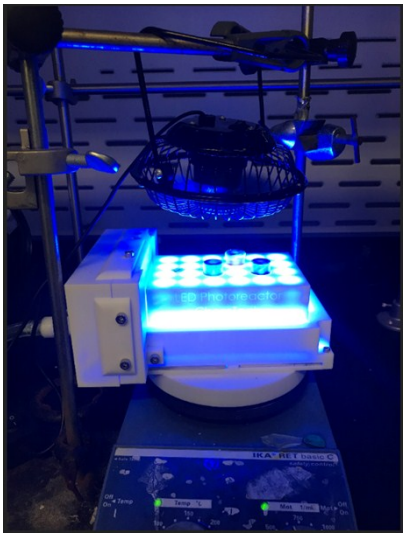
General information

All experiments were conducted under a nitrogen atmosphere unless otherwise noted. 4ml Vial with red pressure relief cap and vial with TFE Septa green open top cap (purchased from Chemglass) were used. Chemtech blue LED reactor was manufactured in the Novartis Institute of Biomedical Research Cambridge USA (2W, λ_{max} = 455 nm). The reaction vessels equipped with a stirring bar were placed on the reactor. A fan attached to hold the temperature.



The solvents were all ACS reaction grade, purchased from Sigma-Aldrich and used without further purification. All carboxylic acids used in this study were purchased from commercial vendors, potassium trifluroborate were purchased from Accela or prepared following the literature procedures.[1] Photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ was purchased from Strem Chemicals, photocatalyst 4CzIPN was purchased from Bide pharm (Shanghai China).

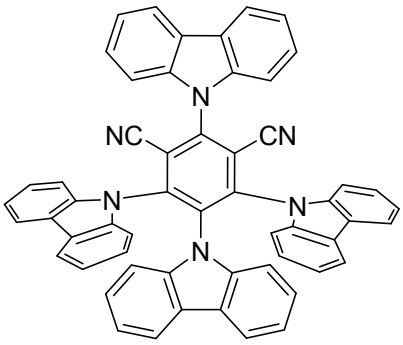
Reactions were monitored by LC/MS and thin layer chromatography (TLC). The mass spectrometric analysis was performed on an Agilent System (Agilent 1260 HPLC and an Agilent 6130 mass spectrometer detector; Column: Phenomenex Kinetex 2.6 um C18, column size 4.6 x 50 mm; column temperature 40°C. gradient: 5-95% methanol in water with 0.1% FA over a 2 min period; flow rate 2.0 mL/min (or Polar gradient 5-50% over 2.0 min, or Non-Polar gradient 50-95% over 2.0 min); Mass Spectrometer molecular weight scan range 100-1000; or 100-1500. capillary voltage 4000 V. All masses were reported as those of the protonated parent ions, unless otherwise indicated. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using a water bath. Flash chromatography was performed using Combiflash Rf workstation over pre-filled Agela® Silica Flash Column. NMR spectra were recorded at at 25 °C either on a Bruker AVANCE III 400 MHz spectrometer or on a Bruker NEO 400 MHz spectrometer equipped with a gradient BBFO cryoprobe, and are calibrated using residual undeuterated solvent ($CHCl_3$, 7.26 ppm ^{1}H NMR, 77.2 ppm ^{13}C NMR). Coupling constants (*J*) were quoted in Hz. High-resolution mass spectra (HRMS) were recorded on an Agilent 6224 TOF LC/MS equipped with an electrospray ionization (ESI) source.

[1]. (a) E. E. Stache, T. Rovis, A. G. Doyle, *Angew. Chem. Int. Ed*. **2017**, *56*, 3679-3683. (b) S. D. Dreher, P. G. Dormer, D. L. Sandrock, G. A. Molander, *J. Am. Chem. Soc*. **2008**, *130*, 9257-9259.

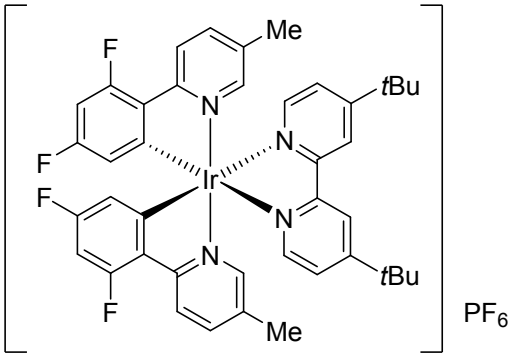
Further purified by preparational High performance liquid chromatography (HPLC) was performed using an Agilent 1260 HPLC System (Santa Clara, CA).The analytical column was reversed phase Phenomenex Kinetex C18-2.6 µm, 4.6 x 50 mm. A gradient elution was used (flow rate 2.0 mL/min), starting with 5% methanol/95% water and progressing to 95% acetonitrile/5% water over a period of 10 minutes. All solvents contained 0.1% formic acid (FA). Compounds were detected by ultraviolet light (UV) absorption at 214, 254 and 300 nm. HPLC solvents were purchased from Sigma Aldrich (St. Louis, MO).

Chiral Preparative HPLC Methods also employed in Purification of Examples. SFC chiral screening was carried out on a Thar Insturments Investigator system. The typical solvents screened were, MeOH, EtOH, IPA, MeOH+0.5%NH_3, EtOH+0.5%NH_3, IPA+0.1%NH_3. Once separation was detected using one of the gradient methods, an isocratic method can be developed, and if necessary, scaled up for separation on the Thar Prep 80 system.

The fluorescence quenching experiments[2] were monitored on a Perkin Elmer Enspire Alpha Multinode Plate Reader by using a Perkin Elmer 96-well plate with black wall and clear bottom.



4CzIPN

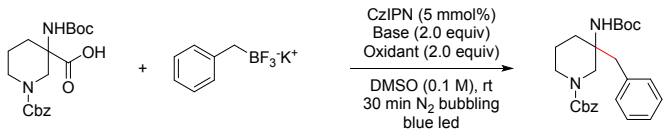


Ir[dF(Me)ppy]$_2$(dtbbpy)PF$_6$

[2]. M. H. ABDEL-KADERP, A. M. BRAU, *J. Chem. SOC., Furuday Trans*. **1985**, *81*, 245-253.

Procedures and method development

Table 1. Optimization of the reaction between **1a** and **1b** to form **1c**

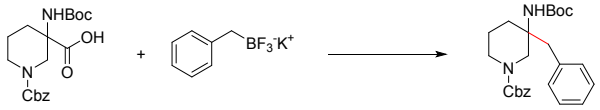


A B C

Entry	Base	Oxidant	Photocatalyst	yield(%)[a]
1	None	$(NH_4)_2S_2O_8$	4-CzIPN	46[b]
2	Na_2CO_3	$(NH_4)_2S_2O_8$	4-CzIPN	46[b]
3	K_2CO_3	$(NH_4)_2S_2O_8$	4-CzIPN	49[b]
4	Cs_2CO_3	$(NH_4)_2S_2O_8$	4-CzIPN	50[b]
5	K_2HPO_4	$(NH_4)_2S_2O_8$	4-CzIPN	31[b]
6	Barton's Base	$(NH_4)_2S_2O_8$	4-CzIPN	26[b]
7	Cs_2CO_3	$K_2S_2O_8$	4-CzIPN	26[b]
8	Cs_2CO_3	BIOAc	4-CzIPN	40[b]
9	Cs_2CO_3	$(NH_4)_2S_2O_8$	4-CzIPN[c]	43[b]
10	Cs_2CO_3	$(NH_4)_2S_2O_8$	$Ir[dF(Me)ppy]_2(dtbbpy)PF_6$	44[b]
11	Cs_2CO_3	$(NH_4)_2S_2O_8$	4-CzIPN	73[d] (65)[e]

[a] General conditions, unless otherwise noted, DMSO (0.1 M), base (2.0 equiv), oxidant (2.0 equiv), PC (5 mmol%), rt, 30 min N_2 bubbling, 2W blue LED. **1c** yields determined by LCMS trace integration compared to the standard solution of **1c**. [b] **1a** (1 equiv), **1b** (1.5 equiv), yield was calculated based on **1a** loading. [c] PC (2.5 mmol %). [d] **1a** (2 equiv), **1b** (1 equiv), yield was calculated based on **1b** loading. [e] isolated yield (0.3 mmol).

Table 2. Control experiments



Entry	Condition	Yield%
1	no light	0
2	no photocatalyst	<5
3	no base	9
4	no oxidant	11

Series of control experiments was conducted, proved that the light, base, oxidant and photocatalyst are essential for this transformation.

Method (standard condition)

To a 4 ml vial equipped with a stirring bar was added photocatalyst (3.9 mg, 5.0 µmol, 5 mmol %.), carboxylic acid (0.2mmol, 2.0 equiv.), potassium trifluoroborate (0.1 mmol, 1.0 equiv.), potassium persulfate (45.6 mg, 0.2 mmol, 2.0 equiv,), cesium carbonate (65.2 mg, 0.2 mmol, 2.0 equiv.), and DMSO (1.0 ml). The mixture was degassed by bubbling industry grade nitrogen using a long-neck syringe for 30 min before sealing with parafilm, and then was put on the reactor, stirred overnight (12-16 h) under the irradiation of Blue LEDs with a fan placed nearby for cooling. The reaction was washed with brine and extracted with EA. The combined organic layer was purified by flash column chromatography on silica gel to afford the pure products.

Mechanistic Investigations

Fluorescence quenching experiments on the model reaction

1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (**1a**) and potassium benzyltrifluoroborate (**1b**) were used in this reaction. Catalyst 4-CzIPN was excited at 455 nm in DMSO solution and the emission intensity was observed from 475- 675 nm. The highest emission intensity is at 551nm. The solvent was degassed by bubbling with N_2 balloon for 30 min. A photocatalyst concentration of 1.0 x 10^{-4} M was used throughout the experiments. First, the emission spectrum of a solution of 4-Czipn in DMSO was collected. Then, different concentration of **1a** or **1b** solution was added to the measured solution and the emission spectrum of the mixture was collected.

1. Fluorescence quenching of 4-CzIPN by carboxylic acid **1a**

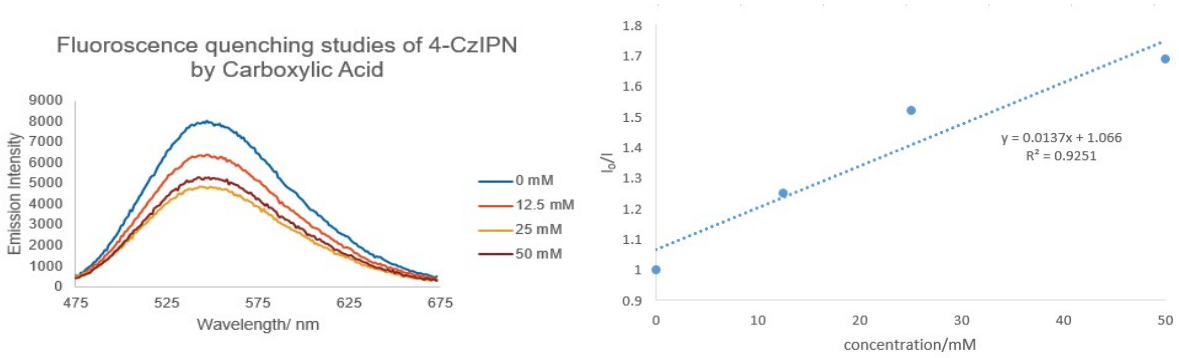


Figure 1.1. Luminescence spectra with different concentration of carboxylic acid **1a** in DMSO.

The emission intensity of PC*-PC fluorescent signal was affected by the gradual increase of the concentration of **1a**.

2. Fluorescence quenching of 4-CzIPN by trifluoroborate **1b**

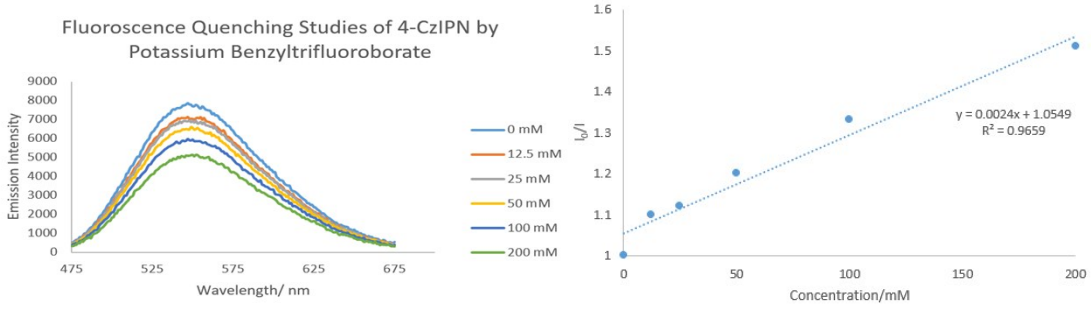


Figure 1.2. Luminescence spectra with different concentration of potassium trifluoroborate **1b** in DMSO.

The emission intensity of PC*-PC fluorescent signal was affected by the gradual increase of the concentration of **1b**.

3. Fluorescence quenching of 4-CzIPN by mixture of **1a** and **1b**.

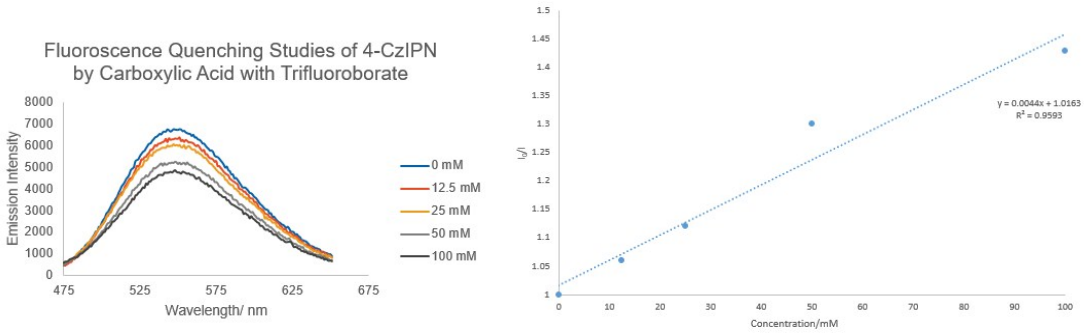


Figure 1.3. Luminescence spectra of 4-CzIPN after the addition of mixture of **1a** and **1b** in DMSO.

The emission intensity of PC*-PC fluorescent signal was affected by the gradual addition of mixture of carboxylic acid **1a** and potassium trifluoroborate **1b** (**1a**: **1b** = 1: 1).

4. Fluorescence quenching of 4-CzIPN by persulfate

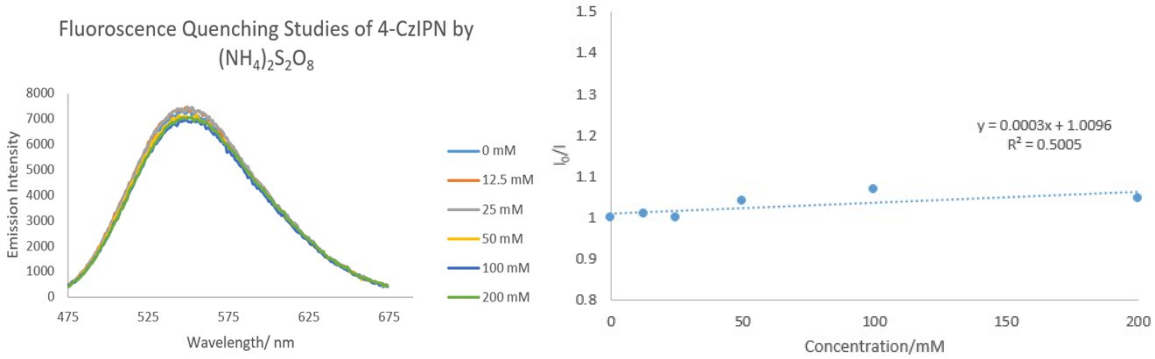


Figure 1.4. Luminescence spectra of 4-CzIPN with different concentration of potassium persulfate in DMSO.

The emission intensity of PC*-PC fluorescent signal was nearly unaffected by the gradual concentration increase of persulfate salt. This demonstrated the persulfate did not act on the PC*. It oxidized the $PC^{\cdot-}$ back to PC instead.

Light om-off reaction for radical chain-transfer process analysis

A vial equipped with magnetic stir bar was charged with carboxylic acid **1a** (0.2 mmol), potassium trifluoroborate **1b** (0.1 mmol), 4-CzIPN（5 ummol), Cs_2CO_3 (0.2 mmol), $(NH_4)_2S_2O_8$ (0.2 mmol) followed by DMSO (1 ml). After N_2 bubbling for 30 min, the vial was put on the photoreactor and irradiated with the bule light. After 1.5 h, a potion of 15 ul mixture was sent to LC-MS to perform the measurement. Then turn off the light until another measurement was carried out after 1.5 h. The process was repeated for 9 h. The yield was calculated by comparing the LC-MS trace to a standard solution.

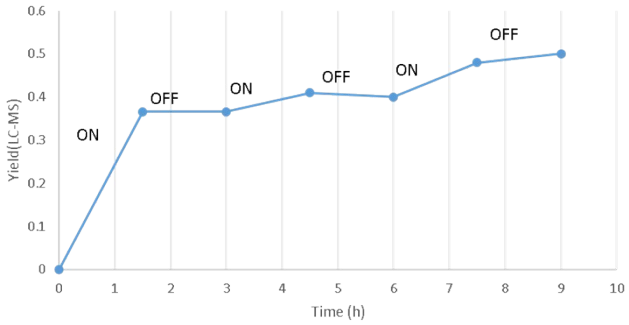
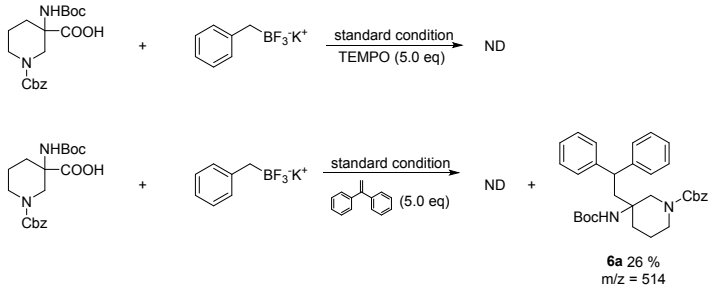


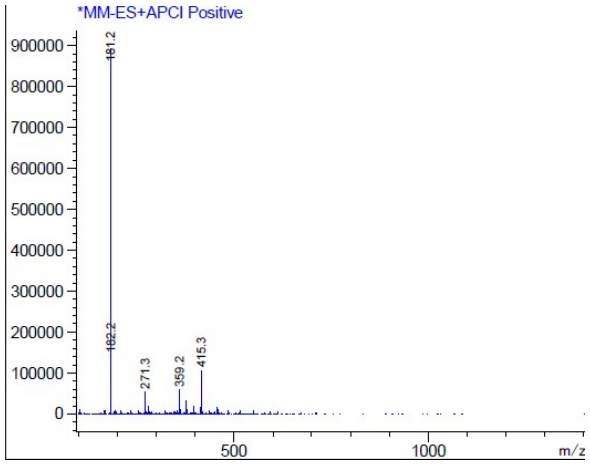
Figure 1.5. light on-off studies

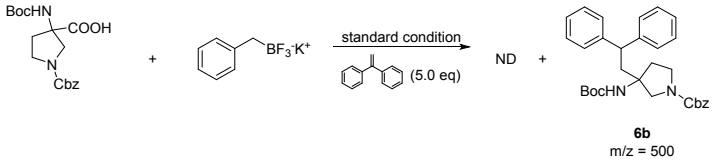
Radical trapping experiments

The results of adding radical scavenger TEMPO and 1, 1-Diphenylthylene was shown in Scheme 1. When TEMPO was added in no product was detected. When 1, 1-diphenylthylene added was detected. Spectrum of **6a** is included in the next session.

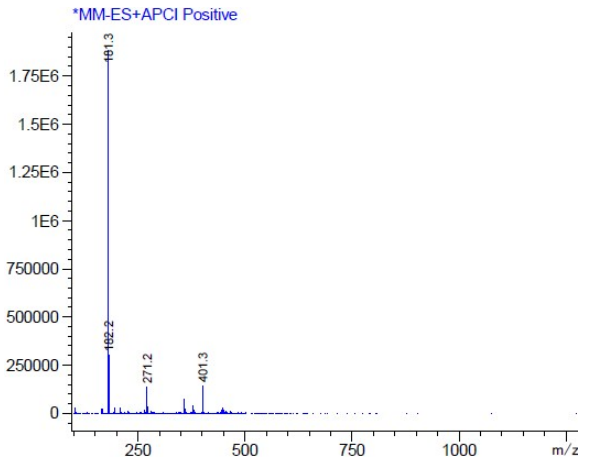


6a 26 %
m/z = 514



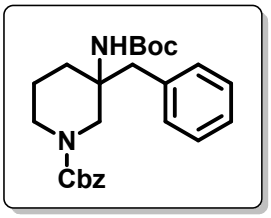


6b
m/z = 500



Scheme 1. Radical trapping experiments

Benzyl 3-benzyl-3-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (1c)



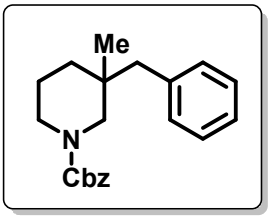
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 65 % yield (27.6 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (dt, *J* = 8.4, 4.0 Hz, 5H), 7.27 (s, 1H), 7.26 – 7.17 (m, 2H), 7.16 – 7.10 (m, 2H), 5.13 (t, *J* = 17.8 Hz, 2H), 4.30 (d, *J* = 94.8 Hz, 1H), 3.99 (d, *J* = 13.4 Hz, 1H), 3.13 (d, *J* = 99.2 Hz, 2H), 2.90 (s, 2H), 1.74 – 1.55 (m, 4H), 1.45 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.53, 136.54, 130.43, 128.45, 128.04, 127.88, 127.56, 126.48, 79.00, 67.11, 54.04, 51.98, 44.34, 40.93, 32.72, 28.43, 20.93.

HR-MS (ESI-TOF) calculated for $C_{25}H_{33}N_2O_4$ $[M+H]^+$: 425.2435, found: 425.2434.

Benzyl 3-benzyl-3-methylpiperidine-1-carboxylate (2a)



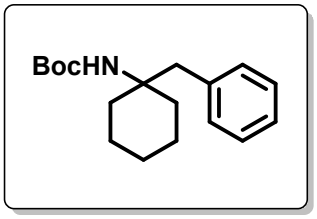
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-methylpiperidine-3-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 65 % yield (13.2 mg) as a pale yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.28 (m, 5H), 7.20 (dd, *J* = 10.1, 3.9 Hz, 3H), 7.12 (s, 2H), 5.14 (s, 2H), 3.63 – 3.51 (m, 1H), 3.41 – 3.10 (m, 3H), 2.56 (s, 2H), 1.62 (s, 2H), 1.45 (ddd, *J* = 13.0, 8.1, 4.7 Hz, 1H), 1.38 – 1.28 (m, 1H), 0.83 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.68, 137.84, 130.55, 128.44, 127.81, 126.05, 66.96, 54.33, 45.70, 44.49, 35.38, 34.56, 22.82, 21.73.

HR-MS (ESI-TOF) calculated for $C_{21}H_{26}NO_2$ $[M+H]^+$: 324.1958, found: 324.1959.

Tert-butyl (1-benzylcyclohexyl) carbamate (2b)



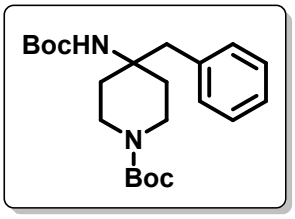
Prepared following general procedure using 1-((tert-butoxycarbonyl) amino) cyclohexane-1-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-30% ethyl acetate in hexanes as the eluent affording the title compound in 39 % yield (11.3 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (dd, *J* = 8.2, 6.0 Hz, 2H), 7.26 – 7.22 (m, 1H), 7.18 – 7.13 (m, 2H), 4.08 (s, 1H), 3.00 (s, 2H), 1.96 (d, *J* = 9.7 Hz, 2H), 1.65 – 1.61 (m, 1H), 1.61 – 1.57 (m, 2H), 1.56 (d, *J* = 5.5 Hz, 2H), 1.50 (s, 9H), 1.46 (d, *J* = 3.4 Hz, 1H), 1.44 – 1.38 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.53, 137.80, 130.69, 127.71, 126.03, 78.54, 54.80, 44.12, 35.03, 28.54, 25.73, 21.54.

HR-MS (ESI-TOF) calculated for $C_{18}H_{28}NO_2$ $[M+H]^+$: 290.2115, found: 290.2112.

Tert-butyl 4-benzyl-4-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (2c)



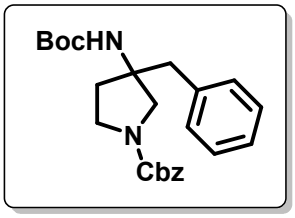
Prepared following general procedure using 1-Boc-(4-N-Boc-amino) piperidine-4-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the title compound in 61 % yield (23.8 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 7.7 Hz, 2H), 7.21 (d, *J* = 14.5 Hz, 1H), 7.11 (d, *J* = 7.2 Hz, 2H), 4.04 (s, 1H), 3.93 – 3.76 (m, 2H), 2.95 (d, *J* = 24.2 Hz, 4H), 2.17 – 1.82 (m, 3H), 1.48 (s, 9H), 1.45 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.78, 136.82, 130.63, 128.00, 126.45, 79.54, 53.47, 39.02, 34.45, 28.48.

HR-MS (ESI-TOF) calculated for $C_{22}H_{35}N_2O_4$ $[M+H]^+$: 391.2591, found: 391.2595.

Benzyl 3-benzyl-3-((tert-butoxycarbonyl) amino) pyrrolidine-1-carboxylate (2d)



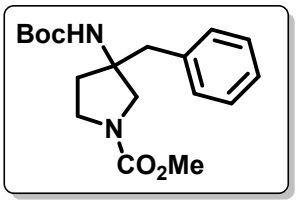
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) pyrrolidine-3-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 67 % yield (27.4 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 4.8 Hz, 4H), 7.34 – 7.30 (m, 1H), 7.28 (d, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 2.1 Hz, 1H), 7.16 – 7.09 (m, 2H), 5.18 – 5.08 (m, 2H), 4.32 (s, 1H), 3.58 – 3.43 (m, 3H), 3.26 – 2.95 (m, 2H), 1.94 (dt, *J* = 12.9, 8.4 Hz, 2H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.73, 137.21, 136.81, 130.05, 128.49, 128.31, 127.97, 126.74, 79.62, 66.87, 61.97, 61.46, 56.56, 55.85, 44.18, 40.04, 35.05, 28.45.

HR-MS (ESI-TOF) calculated for $C_{24}H_{31}N_2O_4$ $[M+H]^+$: 411.2278, found: 411.2277.

Methyl 3-benzyl-3-((tert-butoxycarbonyl) amino) pyrrolidine-1-carboxylate (2e)



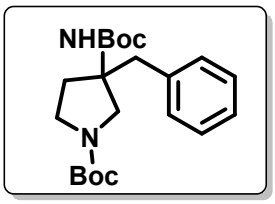
Prepared following general procedure using 3-((tert-butoxycarbonyl) amino)-1-(methoxycarbonyl) pyrrolidine-3-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 51 % yield (17.0 mg) as a yellow solid.

1H NMR (400 MHz, Chloroform-d) δ 7.33 – 7.21 (m, 3H), 7.15 – 7.10 (m, 2H), 4.31 (s, 1H), 3.69 (d, J = 2.5 Hz, 3H), 3.60 – 3.37 (m, 4H), 3.26 – 2.99 (m, 2H), 2.19 – 1.85 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.65, 154.70, 137.22, 130.01, 128.28, 126.70, 82.13, 61.70, 56.26, 52.40, 44.18, 40.06, 34.70, 28.42.

HR-MS (ESI-TOF) calculated for $C_{18}H_{27}N_2O_4$ $[M+H]^+$: 335.1965, found: 335.1968.

Tert-butyl 3-benzyl-3-((tert-butoxycarbonyl) amino) pyrrolidine-1-carboxylate (2f)



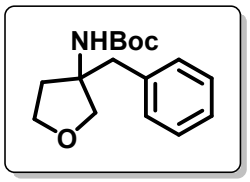
Prepared following general procedure using 1-(tert-butoxycarbonyl)-3-((tert-butoxycarbonyl) amino) pyrrolidine-3-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 42 % yield (15.8 mg) as a white solid.

1H NMR (400 MHz, Chloroform-d) δ 7.29 (dp, J = 18.8, 7.7, 5.8 Hz, 3H), 7.16 – 7.09 (m, 2H), 4.33 (s, 1H), 3.54 – 3.32 (m, 4H), 3.19 (s, 1H), 3.09 – 2.88 (m, 1H), 2.38 (s, 1H), 2.08 – 1.85 (m, 2H), 1.48 (s, 9H), 1.45 (s, 9H).

13C NMR (101 MHz, Chloroform-d) δ 153.69, 136.35, 132.53 – 130.23, 129.01, 127.22, 125.62, 78.47, 60.66, 58.16 – 52.10, 43.27, 42.61, 38.97, 34.03, 28.67, 27.45.

HR-MS (ESI-TOF) calculated for $C_{21}H_{33}N_2O_4$ $[M+H]^+$: 377.2435, found: 377.2437.

Tert-butyl (3-benzyltetrahydrofuran-3-yl) carbamate (2g)



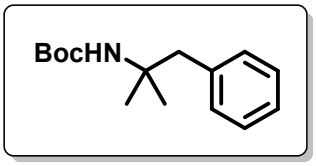
Prepared following general procedure using 1-(tert-butoxycarbonyl)-3-((tert-butoxycarbonyl) amino) pyrrolidine-3-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-50% ethyl acetate in hexanes as the eluent affording the title compound in 40 % yield (11.0 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (dd, *J* = 8.0, 6.1 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.17 – 7.12 (m, 2H), 4.46 (s, 1H), 4.03 – 3.88 (m, 2H), 3.82 (d, *J* = 3.9 Hz, 2H), 3.15 (q, *J* = 13.7 Hz, 2H), 2.06 (t, *J* = 7.0 Hz, 2H), 1.48 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.95, 137.84, 130.08, 128.25, 126.59, 79.43, 67.00, 63.15, 40.92 – 38.74, 37.57, 28.47.

HR-MS (ESI-TOF) calculated for $C_{16}H_{24}NO_3$ $[M+H]^+$: 278.1751, found: 278.1752.

Tert-butyl (2-methyl-1-phenylpropan-2-yl) carbamate (2h)



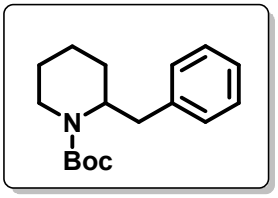
Prepared following general procedure using 2-((tert-butoxycarbonyl) amino)-2-methylpropanoic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-30% ethyl acetate in hexanes as the eluent affording the title compound in 53 % yield (13.2 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.22 (m, 3H), 7.20 – 7.13 (m, 2H), 4.28 (s, 1H), 2.98 (s, 2H), 1.48 (s, 9H), 1.27 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.61, 138.17, 130.57, 127.87, 126.19, 78.76, 52.80, 44.96, 28.51, 27.54.

HR-MS (ESI-TOF) calculated for $C_{15}H_{24}NO_2$ $[M+H]^+$: 250.1802, found: 250.1804.

Tert-butyl 2-benzylpiperidine-1-carboxylate (2i)



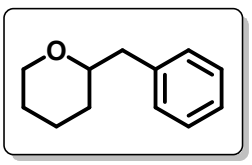
Prepared following general procedure using 1-(tert-butoxycarbonyl) piperidine-2-carboxylic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-30% ethyl acetate in hexanes as the eluent affording the title compound in 61 % yield (16.8 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (t, *J* = 7.4 Hz, 3H), 7.22 – 7.13 (m, 3H), 4.41 (s, 1H), 4.05 (d, *J* = 13.5 Hz, 1H), 2.97 – 2.84 (m, 2H), 2.76 (dd, *J* = 13.3, 8.2 Hz, 1H), 1.64 (dtt, *J* = 14.1, 6.1, 2.9 Hz, 4H), 1.54 (t, *J* = 4.2 Hz, 2H), 1.33 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.90, 139.38, 129.22, 128.34, 126.08, 79.06, 52.86 – 50.94, 38.99, 36.07, 29.68, 28.31, 25.54, 18.94.

HR-MS (ESI-TOF) calculated for $C_{17}H_{26}NO_2$ $[M+H]^+$: 276.1958, found: 276.1961.

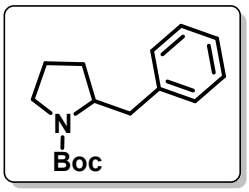
2-benzyltetrahydro-2H-pyran (2j)



Prepared following general procedure using tetrahydro-2H-pyran-2-carboxylic acid (0.4 mmol), Potassium benzyltrifluoroborate (0.2 mmol). Chromatography using 0-30% ethyl acetate in hexanes as the eluent affording the title compound in 43 % yield (15.1 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.21 (d, *J* = 7.3 Hz, 3H), 4.02 – 3.94 (m, 1H), 3.49 (dtd, *J* = 10.7, 6.6, 2.1 Hz, 1H), 3.41 (td, *J* = 11.6, 2.5 Hz, 1H), 2.76 (ddd, *J* = 95.5, 13.6, 6.6 Hz, 2H), 1.81 (dd, *J* = 12.5, 2.8 Hz, 1H), 1.58 (dt, *J* = 12.9, 4.0 Hz, 2H), 1.49 (q, *J* = 2.4 Hz, 1H), 1.43 (dt, *J* = 12.7, 3.8 Hz, 1H), 1.33 – 1.25 (m, 1H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.82, 129.37, 128.19, 126.07, 78.78, 68.63, 43.18, 31.42, 26.03, 23.48.
HR-MS (ESI-TOF) calculated for $C_{12}H_{17}O$ $[M+H]^+$:177.1274, found: 177.1274.

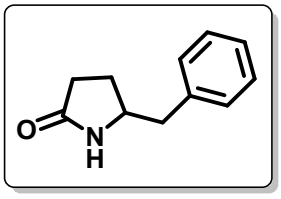
Tert-butyl 2-benzylpyrrolidine-1-carboxylate (2k)



Prepared following general procedure using (tert-butoxycarbonyl)proline (0.4 mmol), Potassium benzyltrifluoroborate (0.2 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the title compound in 37 % yield (19.3 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, *J* = 7.5 Hz, 2H), 7.20 (q, *J* = 7.0 Hz, 3H), 3.99 (s, 1H), 3.39 – 3.28 (m, 2H), 3.09 (d, *J* = 12.5 Hz, 1H), 2.54 (dd, *J* = 13.0, 9.2 Hz, 1H), 1.79 – 1.66 (m, 4H), 1.51 (s, 9H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.55, 139.21, 129.46, 128.33, 126.13, 79.16, 58.78, 46.49, 40.98, 29.51, 28.60, 22.86.
HR-MS (ESI-TOF) calculated for $C_{16}H_{24}NO_2$ $[M+H]^+$:262.1802, found: 261.1803.

5-benzylpyrrolidin-2-one (2l)



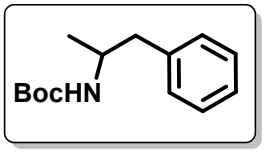
Prepared following general procedure using 5-oxopyrrolidine-2-carboxylic acid (0.4 mmol), Potassium benzyltrifluoroborate (0.2 mmol). Chromatography using 0-30% methanol in Dichloromethane as the eluent affording the title compound in 56 % yield (19.6 mg) as a brown solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (t, *J* = 7.3 Hz, 3H), 7.17 (d, *J* = 7.3 Hz, 2H), 5.62 (s, 1H), 3.88 (dq, *J* = 11.2, 6.1 Hz, 1H), 2.86 (dd, *J* = 13.5, 5.3 Hz, 1H), 2.70 (dd, *J* = 13.4, 8.5 Hz, 1H), 2.43 – 2.21 (m, 3H), 1.92 – 1.79 (m, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.72, 137.52, 128.95, 128.83, 126.90, 55.68, 43.09, 30.01, 27.04.

HR-MS (ESI-TOF) calculated for $C_{11}H_{14}NO$ $[M+H]^+$:176.1070, found: 176.1071.

Tert-butyl (1-phenylpropan-2-yl) carbamate (2m)



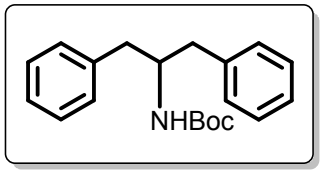
Prepared following general procedure using (tert-butoxycarbonyl) alanine (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the title compound in 57 % yield (13.3 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (t, *J* = 7.2 Hz, 2H), 7.22 (d, *J* = 7.1 Hz, 1H), 7.20 – 7.15 (m, 2H), 4.38 (s, 1H), 3.91 (s, 1H), 2.75 (ddd, *J* = 75.1, 13.5, 6.4 Hz, 2H), 1.43 (s, 9H), 1.08 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.18, 138.23, 129.48, 128.27, 126.26, 79.10, 47.42, 43.00, 28.38, 20.15.

HR-MS (ESI-TOF) calculated for $C_{14}H_{22}NO_2$ $[M+H]^+$:236.1645, found: 236.1643.

Tert-butyl (1, 3-diphenylpropan-2-yl) carbamate (2n)



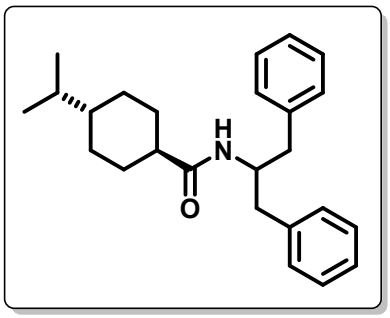
Prepared following general procedure using (tert-butoxycarbonyl) alanine (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the title compound in 62 % yield (19.2 mg) as a colorless solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (dd, *J* = 8.0, 6.6 Hz, 2H), 7.25 – 7.16 (m, 3H), 4.48 – 4.02 (m, 1H), 2.80 (td, *J* = 16.5, 15.2, 6.5 Hz, 2H), 1.36 (s, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.23, 138.15, 129.38, 128.36, 126.33, 79.10, 52.51, 40.20, 28.29.

HR-MS (ESI-TOF) calculated for $C_{20}H_{26}NO_2$ $[M+H]^+$:312.1958, found: 312.1960.

(1r, 4r)-N-(1, 3-diphenylpropan-2-yl)-4-isopropylcyclohexane-1-carboxamide (2o)



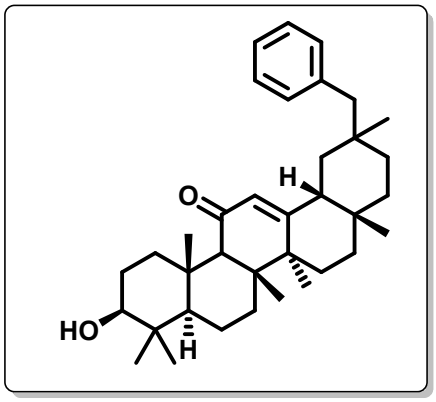
Prepared following general procedure using Nateglinide (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the title compound in 53 % yield (19.1 mg) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 4H), 7.25 – 7.21 (m, 2H), 7.21 – 7.15 (m, 4H), 5.15 (d, *J* = 8.4 Hz, 1H), 4.54 – 4.41 (m, 1H), 2.90 – 2.72 (m, 4H), 1.89 – 1.78 (m, 1H), 1.76 – 1.66 (m, 4H), 1.59 (s, 1H), 1.43 – 1.32 (m, 1H), 1.32 – 1.18 (m, 2H), 1.06 – 0.87 (m, 3H), 0.84 (s, 3H), 0.82 (s, 3H).

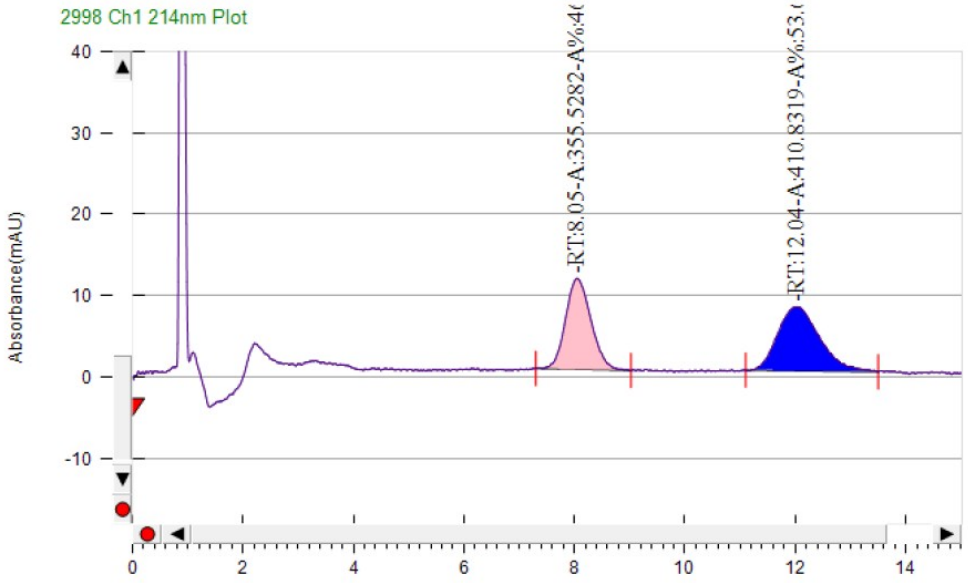
^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.53, 137.95, 129.40, 128.38, 126.44, 50.55, 45.80, 43.20, 39.82, 32.74, 29.65, 28.97, 19.70.

HR-MS (ESI-TOF) calculated for $C_{25}H_{34}NO$ $[M+H]^{+}$:364.2635, found: 364.2639.

(2S, 4aR, 6aS, 6bR, 8aR, 10S, 12aS, 14bR)-2-benzyl-10-hydroxy-2,4a,6a,6b,9,9,12a-heptamethyl-1, 3, 4, 4a, 5, 6, 6a, 6b, 7, 8, 8a, 9, 10, 11, 12, 12a, 12b, 14b -octadecahydropicen-13 (2H)-one (2p)



Prepared following general procedure using Enoxolone (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the two title compounds in 60 % total yield (31 mg) as two white solid. (P1: P2 = 1:1)



Peak #	Ret. Time	Area	Area Sum	Area %	SelectivityPeak1	SelectivityPeak2	ResolutionPeak1	ResolutionPeak2
1	8.05 min	355.5282		46.3918	1	1.4959	0	3.6124
2	12.04 min	410.8319	766.36	53.6082	0.6685	1	-3.6124	0

P1:**^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.31 – 7.26 (m, 1H), 7.25 (s, 1H), 7.23 – 7.17 (m, 1H), 7.15 – 7.09 (m, 2H), 5.66 (s, 1H), 3.22 (dd, *J* = 11.0, 5.3 Hz, 1H), 2.78 (dt, *J* = 13.4, 3.6 Hz, 1H), 2.70 – 2.52 (m, 2H), 2.43 – 2.30 (m, 2H), 2.10 (td, *J* = 13.7, 4.5 Hz, 1H), 1.85 (td, *J* = 13.6, 4.7 Hz, 1H), 1.74 – 1.55 (m, 8H), 1.47 – 1.39 (m, 3H), 1.35 (s, 6H), 1.15 (d, *J* = 2.9 Hz, 6H), 1.00 (s, 4H), 0.95 (s, 4H), 0.80 (d, *J* = 8.3 Hz, 6H), 0.72 – 0.63 (m, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.22, 170.17, 138.97, 130.38, 128.15, 127.83, 125.92, 78.75, 61.78, 54.90, 53.40, 47.06, 45.45, 43.40, 42.58, 41.15, 39.09, 37.06, 36.14, 34.68, 32.94, 32.75, 32.43, 29.76, 28.86, 28.08, 27.29, 26.66, 26.46, 23.46, 18.71, 17.48, 16.35, 15.56.

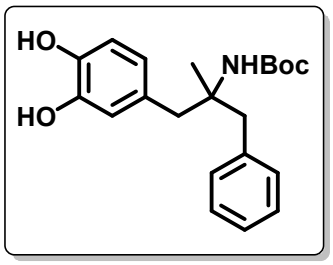
HR-MS (ESI-TOF) calculated for $C_{36}H_{53}O_2$ $[M+H]^+$:517.4040, found: 517.4036.

P2: **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.28 – 7.24 (m, 2H), 7.22 – 7.17 (m, 1H), 7.11 – 7.06 (m, 2H), 5.55 (s, 1H), 3.22 (dd, *J* = 10.6, 5.7 Hz, 1H), 2.79 (d, *J* = 13.5 Hz, 1H), 2.48 (s, 2H), 2.34 (s, 1H), 2.17 – 2.08 (m, 1H), 1.96 – 1.85 (m, 1H), 1.83 – 1.72 (m, 2H), 1.62 (dtd, *J* = 14.5, 11.7, 10.6, 3.4 Hz, 6H), 1.46 – 1.37 (m, 4H), 1.31 (s, 3H), 1.30 – 1.25 (m, 1H), 1.12 (d, *J* = 5.3 Hz, 8H), 1.00 (s, 4H), 0.89 (s, 4H), 0.82 (d, *J* = 12.7 Hz, 6H), 0.69 (dd, *J* = 11.6, 1.9 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 200.32, 170.47, 138.14, 130.65, 128.13, 127.64, 125.94, 78.80, 61.78, 54.95, 51.97, 47.20, 45.39, 43.29, 42.98, 39.13, 37.08, 35.99, 34.90, 32.73, 32.48, 31.91, 28.67, 28.09, 27.30, 26.28, 23.38, 21.56, 18.73, 17.48, 16.33, 15.54.

HR-MS (ESI-TOF) calculated for $C_{36}H_{53}O_2$ $[M+H]^+$:517.4040, found: 517.4033.

Tert-butyl (1-(3, 4-dihydroxyphenyl)-2-methyl-3-phenylpropan-2-yl) carbamate (2q)



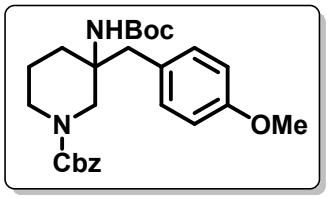
Prepared following general procedure using 2-((tert-butoxycarbonyl) amino)-3-(3, 4-dihydroxyphenyl)-2-methylpropanoic acid (0.2 mmol), Potassium benzyltrifluoroborate (0.1 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the title compounds in 45% total yield (16 mg) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (s, 1H), 7.24 (d, *J* = 7.5 Hz, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 2H), 6.63 (d, *J* = 9.0 Hz, 2H), 3.92 (d, *J* = 6.8 Hz, 2H), 3.14 – 3.01 (m, 2H), 1.56 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.72, 143.42, 142.00, 140.92, 132.63, 128.69, 128.45, 126.02, 125.38, 117.38, 117.14, 60.59, 38.87, 38.21, 28.34, 22.99.

HR-MS (ESI-TOF) calculated for $C_{21}H_{28}NO_4$ $[M+H]^+$:358.2013, found: 358.2011.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-methoxybenzyl) piperidine-1-carboxylate (3a)



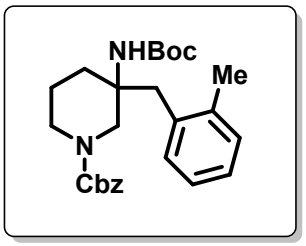
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), Potassium (4-methoxybenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 68 % yield (30.8 mg) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (q, *J* = 6.1 Hz, 5H), 7.09 – 6.97 (m, 2H), 6.86 – 6.75 (m, 2H), 5.13 (t, *J* = 18.3 Hz, 2H), 4.51 – 3.85 (m, 3H), 3.79 (s, 3H), 3.12 – 2.66 (m, 4H), 1.77 – 1.54 (m, 3H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.29, 154.56, 136.65, 131.33, 128.59, 113.48, 78.97, 67.12, 55.18, 53.94, 51.91, 44.35, 40.54, 32.70, 28.44, 20.96.

HR-MS (ESI-TOF) calculated for $C_{26}H_{35}N_2O_2$ $[M+H]^+$:455.2540, found: 455.2541.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-methylbenzyl) piperidine-1-carboxylate (3b)



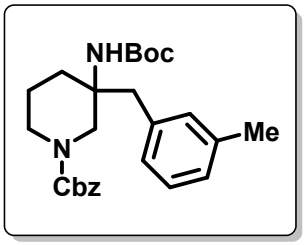
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), Potassium (2-methylbenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 33 % yield (14.4 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.32 (dq, J = 14.3, 7.4 Hz, 5H), 7.14 (d, J = 2.7 Hz, 2H), 7.13 – 7.07 (m, 2H), 5.13 (t, J = 17.4 Hz, 2H), 4.48 (d, J = 106.0 Hz, 1H), 4.26 – 3.89 (m, 2H), 3.08 (s, 2H), 2.73 (td, J = 12.3, 3.2 Hz, 2H), 2.35 (d, J = 7.1 Hz, 3H), 1.65 (ddt, J = 12.7, 8.4, 4.2 Hz, 3H), 1.46 (d, J = 5.7 Hz, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.66, 154.50, 136.88 (d, *J* = 47.2 Hz), 134.89, 131.60, 130.53, 128.46, 127.73, 126.55, 125.46, 79.03, 67.14, 56.47 – 54.66 (m), 52.18, 44.37, 38.32, 31.82, 28.45, 21.09, 20.35.

HR-MS (ESI-TOF) calculated for $C_{26}H_{35}N_2O_4$ $[M+H]^+$:439.2591, found: 439.2591.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(3-methylbenzyl) piperidine-1-carboxylate (3c)



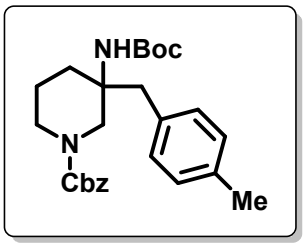
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), Potassium (3-methylbenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 45 % yield (19.7 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (q, *J* = 6.9, 6.5 Hz, 4H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.97 – 6.89 (m, 2H), 5.13 (t, *J* = 18.9 Hz, 2H), 4.54 – 4.07 (m, 2H), 4.00 (d, *J* = 13.2 Hz, 2H), 2.95 (d, *J* = 52.0 Hz, 4H), 2.32 (s, 3H), 1.98 – 1.52 (m, 4H), 1.46 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.38, 154.52, 137.50, 136.50, 131.24, 128.43, 127.96, 78.94, 67.10, 54.12, 52.28, 44.41, 41.42, 32.79, 28.45, 21.36.

HR-MS (ESI-TOF) calculated for $C_{26}H_{35}N_2O_4$ $[M+H]^+$:439.2591, found: 439.2591.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-methylbenzyl) piperidine-1-carboxylate (3d)



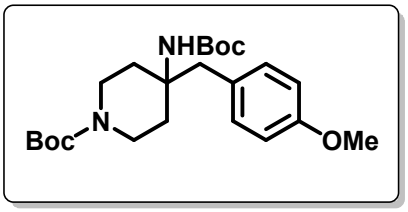
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), Potassium (4-methylbenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 52 % yield (22.6 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.26 (m, 5H), 7.07 (dd, *J* = 8.1, 2.6 Hz, 2H), 7.01 (dd, *J* = 8.1, 2.7 Hz, 2H), 5.20 – 4.96 (m, 2H), 4.54 – 4.14 (m, 1H), 4.14 – 3.82 (m, 2H), 3.05 (d, *J* = 129.0 Hz, 4H), 2.32 (s, 3H), 1.93 – 1.51 (m, 3H), 1.45 (s, 10H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.64, 154.52, 136.66, 135.97, 133.28, 130.30, 128.75, 128.43, 127.71, 78.95, 67.11, 54.15, 52.68, 44.35, 41.01, 32.70, 28.44, 21.00.

HR-MS (ESI-TOF) calculated for $C_{26}H_{35}N_2O_4$ $[M+H]^+$:439.2591, found: 439.2596.

Tert-butyl 4-((tert-butoxycarbonyl) amino)-4-(4-methoxybenzyl) piperidine-1-carboxylate (3e)



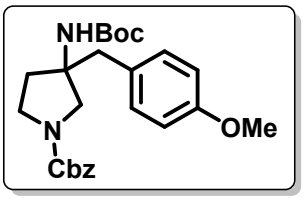
Prepared following general procedure using 1-(tert-butoxycarbonyl)-4-((tert-butoxycarbonyl) amino) piperidine-4-carboxylic acid (0.2 mmol), Potassium (4-methoxybenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 61 % yield (25.6 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.02 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 4.03 (s, 1H), 3.84 (s, 2H), 3.79 (s, 3H), 3.08 – 2.78 (m, 4H), 1.95 (s, 2H), 1.64 – 1.51 (m, 2H), 1.48 (s, 9H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.29, 154.88, 131.48, 128.79, 113.40, 79.50, 55.22, 53.66, 44.43, 39.11, 34.36, 28.45.

HR-MS (ESI-TOF) calculated for $C_{23}H_{37}N_2O_5$ $[M+H]^+$:421.2697, found: 421.2703.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-methoxybenzyl) pyrrolidine-1-carboxylate (3f)



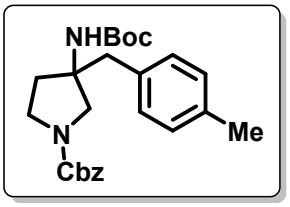
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) pyrrolidine-3-carboxylic acidd (0.2 mmol), Potassium (4-methoxybenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 58 % yield (25.5 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.28 (m, 5H), 7.04 (t, *J* = 8.0 Hz, 2H), 6.85 – 6.79 (m, 2H), 5.19 – 5.06 (m, 2H), 4.31 (s, 1H), 3.79 (s, 3H), 3.66 – 3.42 (m, 4H), 3.24 – 2.86 (m, 2H), 2.08 – 1.87 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.46, 154.70, 136.80, 130.95, 129.21, 128.46, 127.93, 113.70, 79.54, 66.83, 62.06, 61.55, 56.47, 55.73, 55.23, 50.20, 44.17, 39.14, 34.67, 28.42.

HR-MS (ESI-TOF) calculated for $C_{25}H_{33}N_2O_5$ $[M+H]^+$:441.2384, found: 441.2378.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-methylbenzyl) pyrrolidine-1-carboxylate (3g)



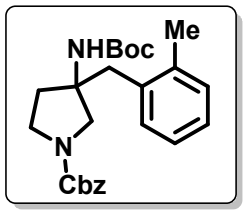
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) pyrrolidine-3-carboxylic acidd (0.2 mmol), Potassium (4-methylbenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 58 % yield (25.5 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.28 (m, 5H), 7.10 (d, *J* = 7.7 Hz, 2H), 7.01 (t, *J* = 6.9 Hz, 2H), 5.19 – 5.07 (m, 2H), 4.32 (s, 1H), 3.68 – 3.43 (m, 4H), 3.20 – 2.91 (m, 2H), 2.33 (s, 4H), 2.09 – 1.87 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.70, 136.80, 136.27, 134.04, 129.90, 128.97, 128.45, 127.92, 79.53, 66.81, 61.98, 61.46, 56.50, 55.78, 44.16, 39.55, 34.95, 28.42, 21.01.

HR-MS (ESI-TOF) calculated for $C_{25}H_{33}N_2O_4$ $[M+H]^+$:425.2435, found: 425.2433.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-methylbenzyl) pyrrolidine-1- carboxylate (3h)



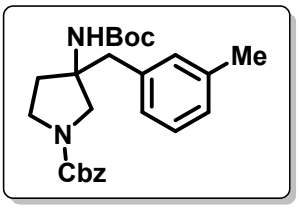
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) pyrrolidine-3-carboxylic acidd (0.2 mmol), Potassium (2-methylbenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 47 % yield (19.9 mg) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.27 (m, 5H), 7.18 – 7.02 (m, 4H), 5.17 – 5.04 (m, 2H), 4.49 (d, *J* = 19.0 Hz, 1H), 3.76 – 3.40 (m, 4H), 3.26 – 3.01 (m, 2H), 2.33 (d, *J* = 4.6 Hz, 3H), 1.96 (dq, *J* = 16.0, 8.1 Hz, 1H), 1.46 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.62, 137.20, 136.77, 135.32, 131.30, 130.67, 128.44, 127.91, 126.77, 125.63, 79.61, 66.84, 62.53, 61.95, 55.69, 55.08, 44.12, 36.67, 34.41, 28.40, 19.97.

HR-MS (ESI-TOF) calculated for $C_{25}H_{33}N_2O_4$ $[M+H]^+$:425.2435, found: 425.2441.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(3-methylbenzyl) pyrrolidine-1-carboxylate (3i)



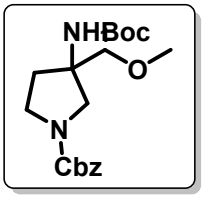
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) pyrrolidine-3-carboxylic acidd (0.2 mmol), Potassium (3-methylbenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 56 % yield (23.6 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.27 (m, 5H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 6.93 (d, *J* = 5.9 Hz, 2H), 5.22 – 5.06 (m, 2H), 4.32 (s, 1H), 3.75 – 3.40 (m, 4H), 3.25 – 2.88 (m, 2H), 2.32 (s, 3H), 2.12 – 1.87 (m, 2H), 1.48 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.71, 137.80, 136.79, 130.87, 128.46, 128.37, 127.42, 127.03, 79.50, 66.82, 61.91, 61.43, 56.59, 55.84, 52.35, 44.22, 39.83, 34.80, 28.44, 21.37.

HR-MS (ESI-TOF) calculated for $C_{25}H_{33}N_2O_4$ $[M+H]^+$:425.2435, found: 425.2433.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(methoxymethyl) pyrrolidine-1-carboxylate (3j)



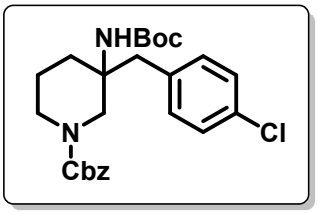
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) pyrrolidine-3-carboxylic acidd (0.2 mmol), Potassium (3-methylbenzyl) trifluoroborate (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 40 % yield (14.4 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.28 (m, 5H), 5.12 (s, 2H), 3.68 – 3.42 (m, 6H), 3.36 (s, 3H), 2.31 (dt, *J* = 36.4, 6.7 Hz, 2H), 1.43 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.82, 136.75, 128.55, 128.44, 127.90, 79.76, 73.78, 66.84, 61.72, 60.98, 59.34, 53.45, 52.74, 44.10, 29.68, 28.32.

HR-MS (ESI-TOF) calculated for $C_{19}H_{29}N_2O_5$ $[M+H]^+$:365.2071, found: 365.2071.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-chlorobenzyl) piperidine-1-carboxylate (4a)



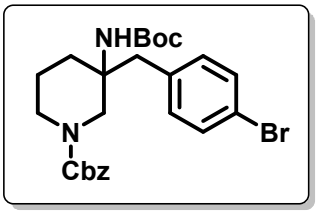
Prepared following general procedure using 1 - ((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(4-chlorophenyl) acetic acid (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 43 % yield (19.6 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (dd, *J* = 11.4, 6.5 Hz, 5H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.09 – 6.99 (m, 2H), 5.19 – 5.00 (m, 2H), 4.50 – 3.80 (m, 3H), 3.37 – 2.35 (m, 4H), 1.73 – 1.52 (m, 3H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.65, 154.49, 136.53, 134.93, 132.46, 131.68, 128.48, 128.08, 79.19, 67.22, 54.09, 51.74, 44.15, 40.26, 32.78, 28.42, 20.91.

HR-MS (ESI-TOF) calculated for $C_{25}H_{32}ClN_2O_4$ $[M+H]^+$:459.2045, found: 459.2046.

Benzyl 3-(4-bromobenzyl)-3-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (4b)



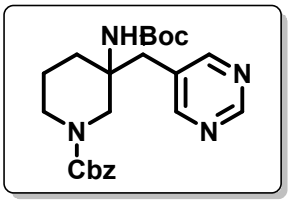
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(4-bromophenyl) acetic acid (0.1 mmol). Chromatography using 0-60% ethyl acetate in hexanes as the eluent affording the title compound in 45 % yield (22.6 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 8.2 Hz, 2H), 7.36 – 7.26 (m, 5H), 6.99 (d, *J* = 8.0 Hz, 2H), 5.26 – 4.95 (m, 2H), 4.53 – 3.72 (m, 3H), 3.32 – 2.38 (m, 5H), 1.80 – 1.51 (m, 3H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.45, 136.51, 135.43, 132.05, 131.11, 128.02, 127.96, 120.55, 79.17, 67.20, 51.91, 44.34, 40.28, 32.75, 29.66, 28.40, 20.92.

HR-MS (ESI-TOF) calculated for $C_{25}H_{32}BrN_2O_4$ $[M+H]^+$: 503.1540, found: 503.1536.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(pyrimidin-5-ylmethyl) piperidine-1- carboxylate (4c)



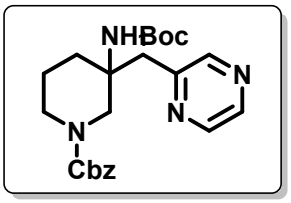
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(pyrimidin-5-yl) acetic acid (0.1 mmol). Chromatography using 0-100% ethyl acetate in hexanes as the eluent affording the title compound in 50 % yield (21.3 mg) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.10 (s, 1H), 8.53 (s, 2H), 7.32 (td, *J* = 10.0, 8.6, 4.8 Hz, 5H), 5.24 – 4.98 (m, 2H), 4.58 – 4.18 (m, 1H), 4.15 – 3.76 (m, 2H), 3.39 – 2.35 (m, 4H), 1.62 (dd, *J* = 10.0, 5.2 Hz, 3H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.93, 156.93, 154.43, 136.38, 130.28, 128.49, 127.88, 79.84, 67.36, 53.75, 44.27, 35.68, 32.67, 28.32, 20.97.

HR-MS (ESI-TOF) calculated for $C_{23}H_{31}N_4O_4$ $[M+H]^+$: 427.2340, found: 427.2345.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(pyrazin-2-ylmethyl) piperidine-1-carboxylate (4d)



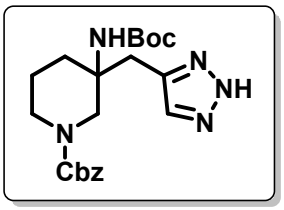
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(pyrazin-2-yl) acetic acid (0.1 mmol). Chromatography using 0-100% ethyl acetate in hexanes as the eluent affording the title compound in 41 % yield (17.4 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 – 8.38 (m, 3H), 7.32 (q, *J* = 7.1, 6.6 Hz, 5H), 5.11 (q, *J* = 12.7 Hz, 2H), 4.74 – 4.39 (m, 1H), 4.36 – 3.85 (m, 2H), 3.05 (d, *J* = 59.1 Hz, 3H), 2.45 – 1.77 (m, 3H), 1.64 (d, *J* = 10.7 Hz, 2H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.53, 153.56, 146.05, 143.71, 142.58, 136.55, 128.48, 127.82, 79.42, 67.25, 56.25, 45.93, 32.22, 29.68, 28.34, 22.72.

HR-MS (ESI-TOF) calculated for $C_{23}H_{31}N_4O_4$ $[M+H]^+$: 427.2340, found: 427.2343.

Benzyl 3-((2H-1, 2, 3-triazol-4-yl) methyl)-3-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (4e)



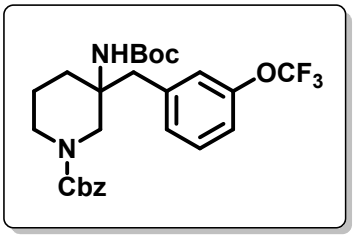
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(2H-1, 2, 3-triazol-4-yl) acetic acid (0.1 mmol). Chromatography using 0-100% ethyl acetate in hexanes as the eluent affording the title compound in 32 % yield (13.3 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (s, 1H), 7.44 – 7.28 (m, 5H), 5.79 (s, 2H), 5.23 – 5.08 (m, 2H), 4.91 – 4.18 (m, 1H), 3.79 (q, *J* = 8.3, 6.3 Hz, 1H), 3.38 (d, *J* = 167.2 Hz, 4H), 2.66 – 2.13 (m, 1H), 1.66 (d, *J* = 18.8 Hz, 3H), 1.38 (s, 8H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.39, 154.84, 149.29, 136.27, 128.17, 79.91, 67.72, 53.43, 50.18, 44.47, 33.35, 28.27, 27.96, 21.95.

HR-MS (ESI-TOF) calculated for $C_{21}H_{30}N_5O_4$ $[M+H]^+$: 416.2292, found: 416.2297.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(3-(trifluoromethoxy) benzyl) piperidine-1-carboxylate (4f)



Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(3-(trifluoromethoxy) phenyl) acetic acid (0.1 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the title compound in 32 % yield (16.3 mg) as a yellow syrup.

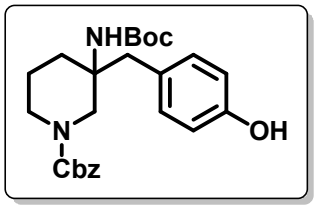
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 5H), 7.10 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 7.00 (s, 1H), 5.20 – 4.99 (m, 2H), 4.51 – 3.85 (m, 3H), 3.45 – 2.45 (m, 4H), 1.63 (ddd, *J* = 23.1, 11.0, 5.5 Hz, 3H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.50, 149.05, 138.80, 136.55, 129.21, 128.82, 128.47, 127.80, 123.01, 122.03, 119.03, 79.32, 67.23, 55.28, 51.67, 44.37, 41.00, 32.85, 29.68, 28.35, 21.54 – 20.57 (m).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -57.69.

HR-MS (ESI-TOF) calculated for $C_{26}H_{32}F_3N_2O_5$ $[M+H]^+$: 509.2258, found: 509.2256.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-hydroxybenzyl) piperidine-1-carboxylate (4g)



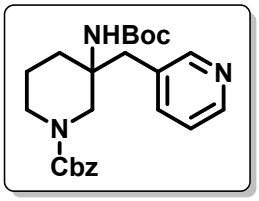
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(4-hydroxyphenyl) acetic acid (0.1 mmol). Chromatography using 0-40% ethyl acetate in hexanes as the eluent affording the title compound in 30 % yield (13.2 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (dd, *J* = 10.0, 4.3 Hz, 5H), 7.01 – 6.92 (m, 2H), 6.76 – 6.63 (m, 2H), 5.13 (t, *J* = 16.4 Hz, 2H), 4.61 – 4.12 (m, 1H), 3.97 (s, 2H), 2.84 (d, *J* = 34.9 Hz, 4H), 1.73 – 1.50 (m, 3H), 1.43 (d, *J* = 6.4 Hz, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.54, 136.54, 131.46, 128.48, 127.96, 114.97, 79.05, 68.15, 54.28, 52.05, 44.31, 41.02, 32.07, 29.68, 28.46, 21.28.

HR-MS (ESI-TOF) calculated for $C_{25}H_{33}F_3N_2O_5$ $[M+H]^+$: 441.2384, found: 441.2387.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(pyridin-3-ylmethyl) piperidine-1-carboxylate (4i)



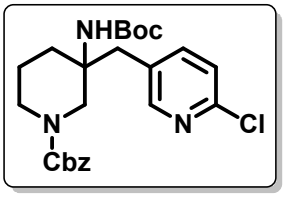
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.4 mmol), 2-(pyridin-3-yl) acetic acid (0.2 mmol). Chromatography using 0-80% ethyl acetate in hexanes as the eluent affording the title compound in 23 % yield (19.5 mg) as a brown solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.52 (t, *J* = 4.0 Hz, 1H), 8.43 (d, *J* = 2.8 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.42 – 7.30 (m, 5H), 7.28 (s, 1H), 5.25 – 4.99 (m, 2H), 4.35 (d, *J* = 83.0 Hz, 1H), 4.00 (d, *J* = 12.9 Hz, 2H), 2.99 (q, *J* = 46.9, 26.0 Hz, 5H), 1.77 – 1.56 (m, 2H), 1.47 (d, *J* = 3.7 Hz, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.45, 150.81, 147.57, 138.02, 136.51, 128.48, 127.82, 125.89, 123.30, 79.45, 67.26, 53.74, 52.01, 44.34, 38.10, 32.85, 28.39, 21.31.

HR-MS (ESI-TOF) calculated for $C_{24}H_{32}N_3O_4$ $[M+H]^{+.}$426.2387, found: 426.2385.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-((6-chloropyridin-3-yl) methyl) piperidine-1-carboxylate (4j)



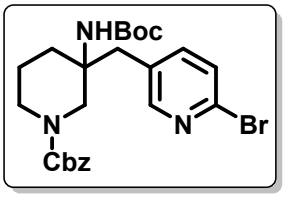
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.1 mmol), 2-(6-chloropyridin-3-yl) acetic acid (0.2 mmol). Chromatography using 0-100% ethyl acetate in hexanes as the eluent affording the title compound in 43 % yield (19.7 mg) as a brown syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 2.4 Hz, 1H), 7.41 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.38 – 7.27 (m, 5H), 7.23 (d, *J* = 8.2 Hz, 1H), 5.20 – 4.99 (m, 2H), 4.53 – 3.75 (m, 3H), 3.38 – 2.84 (m, 4H), 1.87 (s, 1H), 1.70 – 1.50 (m, 2H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.43, 150.86, 149.80, 140.54, 136.43, 131.06, 128.51, 127.87, 123.71, 79.61, 67.33, 53.88, 51.78, 44.32, 37.37, 32.84, 29.67, 28.38, 22.29.

HR-MS (ESI-TOF) calculated for $C_{24}H_{31}ClN_3O_4$ $[M+H]^+$: 460.1998, found: 460.2000.

Benzyl 3-((6-bromopyridin-3-yl) methyl)-3-((tert-butoxycarbonyl) amino) piperidine -1-carboxylate (4k)



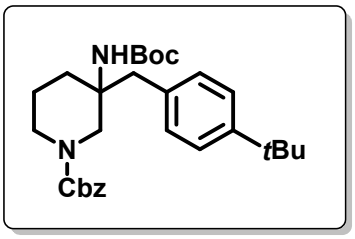
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(6-bromopyridin-3-yl) acetic acid (0.1 mmol). Chromatography using 0-100% ethyl acetate in hexanes as the eluent affording the title compound in 31 % yield (15.5 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.59 (d, *J* = 7.3 Hz, 1H), 7.91 – 7.61 (m, 1H), 7.33 (td, *J* = 6.9, 2.3 Hz, 5H), 7.14 (d, *J* = 24.9 Hz, 1H), 5.18 – 5.00 (m, 2H), 4.86 – 4.56 (m, 1H), 4.26 – 3.80 (m, 2H), 3.54 – 2.97 (m, 4H), 1.63 (dt, *J* = 14.4, 5.2 Hz, 2H), 1.40 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.54, 148.60, 140.21, 139.78, 136.52, 128.48, 128.00, 127.66, 119.08, 79.30, 67.25, 54.30, 51.72, 44.27, 41.98, 32.45, 30.91, 28.37, 21.13.

HR-MS (ESI-TOF) calculated for $C_{24}H_{31}BrN_3O_4$ $[M+H]^+$: 504.1492, found: 504.1496.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-(tert-butyl) benzyl) piperidine-1-carboxylate (4o)



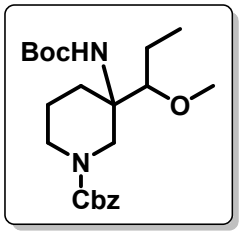
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.1 mmol), 2-(4-(tert-butyl) phenyl) acetic acid (0.2 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound in 68% yield (32.7 mg) as a white solid.

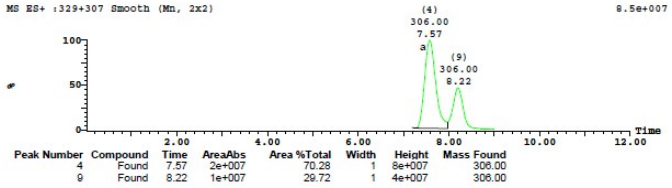
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 6.9 Hz, 5H), 7.24 (s, 2H), 7.03 (d, *J* = 8.1 Hz, 2H), 5.21 – 4.94 (m, 2H), 4.50 – 3.84 (m, 3H), 3.33 – 2.49 (m, 4H), 1.60 (dd, *J* = 27.7, 15.9 Hz, 3H), 1.44 (s, 9H), 1.29 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.52, 149.21, 136.64, 133.28, 130.11, 128.46, 127.77, 124.95, 78.97, 67.16, 55.80, 44.40, 41.51, 40.38, 34.36, 32.85, 31.35, 29.67, 28.46, 20.95.

HR-MS (ESI-TOF) calculated for $C_{29}H_{41}N_2O_4$ $[M+H]^+$: 481.3061, found: 481.3061.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(1-methoxypropyl) piperidine-1-carboxylate (4p)





Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-methoxybutanoic acid (0.1 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound P_1 and P_2 in 32 % total yield (12.9 mg) as two yellow solids. (P1:P2 = 2.3:1)

P1: **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.40 – 7.27 (m, 5H), 5.27 – 4.99 (m, 2H), 4.38 (dd, *J* = 44.0, 30.0 Hz, 2H), 4.16 – 3.94 (m, 1H), 3.47 (s, 3H), 3.15 – 2.70 (m, 2H), 2.12 – 1.77 (m, 2H), 1.58 (tdd, *J* = 16.3, 8.3, 4.9 Hz, 4H), 1.39 (s, 9H), 1.00 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.18, 136.79, 128.46, 127.81, 84.83, 80.80, 67.13, 61.34, 57.85, 47.52, 44.36, 29.68, 28.38, 27.40, 22.98, 11.44.

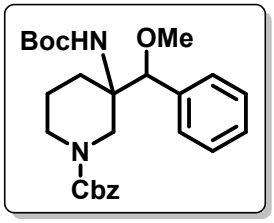
HR-MS (ESI-TOF) calculated for $C_{22}H_{35}N_2O_5$ [M+H] $^+$: 407.2540, found: 407.2543.

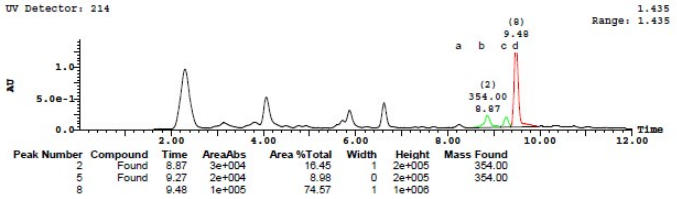
P2: **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.39 – 7.28 (m, 5H), 5.22 – 5.07 (m, 2H), 4.71 (d, *J* = 94.9 Hz, 1H), 4.01 – 3.78 (m, 2H), 3.58 – 3.37 (m, 4H), 3.16 – 2.84 (m, 2H), 2.68 – 2.49 (m, 1H), 1.94 (dt, *J* = 43.3, 6.5 Hz, 2H), 1.75 – 1.57 (m, 3H), 1.40 (s, 9H), 1.01 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.60, 136.66, 128.51, 128.02, 127.74, 86.23, 79.01, 67.26, 61.22, 58.95, 47.96, 44.60, 29.67, 28.37, 28.20, 22.78, 11.42.

HR-MS (ESI-TOF) calculated for $C_{22}H_{35}N_2O_5$ [M+H] $^+$: 407.2540, found: 407.2542.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(methoxy(phenyl)methyl)piperidine-1-carboxylate (4q)





Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
2	Found	8.87	3e+004	16.45	1	2e+005	354.00
5	Found	9.27	2e+004	8.98	0	2e+005	354.00
8		9.48	1e+005	74.57	1	1e+006	

Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-methoxy-2-phenylacetic acid (0.1 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound P_1 and P_2 in 44 % total yield (20.0 mg) as two yellow solids. (P1:P2=1.8:1)

P1:**^{1}H NMR (400 MHz, Chloroform-d)** δ 7.37 (t, J = 11.7 Hz, 4H), 7.30 (q, J = 4.8, 4.1 Hz, 6H), 5.39 – 4.96 (m, 2H), 4.96 – 4.44 (m, 3H), 4.32 – 3.93 (m, 2H), 3.23 (s, 3H), 2.91 – 2.12 (m, 1H), 1.64 (d, J = 52.7 Hz, 2H), 1.43 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.14, 154.60, 137.18, 128.36, 127.76, 83.24, 79.10, 67.05, 57.33 (d, *J* = 61.0 Hz), 48.21, 44.03, 29.68, 28.39, 27.40, 20.20.

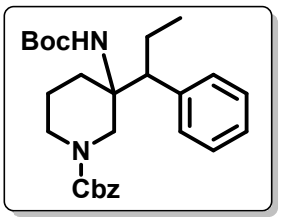
HR-MS (ESI-TOF) calculated for $C_{26}H_{35}N_2O_5$ [M+H] $^+$: 455.2540, found: 455.2541.

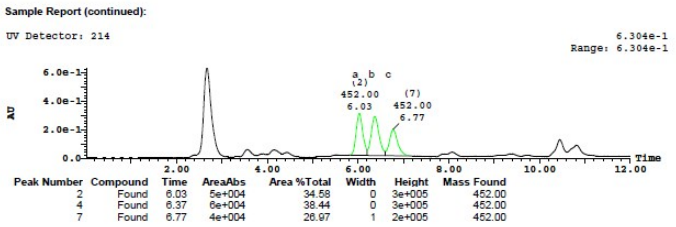
P2: **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.37 – 7.28 (m, 6H), 7.27 (d, *J* = 2.2 Hz, 2H), 7.25 (d, *J* = 2.3 Hz, 1H), 5.06 (s, 2H), 4.70 (s, 1H), 4.52 – 4.24 (m, 1H), 3.92 (dd, *J* = 94.0, 13.3 Hz, 2H), 3.22 (s, 3H), 2.87 – 2.56 (m, 2H), 1.88 (s, 1H), 1.75 – 1.51 (m, 2H), 1.42 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.56, 154.73, 137.17, 128.45, 128.11, 84.22, 79.05, 67.05, 57.74, 47.72, 46.36, 28.42, 27.54, 21.44.

HR-MS (ESI-TOF) calculated for $C_{26}H_{35}N_2O_5$ [M+H] $^+$: 455.2540, found: 455.2536.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(1-phenylpropyl) piperidine-1-carboxylate (4r)





Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.1 mmol), 2-phenylbutanoic acid (0.2 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound P_1 and P_2 in 58 % total yield (26.2 mg) as two yellow solids. (P1:P2=1.5:1)

P1:**^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.30 (dt, *J* = 14.0, 3.4 Hz, 5H), 7.25 – 7.19 (m, 2H), 7.19 – 7.13 (m, 2H), 5.18 – 4.94 (m, 2H), 4.39 – 3.99 (m, 3H), 3.31 (d, *J* = 33.8 Hz, 1H), 2.91 – 2.56 (m, 2H), 1.87 (ddd, *J* = 13.4, 7.4, 3.2 Hz, 1H), 1.78 – 1.49 (m, 5H), 1.40 (s, 9H), 0.70 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ155.76, 154.30, 139.95, 136.55, 129.66, 127.99, 127.97, 126.60, 78.77, 67.08, 56.93, 52, 49.29, 44.25, 28.39, 21.28 (d, *J* = 60.4 Hz), 12.99.

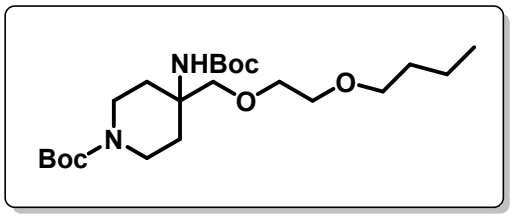
HR-MS (ESI-TOF) calculated for $C_{27}H_{37}N_2O_4$ $[M+H]^+$: 453.2748, found: 453.2746.

P2: **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.39 – 7.30 (m, 5H), 7.30 – 7.27 (m, 2H), 7.25 – 7.21 (m, 1H), 7.21 – 7.12 (m, 2H), 5.14 (t, *J* = 11.8 Hz, 2H), 4.82 – 3.92 (m, 3H), 3.32 – 3.16 (m, 1H), 2.92 – 2.45 (m, 3H), 2.04 – 1.53 (m, 5H), 1.44 (s, 9H), 0.69 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.49, 140.05, 136.62, 128.51, 128.00, 127.63, 126.61, 78.90, 67.22, 57.29, 53.35, 49.92, 44.46, 29.86, 28.44, 20.97, 12.86.

HR-MS (ESI-TOF) calculated for $C_{27}H_{37}N_2O_4$ $[M+H]^+$: 453.2748, found: 453.2743.

Tert-butyl 4-((2-(tert-butoxy) ethoxy) methyl)-4-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (4s)



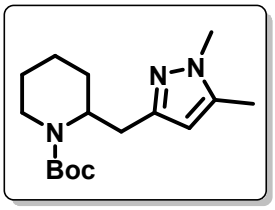
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.1 mmol), 2-(2-butoxyethoxy) acetic acid (0.2 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound in 38 % yield (16.3 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.44 (s, 1H), 3.75 (d, *J* = 13.4 Hz, 2H), 3.63 – 3.57 (m, 2H), 3.56 – 3.51 (m, 4H), 3.45 (t, *J* = 6.6 Hz, 2H), 3.16 – 3.02 (m, 3H), 2.04 (d, *J* = 13.8 Hz, 2H), 1.60 – 1.49 (m, 4H), 1.44 (s, 9H), 1.42 (s, 9H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.86, 79.45, 74.67, 71.12, 71.00, 69.94, 53.80, 45.85, 39.13, 31.75, 31.38, 29.69, 28.40, 19.28, 13.90, 8.62.

HR-MS (ESI-TOF) calculated for $C_{22}H_{43}N_2O_6$ $[M+H]^+$: 431.3116, found: 431.3114.

Tert-butyl 2-((1, 5-dimethyl-1H-pyrazol-3-yl) methyl) piperidine-1-carboxylate (5a)



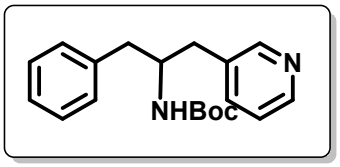
Prepared following general procedure using 1-(tert-butoxycarbonyl) piperidine-2-carboxylic acid (0.1 mmol), 2-(1, 5-dimethyl-1H-pyrazol-3-yl) acetic acid (0.2 mmol). Chromatography using 0- 80% ethyl acetate in hexanes as the eluent affording the title compound in 48 % yield (14.0 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.90 (s, 1H), 4.48 (s, 1H), 4.06 – 3.88 (m, 1H), 3.76 (s, 3H), 2.95 – 2.73 (m, 3H), 2.22 (s, 3H), 1.70 – 1.53 (m, 5H), 1.38 (s, 10H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.92, 148.47, 104.65, 78.96, 50.83, 45.81, 38.81, 35.53, 29.67, 28.34, 25.51, 18.85, 11.08.

HR-MS (ESI-TOF) calculated for $C_{16}H_{28}N_3O_2$ $[M+H]^+$: 294.2176, found: 294.2178.

Tert-butyl (1-phenyl-3-(pyridin-3-yl) propan-2-yl) carbamate (5b)



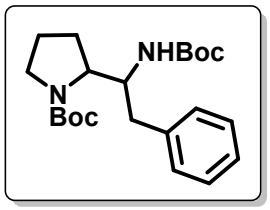
Prepared following general procedure using (tert-butoxycarbonyl) phenylalanine (0.1 mmol), 2-(pyridin-3-yl) acetic acid (0.2 mmol). Chromatography using 0- 80% ethyl acetate in hexanes as the eluent affording the title compound in 36 % yield (11.2 mg) as a white solid.

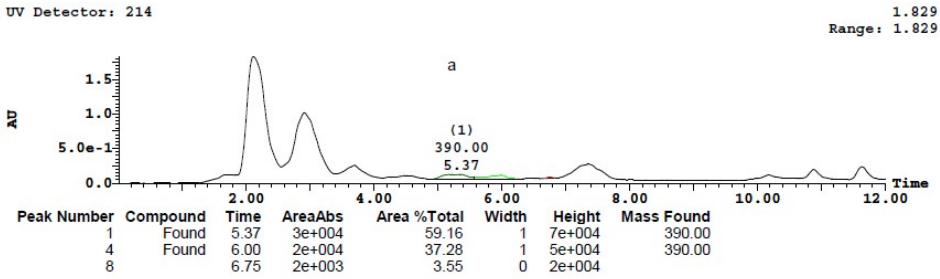
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.50 (d, *J* = 5.9 Hz, 2H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.36 (dd, *J* = 7.9, 4.9 Hz, 1H), 7.31 (dd, *J* = 8.1, 6.5 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.21 – 7.17 (m, 2H), 4.53 (s, 1H), 4.11 (s, 1H), 2.93 – 2.71 (m, 4H), 1.32 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.23, 148.20, 145.42, 139.07, 137.48, 135.28, 129.27, 128.57, 126.67, 124.06, 79.53, 52.32, 40.74, 37.47, 29.67, 28.19.

HR-MS (ESI-TOF) calculated for $C_{19}H_{25}N_2O_2$ [M+H] $^{+}$: 313.1911, found: 313.1915.

Tert-butyl 2-(1-((tert-butoxycarbonyl) amino)-2-phenylethyl) pyrrolidine-1-carboxylate (5c)





Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
1	Found	5.37	3e+004	59.16	1	7e+004	390.00
4	Found	6.00	2e+004	37.28	1	5e+004	390.00
8		6.75	2e+003	3.55	0	2e+004	

Prepared following general procedure using (tert-butoxycarbonyl) proline (0.4 mmol), (tert-butoxycarbonyl) phenylalanine (0.2 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound P1 and P2 in 25 % total yield (19.6 mg) as a white solid and yellow syrup. (P1:P2=1.6:1)

P1:**^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.27 (s, 1H), 7.24 (s, 1H), 7.19 (d, *J* = 7.5 Hz, 3H), 4.72 – 4.02 (m, 2H), 3.81 (d, *J* = 39.7 Hz, 1H), 3.53 (d, *J* = 39.3 Hz, 1H), 3.25 (s, 1H), 2.89 – 2.42 (m, 3H), 2.06 – 1.67 (m, 4H), 1.48 (s, 9H), 1.30 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.56, 138.66, 128.73, 126.19, 79.72, 61.93, 60.04, 54.21, 47.58, 37.52, 29.68, 28.38, 23.73.

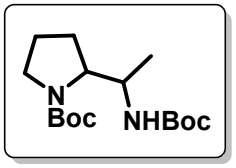
HR-MS (ESI-TOF) calculated for $C_{22}H_{35}N_2O_4$ [M+H] $^{+}$: 391.2591, found: 391.2592.

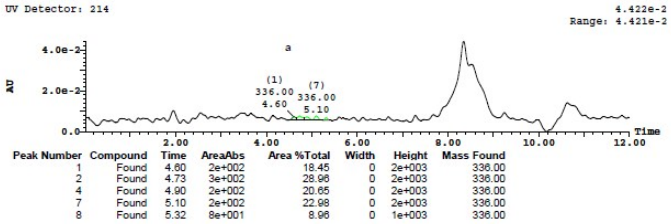
P2: **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.28 (d, J = 7.5 Hz, 1H), 7.24 (s, 1H), 7.22 – 7.13 (m, 3H), 4.83 (d, J = 37.4 Hz, 1H), 3.97 – 3.59 (m, 2H), 3.29 (d, J = 8.8 Hz, 1H), 2.98 – 2.58 (m, 2H), 2.10 – 1.61 (m, 4H), 1.46 (s, 9H), 1.37 (s, 9H).

^{13}C NMR (101 MHz, Chloroform-d) δ 156.07, 137.94, 130.86, 126.30, 79.43, 59.41, 56.03, 54.78, 46.47, 39.15, 29.87, 23.52.

HR-MS (ESI-TOF) calculated for $C_{22}H_{35}N_2O_4$ [M+H] $^{+}$: 391.2591, found: 391.2593.

Tert-butyl 2-(1-((tert-butoxycarbonyl) amino) ethyl) pyrrolidine-1-carboxylate (5d)





Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
1	Found	4.60	2e+002	18.45	0	2e+003	336.00
2	Found	4.73	3e+002	28.96	0	2e+003	336.00
4	Found	4.90	2e+002	20.65	0	2e+003	336.00
7	Found	5.10	2e+002	22.98	0	2e+003	336.00
8	Found	5.32	8e+001	8.96	0	1e+003	336.00

Prepared following general procedure using (tert-butoxycarbonyl) proline (0.4 mmol), (tert-butoxycarbonyl) phenylalanine (0.2 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound P1 and P2 in 21 % total yield (13.2 mg) as two yellow solids. (P1:P2=1.3:1)

P1:**^{1}H NMR (400 MHz, Chloroform-*d*)** δ 3.81 (t, *J* = 6.6 Hz, 1H), 3.58 – 3.15 (m, 3H), 2.14 – 1.77 (m, 4H), 1.47 (s, 9H), 1.44 (s, 9H), 1.25 – 0.72 (m, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.39, 155.13 (d, *J* = 108.2 Hz), 79.55 – 79.26 (m), 79.02, 62.50 – 61.29 (m), 60.21 – 58.17 (m), 46.76 (d, *J* = 59.8 Hz), 29.45 (d, *J* = 45.6 Hz), 28.45 (d, *J* = 3.3 Hz), 24.03, 23.59 – 22.03 (m), 15.94 – 15.34 (m).

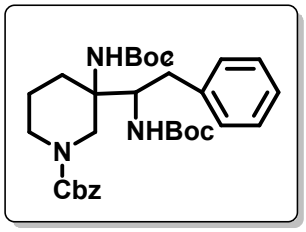
HR-MS (ESI-TOF) calculated for $C_{16}H_{31}N_2O_4$ [M+H] $^{+}$: 315.2278, found: 315.2282.

P2:**^{1}H NMR (400 MHz, Chloroform-*d*)** δ 3.77 – 3.61 (m, 1H), 3.60 – 3.15 (m, 3H), 2.03 – 1.76 (m, 4H), 1.75 – 1.61 (m, 1H), 1.47 (s, 9H), 1.42 (s, 9H), 1.12 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.25, 156.16, 79.65, 78.44, 61.02, 51.26, 46.47, 29.67, 28.42, 23.59, 19.46, 14.10.

HR-MS (ESI-TOF) calculated for $C_{16}H_{31}N_2O_4$ [M+H] $^{+}$: 315.2278, found: 315.2280.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(1-((tert-butoxycarbonyl) amino)-2-phenylethyl) piperidine-1-carboxylate (5e)



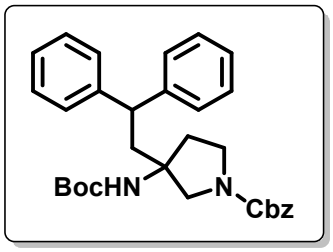
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), (tert-butoxycarbonyl) phenylalanine (0.1 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound in 26 % yield (14.3 mg) as a brown solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.27 (m, 6H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 7.3 Hz, 3H), 5.19 (d, *J* = 26.6 Hz, 2H), 4.78 – 4.43 (m, 1H), 3.89 (dd, *J* = 58.9, 22.3 Hz, 2H), 2.65 (dt, *J* = 109.8, 12.2 Hz, 3H), 2.09 – 1.74 (m, 4H), 1.58 (s, 2H), 1.47 (s, 9H), 1.25 (s, 10H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.90, 155.34, 138.57, 136.40, 129.27, 128.59, 128.46, 128.20, 127.89, 126.12, 79.75, 78.70, 67.54, 67.11, 57.16, 53.00, 44.45, 37.60, 36.66, 29.68, 28.31, 27.84, 21.76.

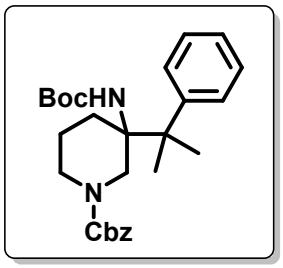
HR-MS (ESI-TOF) calculated for $C_{31}H_{44}N_3O_6$ [M+H] $^+$: 554.3225, found: 554.3226.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2, 2-diphenylethyl) pyrrolidine-1-carboxylate (6b)



^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.41 (m, 2H), 7.41 – 7.27 (m, 8H), 7.25 – 7.01 (m, 5H), 5.15 – 5.01 (m, 2H), 4.31 (d, *J* = 7.4 Hz, 1H), 4.03 (d, *J* = 6.9 Hz, 1H), 3.38 (dq, *J* = 34.0, 15.6, 13.4 Hz, 3H), 2.91 – 2.60 (m, 2H), 2.41 (dd, *J* = 68.1, 15.1 Hz, 2H), 1.75 – 1.53 (m, 2H), 1.42 (s, 9H).

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-phenylpropan-2-yl) piperidine-1-carboxylate (7a)



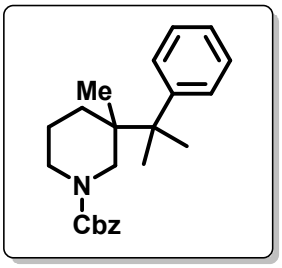
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-methyl-2-phenylpropanoic acid (0.1 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound in 41 % yield (18.5 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (td, *J* = 18.4, 17.6, 10.8 Hz, 8H), 7.19 – 7.03 (m, 2H), 5.02 (dt, *J* = 22.5, 11.3 Hz, 2H), 4.19 – 3.81 (m, 2H), 3.02 (t, *J* = 17.5 Hz, 1H), 2.71 – 2.38 (m, 2H), 1.60 (s, 4H), 1.38 (d, *J* = 10.2 Hz, 6H), 1.35 (d, *J* = 4.1 Hz, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.88, 145.19, 136.79, 128.50, 128.41 – 127.13 (m), 126.27, 78.39, 67.16, 60.27, 59.77, 50.68, 46.05, 44.37, 29.68, 28.44, 26.04, 24.61, 22.15.

HR-MS (ESI-TOF) calculated for $C_{27}H_{37}N_2O_4$ [M+H] $^+$: 453.2748, found: 453.2752.

Benzyl 3-methyl-3-(2-phenylpropan-2-yl) piperidine-1-carboxylate (7b)



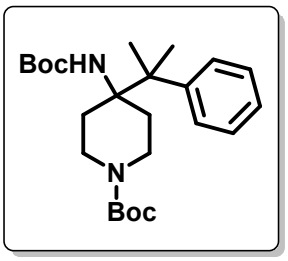
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-methylpiperidine-3-carboxylic acid (0.2 mmol), 2-methyl-2-phenylpropanoic acid (0.1 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound in 30 % yield (10.5 mg) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 7H), 7.24 – 7.11 (m, 3H), 5.08 (d, *J* = 11.9 Hz, 2H), 4.25 – 3.75 (m, 2H), 2.84 – 2.33 (m, 2H), 1.64 (s, 6H), 1.39 (s, 6H), 1.25 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.79, 146.21, 137.03, 128.42, 128.31, 126.12, 125.67, 66.76, 50.10, 44.16, 42.98, 38.52, 30.35, 23.81, 21.50, 16.42.

HR-MS (ESI-TOF) calculated for $C_{23}H_{30}NO_2$ [M+H] $^{+}$: 352.2271, found: 352.2273.

Tert-butyl 4-((tert-butoxycarbonyl) amino)-4-(2-phenylpropan-2-yl) piperidine-1-carboxylate (7c)



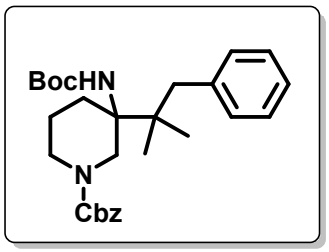
Prepared following general procedure using 1-(tert-butoxycarbonyl)-4-((tert-butoxycarbonyl) amino) piperidine-4-carboxylic acid (0.2 mmol), 2-methyl-2-phenylpropanoic acid (0.1 mmol). Chromatography using 0- 40% ethyl acetate in hexanes as the eluent affording the title compound in 27 % yield (11.3 mg) as a yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.27 (m, 4H), 7.25 – 7.14 (m, 1H), 3.93 (d, *J* = 14.5 Hz, 2H), 2.76 (t, *J* = 12.4 Hz, 2H), 2.11 – 1.86 (m, 2H), 1.53 (dd, *J* = 13.2, 4.5 Hz, 3H), 1.44 (s, 8H), 1.43 (s, 9H), 1.41 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.02, 154.85, 145.21, 128.25, 127.55, 126.14, 79.37, 59.09, 46.87, 28.44, 24.34.

HR-MS (ESI-TOF) calculated for $C_{24}H_{39}N_2O_4$ [M+H] $^{+}$: 419.2904, found: 419.2912.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-methyl-1-phenylpropan-2-yl) piperidine-1-carboxylate (7d)



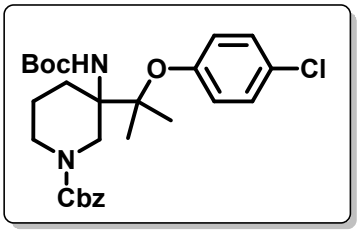
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2, 2-dimethyl-3-phenylpropanoic acid (0.1 mmol). Chromatography using 0- 20% ethyl acetate in hexanes as the eluent affording the title compound in 27 % yield (12.6 mg) as a yellow syrup.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.28 (m, 5H), 7.25 – 7.16 (m, 3H), 7.11 (d, *J* = 7.3 Hz, 2H), 5.17 (q, *J* = 12.6 Hz, 2H), 4.21 (q, *J* = 16.9, 12.8 Hz, 2H), 3.18 – 2.80 (m, 2H), 2.69 (q, *J* = 13.8 Hz, 3H), 1.40 (s, 9H), 0.85 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.23, 138.67, 131.21, 128.57, 128.35, 127.46, 125.91, 78.43, 67.29, 61.28, 50.00, 44.76, 42.38, 29.69, 28.43, 25.35, 21.

HR-MS (ESI-TOF) calculated for $C_{28}H_{39}N_2O_4$ [M+H] $^{+}$: 467.2904, found: 467.2901.

Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-(4-chlorophenoxy) propan-2-yl) piperidine-1-carboxylate (7e)



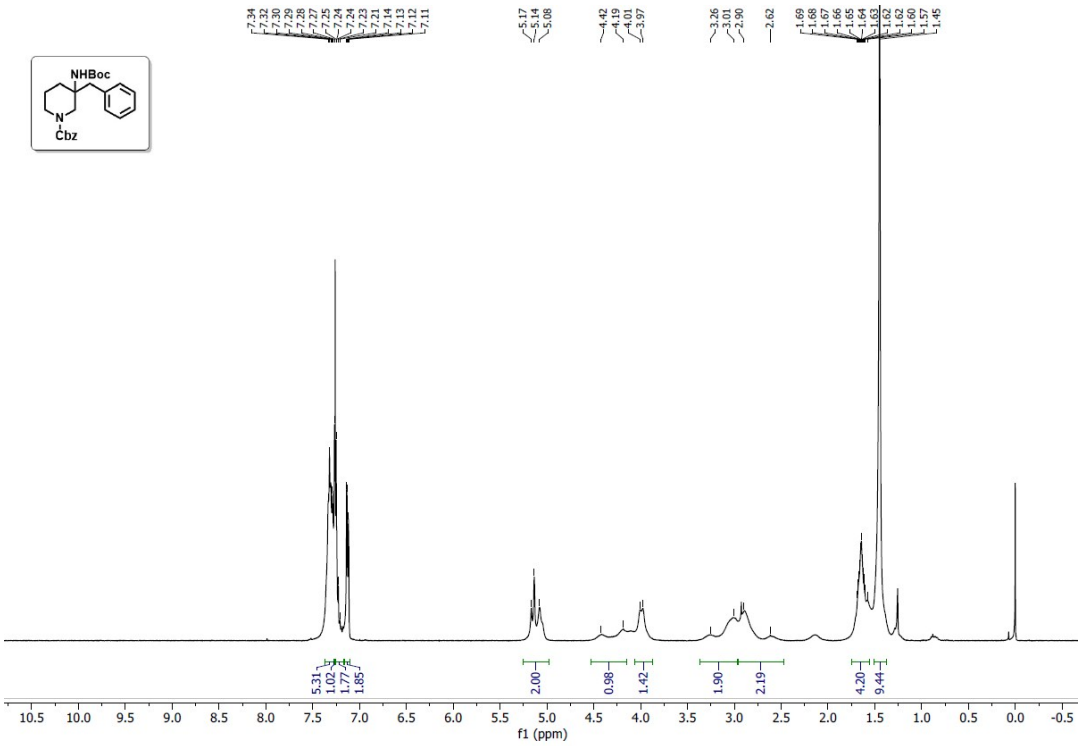
Prepared following general procedure using 1-((benzyloxy) carbonyl)-3-((tert-butoxycarbonyl) amino) piperidine-3-carboxylic acid (0.2 mmol), 2-(4-chlorophenoxy)-2-methylpropanoic acid (0.1 mmol). Chromatography using 0- 20% ethyl acetate in hexanes as the eluent affording the title compound in 34 % yield (17.0 mg) as a yellow syrup.

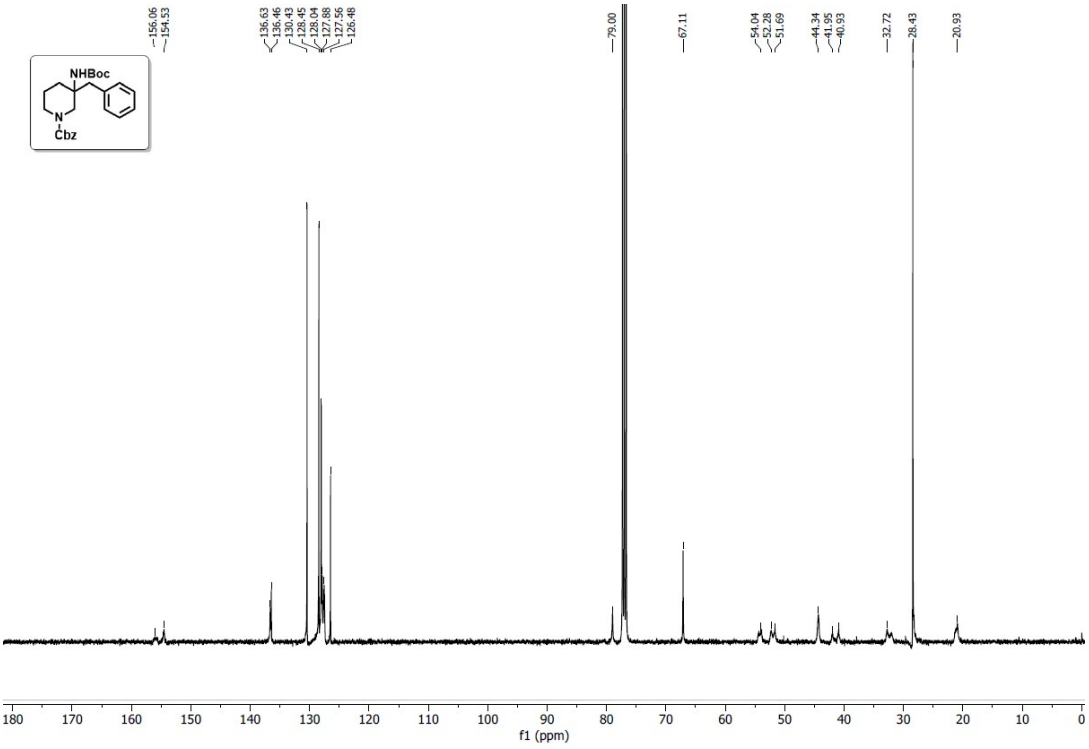
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (dt, *J* = 18.4, 3.9 Hz, 5H), 7.22 (d, *J* = 8.3 Hz, 2H), 6.90 – 6.81 (m, 2H), 5.25 – 5.11 (m, 2H), 4.38 – 4.11 (m, 2H), 3.21 – 2.90 (m, 2H), 2.88 – 2.67 (m, 1H), 1.81 – 1.57 (m, 4H), 1.40 (s, 9H), 1.26 (s, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.85, 153.07, 129.11, 128.99, 128.54, 127.87, 125.66, 85.52, 78.74, 67.25, 61.13, 49.41, 44.57, 29.68, 28.40, 25.31, 22.55, 21.84.

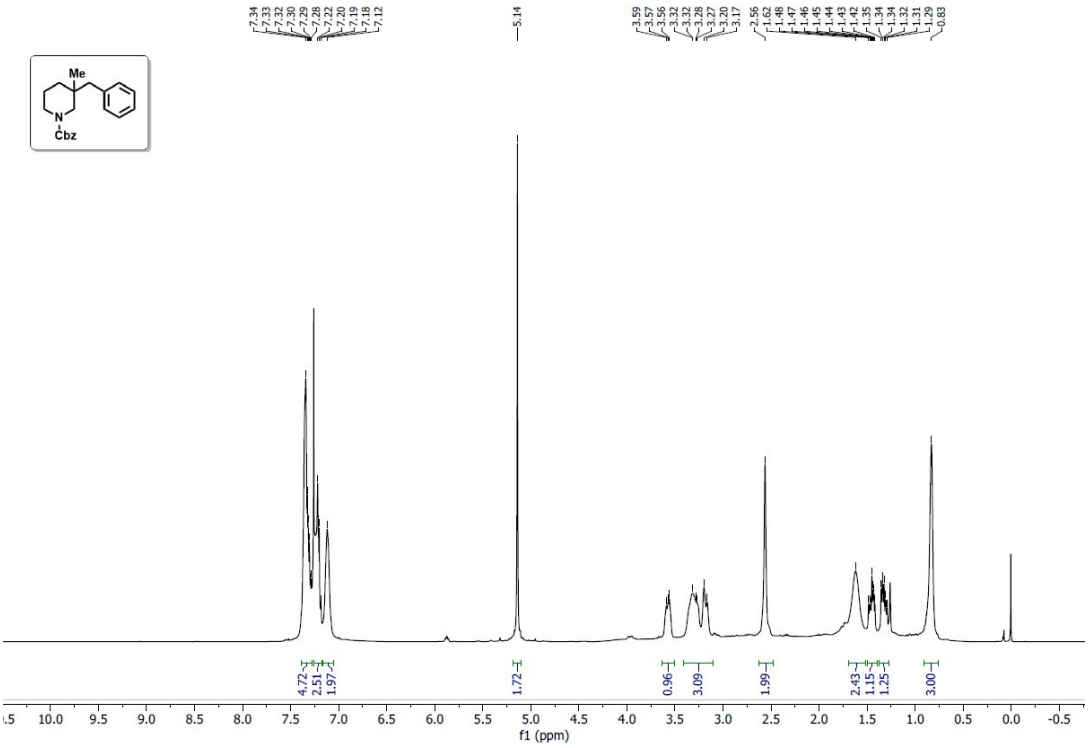
HR-MS (ESI-TOF) calculated for $C_{27}H_{35}ClN_2O_5$ [M+H] $^{+}$: 503.2307, found: 503.2310.

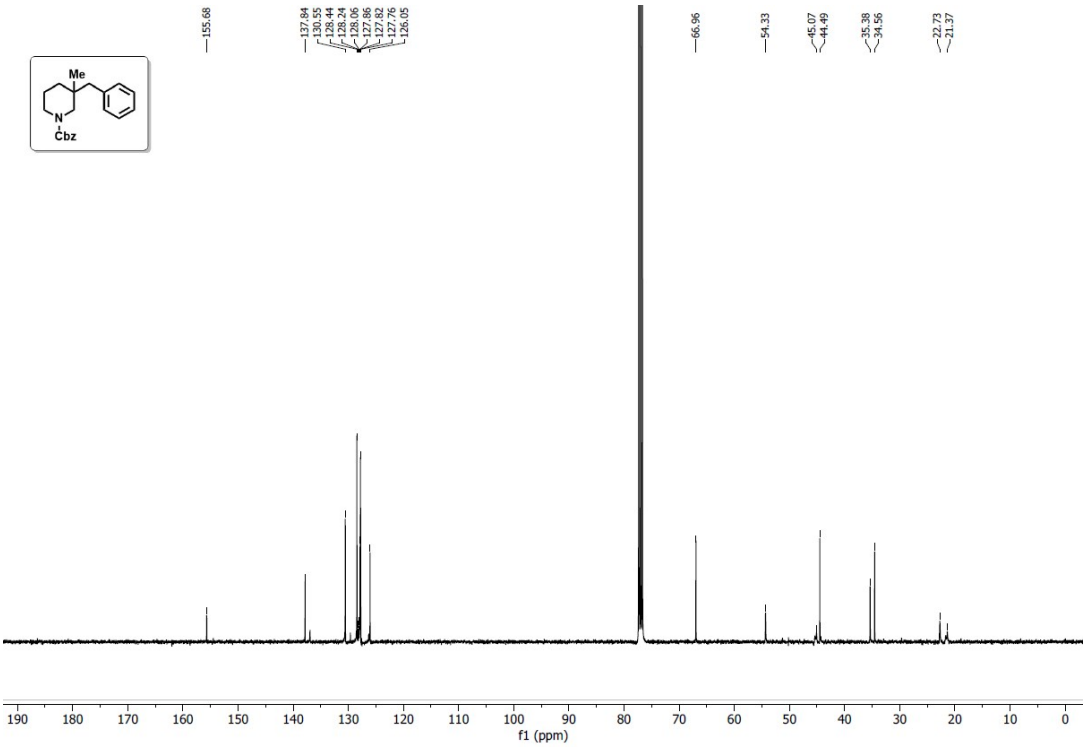
Benzyl 3-benzyl-3-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (1c)



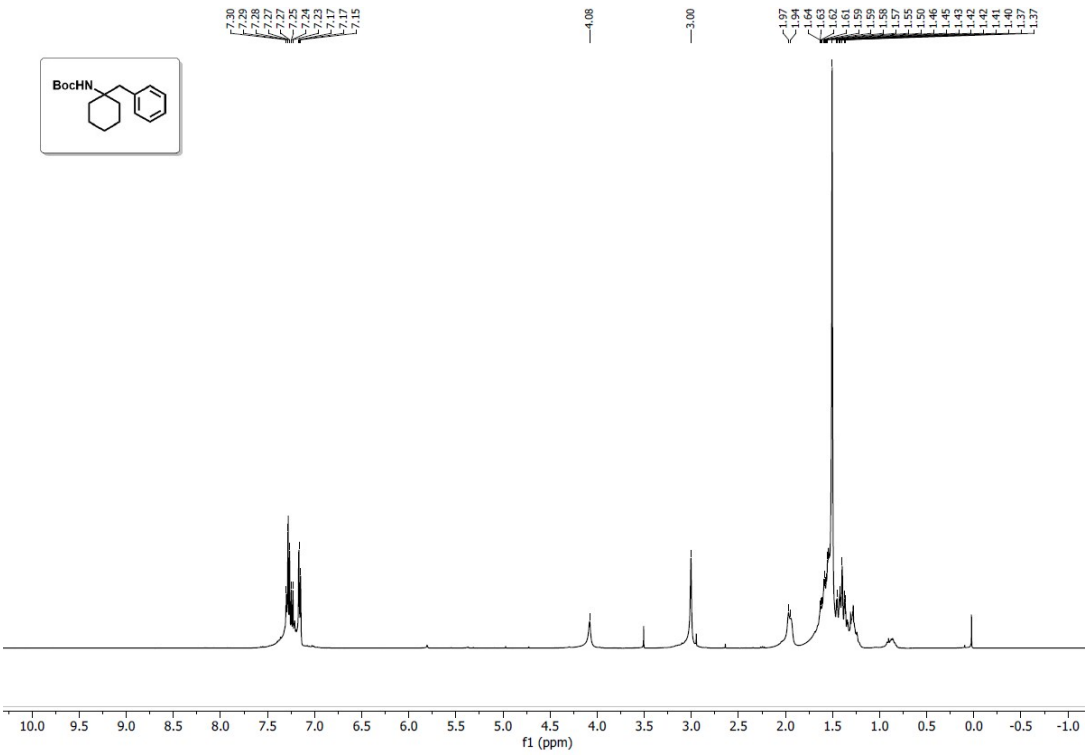


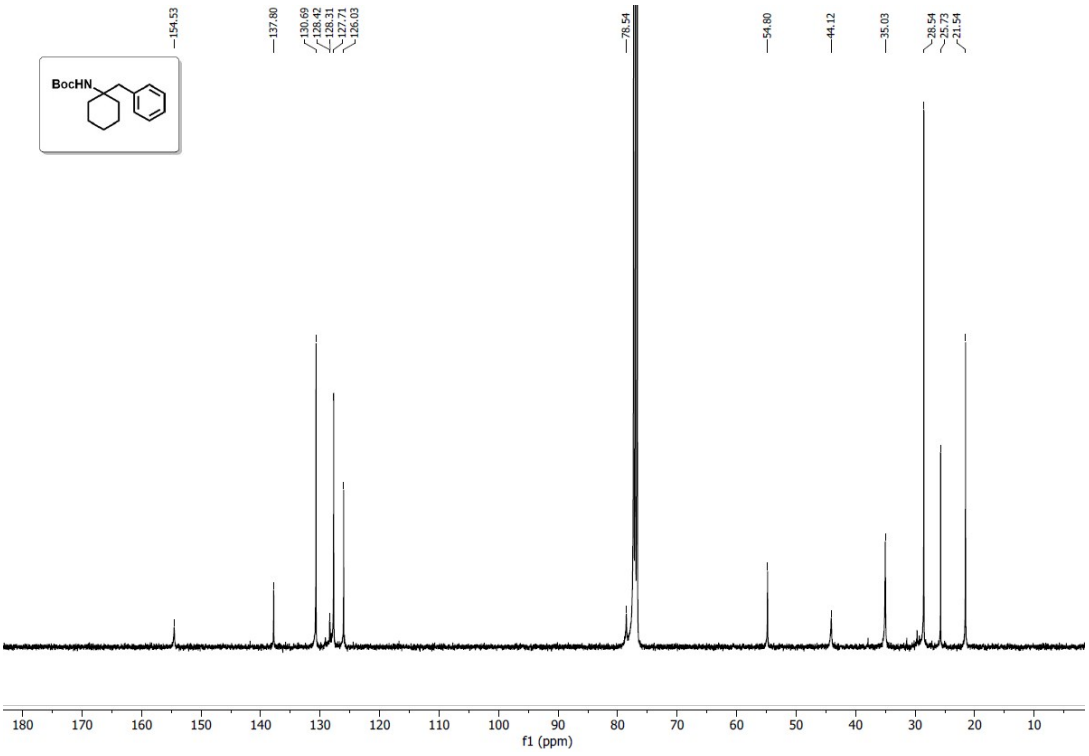
Benzyl 3-benzyl-3-methylpiperidine-1-carboxylate (2a)



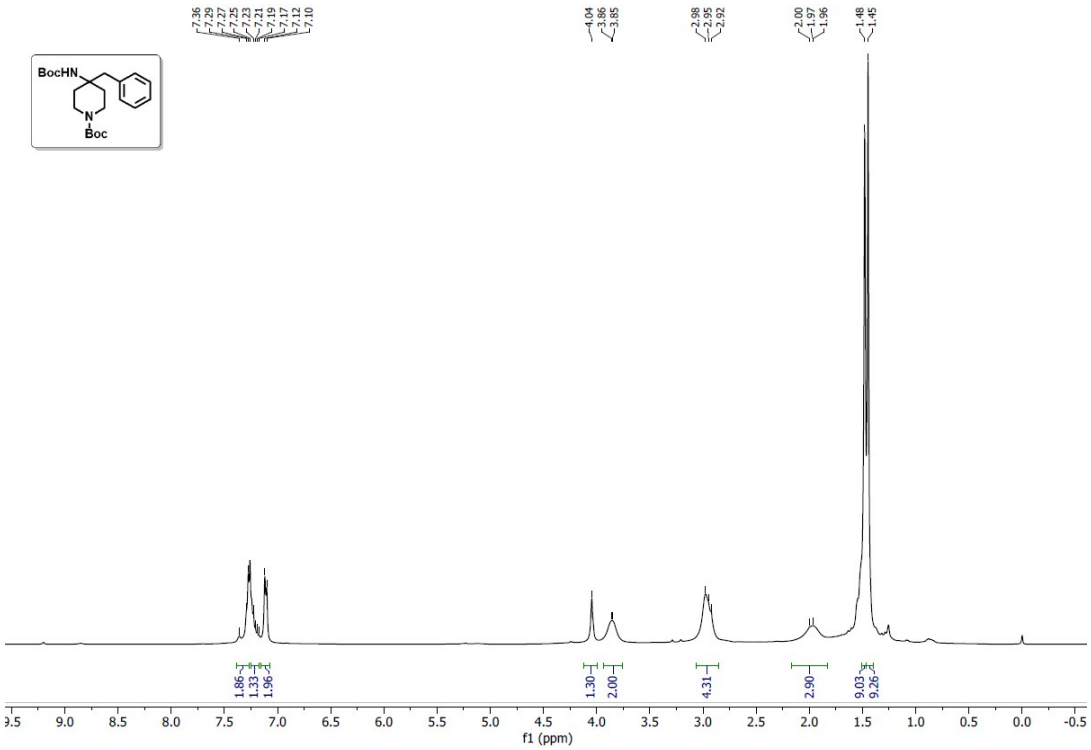


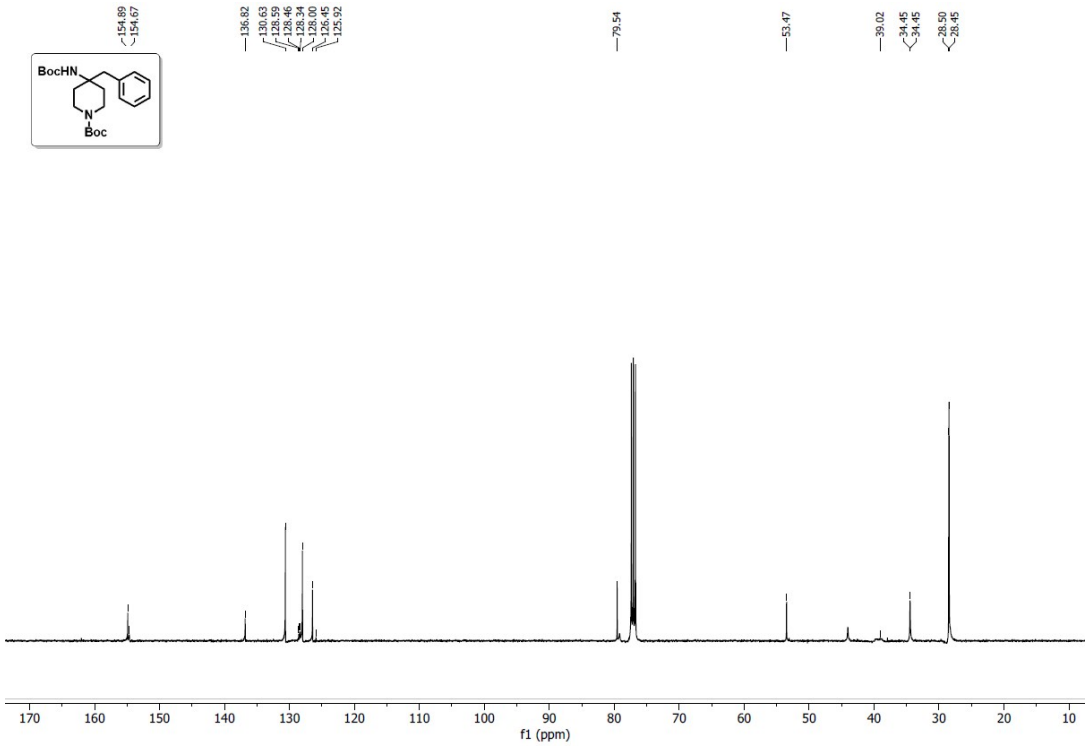
Tert-butyl (1-benzylcyclohexyl) carbamate (2b)



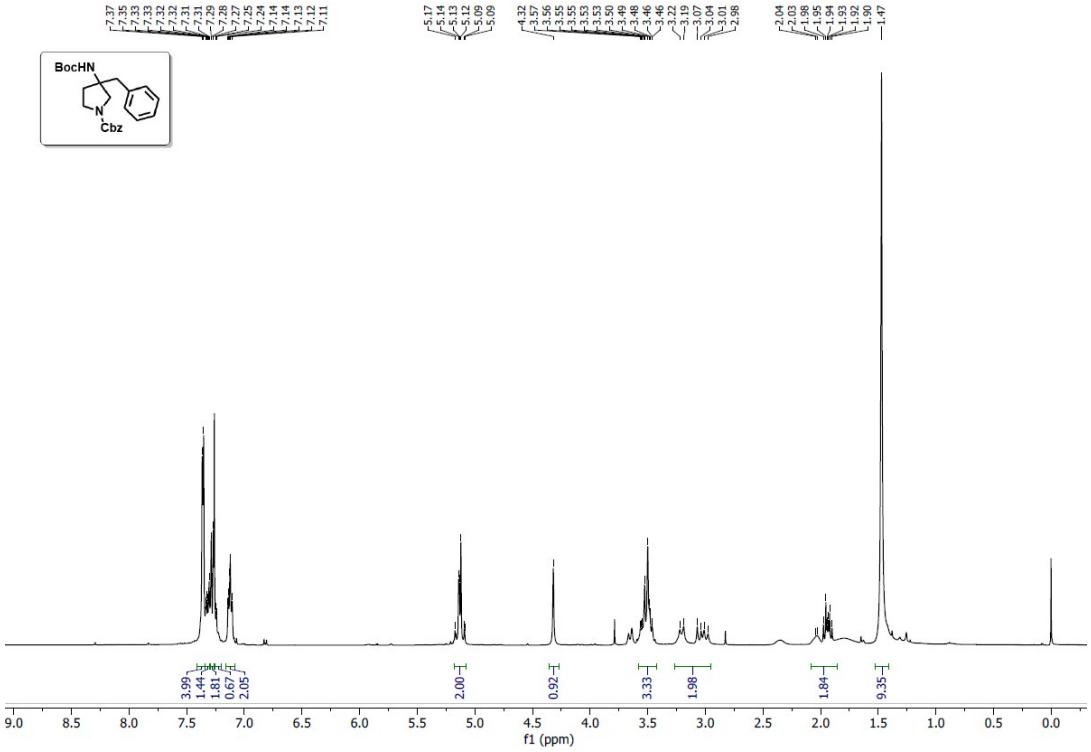


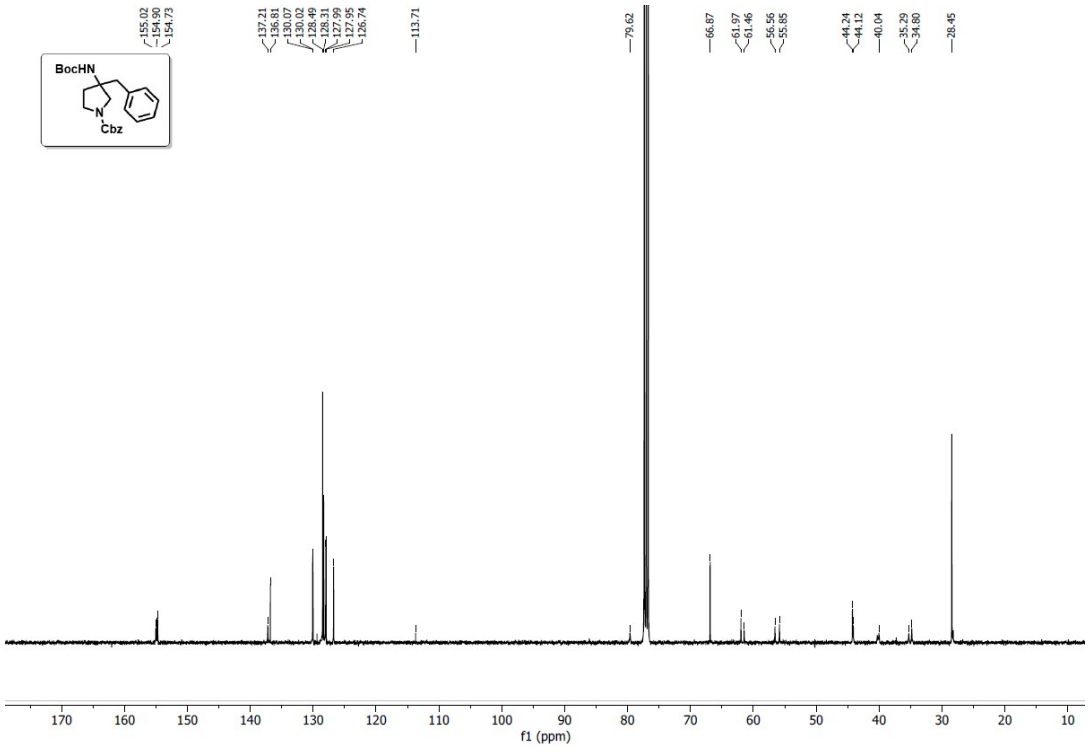
Tert-butyl 4-benzyl-4-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (2c)



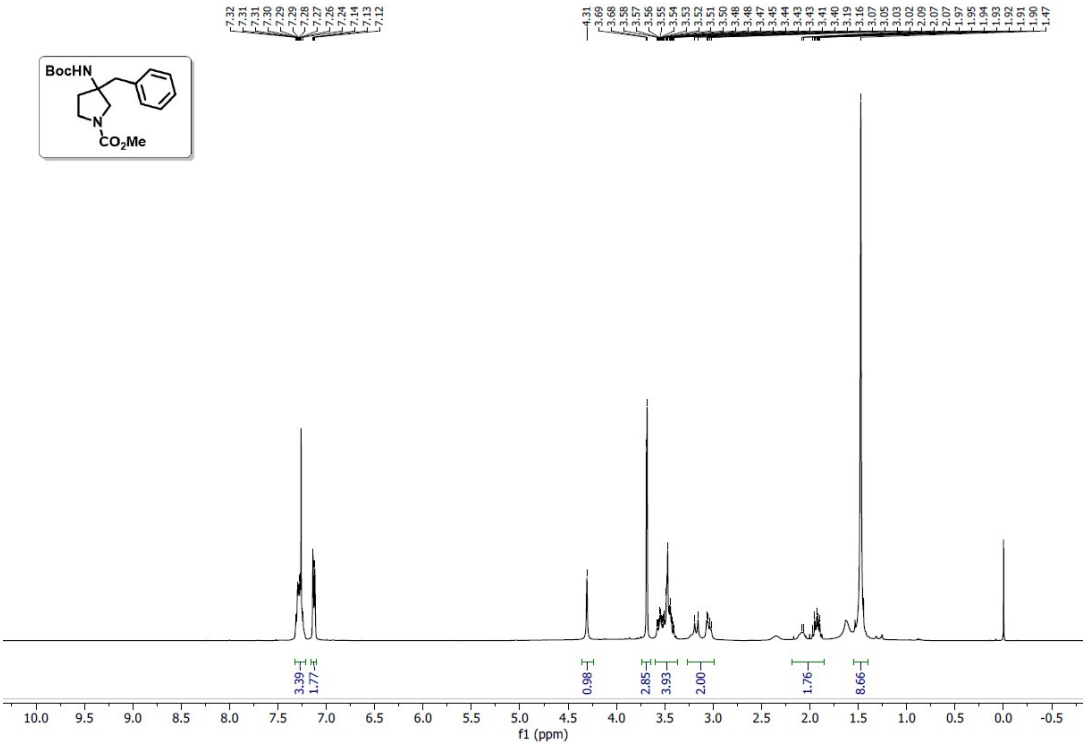


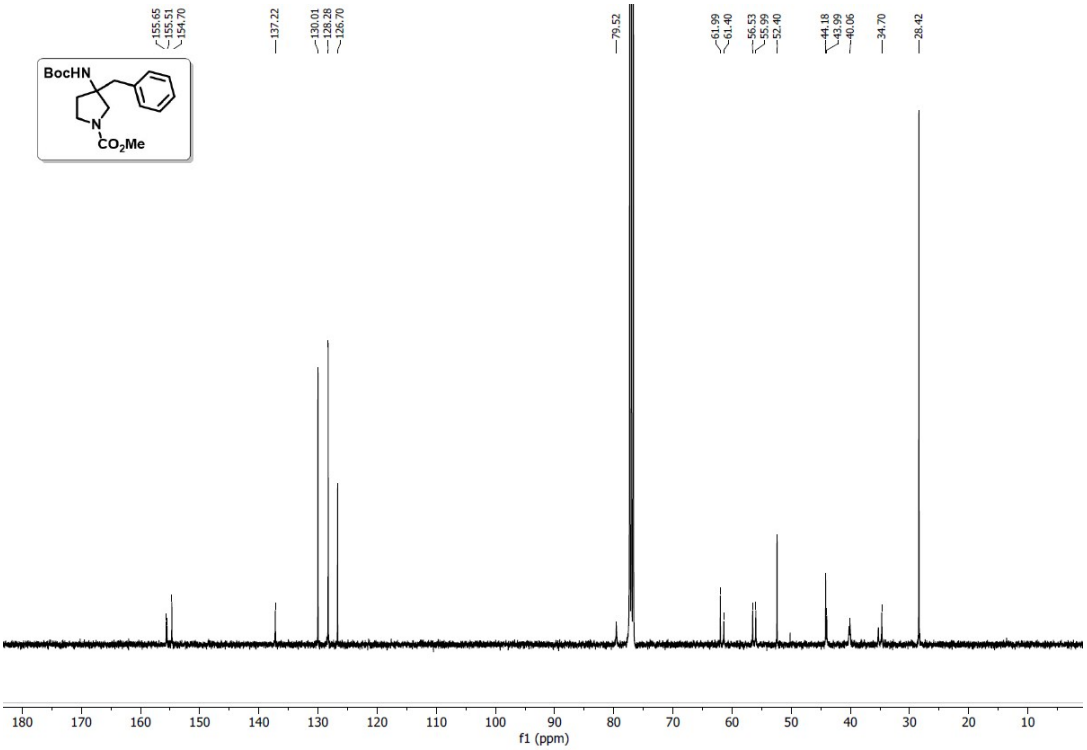
Benzyl 3-benzyl-3-((tert-butoxycarbonyl) amino) pyrrolidine-1-carboxylate (2d)



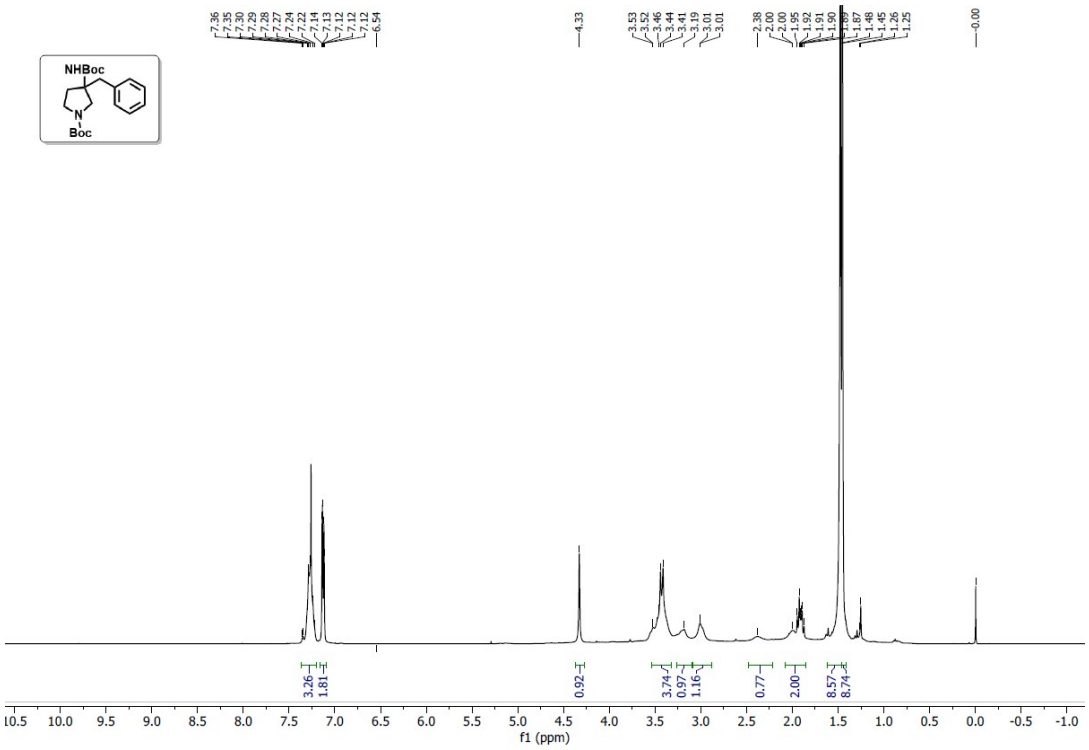


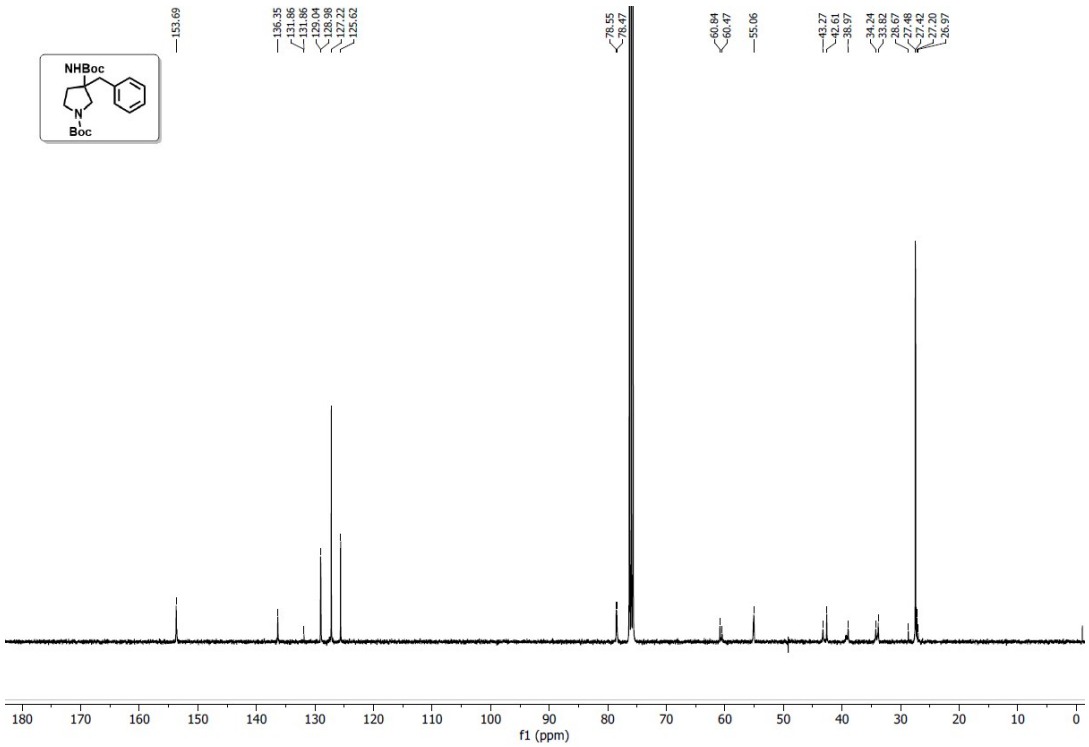
Methyl 3-benzyl-3-((tert-butoxycarbonyl) amino) pyrrolidine-1-carboxylate (2e)



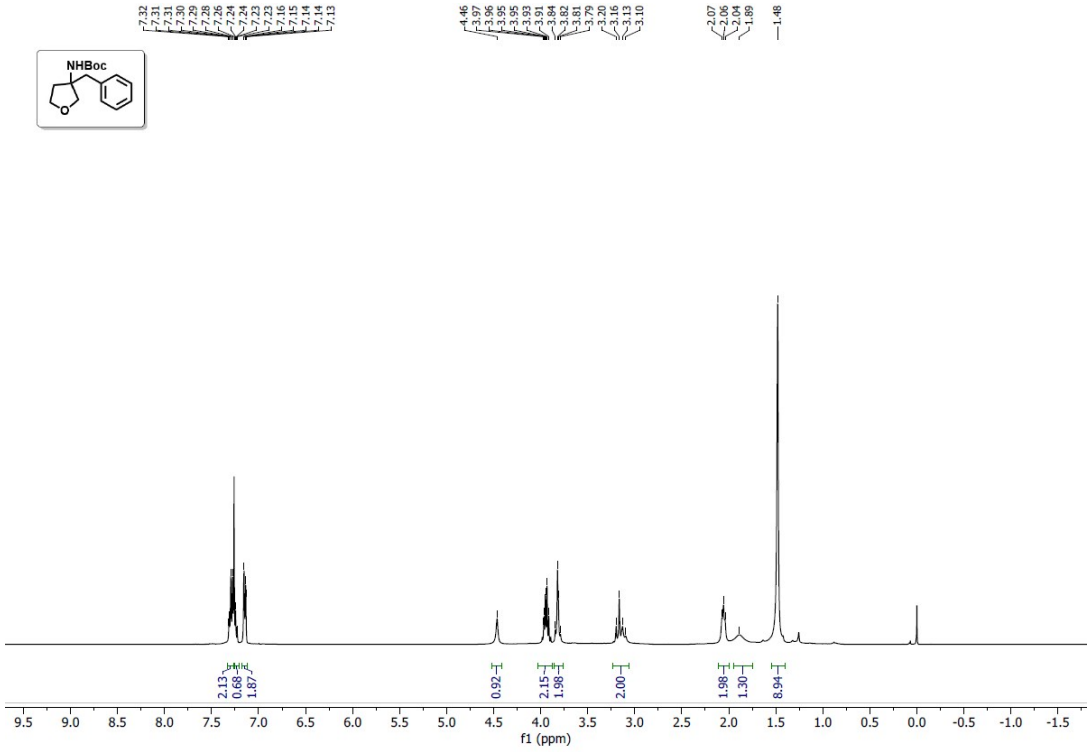


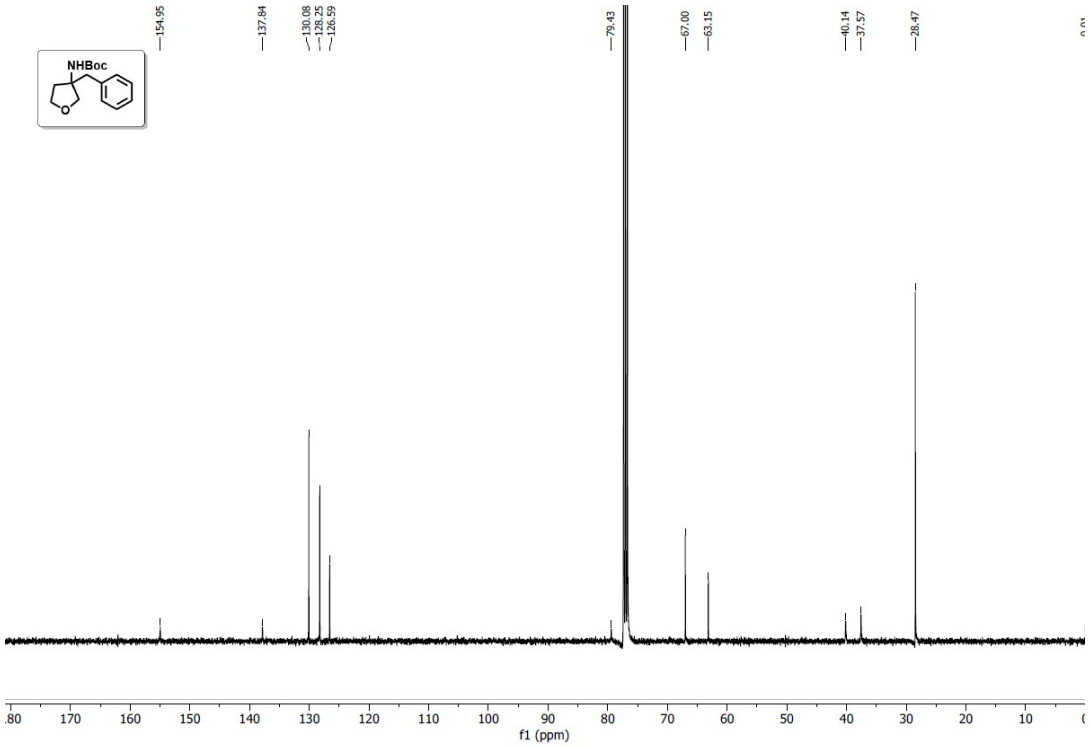
Tert-butyl 3-benzyl-3-((tert-butoxycarbonyl) amino) pyrrolidine-1-carboxylate (2f)



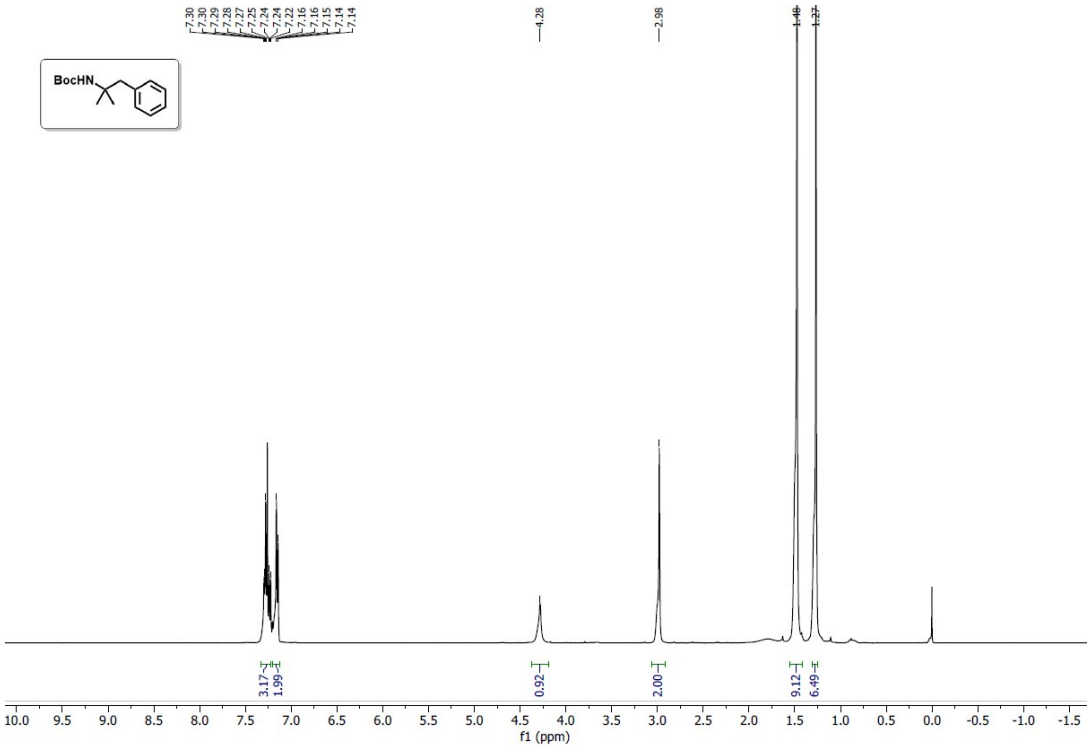


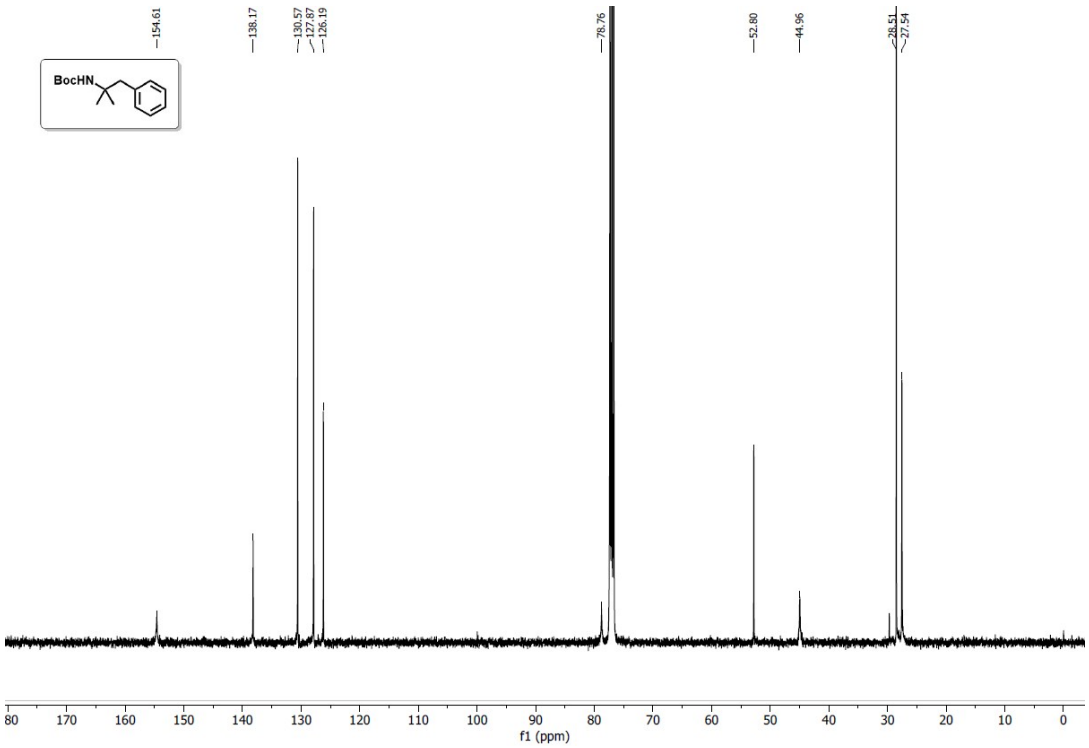
Tert-butyl (3-benzyltetrahydrofuran-3-yl) carbamate (2g)



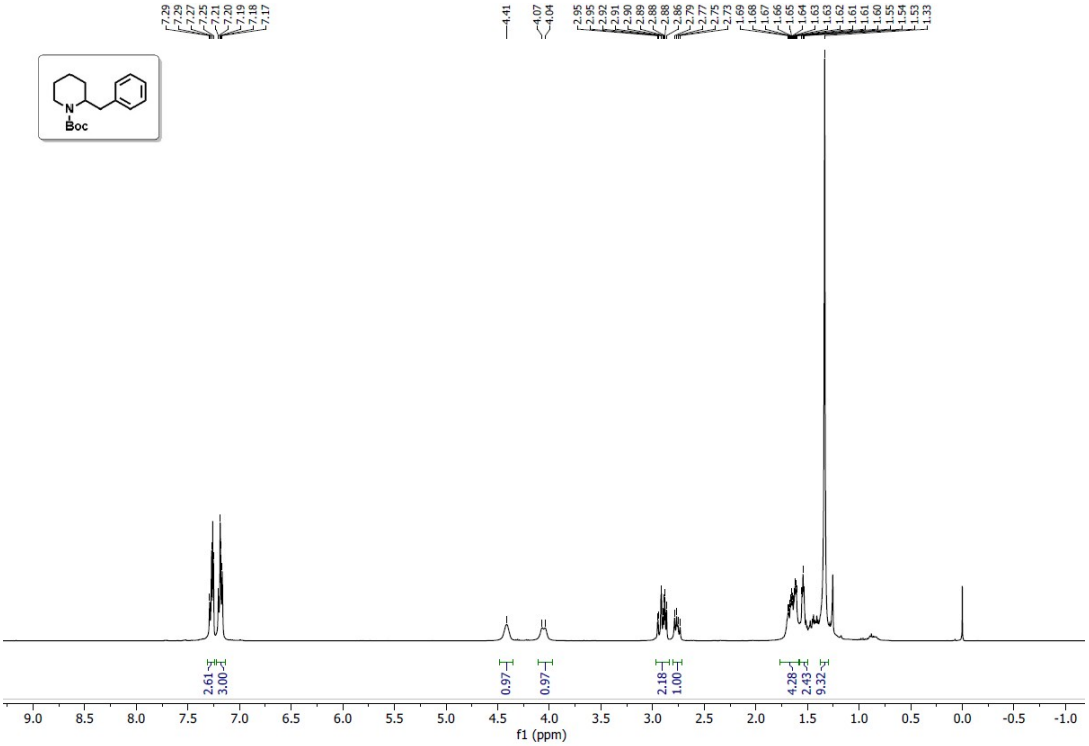


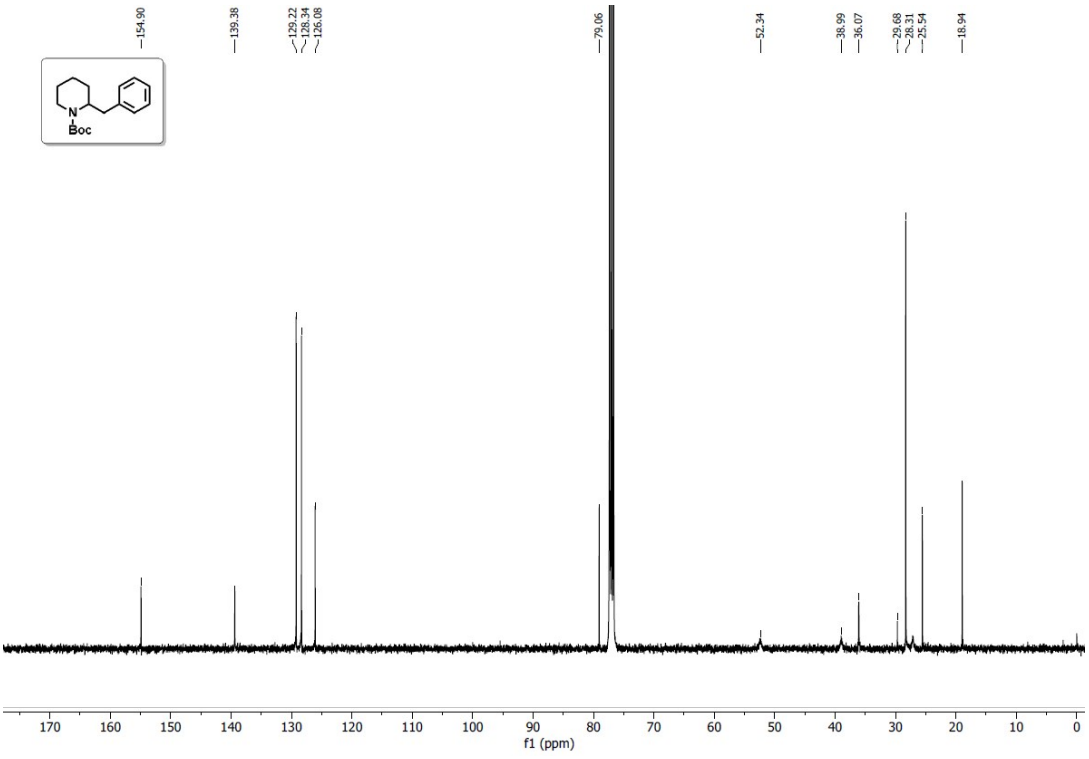
Tert-butyl (2-methyl-1-phenylpropan-2-yl) carbamate (2h)



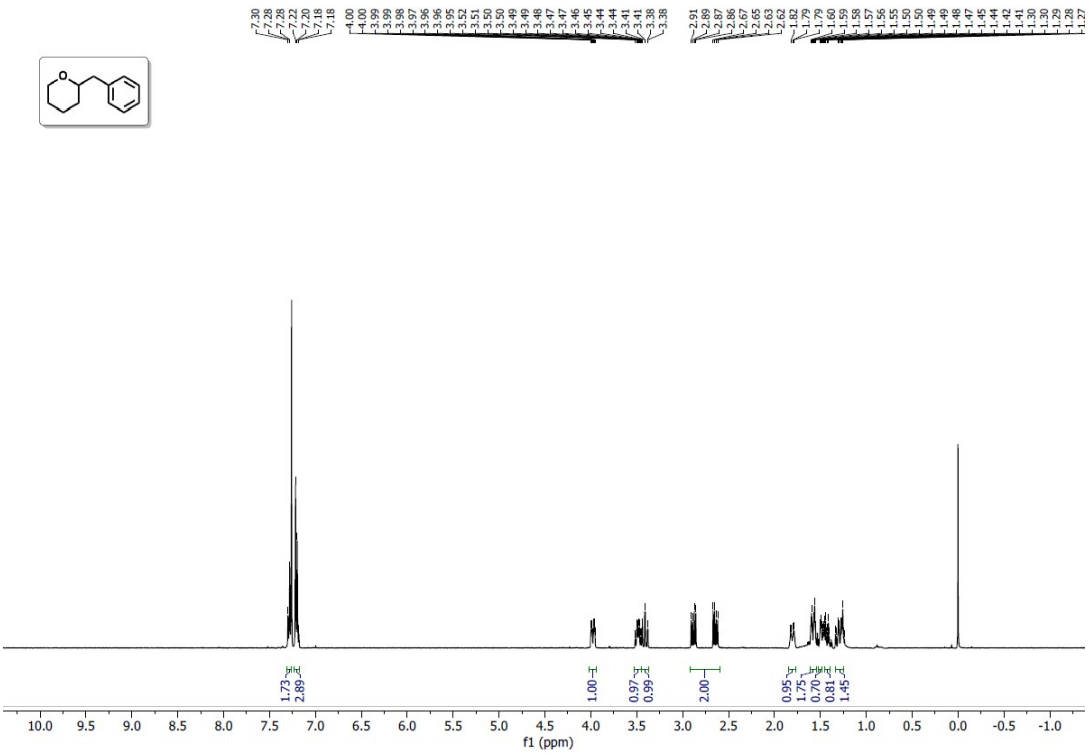


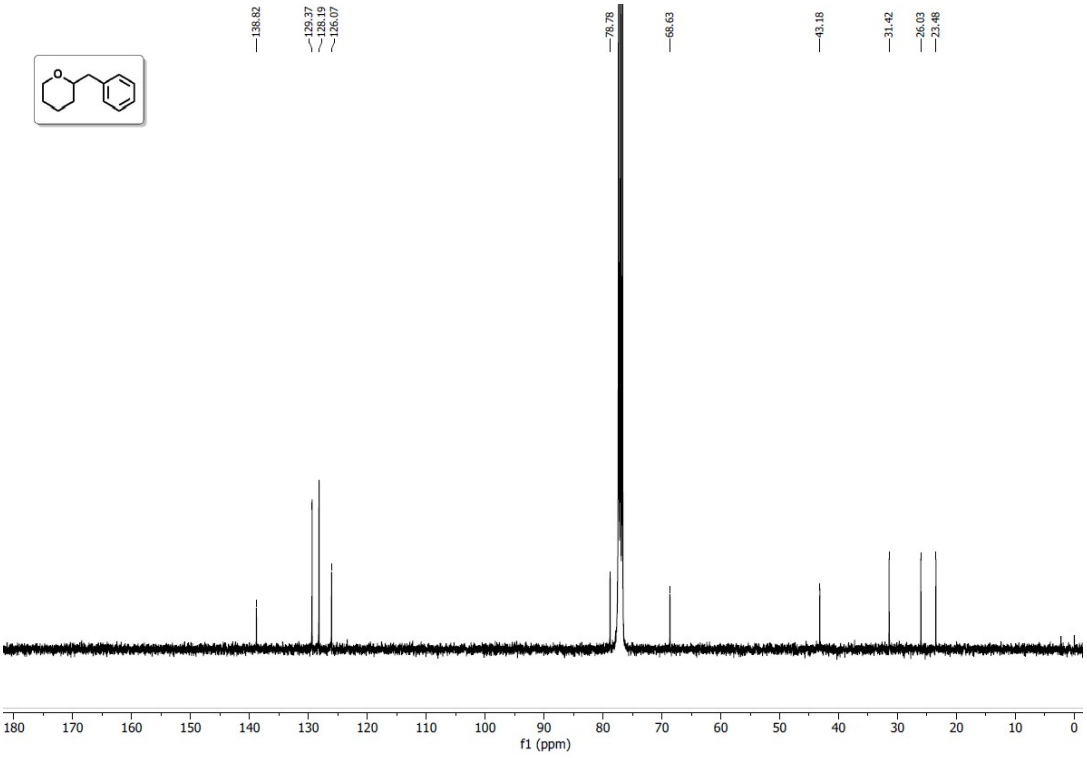
Tert-butyl 2-benzylpiperidine-1-carboxylate (2i)



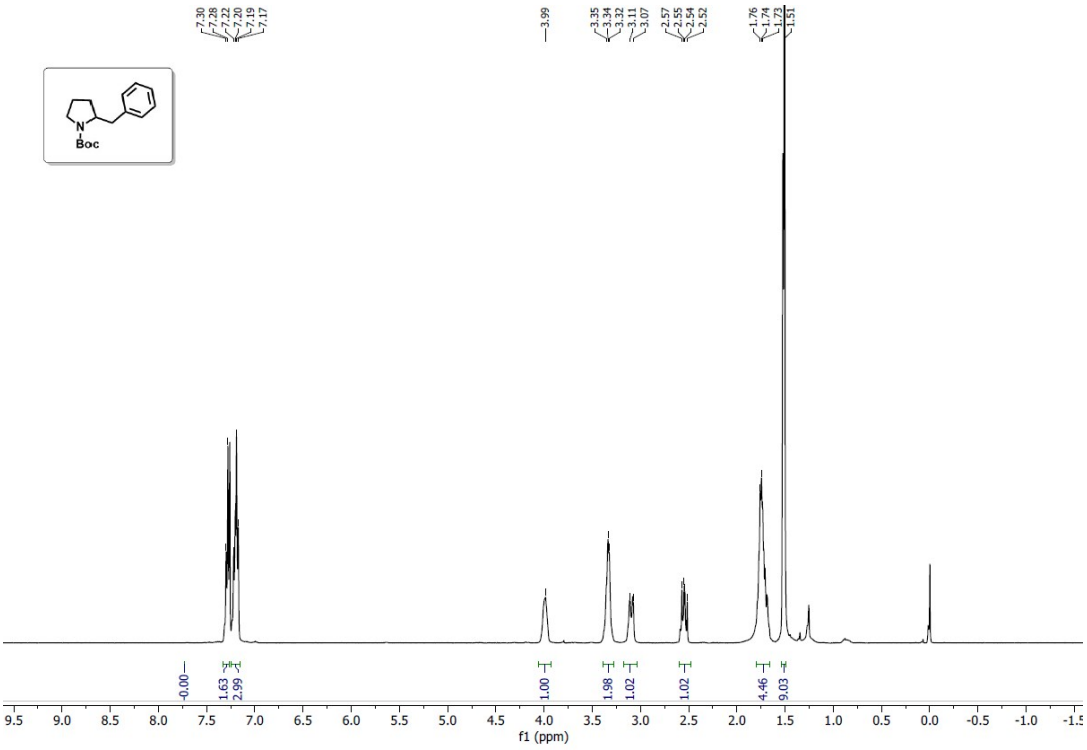


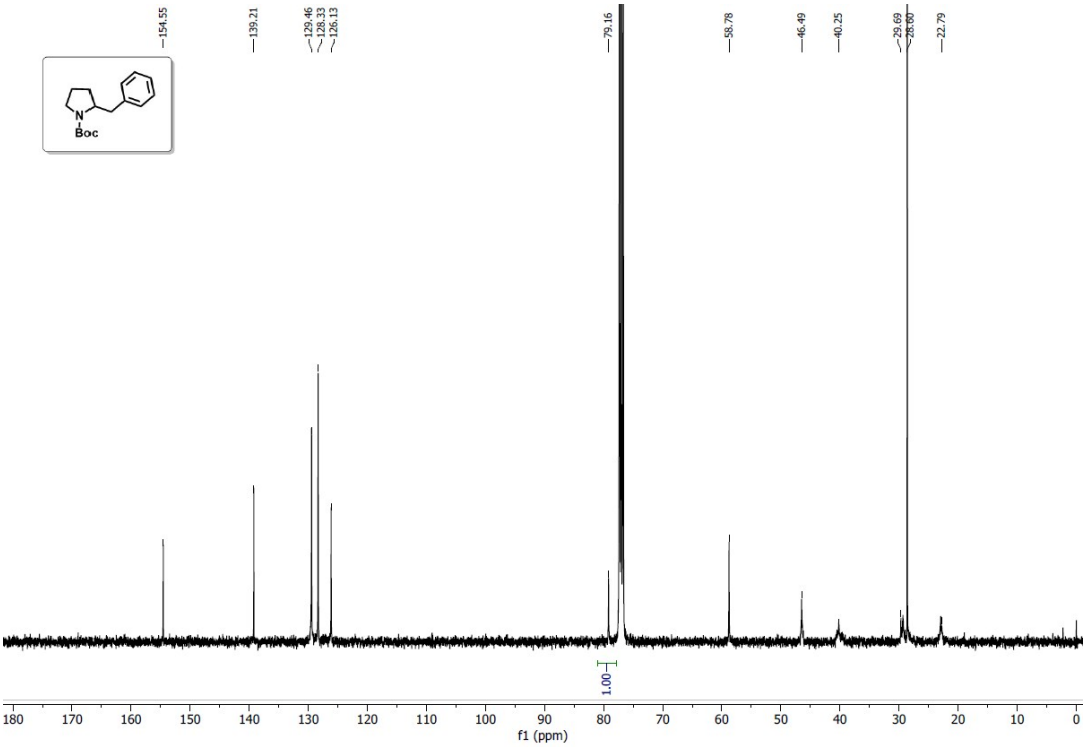
2-benzyltetrahydro-2H-pyran (2j)



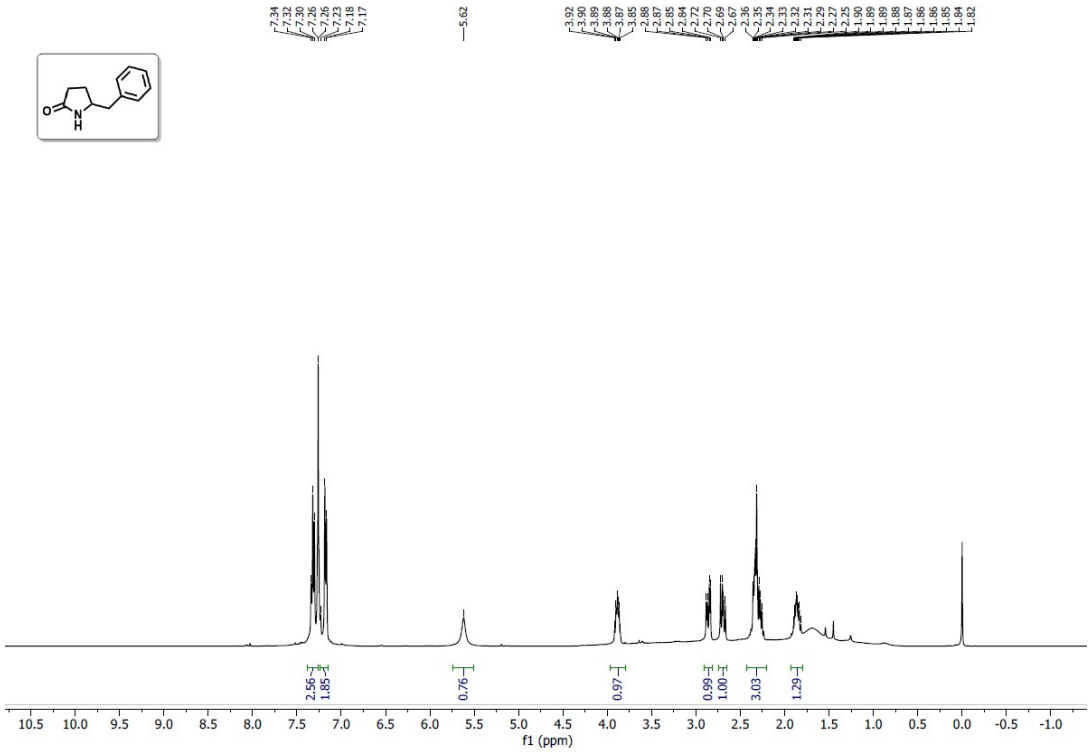


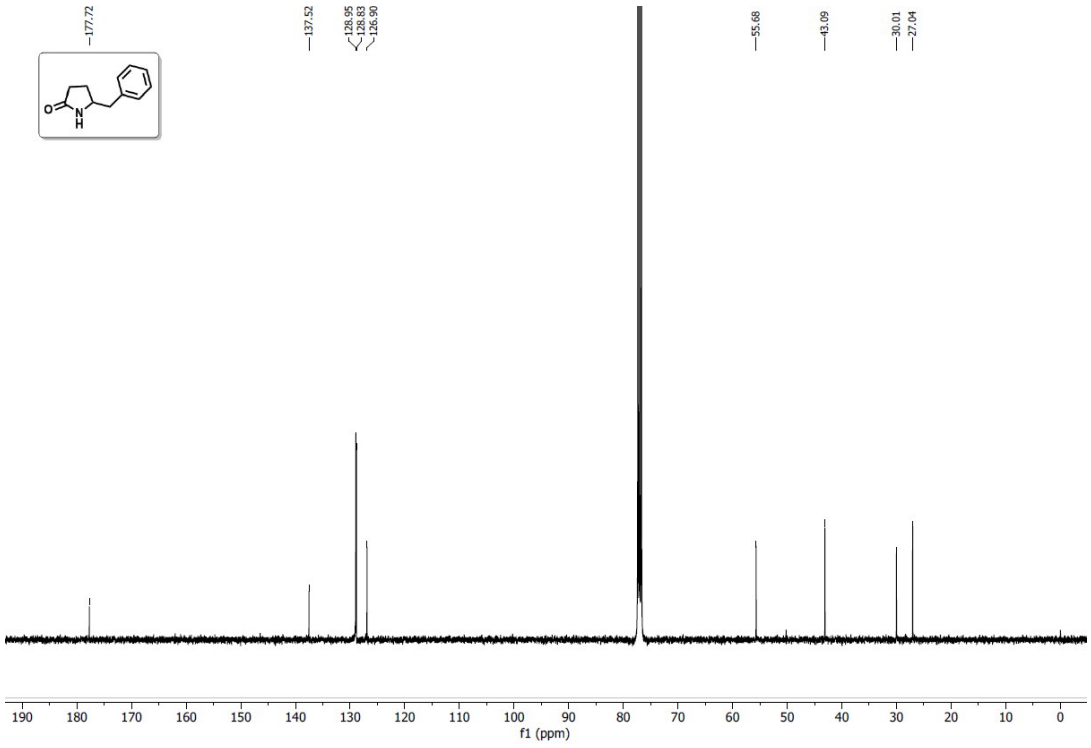
Tert-butyl 2-benzylpyrrolidine-1-carboxylate (2k)



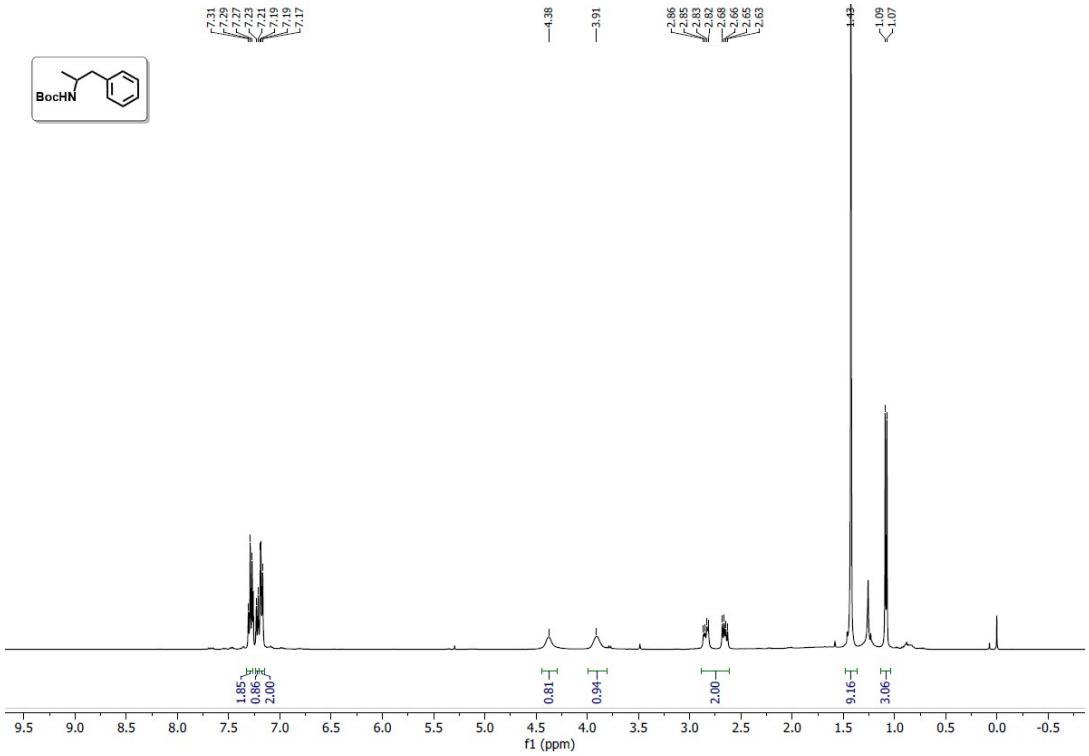


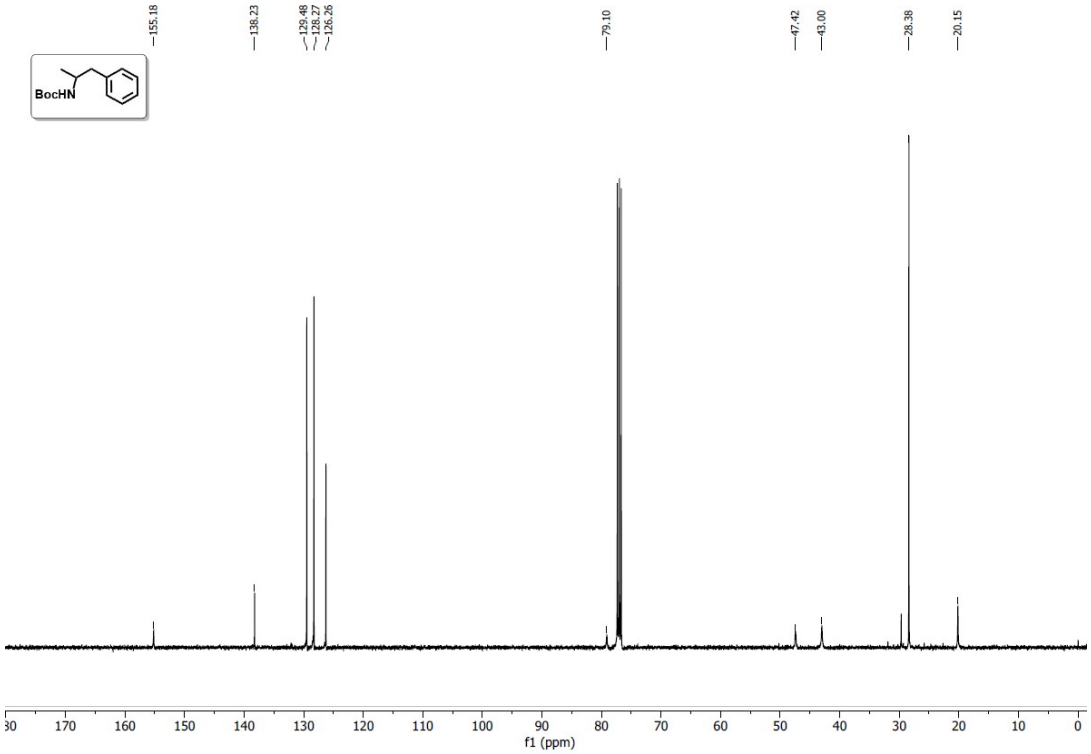
5-benzylpyrrolidin-2-one (2l)



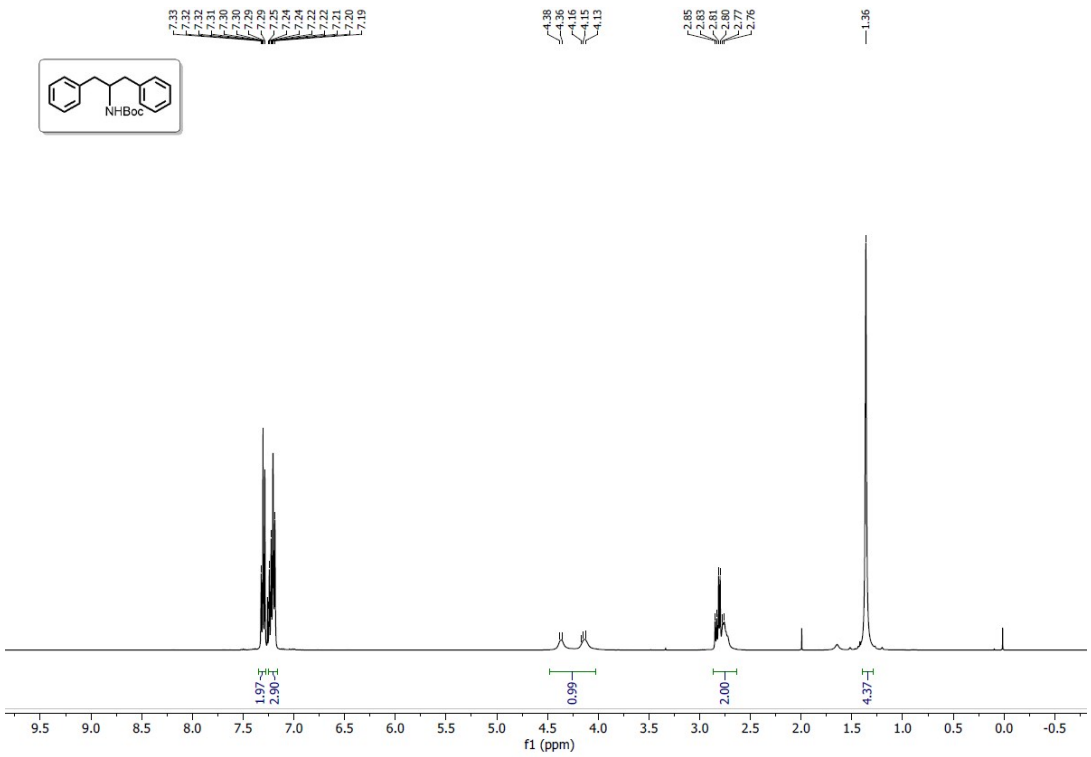


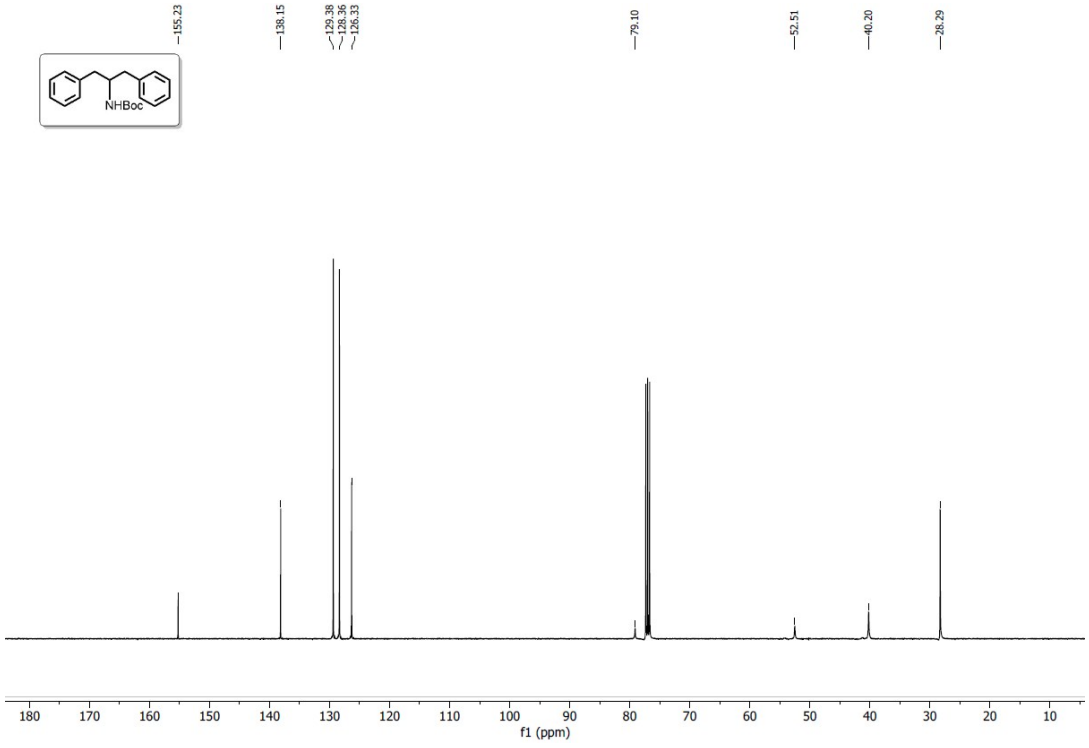
Tert-butyl (1-phenylpropan-2-yl) carbamate (2m)



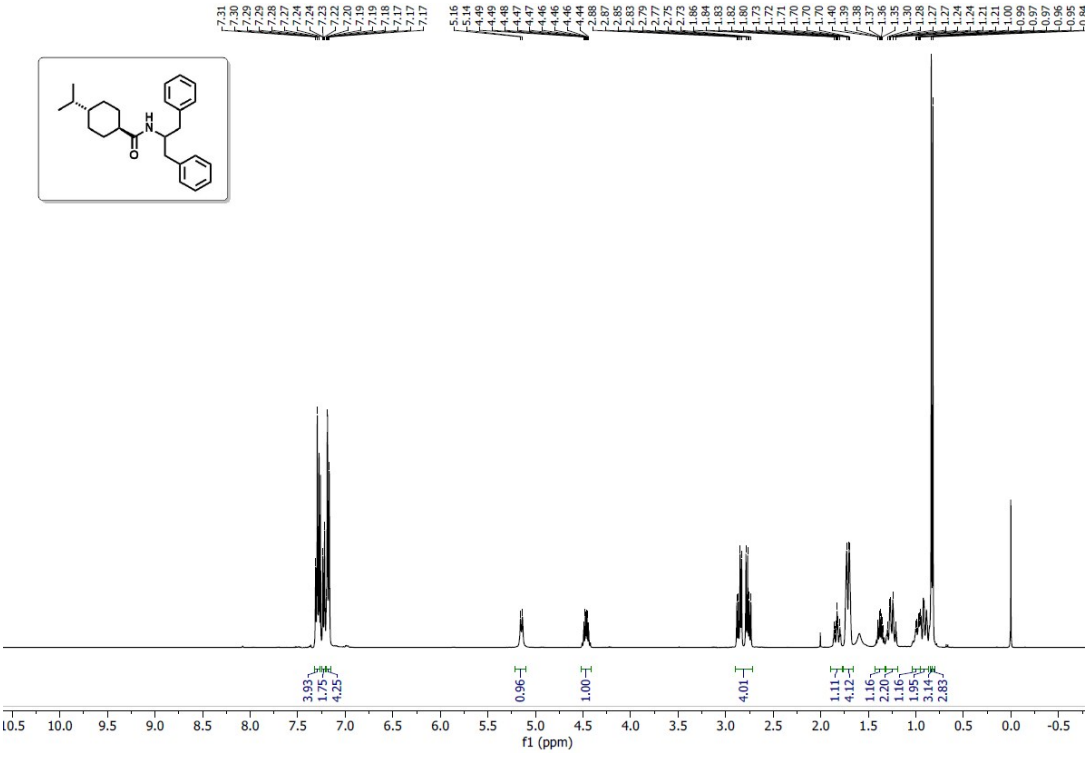


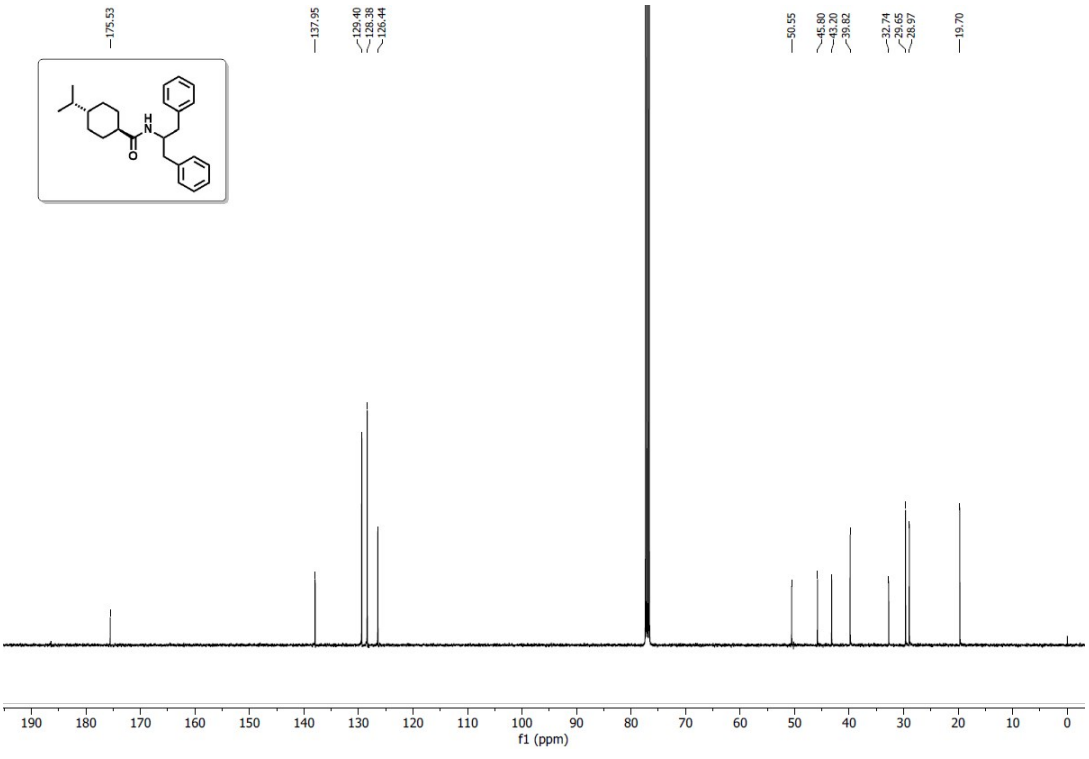
Tert-butyl (1, 3-diphenylpropan-2-yl) carbamate (2n)



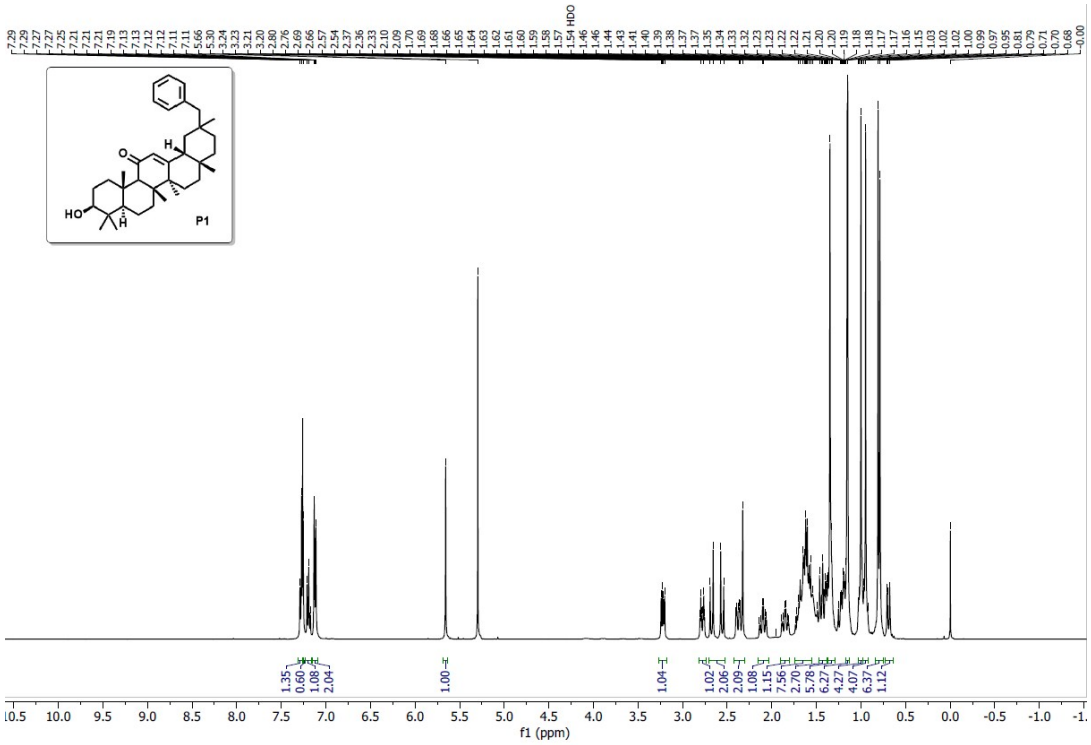


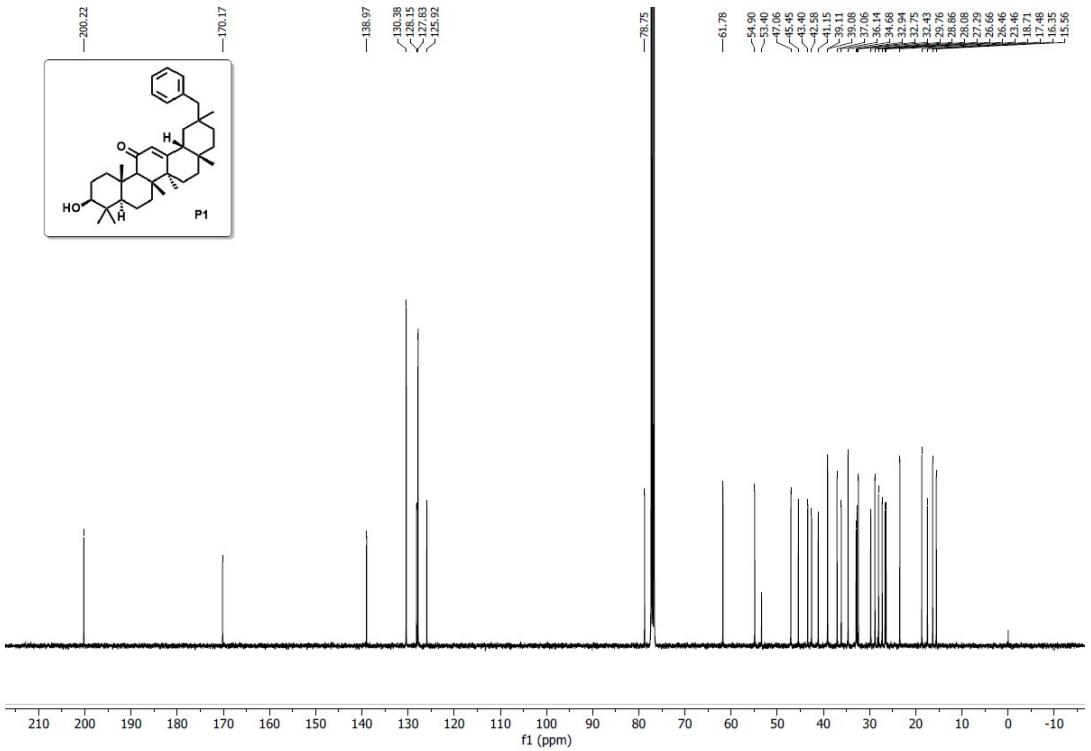
(1r, 4r)-N-(1, 3-diphenylpropan-2-yl)-4-isopropylcyclohexane-1-carboxamide (2o)

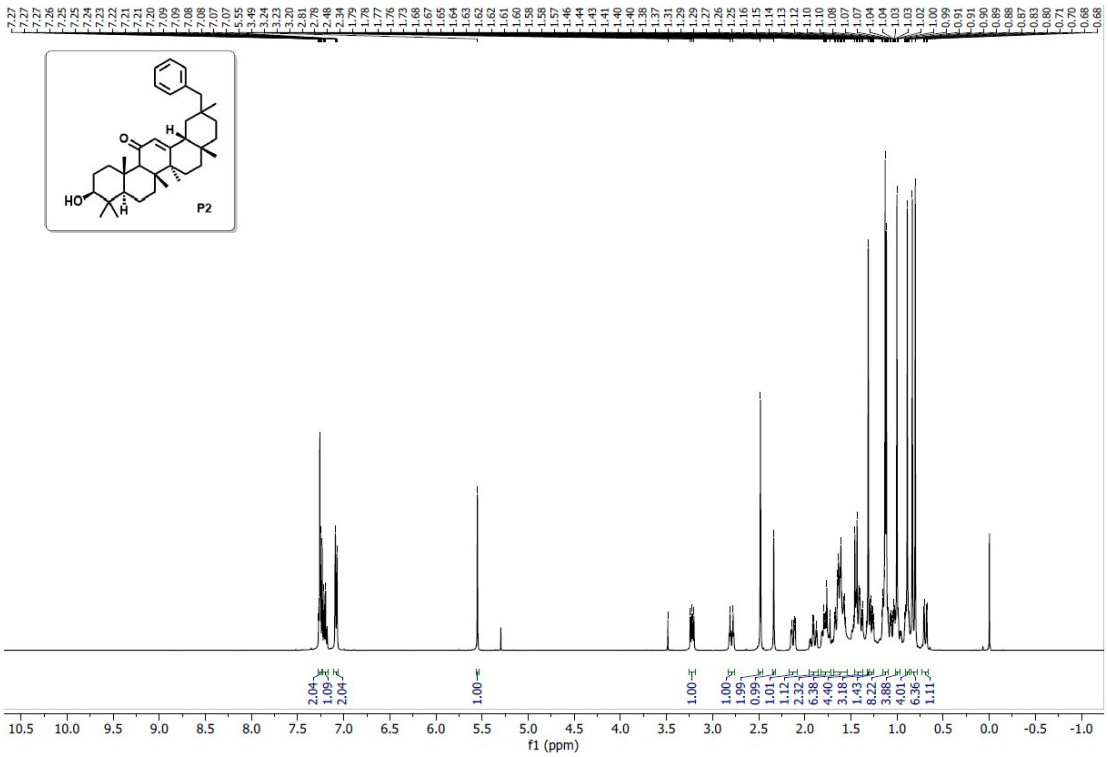


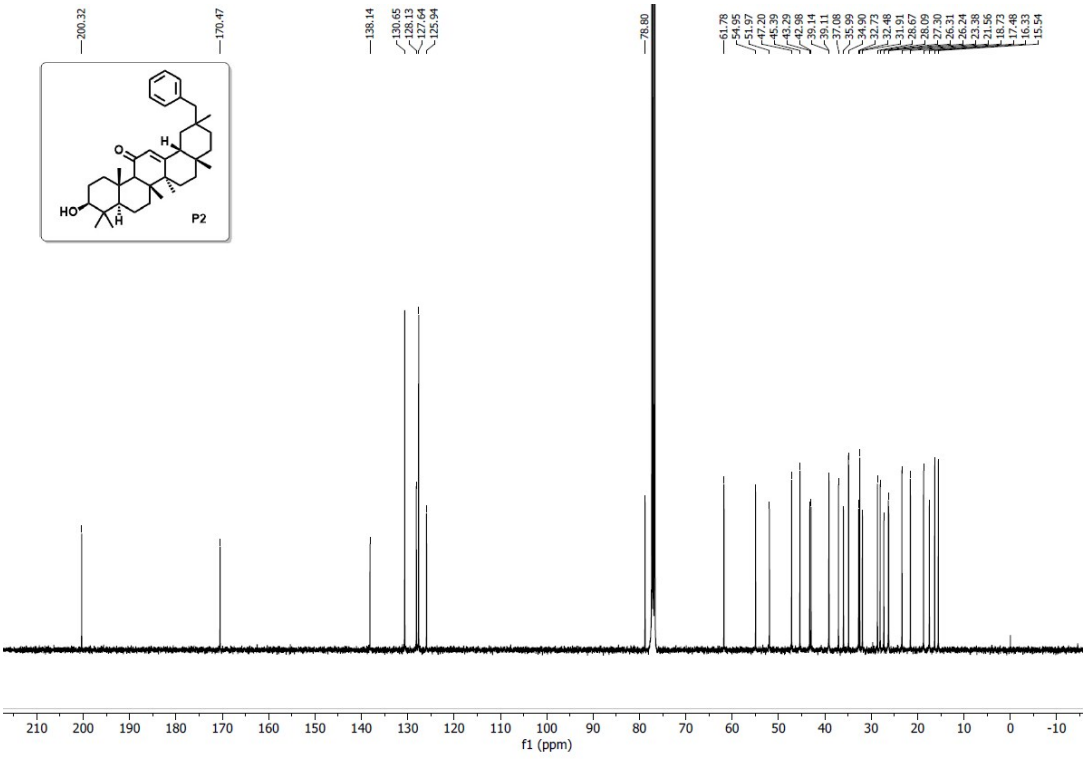


(2S, 4aR, 6aS, 6bR, 8aR, 10S, 12aS, 14bR)-2-benzyl-10-hydroxy-2,4a,6a,6b,9,9,12a-heptamethyl-1, 3, 4, 4a, 5, 6, 6a, 6b, 7, 8, 8a, 9, 10, 11, 12, 12a, 12b, 14b -octadecahydropicen-13 (2H)-one (2p)

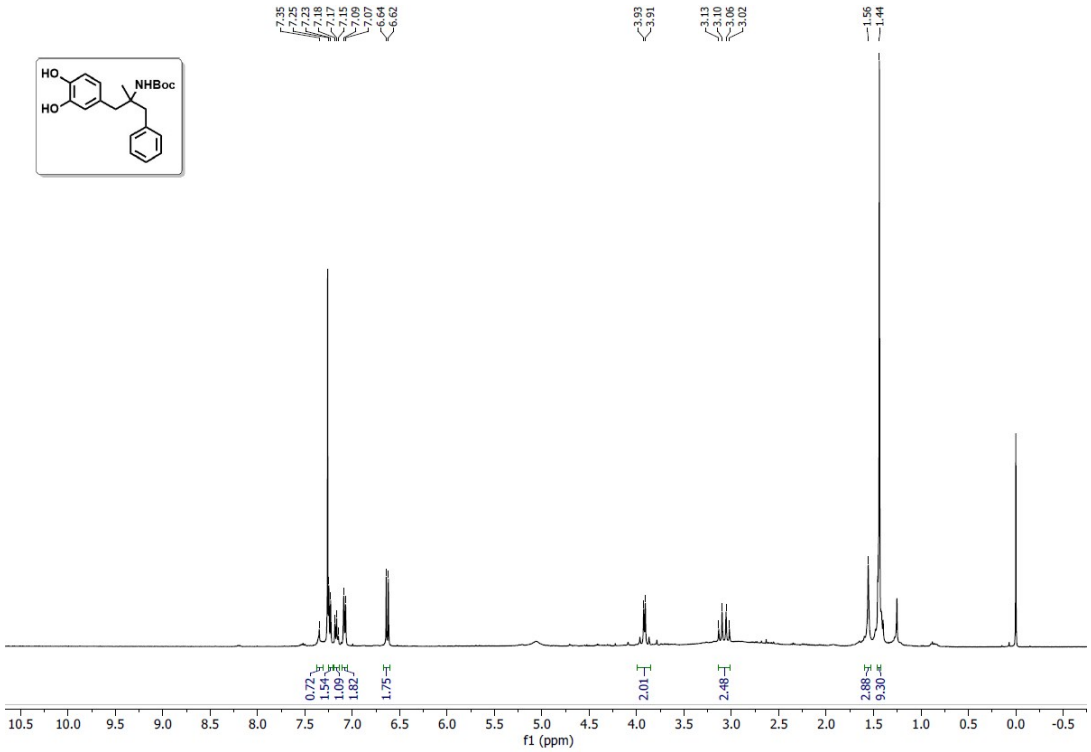


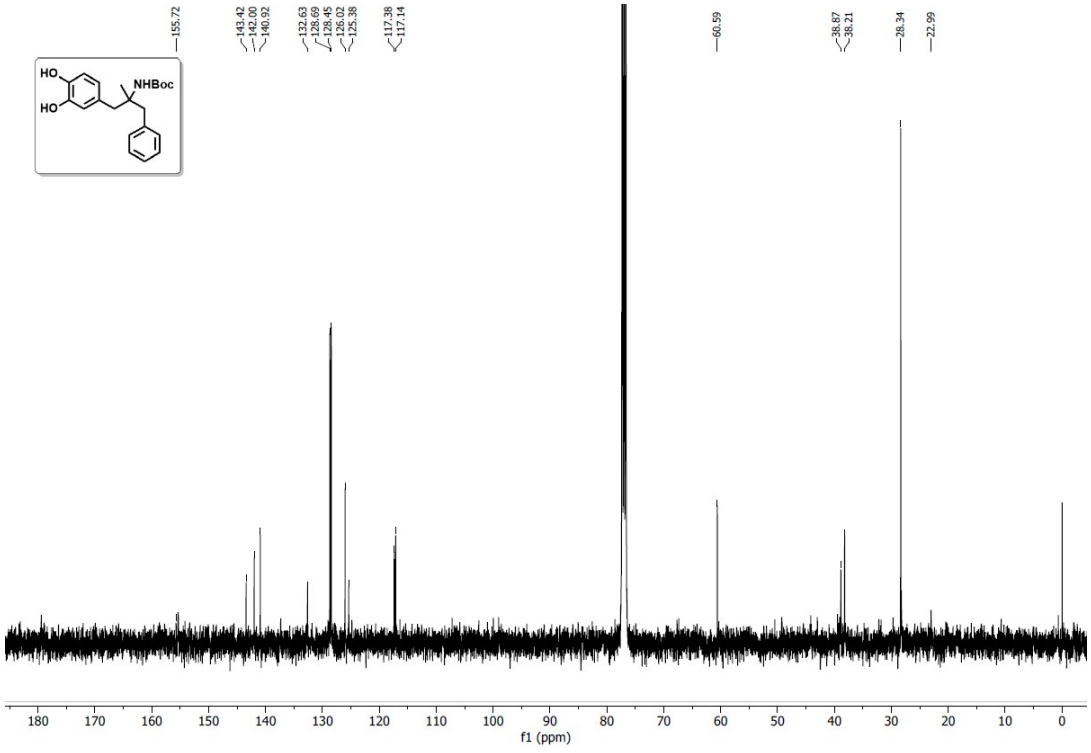




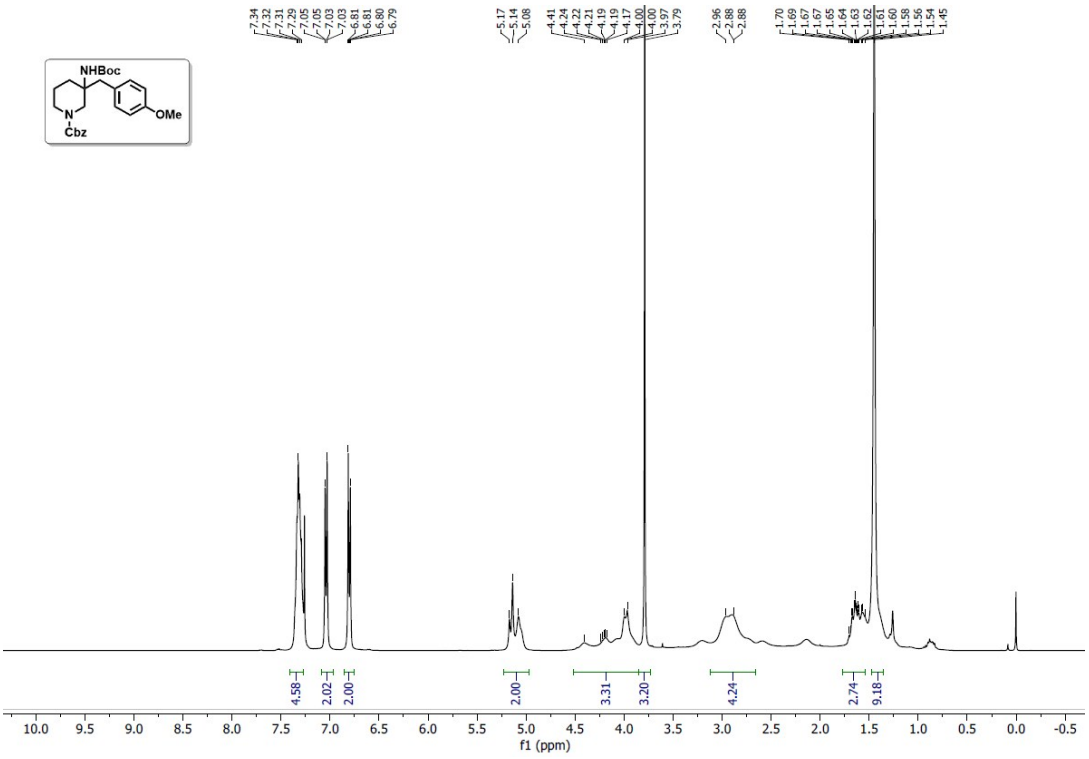


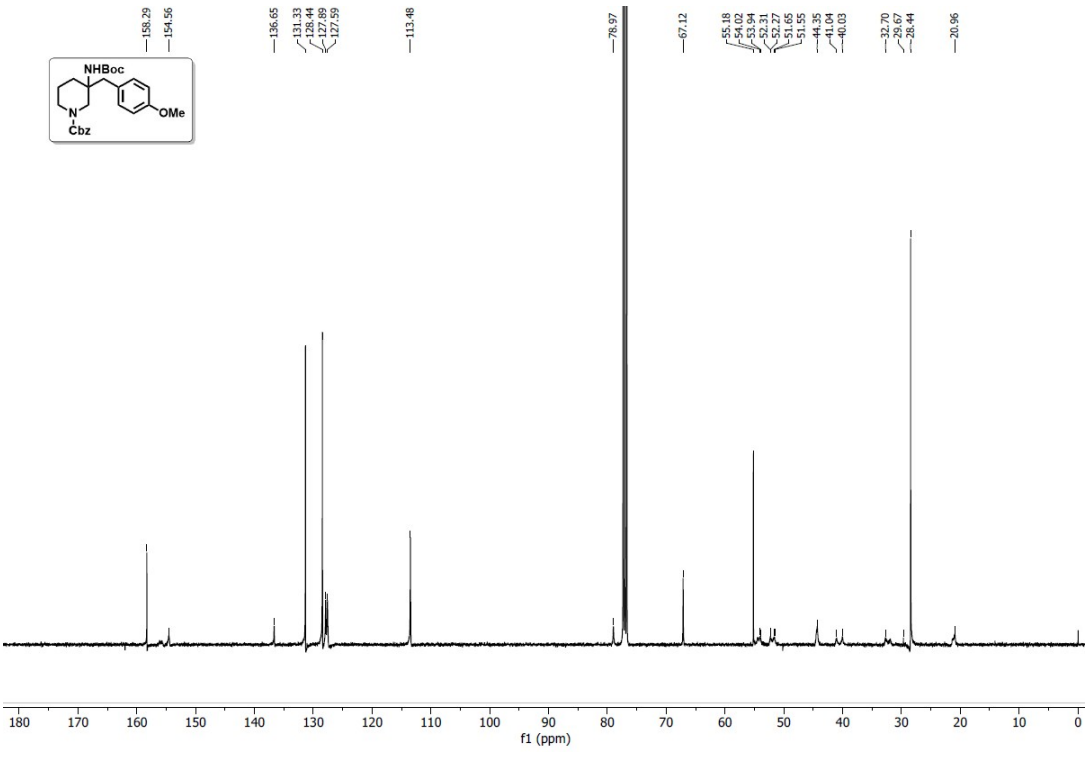
Tert-butyl (1-(3, 4-dihydroxyphenyl)-2-methyl-3-phenylpropan-2-yl) carbamate (2q)



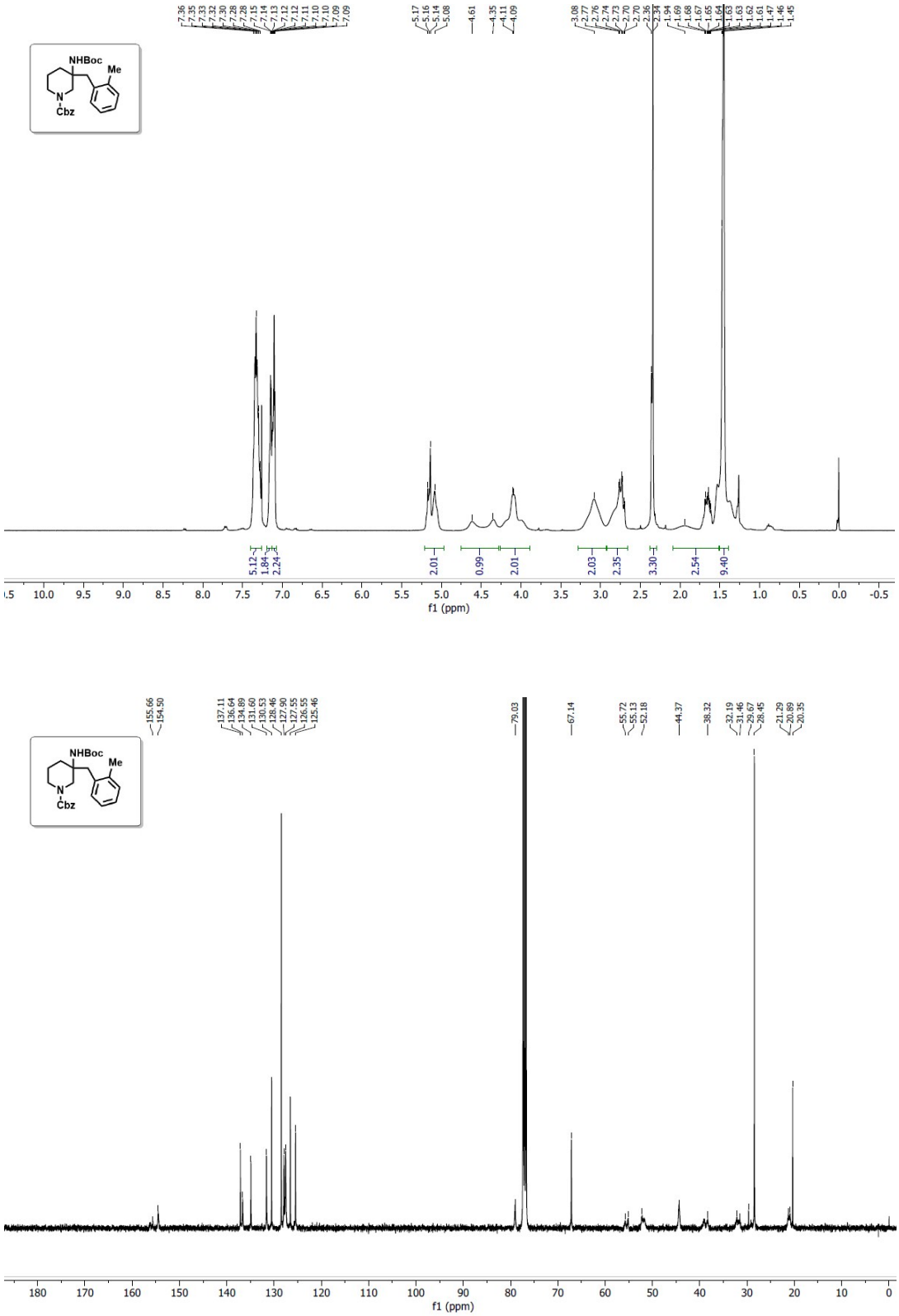


Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-methoxybenzyl) piperidine-1-carboxylate (3a)

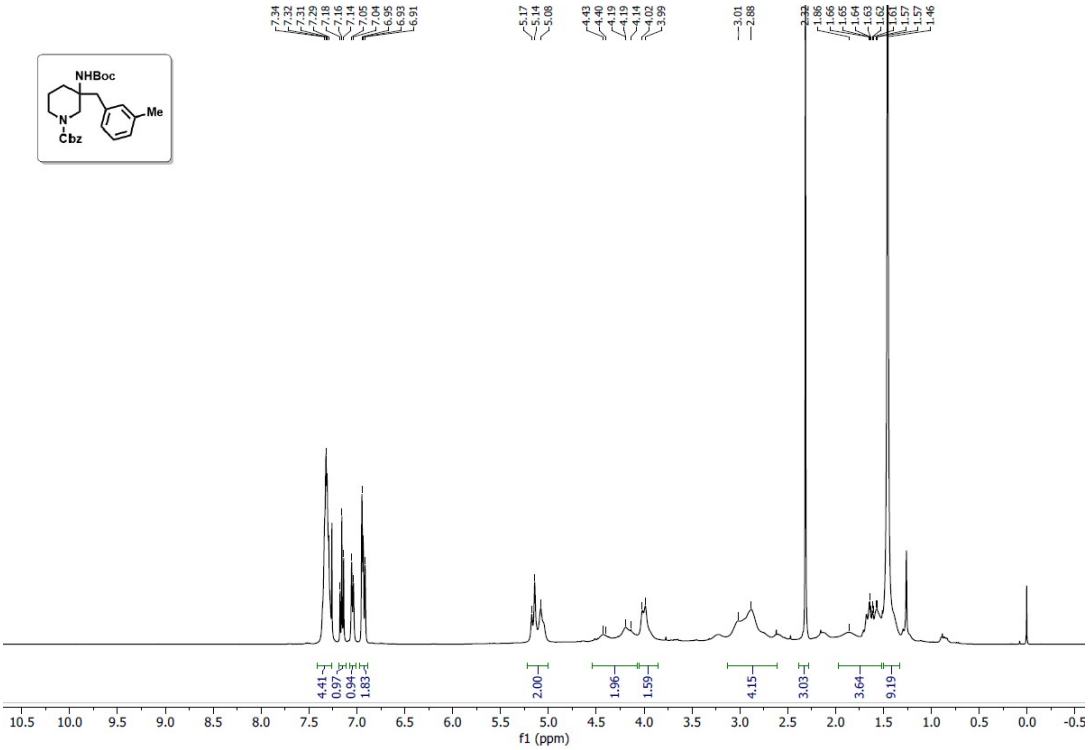


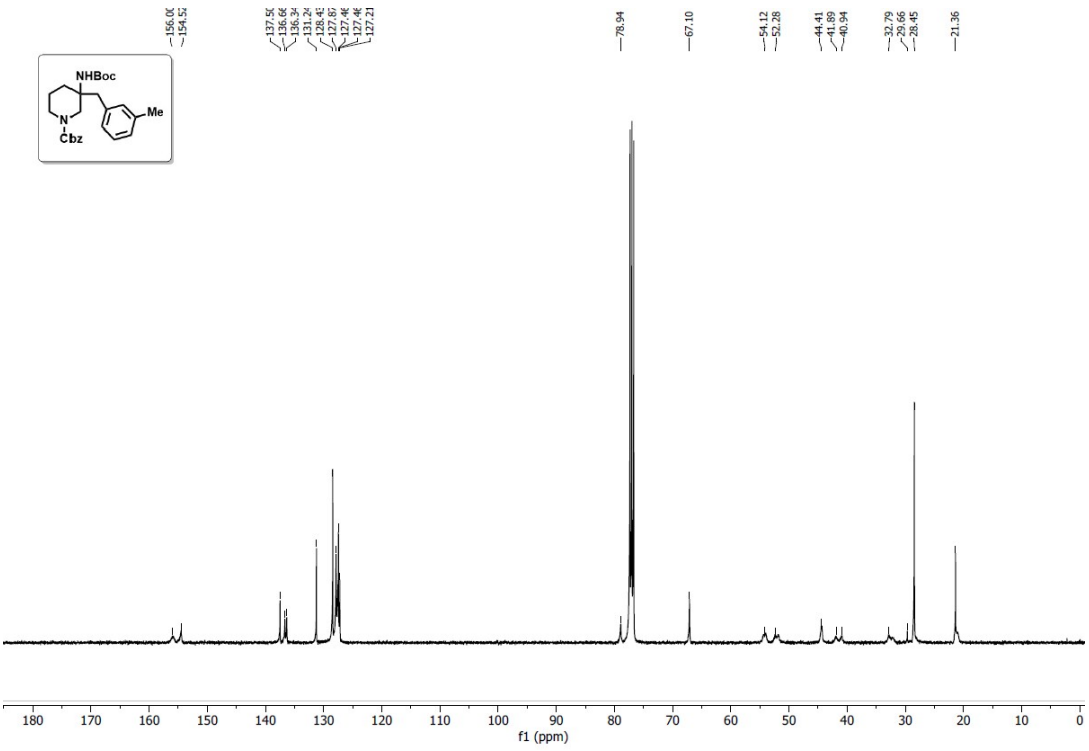


Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-methylbenzyl) piperidine-1-carboxylate (3b)

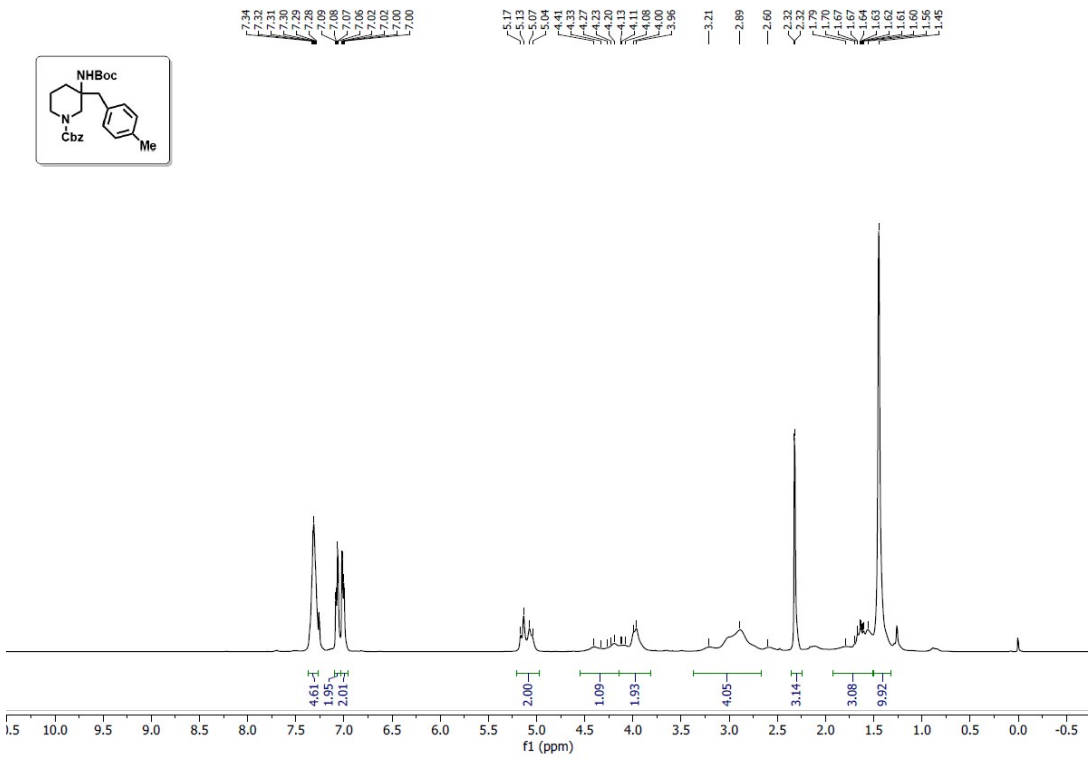


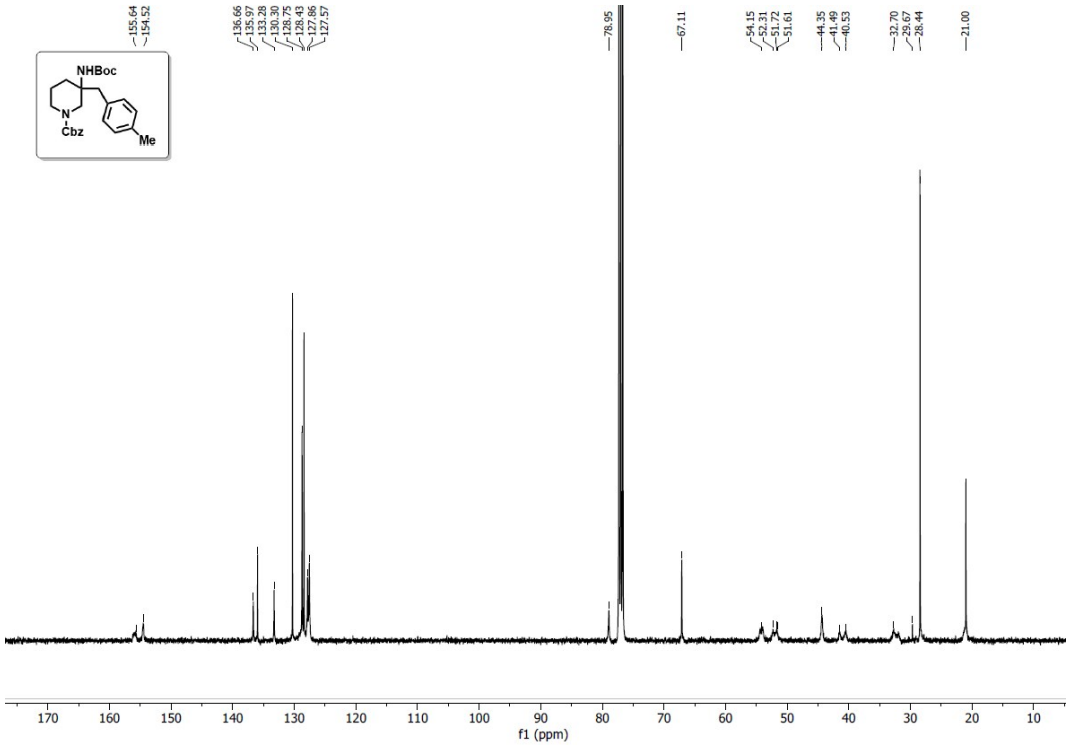
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(3-methylbenzyl) piperidine-1-carboxylate (3c)



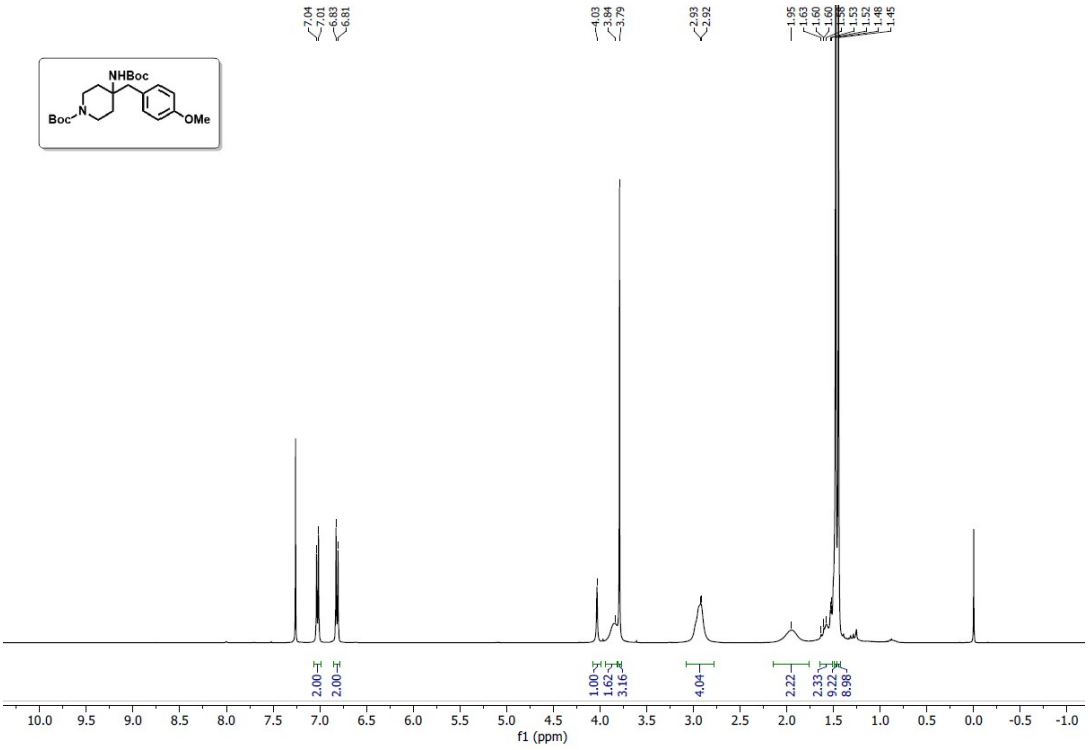


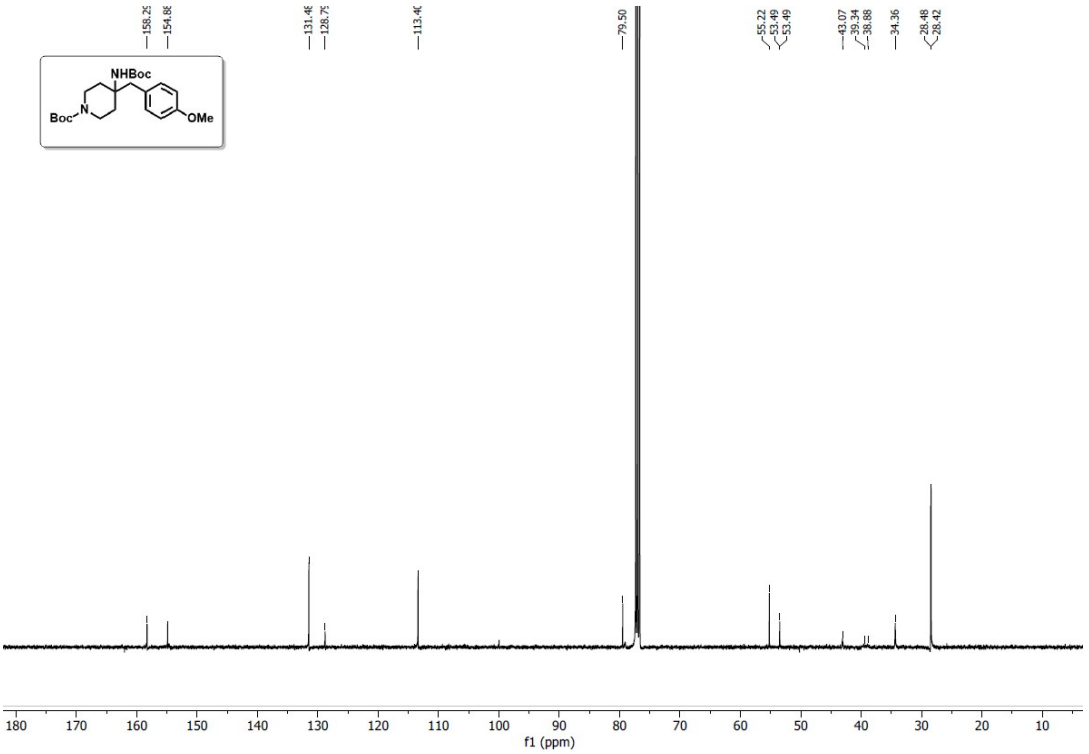
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-methylbenzyl) piperidine-1-carboxylate (3d)



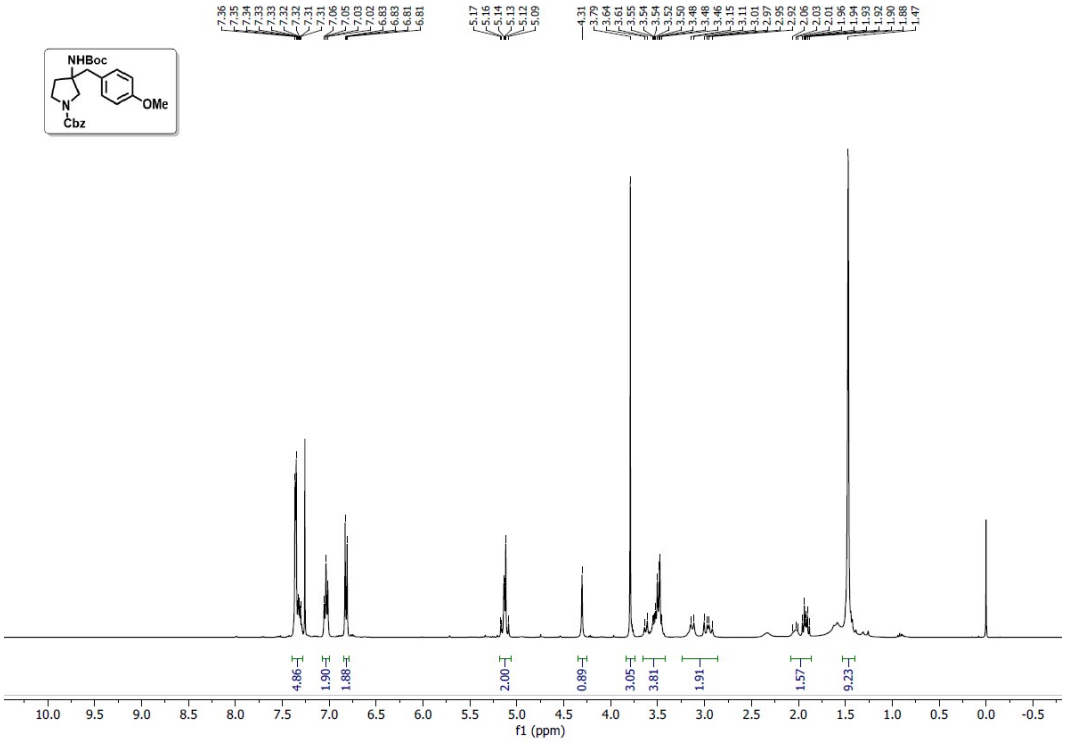


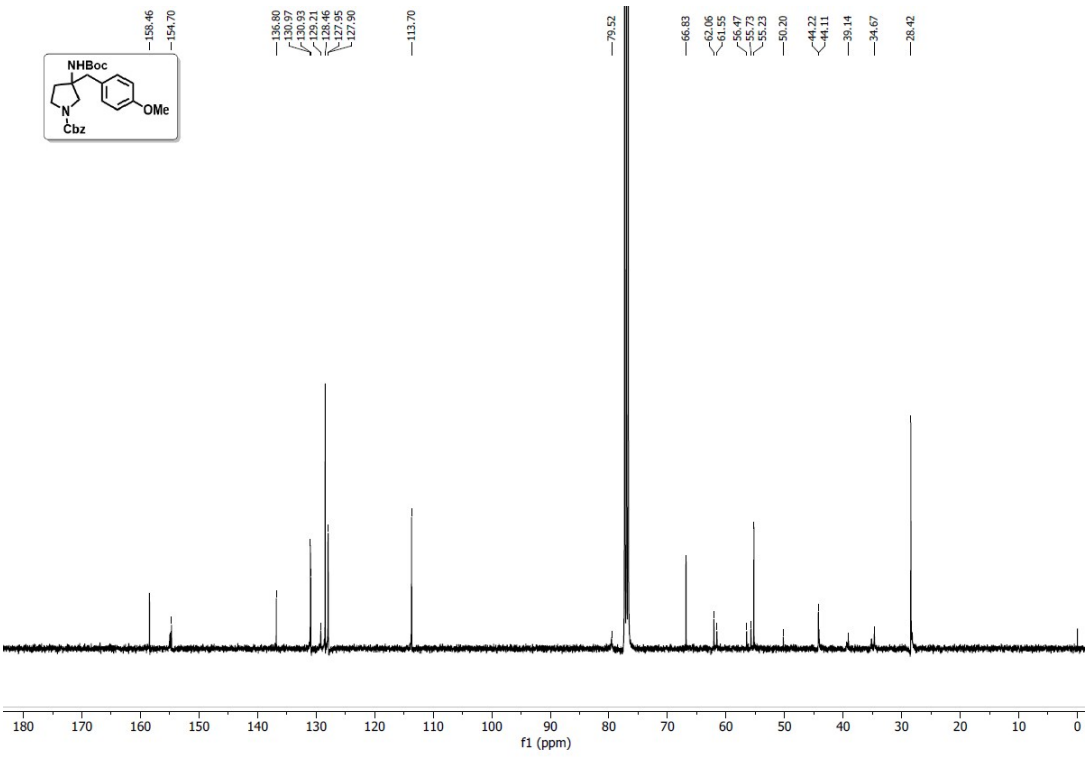
Tert-butyl 4-((tert-butoxycarbonyl) amino)-4-(4-methoxybenzyl) piperidine-1-carboxylate (3e)



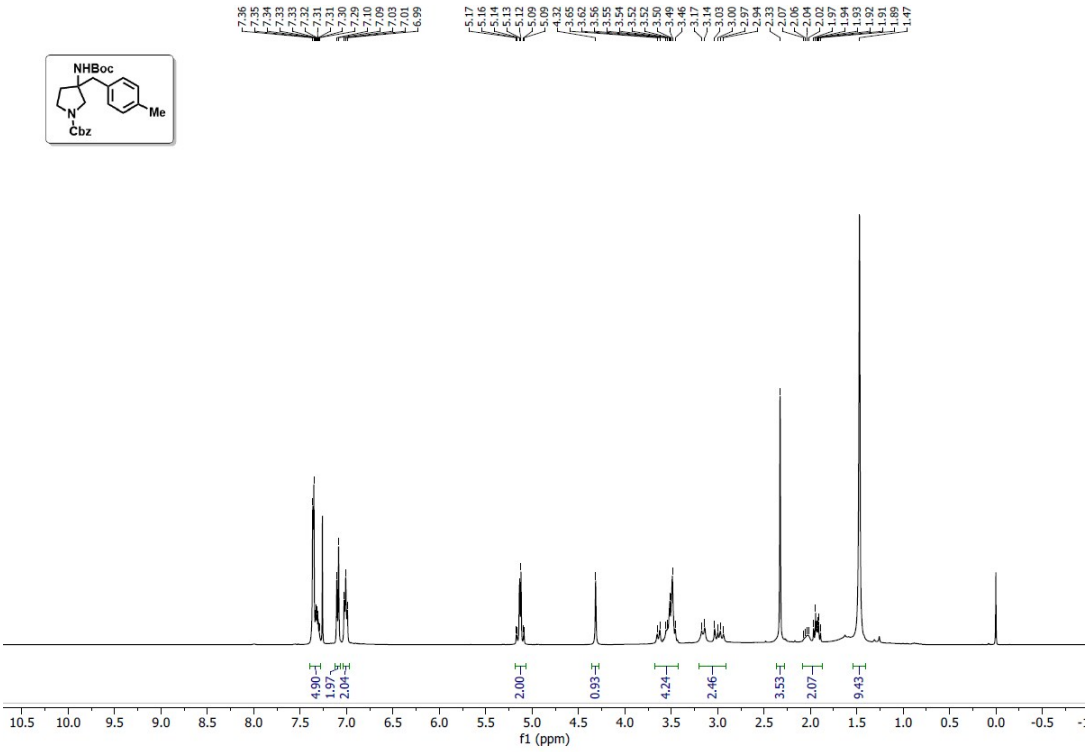


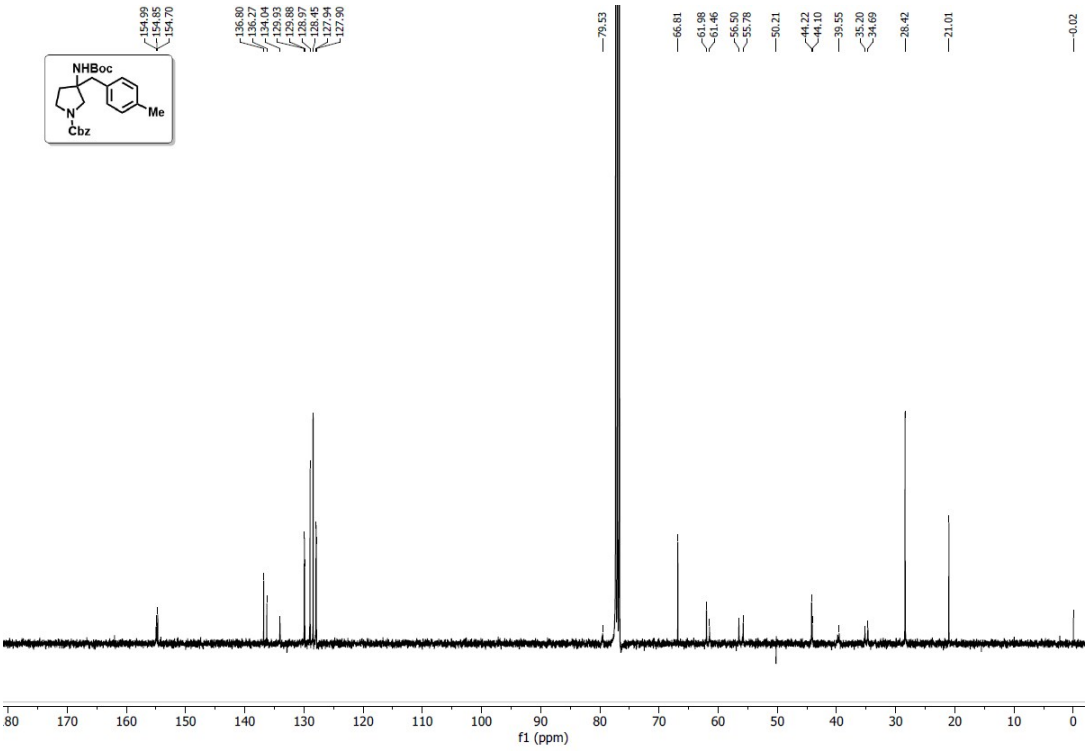
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-methoxybenzyl) pyrrolidine-1-carboxylate (3f)



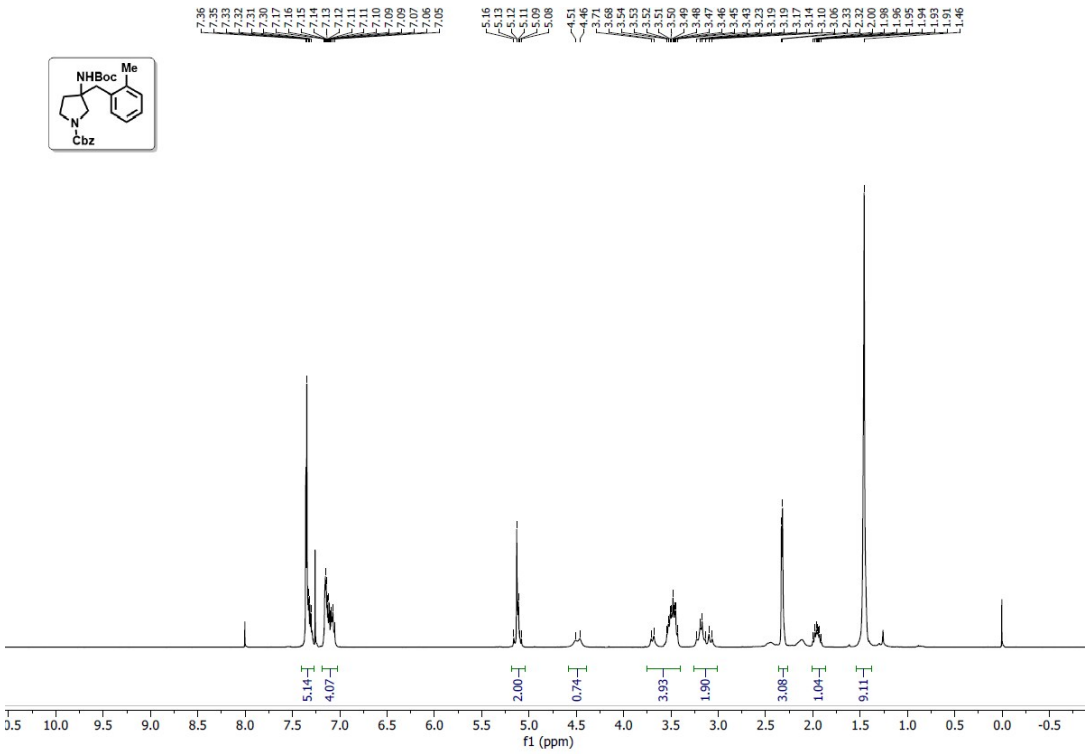


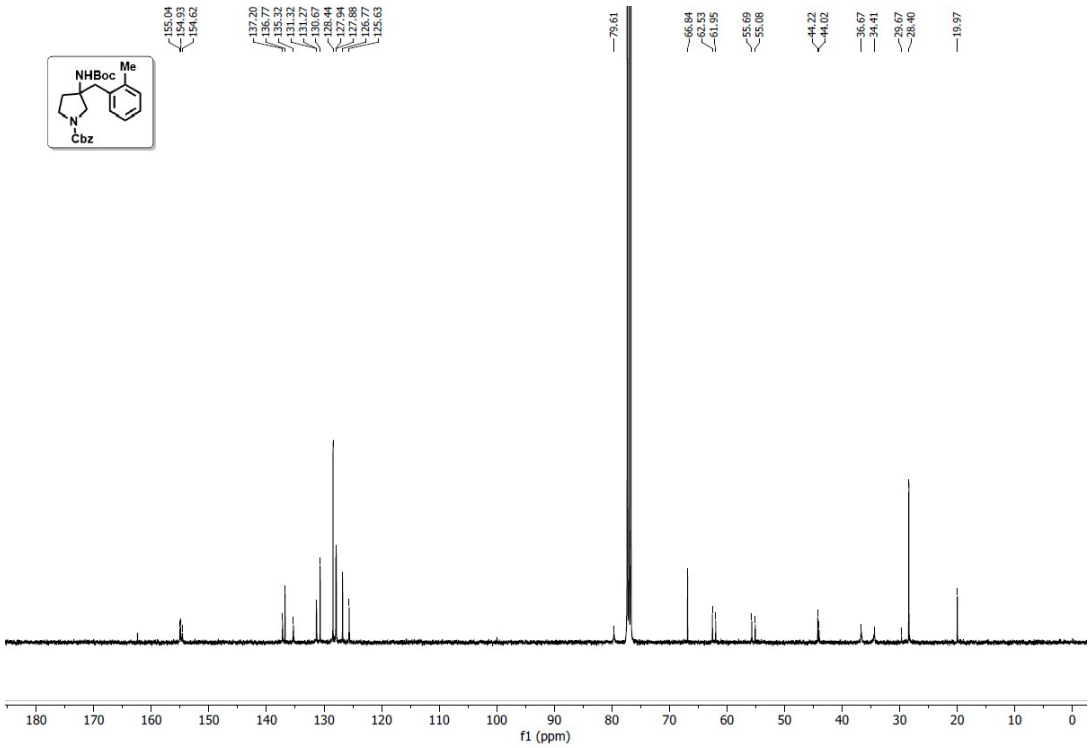
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-methylbenzyl) pyrrolidine-1-carboxylate (3g)



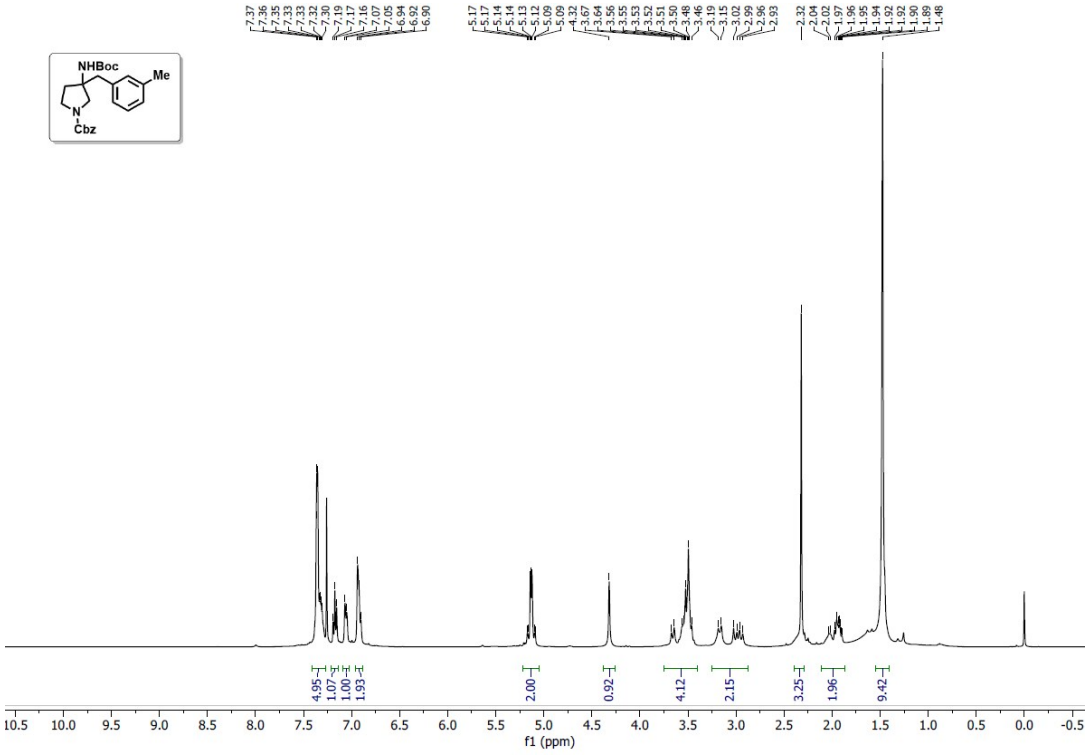


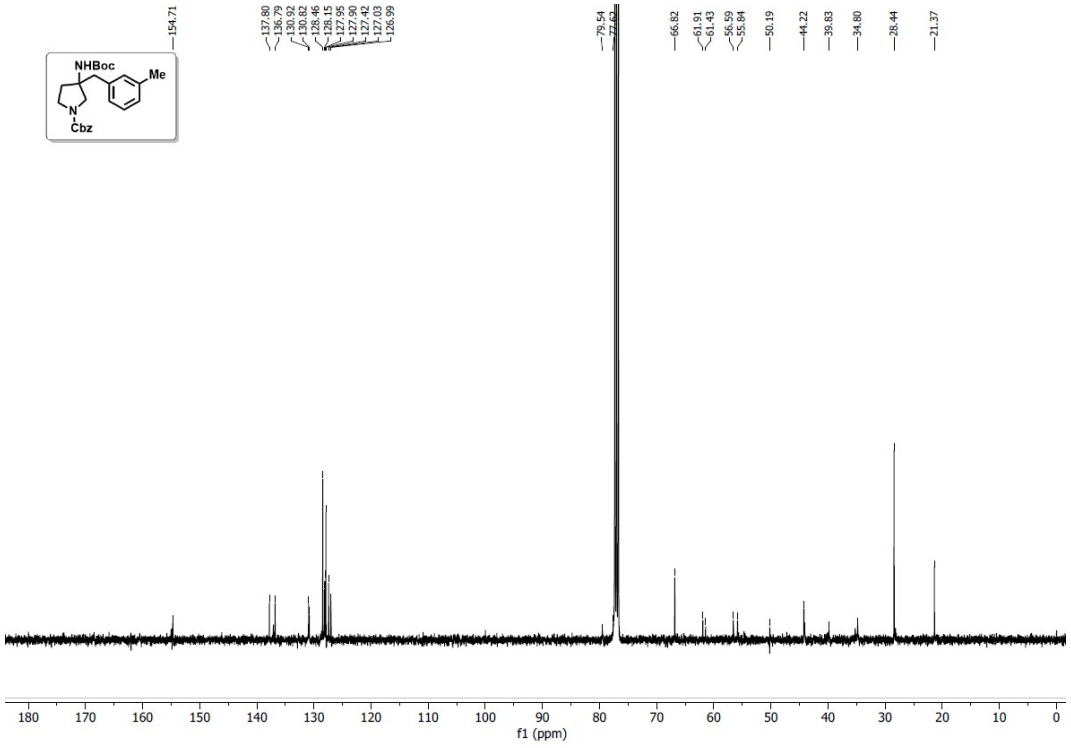
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-methylbenzyl) pyrrolidine-1- carboxylate (3h)



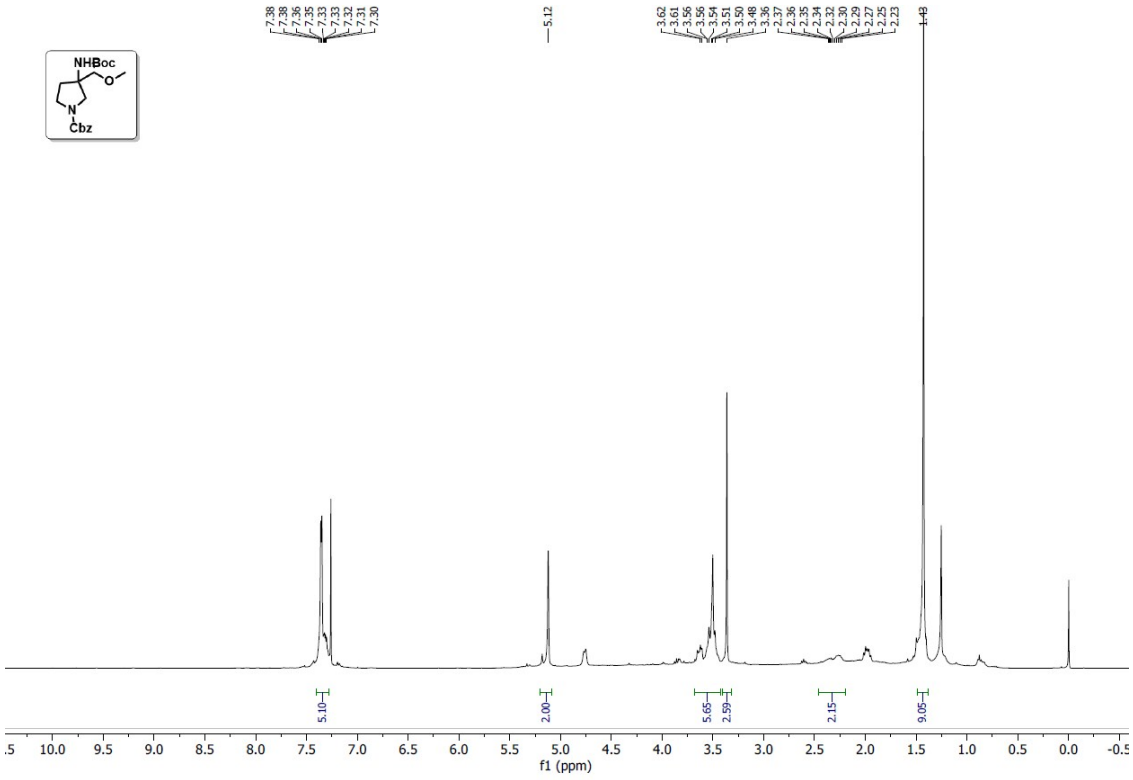


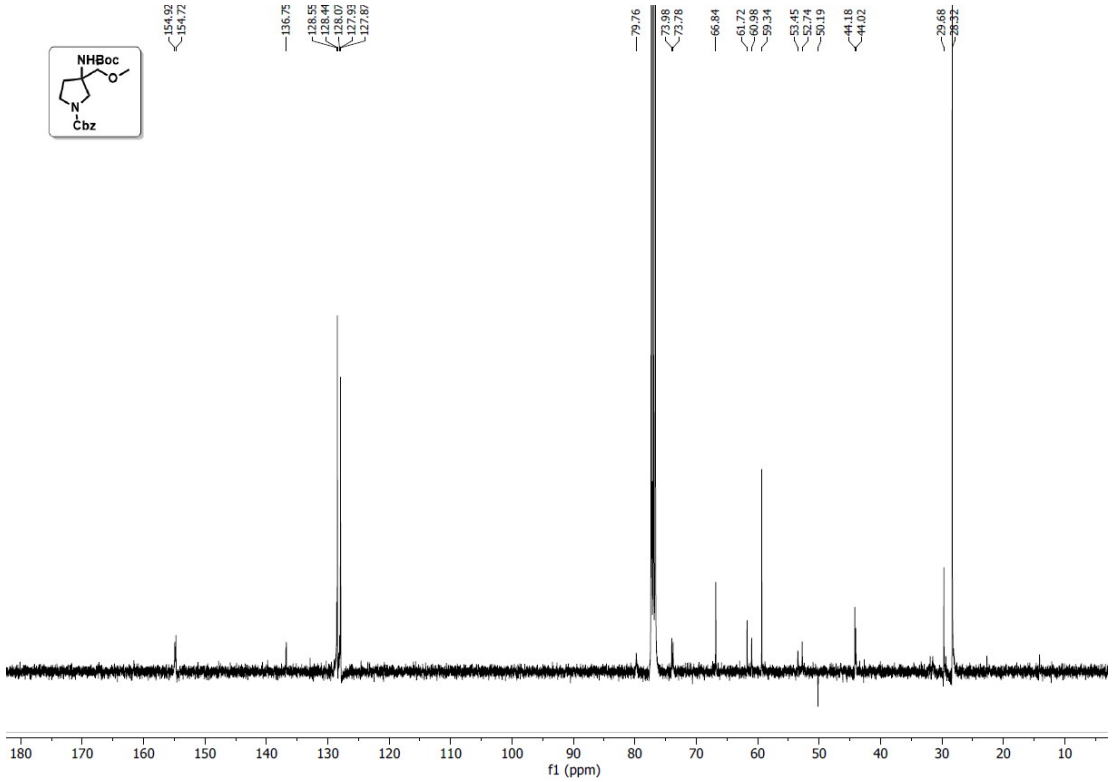
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(3-methylbenzyl) pyrrolidine-1-carboxylate (3i)



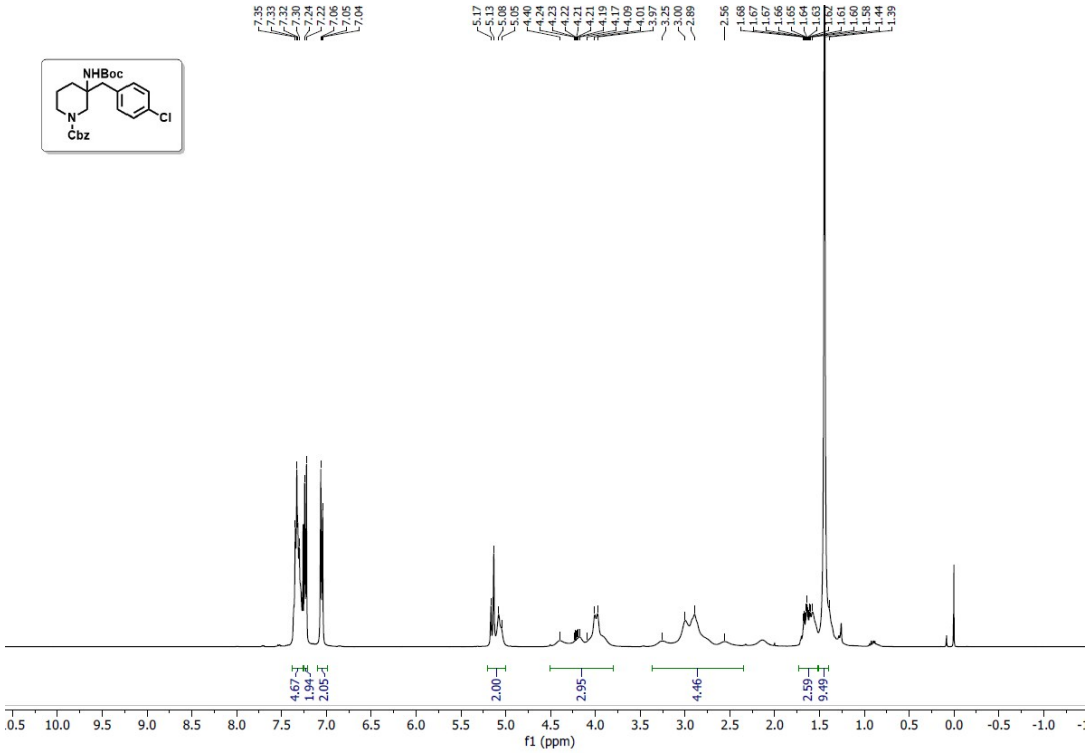


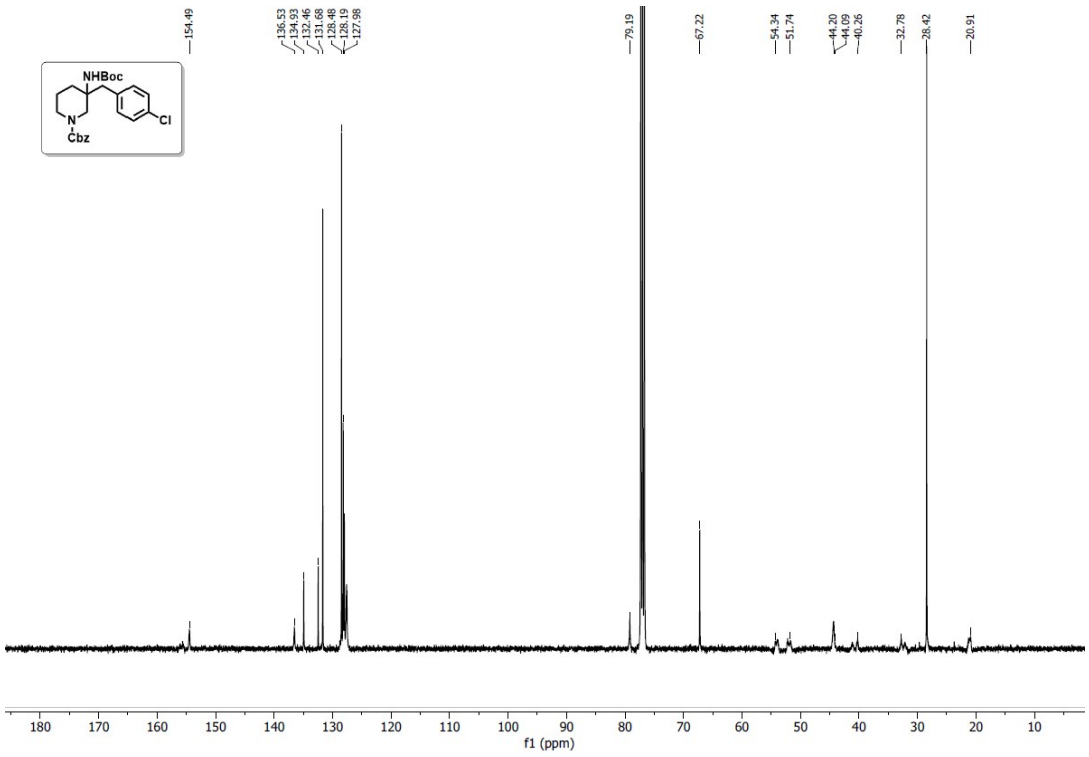
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(methoxymethyl) pyrrolidine-1-carboxylate (3j)



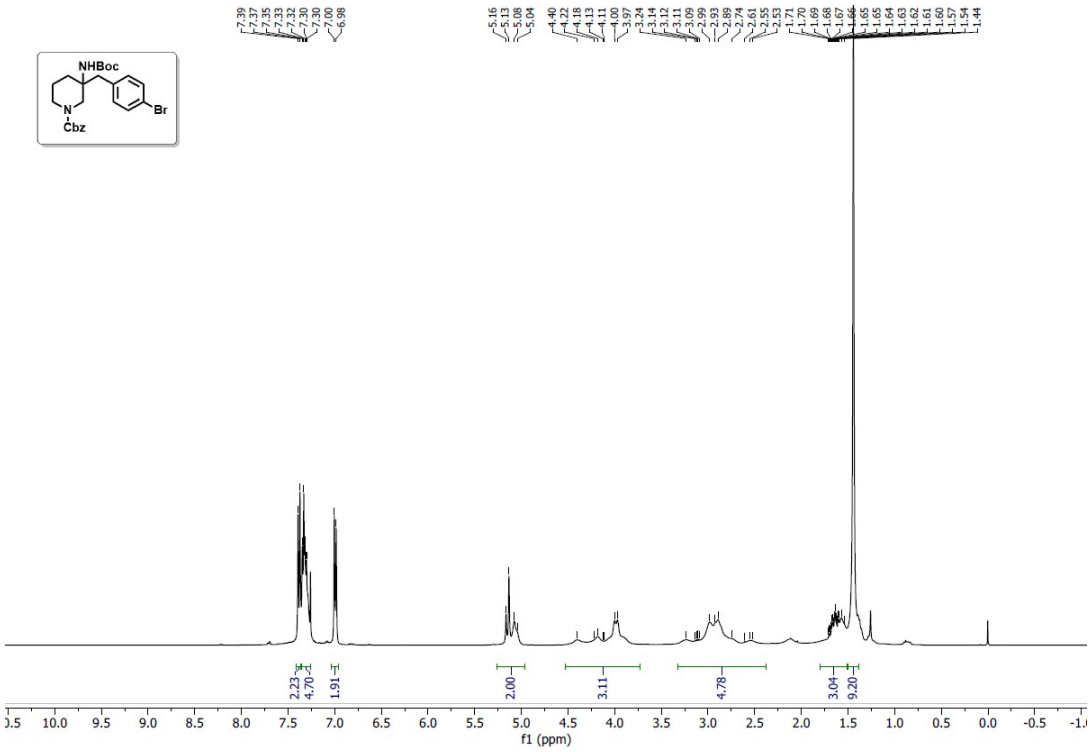


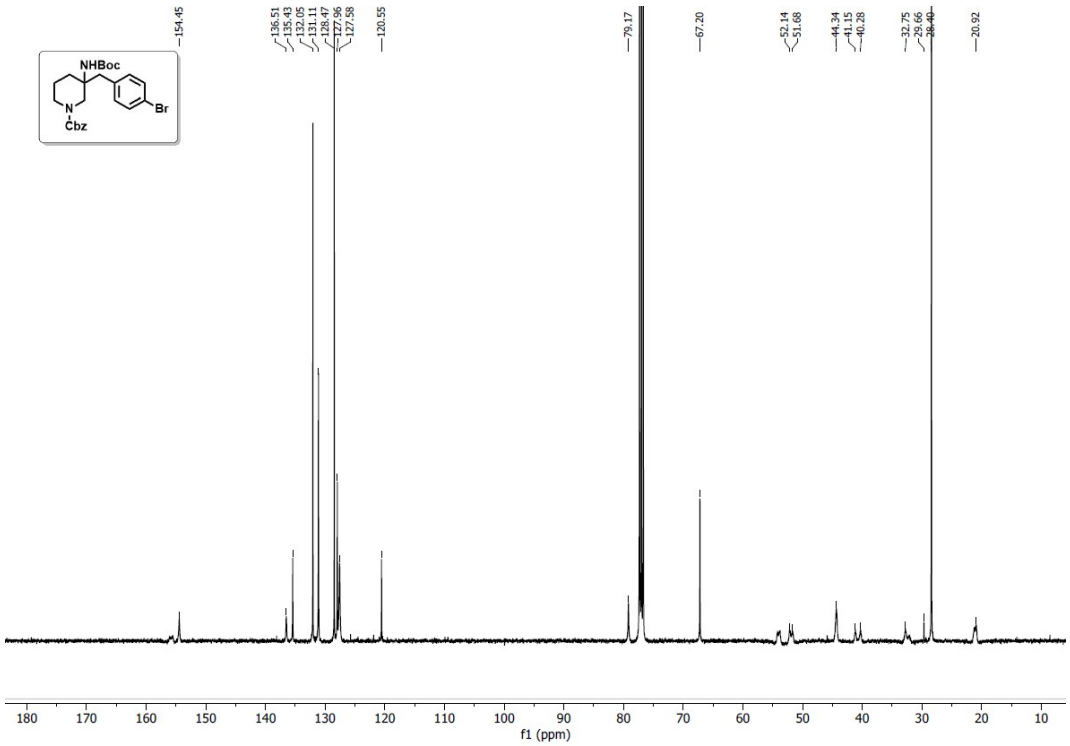
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-chlorobenzyl) piperidine-1-carboxylate (4a)



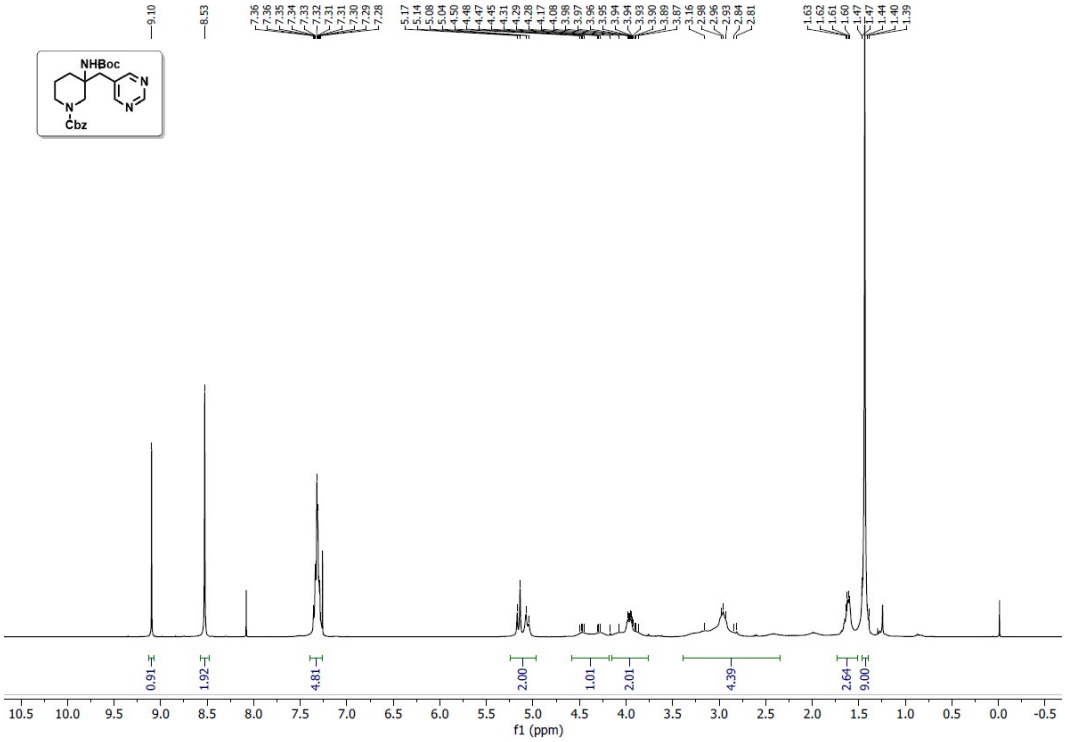


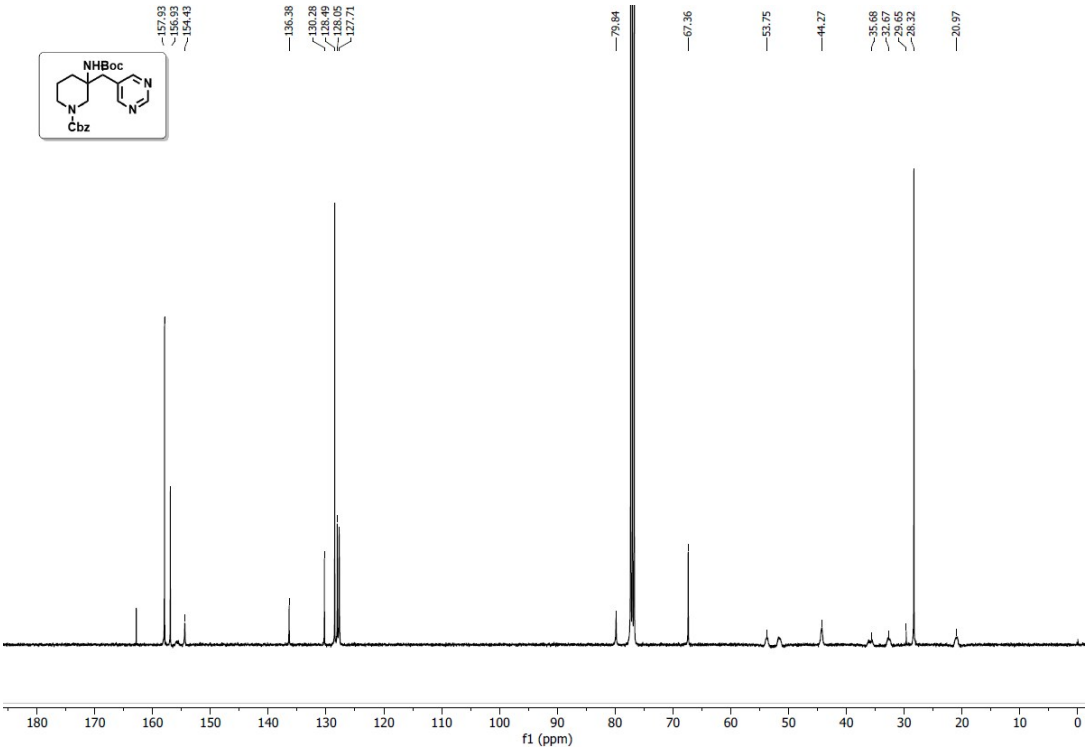
Benzyl 3-(4-bromobenzyl)-3-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (4b)



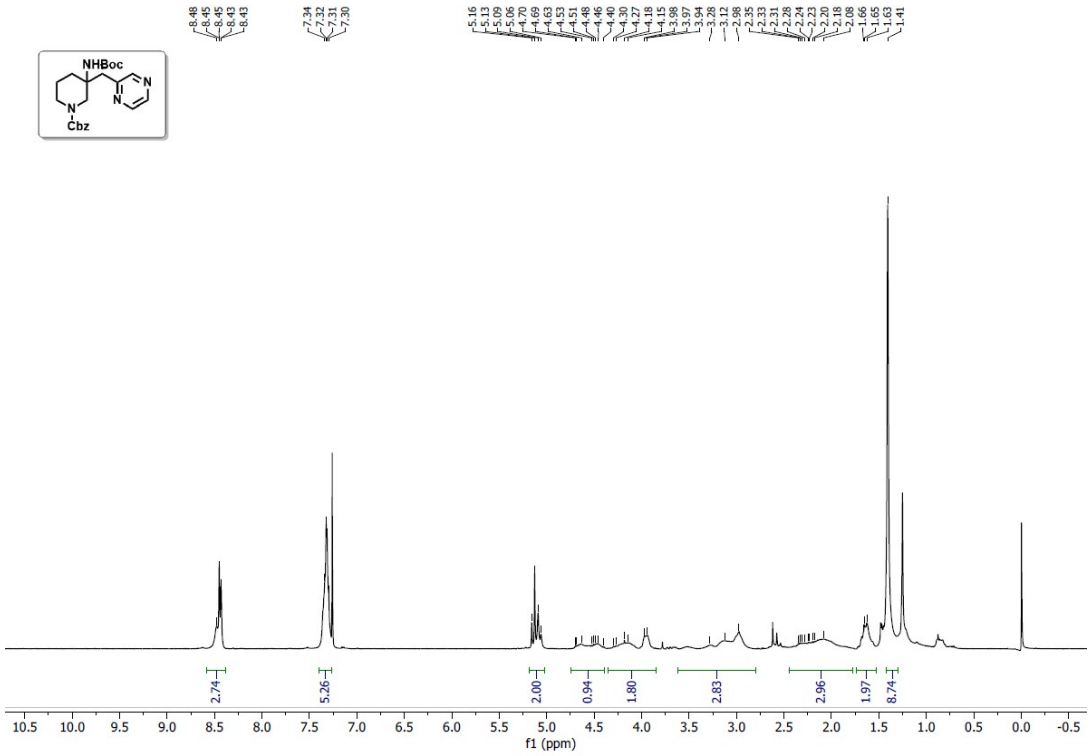


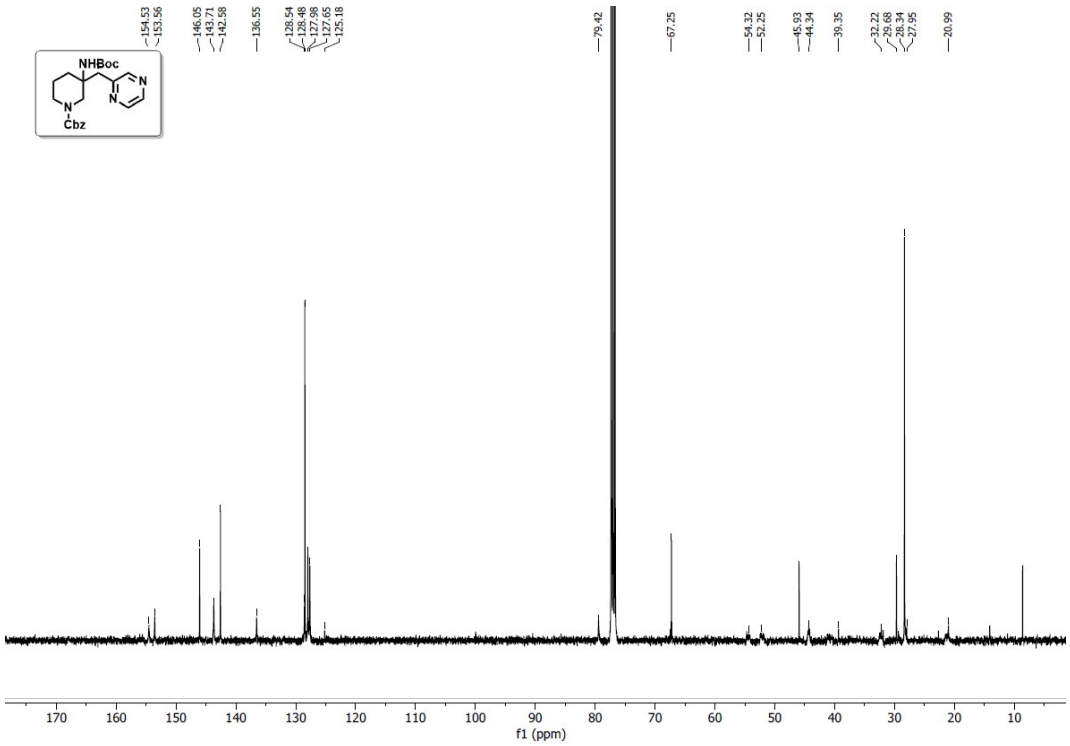
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(pyrimidin-5-ylmethyl) piperidine-1- carboxylate (4c)



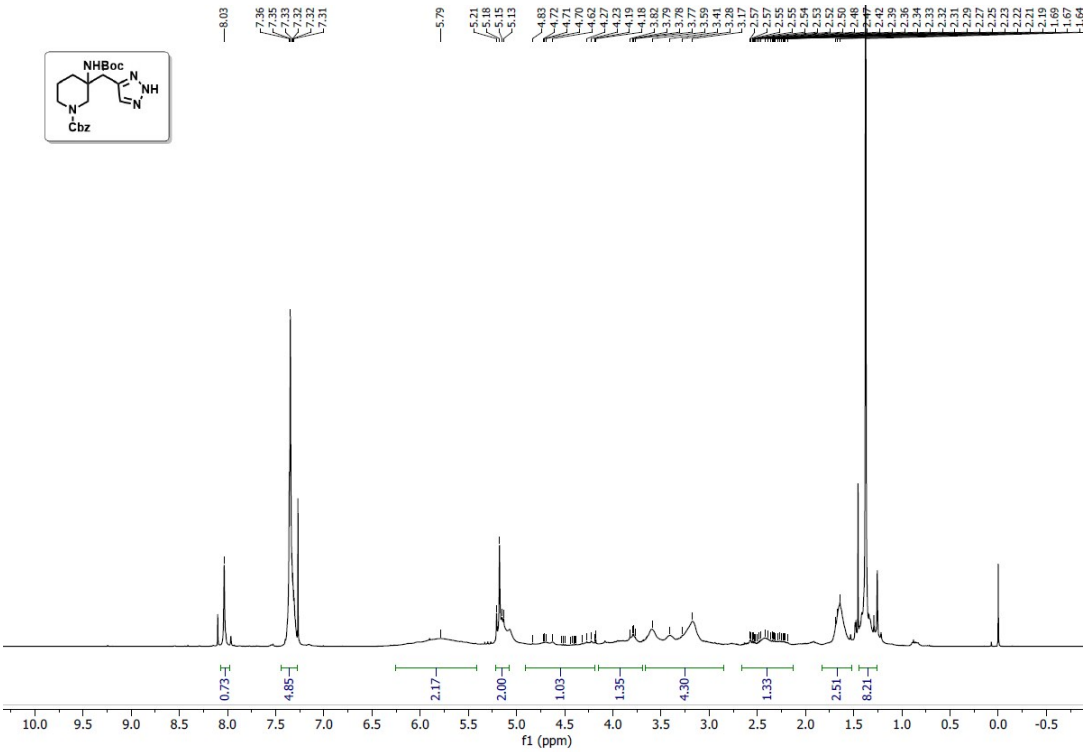


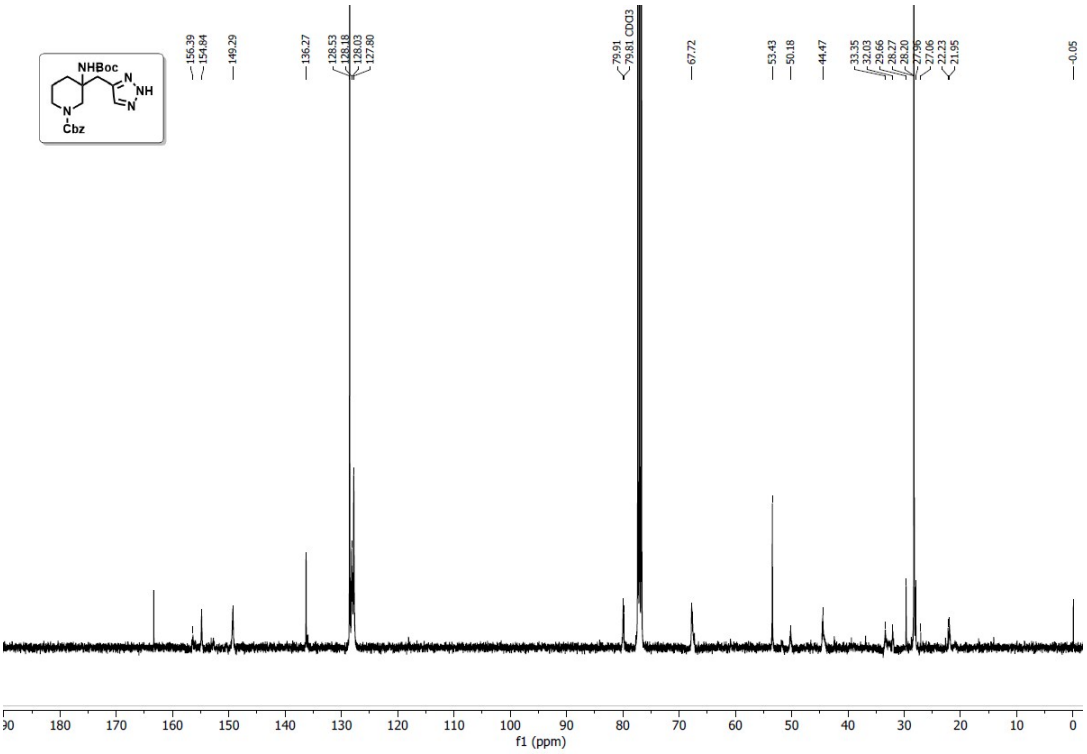
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(pyrazin-2-ylmethyl) piperidine-1-carboxylate (4d)



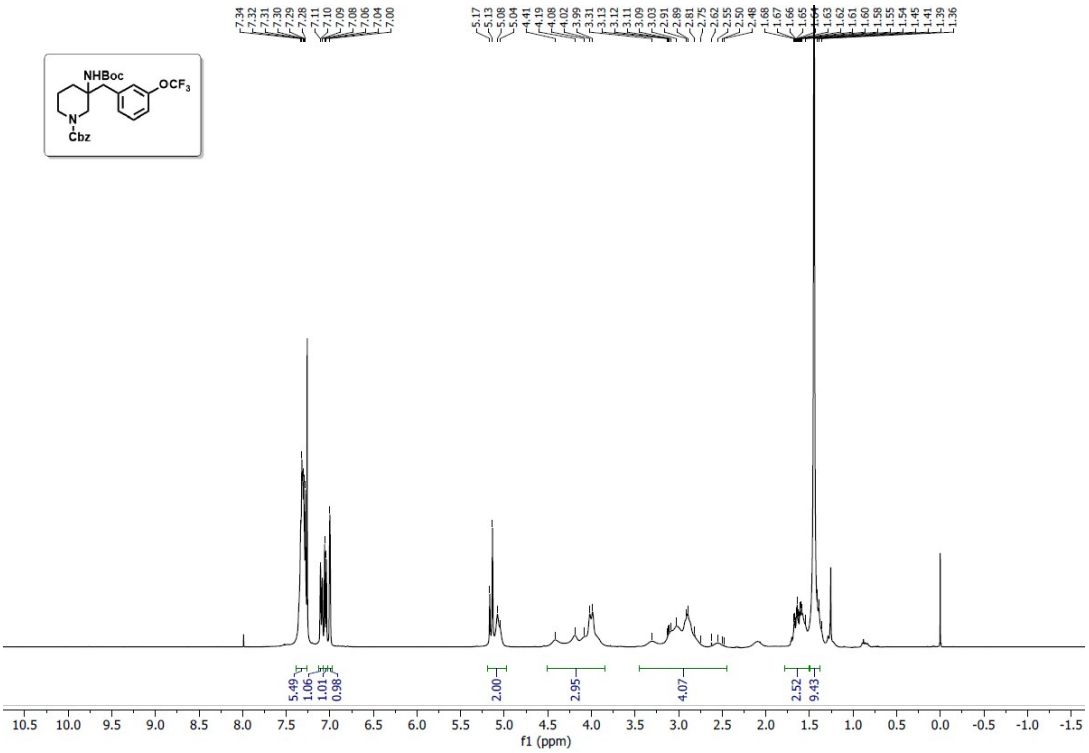


Benzyl 3-((2H-1, 2, 3-triazol-4-yl) methyl)-3-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (4e)





Benzyl 3-((tert-butoxycarbonyl) amino)-3-(3-(trifluoromethoxy) benzyl) piperidine-1-carboxylate (4f)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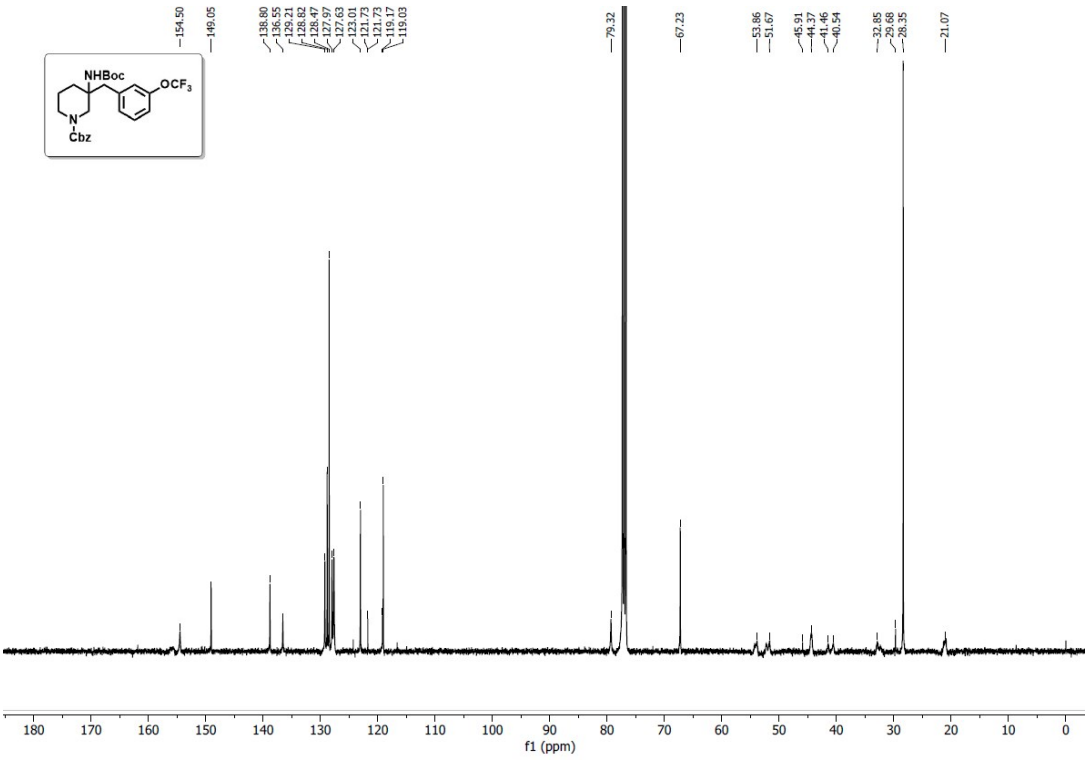
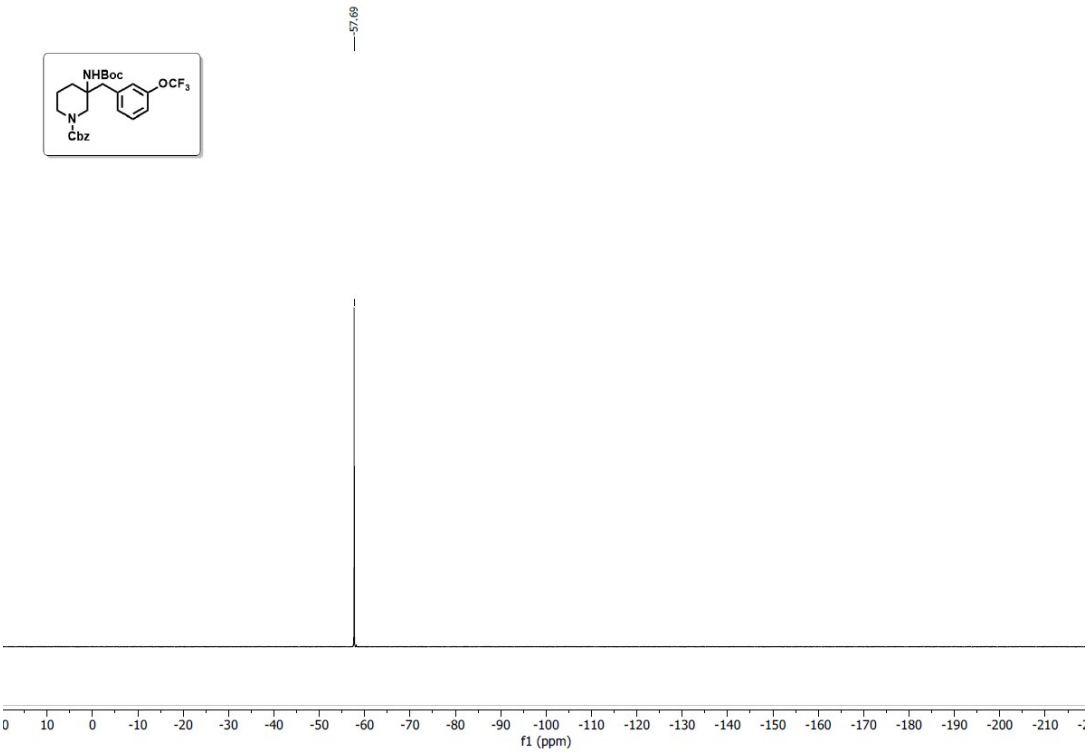
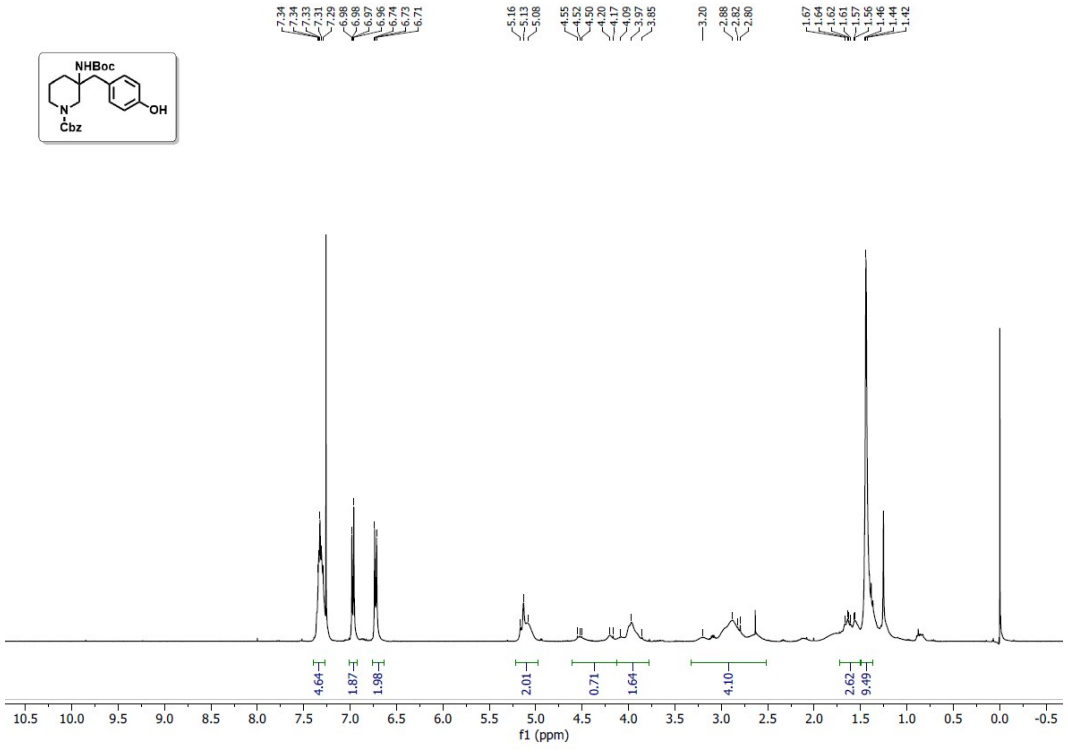
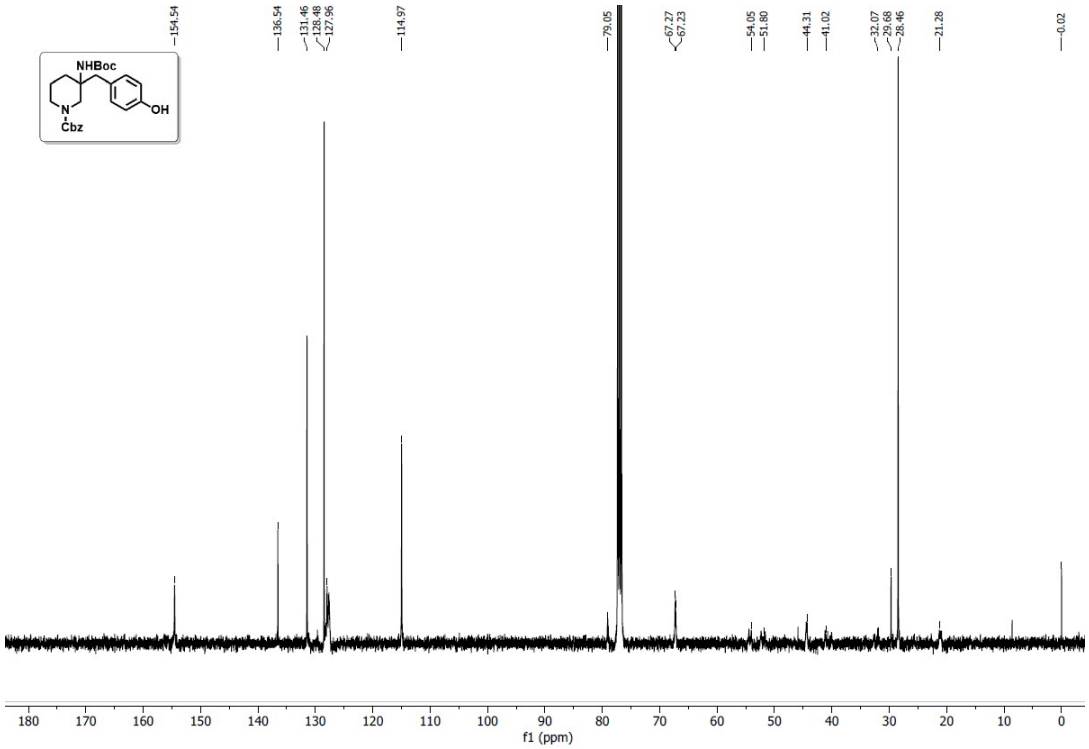
2.52
9.43
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)


NHBoc
OCF3
N
Cbz
154.50
149.05
138.80
136.55
129.21
128.92
128.47
127.97
127.63
123.01
121.73
121.73
119.17
119.03
79.32
67.23
53.86
51.67
45.91
44.37
41.46
40.54
32.85
29.68
28.35
21.07
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

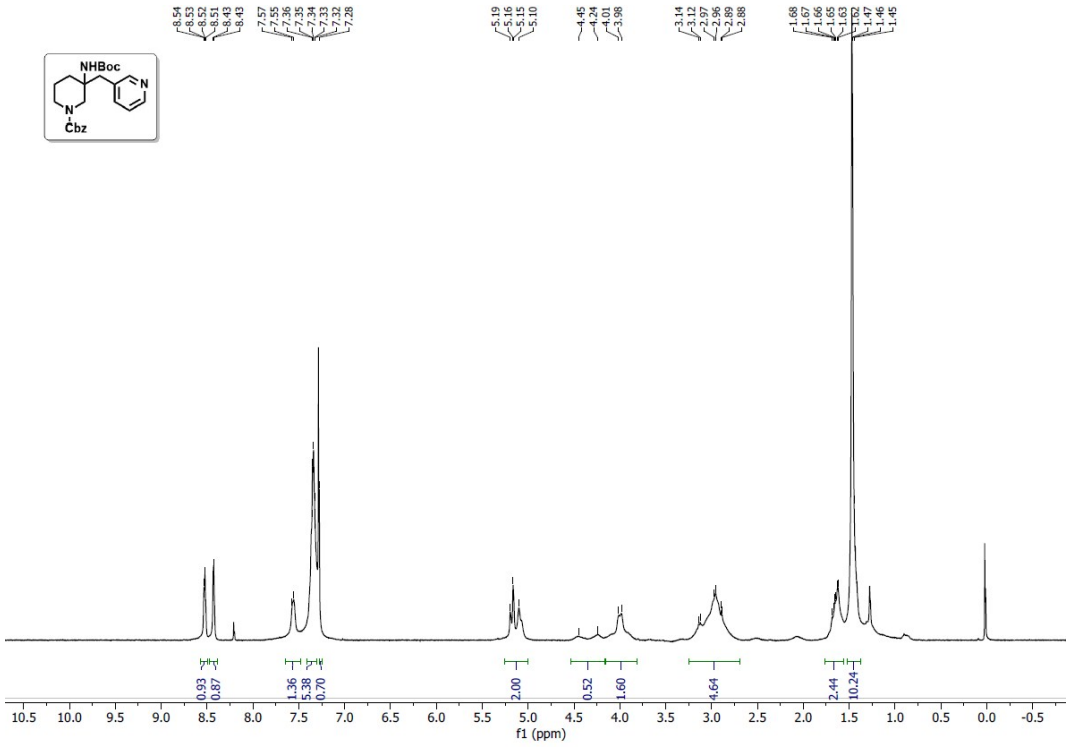


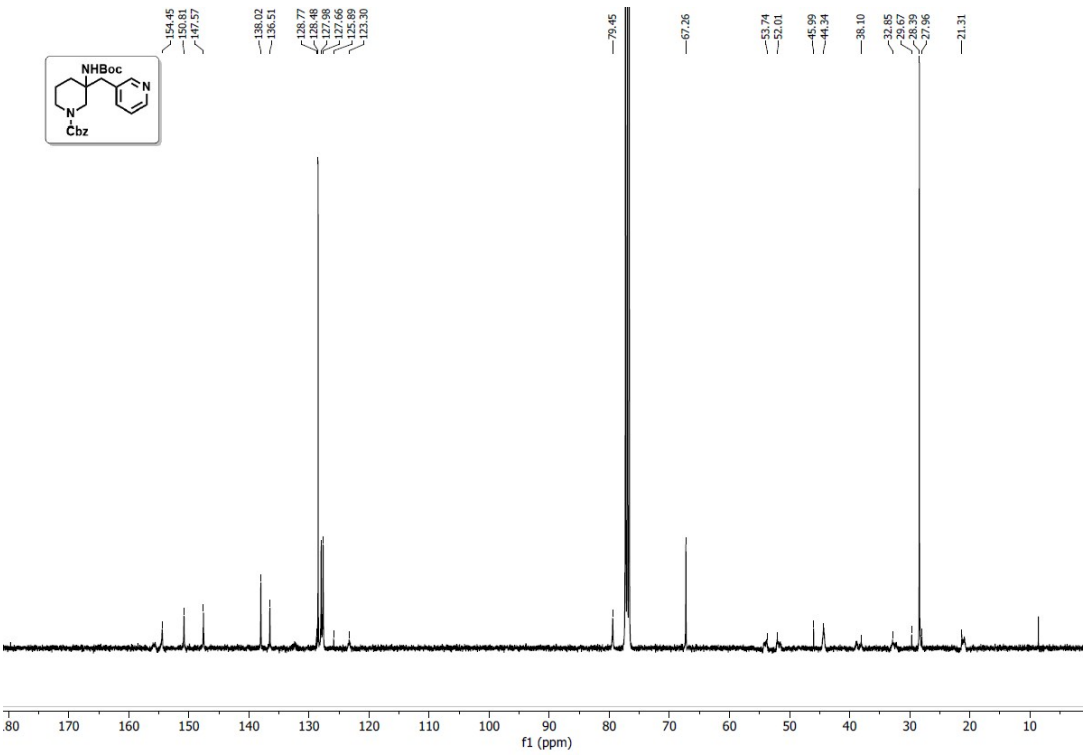
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-hydroxybenzyl) piperidine-1-carboxylate (4g)



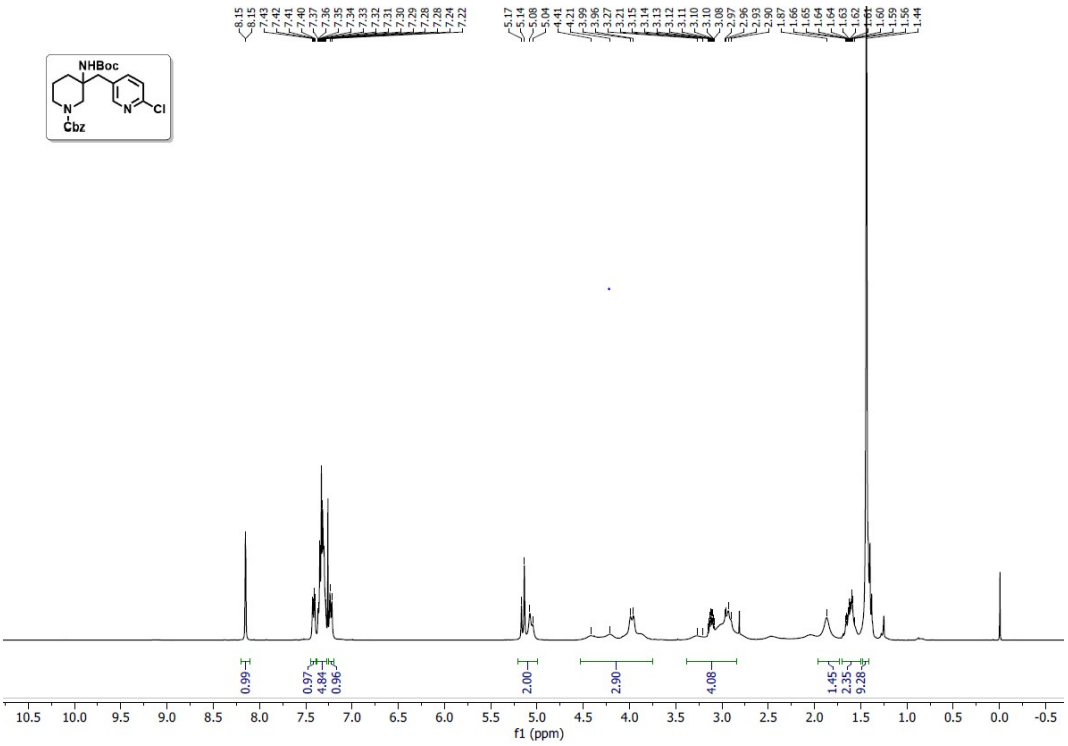


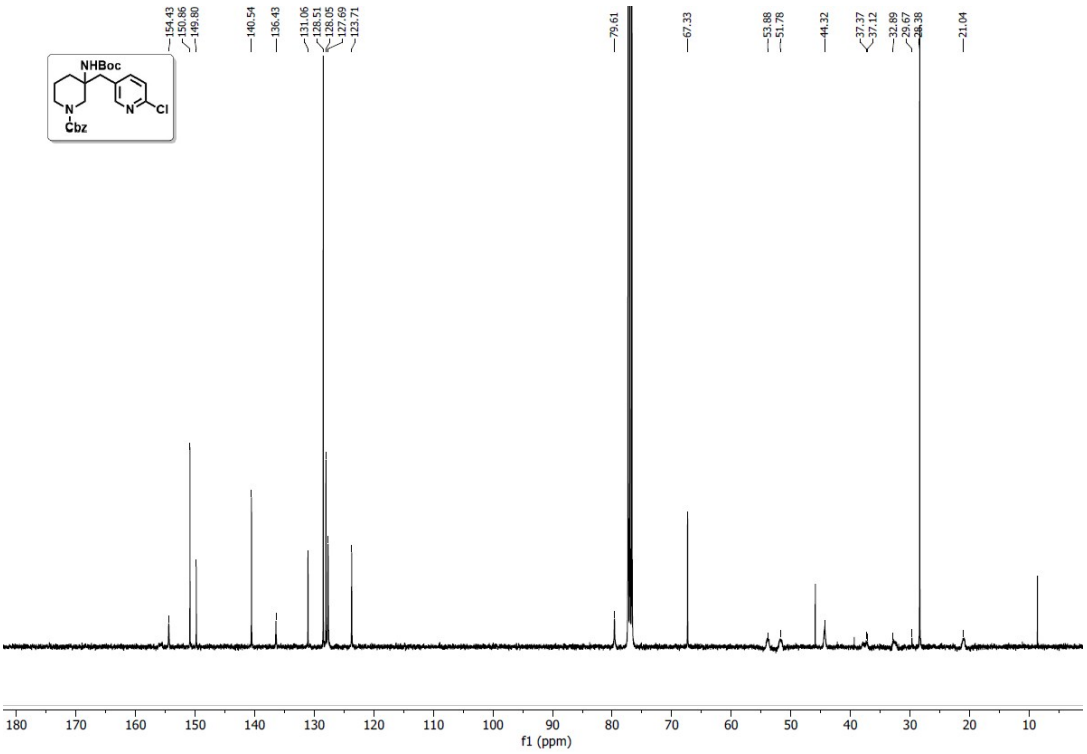
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(pyridin-3-ylmethyl) piperidine-1-carboxylate (4i)



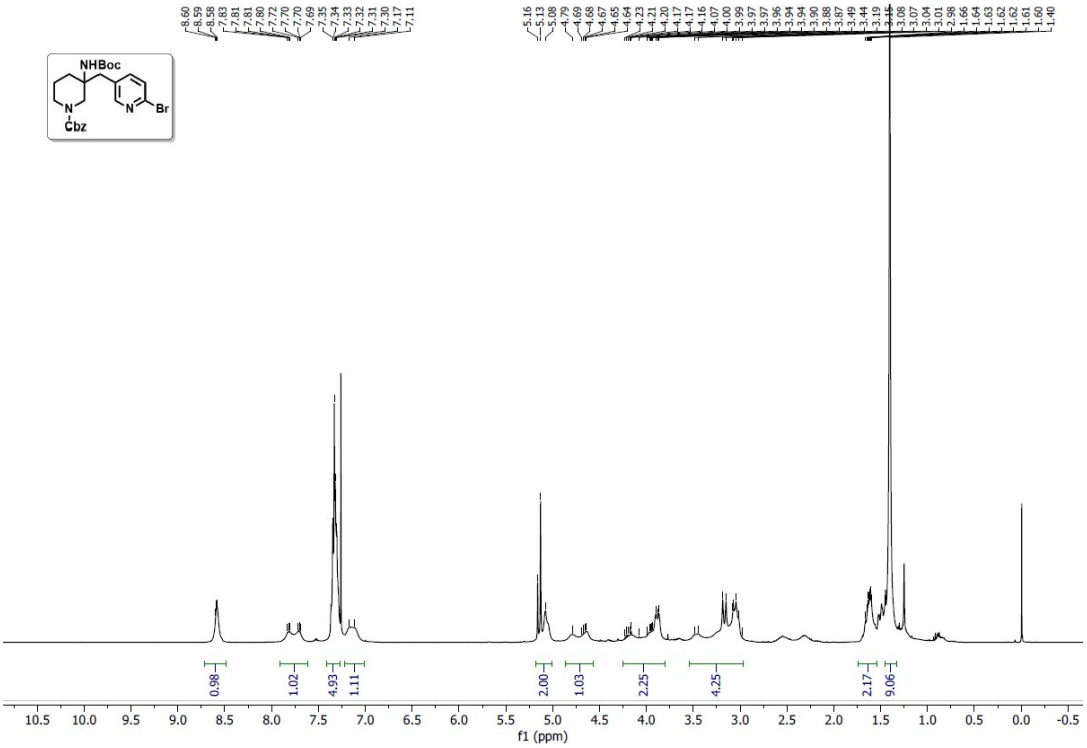


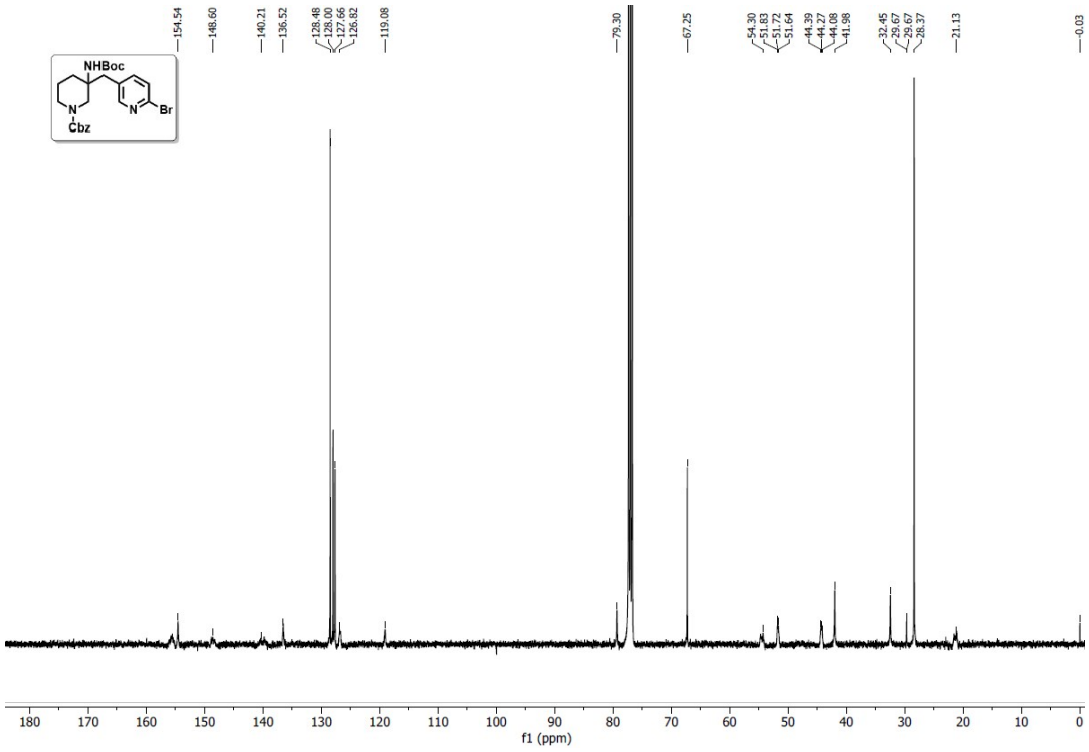
Benzyl 3-((tert-butoxycarbonyl) amino)-3-((6-chloropyridin-3-yl) methyl) piperidine-1-carboxylate (4j)



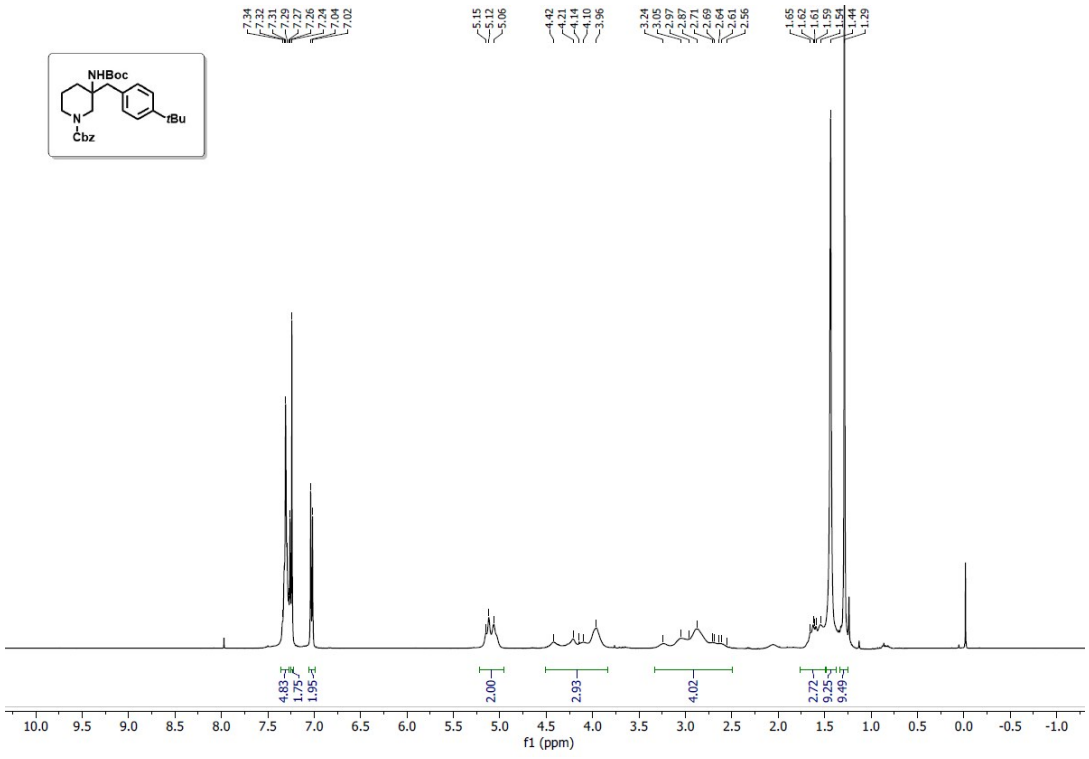


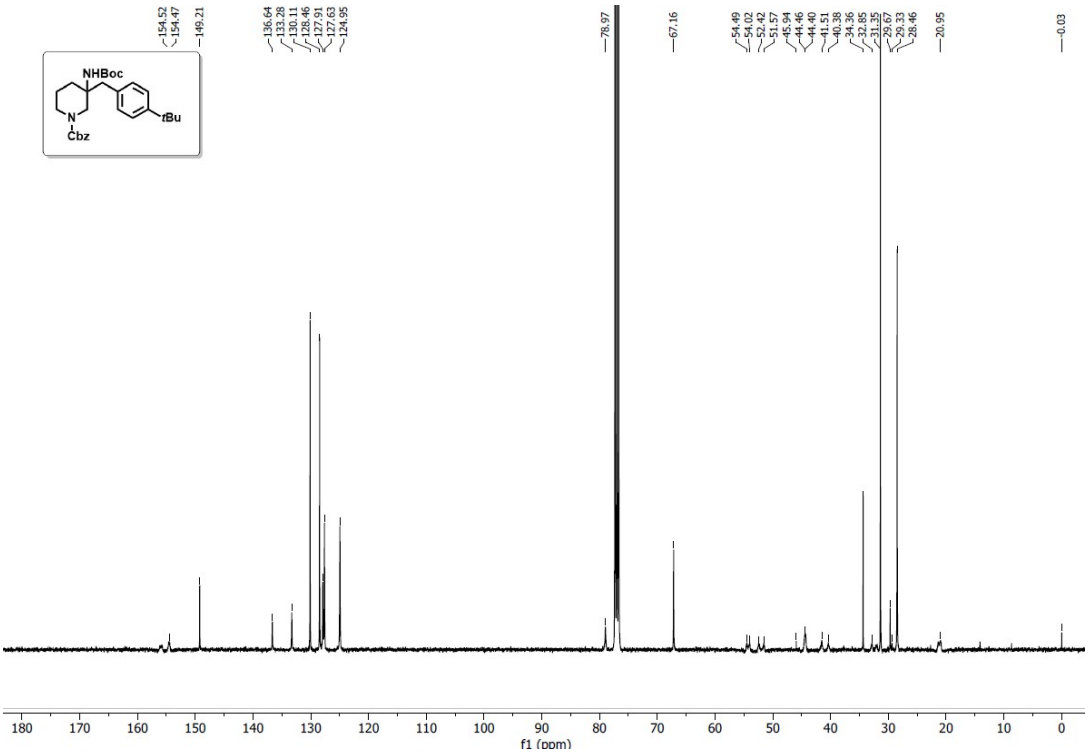
Benzyl 3-((6-bromopyridin-3-yl) methyl)-3-((tert-butoxycarbonyl) amino) piperidine -1-carboxylate (4k)



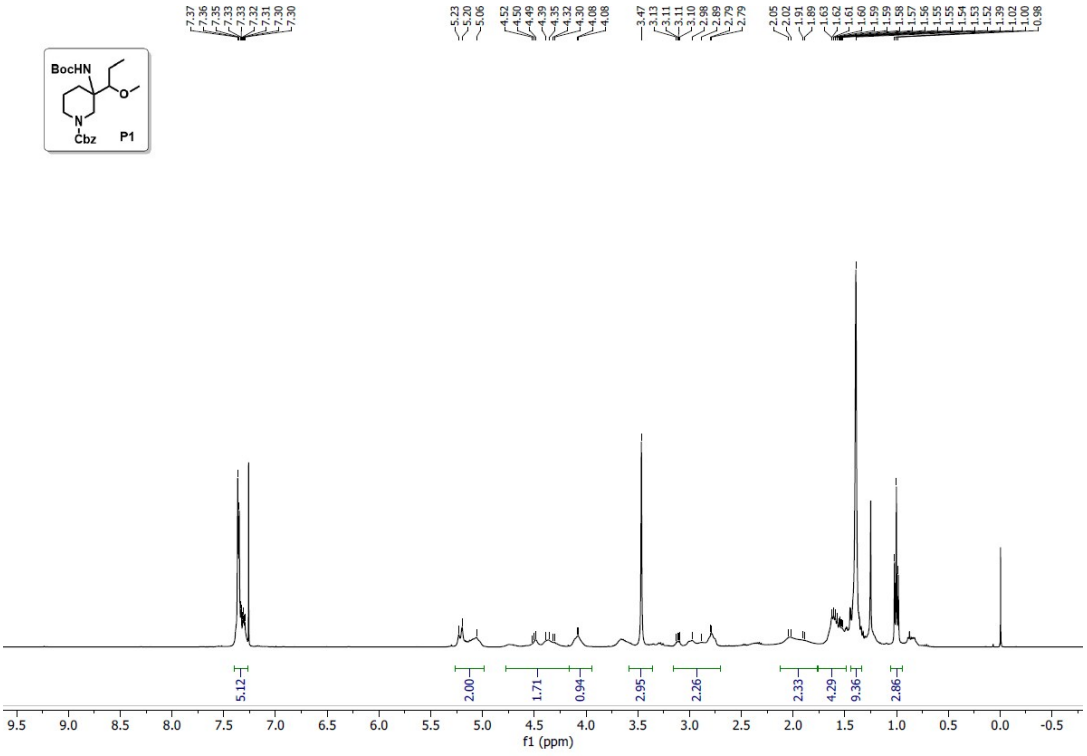


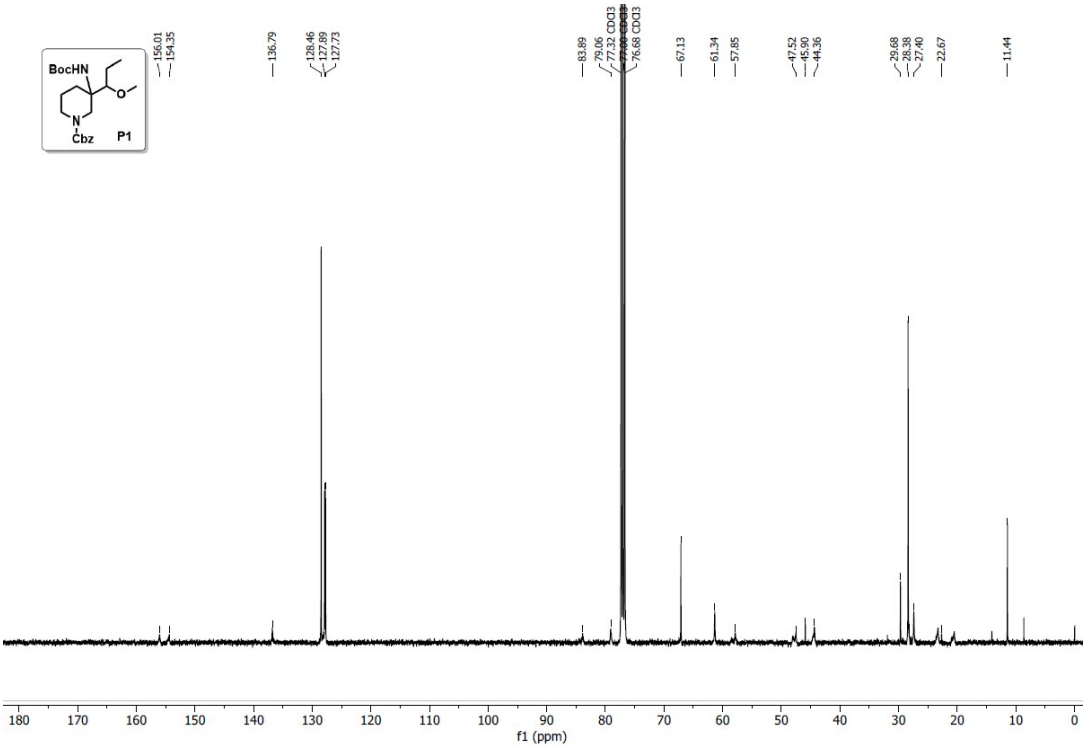
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(4-(tert-butyl) benzyl) piperidine-1-carboxylate (4o)l

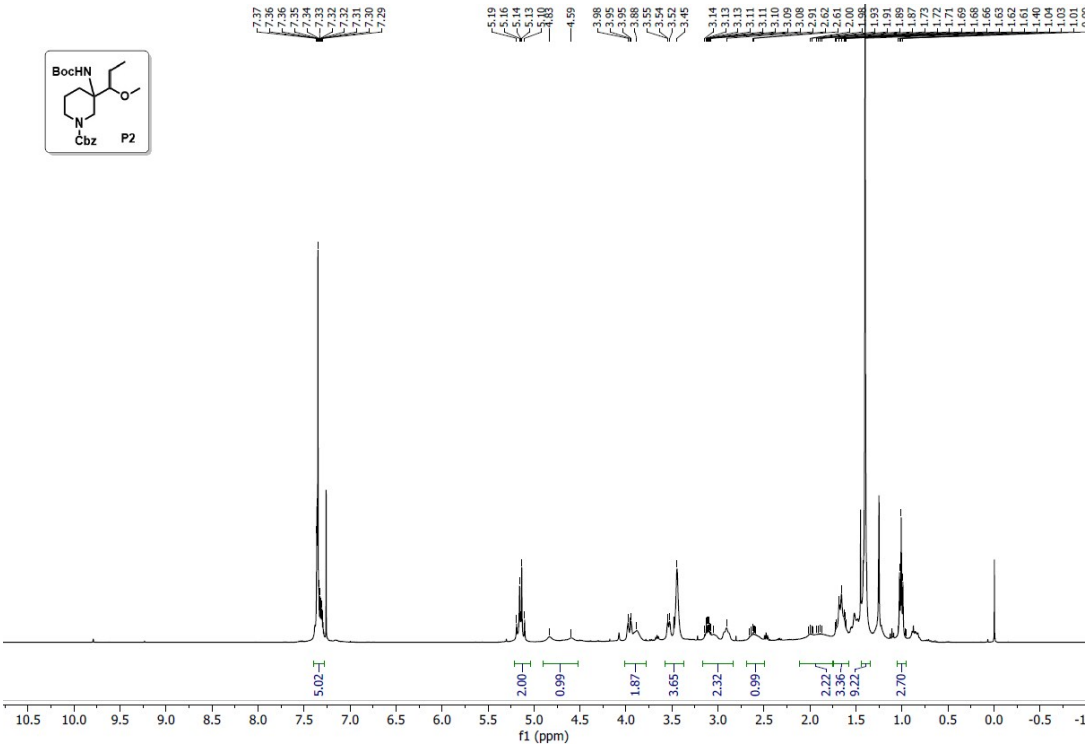


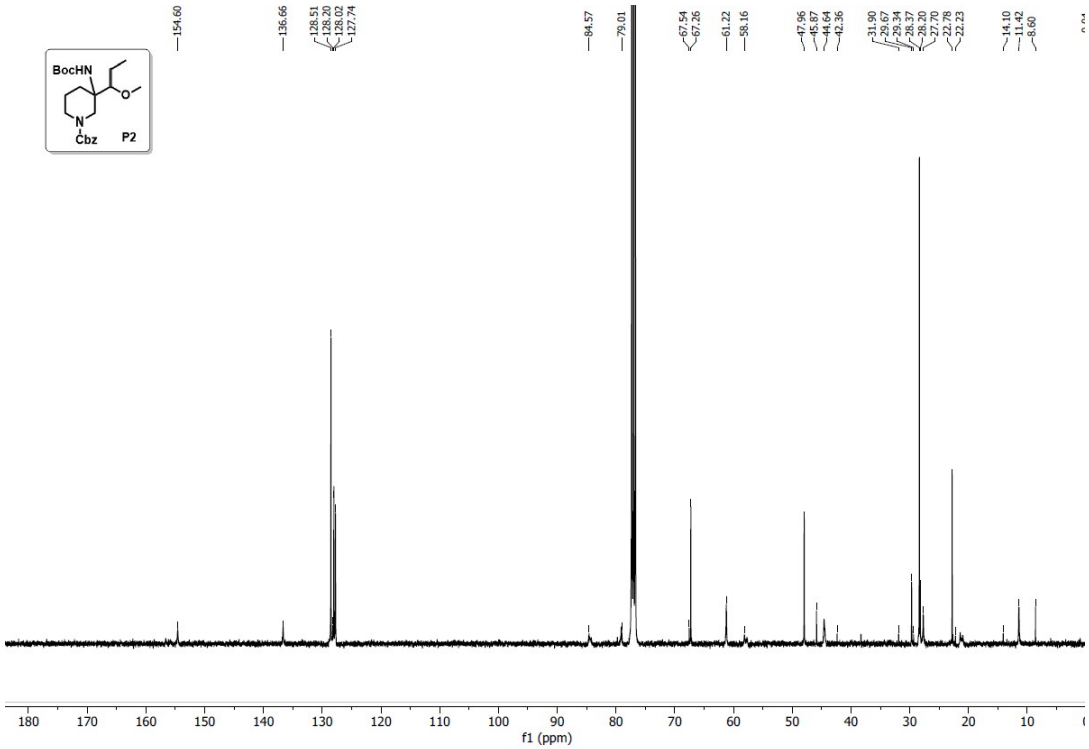


Benzyl 3-((tert-butoxycarbonyl) amino)-3-(1-methoxypropyl) piperidine-1-carboxylate (4p)

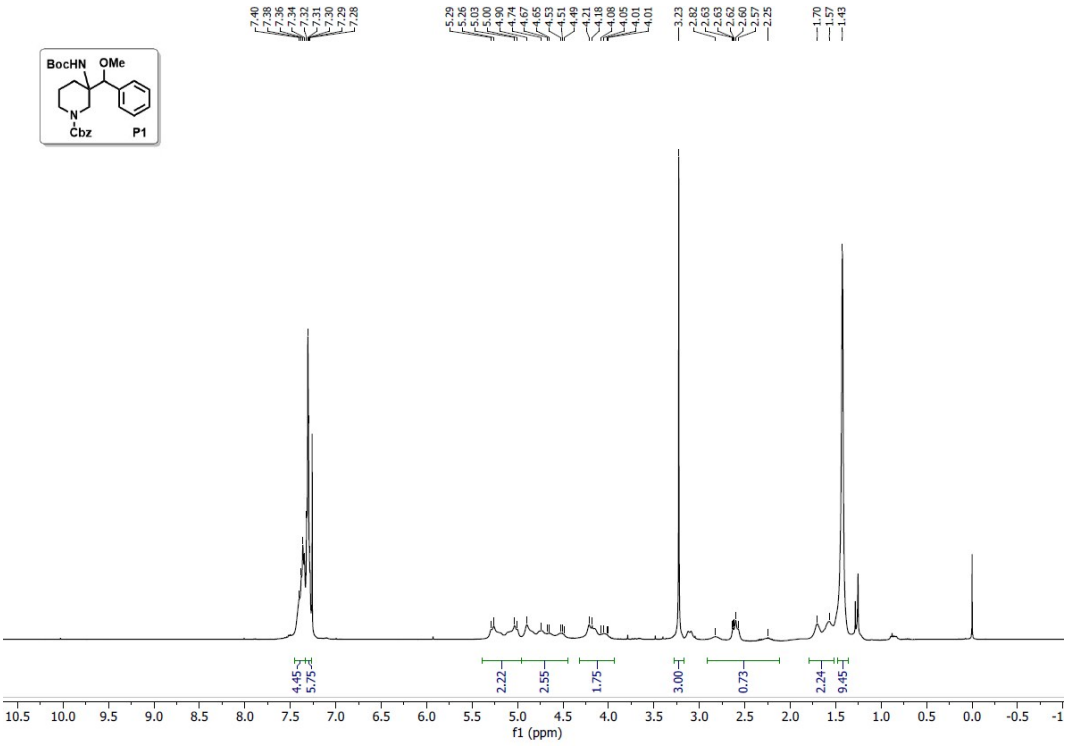


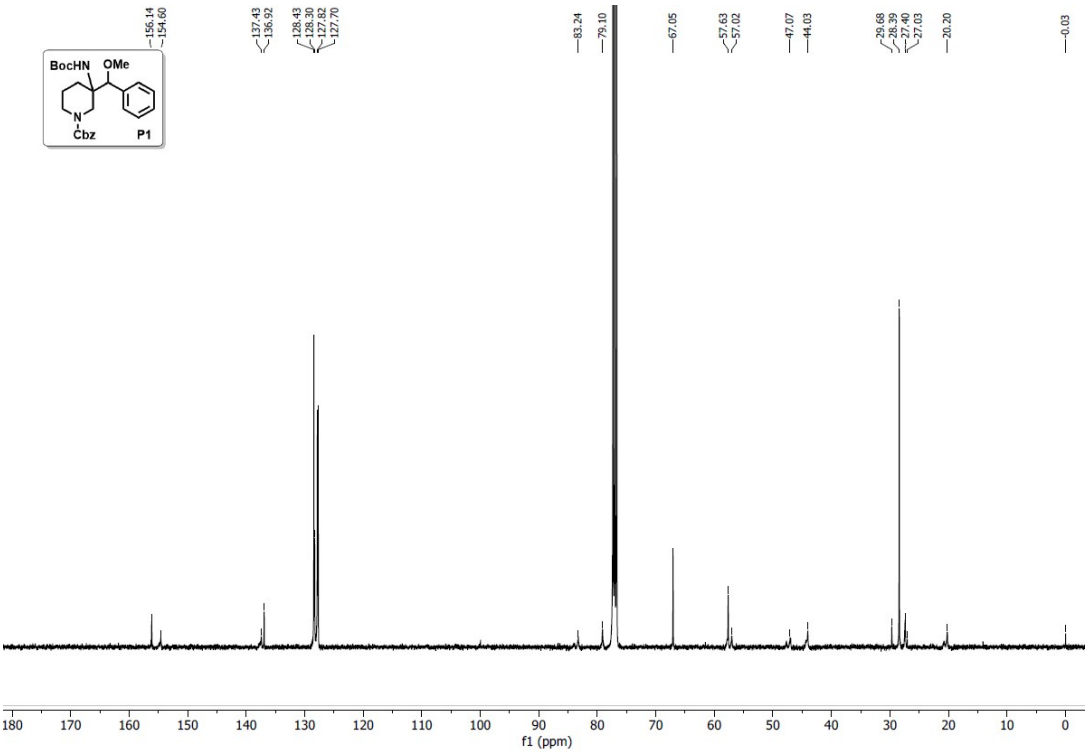

BocHN
N
Cbz
P1
156.01
154.35
136.79
128.46
127.89
127.73
83.89
79.06
77.32 CDCl3
76.68 CDCl3
67.13
61.34
57.85
47.52
45.90
44.36
29.68
28.38
27.40
22.67
11.44
f1 (ppm)

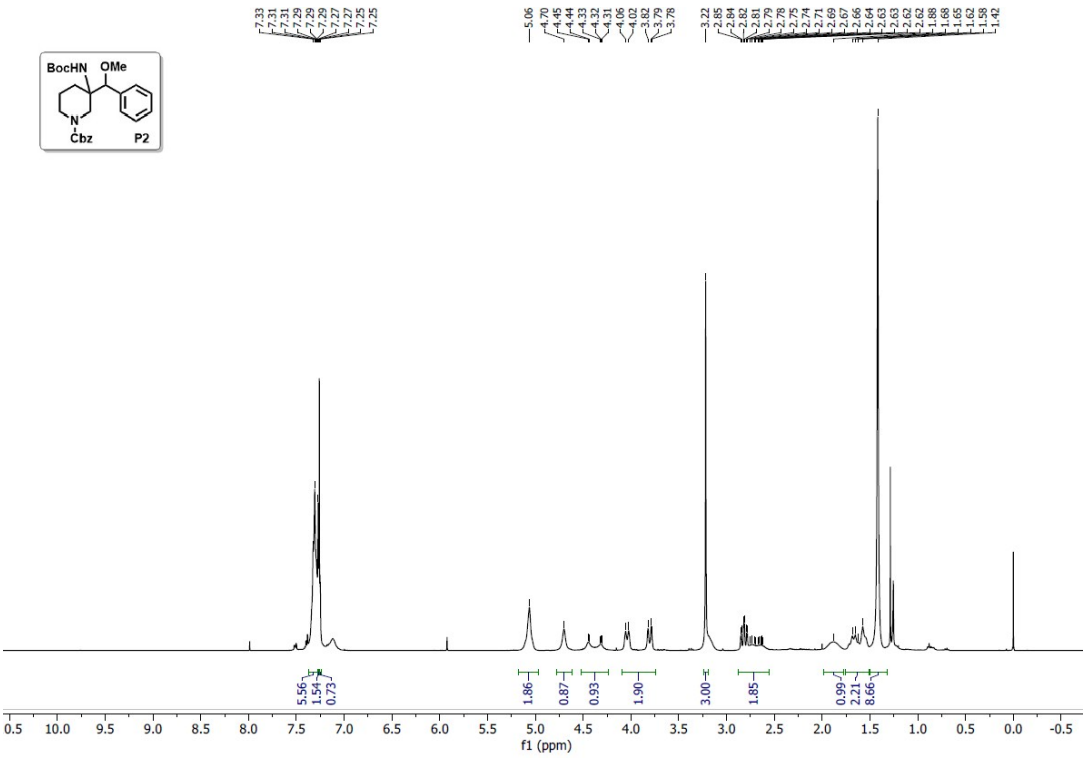

BocHN
N
Cbz
P2
7.37
7.36
7.36
7.35
7.34
7.33
7.32
7.32
7.31
7.30
7.29
5.19
5.16
5.14
5.13
4.60
4.59
3.98
3.95
3.95
3.88
3.55
3.54
3.52
3.45
3.14
3.13
3.13
3.11
3.11
3.10
3.09
3.08
2.91
2.62
2.61
2.00
1.98
1.93
1.91
1.89
1.87
1.73
1.72
1.71
1.69
1.68
1.66
1.63
1.62
1.61
1.40
1.04
1.03
1.01
5.02
2.00
0.99
1.87
3.65
2.32
0.99
2.22
3.36
9.22
2.70
f1 (ppm)

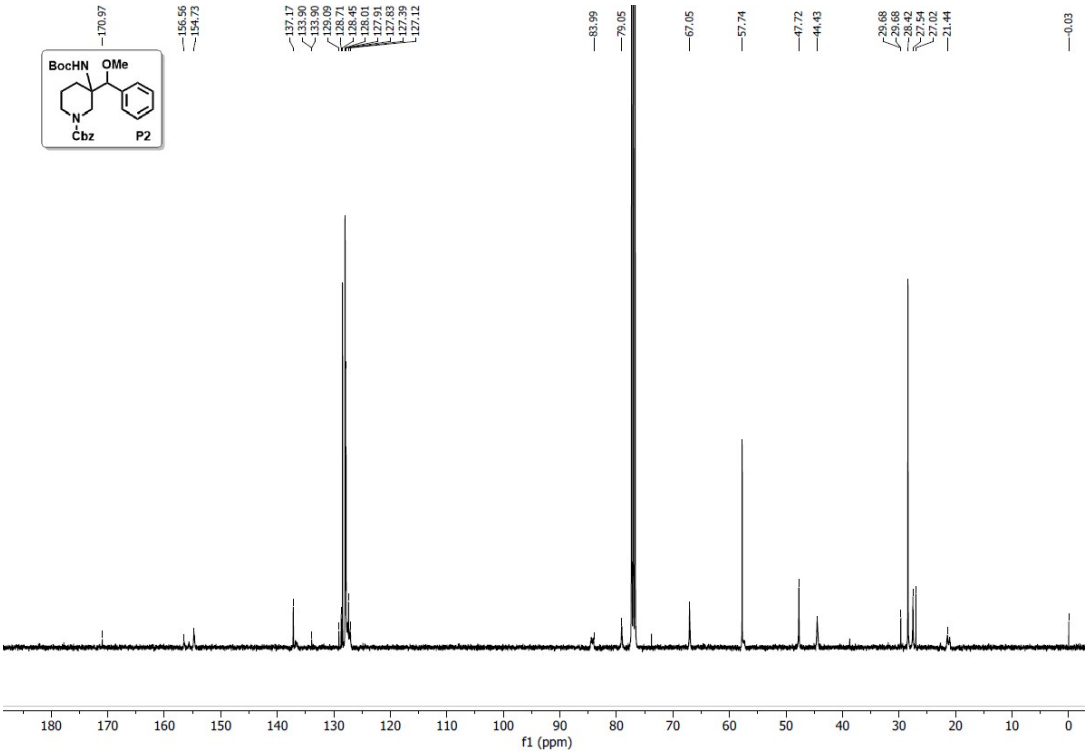


Benzyl 3-((tert-butoxycarbonyl) amino)-3-(methoxy(phenyl)methyl)piperidine-1-carboxylate (4q)

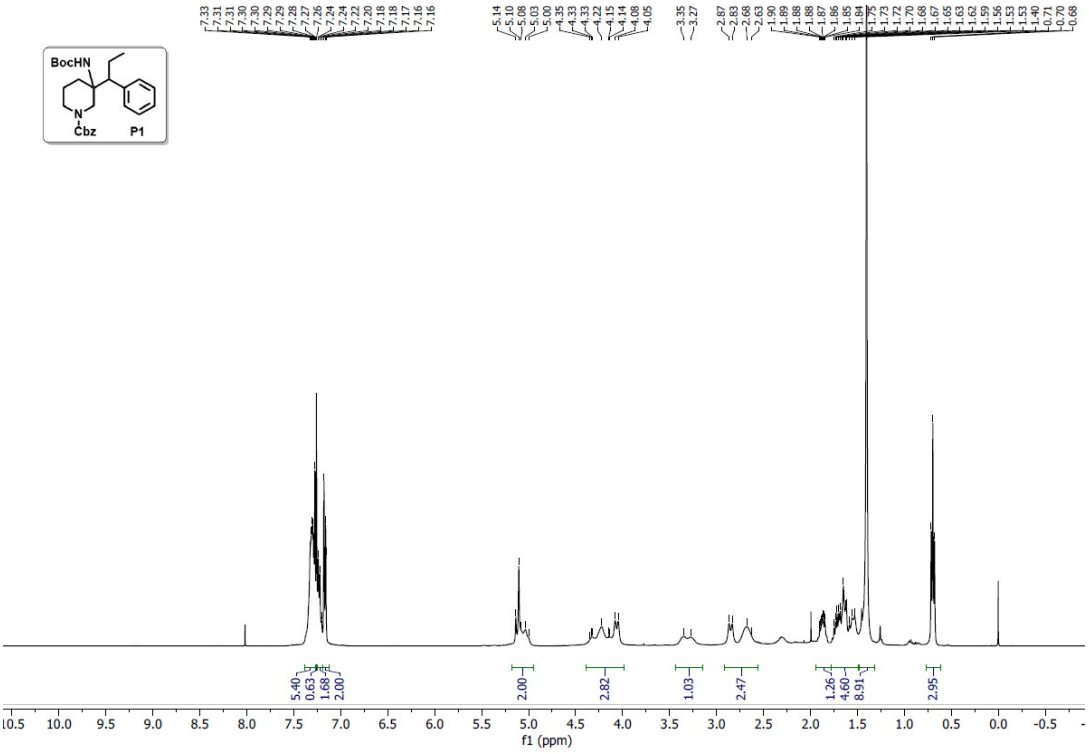


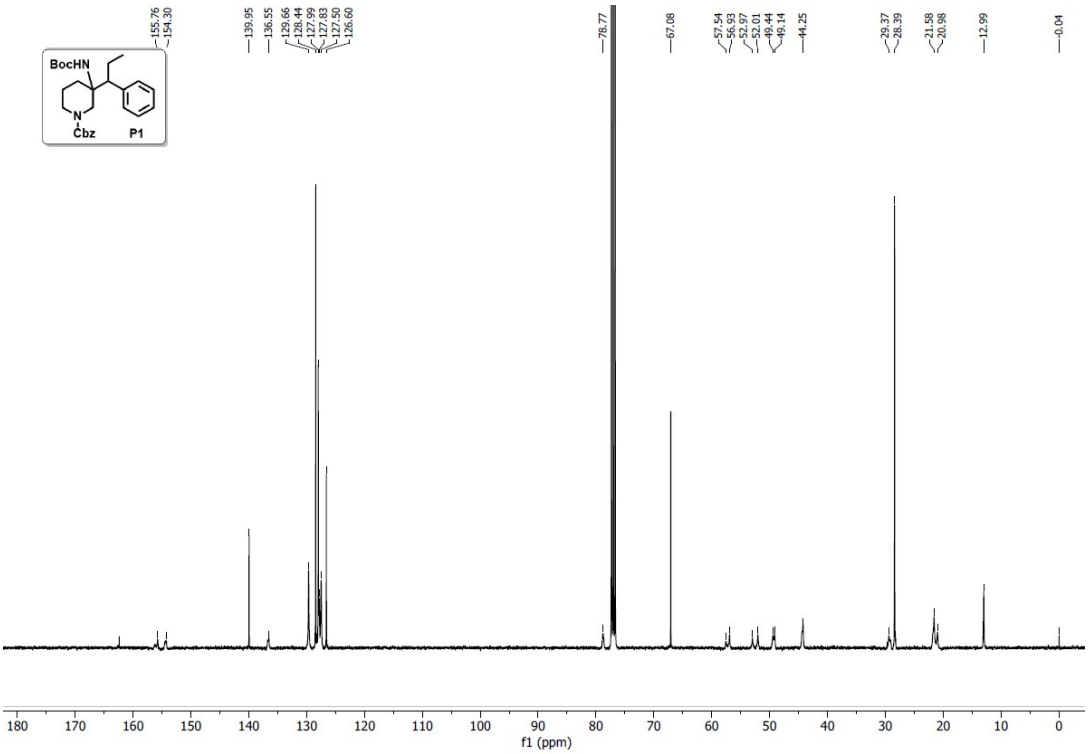

BocHN OMe
N
Cbz
P1
156.14
154.60
137.43
136.92
128.43
128.30
127.82
127.70
83.24
79.10
67.05
57.63
57.02
47.07
44.03
29.68
28.39
27.40
27.03
20.20
-0.03
f1 (ppm)

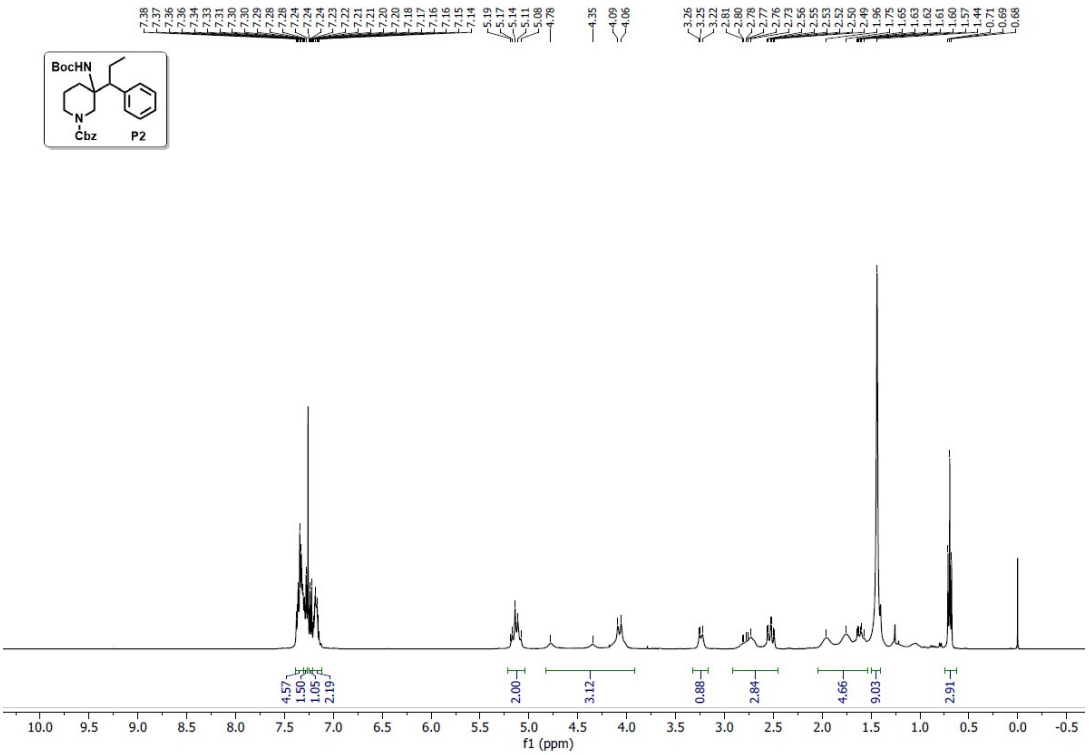

BocHN OMe
N
Cbz
P2
7.33
7.31
7.31
7.29
7.29
7.29
7.29
7.27
7.27
7.25
7.25
5.06
4.70
4.45
4.44
4.33
4.32
4.31
4.06
4.02
3.82
3.79
3.78
3.22
2.85
2.84
2.82
2.81
2.79
2.78
2.75
2.74
2.71
2.69
2.67
2.66
2.64
2.63
2.63
2.62
2.62
1.68
1.68
1.65
1.62
1.58
1.42
5.56
1.54
0.73
1.86
0.87
0.93
1.90
3.00
1.85
0.99
2.21
8.66
f1 (ppm)

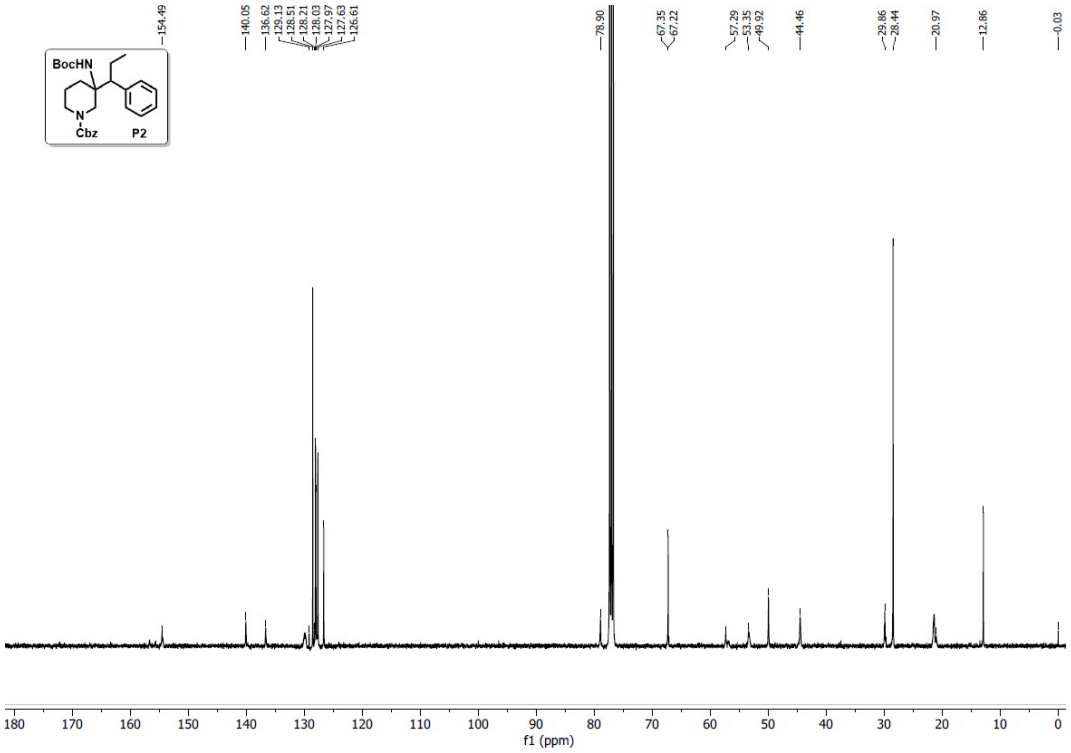


Benzyl 3-((tert-butoxycarbonyl) amino)-3-(1-phenylpropyl) piperidine-1-carboxylate (4r)

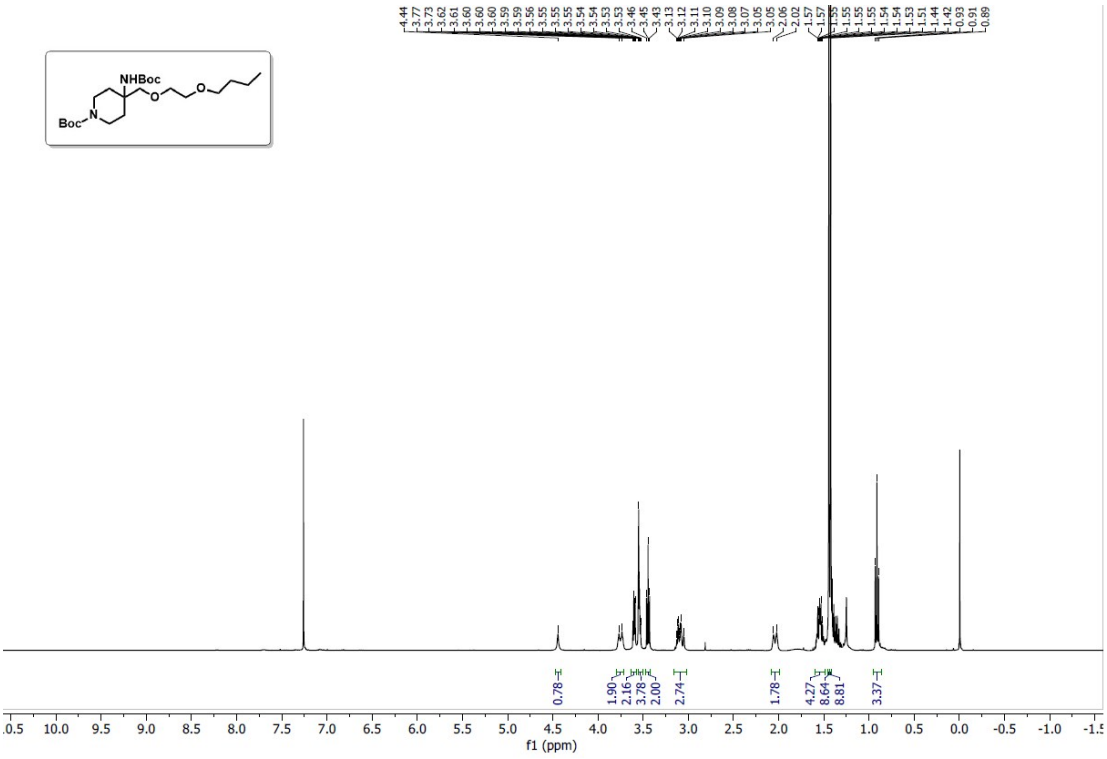


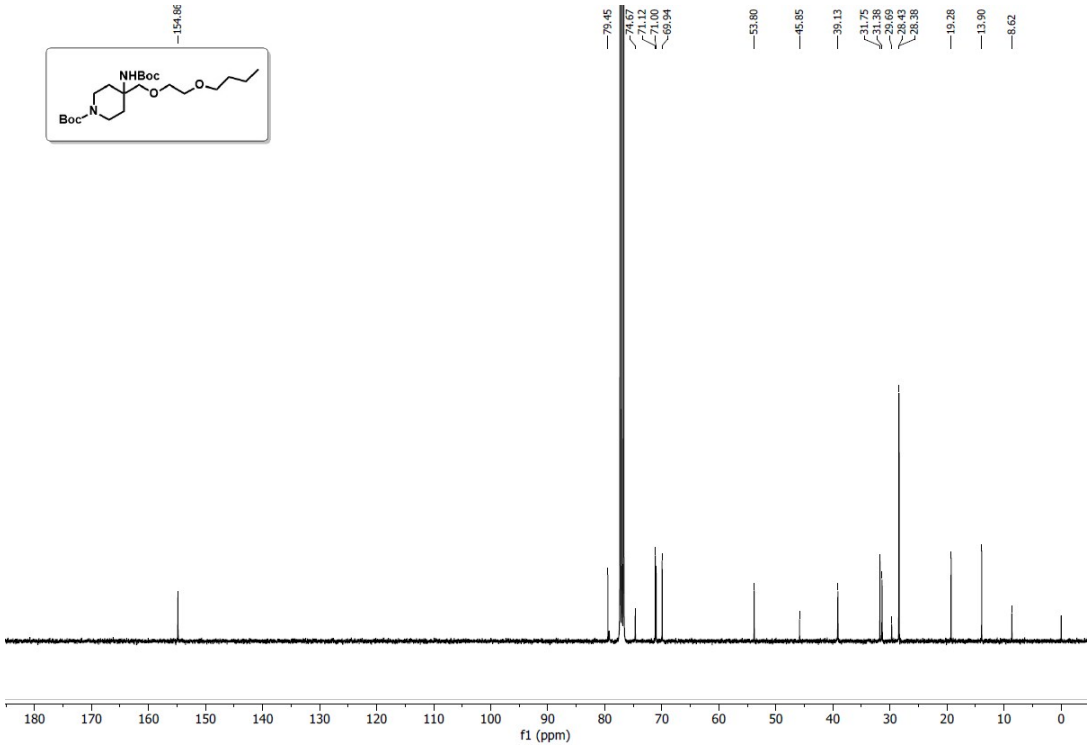

BocHN
N
Cbz
P1
155.76
154.30
139.95
136.55
129.66
128.44
127.99
127.83
127.50
126.60
78.77
67.08
57.54
56.93
52.97
52.01
49.44
49.14
44.25
29.37
28.39
21.58
20.98
12.99
-0.04
f1 (ppm)


BocHN
N
Cbz
P2
4.57
1.50
1.05
2.19
2.00
3.12
0.88
2.84
4.66
9.03
2.91
f1 (ppm)

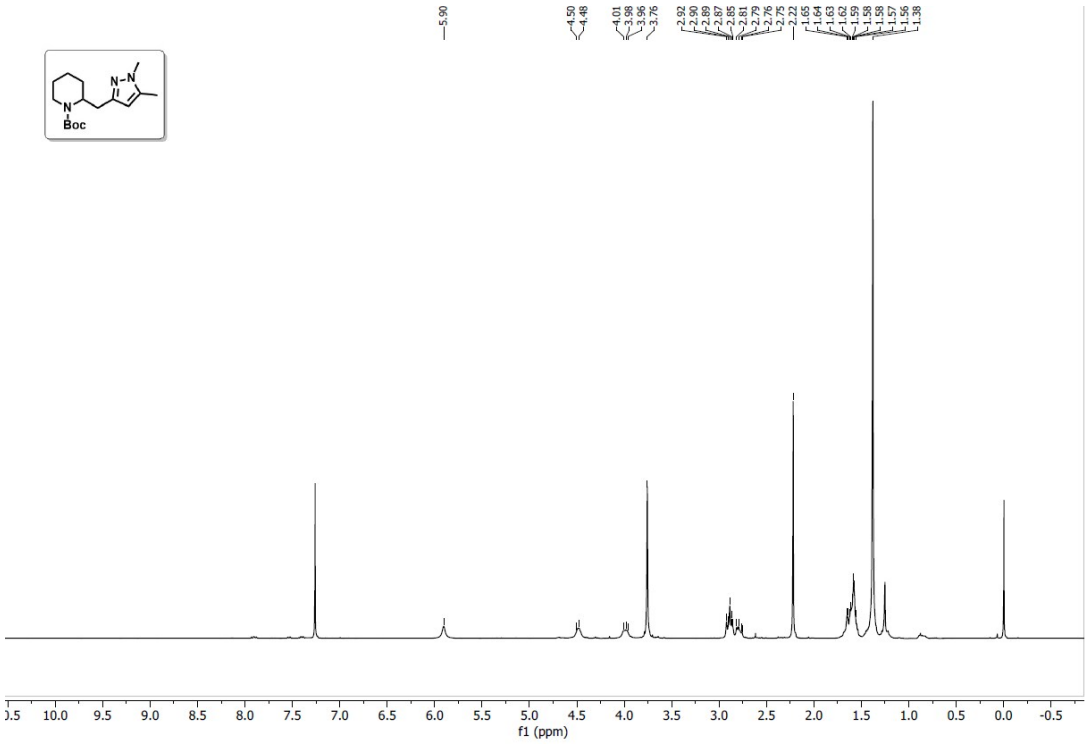


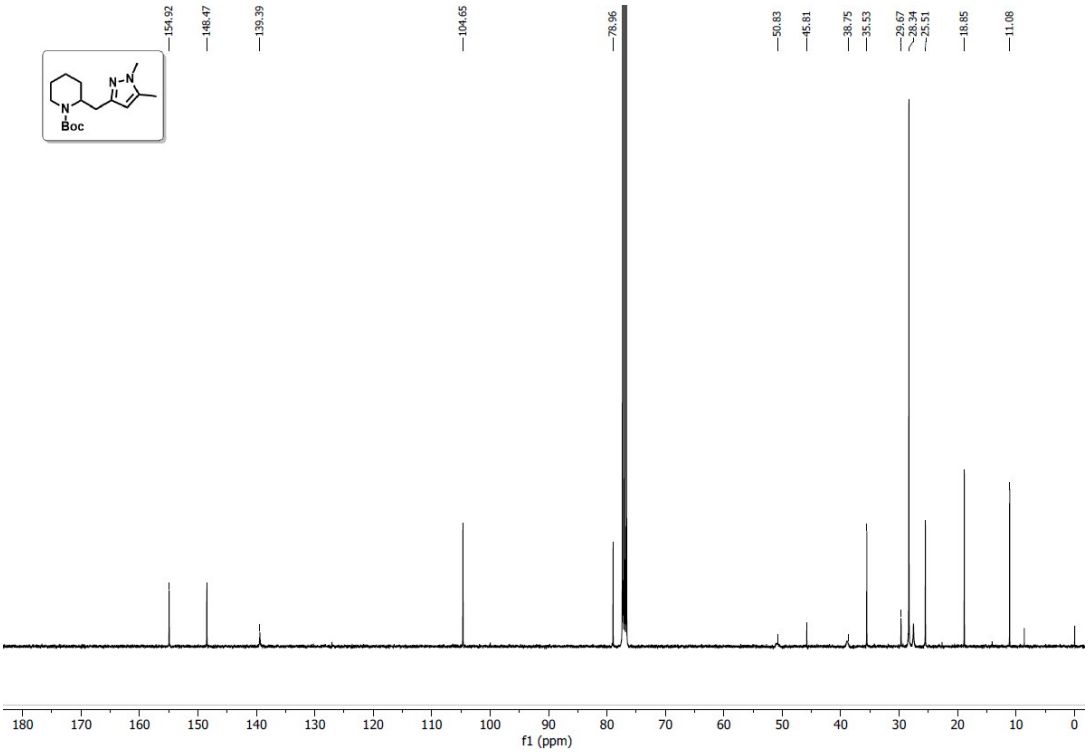
Tert-butyl 4-((2-(tert-butoxy) ethoxy) methyl)-4-((tert-butoxycarbonyl) amino) piperidine-1-carboxylate (4s)



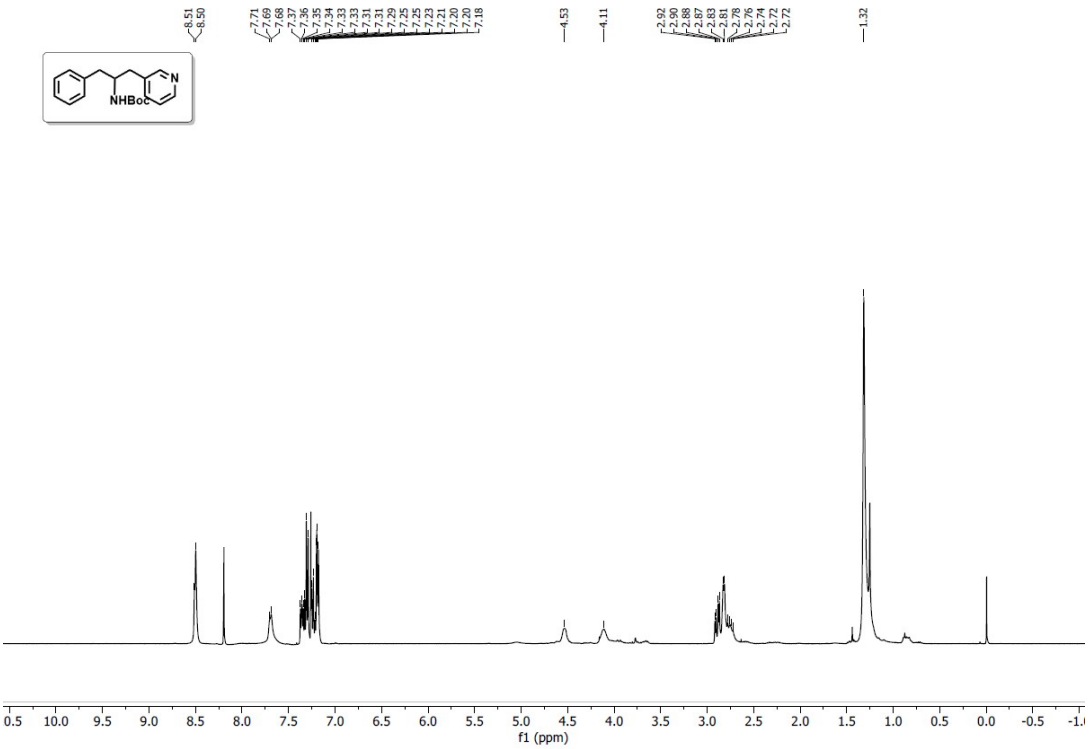


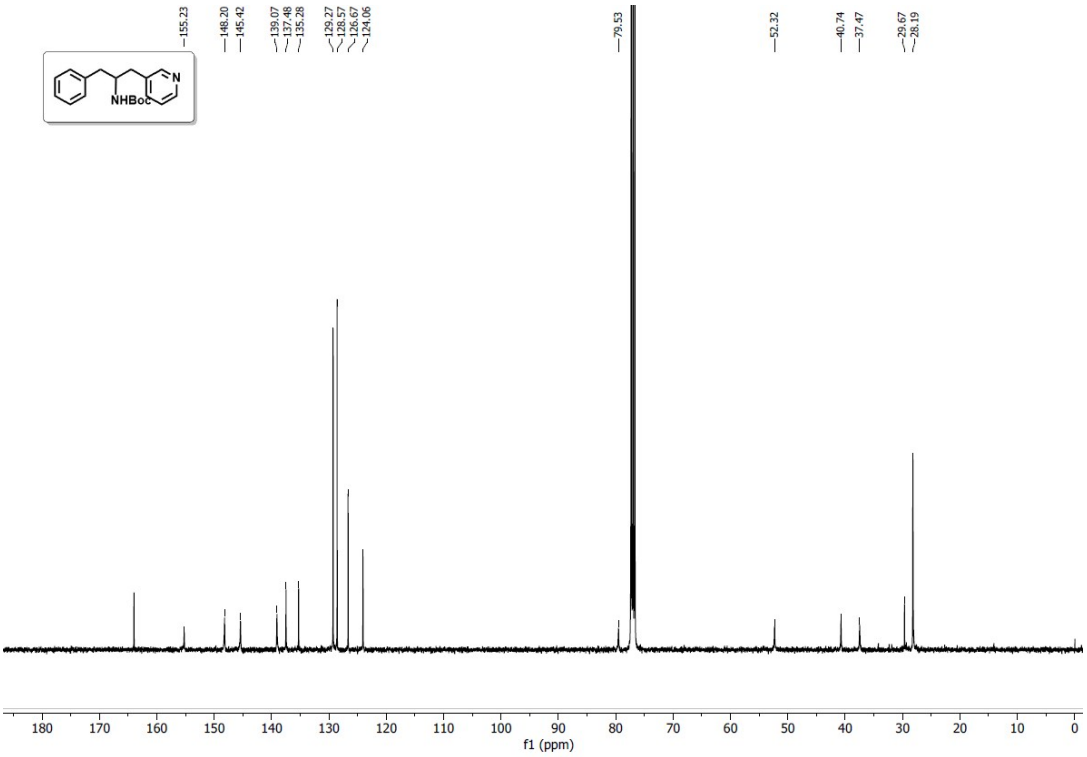
Tert-butyl 2-((1, 5-dimethyl-1H-pyrazol-3-yl) methyl) piperidine-1-carboxylate (5a)



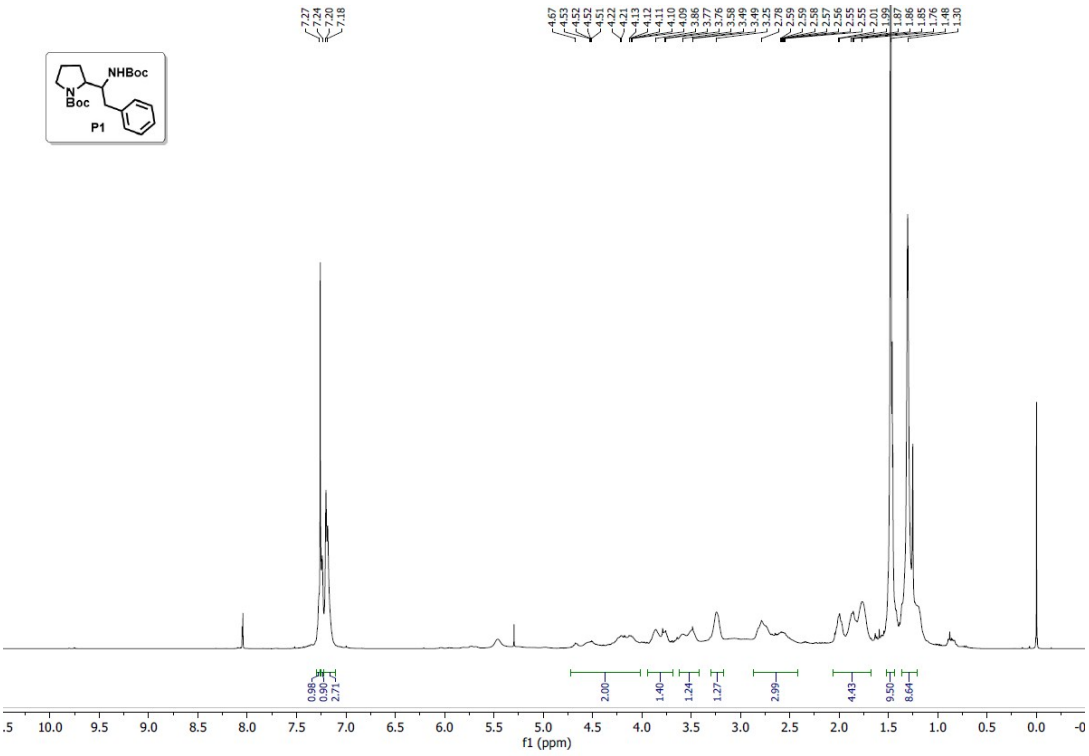


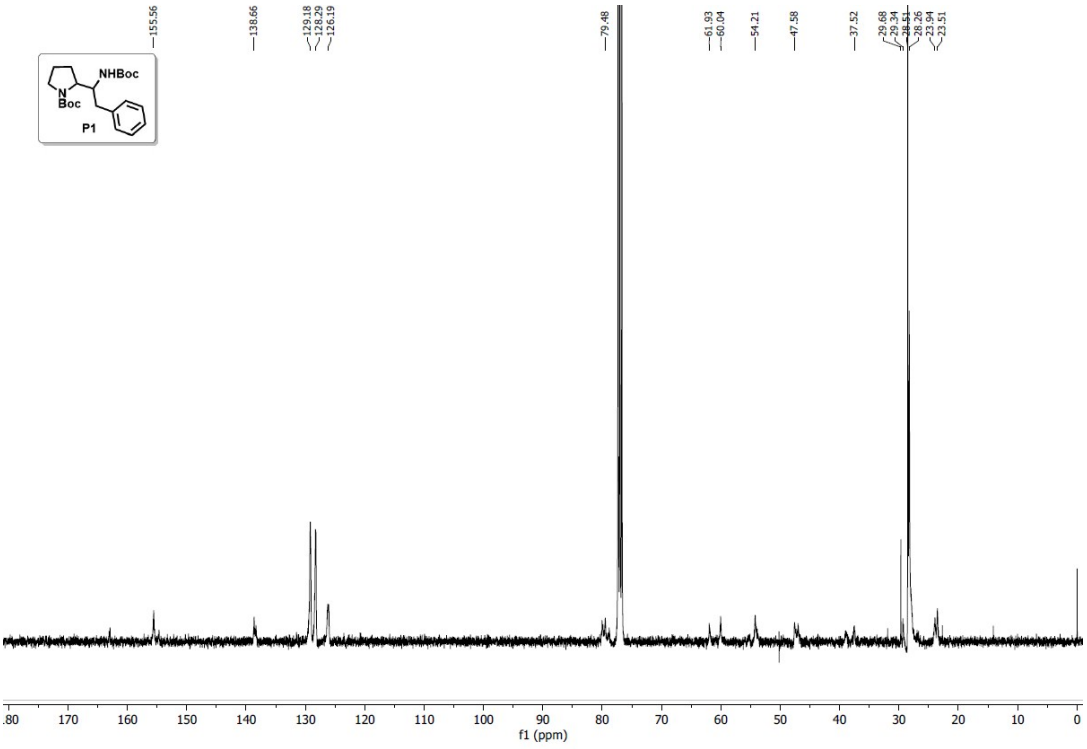
Tert-butyl (1-phenyl-3-(pyridin-3-yl) propan-2-yl) carbamate (5b)

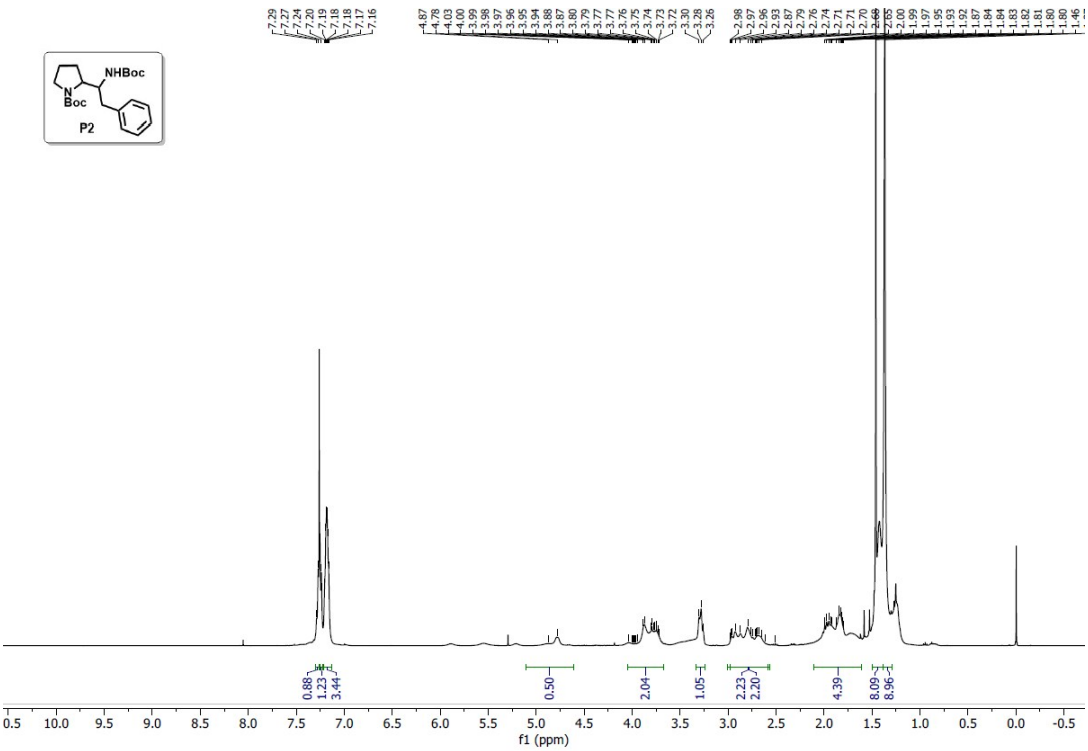


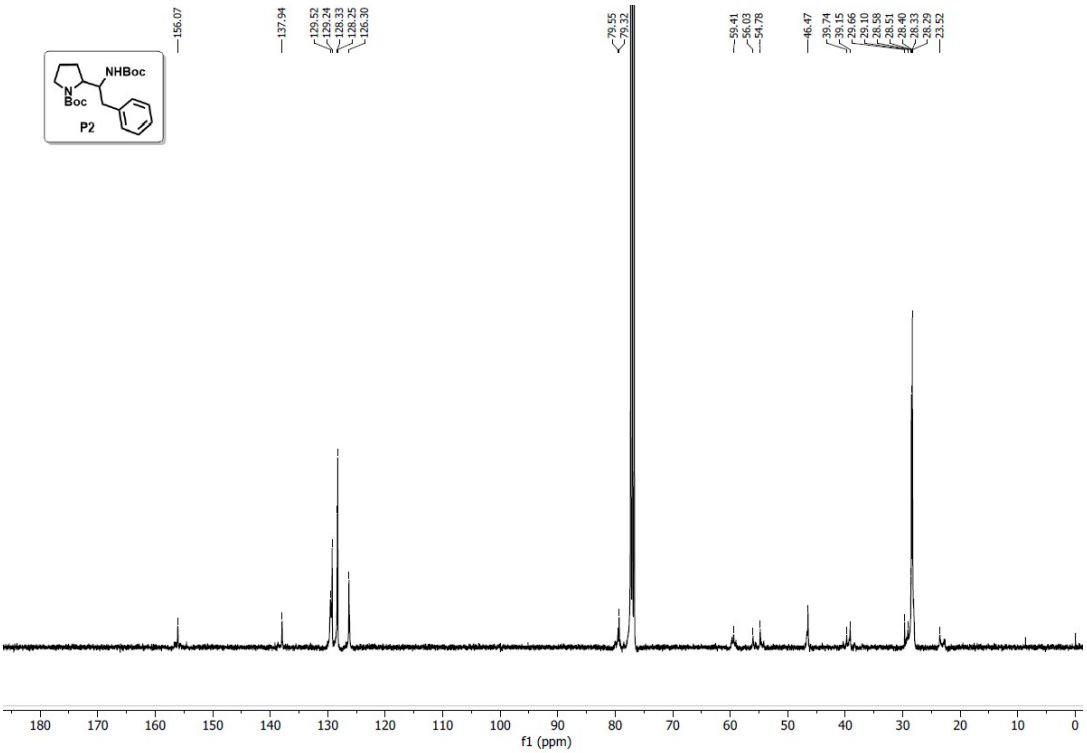


Tert-butyl 2-(1-((tert-butoxycarbonyl) amino)-2-phenylethyl) pyrrolidine-1-carboxylate (5c)

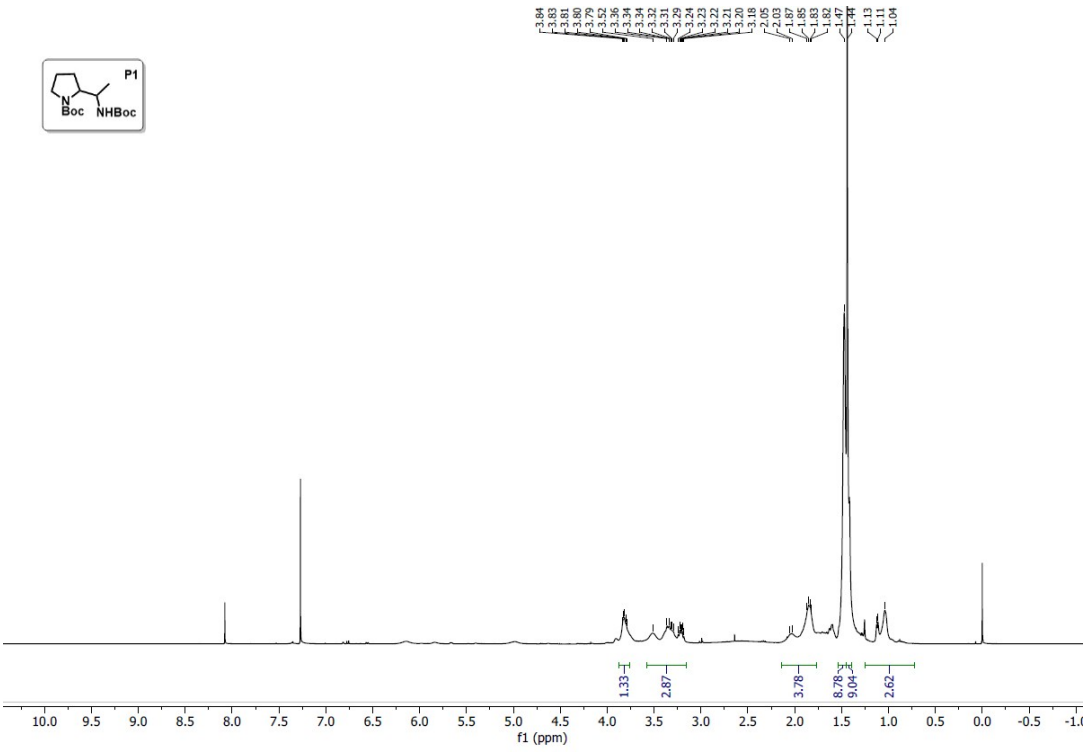


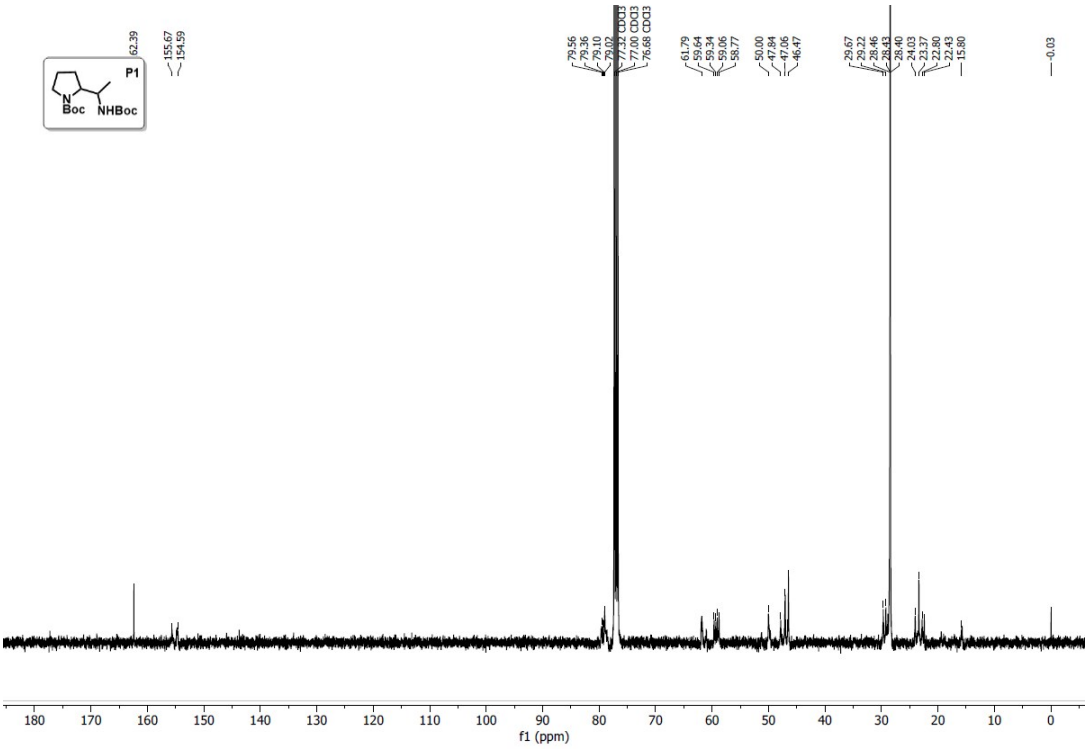

155.56
138.66
129.18
128.29
126.19
79.48
61.93
60.04
54.21
47.58
37.52
29.68
29.34
28.51
28.35
23.94
23.51
NHBoc
Boc
P1
f1 (ppm)

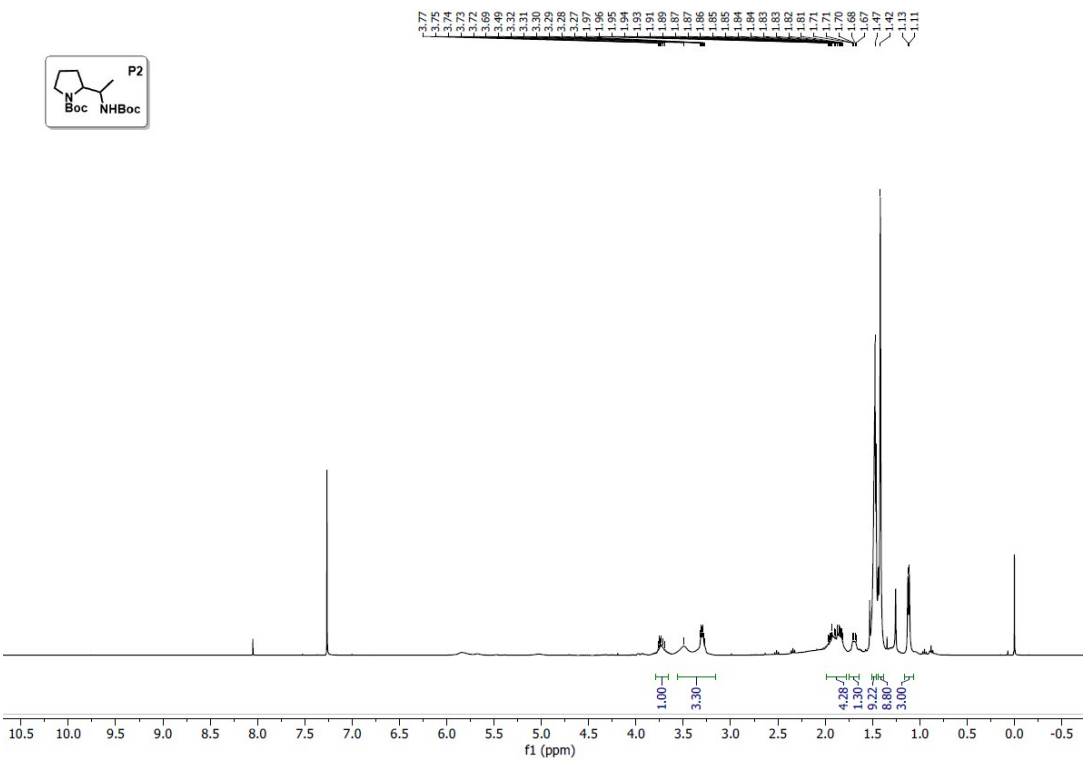

NHBoc
Boc
P2
0.88
1.23
3.44
0.50
2.04
1.05
2.23
2.20
4.39
8.09
8.96
f1 (ppm)

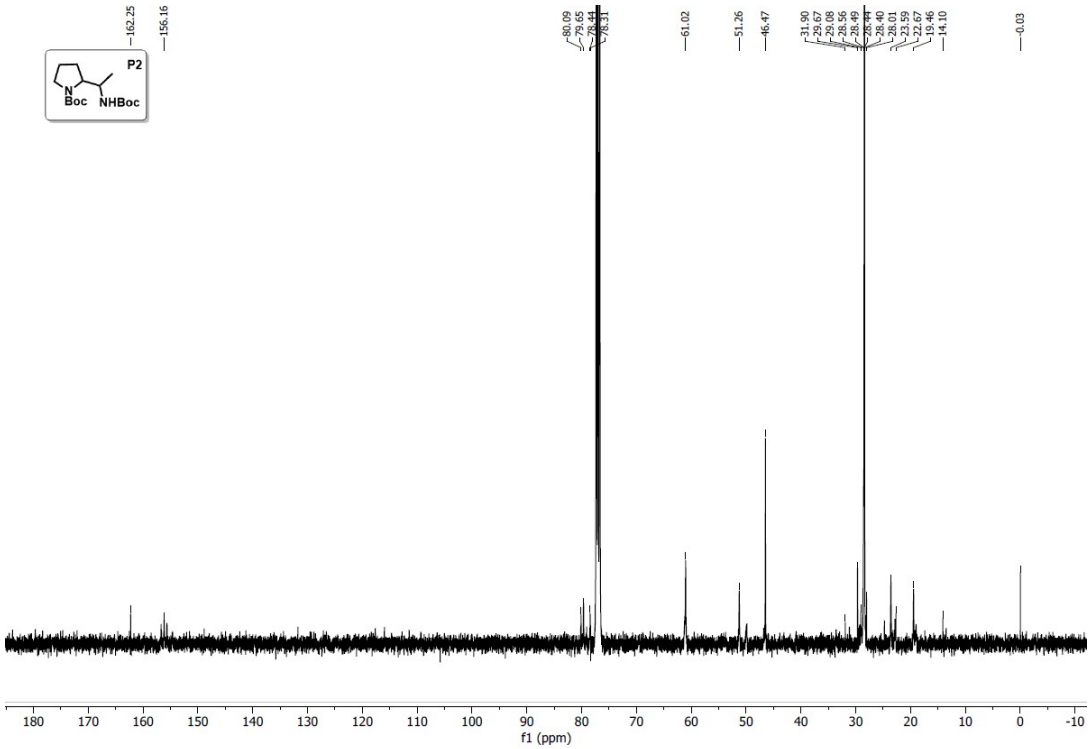


Tert-butyl 2-(1-((tert-butoxycarbonyl) amino) ethyl) pyrrolidine-1-carboxylate (5d)

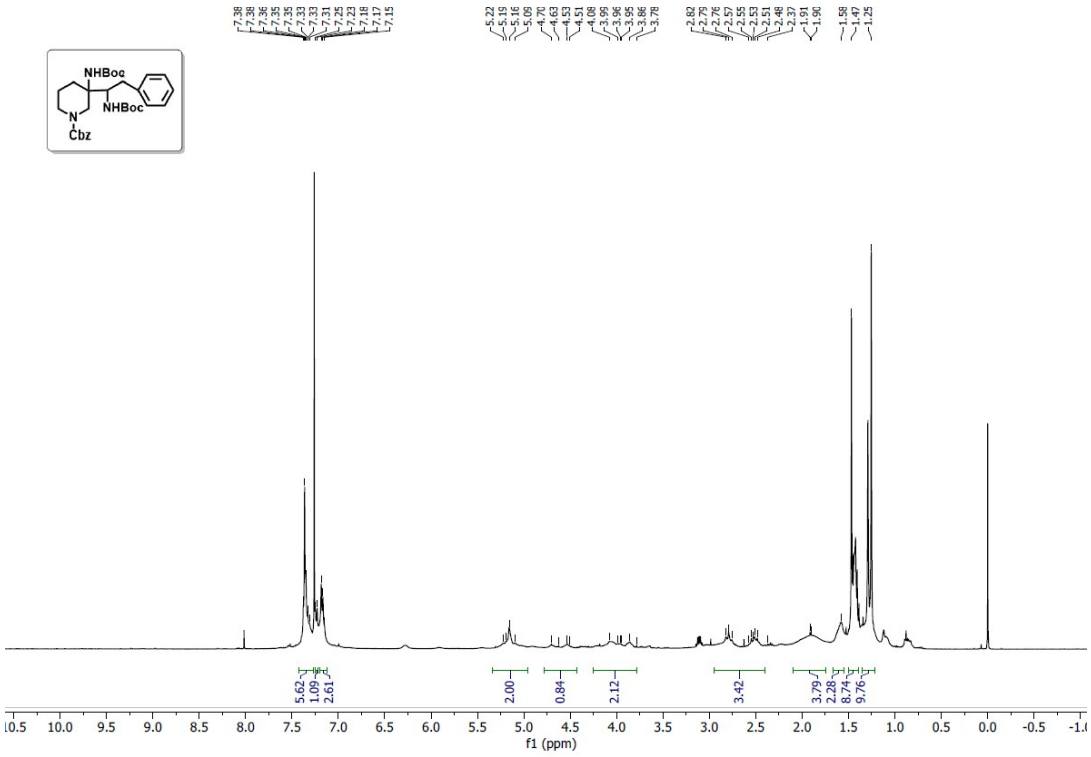


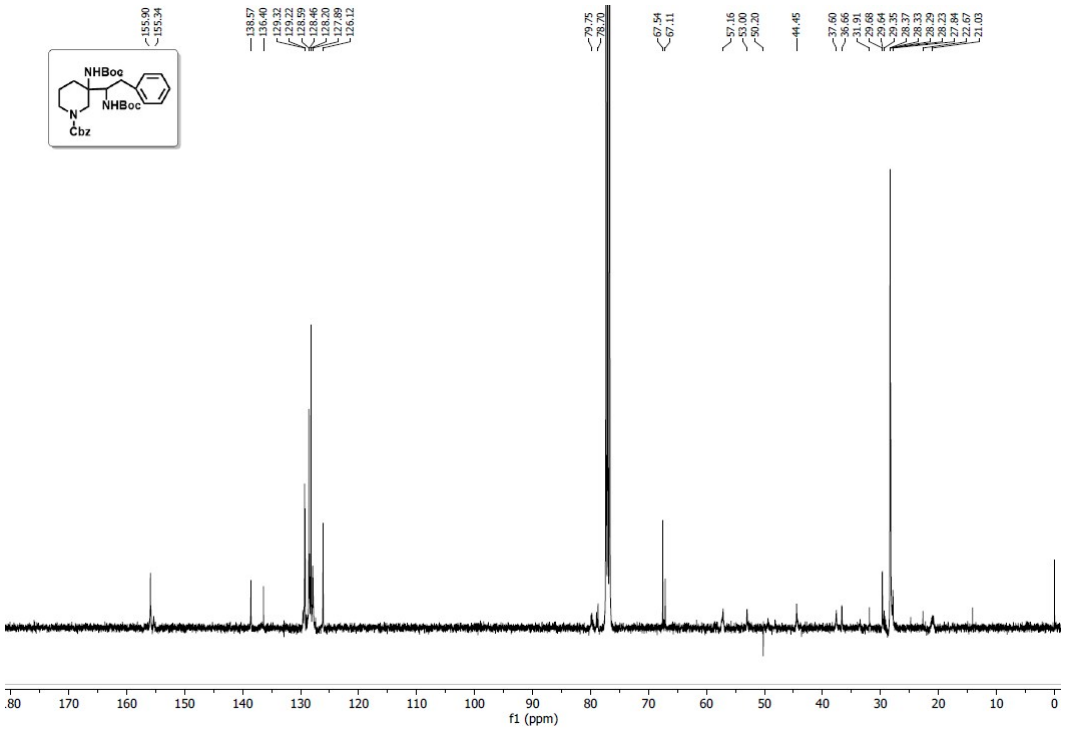

P1
Boc
NHBoc
62.39
155.67
154.59
79.56
79.36
79.10
78.77
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
61.79
59.64
59.34
59.06
58.77
50.00
47.84
47.06
46.47
29.67
29.22
28.46
28.43
28.40
24.03
23.37
22.80
22.43
15.80
-0.03
f1 (ppm)


P2
Boc
NHBoc
3.77
3.75
3.74
3.73
3.72
3.69
3.69
3.32
3.31
3.30
3.29
3.28
3.27
1.97
1.96
1.95
1.94
1.93
1.91
1.89
1.87
1.87
1.86
1.85
1.85
1.84
1.84
1.83
1.83
1.82
1.81
1.71
1.71
1.70
1.68
1.67
1.47
1.43
1.13
1.11
1.00
3.30
4.28
1.30
9.22
8.80
3.00
f1 (ppm)

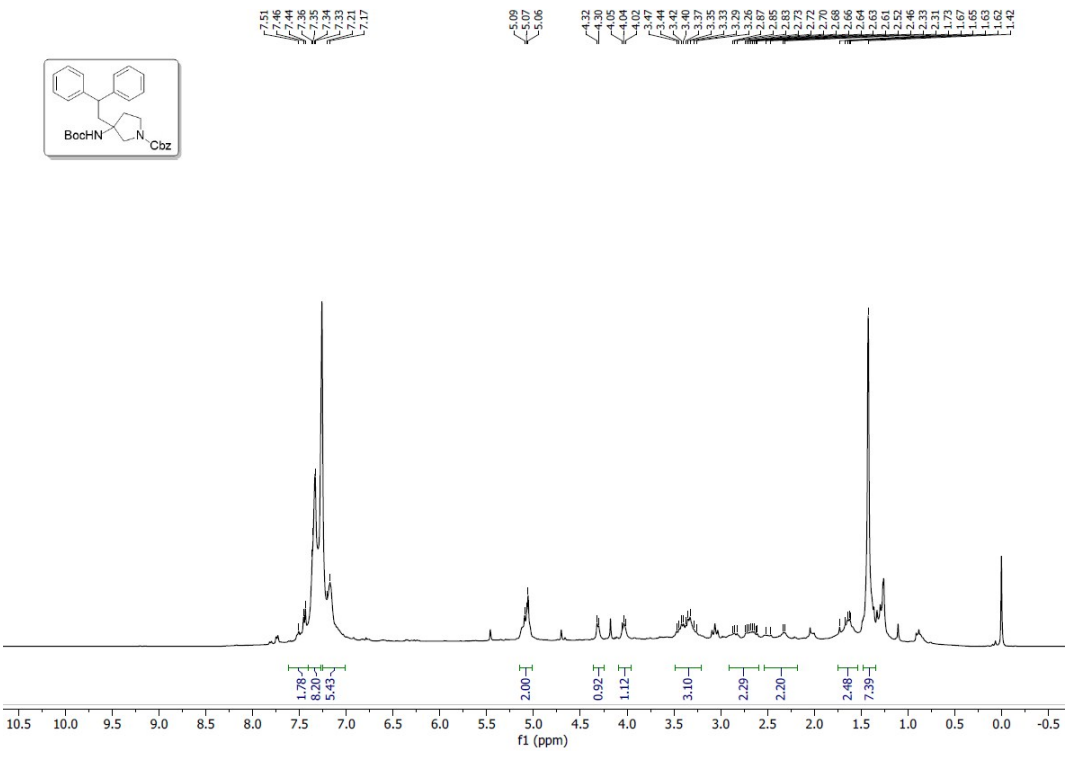


Benzyl 3-((tert-butoxycarbonyl) amino)-3-(1-((tert-butoxycarbonyl) amino)-2-phenylethyl) piperidine-1-carboxylate (5e)

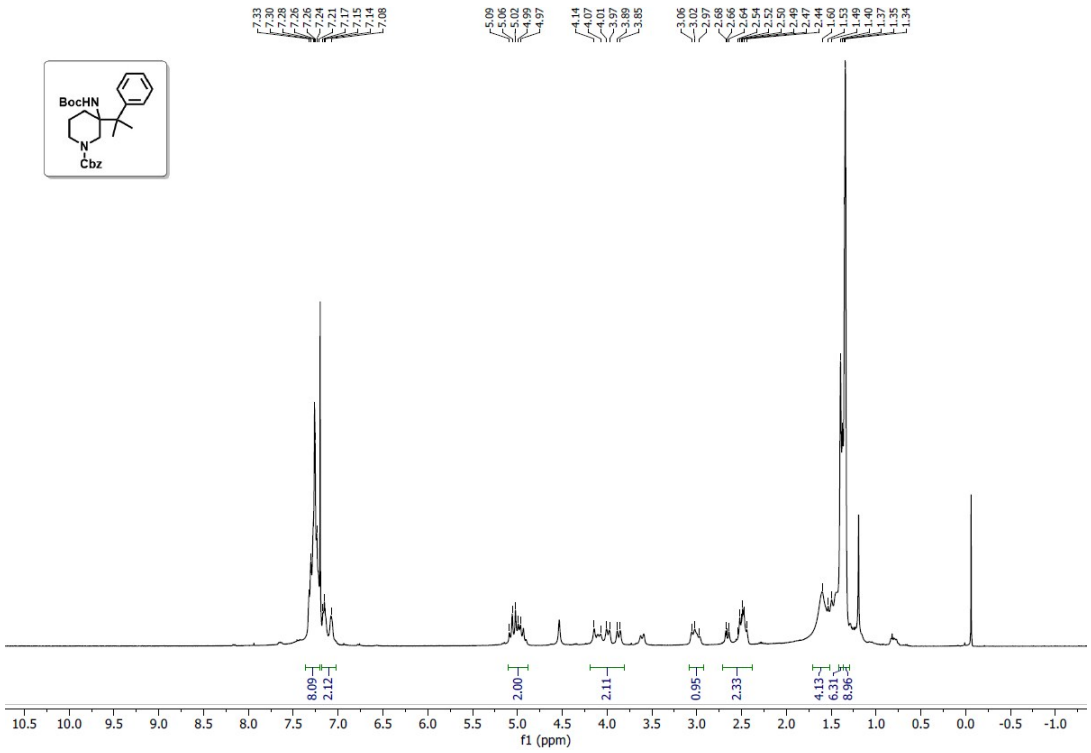


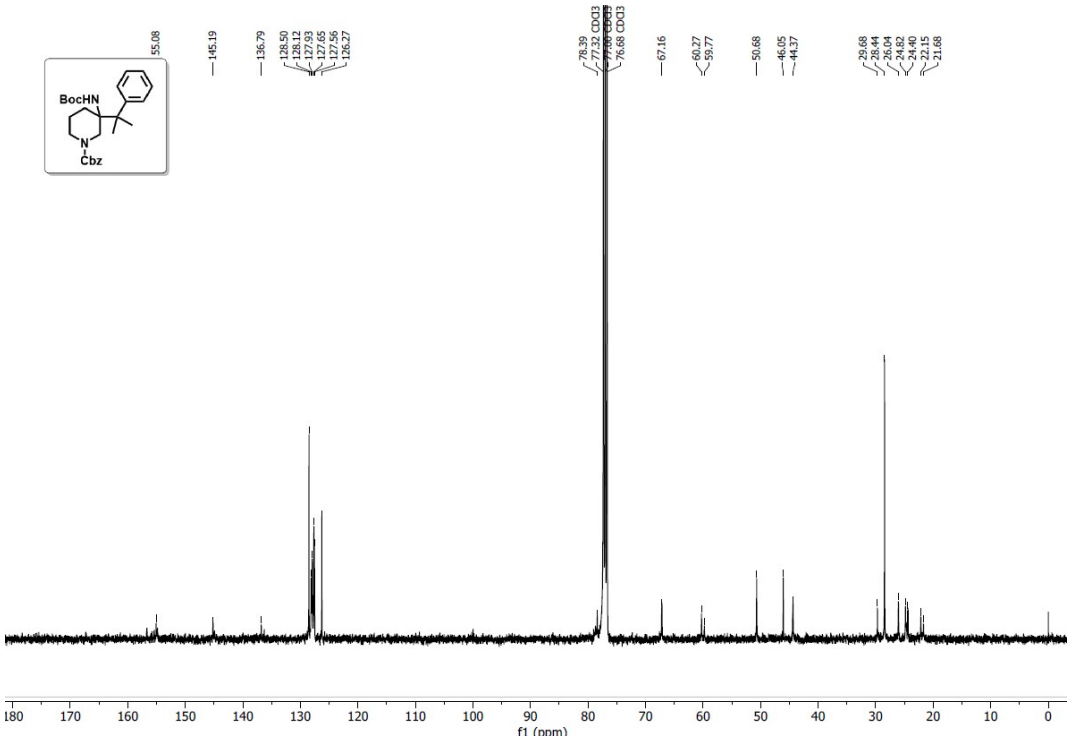


Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2, 2-diphenylethyl) pyrrolidine-1-carboxylate (6b)

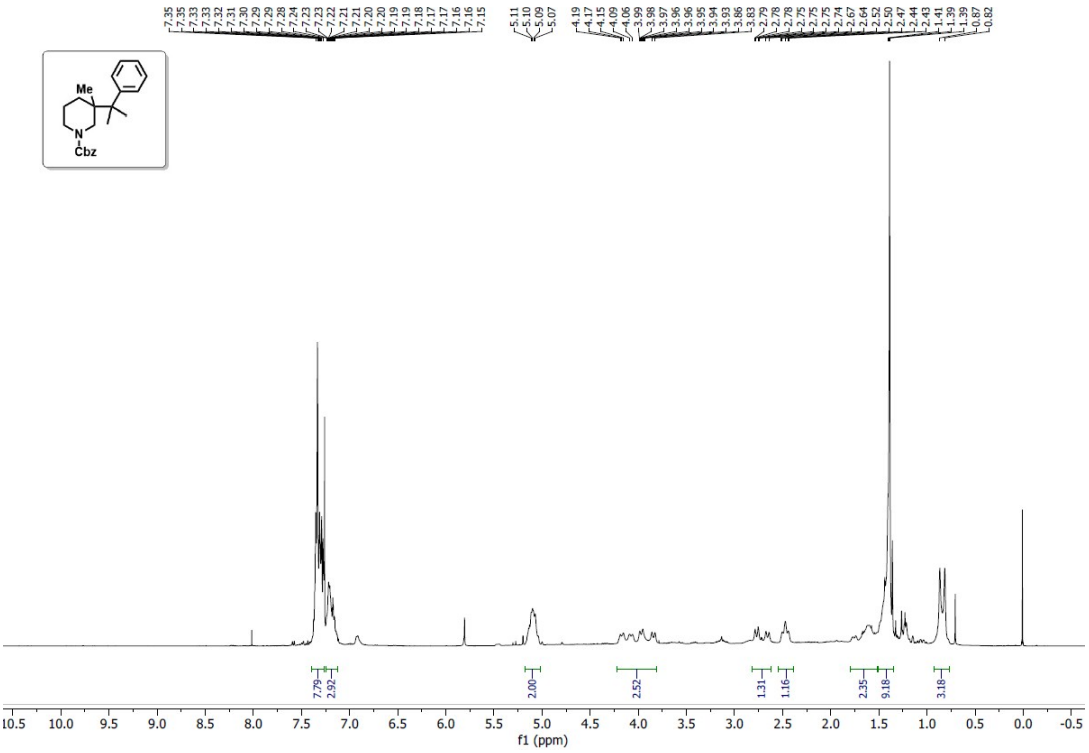


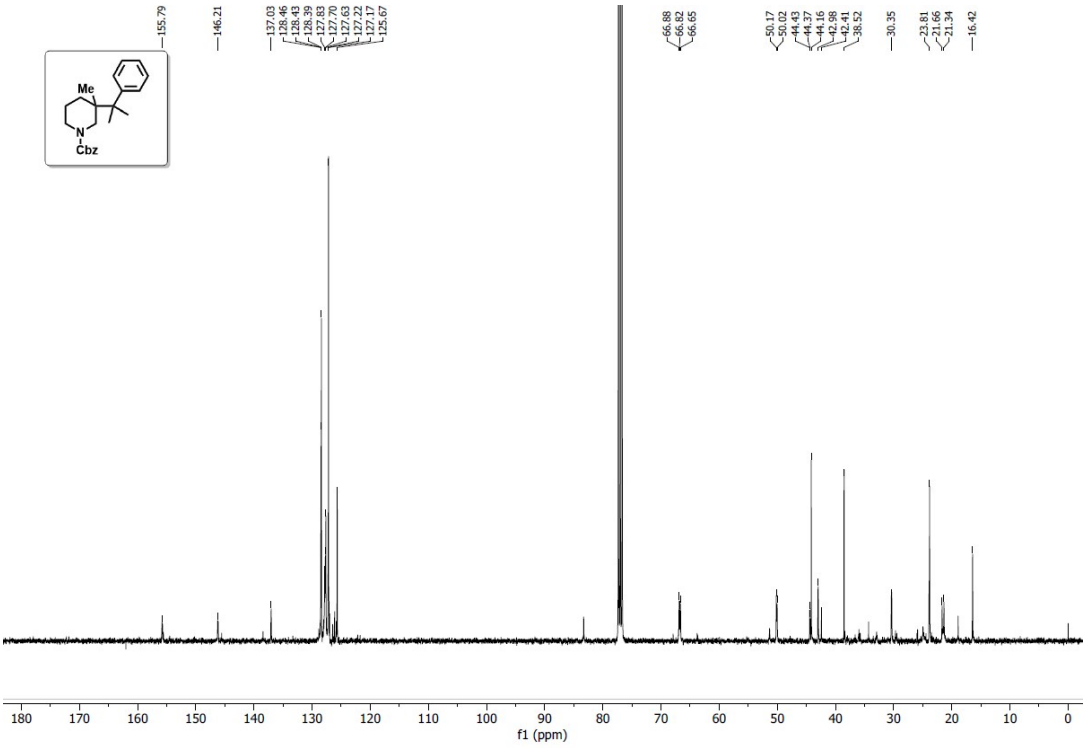
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-phenylpropan-2-yl) piperidine-1-carboxylate (7a)



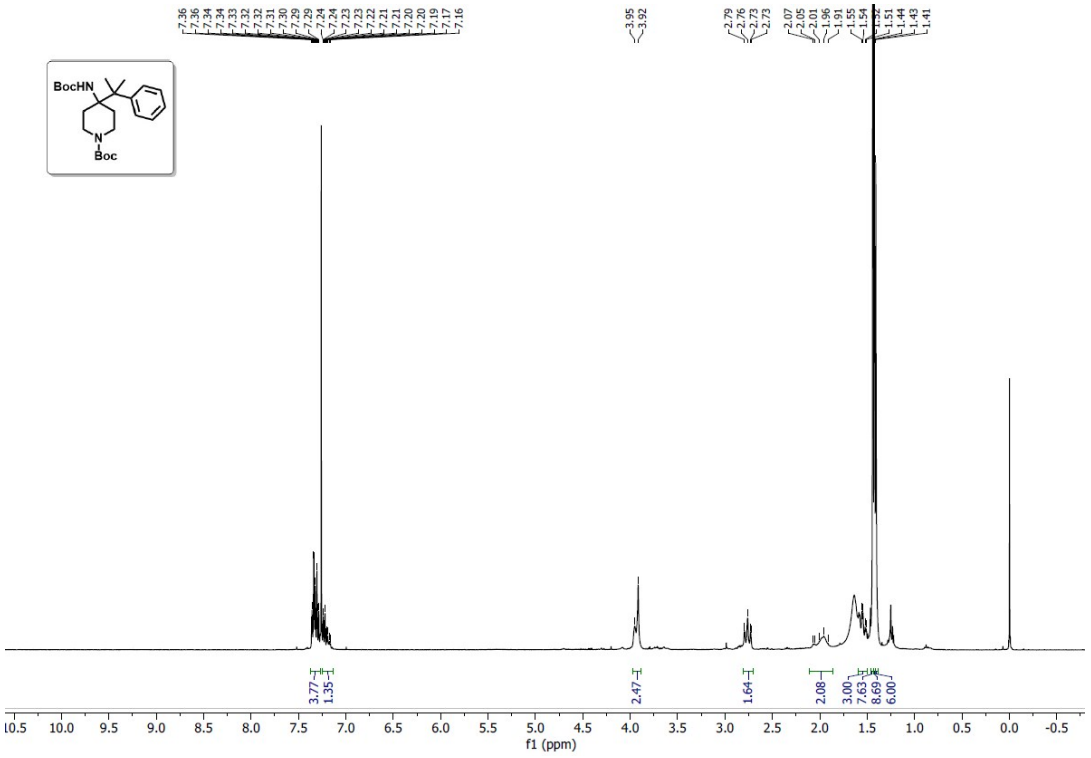


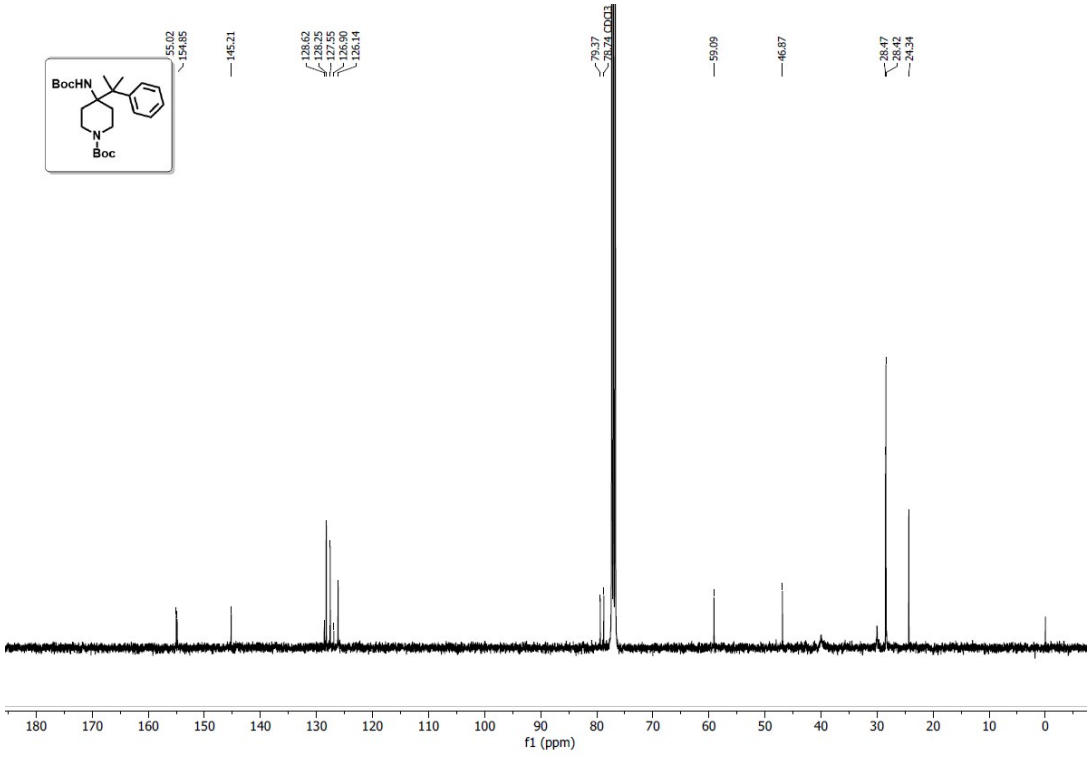
Benzyl 3-methyl-3-(2-phenylpropan-2-yl) piperidine-1-carboxylate (7b)



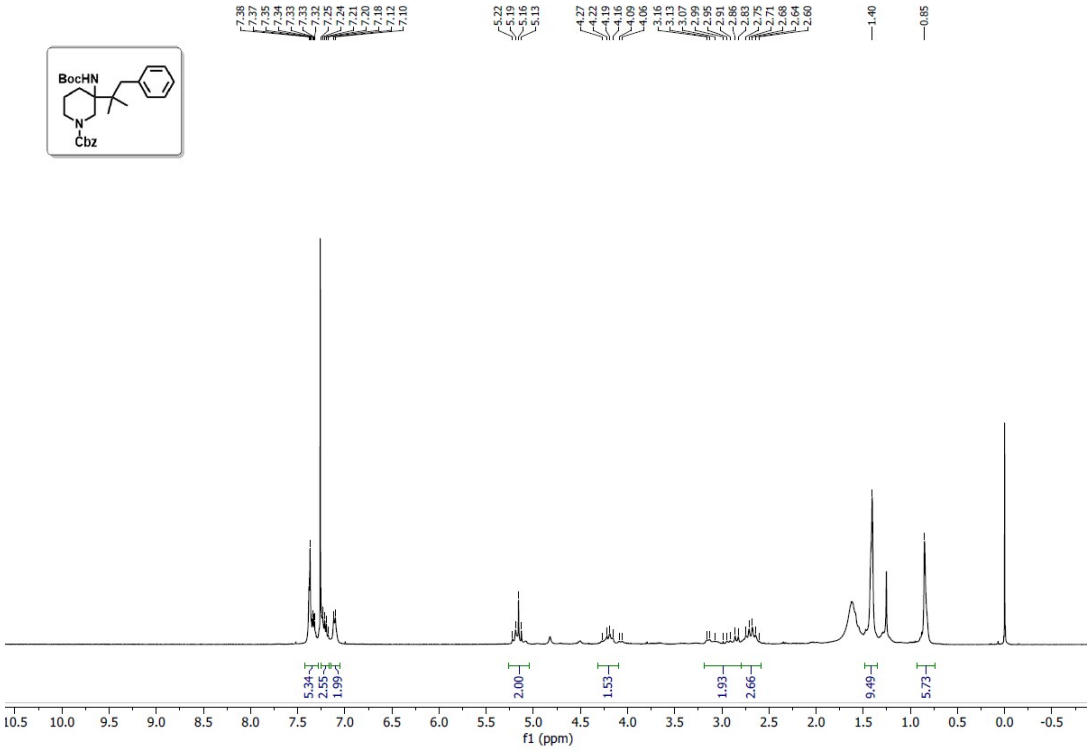


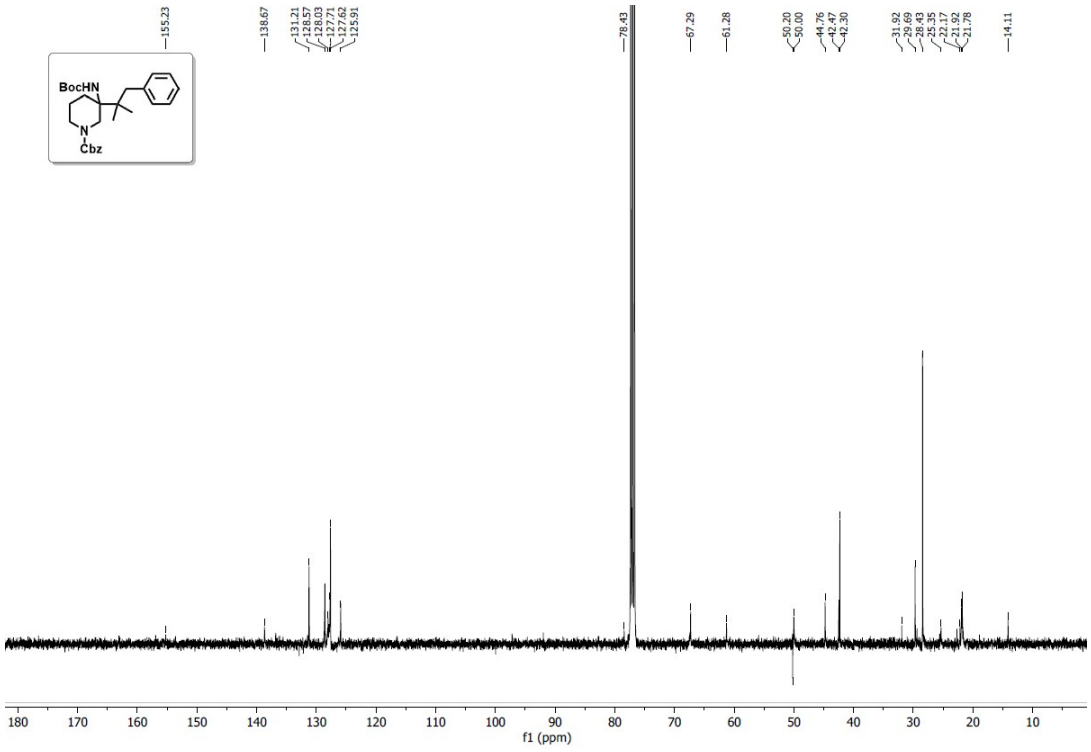
Tert-butyl 4-((tert-butoxycarbonyl)amino)-4-(2-phenylpropan-2-yl)piperidine-1-carboxylate (7c)



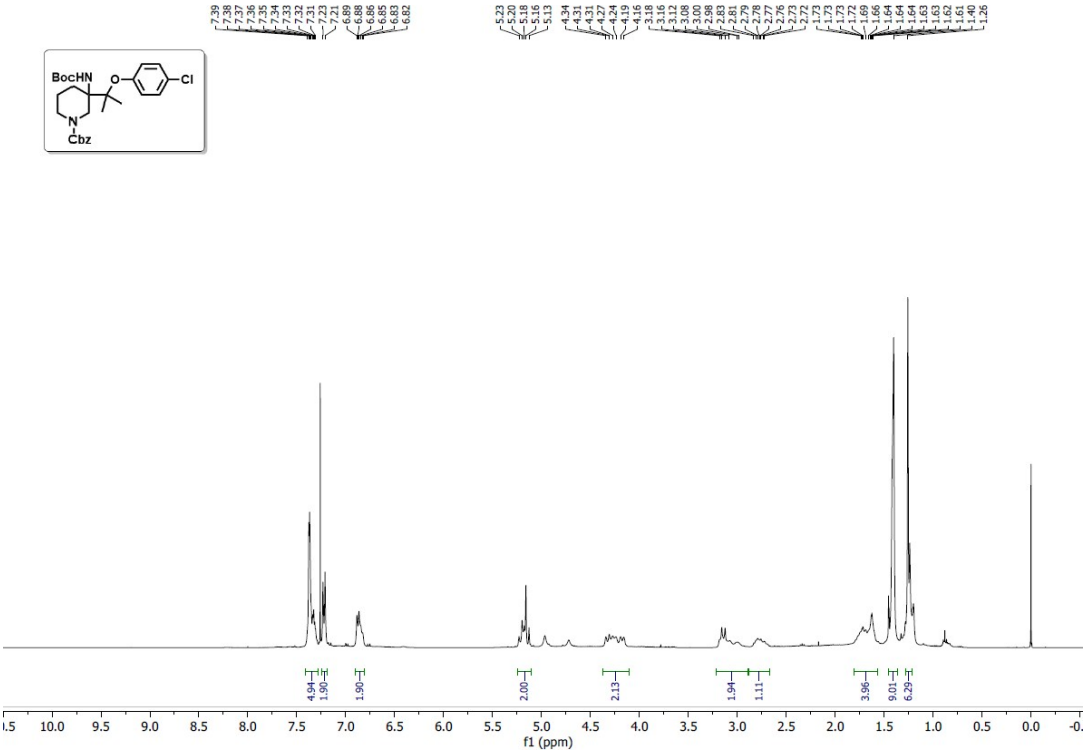


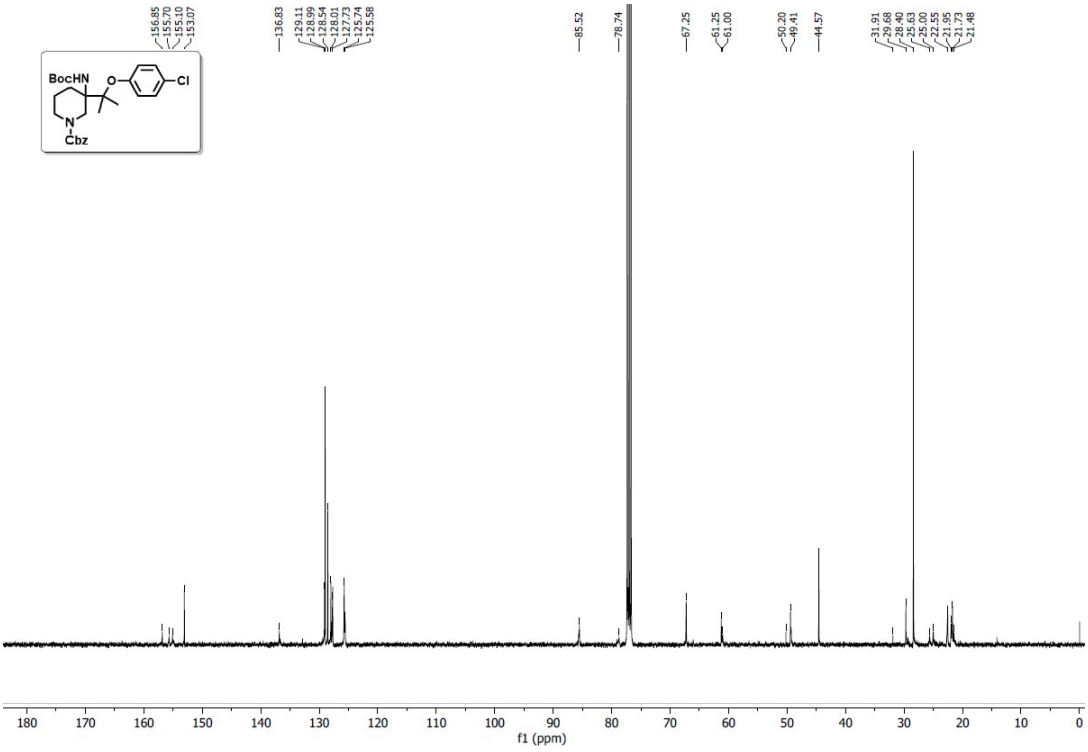
Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-methyl-1-phenylpropan-2-yl) piperidine-1-carboxylate (7d)





Benzyl 3-((tert-butoxycarbonyl) amino)-3-(2-(4-chlorophenoxy) propan-2-yl) piperidine-1-carboxylate (7e)


BocHN
O
Cl
N
Cbz
f1 (ppm)


BocHN
O
Cl
N
Cbz
f1 (ppm)