One Step Synthesis of Saturated Spirocyclic N-Heterocycles with SnAP Reagents and Ketones

Supplementary Information

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Table of contents

1. General methods

1.1. Reagents and purification

All reactions were performed in dried glassware under an atmosphere of dry N_2. Reaction mixtures were stirred magnetically unless otherwise stated and monitored by thin layer chromatography (TLC) on silica-coated aluminum sheets (*Merck*, TLC silica gel 60, F_{254}) or on coated glass plates (*Merck*, TLC silicagel 60, F_{254}) by fluorescene quenching of 254 nm. TLC plates were stained using phosphomolybdic acid (PMA), ninhydrin or potassium permanganate stain. Chromatographic purification of products (flash column chromatography) was performed on Silicycle Silica Flash F60 (230-400 mesh) silica gel using a forced flow of eluent at 0.3–0.5 bar. Concentration of reaction product solutions and chromatography fractions under reduced pressure was performed by rotary evaporaton at 35–40 ^{o}C at the appropriate pressure and then at 23 ^{o}C, ca. 0.1 mmHg (vacuum pump) unless otherwise indicated. Anydrous KF was used as a precolumn (ca. 3 cm) on top of the silica gel for the purification of N-heterocyclic products.

1.2. Materials

All materials were purchased from Acros, Aldrich, Fluka, Merck, ABCR, Fluorochem, TCI, Alfa Aesar or Strem and used directly unless otherwise stated. Commercial grade reagents and solvents were used without further purification except as indicated below. Dichloromethane was distilled from CaH_2. *N,N*-dimethylformamide (DMF), Et_2O and tetrahydrofuran (THF) were purified by pressure filtration through activated alumina. 1,1,1,3,3,3-Hexafluoroisopropanol (HFIP) was distilled from MS 4A. $Cu(OTf)_2$ was dried at 110^{o}C under high vacuum (ca. 0.1 mmHg) for 2 h and stored in desiccator. Yields given refer to chromatographically purified and spectroscopically pure compounds unless otherwise stated. The SnAP reagents used were synthesized based on a previously reported method[1] and were purified by column chromatography prior to use.

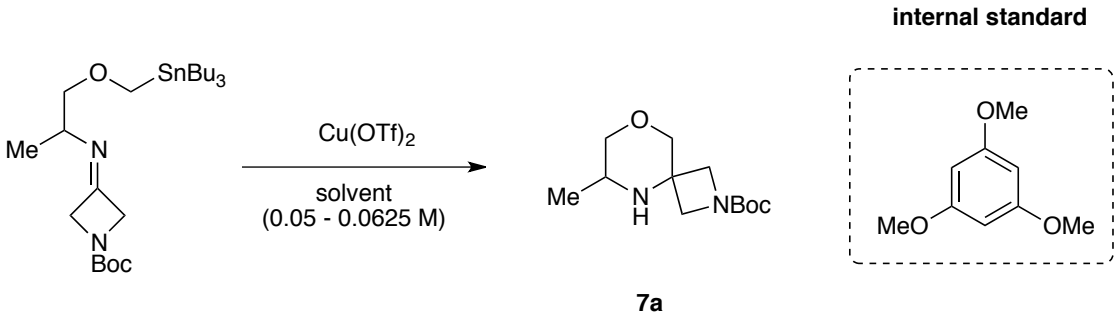
1.3. Instrumentation

^{1}H NMR was performed on a Varian Mercury 300 (300 MHz) or Varian AV400 (400 MHz) and spectra were referenced to residual protonated solvent ($CDCl_3$: 7.26 ppm). ^{13}C NMR was

(1) Luescher, M. U.; Vo, V.-C.; Bode, J. W. *Org. Lett.* **2014**, *16*, 1236–1239.

performed on a Varian Mercury 300 (75 MHz) or a Varian AV400 (100 MHz) and spectra were referenced to the solvent ($CDCl_3$: 77.0 ppm). All chemical shifts are reported in ppm (δ). Splitting patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublet; ddd, doublet of doublet of doublet; t, triplet; q, quartet; quint, quintet; m, multiplet. LCMS analysis was performed on Dionex UltiMate 3000 RSLC connected to a Surveyor MSQ Plus mass spectrometer; a reversed-phase RESTEK Pinnacle II C18 (4.6 x 50 mm) column was used, running a gradient of 5 to 100% CH_3CN in H_2O over 4.5 min, 100% CH_3CN for 2.5 min. IR spectra were obtained on a JASCO FT:IR-4100 spectrophotometer and reported as wavenumber (cm^{-1}) of the absorption maxima for the range between 4000 and 750cm^{-1} with only major peaks reported. High-resolution mass spectra (ESI-HRMS and MALDI-HRMS) for small molecules were performed by the mass spectrometry service of ETH Zürich Laboratorium für Organische Chemie on Varian IonSpec FT-ICR (ESI), Bruker Daltonics maXis ESI-QTOF spectrometer (ESI), Bruker Daltonics SOLARIX spectrometer (MALDI) or Bruker Daltonics UltraFlex II spectrometer (MALDI-TOF). Melting points were measured on an Electrothermal Mel-Temp melting point apparatus and are uncorrected.

2. Optimization of reaction conditions



7a

To an oven-dried flask was charged with $Cu(OTf)_2$ (0.5 mmol, 1.00 equiv) and 1,1,1,3,3,3-hexafluoro-2-propanol (abbreviated as HFIP) was added 2,6-lutidine (0.5 mmol, 1.00 equiv). This reaction mixture was stirred for 1 h at 23 ^{o}C during which time the dark purple mixture turned into homogeneous green solution. Ketimine was dissolved in 1,2-dichloroethane (abbreviated as DCE) and HFIP and added to the $Cu(OTf)_2$ solution. The reaction flask was sealed and the reaction mixture was allowed to stir at the indicated temperature for 14 h (Table 1). The reaction mixture was concentrated under reduced pressure to remove most of the HFIP and re-dissolved in CH_2Cl_2. Sat. aq. $NaHCO_3$ (4 mL) and 2 M NH_4OH (2 mL) were added to the residue and stirred vigorously for 15 min. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were

washed with H_2O (2 x 15 mL) and brine (15 mL), dried over Na_2SO_4, filtered and concentrated. To this residue was added a solution of 1,3,5-dimethoxybenzene (200 μL of a stock solution of 100.8 mg in 1200 μL) as an internal standard; the product **7a** yield was calculated based on ^{1}H NMR integration.

Table S1. Reaction optimization

Temp (^{o}C)	Time (h)	Solvent	Yield[a] (%)
rt	14	HFIP: DCE = 1: 4 (total volume = 10 mL)	59
rt	14	HFIP: DCE = 3: 1 (total volume = 8 mL)	66
rt	14	HFIP: DCE = 3: 1 (total volume = 8 mL)	64[b]
rt	14	HFIP: DCE = 3: 1(total volume = 8 mL)[c]	71 (69)
60 ^{o}C	14	HFIP: DCE = 3: 1 (total volume = 8 mL)	62
rt	14	HFIP: DCE = 5: 1 (total volume = 12 mL)	62

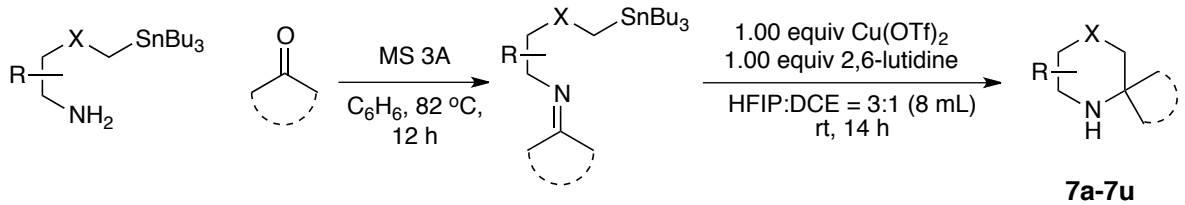
a) NMR yield, number in parentheses showed the isolated yield. b) 1.50 equiv of $Cu(OTf)_2$ was used. c) HFIP and DCE were further pre-treated with MS 4A prior to use.

3. General procedure for the synthesis of spiro N-heterocycles

3.1. Notes on the purification of spiro compound (0.5 mmol scale):

- Precolumn: anhydrous KF (~ 3 cm on top of the silica gel)
- Fast flow rate (0.3 – 0.5 bar) is preferred
- Dry loading (the crude reaction mixture was mixed with silica gel and dried carefully under reduced pressure and further dried on high vacuum (0.1 mm Hg) for ease of purification.)

3.2. General procedure for N-heterocycle synthesis:



SnAP reagents **ketones**

7a-7u
R = Me
X = O, NBoc

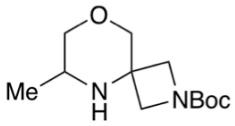
An oven-dried vial was charged with freshly prepared SnAP reagent (0.53 mmol, 1.05 equiv), ketone (0.50 mmol, 1.00 equiv) and MS 3A (240 mg) to which was then added C_6H_6 (2 mL)

and the vial was sealed with Teflon crimp seal. The resulting mixture was stirred at 82°C for 12 h, cooled to 23 °C and filtered through a pad of Celite and washed with CH_2Cl_2 (5 mL). The solvent was removed to afford the unpurified ketimine without any further purification. Separately, 2,6-lutidine (0.50 mmol, 1.00 equiv) was added to a solution of $Cu(OTf)_2$ in HFIP* (2 mL) and the mixture was allowed to stir at 23 °C for 1 h. The ketimine was dissolved in DCE (2 mL) and HFIP (4 mL) and added to the $Cu(OTf)_2$ solution. The resulting reaction mixture was stirred vigorously overnight (14 h) before it was concentrated under reduced pressure to remove most of the HFIP. The reaction mixture was dissolved in CH_2Cl_2, followed by the addition of sat. aq. $NaHCO_3$ (4 mL) and 2 M NH_4OH (2 mL) and stirred vigorously for 15 min. The phases were separated and aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with H_2O (2 x 15 mL) and brine (15 mL) and dried over Na_2SO_4, filtered and concentrated. Purification by column chromatography afforded the desired products.

**These solvents were treated with activated MS 4A prior to use.*

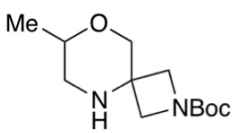
3.3. Characterization data:

***tert*-Butyl 6-methyl-8-oxa-2,5-diazaspiro[3.5]nonane-2-carboxylate (7a):**



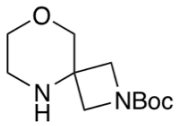
Prepared by the general procedure stated above and isolated as a colorless solid (84.0 mg, 69% yield). **IR** (thin film) v 2966, 2874, 1697, 1159 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.03 (d, *J* = 8.8 Hz, 1H), 3.88 (d, *J* = 11.0 Hz, 1H), 3.76 – 3.68 (m, 2H), 3.66 (d, *J* = 9.5 Hz, 1H), 3.55 (d, *J* = 9.5 Hz, 1H), 3.38 (d, *J* = 11.0 Hz, 1H), 3.06 (t, *J* = 10.4 Hz, 1H), 2.97 (dtt, *J* = 9.5, 6.1, 2.7 Hz, 1H), 1.66 (s, 1H), 1.44 (s, 9H), 0.97 (d, *J* = 6.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.4, 79.7, 72.8, 72.6, 60.4, 57.6, 52.0, 46.9, 28.4, 17.6; m.p.= 82–86 °C **HRMS** (ESI) calc'd for $C_{12}H_{22}N_2O_3$ $[M+H]^+$: 243.1703, found: 243.1704.

***tert*-Butyl 7-methyl-8-oxa-2,5-diazaspiro[3.5]nonane-2-carboxylate (7b):**



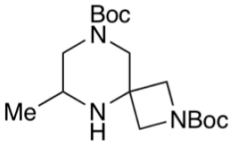
Prepared by the general procedure stated above and isolated as a yellow oil (70.3 mg, 58% yield). **IR** (thin film) v 2972, 2874, 1699, 1408, 1107 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.07 – 4.02 (m, 3H), 3.91 (ddd, *J* = 11.7, 9.0, 2H), 3.24 (dd, *J* = 11.7, 6.1 Hz, 1H), 2.61 (dd, *J* = 11.7, 7.0 Hz, 1H), 2.17 (s, 2H), 1.61 (s, 1H), 1.43 (s, 9H), 1.22 (d, *J* = 6.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.2, 90.8, 79.6, 74.0, 62.4, 52.0, 30.9, 28.4, 28.3, 20.0; **HRMS** (ESI) calc'd for $C_{12}H_{22}N_2O_3$ $[M+H]^+$: 243.1703, found: 243.1700.

***tert*-Butyl 8-oxa-2,5-diazaspiro[3.5]nonane-2-carboxylate (7c):**



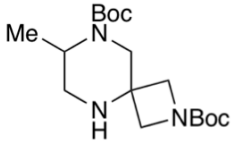
Prepared by the general procedure stated above and isolated as a yellow oil (71.2 mg, 62% yield). **IR** (thin film) ν 2964, 1697, 1410, 1366, 1088 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.83 (d, *J* = 9.1 Hz, 2H), 3.64 (dd, *J* = 10.2, 5.8 Hz, 6H), 2.90 - 2.80 (m, 2H), 1.84 (s, 1H), 1.43 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.4, 79.7, 73.2, 66.9, 58.8, 51.7, 42.6, 28.3; **HRMS** (ESI) calc'd for $C_{11}H_{20}N_2O_3$ $[M+H]^+$: 229.1547, found: 229.1547.

di-*tert*-Butyl 6-methyl-2,5,8-triazaspiro[3.5]nonane-2,8-dicarboxylate (7d):



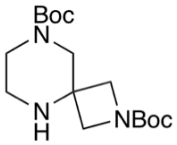
Prepared by the general procedure stated above and isolated as a yellow oil (170.1 mg, 50% yield). **IR** (thin film) ν 2974, 1696, 1418, 1153 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.12 (s, 1H), 3.99 (s, 1H), 3.84 (d, *J* = 8.9 Hz, 1H), 3.74 (d, *J* = 9.3 Hz, 1H), 3.63 (d, *J* = 8.6 Hz, 1H), 3.58 (d, *J* = 9.3 Hz, 1H), 2.78 (dtd, *J* = 9.0, 6.2, 3.4 Hz, 2H), 2.34 (s, 1H), 1.66 (s, 1H), 1.46 (s, 9H), 1.44 (s, 9H), 1.05 (d, *J* = 6.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.4, 154.6, 80.2, 79.7, 60.0, 58.7, 52.3, 51.0, 49.1, 46.8, 28.4, 19.2; **HRMS** (ESI) calc'd for $C_{17}H_{31}N_3O_4$ $[M+H]^+$: 342.2387, found: 342.2389.

di-*tert*-Butyl 7-methyl-2,5,8-triazaspiro[3.5]nonane-2,8-dicarboxylate (7e):



Prepared by the general procedure stated above and isolated as a yellow oil (78.5 mg, 46% yield). **IR** (thin film) ν 2975, 1694, 1408, 1162 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.16 (s, 1H), 3.98 (d, *J* = 13.0 Hz, 1H), 3.81 (d, *J* = 8.6 Hz, 1H), 3.71 (d, *J* = 9.3 Hz, 1H), 3.64 (d, *J* = 8.6 Hz, 1H), 3.59 (d, *J* = 9.3 Hz, 1H), 2.97 (d, *J* = 13.0 Hz, 1H), 2.91 (dd, *J* = 12.1, 4.2 Hz, 1H), 2.67 (d, *J* = 12.1 Hz, 1H), 1.59 (s, 1H), 1.46 (s, 9H), 1.44 (s, 9H), 1.21 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ156.4, 154.9, 80.0, 79.7, 60.4, 58.9, 52.0, 46.1, 45.5, 28.4, 28.4, 21.0, 14.6, 14.2; **HRMS** (ESI) calc'd for $C_{17}H_{31}N_3O_4$ $[M+Na]^+$: 364.2207, found: 364.2207.

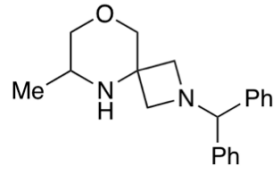
di-*tert*-Butyl 2,5,8-triazaspiro[3.5]nonane-2,8-dicarboxylate (7f):



Prepared by the general procedure stated above and isolated as a yellow oil (78.6 mg, 48% yield). **IR** (thin film) ν 2976, 2875, 1695, 1416; 1159 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.78 (d, *J* = 9.0 Hz, 2H), 3.60 (d, *J* = 9.0 Hz, 2H), 3.46 (s, 2H), 3.37 (s, 2H), 2.78 (t, *J* = 5.0 Hz, 2H), 1.77 (s, 1H), 1.46 (s, 9H), 1.43 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ

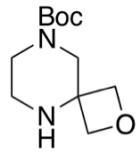
161.6, 156.4, 154.8, 80.1, 79.7, 59.0, 52.0, 51.4, 50.3, 43.9, 42.8, 41.9, 28.4, 28.3; **HRMS** (ESI) calc'd for $C_{16}H_{29}N_3O_4$ $[M+Na]^+$: 350.2050, found: 350.2050.

2-Benzhydryl-6-methyl-8-oxa-2,5-diazaspiro[3.5]nonane (7g):



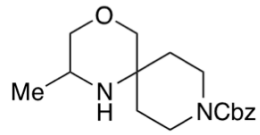
Prepared by the general procedure stated above and isolated as a yellow solid (89.4 mg, 58% yield). **IR** (thin film) v 2963, 1691, 1423, 1162 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 4H), 7.30 – 7.22 (m, 4H), 7.17 (t, *J* = 7.3 Hz, 2H), 4.34 (s, 1H), 4.09 (d, *J* = 10.9 Hz, 1H), 3.68 (dd, *J* = 10.9, 3.0 Hz, 1H), 3.54 (dd, *J* = 7.5, 1.7 Hz, 1H), 3.43 (dd, *J* = 10.9, 1.7 Hz, 1H), 3.12 – 3.02 (m, 2H), 2.93 (dqd, *J* = 9.5, 6.3, 3.0 Hz, 1H), 2.76 (dd, *J* = 7.5, 1.7 Hz, 1H), 2.69 (d, *J* = 8.1 Hz, 1H), 1.65 (s, 1H), 0.93 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.2, 142.1, 128.4, 128.3, 127.4, 127.3, 127.1, 127.0, 77.9, 73.3, 73.1, 64.3, 62.2, 52.0, 46.8, 17.7; m.p. = 131–133 °C **HRMS** (MALDI) calc'd for $C_{20}H_{24}N_2O$ $[M+H]^+$: 309.1961, found: 309.1961.

***tert*-Butyl 2-oxa-5,8-diazaspiro[3.5]nonane-8-carboxylate (7h):**



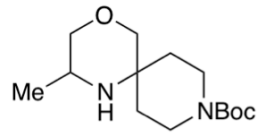
Prepared by the general procedure stated above and isolated as a yellow oil (55.2 mg, 48% yield). **IR** (thin film) v 1974, 1694, 1421, 1161cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.49 (d, *J* = 6.6 Hz, 2H), 4.41 (d, *J* = 6.6 Hz, 2H), 3.64 (s, 2H), 3.38 (t, *J* = 5.1 Hz, 2H), 2.84 – 2.72 (m, 2H), 2.30 (s, 1H), 1.47 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.8, 81.2, 80.1, 79.6, 63.0, 56.6, 41.9, 28.5, 28.4; **HRMS** (MALDI) calc'd for $C_{11}H_{20}N_2O_3$ $[M+H]^+$: 229.1547, found: 229.1547.

Benzyl 2-methyl-4-oxa-1,9-diazaspiro[5.5]undecane-9-carboxylate (7i):



Prepared by the general procedure stated above and isolated as a yellow oil (79.1 mg, 52% yield). **IR** (thin film) v 2954, 2849, 1697, 1430, 1250 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 5H), 5.12 (s, 2H), 3.80 (dd, *J* = 10.7, 3.3 Hz, 1H), 3.70 (d, *J* = 11.1 Hz, 1H), 3.60 – 3.42 (m, 4H), 3.11 (d, *J* = 6.3 Hz, 1H), 3.07 (d, *J* = 11.1 Hz, 1H), 2.90 (t, *J* = 10.7 Hz, 1H), 1.95 – 1.68 (m, 2H), 1.49 – 1.37 (m, 1H), 1.32 – 1.21 (m, 2H), 0.92 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.3, 136.8, 128.5, 128.0, 127.9, 74.7, 74.6, 67.0, 49.5, 44.1, 40.1, 39.1, 35.4, 30.6, 17.9; **HRMS** (ESI) calc'd for $C_{17}H_{24}N_2O_3$ $[M+H]^+$: 305.1860, found: 305.1865.

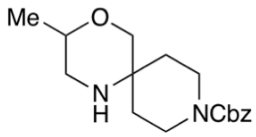
***tert*-Butyl 2-methyl-4-oxa-1,9-diazaspiro[5.5]undecane-9-carboxylate (7j):**



Prepared by the general procedure stated above and isolated as a yellow oil (57.0 mg, 42% yield). **IR** (thin film) v 2963, 1691, 1423, 1162 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.79 (dd, *J* = 10.7, 3.3 Hz, 1H), 3.71 (d, *J* = 11.1

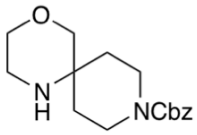
Hz, 1H), 3.48 – 3.34 (m, 4H), 3.18 – 3.10 (m, 1H), 3.08 (d, *J* = 11.1 Hz, 1H), 2.91 (t, *J* = 10.7 Hz, 1H), 1.80 (m, 2H), 1.45 (s, 9H), 1.34 – 1.19 (m, 3H), 0.92 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.8, 79.4, 74.5, 74.5, 49.6, 44.1, 39.9, 38.9, 35.5, 30.6, 28.4, 17.9; **HRMS** (ESI) calc'd for $C_{14}H_{26}N_2O_3$ $[M+H]^+$: 271.2016, found: 271.2016.

Benzyl 3-methyl-4-oxa-1,9-diazaspiro[5.5]undecane-9-carboxylate (7k):



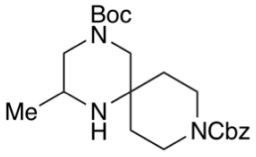
Prepared by the general procedure stated above and isolated as a yellow oil (73.1 mg, 48% yield). **IR** (thin film) v 2933, 1697, 1433, 1245, 1095 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.28 (m, 5H), 5.12 (s, 2H), 3.71 (d, *J* = 11.3 Hz, 1H), 3.66 – 3.51 (m, 2H), 3.43 (m, 3H), 3.24 (d, *J* = 11.3 Hz, 1H), 2.68 (d, *J* = 6.1 Hz, 2H), 1.91 (s, 1H), 1.75 – 1.50 (b, 2H), 1.48 - 1.35 (m, 1H), 1.27 (d, *J* = 3.2 Hz, 1H), 1.13 (d, *J* = 6.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.2, 136.8, 128.4, 127.9, 127.8, 75.8, 73.7, 67.0, 48.1, 47.0, 40.0, 39.1, 35.0, 28.4, 18.7; **HRMS** (ESI) calc'd for $C_{17}H_{24}N_2O_3$ $[M+H]^+$: 305.1860, found: 305.1859.

Benzyl 4-oxa-1,9-diazaspiro[5.5]undecane-9-carboxylate (7l):



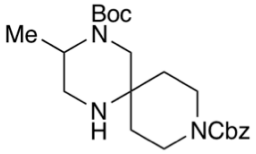
Prepared by the general procedure stated above and isolated as a yellow oil (79.0 mg, 54% yield). **IR** (thin film) v 2949, 2851, 1696, 1434, 1096 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H), 5.12 (s, 2H), 3.68 – 3.51 (m, 4H), 3.50 – 3.39 (m, 4H), 2.94 – 2.77 (m, 2H), 2.21 (s, 1H), 1.59 (h, *J* = 10.0, 9.2 Hz, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.2, 136.8, 128.5, 128.4, 128.0, 127.9, 127.8, 75.5, 68.4, 67.0, 49.0, 40.2, 39.4, 32.3; **HRMS** (ESI) calc'd for $C_{16}H_{22}N_2O_3$ $[M+H]^+$: 291.1703, found: 291.1703.

9-Benzyl 4-*tert*-butyl 2-methyl-1,4,9-triazaspiro[5.5]undecane-4,9-dicarboxylate (7m):



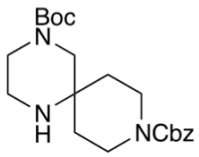
Prepared by the general procedure stated above and isolated as a yellow oil (81.0 mg, 40% yield). **IR** (thin film) v 2971, 1427, 1242, 1161 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.12 (s, 2H), 4.04 (b, 2H), 3.72 – 3.53 (m, 2H), 3.40 (m, 2H), 2.99 (s, 1H), 2.53 – 2.19 (m, 2H), 1.69 (s, 1H), 1.52 (s, 2H), 1.45 (s, 9H), 1.38 (s, 2H), 0.99 (d, *J* = 6.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.2, 136.8, 128.4, 128.4, 127.9, 127.8, 79.8, 67.0, 51.9, 50.5, 44.1, 40.3, 39.5, 36.8, 30.7, 28.4, 28.4, 19.5; **HRMS** (ESI) calc'd for $C_{22}H_{33}N_3O_4$ $[M+H]^+$: 404.2544, found: 404.2545.

9-Benzyl 4-*tert*-butyl 3-methyl-1,4,9-triazaspiro[5.5]undecane-4,9-dicarboxylate (7n):



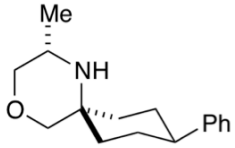
Prepared by the general procedure stated above and isolated as a yellow oil (86.8 mg, 43% yield). **IR** (thin film) v 2934, 1690, 1420, 1163 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 5H), 5.12 (s, 2H), 4.18 (s, 1H), 3.79 (d, *J* = 13.5 Hz, 1H), 3.51 (m, 4H), 3.11 (dd, *J* = 13.5, 4.8 Hz, 1H), 2.66 (d, *J* = 13.5 Hz, 1H), 2.50 (dd, *J* = 13.5, 2.0 Hz, 1H), 1.66 (s, 1H), 1.53 (s, 2H), 1.47 (s, 1H), 1.45 (s, 9H), 1.37 (s, 1H), 1.16 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) 161.5, 155.2, 154.9, 136.8, 128.4, 127.9, 127.8, 79.6, 67.0, 49.6, 46.9, 45.9, 44.0, 40.0, 39.3, 36.6, 29.9, 28.5, 28.4, 28.4, 28.3, 14.7; **HRMS** (ESI) calc'd for $C_{22}H_{33}N_3O_4$ $[M+H]^+$: 404.2544, found: 404.2541.

9-Benzyl 4-*tert*-butyl 1,4,9-triazaspiro[5.5]undecane-4,9-dicarboxylate (7o):



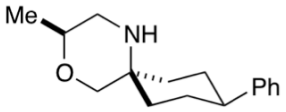
Prepared by the general procedure stated above and isolated as a yellow oil (rotamers, 3:1) (80.8 mg, 42% yield). **IR** (thin film) v 2975, 2932, 1694, 1427, 1246, 1161 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 5.12 (s, 2H), 3.50 (dtd, *J* = 13.8, 9.2, 8.4, 5.2 Hz, 4H), 3.38 (s, 2H), 3.24 (s, 2H), 2.83 (t, *J* = 5.2 Hz, 2H), 1.56 (s, 2H), 1.47 (s, 3H), 1.46 (s, 3H, minor rotamer), 1.44 (s, 9H, major rotamer); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.1, 154.7, 136.7, 128.4, 127.9, 127.8, 79.7, 79.4, 67.0, 63.1, 53.1, 49.7, 45.5, 45.2, 44.4, 39.8, 39.7, 33.2, 28.4, 28.3, 28.0; **HRMS** (ESI) calc'd for $C_{21}H_{31}N_3O_4$ $[M+H]^+$: 390.2387, found: 390.2393.

2-Methyl-9-phenyl-4-oxa-1-azaspiro[5.5]undecane (7p):



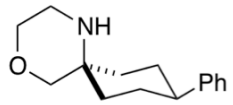
Prepared by the general procedure stated above and isolated as a yellow oil (dr > 10:1) (57.5 mg, 47% yield). **IR** (thin film) v 2928, 2854, 1715, 1451, 1067 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.29 (m, 2H), 7.26 – 7.19 (m, 3H), 4.21 (d, *J* = 11.2 Hz, 1H), 3.84 (dd, *J* = 10.9, 3.4 Hz, 1H), 3.31 (dqd, *J* = 9.9, 6.3, 3.4 Hz, 1H), 3.08 (dd, *J* = 11.3, 1.9 Hz, 1H), 2.97 (t, *J* = 10.9 Hz, 1H), 2.74 (dq, *J* = 13.1, 3.1 Hz, 1H), 2.57 (tt, *J* = 12.0, 3.6 Hz, 1H), 1.95 – 1.86 (m, 1H), 1.81 (dt, *J* = 12.0, 2.7 Hz, 1H), 1.65 (dt, *J* = 13.2, 3.3 Hz, 1H), 1.54 (dd, *J* = 13.2, 3.3 Hz, 1H), 1.51 – 1.43 (m, 2H), 1.23 (tdd, *J* = 13.1, 3.1, 1.9 Hz, 2H), 0.96 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.6, 128.3, 128.3, 126.7, 126.0, 74.5, 71.8, 50.8, 44.4, 44.3, 38.0, 32.2, 30.5, 30.1, 18.1; **HRMS** (ESI) calc'd for $C_{16}H_{23}NO$ $[M+H]^+$: 246.1852, found: 246.1856.

3-Methyl-9-phenyl-4-oxa-1-azaspiro[5.5]undecane (7q):



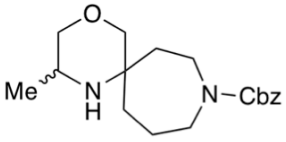
Prepared by the general procedure stated above and isolated as a yellow oil (dr > 10:1) (52.1 mg, 43% yield). **IR** (thin film) ν 2931, 2851, 1449, 1091 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.25 – 7.16 (m, 3H), 3.53 (d, *J* = 11.0 Hz, 1H), 3.51 – 3.43 (m, 1H), 3.35 (d, *J* = 11.1 Hz, 1H), 2.70 (d, *J* = 6.5 Hz, 2H), 2.51 (m, 2H), 1.78 – 1.68 (m, 3H), 1.64 (dd, *J* = 12.4, 3.4 Hz, 1H), 1.55 (b, 1H), 1.40 (dt, *J* = 6.9, 2.0 Hz, 2H), 1.22 (dd, *J* = 13.5, 3.9 Hz, 1H), 1.15 (d, *J* = 6.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.0, 128.3, 126.8, 125.9, 78.6, 73.6, 48.5, 47.0, 44.5, 35.4, 29.0, 28.4, 28.1, 18.8; **HRMS** (ESI) calc'd for $C_{16}H_{23}NO$ $[M+H]^+$: 246.1852, found: 246.1856.

9-Phenyl-4-oxa-1-azaspiro[5.5]undecane (7r):



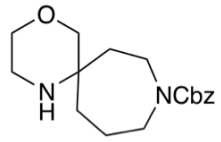
Prepared by the general procedure stated above and isolated as a yellow oil (dr > 10:1) (45.0 mg, 39% yield). **IR** (thin film) ν 2923, 2850, 1111, 1092 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.1 Hz, 1H), 3.71 – 3.62 (m, 2H), 3.39 (s, 2H), 2.95 – 2.84 (m, 2H), 2.50 (tt, *J* = 11.5, 4.4 Hz, 1H), 2.02 (dd, *J* = 14.2, 3.2 Hz, 2H), 1.91 – 1.78 (m, 1H), 1.77 – 1.63 (m, 4H), 1.29 (td, *J* = 13.2, 4.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.9, 128.3, 126.8, 126.0, 78.5, 68.5, 49.4, 44.5, 40.4, 32.3, 28.2; **HRMS** (ESI) calc'd for $C_{15}H_{21}NO$ $[M+H]^+$: 232.1696, found: 232.1700.

Benzyl 2-methyl-4-oxa-1,9-diazaspiro[5.6]d-odecane-9-carboxylate (7s):



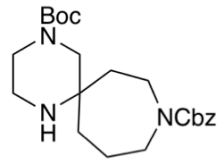
Prepared by the general procedure stated above and isolated as a yellow oil (inseparable 1:1 mixture of diastereomers) (62.1 mg, 39% yield). **IR** (thin film) ν 2928, 1694, 1421, 1216, 1105 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H), 5.14 (s, 2H), 3.81 – 3.66 (m, 2H), 3.61 (ddd, *J* = 14.4, 10.5, 3.9 Hz, 1H), 3.56 – 3.47 (m, 1H), 3.42 (dq, *J* = 14.1, 5.4, 4.6 Hz, 1H), 3.25 (dddd, *J* = 13.5, 9.1, 3.9 Hz, 1H), 3.02 (ddd, *J* = 9.9, 3.8 Hz, 2H), 2.89 (td, *J* = 10.6, 5.8 Hz, 1H), 2.26 (ddt, *J* = 15.2, 4.7 Hz, 1H), 1.72 (ddq, *J* = 15.1, 5.0 Hz, 3H), 1.43 (dt, *J* = 14.4, 4.1 Hz, 1H), 1.38 – 1.27 (m, 2H), 0.87 (dd, *J* = 12.8, 6.2 Hz, 3H, two sets of double of methyl group); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.0, 156.0, 137.0, 136.9, 128.4, 127.9, 127.7, 76.0, 75.9, 75.7, 74.2, 74.1, 66.9, 66.9, 53.3, 53.1, 46.6, 45.4, 45.2, 44.7, 44.6, 44.0, 41.6, 41.3, 40.7, 38.9, 37.8, 37.6, 31.8, 31.4, 29.6, 29.3, 22.5, 22.0, 21.3, 17.8, 17.8; **HRMS** (ESI) calc' for $C_{18}H_{26}N_2O_3$ $[M+H]^+$: 319.2016, found: 319.2020.

Benzyl 4-oxa-1,9-diazaspiro[5.6]dodecane-9-carboxylate (7t):



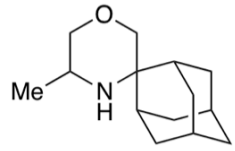
Prepared by the general procedure stated above and isolated as a yellow oil (51.7 mg, 34% yield). **IR** (thin film) v 2931, 1692, 1421, 1106 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 5H), 5.14 (s, 2H), 3.57 (m, 3H), 3.50 – 3.38 (m, 2H), 3.38 – 3.27 (m, 2H), 2.81 (dt, *J* = 9.7, 4.9 Hz, 2H), 1.90 – 1.55 (m, 5H), 1.46 (s, 1H), 1.35 (ddd, *J* = 14.2, 11.0, 3.1 Hz, 1H), 1.25 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.0, 136.9, 128.4, 127.9, 127.8, 127.7, 68.3, 66.9, 66.9, 52.3, 46.1, 45.9, 41.3, 41.0, 40.7, 40.6, 35.1, 34.9, 33.2, 21.9, 21.5; **HRMS** (ESI) calc'd for $C_{15}H_{21}NO$ $[M+H]^+$: 305.1860, found: 305.1859.

9-Benzyl 4-*tert*-butyl 1,4,9-triazaspiro[5.6]dodecane-4,9-dicarboxylate (7u):



Prepared by the general procedure stated above and isolated as a yellow oil (rotamers, 3:1) (62.0 mg, 31% yield). **IR** (thin film) v 2929, 1694, 1422, 1165, 1105 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 5H), 5.13 (s, 2H), 3.74 – 3.20 (m, 7H), 3.20 – 3.07 (m, 2H), 2.76 (dt, *J* = 10.0, 5.2 Hz, 2H), 1.70 (dt, *J* = 18.2, 7.9 Hz, 5H), 1.46 (s, 3H, minor rotamer), 1.44 (s, 9H, major rotamer), 1.25 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.0, 154.8, 136.9, 128.4, 127.8, 127.7, 127.7, 79.6, 79.4, 66.9, 66.9, 63.1, 54.6, 53.3, 52.9, 46.1, 45.9, 45.2, 44.1, 41.2, 40.8, 40.2, 40.1, 36.3, 35.9, 34.1, 33.9, 33.6, 33.4, 28.4, 28.4, 21.7, 21.4; **HRMS** (ESI) calc'd for $C_{22}H_{33}N_3O_4$ $[M+H]^+$:404.2544, found: 404.2543.

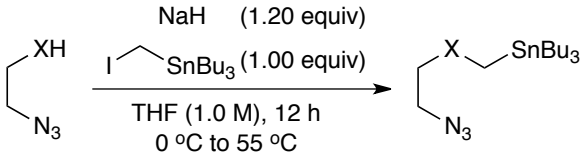
(1*r*,3*r*,5*r*,7*r*)-5'-Methylspiro[adamantane-2,3'-morpholine] (9):



Prepared by the general procedure stated above and isolated as a colorless solid (348.0 mg, 31% yield). **IR** (thin film) v 2909, 2859, 1457, 1076 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.39 (d, *J* = 11.3 Hz, 1H), 3.75 (dd, *J* = 10.6, 3.3 Hz, 1H), 3.14 (dqd, *J* = 9.7, 6.3, 3.3 Hz, 1H), 3.03 – 2.89 (m, 2H), 2.52 – 2.38 (m, 1H), 2.06 (dq, *J* = 13.4, 3.3 Hz, 1H), 1.97 (dt, *J* = 12.9, 3.0 Hz, 2H), 1.88 – 1.81 (m, 2H), 1.75 (dtd, *J* = 13.0, 6.3, 5.7, 3.0 Hz, 3H), 1.69 (d, *J* = 3.0 Hz, 2H), 1.61 (tq, *J* = 13.0, 2.8 Hz, 2H), 1.51 (dq, *J* = 13.4, 2.7 Hz, 1H), 1.43 (s, 1H), 0.93 (d, *J* = 6.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 74.0, 72.8, 54.5, 43.3, 38.6, 36.2, 33.7, 33.4, 31.8, 31.7, 28.1, 27.9, 27.6, 18.2; m.p. = 75–78 °C **HRMS** (ESI) calc'd for $C_{14}H_{23}NO$ $[M+H]^+$: 222.1852, found: 222.1852.

4. Preparation of azido SnAP reagent* and their application

4.1. Synthesis of azido SnAP reagent:



15, X = O, NBoc

Sodium hydride (60% suspension in mineral oil, 1.20 equiv) was washed with pentane and suspended in THF. The suspension was cooled to 0 °C and azido compound (2.00 equiv) in THF was added dropwise over 10 min. The resulting suspension was warmed to 23 °C and allowed to stir for 1 h. After re-immersion of the reaction mixture to the ice-bath, tributyl(iodomethyl)stannane (1.00 equiv) was added dropwise over 10 min. The resulting mixture was allowed to stir at 55 °C for overnight before it was cooled and quenched carefully by H_2O (15 mL). The layers were separated the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic layer was washed twice with H_2O (15 mL each), brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by flash column chromatography (EtOAc:hexanes = 0:1 to 1:4) afforded the desired product **15** as stated below.

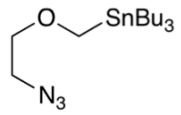
** Organic azides are potentially explosive substances that can decompose with the slight input of energy from external sources (heat, light, pressure). We always keep in mind the following equation:*

$(N_C + N_O)/(N_N) \geq 3$ *(N = number of atom)*

*It is noted that this equation takes into account all nitrogen atoms in the organic azide, not just those in the azido group. Azido compound **15** is stable in the freezer for months without any sign of decomposition.*

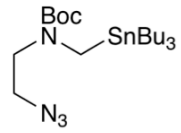
4.2. Characterization data:

((2-Azidoethoxy)methyl)tributylstannane (15a):



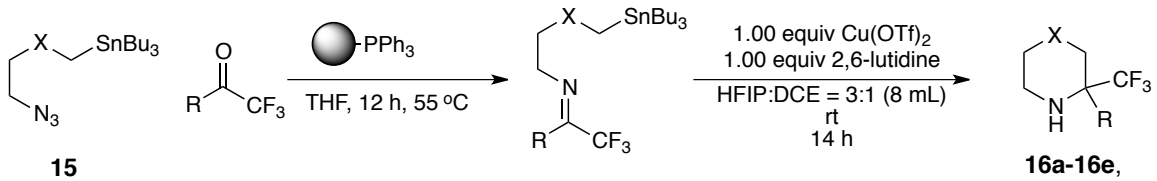
Prepared by the general procedure stated above and isolated as a colorless liquid (6.89 g, 88% yield). **IR** (thin film) v 2956, 2097, 1462, 1287 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.74 (s, $J(^{117/119}Sn\text{-}H$ = 7.8 Hz), 2H), 3.53 (t, J = 5.0 Hz, 2H), 3.36 – 3.24 (m, 2H), 1.59 – 1.45 (m, 6H), 1.39 – 1.23 (m, 6H), 0.91 (q, J = 7.6, 7.1 Hz, 15H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 74.3, 62.5, 50.6, 29.0, 27.2, 13.7, 8.9; **HRMS** (ESI) calc'd for $C_{15}H_{33}N_3OSn$ $[M+Na]^+$: 414.1540, found: 414.1538.

***tert*-Butyl (2-azidoethyl)((tributylstannyl)methyl)carbamate (15b):**



Prepared by the general procedure stated above and isolated as a colorless liquid (4.12 g, 73% yield). **IR** (thin film) v 2978, 1696, 1366, 1251 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.49 – 3.25 (m, 4H), 3.12 (s, 0.64H), 2.83 (s, 1.24H), 1.54 – 1.39 (m, 15H), 1.29 (h, J = 7.2 Hz, 6H), 0.87 (dt, J = 14.4, 7.6 Hz, 15H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.1, 79.9, 79.5, 49.5, 49.5, 49.4, 48.6, 34.3, 34.2, 29.1, 28.5, 28.4, 27.4, 13.7, 10.5, 9.6; **HRMS** (ESI) calc'd for $C_{20}H_{42}N_4O_2Sn$ $[M+H]^+$: 491.2406, found: 491.2402.

5. General procedure for the synthesis of α-trifluoromethyl N-heterocycles



15 **16a-16e**, X = O, NBoc, R = C_6H_5, 4-ClC_6H_4, Me

An oven-dried Schlenk flask was charged with azide SnAP reagent **15** (411 mg, 1.05 mmol, 1.00 equiv) under N_2 atmosphere. THF (10 mL) and polymer-bound triphenylphosphine (3mmol/g, 368 mg, 1.11 mmol, 1.05 equiv) were added (Note: N_2 is evolved!). The resulting mixture was stirred at 23 °C for half an hour before the addition of ketone (1.00 mmol, 0.95 equiv). The reaction mixture was heated to 55 °C for overnight before it was cooled and filtered through a pad of Celite and concentrated under reduced pressure to afford crude ketimine without any further treatment.

Separately, 2,6-lutidine (116.5 μL, 1.00 mmol, 0.95 equiv) was added to a solution of $Cu(OTf)_2$ (361.7 mg, 1.00 mmol, 0.95 equiv) in HFIP* (4 mL) and it was allowed to stir at rt for 1 h during which time the dark purple mixture turned into homogeneous green solution. The crude ketimine was re-dissolved in DCE* (4 mL) and HFIP (8 mL) and added to the $Cu(OTf)_2$ solution. The resulting reaction mixture was stirred vigorously for overnight before it was concentrated to remove most of the HFIP. The reaction crude was re-dissolved in CH_2Cl_2 and followed by the addition of sat aq $NaHCO_3$ (4 mL) and 2 M NH_4OH (2 mL), stirred vigorously for 15 min. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with H_2O (2 x 15 mL) and brine (15 mL), dried over Na_2SO_4, filtered and concentrated. Purification on column afforded the desired products as stated below.

**These solvents were further pre-treated with activated MS 4A prior to use.*

5.1. Easy access to the ketimine with polymer-bound triphenylphosphine

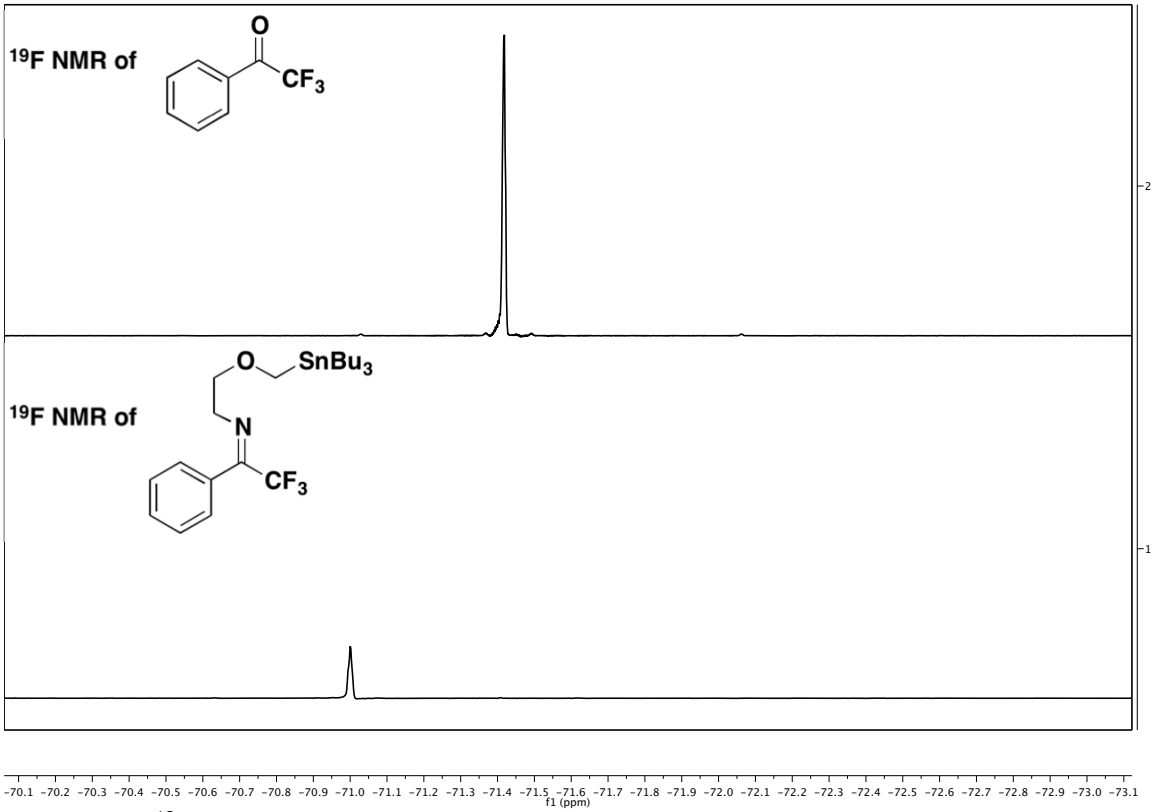
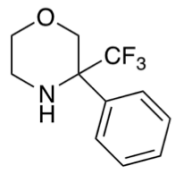


Figure S1. ^{19}F NMR of 2,2,2-trifluoro-1-phenylethanone and its corresponding ketimine.

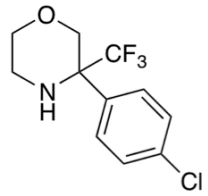
5.2. Characterization data:

3-Phenyl-3-(trifluoromethyl)morpholine (16a):



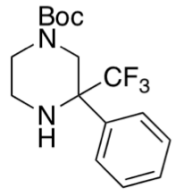
Prepared by the general procedure stated above and isolated as a colorless liquid (104.0 mg, 45% yield). **IR** (thin film) v 2920, 2860, 1295, 1152 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 2H), 7.48 – 7.34 (m, 3H), 4.41 (d, *J* = 11.8 Hz, 1H), 4.08 (d, *J* = 11.8 Hz, 1H), 3.70 (dd, *J* = 6.3, 3.6 Hz, 2H), 2.97 – 2.83 (m, 2H), 2.34 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 134.5, 128.6, 128.5, 128.0, 125.6(q), 68.5(q), 67.8, 60.52(q), 40.5; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -76.1; **HRMS** (MALDI) calc'd for $C_{11}H_{12}F_3NO$ $[M+H]^+$: 232.0944, found: 232.0944.

3-(4-Chlorophenyl)-3-(trifluoromethyl)morpholine (16b):



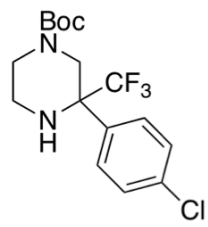
Prepared by the general procedure stated above and isolated as a colorless liquid (106.2 mg, 40% yield). **IR** (thin film) v 2926, 1493, 1154, 1097 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.5 Hz, 2H), 7.44 – 7.38 (m, 2H), 4.37 (d, *J* = 11.9 Hz, 1H), 4.02 (d, *J* = 11.9 Hz, 1H), 3.76 – 3.62 (m, 2H), 2.91 (dt, *J* = 12.8, 3.5 Hz, 1H), 2.84 (ddd, *J* = 13.0, 8.7, 4.4 Hz, 1H), 2.23 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 134.6, 133.0, 129.6, 128.8, 125.22(q), 126.6, 123.8, 68.3 (q), 67.9, 60.41(q), 40.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -76.3; **HRMS** (MALDI) calc'd for $C_{11}H_{11}ClF_3NO$ $[M+H]^+$: 266.0554, found: 266.0554.

***tert*-Butyl 3-phenyl-3-(trifluoromethyl)piperazine-1-carboxylate (16c):**



Prepared by the general procedure stated above and isolated as a colorless liquid (138.8 mg, 42% yield). **IR** (thin film) v 2975, 1694, 1428, 1151 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.8 Hz, 2H), 7.50 – 7.33 (m, 3H), 4.60 (s, 1H), 3.74 (s, 1H), 3.62 – 3.36 (m, 1H), 3.10 – 2.95 (m, 1H), 2.90 (s, 1H), 2.75 (s, 1H), 2.24 (s, 1H), 1.46 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.1, 137.6, 134.0, 128.5, 128.4, 128.4, 125.5(q), 80.3, 62.0(q), 46.5, 43.2, 40.0, 28.3; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -77.5, -77.8; **HRMS** (MALDI) calc'd for $C_{16}H_{21}F_3N_2O_2$ $[M+H]^+$: 331.1628, found: 331.1628.

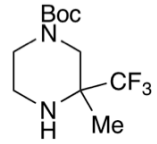
***tert*-Butyl 3-(4-chlorophenyl)-3-(trifluoromethyl)piperazine-1-carboxylate (16d):**



Prepared by the general procedure stated above and isolated as colorless liquid (138.6 mg, 38% yield). **IR** (thin film) v 2976, 1693, 1429, 1155 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.3 Hz, 2H), 7.46 – 7.33 (m, 2H), 4.66 (d, *J* = 98.7 Hz, 1H), 3.74 (s, 1H), 3.42 (s, 1H), 2.99 (ddd, *J* = 13.0, 10.9, 3.6 Hz, 1H), 2.88 (s, 1H), 2.69 (s, 1H), 2.14 (s, 1H), 1.44 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$)

δ 154.0, 134.8, 132.5, 130.1, 128.6, 125.2(q), 80.5, 62.1(q), 46.4, 45.1, 44.5, 43.5, 39.8, 28.3; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -77.3, -77.8; **HRMS** (MALDI) calc'd for $C_{16}H_{20}ClF_3N_2O_2$ $[M+H]^+$: 365.1238, found: 365.1238.

***tert*-Butyl 3-methyl-3-(trifluoromethyl)piperazine-1-carboxylate (16e):**



Prepared by the general procedure stated above (Note: ketimine formation was carried out at the range of 15–18 °C instead of 55 °C for 12 h) and isolated as colorless liquid (114.7 mg, 43% yield). **IR** (thin film) v 2932, 2102, 1697, 1428 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.70 (s, 1H), 3.52 – 3.30 (m, 3H), 3.02 (dq, *J* = 11.3, 5.2 Hz, 1H), 2.90 - 2.83 (m, 1H), 1.47 (s, 9H), 1.25 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.3, 125.7, 80.1, 55.3, 51.2, 47.9, 46.3, 44.2, 42.8, 40.2, 28.3, 19.1, 13.6, 8.75; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -77.5, -78.8; **HRMS** (MALDI) calc'd for $C_{11}H_{19}F_3N_2O_2$ $[M+H]^+$: 269.1471, found: 269.1472.

6. Miscellaneous study

6.1. Importance of ketimine

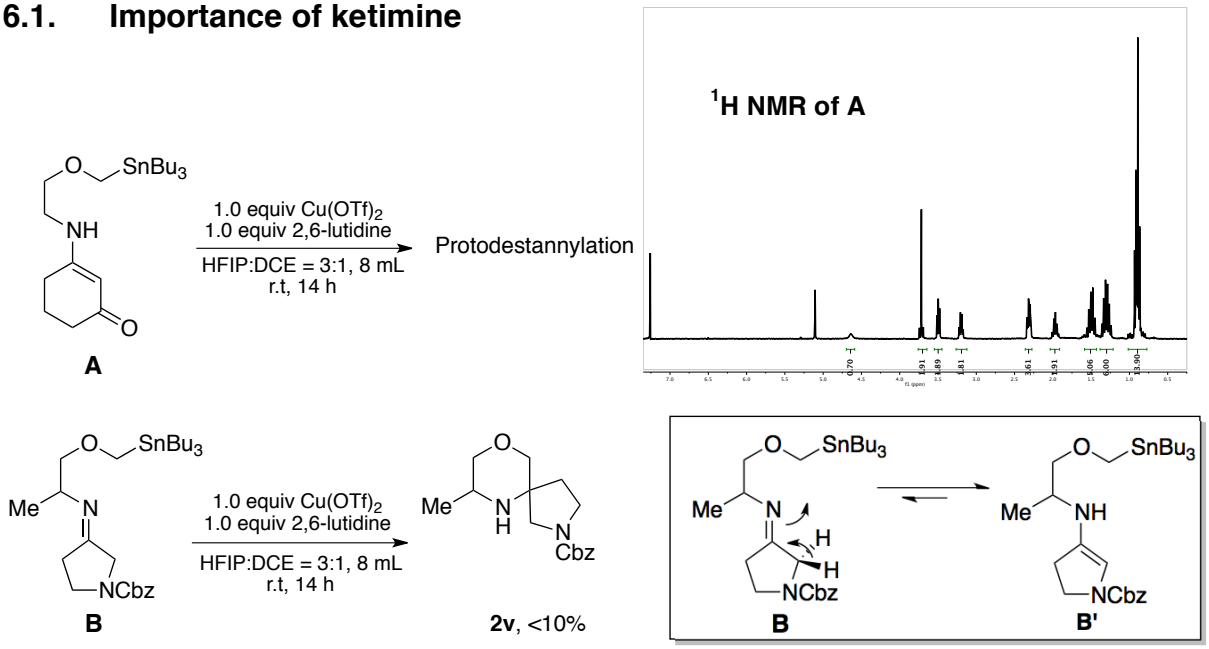


Figure S2. Investigation of enamine cyclization

The integrity of the ketimine formation is crucial for the cyclization. The enamine form of **A** (vinylagous amide) leaded to mainly protodestannylation reaction. No desired cyclization product was observed. The α-proton adjacent to *N*-Cbz group is prone to be abstracted and we attributed to the fact that low yield of spiro-compound **2v** was isolated may due to the ketimine-enamine tautomerization during the course of reaction. The enamine **B'** is detrimental to the cyclization.

7. X-ray crystallography

7.1. X-ray crystal of compound 9

Crystals of (1*r*,3*r*,5*r*,7*r*)-5'-Methylspiro[adamantane-2,3'-morpholine] (**9**) (Scheme 3) were obtained by vapor diffusion method, from of pentane/Et_2O . The X-ray data was collected to establish the relative stereochemistry.

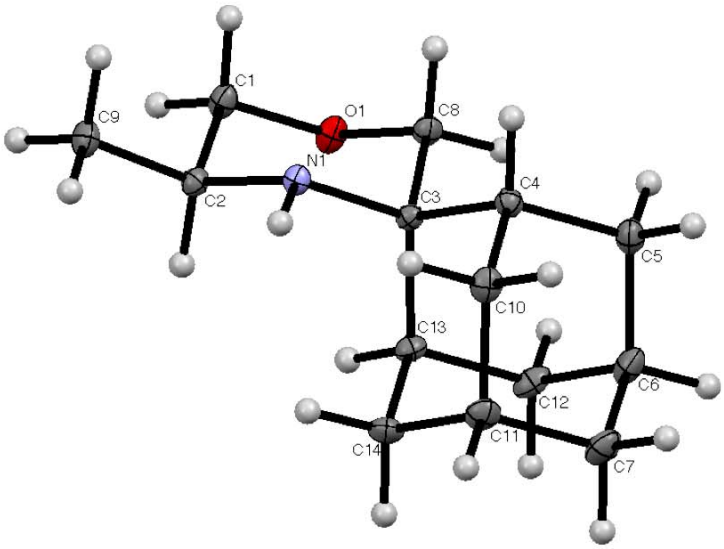


Figure S3. ORTEP diagram showing numbering scheme and the molecular conformation of **9** in crystals.

7.2. Experimental

A suitable single crystal of $C_{14}H_{23}NO$ [jb290714_0m] was selected and measured on a ETH_LOC_ApexIINonius_Mo diffractometer. The crystal was kept at 100.02 K during data collection. Using Olex2, the structure was solved with the XS [SHELX, G.M. Sheldrick, Acta Cryst. (2008). A64, 112-122] structure solution program using Direct Methods and refined with the XL [SHELXL-97 (Sheldrick, 2008)] refinement package using Least Squares minimisation.

Table S2. Crystal data and structure refinement for **9**

Identification code	jb290714_0m
Empirical formula	$C_{14}H_{23}NO$
Formula weight	221.33
Temperature/K	100.0(2)
Crystal system	monoclinic

Space group	C2/c
a/Å	13.9447(18)
b/Å	20.027(2)
c/Å	10.2082(13)
α/°	90
β/°	123.760(4)
γ/°	90
Volume/Å^3	2370.1(5)
Z	8
ρ_{calc}g/cm^3	1.241
μ/mm^{-1}	0.077
F(000)	976.0
Crystal size/mm^3	0.39 × 0.34 × 0.16
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.06 to 61.164
Index ranges	-19 ≤ h ≤ 19, -28 ≤ k ≤ 28, -12 ≤ l ≤ 14
Reflections collected	26374
Independent reflections	3625 [R_{int} = 0.0309, R_{sigma} = 0.0227]
Data/restraints/parameters	3625/1/149
Goodness-of-fit on F^2	1.056
Final R indexes [I>=2σ (I)]	R_1 = 0.0382, wR_2 = 0.1026
Final R indexes [all data]	R_1 = 0.0488, wR_2 = 0.1109
Largest diff. peak/hole / e Å^{-3}	0.43/-0.18

Table S3. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for jb290714_0m. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor

Atom	***x***	***y***	***z***	**U(eq)**
O1	891.6(5)	2405.9(3)	678.2(7)	13.43(14)
N1	3108.6(6)	2547.8(3)	3380.4(8)	9.77(15)
C1	1688.3(7)	1863.5(4)	1231.5(10)	13.19(17)
C2	2922.1(7)	2108.8(4)	2113.6(10)	10.77(16)
C3	2319.4(7)	3124.7(4)	2841.7(9)	9.11(16)
C4	2568.8(7)	3510.2(4)	4308(1)	11.09(16)
C5	1748.3(8)	4107.5(4)	3833.4(11)	14.59(18)
C6	1885.5(8)	4586.9(4)	2780.7(11)	15.49(18)
C7	3128.3(8)	4846.1(4)	3688.0(11)	17.23(19)
C8	1115.5(7)	2814.5(4)	1971.3(10)	11.80(16)
C9	3762.3(8)	1527.9(4)	2816.3(11)	14.70(18)
C10	3804.4(7)	3784.4(4)	5228.3(10)	13.37(17)
C11	3959.9(8)	4255.8(4)	4176.8(11)	14.80(18)
C12	1629.3(8)	4216.8(4)	1308.6(10)	15.02(18)
C13	2451.7(7)	3619.6(4)	1781.7(10)	11.24(16)
C14	3694.1(8)	3884.5(5)	2695.9(11)	14.31(18)

Table S4. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for jb290714_0m. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	10.1(3)	11.9(3)	12.6(3)	-2.5(2)	2.7(2)	0.1(2)
N1	8.1(3)	9.9(3)	9.1(3)	-0.5(2)	3.4(3)	0.3(2)
C1	11.6(4)	10.4(4)	14.4(4)	-1.6(3)	5.3(3)	0.3(3)
C2	11.2(4)	10.2(3)	10.2(3)	-0.1(3)	5.5(3)	0.0(3)
C3	7.7(3)	8.7(3)	9.7(3)	0.1(3)	4.0(3)	-0.5(3)
C4	11.4(4)	11.5(4)	11.0(4)	-0.8(3)	6.6(3)	-0.4(3)
C5	13.0(4)	13.5(4)	17.3(4)	-3.2(3)	8.4(3)	0.2(3)
C6	13.9(4)	9.5(4)	18.7(4)	-0.9(3)	6.3(3)	0.9(3)
C7	16.9(4)	10.8(4)	20.5(4)	-2.5(3)	8.2(4)	-3.4(3)
C8	9.8(4)	11.0(3)	13.4(4)	-1.6(3)	5.7(3)	-1.1(3)
C9	14.9(4)	12.9(4)	15.3(4)	0.3(3)	7.7(3)	3.4(3)
C10	11.2(4)	14.0(4)	11.2(4)	-3.0(3)	4.0(3)	-1.3(3)
C11	11.7(4)	13.1(4)	17.2(4)	-2.7(3)	6.5(3)	-4.2(3)
C12	15.5(4)	10.9(4)	13.3(4)	2.1(3)	4.6(3)	-0.4(3)
C13	12.3(4)	10.3(3)	10.2(4)	1.0(3)	5.6(3)	-0.9(3)
C14	14.1(4)	13.6(4)	17.6(4)	0.3(3)	10.3(3)	-3.1(3)

Table S5. Bond Lengths for jb290714_0m

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.4268(10)	C4	C10	1.5342(12)
O1	C8	1.4323(10)	C5	C6	1.5301(13)
N1	C2	1.4626(11)	C6	C7	1.5319(13)
N1	C3	1.4750(10)	C6	C12	1.5292(13)
C1	C2	1.5134(12)	C7	C11	1.5323(13)
C2	C9	1.5188(12)	C10	C11	1.5329(13)
C3	C4	1.5424(12)	C11	C14	1.5339(13)
C3	C8	1.5284(11)	C12	C13	1.5373(12)
C3	C13	1.5522(12)	C13	C14	1.5352(12)
C4	C5	1.5358(12)			

Table S6. Bond Angles for jb290714_0m

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C1	O1	C8	110.32(6)	C6	C5	C4	110.38(7)
C2	N1	C3	114.33(6)	C5	C6	C7	109.21(7)
O1	C1	C2	111.48(7)	C12	C6	C5	109.51(7)
N1	C2	C1	107.82(7)	C12	C6	C7	109.04(8)
N1	C2	C9	109.35(7)	C6	C7	C11	109.43(7)
C1	C2	C9	110.85(7)	O1	C8	C3	111.99(7)
N1	C3	C4	108.13(6)	C11	C10	C4	109.85(7)

N1	C3	C8	104.44(6)	C7	C11	C10	109.10(8)
N1	C3	C13	114.02(7)	C7	C11	C14	109.17(8)
C4	C3	C13	107.87(6)	C10	C11	C14	109.92(7)
C8	C3	C4	110.49(7)	C6	C12	C13	110.01(7)
C8	C3	C13	111.83(7)	C12	C13	C3	111.04(7)
C5	C4	C3	110.92(7)	C14	C13	C3	109.14(7)
C10	C4	C3	110.13(7)	C14	C13	C12	108.36(7)
C10	C4	C5	107.50(7)	C11	C14	C13	109.86(7)

Table S7. Torsion Angles for jb290714_0m

A	**B**	**C**	**D**	**Angle/°**	**A**	**B**	**C**	**D**	**Angle/°**
O1	C1	C2	N1	55.41(9)	C4	C10	C11	C14	-58.14(9)
O1	C1	C2	C9	175.08(7)	C5	C4	C10	C11	-61.20(9)
N1	C3	C4	C5	-178.21(7)	C5	C6	C7	C11	59.29(10)
N1	C3	C4	C10	62.91(8)	C5	C6	C12	C13	-58.67(9)
N1	C3	C8	O1	-59.04(8)	C6	C7	C11	C10	-59.89(10)
N1	C3	C13	C12	-178.30(6)	C6	C7	C11	C14	60.25(10)
N1	C3	C13	C14	-58.91(9)	C6	C12	C13	C3	59.50(9)
C1	O1	C8	C3	61.65(9)	C6	C12	C13	C14	-60.36(9)
C2	N1	C3	C4	176.32(6)	C7	C6	C12	C13	60.77(9)
C2	N1	C3	C8	58.64(8)	C7	C11	C14	C13	-60.52(9)
C2	N1	C3	C13	-63.71(9)	C8	O1	C1	C2	-58.62(9)
C3	N1	C2	C1	-58.01(9)	C8	C3	C4	C5	-64.49(9)
C3	N1	C2	C9	-178.62(7)	C8	C3	C4	C10	176.64(7)
C3	C4	C5	C6	-59.60(9)	C8	C3	C13	C12	63.50(9)
C3	C4	C10	C11	59.75(9)	C8	C3	C13	C14	-177.11(7)
C3	C13	C14	C11	-60.94(9)	C10	C4	C5	C6	60.86(9)
C4	C3	C8	O1	-175.09(6)	C10	C11	C14	C13	59.11(9)
C4	C3	C13	C12	-58.19(8)	C12	C6	C7	C11	-60.34(10)
C4	C3	C13	C14	61.20(8)	C12	C13	C14	C11	60.09(9)
C4	C5	C6	C7	-60.53(9)	C13	C3	C4	C5	58.04(9)
C4	C5	C6	C12	58.81(9)	C13	C3	C4	C10	-60.84(8)
C4	C10	C11	C7	61.54(9)	C13	C3	C8	O1	64.74(9)

7.3. X-ray crystal of compound 7p

Crystals of the HCl salt of 2-Methyl-9-phenyl-4-oxa-1-azaspiro[5.5]undecane (**7p**) were obtained by slow evaporation method, from CH_3Cl/pentane and $CHCl_3$ was cocrystallized.

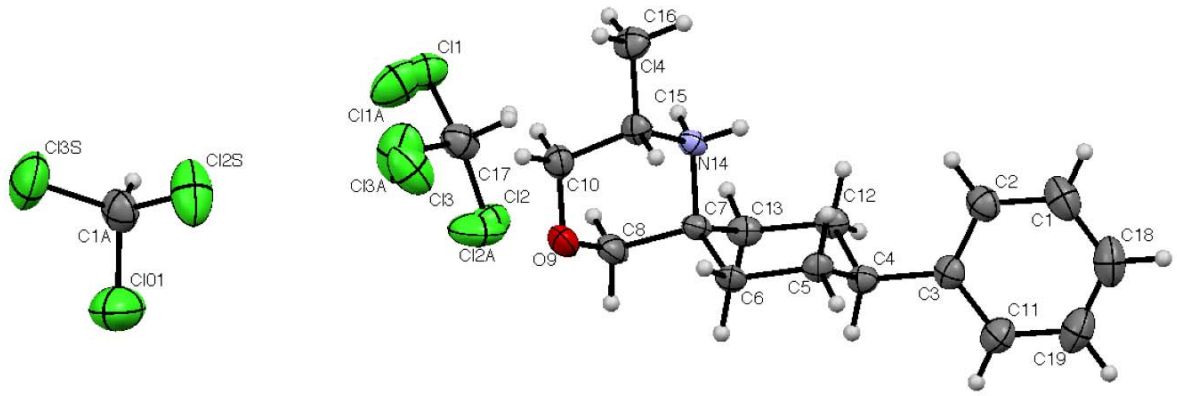


Figure S4. ORTEP diagram showing numbering scheme and the molecular conformation of **7p** in crystals.

7.4. Experimental

A suitable single crystal of $C_{18}H_{26}Cl_7NO$ [jb221014_0m] was selected and measured on a ETH_LOC_ApexIINonius_Mo diffractometer. The crystal was kept at 223.22 K during data collection. Using Olex2, the structure was solved with the XS [SHELX, G.M. Sheldrick, Acta Cryst. (2008). A64, 112-122] structure solution program using Direct Methods and refined with the XL [SHELXL-97 (Sheldrick, 2008)] refinement package using Least Squares minimisation.

Table S8. Crystal data and structure refinement for **7p**

Identification code	mo_jb221014_0m
Empirical formula	$C_{18}H_{26}Cl_7NO$
Formula weight	520.55
Temperature/K	223.2(2)
Crystal system	triclinic

Space group	P-1
a/Å	9.0230(8)
b/Å	10.7212(10)
c/Å	13.9030(13)
α/°	103.245(2)
β/°	94.106(2)
γ/°	110.337(2)
Volume/Å^3	1210.59(19)
Z	2
ρ_{calc}g/cm^3	1.428
μ/mm^{-1}	0.830
F(000)	536.0
Crystal size/mm^3	0.28 × 0.22 × 0.18
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.21 to 61.186
Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 15, -19 ≤ l ≤ 19
Reflections collected	23944
Independent reflections	7418 [R_{int} = 0.0214, R_{sigma} = 0.0227]
Data/restraints/parameters	7418/279/273
Goodness-of-fit on F^2	1.048
Final R indexes [I>=2σ (I)]	R_1 = 0.0487, wR_2 = 0.1239
Final R indexes [all data]	R_1 = 0.0649, wR_2 = 0.1347
Largest diff. peak/hole / e Å^{-3}	0.87/-0.73

Table S9. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for mo_jb221014_0m. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor

Atom	***x***	***y***	***z***	**U(eq)**
Cl01	3487.4(13)	9038.9(11)	637.3(10)	106.9(4)
Cl1	2090(4)	3460(4)	2786(5)	53.5(9)
Cl2	5220(6)	5324(5)	3788(5)	57.8(9)
Cl2S	2678.9(14)	6215.7(10)	653.6(6)	88.8(3)
Cl3	5114(10)	3285(4)	1949(4)	67(1)
Cl3S	1273.7(11)	6896.2(12)	-979.1(6)	88.3(3)
C1	10263(3)	465(2)	8572.4(17)	47.9(5)
C2	9822(2)	892(2)	7763.1(14)	38.0(4)
C3	10631(2)	2231.9(19)	7695.7(13)	31.2(3)
C4	10194.4(19)	2699.9(17)	6805.2(12)	28.4(3)
C5	10437.9(19)	1859.0(18)	5820.3(12)	28.3(3)
C6	10083.3(18)	2394.6(18)	4939.2(13)	28.4(3)
C7	8396.8(18)	2432.4(16)	4812.9(12)	26.0(3)
C8	8184(2)	3174.6(18)	4028.1(14)	34.8(4)
O9	8381.1(16)	2513.2(15)	3065.1(10)	38.7(3)
C10	7151(2)	1174(2)	2699.4(14)	35.1(4)
C11	11874(3)	3130(2)	8465.2(15)	42.1(4)
C12	8459(2)	2631.3(18)	6693.0(13)	30.7(3)

C13	8041(2)	3134.1(17)	5805.8(13)	30.1(3)
N14	7128.6(15)	979.7(13)	4418.9(10)	23.8(2)
C15	7201(2)	249.0(18)	3369.1(12)	28.8(3)
C16	5820(2)	-1141(2)	3009.3(14)	36.9(4)
C17	4094(2)	3671(2)	2961.6(18)	44.0(4)
C18	11505(3)	1373(3)	9329.0(17)	53.8(6)
C19	12306(3)	2704(3)	9274.7(17)	54.0(6)
C1A	1982(3)	7401(3)	303.2(17)	51.5(5)
Cl4	3746.1(5)	1276.7(4)	4355.1(3)	30.85(10)
Cl3A	4719(10)	3174(6)	1847(4)	80.7(13)
Cl1A	2208(7)	3645(7)	2470(8)	76.5(15)
Cl2A	5322(7)	5349(5)	3623(7)	75.6(15)

Table S10. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for mo_jb221014_0m. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
Cl01	85.3(6)	80.4(6)	130.9(9)	41.1(6)	-15.7(6)	0.6(5)
Cl1	35.1(7)	54.9(11)	67.0(18)	11.8(9)	6.2(8)	16.4(7)
Cl2	47.3(13)	55.8(16)	69.5(15)	15.4(9)	-4.4(11)	22.1(13)
Cl2S	149.1(9)	83.8(5)	55.7(4)	19.4(4)	15.6(5)	70.3(6)
Cl3	73(2)	72.2(15)	87.7(17)	43.2(12)	38.7(15)	47.1(13)
Cl3S	88.3(6)	127.1(8)	49.2(4)	25.0(4)	-0.9(3)	41.9(5)
C1	64.8(14)	48.0(11)	43.0(11)	21.4(9)	20.2(10)	27.9(10)
C2	43.6(10)	37.5(9)	34.2(9)	10.2(7)	10.9(7)	15.6(8)
C3	32.6(8)	35.4(8)	27.3(7)	6.6(6)	8.7(6)	15.5(7)
C4	26.4(7)	27.9(7)	29.3(7)	6.6(6)	6.1(6)	8.6(6)
C5	23.6(7)	33.8(8)	30.4(8)	9.6(6)	8.0(6)	13.0(6)
C6	20.5(7)	34.2(8)	30.8(8)	11.9(6)	8.1(6)	7.9(6)
C7	21.9(7)	23.3(7)	32.9(8)	10.7(6)	5.4(5)	6.5(5)
C8	32.3(8)	29.6(8)	44.5(10)	18.5(7)	5.3(7)	8.9(7)
O9	35.8(7)	44.0(7)	39.3(7)	23.7(6)	10.8(5)	9.8(6)
C10	34.9(9)	41.7(9)	31.2(8)	14.6(7)	6.5(7)	14.2(7)
C11	43.7(10)	42.1(10)	35.6(9)	6.9(8)	2.0(8)	13.5(8)
C12	29.4(8)	31.5(8)	31.6(8)	5.3(6)	10.7(6)	13.0(7)
C13	27.2(7)	25.9(7)	38.0(8)	6.0(6)	7.6(6)	12.0(6)
N14	21.0(6)	23.8(6)	29.0(6)	10.0(5)	8.0(5)	8.8(5)
C15	28.0(7)	32.7(8)	28.8(7)	9.2(6)	9.1(6)	13.6(6)
C16	37.3(9)	33.4(9)	35.4(9)	3.4(7)	5.7(7)	11.3(7)
C17	40.5(10)	40.9(10)	58.8(12)	22.4(9)	12.4(9)	18.8(8)
C18	70.2(15)	70.8(15)	35.8(10)	21.7(10)	12.4(10)	39.7(13)
C19	57.2(13)	67.5(15)	34.5(10)	8.1(10)	-3.2(9)	25.7(12)
C1A	54.8(13)	63.6(14)	41.5(11)	19.1(10)	17.5(9)	23.8(11)
Cl4	26.38(18)	30.10(19)	40.1(2)	15.79(16)	8.58(15)	10.79(15)
Cl3A	76(2)	125(3)	62.1(14)	22.9(13)	28.5(14)	61.7(17)
Cl1A	49.2(12)	83.3(18)	92(3)	7.5(19)	-7.4(16)	33.5(12)
Cl2A	56.7(14)	42.7(13)	108(3)	14.9(14)	8.4(15)	-0.3(11)

Table S11. Bond Lengths for mo_jb221014_0m

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cl01	C1A	1.738(3)	C7	C8	1.528(2)
Cl1	C17	1.734(4)	C7	C13	1.527(2)
Cl2	C17	1.772(5)	C7	N14	1.522(2)
Cl2S	C1A	1.745(3)	C8	O9	1.419(2)
Cl3	C17	1.785(5)	O9	C10	1.424(2)
Cl3S	C1A	1.742(2)	C10	C15	1.517(2)
C1	C2	1.390(3)	C11	C19	1.387(3)
C1	C18	1.383(4)	C12	C13	1.528(2)
C2	C3	1.395(3)	N14	C15	1.508(2)
C3	C4	1.514(2)	C15	C16	1.518(2)
C3	C11	1.391(3)	C17	Cl3A	1.720(5)
C4	C5	1.533(2)	C17	Cl1A	1.777(4)
C4	C12	1.537(2)	C17	Cl2A	1.737(5)
C5	C6	1.525(2)	C18	C19	1.380(4)
C6	C7	1.535(2)			

Table S12. Bond Angles for mo_jb221014_0m

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C18	C1	C2	120.2(2)	C19	C11	C3	120.9(2)
C1	C2	C3	120.7(2)	C13	C12	C4	112.10(13)
C2	C3	C4	121.34(16)	C7	C13	C12	114.47(13)
C11	C3	C2	118.22(18)	C15	N14	C7	113.97(12)
C11	C3	C4	120.44(17)	C10	C15	C16	111.36(15)
C3	C4	C5	112.21(14)	N14	C15	C10	108.03(14)
C3	C4	C12	112.49(14)	N14	C15	C16	110.30(13)
C5	C4	C12	108.70(13)	Cl1	C17	Cl2	109.0(2)
C6	C5	C4	111.58(14)	Cl3A	C17	Cl1	111.9(2)
C5	C6	C7	113.42(13)	Cl3A	C17	Cl2	119.0(4)
C8	C7	C6	111.53(13)	Cl1A	C17	Cl3	108.9(3)
C13	C7	C6	111.10(13)	Cl2A	C17	Cl3	103.4(5)
C13	C7	C8	109.44(14)	Cl2A	C17	Cl1A	109.6(3)
N14	C7	C6	110.95(13)	C19	C18	C1	119.6(2)
N14	C7	C8	104.85(13)	C18	C19	C11	120.3(2)
N14	C7	C13	108.76(12)	Cl01	C1A	Cl2S	110.53(14)
O9	C8	C7	112.45(14)	Cl01	C1A	Cl3S	109.93(13)
C8	O9	C10	110.06(13)	Cl3S	C1A	Cl2S	111.27(15)
O9	C10	C15	111.92(14)				

Table S13. Torsion Angles for mo_jb221014_0m

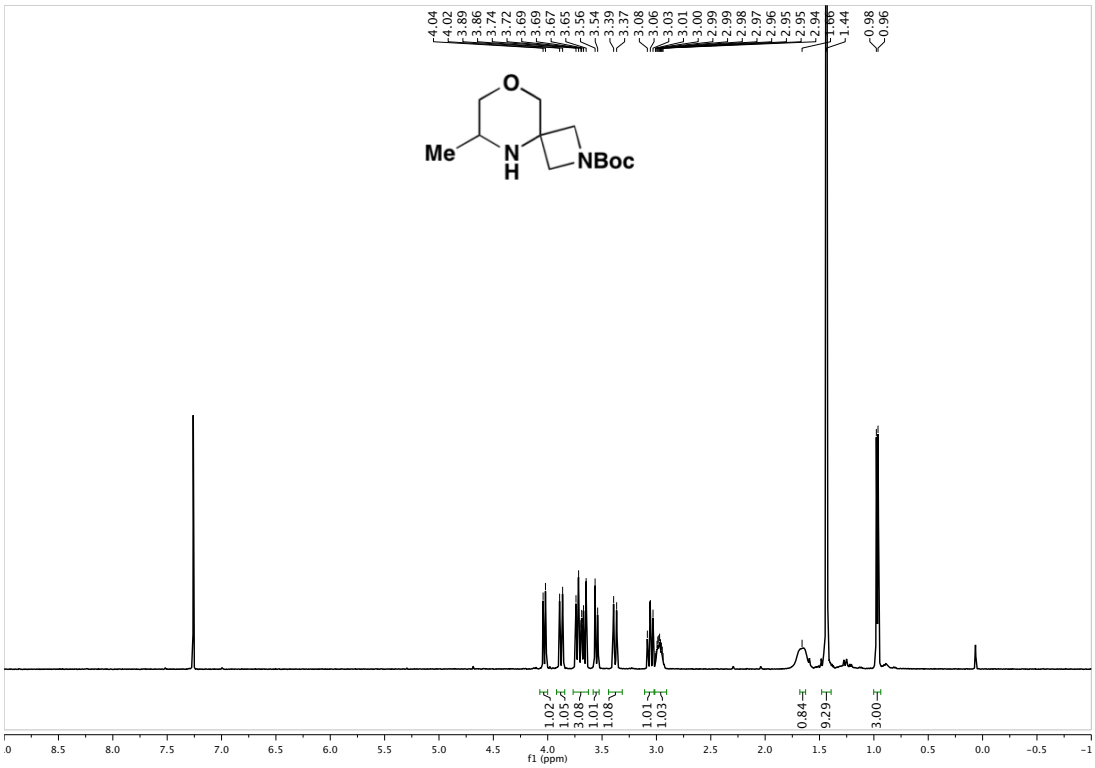
A	B	C	D	Angle/°	A	B	C	D	Angle/°

C1	C2	C3	C4	178.29(18)	C6	C7	C13	C12	-47.45(18))
C1	C2	C3	C11	-0.8(3)	C6	C7	N14	C15	-66.02(16))
C1	C18	C19	C11	-0.2(4)	C7	C8	O9	C10	64.68(18))
C2	C1	C18	C19	-0.1(4)	C7	N14	C15	C10	-53.63(17))
C2	C3	C4	C5	-61.6(2)	C7	N14	C15	C16	-175.56(13)
C2	C3	C4	C12	61.3(2)	C8	C7	C13	C12	-171.04(14))
C2	C3	C11	C19	0.4(3)	C8	C7	N14	C15	54.52(16))
C3	C4	C5	C6	-176.80(13)	C8	O9	C10	C15	-61.38(19))
C3	C4	C12	C13	178.79(14)	O9	C10	C15	N14	54.97(18))
C3	C11	C19	C18	0.1(4)	O9	C10	C15	C16	176.24(15))
C4	C3	C11	C19	-178.7(2)	C11	C3	C4	C5	117.43(19))
C4	C5	C6	C7	-55.95(19)	C11	C3	C4	C12	-119.62(19))
C4	C12	C13	C7	52.63(19)	C12	C4	C5	C6	58.14(17))
C5	C4	C12	C13	-56.32(18)	C13	C7	C8	O9	-175.64(13))
C5	C6	C7	C8	171.37(14)	C13	C7	N14	C15	171.50(13))
C5	C6	C7	C13	48.98(18)	N14	C7	C8	O9	-59.12(17))
C5	C6	C7	N14	-72.14(17)	N14	C7	C13	C12	74.95(17))
C6	C7	C8	O9	61.03(18)	C18	C1	C2	C3	0.7(3))

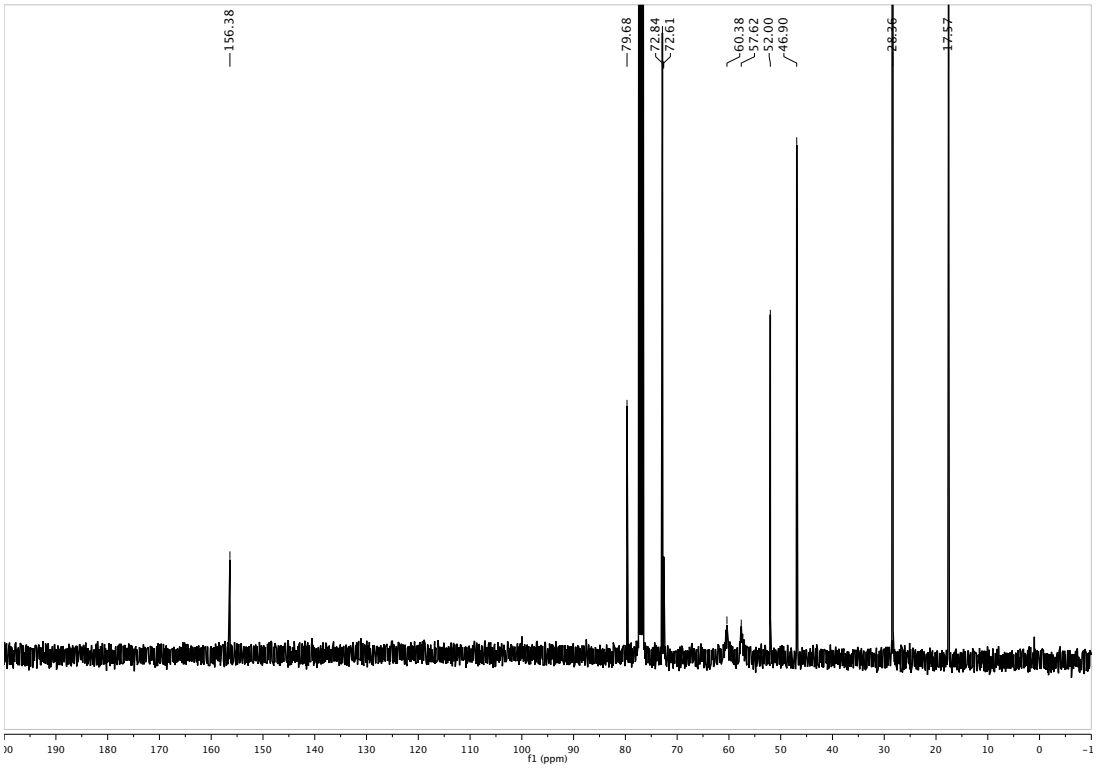
8. Spectroscopic data

tert-Butyl 6-methyl-8-oxa-2,5-diazaspiro[3.5]nonane-2-carboxylate (7a):

^{1}H NMR (400 MHz, $CDCl_3$)

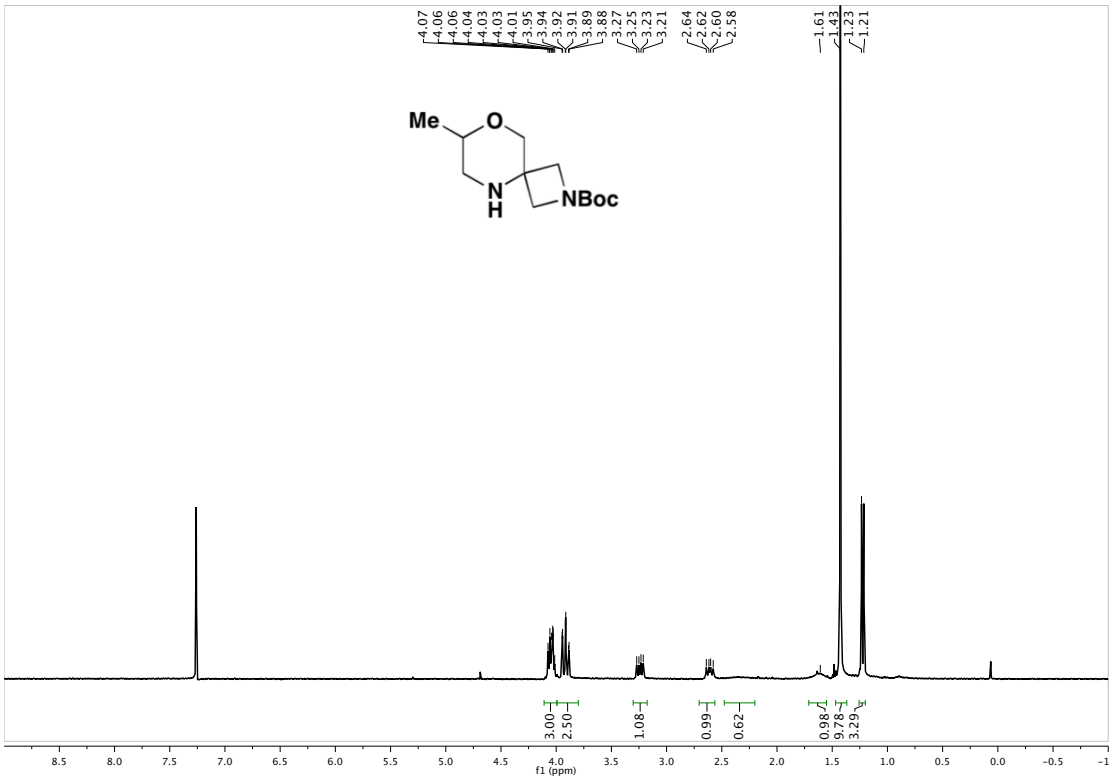


^{13}C NMR (100 MHz, $CDCl_3$)

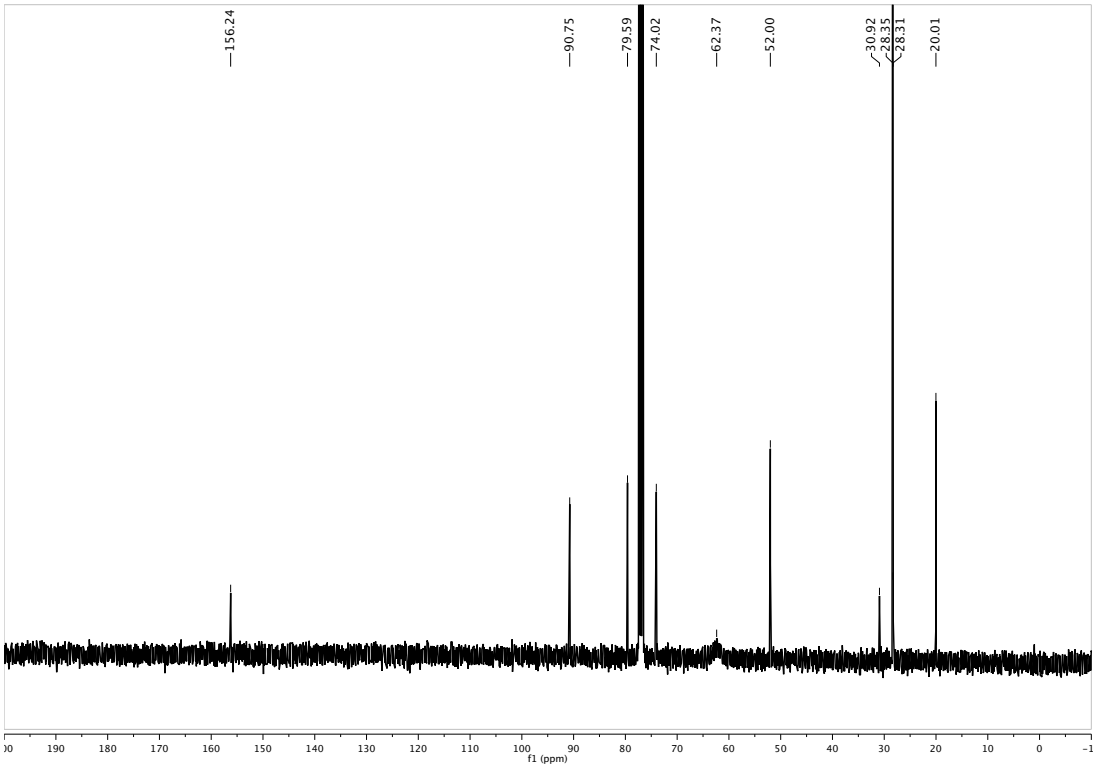


***tert*-Butyl 7-methyl-8-oxa-2,5-diazaspiro[3.5]nonane-2-carboxylate (7b):**

^{1}H NMR (400 MHz, $CDCl_3$)

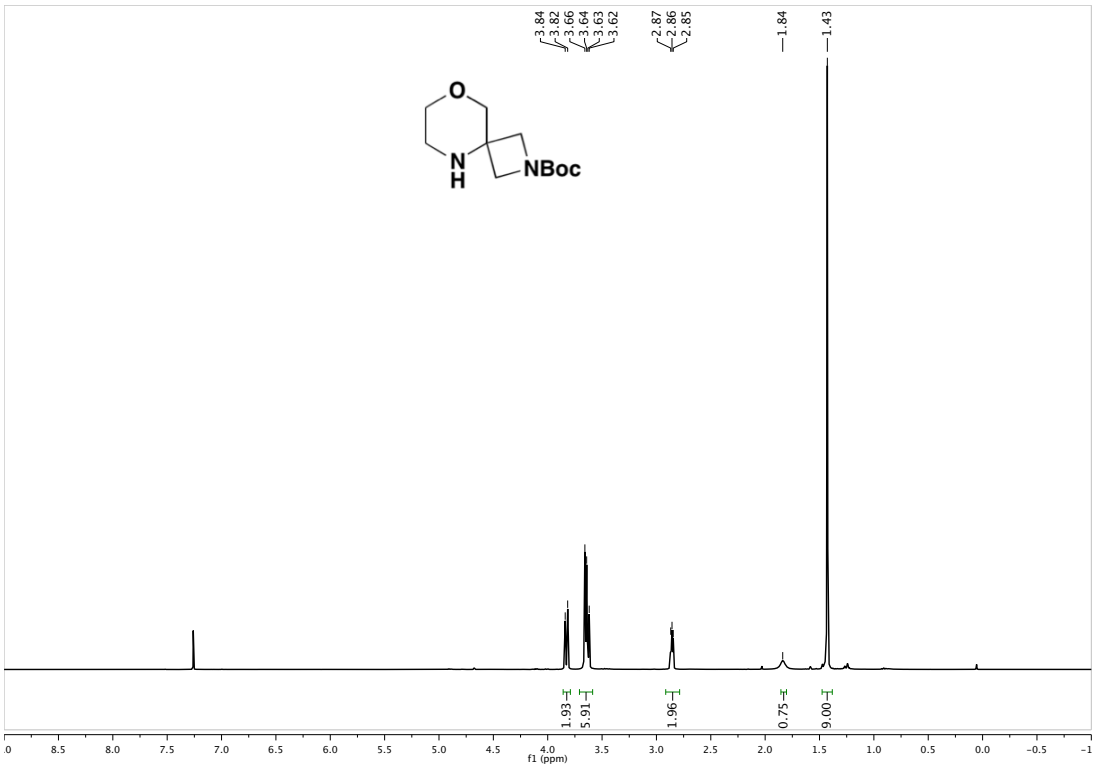


^{13}C NMR (100 MHz, $CDCl_3$)

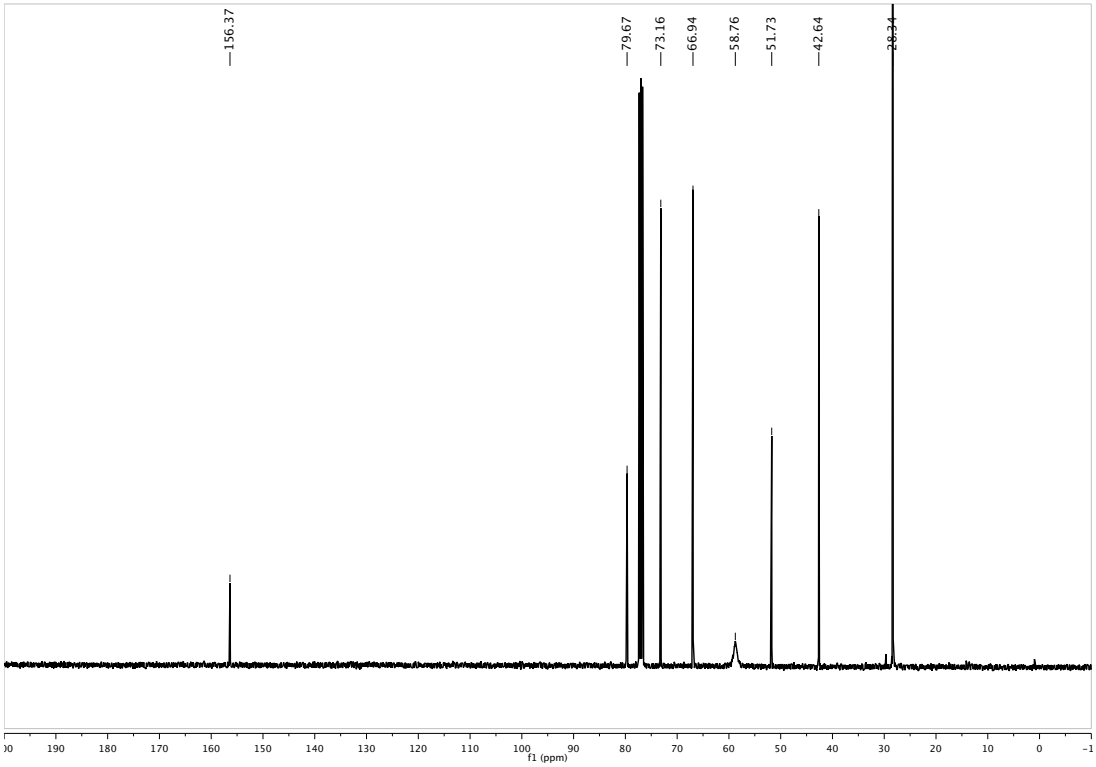


***tert*-Butyl 8-oxa-2,5-diazaspiro[3.5]nonane-2-carboxylate (7c):**

^{1}H NMR (400 MHz, $CDCl_3$

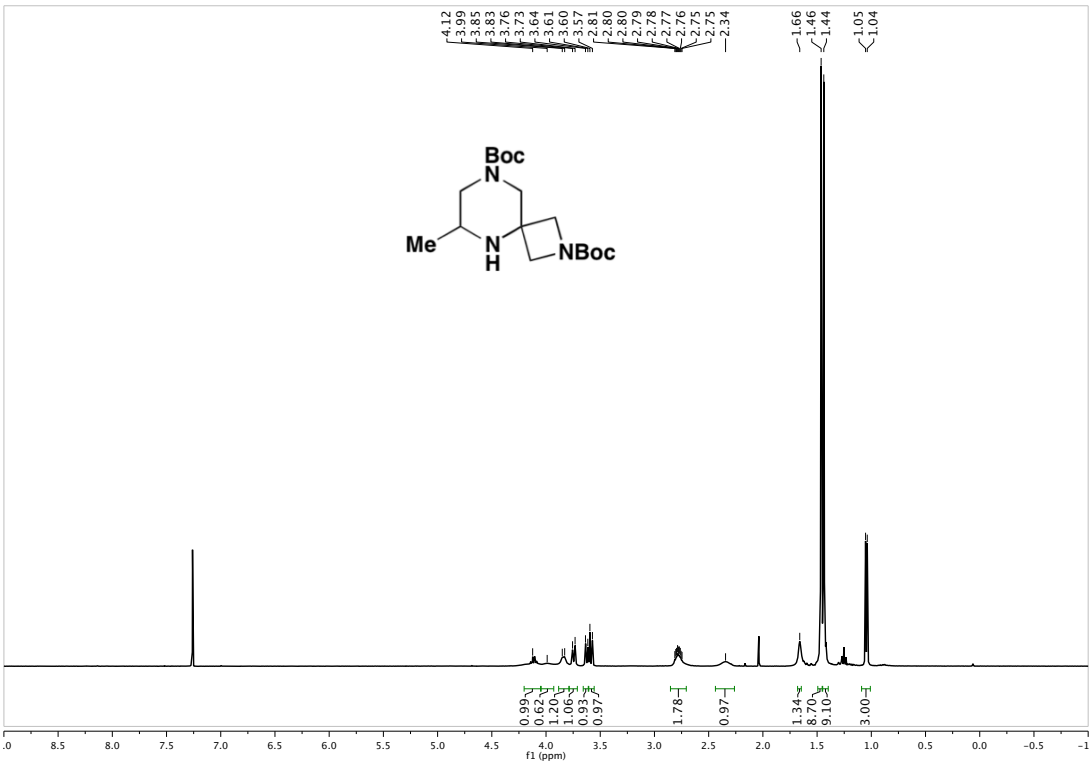


^{13}C NMR (100 MHz, $CDCl_3$)

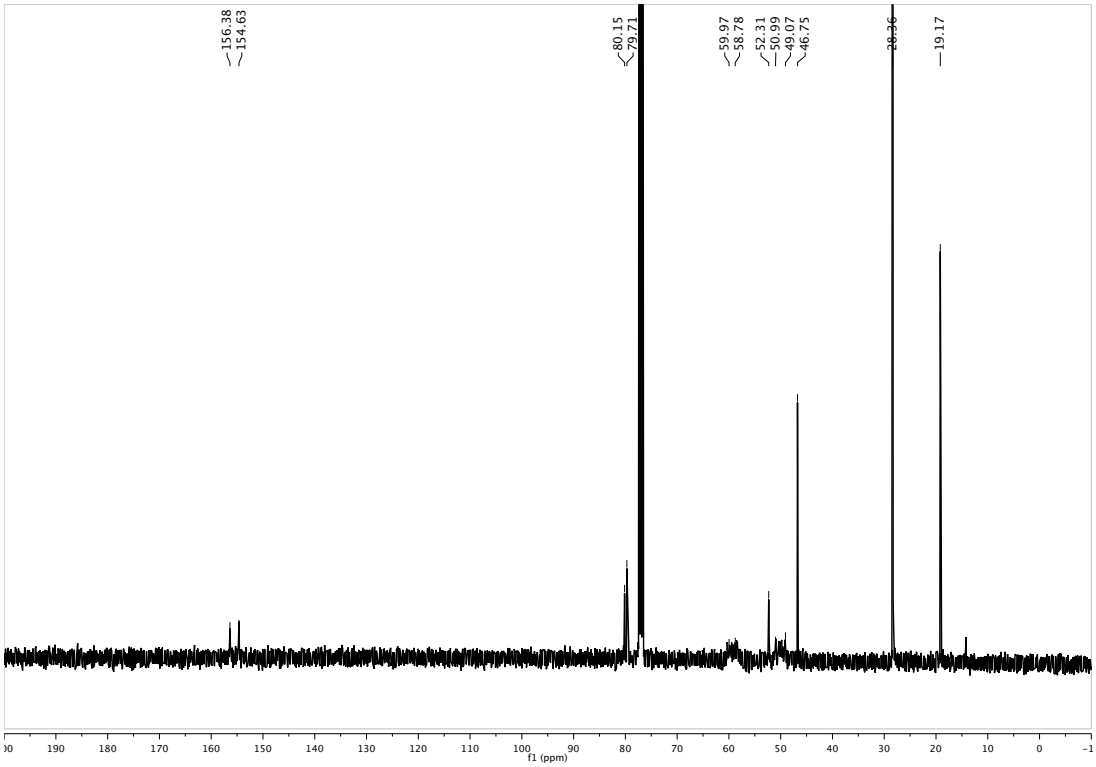


di-*tert*-Butyl 6-methyl-2,5,8-triazaspiro[3.5]nonane-2,8-dicarboxylate (7d):

^{1}H NMR (400 MHz, $CDCl_3$)

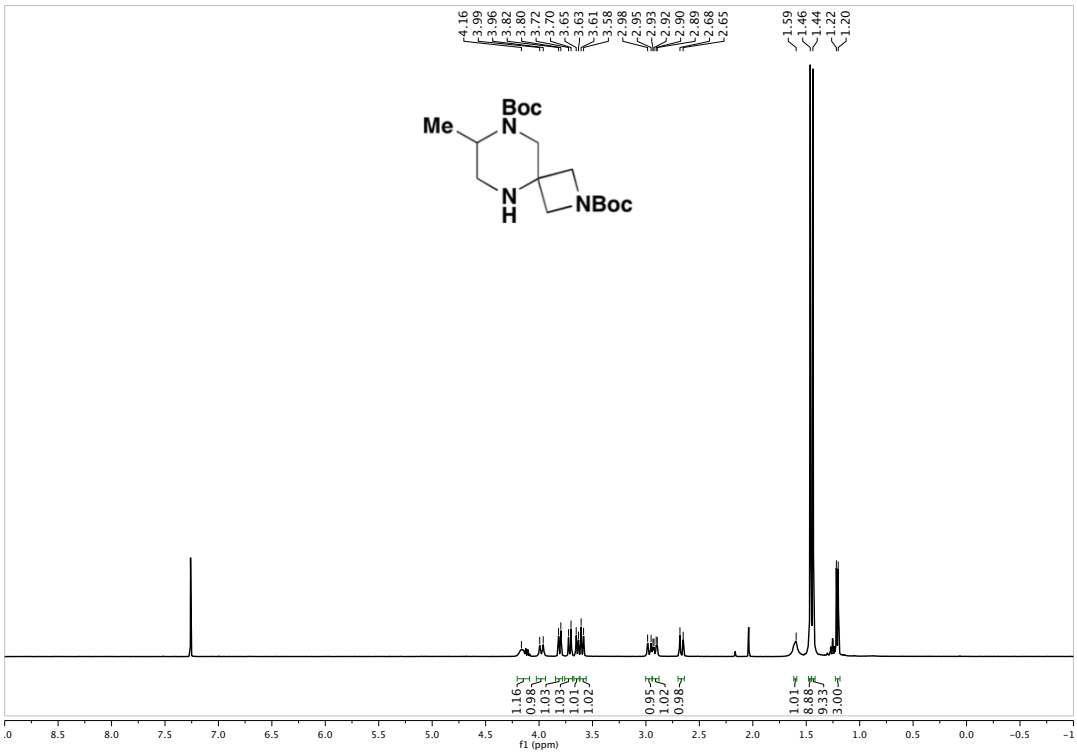


^{13}C NMR (100 MHz, $CDCl_3$)

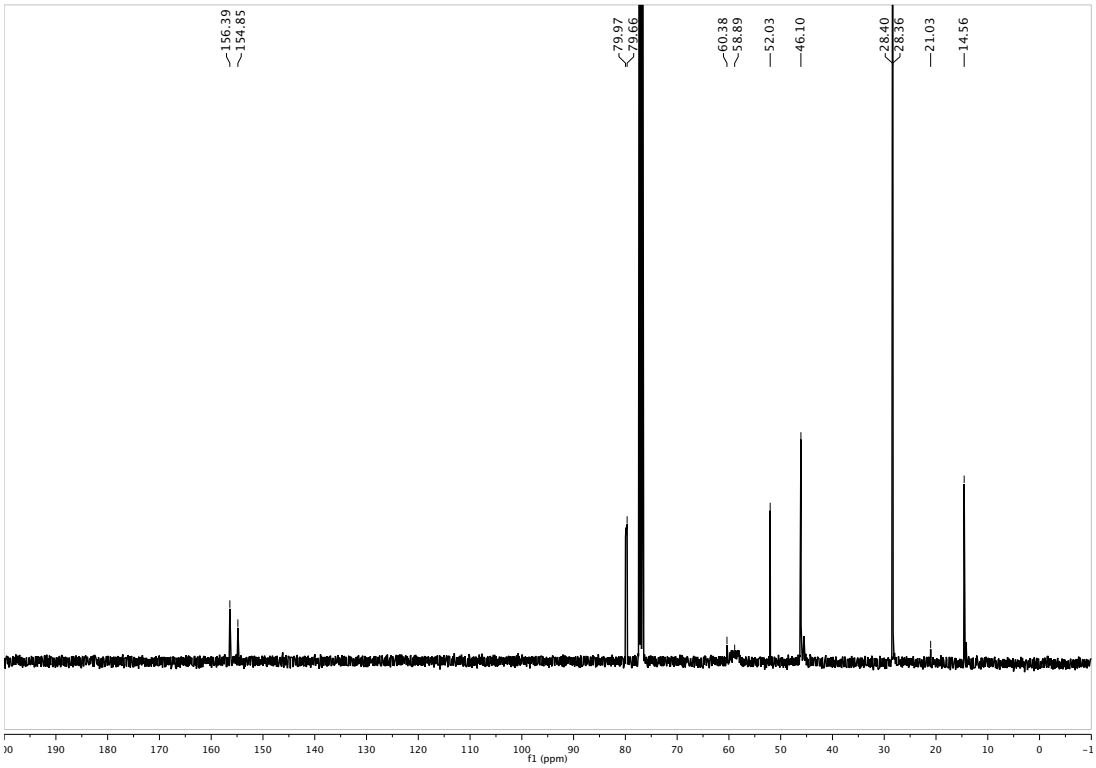


di-*tert*-Butyl 7-methyl-2,5,8-triazaspiro[3.5]nonane-2,8-dicarboxylate (7e):

^{1}H NMR (400 MHz, $CDCl_3$)

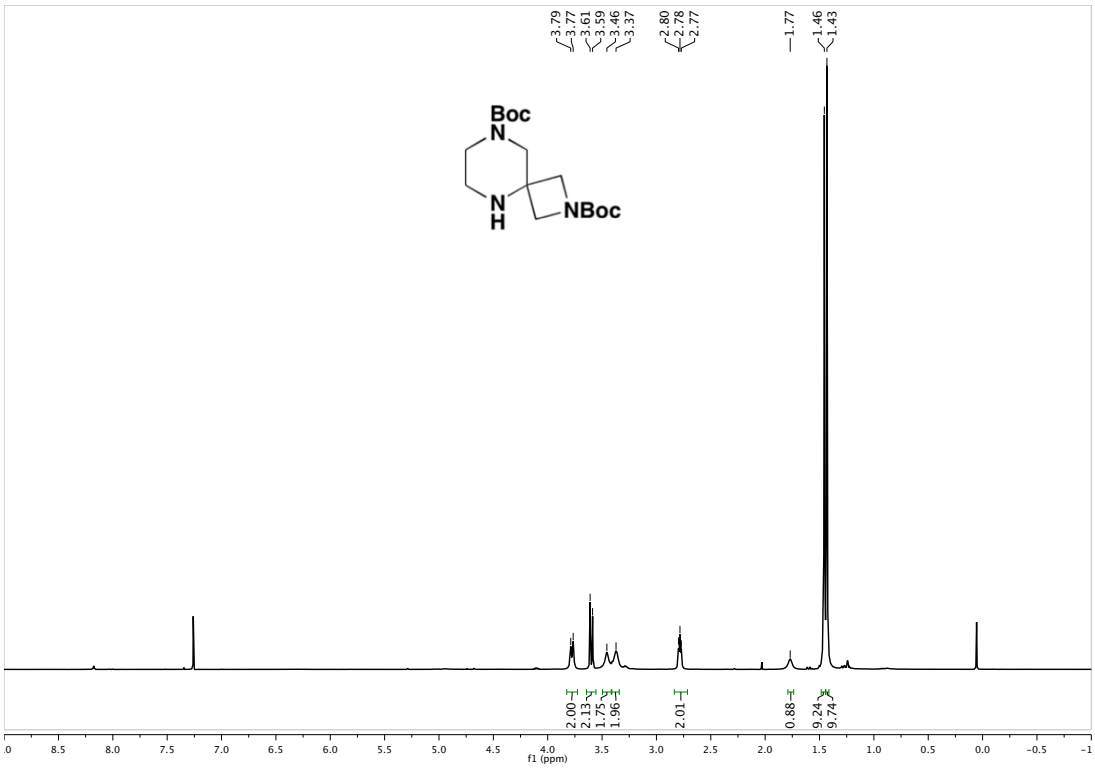


^{13}C NMR (100 MHz, $CDCl_3$)

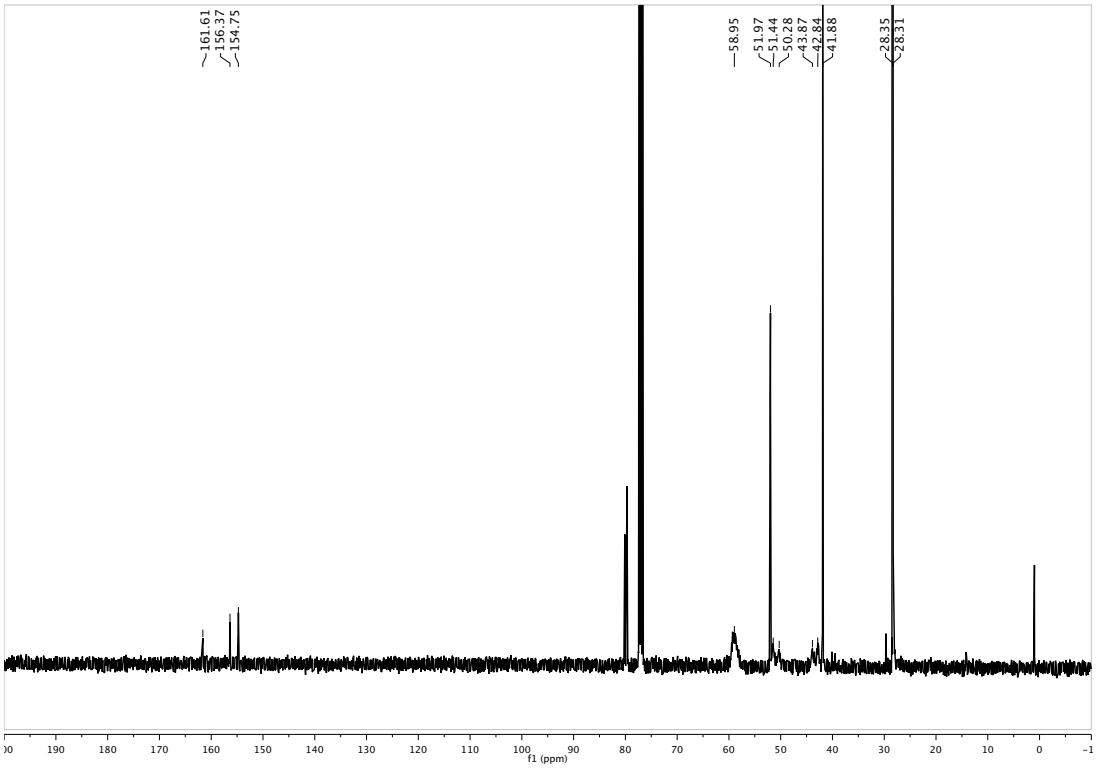


di-*tert*-Butyl 2,5,8-triazaspiro[3.5]nonane-2,8-dicarboxylate (7f):

^{1}H NMR (400 MHz, $CDCl_3$)

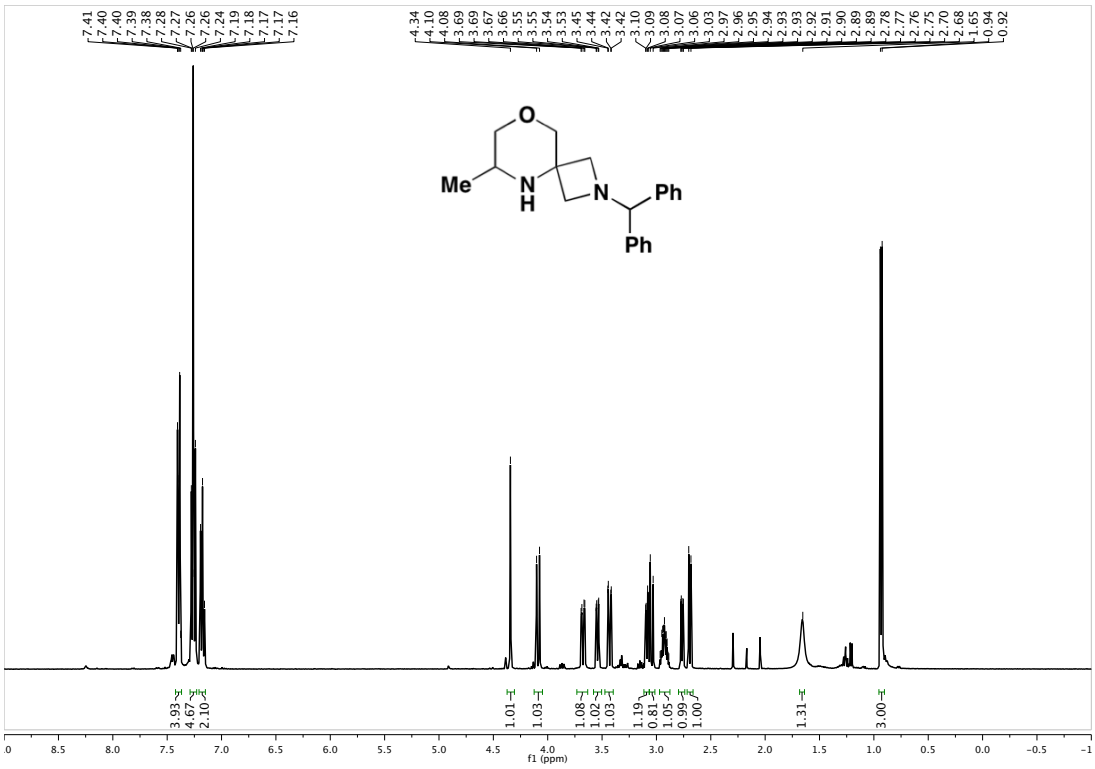


^{13}C NMR (100 MHz, $CDCl_3$)

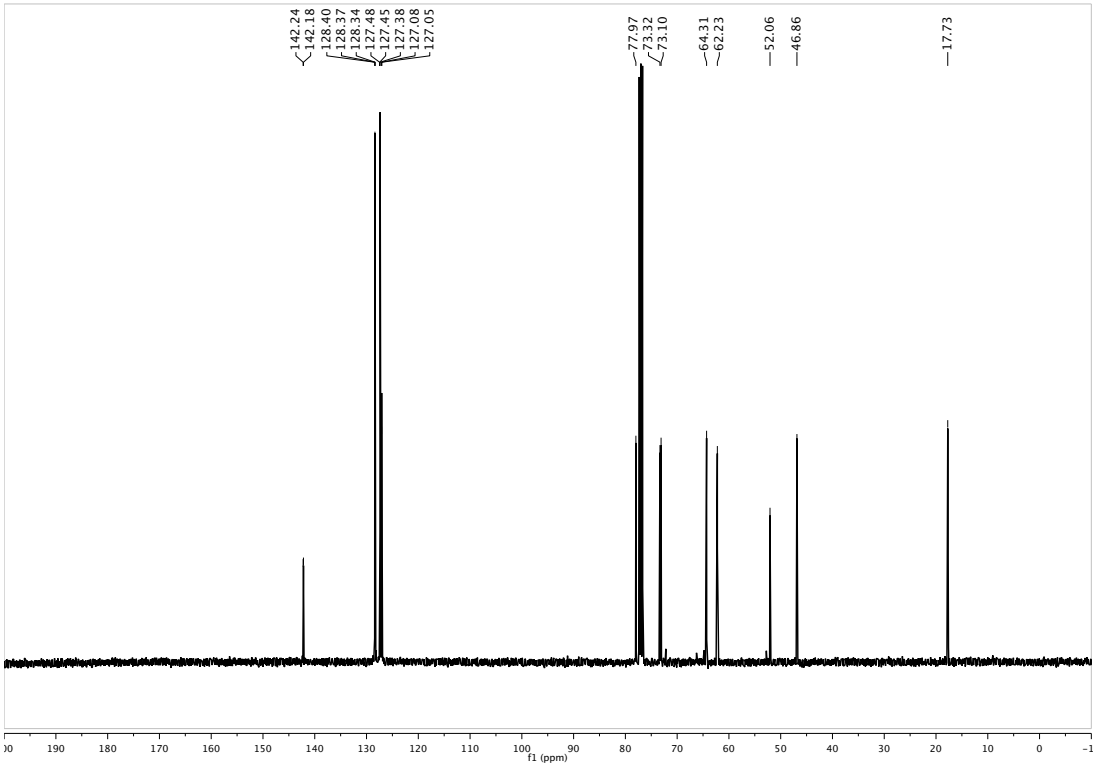


2-Benzhydryl-6-methyl-8-oxa-2,5-diazaspiro[3.5]nonane (7g):

^{1}H NMR (400 MHz, $CDCl_3$)

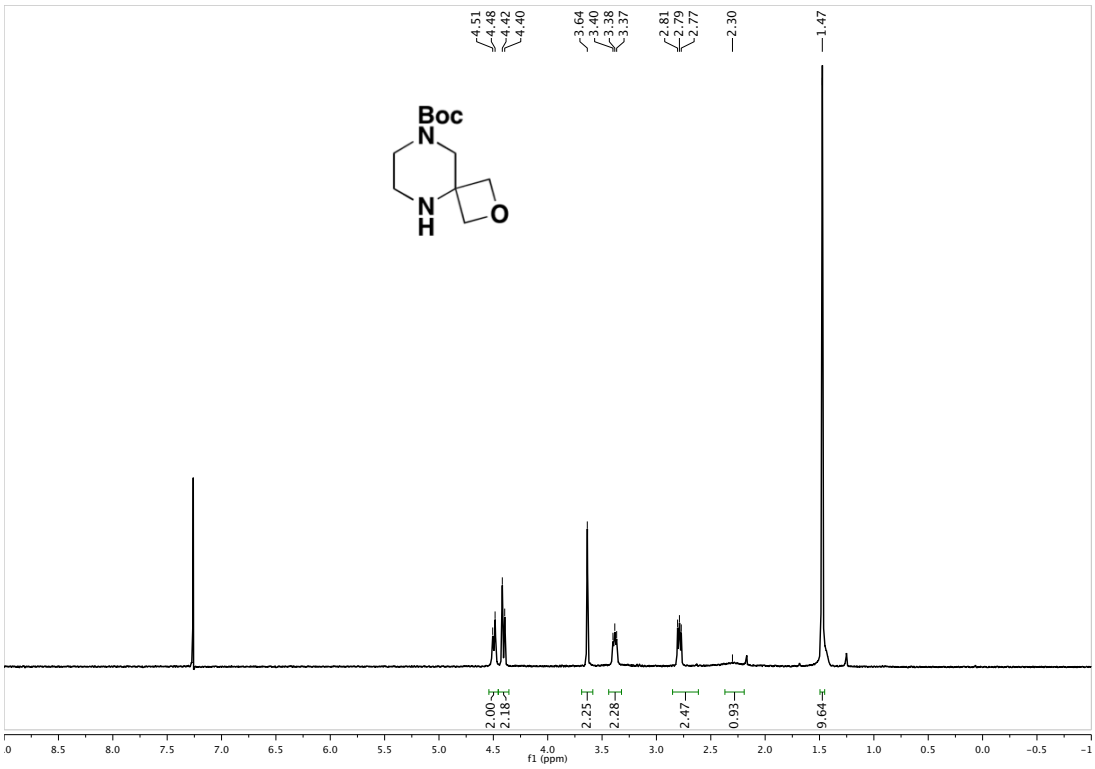


^{13}C NMR (100 MHz, $CDCl_3$)

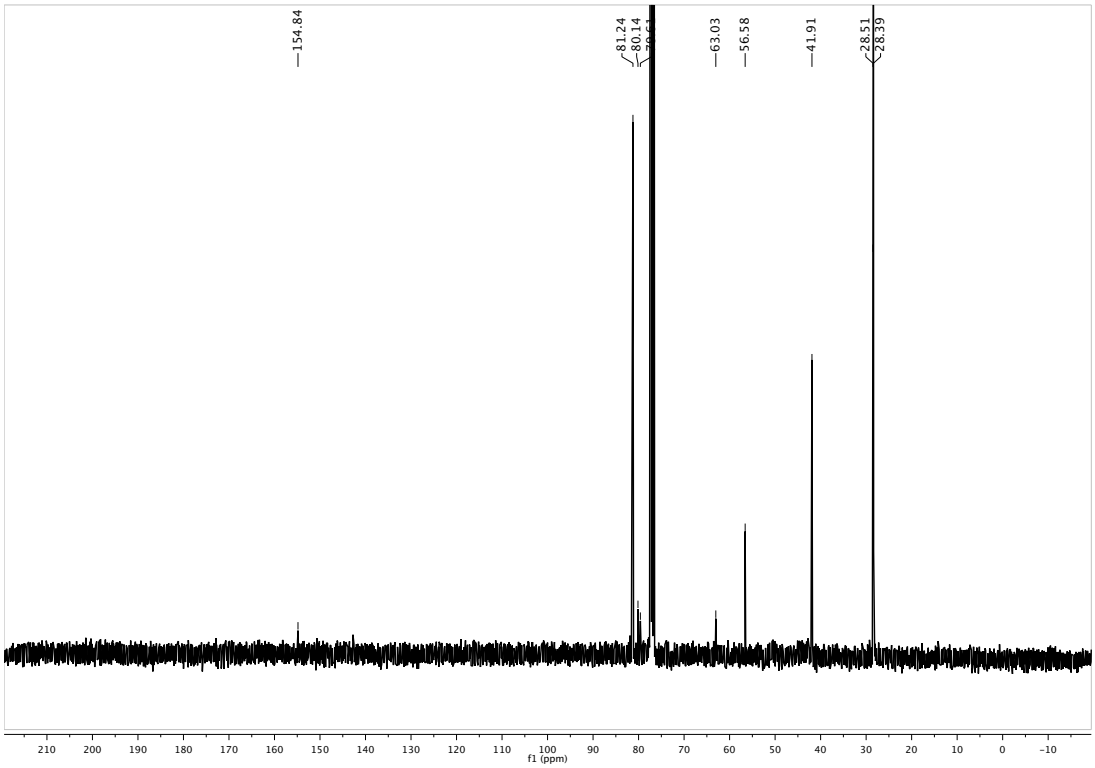


***tert*-Butyl 2-oxa-5,8-diazaspiro[3.5]nonane-8-carboxylate (7h):**

^{1}H NMR (400 MHz, $CDCl_3$)

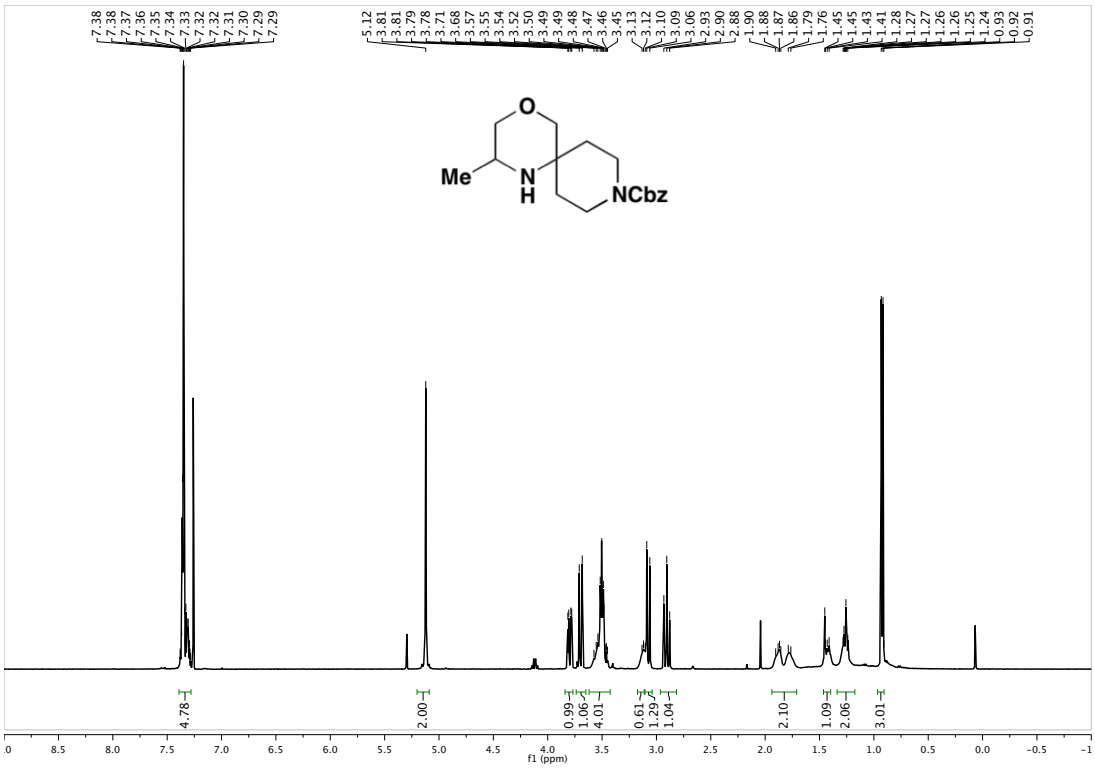


^{13}C NMR (100 MHz, $CDCl_3$)

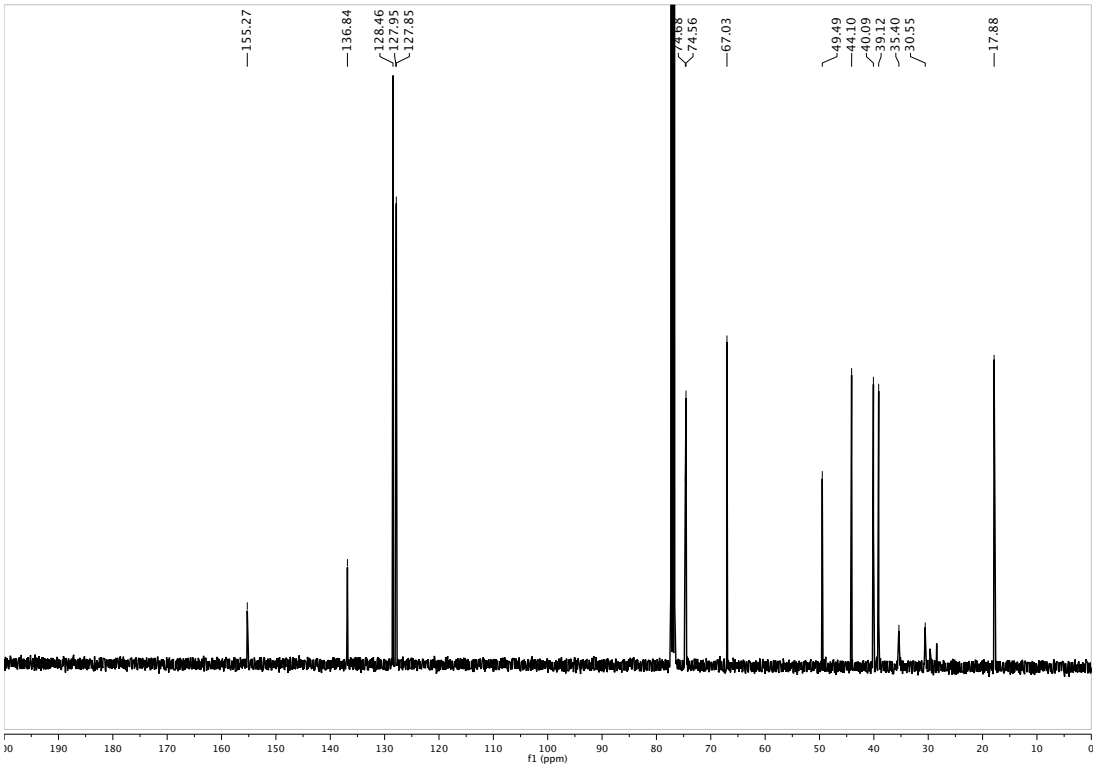


Benzyl 2-methyl-4-oxa-1,9-diazaspiro[5.5]undecane-9-carboxylate (7i):

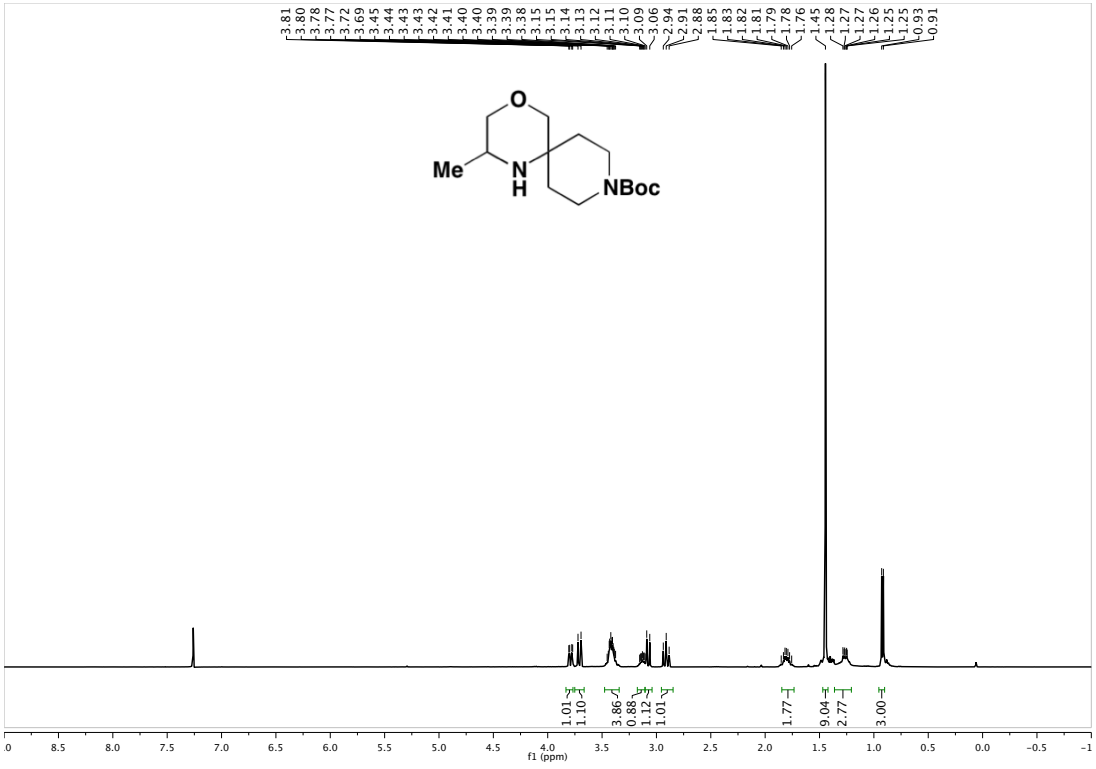
^{1}H NMR (400 MHz, $CDCl_3$)



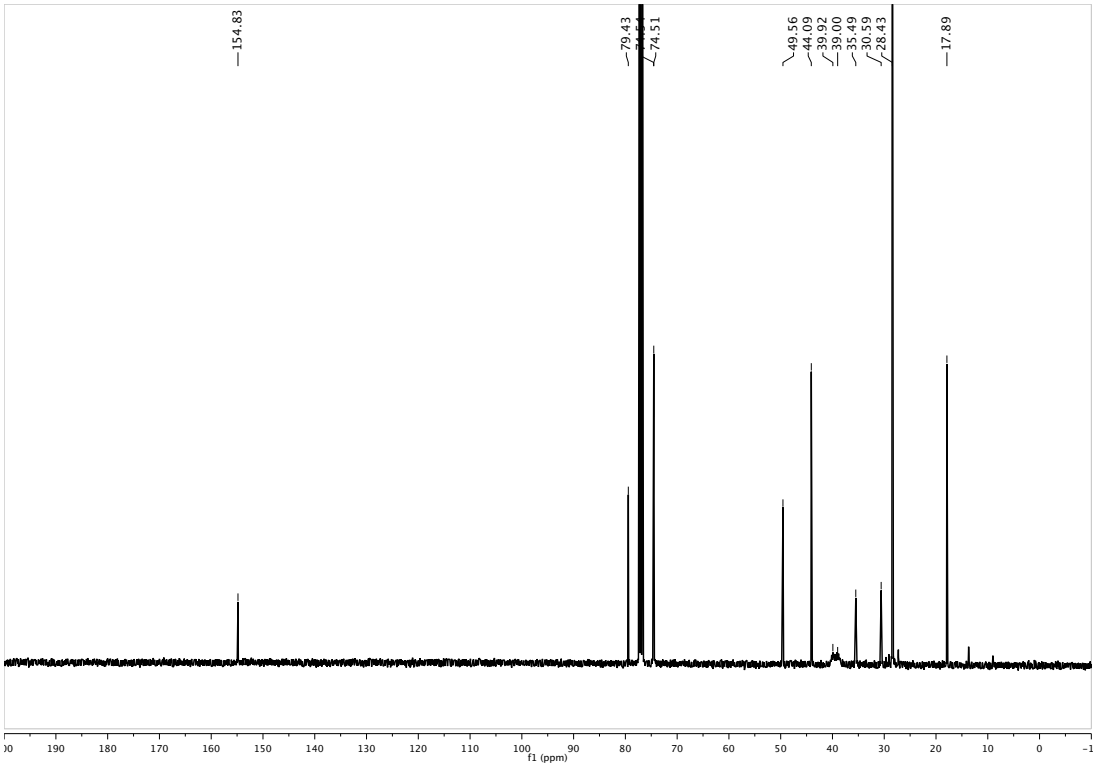
^{13}C NMR (100 MHz, $CDCl_3$)



tert-Butyl 2-methyl-4-oxa-1,9-diazaspiro[5.5]undecane-9-carboxylate (7j):
^{1}H NMR (400 MHz, $CDCl_3$)

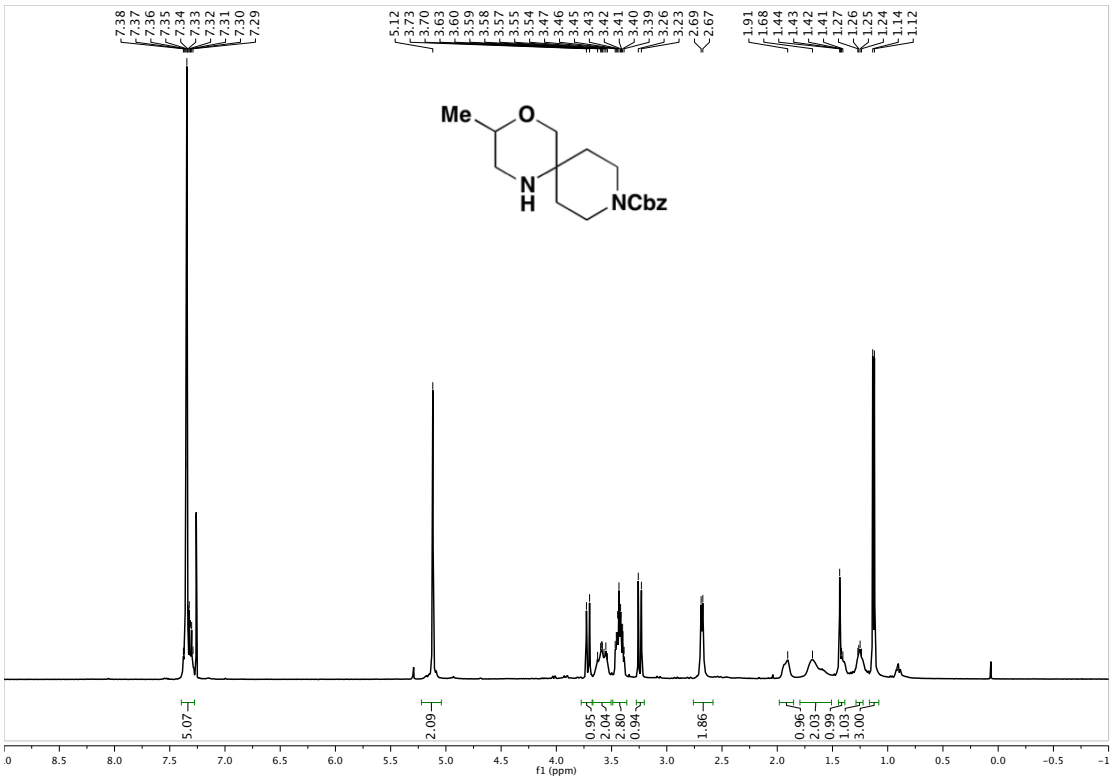


^{13}C NMR (100 MHz, $CDCl_3$)

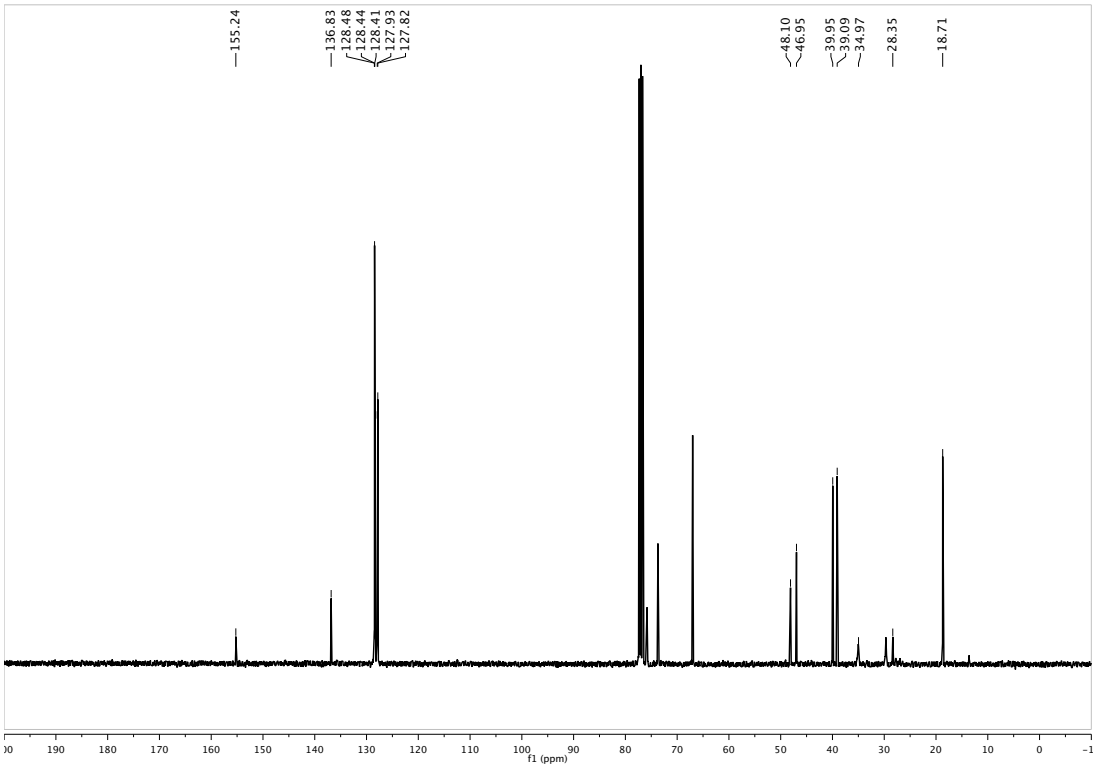


Benzyl 3-methyl-4-oxa-1,9-diazaspiro[5.5]undecane-9-carboxylate (7k):

^{1}H NMR (400 MHz, $CDCl_3$)

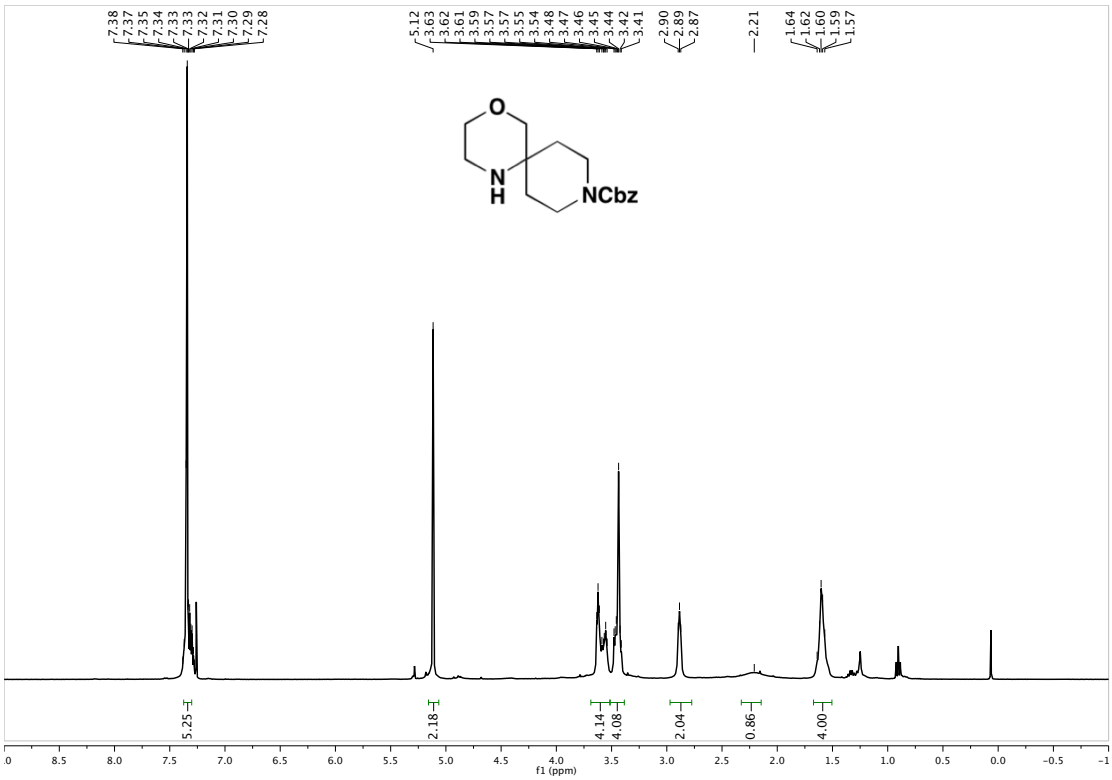


^{13}C NMR (100 MHz, $CDCl_3$)

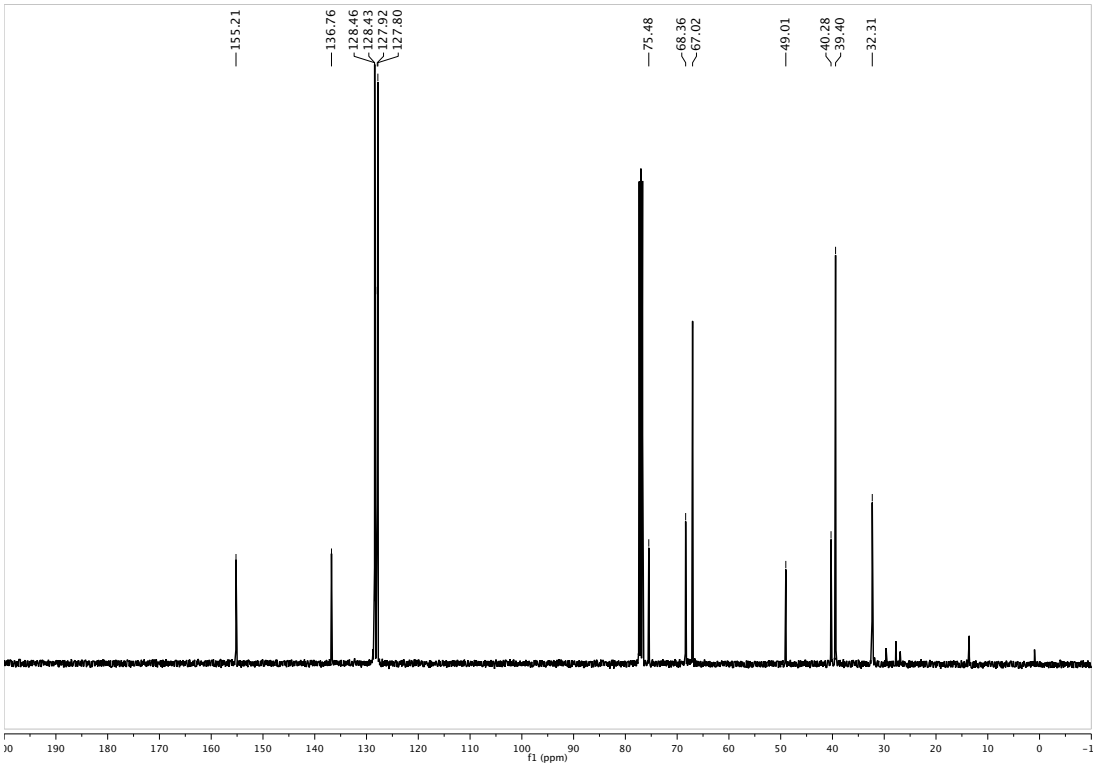


Benzyl 4-oxa-1,9-diazaspiro[5.5]undecane-9-carboxylate (7l):

^{1}H NMR (400 MHz, $CDCl_3$)

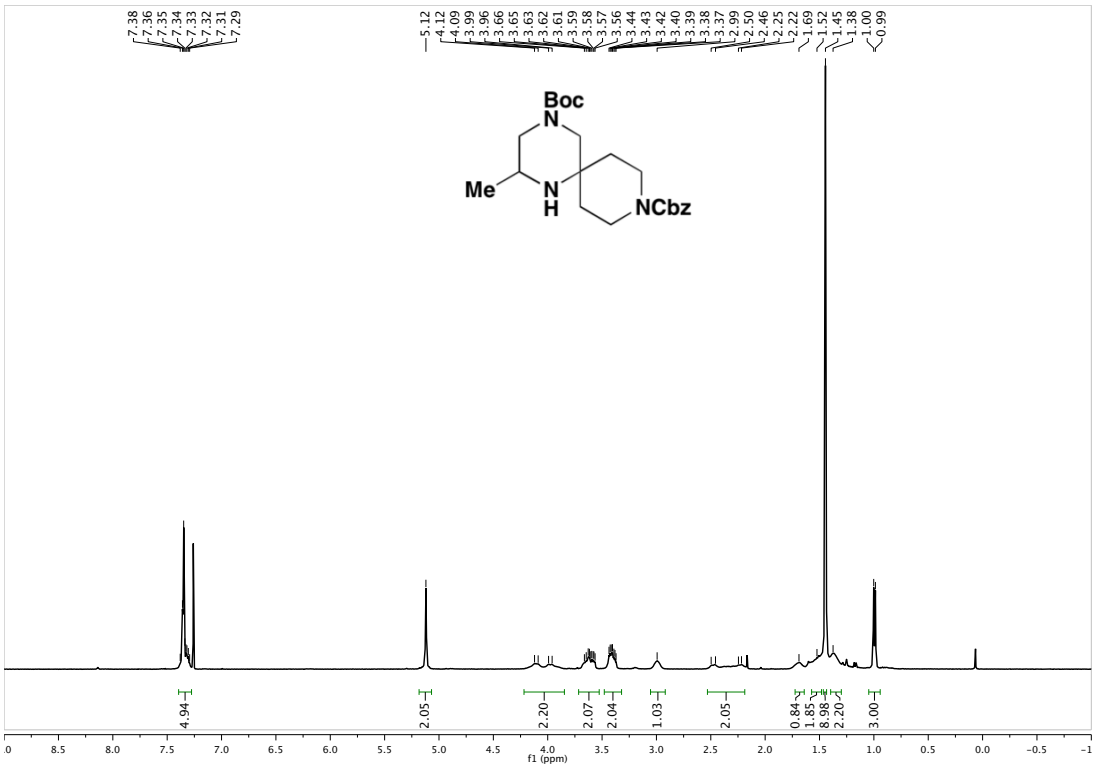


^{13}C NMR (100 MHz, $CDCl_3$)

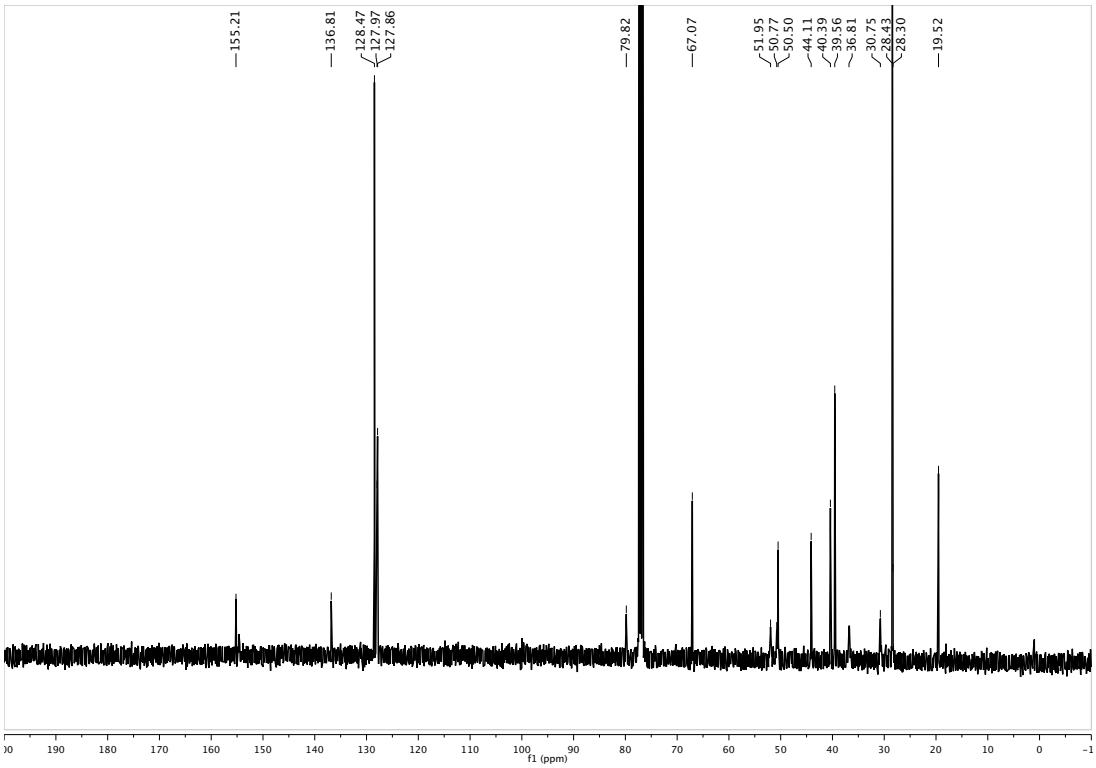


9-Benzyl 4-*tert*-butyl 2-methyl-1,4,9-triazaspiro[5.5]undecane-4,9-dicarboxylate (7m):

^{1}H NMR (400 MHz, $CDCl_3$)

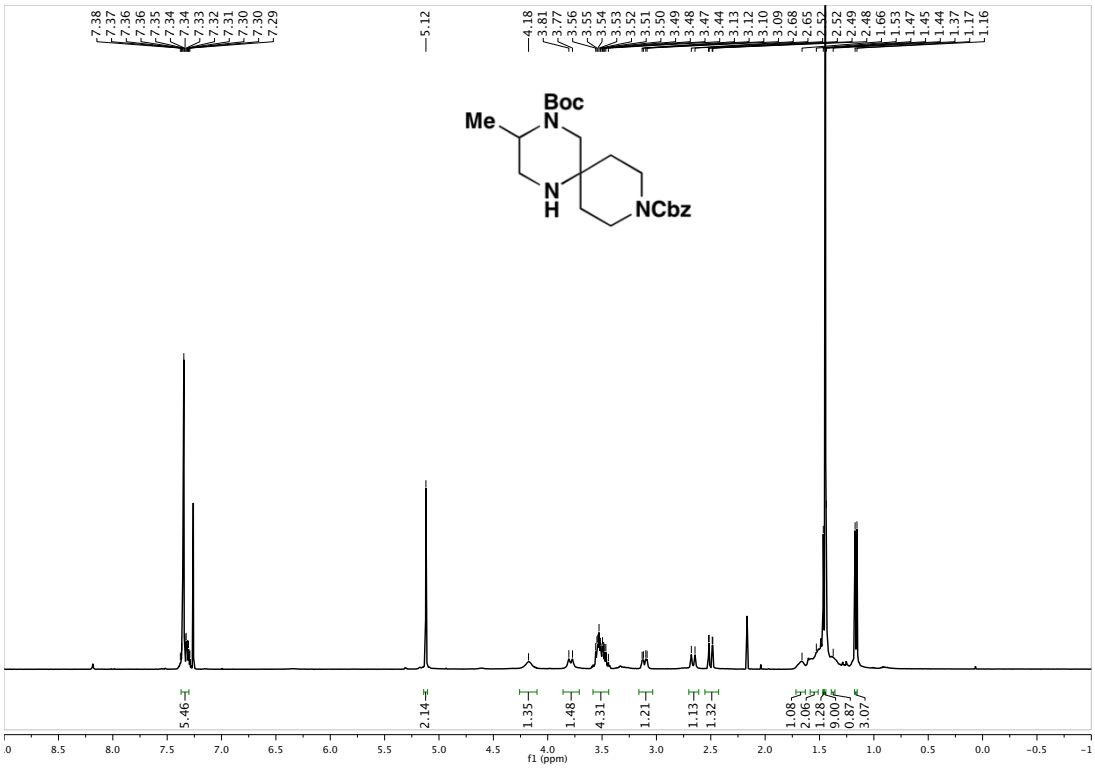


^{13}C NMR (100 MHz, $CDCl_3$)

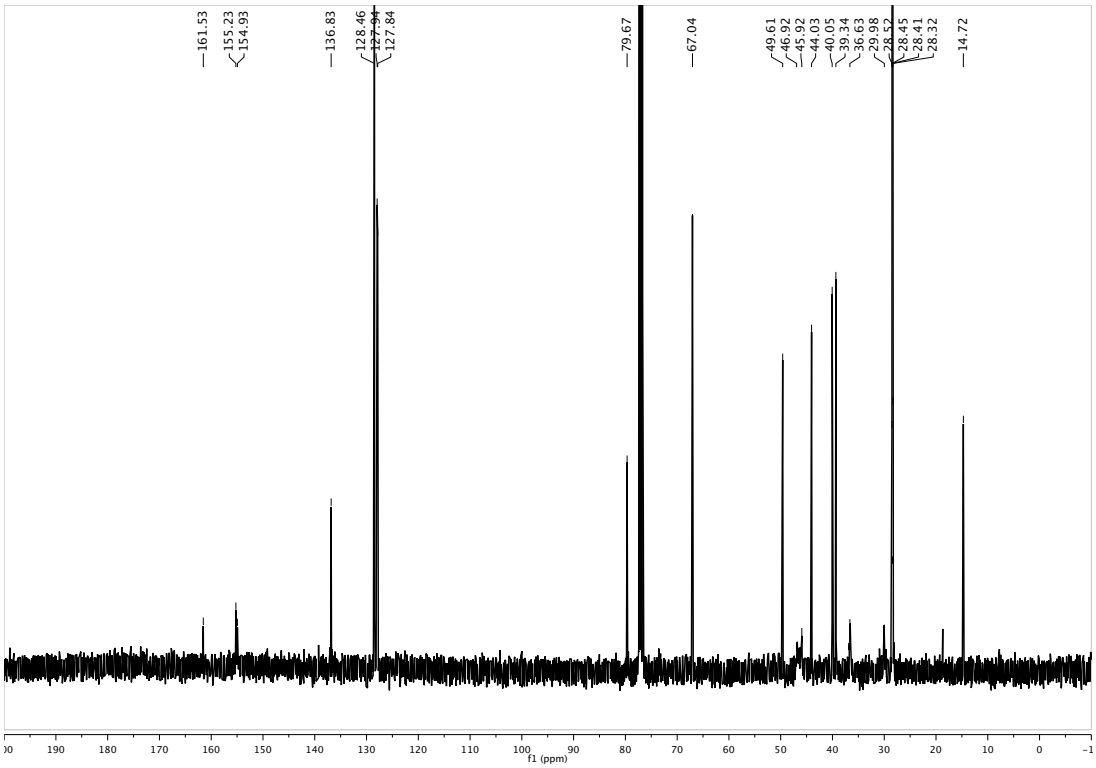


9-Benzyl 4-*tert*-butyl 3-methyl-1,4,9-triazaspiro[5.5]undecane-4,9-dicarboxylate (7n):

^{1}H NMR (400 MHz, $CDCl_3$)

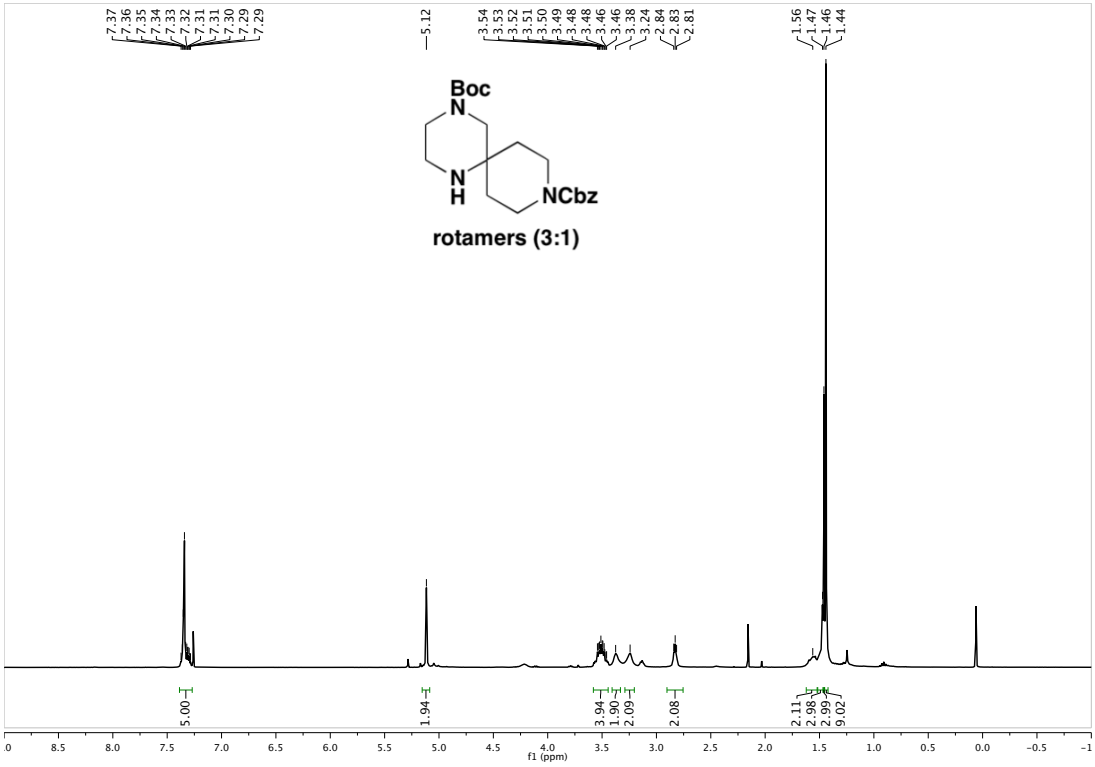


^{13}C NMR (100 MHz, $CDCl_3$)

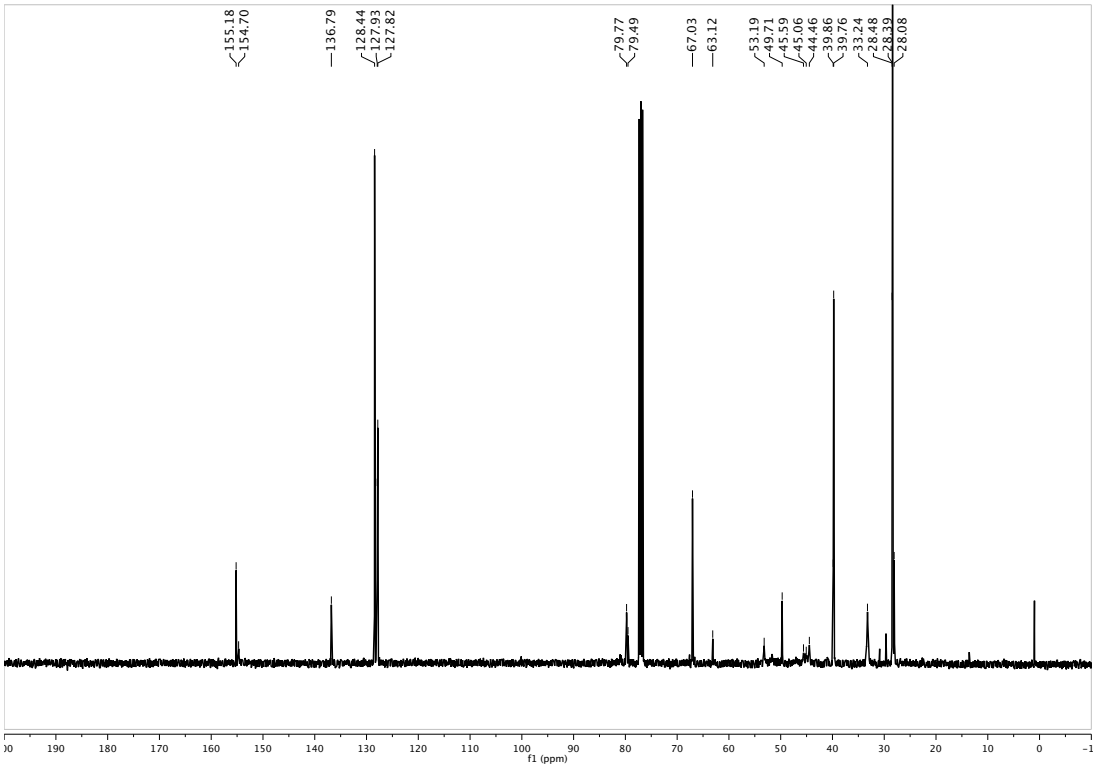


9-Benzyl 4-*tert*-butyl 1,4,9-triazaspiro[5.5]undecane-4,9-dicarboxylate (7o):

^{1}H NMR (400 MHz, $CDCl_3$)

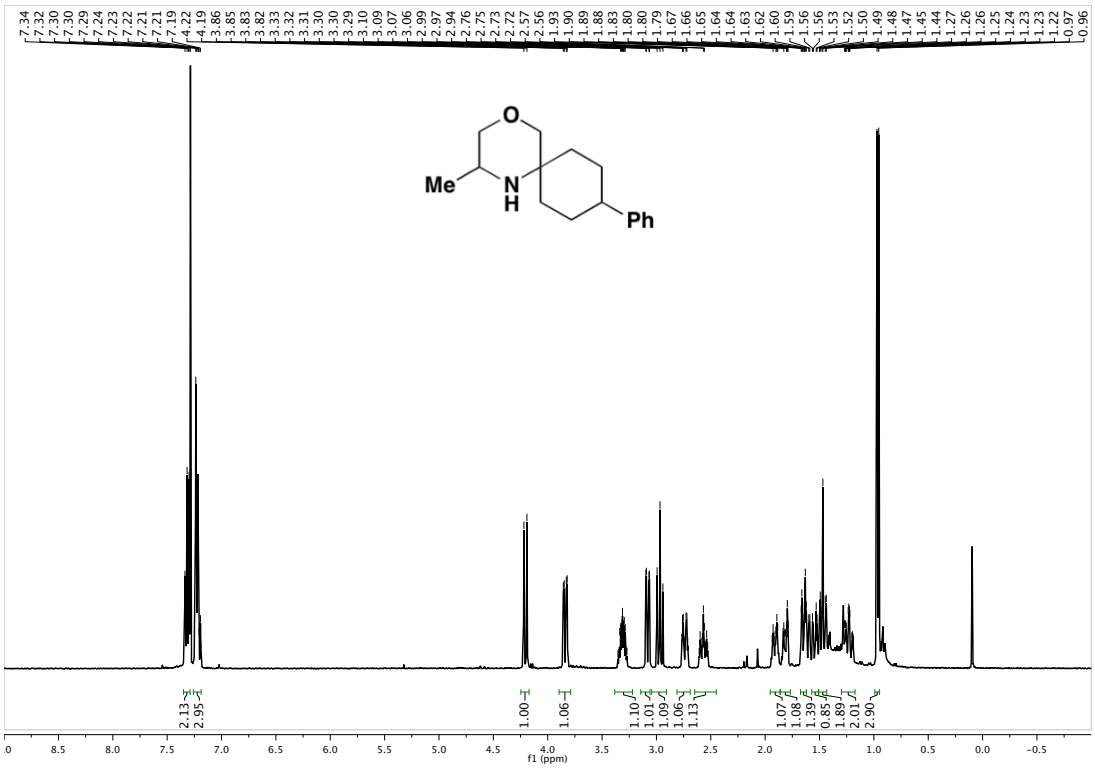


^{13}C NMR (100 MHz, $CDCl_3$)

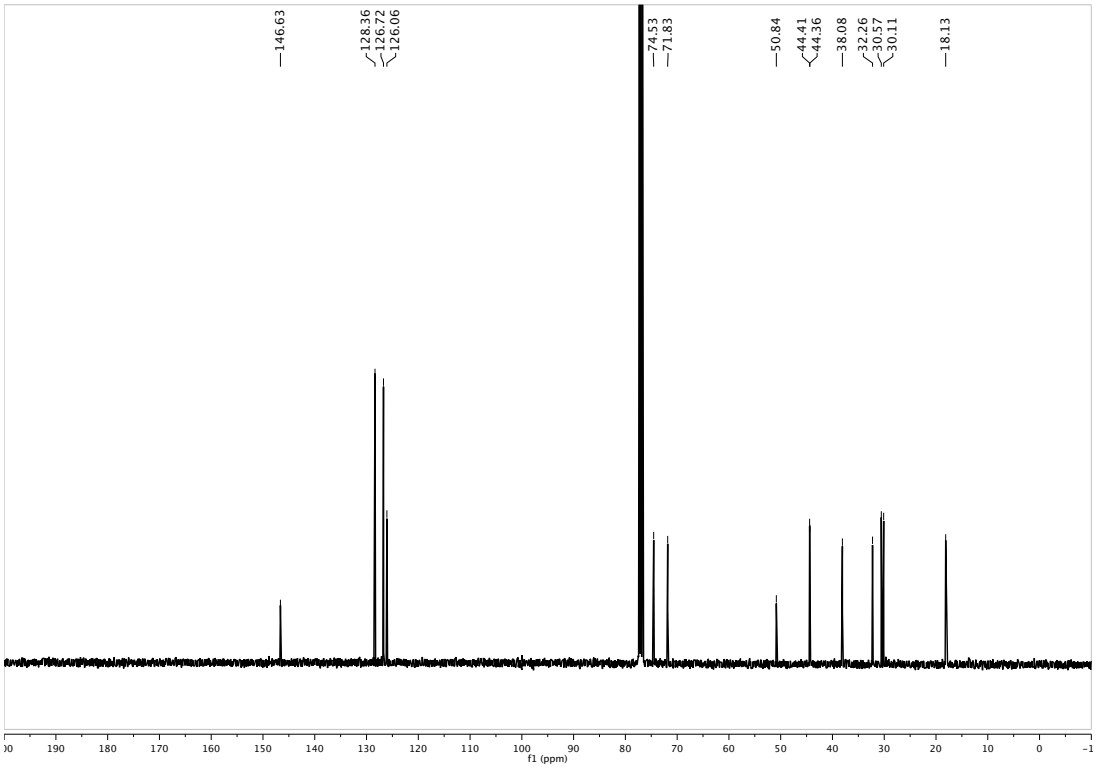


2-Methyl-9-phenyl-4-oxa-1-azaspiro[5.5]undecane (7p):

^{1}H NMR (400 MHz, $CDCl_3$)

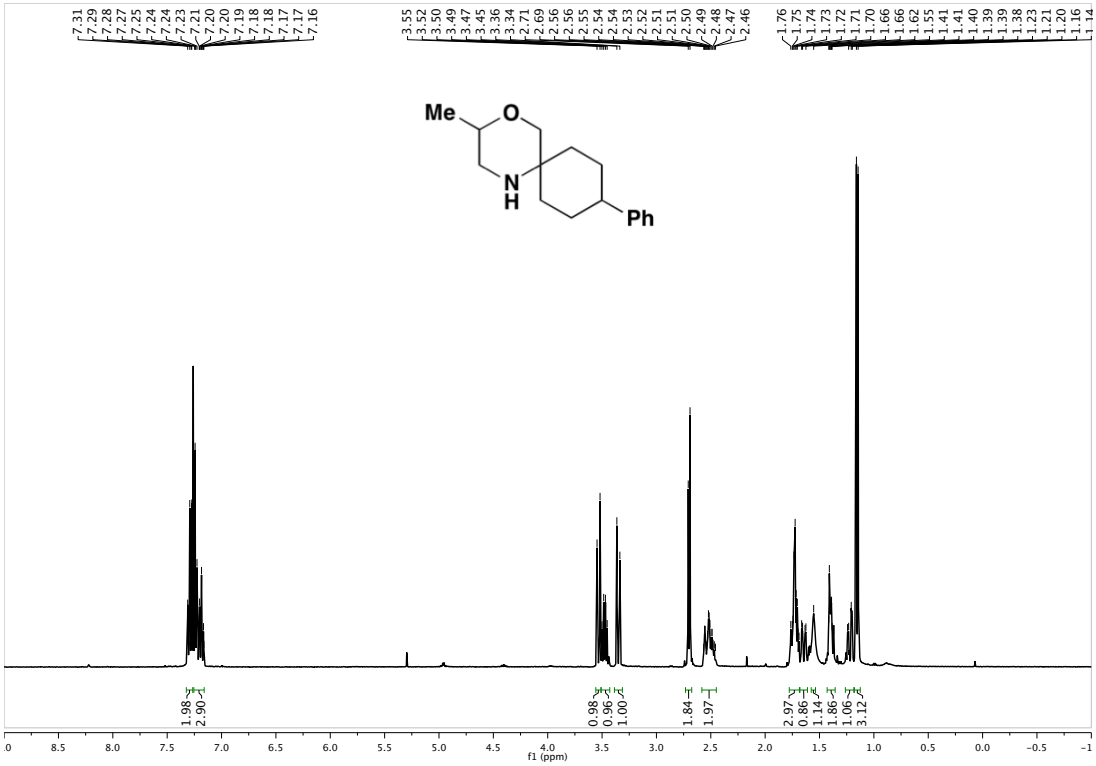


^{13}C NMR (100 MHz, $CDCl_3$)

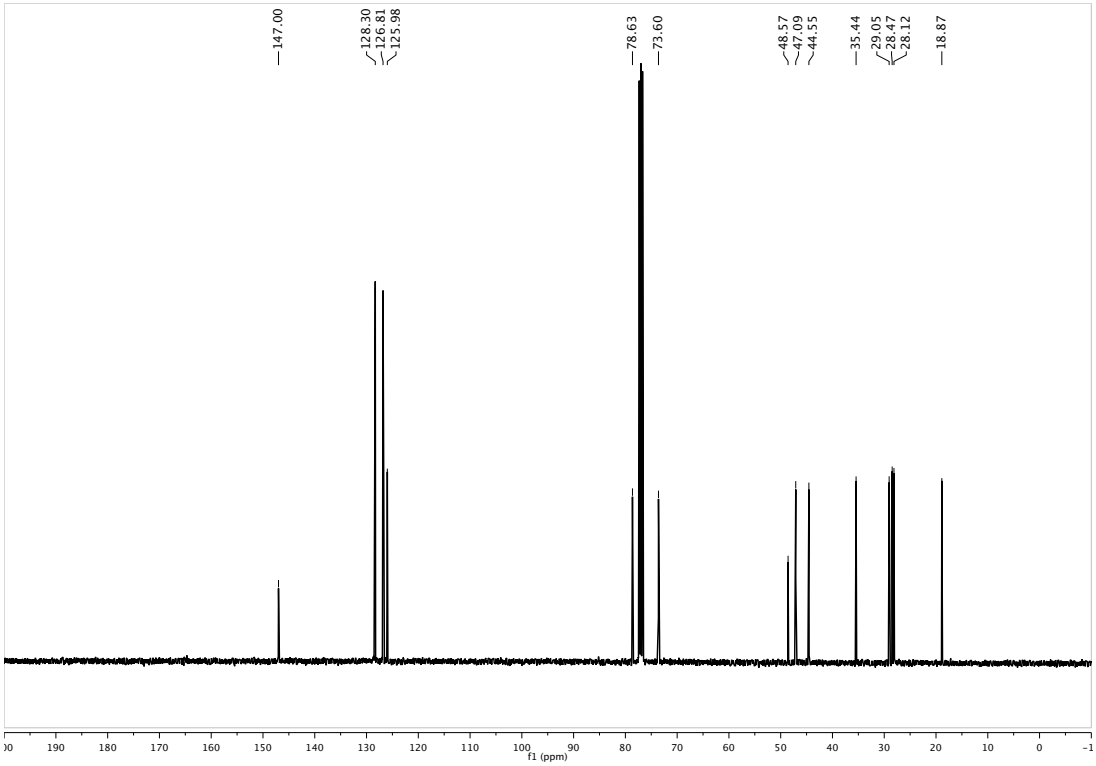


3-Methyl-9-phenyl-4-oxa-1-azaspiro[5.5]undecane (7q):

^{1}H NMR (400 MHz, $CDCl_3$)

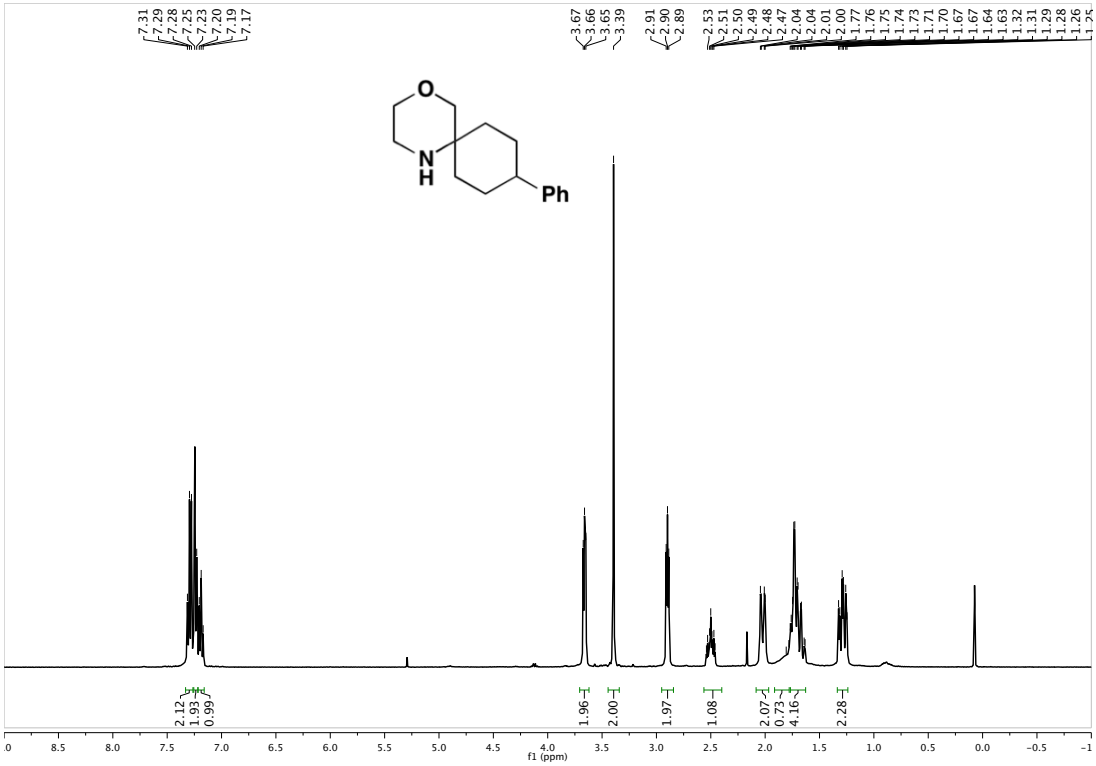


^{13}C NMR (100 MHz, $CDCl_3$)

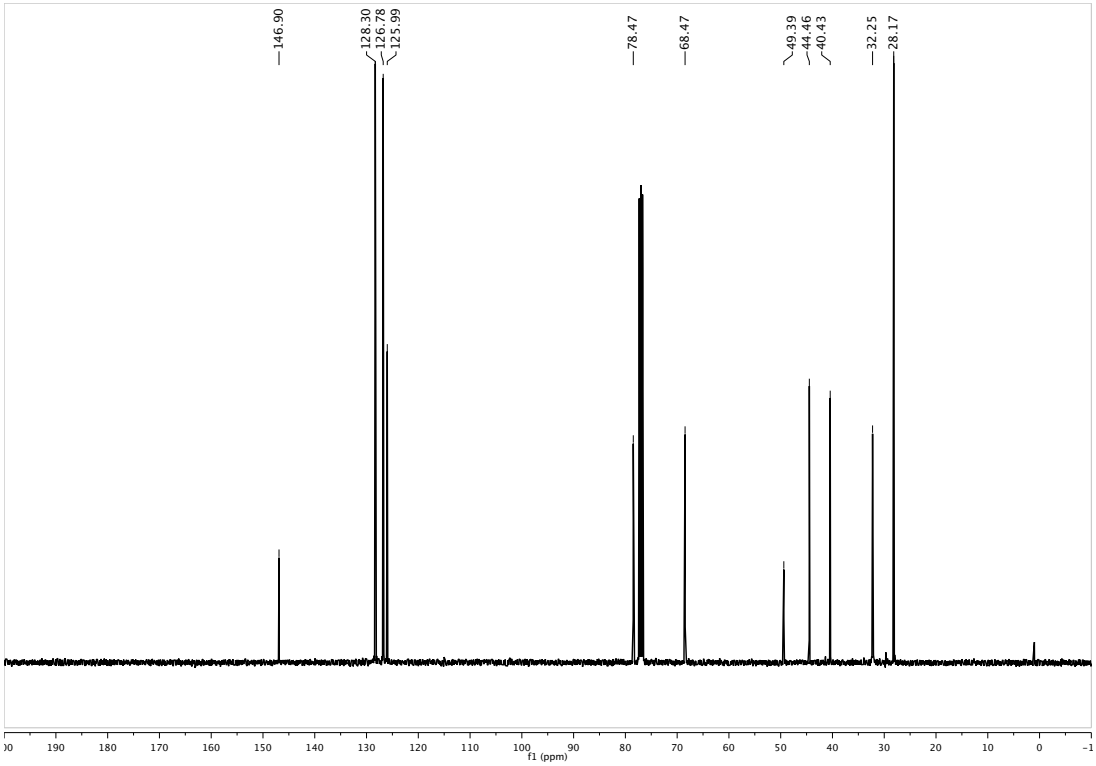


9-Phenyl-4-oxa-1-azaspiro[5.5]undecane (7r):

^{1}H NMR (400 MHz, $CDCl_3$)

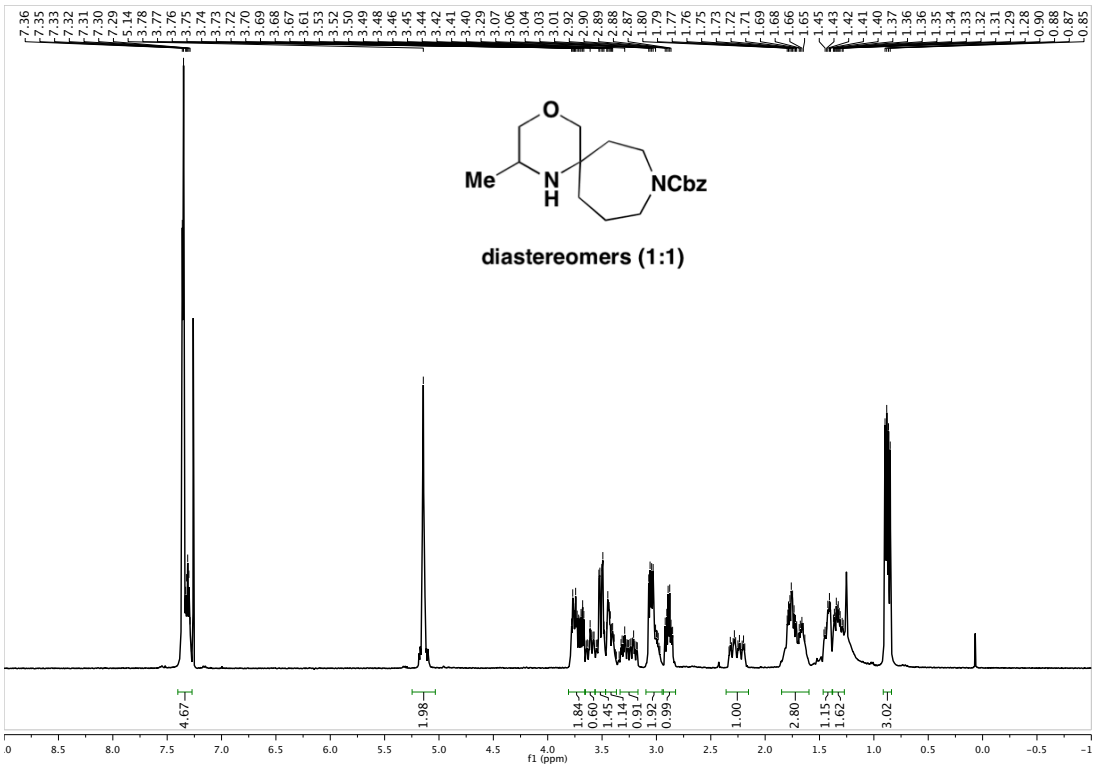


^{13}C NMR (100 MHz, $CDCl_3$)

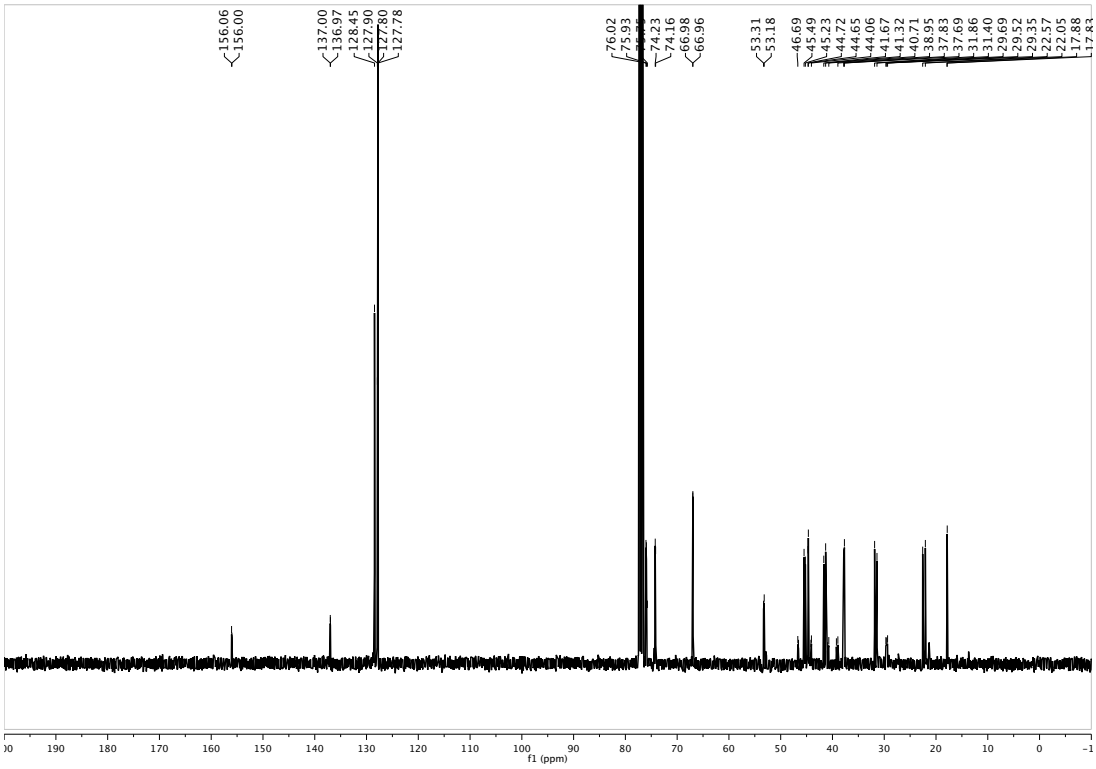


Benzyl 2-methyl-4-oxa-1,9-diazaspiro[5.6]dodecane-9-carboxylate (7s):

^{1}H NMR (400 MHz, $CDCl_3$)

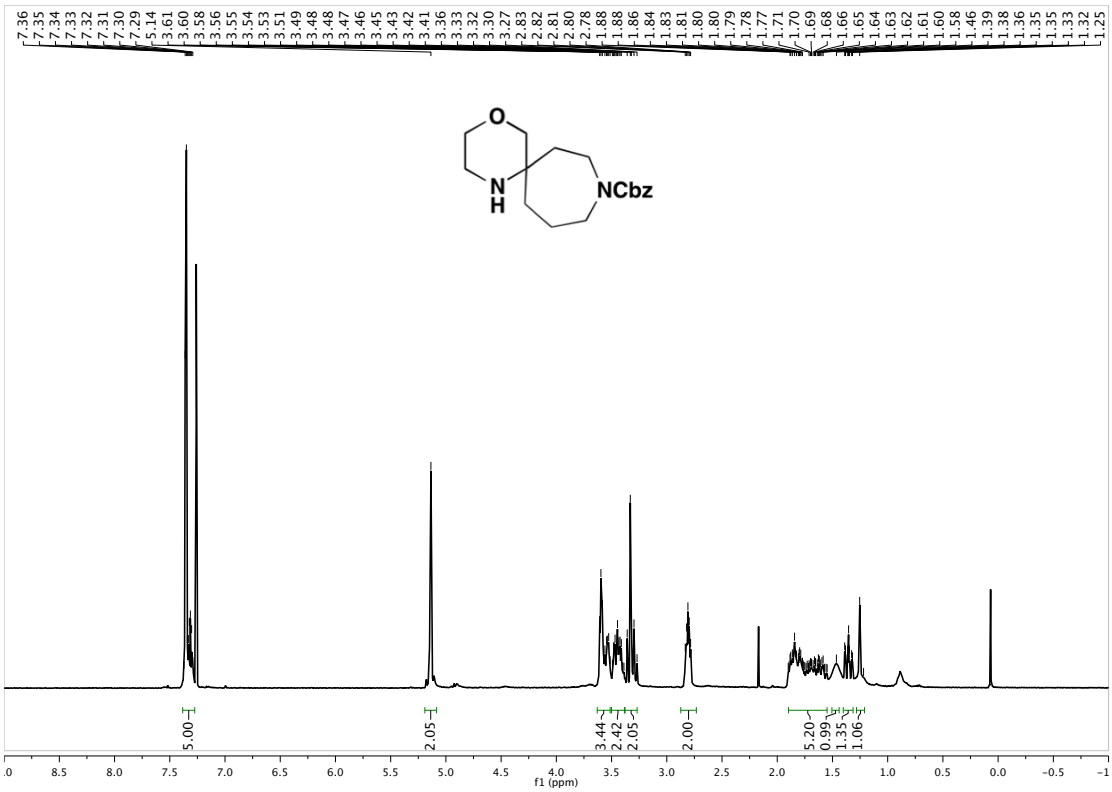


^{13}C NMR (100 MHz, $CDCl_3$)

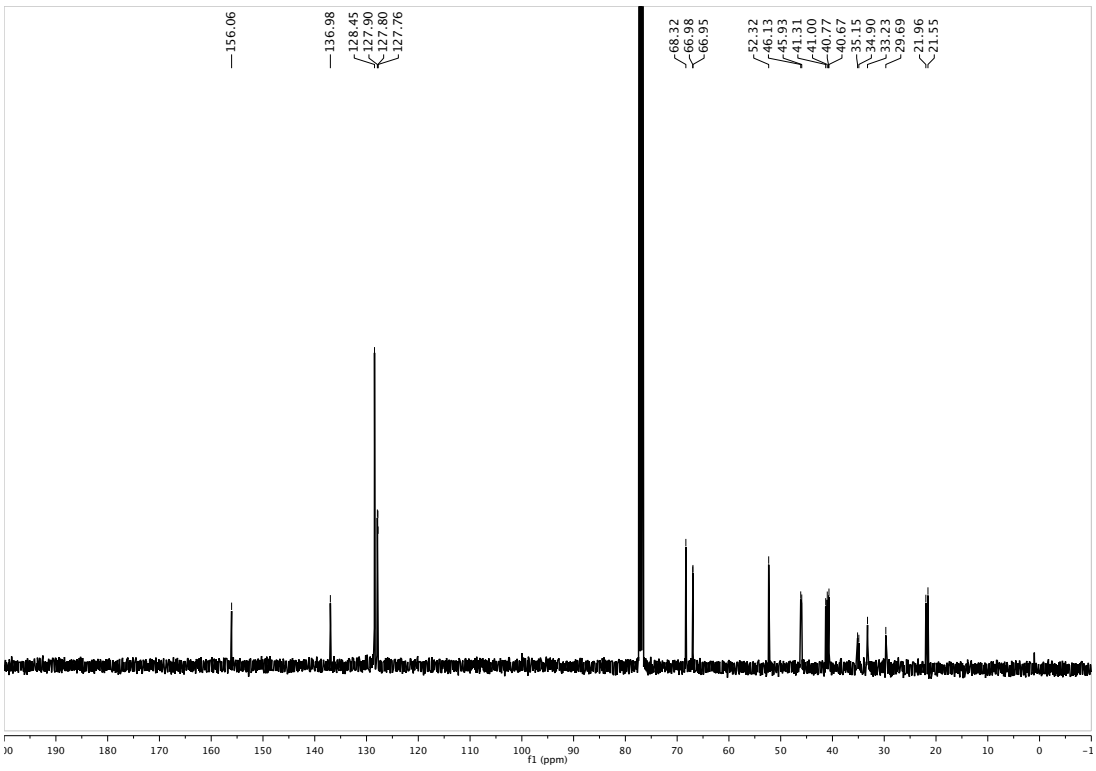


Benzyl 4-oxa-1,9-diazaspiro[5.6]dodecane-9-carboxylate (7t):

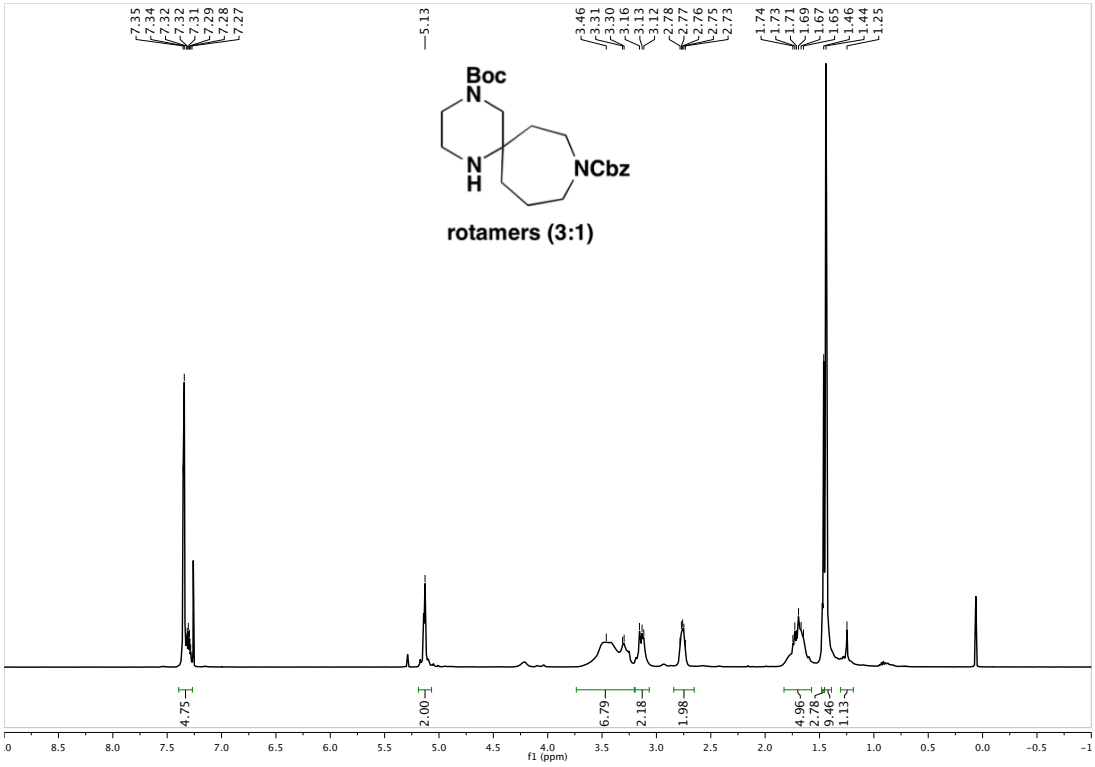
^{1}H NMR (400 MHz, $CDCl_3$)



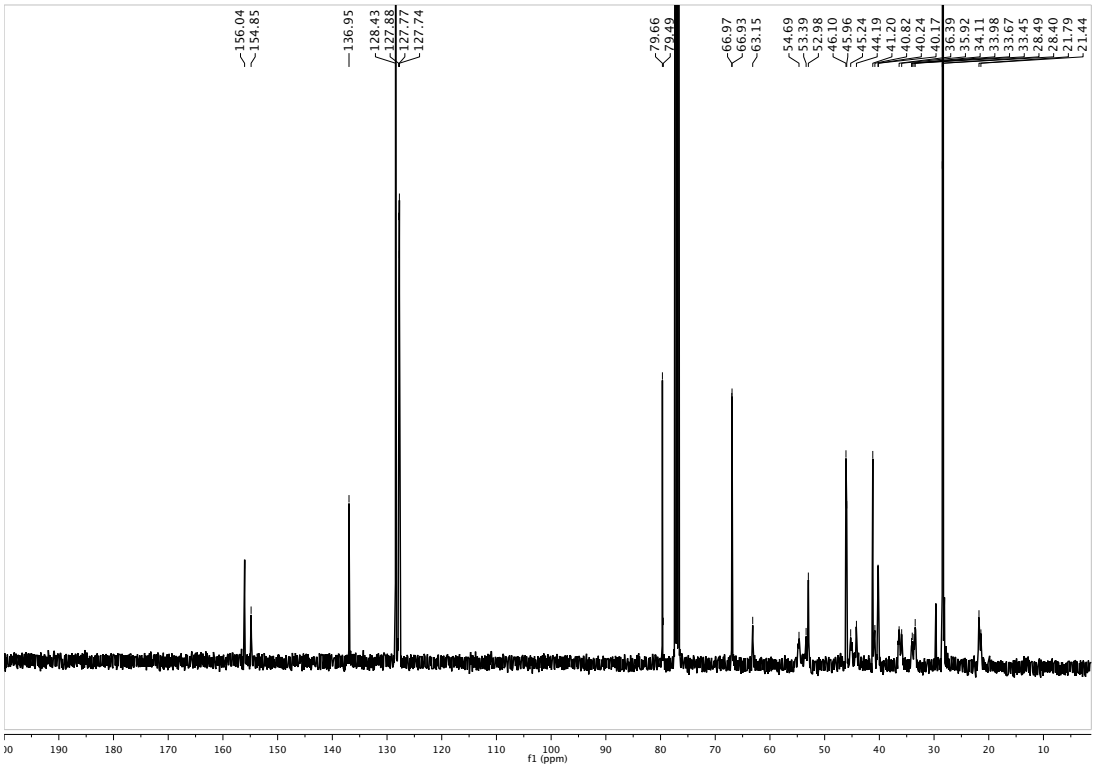
^{13}C NMR (100 MHz, $CDCl_3$)



9-Benzyl 4-*tert*-butyl 1,4,9-triazaspiro[5.6]dodecane-4,9-dicarboxylate (7u):
^{1}H NMR (400 MHz, $CDCl_3$)

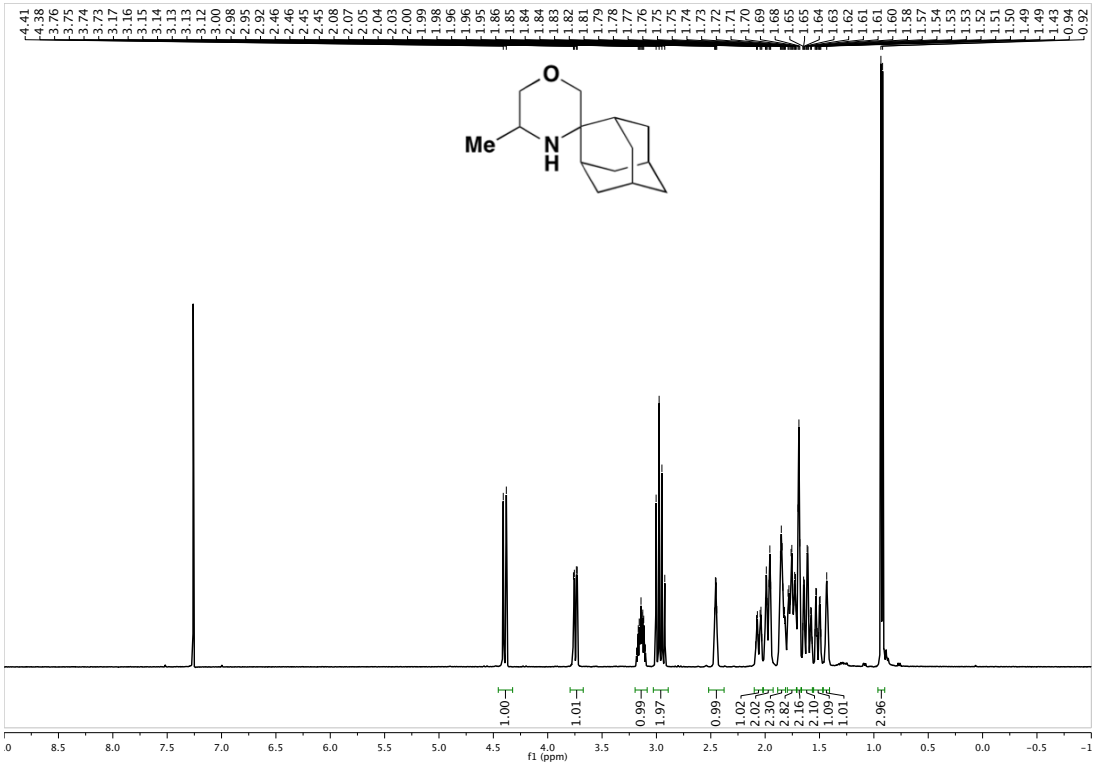


^{13}C NMR (100 MHz, $CDCl_3$)

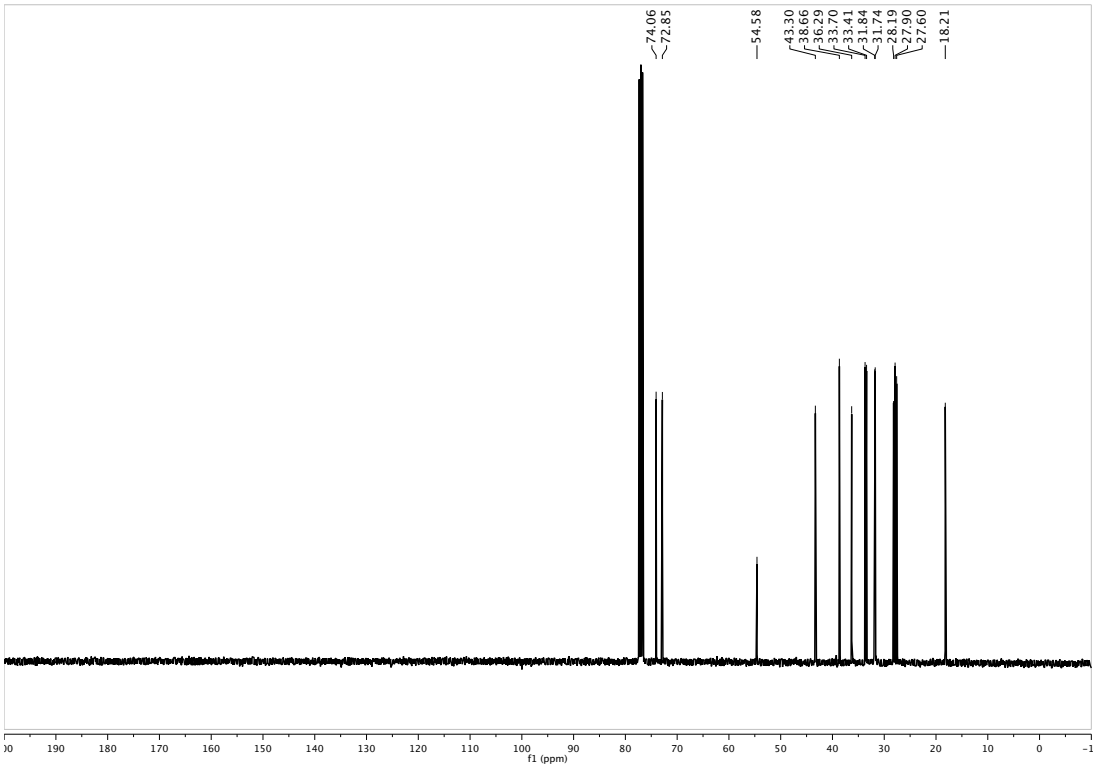


(1*r*,3*r*,5*r*,7*r*)-5'-Methylspiro[adamantane-2,3'-morpholine] (9):

^{1}H NMR (400 MHz, $CDCl_3$)

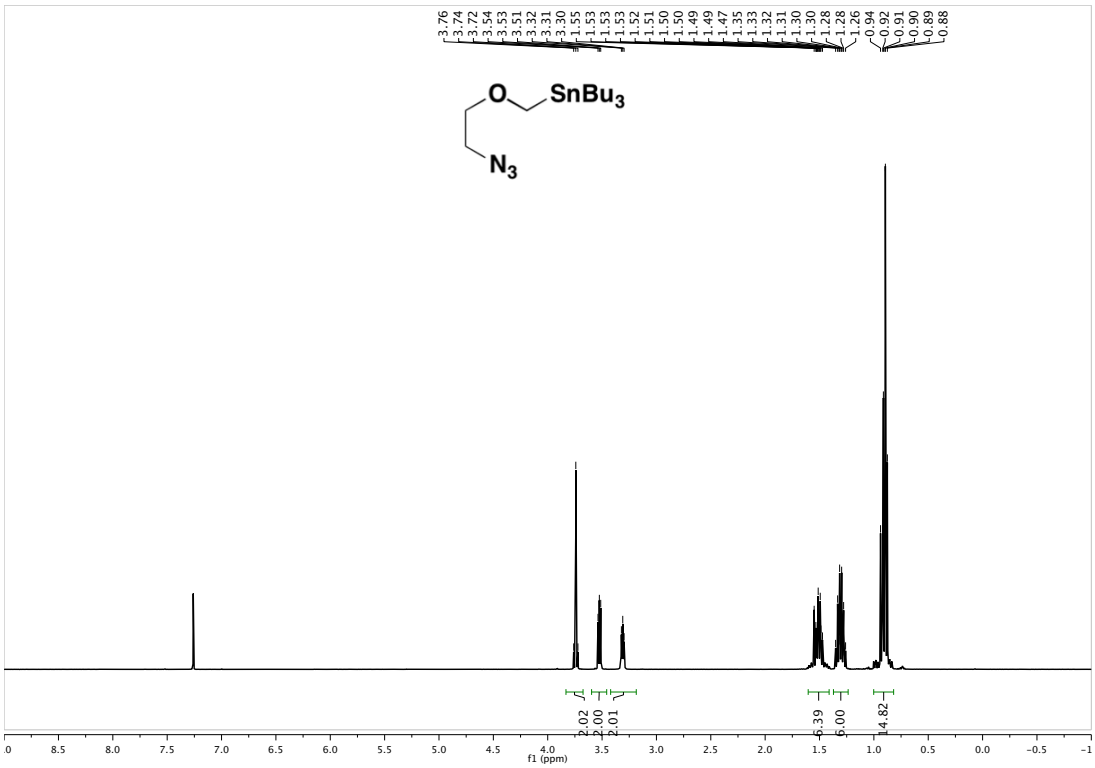


^{13}C NMR (100 MHz, $CDCl_3$)

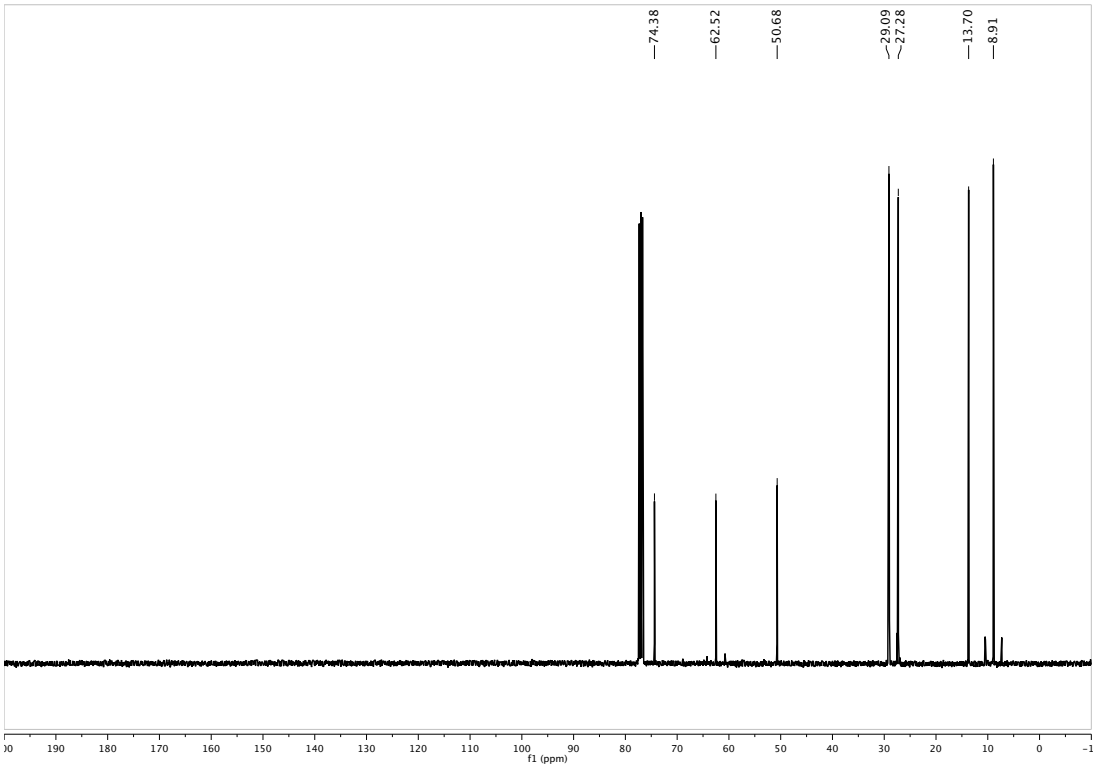


((2-Azidoethoxy)methyl)tributylstannane (15a):

^{1}H NMR (400 MHz, $CDCl_3$)

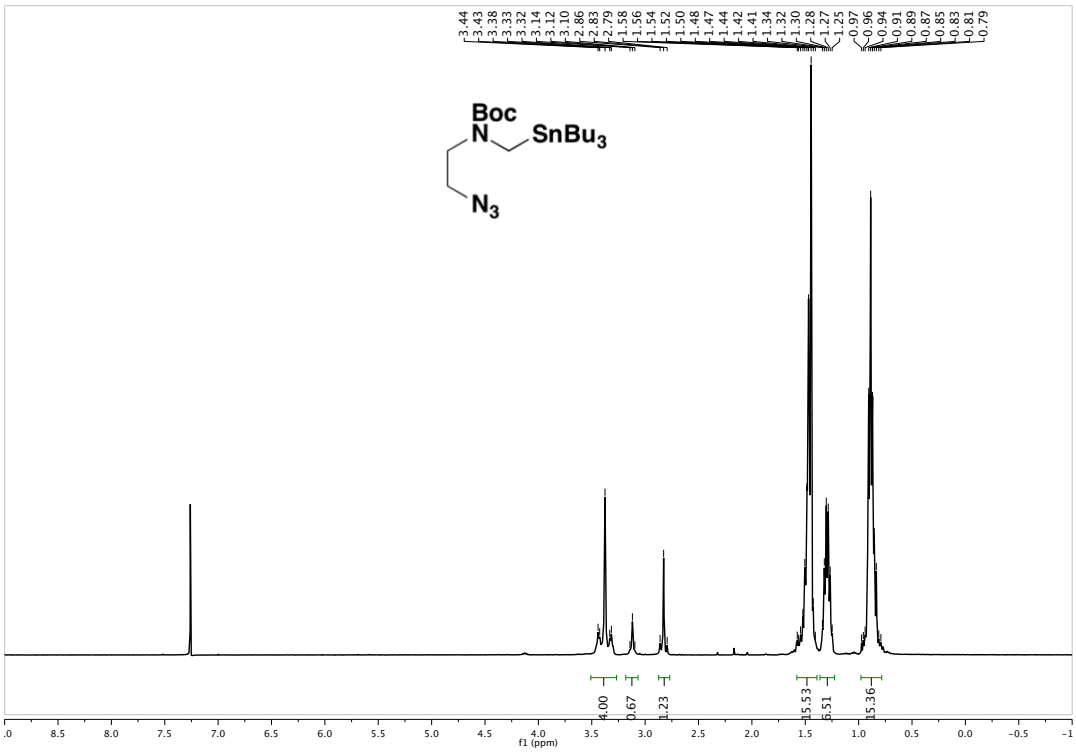


^{13}C NMR (100 MHz, $CDCl_3$)

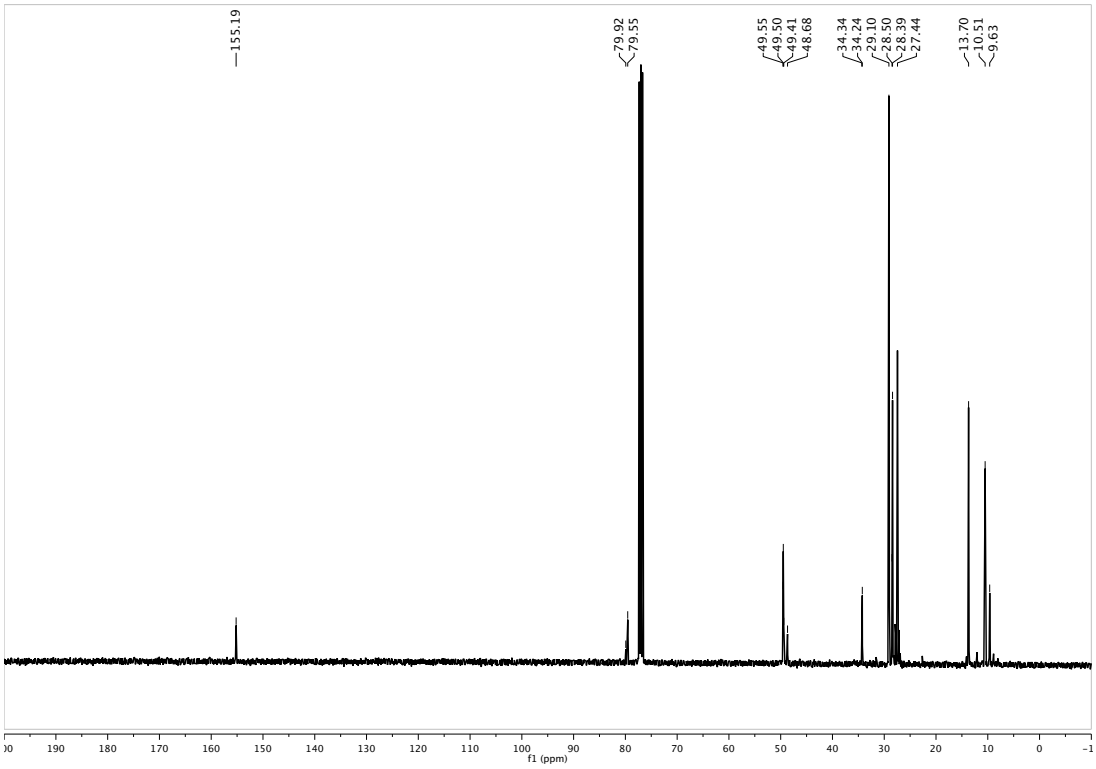


***tert*-Butyl (2-azidoethyl)((tributylstannyl)methyl)carbamate (15b):**

^{1}H NMR (400 MHz, $CDCl_3$)

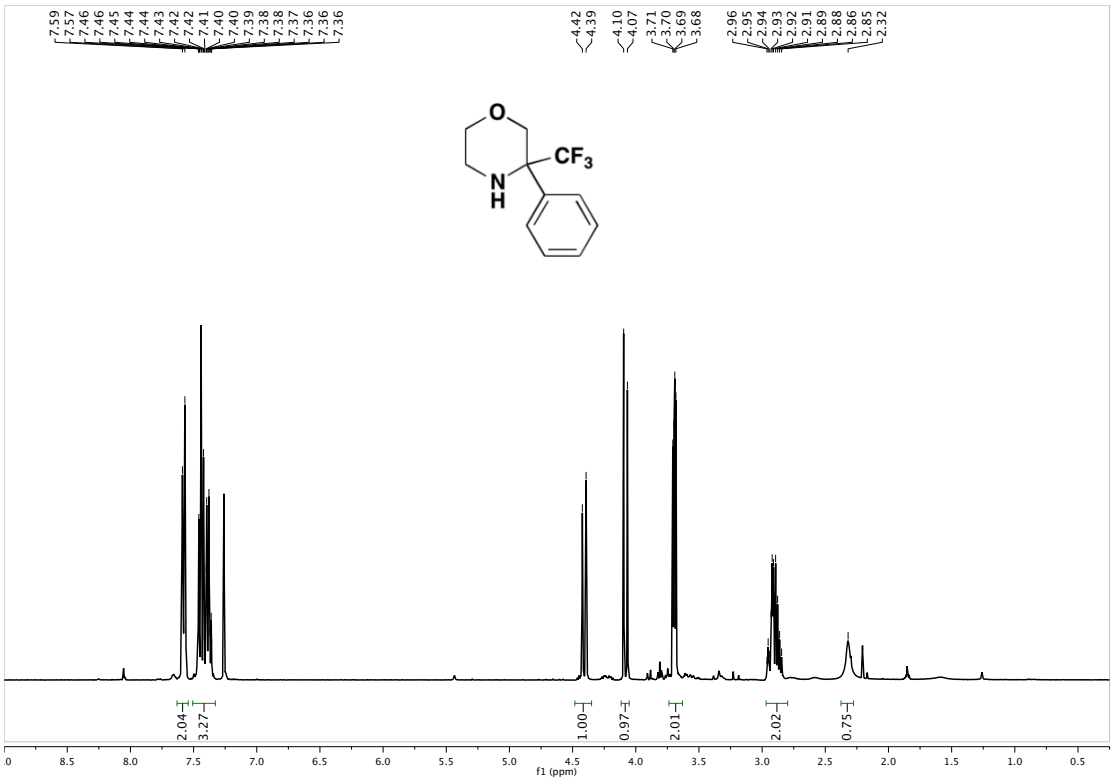


^{13}C NMR (100 MHz, $CDCl_3$)

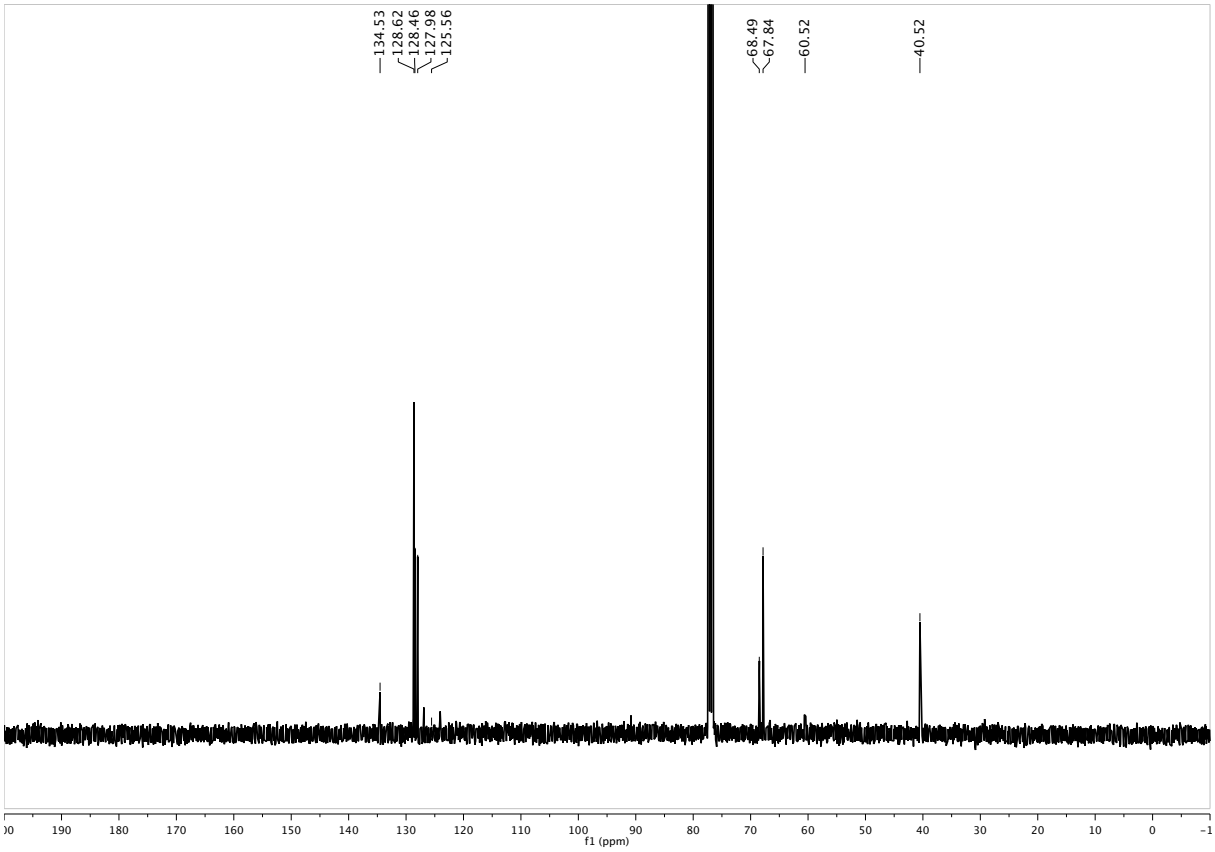


3-Phenyl-3-(trifluoromethyl)morpholine (16a):

^{1}H NMR (400 MHz, $CDCl_3$)

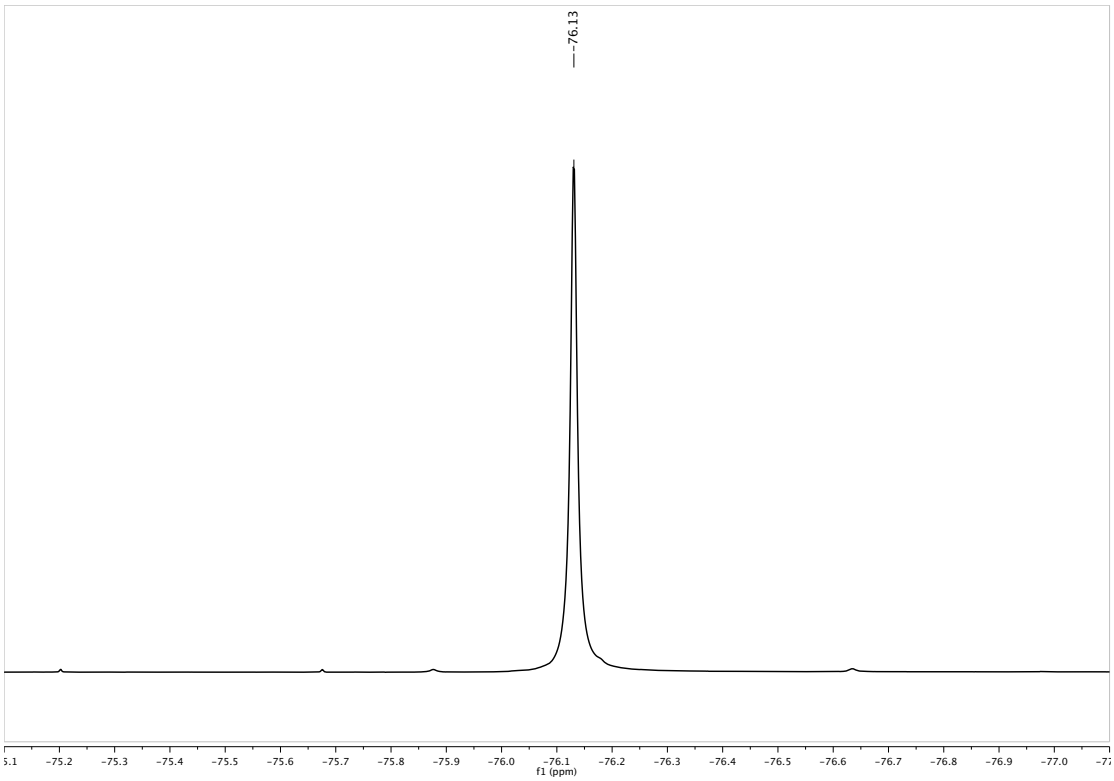


^{13}C NMR (100 MHz, $CDCl_3$)



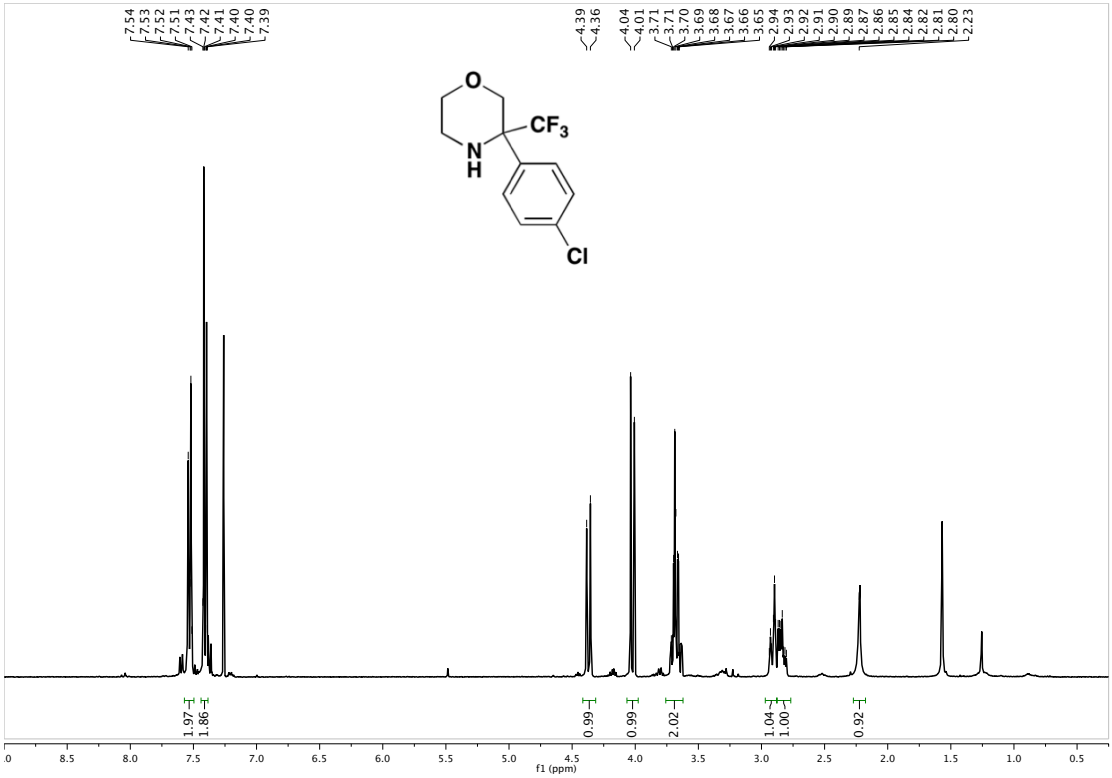
3-Phenyl-3-(trifluoromethyl)morpholine (16a):

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

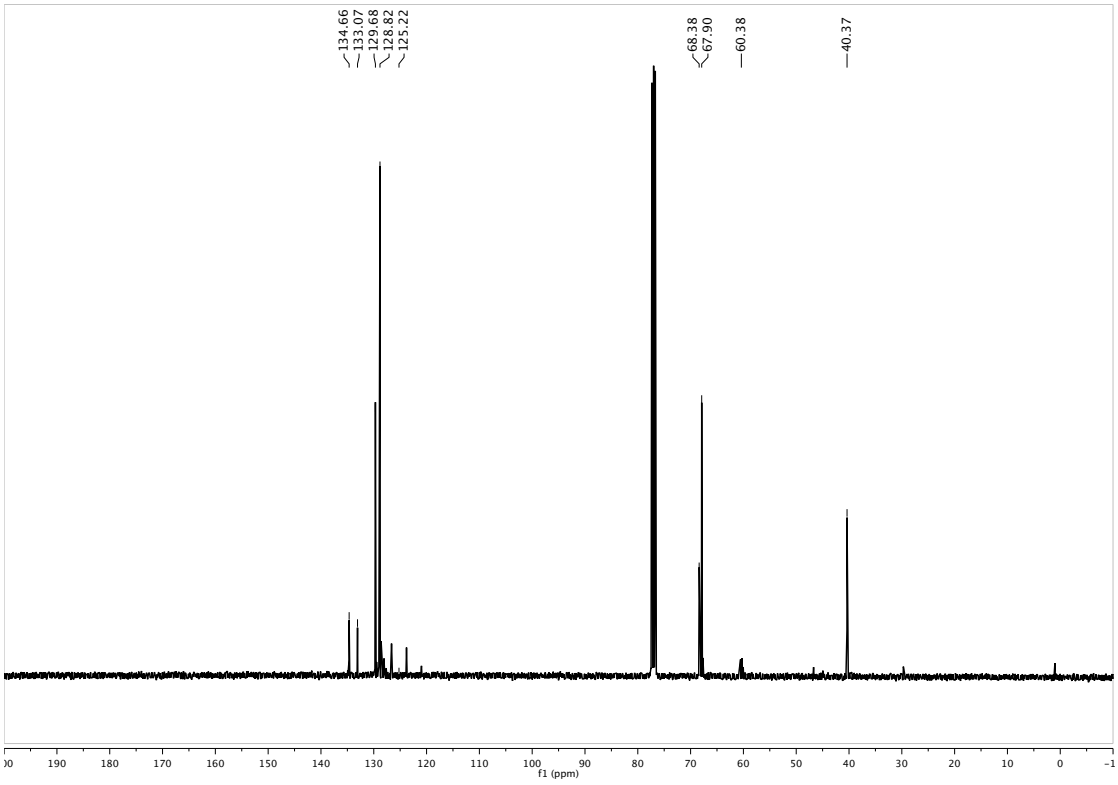


3-(4-Chlorophenyl)-3-(trifluoromethyl)morpholine (16b):

^{1}H NMR (400 MHz, $CDCl_3$)

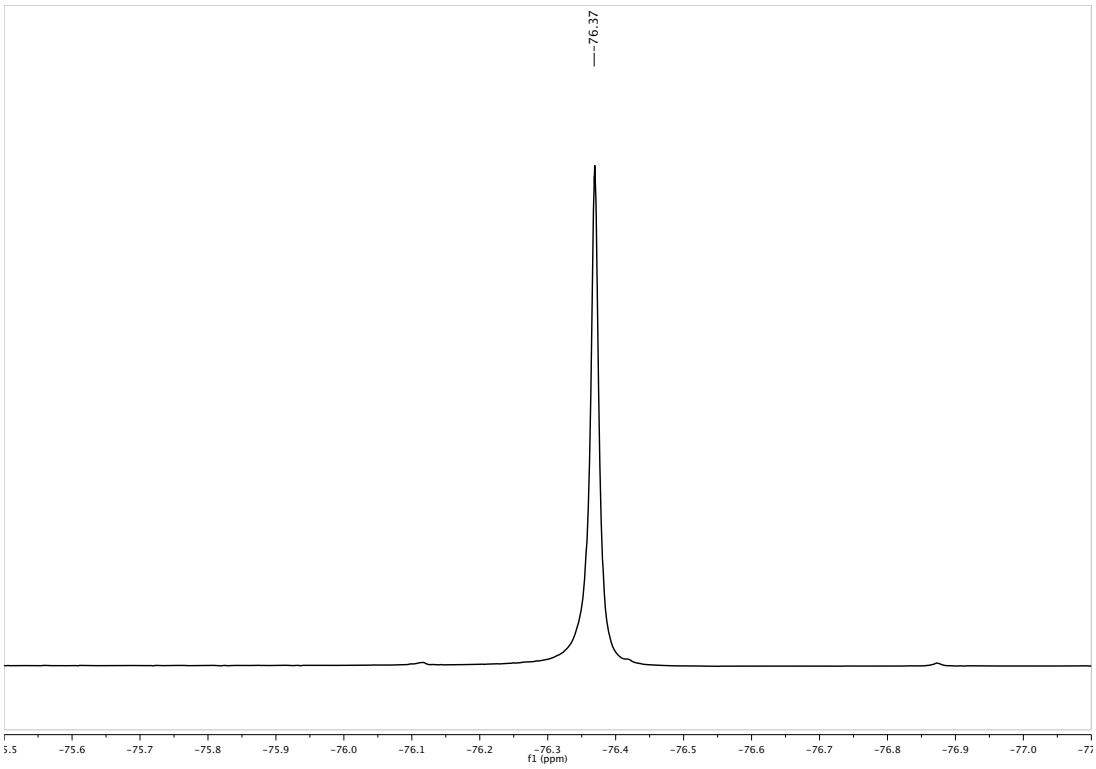


^{13}C NMR (100 MHz, $CDCl_3$)



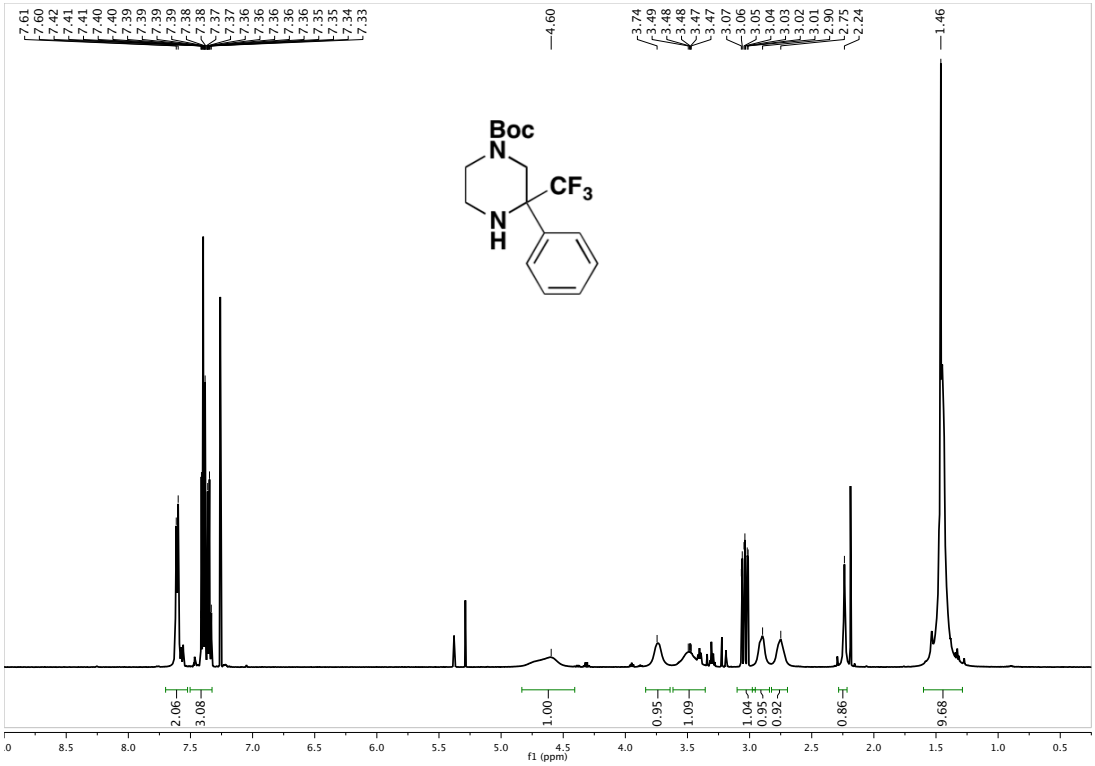
3-(4-Chlorophenyl)-3-(trifluoromethyl)morpholine (16b):

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

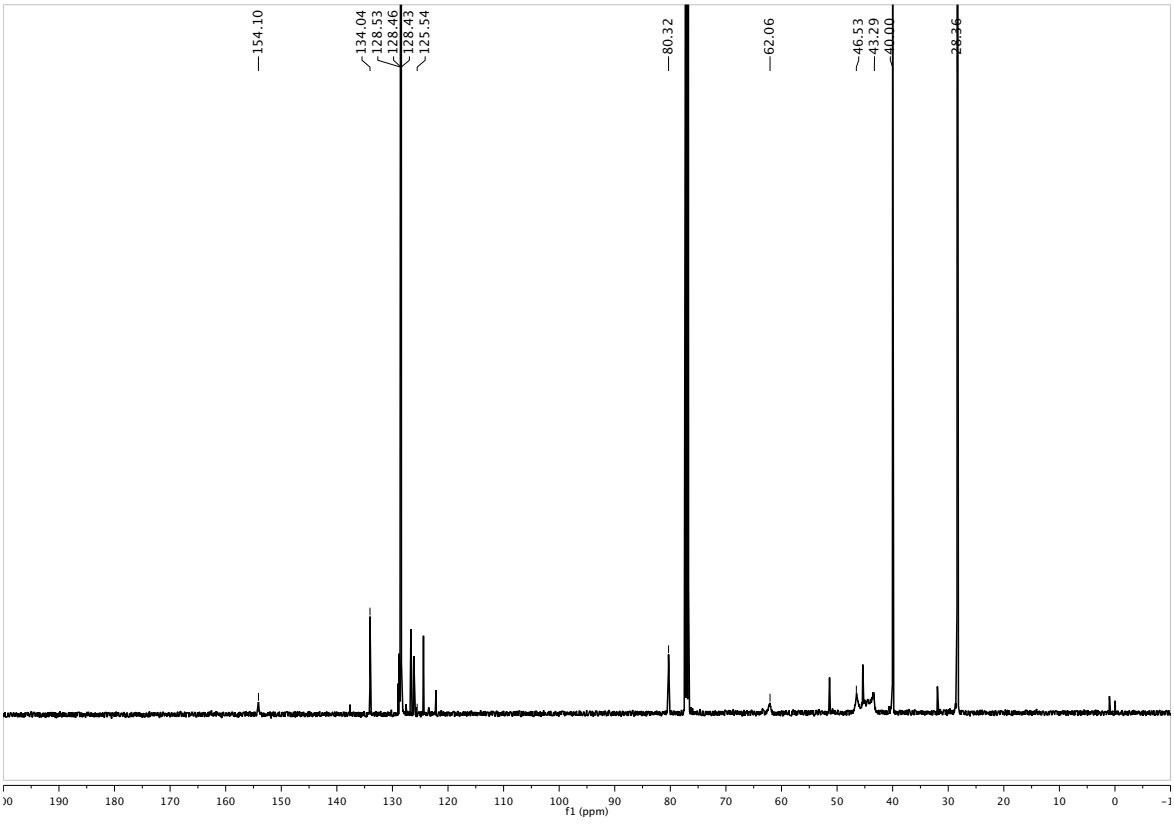


***tert*-Butyl 3-phenyl-3-(trifluoromethyl)piperazine-1-carboxylate (16c):**

^{1}H NMR (500 MHz, $CDCl_3$)@50 ^{o}C

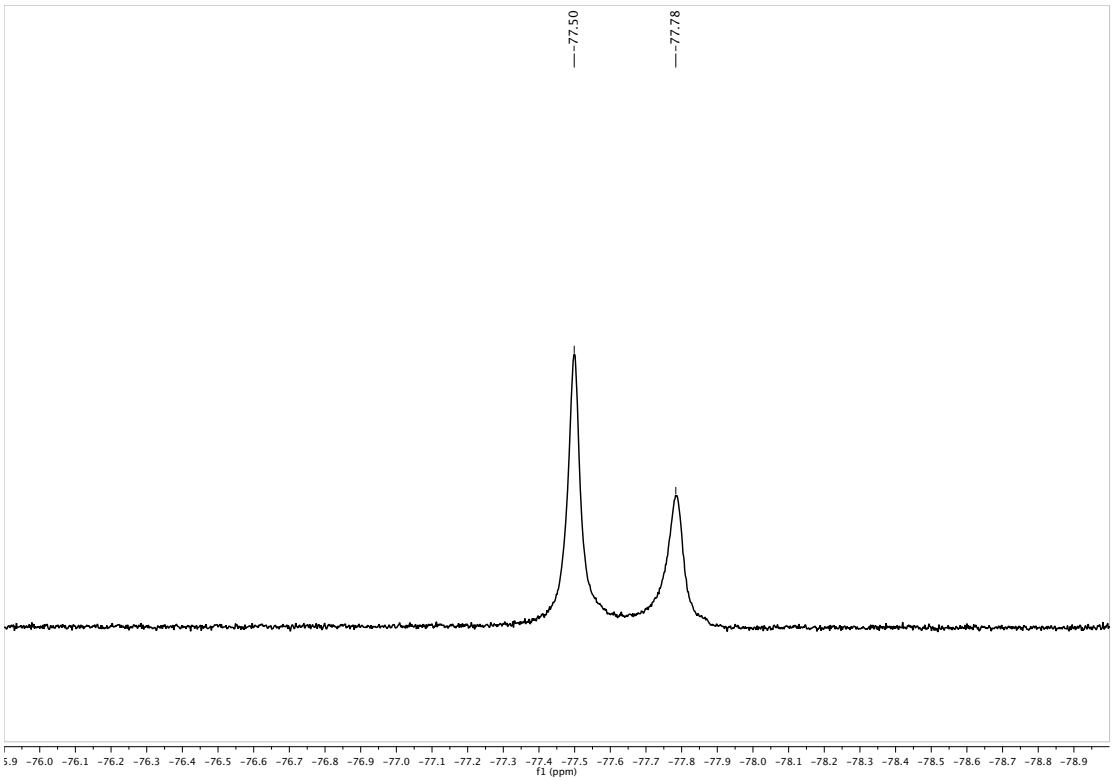


^{13}C NMR (125 MHz, $CDCl_3$)



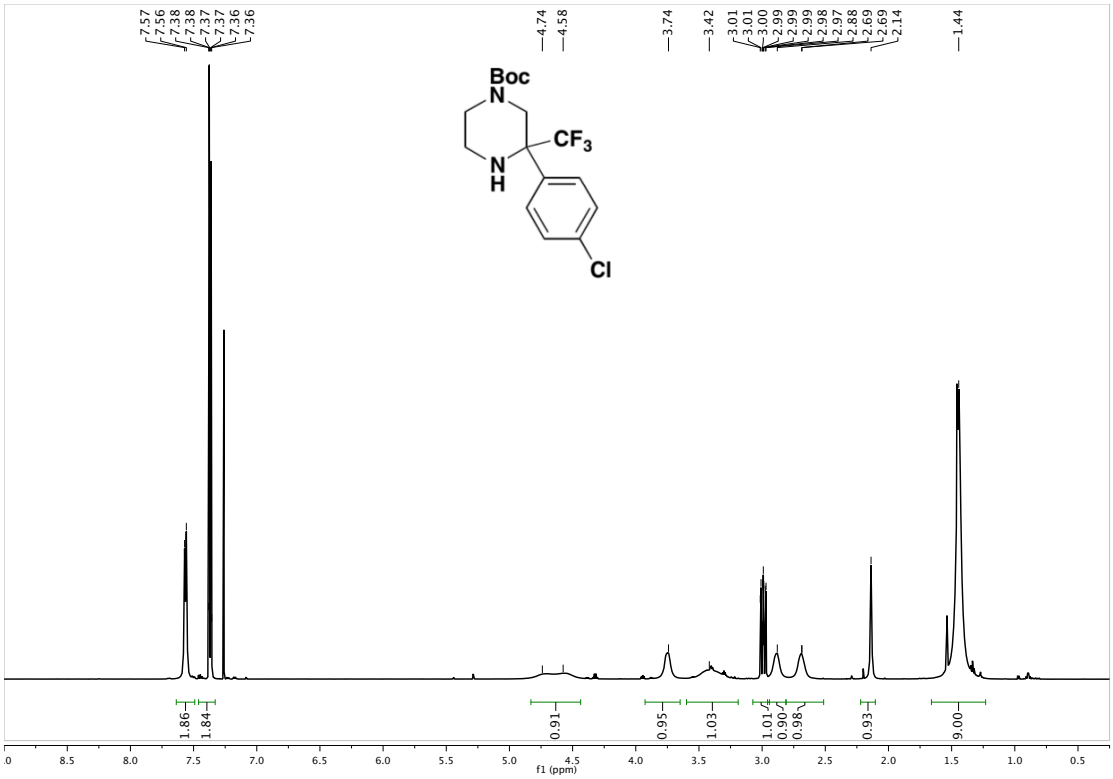
***tert*-Butyl 3-phenyl-3-(trifluoromethyl)piperazine-1-carboxylate (16c):**

^{19}F NMR (470 MHz, $CDCl_3$)

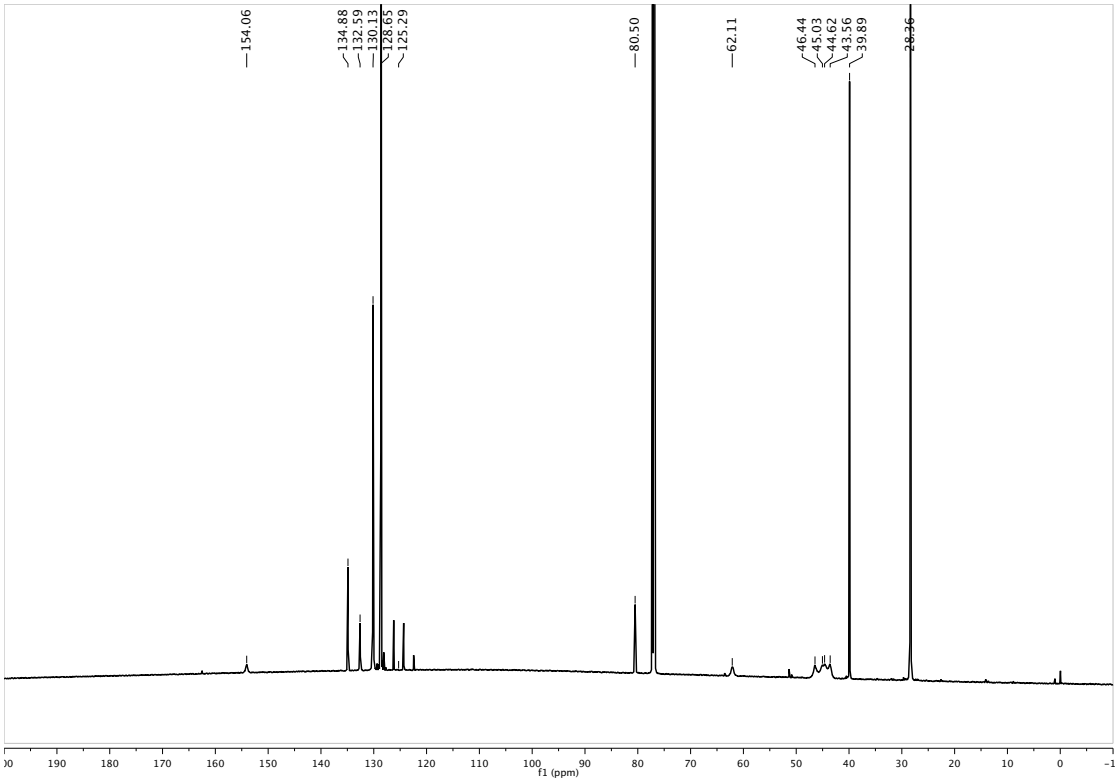


***tert*-Butyl 3-(4-chlorophenyl)-3-(trifluoromethyl)piperazine-1-carboxylate (16d):**

^{1}H NMR (500 MHz, $CDCl_3$)@50 ^{o}C

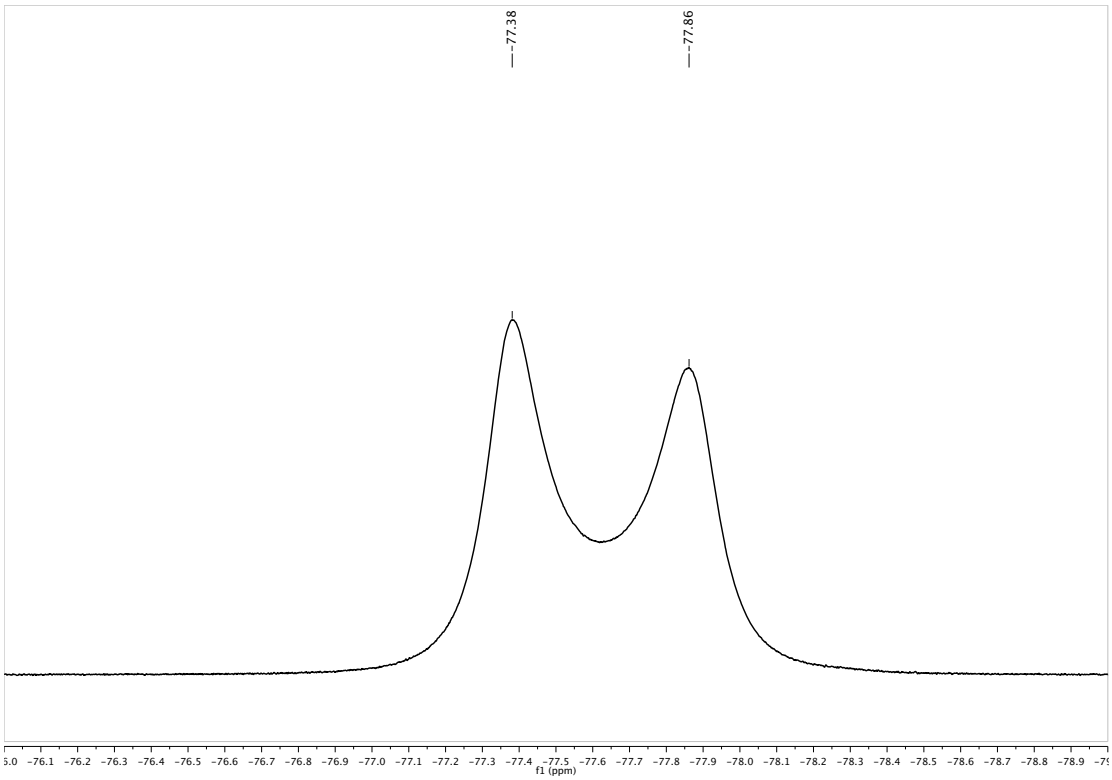


^{13}C NMR (125 MHz, $CDCl_3$)



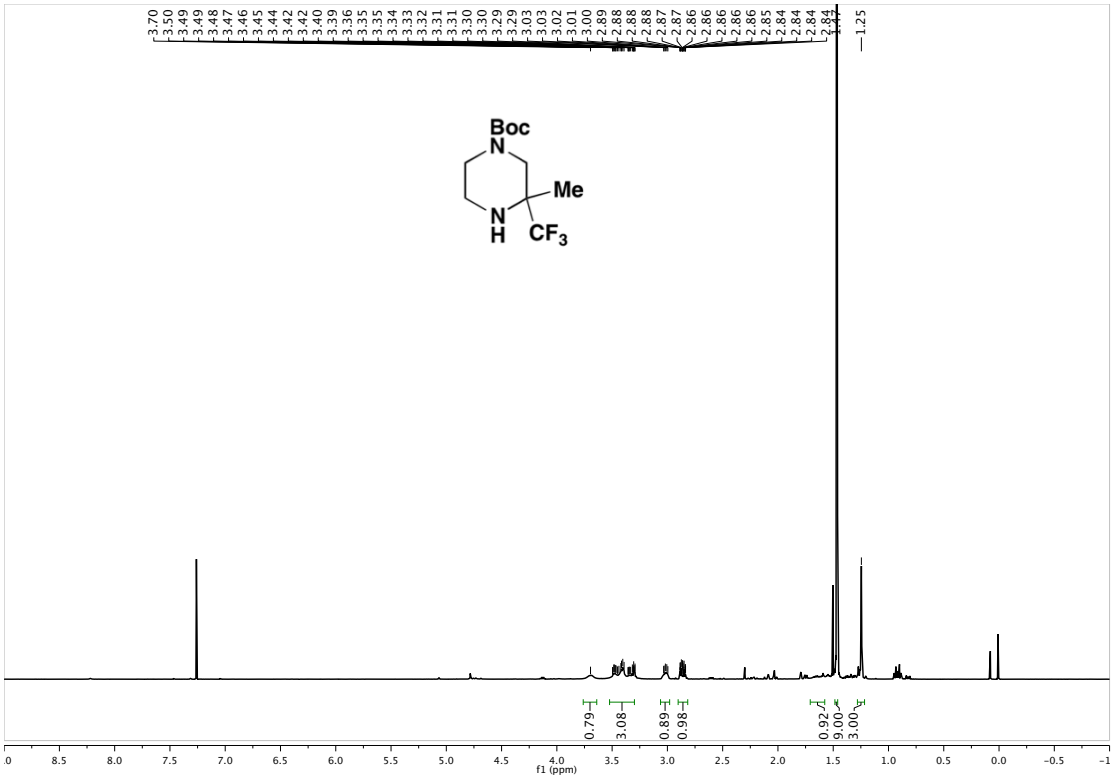
tert-Butyl 3-(4-chlorophenyl)-3-(trifluoromethyl)piperazine-1-carboxylate (16d):

^{19}F NMR (470 MHz, $CDCl_3$)

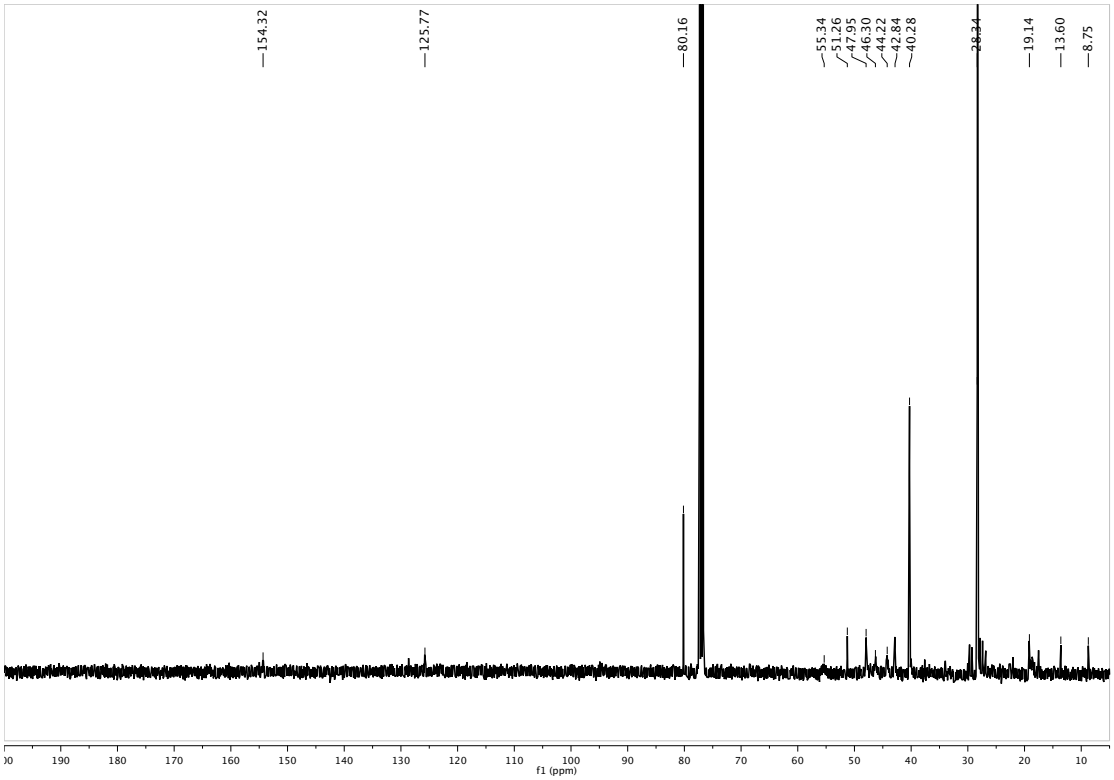


***tert*-Butyl 3-methyl-3-(trifluoromethyl)piperazine-1-carboxylate (16e):**

^{1}H NMR (500 MHz, $CDCl_3$)@50 ^{o}C



^{13}C NMR (125 MHz, $CDCl_3$)



***tert*-Butyl 3-methyl-3-(trifluoromethyl)piperazine-1-carboxylate (16e):**

^{19}F NMR (470 MHz, $CDCl_3$)