous to that used for the preparation of **1h**. Spectral data were in full agreement with the reported literature values (*51*).



Methyl Benzoyl-*L*-prolinate (1o) was prepared from L-proline methyl ester hydrochloride using a procedure analogous to that used for the synthesis of **1h**. Spectral data were in full agreement with the reported literature values (*52*).

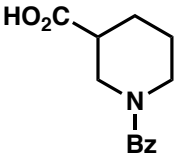


1-Pivaloylpiperidin-2-one (1r) was prepared from 2-piperidinone and pivaloyl chloride using a procedure analogous to that used for the synthesis of **1h**. The title compound was obtained as a colorless oil (456 mg, 83%).

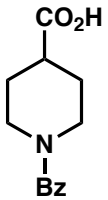
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.50 (br s, 2H), 2.46 (t, J = 5.8 Hz, 2H), 1.85–1.84 (m, 4H), 1.28 (s, 9H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 190.0, 173.2, 47.2, 43.7, 34.0, 27.7, 22.7, 21.5;

HRMS (ESI): Calc'd for $C_{10}H_{18}NO_2$ $[M+H]^+$: 184.1332, found: 184.1333.



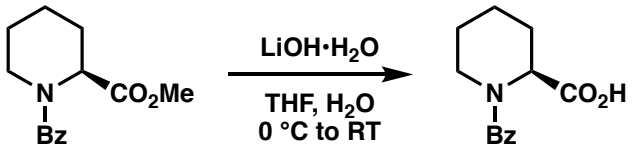
1-Benzoylpiperidine-3-carboxylic acid (1s) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*53*).



1-Benzoylpiperidine-4-carboxylic acid (1t) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*54*).

2.2. Preparation of Peptides

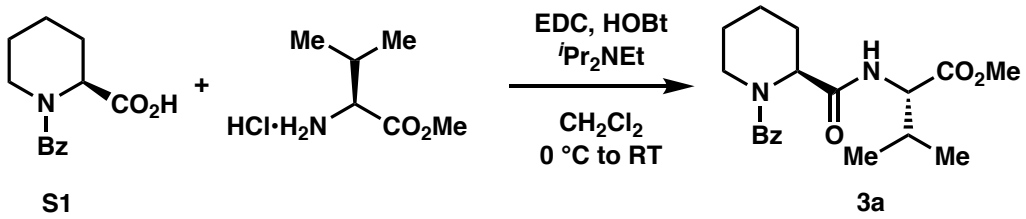
Representative Procedure for Methyl Ester Hydrolysis



1p **S1**

A 100 mL round-bottom flask was charged with a solution of **1p** (1.24 g, 5.00 mmol) in 3:1 THF: H_2O (10 mL) and cooled to 0 °C. LiOH•H_2O (210 mg, 25.0 mmol) was added and the resulting mixture was warmed to room temperature. After 13 h, the reaction mixture was cooled to 0 °C and acidified with 1 M HCl aq. (10 mL) to pH <2. The solution was then diluted with EtOAc (10 mL) and the aqueous layer was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine (5.0 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford **S1**, which was used in the next step without further purification.

Representative Procedure for Condensation Reaction



S1 **3a**

Methyl ((*S*)-1-Benzoylpiperidine-2-carbonyl)-*L*-valinate (3a): A 100 mL round-bottomed flask was charged with a solution of *L*-valine methyl ester hydrochloride (922 mg, 5.50 mmol) in CH_2Cl_2 (45 mL) and cooled to 0 °C. *i*Pr_2NEt (0.96 mL, 5.5 mmol) was added dropwise over 5 min and the resulting mixture was stirred at 0 °C for 10 min. To this solution were added the crude **S1**, hydroxybenzotriazole (HOBt: 676 mg, 5.00 mmol) followed by 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC: 1.05 g, 5.50 mmol) and the resulting mixture was warmed to room temperature. After 19 h, the reaction mixture was cooled to 0 °C and quenched with 1 M HCl aq. (10 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, 25% to 50% EtOAc/ hexanes) to provide the title compound (1.23 g, 71% over 2

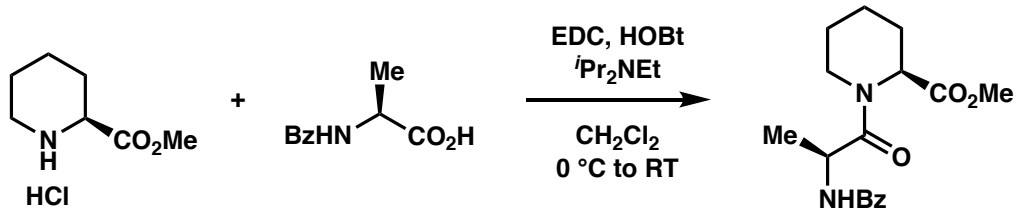
steps) as a white amorphous solid.

Optical Rotation: $[\alpha]^{22}_{D} = -100$ (*c* 0.770, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$, *ca.* 3:1 mixture of rotamers): δ 7.44 (br s, 5H), 7.10 (d, *J* = 6.6 Hz, 0.75H), 6.60 (br, 0.25H), 5.29 (s, 0.75H), 4.79 (br, 0.25H), 4.64 (br, 0.25H), 4.52 (s, 0.75H), 4.42 (br, 0.25H), 3.76 (s, 3H), 3.72 (s, 0.75H), 3.04 (t, *J* = 12.4 Hz, 0.75H), 2.86 (br, 0.25H), 2.35–2.30 (m, 1H), 2.27–2.20 (m, 1H), 1.93–1.84 (m, 0.75H), 1.76–1.74 (m, 1.25H), 1.68–1.47 (m, 3H), 0.93 (d, *J* = 6.9 Hz, 6H);

^{13}C NMR (151 MHz, $CDCl_3$, peaks of major rotamer are listed): δ 172.5, 172.0, 170.9, 135.2, 130.2, 128.6, 127.1, 57.1, 52.6, 52.1, 46.1, 30.9, 25.5, 25.3, 20.5, 19.2, 17.7;

HRMS (ESI): Calc'd for $C_{19}H_{27}N_2O_4$ $[M+H]^+$: 347.1965, found: 347.1959.



3b

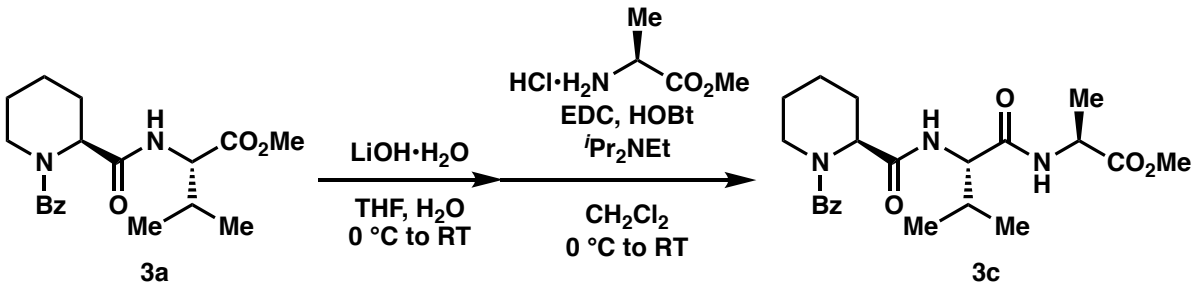
Methyl (*S*)-1-(Benzoyl-*L*-alanyl)piperidine-2-carboxylate (3b) was prepared from methyl (*S*)-piperidine-2-carboxylate (*55*) and *N*-benzoyl-*L*-alanine according to the representative procedure. The title compound was obtained as a colorless foam (1.37 g, 86% over 2 steps).

Optical Rotation: $[\alpha]^{22}_{D} = -54$ (*c* 1.7, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$, *ca.* 4:4:1:1 mixture of rotamers): δ 7.78 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.42–7.41 (m, 1H), 7.38 (t, *J* = 7.5 Hz, 2H), 5.35 (d, *J* = 5.3 Hz, 0.4H), 5.29 (d, *J* = 5.3 Hz, 0.4H), 5.14 (quint, *J* = 6.8 Hz, 0.4H), 5.10 (quint, *J* = 6.8 Hz, 0.4H), 5.04 (quint, *J* = 6.8 Hz, 0.1H), 4.94 (quint, *J* = 6.8 Hz, 0.1H), 4.87 (d, *J* = 4.0 Hz, 0.1H), 4.62 (d, *J* = 4.9 Hz, 0.1H), 4.54 (d, *J* = 12.8 Hz, 0.1H), 4.48 (d, *J* = 13.9 Hz, 0.1H), 3.86 (d, *J* = 12.8 Hz, 0.4H), 3.80 (d, *J* = 13.3 Hz, 0.4H), 3.75 (s, 0.3H), 3.70 (s, 1.2H), 3.68 (s, 1.2H), 3.59 (s, 0.3H), 3.28–3.21 (m, 0.8H), 2.77–2.69 (m, 0.2H), 2.33 (d, *J* = 13.6 Hz, 0.1H), 2.27–2.23 (m, 0.9H), 1.72–1.71 (m, 2H), 1.65–1.59 (m, 1H), 1.51–1.28 (m, 3H), 1.42 (d, *J* = 6.8 Hz, 1.5H), 1.41 (d, *J* = 6.8 Hz, 1.5H);

^{13}C NMR (151 MHz, $CDCl_3$, peaks of 2 major rotamers are listed): δ 172.6, 172.4, 171.3, 171.2, 166.3, 166.2, 134.2, 134.2, 131.5, 128.5, 128.5, 127.1, 127.0, 52.5, 52.4, 52.3, 52.3, 46.0, 45.8, 43.5, 43.4, 26.6, 26.4, 25.2, 25.1, 20.9, 19.6, 18.2 (*Two ^{13}C signals are overlapping with others)*;

HRMS (ESI): Calc'd for $C_{17}H_{22}N_2O_4Na$ $[M+Na]^+$: 341.1472, found: 341.1471.



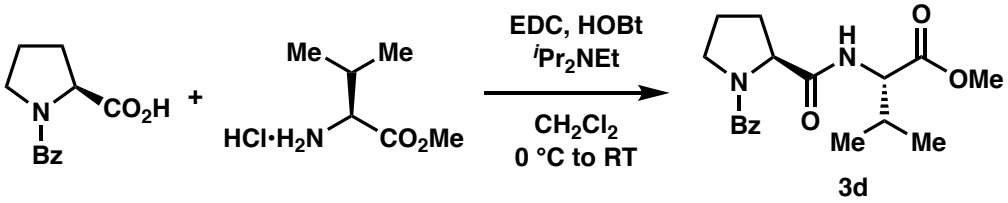
Methyl ((*S*)-1-Benzoylpiperidine-2-carbonyl)-*L*-valyl-*L*-alaninate (3c) was prepared from **3a** and *L*-alanine methyl ester hydrochloride according to the representative procedure. The title compound was obtained as a white amorphous solid (864 mg, 69% over 2 steps).

Optical Rotation: $[\alpha]^{22}_{D} = -105$ (*c* 2.01, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$, *ca.* 4:1 mixture of rotamers): δ 7.43 (br s, 5H), 7.17 (d, *J* = 7.3 Hz, 0.8H), 6.79 (br, 0.2H), 6.62 (d, *J* = 5.0 Hz, 0.8H), 6.46 (br, 0.2H), 5.29 (s, 0.8H), 4.79 (br, 0.2H), 4.58 (quint, *J* = 7.2 Hz, 1H), 4.35 (br, 0.2H), 4.33–4.30 (m, 1H), 3.74 (s, 3H), 3.71 (br, 0.8H), 3.05 (t, *J* = 12.8 Hz, 0.8H), 2.88 (br, 0.2H), 2.32–2.12 (m, 2H), 1.85–1.52 (m, 5H), 1.41 (d, *J* = 7.2 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 6H);

^{13}C NMR (151 MHz, $CDCl_3$, peaks of major rotamer are listed): δ 173.2, 172.7, 171.3, 170.5, 135.2, 130.4, 128.7, 127.3, 58.4, 53.0, 52.5, 48.2, 46.2, 30.8, 25.7, 25.5, 20.8, 19.5, 18.2, 17.9;

HRMS (ESI): Calc'd for $C_{22}H_{31}N_3O_5Na$ $[M+Na]^+$: 440.2156, found: 440.2151.



Methyl Benzoyl-*L*-prolyl-*L*-valinate (3d) was prepared from *N*-benzoyl-*L*-proline (*56*) and *L*-valine methyl ester hydrochloride according to the representative procedure. The title compound was obtained as a white solid (538 mg, 81%).

Melting Point: 104–106 °C;

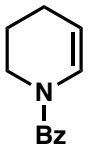
Optical Rotation: $[\alpha]^{22}_{D} = -142$ (*c* 0.960, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45–7.38 (m, 5H), 7.33 (br, 1H), 4.80 (s, 1H), 4.49 (t, *J* = 6.4 Hz, 1H), 3.71 (s, 3H), 3.51 (s, 1H), 3.44 (s, 1H), 2.43 (s, 1H), 2.18–2.16 (m, 1H), 2.02 (s, 2H), 1.81 (s, 1H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.89 (d, *J* = 6.4 Hz, 3H);

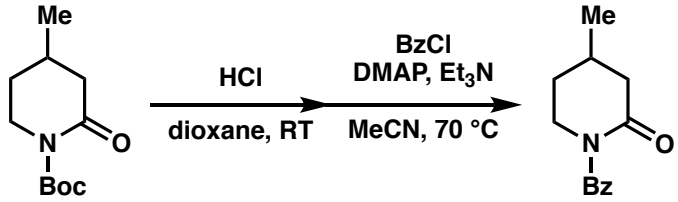
^{13}C NMR (151 MHz, $CDCl_3$): δ172.2, 171.1, 171.0, 136.4, 130.3, 128.5, 127.0, 59.8, 57.6, 52.1, 50.4, 31.1, 27.1, 25.5, 19.2, 17.8;

HRMS (ESI): Calc'd for $C_{18}H_{24}N_2O_4Na$ $[M+Na]^+$: 355.1628, found: 355.1627.

2.3. Preparation of Enamides



(3,4-Dihydropyridin-1(2*H*)-yl)(phenyl)methanone (10a) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*57*).



S2

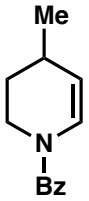
A 100 mL round-bottomed flask was charged with a solution of *tert*-butyl 4-methyl-2-oxopiperidine-1-carboxylate (*58*) (2.00 g, 9.38 mmol) in dioxane (40 mL) and cooled to 0 °C. HCl (4.0 M solution in dioxane, 7.00 mL, 28.1 mmol) was added and the resulting mixture was warmed to room temperature. After 16 h, the reaction mixture was concentrated under reduced pressure to afford a white solid, which was used in the next step without further purification. The solid was dissolved in MeCN (30 mL) and the resulting solution was cooled to 0 °C. To this solution was added Et_3N (3.92 mL, 28.1 mmol), DMAP (115 mg, 0.938 mmol) and BzCl (1.31 mL, 11.3 mmol) and the reaction mixture was heated to 70 °C. After 12 h, H_2O (1.0 mL) was added and the reaction mixture was allowed to continue to stir at 70 °C for an additional 1 h. The solution was then allowed to cool to room temperature, poured into a separatory funnel, and washed with sat. $NaHCO_3$ aq. (20 mL). The aqueous phase was extracted with EtOAc (10 mL × 2). The combined organic layers were washed with 1 M HCl (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, 5% to 15% EtOAc/ hexanes) to provide **S2** (1.47 g, 73% over 2 steps) as a white solid.

Melting Point: 74–77 °C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.4 Hz, 2H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 2H), 3.95 (dt, *J* = 12.9, 4.3 Hz, 1H), 3.64 (ddd, *J* = 12.9, 11.5, 4.0 Hz, 1H), 2.59 (ddd, *J* = 16.4, 4.6, 1.9 Hz, 1H), 2.23 (dd, *J* = 16.4, 10.9 Hz, 1H), 2.13–2.05 (m, 2H), 1.65–1.57 (m, 1H), 1.10 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.8, 173.4, 136.2, 131.6, 128.2, 128.0, 45.4, 42.9, 30.9, 28.8, 21.3;

HRMS (ESI): Calc'd for $C_{13}H_{16}NO_2$ $[M+H]^+$: 218.1176, found: 218.1183.

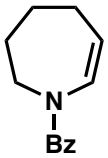


(4-Methyl-3,4-dihydropyridin-1(2*H*)-yl)(phenyl)methanone (10b) was prepared from **S2** according to a published procedure (*57*). The title compound was obtained as a colorless oil (323 mg, 74%).

^{1}H NMR (500 MHz, $CDCl_3$, *ca.* 3:1 mixture of conformers): δ 7.45–7.35 (m, 5H), 7.22 (br, 0.25H), 6.37 (d, *J* = 7.9 Hz, 0.75H), 5.08 (br, 0.25H), 4.68 (d, *J* = 7.9 Hz, 0.75H), 4.03 (br, 0.75H), 3.59–3.55 (m, 1H), 3.47 (br, 0.25H), 2.34 (br, 1H), 2.02 (br, 0.75H), 1.83 (br, 0.25H), 1.55 (br, 0.75H), 1.40 (br, 0.25H), 1.02 (d, *J* = 7.0 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$, peaks of major conformer are listed): δ 169.3, 135.1, 130.2, 128.4, 128.2, 126.3, 113.8, 39.9, 30.0, 27.4, 21.3;

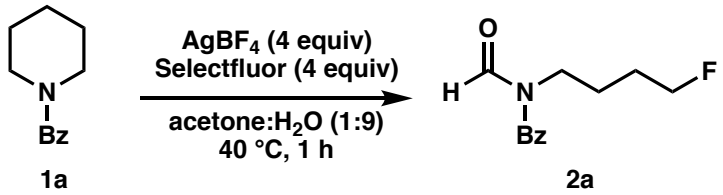
HRMS (ESI): Calc'd for $C_{13}H_{16}NO$ $[M+H]^+$: 202.1226, found: 202.1226.



Phenyl(2,3,4,5-tetrahydro-1*H*-azepin-1-yl)methanone (10c) was prepared according to a published procedure. Spectral data were in full agreement with the reported literature values (*59*).

3. Experimental Procedures for the Silver-Mediated Fluorination

3.1. Representative Procedure for the Silver-Mediated Monofluorination of Cyclic Amines



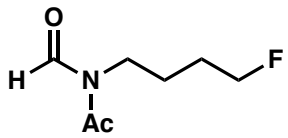
To a 1-dram vial was added sequentially **1a** (18.9 mg, 0.100 mmol), $AgBF_4$ (77.9 mg, 0.400 mmol), Selectfluor® (142 mg, 0.400 mmol) and 1:9 acetone: H_2O (0.5 mL) The resulting mixture was heated to 40 °C and held at this temperature. After 1 h, the reaction mixture was partitioned with EtOAc (0.5 mL) and H_2O (0.5 mL) and the phases were separated. The aqueous phase was extracted with EtOAc (1.5 mL × 3) and the combined organic layers were concentrated under reduced pressure. The crude residue was purified by preparative thin-layer chromatography (50% EtOAc/hexanes) to provide *N*-(4-fluorobutyl)-*N*-formylbenzamide (**2a**) (18.0 mg, 81%) as a pale yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.93 (s, 1H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.53–7.48 (m, 4H), 4.48 (dt, *J* = 47.6, 5.6 Hz, 2H), 3.92 (t, *J* = 7.1 Hz, 2H), 1.82–1.72 (m, 4H);

^{13}C NMR (151 MHz, $CDCl_3$): 172.5, 164.3, 133.7, 132.3, 129.1, 128.9, 83.6 (d, *J* = 165.2 Hz), 40.2, 28.0 (d, *J* = 20.2 Hz), 24.2 (d, *J* = 5.0 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −217.5 – −217.9 (m, 1F);

HRMS (ESI): Calc'd for $C_{12}H_{14}FNO_2Na$ $[M+Na]^+$: 246.0906, found: 246.0906.



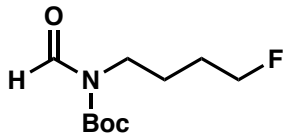
***N*-(4-Fluorobutyl)-*N*-formylacetamide (2b):** The title compound was prepared according to the representative procedure using **1b**. Purification by preparative thin-layer chromatography (25% EtOAc/hexanes) provided the title compound (7.2 mg, 45%) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 9.16 (s, 1H), 4.45 (dt, *J* = 47.0, 5.7 Hz, 2H), 3.73 (t, *J* = 7.3 Hz, 2H), 2.41 (s, 3H), 1.74–1.62 (m, 4H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 171.2, 162.8, 83.6 (d, *J* = 165.3 Hz), 39.6, 27.9 (d, *J* = 20.0 Hz), 24.3 (d, *J* = 4.3 Hz), 23.0;

^{19}F NMR (376 MHz, $CDCl_3$): δ −217.8 (tt, *J* = 47.9, 24.4 Hz, 1F);

HRMS (EI): Calc'd for $C_7H_{13}FNO_2$ $[M+H]^+$: 162.0925, found: 162.0933.



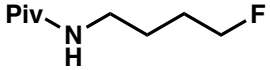
***tert*-Butyl (4-Fluorobutyl)(formyl)carbamate (2c):** The title compound was prepared according to the representative procedure using **1c**. Purification by preparative thin-layer chromatography (25% EtOAc/hexanes) provided the title compound (8.6 mg, 39%) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 9.17 (s, 1H), 4.45 (dt, *J* = 47.0, 5.7 Hz, 2H), 3.63 (t, *J* = 7.1 Hz, 2H), 1.73–1.63 (m, 4H), 1.54 (s, 9H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 163.2, 152.6, 84.2, 83.6 (d, *J* = 165.2 Hz), 40.2, 28.2, 27.8 (d, *J* = 20.0 Hz), 24.4 (d, *J* = 5.0 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −217.9 (tt, *J* = 48.1, 25.7 Hz, 1F);

HRMS (ESI): Calc'd for $C_{10}H_{19}FNO_3$ $[M+H]^+$: 220.1343, found: 220.1351.



***N*-(4-Fluorobutyl)pivalamide (2d):** The title compound was prepared according to the representative procedure using **1d**. Purification by preparative thin-layer chromatography (25% EtOAc/hexanes) provided the title compound (12.3 mg, 70%) as a white solid.

Melting Point: 67–69 °C;

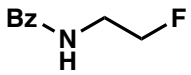
^{1}H NMR (600 MHz, $CDCl_3$): δ 5.70 (br, 1H), 4.47 (dt, *J* = 47.2, 5.8 Hz, 2H), 3.29 (t, *J* = 6.8 Hz, 2H), 1.76–

1.61 (m, 4H), 1.19 (s, 9H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 178.6, 83.9 (d, *J* = 164.6 Hz), 39.1, 38.8, 27.9 (d, *J* = 19.9 Hz), 27.7, 25.9 (d, *J* = 4.4 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −219.0 (tt, *J* = 47.4, 25.8 Hz, 1F);

HRMS (ESI): Calc'd for $C_9H_{19}FNO$ $[M+H]^+$: 176.1445, found: 176.1442.



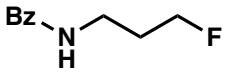
***N*-(2-Fluoroethyl) benzamide (2e):** The title compound was prepared according to the representative procedure using **1e**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (6.7 mg, 40%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.5 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 6.63 (br, 1H), 4.60 (dt, *J* = 47.4, 4.9 Hz, 2H), 3.77 (dq, *J* = 28.3, 4.9 Hz, 2H);

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.8, 134.2, 131.8, 128.7, 127.1, 83.0 (d, *J* = 166.4 Hz), 40.6 (d, *J* = 19.7 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −223.0 – −223.5 (m, 1F);

HRMS (ESI): Calc'd for $C_9H_{11}FNO$ $[M+H]^+$: 168.0819, found: 168.0825.



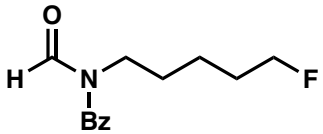
***N*-(3-Fluoropropyl) benzamide (2f):** The title compound was prepared according to the representative procedure using **1f**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (6.0 mg, 33%) as a pale yellow waxy solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 6.9 Hz, 2H), 7.51 (t, *J* = 6.9 Hz, 1H), 7.43 (t, *J* = 6.9 Hz, 2H), 6.44 (br, 1H), 4.61 (dt, *J* = 47.3, 6.0 Hz, 2H), 3.63 (q, *J* = 6.0 Hz, 2H), 2.04 (dquint, J = 28.2, 6.0 Hz, 2H);

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.8, 134.6, 131.6, 128.7, 127.0, 83.0 (d, *J* = 163.9 Hz), 37.4 (d, *J* = 4.1 Hz), 30.3 (d, *J* = 19.2 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −218.9 – −219.3 (m, 1F);

HRMS (ESI): Calc'd for $C_{10}H_{13}FNO$ $[M+H]^+$: 182.0976, found: 182.0976.



***N*-(5-Fluoropentyl)-*N*-formylbenzamide (2g):** The title compound was prepared according to the representative procedure using **1g**. Purification by preparative thin-layer chromatography (50%

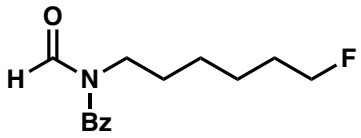
EtOAc/hexanes) provided the title compound (15.6 mg, 67%) as a colorless oil.

^{1}H NMR (700 MHz, $CDCl_3$): δ 8.92 (s, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 2H), 4.45 (dt, *J* = 47.3, 6.1 Hz, 2H), 3.88 (t, *J* = 7.5 Hz, 2H), δ 1.81–1.68 (m, 4H), 1.49 (quint, J = 7.5 Hz, 2H);

^{13}C NMR (176 MHz, $CDCl_3$): δ 172.5, 164.4, 133.7, 132.3, 129.1, 128.9, 83.9 (d, *J* = 164.7 Hz), 40.5, 30.1 (d, *J* = 19.8 Hz), 27.7, 22.8 (d, *J* = 5.3 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −217.9 (tt, *J* = 47.3, 25.5 Hz, 1F);

HRMS (ESI): Calc'd for $C_{13}H_{17}FNO_2$ $[M+H]^+$: 238.1238, found: 238.1238.



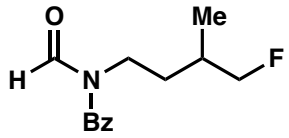
***N*-(6-Fluorohexyl)-N-formylbenzamide (2h):** The title compound was prepared according to the representative procedure using **1h**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (12.4 mg, 49%) as a colorless oil.

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.92 (s, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.53–7.48 (m, 4H), 4.47 (dt, *J* = 47.3, 6.0 Hz, 2H), 3.87 (t, *J* = 7.4 Hz, 2H), 1.73–1.63 (m, 4H), 1.47–1.41 (m, 4H);

^{13}C NMR (176 MHz, $CDCl_3$) δ 172.5, 164.4, 133.8, 132.3, 129.1, 128.9, 84.2 (d, *J* = 164.4 Hz), 40.6, 30.4 (d, *J* = 19.7 Hz), 28.0, 26.7, 25.0 (d, *J* = 5.2 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −217.5 (tt, *J* = 48.9, 24.5 Hz, 1F);

HRMS (ESI): Calc'd for $C_{14}H_{18}FNO_2Na$ $[M+Na]^+$: 274.1214, found: 274.1216.



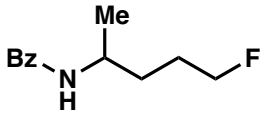
***N*-(4-Fluoro-3-methylbutyl)-*N*-formylbenzamide (2i):** The title compound was prepared according to the representative procedure using **1i**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (14.0 mg, 59%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.92 (s, 1H), 7.60–7.47 (m, 5H), 4.32 (ddd, *J* = 47.5, 8.9, 5.7 Hz, 1H), 4.29 (ddd, *J* = 47.5, 8.9, 5.9 Hz, 1H), 3.94 (t, *J* = 7.6 Hz, 2H), 1.98–1.77 (m, 2H), 1.58–1.47 (m, 1H), 1.05 (dd, *J* = 6.7, 0.9 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$): δ 172.4, 164.3, 133.7, 132.4, 129.1, 128.9, 88.0 (d, *J* = 169.7 Hz), 38.8, 32.4 (d, *J* = 18.5 Hz), 31.1 (d, *J* = 5.1 Hz), 15.8 (d, *J* = 6.8 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −221.2 (td, *J* = 47.4, 19.4 Hz, 1F);

HRMS (ESI): Calc'd for $C_{12}H_{16}FNONa$ $[M-CO+Na]^+$: 232.1108, found: 232.1107.



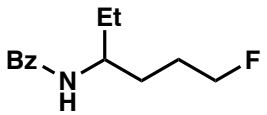
***N*-(5-Fluoropentan-2-yl)benzamide (2j):** The title compound was prepared according to the representative procedure using **1j**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (17.0 mg, 81%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.3 Hz, 1H), 7.42 (d, *J* = 7.3 Hz, 2H), 5.96 (br, 1H), 4.47 (dddd, *J* = 47.2, 9.0, 6.4, 3.7 Hz, 2H), 4.26 (hept, *J* = 6.6 Hz, 1H), 1.86–1.60 (m, 4H), 1.27 (d, *J* = 6.6 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.1, 134.9, 131.5, 128.7, 126.9, 83.9 (d, *J* = 164.8 Hz), 45.5, 33.0 (d, *J* = 4.3 Hz), 27.3 (d, *J* = 19.9 Hz), 21.3;

^{19}F NMR (376 MHz, $CDCl_3$): δ −217.6 – −218.0 (m, 1F);

HRMS (ESI): Calc'd for $C_{12}H_{16}FNONa$ $[M+Na]^+$: 232.1108, found: 232.1111.



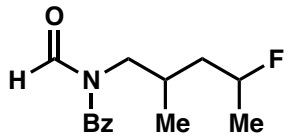
***N*-(6-Fluorohexan-3-yl) benzamide (2k):** The title compound was prepared according to the representative procedure using **1k**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (19.0 mg, 85%) as a colorless oil.

^{1}H NMR (700 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 5.92 (br, 1H), 4.53–4.41 (m, 2H), 4.11 (ddq, *J* = 13.6, 8.9, 4.9 Hz, 1H), 1.85–1.72 (m, 3H), 1.70–1.64 (m, 1H), 1.60–1.49 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 167.6, 134.9, 131.5, 128.7, 126.9, 84.0 (d, *J* = 164.7 Hz), 50.8, 30.9 (d, *J* = 4.4 Hz), 28.4, 27.2 (d, *J* = 19.8 Hz), 10.5;

^{19}F NMR (376 MHz, $CDCl_3$): δ −217.8 – −218.2 (m, 1F);

HRMS (ESI): Calc'd for $C_{13}H_{19}FNO$ $[M+H]^+$: 224.1445, found: 224.1450.



***N*-(4-Fluoro-2-methylpentyl)-*N*-formylbenzamide (2l):** The title compound was prepared according to the representative procedure using **1l**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (12.6 mg, 50%) as a colorless oil as a 1:1 mixture of

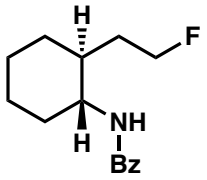
diastereomers.

^{1}H NMR (400 MHz, $CDCl_3$): (400 MHz, 1H), 8.95 (s, 1H), 7.59–7.47 (m, 10H), 4.91–4.68 (m, 2H), 3.88–3.74 (m, 4H), 2.25– 2.10 (m, 2H), 1.80–1.49 (m, 3H), 1.42–1.26 (m, 1H), 1.34 (dd, J = 23.7, 6.1 Hz, 3H), 1.33 (dd, J = 23.7, 6.1 Hz, 3H), 1.00 (d, J = 6.6 Hz, 3H), 0.99 (d, J = 6.6 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$): δ 172.7 (2C), 164.7, 164.6, 133.84, 133.79, 132.4, 132.3, 129.14, 129.13, 128.94, 128.92, 89.6 (d, J = 164.6 Hz), 88.7 (d, J = 165.0 Hz), 46.0, 45.8, 41.90 (d, J = 20.7 Hz), 41.86 (d, J = 20.6 Hz), 29.7 (d, J = 4.0 Hz), 29.1 (d, J = 2.9 Hz), 21.8 (d, J = 22.6 Hz), 21.4 (d, J = 22.8 Hz), 18.3, 17.6;

^{19}F NMR (376 MHz, $CDCl_3$): δ −169.8 – −170.3 (m, 1F), −172.6 – −173.1 (m, 1F);

HRMS (ESI): Calc'd for $C_{14}H_{18}FNO_2Na$ $[M+Na]^+$: 274.1214, found: 274.1212.



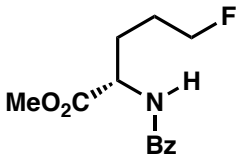
***trans*-*N*-(2-(2-Fluoroethyl)cyclohexyl)benzamide (2m):** The title compound was prepared according to the representative procedure using **1m**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (10.7 mg, 43%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 7.3 Hz, 2H), 7.50 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.3 Hz, 2H), 5.92 (br, 1H), 4.52 (ddd, J = 47.4, 7.2, 3.7 Hz, 2H), 3.83 (dq, J = 10.6, 3.9 Hz, 1H), 2.16–2.05 (m, 2H), 2.00–1.96 (m, 1H), 1.81–1.74 (m, 2H), 1.63–1.09 (m, 6H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 167.2, 135.0, 131.5, 128.7, 127.0, 82.4 (d, J = 163.6 Hz), 53.0, 40.1 (d, J = 3.3 Hz), 34.2, 33.8 (d, J = 19.5 Hz), 31.6, 25.7, 25.4;

^{19}F NMR (400 MHz, $CDCl_3$): δ −217.5 – −217.9 (m, 1F);

HRMS (ESI): Calc'd for $C_{15}H_{21}FNO$ $[M+H]^+$: 250.1602, found: 250.1595.



Methyl (*S*)-2-Benzamido-5-fluoropentanoate (2n): The title compound was prepared according to the representative procedure using **1n**. Purification by preparative thin-layer chromatography (25% EtOAc/hexanes) provided the title compound (17.2 mg, 68%) as a white solid.

Melting Point: 63–65 °C;

Optical Rotation: $[\alpha]^{22}_D$ = +17 (c 0.67, $CHCl_3$);

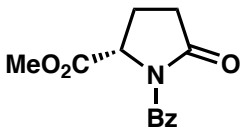
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.80 (d, J = 7.4 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.4 Hz, 2H), 6.78 (d, J = 7.4 Hz, 1H), 4.87 (dt, J = 7.4, 5.3 Hz, 1H), 4.54–4.41 (m, 2H), 3.79 (s, 3H), 2.16–2.10 (m, 1H),

1.95–1.89 (m, 1H), 1.88–1.72 (m, 2H);

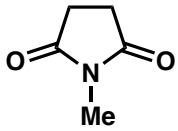
^{13}C NMR (151 MHz, $CDCl_3$): δ 172.9, 167.2, 133.9, 132.0, 128.8, 127.2, 83.4 (d, *J* = 165.5 Hz), 52.7, 52.2, 28.9 (d, *J* = 4.7 Hz), 26.6 (d, *J* = 20.2 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −218.4 (tt, *J* = 47.3, 25.7 Hz, 1F);

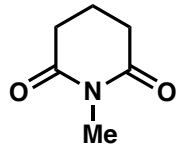
HRMS (ESI): Calc'd for $C_{13}H_{17}FNO_3$ $[M+H]^+$: 254.1187, found: 254.1185.



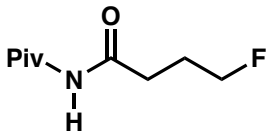
Methyl (*S*)-1-Benzoyl-5-oxopyrrolidine-2-carboxylate (1o): The title compound was prepared according to the representative procedure using **1o**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (11.4 mg, 46% yield). Spectroscopic data is fully consistent with previously reported data (*60*).



1-Methylpyrrolidine-2,5-dione (1p): The title compound was prepared according to the representative procedure using **1p**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (9.2 mg, 81% yield). Spectroscopic data is fully consistent with previously reported data (*10*).



1-Methylpiperidine-2,6-dione (1q): The title compound was prepared according to the representative procedure using **1p**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (7.1 mg, 56% yield). Spectroscopic data is fully consistent with previously reported data (*10*).



4-Fluoro-*N*-pivaloylbutanamidebenzamide (2r): The title compound was prepared according to the representative procedure using **1r**. Purification by preparative thin-layer chromatography (30%

EtOAc/hexanes) provided the title compound (8.1 mg, 43% yield) as a white solid.

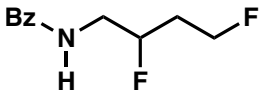
Melting Point: 63–65 °C;

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (br, 1H), 4.51 (dt, *J* = 47.2, 5.9 Hz, 2H), 3.01 (t, *J* = 7.2 Hz, 2H), 2.05 (ddd, *J* = 25.8, 7.2, 5.9 Hz, 2H), 1.25 (s, 9H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 177.2, 175.3, 83.2 (d, *J* = 165.1 Hz), 40.2, 33.4 (d, *J* = 5.2 Hz), 27.2, 25.0 (d, *J* = 20.3 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −219.1 (tt, *J* = 47.2, 25.8 Hz, 1F);

HRMS (ESI): Calc'd for $C_9H_{17}FNO_2$ $[M+H]^+$: 190.1238, found: 190.1245.



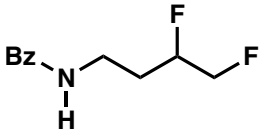
***N*-(2,4-Difluorobutyl)benzamide (2s):** The title compound was prepared according to the representative procedure using **1s**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (6.0 mg, 28% yield) as a waxy white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.3 Hz, 2H), 6.52 (br, 1H), 4.90 (dtt, *J* = 48.4, 7.2, 3.6 Hz, 1H), 4.62 (dt, *J* = 47.3, 5.9 Hz, 2H), 3.89 (dddd, *J* = 28.2, 14.7, 6.6, 3.0 Hz, 1H), 3.66–3.54 (m, 1H), 2.20–1.93 (m, 2H);

^{13}C NMR (101 MHz, $CDCl_3$): δ167.8, 134.1, 131.9, 128.8, 127.1, 89.8 (dd, *J* = 169.6, 3.6 Hz), 79.7 (dd, *J* = 165.6, 5.1 Hz), 43.6 (d, *J* = 20.1 Hz), 33.5 (t, *J* = 20.1 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −188.7 – −189.1 (m, 1F), −220.3 – −220.7 (m, 1F);

HRMS (ESI): Calc'd for $C_{11}H_{14}F_2NO$ $[M+H]^+$: 214.1038, found: 214.1038.



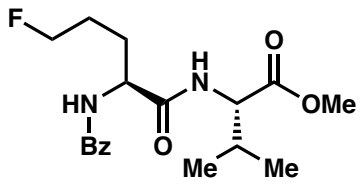
***N*-(3,4-Difluorobutyl)benzamide (2t):** The title compound was prepared according to the representative procedure using **1t**. Purification by preparative thin-layer chromatography (50% EtOAc/hexanes) provided the title compound (4.7 mg, 22% yield) as a waxy white solid.

^{1}H NMR (700 MHz, $CDCl_3$) 7.78 (d, *J* = 7.4 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.46–7.41 (m, 2H), 6.45 (br, 1H), 4.98–4.74 (m, 1H), 4.69–4.41 (m, 2H), 3.73–3.62 (m, 2H), 2.14–1.98 (m, 2H);

^{13}C NMR (176 MHz, $CDCl_3$) δ 167.9, 134.4, 131.8, 128.8, 127.0, 90.8 (dd, *J* = 172.6, 19.7 Hz), 84.0 (dd, *J* = 174.5, 22.4 Hz), 36.5 (d, *J* = 4.3 Hz), 36.5 (dd, *J* = 20.2, 6.0 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −189.5 – −190.0 (m, 1F), −229.4 – −229.8 (m, 1F);

HRMS (ESI): Calc'd for $C_{11}H_{14}F_2NO$ $[M+H]^+$: 214.1038, found: 214.1038.



Methyl ((*S*)-2-Benzamido-5-fluoropentanoyl)-*L*-valinate (4a): The title compound was prepared according to the representative procedure using **3a** with the following modifications: reaction time of 15 h at room temperature. Purification by preparative thin-layer chromatography (20% to 50% EtOAc/hexanes) provided the title compound (17.5 mg, 50% yield) as a white amorphous solid along with recovered **3a** (8.7 mg, 25%).

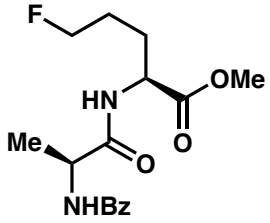
Optical Rotation: $[\alpha]^{22}_{D} = -13$ (*c* 0.47, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.4 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.80 (t, *J* = 7.4 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 1H), 6.89 (d, *J* = 8.5 Hz, 1H), 4.84 (q, *J* = 8.5 Hz, 1H), 4.51 (dd, *J* = 8.3, 5.0 Hz, 1H), 4.50 (dt, *J* = 47.4, 5.7 Hz, 2H), 3.75 (s, 3H), 2.21–2.14 (m, 1H), 2.09 (ddt, *J* = 13.4, 9.4, 6.1 Hz, 1H), 1.97–1.76 (m, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 172.1, 171.6, 167.5, 133.8, 132.0, 128.7, 127.2, 83.9 (d, *J* = 164.8 Hz), 57.6, 53.0, 52.3, 31.1, 29.1 (d, *J* = 4.1 Hz), 26.6 (d, *J* = 20.0 Hz), 19.1, 17.8;

^{19}F NMR (376 MHz, $CDCl_3$): δ −217.1 – −217.5 (m, 1F);

HRMS (ESI): Calc'd for $C_{18}H_{25}FN_2O_4Na$ $[M+Na]^+$: 375.1691, found: 375.1692.



Methyl (*S*)-2-((*S*)-2-Benzamidopropanamido)-5-fluoropentanoate (4b): The title compound was prepared according to the representative procedure using **3b** with the following modifications: reaction time of 15 h at room temperature. Purification by preparative thin-layer chromatography (20% to 50% EtOAc/hexanes) provided the title compound (12.3 mg, 38% yield) as a white amorphous solid along with recovered **3b** (12.7 mg, 40%).

Optical Rotation: $[\alpha]^{22}_{D} = +7.1$ (*c* 0.63, $CHCl_3$);

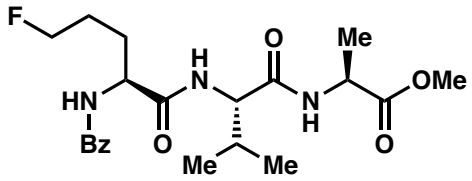
^{1}H NMR (600 MHz, $CDCl_3$, *ca.* 1:1 mixture of rotamers): δ 7.81–7.79 (m, 2H), 7.52–7.49 (m, 1H), 7.45–7.40 (m, 2H), 7.33 (d, *J* = 7.9 Hz, 0.5H), 7.23 (d, *J* = 7.9 Hz, 0.5H), 7.09 (d, *J* = 7.3 Hz, 1H), 4.83 (dq, *J* = 14.3, 7.3 Hz, 1H), 4.63–4.59 (m, 1H), 4.49–4.47 (m, 0.5H), 4.42–4.39 (m, 1H), 4.34–4.32 (m, 0.5H), 3.75 (s, 1.5H), 3.68 (s, 1.5H), 2.03–1.98 (m, 1H), 1.86–1.66 (m, 3H), 1.495 (d, *J* = 7.0 Hz, 1.5H), 1.491 (d, *J* = 7.0 Hz, 1.5H);

^{13}C NMR (151 MHz, $CDCl_3$, mixture of rotamers): δ 172.6, 172.5, 172.4, 172.3, 167.5, 167.4, 133.9 (2C), 131.9 (2C), 128.7 (2C), 127.23, 127.20, 82.23 (d, *J* = 165.7 Hz), 82.20 (d, *J* = 165.7 Hz), 52.61, 52.58, 52.1,

52.0, 49.29, 49.26, 28.33 (d, J = 4.7 Hz), 28.30 (d, J = 4.7 Hz), 26.61 (d, J = 20.2 Hz), 26.55 (d, J = 20.2 Hz), 18.7, 18.6;

^{19}F NMR (376 MHz, $CDCl_3$): δ −218.4 – −218.9 (m, 1F);

HRMS (ESI): Calc'd for $C_{16}H_{21}FN_2O_4Na$ $[M+Na]^+$: 347.1378, found: 347.1379.



Methyl ((*S*)-2-Benzamido-5-fluoropentanoyl)-*L*-valyl-*L*-alaninate (4c): The title compound was prepared according to the representative procedure using **3c** with the following modifications: reaction time of 15 h at room temperature. Purification by preparative thin-layer chromatography (5% $MeOH/CH_2Cl_2$) provided the title compound (16.5 mg, 39% yield) as a white amorphous solid along with recovered **3c** (10.4 mg, 25%).

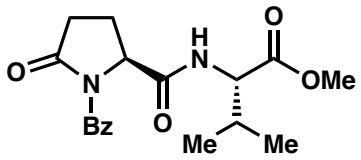
Optical Rotation: $[\alpha]^{22}_D$ = −41 (*c* 0.39, MeOH);

^{1}H NMR (700 MHz, CD_3OD): δ 7.85–7.84 (m, 2H), 7.55–7.53 (m, 1H), 7.47–7.45 (m, 2H), 4.64 (dt, J = 8.8, 4.7 Hz, 1H), 4.47 (d, J = 47.6 Hz, 2H), 4.39 (dt, J = 13.5, 6.7 Hz, 1H), 4.24 (dd, J = 6.6, 4.2 Hz, 1H), 3.69 (s, 3H), 2.08 (dt, J = 12.1, 5.5 Hz, 1H), 2.01 (tt, J = 10.4, 5.3 Hz, 1H), 1.90–1.77 (m, 3H), 1.39 (br s, 3H), 0.99 (br s, 9H);

^{13}C NMR (176 MHz, CD_3OD): δ 174.4, 174.2, 173.3, 170.5, 135.2, 132.9, 129.6, 128.5, 84.4 (d, J = 164.3 Hz), 59.8, 55.0, 52.6, 49.4, 32.3, 28.9 (d, J = 5.3 Hz), 28.3 (d, J = 20.0 Hz), 19.6, 18.6, 17.3;

^{19}F NMR (376 MHz, CD_3OD): δ −219.7 (tt, J = 47.7, 24.8 Hz, 1F);

HRMS (ESI): Calc'd for $C_{21}H_{30}FN_3O_5Na$ $[M+Na]^+$: 446.2062, found: 446.2060.



Methyl ((*S*)-1-Benzoyl-5-oxopyrrolidine-2-carbonyl)-*L*-valinate (4d): The title compound was prepared according to the representative procedure using **3d** with the following modifications: 0.2 mmol scale with a reaction time of 15 h at room temperature. Purification by preparative thin-layer chromatography (20% to 50% EtOAc/hexanes) provided the title compound (52.6 mg, 76% yield) as a white solid.

Melting Point: 155–158 °C;

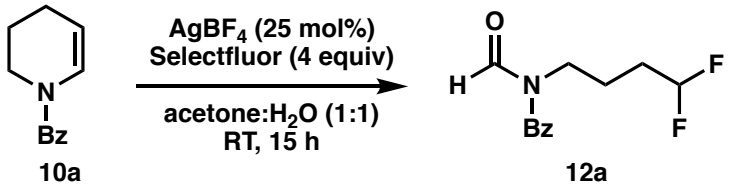
Optical Rotation: $[\alpha]^{22}_D$ = −256 (*c* 0.46, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.62–7.61 (m, 2H), 7.52–7.48 (m, 1H), 7.40 (t, J = 7.8 Hz, 2H), 4.83 (dd, J = 8.3, 3.6 Hz, 1H), 4.57 (dd, J = 8.9, 4.8 Hz, 1H), 3.75 (s, 3H), 2.89–2.83 (m, 1H), 2.53 (ddd, J = 17.8, 9.1, 4.3 Hz, 1H), 2.36–2.25 (m, 2H), 2.23–2.17 (m, 1H), 0.95 (d, J = 6.9 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 174.1, 172.4, 170.9, 170.4, 134.0, 132.2, 129.0, 128.0, 60.0, 57.5, 52.4, 32.1, 31.4, 22.2, 19.0, 17.8;

HRMS (ESI): Calc'd for $C_{18}H_{23}N_2O_5$ $[M+H]^+$: 347.1601, found: 347.1599.

3.2. Representative Procedure for the Silver-Mediated Difluorination of Enamides



10a **12a**

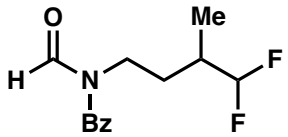
To a 1-dram vial containing a solution of **10a** (18.7 mg, 0.100 mmol) in 1:1 acetone: H_2O (0.5 mL) was added Selectfluor® (142 mg, 0.400 mmol) followed by $AgBF_4$ (4.9 mg, 0.025 mmol). The resulting mixture was stirred at room temperature. After 15 h, the reaction mixture was partitioned with EtOAc (0.5 mL) and H_2O (0.5 mL) and the phases were separated. The aqueous phase was extracted with EtOAc (1.5 mL × 3) and the combined organic layers were concentrated under reduced pressure. The crude residue was purified by preparative thin-layer chromatography (25% EtOAc/hexanes) to provide *N*-(4,4-difluorobutyl)-*N*-formylbenzamide (**12a**) (18.7 mg, 78%) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.93 (s, 1H), 7.59 (d, *J* = 7.1 Hz, 1H), 7.54–7.49 (m, 4H), 5.87 (tt, *J* = 56.5, 4.2 Hz, 1H), 3.93 (t, *J* = 7.2 Hz, 2H), 1.96–1.82 (m, 4H);

^{13}C NMR (151 MHz, $CDCl_3$): δ 178.6, 83.9 (d, *J* = 164.6 Hz), 39.1, 38.8, 27.9 (d, *J* = 19.9 Hz), 27.7, 25.9 (d, *J* = 4.4 Hz) ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.4, 164.3, 133.5, 132.5, 129.2, 128.9, 116.8 (t, *J* = 239.2 Hz), 39.9, 31.8 (t, *J* = 21.5 Hz), 20.9 (t, *J* = 5.5 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −115.3 (dt, *J* = 56.5, 16.9 Hz, 2F);

HRMS (ESI): Calc'd for $C_{11}H_{14}F_2NO$ $[M-CO+H]^+$: 214.1038, found: 214.1038.



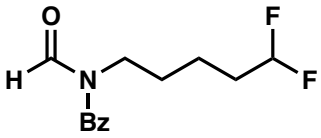
***N*-(4,4-Difluoro-3-methylbutyl)-*N*-formylbenzamide (12b):** The title compound was prepared according to the representative procedure using **10b**. Purification by preparative thin-layer chromatography (20% EtOAc/hexanes) provided the title compound (13.9 mg, 54%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 1H), 7.58 (t, *J* = 6.9 Hz, 1H), 7.54–7.48 (m, 4H), 5.68 (td, *J* = 56.7, 3.5 Hz, 1H), 3.94 (t, *J* = 7.5 Hz, 2H), 2.01–1.90 (m, 2H), 1.59–1.53 (m, 1H), 1.11(d, *J* = 6.9 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.4, 164.3, 133.5, 132.5, 129.2, 128.9, 118.8 (t, *J* = 242.5 Hz), 38.4, 35.7 (t, *J* = 19.9 Hz), 28.3 (t, *J* = 4.4 Hz), 12.6 (t, *J* = 5.2 Hz);

^{19}F NMR (376 MHz, $CDCl_3$): δ −122.4 (ddd, *J* = 56.6, 29.6, 14.7 Hz, 2F);

HRMS (ESI): Calc'd for $C_{13}H_{16}F_2NO$ $[M-CO+H]^+$: 256.1144, found: 256.1143.



***N*-(5,5-Difluoropentyl)-*N*-formylbenzamide (12c):** The title compound was prepared according to the representative procedure using **10c**. Purification by preparative thin-layer chromatography (20% EtOAc/hexanes) provided the title compound (15.6 mg, 61%) as a colorless oil.

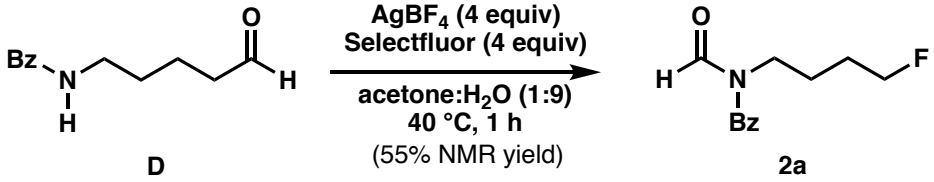
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.92 (s, 1H), 7.59–7.56 (m, 1H), 7.53–7.48 (m, 4H), 5.82 (tt, *J* = 56.8, 4.4 Hz, 1H), 3.88 (t, *J* = 7.4 Hz, 2H), 1.95–1.83 (m, 2H), 1.72 (quint, *J* = 7.4 Hz, 2H), 1.53 (quint, *J* = 7.4 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.5, 164.4, 133.6, 132.4, 129.1, 128.9, 117.1 (t, *J* = 238.8 Hz), 40.2, 33.7 (t, *J* = 21.0 Hz), 27.5, 19.6 (t, *J* = 5.6 Hz);

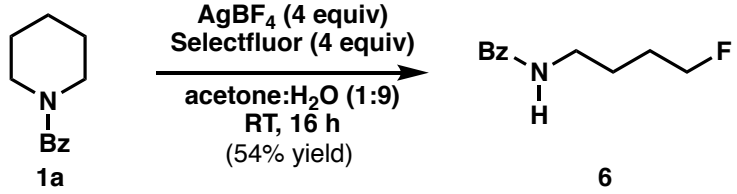
^{19}F NMR (376 MHz, $CDCl_3$): δ −115.3 (dt, *J* = 56.7, 17.5 Hz, 2F);

HRMS (EI): Calc'd for $C_{13}H_{15}F_2NO_2$ $[M]^+$: 255.1065, found: 255.1070.

4. Mechanistic Studies



According to the representative procedure, aldehyde **D** (*61*) was used as a starting material. Triphenylmethane was used as an internal standard and ^{1}H NMR analysis showed the formation of **2a** in 55% yield.



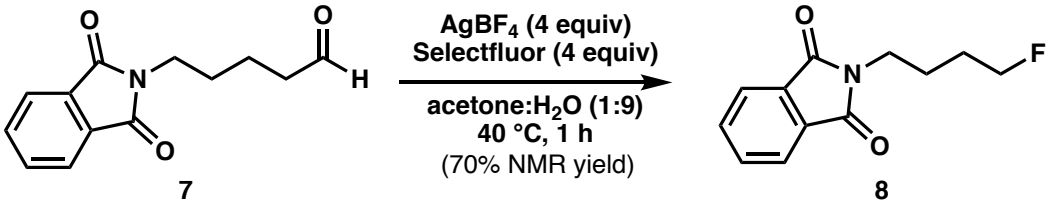
To a 1-dram vial containing **1a** (94.5 mg, 0.5 mmol), $AgBF_4$ (390 mg, 2.00 mmol) and Selectfluor® (710 mg, 2.00 mmol) was added 1:9 acetone: H_2O (2.5 mL), and the resulting mixture was stirred at room temperature. After 16 h, the reaction mixture was partitioned with EtOAc (2.5 mL) and H_2O (0.5 mL) and the phases were separated. The aqueous phase was extracted with EtOAc (5.0 mL × 3) and the combined organic layers were concentrated under reduced pressure. The crude residue was purified by preparative thin-layer chromatography (50% EtOAc/hexanes) to provide *N*-(4-fluorobutyl)benzamide (**6**) (52.7 mg, 54%) as a waxy white solid.

^{1}H NMR (700 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 6.31 (br, 1H), 4.50 (dt, *J* = 46.9, 5.6 Hz, 2H), 3.51 (q, *J* = 6.5 Hz, 2H), 1.86–1.72 (m, 4H);

^{13}C NMR (176 MHz, $CDCl_3$): δ 167.6, 134.6, 131.4, 128.5, 126.8, 83.7 (d, *J* = 164.7 Hz), 39.5, 27.8 (d, *J* = 19.9 Hz), 25.7 (d, *J* = 4.4 Hz);

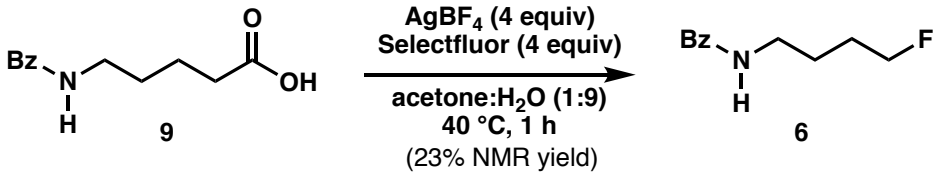
^{19}F NMR (376 MHz, $CDCl_3$): δ −217.4 (tt, *J* = 47.5, 26.2 Hz, 1F);

HRMS (ESI): Calc'd for $C_{11}H_{14}FNONa$ $[M+Na]^+$: 218.0952, found: 218.0952.



7 **8**

According to the representative procedure, aldehyde **7** (*62*) was used as a starting material. Triphenylmethane was used as an internal standard and ^{1}H NMR analysis showed theformation of **8** (*63*) in 70% yield.



9 **6**

According to the representative procedure, carboxylic acid **9** (*10*) was used as a starting material. Triphenylmethane was used as an internal standard and ^{1}H NMR analysis showed the formation of **6** in 23% yield.

5. Electrochemical Measurement

Non-aqueous electrochemical experiments were conducted under an Ar atmosphere in 0.1 M NBu_4PF_6 electrolyte in acetonitrile. Cyclic voltammetry experiments were performed using an Epsilon potentiostat from Bioanalytical Systems, Inc. The working electrode was a 3.0 mm diameter glassy carbon disk (from Bioanalytical Systems, Inc.) and was polished between every scan with 0.05-micron alumina powder on a felt pad. The counter electrode was a platinum wire. A silver wire in porous Vycor tip glass tube filled with 0.1 M NBu_4PF_6 in acetonitrile was used as a pseudo-reference electrode. At the conclusion of the series of experiments, the pseudo-reference potentials were referenced against ferrocene/ferrocenium as an external standard. The scan rate for all cyclic voltammograms was 100 mV/sec unless otherwise noted. All scans were compensated for internal resistance. Data measured with respect to Fc/Fc^+ and reported to SCE.

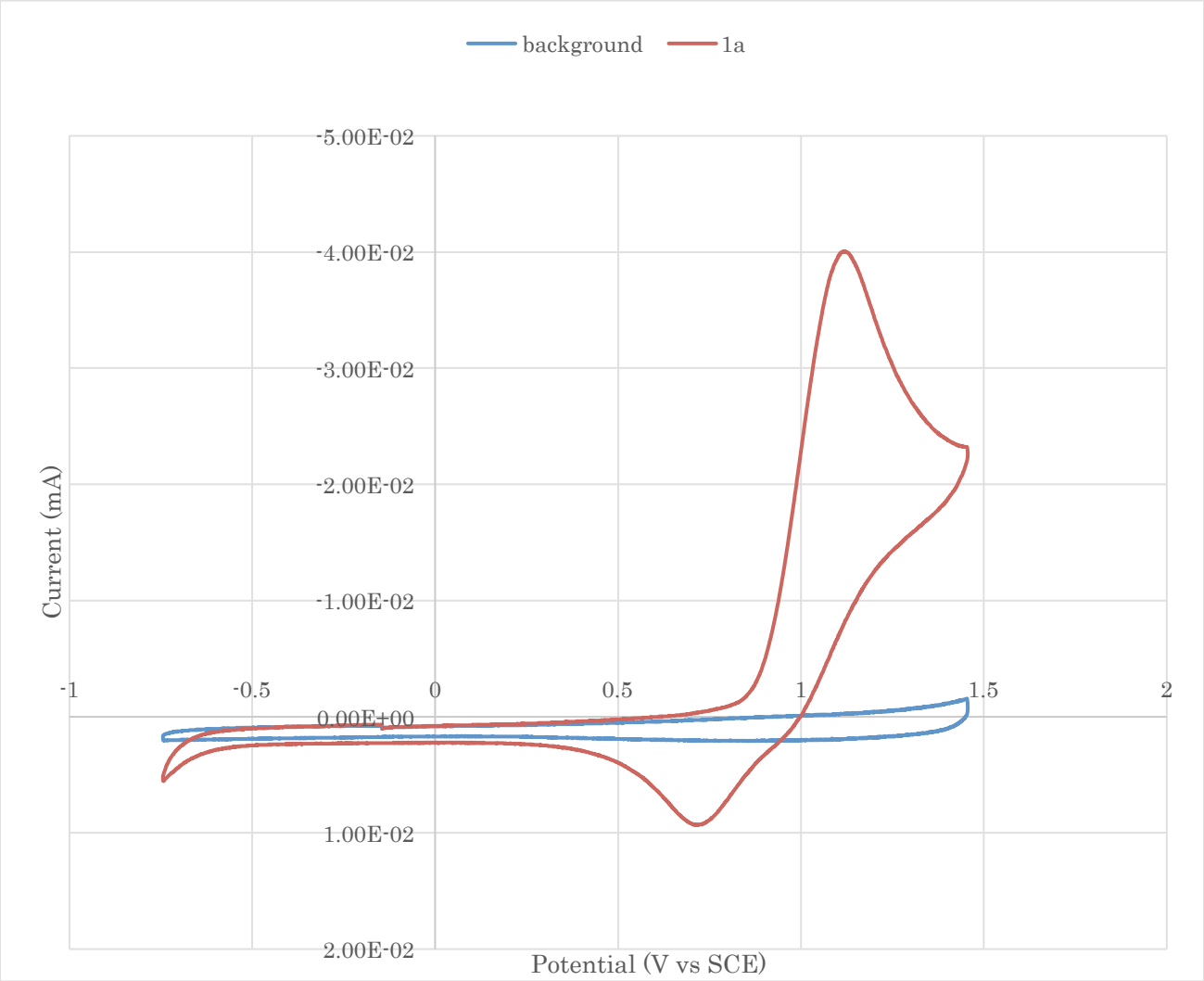


Fig. S1, Cyclic voltammograms of **1a** (1mM) and Ar background in 0.10 M NBu_4PF_6 in acetonitrile. Data was collected with a scan rate of 100mV/s.

6. NMR Studies

6.1. Interaction of $AgBF_4$ with Selectfluor®

Procedure: To a 4 ml vial containing Selectfluor® (35.4 mg, 0.100 mmol) and $AgBF_4$ (19.4 mg, 0.100 mmol) was added 1:9 (v/v) Acetone-*d6*/D_2O (1.0 ml). The resulting solution was allowed to stir at 40 °C for 1 h. The contents of the reaction vial were then transferred into a NMR tube and an NMR spectrum was taken directly afterwards to measure consumption of Selectfluor®.

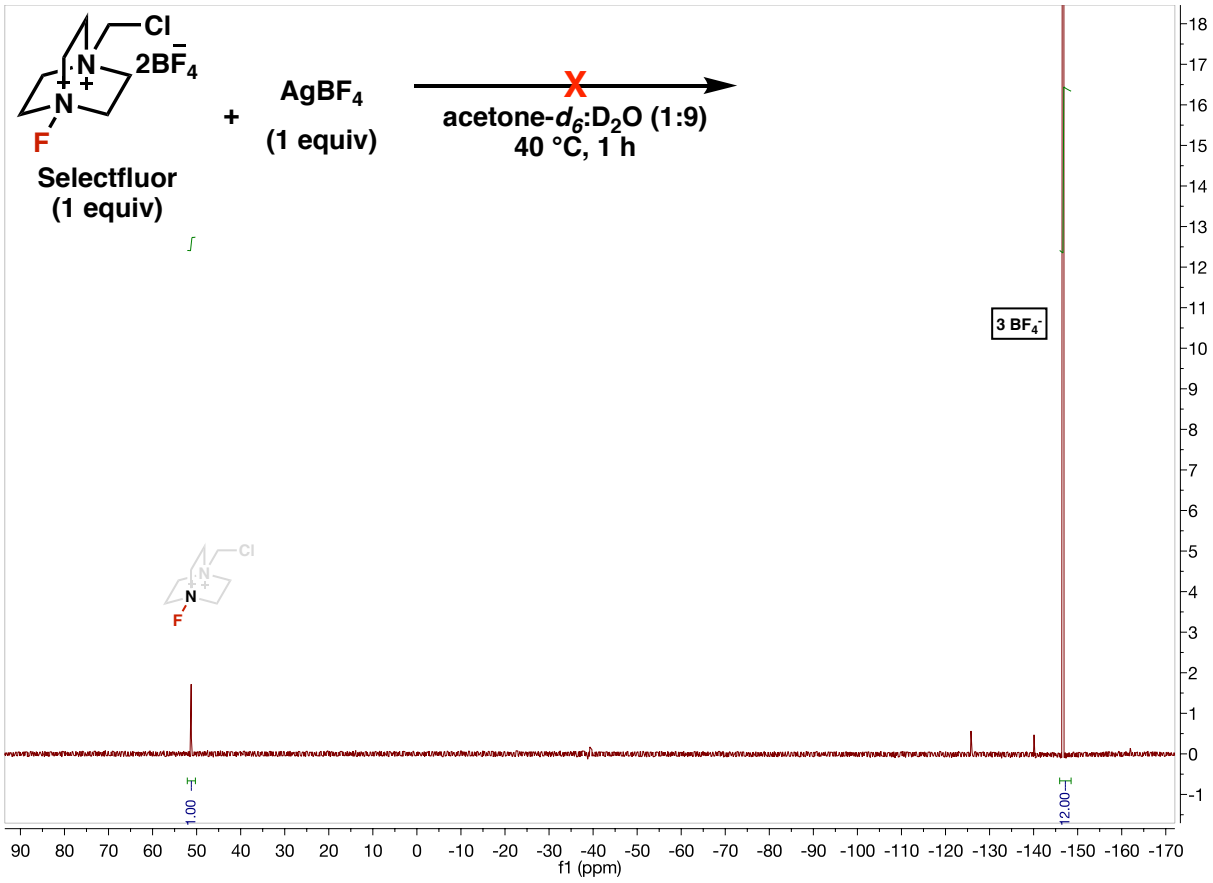


Fig. S2. ^{19}F NMR monitoring of Selectfluor® consumption in the presence of $AgBF_4$

6.2. Interaction of $AgBF_4$ with 1a.

Procedure: To a 4 ml vial containing **1a** (18.9 mg, 0.100 mmol) and $AgBF_4$ (19.4 mg, 0.100 mmol) was added 1:9 (v/v) Acetone-*d6*/D_2O (1.0 ml). The contents of the reaction vial were then transferred into a NMR tube and spectroscopic data was collected right after. The same procedure was followed with varying amounts of $AgBF_4$. The residual signal of acetone was used as internal reference.

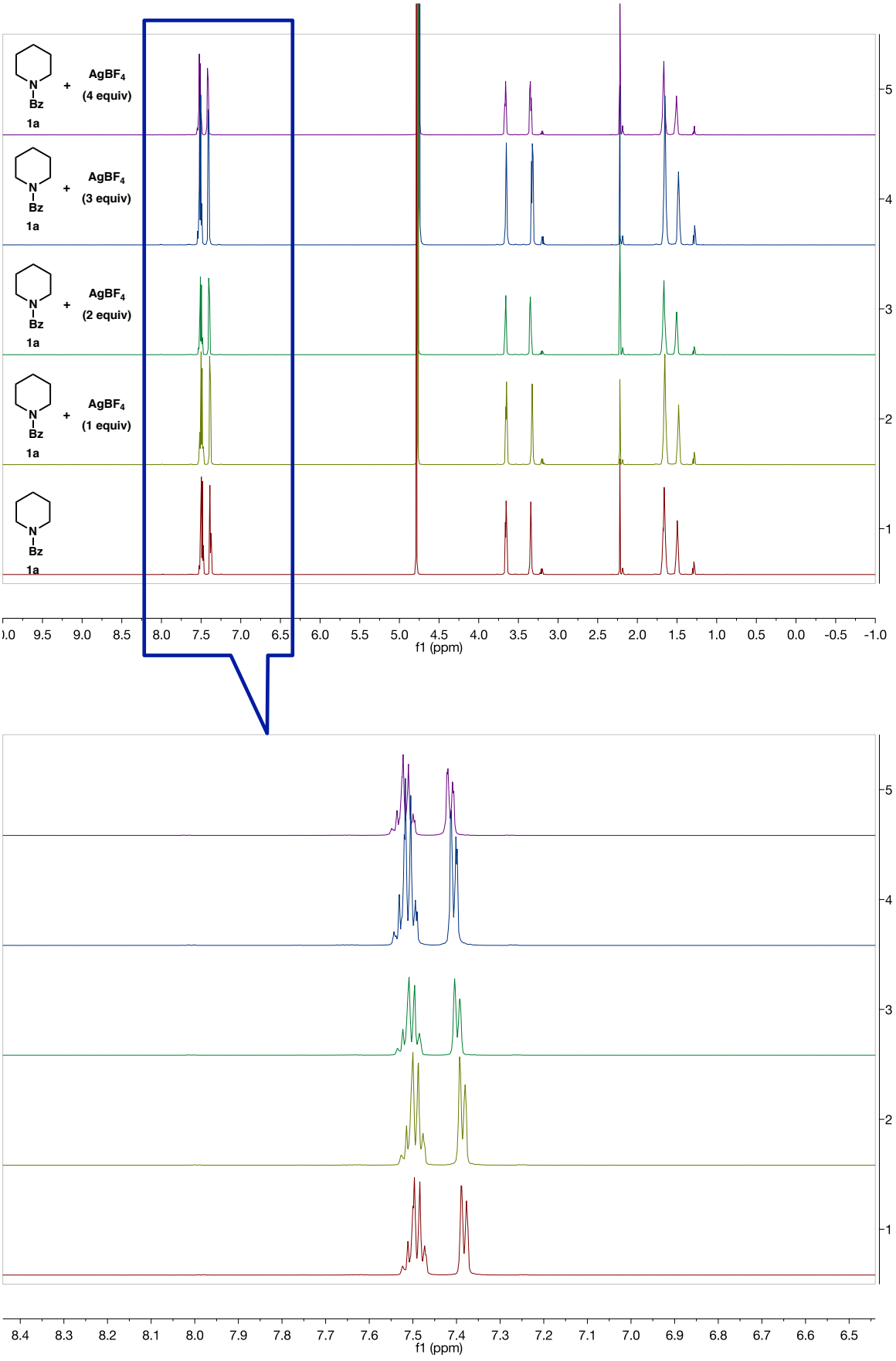
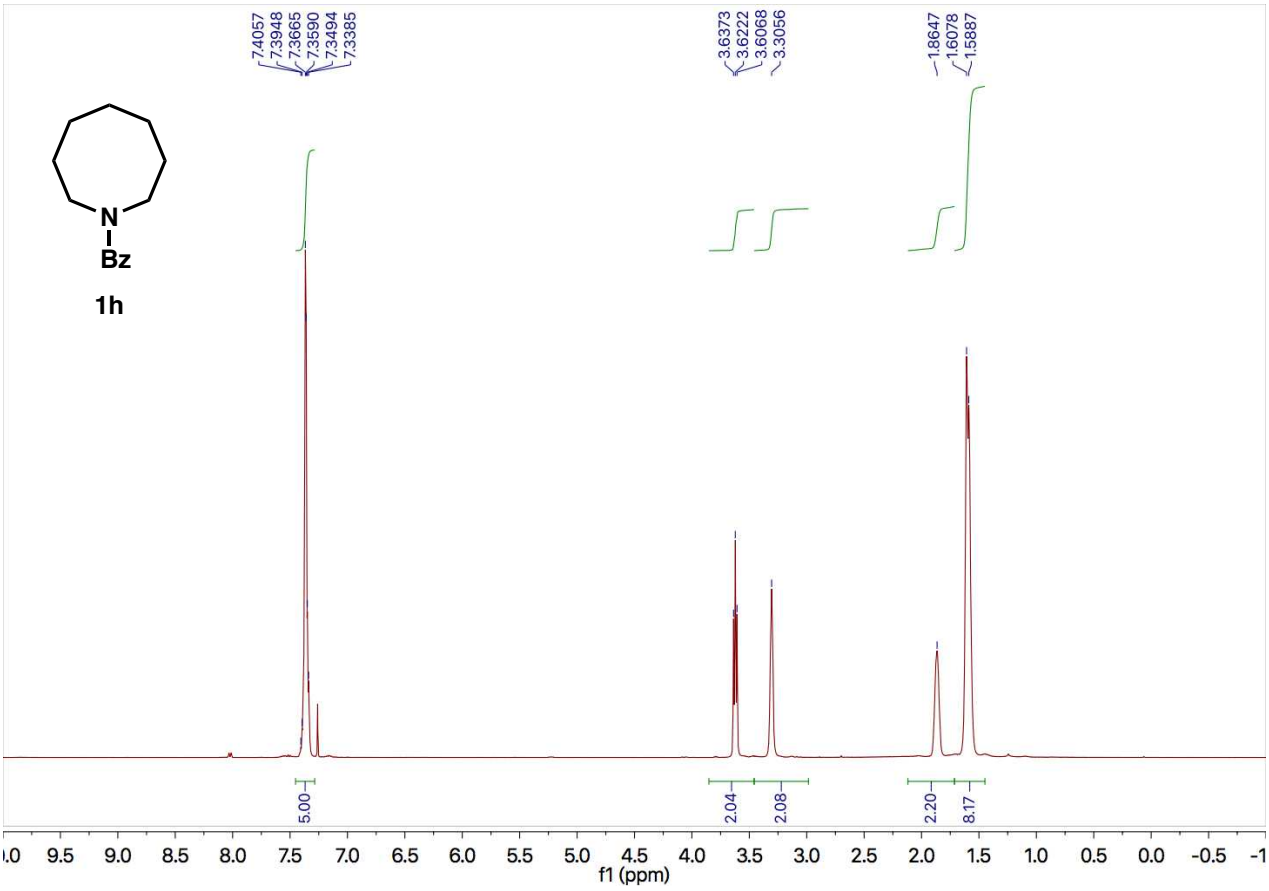
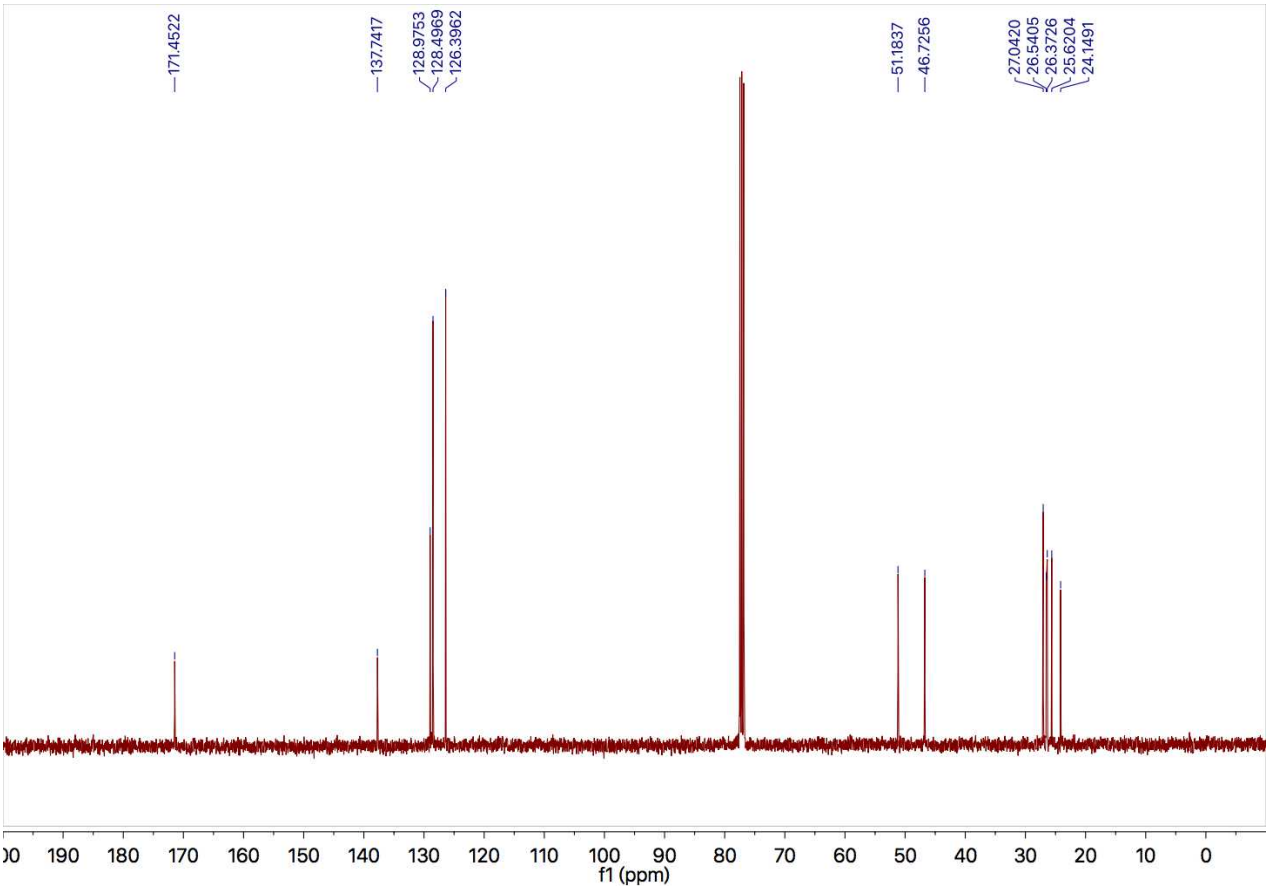
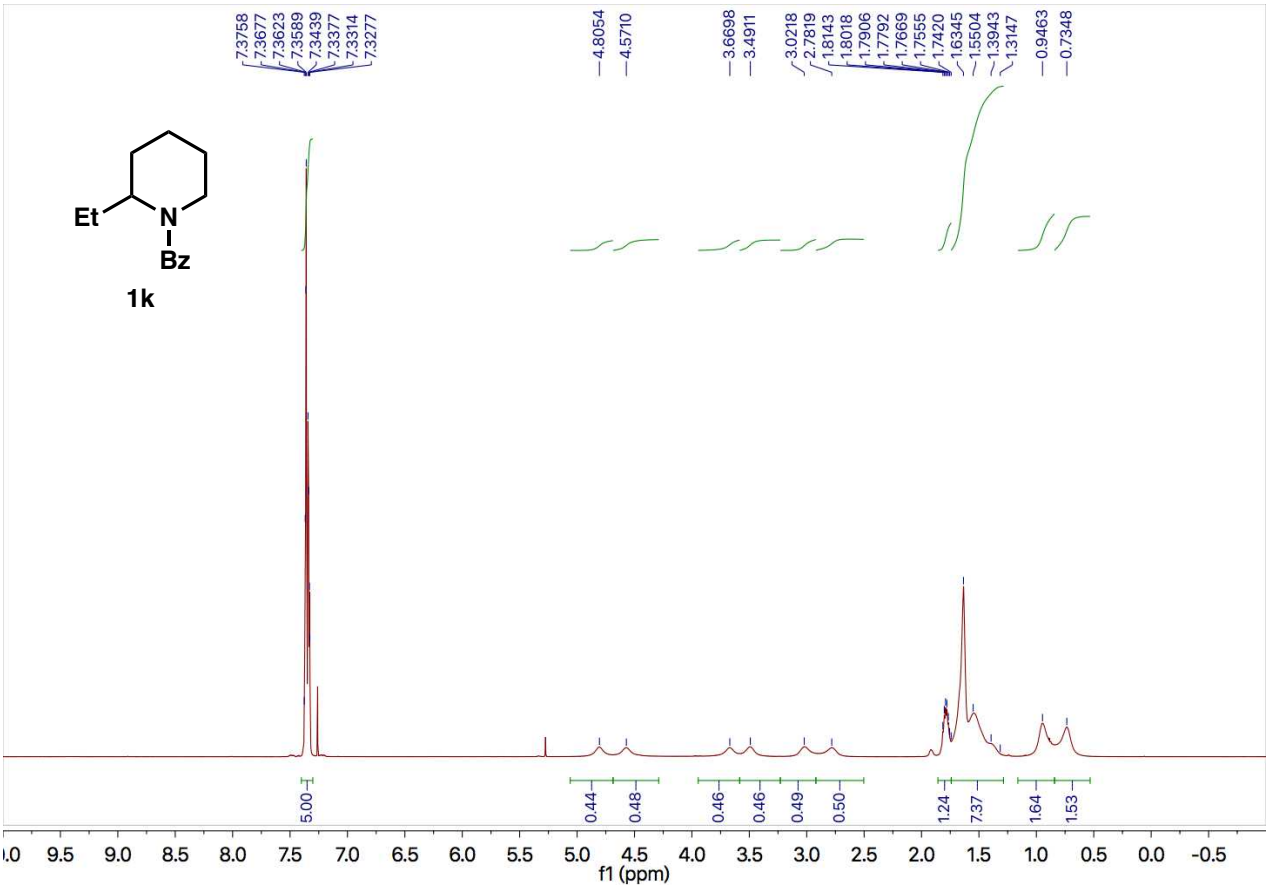


Fig. S3. ^{1}H NMR monitoring of interaction of $AgBF_4$ and **1a**

7. NMR Spectra



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3.4911
3.0218
2.7819
1.8143
1.8018
1.7906
1.7792
1.7669
1.7555
1.7420
1.6345
1.5504
1.3943
1.3147
0.9463
0.7348
Et
N
Bz
1k
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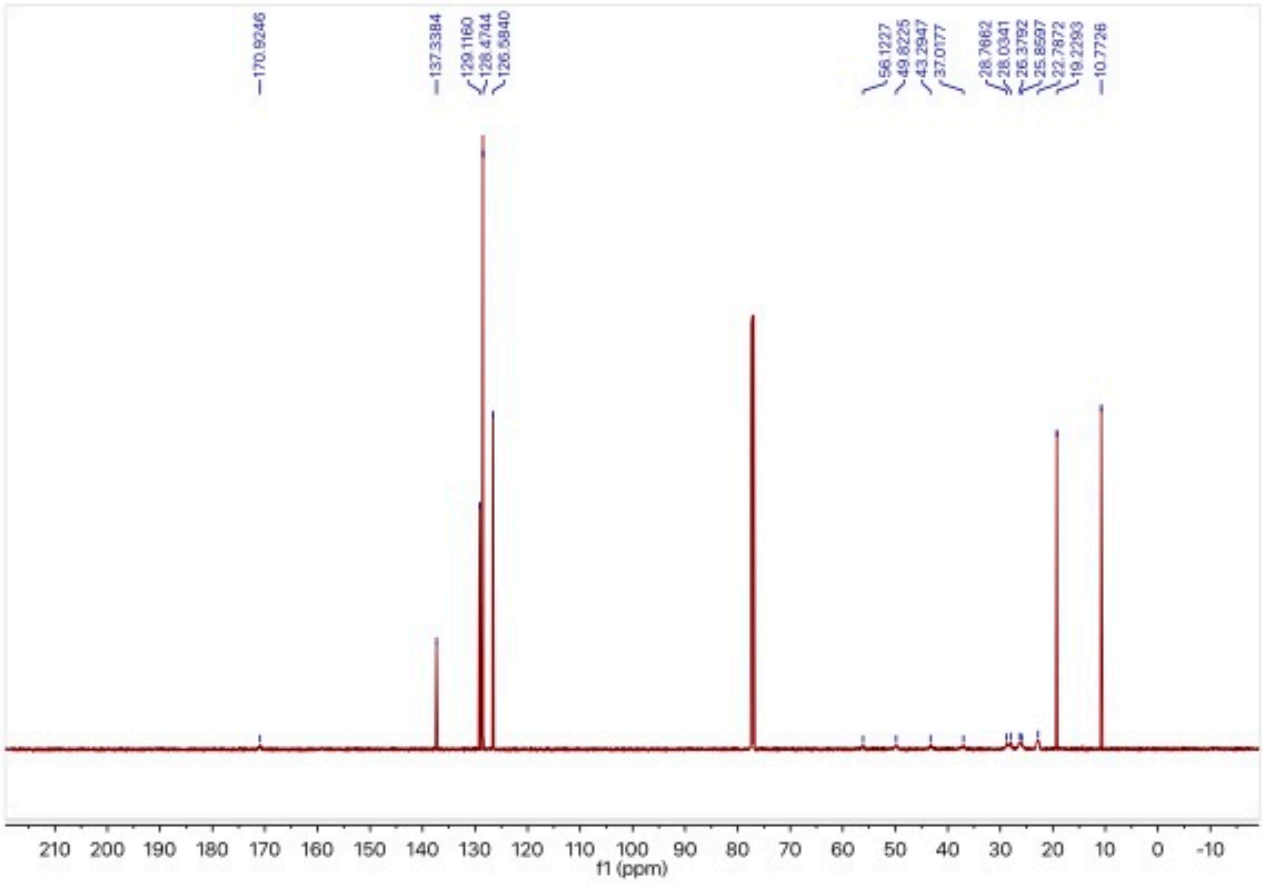
0.48
0.46
0.46
0.49
0.50
1.24
7.37
1.64
1.53
f1 (ppm)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129.1160
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126.5840
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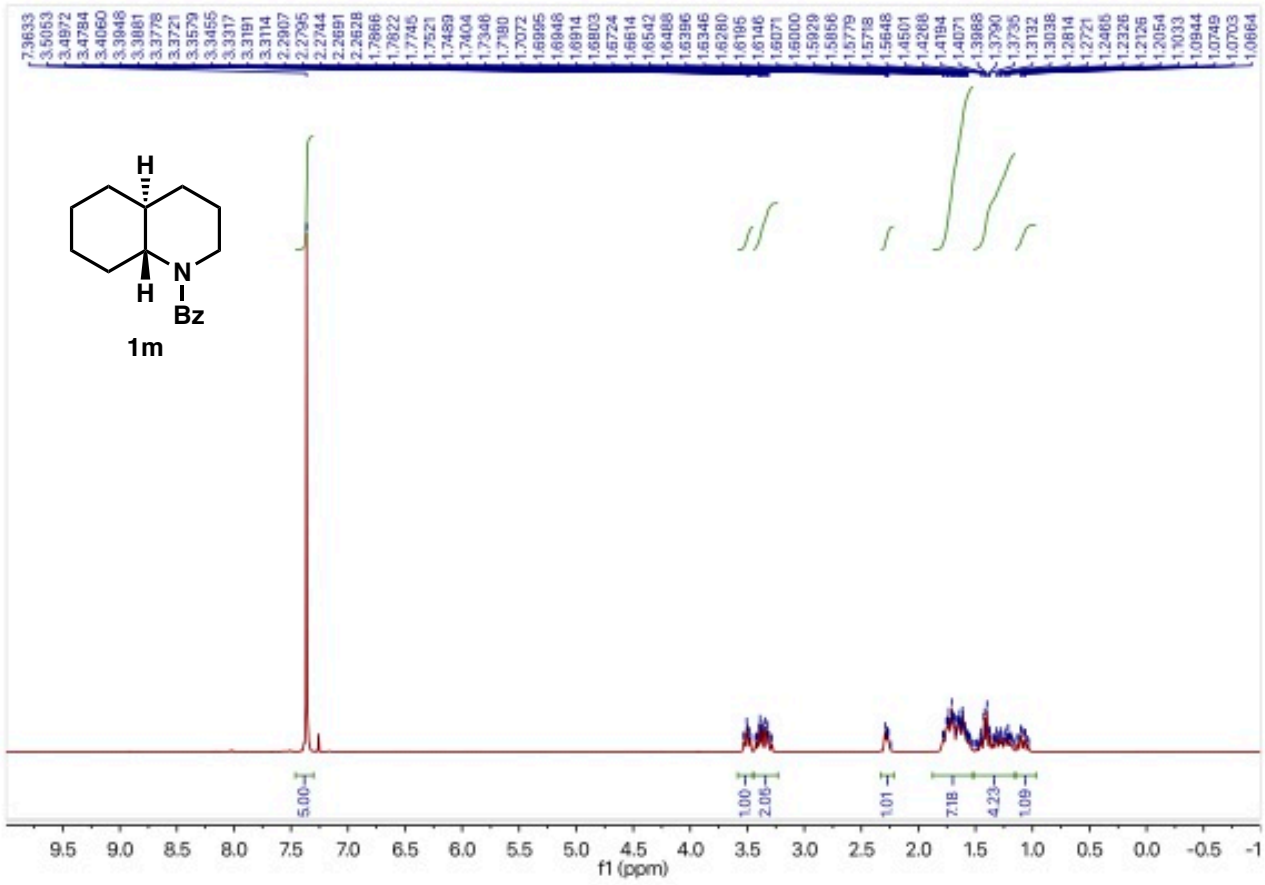
28.0341
26.3792
25.8597
22.7872
19.2293
10.7726
f1 (ppm)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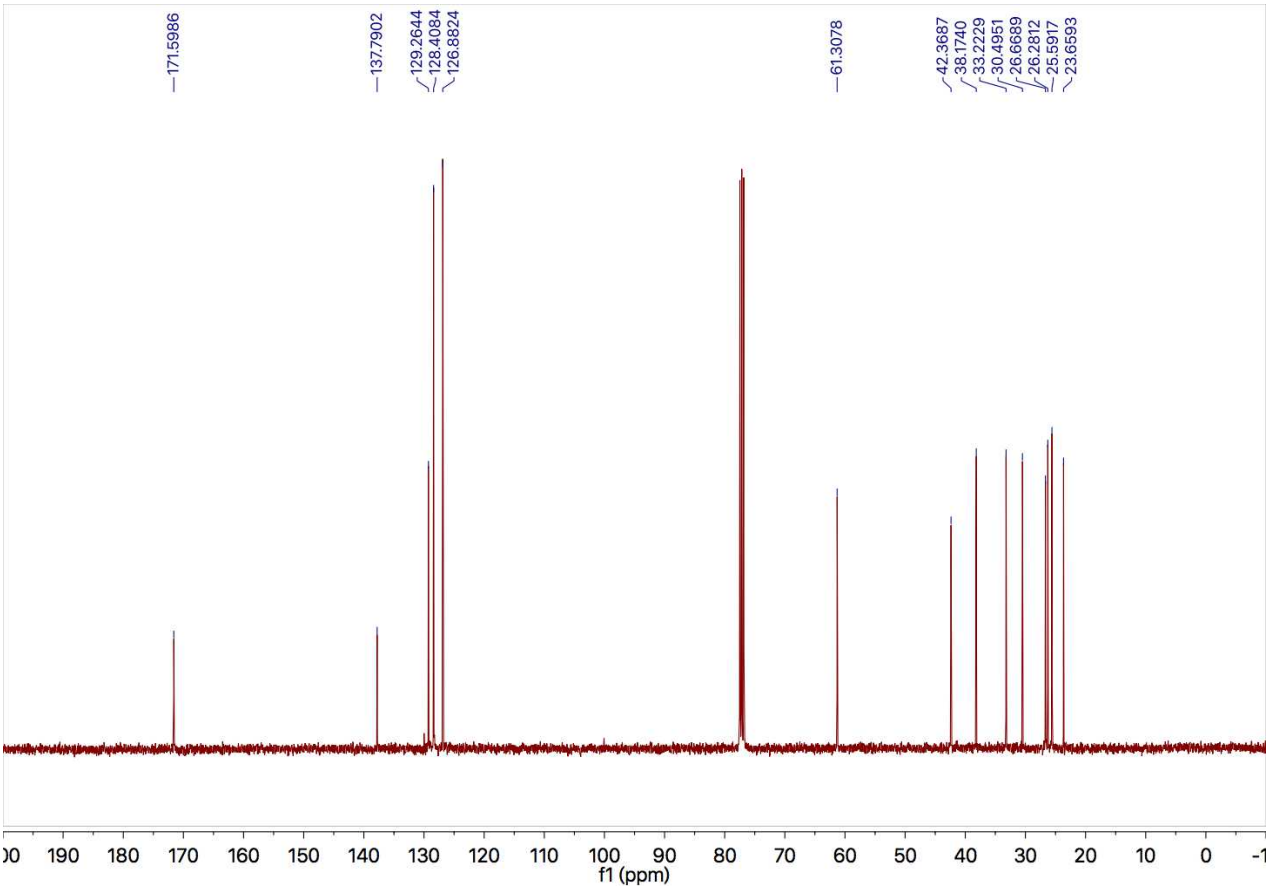
H
N
Bz
1m
f1 (ppm)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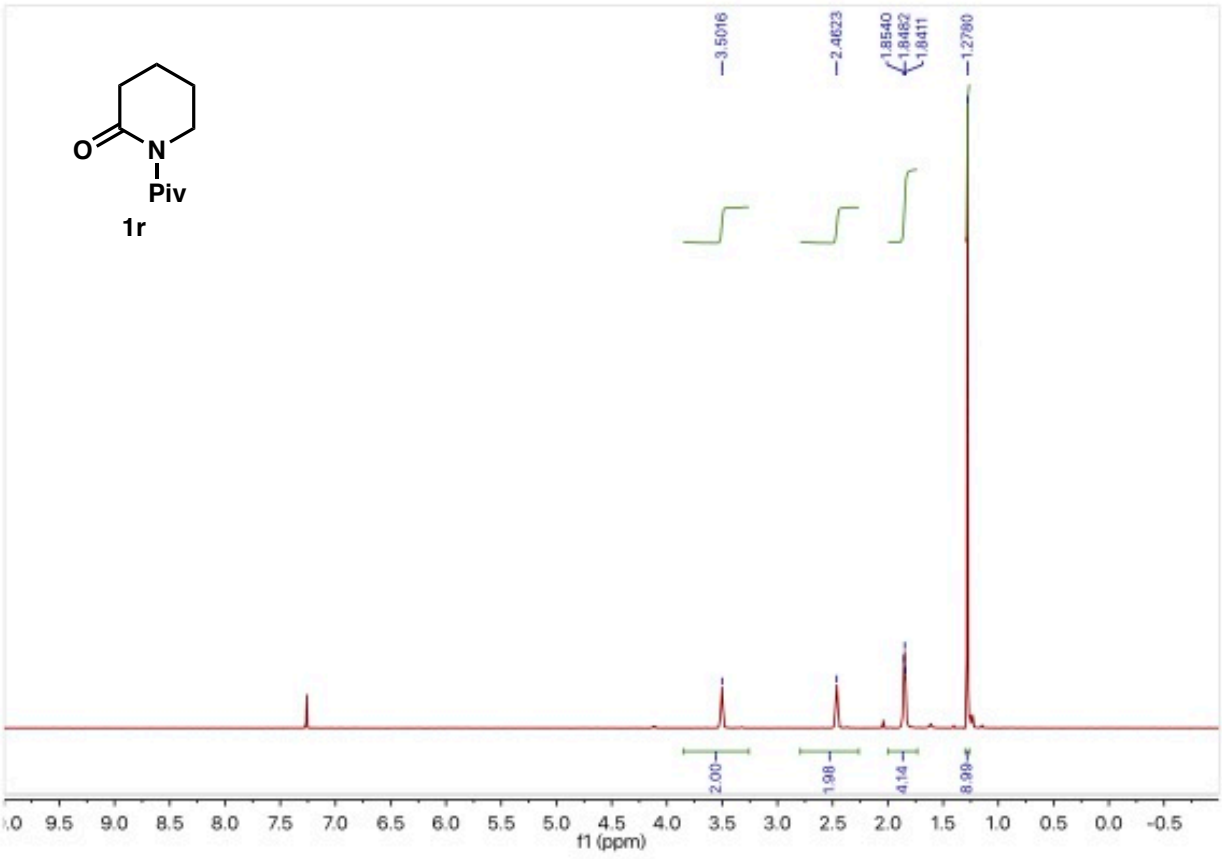
26.2812
25.5917
23.6593
f1 (ppm)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N
Piv
1r
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2.00
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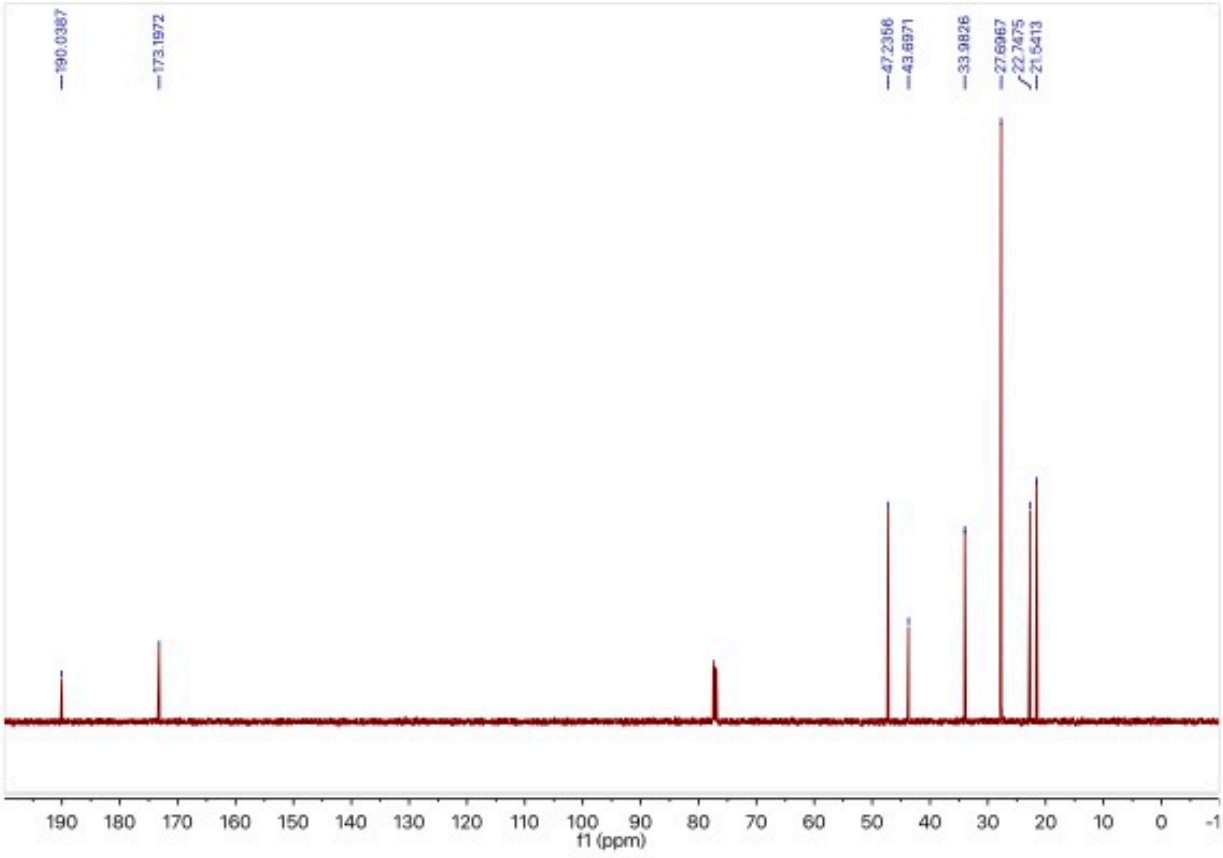
8.99
f1 (ppm)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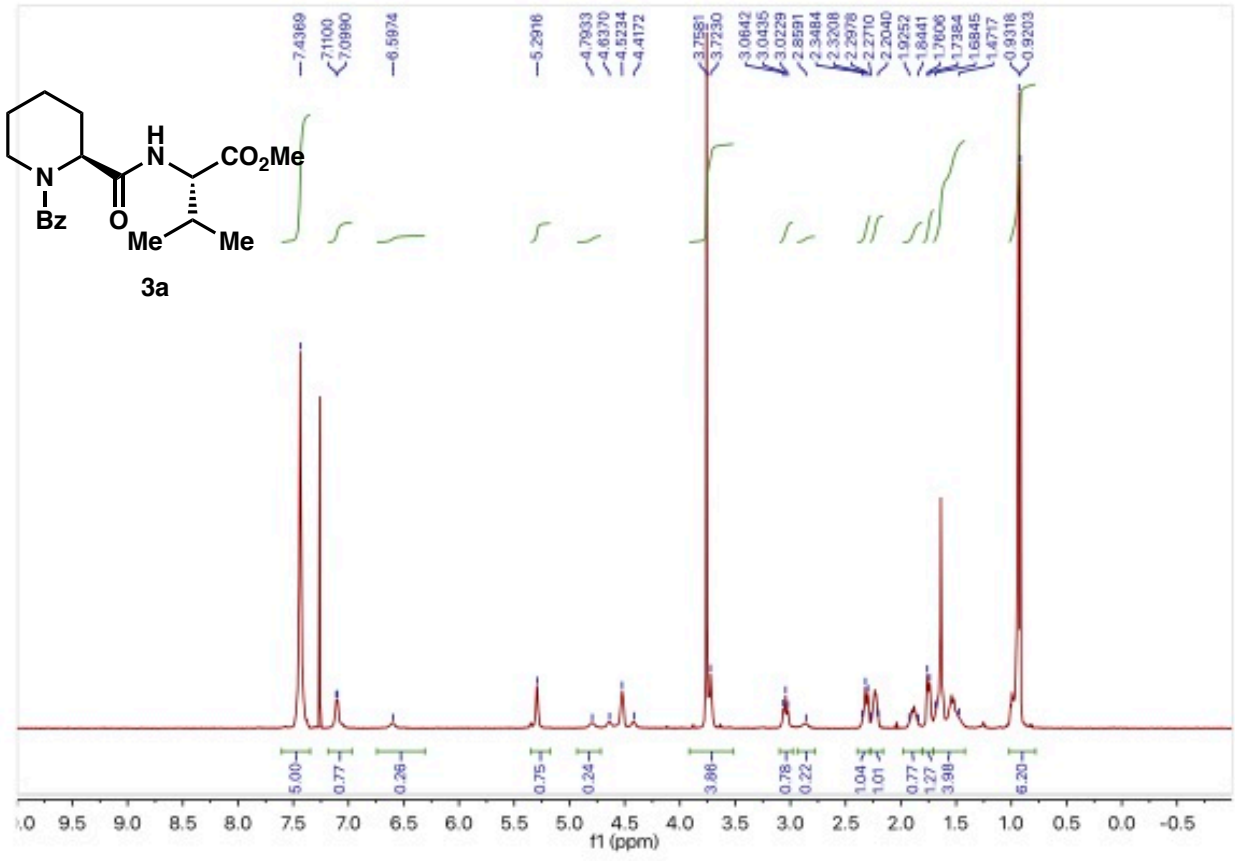
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3.0642
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3.0229
2.8591
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2.2978
2.2710
2.2040
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1.8441
1.7606
1.7384
1.6845
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0.9203
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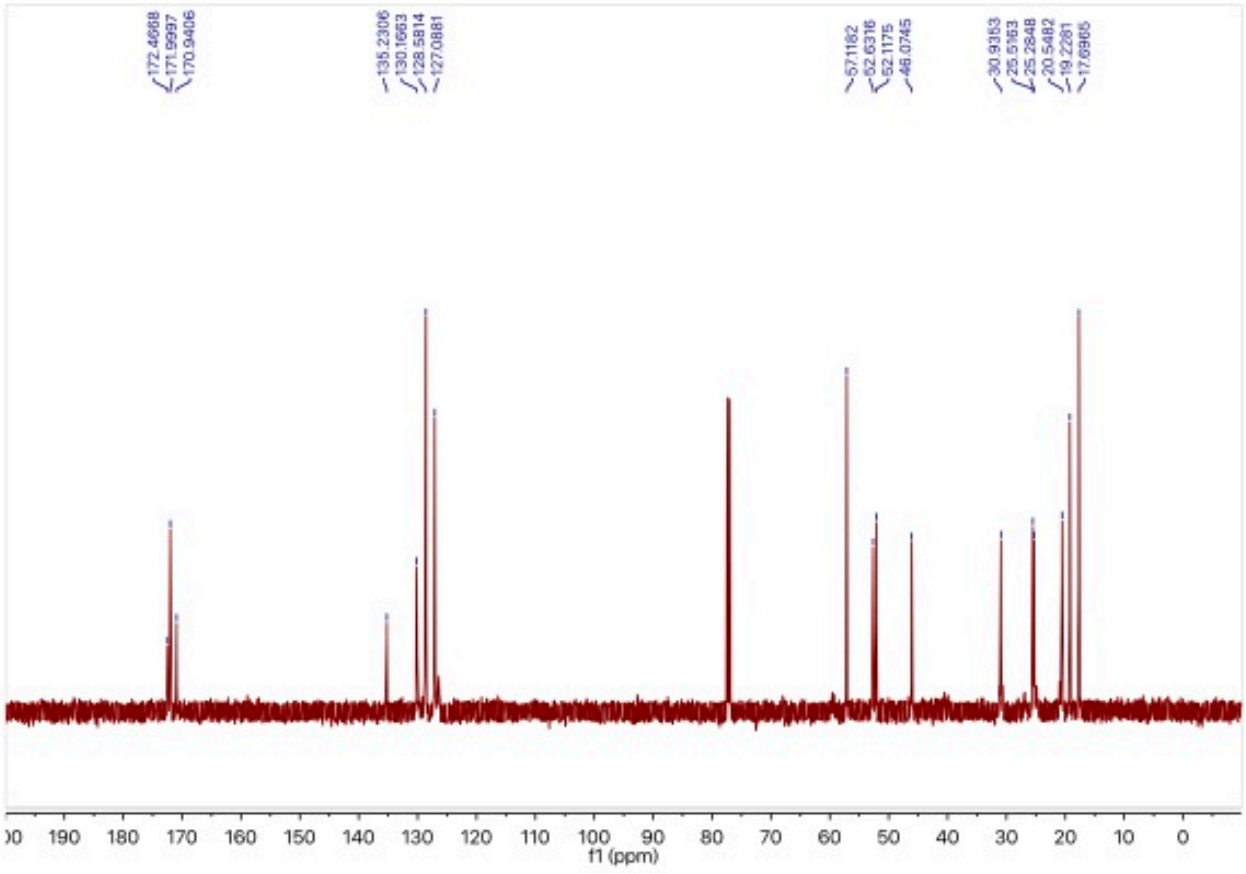
f1 (ppm)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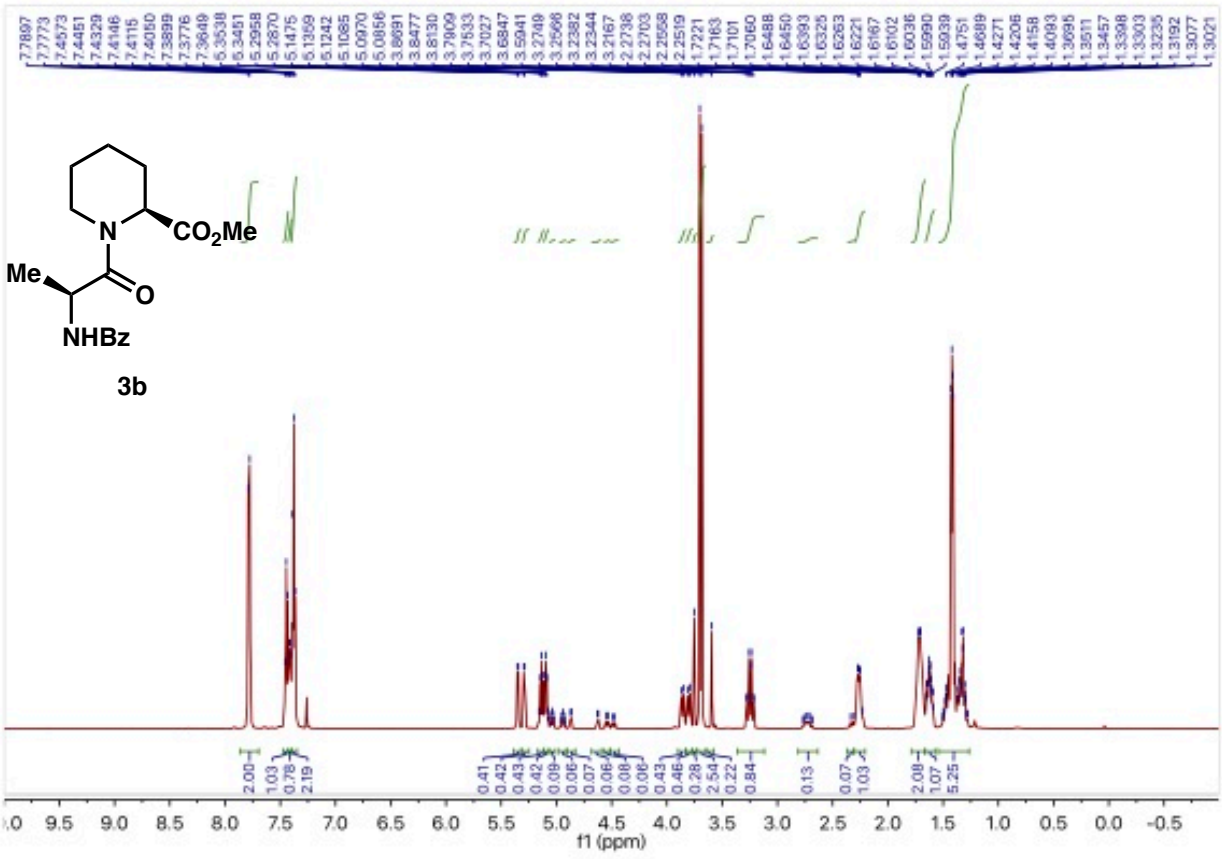
20.5482
19.2261
17.6965
f1 (ppm)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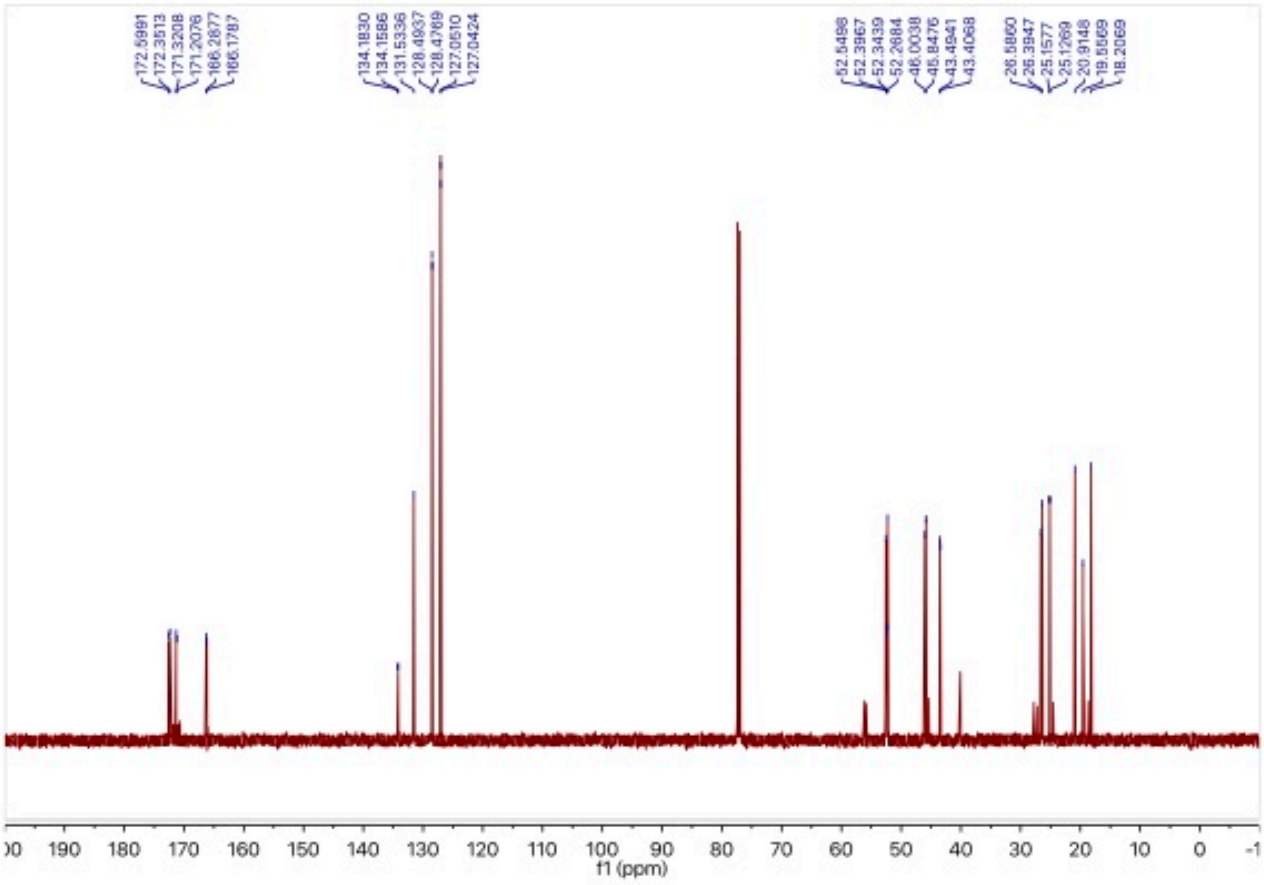
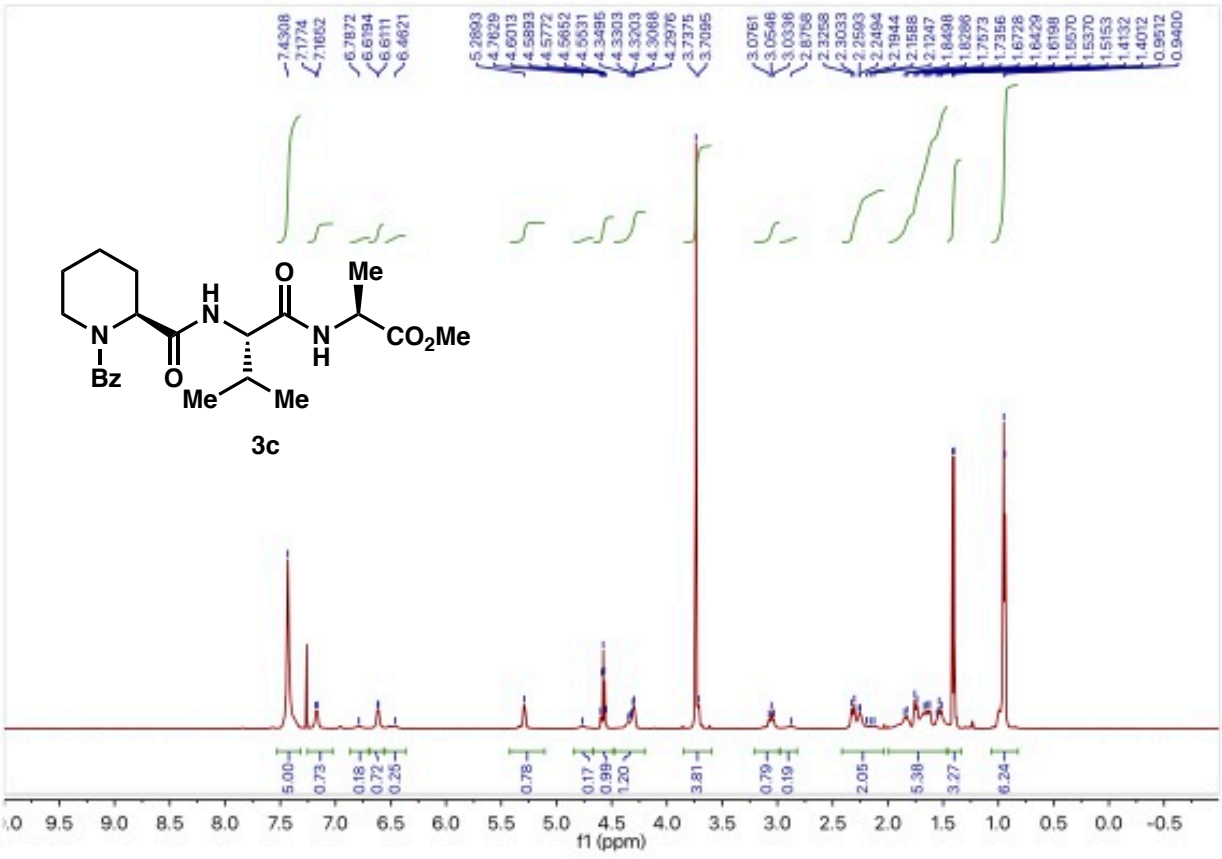
N
Me
O
NHBz
3b
f1 (ppm)


f1 (ppm)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3.7375
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0.9400
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0.73
0.18
0.72
0.25
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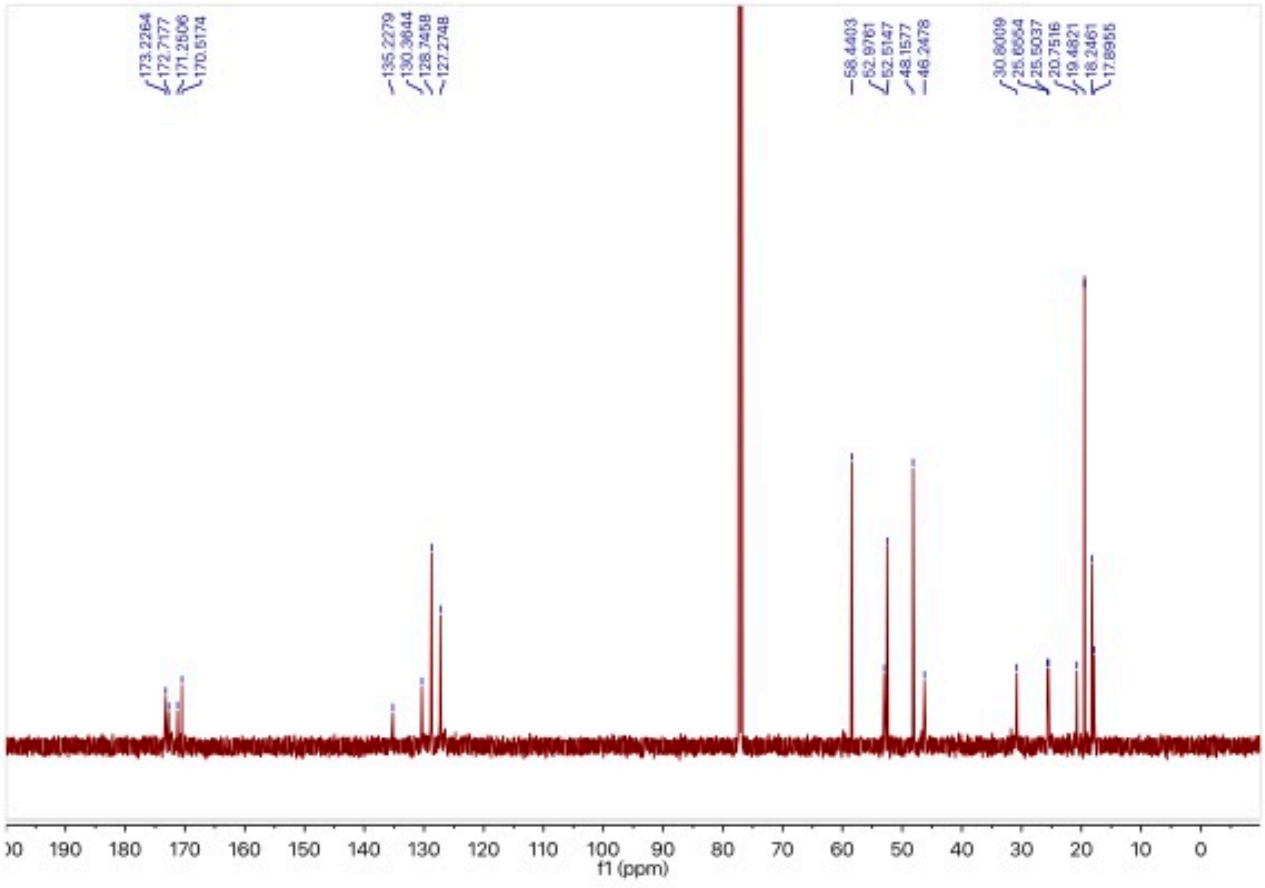
f1 (ppm)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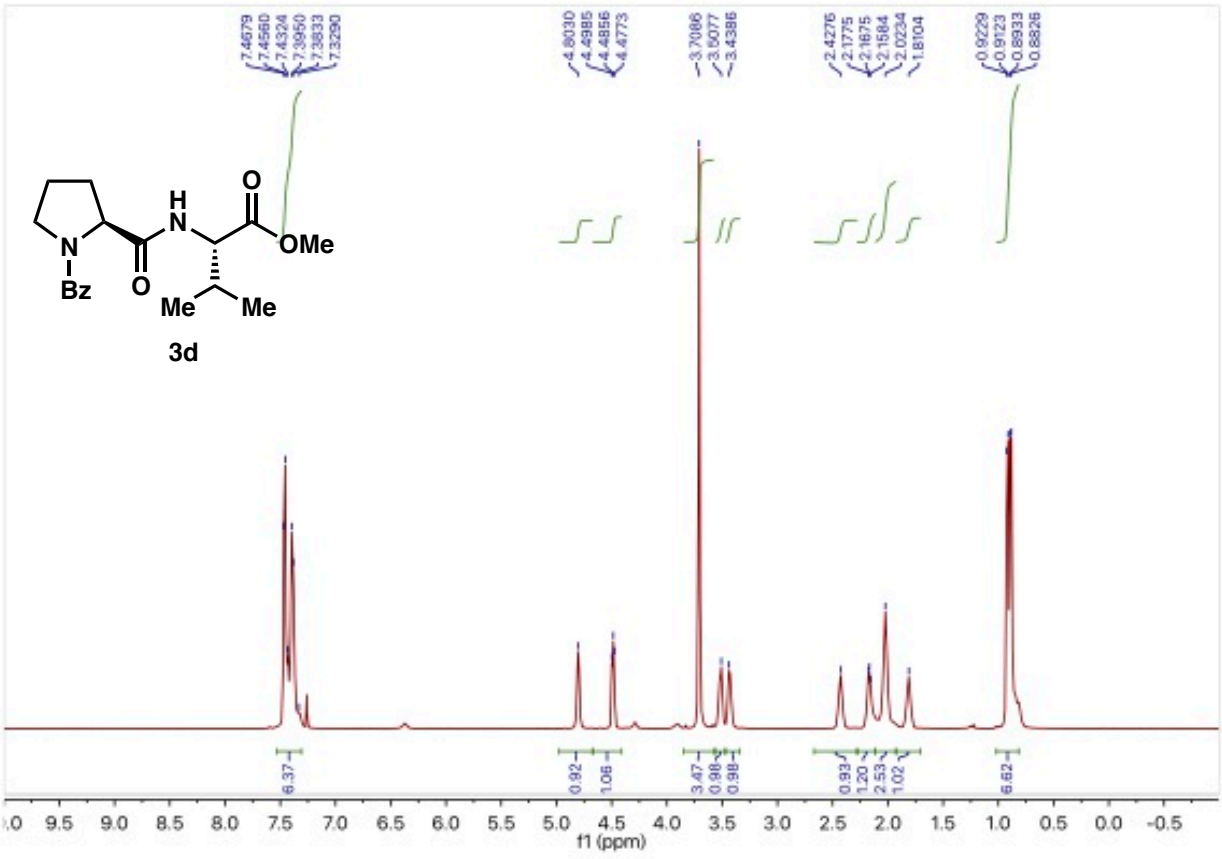
f1 (ppm)

3c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3.5077
3.4386
2.4276
2.1775
2.1675
2.1584
2.0234
1.8104
0.9229
0.9123
0.8933
0.8826
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0.98
0.93
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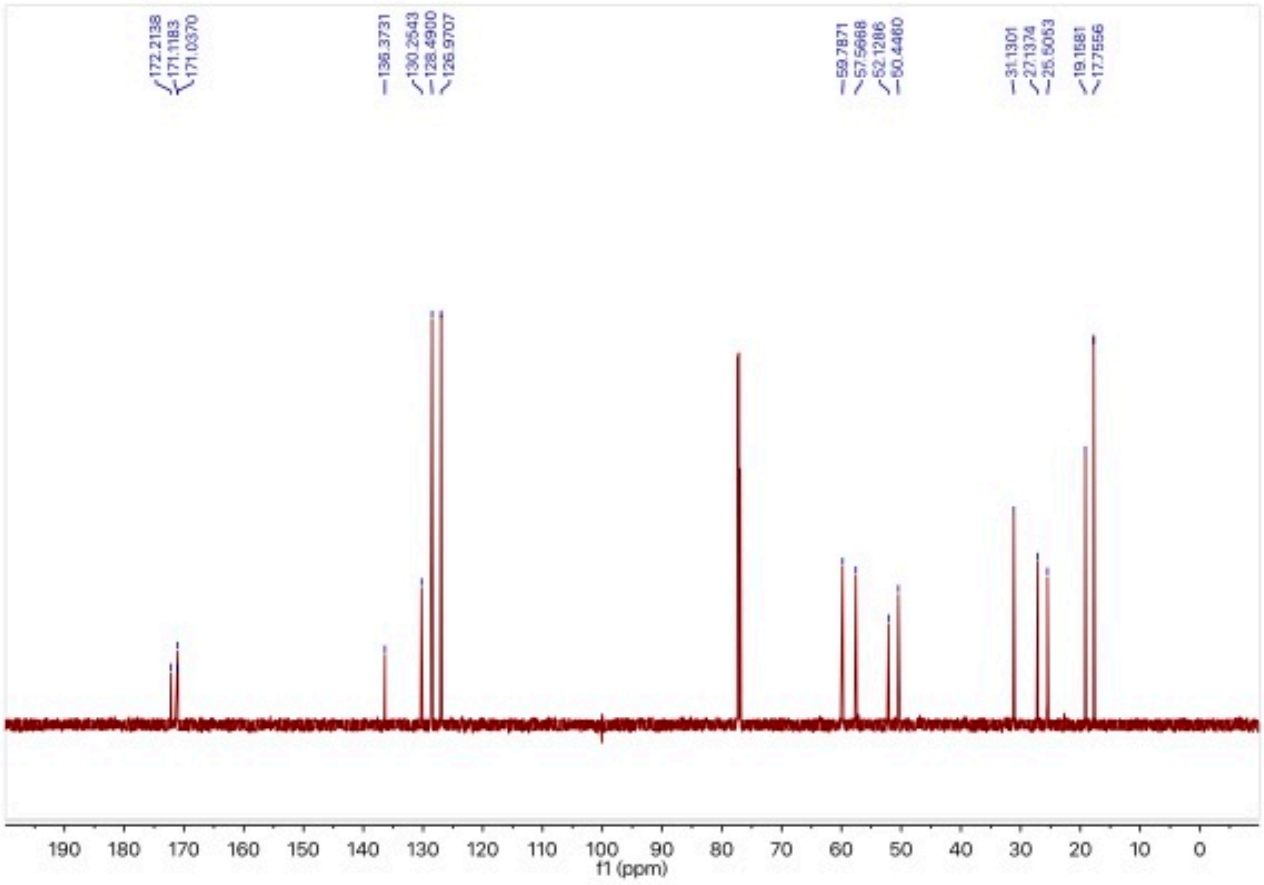
3d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25.5053
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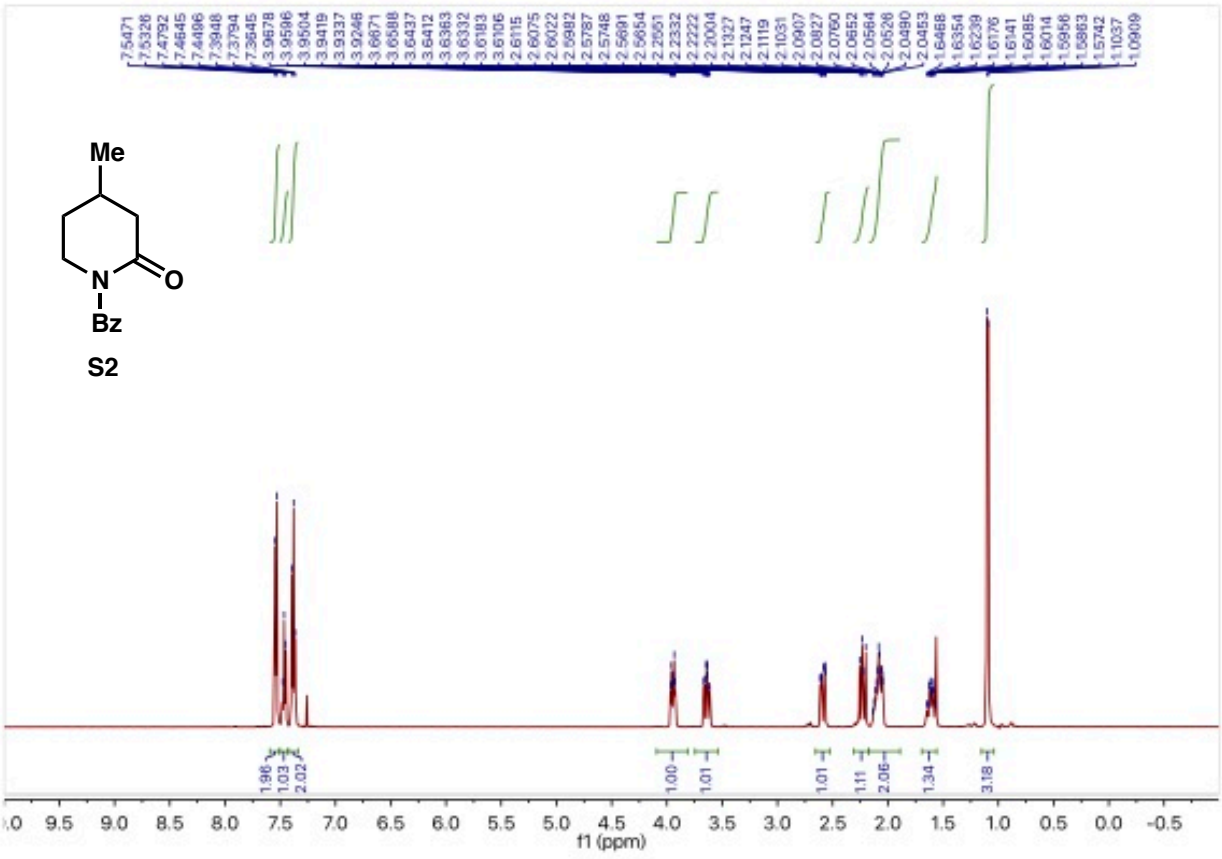
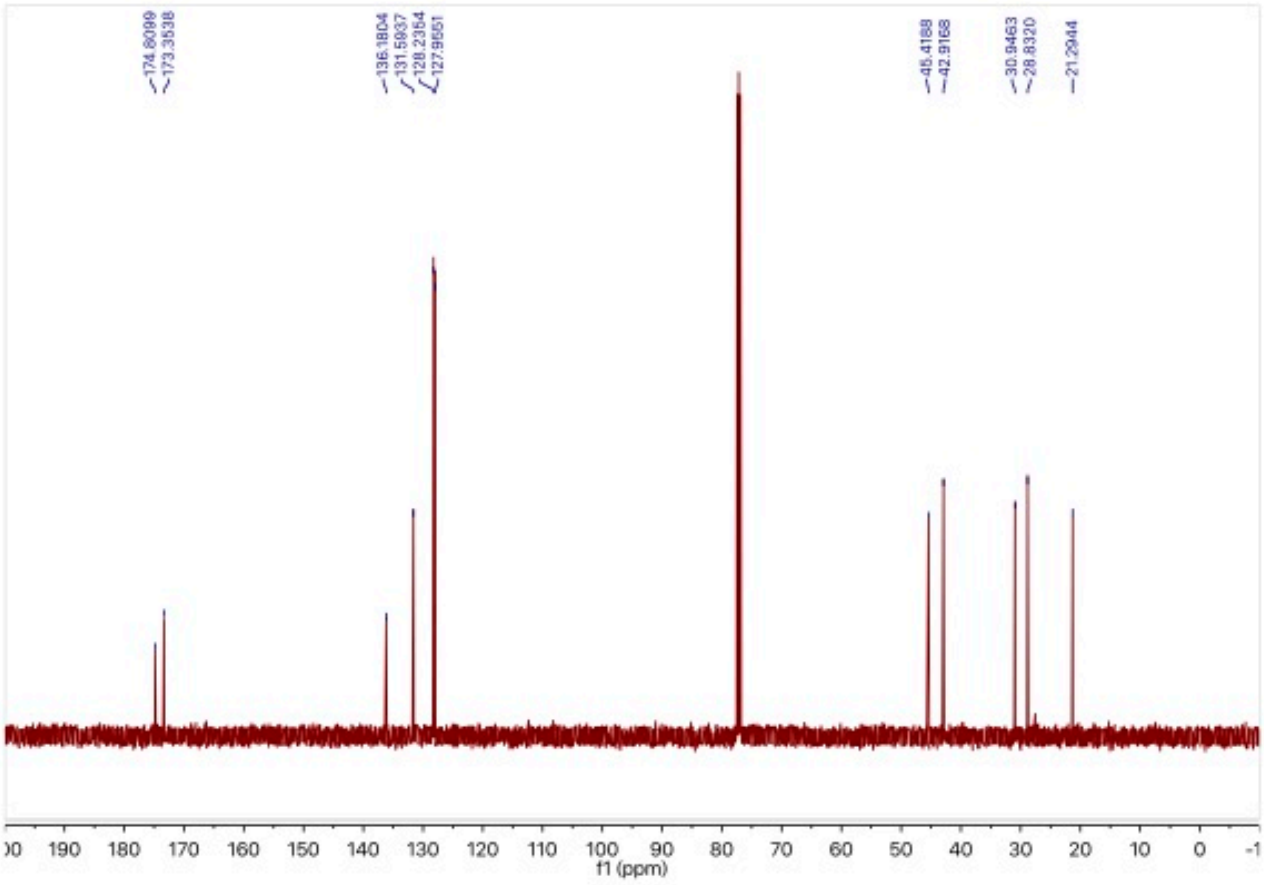
f1 (ppm)


Me
N
O
Bz
S2
f1 (ppm)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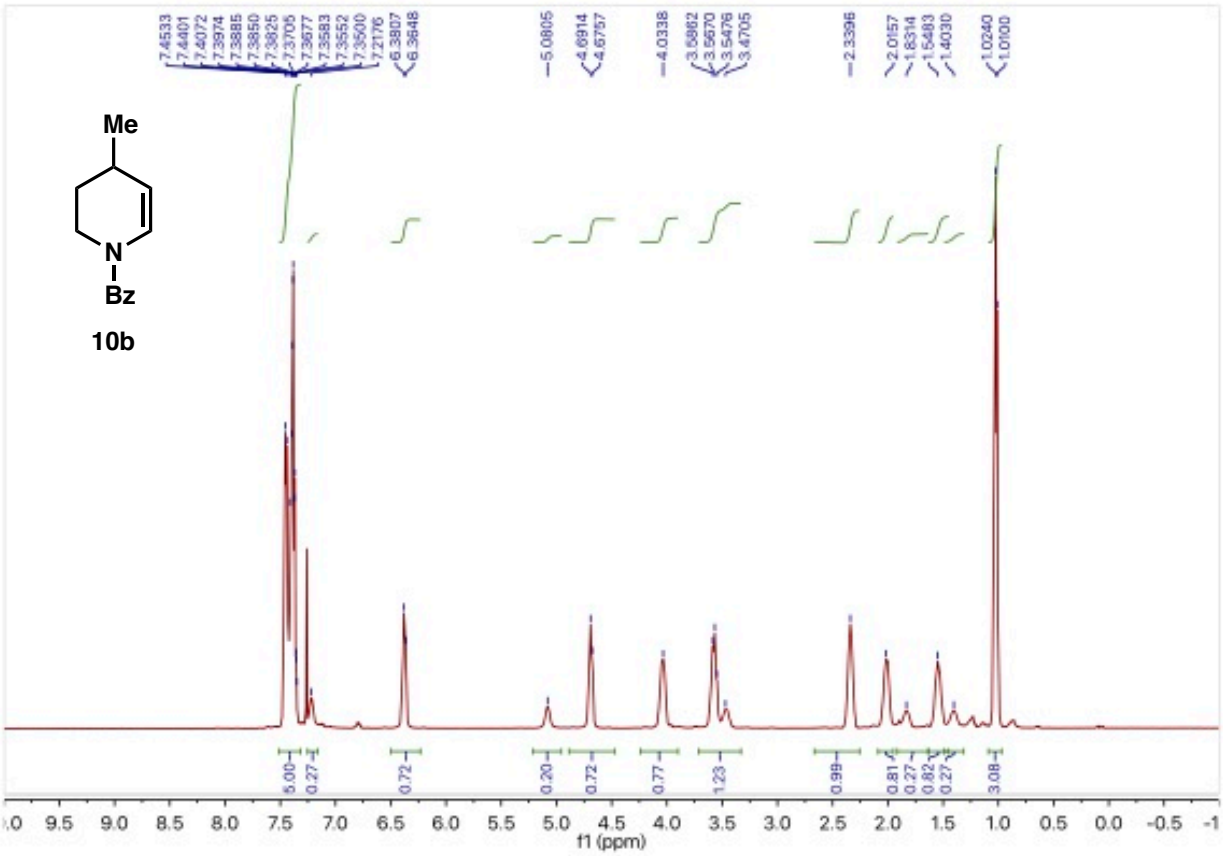
f1 (ppm)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N
Bz
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3.4705
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2.0157
1.8314
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1.0240
1.0100
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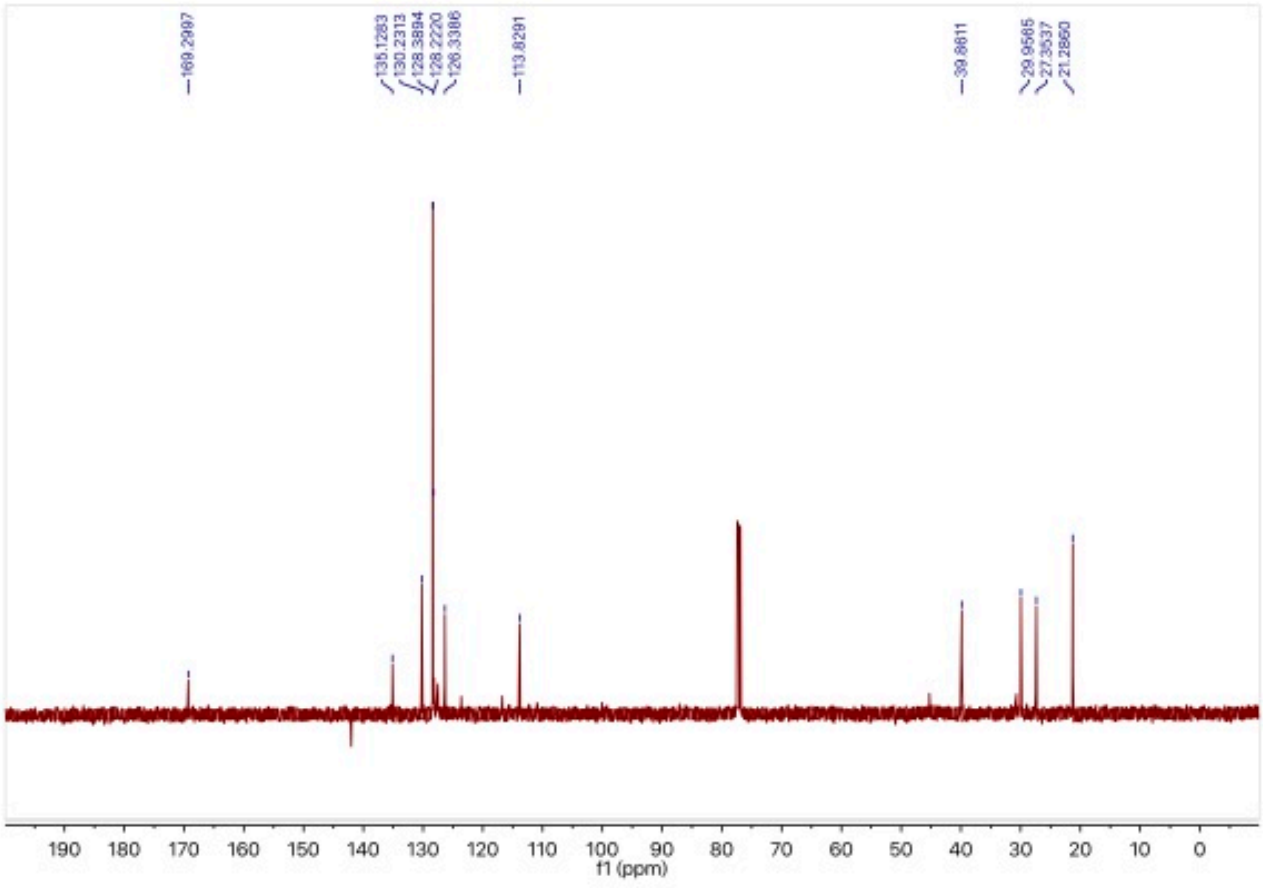
0.20
0.72
0.77
1.23
0.99
0.81
0.27
0.82
0.27
3.08
f1 (ppm)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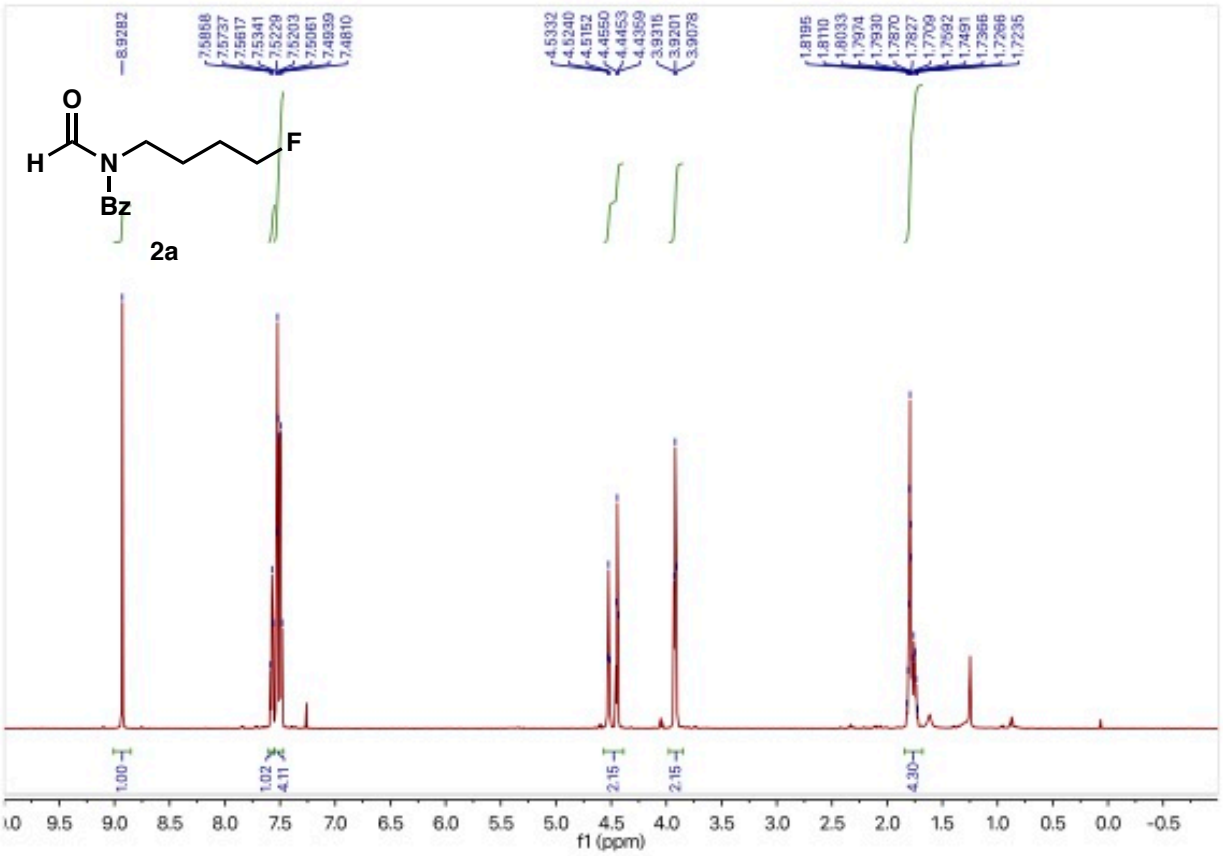
113.8291
39.8811
29.9565
27.3537
21.2860
f1 (ppm)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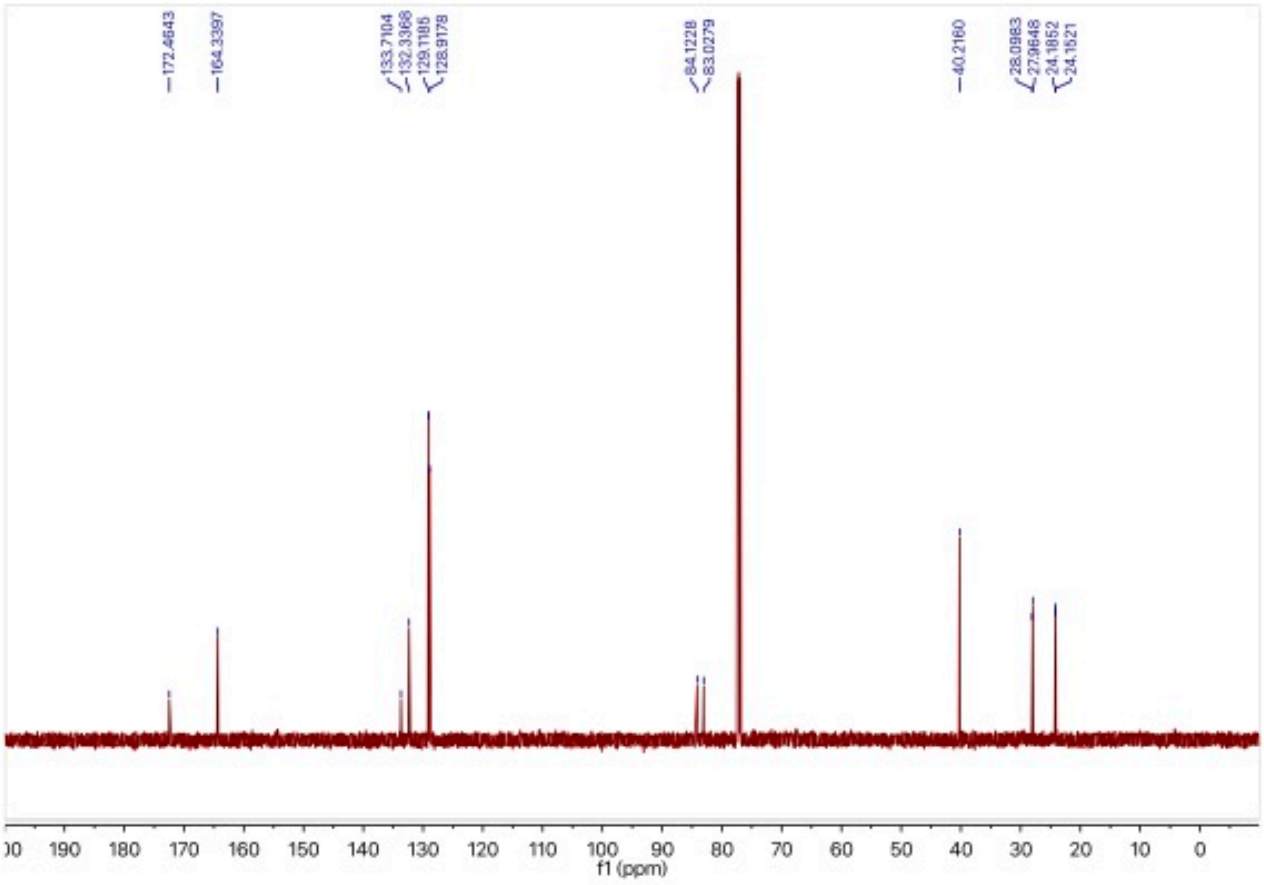
7.5341
7.5229
7.5203
7.5061
7.4939
7.4810
4.5332
4.5240
4.5152
4.4550
4.4453
4.4359
3.9315
3.9201
3.9078
1.8195
1.8110
1.8033
1.7974
1.7930
1.7870
1.7827
1.7709
1.7592
1.7491
1.7366
1.7266
1.7235
O
H
N
Bz
F
2a
1.00
1.02
4.11
2.15
2.15
4.30
f1 (ppm)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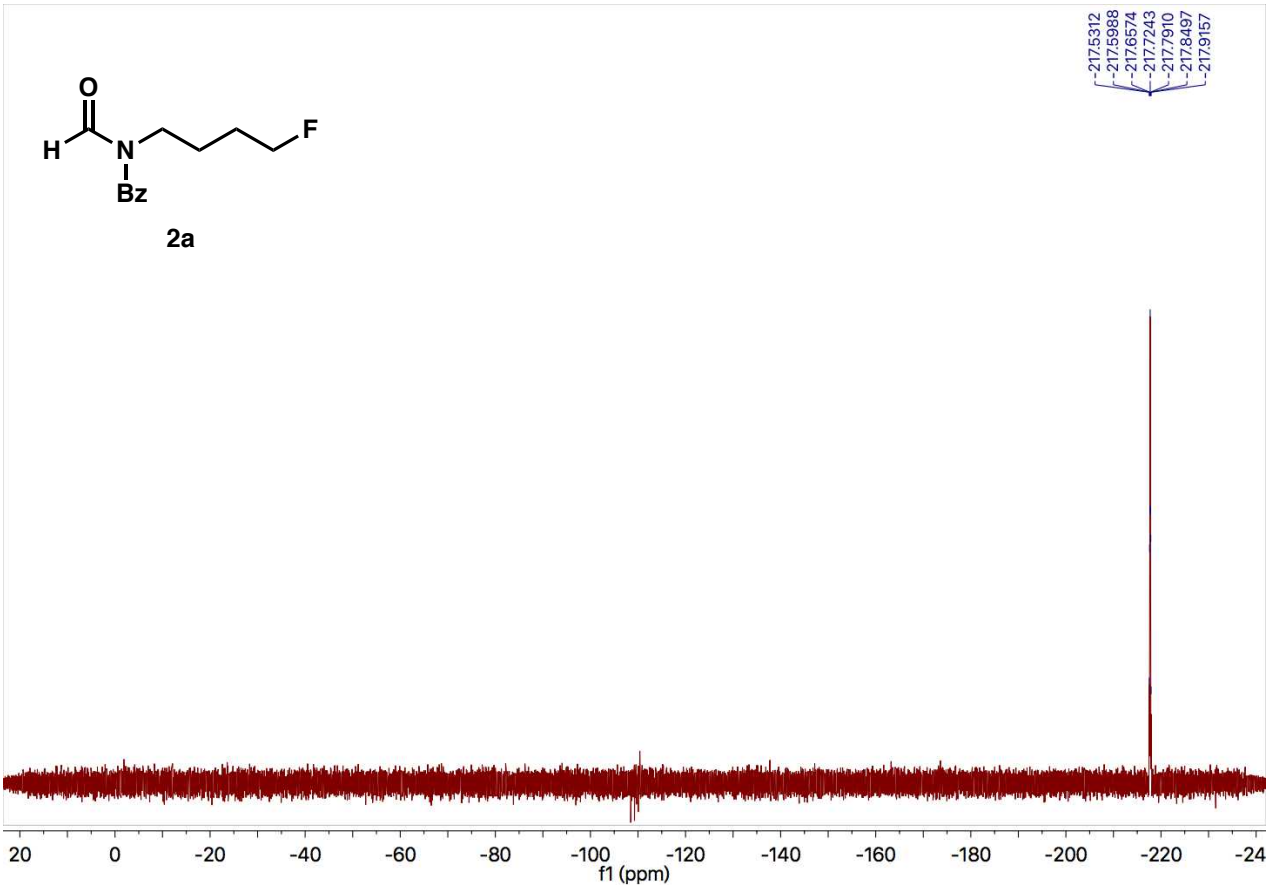
133.7104
132.3368
129.1185
128.9178
84.1228
83.0279
40.2160
28.0983
27.9648
24.1852
24.1521
f1 (ppm)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H
N
F
Bz
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-217.5988
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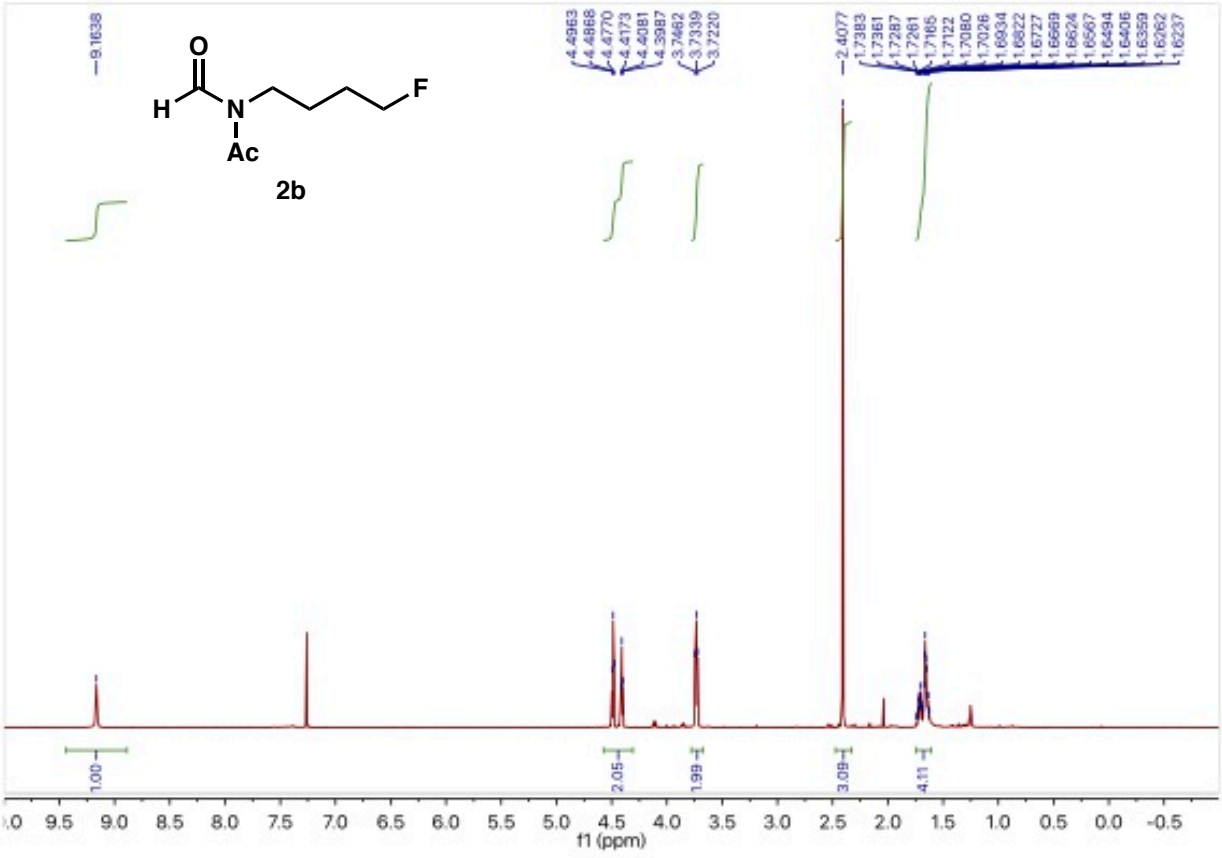
-217.7243
-217.7910
-217.8497
-217.9157
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-24
f1 (ppm)

2a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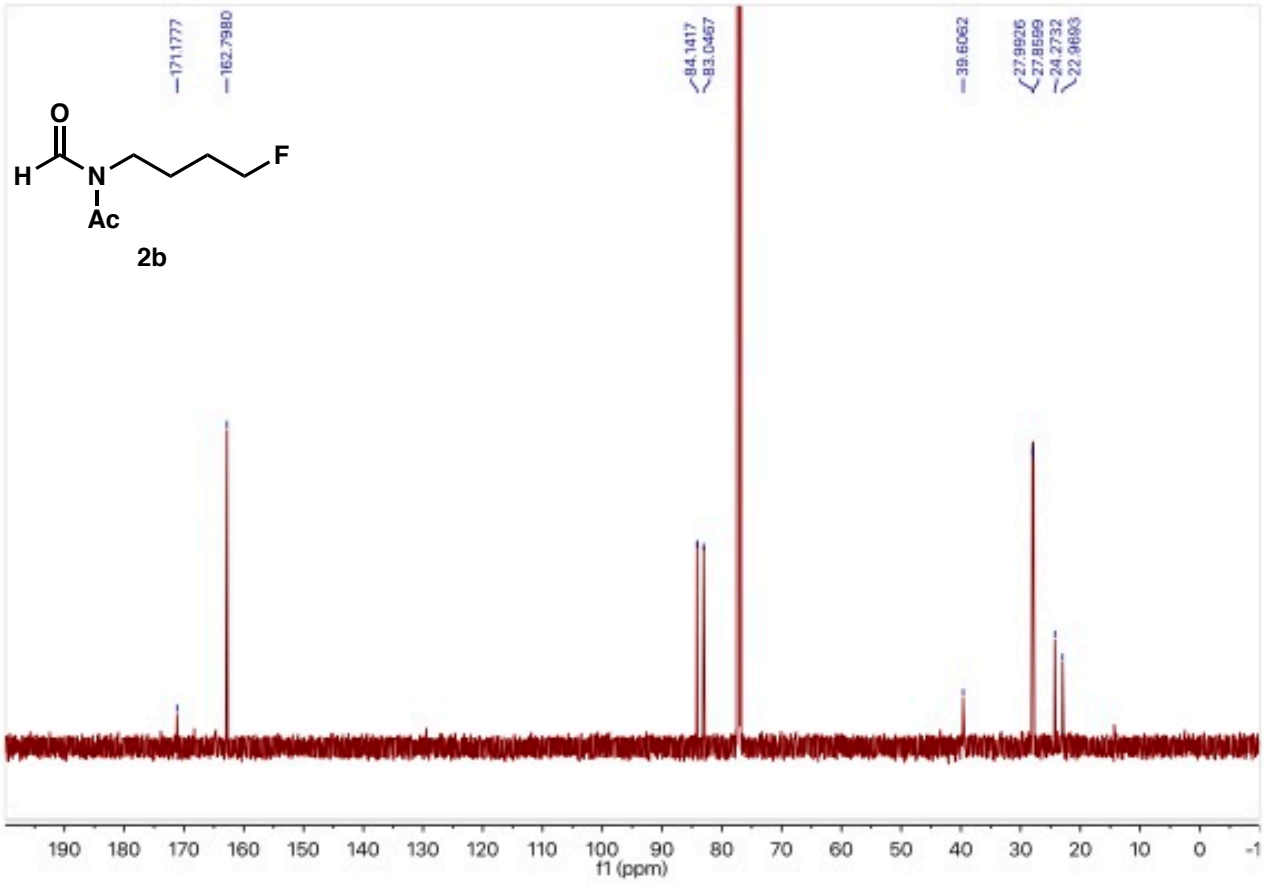
4.4866
4.4770
4.4173
4.4081
4.3987
3.7462
3.7339
3.7220
2.4077
1.7383
1.7361
1.7287
1.7261
1.7165
1.7122
1.7080
1.7026
1.6934
1.6822
1.6727
1.6669
1.6624
1.6567
1.6494
1.6406
1.6359
1.6262
1.6237
O
H
N
F
Ac
1.00
2.05
1.99
3.09
4.11
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

2b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162.7980
84.1417
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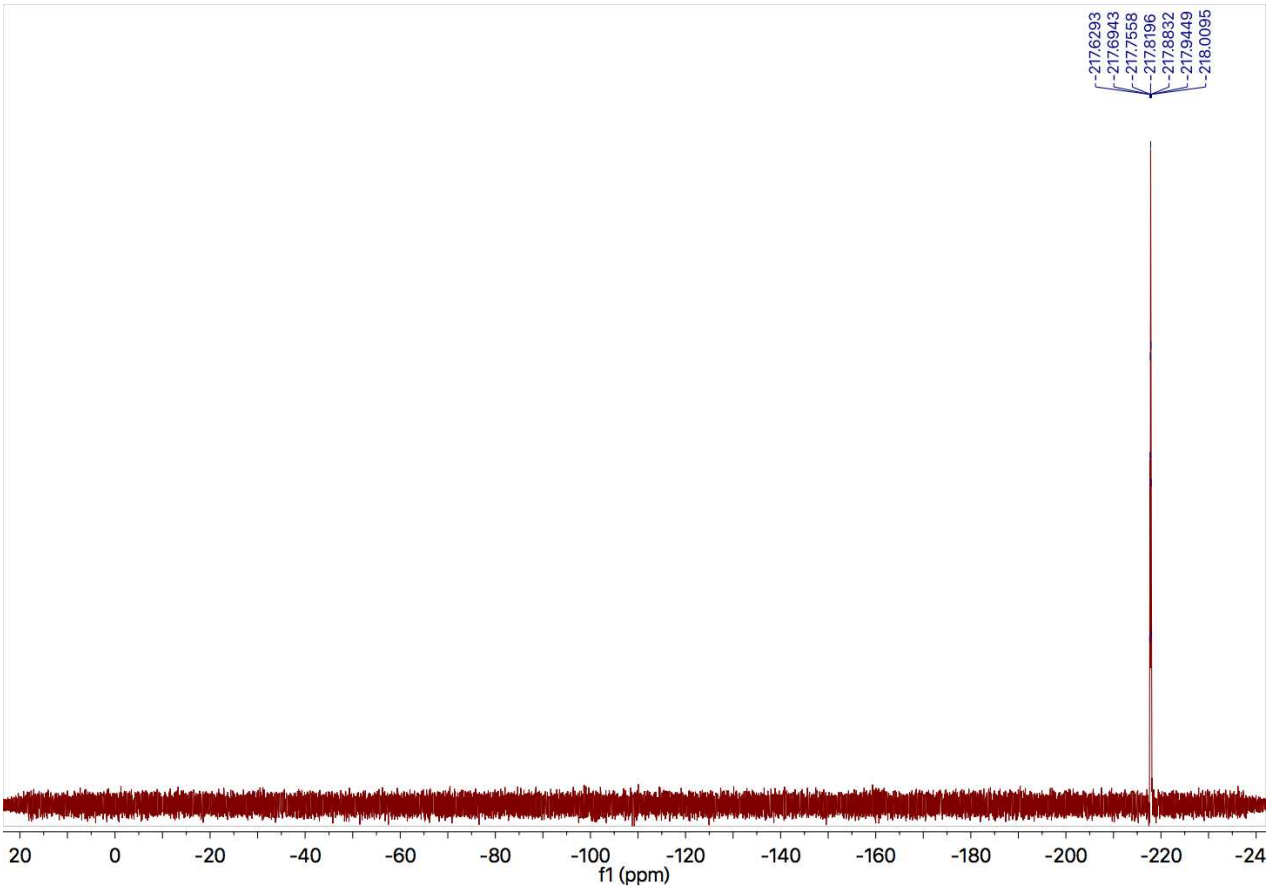
39.6062
27.9926
27.8599
24.2732
22.9693
O
H
N
Ac
F
2b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)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217.6943
217.7558
217.8196
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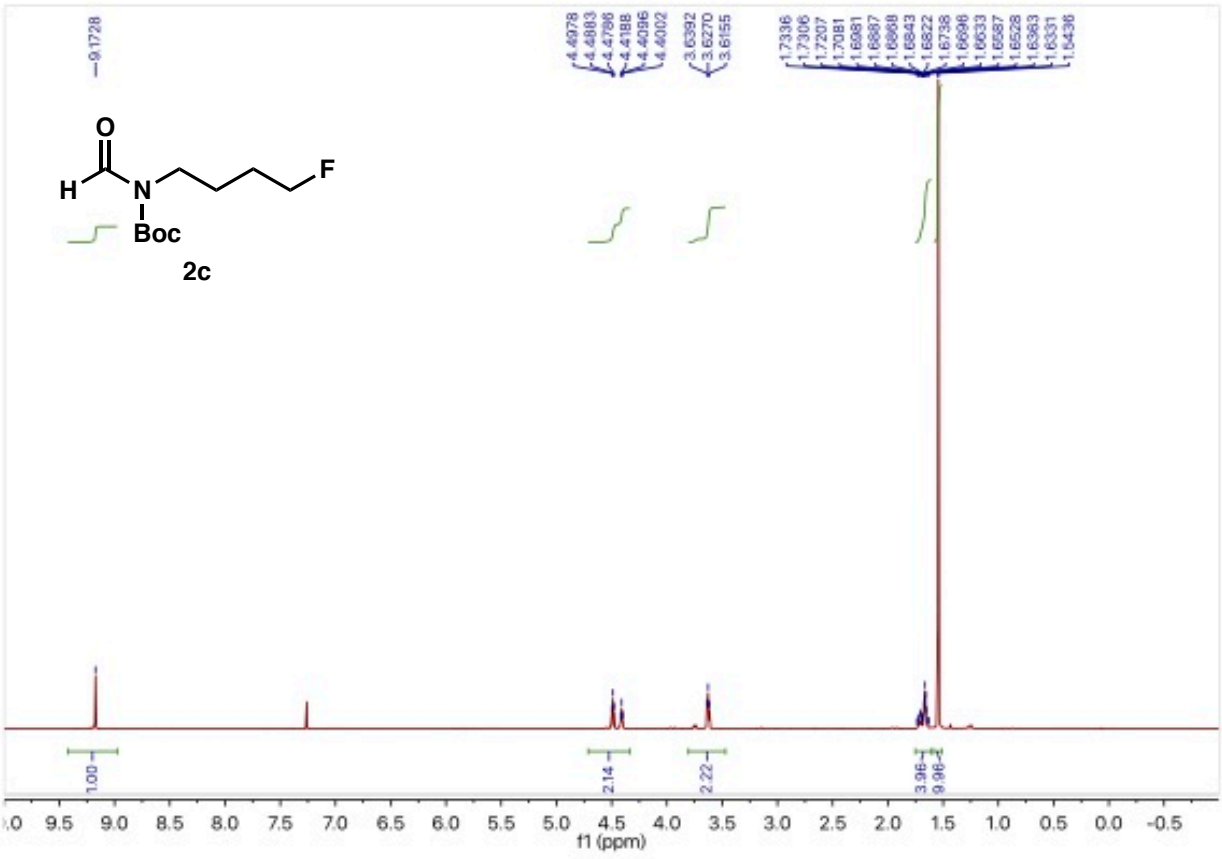
217.9449
218.0095
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -24
f1 (ppm)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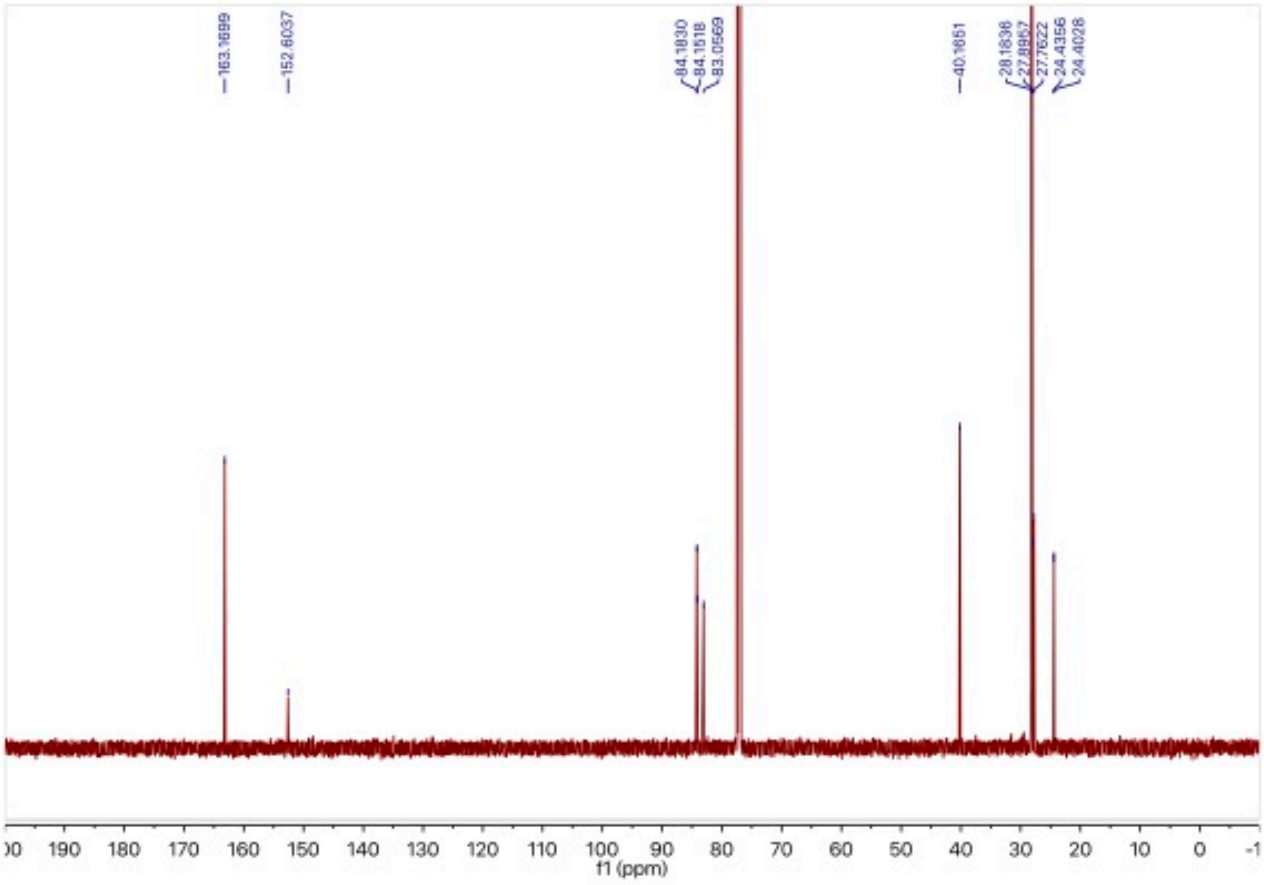
4.4883
4.4786
4.4188
4.4096
4.4002
3.6392
3.6270
3.6155
1.7336
1.7306
1.7207
1.7081
1.6981
1.6887
1.6868
1.6843
1.6822
1.6738
1.6696
1.6633
1.6587
1.6528
1.6383
1.6331
1.5436
O
H
N
F
Boc
2c
1.00
2.14
2.22
3.96
9.96
f1 (ppm)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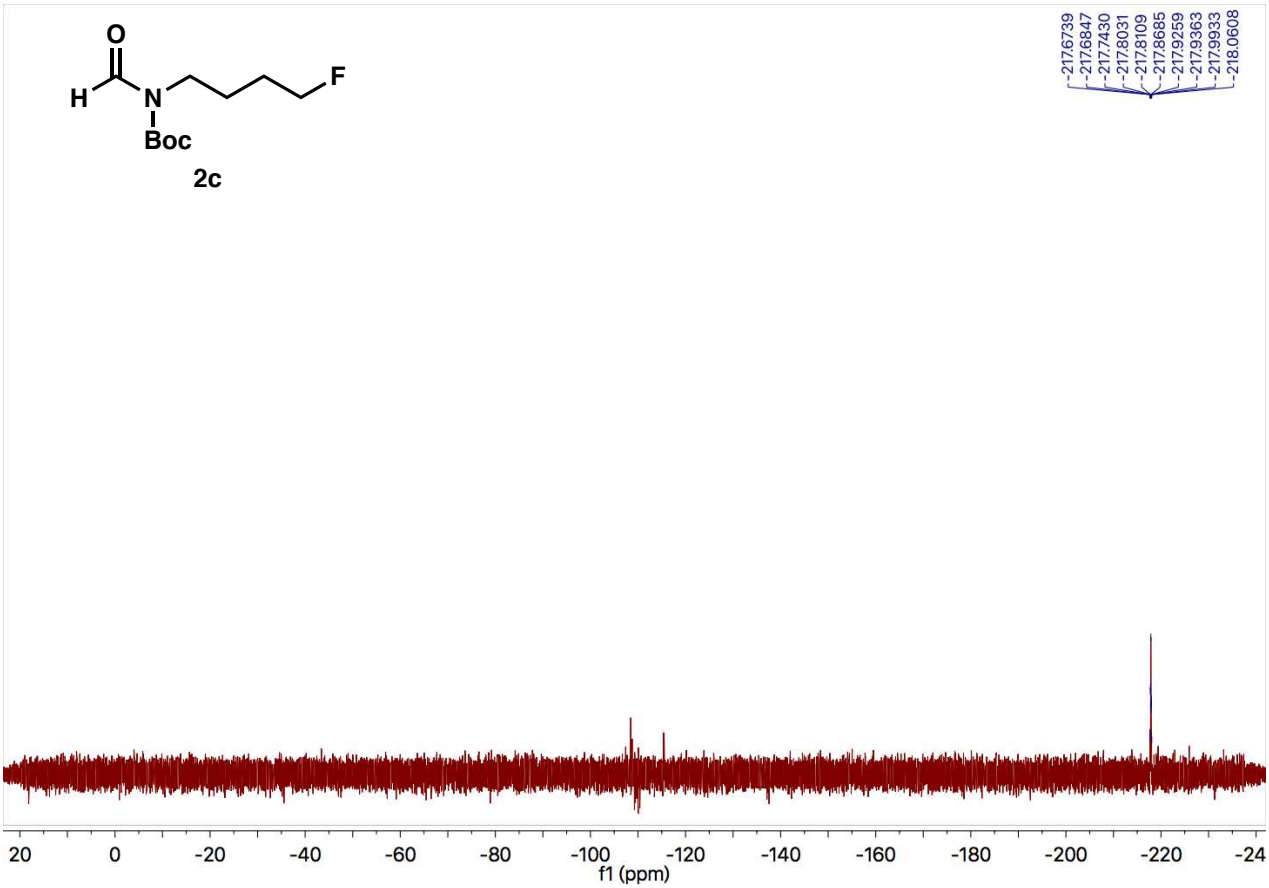
152.6037
84.1830
84.1518
83.0569
40.1651
28.1836
27.8957
27.7622
24.4356
24.4028
f1 (ppm)


O
H
N
Boc
F
2c
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-217.6847
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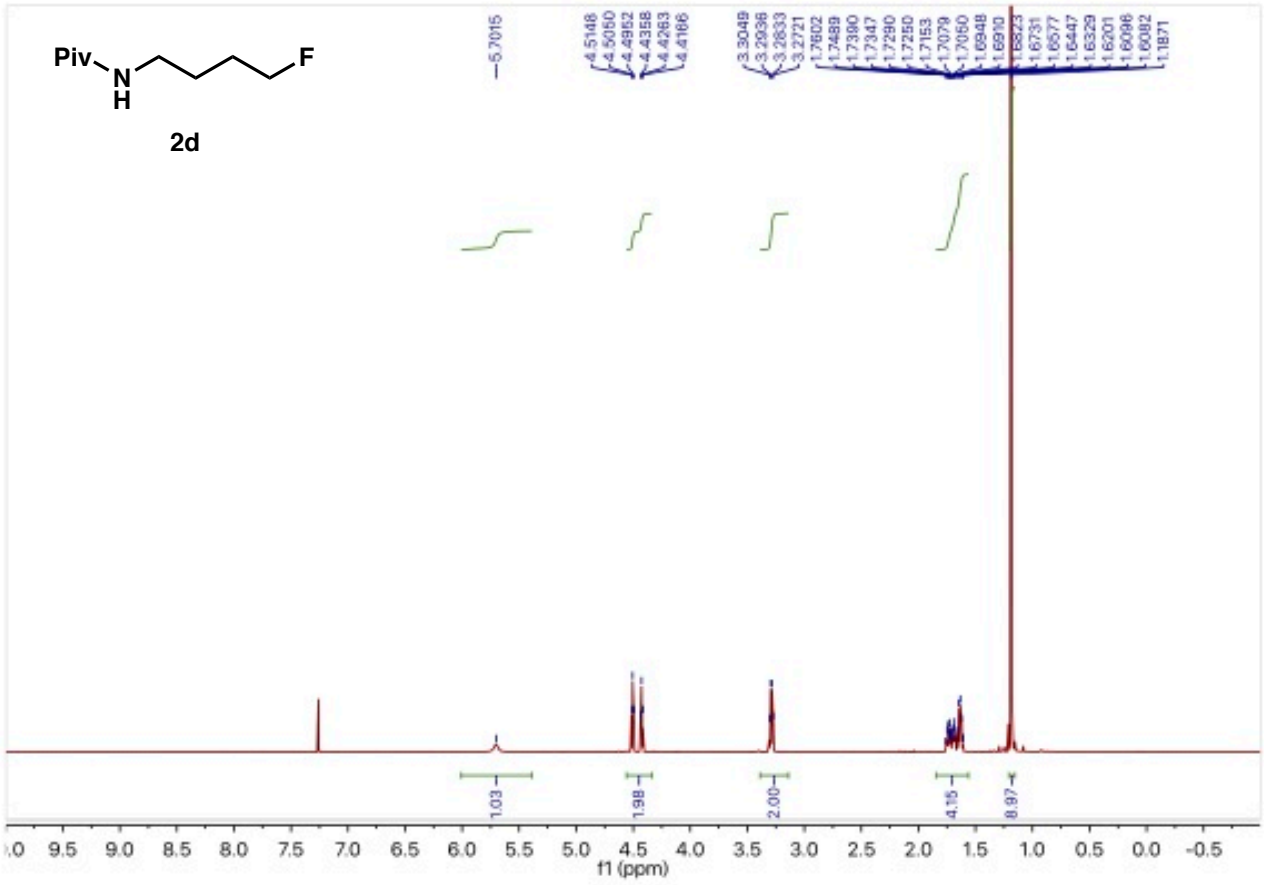
-217.8109
-217.8685
-217.9259
-217.9363
-217.9933
-218.0608
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-24
f1 (ppm)


Piv
N
H
F
2d
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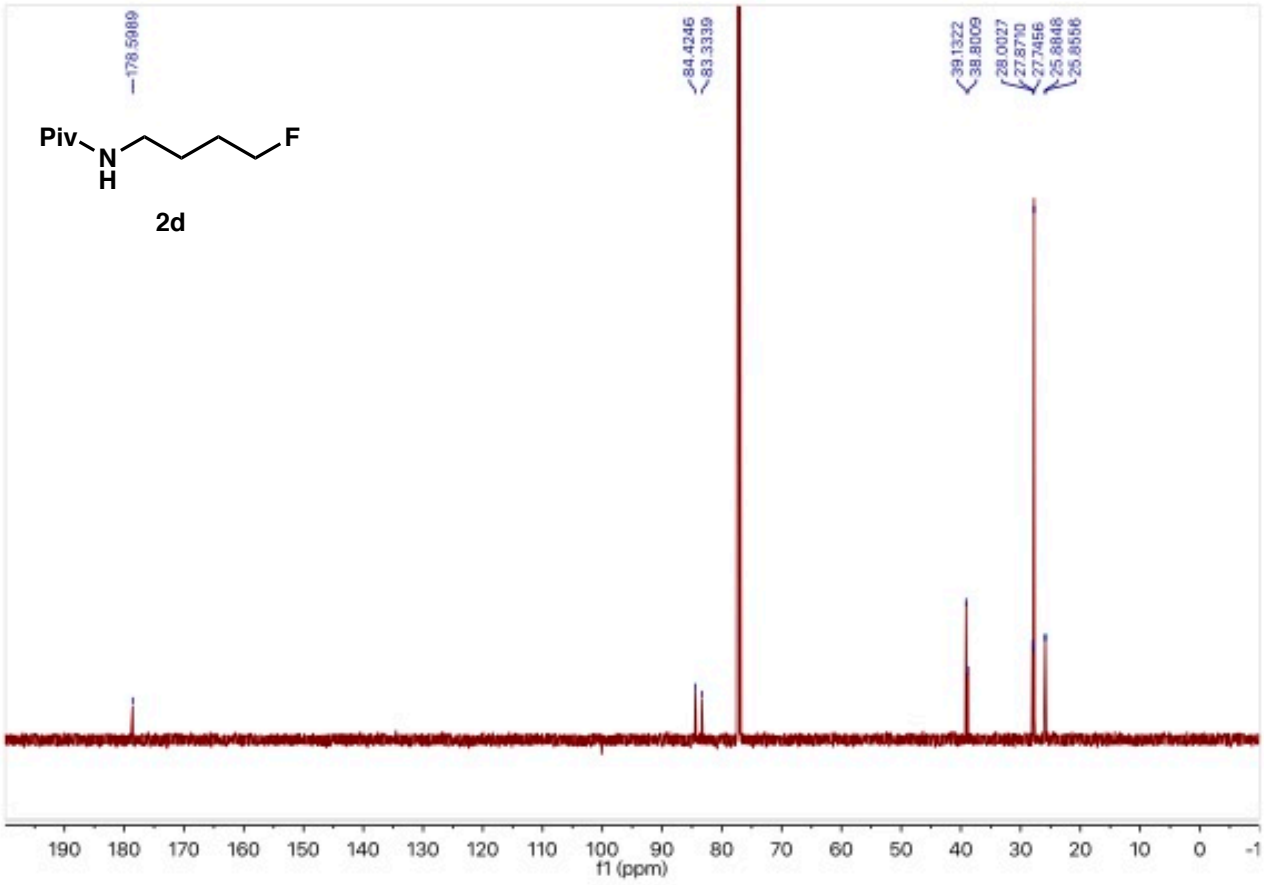
4.5148
4.5050
4.4952
4.4358
4.4263
4.4166
3.3049
3.2936
3.2833
3.2721
1.7602
1.7489
1.7390
1.7347
1.7290
1.7250
1.7153
1.7079
1.7060
1.6948
1.6910
1.6731
1.6577
1.6447
1.6329
1.6201
1.6096
1.6082
1.1871
1.03
1.98
2.00
4.15
8.97
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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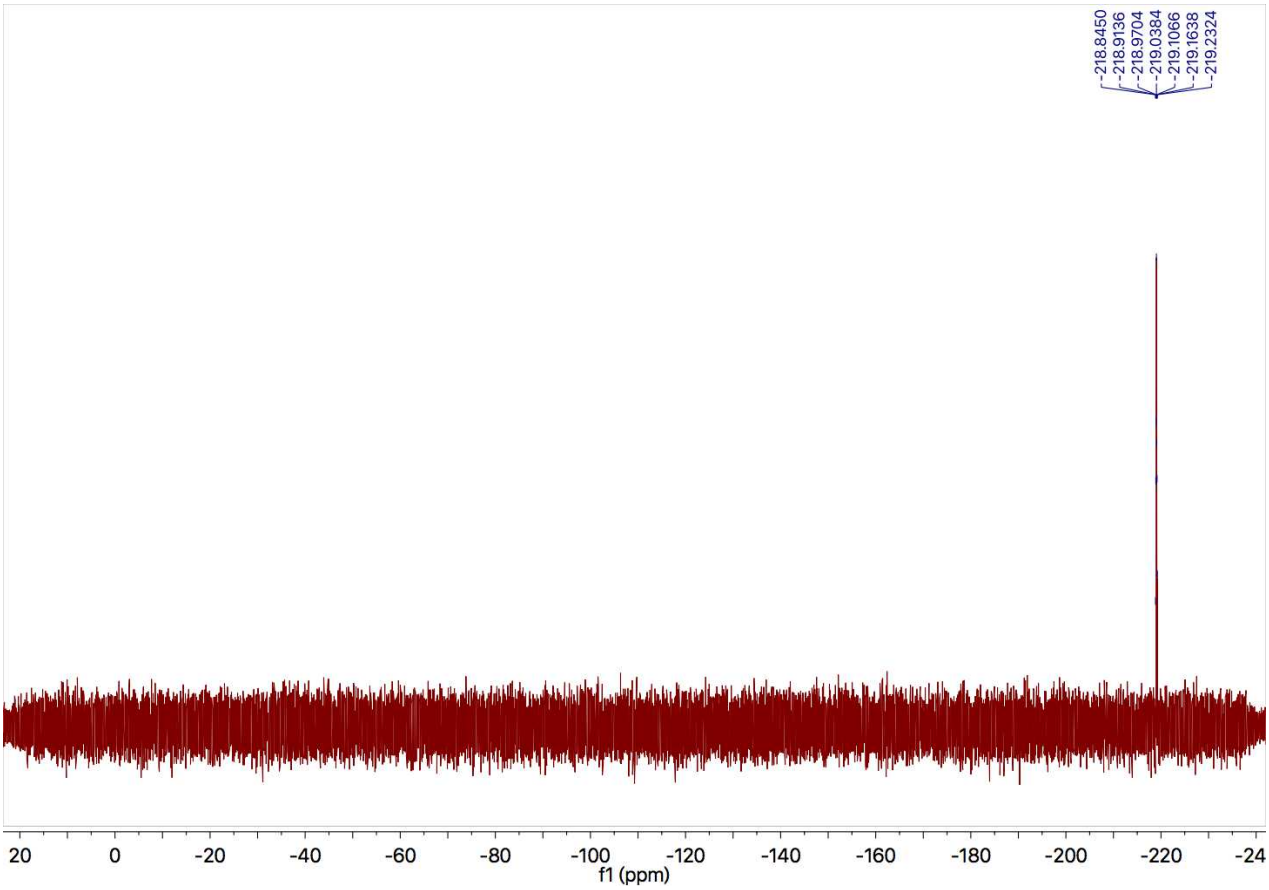
83.3339
39.1322
38.9009
28.0027
27.8710
27.7456
25.8848
25.8556
Piv
N
H
F
2d
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)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-218.9136
-218.9704
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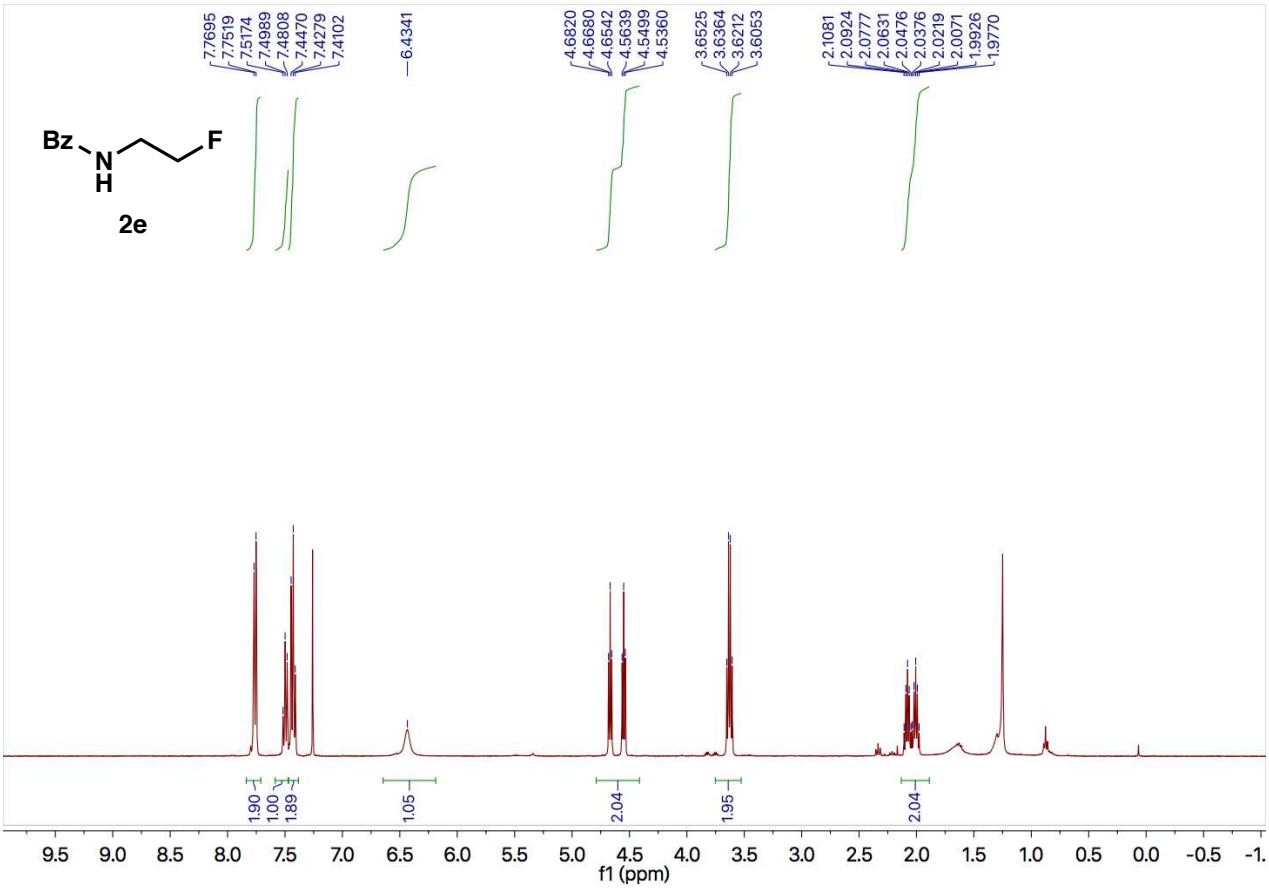
-219.1066
-219.1638
-219.2324
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -24
f1 (ppm)


7.7695
7.7519
7.5174
7.4989
7.4808
7.4470
7.4279
7.4102
6.4341
4.6820
4.6680
4.6542
4.5639
4.5499
4.5360
3.6525
3.6364
3.6212
3.6053
2.1081
2.0924
2.0777
2.0631
2.0476
2.0376
2.0219
2.0071
1.9926
1.9770
Bz
N
H
F
2e
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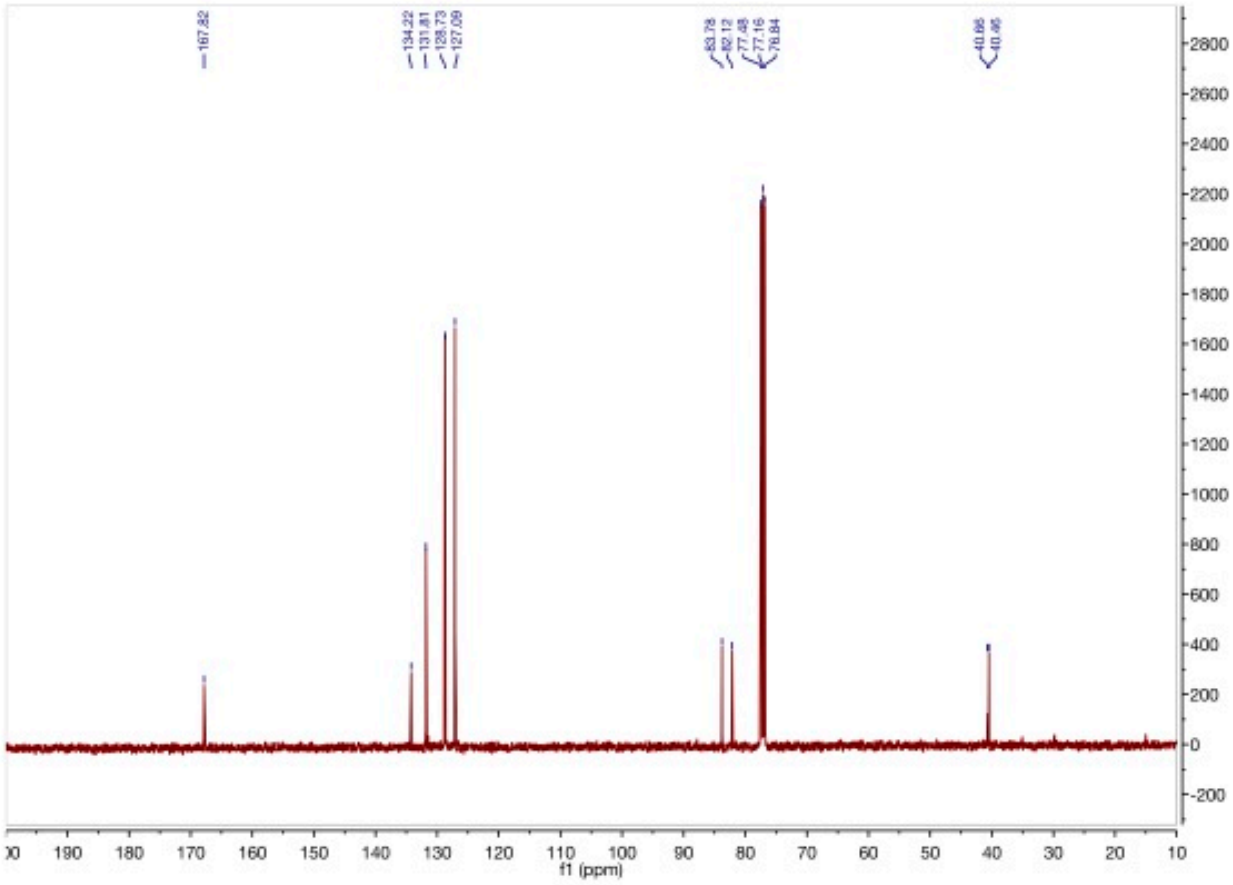
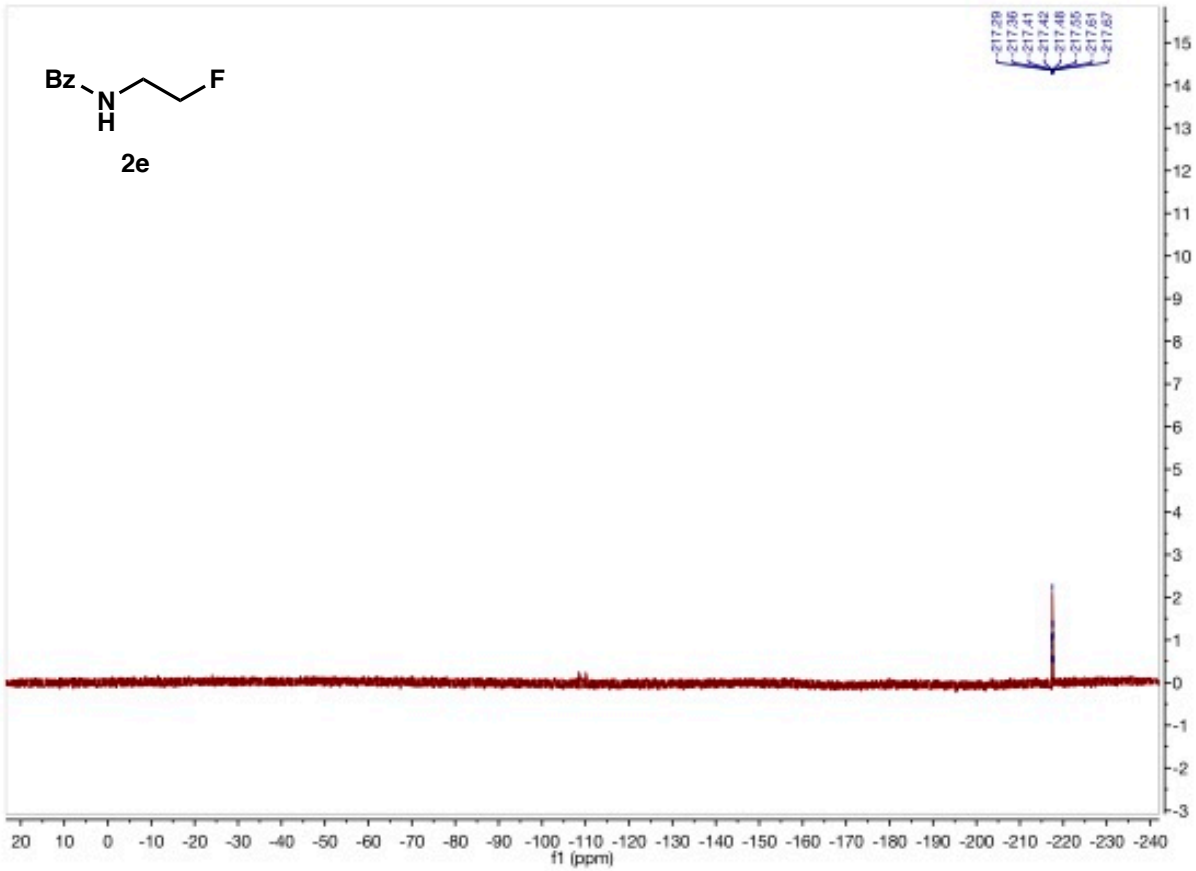
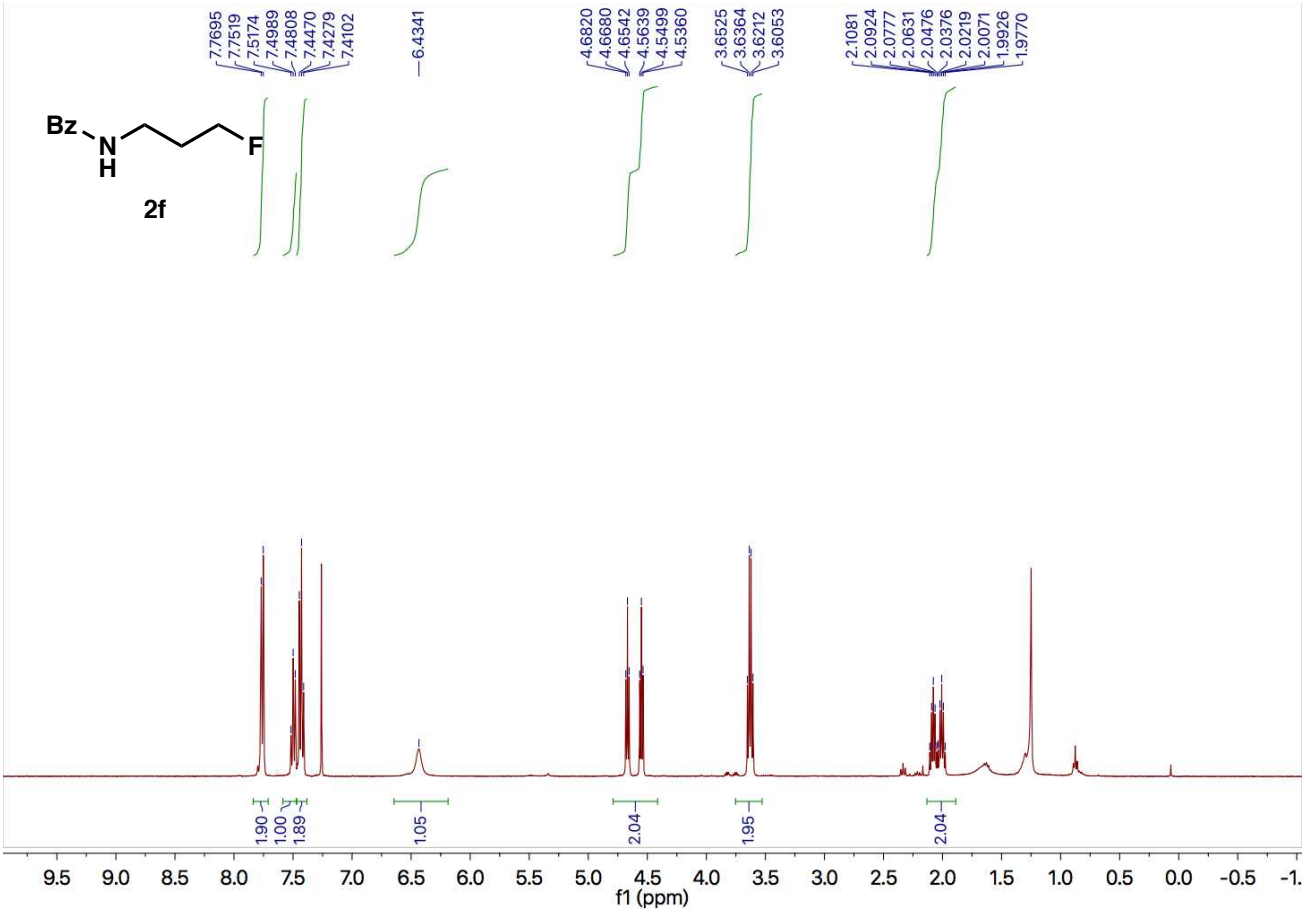
1.00
1.89
1.05
2.04
1.95
2.04
f1 (ppm)


167.82
134.22
131.81
128.73
127.09
83.78
82.12
77.48
77.16
76.84
40.86
40.46
f1 (ppm)


Bz
N
H
F
2e
f1 (ppm)


Bz
N
H
F
2f
7.7695
7.7519
7.5174
7.4989
7.4808
7.4470
7.4279
7.4102
6.4341
4.6820
4.6680
4.6542
4.5639
4.5499
4.5360
3.6525
3.6364
3.6212
3.6053
2.1081
2.0924
2.0777
2.0631
2.0476
2.0376
2.0219
2.0071
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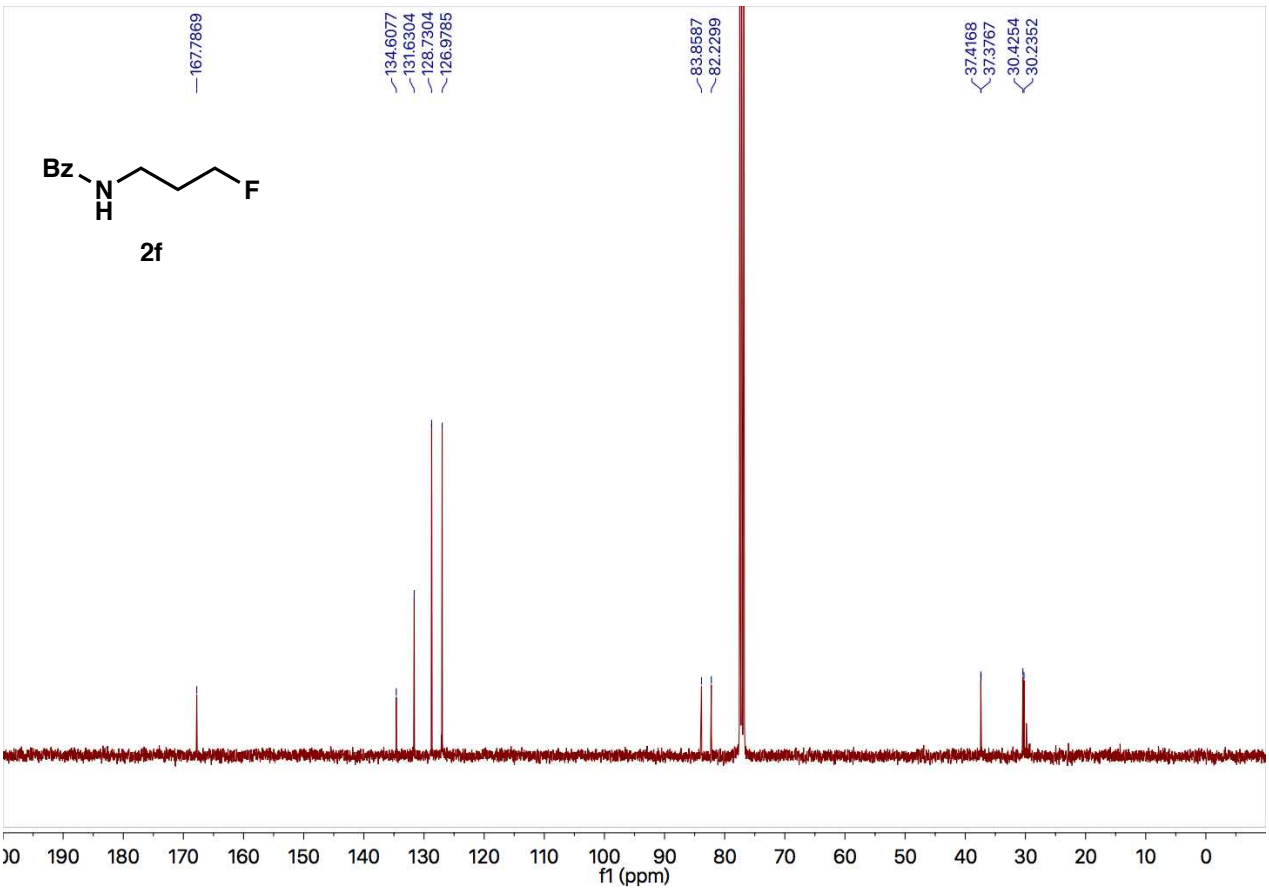
1.9770
1.90
1.00
1.89
1.05
2.04
1.95
2.04
f1 (ppm)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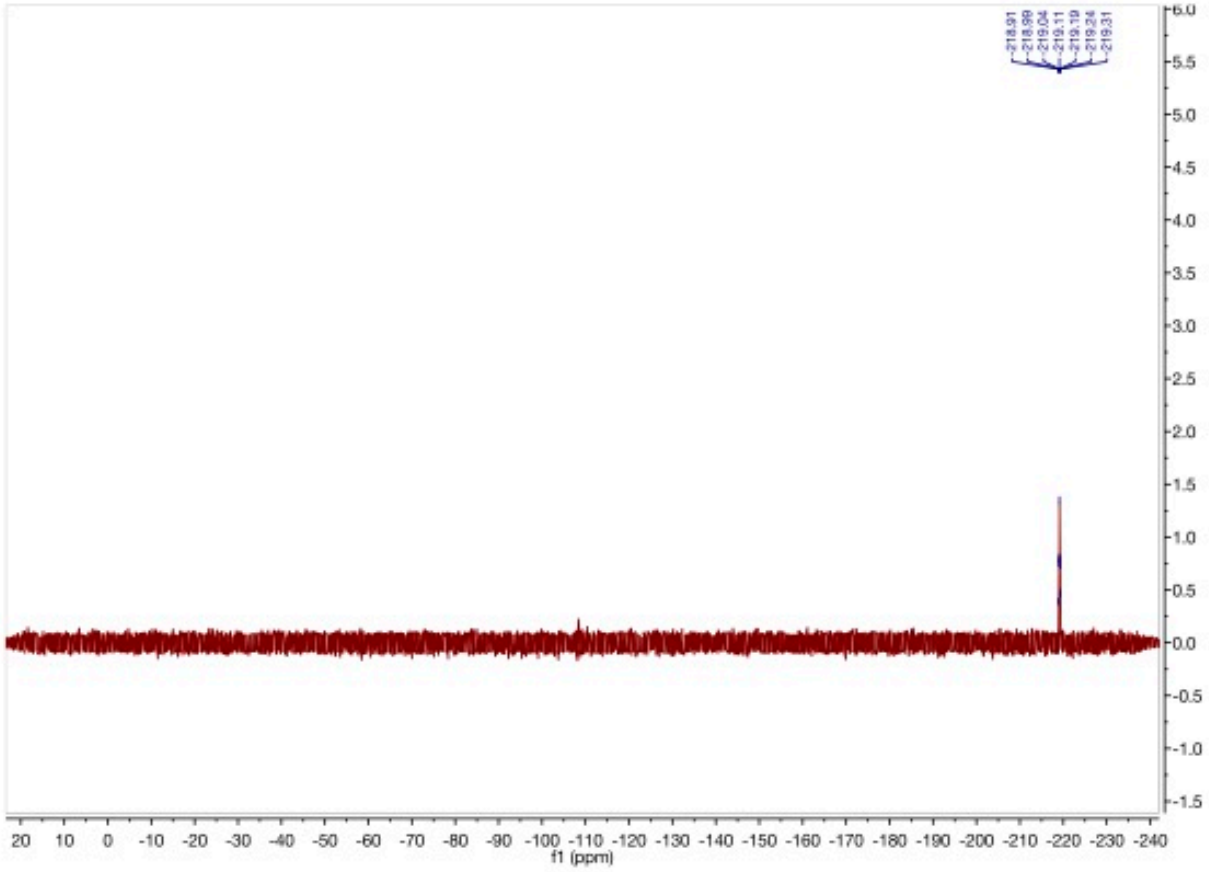
82.2299
37.4168
37.3767
30.4254
30.2352
Bz
N
H
F
2f
f1 (ppm)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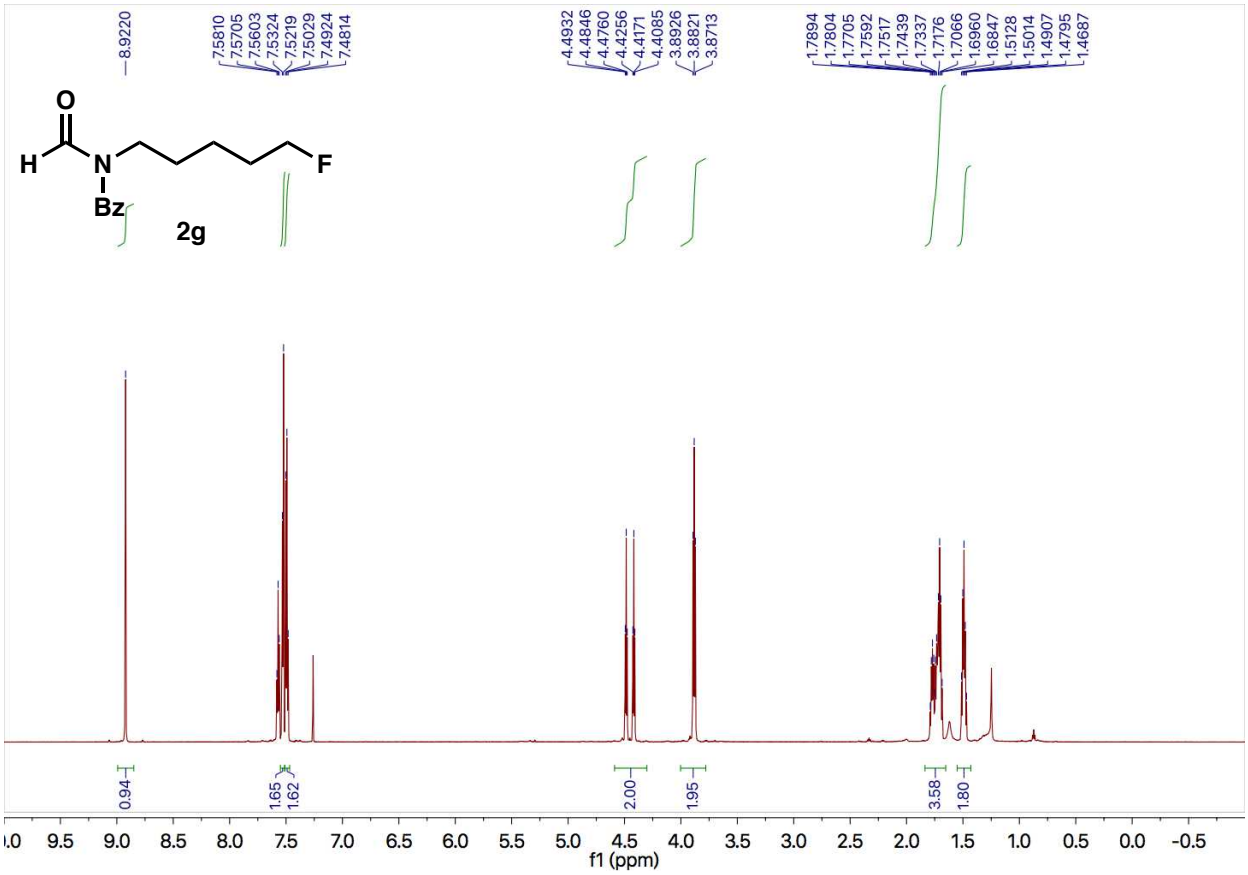
219.11
219.19
219.24
219.31
f1 (ppm)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7.5705
7.5603
7.5324
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7.5029
7.4924
7.4814
4.4932
4.4846
4.4760
4.4256
4.4171
4.4085
3.8926
3.8821
3.8713
1.7894
1.7804
1.7705
1.7592
1.7517
1.7439
1.7337
1.7176
1.7066
1.6960
1.6847
1.5128
1.5014
1.4907
1.4795
1.4687
O
H
N
Bz
F
2g
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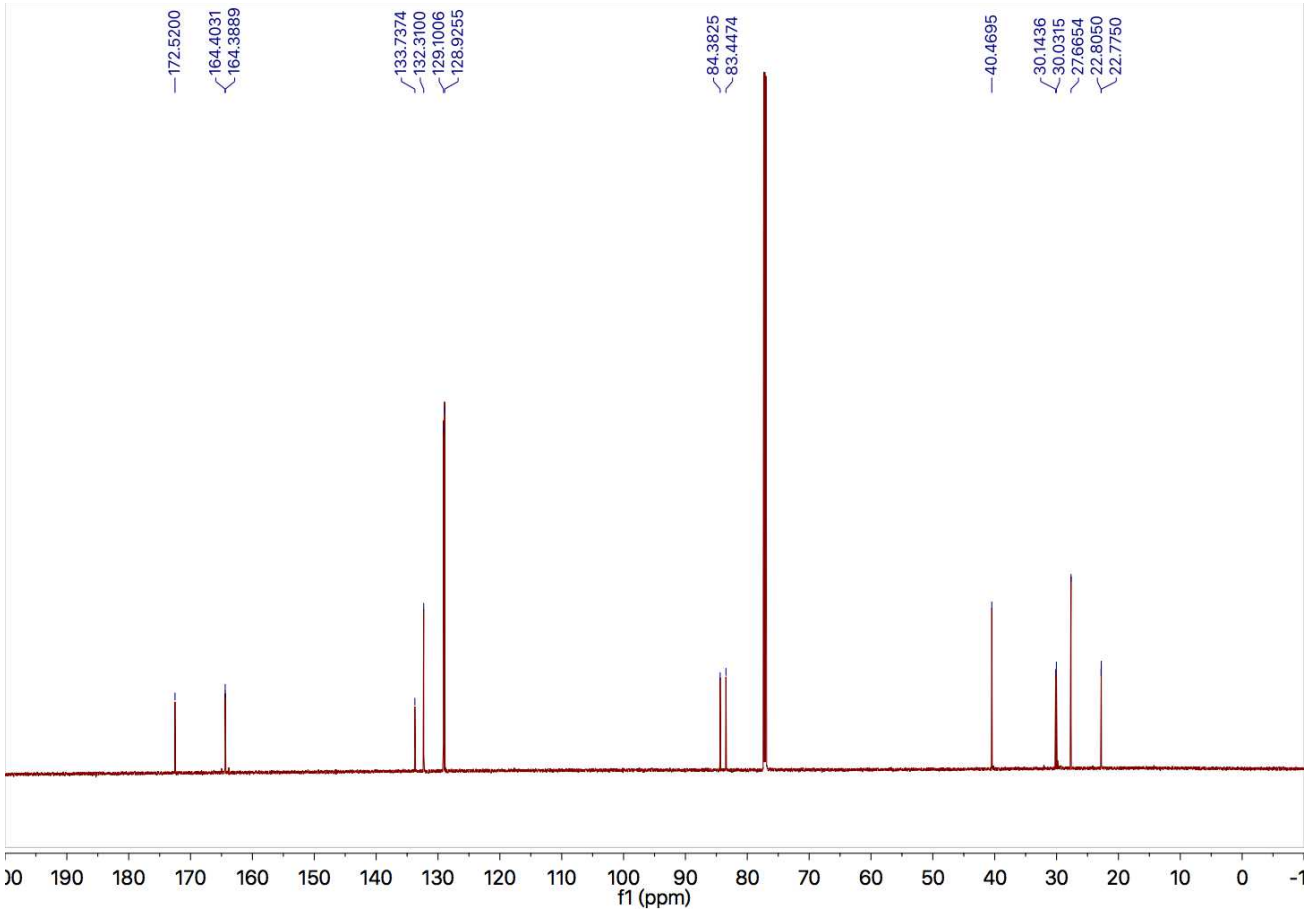
1.65
1.62
2.00
1.95
3.58
1.80
f1 (ppm)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133.7374
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129.1006
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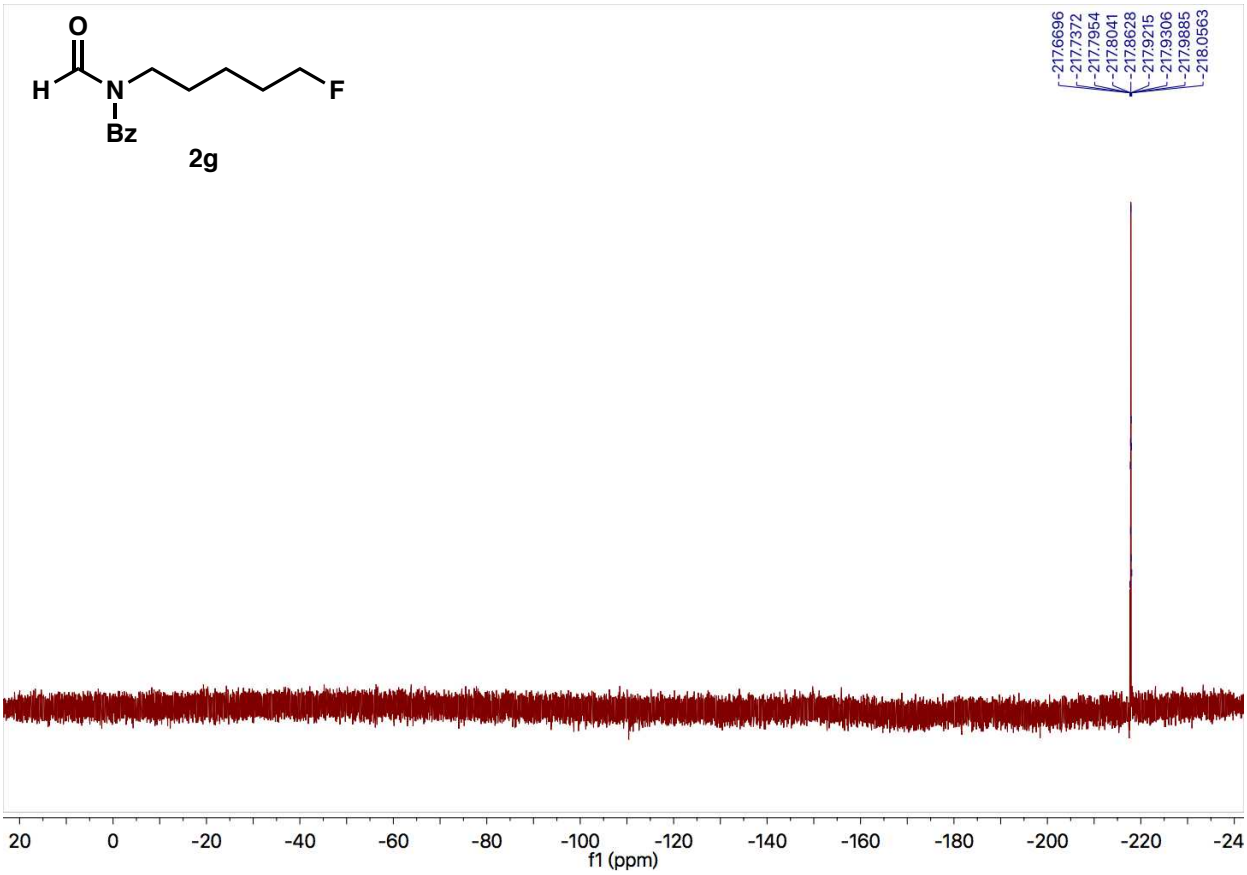
83.4474
40.4695
30.1436
30.0315
27.6654
22.8050
22.7750
f1 (ppm)


O
H
N
Bz
F
2g
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-217.7372
-217.7954
-217.8041
-217.8628
-217.9215
-217.9306
-217.9885
-218.0563
20
0
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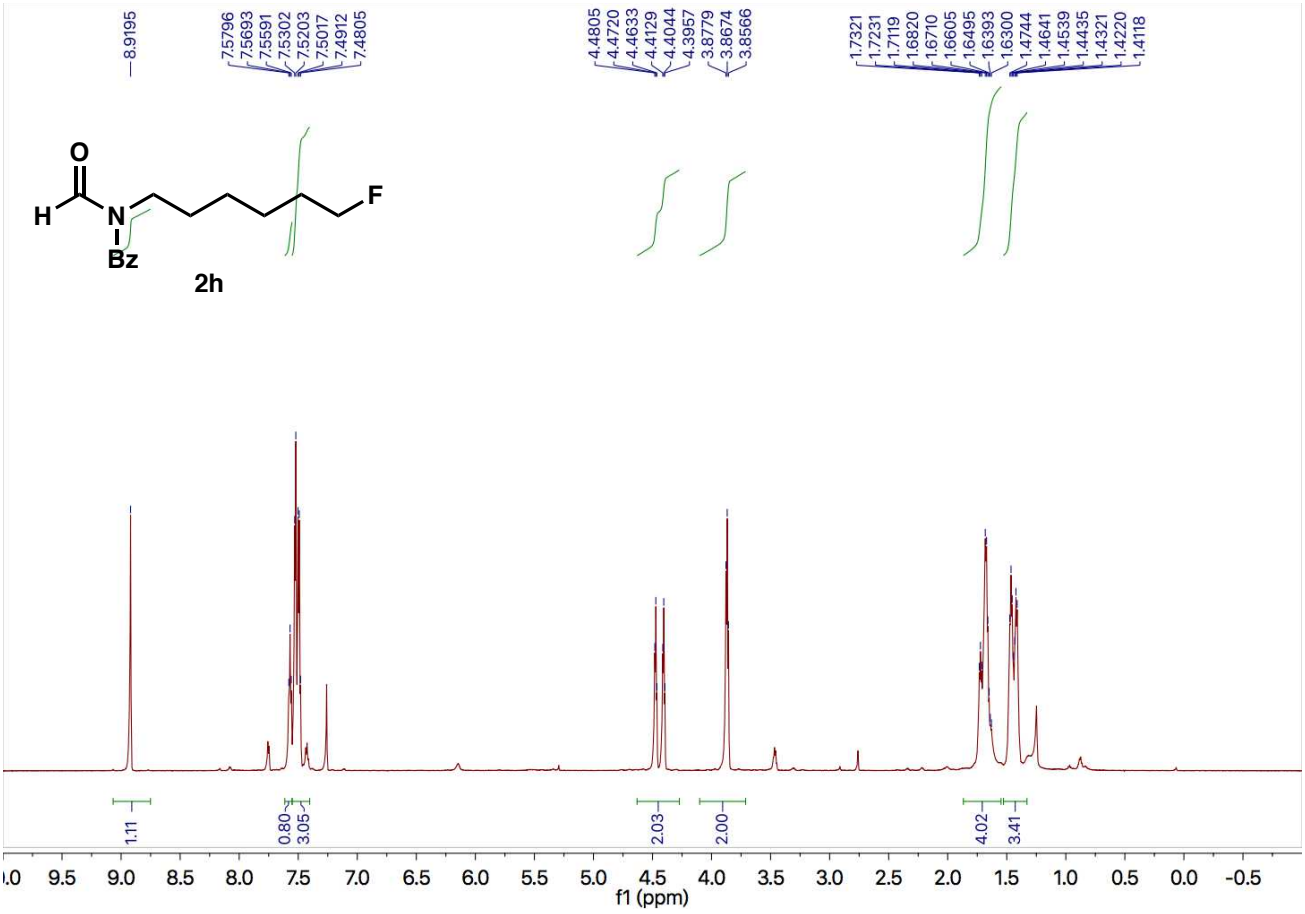
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-24
f1 (ppm)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7.5017
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7.4805
4.4805
4.4720
4.4633
4.4129
4.4044
4.3957
3.8779
3.8674
3.8566
1.7321
1.7231
1.7119
1.6820
1.6710
1.6605
1.6495
1.6393
1.6300
1.4744
1.4641
1.4539
1.4435
1.4321
1.4220
1.4118
O
H
N
Bz
F
2h
1.11
0.80
3.05
2.03
2.00
4.02
3.41
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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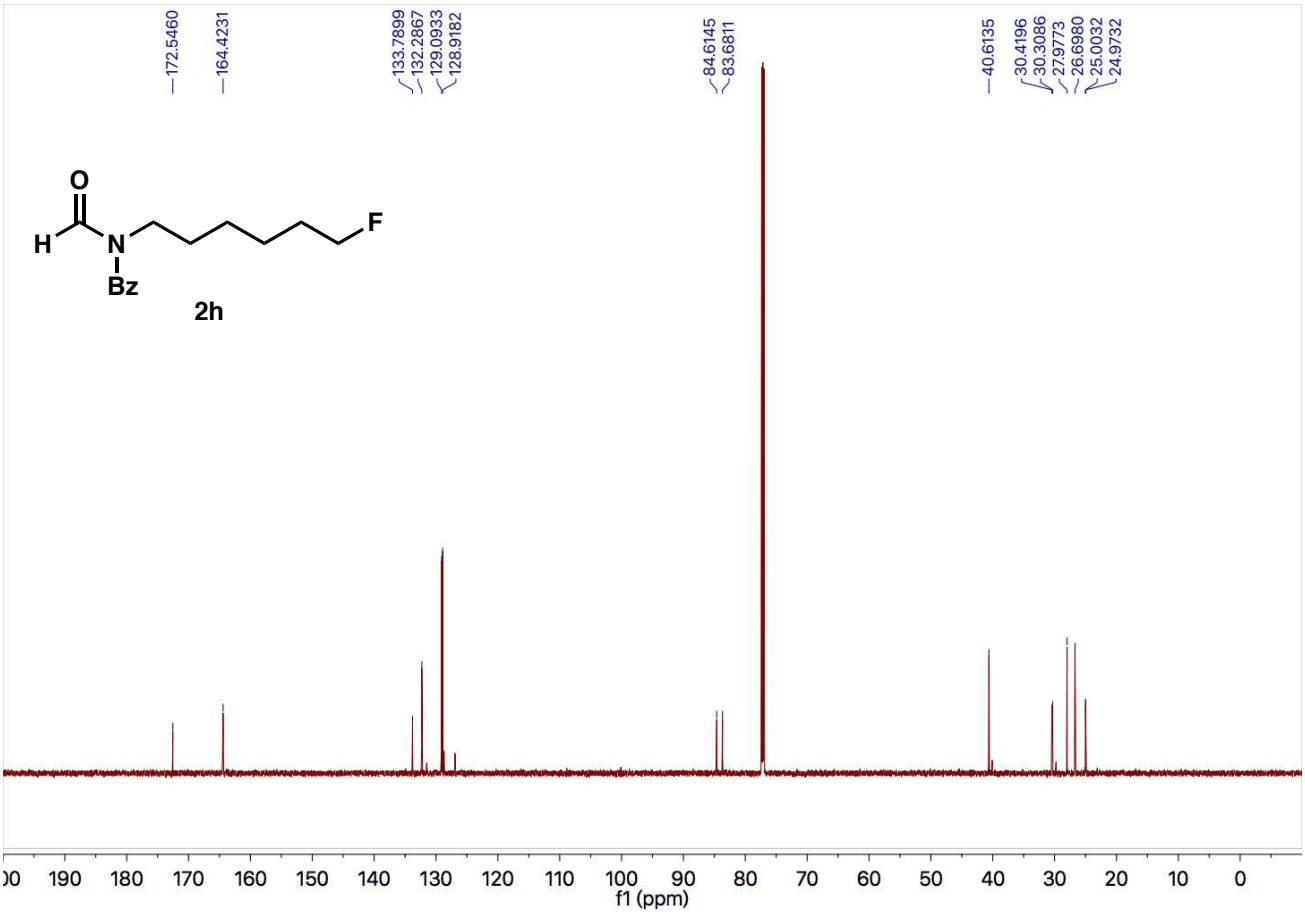
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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132.2867
129.0933
128.9182
84.6145
83.6811
40.6135
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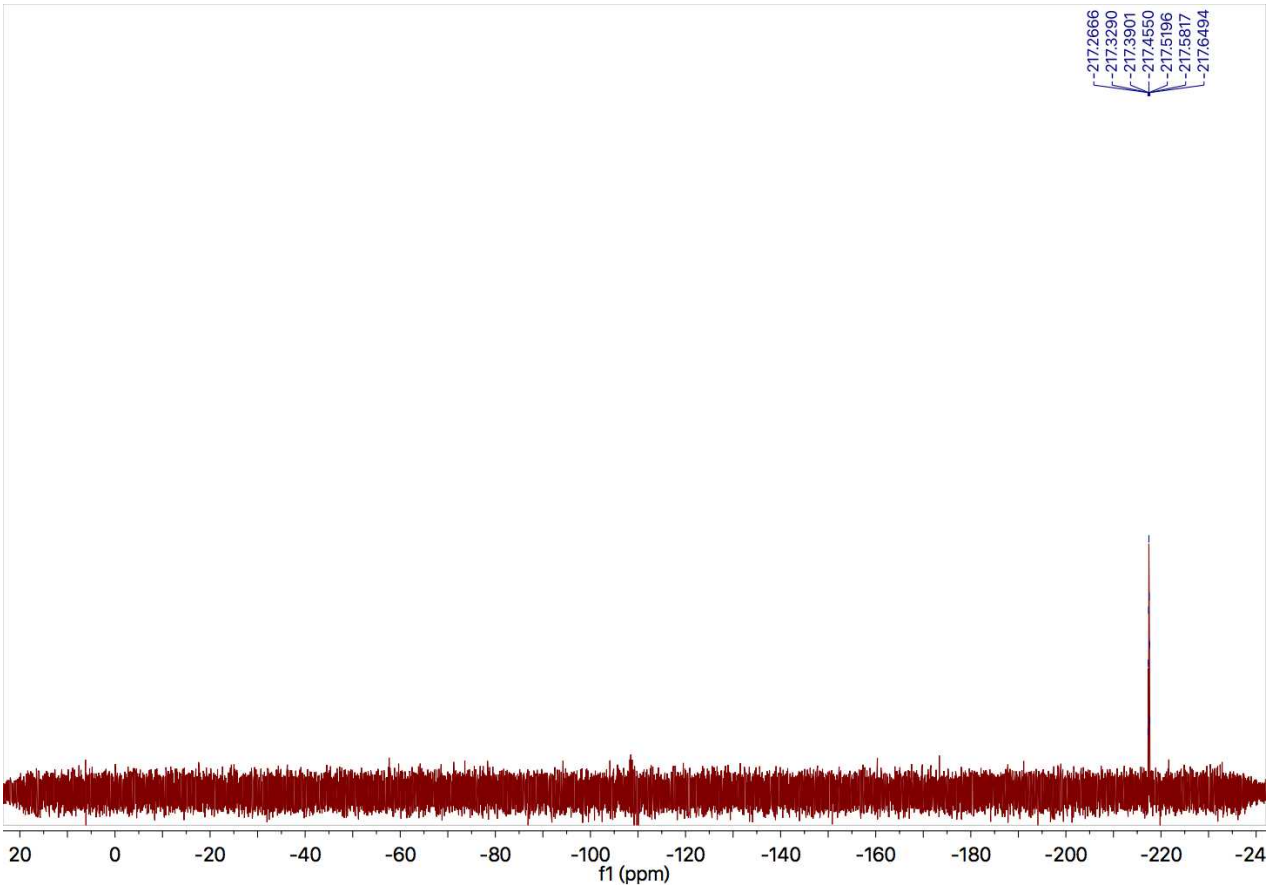
30.3086
27.9773
26.6980
25.0032
24.9732
O
H
N
Bz
F
2h
f1 (ppm)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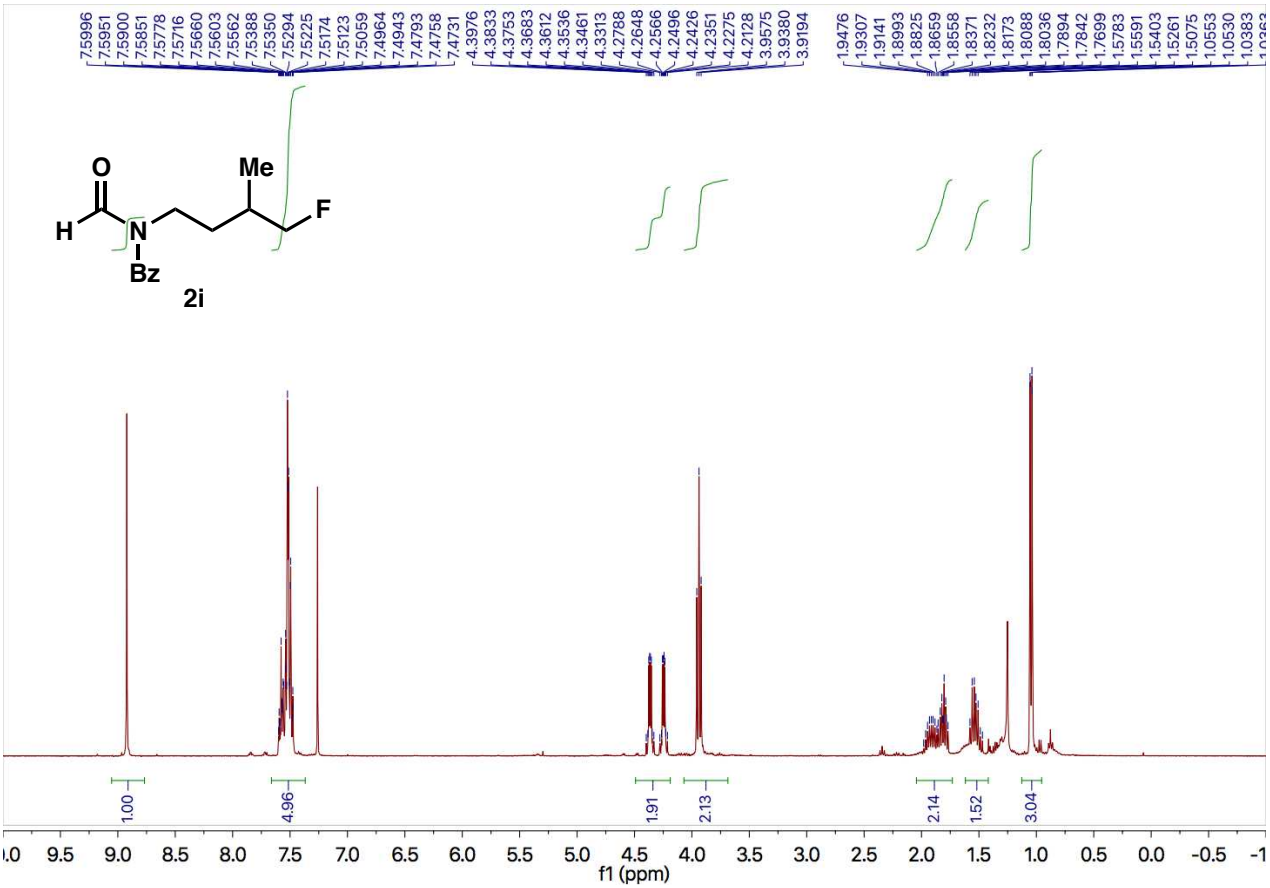
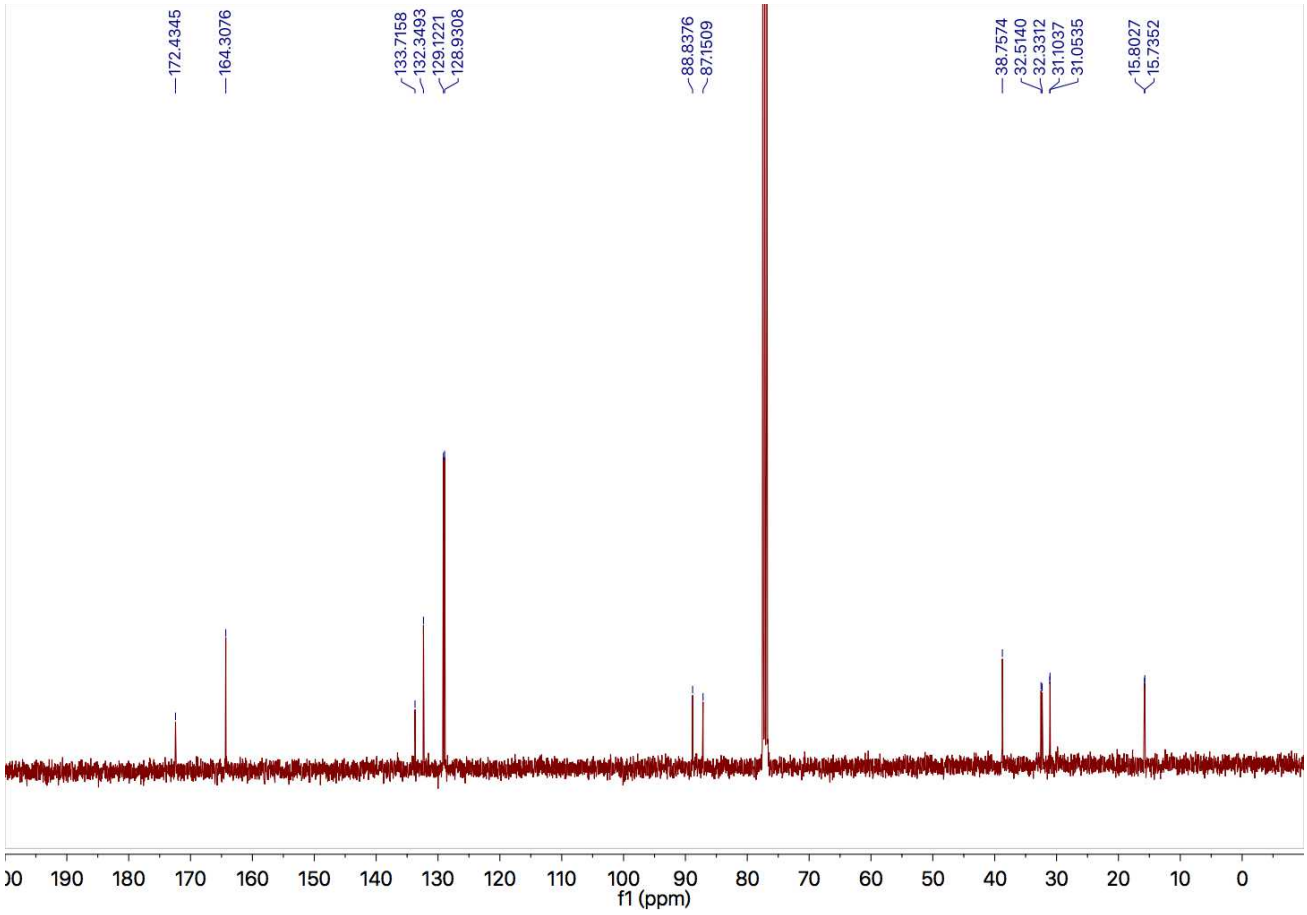
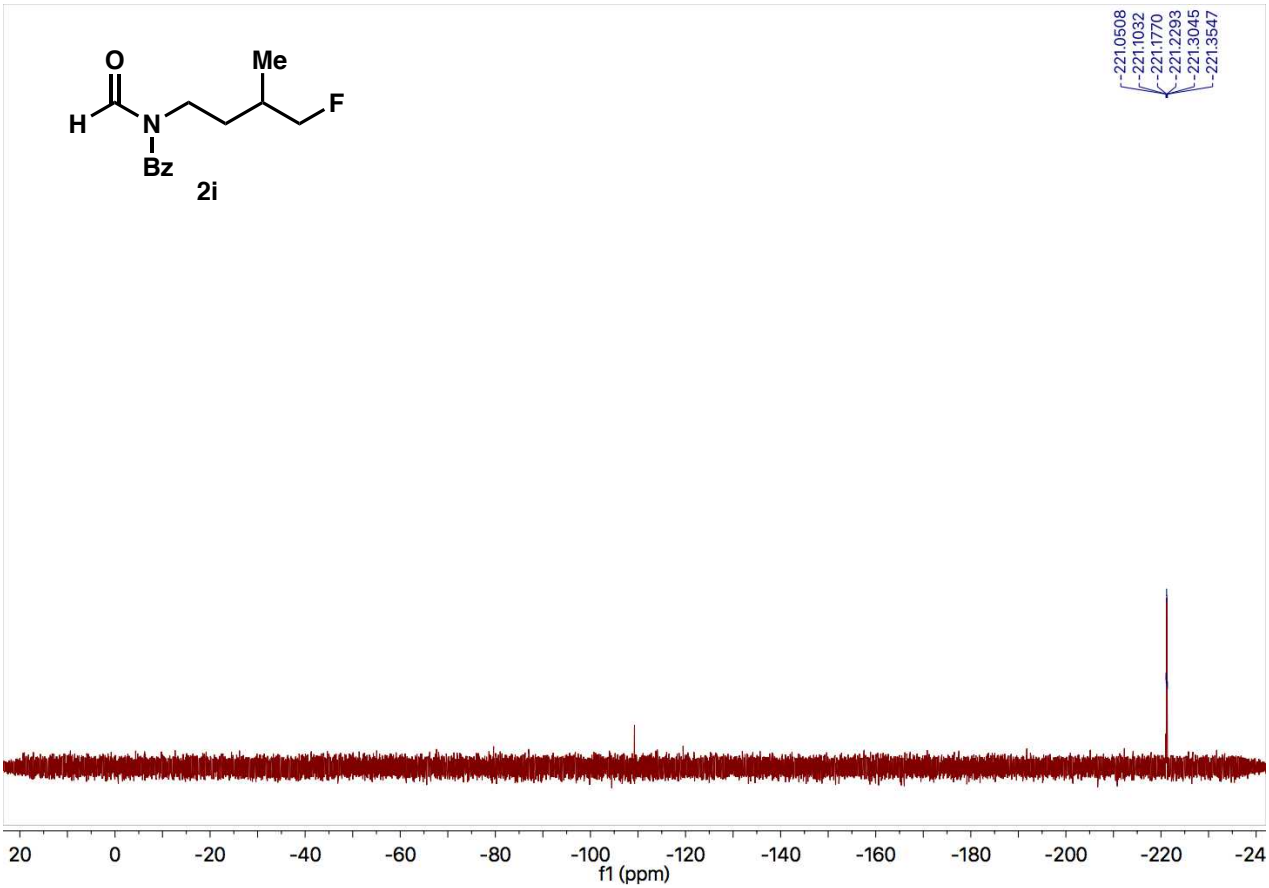
217.3290
217.3901
217.4550
217.5196
217.5817
217.6494
f1 (ppm)


O
Me
F
H
N
Bz
2i
f1 (ppm)


f1 (ppm)


O
Me
H
N
F
Bz
2i
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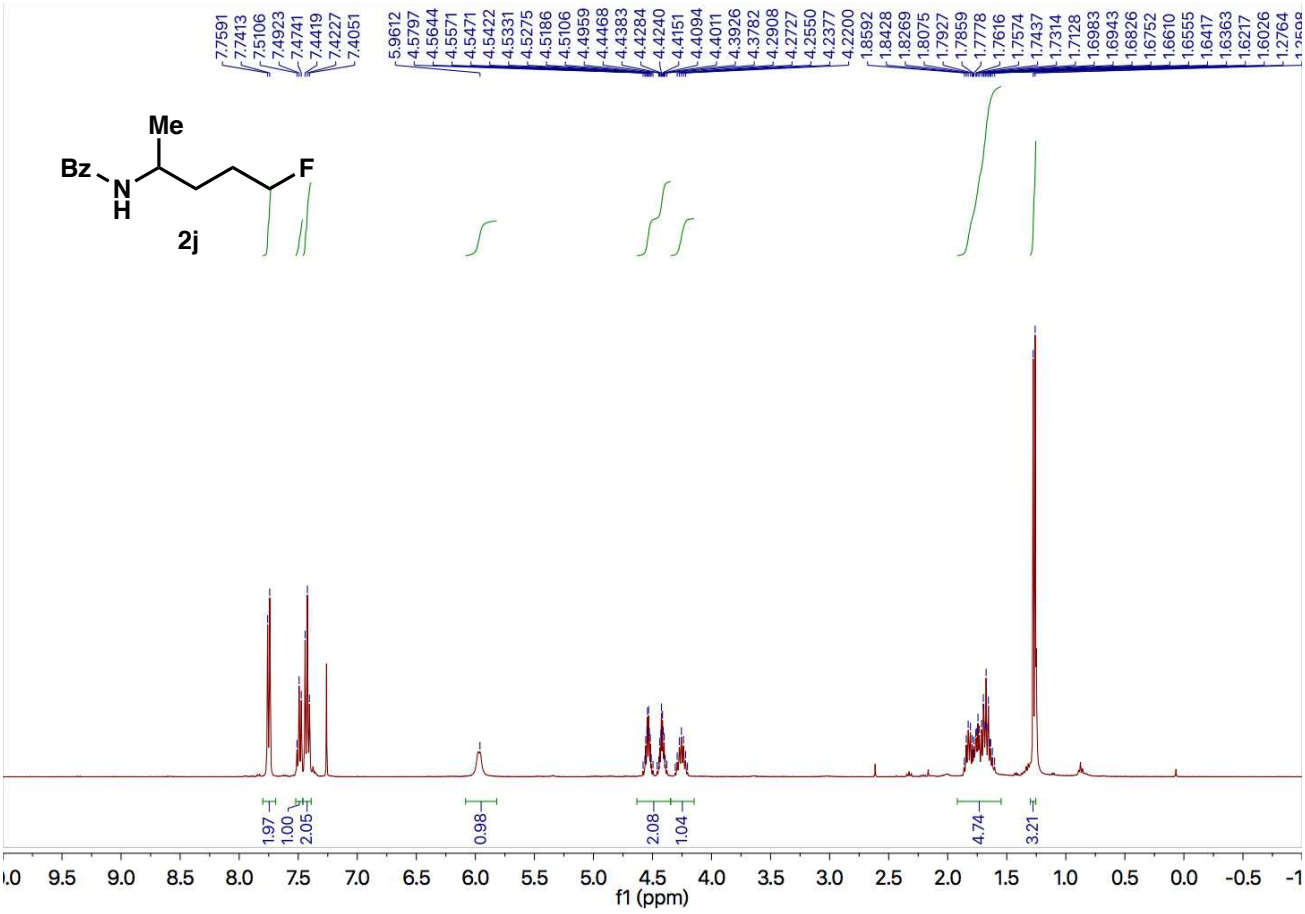
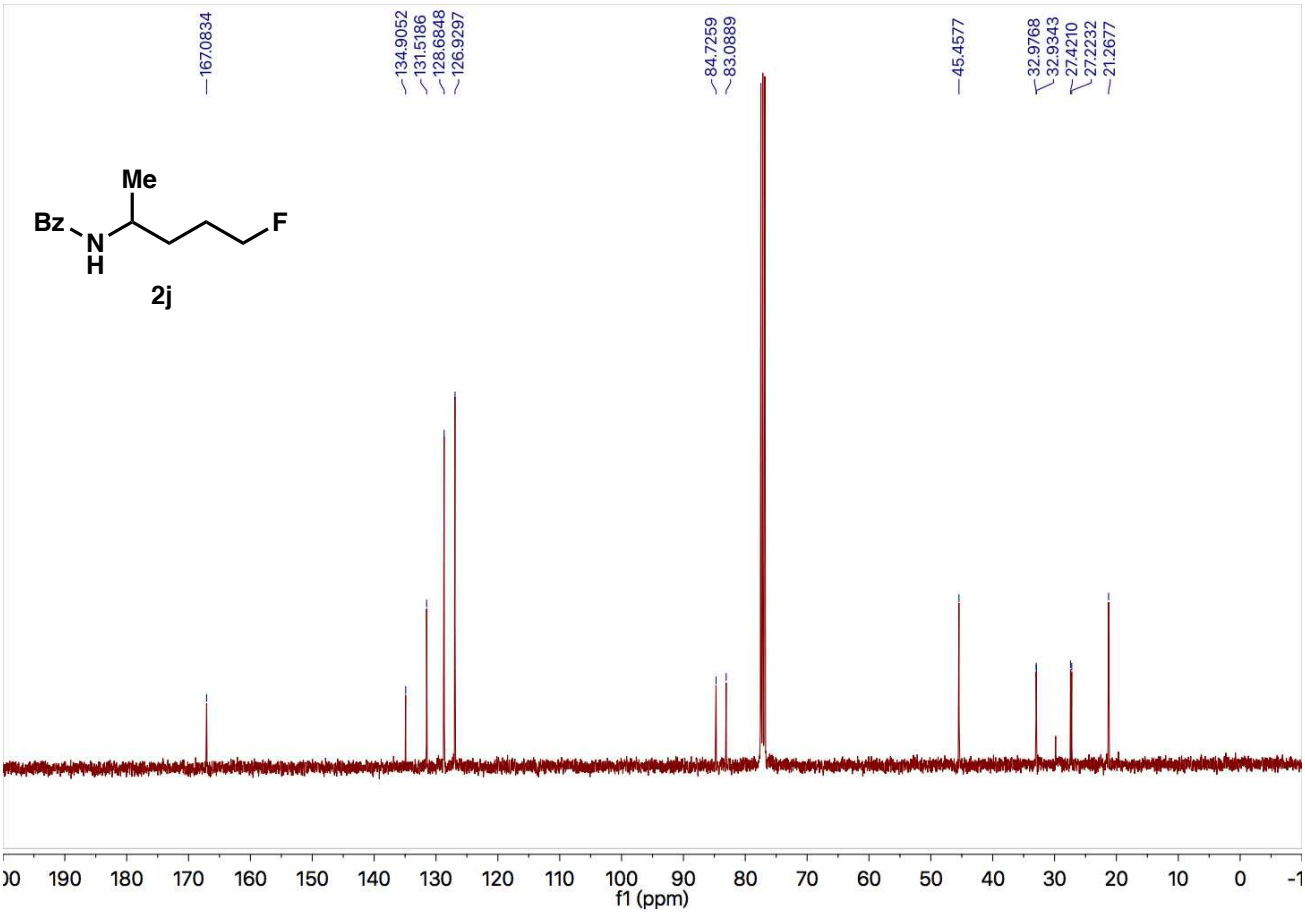
-221.1032
-221.1770
-221.2293
-221.3045
-221.3547
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-24
f1 (ppm)


Me
Bz
N
H
F
2j
1.97
1.00
2.05
0.98
2.08
1.04
4.74
3.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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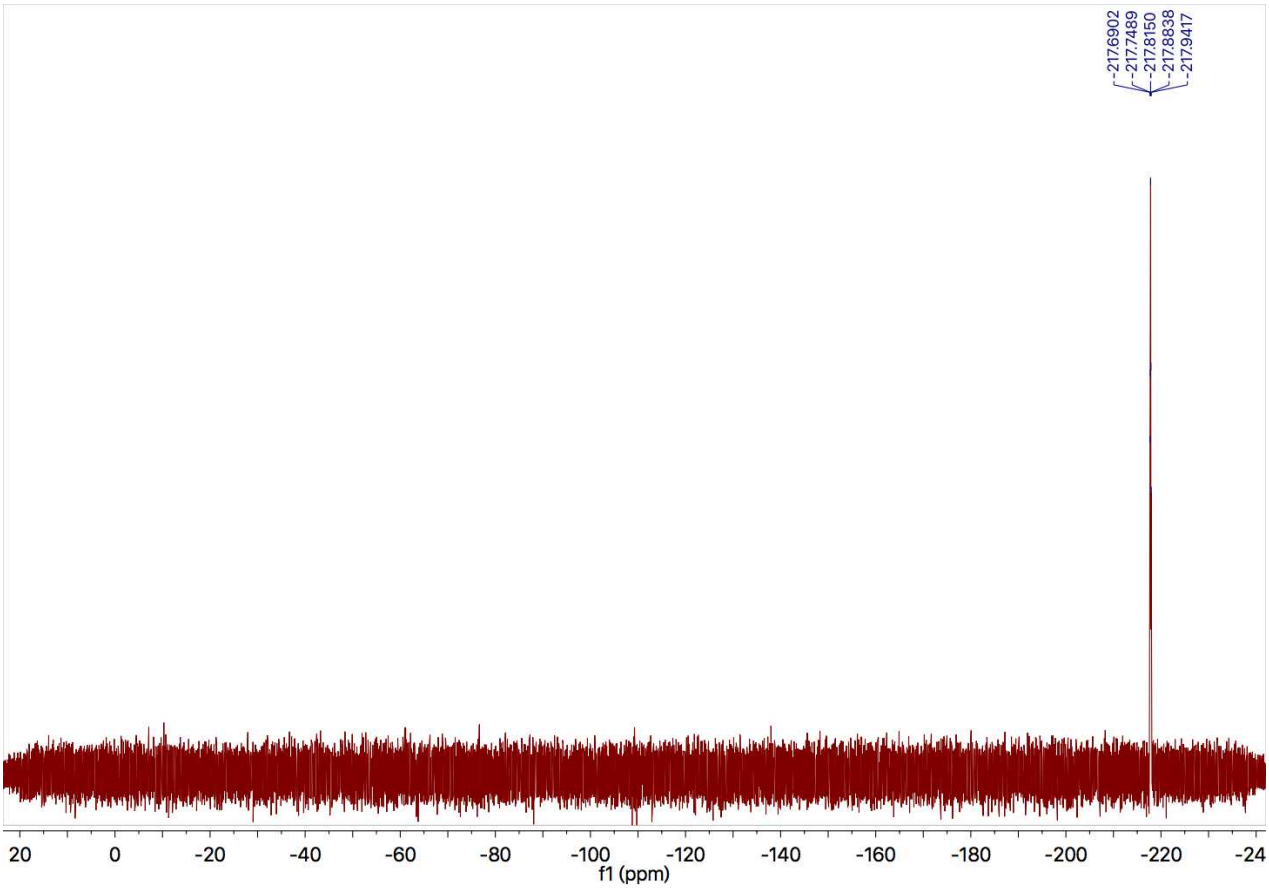
131.5186
128.6848
126.9297
84.7259
83.0889
45.4577
32.9768
32.9343
27.4210
27.2232
21.2677
Me
Bz
N
H
F
2j
f1 (ppm)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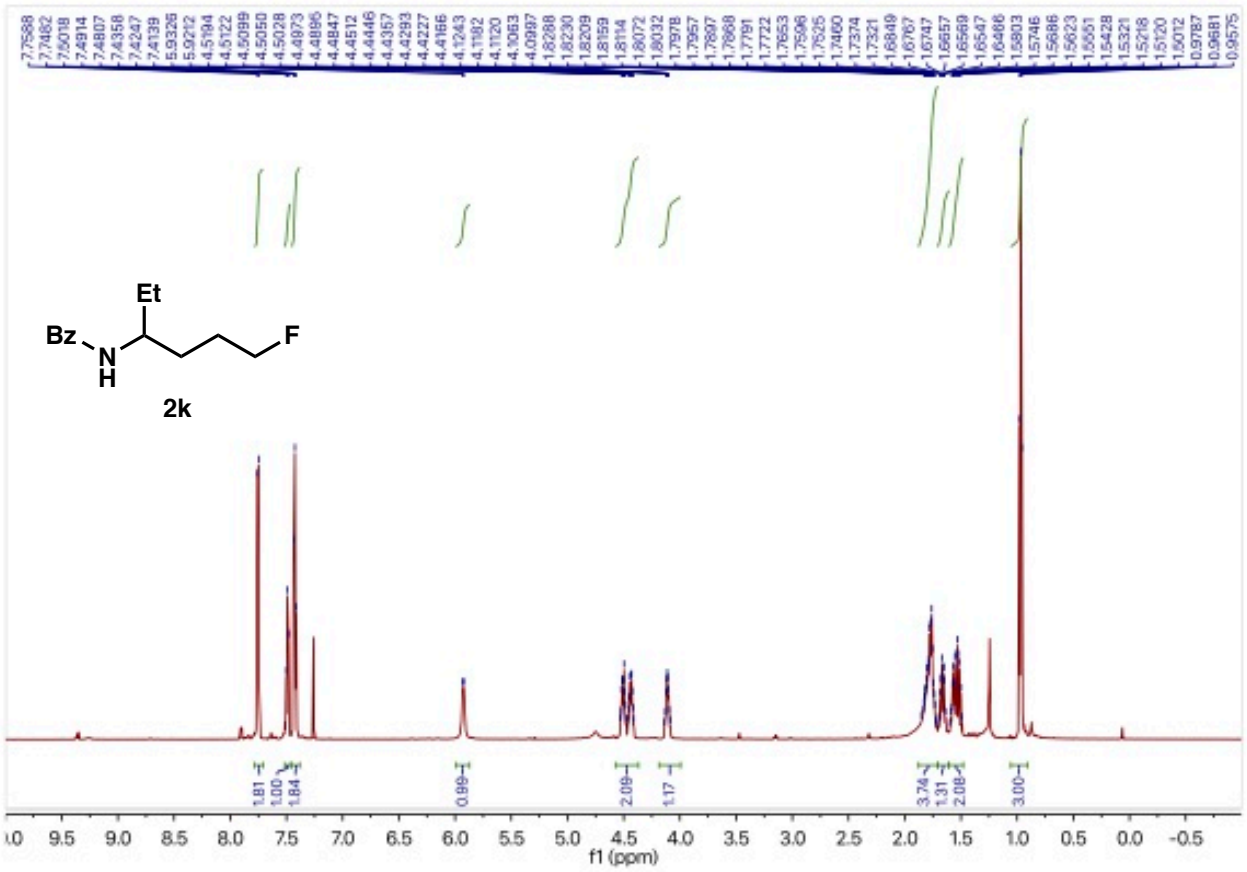
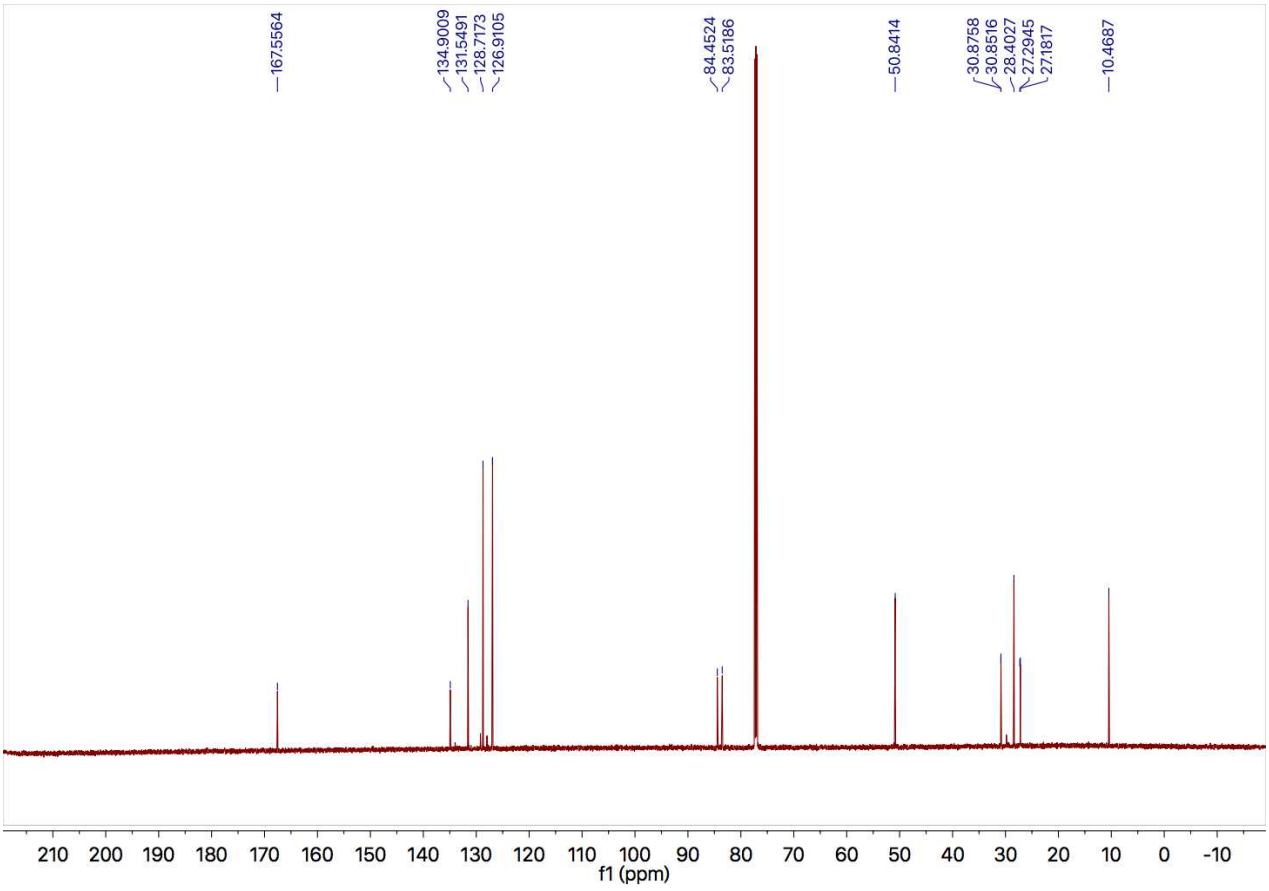
-217.7489
-217.8150
-217.8838
-217.9417
f1 (ppm)


Et
Bz
N
H
F
2k
f1 (ppm)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134.9009
131.5491
128.7173
126.9105
84.4524
83.5186
50.8414
30.8758
30.8516
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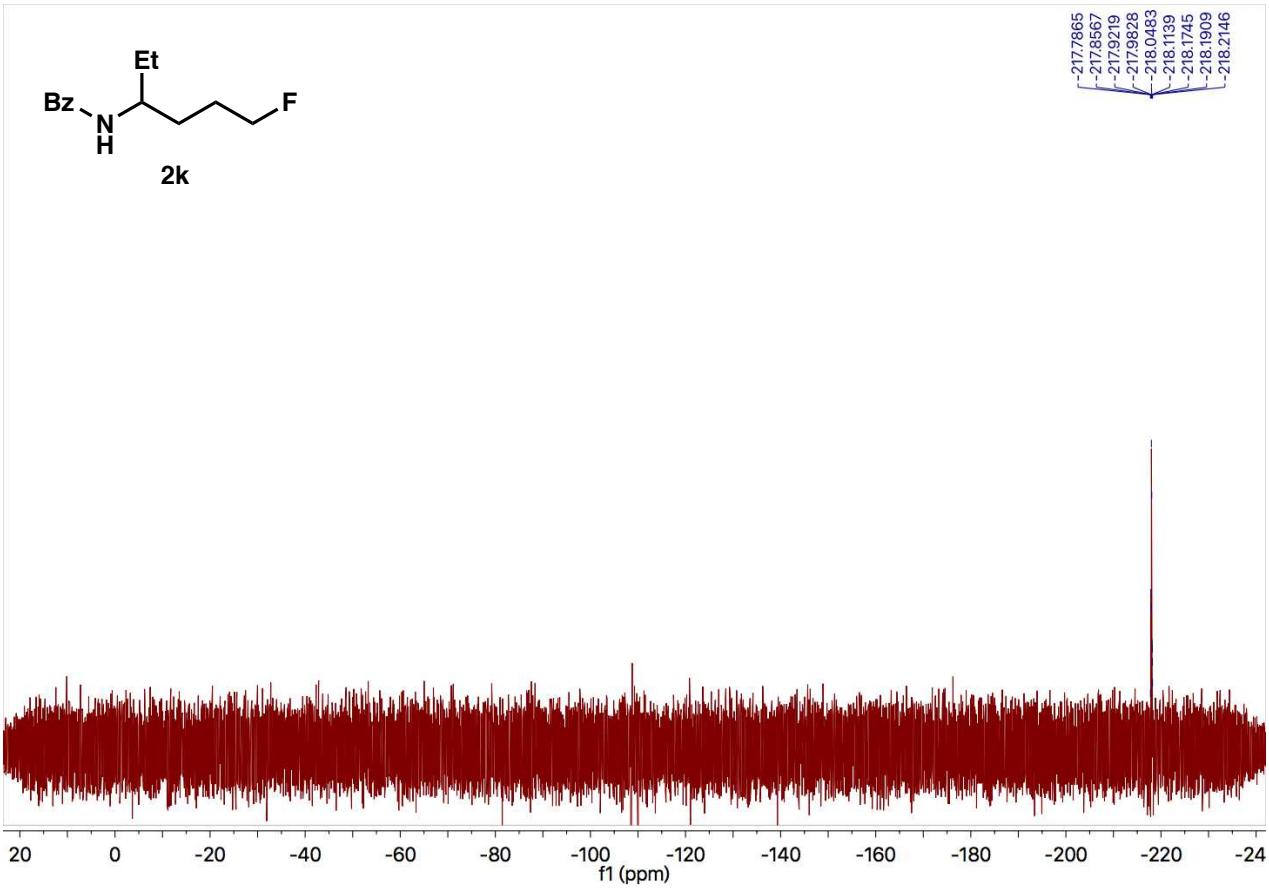
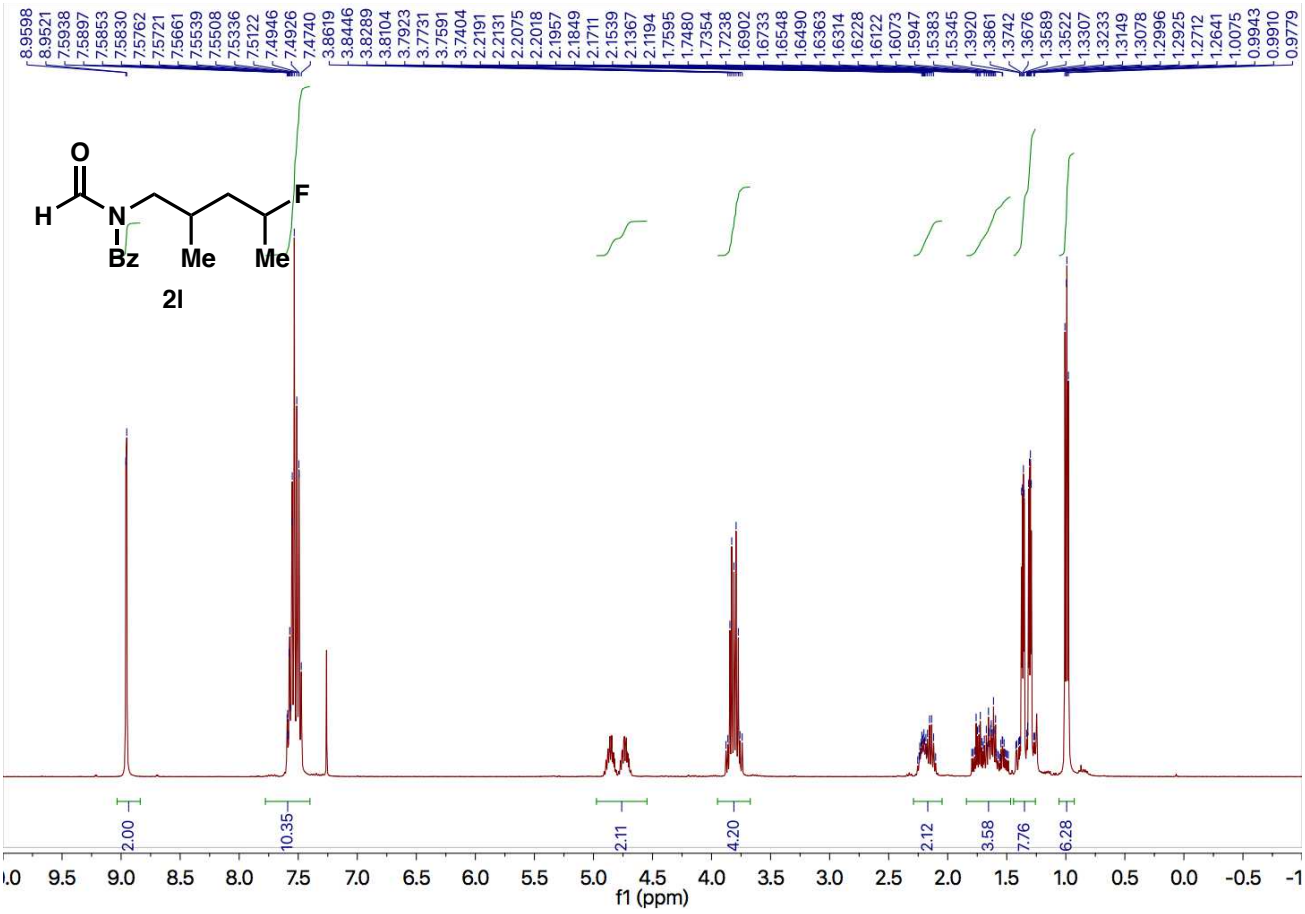
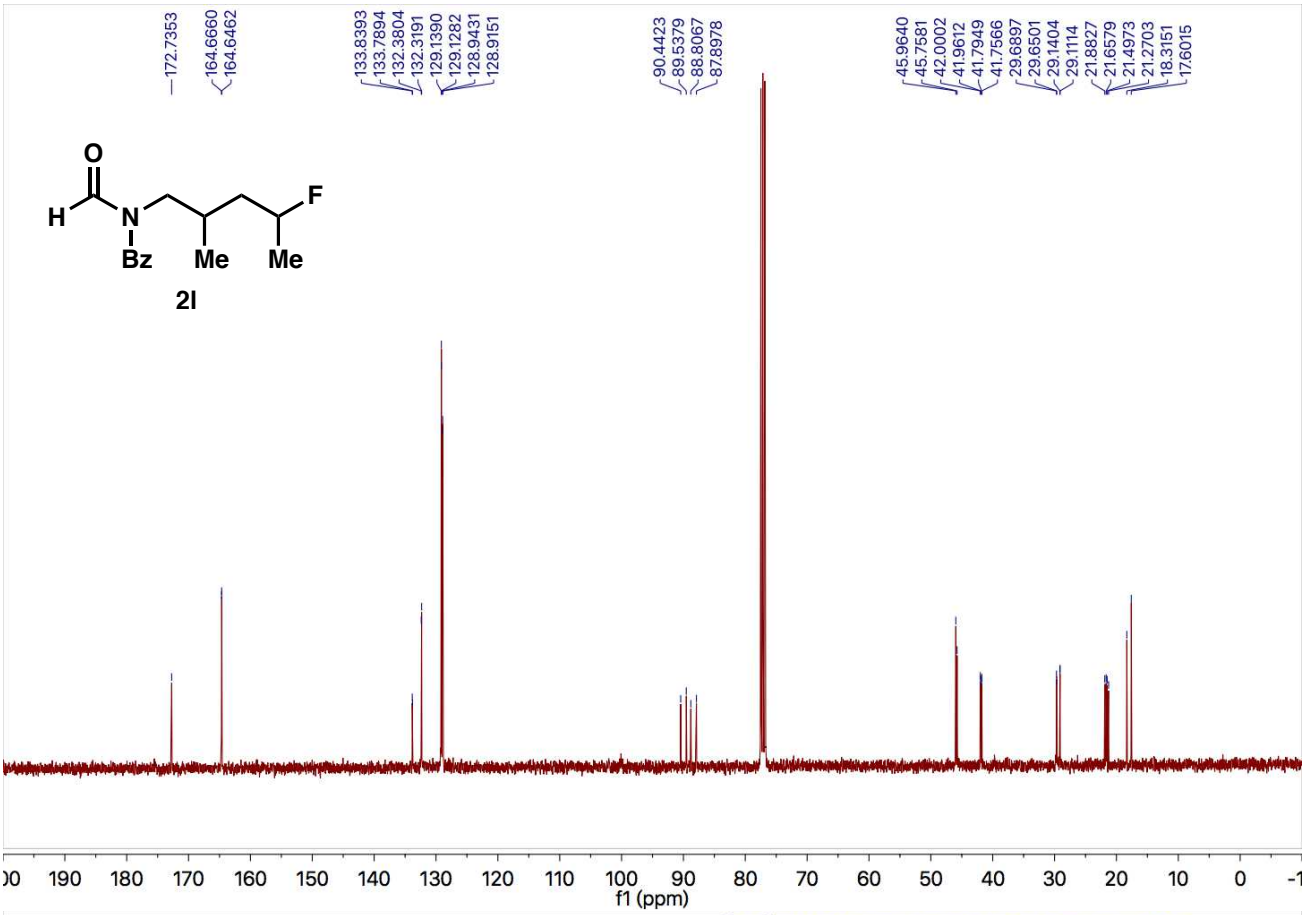
27.2945
27.1817
10.4687
f1 (ppm)


Et
Bz
N
H
F
2k
-217.7865
-217.8567
-217.9219
-217.9828
-218.0483
-218.1139
-218.1745
-218.1909
-218.2146
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-24
f1 (ppm)


O
H
N
Bz
Me
Me
F
2l
2.00
10.35
2.11
4.20
2.12
3.58
7.76
6.28
f1 (ppm)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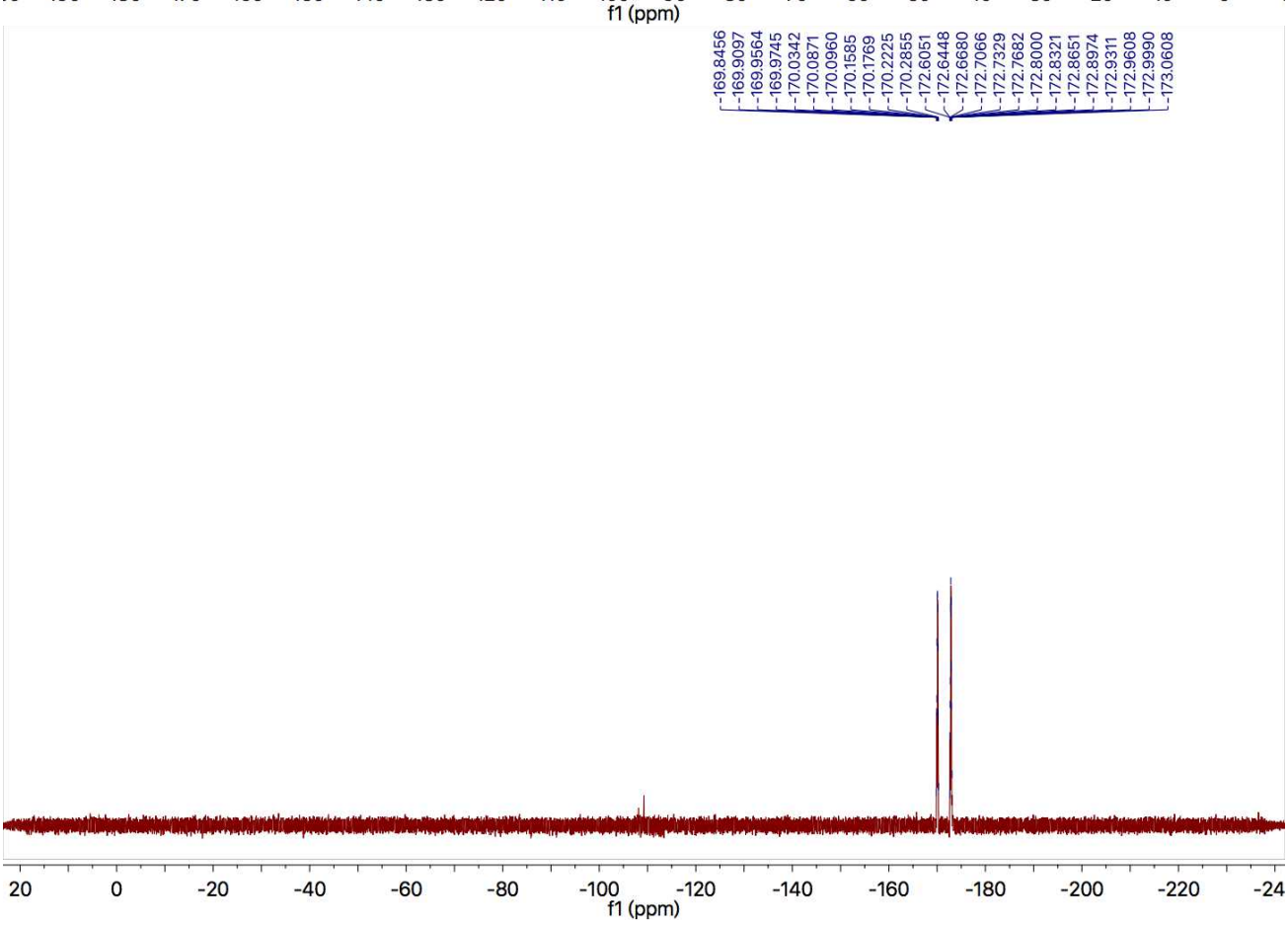
164.6462
133.8393
133.7894
132.3804
132.3191
129.1390
129.1282
128.9431
128.9151
90.4423
89.5379
88.8067
87.8978
45.9640
45.7581
42.0002
41.9612
41.7949
41.7566
29.6897
29.6501
29.1404
29.1114
21.8827
21.6579
21.4973
21.2703
18.3151
17.6015
O
H
N
Bz
Me
Me
F
2l
f1 (ppm)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169.9097
169.9564
169.9745
170.0342
170.0871
170.0960
170.1585
170.1769
170.2225
170.2855
172.6051
172.6448
172.6680
172.7066
172.7329
172.7682
172.8000
172.8321
172.8651
172.8974
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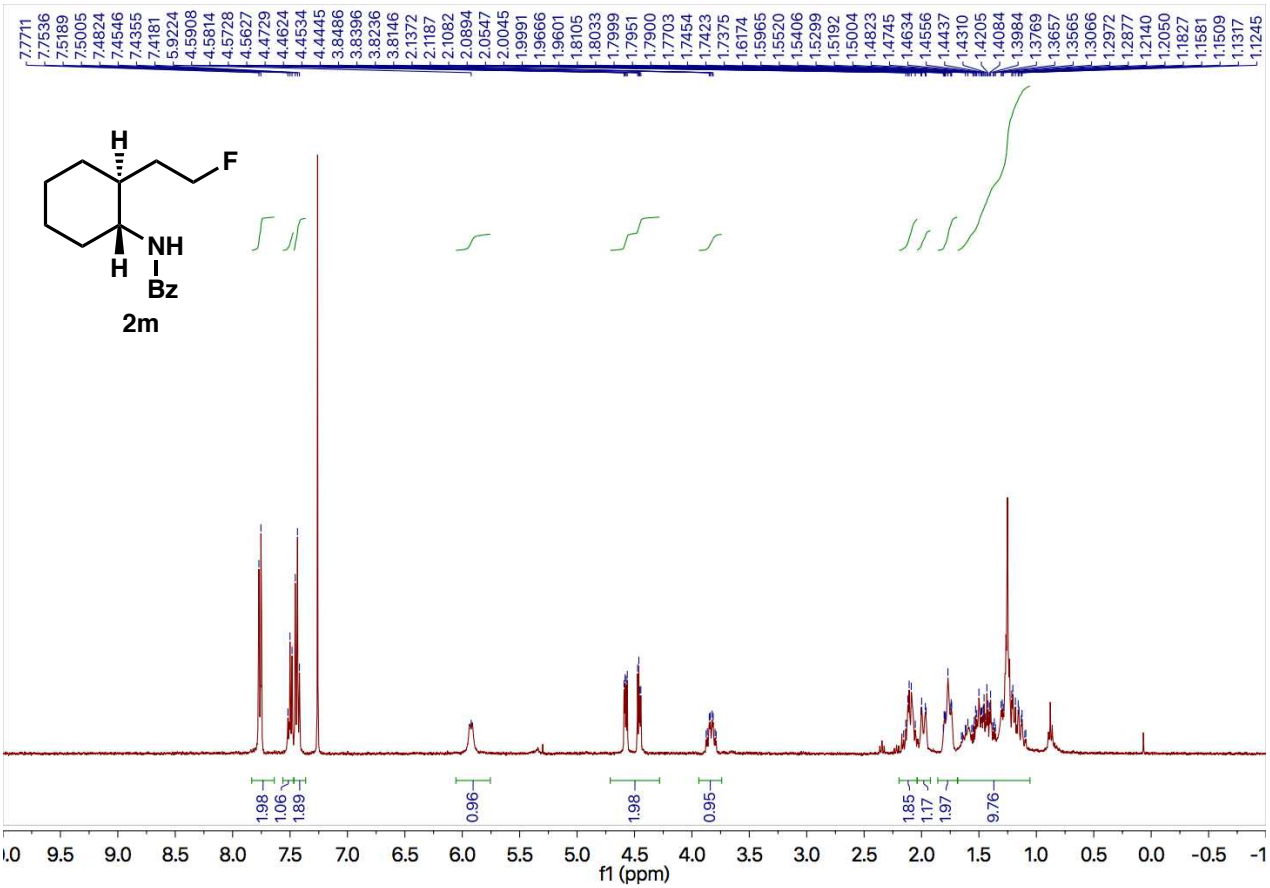
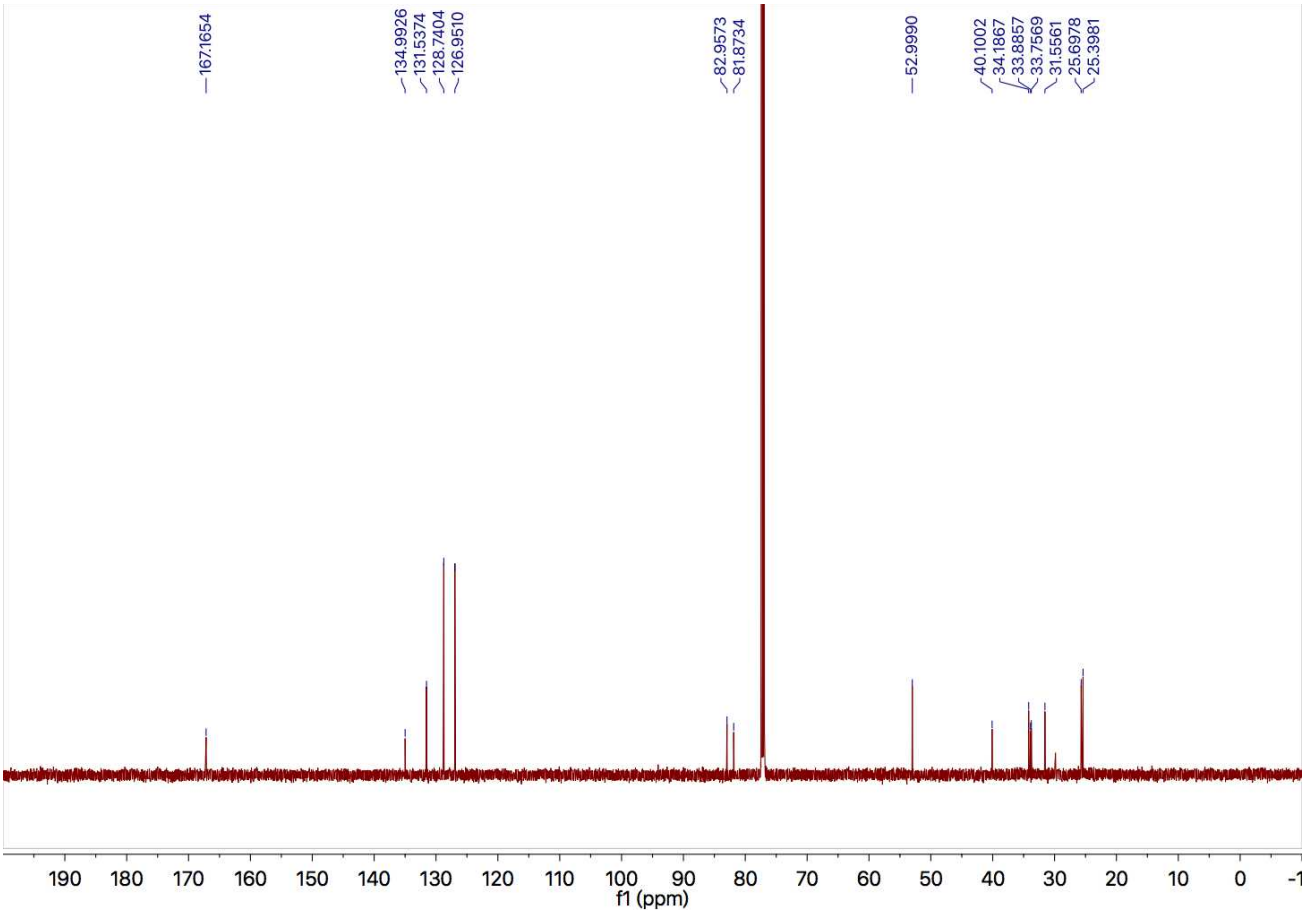
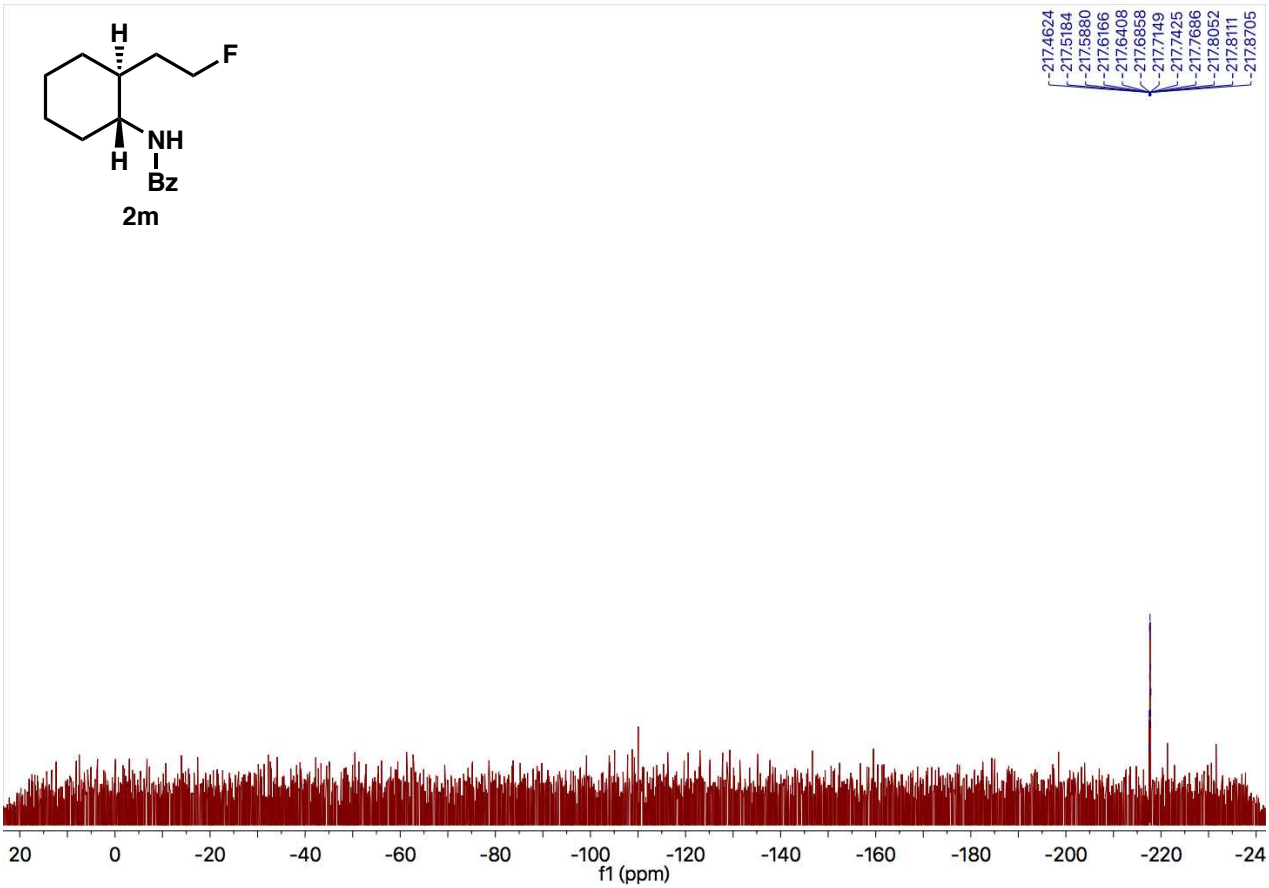
172.9608
172.9990
173.0608
f1 (ppm)


H
F
NH
H
Bz
2m
f1 (ppm)


167.1654
134.9926
131.5374
128.7404
126.9510
82.9573
81.8734
52.9990
40.1002
34.1867
33.8857
33.7569
31.5561
25.6978
25.3981
f1 (ppm)


H
F
NH
H
Bz
2m
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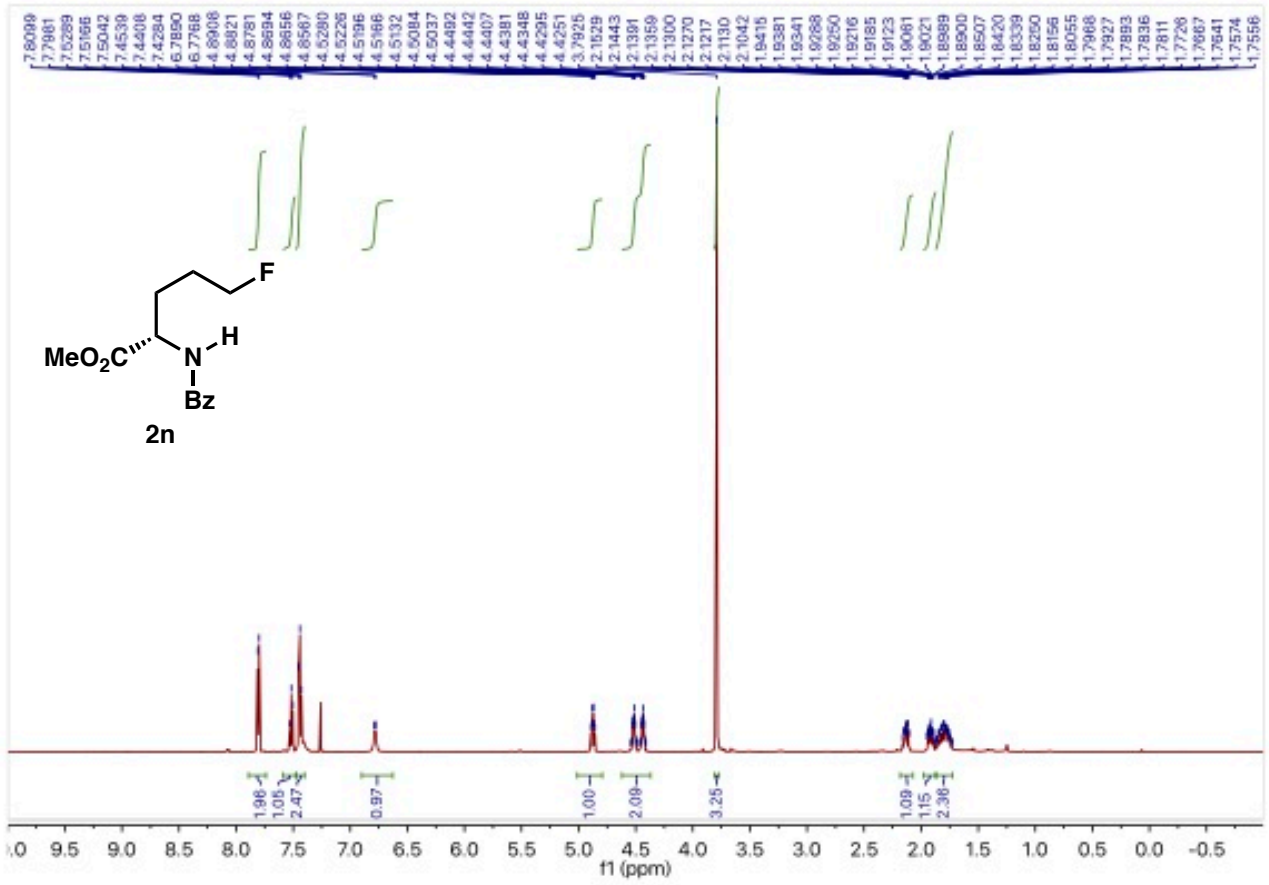
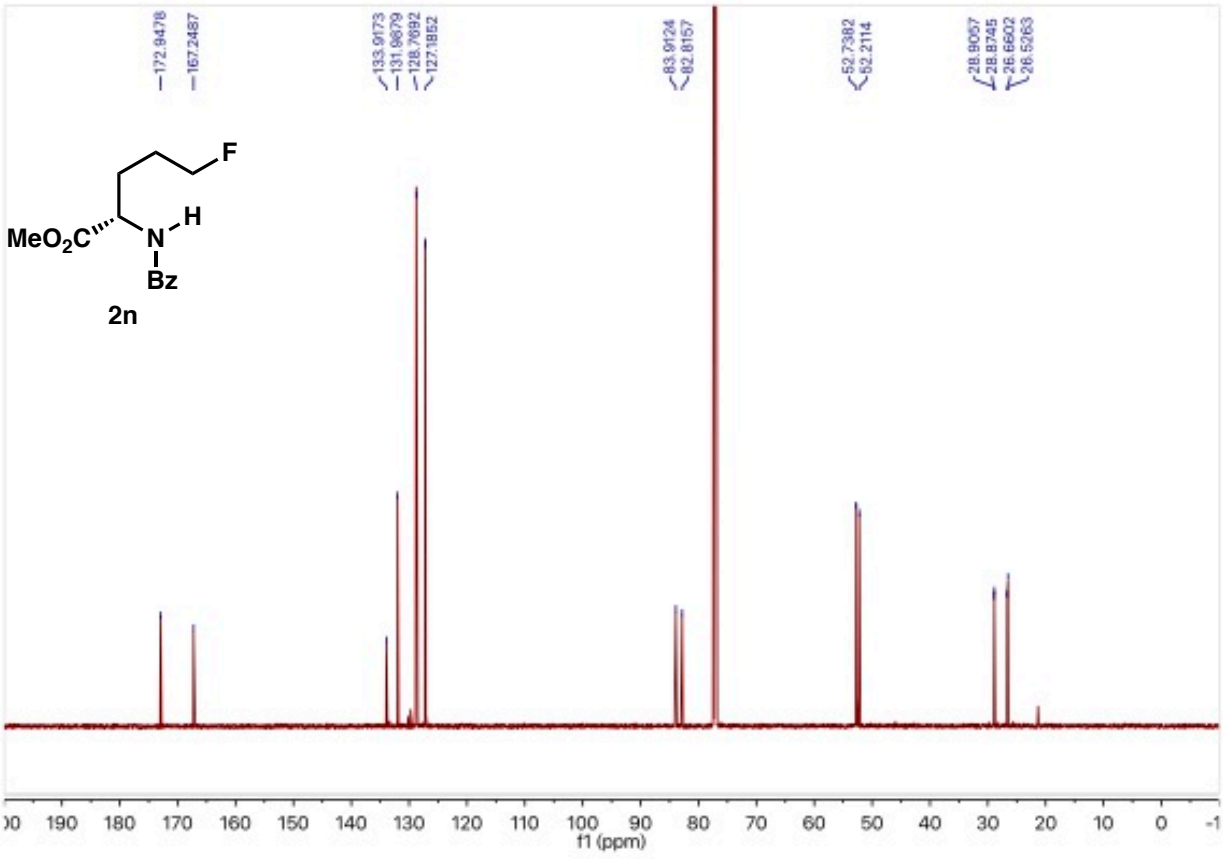
-217.5184
-217.5880
-217.6166
-217.6408
-217.6858
-217.7149
-217.7425
-217.7686
-217.8052
-217.8111
-217.8705
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-24
f1 (ppm)


F
MeO2C
N
H
Bz
2n
1.96
1.05
2.47
0.97
1.00
2.09
3.25
1.09
1.15
2.36
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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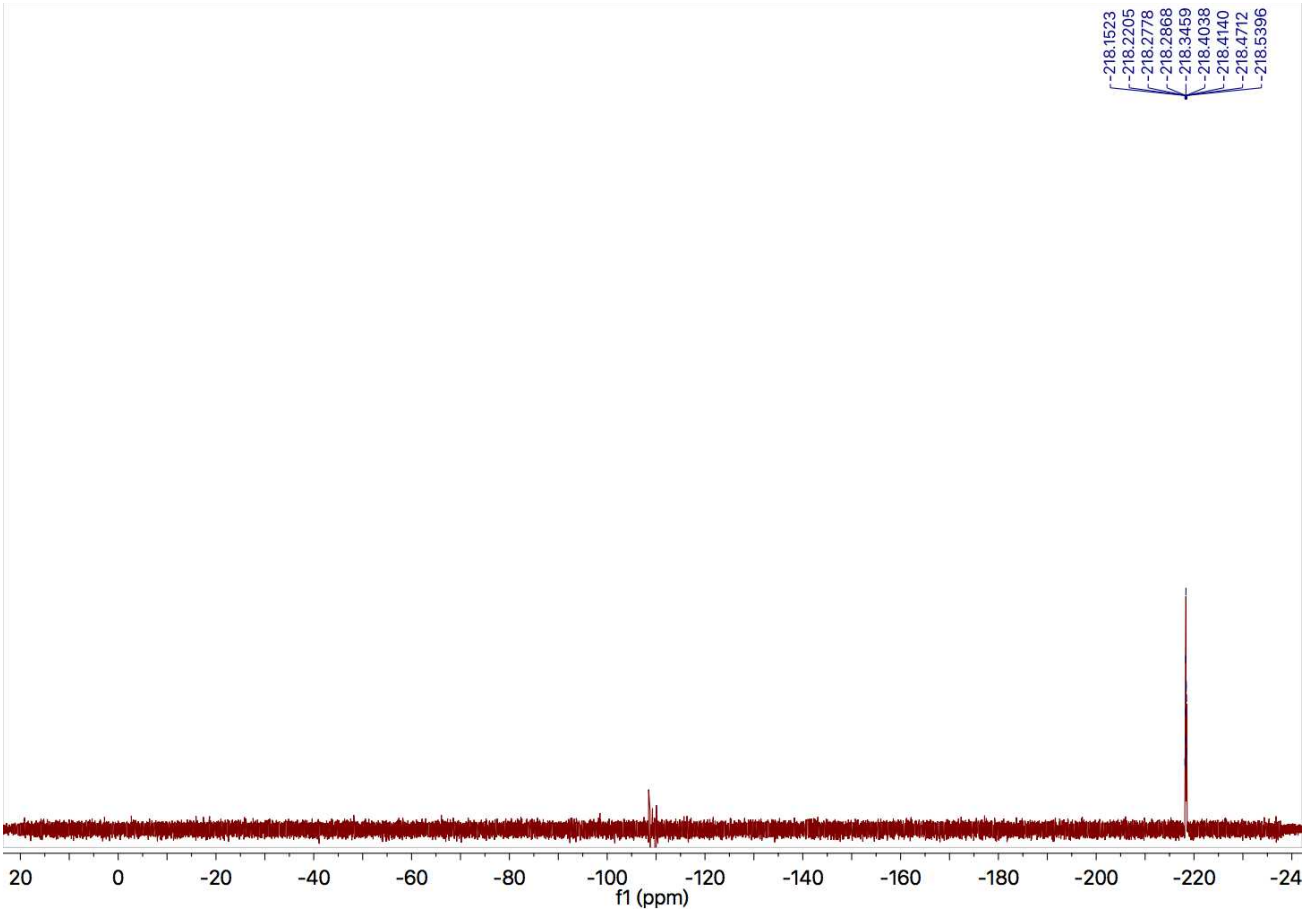
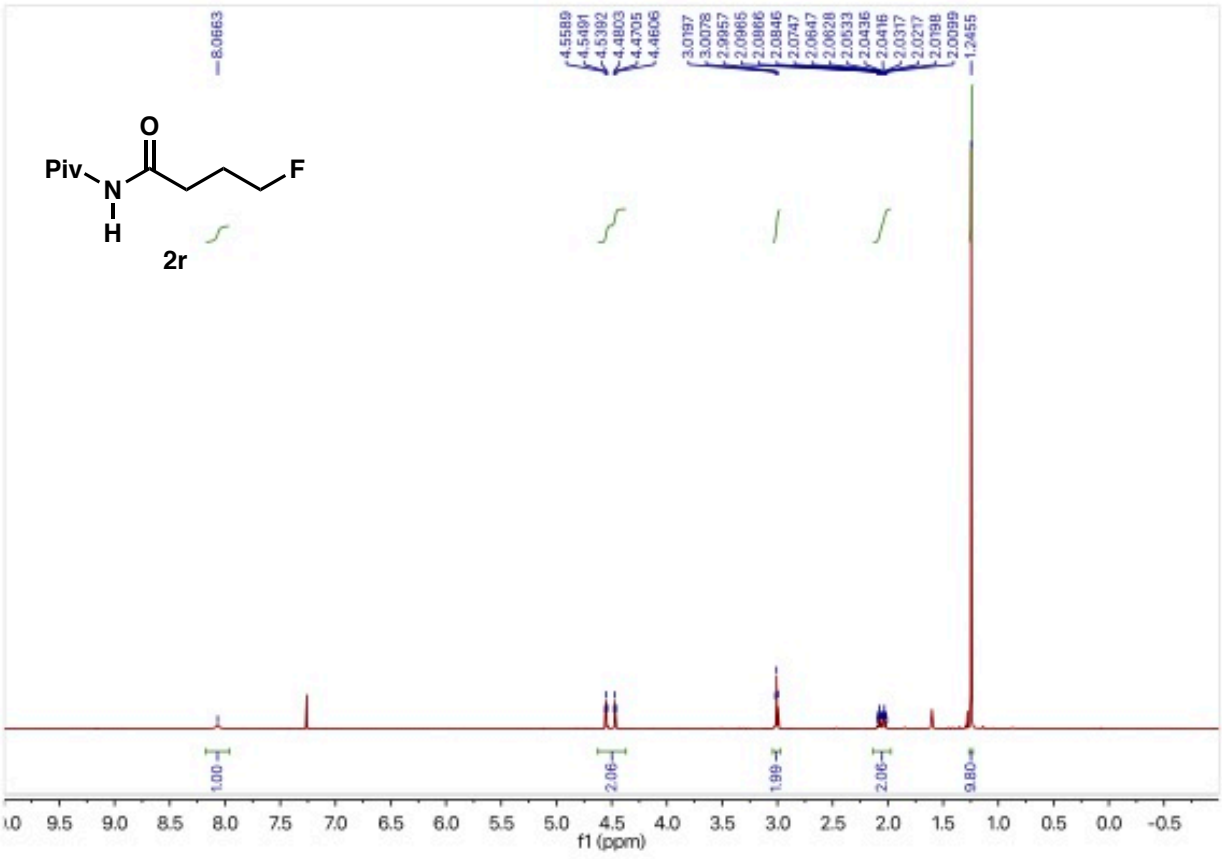
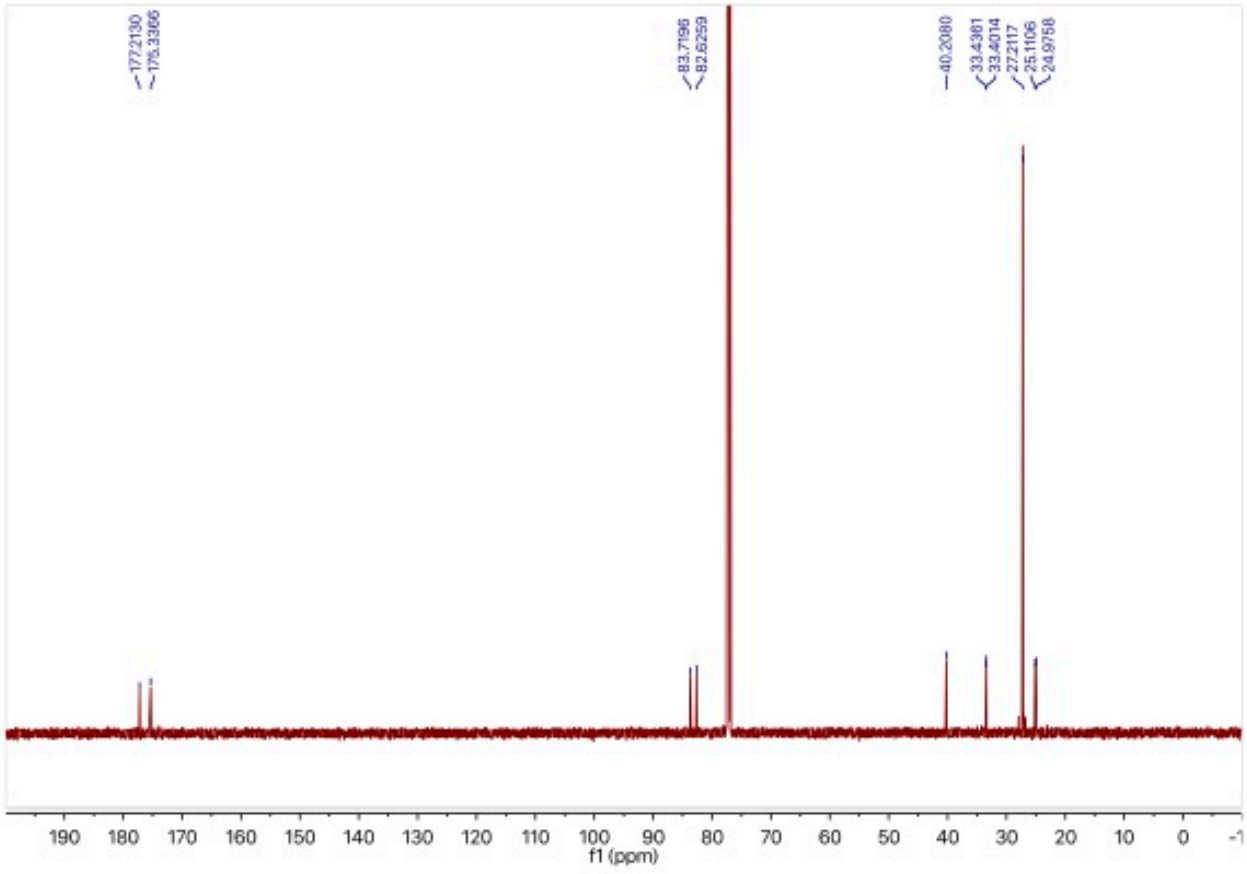
133.9173
131.9879
128.7692
127.1852
83.9124
82.8157
52.7382
52.2114
28.9057
28.8745
26.6602
26.5263
F
H
N
MeO2C
Bz
2n
f1 (ppm)


218.1523
218.2205
218.2778
218.2868
218.3459
218.4038
218.4140
218.4712
218.5396
f1 (ppm)


8.0663
4.5589
4.5491
4.5392
4.4803
4.4705
4.4606
3.0197
3.0078
2.9957
2.0965
2.0866
2.0846
2.0747
2.0647
2.0628
2.0533
2.0436
2.0416
2.0317
2.0217
2.0198
2.0099
1.2455
1.00
2.06
1.99
2.06
9.80
f1 (ppm)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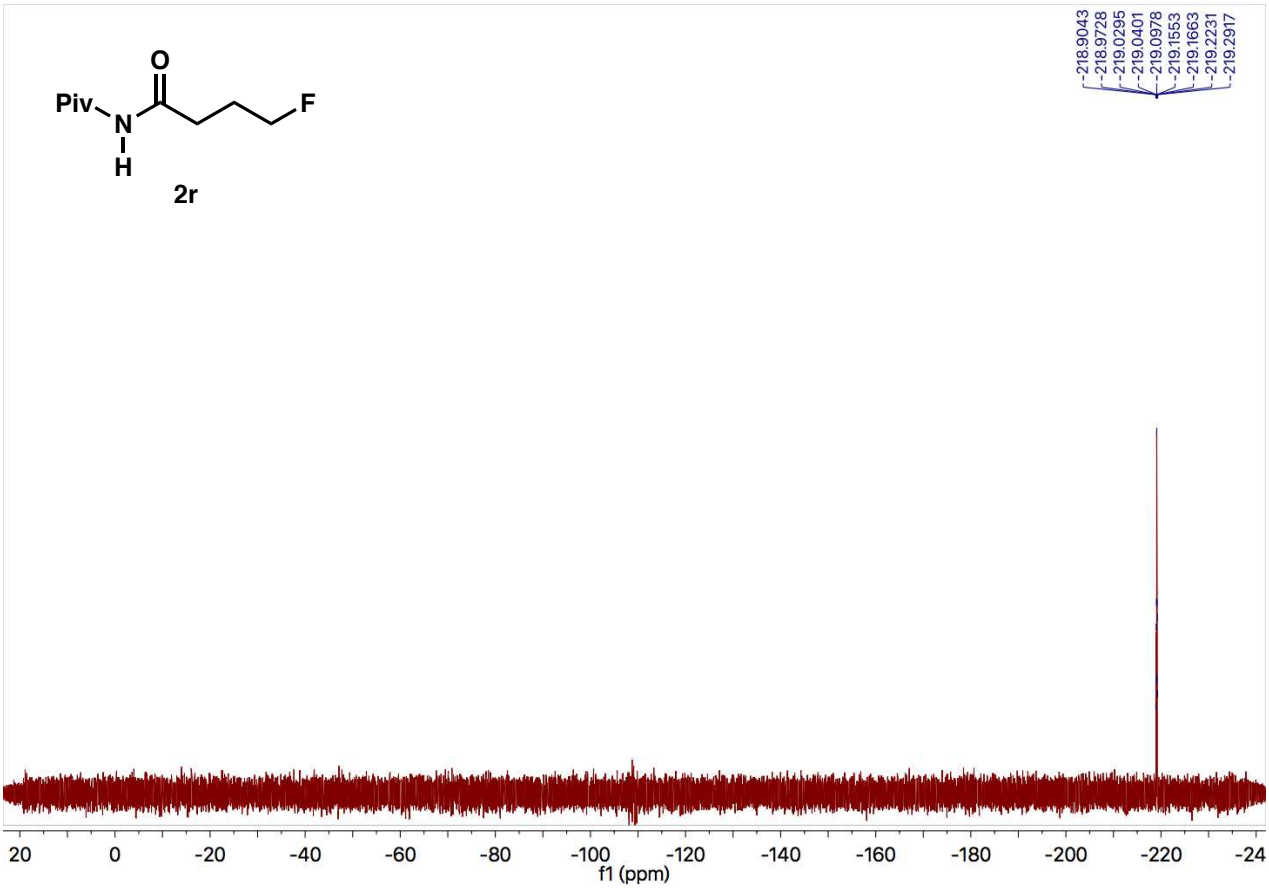
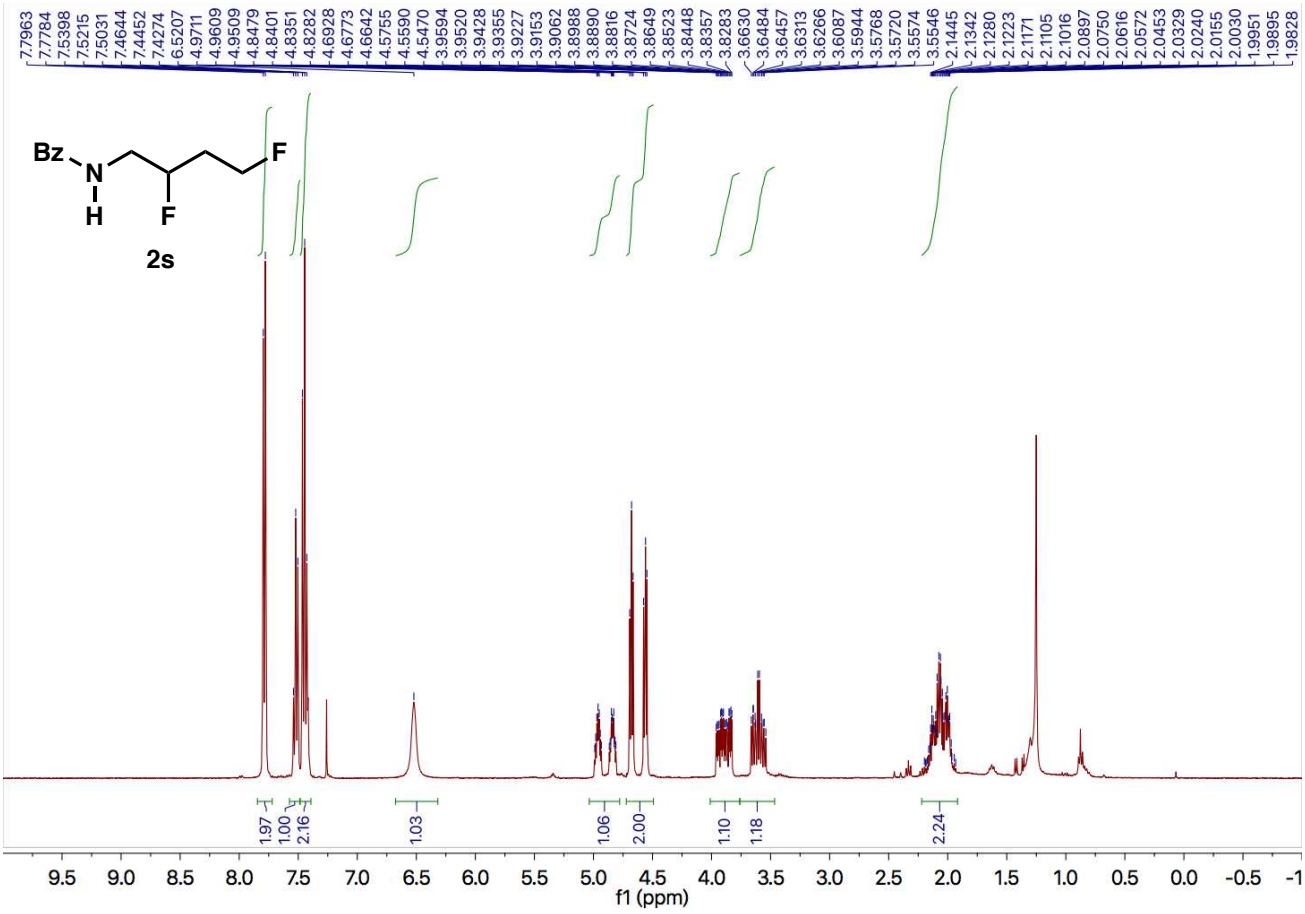
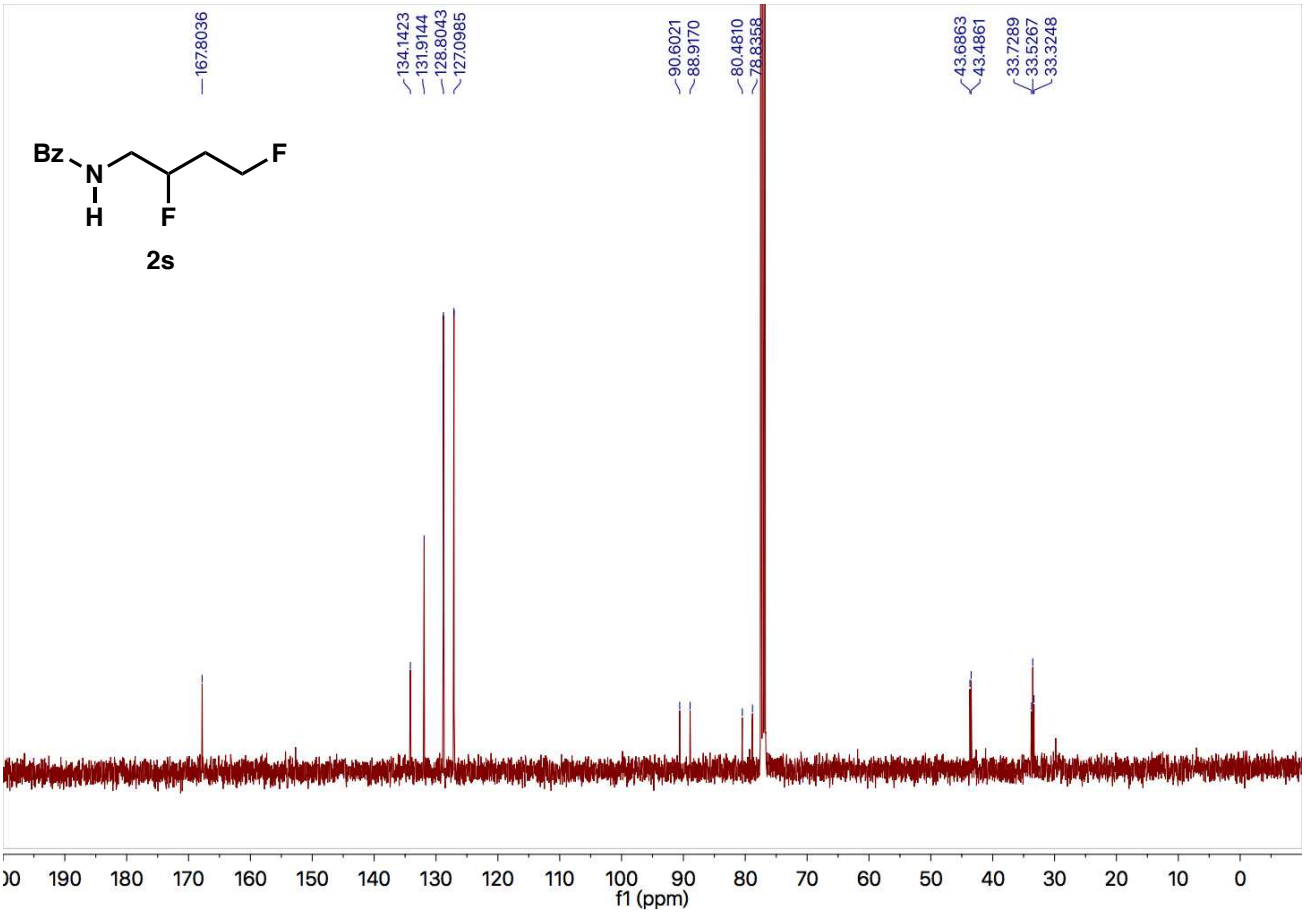
175.3366
83.7796
82.6259
40.2080
33.4361
33.4014
27.2117
25.1106
24.9758
f1 (ppm)


Piv
N
H
O
F
2r
218.9043
218.9728
219.0295
219.0401
219.0978
219.1553
219.1663
219.2231
219.2917
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-24
f1 (ppm)


Bz
N
H
F
F
2s
1.97
1.00
2.16
1.03
1.06
2.00
1.10
1.18
2.24
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)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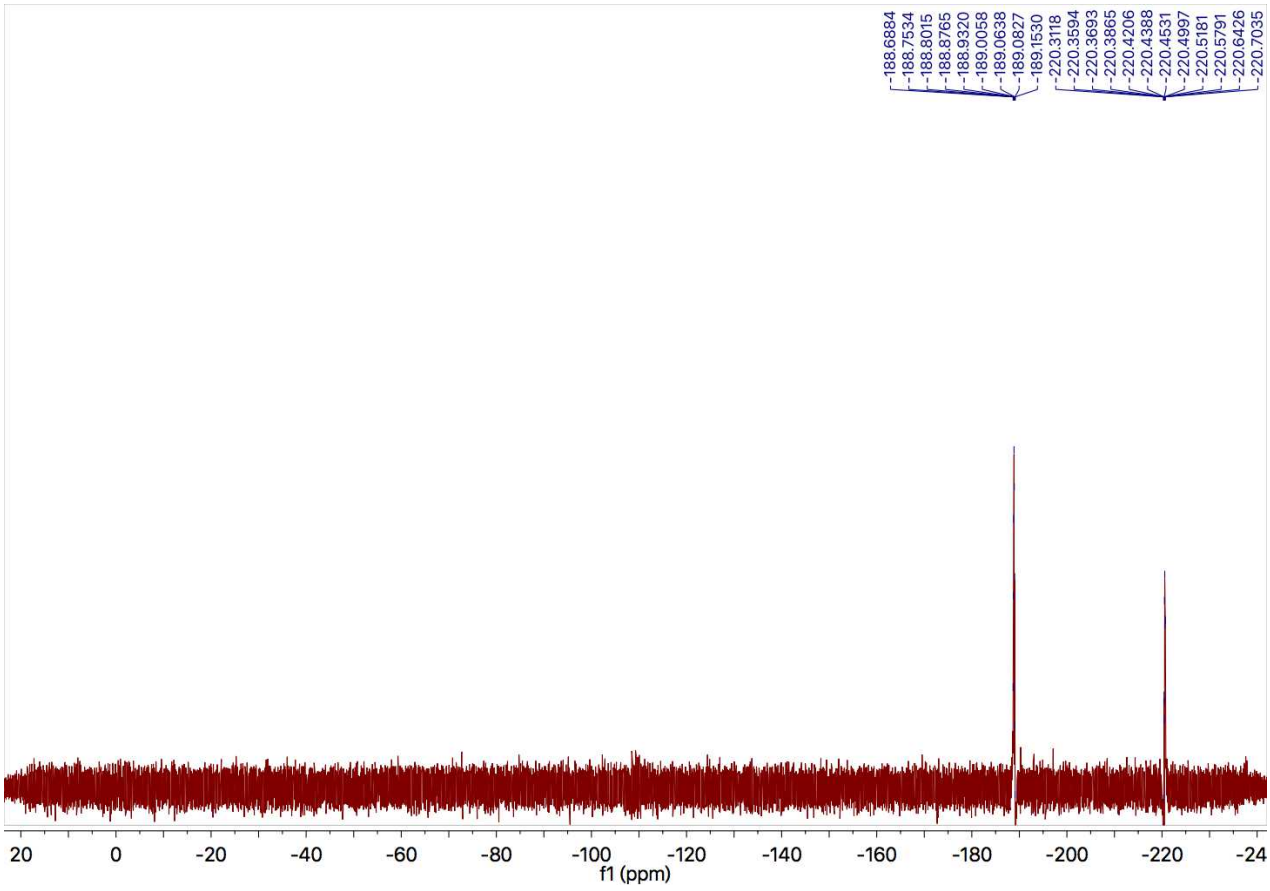
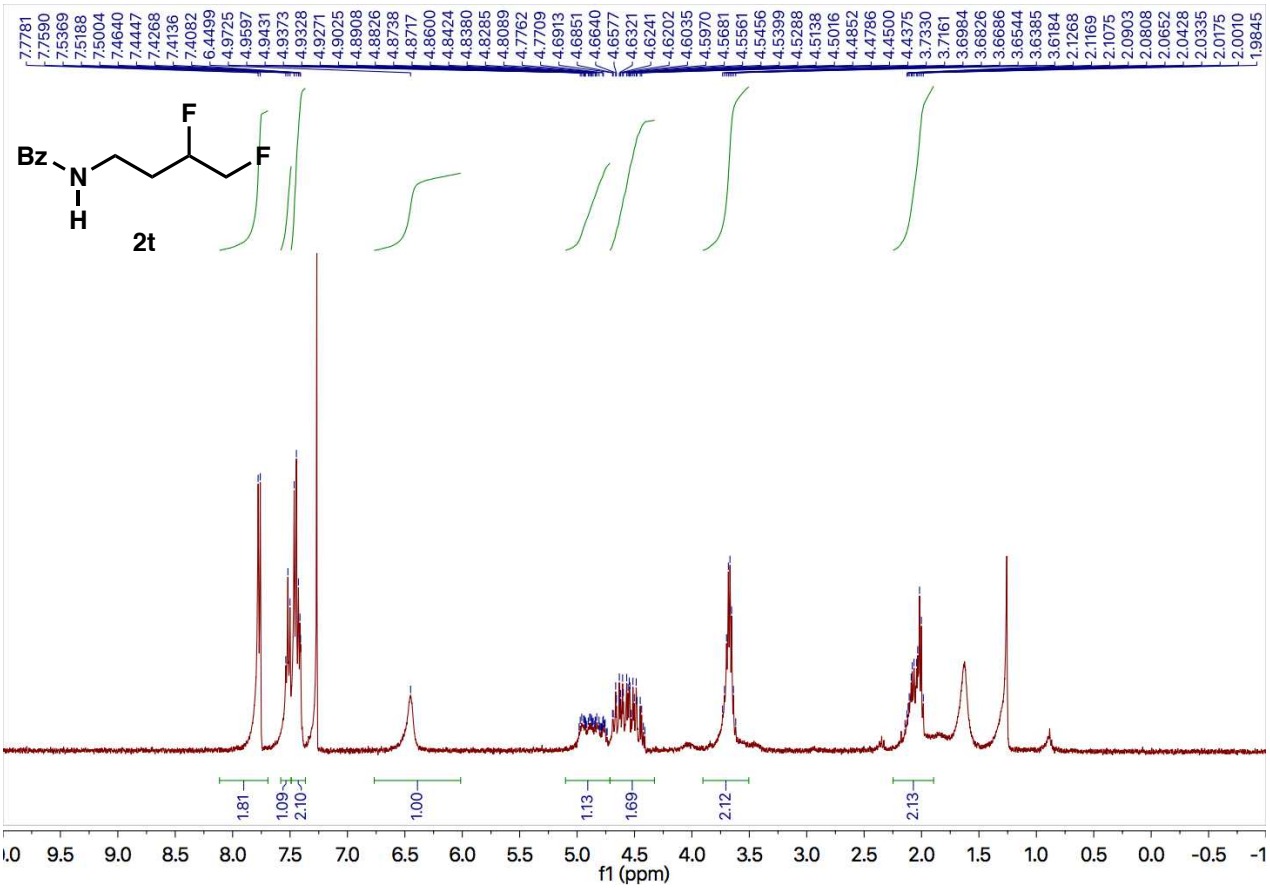
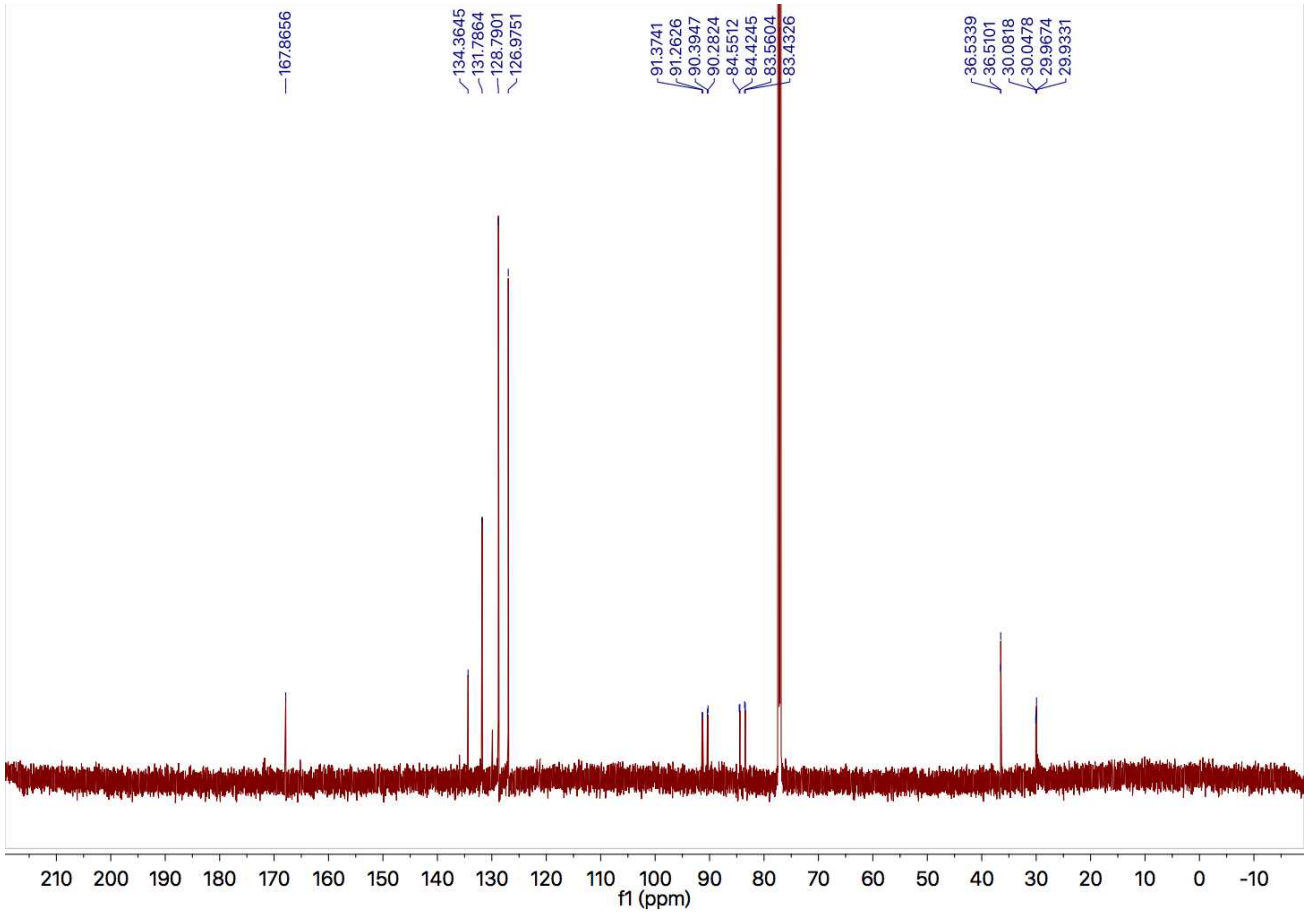
131.9144
128.8043
127.0985
90.6021
88.9170
80.4810
78.8358
43.6863
43.4861
33.7289
33.5267
33.3248
Bz
N
H
F
F
2s
f1 (ppm)


-188.6884
-188.7534
-188.8015
-188.8765
-188.9320
-189.0058
-189.0638
-189.0827
-189.1530
-220.3118
-220.3594
-220.3693
-220.3865
-220.4206
-220.4388
-220.4531
-220.4997
-220.5181
-220.5791
-220.6426
-220.7035
f1 (ppm)


Bz
N
H
F
F
2t
1.81
1.09
2.10
1.00
1.13
1.69
2.12
2.13
f1 (ppm)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131.7864
128.7901
126.9751
91.3741
91.2626
90.3947
90.2824
84.5512
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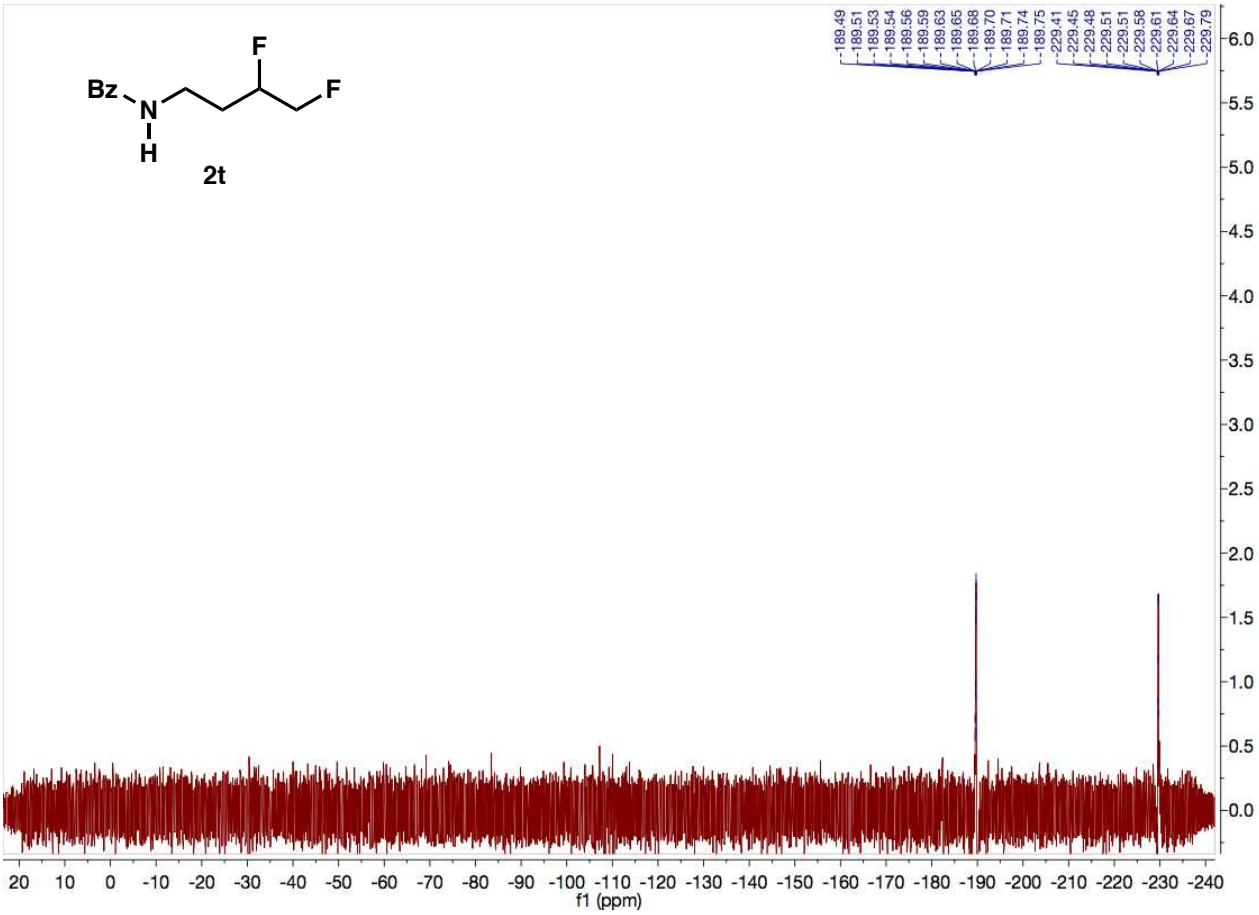
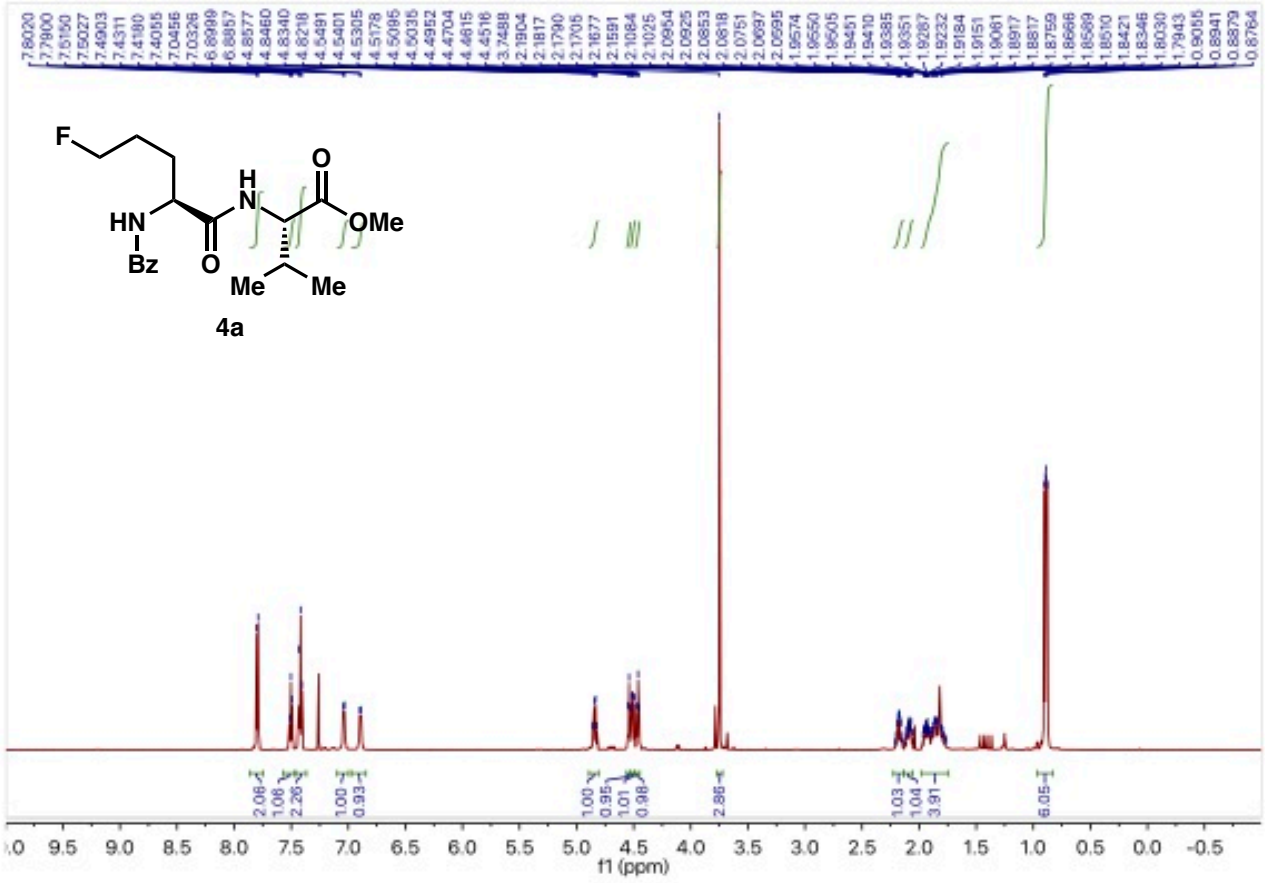
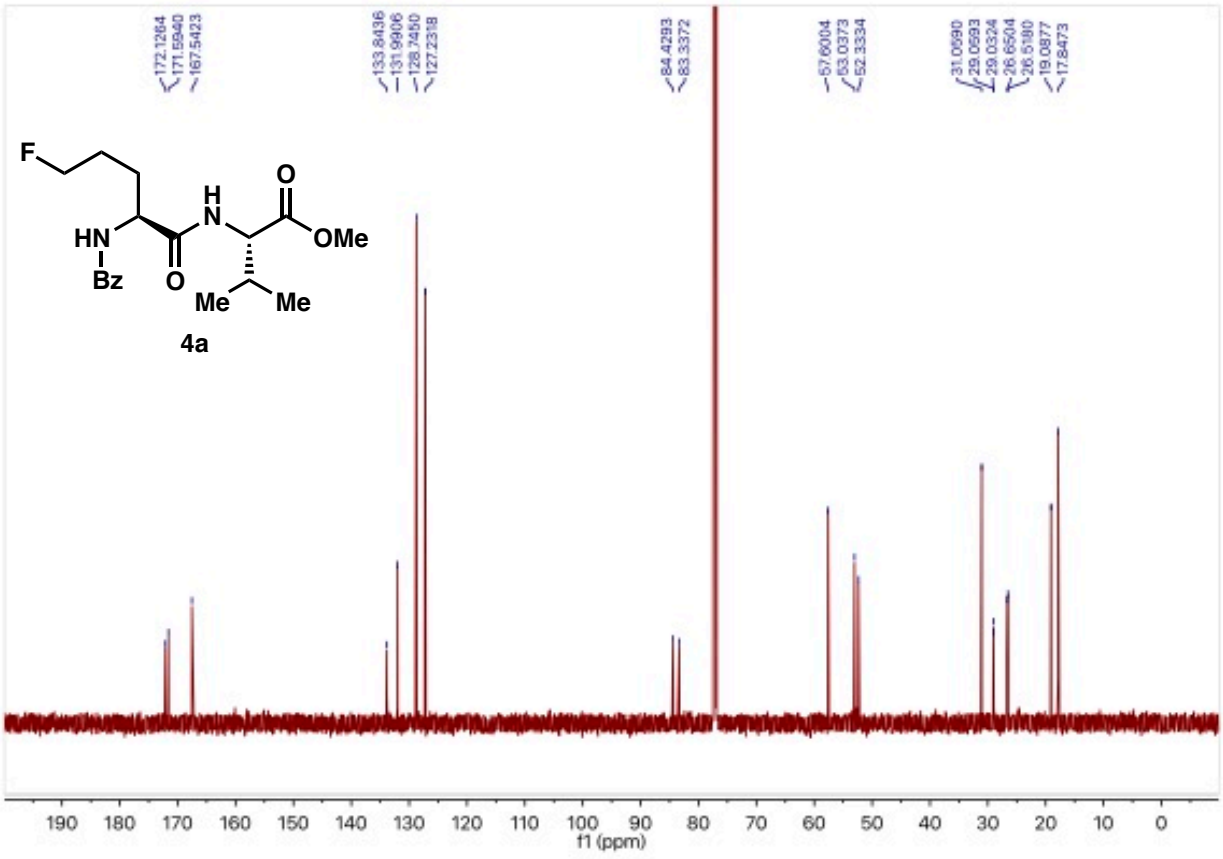
83.4326
36.5339
36.5101
30.0818
30.0478
29.9674
29.9331
f1 (ppm)


F
Bz
N
H
F
2t
f1 (ppm)


F
HN
Bz
O
H
N
O
OMe
Me
Me
4a
f1 (ppm)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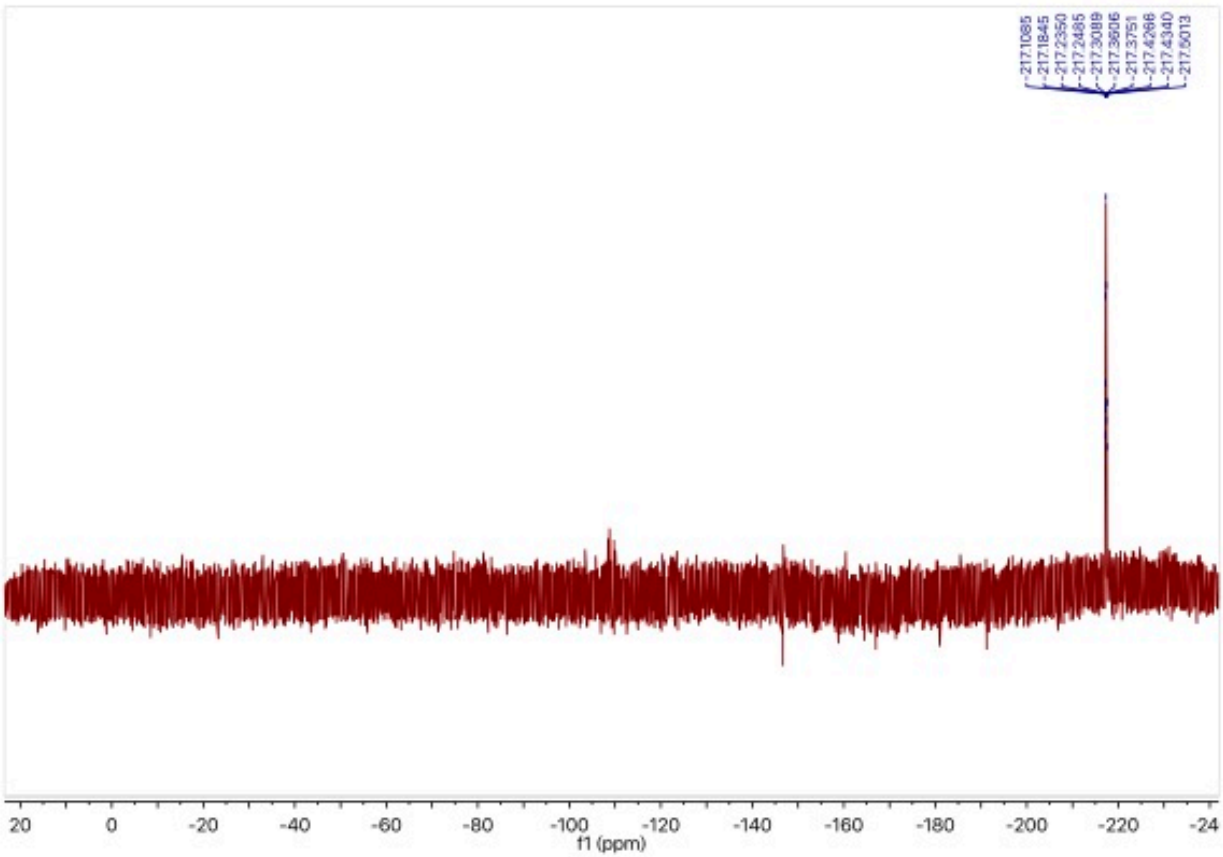
171.5940
167.5423
133.8436
131.9906
128.7450
127.2318
84.4293
83.3372
57.6004
53.0373
52.3334
31.0590
29.0593
29.0324
26.6504
26.5180
19.0877
17.8473
F
HN
Bz
O
H
N
O
OMe
Me
Me
4a
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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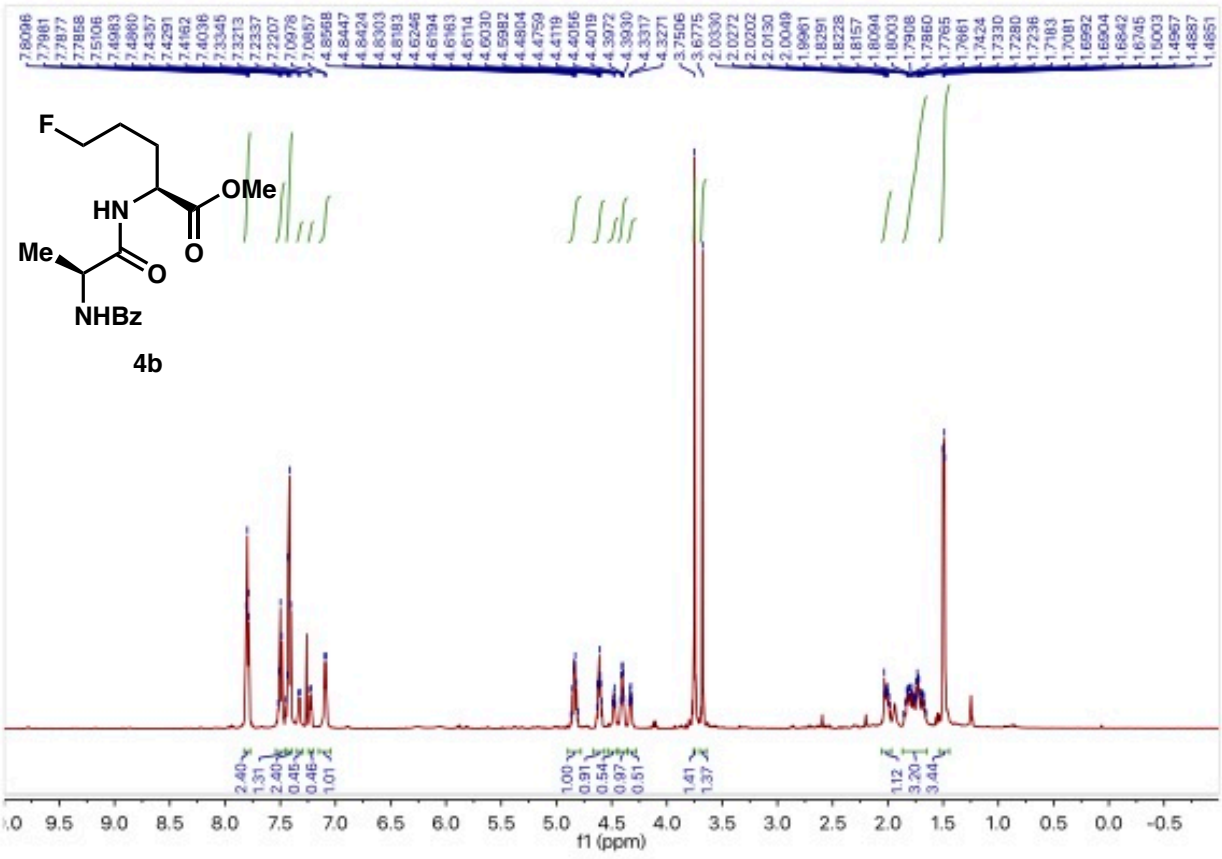
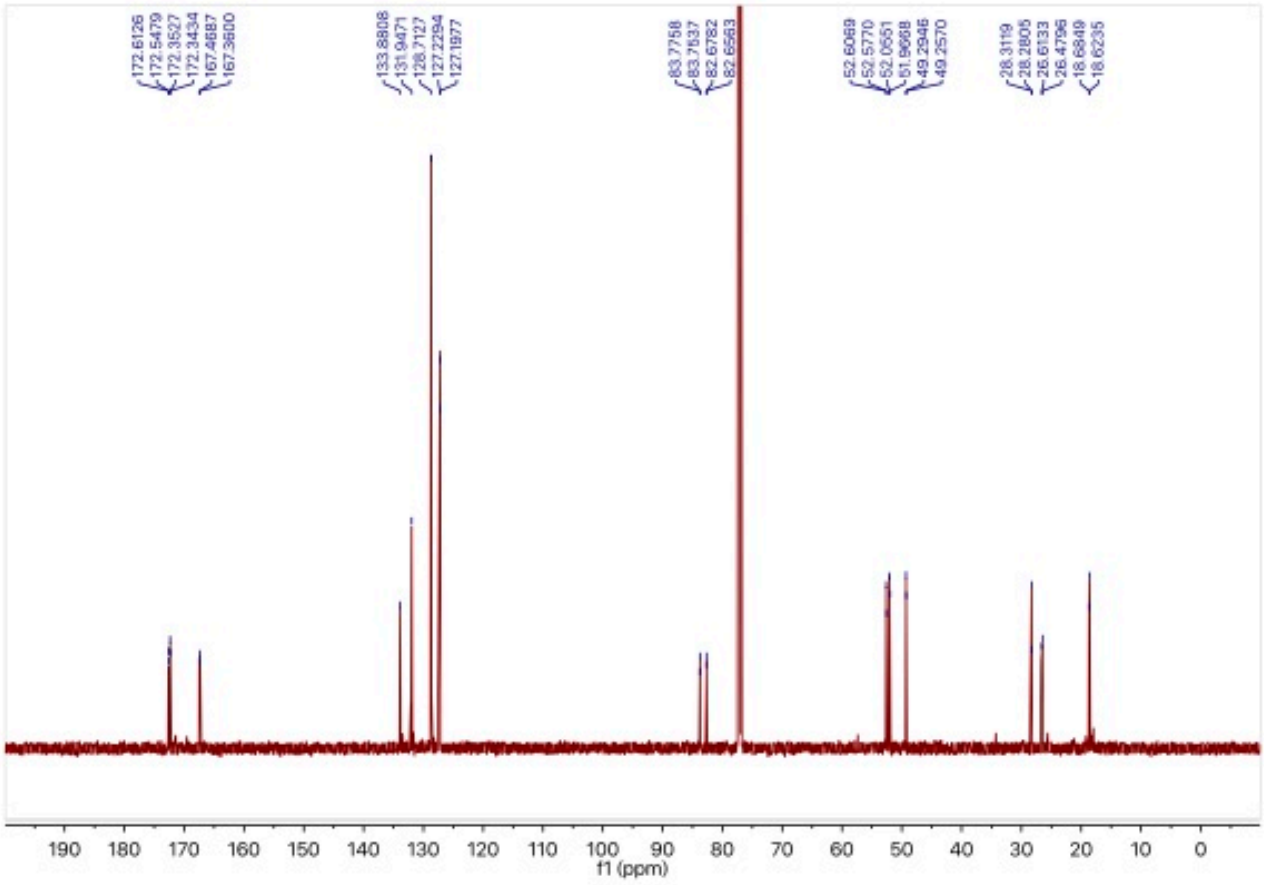
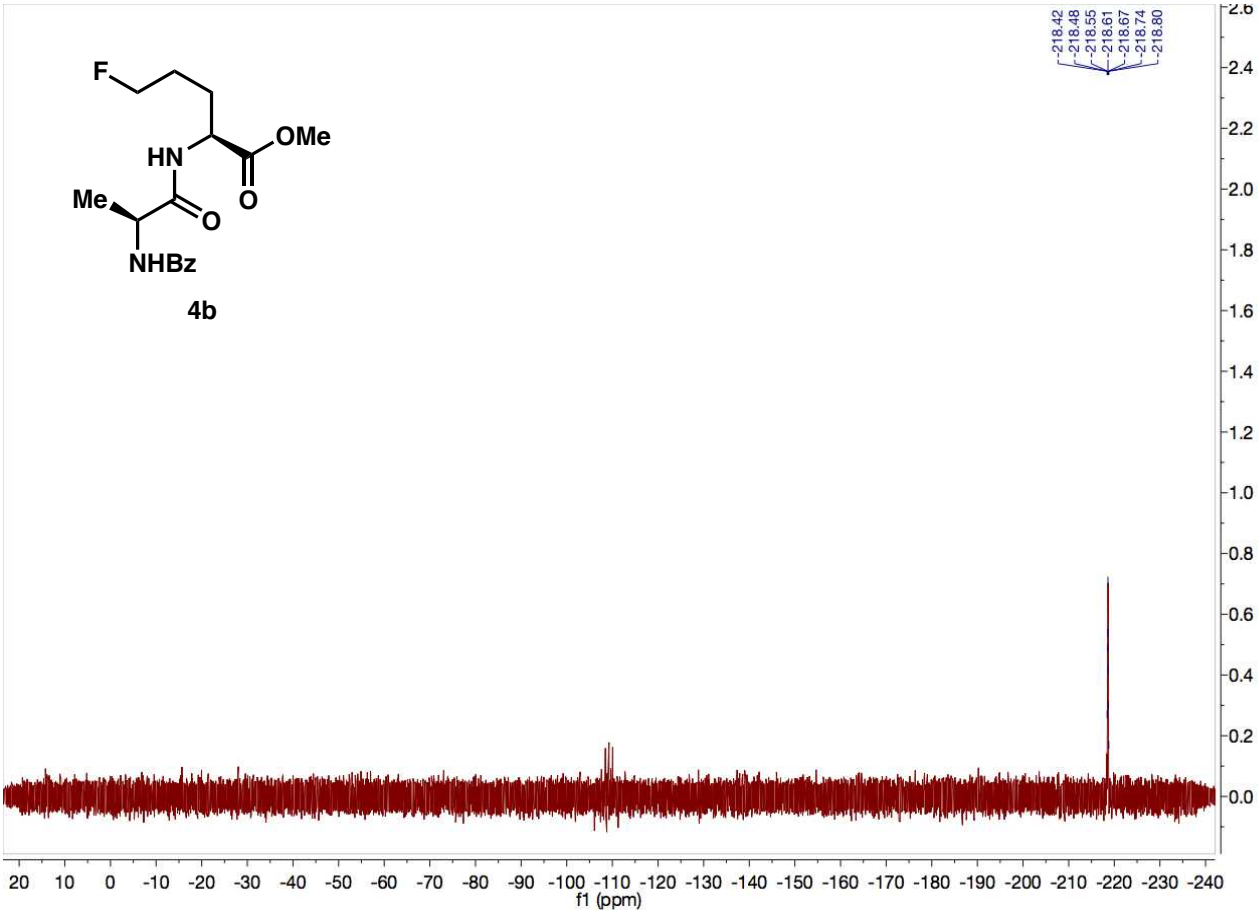
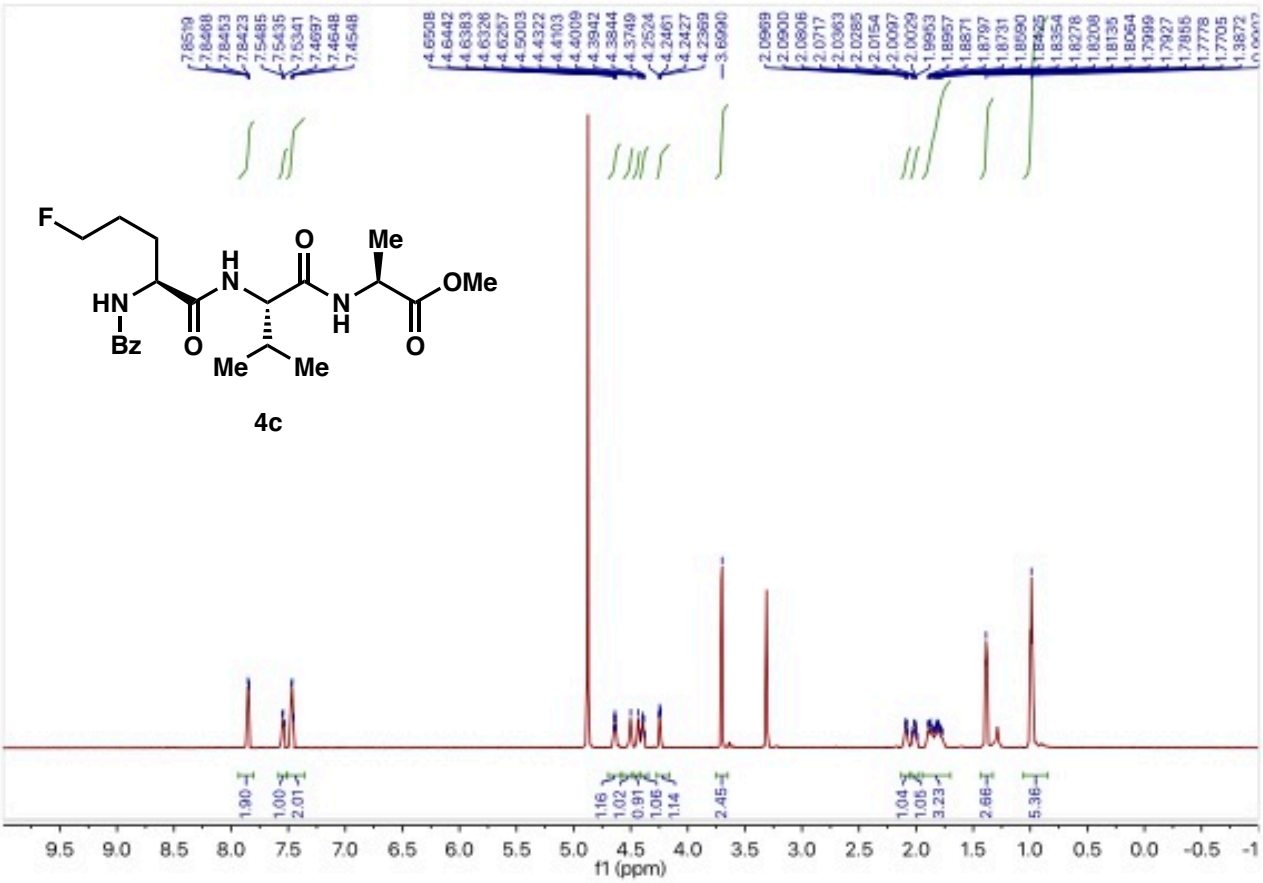
-217.1845
-217.2350
-217.2485
-217.3089
-217.3606
-217.3751
-217.4266
-217.4340
-217.5013
20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -24
f1 (ppm)


F
HN
OMe
O
Me
O
NHBz
4b
f1 (ppm)

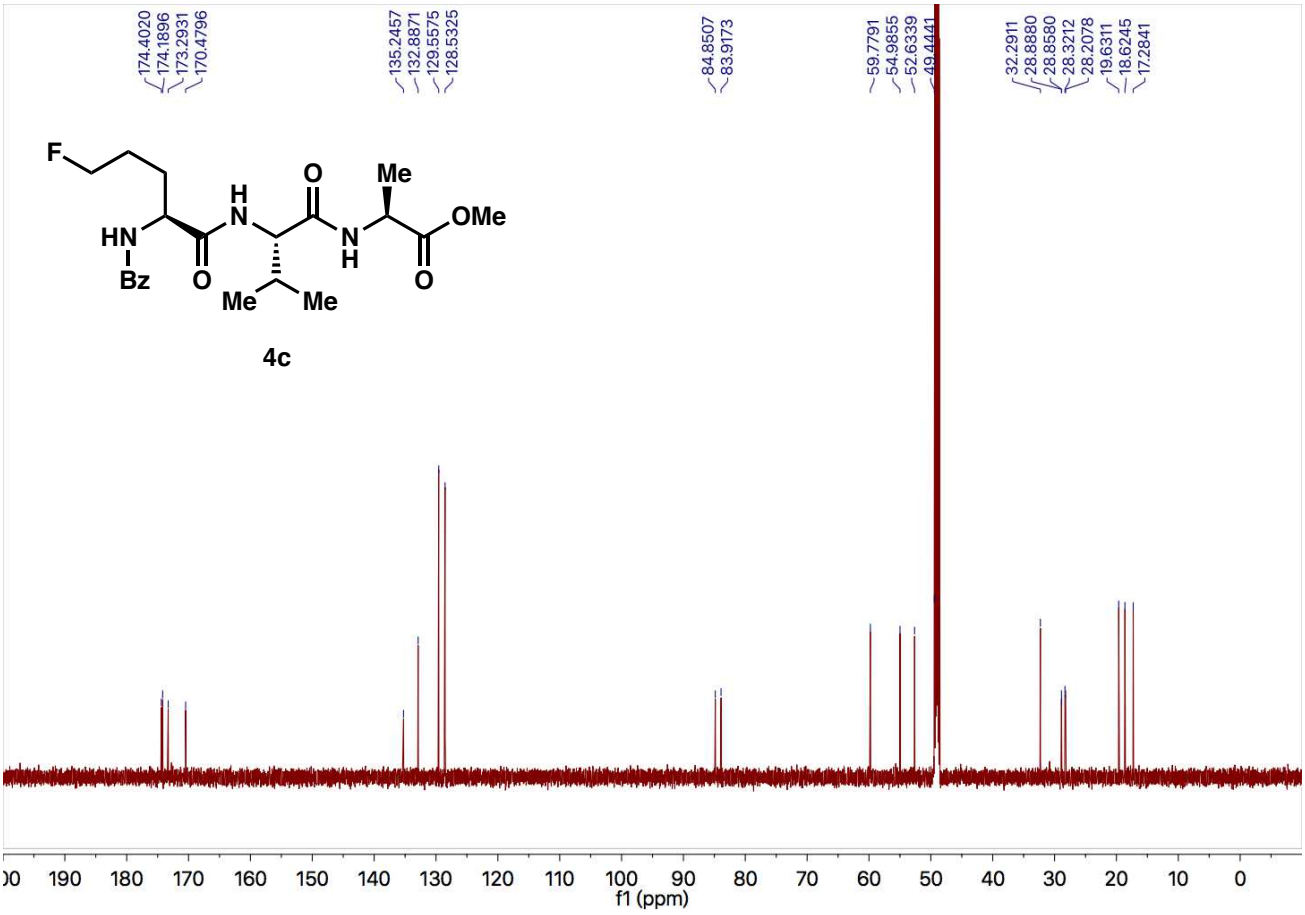

f1 (ppm)


F
HN
OMe
O
Me
O
NHBz
-218.42
-218.48
-218.55
-218.61
-218.67
-218.74
-218.80
f1 (ppm)

4b


F
HN
Bz
O
H
N
O
Me
N
H
OMe
O
Me
Me
f1 (ppm)

4c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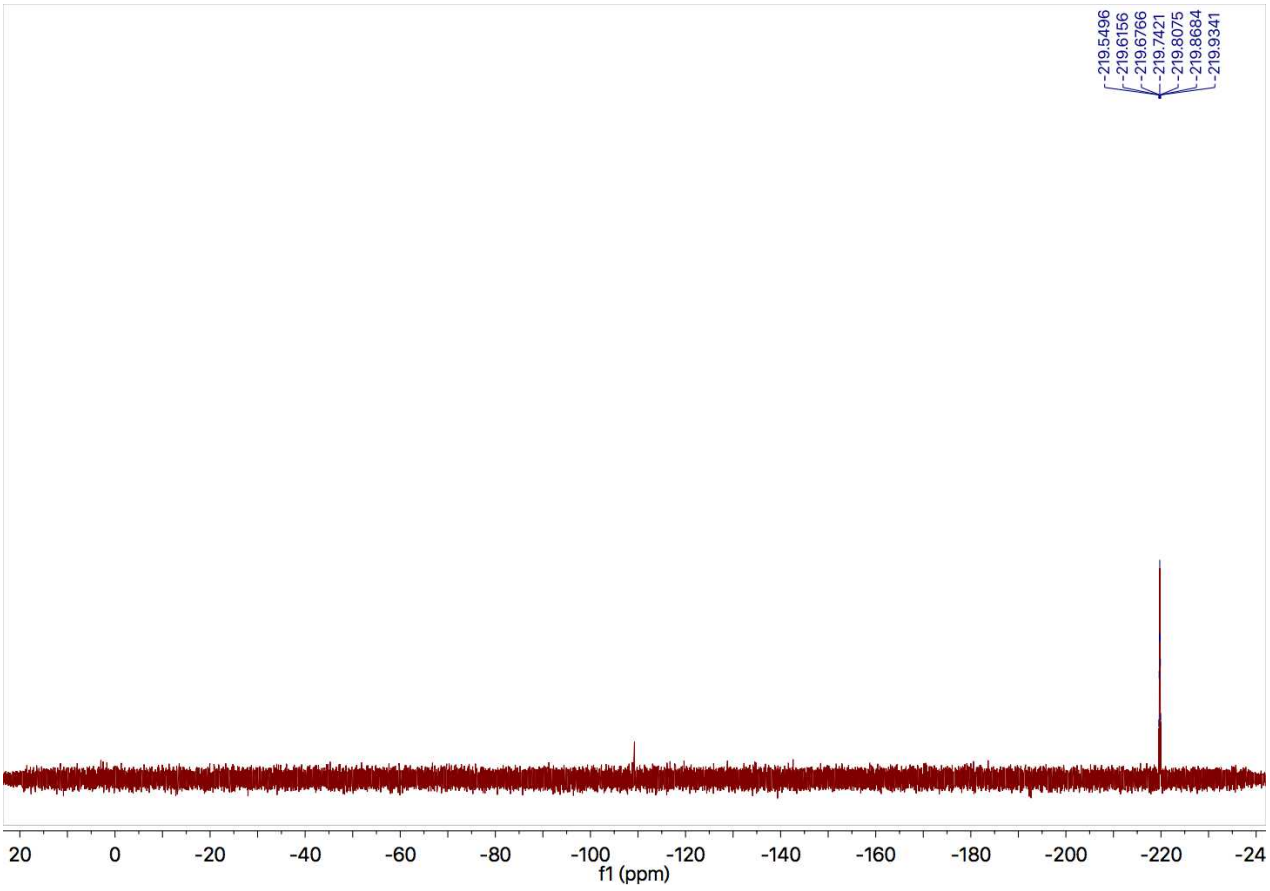
173.2931
170.4796
135.2457
132.8871
129.5575
128.5325
84.8507
83.9173
59.7791
54.9855
52.6339
49.4441
32.2911
28.8880
28.8580
28.3212
28.2078
19.6311
18.6245
17.2841
F
HN
Bz
O
H
N
O
Me
Me
N
H
OMe
O
f1 (ppm)

4c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-219.7421
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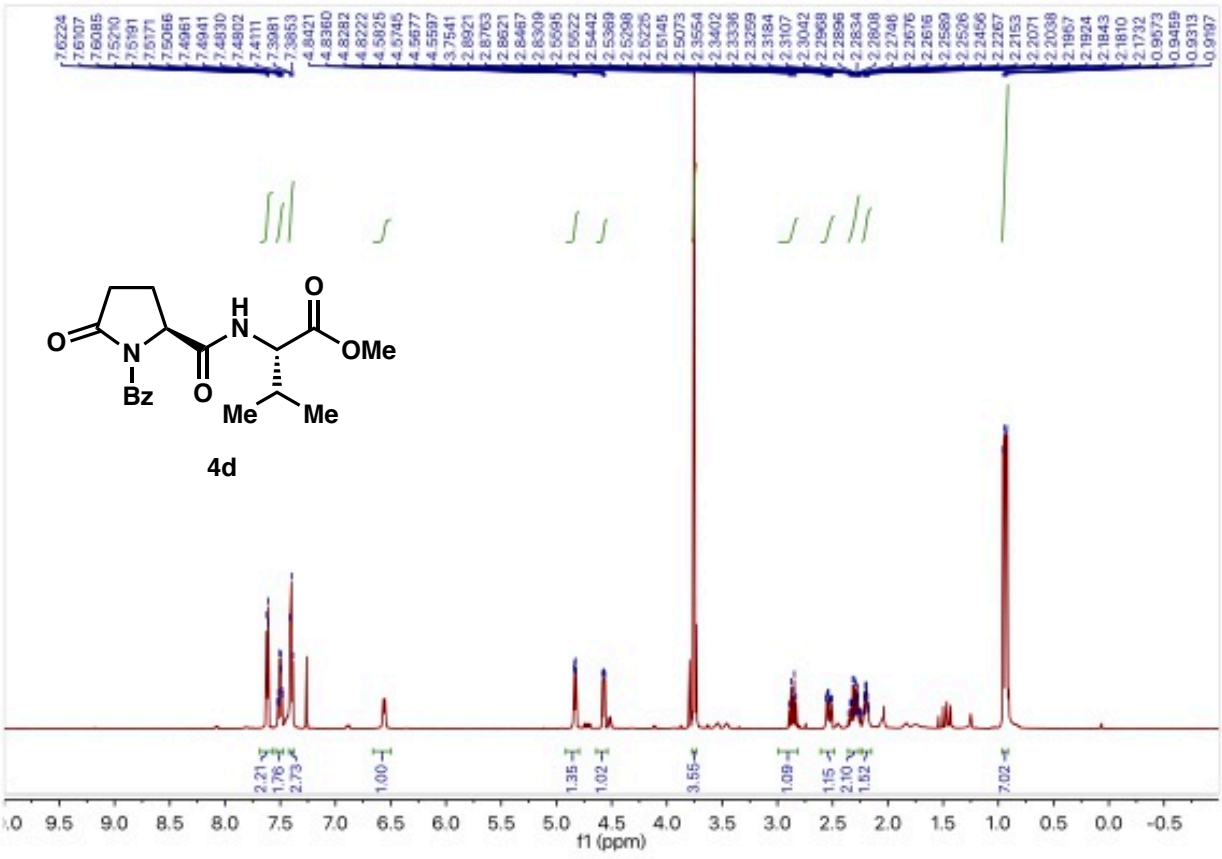
-219.8684
-219.9341
f1 (ppm)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7.6085
7.5240
7.5191
7.5171
7.5066
7.4961
7.4941
7.4830
7.4802
7.4111
7.3981
7.3853
4.8421
4.8360
4.8282
4.8222
4.5925
4.5745
4.5677
4.5597
3.7541
2.8921
2.8763
2.8621
2.8467
2.8309
2.5695
2.5522
2.5442
2.5369
2.5298
2.5225
2.5145
2.5073
2.3554
2.3402
2.3336
2.3259
2.3184
2.3107
2.3042
2.2968
2.2895
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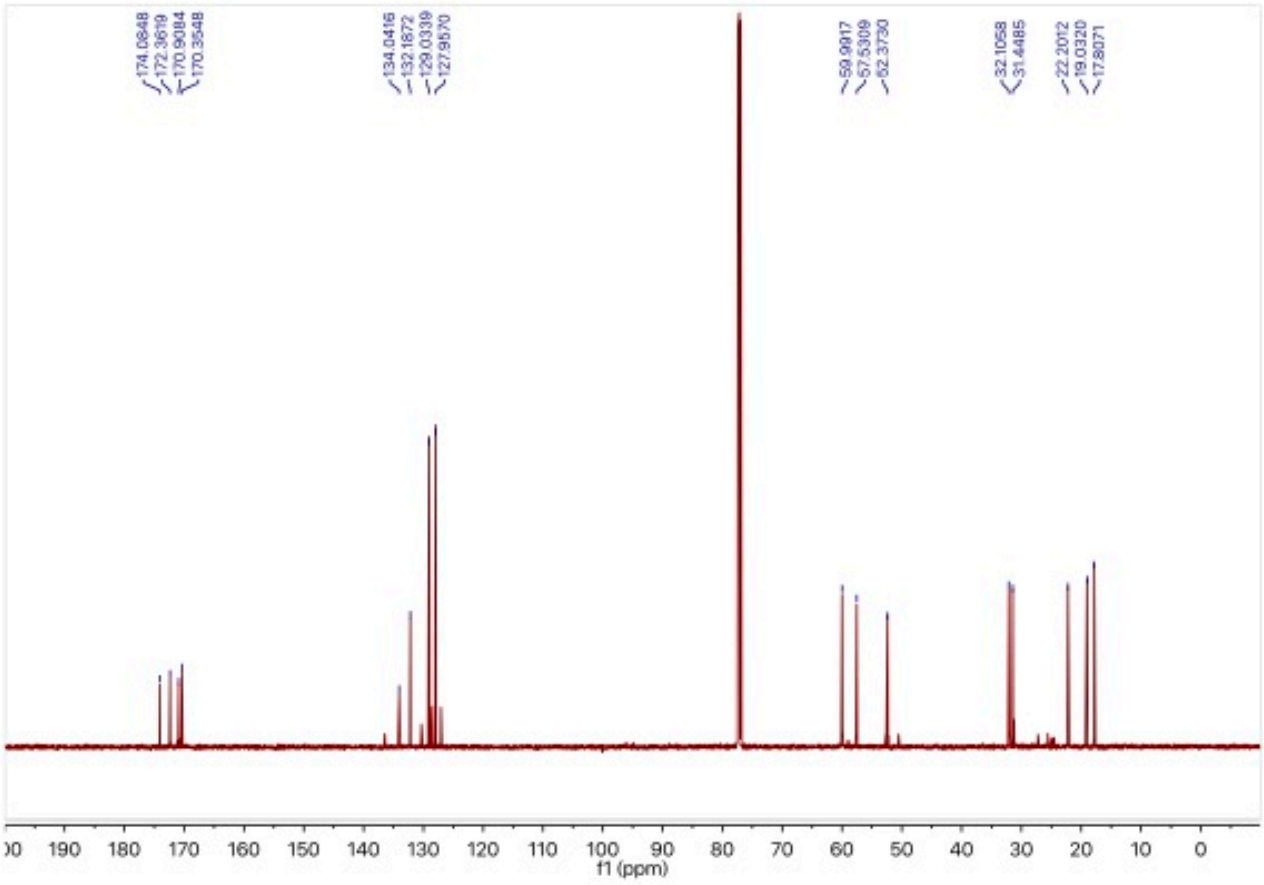
2.2526
2.2456
2.2267
2.2153
2.2071
2.2038
2.1967
2.1924
2.1843
2.1810
2.1732
0.9573
0.9459
0.9313
0.9197
O
H
N
O
OMe
O
N
Bz
O
Me
Me
4d
2.21
1.76
2.73
1.00
1.35
1.02
3.55
1.09
1.15
2.10
1.52
7.02
f1 (ppm)


174.0848
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170.9084
170.3548
134.0416
132.1872
129.0339
127.9570
59.9917
57.5309
52.3730
32.1058
31.4485
22.2012
19.0320
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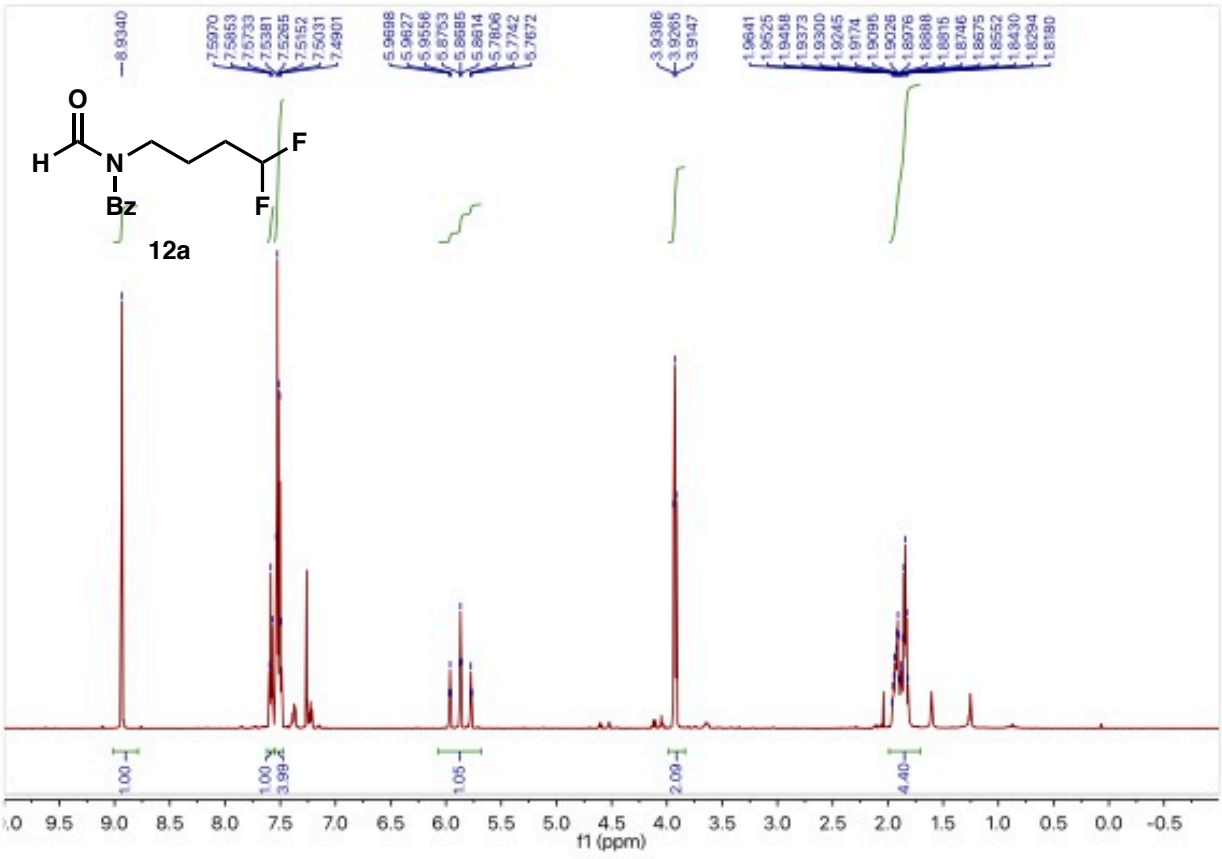
f1 (ppm)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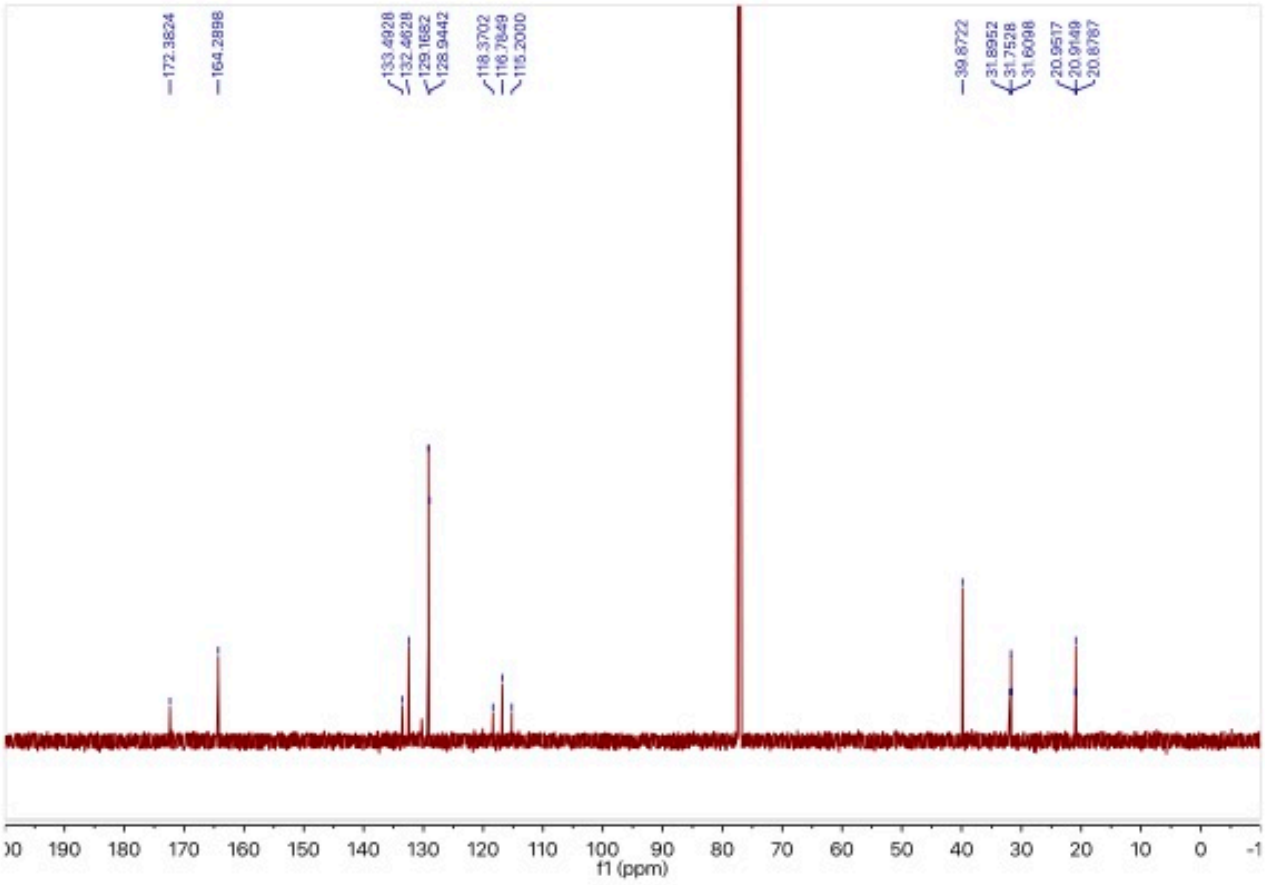
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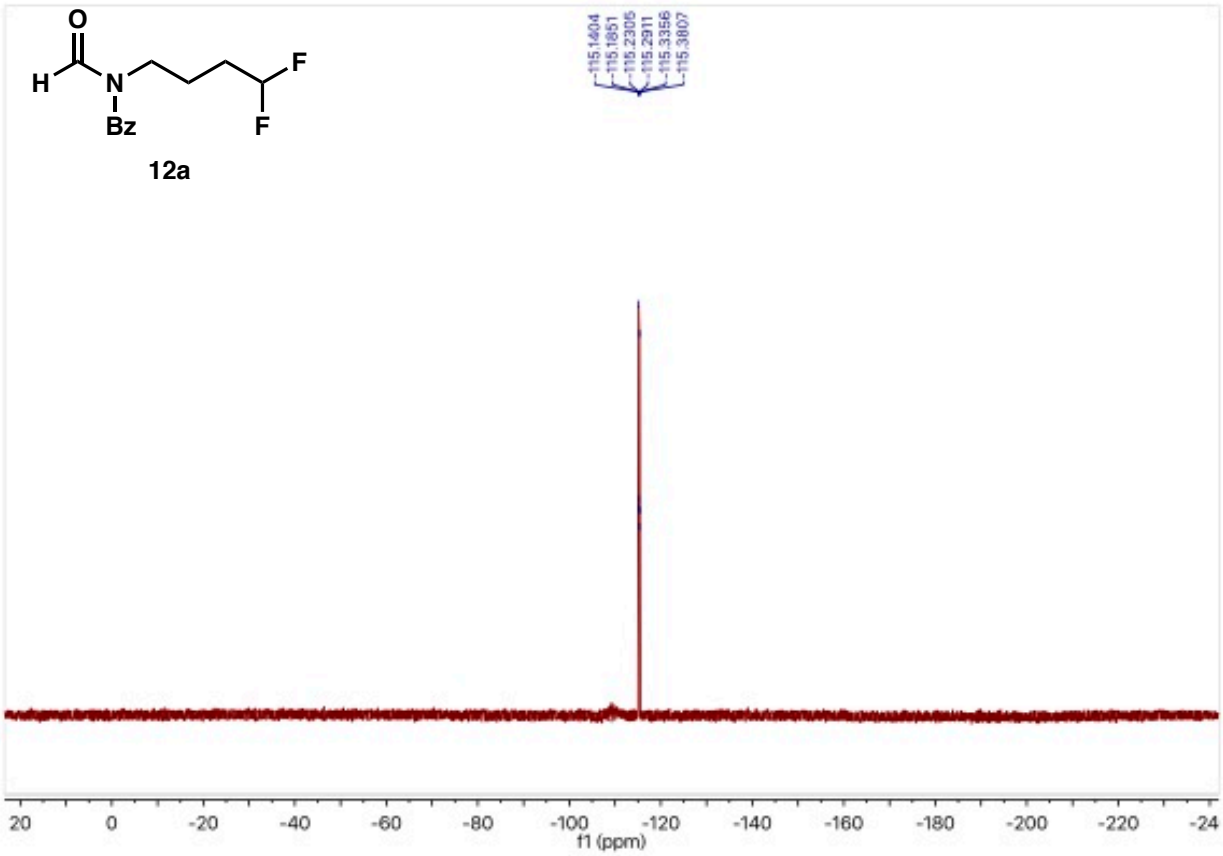
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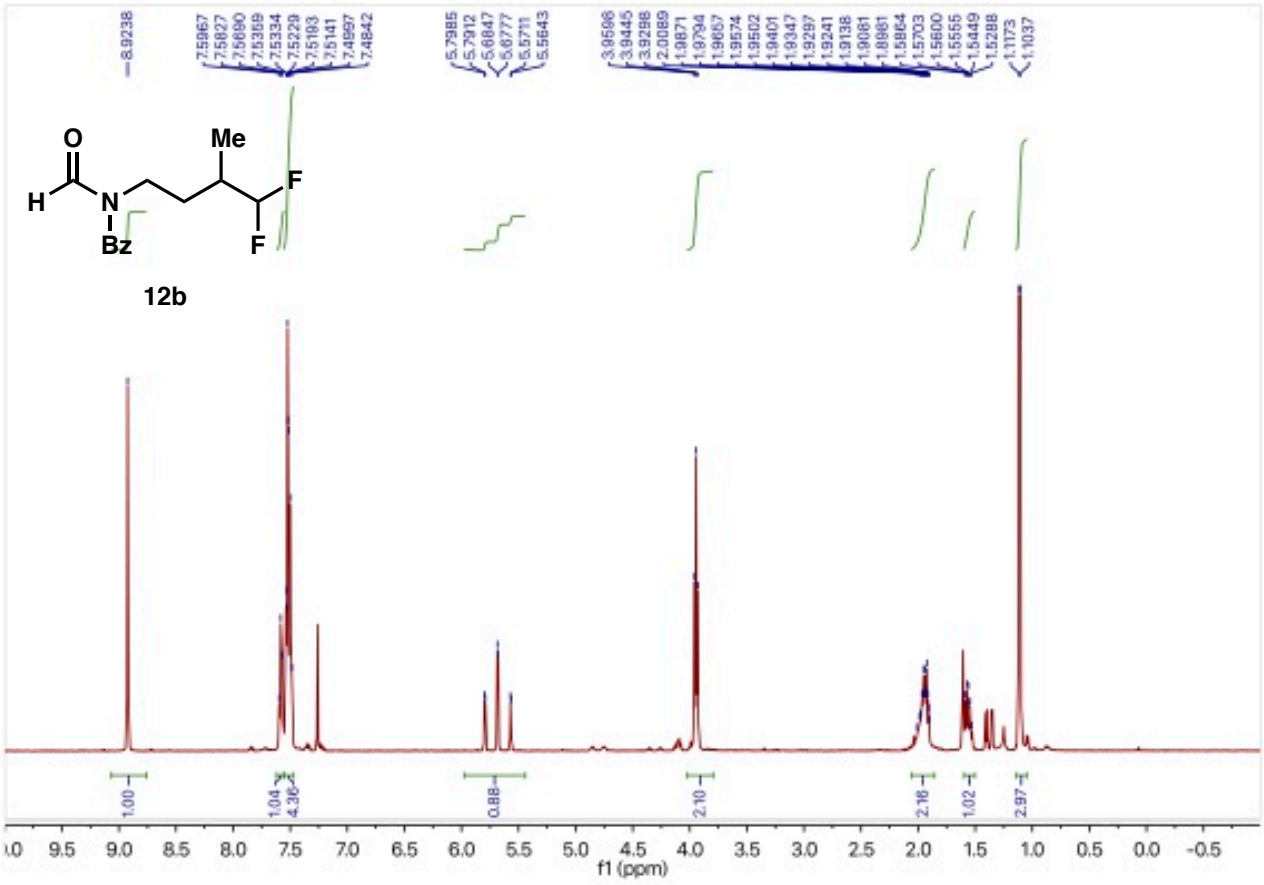
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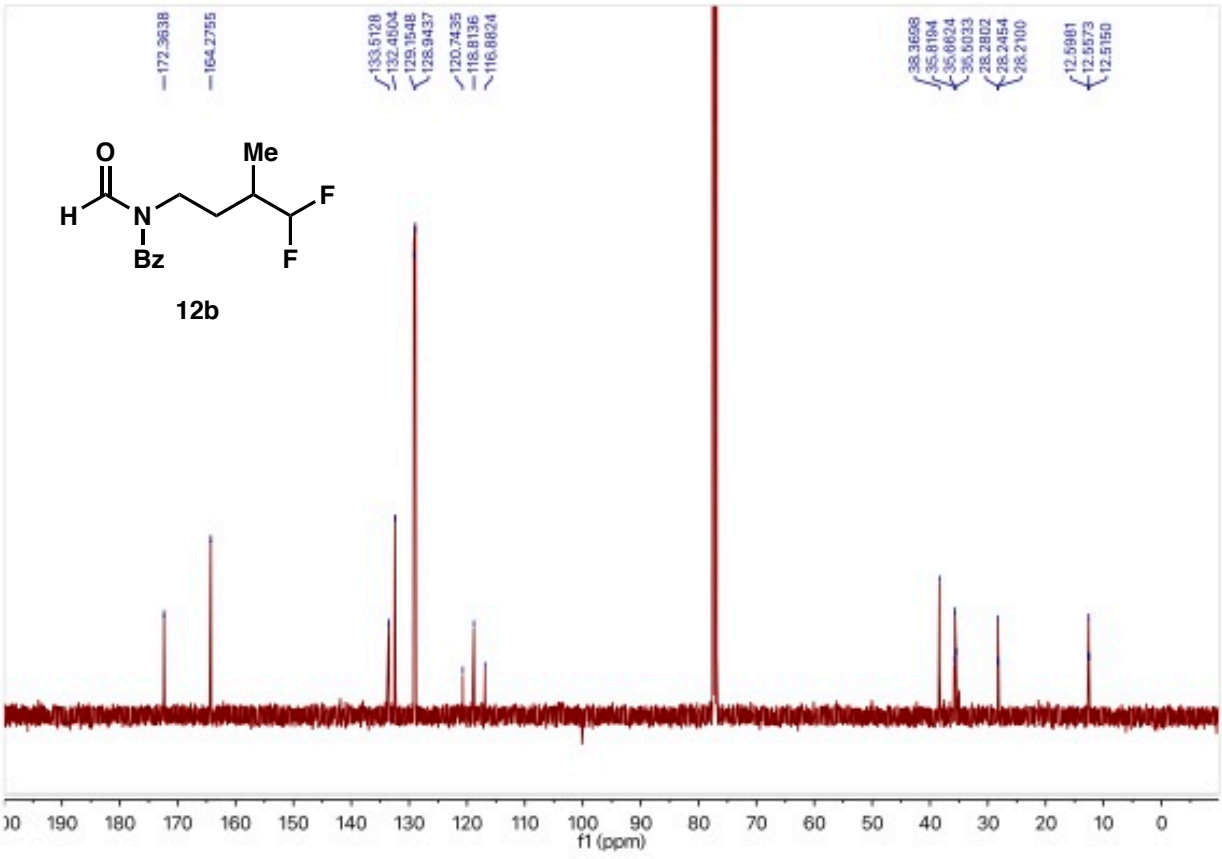
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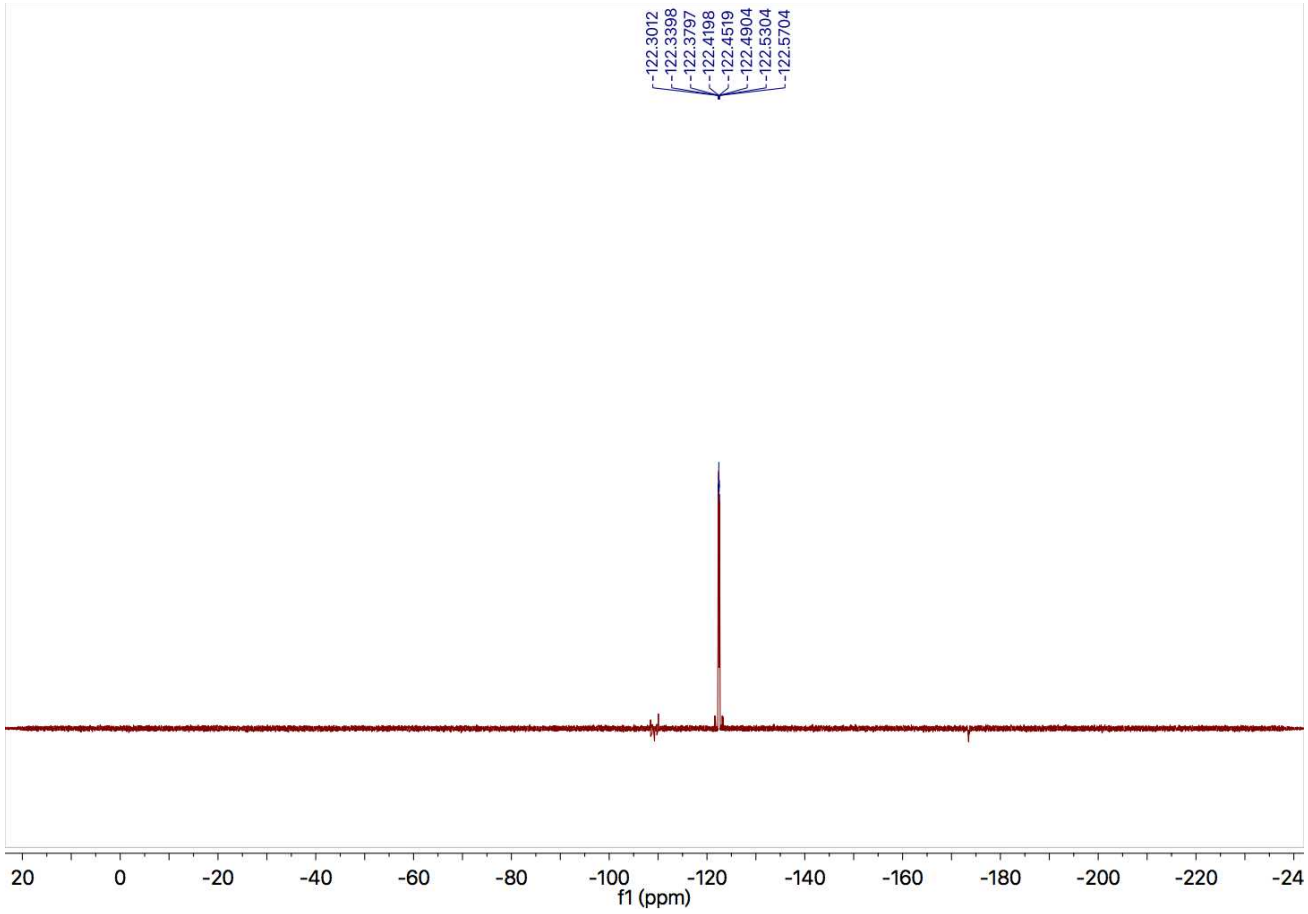
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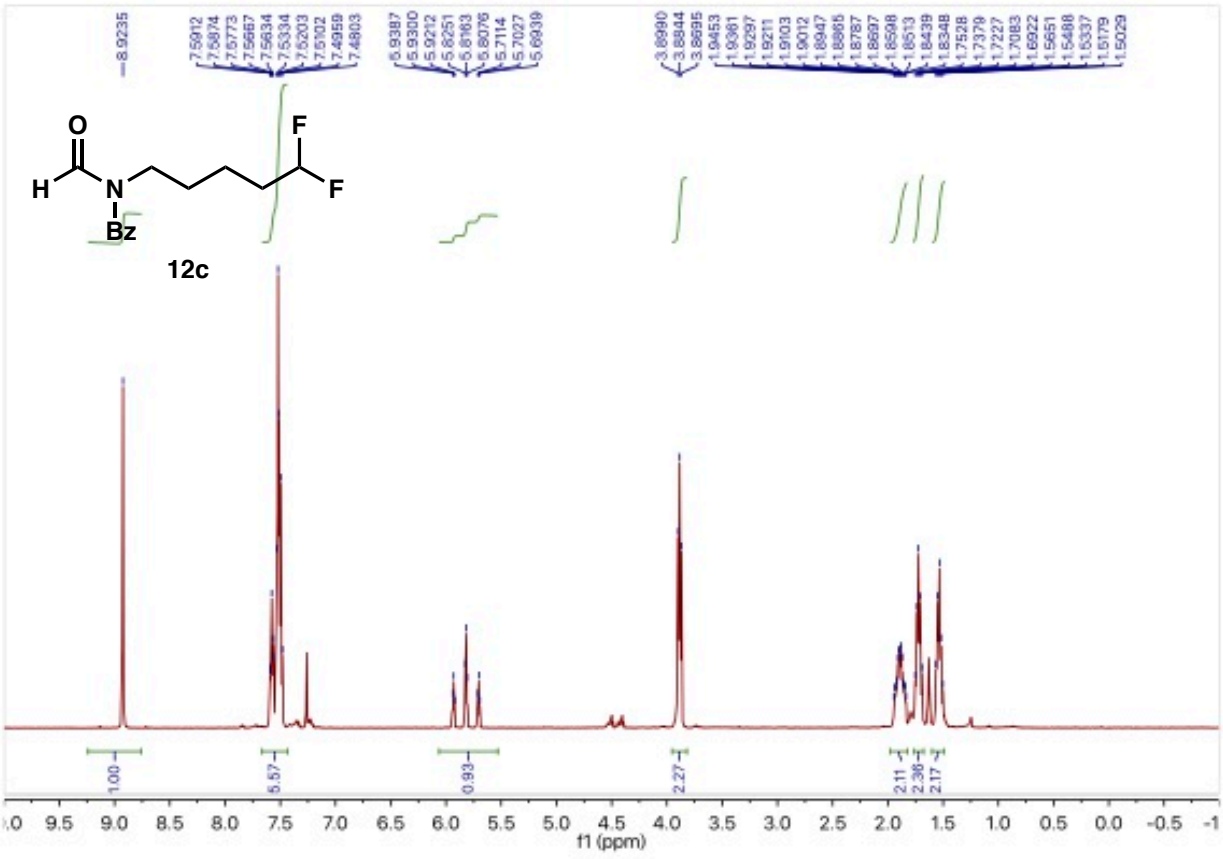
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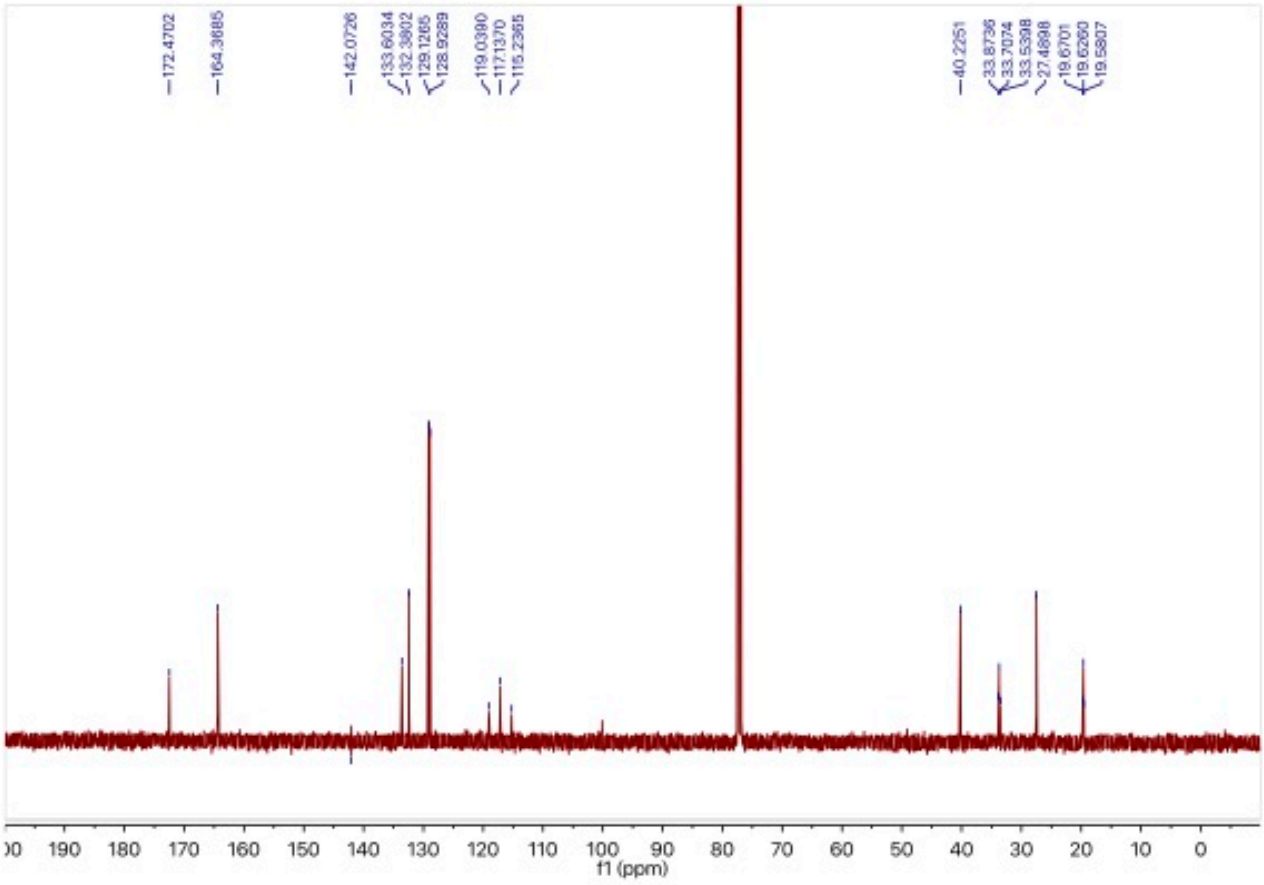
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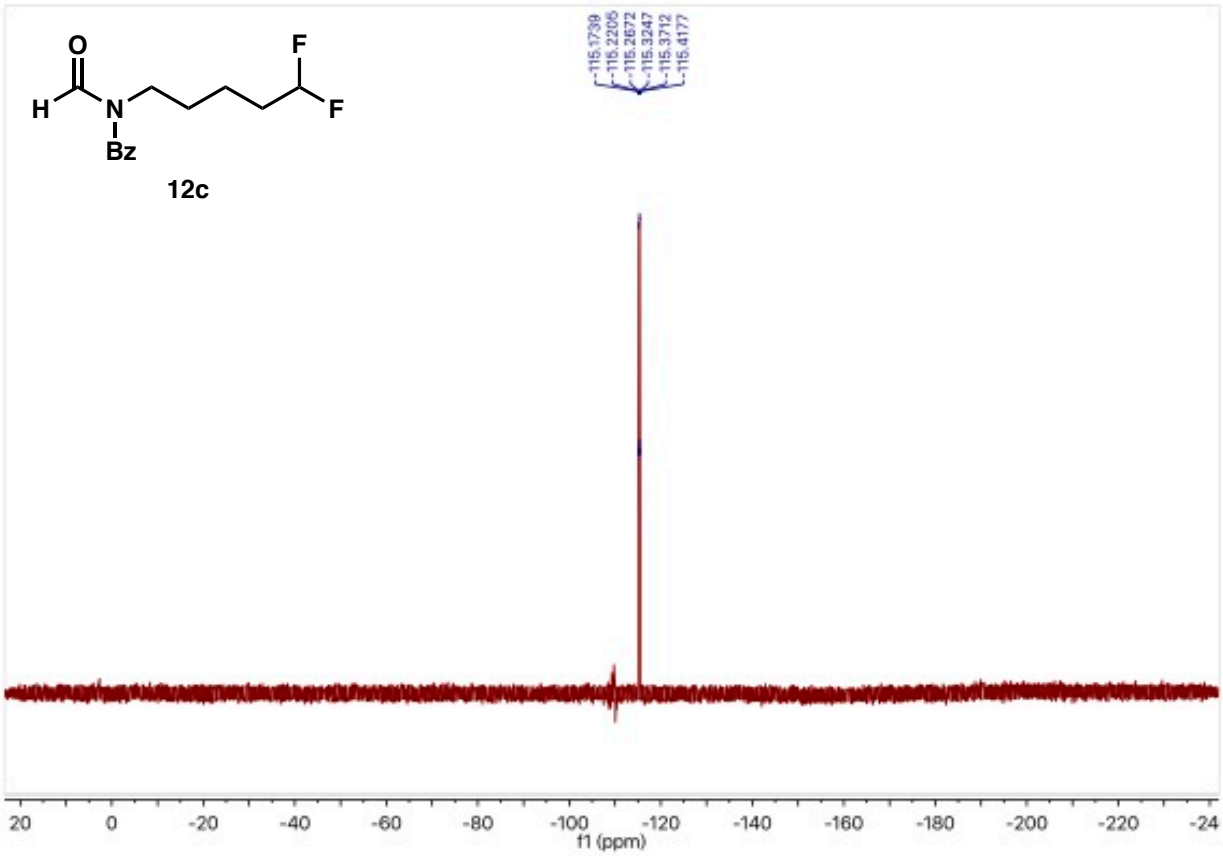
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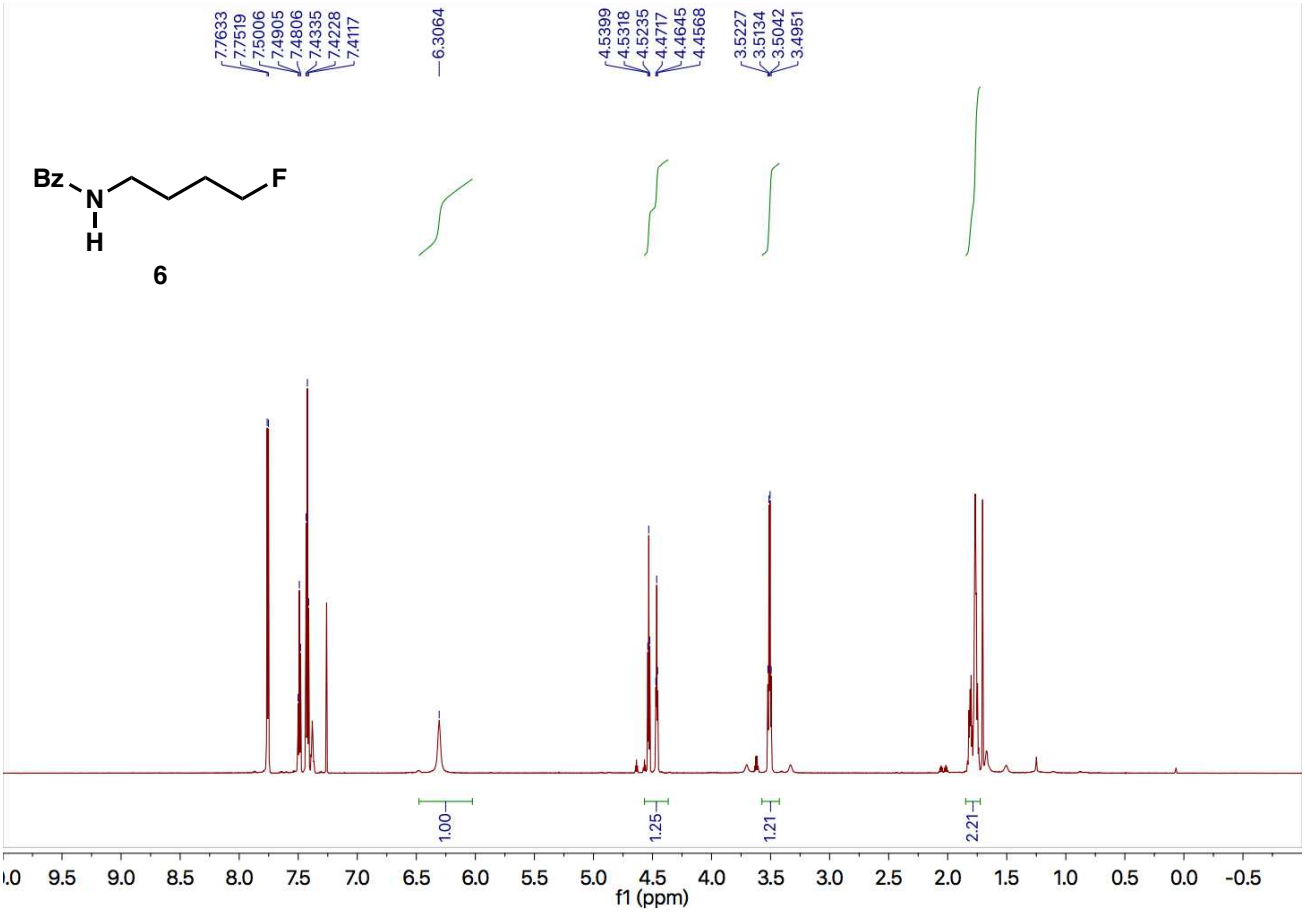
f1 (ppm)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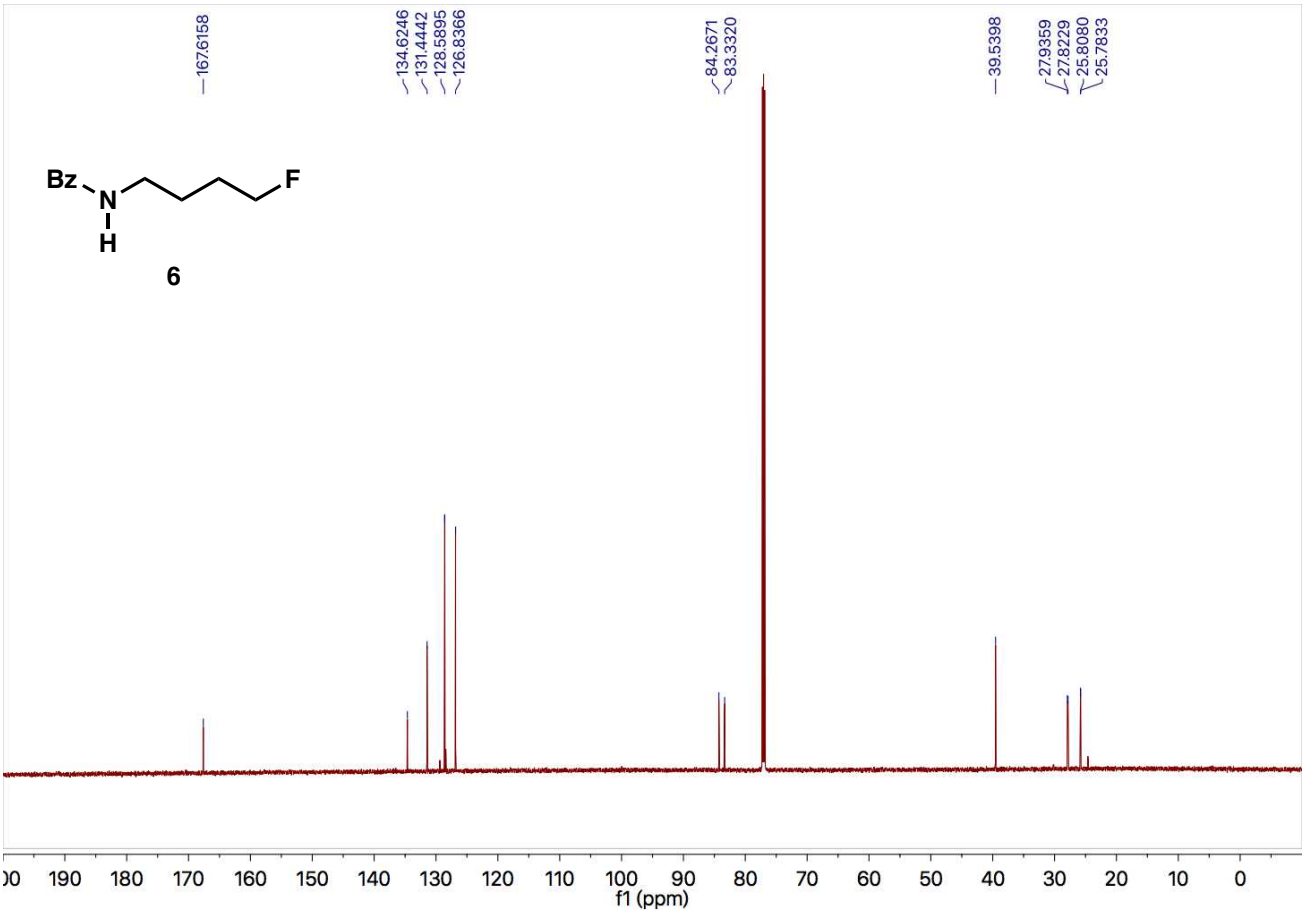
f1 (ppm)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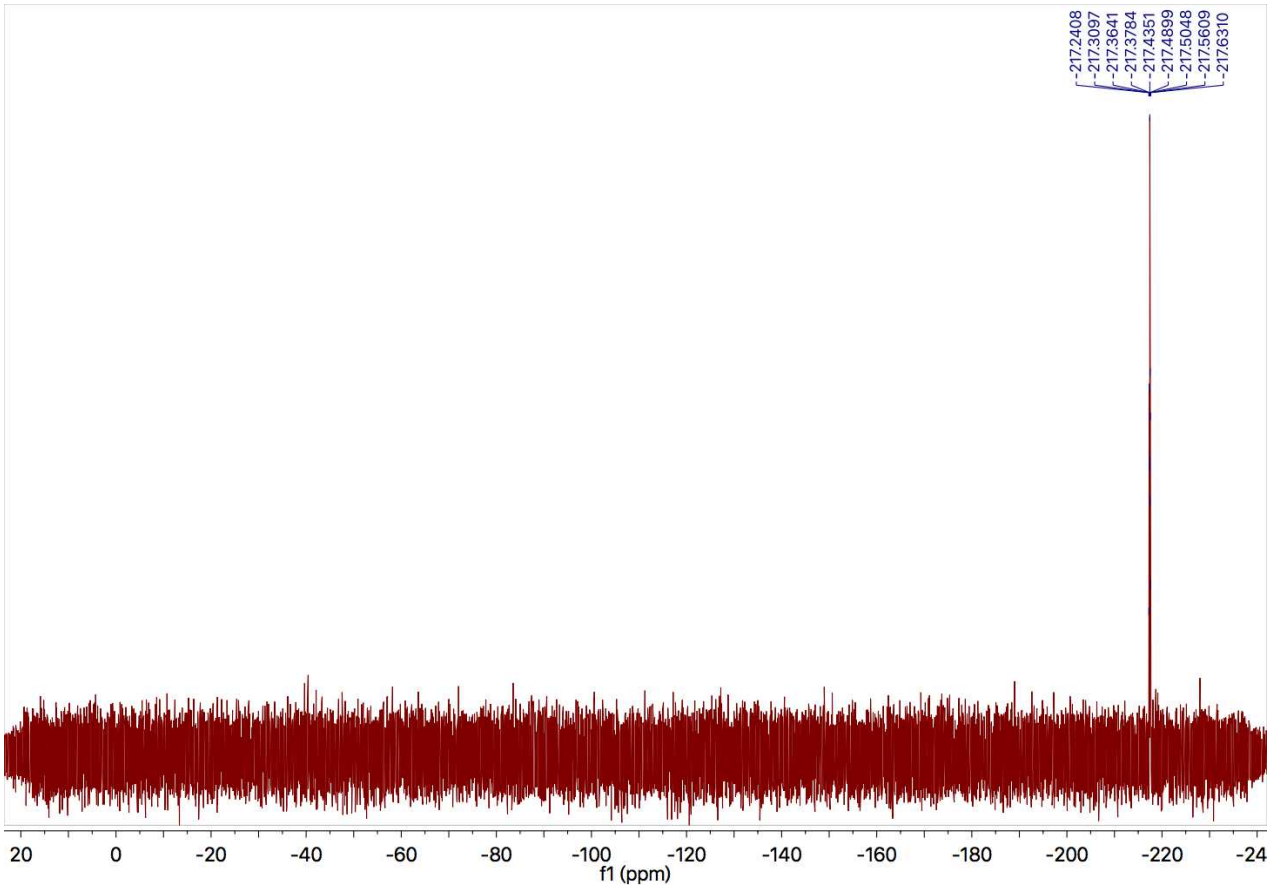
f1 (ppm)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f1 (ppm)

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