Iridium(I)-catalyzed α-C(sp^3)–H Alkylation of Saturated Azacycles

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Supporting Information

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1. General Information

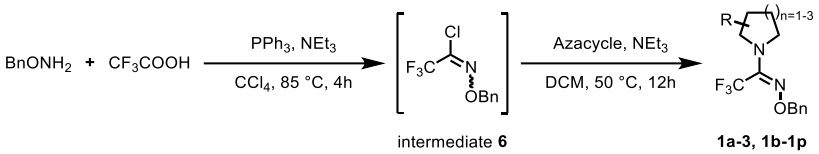
Unless stated otherwise, all materials were used as received from commercial suppliers without further purification. All Iridium catalysts were purchased from Sigma-Aldrich. Iridium pre-catalysts were synthesized according to literature procedures.[1] Anhydrous carbon tetrachloride and 1,2-dimethoxyethane were purchased from Sigma Aldrich. Anhydrous chlorobenzene was purchased from Acros. Other anhydrous solvents were obtained from the solvent purification system produced by JC Meyer Solvent Systems. All glassware and stirring bars were dried in an oven at 100 °C overnight unless otherwise stated. Ambient temperatures refer to 21–24 °C. Low temperatures were maintained using ice/water (0 °C) and acetone/CO_2(s) (-78 °C) baths. Elevated temperatures were maintained by Ika hot plates calibrated to an external thermometer, with heating blocks for 2-dram vials and silicone oil baths for larger vessels. Prior to beginning an experiment, the hot plate was turned on, and the heating block and oil bath were equilibrated to the desired temperature for 30 minutes. Analytical thin layer chromatography (TLC) was performed on Merck Millipore precoated (0.25 mm thickness) silica gel plates with F254 indicator. Visualization was accomplished by irradiation with UV light at 254 nm or potassium permanganate stain solution. Flash column chromatography was performed on silica gel (32-63 μm) supplied by Dynamic Adsorbents. Preparative TLC was used to purify reactions run at 0.1 mmol scale using Analtech Preparative TLC uniplates (20x20cm, 1000mm thickness), unless otherwise noted. ^{1}H NMR spectra were recorded on a Bruker DRX-600 spectrometer (600 MHz), unless otherwise noted. Chemical shifts were reported in parts per million (ppm) referenced to 0.0 ppm for tetramethylsilane. ^{13}C NMR spectra were recorded on a Bruker DRX-600 spectrometer (151 MHz) and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in parts per million (ppm) referenced to 77.16 ppm for center line of chloroform. ^{19}F NMR spectra were recorded on Bruker AMX-400 spectrometer (376 MHz) and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in parts per million (ppm) referenced to -164.9 ppm for hexafluorobenzene. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q =quartet, m = multiplet, br = broad. Coupling constants, *J*, were reported in Hertz unit (Hz). All 2D-NMR experiments were carried out on a Bruker DRX-600 spectrometer (600 MHz) using $CDCl_3$ as solvent. All NMR spectra were

recorded at room temperature, unless otherwise noted. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer.

2. Experimental Section

A. Preparation of Substrates

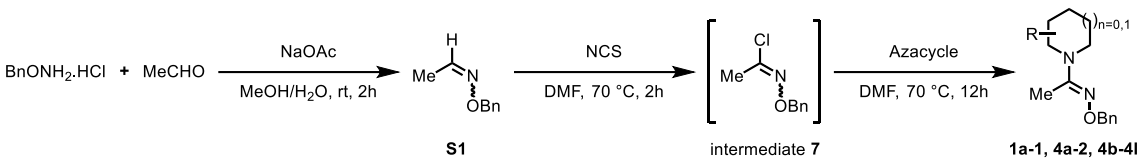
- *General procedure A for the preparation of substrates **1a-3**, **1b-1p**.*[2]



A 100 mL 2-neck flask equipped with a reflux condenser was charged with a stir bar and triphenylphosphine (25 mmol). The system was sealed and brought under N_2 atmosphere. Anhydrous carbon tetrachloride (10 mL) and triethylamine (10 mmol) were added consecutively. The reaction mixture was cooled to 0 °C and stirred for 10 minutes. Trifluoroacetic acid (10 mmol) was added dropwise and the stirring was continued at 0 °C for an additional 10 minutes. Next, *O*-benzylhydroxylamine (10 mmol) was added dropwise and the reaction mixture was heated to 85 °C. After 4 hours, the solvent was removed *in vacuo* to give a light yellow solid. The solid was thoroughly washed with hexanes. The filtrate was concentrated *in vacuo* to give intermediate **6**, which was used in the next step without further purification.

To a stirring solution of **6** in DCM (20 mL) were added triethylamine (10 mmol) and the corresponding azacycle (8.3 mmol) dropwise at rt. The reaction mixture was stirred at 50 °C for 12 hours. Upon completion, the system was cooled, and the organic layer was washed consecutively with saturated $NaHCO_3$ (aq), 1 N HCl (aq), and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography to afford the corresponding substrate in 75-90% yield over two steps. (When a hydrochloride salt of azacycle was used, the amount of triethylamine was increased to 20 mmol).

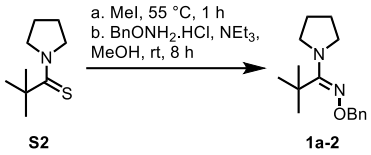
- *General procedure B for the preparation of substrates **1a-1**, **4a-2**, **4b-4l**.*[3]



To a stirred solution of sodium acetate (36 mmol) in 400 mL H_2O/MeOH (4:1) were added *O*-benzylhydroxylamine hydrochloride (30 mmol) and acetaldehyde (90 mmol). The reaction mixture was stirred at rt for 2h and then extracted with DCM (3 x 40 mL). The organic layer was washed with saturated $NaHCO_3$ (aq), dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* to give **S1**, which was used in the next step without further purification.

A 100 mL flask was charged with **S1** (30 mmol) and anhydrous DMF (20 mL). *N*-Chlorosuccinamide (30 mmol) was added in portions, and the reaction mixture was heated at 70 °C for 2 hours. After 2 hours, the system was cooled to rt and the corresponding azacycle (25 mmol) was added dropwise. The reaction mixture was re-heated to 70 °C and the stirring was continued for 12 hours. Upon completion, the reaction mixture was poured into ice water (100 mL) and the resulting mixture was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with saturated $NaHCO_3$ (aq), brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography to afford the corresponding substrate in 70-90% yield over two steps.

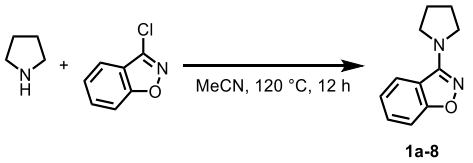
- *Procedure for the preparation of substrate **1a-2**.*



S2 was prepared according to a literature procedure.[4] A solution of **S2** (1 mmol) in methyl iodide (10 mmol) was refluxed at 55 °C for 1 hour. Upon completion, methyl iodide was removed *in vacuo*. The crude reaction mixture was charged with anhydrous methanol (10 mL), *O*-benzylhydroxylamine hydrochloride (1.2 mmol), and triethylamine (1.2 mmol). The solution was stirred at rt for 8 hours. Upon completion, the reaction mixture was concentrated *in vacuo* and diluted with water (10 mL) and ethyl acetate (10 mL). The layers were separated, and the aqueous

layer was back extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by flash chromatography to afford substrate **1a-2**.

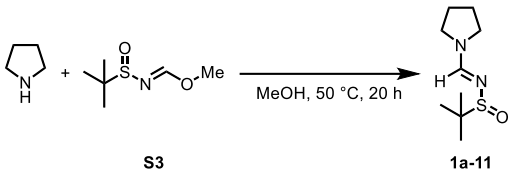
- *Procedure for the preparation of substrate **1a-8**.*



1a-8

To a stirred solution of 3-chloro-1,2-benzisoxazole (6.51 mmol) in MeCN (13 mL) was added pyrrolidine (19.53 mmol) and the reaction mixture was refluxed at 120 °C for 12 hours. Upon completion, the reaction mixture was concentrated in vacuo and diluted with DCM (15 mL), washed with saturated $NaHCO_3$ (aq), 1 N HCl (aq), and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography to afford substrate **1a-8** in 76% yield.

- *Procedure for the preparation of substrate **1a-12**.*



S3 **1a-11**

S3 (5 mmol) was prepared according to a literature procedure.[5] To a 50 mL flask charged with **S3** were added MeOH (5 mL) and pyrrolidine (10 mmol). The solution was stirred at 50 °C for 20 hours and the solvent was removed *in vacuo*. The crude residue was diluted with DCM and washed with water and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography to afford substrate **1a-12** in 55% yield over two steps.

- *Notes.*

Substrates **1a-4** and **4a-1** were prepared using the general procedure A, wherein perfluoropropionic acid was used instead of trifluoroacetic acid.

Substrate **1a-5** was prepared using the general procedure A, wherein *O*-tritylhydroxylamine was used instead of *O*-benzylhydroxylamine.

Substrate **1a-6** was prepared using the general procedure A, wherein *O*-(4-nitrobenzyl)hydroxylamine was used instead of *O*-benzylhydroxylamine. *O*-(4-nitrobenzyl)hydroxylamine was obtained from the commercially available *O*-(4-nitrobenzyl)hydroxylamine hydrochloride salt according to a literature procedure.[6]

Substrate **1a-7** was prepared using the general procedure A, wherein *O*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine was used instead of *O*-benzylhydroxylamine. *O*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine was obtained from the commercially available *O*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine hydrochloride salt according to a literature procedure.[6]

Substrate **1a-9** was prepared using the general procedure A, wherein ethyl 2-(aminooxy)acetate was used instead of *O*-benzylhydroxylamine. Ethyl 2-(aminooxy)acetate was obtained according to a literature procedure.[7]

Substrate **1a-10** was prepared using the general procedure A, wherein O-(pyridin-2-ylmethyl)hydroxylamine was used instead of *O*-benzylhydroxylamine. O-(pyridin-2-ylmethyl)hydroxylamine was obtained according to a literature procedure.[8]

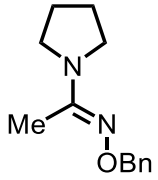
Substrate **1a-11** was prepared using the general procedure A, wherein *O*-phenylhydroxylamine was used instead of *O*-benzylhydroxylamine.

Substrate **4a-3** was prepared using the general procedure B, wherein propionaldehyde was used instead of acetaldehyde.

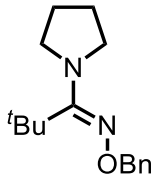
Substrate **4a-4** was prepared using the general procedure B, wherein isovaleraldehyde was used instead of acetaldehyde.

Deuterated benzyl acrylate was prepared using a reported literature procedure.[9]

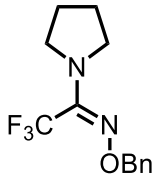
- *Full characterization of all substrates.*



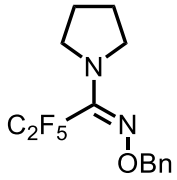
(*E*)-1-(pyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1a-1). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 – 7.22 (m, 5H), 4.90 (s, 2H), 3.29 – 3.20 (m, 4H), 2.02 (s, 3H), 1.90 – 1.83 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.60, 138.75, 128.34, 128.14, 127.37, 75.32, 46.70, 25.04, 12.73. **HRMS** (ESI-TOF): *m/z* calculated for $C_{13}H_{19}N_2O^+$ $[M+H]^+$ 219.1492, found 219.1491.



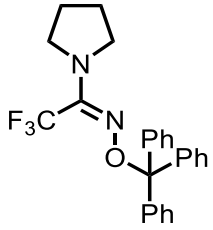
(*E*)-2,2-dimethyl-1-(pyrrolidin-1-yl)propan-1-one *O*-benzyl oxime (1a-2). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 – 7.22 (m, 5H), 4.93 (s, 2H), 3.43 – 3.34 (m, 4H), 1.78 – 1.70 (m, 4H), 1.21 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.26, 138.78, 128.26, 128.05, 127.28, 75.41, 51.06, 37.10, 29.08, 25.69. **HRMS** (ESI-TOF): *m/z* calculated for $C_{16}H_{25}N_2O^+$ $[M+H]^+$ 261.1961, found 216.1963.



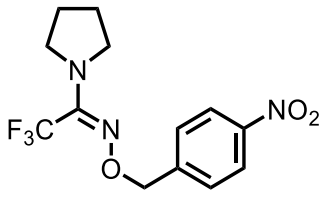
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1a-3). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 4H), 7.36 – 7.32 (m, 1H), 5.03 (s, 2H), 3.67 – 3.50 (m, 4H), 1.91 – 1.76 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.17 (q, *J* = 30.3 Hz), 137.24, 128.12 (d, *J* = 67.7 Hz), 119.39 (q, *J* = 277.3 Hz), 76.88, 49.94 (q, *J* = 2.2 Hz), 25.31. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.26. **HRMS** (ESI-TOF): *m/z* calculated for $C_{13}H_{16}F_3N_2O^+$ $[M+H]^+$ 273.1209, found 273.1212.



(*E*)-2,2,3,3,3-pentafluoro-1-(pyrrolidin-1-yl)propan-1-one *O*-benzyl oxime (1a-4). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 – 7.27 (m, 5H), 4.96 (d, *J* = 1.5 Hz, 2H), 3.59 – 3.52 (m, 4H), 1.83 – 1.74 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.56 (t, *J* = 26.2 Hz), 137.33, 128.61, 128.29, 127.93, 122.11 – 114.97 (m), 113.83 – 109.18 (m), 76.95, 49.83 (t, *J* = 2.9 Hz), 25.34. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -79.72, -110.46. **HRMS** (ESI-TOF): *m/z* calculated for $C_{14}H_{16}F_5N_2O^+$ $[M+H]^+$ 323.1177, found 323.1171.

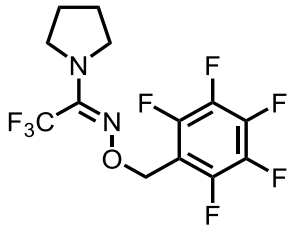


(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-trityl oxime (1a-5). White solid. **^{1}H NMR** (600 MHz, $CDCl_3$, 93:7 mixture of geometrical isomers, only the major geometrical isomer is characterized) δ 7.34 – 7.21 (m, 15H), 3.67 – 3.61 (m, 4H), 1.88 – 1.79 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$, 93:7 mixture of geometrical isomers, only the major geometrical isomer is characterized) δ 144.14, 140.15 (q, *J* = 30.5 Hz), 129.41, 127.37, 127.06, 119.38 (q, *J* = 277.6 Hz), 91.92, 49.90 (d, *J* = 2.3 Hz), 25.41. **^{19}F NMR** (376 MHz, $CDCl_3$, 93:7 mixture of geometrical isomers) δ -63.69 (minor), -66.09. **HRMS** (ESI-TOF): *m/z* calculated for $C_{25}H_{24}F_3N_2O^+$ $[M+H]^+$ 425.1835, found 425.1834.

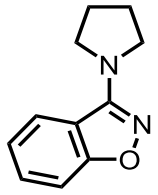


(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-(4-nitrobenzyl) oxime (1a-6). Dark green solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.25 – 8.19 (m, 2H), 7.54 – 7.48 (m, 2H), 5.08 (s, 2H), 3.62

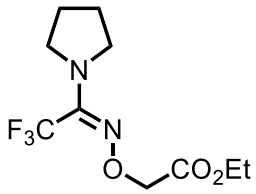
– 3.57 (m, 4H), 1.89 – 1.80 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.55, 145.01, 141.56 (q, *J* = 30.5 Hz), 128.49, 123.64, 119.24 (q, *J* = 277.8 Hz), 75.28, 50.06 (d, *J* = 2.3 Hz), 25.32. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.35. **HRMS** (ESI-TOF): *m/z* calculated for $C_{13}H_{15}F_3N_3O_3^+$ $[M+H]^+$ 318.1060, found 318.1051.



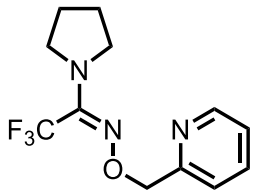
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-((perfluorophenyl)methyl) oxime (1a-7). Pale yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 78:22 mixture of isomers) δ 5.17 – 4.90 (m, 2H), 3.69 – 3.45 (m, 4H), 1.98 – 1.74 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$, 78:22 mixture of isomers, only the major isomer is characterized) δ 147.07 – 146.26 (m), 145.41 – 144.64 (m), 142.71 – 142.10 (m), 141.46 (q), 138.70 – 137.84 (m), 136.89 – 136.20 (m), 119.16 (q, *J* = 277.8 Hz), 113.18 – 108.68 (m), 62.84, 49.93 (q, *J* = 2.3 Hz), 25.30. **^{19}F NMR** (376 MHz, $CDCl_3$, 78:22 mixture of isomers) δ -66.37 (minor), -66.50, -142.40 (dd, *J* = 22.0, 8.6 Hz), -146.44 – -146.60 (m, minor), -153.75 (t, *J* = 20.6 Hz), -156.57 – -156.73 (m, minor), -162.44 (td, *J* = 21.9, 8.6 Hz). **HRMS** (ESI-TOF): *m/z* calculated for $C_{13}H_{11}F_8N_2O^+$ $[M+H]^+$ 363.0738, found 363.0733.



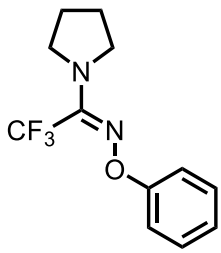
3-(pyrrolidin-1-yl)benzo[*d*]isoxazole (1a-8). White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.76 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.46 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.40 (dt, *J* = 8.4, 0.9 Hz, 1H), 7.17 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 3.74 – 3.65 (m, 4H), 2.10 – 2.02 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.73, 158.89, 129.45, 122.52, 121.77, 116.71, 110.17, 48.50, 25.52. **HRMS** (ESI-TOF): *m/z* calculated for $C_{11}H_{13}N_2O^+$ $[M+H]^+$ 189.1022, found 189.1021.



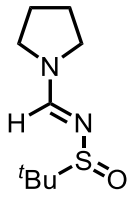
ethyl (*E*)-2-(((2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethylidene)amino)oxy)acetate (1a-9). Yellow oil. Isolated as a mixture of isomers, only the major isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.52 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.69 – 3.62 (m, 4H), 1.87 – 1.80 (m, 4H), 1.28 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 169.78, 141.94 (q, *J* = 30.7 Hz), 119.24 (q, *J* = 277.8 Hz), 71.19, 60.85, 50.02 (q, *J* = 2.4 Hz), 25.35, 14.18. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.46. HRMS (ESI-TOF): *m/z* calculated for $C_{10}H_{16}F_3N_2O_3^+$ $[M+H]^+$ 269.1108, found 269.1109.



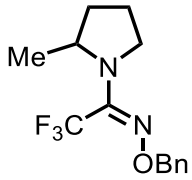
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-pyridin-2-ylmethyl oxime (1a-10). Yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 97:3 mixture of geometrical isomers) δ 8.60 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.71 (td, *J* = 7.7, 1.8 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.23 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 5.13 (s, 2H), 3.64 – 3.58 (m, 4H), 1.88 – 1.78 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$, 97:3 mixture of geometrical isomers, only the major geometrical isomer is characterized) δ 157.72, 149.23, 141.45 (q, *J* = 30.5 Hz), 136.49, 122.52, 122.11, 119.34 (q, *J* = 277.5 Hz), 77.38, 50.03 (q, *J* = 2.2 Hz), 25.33. **^{19}F NMR** (376 MHz, $CDCl_3$, 97:3 mixture of geometrical isomers) δ -63.28 (minor), -66.29. **HRMS** (ESI-TOF): *m/z* calculated for $C_{12}H_{15}F_3N_3O^+$ $[M+H]^+$ 274.1162, found 274.1159.



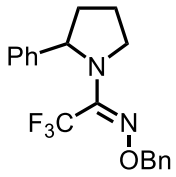
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one O-phenyl oxime (1a-11). Dark green oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 2H), 7.20 – 7.15 (m, 2H), 6.98 (tt, *J* = 7.3, 1.1 Hz, 1H), 3.74 – 3.69 (m, 4H), 1.93 – 1.84 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.13, 143.12 (q, *J* = 30.6 Hz), 129.27, 121.89, 119.45 (q, *J* = 278.2 Hz), 114.09, 50.31 (q, *J* = 2.4 Hz), 25.37. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.34. **HRMS** (ESI-TOF): *m/z* calculated for $C_{12}H_{14}F_3N_2O^+$ $[M+H]^+$ 259.1053, found 259.1059.



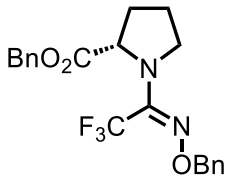
(*E*)-2-methyl-*N*-(pyrrolidin-1-ylmethylene)propane-2-sulfinamide (1a-12). Light orange solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.89 (s, 1H), 3.51 (t, *J* = 6.5 Hz, 2H), 3.47 – 3.37 (m, 2H), 2.00 – 1.88 (m, 4H), 1.14 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 152.23, 55.56, 49.19, 45.61, 25.22, 24.64, 21.85. **HRMS** (ESI-TOF): *m/z* calculated for $C_9H_{19}N_2OS^+$ $[M+H]^+$ 203.1213, found 203.1210.



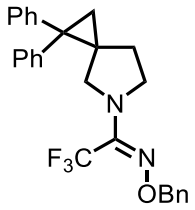
(*E*)-2,2,2-trifluoro-1-(2-methylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1b). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.46 – 7.27 (m, 5H), 5.03 (d, *J* = 2.7 Hz, 2H), 4.35 (h, *J* = 6.3 Hz, 1H), 3.53 (dddd, *J* = 9.6, 8.1, 6.9, 1.2 Hz, 1H), 3.33 (ddd, *J* = 9.8, 7.4, 4.4 Hz, 1H), 2.04 (dtd, *J* = 12.5, 7.2, 5.4 Hz, 1H), 1.92 – 1.81 (m, 1H), 1.76 (dddd, *J* = 13.2, 8.4, 6.6, 4.2 Hz, 1H), 1.44 (ddt, *J* = 12.6, 8.5, 6.5 Hz, 1H), 1.01 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.47 (q, *J* = 30.6 Hz), 136.97, 128.45 (d, *J* = 29.2 Hz), 128.02, 119.55 (q, *J* = 278.1 Hz), 77.15, 55.99, 48.97 (d, *J* = 2.9 Hz), 33.28, 24.14, 20.49. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.18. **HRMS** (ESI-TOF): *m/z* calculated for $C_{14}H_{18}F_3N_2O^+$ $[M+H]^+$ 287.1366, found 287.1366.



(*E*)-2,2,2-trifluoro-1-(2-phenylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1c). Pale yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 5H), 7.23 – 7.16 (m, 3H), 7.10 – 7.02 (m, 2H), 5.30 (t, *J* = 7.0 Hz, 1H), 4.71 (dd, *J* = 166.7, 11.4 Hz, 2H), 3.85 (q, *J* = 7.7 Hz, 1H), 3.55 (ddd, *J* = 9.8, 7.4, 4.7 Hz, 1H), 2.28 (dq, *J* = 12.7, 6.5 Hz, 1H), 1.97 – 1.79 (m, 2H), 1.71 (ddt, *J* = 12.8, 8.6, 6.6 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.83, 140.13 (q, *J* = 30.9 Hz), 136.79, 128.49, 128.26 (d, *J* = 6.5 Hz), 127.88, 126.68, 125.46, 119.54 (q, *J* = 277.9 Hz), 76.93, 64.73, 50.72 (d, *J* = 3.0 Hz), 36.50, 24.17. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.81. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{20}F_3N_2O^+$ $[M+H]^+$ 349.1522, found 349.1522.

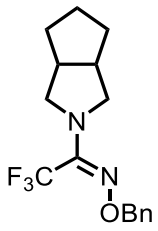


benzyl (*E*)-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-*L*-prolinate (1d). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 – 7.17 (m, 10H), 5.05 – 4.68 (m, 5H), 3.58 (ddt, *J* = 43.3, 9.0, 6.1 Hz, 2H), 2.17 (ttd, *J* = 10.7, 6.9, 3.1 Hz, 1H), 1.96 – 1.70 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.03, 139.85 (q, *J* = 31.0 Hz), 136.69, 135.63, 128.63, 128.49, 128.29 (d, *J* = 4.3 Hz), 128.02, 119.25 (q, *J* = 277.1 Hz), 77.16, 66.53, 62.84, 49.54 (q, *J* = 3.6 Hz), 30.49, 23.47. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.20. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{22}F_3N_2O_3^+$ $[M+H]^+$ 407.1577, found 407.1578.

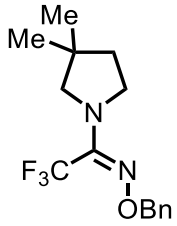


(*E*)-1-(1,1-diphenyl-5-azaspiro[2.4]heptan-5-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1e). Pale yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.60 – 6.94 (m, 15H), 4.94 (s, 2H), 3.80

(ddd, *J* = 10.1, 7.4, 5.9 Hz, 1H), 3.74 – 3.63 (m, 2H), 3.19 (d, *J* = 11.0 Hz, 1H), 1.85 (dt, *J* = 12.6, 7.1 Hz, 1H), 1.52 – 1.43 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.96, 142.68, 140.97 (q, *J* = 30.4 Hz), 137.06, 129.22, 129.07, 128.56, 128.50, 128.31, 128.15, 127.78, 126.63, 126.49, 119.31 (q, *J* = 277.7 Hz), 76.87, 55.73, 49.87 (d, *J* = 2.5 Hz), 39.35, 32.64, 31.43, 22.37. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.13. **HRMS** (ESI-TOF): *m/z* calculated for $C_{27}H_{26}F_3N_2O^+$ $[M+H]^+$ 451.1991, found 451.1990.

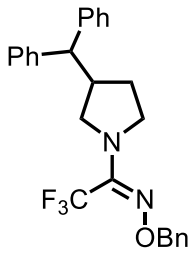


(*E*)-2,2,2-trifluoro-1-(hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)ethan-1-one *O*-benzyl oxime (1f). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 95:5 mixture of geometrical isomers) δ 7.44 – 7.30 (m, 5H), 5.03 (s, 2H), 3.72 (dd, *J* = 10.9, 7.3 Hz, 2H), 3.36 (dd, *J* = 10.9, 3.6 Hz, 2H), 2.62 – 2.51 (m, 2H), 1.88 – 1.64 (m, 3H), 1.63 – 1.50 (m, 1H), 1.49 – 1.34 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$, 95:5 mixture of geometrical isomers, only the major geometrical isomer is characterized) δ 140.81 (q, *J* = 30.4 Hz), 137.25, 128.34, 128.25, 127.88, 119.41 (q, *J* = 277.5 Hz), 76.90, 55.98 (q, *J* = 2.2 Hz), 42.35, 32.17, 25.63. **^{19}F NMR** (376 MHz, $CDCl_3$, 95:5 mixture of geometrical isomers) δ -63.91 (minor), -65.99. **HRMS** (ESI-TOF): *m/z* calculated for $C_{16}H_{20}F_3N_2O^+$ $[M+H]^+$ 313.1522, found 313.1527.

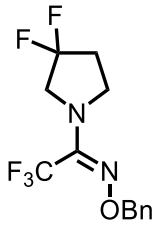


(*E*)-1-(3,3-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1g). Pale yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.43 – 7.28 (m, 5H), 5.00 (s, 2H), 3.66 (t, *J* = 7.1 Hz, 2H), 3.28 (s, 2H), 1.58 (t, *J* = 7.1 Hz, 2H), 1.05 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.20 (q, *J* = 30.5 Hz), 137.32, 128.33, 128.25, 127.85, 119.36 (q, *J* = 277.6 Hz), 76.82, 62.80 (d, *J* = 1.9

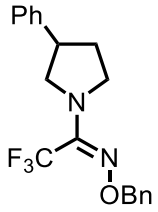
Hz), 49.14 (q, *J* = 2.1 Hz), 38.64, 37.46, 25.69. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.17. **HRMS** (ESI-TOF): *m/z* calculated for $C_{15}H_{20}F_3N_2O^+$ $[M+H]^+$ 301.1522, found 301.1521.



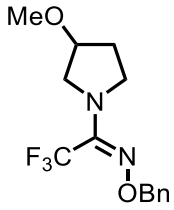
(*E*)-1-(3-benzhydrylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1h/1k). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 11H), 7.22 – 7.12 (m, 4H), 4.93 (d, *J* = 1.9 Hz, 2H), 3.69 – 3.47 (m, 4H), 3.31 (dd, *J* = 10.8, 8.7 Hz, 1H), 3.01 – 2.84 (m, 1H), 1.88 – 1.77 (m, 1H), 1.56 – 1.40 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.53, 143.45, 141.08 (q, *J* = 30.6 Hz), 136.95, 128.66, 128.64, 128.31, 128.23, 127.81, 127.70, 127.55, 126.59, 126.52, 119.26 (q, *J* = 277.7 Hz), 76.87, 55.76, 55.35, 49.64 (d, *J* = 2.5 Hz), 43.09, 30.76. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.22. **HRMS** (ESI-TOF): *m/z* calculated for $C_{26}H_{26}F_3N_2O^+$ $[M+H]^+$ 439.1992, found 439.1995.



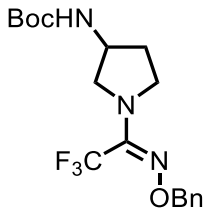
(*E*)-1-(3,3-difluoropyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1i). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 – 7.28 (m, 5H), 5.02 (s, 2H), 3.90 (t, *J* = 13.2 Hz, 2H), 3.77 (t, *J* = 7.3 Hz, 2H), 2.34 – 2.13 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.58 (q, *J* = 31.2 Hz), 136.60, 128.49, 128.23, 127.10 (t, *J* = 247.6), 118.97 (q, *J* = 277.2 Hz), 77.41, 56.46 (t, *J* = 32.6 Hz), 47.59 (q, *J* = 2.9 Hz), 33.48 (t, *J* = 23.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.20, -102.70. **HRMS** (ESI-TOF): *m/z* calculated for $C_{13}H_{14}F_5N_2O^+$ $[M+H]^+$ 309.1021, found 309.1024.



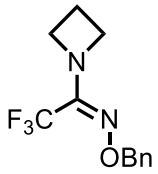
(*E*)-2,2,2-trifluoro-1-(3-phenylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1j). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 97:3 mixture of geometrical isomers) δ 7.49 – 7.11 (m, 10H), 5.05 (s, 2H), 3.99 (dd, *J* = 10.4, 7.5 Hz, 1H), 3.86 – 3.72 (m, 2H), 3.65 (t, *J* = 9.7 Hz, 1H), 3.38 – 3.26 (m, 1H), 2.32 – 2.20 (m, 1H), 2.05 – 1.88 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$, 97:3 mixture of geometrical isomers, only the major geometrical isomer is characterized) δ 140.96, 140.80 (q, *J* = 30.7 Hz), 137.20, 128.63, 128.35, 128.33, 127.92, 127.08, 126.89, 119.35 (q, *J* = 277.6 Hz), 76.94, 56.19 (t, *J* = 2.1 Hz), 49.96 (d, *J* = 2.2 Hz), 43.61, 32.65. **^{19}F NMR** (376 MHz, $CDCl_3$, 97:3 mixture of geometrical isomers) δ -63.28 (minor), -66.15. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{20}F_3N_2O^+$ $[M+H]^+$ 349.1522, found 349.1525.



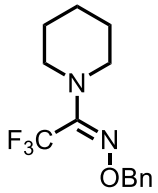
(*E*)-2,2,2-trifluoro-1-(3-methoxypyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1l). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 5.00 (s, 2H), 3.94 – 3.83 (m, 1H), 3.77 – 3.56 (m, 4H), 3.30 (s, 3H), 2.05 – 1.93 (m, 1H), 1.89 – 1.74 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.78 (q, *J* = 30.7 Hz), 137.14, 128.37, 128.35, 127.93, 119.29 (q, *J* = 277.4 Hz), 78.91, 76.96, 56.44, 54.88, 47.71 (q, *J* = 2.4 Hz), 30.29. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.26. **HRMS** (ESI-TOF): *m/z* calculated for $C_{14}H_{18}F_3N_2O_2^+$ $[M+H]^+$ 303.1315, found 303.1323.



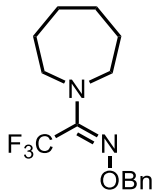
tert-butyl (*E*)-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-3-yl)carbamate (1m). White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 5H), 5.00 (s, 2H), 4.58 (*br* s, 1H), 4.17 (*br* s, 1H), 3.77 (dd, *J* = 11.1, 5.8 Hz, 1H), 3.72 – 3.54 (m, 2H), 3.42 (dd, *J* = 11.1, 3.9 Hz, 1H), 2.12 – 1.94 (m, 1H), 1.79 (s, 1H), 1.44 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.17, 140.59 (q, *J* = 30.4 Hz), 136.93, 128.45, 128.41, 128.05, 119.20 (q, *J* = 277.4 Hz), 79.84, 77.11, 55.60, 49.87, 47.84, 31.38, 28.35. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.25. **HRMS** (ESI-TOF): *m/z* calculated for $C_{18}H_{25}F_3N_3O_3^+$ $[M+H]^+$ 388.1843, found 388.1841.



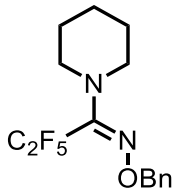
(*E*)-1-(azetidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1n). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H), 4.94 (s, 2H), 4.34 – 4.29 (m, 4H), 2.31 – 2.22 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.88 (q, *J* = 31.3 Hz), 137.28, 128.34, 128.18, 127.88, 118.84 (q, *J* = 276.5 Hz), 76.70, 54.88, 18.14. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -67.62. **HRMS** (ESI-TOF): *m/z* calculated for $C_{12}H_{14}F_3N_2O^+$ $[M+H]^+$ 259.1053, found 259.1049.



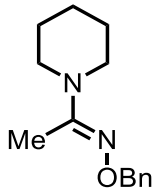
(*E*)-2,2,2-trifluoro-1-(piperidin-1-yl)ethan-1-one *O*-benzyl oxime (1o). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 85:15 mixture of geometrical isomers) δ 7.46 – 7.28 (m, 5H), 5.05 (s, 2H), 3.28 – 3.23 (m, 3.55H), 3.01 – 2.92 (m, 0.45H, minor), 1.63 – 1.52 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$, 85:15 mixture of geometrical isomers, only the major geometrical isomer is characterized) δ 143.18 (q, *J* = 30.7 Hz), 137.05, 128.37, 128.18, 127.97, 119.73 (q, *J* = 278.8 Hz), 77.08, 49.06, 26.07, 24.14. **^{19}F NMR** (376 MHz, $CDCl_3$, 85:15 mixture of geometrical isomers) δ -64.32, -64.51 (minor). **HRMS** (ESI-TOF): *m/z* calculated for $C_{14}H_{18}F_3N_2O^+$ $[M+H]^+$ 287.1366, found 287.1359.



(*E*)-1-(azepan-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1p). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 94:6 mixture of geometrical isomers) δ 7.41 – 7.28 (m, 5H), 5.02 (s, 2H), 3.42 – 3.29 (m, 4H), 1.69 – 1.62 (m, 4H), 1.61 – 1.54 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$, 94:6 mixture of geometrical isomers, only the major geometrical isomer is characterized) δ 142.35 (q, *J* = 30.0 Hz), 136.55, 127.96, 127.86, 127.51, 119.22 (q, *J* = 278.7 Hz), 76.64, 51.38, 28.99, 26.19. **^{19}F NMR** (376 MHz, $CDCl_3$, 94:6 mixture of geometrical isomers) δ -63.15 (minor), -64.24. **HRMS** (ESI-TOF): *m/z* calculated for $C_{15}H_{20}F_3N_2O^+$ $[M+H]^+$ 301.1522, found 301.1527.

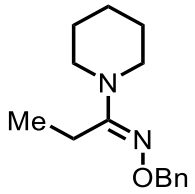


(*E*)-2,2,3,3,3-pentafluoro-1-(piperidin-1-yl)propan-1-one *O*-benzyl oxime (4a-1). Pale yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 5.03 (s, 2H), 3.27 – 3.19 (m, 4H), 1.58 – 1.51 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.97 (t, *J* = 25.6 Hz), 137.05, 128.42, 128.33, 128.02, 122.73 – 115.07 (m), 114.03 – 107.67 (m), 77.23, 49.24, 26.06, 24.14. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -80.84, -110.42. **HRMS** (ESI-TOF): *m/z* calculated for $C_{15}H_{18}F_5N_2O^+$ $[M+H]^+$ 337.1334, found 337.1329.

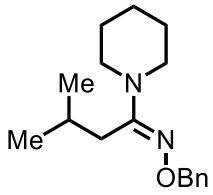


(*E*)-1-(piperidin-1-yl)ethan-1-one *O*-benzyl oxime (4a-2/4b). Yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 5H), 4.93 (s, 2H), 3.17 – 3.04 (m, 4H), 1.96 (s, 3H), 1.60 – 1.47 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.03, 138.67, 128.22, 128.13, 127.38, 75.28, 47.02, 25.41,

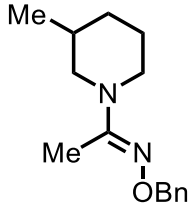
24.60, 11.91. **HRMS** (ESI-TOF): *m/z* calculated for $C_{14}H_{21}N_2O^+$ $[M+H]^+$ 233.1648, found 233.1652.



(*E*)-1-(piperidin-1-yl)propan-1-one *O*-benzyl oxime (4a-3). Yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 – 7.22 (m, 5H), 4.92 (s, 2H), 3.13 – 3.07 (m, 4H), 2.45 (q, *J* = 7.6 Hz, 2H), 1.58 – 1.53 (m, 6H), 1.05 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.43, 138.82, 128.17, 128.12, 127.33, 75.26, 46.87, 25.55, 24.65, 19.08, 11.05. **HRMS** (ESI-TOF): *m/z* calculated for $C_{15}H_{23}N_2O^+$ $[M+H]^+$ 247.1805, found 247.1807.

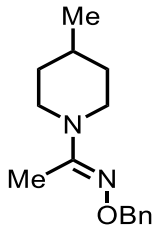


(*E*)-3-methyl-1-(piperidin-1-yl)butan-1-one *O*-benzyl oxime (4a-4). Pale yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 – 7.22 (m, 5H), 4.90 (s, 2H), 3.14 – 3.09 (m, 4H), 2.37 (d, *J* = 7.4 Hz, 2H), 1.93 – 1.83 (m, 1H), 1.59 – 1.50 (m, 6H), 0.91 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.42, 138.79, 128.20, 128.08, 127.27, 75.14, 47.02, 32.81, 26.71, 25.65, 24.71, 22.55. **HRMS** (ESI-TOF): *m/z* calculated for $C_{17}H_{27}N_2O^+$ $[M+H]^+$ 275.2118, found 275.2115.

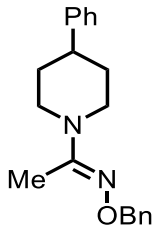


(*E*)-1-(3-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (4c). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 (ddt, *J* = 7.5, 1.3, 0.6 Hz, 2H), 7.33 (ddd, *J* = 7.6, 6.7, 1.1 Hz, 2H), 7.29 – 7.25 (m, 1H), 4.93 (s, 2H), 3.67 – 3.55 (m, 2H), 2.52 (ddd, *J* = 12.7, 12.0, 3.0 Hz, 1H), 2.20 (dd, *J* = 12.6, 10.6 Hz, 1H), 1.96 (s, 3H), 1.76 (dtt, *J* = 12.7, 3.7, 2.1 Hz, 1H), 1.67 – 1.55 (m, 2H), 1.49

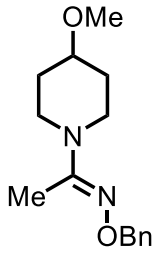
(dtt, *J* = 13.3, 12.1, 4.1 Hz, 1H), 1.02 (tdd, *J* = 12.7, 11.1, 4.0 Hz, 1H), 0.88 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.94, 138.65, 128.23, 128.13, 127.38, 75.29, 53.79, 46.43, 33.17, 30.58, 24.87, 19.35, 11.97. **HRMS** (ESI-TOF): *m/z* calculated for $C_{15}H_{23}N_2O^+$ $[M+H]^+$ 247.1805, found 247.1808.



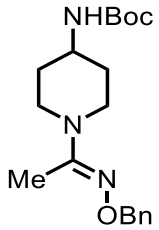
(*E*)-1-(4-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (4d). White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 (ddt, *J* = 7.5, 1.3, 0.6 Hz, 2H), 7.33 (ddd, *J* = 7.6, 6.7, 1.1 Hz, 2H), 7.29 – 7.26 (m, 1H), 4.93 (s, 2H), 3.68 (dq, *J* = 12.8, 2.7, 2.2 Hz, 2H), 2.64 – 2.47 (m, 2H), 1.96 (s, 3H), 1.67 – 1.59 (m, 2H), 1.54 – 1.40 (m, 1H), 1.22 – 1.09 (m, 2H), 0.92 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.95, 138.67, 128.23, 128.13, 127.38, 75.28, 46.40, 33.66, 31.00, 21.91, 11.95. **HRMS** (ESI-TOF): *m/z* calculated for $C_{15}H_{23}N_2O^+$ $[M+H]^+$ 247.1805, found 247.1810.



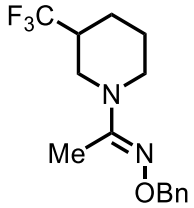
(*E*)-1-(4-phenylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (4e). White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.37 (m, 2H), 7.36 – 7.26 (m, 5H), 7.23 – 7.17 (m, 3H), 4.96 (s, 2H), 3.86 (dp, *J* = 12.8, 1.9 Hz, 2H), 2.72 – 2.66 (m, 2H), 2.65 – 2.58 (m, 1H), 2.01 (s, 3H), 1.86 – 1.79 (m, 2H), 1.70 (dtd, *J* = 13.2, 12.2, 3.9 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.68, 145.98, 138.66, 128.45, 128.24, 128.17, 127.42, 126.78, 126.26, 75.34, 46.85, 42.75, 32.75, 11.97. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{25}N_2O^+$ $[M+H]^+$ 309.1961, found 309.1963.



(*E*)-1-(4-methoxypiperidin-1-yl)ethan-1-one *O*-benzyl oxime (4f). Yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 5H), 4.93 (s, 2H), 3.52 (dddd, *J* = 12.9, 5.4, 3.9, 1.2 Hz, 2H), 3.35 (s, 3H), 3.31 (tt, *J* = 8.5, 3.9 Hz, 1H), 2.81 (ddd, *J* = 13.1, 9.7, 3.2 Hz, 2H), 1.96 (s, 3H), 1.93 – 1.81 (m, 2H), 1.58 – 1.43 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.37, 138.60, 128.22, 128.16, 127.42, 76.32, 75.33, 55.53, 43.67, 30.28, 11.85. **HRMS** (ESI-TOF): *m/z* calculated for $C_{15}H_{23}N_2O_2^+$ $[M+H]^+$ 263.1754, found 263.1760.

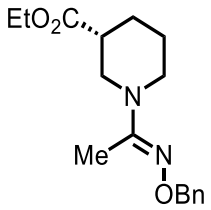


tert-butyl (*E*)-(1-(1-((benzyloxy)imino)ethyl)piperidin-4-yl)carbamate (4g). White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 5H), 4.93 (s, 2H), 4.42 (br s, 1H), 3.67 – 3.60 (m, 2H), 3.58 (br s, 1H), 2.70 (ddd, *J* = 13.7, 11.6, 2.7 Hz, 2H), 1.95 (s, 3H), 1.94 – 1.87 (m, 2H), 1.44 (s, 9H), 1.34 (dtd, *J* = 12.7, 11.2, 4.0 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.23, 155.09, 138.57, 128.23, 128.16, 127.45, 79.37, 75.35, 47.89, 44.98, 31.91, 28.41, 11.88. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{30}N_3O_3^+$ $[M+H]^+$ 348.2282, found 348.2283.

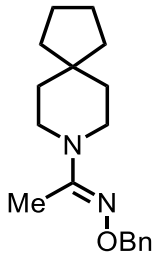


(*E*)-1-(3-(trifluoromethyl)piperidin-1-yl)ethan-1-one *O*-benzyl oxime (4h). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 5H), 4.94 (s, 2H), 4.00 – 3.92 (m, 1H), 3.70 – 3.60 (m,

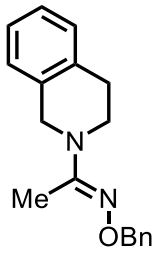
1H), 2.63 – 2.52 (m, 2H), 2.38 – 2.24 (m, 1H), 2.04 – 1.97 (m, 1H), 1.96 (s, 3H), 1.77 – 1.66 (m, 1H), 1.52 – 1.40 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.61, 138.47, 128.40, 128.17, 127.53, 126.8 (q), 75.50, 46.56, 45.15 (q, *J* = 3.4 Hz), 39.35 (q, *J* = 26.1 Hz), 23.61 (q, *J* = 2.5 Hz), 23.45, 11.82. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -72.81. **HRMS** (ESI-TOF): *m/z* calculated for $C_{15}H_{20}F_3N_2O^+$ $[M+H]^+$ 301.1522, found 301.1523.



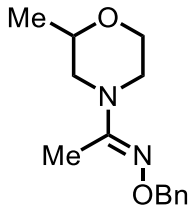
ethyl (*R*,*E*)-1-(1-((benzyloxy)imino)ethyl)piperidine-3-carboxylate (4i). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 5H), 4.93 (s, 2H), 4.14 (qd, *J* = 7.1, 0.6 Hz, 2H), 3.78 – 3.69 (m, 1H), 3.53 – 3.45 (m, 1H), 2.94 – 2.86 (m, 1H), 2.79 – 2.71 (m, 1H), 2.56 – 2.48 (m, 1H), 2.01 – 1.95 (m, 4H), 1.72 – 1.61 (m, 2H), 1.55 – 1.46 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.73, 158.22, 138.57, 128.30, 128.15, 127.44, 75.38, 60.45, 48.21, 46.36, 40.86, 27.23, 23.73, 14.22, 11.89. **HRMS** (ESI-TOF): *m/z* calculated for $C_{17}H_{25}N_2O_3^+$ $[M+H]^+$ 305.1860, found 305.1861.



(*E*)-1-(8-azaspiro[4.5]decan-8-yl)ethan-1-one *O*-benzyl oxime (4j). White solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 5H), 4.93 (s, 2H), 3.15 – 3.05 (m, 4H), 1.97 (s, 3H), 1.65 – 1.57 (m, 4H), 1.48 – 1.37 (m, 8H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.09, 138.66, 128.24, 128.14, 127.40, 75.29, 44.00, 41.08, 37.69, 36.92, 24.30, 11.95. **HRMS** (ESI-TOF): *m/z* calculated for $C_{18}H_{27}N_2O^+$ $[M+H]^+$ 287.2118, found 287.2121.



(*E*)-1-(3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one *O*-benzyl oxime (4k). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 5H), 7.19 – 7.08 (m, 4H), 4.97 (s, 2H), 4.37 (d, *J* = 1.1 Hz, 2H), 3.44 (t, *J* = 5.9 Hz, 2H), 2.87 (t, *J* = 5.9 Hz, 2H), 2.07 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.17, 138.54, 134.42, 133.99, 128.64, 128.25, 128.18, 127.46, 126.50, 126.20, 126.00, 75.43, 48.05, 43.54, 28.91, 11.91. **HRMS** (ESI-TOF): *m/z* calculated for $C_{18}H_{21}N_2O^+$ $[M+H]^+$ 281.1648, found 281.1645.

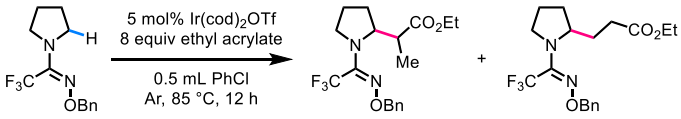


(*E*)-1-(2-methylmorpholino)ethan-1-one *O*-benzyl oxime (4l). Colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 5H), 4.94 (s, 2H), 3.86 (ddd, *J* = 11.5, 3.5, 1.5 Hz, 1H), 3.65 – 3.54 (m, 2H), 3.48 (dt, *J* = 12.6, 2.2 Hz, 1H), 3.42 (ddt, *J* = 12.8, 3.1, 1.7 Hz, 1H), 2.74 (ddd, *J* = 12.8, 11.9, 3.4 Hz, 1H), 2.40 (dd, *J* = 12.6, 10.3 Hz, 1H), 1.96 (s, 3H), 1.17 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.20, 138.43, 128.22, 128.19, 127.50, 75.43, 71.43, 66.31, 52.42, 45.83, 18.91, 11.49. **HRMS** (ESI-TOF): *m/z* calculated for $C_{14}H_{21}N_2O_2^+$ $[M+H]^+$ 249.1598, found 249.1595.

B. Optimization of Reaction Conditions

Optimization for pyrrolidine substrate

- Solvent screening.[a]

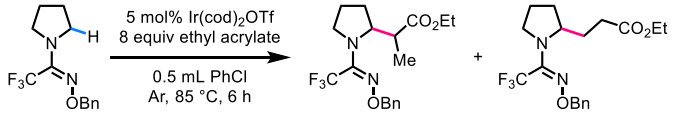


1a-3 **2a-3-B** **2a-3-L**

Change from reaction conditions	Yield (%)	B (%)	L (%)
No change	86	63	23
Toluene	27	22	5
1,4-Dioxane	54	40	14
Dichloroethane	76	39	37
1,2-Dimethoxyethane	73	51	22
Tetrahydrofuran	39	27	12
1,2-Dichlorobenzene	43	27	16
m-Xylene	21	16	5
n-Heptane	51	31	20

[a]Determined by ^{1}H NMR analysis of the crude products using mesitylene as the internal standard.

- Catalyst screening: Part A.[a]

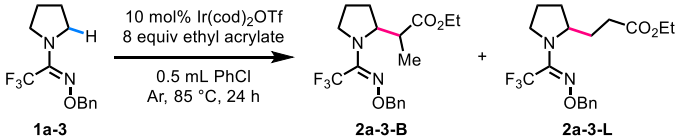


1a-3 **2a-3-B** **2a-3-L**

Change from reaction conditions	Yield (%)	B (%)	L (%)
No change	79	57	22
$Ir(cod_2)NTf_2$	80	56	24
$Ir(cod)_2SbF_6$	72	44	28
$Ir(cod)_2BF_4$	85	56	29
$Ir(cod)_2PF_6$	32	25	7
$Ir(cod)_2BARF$	57	25	32
Ir(cod)acac	0	0	0
$Ir(cod)(quinoline)BF_4$	0	0	0
$[Ir(cod)Cl]_2$	0	0	0

[a]Determined by ^{1}H NMR analysis of the crude products using mesitylene as the internal standard.

- *Catalyst screening: Part B.*[a]

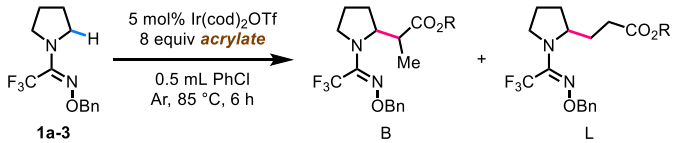


1a-3 **2a-3-B** **2a-3-L**

Change from reaction conditions	Yield (%)	B (%)	L (%)
5% $[Ir(cod)Cl]_2$ + 10% AgOTf	84	64	20
5% $[Ir(cod)Cl]_2$ + 10% $AgNTf_2$*	67	52	15
5% $[Ir(cod)Cl]_2$ + 10% $AgBF_4$	76	54	22
5% $[Ir(cod)Cl]_2$ + 10% $AgPF_6$*	37	25	12
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$*	72	50	22
5% $[Ir(cod)Cl]_2$ + 20% NaBARF	65	30	35
5% $[Rh(cod)Cl]_2$ + 10% AgOTf/ $AgNTf_2$/$AgBF_4$/$AgPF_6$/$AgSbF_6$/NaBARF	0	0	0
$[Ir(cod)Cl]_2$ + 10% $NaOTf/NaBF_4$	0	0	0
$[Ir(cod)Cl]_2$ + 10% AgOAc/AgTFA/Ag_2CO_3/Ag_3PO_4	0	0	0
10% $[Ir(dbcot)Cl]_2$ + 10% AgOTf	35	17	18
10% $[Ir(dbcot)Cl]_2$ + 10% $AgNTf_2$	63	32	31
10% $[Ir(dbcot)Cl]_2$ + 20% NaBARF	31	15	16
5% $[Ir(coe)Cl]_2$ + 10% AgOTf	0	0	0
5% $[Ir(coe)Cl]_2$ + 10% $AgNTf_2$	0	0	0
5% $[Ir(coe)Cl]_2$ + 20% NaBARF	0	0	0

[a]Determined by ^1H NMR analysis of the crude products using mesitylene as the internal standard. *6 h instead of 24 h.

- *Screening of the ester substituent on acrylate coupling partner.*[a]

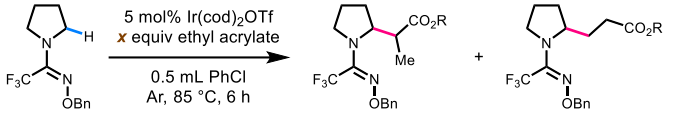


1a-3 B L

acrylate	Yield (%)	B (%)	L (%)
Ethyl acrylate	79	57	22
Methyl acrylate	71	54	17
Benzyl acrylate	61	43	18
n-Butyl acrylate	47	32	15

[a]Determined by ^1H NMR analysis of the crude products using mesitylene as the internal standard.

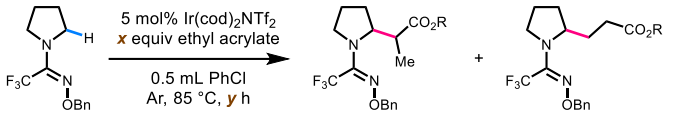
- Screening of the equivalents of ethyl acrylate coupling partner.[a]



1a-3 B L

x	Yield (%)	B (%)	L (%)
2	33	24	9
4	62	44	18
6	69	49	20
8	79	57	22
10	77	55	22

[a]Determined by ^{1}H NMR analysis of the crude products using mesitylene as the internal standard.

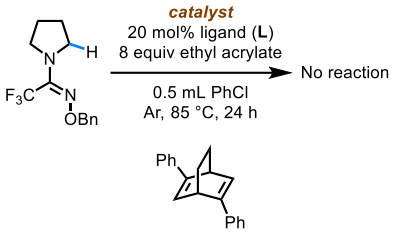


1a-3 B L

x	*y*	Yield (%)	B (%)	L (%)
2	6 h	54	34	20
4	6 h	64	40	24
6	6h	77	51	26
8	6h	80	56	24
10	6h	80	54	26
2	24 h	70	45	25
4	24 h	80	53	27

[a]Determined by ^{1}H NMR analysis of the crude products using mesitylene as the internal standard.

- Reaction with chiral diene ligand.

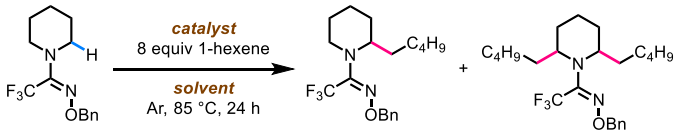


L (1*S*, 4*S*)

catalyst
5 mol% $[Ir(coe)_2Cl]_2$ + 10 mol% AgOTf
5 mol% $[Ir(coe)_2Cl]_2$ + 20 mol% NaBARF
5 mol% $[Ir(ethylene)_2Cl]_2$ + 10 mol% AgOTf
5 mol% $[Ir(ethylene)_2Cl]_2$ + 20 mol% NaBARF

Optimization for piperidine substrate

- Catalyst, solvent, and concentration screening.[a]

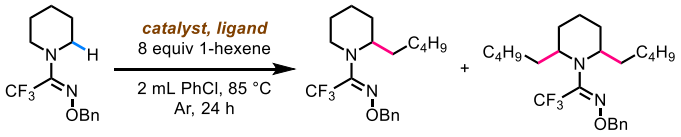


4b **5b-mono** **5b-di**

catalyst	*solvent*	5b-mono (%)	5b-di (%)
5% $[Ir(cod)Cl]_2$ + 10% AgOTf	0.5 mL PhCl	38	5
5% $[Ir(cod)Cl]_2$ + 10% $AgNTf_2$	0.5 mL PhCl	36	19
5% $[Ir(cod)Cl]_2$ + 10% $AgBF_4$	0.5 mL PhCl	38	8
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	0.5 mL PhCl	40	20
5% $[Ir(cod)Cl]_2$ + 20% NaBARF	0.5 mL PhCl	30	20
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	0.5 mL DCE	27	11
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	0.5 mL 1,2-DME	41	7
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	0.5 mL THF	42	8
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	0.5 mL 1,4-dioxane	41	6
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	0.1 mL PhCl	34	18
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	0.5 mL PhCl	40	20
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	1.0 mL PhCl	45	15
5% $[Ir(cod)Cl]_2$ + 10% $AgSbF_6$	2.0 mL PhCl	50	15
10% $Ir(cod)_2NTf_2$	0.1 mL PhCl	25	25
10% $Ir(cod)_2NTf_2$	0.5 mL PhCl	33	20
10% $Ir(cod)_2NTf_2$	1.0 mL PhCl	37	19
10% $Ir(cod)_2NTf_2$	2.0 mL PhCl	44	12

[a]Determined by ^1H NMR analysis of the crude products using mesitylene as the internal standard.

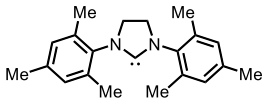
- Screening of ligands and additives.[a]



4b **5b-mono** **5b-di**

catalyst	*ligand*	5b-mono (%)	5b-di (%)
5 mol% $[Ir(dbcot)Cl]_2$	-	26	13
10 mol% Ir(**NHC-1**)(cod)Cl	-	N.R.	N.R.
10 mol% Ir(**NHC-2**)(cod)Cl	-	N.R.	N.R.
10 mol% $Ir(cod)(MeCN)_2Cl$	-	46	14
5 mol% $[Ir(cod)Cl]_2$ + 10 mol% $AgSbF_6$	**L1**	9	10
5 mol% $[Ir(cod)Cl]_2$ + 10 mol% $AgSbF_6$	**L2**	21	17
5 mol% $[Ir(cod)Cl]_2$ + 10 mol% $AgSbF_6$	$P(Cy)_3$	25	18
5 mol% $[Ir(cod)Cl]_2$ + 10 mol% $AgSbF_6$	$P(o\text{-}tolyl)_3$	24	36
5 mol% $[Ir(cod)Cl]_2$ + 10 mol% $AgSbF_6$	(*R*)-BINAP	N.R.	N.R.
5 mol% $[Ir(cod)Cl]_2$ + 10 mol% $AgSbF_6$	(-)-DIOP	N.R.	N.R.
5 mol% $[Ir(cod)Cl]_2$ + 10 mol% $AgSbF_6$	dfppe	N.R.	N.R.
5 mol% $[Ir(cod)Cl]_2$ + 10 mol% $AgSbF_6$	dppf	N.R.	N.R.

NHC-1 =



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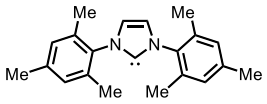

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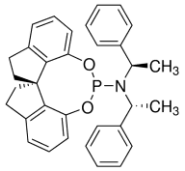

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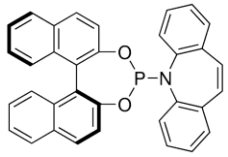
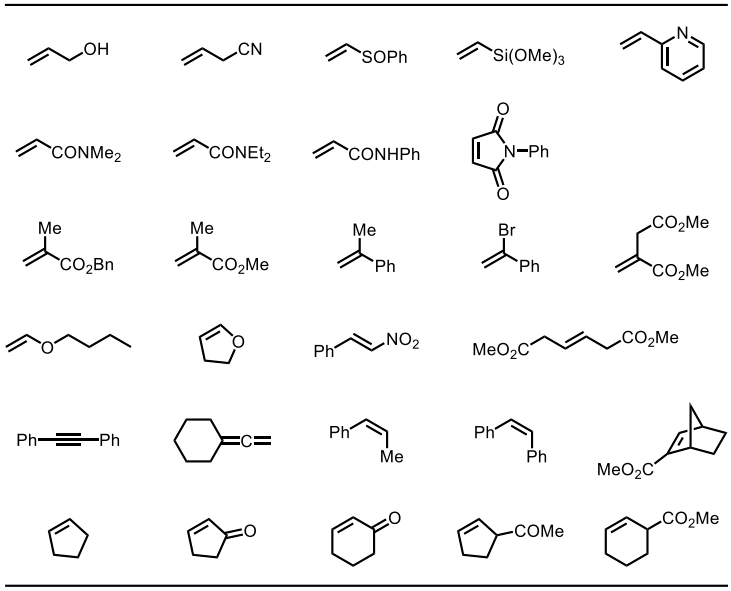


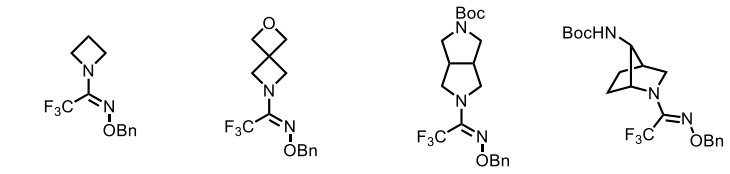
[a]Determined by ^1H NMR analysis of the crude products using mesitylene as the internal standard.

C. Current Limitations

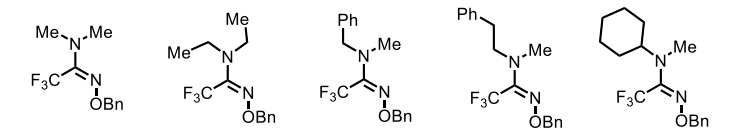
- Olefin coupling partners (<10% yield).



- Saturated azacycle substrates (<10% yield).



- Acyclic amine substrates.



Decomposition of starting material	36%[a] (5% B, 31% L)	No reaction	No reaction	No reaction

[a] 10 mol% $Ir(cod)_2NTf_2$, 8 equiv ethyl acrylate, 0.1 mL PhCl, 85 °C, 24 h

D. Procedure for Ir-catalyzed α-C(sp^3)–H Alkylation

- *General procedure C*

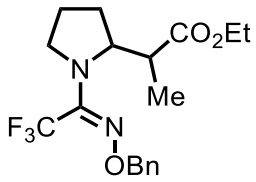
A 2-dram vial was charged with the substrate (0.1 mmol, 1.0 equiv) and taken inside an argon glovebox. $Ir(cod)_2NTf_2$ (6.9 mg, 0.01 mmol, 0.1 equiv, unless otherwise noted) was added followed by a magnetic stir bar. The vial was sealed with a PTFE septum and taken out of the glovebox. Degassed PhCl (0.1 mL, unless otherwise noted) and olefin coupling partner (0.8 mmol, 8.0 equiv, unless otherwise noted) were added to the vial. The solution was stirred at 85 °C for 24 hours (unless otherwise noted). Upon completion, the reaction mixture was cooled to rt and diluted with 2 mL EtOAc. The mixture was filtered through a pad of celite. The celite was washed thoroughly with EtOAc and the combined organics were concentrated *in vacuo*. The crude reside was purified by preparative TLC with the solvent noted to provide the alkylated product(s).

- *Notes*

Wherever applicable, $HBF_4.Et_2O$ (1.4 µL, 0.01 mmol, 0.1 equiv) was added along with solvent outside the glovebox.

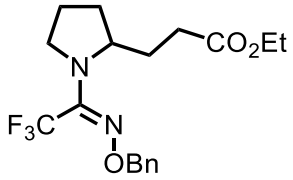
Wherever applicable, $Ir(cod)_2OTf$, or $[Ir(cod)Cl]_2$ and $AgSbF_6$, were added inside the glovebox.

- *Full characterization of all products*

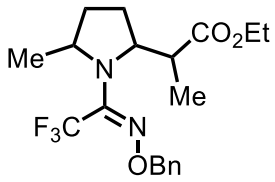


ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (2a-3-B). Prepared via Procedure C (described above) using 27.2 mg (0.1 mmol, 1.0 equiv) of **1a-3**, 2.8 mg of $[Ir(cod)_2]OTf$ (0.005 mmol, 0.05 equiv), 44 µL of ethyl acrylate (0.4 mmol, 4.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 6 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **2a-3-B** (21.2 mg, 57%) and **2a-3-L** (9.7 mg, 26%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 67:33 mixture of diastereomers) δ 7.43 – 7.29 (m, 5H), 5.07 – 4.98

(m, 2H), 4.78 (td, *J* = 7.3, 4.6 Hz, 0.67H), 4.41 (q, *J* = 6.3 Hz, 0.33H), 4.17 – 3.97 (m, 2H), 3.44 (q, *J* = 8.7 Hz, 1H), 3.37 (td, *J* = 9.8, 8.6, 3.3 Hz, 0.67H), 3.31 (td, *J* = 9.3, 8.6, 4.2 Hz, 0.33H), 2.78 (qd, *J* = 7.1, 4.6 Hz, 0.67H), 2.74 – 2.67 (m, 0.33H), 1.95 – 1.66 (m, 4H), 1.20 (dt, *J* = 25.7, 7.1 Hz, 3H), 0.96 (dd, *J* = 34.2, 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 67:33 mixture of diastereomers, only the major diastereomer is characterized) δ 174.16, 139.98 (q, *J* = 31.0 Hz), 136.70, 128.69, 128.31, 128.10, 119.57 (q, *J* = 278.1 Hz), 77.42, 60.60, 60.34, 50.31 (q, *J* = 2.7 Hz), 40.81, 26.08, 24.50, 14.15, 9.52. **^{19}F NMR** (376 MHz, $CDCl_3$, 67:33 mixture of diastereomers) δ -65.59 (minor), -65.71. **HRMS** (ESI-TOF): *m/z* calculated for $C_{18}H_{24}F_3N_2O_3^+$ $[M+H]^+$ 373.1734, found 373.1734.

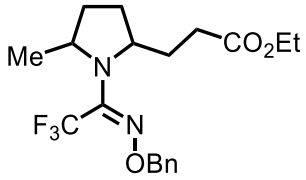


ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (2a-3-L). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 5H), 5.06 – 4.98 (m, 2H), 4.21 (tq, *J* = 9.2, 5.9, 4.8 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.51 (q, *J* = 7.9 Hz, 1H), 3.33 (ddd, *J* = 9.9, 7.4, 4.7 Hz, 1H), 2.15 – 2.00 (m, 2H), 2.00 – 1.93 (m, 1H), 1.92 – 1.82 (m, 2H), 1.81 – 1.71 (m, 1H), 1.53 – 1.42 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.07, 140.20 (q, *J* = 30.8 Hz), 136.78, 128.79, 128.42, 128.17, 119.53 (q, *J* = 278.0 Hz), 77.35, 60.42, 59.61, 49.25 (q, *J* = 2.8 Hz), 30.79, 30.44, 29.63, 23.96, 14.23. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.97. **HRMS** (ESI-TOF): *m/z* calculated for $C_{18}H_{24}F_3N_2O_3^+$ $[M+H]^+$ 373.1734, found 373.1730.

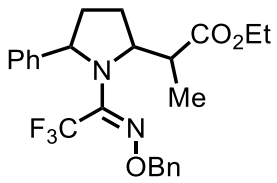


ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-methylpyrrolidin-2-yl)propanoate (2b-B). Prepared via Procedure C (described above) using 28.6 mg (0.1 mmol, 1.0 equiv) of **1b**, 5.6 mg of $[Ir(cod)_2]OTf$ (0.01 mmol, 0.1 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by

preparative TLC (6% EtOAc/hexanes) to afford **2b-B** (16.2 mg, 42%) and **2b-L** (14.5 mg, 38%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, mixture of diastereomers) δ 7.44 – 7.29 (m, 5H), 5.17 – 4.99 (m, 2H), 4.97 – 3.62 (m, 4H), 2.79 – 2.27 (m, 1H), 2.16 – 1.66 (m, 3H), 1.52 – 1.37 (m, 1H), 1.32 – 0.80 (m, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ 174.68, 142.22 (q, *J* = 31.2 Hz), 136.82, 128.50, 128.40, 128.34, 119.77 (q, *J* = 279.3 Hz), 77.40, 62.24, 60.36, 56.66, 42.28, 33.22, 30.43, 25.23, 14.15, 10.88. **^{19}F NMR** (376 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ -65.20. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{26}F_3N_2O_3^+$ $[M+H]^+$ 387.1890, found 387.1890.

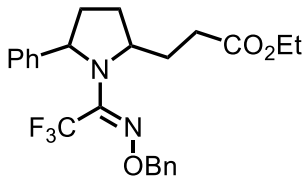


ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-methylpyrrolidin-2-yl)propanoate (2b-L). ^{1}H NMR (500 MHz, CD_3CN, 333 K, 56:44 mixture of diastereomers) δ 7.53 – 7.40 (m, 5H), 5.15 (d, *J* = 13.7 Hz, 2H), 4.29 – 4.10 (m, 3H), 4.08 – 3.96 (m, 1H), 2.35 – 2.20 (m, 2H), 2.20 – 2.00 (m, 2H), 1.88 – 1.52 (m, 4H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.27 (d, *J* = 6.3 Hz, 1.68H), 1.06 (d, *J* = 6.2 Hz, 1.32H). **^{13}C NMR** (151 MHz, $CDCl_3$, 56:44 mixture of diastereomers, only the major diastereomer is characterized) δ 173.11, 141.46 (q, *J* = 30.2 Hz), 136.71, 128.78, 128.56, 128.39, 119.54 (q, *J* = 278.3 Hz), 77.39, 60.42, 60.36, 57.64, 32.45, 31.46, 29.40, 28.16, 22.60, 14.21. **^{19}F NMR** (376 MHz, $CDCl_3$, 56:44 mixture of diastereomers) δ -64.56 (major), -65.45. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{26}F_3N_2O_3^+$ $[M+H]^+$ 387.1890, found 387.1892.

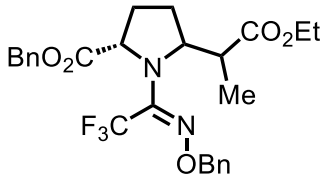


ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-phenylpyrrolidin-2-yl)propanoate (2c-B). Prepared via Procedure C (described above) using 34.8 mg (0.1 mmol, 1.0

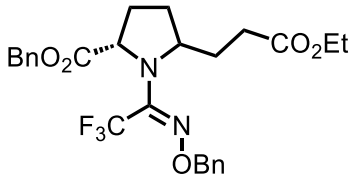
equiv) of **1c**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), 1.4 µL of $HBF_4.Et_2O$ (0.01 mmol, 0.1 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **2c-B** (21.4 mg, 48%) and **2c-L** (15.6 mg, 35%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, mixture of diastereomers) δ 7.54 – 6.98 (m, 10H), 5.30 – 4.21 (m, 4H), 4.21 – 3.99 (m, 2H), 2.95 – 2.62 (m, 1H), 2.37 – 1.59 (m, 4H), 1.40 – 0.92 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ 174.53, 143.75, 140.65 (q, *J* = 32.3 Hz), 136.75, 128.83, 128.51, 128.48, 128.38, 128.14, 125.26, 119.46 (q), 77.82, 64.54, 64.13, 60.46, 40.33, 34.11, 29.72, 24.39, 14.19. **^{19}F NMR** (376 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ -64.53. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 449.2047, found 449.2048.



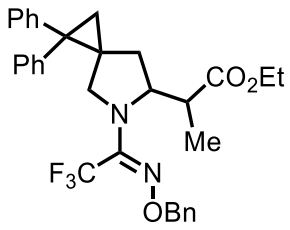
ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-phenylpyrrolidin-2-yl)propanoate (2c-L). ^{1}H NMR (600 MHz, $CDCl_3$, mixture of diastereomers) δ 7.54 – 6.96 (m, 10H), 5.43 – 4.65 (m, 3H), 4.64 – 3.77 (m, 3H), 2.41 – 1.59 (m, 8H), 1.26 (dt, *J* = 10.8, 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ 173.05, 144.25, 140.13 (q, *J* = 31.4 Hz), 136.47, 128.63, 128.44, 128.17, 128.07, 126.97, 125.62, 119.38 (q, *J* = 278.6 Hz), 77.51, 65.48, 62.79, 60.48, 34.50, 31.94, 30.84, 29.71, 14.23. **^{19}F NMR** (376 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ -64.37. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 449.2047, found 449.2045.



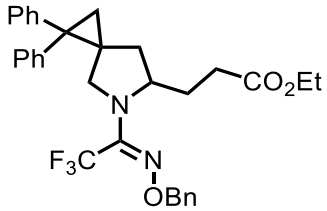
benzyl (2*S*)-1-(*E*-1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-(1-ethoxy-1-oxopropan-2-yl)pyrrolidine-2-carboxylate (2d-B). Prepared via Procedure C (described above) using 40.6 mg (0.1 mmol, 1.0 equiv) of **1d**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (10% EtOAc/hexanes) to afford **2d-B** (4.1 mg, 8%) and **2d-L** (30.2 mg, 60%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, mixture of diastereomers) δ 7.38 – 7.27 (m, 10H), 5.21 – 3.91 (m, 8H), 2.88 – 2.49 (m, 1H), 2.25 – 1.73 (m, 4H), 1.20 – 1.14 (m, 3H), 1.02 – 0.81 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ 174.40, 173.85, 142.01 (q, *J* = 32.0 Hz), 136.56, 135.44, 128.73, 128.56, 128.38, 128.31, 128.24, 128.09, 119.48 (q, *J* = 278.5 Hz), 77.57, 66.93, 65.03, 61.06, 60.47, 42.25, 29.35, 25.05, 14.11, 11.54. **^{19}F NMR** (376 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ -64.93. **HRMS** (ESI-TOF): *m/z* calculated for $C_{26}H_{30}F_3N_2O_5^+$ $[M+H]^+$ 507.2101, found 507.2107.



benzyl (2*S*)-1-(*E*-1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-(3-ethoxy-3-oxopropyl)pyrrolidine-2-carboxylate (2d-L). **^{1}H NMR** (600 MHz, $CDCl_3$, 77:23 mixture of diastereomers) δ 7.40 – 7.19 (m, 10H), 5.15 – 4.92 (m, 1H), 4.93 – 4.83 (m, 2H), 4.80 – 4.65 (m, 1H), 4.20 (dd, *J* = 8.7, 2.9 Hz, 1H), 4.10 (qd, *J* = 7.1, 2.5 Hz, 2H), 3.99 (dq, *J* = 11.5, 6.4 Hz, 1H), 2.29 – 2.17 (m, 2H), 2.17 – 2.04 (m, 2H), 2.04 – 1.91 (m, 2H), 1.91 – 1.75 (m, 1H), 1.68 – 1.48 (m, 1H), 1.24 (td, *J* = 7.2, 2.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 77:23 mixture of diastereomers, only the major diastereomer is characterized) δ 173.36, 172.93, 141.14 (q, *J* = 31.2 Hz), 136.51, 135.72, 128.91, 128.64, 128.50, 128.33, 128.26, 128.15, 119.19 (q, *J* = 278.0 Hz), 77.32, 66.86, 66.40, 60.52, 60.40, 31.25, 30.07, 29.42, 28.46, 14.20. **^{19}F NMR** (376 MHz, $CDCl_3$, 77:23 mixture of diastereomers) δ -64.74 (major), -65.29. **HRMS** (ESI-TOF): *m/z* calculated for $C_{26}H_{30}F_3N_2O_5^+$ $[M+H]^+$ 507.2101, found 507.2103.

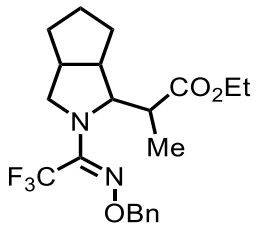


ethyl (*E*)-2-(5-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-1,1-diphenyl-5-azaspiro[2.4]heptan-6-yl)propanoate (2e-B). Prepared via Procedure C (described above) using 45.0 mg (0.1 mmol, 1.0 equiv) of **1e**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **2e-B** (21.0 mg, 38%) and **2e-L** (33.2 mg, 60%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, mixture of diastereomers) δ 7.54 – 7.02 (m, 15H), 5.38 – 4.23 (m, 3H), 4.20 – 3.86 (m, 2H), 3.85 – 2.28 (m, 3H), 2.12 – 1.24 (m, 4H), 1.24 – 0.81 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ 174.45, 143.08, 142.51, 140.50 (q, *J* = 65.8 Hz), 136.73, 129.29, 129.05, 128.99, 128.64, 128.53, 128.43, 128.16, 126.72, 126.48, 119.48 (q, *J* = 278.3 Hz), 77.47, 63.02, 60.47, 54.48, 40.93, 37.34, 32.65, 31.32, 19.32, 13.97, 9.52. **^{19}F NMR** (376 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ -65.50. **HRMS** (ESI-TOF): *m/z* calculated for $C_{32}H_{34}F_3N_2O_3^+$ $[M+H]^+$ 551.2516, found 551.2516.

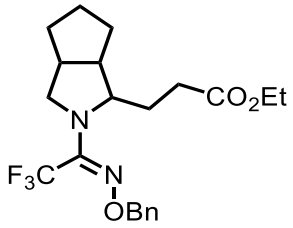


ethyl (*E*)-3-(5-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-1,1-diphenyl-5-azaspiro[2.4]heptan-6-yl)propanoate (2e-L). **^{1}H NMR** (600 MHz, $CDCl_3$, 64:36 mixture of diastereomers) δ 7.41 – 7.10 (m, 15H), 5.12 – 5.03 (m, 1.28H), 4.99 (q, *J* = 11.3 Hz, 0.72H), 4.54 – 4.46 (m, 0.64H), 4.30 – 4.23 (m, 0.36H), 4.11 – 4.02 (m, 2H), 3.86 (d, *J* = 10.3 Hz, 0.36H), 3.37 (d, *J* = 10.5 Hz, 0.64H), 3.16 (d, *J* = 10.5 Hz, 0.64H), 2.63 (d, *J* = 10.3 Hz, 0.36H), 2.08 – 2.02 (m, 1.28H), 2.00 – 1.89 (m, 1.72H), 1.86 – 1.77 (m, 1H), 1.70 – 1.59 (m, 1H), 1.53 (d, *J* = 5.3 Hz, 0.64H), 1.49 – 1.42 (m, 1.36H), 1.42 – 1.33 (m, 1H), 1.21 (dt, *J* = 10.2, 7.1 Hz, 3H). **^{13}C NMR**

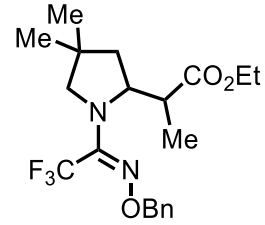
(151 MHz, $CDCl_3$, 64:36 mixture of diastereomers, only the major diastereomer is characterized) δ 172.95, 142.65, 142.57, 140.35 (q, *J* = 31.0 Hz), 136.87, 129.24, 129.08, 128.65, 128.55, 128.52, 128.46, 128.13, 126.71, 126.50, 119.44 (q, *J* = 278.0 Hz), 77.33, 60.40, 60.13, 54.16 (d, *J* = 2.5 Hz), 39.49, 36.33, 31.94, 30.51, 29.72, 21.30, 14.17. **^{19}F NMR** (376 MHz, $CDCl_3$, 64:36 mixture of diastereomers) δ -65.77 (minor), -65.88. **HRMS** (ESI-TOF): *m/z* calculated for $C_{32}H_{34}F_3N_2O_3^+$ $[M+H]^+$ 551.2516, found 551.2515.



ethyl (*E*)-2-(2-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)octahydrocyclopenta[*c*]pyrrol-1-yl)propanoate (2f-B). Prepared via Procedure C (described above) using 31.2 mg (0.1 mmol, 1.0 equiv) of **1f**, 2.8 mg of $[Ir(cod)_2]OTf$ (0.005 mmol, 0.05 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 12 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **2f-B** (22.6 mg, 55%) and **2f-L** (10.4 mg, 25%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 60:40 mixture of diastereomers) δ 7.42 – 7.28 (m, 5H), 5.04 (dd, *J* = 3.7, 1.5 Hz, 2H), 4.58 (dd, *J* = 5.3, 2.9 Hz, 0.60H), 4.23 (dd, *J* = 6.8, 1.7 Hz, 0.40H), 4.17 – 3.97 (m, 2H), 3.80 (dd, *J* = 10.6, 7.8 Hz, 0.60H), 3.69 (dd, *J* = 10.8, 7.2 Hz, 0.40H), 3.17 – 3.09 (m, 1H), 2.73 – 2.64 (m, 0.80H), 2.61 – 2.46 (m, 1.60H), 2.40 (ddt, *J* = 8.8, 6.6, 3.2 Hz, 0.60H), 1.89 – 1.77 (m, 2H), 1.73 – 1.62 (m, 1H), 1.54 – 1.28 (m, 3H), 1.19 (dt, *J* = 25.9, 7.1 Hz, 3H), 1.01 (dd, *J* = 32.3, 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 60:40 mixture of diastereomers, only the major diastereomer is characterized) δ 173.98, 139.99 (q, *J* = 31.0 Hz), 136.99, 128.40, 128.28, 127.96, 119.53 (q, *J* = 278.3 Hz), 77.18, 68.23, 60.36, 57.11 (q, *J* = 2.3 Hz), 44.82, 42.63, 42.13, 33.98, 33.41, 26.04, 14.15, 10.68. **^{19}F NMR** (376 MHz, $CDCl_3$, 60:40 mixture of diastereomers) δ -64.91 (minor), -65.35. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 413.2047, found 413.2043.

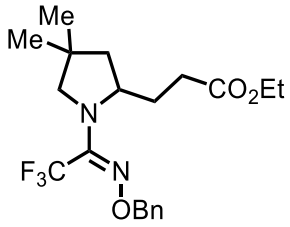


ethyl (*E*)-3-(2-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)octahydrocyclopenta[*c*]pyrrol-1-yl)propanoate (2f-L). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.05 – 4.98 (m, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 4.03 (ddd, *J* = 7.9, 5.0, 2.1 Hz, 1H), 3.74 (dd, *J* = 10.9, 7.8 Hz, 1H), 3.19 (dd, *J* = 10.8, 2.8 Hz, 1H), 2.56 (qdd, *J* = 8.1, 5.5, 2.8 Hz, 1H), 2.24 (tdd, *J* = 8.3, 5.7, 2.3 Hz, 1H), 2.21 – 2.06 (m, 2H), 1.88 – 1.72 (m, 3H), 1.71 – 1.58 (m, 2H), 1.52 – 1.31 (m, 3H), 1.25 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.10, 140.41 (q, *J* = 30.7 Hz), 137.05, 128.41, 128.37, 128.00, 119.48 (q, *J* = 278.1 Hz), 77.09, 66.47, 60.42, 55.33 (q, *J* = 2.3 Hz), 47.98, 41.42, 33.41, 33.34, 30.75, 29.87, 26.23, 14.22. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.44. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 413.2047, found 413.2047.

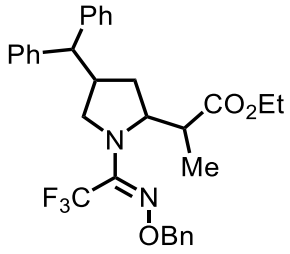


ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (2g-B). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 5.6 mg of $[Ir(cod)_2]OTf$ (0.01 mmol, 0.1 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **2g-B** (10.3 mg, 26%) and **2g-L** (24.0 mg, 60%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ 7.41 – 7.29 (m, 5H), 5.08 – 4.98 (m, 2H), 4.85 (ddd, *J* = 9.6, 7.5, 4.5 Hz, 0.5H), 4.44 (ddd, *J* = 9.6, 7.6, 4.4 Hz, 0.5H), 4.15 – 4.08 (m, 0.5H), 4.08 – 3.97 (m, 1.5H), 3.14 (dd, *J* = 9.4, 7.2 Hz, 1H), 3.03 (dd, *J* = 9.5, 1.7 Hz, 0.5H), 2.98 (d, *J* = 9.3 Hz, 0.5H), 2.80 (ddt, *J* = 22.0, 11.7, 7.1 Hz, 1H), 1.76 (dd, *J* = 12.4, 9.5 Hz, 0.5H), 1.63 (ddd, *J* = 12.4, 7.6, 1.7 Hz, 0.5H), 1.60 – 1.54 (m, 0.5H), 1.48 (dd, *J* = 12.6, 9.5 Hz, 0.5H), 1.19 (dt, *J* = 22.9, 7.1 Hz, 3H), 1.10 – 1.00 (m, 6H), 0.98 (d, *J* = 7.0 Hz, 1.5H),

0.88 (d, *J* = 7.2 Hz, 1.5H). **^{13}C NMR** (151 MHz, $CDCl_3$, 50:50 mixture of diastereomers, only one diastereomer is characterized) δ 174.02, 140.19 (q, *J* = 31.1 Hz), 136.79, 128.48, 128.28, 128.00, 119.61 (q, *J* = 278.3), 77.29, 63.17 (d, *J* = 2.7 Hz), 60.41, 60.32, 40.35, 39.17, 37.66, 26.23, 25.55, 14.16, 13.84. **^{19}F NMR** (376 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ -65.44, -65.49. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 401.2047, found 401.2052.

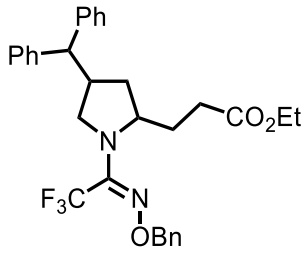


ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (2g-L). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.07 – 4.99 (m, 2H), 4.23 (tdd, *J* = 9.5, 7.1, 3.1 Hz, 1H), 4.10 (qd, *J* = 7.1, 0.8 Hz, 2H), 3.21 (d, *J* = 9.4 Hz, 1H), 3.00 (dd, *J* = 9.6, 1.8 Hz, 1H), 2.15 – 1.99 (m, 2H), 1.92 (dddd, *J* = 13.0, 10.7, 5.7, 3.1 Hz, 1H), 1.76 (ddd, *J* = 12.3, 7.2, 1.8 Hz, 1H), 1.47 (dtd, *J* = 13.0, 10.0, 5.6 Hz, 1H), 1.29 – 1.23 (m, 4H), 1.07 (s, 3H), 1.02 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.03, 140.54 (q, *J* = 31.2 Hz), 136.96, 128.57, 128.39, 128.07, 119.56 (q, *J* = 278.1 Hz), 77.24, 62.09 (q, *J* = 2.4 Hz), 60.43, 59.30, 45.08, 37.94, 30.44, 29.96, 26.13, 25.85, 14.22. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.84. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 401.2047, found 401.2041.



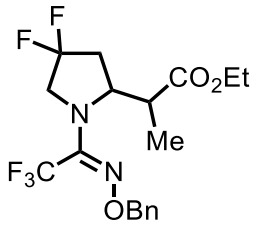
ethyl (*E*)-2-(4-benzhydryl-1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (2h-B). Prepared via Procedure C (described above) using 43.8 mg (0.1 mmol, 1.0 equiv) of **1h**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **2h-B** (24.8 mg, 46%) and **2h-L** (24.2 mg, 45%)

as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 41:24:22:12 mixture of diastereomers) δ 7.41 – 7.09 (m, 15H), 5.09 – 4.96 (m, 2H), 4.85 (dt, *J* = 8.1, 5.3 Hz, 0.41H), 4.79 (ddd, *J* = 9.6, 7.3, 4.3 Hz, 0.24H), 4.50 (ddd, *J* = 8.1, 5.9, 4.1 Hz, 0.22H), 4.36 (ddd, *J* = 9.4, 7.5, 4.6 Hz, 0.12H), 4.17 – 3.91 (m, 2H), 3.69 – 3.51 (m, 1.65H), 3.27 – 3.17 (m, 0.35H), 3.08 – 2.91 (m, 2H), 2.81 – 2.62 (m, 1H), 1.96 (ddd, *J* = 13.2, 6.5, 4.1 Hz, 0.22H), 1.90 – 1.81 (m, 0.36H), 1.78 – 1.70 (m, 0.53H), 1.67 – 1.58 (m, 0.65H), 1.36 (ddd, *J* = 12.9, 11.5, 9.6 Hz, 0.24H), 1.20 (dt, *J* = 22.1, 7.2 Hz, 1H), 1.10 (dt, *J* = 19.2, 7.1 Hz, 2H), 1.01 (dd, *J* = 12.4, 7.0 Hz, 2H), 0.87 (dd, *J* = 23.4, 7.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$, 41:24:22:12 mixture of diastereomers, only the major diastereomer is characterized) δ 173.90, 143.48, 143.34, 140.25 (q, *J* = 31.2 Hz), 136.80, 128.72, 128.67, 128.51, 128.33, 127.85, 127.70, 126.60, 126.52, 123.44 – 115.82 (m), 77.33, 60.52, 60.35, 55.24, 54.74 (d, *J* = 2.4 Hz), 41.75, 41.56, 31.45, 13.99, 10.29. **^{19}F NMR** (376 MHz, $CDCl_3$, 41:24:22:12 mixture of diastereomers) δ -65.36, -65.54, -65.56, -65.59. **HRMS** (ESI-TOF): *m/z* calculated for $C_{31}H_{34}F_3N_2O_3^+$ $[M+H]^+$ 539.2516, found 539.2518.

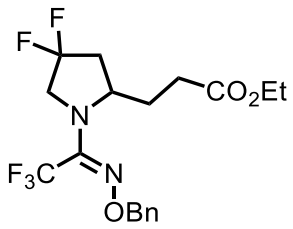


ethyl (*E*)-3-(4-benzhydryl-1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (2h-L). ^{1}H NMR (600 MHz, $CDCl_3$, 78:22 mixture of diastereomers) δ 7.36 – 7.13 (m, 15H), 5.04 – 4.94 (m, 2H), 4.31 (tt, *J* = 8.1, 4.0 Hz, 0.22H), 4.14 (tdd, *J* = 9.6, 6.9, 3.1 Hz, 0.78H), 4.06 (qd, *J* = 7.1, 2.8 Hz, 2H), 3.69 – 3.59 (m, 1.22H), 3.24 (dd, *J* = 9.8, 6.6 Hz, 0.78H), 3.17 – 3.02 (m, 1H), 2.97 (qd, *J* = 11.4, 10.9, 5.5 Hz, 1H), 2.10 – 1.95 (m, 2.78H), 1.90 (dddd, *J* = 16.3, 10.7, 5.5, 3.1 Hz, 0.78H), 1.87 – 1.79 (m, 0.22H), 1.66 (dt, *J* = 12.9, 7.8 Hz, 0.22H), 1.62 – 1.51 (m, 0.22H), 1.44 (dtd, *J* = 13.0, 10.0, 5.7 Hz, 0.78H), 1.33 – 1.27 (m, 0.22H), 1.21 (td, *J* = 7.1, 2.7 Hz, 3H), 1.13 (td, *J* = 12.1, 9.3 Hz, 0.78H). **^{13}C NMR** (151 MHz, $CDCl_3$, 78:22 mixture of diastereomers, only the major diastereomer is characterized) δ 172.93, 143.41, 143.28, 140.23 (q, *J* = 31.4 Hz), 136.57, 128.81, 128.72, 128.68, 128.42, 128.22, 127.59, 127.34, 126.69, 126.58, 119.38 (q, *J* = 278.3 Hz), 77.43, 60.44, 60.21, 56.22, 54.78 (d, *J* = 2.3 Hz), 43.17, 37.54, 30.43,

29.87, 14.18. **^{19}F NMR** (376 MHz, $CDCl_3$, 78:22 mixture of diastereomers) δ -65.65 (minor), -65.97. **HRMS** (ESI-TOF): *m/z* calculated for $C_{31}H_{34}F_3N_2O_3^+$ $[M+H]^+$ 539.2516, found 539.2520.

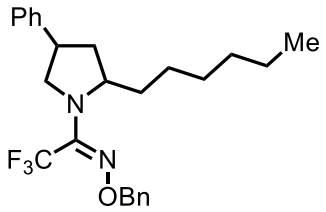


ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-difluoropyrrolidin-2-yl)propanoate (2i-B). Prepared via Procedure C (described above) using 30.8 mg (0.1 mmol, 1.0 equiv) of **1i**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), 1.4 µL of $HBF_4.Et_2O$ (0.01 mmol, 0.1 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **2i-B** (2.5 mg, 6%) and **2i-L** (12.2 mg, 30%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ 7.33 – 7.24 (m, 5H), 5.00 (s, 2H), 4.82 (td, *J* = 7.7, 4.9 Hz, 0.5H), 4.45 (q, *J* = 7.1 Hz, 0.5H), 4.10 – 3.93 (m, 2H), 3.74 (ddd, *J* = 22.6, 11.6, 7.8 Hz, 1H), 3.53 – 3.46 (m, 1H), 2.69 (dq, *J* = 20.9, 6.7 Hz, 1H), 2.56 – 2.43 (m, 0.5H), 2.40 – 2.21 (m, 1H), 2.18 – 2.05 (m, 0.5H), 1.16 – 1.09 (m, 3H), 1.01 (d, *J* = 7.1 Hz, 1.5H), 0.89 (d, *J* = 7.2 Hz, 1.5H). **^{13}C NMR** (151 MHz, $CDCl_3$, 50:50 mixture of diastereomers, only one diastereomer is characterized) δ 172.11, 137.98 (q, *J* = 62.0 Hz), 135.17, 127.67, 127.42, 127.34, 125.60, 118.10 (q, *J* = 278.0 Hz), 76.82, 59.75 (d, *J* = 3.1 Hz), 56.34 – 55.43 (m), 40.00, 33.57, 28.69, 12.89, 8.64. **^{19}F NMR** (376 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ -65.71, -65.82, -96.66 (d, *J* = 96.9 Hz), -97.27 (d, *J* = 96.8 Hz), -104.76 (d, *J* = 89.4 Hz), -105.37 (d, *J* = 89.5 Hz). **HRMS** (ESI-TOF): *m/z* calculated for $C_{18}H_{22}F_5N_2O_3^+$ $[M+H]^+$ 409.1545, found 409.1543.

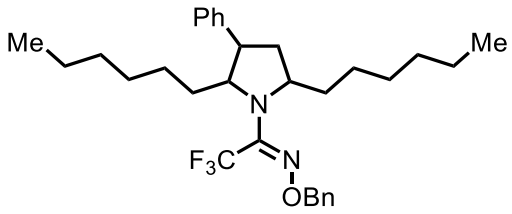


ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-difluoropyrrolidin-2-yl)propanoate (2i-L). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 5H), 4.99 (d, *J* = 1.3 Hz,

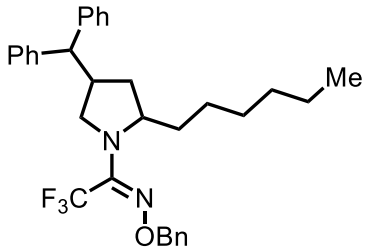
2H), 4.34 (tt, *J* = 9.1, 5.0 Hz, 1H), 4.04 (q, *J* = 7.1 Hz, 2H), 3.82 (dt, *J* = 18.0, 11.2 Hz, 1H), 3.54 (dddd, *J* = 13.6, 11.9, 6.5, 1.5 Hz, 1H), 2.44 – 2.33 (m, 1H), 2.11 – 1.90 (m, 3H), 1.89 – 1.81 (m, 1H), 1.67 – 1.57 (m, 1H), 1.18 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.87, 138.61 (q, *J* = 32.0 Hz), 135.85, 128.29, 128.07, 127.95, 126.43, 118.64 (q, *J* = 277.7 Hz), 77.31, 60.20, 58.10 (d, *J* = 3.3 Hz), 56.06 – 55.06 (m), 38.27 (dd, *J* = 24.2, 21.9 Hz), 29.77, 28.91, 13.72. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.99, -98.02 (d, *J* = 232.1 Hz), -100.56 (d, *J* = 232.1 Hz). **HRMS** (ESI-TOF): *m/z* calculated for $C_{18}H_{22}F_5N_2O_3^+$ $[M+H]^+$ 409.1545, found 409.1546.



(*E*)-2,2,2-trifluoro-1-(2-hexyl-4-phenylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (2j-mono). Prepared via Procedure C (described above) using 34.8 mg (0.1 mmol, 1.0 equiv) of **1j**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), 1.4 µL of $HBF_4.Et_2O$ (0.01 mmol, 0.1 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **2j-mono** (27.4 mg, 63%) and **2j-di** (4.7 mg, 10%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 62:38 mixture of diastereomers) δ 7.35 – 7.12 (m, 10H), 5.03 – 4.90 (m, 2H), 4.37 (ddt, *J* = 10.8, 7.4, 3.5 Hz, 0.38H), 4.20 (tdd, *J* = 9.6, 6.8, 3.1 Hz, 0.62H), 3.96 – 3.90 (m, 0.38H), 3.60 (dd, *J* = 9.2, 7.0 Hz, 0.62H), 3.38 – 3.17 (m, 2H), 2.36 (dtd, *J* = 12.2, 6.7, 1.4 Hz, 0.62H), 1.99 (dt, *J* = 12.5, 7.9 Hz, 0.38H), 1.91 (ddd, *J* = 12.6, 6.6, 3.6 Hz, 0.38H), 1.63 – 1.50 (m, 1.62H), 1.24 – 0.91 (m, 9H), 0.80 (td, *J* = 7.2, 4.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 62:38 mixture of diastereomers, only the major diastereomer is characterized) δ 139.77, 139.36 (q, *J* = 30.6 Hz), 136.36, 128.29, 128.14, 127.93, 127.71, 126.72, 126.49, 119.12 (q, *J* = 278.4 Hz), 76.92, 60.62, 54.92, 43.33, 38.71, 34.20, 31.42, 28.95, 25.01, 22.13, 13.63. **^{19}F NMR** (376 MHz, $CDCl_3$, 62:38 mixture of diastereomers) δ -65.75 (minor), -66.02. **HRMS** (ESI-TOF): *m/z* calculated for $C_{25}H_{32}F_3N_2O^+$ $[M+H]^+$ 433.2461, found 433.2460.

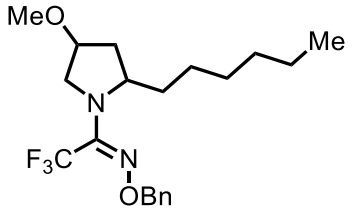


(*E*)-1-(2,5-dihexyl-3-phenylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (2j-di). The major diastereomer was isolated and characterized (other diastereomer = 7%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 – 7.06 (m, 10H), 4.96 (s, 2H), 3.92 (dt, *J* = 9.2, 4.4 Hz, 1H), 3.81 (ddt, *J* = 10.4, 6.5, 3.1 Hz, 1H), 3.07 – 3.04 (m, 1H), 2.00 – 1.89 (m, 2H), 1.81 – 1.71 (m, 1H), 1.69 – 1.59 (m, 1H), 1.39 – 1.23 (m, 2H), 1.23 – 0.89 (m, 16H), 0.78 (dt, *J* = 27.9, 7.3 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.87, 140.29 (q, *J* = 30.3 Hz), 135.63, 127.87, 127.53, 127.33, 127.14, 126.28, 125.40, 118.63 (q, *J* = 278.5 Hz), 76.39, 66.66, 61.96, 48.15, 38.53, 37.26, 35.75, 30.85, 30.66, 28.26, 28.19, 26.20, 25.32, 21.59, 21.54, 13.07, 13.02. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -64.21. **HRMS** (ESI-TOF): *m/z* calculated for $C_{31}H_{44}F_3N_2O^+$ $[M+H]^+$ 517.3400, found 517.3403.

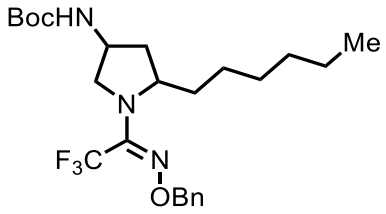


(*E*)-1-(4-benzhydryl-2-hexylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (2k). Prepared via Procedure C (described above) using 43.8 mg (0.1 mmol, 1.0 equiv) of **1k**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **2k** (44.7 mg, 86%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 60:40 mixture of diastereomers) δ 7.42 – 7.07 (m, 15H), 5.04 – 4.93 (m, 2H), 4.31 – 4.24 (m, 0.4H), 4.16 – 4.07 (m, 0.6H), 3.69 – 3.59 (m, 1.4H), 3.25 – 3.18 (m, 0.6H), 3.13 – 3.06 (m, 0.6H), 3.06 – 2.92 (m, 1.4H), 2.06 – 1.98 (m, 0.6H), 1.71 – 1.62 (m, 0.4H), 1.60 – 1.51 (m, 0.6H), 1.51 – 1.44 (m, 0.4H), 1.34 – 0.91 (m, 10H), 0.89 – 0.82 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 60:40 mixture of diastereomers, only the major diastereomer is characterized) δ 143.65, 140.49 (q, *J* = 31.2 Hz), 136.74, 128.68, 128.65, 128.45, 128.35, 128.12, 127.64, 127.35, 126.61, 126.49, 119.46 (q, *J* =

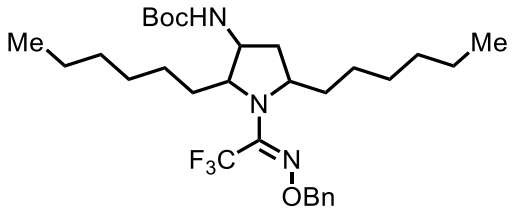
278.2 Hz), 77.29, 61.10, 56.27, 37.95, 34.80, 31.82, 29.39, 25.37, 22.58, 14.07. **^{19}F NMR** (376 MHz, $CDCl_3$, 60:40 mixture of diastereomers) δ -65.71(minor), -65.98. **HRMS** (ESI-TOF): *m/z* calculated for $C_{32}H_{38}F_3N_2O^+$ $[M+H]^+$ 523.2931, found 523.2931.



(*E*)-2,2,2-trifluoro-1-(2-hexyl-4-methoxypyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (2l). Prepared via Procedure C (described above) using 30.2 mg (0.1 mmol, 1.0 equiv) of **1l**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 μL of 1-hexene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (8% EtOAc/hexanes) to afford **2l** as a mixture of two separable diastereomers in a ratio of 77:23. Colorless oil. First diastereomer (19.8 mg, 51%): **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H), 5.05 – 4.98 (m, 2H), 4.20 (tq, *J* = 9.6, 5.7, 4.7 Hz, 1H), 3.88 (p, *J* = 6.3 Hz, 1H), 3.56 (dd, *J* = 10.3, 6.2 Hz, 1H), 3.45 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.31 (s, 3H), 2.18 (dt, *J* = 13.6, 7.2 Hz, 1H), 1.63 – 1.49 (m, 2H), 1.34 – 1.08 (m, 8H), 1.07 – 0.99 (m, 1H), 0.87 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.01 (q, *J* = 30.9 Hz), 136.83, 128.68, 128.38, 128.14, 119.47 (q, *J* = 277.9 Hz), 78.61, 77.34, 59.62, 57.13, 53.49 (q, *J* = 2.6 Hz), 35.48, 34.63, 31.84, 29.28, 25.76, 22.59, 14.09. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.94. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{30}F_3N_2O_2^+$ $[M+H]^+$ 387.2254, found 387.2249. Second diastereomer (5.7 mg, 15%): **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.06 – 4.98 (m, 2H), 4.28 (qd, *J* = 7.7, 3.1 Hz, 1H), 3.87 (tt, *J* = 4.2, 1.8 Hz, 1H), 3.55 (dd, *J* = 11.2, 4.2 Hz, 1H), 3.45 – 3.39 (m, 1H), 3.28 (s, 3H), 2.15 (ddt, *J* = 13.4, 7.4, 2.1 Hz, 1H), 1.60 – 1.53 (m, 1H), 1.25 – 0.96 (m, 10H), 0.87 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.31 (q, *J* = 31.0 Hz), 136.97, 128.67, 128.32, 128.03, 119.55 (q, *J* = 278.1 Hz), 78.90, 77.23, 59.07, 56.45, 53.80 (q, *J* = 2.5 Hz), 36.70, 34.80, 31.84, 29.33, 25.48, 22.70, 14.08. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.95. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{30}F_3N_2O_2^+$ $[M+H]^+$ 387.2254, found 387.2247.

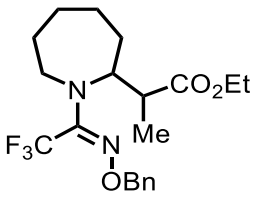


tert-butyl (*E*)-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-hexylpyrrolidin-3-yl)carbamate (2m-mono). Prepared via Procedure C (described above) using 38.7 mg (0.1 mmol, 1.0 equiv) of **1m**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (10% EtOAc/hexanes) to afford **2m-mono** (30.0 mg, 64%) and **2m-di** (7.4 mg, 13%) as white solids. **^{1}H NMR** (600 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ 7.42 – 7.28 (m, 5H), 5.07 – 4.98 (m, 2H), 4.72 (br d, *J* = 8.0 Hz, 0.5H), 4.51 (br s, 0.5H), 4.28 – 3.89 (m, 2H), 3.69 – 3.60 (m, 1H), 3.19 (dt, *J* = 10.6, 2.0 Hz, 0.5H), 3.13 (t, *J* = 9.2 Hz, 0.5H), 2.36 (dt, *J* = 13.6, 7.1 Hz, 0.5H), 1.99 – 1.92 (m, 0.5H), 1.73 (dt, *J* = 13.3, 6.6 Hz, 0.5H), 1.60 – 1.49 (m, 1H), 1.43 (d, *J* = 3.9 Hz, 9H), 1.34 – 0.96 (m, 9.5H), 0.87 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 50:50 mixture of diastereomers, only one diastereomer is characterized) δ 155.22, 140.00 (q, *J* = 30.9 Hz), 136.73, 128.78, 128.42, 128.24, 119.44 (q, *J* = 278.0 Hz), 79.77, 77.46, 59.32, 55.04 (d, *J* = 2.7 Hz), 49.63, 37.54, 34.43, 31.82, 29.25, 28.35, 25.44, 22.57, 14.07. **^{19}F NMR** (376 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ -66.00, -66.03. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{37}F_3N_3O_3^+$ $[M+H]^+$ 472.2782, found 472.2787 .

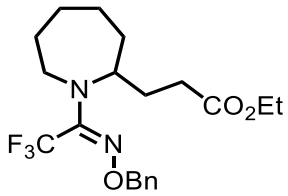


tert-butyl (*E*)-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-2,5-dihexylpyrrolidin-3-yl)carbamate (2m-di). **^{1}H NMR** (600 MHz, $CDCl_3$, mixture of diastereomers) δ 7.40 – 7.29 (m, 5H), 5.15 – 4.95 (m, 2H), 4.77 – 4.17 (m, 1H), 4.14 – 3.28 (m, 3H), 2.38 – 1.66 (m, 3H), 1.43 (d, *J* = 5.3 Hz, 9H), 1.33 – 1.01 (m, 19H), 0.91 – 0.82 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ 155.04, 141.56 (q), 136.41, 128.96, 128.43, 128.31, 119.57 (q, *J* = 278.4 Hz), 79.56, 77.58, 69.51, 58.82, 54.32, 38.50, 36.40,

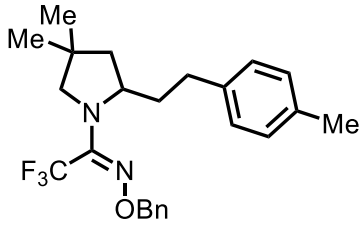
35.83, 31.78, 31.70, 29.30, 29.16, 28.40, 26.34, 25.94, 22.61, 22.57, 14.07. **^{19}F NMR** (376 MHz, $CDCl_3$, mixture of diastereomers, only the major diastereomer is characterized) δ -64.61. **HRMS** (ESI-TOF): *m/z* calculated for $C_{30}H_{49}F_3N_3O_3^+$ $[M+H]^+$ 556.3721, found 556.3728.



ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)azepan-2-yl)propanoate (2p-B). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1p**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 87 µL of ethyl acrylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **2p-B** and **2p-L** (18.1 mg, 45%) as colorless oils. **2p-B** was obtained as a mixture of two separable diastereomers in a ratio of 56:44. First diastereomer (5.5 mg, 14%): **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 – 7.28 (m, 5H), 5.13 – 5.04 (m, 2H), 4.19 (td, *J* = 9.7, 6.6 Hz, 1H), 4.10 (qd, *J* = 7.1, 1.7 Hz, 2H), 3.64 (d, *J* = 15.5 Hz, 1H), 2.83 – 2.75 (m, 1H), 2.43 (dq, *J* = 9.0, 7.0 Hz, 1H), 2.03 – 1.95 (m, 1H), 1.84 – 1.74 (m, 1H), 1.70 – 1.57 (m, 3H), 1.37 – 1.27 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.20 – 1.12 (m, 1H), 1.07 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.97, 142.50 (q, *J* = 30.1 Hz), 136.88, 128.35, 128.33, 128.02, 119.86 (q, *J* = 279.9 Hz), 77.34, 60.40, 60.20, 46.05, 44.34, 32.71, 30.35, 29.84, 23.92, 14.52, 14.12. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.58. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 401.2047, found 401.2044. Second diastereomer (4.3 mg, 11%): **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H), 5.13 – 5.03 (m, 2H), 4.36 (td, *J* = 9.9, 6.8 Hz, 1H), 4.03 (qd, *J* = 7.2, 4.5 Hz, 2H), 3.49 (d, *J* = 15.5 Hz, 1H), 2.88 (ddd, *J* = 15.7, 11.8, 1.3 Hz, 1H), 2.53 (dq, *J* = 9.1, 7.0 Hz, 1H), 2.06 – 1.98 (m, 1H), 1.80 (d, *J* = 13.8 Hz, 1H), 1.77 – 1.58 (m, 3H), 1.33 – 1.26 (m, 2H), 1.21 – 1.11 (m, 4H), 1.08 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.46, 142.04 (q, *J* = 30.2 Hz), 137.01, 128.32, 128.20, 127.94, 119.72 (q, *J* = 279.7 Hz), 77.23, 60.36, 59.51, 46.23, 45.08, 31.94, 30.52, 29.97, 23.94, 14.07, 13.95. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.62. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 401.2047, found 401.2039.

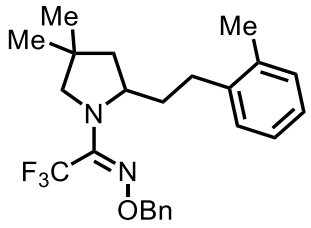


ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)azepan-2-yl)propanoate (2p-L). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 5H), 5.06 (s, 2H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.93 (dq, *J* = 10.2, 6.8 Hz, 1H), 3.61 (d, *J* = 15.5 Hz, 1H), 2.84 (ddd, *J* = 15.9, 11.6, 1.4 Hz, 1H), 2.32 – 2.22 (m, 1H), 2.22 – 2.12 (m, 1H), 2.04 – 1.96 (m, 1H), 1.83 – 1.75 (m, 1H), 1.72 – 1.66 (m, 2H), 1.66 – 1.59 (m, 3H), 1.34 – 1.15 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.40, 142.62 (q, *J* = 29.8 Hz), 136.89, 128.37, 128.30, 128.03, 119.87 (q, *J* = 280.0 Hz), 60.35, 57.30, 43.86, 34.96, 30.87, 30.71, 30.43, 29.85, 29.72, 24.05, 14.19. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.98. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{28}F_3N_2O_3^+$ $[M+H]^+$ 401.2047, found 401.2043.

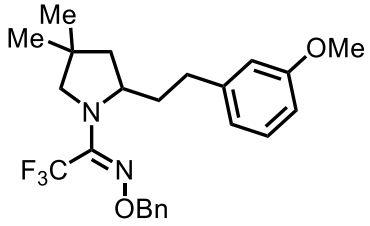


(*E*)-1-(4,4-dimethyl-2-(4-methylphenethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3a). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 105 µL of 4-methylstyrene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3a** (29.3 mg, 70%) as a colorless oil. Isolated as a 95:5 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 7.09 – 7.03 (m, 2H), 6.98 – 6.92 (m, 2H), 5.07 – 4.93 (m, 2H), 4.30 (tdd, *J* = 9.7, 7.1, 3.1 Hz, 1H), 3.22 (d, *J* = 9.4 Hz, 1H), 3.01 (dd, *J* = 9.3, 1.7 Hz, 1H), 2.40 (ddd, *J* = 13.6, 11.7, 5.0 Hz, 1H), 2.36 – 2.28 (m, 4H), 1.93 (dddd, *J* = 12.7, 11.6, 5.6, 3.1 Hz, 1H), 1.85 (ddd, *J* = 12.2, 7.2, 1.8 Hz, 1H), 1.44 – 1.31 (m, 2H), 1.09 (s, 3H), 1.04 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.66 (q, *J* = 30.9 Hz), 138.71, 137.14, 135.24, 129.01, 128.38, 128.09, 127.97, 119.60 (q, *J* = 278.3 Hz), 77.07, 61.88 (d, *J* = 2.3 Hz),

59.92, 45.60, 37.97, 36.86, 31.29, 26.21, 25.93, 20.98. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.86. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{30}F_3N_2O^+$ $[M+H]^+$ 419.2305, found 419.2300.

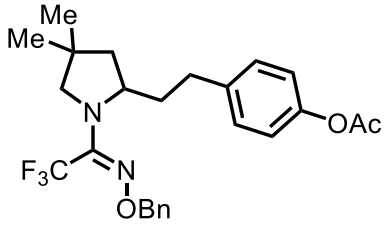


(*E*)-1-(4,4-dimethyl-2-(2-methylphenethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3b). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 103 µL of 2-methylstyrene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3b** (31.8 mg, 76%) as a colorless oil. Isolated as a 97:3 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 5H), 7.12 – 7.05 (m, 3H), 7.00 – 6.95 (m, 1H), 5.06 – 4.95 (m, 2H), 4.35 (tdd, *J* = 9.5, 7.1, 3.0 Hz, 1H), 3.25 (d, *J* = 9.4 Hz, 1H), 3.02 (dd, *J* = 9.4, 1.7 Hz, 1H), 2.42 (ddd, *J* = 13.7, 12.1, 4.9 Hz, 1H), 2.34 (ddd, *J* = 13.6, 11.7, 5.1 Hz, 1H), 2.21 (s, 3H), 1.94 – 1.84 (m, 2H), 1.39 (tdd, *J* = 12.2, 9.4, 3.9 Hz, 2H), 1.10 (s, 3H), 1.06 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.76 (q, *J* = 31.0 Hz), 139.96, 137.10, 135.67, 130.12, 128.57, 128.35, 128.29, 127.95, 126.00, 125.97, 119.61 (q, *J* = 278.3 Hz), 77.05, 62.06 (d, *J* = 2.7 Hz), 60.05, 45.59, 38.01, 35.48, 28.99, 26.21, 25.94, 19.15. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.76. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{30}F_3N_2O^+$ $[M+H]^+$ 419.2305, found 419.2301.

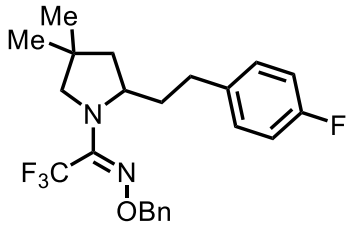


(*E*)-2,2,2-trifluoro-1-(2-(3-methoxyphenethyl)-4,4-dimethylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (3c). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 111 µL of 3-vinylanisole (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by

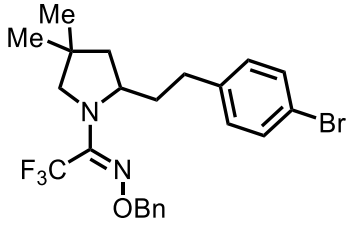
preparative TLC (6% EtOAc/hexanes) to afford **3c** (28.7 mg, 66%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 7.16 (t, *J* = 7.9 Hz, 1H), 6.71 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 6.67 – 6.61 (m, 2H), 5.06 – 4.95 (m, 2H), 4.30 (tdd, *J* = 9.6, 7.0, 3.0 Hz, 1H), 3.78 (s, 3H), 3.23 (d, *J* = 9.4 Hz, 1H), 3.04 – 2.99 (m, 1H), 2.42 (ddd, *J* = 13.6, 11.6, 5.0 Hz, 1H), 2.34 (ddd, *J* = 13.6, 11.1, 5.6 Hz, 1H), 1.95 (dddd, *J* = 12.7, 11.6, 5.7, 3.1 Hz, 1H), 1.85 (ddd, *J* = 12.2, 7.2, 1.8 Hz, 1H), 1.41 – 1.40 (m, 1H), 1.34 (dd, *J* = 12.2, 9.0 Hz, 1H), 1.09 (s, 3H), 1.04 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.63, 143.45, 140.66 (q, *J* = 31.1 Hz), 137.11, 129.30, 128.38, 128.37, 127.99, 120.66, 119.60 (q, *J* = 278.2 Hz), 114.16, 110.98, 77.08, 61.93, 59.89, 55.14 (d, *J* = 2.4 Hz), 45.58, 37.99, 36.59, 31.78, 26.21, 25.93. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.83. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{30}F_3N_2O_2^+$ $[M+H]^+$ 435.2254, found 435.2254.



(*E*)-4-(2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)ethyl)phenyl acetate (3d). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 122 µL of 4-acetoxystyrene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **3d** (35.2 mg, 76%) as a colorless oil. Isolated as a 97:3 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 7.05 – 6.99 (m, 2H), 6.98 – 6.91 (m, 2H), 5.06 – 4.96 (m, 2H), 4.31 (tdd, *J* = 9.6, 7.1, 3.0 Hz, 1H), 3.22 (d, *J* = 9.4 Hz, 1H), 3.04 – 2.99 (m, 1H), 2.46 – 2.38 (m, 1H), 2.38 – 2.30 (m, 1H), 2.29 (s, 3H), 1.91 (tdd, *J* = 12.2, 5.5, 3.0 Hz, 1H), 1.85 (ddd, *J* = 12.2, 7.1, 1.8 Hz, 1H), 1.44 – 1.30 (m, 2H), 1.09 (s, 3H), 1.05 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 169.65, 148.74, 140.60 (q, *J* = 30.9 Hz), 139.34, 137.13, 129.11, 128.44, 128.40, 128.03, 121.32, 119.59 (q, *J* = 278.3 Hz), 77.11, 62.01 – 61.81 (m), 59.84, 45.56, 37.99, 36.56, 31.07, 26.20, 25.92, 21.14. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.85. **HRMS** (ESI-TOF): *m/z* calculated for $C_{25}H_{30}F_3N_2O_3^+$ $[M+H]^+$ 463.2203, found 463.2201.

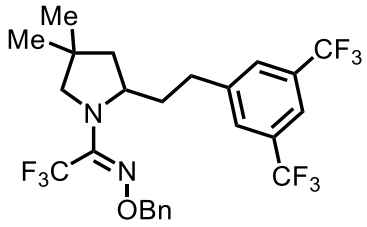


(*E*)-2,2,2-trifluoro-1-(2-(4-fluorophenethyl)-4,4-dimethylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (3e). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 95 µL of 4-fluorostyrene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3e** (33.1 mg, 79%) as a colorless oil. Isolated as a 97:3 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 6.99 – 6.94 (m, 2H), 6.93 – 6.88 (m, 2H), 5.06 – 4.96 (m, 2H), 4.29 (tdd, *J* = 9.6, 7.1, 3.1 Hz, 1H), 3.22 (d, *J* = 9.4 Hz, 1H), 3.02 (dd, *J* = 9.4, 1.7 Hz, 1H), 2.40 (ddd, *J* = 13.7, 11.4, 5.0 Hz, 1H), 2.31 (ddd, *J* = 13.8, 11.1, 5.7 Hz, 1H), 1.90 (dddd, *J* = 12.7, 11.5, 5.7, 3.1 Hz, 1H), 1.84 (ddd, *J* = 12.1, 7.2, 1.8 Hz, 1H), 1.43 – 1.29 (m, 2H), 1.09 (s, 3H), 1.05 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.03, 160.41, 140.62 (q, *J* = 31.2 Hz), 137.32 (d, *J* = 3.1 Hz), 137.12, 129.53, 129.48, 128.39, 128.03, 119.59 (q, *J* = 278.2 Hz), 115.09, 114.95, 77.12 (d, *J* = 2.4 Hz), 61.91 (d, *J* = 2.6 Hz), 59.78, 45.58, 37.99, 36.72, 30.89, 26.19, 25.92. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.84, -117.98. **HRMS** (ESI-TOF): *m/z* calculated for $C_{23}H_{27}F_4N_2O^+$ $[M+H]^+$ 423.2054, found 423.2054.

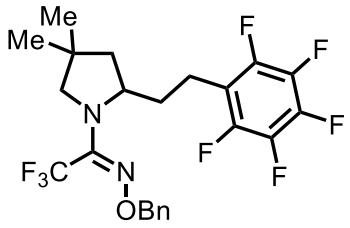


(*E*)-1-(2-(4-bromophenethyl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3f). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 105 µL of 4-bromostyrene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3f** (38.7 mg, 80%) as a colorless oil.

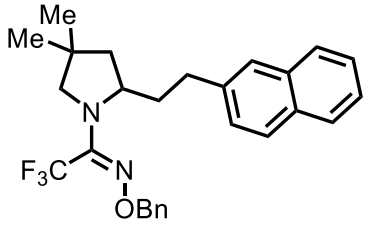
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 7H), 6.90 – 6.85 (m, 2H), 5.06 – 4.95 (m, 2H), 4.29 (tdd, *J* = 9.6, 7.1, 3.1 Hz, 1H), 3.22 (d, *J* = 9.4 Hz, 1H), 3.04 – 2.99 (m, 1H), 2.37 (ddd, *J* = 13.8, 11.5, 5.0 Hz, 1H), 2.28 (ddd, *J* = 13.8, 11.1, 5.7 Hz, 1H), 1.93 – 1.80 (m, 2H), 1.42 – 1.29 (m, 2H), 1.09 (s, 3H), 1.04 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.09, 131.34, 129.96, 128.40, 128.05, 122.76 – 115.86 (m), 77.12, 61.89 (q, *J* = 2.4 Hz), 59.73, 45.52, 37.98, 36.37, 31.09, 26.17, 25.90. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.82. **HRMS** (ESI-TOF): *m/z* calculated for $C_{23}H_{27}BrF_3N_2O^+$ $[M+H]^+$ 483.1253, found 483.1249.



(*E*)-1-(2-(3,5-bis(trifluoromethyl)phenethyl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3g). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 144 µL of 3,5-bis(trifluoromethyl)styrene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3g** (43.8 mg, 81%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.43 (s, 2H), 7.38 – 7.26 (m, 5H), 5.09 – 4.94 (m, 2H), 4.34 (tdd, *J* = 9.6, 7.0, 3.0 Hz, 1H), 3.24 (d, *J* = 9.4 Hz, 1H), 3.05 (d, *J* = 9.4 Hz, 1H), 2.50 (ddd, *J* = 13.8, 12.2, 4.8 Hz, 1H), 2.36 (ddd, *J* = 13.9, 11.7, 5.3 Hz, 1H), 1.93 – 1.84 (m, 2H), 1.45 – 1.31 (m, 2H), 1.10 (d, *J* = 21.7 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.18, 140.48 (q, *J* = 31.1 Hz), 136.97, 131.56 (q, *J* = 33.0 Hz), 128.44 (d, *J* = 1.8 Hz), 128.37 (d, *J* = 3.8 Hz), 128.22, 128.04 (q, *J* = 29.6 Hz), 123.41 (q, *J* = 272.8 Hz), 120.01 (p, *J* = 4.0 Hz), 119.57 (q, *J* = 278.1 Hz), 77.28, 61.97 (q, *J* = 2.4 Hz), 59.65, 45.67, 38.06, 36.31, 31.48, 26.17, 25.87. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.01, -65.87. **HRMS** (ESI-TOF): *m/z* calculated for $C_{25}H_{26}F_9N_2O^+$ $[M+H]^+$ 541.1896, found 541.1894.

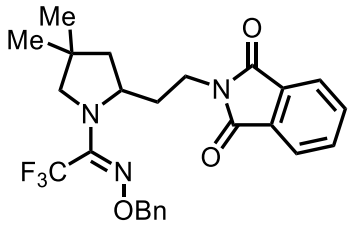


(*E*)-1-(4,4-dimethyl-2-(2-(perfluorophenyl)ethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3h). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 110 µL of 2,3,4,5,6-pentafluorostyrene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3h** (38.9 mg, 79%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 5H), 5.06 – 4.96 (m, 2H), 4.30 (tdd, *J* = 9.6, 7.0, 3.1 Hz, 1H), 3.23 (d, *J* = 9.4 Hz, 1H), 3.05 – 3.00 (m, 1H), 2.56 – 2.44 (m, 2H), 1.94 – 1.83 (m, 2H), 1.40 – 1.31 (m, 2H), 1.11 (s, 3H), 1.07 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.17 – 145.30 (m), 144.37 – 143.85 (m), 140.47 (q, *J* = 31.2 Hz), 139.04 – 138.51 (m), 138.60 – 137.86 (m), 136.88, 136.84 – 136.29 (m), 128.35, 128.16, 128.00, 119.53 (q, *J* = 278.2 Hz), 114.60 (td, *J* = 18.9, 3.7 Hz), 77.08, 61.88 (q, *J* = 2.3 Hz), 59.35, 45.23, 38.04, 34.05, 26.18, 25.87, 18.32. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.01, -144.86 (dd, *J* = 22.7, 8.4 Hz), -157.79 (t, *J* = 20.9 Hz), -162.97 (td, *J* = 21.8, 8.2 Hz). **HRMS** (ESI-TOF): *m/z* calculated for $C_{23}H_{23}F_8N_2O^+$ $[M+H]^+$ 495.1677, found 495.1671.

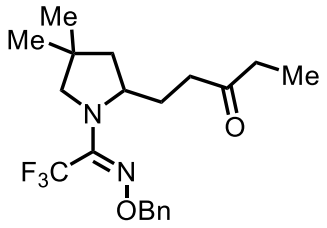


(*E*)-1-(4,4-dimethyl-2-(2-(naphthalen-2-yl)ethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3i). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 123.4 mg of 2-vinylnaphthalene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3i** (36.4 mg, 80%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.82 – 7.70 (m, 3H), 7.49 – 7.37 (m, 3H), 7.36 – 7.25 (m, 5H), 7.18

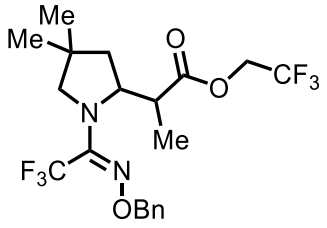
(dd, *J* = 8.4, 1.8 Hz, 1H), 5.07 – 4.95 (m, 2H), 4.36 (tdd, *J* = 9.7, 7.1, 3.1 Hz, 1H), 3.25 (d, *J* = 9.4 Hz, 1H), 3.03 (dd, *J* = 9.4, 1.7 Hz, 1H), 2.60 (ddd, *J* = 13.7, 11.5, 5.0 Hz, 1H), 2.51 (ddd, *J* = 13.7, 11.1, 5.6 Hz, 1H), 2.04 (dddd, *J* = 12.7, 11.5, 5.7, 3.1 Hz, 1H), 1.89 (ddd, *J* = 12.2, 7.1, 1.7 Hz, 1H), 1.53 – 1.45 (m, 1H), 1.39 (dd, *J* = 12.2, 9.1 Hz, 1H), 1.10 (s, 3H), 1.06 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.65 (q, *J* = 31.0 Hz), 139.27, 137.11, 133.59, 131.98, 128.40, 128.37, 128.00, 127.87, 127.61, 127.37, 127.15, 126.09, 125.91, 125.14, 119.61 (q, *J* = 278.2 Hz), 77.11, 61.96 – 61.85 (m), 59.94, 45.64, 38.00, 36.50, 31.88, 26.22, 25.94. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.80. **HRMS** (ESI-TOF): *m/z* calculated for $C_{27}H_{30}F_3N_2O^+$ $[M+H]^+$ 455.2305, found 455.2301.



(*E*)-2-(2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)ethyl)isoindoline-1,3-dione (3j). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 138.5 mg of *N*-vinylphthalimide (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (8% EtOAc/hexanes) to afford **3j** (36.8 mg, 78%) as a colorless oil. Isolated as a 97:3 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 2H), 7.73 – 7.67 (m, 2H), 7.40 – 7.35 (m, 2H), 7.33 – 7.28 (m, 2H), 7.27 – 7.22 (m, 1H), 5.01 (s, 2H), 4.30 (tdd, *J* = 9.8, 7.1, 3.0 Hz, 1H), 3.61 – 3.49 (m, 2H), 3.21 (d, *J* = 9.3 Hz, 1H), 3.00 (dd, *J* = 9.3, 1.6 Hz, 1H), 2.11 – 2.03 (m, 1H), 1.97 (ddd, *J* = 12.2, 7.1, 1.7 Hz, 1H), 1.51 – 1.42 (m, 1H), 1.40 (d, *J* = 9.1 Hz, 1H), 1.10 (s, 3H), 1.04 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 168.13, 140.37 (q, *J* = 31.3 Hz), 136.98, 133.92, 132.08, 128.42, 128.33, 127.89, 123.20, 119.49 (q, *J* = 278.3 Hz), 77.08, 61.67 (d, *J* = 2.7 Hz), 57.87, 45.43, 38.07, 34.68, 33.58, 26.15, 25.84. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.00. **HRMS** (ESI-TOF): *m/z* calculated for $C_{25}H_{27}F_3N_3O_3^+$ $[M+H]^+$ 474.1999, found 474.2003.

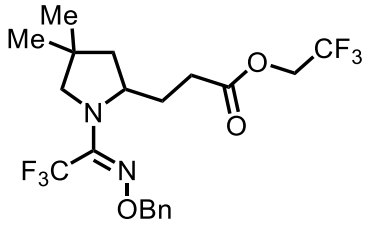


(*E*)-1-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)pentan-3-one (3k). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 80 µL of ethyl vinyl ketone (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **3k** (24.9 mg, 65%) as a colorless oil. Isolated as a 97:3 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 5.06 – 4.98 (m, 2H), 4.23 (tdd, *J* = 9.3, 7.1, 3.2 Hz, 1H), 3.20 (d, *J* = 9.4 Hz, 1H), 3.03 – 2.98 (m, 1H), 2.30 (q, *J* = 7.3 Hz, 2H), 2.17 (ddd, *J* = 16.3, 10.9, 5.2 Hz, 1H), 2.07 (ddd, *J* = 16.2, 10.6, 5.3 Hz, 1H), 1.83 (dddd, *J* = 13.2, 10.9, 5.4, 3.2 Hz, 1H), 1.74 (ddd, *J* = 12.2, 7.2, 1.7 Hz, 1H), 1.42 (dddd, *J* = 13.2, 10.6, 9.2, 5.2 Hz, 1H), 1.23 (dd, *J* = 12.2, 9.1 Hz, 1H), 1.07 (s, 3H), 1.04 – 0.98 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 210.61, 140.55 (q, *J* = 31.0 Hz), 137.04, 128.55, 128.38, 128.07, 119.57 (q, *J* = 278.1 Hz), 77.22, 62.10 (d, *J* = 2.3 Hz), 59.41, 45.20, 38.11, 37.92, 35.66, 28.83, 26.17, 25.86, 7.80. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.79. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{28}F_3N_2O_2^+$ $[M+H]^+$ 385.2097, found 385.2090.

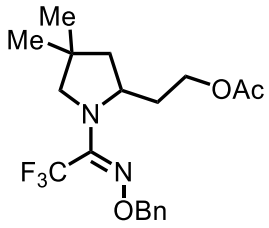


2,2,2-trifluoroethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (3l-B). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 101 µL of 2,2,2-trifluoroethylacrylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **3l-B** (15.9

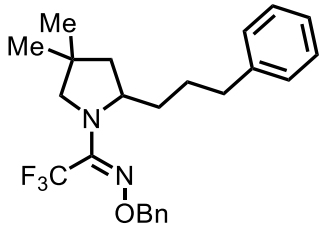
mg, 35%) and **3l-L** (22.1 mg, 49%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ 7.39 – 7.28 (m, 5H), 5.08 – 5.00 (m, 2H), 4.88 (ddd, *J* = 9.6, 7.4, 4.4 Hz, 0.5H), 4.56 – 4.37 (m, 1.5H), 4.36 – 4.19 (m, 1H), 3.15 (dd, *J* = 9.4, 3.9 Hz, 1H), 3.04 (d, *J* = 9.2 Hz, 0.5H), 3.00 – 2.95 (m, 0.5H), 2.90 (qd, *J* = 7.1, 4.4 Hz, 0.5H), 2.83 (qd, *J* = 7.2, 4.5 Hz, 0.5H), 1.74 (dd, *J* = 12.4, 9.7 Hz, 0.5H), 1.66 (ddd, *J* = 12.4, 7.6, 1.7 Hz, 0.5H), 1.60 – 1.54 (m, 0.5H), 1.46 (dd, *J* = 12.6, 9.6 Hz, 0.5H), 1.10 – 1.03 (m, 4.5H), 1.03 – 1.00 (m, 3H), 0.92 (d, *J* = 7.2 Hz, 1.5H). **^{13}C NMR** (151 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ 172.77, 172.41, 140.15 (q, *J* = 26.3 Hz), 136.79, 136.69, 128.70, 128.57, 128.46, 128.32, 128.29, 128.08, 122.89 (qd, *J* = 277.6, 3.3 Hz), 119.52 (q, *J* = 278.0 Hz), 77.48, 77.38, 63.10 (d, *J* = 2.3 Hz), 62.32 (d, *J* = 2.6 Hz), 62.26, 60.11, 60.00 (q, *J* = 36.5 Hz), 40.69, 40.12, 39.96, 39.08, 37.70, 37.55, 26.20, 26.17, 25.52, 25.47, 13.78, 8.69 (Due to similar peak intensities, the diastereomeric carbon peaks could not be distinguished). **^{19}F NMR** (376 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ -65.55, -65.76, -73.76, -73.98. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{25}F_6N_2O_3^+$ $[M+H]^+$ 455.1764, found 455.1762.



2,2,2-trifluoroethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (3l-L). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H), 5.07 – 4.98 (m, 2H), 4.46 – 4.33 (m, 2H), 4.24 (tdd, *J* = 9.4, 7.1, 3.1 Hz, 1H), 3.21 (d, *J* = 9.4 Hz, 1H), 3.04 – 2.99 (m, 1H), 2.20 (ddd, *J* = 16.1, 10.5, 5.6 Hz, 1H), 2.12 (ddd, *J* = 15.9, 10.2, 5.9 Hz, 1H), 1.93 (dddd, *J* = 13.5, 10.5, 5.9, 3.2 Hz, 1H), 1.77 (ddd, *J* = 12.2, 7.1, 1.7 Hz, 1H), 1.54 – 1.45 (m, 1H), 1.25 (dd, *J* = 12.2, 9.1 Hz, 1H), 1.08 (s, 3H), 1.03 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.36, 140.42 (q, *J* = 31.3 Hz), 136.87, 128.60, 128.42, 128.15, 122.95 (q, *J* = 277.2 Hz), 119.52 (q, *J* = 278.3 Hz), 77.31, 62.08 (d, *J* = 2.5 Hz), 60.29 (q, *J* = 36.4 Hz), 59.03, 45.03, 37.96, 29.66, 29.57, 26.09, 25.81. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.89, -74.00. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{25}F_6N_2O_3^+$ $[M+H]^+$ 455.1764, found 455.1767.

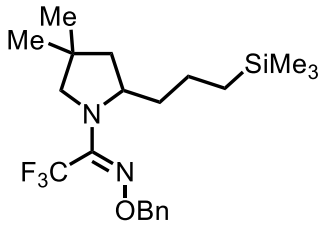


(*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)ethyl acetate (3m). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 74 µL of vinyl acetate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **3m** (25.1 mg, 65%) as a colorless oil. Isolated as a 96:4 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 5.03 (d, *J* = 1.9 Hz, 2H), 4.29 (tdd, *J* = 9.7, 7.1, 3.1 Hz, 1H), 3.96 – 3.86 (m, 2H), 3.20 (d, *J* = 9.4 Hz, 1H), 3.02 – 2.97 (m, 1H), 1.97 (s, 3H), 1.96 – 1.89 (m, 1H), 1.86 – 1.79 (m, 1H), 1.43 (ddt, *J* = 13.1, 9.8, 6.6 Hz, 1H), 1.32 (dd, *J* = 12.3, 9.2 Hz, 1H), 1.08 (s, 3H), 1.04 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.98, 140.52 (q, *J* = 31.2 Hz), 136.97, 128.47, 128.41, 128.09, 119.52 (q, *J* = 278.0 Hz), 77.22, 61.77 (q, *J* = 2.4 Hz), 61.53, 57.63, 45.69, 38.03, 33.53, 26.06, 25.85, 20.88. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.96. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{26}F_3N_2O_3^+$ $[M+H]^+$ 387.1890, found 387.1898.

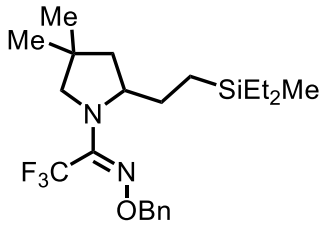


(*E*)-1-(4,4-dimethyl-2-(3-phenylpropyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3n). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 106 µL of allylbenzene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3n** (21.4 mg, 51%) as a colorless oil. Isolated as a 97:3 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H), 7.29 – 7.23 (m, 2H), 7.20 – 7.15 (m, 1H), 7.13 – 7.07 (m, 2H), 5.07

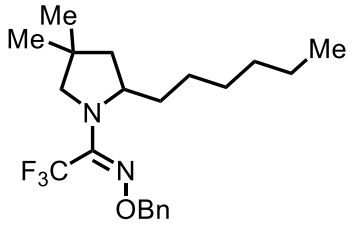
– 4.90 (m, 2H), 4.22 (tdd, *J* = 9.7, 7.0, 3.2 Hz, 1H), 3.18 (d, *J* = 9.3 Hz, 1H), 3.01 – 2.96 (m, 1H), 2.46 (ddd, *J* = 8.8, 6.7, 3.3 Hz, 2H), 1.76 (ddd, *J* = 12.2, 7.2, 1.8 Hz, 1H), 1.64 (tdd, *J* = 12.0, 5.1, 3.2 Hz, 1H), 1.48 – 1.39 (m, 1H), 1.39 – 1.30 (m, 1H), 1.27 – 1.20 (m, 1H), 1.13 (dddd, *J* = 12.5, 11.2, 9.6, 4.7 Hz, 1H), 1.05 (s, 3H), 1.01 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.40, 140.69 (q, *J* = 30.8 Hz), 137.12, 128.51, 128.36, 128.30, 128.02, 125.74, 119.62 (q, *J* = 278.3 Hz), 77.10, 61.83 (q, *J* = 2.4 Hz), 59.96, 45.52, 37.87, 35.96, 34.53, 27.31, 26.17, 25.88. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.85. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{30}F_3N_2O^+$ $[M+H]^+$ 419.2305, found 419.2303.



(*E*)-1-(4,4-dimethyl-2-(3-(trimethylsilyl)propyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3o). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 127 µL of allyltrimethylsilane (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3o** (29.3 mg, 71%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.06 – 4.98 (m, 2H), 4.20 (tdd, *J* = 9.4, 7.0, 3.0 Hz, 1H), 3.19 (d, *J* = 9.3 Hz, 1H), 3.01 – 2.96 (m, 1H), 1.78 (ddd, *J* = 12.3, 7.2, 1.8 Hz, 1H), 1.65 – 1.57 (m, 1H), 1.24 (dd, *J* = 12.5, 9.4 Hz, 1H), 1.18 – 0.98 (m, 9H), 0.42 – 0.30 (m, 2H), -0.05 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.80 (q, *J* = 30.9 Hz), 137.12, 128.47, 128.34, 127.98, 119.64 (q, *J* = 278.3 Hz), 77.08, 61.76 (d, *J* = 3.7 Hz), 59.94, 45.61, 38.78, 37.90, 26.19, 25.95, 19.78, 16.73, -1.72. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.89. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{34}F_3N_2OSi^+$ $[M+H]^+$ 415.2387, found 415.2387.

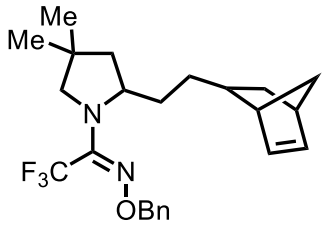


(*E*)-1-(2-(2-(diethyl(methyl)silyl)ethyl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3p). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 0.14 mL of diethylmethylvinylsilane (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3p** (31.7 mg, 74%) as a colorless oil. Isolated as a 98:2 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 5.08 – 4.95 (m, 2H), 4.18 (tdd, *J* = 9.3, 7.0, 3.0 Hz, 1H), 3.23 (d, *J* = 9.5 Hz, 1H), 3.02 – 2.97 (m, 1H), 1.80 (ddd, *J* = 12.3, 7.1, 1.8 Hz, 1H), 1.62 – 1.53 (m, 1H), 1.25 (dd, *J* = 12.2, 9.1 Hz, 1H), 1.14 – 1.05 (m, 4H), 1.02 (s, 3H), 0.88 (t, *J* = 7.9 Hz, 6H), 0.44 (q, *J* = 8.0 Hz, 4H), 0.26 (dtd, *J* = 36.8, 14.1, 4.3 Hz, 2H), -0.12 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.98 (q, *J* = 30.9 Hz), 137.17, 128.33, 128.29, 127.92, 119.67 (q, *J* = 278.4 Hz), 76.99, 62.52 – 62.44 (m), 62.41, 45.05, 37.79, 28.73, 26.25, 25.92, 7.84, 7.34, 4.87, 4.86, -6.31. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.69. **HRMS** (ESI-TOF): *m/z* calculated for $C_{22}H_{36}F_3N_2OSi^+$ $[M+H]^+$ 429.2544, found 429.2544.

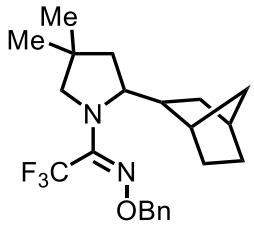


(*E*)-2,2,2-trifluoro-1-(2-hexyl-4,4-dimethylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (3q). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3q** (28.1 mg, 73%) as a colorless oil. Isolated as a 97:3 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.06 – 4.98 (m, 2H), 4.19 (tdd, *J* = 9.5, 7.0, 3.1 Hz, 1H), 3.19 (d, *J* = 9.3 Hz, 1H), 3.01 – 2.96 (m, 1H), 1.78 (ddd, *J* = 12.2, 7.1, 1.8 Hz, 1H), 1.62 – 1.54 (m, 1H), 1.29 – 1.13 (m, 7H), 1.12 – 0.95 (m, 9H), 0.87 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.81 (q, *J* = 30.9 Hz), 137.16, 128.47, 128.32, 127.97, 119.65 (q, *J* = 278.2 Hz), 77.09, 61.83 (q, *J* = 2.2 Hz), 60.15, 45.67, 37.88, 34.90, 31.88, 29.37, 26.20, 25.94, 25.41, 22.59, 14.09. **^{19}F**

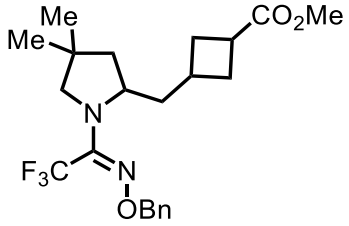
NMR (376 MHz, $CDCl_3$) δ -65.87. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{32}F_3N_2O^+$ $[M+H]^+$ 385.2461, found 385.2460.



(*E*)-1-(2-(2-(bicyclo[2.2.1]hept-5-en-2-yl)ethyl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3r). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 114 µL of 5-vinyl-2-norbornene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3r** (30.6 mg, 73%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 47(*endo*):39(*endo*):7(*exo*):7(*exo*) mixture of diastereomers) δ 7.40 – 7.28 (m, 5H), 6.10 – 6.05 (m, 0.93H), 6.03 (dd, *J* = 5.7, 2.9 Hz, 0.07H), 5.99 (dd, *J* = 5.7, 2.9 Hz, 0.14H), 5.85 (dd, *J* = 5.7, 2.9 Hz, 0.39H), 5.81 (dd, *J* = 5.8, 2.9 Hz, 0.47H), 5.08 – 4.98 (m, 2H), 4.21 – 4.09 (m, 1H), 3.23 – 3.15 (m, 1H), 3.02 – 2.95 (m, 1H), 2.77 – 2.64 (m, 1.86H), 2.41 (dd, *J* = 11.0, 2.3 Hz, 0.14H), 1.85 – 1.71 (m, 3H), 1.69 – 1.56 (m, 1H), 1.38 – 1.33 (m, 1H), 1.30 – 1.10 (m, 3H), 1.08 – 0.99 (m, 6H), 0.96 – 0.77 (m, 2H), 0.40 (tt, *J* = 10.3, 3.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$, 47(*endo*):39(*endo*):7(*exo*):7(*exo*) mixture of diastereomers, only the major diastereomer is characterized) δ 140.95 (q, *J* = 30.9 Hz), 137.08, 137.07, 132.25, 128.48, 128.33, 127.93, 119.64 (q, *J* = 278.3 Hz), 77.09, 62.04 (d, *J* = 2.5 Hz), 60.23, 49.58, 45.66, 45.18, 42.52, 38.87, 37.89, 33.95, 32.44, 30.38, 26.17, 26.16. **^{19}F NMR** (376 MHz, $CDCl_3$, 47(*endo*):39(*endo*):7(*exo*):7(*exo*) mixture of diastereomers, only the two *endo* diastereomers are characterized) δ -65.78, -65.84. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{32}F_3N_2O^+$ $[M+H]^+$ 421.2461, found 421.2460.

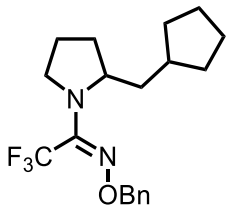


(*E*)-1-(2-(bicyclo[2.2.1]heptan-2-yl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3s). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 75.3 mg of 2-norbornene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3m** (30.6 mg, 78%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 88:6:6 mixture of diastereomers) δ 7.40 – 7.28 (m, 5H), 5.06 (s, 2H), 4.26 (q, *J* = 7.8 Hz, 0.88H), 4.18 (q, *J* = 7.2 Hz, 0.06H), 4.06 (m, 0.06H), 3.17 (d, *J* = 9.7 Hz, 1H), 2.94 (dd, *J* = 9.8, 1.5 Hz, 1H), 2.19 – 2.06 (m, 1H), 2.02 – 1.86 (m, 1H), 1.76 – 1.59 (m, 2H), 1.52 – 1.37 (m, 2H), 1.31 (dd, *J* = 12.4, 7.9 Hz, 1H), 1.24 – 1.13 (m, 2H), 1.12 – 0.90 (m, 10H). **^{13}C NMR** (151 MHz, $CDCl_3$, 88:6:6 mixture of diastereomers, only the major diastereomer is characterized) δ 141.98 (q, *J* = 31.1 Hz), 137.27, 128.33, 128.19, 127.88, 119.79 (q, *J* = 278.9 Hz), 76.95, 62.73, 62.61, 47.11, 42.70, 38.77, 38.00, 36.34, 35.65, 33.52, 30.84, 28.64, 26.92, 26.27. **^{19}F NMR** (376 MHz, $CDCl_3$, 88:6:6 mixture of diastereomers) δ -64.49, -65.16 (major), -65.39. **HRMS** (ESI-TOF): *m/z* calculated for $C_{22}H_{30}F_3N_2O^+$ $[M+H]^+$ 395.2305, found 395.2299.

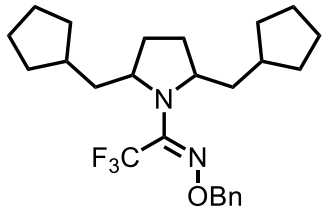


methyl (*E*)-3-((1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)methyl)cyclobutane-1-carboxylate (3t). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **1g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 0.1 mL of methyl 3-methylenecyclobutanecarboxylate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **3t** (23.4 mg, 55%) as a colorless oil. Isolated as a 96:4 ratio of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$, 70:30 mixture of diastereomers) δ 7.41 – 7.29 (m, 5H), 5.04 (d, *J* = 5.1 Hz, 2H), 4.13 (dqd, *J* = 9.6, 6.6, 6.1, 2.7 Hz, 1H), 3.67 (d, *J* = 12.4 Hz, 3H), 3.17 (d, *J* = 9.3 Hz, 1H), 3.01 – 2.94 (m, 1H), 2.94 – 2.83 (m, 1H), 2.33 – 1.95 (m, 3H), 1.90 – 1.64 (m, 4H), 1.33 – 1.14 (m, 2H), 1.05 (s, 3H), 1.01 (d, *J* = 3.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 70:30 mixture of diastereomers, only the major diastereomer

is characterized) δ 176.60, 140.68 (q, *J* = 31.0 Hz), 137.07, 128.60, 128.37, 128.10, 119.58 (q, *J* = 278.4 Hz), 77.19, 61.66, 58.47, 51.66 (d, *J* = 2.2 Hz), 45.67, 41.02, 37.94, 35.09, 31.13, 29.57, 29.33, 26.05, 25.90. **^{19}F NMR** (376 MHz, $CDCl_3$, 70:30 mixture of diastereomers) δ -65.86. **HRMS** (ESI-TOF): *m/z* calculated for $C_{22}H_{30}F_3N_2O_3^+$ $[M+H]^+$ 427.2203, found 427.2193.

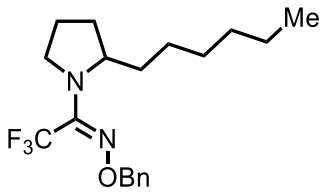


(*E*)-1-(2-(cyclopentylmethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3u-mono). Prepared via Procedure C (described above) using 27.2 mg (0.1 mmol, 1.0 equiv) of **1a-3**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 84 µL of methylenecyclopentane (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3u-mono** (14.2 mg, 40%) and **3u-di** (4.3 mg, 10%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 – 7.28 (m, 5H), 5.06 – 4.97 (m, 2H), 4.21 (dtd, *J* = 10.2, 6.6, 3.3 Hz, 1H), 3.47 (dddd, *J* = 9.8, 8.4, 6.9, 1.2 Hz, 1H), 3.32 (ddd, *J* = 9.8, 7.5, 4.0 Hz, 1H), 2.01 (dtd, *J* = 12.3, 7.2, 5.1 Hz, 1H), 1.85 (tdd, *J* = 11.7, 6.8, 4.5 Hz, 1H), 1.79 – 1.71 (m, 1H), 1.71 – 1.64 (m, 1H), 1.62 – 1.36 (m, 8H), 1.17 (ddd, *J* = 12.4, 10.5, 4.6 Hz, 1H), 0.99 (dq, *J* = 12.4, 8.1 Hz, 1H), 0.88 (dq, *J* = 12.2, 8.7, 8.3 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.47 (q, *J* = 30.6 Hz), 137.01, 128.75, 128.29, 128.03, 119.61 (q, *J* = 278.3 Hz), 77.21, 59.85, 48.90 (q, *J* = 2.7 Hz), 40.32, 37.28, 33.64, 31.52, 30.86, 25.05, 24.85, 24.26. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.89. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{26}F_3N_2O^+$ $[M+H]^+$ 355.1992, found 355.1990.

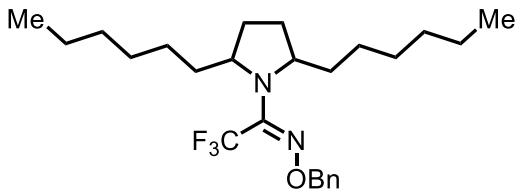


(*E*)-1-(2,5-bis(cyclopentylmethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3u-di). ^{1}H NMR (600 MHz, $CDCl_3$, 92:8 mixture of diastereomers) δ 7.41 – 7.28 (m, 5H), 5.02

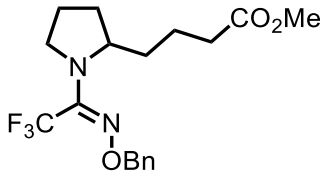
(s, 2H), 3.84 – 3.79 (m, 1.86H), 3.75 – 3.67 (m, 0.14H), 1.90 – 1.82 (m, 2H), 1.74 – 1.65 (m, 6H), 1.54 – 1.31 (m, 14H), 1.02 – 0.87 (m, 4H). **^{13}C NMR** (151 MHz, CDCl3, 92:8 mixture of diastereomers, only the major diastereomer is characterized) δ 141.72 (q, *J* = 29.8 Hz), 136.97, 128.98, 128.28, 128.04, 119.63 (q, *J* = 278.9 Hz), 76.30, 61.17, 42.82, 38.00, 33.55, 31.31, 29.66, 24.90, 24.79. **^{19}F NMR** (376 MHz, $CDCl_3$, 92:8 mixture of diastereomers, only the major diastereomer is characterized) δ -63.98. **HRMS** (ESI-TOF): *m/z* calculated for $C_{25}H_{36}F_3N_2O^+$ $[M+H]^+$ 437.2774, found 437.2765.



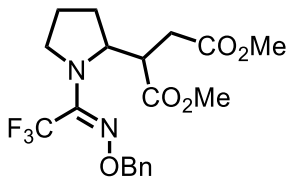
(*E*)-2,2,2-trifluoro-1-(2-hexylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (3v-mono). Prepared via Procedure C (described above) using 27.2 mg (0.1 mmol, 1.0 equiv) of **1a-3**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 101 µL of *cis*-2-hexene (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (4% EtOAc/hexanes) to afford **3v-mono** (16.1 mg, 45%) and **3v-di** (2.7 mg, 6%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 5H), 5.01 (q, *J* = 11.3 Hz, 2H), 4.17 (dtd, *J* = 9.2, 6.2, 3.2 Hz, 1H), 3.47 (dddd, *J* = 9.5, 8.1, 6.8, 1.2 Hz, 1H), 3.32 (ddd, *J* = 9.8, 7.4, 4.3 Hz, 1H), 1.98 (dtd, *J* = 12.5, 7.3, 5.3 Hz, 1H), 1.84 (tdd, *J* = 11.9, 6.8, 4.7 Hz, 1H), 1.74 (dddd, *J* = 15.6, 12.2, 8.3, 7.4 Hz, 1H), 1.56 – 1.44 (m, 2H), 1.30 – 0.99 (m, 9H), 0.87 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.43 (q, *J* = 30.7 Hz), 136.96, 128.69, 128.34, 128.07, 119.62 (q, *J* = 278.3 Hz), 77.22, 60.49, 49.03 (q, *J* = 2.9 Hz), 34.47, 31.88, 30.70, 29.41, 25.83, 24.17, 22.60, 14.10. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.95. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{28}F_3N_2O^+$ $[M+H]^+$ 357.2148, found 357.2147.



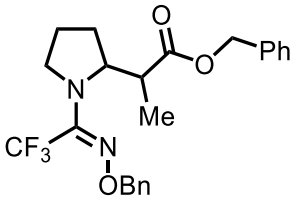
(*E*)-1-(2,5-dihexylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3v-di). **^{1}H NMR** (600 MHz, $CDCl_3$, 90:10 mixture of diastereomers) δ 7.40 – 7.29 (m, 5H), 5.00 (s, 2H), 3.76 – 3.71 (m, 1.80H), 3.67 – 3.60 (m, 0.20H), 1.88 – 1.79 (m, 2H), 1.76 – 1.67 (m, 2H), 1.64 – 1.57 (m, 2H), 1.22 – 1.07 (m, 16H), 1.05 – 0.98 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$, 90:10 mixture of diastereomers, only the major diastereomer is characterized) δ 141.68 (q), 136.80, 128.91, 128.31, 128.10, 119.61 (q, *J* = 278.9 Hz), 77.31, 61.87, 37.23, 31.86, 29.59, 29.29, 26.97, 22.61, 14.09. **^{19}F NMR** (376 MHz, $CDCl_3$, 90:10 mixture of diastereomers, only the major diastereomer is characterized) δ -64.25. **HRMS** (ESI-TOF): *m/z* calculated for $C_{25}H_{40}F_3N_2O^+$ $[M+H]^+$ 441.3087, found 441.3087.



methyl (*E*)-4-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)butanoate (3w). Prepared via Procedure C (described above) using 27.2 mg (0.1 mmol, 1.0 equiv) of **1a-3**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 85 µL of methylcrotonate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **3w** (14.2 mg, 35%) as a colorless oil. Isolated as a 97:3 mixture of geometrical isomers. Only the major diastereomer isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 – 7.29 (m, 5H), 5.06 – 4.96 (m, 2H), 4.19 (dtd, *J* = 9.8, 6.4, 2.7 Hz, 1H), 3.66 (s, 3H), 3.50 – 3.43 (m, 1H), 3.32 (ddd, *J* = 9.8, 7.4, 4.4 Hz, 1H), 2.20 – 2.09 (m, 2H), 2.00 (dtd, *J* = 12.6, 7.3, 5.4 Hz, 1H), 1.85 (tdd, *J* = 12.0, 6.8, 4.8 Hz, 1H), 1.80 – 1.70 (m, 1H), 1.56 – 1.42 (m, 3H), 1.39 – 1.27 (m, 1H), 1.12 – 1.04 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.82, 140.26 (q, *J* = 30.8 Hz), 136.90, 128.81, 128.41, 128.16, 119.56 (q, *J* = 278.1 Hz), 77.30, 60.01, 51.50, 49.08 (q, *J* = 2.9 Hz), 33.90, 33.88, 30.63, 24.13, 21.16. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.97. **HRMS** (ESI-TOF): *m/z* calculated for $C_{18}H_{24}F_3N_2O_3^+$ $[M+H]^+$ 373.1734, found 373.1731.

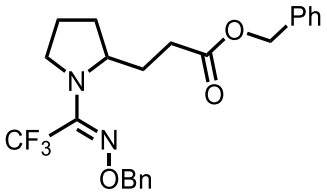


dimethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)succinate (3x). Prepared via Procedure C (described above) using 27.2 mg (0.1 mmol, 1.0 equiv) of **1a-3**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 0.1 mL of dimethylmaleate (0.8 mmol, 8.0 equiv), and 0.1 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (8% EtOAc/hexanes) to afford **3x** (9.6 mg, 23%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 92:8 mixture of diastereomers, only the major diastereomer is characterized) δ 7.39 – 7.30 (m, 5H), 5.07 – 4.98 (m, 2H), 4.44 – 4.38 (m, 1H), 3.68 – 3.62 (m, 6H), 3.41 – 3.29 (m, 2H), 3.16 (ddd, *J* = 11.6, 4.8, 3.5 Hz, 1H), 2.58 (dd, *J* = 16.7, 11.6 Hz, 1H), 1.96 – 1.83 (m, 2H), 1.83 – 1.68 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 92:8 mixture of diastereomers, only the major diastereomer is characterized) δ 173.35, 171.76, 140.02 (q, *J* = 31.1 Hz), 136.42, 128.90, 128.46, 128.36, 119.53 (q, *J* = 277.9 Hz), 77.59, 61.46, 51.96, 51.83, 49.67 (q, *J* = 3.1 Hz), 43.22, 33.49, 26.92, 23.77. **^{19}F NMR** (376 MHz, $CDCl_3$, 92:8 mixture of diastereomers) δ -65.70 (minor), -65.74. **HRMS** (ESI-TOF): *m/z* calculated for $C_{19}H_{24}F_3N_2O_5^+$ $[M+H]^+$ 417.1632, found 417.1626.

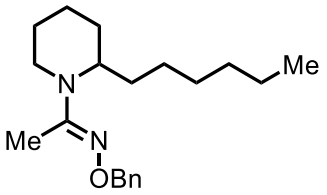


benzyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (3y-B). Prepared via Procedure C (described above) using 27.2 mg (0.1 mmol, 1.0 equiv) of **1a-3**, 2.8 mg of $[Ir(cod)_2]OTf$ (0.005 mmol, 0.05 equiv), 0.12 mL of benzyl acrylate (0.8 mmol, 8.0 equiv), and 0.5 mL of degassed PhCl at 85 °C under Ar for 6 h. The reaction was purified by preparative TLC (8% EtOAc/hexanes) to afford **3y-B** (24.9 mg, 57%) and **3y-L** (9.5 mg, 22%) as colorless oils. **3y-B** was isolated as a 96:4 mixture of geometrical isomers. Only the major geometrical isomer is characterized. **^{1}H NMR** (600 MHz, $CDCl_3$, 69:31 mixture of diastereomers) δ 7.39 – 7.23 (m, 10H), 5.15 – 4.96 (m, 4H), 4.81 (td, *J* = 7.1, 4.5 Hz, 0.69H), 4.41 (dt, *J* = 7.7, 5.8 Hz, 0.31H), 3.46 – 3.39 (m, 0.69H), 3.39 – 3.32 (m, 1H), 3.29 – 3.22 (m, 0.31H), 2.85 (qd, *J* = 7.1, 4.5 Hz, 0.69H), 2.73 (qd, *J* = 7.1, 5.3 Hz, 0.31H), 1.94 – 1.60 (m, 4H), 1.00 (d, *J* = 7.1 Hz, 2.07H), 0.94 (d, *J* = 7.2 Hz, 0.93H). **^{13}C NMR** (151 MHz, $CDCl_3$, 69:31 mixture of diastereomers, only the major diastereomer is characterized) δ 173.94, 139.87 (q, *J* = 31.0 Hz), 136.63, 136.04, 128.73, 128.52, 128.41, 128.30, 128.16, 128.05, 119.55 (q, *J* = 278.2 Hz), 77.42, 66.12, 60.55, 50.29 (q, *J*

= 2.7 Hz), 40.82, 25.99, 24.49, 9.42. **^{19}F NMR** (376 MHz, $CDCl_3$, 69:31 mixture of diastereomers) δ -65.48 (minor), -65.64. **HRMS** (ESI-TOF): *m/z* calculated for $C_{23}H_{26}F_3N_2O_3^+$ $[M+H]^+$ 435.1890, found 435.1881.

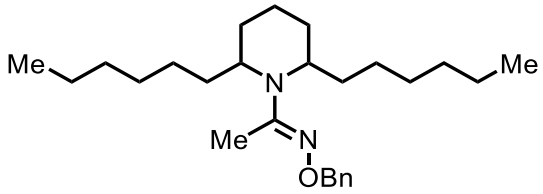


benzyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (3y-L). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 10H), 5.09 (d, *J* = 1.5 Hz, 2H), 5.00 (q, *J* = 11.2 Hz, 2H), 4.21 (dddd, *J* = 9.4, 7.2, 5.8, 3.6 Hz, 1H), 3.53 – 3.46 (m, 1H), 3.32 (ddd, *J* = 9.8, 7.5, 4.7 Hz, 1H), 2.16 (ddd, *J* = 16.2, 10.9, 5.6 Hz, 1H), 2.08 (ddd, *J* = 15.8, 10.5, 5.6 Hz, 1H), 1.99 – 1.80 (m, 3H), 1.79 – 1.70 (m, 1H), 1.53 – 1.43 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 172.86, 140.16 (q, *J* = 30.8 Hz), 136.72, 135.93, 128.77, 128.58, 128.41, 128.31, 128.29, 128.16, 119.51 (q, *J* = 278.1 Hz), 77.35, 66.31, 59.57, 49.24 (q, *J* = 2.8 Hz), 30.70, 30.44, 29.57, 23.94. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -65.89. **HRMS** (ESI-TOF): *m/z* calculated for $C_{23}H_{26}F_3N_2O_3^+$ $[M+H]^+$ 435.1890, found 435.1885.

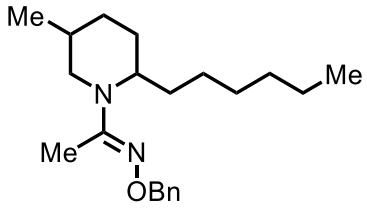


(*E*)-1-(2-hexylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5b-mono). Prepared via Procedure C (described above) using 23.2 mg (0.1 mmol, 1.0 equiv) of **4b**, 3.4 mg of $[Ir(cod)Cl]_2$ (0.005 mmol, 0.05 equiv), 3.4 mg of $AgSbF_6$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **5b-mono** (16.0 mg, 50%) and **5b-di** (5.9 mg, 15%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 – 7.24 (m, 5H), 4.96 – 4.86 (m, 2H), 3.71 (ddt, *J* = 9.2, 6.0, 3.1 Hz, 1H), 3.60 (ddd, *J* = 13.2, 4.2, 2.5 Hz, 1H), 2.75 (td, *J* = 13.1, 2.5 Hz, 1H), 1.96 (s, 3H), 1.65 – 1.50 (m, 6H), 1.49 – 1.38 (m, 2H), 1.34 – 1.13 (m, 8H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.82, 138.86, 128.25, 128.09, 127.30, 75.19, 52.30,

40.44, 31.83, 29.39, 28.38, 27.48, 26.78, 25.16, 22.65, 19.10, 14.10, 11.72. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{33}N_2O^+$ $[M+H]^+$ 317.2587, found 317.2586.

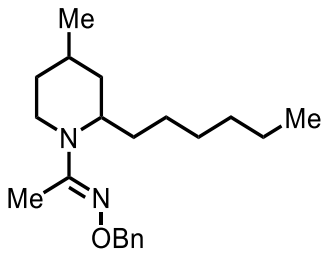


(*E*)-1-(2,6-dihexylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5b-di). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.22 (m, 5H), 5.01 – 4.92 (m, 2H), 3.18 (qd, *J* = 6.5, 3.8 Hz, 2H), 1.90 (s, 3H), 1.77 – 1.68 (m, 2H), 1.63 – 1.46 (m, 6H), 1.43 – 1.33 (m, 2H), 1.32 – 1.09 (m, 16H), 0.88 (t, *J* = 7.2 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.88, 139.45, 128.08, 127.85, 127.19, 75.10, 53.78, 31.95, 31.44, 29.41, 27.44, 26.66, 22.68, 19.13, 14.29, 14.13. **HRMS** (ESI-TOF): *m/z* calculated for $C_{26}H_{45}N_2O^+$ $[M+H]^+$ 401.3526, found 401.3522.

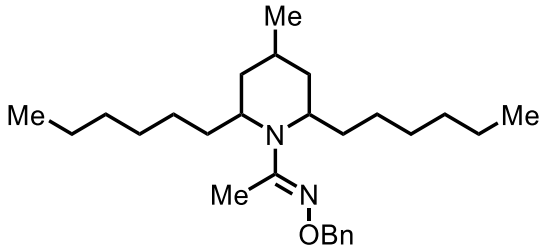


(*E*)-1-(2-hexyl-5-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5c). Prepared via Procedure C (described above) using 24.6 mg (0.1 mmol, 1.0 equiv) of **4c**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **5c** (23.9 mg, 72%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ 7.41 – 7.34 (m, 2H), 7.34 – 7.29 (m, 2H), 7.29 – 7.23 (m, 1H), 4.97 – 4.85 (m, 2H), 3.76 – 3.67 (m, 1H), 3.60 – 3.53 (m, 0.5H), 3.26 – 3.18 (m, 0.5H), 3.01 (dd, *J* = 13.3, 3.3 Hz, 0.5H), 2.36 (dd, *J* = 13.3, 11.2 Hz, 0.5H), 1.95 (d, *J* = 9.3 Hz, 3H), 1.88 – 1.76 (m, 1.5H), 1.67 – 1.57 (m, 1H), 1.57 – 1.35 (m, 3.5H), 1.34 – 1.13 (m, 9H), 0.96 (d, *J* = 6.9 Hz, 1.5H), 0.92 – 0.83 (m, 4.5H). **^{13}C NMR** (151 MHz, $CDCl_3$, 50:50 mixture of diastereomers) δ 159.35, 158.75, 138.95, 138.83, 128.28, 128.25, 128.08, 128.06, 127.31, 127.27, 75.21, 75.15, 52.55, 51.57, 47.37, 46.59, 31.85, 31.84, 30.70, 29.43, 29.39, 28.80, 28.35, 28.09, 27.95, 27.45, 26.81, 26.67, 25.84, 22.69, 22.67, 22.65, 19.58, 17.43, 14.11, 14.10, 11.93, 11.80 (Due to similar peak intensities, the

diastereomeric carbon peaks could not be distinguished). **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{35}N_2O^+$ $[M+H]^+$ 331.2744, found 331.2748.

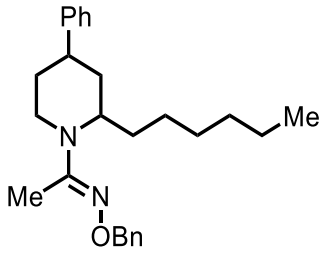


(*E*)-1-(2-hexyl-4-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5d-mono). Prepared via Procedure C (described above) using 24.6 mg (0.1 mmol, 1.0 equiv) of **4d**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **5d-mono** (16.2 mg, 49%) and **5d-di** (13.6 mg, 33%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 75:25 mixture of diastereomers) δ 7.42 – 7.22 (m, 5H), 5.03 – 4.86 (m, 2H), 3.74 (q, *J* = 6.7 Hz, 0.25H), 3.68 – 3.60 (m, 0.25H), 3.25 – 2.95 (m, 2.25H), 2.76 (td, *J* = 13.2, 2.8 Hz, 0.25H), 1.99 – 1.82 (m, 3H), 1.78 – 1.36 (m, 5H), 1.34 – 1.02 (m, 10H), 1.00 – 0.81 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$, 75:25 mixture of diastereomers, only the major diastereomer is characterized) δ 158.41, 139.04, 128.12, 128.08, 127.31, 75.21, 56.26, 44.57, 36.79, 33.83, 32.31, 31.91, 29.47, 28.64, 26.20, 22.67, 21.84, 14.13, 12.98. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{35}N_2O^+$ $[M+H]^+$ 331.2744, found 331.2744.

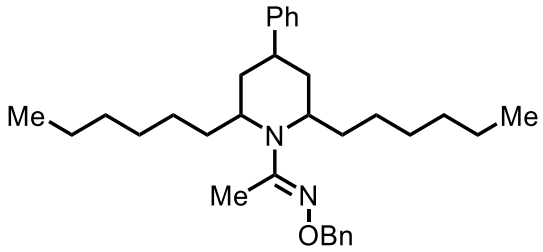


(*E*)-1-(2,6-dihexyl-4-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5d-di). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.21 (m, 5H), 5.01 – 4.93 (m, 2H), 3.31 (tdd, *J* = 7.5, 5.1, 2.3 Hz, 1H), 2.97 (dtd, *J* = 11.1, 6.4, 3.2 Hz, 1H), 1.89 (s, 3H), 1.88 – 1.80 (m, 1H), 1.72 – 1.57 (m, 2H), 1.48 (ddt, *J* = 13.2, 3.9, 2.0 Hz, 1H), 1.43 – 1.33 (m, 3H), 1.34 – 1.22 (m, 10H), 1.22 – 1.14 (m, 4H), 1.14 – 1.03 (m, 4H), 0.91 – 0.82 (m, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.84, 139.46, 128.10, 127.85,

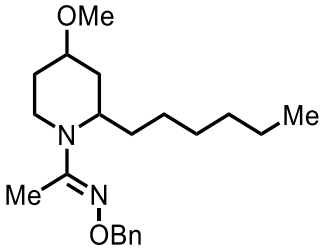
127.21, 75.10, 55.23, 53.05, 37.60, 35.85, 33.23, 32.01, 31.90, 29.60, 29.42, 29.40, 27.05, 26.28, 25.96, 22.70, 22.66, 22.49, 14.64, 14.15, 14.11. **HRMS** (ESI-TOF): *m/z* calculated for $C_{27}H_{47}N_2O^+$ $[M+H]^+$ 415.3683, found 415.3687.



(*E*)-1-(2-hexyl-4-phenylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5e-mono). Prepared via Procedure C (described above) using 30.8 mg (0.1 mmol, 1.0 equiv) of **4e**, 3.4 mg of $[Ir(cod)Cl]_2$ (0.005 mmol, 0.05 equiv), 3.4 mg of $AgSbF_6$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **5e-mono** (10.9 mg, 28%) and **5e-di** (16.2 mg, 34%) as colorless oils. ^{1}H NMR (600 MHz, $CDCl_3$, 77:23 mixture of diastereomers) δ 7.41 – 7.26 (m, 7H), 7.23 – 7.14 (m, 3H), 5.02 – 4.90 (m, 2H), 3.94 – 3.83 (m, 0.23H), 3.77 (ddd, *J* = 13.6, 4.3, 2.2 Hz, 0.23H), 3.35 (dt, *J* = 13.3, 5.3 Hz, 0.77H), 3.27 (ddt, *J* = 9.8, 7.6, 4.7 Hz, 0.77H), 3.08 (ddd, *J* = 13.2, 8.6, 4.6 Hz, 0.77H), 2.96 – 2.84 (m, 0.46H), 2.65 (tt, *J* = 11.6, 4.4 Hz, 0.77H), 1.99 (d, *J* = 13.0 Hz, 3H), 1.94 – 1.88 (m, 1H), 1.87 – 1.57 (m, 4H), 1.47 – 1.37 (m, 1H), 1.33 – 1.12 (m, 8H), 0.88 (dt, *J* = 14.4, 7.1 Hz, 3H).**^{13}C NMR** (151 MHz, $CDCl_3$, 77:23 mixture of diastereomers, only the major diastereomer is characterized) δ 158.01, 146.34, 139.09, 128.41, 128.16, 128.05, 127.35, 126.90, 126.09, 75.27, 57.25, 46.04, 40.61, 36.24, 33.77, 31.88, 31.68, 29.43, 26.03, 22.65, 14.12, 13.17. **HRMS** (ESI-TOF): *m/z* calculated for $C_{26}H_{37}N_2O^+$ $[M+H]^+$ 393.2900, found 393.2892.

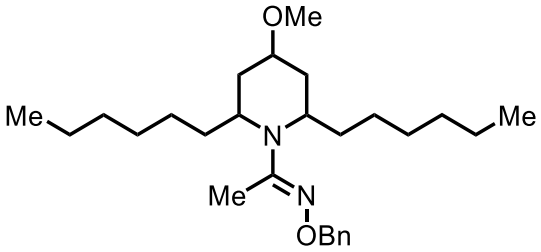


(*E*)-1-(2,6-dihexyl-4-phenylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5e-di). The major diastereomer was isolated and characterized (other diastereomer = 6%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 2H), 7.38 – 7.33 (m, 2H), 7.33 – 7.28 (m, 3H), 7.24 – 7.19 (m, 1H), 7.19 – 7.14 (m, 2H), 5.04 (d, *J* = 1.3 Hz, 2H), 3.42 (tdd, *J* = 7.5, 5.0, 2.3 Hz, 1H), 3.11 (dtd, *J* = 11.6, 6.4, 2.9 Hz, 1H), 2.85 (tt, *J* = 12.6, 4.0 Hz, 1H), 2.01 – 1.88 (m, 5H), 1.85 – 1.72 (m, 2H), 1.72 – 1.66 (m, 1H), 1.63 – 1.49 (m, 2H), 1.50 – 1.41 (m, 1H), 1.41 – 1.08 (m, 16H), 0.95 – 0.86 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.55, 146.72, 139.54, 128.35, 128.14, 127.86, 127.23, 126.97, 126.01, 75.15, 55.26, 53.27, 37.79, 36.45, 34.70, 33.01, 31.98, 31.89, 29.38, 26.99, 26.30, 22.67 (d, *J* = 3.7 Hz), 14.72, 14.14, 14.11. **HRMS** (ESI-TOF): *m/z* calculated for $C_{32}H_{49}N_2O^+$ $[M+H]^+$ 477.3839, found 477.3842.

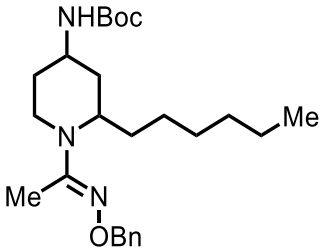


(*E*)-1-(2-hexyl-4-methoxypiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5f-mono). Prepared via Procedure C (described above) using 26.2 mg (0.1 mmol, 1.0 equiv) of **4f**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 μL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (8% EtOAc/hexanes) to afford **5f-mono** (12.1 mg, 35%) and **5f-di** (14.3 mg, 33%) as colorless oils. **5f-mono** was obtained as a mixture of two separable diastereomers in a ratio of 57:43. First diastereomer (20% isolated yield): **^{1}H NMR** (600 MHz, $CDCl_3$, 4.1:1 mixture of rotational/geometrical isomers) δ 7.42 – 7.27 (m, 5H), 4.98 – 4.90 (m, 2H), 3.94 – 3.62 (m, 1H), 3.49 (p, *J* = 3.6 Hz, 1H), 3.45 (dt, *J* = 13.6, 4.0 Hz, 1H), 3.31 (s, 3H), 3.10 (ddd, *J* = 13.5, 11.6, 3.5 Hz, 1H), 2.10 – 1.83 (m, 4H), 1.77 – 1.65 (m, 4H), 1.45 – 1.20 (m, 9H), 0.94 – 0.88 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 4.1:1 mixture of rotational/geometrical isomers, only the major isomer is characterized) δ 158.40, 138.87, 128.27, 128.11, 127.34, 75.23, 74.57, 55.96, 52.10, 36.37, 31.87, 31.67, 30.32, 29.35, 28.74, 27.08, 22.66, 14.11, 11.88. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{35}N_2O_2^+$ $[M+H]^+$ 347.2693, found 347.2694. Second diastereomer (15% isolated yield): **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 – 7.23 (m, 5H), 4.95 – 4.87 (m, 2H), 3.86 (q, *J* = 6.9 Hz, 1H), 3.75 (ddt, *J* = 13.5, 4.7, 2.2 Hz, 1H), 3.45

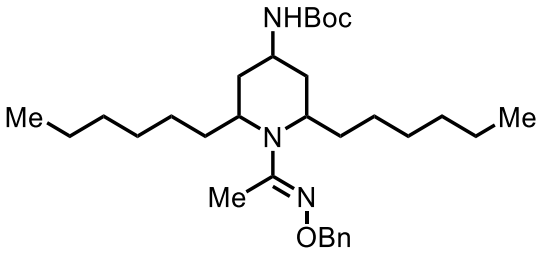
(tt, *J* = 11.3, 4.4 Hz, 1H), 3.34 (s, 3H), 2.76 (td, *J* = 13.5, 2.7 Hz, 1H), 2.04 – 1.93 (m, 5H), 1.49 – 1.40 (m, 3H), 1.37 – 1.18 (m, 9H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.07, 138.75, 128.25, 128.14, 127.39, 75.27, 73.85, 55.41, 52.64, 38.92, 33.51, 31.78, 30.94, 29.69, 29.27, 26.81, 22.63, 14.09, 11.73. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{35}N_2O_2^+$ $[M+H]^+$ 347.2693, found 347.2698.



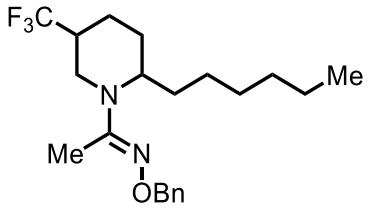
(*E*)-1-(2,6-dihexyl-4-methoxypiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5f-di). 5f-di was obtained as a mixture of two separable diastereomers in a ratio of 76:24. First diastereomer (25% isolated yield): **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 – 7.22 (m, 5H), 4.99 – 4.92 (m, 2H), 3.49 – 3.37 (m, 2H), 3.31 (s, 3H), 3.06 – 2.99 (m, 1H), 1.99 – 1.91 (m, 1H), 1.91 – 1.85 (m, 4H), 1.79 – 1.73 (m, 1H), 1.72 – 1.61 (m, 2H), 1.49 – 1.05 (m, 19H), 0.88 (td, *J* = 7.1, 6.3 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.12, 139.36, 128.13, 127.89, 127.26, 75.17, 74.70, 55.36, 53.81, 52.27, 33.64, 32.91, 32.76, 31.94, 31.87, 30.75, 29.28, 26.92, 26.45, 22.68, 22.65, 14.39, 14.13, 14.10. **HRMS** (ESI-TOF): *m/z* calculated for $C_{27}H_{47}N_2O_2^+$ $[M+H]^+$ 431.3632, found 431.3625. Second diastereomer (8% isolated yield): **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 – 7.23 (m, 5H), 4.97 (s, 2H), 3.37 – 3.25 (m, 6H), 2.04 (dt, *J* = 13.4, 5.1 Hz, 2H), 1.90 (s, 3H), 1.53 – 1.38 (m, 5H), 1.36 – 1.11 (m, 17H), 0.88 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.64, 138.95, 128.12, 127.37, 75.71, 75.39, 55.76, 53.81, 36.01, 33.59, 31.85, 29.39, 26.47, 22.70, 14.11, 11.47. **HRMS** (ESI-TOF): *m/z* calculated for $C_{27}H_{47}N_2O_2^+$ $[M+H]^+$ 431.3632, found 431.3623.



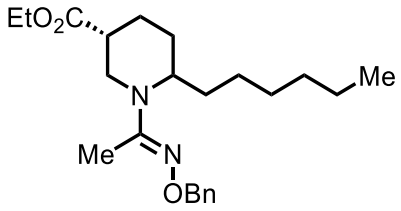
tert-butyl (*E*)-(1-(1-((benzyloxy)imino)ethyl)-2-hexylpiperidin-4-yl)carbamate (5g-mono). Prepared via Procedure C (described above) using 34.7 mg (0.1 mmol, 1.0 equiv) of **4g**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (10% EtOAc/hexanes) to afford **5g-mono** (10.8 mg, 25%) and **5g-di** (24.6 mg, 48%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$, 73:27 mixture of diastereomers) δ 7.39 – 7.24 (m, 5H), 4.98 – 4.85 (m, 2H), 4.55 – 4.19 (m, 1H), 3.89 – 3.72 (m, 1.46H), 3.72 – 3.63 (m, 1H), 3.41 – 3.30 (m, 0.27H), 3.22 (ddd, *J* = 13.7, 6.6, 4.3 Hz, 0.27H), 3.11 (ddd, *J* = 13.7, 8.6, 3.7 Hz, 0.27H), 2.83 (td, *J* = 13.4, 2.7 Hz, 0.73H), 1.94 (d, *J* = 13.4 Hz, 3H), 1.92 – 1.65 (m, 2H), 1.57 – 1.48 (m, 2H), 1.44 (s, 9H), 1.38 – 1.13 (m, 10H), 0.90 – 0.85 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 73:27 mixture of diastereomers, only the major diastereomer is characterized) δ 158.07, 155.13, 138.77, 128.26, 128.13, 127.39, 79.31, 75.27, 52.46, 44.11, 39.26, 34.74, 32.45, 31.77, 30.32, 29.31, 29.25, 28.43, 26.77, 22.65, 14.09, 11.76. **HRMS** (ESI-TOF): *m/z* calculated for $C_{25}H_{42}N_3O_3^+$ $[M+H]^+$ 432.3221, found 432.3226.



tert-butyl (*E*)-(1-(1-((benzyloxy)imino)ethyl)-2,6-dihexylpiperidin-4-yl)carbamate (5g-di). Isolated yield consists of two separable diastereomers (38% + 10%). Only the major diastereomer was characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 – 7.22 (m, 5H), 5.00 – 4.91 (m, 2H), 4.26 (d, *J* = 8.3 Hz, 1H), 3.75 (s, 1H), 3.34 (dtd, *J* = 8.6, 5.9, 2.2 Hz, 1H), 2.97 (dtd, *J* = 10.1, 6.6, 3.0 Hz, 1H), 1.88 (m, 4H), 1.80 – 1.51 (m, 4H), 1.44 (s, 9H), 1.42 – 1.01 (m, 19H), 0.87 (td, *J* = 7.1, 4.9 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.33, 155.17, 139.40, 128.14, 127.90, 127.30, 79.09, 75.18, 55.09, 52.27, 44.87, 35.28, 34.09, 32.38, 31.92, 31.81, 30.11, 29.24, 29.22, 28.45, 26.84, 26.34, 22.67, 22.64, 14.64, 14.13, 14.09. **HRMS** (ESI-TOF): *m/z* calculated for $C_{31}H_{54}N_3O_3^+$ $[M+H]^+$ 516.4160, found 516.4151.

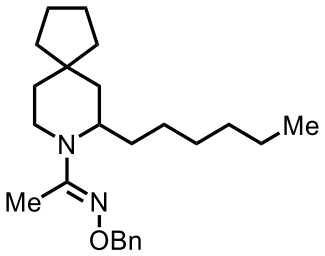


(*E*)-1-(2-hexyl-5-(trifluoromethyl)piperidin-1-yl)ethan-1-one *O*-benzyl oxime (5h). Prepared via Procedure C (described above) using 30.0 mg (0.1 mmol, 1.0 equiv) of **4h**, 3.4 mg of $[Ir(cod)Cl]_2$ (0.005 mmol, 0.05 equiv), 3.4 mg of $AgSbF_6$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 24 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **5h** (29.6 mg, 77%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 83:17 mixture of diastereomers) δ 7.40 – 7.23 (m, 5H), 4.96 – 4.88 (m, 2H), 3.88 (ddd, *J* = 13.0, 4.3, 1.8 Hz, 0.83H), 3.64 (ddd, *J* = 11.1, 6.5, 2.9 Hz, 1H), 3.62 – 3.57 (m, 0.17H), 3.13 (dd, *J* = 14.4, 5.0 Hz, 0.17H), 2.75 (dd, *J* = 13.3, 11.7 Hz, 0.83H), 2.35 – 2.20 (m, 1H), 1.95 (d, *J* = 0.9 Hz, 3H), 1.91 – 1.69 (m, 1H), 1.69 – 1.40 (m, 5H), 1.34 – 1.10 (m, 8H), 0.88 (td, *J* = 7.1, 1.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 83:17 mixture of diastereomers, only the major diastereomer is characterized) δ 157.68, 138.63, 126.93 (q), 128.48, 128.15, 127.49, 75.45, 51.75, 39.12 (q, *J* = 26.0 Hz), 38.58 (q, *J* = 3.4 Hz), 31.81, 29.27, 28.33, 26.69, 25.95, 22.63, 18.44 (q, *J* = 2.5 Hz), 14.08, 11.87. **^{19}F NMR** (376 MHz, $CDCl_3$, 83:17 mixture of diastereomers) δ -69.78 (minor), -72.98. **HRMS** (ESI-TOF): *m/z* calculated for $C_{21}H_{32}F_3N_2O^+$ $[M+H]^+$ 385.2461, found 385.2457.

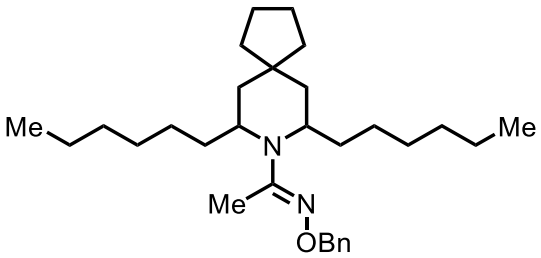


ethyl (3*R*)-1-((*E*)-1-((benzyloxy)imino)ethyl)-6-hexylpiperidine-3-carboxylate (5i). Prepared via Procedure C (described above) using 30.4 mg (0.1 mmol, 1.0 equiv) of **4i**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (8% EtOAc/hexanes) to afford **5i** (17.6 mg, 45%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 68:32 mixture of diastereomers) δ 7.43 – 7.20 (m, 5H), 4.95 – 4.86 (m, 2H), 4.19 – 4.08 (m, 2H), 4.01 –

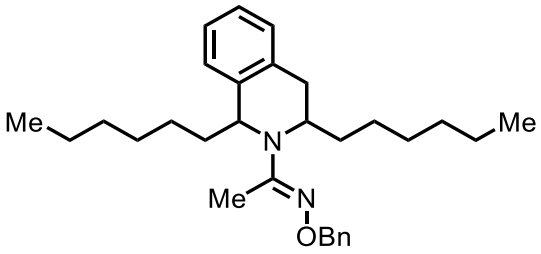
3.95 (m, 0.32H), 3.91 – 3.84 (m, 0.68H), 3.80 – 3.74 (m, 0.32H), 3.74 – 3.68 (m, 0.68H), 3.00 (dd, *J* = 13.6, 3.9 Hz, 0.32H), 2.85 (dd, *J* = 13.5, 11.8 Hz, 0.68H), 2.54 – 2.44 (m, 1H), 1.96 (d, *J* = 7.1 Hz, 3H), 1.88 – 1.68 (m, 2H), 1.67 – 1.42 (m, 4H), 1.34 – 1.13 (m, 11H), 0.88 (td, *J* = 7.0, 1.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 68:32 mixture of diastereomers, only the major diastereomer is characterized) δ 174.20, 158.04, 138.75, 128.40, 128.12, 127.40, 75.34, 60.38, 51.57, 41.62, 40.90, 31.82, 29.30, 28.40, 26.69, 22.64, 22.41, 14.23, 14.09, 11.83. **HRMS** (ESI-TOF): *m/z* calculated for $C_{23}H_{37}N_2O_3^+$ $[M+H]^+$ 389.2799, found 389.2796.



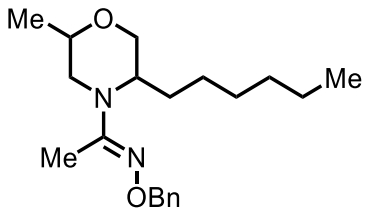
(*E*)-1-(7-hexyl-8-azaspiro[4.5]decan-8-yl)ethan-1-one *O*-benzyl oxime (5j-mono). Prepared via Procedure C (described above) using 28.6 mg (0.1 mmol, 1.0 equiv) of **4j**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **5j-mono** (13.2 mg, 36%) and **5j-di** (10.1 mg, 22%) as colorless oils. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.22 (m, 5H), 4.95 – 4.88 (m, 2H), 3.64 (dtd, *J* = 8.5, 6.5, 3.0 Hz, 1H), 3.55 – 3.49 (m, 1H), 2.88 (ddd, *J* = 13.7, 11.9, 3.1 Hz, 1H), 1.95 (s, 3H), 1.72 – 1.58 (m, 4H), 1.57 – 1.43 (m, 5H), 1.42 – 1.17 (m, 13H), 0.88 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.64, 138.90, 128.26, 128.10, 127.32, 75.21, 53.13, 42.71, 40.68, 39.05, 38.79, 36.73, 35.65, 31.84, 31.35, 29.38, 27.14, 25.06, 22.90, 22.66, 14.10, 11.92. **HRMS** (ESI-TOF): *m/z* calculated for $C_{24}H_{39}N_2O^+$ $[M+H]^+$ 371.3057, found 371.3054.



(*E*)-1-(7,9-dihexyl-8-azaspiro[4.5]decan-8-yl)ethan-1-one *O*-benzyl oxime (5j-di). Isolated yield consists of two separable diastereomers (15% + 7%). Only the major diastereomer was characterized. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.21 (m, 5H), 4.94 (q, *J* = 12.4 Hz, 2H), 3.21 (qd, *J* = 6.9, 4.5 Hz, 2H), 1.89 (s, 3H), 1.84 – 1.75 (m, 2H), 1.60 – 1.51 (m, 5H), 1.48 – 1.32 (m, 8H), 1.32 – 1.12 (m, 17H), 0.88 (t, *J* = 7.2 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.57, 139.55, 128.07, 127.94, 127.17, 75.07, 53.41, 41.41, 41.00, 38.70, 32.72, 31.95, 29.37, 27.01, 23.99, 22.70, 14.12, 14.02. **HRMS** (ESI-TOF): *m/z* calculated for $C_{30}H_{51}N_2O^+$ $[M+H]^+$ 455.3996, found 455.4001.

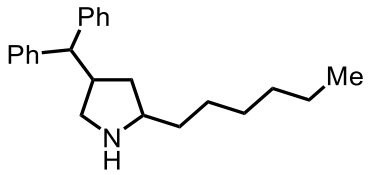


(*E*)-1-(1,3-dihexyl-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one *O*-benzyl oxime (5k). Prepared via Procedure C (described above) using 28.0 mg (0.1 mmol, 1.0 equiv) of **4k**, 6.9 mg of $[Ir(cod)_2]NTf_2$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **5k** (23.7 mg, 53%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 2H), 7.35 – 7.29 (m, 2H), 7.28 – 7.22 (m, 1H), 7.19 – 7.12 (m, 2H), 7.12 – 7.07 (m, 1H), 7.07 – 7.01 (m, 1H), 4.99 (d, *J* = 12.2 Hz, 1H), 4.94 (d, *J* = 12.2 Hz, 1H), 4.69 (dd, *J* = 8.3, 3.7 Hz, 1H), 3.93 – 3.87 (m, 1H), 2.99 (dd, *J* = 15.1, 4.9 Hz, 1H), 2.79 (dd, *J* = 15.2, 3.2 Hz, 1H), 2.10 (s, 3H), 1.75 – 1.66 (m, 1H), 1.58 – 1.49 (m, 1H), 1.32 – 1.03 (m, 17H), 0.99 – 0.90 (m, 1H), 0.83 (td, *J* = 7.2, 1.8 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.90, 139.36, 138.56, 133.99, 128.51, 128.12, 128.11, 127.25, 127.17, 126.34, 125.75, 75.22, 56.41, 52.31, 36.54, 32.56, 31.97, 31.89, 31.75, 29.23, 29.04, 26.45, 25.78, 22.66, 22.55, 14.09, 14.06, 12.20. **HRMS** (ESI-TOF): *m/z* calculated for $C_{30}H_{45}N_2O^+$ $[M+H]^+$ 449.3526, found 449.3523.

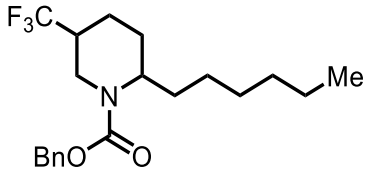


(*E*)-1-(5-hexyl-2-methylmorpholino)ethan-1-one *O*-benzyl oxime (5l). Prepared via Procedure C (described above) using 24.8 mg (0.1 mmol, 1.0 equiv) of **4l**, 3.4 mg of $[Ir(cod)Cl]_2$ (0.005 mmol, 0.05 equiv), 3.4 mg of $AgSbF_6$ (0.01 mmol, 0.1 equiv), 99 µL of 1-hexene (0.8 mmol, 8.0 equiv), and 2.0 mL of degassed PhCl at 85 °C under Ar for 48 h. The reaction was purified by preparative TLC (6% EtOAc/hexanes) to afford **5l** (6.6 mg, 20%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$, 69:31 mixture of diastereomers) δ 7.40 – 7.26 (m, 5H), 4.99 – 4.88 (m, 2H), 3.90 (dd, *J* = 11.7, 3.5 Hz, 0.31H), 3.89 – 3.84 (m, 0.31H), 3.80 (dd, *J* = 11.5, 1.2 Hz, 0.69H), 3.66 (ddd, *J* = 11.5, 3.0, 1.2 Hz, 0.69H), 3.57 – 3.49 (m, 0.69H), 3.46 – 3.38 (m, 1H), 3.38 – 3.32 (m, 0.69H), 3.32 – 3.25 (m, 0.31H), 3.20 (dd, *J* = 12.8, 3.6 Hz, 0.31H), 2.87 (dd, *J* = 12.9, 4.7 Hz, 0.31H), 2.65 (dd, *J* = 13.3, 10.8 Hz, 0.69H), 1.95 (d, *J* = 7.3 Hz, 3H), 1.84 – 1.75 (m, 0.69H), 1.64 – 1.57 (m, 0.31H), 1.54 – 1.47 (m, 0.31H), 1.41 – 1.33 (m, 0.69H), 1.33 – 1.26 (m, 4H), 1.25 – 1.19 (m, 4H), 1.17 (d, *J* = 6.2 Hz, 3H), 0.88 (td, *J* = 7.0, 2.5 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 69:31 mixture of diastereomers, only the major diastereomer is characterized) δ 157.85, 138.64, 128.23, 128.17, 127.45, 75.34, 71.64, 68.19, 52.50, 47.04, 31.80, 29.31, 27.12, 26.69, 22.62, 18.99, 14.08, 11.34. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{33}N_2O_2^+$ $[M+H]^+$ 333.2537, found 333.2540.

E. Removal of Directing Group[10]



4-benzhydryl-2-hexylpyrrolidine (8). To a 2-dram vial equipped with a magnetic stir bar was added (*E*)-1-(4-benzhydryl-2-hexylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (**2k**, 52.3 mg, 0.1 mmol, 1.0 equiv). The vial was sealed with a septum, purged with N_2, and cooled to 0 °C. DIBAL-H solution (1M in toluene, 0.5 mL, 0.5 mmol, 5.0 equiv) was added dropwise. The reaction was stirred at 0 °C for 2 hours. Upon completion, the reaction was carefully quenched with 0.02 mL water, 0.02 mL 15% NaOH (aq), and 0.05 mL water. The reaction mixture was warmed to rt and stirred for 30 minutes, followed by filtration over celite. The filtrate was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified by preparative TLC (5% MeOH/DCM) to provide the title compound as a colorless oil (29.1 mg, 91% yield). **^{1}H NMR** (600 MHz, $CDCl_3$, 58:42 mixture of diastereomers) δ 7.42 – 7.07 (m, 10H), 3.69 (dd, *J* = 14.8, 11.1 Hz, 1H), 3.41 – 2.82 (m, 4H), 2.72 (dd, *J* = 10.8, 6.8 Hz, 0.58H), 2.53 (dt, *J* = 10.6, 6.1 Hz, 0.42H), 2.02 – 0.98 (m, 12H), 0.85 (td, *J* = 7.0, 4.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 58:42 mixture of diastereomers, only the major diastereomer is characterized) δ 144.35, 144.23, 128.58, 128.53, 127.84, 127.71, 126.36, 126.29, 60.14, 57.41, 50.77, 43.76, 38.96, 36.22, 31.74, 29.33, 27.19, 22.58, 14.06. **HRMS** (ESI-TOF): *m/z* calculated for $C_{23}H_{32}N^+$ $[M+H]^+$ 322.2529, found 322.2529.



benzyl 2-hexyl-5-(trifluoromethyl)piperidine-1-carboxylate (9). To a 2-dram vial equipped with a magnetic stir bar was added (*E*)-1-(2-hexyl-5-(trifluoromethyl)piperidin-1-yl)ethan-1-one *O*-benzyl oxime (**5h**, 38.4 mg, 0.1 mmol, 1.0 equiv). The vial was sealed with a septum, purged with N_2, and cooled to 0 °C. DIBAL-H solution (1M in toluene, 0.5 mL, 0.5 mmol, 5.0 equiv) was

added dropwise. The reaction was stirred at 0 °C for 2 hours. The reaction was carefully quenched with 0.02 mL water, 0.02 mL 15% NaOH (aq), and 0.05 mL water. The reaction mixture was warmed to rt and stirred for 30 minutes, followed by filtration over celite. The filtrate was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. To a solution of the crude reaction mixture under N_2 in DCM (1 mL) were added triethylamine (42 µL, 0.3 mmol, 3.0 equiv) and Cbz-Cl (42 µL, 0.3 mmol, 3.0 equiv). The solution was stirred at rt for 12 hours. Upon completion, the reaction mixture was washed with water, brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude reaction mixture was purified by preparative TLC (6% EtOAc/hexanes) to provide the title compound as a colorless oil (31.5 mg, 85% yield). **^{1}H NMR** (600 MHz, $CDCl_3$, 84:16 mixture of diastereomers) δ 7.39 – 7.27 (m, 5H), 5.21 – 5.07 (m, 2H), 4.39 – 4.33 (m, 1H), 4.30 – 4.20 (m, 1H), 3.11 (dd, *J* = 15.0, 5.3 Hz, 0.16H), 2.86 (t, *J* = 12.7 Hz, 0.38H), 2.79 (t, *J* = 12.7 Hz, 0.46H), 2.38 – 2.09 (m, 1H), 1.99 – 1.16 (m, 14H), 0.87 (tt, *J* = 7.1, 2.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, 84:16 mixture of diastereomers, only the major diastereomer is characterized) δ 155.68, 136.62, 128.51, 127.99, 127.76, 126.45 (q, *J* = 278.9 Hz), 67.39, 50.23, 40.45 (q, *J* = 26.5 Hz), 37.13, 31.78, 29.43, 29.07, 27.12, 26.13, 22.59, 18.27, 14.08. **^{19}F NMR** (376 MHz, $CDCl_3$, 84:16 mixture of diastereomer) δ -69.62, -72.94, -72.95. **HRMS** (ESI-TOF): *m/z* calculated for $C_{20}H_{29}F_3NO_2^+$ $[M+H]^+$ 372.2145, found 372.2144. (Note: Rotational isomers are present in a ratio of 38:46).

F. Product Diastereomeric Ratios.

Name	***d.r.***	***Name***	***d.r.***
2a-3-B	67:33	**3r**	47:39:7:7
2a-3-L	*Note (a)*	**3s**	88:6:6 *[Note (f)]*
2b-B	*Note (b)*	**3t**	70:30
2b-L	56:44	**3u-mono**	*Note (a)*
2c-B	*Note (b)*	**3u-di**	92:8
2c-L	*Note (b)*	**3v-mono**	*Note (a)*
2d-B	*Note (b)*	**3v-di**	90:10
2d-L	77:23	**3w**	*Note (a)*
2e-B	*Note (c)*	**3x**	92:8
2e-L	64:36	**3y-B**	69:31
2f-B	60:40 *[Note (d)]*	**3y-L**	*Note (a)*
2f-L	*Note (e)*	**5b-mono**	*Note (a)*
2g-B	50:50	**5b-di**	*Note (g)*
2g-L	*Note (a)*	**5c**	50:50
2h-B	41:24:22:12	**5d-mono**	75:25
2h-L	78:22	**5d-di**	*Note (g)*
2i-B	50:50	**5e-mono**	77:23
2i-L	*Note (a)*	**5e-di**	85:15
2j-mono	62:38	**5f-mono**	57:43
2j-di	59:41	**5f-di**	76:24
2k	60:40	**5g-mono**	73:27
2l	77:23	**5g-di**	79:21
2m-mono	50:50	**5h**	83:17
2m-di	*Note (b)*	**5i**	68:32
2p-B	56:44	**5j-mono**	*Note (a)*
2p-L	*Note (a)*	**5j-di**	68:32
3a to 3k	*Note (a)*	**5k**	*Note (h)*
3l-B	50:50	**5l**	69:31
3l-L	*Note (a)*	**8**	58:42
3m to 3q	*Note (a)*	**9**	84:16

Notes:

(a) Diastereomeric ratio is not applicable here.

(b) The diastereomeric ratios of **2b-B**, **2c-B**, **2c-L**, **2d-B**, and **2m-di** could not be determined due to rotamers in the molecule leading to broad NMR peaks.

(c) The diastereomeric ratio of **2e-B** could not be determined accurately due to overlapping peaks.

(d) **2f-B**: Only two diastereomers were observed (out of possible four); *anti*-selective.

(e) **2f-L**: Only a single diastereomer was observed (out of possible two); *anti*-selective.

(f) **3s**: Only 3 diastereomers were observed (out of possible four).

(g) **5b-di** and **5d-di**: Only a single diastereomer was observed (out of possible three); *anti*-selective for the two α- and α'-functionalizations.

(h) **5k**: Only a single diastereomer was observed (out of possible two); *anti*-selective.

(i) **3x**: A higher diastereomeric ratio of 92:8 might be attributed to *cis*-geometry of the olefin coupling partner.

(j) Unless otherwise noted, all product diastereomeric ratios are calculated by integration of the product's 1H NMR spectra. The integrals are included in the NMR characterization data, as well as marked on the NMR spectra. For **2b-L**, **2d-L**, and **3x**, product diastereomeric ratios are calculated by integration of their 19F NMR spectra. For **2l**, **2p-B**, **2j-di**, **5e-di**, **5f-mono**, **5f-di**, **5g-di**, and **5j-di**, the diastereomers are separable and the ratios are calculated based on their isolated yields. *Anti*-stereochemistry was determined by *NOESY* experiments on the representative compound **5d-di**.

3. References

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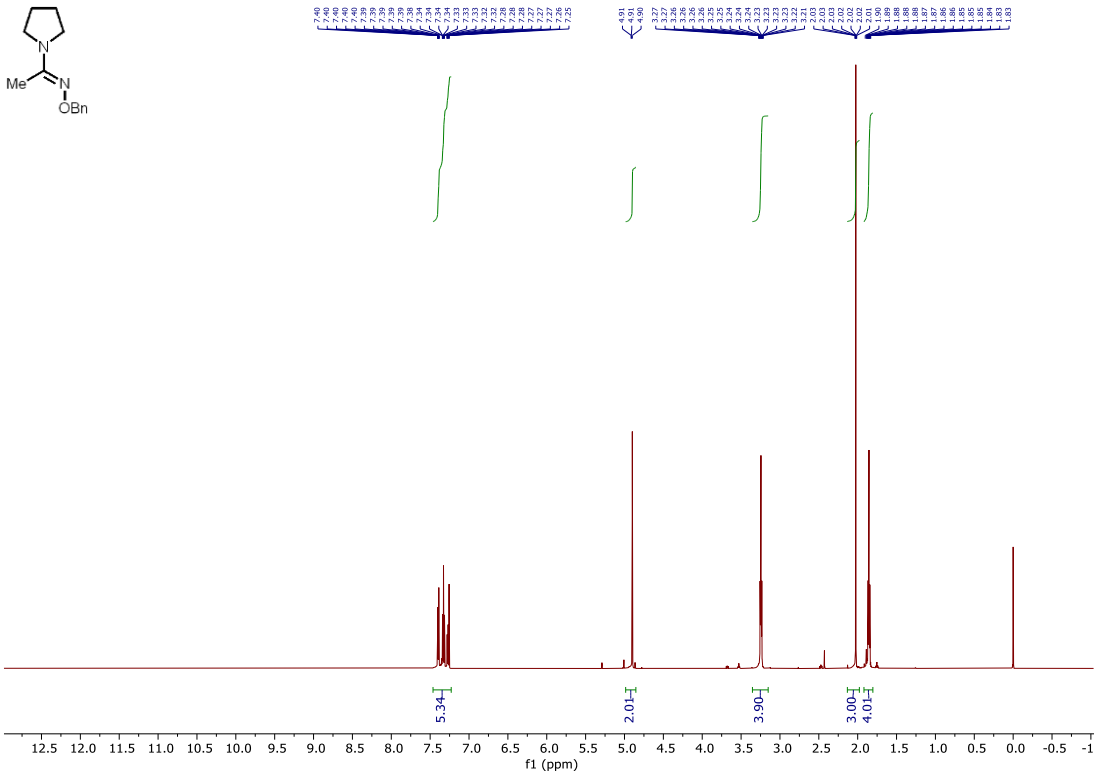
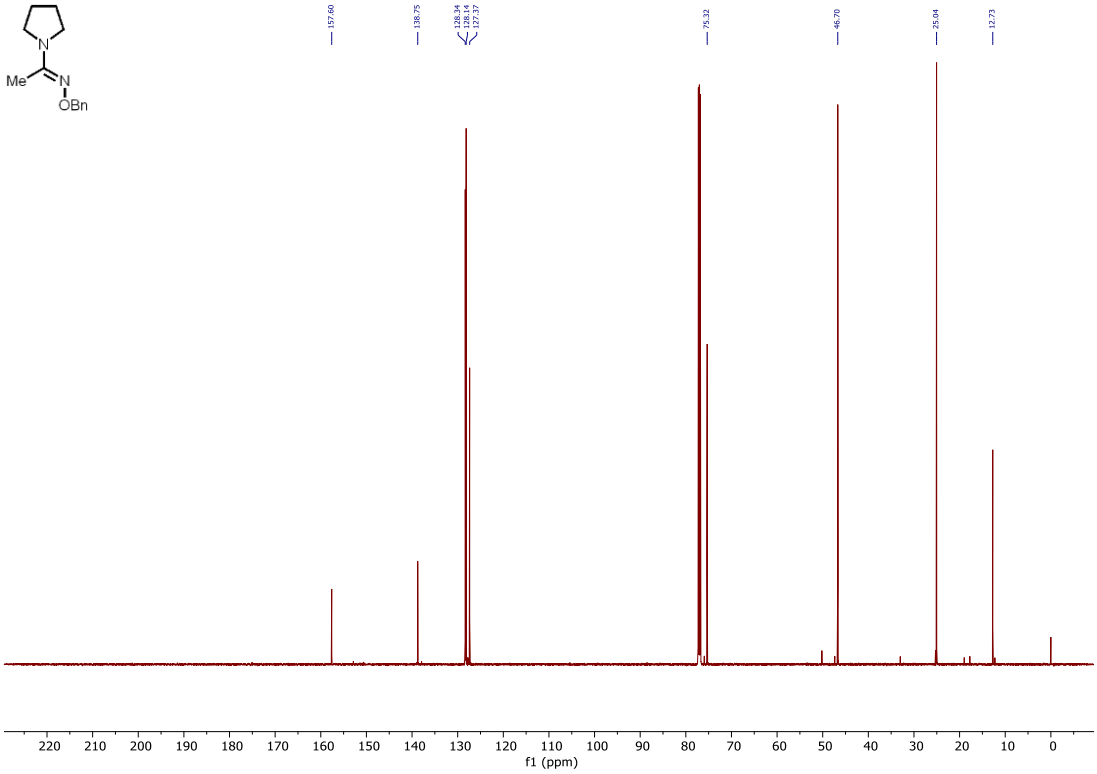
4. NMR Spectra

(*E*)-1-(pyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1a-1)





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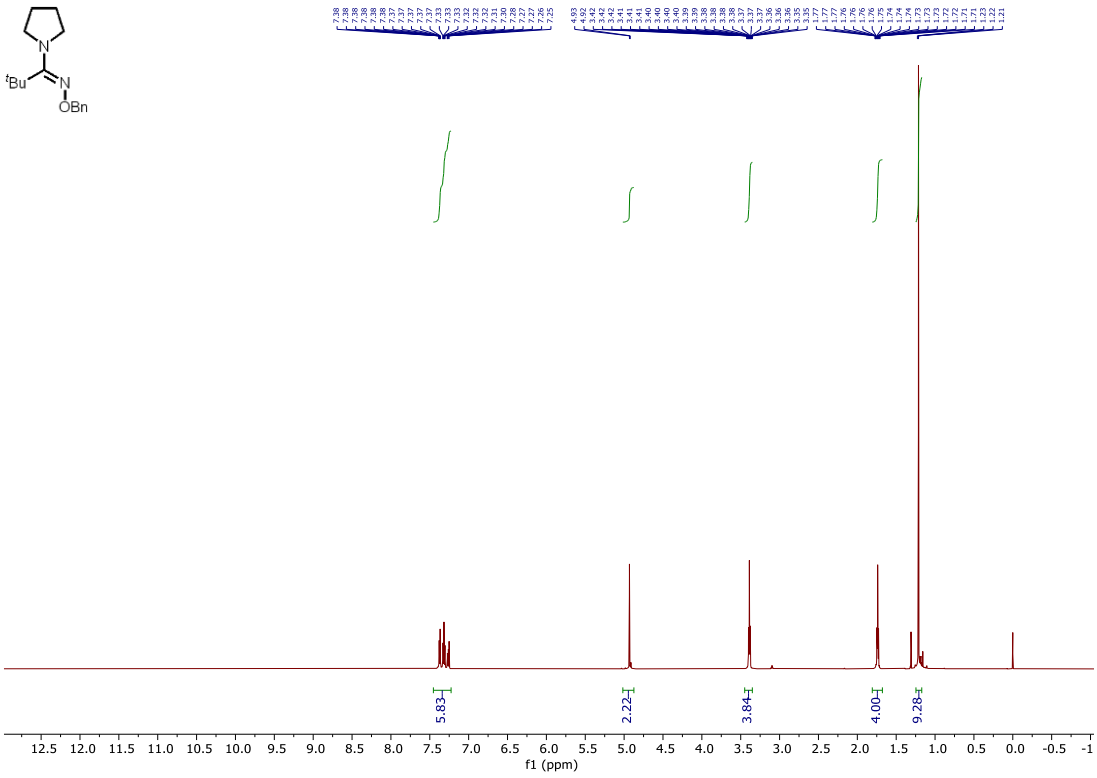

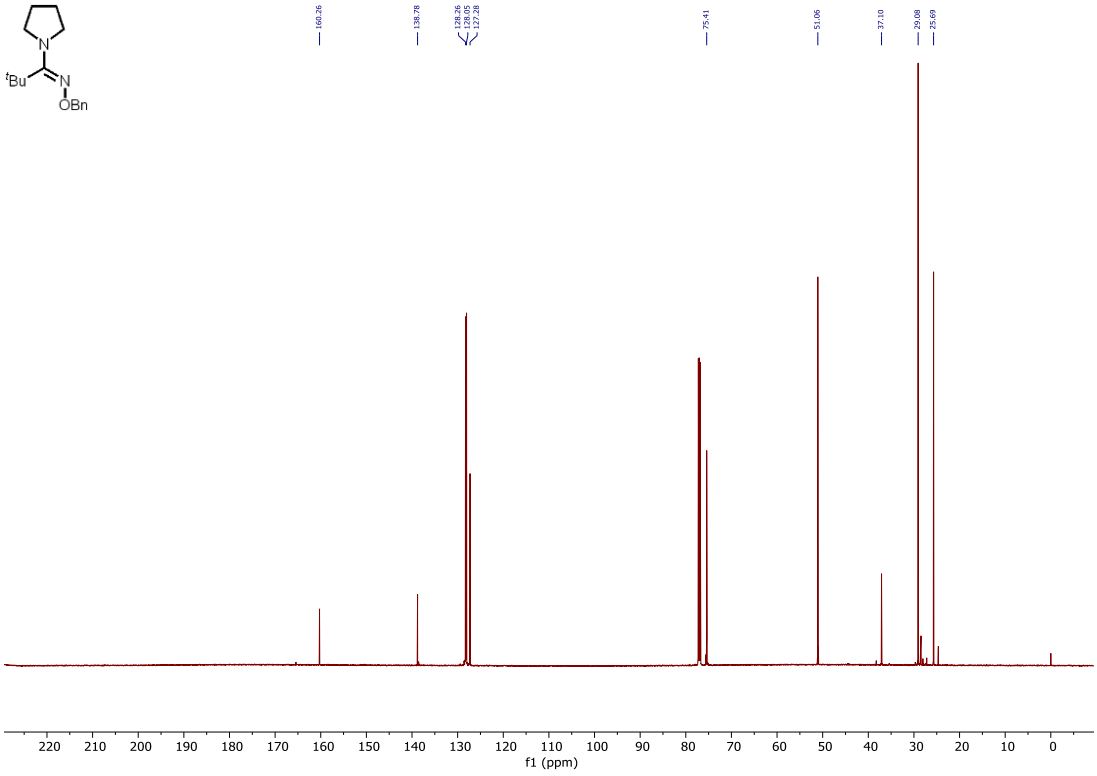

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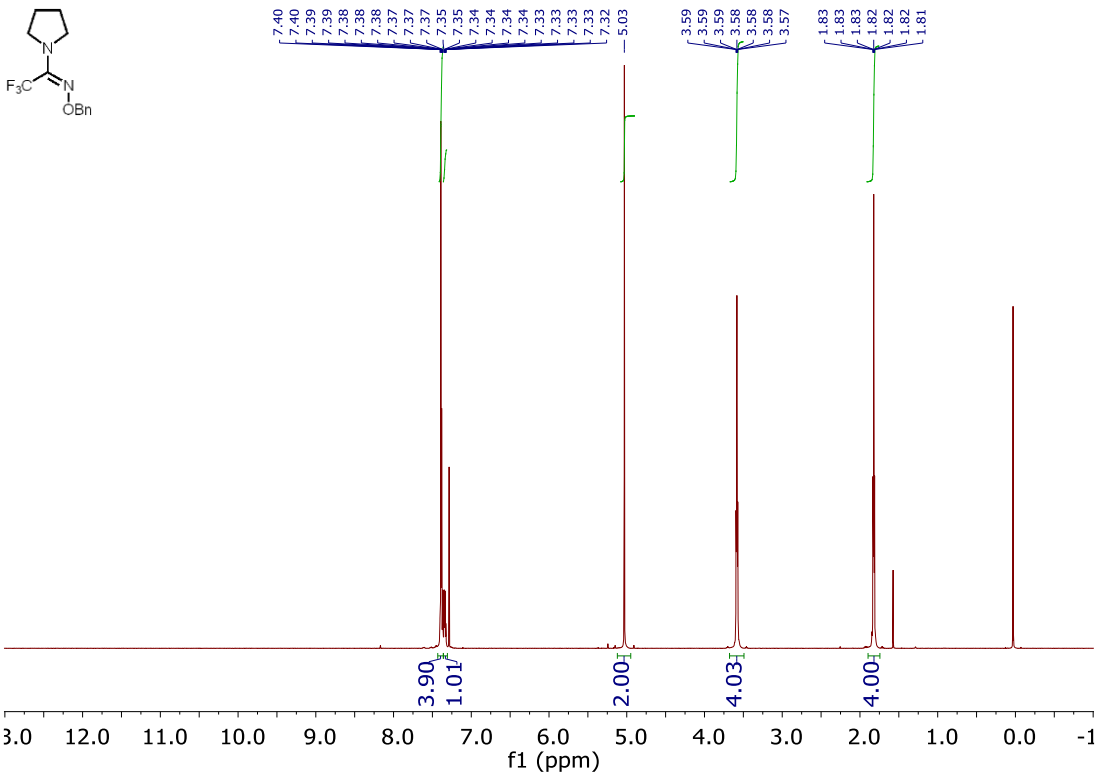

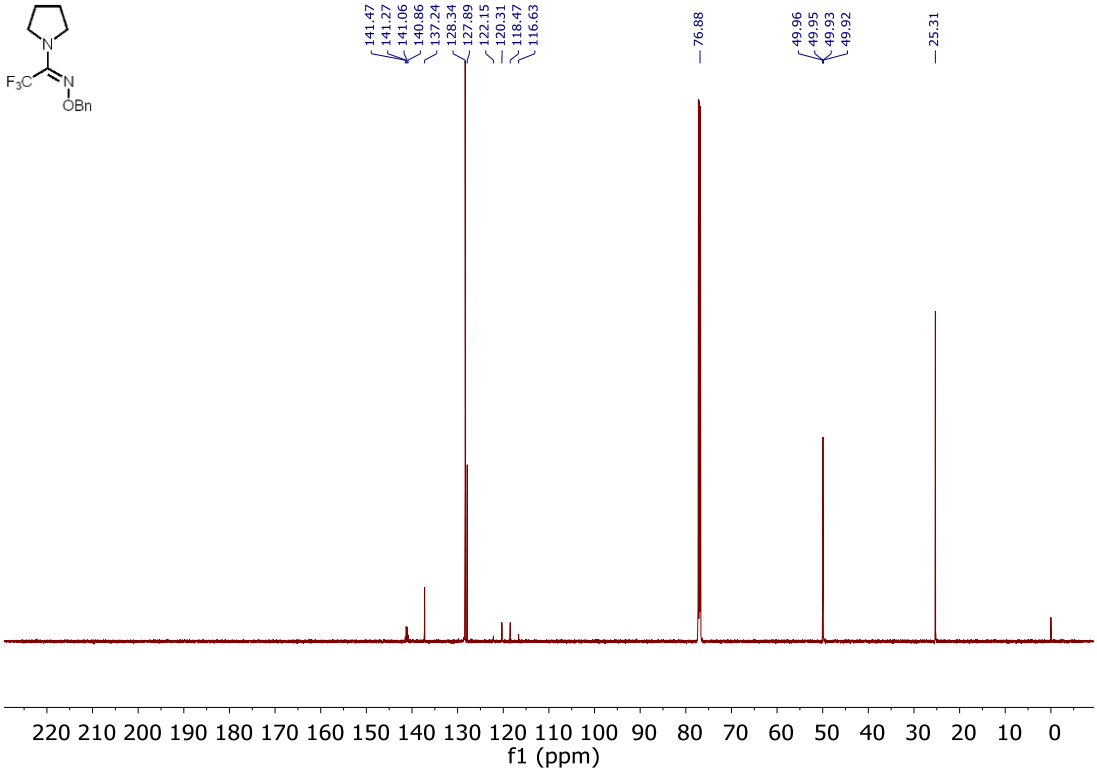

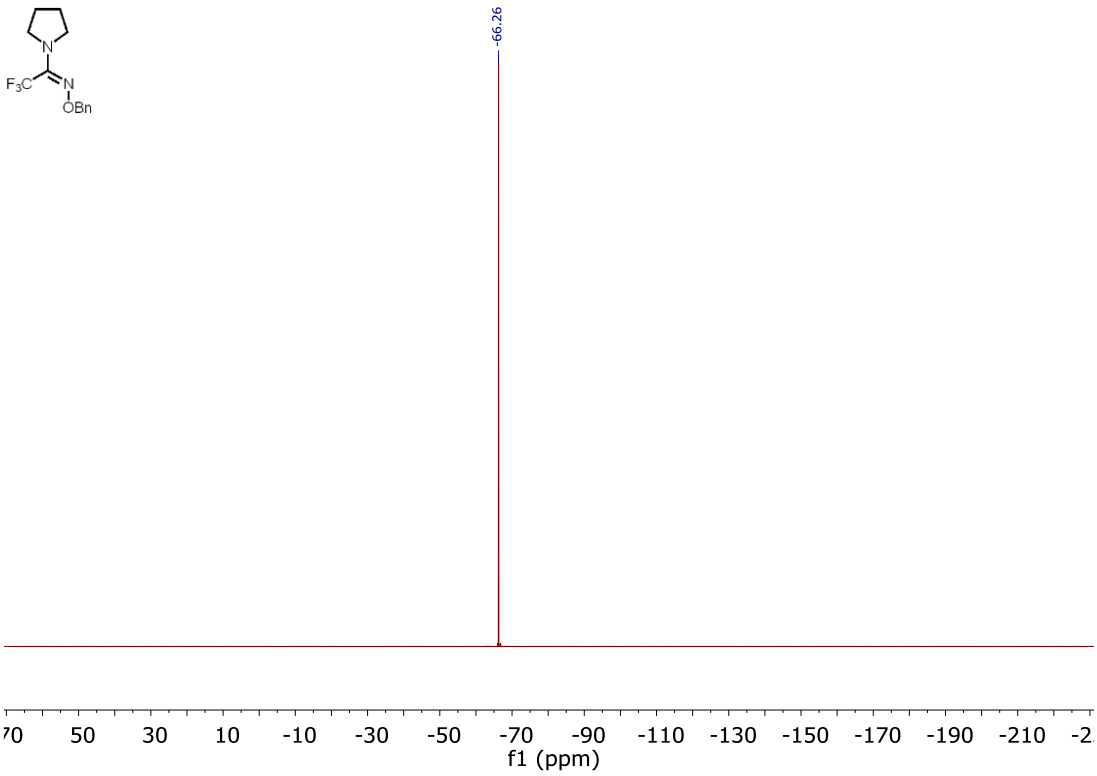
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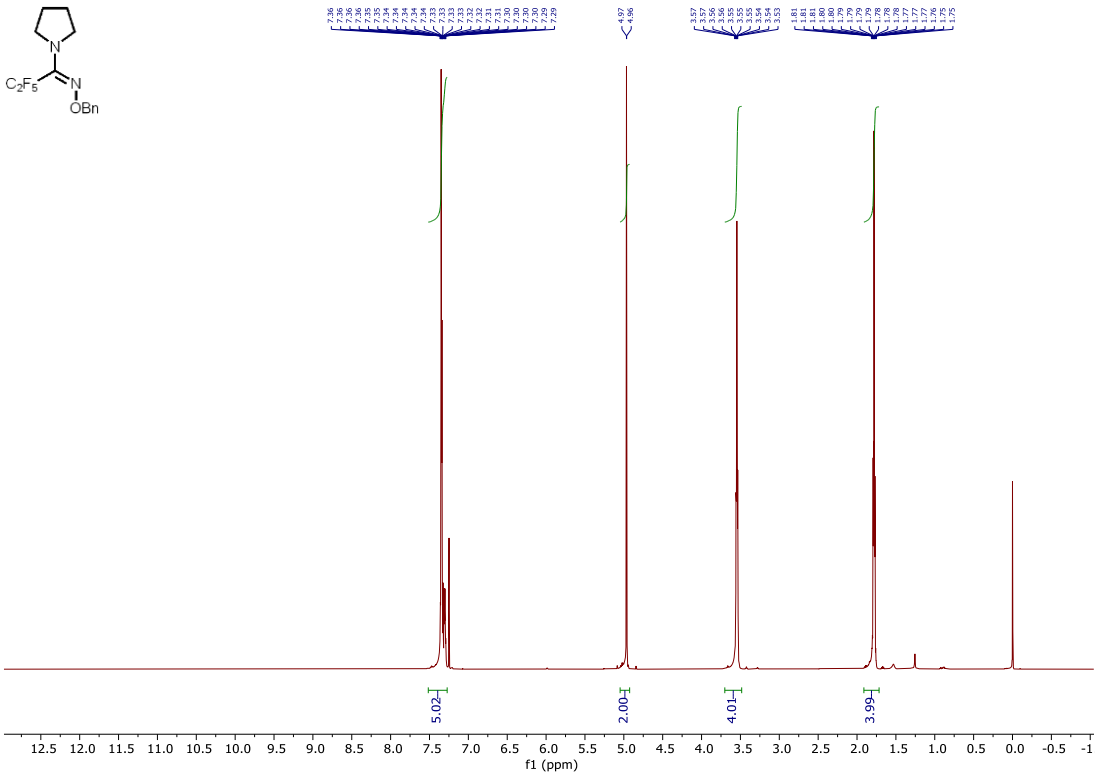
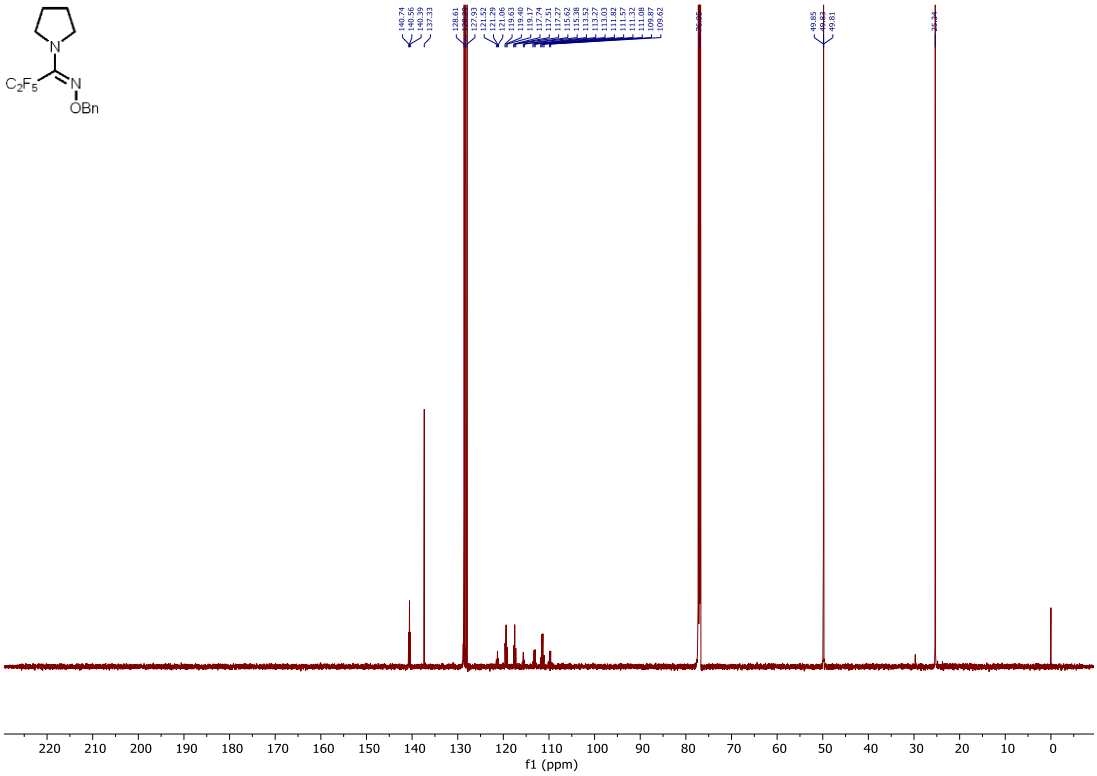
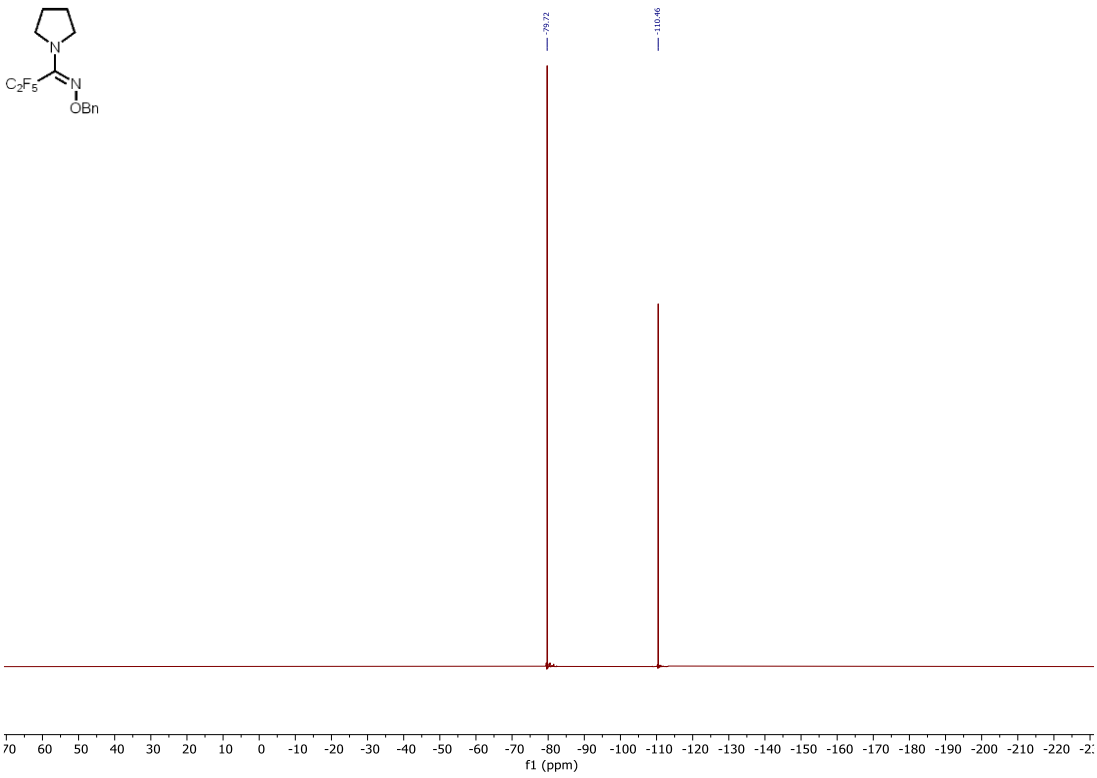
f1 (ppm)

(*E*)-2,2,3,3,3-pentafluoro-1-(pyrrolidin-1-yl)propan-1-one *O*-benzyl oxime (1a-4)



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C2F5
N
OBn
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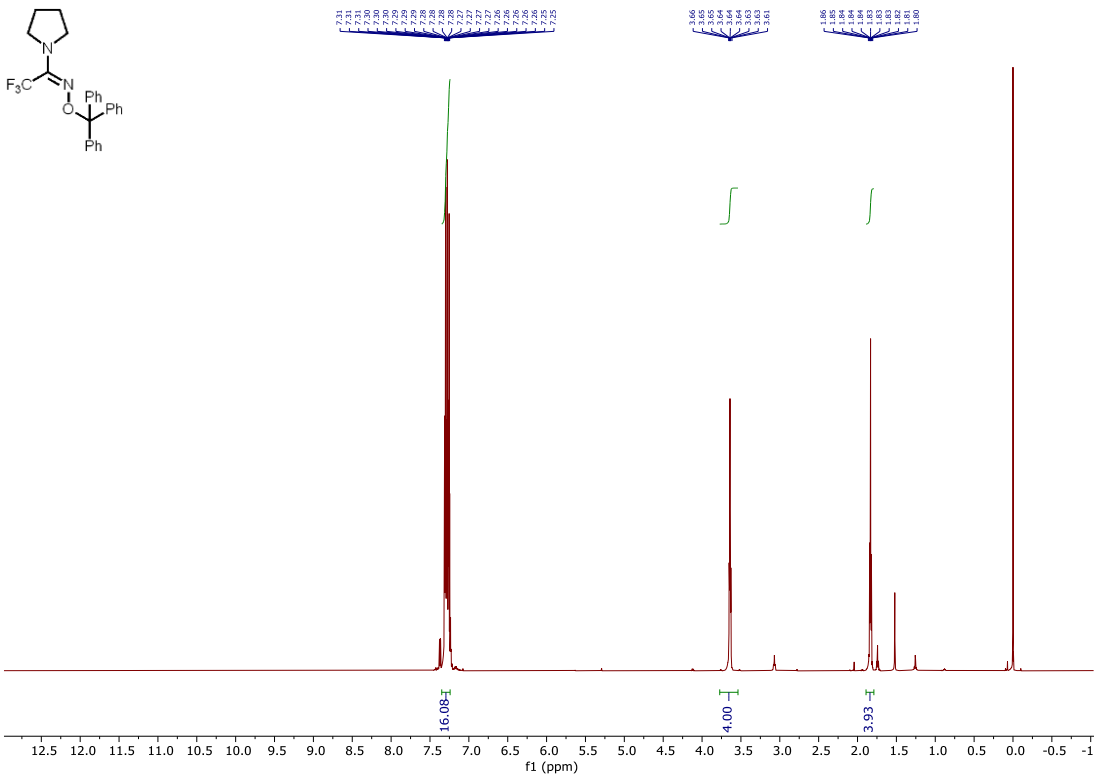
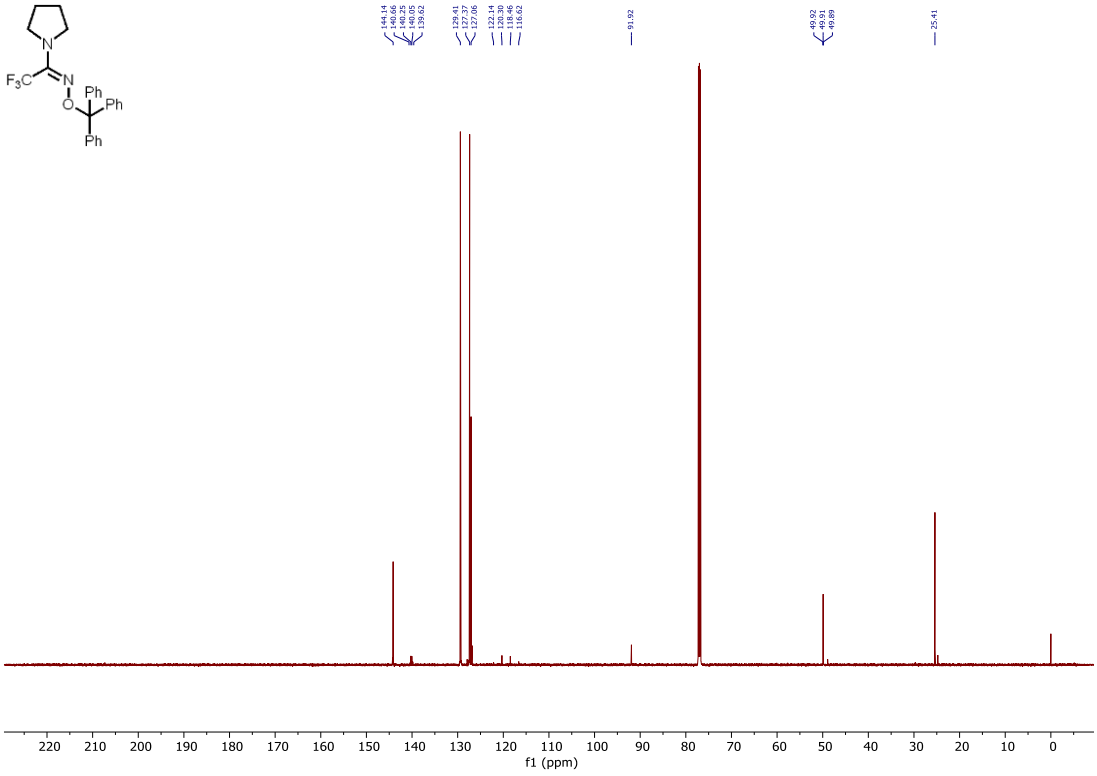
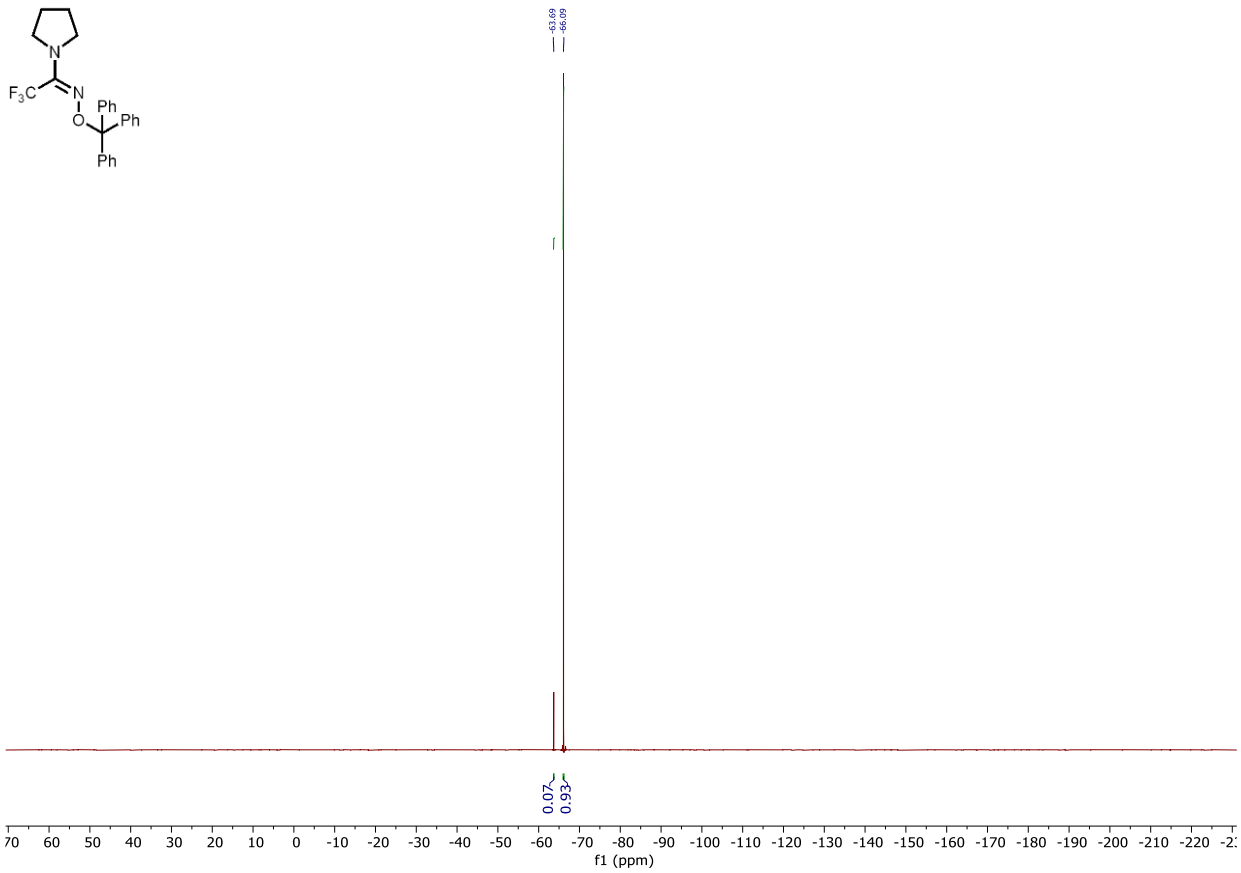
f1 (ppm)

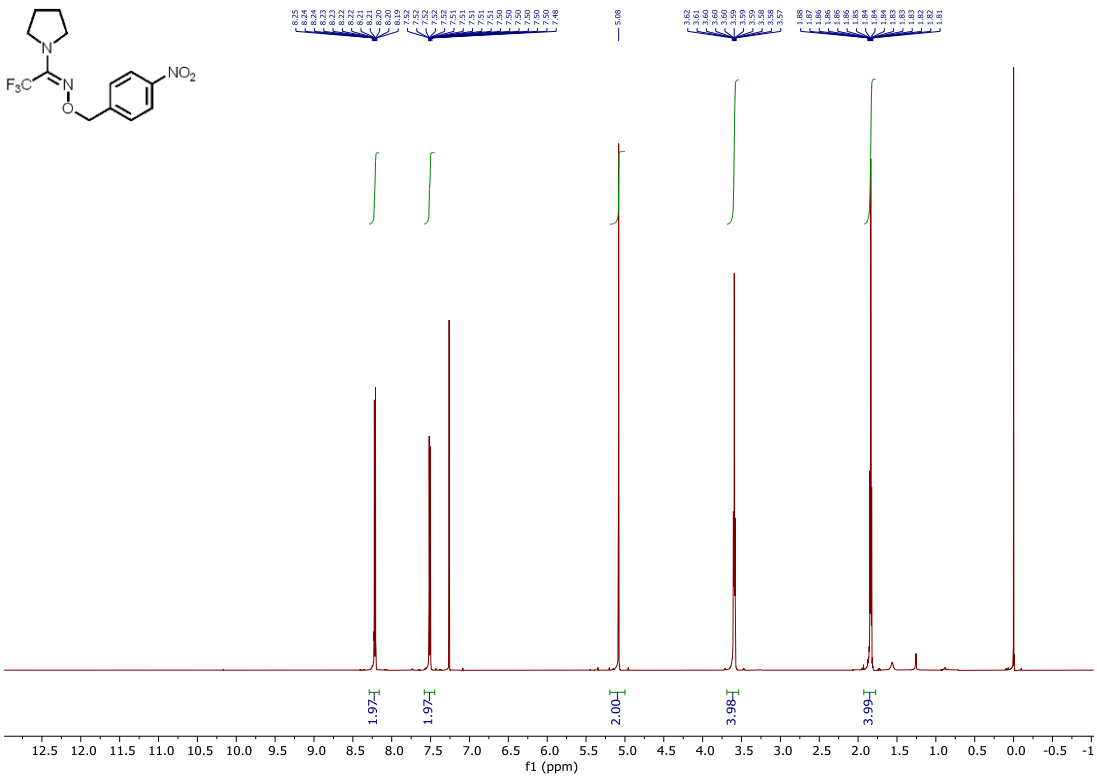
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-trityl oxime (1a-5)

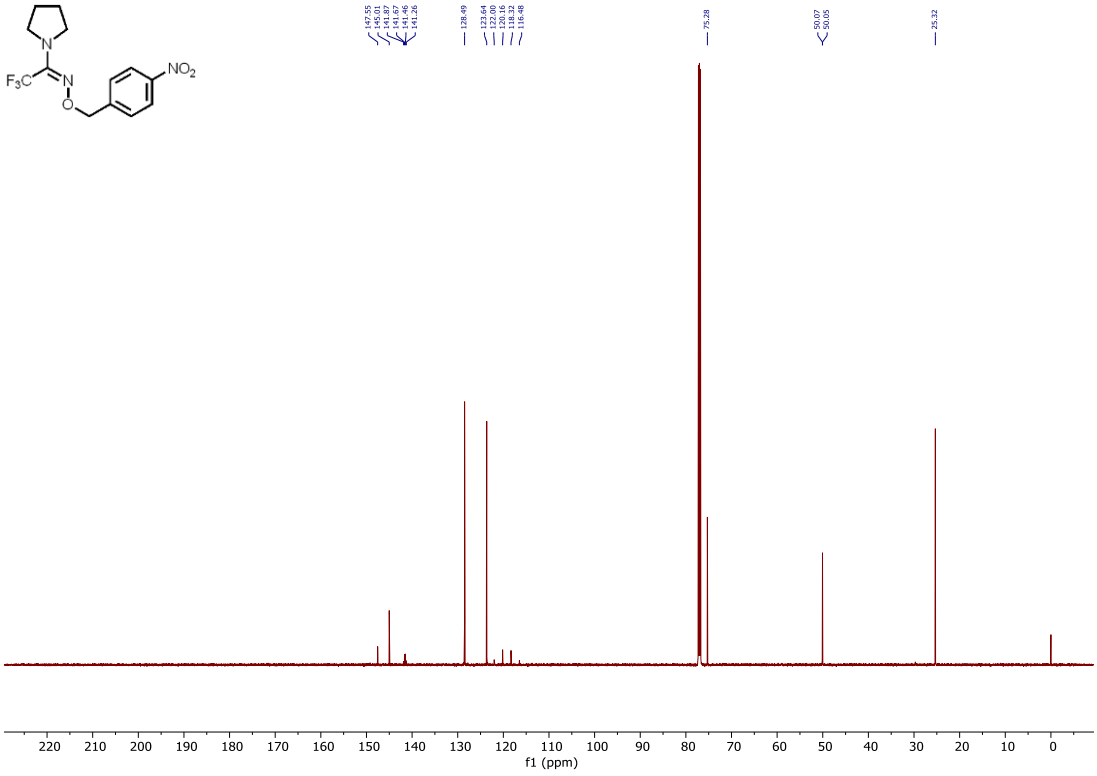


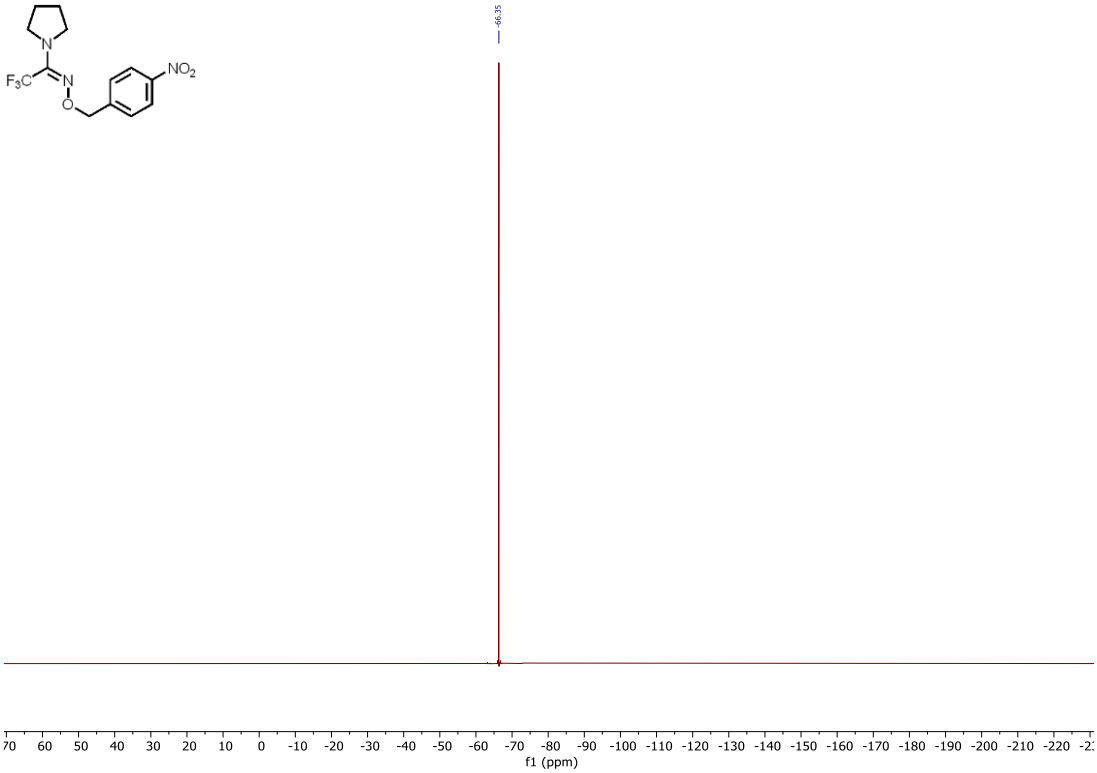



-63.69
-66.09
0.07
0.93
f1 (ppm)

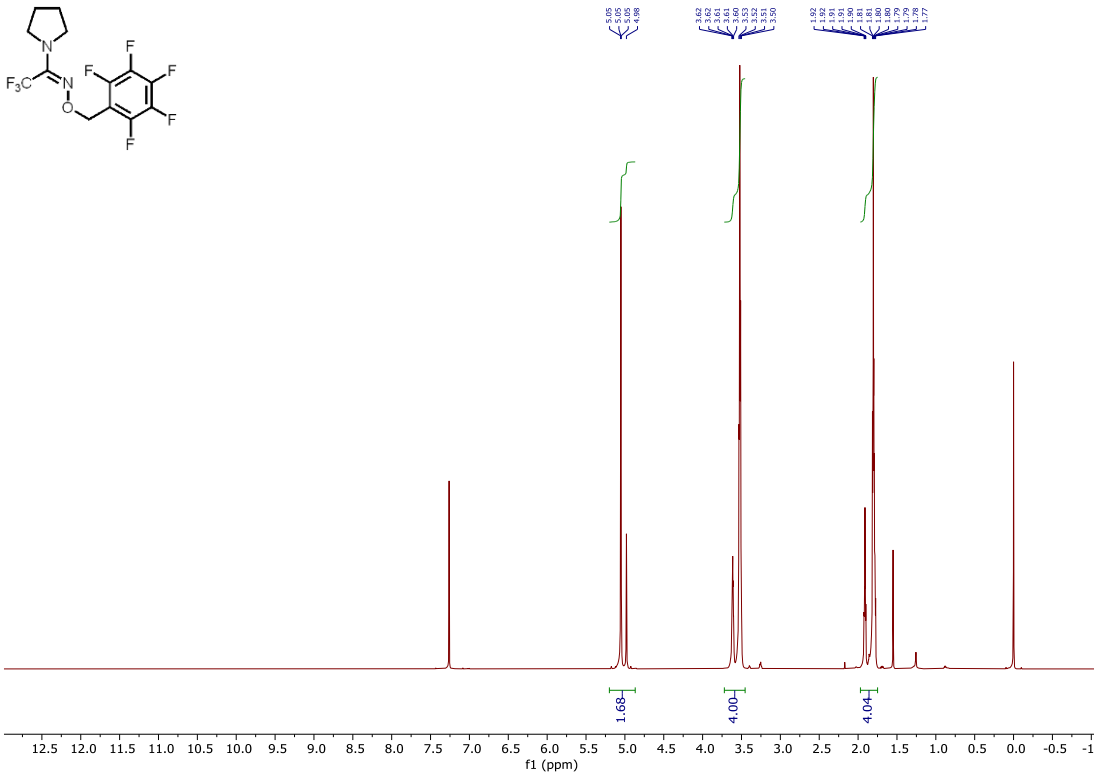
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-(4-nitrobenzyl) oxime (1a-6)

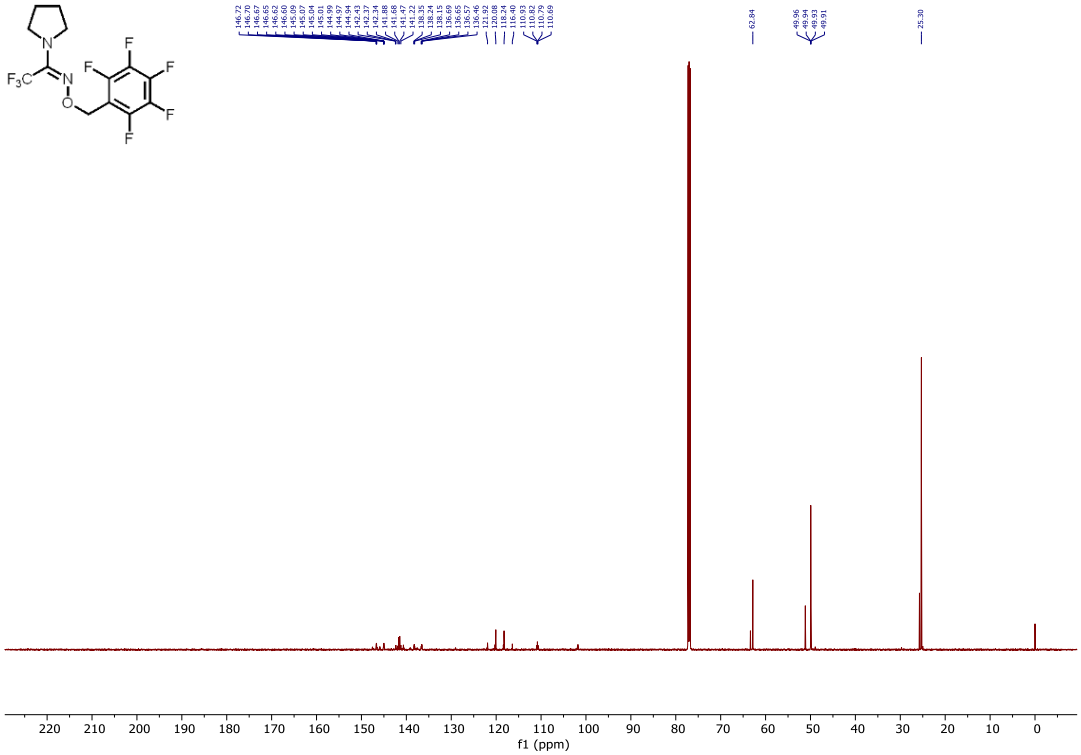


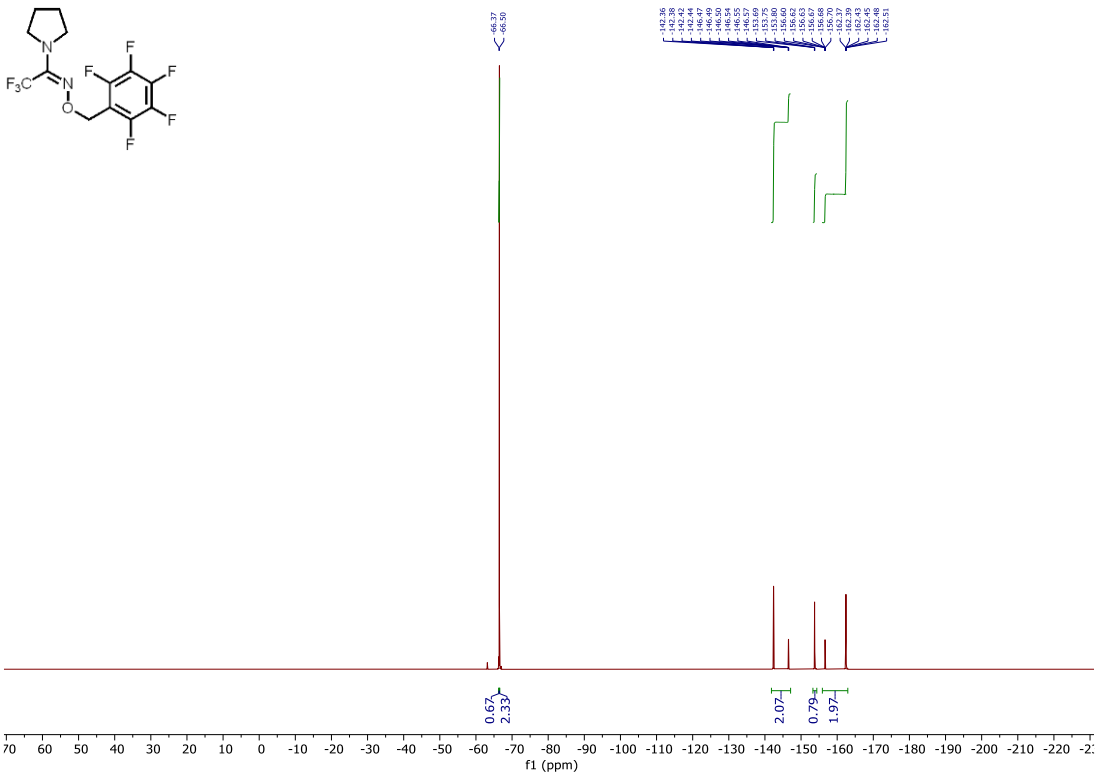



-66.35
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

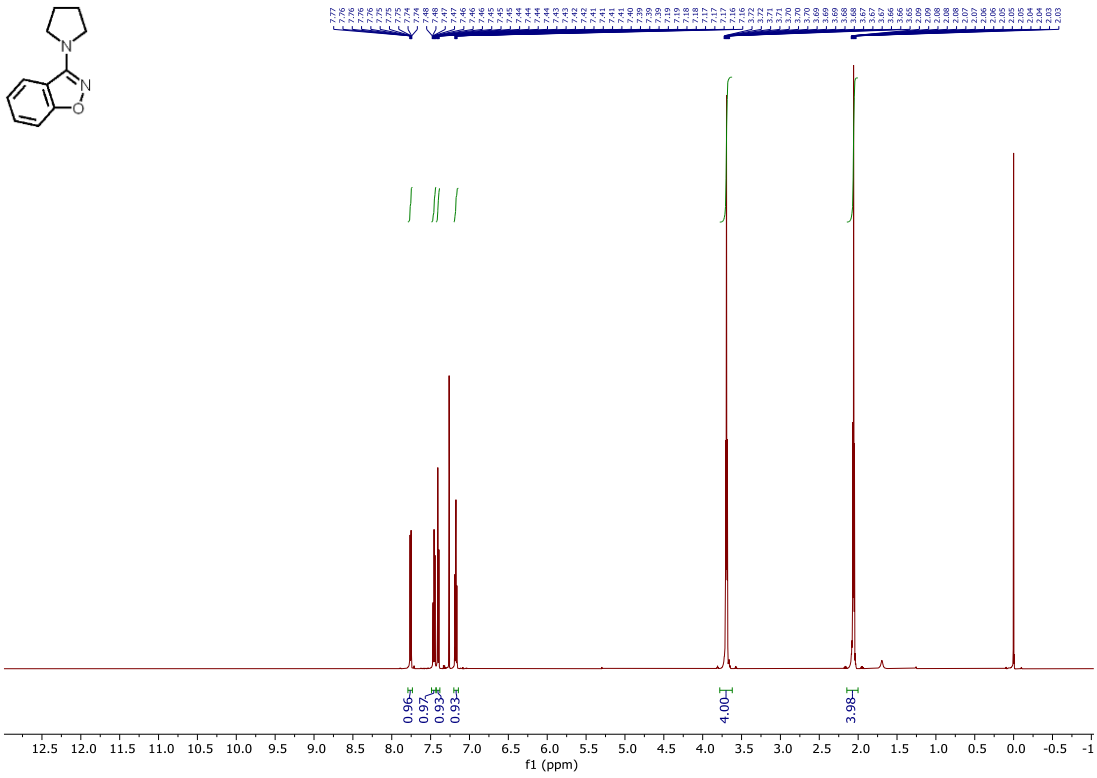
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-((perfluorophenyl)methyl) oxime (1a-7)

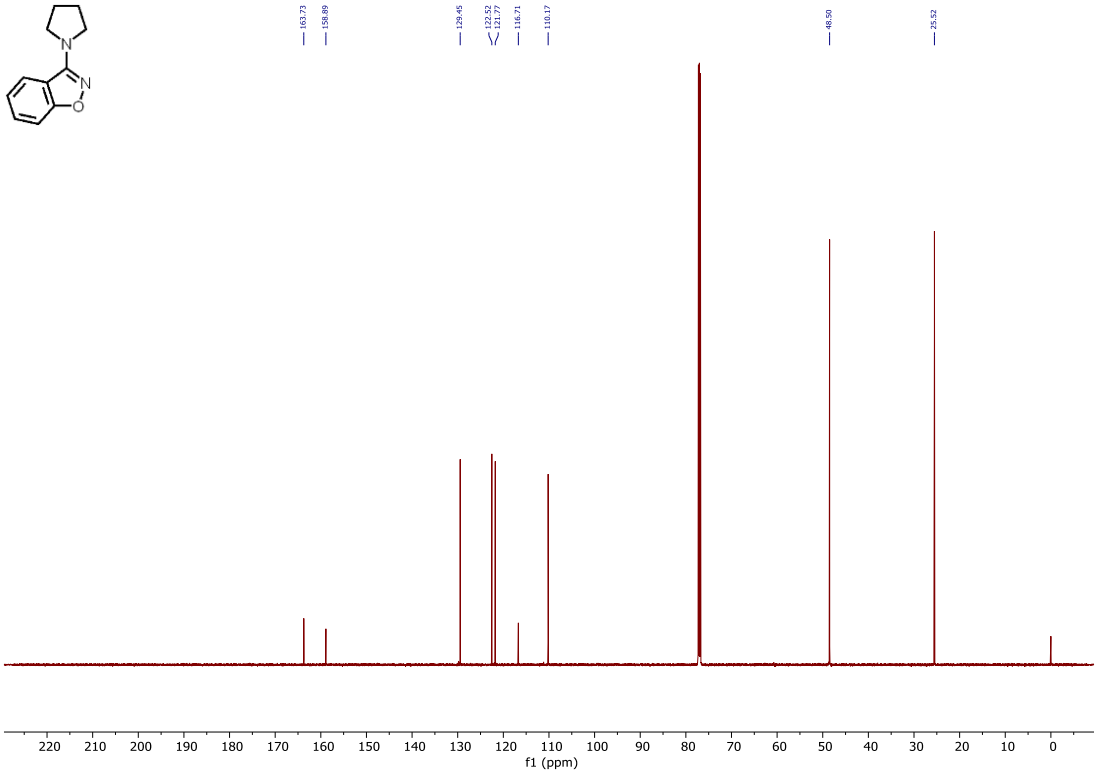




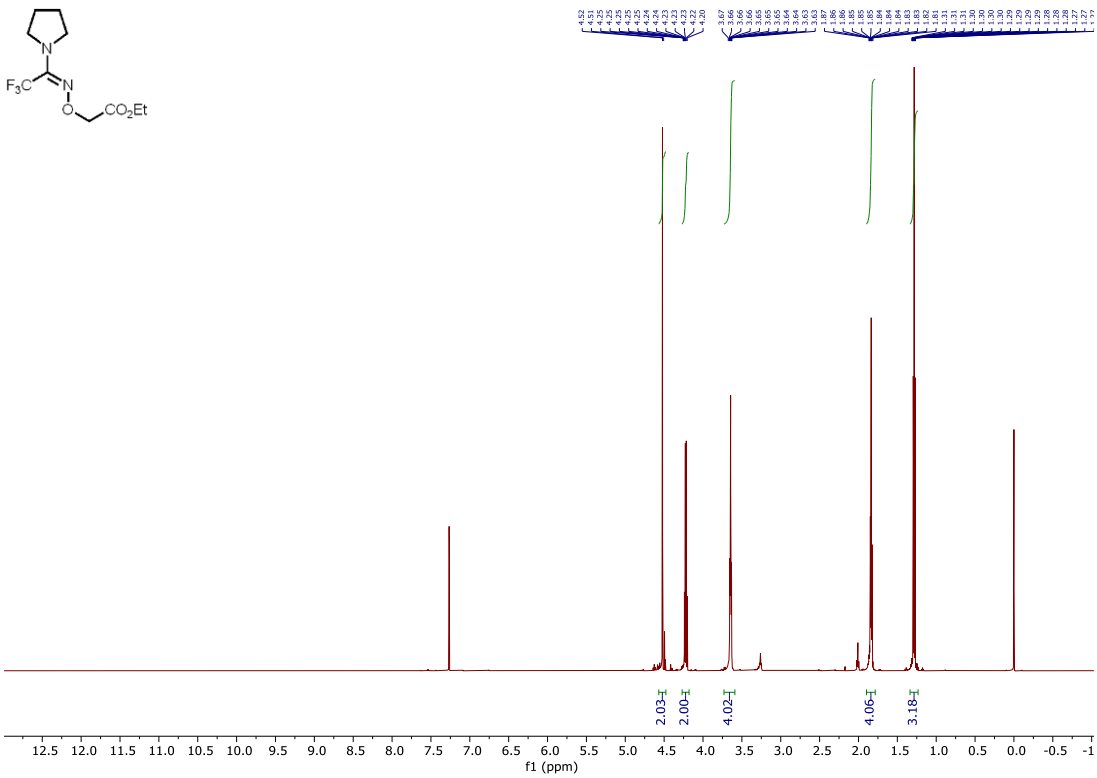

F3C
N
O
F
F
F
F
F
-66.37
-66.50
0.67
2.33
2.07
0.79
1.97
f1 (ppm)

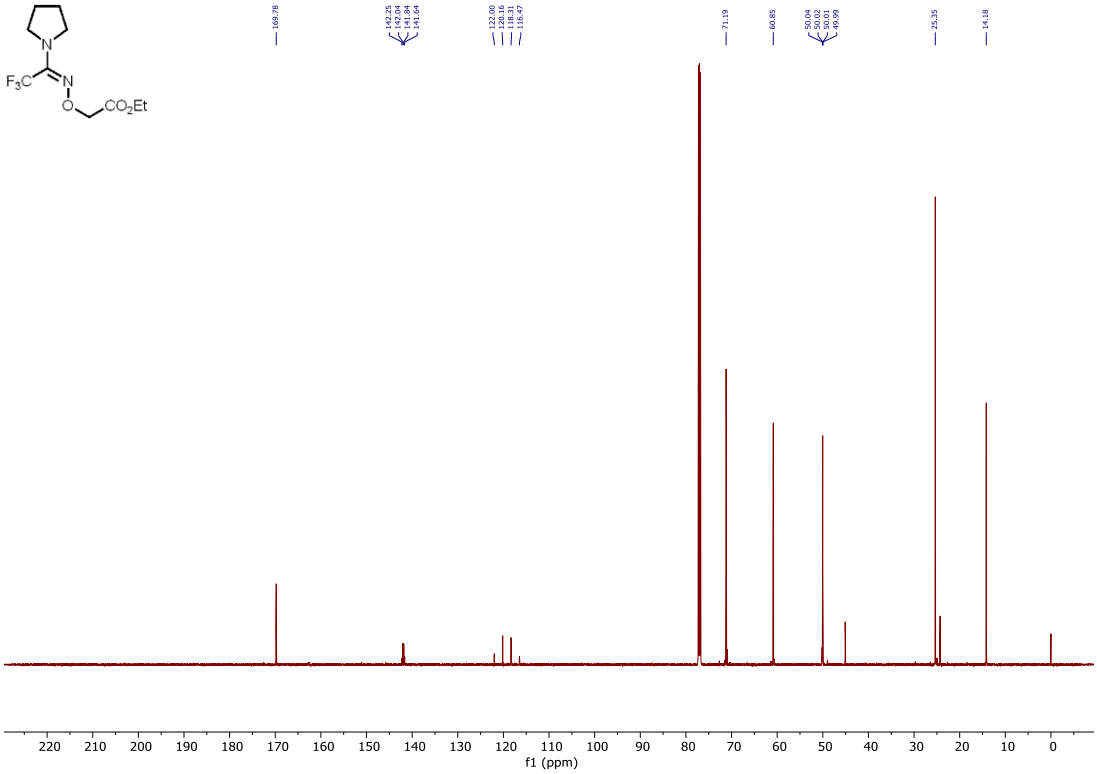
3-(pyrrolidin-1-yl)benzo[*d*]isoxazole (1a-8)

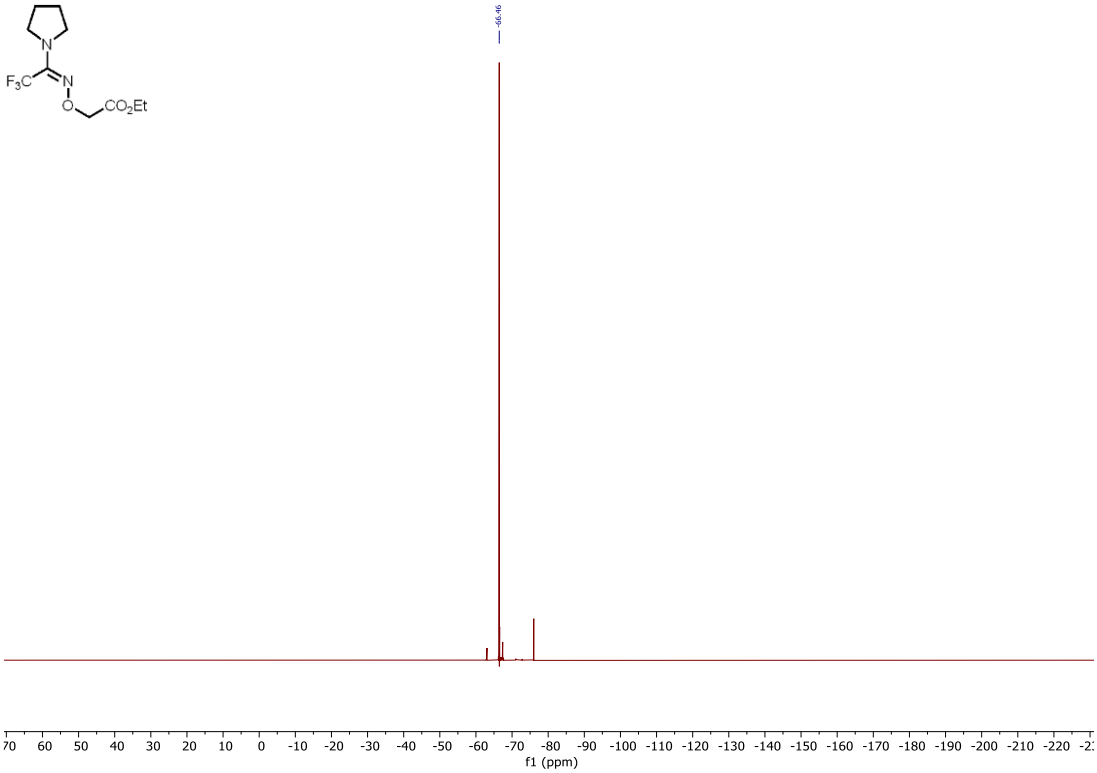




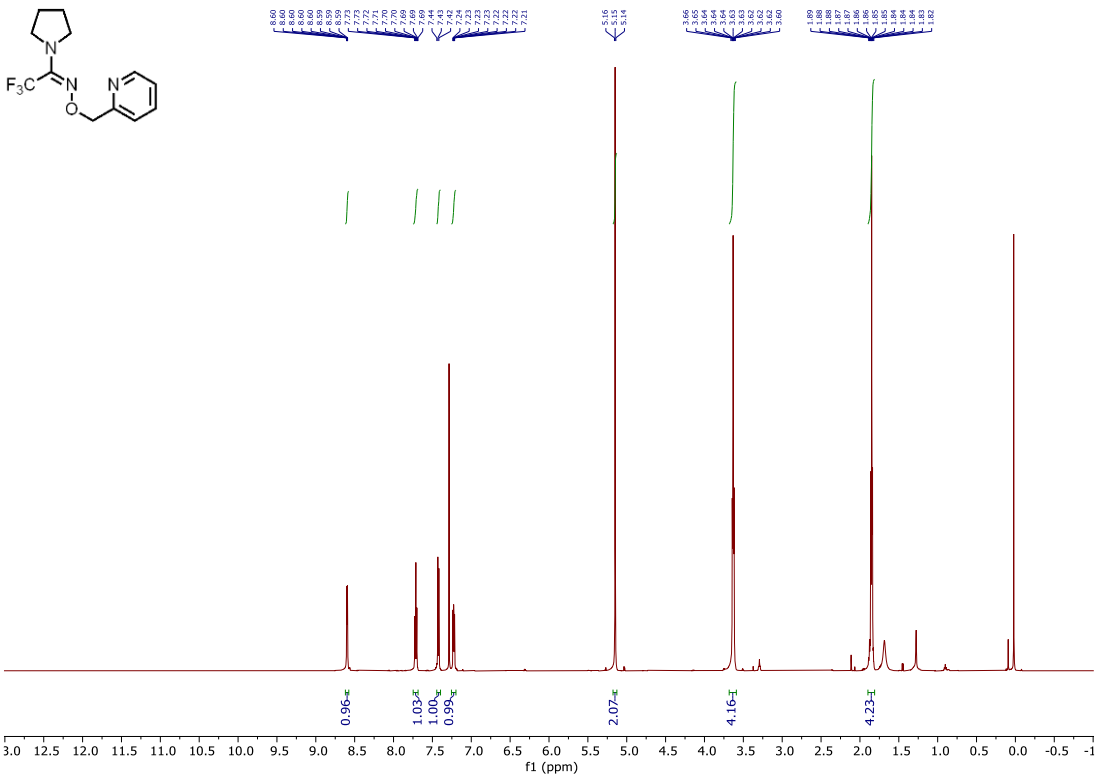
ethyl (*E*)-2-(((2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethylidene)amino)oxy)acetate (1a-9)

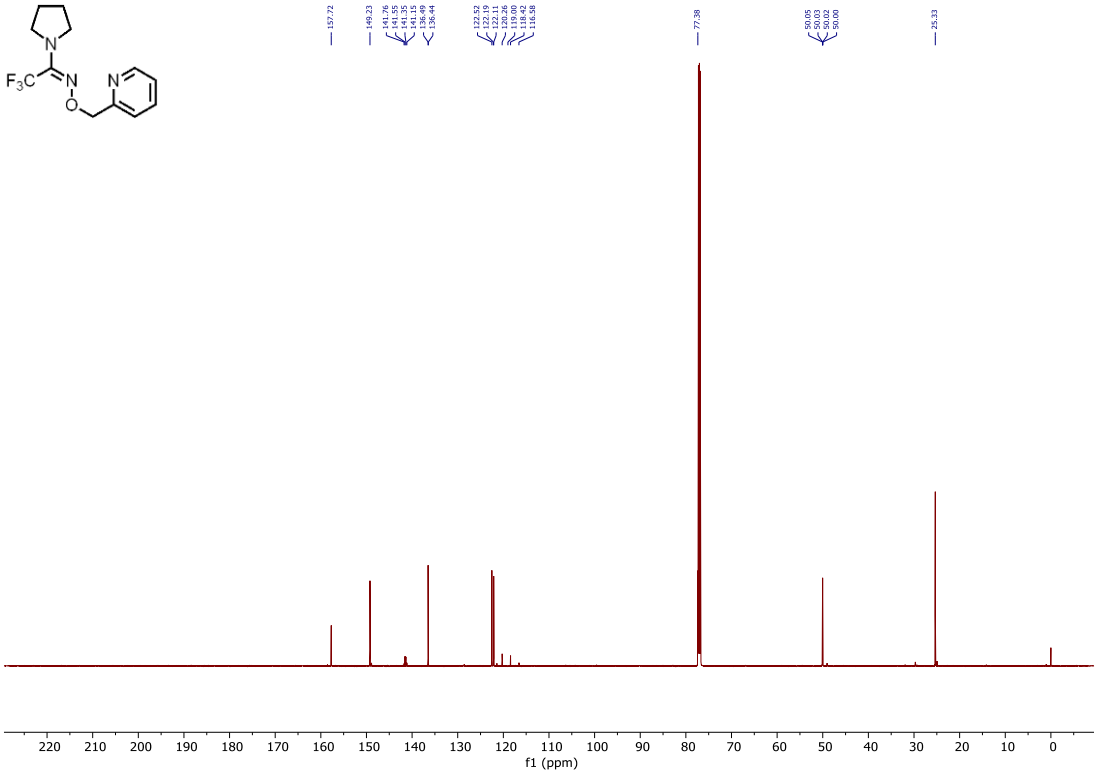


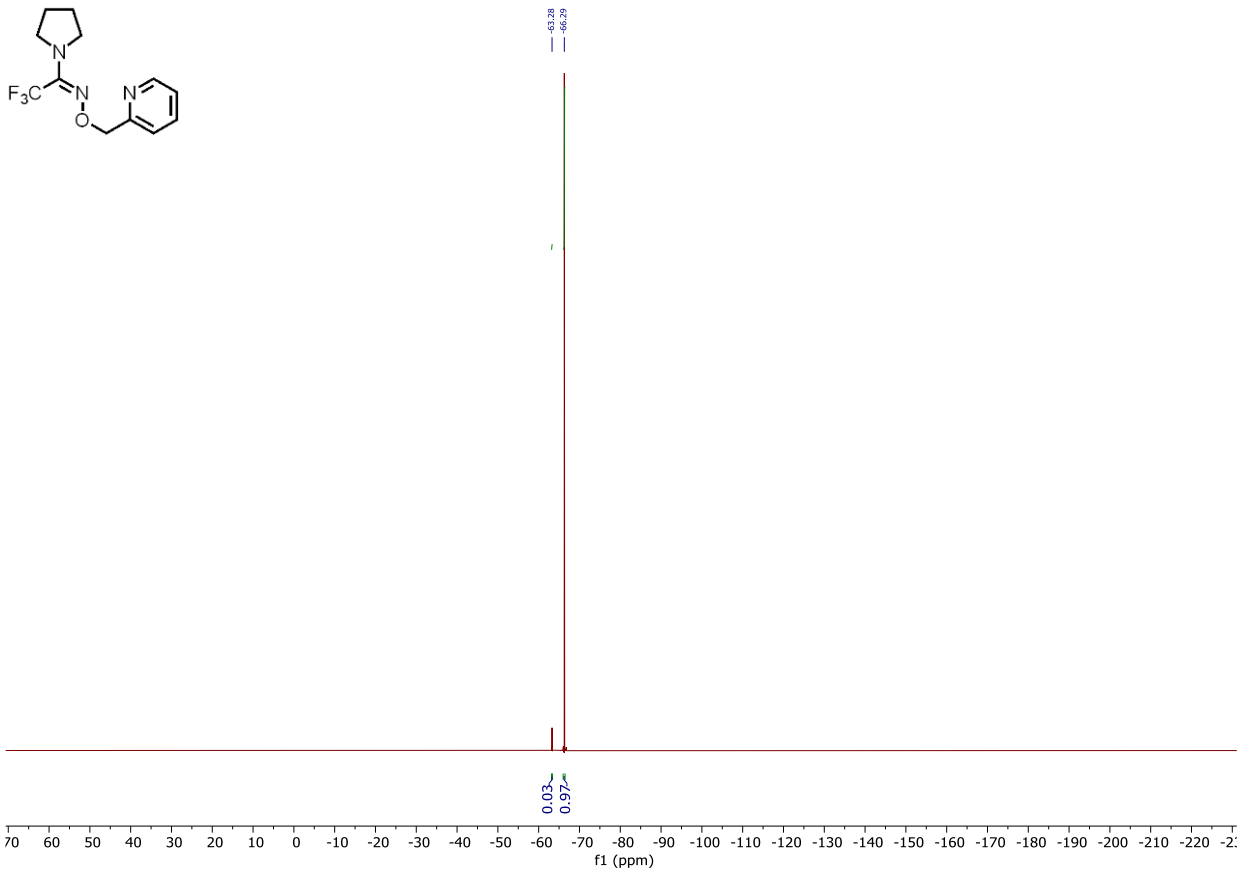



-66.46
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

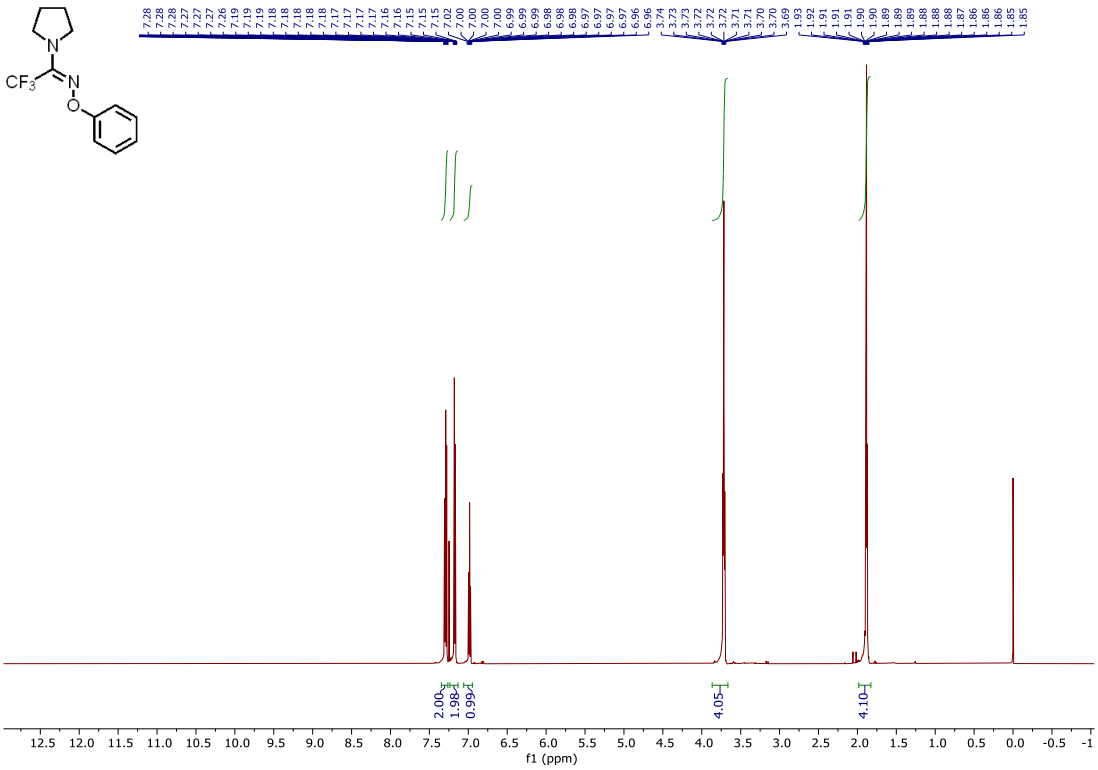
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one *O*-pyridin-2-ylmethyl oxime (1a-10)

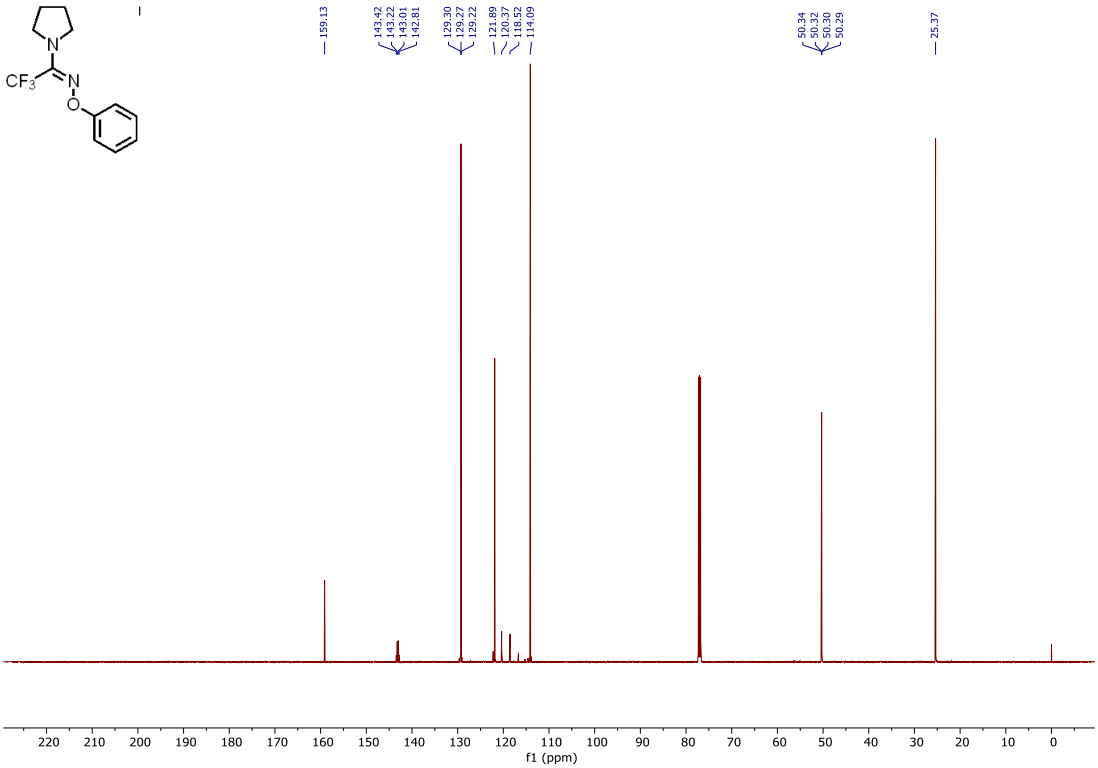


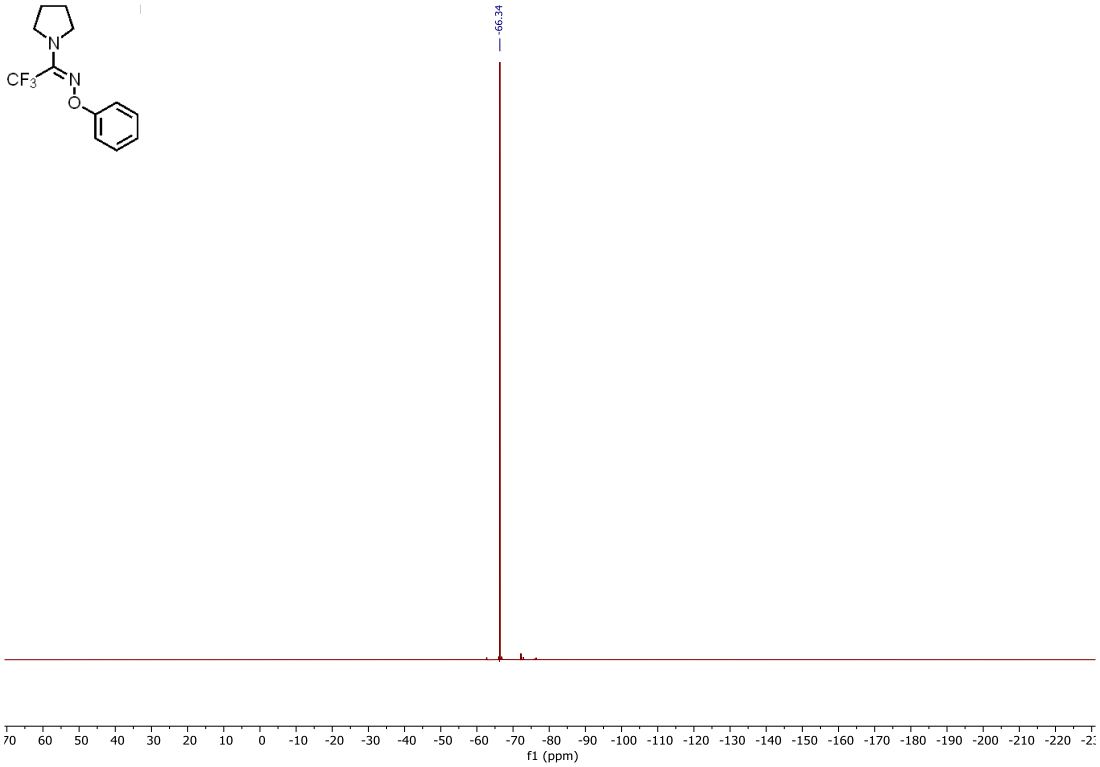



-63.28
-66.29
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

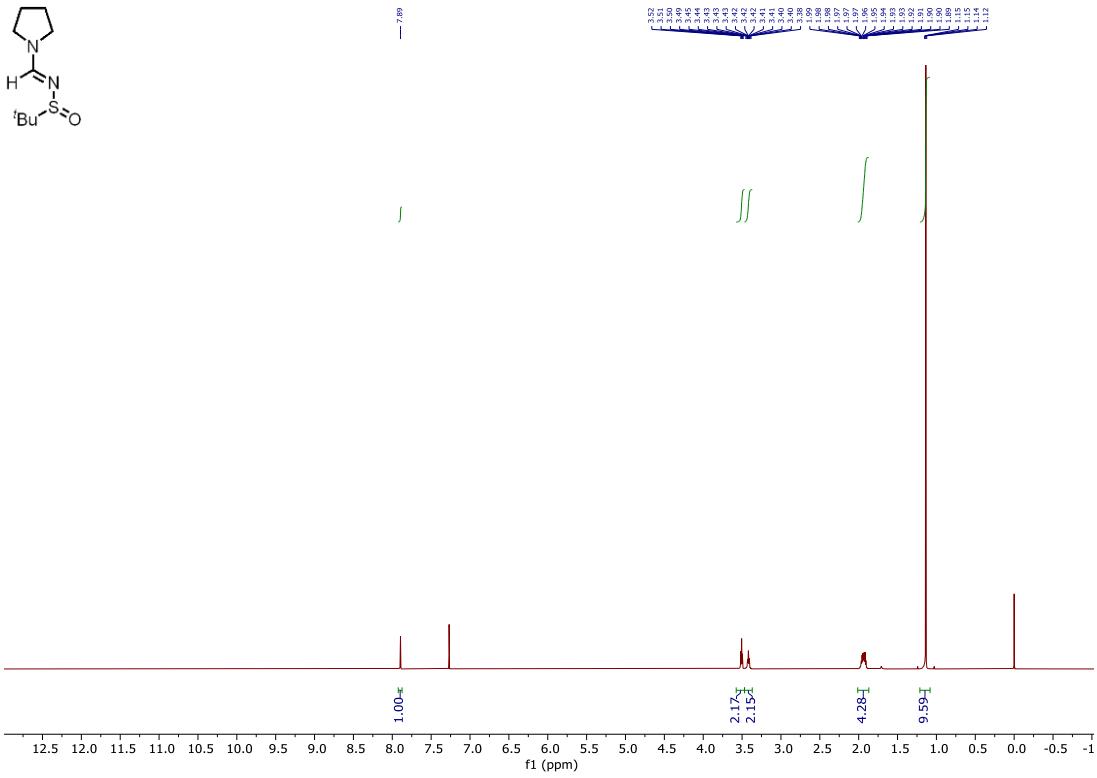
(*E*)-2,2,2-trifluoro-1-(pyrrolidin-1-yl)ethan-1-one O-phenyl oxime (1a-11)

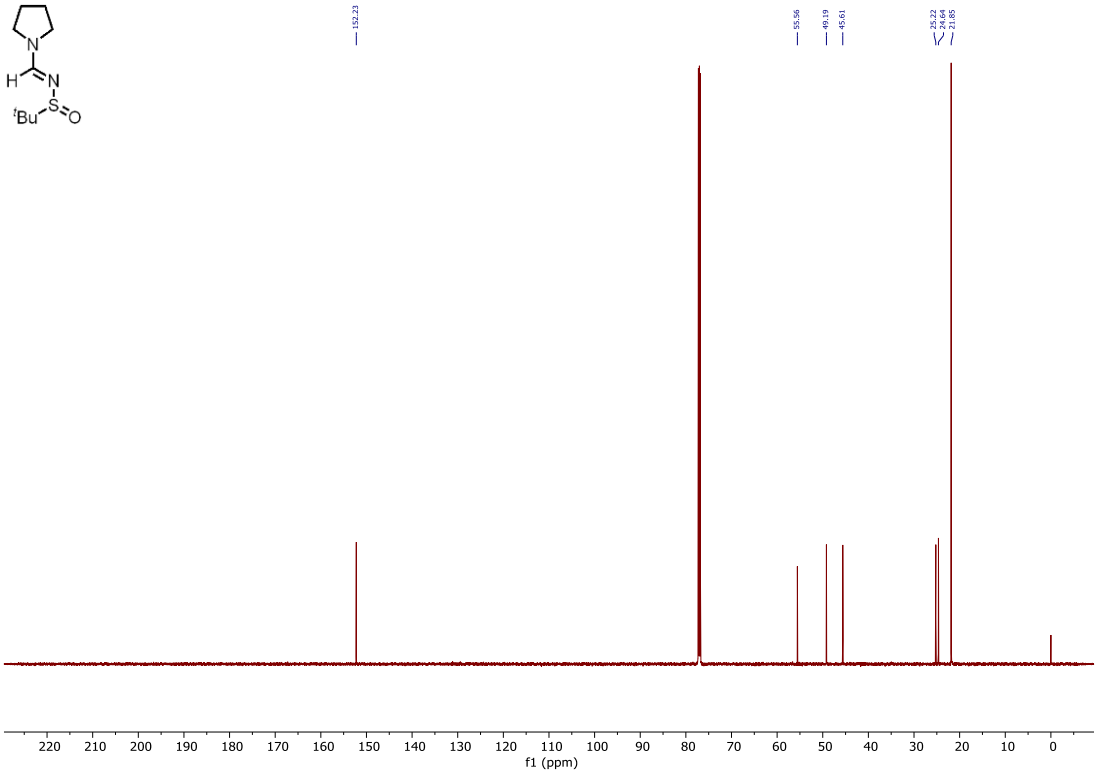




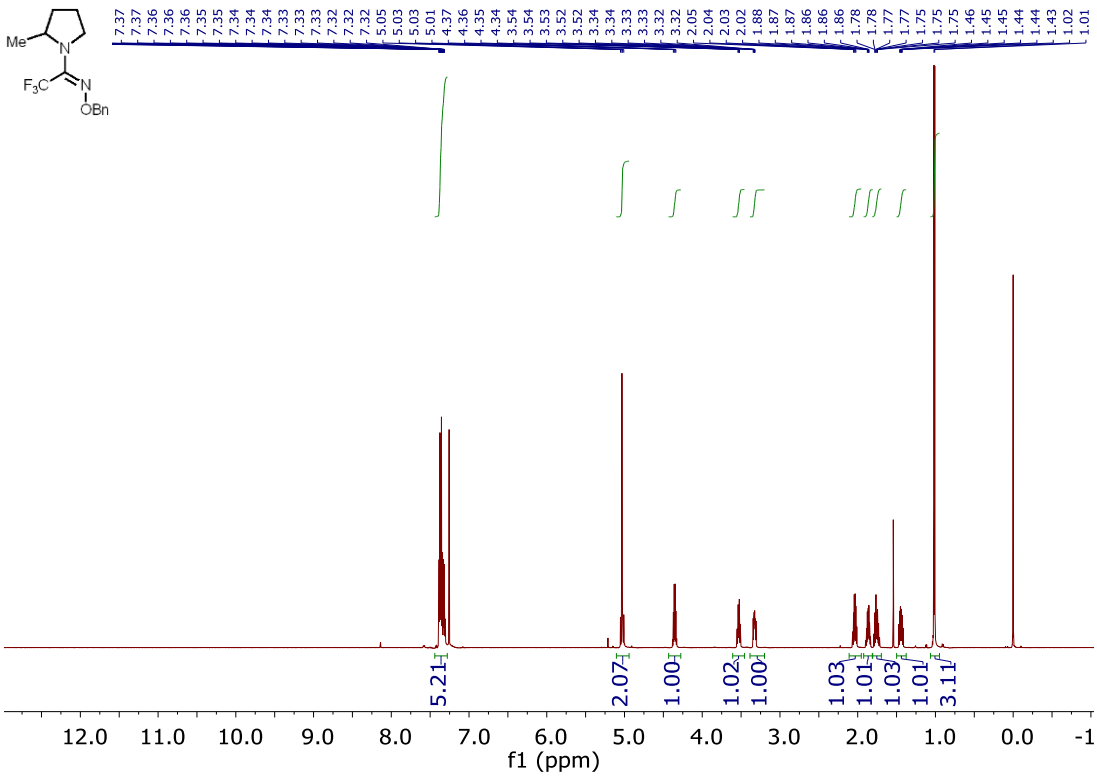

-66.34
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

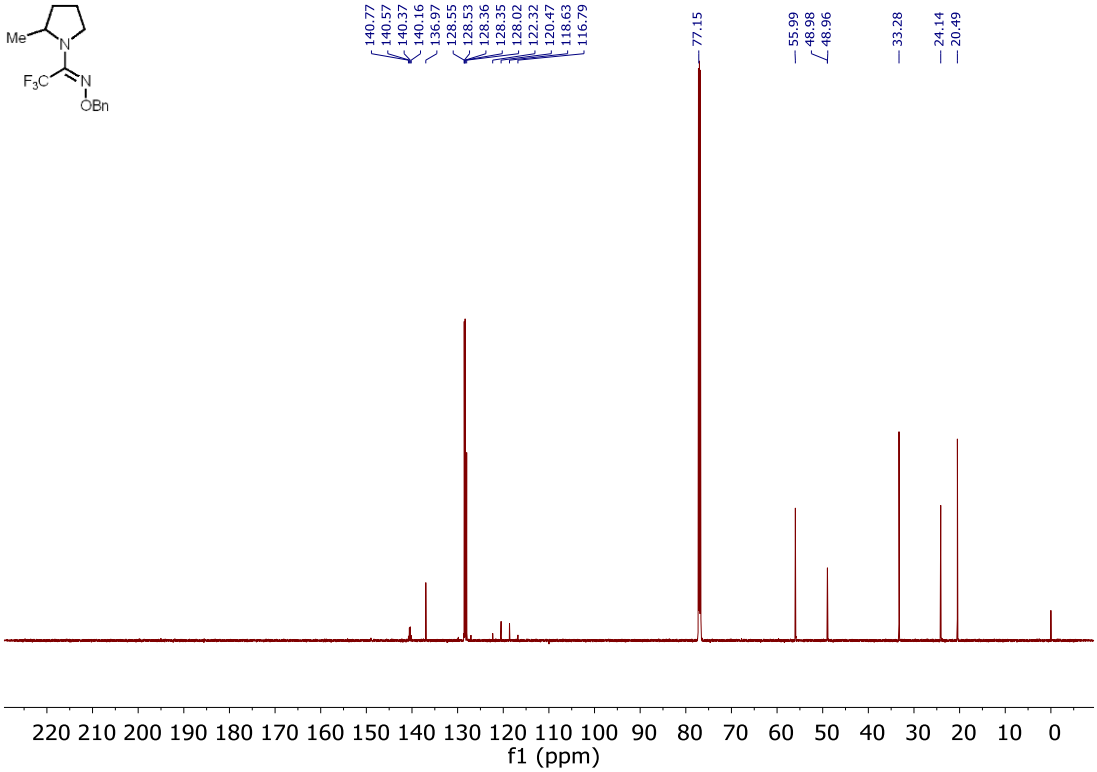
(*E*)-2-methyl-*N*-(pyrrolidin-1-ylmethylene)propane-2-sulfinamide (1a-12)

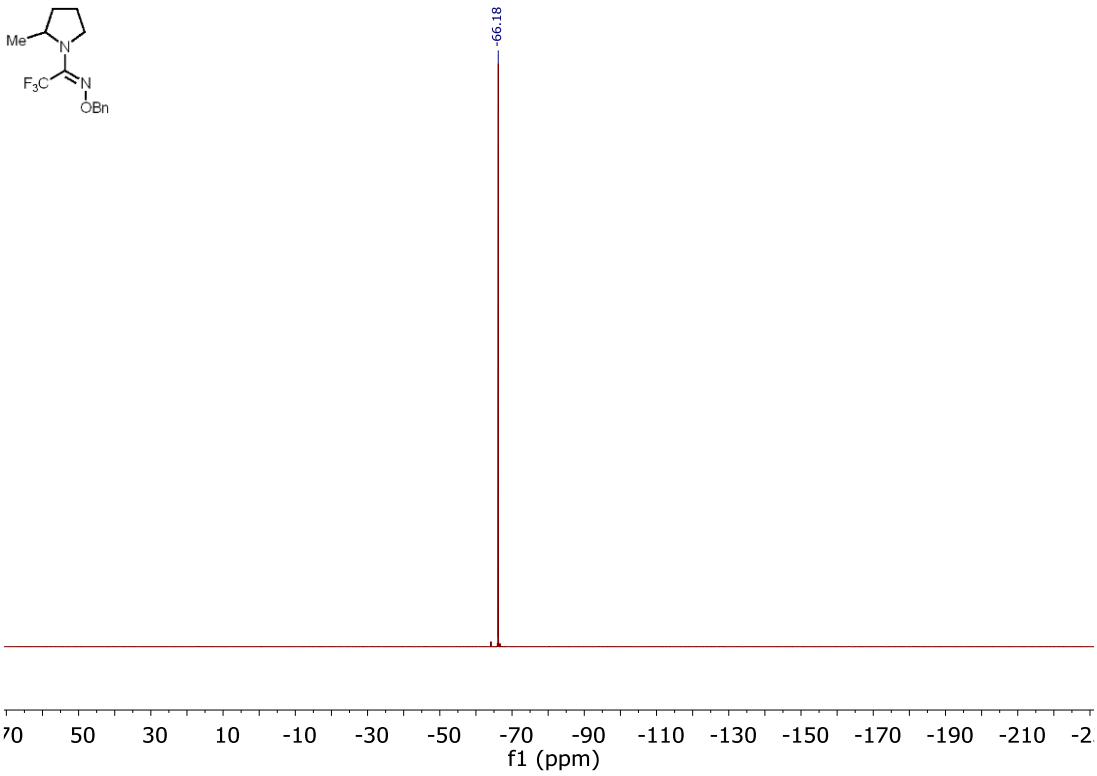




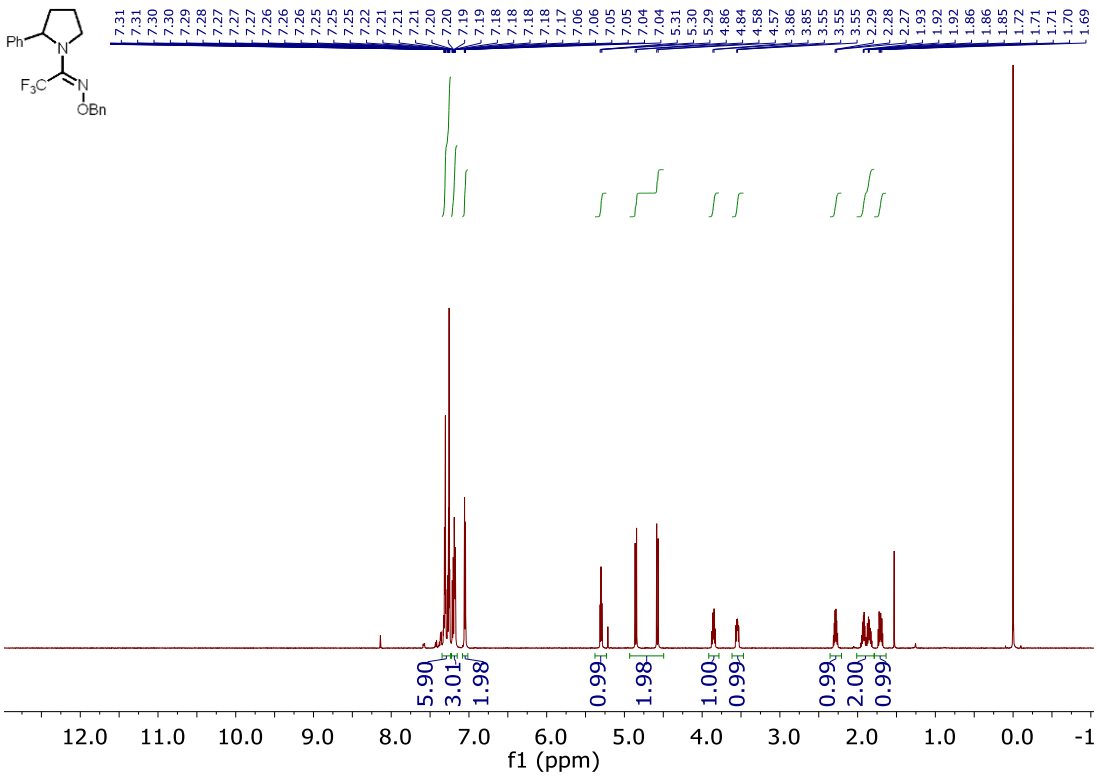
(*E*)-2,2,2-trifluoro-1-(2-methylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1b)

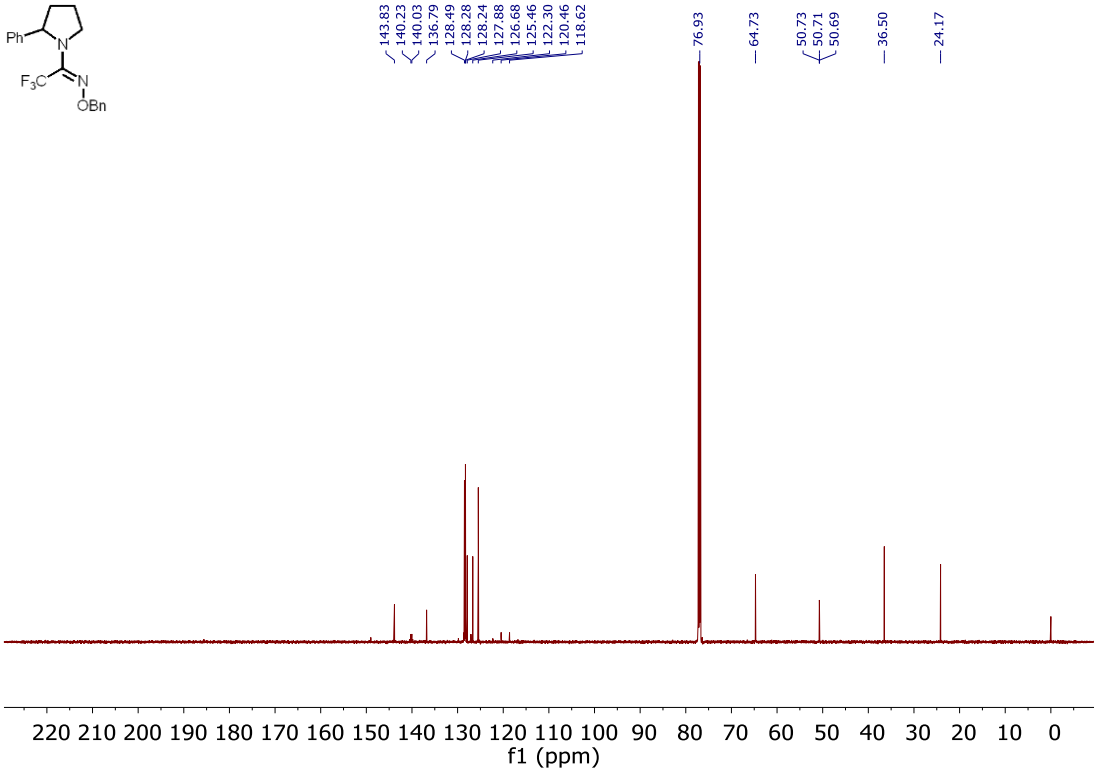


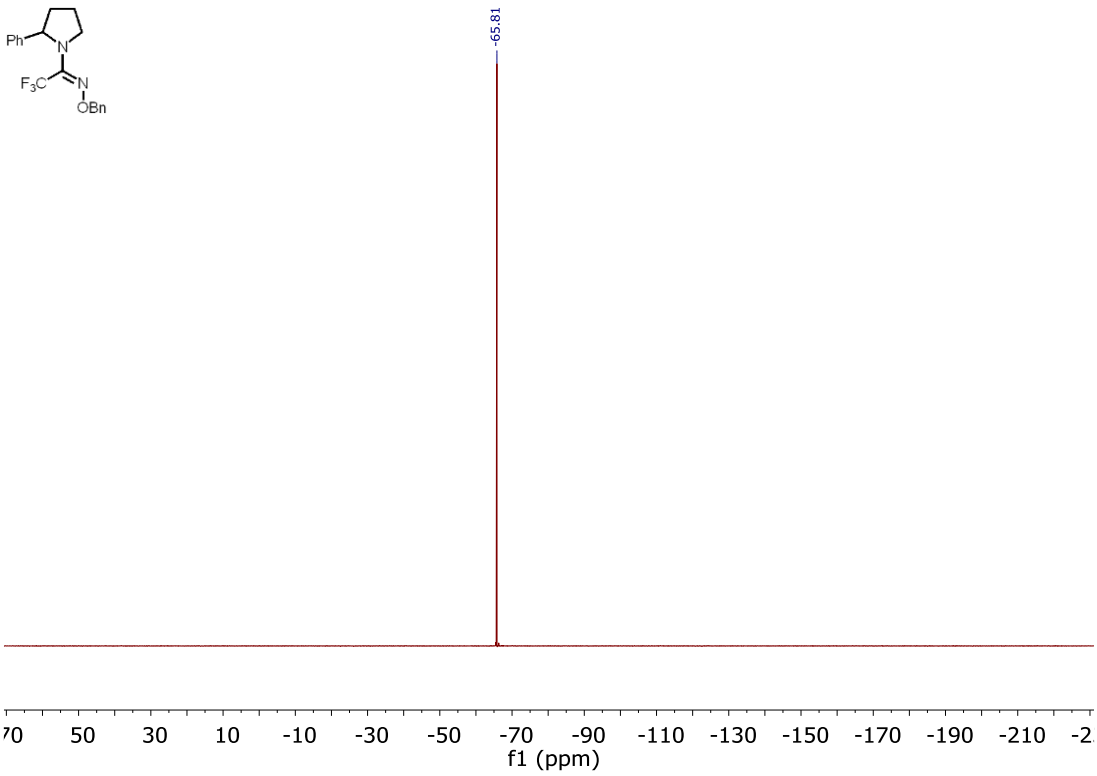



Me
N
F3C
N
OBn
-66.18
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

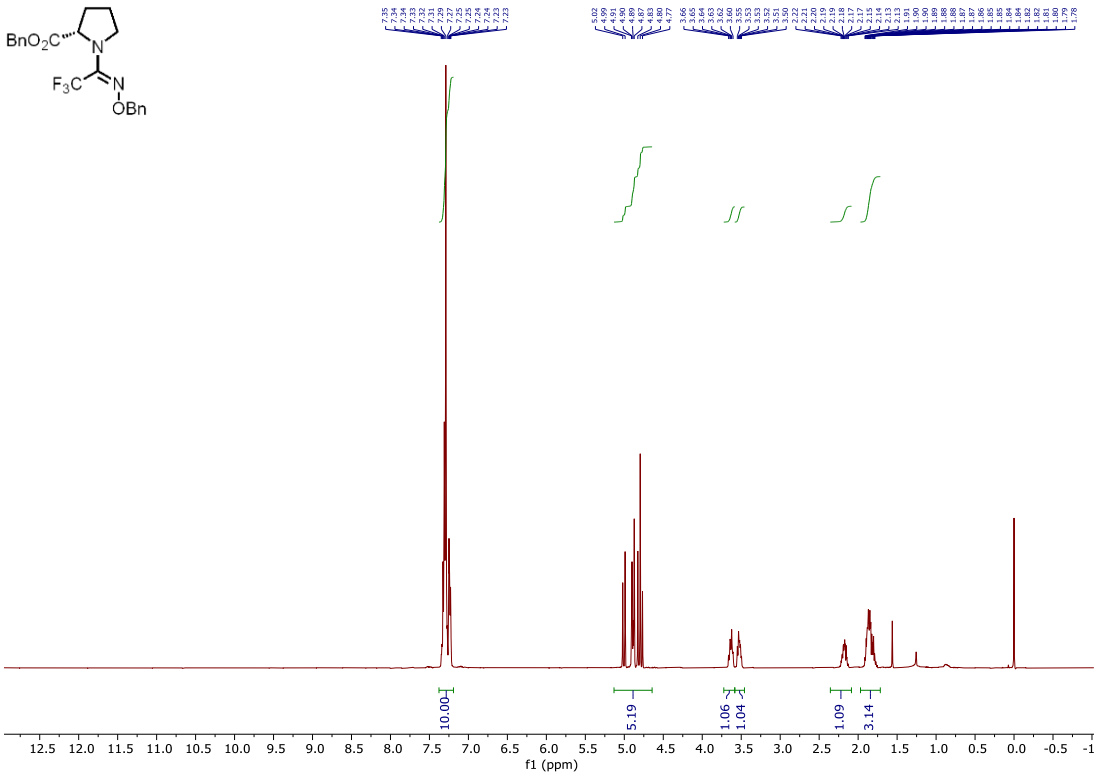
(*E*)-2,2,2-trifluoro-1-(2-phenylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1c)

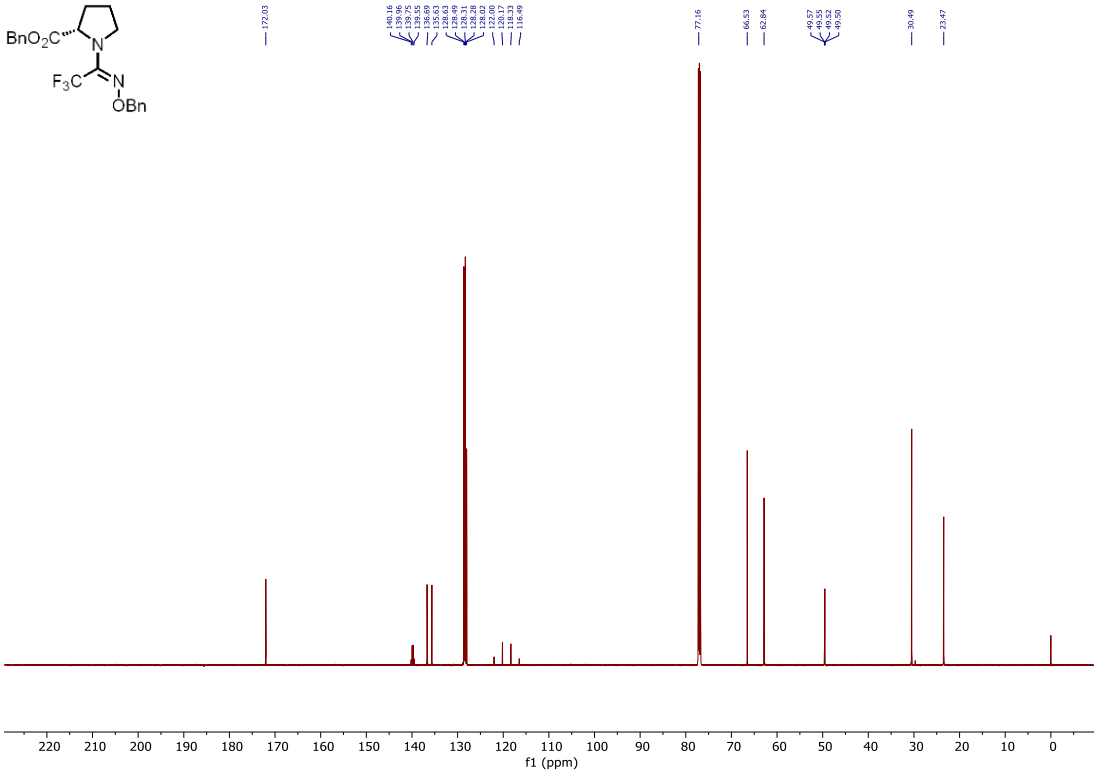


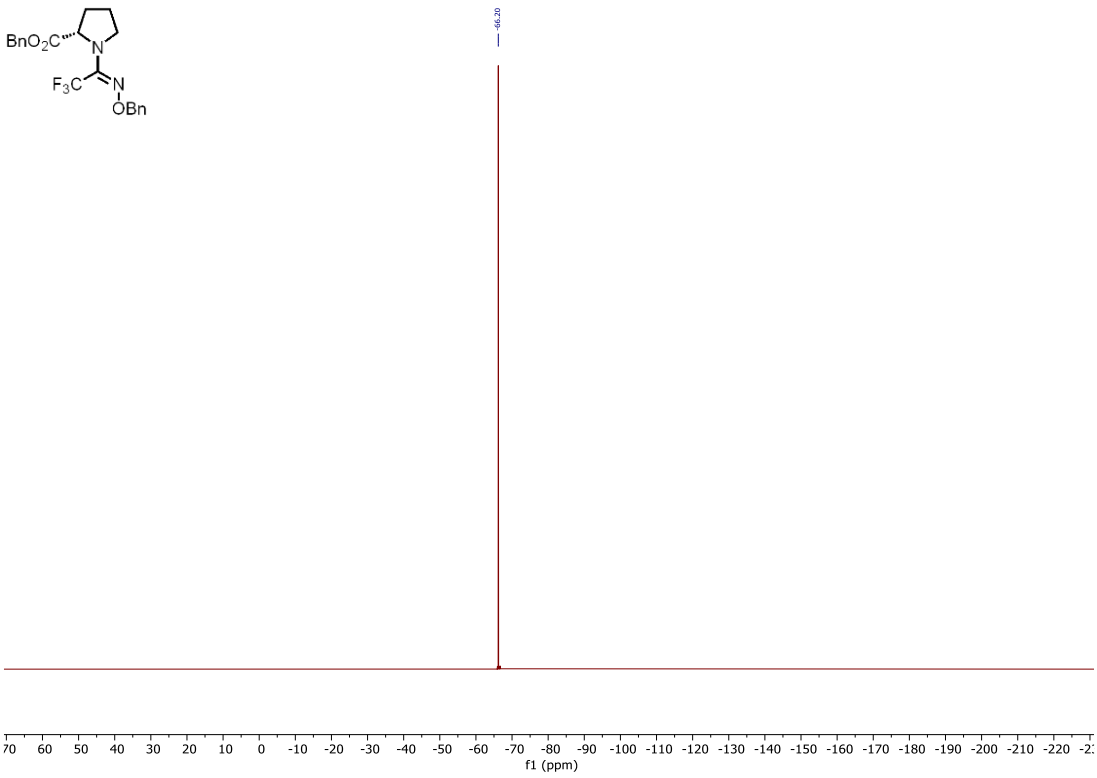



Ph
N
F3C
N
OBn
-65.81
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

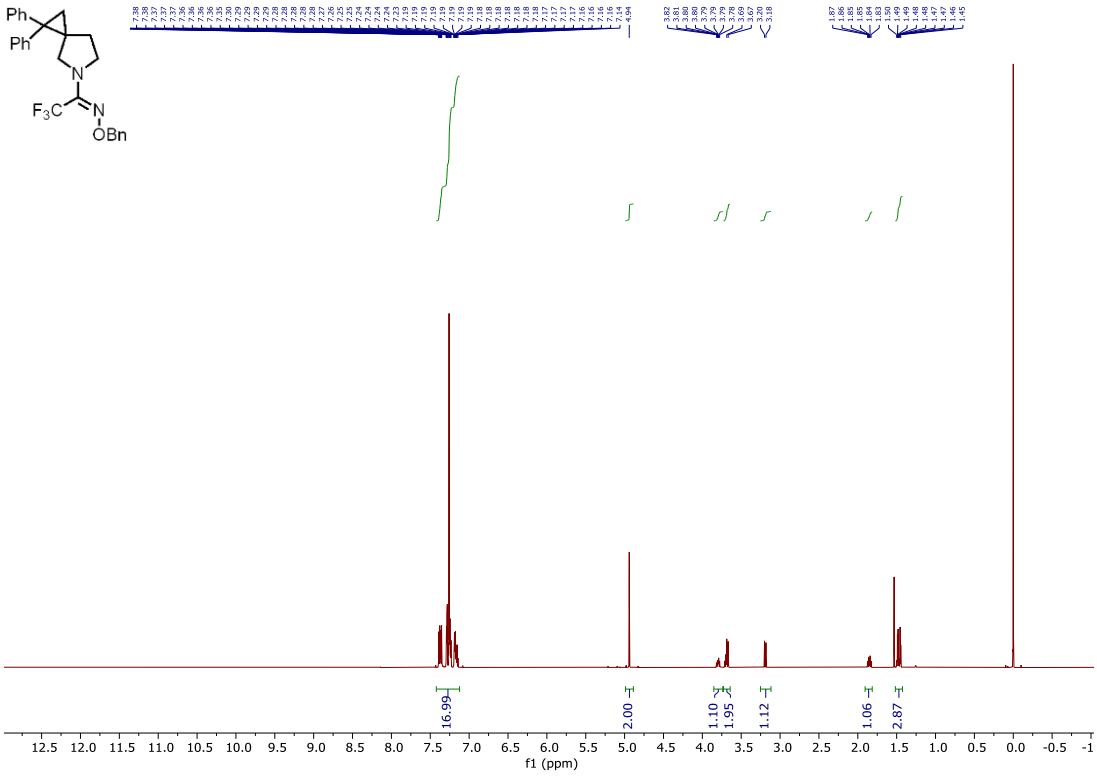
benzyl (*E*)-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-*L*-prolinate (1d)

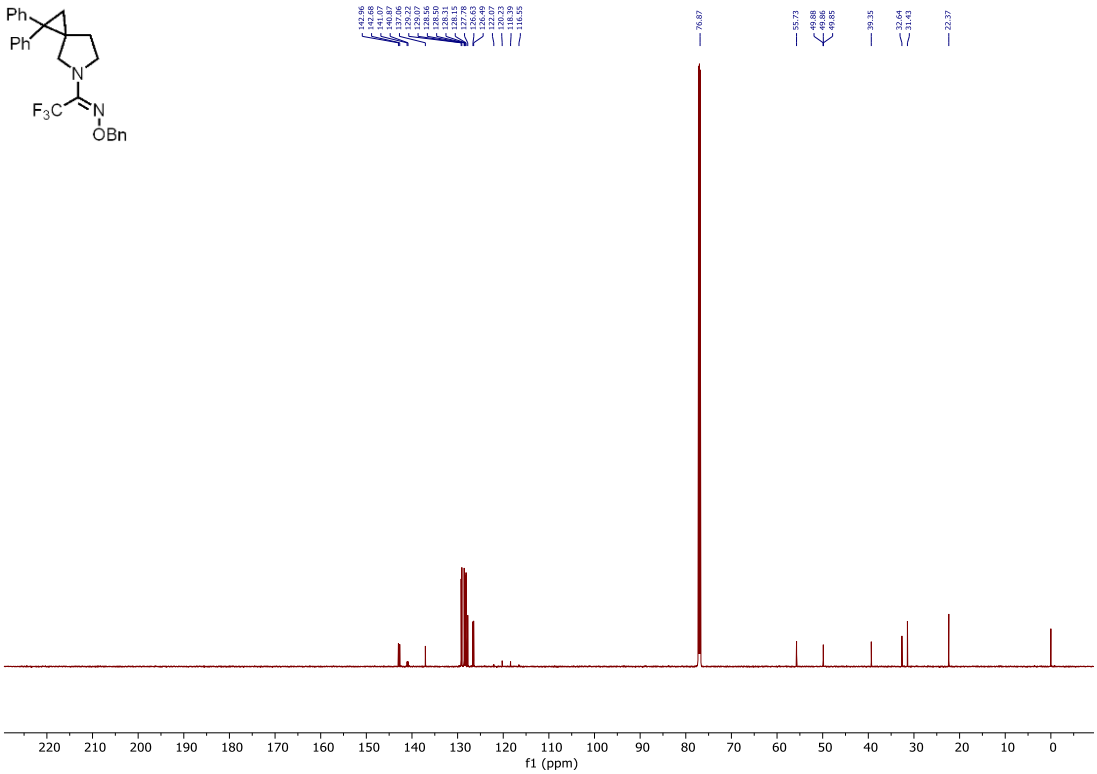


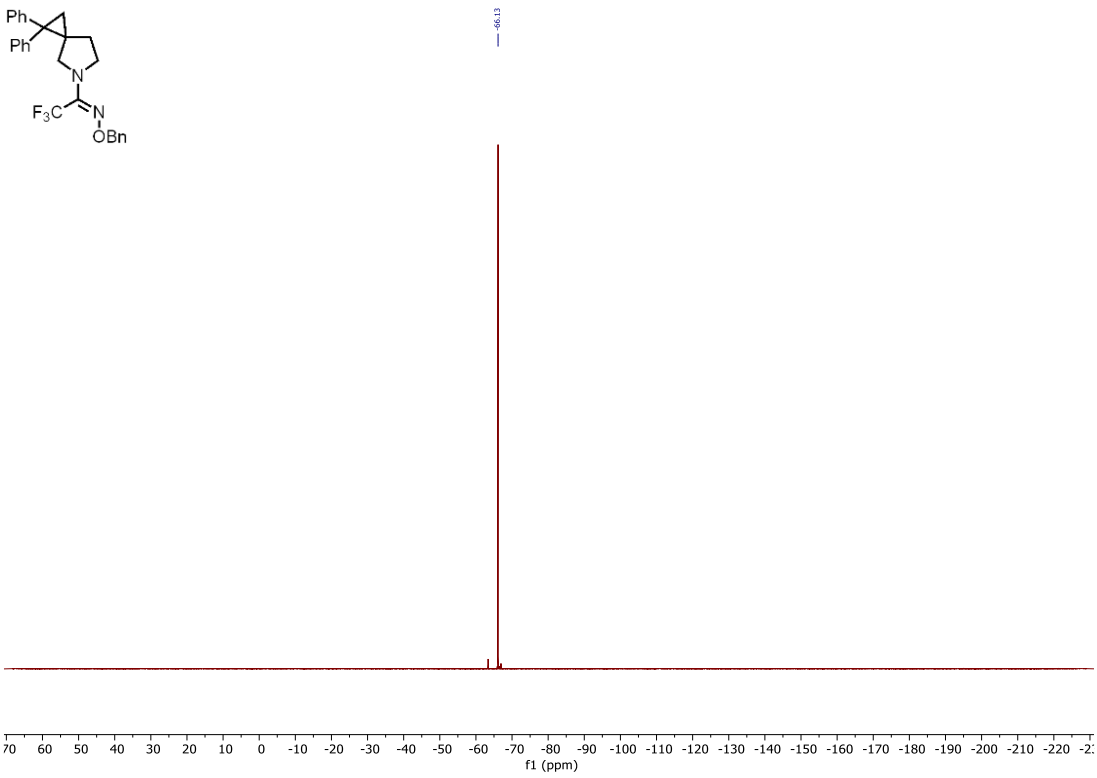



BnO2C
N
F3C
N
OBn
-66.20
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

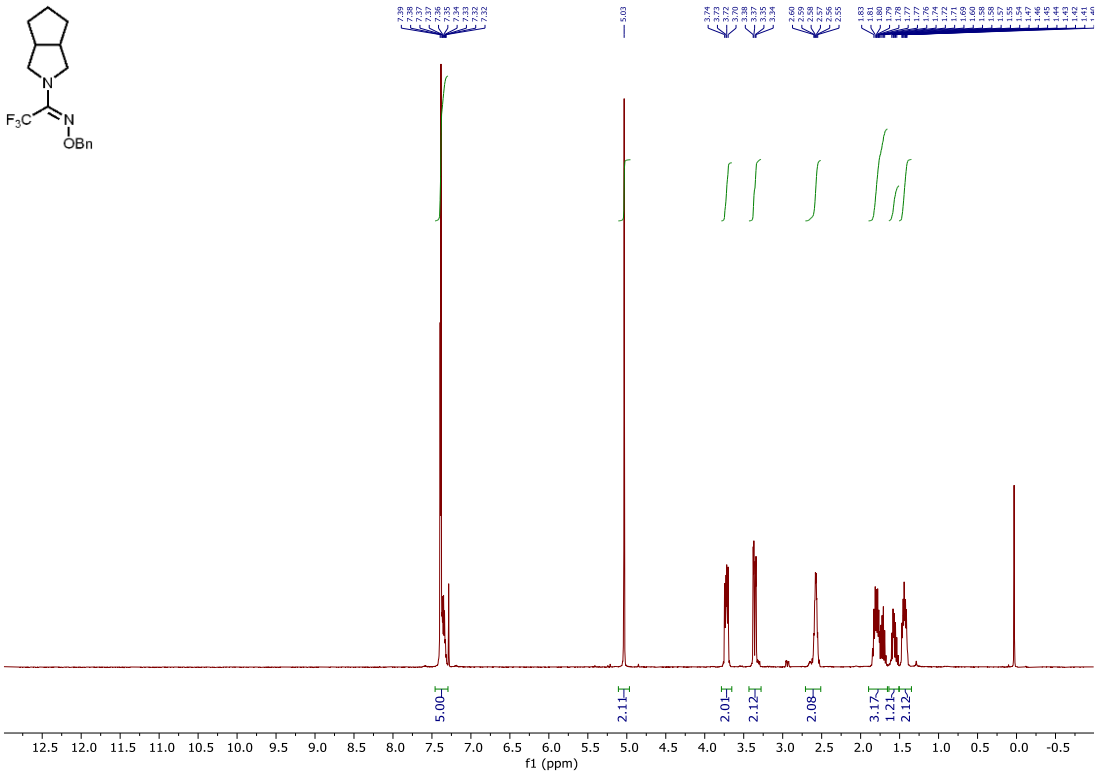
(*E*)-1-(1,1-diphenyl-5-azaspiro[2.4]heptan-5-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1e)

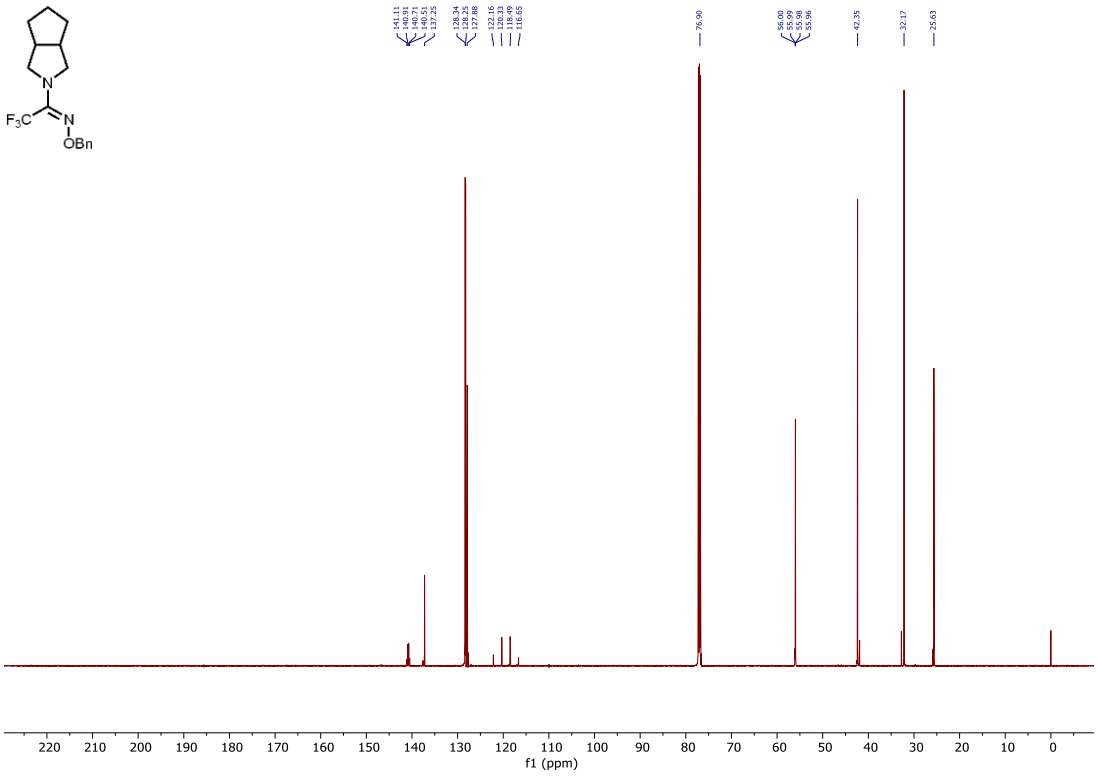


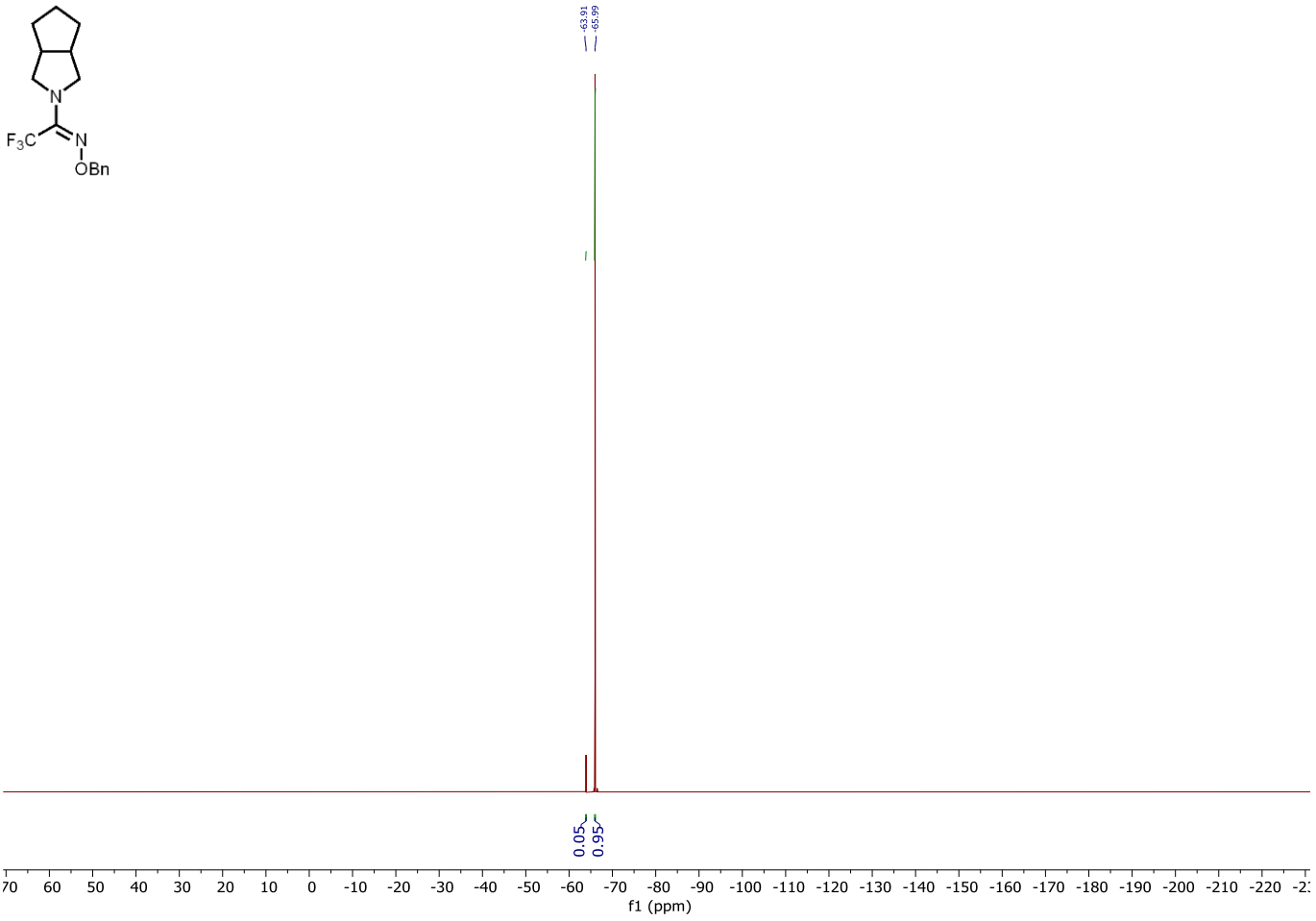



Ph
Ph
N
F3C
N
OBn
-66.13
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

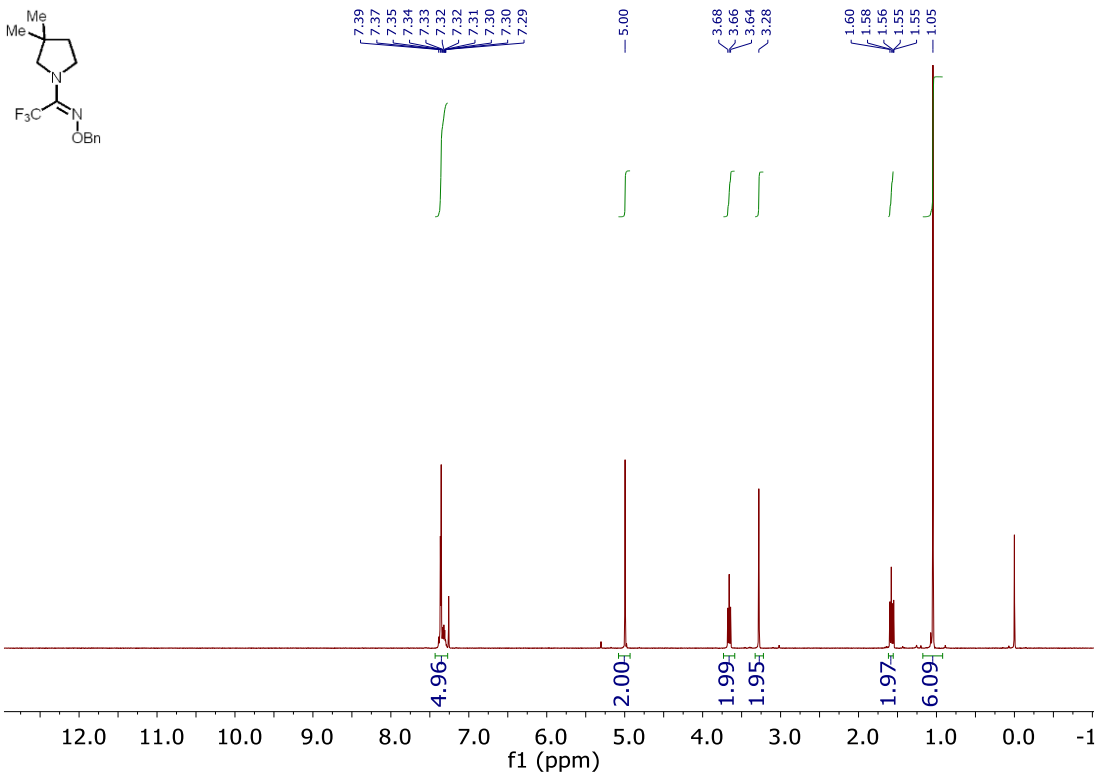
(*E*)-2,2,2-trifluoro-1-(hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)ethan-1-one *O*-benzyl oxime (1f)

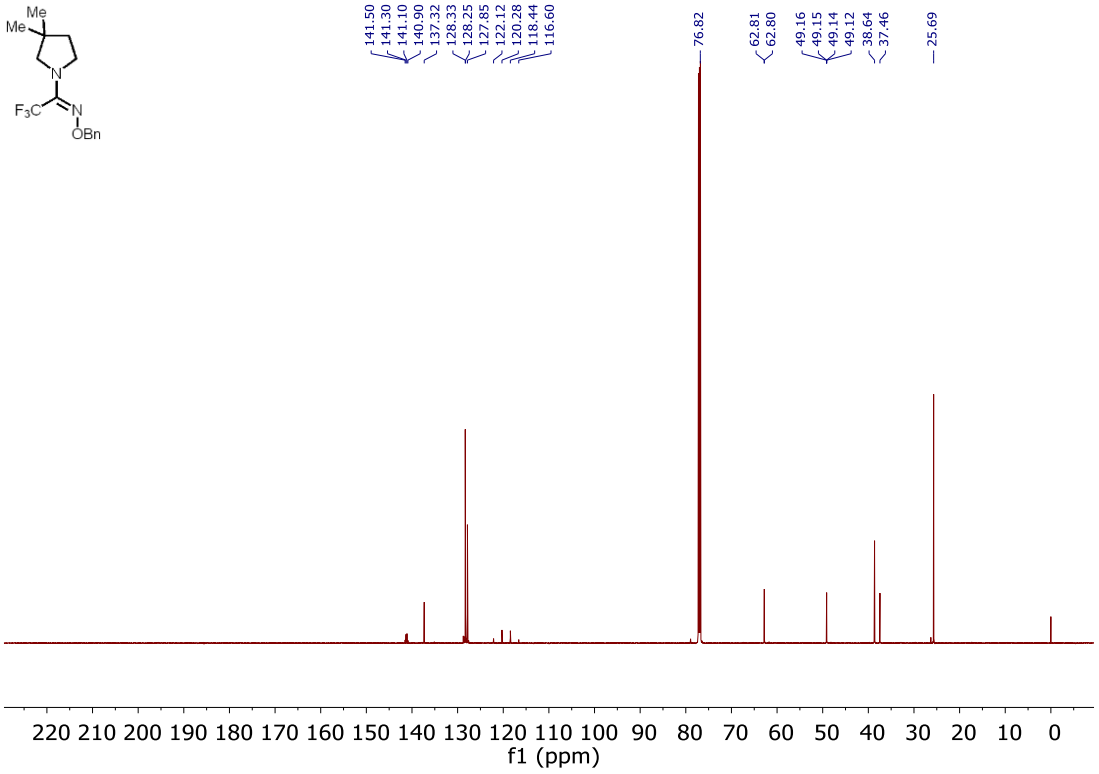


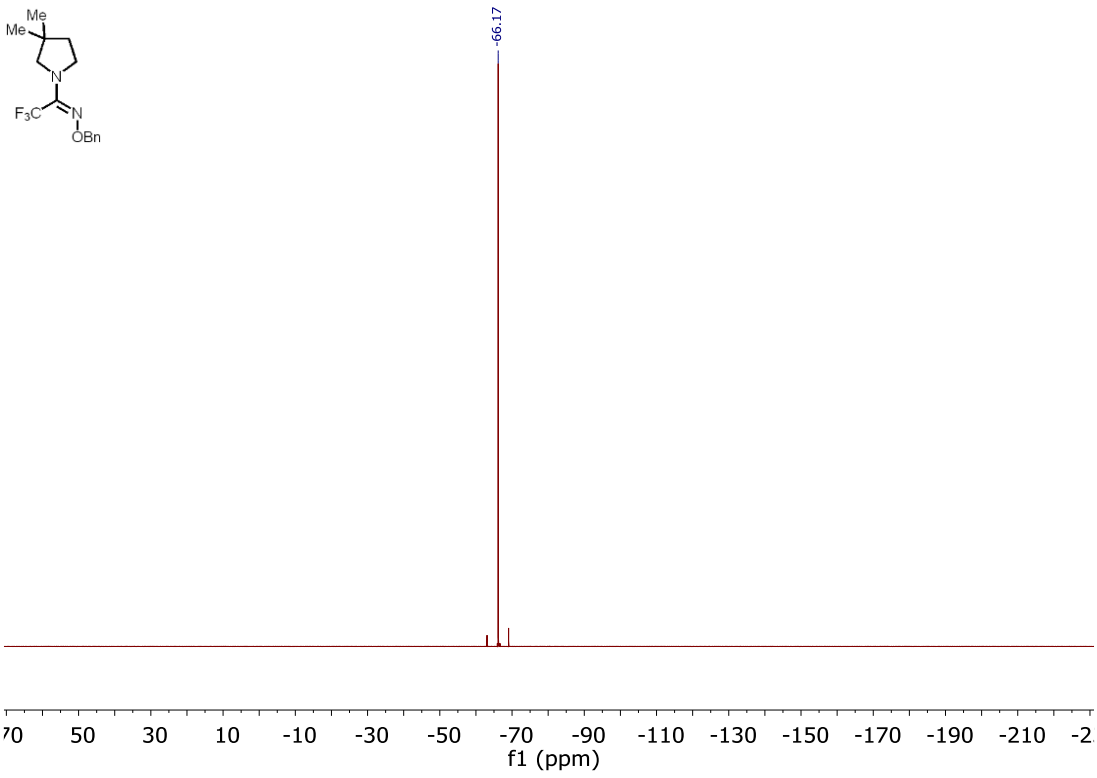



-63.91
-65.99
0.05
0.95
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

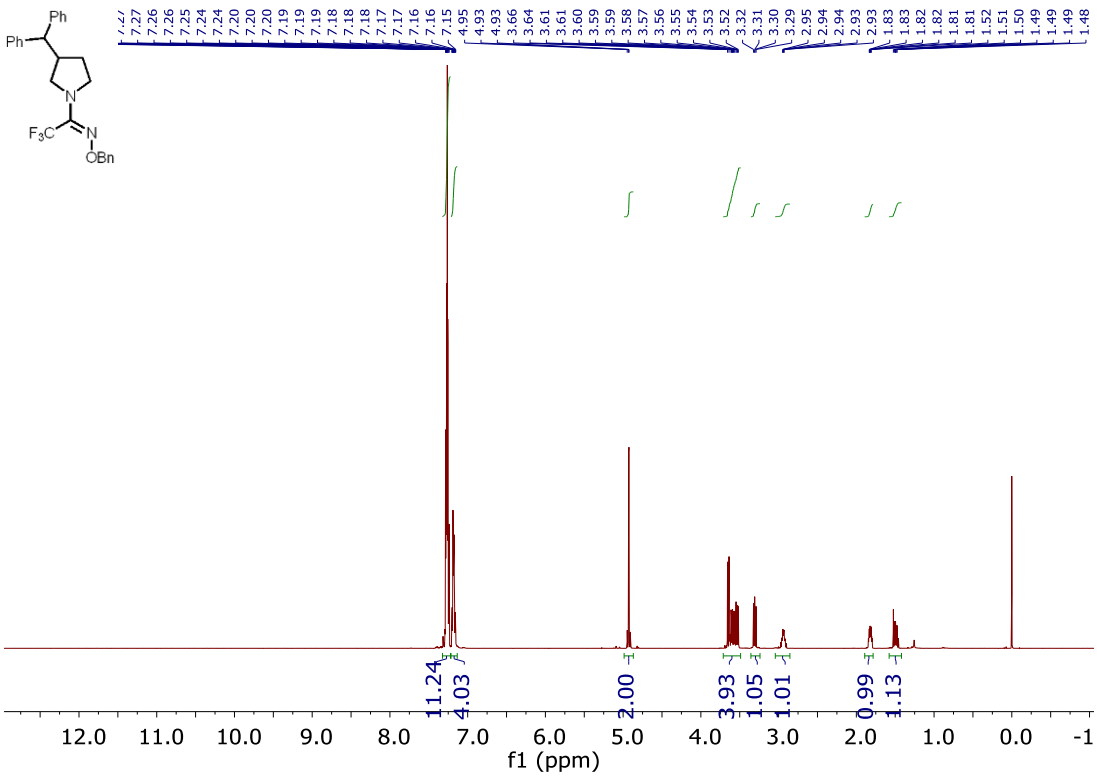
(*E*)-1-(3,3-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1g)

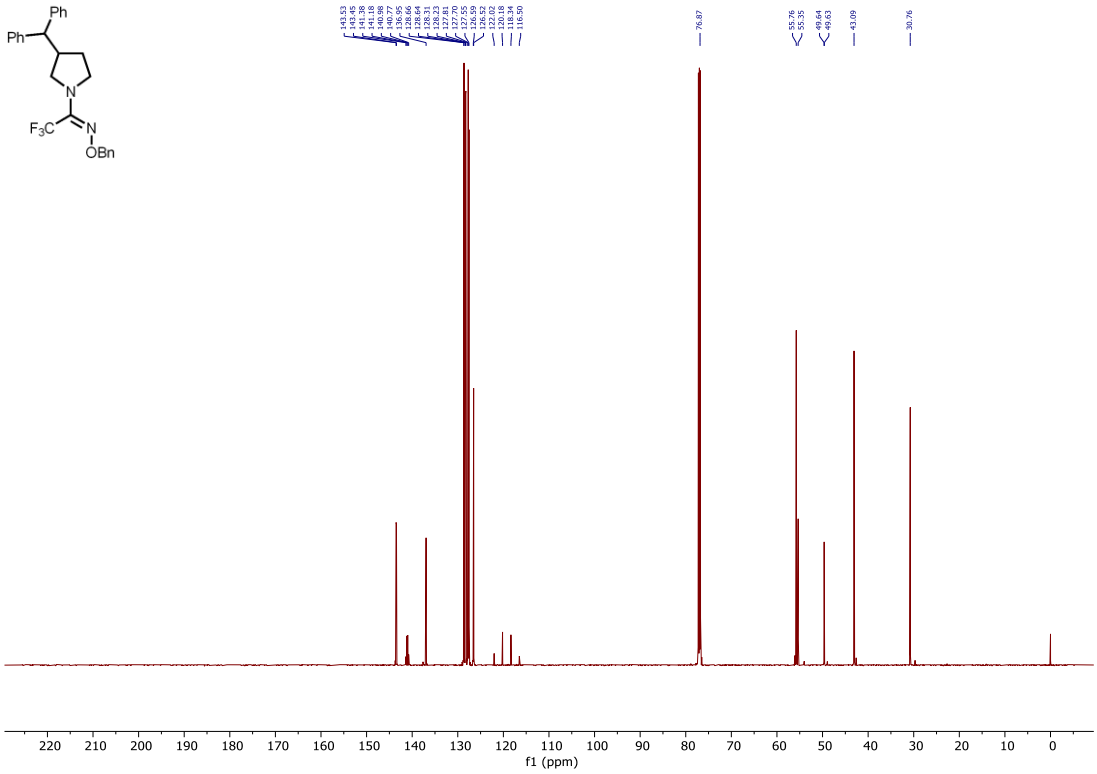


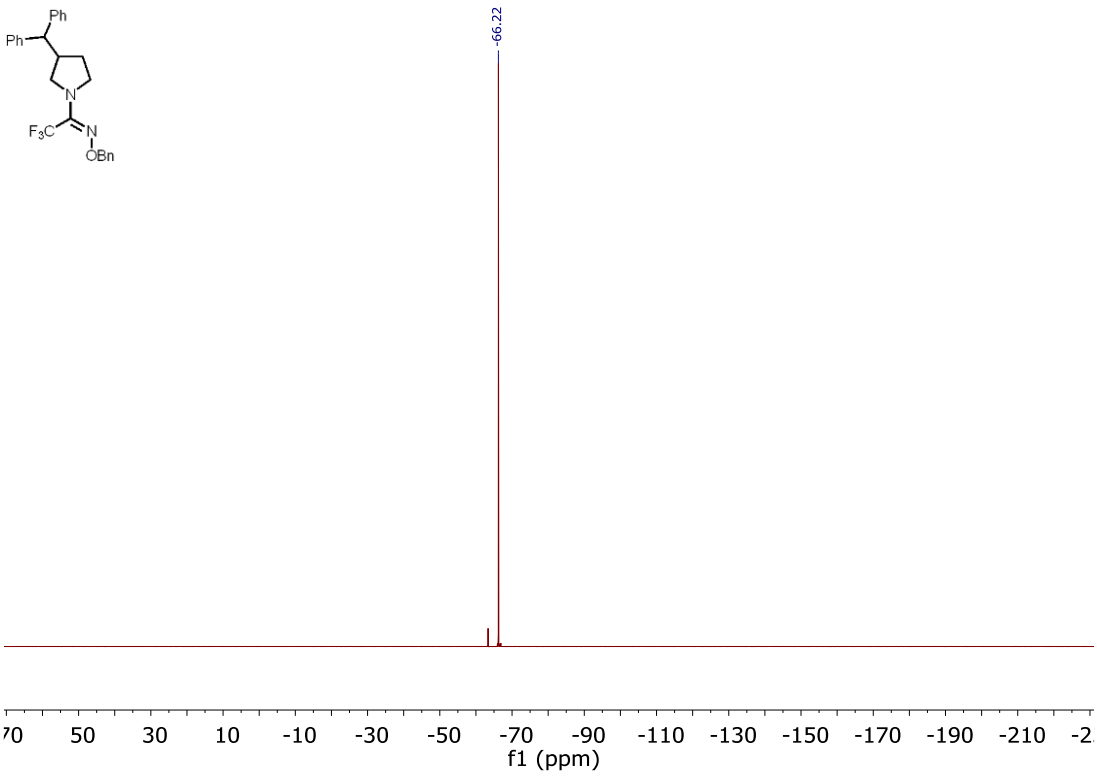



Me
Me
N
F3C
N
OBn
-66.17
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

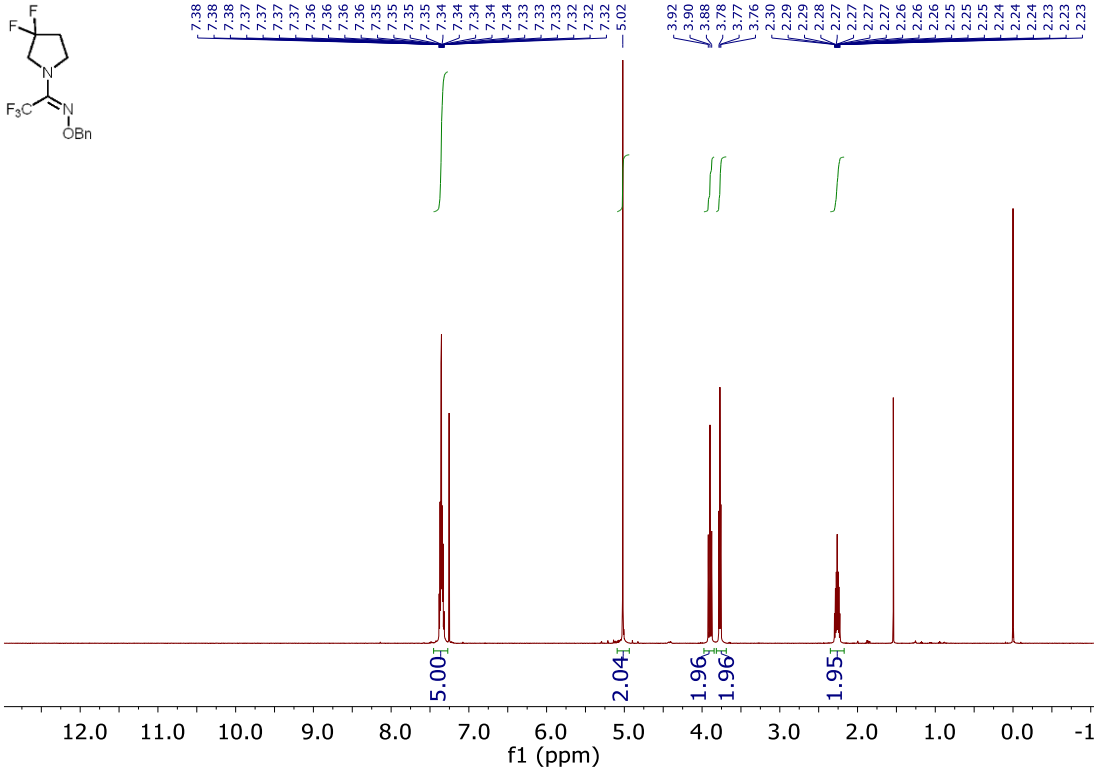
(*E*)-1-(3-benzhydrylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1h/1k)

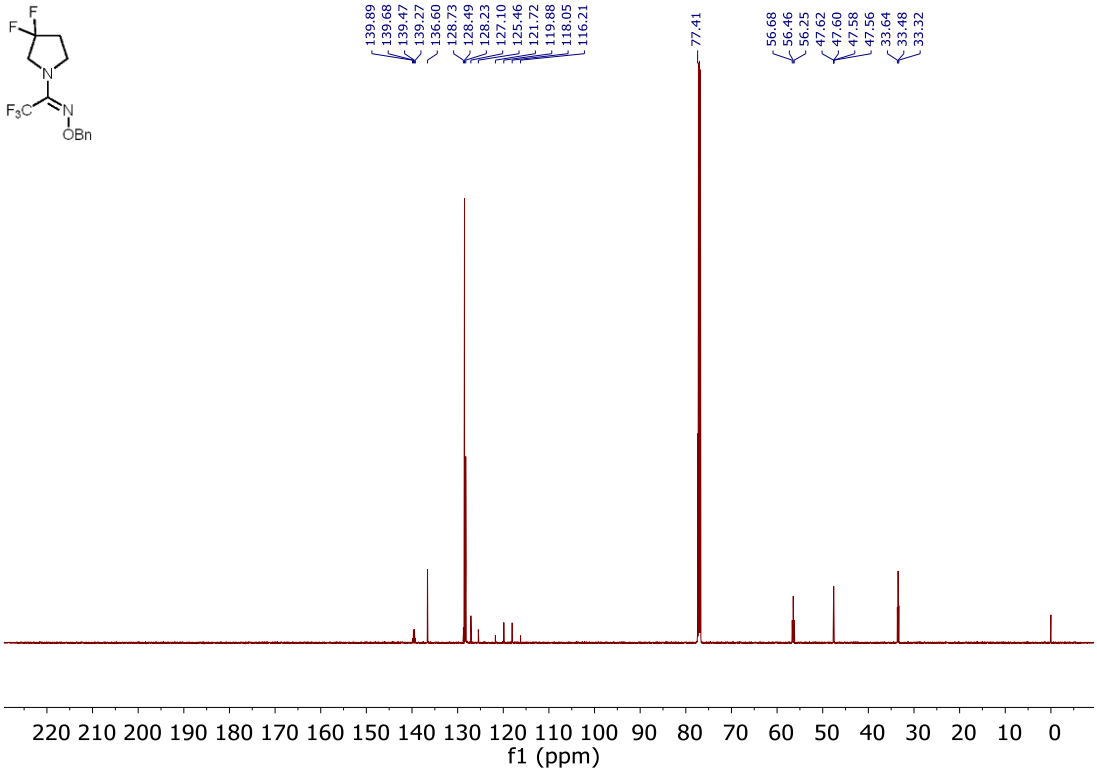


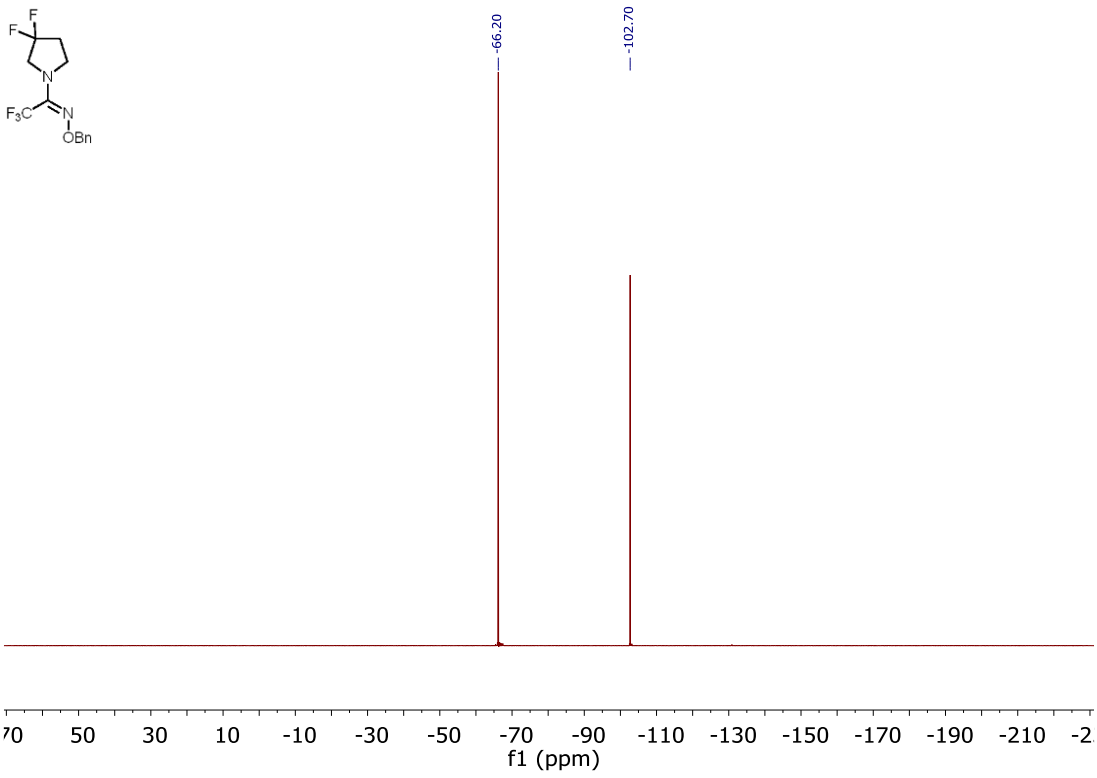



Ph
Ph
N
F3C
N
OBn
-66.22
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

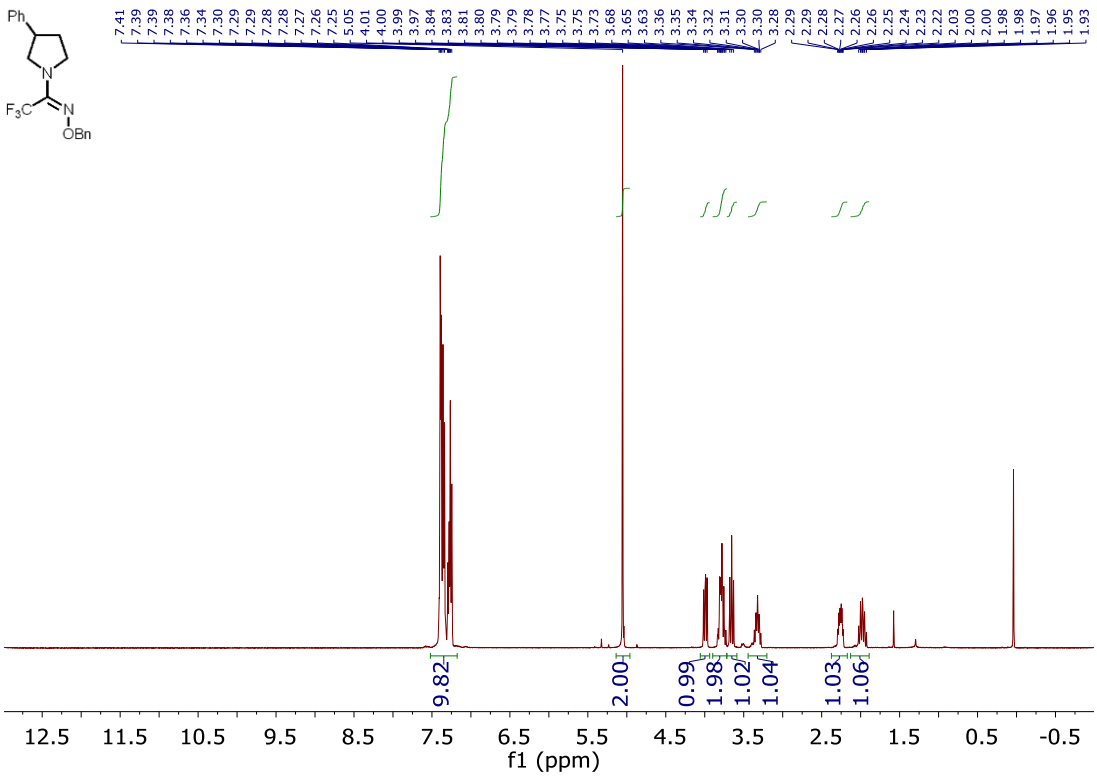
(*E*)-1-(3,3-difluoropyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1i)

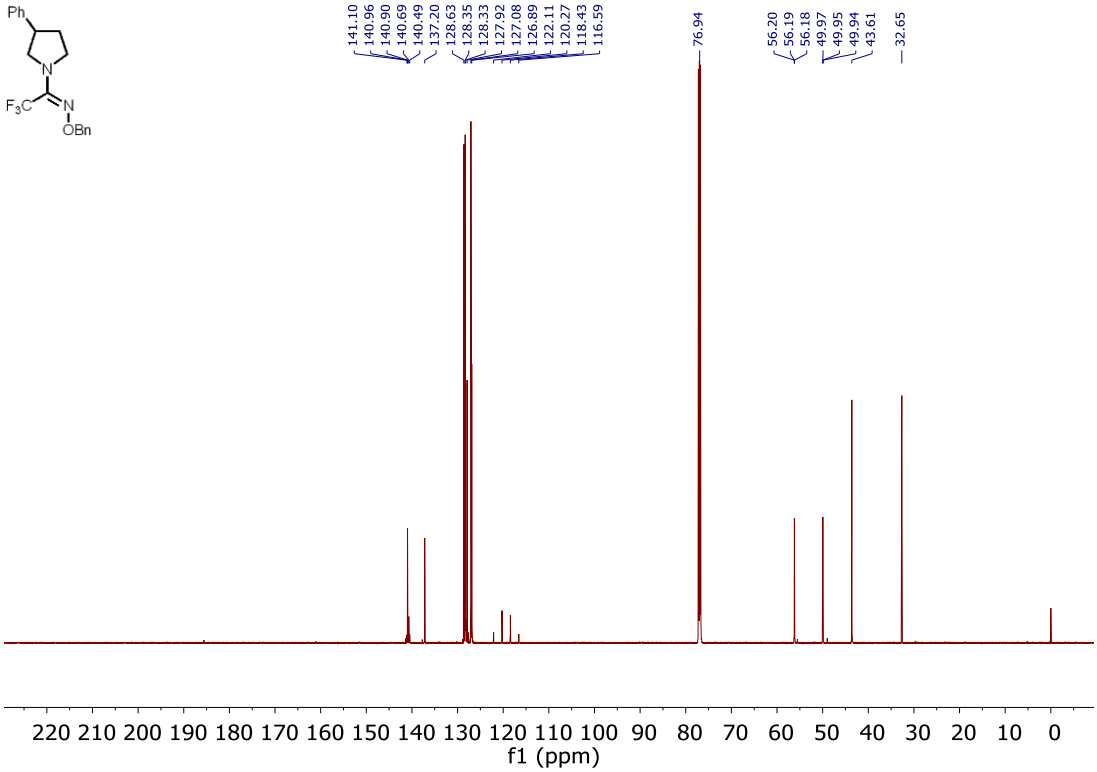


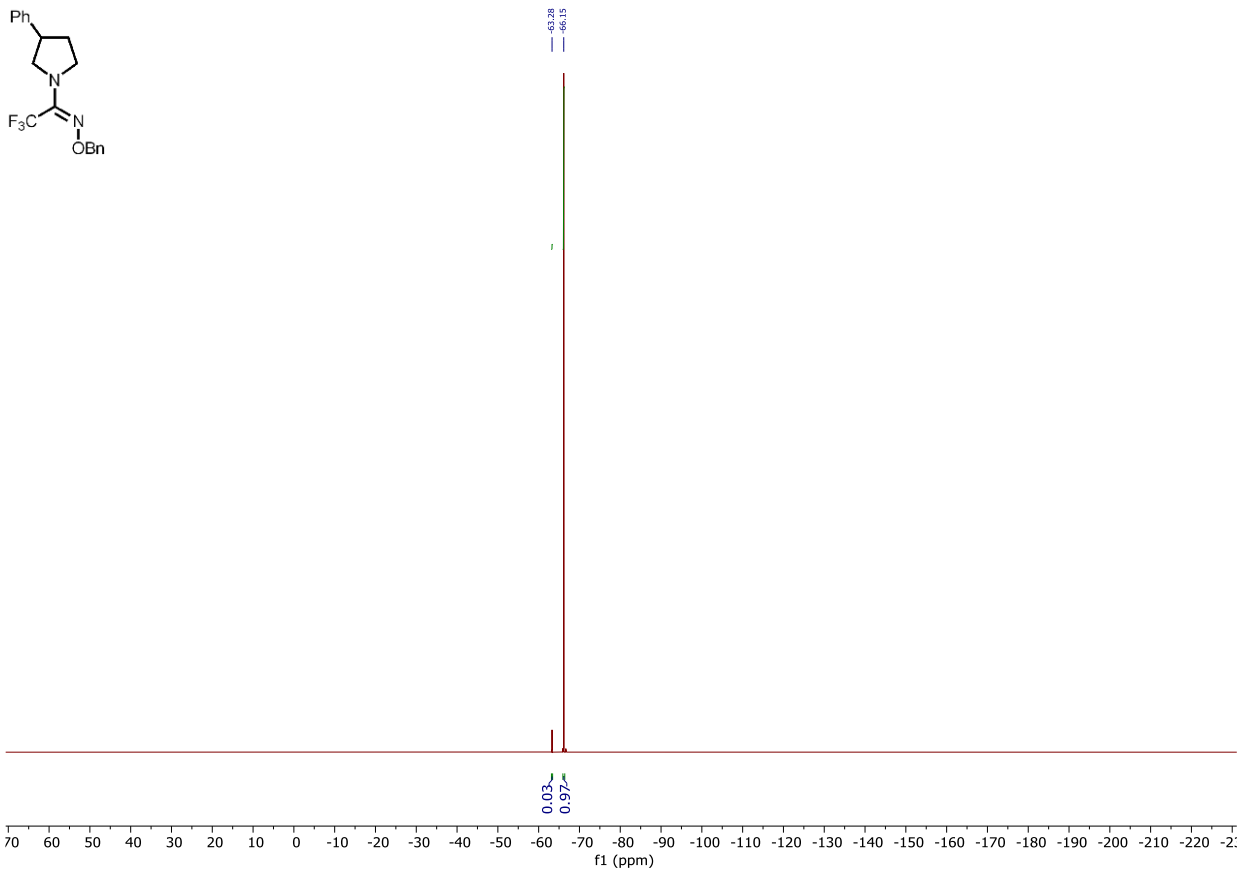



F
F
N
F3C
N
OBn
-66.20
-102.70
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

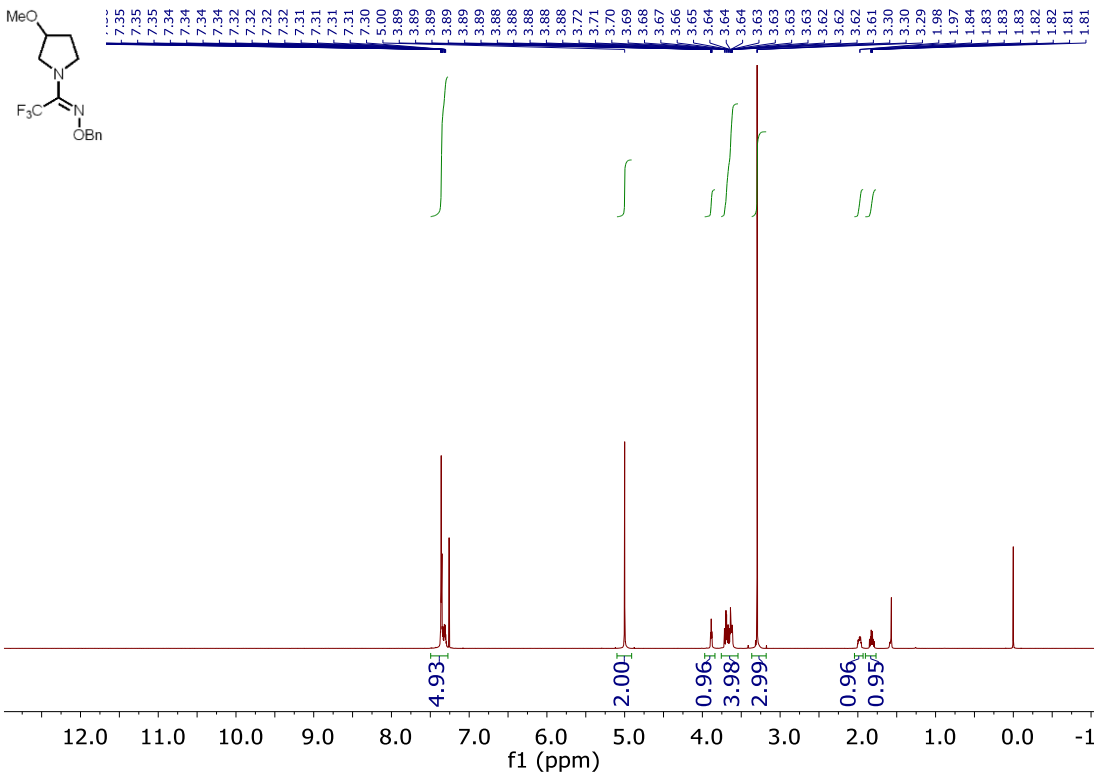
(*E*)-2,2,2-trifluoro-1-(3-phenylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1j)

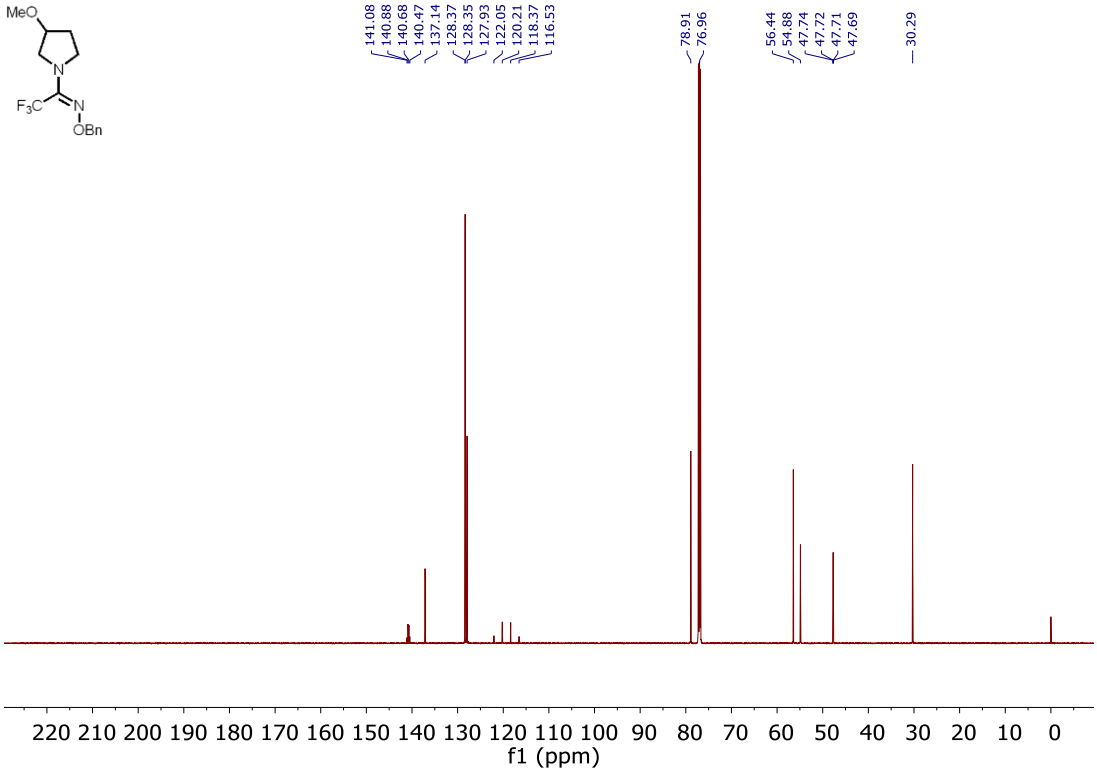


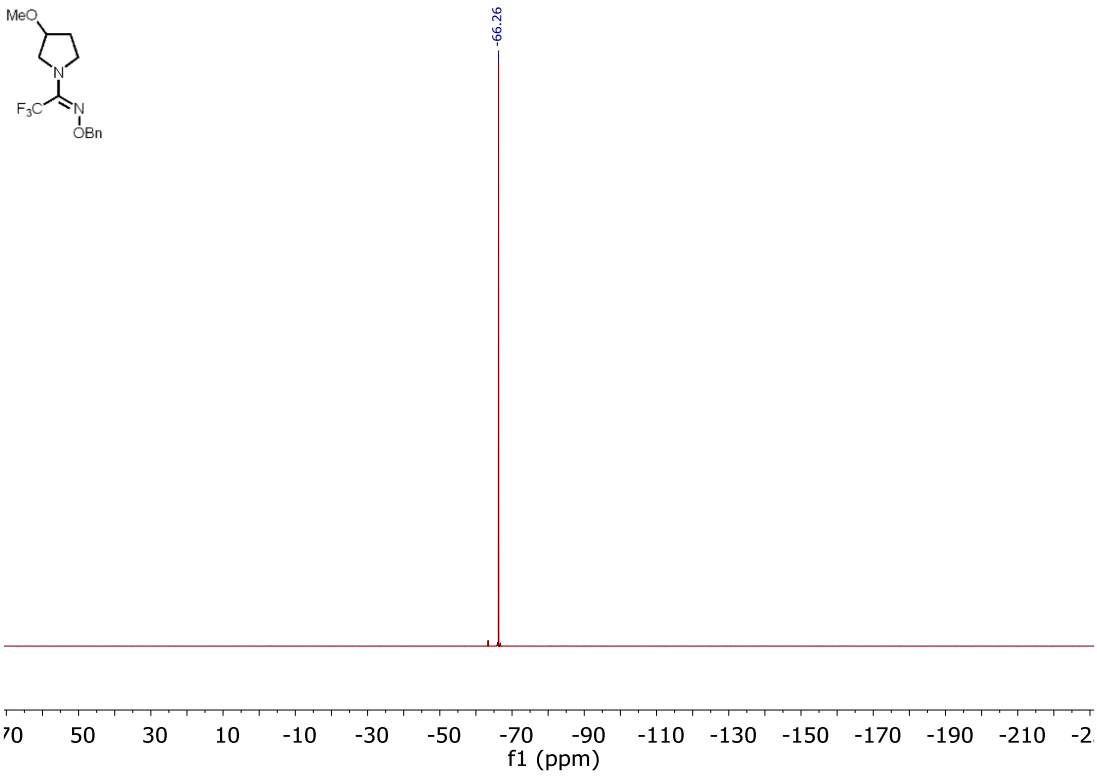



Ph
N
F3C
N
OBn
-63.28
-66.15
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

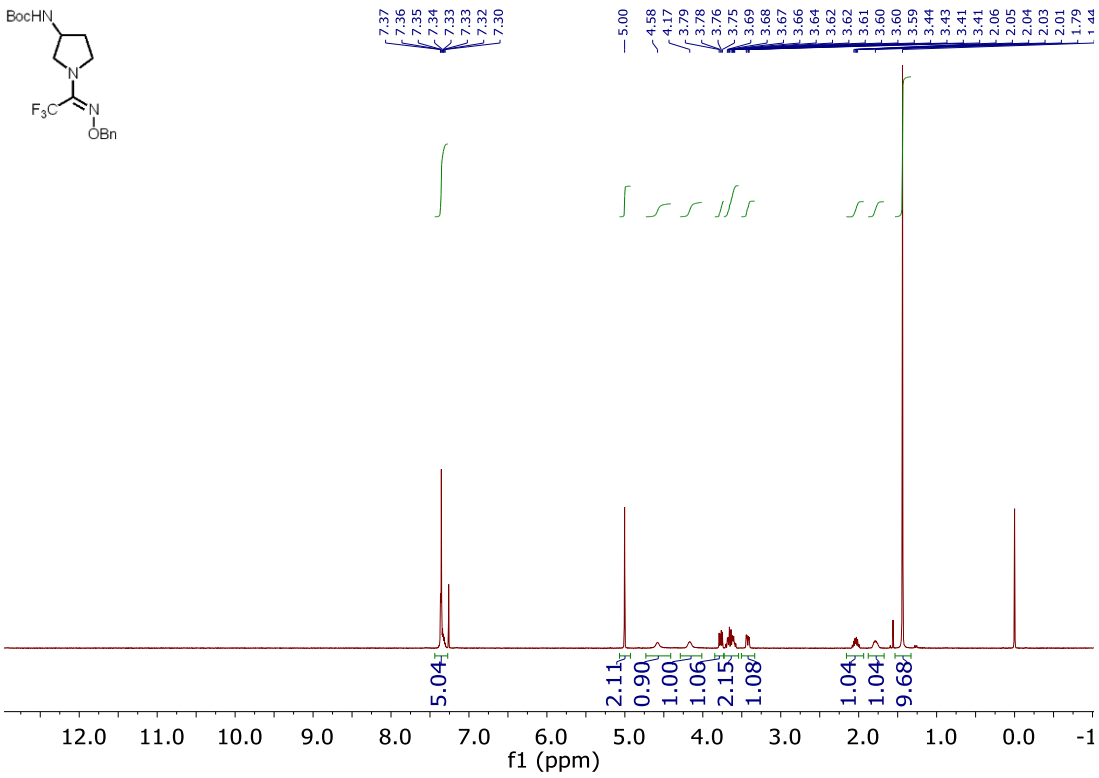
(*E*)-2,2,2-trifluoro-1-(3-methoxypyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (1l)

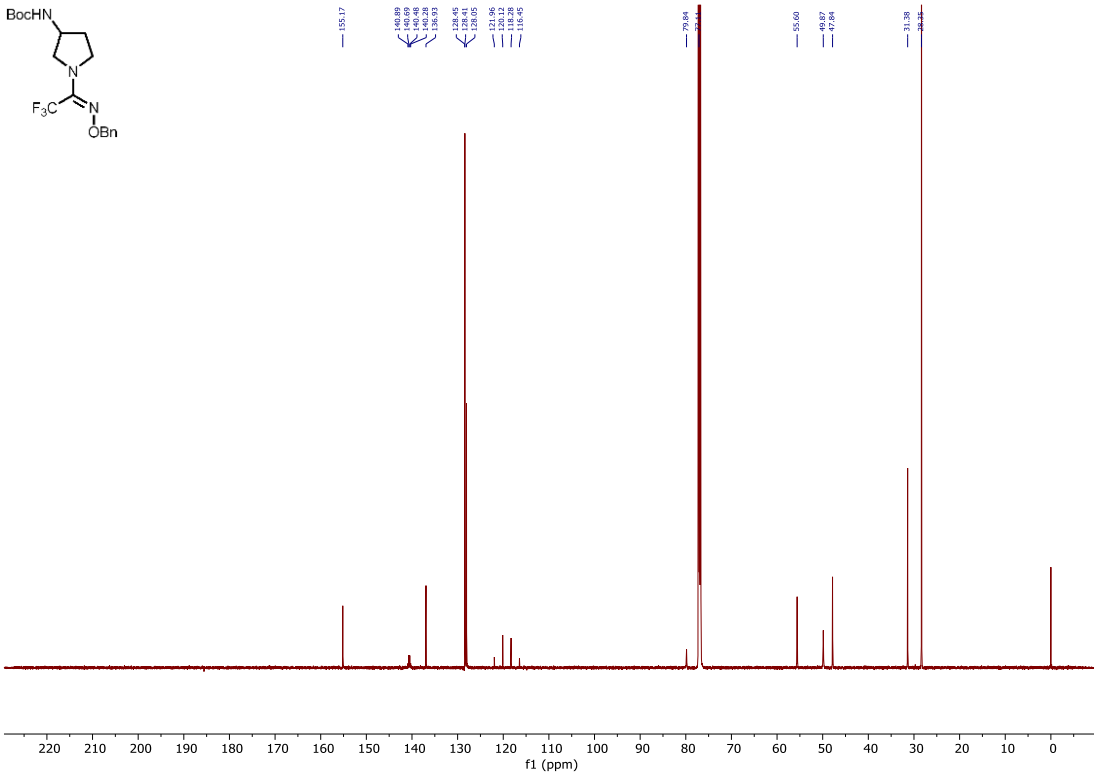


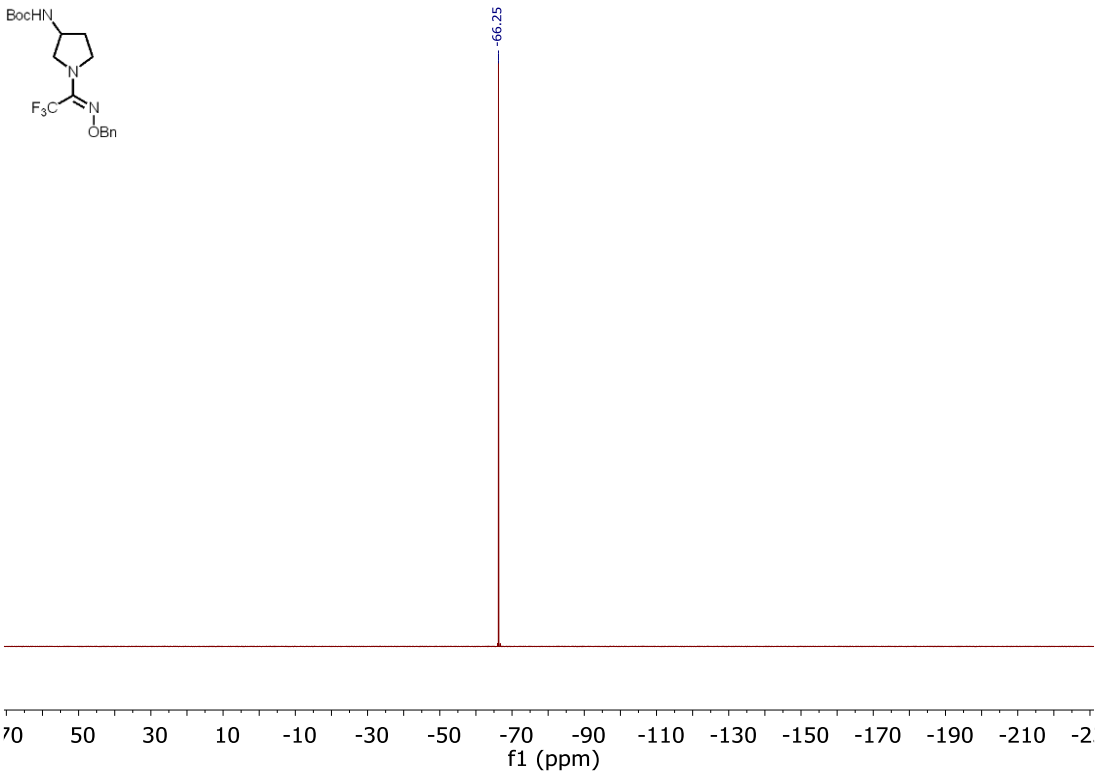



MeO
N
F3C
N
OBn
-66.26
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

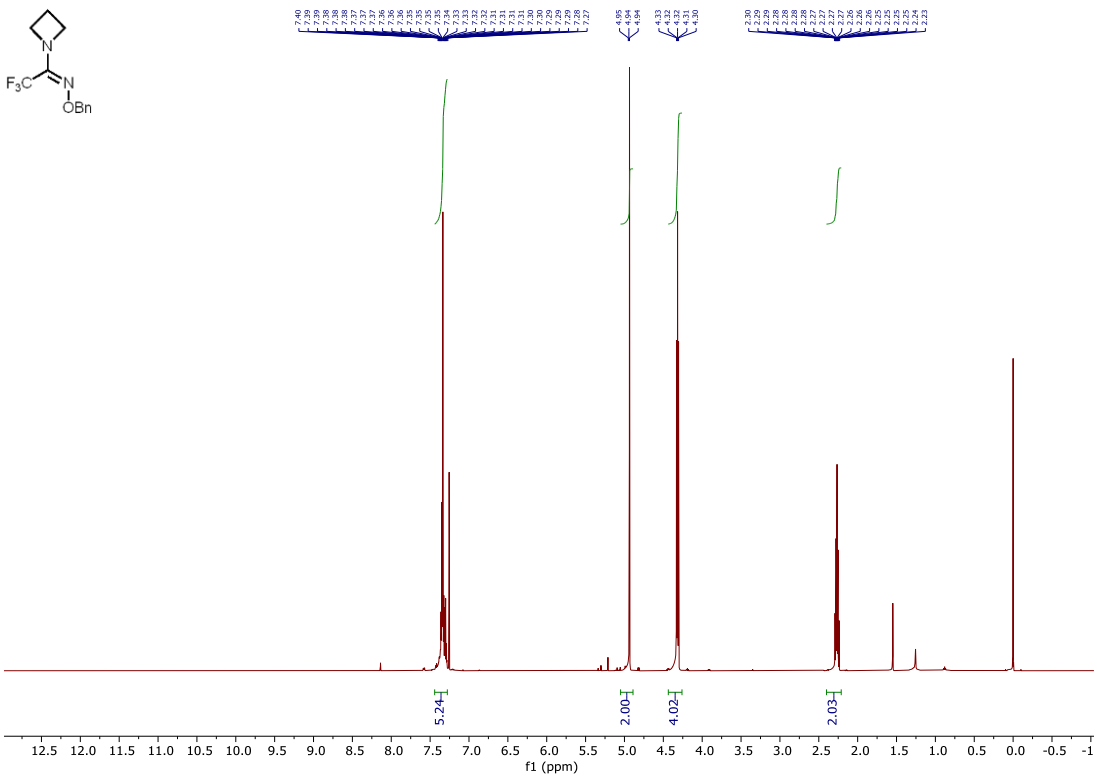
tert-butyl (*E*)-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-3-yl)carbamate (1m)

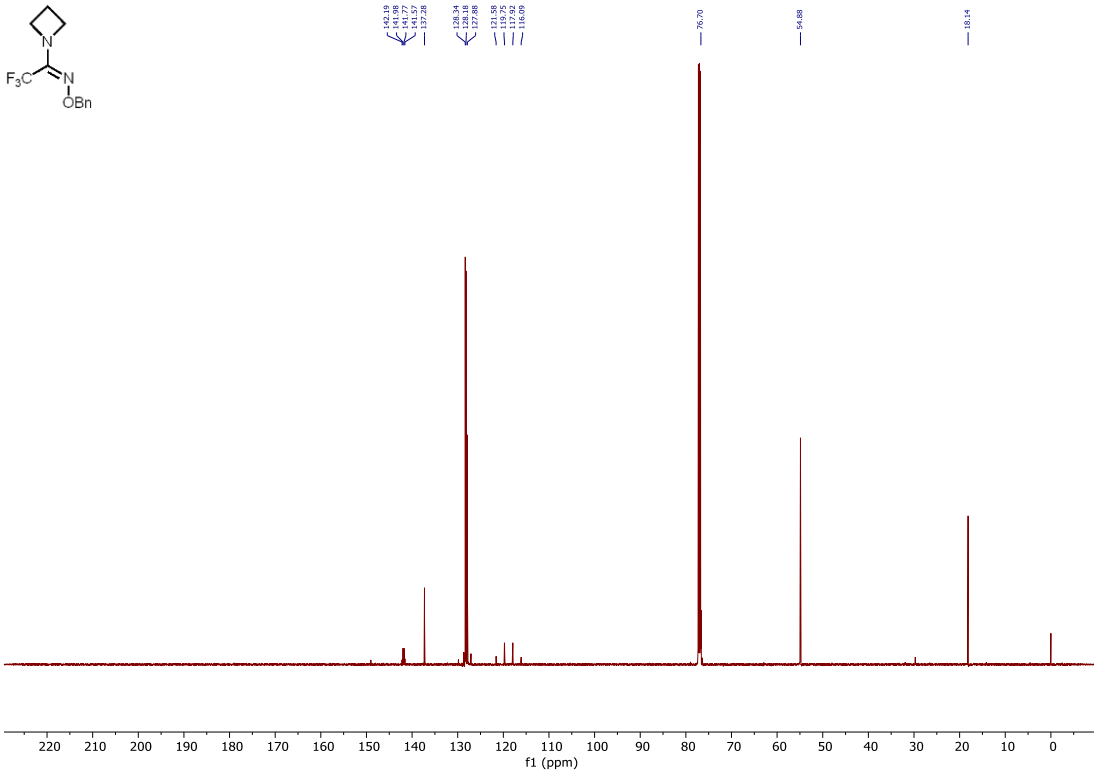


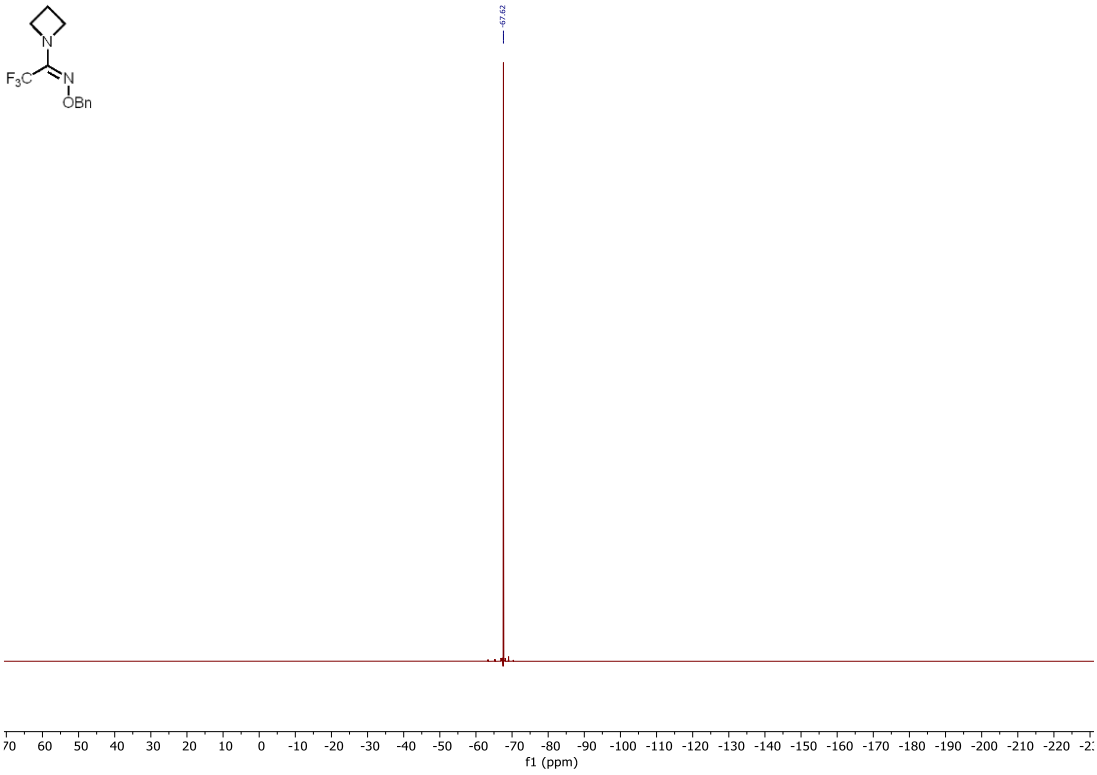



BocHN
N
F3C
N
OBn
-66.25
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

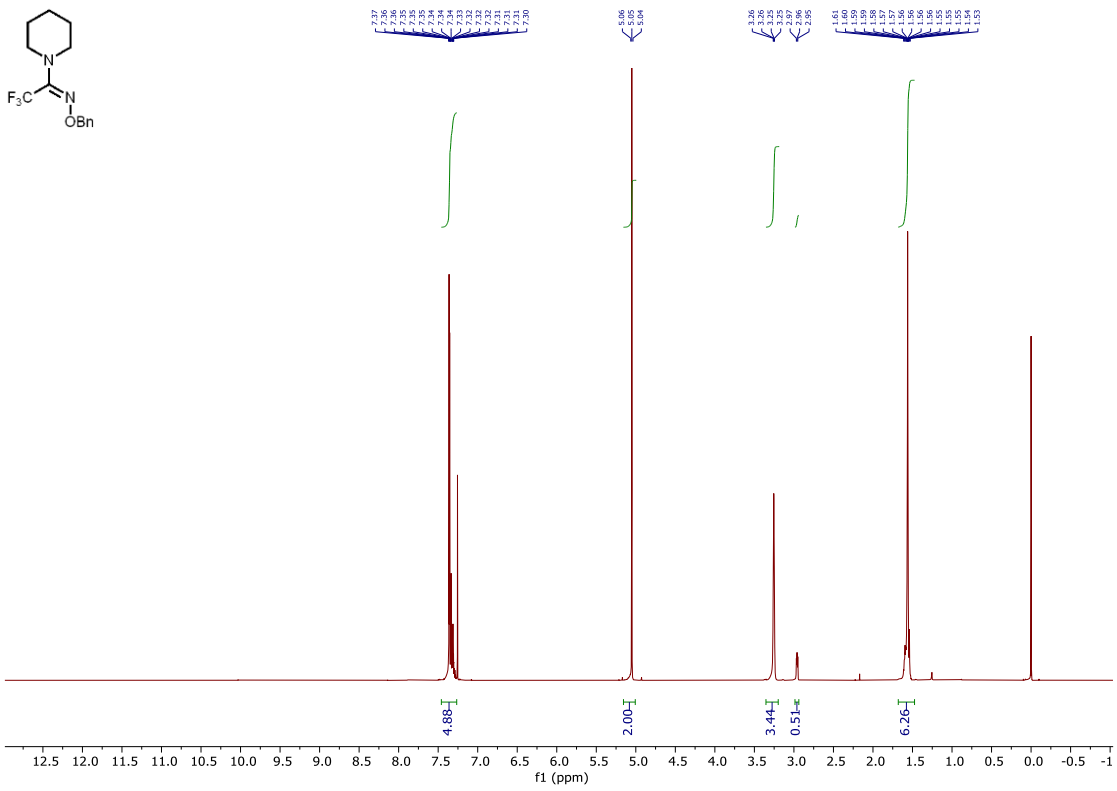
(*E*)-1-(azetidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1n)

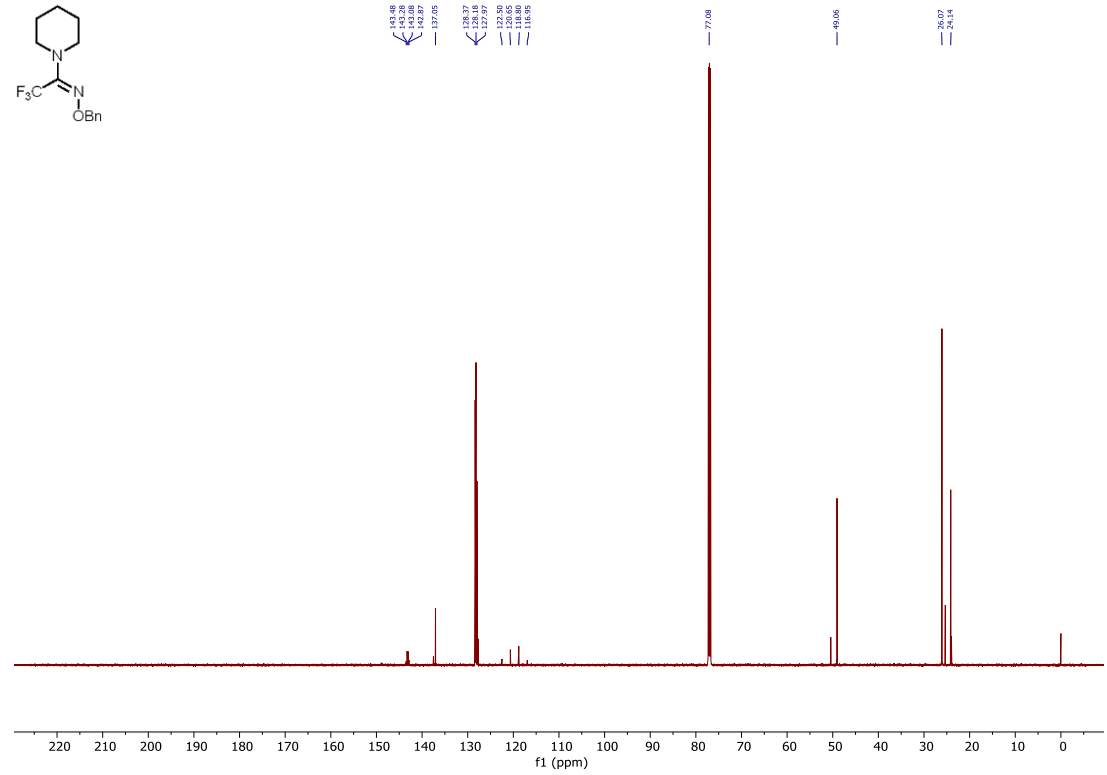


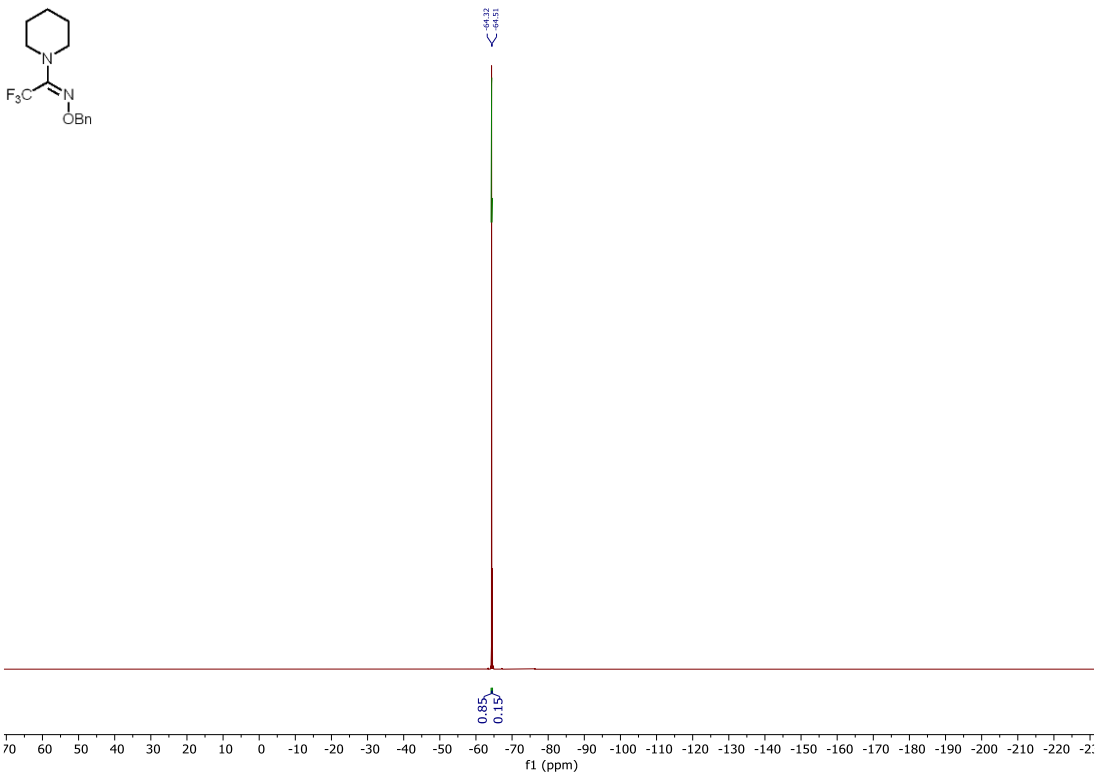



N
F3C
N
OBn
-67.62
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

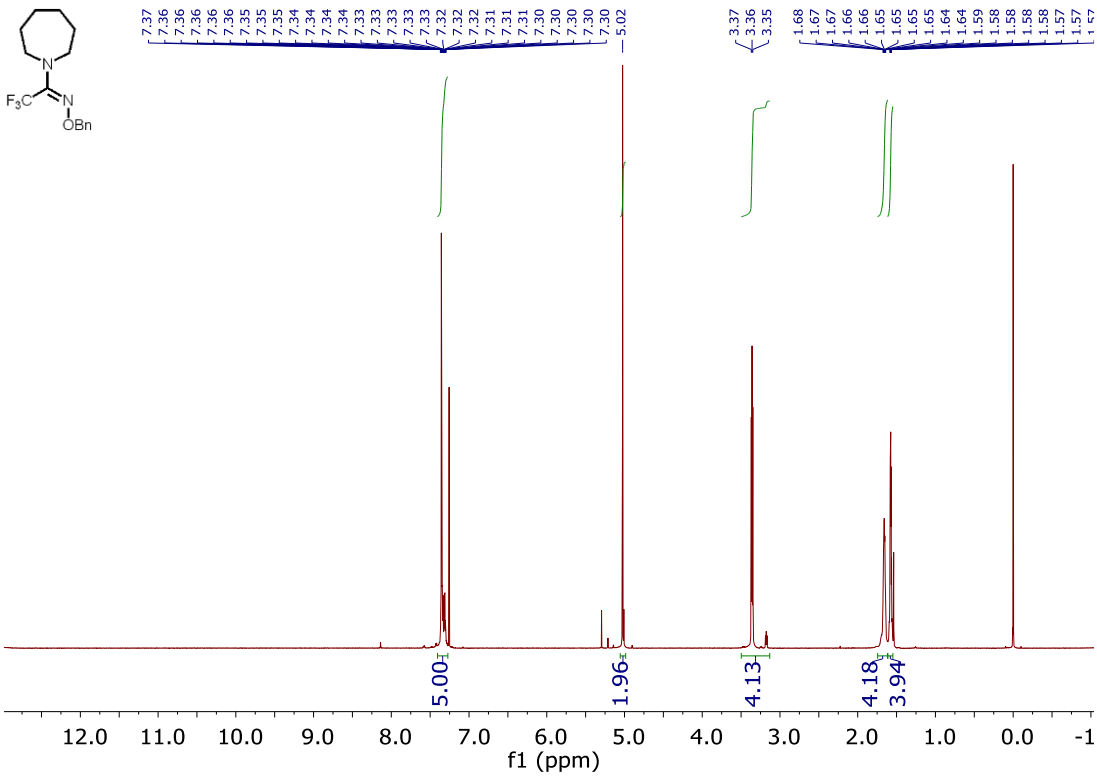
(*E*)-2,2,2-trifluoro-1-(piperidin-1-yl)ethan-1-one *O*-benzyl oxime (1o)

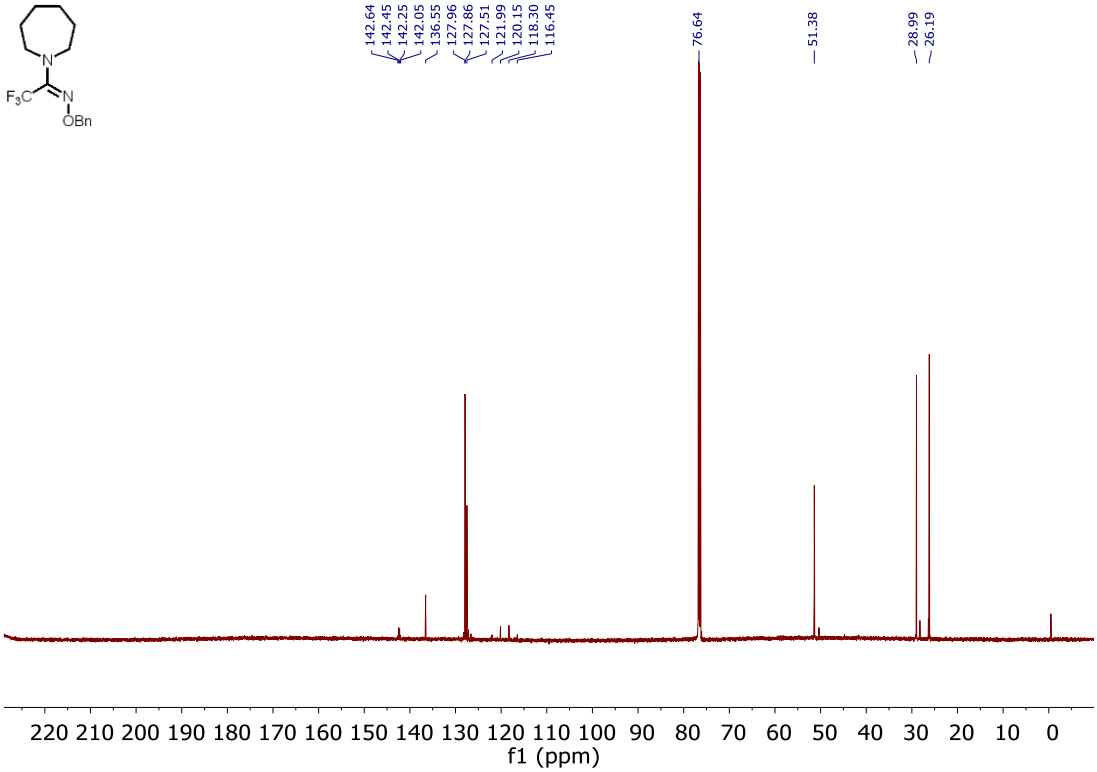


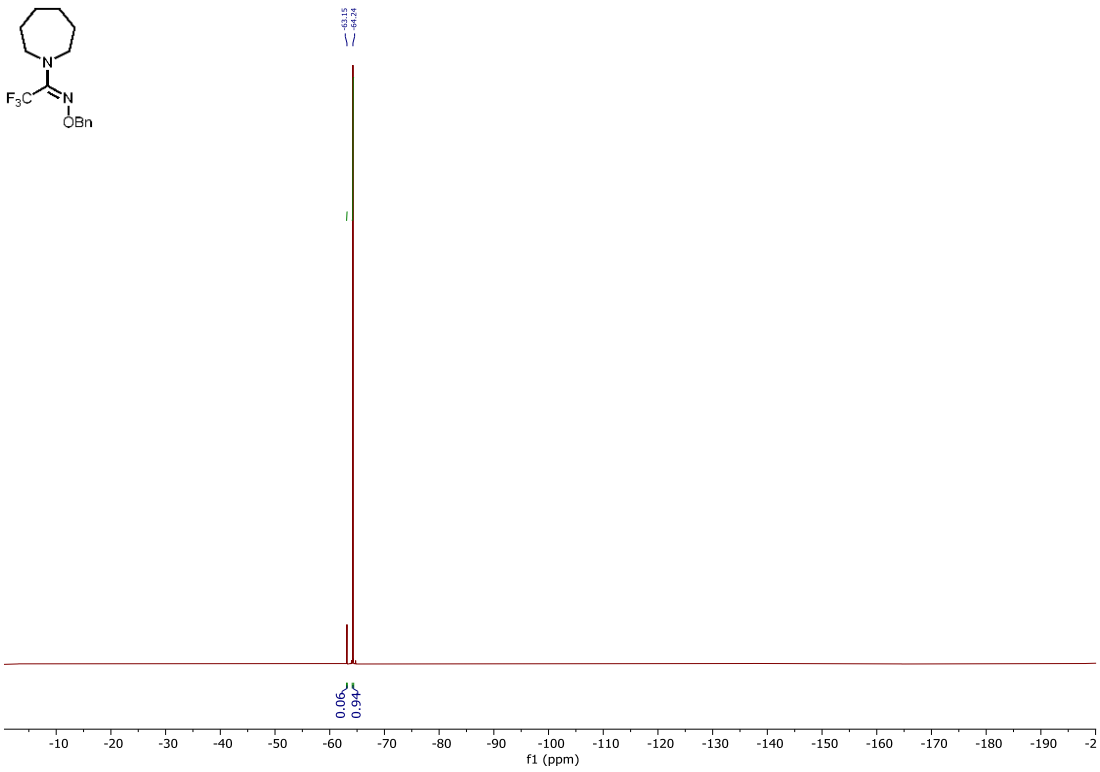



-64.32
-64.51
N
F3C
N
OBn
0.85
0.15
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

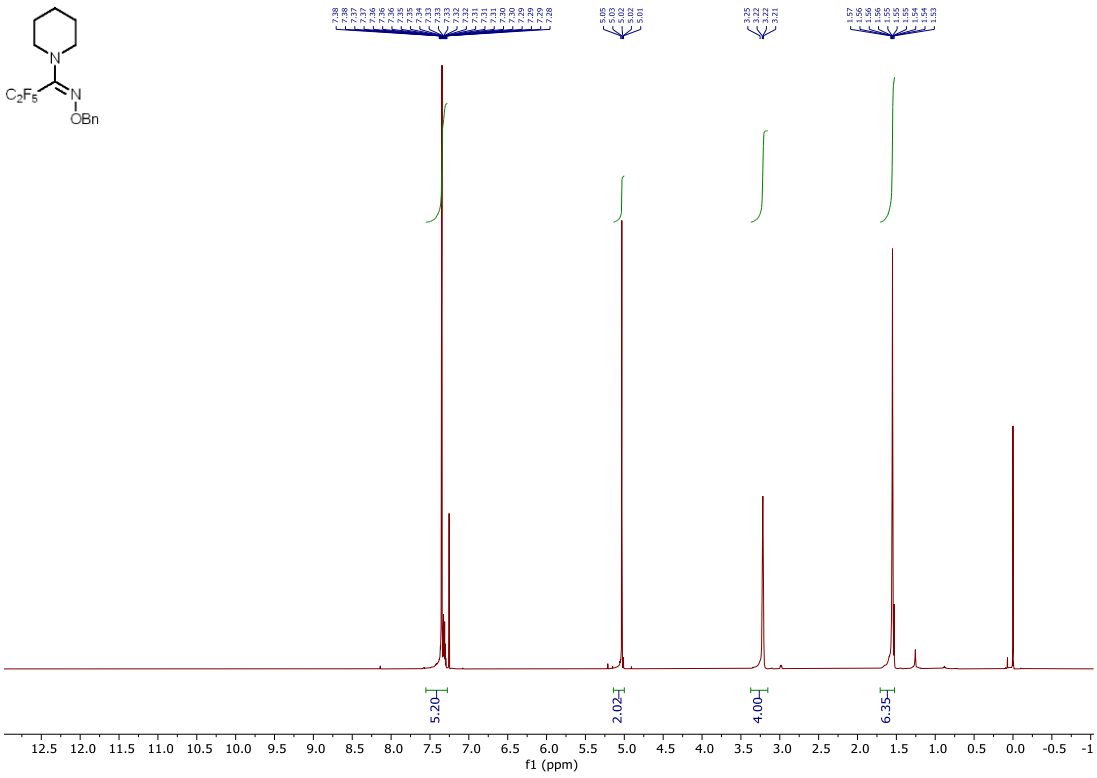
(*E*)-1-(azepan-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (1p)

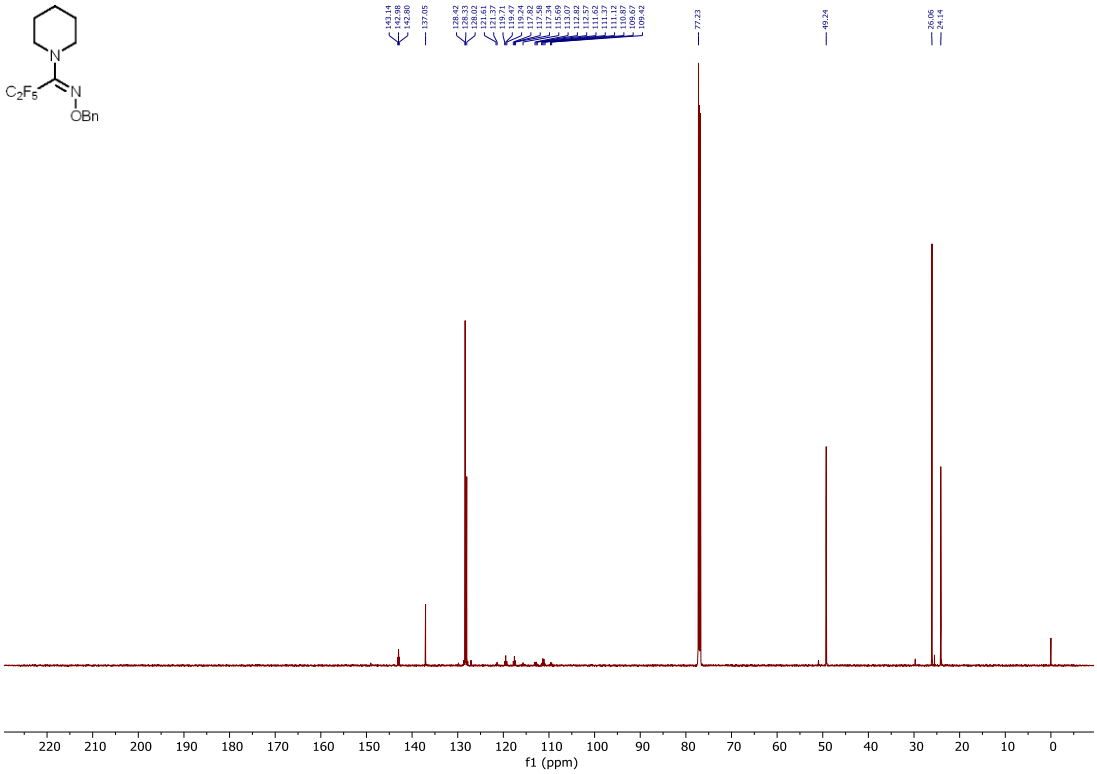


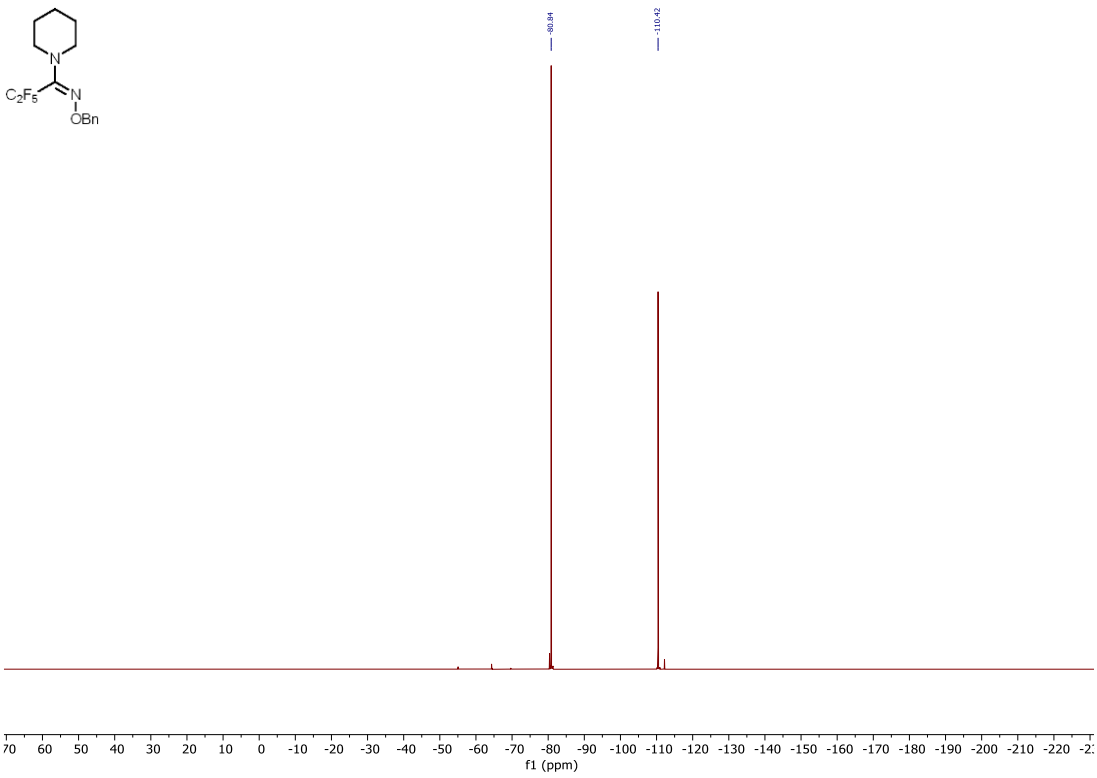



-63.15
-64.24
0.06
0.94
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-2
f1 (ppm)

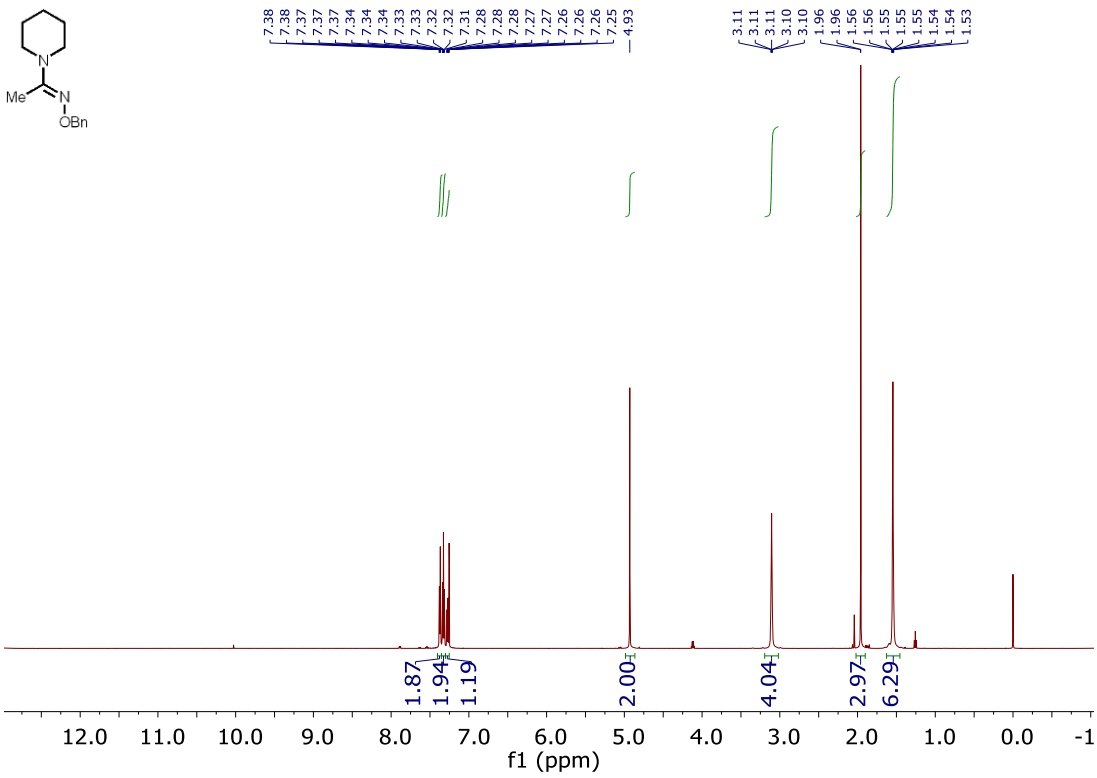
(*E*)-2,2,3,3,3-pentafluoro-1-(piperidin-1-yl)propan-1-one *O*-benzyl oxime (4a-1)

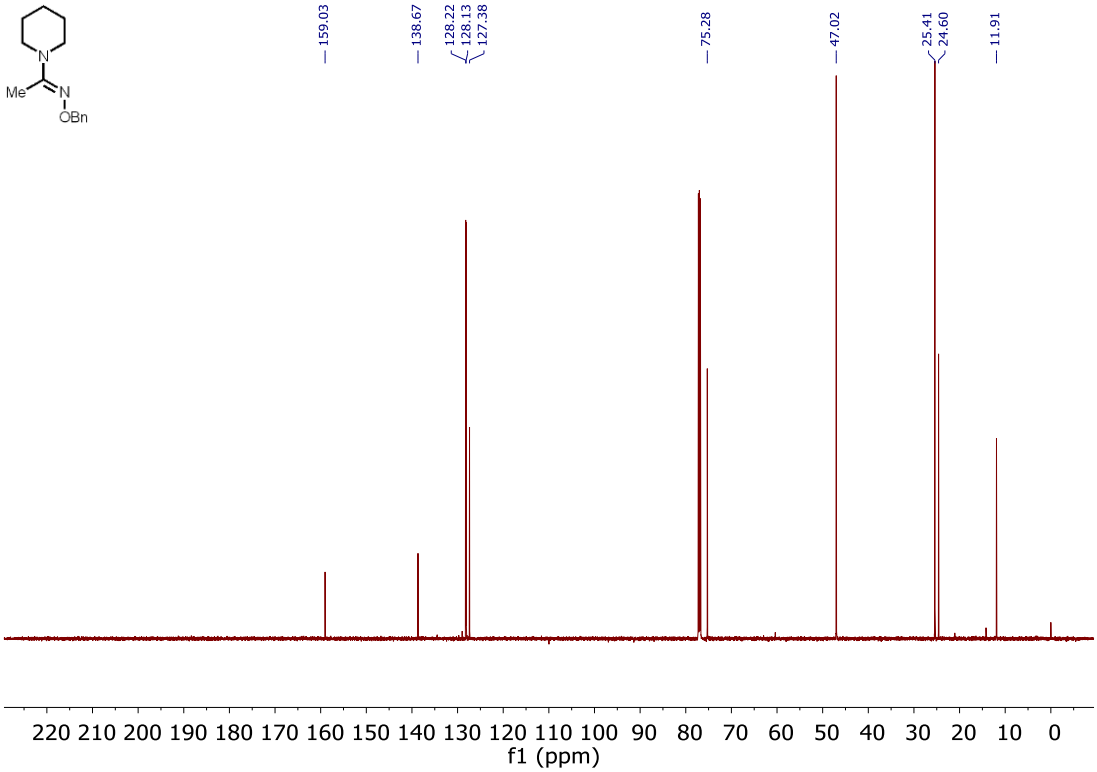




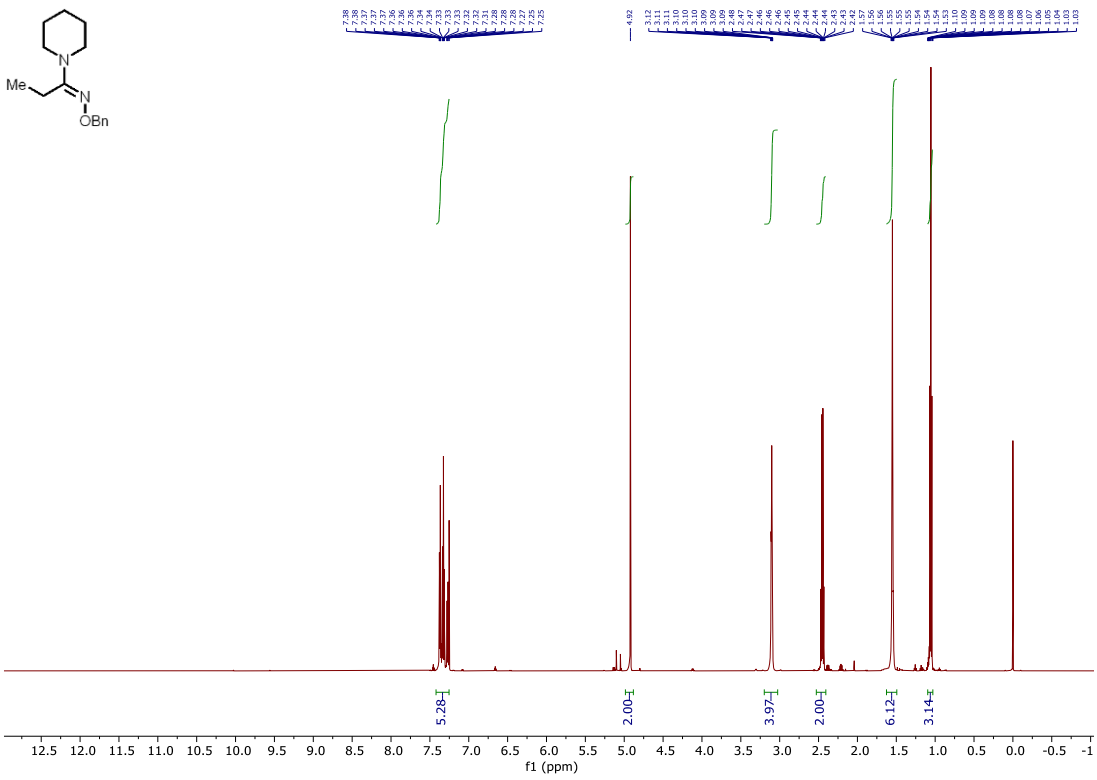

-80.84
-110.42
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

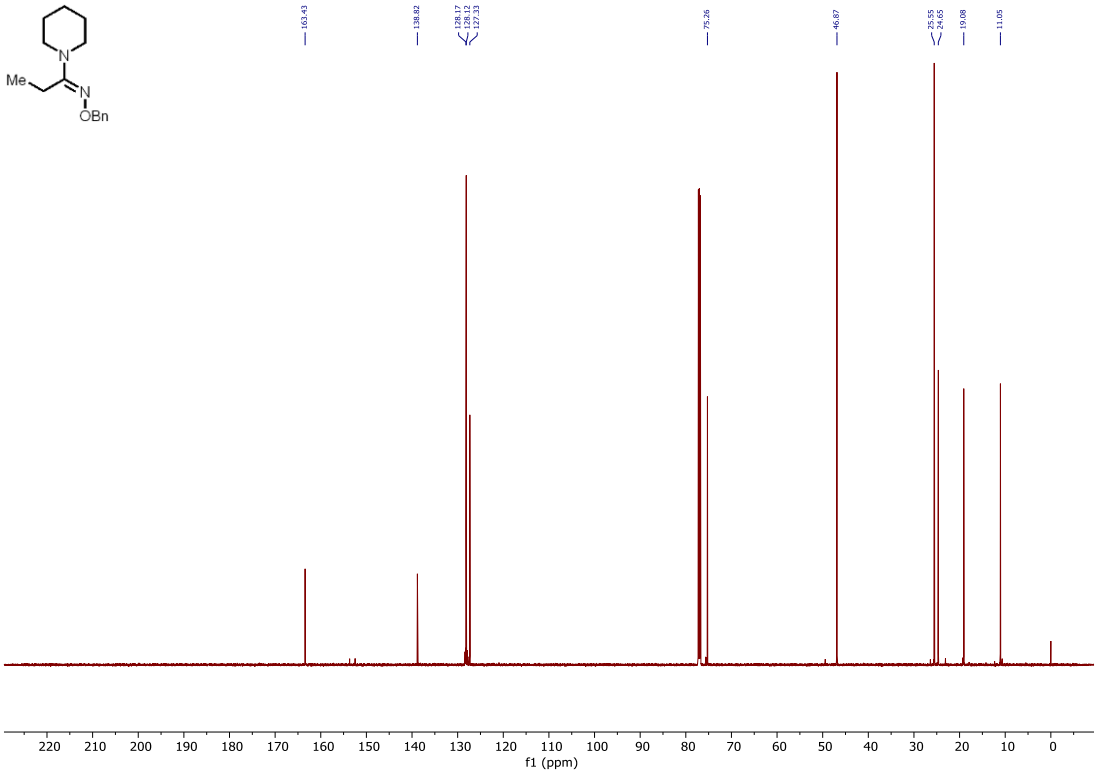
(*E*)-1-(piperidin-1-yl)ethan-1-one *O*-benzyl oxime (4a-2/4b)



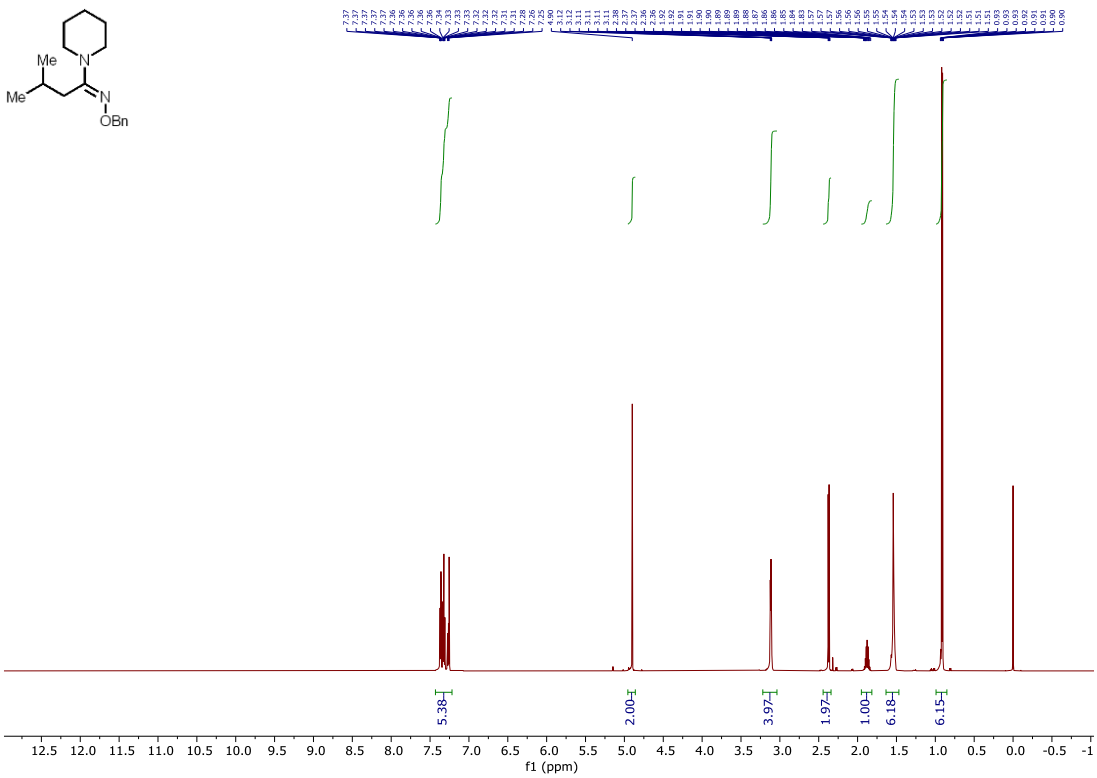


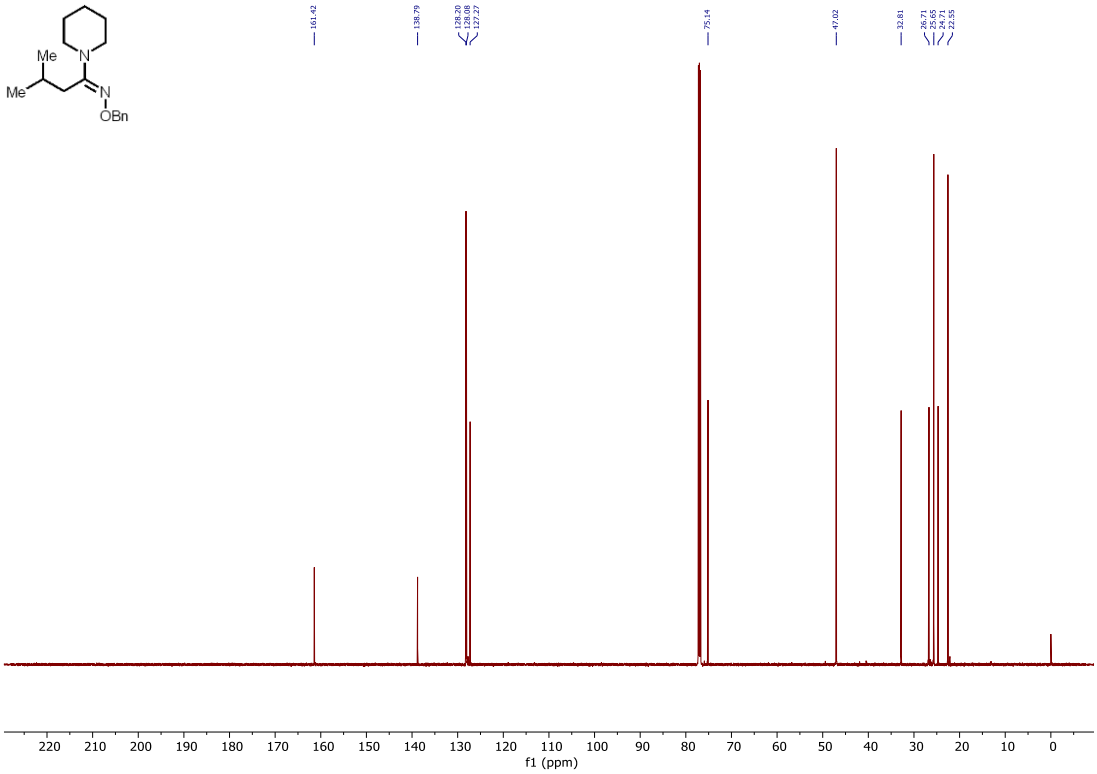
(*E*)-1-(piperidin-1-yl)propan-1-one *O*-benzyl oxime (4a-3)



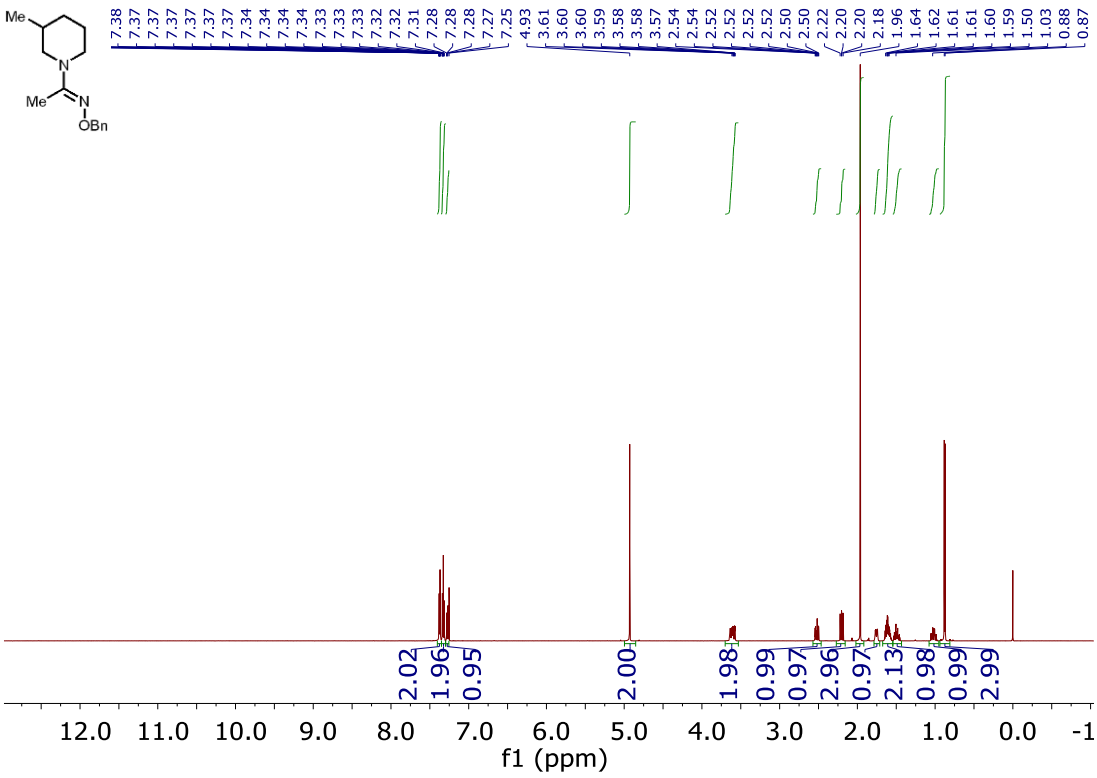


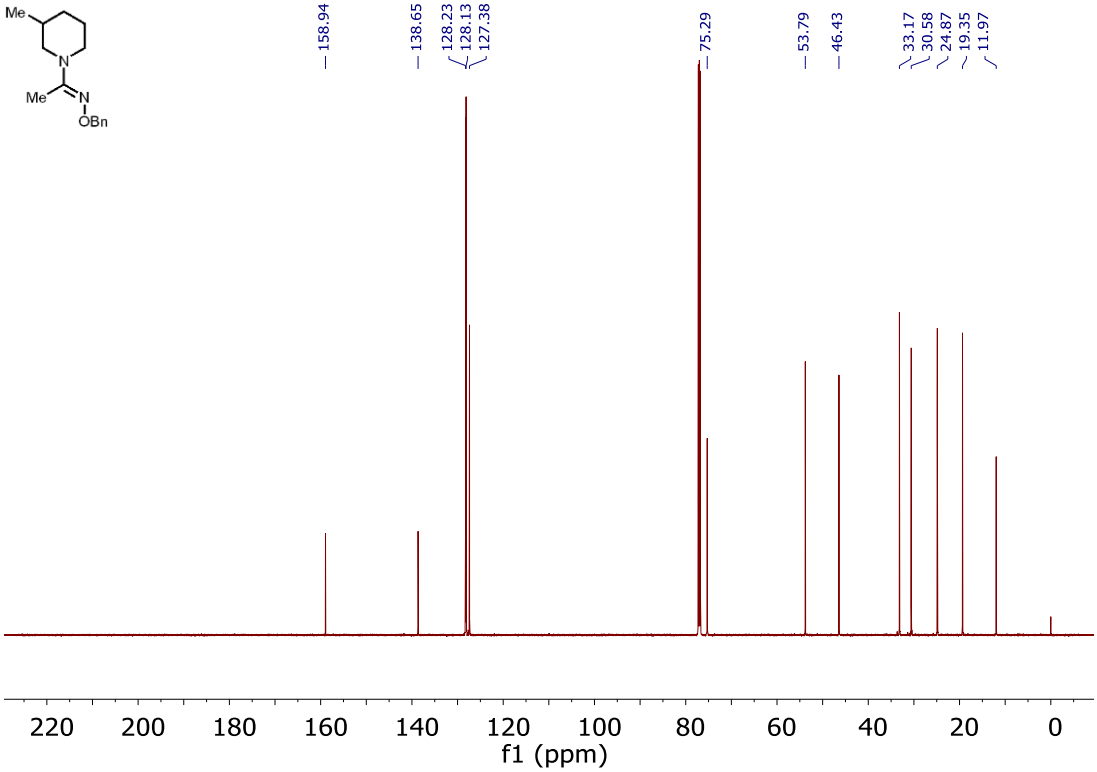
(*E*)-3-methyl-1-(piperidin-1-yl)butan-1-one *O*-benzyl oxime (4a-4)



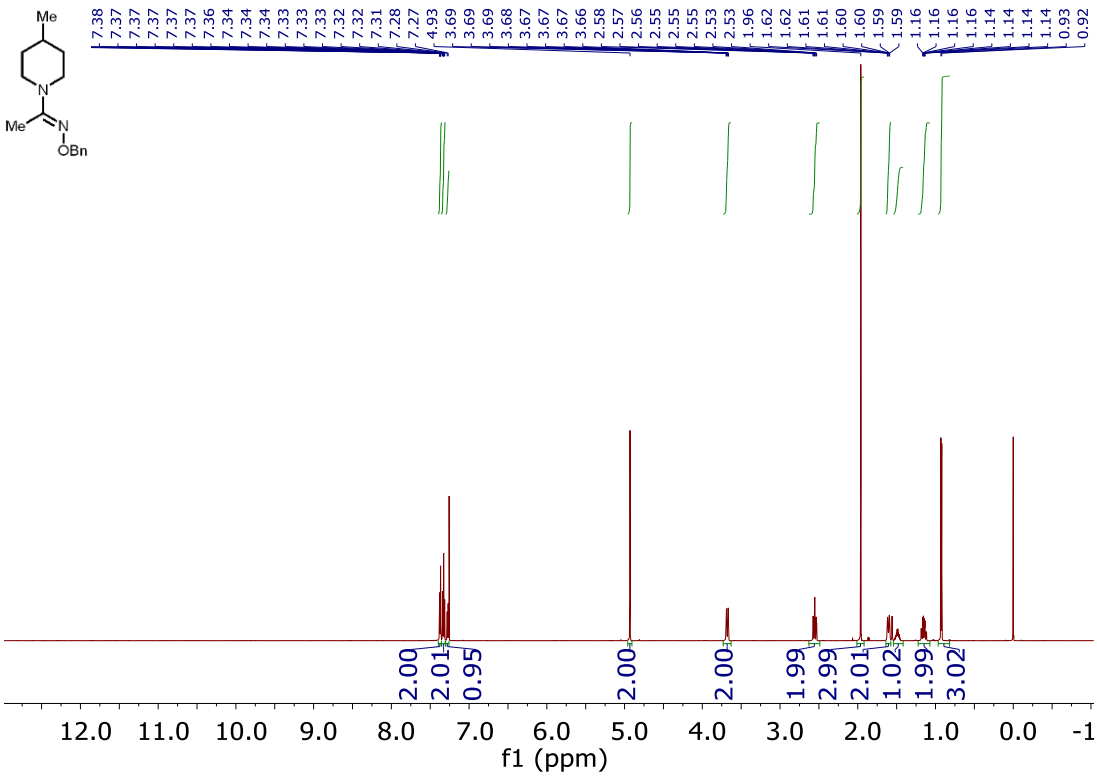


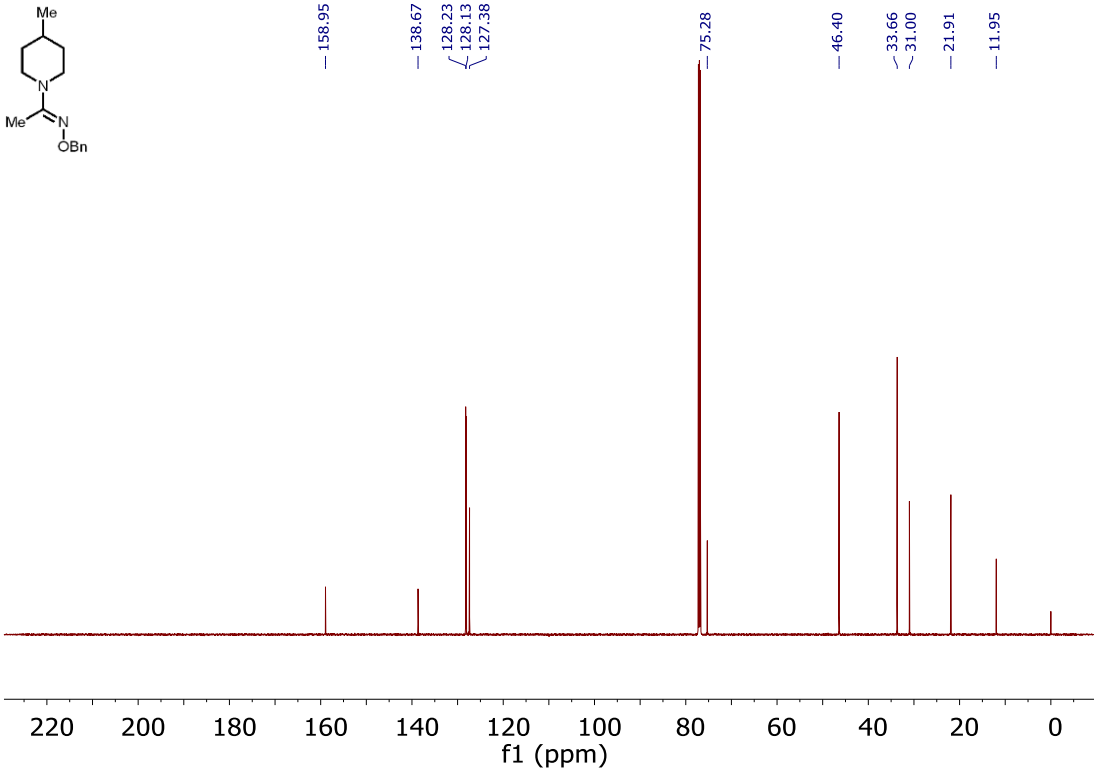
(*E*)-1-(3-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (4c)



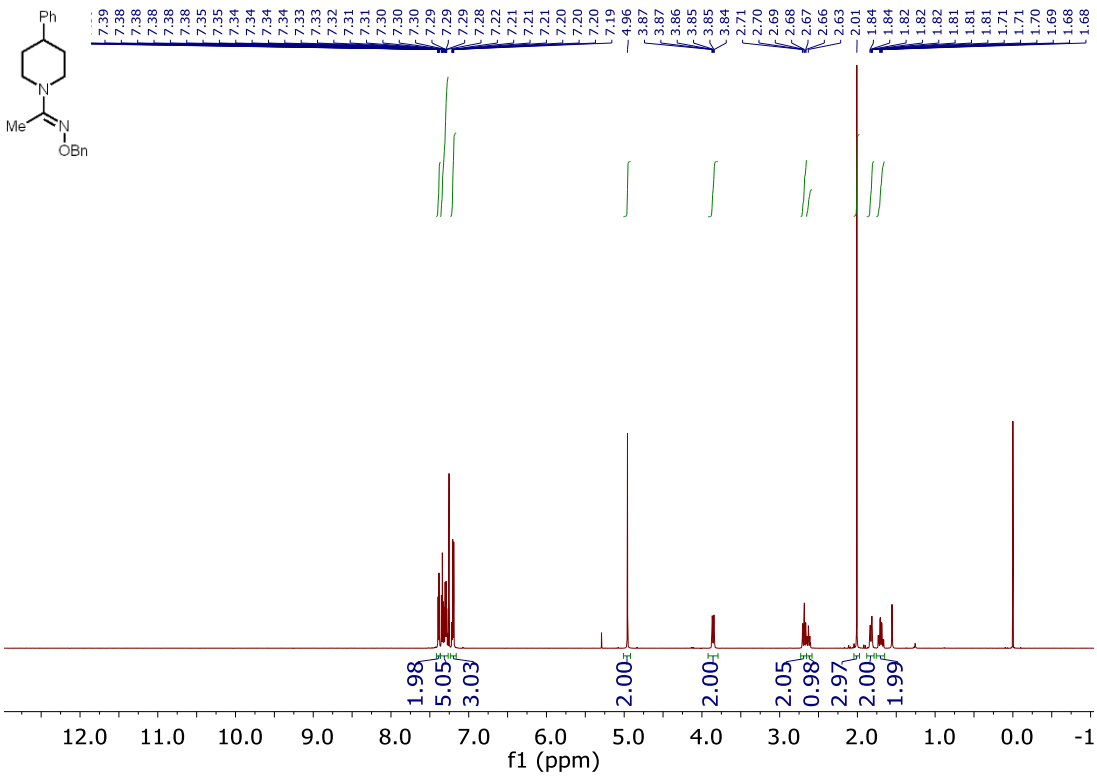


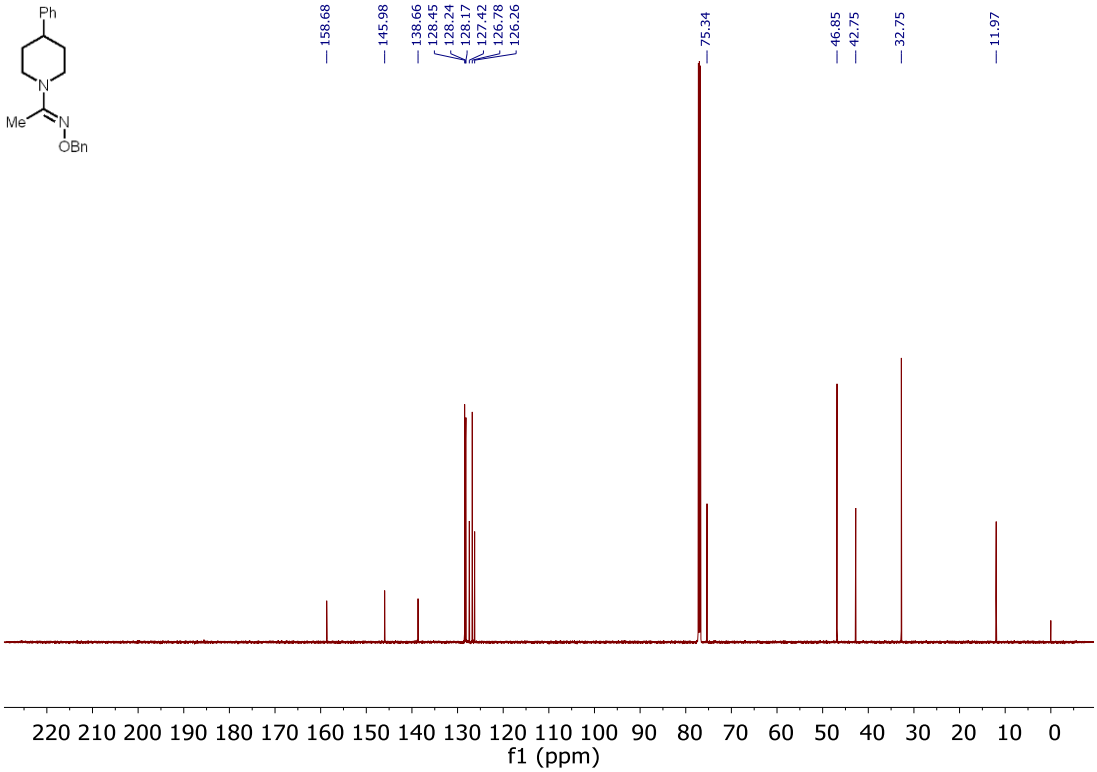
(*E*)-1-(4-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (4d)



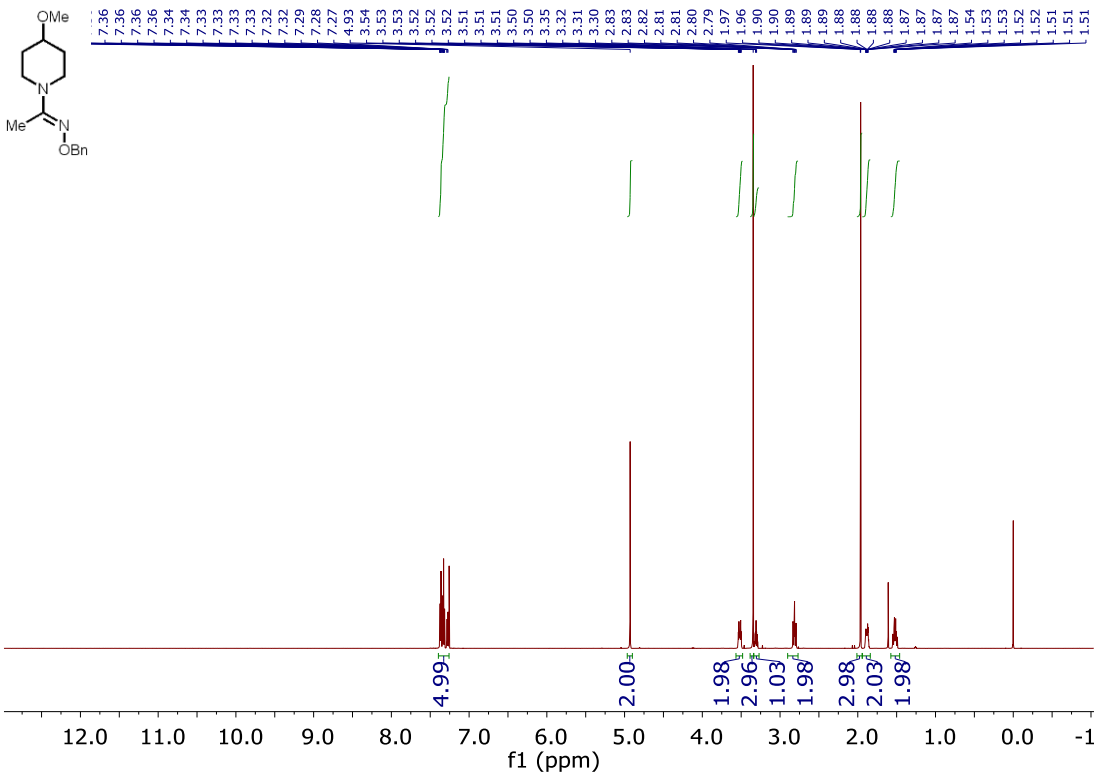


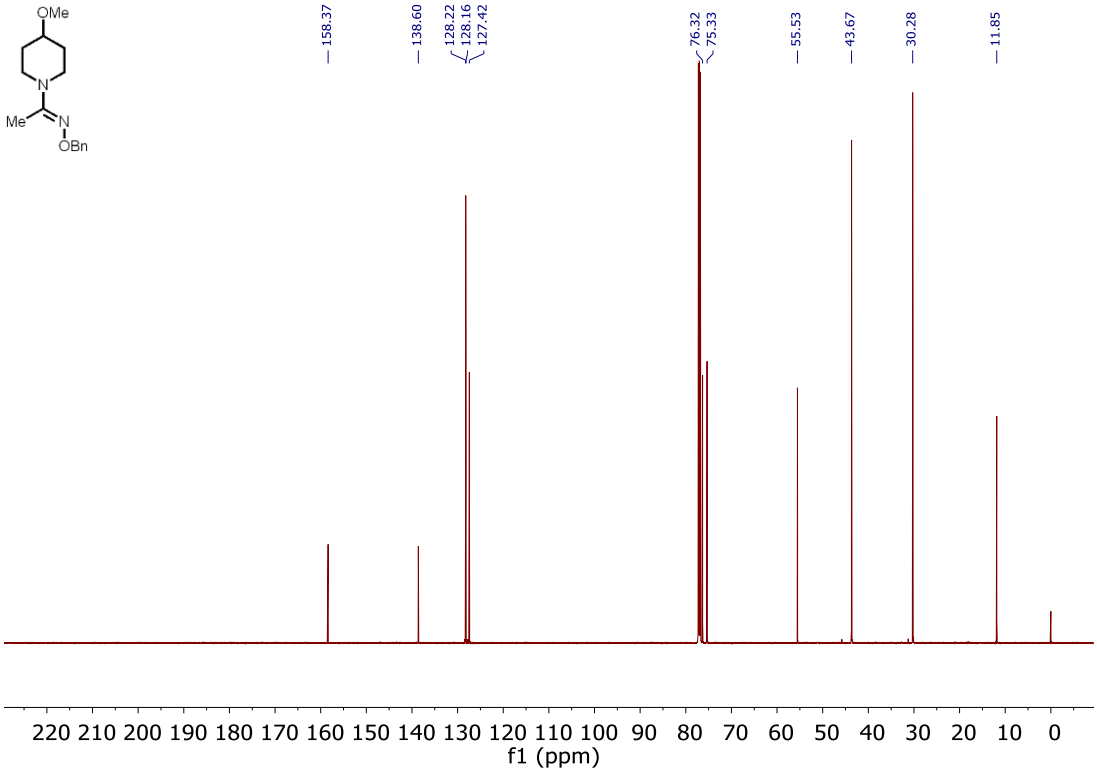
(*E*)-1-(4-phenylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (4e)



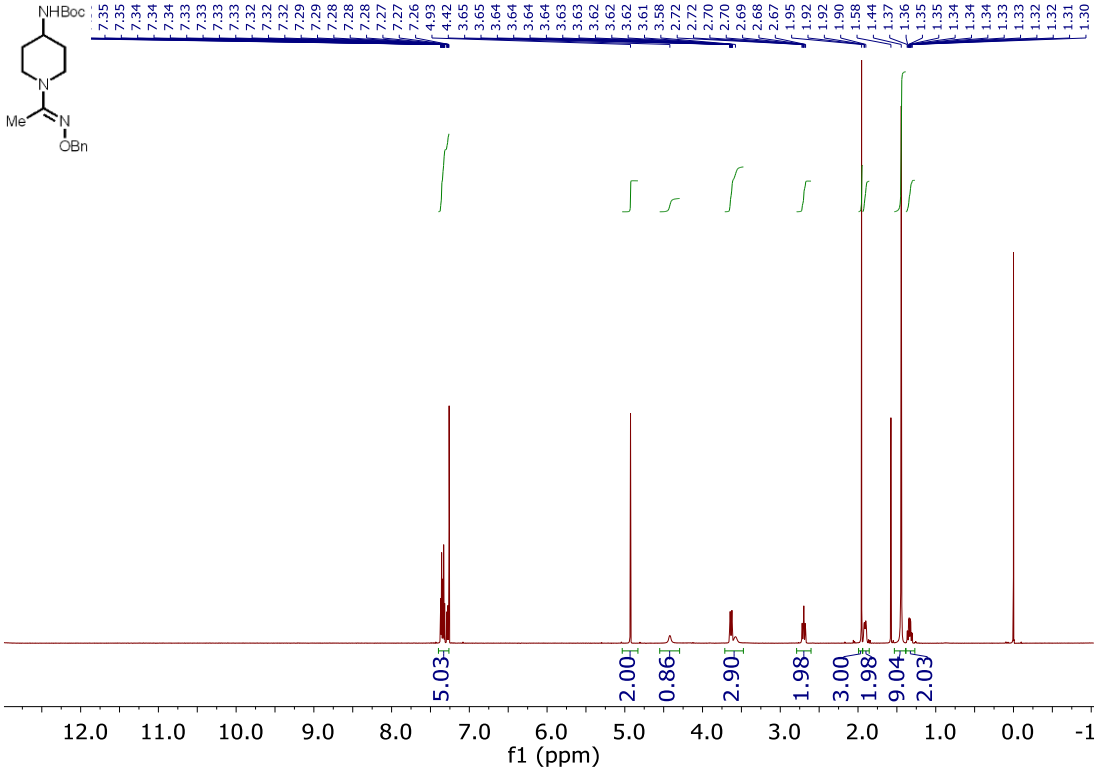


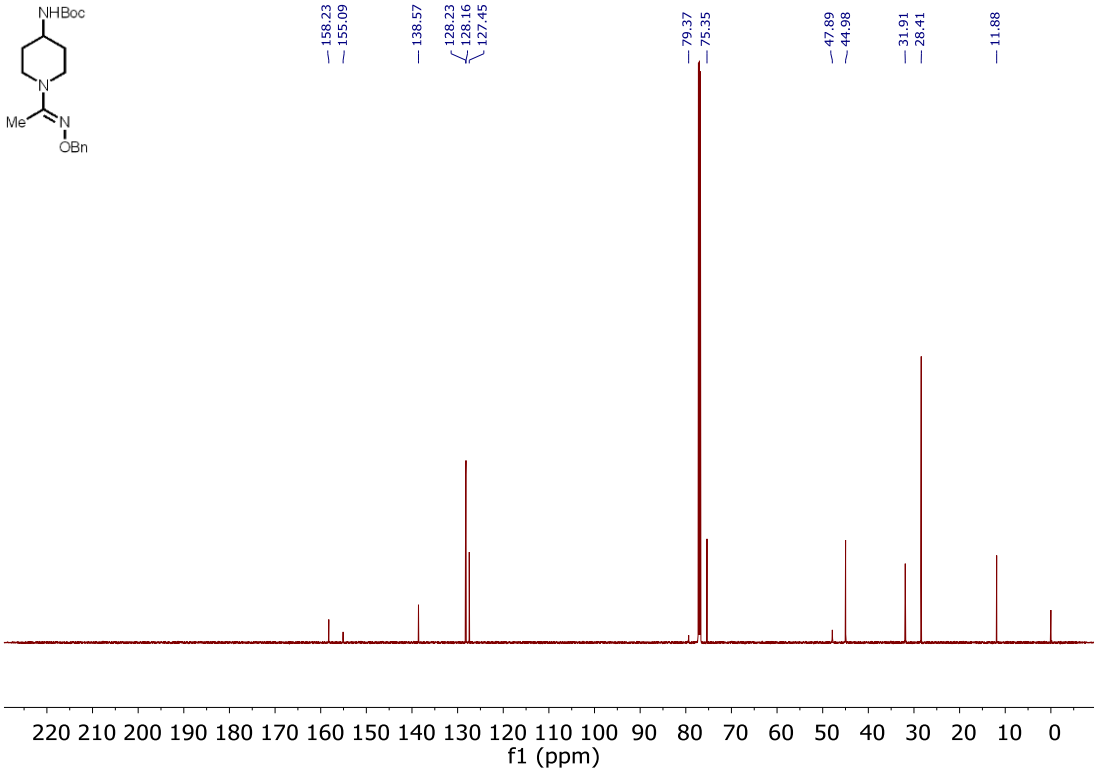
(*E*)-1-(4-methoxypiperidin-1-yl)ethan-1-one *O*-benzyl oxime (4f)



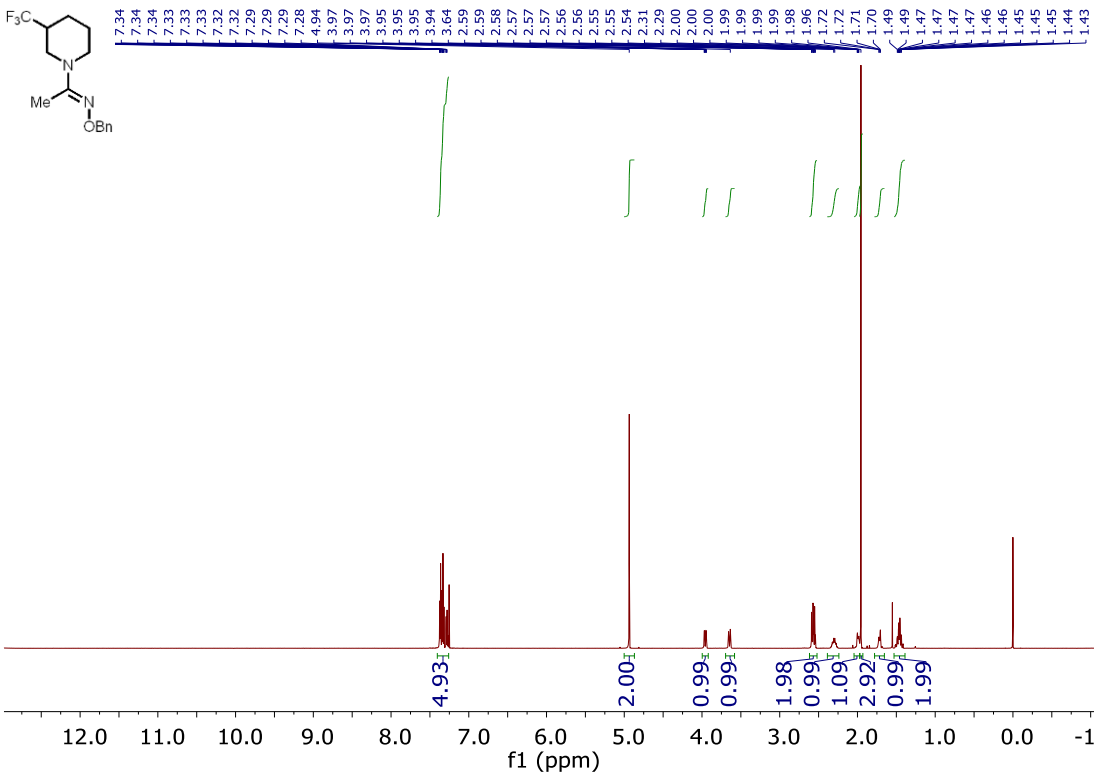


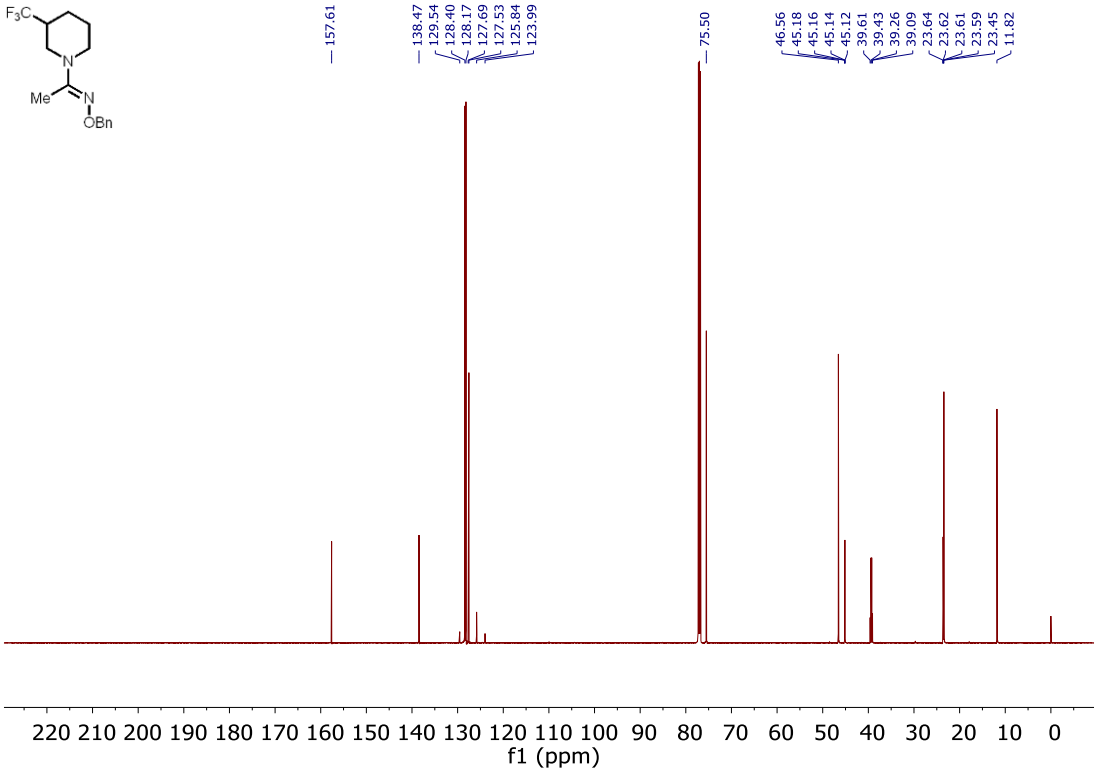
tert-butyl (*E*)-(1-(1-((benzyloxy)imino)ethyl)piperidin-4-yl)carbamate (4g)

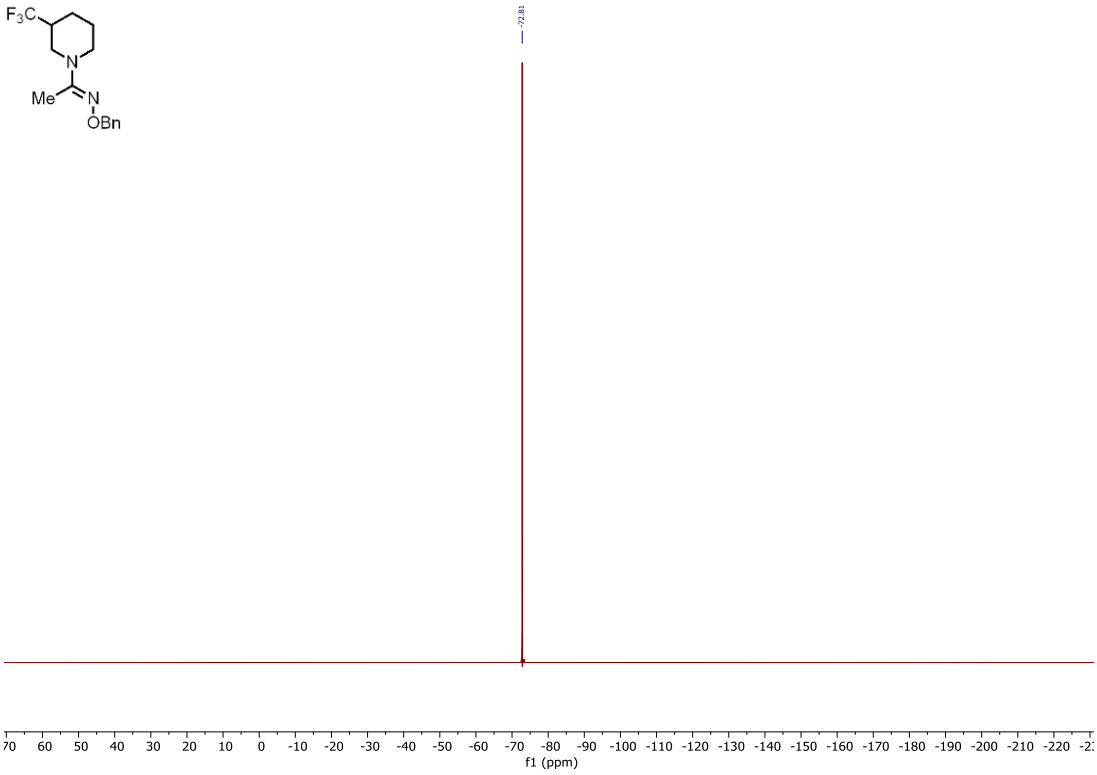




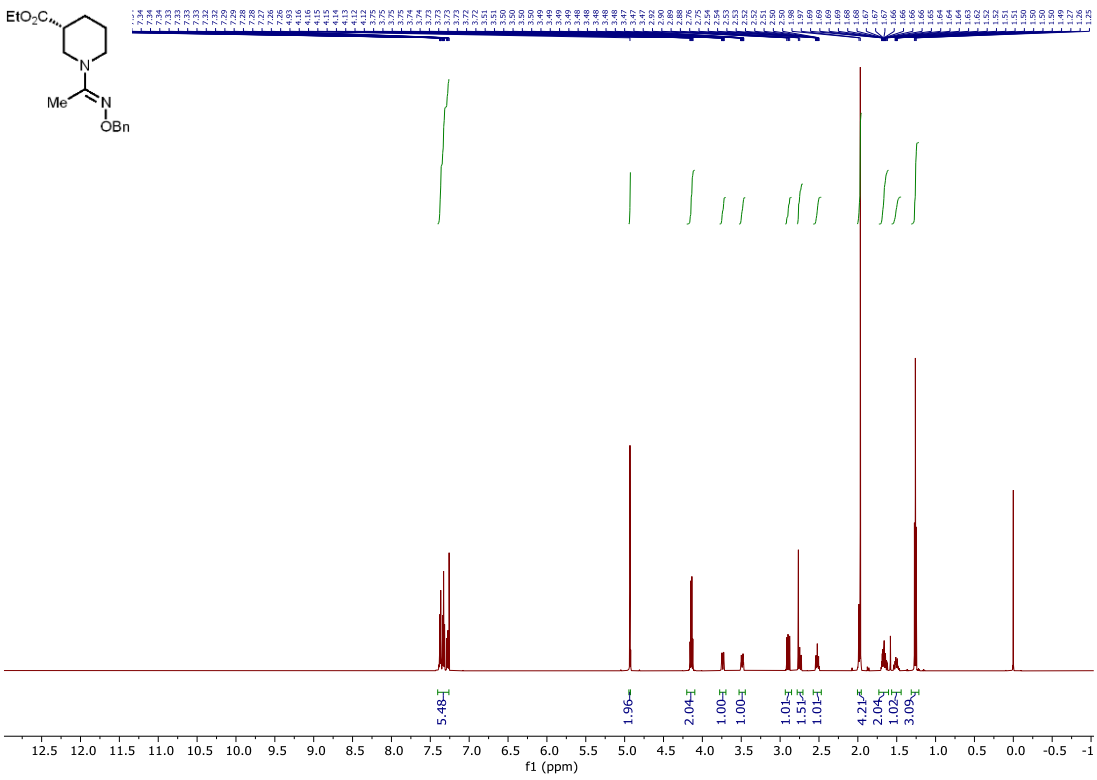
(*E*)-1-(3-(trifluoromethyl)piperidin-1-yl)ethan-1-one *O*-benzyl oxime (4h)

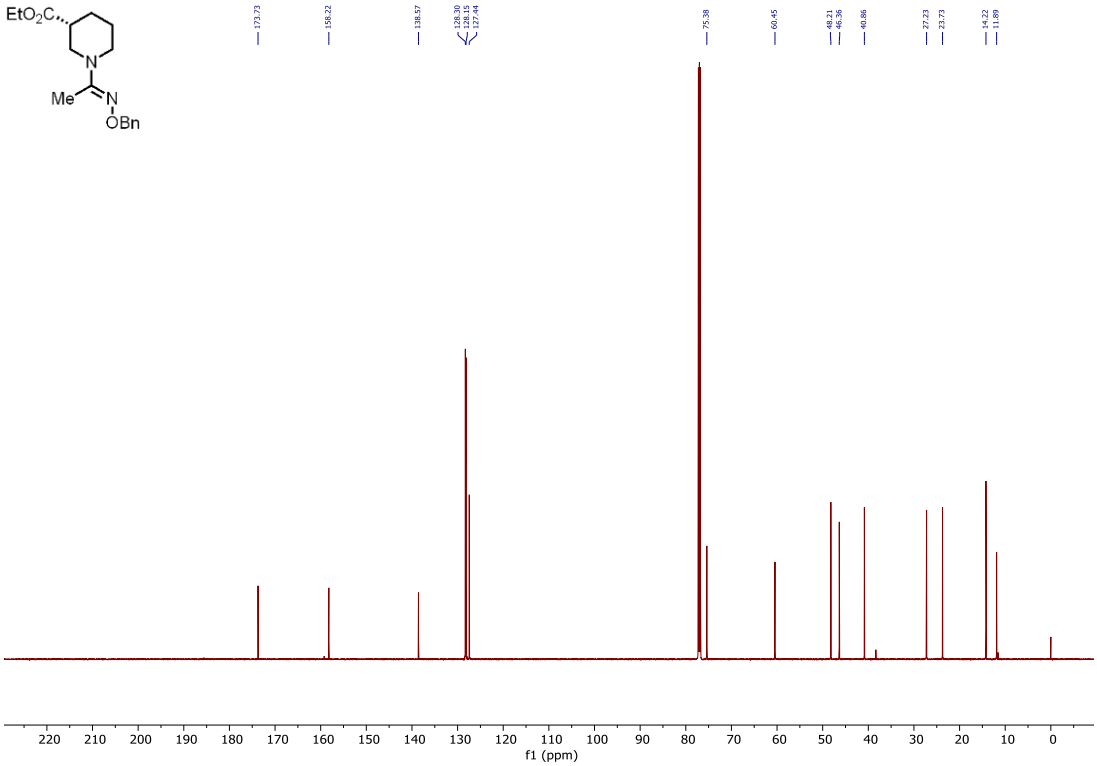




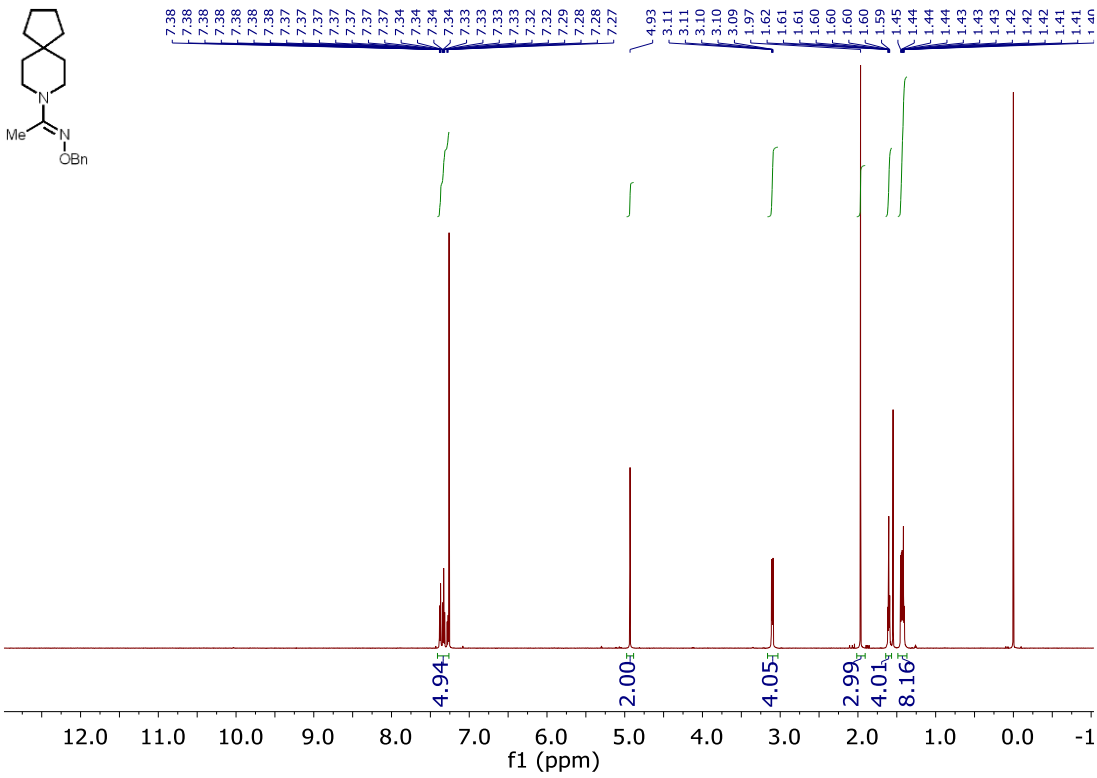

F3C
N
Me
N
OBn
-72.81
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

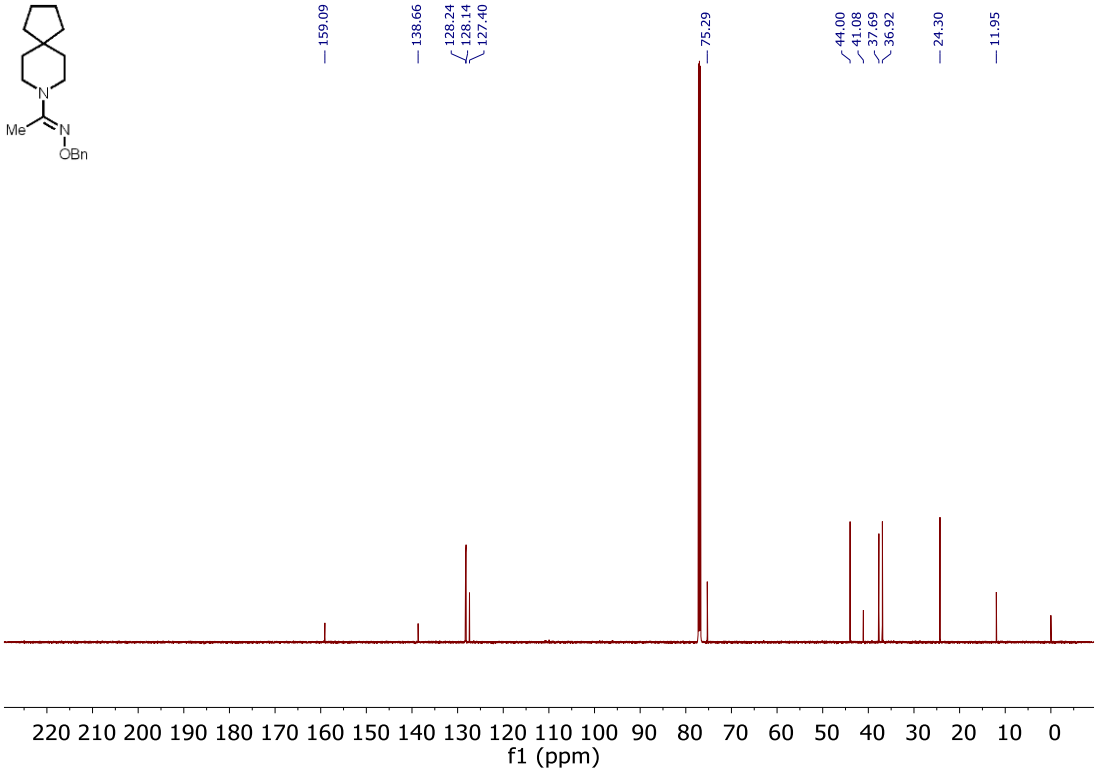
ethyl (*R*,*E*)-1-(1-((benzyloxy)imino)ethyl)piperidine-3-carboxylate (4i)



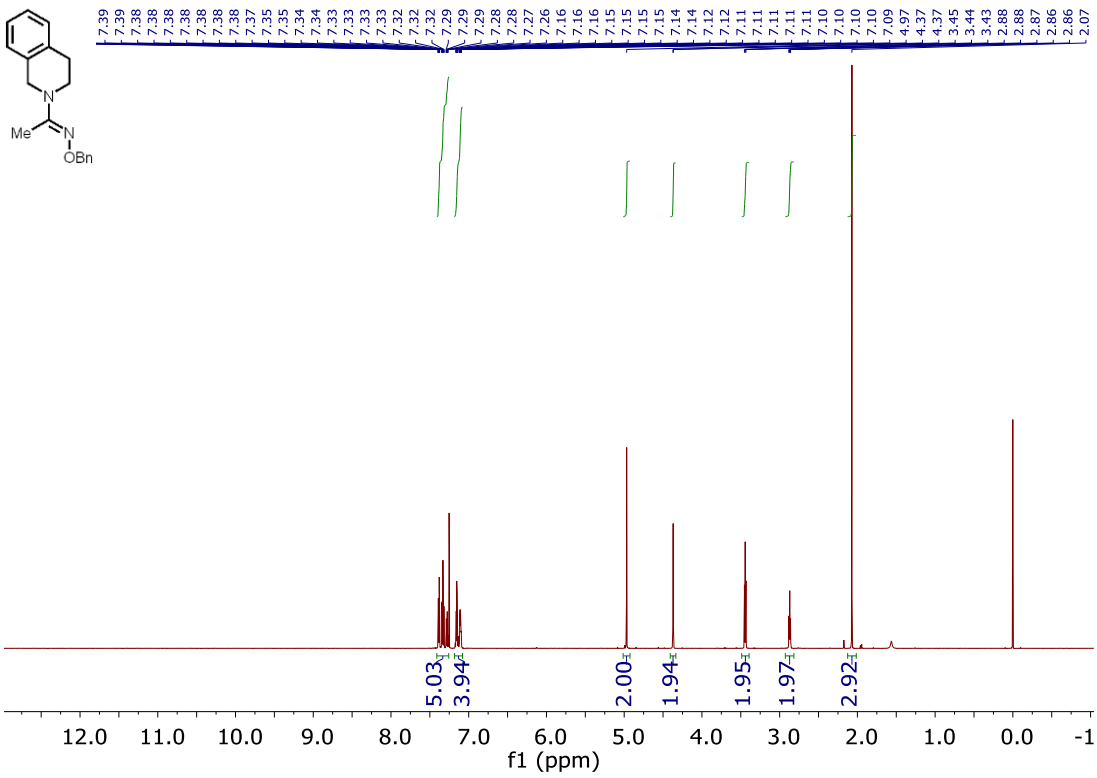


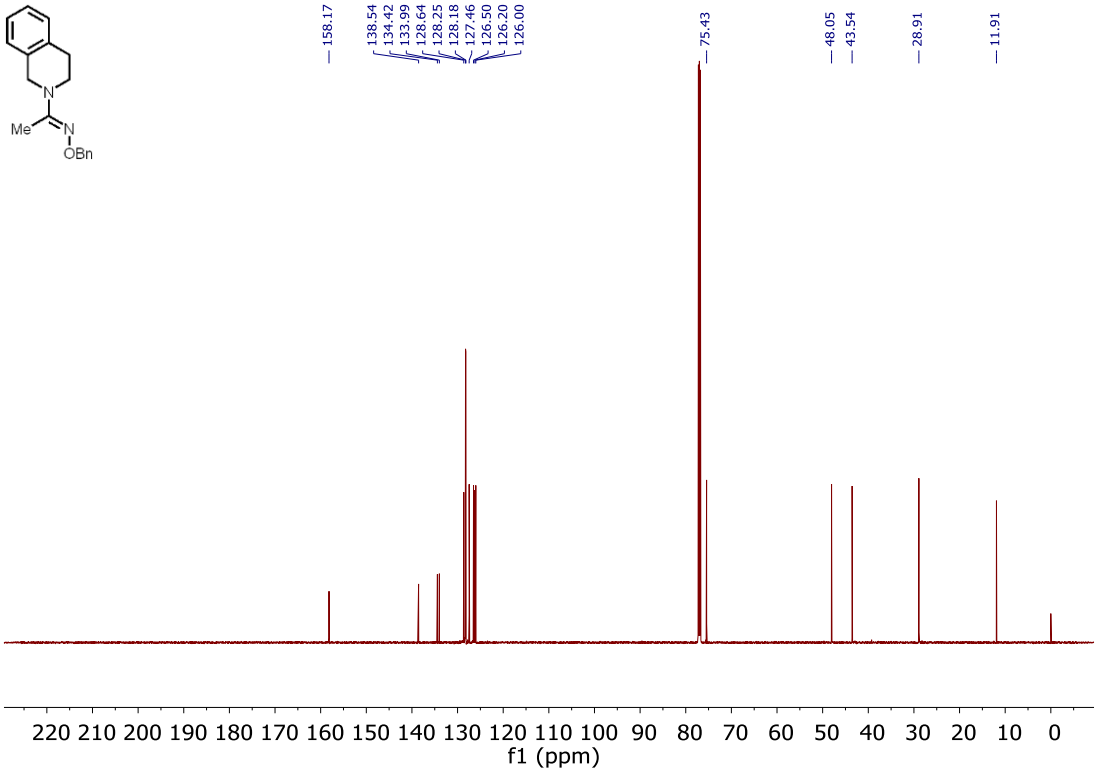
(*E*)-1-(8-azaspiro[4.5]decan-8-yl)ethan-1-one *O*-benzyl oxime (4j)



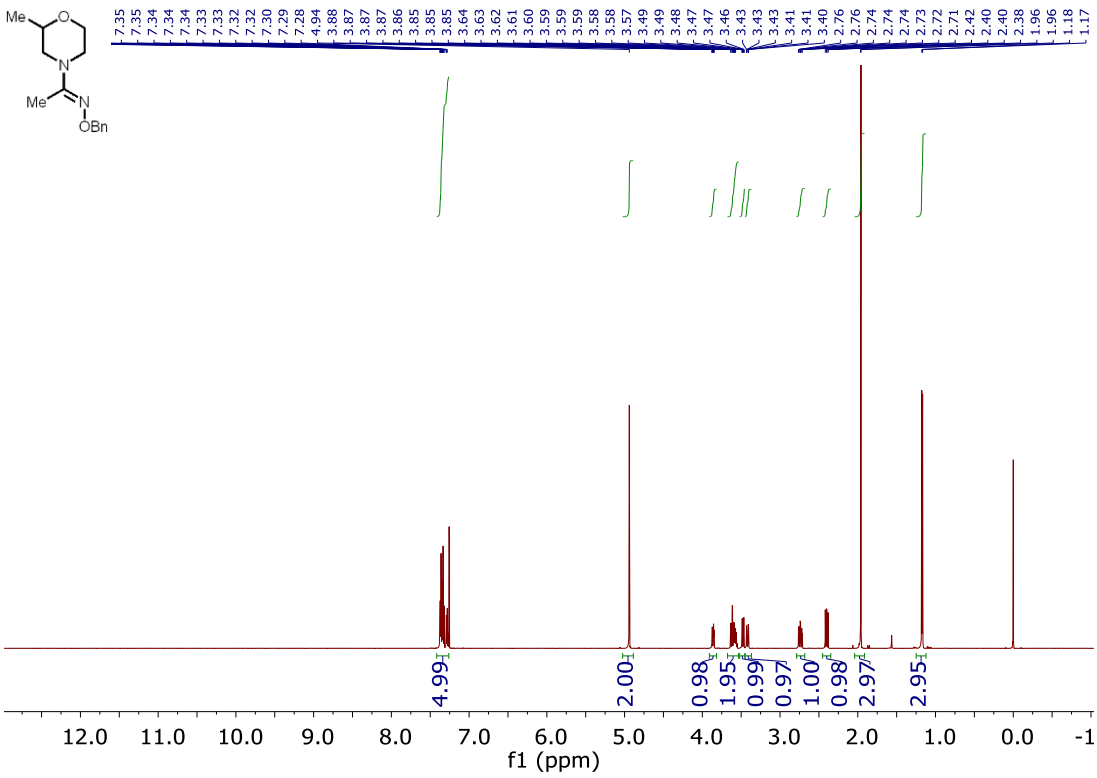


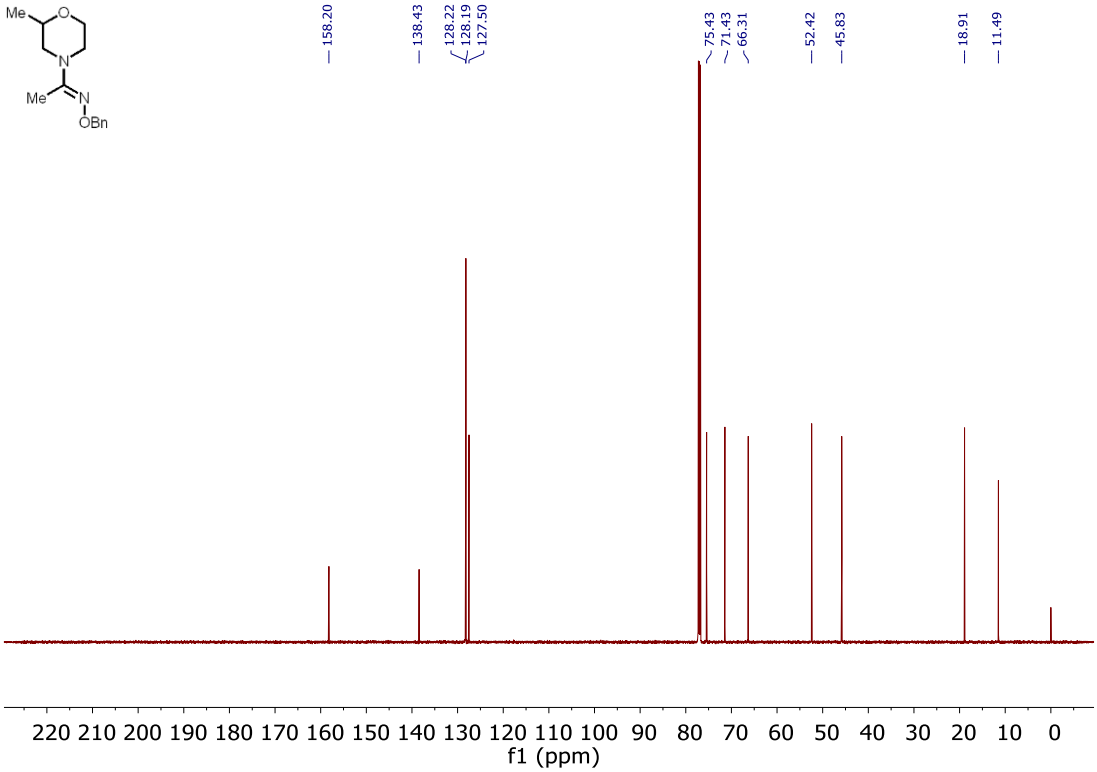
(*E*)-1-(3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one *O*-benzyl oxime (4k)



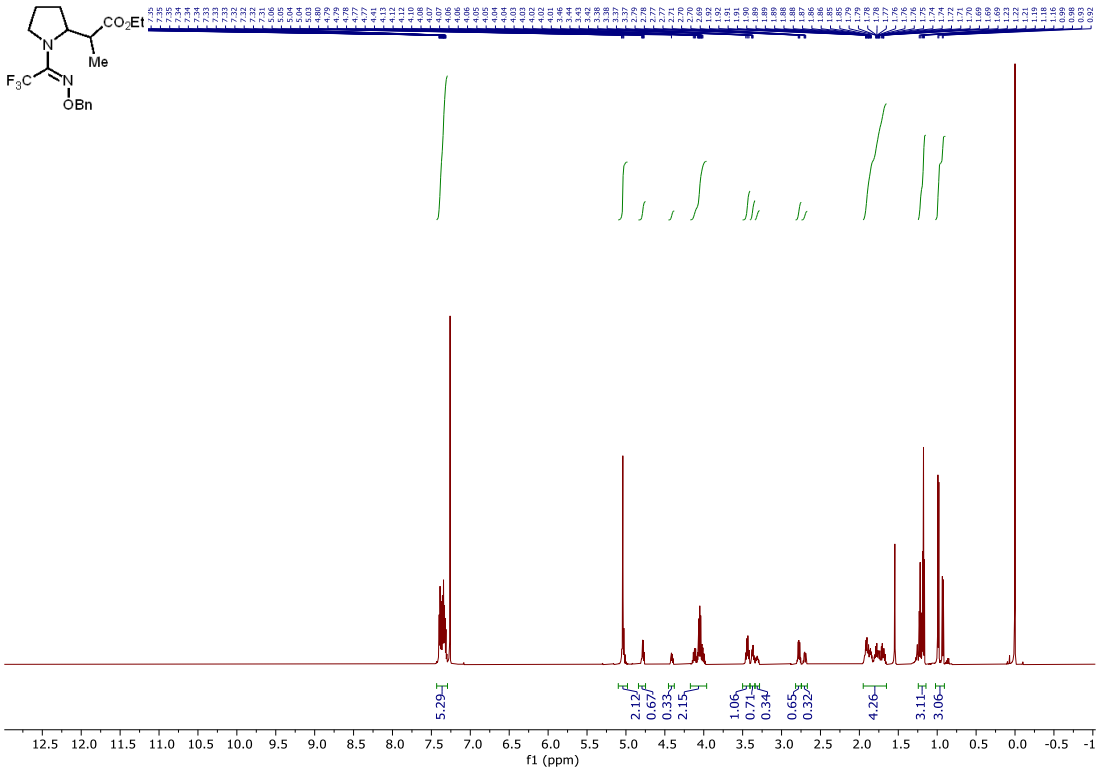


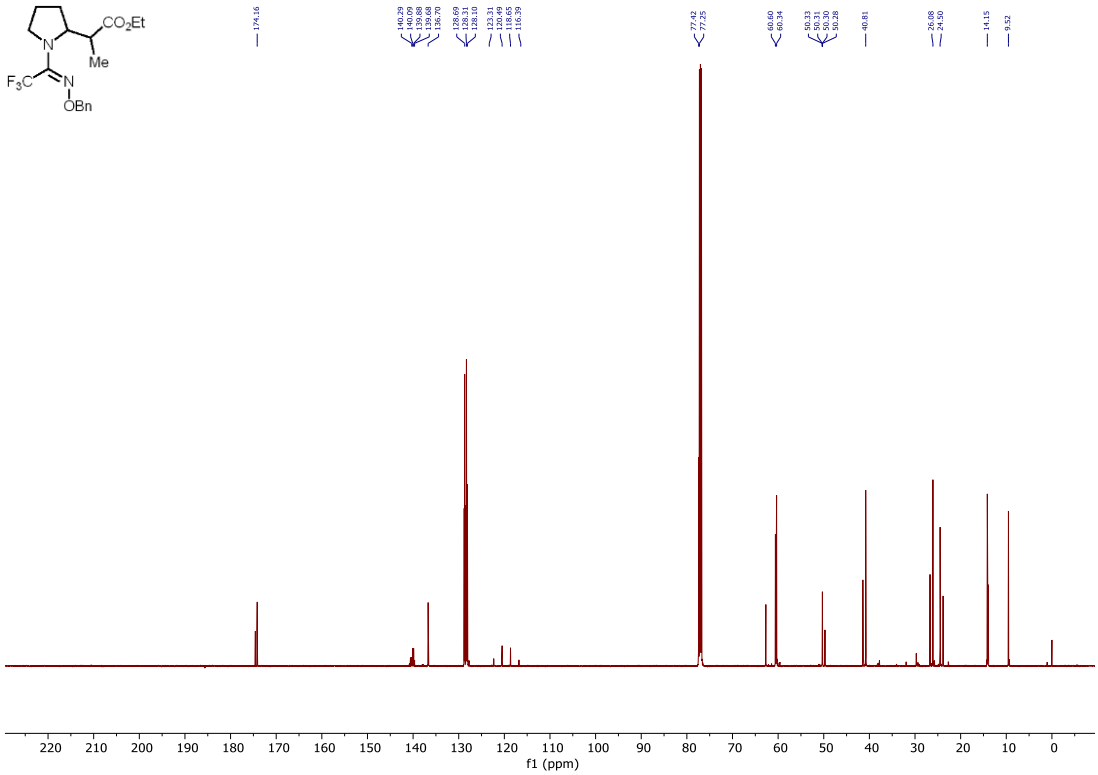
(*E*)-1-(2-methylmorpholino)ethan-1-one *O*-benzyl oxime (4l)

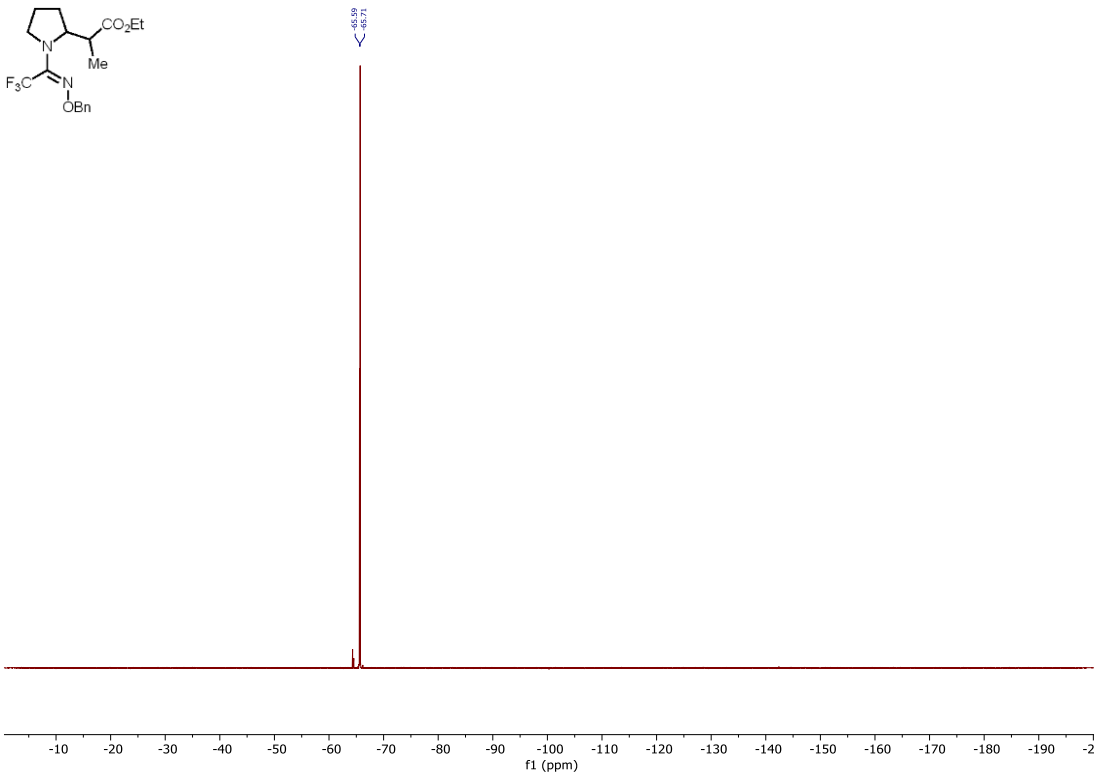




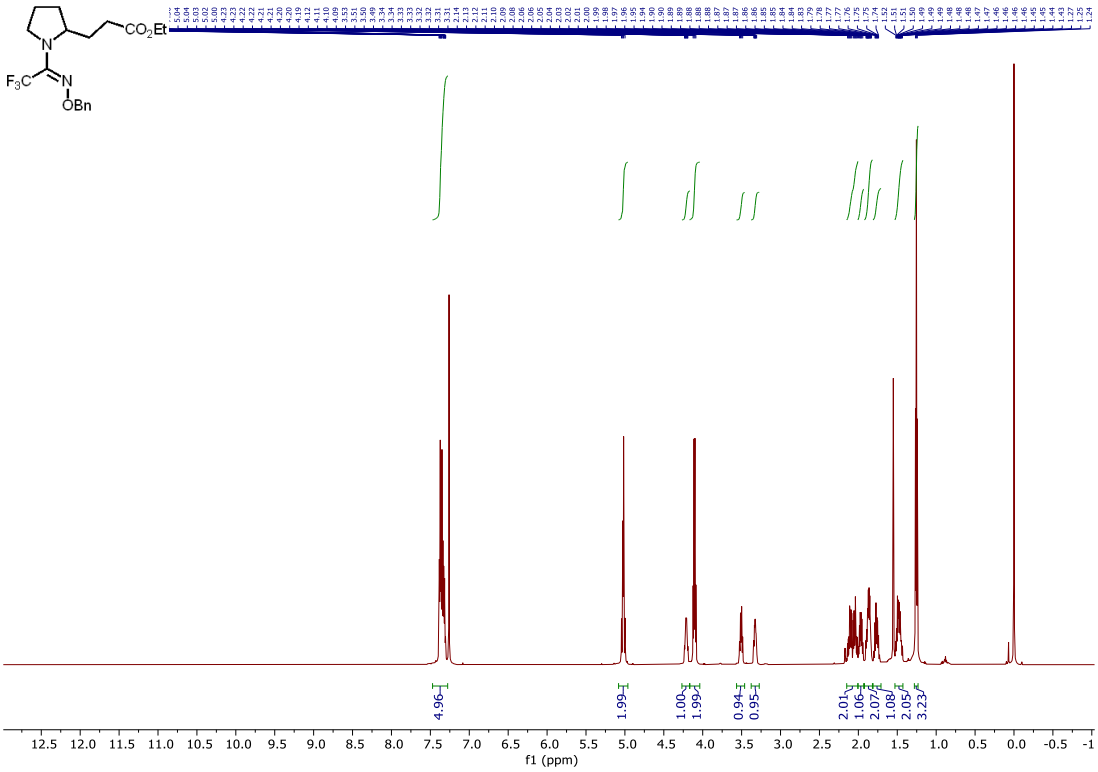
ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (2a-3-B)

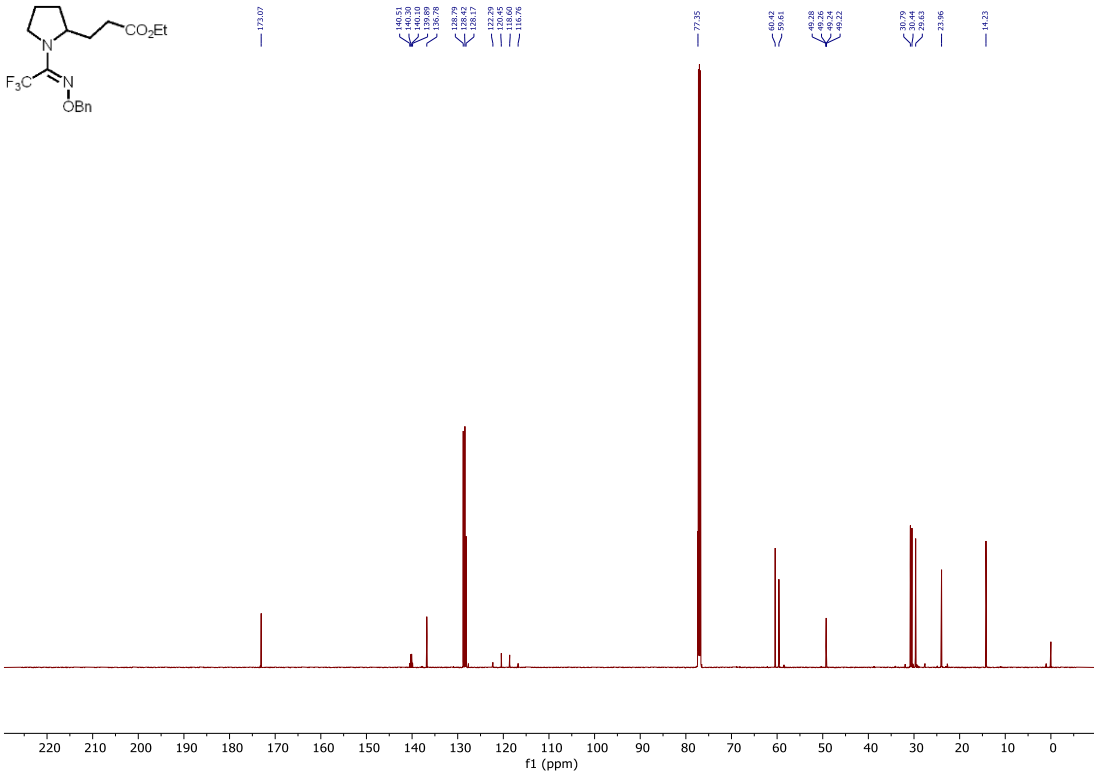


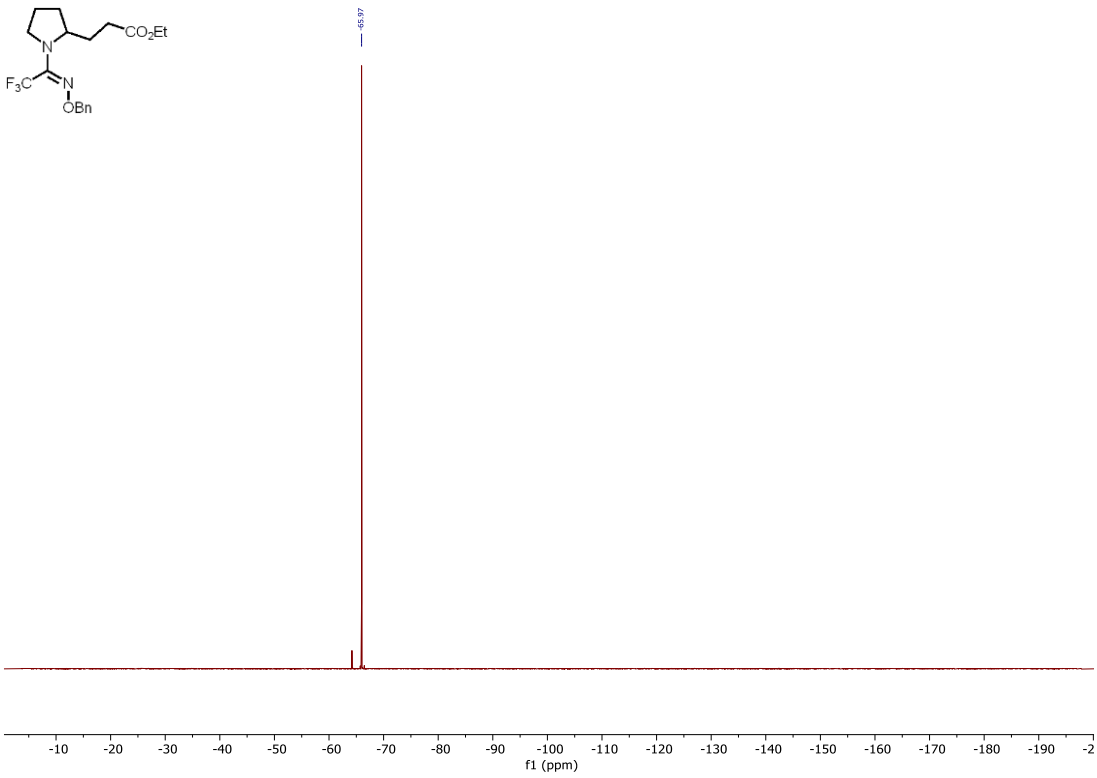



CO2Et
Me
F3C
N
OBn
-65.59
-65.71
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-2
f1 (ppm)

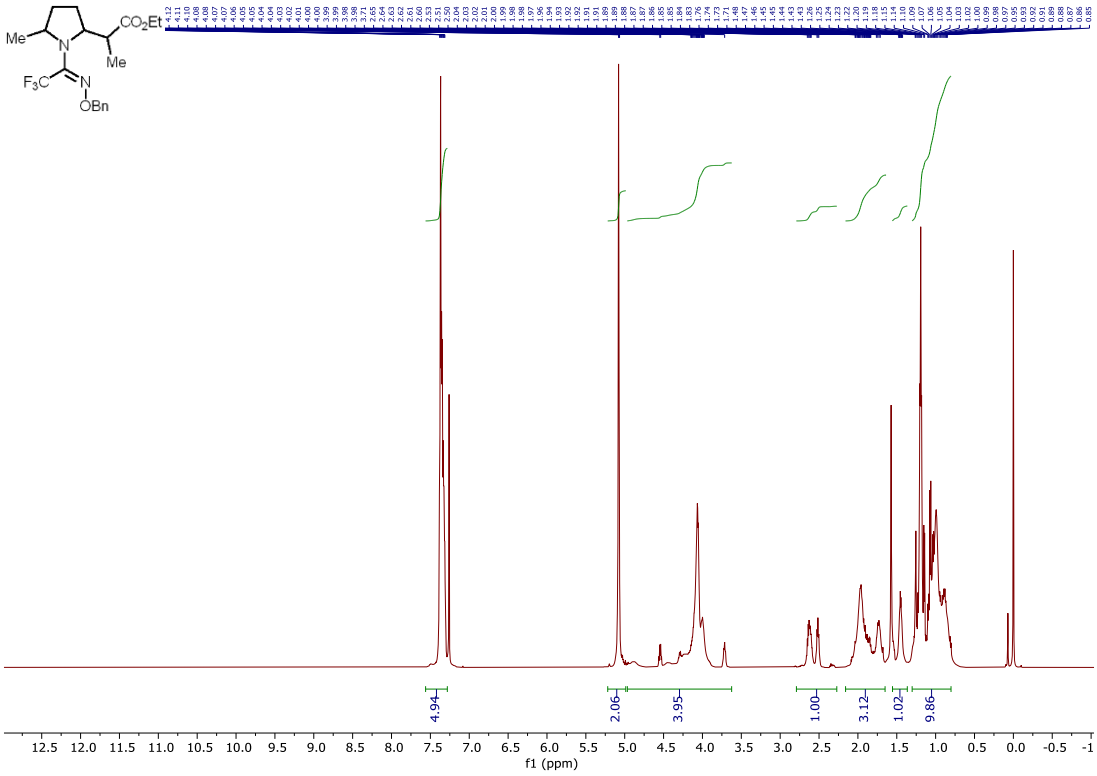
ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (2a-3-L)

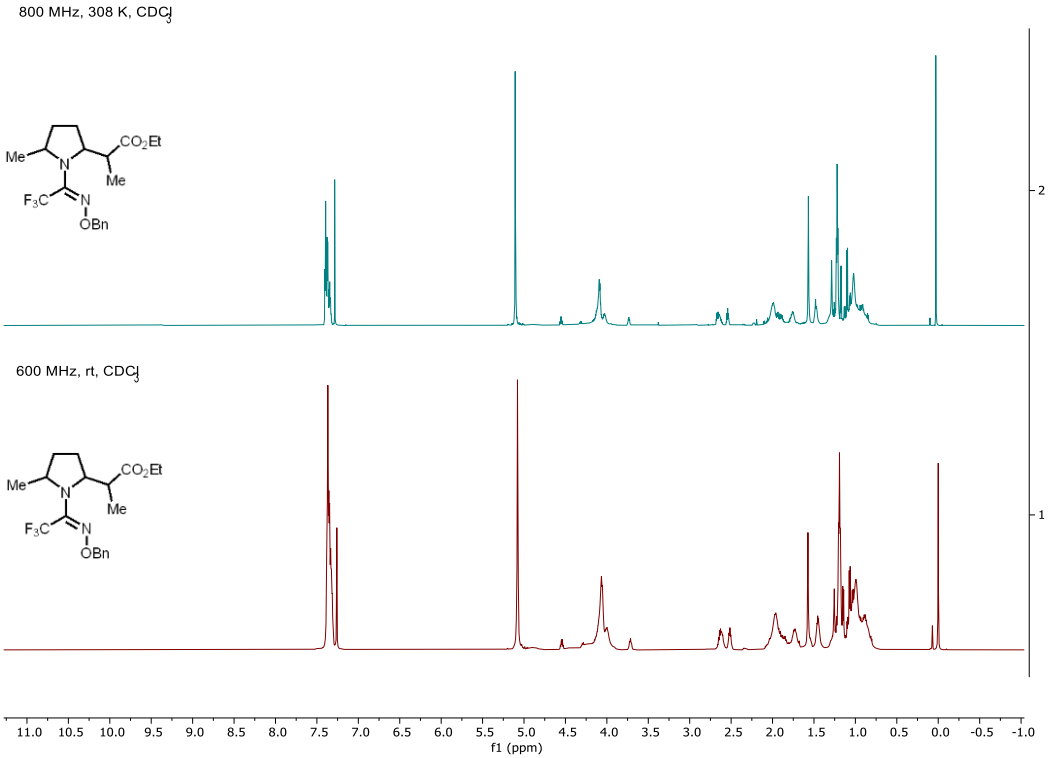


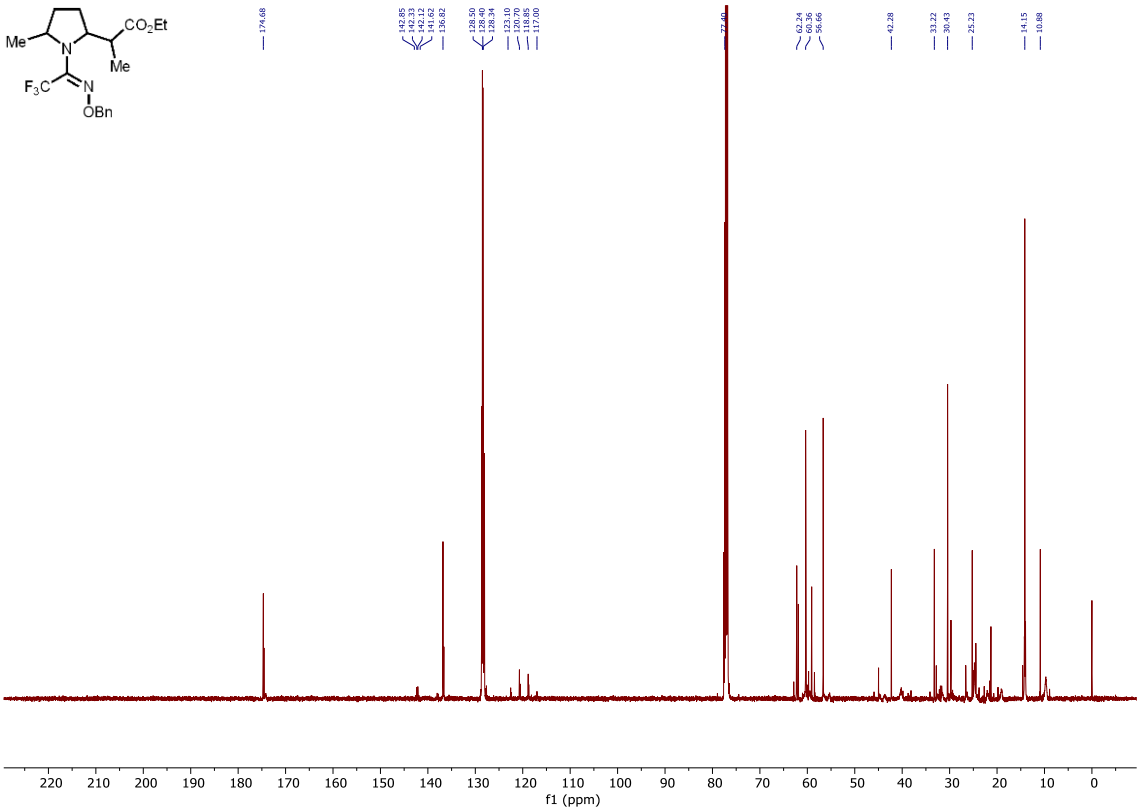


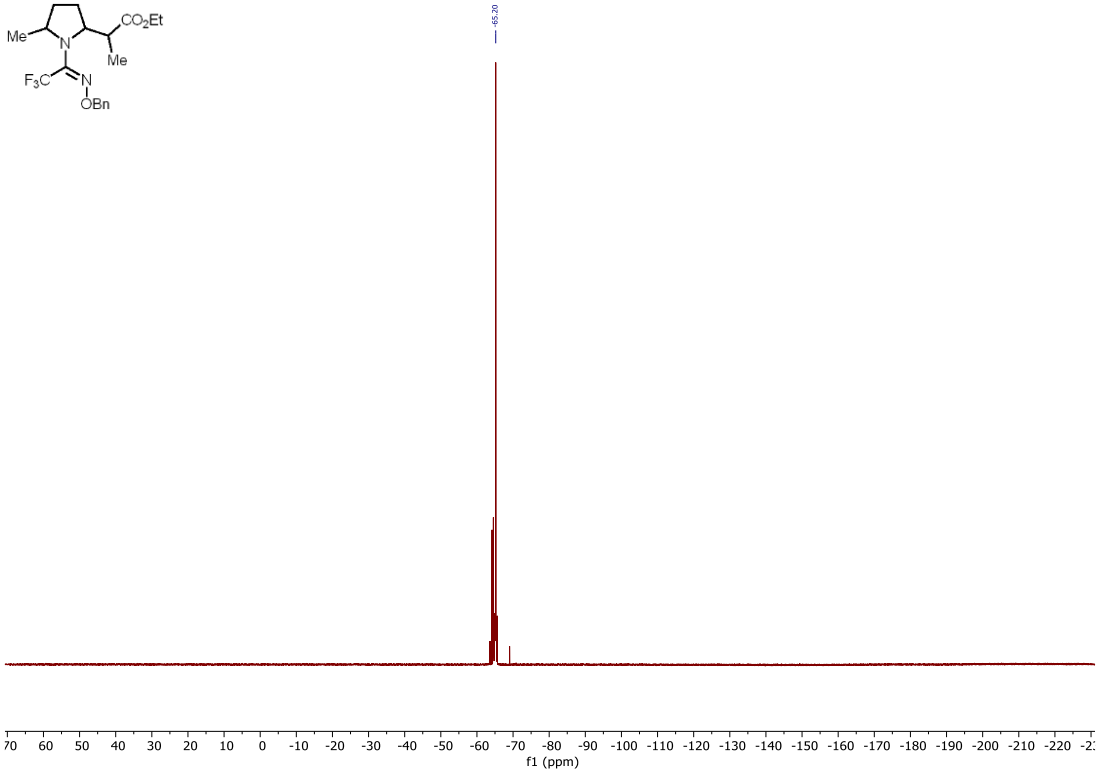

CO2Et
N
F3C
N
OBn
-65.97
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-2
f1 (ppm)

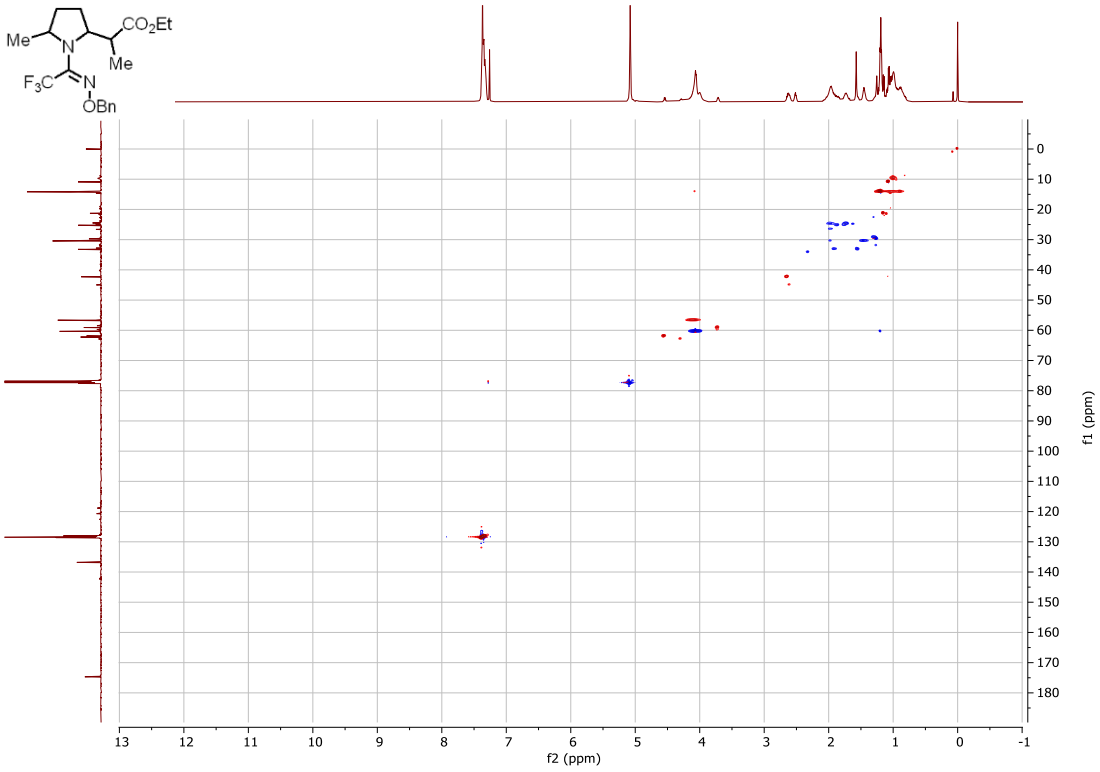
ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-methylpyrrolidin-2-yl)propanoate (2b-B)



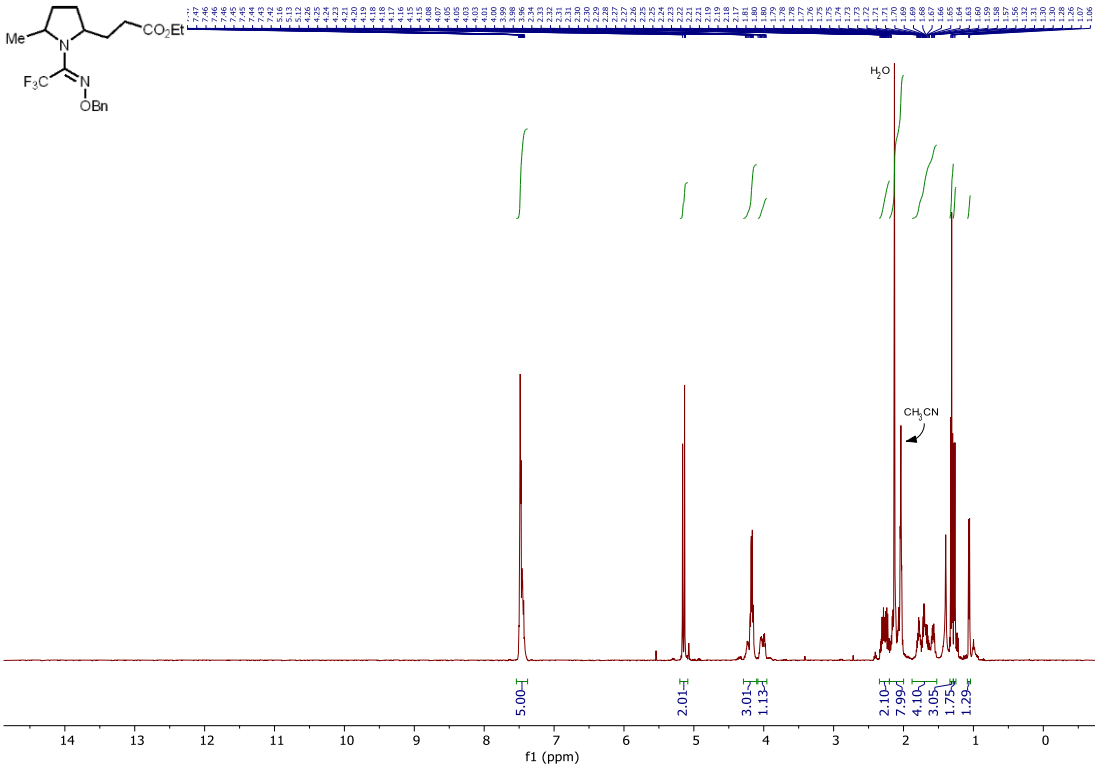


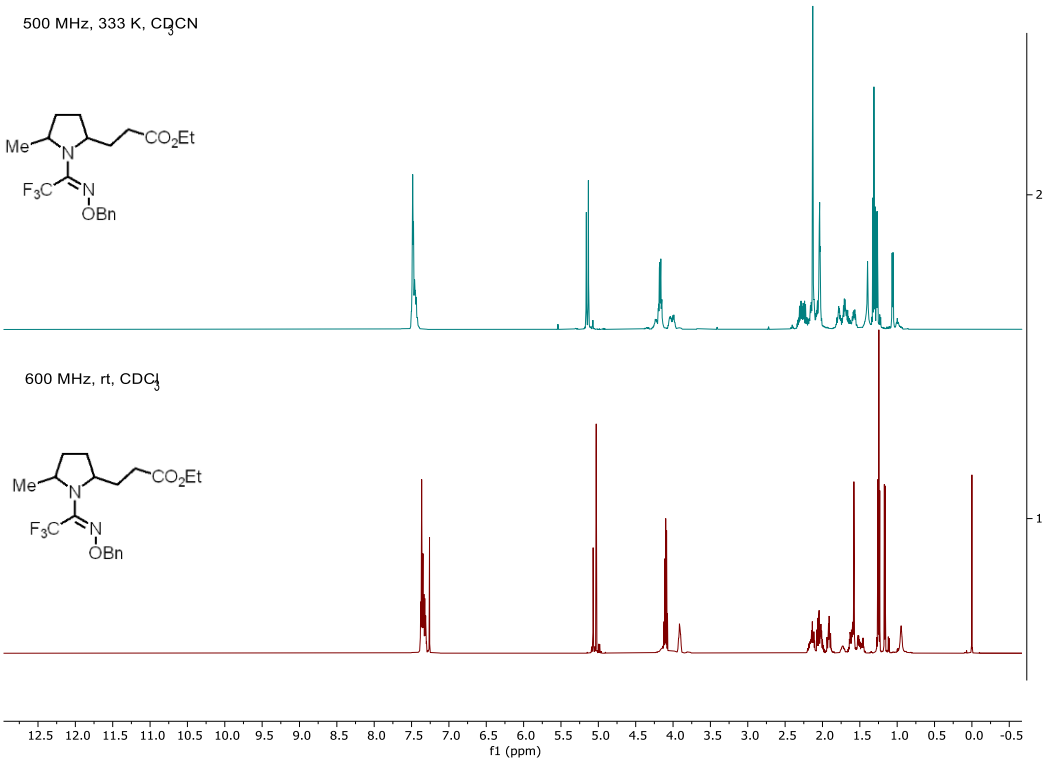

Me
CO2Et
N
Me
F3C
N
OBn
174.68
142.85
142.33
142.12
141.62
136.82
128.50
128.40
128.34
123.10
120.70
119.85
117.00
77.40
62.24
60.36
56.66
42.28
33.22
30.43
25.23
14.15
10.88
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

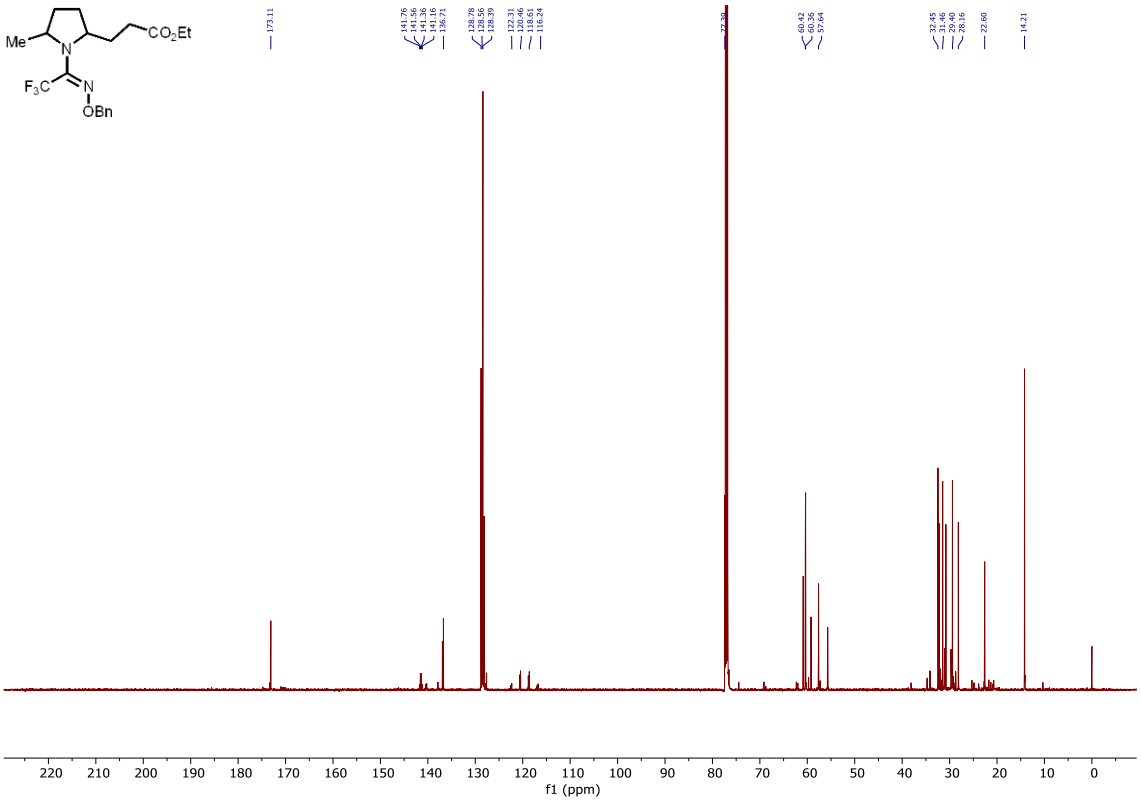

Me
CO2Et
N
Me
F3C
N
OBn
-65.20
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

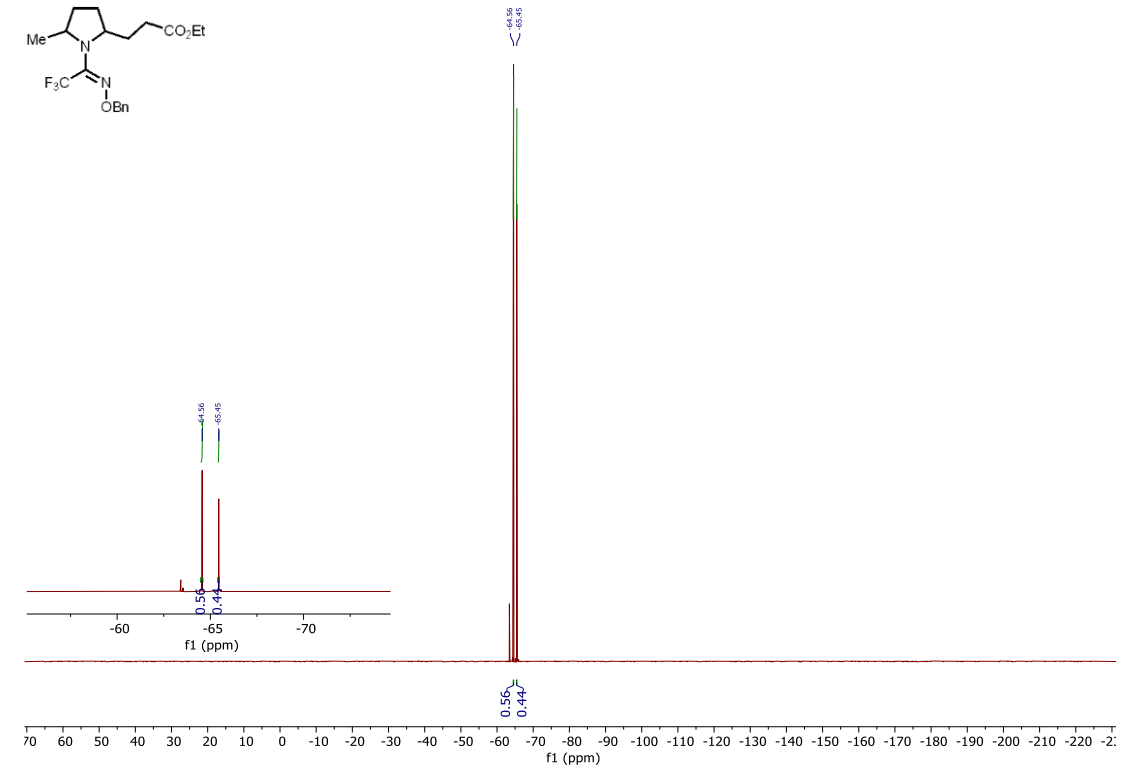

Me
N
CO2Et
Me
F3C
N
OBn
f2 (ppm)
f1 (ppm)

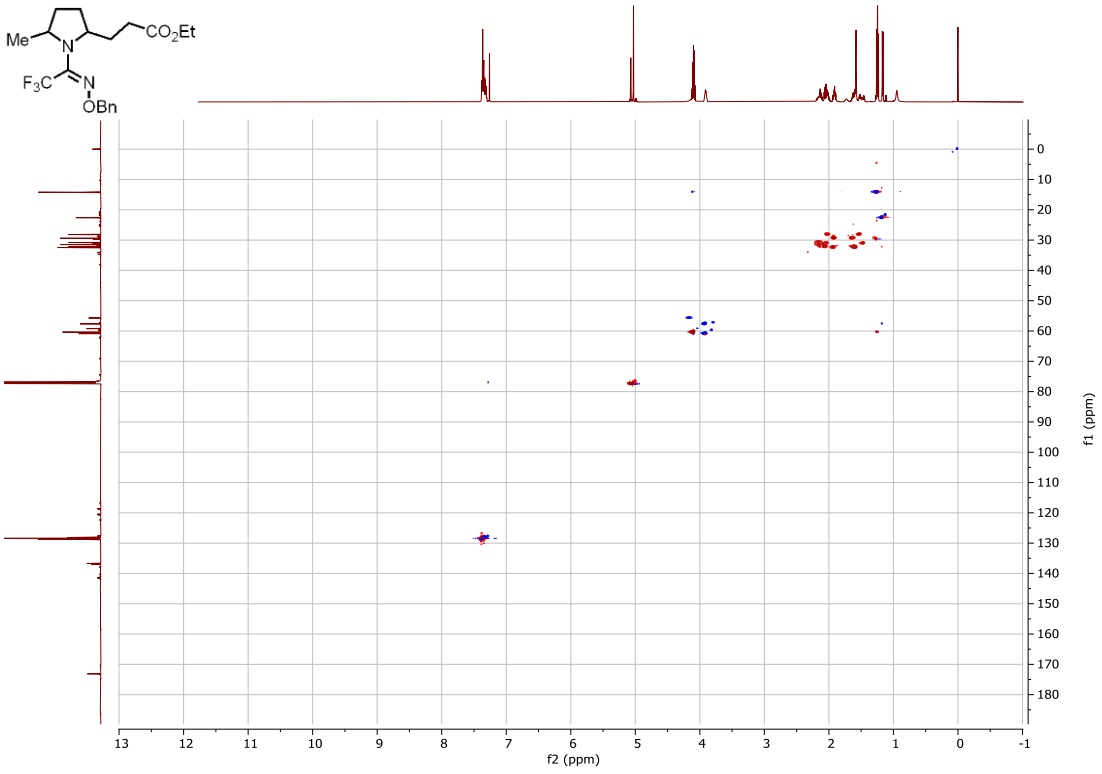
ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-methylpyrrolidin-2-yl)propanoate (2b-L)



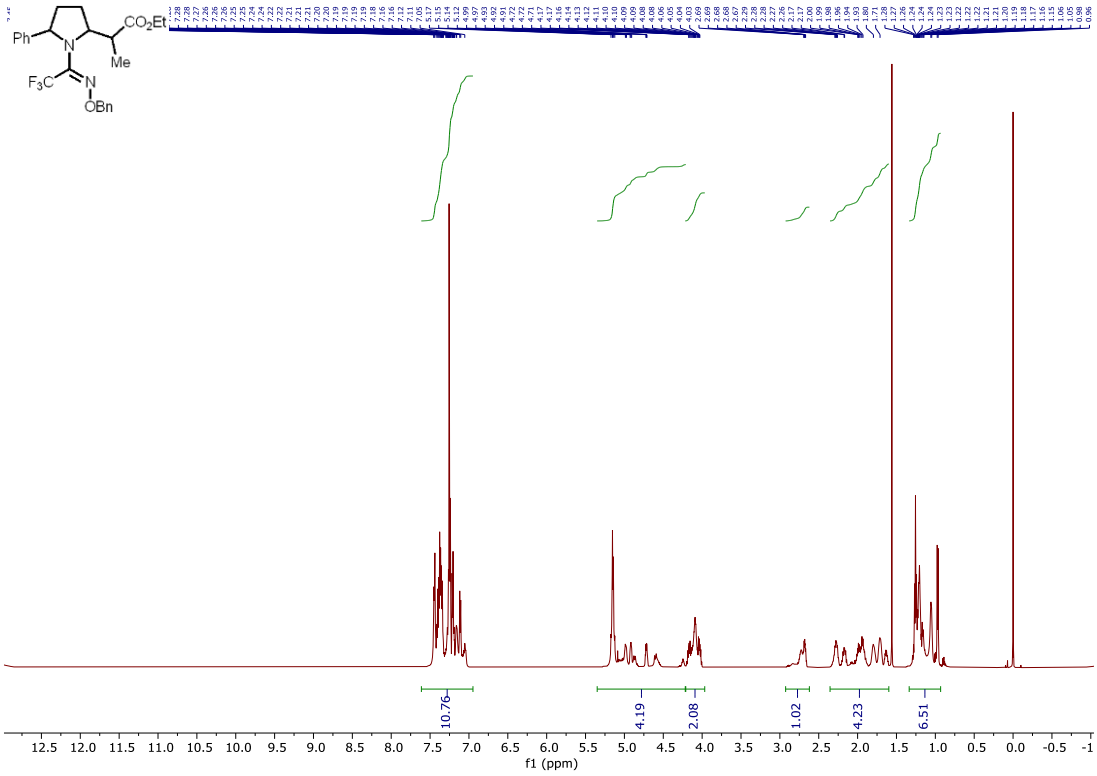


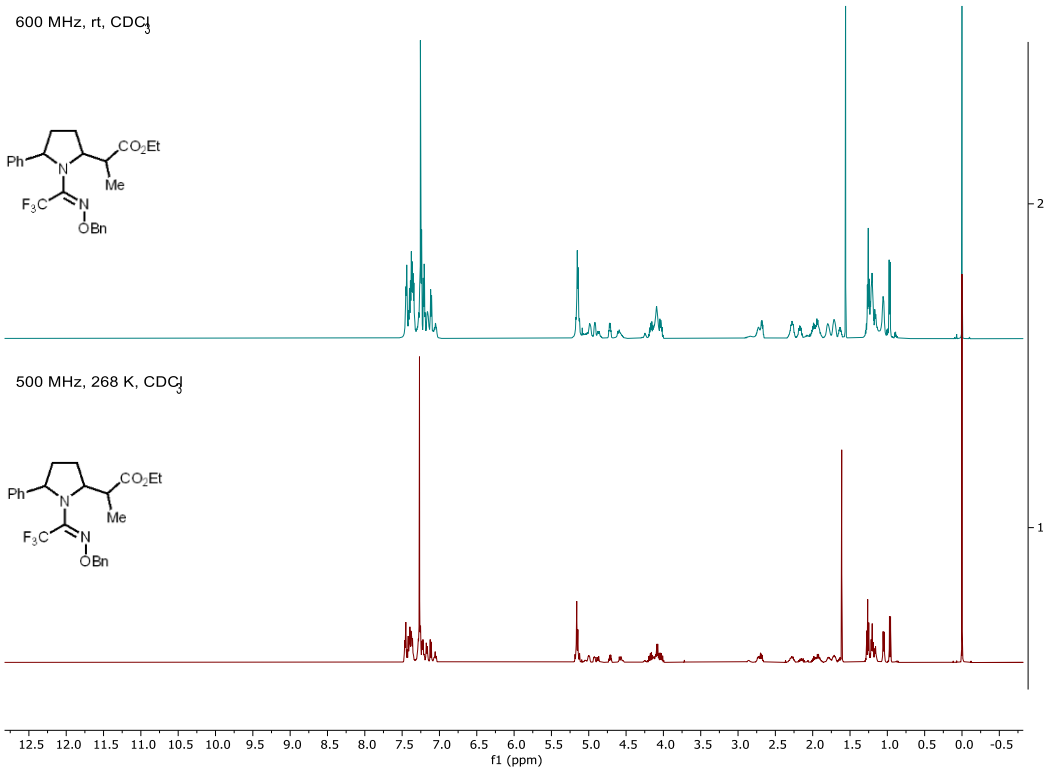

Me
N
CO2Et
F3C
N
OBn
173.11
141.76
141.56
141.36
141.16
136.71
128.78
128.56
128.39
122.31
120.46
118.61
116.24
77.38
60.42
60.36
57.64
32.45
31.46
29.40
28.16
22.60
14.21
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

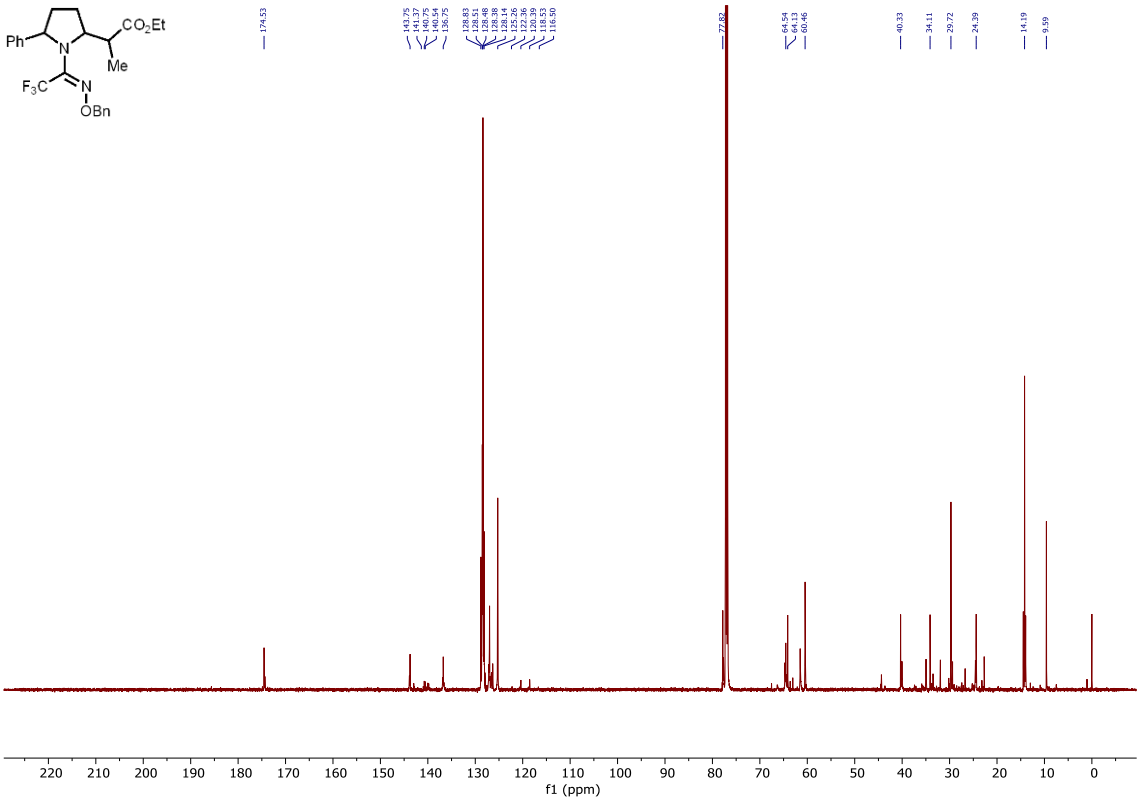

Me
N
CO2Et
F3C
N
OBn
-64.56
-65.45
0.56
0.44
-60
-65
-70
f1 (ppm)
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

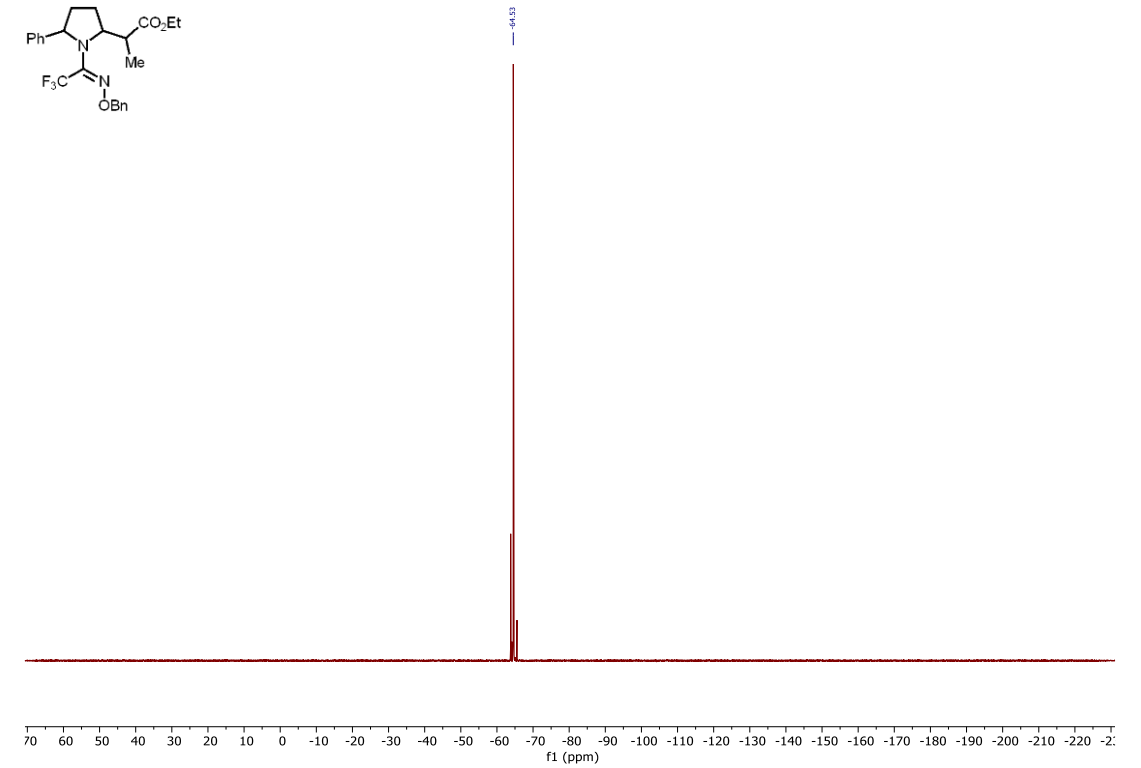

Me
N
CO2Et
F3C
N
OBn
f2 (ppm)
f1 (ppm)

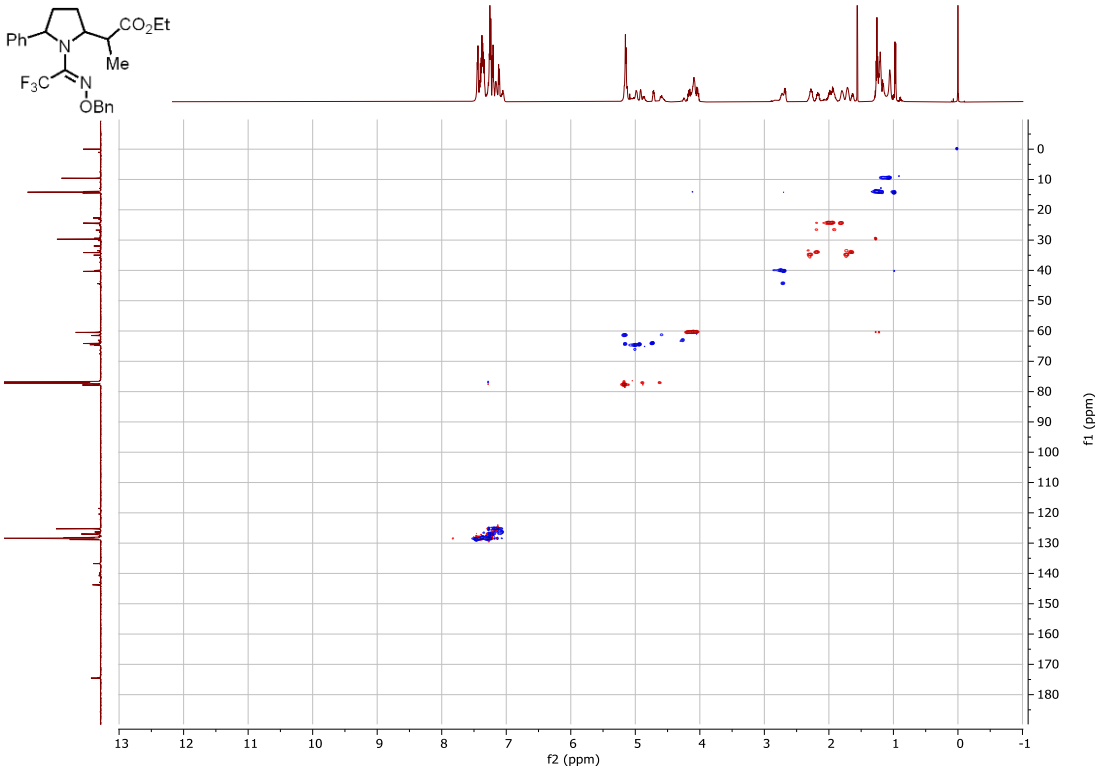
ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-phenylpyrrolidin-2-yl)propanoate (2c-B)



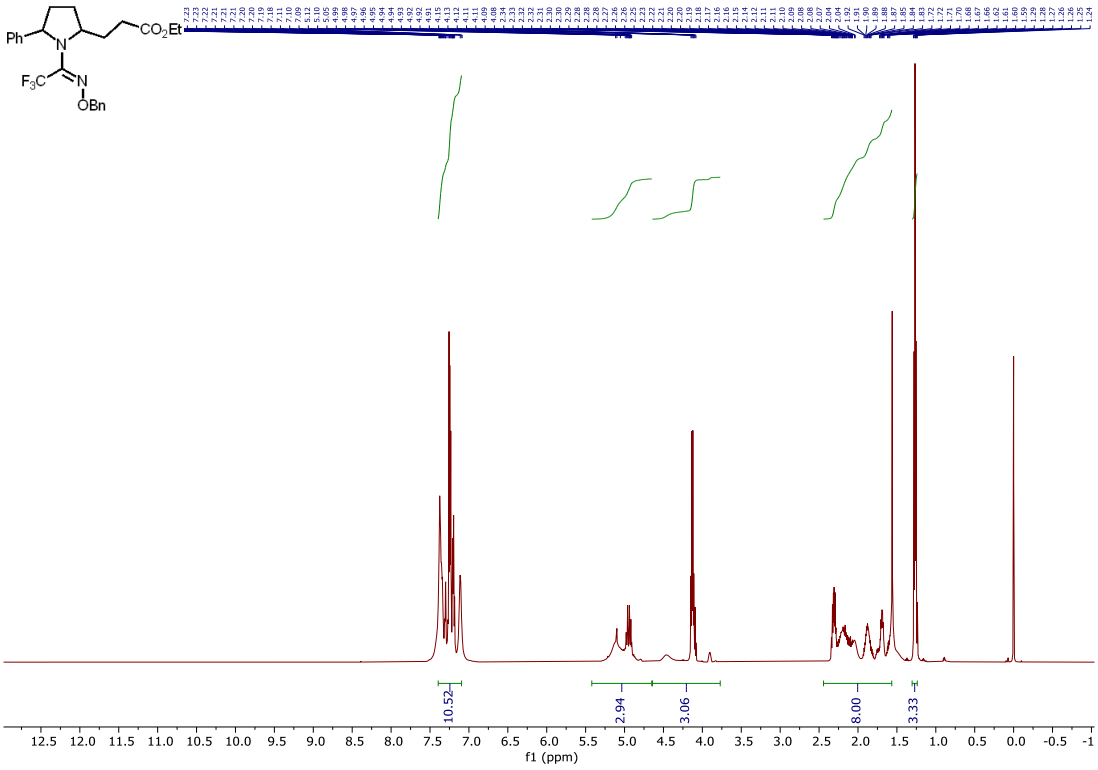


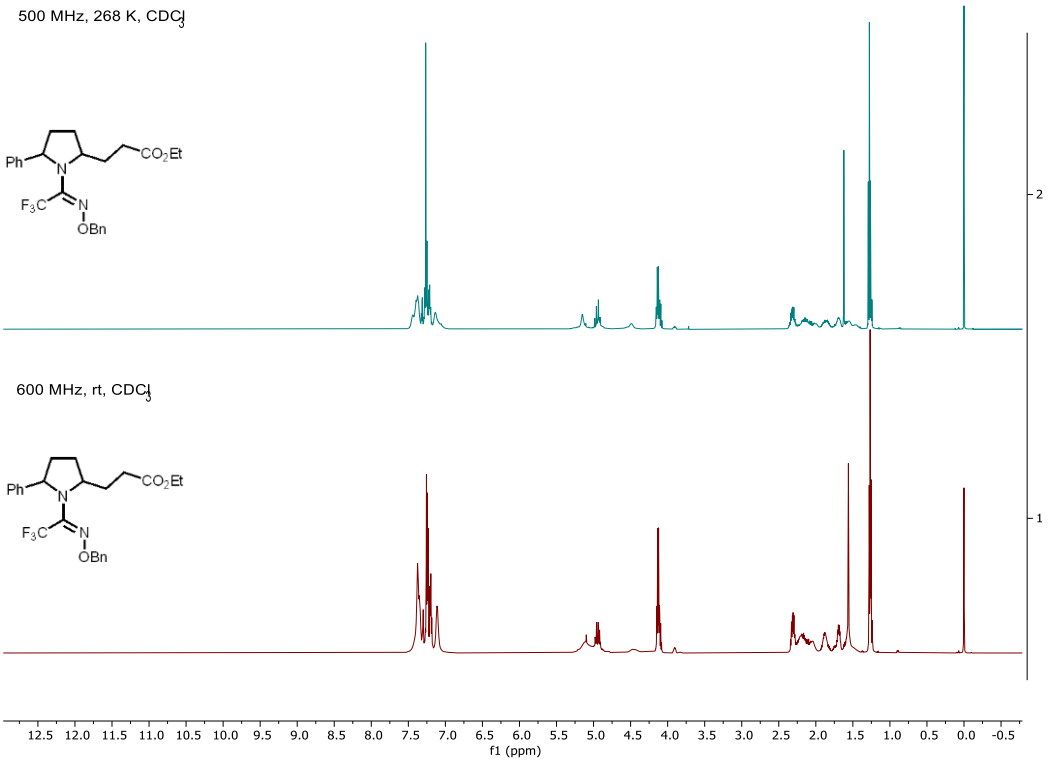

Ph
N
CO2Et
Me
F3C
N
OBn
174.53
143.75
141.37
140.95
140.54
136.75
128.83
128.51
128.48
128.36
128.14
123.26
121.36
120.39
118.53
116.50
77.82
64.54
64.13
60.46
40.33
34.11
29.72
24.39
14.19
9.99
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

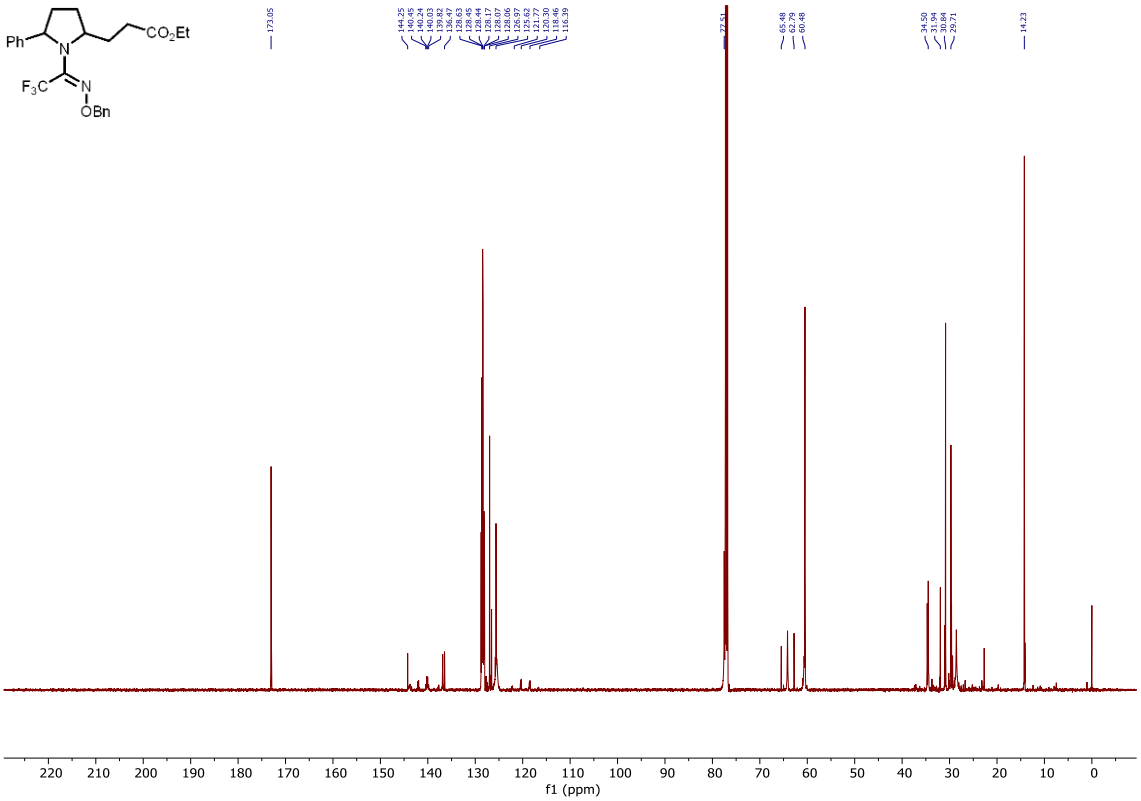

Ph
N
CO2Et
Me
F3C
N
OBn
-64.53
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

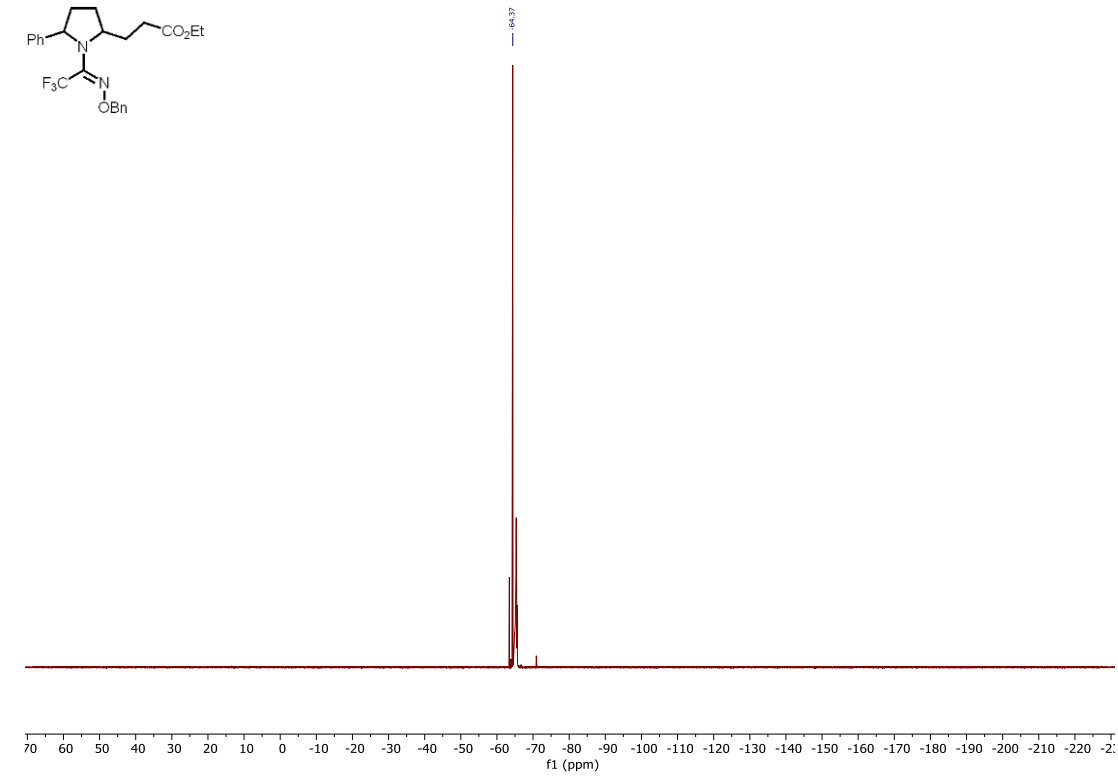

Ph
N
CO2Et
Me
F3C
N
OBn
f2 (ppm)
f1 (ppm)

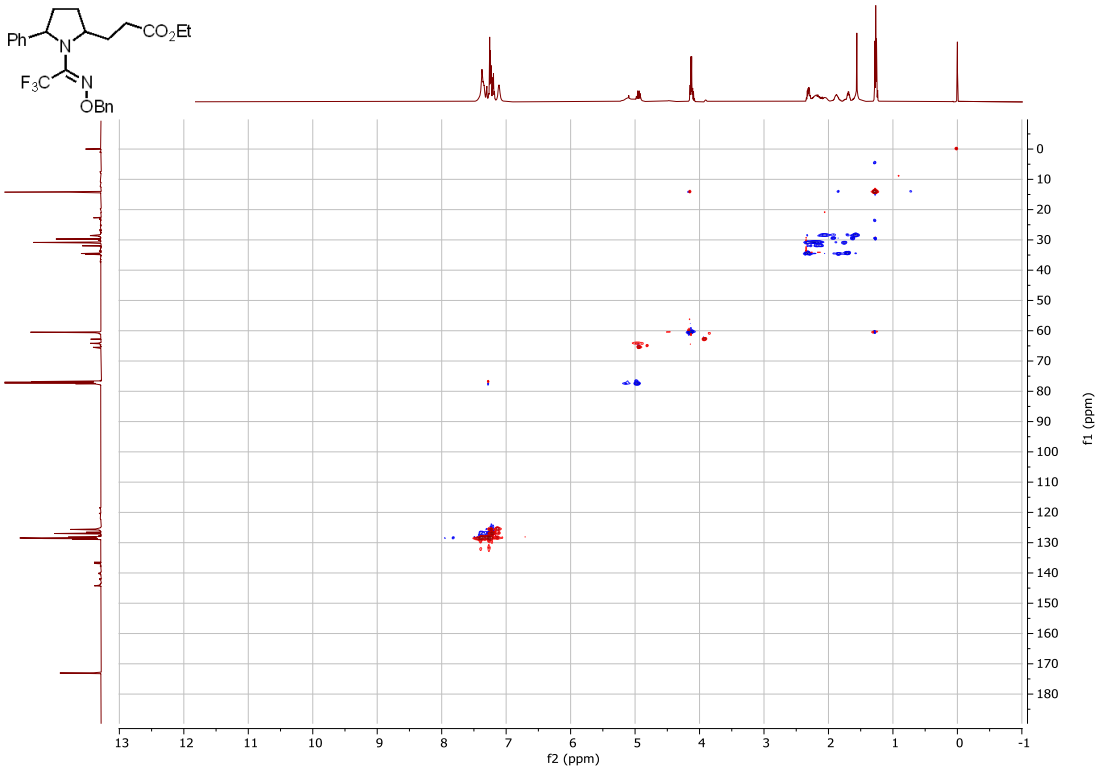
ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-phenylpyrrolidin-2-yl)propanoate (2c-L)



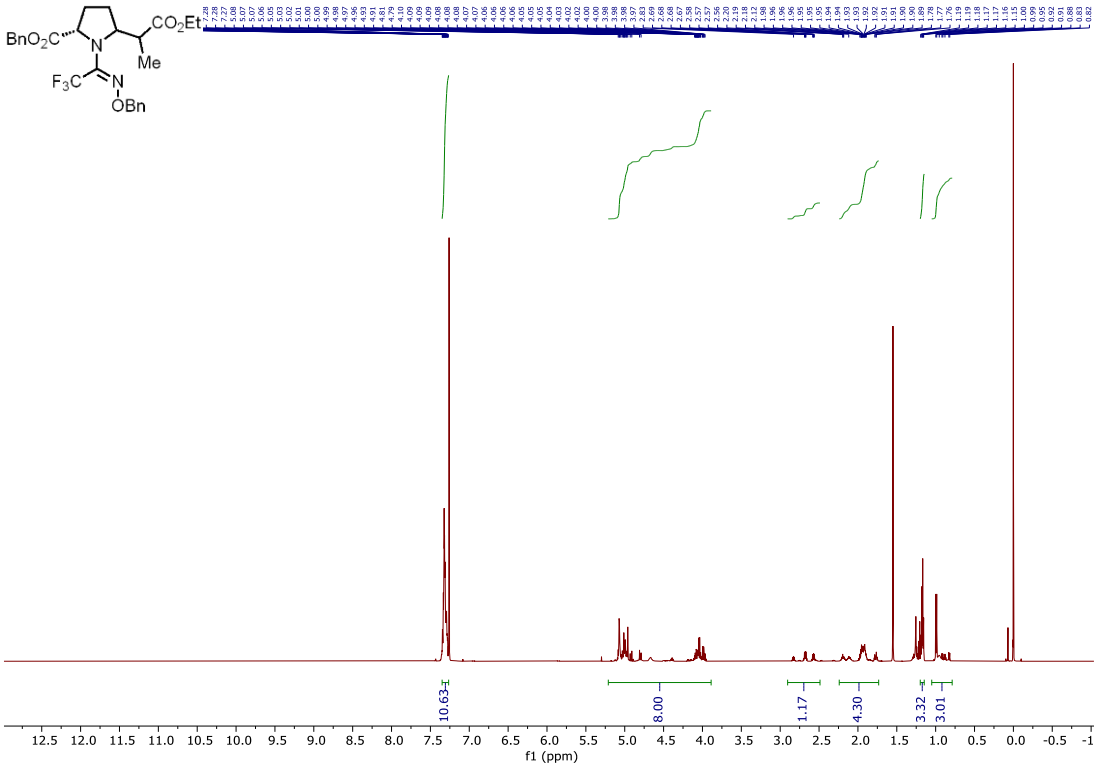


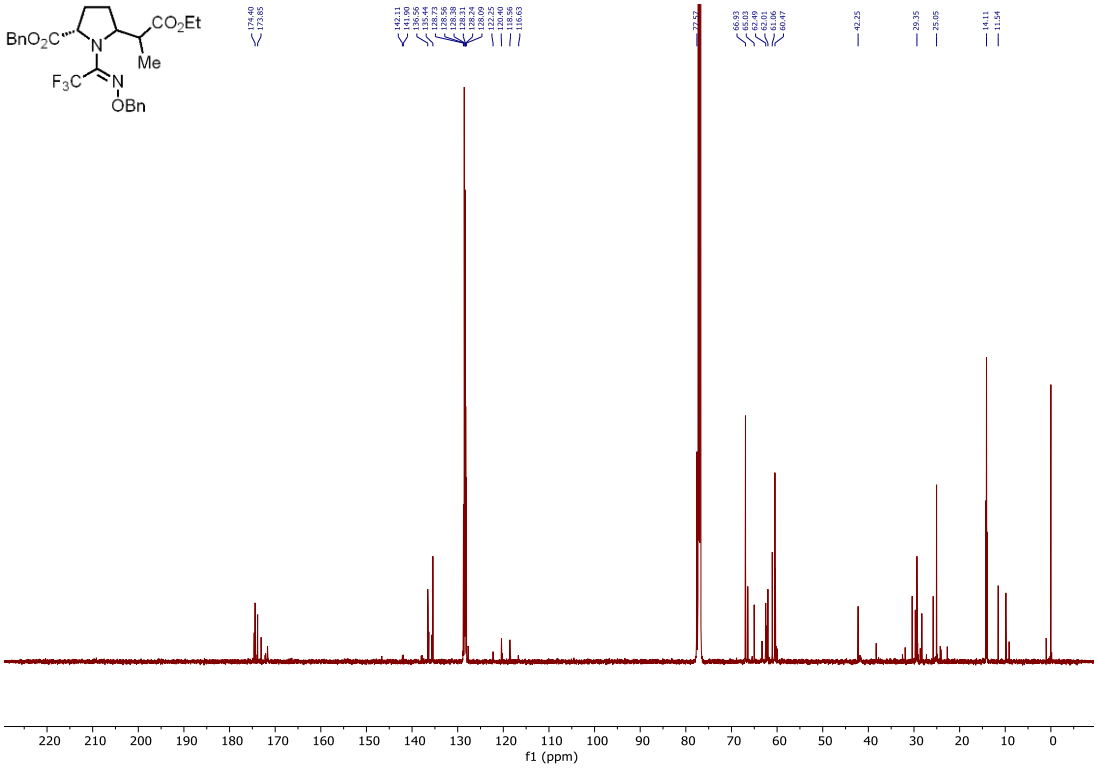

Ph
N
CO2Et
F3C
N
OBn
173.05
144.25
140.65
140.24
140.03
136.97
136.47
128.63
128.45
128.44
128.17
128.07
127.96
126.97
125.62
121.77
120.30
118.46
116.99
77.51
65.48
62.29
60.48
34.50
31.94
30.84
29.71
14.23
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

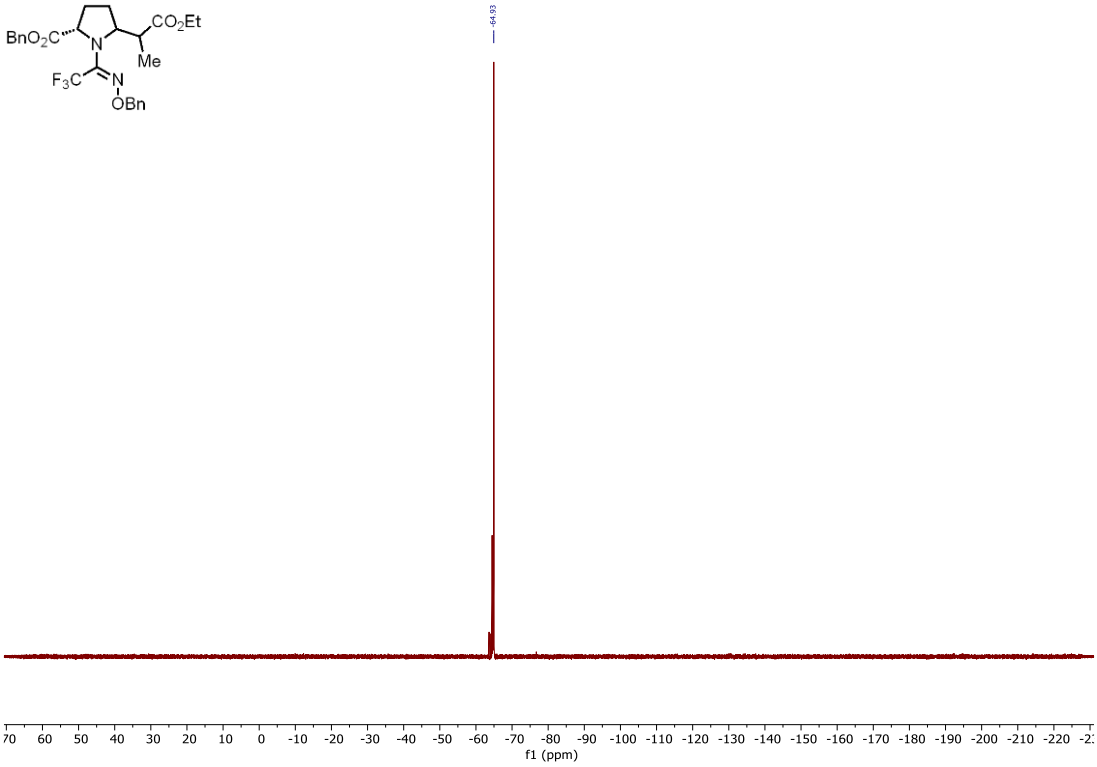

Ph
N
CO2Et
F3C
N
OBn
-64.37
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

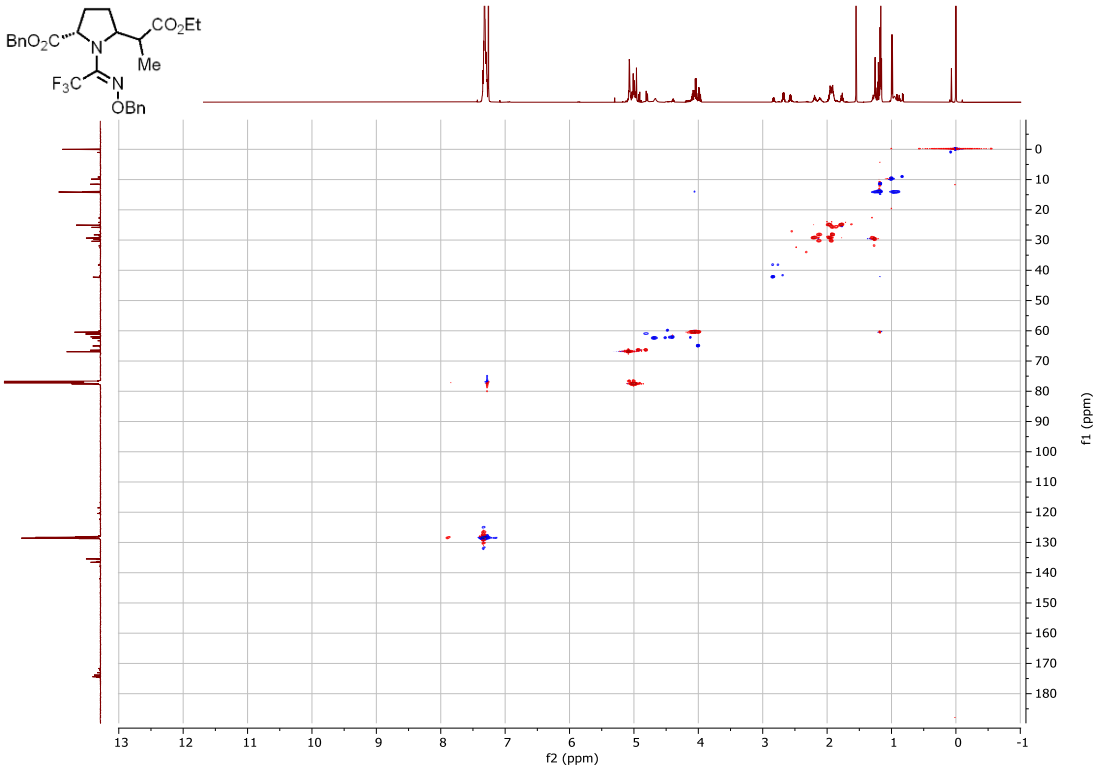

Ph
N
CO2Et
F3C
N
OBn
f2 (ppm)
f1 (ppm)

benzyl (2*S*)-1-((*E*)-1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-(1-ethoxy-1-oxopropan-2-yl)pyrrolidine-2-carboxylate (2d-B)

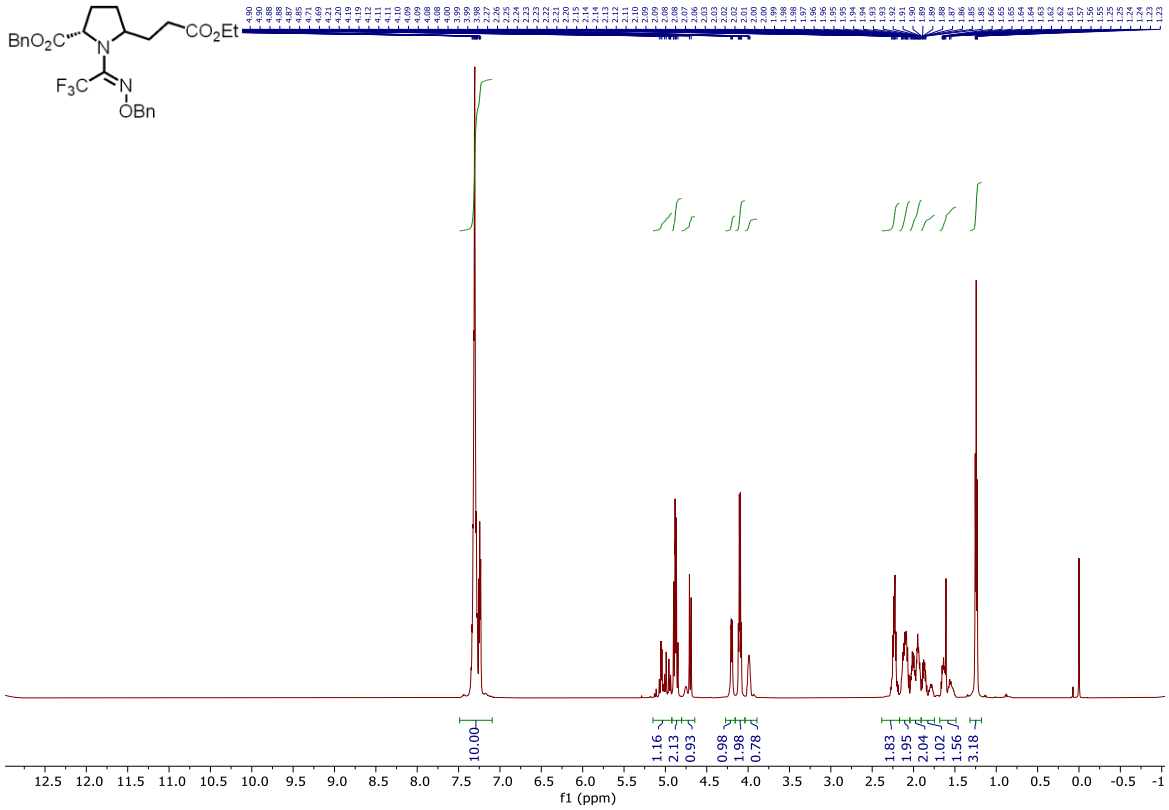


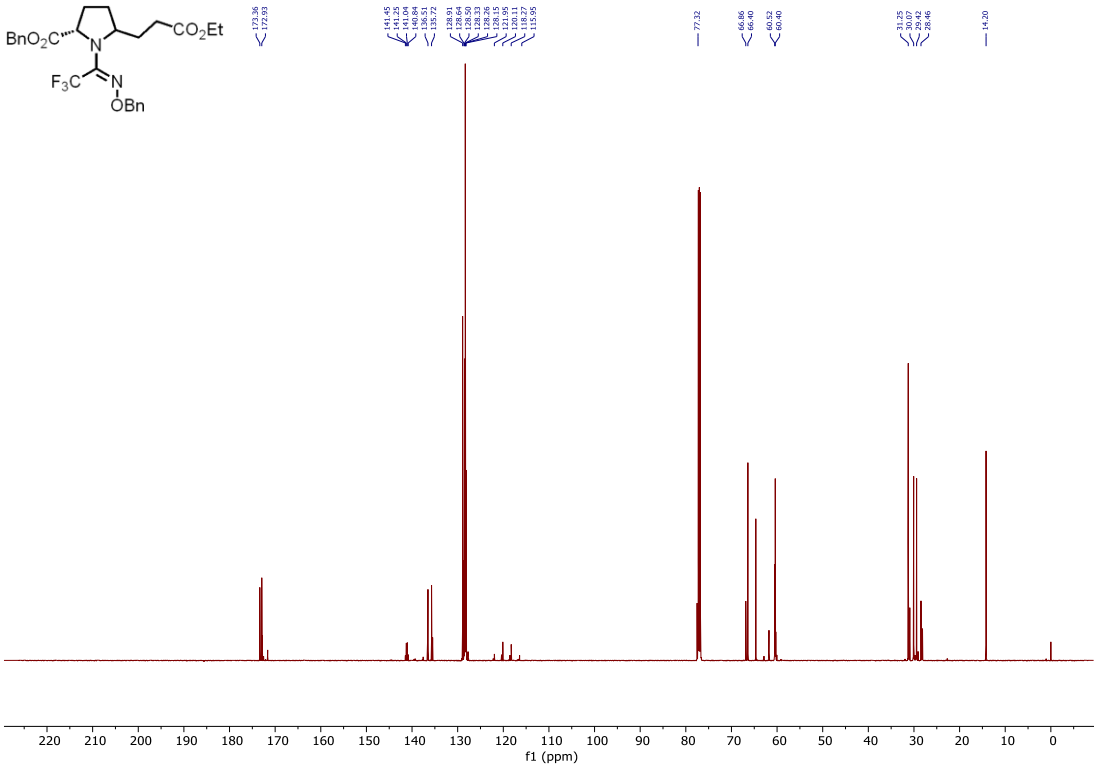


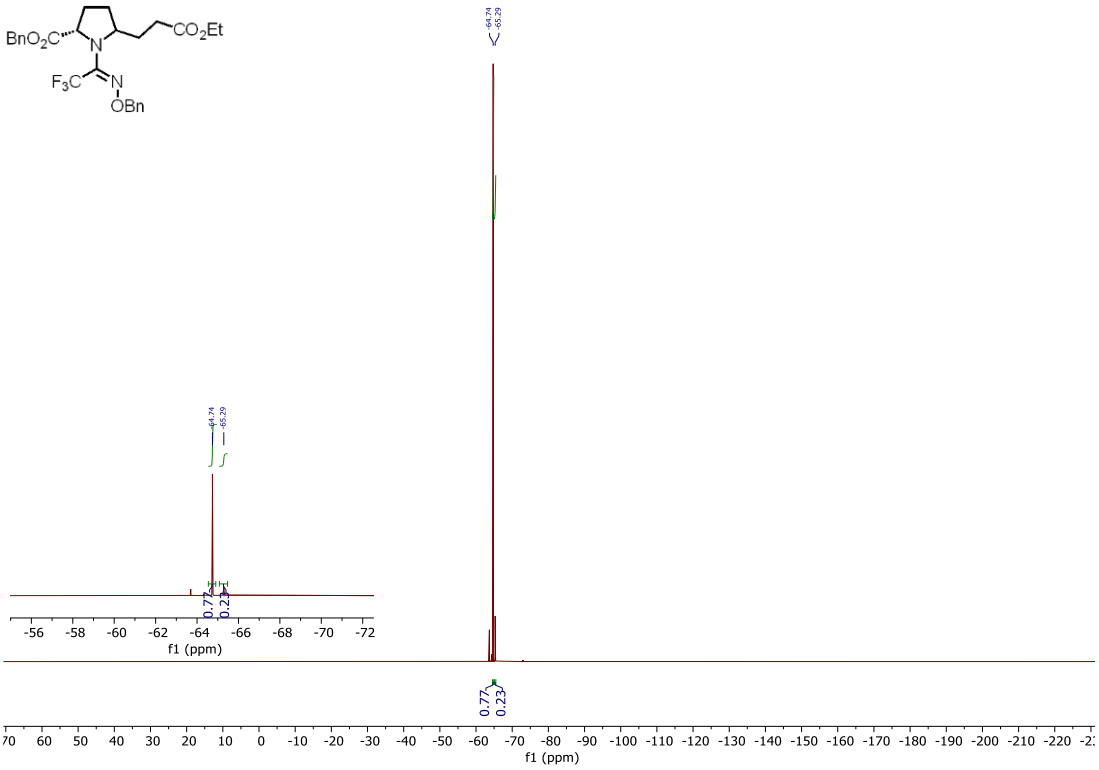

BnO2C
CO2Et
Me
F3C
N
OBn
-64.93
f1 (ppm)

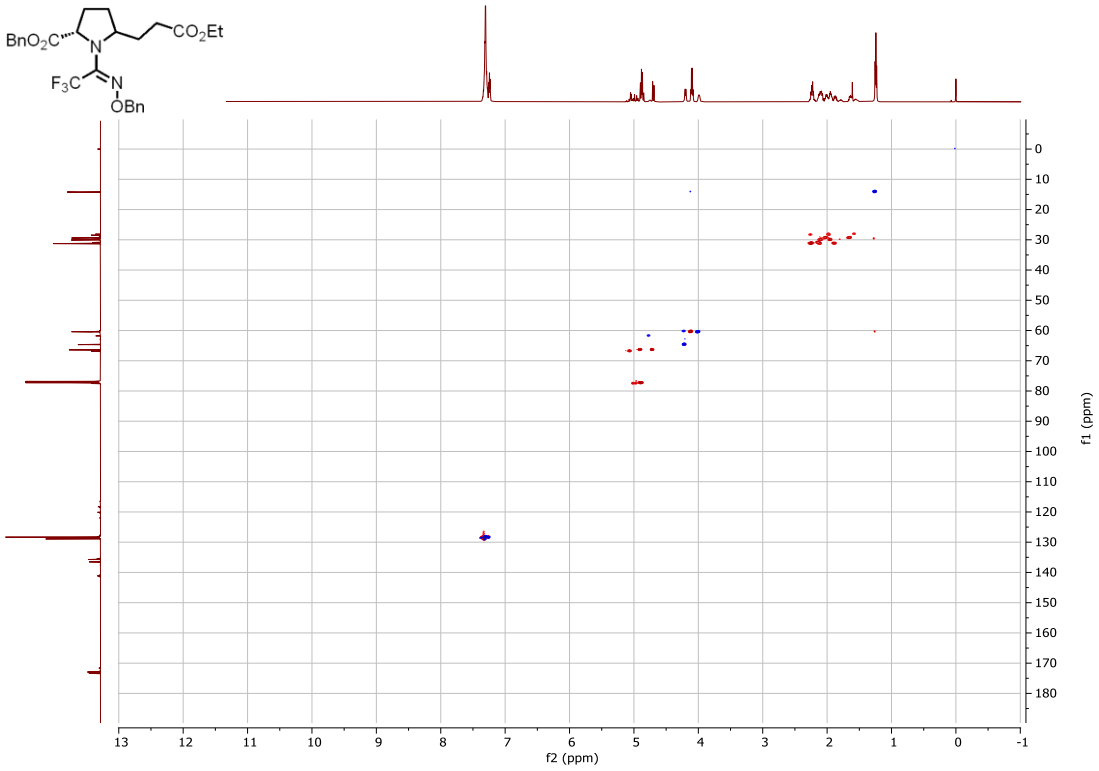

BnO2C
CO2Et
Me
F3C
N
OBn
f2 (ppm)
f1 (ppm)

benzyl (2*S*)-1-((*E*)-1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-(3-ethoxy-3-oxopropyl)pyrrolidine-2-carboxylate (2d-L)

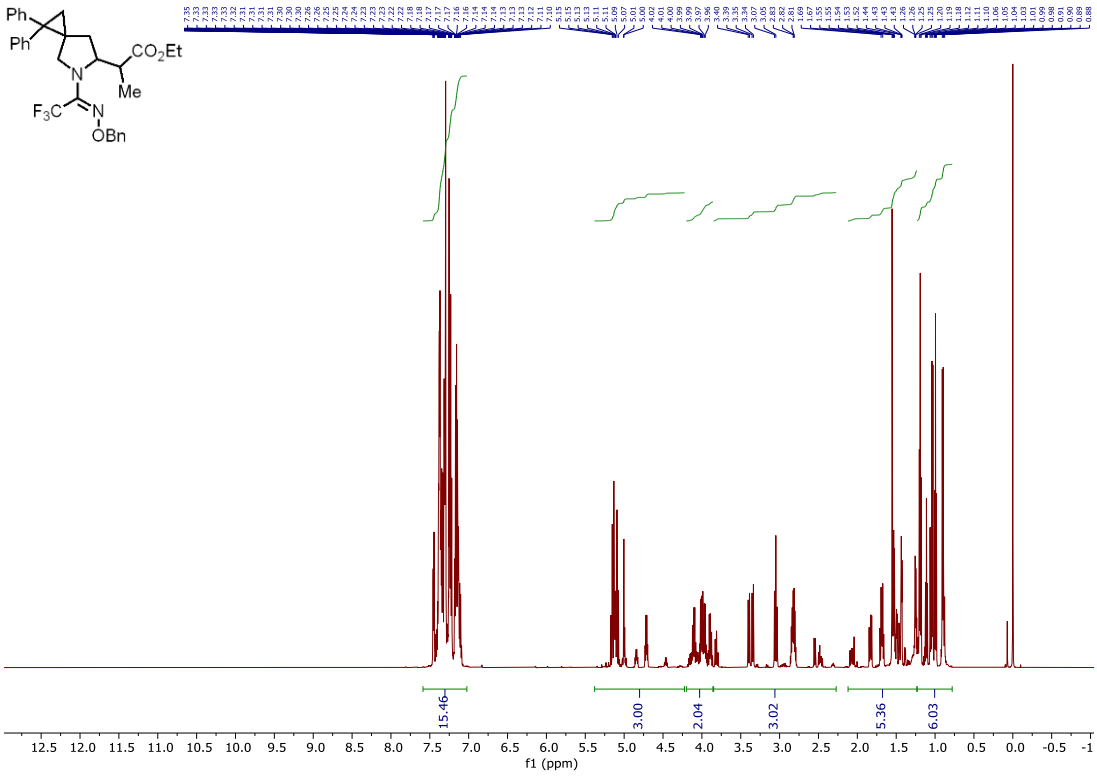


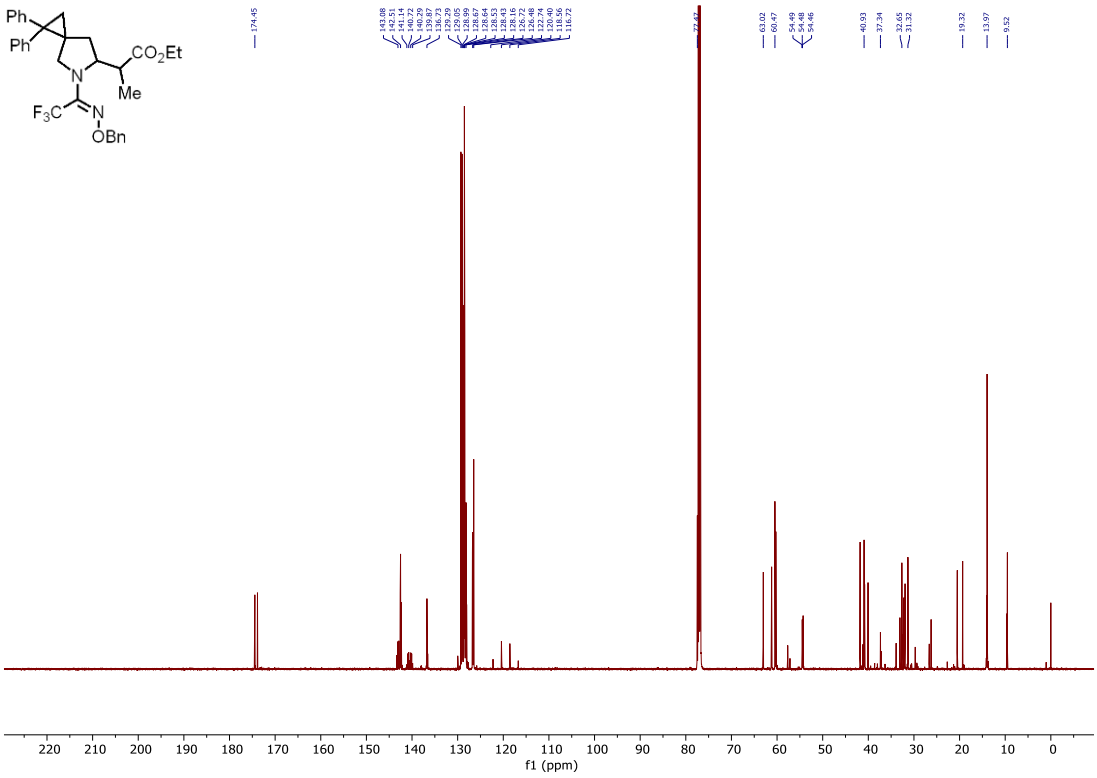


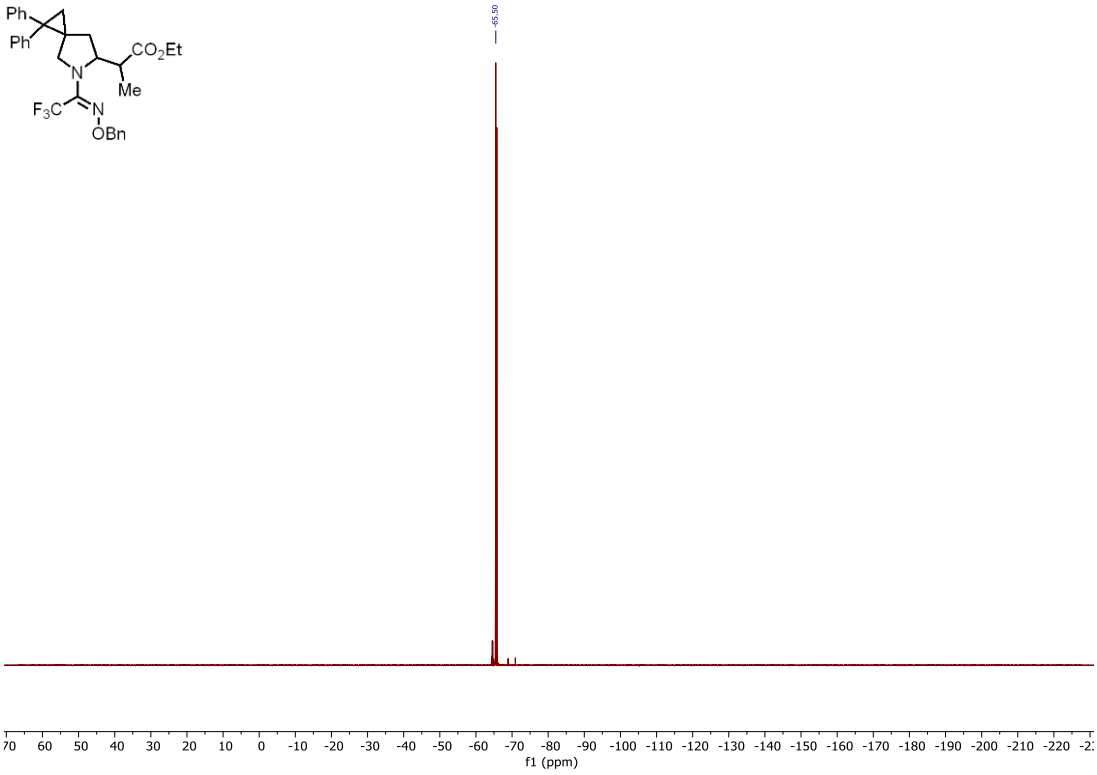

BnO2C
CO2Et
F3C
N
OBn
-64.74
-65.29
0.77
0.23
f1 (ppm)

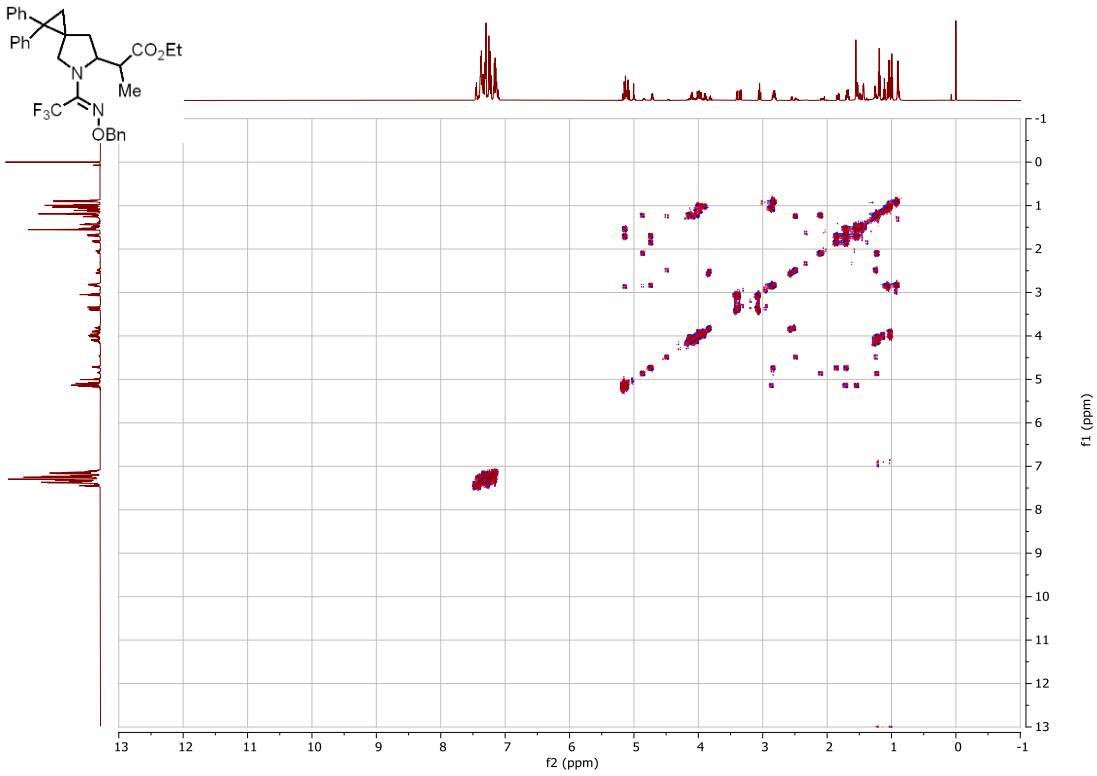

BnO2C
CO2Et
F3C
N
OBn
f2 (ppm)
f1 (ppm)

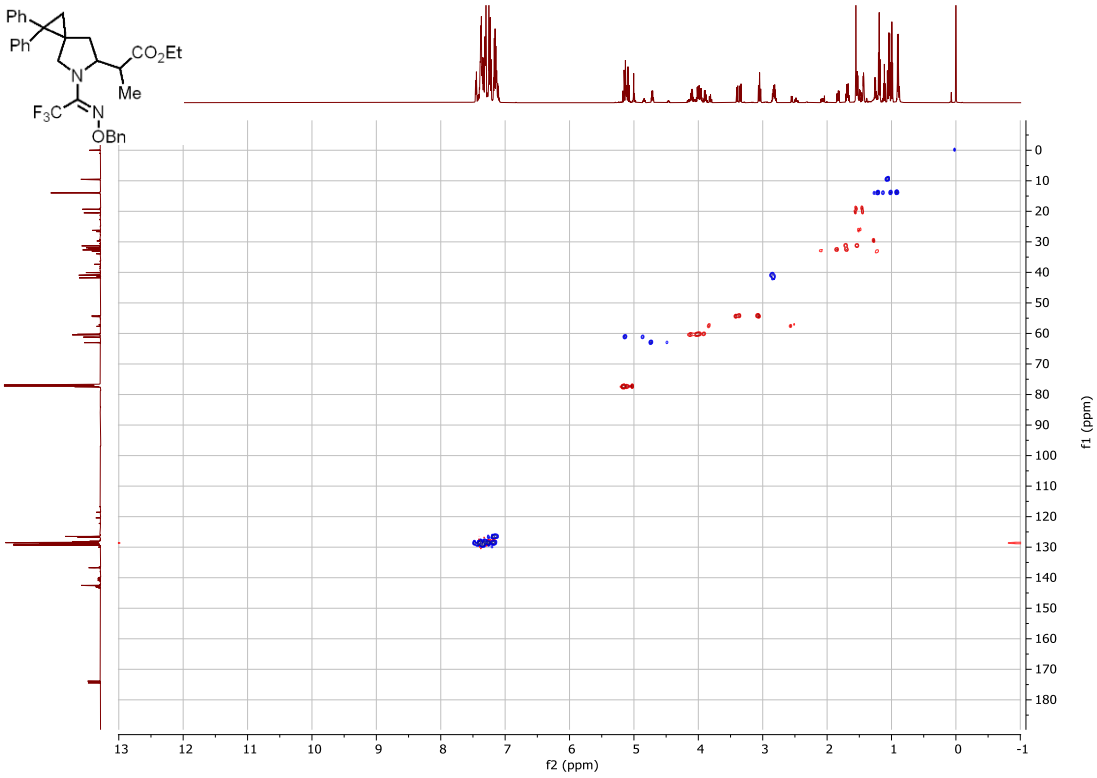
ethyl (*E*)-2-(5-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-1,1-diphenyl-5-azaspiro[2.4]heptan-6-yl)propanoate (2e-B)



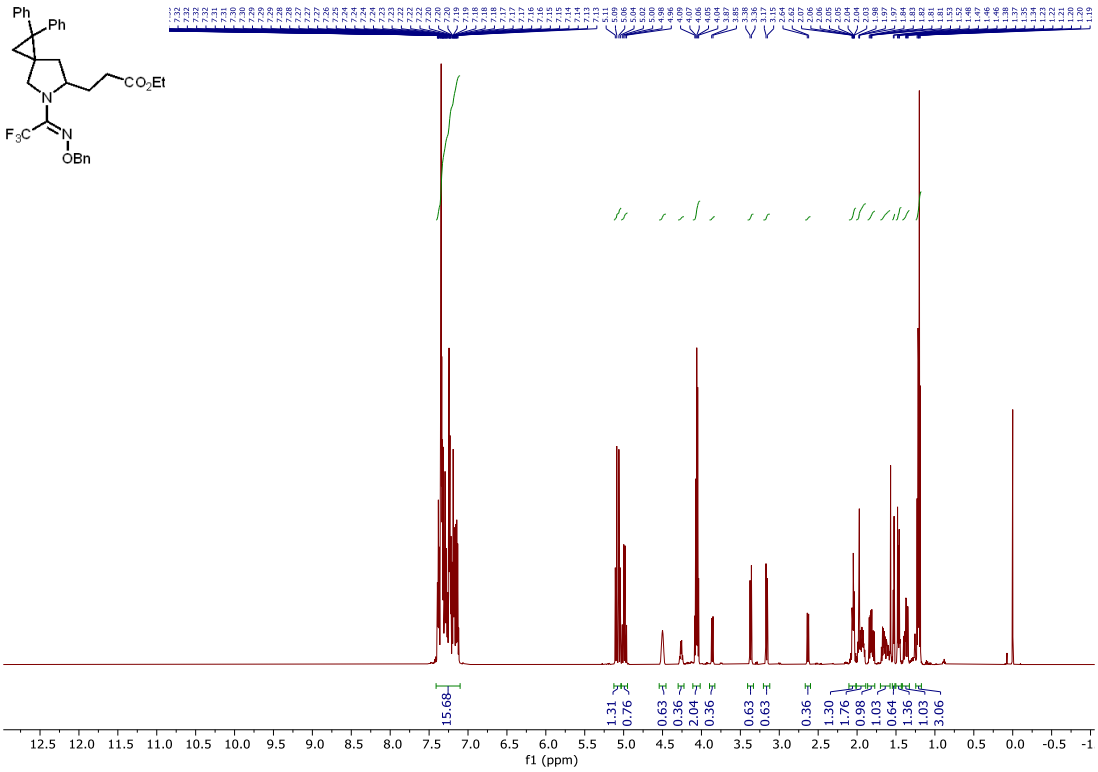


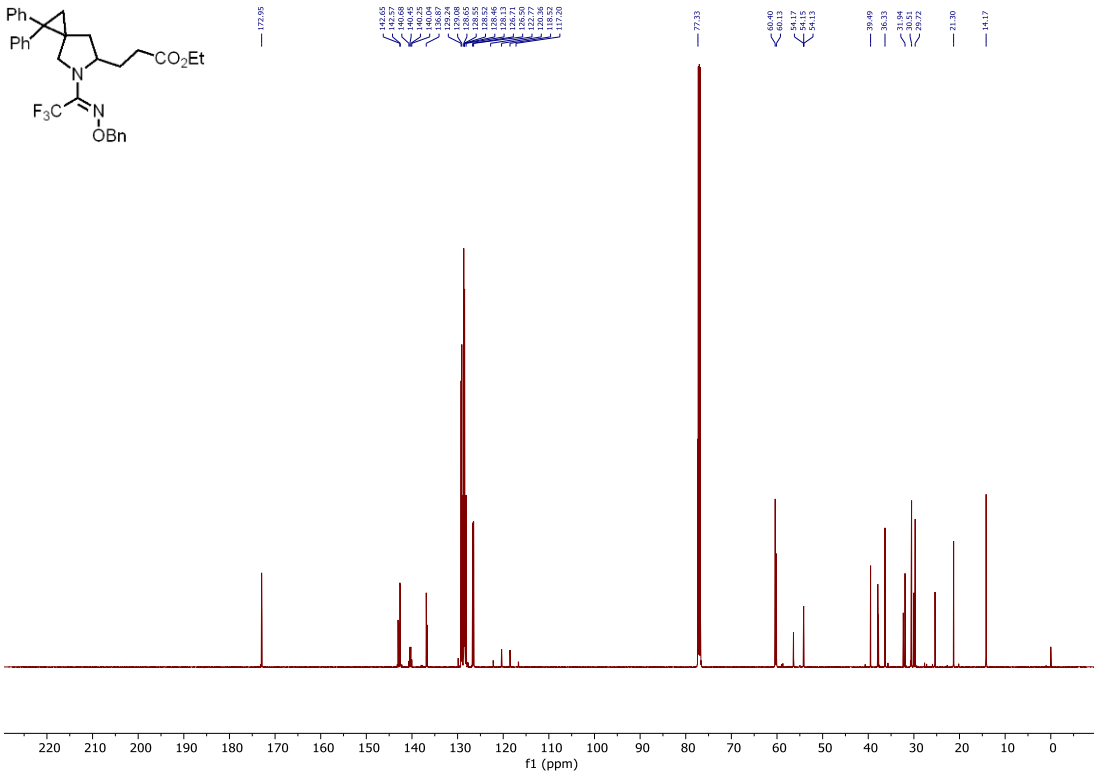

Ph
Ph
CO2Et
Me
F3C
N
N
OBn
-65.50
f1 (ppm)

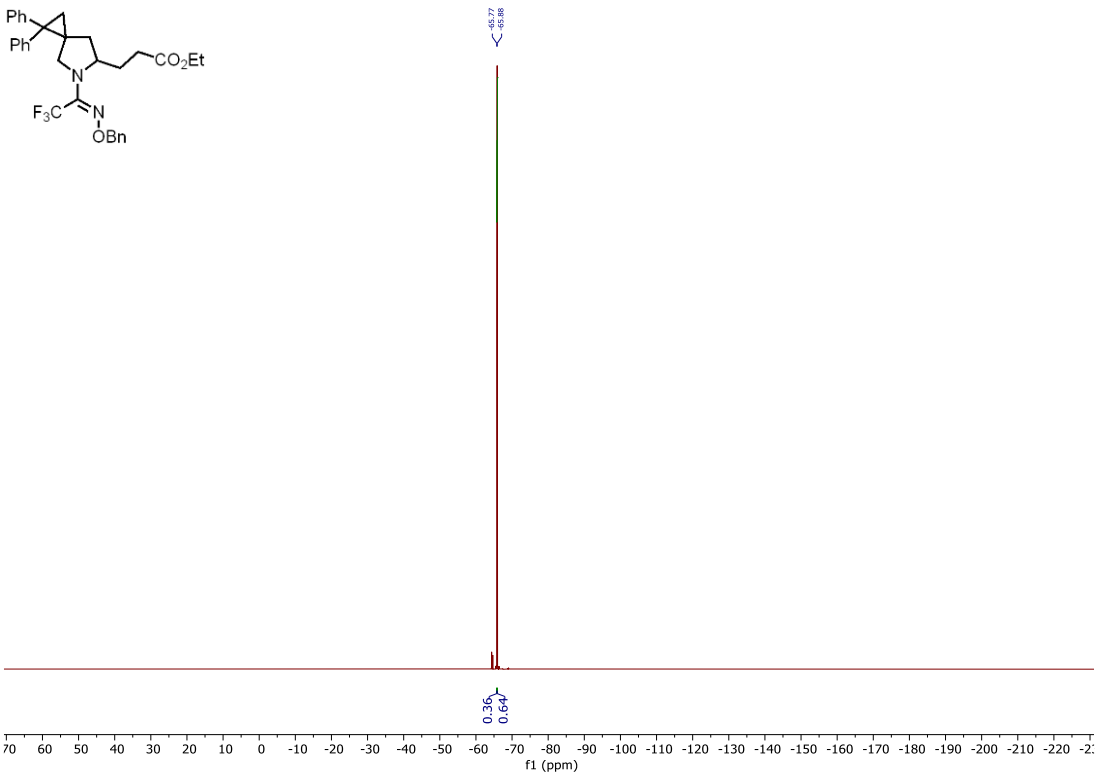

Ph
Ph
CO2Et
Me
F3C
N
N
OBn
f2 (ppm)
f1 (ppm)

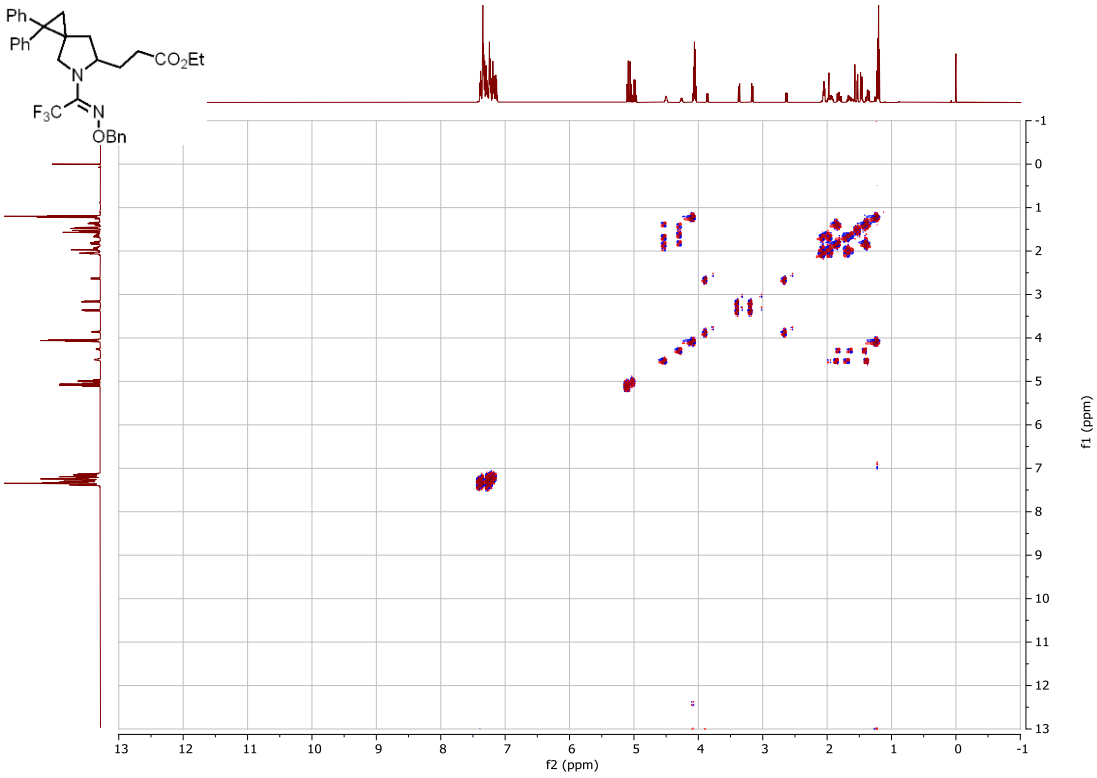

Ph
Ph
CO2Et
Me
F3C
N
N
OBn
f2 (ppm)
f1 (ppm)

ethyl (*E*)-3-(5-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-1,1-diphenyl-5-azaspiro[2.4]heptan-6-yl)propanoate (2e-L)

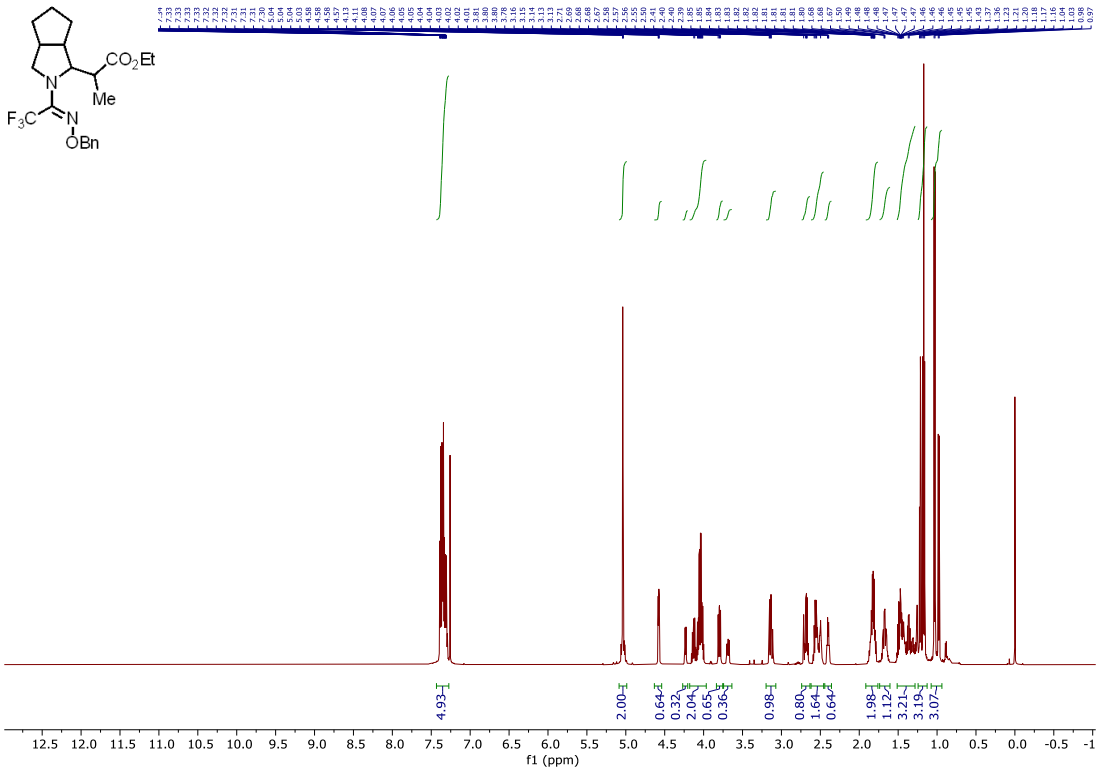


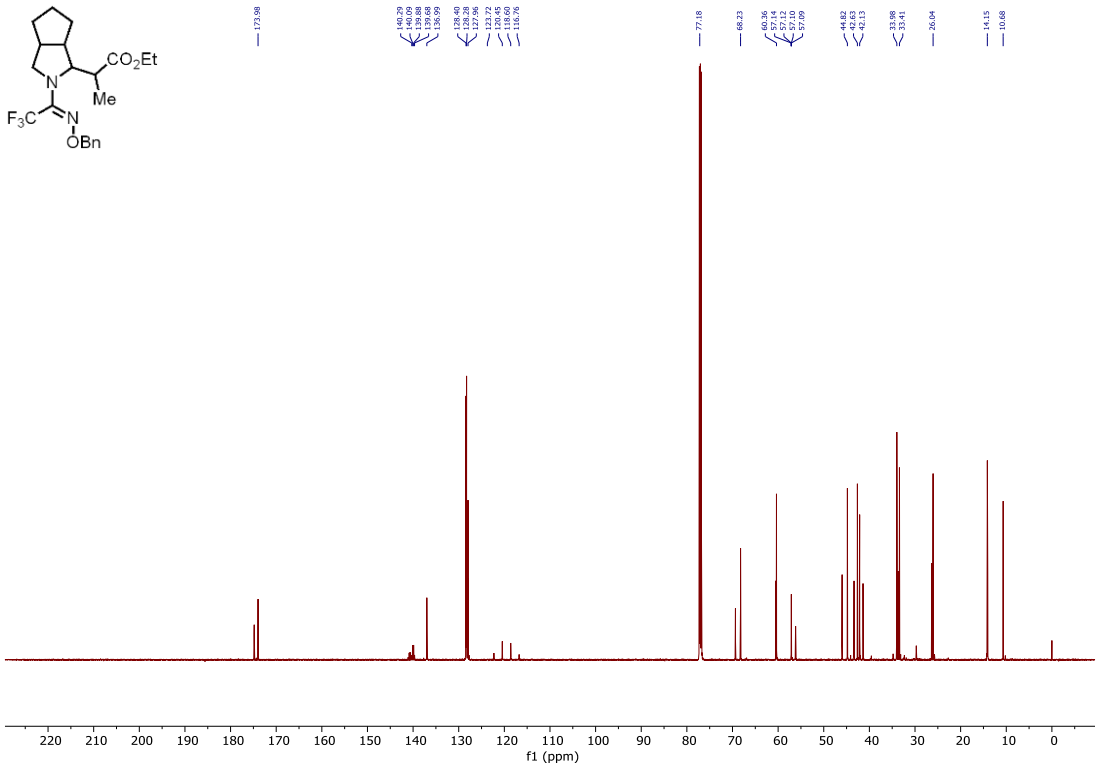


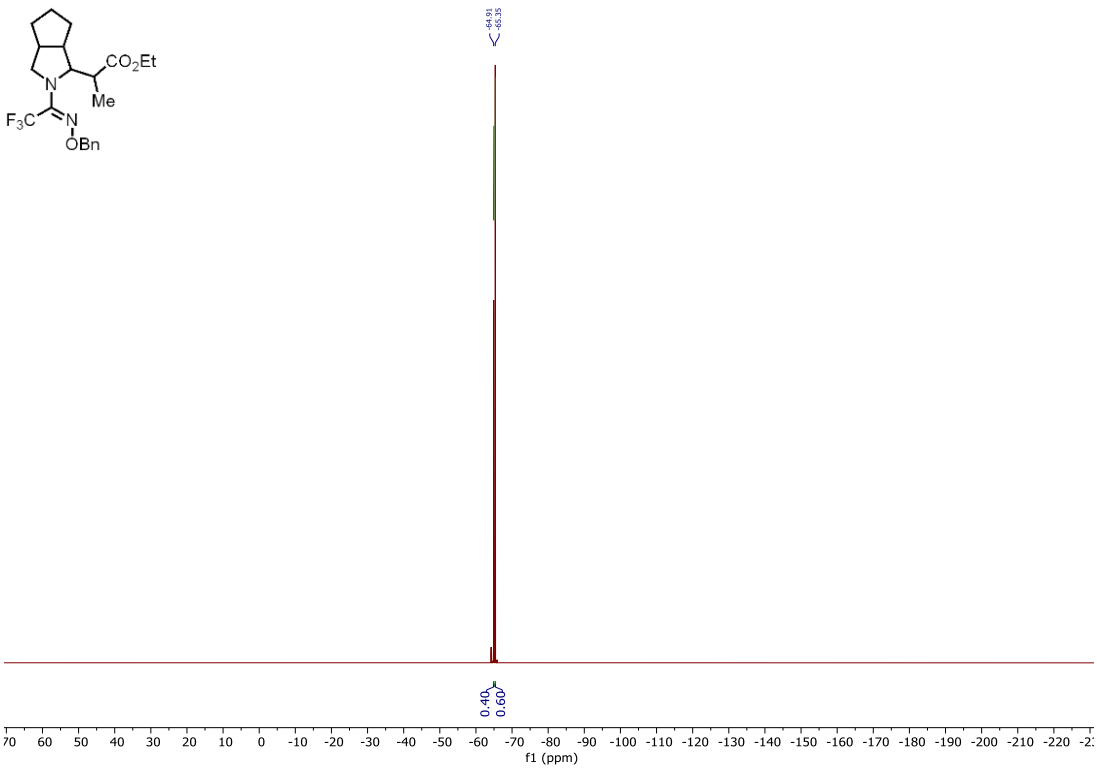

Ph
Ph
CO2Et
N
F3C
N
OBn
-65.77
-65.86
0.36
0.64
f1 (ppm)


Ph
Ph
CO2Et
N
F3C
N
OBn
f2 (ppm)
f1 (ppm)

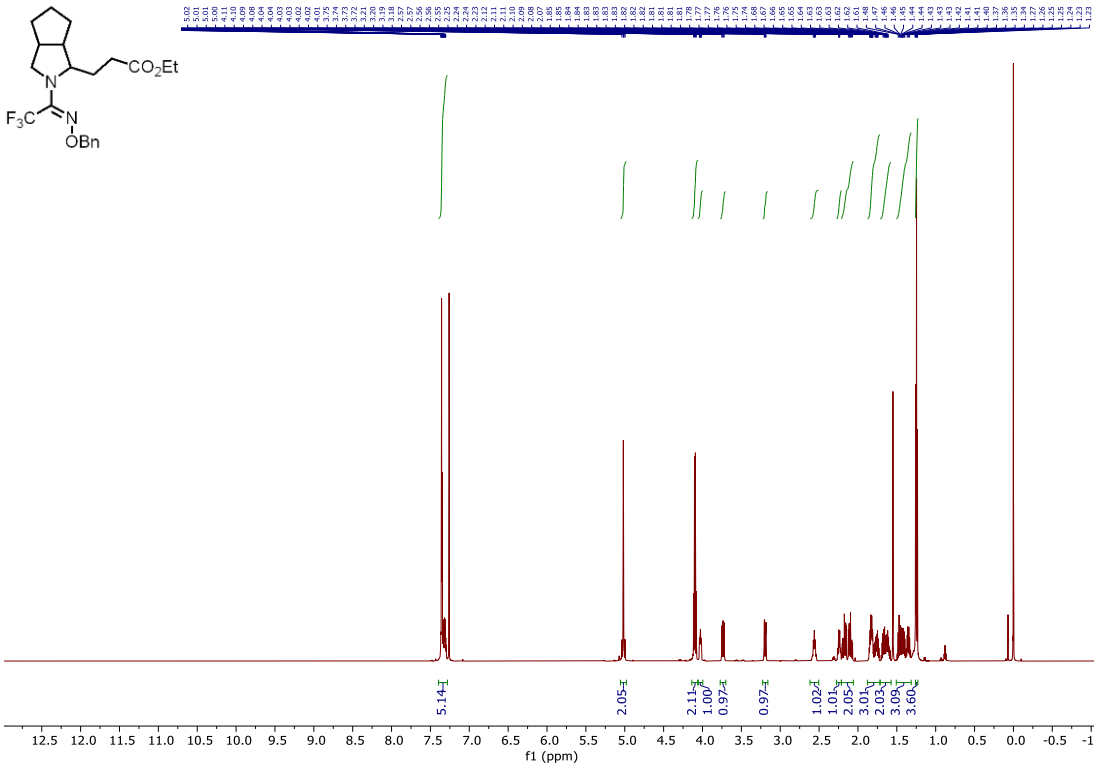
ethyl (*E*)-2-(2-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)octahydrocyclopenta[*c*]pyrrol-1-yl)propanoate (2f-B)

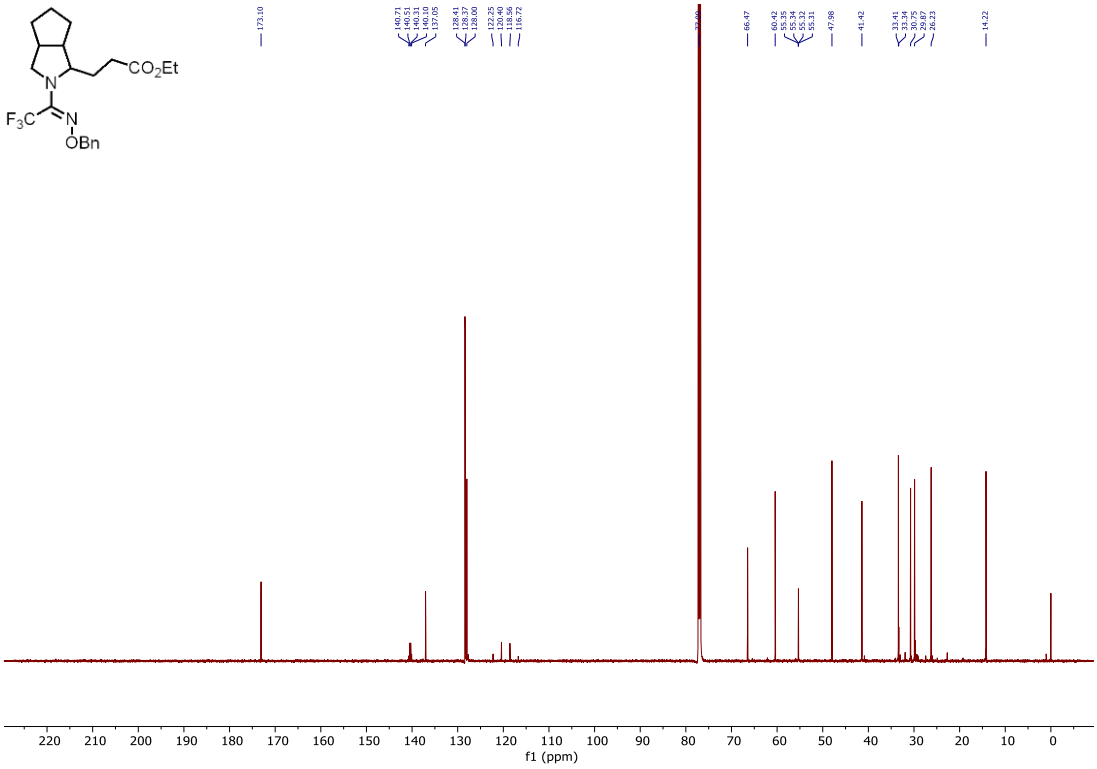


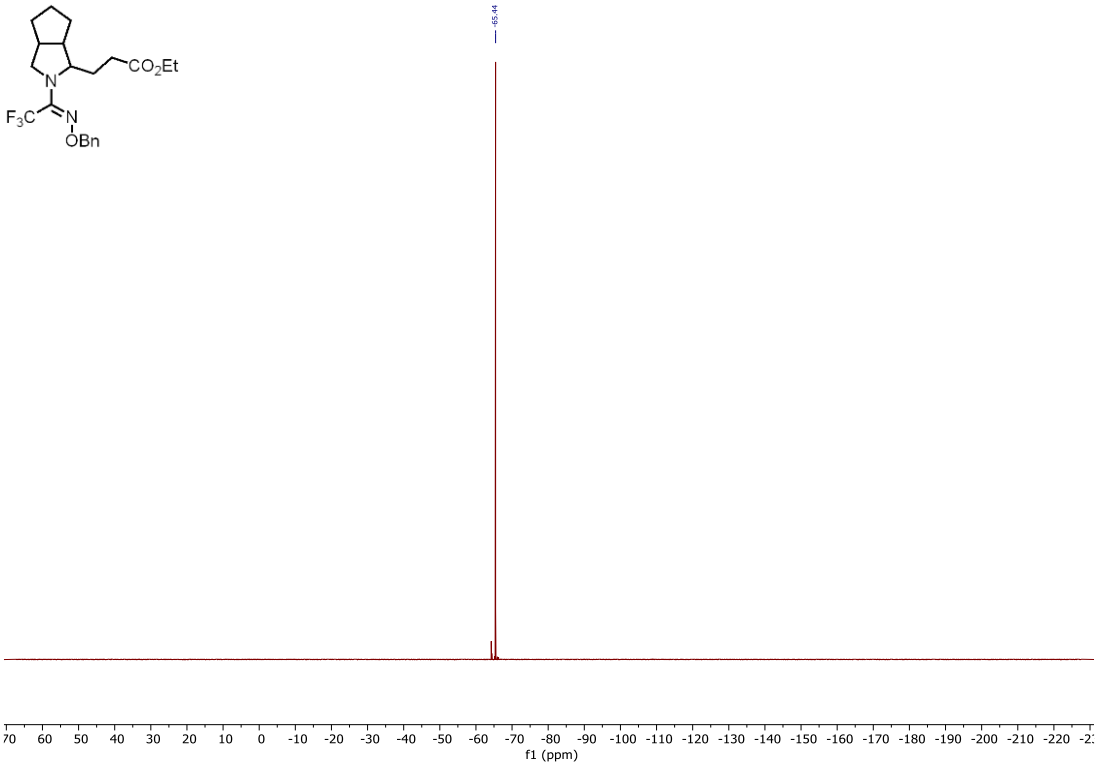



CO2Et
Me
F3C
N
OBn
-64.91
-65.35
0.40
0.60
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

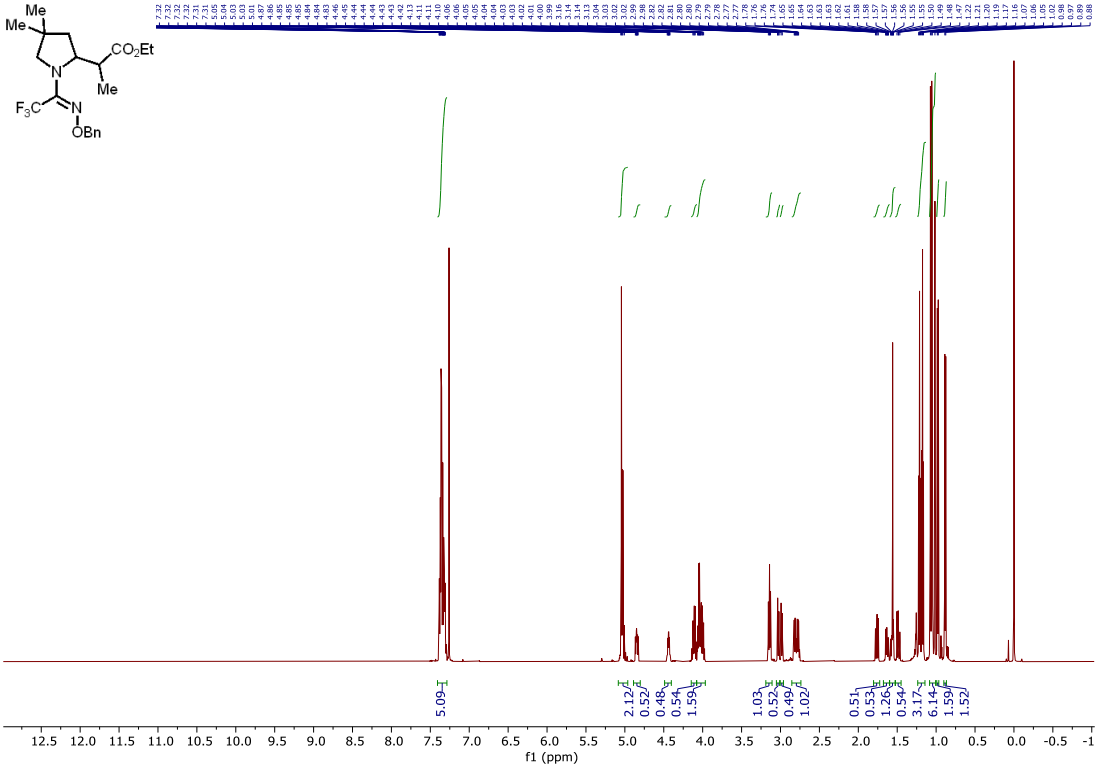
ethyl (*E*)-3-(2-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)octahydrocyclopenta[*c*]pyrrol-1-yl)propanoate (2f-L)

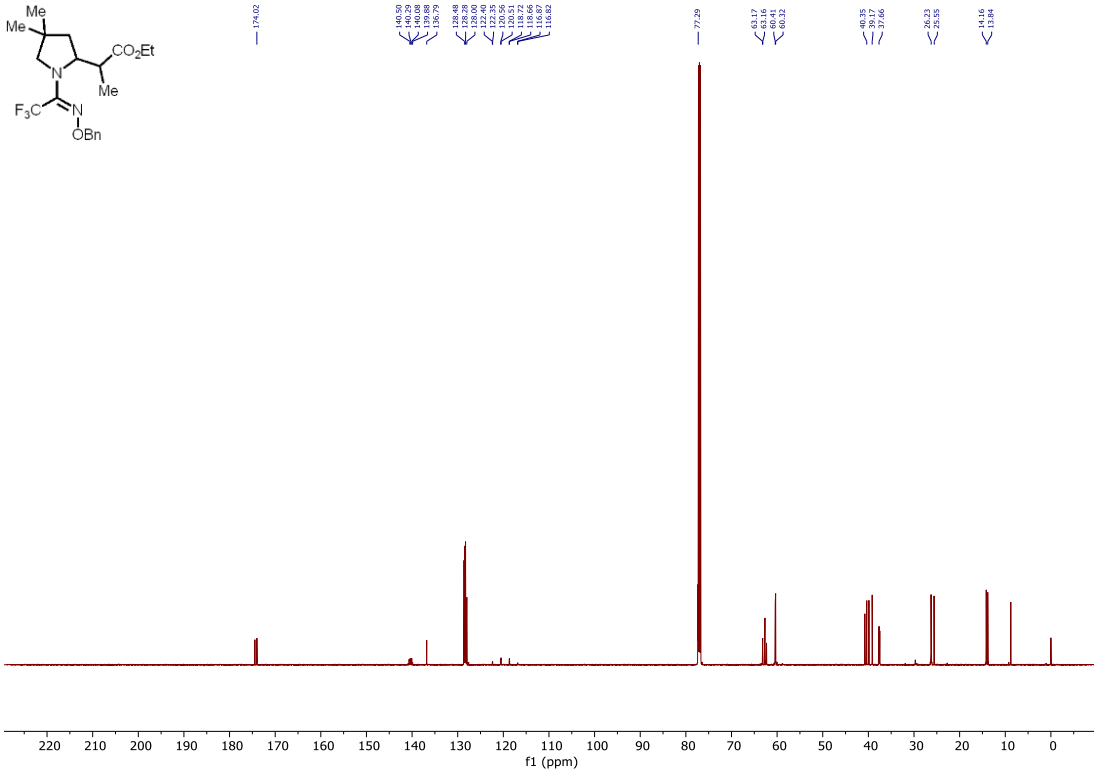


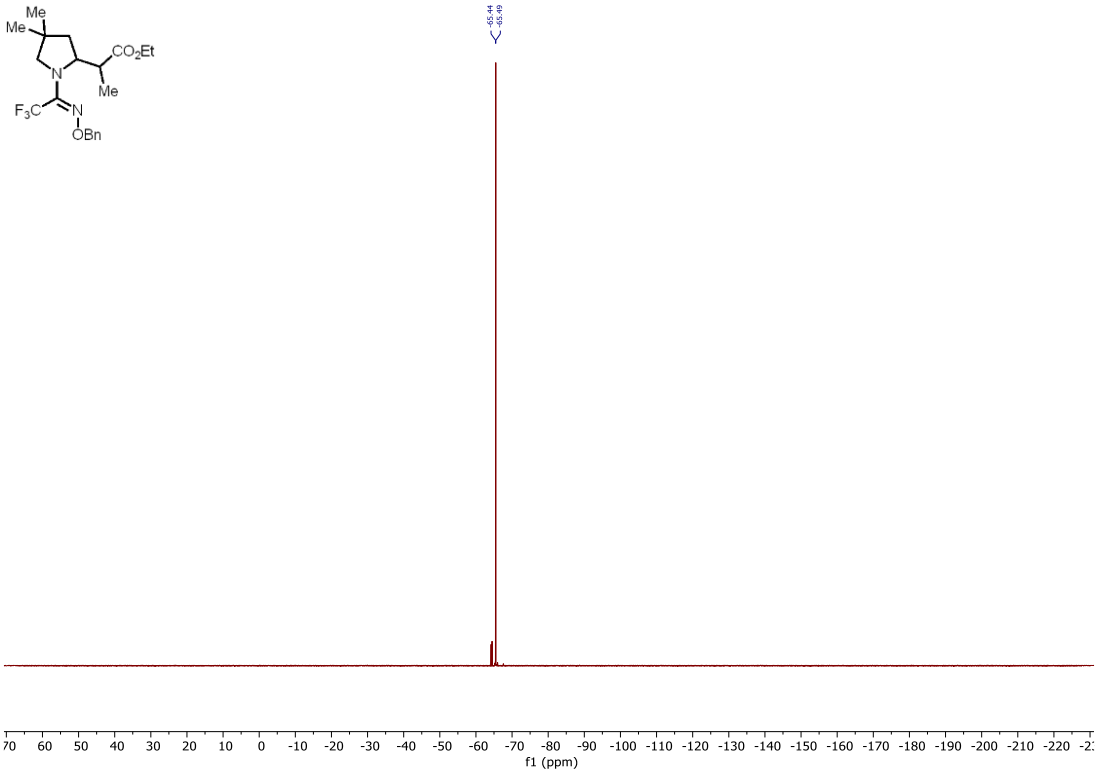


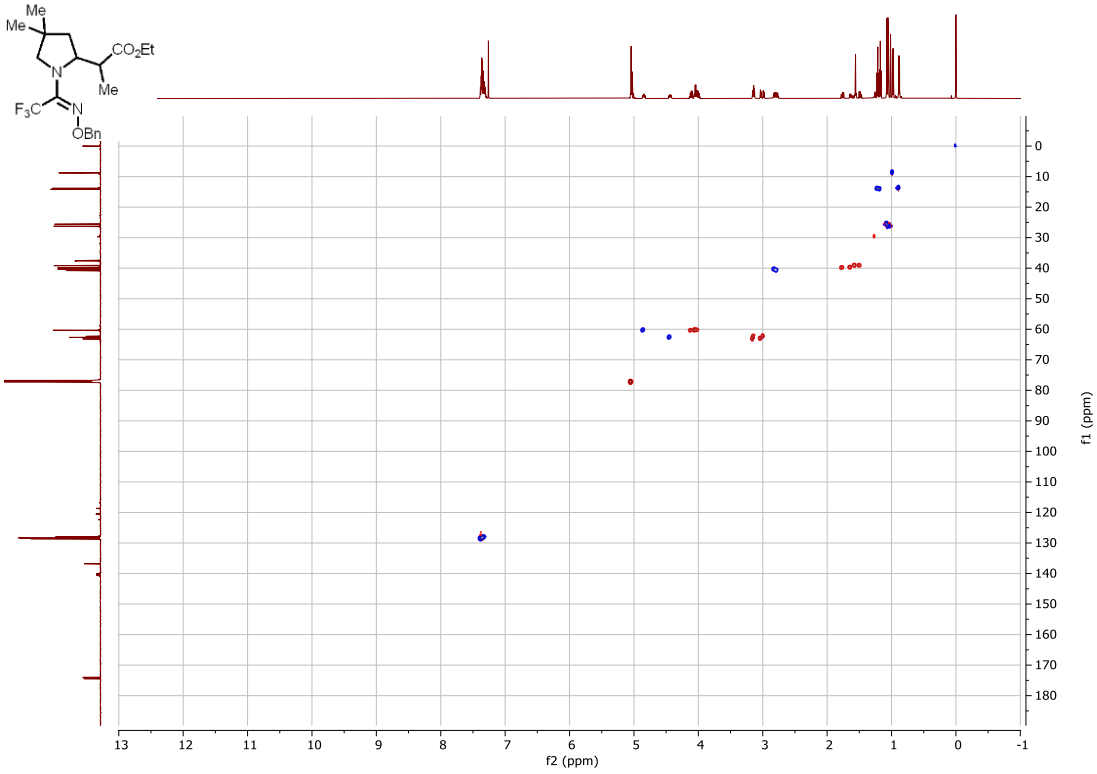

-65.44
CO2Et
N
F3C
N
OBn
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (2g-B)

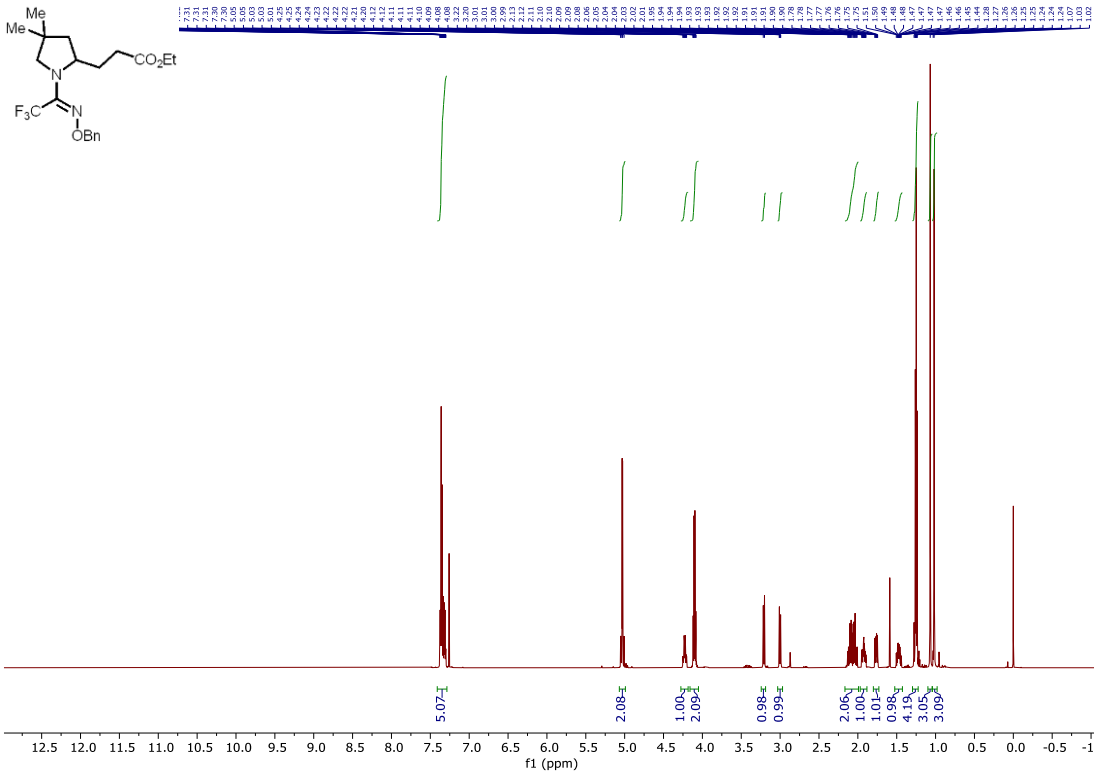


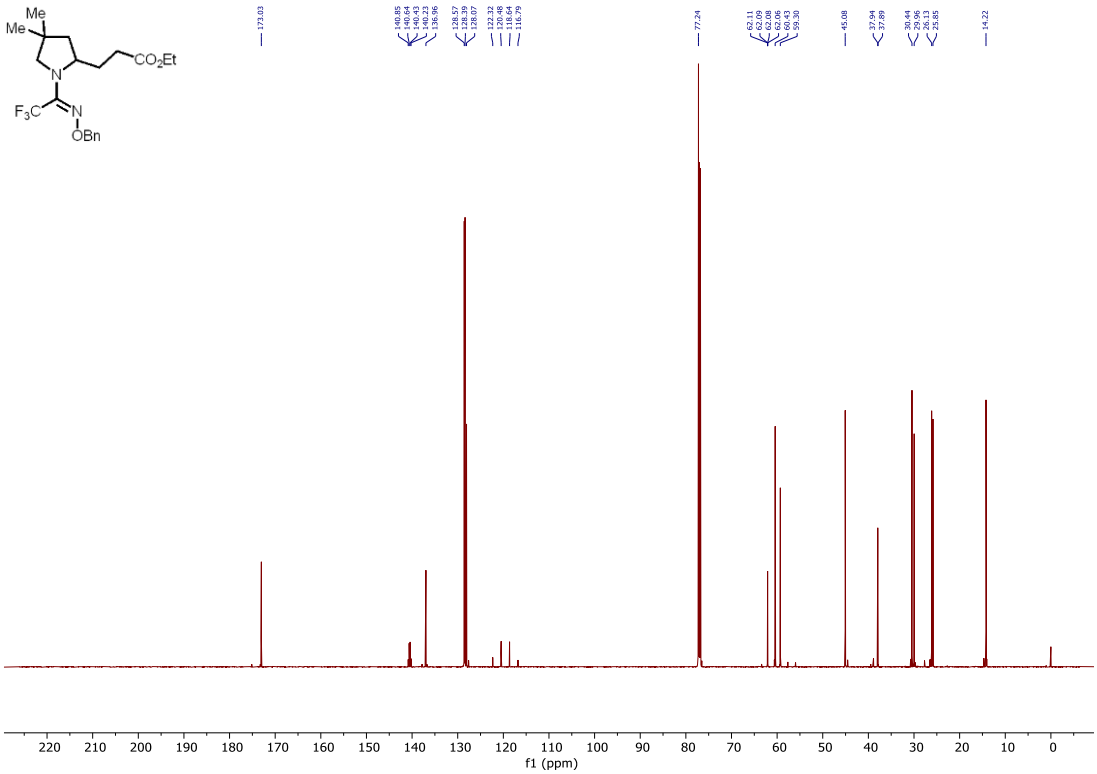


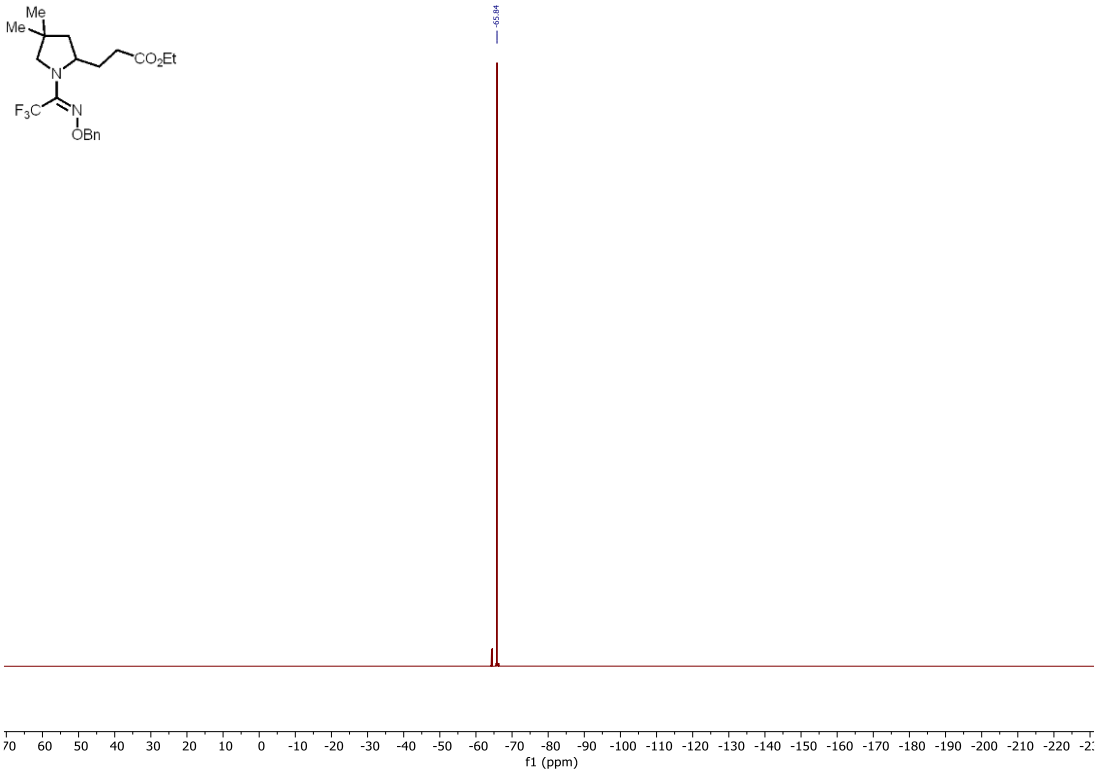

Me
Me
CO2Et
N
Me
F3C
N
OBn
-65.44
-65.49
f1 (ppm)

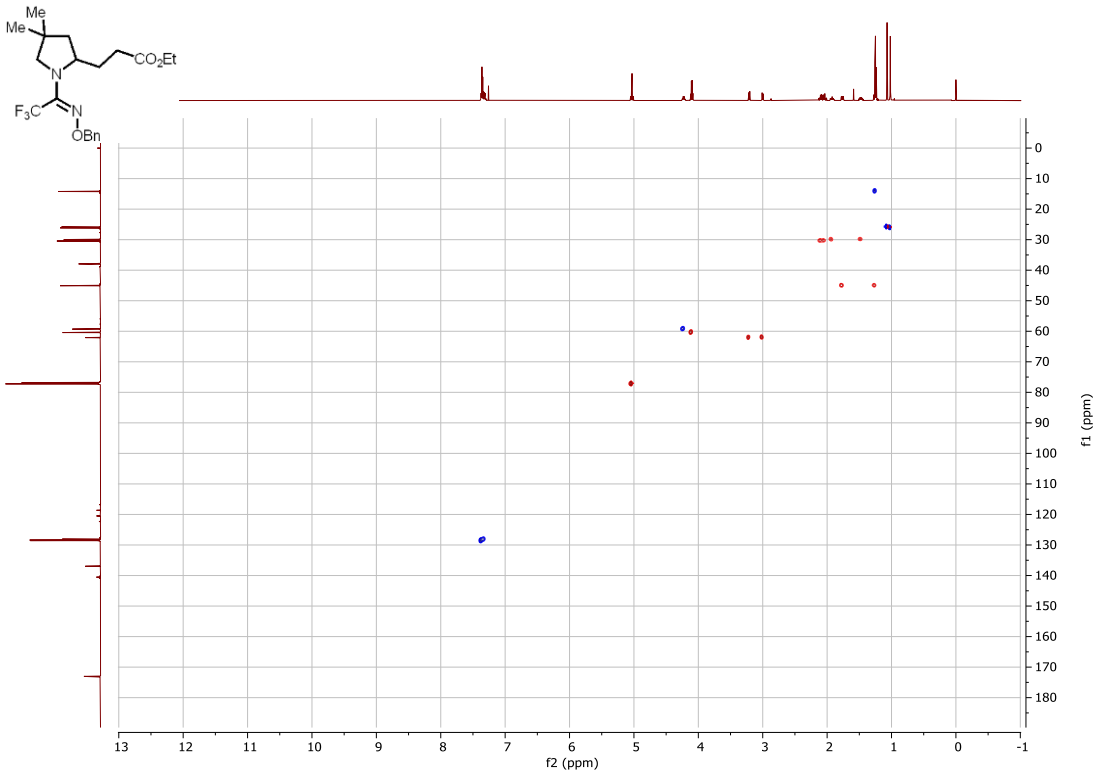

Me
Me
CO2Et
N
Me
F3C
N
OBn
f2 (ppm)
f1 (ppm)

ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (2g-L)

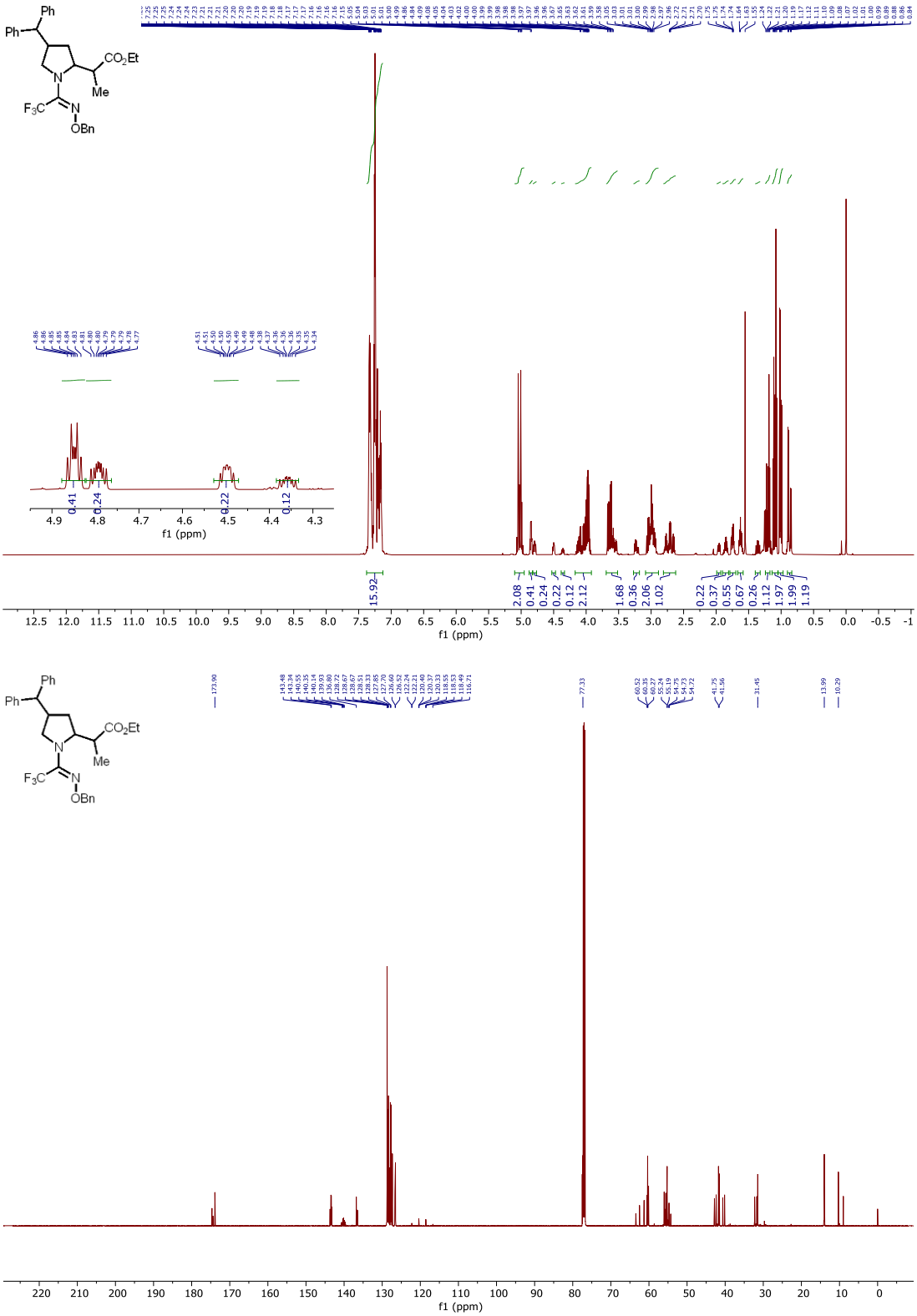


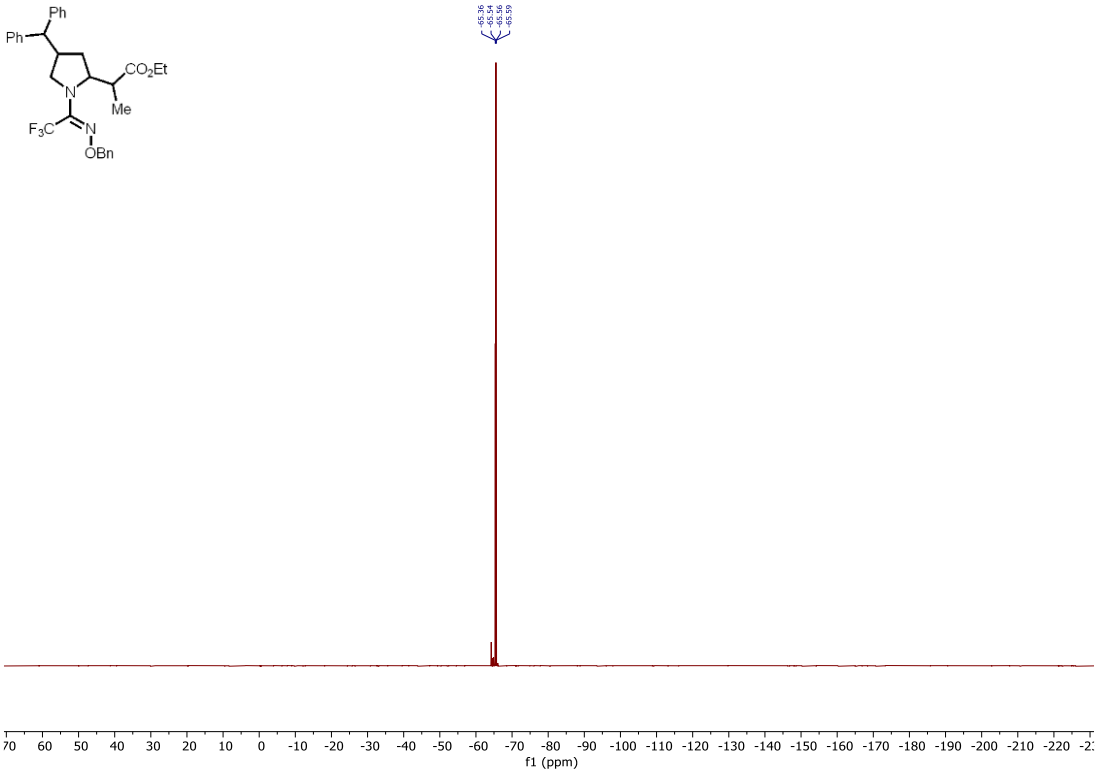


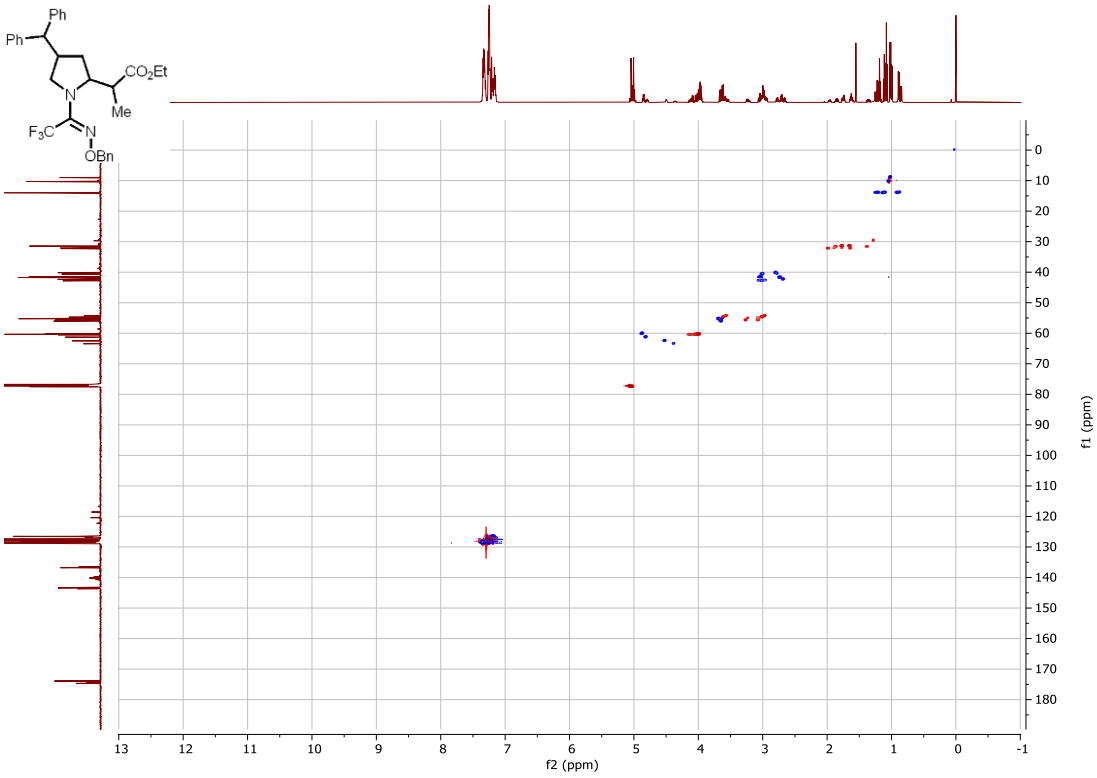

Me
Me
CO2Et
N
F3C
N
OBn
-65.84
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)


Me
Me
CO2Et
N
F3C
N
OBn
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
f1 (ppm)

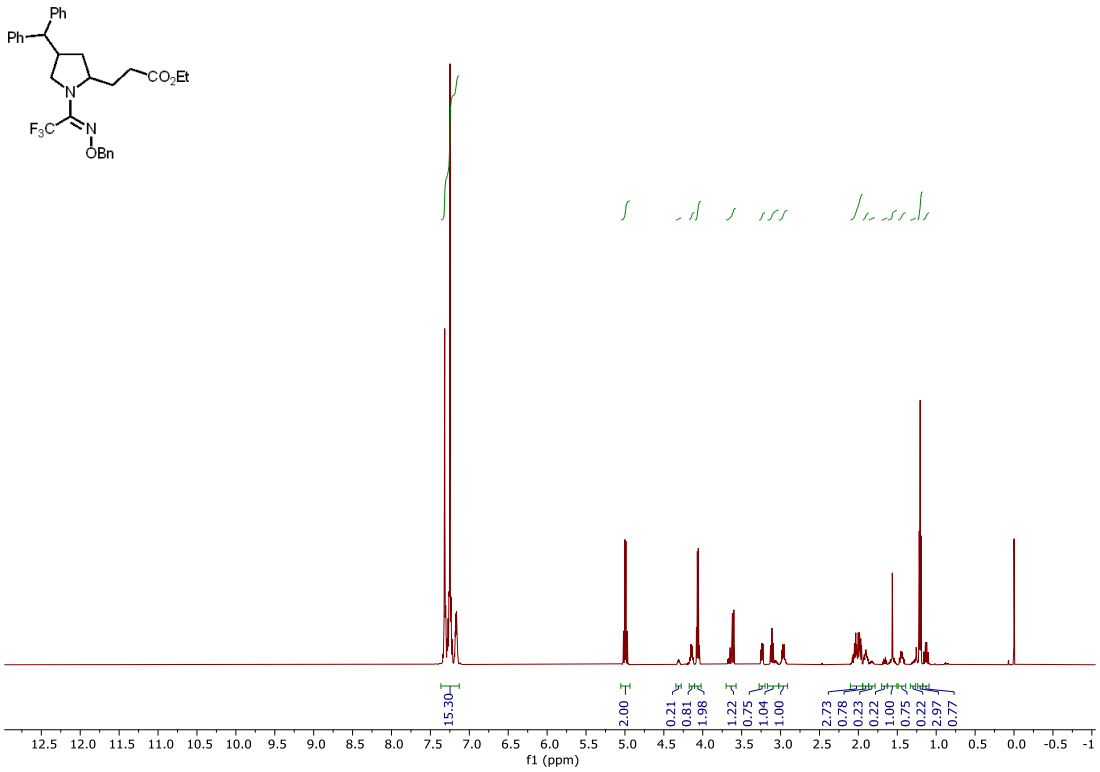
ethyl (*E*)-2-(4-benzhydryl-1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (2h-B)

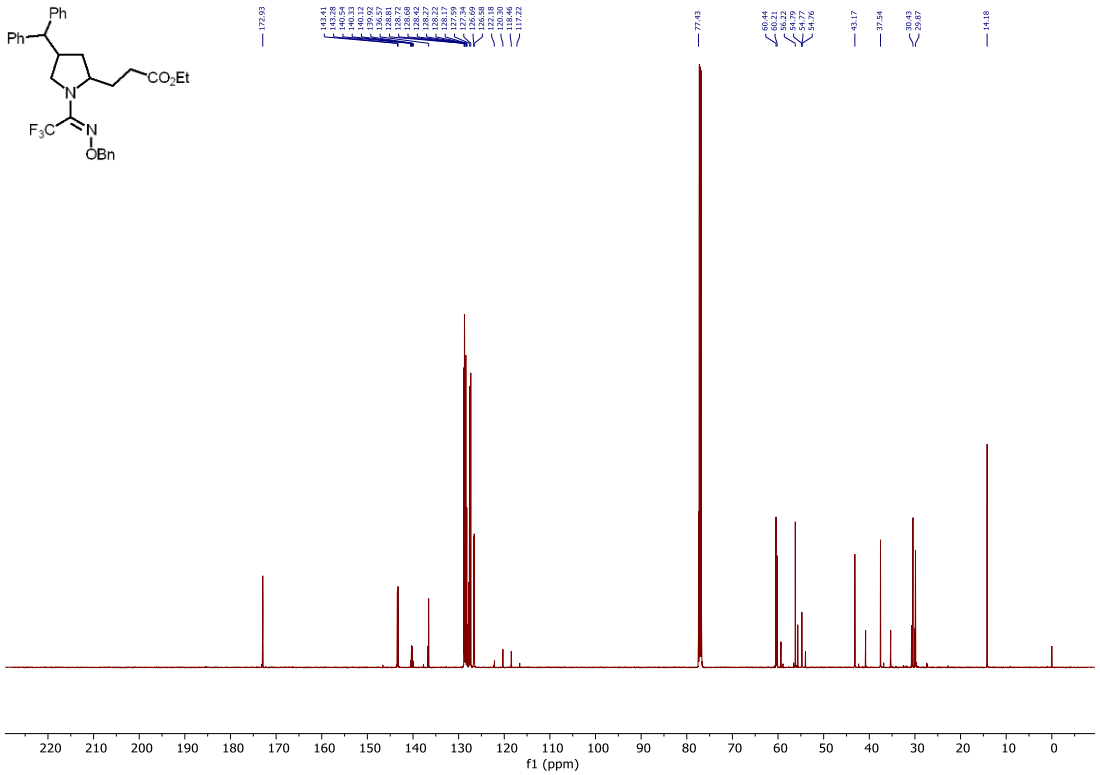


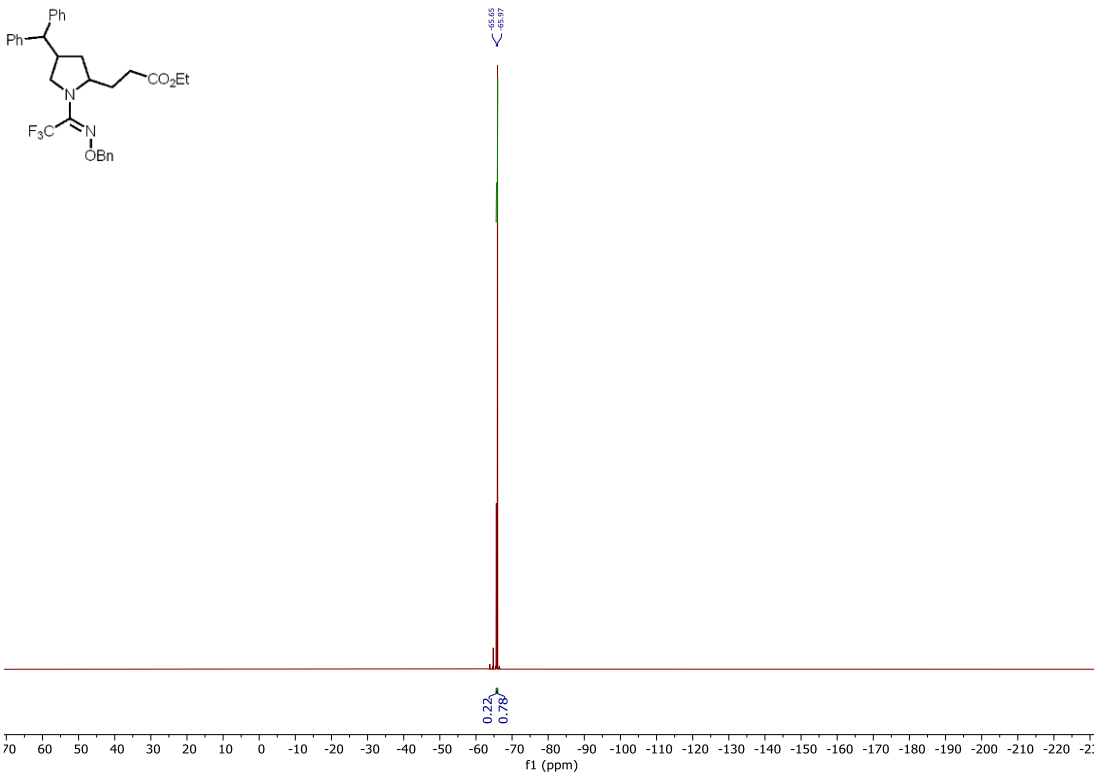

Ph
Ph
CO2Et
N
Me
F3C
N
OBn
-65.36
-65.44
-65.54
-65.58
-65.59
f1 (ppm)


Ph
Ph
CO2Et
N
Me
F3C
N
OBn
f2 (ppm)
f1 (ppm)

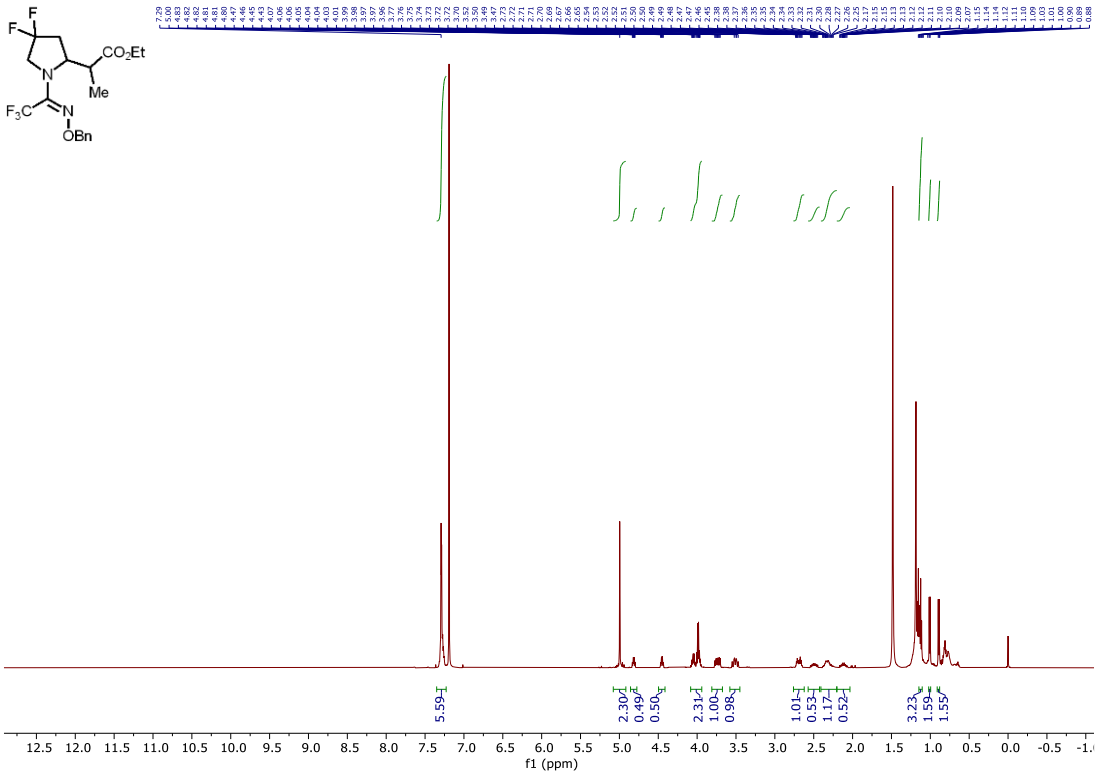
ethyl (*E*)-3-(4-benzhydryl-1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (2h-L)

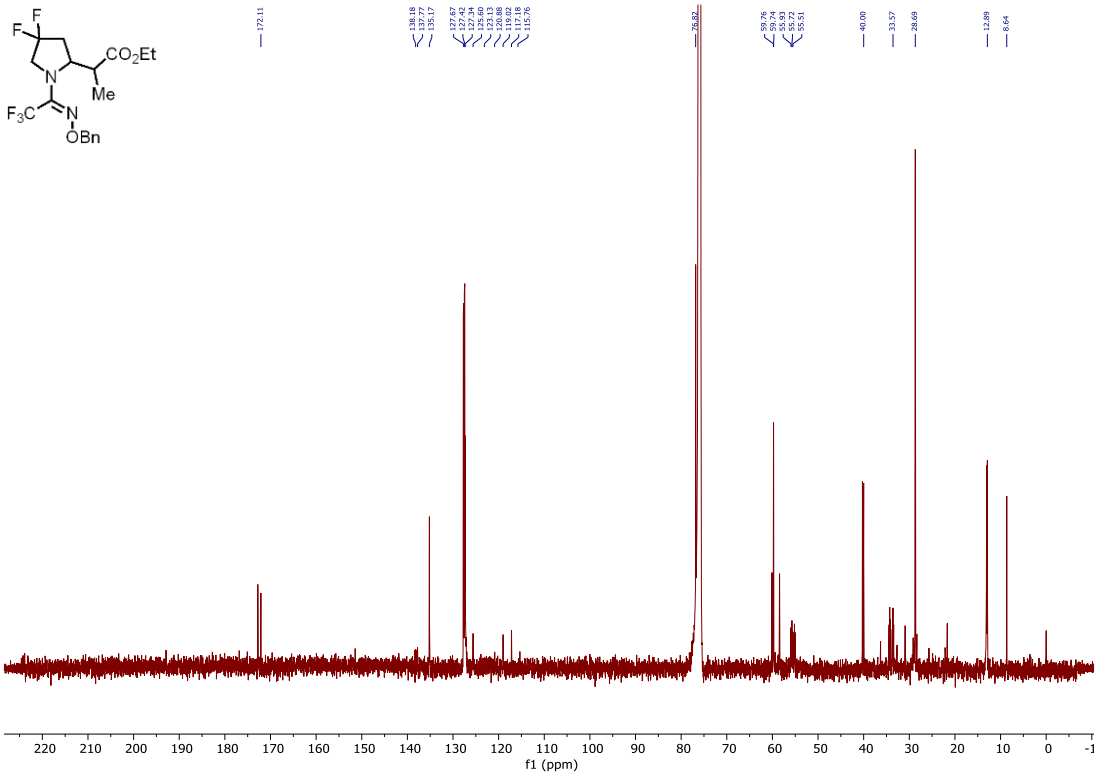


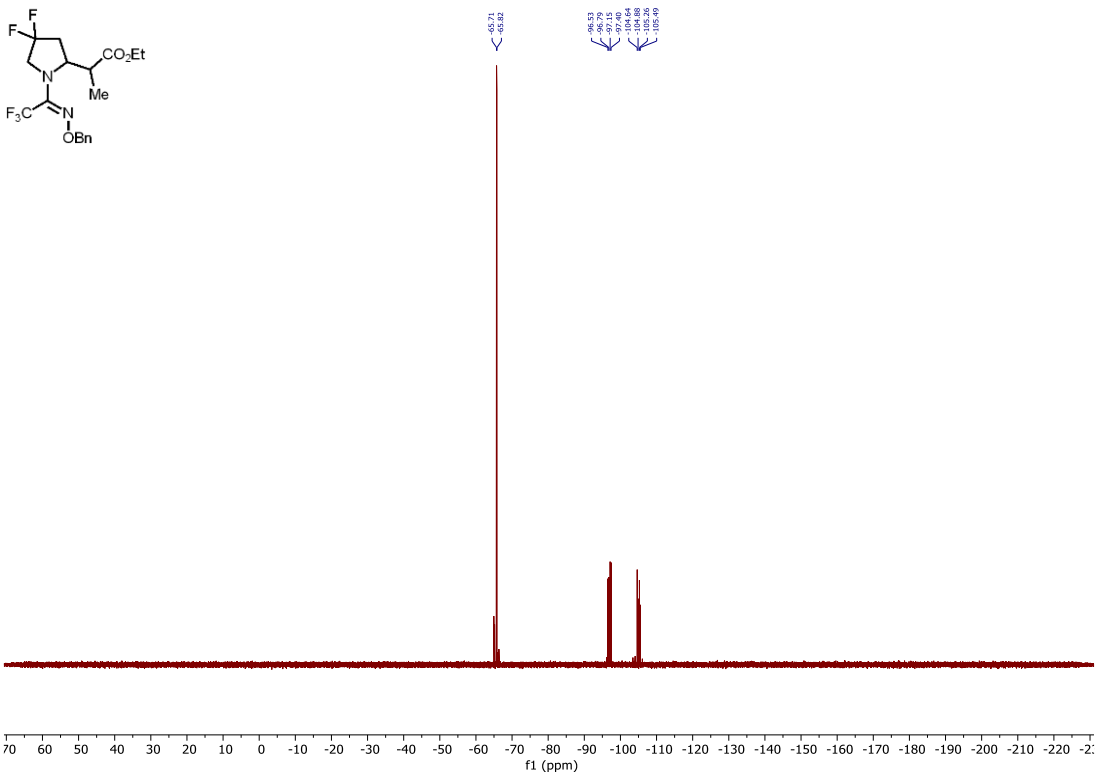



Ph
Ph
CO2Et
N
F3C
N
OBn
-65.65
-65.97
0.22
0.78
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

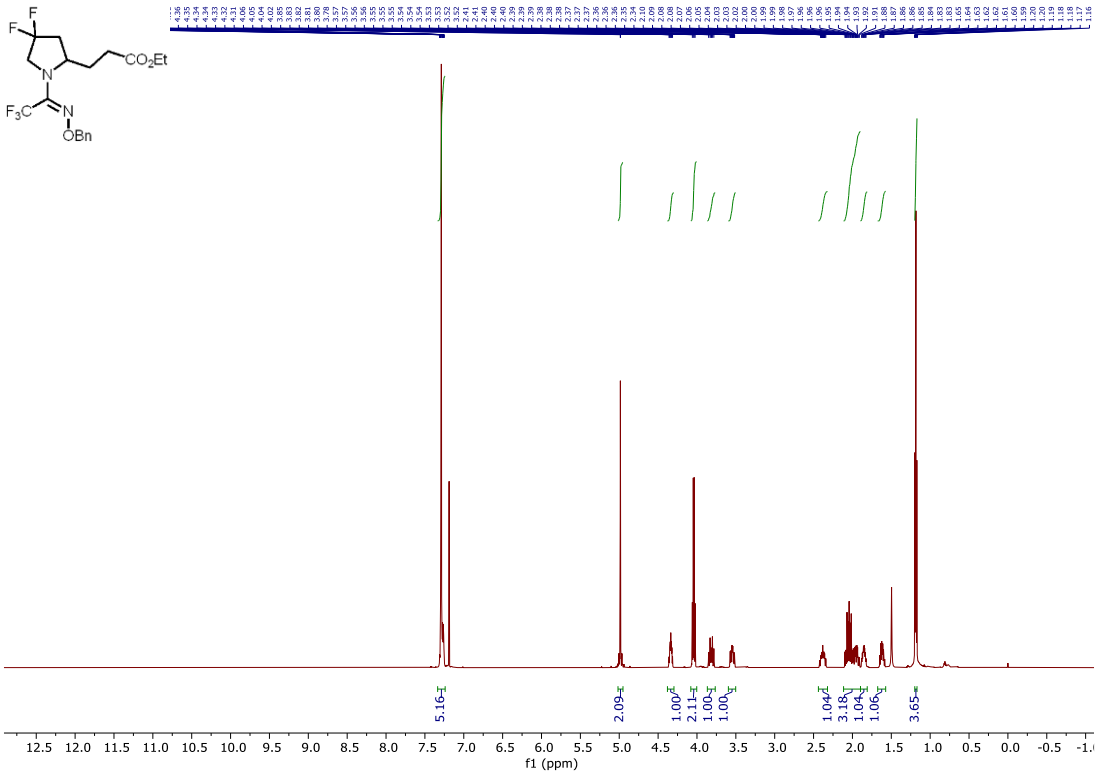
ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-difluoropyrrolidin-2-yl)propanoate (2i-B)

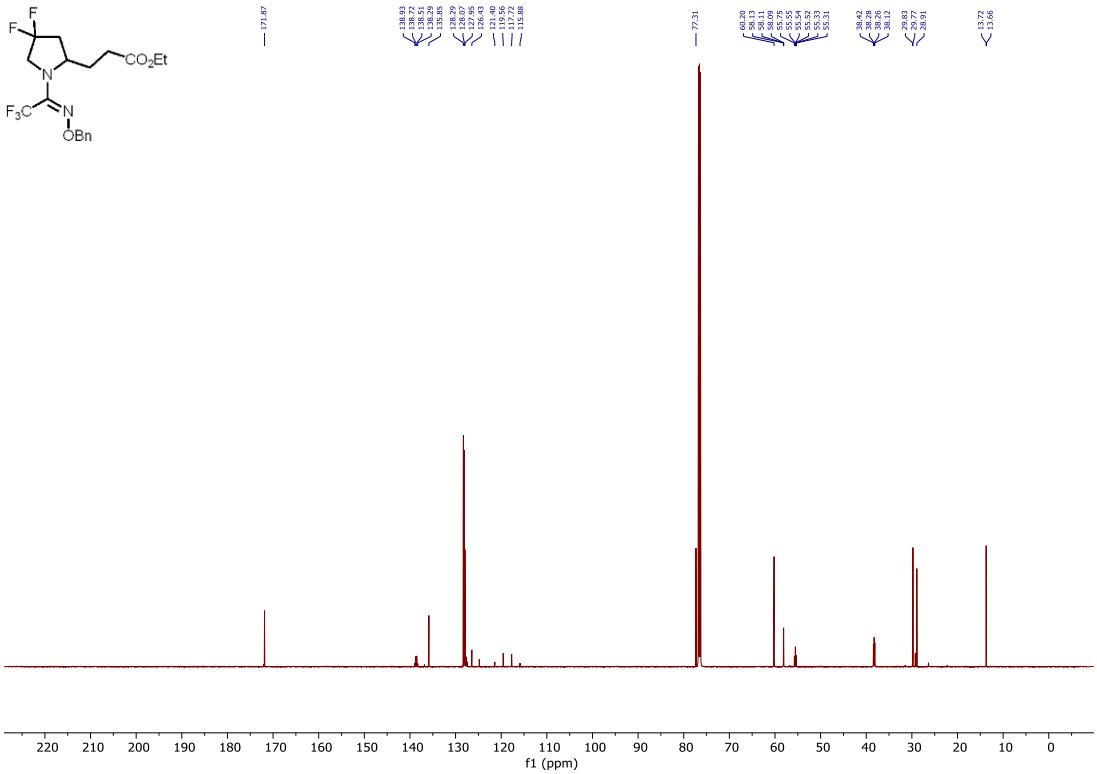


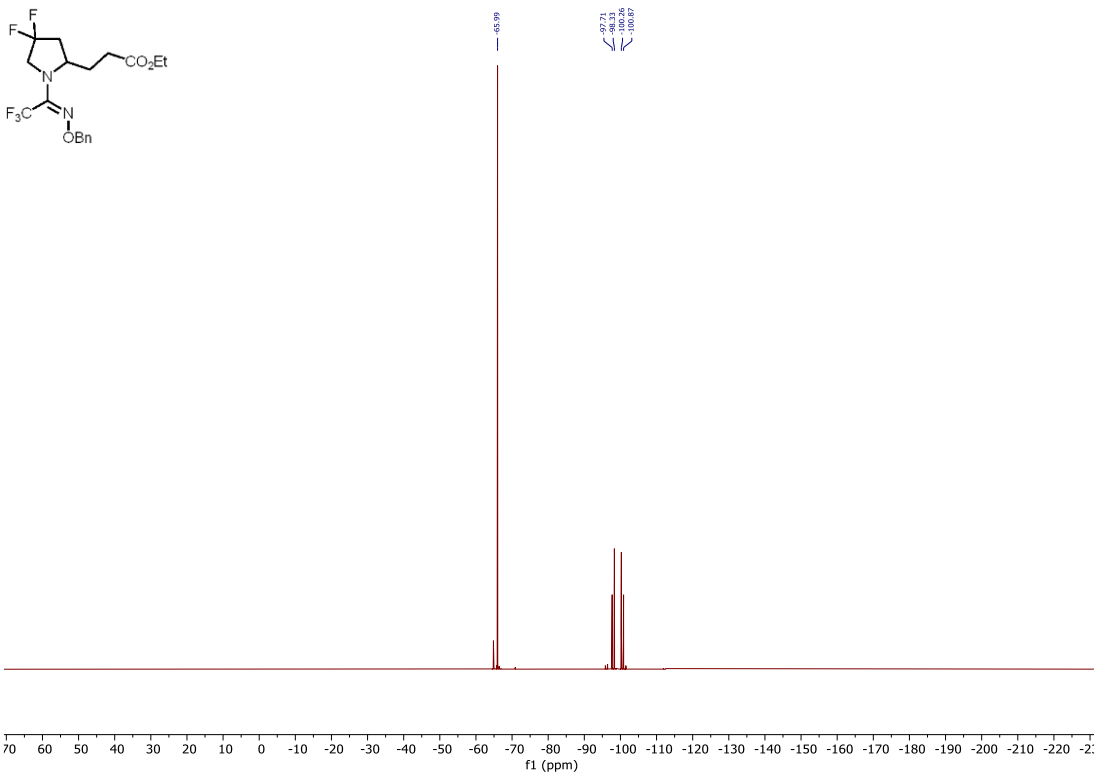



F
F
CO2Et
N
Me
F3C
N
OBn
-65.71
-65.82
-96.53
-96.79
-97.15
-97.40
-104.64
-104.88
-105.26
-105.49
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

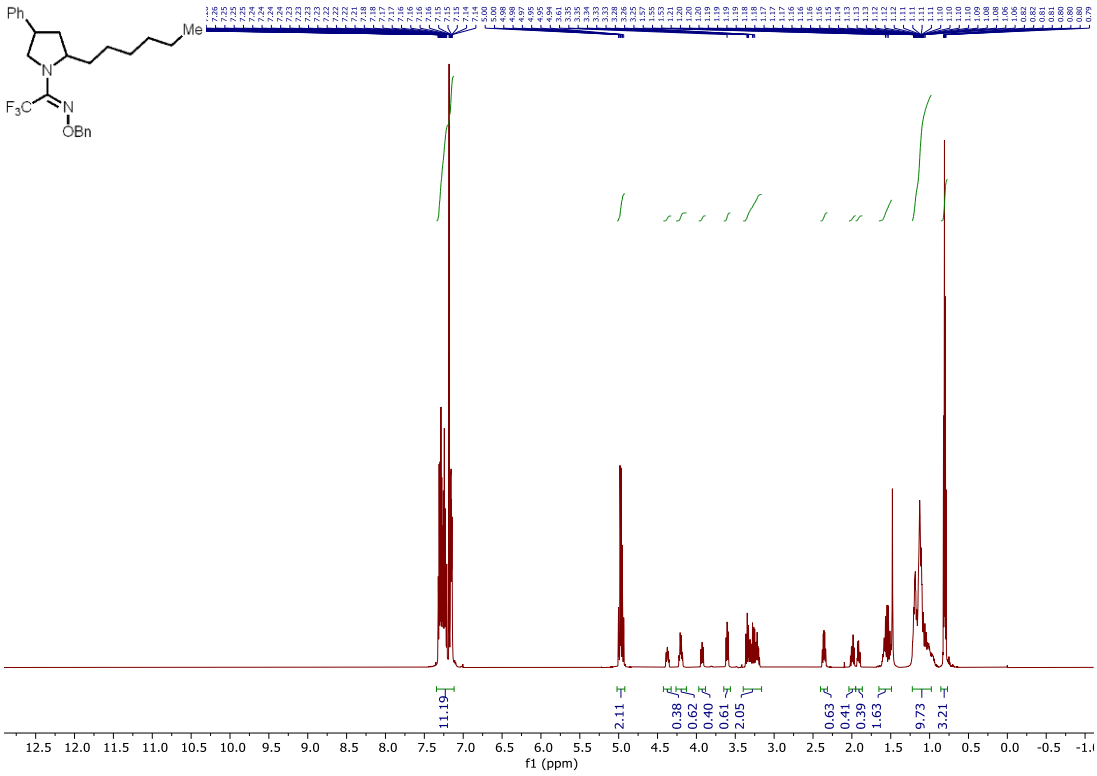
ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-difluoropyrrolidin-2-yl)propanoate (2i-L)

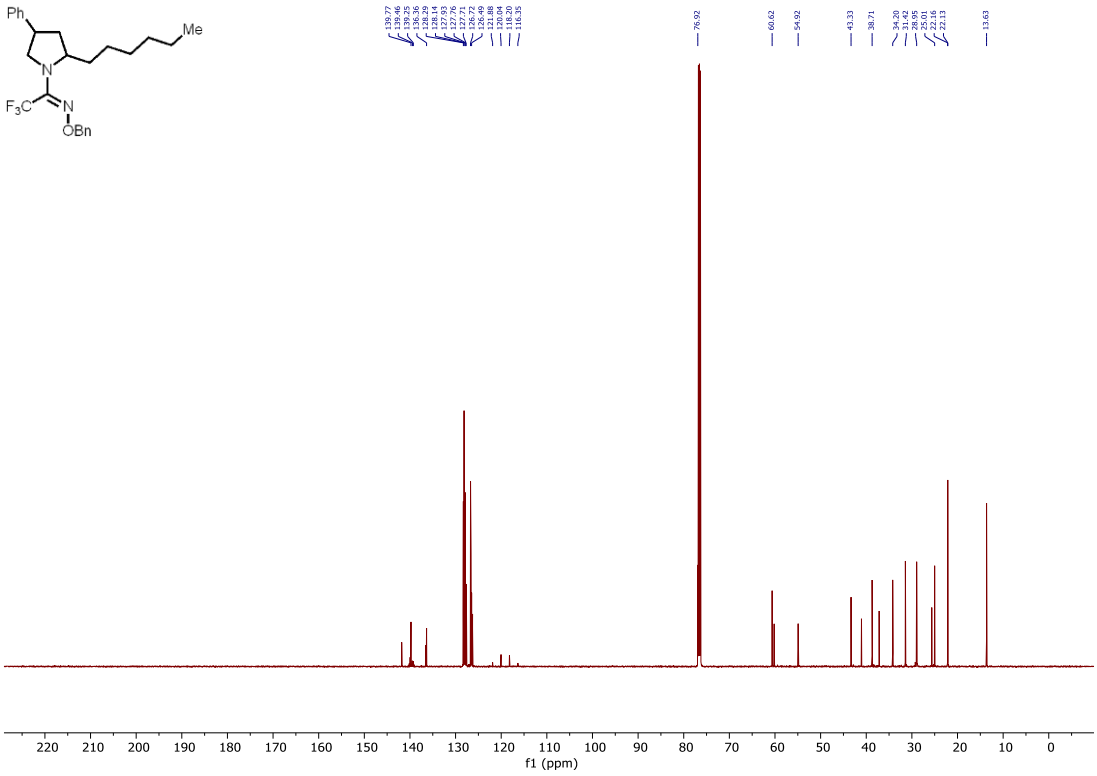


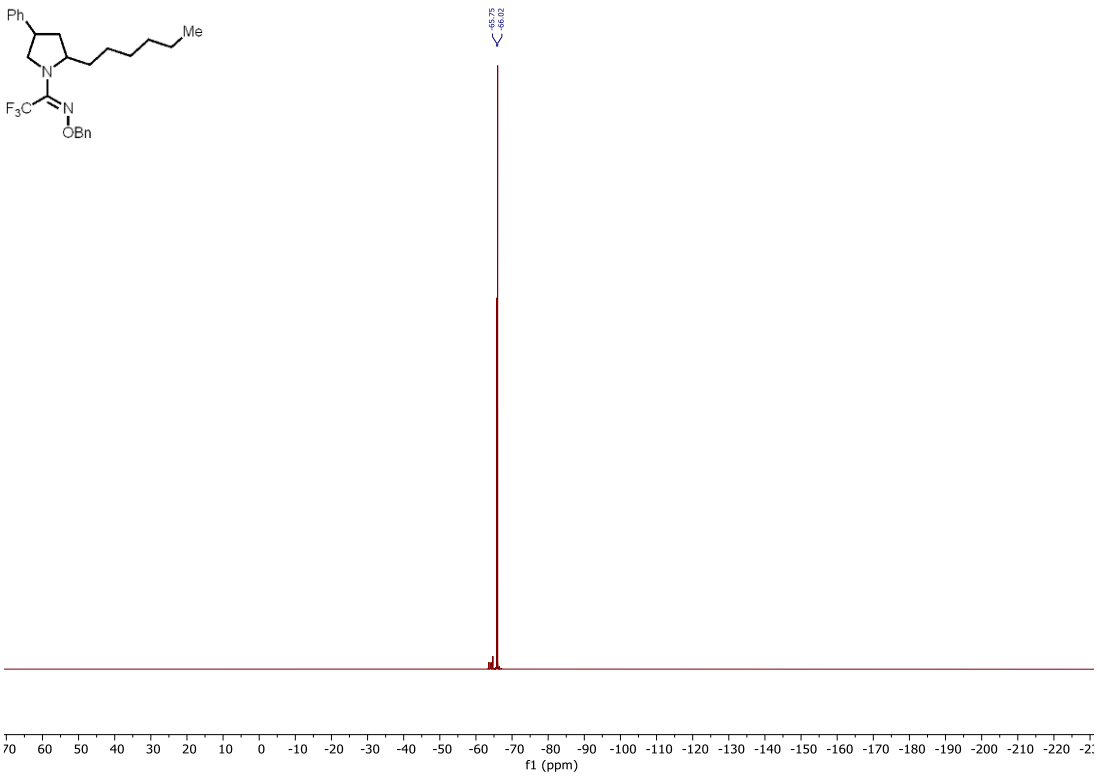


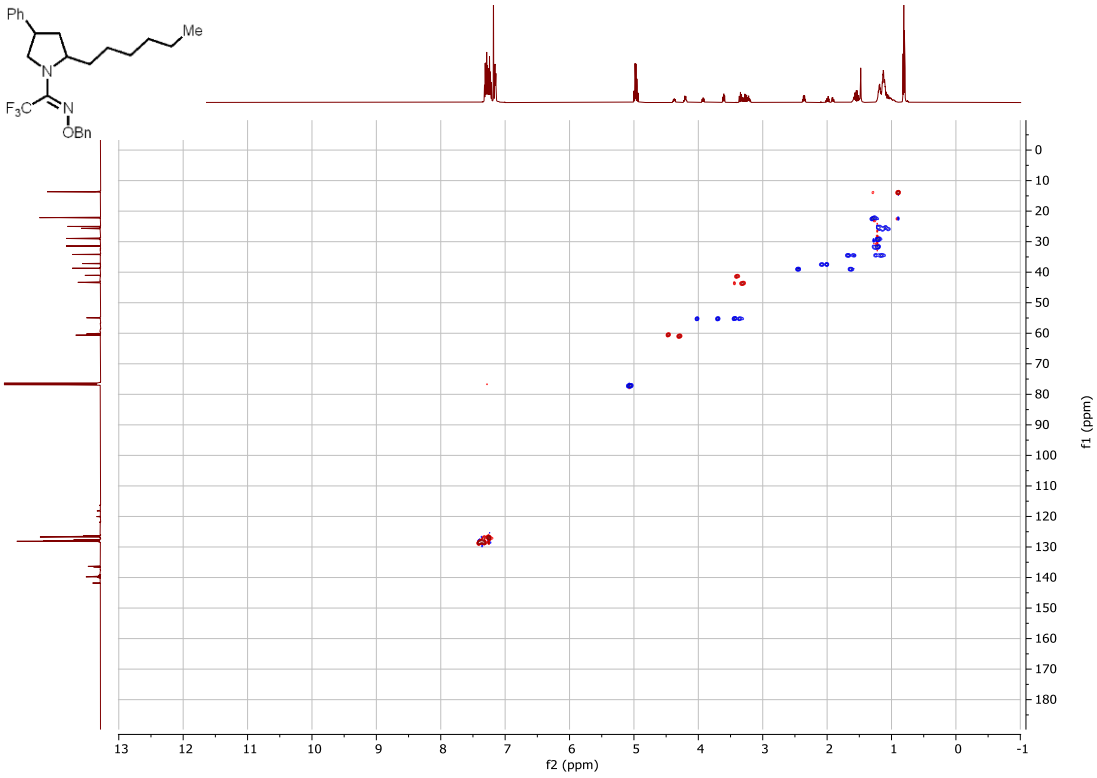

F
F
CO2Et
N
F3C
N
OBn
-65.99
-97.71
-98.23
-100.26
-100.87
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

(*E*)-2,2,2-trifluoro-1-(2-hexyl-4-phenylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (2j-mono)

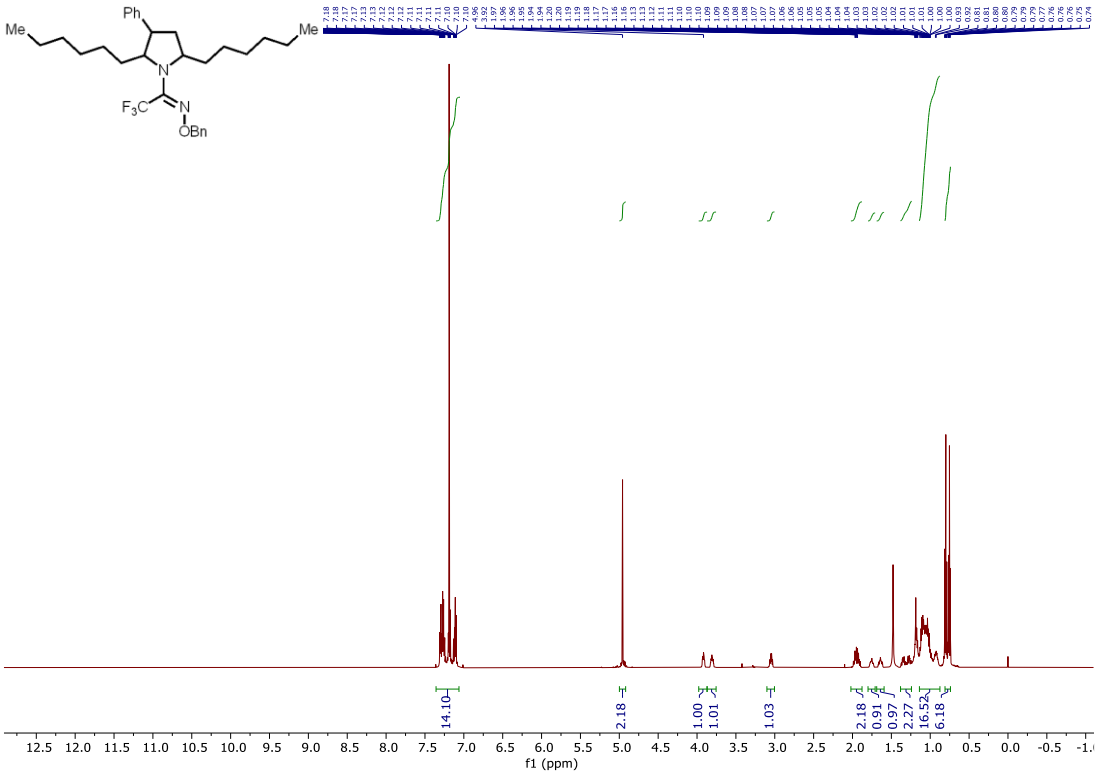


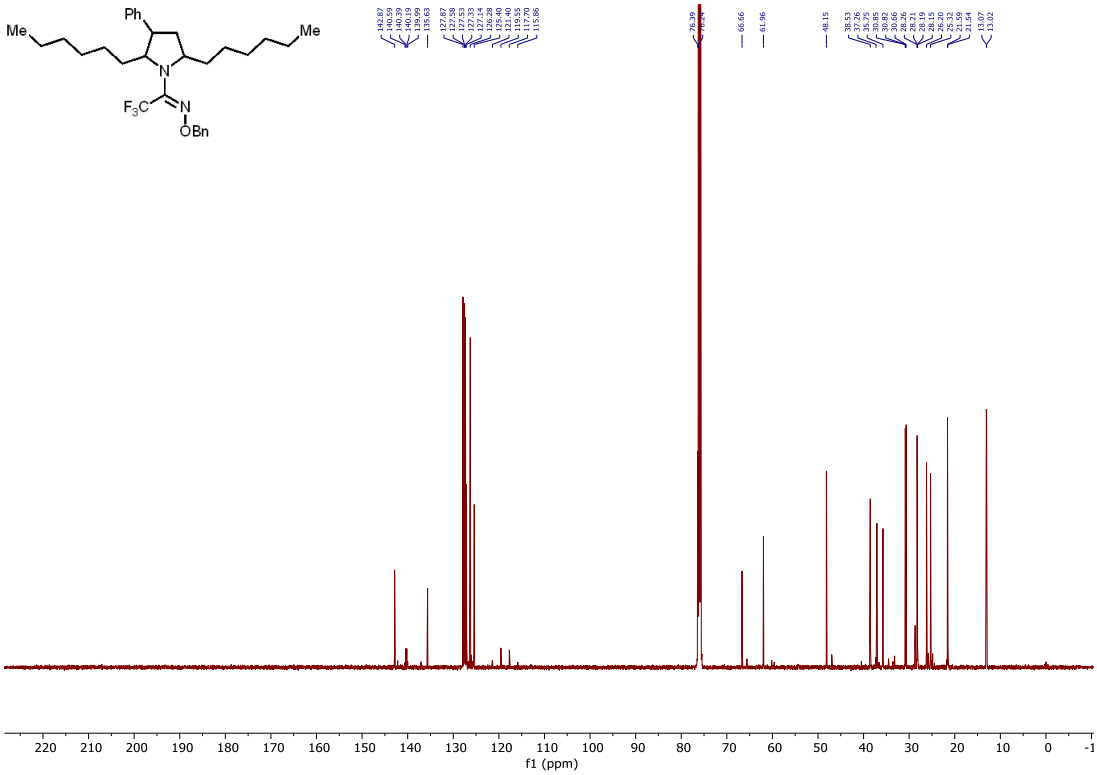


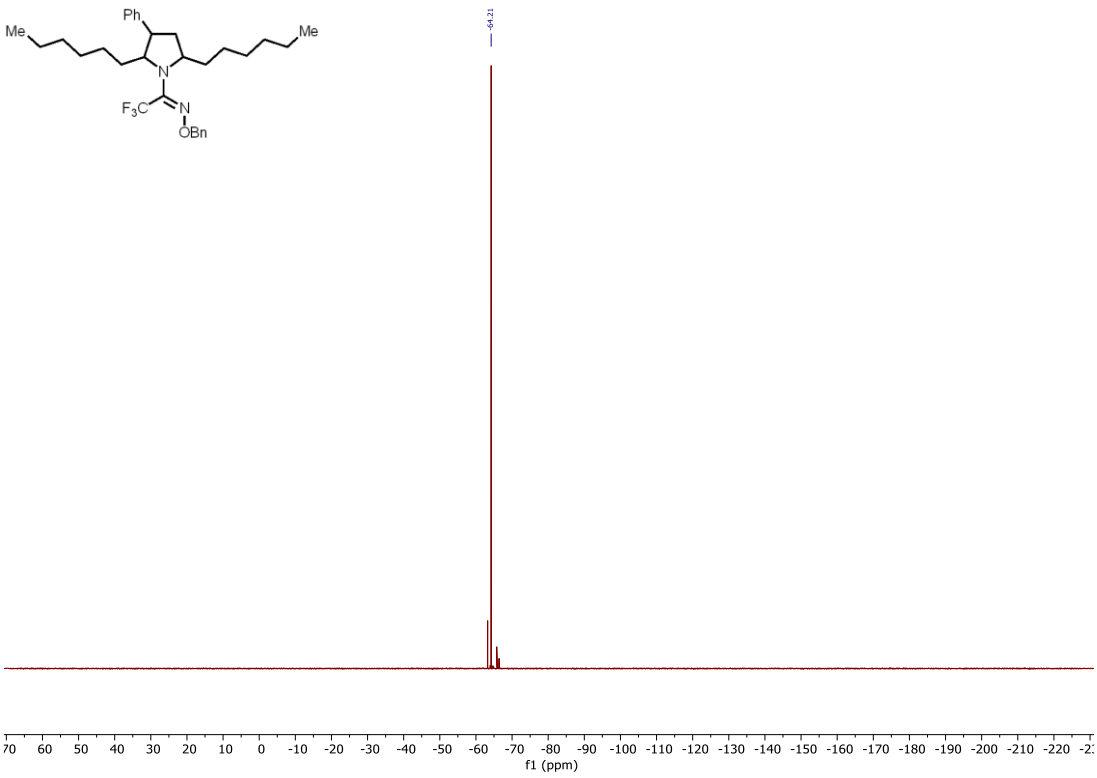

Ph
Me
N
F3C
N
OBn
-65.75
-66.02
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)


Ph
Me
N
F3C
N
OBn
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
f1 (ppm)

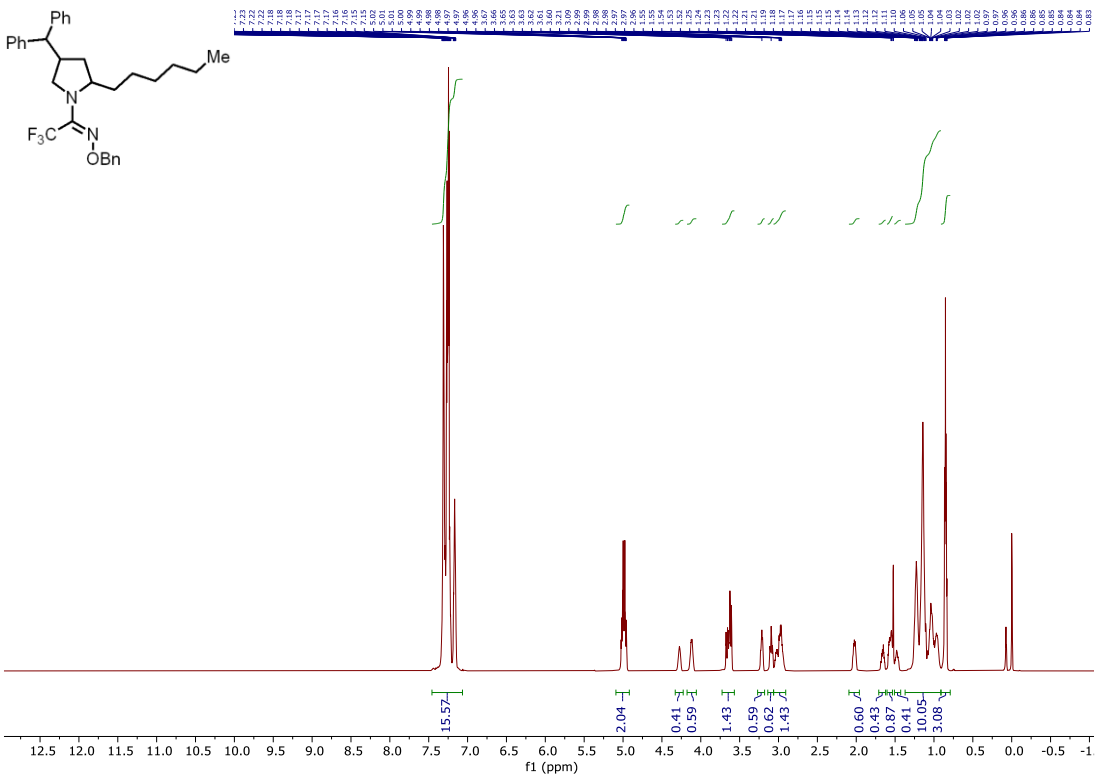
(*E*)-1-(2,5-dihexyl-3-phenylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (2j-di)

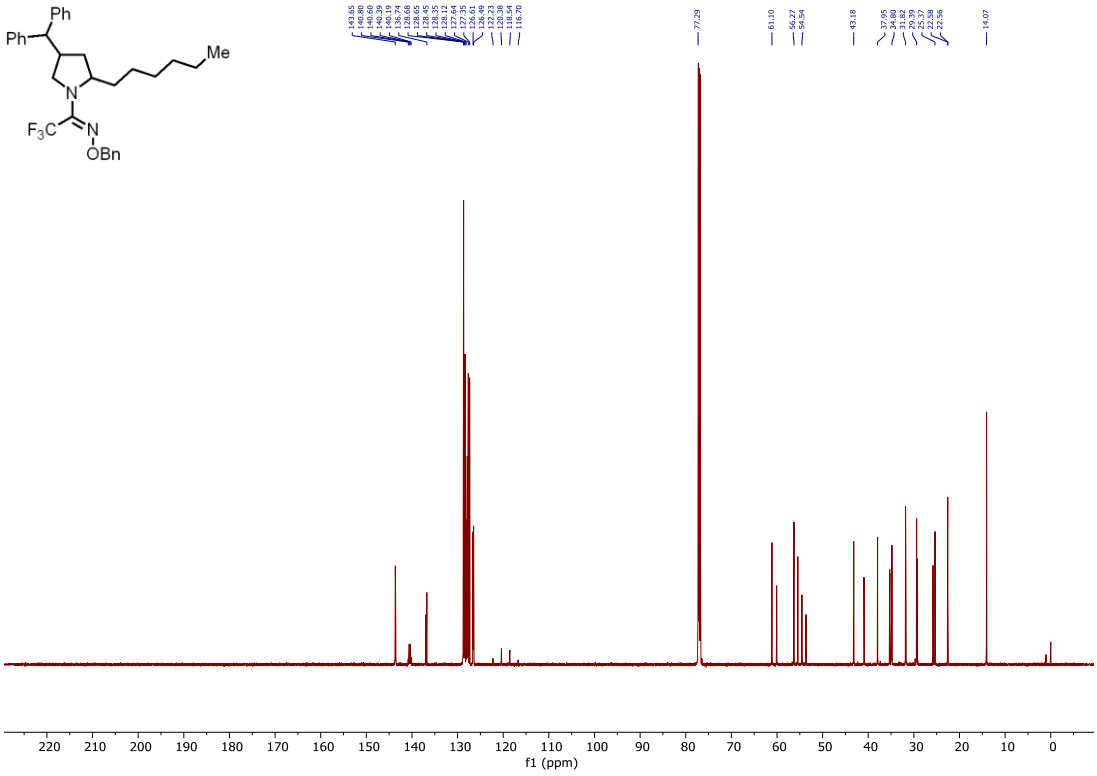


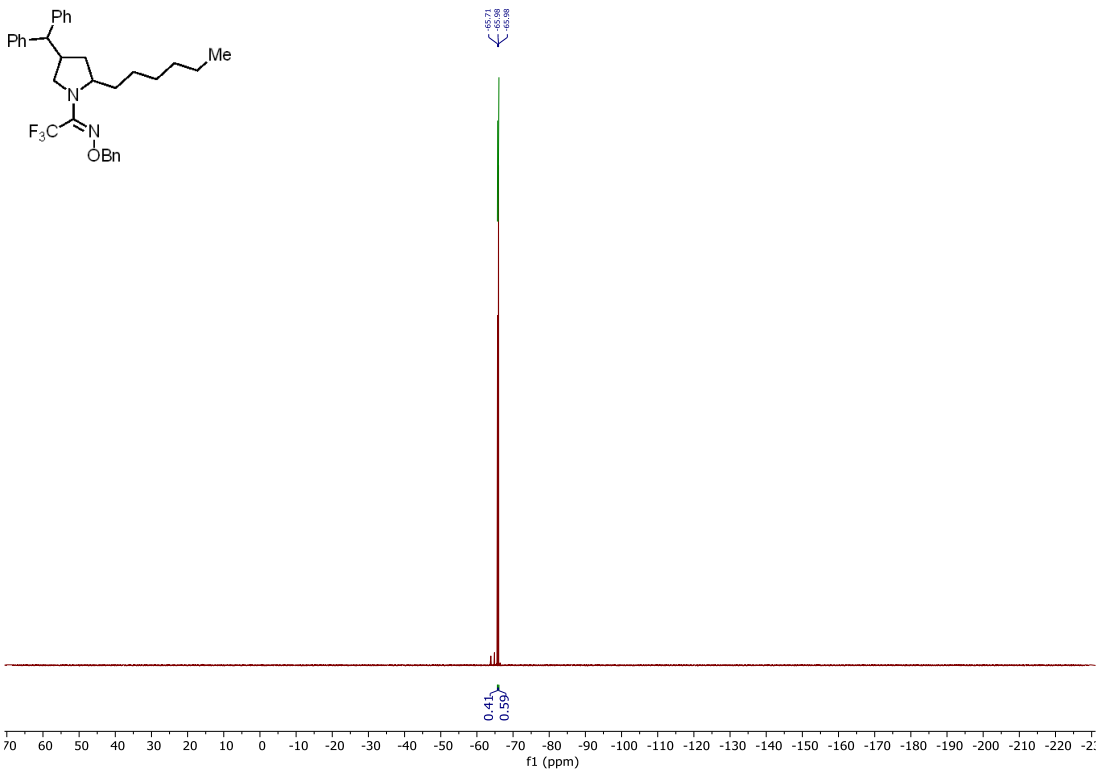



Ph
Me
Me
N
F3C
N
OBn
-64.21
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

(*E*)-1-(4-benzhydryl-2-hexylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (2k)

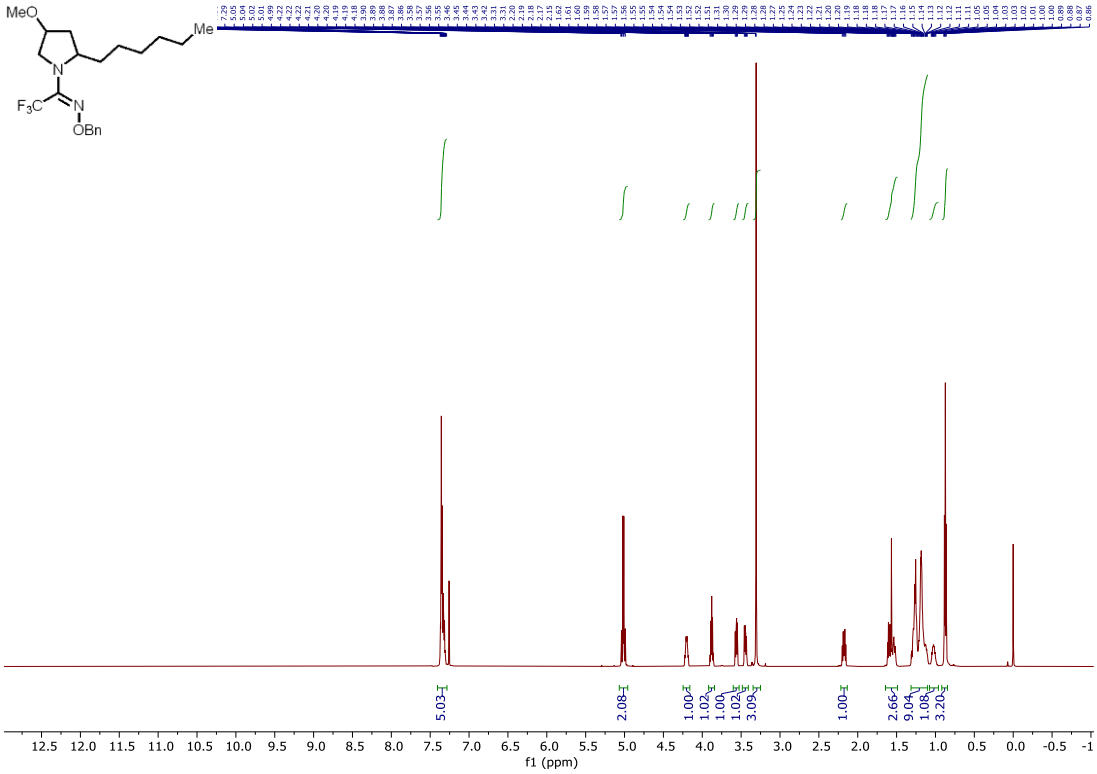


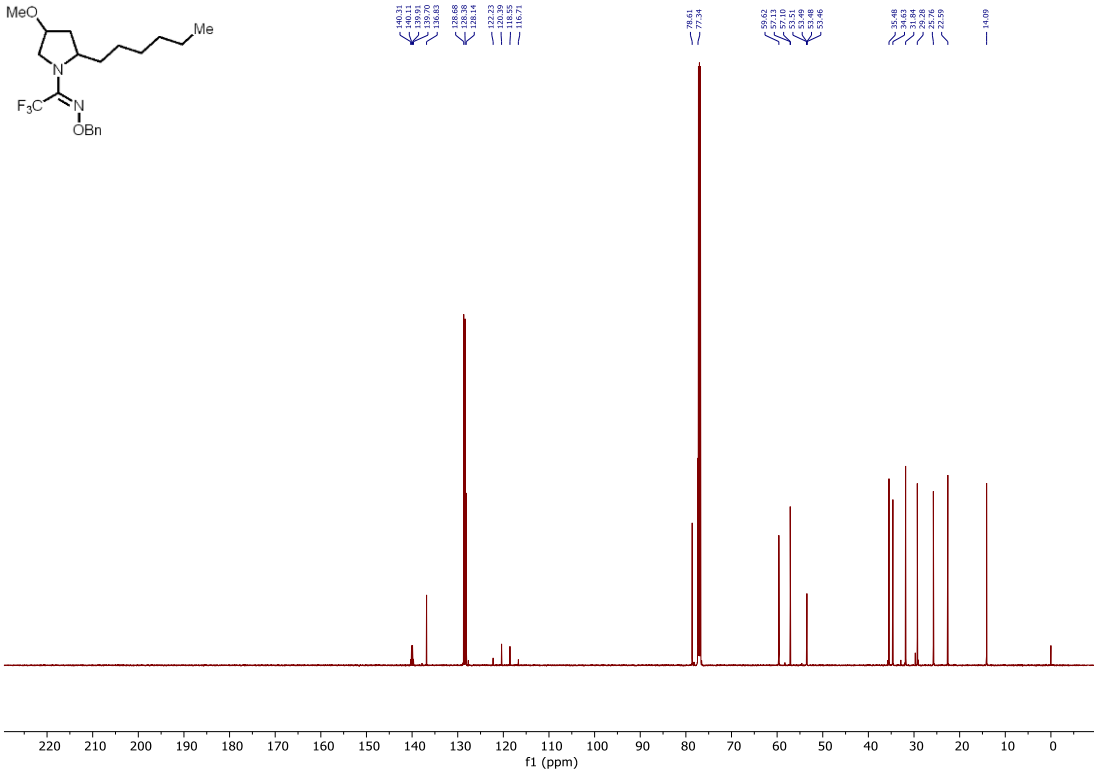


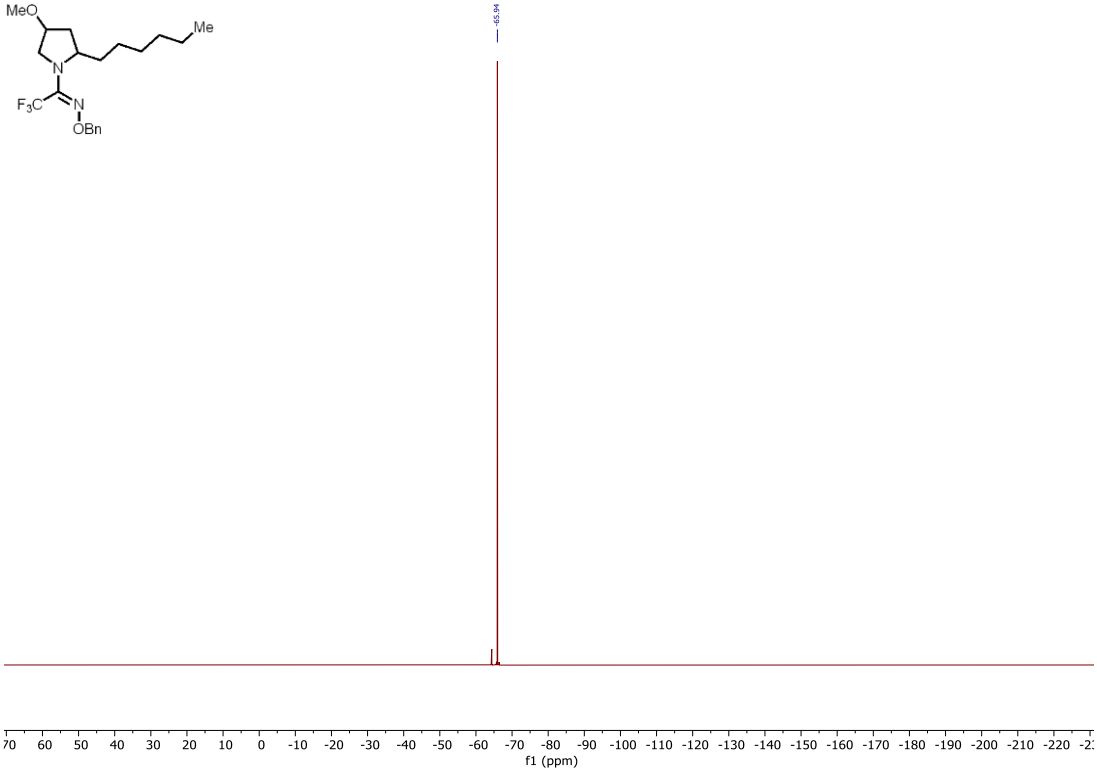

Ph
Ph
Me
N
F3C
N
OBn
-65.71
-65.98
-65.98
0.41
0.59
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

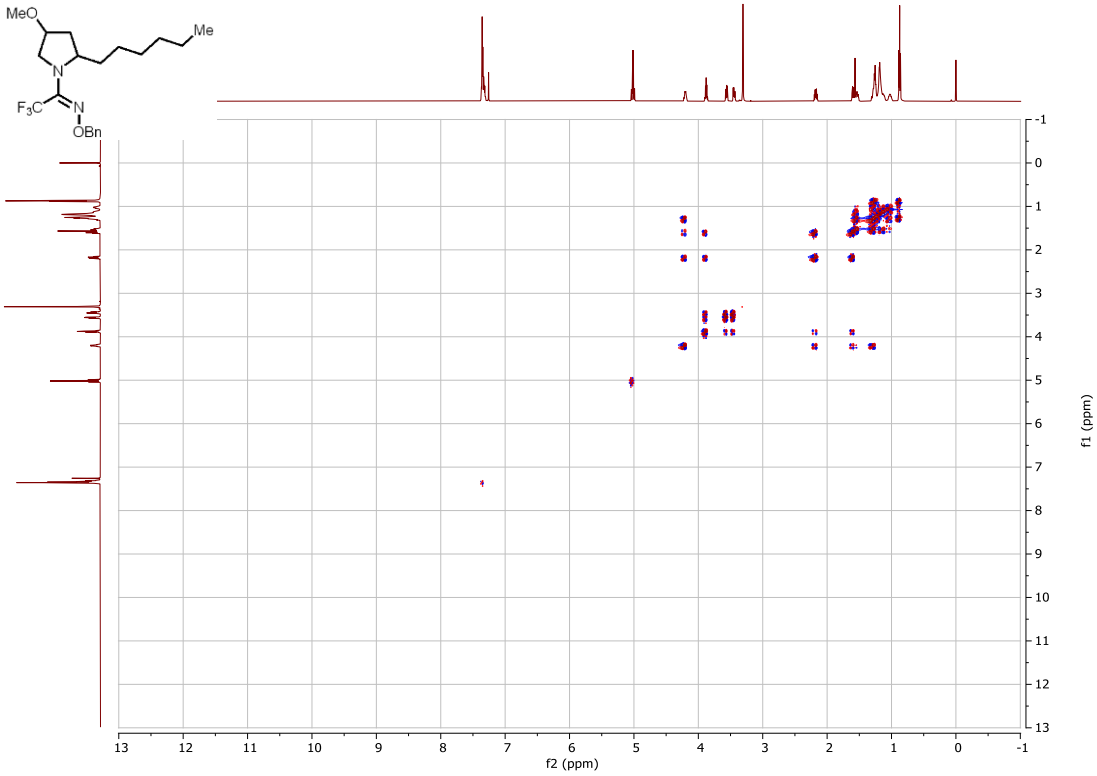
(*E*)-2,2,2-trifluoro-1-(2-hexyl-4-methoxypyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (2l)

First diastereomer

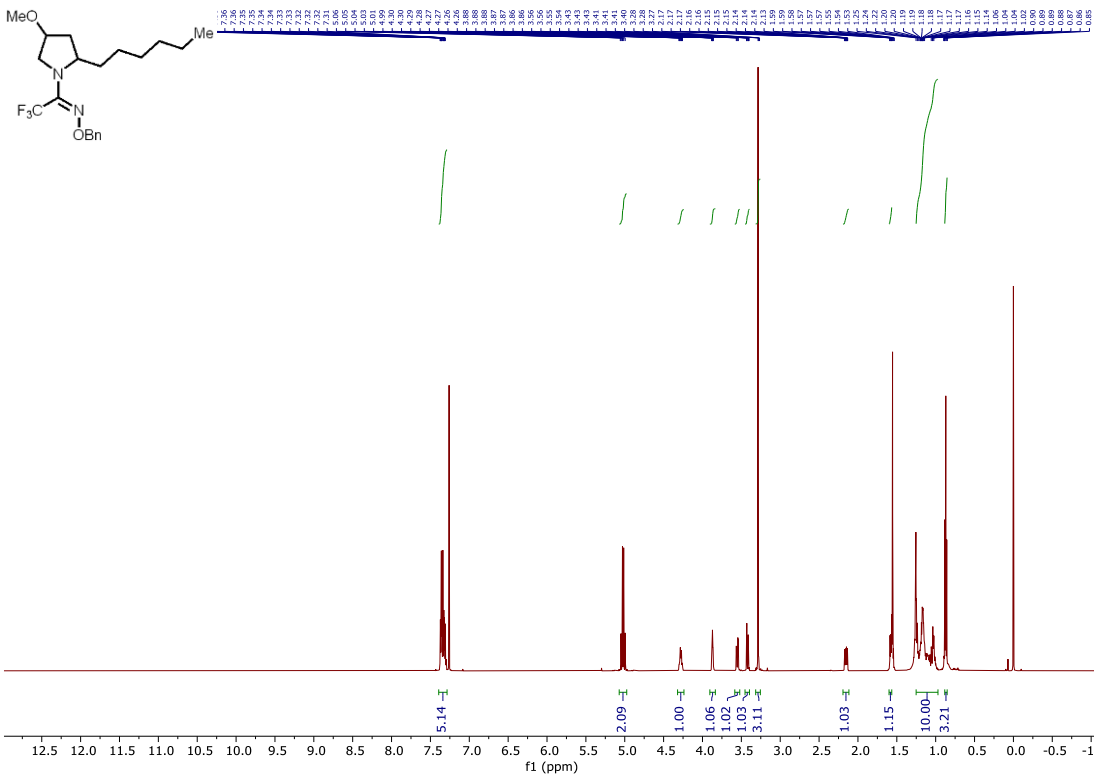


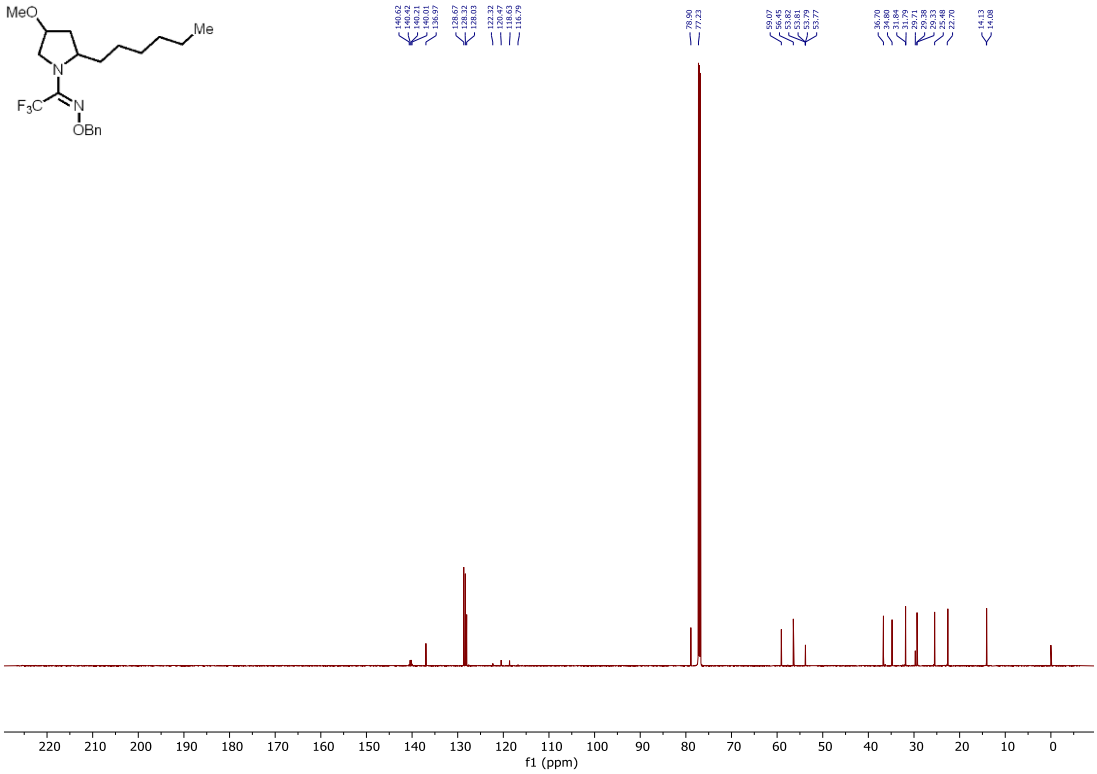


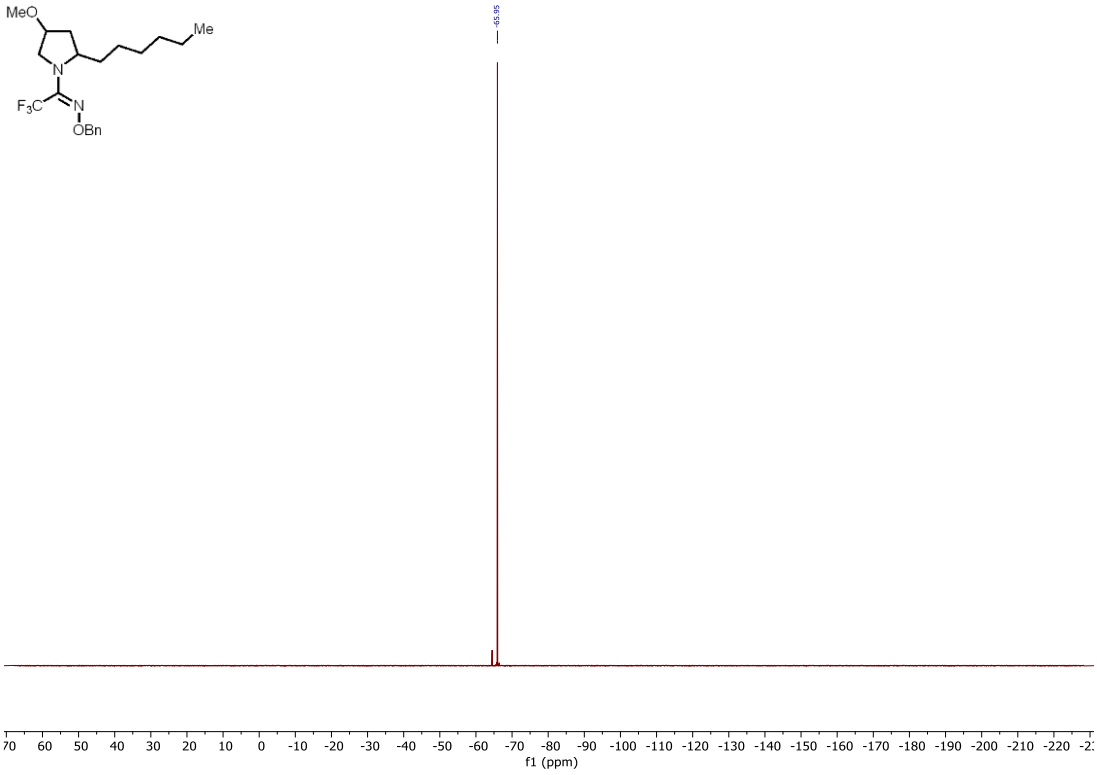

MeO
Me
N
F3C
N
OBn
-65.94
f1 (ppm)

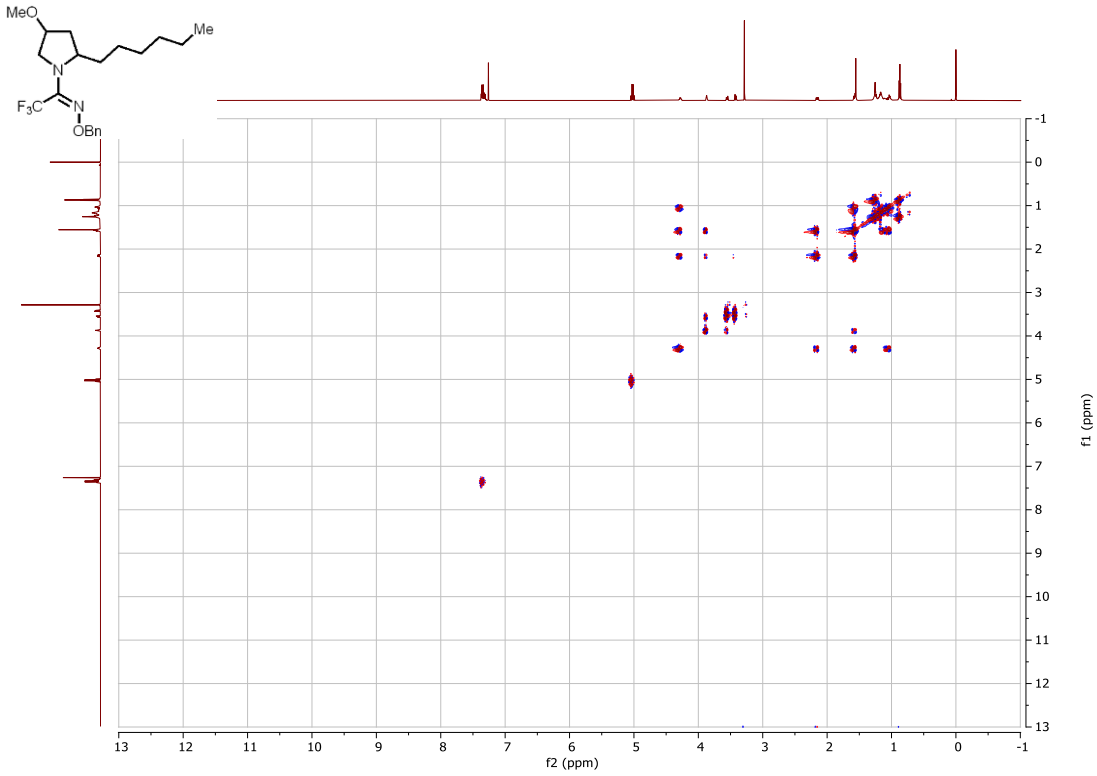

MeO
Me
N
F3C
N
OBn
f2 (ppm)
f1 (ppm)

Second diastereomer

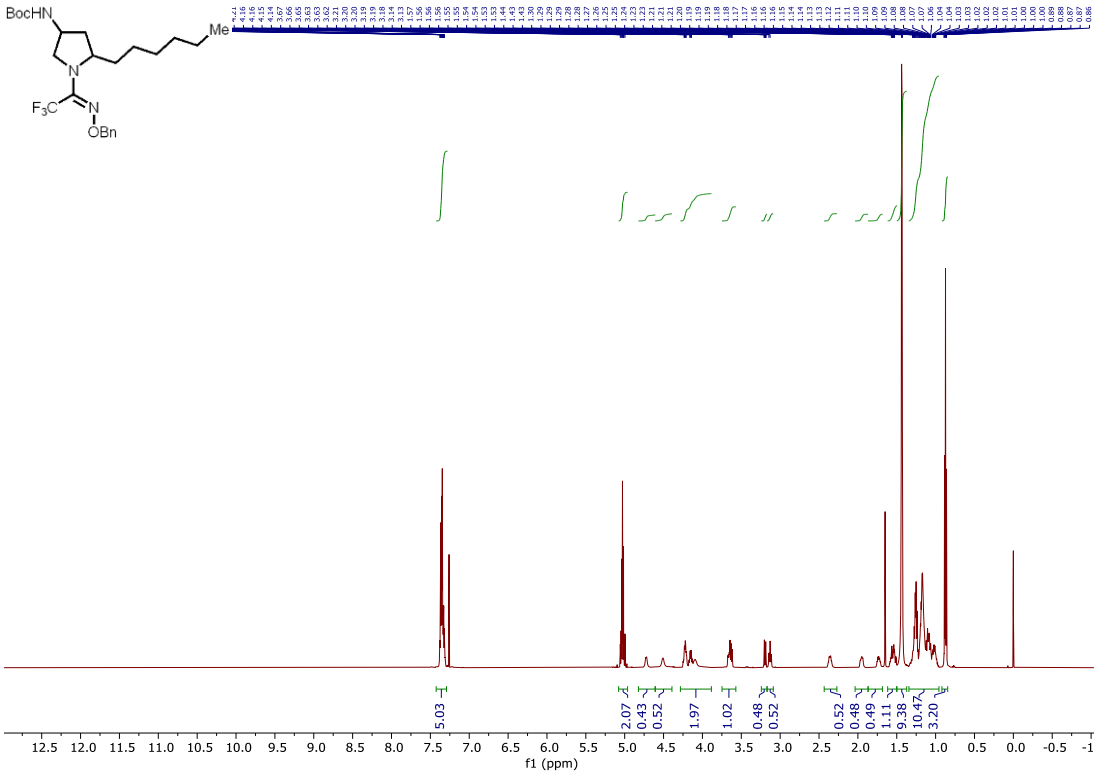


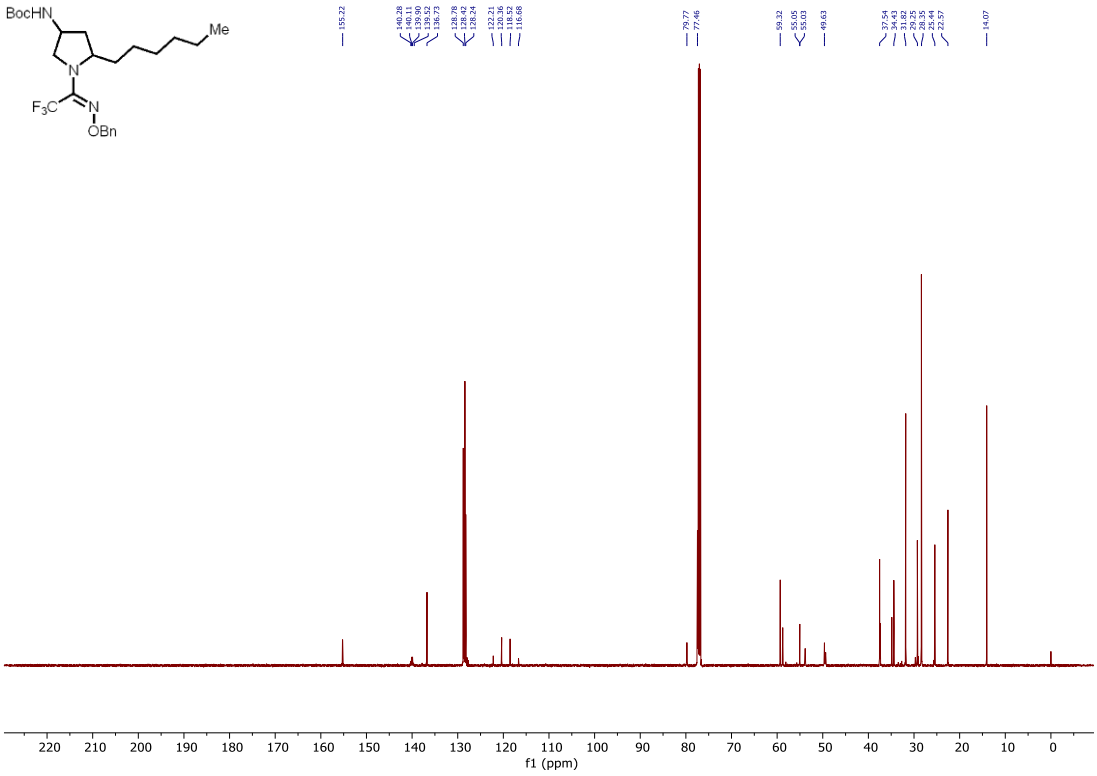


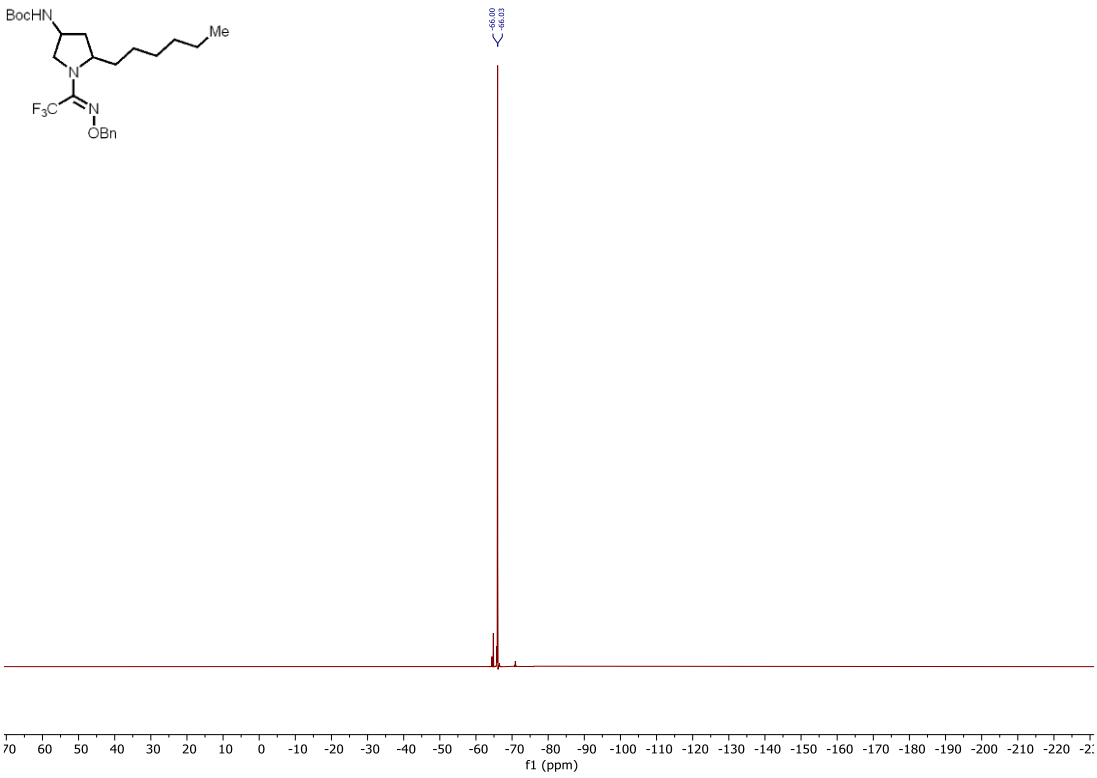

MeO
Me
N
F3C
N
OBn
-65.95
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

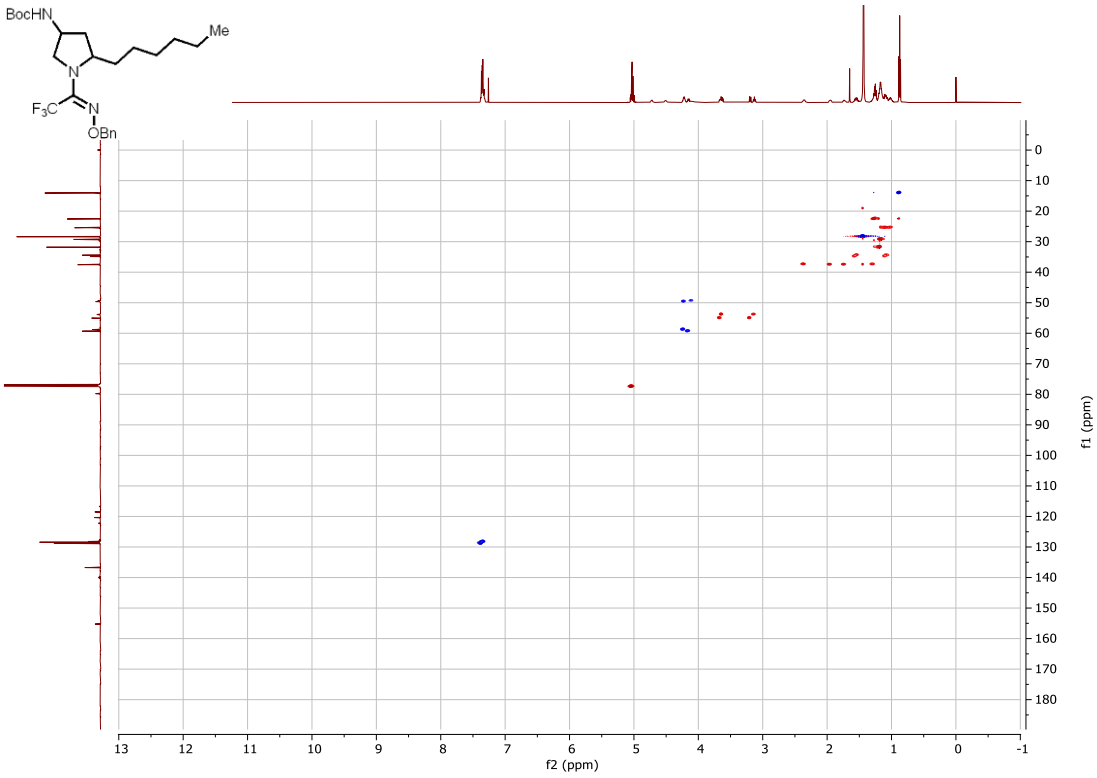

MeO
Me
N
F3C
N
OBn
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f2 (ppm)
-1 0 1 2 3 4 5 6 7 8 9 10 11 12 13
f1 (ppm)

tert-butyl (*E*)-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-5-hexylpyrrolidin-3-yl)carbamate (2m-mono)

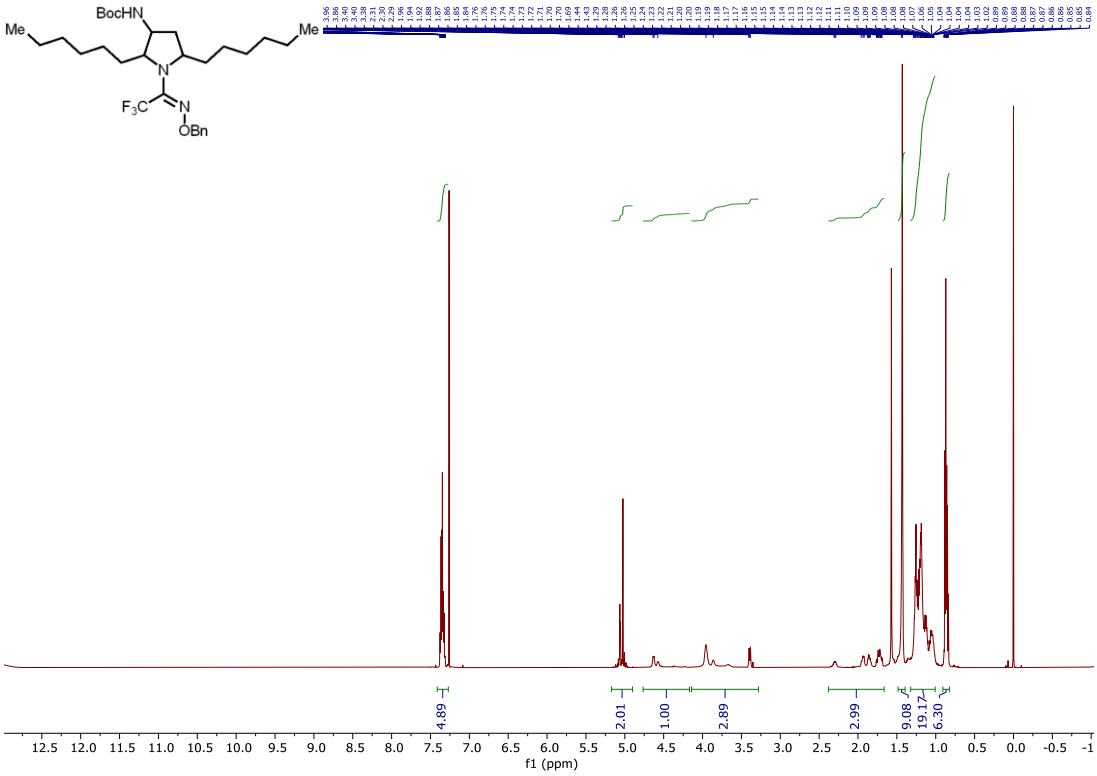


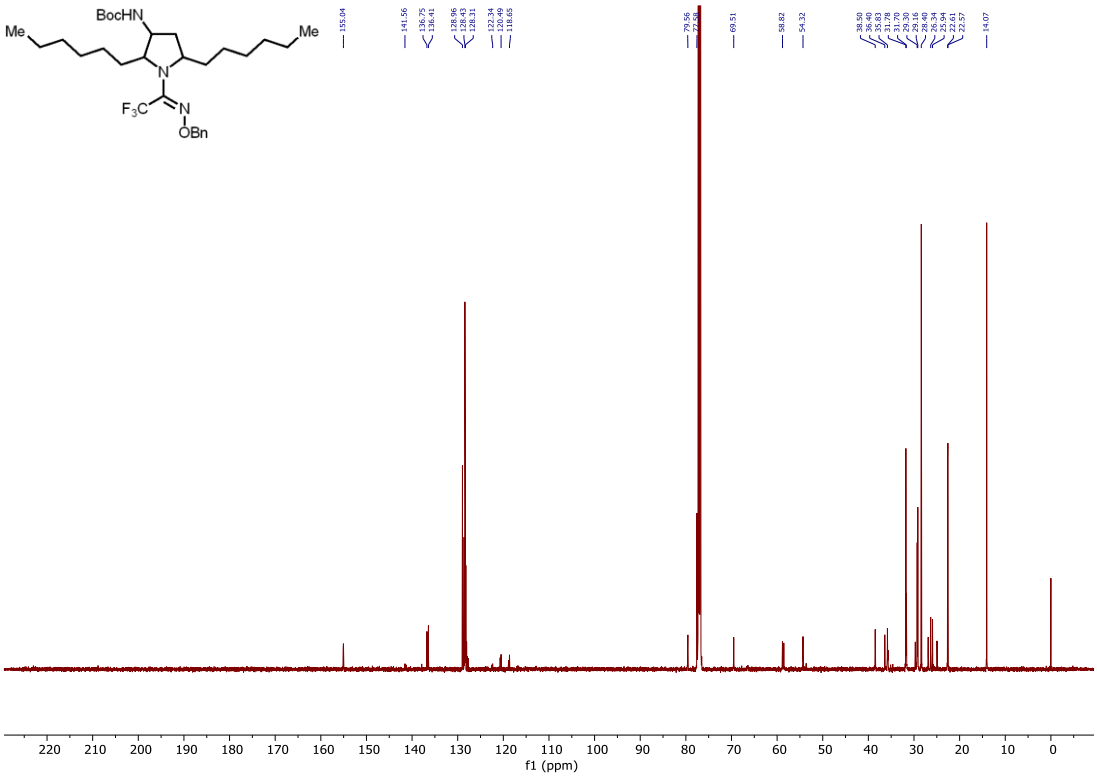


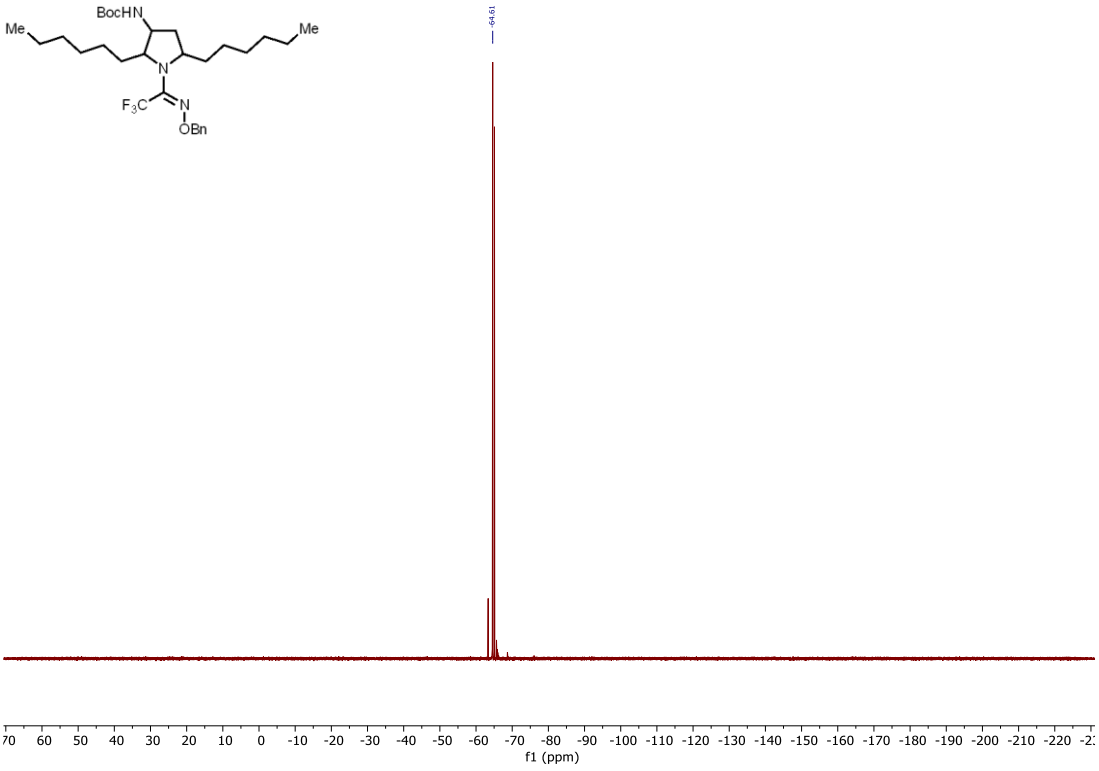

BocHN
Me
N
F3C
N
OBn
-66.00
-66.03
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

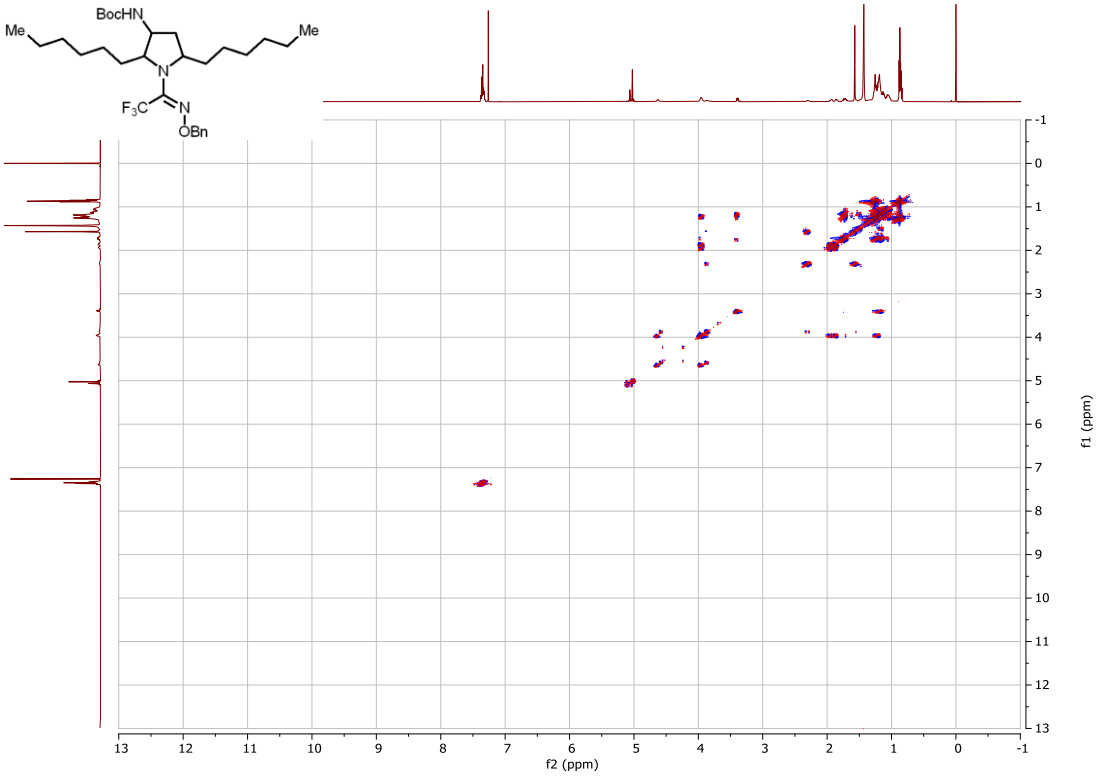

BocHN
Me
N
F3C
N
OBn
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
f1 (ppm)

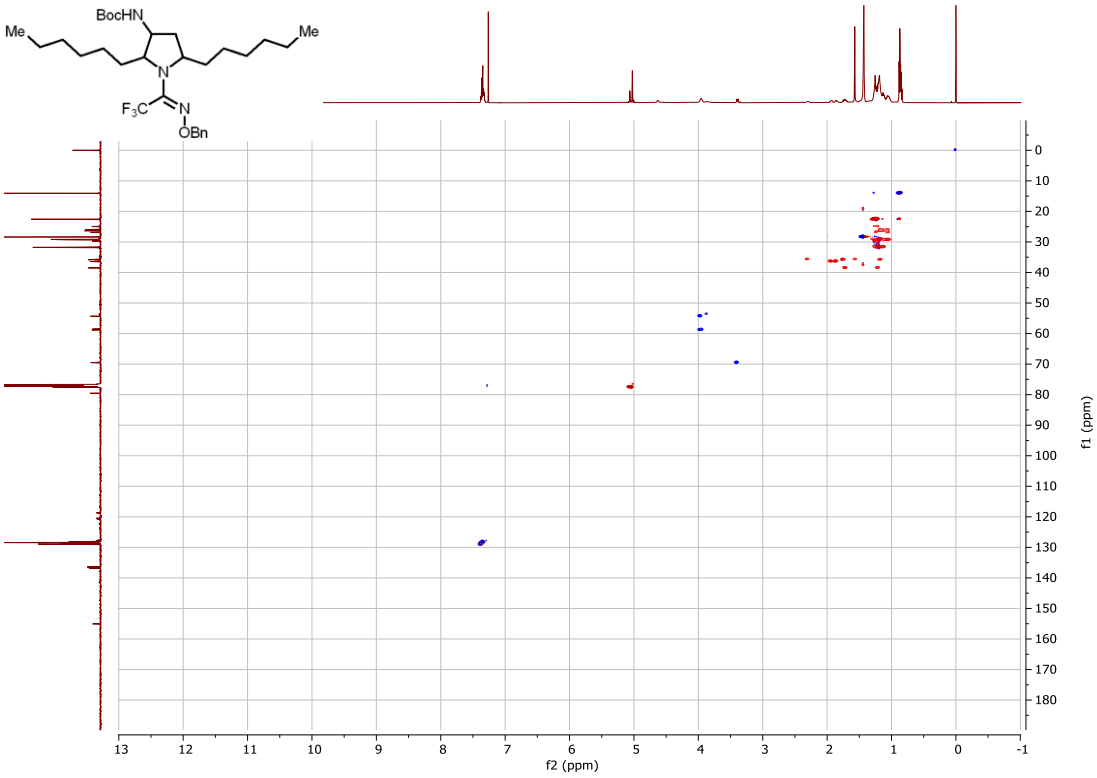
tert-butyl (*E*)-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-2,5-dihexylpyrrolidin-3-yl)carbamate (2m-di)





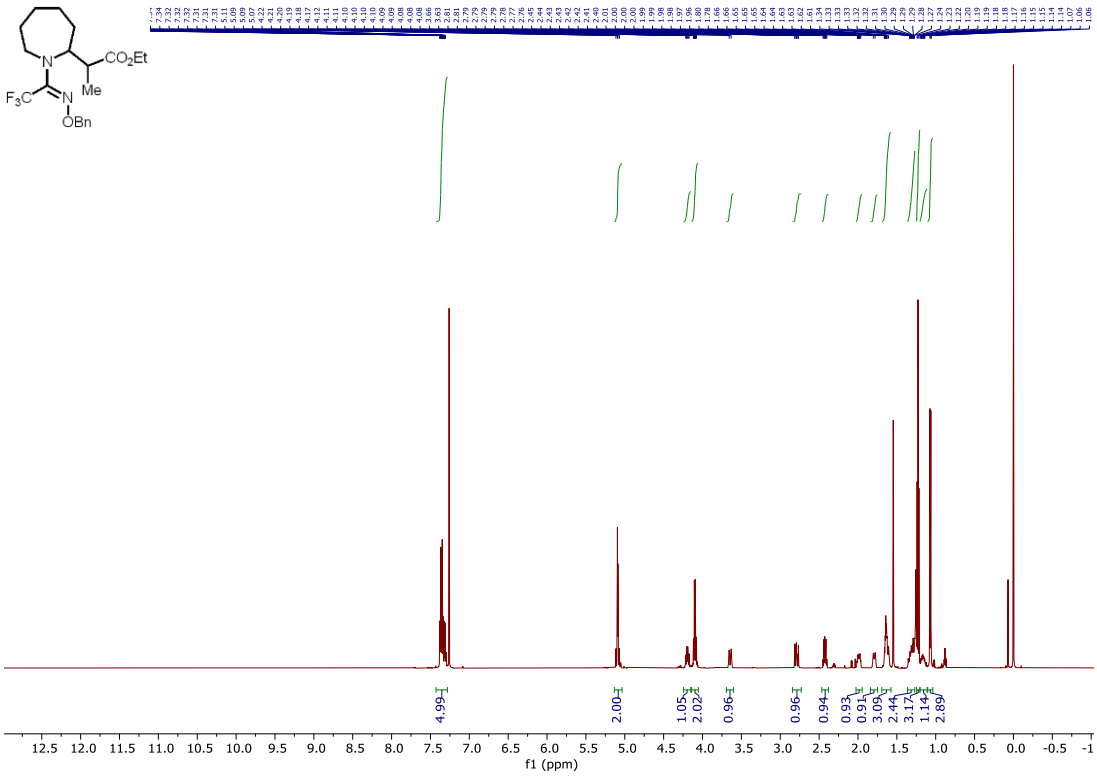

BocHN
Me
Me
N
F3C
N
OBn
-64.61
f1 (ppm)

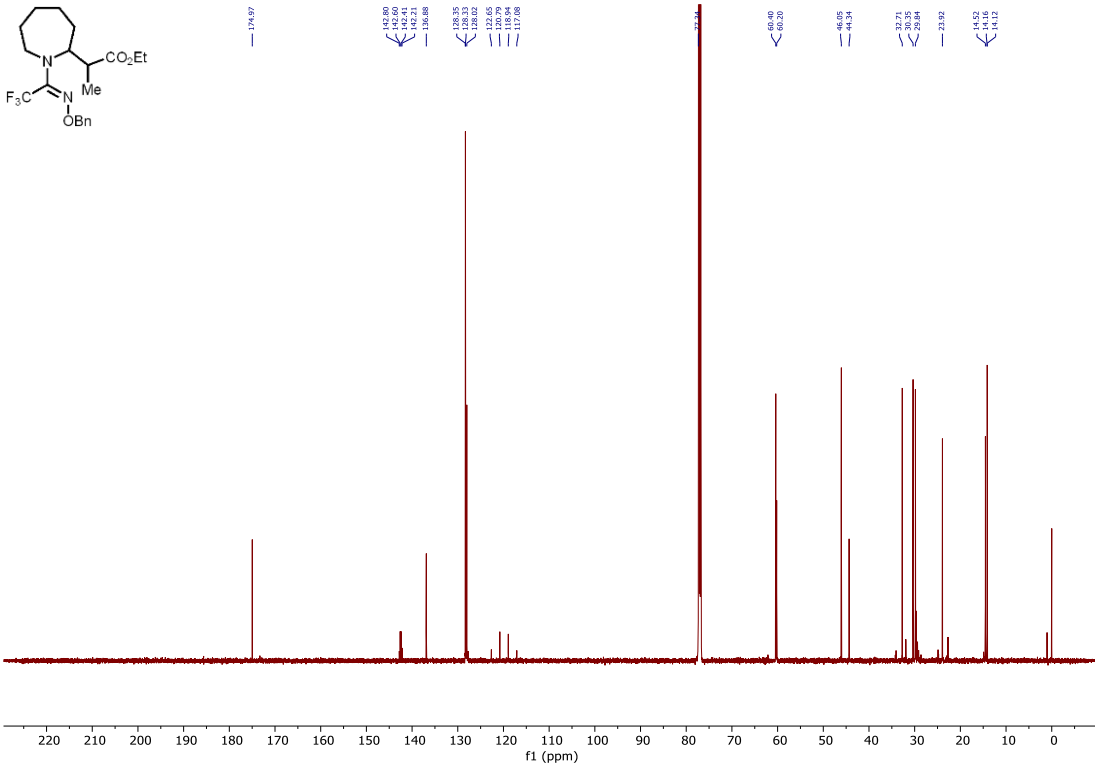

BocHN
Me
Me
N
F3C
N
OBn
f2 (ppm)
f1 (ppm)

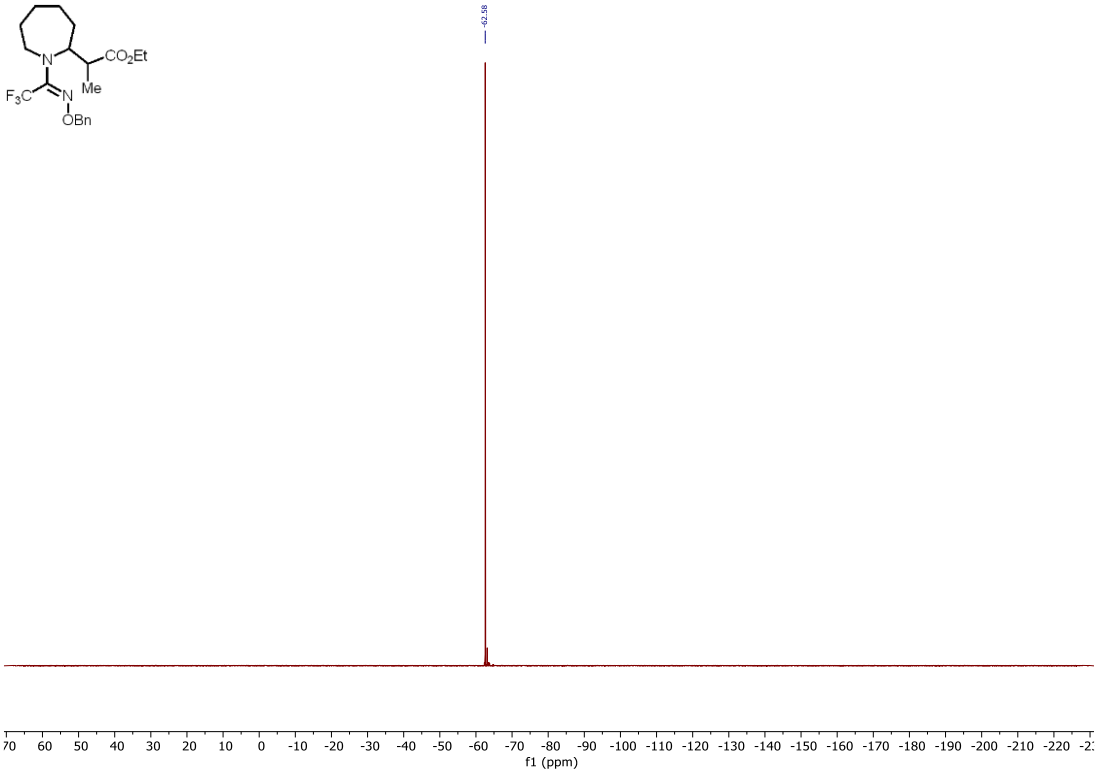

BocHN
Me
Me
N
F3C
N
OBn
f2 (ppm)
f1 (ppm)

ethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)azepan-2-yl)propanoate (2p-B)

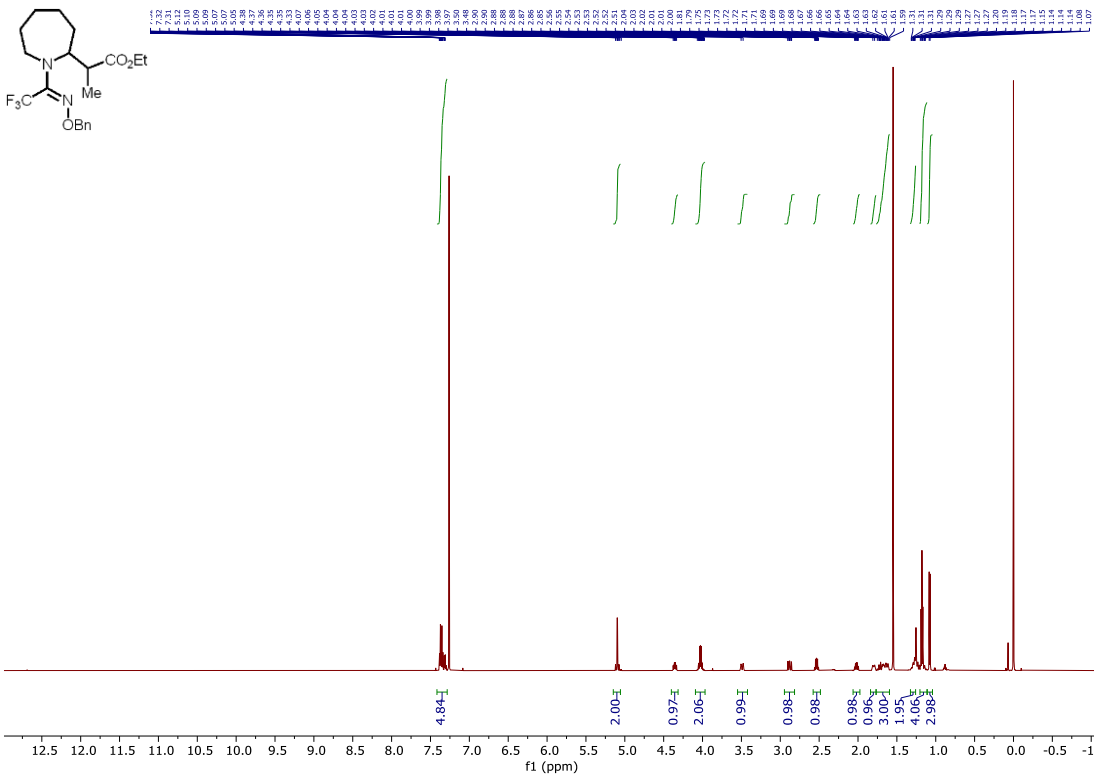
First diastereomer

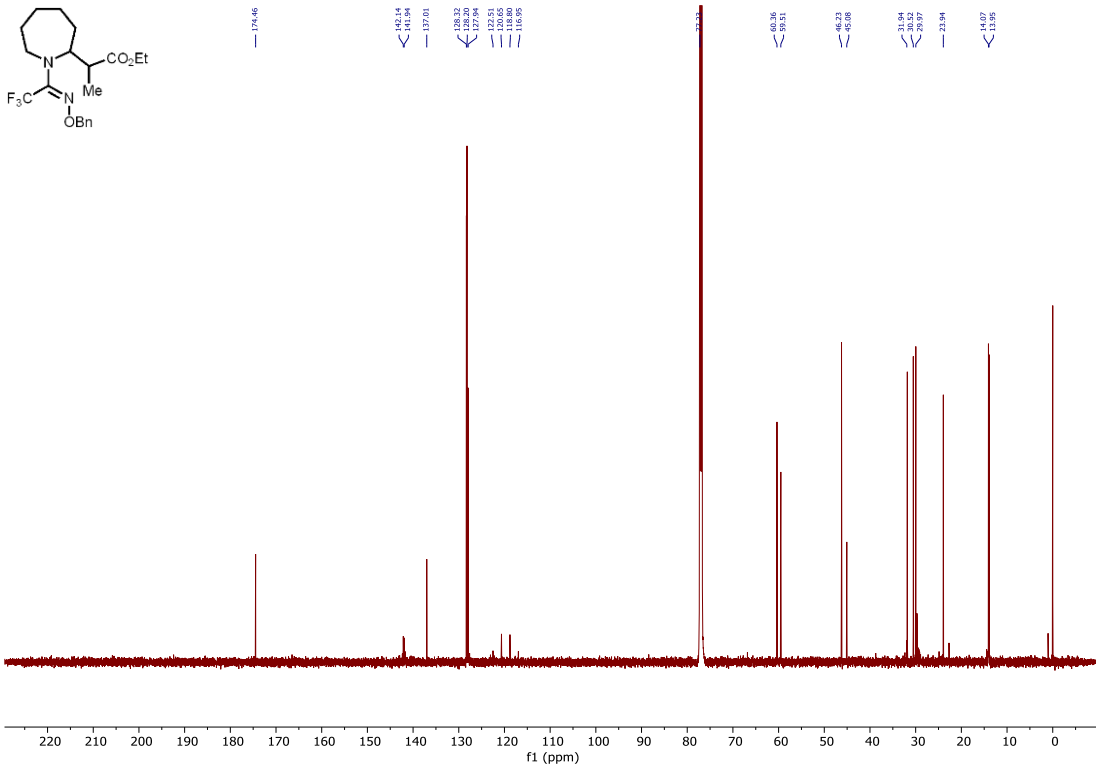


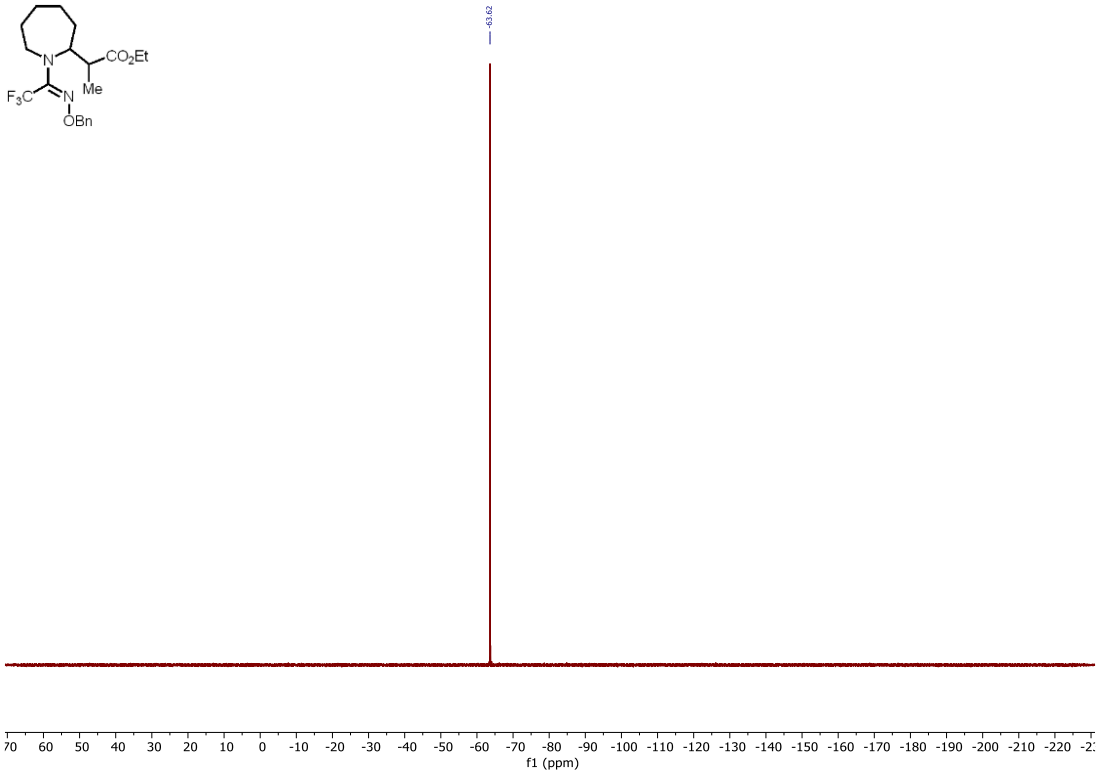




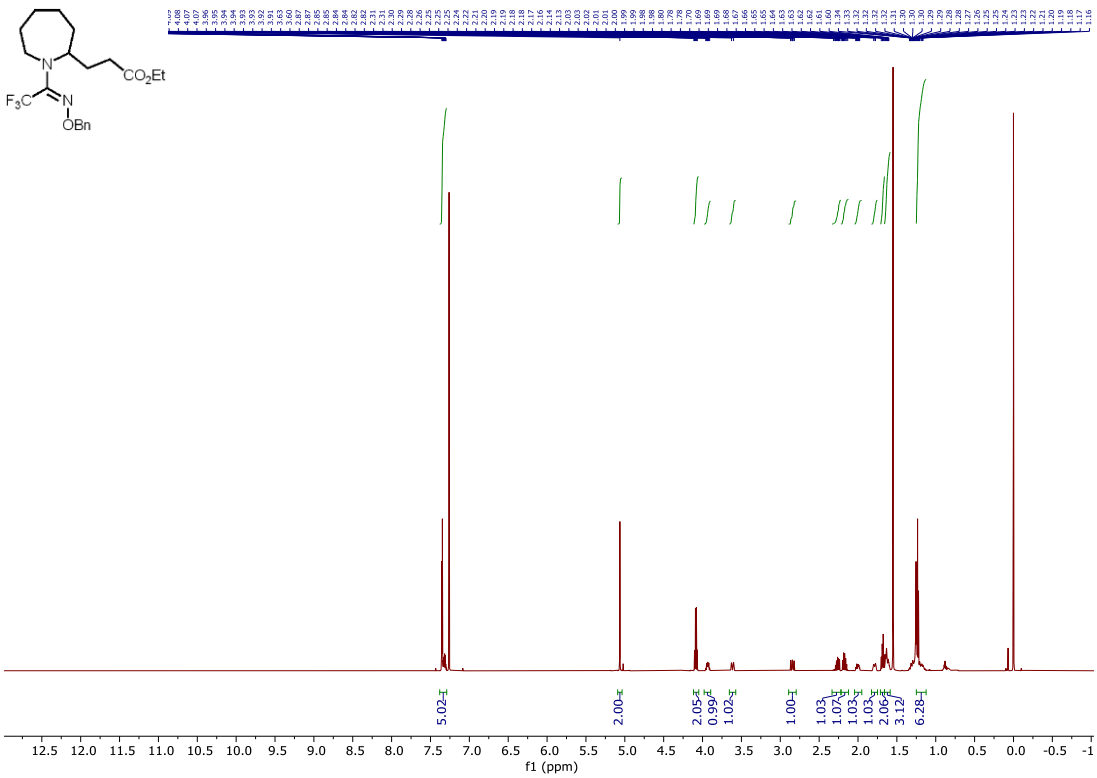
Second diastereomer

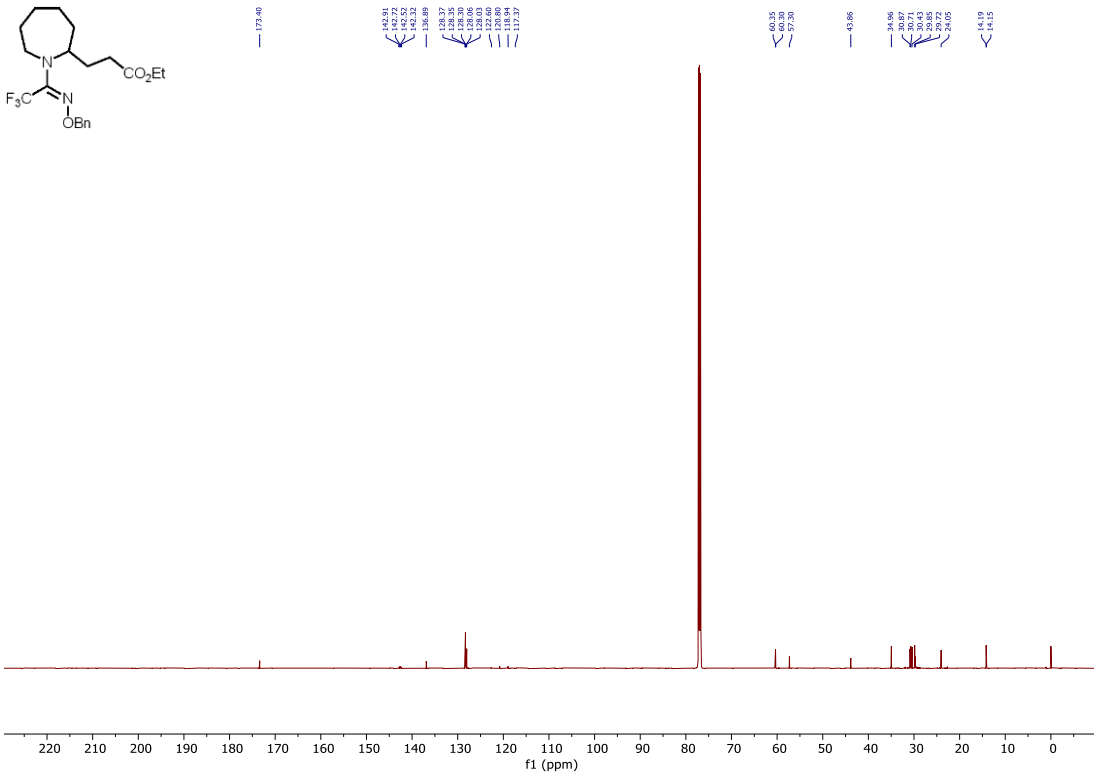


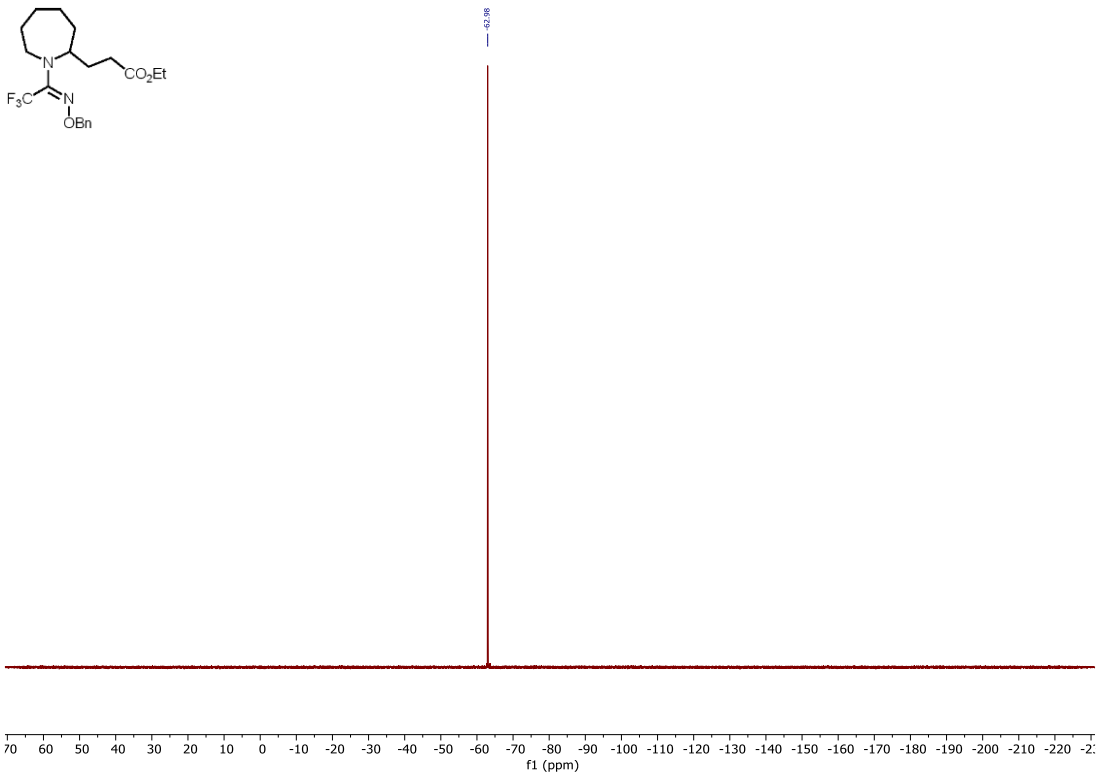

CO2Et
Me
F3C
N
OBn
174.46
142.14
141.94
137.01
128.32
128.20
127.94
77.32
60.36
59.51
46.23
45.08
31.94
30.53
29.97
23.94
14.07
13.95
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CO2Et
Me
F3C
N
OBn
-63.62
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

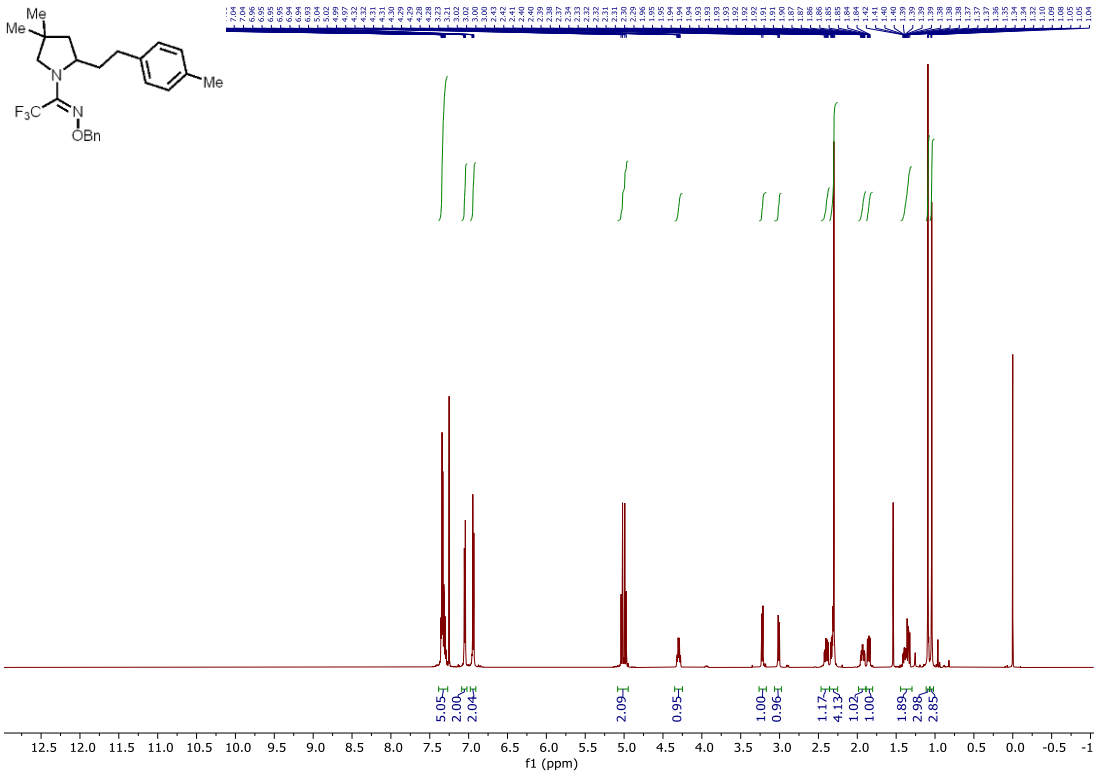
ethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)azepan-2-yl)propanoate (2p-L)

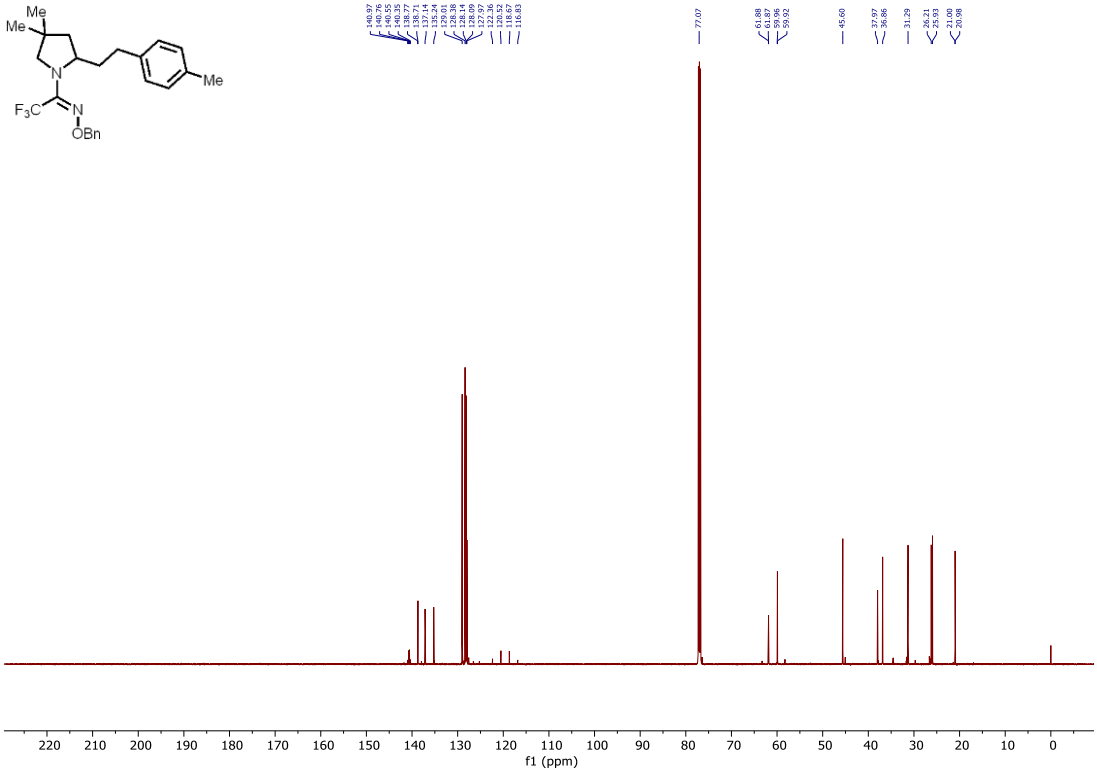


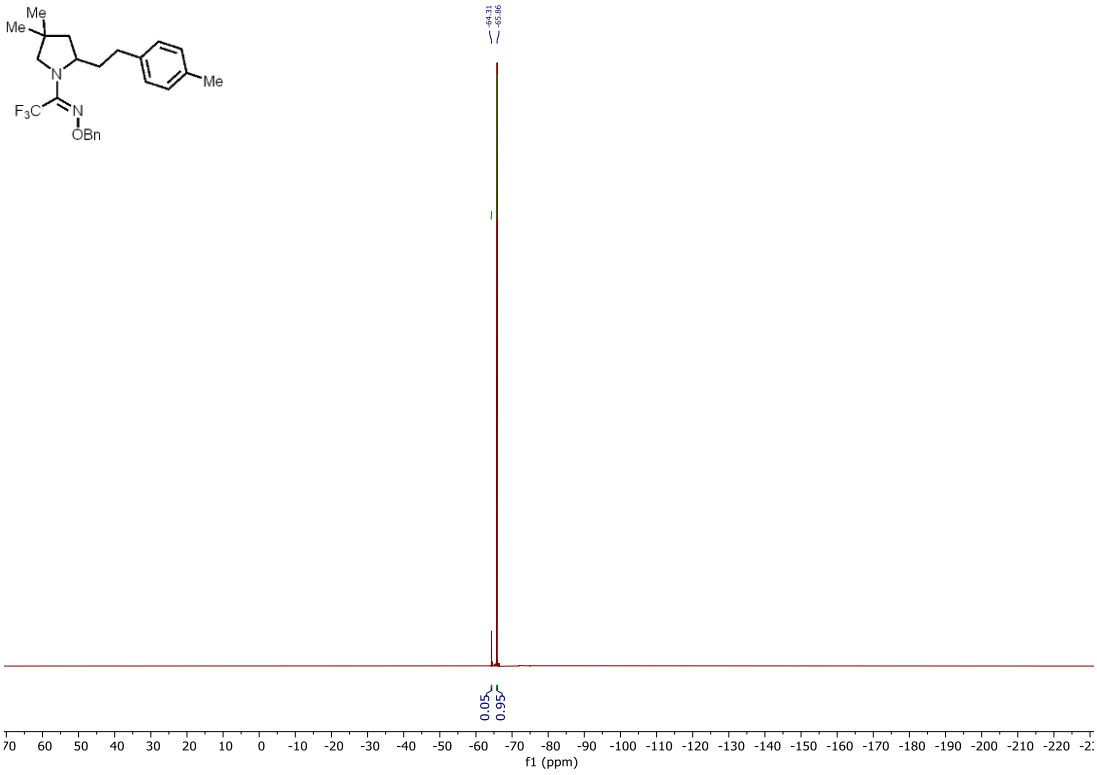



-62.98
CO2Et
F3C
N
OBn
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

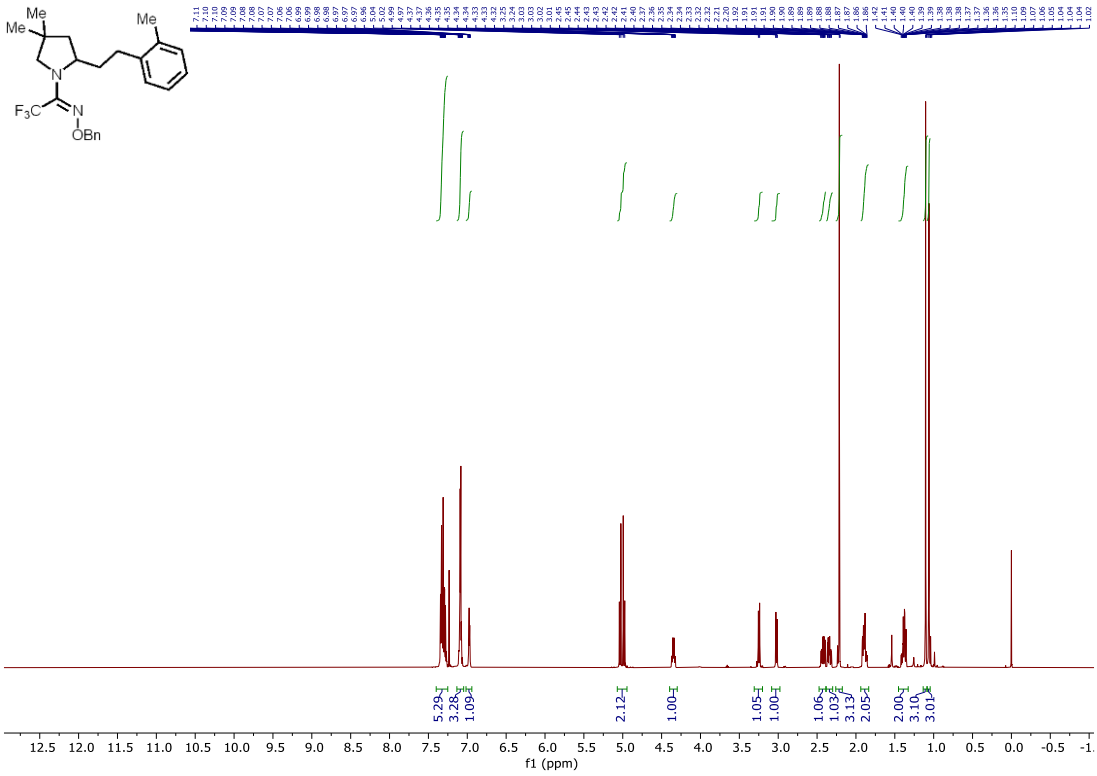
(*E*)-1-(4,4-dimethyl-2-(4-methylphenethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3a)

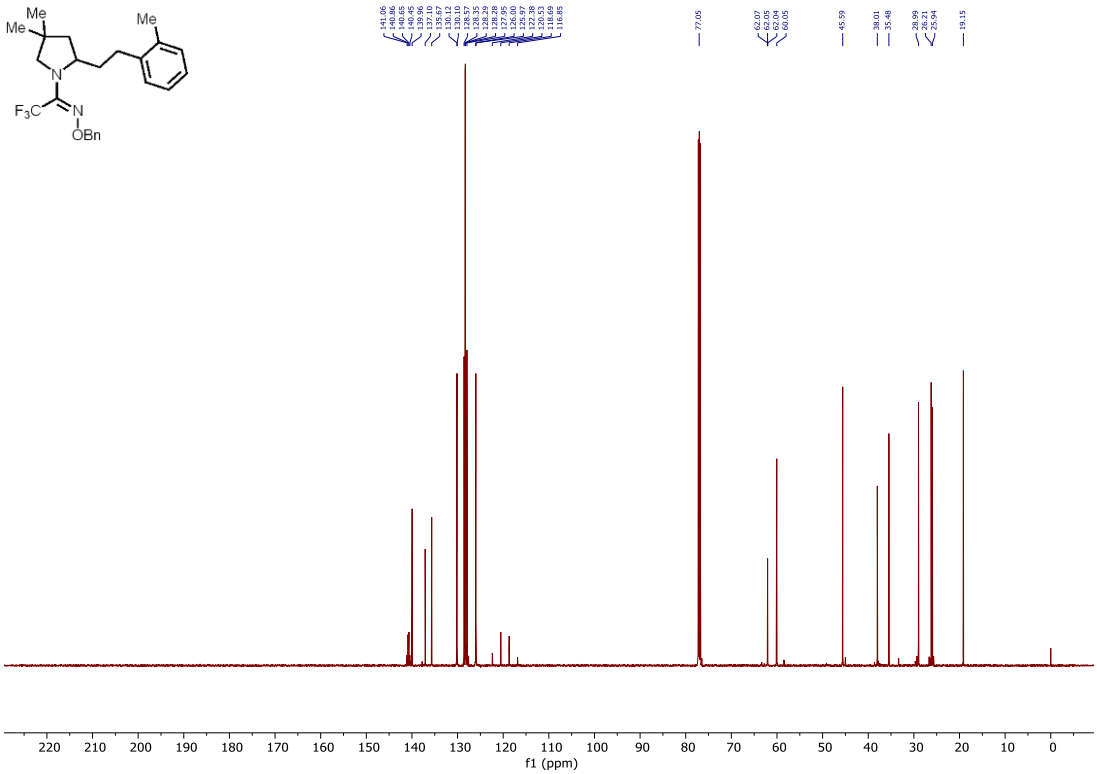


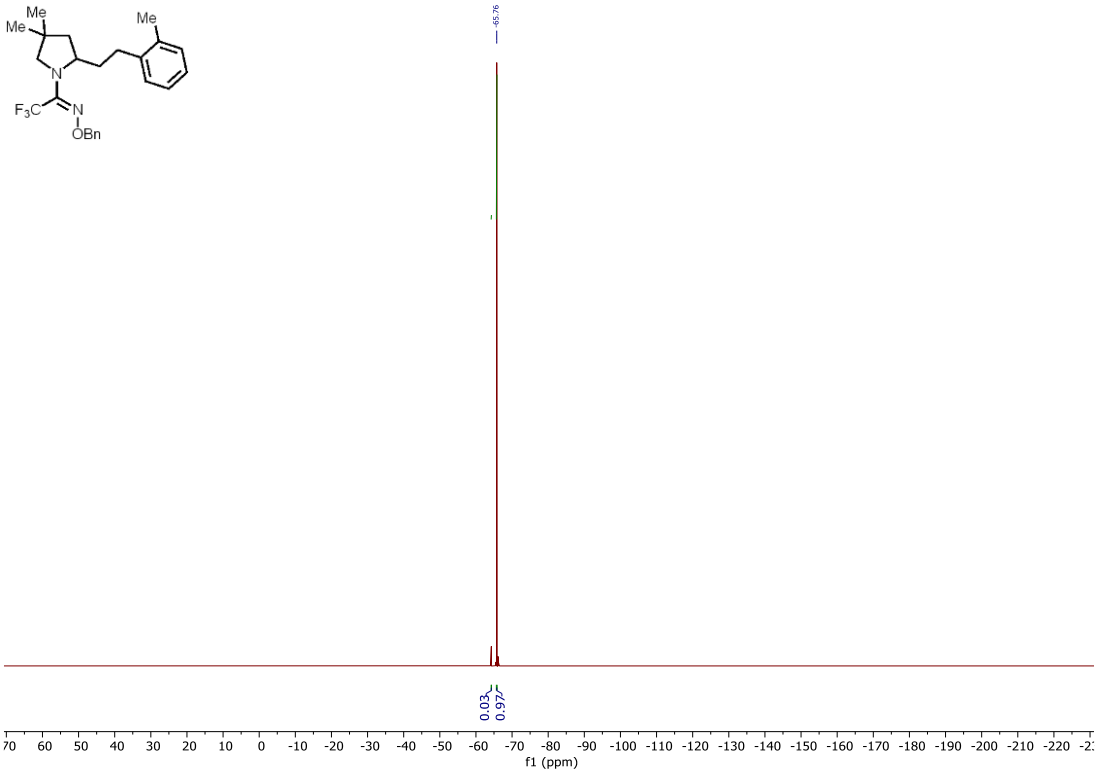



Me
Me
N
F3C
N
OBn
Me
-64.31
-65.86
0.05
0.95
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

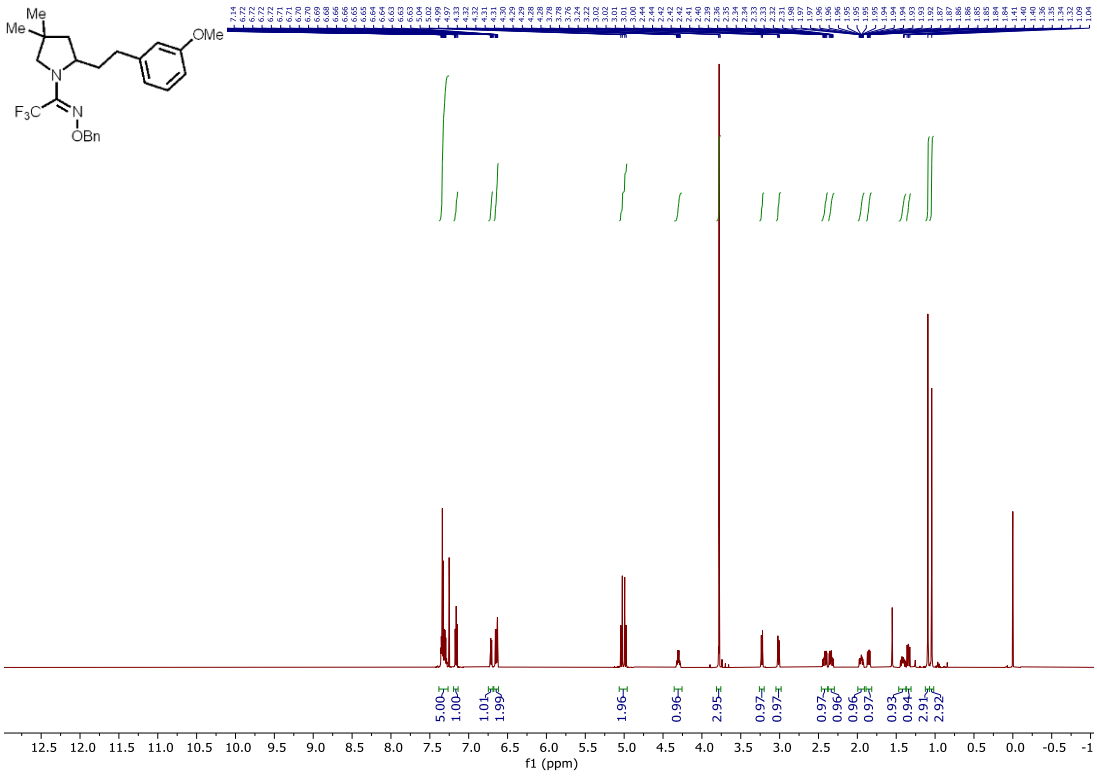
(*E*)-1-(4,4-dimethyl-2-(2-methylphenethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3b)

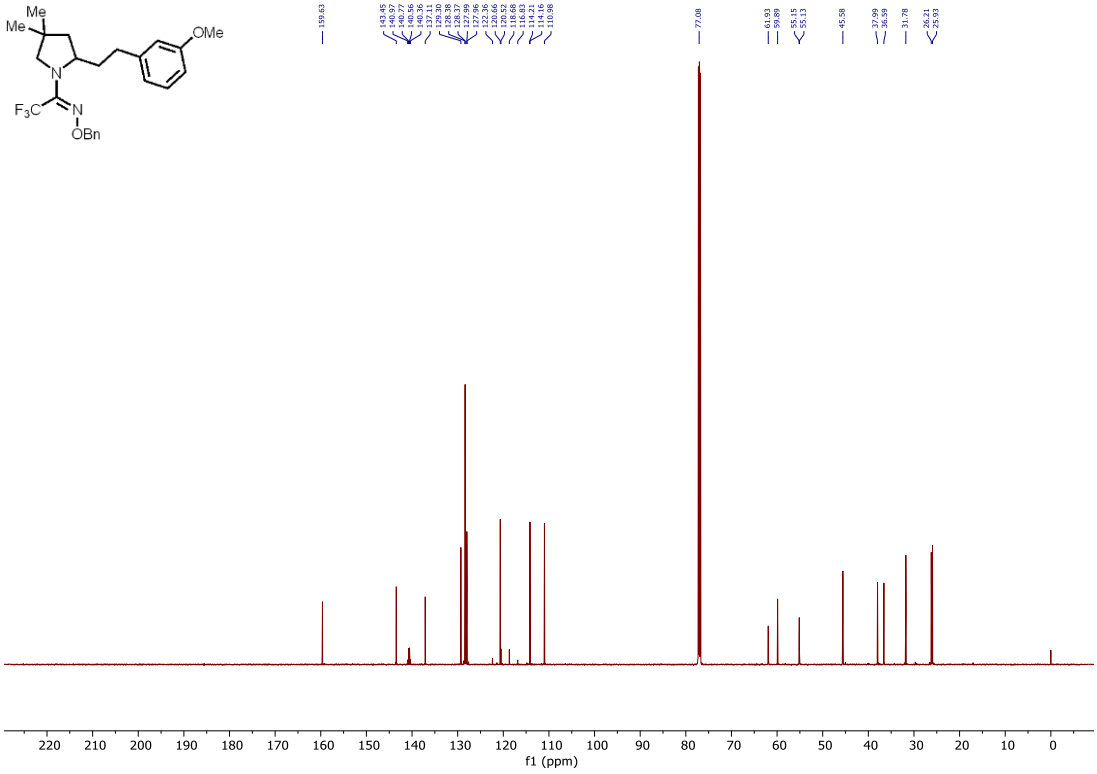


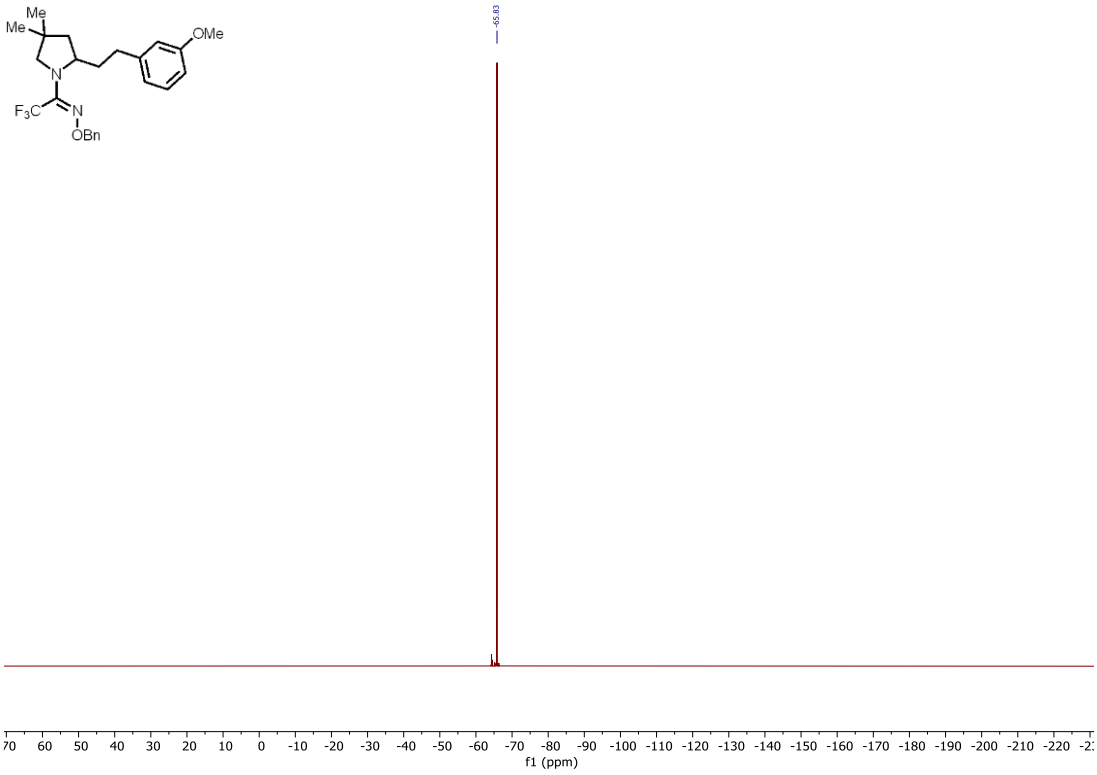



Me
Me
Me
N
F3C
N
OBn
-65.76
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

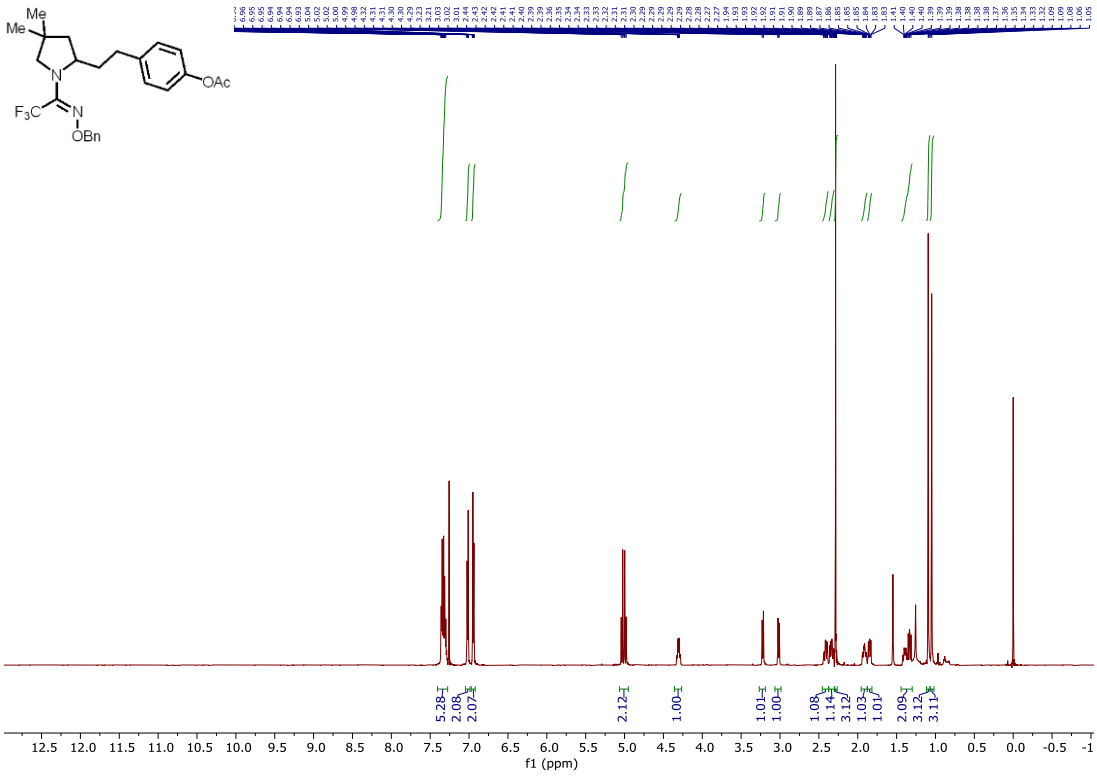
(*E*)-2,2,2-trifluoro-1-(2-(3-methoxyphenethyl)-4,4-dimethylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (3c)

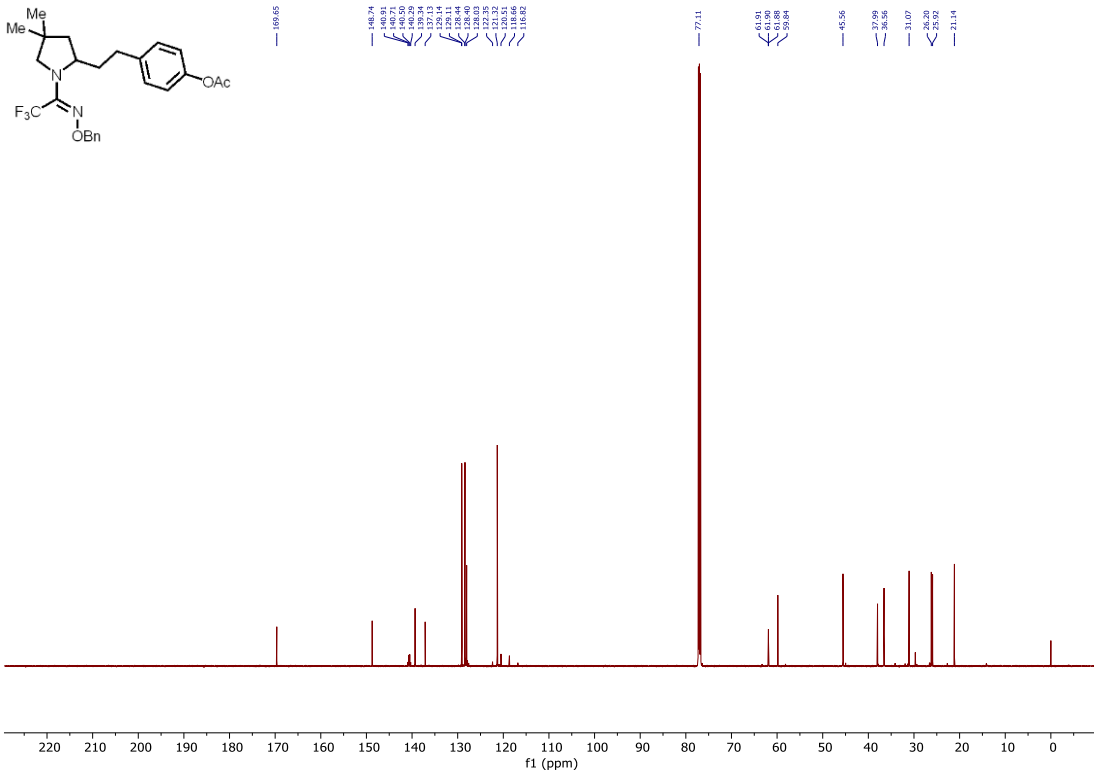


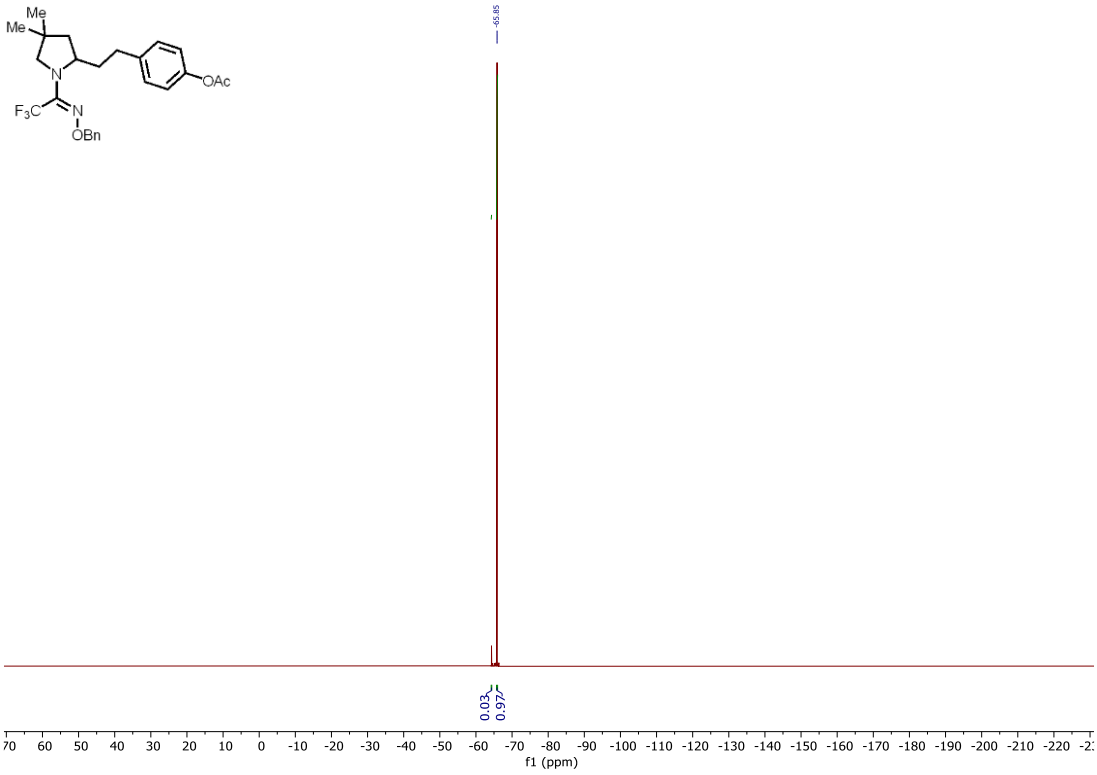



Me
Me
OMe
N
F3C
N
OBn
-65.83
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

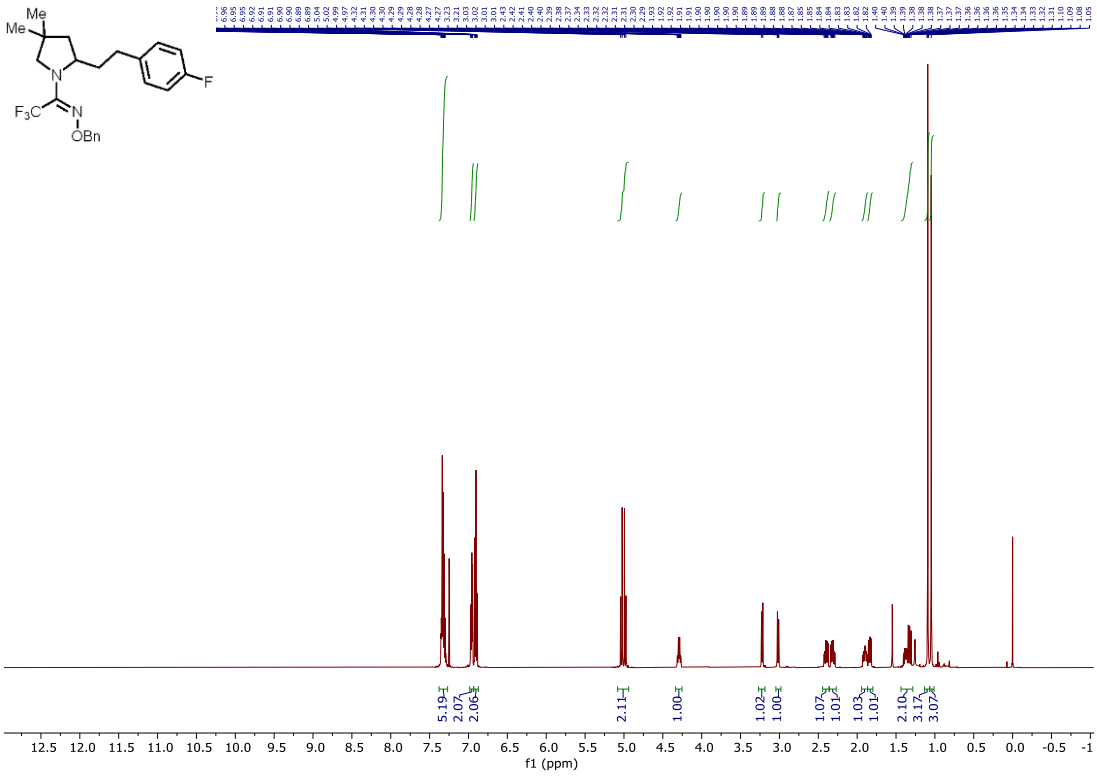
(*E*)-4-(2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)ethyl)phenyl acetate (3d)

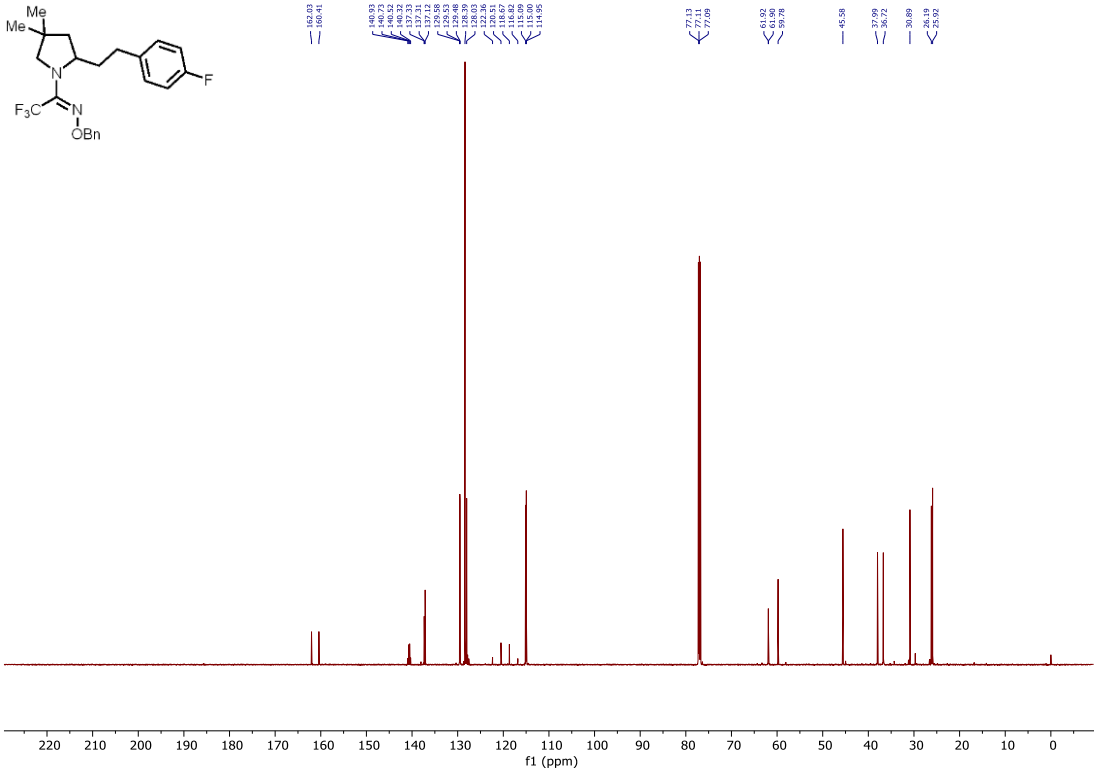


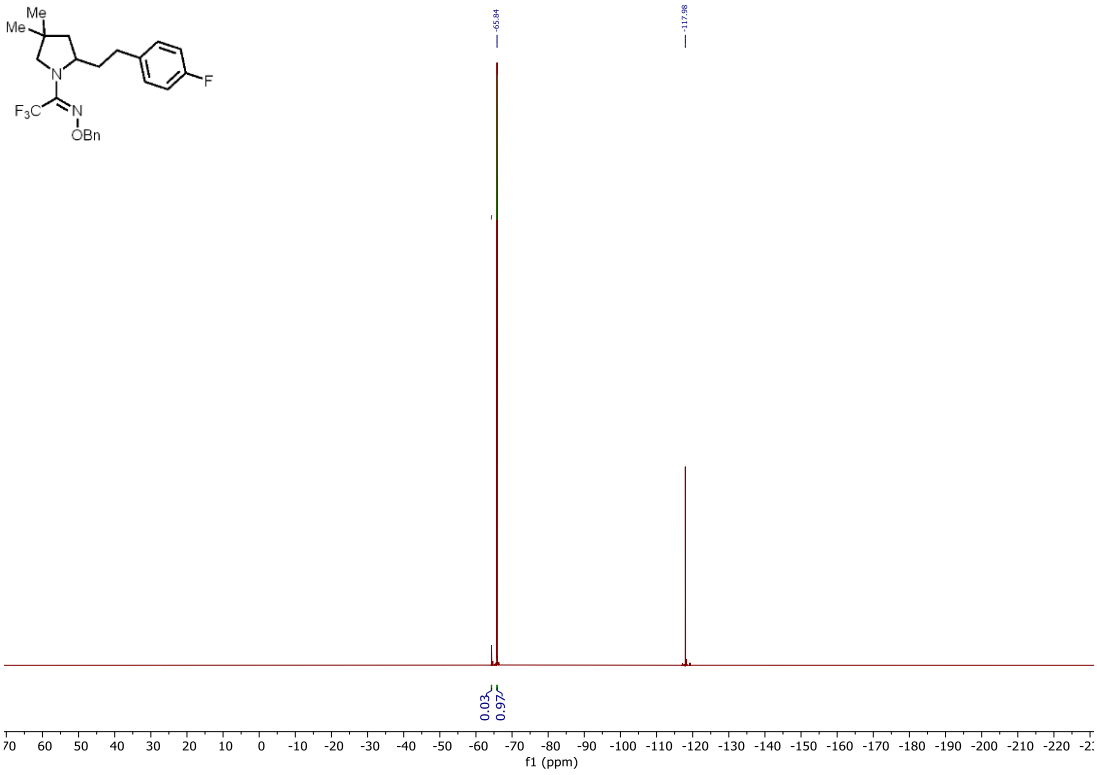


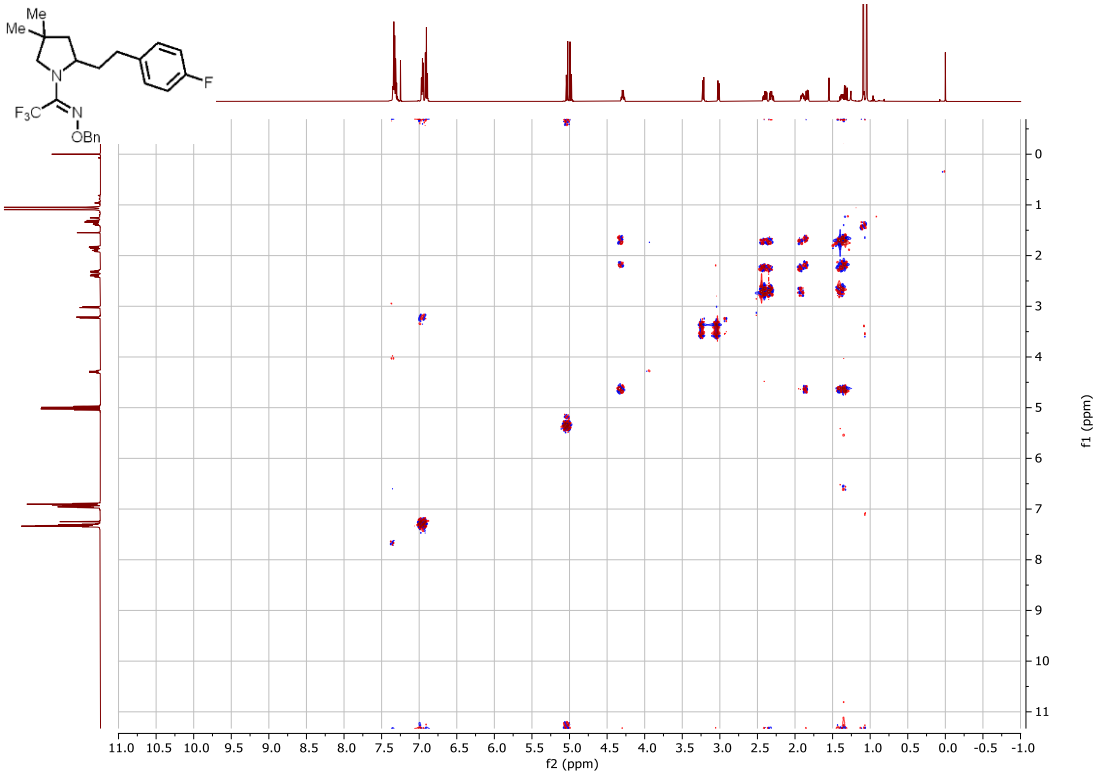

Me
Me
N
F3C
N
OBn
OAc
-65.85
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

(*E*)-2,2,2-trifluoro-1-(2-(4-fluorophenethyl)-4,4-dimethylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (3e)

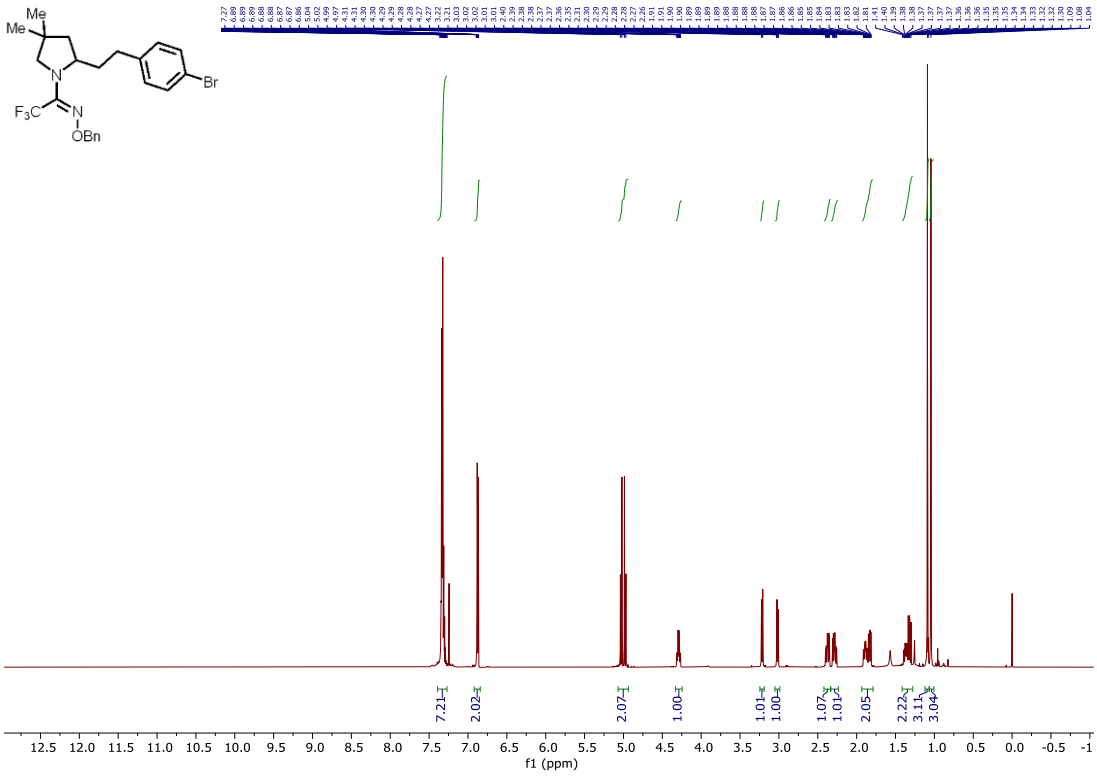


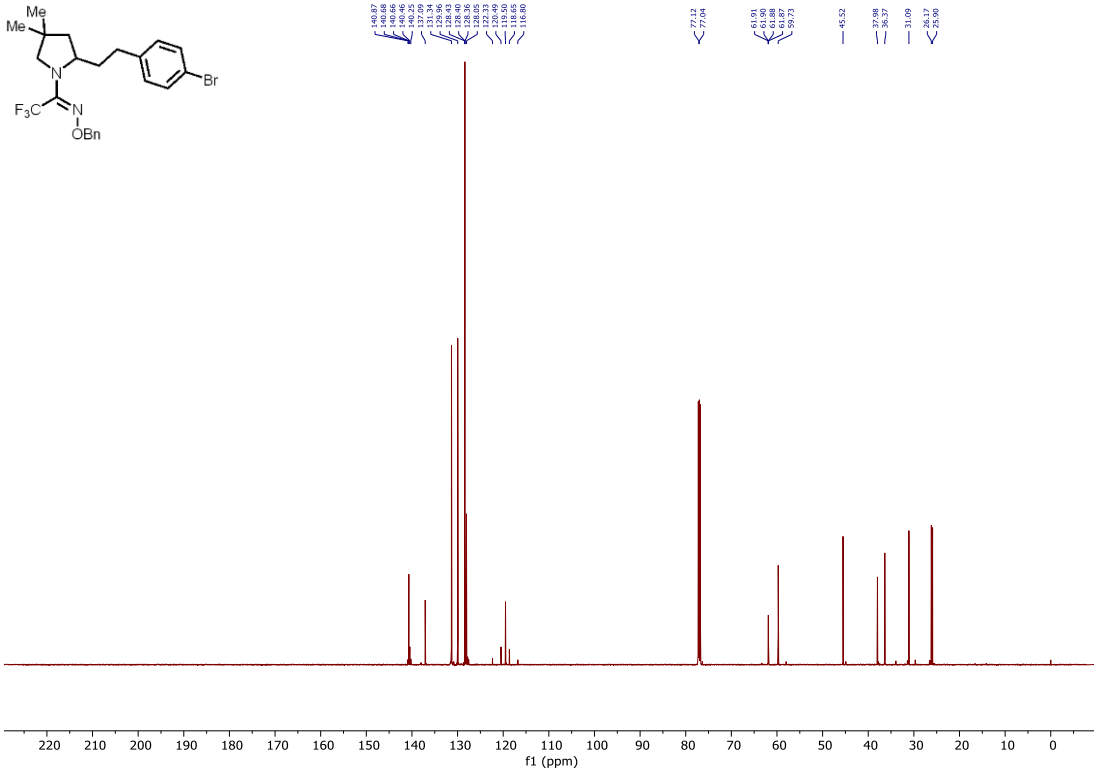


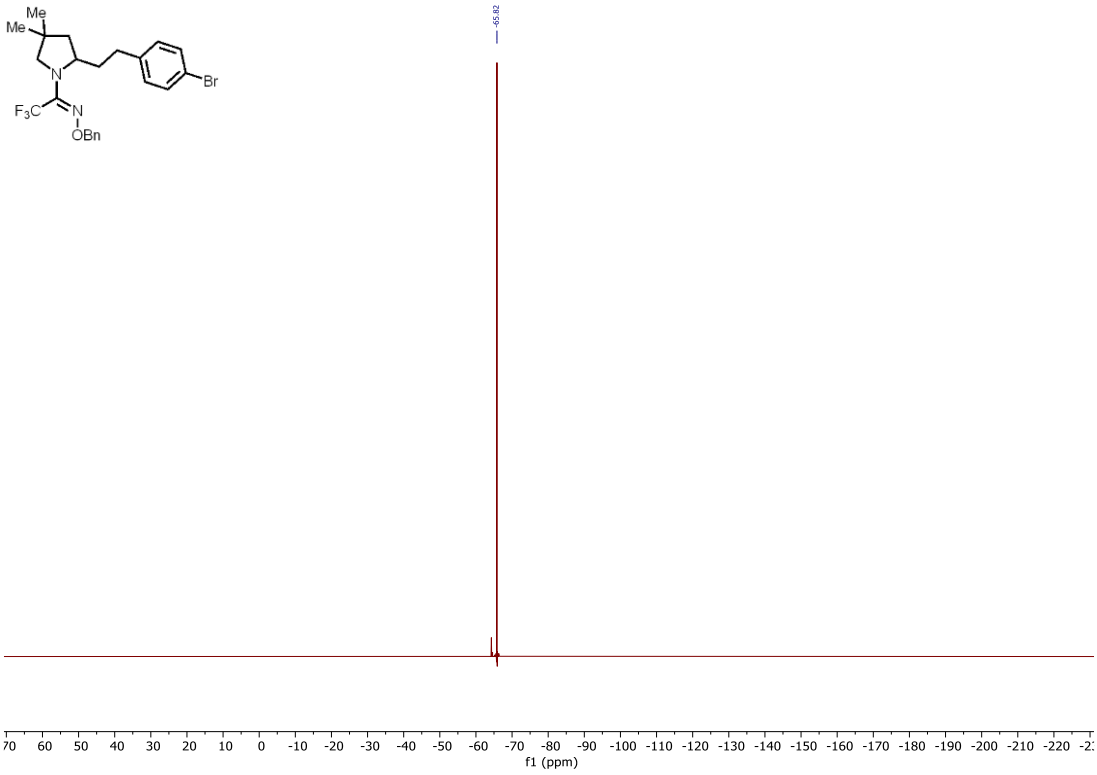

Me
Me
N
F
F3C
N
OBn
-65.84
-117.98
0.03
0.97
f1 (ppm)


Me
Me
N
F
F3C
N
OBn
f2 (ppm)
f1 (ppm)

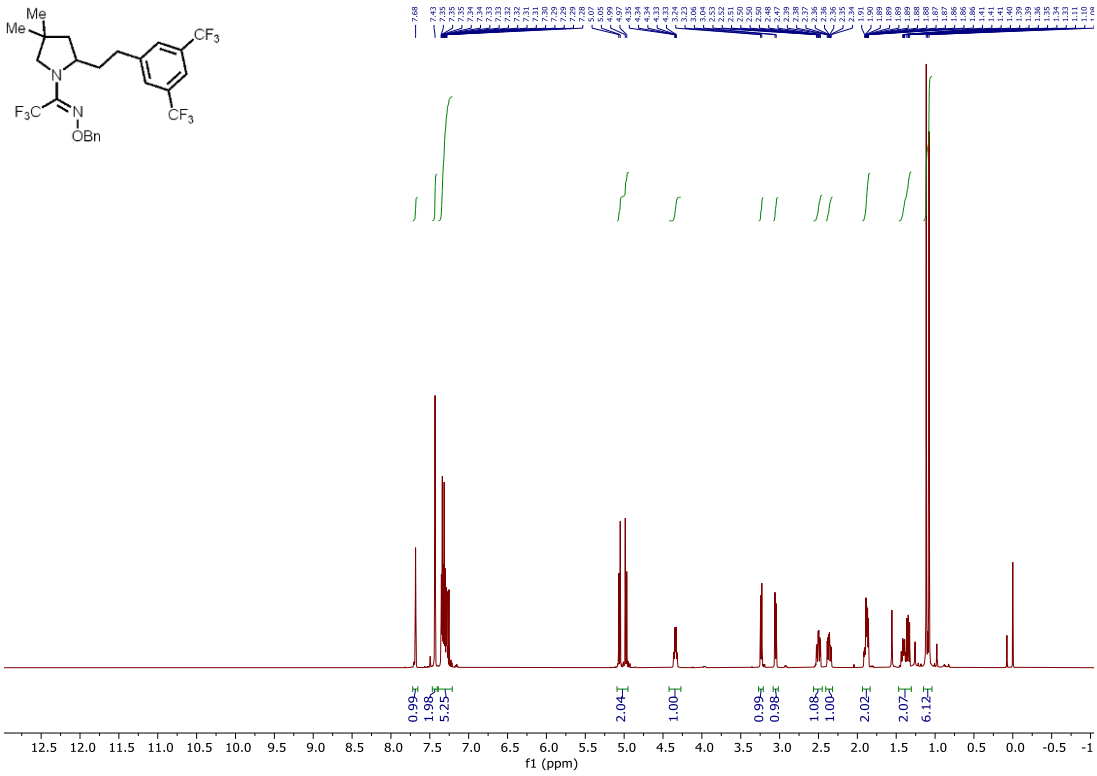
(*E*)-1-(2-(4-bromophenethyl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3f)

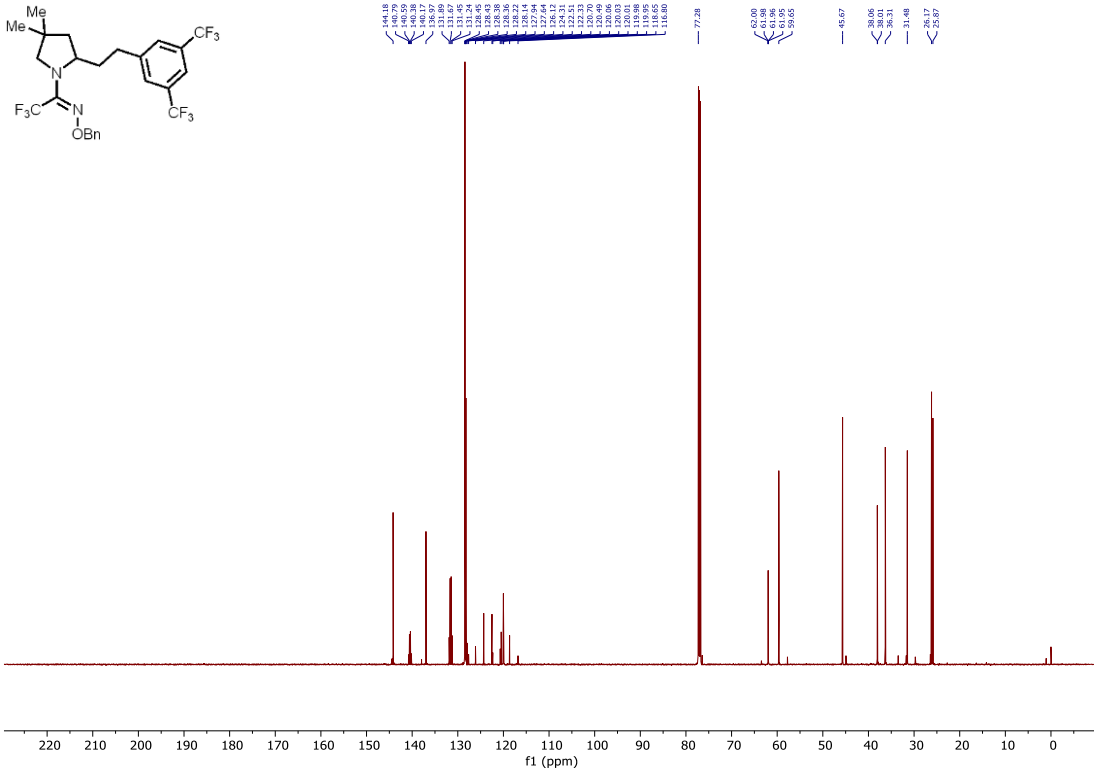


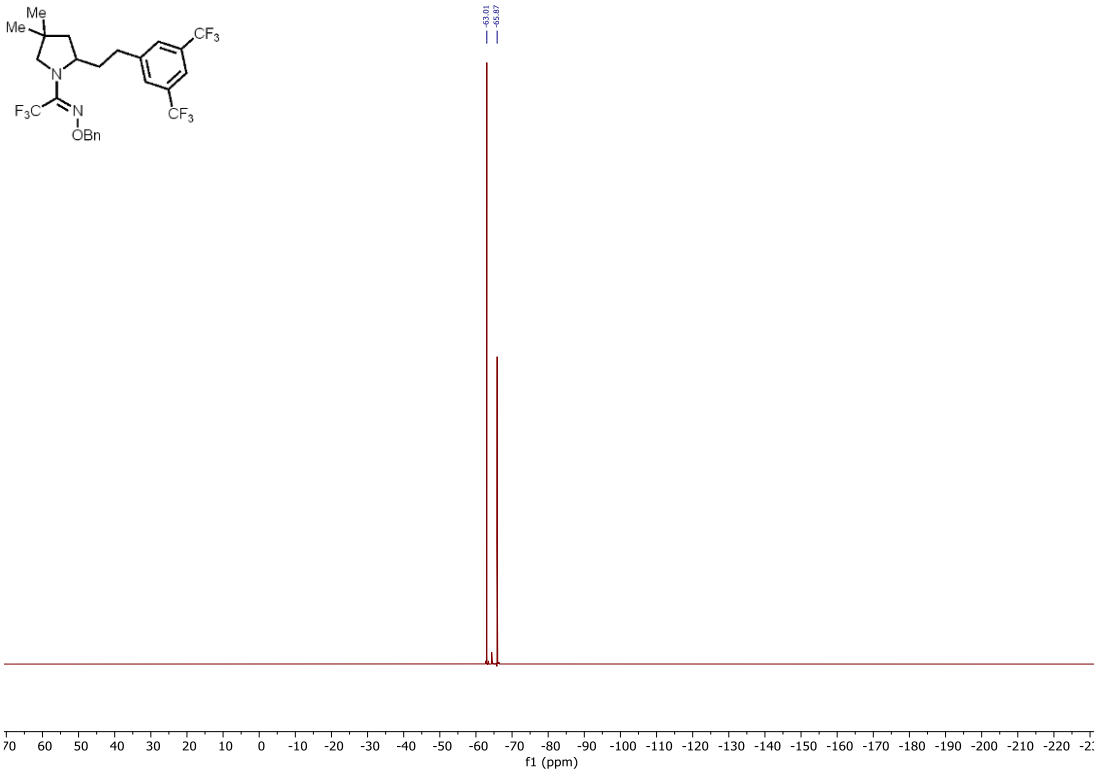



Me
Me
N
F3C
N
OBn
Br
-65.82
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

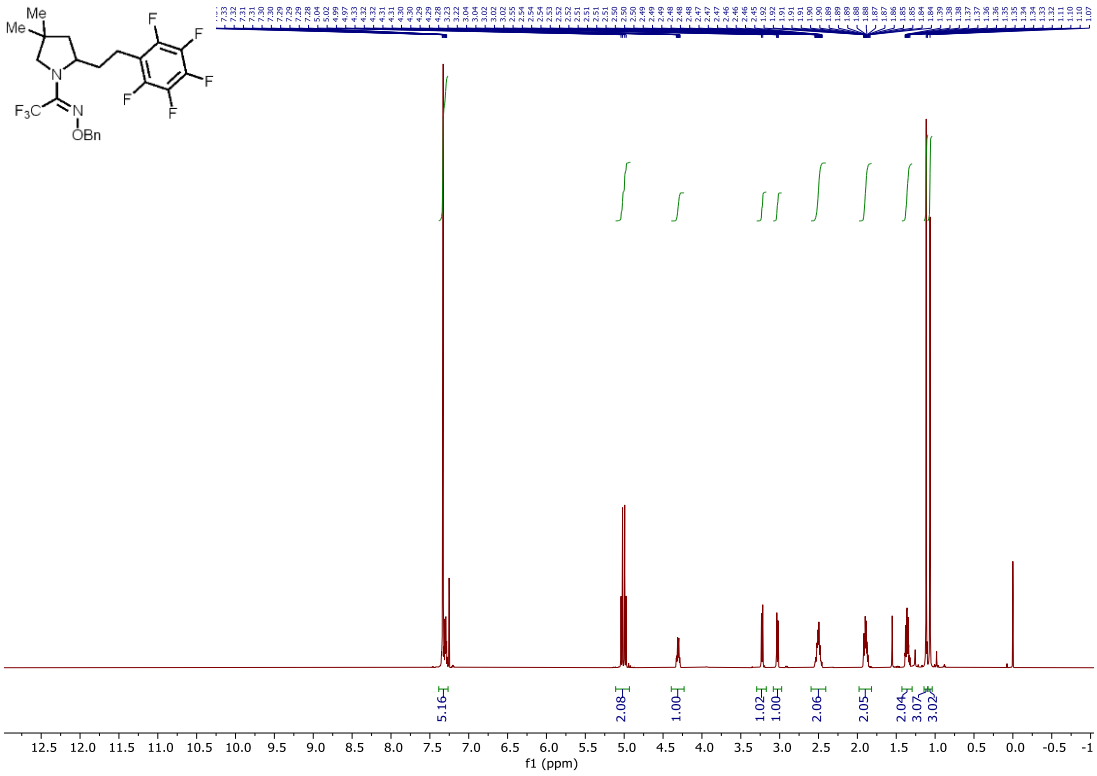
(*E*)-1-(2-(3,5-bis(trifluoromethyl)phenethyl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3g)

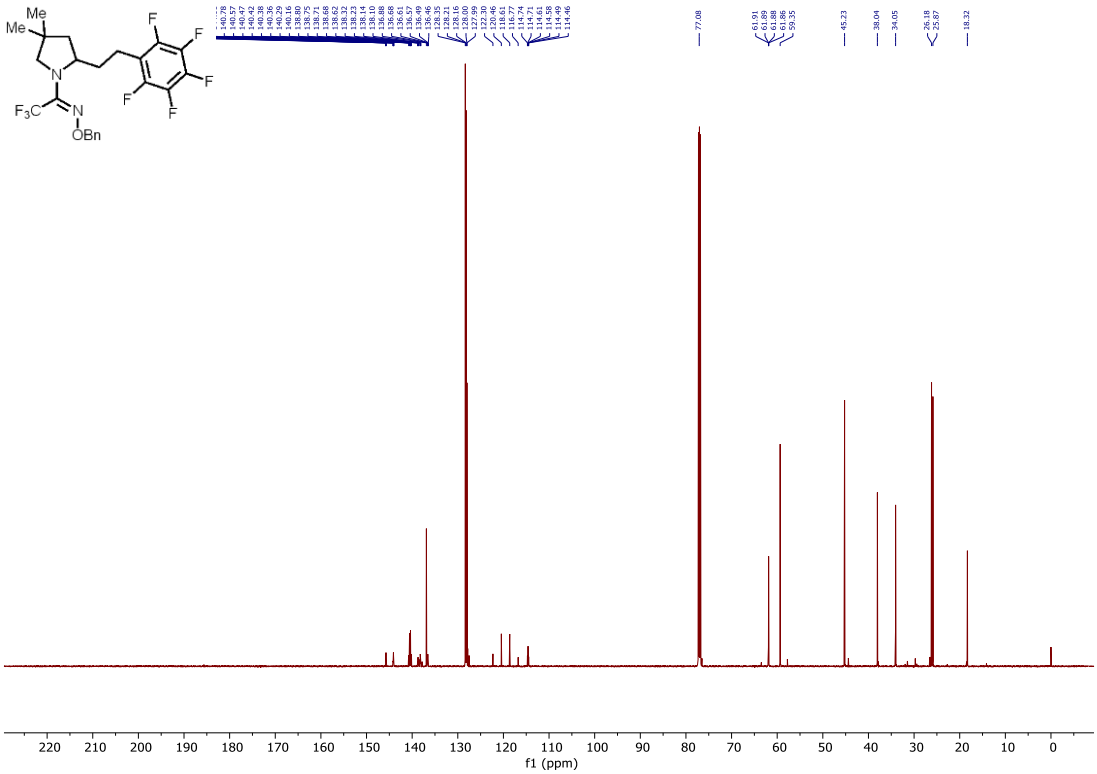


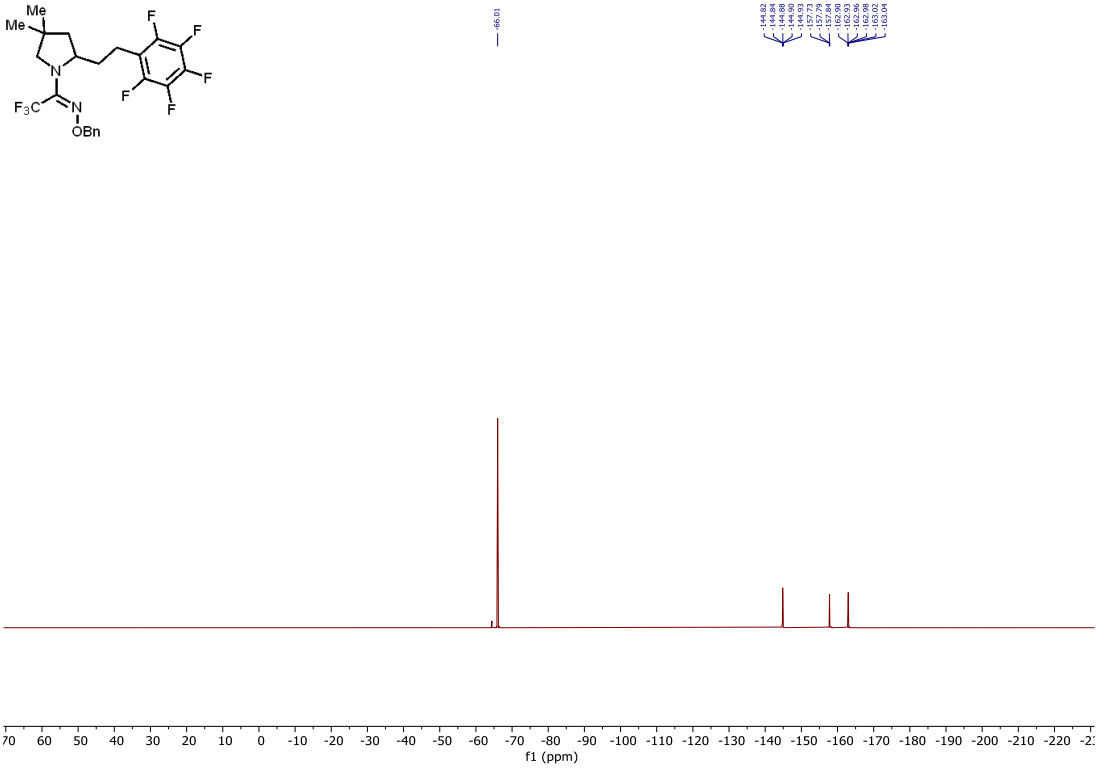



Me
Me
N
F3C
N
OBn
CF3
CF3
-63.01
-65.87
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

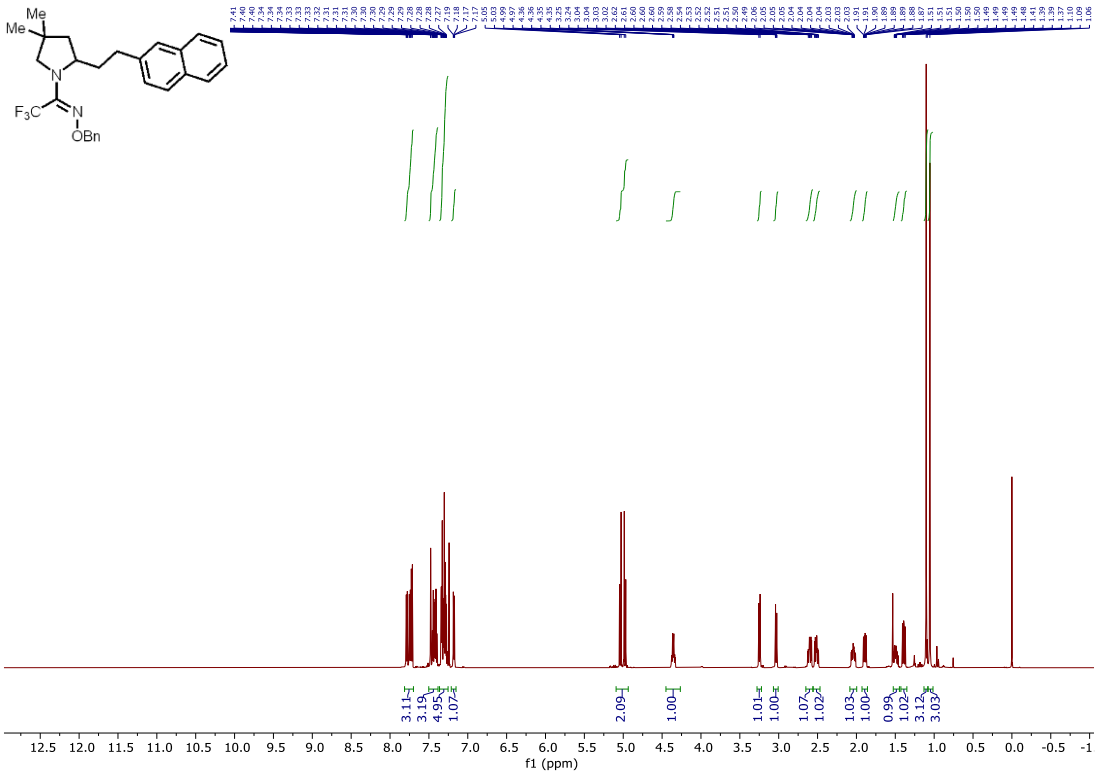
(*E*)-1-(4,4-dimethyl-2-(2-(perfluorophenyl)ethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3h)

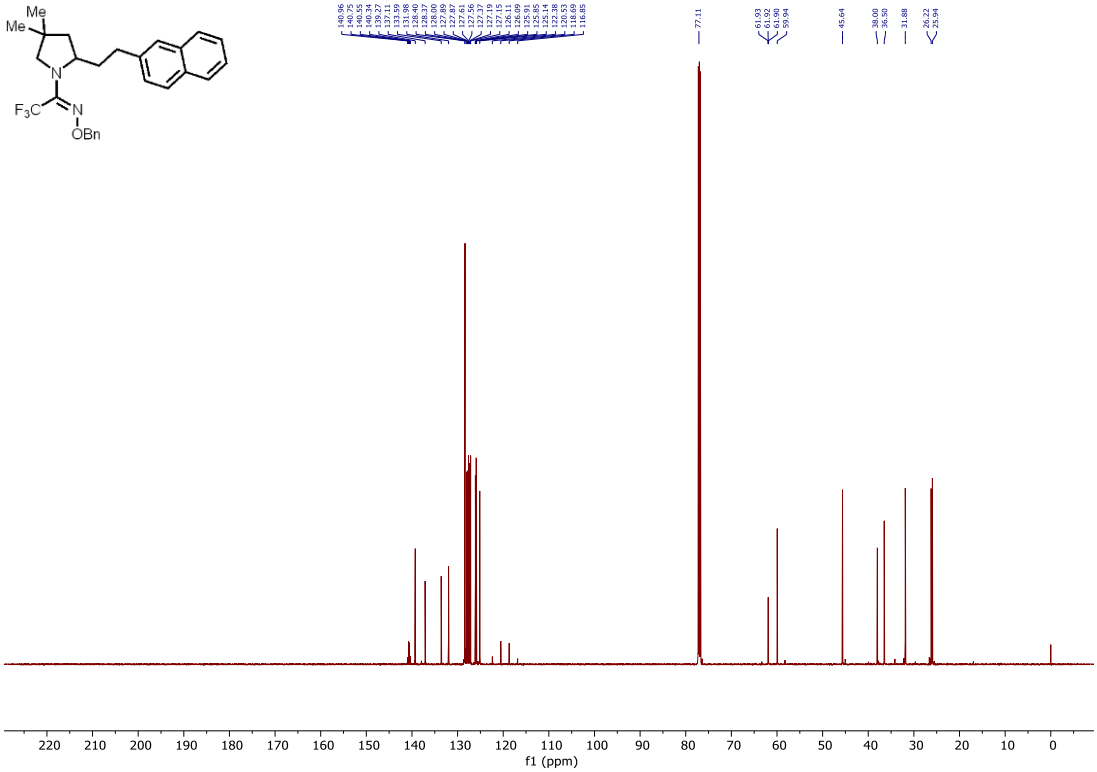


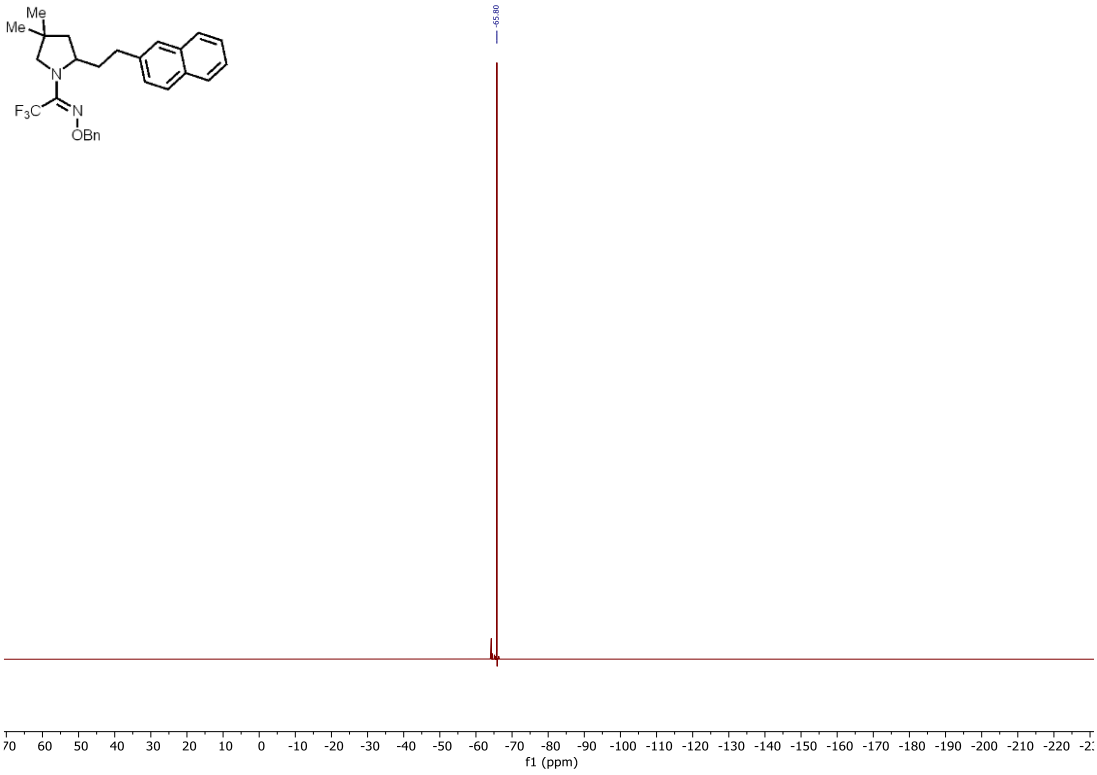



Me
Me
N
F3C
N
OBn
F
F
F
F
F
-66.01
-144.82
-144.84
-144.88
-144.90
-144.93
-157.73
-157.79
-157.84
-157.90
-162.93
-162.96
-162.98
-163.02
-163.04
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

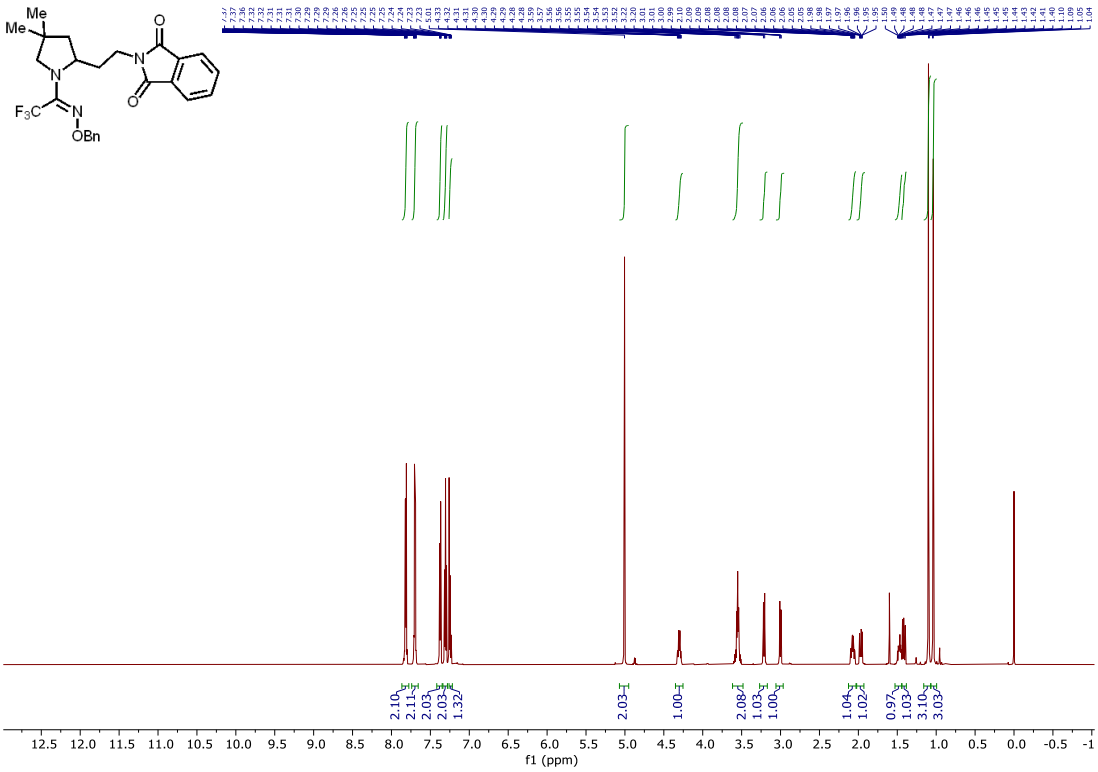
(*E*)-1-(4,4-dimethyl-2-(2-(naphthalen-2-yl)ethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3i)

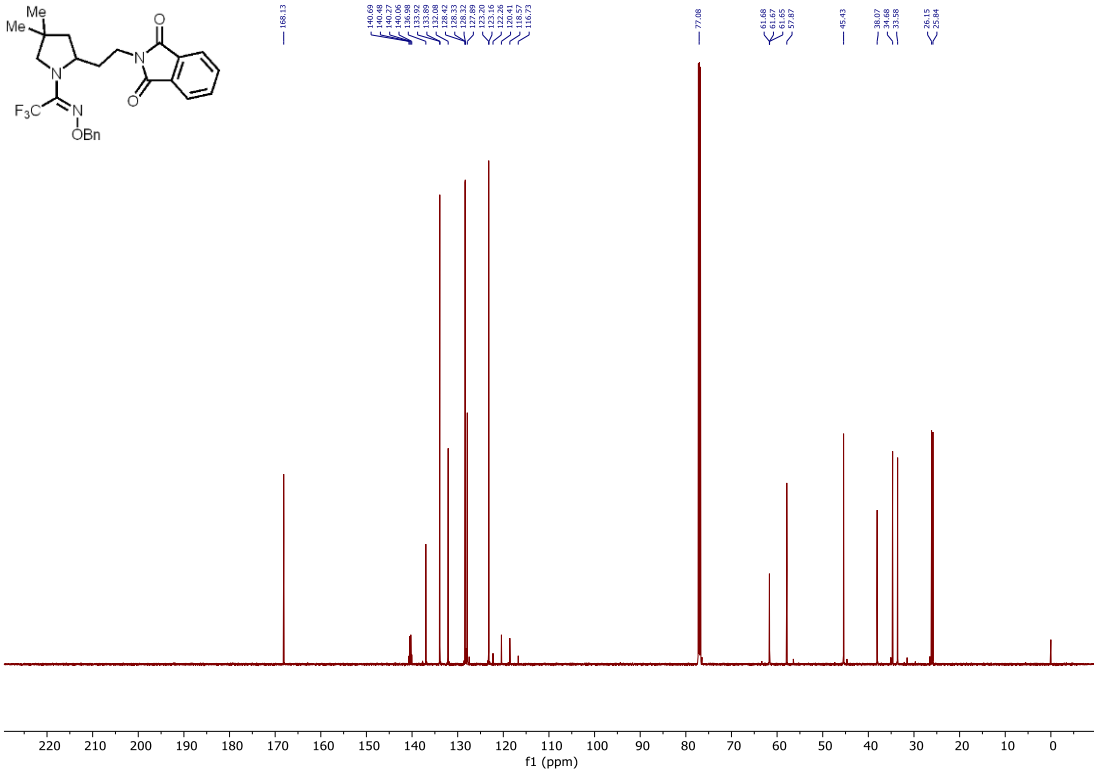


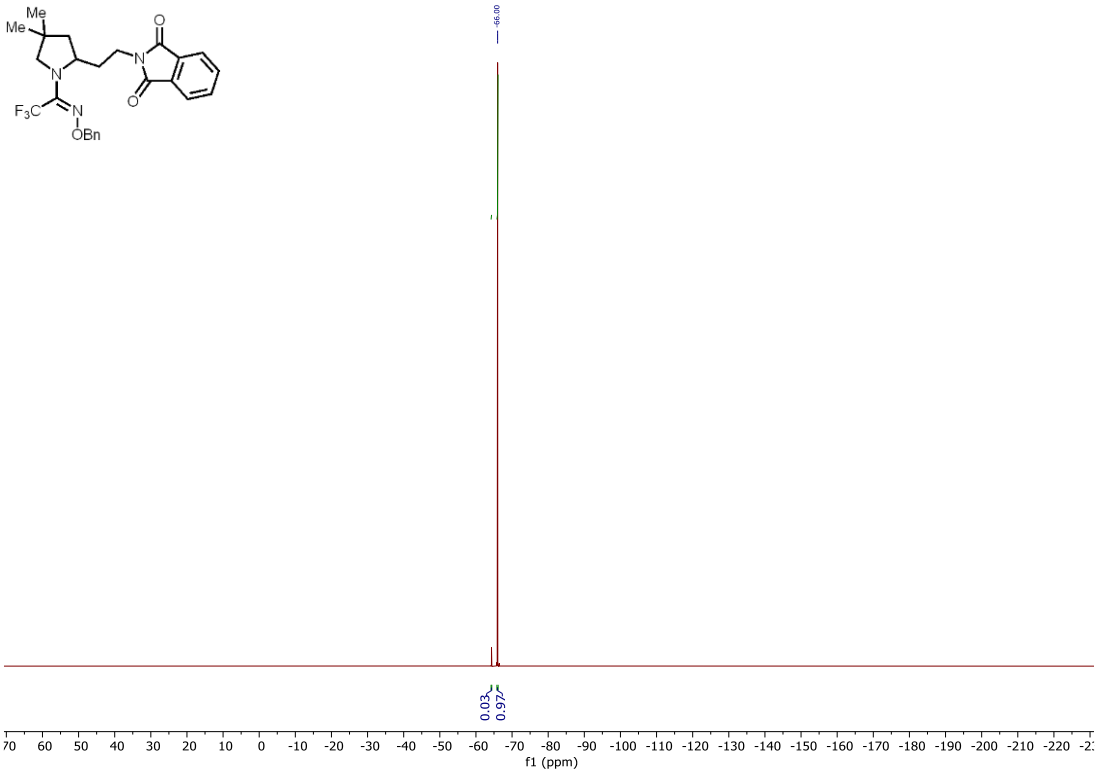



Me
Me
N
F3C
N
OBn
-65.80
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

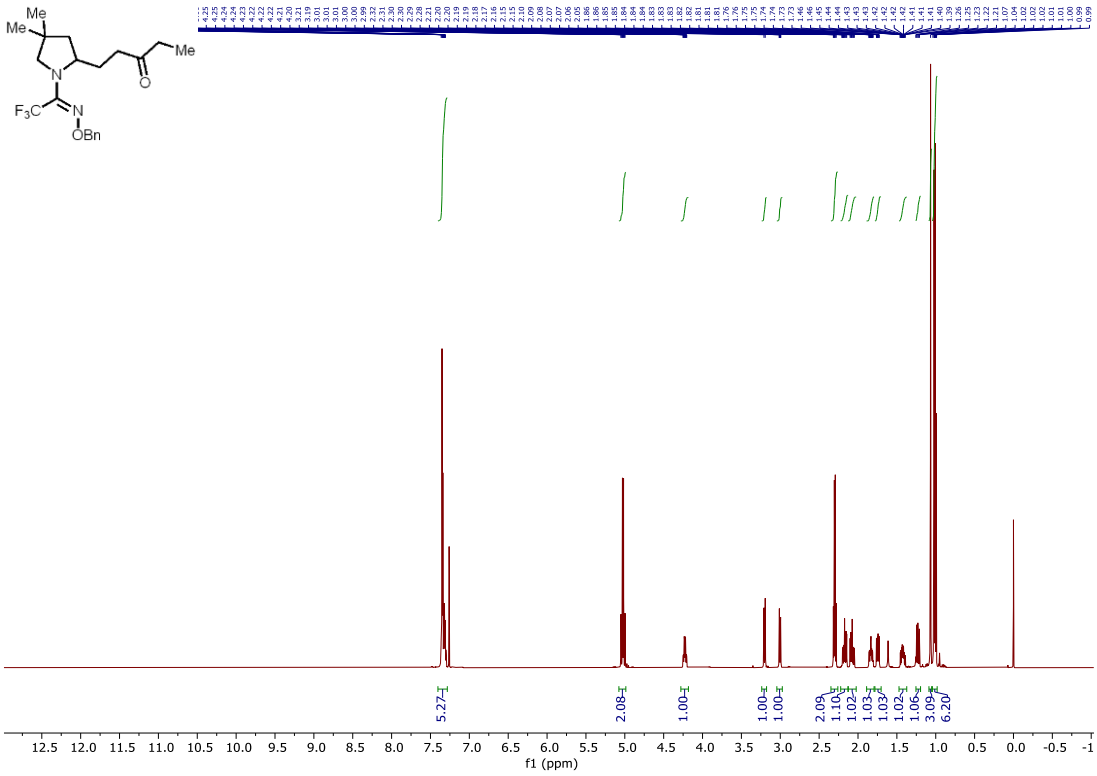
(*E*)-2-(2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)ethyl)isoindoline-1,3-dione (3j)

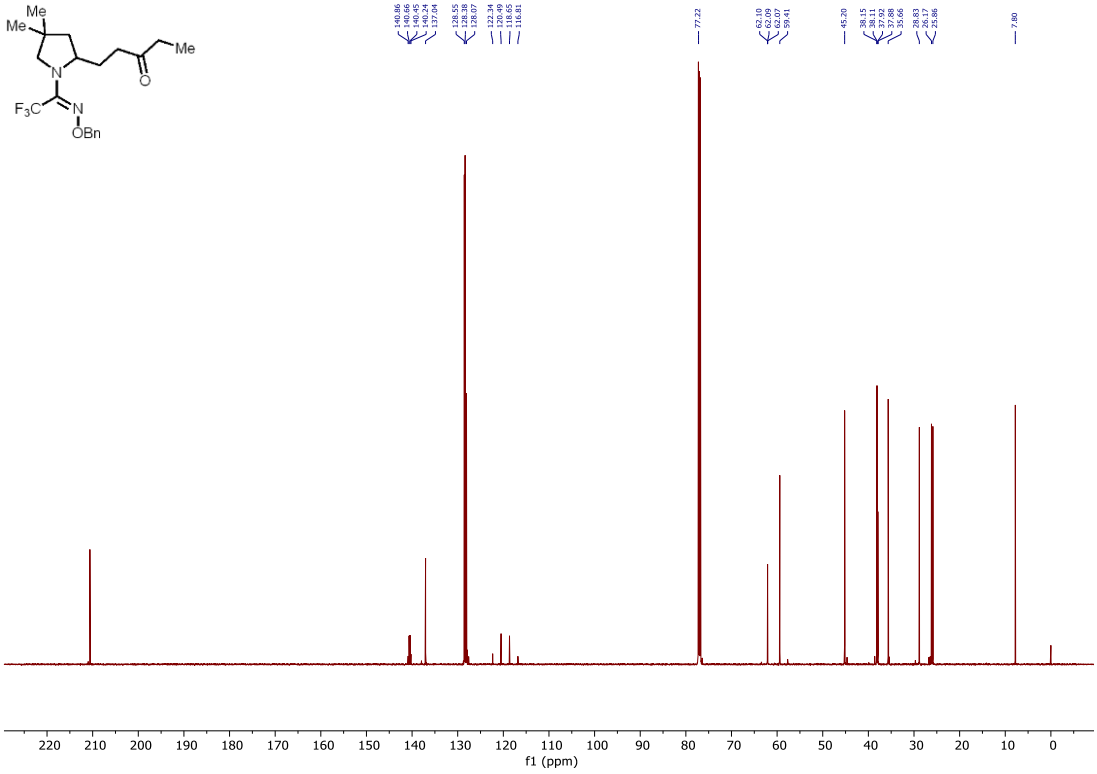


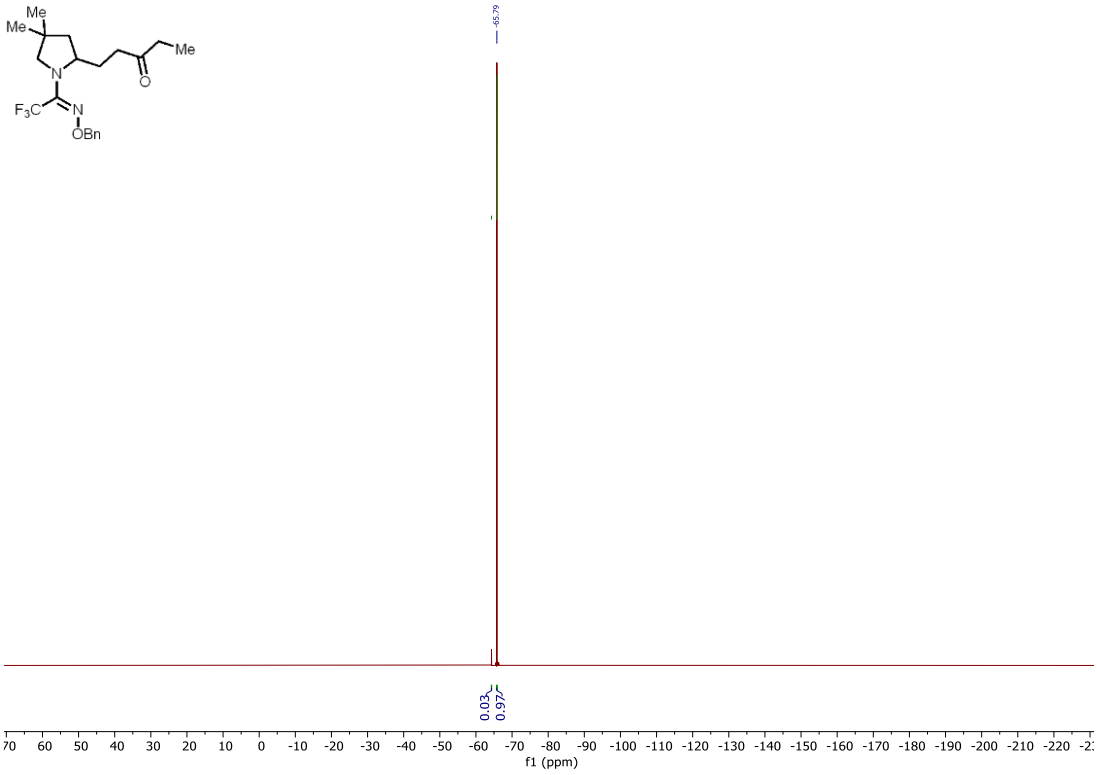



Me
Me
N
F3C
N
OBn
O
N
O
-66.00
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

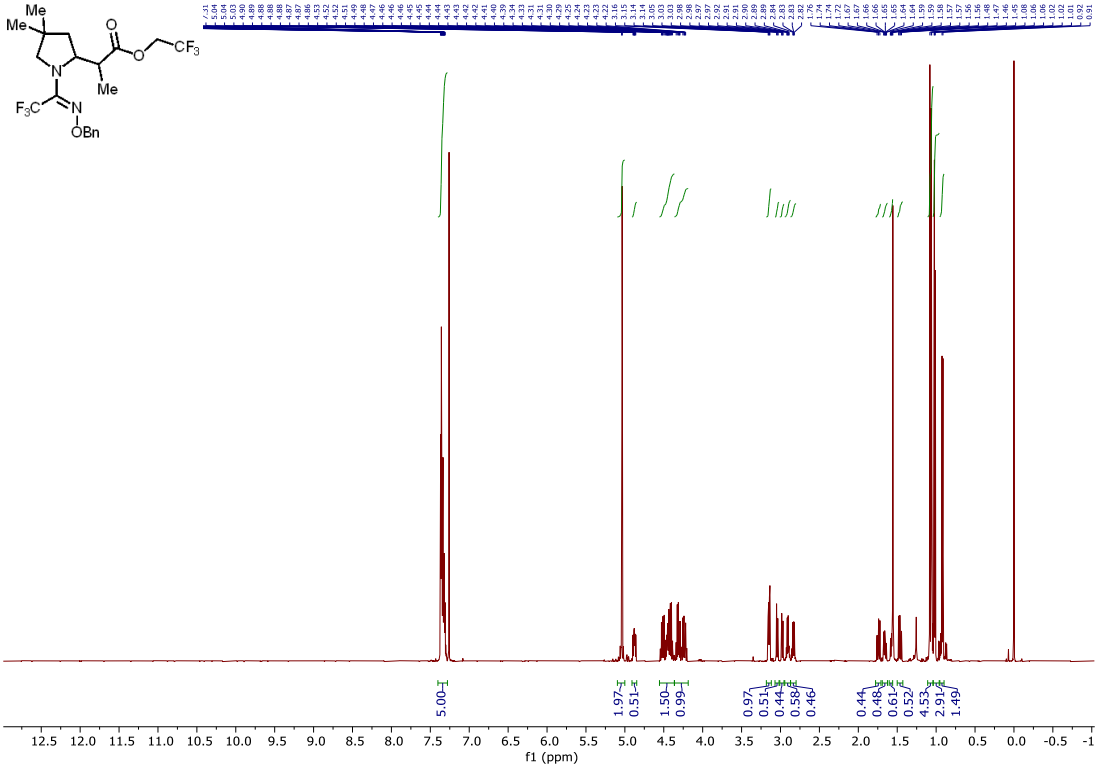
(*E*)-1-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)pentan-3-one (3k)

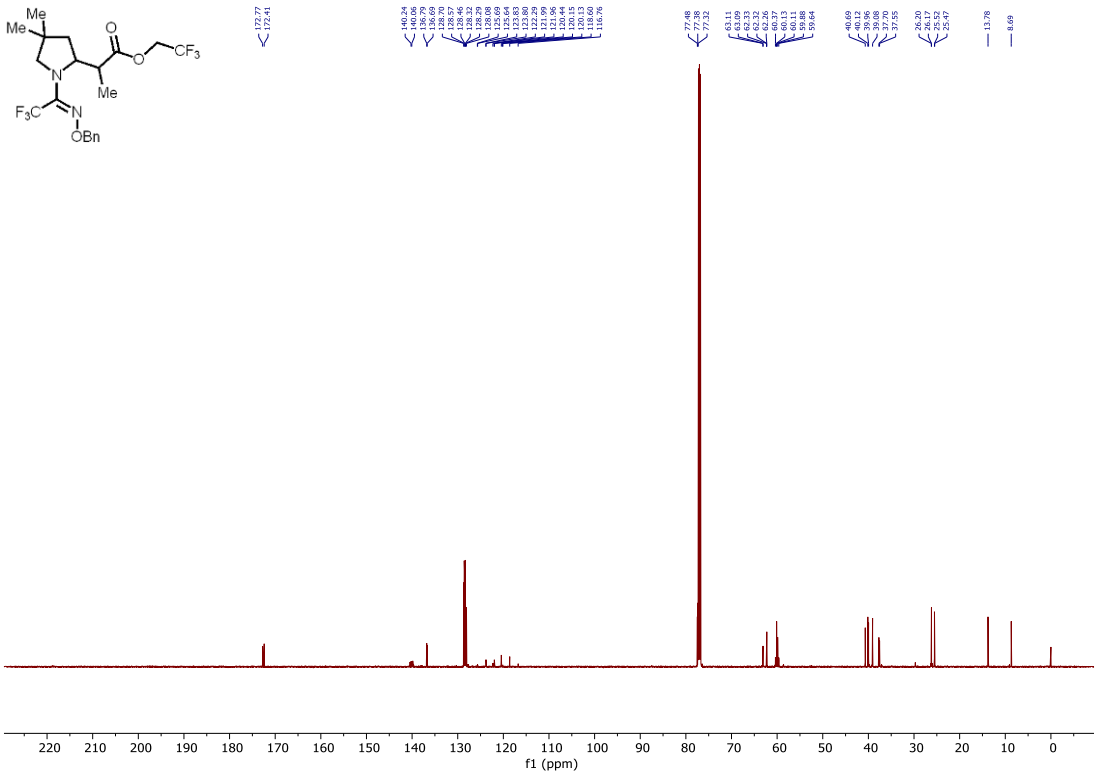


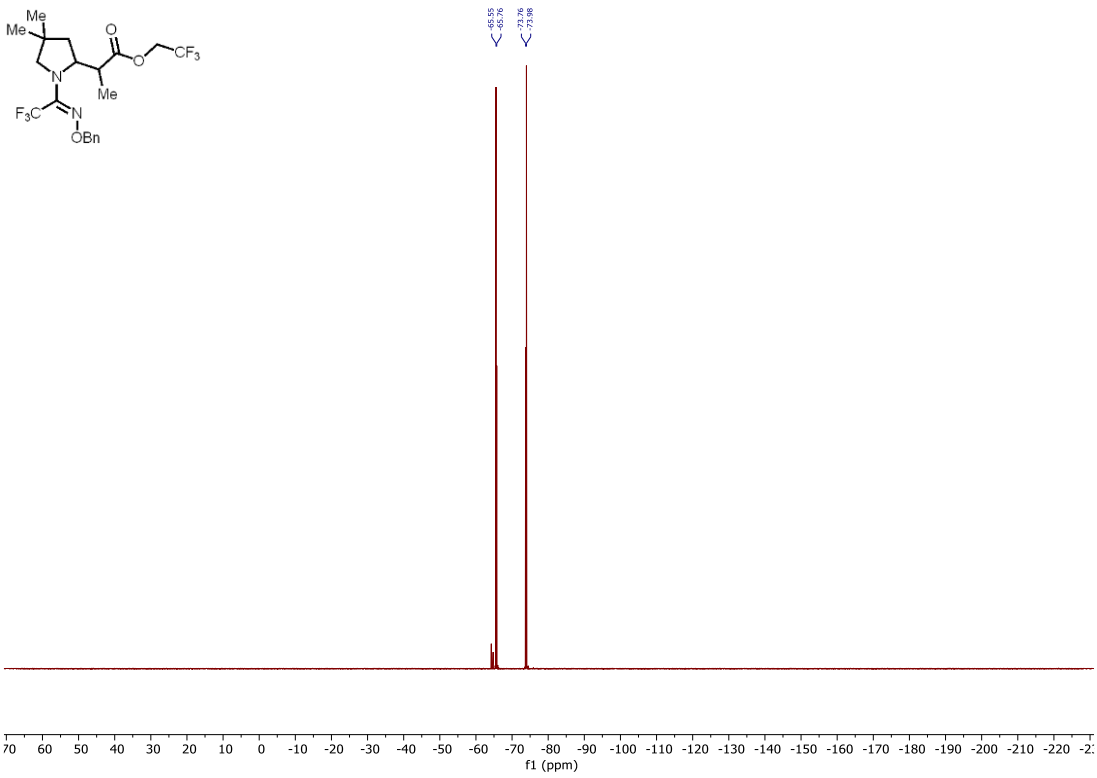



Me
Me
Me
N
O
F3C
N
OBn
-65.79
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

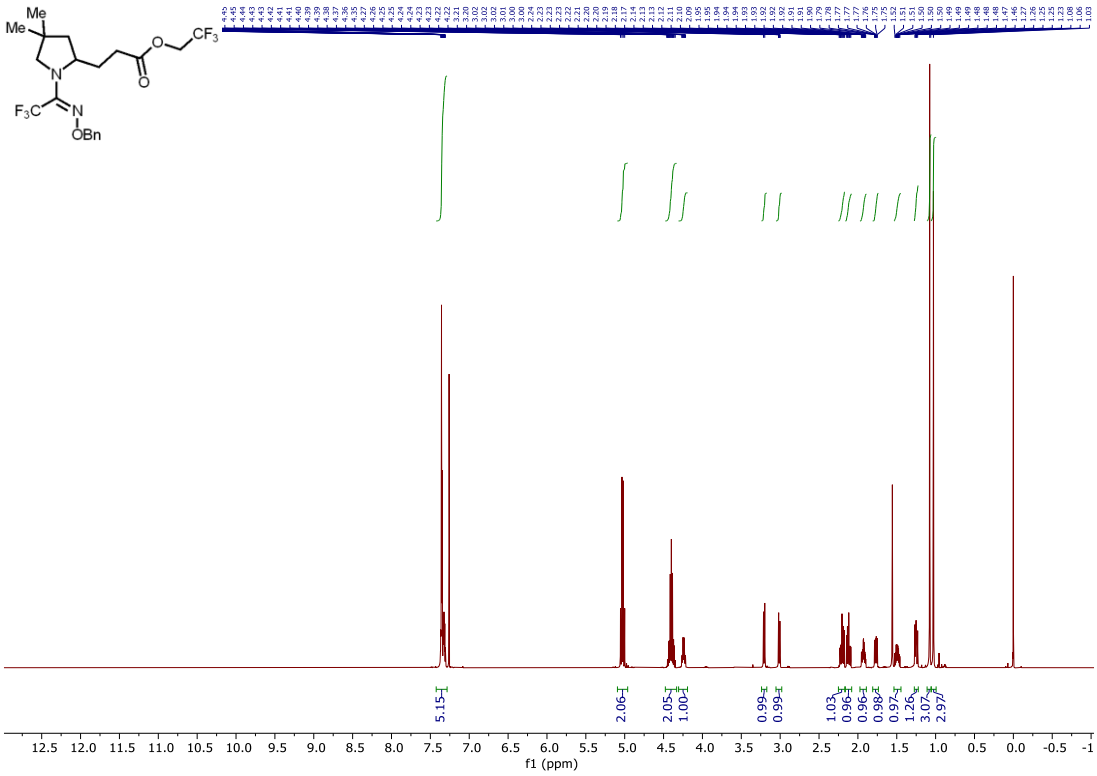
2,2,2-trifluoroethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (3l-B)

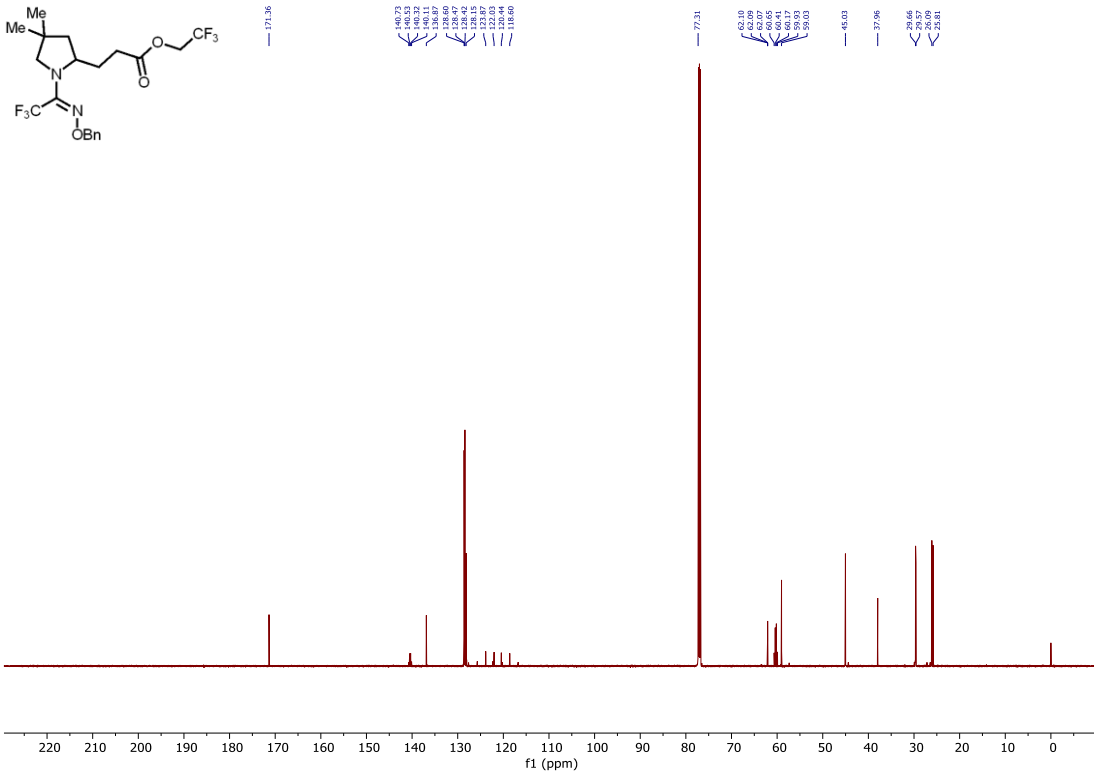


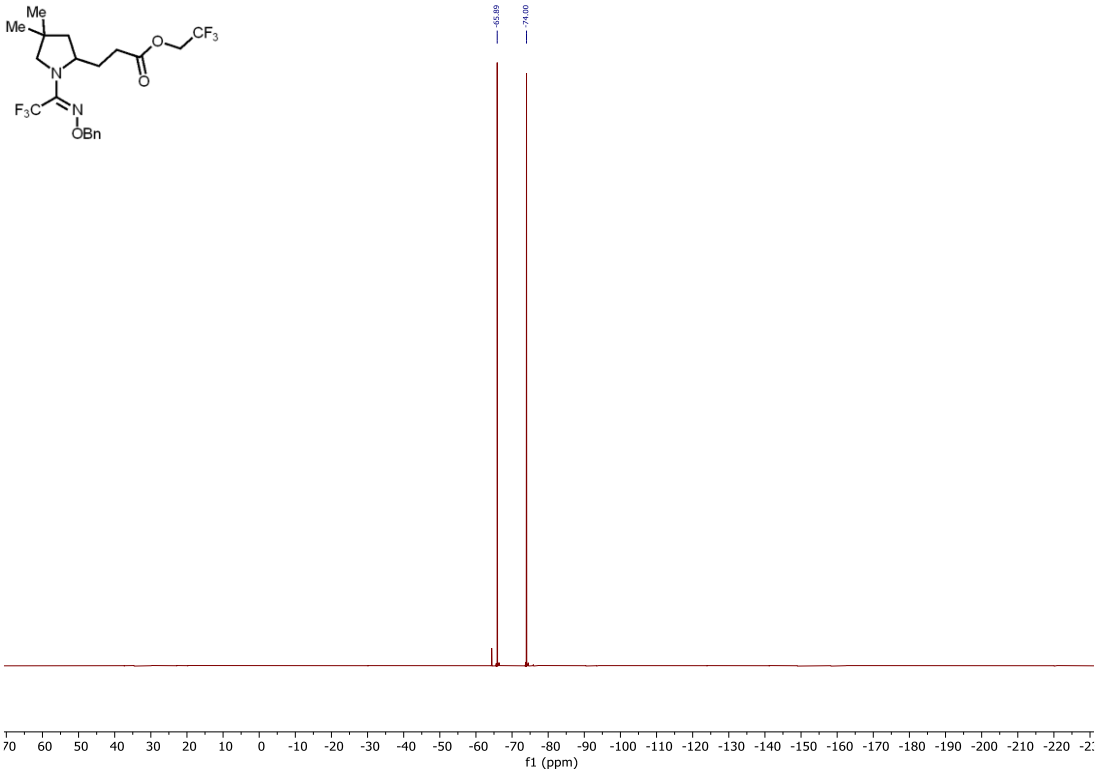



Me
Me
O
O
CF3
N
Me
F3C
N
OBn
-65.55
-65.70
-73.76
-73.98
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

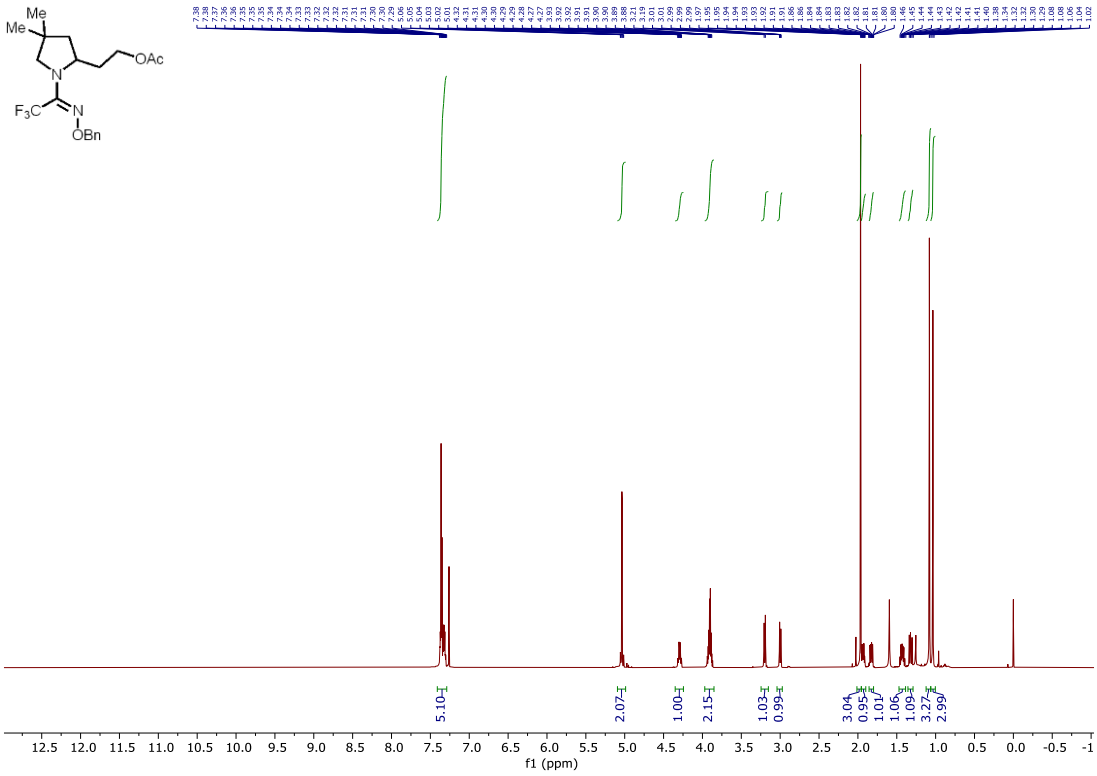
2,2,2-trifluoroethyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)propanoate (3l-L)

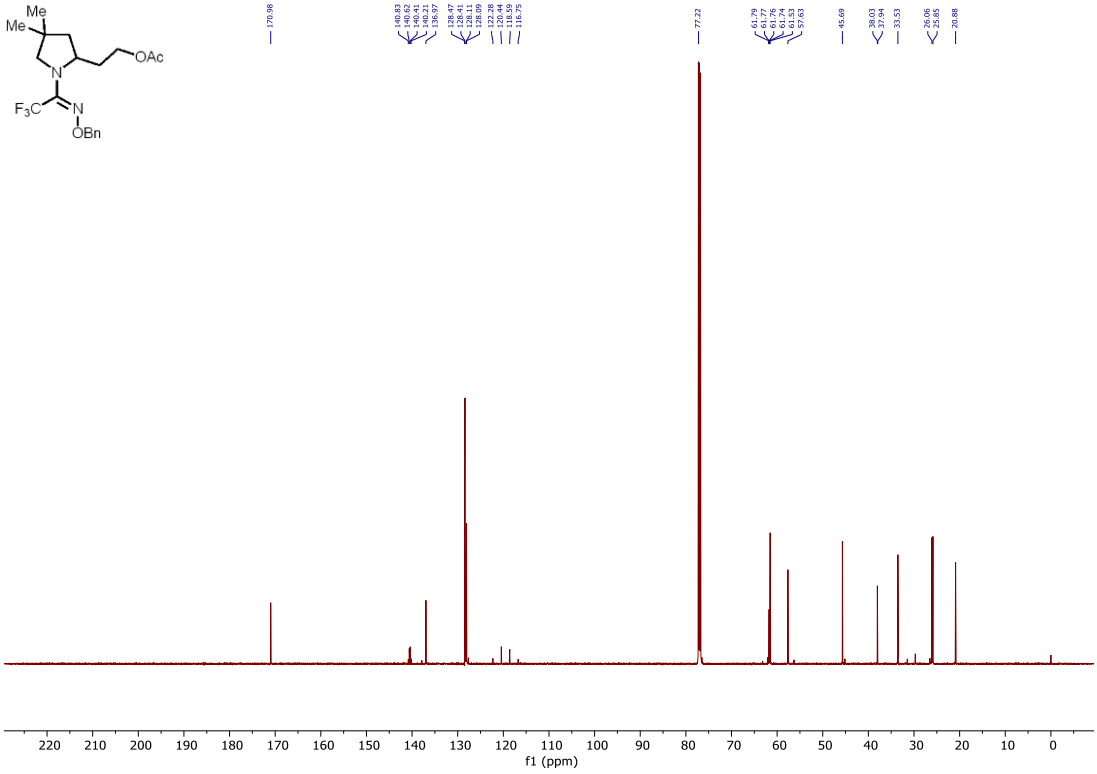


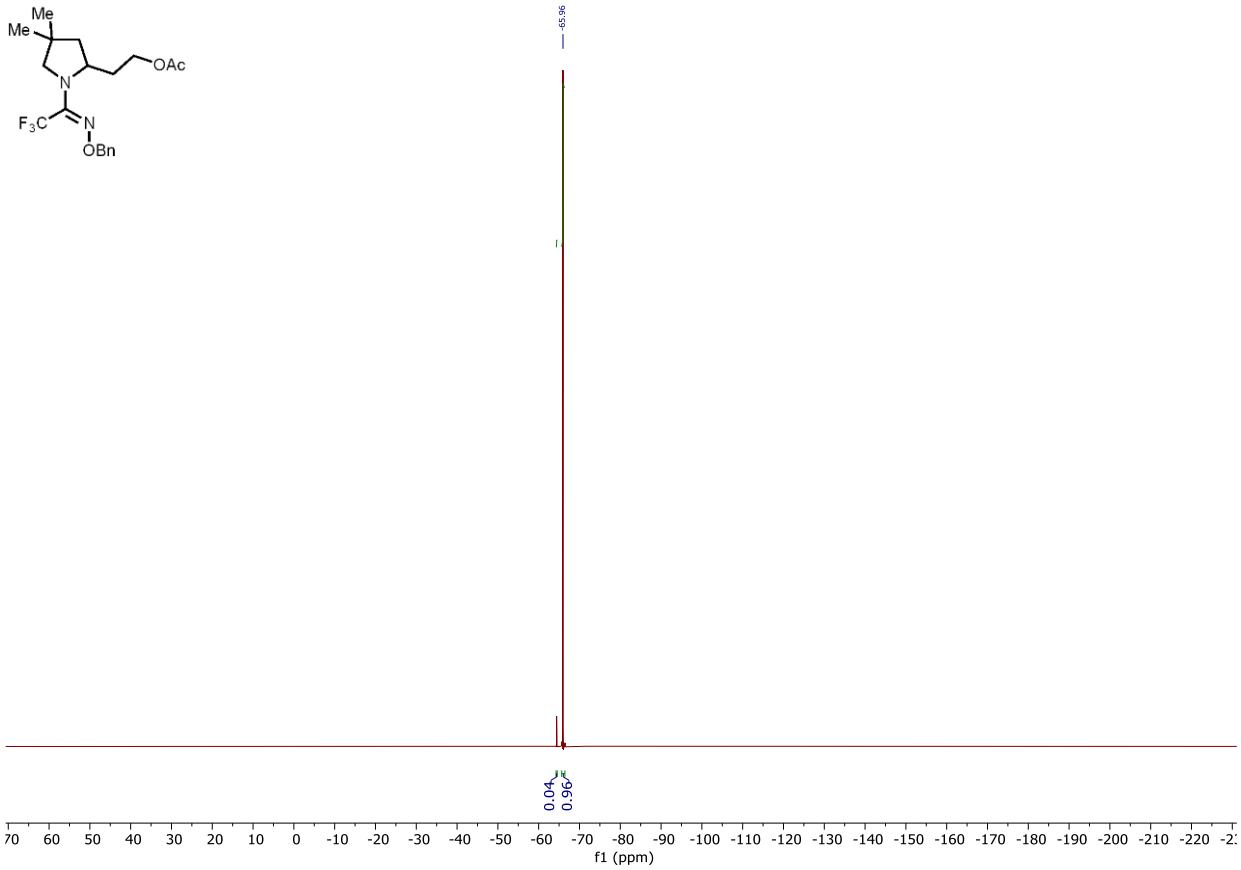



Me
Me
N
O
O
CF3
F3C
N
OBn
-65.89
-74.00
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

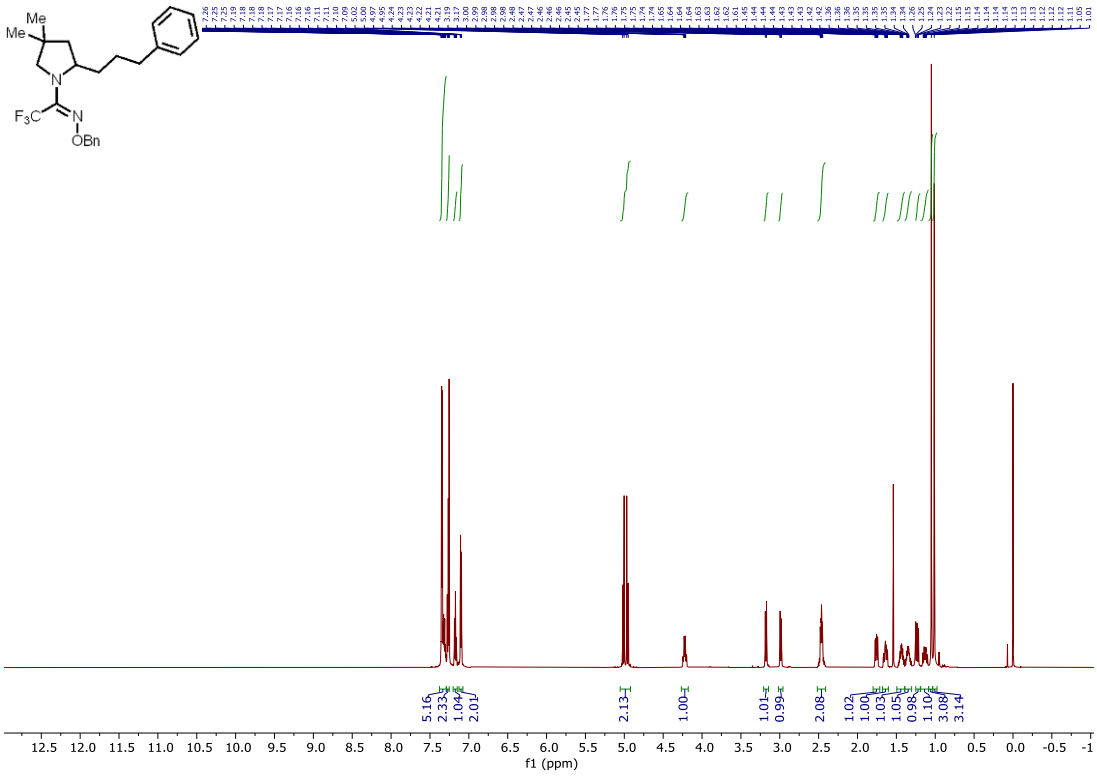
(*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)ethyl acetate (3m)

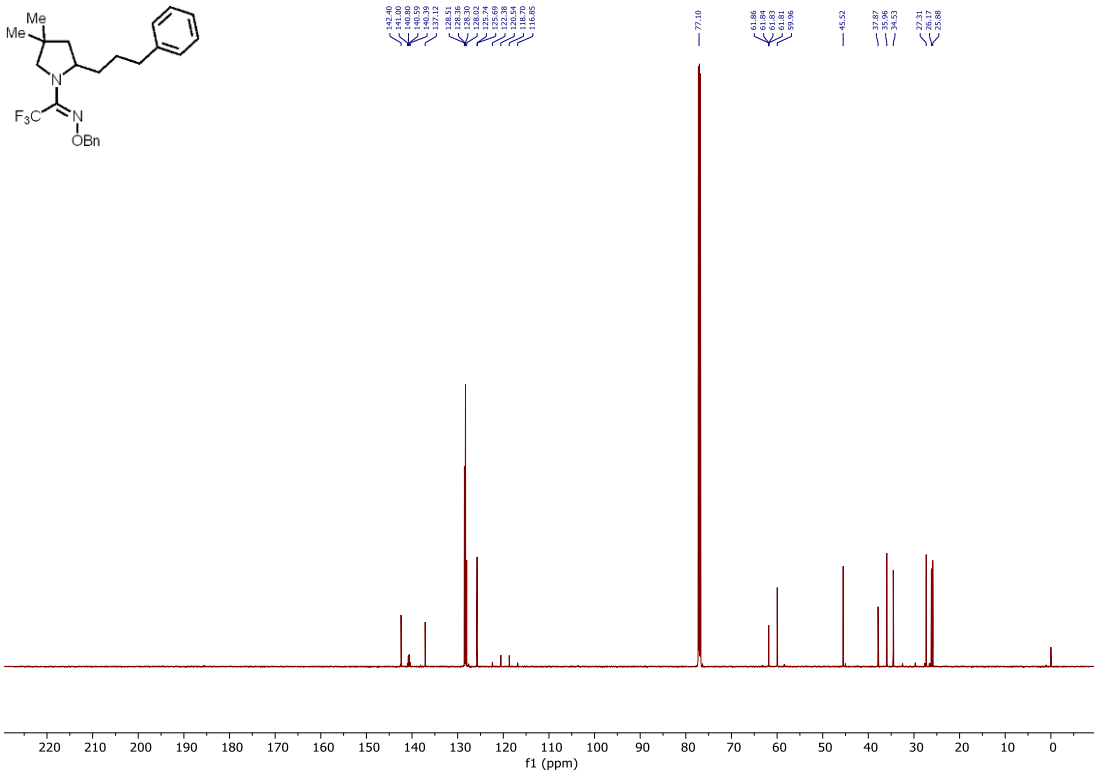


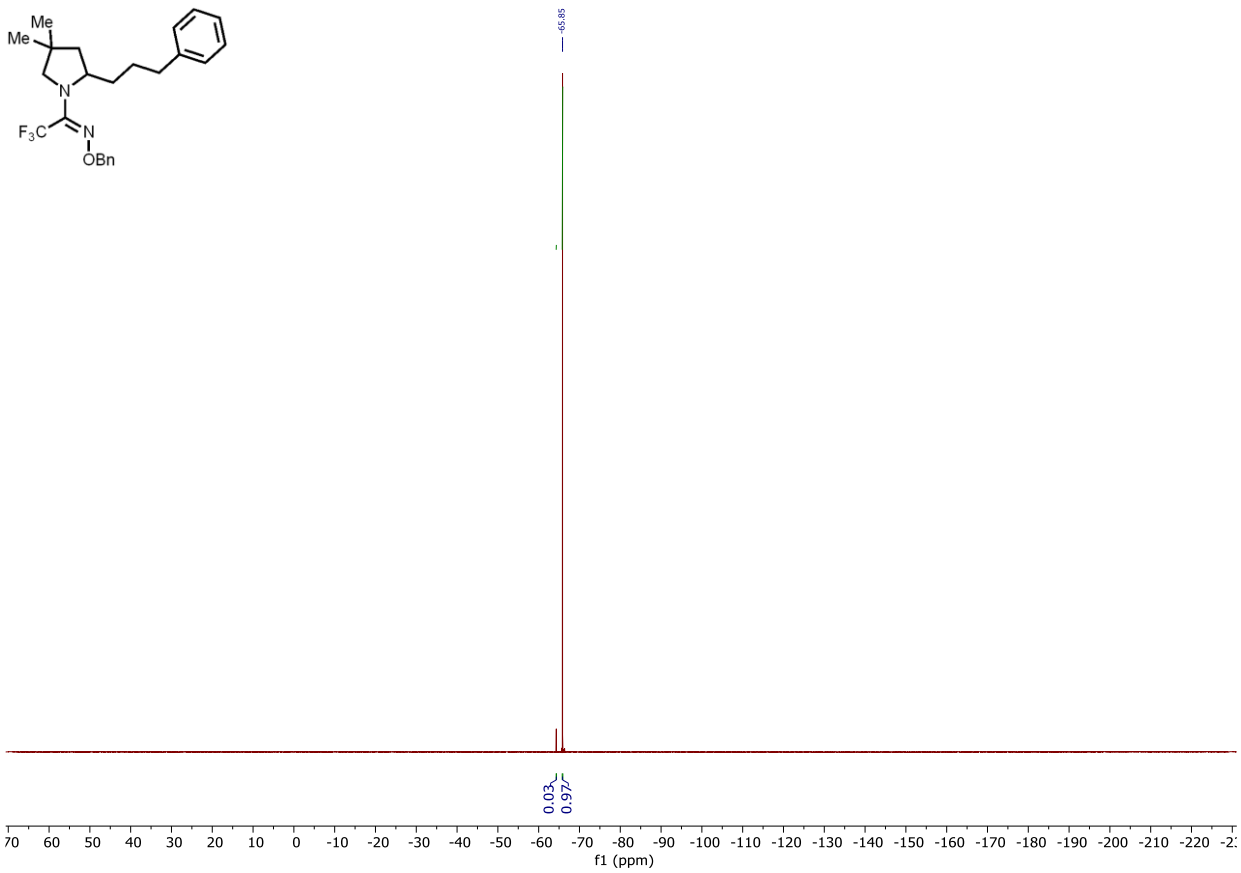



Me
Me
OAc
N
F3C
N
OBn
-65.96
0.04
0.96
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

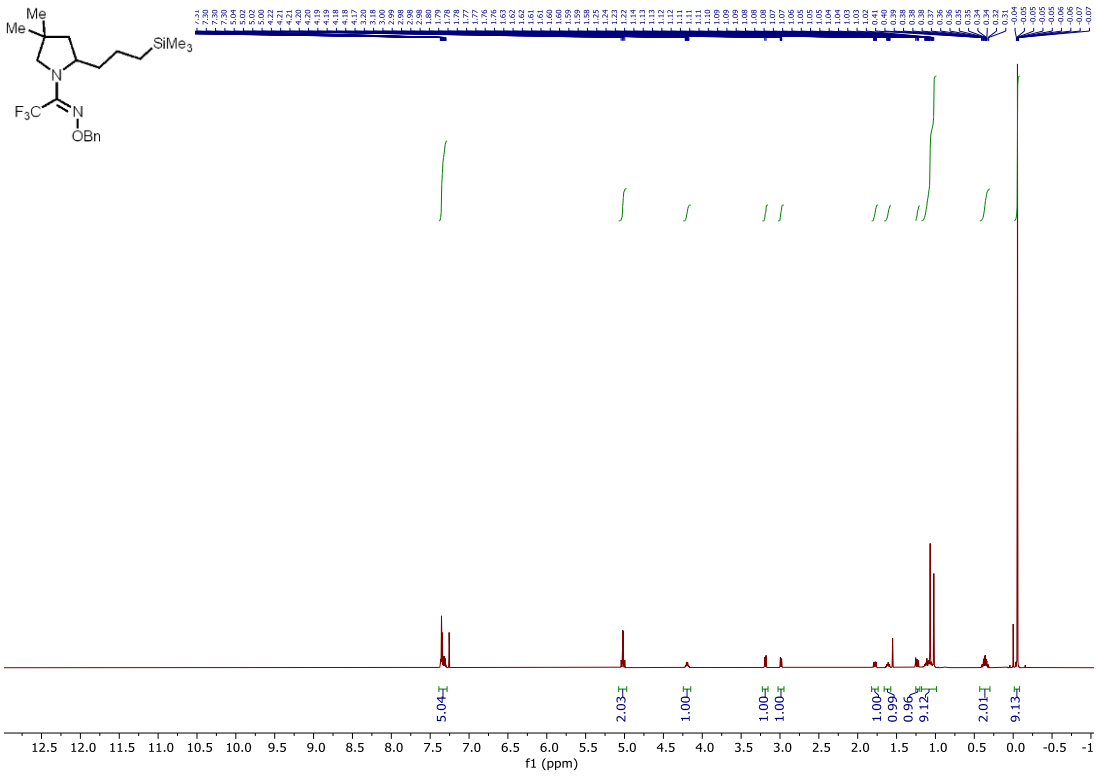
(*E*)-1-(4,4-dimethyl-2-(3-phenylpropyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3n)

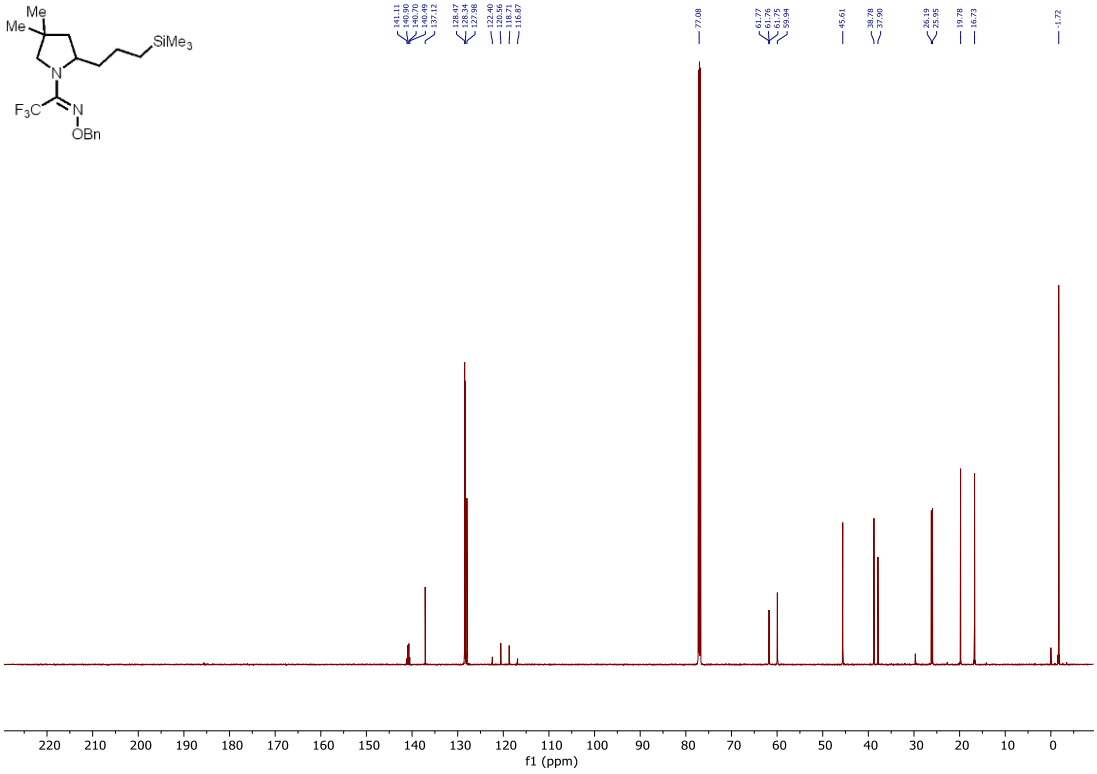


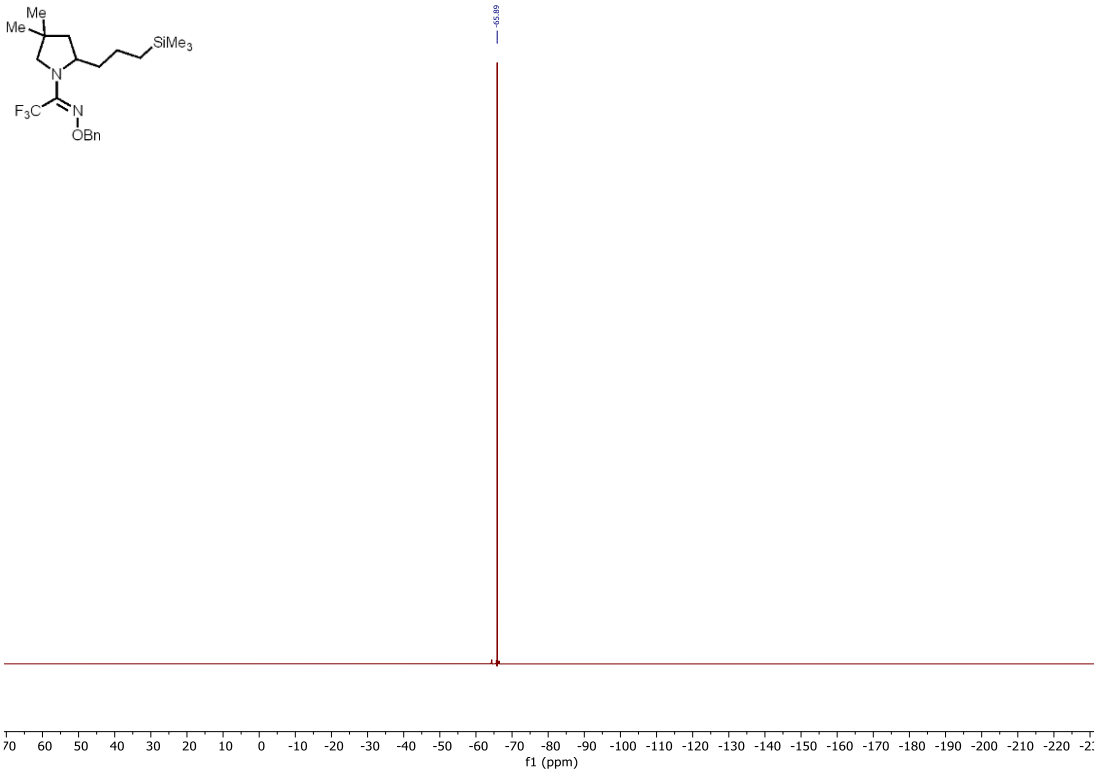



Me
Me
N
F3C
N
OBn
-65.85
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

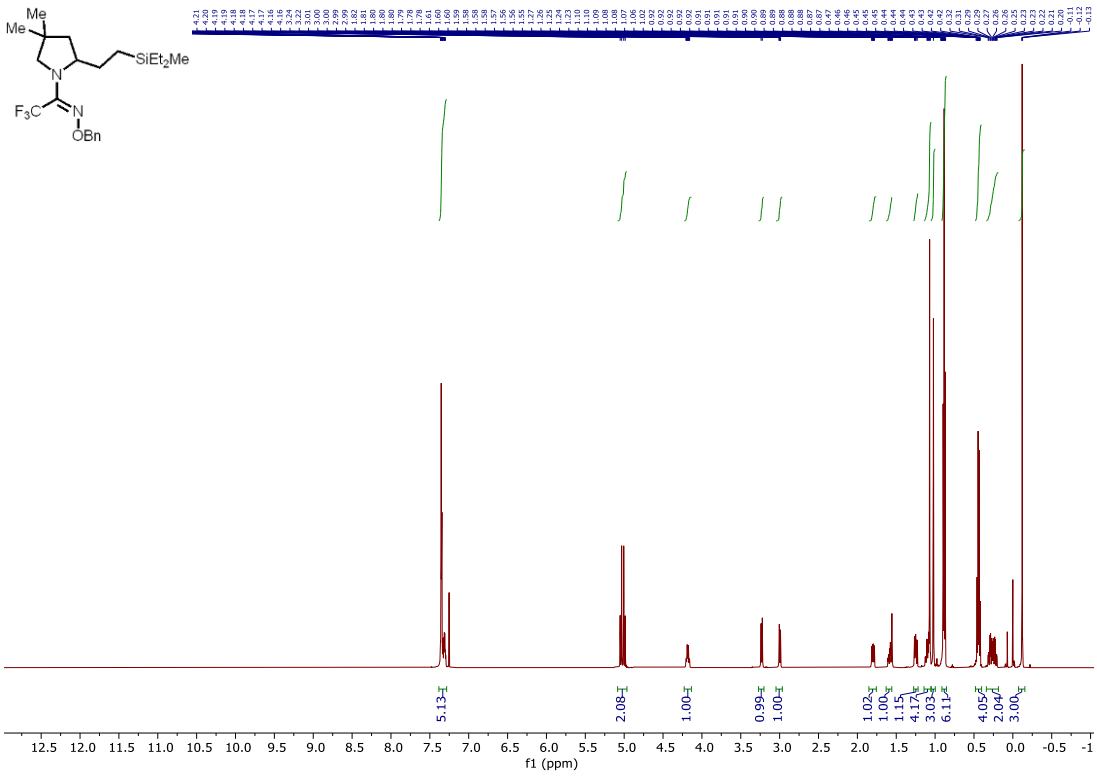
(*E*)-1-(4,4-dimethyl-2-(3-(trimethylsilyl)propyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3o)

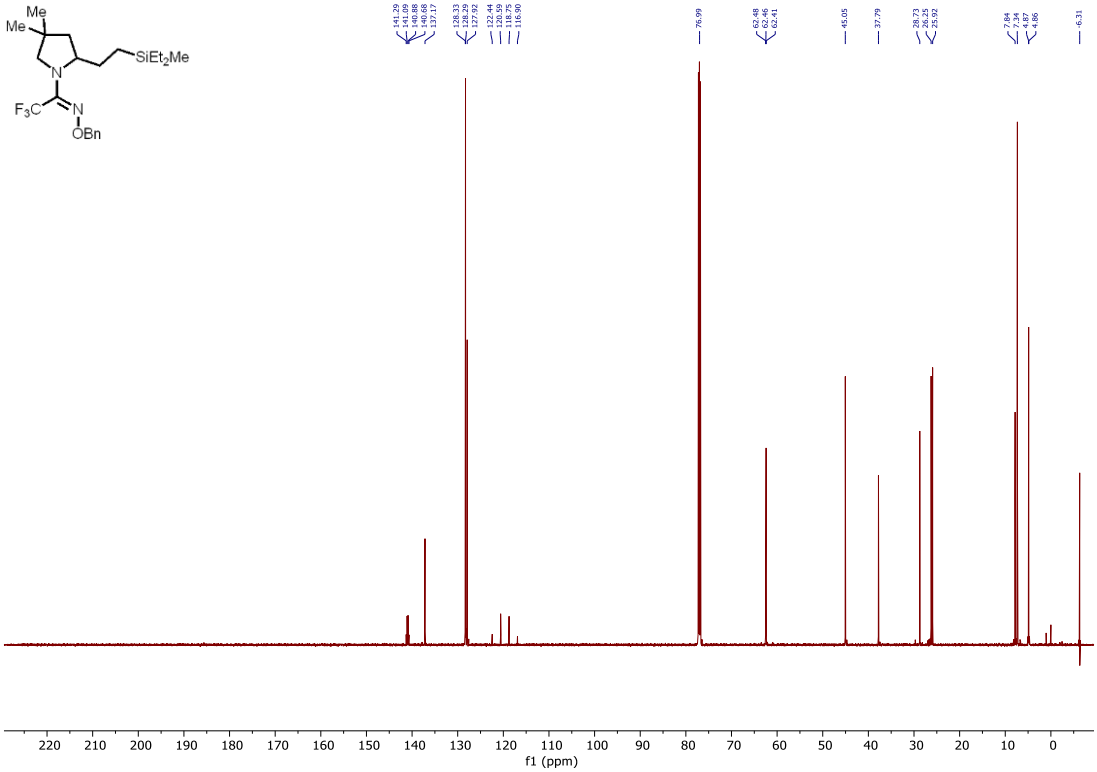


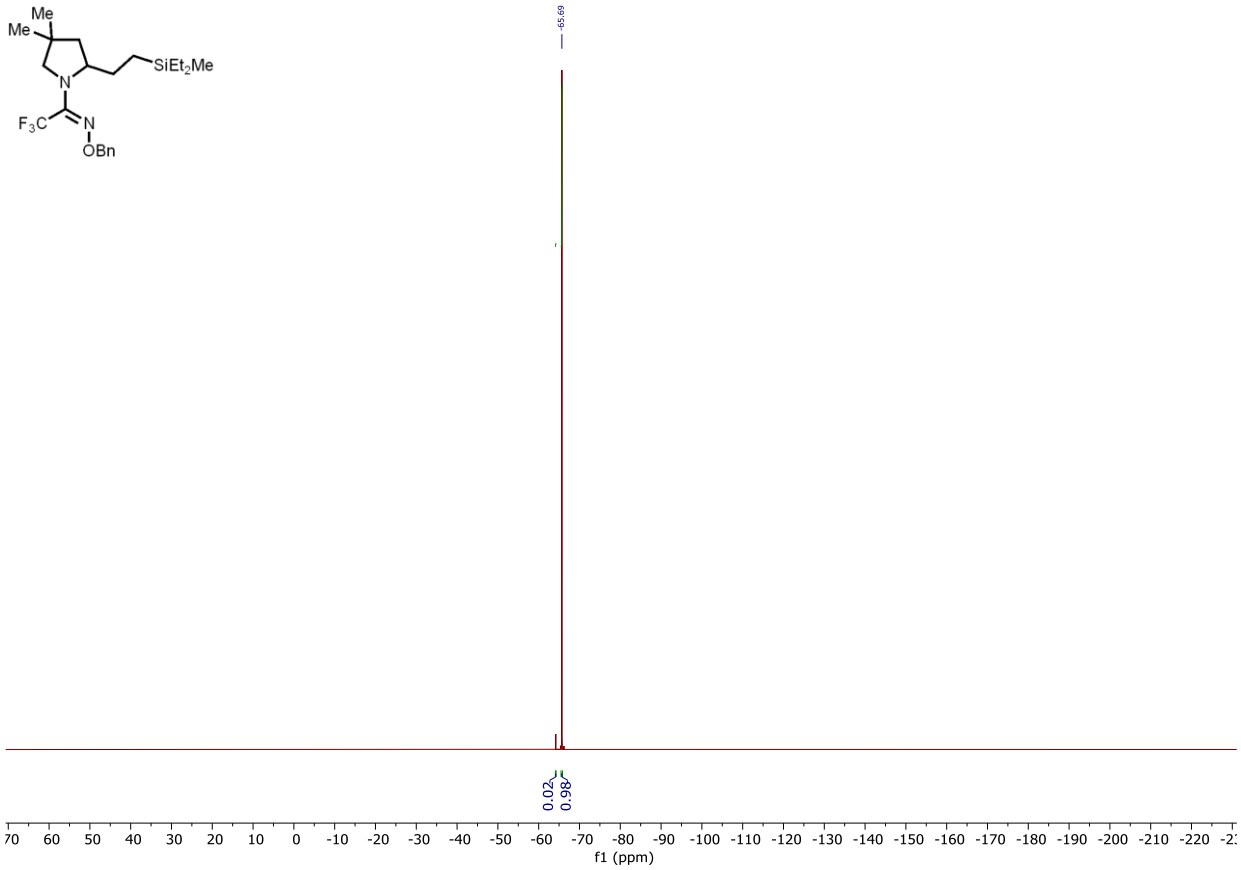



Me
Me
SiMe3
N
F3C
N
OBn
-65.89
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

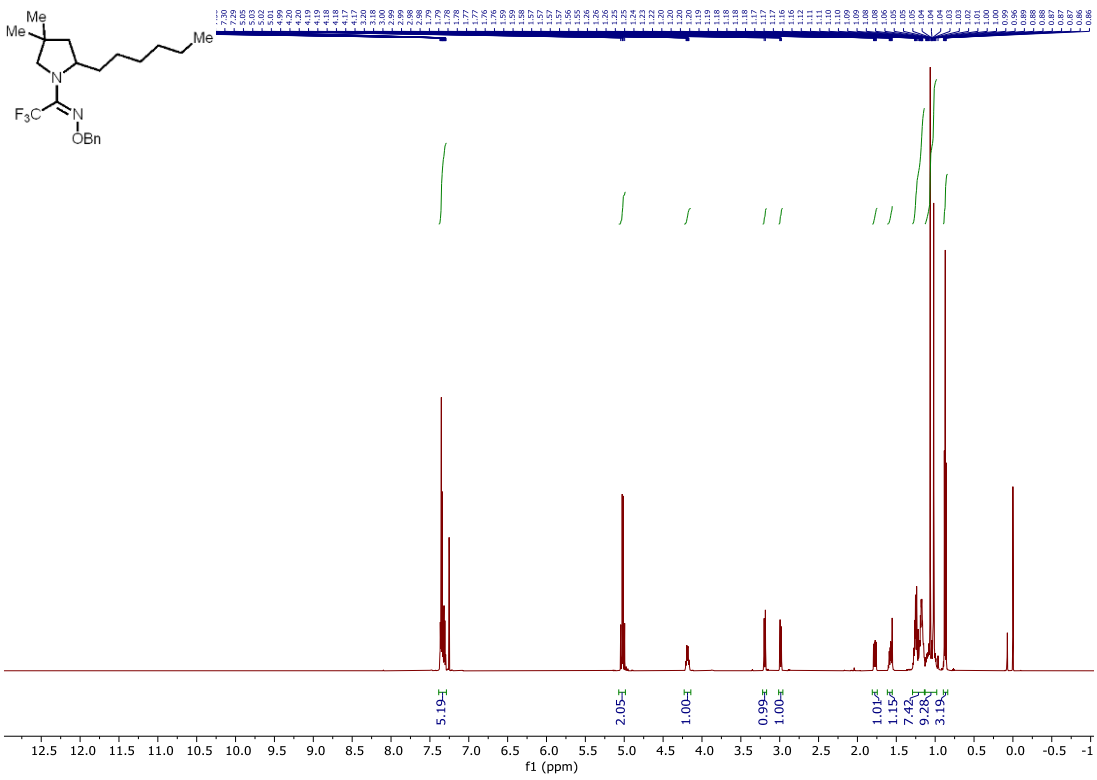
(*E*)-1-(2-(2-(diethyl(methyl)silyl)ethyl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3p)

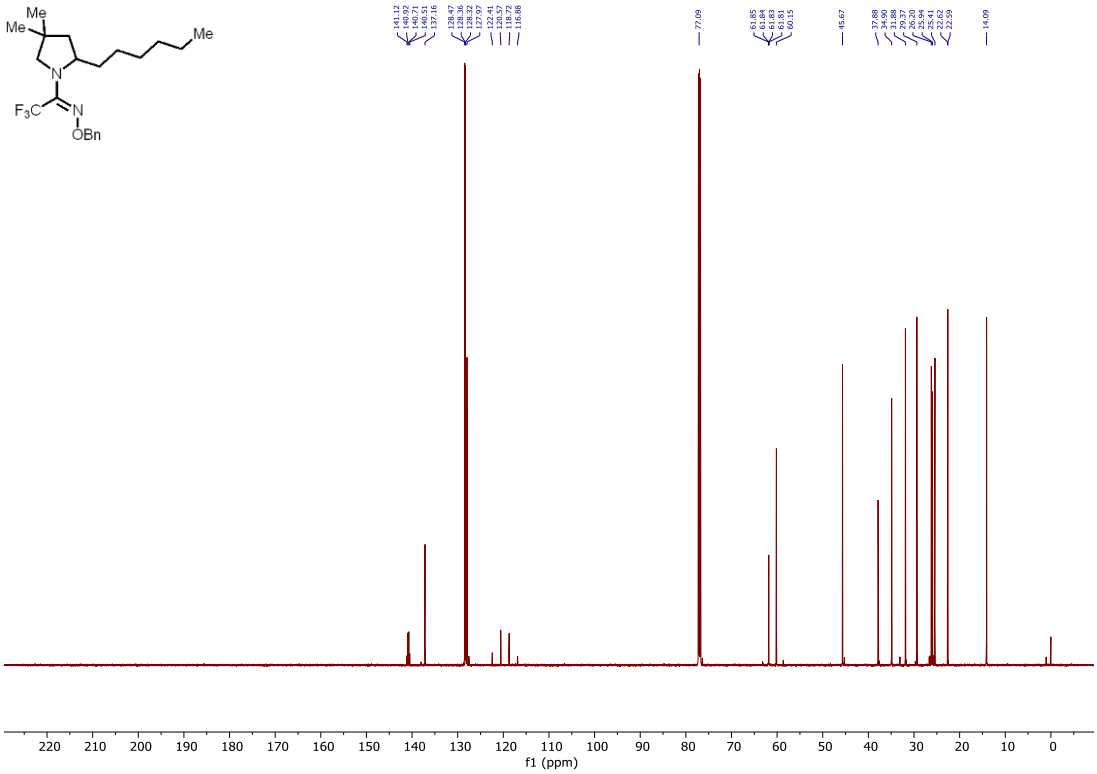


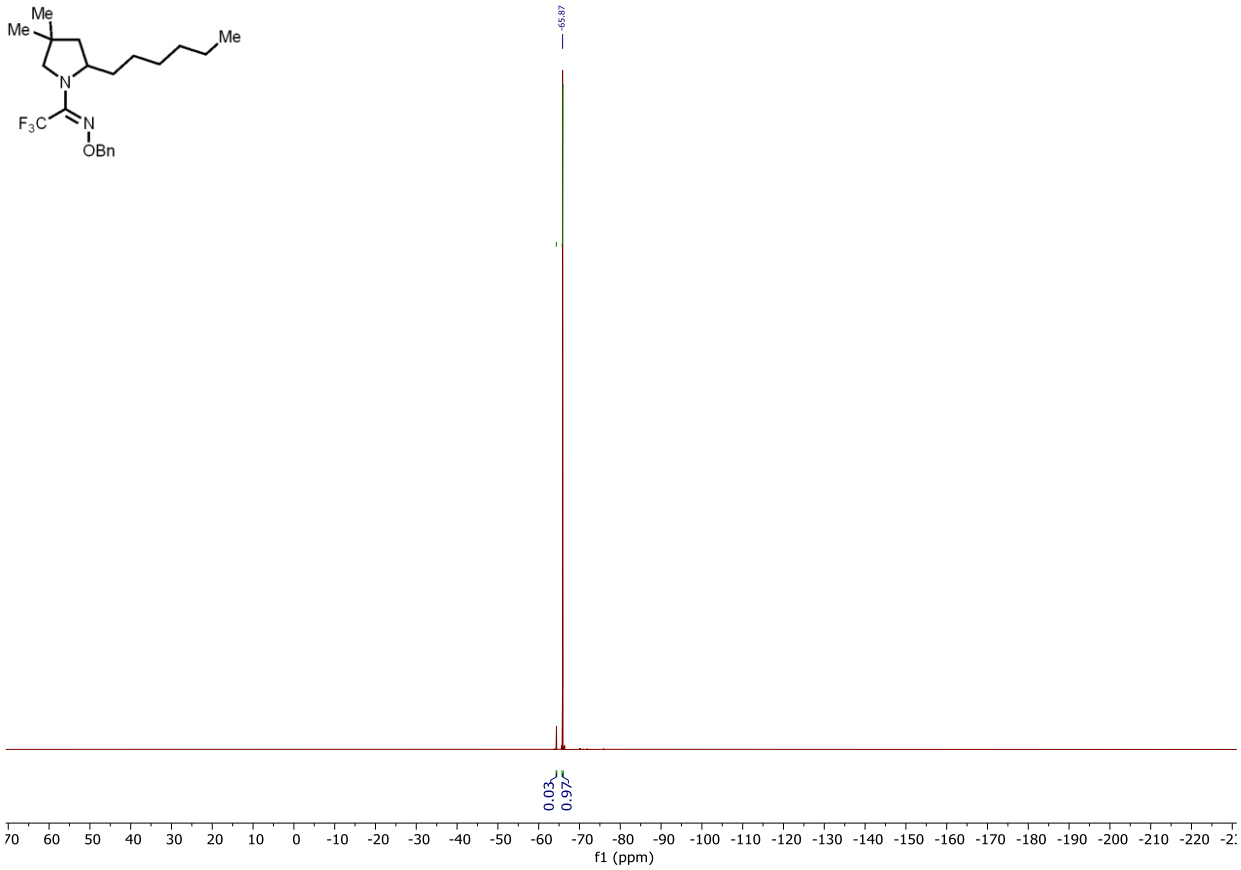



Me
Me
SiEt2Me
N
F3C
N
OBn
-65.69
0.02
0.98
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

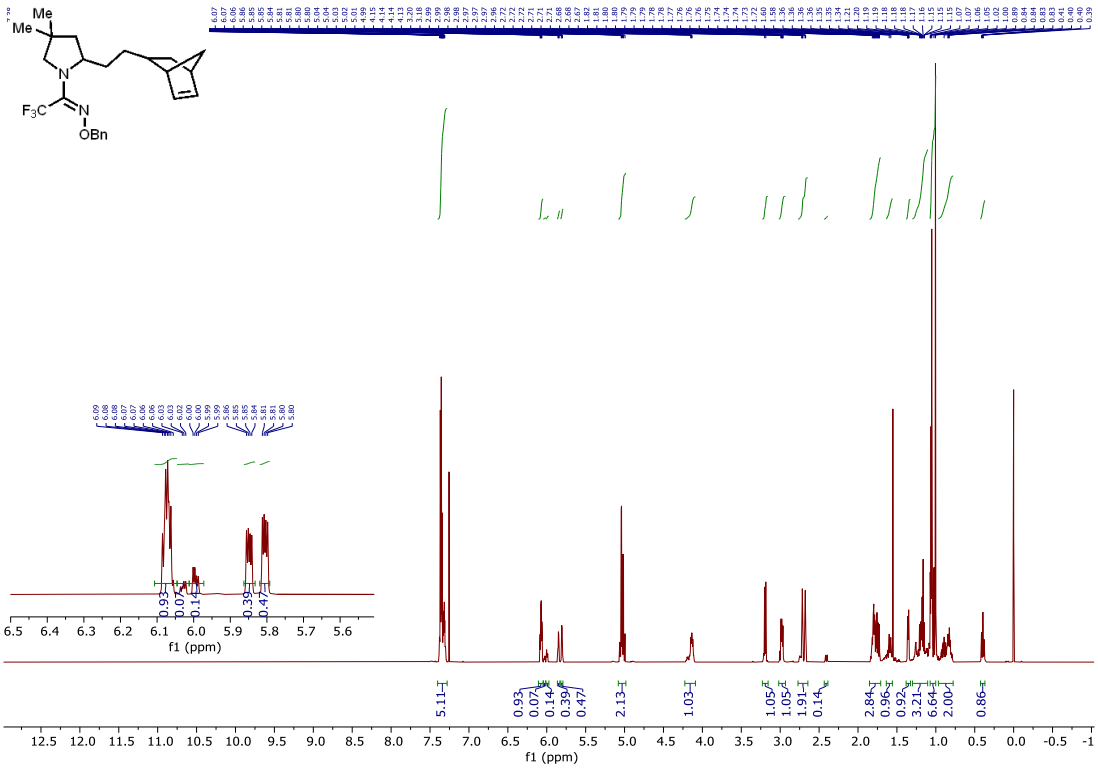
(*E*)-2,2,2-trifluoro-1-(2-hexyl-4,4-dimethylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (3q)

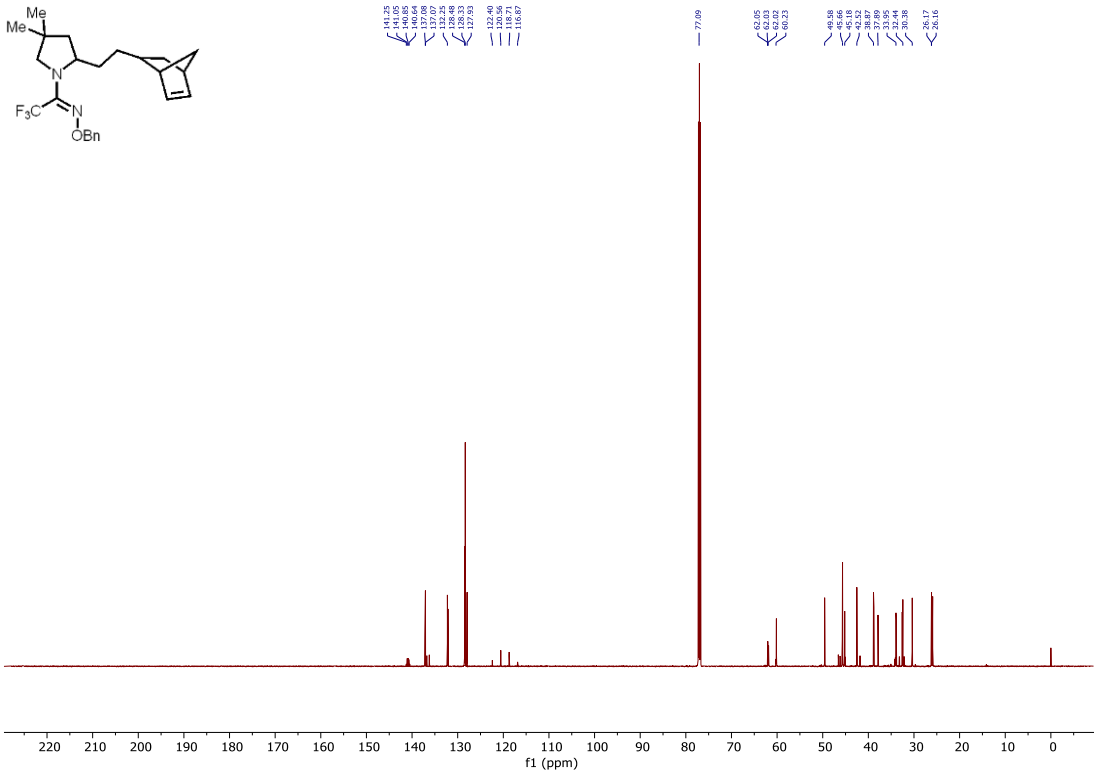


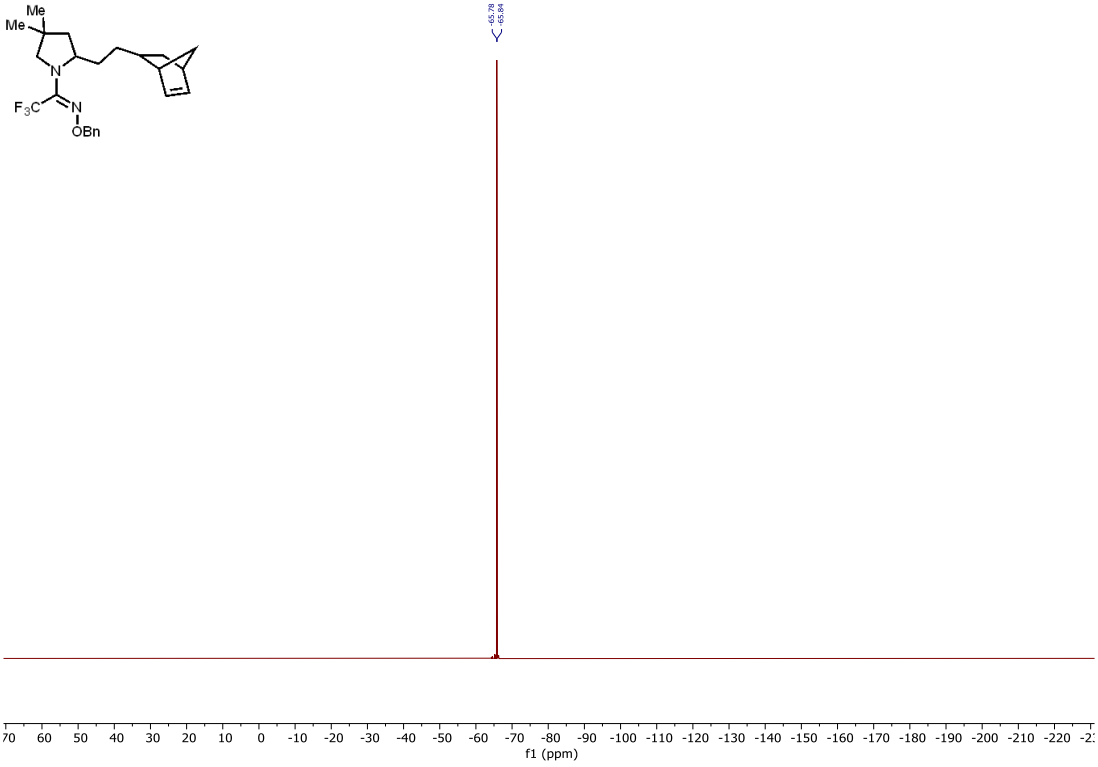


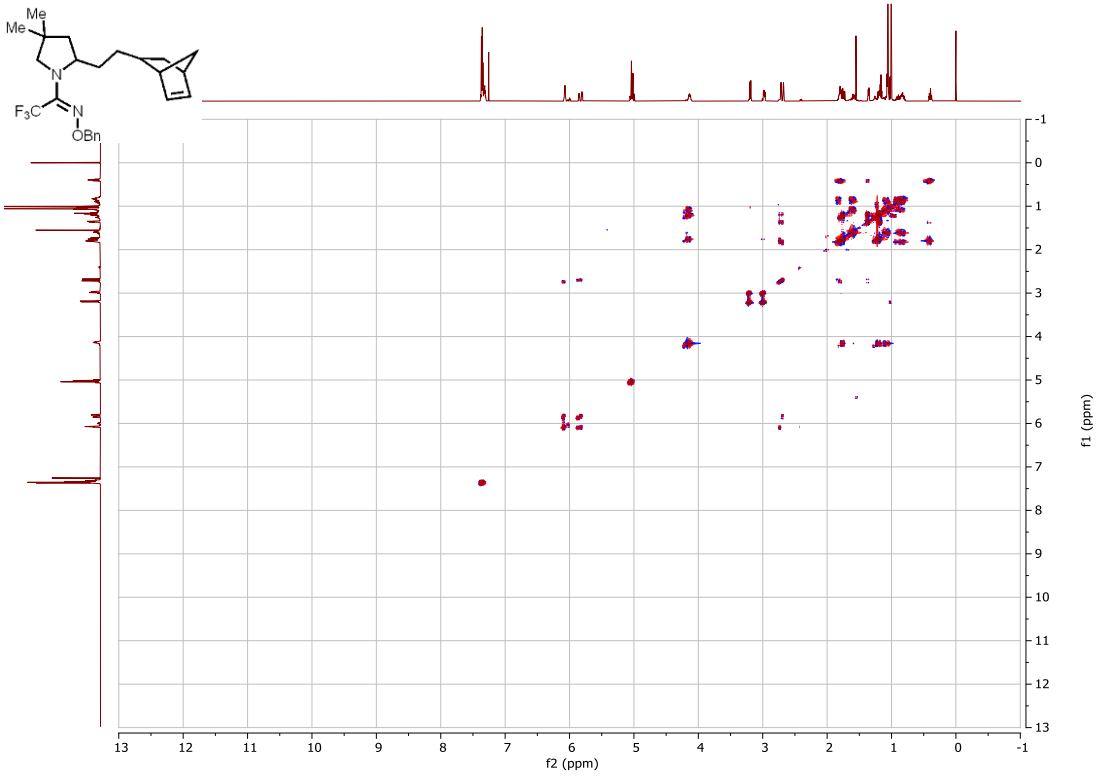

Me
Me
Me
N
F3C
N
OBn
-65.87
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

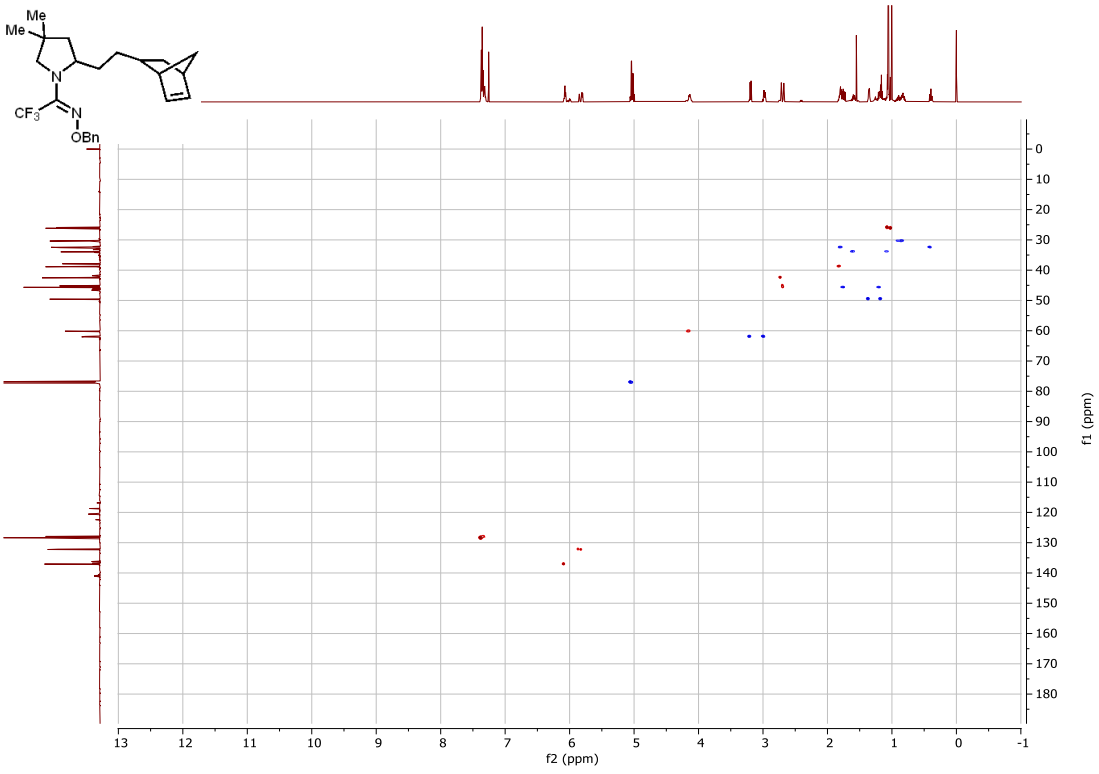
(*E*)-1-(2-(2-(bicyclo[2.2.1]hept-5-en-2-yl)ethyl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3r)

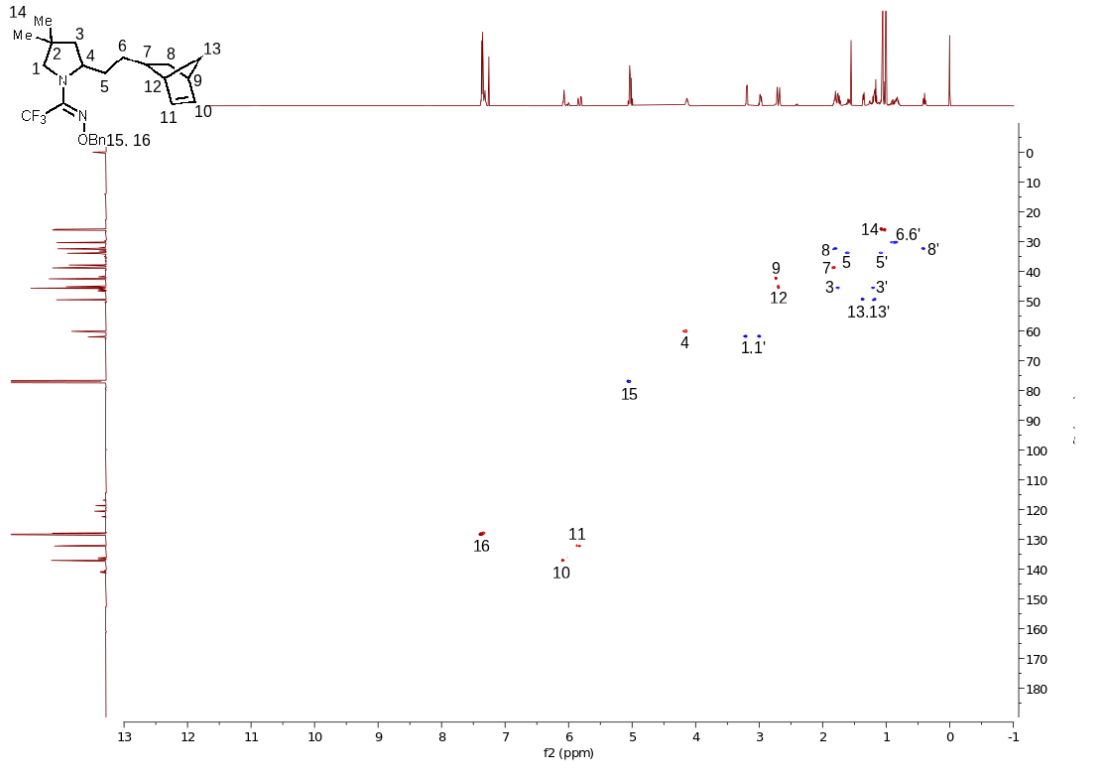


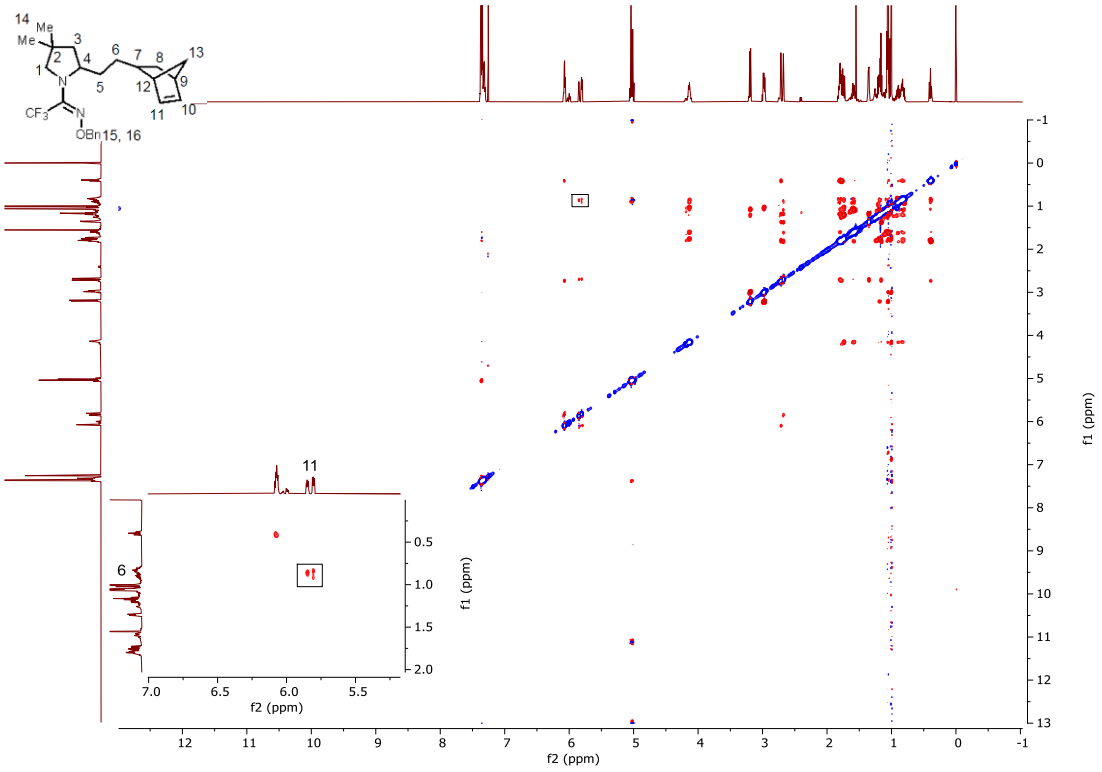



Me
Me
N
F3C
N
OBn
-65.78
-65.94
f1 (ppm)

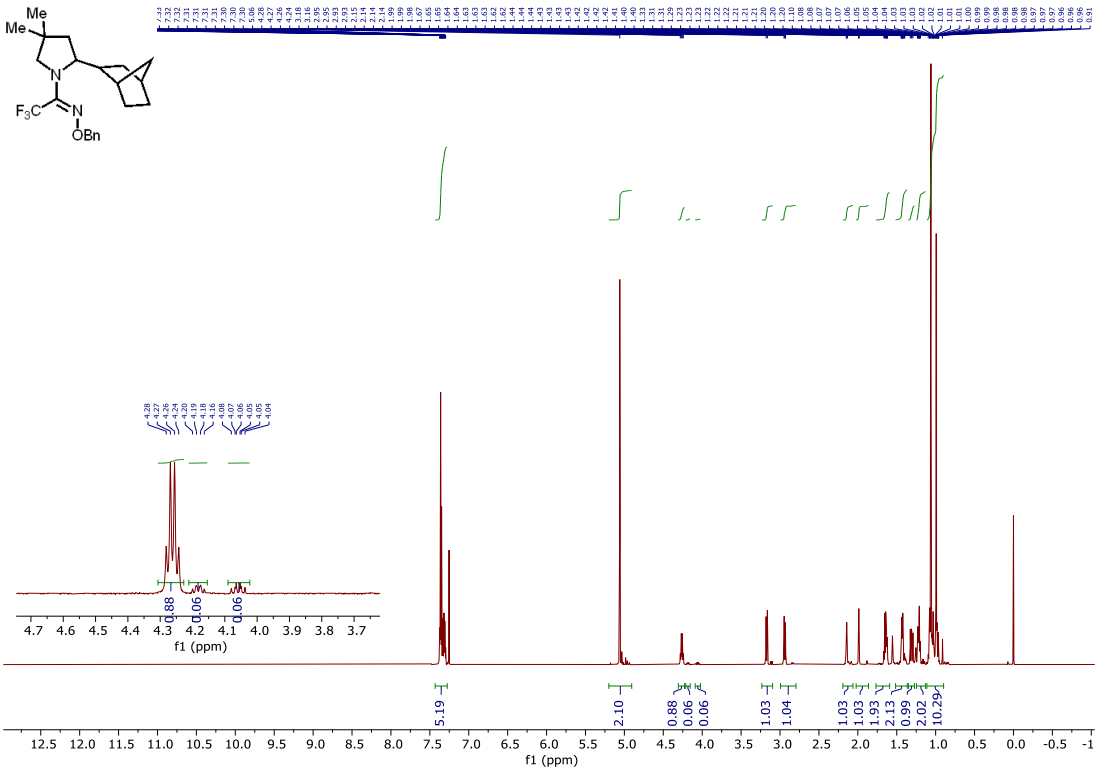

Me
Me
N
F3C
N
OBn
f2 (ppm)
f1 (ppm)

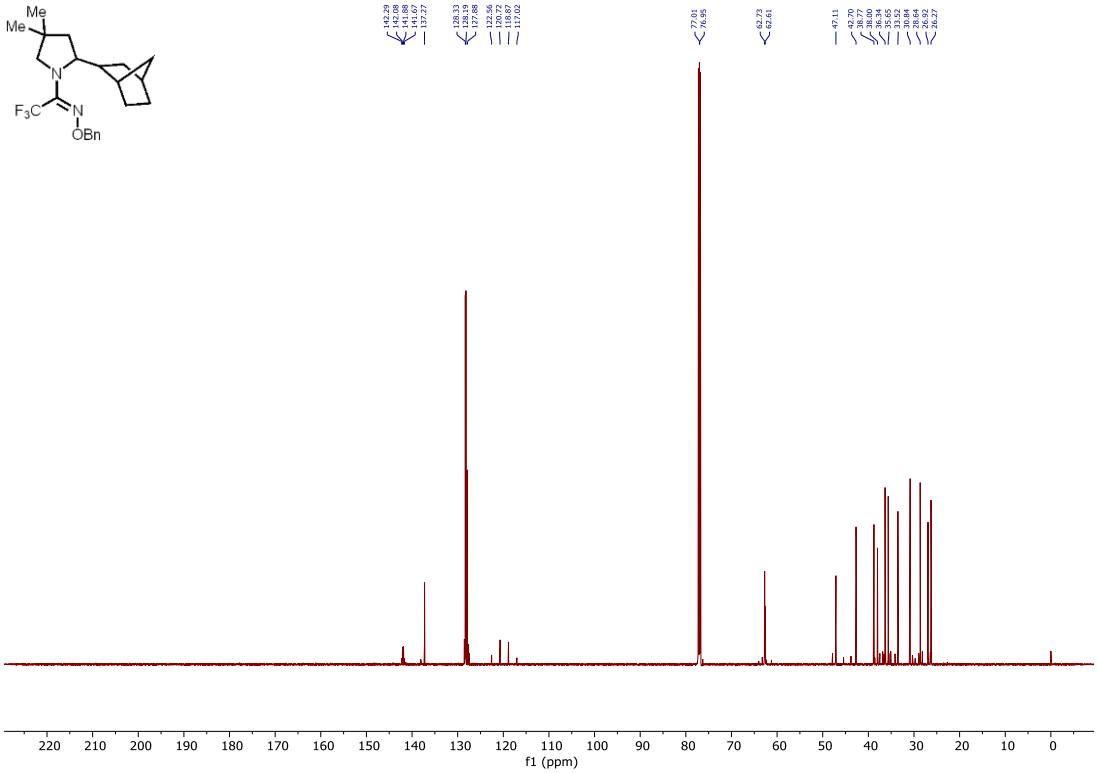

Me
Me
N
CF3
N
OBn
f2 (ppm)
f1 (ppm)

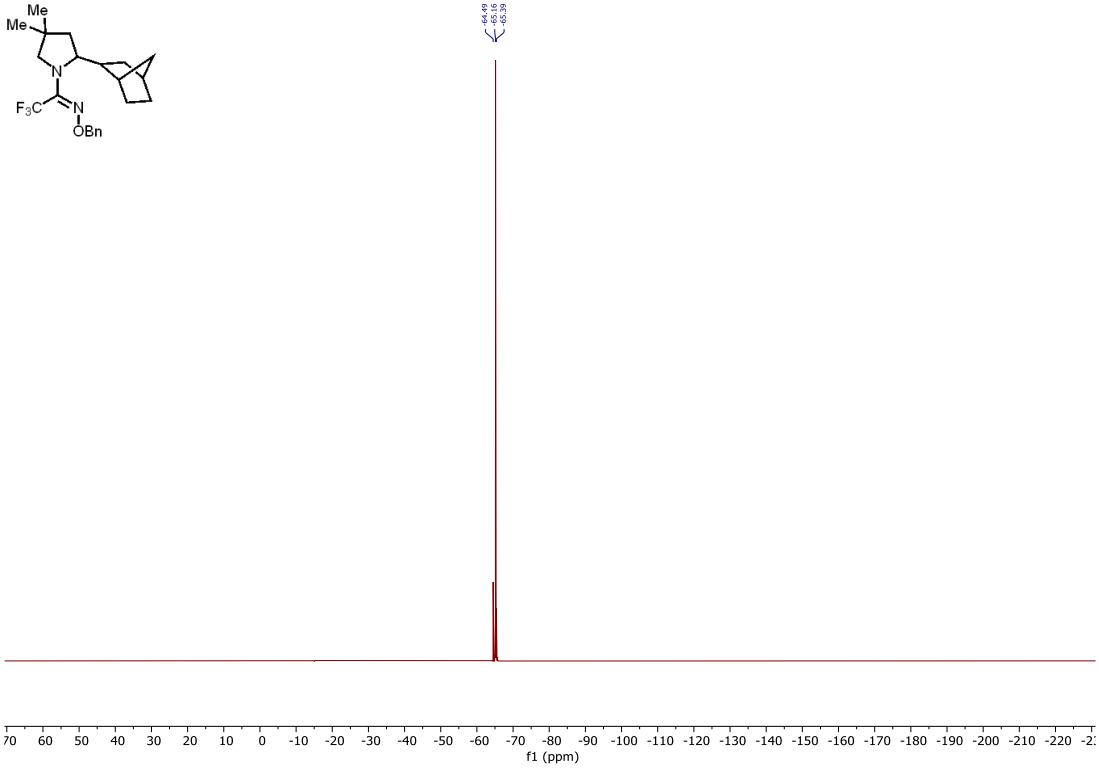

14
Me
Me
3
2
1
4
N
5
6
7
8
13
12
9
11
10
CF3
N
OBn
15, 16
14
6,6'
8'
8
7
5
5'
9
12
3
3'
13,13'
4
1,1'
15
16
11
10
f2 (ppm)

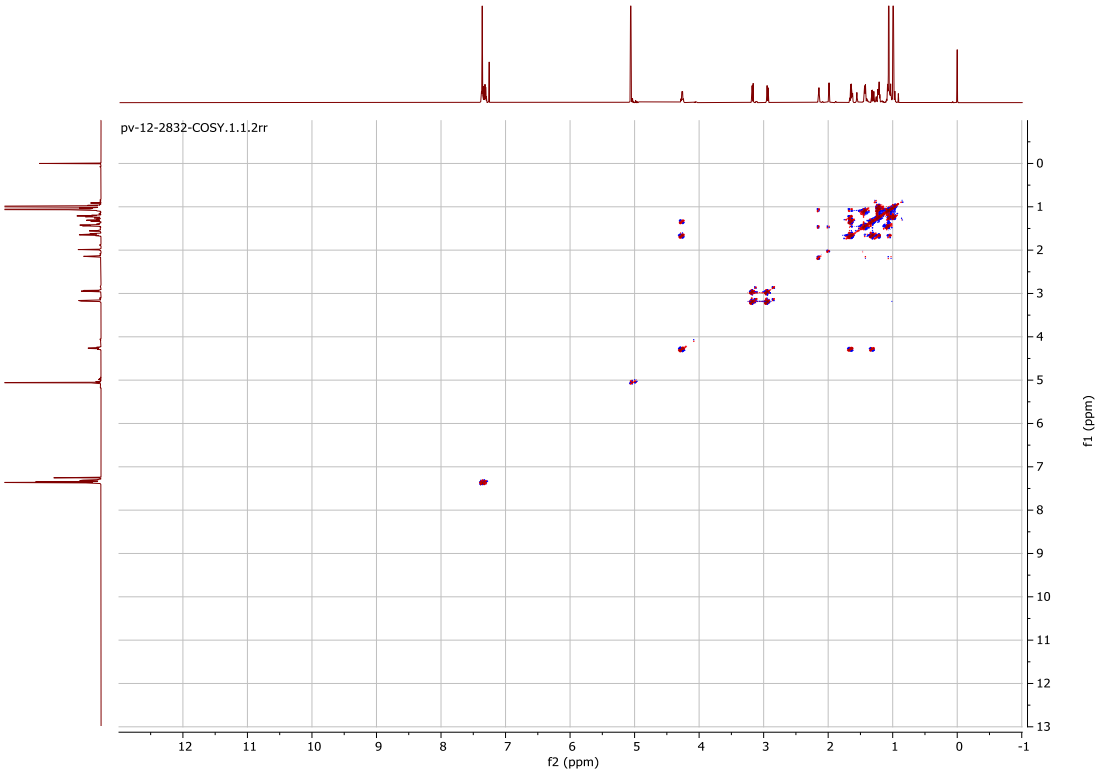

14
Me
Me
3
2
4
6
7
8
13
1
N
5
12
9
CF3
N
11
10
OBn
15, 16
11
6
0.5
1.0
1.5
2.0
7.0
6.5
6.0
5.5
f2 (ppm)
f1 (ppm)
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f2 (ppm)
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
f1 (ppm)

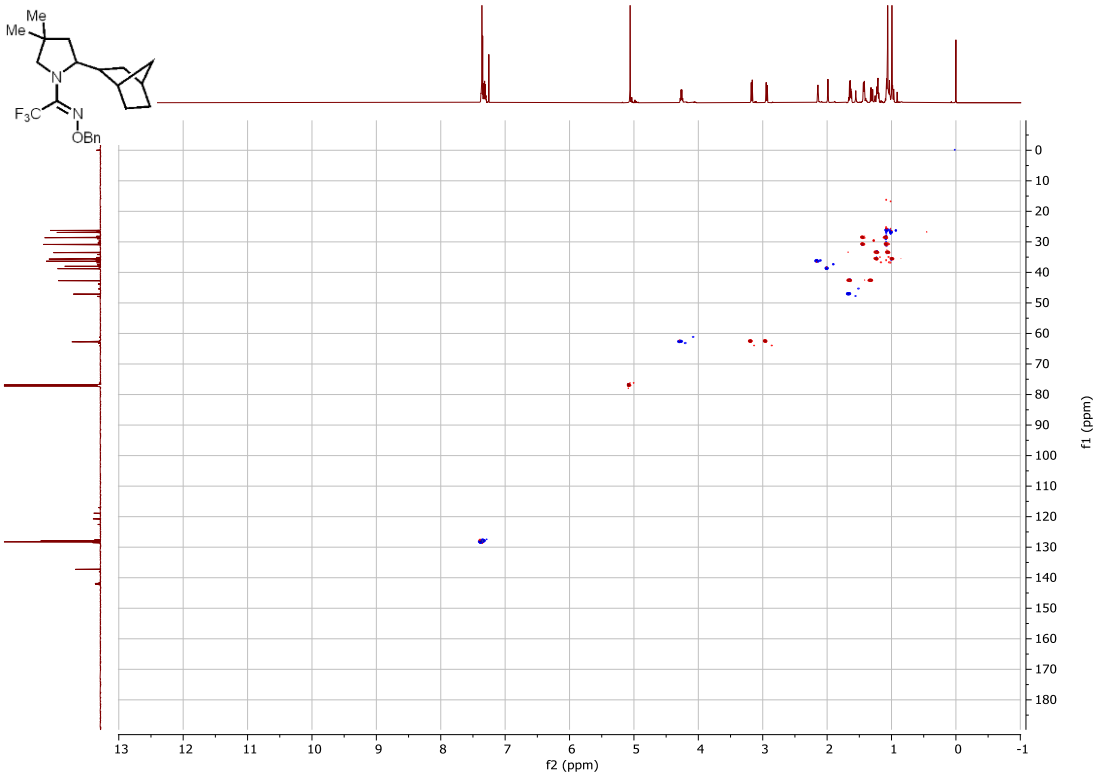
(*E*)-1-(2-(bicyclo[2.2.1]heptan-2-yl)-4,4-dimethylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3s)



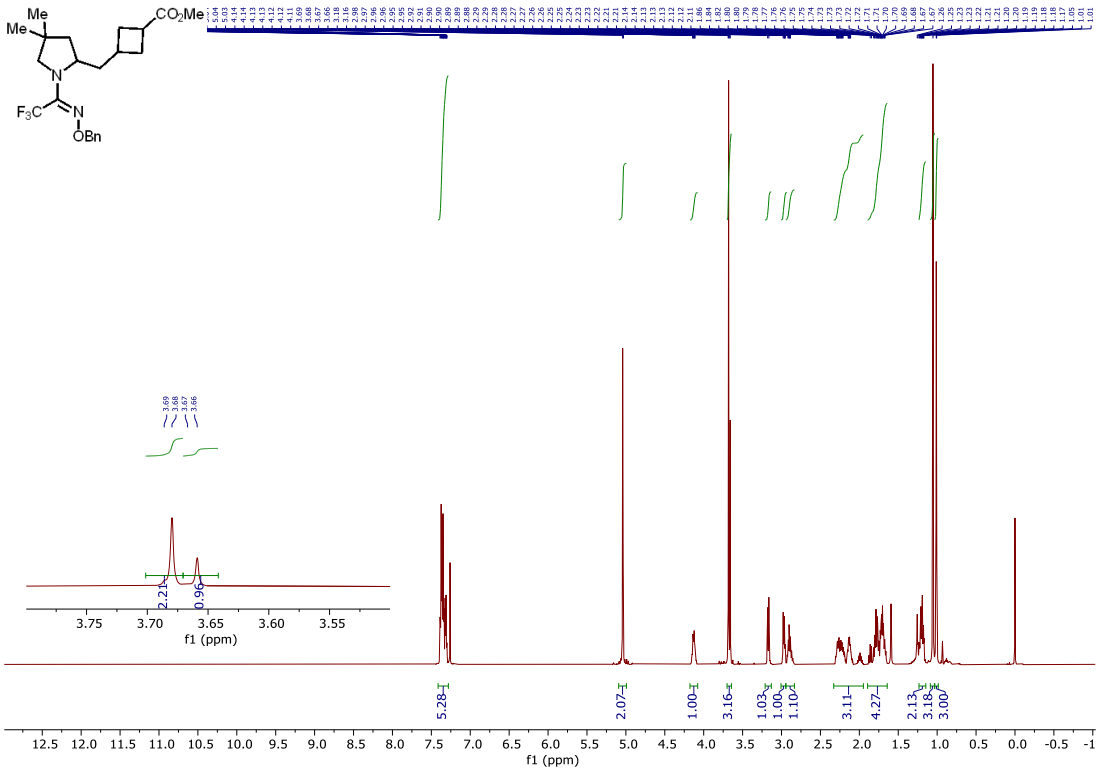


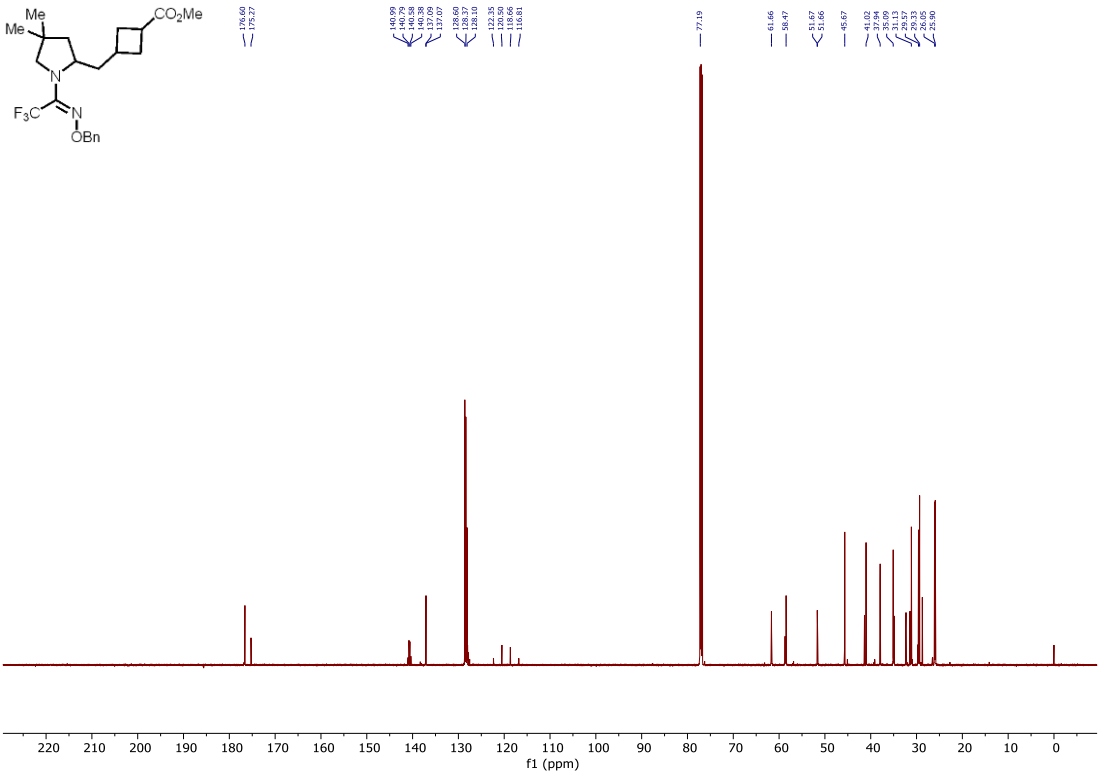

Me
Me
N
F3C
N
OBn
-64.49
-65.16
-65.59
f1 (ppm)

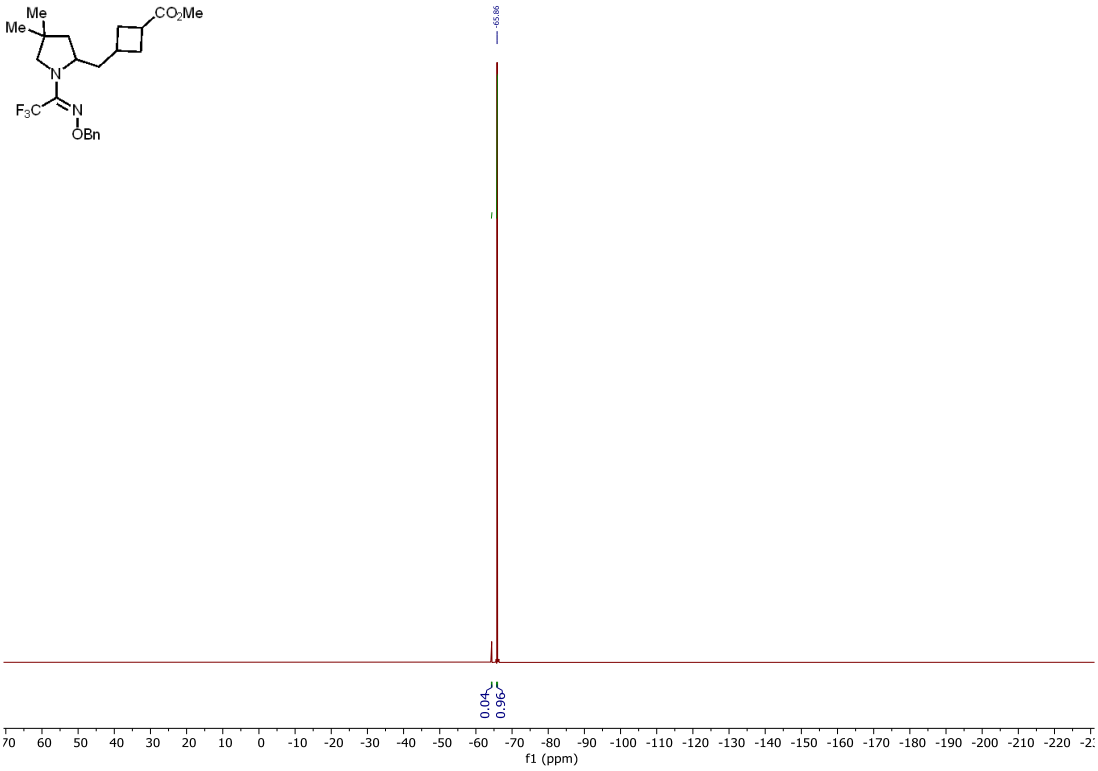

pv-12-2832-COSY.1.1.2rr
f2 (ppm)
f1 (ppm)


Me
Me
N
F3C
N
OBn
f2 (ppm)
f1 (ppm)

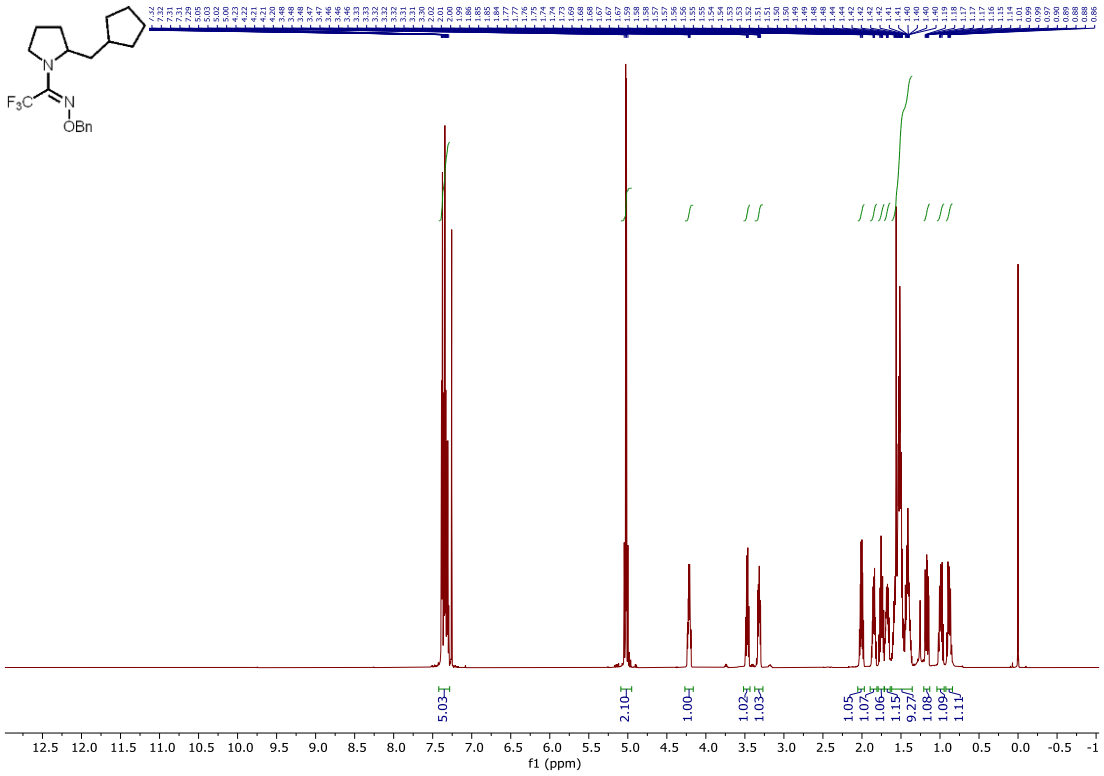
methyl (*E*)-3-((1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)-4,4-dimethylpyrrolidin-2-yl)methyl)cyclobutane-1-carboxylate (3t)

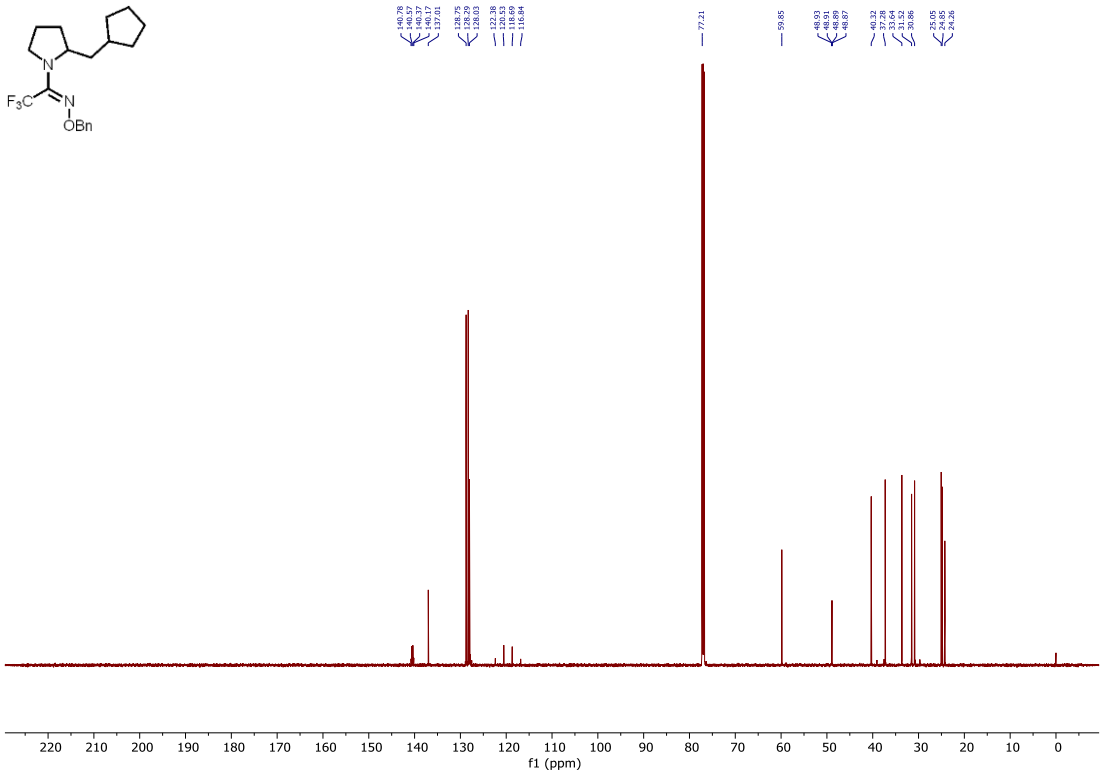


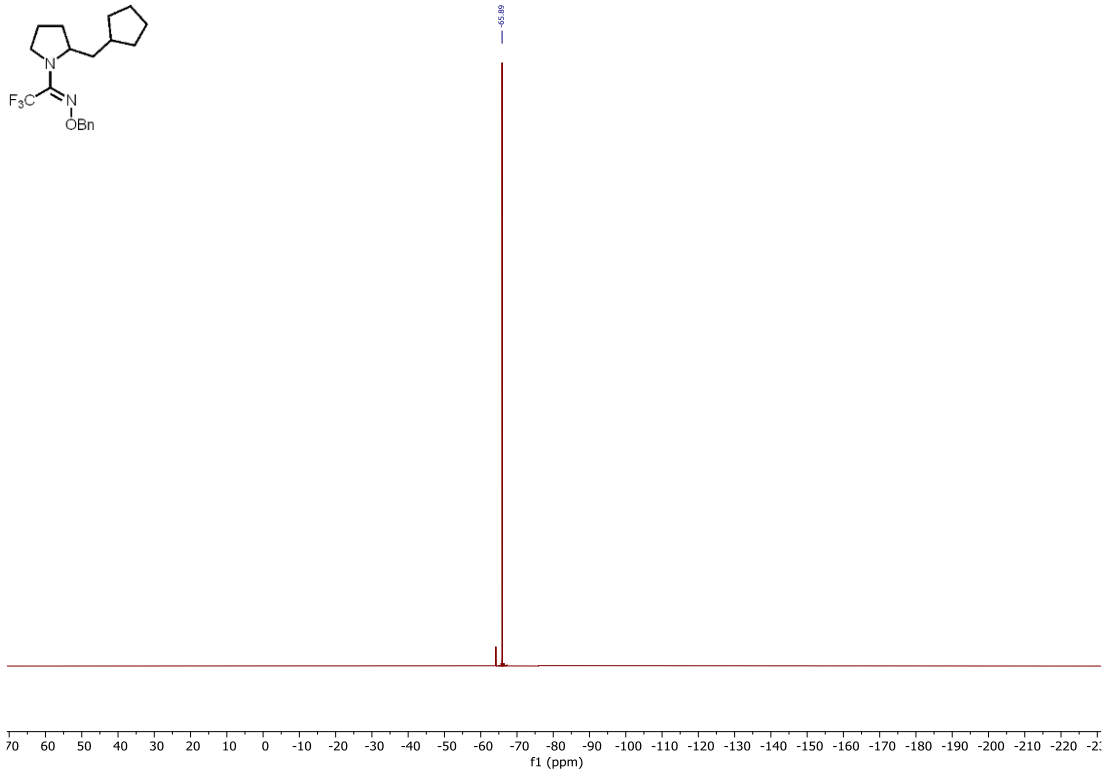



Me
Me
CO2Me
N
F3C
N
OBn
-65.86
0.04
0.96
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

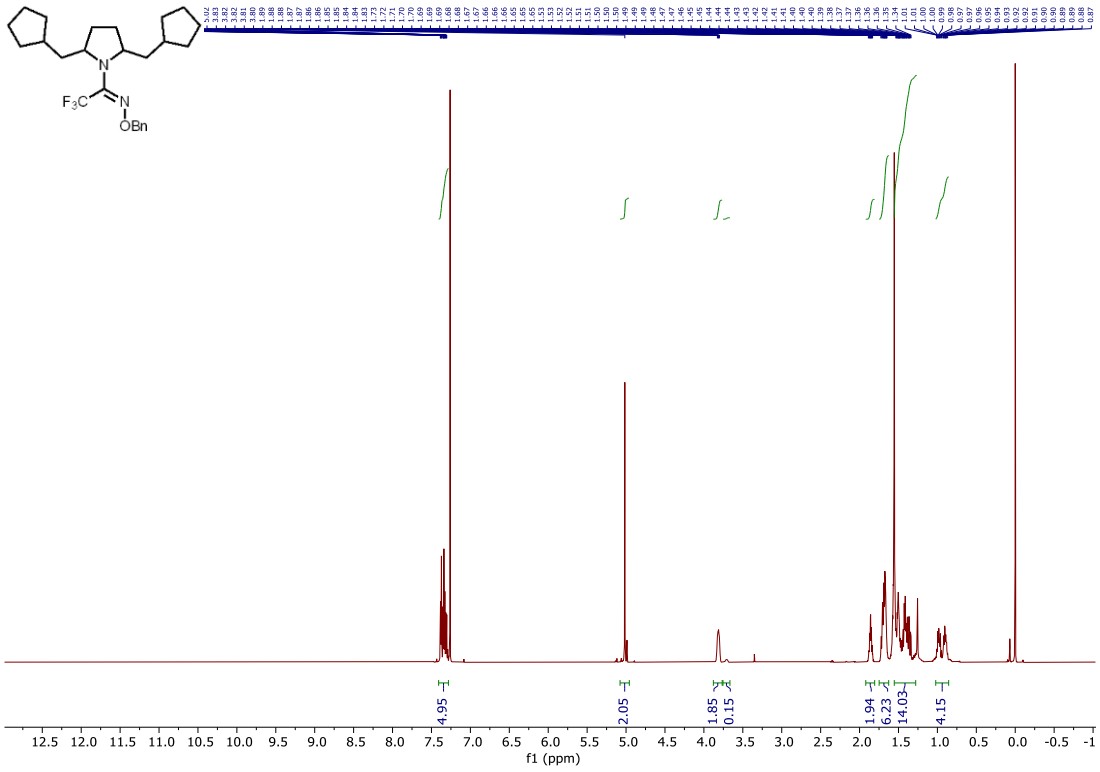
(*E*)-1-(2-(cyclopentylmethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3u-mono)

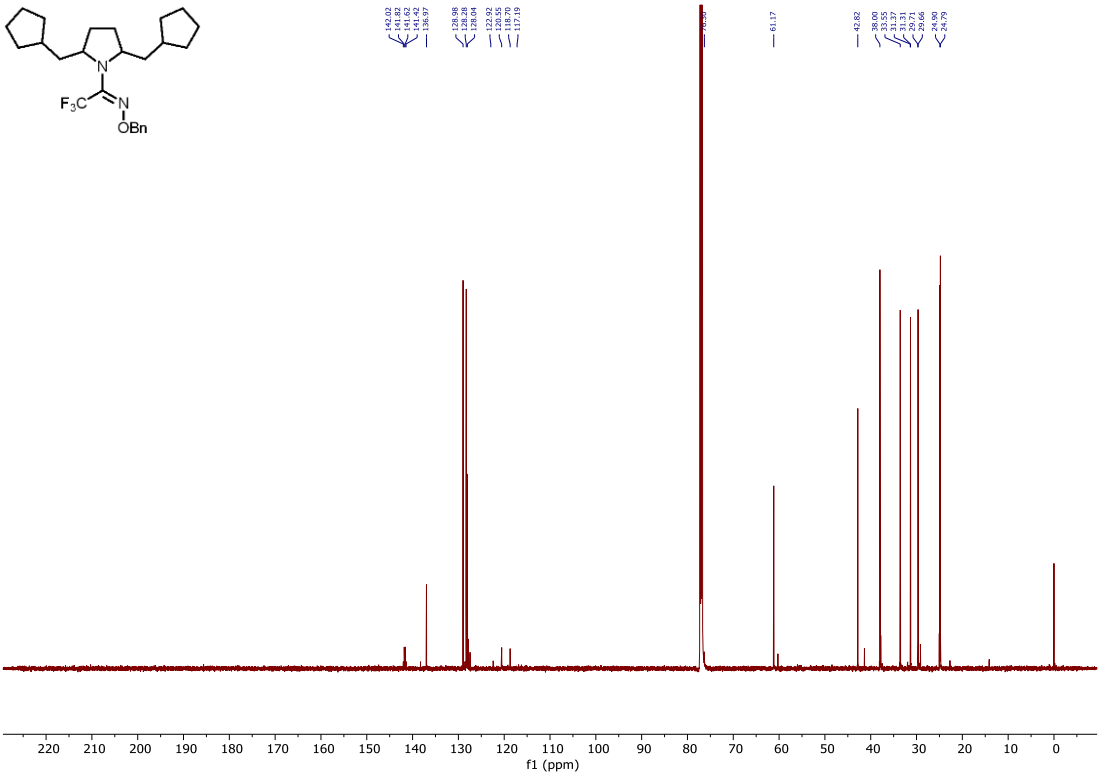


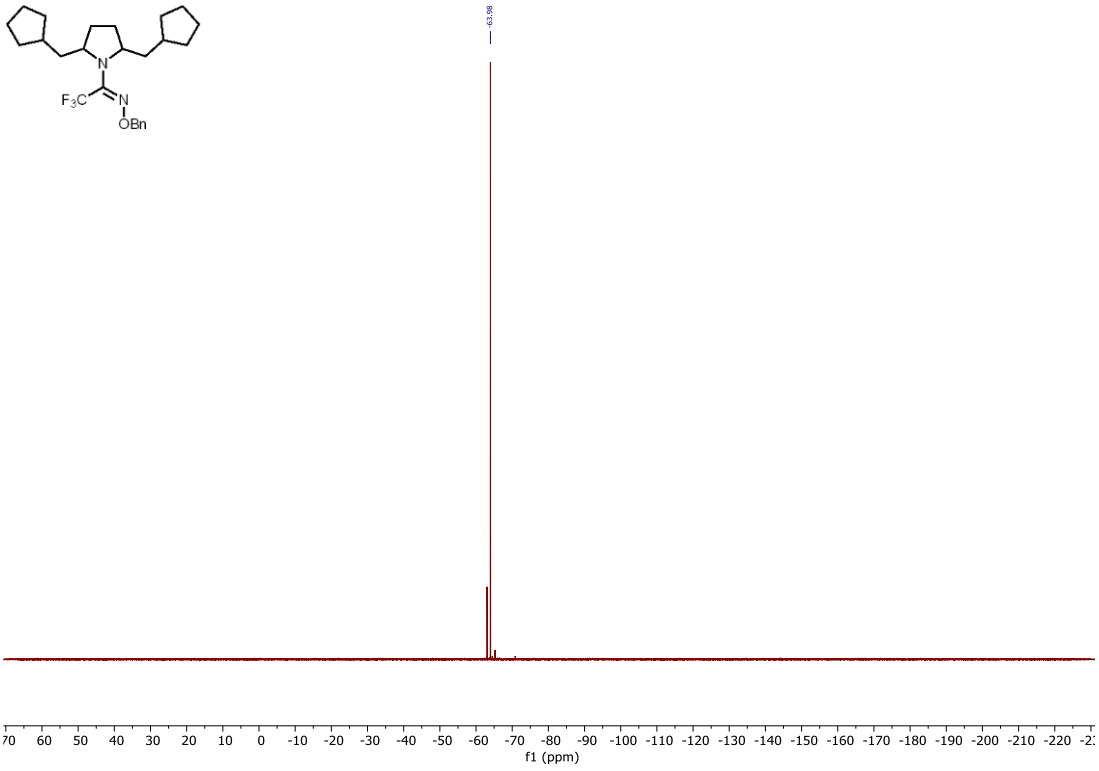



-65.89
F3C
N
N
OBn
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

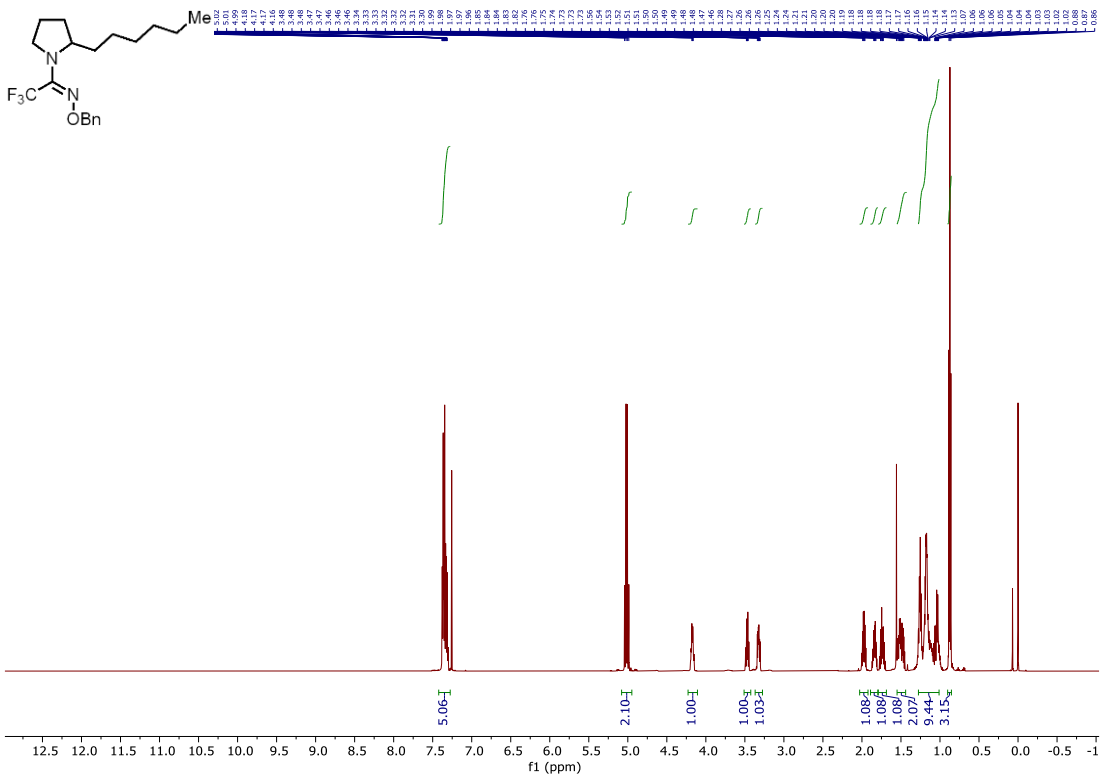
(*E*)-1-(2,5-bis(cyclopentylmethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3u-di)

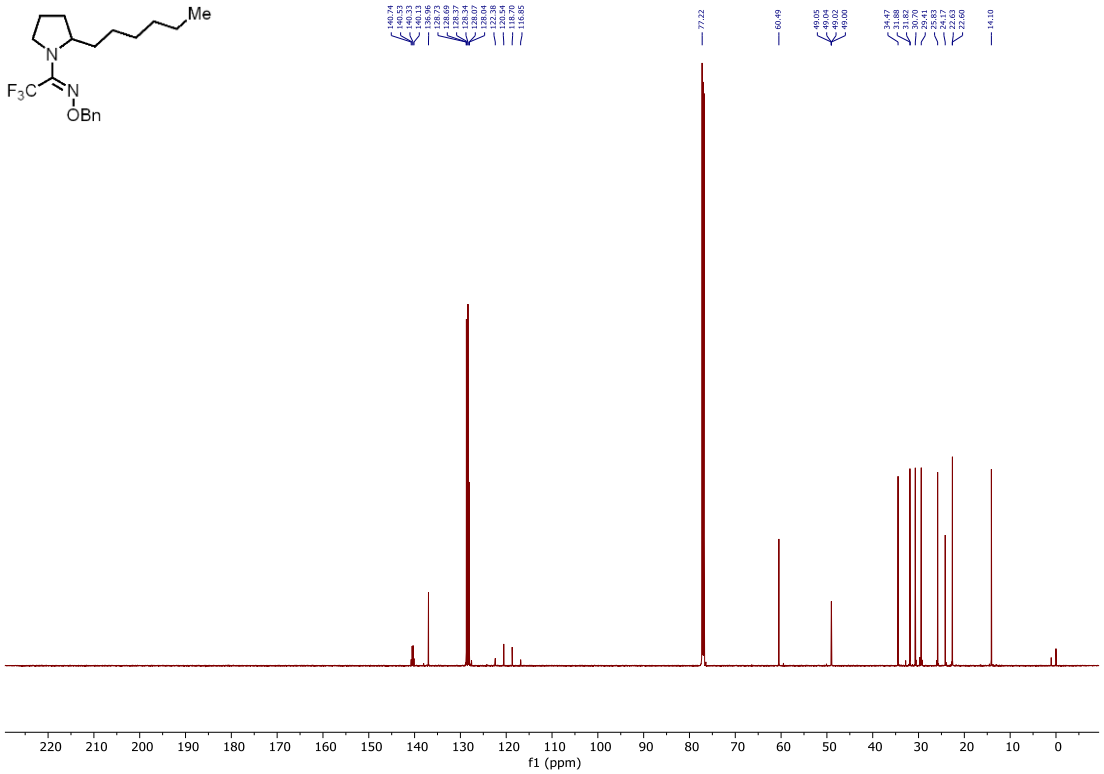


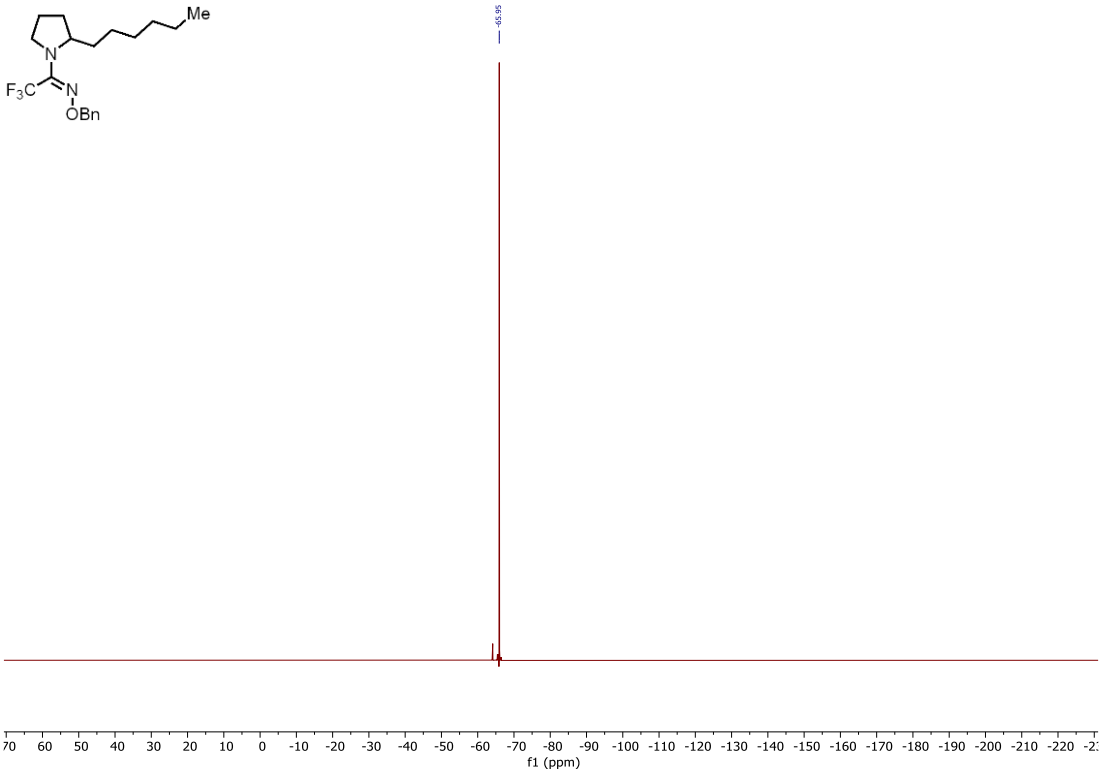


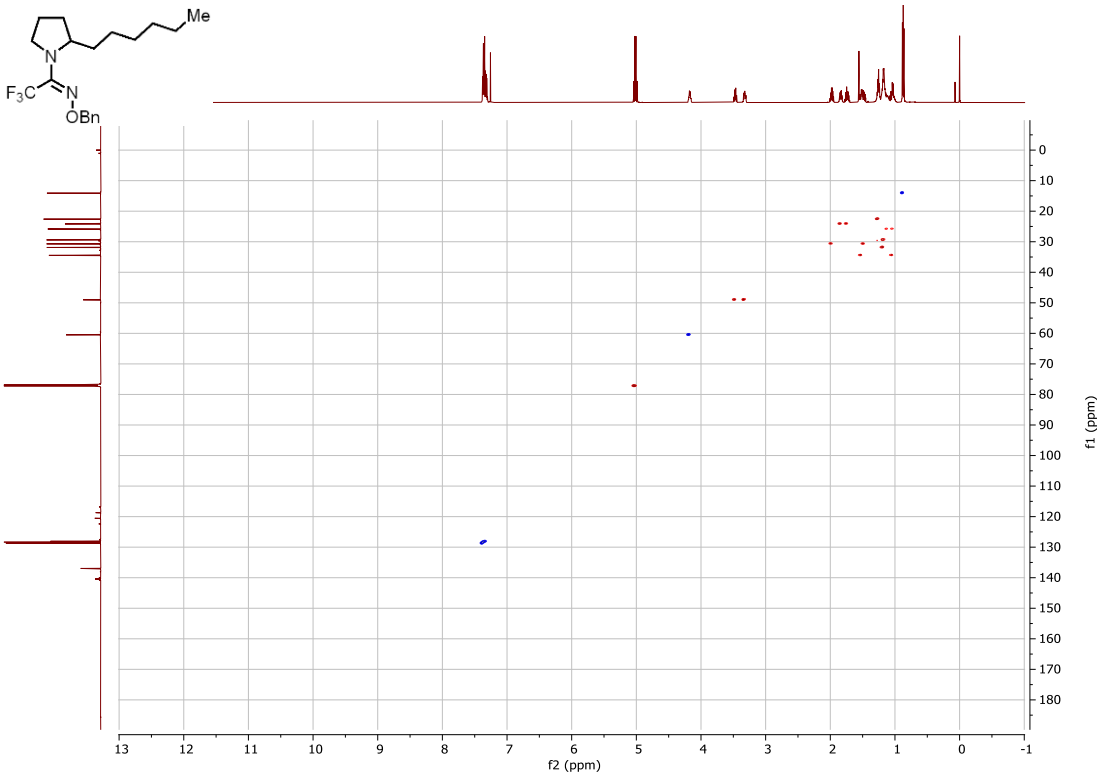

F3C
N
OBn
-63.98
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

(*E*)-2,2,2-trifluoro-1-(2-hexylpyrrolidin-1-yl)ethan-1-one *O*-benzyl oxime (3v-mono)

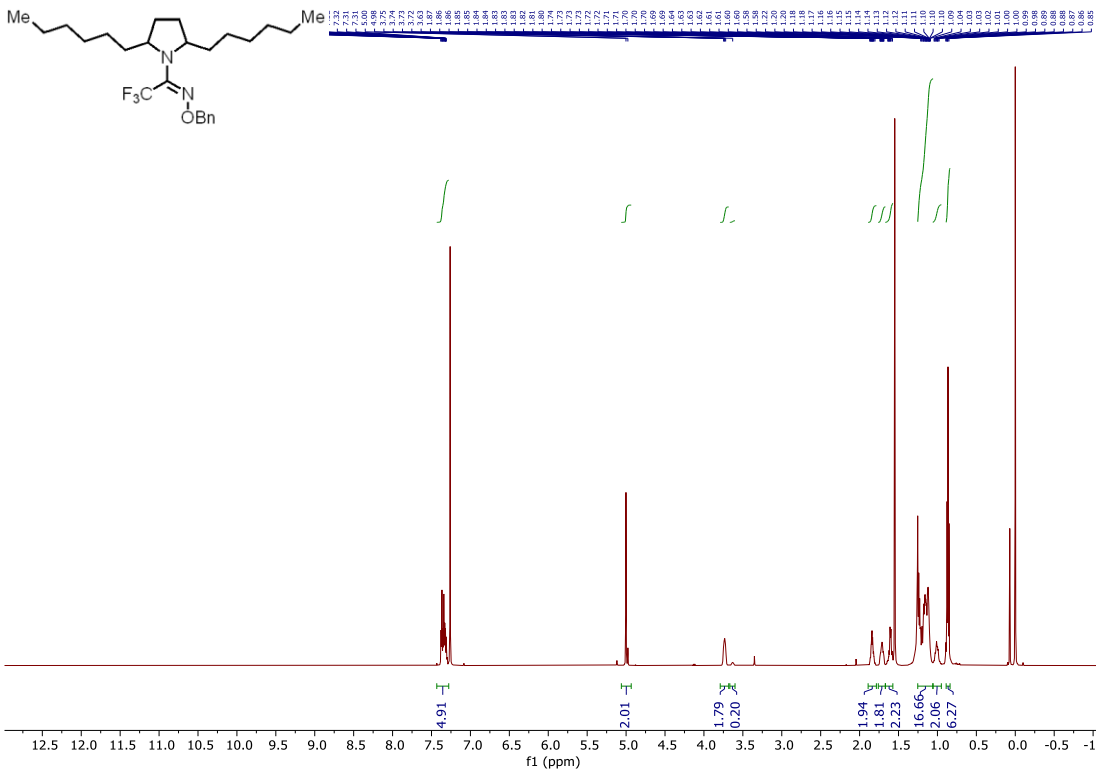


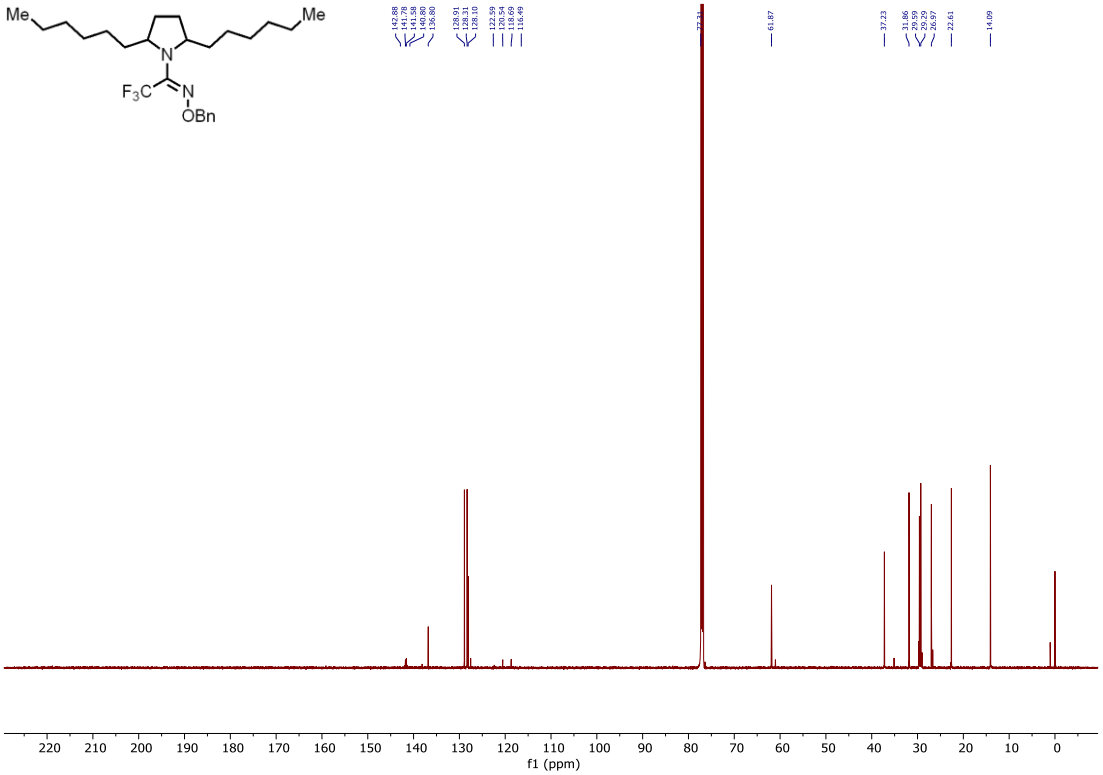


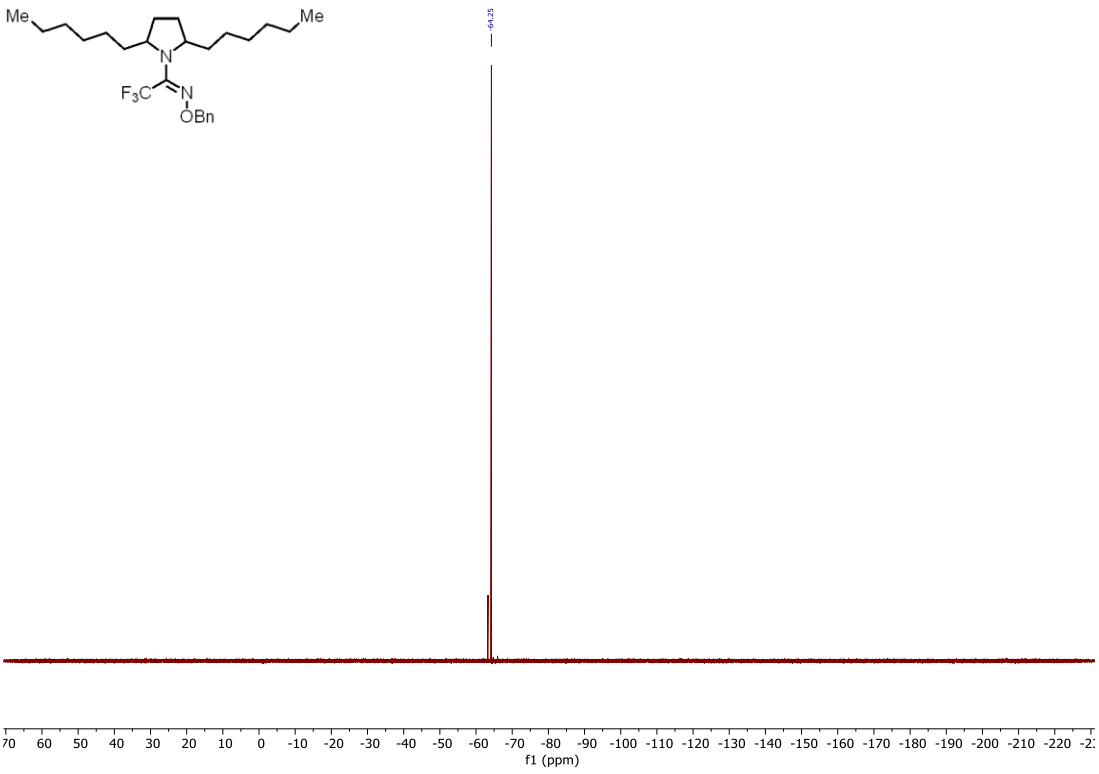

Me
N
F3C
N
OBn
-65.95
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)


Me
N
F3C
N
OBn
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
f1 (ppm)
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f2 (ppm)

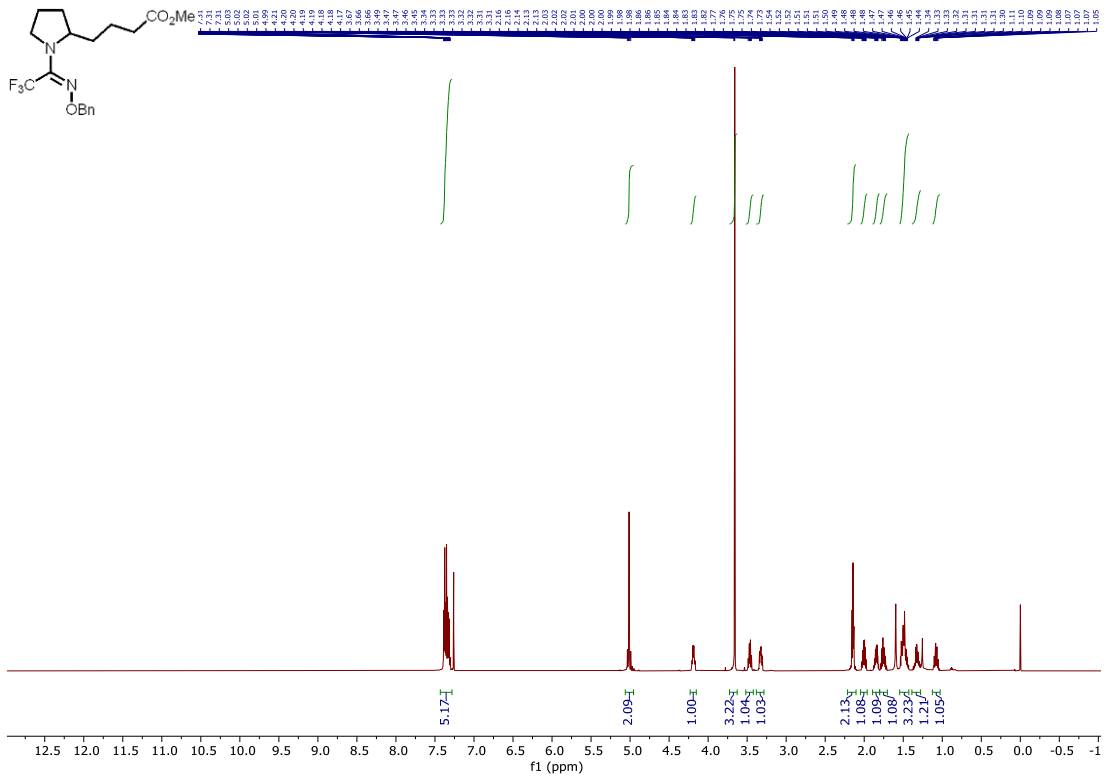
(*E*)-1-(2,5-dihexylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one *O*-benzyl oxime (3v-di)

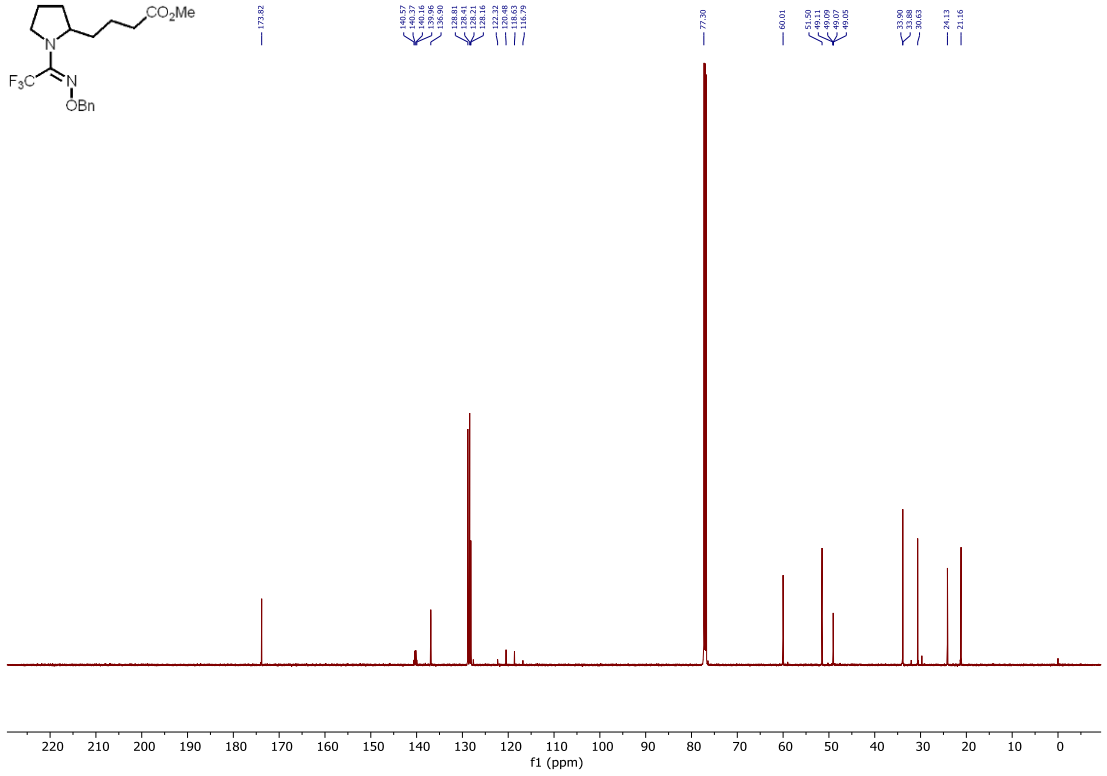


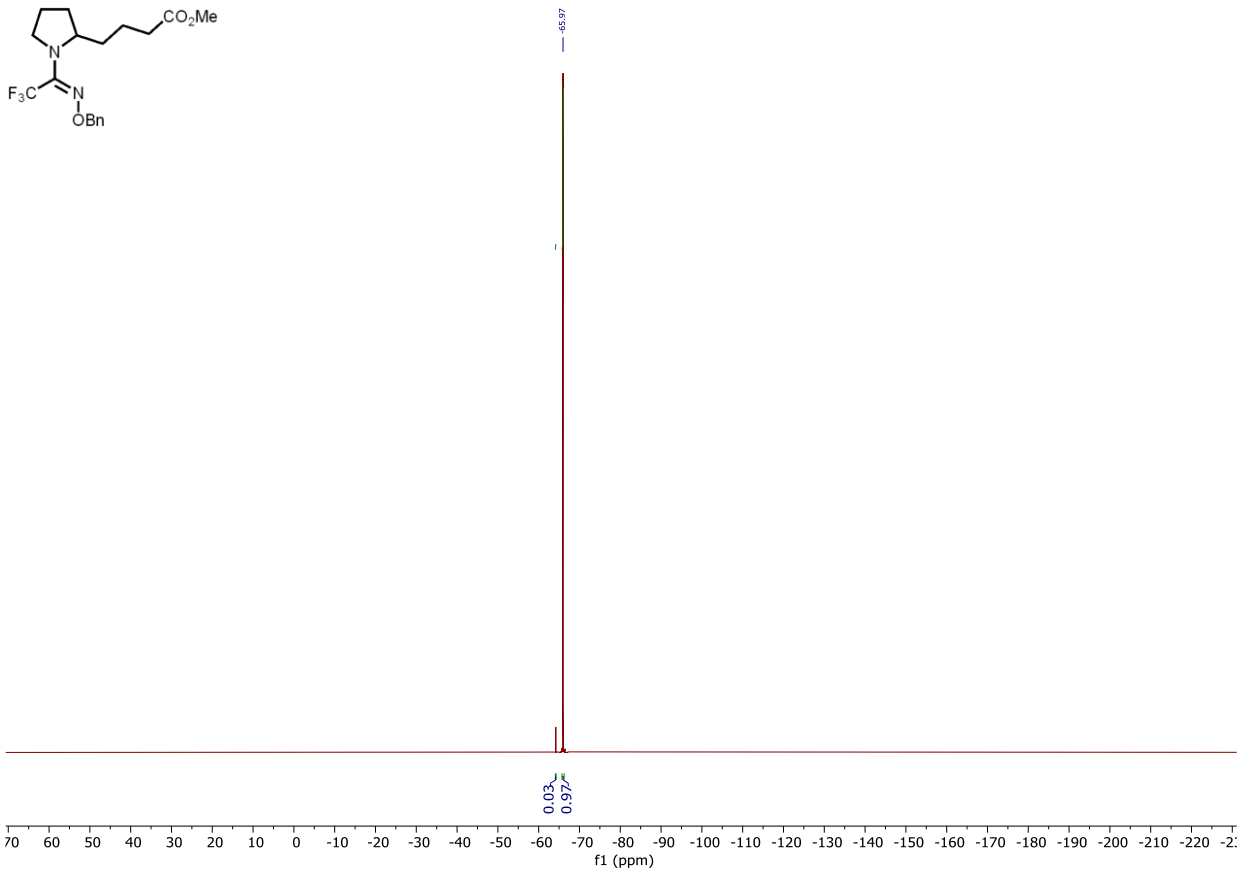



Me
Me
N
F3C
N
OBn
-64.25
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

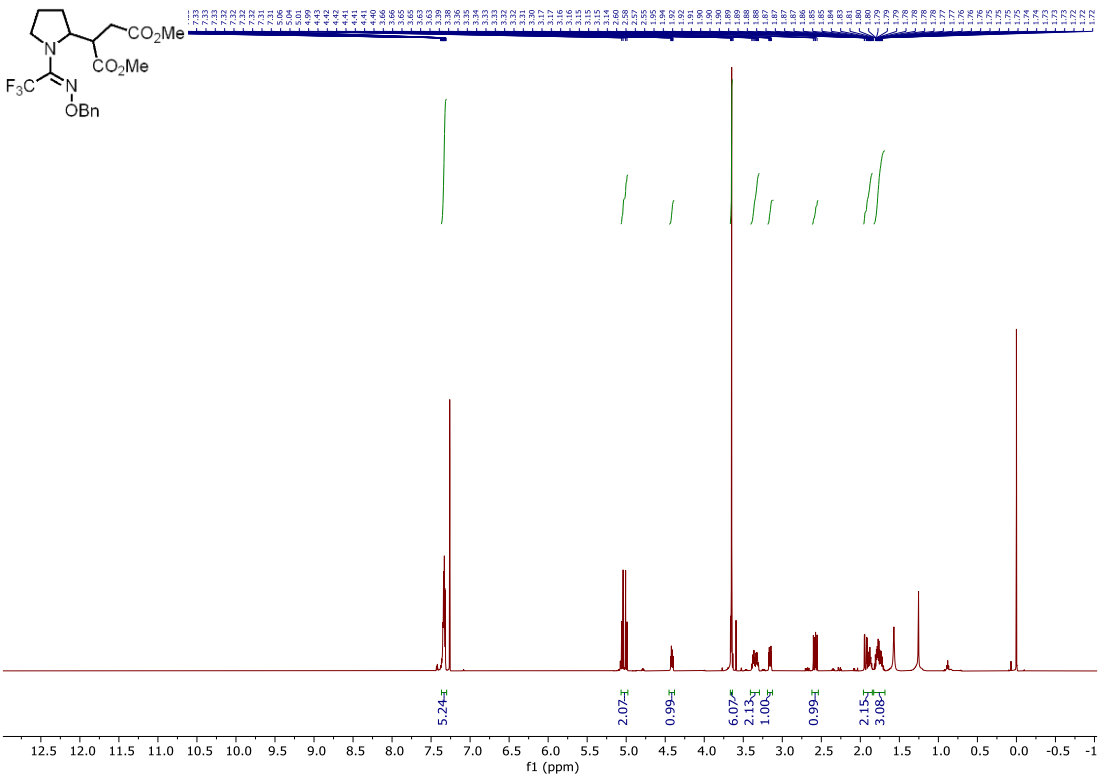
methyl (*E*)-4-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)butanoate (3w)

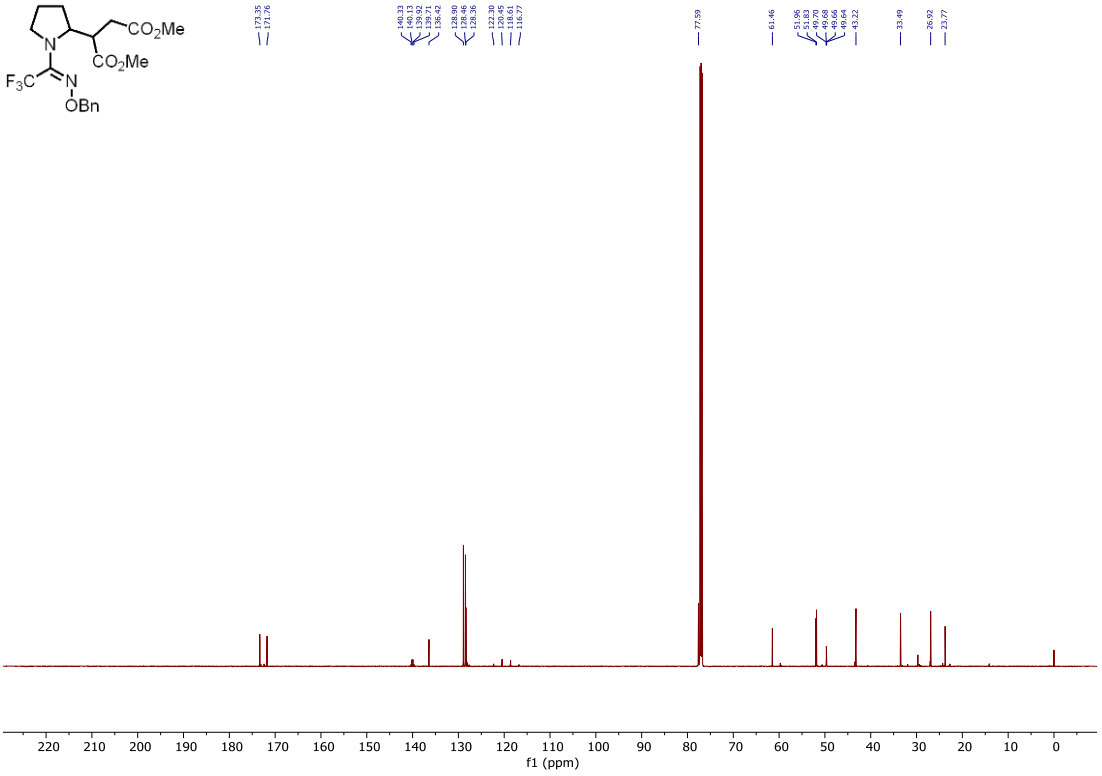


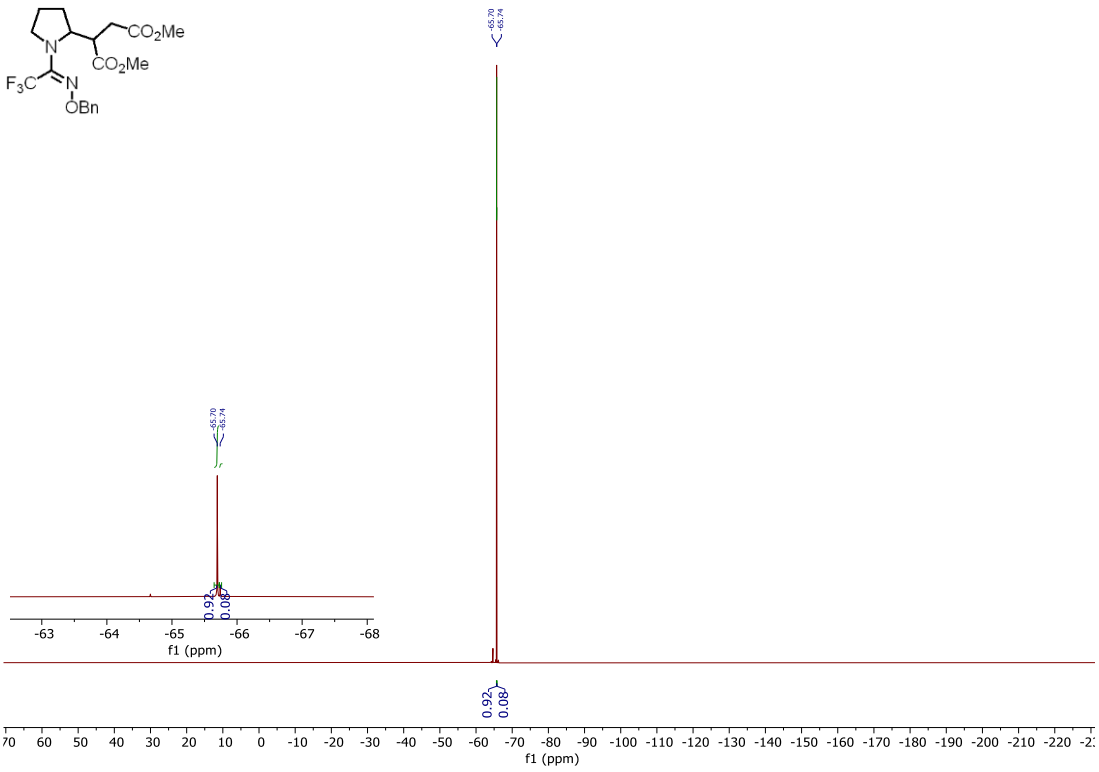



CO2Me
N
F3C
N
OBn
-65.97
0.03
0.97
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

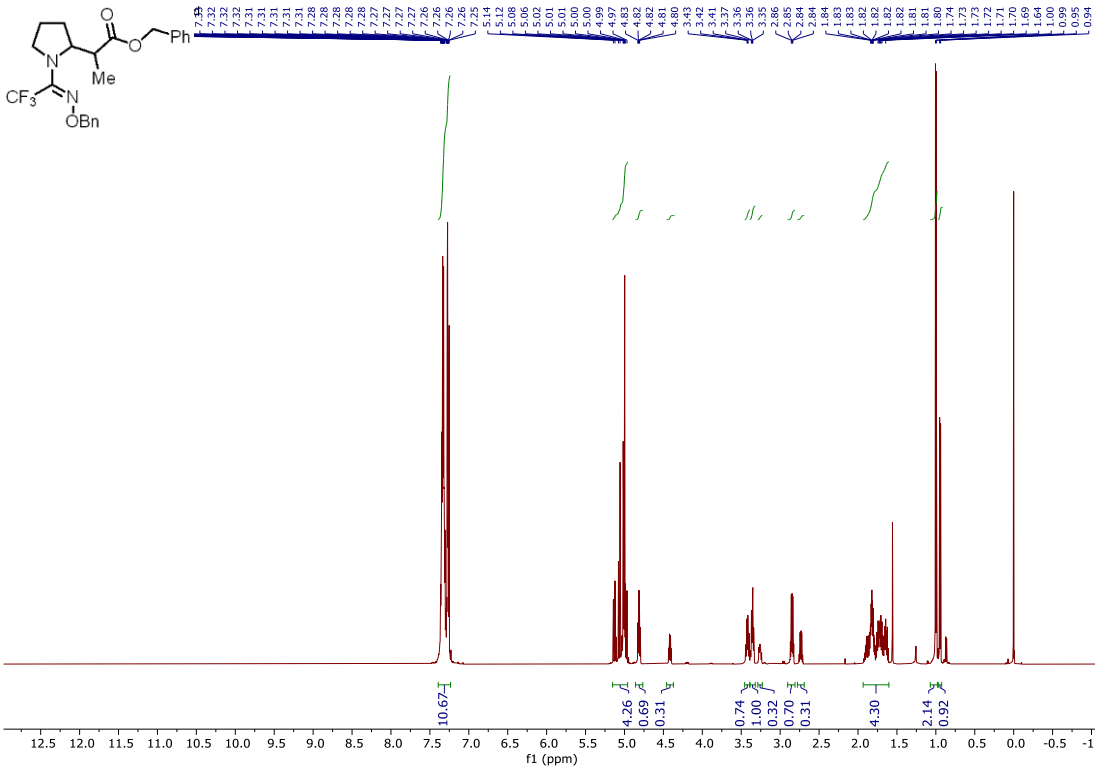
dimethyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)succinate (3x)

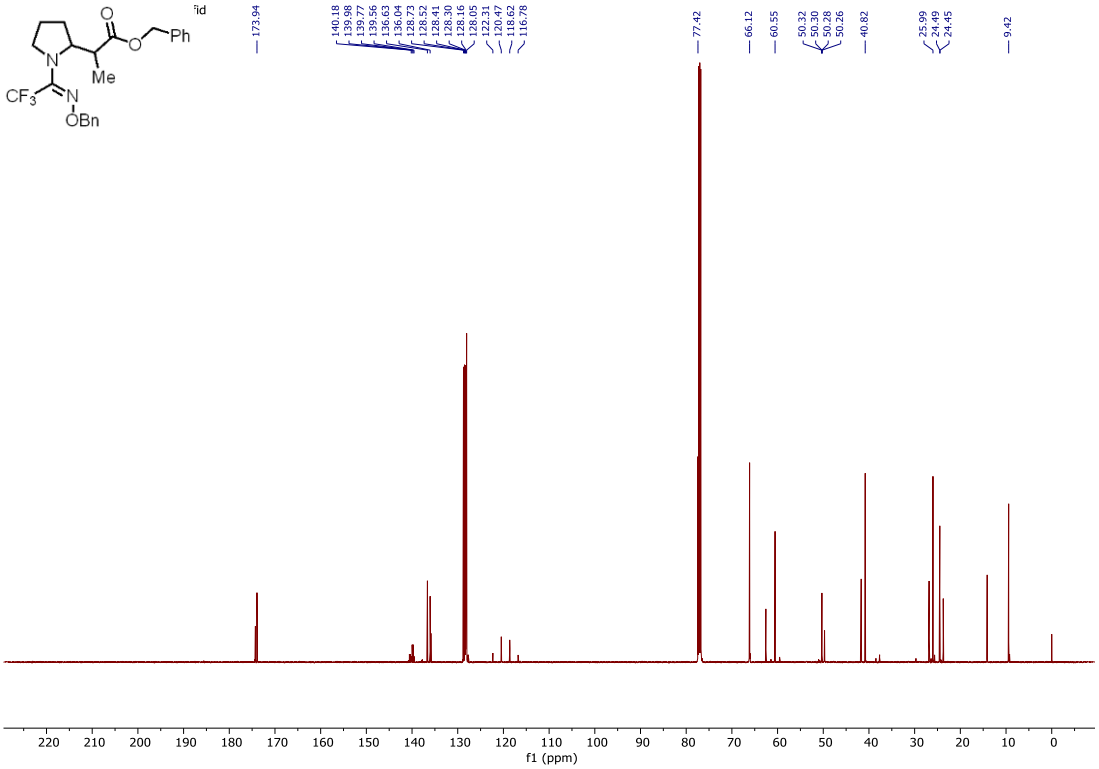


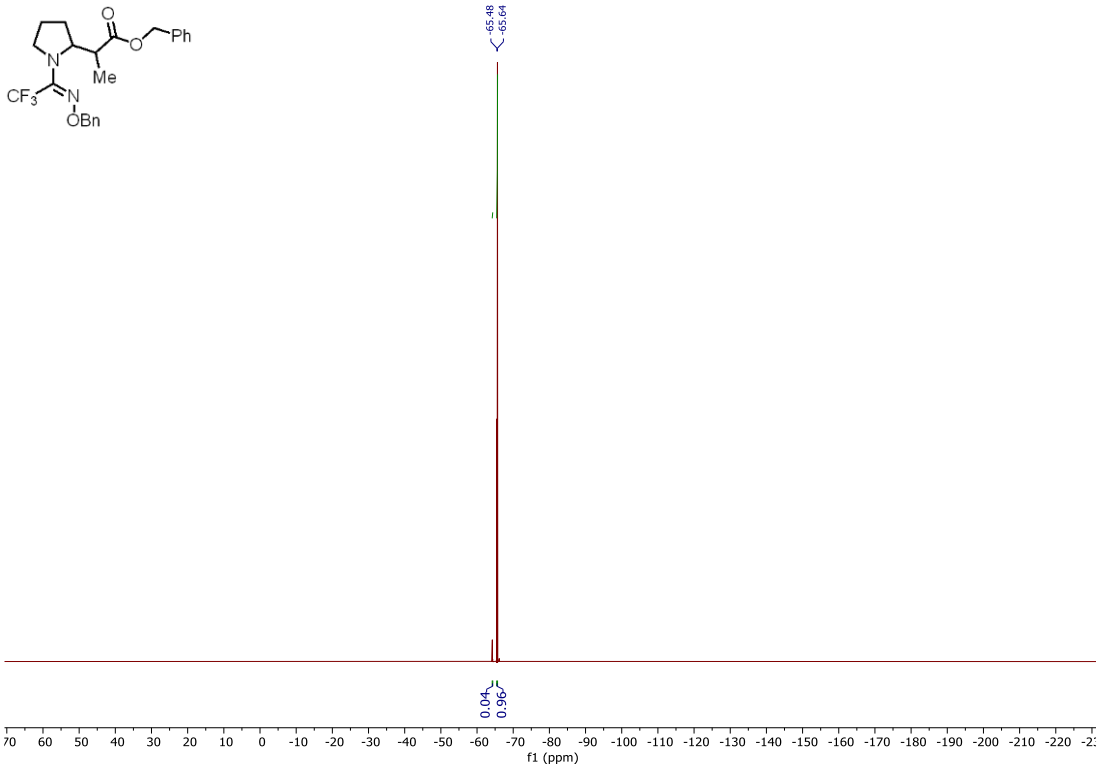


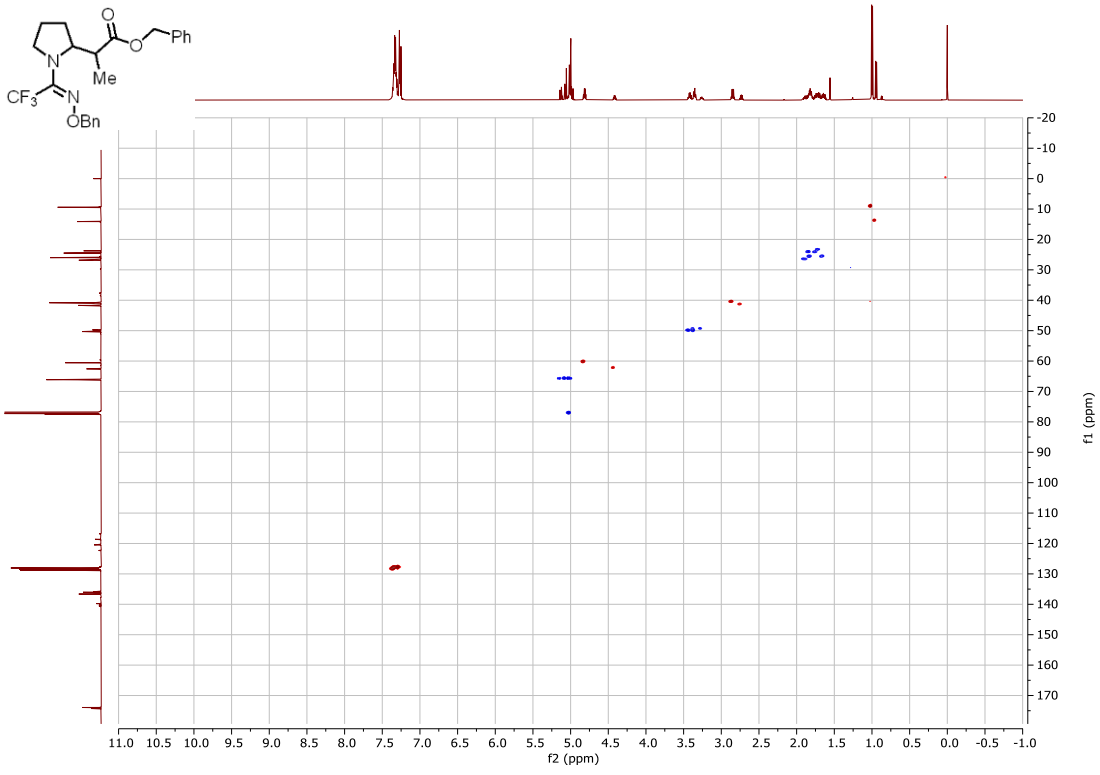

CO2Me
CO2Me
F3C
N
N
OBn
-65.70
-65.74
0.92
0.08
-63
-64
-65
-66
-67
-68
f1 (ppm)
0.92
0.08
f1 (ppm)

benzyl (*E*)-2-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (3y-B)

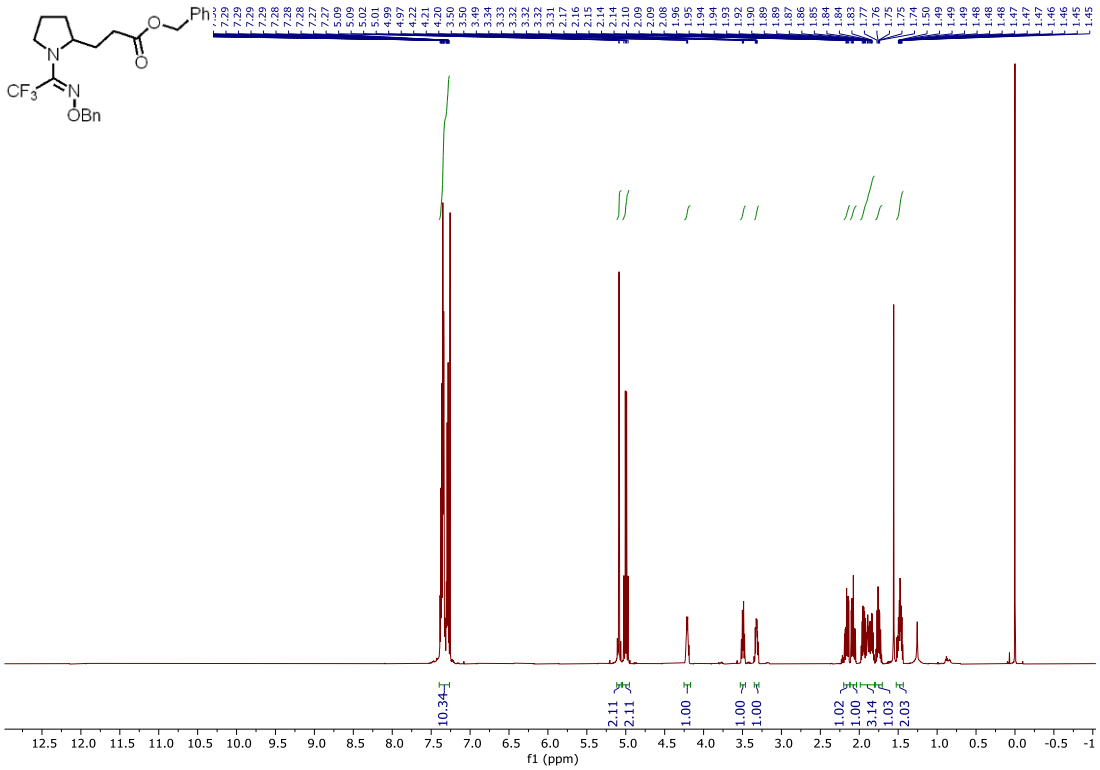


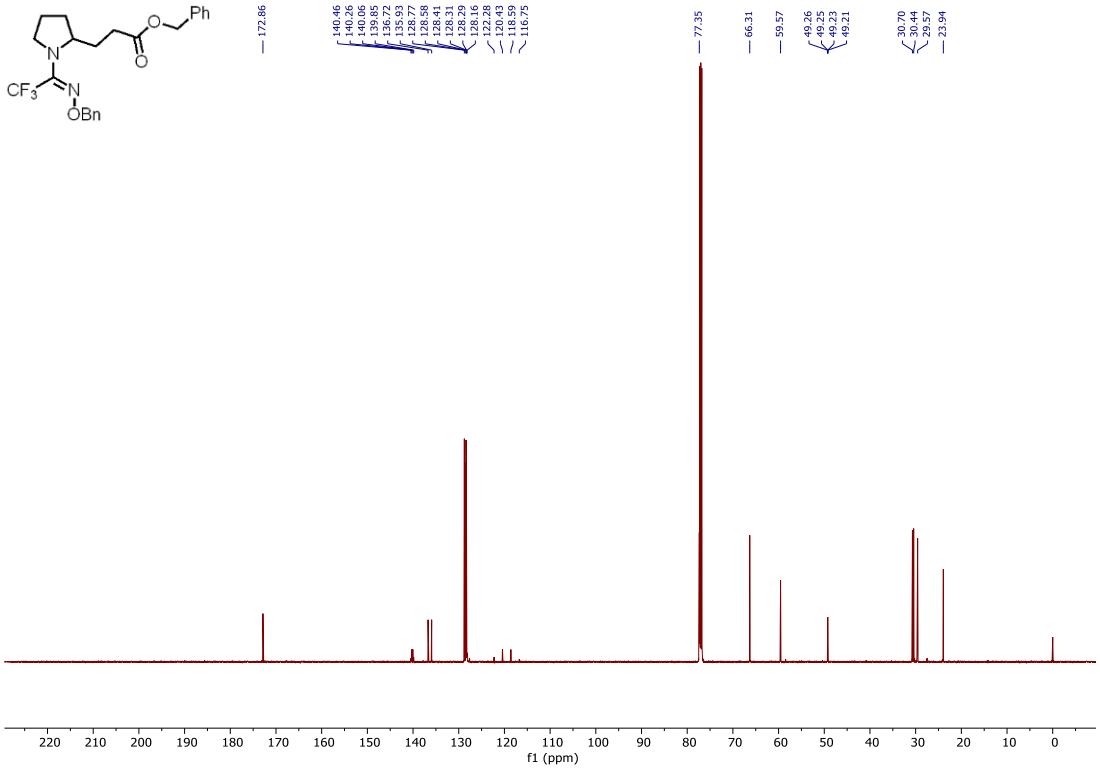


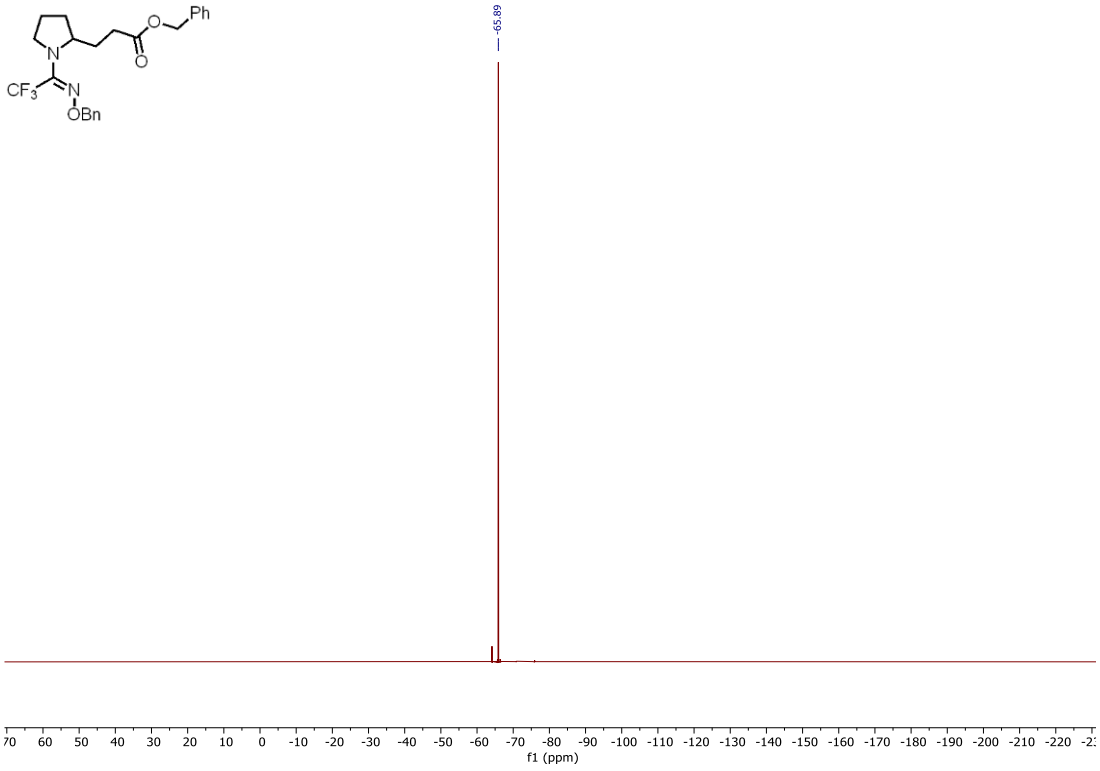

-65.48
-65.64
0.04
0.96
f1 (ppm)

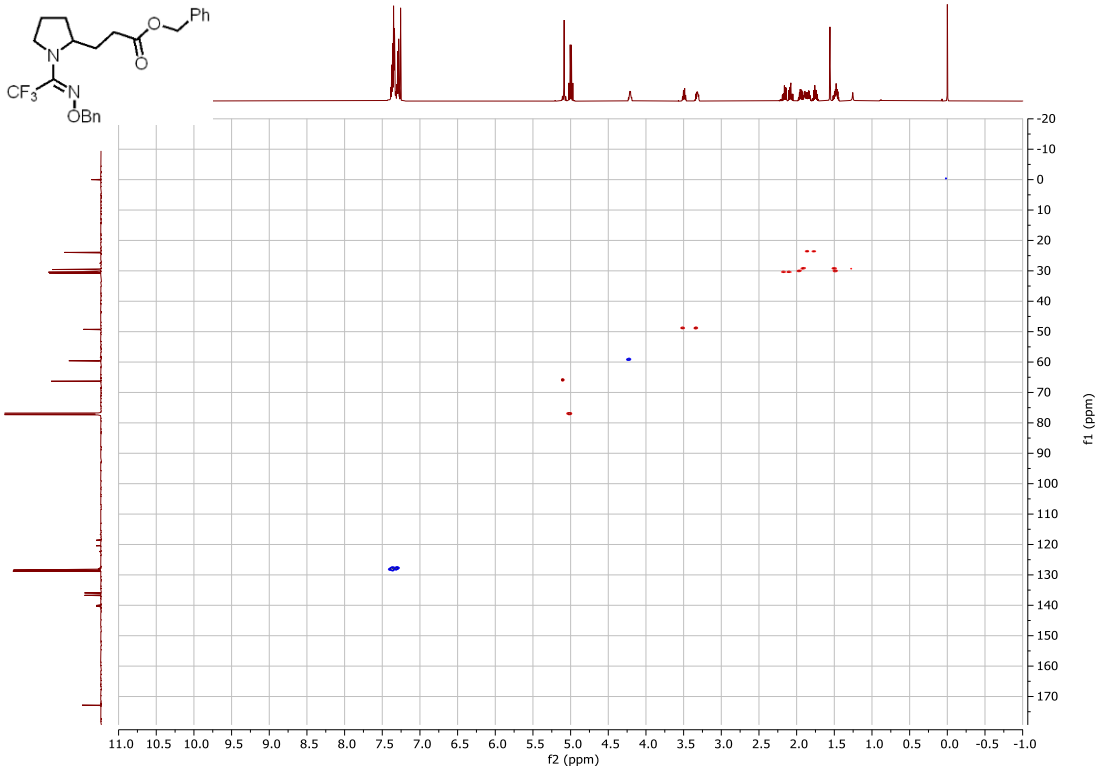

f2 (ppm)
f1 (ppm)

benzyl (*E*)-3-(1-(1-((benzyloxy)imino)-2,2,2-trifluoroethyl)pyrrolidin-2-yl)propanoate (3y-L).

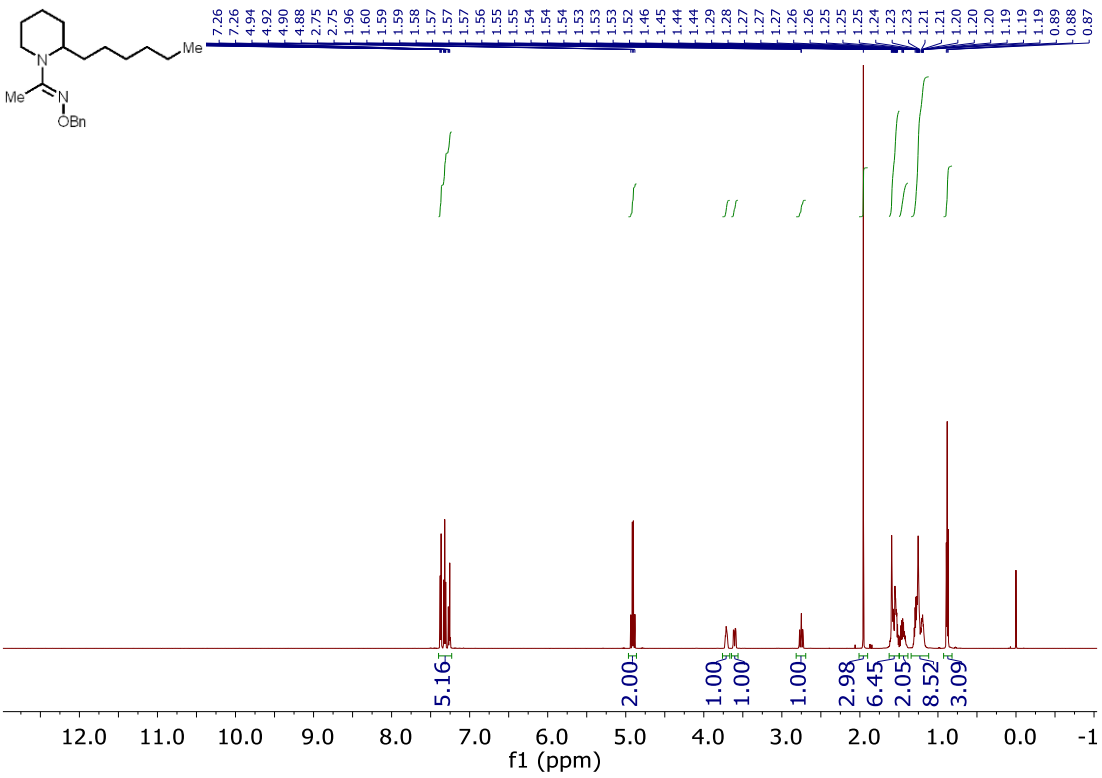


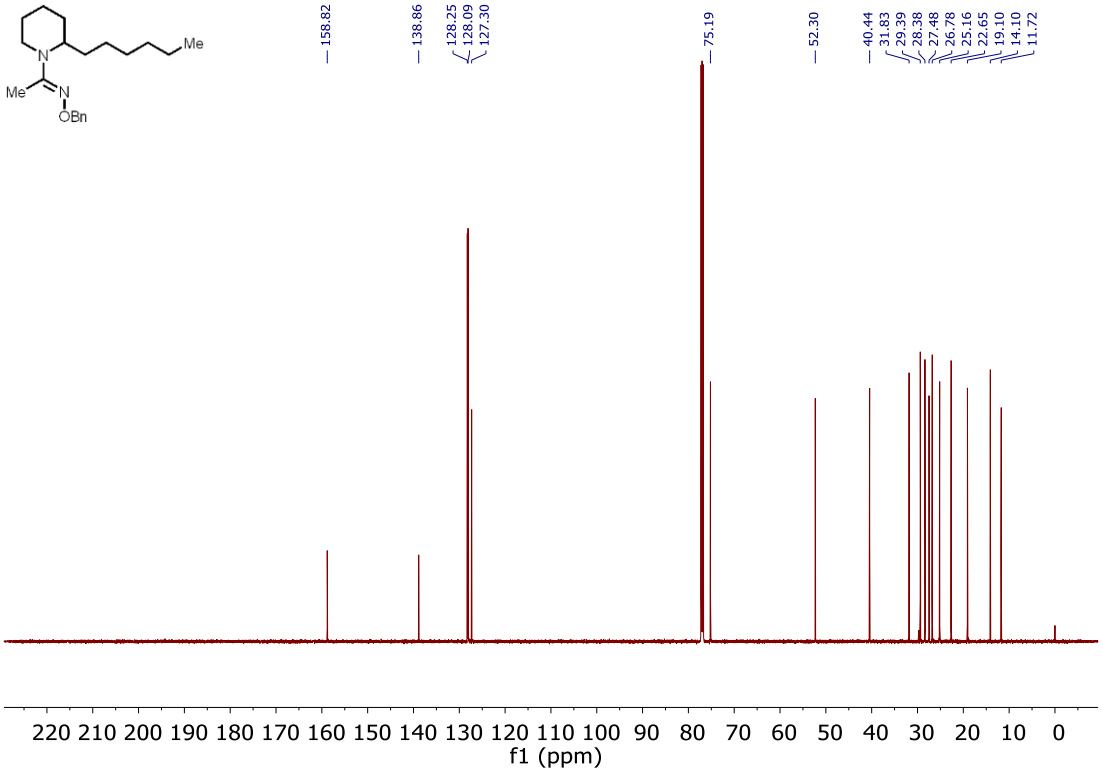



-65.89
f1 (ppm)

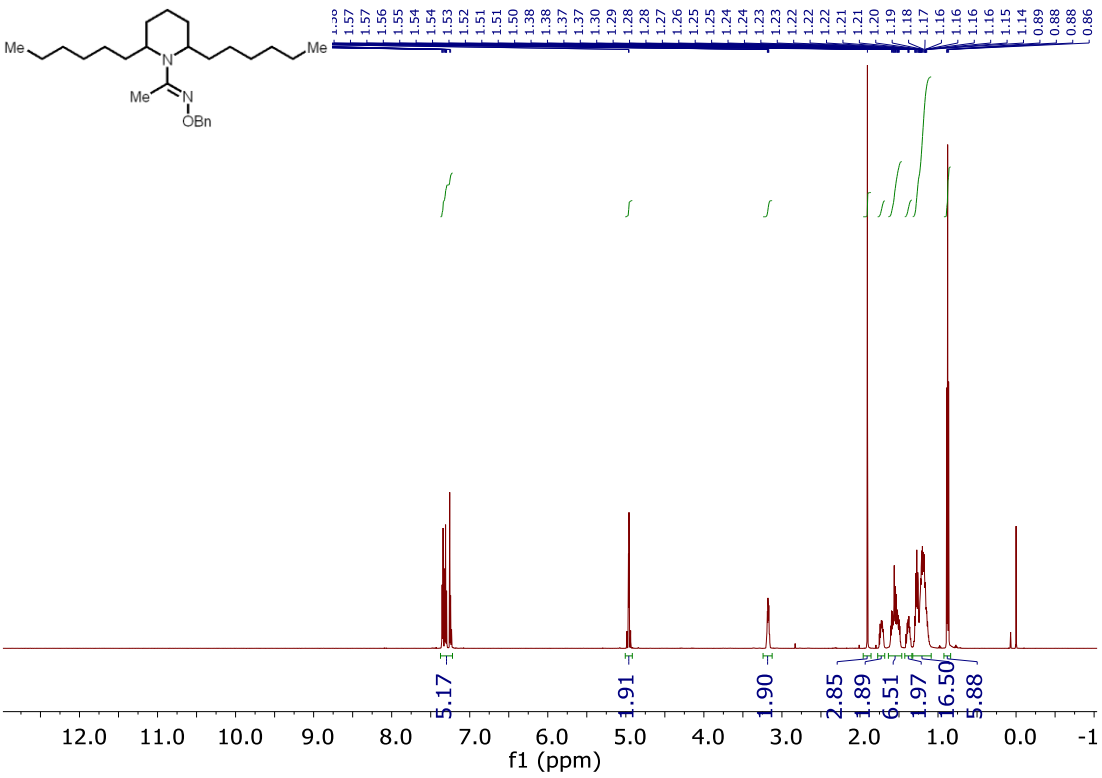

f2 (ppm)
f1 (ppm)

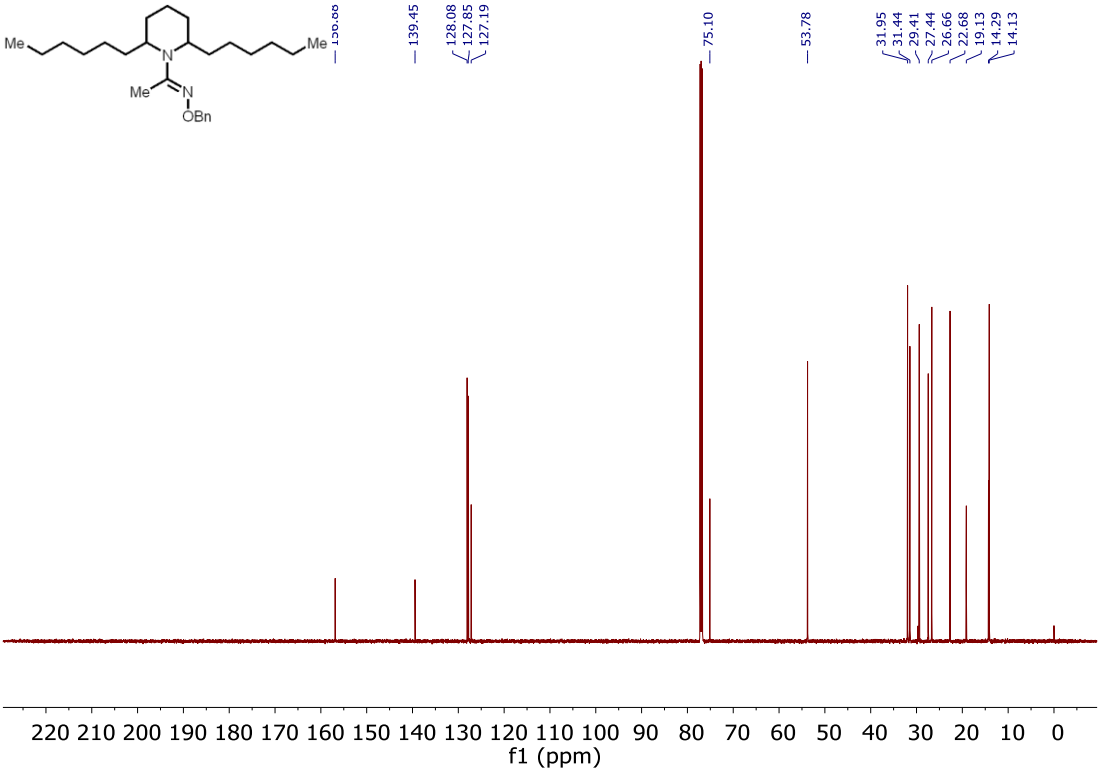
(*E*)-1-(2-hexylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5b-mono)

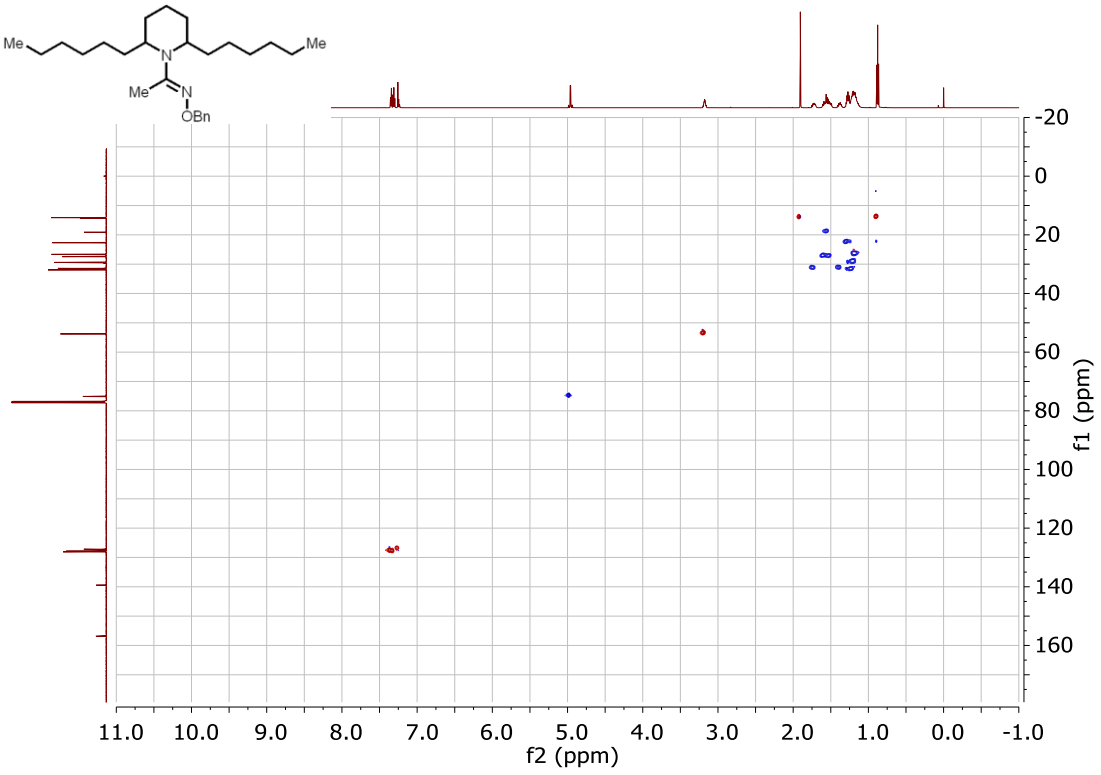




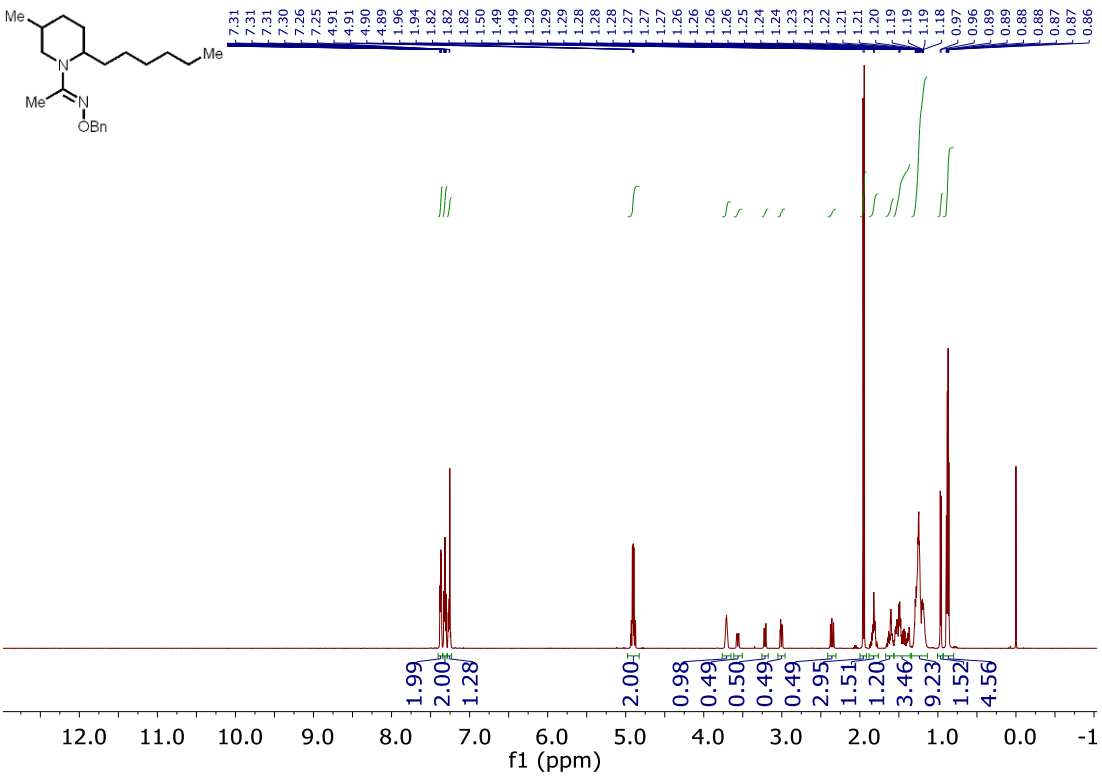
(*E*)-1-(2,6-dihexylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5b-di)

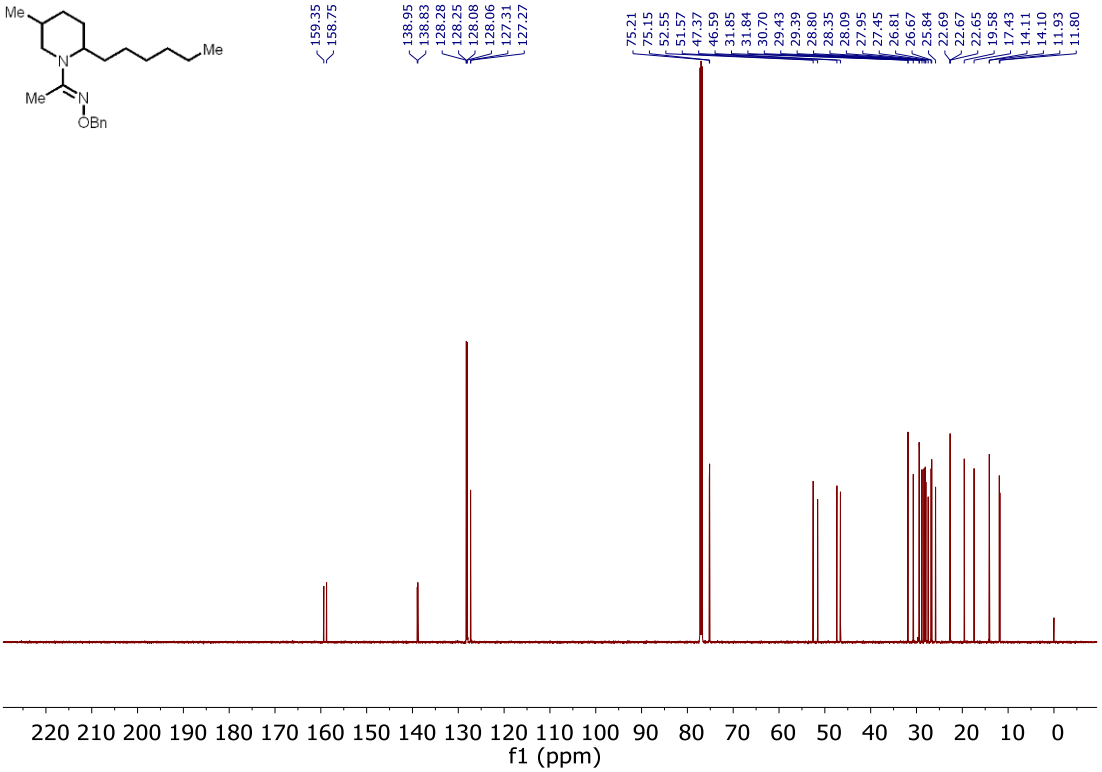


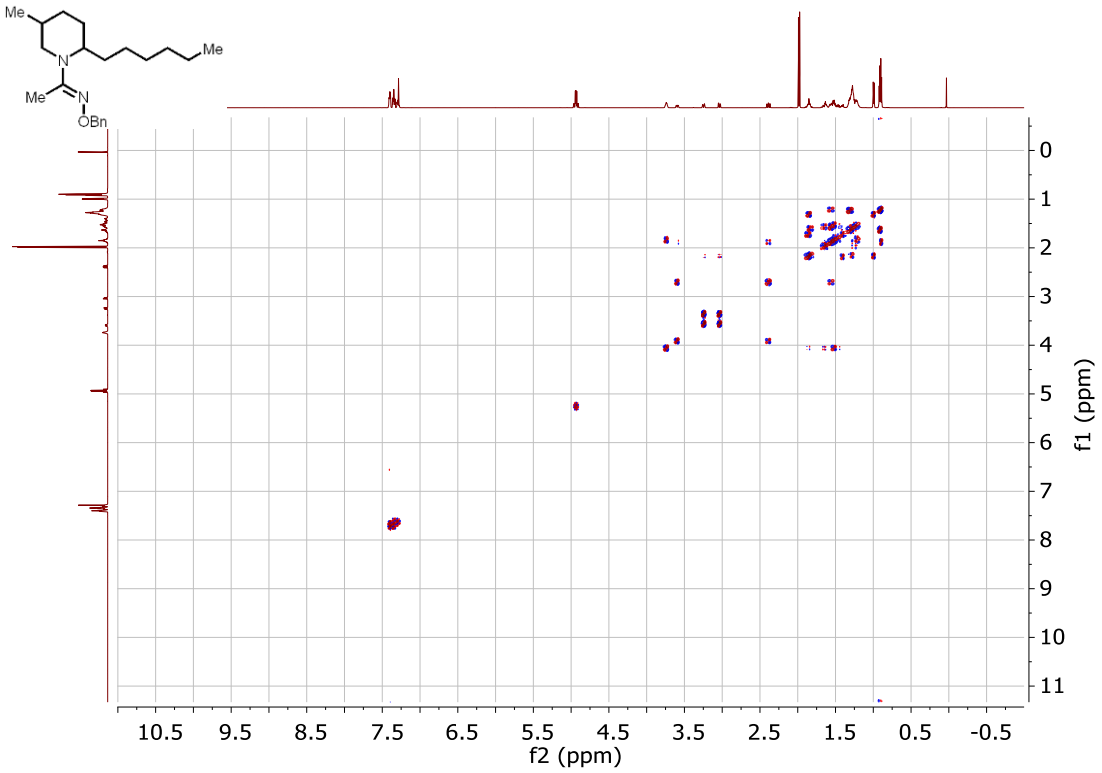


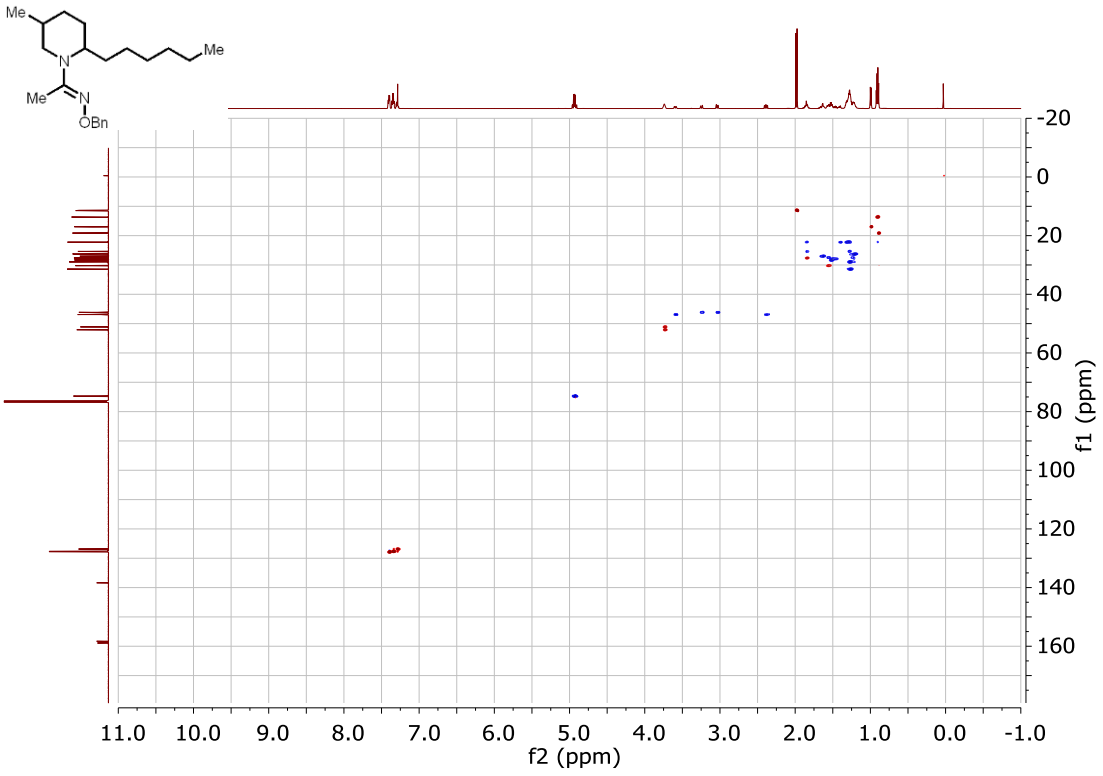

Me
N
Me
Me
N
OBn
-20
0
20
40
60
80
100
120
140
160
f1 (ppm)
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f2 (ppm)

(*E*)-1-(2-hexyl-5-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5c)

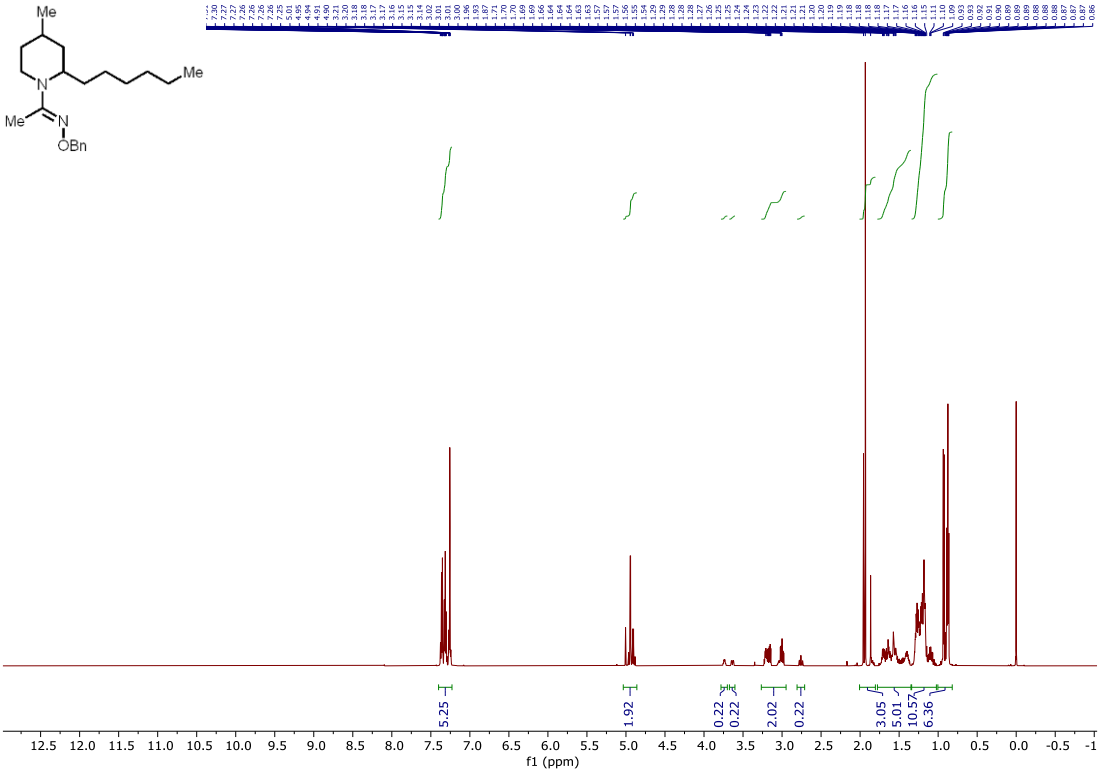


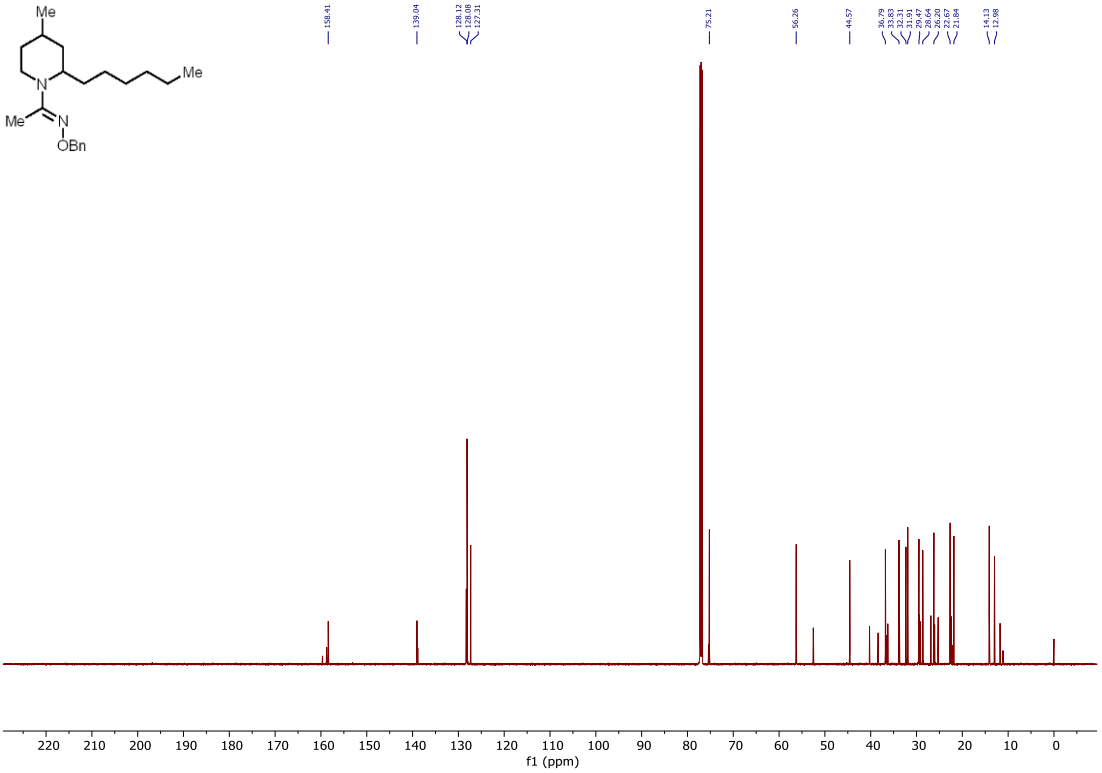


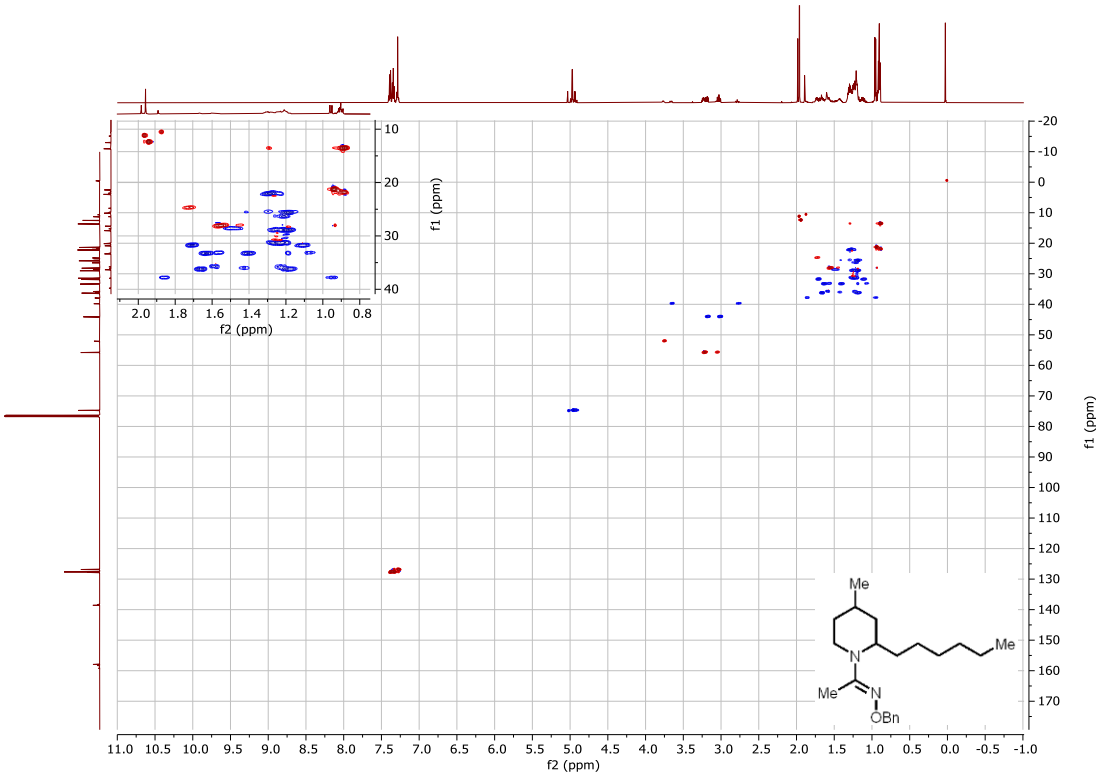

Me
Me
N
Me
N
OBn
0
1
2
3
4
5
6
7
8
9
10
11
f1 (ppm)
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f2 (ppm)


Me
Me
N
Me
N
OBn
-20
0
20
40
60
80
100
120
140
160
f1 (ppm)
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
f2 (ppm)

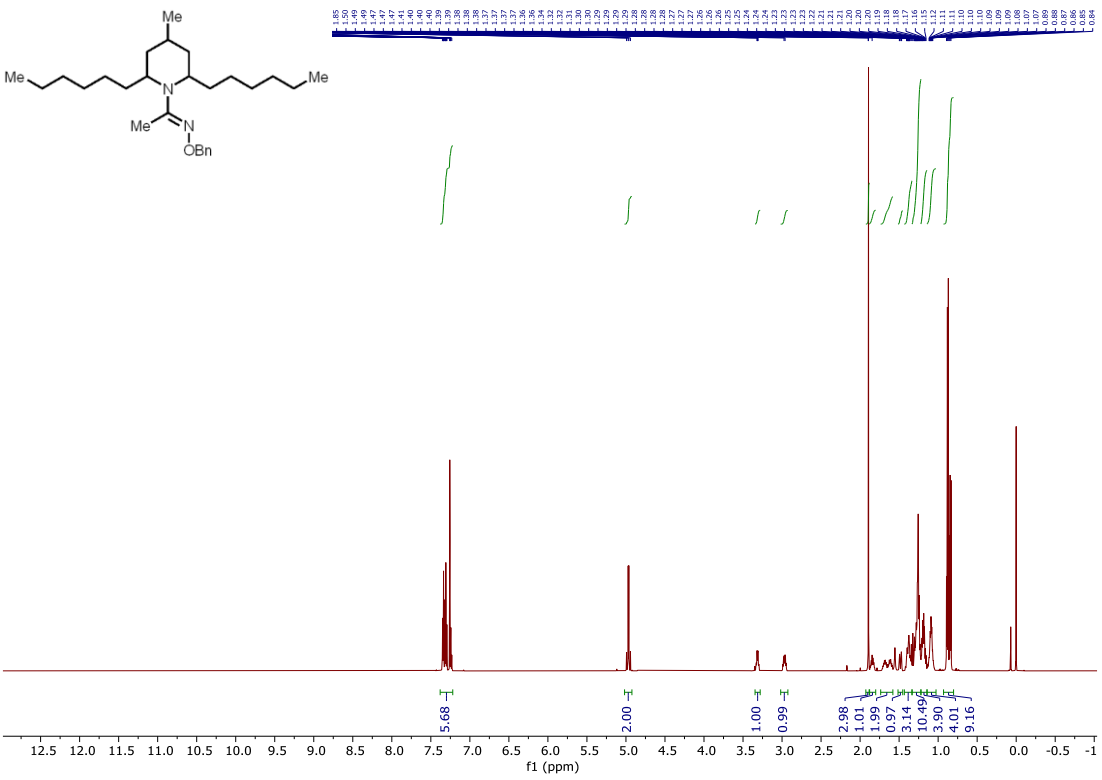
(*E*)-1-(2-hexyl-4-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5d-mono)

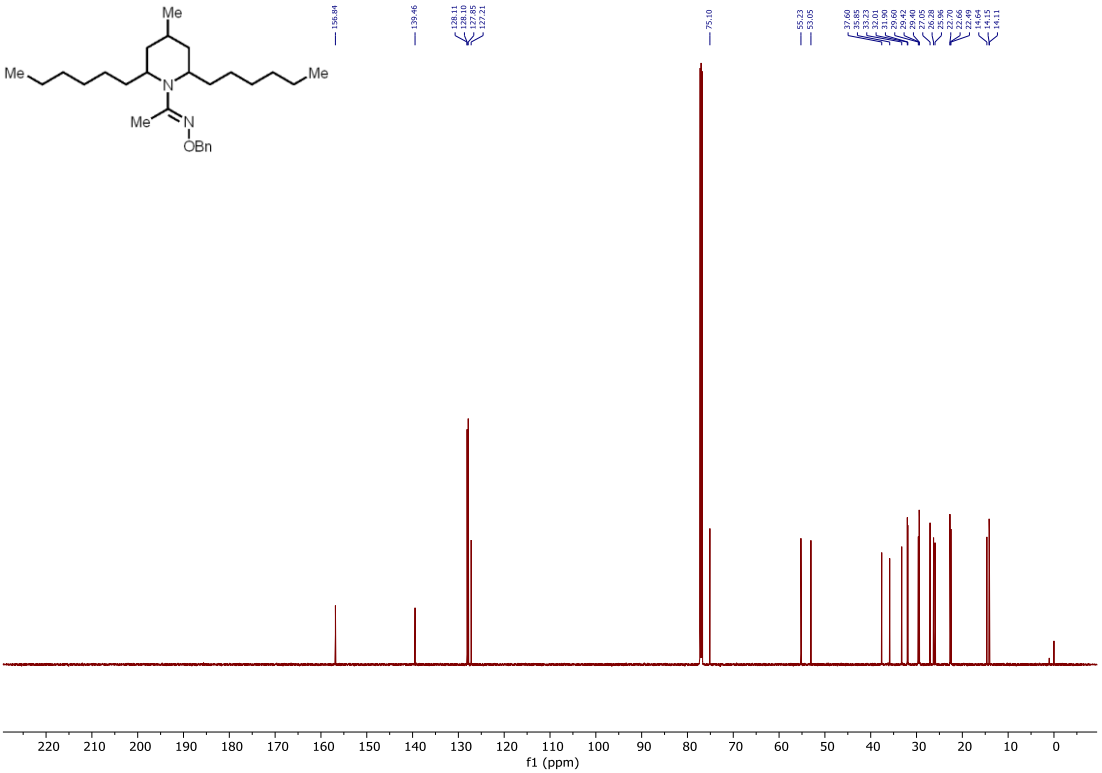


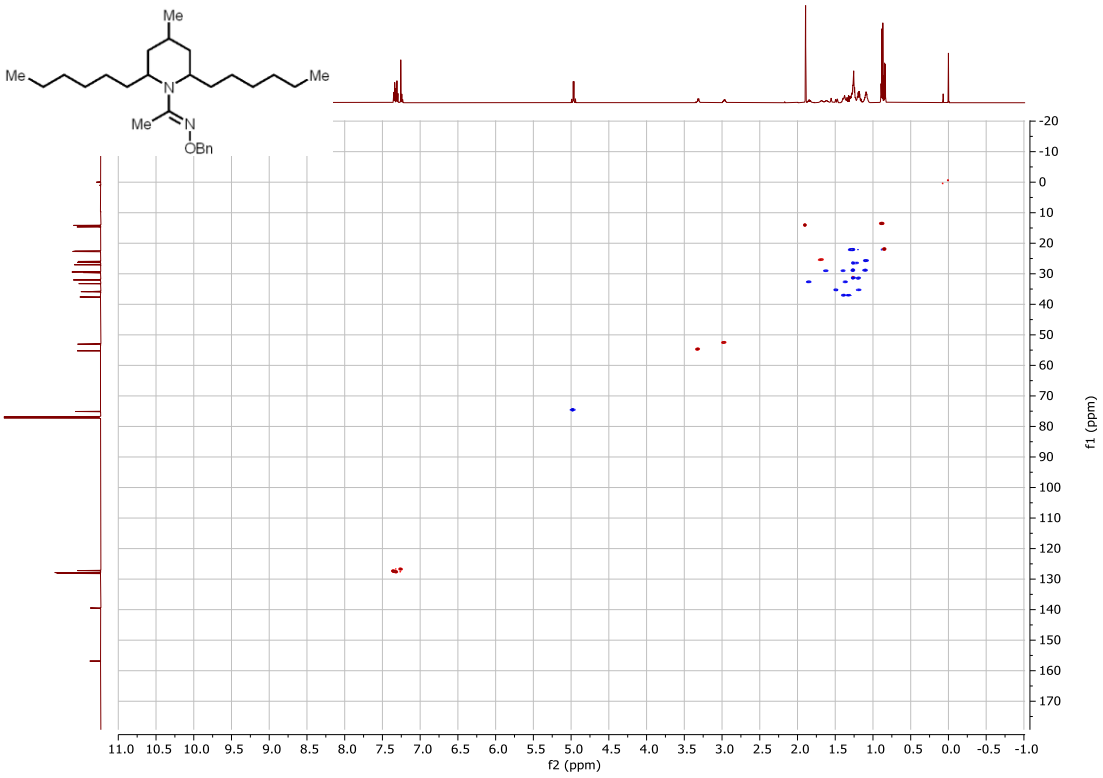


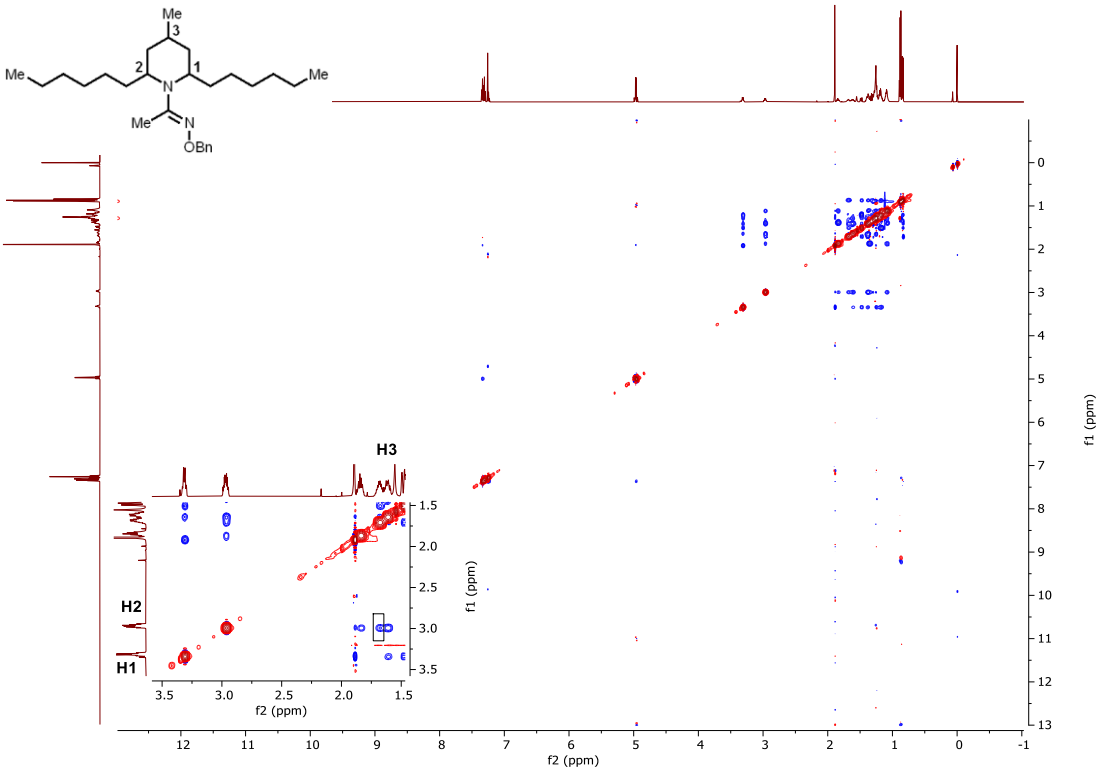

f1 (ppm)
f2 (ppm)
Me
N
Me
Me
N
OBn

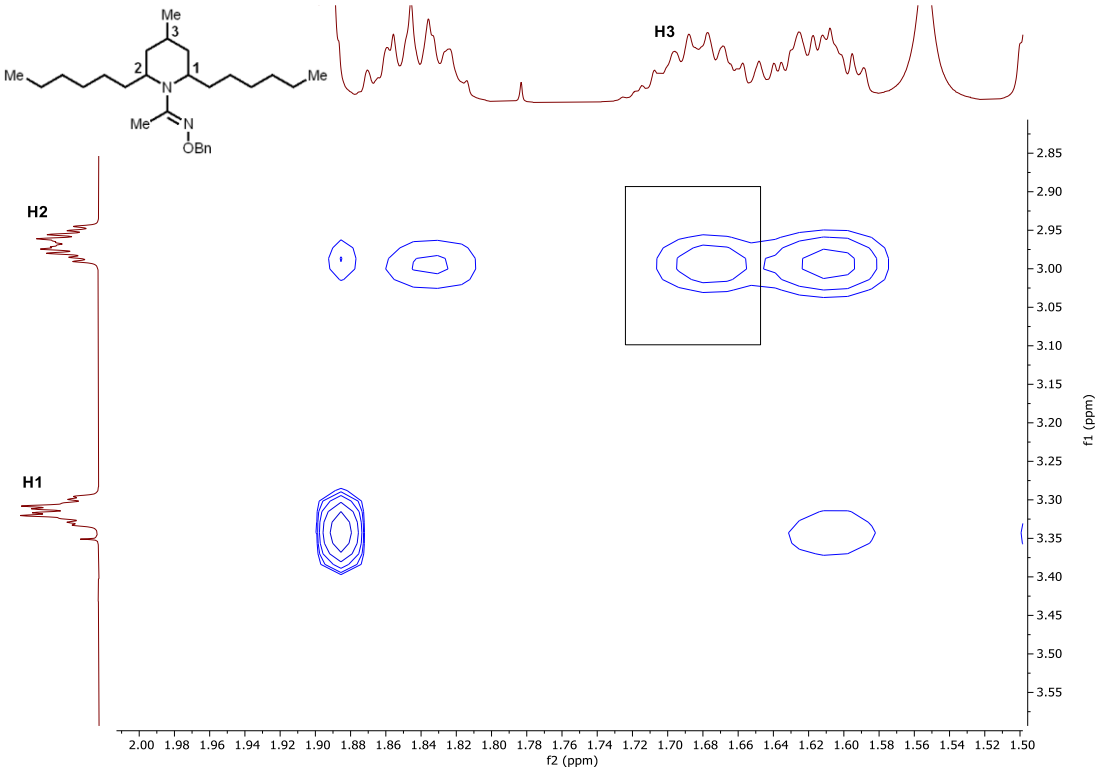
(*E*)-1-(2,6-dihexyl-4-methylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5d-di)



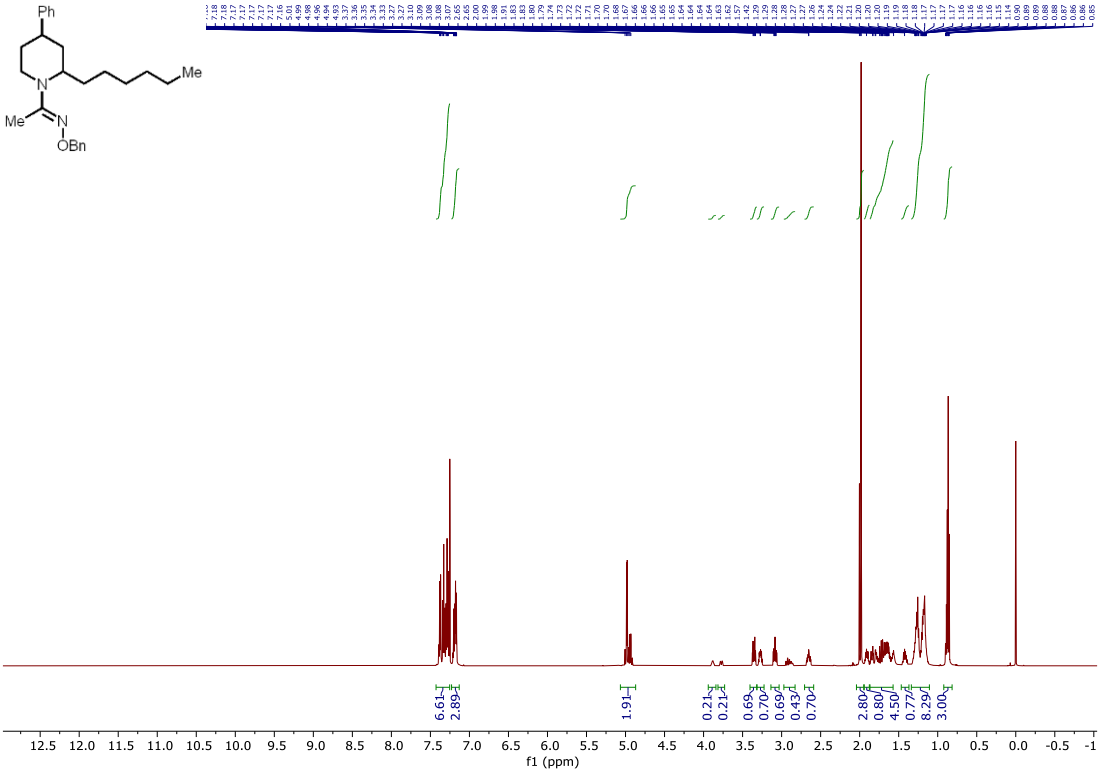


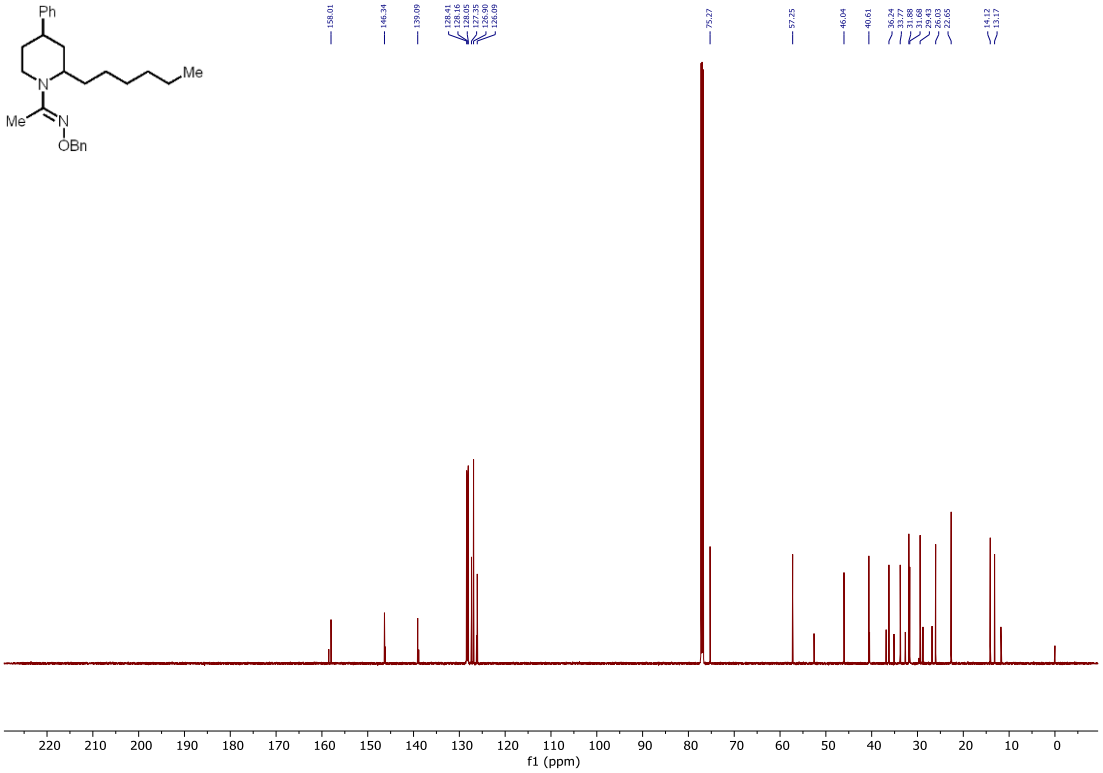

Me
Me
N
Me
N
OBn
f2 (ppm)
f1 (ppm)

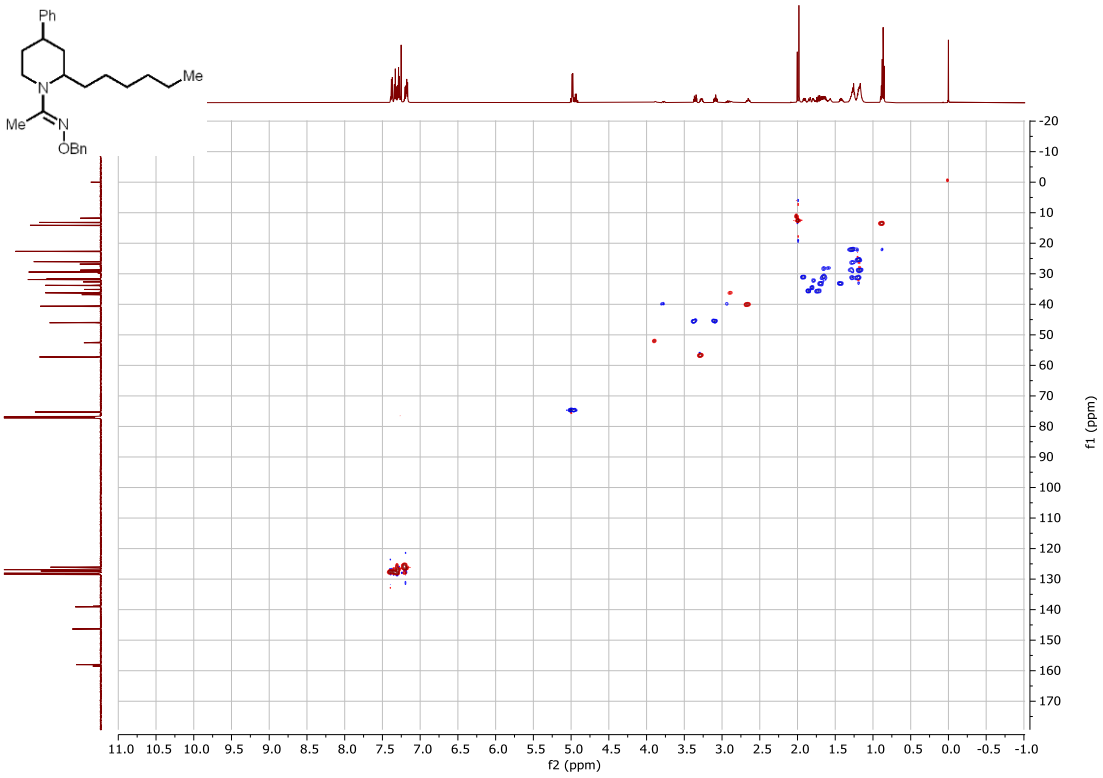

Me
3
2
1
N
Me
Me
N
OBn
H3
H2
H1
f2 (ppm)
f1 (ppm)


Me
3
2
1
N
Me
Me
Me
N
OBn
H3
H2
H1
2.85
2.90
2.95
3.00
3.05
3.10
3.15
3.20
3.25
3.30
3.35
3.40
3.45
3.50
3.55
f1 (ppm)
2.00 1.98 1.96 1.94 1.92 1.90 1.88 1.86 1.84 1.82 1.80 1.78 1.76 1.74 1.72 1.70 1.68 1.66 1.64 1.62 1.60 1.58 1.56 1.54 1.52 1.50
f2 (ppm)

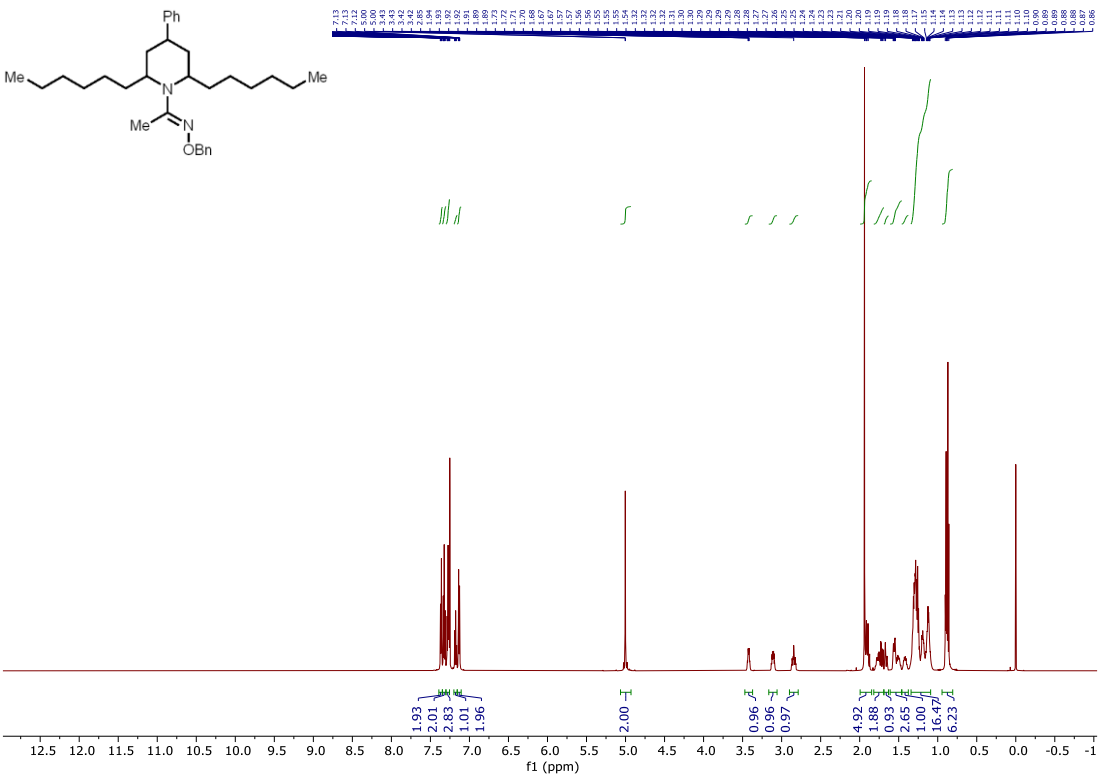
(*E*)-1-(2-hexyl-4-phenylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5e-mono)

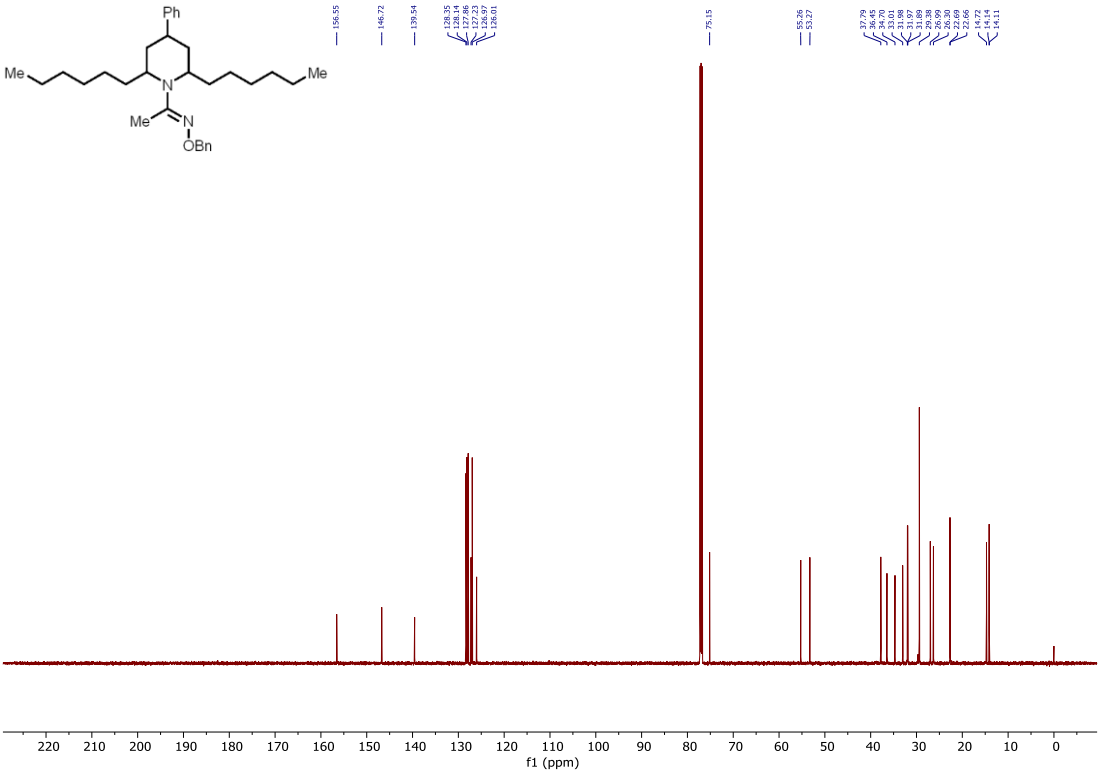


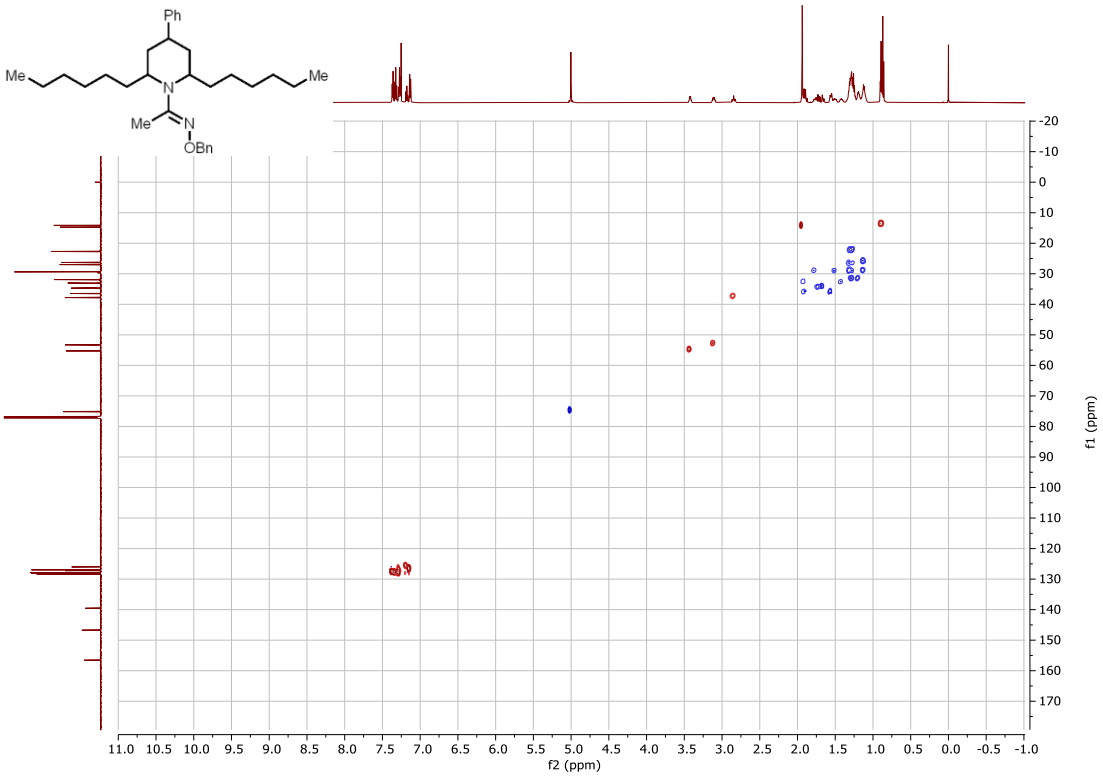



Ph
N
Me
Me
N
OBn
f2 (ppm)
f1 (ppm)

(*E*)-1-(2,6-dihexyl-4-phenylpiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5e-di)

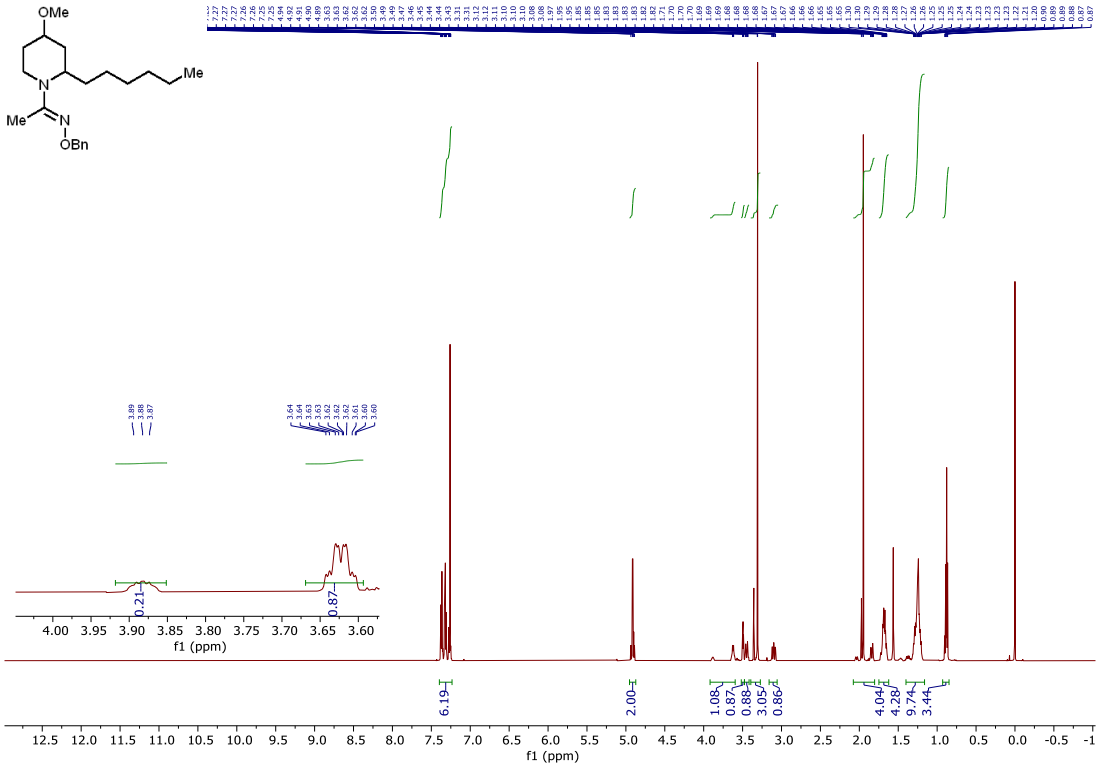


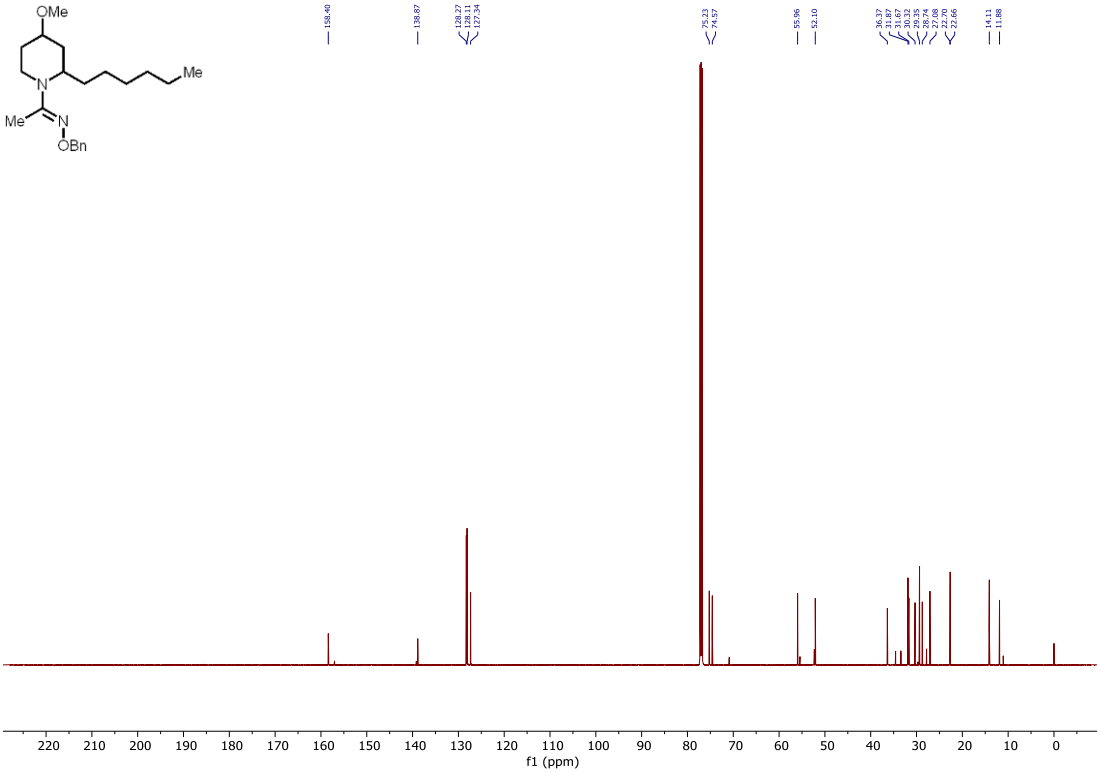


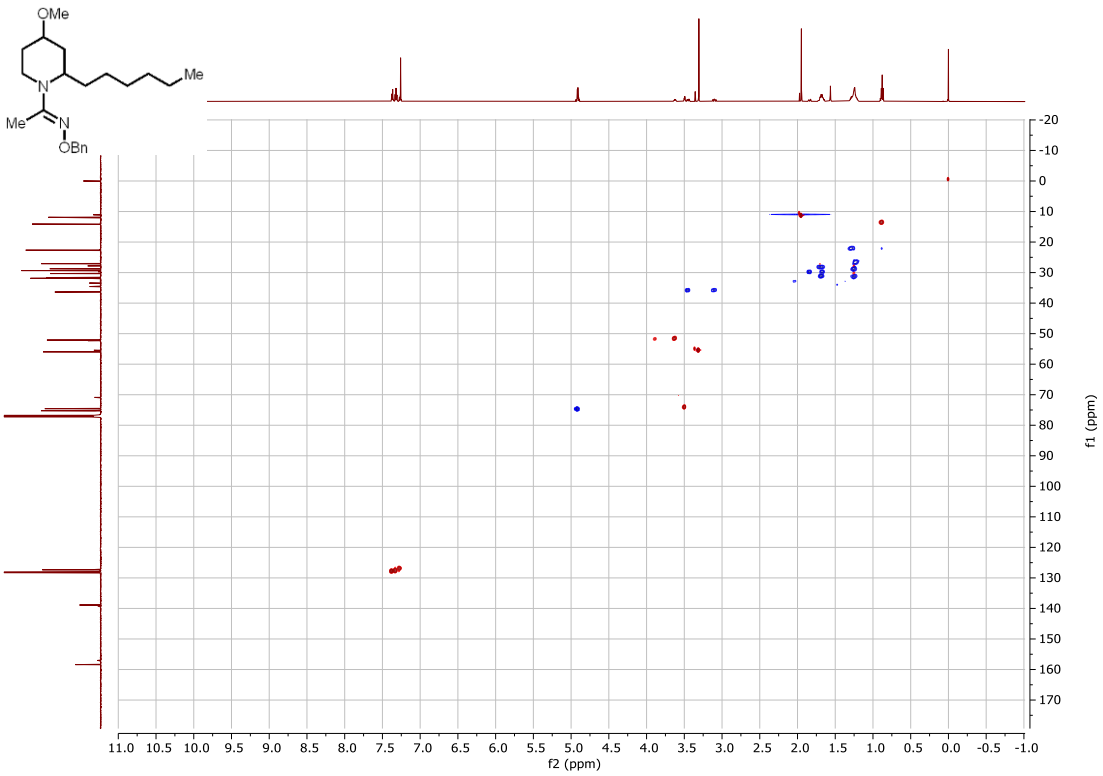

Ph
Me
Me
N
Me
N
OBn
f1 (ppm)
f2 (ppm)

(*E*)-1-(2-hexyl-4-methoxypiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5f-mono)

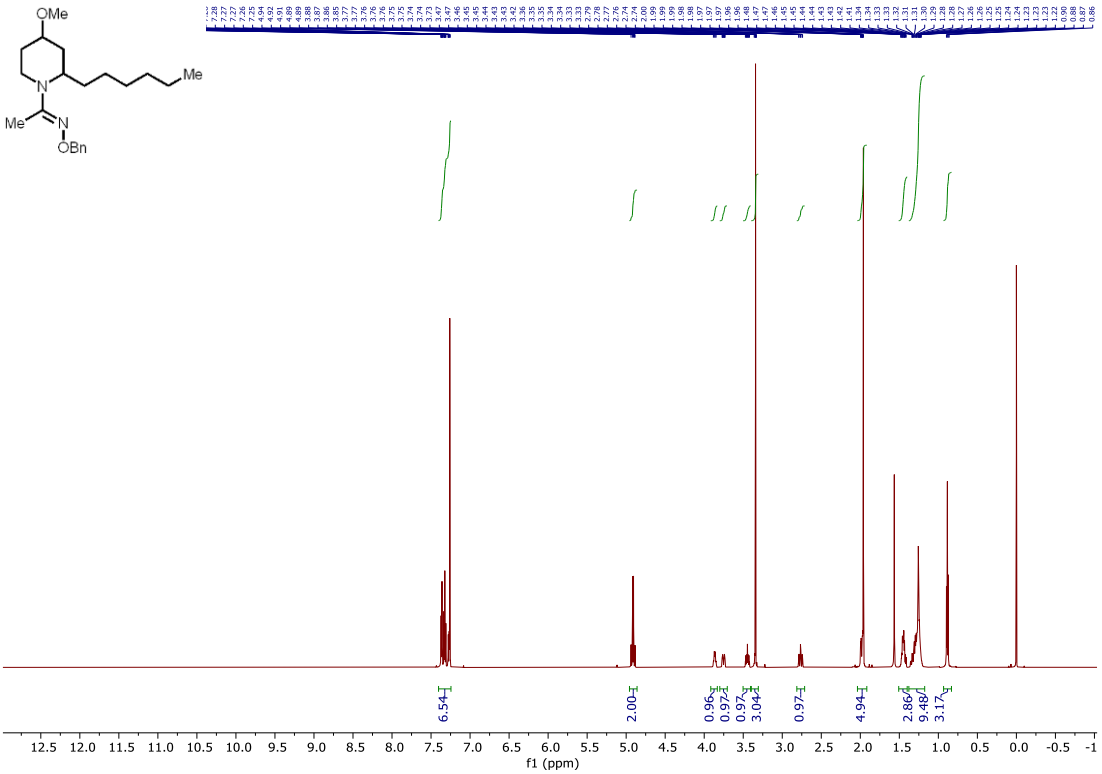
First diastereomer

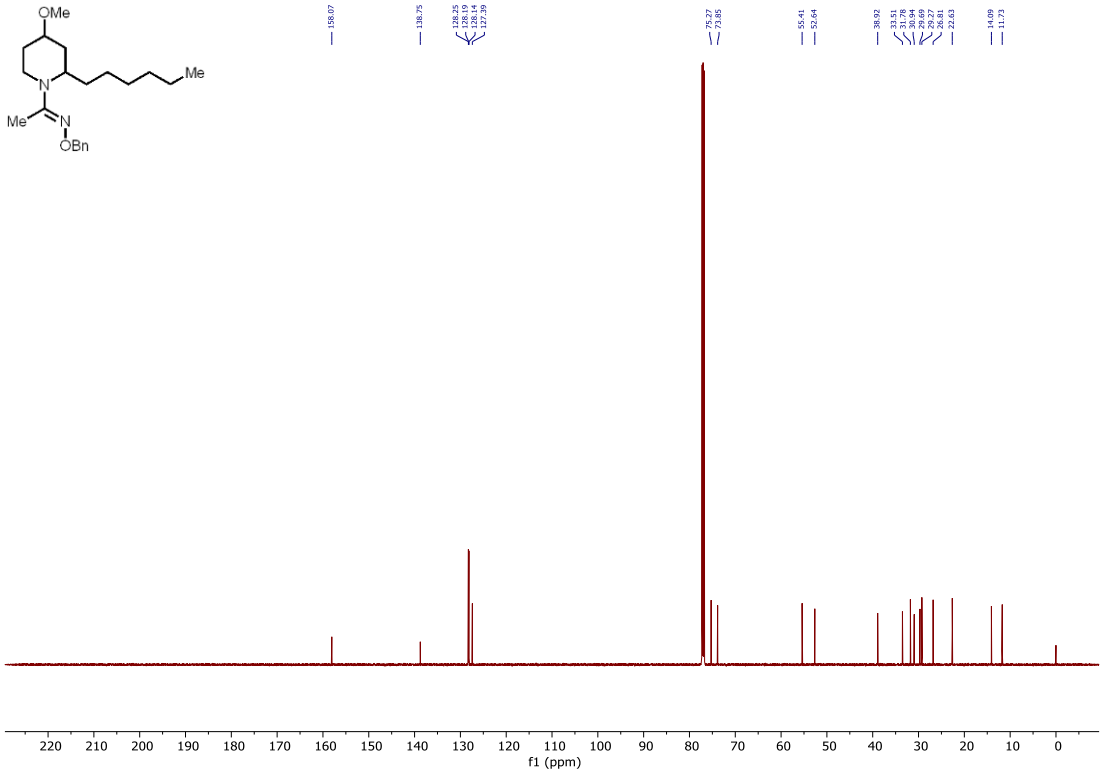


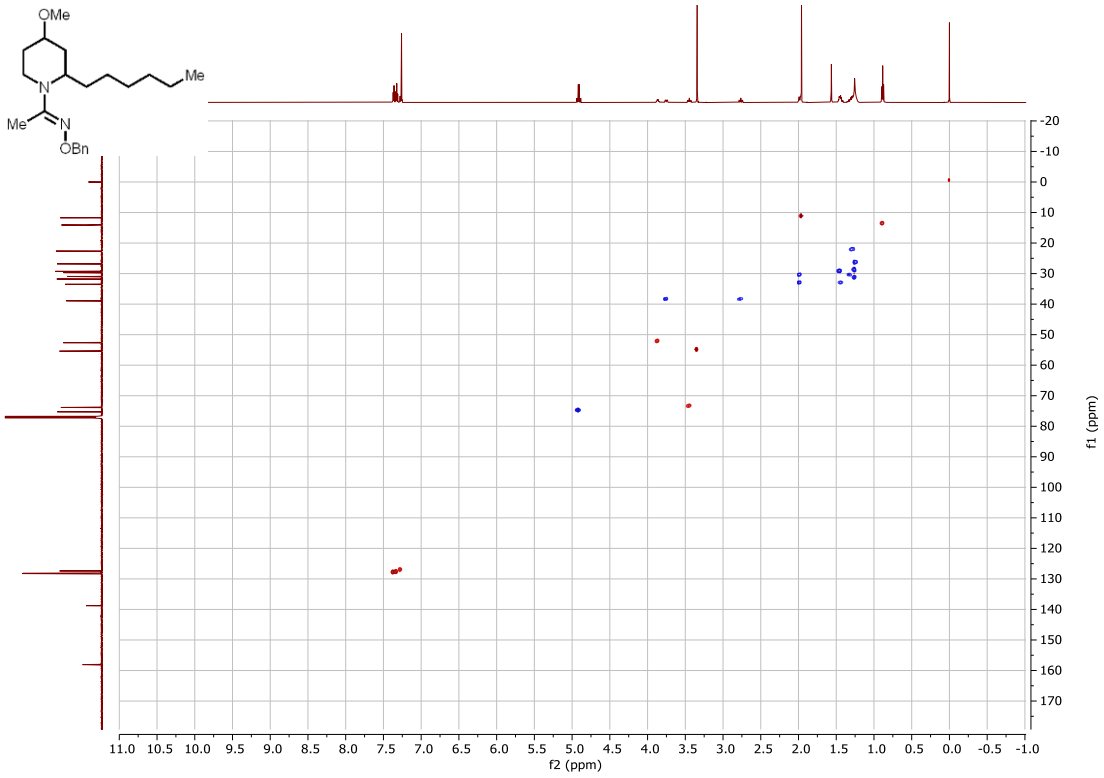




Second diastereomer

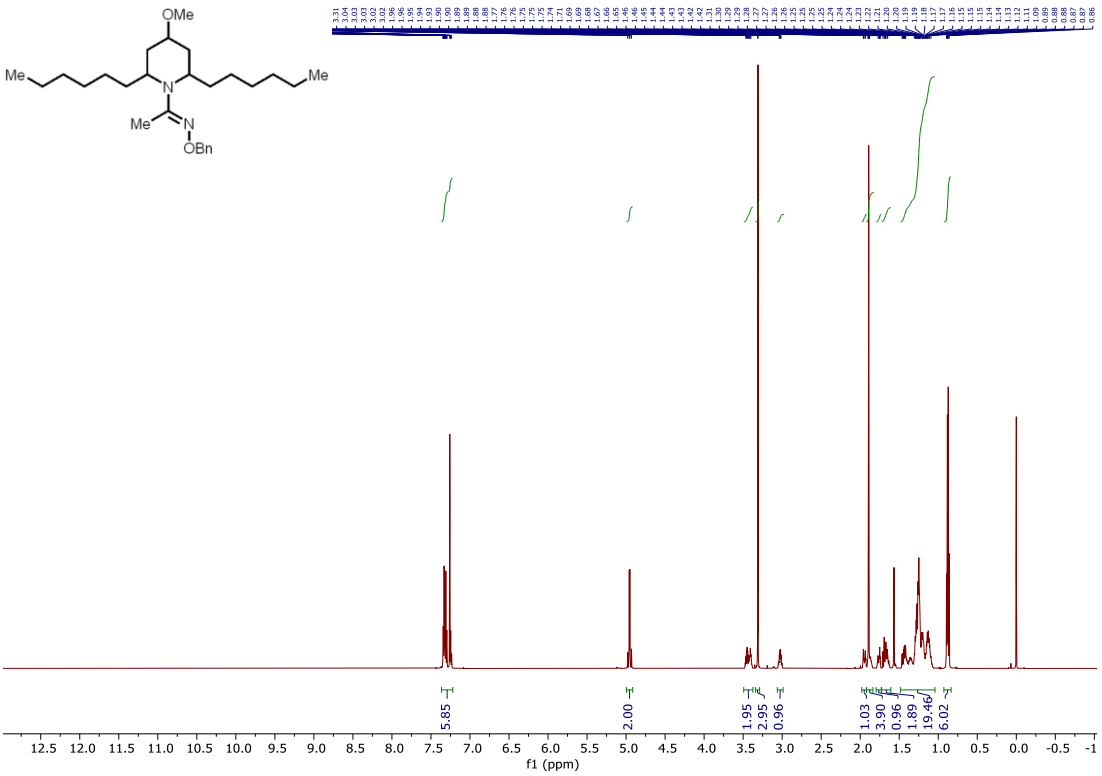


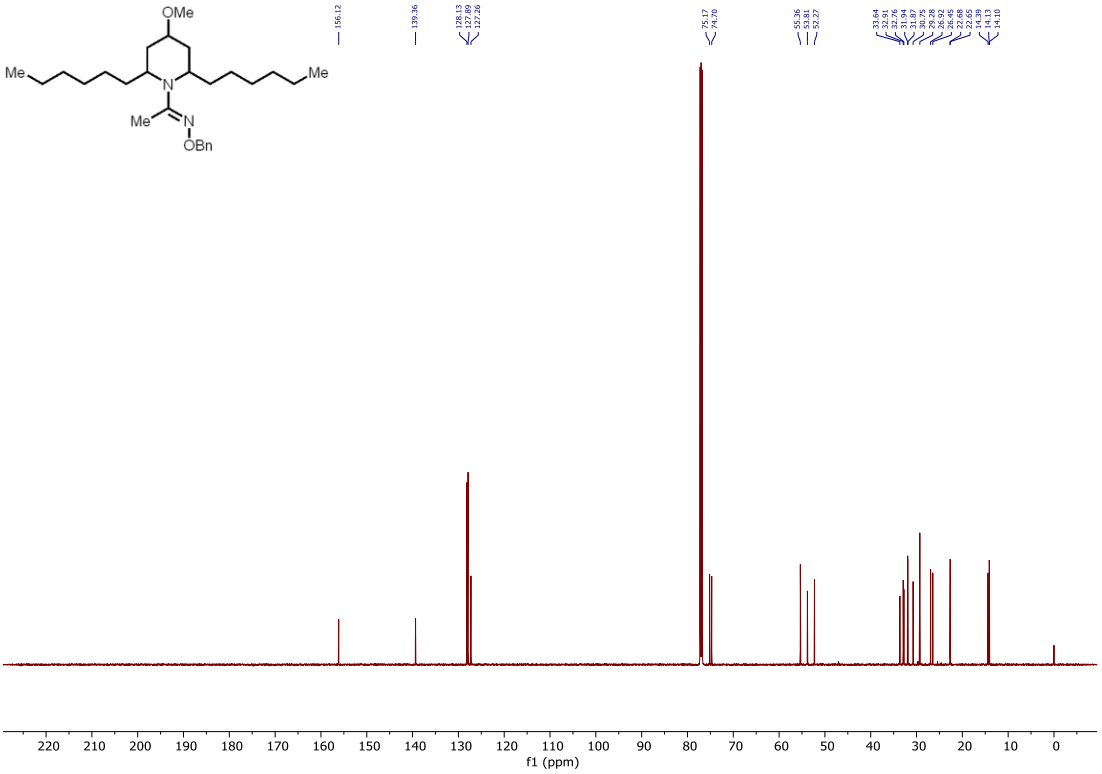

OMe
Me
N
Me
N
OBn
158.07
138.75
128.25
128.09
128.14
127.39
75.27
73.85
55.41
52.64
38.92
33.51
31.78
30.84
29.69
29.27
26.81
22.63
14.09
11.73
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

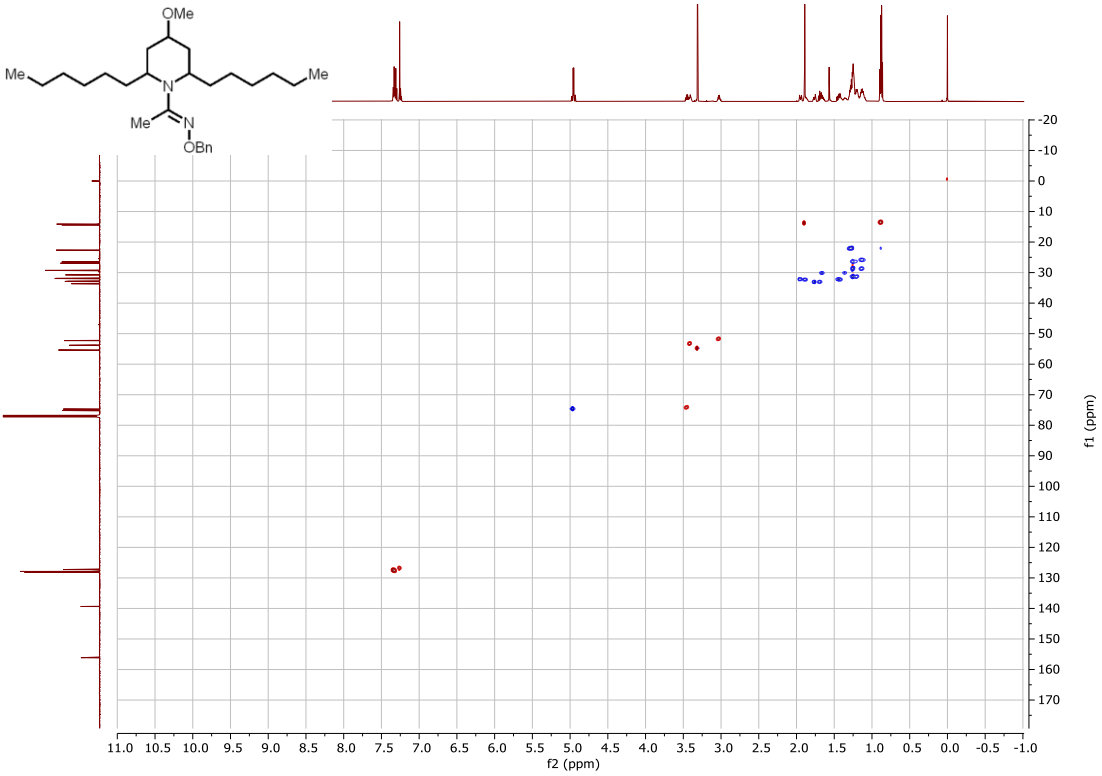

OMe
Me
N
Me
N
OBn
-20 -10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170
f1 (ppm)
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f2 (ppm)

(*E*)-1-(2,6-dihexyl-4-methoxypiperidin-1-yl)ethan-1-one *O*-benzyl oxime (5f-di)

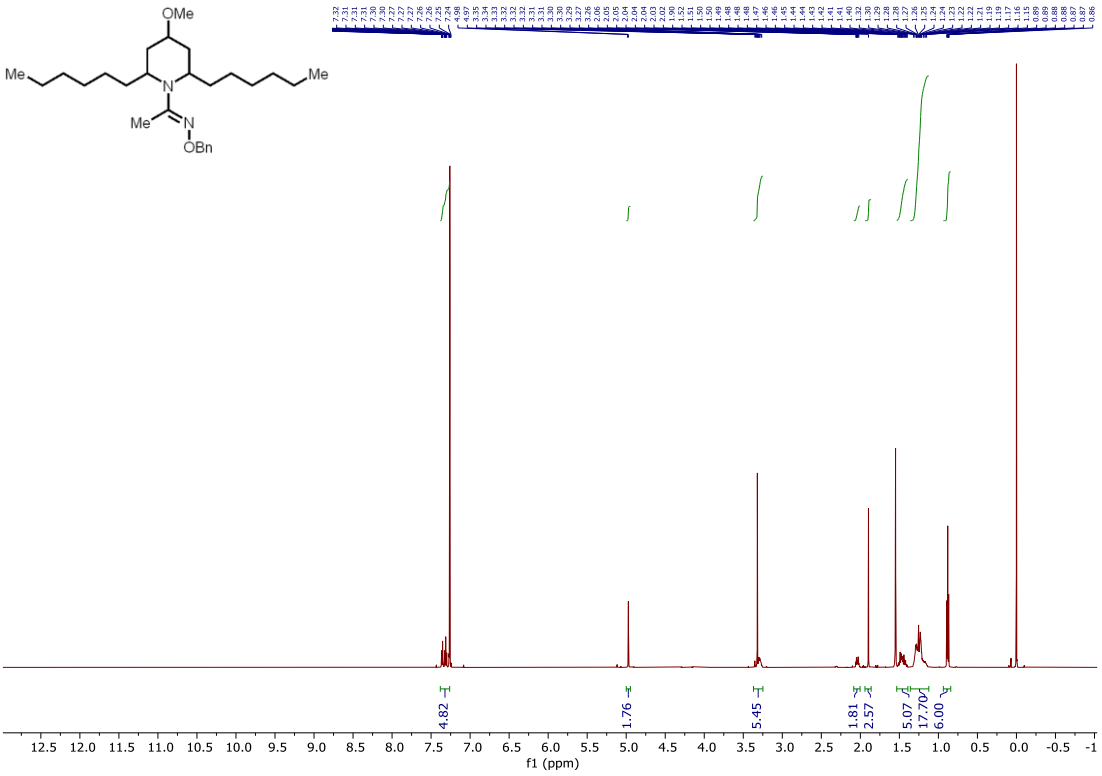
First diastereomer

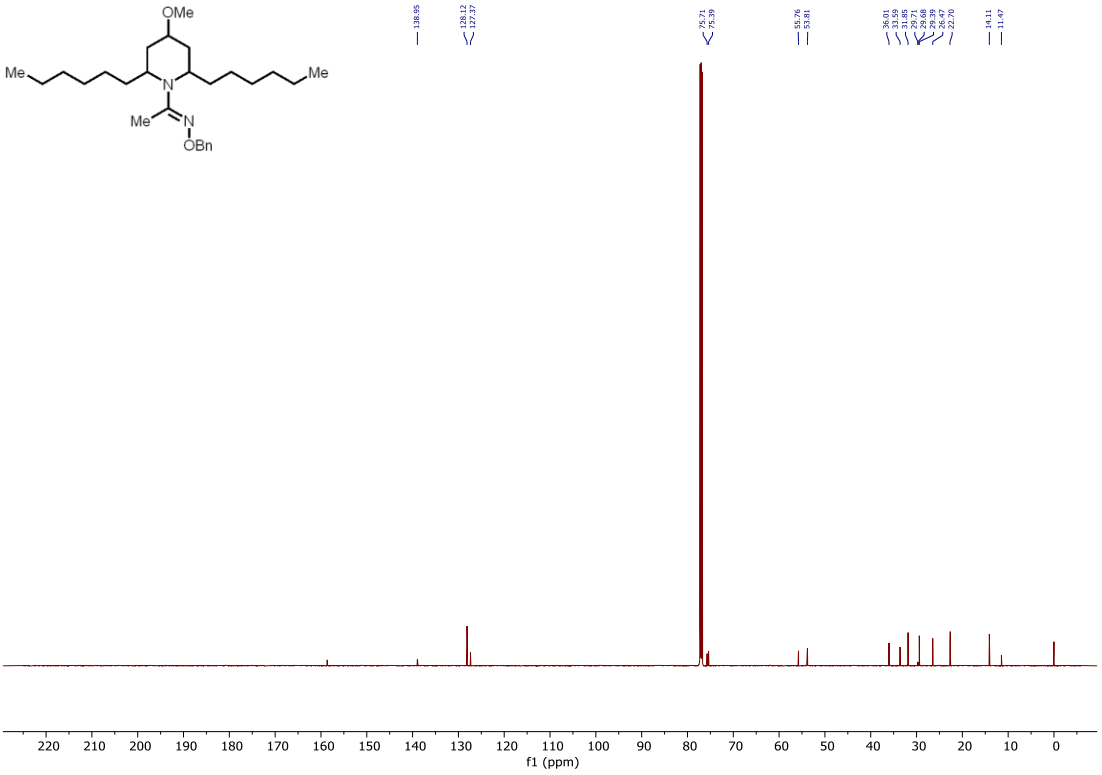


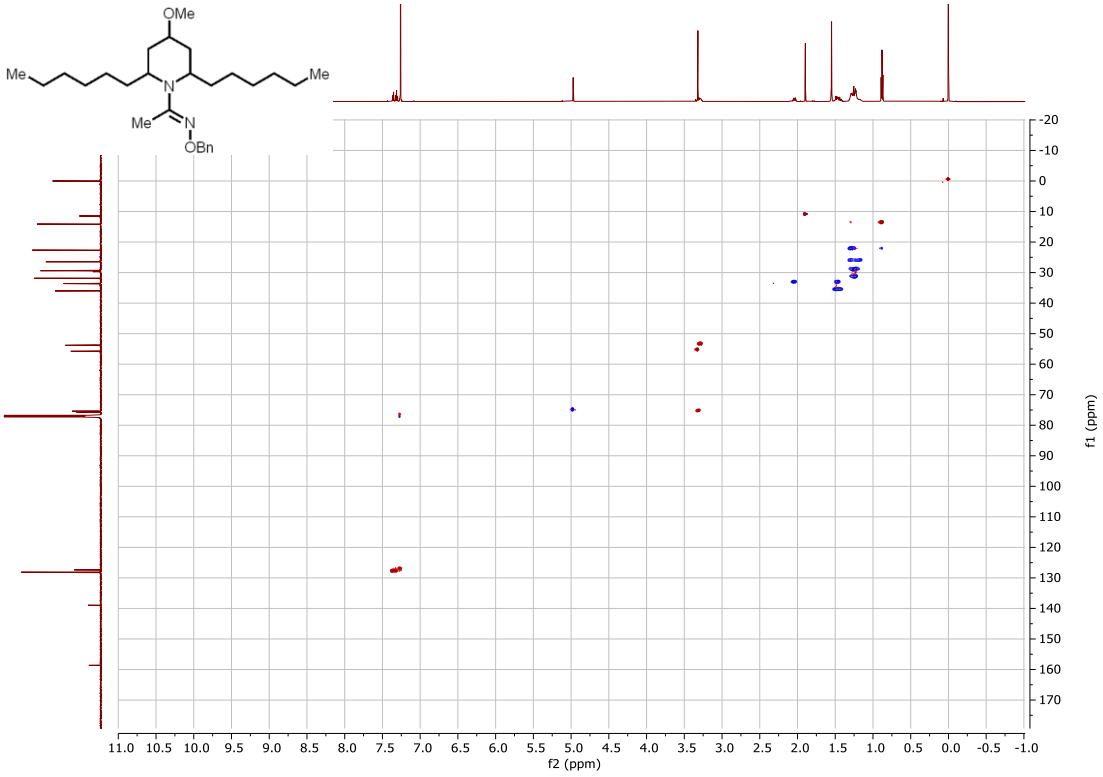




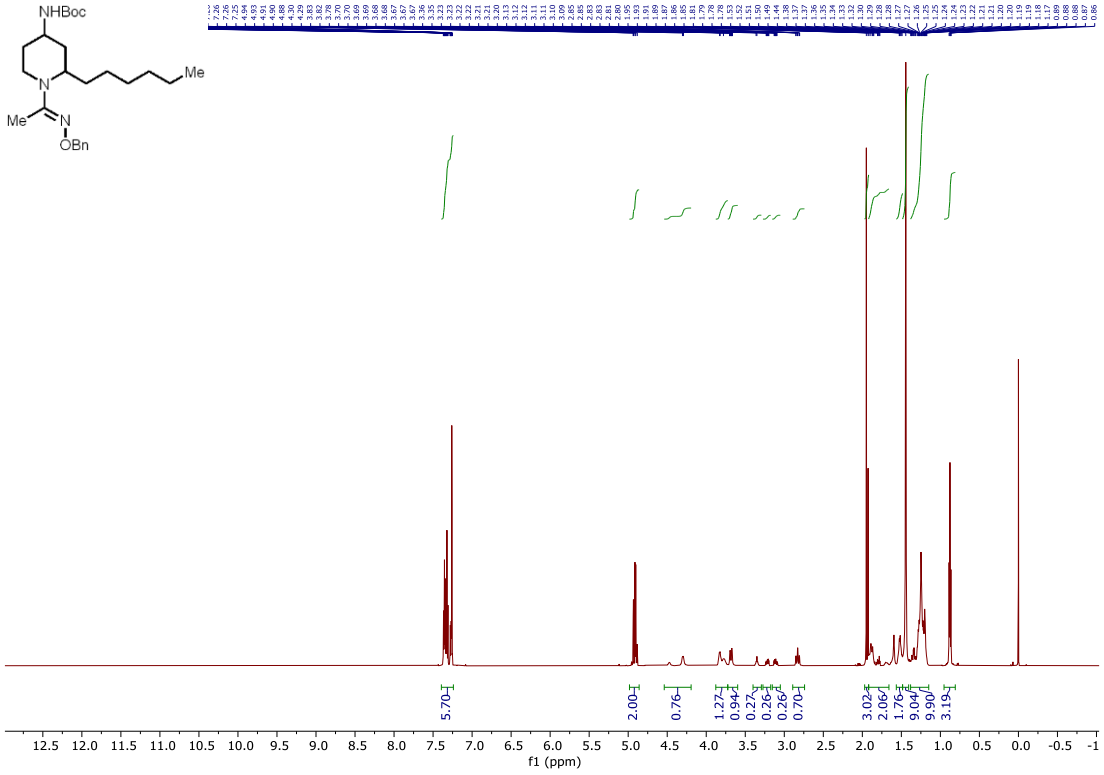
Second diastereomer

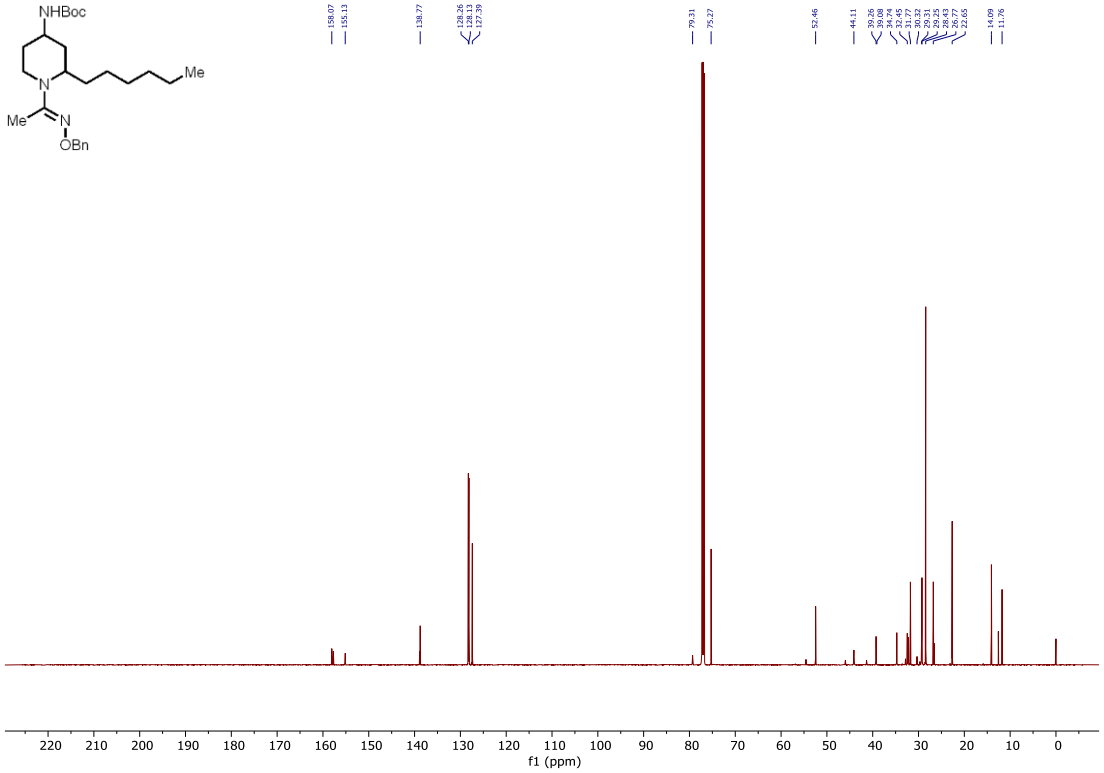


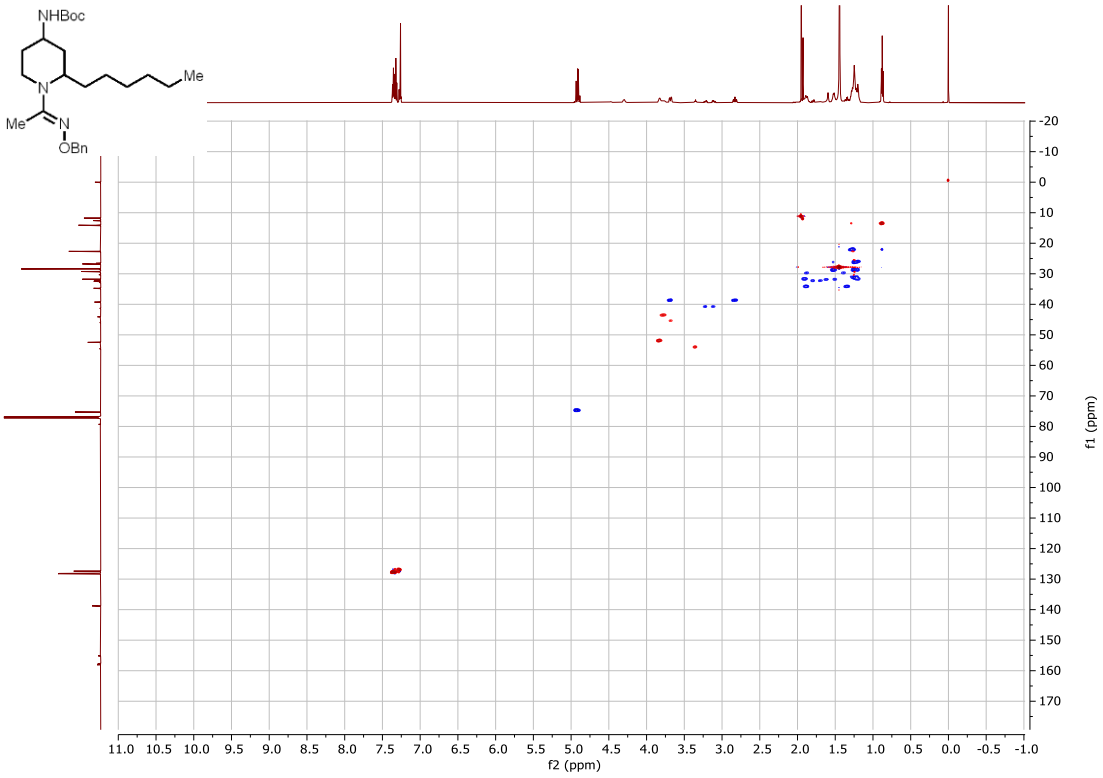

OMe
Me
N
Me
Me
N
OBn
138.95
129.12
127.37
75.71
75.39
55.76
53.81
36.01
33.99
31.85
29.71
29.68
29.39
26.47
22.70
14.11
11.47
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OMe
Me
N
Me
Me
N
OBn
-20 -10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170
f1 (ppm)
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f2 (ppm)

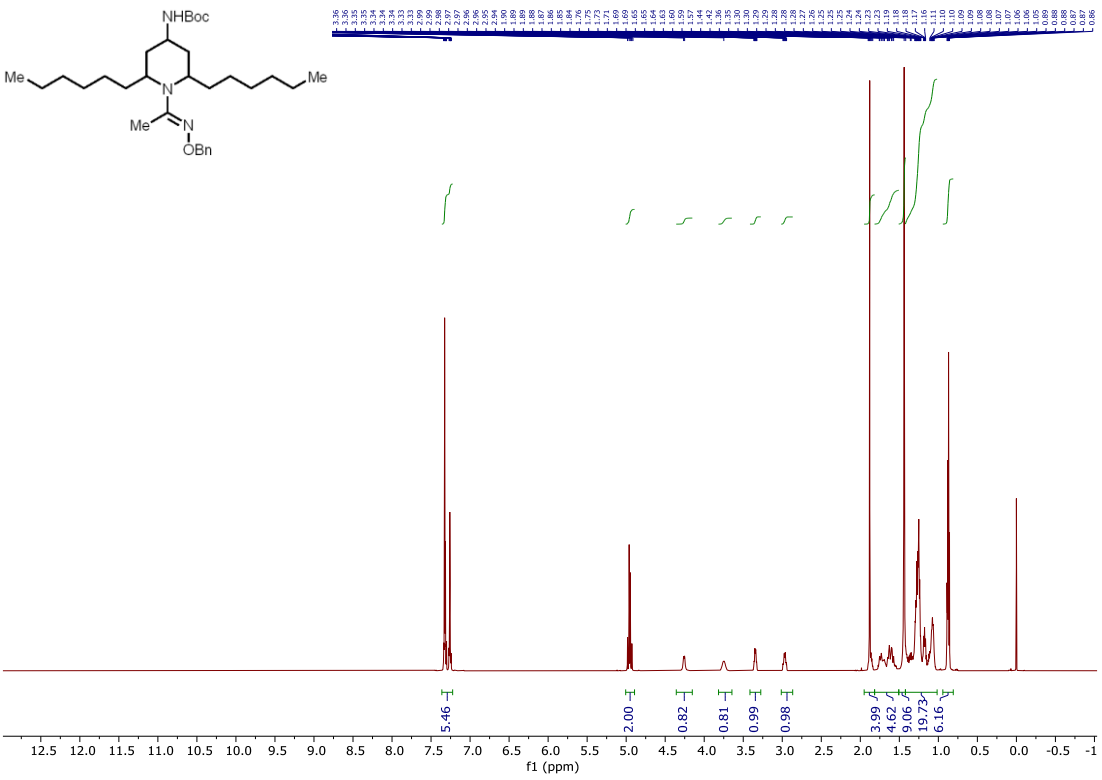
tert-butyl (*E*)-(1-(1-((benzyloxy)imino)ethyl)-2-hexylpiperidin-4-yl)carbamate (5g-mono)

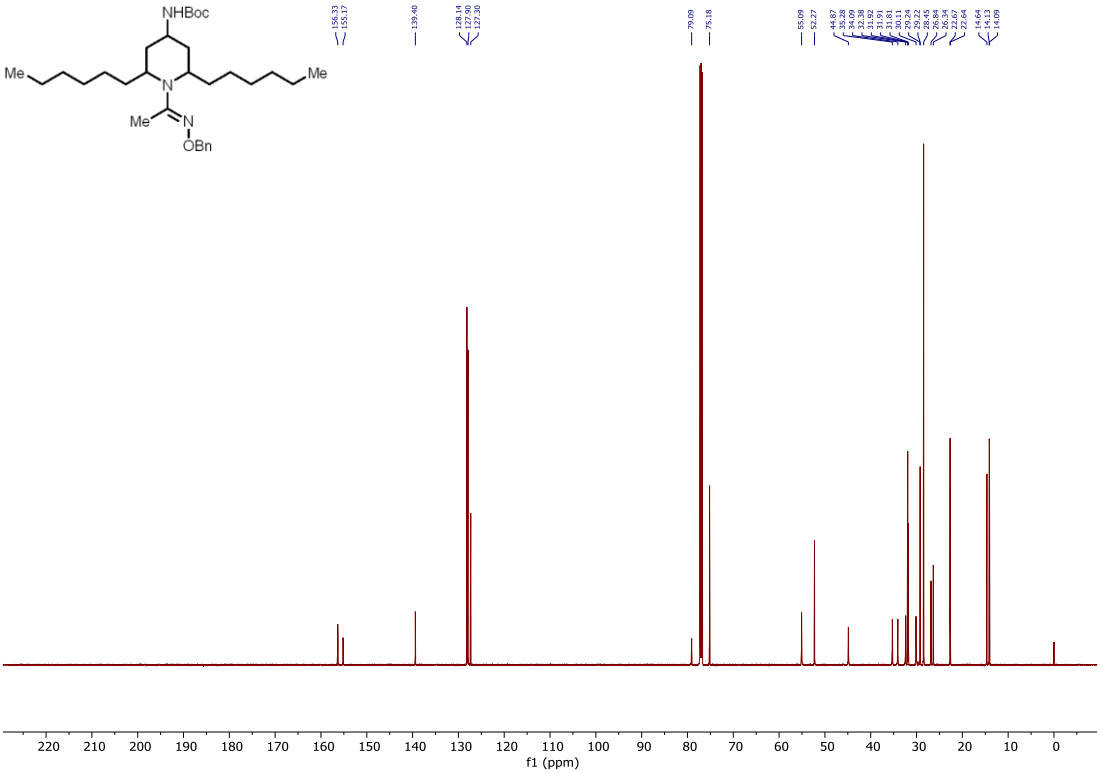




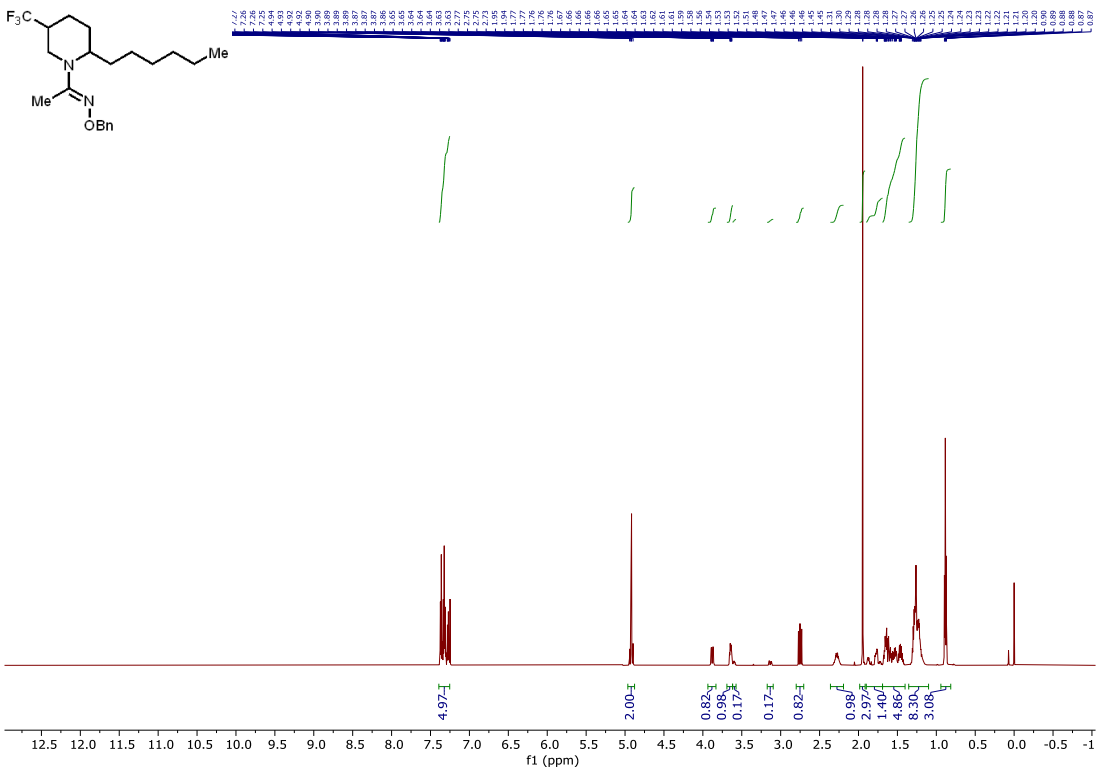

NHBoc
Me
N
Me
N
OBn
f1 (ppm)
f2 (ppm)

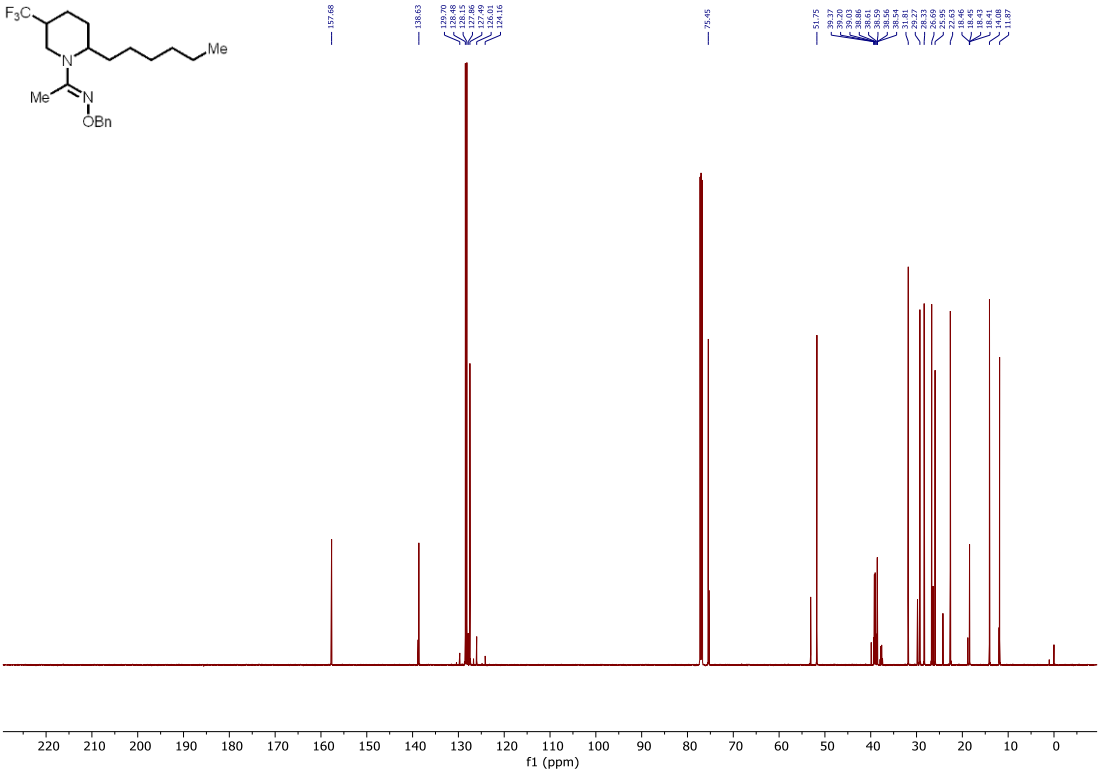
tert-butyl (*E*)-(1-(1-((benzyloxy)imino)ethyl)-2,6-dihexylpiperidin-4-yl)carbamate (5g-di)

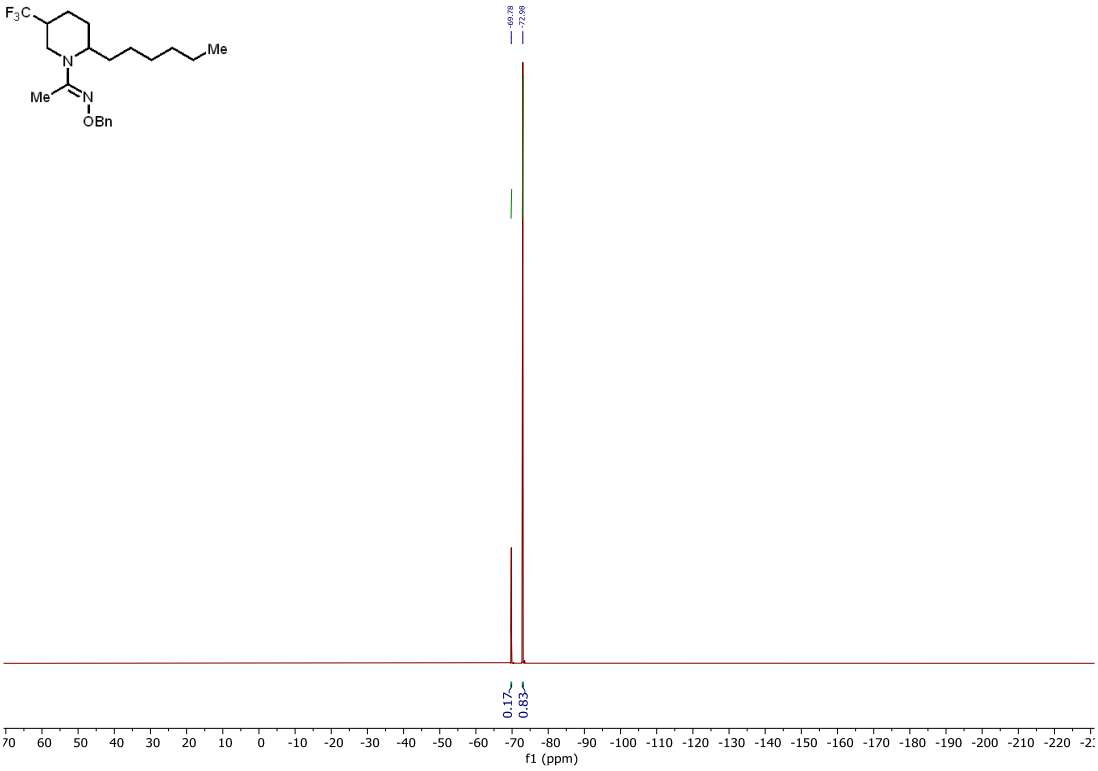


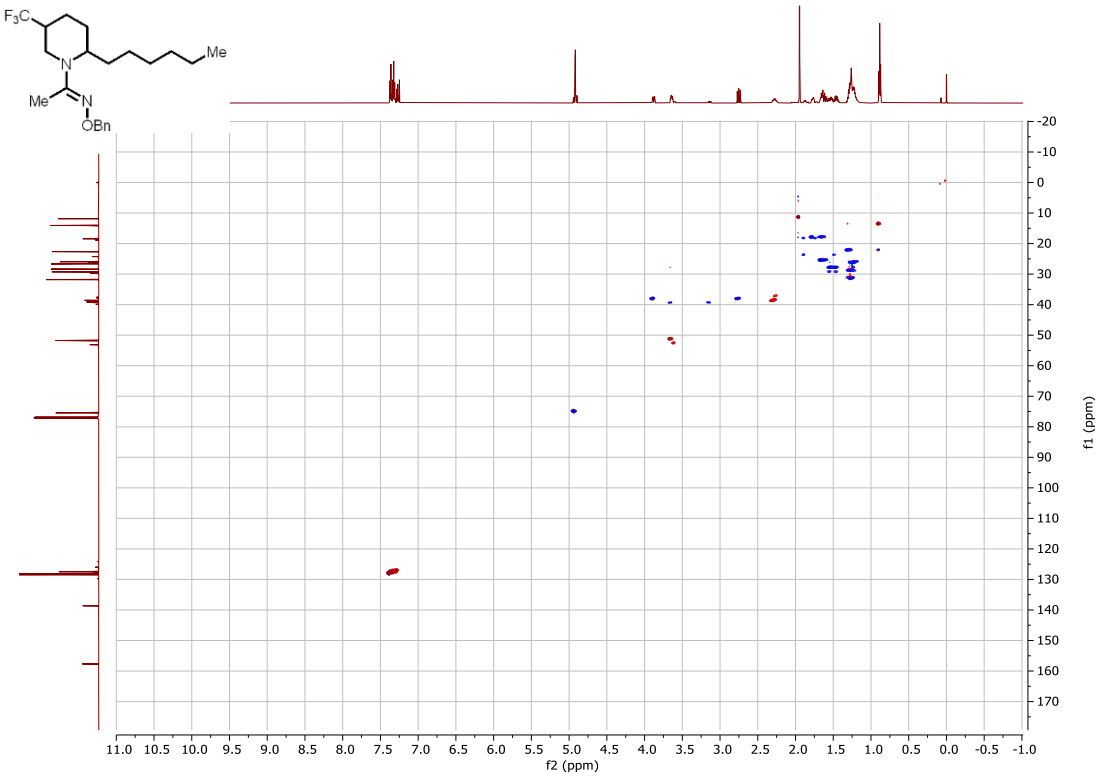


(*E*)-1-(2-hexyl-5-(trifluoromethyl)piperidin-1-yl)ethan-1-one *O*-benzyl oxime (5h)

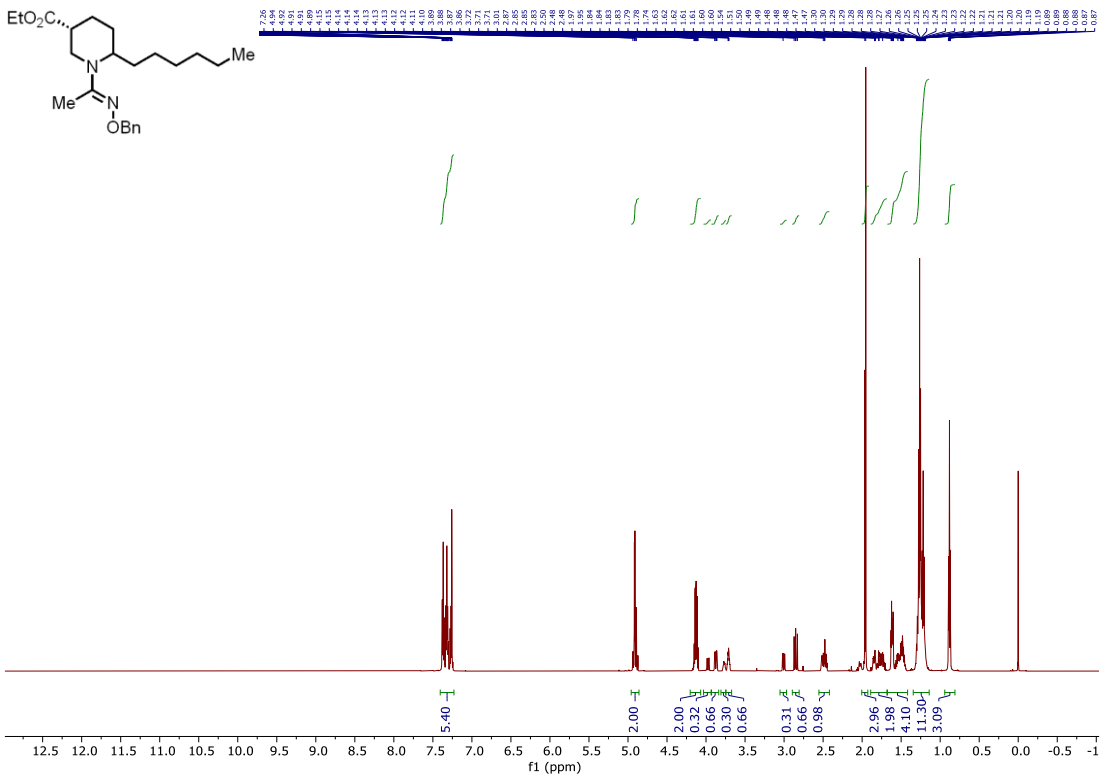


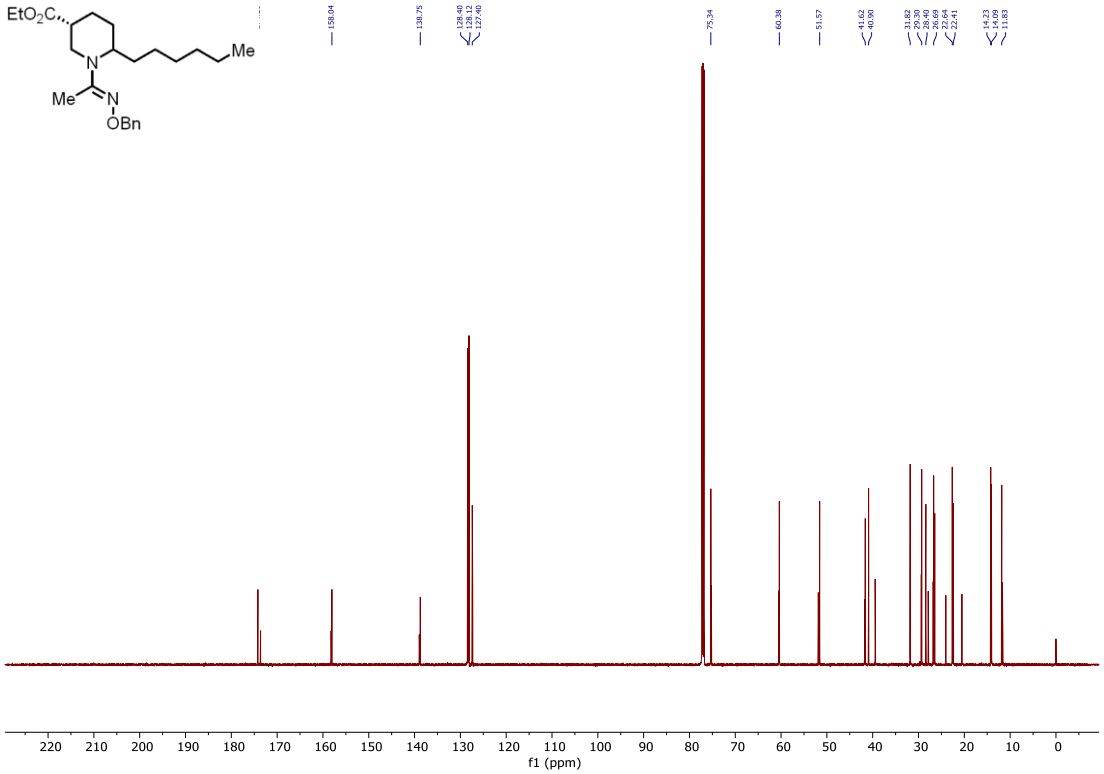


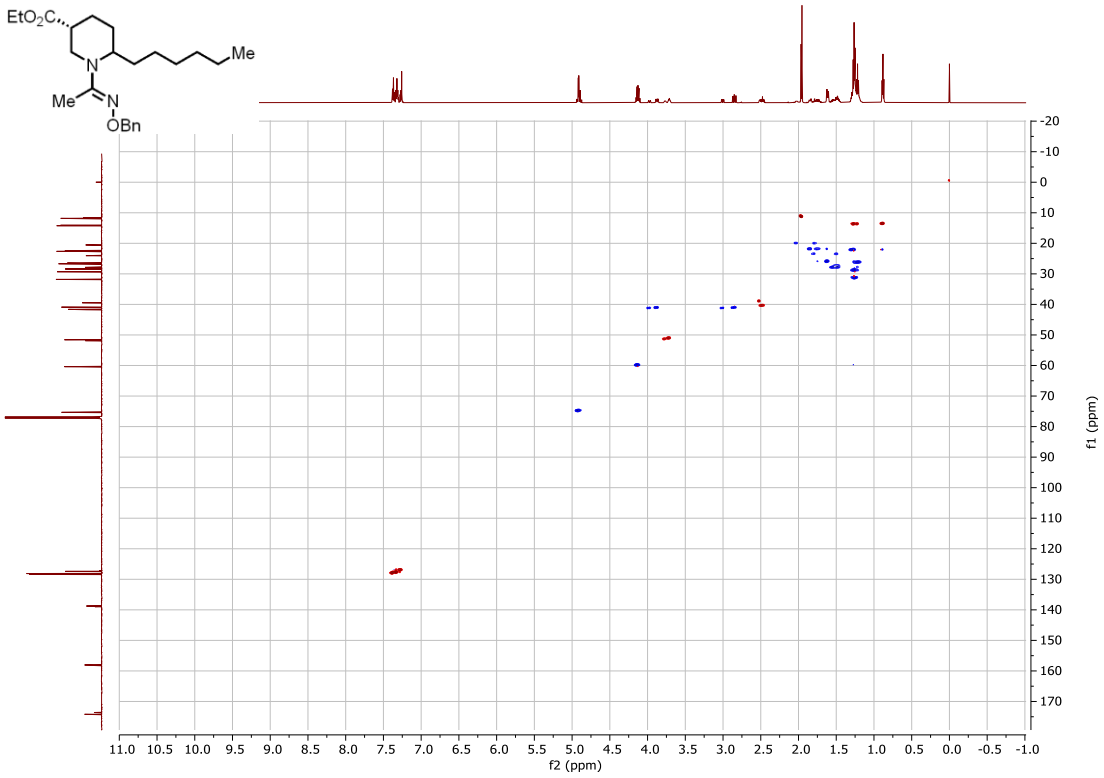

F3C
N
Me
Me
N
OBn
-69.78
-72.98
0.17
0.83
f1 (ppm)


F3C
N
Me
Me
N
OBn
f2 (ppm)
f1 (ppm)

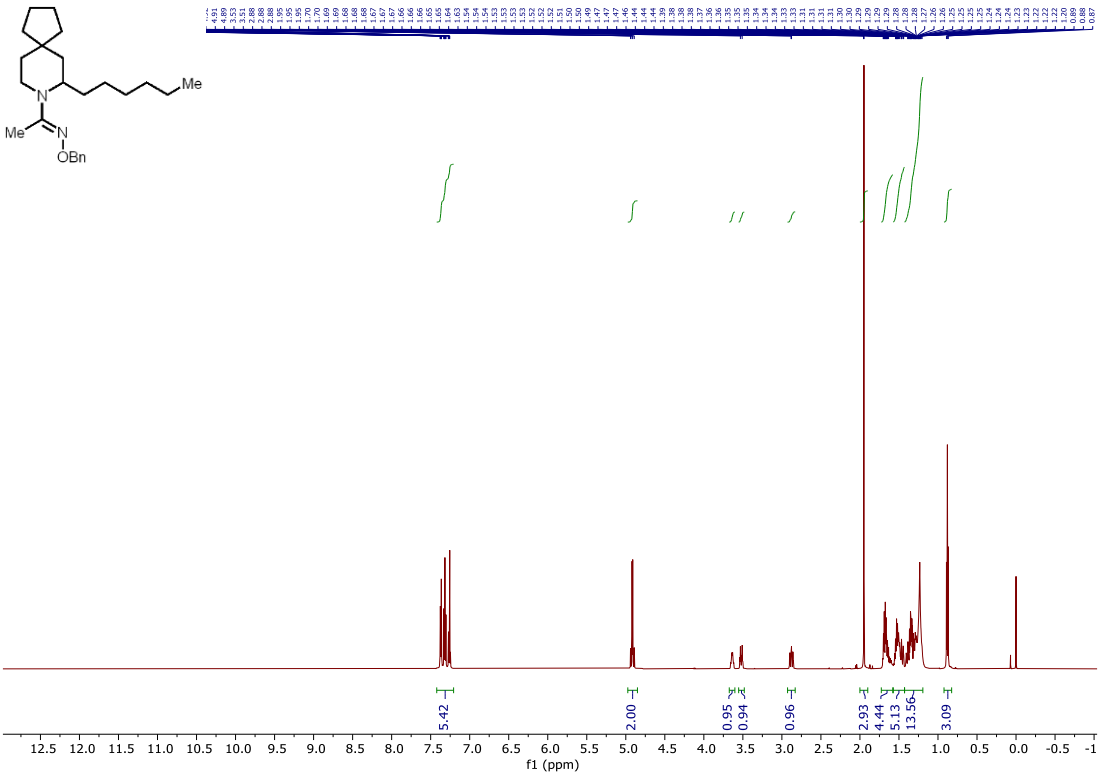
ethyl (3*R*)-1-((*E*)-1-((benzyloxy)imino)ethyl)-6-hexylpiperidine-3-carboxylate (5i)

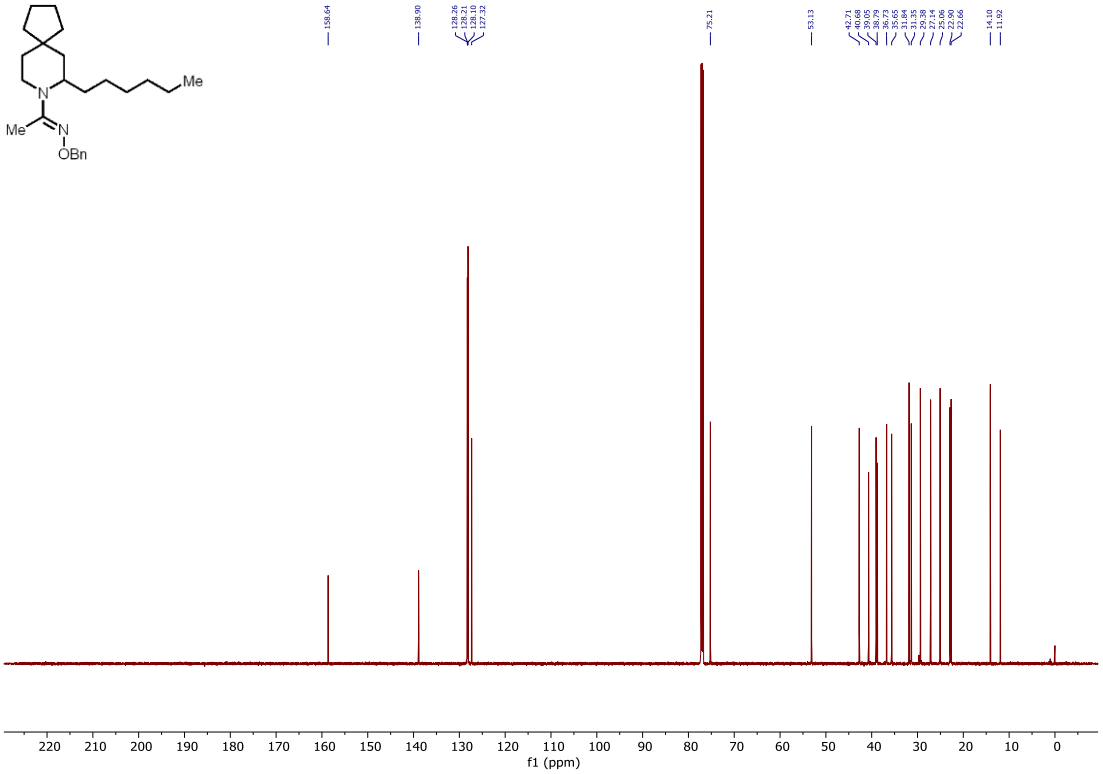




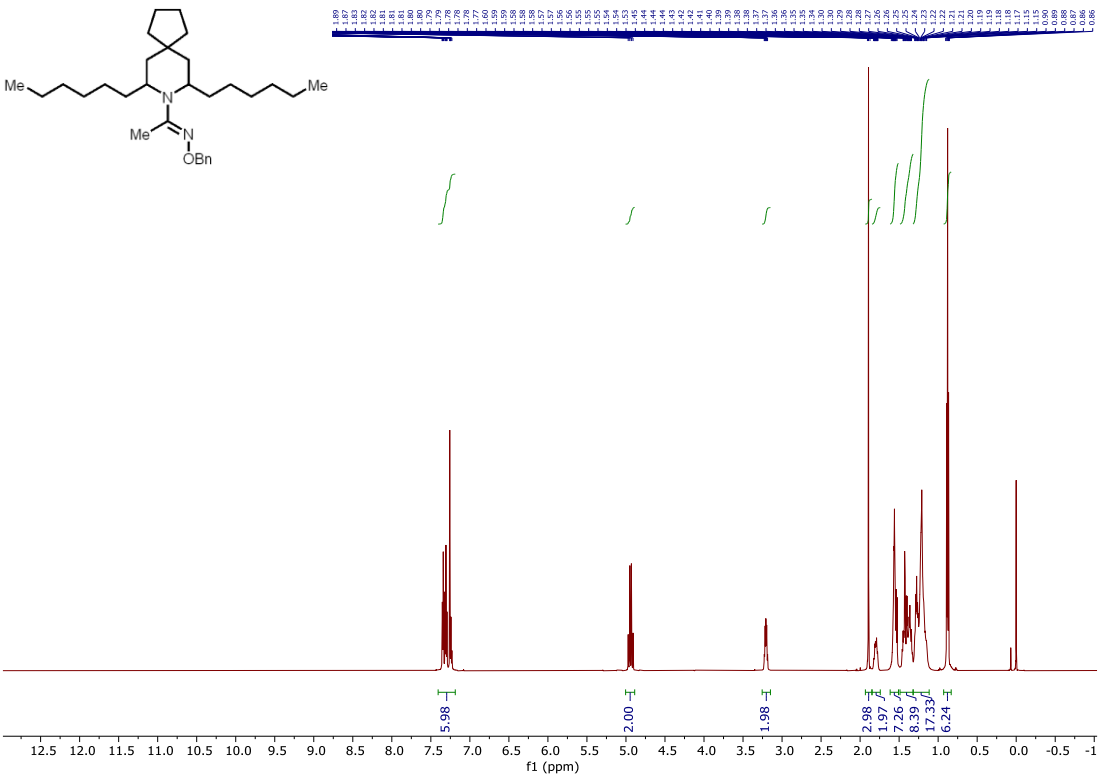

EtO2C
Me
N
Me
N
OBn
f2 (ppm)
f1 (ppm)

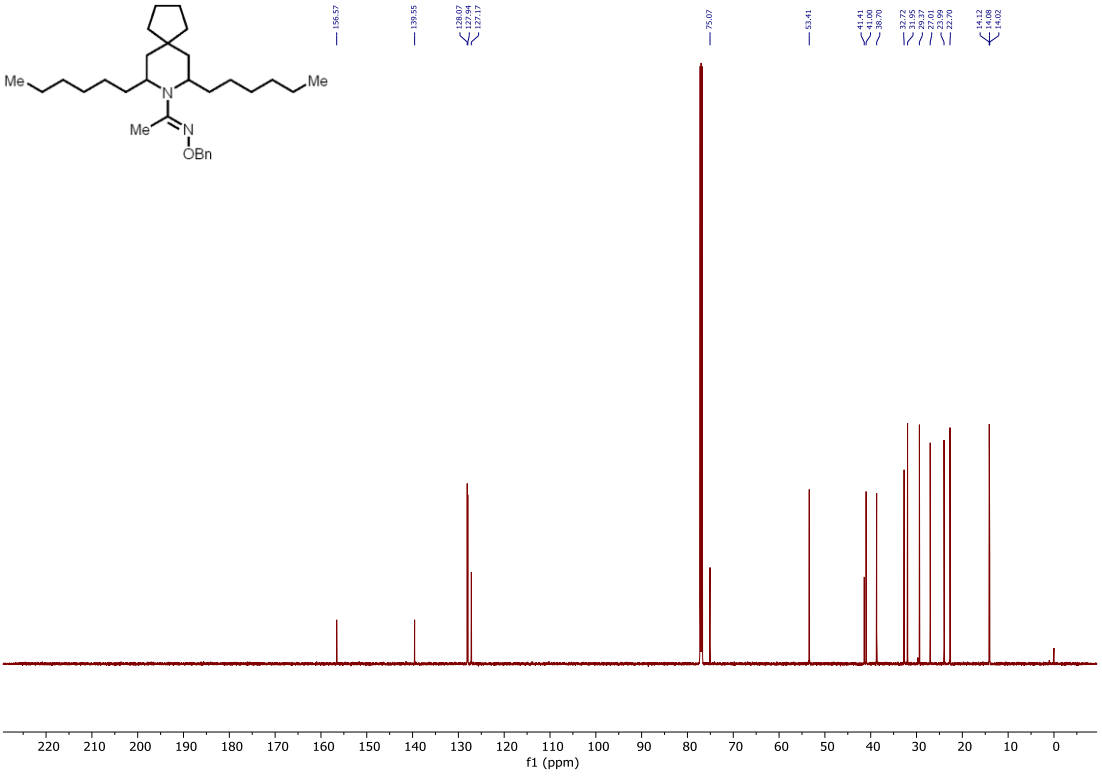
(*E*)-1-(7-hexyl-8-azaspiro[4.5]decan-8-yl)ethan-1-one *O*-benzyl oxime (5j-mono)



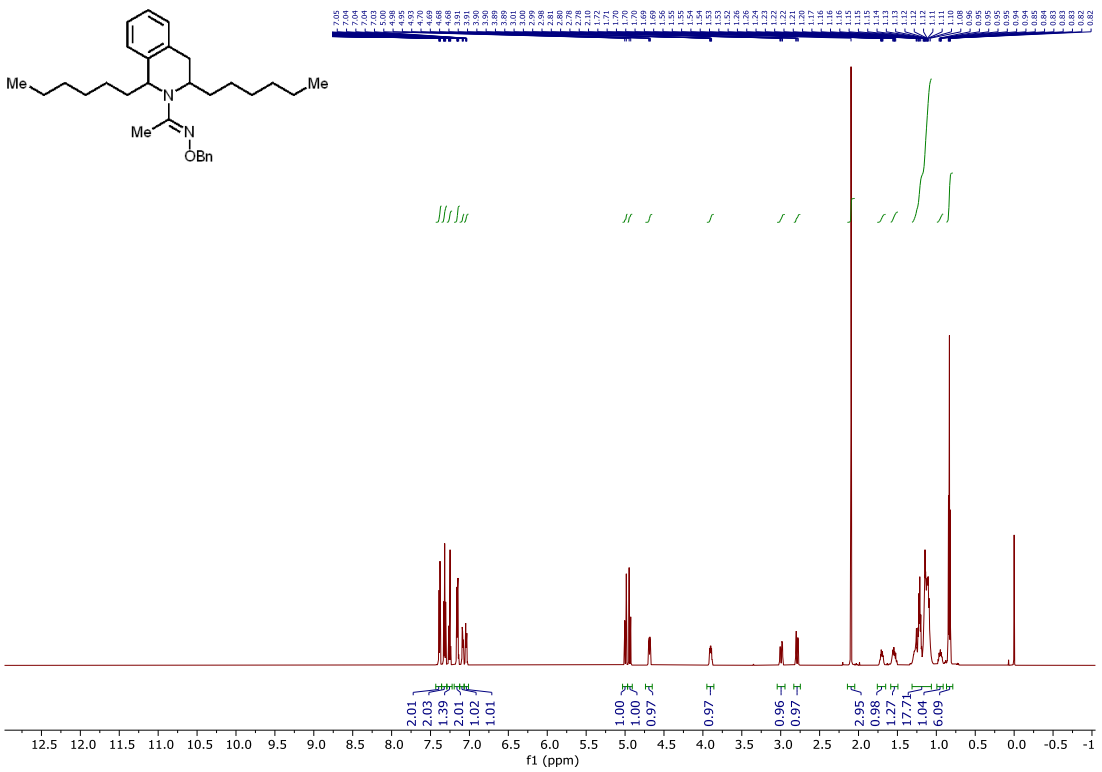


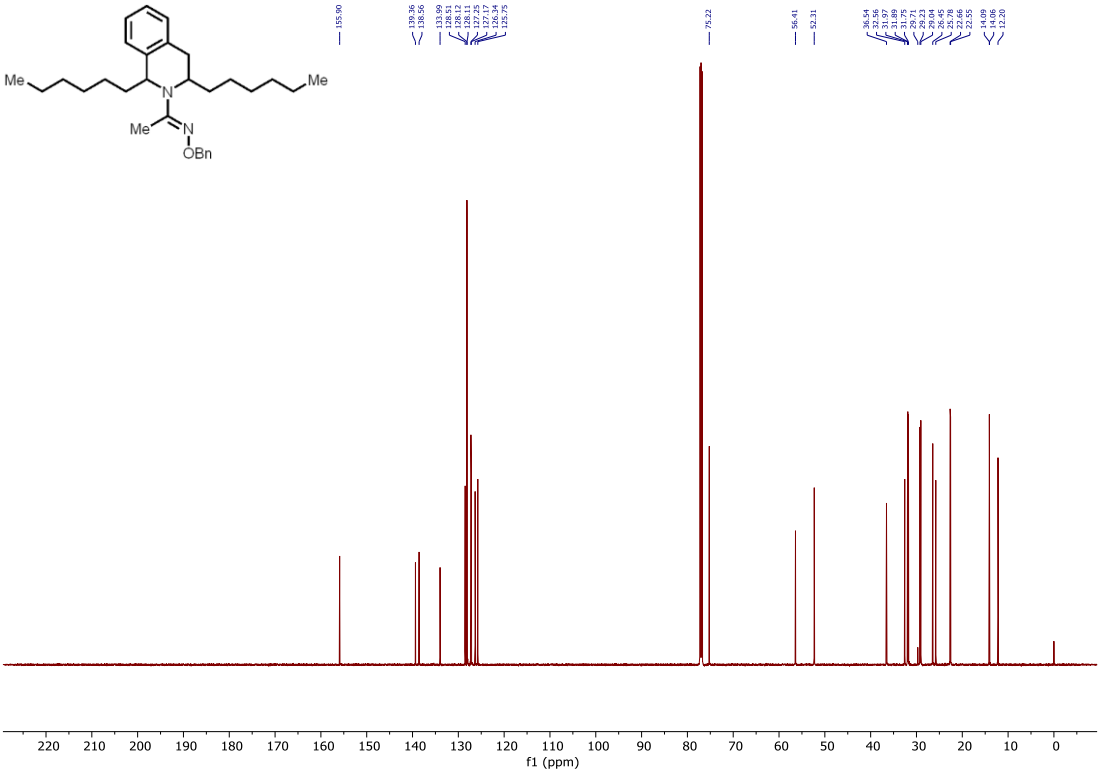
(*E*)-1-(7,9-dihexyl-8-azaspiro[4.5]decan-8-yl)ethan-1-one *O*-benzyl oxime (5j-di)



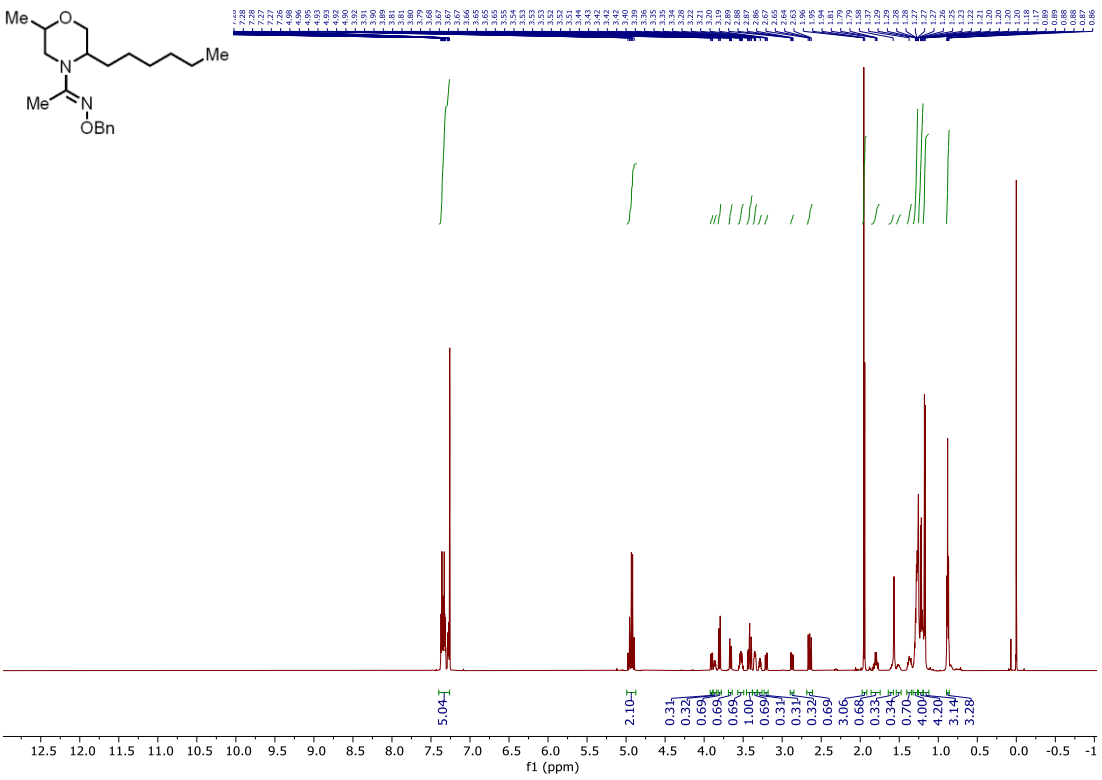


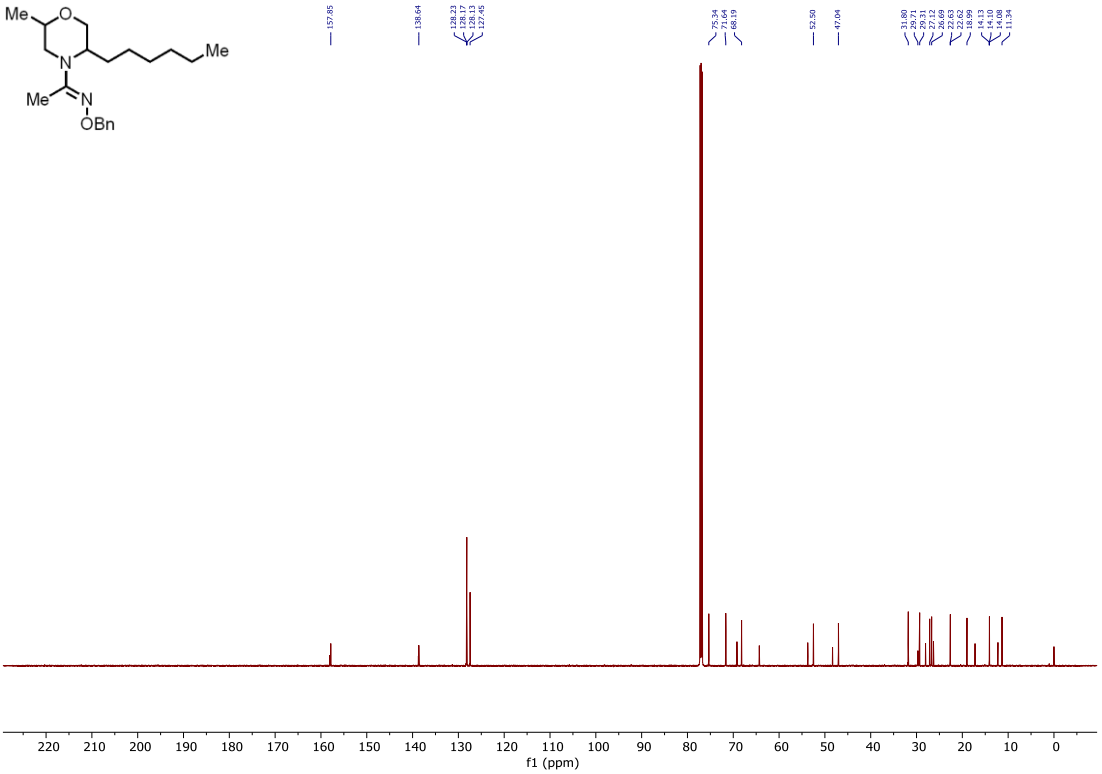
(*E*)-1-(1,3-dihexyl-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one *O*-benzyl oxime (5k)

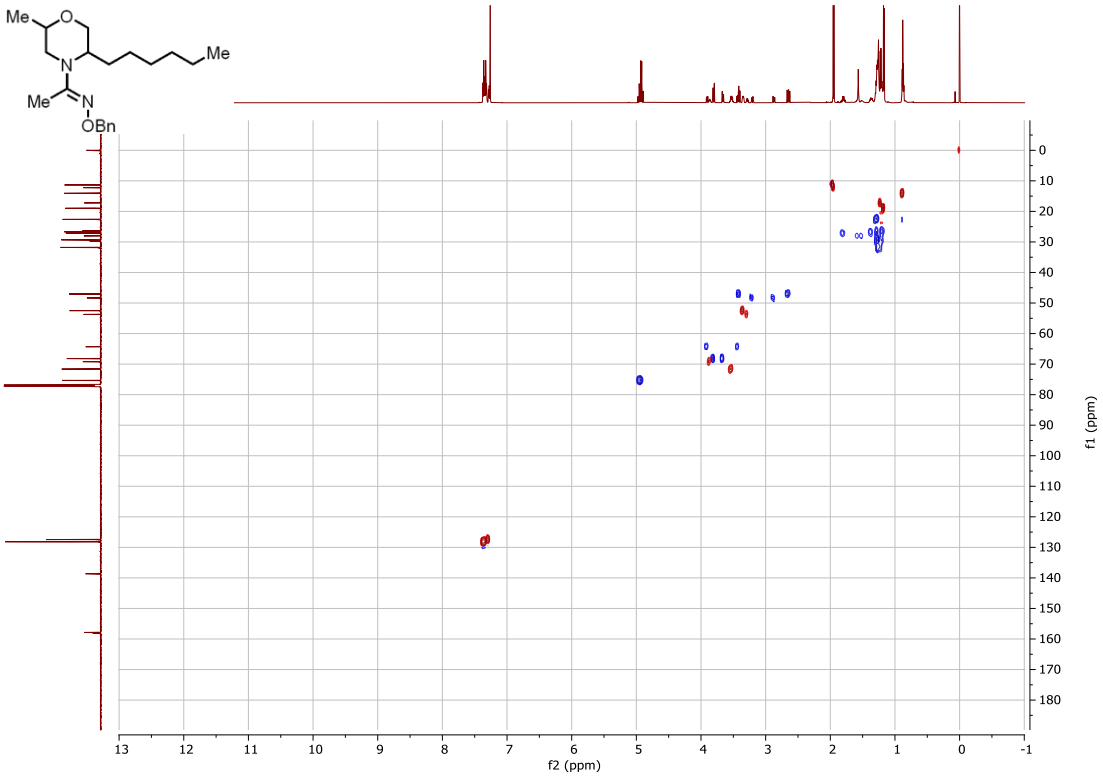




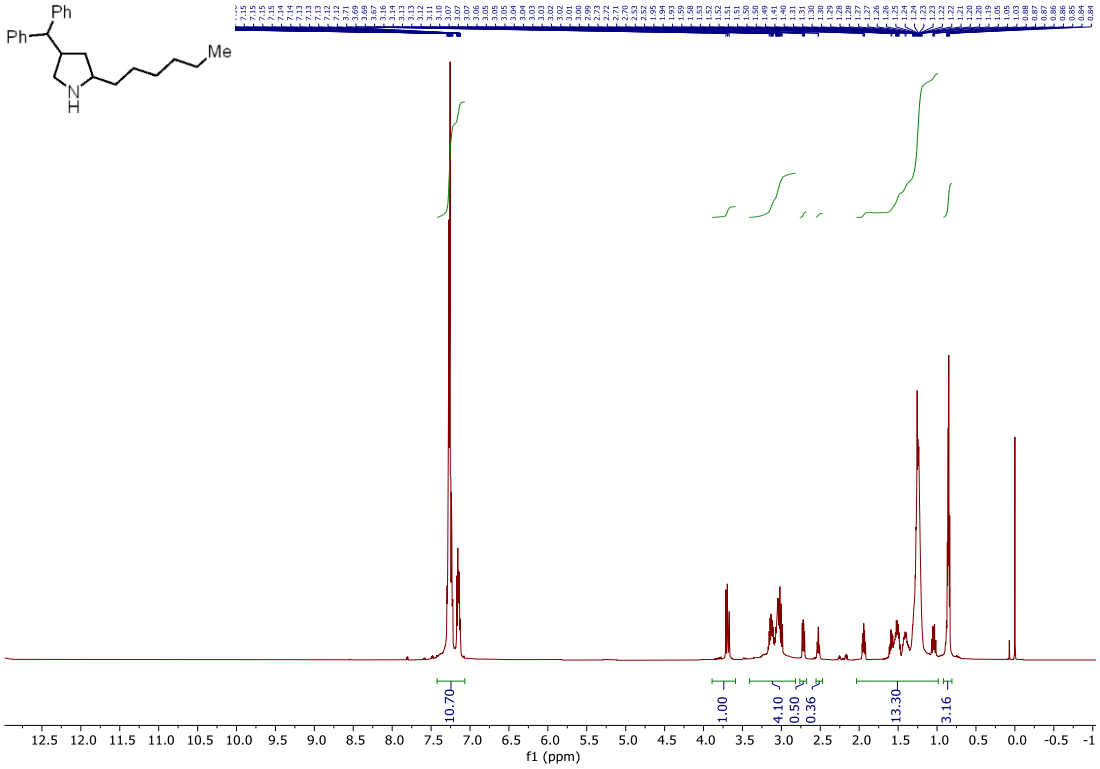
(*E*)-1-(5-hexyl-2-methylmorpholino)ethan-1-one *O*-benzyl oxime (5l)

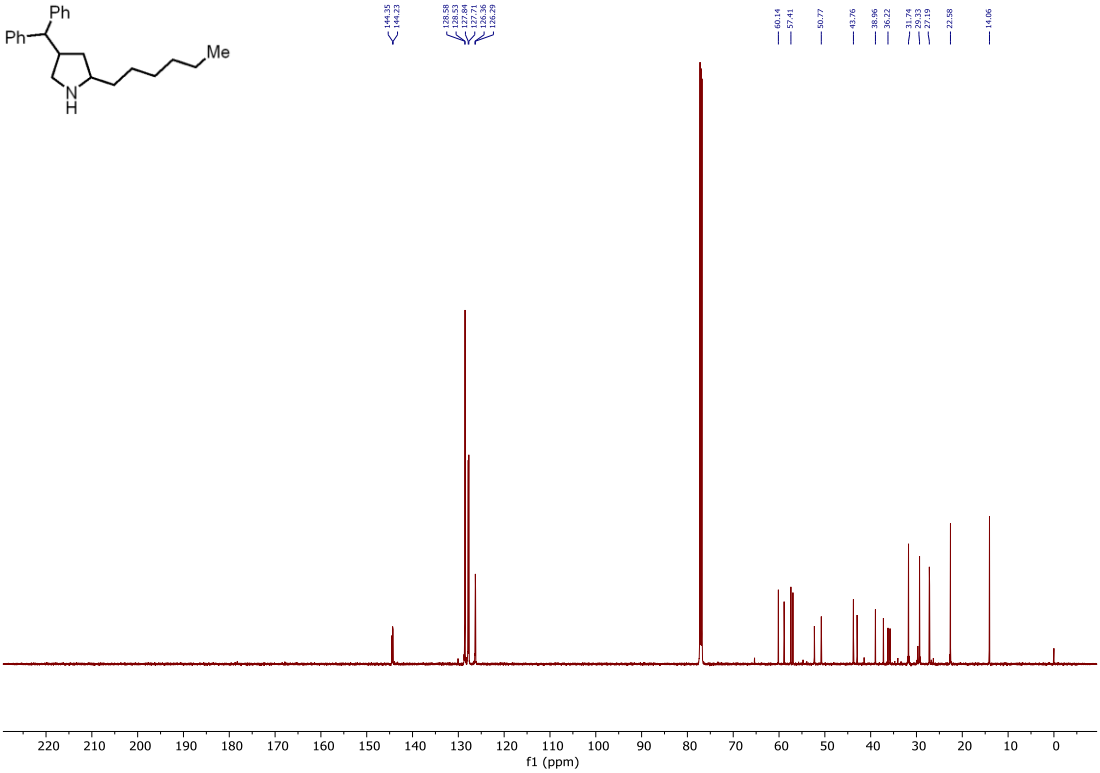


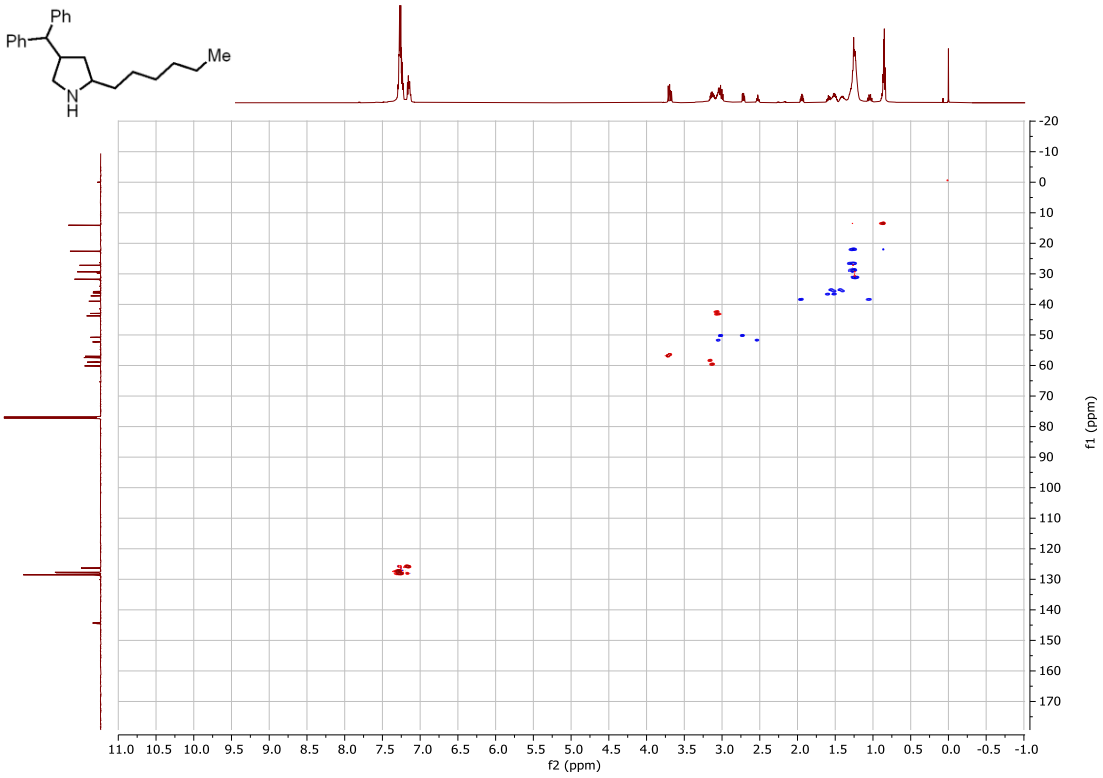


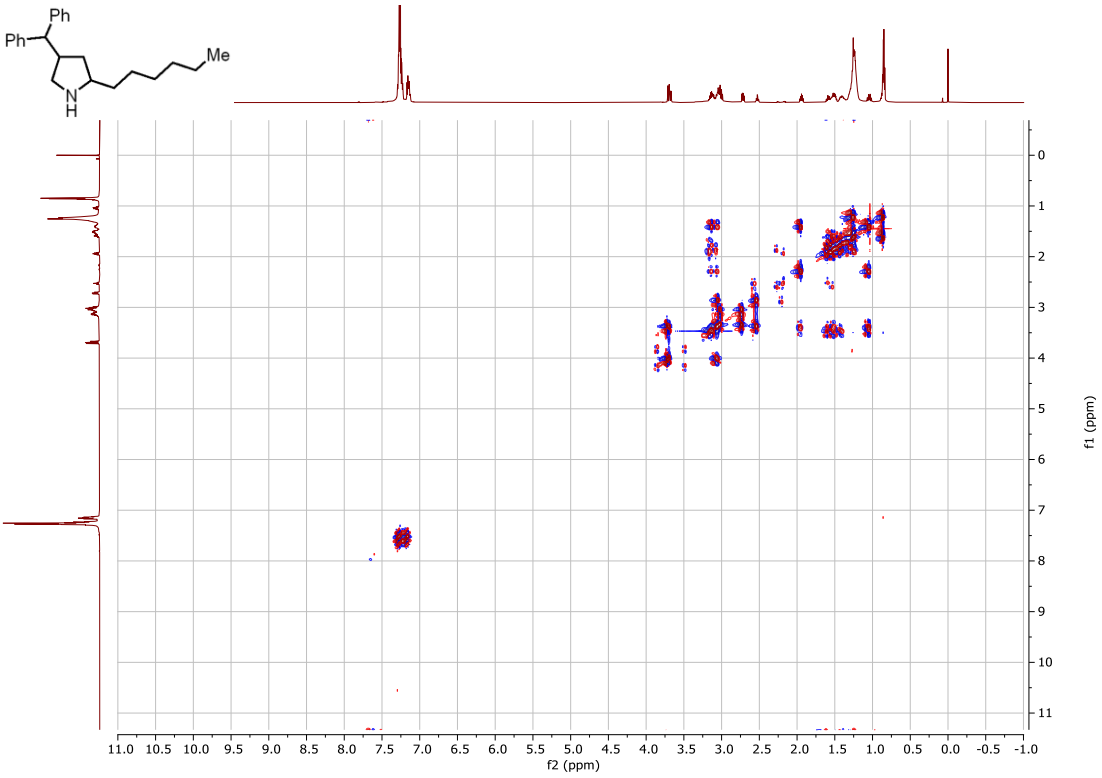

Me
O
N
Me
Me
N
OBn
f2 (ppm)
f1 (ppm)

4-benzhydryl-2-hexylpyrrolidine (8)

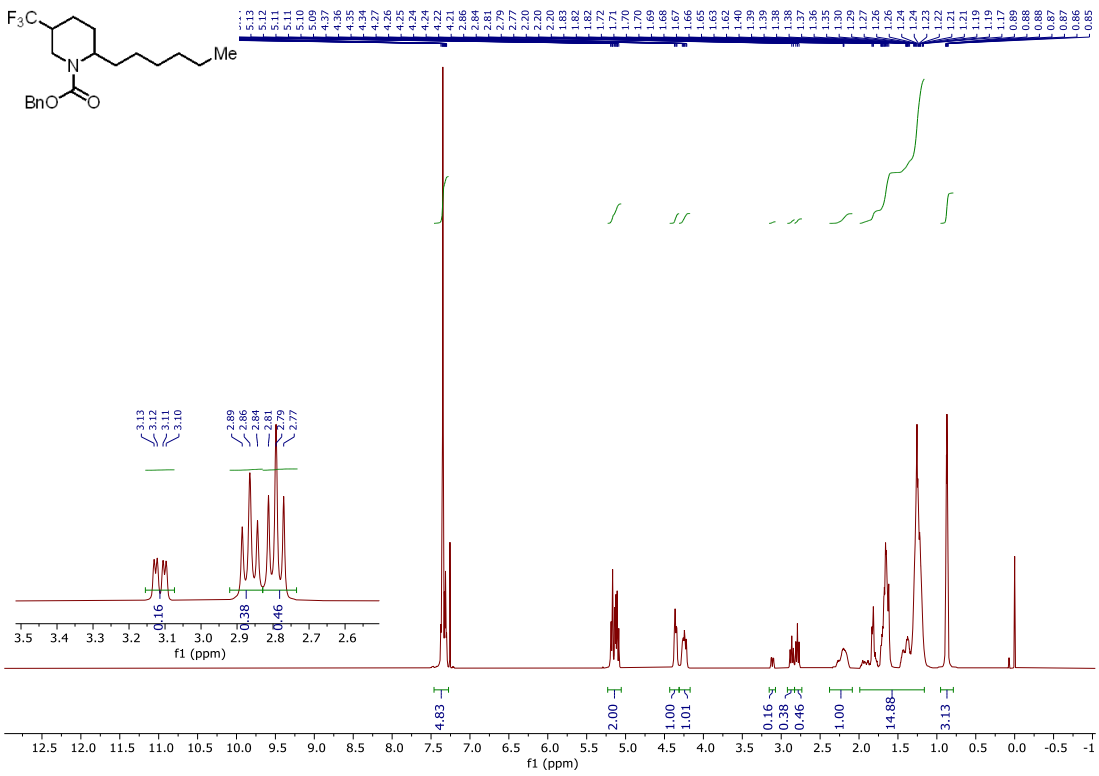


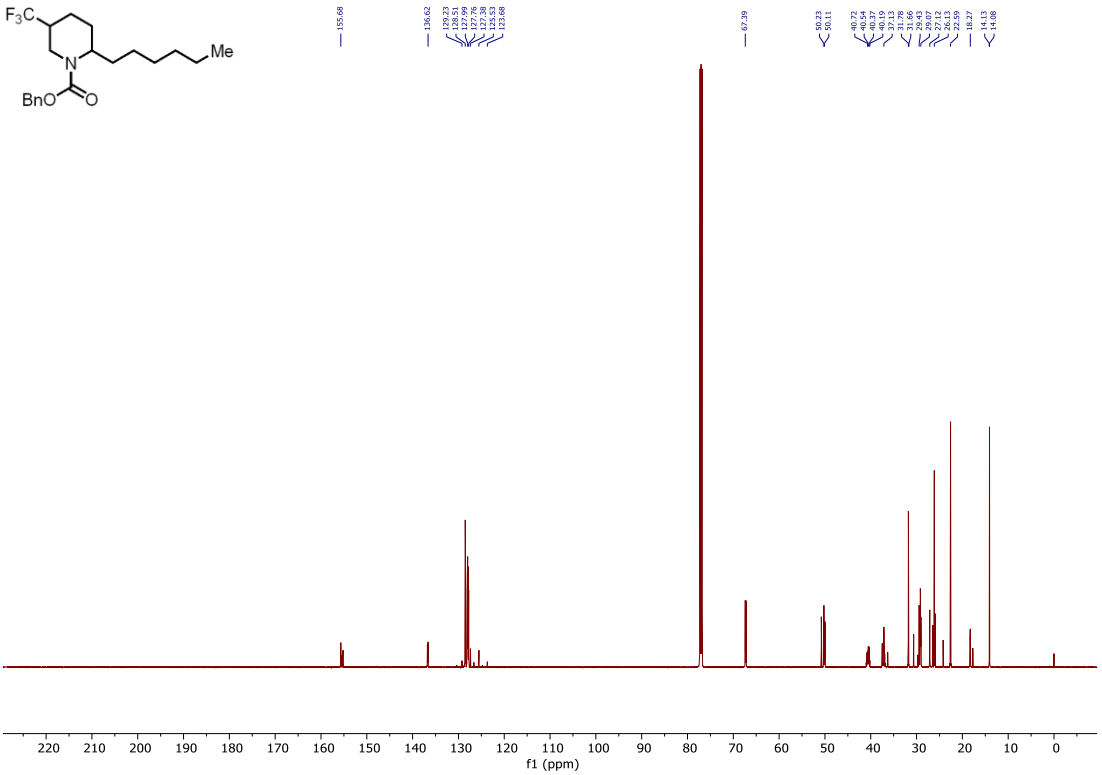


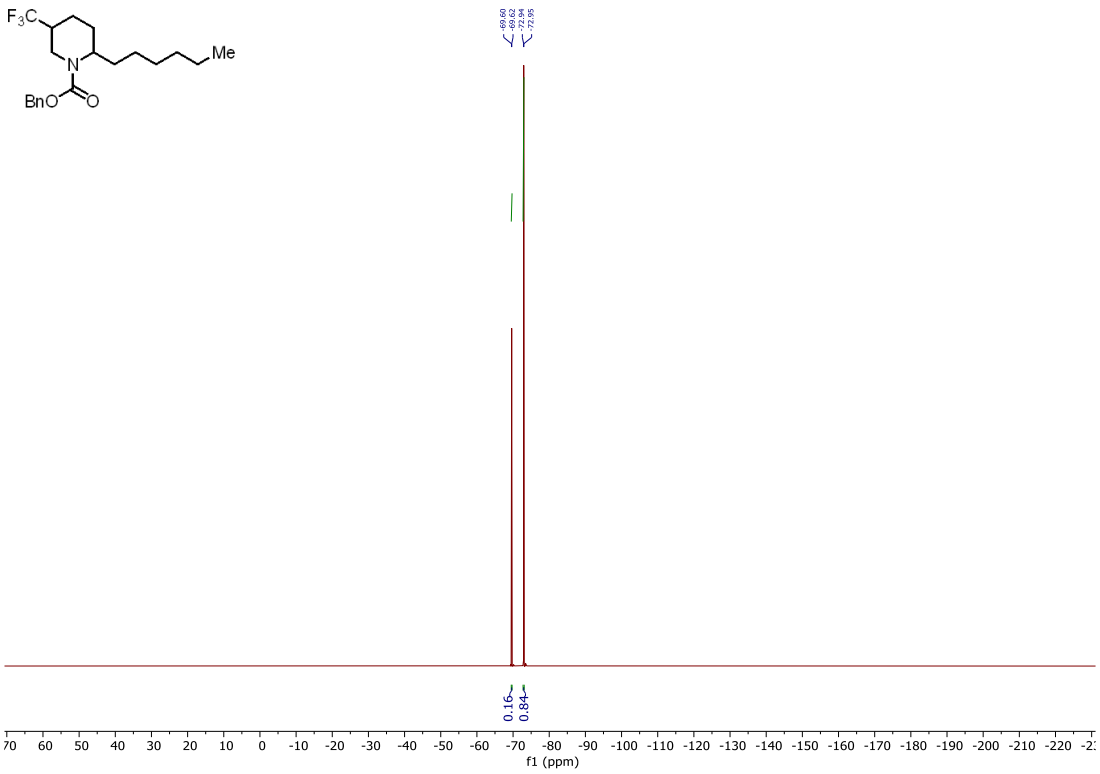

Ph
Ph
Me
N
H
f2 (ppm)
f1 (ppm)

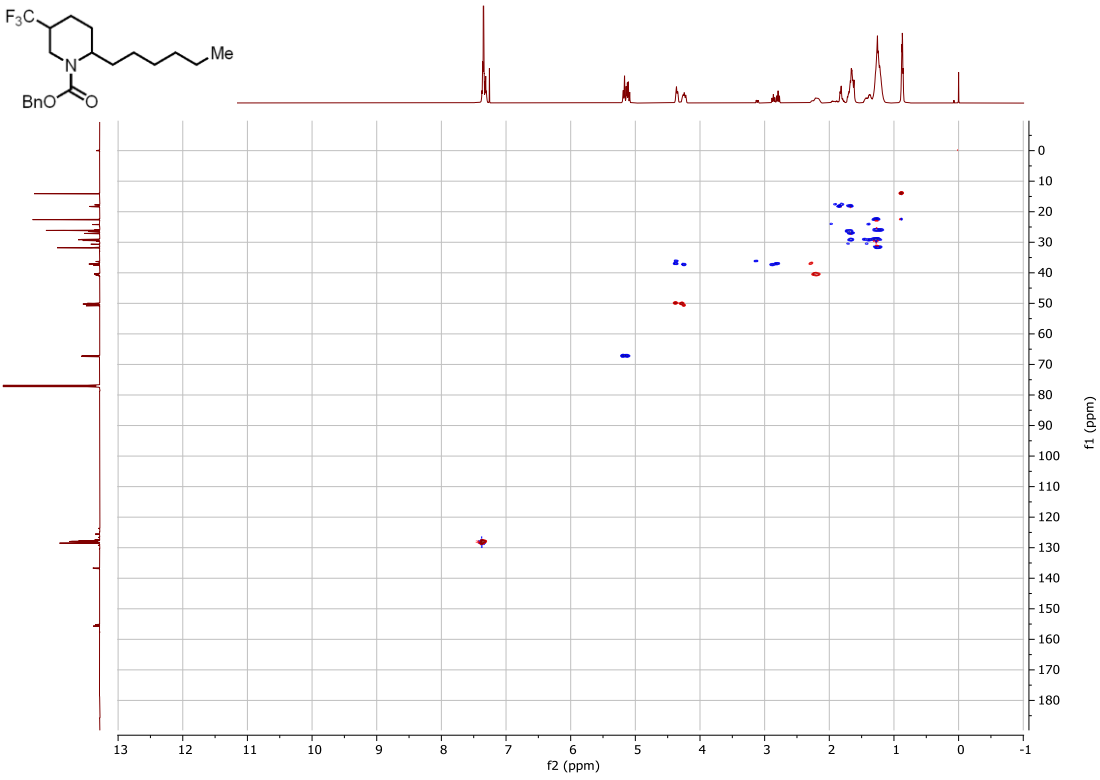

Ph
Ph
Me
N
H
f2 (ppm)
f1 (ppm)

benzyl 2-hexyl-5-(trifluoromethyl)piperidine-1-carboxylate (9)






F3C
Me
N
BnO
O
-69.60
-69.62
-72.94
-72.95
0.16
0.84
f1 (ppm)


F3C
Me
N
BnO
O
f2 (ppm)
f1 (ppm)