Electronic Supplementary Material (ESI) for ChemComm.

Fragment-Oriented Synthesis: β-Elaboration of Cyclic Amine Fragments using Enecarbamates as Platform Intermediates

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SUPPORTING INFORMATION

Contents:

General Information

Dichloromethane, toluene, methanol, THF and acetonitrile were dried under nitrogen using a PureSolv MD5 solvent purification System. All reactions were performed in oven-dried glassware under nitrogen atmosphere. The photoredox catalysts were purchased from Aldrich. All other reagents were purchased from commercial sources like Aldrich, Alpha-Aesar or Fluorochem and used without further purification.

Electrochemical experiments were performed on an IKA Electrasyn 2.0. The Electrasyn vial was sealed with an ElectraSyn Teflon cap fitted with a graphite anode and graphite cathode, and reactions were stirred with Teflon-coated magnetic stirrer bars.

Photochemical reactions were carried out using a Kessil lamp (32W, model H150) without external cooling.

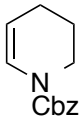
Preparative thin layer chromatography (TLC) plates were prepared with silica gel 60 GF254 Merck. Reaction mixtures were analysed by TLC using ALUGRAM® SIL G/UV254, and visualisation of TLC spots was achieved using ultraviolet (UV) and potassium permanganate solution. Nuclear magnetic resonance (NMR) spectra were recorded in a Bruker AV3-300, Bruker AV3HD-400, Bruker AV4-NEO using $CDCl_3$, CD_3OD and $(CD_3)_2SO$ as solvents and $(CH_3)_4Si$ (^1H) as internal standard. Data was collected at 300 K unless otherwise stated. Chemical shifts (δ) are given in parts per million (ppm) and they are referenced to the residual solvent peak. All coupling constants are expressed in Hz, splitting patterns are reported in an abbreviated manner: app. (apparent), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Assignments were made using COSY, DEPT, HMQC and NOESY experiments. Electrospray ionization (ESI) mass spectra were recorded in a mass spectrometer (Micromass Quattro Micro API, Waters, Ireland) with a Triple Quadrupole (TQ) and with an electrospray ion source operating in positive mode. A Bruker Daltonics micrOTOF spectrometer with electrospray (ES) ionisation source was used for high-resolution mass spectrometry (HRMS).

Synthesis of Enecarbamates and Enamides

General method for enamide synthesis via electrochemical oxidation/elimination (procedure A; Scheme 1)

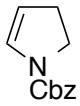
An Electrasyn vial (10 mL) with a stir bar was charged with Cbz protected amine (1.0 g), in anhydrous methanol (10 mL) containing tetraethylammonium tosylate (83 mg, 0.28 mmol) and the mixture was electrolysed (graphite electrodes) under a constant current of 200 mA (terminal voltage 1-2 V) at 25 °C. After the passage of 2.5 $Fmol^{-1}$ of electricity, the mixture was concentrated under reduced pressure. The residue was taken up in anhydrous DCM (0.5 M) and transferred to 100 mL RBF and placed under an inert atmosphere. Me_3SiOTf (1.8 mL, 10.0 mmol) was added dropwise over 10 minutes to the ice-cooled solution of electrolysed amine and $^{i}Pr_2NEt$ (10.0 mmol) in DCM (0.5 M) over 10 minutes. After 3 hours the reaction mixture was diluted with 40 mL of hexane. The reaction was filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by flash chromatography with mixtures of ethyl acetate/hexanes to yield pure enecarbamates.

Benzyl 3,4-dihydropyridine-1(2*H*)-carboxylate (6a)



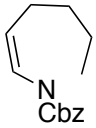
6a was isolated in a 90% yield through procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.51 – 7.29 (5H, m), 6.94 (0.4H, br), 6.83 (0.6H, br), 5.21 (2H, s), 4.99 (0.4H, m), 4.87 (0.6H, m), 3.66 (2H, m), 2.0 4(2H, m), 1.97 – 1.78 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 153.6, 153.2, 136.4, 128.6, 128.2, 128.04, 127.98, 125.4, 124.9, 106.7, 106.4, 67.5, 67.4, 42.4, 42.2, 21.7, 21.5, 21.2. (18 signals observed). Data in accordance with literature values.[1]

Benzyl-2,3-dihydro-1*H*-pyrrole-1-carboxylate (6b)



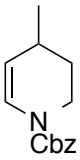
6b was isolated in a 76% yield through general procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.34 – 7.21 (m, 5H), 6.56 (0.4H, br), 6.47 (0.6H. br), 5.10 (2H, s), 5.02 (0.4H, br), 4.99 (0.6H, br), 3.64 (m, 2H), 2.50 (m, 2H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 153.6, 153.2, 136.6, 129.7, 129.1, 128.5, 128.1, 128.0, 127.9, 108.8, 108.7, 67.1, 66.9, 45.3, 45.1, 29.7, 28.7 (17 signals observed). Data in accordance with literature values. [2]

Benzyl 2,3,4,5-tetrahydro-1*H*-azepine-1-carboxylate (6c)



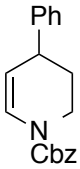
6c was isolated in a 72% yield through general procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.25 – 7.08 (5H, m), 6.35 (1H, H6), 4.96 (2H, s), 4.92 – 4.78 (1H, m), 3.50 (2H, m), 2.02 – 1.93 (2H, m), 1.66 – 1.46 (4H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.4, 136.6, 130.7, 129.9, 128.5, 128.1, 127.9, 115.9, 77.3, 67.4, 47.7, 28.1, 26.3, 26.0, 25.1 (15 signals observed). **HRMS [M+Na]$^+$** $C_{14}H_{17}NNaO_2^+$ calc., 254.1151 found, 254.1151.

Benzyl 4-methyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6d)



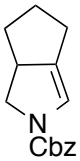
6d was isolated in a 68% yield through general procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.29 – 7.04 (5H, m), 6.77 (0.4H, br), 6.68 (0.6H, br), 5.04 (2H, s), 4.77 (0.4H, m), 4.65 (0.6H, m), 3.65 (1H, m), 3.31 (1H, m), 2.13 (1H, m), 1.89–1.51 (1H, m), 1.36–1.20 (1H, m), 0.94 (3H, m, *J* = 7.0 Hz). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 153.5, 153.1, 136.4, 128.5, 128.2, 128.1, 124.2, 123.7, 113.2, 112.8, 77.3, 67.5, 67.4, 41.0, 40.8, 29.9, 26.8, 26.2, 21.3 (19 signals observed). **HRMS [M+H]$^+$** $C_{14}H_{18}NO_2^+$ calc., 232.1332 found 232.1332.

Benzyl 4-phenyl-3,4-dihydropyridine-1(2H)-carboxylate (6e)



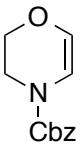
6e was isolated in 83% over 2-steps through procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43-7.23 (10H, m), 7.14 (0.4H, d, J = 8.3Hz), 7.04 (0.6H, d, *J* = 8.3 Hz), 5.24 (2H, s), 5.08 (0.4H, dd, *J* = 8.2, 2.8 Hz), 4.96 (0.4H, dd, *J* = 8.2, 2.8 Hz), 3.75-3.51 (3H, m), 2.18-2.16 (1H, m), 1.85-1.84 (1H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 153.7, 153.2, 145.1, 136.4, 128.7, 128.6, 128.4, 128.3, 127.8, 126.6, 126.3, 125.8, 109.4, 109.1, 67.8, 40.5, 38.3, 38.0, 31.2 (19 signals observed). **HRMS [M+H]$^+$** $C_{19}H_{20}NO_2$ calc. 294.1486 found 294.1487.

Benzyl 4,5,6,6a-tetrahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate (6f)



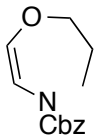
6f was isolated in a 69% yield through general procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.25 – 6.96 (5H, m), 6.05 (0.4H, br), 5.97 (0.6H, m), 4.93 (2H, s), 3.86 – 3.69 (1H, m), 3.24 – 2.88 (2H, m), 2.15 – 1.87 (2H, m), 1.87 – 1.50 (2H, m), 1.12 – 0.90 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 152.5, 151.9, 136.9, 136.8, 133.2, 132.7, 128.5, 128.4, 128.0, 127.9, 119.2, 118.6, 66.8, 66.7, 52.2, 52.1, 49.2, 48.1, 31.32, 31.29, 27.6, 21.70, 21.67 (23 signals observed). **HRMS $[M+H]^+$** $C_{15}H_{18}NO_2^+$ calc., 244.1332 found 244.1332.

Benzyl 2H-1,4-oxazine-4(3H)-carboxylate (6g)



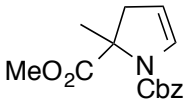
6g was isolated in 64% yield over 2-steps through procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.38-7.26 (5H, m), 6.34 (0.4H, br), 6.21 (0.6H, m), 6.03 (0.4H, m), 5.89 (0.6H, m), 5.19-5.18 (2H, m), 4.09-4.03 (2H, m), 3.75-3.73 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 152.2, 151.9, 136.26, 136.22, 130.3, 129.2, 128.7, 128.44, 128.39, 128.3, 128.2, 106.2, 105.7, 67.8, 67.7, 64.8, 64.3, 42.3, 41.6 (19 signals observed). **HRMS $[M+Na]^+$** $C_{12}H_{13}NNaO_3$ calc. 242.0787 found 242.0784.

Benzyl 6,7-dihydro-1,4-oxazepine-4(5*H*)-carboxylate (6h)



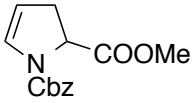
6h was isolated in a 59% yield through general procedure A as a thick oil. **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.33 – 7.19 (5H, m), 5.74 (1H, m), 5.65 (1H, m), 5.07 (2H, s), 4.06 – 3.93 (2H, m), 3.75 (2H, m), 1.89 (2H, m). **^{13}C NMR (126 MHz,$CDCl_3$)** δ 153.9, 136.3, 134.8, 128.6, 128.0, 110.3, 70.8, 68.9, 67.8, 46.6, 28.5. **HRMS $[M+Na]^+$** $C_{13}H_{15}NNaO_3^+$ calc. 256.0944 found 256.0944.

1-Benzyl 2-methyl 2-methyl-2,3-dihydro-1H-pyrrole-1,2-dicarboxylate (6i)



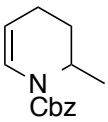
6i isolated in 21% over 2-steps through procedure A as a thick oil (mixture of rotamers. **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.36-7.30 (5H, m), 6.65 (0.45H, dt, *J* = 4.3, 2.1 Hz), 6.56 (0.55H, dt, *J* = 4.3, 2.1 Hz), 5.26-5.03 (2H, m Cbz), 4.97 (0.45H, dt, *J* = 4.7, 2.5 Hz), 4.89 (0.55H, dt, *J* = 4.7, 2.5 Hz), 3.74 (1.6H, s), 3.47 (1.4H, s), 3.03-2.95 (1H, m), 2.62-2.55 (1H, m), 1.68 (1.6H, s), 1.59 (1.4H, s). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 173.7, 173.6, 152.3, 151.7, 136.4, 136.0, 129.9, 129.2, 128.7, 128.6, 128.40, 128.36, 128.30, 128.25, 128.16, 128.09, 104.8, 104.7, 67.5, 67.3, 65.9, 65.5, 52.8, 52.5, 45.7, 44.2, 23.4, 22.5 (28 signals observed). **HRMS $[M+H]^+$** $C_{15}H_{18}NO_4$ calc. 276.1230 found 276.1226.

1-Benzyl 2-methyl 2,3-dihydro-1*H*-pyrrole-1,2-dicarboxylate (6j)



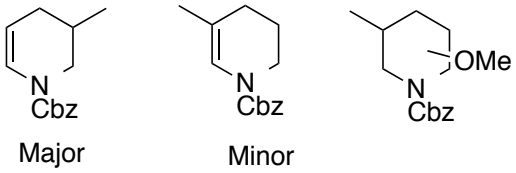
6j was isolated in a 67% yield through general procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44–7.29 (5H, m), 6.70 (0.45H, m), 6.60 (0.55H, m), 5.27–5.05 (2H, m), 4.97 (1H, m), 4.70 (1H, m), 3.77 (1.65H, s), 3.60 (1.35H, s), 3.19–2.97 (1H, m), 2.78–2.58 (1H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.1, 171.9, 152.2, 152.2, 136.2, 136.1, 130.0, 129.3, 128.54, 128.50, 128.22, 128.18 128.1, 128.0, 106.4, 106.2, 67.5, 67.3, 58.1, 58.8, 52.5, 52.3, 35.5, 34.3. **HRMS $[M+H]^+$** $C_{14}H_{16}NO_4$ calc. 262.1079, found 262.1079.

Benzyl 2-methyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6k)



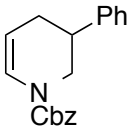
6k was isolated in a 71% yield through general procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.34–7.19 (m, 5H), 6.71 (0.4H, m), 6.63 (0.6H, m), 5.17–5.01 (2H, m), 4.84 (0.4H, m), 4.72 (0.6H, m), 4.43 – 4.24 (1H, m), 2.12–1.96 (1H, m), 1.95–1.78 (1H, m), 1.78–1.45 (2H, m), 1.03 (3H, d, *J* = 7.0 Hz). **^{13}C NMR (126 MHz, $CDCl_3$) δ** 153.4, 152.7, 136.9, 128.5, 128.1, 127.99, 127.95, 123.8, 123.4, 105.8, 105.4, 67.2, 46.5, 46.3, 26.4 17.3 (16 signals observed). **HRMS $[M+H]^+$** $C_{14}H_{18}NO_2^+$ calc. 232.1332 found 232.1332.

Benzyl 3-methyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6l and 6l')



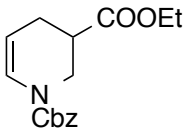
Following general procedure A gave an inseparable mixture of regioisomers **6l** and **6l'** and aminoacetals (1:0.5:1) equating to a 40% yield of **6l**/**6l'** (major regiosiomer showed a 0.7:1 ratio of rotamers, minor showed a 1:1 mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.27 – 7.12 (12.5H, m), 6.81 (0.4H, d, *J* = 8.3 Hz), 6.71 (0.60H, d, *J* = 8.3 Hz), 6.62 (0.25H, br), 6.61 (0.25H, br), 5.03 (5.8H, m), 4.79 (0.4H, m), 4.68 (0.6H, m), 3.85–3.67 (2H, m), 3.53–3.39 (1H, m), 3.11 (1.5H, s), 3.02 (1.5H, s), 2.78 (1.7H, m), 1.95 (1.3H, m), 1.82-1.20 (10.5H, m), 0.84 (6H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 155.7, 155.3, 153.7, 153.3, 153.1, 153.0, 136.7, 136.63, 136.55, 136.4, 128.5, 128.1, 128.00, 127.97, 127.7, 125.0, 124.5, 120.1, 115.5, 115.1, 106.0, 105.8, 85.8, 85.7, 67.4, 67.2, 67.1, 66.9, 55.0. 54.6, 48.5, 48.3, 41.6, 38.2, 38.0, 35.7, 35.5, 29.8, 29.6, 26.9, 25.6, 25.5, 25.1, 21.7, 20.9, 18.7, 17.7, 17.6 (4 signals observed). **HRMS [M+H]$^+$** $C_{14}H_{18}NO_2^+$ calc., 232.1332 found 232.1332.

Benzyl 3-phenyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6m)



6m was isolated in a 67% yield through general procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.38–7.09 (10H, m), 6.93 (0.5H, m), 6.83 (0.5H), 5.21–5.04 (2.5H, m), 4.93 (0.5H, m), 4.18 (0.5H, m), 4.05 (0.5H, m), 3.19 (1H, m), 2.92 (1H, m), 2.22 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 153.5, 153.1, 143.0, 142.8, 136.3, 136.2, 128.72, 128.68, 128.57, 128.5, 128.25, 128.21, 128.14, 128.08, 127.3, 127.2, 126.9, 126.1, 125.3, 124.9, 106.6, 106.3, 67.7, 67.6, 47.9, 47.7, 38.6, 38.5, 31.6 (29 signals observed). **HRMS [M+H]$^+$** $C_{19}H_{20}NO_2^+$ 294.1489 found 294.1487.

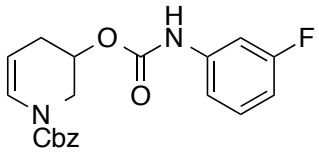
1-Benzyl 3-ethyl 3,4-dihydropyridine-1,3(2*H*)-dicarboxylate (6n)



6n was isolated in a 73% yield through general procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.56–6.95 (5H, m), 6.86 (0.5H), 6.76 (0.5H), 5.03 (2H, s), 4.91 (0.5H, m), 4.79 (0.5H, m), 4.00 (2H, q, *J* = 7.1 Hz), 3.55 (2H, m), 3.0–2.91 (1H, m), 1.95 (1H, m), 1.81 (1H, m), 1.10 (3H, t, *J* = 7.1 Hz). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.2, 153.4, 152.9, 136.1, 129.6, 128.6, 128.3, 128.1, 126.6, 126.2, 103.3,

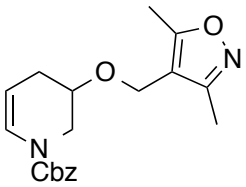
103.0, 67.7, 60.9, 40.3, 40.2, 37.5, 37.2, 23.9, 23.8, 14.2 (21 signals observed). **HRMS [M+Na]$^+$** $C_{16}H_{19}NNaO_4^+$ calc., 312.1206 found, 312.1203.

Benzyl 3-(((3-fluorophenyl)carbamoyl)oxy)-3,4-dihydropyridine-1(2H)-carboxylate (6o)



6p was isolated in a 63% yield through procedure A as a thick oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.39-7.22 (6H, m), 7.00-6.98 (1H, m), 6.92 (1H, dd, *J* = 8.4 Hz), 6.77-6.74 (1H, m), 6.68 (1H, bs), 5.30-5.18 (3H, m), 4.93-4.81 (1H, m), 4.03 (1H, dd, *J*= 13.1, 4.6 Hz), 3.58 (1H, d, *J* = 13.2Hz), 2.48-2.44 (1H, m), 2.27-2.23 (1H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 164.3 (d, J_{C-F} = 244.1 Hz), 153.7, 153.4, 152.3, 139.3 (d, J_{C-F} = 11 Hz), 139.2, 136.0, 130.2 (d, *J* = 8.8 Hz), 128.6, 128.3, 128.2, 128.1, 125.5, 125.0, 113.8, 110.3 (d, *J* = 20.1 Hz), 106.1 (d, *J* = 20.1 Hz), 102.9, 102.5, 67.9, 67.7, 66.3, 45.2, 45.0, 27.4, 27.2 (26 signals observed). **HRMS [M+Na]$^+$** $C_{20}H_{19}FN_2NaO_4$ calc. 393.1221 found 393.1215.

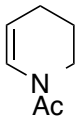
Benzyl 3-((3,5-dimethylisoxazol-4-yl)methoxy)-3,4-dihydropyridine-1(2H)-carboxylate (6p)



6o was isolated in 41% yield as a thick oil (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37-7.36 (5H, m), 6.89 (0.3H, d, *J* = 8.3 Hz), 6.80 (0.7H, d, *J* = 8.3 Hz), 5.19 (2H, m), 4.81-4.79 (1H, m), 4.40-4.27 (2H, m), 3.79-3.56 (3H, m), 2.38-2.08 (8H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.1, 159.8, 153.4, 136.1, 128.6, 128.3, 128.2, 128.1, 125.5, 125.0, 111.0, 103.4, 103.2, 69.9, 69.8, 67.8, 67.7, 59.4, 45.0, 44.0, 28.5, 27.9, 10.9, 10.0 (24 signals observed). **HRMS [M+H]$^+$** $C_{19}H_{23}N_2O_4$ calc. 343.1652 found 343.1659.

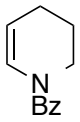
ADDITIONAL SUBSTRATES NOT IN PAPER:

1-(3,4-Dihydropyridin-1(2*H*)-yl)ethenone



7 was isolated in a 75% yield as a brown oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 6.58 (1H, dt, *J* = 8.4, 2.0 Hz), 4.98 (1H, dt, *J* = 8.1, 3.9 Hz), 3.75 – 3.68 (2H, m), 2.17 (3H, s), 2.10 (2H, tdd, *J* = 6.2, 3.9, 2.0 Hz), 1.89 – 1.77 (2H, m, H-1). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 173.2, 168.1, 167.9, 125.7, 123.8, 108.6, 108.3, 44.3, 40.1, 21.7, 21.7, 21.4 (12 signals observed). **HRMS $[M+H]^+$** $C_7H_{12}NO$ calc. 126.0913 found 126.0909

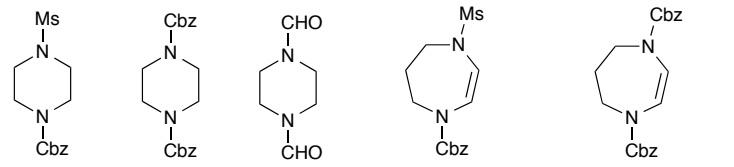
(3,4-dihydropyridin-1(2*H*)-yl)(phenyl)methanone



8 was isolated in a 79% yield through procedure A as a colourless oil (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.47 – 7.29 (5H, m), 6.38 (1H, d, *J* = 8.2 Hz), 4.78 (1H, m), 3.77 (2H, m), 2.06 (2H, m), 1.89 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 169.3, 135.2, 130.2, 128.4, 128.2, 127.5, 124.8, 107.6, 41.1, 21.9 (10 signals observed). **HRMS $[M+H]^+$** $C_{12}H_{14}NO$ calc. 188.1070 found 188.1071

UNSUCCESSFUL SUBSTRATES:

The following substrates were unsuccessful in the electrochemical oxidation. For the diazepane substrates, some conversion was observed but analytically pure material could not be obtained: indicative yields are given for information.



no product | no product | no product | 43% (not analytically pure) | 38% (not analytically pure)

Enamide Substrates Prepared by Alternative Routes

General method for formation of Cbz-imides

In an oven-dried round bottom flask was added unprotected amides (7.6 mmols) and kept under nitrogen. Then, 38 mL of dried THF was added and the solution cooled down to -78 ^{o}C. n-BuLi solution in hexanes (6.3 mL, 1.3M, 8.4 mmols) was added dropwise into the reaction mixture and stirred 1 hour at -78 ^{o}C before neat benzyl chloroformate (1.2 mL, 9.1 mmols) was added, again dropwise. The reaction is allowed to stir at -78oC for 4 hours before quenched with a saturated NH_4Cl solution (40 mL). The reaction mixture was stirred until it reached room temperature, when 50 mL of DCM was added. The aqueous phase was extracted trice with DCM (50 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography with mixtures of ethyl acetate/hexanes to yield pure imides.

General method for reduction of Cbz-imides to enamides:

Method A ($LiBHEt_3$): In an oven-dried round bottom flask imide (2.9 mmols) was dissolved in dry toluene (6.7 mL). Then, 3.2 mL of $LiBHEt_3$ solution in THF (1M, 3.2 mmol) was added dropwise at -78 ^{o}C. The reaction mixture was stirred 1 hour at -78 ^{o}C before DIPEA (2.9 mL, 16.6 mmols), DMAP (10 mg) and TFAA (0.49 mL, 3.5 mmols) were added slowly at -78 ^{o}C. The reaction mixture was allowed to warm to room temperature and stirred for additional 2 hours. The reaction was quenched by addition of saturated NH_4Cl solution (20 mL) and diluted with 20 mL of DCM. The aqueous phase was extracted trice with DCM (20 mL), and the combined organic phases were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography with mixtures of ethyl acetate/hexanes to yield pure enamides.

Method B (DiBAL-H): In an oven-dried round bottom flask imide (1.8 mmols) was dissolved in dry THF (6 mL). Then, 2.5 mL of DiBAL-H solution in hexanes (1M, 2.5 mmol) was added dropwise at -78 ^{o}C. The reaction mixture was stirred 1 hour -78 ^{o}C before quenched with a saturated NH_4Cl solution (20 mL). The reaction mixture was allowed to warm till room temperature followed by the addition of 5 mL of 10% Na_2CO_3 solution and 15mL of DCM. The aqueous phase was extracted 4 times with DCM (15 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was dissolved in 4 mL of THF and 0.02 mL of sulfuric acid was added. The mixture was stirred for 1.5 hours at room temperature before being quenched with saturated $NaHCO_3$ solution and diluted with 15 mL of DCM. The aqueous phase was extracted trice with DCM (15 mL), and the combined organic phases were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography with mixtures of ethyl acetate/hexanes to yield pure enamides.

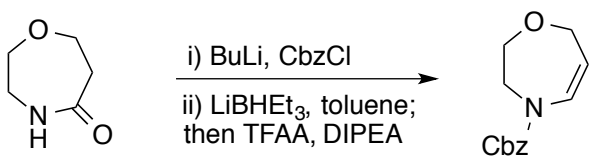
General method for lactam synthesis via Beckmann rearrangement

In a round bottom flask $NH_2OH.HCl$ (0.52 g, 7.5 mmols) and NaOH (0.6 g, 15 mmols) were dissolved in distilled water (7.5 mL) and stirred at room temperature for 30 minutes. To this solution was added ketone (4 mmols) dissolved in 20 mL of ethanol. The mixture was allowed to react for 30 minutes under reflux. Then, the mixture was concentrated under reduced pressure, diluted with distilled water (10 mL) and extracted trice with DCM (20 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue (2.1 mmols) was redissolved in a mixture of DME (6.3 mL) and distilled water (4.2 mL), followed by the addition of tosyl chloride (582 mg, 3 mmols) and K_2CO_3 (707 mg, 5 mmols). The mixture was heated at 82 ^oC for 3 hours. The reaction diluted with 20 mL of DCM and 10 mL of distilled water. The aqueous phase was extracted trice with DCM (20 mL), and the combined organic phases were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was proceeded to the following steps without further purification.

General procedure for enamide synthesis by elimination of N*-chloroamines*

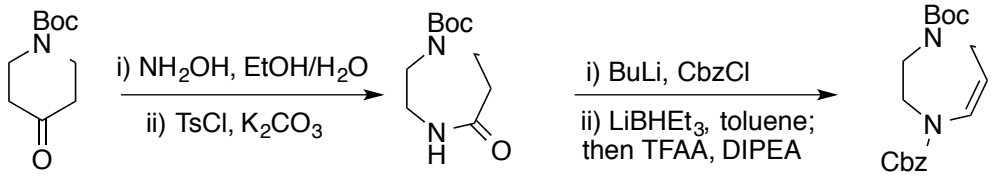
Into a 100ml round bottom flask fitted with a magnetic stirrer, was added NCS (3.02 g, 22.6 mmol), MTBE (11 mL) and distilled water (11 mL). The suspension was stirred for 5 minutes at 0 ^oC, before dropwise addition amine (20.2 mmol). Stirring at 0 ^oC was continued for an additional 5 minutes, followed by 30 minutes at room temperature. The reaction mixture was diluted with MTBE (6 mL), extracted and the aqueous layer was extracted once with MTBE (11mL). The organic phase was dried with MgSO4, filtered and diluted with 25% NaOMe (in methanol, 6.2 mL). The reaction mixture was refluxed for 45 minutes, cooled down to room temperature with stirring. The white precipitate was dissolved by adding the minimal amount of water. The mixture was extracted three times with diethyl ether (20 mL), followed by drying with MgSO4, filtration and concentrated under reduced pressure. Note: A thorough drying of the organic phase will be essential for higher yields on the following step. The crude imine was dissolved in chloroform (4.1ml/mmol imine), followed by the addition of 2,6-lutidine (1 equiv.). The reaction mixture was added dropwise into a stirred solution of CbzCl (1 equiv., or other acylating reagent) in chloroform (4.1ml/mmol imine). Upon complete addition, the reaction was concentrated under reduced pressure and the crude purified by flash chromatography with mixtures of ethyl acetate/hexanes to yield pure enamides.

Benzyl 2,3-dihydro-1,4-oxazepine-4(7H)-carboxylate



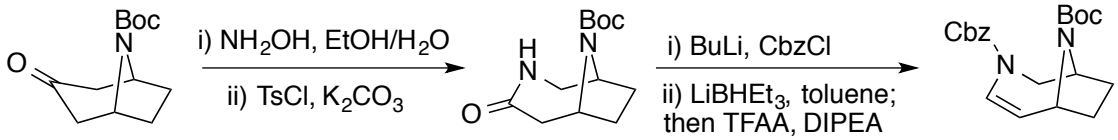
Isolated in 25% yield over 2 steps. (Mixture of rotamers) **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38-7.31 (5H, m), 6.82-6.74 (1H, m), 5.19 (2H, s), 4.95 (1H, bs), 4.22-4.21 (2H, m), 3.88-3.81 (4H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.3, 136.1, 129.8, 128.7, 128.4, 128.3, 111.5, 70.0, 68.2, 67.3, 49.6. **HRMS [M+H]$^+$** $C_{13}H_{16}NO_3^+$ calc. 234.1125 found 234.1120.

1-Benzyl 4-*tert*-butyl 2,3-dihydro-1H-1,4-diazepine-1,4(5H)-dicarboxylate



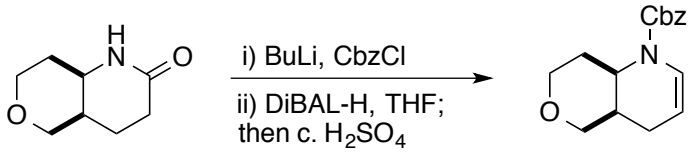
Isolated in 18% yield over four steps. (Mixture of rotamers) **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.39-7.32 (5H, m), 6.71-6.60 (1H, m), 5.18 (2H, s), 4.97 (1H, bs), 4.04-3.98 (2H, m), 3.87 (2H, bs), 3.66 (2H, bs), 1.43 (9H, s). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 155.3, 154.0, 136.1, 129.5, 128.6, 128.3, 128.1, 110.6, 80.1, 67.9, 46.9, 46.7, 43.3, 42.5, 28.4 (15 signals observed). **HRMS [M+Na]$^+$** $C_{18}H_{24}N_2NaO_4^+$ calc. 355.1628 found 355.1624.

3-Benzyl 9-*tert*-butyl 3,9-diazabicyclo[4.2.1]non-4-ene-3,9-dicarboxylate



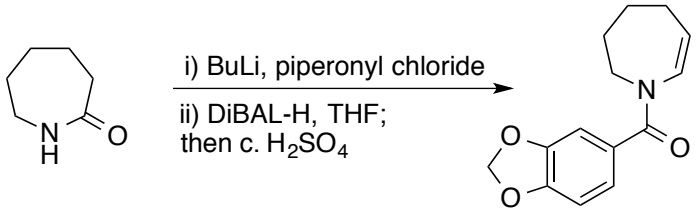
Isolated in 20% yield over 4-steps. (Mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.27-7.19 (5H, m), 6.43 (1H, bm) 5.40-5.36 (1H, m), 5.13-5.06 (2H, m), 4.42-4.21 (3H, m), 3.18-3.15 (1H, m), 2.02-1.94 (2H, m), 1.63-1.59 (2H, m), 1.36 (9H, s). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.2, 153.0, 152.7, 141.3, 136.1, 128.6, 128.4, 128.3, 128.0, 127.4, 126.9, 120.1, 119.6, 118.3, 79.8, 79.6, 68.1, 65.0, 54.0, 53.2, 51.5, 50.3, 32.1, 31.4, 28.5, 26.0, 25.0 (27 signals observed). **HRMS [M+Na]$^+$** $C_{20}H_{26}N_2NaO_4$ calc. 381.1784 found 381.1785.

Benzyl 4,4a,5,7,8,8a-hexahydro-1H-pyrano[4,3-b]pyridine-1-carboxylate



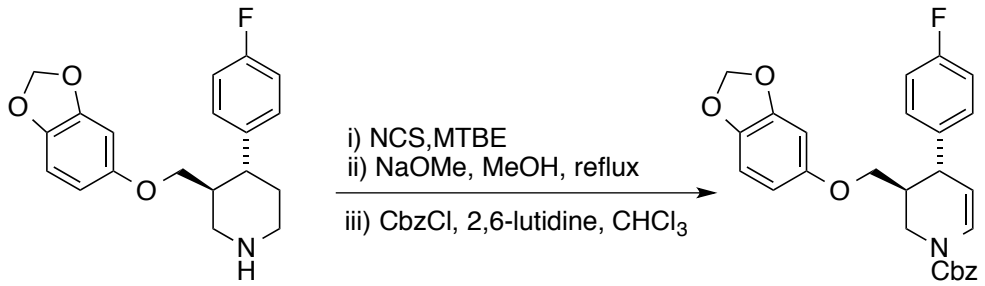
Isolated in 6 % yield over 4-steps. (Mixture of rotamers) **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37-7.32 (5H, m), 6.85 (0.4H, br m), 6.78 (0.6H, br m), 5.21-5.18 (2H, m), 4.97 (0.4H, br m), 4.85 (0.6H, br m), 4.38 (0.6H, m), 4.24 (0.4H, m), 3.99-3.96 (1H, m), 3.80-3.77 (1H, d, *J* = 11.7 Hz), 3.65- 3.39 (2H, m), 2.55-2.46 (1H, m), 1.96-1.53 (4H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 153.1, 152.6, 136.3, 128.6, 128.2, 128.1, 128.0, 123.2, 122.7, 105.0, 104.8, 70.8, 67.5, 67.4, 50.8, 50.4, 31.9, 31.8, 26.5, 25.7, 21.1, 21.0 (22 signals observed). **HRMS [M+H]$^+$** $C_{16}H_{20}NO_3$ calc. 274.1437 found 274.1432.

Benzo[d][1,3]dioxol-5-yl(2,3,4,5-tetrahydro-1H-azepin-1-yl)methanone (13)



Isolated in 48% yield over 3 steps. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.04 (1H, d, *J* = 7.7 Hz), 6.99 (1H, s), 6.76 (1H, d, *J* = 8.0 Hz), 6.23 (1H, bs), 5.95 (2H, s), 5.03 (1H, bs), 3.87 (2H, bs), 2.24-2.21 (2H, m), 1.83- 1.73 (4H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.1, 149.2, 147.3, 133.1, 129.7, 123.4, 116.6, 109.1, 107.8, 101.5, 46.4, 28.2, 26.7, 24.8. **HRMS $[M+Na]^+$** $C_{14}H_{15}NNaO_3^+$ calc. 268.0944 found 268.0948.

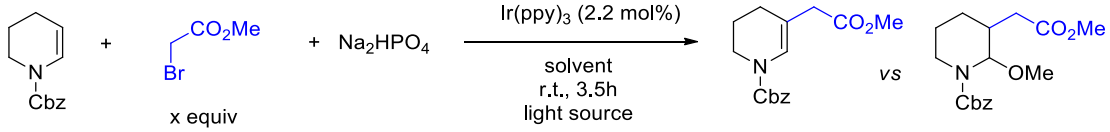
(3S,4R)-Benzyl 3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)-3,4-dihydropyridine-1(2H)-carboxylate (16)



Isolated in 7% yield over 3-steps. (Mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.41-7.37 (5H, m), 7.18-7.11 (2.5H, m), 7.01-6.98 (2.5H, m), 6.68-6.66 (1H, d, *J* = 8.5 Hz), 6.43-6.42 (1H, m), 6.23 (1H, m), 5.91 (2H, s), 5.23-5.21 (2H, s), 4.97 (0.5H, br d, *J* = 2.4 Hz), 4.83 (0.5H, br d, *J* = 2.4 Hz), 4.01-3.98 (0.5H, dd, *J* = 12.9, 2.8 Hz), 3.85-3.81 (1.5H, m), 3.74-3.70 (1H, m), 3.67-3.54 (1H, dd, *J* = 12.6, 8.2 Hz), 3.51-3.47 (1H, m), 2.17 (1H, bs). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 161.8 (J_{F-C} = 244.4 Hz), 154.2, 154.2, 153.6, 153.1, 148.3, 141.8, 139.3 (J_{C-F} = 2.5 Hz), 136.1, 129.6 (J_{C-F} = 7.6 Hz), 128.6, 128.2, 128.1, 115.5 (J_{C-F} = 21.4 Hz), 108.5, 107.9, 105.63, 105.56, 101.2, 98.1, 68.6, 67.9, 67.7, 42.9, 42.6, 40.4, 39.7, 39.5 (28 signals observed). **HRMS $[M+H]^+$** $C_{27}H_{25}FNO_5$ calc. 462.1711 found 462.1709.

Optimization procedures for methyl bromoacetate photoredox alkylations

Into an oven-dried 7 mL Supelco vial fitted with a Teflon septum was weighed base (0.135 mmol), methyl bromoacetate (0.225 or 0.45 mmol), and *N*-(benzyloxycarbonyl)-1,2,3,4-tetrahydropyridine **6a** (0.069 mmol). The vial was then purged with nitrogen for 5 minutes, before the addition of a dry solvent solution of $Ir(ppy)_3$ (1 mg in 1 mL, prepared in an oven-dried vial under nitrogen flow). The vial was sealed and stirred for 3-5 hours under light irradiation. After this period the solvent was removed under reduced pressure and the crude mixture was analysed by NMR spectroscopy against 1,3,5-trimethoxybenzene as internal standard to determine the starting material conversion and product yield.

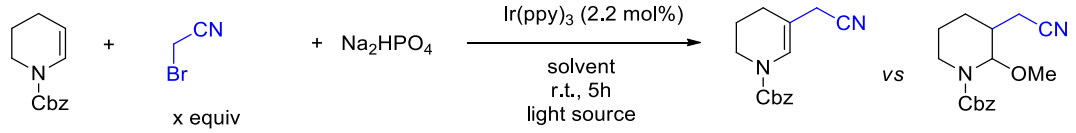


Solvent	Halide equiv	Base	Catalyst	Light source	Aminal/ enamine ratio	Yield %[a]
MeCN	3 equiv	As shown	As shown	32W LED blue	n/a	65 (50)
MeCN	3 equiv	2,6-lutidine	As shown	32W LED blue	n/a	54
MeCN	6 equiv	As shown	As shown	32W LED blue	n/a	62
MeCN	3 equiv	As shown	$Ir(ppy)_2(dtbbpy)PF_6$	32W LED blue	-	n.r.
MeCN	3 equiv	As shown	As shown	20W CFL	n/a	55
MeCN	3 equiv	As shown	$Ir(ppy)_3$ (0.2 mol%)	32W LED blue	n/a	50
CH_2Cl_2	3 equiv	As shown	As shown	32W LED blue	n/a	24
MeOH	3 equiv	As shown	As shown	32W LED blue	<1:20	82
MeOH/MeCN 1:4	3 equiv	As shown	As shown	32W LED blue	<1:20	53
MeOH/MeCN 1:1[b]	3 equiv	As shown	As shown	32W LED blue	-	n.r.
MeOH[c]	3 equiv	2,6-lutidine	As shown	32W LED blue	>20:1	95 (86)
MeOH[d]	3 equiv	2,6-lutidine	$Ir(ppy)_3$ (0.2 mol%)	32W LED blue	>20:1	80
MeOH	3 equiv	As shown	-	32W LED blue	-	n.r.

Table 1: Optimisation procedures for methyl bromoacetate photoredox alkylations. [a)] NMR yields vs. internal standard (1,3,5-trimethoxybenzene); isolated yields in parentheses [b)] Sodium ascorbate used as additive (1 equiv) [c)] isolated yield after TES/BF_3 reductive quench as reduced *N*-Cbz amine [d)] 16 hours.

Optimisation procedures for bromoacetonitrile photoredox alkylation

Into an oven-dried 7 mL Supelco vial fitted with a Teflon septum was weighed base (0.135 mmol), bromoacetonitrile (x mmol), and *N*-(benzyloxycarbonyl)-1,2,3,4-tetrahydropyridine (0.069 mmol). The vial was then purged with nitrogen for 5 minutes, before the addition of a dry solvent solution of $Ir(ppy)_3$ (1 mg in 1 mL, prepared in an oven-dried vial under nitrogen flow). The vial was sealed and stirred for 3-5 hours under light irradiation. After this period the solvent was removed under reduced pressure and the crude mixture was analysed by NMR spectroscopy against 1,3,5-trimethoxybenzene as internal standard to determine the product yield and starting material conversion.



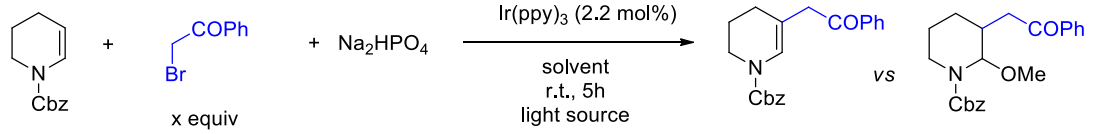
Solvent	Halide equiv	Base	Catalyst	Light source	Aminal/enamine ratio	Yield %
MeCN	3	As shown	As shown	20W CFL	<1:20	36
MeCN	1.7	As shown	As shown	32W LED blue	<1:20	39
MeOH/MeCN 1:1[a]	3	As shown	As shown	32W LED blue	<1:20	38
MeCN	5	As shown	As shown	32W LED blue	<1:20	50
MeCN	3	TMG, DABCO, Quinuclidine, Cs_2CO_3, Na_2CO_3, K_3PO_4, K_3CO_3, NaAc	As shown	32W LED blue	<1:20	11-38
MeOH	3	lutidine	As shown	32W LED blue	>20:1	40[b]

[a] Sodium ascorbate used as additive (1 equiv) [b] isolated yield after TES/BF_3 reductive quench as reduced *N*-Cbz amine.

Optimisation procedures for phenacyl bromide photoredox alkylations

Into an oven-dried 7 mL Supelco vial fitted with a Teflon septum was weighed base (0.135 mmol), phenacyl bromide (x mmol), and *N*-(benzyloxycarbonyl)-1,2,3,4-tetrahydropyridine (0.069 mmol). The vial was then purged with nitrogen for 5 minutes, before the addition of a dry solvent solution of $Ir(ppy)_3$ (1 mg in 1 mL, prepared in an oven-dried vial under nitrogen flow). The vial was sealed and stirred for 3-5 hours under light irradiation. After this period the solvent was removed under reduced pressure and the crude mixture

was analysed by NMR spectroscopy against 1,3,5-trimethoxybenzene as internal standard to determine the product yield and starting material conversion.

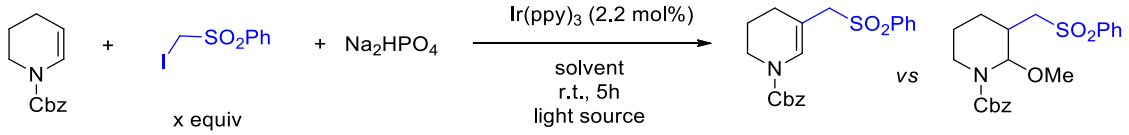


Solvent	Halide equiv	Base	Catalyst	Light source	Aminal/enamine ratio	Yield %
MeCN	3	As shown	As shown	20W CFL	<1:20	28
MeOH	3	lutidine	As shown	32W LED blue	>20:1	40[b]

[a] Sodium ascorbate used as additive (1 equiv); [b] isolated yield after TES/BF_3 reductive quench as reduced *N*-Cbz amine.

Optimization procedures for iodomethyl phenyl sulfone photoredox alkylations

Into an oven-dried 7 mL Supelco vial fitted with a Teflon septum was weighed base (0.135 mmol), iodomethyl phenyl sulfone (x mmol), and *N*-(benzyloxycarbonyl)-1,2,3,4-tetrahydropyridine (0.069 mmol). The vial was then purged with nitrogen for 5 minutes, before the addition of a dry solvent solution of $Ir(ppy)_3$ (1 mg in 1 mL, prepared in an oven-dried vial under nitrogen flow). The vial was sealed and stirred for 5 hours under light irradiation. After this period the solvent was removed under reduced pressure and the crude mixture was analysed by NMR spectroscopy against 1,3,5-trimethoxybenzene as internal standard to determine the product yield and starting material conversion.

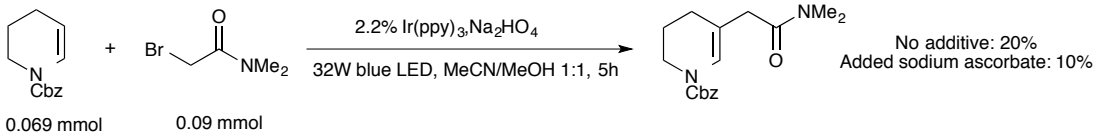


Solvent	Halide equiv	Base	Catalyst	Light source	Aminal/enamine ratio	Yield %
MeOH/MeCN 1:1[a]	2	As shown	As shown	26 W CFL	<1:20	30
MeOH/MeCN 1:1[a,b]	2	2,6-lutidine	As shown	32W LED blue	>20:1	33

[a] Sodium ascorbate used as additive (1 equiv); [b] isolated yield after TES/BF_3 reductive quench as reduced *N*-Cbz amine.

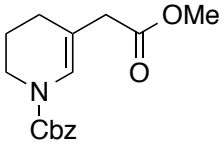
Attempted photoredox alkylation with bromoacetamides

Despite extensive efforts we were unable to achieve efficient coupling of our cyclic enecarbamates with a range of α-bromoacetamides (maximum yield of 20%):



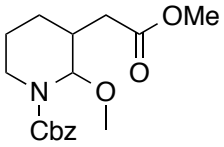
Characterisation of β-Carboxyalkylated Enecarbamates

Benzyl 5-(2-methoxy-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate



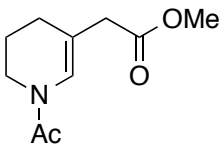
9a was isolated as a viscous oil in a 50% yield, as mixture of rotamers. **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.29-7.25 (5H, m), 6.79 (0.5H, br s), 6.68 (0.5H, br s), 5.10 (2H, s), 3.60-3.51 (5H, m), 2.94-2.90 (2H, s), 2.02-1.98 (2H, m), 1.80-1.76 (2H, M). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.1, 153.5, 153.0, 136.3, 128.5, 128.2, 123.8, 123.4, 111.6, 67.6, 51.8, 41.7, 40.5, 25.3, 21.4 (15 signals observed). **MS [M+H]$^+$** $C_{16}H_{20}NO_4$ calc. 290.1 found 290.2.

Benzyl 2-methoxy-3-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate (7a)



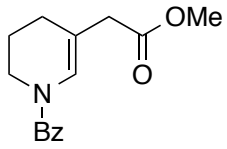
10a was isolated as a viscous oil in 86% yield, as a mixture of rotamers/diastereomers containing ca. 8% contamination of the respective enecarbamate **9a** (Note: evaporation of MeOH using nitrogen flow minimised the amount of enecarbamate formed compared to evaporation using a rotary evaporator). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.36-7.31 (5H, m), 5.33-5.10 (3H, m), 4.01-3.90 (1H, m), 3.67-3.47 (3H, m), 3.23-3.15 (3H, m), 3.00-2.87 (1H, m), 2.45-2.40 (1.2H, m), 2.29-2.25 (1H, m), 2.07-2.05 (1.2H, m), 1.57-1.54 (3.6H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 173.0, 172.9, 172.7, 172.2, 155.6, 155.2, 136.64, 136.58, 136.5, 136.3, 128.6, 128.5, 128.2, 128.09, 128.05, 127.9, 122.8, 111.6, 85.0, 84.03, 84.01, 67.6, 67.3, 67.2, 67.1, 55.1, 54.7, 51.6, 51.5, 50.8, 41.7, 40.5, 38.4, 38.0, 37.5, 37.4, 37.1, 37.0, 34.5, 34.0, 29.7, 25.3, 25.1, 25.0, 24.9, 24.7, 21.4, 19.6 (48 signals observed). **MS [M+Na]$^+$** $C_{17}H_{23}NNaO_5$ calc. 344.1468 found 344.1479.

Methyl 2-(1-acetyl-1,4,5,6-tetrahydropyridin-3-yl)acetate



9e was isolated as a viscous oil in 56% yield as mixture of rotamers, following a reductive quench. **^{1}H NMR (501 MHz, CH_2Cl_2)** δ 7.14 (0.3H, s), 6.51 (0.7H, s), 3.69-3.52 (5H, m), 3.01 (2H, s), 2.15-2.08 (5H, m), 1.90-1.79 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.0, 171.9, 168.0, 167.7, 124.4, 122.6, 113.9, 113.2, 52.0, 51.8, 43.8, 40.06, 40.66, 39.7, 25.7, 25.2, 22.02, 21.96, 21.5, 21.3. **HRMS [M+H]$^+$** $C_{10}H_{16}NO_3^+$ calc. 198.1124 found 198.1123.

Methyl 2-(1-benzoyl-1,4,5,6-tetrahydropyridin-3-yl)acetate

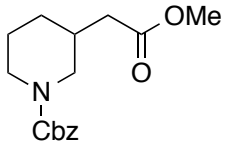


9f was isolated in a 91% yield as mixture of rotamers, following a reductive quench. **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.46-7.36 (5H, m), 7.23 (0.4H, s), 6.38 (0.6H, s), 3.79-3.50 (5H, m), 3.08-2.86 (2H, s), 2.14-2.12 (2H, bs), 1.96-1.79 (2H, bs). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 171.8, 170.3, 169.2, 168.4, 136.5, 135.0, 130.3, 130.1, 129.5, 128.6, 128.4, 128.2, 127.4, 126.9, 126.8, 125.9, 123.4, 115.9, 112.7, 51.9, 48.8, 46.1, 40.7, 40.4, 29.7, 25.8, 24.6, 22.2, 21.4 (29 signals observed). **HRMS $[M+H]^+$** $C_{15}H_{18}NO_3^+$ calc. 260.1281 found 260.1288.

General Methods for the Synthesis of Elaborated Enecarbamates and Enamides (Scheme 2)

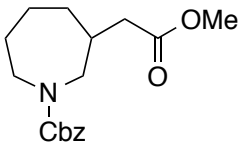
Into an oven-dried 7mL Supelco vial fitted with a Teflon septum was weighed lutidine (29mg, 0.27mmol), methyl bromoacetate (60mg, 0.39mmol), and the enamide/enecarbamate (0.138mmol). The vial was then purged with nitrogen for 5 minutes, before the addition of a dry MeOH solution of $Ir(ppy)_3$ (2mg in 2 mL, prepared in an oven-dried vial under nitrogen flow). The vial was sealed and stirred for 3 hours under blue LED irradiation (32W blue LED Kessil H150). After this period the solvent was removed under reduced pressure and replaced with dry dichloromethane under nitrogen. Et_3SiH (0.2 mL) was added followed by $BF_3.Et_2O$ (0.17 mL). Once the intermediate *N*,*O*-aminal have been completely reduced, as judged by LCMS, the reaction mixture was concentrated under vacuum and the residue purified by flash chromatography (eluents: ethyl acetate mixtures in hexanes).

Benzyl 3-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate (8a)



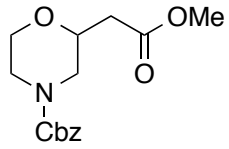
8a was isolated as a viscous oil in 92% yield as a mixture of rotamers. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35-7.26 (5H, m), 5.12 (2H, s), 3.97-3.93 (2H, m), 3.64 (3H, bs), 2.92-2.90 (1H, m), 2.72-2.62 (1H, m), 2.26- 2.16 (2H, m), 2.02-1.99 (1H, m), 1.86-1.84 (1H, m), 1.64 (1H, m), 1.50 (1H, m), 1.20-1.17 (1H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.7, 155.5, 137.1, 128.7, 128.1, 128.0, 67.2, 51.8, 49.4, 44.6, 38.2, 33.0, 30.6, 24.5. **HRMS [M+H]$^+$** $C_{16}H_{22}NO_4^+$ calc. 292.1543 found 292.1540.

Benzyl 3-(2-methoxy-2-oxoethyl)azepane-1-carboxylate (8b)



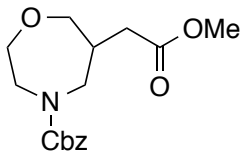
8b was isolated as a viscous oil as a mixture of rotamers, in 59% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36-7.26 (5H, m), 5.13 (2H, s), 3.67-3.57 (4.4H, m), 3.47-3.32 (1.6H, m), 3.14-3.03 (1H, m), 2.39-2.18 (3H, m), 1.85-1.71 (3H, m), 1.61-1.54 (1H, m), 1.46-1.39 (1H, m), 1.27-1.22 (1H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.9, 172.8, 156.1, 137.0, 128.5, 127.9, 127.8, 127.7, 66.99, 66.95, 51.6, 51.5, 50.9, 47.7, 47.2, 38.9, 38.8, 36.4, 36.1, 33.6, 33.0, 28.2, 27.8, 25.1, 24.5 (25 signals observed). **HRMS [M+H]$^+$** $C_{17}H_{24}NO_4^+$ calc. 306.1699 found 306.1695.

Benzyl 2-(2-methoxy-2-oxoethyl)morpholine-4-carboxylate (8c)



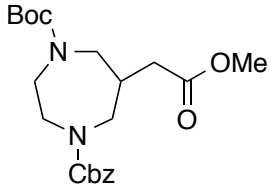
8c was isolated as a mixture of rotamers as a viscous oil in 87% yield. **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.40-7.30 (5H, m), 5.26- 5.12 (2H, m), 4.06-3.85 (4H, m), 3.70 (3H, s), 3.56-3.55 (1H, m), 3.01 (1H, m), 2.75 (1H, m), 2.58-2.42 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.8, 155.2, 136.5, 128.9, 128.8, 128.6, 128.2, 128.0, 72.0, 69.1, 67.4, 66.5, 52.0, 47.8, 43.6, 38.2, 35.7 (17 signals observed). **HRMS [M+Na]$^+$** $C_{15}H_{19}NNaO_5$ calc. 316.1155 found 316.1157.

Benzyl 6-(2-methoxy-2-oxoethyl)-1,4-oxazepane-4-carboxylate (8d)



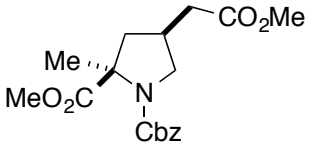
8d was isolated as a viscous oil isolated in a 69% yield.**^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36-7.26 (5H, m), 5.14 (2H, s), 3.78-3.61 (6H, m), 3.58 (3H, s), 3.56-3.31 (2H, m), 2.52-2.40 (1H, m), 2.38-2.30 (2H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.5, 172.5, 156.0, 155.9, 136.7, 136.6, 128.5, 128.1, 128.0, 127.9, 74.10, 74.07, 71.1, 70.8, 67.3, 51.7, 51.6, 50.5, 50.2, 50.0, 49.9, 36.9, 36.7, 35.4, 35.3 (25 signals observed). **HRMS [M+H]$^+$** $C_{16}H_{22}NO_5^+$ calc. 308.1492 found 308.1494.

1-Benzyl 4-*tert* butyl 6-(2-methoxy-2-oxoethyl)-1,4-diazepane-1,4-dicarboxylate (8e)



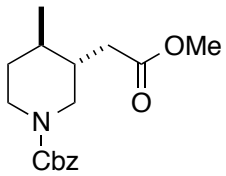
8e was isolated as a viscous oil in a 13% yield as a mixture of rotamers after Boc reprotection. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.29-7.19 (5H, m), 5.07-5.05 (2H, m), 3.61-3.14 (11H, m), 2.47-2.45 (1H, m), 2.33-2.22 (2H, m), 1.38 (9H, s). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.4, 155.9, 155.2, 136.5, 128.5, 128.1, 127.9, 80.2, 67.3, 51.5, 50.8, 50.5, 50.3, 47.9, 35.9, 35.2, 28.4 (17 signals observed). **HRMS [M+H]$^+$** $C_{21}H_{31}N_2O_6^+$ calc. 407.2177 found 407.2176.

1-Benzyl 2-methyl 4-(2-methoxy-2-oxoethyl)-2-methylpyrrolidine-1,2-dicarboxylate (8f)



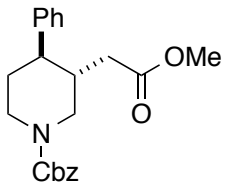
8f isolated as a 2:1 mixture of diastereomers as a viscous oil in 87% yield (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.28-7.20 (5H, m), 5.13-4.92 (2H, m), 4.02-3.92 (0.33H, m), 3.86-3.79 (0.66H, m), 3.63-3.59 (4.6H, m), 3.42-3.35 (1.4H, m), 3.15-3.00 (1H, m), 2.67-2.60 (1H, m), 2.39-2.29 (2.33H, m), 2.07-2.01 (0.67H, m), 1.85-1.76 (0.67H, m), 1.60-1.47 (3.33H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 174.49, 174.45, 174.3, 172.2, 172.11, 172.08, 154.3, 154.2, 153.9, 136.8, 136.4, 136.3, 128.4, 128.14, 128.05, 128.01, 127.93, 127.8, 67.1, 66.7, 65.9, 65.3, 53.3, 52.7, 52.4, 51.78, 51.75, 44.4, 37.1, 36.8, 33.3, 32.0, 24.5, 23.3, 23.0, 21.9 (36 signals observed). **HRMS $[M+K]^+$** $C_{18}H_{23}NKO_6$ calc. 388.1157 found 388.1153.

Benzyl 3-(2-methoxy-2-oxoethyl)-4-methylpiperidine-1-carboxylate (8g)



8g was isolated as a viscous oil as 2:1 mixture of *trans*:*cis* disastereoisomers in 45% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35-7.30 (5H, m), 5.12-5.10 (2H, m), 4.10 (1.4H, m), 3.92-3.52 (3.6H, m), 3.15-3.02 (0.6H, m), 2.77-2.71 (0.65H, t, *J* = 12.1 Hz), 2.58 (0.65H, m), 2.50-2.47 (0.7H, dd, *J* = 15.4 and 4.4 Hz), 2.24-2.13 (1.7H, m), 1.87-1.86 (0.4H, m), 1.63 (1.4H, m), 1.43-1.41 (0.4H, m), 1.27-1.18 (1.5H, m), 0.90-0.84 (3H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.4, 172.8, 155.7, 155.1, 136.92, 136.88, 128.5, 128.3, 127.9, 127.8, 67.02, 67.00, 51.6, 48.4, 47.2, 44.0, 39.6, 36.0, 35.6, 35.2, 33.5, 31.9, 30.7, 29.7, 19.2, 17.1 (26 signals observed). **HRMS $[M+H]^+$** $C_{17}H_{24}NO_4$ calc. 306.1699 found 306.1699.

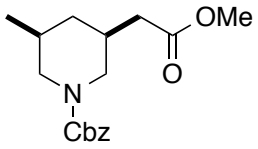
Benzyl 3-(2-methoxy-2-oxoethyl)-4-phenylpiperidine-1-carboxylate (8h)



8h was isolated as a viscous oil in a 53% yield as an inseparable 4:1 mixture of *trans*:*cis* diastereomers (mixture of rotamers; signals for major isomer only). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40-7.15 (10H, m), 5.19-5.17 (2H, m), 4.42-4.07 (2H, m), 3.49 (3H, m), 2.91-2.86 (1H, m), 2.62 (1H, t, *J* = 12.1 Hz), 2.42 (1H, td, *J* = 11.5, 3.2 Hz), 2.23-2.16 (2H, m), 1.96-1.92 (1H, m), 1.82-1.72 (2H, m). Signals for minor diastereomer visible at 3.65 (m), 3.02 (m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.3, 171.7, 155.1, 143.1, 142.5, 141.2, 136.9, 128.7,

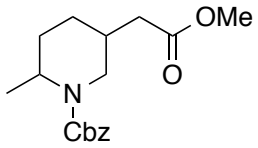
128.50, 128.47, 128.0, 127.9, 127.6, 127.3, 127.2, 126.9, 67.2, 51.9, 51.5, 49.0, 48.4, 44.6, 44.1, 38.4, 37.0, 36.5, 36.1, 34.1 (28 signals observed). **HRMS [M+Na]$^+$** $C_{22}H_{25}NNaO_4^+$ calc. 390.1676 found 390.1687.

Benzyl 3-(2-methoxy-2-oxoethyl)-5-methylpiperidine-1-carboxylate (8i)



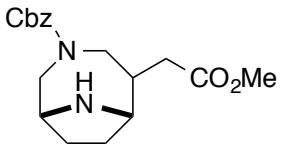
8i was isolated as a viscous oil in a 69% yield as an inseparable 2:1 mixture of *cis*:*trans* diastereomers (d.r. evaluated on unprotected product; see below). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38-7.28 (5H, m), 5.14-5.12 (2H, m), 4.22-4.10 (1.3H, m), 3.86-3.84 (0.2H, m), 3.68-3.59 (3.3H, m), 3.42 (0.35H, m), 3.28-3.25 (0.2H, m), 2.99-2.97 (0.15H, m), 2.74 (0.2H, m), 2.41-2.14 (3.6H, m), 2.01 (0.7H, bm), 1.91-1.83 (1H, m), 1.64-1.56 (1H, m), 1.45-1.41 (0.34H, m), 0.91 (3H, d, *J* = 6.8 Hz), 0.75 (0.66H, dt, *J* = 12.3 ,12.0 Hz). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.9, 172.4, 155.7, 155.1, 136.9, 128.5, 127.9, 127.8, 67.0, 51.6, 51.0, 50.8, 49.0, 48.4, 48.1, 39.7, 38.5, 37.3, 33.4, 31.0, 29.7, 18.9 (22 signals observed). **HRMS [M+H]$^+$** $C_{17}H_{24}NO_4^+$ calc. 306.1670 found 306.1696.

Benzyl 5-(2-methoxy-2-oxoethyl)-2-methylpiperidine-1-carboxylate (8j)



8j was isolated as a viscous oil in an 87% yield as an inseparable 1:1 mixture of diastereomers (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.28-7.26 (5H, m), 5.08-4.99 (2H, m), 4.38-4.37 (1H, m), 3.98 (0.5H, bd, *J* = 11.2 Hz), 3.81 (0.5H, d, *J* = 13.9 Hz), 3.55 (3H, s), 3.06 (0.5H, dd, *J* = 13.9, 3.4 Hz), 2.52 (0.5H, t, *J* = 12.5 Hz), 2.38 (0.5H, dd, *J* = 15.4, 7.5 Hz), 2.25-2.12 (2H, m), 1.79-1.58 (2.5H, m), 1.46 (0.5H, m), 1.35-1.22 (1.5H, m), 1.10-1.05 (3H, d, *J* = 6.9 Hz). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.2, 172.4, 155.8, 137.0, 136.9, 128.5, 127.9, 127.73, 127.68, 67.0, 51.6, 51.5, 46.6, 45.8, 43.7, 42.1, 38.7, 35.0, 33.5, 29.9, 29.7, 25.2, 25.0, 23.0, 16.0 (25 signals observed). **HRMS [M+H]$^+$** $C_{17}H_{24}NO_4^+$ calc. 306.1700 found 306.1696.

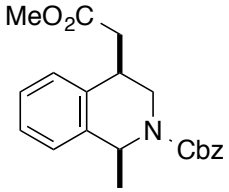
3-Benzyl 5-(2-methoxy-2-oxoethyl)-3,9-diazabicyclo[4.2.1]nonane-3-carboxylate (8k)



8k was isolated in 50% yield as an inseparable 1.3:1 mixture of diastereoisomers (mixture of rotamers). Signal overlap identification of relative configuration in major/minor diastereomer by nOe. **^{1}H NMR (501**

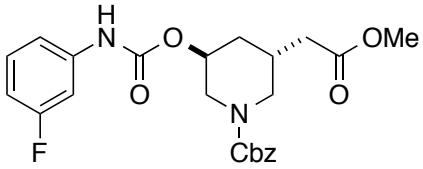
MHz, $CDCl_3$) δ 7.37-7.31 (5H, m), 5.17-5.06 (2H, m), 4.10-3.88 (2H, m), 3.66 (3H, s), 3.52-3.36 (2H, m), 2.85-2.83 (2H, m), 2.34-2.30 (2H, m), 2.23-2.19 (1H, m), 2.09-2.06 (1H, m), 1.87-1.85 (1H, m), 1.64-1.62 (1H, m), 1.44 (1H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 173.1, 156.0, 155.6, 137.0, 136.8, 128.5, 128.11, 128.06, 127.94, 127.86, 67.2, 67.1, 61.0, 59.7, 59.3, 54.9, 51.6, 49.7, 41.7, 40.8, 37.7, 37.6, 33.8, 33.6, 30.1, 29.9, 29.7 (27 signals observed). **HRMS [M+H]$^+$** $C_{18}H_{25}N_2O_4^+$ calc. 333.1809 found 333.1806.

Benzyl 4-(2-methoxy-2-oxoethyl)-1-methyl-3,4-dihydroisoquinoline-2(1H)-carboxylate (8l)



8l was isolated as a viscous oil in 51% yield as an inseparable 4:1 mixture of *cis*/*trans* diastereomers. **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.39-7.32 (5H, m), 7.19-7.12 (4H, m), 5.21-5.17 (3H, m), 4.25 (0.8H, bm), 3.69-3.41 (4H, m), 3.18 (1H, m), 2.92-2.53 (2.2H, m), 1.55-1.50 (3H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.5, 171.6, 136.9, 128.7, 128.1, 128.0, 127.3, 126.7, 126.9, 126.5, 67.3, 52.0, 51.8, 51.0, 42.5, 37.4, 34.3, 22.3 (18 signals observed). **HRMS [M+H]$^+$** $C_{21}H_{24}NO_4$ calc 354.1700 found 354.1697.

Benzyl 3-(((3-fluorophenyl)carbamoyl)oxy)piperidine-1-carboxylate (8m)

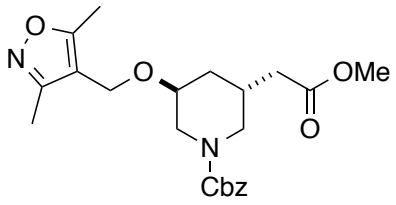


11m was isolated as a viscous oil in 55% yield as an inseparable ~4:1 mixture of *trans*:*cis* diastereomers (mixture of rotamers; signals for major isomer only). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.35-7.20 (7H, m), 6.96 (1H, bs), 6.76-6.75 (2H, bs), 5.15-5.00 (2H, m), 4.95 (1H, m), 4.40-4.12 (2H, m), 3.68 (3H, bs), 3.02 (1H, dd, *J* = 12.5, 2.5 Hz), 2.66-2.52 (1H, m), 2.39 (1H, bs), 2.34-2.23 (2H, m), 2.11 (1H, d, *J* = 13.6 Hz), 1.48-1.43 (1H, t, *J* = 12.6 Hz). Signal for minor diastereomer visible at 4.75 (m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.1, 163.3 (d, *J* = 244.4 Hz), 155.8, 155.4, 152.4, 139.5 (d, *J* = 10.1 Hz), 136.6, 128.6 (d, *J* = 10.1 Hz), 128.14, 128.05, 122.9, 114.0, 110.2 (d, *J* = 21.4 Hz), 106.2 (d, *J* = 26.5 Hz), 68.3, 67.6, 67.4, 51.9, 49.0, 48.4, 47.6, 47.4, 37.9, 35.6, 34.8, 28.6, 28.3 (27 signals observed). **HRMS [M+H]$^+$** $C_{23}H_{26}N_2FO_6$ calc. 445.1769 found 445.1777.

Benzyl 3-((3,5-dimethylisoxazol-4-yl)methoxy)-5-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate (8n)

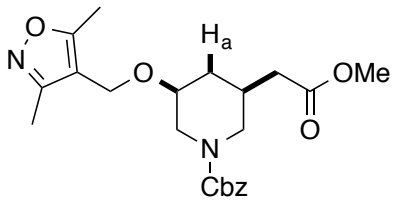
8n was isolated as a viscous oil, as a separable 7:2 mixture of *trans*:*cis* diastereomers in a combined 54% yield (mixtures of rotamers)

Major (*trans*) diastereomer



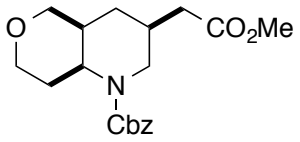
^{1}H NMR (501 MHz, $CDCl_3$) δ 7.34-7.31 (5H, m), 5.12 (2H, m), 4.49-4.46 (0.6H, d, *J* = 11.4 Hz), 4.22-4.01 (3.4H, m), 3.67-3.50 (4H, m), 3.01 (1H, d, *J* = 13.9 Hz), 2.75 (0.6H, t, *J* = 11.5 Hz), 2.62 (0.4H, t, *J* = 11.5 Hz), 2.37-2.14 (9H, m), 2.03 (0.4H, br d, *J* = 12.6 Hz), 1.91 (0.6H, br d, *J* = 12.6 Hz), 1.44-1.32 (1H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.2, 167.1, 166.8, 160.1, 159.8, 155.7, 136.8, 128.6, 128.2, 128.1, 128.0, 127.7, 111.3, 111.1, 71.0, 67.4, 62.2, 59.5, 59.3, 51.7, 49.0, 46.6, 45.7, 37.8, 35.9, 35.9, 34.7, 28.5, 28.1, 11.0, 10.2 (31 signals observed). **HRMS $[M+H]^+$** $C_{22}H_{29}N_2O_6$ calc. 417.2026 found 417.2043.

Minor (*cis*) diastereomer



^{1}H NMR (501 MHz, $CDCl_3$) δ 7.38-7.31 (5H, m), 5.19-5.10 (2H, m), 4.41-4.23 (3H, m), 4.14-4.05 (1H, m), 3.71-3.59 (3H, m), 3.41-3.37 (1H, bm), 2.65-2.39 (2H, m), 2.36-2.14 (9H, m), 2.05-2.04 (1H, bm), 1.16-1.14 (1H, bm – H_a). Signal for Ha resolves on VT NMR to a quartet with *J* = 11Hz, indicating 3,5-*cis* stereochemistry. **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.3, 167.2, 159.9, 136.7, 128.74, 127.68, 128.5, 128.4, 128.3, 128.0, 111.2, 72.7, 67.5, 59.7, 59.6, 52.1, 51.9, 48.8, 47.7, 40.2, 37.8, 37.1, 32.0, 29.8, 11.1, 10.2 (26 signals observed). **HRMS $[M+H]^+$** $C_{22}H_{29}N_2O_6$ calc. 417.2026 found 417.2043.

Benzyl 3-(2-methoxy-2-oxoethyl)octahydro-1H-pyrano[4,3-b]pyridine-1-carboxylate (8o)

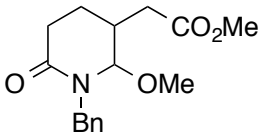


8o was isolated as a viscouse oil in a 96% yield as an inseparable 2:1 mixture of *cis*:*trans* diastereomers. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37- 7.34 (5H, m), 5.18-5.09 (2H, m), 4.48-4.31 (1H, m), 4.12-4.03 (0.6H, m), 3.98-3.93 (1.4H, m), 3.74-3.58 (5H, m), 3.44-3.38 (1H, m), 3.11 (0.4H, dd, *J* =13.9, 2.9 Hz), 2.60-2.53 (0.6H,

m), 2.50-2.45 (0.6H, m), 2.32 (0.4H, bs), 2.32-2.23 (1.2H, m), 2.22-1.96 (2H, m), 1.85-1.81 (0.6H, m), 1.77-1.58 (1.8H, m), 1.43-1.37 (1.4H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.0, 172.3, 155.8, 155.1, 136.7, 128.5, 128.0, 127.8, 127.7, 71.9, 67.4, 67.3, 67.2, 51.63, 51.56, 49.9, 49.5, 43.7, 42.0, 38.4, 35.7, 35.5, 35.2, 33.3, 33.0, 30.2, 30.0, 29.6, 27.2, 24.5, 23.9 (31 signals observed). **HRMS [M+H]$^+$** $C_{19}H_{26}NO_5$ calc. 348.1805 found 348.1805.

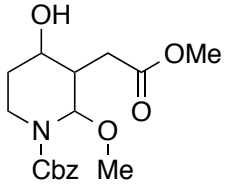
Additional Alkylation Reactions:

Methyl 2-(1-benzyl-2-methoxy-6-oxopiperidin-3-yl)acetate



Isolated as a viscous oil in 56% yield as an inseparable 1:1 mixture of diastereomers. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35-7.25 (5H, m), 5.42 (0.5H, d, *J* = 14.9 Hz), 5.36 (0.5H, d, *J* = 14.9 Hz), 4.49 (0.5H, d, *J* = 2.8, Hz), 4.25-4.24 (0.5H, d, *J* = 2.8 Hz), 4.17 (0.5H, d, *J* = 15.2 Hz), 3.90 (0.5H, d, *J* = 15.2 Hz), 3.64 (1.5H, s), 3.58 (1.5H, s), 3.42 (1.5H, s), 3.33 (1.5H, s), 2.66-2.20 (5.5H, m), 1.96-1.88 (0.5H, m), 1.75-1.71 (0.5H, m), 1.55-1.50 (0.5H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.5, 172.2, 170.5, 170.2, 137.5, 137.4, 128.8, 128.7, 127.9, 127.6, 127.5, 89.7, 89.5, 59.0, 55.1, 51.82, 51.79, 49.7, 47.4, 36.7, 36.1, 34.3, 31.28, 31.26, 28.8, 21.9, 20.7 (27 signals observed). **HRMS [M+H]$^+$** $C_{16}H_{22}NO_4$ calc. 292.1543, found 292.1538.

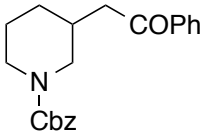
Benzyl 4-hydroxy-2-methoxy-3-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate



Isolated as a viscous oil in 50% yield as an inseparable 1:1 mixture of diastereomers (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.35-7.32 (5H, m), 5.43-5.36 (1H, m), 5.23-5.10 (2H, m), 4.10-3.90 (1.2H, m), 3.81-3.74 (1H, m), 3.69-3.66 (3.2H, m), 3.58 (0.6H, m), 3.28-2.15 (2.7H, m), 2.08-1.97 (1.3H, m), 1.72 (1.4H, m), 1.51-1.45 (0.6H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 174.4, 174.2, 171.9, 155.5, 155.1, 136.50, 136.46, 128.70, 128.67, 128.5, 128.4, 128.3, 128.1, 128.03, 127.99, 86.2, 85.5, 85.2, 68.5, 67.7, 67.6, 55.4, 55.3, 55.1, 52.0, 51.9, 45.4, 45.2, 39.9, 37.5, 37.3, 34.8, 34.7, 34.4, 33.9, 32.9, 27.7 (37 signals observed). **HRMS [M+Na]$^+$** $C_{17}H_{23}NNaO_6$ calc. 360.1418 found 360.1420.

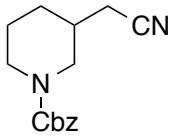
Alkylation of Enecarbamate 6a with Alternative Electrophiles:

Benzyl 3-(2-oxo-2-phenylethyl)piperidine-1-carboxylate



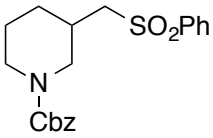
Isolated as a viscous oil in 41% yield (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.93 (2H, d, *J* = 7.5 Hz), 7.58-7.55 (1H, m), 7.47-7.44 (2H, m), 7.33 (5H, m), 5.11 (2H, s), 3.90 (2H, br m), 2.95-2.79 (4H, m), 2.27-2.23 (1H, m), 1.92-1.89 (1H, m), 1.69 (1H, m), 1.53 (1H, m), 1.26 (1H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 198.6, 155.4, 137.1, 136.9, 133.1, 129.0, 128.7, 128.5, 128.1, 127.9, 127.8, 67.0, 49.5, 44.6, 42.0, 41.7, 31.9, 30.6, 24.7, 24.2 (20 signals observed). **HRMS $[M+H]^+$** $C_{21}H_{24}NO_3$ calc. 338.1751 found 338.1744

Benzyl 3-(cyanomethyl)piperidine-1-carboxylate



Isolated as a viscous oil in 40% yield (95% purity; mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37-7.30 (5H, m), 5.13 (2H, m), 3.98-3.94 (2H, m), 2.94-2.80 (2H, m), 2.30-2.25 (2H, m), 1.95-1.90 (2H, m), 1.73-1.70 (1H, m), 1.52-1.51 (1H, m), 1.39-1.36 (1H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.4, 155.3, 137.4, 136.7, 128.7, 128.2, 128.1, 117.9, 67.4, 48.6, 44.34, 44.30, 32.7, 29.8, 29.3, 24.4, 24.0, 21.3 (18 signals observed). **HRMS $[M+Na]^+$** $C_{15}H_{18}N_2NaO_2$ calc. 281.1260 found 281.1261.

Benzyl 3-((phenylsulfonyl)methyl)piperidine-1-carboxylate

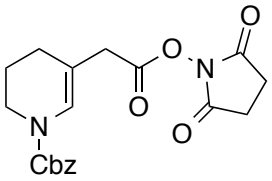


Isolated as a viscous oil in 33% yield (mixture of rotamers). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.88-7.30 (10H, m), 5.14-5.11 (2H, m), 4.02-3.79 (2H, m), 3.02-2.86 (4H, m), 2.15-1.91 (2H, m), 1.66-1.61 (1H, m), 1.50-1.39 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 155.2, 139.6, 136.7, 133.8, 129.4, 128.5, 128.1, 127.9, 127.9, 67.2, 59.1, 48.9, 44.3, 31.0, 23.9 (15 signals observed). **HRMS $[M+Na]^+$** $C_{20}H_{23}NNaO_4S$ calc. 396.1240 found 396.1239.

Fragment Growth with Activated Esters (one-pot acetamidation, Scheme 3): General Methods for the Synthesis of Grown Enecarbamates and Enamides

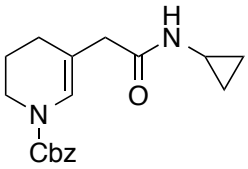
Into an oven-dried 7mL Supelco vial fitted with a Teflon septum was weighed Na_2HPO_4 (29 mg, 0.27 mmol), succinimidyl bromoacetate (60 mg, 0.39 mmol), and the enamide/enecarbamate (0.138 mmol). The vial was then purged with nitrogen for 5 minutes, before the addition of a dry MeCN solution of $Ir(ppy)_3$ (2 mg in 2 mL, prepared in an oven-dried vial under nitrogen flow). The vial was sealed, and the slurry was stirred for 5 hours under blue LED irradiation (32 W blue LED Kessil H150). After this period, the respective amine (0.28 mmol) was added neat and the reaction mixture stirred for one additional hour in the dark. Once the intermediate activated ester enamide had been completely consumed by the amine, as judged by LCMS, the reaction mixture was diluted with dichloromethane and filtered. The inorganic precipitate was washed thoroughly with dichloromethane and the combined filtrates concentrated under reduced pressure. The residue was purified by flash chromatography (eluents: ethyl acetate mixtures in hexanes).

Benzyl 5-(2-((2,5-dioxopyrrolidin-1-yl)oxy)-2-oxoethyl)-3,4-dihydropyridine-1(2*H*)-carboxylate (10)



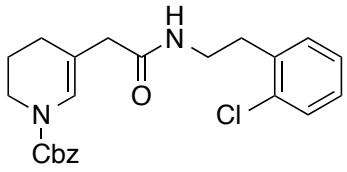
10 was formed in 77% NMR yield (internal standard: 1,3,5-trimethoxybenzene); it was typically used crude but could be isolated as a viscous oil in 42% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.38-7.32 (5H, m), 6.98 (0.5H, s), 6.86 (0.5H, s), 5.18 (2H, s), 3.60-3.59 (2H, m), 3.29 (1H, s), 3.25 (1H, s), 2.81 (4H, s), 2.15-2.12 (2H, m), 1.87-1.86 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 169.1, 166.8, 153.6, 153.0, 136.2, 128.7, 128.4, 128.2, 125.4, 124.9, 109.7, 109.2, 67.8, 67.7, 41.9, 41.7, 37.7, 25.7, 25.0, 24.7, 21.5, 21.4 (22 signals observed). **MS [M+H]$^+$** $C_{19}H_{21}N_2O_6$ calc. 373.1 found 373.0.

Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11a)



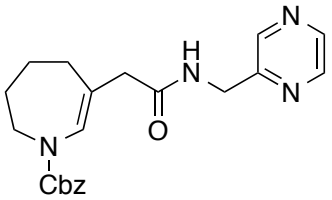
11a was isolated as a viscous oil in a 69% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.37-7.34 (5H, m), 6.86 (0.5H, s), 6.74 (0.5H, s), 5.79-5.74 (1H, m), 5.18 (2H, s), 3.60-3.56 (2H, m), 2.87 (1H, s), 2.83 (1H, s), 2.68-2.64 (1H, m), 2.02-2.00 (2H, m), 1.86-1.80 (2H, m), 0.84-0.74 (2H, m), 0.46 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.3, 172.2, 153.7, 153.1, 136.3, 128.7, 128.5, 128.4, 128.2, 113.7, 112.9, 67.9, 67.7, 43.5, 43.4, 42.0, 41.8, 25.3, 25.0, 22.8, 21.7, 21.6, 6.8 (23 signals observed). **HRMS [M+H]$^+$** $C_{18}H_{23}N_2O_3$ calc. 315.1703 found 315.1699.

Benzyl 5-(2-((2-chlorophenethyl)amino)-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11b)



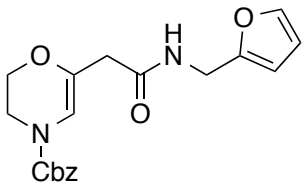
11b was isolated as a viscous oil in 50% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.39-7.32 (6H, m), 7.15-7.13 (3H, m), 6.85 (0.5H, s), 6.73 (0.5H, s), 5.79-5.75 (1H, m), 5.19 (2H, s), 3.57-3.51 (4H, m), 2.97-2.94 (2H, t, *J* = 6.8 Hz), 2.88 (1H, s), 2.84 (1H, s), 1.96-1.94 (2H, m), 1.81-1.75 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.9, 170.8, 153.0, 136.6, 134.2, 131.1, 129.7, 128.7, 128.4, 128.2, 127.0, 113.4, 112.7, 67.8, 67.7, 43.5, 43.4, 41.9, 41.7, 39.3, 39.2, 33.3, 33.2, 25.3, 25.0, 21.6, 21.5 (27 signals observed). **HRMS $[M+Na]^+$** $C_{23}H_{25}{}^{35}ClN_2NaO_3$ calc. 435.1445 found 435.1441.

Benzyl 6-(2-oxo-2-((pyrazin-2-ylmethyl)amino)ethyl)-2,3,4,5-tetrahydro-1H-azepine-1-carboxylate (11c)



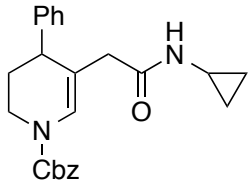
11c was isolated as a viscous oil in 76% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 8.56-8.43 (3H, m), 7.34-7.30 (5H, m), 6.83 (1H, bs), 6.61 (0.5H, s), 6.52 (0.5H, bs), 5.15 (2H, s), 4.57 (2H, bs), 3.73-3.70 (2H, m), 2.98-2.96 (2H, m), 2.22-2.20 (2H, m), 1.80-1.68 (4H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 171.2, 171.0, 154.7, 154.4, 152.7, 152.4, 144.0, 143.8, 143.6, 136.5, 130.6, 129.9, 128.6, 128.2, 128.0, 124.0, 123.8, 67.7, 67.6, 47.8, 45.1, 42.4, 42.3, 30.9, 30.3, 28.1, 24.3 (27 signals observed). **HRMS $[M+H]^+$** $C_{21}H_{25}N_4O_3$ calc. 381.1921 found 381.1926.

Benzyl 6-(2-((furan-2-ylmethyl)amino)-2-oxoethyl)-2H-1,4-oxazine-4(3H)-carboxylate (11d)



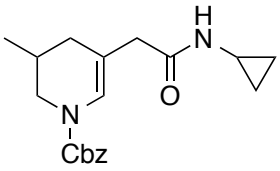
11d was isolated as a viscous oil in 56% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.37-7.33 (6H, m), 6.38-6.19 (4H, m), 5.17 (2H, s), 4.43-4.42 (2H, m), 4.10-4.05 (2H, m), 3.70-3.69 (2H, m), 3.01 (0.8H, s), 2.97 (1.2H, s). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 169.0, 168.9, 152.1, 151.3, 142.3, 136.0, 133.7, 128.8, 128.7, 128.5, 128.4, 128.3, 110.6, 107.4, 105.0, 104.4, 68.0, 67.8, 65.0, 64.6, 41.5, 40.8, 40.32, 40.27, 36.7 (25 signals observed). **HRMS $[M+H]^+$** $C_{19}H_{21}N_2O_5$ calc. 357.1444 found 357.1441.

Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-4-phenyl-3,4-dihydropyridine-1(2H)-carboxylate (11e)



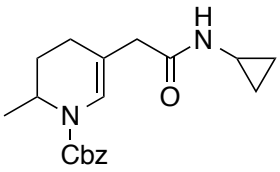
11e isolated as a viscous oil in 60% yield (mixture of rotamers).**^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.43-7.02 (11H, m), 5.62 (0.5H, s), 5.50 (0.5H, bs), 5.24-5.18 (2H, m), 3.77-3.74 (1H, m), 3.53-3.49 (1H, m), 3.41-3.36 (1H, m), 2.84-2.60 (3H, m), 2.15-2.13 (1H, m), 1.88-1.87 (1H, m), 0.72-0.71 (2H, m), 0.41- 0.38 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.13, 172.09, 136.2, 128.7, 128.6, 128.5, 128.40, 128.36, 126.93, 126.90, 114.1, 113.3, 68.0, 67.8, 41.4, 41.3, 41.0, 40.5, 38.7, 30.8, 22.7, 6.7, 6.6 (23 signals observed). **HRMS $[M+H]^+$** $C_{24}H_{27}N_2O_3$ calc. 391.2016 found 391.2019.

Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-3-methyl-3,4-dihydropyridine-1(2H)-carboxylate (11f)



11f was isolated as a viscous oil in a 72% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.38-7.34 (5H, m), 6.85 (0.5H, s), 6.73 (0.5H, s), 5.80-5.75 (1H, m), 5.18 (2H, s), 3.89 (0.5H, dd, *J* = 12.4, 2.3 Hz), 3.78 (0.5H, dd, *J* = 12.4, 2.3 Hz), 2.94-2.82 (3H, m), 2.67-2.65 (1H, m), 2.07-2.02 (1H, m), 1.92 (1H, bs), 1.69 (1H, dd, *J* = 17.0, 9.0 Hz), 0.99 (3H, d, *J* = 6.8 Hz), 0.76-0.74 (2H, m), 0.45 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.3, 172.2, 153.8, 153.2, 136.28, 136.25, 128.7, 128.44, 128.40, 128.2, 113.0, 112.4, 68.4, 67.8, 67.7, 48.2, 48.0, 43.2, 43.1, 33.6, 33.3, 27.02, 26.97, 22.8, 18.7, 18.6, 6.8, 6.74, 6.70 (29 signals observed). **HRMS $[M+Na]^+$** $C_{19}H_{24}N_2NaO_3$ calc. 351.1679 found 351.1683.

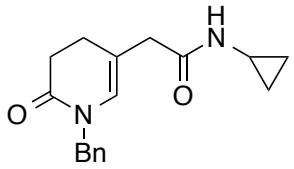
Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-2-methyl-3,4-dihydropyridine-1(2H)-carboxylate (11g)



11g was isolated as a viscous oil in a 68% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.38-7.32 (5H, m), 6.79 (0.5H, s), 6.67 (0.5H, s), 5.79-5.76 (1H, m), 5.18 (2H, s), 4.44-4.37 (1H, m), 2.88-2.84 (2H, s), 2.68-2.65 (1H, m) 2.14-2.11 (1H, m), 1.92-1.88 (1H, m), 1.78-1.74 (2H, m), 1.10 (3H, bs), 0.76-0.74 (2H, m), 0.44-0.43 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.4, 153.5, 152.6, 136.3, 128.7, 128.4, 128.1, 122.9,

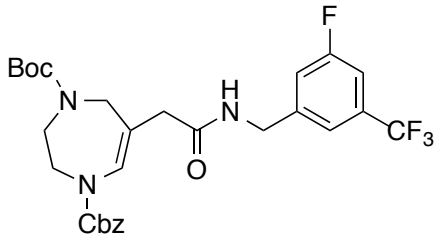
122.4, 112.7, 111.9, 67.7, 46.1, 45.8, 43.4, 26.6, 26.4, 22.7, 21.2, 20.9, 17.5, 16.9, 6.8, 6.7 (24 signals observed). **HRMS [M+H]$^+$** $C_{19}H_{25}N_2O_3$ calc. 329.185969 found 329.186739.

2-(1-Benzyl-6-oxo-1,4,5,6-tetrahydropyridin-3-yl)-*N*-cyclopropylacetamide (11h)



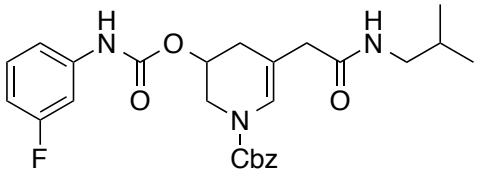
11h was isolated as a viscous oil in 60% yield. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.28-7.15 (5H, m), 5.85 (1H, s), 5.62 (1H, bs), 4.61 (2H, s), 2.78 (2H, s), 2.60-2.57 (1H, m), 2.56-2.52 (2H, t, *J* = 8.0 Hz), 2.28-2.24 (2H, t, *J* = 8.0 Hz), 0.71-0.66 (2H, m), 0.37-0.33 (2H, m). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 171.4, 168.8, 137.2, 128.9, 127.8, 127.6, 114.1, 49.0, 41.5, 31.2, 24.4, 22.8, 6.8 (13 signals observed). **HRMS [M+H]$^+$** $C_{17}H_{21}N_2O_2$ calc. 285.1598 found 285.1595.

1-Benzyl 4-*tert*-butyl 6-(2-((3-fluoro-5-(trifluoromethyl)benzyl)amino)-2-oxoethyl)-2,3-dihydro-1H-1,4-diazepine-1,4(5H)-dicarboxylate (11i)



11i was isolated as a viscous oil in 24% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 8.53 (1H, bs), 7.39-7.18 (8H, m), 6.66 (0.4H, s), 6.54 (0.6H, bs), 5.18-5.15 (2H, m), 4.48-4.47 (2H, m), 3.91 (2H, s), 3.84-3.67 (4H, m), 3.03-3.00 (2H, m), 1.26 (9H, s). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.5, 163.7 (d, *J* = 249.5 Hz), 157.2, 153.8, 143.1, 135.9, 131.7, 130.8, 128.7, 128.6, 128.4, 120.9, 120.7, 118.7 (d, *J* = 21.4 Hz), 117.1, 111.6 (d, *J* = 26.5 Hz), 81.3, 68.2, 47.3, 47.1, 46.9, 46.8, 43.1, 42.9, 40.3, 28.2, 28.1 (27 signals observed). **HRMS [M+Na]$^+$** $C_{28}H_{31}F_4N_3NaO_5$ calc. 588.2092 found 588.2091.

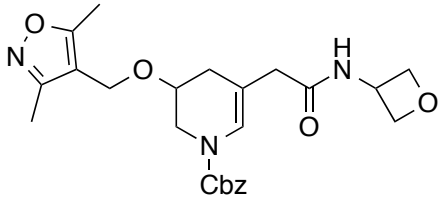
Benzyl 3-(((3-fluorophenyl)carbamoyl)oxy)-5-(2-(isobutylamino)-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11j)



11j was isolated as a viscous oil in a 67% yield (mixture of rotamers).**^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.38-6.74 (11H, m), 5.81 (0.5H, s), 5.75 (0.5H, s), 5.23-5.18 (3H, m), 4.08-4.06 (1H, m), 3.47 (1H, t, *J* = 11.9 Hz), 3.05-3.00 (2H, m), 2.93 (1H, s), 2.89 (1H, bs), 2.47 (1H, dd, *J* = 17.8, 3.2 Hz), 2.23 (1H, dd, *J* = 17.8, 3.2 Hz), 1.72-

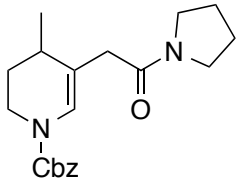
1.70 (1H, m), 0.86-0.84 (6H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.4, 170.3, 163.3 (d, *J* = 239.4 Hz), 153.8, 153.3, 152.4, 136.0, 130.3 (d, *J* = 10.1 Hz), 128.76, 128.70, 128.6, 128.5, 128.1, 114.0, 110.3 (d, *J* = 21.4 Hz), 110.1, 109.4, 106.1 (d, *J* = 26.5 Hz), 68.2, 68.0, 66.1, 56.6, 55.7, 47.1, 44.9, 44.8, 42.8, 42.7, 31.1, 30.8, 29.9, 28.9, 20.2 (33 signals observed). **HRMS [M+H]$^+$** $C_{26}H_{31}FN_3O_5$ calc. 484.2242 found 484.224.

Benzyl 3-((3,5-dimethylisoxazol-4-yl)methoxy)-5-(2-(3-oxetanyl)amino-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11k)



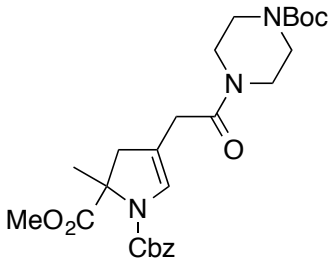
11k was isolated as a viscous oil in 50% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.39-7.35 (5H, m), 6.95 (0.4H, s), 6.81 (0.6H, s), 6.47-6.42 (1H, m), 5.23-5.20 (2H, m), 4.94-4.91 (1H, m), 4.82-4.79 (2H, m), 4.43-4.19 (4.6H, m), 3.97-3.84 (1.4H, m), 3.39-3.35 (1H, m), 3.00-2.86 (2H, m), 2.40-2.27 (4H, m), 2.16-2.12 (4H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.30, 170.25, 167.5, 167.3, 159.8, 159.7, 153.6, 153.4, 135.9, 128.8, 128.7, 128.6, 128.5, 124.8, 124.4, 110.8, 108.9, 108.5, 78.4, 78.3, 78.2, 68.9, 68.3, 59.5, 59.4, 44.9, 43.7, 42.8, 42.3, 42.2, 32.2, 31.6, 11.0, 10.04, 9.98 (35 signals observed). **HRMS [M+H]$^+$** $C_{24}H_{30}N_3O_6$ calc. 456.2129 found 456.2121.

Benzyl 4-methyl-5-(2-oxo-2-(pyrrolidin-1-yl)ethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11l)



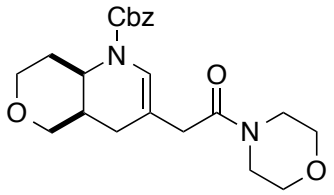
11l was isolated as a viscous oil in a 49% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.35-7.30 (5H, m), 6.73 (0.5H, s), 6.61 (0.5H, s), 5.16-5.15 (2H, m), 3.73-3.68 (1H, m), 3.53-3.38 (5H, m), 3.08-2.90 (2H, m), 2.41-2.35 (1H, m), 1.93-1.79 (5H, m), 1.57-1.56 (1H, m), 1.05, (1.5H, d, *J* = 6.9 Hz), 1.03 (1.5H, d, *J* = 6.9 Hz). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 169.6, 153.5, 153.0, 136.5, 128.63, 128.60, 128.5, 128.3, 128.1, 122.5, 121.8, 117.6, 117.0, 67.6, 67.5, 46.9, 46.8, 46.0, 45.9, 39.7, 39.5, 39.2, 39.1, 29.53, 29.49, 29.0, 28.5, 26.4, 26.3, 26.2, 24.4, 19.4, 19.1 (33 signals observed). **HRMS [M+H]$^+$** $C_{20}H_{27}N_2O_3$ calc. 343.2016 found 343.2019.

1-Benzyl 2-methyl 4-(2-(4-(*tert*-butoxycarbonyl)piperazin-1-yl)-2-oxoethyl)-2-methyl-2,3-dihydro-1H-pyrrole-1,2-dicarboxylate (11m)



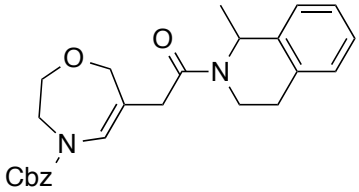
11m was isolated as a viscous oil in 85% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.35-7.29 (5H, m), 6.52 (0.5H, bs), 6.43 (0.5H, bs), 5.22 (0.5H, d, *J* = 12.5 Hz), 5.13 (1H, s), 5.03 (0.5H, *J* = 12.5 Hz), 3.73 (1.5H, s), 3.56 (2H, m), 3.46-3.36 (7.5H, m), 3.16-3.12 (2H, m), 3.01-2.92 (1H, m), 2.66-2.59 (1H, m), 1.69-1.60 (3H, s), 1.47 (9H, s). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 173.4, 173.3, 168.5, 154.6, 152.1, 151.5, 136.3, 128.7, 128.40, 128.36, 128.3, 128.2, 126.8, 126.1, 112.7, 80.6, 80.5, 67.5, 67.4, 66.5, 52.8, 52.5, 46.6, 45.9, 41.7, 33.7, 33.5, 28.5, 23.6, 22.7 (30 signals observed). **HRMS [M+H]$^+$** $C_{26}H_{36}N_3O_7$ calc. 502.2548 found 502.2548.

Benzyl 3-(2-morpholino-2-oxoethyl)-4,4a,5,7,8,8a-hexahydro-1H-pyrano[4,3-b]pyridine-1-carboxylate (11n)



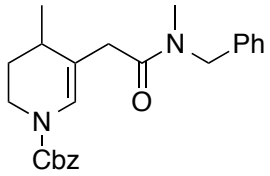
11n was isolated as a viscous oil in 93% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.37-7.31 (5H, m), 6.74 (0.4H), 6.60 (0.6H, s), 5.19-5.14 (2H, m), 4.35-4.33 (0.6H, m), 4.20-4.18 (0.4H, m), 3.97-3.96 (1H, m), 3.79-3.77 (1H, m), 3.65-3.41 (10H, m), 3.08 (0.8H, s), 3.02 (1.2H, s), 2.55-2.49 (1H, m), 2.01-1.99 (1H, m), 1.91-1.87 (1H, m), 1.75-1.73 (1H, m), 1.62-1.54 (1H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 169.3, 153.1, 152.5, 136.1, 128.7, 128.42, 128.39, 128.3, 128.0, 121.0, 120.4, 111.5, 111.2, 70.6, 67.8, 67.6, 67.5, 67.4, 67.0, 66.9, 66.7, 66.6, 50.4, 50.0, 46.3, 42.1, 39.9, 39.6, 32.1, 31.9, 26.7, 25.9, 25.3, 24.8 (34 signals observed). **HRMS [M+H]$^+$** $C_{22}H_{29}N_2O_5$ calc. 401.2071 found 401.2078.

Benzyl 6-(2-(1-methyl-3,4-dihydroisoquinolin-2(1H)-yl)-2-oxoethyl)-2,3-dihydro-1,4-oxazepine-4(7H)-carboxylate (11o)



11o was isolated as a viscous oil in 36% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.35-7.34 (5H, m), 7.20-7.12 (4H, m), 6.66 (0.34H, s), 6.50 (0.66H, s), 5.59-5.57 (0.66H, m), 5.16 (2H, m), 5.00-4.94 (0.34H, m), 4.66-4.62 (0.34H, m), 4.25 (2H, m), 3.90-3.74 (4.67H, m), 3.47-3.43 (0.66H, m), 3.18-3.12 (2H, m), 3.03 (0.34H, m), 2.91-2.72 (2H, m), 1.57-1.38 (3H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 168.7, 168.5, 154.2, 138.6, 136.2, 134.3, 133.2, 129.4, 128.7, 128.4, 128.2, 127.3, 127.0, 126.7, 126.6, 126.4, 120.6, 70.1, 70.0, 69.9, 68.2, 52.3, 49.0, 48.5, 40.2, 39.9, 39.6, 35.3, 29.8, 29.5, 28.6, 23.1, 21.7 (33 signals observed). **HRMS [M+H]$^+$** $C_{25}H_{29}N_2O_4$ calc. 421.2121 found 421.2119.

Benzyl 5-(2-(benzyl(methyl)amino)-2-oxoethyl)-4-methyl-3,4-dihydropyridine-1(2H)-carboxylate (11p)

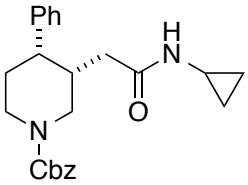


11p was isolated as a viscous oil in 70% yield (mixture of amide and carbamate rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.36-7.13 (10H, m), 6.79 (0.3H, s), 6.72 (0.2H, s), 6.67 (0.3H, s), 6.61 (0.2H, s), 5.18-5.16 (2H, m), 4.68-4.49 (2H, m), 3.71-3.70 (1H, m), 3.53-3.48 (1H, m), 3.18-3.06 (2H, m), 2.96-2.91 (3H, m), 2.41-2.40 (1H, m), 1.93-1.90 (1H, m), 1.60-1.58 (1H, m), 1.07-1.00 (3H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 171.49, 171.46, 171.1, 171.0, 153.44, 153.38, 153.0, 152.9, 137.39, 137.35, 136.4, 129.0, 128.61, 128.54, 128.2, 128.1, 128.0, 127.6, 127.4, 126.3, 126.2, 122.3, 122.1, 117.6, 116.9, 67.5, 67.4, 53.6, 51.0, 39.1, 38.1, 35.0, 34.2, 29.42, 29.40, 28.9, 19.0 (37 signals observed). **HRMS [M+H]$^+$** $C_{24}H_{29}N_2O_3$ calc. 393.2172 found 393.2179.

Benzyl 3-(2-(cyclopropylamino)-2-oxoethyl)-4-phenylpiperidine-1-carboxylate (12a)

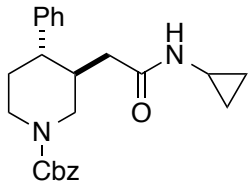
12a was isolated as a viscous oil in a combined 77% yield as a separable 3:2 mixture of *cis*/*trans* diastereomers (mixtures of rotamers).

Major Diastereomer



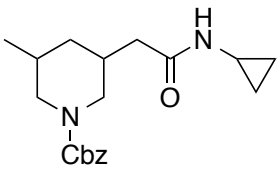
^{1}H NMR (501 MHz, $CDCl_3$) δ 7.38-7.14 (10H, m), 6.46 (0.4H, br), 5.16 (2H, s), 4.39-4.22 (2H, m), 3.07-2.93 (3H, m), 2.65 (0.6H, br), 2.58-2.51 (1H, m), 1.81-1.68 (5H, m), 0.71-0.18 (4H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 173.7, 156.2, 142.3, 136.8, 128.8, 126.6, 128.51, 128.47, 128.2, 127.8, 127.3, 126.7, 126.6, 67.5, 67.0, 48.0, 45.1, 44.6, 38.3, 37.1, 35.8, 35.8, 32.8, 31.9, 31.5, 30.2, 30.1, 29.4, 25.1, 23.4, 22.7, 8.2, 7.9, 6.4 (34 signals observed). **HRMS [M+H]$^+$** $C_{24}H_{29}N_2O_3$ calc. 393.2173 found 393.2173.

Minor Diastereomer



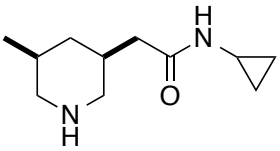
^{1}H NMR (501 MHz, $CDCl_3$) δ 7.31-7.08 (10H, m), 5.09 (3H, m), 4.33-4.23 (2H, m), 2.82-2.81 (1H, m), 2.67 (1H, dd, *J* = 13.2, 11.3Hz), 2.69-2.21 (2H, m), 2.10, 2.09-2.08 (1H, m), 1.94-1.90 (1H, m), 1.74-1.62 (3H, m), 0.61-0.60 (2H, m), 0.26 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.5, 155.3, 143.5, 137.0, 129.0, 128.9, 128.8, 128.7, 128.08, 128.05, 127.8, 127.0, 67.3, 49.1, 44.7, 39.0, 38.3, 34.4, 22.6, 6.7, 6.6. **HRMS [M+H]$^+$** $C_{24}H_{29}N_2O_3$ calc. 393.2173 found 393.2173.

Benzyl 3-(2-(cyclopropylamino)-2-oxoethyl)-5-methylpiperidine-1-carboxylate (12b)



12b isolated as a viscous oil, with unknown d.r. 7:3 (estimated from free amine, see below) in 65% yield. Due to extensive rotameric effects ^{1}H and ^{13}C spectra were found to be highly broadened, hence full characterization was addressed after Cbz removal (see next compound). Obtained spectra are displayed below. **HRMS [M+Na]$^+$** $C_{19}H_{27}N_2O_3$ calc. 331.2016 found 331.2025.

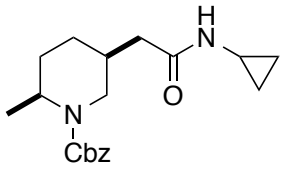
***N*-Cyclopropyl-2-(5-methylpiperidin-3-yl)acetamide**



Isolated as a viscous oil, inseparable 7:3 mixture of *cis*:*trans* diastereomers. Relative diastereoselectivity was assigned by comparison with ester analogue.

^{1}H NMR (501 MHz, MeOD) δ 3.07-2.99 (1.4H, m), 2.91-2.85 (0.6H, m), 2.65-2.58 (1.3H, m), 2.46-2.42 (0.3H, m), 2.25-2.14 (2.4H, m), 2.03-1.99 (2H, m), 1.82-1.80 (1H, m), 1.65-1.63 (1H, m), 1.51-1.37 (1H, m), 0.96-0.94 (0.9H, d, *J* = 6.9 Hz), 0.89-0.88 (2.1H, m), 0.72-0.71 (3H, m), 0.47-0.46 (2H, m). **^{13}C NMR (126 MHz, MeOD)** δ 175.0, 174.4, 50.04, 49.99, 48.1, 47.8, 47.6, 47.5, 47.3, 47.1, 40.0, 38.9, 38.5, 36.2, 33.7, 30.8, 29.7, 26.4, 21.9, 18.2, 17.4, 5.1. **HRMS [M+Na]$^+$** $C_{11}H_{21}N_2O$ calc. 197.1648 found 197.1653.

Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-2-methylpiperidine-1-carboxylate (12c)



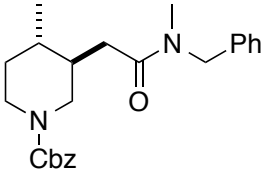
12c was isolated as a viscous oil in 79% yield as an inseparable 2:1 mixture of *cis*:*trans* diastereomers (mixture of rotamers).

^{1}H NMR (501 MHz, $CDCl_3$) δ 7.36-7.31 (5H, m), 5.70 (1H, br s), 5.13-5.11 (2H, m), 4.47-4.39 (1H, m), 4.00 (0.7H, d, *J* = 12.1 Hz), 3.81 (0.3H, d, *J* = 14.1 Hz), 3.07 (0.3H, dd, *J* = 14.1, 2.9 Hz), 2.70-2.68 (1H, m), 2.57 (0.7H, t, *J* = 12.4 Hz), 2.24-1.94 (2.7H, m), 1.92-1.86 (0.7H, m), 1.74-1.67 (1.6H, m), 1.53-1.50 (0.7H, m), 1.34-1.29 (1.3H, m), 1.18 (1H, d, *J* = 6.9 Hz), 1.12 (2H, d, *J* = 6.9 Hz), 0.76-0.73 (2H, m), 0.46 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.7, 156.6, 155.4, 137.2, 137.0, 128.8, 128.7, 128.3, 128.0, 127.9, 67.4, 67.2, 47.4, 46.0, 44.0, 41.3, 38.0, 34.3, 30.0, 25.8, 25.4, 23.0, 22.9, 16.5, 6.93, 6.88, 6.7 (27 signals observed). **HRMS $[M+NH_4]^+$** $C_{19}H_{30}N_3O_3$ calc. 348.2282 found 348.2277.

Benzyl 3-(2-(benzyl(methyl)amino)-2-oxoethyl)-4-methylpiperidine-1-carboxylate (12d)

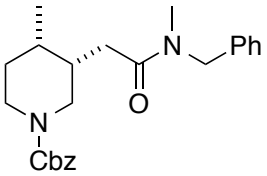
12d was isolated in a combined 66% yield as a separable 3:2 mixture *trans*/*cis* diastereoisomers (mixtures of rotamers)

Major diastereomer



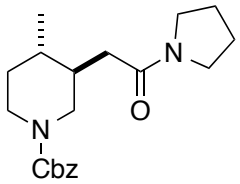
^{1}H NMR (501 MHz, $CDCl_3$) δ 7.40-7.15 (10H, m), 5.16-5.15 (2H, m), 4.59-4.53 (2H, m), 4.20-4.18 (1H, m), 4.04 (1H, m), 2.96-2.91 (4H, m), 2.75-2.55 (2H, m), 2.19 (1H, m), 1.83 (1H, m), 1.71-1.67 (1H, m), 1.45-1.28 (2H, m), 1.03-0.95 (3H, d, *J* = 6.4 Hz). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 171.9, 171.5, 155.2, 137.4, 137.1, 136.6, 129.0, 128.6, 128.5, 128.1, 127.84, 127.76, 127.4, 126.2, 66.9, 53.4, 50.9, 48.3, 43.8, 39.2, 35.3, 35.1, 34.9, 34.7, 34.2, 33.3, 19.3 (27 signals observed). **HRMS $[M+H]^+$** $C_{24}H_{31}N_2O_3$ calc. 393.2173 found 393.2179.

Minor diastereomer



^{1}H NMR (501 MHz, $CDCl_3$) δ 7.35-7.09 (10H, m), 5.15-5.08 (2H, m), 4.72- 4.16 (2H, m), 3.92 (2H, *m, H2 and H4*), 3.14-2.78 (5H, m), 2.40-2.13 (3H, m), 1.85 (1H, m), 1.55-1.50 (1H, m), 1.34-1.25 (1H, m), 0.95 (1.8H, d, *J* = 6.8 Hz), 0.85 (1.2H, d, *J* = 6.8 Hz). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.4, 172.1, 155.9, 137.6, 137.0, 136.8, 129.0, 128.7, 128.6, 128.1, 128.0, 127.8, 127.7, 127.4, 126.4, 67.1, 67.0, 53.3, 51.0, 47.9, 43.6, 35.6, 35.5, 34.8, 34.2, 32.9, 29.9, 28.8, 17.9 (29 signals observed). **HRMS [M+H]$^+$** $C_{24}H_{31}N_2O_3$ calc. 393.2173 found 393.2179.

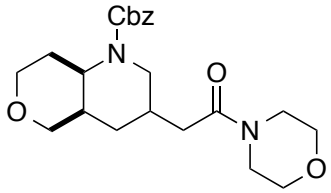
Benzyl 4-methyl-3-(2-oxo-2-(pyrrolidin-1-yl)ethyl)piperidine-1-carboxylate (12e)



12e was isolated as a viscous oil in 50% yield as an inseparable 3:2 mixture of *trans*:*cis* diastereomers (mixture of rotamers)

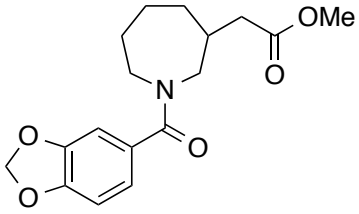
^{1}H NMR (501 MHz, $CDCl_3$) δ 7.35-7.32 (5H, m), 5.10-5.09 (2H, m), 4.11 (0.6H, dd, , *J* = 13.5, 3.5Hz) 4.06-3.90 (1.4H, m), 3.43-3.29 (4H, m), 3.08 (0.4H, dd, *J* = 13.4, 2.5Hz), 2.91-2.87 (1H, m), 2.68 (0.6H, dd*, J* = 13.1, 10.2 Hz), 2.43 (0.6H, dd, *J* = 15.3, 4.3 Hz), 2.37 (0.4H, bs), 2.15-2.06 (1.4H, m), 1.90-1.79 (5H, m), 1.66-1.64 (0.6H, m), 1.52-1.49 (0.4H, m), 1.42 (0.6H, m), 1.29-1.27 (1H, m), 0.98 (2H, d*, J* = 6.9 Hz), 0.93 (1H, d, *J* = 6.9 Hz). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.1, 155.2, 137.1, 128.5, 128.4, 127.9, 127.8, 127.7, 127.6, 66.9, 48.2, 46.8, 45.8, 43.8, 39.1, 36.4, 35.1, 33.2, 32.7, 29.7, 26.1, 26.0, 24.3, 19.3 (24 signals observed). **HRMS [M+H]$^+$** $C_{20}H_{29}N_2O_3$ calc. 345.2173 found 345.2176.

(4a*R,8a*R**)-Benzyl 3-(2-morpholino-2-oxoethyl)octahydro-1H-pyrano[4,3-b]pyridine-1-carboxylate (12f)**



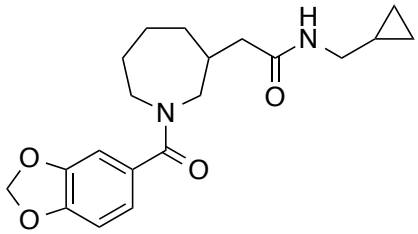
12f was isolated as a viscous oil in 75% yield as an inseparable 1:1 mixture of diastereomers (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 7.37-7.31 (5H*,* m), 5.18-5.13 (2H, m), 4.47-4.30 (1H, m), 4.12-4.11 (0.5H, m), 4.00-3.91 (1.5H, m), 3.68-3.30 (11H, m), 3.11 (0.5H, d, *J* = 13.2 Hz), 2.58 (0.5H, m), 2.52-2.44 (1H, m), 2.23-2.04 (3.25H, m), 1.80-1.65 (2.5H, m), 1.46-1.38 (1.25H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 170.1, 169.6, 155.9, 155.3, 155.2, 136.8, 128.61, 128.55, 128.5, 128.1, 127.9, 127.84, 127.76, 72.0, 71.9, 67.4, 67.2, 66.9, 66.62, 66.57, 50.0, 49.6, 46.1, 44.0, 42.4, 42.0, 41.9, 37.0, 35.7, 35.5, 33.4, 33.3, 30.7, 30.0, 29.8, 24.6, 23.9 (37 signals observed). **HRMS [M+Na]$^+$** $C_{22}H_{30}N_2NaO_5$ calc. 425.2047 found 425.2057.

Methyl 2-(1-(benzo[d][1,3]dioxole-5-carbonyl)azepan-3-yl)acetate (14)



14 was isolated as a viscous oil in 59% yield (mixture of rotamers). **^{1}H NMR (501 MHz, $CDCl_3$)** δ 6.88-6.86 (2H, m), 6.81-6.79 (1H, d, *J* = 7.7 Hz), 5.98 (2H, s), 3.92-3.84 (1H, m), 3.71-3.41 (5H, m), 3.20 (0.5H, br s), 3.01 (0.5H, br s), 2.46-2.10 (3H, m), 1.97-1.73 (3H, m), 1.56-1.25 (3H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.9, 172.3, 171.3, 148.4, 147.5, 130.5, 120.8, 108.2, 107.6, 101.3, 54.6, 52.6, 51.6, 50.7, 50.5, 46.9, 46.0, 39.2, 38.8, 37.6, 35.1, 33.7, 32.7, 32.0, 30.8, 29.3, 26.7, 25.5, 24.2 (29 signals observed). **HRMS $[M+H]^+$** $C_{17}H_{22}NO_5$ calc. 320.1492 found 320.1490.

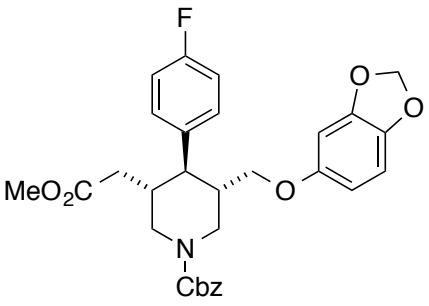
2-(1-(Benzo[d][1,3]dioxole-5-carbonyl)azepan-3-yl)-*N*-cyclopropylacetamide (15)



15 was isolated as a viscous oil in 36% yield (mixture of rotamers, 95% purity).

^{1}H NMR (501 MHz, $CDCl_3$) δ 7.81 (1H, s), 6.90-6.88 (2H, m), 6.83 (1H, d, *J* = 7.8 Hz), 6.00 (1H, s), 3.63-3.47 (3H, m), 3.26-3.22 (1H, m), 2.82-2.80 (1H, m), 2.20-2.19 (3H, m), 1.94-1.91 (1H, m), 1.83-1.80 (2H, m), 1.59-1.56 (1H, m), 1.39-1.37 (1H, m), 1.19-1.26 (2H, m), 0.76-0.74 (2H, m), 0.62-0.61 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 173.5, 172.1, 148.9, 147.8, 130.1, 121.0, 108.4, 107.6, 101.6, 51.7, 49.7, 41.9, 35.9, 35.5, 29.8, 29.6, 24.1, 22.9, 6.7, 6.4, 6.3 (21 signals observed) **HRMS $[M+H]^+$** $C_{19}H_{25}N_2O_4$ calc. 345.1809 found 345.1809.

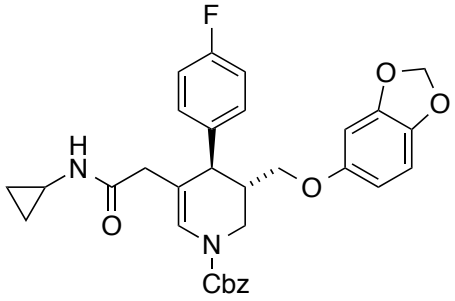
3-(3*S*,4*R*,5*R*)-Benzyl 3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)-5-(2-methoxy-2-oxoethyl)-piperidine-1-carboxylate (17)



17 was isolated as a viscous oil in 29% yield as an inseparable 4:1 mixture of *trans*/*cis* diastereoisomers (mixtures of rotamers)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.25 (5H, m), 7.05-7.02 (2H, m), 6.93-6.89 (2H, m), 6.54 (1H, d, *J* = 8.5 Hz), 6.26 (1H, s), 6.03 (1H, d, *J* = 8.4 Hz), 5.81 (2H, s), 5.12 (2H, bs), 4.37-4.34 (2H, m), 3.62 (0.8H, m), 3.48-3.46 (3.4H, m), 3.33-3.29 (0.8H, m), 2.89-2.83 (1H, m), 2.60 (1H, t, *J* = 12.3 Hz), 2.47 (1H, t, *J* = 11.3 Hz), 2.19 (1H, bs), 2.08-1.88 (3H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 172.2, 162.0 (d, *J* = 245.7 Hz), 155.4, 155.2, 148.3, 141.9, 136.9, 136.3, 129.6, 128.9, 128.7, 128.19, 128.16, 128.0, 115.8 (d, *J* = 20.2 Hz), 110.7, 108.0, 105.7, 101.34, 101.28, 98.1, 68.7, 67.4, 51.7, 49.1, 48.9, 47.4, 42.6, 39.1, 36.2 (30 signals observed). **HRMS $[M+H]^+$** $C_{30}H_{31}FNO_7$ calc. 536.2079 found 536.2075

Benzyl 3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-5-(2-(cyclopropylamino)-2-oxoethyl)-4-(4-fluorophenyl)-3,4-dihydropyridine-1(2H)-carboxylate

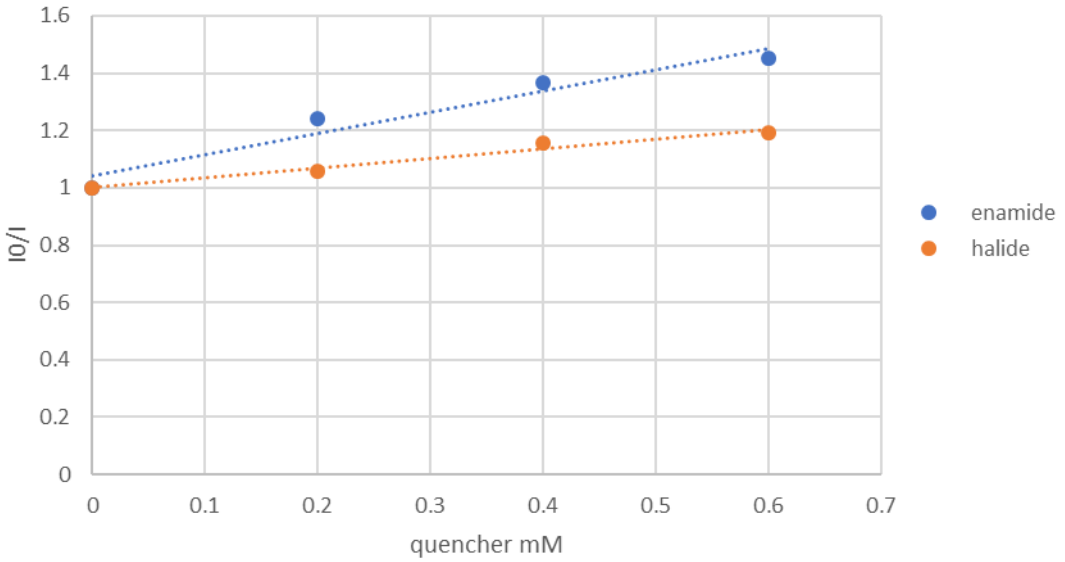


Isolated as a mixture of rotamers, as a viscous oil in 21% yield

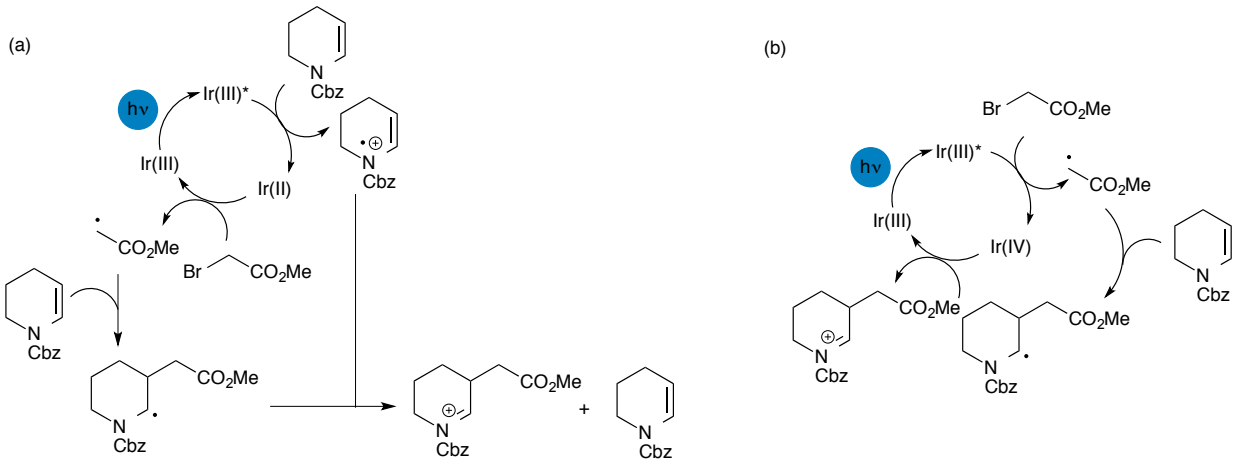
^{1}H NMR (501 MHz, $CDCl_3$) δ 7.34-7.30 (5H, m), 7.19 (2.5H, m), 7.04-6.91 (2.5H, m), 6.60-6.59 (1H, m), 6.37-6.35 (1H, s), 6.19-6.15 (1H, m), 5.83 (2H, s), 5.25 (2H, br s), 4.51-4.44 (2H, m), 3.58 (1H, br), 3.45 (1H, br), 2.98-2.69 (3H, m), 2.14-2.06 (2H, m), 1.37 (1H, br s), 0.75 (2H, m), 0.44 (2H, m). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 171.7, 161.9 (d, *J* = 245.7 Hz), 154.0, 153.8, 153.1, 148.3, 141.9, 137.6, 135.9, 130.0, 128.6-128.0, 125.5, 125.1, 115.7 (d, *J* = 20.2 Hz), 112.9-112.3, 107.9, 105.8, 105.7, 101.2, 98.2, 69.0, 68.8, 68.1, 67.9, 42.5, 40.3, 22.6, 6.6, 6.5. **HRMS $[M+H]^+$** $C_{32}H_{32}FN_2O_6$ calc. 559.2239 found 559.2238.

Mechanistic studies: Stern Volmer Study

A solution of $Ir(ppy)_3$ catalyst in dry and degassed DME (25uM) was prepared and transferred into a quartz cuvette. The catalyst solution was excited at 375 nm and its emission intensity was measured at 518 nm. The solution was submitted to increasing concentrations of enecarbamate **6a** and methyl bromoacetate, and the resulting emission intensity was measured in triplicate. By comparing the slopes of the quenching ability of both analytes we concluded that the enecarbamate was a more efficient quencher of the photo-catalyst excited state than the halide.



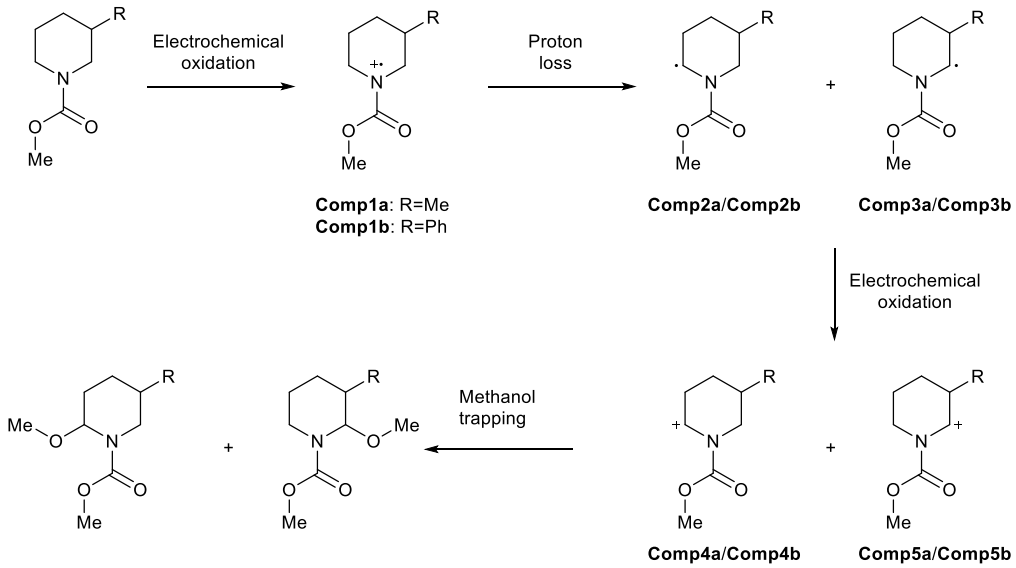
The greater quenching power of the enecarbamate may support a reductive quenching cycle (cycle a below); however, the moderate quenching activity of the bromide means we cannot ignore the possibility of an oxidative quenching cycle (cycle b below).



DFT Calculations

DFT studies employed the M06-2X/6-31+G** level of theory.[5] Solvation energies were computed as single points on the optimized geometries and employed the same level of theory and the IEFPCM formalism.[6] The gas phase and water solvation were used to delimit the extremes of solvent effects. Continuum solvation in methanol was used to check quantitative agreement with experiment. All calculations were performed in Gaussian09.[7] Free energies were computed with the goodvibes program.[8] A range of conformations were studied for each species, where relevant and the relative energies of each was used to compute a Boltzmann factor in order to assign its contribution to the overall population.

Two systems were selected to probe the reaction mechanism, the reactions of **5l** and **5m** that give contrasting outcomes; **5l** gives a mixture of **6l** and **6l'** in a 2:1 ratio while **5m** gives **6m** and **6m'** in a >9:1 ratio; in the following text, ratios are always in this same order to allow for easy comparison. Whereas in the experimental studies, a benzyl carbamate is presented, this has been abbreviated to a methyl carbamate for computational simplicity. The mechanism of the reaction is likely to proceed following loss of an electron from the substrates (Scheme S1). The radical cation that results (**Comp1a**/**b**) can then shed a proton to the solvent leading to two, regioisomeric radicals **Comp2a**/**b** and **Comp3a**/**b**. These can be oxidised by further electrochemistry to give the two cations **Comp4a**/**b** and **Comp5a**/**b** that can be trapped by methanol to give the observed products.



Scheme S1. The proposed mechanism

Initial investigations focused on the energy of the two radicals arising from deprotonation of the radical cation. This indicated that for **Comp1a**, the two radicals **Comp2a** and **Comp3a** are expected to be present in equal amounts in the gas phase (47:53) and in water (48:52) indicating that there is no preference regardless of the polarity of the medium. By contrast for **Comp1b**, **Comp3b** is computed to be the preferred isomer and to be dominant in both gas phase (17:83) and water (also 17:83). This preference is opposite to experiment.

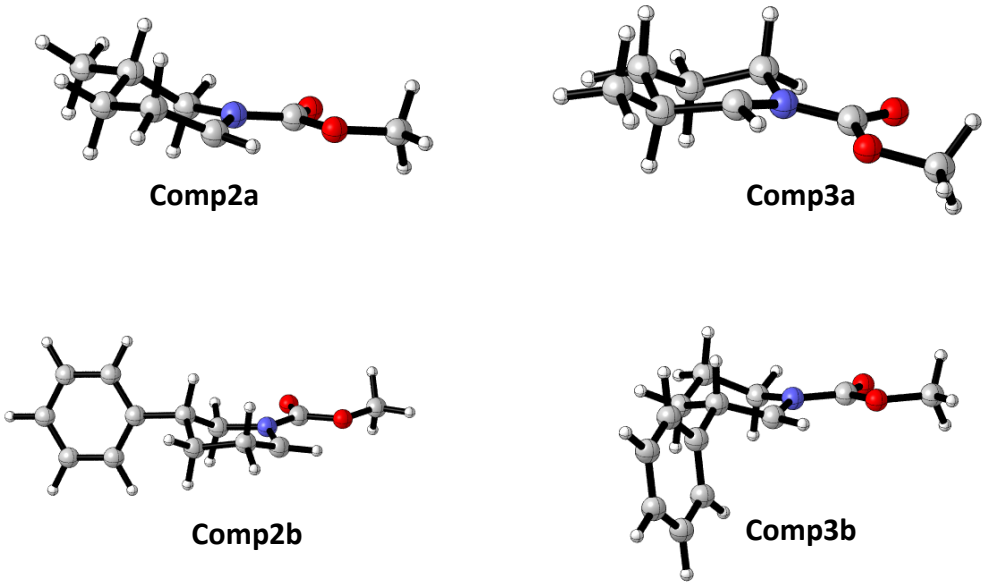
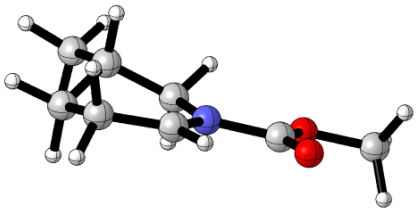
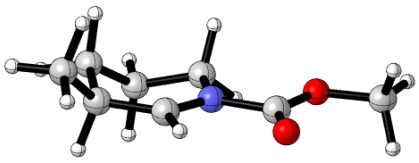


Figure S1. The lowest free energy conformations of each of the radicals.

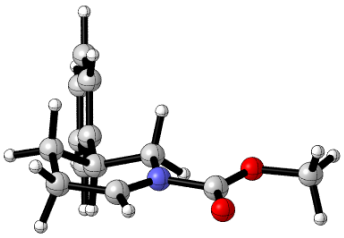
Subsequently, the cations **Comp4a**/**b** and **Comp5a**/**b** were studied. In both cases, there was an effect of solvent polarity computed. A preference for **Comp4a** (65:35 in the gas phase and 84:16 in water) was found. The preference for **Comp5b** (66:34) in the gas phase becomes a preference for **Comp4b** (92:8) in water. Under aqueous conditions, the experimentally observed dominant isomer is preferred but there is little effect of changing Me to Ph predicted. While the error intrinsic to the calculations means that it cannot be precluded that this is in agreement with experiment, it requires a mechanism in which these two isomers are rapidly equilibrated. An alternative, in which the regioselective formation of the radicals takes place, was considered with methanol acting as the base.



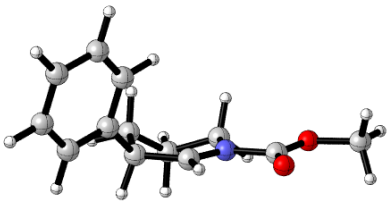
Comp4a



Comp5a



Comp4b



Comp5b

Figure S2. The lowest free energy conformations of each of the cations.

Transition states for the proton transfer from the radical cation to methanol were obtained and structural variations were considered including whether the proton being removed is axial or equatorial (in addition to the methyl or phenyl substituent being axial or equatorial). In the transition state, it was assumed that the OH of methanol orients towards the carbamate (to form a hydrogen bond with either the carbonyl or ester oxygen). Finally, the methyl of methanol could either be placed over the piperidine ring or else away from it. Up to five attempts were made to obtain each of the transition states but some were not found, as noted below). In the gas phase, a kinetic preference of 30:70 in favour of formation of **Comp3a** was computed. In solvent this changed slightly, becoming 15:85 in methanol. By contrast, a 98:2 preference for **Comp2b** becomes 92:8 in methanol. This latter is in near perfect agreement with observation, while the preference for **Comp3a** is within the intrinsic error in the calculations. This provides a plausible explanation for the observed preference given that it does not require any further steps.

In order to understand the origin of selectivity, the transition states for the selective reaction (R=Ph) were examined. The lowest energy transition state TS1->2b (leading to **Comp2b**) features the phenyl group in an equatorial position, during removal of an axial proton. The methanol forms a hydrogen bond with the carbonyl oxygen and the methyl group of methanol is placed away from the piperidine ring. The same features are present in the lowest energy transition state leading to **Comp3b**, TS1->3b, with the exception of the orientation of the methyl of methanol which is placed over the piperidine ring. This suggests that the preference has a steric influence, given that orienting the methyl away from the piperidine would cause it to clash with the phenyl group; a transition state with such a configuration could not be obtained. This steric model provides a consistent rationale for the preference for reaction distal to the substituent and for the enhanced selectivity for the larger phenyl substituted **5m** than for **5l**.

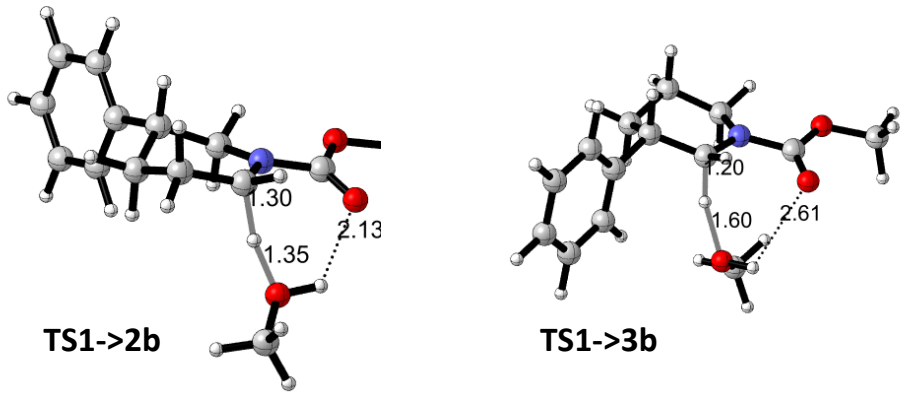


Figure S3. The lowest free energy conformations of the transition states for the formation of **Comp2b** and **Comp3b**.

Computational Studies: Geometries and Energies

In the section below, a brief description of each species is provided (transition state or minimum, is the substituent Me or Ph, is the activated carbon proximal or distal to the substituent, is the substituent in an axial or equatorial orientation, is the hydrogen being removed or the radical (in the starting geometry) in an equatorial or axial orientation, is the oxamate in a syn or anti conformation, is the methyl of methanol placed above (endo) or away (exo) from the ring). The gas phase electronic and free energies obtained with (U)M06-2X/6-31+G** level of theory are then given (in Hartrees with the correction being provided by Goodvibes for 298K and 1M concentration). Energies corrected for solvation by methanol are then provided where the correction has been computed as a single point using the same level of theory as for the geometry optimisation and with the IEFPCM protocol using settings appropriate for methanol. Finally x, y, z coordinates are given.

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -634.273813
Free energy (gas): -634.027224
Electronic energy (MeOH solvation): -634.3491218
Free energy (MeOH solvation): -634.1025328
Coordinates:

C	-1.19970	-0.50703	1.13435
N	-0.20514	-0.36329	0.04013
C	-2.61358	-0.19818	0.65517
H	-0.90796	0.17588	1.94346
H	-1.11025	-1.52829	1.50569
C	-2.62025	1.18587	-0.00112
C	-0.35789	0.58879	-0.96461
C	-1.71136	1.19009	-1.22679
H	-2.27885	1.93660	0.72382
H	-3.63465	1.46643	-0.29717
H	-1.58318	2.20171	-1.62571
H	-2.18106	0.61557	-2.03929
H	0.27432	0.39906	-1.83309
C	0.94486	-1.13144	0.17721
O	1.07227	-2.05438	0.93470
O	1.96202	-0.68421	-0.62925
C	3.09551	-1.59108	-0.71354
H	3.53990	-1.71864	0.27295
H	3.78700	-1.12274	-1.41056
H	2.75240	-2.55186	-1.09502
H	0.87924	1.73349	-0.46866
O	1.88501	1.89224	-0.22990
H	2.24916	0.96662	-0.35673
C	-3.14325	-1.30137	-0.26443
H	-3.26024	-2.23885	0.28519
H	-4.11863	-1.02868	-0.67696
H	-2.46573	-1.49598	-1.10267
H	-3.23815	-0.16229	1.55441
C	2.09493	2.42836	1.11959
H	3.16915	2.54148	1.24472
H	1.60224	3.39729	1.14099
H	1.67123	1.74298	1.85431

C	-0.48348	0.17194	-1.00872
N	0.44095	-0.49512	-0.16560
C	-0.77103	1.60437	-0.33958
H	-1.43613	-0.37088	-0.99126

H	-0.06021	0.30144	-2.00362
C	-1.26284	1.35197	1.08596
C	-0.01259	-0.84118	1.15959
C	-0.29702	0.50475	1.90620
H	-2.23990	0.85850	1.05309
H	-1.39390	2.32308	1.58043
H	0.74287	-1.43355	1.67023
C	1.84030	-0.47218	-0.53030
O	2.58116	-0.94947	0.44196
O	2.18729	-0.05491	-1.59939
H	-0.95271	-1.39262	1.05746
O	-3.21401	-1.15683	-0.05817
H	-3.17361	-2.04535	0.31494
C	4.00529	-0.99194	0.16814
H	4.18514	-1.62922	-0.69813
H	4.36520	0.01901	-0.02470
H	4.45180	-1.40794	1.06681
H	-1.58571	2.00384	-0.95324
H	-0.71984	0.23816	2.87853
C	-4.49300	-1.02369	-0.69040
H	-4.57740	-1.69058	-1.55235
H	-5.30244	-1.22405	0.01650
H	-4.57024	0.01007	-1.03056
H	0.65565	1.01248	2.08598
C	0.44582	2.51310	-0.44630
H	0.79885	2.59356	-1.47769
H	0.17782	3.51716	-0.10461
H	1.28404	2.16958	0.16859

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -634.254044
Free energy (gas): -634.011246
Electronic energy (MeOH solvation): -634.3280459
Free energy (MeOH solvation): -634.0852479
Coordinates:

C	1.57696	-0.36747	1.40412
N	0.23916	-0.10031	0.83368
C	2.52382	-0.68548	0.21551
H	1.48503	-1.23066	2.07081
H	1.90091	0.50153	1.97716
C	1.92287	-1.76203	-0.70190
C	-0.24707	-1.22031	0.14116
C	0.45829	-1.45297	-1.17648
H	1.91770	-2.73492	-0.19800
H	2.53857	-1.86726	-1.60300
H	0.05068	-2.30334	-1.72706
H	0.42905	-0.56512	-1.81462
H	-1.66988	-1.05353	-0.18699
C	-0.02075	1.21191	0.44127
O	0.61836	2.16407	0.79822
O	-1.12012	1.29725	-0.35163
C	-1.38125	2.63698	-0.83862
H	-1.59093	3.30043	0.00034
H	-2.24370	2.54593	-1.49675
H	-0.51408	2.99994	-1.39013
H	-0.22770	-2.09968	0.79524
O	-2.77107	-0.81799	-0.38750
C	-3.69010	-1.42031	0.57374
H	-3.58774	-2.49626	0.45235

H	-3.43030	-1.10622	1.58484
H	-4.69508	-1.10354	0.30162
H	-2.76125	0.15934	-0.35480
C	2.92227	0.56819	-0.56898
H	2.08638	0.98538	-1.14019
H	3.28583	1.35579	0.09512
H	3.71451	0.32418	-1.28131
H	3.43033	-1.10748	0.66804

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: anti
Position of methyl from MeOH: exo
Electronic energy (gas): -634.253056
Free energy (gas): -634.010092
Electronic energy (MeOH solvation): -634.3276842
Free energy (MeOH solvation): -634.0847202
Coordinates:

C	1.81373	-0.18756	1.29712
N	0.40142	0.05498	0.93660
C	2.51477	-0.74215	0.02735
H	1.82630	-0.92578	2.10513
H	2.25806	0.74398	1.64841
C	1.72797	-1.91598	-0.57773
C	-0.23186	-1.13477	0.54757
C	0.20669	-1.60932	-0.81946
H	1.79474	-2.79611	0.07115
H	2.16224	-2.19338	-1.54537
H	-1.69611	-0.93304	0.54419
C	0.09982	1.30073	0.39214
O	0.81246	2.26409	0.47106
O	-1.12550	1.31892	-0.19716
C	-1.45758	2.59697	-0.79380
H	-1.49865	3.36499	-0.02144
H	-2.43102	2.45851	-1.26175
H	-0.70665	2.85981	-1.53867
H	-0.10627	-1.89549	1.32615
O	-2.79986	-0.65576	0.56289
H	-2.76375	0.27630	0.26843
C	-3.64494	-1.49905	-0.27663
H	-3.56311	-2.50420	0.13066
H	-4.66515	-1.13333	-0.17639
H	-3.30255	-1.45734	-1.31086
H	0.07794	-0.83227	-1.57905
H	-0.31000	-2.51726	-1.13992
C	2.79334	0.34813	-1.01180
H	1.87892	0.71365	-1.49097
H	3.29017	1.21068	-0.56158
H	3.43822	-0.04743	-1.80076
H	3.47836	-1.13716	0.37357

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: syn
Position of methyl from MeOH: endo
Electronic energy (gas): -634.265679
Free energy (gas): -634.023142
Electronic energy (MeOH solvation): -634.3312415
Free energy (MeOH solvation): -634.0887045

Coordinates:

C	1.38119	-0.46750	1.39804
N	0.09753	-0.07512	0.79438
C	2.18614	-1.19711	0.28163
H	1.16163	-1.15380	2.22163
H	1.89963	0.40860	1.78476
C	1.34431	-2.30890	-0.35852
C	-0.65234	-1.18791	0.38322
C	-0.05529	-1.83863	-0.86731
H	1.19580	-3.12961	0.35185
H	1.87711	-2.72368	-1.22335
H	-0.65583	-2.68626	-1.20240
H	0.03155	-1.11816	-1.68533
H	-1.88186	-0.83500	-0.03222
C	-0.03957	1.12428	0.09044
O	-0.95947	1.33240	-0.68425
O	0.89415	1.99645	0.40374
C	0.81236	3.27608	-0.26005
H	0.91130	3.13471	-1.33723
H	1.64272	3.85369	0.13745
H	-0.14234	3.74989	-0.03012
H	-0.74239	-1.89902	1.21022
O	-2.95522	-0.40942	-0.52385
C	-4.04812	-0.26734	0.41532
H	-4.32442	-1.27317	0.72442
H	-3.73956	0.33444	1.27207
H	-4.88006	0.20318	-0.10819
H	-2.61714	0.45932	-0.83102
C	2.74362	-0.22414	-0.76124
H	1.95721	0.23291	-1.37281
H	3.30877	0.58312	-0.28826
H	3.41428	-0.75297	-1.44313
H	3.03143	-1.67071	0.79665

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: syn
Position of methyl from MeOH: exo
Electronic energy (gas): -634.264774
Free energy (gas): -634.021644
Electronic energy (MeOH solvation): -634.3306581
Free energy (MeOH solvation): -634.0875281
Coordinates:

C	1.48249	-0.71587	1.28649
N	0.24125	-0.02668	0.90418
C	1.87017	-1.61724	0.07530
H	1.26226	-1.32875	2.16587
H	2.25651	0.00949	1.53309
C	0.68447	-2.48882	-0.36011
C	-0.81617	-0.92286	0.68565
C	-0.63302	-1.69155	-0.62386
H	0.47763	-3.25391	0.39622
H	0.93635	-3.01424	-1.28955
H	-1.97632	-0.24920	0.55627
C	0.26133	1.17582	0.19115
O	-0.71325	1.59959	-0.40813
O	1.41647	1.79627	0.29231
C	1.50763	3.07482	-0.37309
H	1.34636	2.94139	-1.44356
H	2.51512	3.42756	-0.16910
H	0.76215	3.75620	0.03743
H	-0.91118	-1.59456	1.54428

O	-2.98677	0.48154	0.39446
H	-2.53850	1.23899	-0.03801
C	-4.00709	-0.10349	-0.44884
H	-4.39327	-0.96922	0.08589
H	-4.79769	0.63533	-0.57891
H	-3.58612	-0.39272	-1.41395
H	-0.52899	-1.00946	-1.47290
H	-1.46311	-2.37581	-0.81290
C	2.44531	-0.80480	-1.08789
H	1.69364	-0.16747	-1.56751
H	3.26289	-0.16021	-0.75501
H	2.83538	-1.47725	-1.85599
H	2.65587	-2.28466	0.45117

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -634.275124
Free energy (gas): -634.029024
Electronic energy (MeOH solvation): -634.3504797
Free energy (MeOH solvation): -634.1043797
Coordinates:

C	-1.24300	-0.87587	0.58277
N	-0.09299	-0.46516	-0.26287
C	-2.59056	-0.51357	-0.02793
H	-1.13441	-0.38450	1.56085
H	-1.14956	-1.95080	0.74170
C	-2.57462	0.94547	-0.47781
C	-0.16763	0.61350	-1.13997
C	-1.51303	1.13422	-1.55577
H	-2.36591	1.59291	0.38705
H	-3.55434	1.23788	-0.86594
H	-1.41358	2.18240	-1.85565
H	-1.82095	0.59095	-2.46332
H	0.62404	0.61430	-1.89010
C	1.09333	-1.13778	-0.00045
O	1.18559	-2.15083	0.63717
O	2.18424	-0.48123	-0.51810
C	3.41287	-1.25968	-0.49874
H	3.67549	-1.50821	0.52893
H	4.16234	-0.62393	-0.96520
H	3.26294	-2.17076	-1.07673
H	0.83041	1.78350	-0.25998
O	1.74950	1.97556	0.19196
H	2.22006	1.10376	0.01922
C	1.64198	2.31980	1.61404
H	2.65635	2.47476	1.97372
H	1.07294	3.24492	1.65969
H	1.14182	1.51113	2.14784
C	-3.69593	-0.79938	0.98589
H	-4.67658	-0.60300	0.54584
H	-3.67869	-1.84184	1.31602
H	-3.58938	-0.15993	1.86916
H	-2.74703	-1.14568	-0.91341

C	0.49957	-0.42383	-0.91110
N	-0.45912	0.26975	-0.12163
C	0.78036	-1.81603	-0.18472
H	1.44245	0.13480	-0.89356
H	0.10673	-0.59915	-1.91171
C	1.20422	-1.52158	1.25025

C	-0.04855	0.67233	1.19858
C	0.20090	-0.65378	1.99666
H	2.18848	-1.03639	1.24471
H	1.31559	-2.47667	1.77957
H	-0.82183	1.27984	1.66258
C	-1.85124	0.17476	-0.50927
O	-2.61942	0.77491	0.36812
O	-2.16712	-0.39508	-1.51555
H	0.90496	1.20422	1.10368
O	2.85681	1.50073	0.07630
H	3.73385	1.36939	0.45007
C	-4.03725	0.75217	0.06095
H	-4.20239	1.23002	-0.90499
H	-4.38266	-0.28158	0.03530
H	-4.50898	1.30853	0.86581
H	0.56576	-0.35858	2.98397
C	2.83351	2.71334	-0.68624
H	2.09479	3.39589	-0.25772
H	3.80676	3.20751	-0.68472
H	2.56147	2.48330	-1.71990
H	-0.75658	-1.16933	2.13017
C	1.83143	-2.56089	-0.99607
H	2.02437	-3.53369	-0.53445
H	1.49716	-2.73878	-2.02103
H	2.77187	-2.00197	-1.02413
H	-0.16780	-2.36901	-0.19750

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -634.256598
Free energy (gas): -634.014022
Electronic energy (MeOH solvation): -634.3300663
Free energy (MeOH solvation): -634.0874903
Coordinates:

C	-1.59326	-0.02523	-1.18554
N	-0.18242	0.01902	-0.74134
C	-2.45560	-0.07660	0.09818
H	-1.72821	-0.93207	-1.78497
H	-1.81148	0.85212	-1.79440
C	-1.98739	-1.18819	1.04540
H	-2.32972	0.89236	0.59930
C	-3.92843	-0.25045	-0.27887
C	0.15529	-1.14304	-0.03127
C	-0.45300	-1.17073	1.35623
H	-2.24799	-2.16726	0.62255
H	-2.51383	-1.10311	2.00339
H	-0.16333	-2.05716	1.92410
H	-0.18621	-0.27636	1.92850
H	1.61219	-1.21457	0.14613
H	-4.08846	-1.20262	-0.79575
H	-4.26161	0.55727	-0.93557
H	-4.55989	-0.23986	0.61271
C	0.26664	1.27859	-0.32857
O	-0.32163	2.30526	-0.53145
O	1.47333	1.20837	0.28584
C	1.95299	2.48505	0.77690
H	2.09456	3.17033	-0.05865
H	2.89638	2.27082	1.27589
H	1.23125	2.90071	1.47957
H	-0.08486	-2.03045	-0.62664

```
O          2.75311       -1.15000        0.21588
C          3.45075       -1.90927       -0.81765
H          3.21266       -2.95440       -0.63410
H          3.11469       -1.58949       -1.80426
H          4.51650       -1.73534       -0.68193
H          2.88796       -0.18398        0.14244

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: anti
Position of methyl from MeOH: exo
Electronic energy (gas): -634.255471
Free energy (gas): -634.012962
Electronic energy (MeOH solvation): -634.3297935
Free energy (MeOH solvation): -634.0872845
Coordinates:
C         -1.78507        0.26700       -1.06369
N         -0.32207        0.23294       -0.84807
C         -2.43583       -0.13878        0.28024
H         -2.02512       -0.45524       -1.85154
H         -2.08236        1.26616       -1.38227
C         -1.83728       -1.44125        0.82564
C          0.10770       -1.06304       -0.52581
C         -0.27238       -1.45908        0.88541
H         -2.17110       -2.28656        0.21026
H         -2.20677       -1.61950        1.84224
H          1.57713       -1.13409       -0.66911
C          0.21176        1.36167       -0.22066
O         -0.38110        2.39413       -0.06640
O          1.50443        1.17308        0.15036
C          2.09237        2.32536        0.80336
H          2.12840        3.16291        0.10673
H          3.09465        2.01690        1.09629
H          1.49962        2.59516        1.67682
H         -0.23523       -1.77383       -1.28487
O          2.70711       -1.05546       -0.79261
H          2.83884       -0.10043       -0.62385
C          3.43947       -1.88771        0.15723
H          3.17771       -2.91656       -0.07911
H          4.50052       -1.71893       -0.01700
H          3.15250       -1.62601        1.17644
H          0.09120       -0.73138        1.61892
H          0.08608       -2.45490        1.15733
H         -2.22429        0.67209        0.99023
C         -3.95107       -0.25701        0.10219
H         -4.43524       -0.49755        1.05176
H         -4.37563        0.68178       -0.26258
H         -4.19800       -1.04745       -0.61449

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: syn
Position of methyl from MeOH: endo
Electronic energy (gas): -634.267251
Free energy (gas): -634.025154
Electronic energy (MeOH solvation): -634.332602
Free energy (MeOH solvation): -634.090505
Coordinates:
C         -1.45873       -0.07669       -1.14102
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N	-0.06298	0.02339	-0.68559
C	-2.28457	-0.49939	0.10315
H	-1.50503	-0.85362	-1.91192
H	-1.79285	0.87105	-1.56046
C	-1.67790	-1.73614	0.77320
C	0.44120	-1.21463	-0.26035
C	-0.15765	-1.61652	1.09227
H	-1.84099	-2.61653	0.13828
H	-2.19274	-1.92688	1.72307
H	0.25105	-2.56513	1.44538
H	0.02769	-0.84658	1.84767
H	1.76121	-1.14832	0.00167
C	0.38833	1.17594	-0.03044
O	1.44483	1.21417	0.57779
O	-0.42880	2.19463	-0.18792
C	0.00422	3.44840	0.38605
H	0.14046	3.33098	1.46129
H	-0.79510	4.15048	0.16472
H	0.93987	3.75908	-0.07987
H	0.26907	-1.97128	-1.03111
O	2.95213	-0.96072	0.34260
C	3.92780	-1.13320	-0.71350
H	3.92444	-2.19037	-0.97025
H	3.66659	-0.51969	-1.57756
H	4.90250	-0.84928	-0.31702
H	2.85890	-0.02009	0.60791
H	-2.24393	0.34089	0.81024
C	-3.74009	-0.73309	-0.30699
H	-3.81528	-1.55719	-1.02392
H	-4.34931	-0.98603	0.56393
H	-4.16664	0.16202	-0.76697

Transition state
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: syn
Position of methyl from MeOH: exo
Electronic energy (gas): -634.266441
Free energy (gas): -634.024177
Electronic energy (MeOH solvation): -634.3321441
Free energy (MeOH solvation): -634.0898801
Coordinates:

C	1.60500	-0.12776	1.06469
N	0.18050	0.12733	0.80566
C	2.16775	-0.74308	-0.24525
H	1.67398	-0.84839	1.88669
H	2.11387	0.79334	1.34511
C	1.31445	-1.92718	-0.71195
C	-0.53570	-1.05603	0.57505
C	-0.21181	-1.62572	-0.80943
H	1.46529	-2.77862	-0.03601
H	1.64758	-2.24657	-1.70712
H	-1.85942	-0.79819	0.57958
C	-0.22274	1.28250	0.12277
O	-1.34594	1.41469	-0.33258
O	0.72554	2.19236	0.07372
C	0.35839	3.45379	-0.52869
H	0.05198	3.28944	-1.56198
H	1.25661	4.06306	-0.47691
H	-0.45657	3.90487	0.03814
H	-0.33298	-1.77310	1.37559
O	-3.05701	-0.41979	0.55282
H	-2.91090	0.45744	0.13915

H	2.12392	0.04568	-1.00916
C	-3.93264	-1.26220	-0.23338
H	-3.99460	-2.21625	0.28634
H	-4.91501	-0.79074	-0.26174
H	-3.53608	-1.38920	-1.24262
H	-0.41749	-0.89089	-1.59450
H	-0.77666	-2.53763	-1.01558
C	3.62813	-1.14749	-0.03268
H	3.70924	-1.92732	0.73152
H	4.05828	-1.53536	-0.95913
H	4.22974	-0.29188	0.28457

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -634.273029
Free energy (gas): -634.026754
Electronic energy (MeOH solvation): -634.3481533
Free energy (MeOH solvation): -634.1018783
Coordinates:

C	0.92018	-0.90441	-1.43169
N	0.13922	-0.55822	-0.21706
C	2.41637	-0.79615	-1.19282
H	0.61093	-0.21826	-2.23196
H	0.62100	-1.91092	-1.72220
C	2.76024	0.54754	-0.55775
C	0.60463	0.36027	0.72153
C	2.07571	0.68403	0.80523
H	2.43369	1.35834	-1.22327
H	3.84121	0.65482	-0.43353
H	0.06718	0.30504	1.67028
C	-1.14741	-1.08069	-0.18117
O	-1.55442	-1.96219	-0.88769
O	-1.94147	-0.43527	0.73558
C	-3.20905	-1.09819	0.99734
H	-3.80127	-1.13623	0.08365
H	-3.69184	-0.49976	1.76694
H	-3.01323	-2.10743	1.35742
H	-0.44883	1.72814	0.35236
O	-1.43121	2.06508	0.24757
H	-1.93457	1.21833	0.44732
H	2.75269	-1.62241	-0.55850
H	2.91727	-0.91321	-2.15734
H	2.16142	1.72410	1.14465
C	2.73471	-0.19526	1.88772
H	3.79730	0.05053	1.96694
H	2.27648	-0.02519	2.86553
H	2.64234	-1.25927	1.65377
C	-1.72425	2.63294	-1.07281
H	-2.76788	2.93754	-1.05508
H	-1.07427	3.49755	-1.18199
H	-1.53417	1.88445	-1.84275

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: exo
Electronic energy (gas): -634.272734

Free energy (gas): -634.02645
Electronic energy (MeOH solvation): -634.3478549
Free energy (MeOH solvation): -634.1015709
Coordinates:

C	1.17387	-1.31699	-1.09621
N	0.25139	-0.67998	-0.12030
C	2.62394	-0.96082	-0.81781
H	0.87878	-0.97550	-2.09685
H	0.99690	-2.39050	-1.04103
C	2.78351	0.54870	-0.66647
C	0.53310	0.55613	0.45670
C	1.95539	1.05637	0.51790
H	2.45559	1.04252	-1.59073
H	3.83291	0.81637	-0.51611
H	-0.09032	0.76925	1.32675
C	-0.97580	-1.31093	0.01659
O	-1.22647	-2.43054	-0.33310
O	-1.92708	-0.48020	0.57341
C	-3.16889	-1.15412	0.91817
H	-3.62670	-1.56308	0.01808
H	-3.79272	-0.39044	1.37828
H	-2.95311	-1.95411	1.62491
H	-0.60847	1.55526	-0.52958
O	-1.59717	1.63502	-0.82633
H	-2.01151	0.87972	-0.28991
H	2.97047	-1.48054	0.08116
H	3.22471	-1.33443	-1.65122
C	-2.19503	2.95905	-0.62745
H	-1.62238	3.64664	-1.24480
H	-3.22038	2.89030	-0.98267
H	-2.14795	3.22831	0.42726
H	1.91813	2.15264	0.48016
C	2.57572	0.67547	1.87768
H	3.60198	1.04874	1.93456
H	2.01187	1.11526	2.70486
H	2.59330	-0.40805	2.02248

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -634.256887
Free energy (gas): -634.011428
Electronic energy (MeOH solvation): -634.3304724
Free energy (MeOH solvation): -634.0850134
Coordinates:

C	-1.78250	0.04330	-1.54124
N	-0.41728	0.07260	-0.96171
C	-2.74887	-0.15661	-0.36066
H	-1.82337	-0.79714	-2.24120
H	-1.96053	0.97354	-2.07943
C	-2.36716	-1.36260	0.50225
C	-0.13398	-1.13928	-0.30524
C	-0.87169	-1.34095	1.00798
H	-2.53233	-2.29002	-0.05733
H	-3.00031	-1.40715	1.39608
H	1.34717	-1.21760	0.01799
C	-0.00658	1.30753	-0.46788
O	-0.61054	2.33609	-0.61043
O	1.20255	1.23138	0.15264
C	1.61531	2.47077	0.77781
H	1.71868	3.24815	0.02154

H	2.57045	2.25616	1.25426
H	0.87353	2.76843	1.51994
H	-0.27126	-1.97700	-0.99845
O	2.44579	-1.09749	0.15953
C	3.24606	-1.82088	-0.82752
H	3.05316	-2.87691	-0.65436
H	2.95447	-1.51844	-1.83333
H	4.28909	-1.58731	-0.62435
H	2.51659	-0.12035	0.08517
H	-2.76503	0.76346	0.23317
H	-3.76059	-0.29853	-0.75434
C	-0.64553	-0.29379	2.09408
H	0.40380	-0.25564	2.40118
H	-0.95073	0.70899	1.77932
H	-1.24088	-0.55132	2.97318
H	-0.63366	-2.33450	1.40160

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: anti
Position of methyl from MeOH: exo
Electronic energy (gas): -634.255323
Free energy (gas): -634.011004
Electronic energy (MeOH solvation): -634.3296795
Free energy (MeOH solvation): -634.0853605
Coordinates:

C	-2.10464	0.27431	-1.23834
N	-0.64957	0.28706	-0.95565
C	-2.78312	-0.27034	0.03126
H	-2.26644	-0.38531	-2.09652
H	-2.42774	1.28371	-1.49020
C	-2.17583	-1.60003	0.49031
C	-0.18638	-1.01299	-0.68786
C	-0.60662	-1.56468	0.66308
H	-2.42815	-2.39147	-0.22405
H	-2.59422	-1.89505	1.45985
H	1.32953	-1.01621	-0.80869
C	-0.17895	1.40906	-0.28131
O	-0.83118	2.39064	-0.04749
O	1.13921	1.29481	0.04069
C	1.64439	2.40980	0.81313
H	1.55522	3.32963	0.23583
H	2.68831	2.17755	1.01864
H	1.07916	2.49688	1.74184
H	-0.45115	-1.67933	-1.51617
O	2.41495	-0.82185	-0.95766
H	2.46535	0.11876	-0.68095
H	-2.70860	0.48934	0.81661
H	-3.84948	-0.41264	-0.17205
C	3.30375	-1.70658	-0.20864
H	3.07234	-2.71618	-0.54033
H	4.32259	-1.44172	-0.48400
H	3.13144	-1.58878	0.86126
C	-0.18709	-0.76800	1.89537
H	0.90097	-0.67242	1.96558
H	-0.61569	0.23884	1.90662
H	-0.53741	-1.27867	2.79546
H	-0.25586	-2.59839	0.75463

Transition state
Substituent: Me
Regioisomer: proximal

Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: syn
Position of methyl from MeOH: endo
Electronic energy (gas): -634.26753
Free energy (gas): -634.024525
Electronic energy (MeOH solvation): -634.3325807
Free energy (MeOH solvation): -634.0895757
Coordinates:

C	-1.61533	-0.47883	-1.44985
N	-0.35258	0.01822	-0.87353
C	-2.25674	-1.36147	-0.35737
H	-1.36002	-1.07238	-2.33350
H	-2.24528	0.35672	-1.74788
C	-1.28550	-2.41795	0.17009
C	0.52822	-1.02914	-0.55949
C	0.08414	-1.83543	0.67816
H	-1.08675	-3.16493	-0.60589
H	-1.73103	-2.94587	1.02229
H	1.74636	-0.56645	-0.18549
C	-0.30367	1.19764	-0.13349
O	0.70219	1.57199	0.45003
O	-1.43624	1.86825	-0.17744
C	-1.43512	3.15479	0.48025
H	-1.23008	3.02172	1.54278
H	-2.43296	3.55421	0.31982
H	-0.67787	3.79616	0.02875
H	0.64874	-1.68087	-1.43040
O	2.78194	-0.02175	0.23534
C	3.84340	0.12312	-0.73975
H	4.16623	-0.88265	-1.00050
H	3.48270	0.65903	-1.61932
H	4.66029	0.66439	-0.26325
H	2.36945	0.84061	0.47167
H	-2.61127	-0.71434	0.45192
H	-3.13761	-1.85274	-0.78356
C	-0.05640	-1.05646	1.97845
H	0.88976	-0.59502	2.27414
H	-0.81454	-0.27008	1.91624
H	-0.35866	-1.74001	2.77575
H	0.78944	-2.66059	0.81585

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: syn
Position of methyl from MeOH: exo
Electronic energy (gas): -634.266132
Free energy (gas): -634.023231
Electronic energy (MeOH solvation): -634.3317307
Free energy (MeOH solvation): -634.0888297
Coordinates:

C	1.67730	0.98106	-1.22228
N	0.53975	0.09827	-0.91111
C	1.80759	1.92956	-0.01062
H	1.42193	1.53659	-2.13021
H	2.57414	0.39126	-1.40091
C	0.48303	2.61402	0.33137
C	-0.65803	0.81469	-0.77255
C	-0.72042	1.62188	0.53774
H	0.21842	3.32949	-0.45453
H	0.58367	3.18041	1.26530
H	-1.71559	-0.04090	-0.73965

C	0.70707	-1.09262	-0.20344
O	-0.23365	-1.77554	0.16775
O	1.97567	-1.39909	-0.02731
C	2.23553	-2.67369	0.60222
H	1.81513	-2.67680	1.60839
H	3.31844	-2.75962	0.62900
H	1.79135	-3.47229	0.00749
H	-0.79680	1.46574	-1.64115
O	-2.57454	-0.93575	-0.72775
H	-2.04623	-1.63684	-0.28789
H	2.18573	1.35511	0.84181
H	2.56189	2.68818	-0.24412
C	-3.81587	-0.62733	-0.05156
H	-4.27644	0.18839	-0.60540
H	-4.45073	-1.51183	-0.09917
H	-3.62938	-0.33983	0.98465
C	-0.60098	0.83086	1.83382
H	-1.37326	0.06091	1.91647
H	0.36914	0.33586	1.93540
H	-0.71089	1.51052	2.68252
H	-1.64994	2.20040	0.53997

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -634.275644
Free energy (gas): -634.02968
Electronic energy (MeOH solvation): -634.3506891
Free energy (MeOH solvation): -634.1047251
Coordinates:

C	-0.71060	-1.67975	0.89475
N	0.00704	-0.80566	-0.06817
C	-2.18778	-1.79417	0.55906
H	-0.57757	-1.25224	1.89731
H	-0.20856	-2.64691	0.87693
C	-2.79715	-0.41343	0.34071
C	-0.63616	0.21079	-0.76716
C	-2.13762	0.24980	-0.86537
H	-2.64820	0.21051	1.23509
H	-3.87590	-0.48123	0.17519
H	-2.40663	-0.33963	-1.75863
H	-0.07799	0.55573	-1.63953
C	1.38389	-0.98448	-0.10336
O	1.96967	-1.91434	0.38075
O	2.02532	0.06081	-0.72092
C	3.42800	-0.19046	-1.01178
H	3.97575	-0.34214	-0.08212
H	3.77275	0.69300	-1.54483
H	3.50549	-1.07739	-1.63925
H	0.03199	1.64375	0.05496
O	0.89231	2.14062	0.36673
H	1.59925	1.52916	0.00031
C	0.95891	2.30878	1.82297
H	1.90376	2.80278	2.03616
H	0.12112	2.94717	2.09251
H	0.89335	1.33242	2.30466
H	-2.31771	-2.40506	-0.34194
H	-2.67817	-2.32281	1.38037
C	-2.61981	1.68426	-1.09330
H	-2.11407	2.15189	-1.94375
H	-3.69339	1.69667	-1.29557

H -2.44304 2.29910 -0.20233

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: exo
Electronic energy (gas): -634.275886
Free energy (gas): -634.029128
Electronic energy (MeOH solvation): -634.3508405
Free energy (MeOH solvation): -634.1040825
Coordinates:

C	0.94831	-1.82340	-0.75137
N	0.09949	-0.91206	0.05954
C	2.40987	-1.73349	-0.34822
H	0.82076	-1.54397	-1.80487
H	0.54591	-2.82725	-0.61906
C	2.86874	-0.27944	-0.31404
C	0.59886	0.26251	0.60992
C	2.08176	0.48022	0.75118
H	2.71162	0.18866	-1.29673
H	3.93770	-0.21017	-0.09386
H	2.36592	0.06679	1.73415
H	-0.03250	0.67072	1.40115
C	-1.24928	-1.23674	0.07835
O	-1.71226	-2.29239	-0.25311
O	-2.03209	-0.17846	0.48683
C	-3.42523	-0.53051	0.71073
H	-3.86910	-0.88250	-0.21989
H	-3.89917	0.38274	1.06490
H	-3.47675	-1.31120	1.46846
H	-0.16835	1.44345	-0.51842
O	-1.07326	1.75922	-0.91455
H	-1.71015	1.14474	-0.42607
H	2.55403	-2.19448	0.63596
H	2.99158	-2.31750	-1.06607
C	2.39677	1.97769	0.76867
H	1.80358	2.50655	1.52228
H	3.45126	2.14419	1.00138
H	2.20114	2.42576	-0.21334
C	-1.33228	3.19212	-0.73788
H	-0.55163	3.71163	-1.28795
H	-2.30674	3.38594	-1.17953
H	-1.30983	3.43961	0.32323

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -634.258592
Free energy (gas): -634.014009
Electronic energy (MeOH solvation): -634.3324445
Free energy (MeOH solvation): -634.0878615
Coordinates:

C	-1.72429	0.74292	-1.43264
N	-0.36823	0.46856	-0.88981
C	-2.70865	0.48684	-0.27890
H	-1.88807	0.05262	-2.26541
H	-1.76053	1.76819	-1.79858
C	-2.50597	-0.88574	0.36885

C	-0.27599	-0.87424	-0.47404
C	-1.02252	-1.18201	0.80177
H	-2.82090	-1.68254	-0.31718
H	-3.12265	-0.97508	1.27071
H	1.22437	-1.23695	-0.20722
C	0.17276	1.50652	-0.13521
O	-0.25802	2.62663	-0.10286
O	1.30043	1.12633	0.53386
C	1.86673	2.17172	1.36460
H	2.19162	3.00189	0.73790
H	2.70821	1.71165	1.87965
H	1.11879	2.51612	2.07798
H	-0.51285	-1.55354	-1.30213
O	2.30235	-1.22919	-0.05020
C	3.05993	-1.67086	-1.22291
H	2.81941	-2.72277	-1.35679
H	2.77257	-1.07737	-2.09080
H	4.11362	-1.54790	-0.98188
H	2.42127	-0.27334	0.16209
H	-2.58230	1.28238	0.46388
H	-3.73167	0.56480	-0.66080
H	-0.74006	-0.46385	1.58276
C	-0.85278	-2.61145	1.29453
H	0.16575	-2.79573	1.64916
H	-1.53384	-2.81257	2.12491
H	-1.07843	-3.32829	0.49774

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: anti
Position of methyl from MeOH: exo
Electronic energy (gas): -634.256949
Free energy (gas): -634.014016
Electronic energy (MeOH solvation): -634.330622
Free energy (MeOH solvation): -634.087689
Coordinates:

C	2.14287	0.28184	1.18136
N	0.70049	0.43223	0.88052
C	2.76227	-0.35426	-0.07813
H	2.23137	-0.37346	2.05255
H	2.56754	1.25790	1.41224
C	2.01505	-1.61235	-0.52823
C	0.10238	-0.81654	0.65701
C	0.46194	-1.42328	-0.68685
H	2.18328	-2.43207	0.18199
H	2.39341	-1.94758	-1.50119
H	-1.37825	-0.64836	0.76836
C	0.37089	1.54963	0.11029
O	1.12196	2.45611	-0.12585
O	-0.92356	1.51924	-0.30098
C	-1.29894	2.65282	-1.12190
H	-1.20728	3.57220	-0.54370
H	-2.33294	2.47396	-1.41220
H	-0.65408	2.69964	-1.99900
H	0.30283	-1.49011	1.49903
O	-2.44780	-0.31648	0.93363
H	-2.42383	0.58787	0.55886
H	2.76022	0.39672	-0.87582
H	3.80831	-0.60179	0.12929
H	0.28022	-0.69463	-1.48754
C	-0.23844	-2.73986	-0.98379
H	-1.30742	-2.59423	-1.16709

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H          0.18498       -3.20649       -1.87669
H         -0.12192       -3.44319       -0.15238
C         -3.48715       -1.16466        0.35972
H         -3.32176       -2.16043        0.76545
H         -4.44324       -0.77202        0.70086
H         -3.41488       -1.16058       -0.72784

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: syn
Position of methyl from MeOH: endo
Electronic energy (gas): -634.269603
Free energy (gas): -634.02746
Electronic energy (MeOH solvation): -634.3346033
Free energy (MeOH solvation): -634.0924603
Coordinates:
C         -1.32883        1.18751        1.34998
N         -0.50155        0.08420        0.82705
C         -1.35763        2.24023        0.22007
H         -0.83062        1.57847        2.24220
H         -2.31807        0.82300        1.61887
C          0.04522        2.60041       -0.26789
C          0.81702        0.49014        0.57896
C          0.92952        1.37325       -0.67666
H          0.58321        3.16803        0.50179
H         -0.01878        3.24249       -1.15517
H          0.46279        0.85810       -1.52522
H          1.60824       -0.55763        0.23663
C         -1.06123       -0.88094       -0.01596
O         -0.38468       -1.66114       -0.66654
O         -2.37669       -0.87080        0.01318
C         -3.03561       -1.89388       -0.76644
H         -2.78994       -1.76442       -1.82077
H         -4.09698       -1.74260       -0.58911
H         -2.71511       -2.87783       -0.42364
H          1.23486        0.98356        1.46291
O          2.21643       -1.55115       -0.19929
C          2.91604       -2.33726        0.79632
H          3.67023       -1.68527        1.23244
H          2.22085       -2.69453        1.55764
H          3.39569       -3.17136        0.28491
H          1.43829       -2.02231       -0.57112
H         -1.96104        1.84474       -0.60520
H         -1.86484        3.13680        0.59126
C          2.35740        1.77267       -1.00560
H          2.94979        0.90926       -1.31942
H          2.36634        2.49826       -1.82299
H          2.84405        2.23573       -0.14086

Transition state
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: equatorial
Oxamate conformation: syn
Position of methyl from MeOH: exo
Electronic energy (gas): -634.267783
Free energy (gas): -634.025834
Electronic energy (MeOH solvation): -634.3343041
Free energy (MeOH solvation): -634.0910946
Coordinates:
C         -1.46585        1.28116        1.20913
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N	-0.61323	0.13567	0.84705
C	-1.38618	2.23693	-0.00307
H	-1.03803	1.74100	2.10489
H	-2.47911	0.94674	1.42190
C	0.05675	2.53947	-0.40605
C	0.72778	0.50656	0.68020
C	0.94977	1.27353	-0.63351
H	0.54089	3.16825	0.35188
H	0.07052	3.10327	-1.34718
H	1.50242	-0.61308	0.61793
C	-1.11303	-0.89790	0.04569
O	-0.39246	-1.73932	-0.46416
O	-2.42485	-0.86767	-0.05133
C	-3.03085	-1.96259	-0.77423
H	-2.65404	-1.97992	-1.79697
H	-4.09789	-1.75830	-0.75118
H	-2.79992	-2.90236	-0.27181
H	1.06772	1.08089	1.54881
O	2.02019	-1.74375	0.61496
H	1.34617	-2.22087	0.08604
H	-1.92892	1.78055	-0.83894
H	-1.90556	3.16648	0.25147
C	3.37216	-1.90357	0.12434
H	3.99175	-1.20765	0.68725
H	3.68049	-2.92753	0.33506
H	3.42094	-1.69437	-0.94501
H	0.54252	0.69169	-1.46944
C	2.40321	1.63811	-0.88375
H	2.83583	2.14906	-0.01728
H	3.00739	0.75322	-1.10197
H	2.48398	2.30895	-1.74303

Transition state
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -825.944902
Free energy (gas): -825.648879
Electronic energy (MeOH solvation): -826.0210526
Free energy (MeOH solvation): -825.7250296
Coordinates:

C	-0.05304	-0.34647	1.41399
N	-0.84921	0.06393	0.22820
C	1.19762	-1.13002	1.03756
H	-0.69807	-0.96729	2.04820
H	0.18347	0.56159	1.96879
C	0.79436	-2.26731	0.08369
C	-0.84409	-0.66544	-0.95893
C	0.24545	-1.66831	-1.20566
H	0.03846	-2.90066	0.56763
H	1.65135	-2.90502	-0.14401
H	-0.12296	-2.43993	-1.88903
H	1.06188	-1.15388	-1.73680
H	-1.19775	-0.09087	-1.81635
C	-1.66939	1.16651	0.42421
O	-1.58019	1.93968	1.33914
O	-2.64405	1.26268	-0.53862
C	-3.37254	2.52118	-0.52465
H	-3.87232	2.64613	0.43525
H	-4.08397	2.45052	-1.34454
H	-2.67035	3.33734	-0.68967
H	-2.45972	-1.35389	-0.89803

O	-3.48536	-1.17668	-0.79710
H	-3.48080	-0.17542	-0.70663
H	1.56114	-1.57288	1.97263
C	-4.08575	-1.86802	0.34821
H	-5.12830	-1.56139	0.38574
H	-4.00642	-2.93153	0.13697
H	-3.55084	-1.59641	1.25896
C	2.31895	-0.28215	0.45419
C	2.16869	1.06395	0.11260
C	3.56375	-0.88884	0.24296
C	3.23223	1.78320	-0.43633
H	1.22852	1.58136	0.28397
C	4.62502	-0.17511	-0.30313
H	3.71046	-1.92938	0.52453
C	4.46026	1.16593	-0.65024
H	3.09733	2.83013	-0.68858
H	5.58369	-0.66190	-0.45020
H	5.28725	1.72584	-1.07428

Transition state
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: syn
Position of methyl from MeOH: exo
Electronic energy (gas): -825.95452
Free energy (gas): -825.661685
Electronic energy (MeOH solvation): -826.0213105
Free energy (MeOH solvation): -825.7284755
Coordinates:

C	-0.07377	0.34326	1.38533
N	-0.88660	0.28385	0.14883
C	1.09892	-0.63057	1.36199
H	-0.74189	0.10911	2.22393
H	0.26027	1.37495	1.50247
C	0.58992	-2.01710	0.93136
C	-0.99044	-0.85274	-0.64381
C	0.05409	-1.93187	-0.49217
H	-0.19580	-2.35307	1.62055
H	1.39825	-2.75043	0.97776
H	-1.28060	-0.59428	-1.66923
C	-1.83417	1.30602	-0.10720
O	-1.54143	2.41532	0.53048
O	-2.79063	1.12343	-0.83170
H	-2.18722	-1.30738	-0.31927
O	-3.48206	-1.45838	-0.09199
H	-3.84537	-0.64118	-0.48314
C	-2.46253	3.51423	0.33814
H	-2.50978	3.76751	-0.72103
H	-3.44966	3.22894	0.70282
H	-2.04913	4.33253	0.92137
C	-4.09767	-2.64820	-0.63867
H	-5.15964	-2.62945	-0.39389
H	-3.95053	-2.69533	-1.71907
H	-3.62153	-3.49413	-0.14672
H	0.87931	-1.69885	-1.18116
H	-0.36942	-2.88386	-0.82677
H	1.44942	-0.69510	2.39866
C	2.26603	-0.17653	0.49849
C	2.17677	0.86383	-0.43023
C	3.48369	-0.85689	0.62412
C	3.27354	1.20859	-1.22279
H	1.25667	1.43149	-0.54628
C	4.57858	-0.51461	-0.16232

H	3.57942	-1.65656	1.35557
C	4.47473	0.51957	-1.09338
H	3.18583	2.02134	-1.93655
H	5.51590	-1.04848	-0.04397
H	5.32852	0.79029	-1.70542

Transition state
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -825.944558
Free energy (gas): -825.648783
Electronic energy (MeOH solvation): -826.0215429
Free energy (MeOH solvation): -825.7257679
Coordinates:

C	-0.18260	0.51200	-0.09600
N	1.19965	0.36919	0.43000
C	-1.23126	-0.04184	0.86618
H	-0.23797	-0.01846	-1.05648
H	-0.34426	1.57205	-0.29276
C	-0.83942	-1.45881	1.29124
C	1.55510	-0.65935	1.29825
C	0.48447	-1.40166	2.04636
H	-0.74657	-2.10405	0.40703
H	-1.61630	-1.89359	1.92520
H	0.85340	-2.40107	2.29902
H	0.32817	-0.88971	3.00927
H	2.49280	-0.47472	1.82353
C	2.12886	1.24300	-0.11907
O	1.86207	2.22137	-0.76168
O	3.42119	0.83645	0.11540
C	4.42683	1.83444	-0.21241
H	4.38688	2.06273	-1.27702
H	5.37746	1.38705	0.07000
H	4.23357	2.73492	0.36916
H	2.51850	-1.65705	0.19325
O	3.31701	-1.68696	-0.47508
H	3.63768	-0.73545	-0.41487
C	2.92807	-2.09382	-1.82998
H	3.83571	-2.08836	-2.42850
H	2.53222	-3.10249	-1.74195
H	2.18200	-1.39979	-2.21864
H	-1.23185	0.59196	1.76370
C	-2.60170	0.05766	0.22816
C	-3.53183	0.97866	0.71547
C	-2.95638	-0.74812	-0.85945
C	-4.79222	1.09393	0.13204
H	-3.27053	1.60843	1.56228
C	-4.21497	-0.63488	-1.44510
H	-2.25367	-1.47800	-1.25631
C	-5.13589	0.28778	-0.95028
H	-5.50444	1.81201	0.52512
H	-4.47809	-1.26742	-2.28676
H	-6.11672	0.37597	-1.40570

Transition state
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: exo

Electronic energy (gas): -825.944266
Free energy (gas): -825.648169
Electronic energy (MeOH solvation): -826.0213346
Free energy (MeOH solvation): -825.7252376
Coordinates:

C	-0.30069	0.57141	-0.06682
N	1.10136	0.41405	0.40209
C	-1.29751	-0.18356	0.81022
H	-0.35349	0.20259	-1.09973
H	-0.51537	1.64014	-0.08173
C	-0.82824	-1.62842	0.99526
C	1.52987	-0.73088	1.06594
C	0.51431	-1.62614	1.71884
H	-0.73201	-2.12064	0.01863
H	-1.56524	-2.19485	1.57031
H	0.93037	-2.63497	1.80723
H	0.36616	-1.27177	2.75169
H	2.47912	-0.59421	1.58488
C	1.97187	1.41185	-0.01548
O	1.64521	2.48457	-0.43987
O	3.28967	1.01733	0.07062
C	4.24170	2.09277	-0.15625
H	4.11293	2.49276	-1.16134
H	5.22295	1.64161	-0.02397
H	4.07424	2.87554	0.58222
H	2.42730	-1.46778	-0.28918
O	3.17497	-1.32034	-0.99824
H	3.49399	-0.39829	-0.73664
H	-1.31147	0.29754	1.79798
C	-2.68267	-0.05681	0.20876
C	-3.63233	0.77520	0.80563
C	-3.02725	-0.74602	-0.95886
C	-4.90381	0.91490	0.25159
H	-3.37771	1.31664	1.71352
C	-4.29698	-0.60891	-1.51443
H	-2.30743	-1.40238	-1.44271
C	-5.23824	0.22271	-0.90977
H	-5.63164	1.56339	0.72836
H	-4.55205	-1.15334	-2.41786
H	-6.22774	0.32926	-1.34194
C	4.21091	-2.35752	-1.01993
H	3.71503	-3.27534	-1.32573
H	4.93982	-2.05002	-1.76604
H	4.65818	-2.45023	-0.03068

Transition state
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: syn
Position of methyl from MeOH: exo
Electronic energy (gas): -825.953797
Free energy (gas): -825.661802
Electronic energy (MeOH solvation): -826.0212858
Free energy (MeOH solvation): -825.7292908
Coordinates:

C	-0.15163	0.60368	0.11557
N	1.24556	0.39295	0.55500
C	-1.14107	-0.30329	0.84791
H	-0.18866	0.41259	-0.96618
H	-0.38806	1.65682	0.27302
C	-0.62876	-1.74586	0.84069
C	1.71131	-0.82013	1.04569
C	0.70356	-1.81349	1.57930

H	-0.50837	-2.09743	-0.19227
H	-1.35861	-2.40396	1.31898
H	2.62118	-0.68122	1.64134
C	2.24424	1.32811	0.16790
O	1.73200	2.50452	-0.10124
O	3.41382	1.01565	0.09926
H	2.33471	-1.30592	0.01032
O	3.14510	-1.52079	-1.04662
H	3.78839	-0.79344	-0.95645
C	2.67443	3.52001	-0.51852
H	3.41375	3.67413	0.26751
H	3.16366	3.20396	-1.44036
H	2.07469	4.41199	-0.67740
H	-1.19737	0.03243	1.89222
C	3.79140	-2.81218	-1.11609
H	4.43052	-2.83220	-1.99899
H	4.37518	-3.00053	-0.21324
H	2.99725	-3.54890	-1.22167
H	0.55038	-1.59742	2.64598
H	1.14255	-2.81506	1.53293
C	-2.51425	-0.13904	0.22762
C	-3.53696	0.49159	0.93905
C	-2.77645	-0.60496	-1.06524
C	-4.80104	0.65164	0.37251
H	-3.34759	0.85559	1.94604
C	-4.03790	-0.44631	-1.63328
H	-1.99830	-1.10459	-1.63877
C	-5.05333	0.18311	-0.91417
H	-5.58726	1.14073	0.93831
H	-4.22875	-0.81634	-2.63546
H	-6.03680	0.30576	-1.35564

Transition state
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: endo
Electronic energy (gas): -825.939823
Free energy (gas): -825.643795
Electronic energy (MeOH solvation): -826.0156342
Free energy (MeOH solvation): -825.7196062
Coordinates:

C	1.05460	-2.06084	-0.77116
N	1.08816	-0.60737	-0.49339
C	-0.35291	-2.60208	-0.60781
H	1.74266	-2.55635	-0.07229
H	1.43665	-2.20026	-1.78135
C	-0.88342	-2.27185	0.78592
C	0.30073	-0.04594	0.50807
C	-0.93380	-0.76010	1.03637
H	-0.22148	-2.73454	1.52907
H	-1.87652	-2.69822	0.94769
H	0.21084	1.03710	0.41440
C	2.03549	0.12040	-1.20127
O	2.63729	-0.27450	-2.16260
O	2.25521	1.35713	-0.64499
C	3.03612	2.25603	-1.47924
H	4.02969	1.83899	-1.64063
H	3.07583	3.19431	-0.93027
H	2.52644	2.38584	-2.43302
H	1.55203	0.31162	1.69267
O	2.45432	0.80347	1.88225
H	2.63100	1.20852	0.97886

H	-0.98739	-2.17427	-1.39012
H	-0.32488	-3.68396	-0.76312
H	-0.95305	-0.59771	2.12220
C	3.52464	-0.08450	2.34856
H	4.40619	0.53724	2.48617
H	3.18941	-0.49088	3.29944
H	3.69411	-0.86936	1.61077
C	-2.17370	-0.03645	0.49362
C	-2.41474	1.27013	0.93681
C	-3.07692	-0.61612	-0.39865
C	-3.51862	1.98819	0.49085
H	-1.74235	1.72590	1.66257
C	-4.18703	0.10196	-0.84714
H	-2.94539	-1.63703	-0.74070
C	-4.40808	1.40440	-0.41118
H	-3.69241	2.99516	0.85624
H	-4.88314	-0.36622	-1.53558
H	-5.27405	1.95757	-0.75929

Transition state
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: exo
Electronic energy (gas): -825.939616
Free energy (gas): -825.643071
Electronic energy (MeOH solvation): -826.0155952
Free energy (MeOH solvation): -825.7190502
Coordinates:

C	-0.90426	2.36467	0.28086
N	-1.05745	0.94969	-0.13220
C	0.53222	2.65609	0.67152
H	-1.58288	2.54230	1.12543
H	-1.23380	2.97645	-0.55761
C	0.99683	1.67591	1.74674
C	-0.35055	-0.06823	0.50078
C	0.93418	0.22424	1.25962
H	0.34660	1.78479	2.62384
H	2.01220	1.90170	2.08225
H	-0.35942	-0.99919	-0.06679
C	-2.05380	0.70525	-1.06611
O	-2.58192	1.53295	-1.75511
O	-2.42176	-0.62328	-1.09242
C	-3.30771	-0.96807	-2.19243
H	-4.24744	-0.42592	-2.09181
H	-3.45250	-2.04398	-2.11851
H	-2.82303	-0.70665	-3.13202
H	-1.70436	-0.72602	1.46679
O	-2.67057	-1.10631	1.41327
H	-2.81347	-1.09910	0.41040
H	1.15981	2.59745	-0.22279
H	0.58352	3.68407	1.04040
C	-2.84893	-2.40901	2.06098
H	-2.67469	-2.24785	3.12182
H	-3.88049	-2.70368	1.88346
H	-2.14496	-3.12680	1.64062
H	0.93646	-0.42845	2.14280
C	2.11957	-0.24069	0.40216
C	2.24760	-1.61148	0.14450
C	3.08442	0.62566	-0.11445
C	3.29597	-2.10552	-0.62352
H	1.52892	-2.31001	0.57162
C	4.13849	0.13340	-0.88592

H	3.04454	1.68991	0.09008
C	4.24466	-1.22837	-1.14916
H	3.38138	-3.17268	-0.80143
H	4.88091	0.82260	-1.27499
H	5.06679	-1.60667	-1.74747

Transition state
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: axial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: syn
Position of methyl from MeOH: exo
Electronic energy (gas): -825.949447
Free energy (gas): -825.656669
Electronic energy (MeOH solvation): -826.0163262
Free energy (MeOH solvation): -825.7235482
Coordinates:

C	1.17274	-1.40299	1.46906
N	1.14695	-0.58272	0.24085
C	-0.19732	-1.44444	2.12249
H	1.91877	-0.96169	2.14445
H	1.51904	-2.39660	1.18764
C	-0.74986	-0.03183	2.30548
C	0.33373	0.53390	0.10131
C	-0.92050	0.68130	0.96053
H	-0.05479	0.54493	2.92874
H	-1.70434	-0.04409	2.83715
H	0.21551	0.79412	-0.95642
C	2.20651	-0.69613	-0.69264
O	2.81149	-1.85785	-0.60986
O	2.49418	0.21079	-1.44738
H	1.19193	1.52038	0.34704
O	2.22103	2.33073	0.31758
H	2.66491	2.05083	-0.50637
C	3.91928	-2.05814	-1.51731
H	3.56261	-1.99134	-2.54521
H	4.68330	-1.30258	-1.33279
H	4.28928	-3.05494	-1.29314
H	-0.86390	-2.05339	1.50536
H	-0.09463	-1.94734	3.08773
H	-1.03535	1.75595	1.15474
C	1.93517	3.74975	0.33582
H	2.88050	4.28943	0.28032
H	1.28535	4.02083	-0.49798
H	1.44957	3.95322	1.28819
C	-2.14599	0.26792	0.13467
C	-2.43173	0.97616	-1.04004
C	-3.01444	-0.75373	0.52297
C	-3.53990	0.65908	-1.81879
H	-1.79596	1.80642	-1.34360
C	-4.12817	-1.07256	-0.25520
H	-2.85593	-1.30256	1.44474
C	-4.38980	-0.37576	-1.43048
H	-3.74566	1.22525	-2.72134
H	-4.79473	-1.86553	0.06791
H	-5.25606	-0.62675	-2.03323

Transition state
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: endo

Electronic energy (gas): -825.949572
Free energy (gas): -825.652975
Electronic energy (MeOH solvation): -826.0209631
Free energy (MeOH solvation): -825.7243661
Coordinates:

C	-2.19573	2.00836	0.45366
N	-1.81450	0.69167	-0.11829
C	-1.19623	3.08223	0.06260
H	-2.24497	1.90196	1.54311
H	-3.20371	2.23066	0.09900
C	0.21995	2.57989	0.32053
C	-0.58666	0.44769	-0.72068
C	0.53311	1.46375	-0.67387
H	0.27468	2.20710	1.35175
H	0.96024	3.37818	0.22080
H	0.61489	1.92493	-1.67126
H	-0.62929	-0.24241	-1.56553
C	-2.78743	-0.28344	0.00429
O	-3.91036	-0.08305	0.38464
O	-2.32693	-1.53262	-0.32981
C	-3.37794	-2.52832	-0.43001
H	-3.85387	-2.66295	0.54100
H	-2.88354	-3.43882	-0.76426
H	-4.11572	-2.20046	-1.16145
H	0.25231	-1.04570	-0.01204
O	0.18143	-2.01992	0.28487
H	-0.80179	-2.15243	0.34185
C	0.99612	-2.34238	1.46311
H	0.87642	-3.40900	1.63669
H	2.01857	-2.09842	1.17787
H	0.66087	-1.74649	2.31087
H	-1.31707	3.34956	-0.99387
H	-1.41474	3.97752	0.64957
C	1.84245	0.71275	-0.42077
C	2.31351	-0.18155	-1.39454
C	2.57718	0.85898	0.76056
C	3.47873	-0.91711	-1.18912
H	1.77698	-0.28562	-2.33611
C	3.75287	0.13190	0.96271
H	2.25901	1.56084	1.52382
C	4.20374	-0.76166	-0.00591
H	3.83281	-1.59301	-1.96103
H	4.32114	0.27799	1.87605
H	5.12322	-1.31711	0.14808

Transition state
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: anti
Position of methyl from MeOH: exo
Electronic energy (gas): -825.952959
Free energy (gas): -825.656037
Electronic energy (MeOH solvation): -826.0155952
Free energy (MeOH solvation): -825.7186732
Coordinates:

C	2.20515	2.02059	-0.40990
N	1.82321	0.69085	0.12786
C	1.20125	3.08851	-0.00776
H	2.26625	1.93690	-1.50139
H	3.20755	2.23626	-0.03790
C	-0.21991	2.62199	-0.31168
C	0.53622	0.39354	0.55135
C	-0.54855	1.44031	0.60047

H	-0.27830	2.33195	-1.36805
H	-0.95019	3.41930	-0.15226
H	-0.59603	1.82827	1.63131
H	0.48577	-0.40649	1.29192
C	2.81497	-0.27287	0.05317
O	3.96702	-0.05149	-0.20491
O	2.33292	-1.54041	0.28113
C	3.37671	-2.54391	0.39384
H	3.92868	-2.60895	-0.54339
H	2.86029	-3.47529	0.61925
H	4.05045	-2.27116	1.20514
H	-0.10863	-0.85500	-0.62872
O	0.00790	-1.82031	-0.96177
H	0.91920	-2.02538	-0.60617
H	1.30253	3.31909	1.05941
H	1.44389	4.00042	-0.55881
C	-1.87199	0.73093	0.33050
C	-2.55349	0.12612	1.39335
C	-2.39486	0.60186	-0.96273
C	-3.73338	-0.58430	1.17506
H	-2.16813	0.23203	2.40533
C	-3.58170	-0.10017	-1.18221
H	-1.89817	1.07033	-1.80744
C	-4.25227	-0.69730	-0.11496
H	-4.25640	-1.03247	2.01395
H	-3.98772	-0.16784	-2.18667
H	-5.18162	-1.23113	-0.28493
C	-1.04714	-2.69251	-0.41542
H	-0.93287	-3.65499	-0.90786
H	-0.92695	-2.76457	0.66557
H	-1.99098	-2.21613	-0.67742

Transition state
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Hydrogen being attacked by MeOH: axial
Oxamate conformation: syn
Position of methyl from MeOH: endo
Electronic energy (gas): -825.952123
Free energy (gas): -825.658751
Electronic energy (MeOH solvation): -826.0206082
Free energy (MeOH solvation): -825.7272362
Coordinates:

C	-1.81984	1.54982	0.94776
N	-1.52618	0.62033	-0.15888
C	-0.68804	2.53926	1.19029
H	-1.99040	0.92583	1.83855
H	-2.76401	2.04245	0.71301
C	0.66646	1.83883	1.21769
C	-0.22456	0.22615	-0.49584
C	0.91682	1.17378	-0.13691
H	0.69606	1.08706	2.01826
H	1.46854	2.55261	1.42167
H	-0.19811	-0.16090	-1.52279
C	-2.58522	-0.16313	-0.73524
O	-3.76042	0.35371	-0.46186
O	-2.34946	-1.16407	-1.36181
H	-0.10610	-0.82043	0.07148
O	-0.33079	-2.31827	0.59601
H	-0.71319	-2.79847	-0.15398
C	-4.89578	-0.35849	-1.01209
H	-4.79477	-0.41738	-2.09598
H	-4.93754	-1.35991	-0.58228
H	-5.76309	0.22977	-0.72625

H 0.90355 1.96370 -0.90301
C -1.22446 -2.35125 1.70957
H -1.40399 -3.38290 2.02087
H -0.73390 -1.81409 2.52235
H -2.18237 -1.87371 1.46927
H -0.69713 3.30305 0.40462
H -0.89530 3.04912 2.13465
C 2.24818 0.45911 -0.24108
C 3.19683 0.88760 -1.17103
C 2.55556 -0.61767 0.59723
C 4.43591 0.25482 -1.26228
H 2.97029 1.72507 -1.82632
C 3.79057 -1.25411 0.50460
H 1.83186 -0.97007 1.32956
C 4.73384 -0.81717 -0.42541
H 5.16545 0.60146 -1.98678
H 4.01800 -2.08945 1.15882
H 5.69713 -1.31146 -0.49591

Minimum
Type: Radical
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: axial
Oxamate conformation: anti
Electronic energy (gas): -518.253577
Free energy (gas): -518.076247
Electronic energy (MeOH solvation): -518.2602883
Free energy (MeOH solvation): -518.0829583
Coordinates:
C 0.76459 -0.95710 -0.79927
N -0.17390 0.04925 -0.28573
C 2.14877 -0.78463 -0.17481
H 0.82850 -0.84771 -1.89075
H 0.34313 -1.93820 -0.57891
C 2.64009 0.64425 -0.43760
C 2.13499 -1.14004 1.31349
C 0.24452 1.37963 -0.20452
C 1.66756 1.66893 0.15332
H 2.71585 0.80097 -1.52107
H 3.64057 0.78786 -0.01513
H 1.92098 2.67812 -0.18662
H 1.78466 1.68347 1.25106
H -0.53370 2.09594 0.01359
C -1.48839 -0.33346 -0.16301
O -1.90515 -1.45554 -0.38330
O -2.27611 0.68506 0.23733
C -3.65437 0.34390 0.38444
H -4.06136 -0.01408 -0.56316
H -4.14900 1.26317 0.69439
H -3.77567 -0.43326 1.14164
H 1.39791 -0.54343 1.86027
H 3.11591 -0.96539 1.76688
H 1.87654 -2.19358 1.45707
H 2.81656 -1.48378 -0.69361

Minimum
Type: Radical
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: axial
Oxamate conformation: syn
Electronic energy (gas): -518.252972

Free energy (gas): -518.075841
Electronic energy (MeOH solvation): -518.2601077
Free energy (MeOH solvation): -518.0829767
Coordinates:

C	0.44670	-0.85645	-0.78178
N	-0.15658	0.33375	-0.16523
C	1.87782	-1.06318	-0.28222
H	0.44505	-0.72650	-1.87301
H	-0.17318	-1.71837	-0.53843
C	2.69521	0.20489	-0.55317
C	1.89332	-1.46945	1.19319
C	0.60090	1.50564	-0.08064
C	2.07191	1.40735	0.16022
H	2.71179	0.39426	-1.63400
H	3.73216	0.06653	-0.22831
H	2.54806	2.33746	-0.16561
H	2.27511	1.32849	1.24274
H	0.03695	2.37582	0.22531
C	-1.51070	0.42457	0.06060
O	-2.07383	1.41219	0.48929
O	-2.15557	-0.71991	-0.25578
C	-3.56056	-0.69195	-0.00540
H	-3.93244	-1.66324	-0.32768
H	-4.03259	0.11166	-0.57369
H	-3.75445	-0.53763	1.05822
H	1.35645	-0.74307	1.81143
H	2.91903	-1.54190	1.56862
H	1.41166	-2.44209	1.33317
H	2.30006	-1.88437	-0.87503

Minimum
Type: Radical
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: equatorial
Oxamate conformation: anti
Electronic energy (gas): -518.253577
Free energy (gas): -518.076248
Electronic energy (MeOH solvation): -518.2602885
Free energy (MeOH solvation): -518.0829595
Coordinates:

C	0.76447	-0.95740	-0.79871
N	-0.17395	0.04907	-0.28522
C	2.14890	-0.78454	-0.17489
H	0.82790	-0.84854	-1.89028
H	0.34322	-1.93845	-0.57772
C	2.63993	0.64432	-0.43826
C	2.13581	-1.13957	1.31344
C	0.24439	1.37947	-0.20424
C	1.66756	1.66896	0.15296
H	2.71515	0.80085	-1.52179
H	3.64059	0.78814	-0.01630
H	1.92067	2.67814	-0.18723
H	1.78514	1.68368	1.25065
H	-0.53378	2.09572	0.01419
C	-1.48852	-0.33354	-0.16284
O	-1.90531	-1.45555	-0.38338
O	-2.27621	0.68497	0.23760
C	-3.65458	0.34399	0.38411
H	-4.06087	-0.01528	-0.56328
H	-4.14946	1.26365	0.69249
H	-3.77641	-0.43216	1.14226
H	1.39869	-0.54318	1.86039
H	3.11684	-0.96447	1.76643

H	1.87787	-2.19319	1.45739
H	2.81648	-1.48382	-0.69383

Minimum
Type: Radical
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: equatorial
Oxamate conformation: syn
Electronic energy (gas): -518.252972
Free energy (gas): -518.075848
Electronic energy (MeOH solvation): -518.260107
Free energy (MeOH solvation): -518.082983
Coordinates:

C	0.44673	0.85629	0.78195
N	-0.15662	-0.33381	0.16528
C	1.87791	1.06309	0.28241
H	0.44517	0.72610	1.87315
H	-0.17313	1.71826	0.53876
C	2.69526	-0.20512	0.55293
C	1.89342	1.46997	-1.19281
C	0.60081	-1.50570	0.08032
C	2.07184	-1.40748	-0.16045
H	2.71205	-0.39471	1.63372
H	3.73219	-0.06678	0.22793
H	2.54792	-2.33764	0.16537
H	2.27506	-1.32865	-1.24297
H	0.03672	-2.37587	-0.22535
C	-1.51072	-0.42456	-0.06064
O	-2.07387	-1.41230	-0.48895
O	-2.15551	0.72020	0.25516
C	-3.56063	0.69196	0.00549
H	-3.93260	1.66322	0.32785
H	-4.03225	-0.11157	0.57425
H	-3.75503	0.53744	-1.05799
H	1.35669	0.74374	-1.81134
H	2.91912	1.54271	-1.56821
H	1.41160	2.44258	-1.33245
H	2.30018	1.88399	0.87557

Minimum
Type: Radical
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: axial
Oxamate conformation: anti
Electronic energy (gas): -518.254971
Free energy (gas): -518.077708
Electronic energy (MeOH solvation): -518.261666
Free energy (MeOH solvation): -518.084403
Coordinates:

C	0.80204	-0.90166	-0.27280
N	-0.27974	0.07343	-0.08940
C	2.10625	-0.42867	0.36235
H	0.95689	-1.05792	-1.35144
H	0.46884	-1.84645	0.15764
C	2.45776	0.96345	-0.16191
H	1.94610	-0.35790	1.44844
C	3.21438	-1.44131	0.08747
C	-0.00532	1.43139	-0.26651
C	1.33119	1.94658	0.15963
H	2.60224	0.90723	-1.25018
H	3.40113	1.30872	0.27587

H 1.50763 2.91666 -0.31507
H 1.33114 2.12995 1.24961
H -0.86996 2.07812 -0.27562
H 3.39373 -1.53355 -0.98990
H 2.95612 -2.43274 0.47269
H 4.15143 -1.12783 0.55714
C -1.55656 -0.43318 -0.02745
O -1.82870 -1.61922 -0.03871
O -2.48519 0.54075 0.05180
C -3.83020 0.06913 0.13277
H -4.07538 -0.53564 -0.74230
H -4.44968 0.96374 0.16957
H -3.96814 -0.53302 1.03328

Minimum
Type: Radical
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: axial
Oxamate conformation: syn
Electronic energy (gas): -518.254382
Free energy (gas): -518.077218
Electronic energy (MeOH solvation): -518.2615073
Free energy (MeOH solvation): -518.0843433
Coordinates:
C 0.52565 -0.82657 -0.25992
N -0.27252 0.38903 -0.05011
C 1.92257 -0.69772 0.34417
H 0.61385 -1.01190 -1.34157
H -0.00544 -1.66743 0.18457
C 2.59976 0.56896 -0.17681
C 0.33507 1.63565 -0.22160
C 1.76218 1.79702 0.18310
H 2.70108 0.49491 -1.26892
H 3.60892 0.65802 0.24068
H 2.16692 2.70038 -0.28313
H 1.82859 1.95488 1.27515
H -0.35340 2.46918 -0.21344
C -1.64683 0.34539 0.00753
O -2.36586 1.32178 0.08184
O -2.11521 -0.92133 -0.03064
C -3.53578 -1.02536 0.06042
H -3.75277 -2.09124 0.00987
H -4.01007 -0.49437 -0.76705
H -3.88885 -0.60373 1.00379
C 2.73633 -1.95101 0.03291
H 1.80908 -0.60426 1.43440
H 2.86648 -2.06675 -1.04939
H 2.24742 -2.85380 0.41290
H 3.73078 -1.88891 0.48450

Minimum
Type: Radical
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: equatorial
Oxamate conformation: anti
Electronic energy (gas): -518.254971
Free energy (gas): -518.077718
Electronic energy (MeOH solvation): -518.2616662
Free energy (MeOH solvation): -518.0844132
Coordinates:
C -0.80204 -0.90161 0.27294

```
N          0.27974        0.07346        0.08943
C         -2.10622       -0.42873       -0.36233
H         -0.95696       -1.05759        1.35161
H         -0.46876       -1.84647       -0.15725
C         -2.45776        0.96342        0.16187
H         -1.94604       -0.35802       -1.44840
C         -3.21435       -1.44138       -0.08745
C          0.00532        1.43147        0.26641
C         -1.33122        1.94659       -0.15970
H         -2.60228        0.90721        1.25013
H         -3.40109        1.30872       -0.27599
H         -1.50776        2.91667        0.31497
H         -1.33121        2.12992       -1.24968
H          0.86998        2.07817        0.27582
H         -3.39365       -1.53366        0.98992
H         -2.95613       -2.43279       -0.47272
H         -4.15141       -1.12784       -0.55707
C          1.55654       -0.43314        0.02739
O          1.82867       -1.61919        0.03853
O          2.48522        0.54076       -0.05167
C          3.83020        0.06906       -0.13276
H          4.07607       -0.53391        0.74338
H          4.44963        0.96363       -0.17173
H          3.96748       -0.53493       -1.03211
```

Minimum
Type: Radical
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: equatorial
Oxamate conformation: syn
Electronic energy (gas): -518.254382
Free energy (gas): -518.077215
Electronic energy (MeOH solvation): -518.2615067
Free energy (MeOH solvation): -518.0843397
Coordinates:

```
C          0.52560       -0.82663       -0.25940
N         -0.27248        0.38903       -0.04930
C          1.92278       -0.69767        0.34410
H          0.61322       -1.01225       -1.34106
H         -0.00518       -1.66740        0.18563
C          2.59980        0.56903       -0.17706
C          0.33504        1.63557       -0.22176
C          1.76216        1.79700        0.18299
H          2.70087        0.49502       -1.26919
H          3.60902        0.65823        0.24024
H          2.16684        2.70047       -0.28308
H          1.82842        1.95459        1.27508
H         -0.35343        2.46908       -0.21385
C         -1.64689        0.34544        0.00776
O         -2.36586        1.32187        0.08169
O         -2.11531       -0.92127       -0.03065
C         -3.53589       -1.02542        0.06010
H         -3.75253       -2.09138        0.00988
H         -4.01014       -0.49504       -0.76782
H         -3.88970       -0.60364        1.00313
C          2.73650       -1.95101        0.03267
H          1.80961       -0.60419        1.43436
H          2.86643       -2.06673       -1.04966
H          2.24763       -2.85376        0.41276
H          3.73105       -1.88884        0.48402
```

Minimum
Type: Radical

Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: axial
Oxamate conformation: anti
Electronic energy (gas): -518.252651
Free energy (gas): -518.075203
Electronic energy (MeOH solvation): -518.2593948
Free energy (MeOH solvation): -518.0819468
Coordinates:

C	-0.45727	0.77400	-0.73946
N	0.18633	-0.33208	-0.17725
C	-1.91168	0.99311	-0.44189
C	-2.68069	-0.33596	-0.43373
C	-2.08825	1.76118	0.88416
H	-2.31622	1.62457	-1.24248
C	-0.54396	-1.60337	-0.08773
C	-1.96110	-1.37778	0.42230
H	-2.75710	-0.71355	-1.46144
H	-3.70088	-0.17326	-0.06926
H	-2.49597	-2.33259	0.39778
H	-1.92458	-1.05701	1.46980
H	-0.57315	-2.05784	-1.08835
H	0.02554	-2.26232	0.56636
H	-1.66444	1.20199	1.72411
H	-3.14913	1.94217	1.08957
H	-1.57890	2.72813	0.84071
C	1.54469	-0.38467	0.02936
O	2.15705	-1.38823	0.34370
O	2.13089	0.81569	-0.15159
C	3.54366	0.82058	0.05360
H	3.77925	0.54436	1.08341
H	4.02937	0.11696	-0.62525
H	3.86306	1.84067	-0.15376
H	0.18294	1.62000	-0.94689

Minimum
Type: Radical
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: axial
Oxamate conformation: syn
Electronic energy (gas): -518.252013
Free energy (gas): -518.074781
Electronic energy (MeOH solvation): -518.2591838
Free energy (MeOH solvation): -518.0819518
Coordinates:

C	0.74259	-0.89287	-0.70541
N	-0.19903	0.01769	-0.21488
C	2.19111	-0.69804	-0.37268
H	0.34500	-1.88462	-0.87823
C	2.56789	0.78985	-0.41643
C	2.53309	-1.33482	0.98984
H	2.77420	-1.22719	-1.13634
C	0.15614	1.44338	-0.16260
C	1.56854	1.62724	0.37944
H	2.56533	1.13097	-1.45962
H	3.58311	0.93000	-0.02938
H	1.82470	2.69024	0.32433
H	1.58972	1.34612	1.43871
H	0.08871	1.85868	-1.17847
H	-0.57182	1.95614	0.46282
H	1.95138	-0.87885	1.79689
H	3.59759	-1.21233	1.21900

H 2.30452 -2.40411 0.98303
C -1.50541 -0.40262 -0.10875
O -1.87476 -1.55154 -0.24711
O -2.34527 0.61848 0.17026
C -3.71184 0.23249 0.31589
H -4.24854 1.14903 0.55594
H -4.08491 -0.20111 -0.61407
H -3.81813 -0.49999 1.11852

Minimum
Type: Radical
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: equatorial
Oxamate conformation: anti
Electronic energy (gas): -518.252651
Free energy (gas): -518.075202
Electronic energy (MeOH solvation): -518.259394
Free energy (MeOH solvation): -518.081945
Coordinates:
C 0.45729 0.77397 0.73954
N -0.18631 -0.33208 0.17732
C 1.91169 0.99309 0.44190
H -0.18289 1.61996 0.94702
C 2.68069 -0.33600 0.43364
C 2.08815 1.76132 -0.88411
H 2.31627 1.62449 1.24250
C 0.54393 -1.60338 0.08770
C 1.96106 -1.37783 -0.42235
H 2.75710 -0.71364 1.46133
H 3.70089 -0.17334 0.06917
H 2.49591 -2.33267 -0.39777
H 1.92459 -1.05710 -1.46986
H 0.57315 -2.05793 1.08830
H -0.02565 -2.26226 -0.56641
H 1.66397 1.20236 -1.72402
H 3.14903 1.94207 -1.08976
H 1.57905 2.72838 -0.84036
C -1.54466 -0.38464 -0.02937
O -2.15703 -1.38822 -0.34364
O -2.13083 0.81575 0.15145
C -3.54362 0.82053 -0.05356
H -4.02915 0.11700 0.62549
H -3.86305 1.84065 0.15360
H -3.77935 0.54407 -1.08328

Minimum
Type: Radical
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: equatorial
Oxamate conformation: syn
Electronic energy (gas): -518.252013
Free energy (gas): -518.074791
Electronic energy (MeOH solvation): -518.2591839
Free energy (MeOH solvation): -518.0819619
Coordinates:
C 0.74255 -0.89297 -0.70513
N -0.19907 0.01766 -0.21478
C 2.19112 -0.69801 -0.37273
H 0.34498 -1.88469 -0.87808
C 2.56777 0.78990 -0.41673
C 2.53343 -1.33466 0.98978

```
H          2.77413       -1.22718       -1.13644
C          0.15605        1.44332       -0.16235
C          1.56858        1.62724        0.37937
H          2.56486        1.13088       -1.45997
H          3.58310        0.93014       -0.03002
H          1.82463        2.69027        0.32419
H          1.59004        1.34612        1.43863
H          0.08834        1.85883       -1.17812
H         -0.57179        1.95594        0.46332
H          1.95166       -0.87891        1.79690
H          3.59791       -1.21185        1.21886
H          2.30519       -2.40401        0.98293
C         -1.50545       -0.40267       -0.10866
O         -1.87481       -1.55159       -0.24702
O         -2.34531        0.61842        0.17031
C         -3.71186        0.23254        0.31568
H         -4.24872        1.14926        0.55469
H         -4.08455       -0.20196       -0.61401
H         -3.81853       -0.49922        1.11894
```

Minimum
Type: Radical
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: axial
Oxamate conformation: anti
Electronic energy (gas): -518.25486
Free energy (gas): -518.077979
Electronic energy (MeOH solvation): -518.2615067
Free energy (MeOH solvation): -518.0846257
Coordinates:

```
C          0.52277       -0.82017       -0.13360
N         -0.26122        0.33198       -0.05602
C          1.94714       -0.77451        0.32714
C          2.60907        0.55297       -0.05169
C          2.72078       -1.97491       -0.21585
C          0.36314        1.64013       -0.29407
C          1.72626        1.72146        0.37921
H          2.75285        0.58227       -1.14137
H          3.60005        0.61862        0.41088
H          2.18649        2.68023        0.11998
H          1.59500        1.70462        1.46871
H          0.47106        1.78287       -1.37858
H         -0.32109        2.40111        0.07898
C         -1.63638        0.30508       -0.04518
O         -2.34416        1.28970       -0.14632
O         -2.11947       -0.94485        0.09721
C         -3.54459       -1.02606        0.12712
H         -3.94001       -0.45475        0.96942
H         -3.96721       -0.63448       -0.80012
H         -3.77244       -2.08490        0.23899
H         -0.02398       -1.75260       -0.10470
H          1.95687       -0.83466        1.43278
H          2.75703       -1.93941       -1.30975
H          2.24707       -2.91725        0.07667
H          3.74678       -1.97817        0.16463
```

Minimum
Type: Radical
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: axial
Oxamate conformation: syn

Electronic energy (gas): -518.254211
Free energy (gas): -518.077431
Electronic energy (MeOH solvation): -518.2612975
Free energy (MeOH solvation): -518.0845175
Coordinates:

C	-0.78746	-0.89530	0.09011
N	0.25998	0.02436	0.00646
C	-2.16612	-0.48920	-0.32471
H	-0.47455	-1.93011	0.03259
C	-2.46610	0.94989	0.10378
H	-2.22051	-0.51414	-1.43050
C	-3.19968	-1.47487	0.21905
C	-0.01052	1.44080	0.29165
C	-1.33185	1.87279	-0.33267
H	-2.56839	0.98371	1.19802
H	-3.42085	1.27512	-0.32412
H	-1.53056	2.90900	-0.04058
H	-1.23827	1.85200	-1.42603
H	-0.04970	1.57877	1.38152
H	0.81707	2.03182	-0.09615
H	-3.18902	-1.46922	1.31406
H	-2.98836	-2.49484	-0.11619
H	-4.20527	-1.20637	-0.11909
C	1.54535	-0.46754	-0.03874
O	2.46607	0.51068	0.10038
O	1.83098	-1.63911	-0.18393
C	3.81836	0.05795	0.02757
H	4.43047	0.94833	0.16281
H	4.01309	-0.40186	-0.94351
H	4.01672	-0.67250	0.81415

Minimum
Type: Radical
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: equatorial
Oxamate conformation: anti
Electronic energy (gas): -518.254859
Free energy (gas): -518.077976
Electronic energy (MeOH solvation): -518.2615061
Free energy (MeOH solvation): -518.0846231
Coordinates:

C	-0.52267	-0.82025	0.13364
N	0.26118	0.33190	0.05604
C	-1.94705	-0.77467	-0.32698
H	0.02404	-1.75270	0.10472
C	-2.60909	0.55293	0.05167
C	-2.72053	-1.97467	0.21573
C	-0.36324	1.64001	0.29418
C	-1.72623	1.72134	-0.37931
H	-2.75300	0.58244	1.14133
H	-3.60000	0.61849	-0.41105
H	-2.18644	2.68017	-0.12025
H	-1.59487	1.70432	-1.46878
H	-0.47139	1.78264	1.37868
H	0.32103	2.40105	-0.07868
C	1.63636	0.30509	0.04515
O	2.34402	1.28980	0.14623
O	2.11944	-0.94478	-0.09714
C	3.54459	-1.02595	-0.12713
H	3.93985	-0.45486	-0.96967
H	3.96728	-0.63413	0.79996
H	3.77231	-2.08483	-0.23876
H	-1.95689	-0.83455	-1.43269

H -2.75653 -1.93968 1.30970
H -2.24742 -2.91723 -0.07717
H -3.74678 -1.97755 -0.16414

Minimum
Type: Radical
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: equatorial
Oxamate conformation: syn
Electronic energy (gas): -518.254212
Free energy (gas): -518.077421
Electronic energy (MeOH solvation): -518.2612972
Free energy (MeOH solvation): -518.0845062
Coordinates:
C -0.78740 -0.89532 0.09042
N 0.26006 0.02436 0.00668
C -2.16600 -0.48926 -0.32473
H -0.47447 -1.93012 0.03286
C -2.46605 0.94980 0.10387
H -2.21989 -0.51400 -1.43055
C -3.19961 -1.47480 0.21851
C -0.01052 1.44087 0.29173
C -1.33190 1.87281 -0.33252
H -2.56828 0.98347 1.19811
H -3.42085 1.27502 -0.32395
H -1.53069 2.90895 -0.04020
H -1.23837 1.85228 -1.42588
H -0.04970 1.57888 1.38159
H 0.81700 2.03192 -0.09610
H -3.19332 -1.46519 1.31353
H -2.98505 -2.49563 -0.11208
H -4.20442 -1.20963 -0.12454
C 1.54516 -0.46752 -0.03860
O 2.46616 0.51082 0.09984
O 1.83083 -1.63913 -0.18334
C 3.81825 0.05785 0.02728
H 4.43058 0.94693 0.16990
H 4.01510 -0.39549 -0.94647
H 4.01433 -0.67809 0.80926

Minimum
Type: Radical
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: axial
Oxamate conformation: anti
Electronic energy (gas): -709.923666
Free energy (gas): -709.697029
Electronic energy (MeOH solvation): -709.9324717
Free energy (MeOH solvation): -709.7058347
Coordinates:
C 0.52298 0.92314 1.34700
N 1.37244 0.62628 0.18480
C -0.90329 1.28825 0.93821
H 0.54897 0.05566 2.00609
C -0.84404 2.43775 -0.08470
C 1.28859 1.44172 -0.94662
C -0.04633 2.00433 -1.31407
H -0.35644 3.30094 0.38566
H -1.85185 2.74727 -0.37676
H 0.09549 2.84486 -2.00003
H -0.63379 1.24618 -1.86179

H	2.03770	1.25889	-1.70247
C	2.33955	-0.33408	0.35220
O	2.46795	-1.01413	1.35492
O	3.12915	-0.45437	-0.73245
C	4.13833	-1.45861	-0.62330
H	4.79858	-1.24405	0.21913
H	4.68669	-1.42120	-1.56316
H	3.68343	-2.44079	-0.48073
C	-1.73014	0.11618	0.42773
C	-3.08881	0.32277	0.15468
H	-3.52335	1.30606	0.32172
C	-3.89660	-0.70825	-0.31436
H	-4.94756	-0.52214	-0.51409
C	-3.35736	-1.97816	-0.52132
H	-3.98309	-2.78582	-0.88792
C	-2.01220	-2.20070	-0.24425
H	-1.58130	-3.18637	-0.39163
C	-1.20523	-1.16410	0.22785
H	-0.16174	-1.37037	0.44386
H	0.96492	1.77037	1.88774
H	-1.39332	1.66318	1.84657

Minimum
Type: Radical
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: axial
Oxamate conformation: syn
Electronic energy (gas): -709.922874
Free energy (gas): -709.698136
Electronic energy (MeOH solvation): -709.932236
Free energy (MeOH solvation): -709.707498
Coordinates:

C	-1.17666	1.61517	-1.00691
N	-1.42264	0.60555	-0.07274
C	0.18797	2.21217	-1.08752
H	-1.84452	1.60338	-1.85656
C	0.80543	2.38965	0.29840
C	-0.69756	0.59510	1.20770
C	0.75449	1.05911	1.07078
H	0.24044	3.14597	0.85809
H	1.84059	2.73635	0.21761
H	-0.73655	-0.41535	1.61374
C	-2.53232	-0.18647	-0.26324
O	-3.22969	-0.17051	-1.25805
O	-2.75956	-0.99775	0.79306
C	-3.88103	-1.86730	0.63385
H	-4.79596	-1.28668	0.50033
H	-3.92591	-2.45412	1.54979
H	-3.74009	-2.51477	-0.23409
H	-1.21831	1.26308	1.90699
H	0.12520	3.17220	-1.60872
H	0.85452	1.57239	-1.69195
C	1.69592	0.02905	0.46875
C	1.26663	-1.02313	-0.34553
H	0.21078	-1.14369	-0.56759
C	2.18380	-1.92437	-0.88842
H	1.82882	-2.73335	-1.51965
C	3.54418	-1.78957	-0.62681
H	4.25556	-2.49258	-1.04861
C	3.98497	-0.74605	0.18670
H	5.04251	-0.63381	0.40578
C	3.06707	0.15040	0.72604
H	3.41698	0.95816	1.36617

H 1.10102 1.24749 2.09495

Minimum
Type: Radical
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: equatorial
Oxamate conformation: anti
Electronic energy (gas): -709.923666
Free energy (gas): -709.69703
Electronic energy (MeOH solvation): -709.932472
Free energy (MeOH solvation): -709.705836
Coordinates:
C 0.52297 0.92300 1.34696
N 1.37247 0.62617 0.18477
C -0.90327 1.28821 0.93816
H 0.54888 0.05547 2.00598
C -0.84398 2.43768 -0.08478
C 1.28861 1.44158 -0.94667
C -0.04632 2.00417 -1.31415
H -0.35632 3.30086 0.38554
H -1.85180 2.74722 -0.37681
H 0.09550 2.84465 -2.00017
H -0.63380 1.24599 -1.86179
C 2.33968 -0.33408 0.35224
O 2.46813 -1.01407 1.35499
O 3.12928 -0.45437 -0.73240
C 4.13860 -1.45846 -0.62316
H 4.79877 -1.24377 0.21930
H 4.68700 -1.42102 -1.56298
H 3.68383 -2.44070 -0.48056
C -1.73021 0.11619 0.42772
C -3.08893 0.32282 0.15496
H -3.52343 1.30609 0.32222
C -3.89682 -0.70814 -0.31406
H -4.94782 -0.52201 -0.51357
C -3.35761 -1.97801 -0.52131
H -3.98342 -2.78563 -0.88789
C -2.01239 -2.20060 -0.24453
H -1.58154 -3.18625 -0.39214
C -1.20534 -1.16406 0.22755
H -0.16181 -1.37036 0.44333
H 0.96495 1.77016 1.88778
H -1.39327 1.66319 1.84651
H 2.03775 1.25876 -1.70250

Minimum
Type: Radical
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: equatorial
Oxamate conformation: syn
Electronic energy (gas): -709.922874
Free energy (gas): -709.698138
Electronic energy (MeOH solvation): -709.9322365
Free energy (MeOH solvation): -709.7075005
Coordinates:
C 1.17645 1.61504 1.00713
N 1.42268 0.60571 0.07273
C -0.18815 2.21210 1.08758
C -0.80548 2.38965 -0.29838
C 0.69762 0.59526 -1.20772
C -0.75447 1.05914 -1.07081

H	-0.24046	3.14599	-0.85802
H	-1.84065	2.73636	-0.21763
H	0.73676	-0.41516	-1.61382
C	2.53223	-0.18643	0.26332
O	3.22937	-0.17075	1.25830
O	2.75970	-0.99744	-0.79317
C	3.88102	-1.86717	-0.63393
H	4.79600	-1.28670	-0.50009
H	3.92602	-2.45378	-1.55000
H	3.73982	-2.51483	0.23382
H	1.21833	1.26331	-1.90698
H	-0.12542	3.17211	1.60883
H	-0.85481	1.57234	1.69192
C	-1.69584	0.02901	-0.46881
C	-1.26649	-1.02324	0.34534
H	-0.21062	-1.14385	0.56731
C	-2.18363	-1.92452	0.88822
H	-1.82861	-2.73356	1.51935
C	-3.54402	-1.78968	0.62674
H	-4.25539	-2.49271	1.04853
C	-3.98488	-0.74607	-0.18664
H	-5.04244	-0.63381	-0.40560
C	-3.06702	0.15042	-0.72597
H	-3.41695	0.95826	-1.36597
H	-1.10099	1.24751	-2.09499
H	1.84416	1.60305	1.85688

Minimum
Type: Radical
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: axial
Oxamate conformation: anti
Electronic energy (gas): -709.924308
Free energy (gas): -709.700041
Electronic energy (MeOH solvation): -709.9335038
Free energy (MeOH solvation): -709.7092368
Coordinates:

C	-0.33652	-0.29116	-0.27811
N	-1.70645	0.19447	-0.07662
C	0.68273	0.60207	0.43571
H	-0.11936	-0.30967	-1.35592
H	-0.28715	-1.31563	0.09071
C	0.49497	2.05671	-0.00723
C	-1.96185	1.56471	-0.16600
C	-0.92333	2.51544	0.33514
H	0.65192	2.13367	-1.09062
H	1.23763	2.69764	0.47867
H	-1.12135	3.50980	-0.07648
H	-1.00182	2.61266	1.43338
H	-3.00606	1.83986	-0.16747
C	-2.70066	-0.75702	-0.08866
O	-2.50655	-1.95398	-0.18238
O	-3.92676	-0.20867	0.02135
C	-4.99732	-1.15337	0.02585
H	-4.99077	-1.74080	-0.89418
H	-5.90749	-0.56019	0.09855
H	-4.90620	-1.82693	0.88043
C	2.08253	0.07506	0.20510
C	2.79295	-0.52600	1.24756
H	2.33439	-0.59858	2.23084
C	4.07529	-1.03289	1.04349
H	4.60953	-1.49611	1.86741
C	4.66762	-0.94713	-0.21424

```
H          5.66571       -1.34179       -0.37639
C          3.96894       -0.35166       -1.26357
H          4.42193       -0.27985       -2.24773
C          2.68806        0.15404       -1.05452
H          2.15738        0.61625       -1.88325
H          0.47287        0.54678        1.51349

Minimum
Type: Radical
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: axial
Oxamate conformation: syn
Electronic energy (gas): -709.924032
Free energy (gas): -709.699385
Electronic energy (MeOH solvation): -709.9334106
Free energy (MeOH solvation): -709.7087636
Coordinates:
C         -1.96397        1.82220        0.17883
N         -1.80409        0.44095        0.04026
C         -0.86364        2.71930       -0.28267
H         -2.99438        2.14976        0.18427
C          0.51648        2.15600        0.05891
C         -0.47196       -0.14516        0.23606
C          0.61367        0.70797       -0.43117
H          0.66383        2.18710        1.14600
H          1.30744        2.75986       -0.39734
H         -0.46767       -1.15145       -0.17988
C         -2.93667       -0.34299        0.02733
O         -4.07095        0.08567       -0.03938
O         -2.64012       -1.65797        0.09945
C         -3.77524       -2.52284        0.05074
H         -4.45702       -2.30146        0.87394
H         -3.37478       -3.53133        0.14028
H         -4.30556       -2.40003       -0.89591
H         -0.26790       -0.22169        1.31401
H         -1.00117        3.71058        0.15948
H         -0.92376        2.85668       -1.37778
C          1.97444        0.08729       -0.20086
C          2.67427       -0.50094       -1.25771
H          2.23480       -0.49920       -2.25240
C          3.92451       -1.08363       -1.05428
H          4.45234       -1.53321       -1.88984
C          4.49423       -1.08736        0.21651
H          5.46826       -1.53861        0.37740
C          3.80534       -0.50609        1.28029
H          4.24142       -0.50362        2.27466
C          2.55699        0.07558        1.07180
H          2.03448        0.52863        1.91071
H          0.41612        0.70370       -1.51260

Minimum
Type: Radical
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: equatorial
Oxamate conformation: anti
Electronic energy (gas): -709.924308
Free energy (gas): -709.700039
Electronic energy (MeOH solvation): -709.9335042
Free energy (MeOH solvation): -709.7092352
Coordinates:
C         -0.33646       -0.29116       -0.27789
```

N	-1.70643	0.19445	-0.07655
C	0.68277	0.60214	0.43585
H	-0.11925	-0.30985	-1.35568
H	-0.28708	-1.31557	0.09111
C	0.49494	2.05677	-0.00706
C	-1.96188	1.56471	-0.16560
C	-0.92333	2.51541	0.33556
H	0.65171	2.13382	-1.09046
H	1.23767	2.69769	0.47878
H	-1.12143	3.50981	-0.07596
H	-1.00171	2.61255	1.43381
C	-2.70063	-0.75704	-0.08874
O	-2.50649	-1.95403	-0.18204
O	-3.92677	-0.20865	0.02064
C	-4.99733	-1.15336	0.02545
H	-4.99121	-1.74058	-0.89472
H	-5.90747	-0.56021	0.09869
H	-4.90579	-1.82713	0.87983
C	2.08254	0.07508	0.20513
C	2.79279	-0.52654	1.24736
H	2.33413	-0.59955	2.23057
C	4.07512	-1.03346	1.04317
H	4.60924	-1.49709	1.86694
C	4.66757	-0.94715	-0.21445
H	5.66565	-1.34182	-0.37667
C	3.96903	-0.35112	-1.26358
H	4.42211	-0.27890	-2.24768
C	2.68819	0.15459	-1.05442
H	2.15761	0.61717	-1.88301
H	0.47299	0.54687	1.51364
H	-3.00611	1.83984	-0.16683

Minimum
Type: Radical
Substituent: Ph
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: equatorial
Oxamate conformation: syn
Electronic energy (gas): -709.924032
Free energy (gas): -709.699383
Electronic energy (MeOH solvation): 709.9334111
Free energy (MeOH solvation): 710.1580601
Coordinates:

C	-1.96408	1.82223	0.17843
N	-1.80405	0.44096	0.04024
C	-0.86378	2.71934	-0.28316
C	0.51636	2.15621	0.05856
C	-0.47185	-0.14498	0.23610
C	0.61367	0.70813	-0.43131
H	0.66367	2.18754	1.14564
H	1.30728	2.76006	-0.39778
H	-0.46748	-1.15134	-0.17967
C	-2.93655	-0.34310	0.02747
O	-4.07088	0.08544	-0.03938
O	-2.63989	-1.65803	0.09987
C	-3.77494	-2.52300	0.05139
H	-4.45640	-2.30188	0.87493
H	-3.37434	-3.53147	0.14057
H	-4.30566	-2.40003	-0.89501
H	-0.26771	-0.22132	1.31406
H	-1.00142	3.71065	0.15889
H	-0.92391	2.85660	-1.37827
C	1.97443	0.08746	-0.20095
C	2.67367	-0.50204	-1.25749

H 2.23381 -0.50119 -2.25201
C 3.92383 -1.08489 -1.05397
H 4.45119 -1.53546 -1.88929
C 4.49406 -1.08751 0.21659
H 5.46804 -1.53884 0.37754
C 3.80574 -0.50498 1.28007
H 4.24223 -0.50164 2.27427
C 2.55748 0.07682 1.07150
H 2.03540 0.53081 1.91017
H 0.41609 0.70370 -1.51273
H -2.99452 2.14970 0.18363

Minimum
Type: Radical
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: axial
Oxamate conformation: anti
Electronic energy (gas): -709.925634
Free energy (gas): -709.701758
Electronic energy (MeOH solvation): -709.9345547
Free energy (MeOH solvation): -709.7106787
Coordinates:
C -1.87925 1.79332 0.50744
N -1.75794 0.40026 0.05740
C -0.82591 2.67091 -0.15453
H -2.89055 2.12441 0.27467
C 0.57025 2.09640 0.06809
C -0.49003 -0.17071 -0.05801
C 0.65247 0.68029 -0.52678
H 0.78458 2.04446 1.14411
H 1.33931 2.72830 -0.38795
H -0.47243 -1.23621 -0.23803
C -2.91503 -0.34583 0.05510
O -4.01606 0.09395 0.32671
O -2.68995 -1.62789 -0.29005
C -3.85894 -2.44748 -0.32047
H -4.32156 -2.48690 0.66777
H -3.51293 -3.43412 -0.62400
H -4.58087 -2.05313 -1.03805
H -0.90396 3.68104 0.25979
H -1.75632 1.81865 1.59949
H -1.03291 2.74085 -1.23009
C 1.98713 0.02950 -0.22790
C 2.97902 -0.04307 -1.20806
H 2.77203 0.33839 -2.20539
C 4.22549 -0.59943 -0.92330
H 4.98377 -0.65140 -1.69884
C 4.49427 -1.09380 0.35078
H 5.46277 -1.53073 0.57358
C 3.50983 -1.02804 1.33680
H 3.70986 -1.41413 2.33183
C 2.26692 -0.47046 1.04835
H 1.49751 -0.42390 1.81581
H 0.57808 0.79450 -1.62479

Minimum
Type: Radical
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: axial
Oxamate conformation: syn
Electronic energy (gas): -709.924811

Free energy (gas): -709.70038
Electronic energy (MeOH solvation): -709.9343452
Free energy (MeOH solvation): -709.7099142
Coordinates:

C	-0.36931	-0.32509	0.14990
N	-1.67397	0.15670	0.02317
C	0.73359	0.63277	0.48089
H	-0.30239	-1.36306	0.44921
C	0.55169	1.96332	-0.26898
C	-1.89331	1.48169	-0.57500
C	-0.86711	2.48283	-0.05899
H	0.73567	1.79723	-1.33905
H	1.29545	2.68561	0.08289
H	-1.01800	3.43421	-0.57903
H	-1.04162	2.66194	1.00968
H	-2.90571	1.80068	-0.33536
C	-2.70717	-0.74196	0.17694
O	-2.57754	-1.88084	0.57668
O	-3.89676	-0.20569	-0.17089
C	-5.01077	-1.08086	0.00757
H	-4.89707	-1.97187	-0.61303
H	-5.88372	-0.50636	-0.29792
H	-5.09301	-1.38300	1.05360
C	2.09976	0.03430	0.21720
C	3.13083	0.19536	1.14557
H	2.92965	0.71482	2.07974
C	4.40724	-0.30365	0.89095
H	5.19487	-0.17173	1.62653
C	4.66772	-0.97622	-0.30078
H	5.65934	-1.37053	-0.50021
C	3.64484	-1.14434	-1.23401
H	3.83884	-1.67030	-2.16396
C	2.37142	-0.64218	-0.97652
H	1.57391	-0.77951	-1.70301
H	0.68043	0.86936	1.56059
H	-1.81095	1.39213	-1.66757

Minimum
Type: Radical
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: equatorial
Oxamate conformation: anti
Electronic energy (gas): -709.925634
Free energy (gas): -709.701759
Electronic energy (MeOH solvation): -709.9345543
Free energy (MeOH solvation): -709.7106793
Coordinates:

C	-1.87885	1.79326	0.50833
N	-1.75788	0.40009	0.05855
C	-0.82581	2.67060	-0.15445
H	-2.89027	2.12434	0.27607
C	0.57041	2.09608	0.06776
C	-0.49012	-0.17099	-0.05752
C	0.65234	0.67978	-0.52674
H	0.78520	2.04439	1.14370
H	1.33933	2.72782	-0.38876
C	-2.91519	-0.34562	0.05532
O	-4.01631	0.09443	0.32615
O	-2.69021	-1.62769	-0.28985
C	-3.85948	-2.44682	-0.32153
H	-4.32270	-2.48671	0.66640
H	-3.51364	-3.43339	-0.62548
H	-4.58084	-2.05175	-1.03928

H -0.90362 3.68090 0.25950
H -1.75523 1.81881 1.60028
H -1.03331 2.74011 -1.22995
C 1.98709 0.02914 -0.22790
C 2.97928 -0.04222 -1.20786
H 2.77242 0.33990 -2.20495
C 4.22593 -0.59825 -0.92320
H 4.98441 -0.64928 -1.69860
C 4.49458 -1.09349 0.35057
H 5.46322 -1.53014 0.57333
C 3.50983 -1.02895 1.33636
H 3.70973 -1.41574 2.33114
C 2.26674 -0.47169 1.04801
H 1.49712 -0.42603 1.81533
H 0.57779 0.79366 -1.62475
H -0.47267 -1.23656 -0.23718

Minimum
Type: Radical
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: equatorial
Oxamate conformation: syn
Electronic energy (gas): -709.924812
Free energy (gas): -709.700379
Electronic energy (MeOH solvation): -709.9343449
Free energy (MeOH solvation): -709.7099119
Coordinates:
C 0.36938 -0.32513 -0.14994
N 1.67402 0.15672 -0.02316
C -0.73359 0.63272 -0.48069
C -0.55174 1.96310 0.26948
C 1.89336 1.48167 0.57511
C 0.86698 2.48279 0.05947
H -0.73562 1.79673 1.33952
H -1.29561 2.68539 -0.08215
H 1.01785 3.43406 0.57973
H 1.04134 2.66220 -1.00918
H 2.90568 1.80077 0.33526
C 2.70724 -0.74188 -0.17705
O 2.57765 -1.88070 -0.57694
O 3.89682 -0.20561 0.17089
C 5.01086 -1.08067 -0.00783
H 4.89730 -1.97178 0.61265
H 5.88380 -0.50614 0.29765
H 5.09300 -1.38264 -1.05391
C -2.09977 0.03419 -0.21716
C -3.13102 0.19626 -1.14517
H -2.92991 0.71643 -2.07896
C -4.40747 -0.30269 -0.89069
H -5.19524 -0.17001 -1.62599
C -4.66782 -0.97620 0.30055
H -5.65949 -1.37045 0.49986
C -3.64479 -1.14533 1.23340
H -3.83868 -1.67202 2.16295
C -2.37130 -0.64322 0.97606
H -1.57368 -0.78129 1.70227
H -0.68043 0.86958 -1.56035
H 1.81133 1.39198 1.66769
H 0.30254 -1.36303 -0.44953

Minimum
Type: Radical
Substituent: Ph

Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: axial
Oxamate conformation: anti
Electronic energy (gas): -709.924487
Free energy (gas): -709.699247
Electronic energy (MeOH solvation): -709.9333151
Free energy (MeOH solvation): -709.7080751
Coordinates:

C	-1.44587	1.81954	-0.75175
N	-1.50917	0.59720	0.06153
C	-0.00078	2.22704	-1.00526
H	-1.98228	1.62236	-1.67900
C	0.75331	2.35754	0.31411
C	-0.64077	0.44660	1.14507
C	0.74577	1.01139	1.06610
H	0.26329	3.11515	0.93932
H	1.78541	2.68096	0.14629
H	-0.83826	-0.40674	1.77764
C	-2.59720	-0.21992	-0.14533
O	-3.46348	-0.01530	-0.97468
O	-2.58954	-1.29006	0.67339
C	-3.69544	-2.17633	0.49604
H	-4.63626	-1.64957	0.66682
H	-3.55525	-2.96583	1.23228
H	-3.69451	-2.58672	-0.51584
H	0.00279	3.17608	-1.55031
H	0.48701	1.48044	-1.64377
C	1.75540	0.04137	0.44842
C	1.37902	-0.97086	-0.43842
H	0.32973	-1.10960	-0.68415
C	2.33629	-1.81155	-1.00728
H	2.02374	-2.59178	-1.69486
C	3.68393	-1.65706	-0.69306
H	4.42726	-2.31496	-1.13227
C	4.07024	-0.65555	0.19751
H	5.11720	-0.53141	0.45763
C	3.11219	0.18285	0.76088
H	3.41908	0.95973	1.45886
H	-1.97525	2.62078	-0.21727
H	1.07817	1.19325	2.09605

Minimum
Type: Radical
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: axial
Oxamate conformation: syn
Electronic energy (gas): -709.923732
Free energy (gas): -709.698635
Electronic energy (MeOH solvation): -709.9329969
Free energy (MeOH solvation): -709.7078999
Coordinates:

C	0.48344	0.51469	1.24256
N	1.44705	0.43569	0.23364
C	-0.85404	1.12206	0.95099
H	0.59291	-0.23148	2.01809
C	-0.71310	2.32313	-0.00625
C	1.52352	1.49889	-0.77887
C	0.12794	1.92701	-1.21518
H	-0.22098	3.14729	0.52595
H	-1.70340	2.67053	-0.31642
H	0.22494	2.76331	-1.91457
H	-0.35802	1.10324	-1.75220

H	2.09996	1.12534	-1.62304
C	2.45653	-0.48940	0.37940
O	2.47351	-1.36383	1.22270
O	3.43658	-0.31530	-0.53267
C	4.49064	-1.27557	-0.45510
H	4.97841	-1.22506	0.52025
H	5.18605	-1.00781	-1.24907
H	4.09881	-2.28325	-0.60734
H	2.06199	2.35563	-0.34922
C	-1.87031	0.11512	0.40584
C	-3.23465	0.41319	0.49903
H	-3.54546	1.33976	0.97848
C	-4.19591	-0.45903	-0.00315
H	-5.24964	-0.21171	0.08477
C	-3.80510	-1.65268	-0.61052
H	-4.55112	-2.33753	-1.00130
C	-2.45107	-1.96278	-0.70351
H	-2.13642	-2.89322	-1.16670
C	-1.49025	-1.08667	-0.19639
H	-0.43729	-1.34744	-0.26056
H	-1.25660	1.48790	1.90403

Minimum
Type: Radical
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: equatorial
Oxamate conformation: anti
Electronic energy (gas): -709.924486
Free energy (gas): -709.699249
Electronic energy (MeOH solvation): -709.9333146
Free energy (MeOH solvation): -709.7080776
Coordinates:

C	1.44550	1.81908	0.75226
N	1.50898	0.59668	-0.06095
C	0.00038	2.22696	1.00485
H	1.98114	1.62175	1.67994
C	-0.75319	2.35723	-0.31485
C	0.64089	0.44601	-1.14473
C	-0.74569	1.01082	-1.06625
H	-0.26280	3.11450	-0.94018
H	-1.78525	2.68104	-0.14738
C	2.59755	-0.21978	0.14561
O	3.46398	-0.01452	0.97464
O	2.59018	-1.28996	-0.67307
C	3.69674	-2.17551	-0.49624
H	4.63708	-1.64838	-0.66867
H	3.55609	-2.96570	-1.23165
H	3.69729	-2.58498	0.51600
H	-0.00325	3.17613	1.54966
H	-0.48790	1.48066	1.64334
C	-1.75555	0.04109	-0.44843
C	-1.37949	-0.97132	0.43832
H	-0.33025	-1.11045	0.68400
C	-2.33708	-1.81171	1.00713
H	-2.02481	-2.59212	1.69463
C	-3.68466	-1.65670	0.69295
H	-4.42823	-2.31439	1.13208
C	-4.07065	-0.65494	-0.19747
H	-5.11758	-0.53038	-0.45750
C	-3.11229	0.18314	-0.76082
H	-3.41892	0.96022	-1.45869
H	1.97561	2.62010	0.21820
H	-1.07778	1.19216	-2.09638

H 0.83864 -0.40730 -1.77727

Minimum
Type: Radical
Substituent: Ph
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: equatorial
Oxamate conformation: syn
Electronic energy (gas): -709.923732
Free energy (gas): -709.69864
Electronic energy (MeOH solvation): -709.9329983
Free energy (MeOH solvation): -709.7079063
Coordinates:

C	0.48348	0.51485	1.24256
N	1.44716	0.43574	0.23372
C	-0.85407	1.12209	0.95079
C	-0.71318	2.32310	-0.00646
C	1.52367	1.49910	-0.77868
C	0.12812	1.92703	-1.21526
H	-0.22122	3.14738	0.52572
H	-1.70345	2.67043	-0.31683
H	0.22514	2.76331	-1.91466
H	-0.35762	1.10318	-1.75235
H	2.10043	1.12578	-1.62272
C	2.45662	-0.48934	0.37949
O	2.47412	-1.36301	1.22359
O	3.43600	-0.31610	-0.53341
C	4.49055	-1.27583	-0.45523
H	4.97770	-1.22506	0.52040
H	5.18621	-1.00771	-1.24886
H	4.09929	-2.28370	-0.60770
H	2.06181	2.35586	-0.34865
C	-1.87035	0.11511	0.40567
C	-3.23460	0.41319	0.49903
H	-3.54546	1.33979	0.97839
C	-4.19596	-0.45911	-0.00300
H	-5.24966	-0.21169	0.08504
C	-3.80525	-1.65276	-0.61029
H	-4.55131	-2.33766	-1.00091
C	-2.45118	-1.96285	-0.70349
H	-2.13662	-2.89334	-1.16665
C	-1.49032	-1.08672	-0.19659
H	-0.43737	-1.34741	-0.26095
H	-1.25674	1.48781	1.90383
H	0.59278	-0.23135	2.01814

Minimum
Type: Cation
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: NA
Oxamate conformation: anti
Electronic energy (gas): -518.045437
Free energy (gas): -517.864904
Electronic energy (MeOH solvation): -518.120613
Free energy (MeOH solvation): -517.94008
Coordinates:

C	0.77690	-1.06344	-0.61568
N	-0.15855	0.02738	-0.20392
C	2.20542	-0.75228	-0.18113
H	0.67866	-1.15977	-1.70124
H	0.39176	-1.97709	-0.16134
C	2.57291	0.65982	-0.64907

```
C          2.39441       -0.94843        1.32542
C          0.22275        1.23421        0.05615
C          1.62825        1.68621       -0.02646
H          2.50701        0.71952       -1.74063
H          3.60289        0.90078       -0.37684
H          1.62825        2.64617       -0.55797
H          1.90966        1.94673        1.00667
H         -0.55770        1.92863        0.36153
C         -1.58187       -0.36310       -0.13655
O         -1.90129       -1.47956       -0.40173
O         -2.32584        0.65190        0.22281
C         -3.75087        0.37156        0.31995
H         -4.11770        0.04924       -0.65414
H         -4.20001        1.31268        0.62391
H         -3.90992       -0.40607        1.06648
H          1.71449       -0.32579        1.91843
H          3.41611       -0.69457        1.61948
H          2.21394       -1.98859        1.60781
H          2.84201       -1.46951       -0.70910

Minimum
Type: Cation
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: NA
Oxamate conformation: syn
Electronic energy (gas): -518.046487
Free energy (gas): -517.865709
Electronic energy (MeOH solvation): -518.1210617
Free energy (MeOH solvation): -517.9402837
Coordinates:
C          0.44727       -0.99003       -0.55986
N         -0.14750        0.30214       -0.10013
C          1.94295       -1.04268       -0.25766
H          0.23076       -1.06801       -1.62942
H         -0.09749       -1.78085       -0.04360
C          2.60620        0.23935       -0.77146
C          2.20738       -1.29274        1.22995
C          0.54482        1.37083        0.11887
C          2.00651        1.45918       -0.07410
H          2.45773        0.32890       -1.85300
H          3.68403        0.21140       -0.59736
H          2.20637        2.39835       -0.60492
H          2.42684        1.62062        0.93157
H         -0.02774        2.23018        0.46998
C         -1.61154        0.41141        0.10394
O         -2.10016        1.41914        0.51494
O         -2.17979       -0.71007       -0.24083
C         -3.62859       -0.73726       -0.11040
H         -3.91641       -1.74219       -0.40505
H         -4.05795        0.01241       -0.77488
H         -3.89741       -0.53047        0.92524
H          1.73916       -0.53738        1.87165
H          3.28083       -1.28160        1.43540
H          1.81891       -2.26712        1.53639
H          2.33446       -1.89012       -0.82963

Minimum
Type: Cation
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: NA
Oxamate conformation: anti
```

Electronic energy (gas): -518.04645
Free energy (gas): -517.866726
Electronic energy (MeOH solvation): -518.1218329
Free energy (MeOH solvation): -517.9421089
Coordinates:

C	0.83107	-0.93577	-0.10197
N	-0.24988	0.08983	-0.01078
C	2.17266	-0.38046	0.35862
H	0.86204	-1.26652	-1.14621
H	0.50088	-1.78047	0.50402
C	2.43056	0.96205	-0.32460
H	2.11837	-0.21812	1.44465
C	3.26980	-1.40145	0.06501
C	-0.02505	1.35953	0.06246
C	1.32882	1.95583	0.03323
H	2.46565	0.81906	-1.41158
H	3.40009	1.36617	-0.02396
H	1.28695	2.81985	-0.64161
H	1.47639	2.39344	1.03399
H	-0.90216	1.99725	0.15238
H	3.37134	-1.56509	-1.01280
H	3.05833	-2.36344	0.53933
H	4.22976	-1.04444	0.44458
C	-1.62460	-0.45183	-0.02898
O	-1.79350	-1.62721	-0.12123
O	-2.50580	0.51191	0.05758
C	-3.89638	0.08306	0.03687
H	-4.10010	-0.41447	-0.91107
H	-4.47187	0.99880	0.13723
H	-4.07335	-0.59423	0.87197

Minimum
Type: Cation
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: NA
Oxamate conformation: syn
Electronic energy (gas): -518.047604
Free energy (gas): -517.867468
Electronic energy (MeOH solvation): -518.1223686
Free energy (MeOH solvation): -517.9422326
Coordinates:

C	0.54305	-0.86875	-0.05732
N	-0.24197	0.39959	0.01597
C	1.99422	-0.65568	0.35752
H	0.46339	-1.23071	-1.08838
H	0.03841	-1.58489	0.59184
C	2.56245	0.56398	-0.36619
C	0.29839	1.57250	0.05126
C	1.75545	1.81036	-0.01166
H	2.53158	0.39540	-1.44972
H	3.61035	0.71630	-0.09708
H	1.91793	2.64516	-0.70456
H	2.02977	2.21388	0.97674
H	-0.40347	2.40345	0.13325
C	-1.72335	0.35108	0.03831
O	-2.36846	1.34847	0.14670
O	-2.11416	-0.88632	-0.08573
C	-3.55558	-1.08558	-0.09414
H	-3.68807	-2.15827	-0.20111
H	-3.98440	-0.54365	-0.93695
H	-3.97020	-0.72256	0.84599
C	2.79170	-1.92570	0.06734
H	2.01220	-0.46227	1.43954

```
H          2.82112       -2.12913       -1.00809
H          2.35821       -2.79490        0.56949
H          3.82001       -1.81542        0.41867

Minimum
Type: Cation
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: NA
Oxamate conformation: anti
Electronic energy (gas): -518.045367
Free energy (gas): -517.864987
Electronic energy (MeOH solvation): -518.1197149
Free energy (MeOH solvation): -517.9393349
Coordinates:
C         -0.44035        0.80942       -0.29559
N          0.18431       -0.30132       -0.07772
C         -1.90923        0.93189       -0.46094
C         -2.59862       -0.42864       -0.60054
C         -2.44698        1.78512        0.71418
H         -2.04019        1.53063       -1.37376
C         -0.49798       -1.62269        0.04969
C         -1.97199       -1.43568        0.36187
H         -2.49932       -0.79299       -1.62908
H         -3.66690       -0.31286       -0.40320
H         -2.45869       -2.41013        0.27949
H         -2.09078       -1.10761        1.40065
H         -0.33455       -2.14726       -0.89695
H          0.03585       -2.16615        0.82905
H         -2.37763        1.24204        1.65987
H         -3.49689        2.01211        0.52106
H         -1.90968        2.73141        0.81557
C          1.65564       -0.35122        0.03965
O          2.19657       -1.39323        0.24172
O          2.17692        0.83920       -0.11720
C          3.62791        0.89537       -0.02471
H          3.93152        0.59854        0.97891
H          4.05888        0.22646       -0.76912
H          3.88086        1.93226       -0.22633
H          0.17896        1.70364       -0.33998

Minimum
Type: Cation
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: NA
Oxamate conformation: syn
Electronic energy (gas): -518.046543
Free energy (gas): -517.865996
Electronic energy (MeOH solvation): -518.1202449
Free energy (MeOH solvation): -517.9396979
Coordinates:
C          0.71174       -0.90004       -0.32094
N         -0.19120        0.00047       -0.10729
C          2.16244       -0.62992       -0.44944
H          0.33502       -1.92187       -0.39066
C          2.46688        0.86611       -0.56967
C          2.87721       -1.32036        0.73945
H          2.47079       -1.16635       -1.35789
C          0.11159        1.45361        0.05202
C          1.57981        1.65949        0.38690
H          2.29081        1.20033       -1.59827
H          3.52357        1.03864       -0.35283
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H          1.79173        2.72918        0.32165
H          1.76493        1.36120        1.42485
H         -0.17328        1.93651       -0.88780
H         -0.54689        1.82509        0.83645
H          2.63858       -0.82698        1.68486
H          3.95440       -1.25474        0.57618
H          2.60977       -2.37675        0.82074
C         -1.59516       -0.46868       -0.04878
O         -1.85978       -1.62922       -0.12758
O         -2.38695        0.55927        0.08141
C         -3.80675        0.24787        0.14033
H         -4.29856        1.21006        0.24943
H         -4.10061       -0.24923       -0.78406
H         -3.99452       -0.39731        0.99846

Minimum
Type: Cation
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: NA
Oxamate conformation: anti
Electronic energy (gas): -518.045916
Free energy (gas): -517.865719
Electronic energy (MeOH solvation): -518.1203193
Free energy (MeOH solvation): -517.9401223
Coordinates:
C          0.48009       -0.74000        0.28990
N         -0.18423        0.33975        0.03863
C          1.96204       -0.82749        0.34123
C          2.63874        0.45185       -0.15086
C          2.42118       -2.09485       -0.40295
C          0.45408        1.67006       -0.18860
C          1.87645        1.67707        0.34478
H          2.66717        0.44491       -1.24778
H          3.67494        0.46629        0.19439
H          2.35532        2.60124        0.01333
H          1.86038        1.69881        1.44083
H          0.41005        1.85596       -1.26607
H         -0.18723        2.40232        0.30203
C         -1.65759        0.33754       -0.06410
O         -2.23079        1.34886       -0.32477
O         -2.14052       -0.85909        0.15458
C         -3.58926       -0.96420        0.06450
H         -3.90162       -0.70300       -0.94635
H         -3.80931       -2.00291        0.29318
H         -4.04121       -0.28990        0.79141
H         -0.11393       -1.63677        0.46236
H          2.17885       -0.97699        1.41367
H          2.17358       -2.03548       -1.46619
H          1.97282       -2.99912        0.01581
H          3.50585       -2.18166       -0.31295

Minimum
Type: Cation
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: NA
Oxamate conformation: syn
Electronic energy (gas): -518.047099
Free energy (gas): -517.866767
Electronic energy (MeOH solvation): -518.1208968
Free energy (MeOH solvation): -517.9405648
Coordinates:
```

C	-0.74791	-0.81329	-0.31268
N	0.19548	0.04634	-0.10804
C	-2.19778	-0.50129	-0.29539
H	-0.40841	-1.83502	-0.49442
C	-2.47796	0.90891	0.22419
H	-2.49649	-0.57521	-1.35603
C	-2.94921	-1.60417	0.47268
C	-0.04654	1.50217	0.12310
C	-1.44634	1.88816	-0.32746
H	-2.44250	0.90207	1.32104
H	-3.49054	1.20401	-0.05987
H	-1.64145	2.90563	0.01928
H	-1.48880	1.90793	-1.42276
H	0.11086	1.67952	1.19120
H	0.72751	2.03678	-0.42652
H	-2.64443	-1.62701	1.52233
H	-2.78364	-2.59088	0.03385
H	-4.01927	-1.39049	0.43567
C	1.58068	-0.47907	-0.09835
O	2.40552	0.48906	0.18959
O	1.80392	-1.62948	-0.32165
C	3.80886	0.11109	0.25350
H	4.33312	1.02719	0.50942
H	4.11979	-0.26929	-0.71934
H	3.93746	-0.65139	1.02138

Minimum
Type: Cation
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: NA
Oxamate conformation: anti
Electronic energy (gas): -709.716339
Free energy (gas): -709.489108
Electronic energy (MeOH solvation): -709.7919858
Free energy (MeOH solvation): -709.5647548
Coordinates:

C	-0.31502	-0.35065	-0.07990
N	-1.69520	0.21843	-0.01192
C	0.72447	0.65693	0.40401
H	-0.14704	-0.64869	-1.11995
H	-0.32249	-1.25574	0.52814
C	0.50113	2.00321	-0.29182
C	-1.94271	1.48460	0.05012
C	-0.89503	2.52937	0.03211
H	0.61009	1.88748	-1.37582
H	1.25533	2.72446	0.02997
H	-1.23324	3.31278	-0.65780
H	-0.93852	3.00108	1.02751
H	-2.99164	1.76483	0.12350
C	-2.78295	-0.78103	-0.03133
O	-2.51875	-1.93937	-0.11306
O	-3.95284	-0.19781	0.04359
C	-5.09446	-1.10009	0.03045
H	-5.07817	-1.68254	-0.89031
H	-5.96424	-0.45118	0.07581
H	-5.03986	-1.75540	0.89949
C	2.11407	0.09049	0.19154
C	2.90793	-0.24378	1.29038
H	2.52717	-0.09327	2.29761
C	4.18784	-0.76430	1.10634
H	4.79530	-1.01802	1.96873
C	4.68335	-0.95695	-0.18073
H	5.67932	-1.36196	-0.32557

C	3.89586	-0.62885	-1.28377
H	4.27780	-0.77632	-2.28858
C	2.61749	-0.10915	-1.09838
H	2.02008	0.14425	-1.97186
H	0.57755	0.79786	1.48409

Minimum
Type: Cation
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: axial
Radical orientation: NA
Oxamate conformation: syn
Electronic energy (gas): -709.717759
Free energy (gas): -709.490189
Electronic energy (MeOH solvation): -709.7925457
Free energy (MeOH solvation): -709.5649757
Coordinates:

C	-1.95513	1.75103	-0.02223
N	-1.78794	0.47015	-0.01732
C	-0.84822	2.72763	0.05237
H	-2.99211	2.08273	-0.08586
C	0.50410	2.09949	0.38005
C	-0.44695	-0.18825	0.02203
C	0.66114	0.78208	-0.38508
H	0.57537	1.91820	1.45828
H	1.31032	2.78747	0.11729
H	-0.49388	-1.04366	-0.65222
C	-3.01599	-0.35880	-0.04582
O	-4.09425	0.14274	-0.14263
O	-2.68725	-1.61574	0.06034
C	-3.80003	-2.55219	0.06075
H	-4.46103	-2.31926	0.89533
H	-3.34145	-3.52990	0.17611
H	-4.33382	-2.46993	-0.88588
H	-0.30786	-0.56719	1.03934
H	-1.15041	3.50376	0.76656
H	-0.84153	3.23897	-0.92420
C	2.00839	0.11826	-0.18429
C	2.80322	-0.19653	-1.28826
H	2.45632	0.04418	-2.29024
C	4.04231	-0.81144	-1.11585
H	4.65137	-1.04817	-1.98197
C	4.49575	-1.11872	0.16441
H	5.46095	-1.59503	0.30048
C	3.70774	-0.80889	1.27243
H	4.05779	-1.04316	2.27240
C	2.47045	-0.19423	1.09873
H	1.87334	0.04587	1.97626
H	0.54365	0.99156	-1.45756

Minimum
Type: Cation
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: NA
Oxamate conformation: anti
Electronic energy (gas): -709.717244
Free energy (gas): -709.489014
Electronic energy (MeOH solvation): -709.790716
Free energy (MeOH solvation): -709.562486
Coordinates:

C	0.51534	0.80808	1.31875
N	1.34429	0.51845	0.10854

C	-0.88892	1.25480	0.93723
H	0.52227	-0.10072	1.92041
C	-0.77475	2.36512	-0.12158
C	1.05807	0.94805	-1.07667
C	-0.11230	1.79875	-1.37282
H	-0.18118	3.19770	0.27221
H	-1.75787	2.76202	-0.37978
H	0.20549	2.56790	-2.08609
H	-0.80503	1.14801	-1.93426
H	1.73014	0.63749	-1.87409
C	2.53416	-0.31778	0.35502
O	2.71692	-0.78546	1.43591
O	3.26419	-0.41866	-0.72708
C	4.47036	-1.21987	-0.58882
H	5.09623	-0.78885	0.19234
H	4.95339	-1.16614	-1.56031
H	4.19301	-2.24310	-0.33682
C	-1.79601	0.12742	0.45904
C	-3.14666	0.42462	0.23605
H	-3.52115	1.42429	0.44530
C	-4.02583	-0.54863	-0.22645
H	-5.07062	-0.30067	-0.38243
C	-3.56804	-1.84207	-0.47868
H	-4.25262	-2.60292	-0.83810
C	-2.23164	-2.15336	-0.25205
H	-1.86840	-3.16072	-0.42776
C	-1.35177	-1.17445	0.21549
H	-0.32083	-1.46282	0.40765
H	1.04797	1.58341	1.87694
H	-1.32191	1.68499	1.84735

Minimum
Type: Cation
Substituent: Me
Regioisomer: distal
Methyl (on ring) orientation: equatorial
Radical orientation: NA
Oxamate conformation: syn
Electronic energy (gas): -709.718213
Free energy (gas): -709.489671
Electronic energy (MeOH solvation): -709.7911455
Free energy (MeOH solvation): -709.5626035
Coordinates:

C	-0.90428	1.24530	-1.15521
N	-1.35901	0.58658	-0.14015
C	0.30635	2.08677	-1.10677
H	-1.47871	1.13306	-2.07545
C	0.78913	2.35431	0.31500
C	-0.70112	0.57127	1.20274
C	0.74564	1.04305	1.11865
H	0.15146	3.10732	0.79155
H	1.80236	2.75846	0.28558
H	-0.77855	-0.44863	1.57864
C	-2.60318	-0.18443	-0.35658
O	-3.14002	-0.20140	-1.42198
O	-2.94706	-0.77124	0.75672
C	-4.16874	-1.55784	0.69140
H	-5.00016	-0.90267	0.43183
H	-4.28609	-1.97521	1.68712
H	-4.04961	-2.33925	-0.05874
H	-1.30099	1.21778	1.84909
H	0.10436	2.99852	-1.68005
H	1.06391	1.53554	-1.69064
C	1.70446	0.01055	0.53774
C	1.28860	-1.17393	-0.07552

H 0.23600 -1.44254 -0.12720
C 2.21902 -2.06151 -0.62043
H 1.87554 -2.97838 -1.08842
C 3.57856 -1.77652 -0.55490
H 4.30175 -2.46795 -0.97389
C 4.00660 -0.60233 0.06525
H 5.06598 -0.37876 0.13671
C 3.07699 0.28129 0.60355
H 3.42467 1.18598 1.09774
H 1.04950 1.25585 2.14977

Minimum
Type: Cation
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: NA
Oxamate conformation: anti
Electronic energy (gas): -709.717245
Free energy (gas): -709.489212
Electronic energy (MeOH solvation): -709.7886975
Free energy (MeOH solvation): -709.5606645
Coordinates:
C -1.52086 1.81953 -0.64875
N -1.52564 0.50212 0.05482
C -0.11089 2.37372 -0.77005
H -1.99307 1.64996 -1.61638
C 0.61534 2.29369 0.56935
C -0.55468 0.07976 0.79932
C 0.70062 0.83306 1.03647
H 0.07713 2.88433 1.31982
H 1.62569 2.70077 0.49289
H -0.67646 -0.90653 1.24189
C -2.75460 -0.29114 -0.12837
O -3.63770 0.13245 -0.80760
O -2.68664 -1.41835 0.53451
C -3.85581 -2.27507 0.41950
H -4.72490 -1.74688 0.81145
H -3.61969 -3.15132 1.01620
H -4.00683 -2.53449 -0.62819
H -0.18939 3.40905 -1.10994
H 0.44586 1.82714 -1.53839
C 1.82858 0.01579 0.40345
C 1.68993 -0.57317 -0.85824
H 0.75695 -0.49452 -1.41260
C 2.75229 -1.27405 -1.42756
H 2.63497 -1.72780 -2.40597
C 3.95696 -1.39069 -0.74038
H 4.78458 -1.93406 -1.18383
C 4.09814 -0.81060 0.52097
H 5.03528 -0.90089 1.06019
C 3.03688 -0.11754 1.09446
H 3.15112 0.33004 2.07839
H -2.17604 2.47716 -0.06897
H 0.85764 0.79065 2.12329

Minimum
Type: Cation
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: axial
Radical orientation: NA
Oxamate conformation: syn
Electronic energy (gas): -709.718099
Free energy (gas): -709.490067

Electronic energy (MeOH solvation): -709.7892962
Free energy (MeOH solvation): -709.5612642
Coordinates:

C	0.42392	0.07694	0.92705
N	1.46161	0.28987	0.18345
C	-0.78877	0.92638	0.92750
H	0.47636	-0.80654	1.56418
C	-0.56719	2.26394	0.20654
C	1.57550	1.42417	-0.78296
C	0.21282	2.03100	-1.08280
H	-0.01204	2.94537	0.86199
H	-1.53708	2.72183	0.00123
H	0.37863	2.96955	-1.61686
H	-0.35352	1.37533	-1.75288
H	2.05357	1.02309	-1.67658
C	2.59523	-0.64469	0.34954
O	2.51560	-1.58902	1.07461
O	3.59864	-0.24258	-0.38237
C	4.79557	-1.06317	-0.29386
H	5.15048	-1.06478	0.73664
H	5.50994	-0.58913	-0.96063
H	4.55829	-2.07661	-0.61713
H	2.25973	2.14765	-0.32953
C	-1.93962	0.08493	0.37319
C	-3.20884	0.23133	0.94212
H	-3.35084	0.90456	1.78378
C	-4.29187	-0.47227	0.42649
H	-5.27462	-0.34563	0.86829
C	-4.11409	-1.34225	-0.64989
H	-4.95918	-1.89495	-1.04652
C	-2.85071	-1.50383	-1.21123
H	-2.70556	-2.18526	-2.04279
C	-1.76536	-0.79083	-0.70291
H	-0.78628	-0.93021	-1.15739
H	-1.01265	1.09948	1.98940

Minimum
Type: Cation
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: NA
Oxamate conformation: anti
Electronic energy (gas): -709.717794
Free energy (gas): -709.49002
Electronic energy (MeOH solvation): -709.7898132
Free energy (MeOH solvation): -709.5620392
Coordinates:

C	-1.89679	1.80821	0.51413
N	-1.62246	0.44816	-0.03792
C	-0.91203	2.81791	-0.05024
H	-2.93205	2.03558	0.26041
C	0.51732	2.30859	0.10816
C	-0.49580	0.11137	-0.57808
C	0.69700	0.99757	-0.66599
H	0.73768	2.13633	1.16773
H	1.24619	3.03661	-0.25372
H	-0.42936	-0.90135	-0.97198
C	-2.73551	-0.50959	0.08856
O	-3.74470	-0.17509	0.62743
O	-2.42190	-1.66412	-0.44294
C	-3.45639	-2.68258	-0.36453
H	-3.68490	-2.87931	0.68266
H	-3.02637	-3.55499	-0.84815
H	-4.34394	-2.33140	-0.89057

H	-1.05471	3.76168	0.48130
H	-1.82956	1.72408	1.60324
H	-1.13985	3.00671	-1.10612
C	1.91257	0.17763	-0.25636
C	2.96434	-0.02540	-1.15032
H	2.92127	0.40339	-2.14821
C	4.07790	-0.76712	-0.76049
H	4.89746	-0.91215	-1.45633
C	4.13800	-1.31826	0.51797
H	5.00552	-1.89580	0.81915
C	3.08553	-1.12476	1.41194
H	3.13122	-1.55079	2.40870
C	1.97602	-0.37670	1.02655
H	1.16710	-0.21434	1.73798
H	0.79138	1.21102	-1.74436

Minimum
Type: Cation
Substituent: Me
Regioisomer: proximal
Methyl (on ring) orientation: equatorial
Radical orientation: NA
Oxamate conformation: syn
Electronic energy (gas): -709.718567
Free energy (gas): -709.490936
Electronic energy (MeOH solvation): -709.7902668
Free energy (MeOH solvation): -709.5626358
Coordinates:

C	-0.35030	0.07375	0.68212
N	-1.52342	0.27980	0.17603
C	0.79717	1.01433	0.57381
H	-0.22085	-0.88005	1.19555
C	0.50307	2.18714	-0.36829
C	-1.90871	1.54106	-0.52482
C	-0.93541	2.65752	-0.18115
H	0.66278	1.86760	-1.40454
H	1.21671	2.98960	-0.17081
H	-1.15941	3.50960	-0.82730
H	-1.10119	2.98511	0.85216
H	-2.92753	1.77036	-0.21444
C	-2.50762	-0.81500	0.31351
O	-2.24380	-1.81198	0.91330
O	-3.60707	-0.48652	-0.30944
C	-4.66469	-1.48266	-0.26662
H	-4.31500	-2.39417	-0.75135
H	-5.49225	-1.03499	-0.80930
H	-4.92760	-1.67997	0.77247
C	2.02792	0.19572	0.20989
C	3.13621	0.16443	1.05678
H	3.13035	0.73262	1.98326
C	4.25736	-0.58745	0.71033
H	5.12073	-0.60026	1.36698
C	4.26913	-1.31987	-0.47517
H	5.14171	-1.90665	-0.74172
C	3.16075	-1.29748	-1.32081
H	3.16693	-1.86756	-2.24371
C	2.04352	-0.53961	-0.98015
H	1.18742	-0.51667	-1.65353
H	0.93943	1.38720	1.60233
H	-1.92174	1.31635	-1.59566

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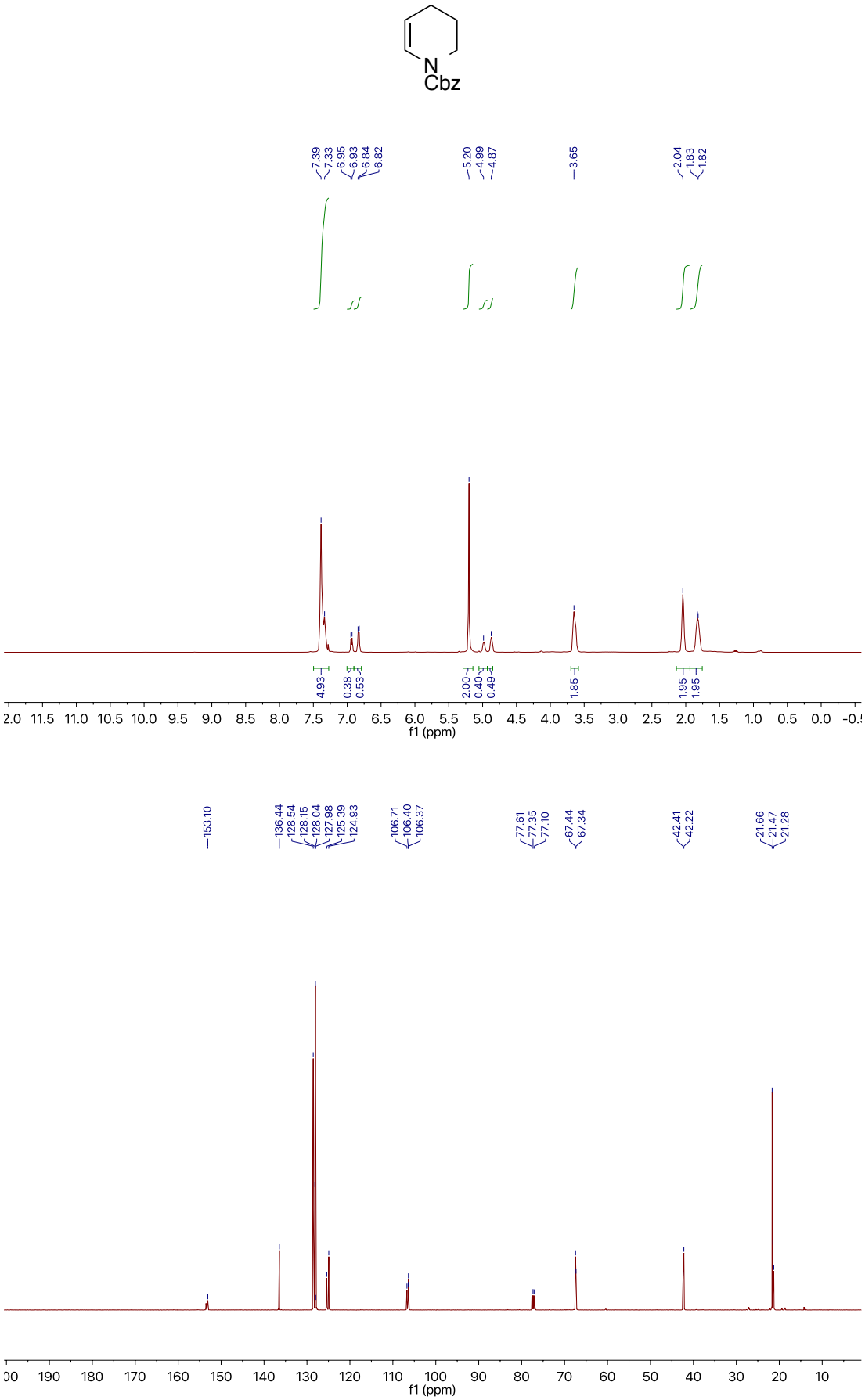
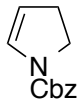
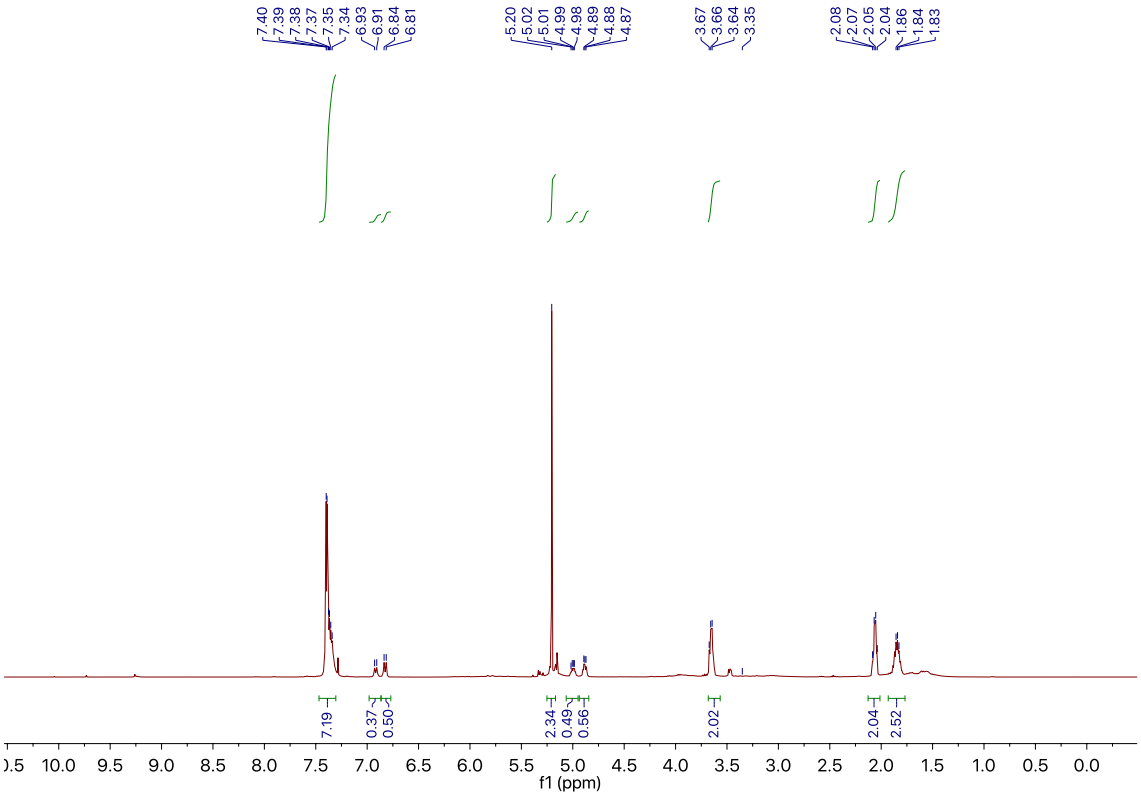
NMR Spectra

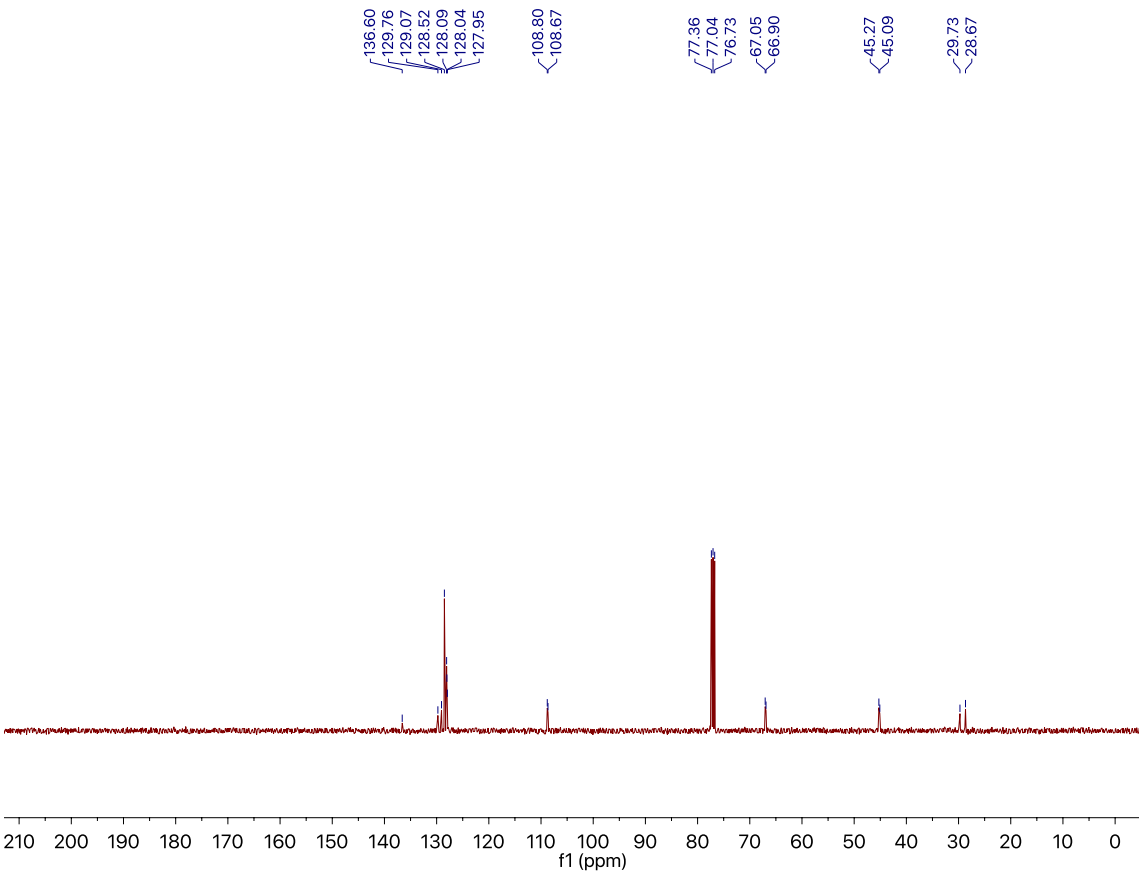
Benzyl 3,4-dihydropyridine-1(2*H*)-carboxylate (6a)



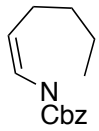
Benzyl-2,3-dihydro-1*H*-pyrrole-1-carboxylate (6b)

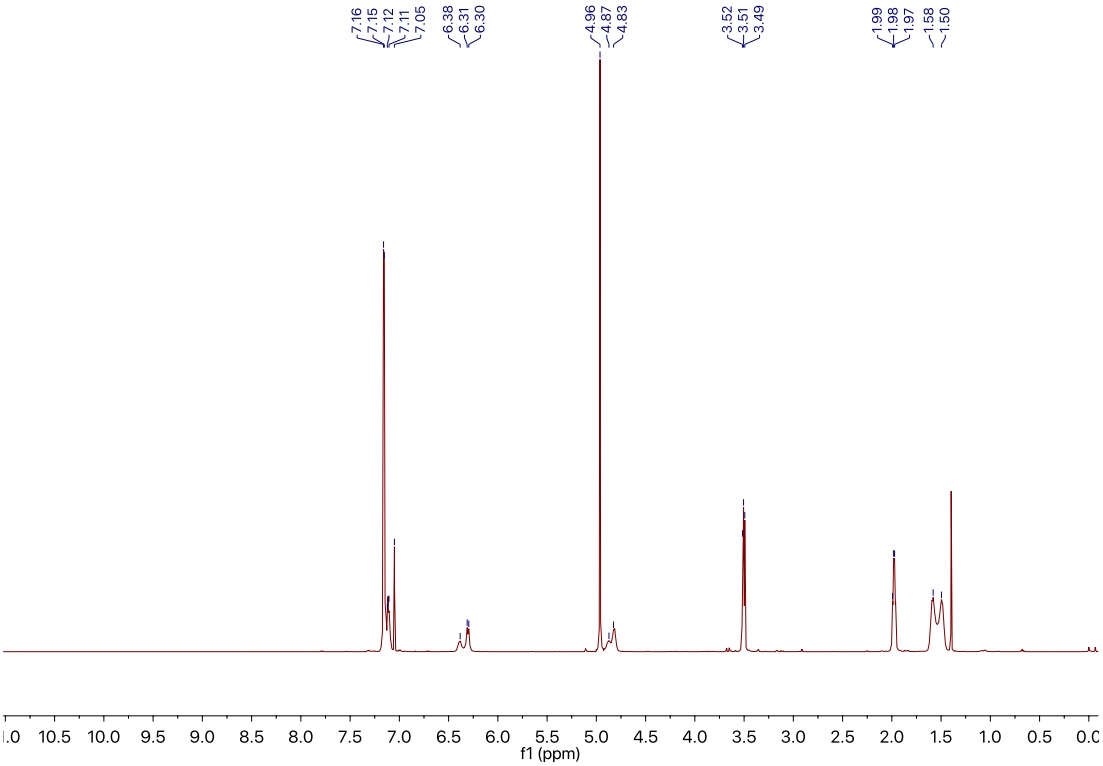


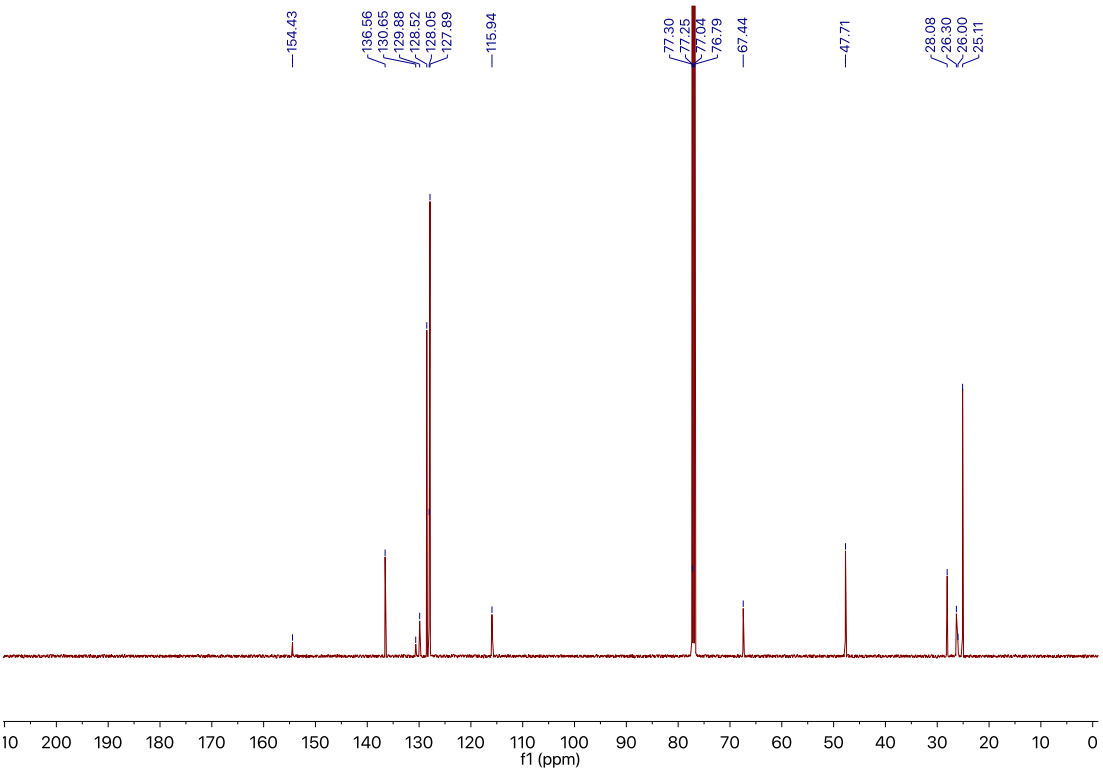




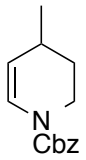
Benzyl 2,3,4,5-tetrahydro-1*H*-azepine-1-carboxylate (6c)

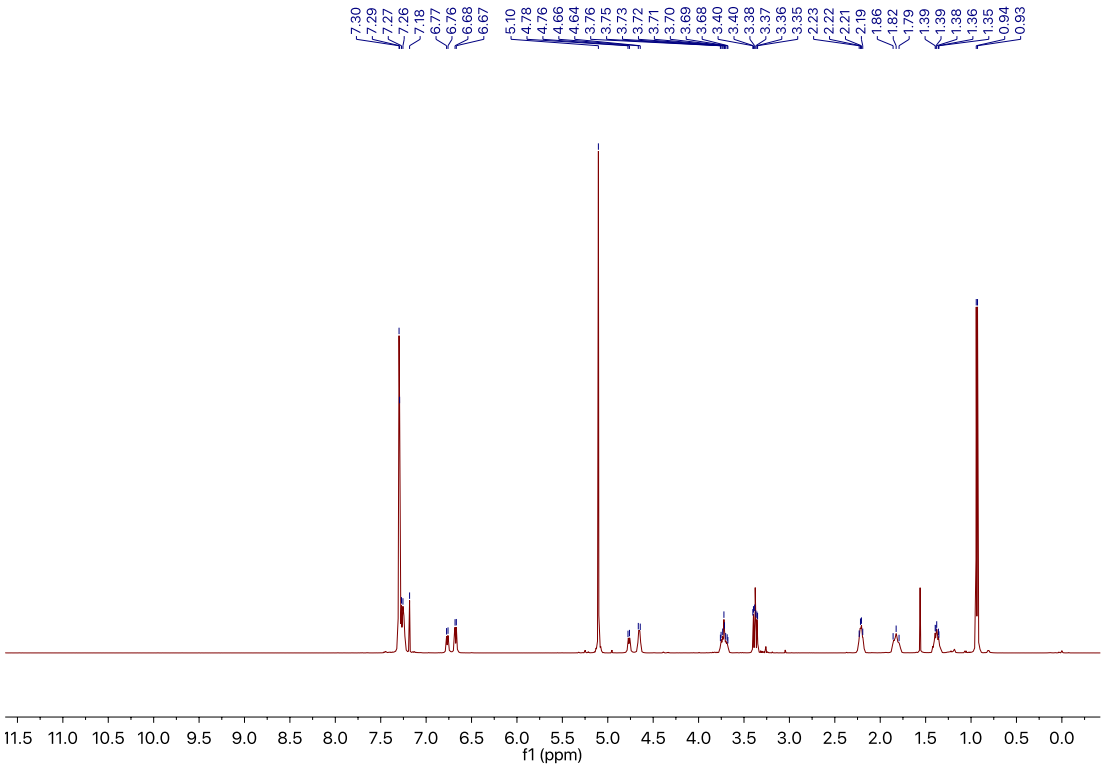


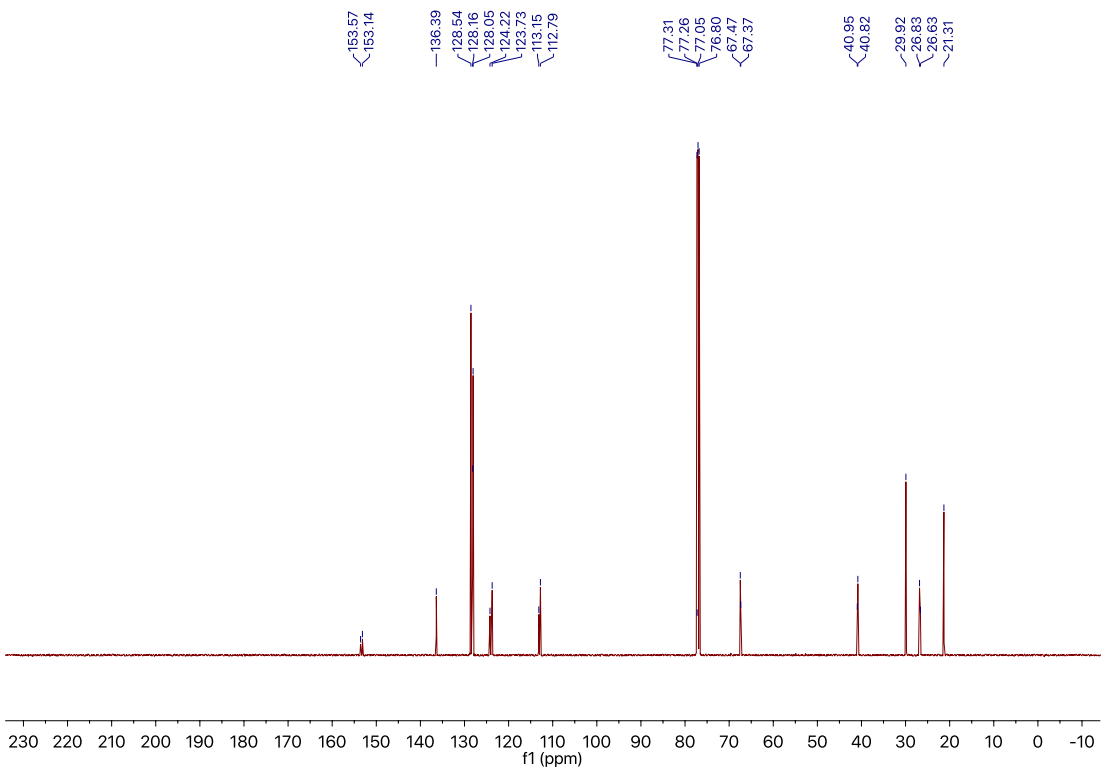




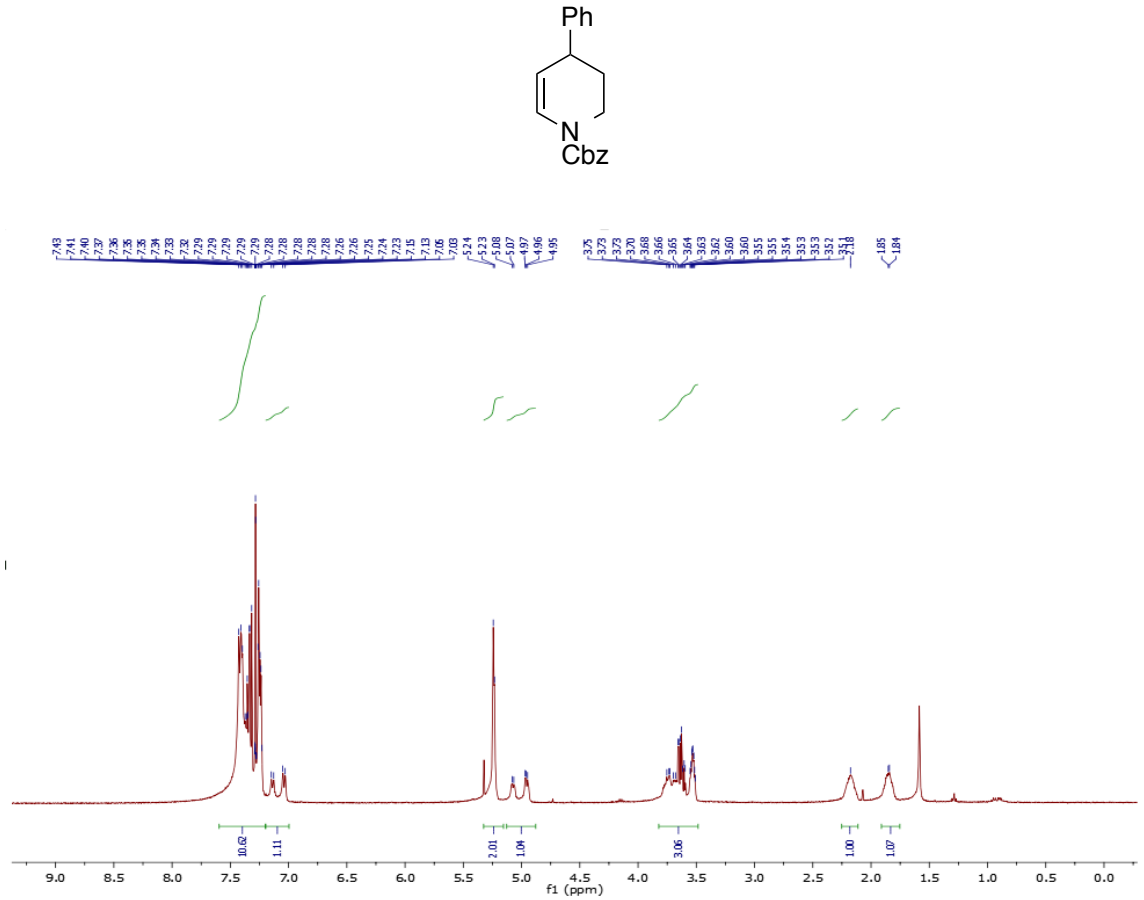
Benzyl 4-methyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6d)

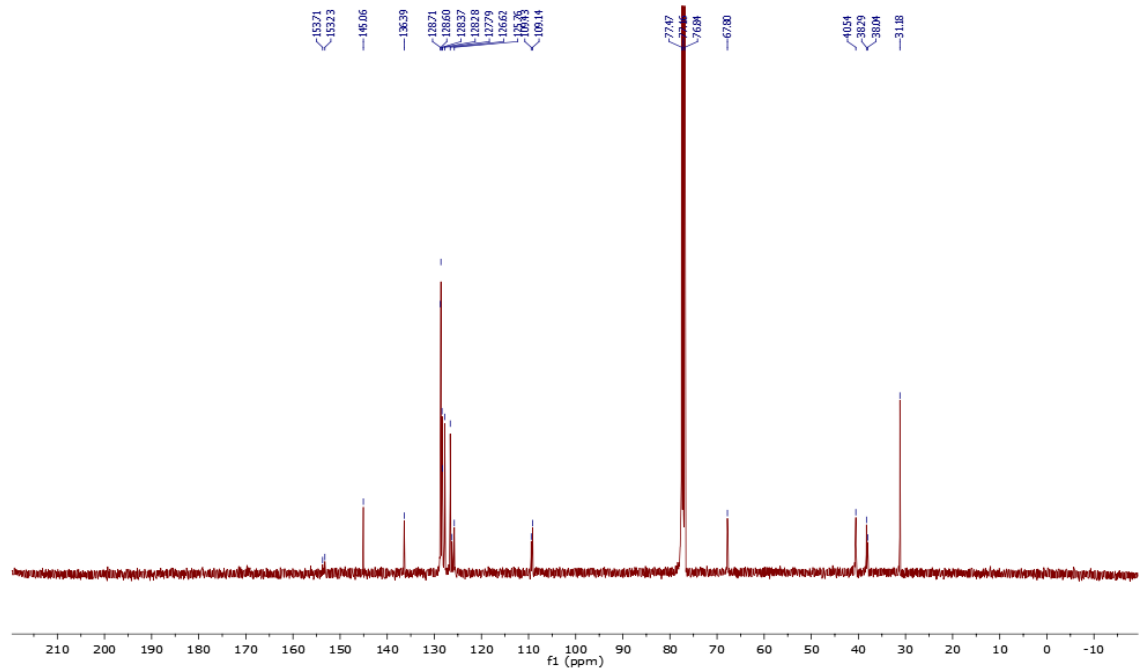




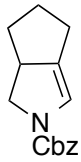


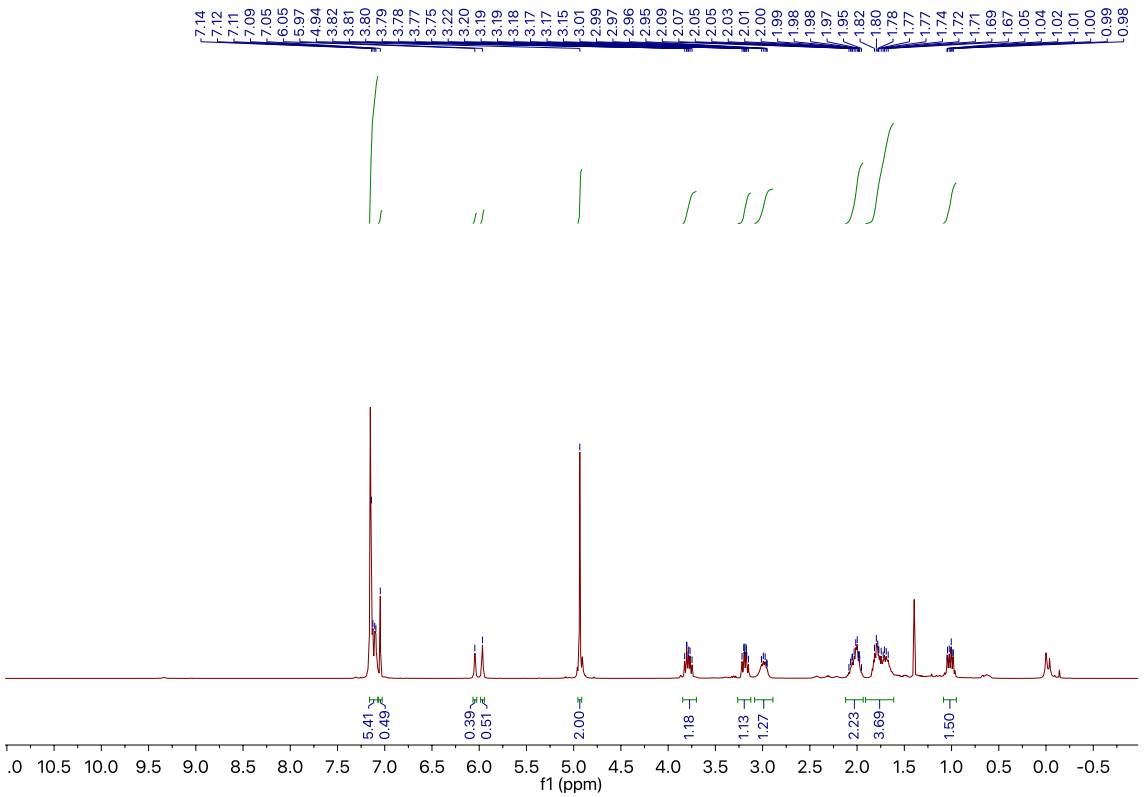
Benzyl 4-phenyl-3,4-dihydropyridine-1(2H)-carboxylate (6e)

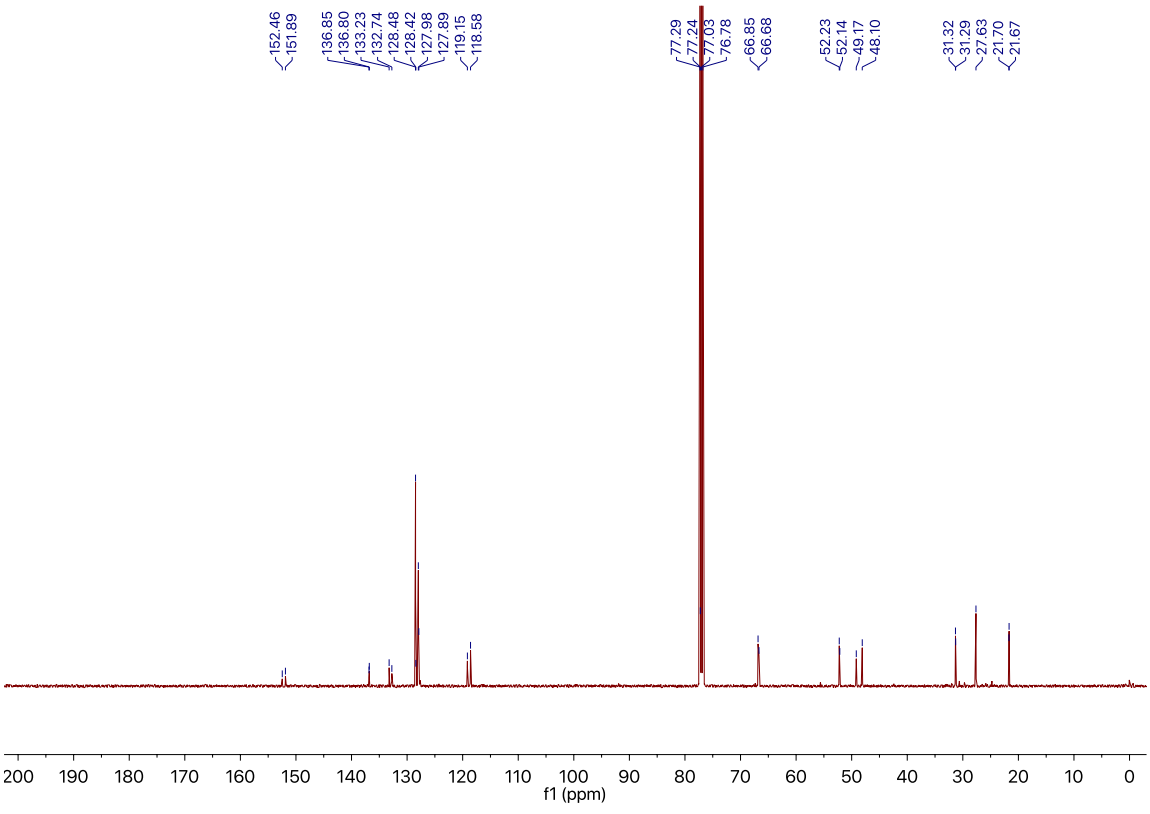




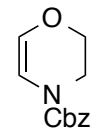
Benzyl 4,5,6,6a-tetrahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate (6f)

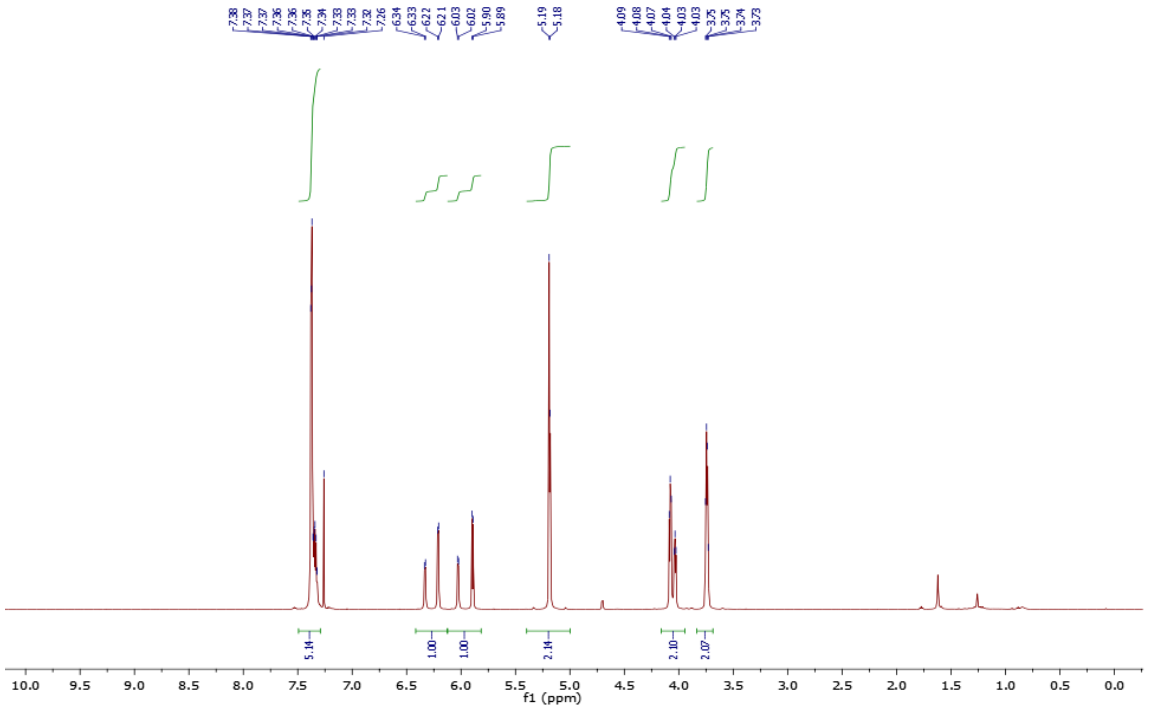


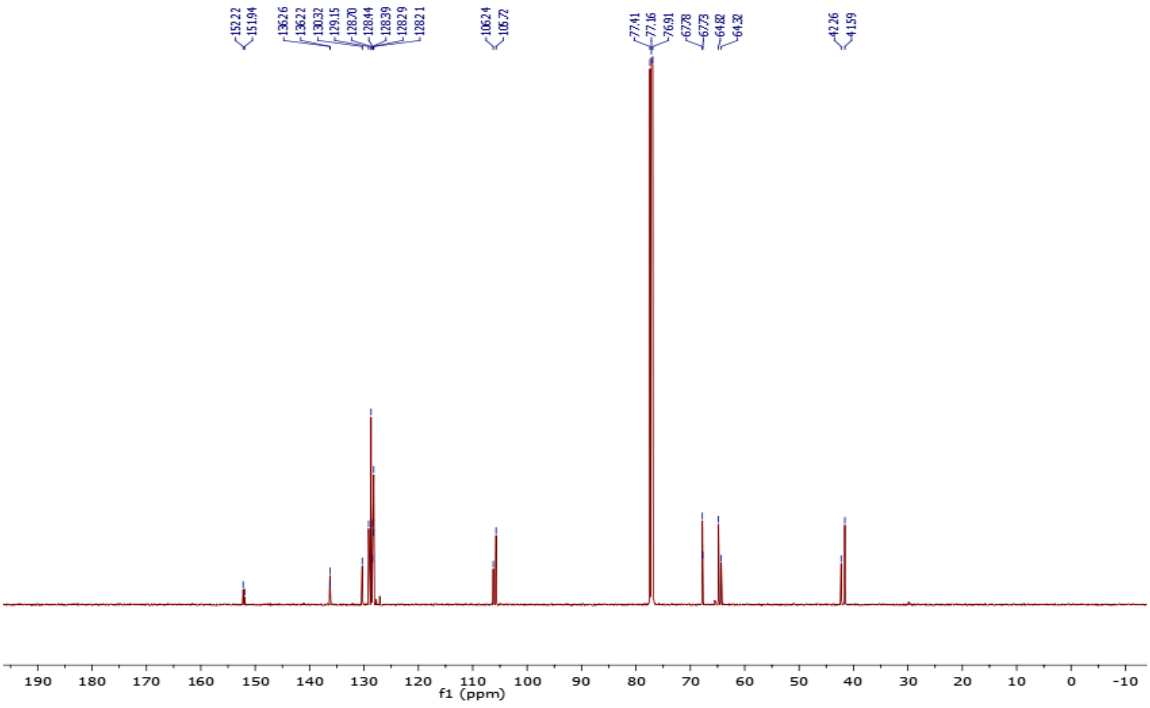




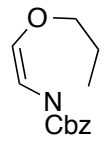
Benzyl 2H-1,4-oxazine-4(3H)-carboxylate (6g)

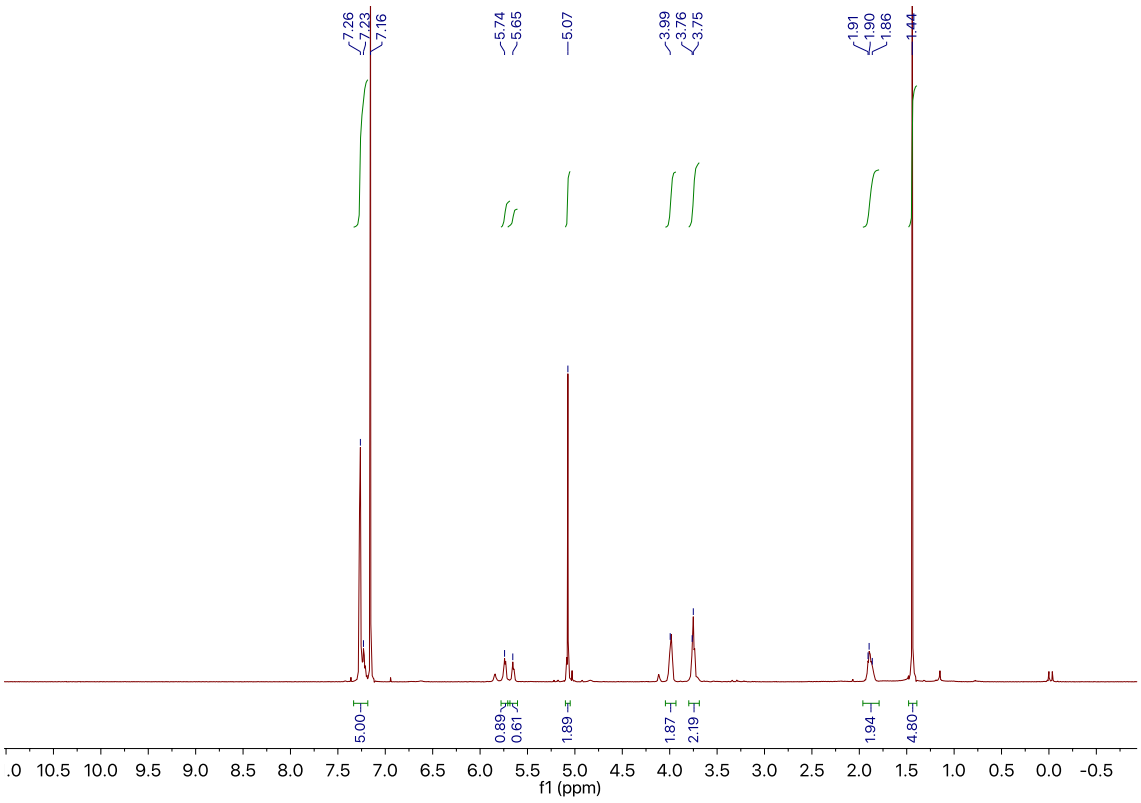


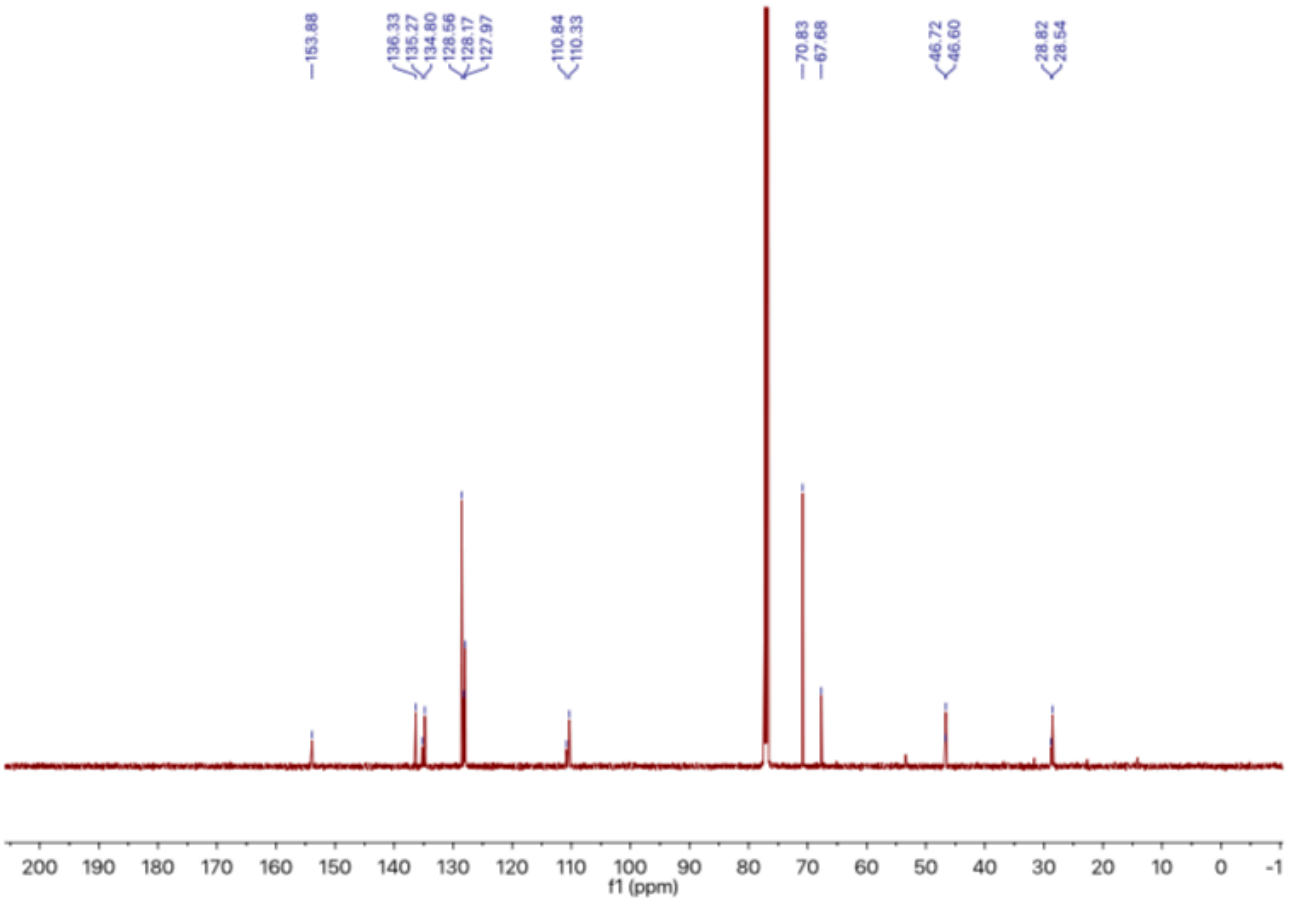




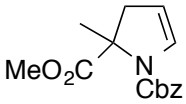
Benzyl 6,7-dihydro-1,4-oxazepine-4(5*H*)-carboxylate (6h)

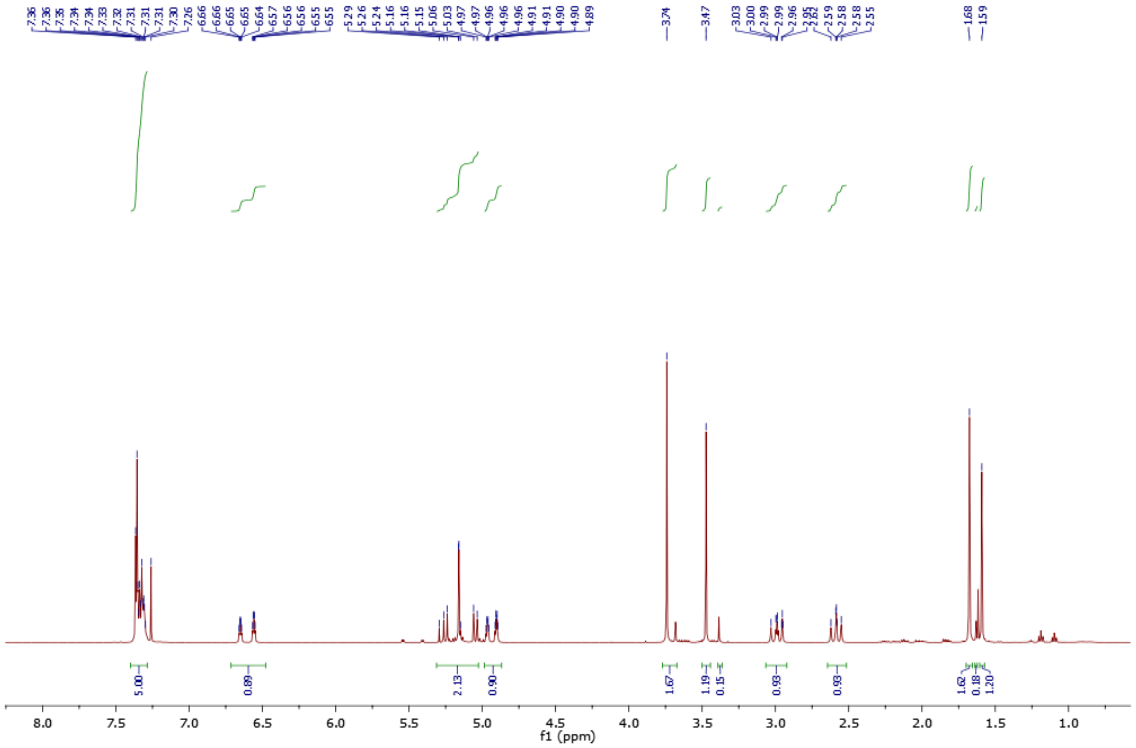


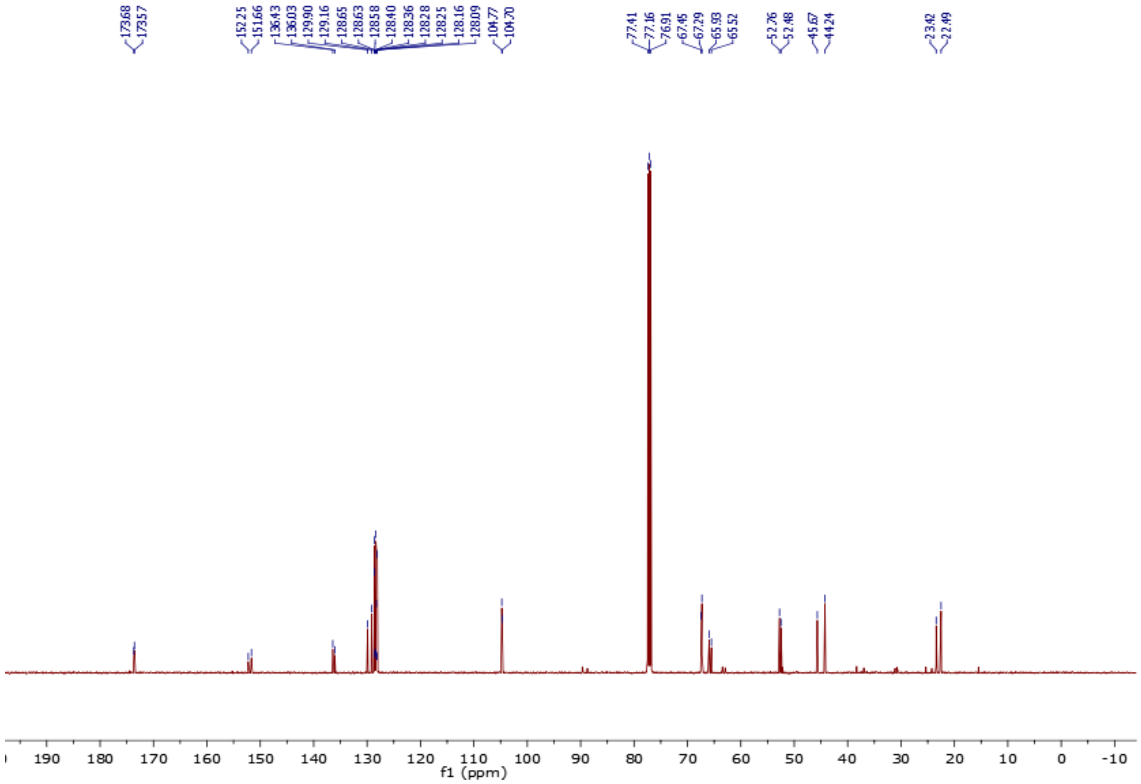




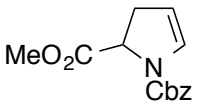
1-Benzyl 2-methyl 2-methyl-2,3-dihydro-1H-pyrrole-1,2-dicarboxylate (6i)

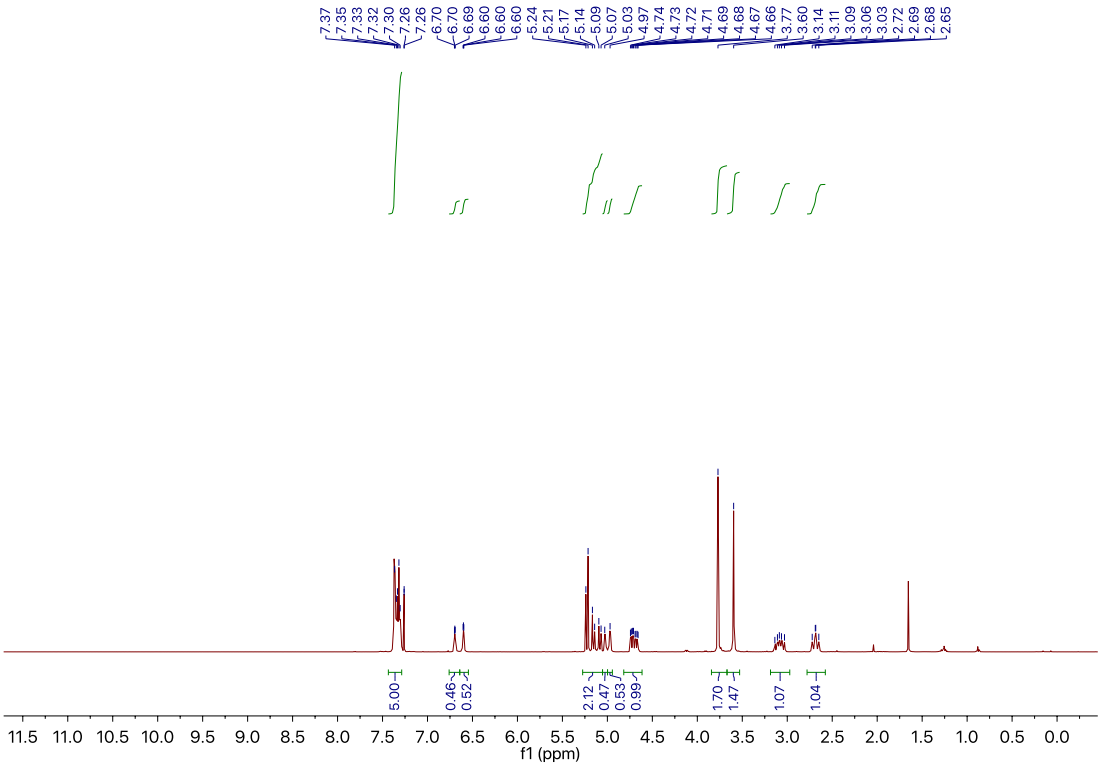


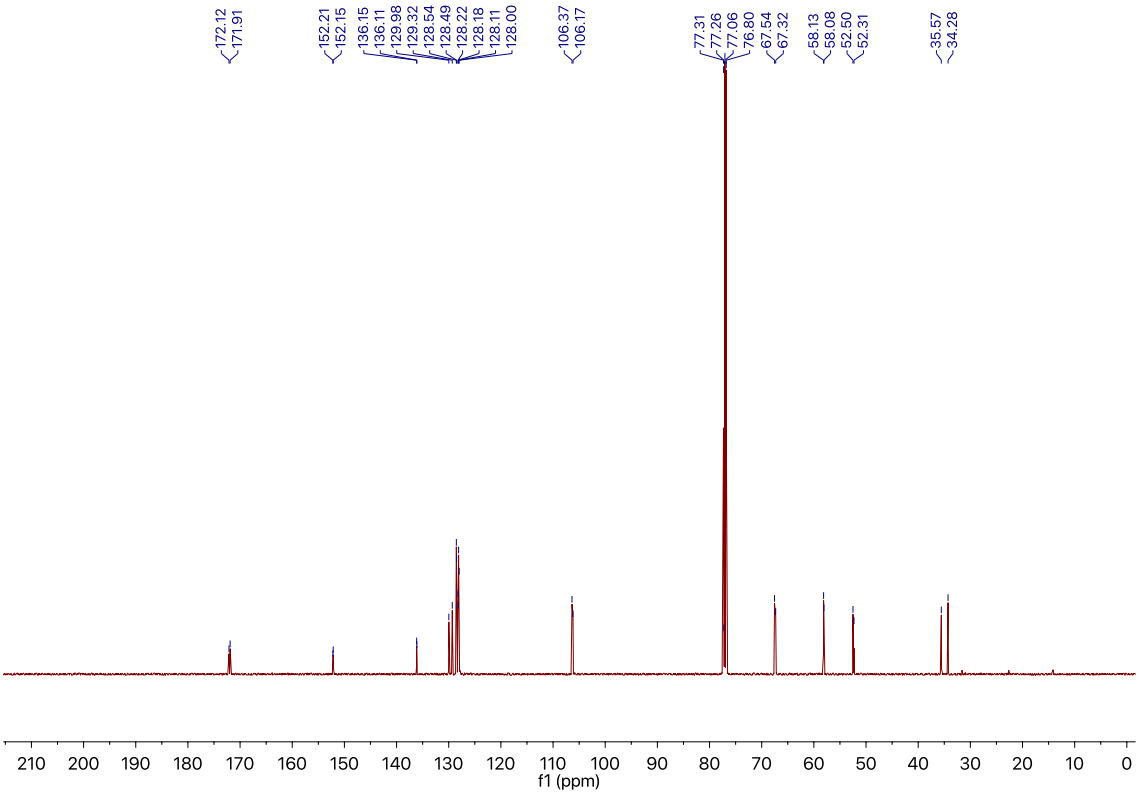




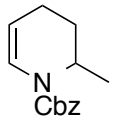
1-Benzyl 2-methyl 2,3-dihydro-1*H*-pyrrole-1,2-dicarboxylate (6j)

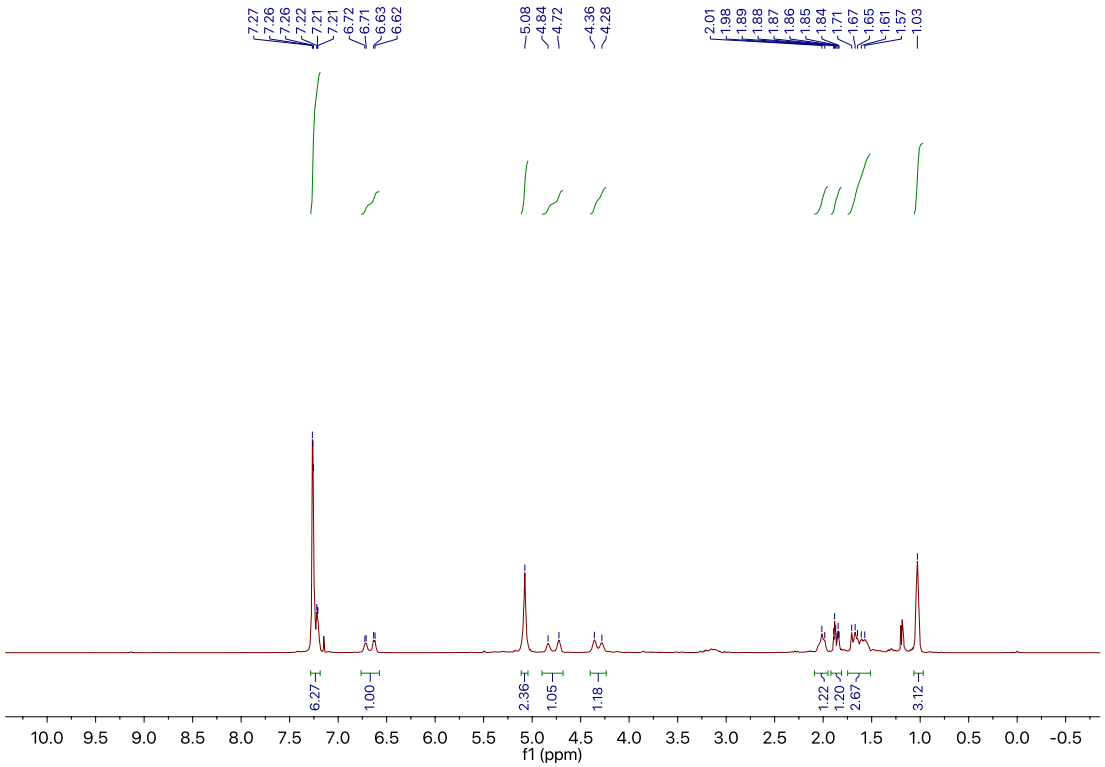


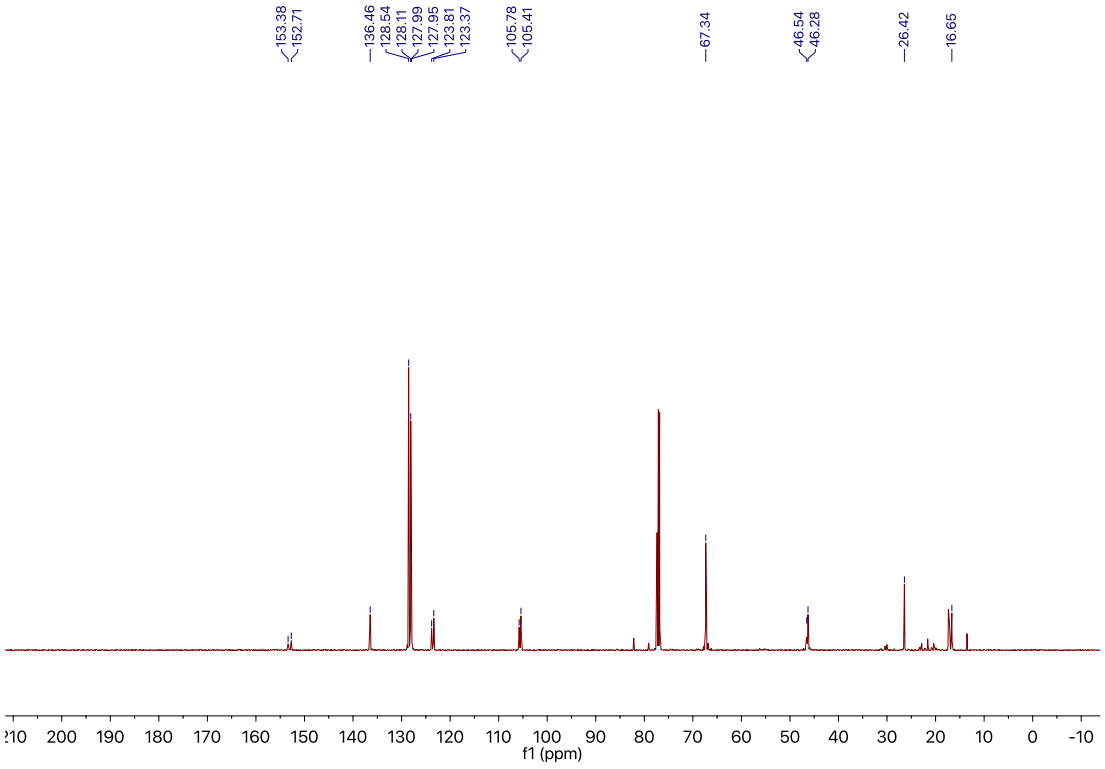




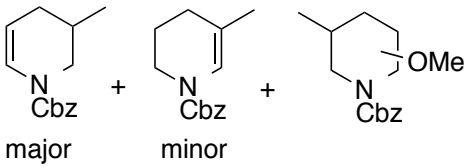
Benzyl 2-methyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6k)





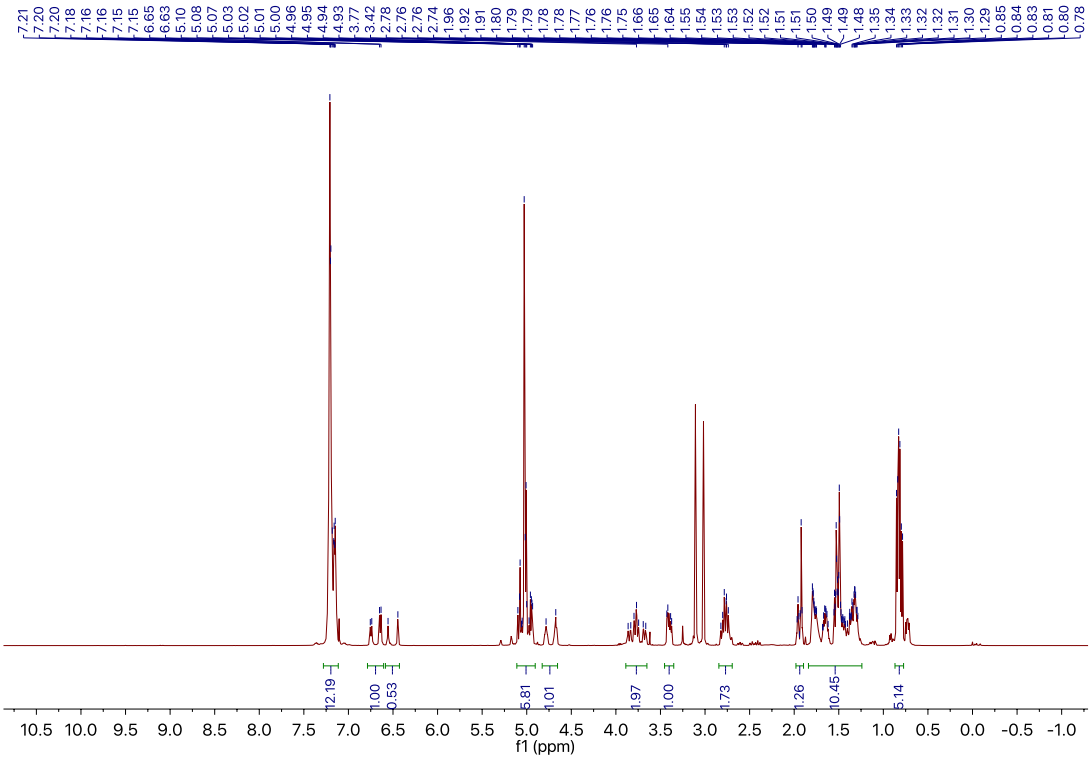


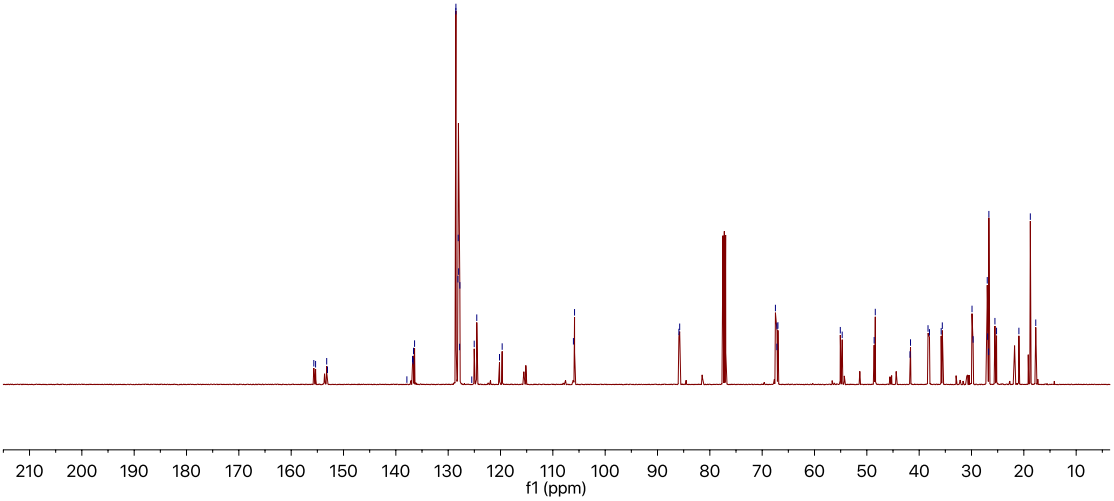
Benzyl 3-methyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6l and 6l')



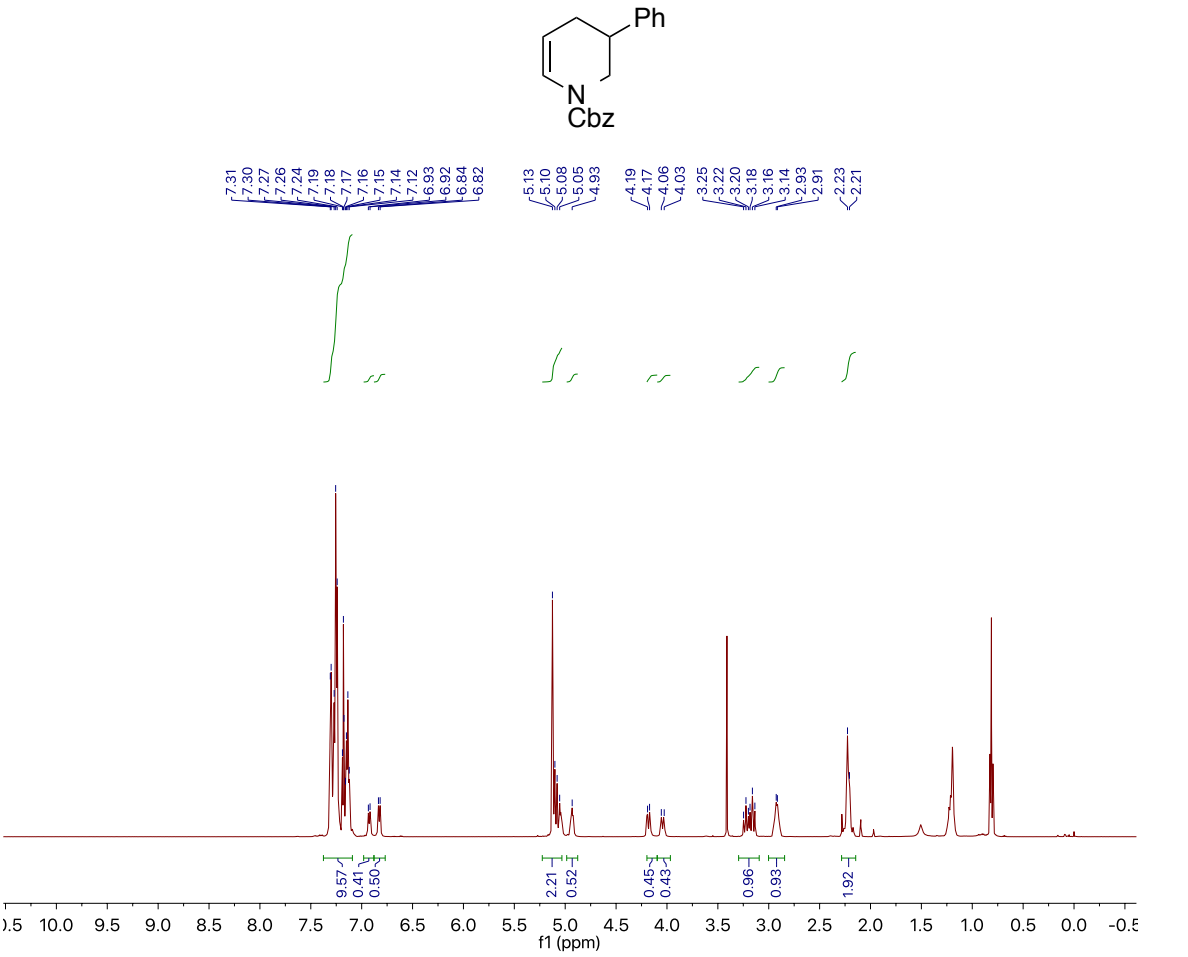
major minor

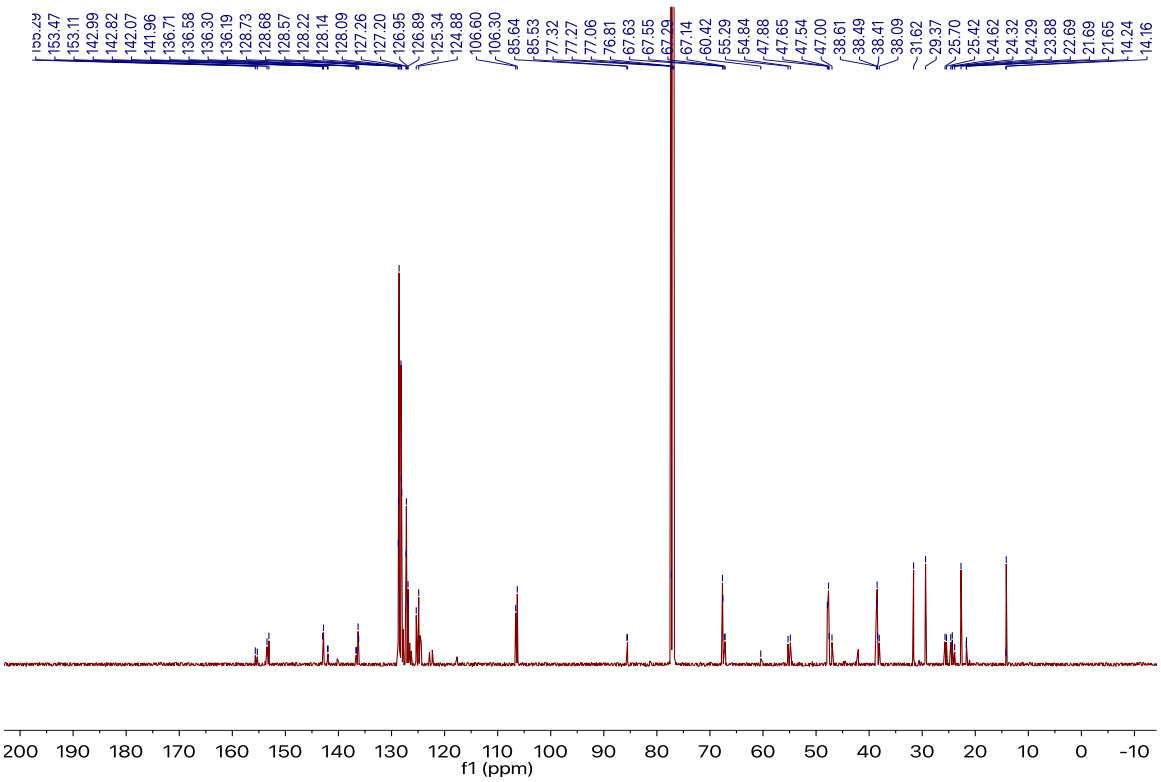
2 : 1 : 2



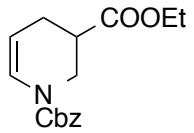


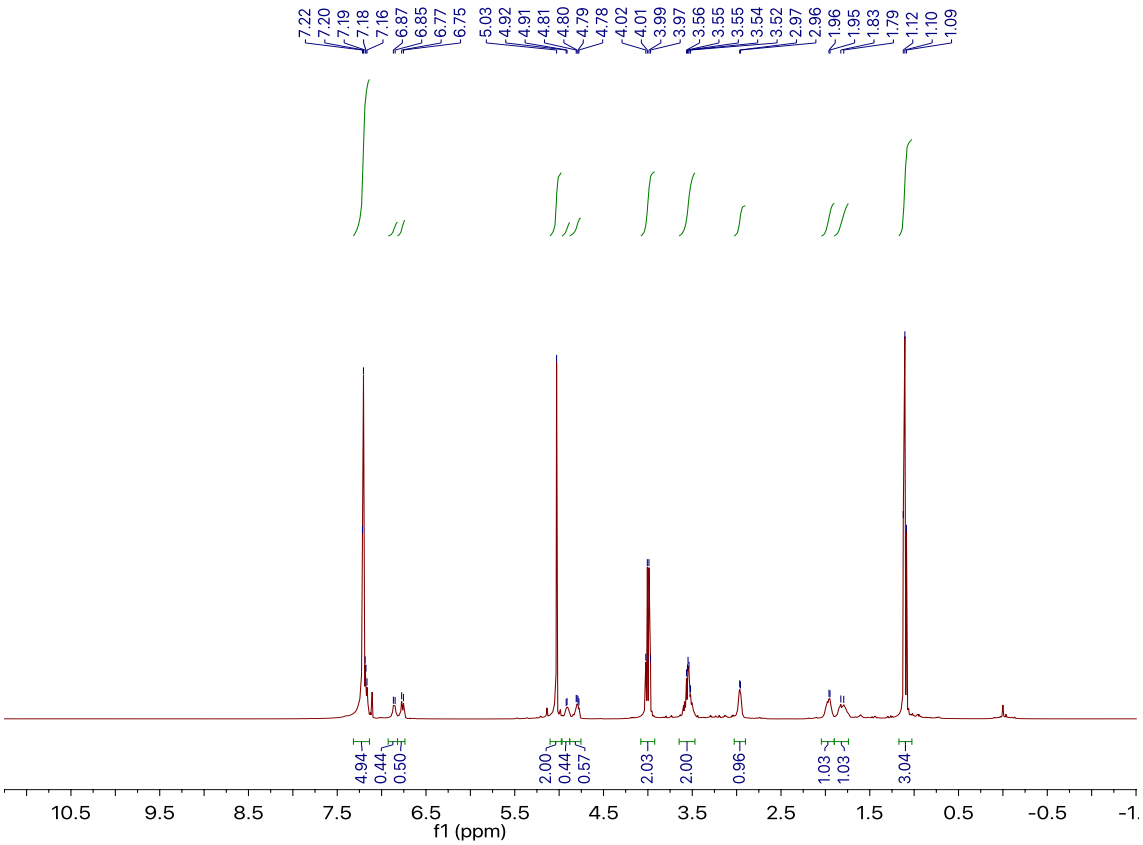
Benzyl 3-phenyl-3,4-dihydropyridine-1(2*H*)-carboxylate (6m)

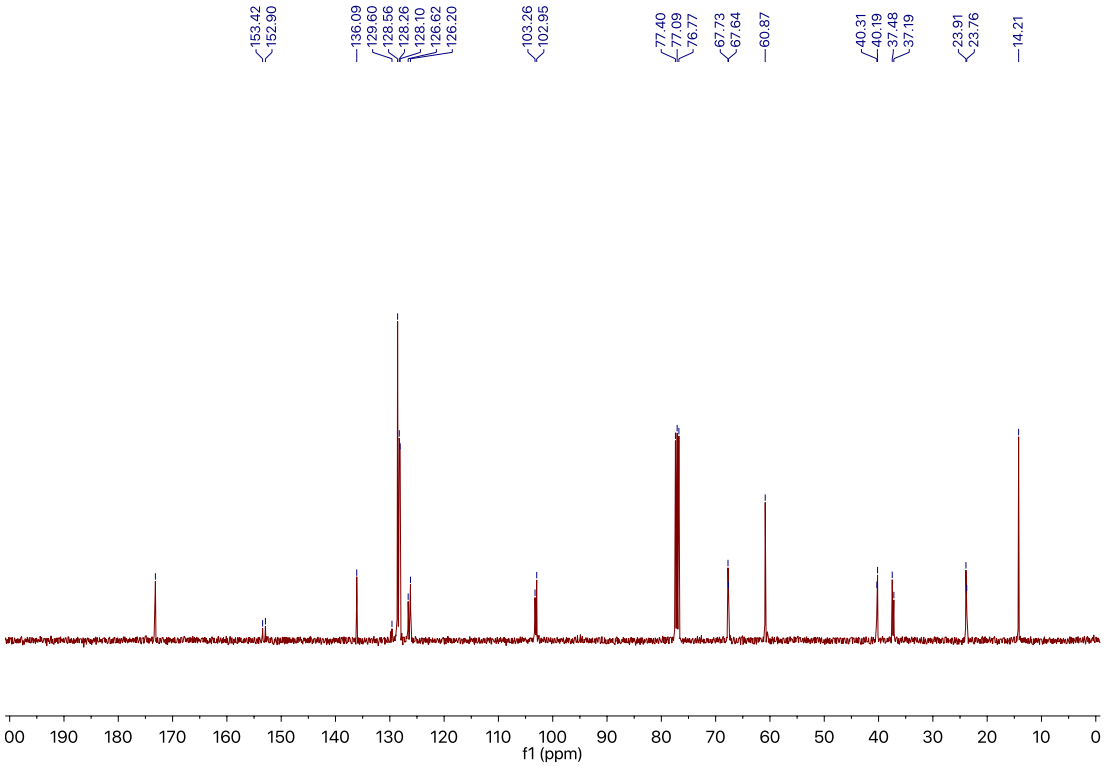




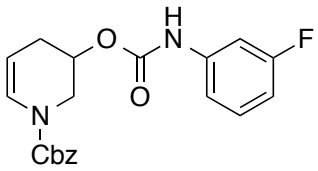
1-Benzyl 3-ethyl 3,4-dihydropyridine-1,3(2*H*)-dicarboxylate (6n)

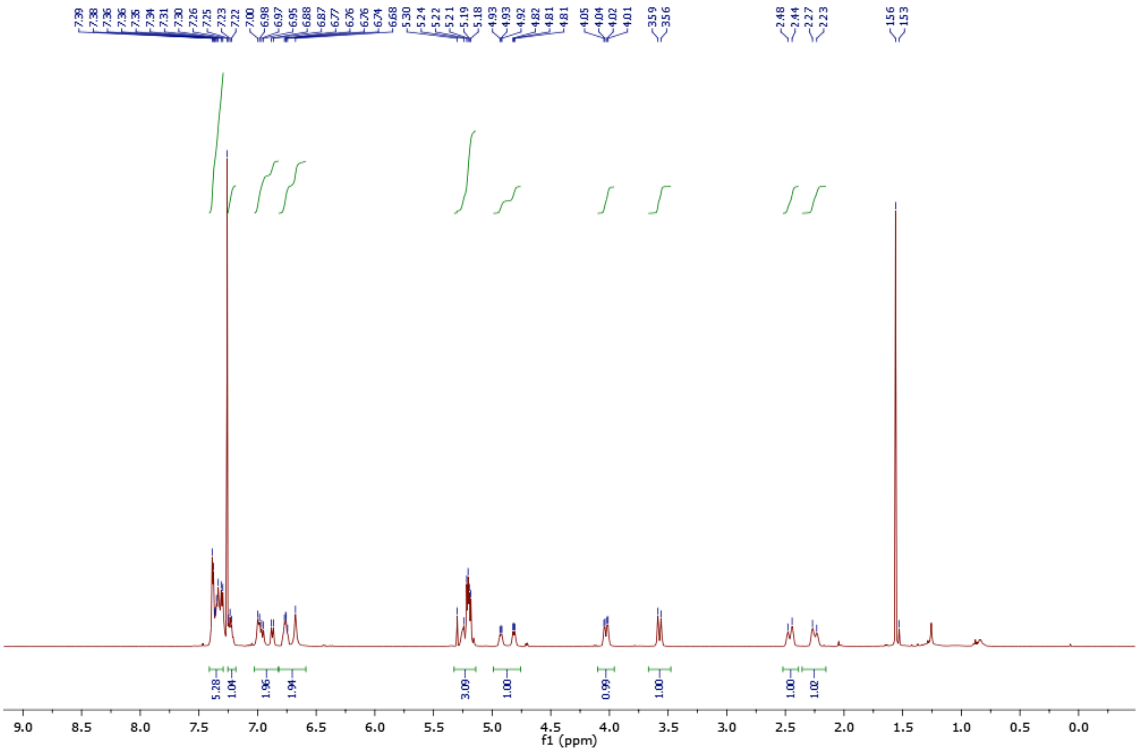


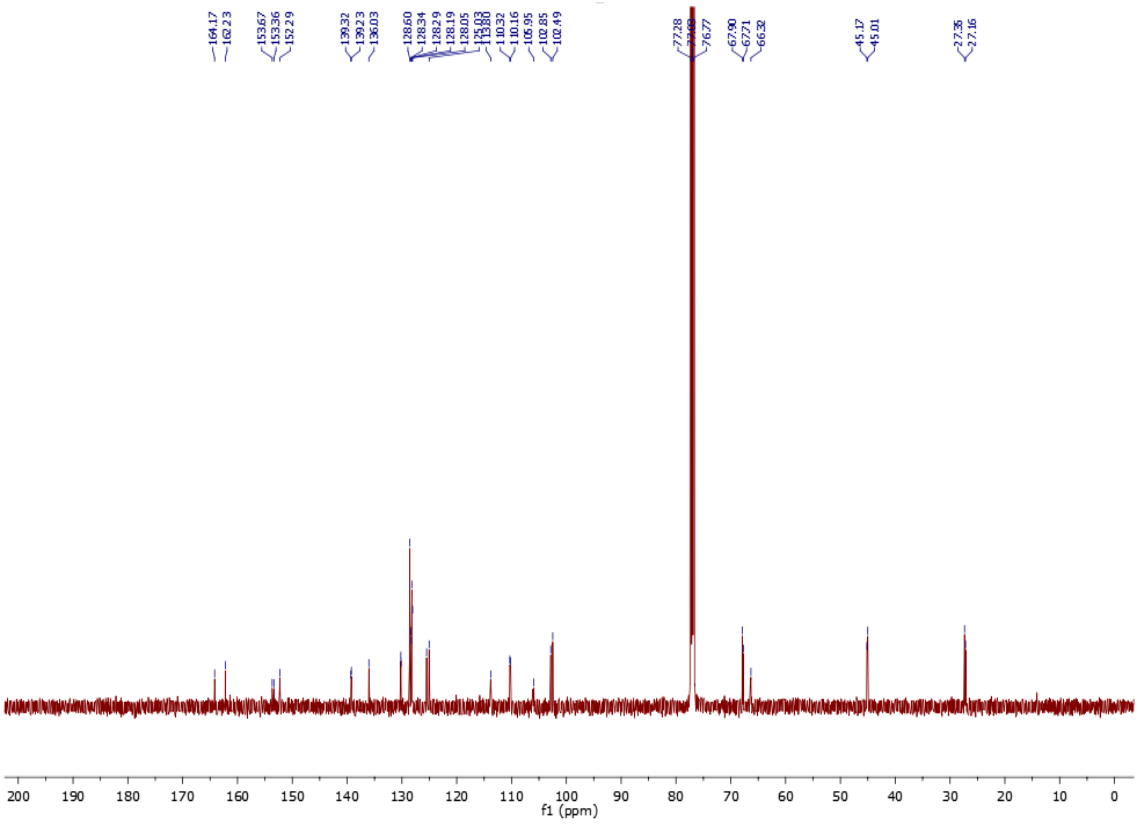




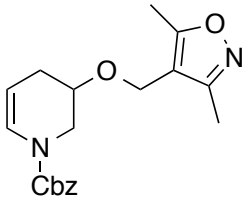
Benzyl 3-(((3-fluorophenyl)carbamoyl)oxy)-3,4-dihydropyridine-1(2H)-carboxylate (6o)

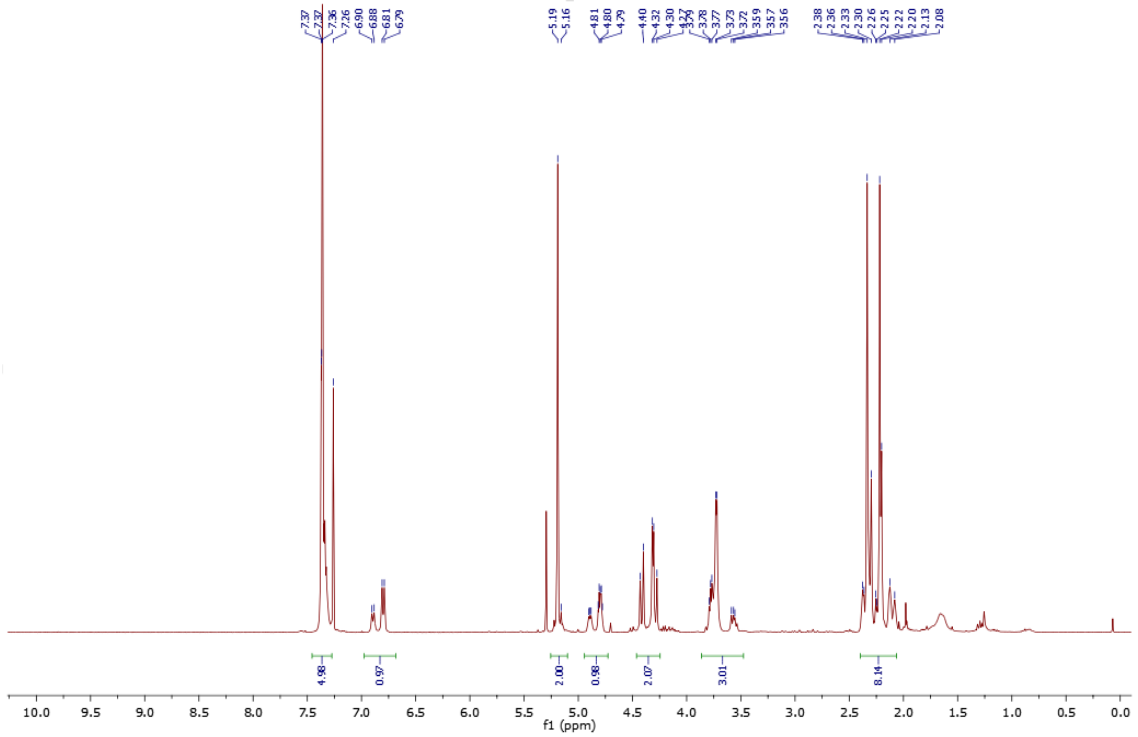


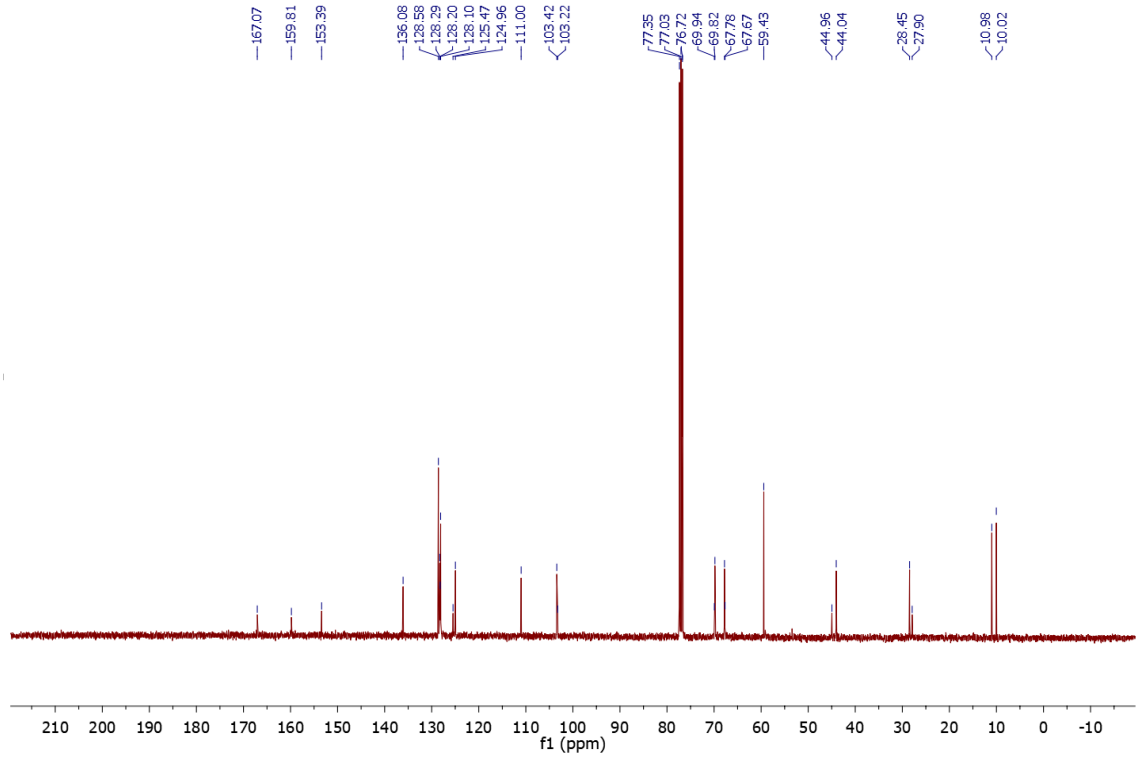




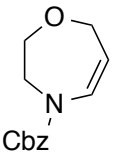
Benzyl 3-((3,5-dimethylisoxazol-4-yl)methoxy)-3,4-dihydropyridine-1(2H)-carboxylate (6p)

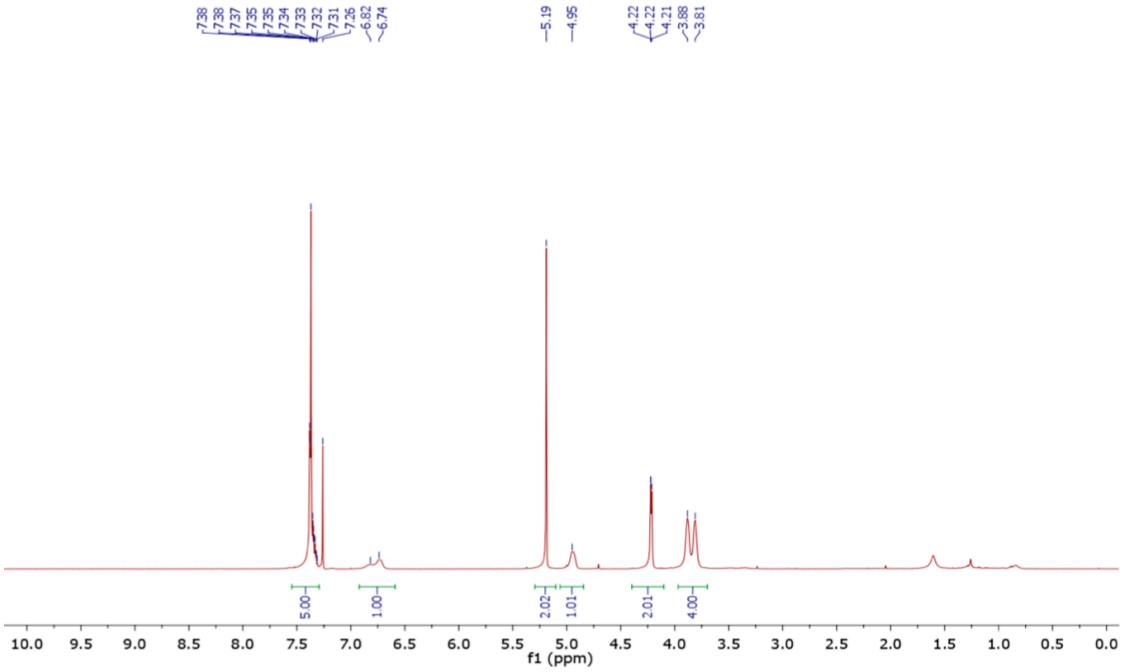


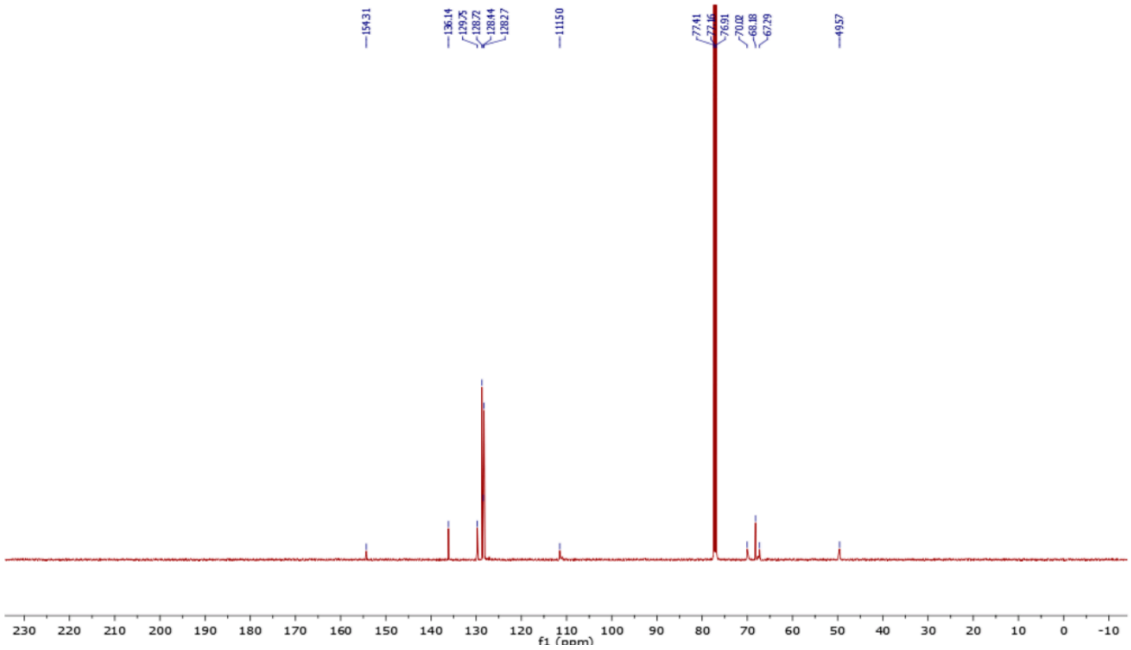




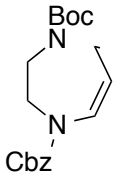
Benzyl 2,3-dihydro-1,4-oxazepine-4(7H)-carboxylate

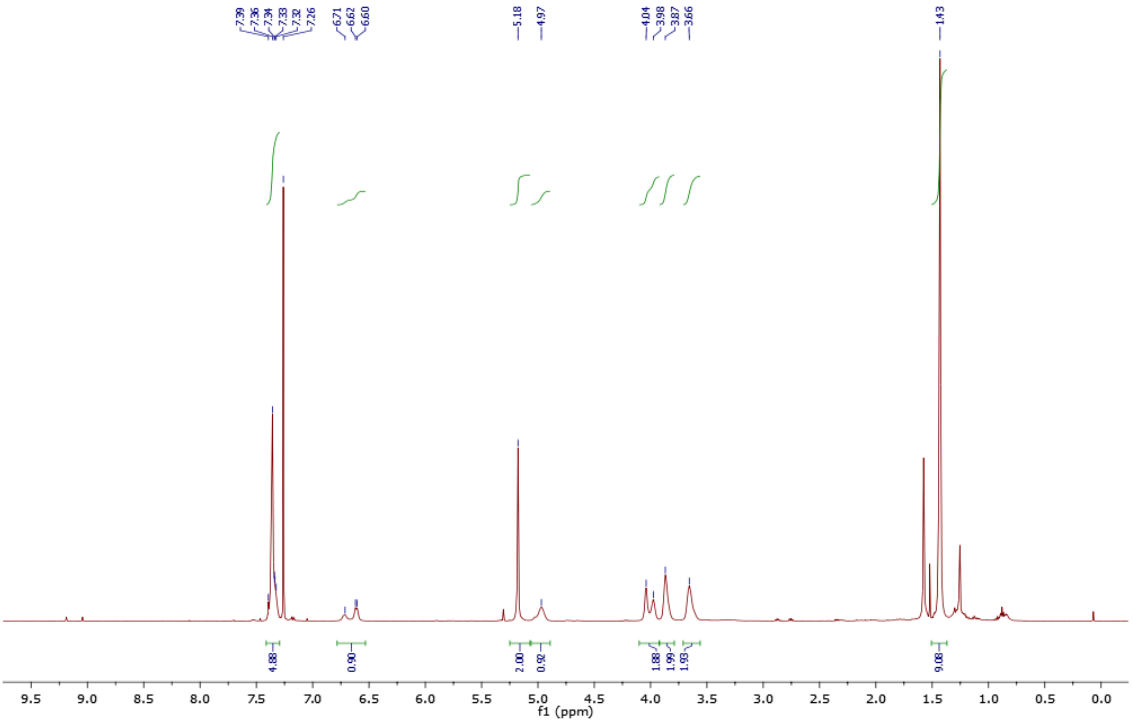


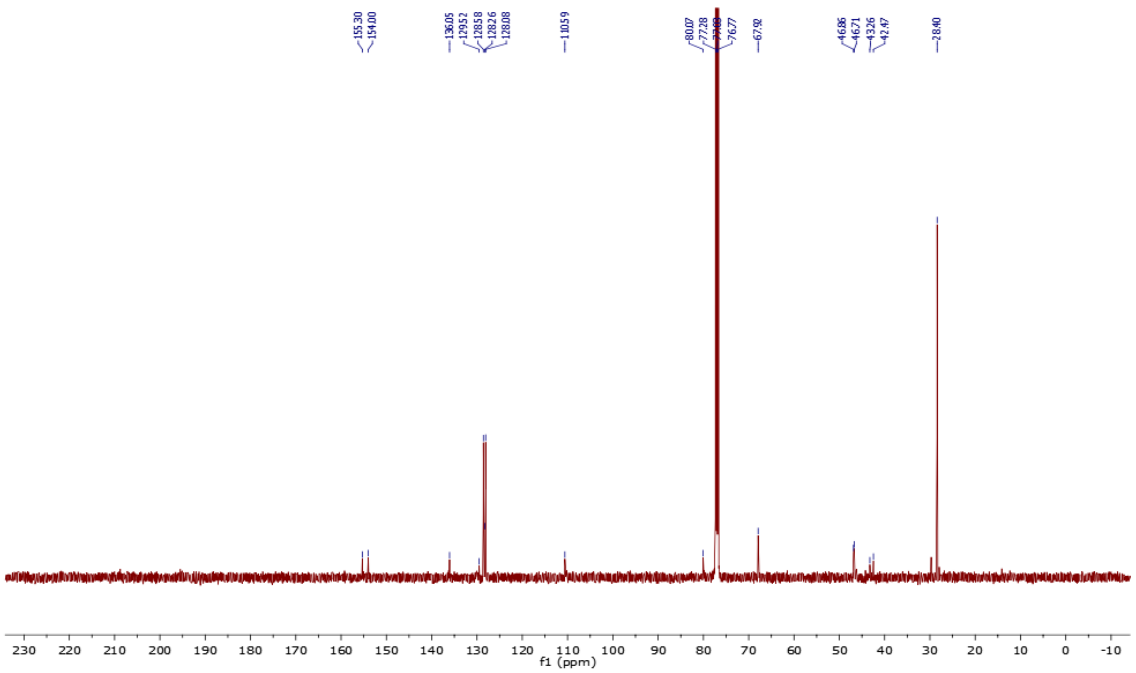




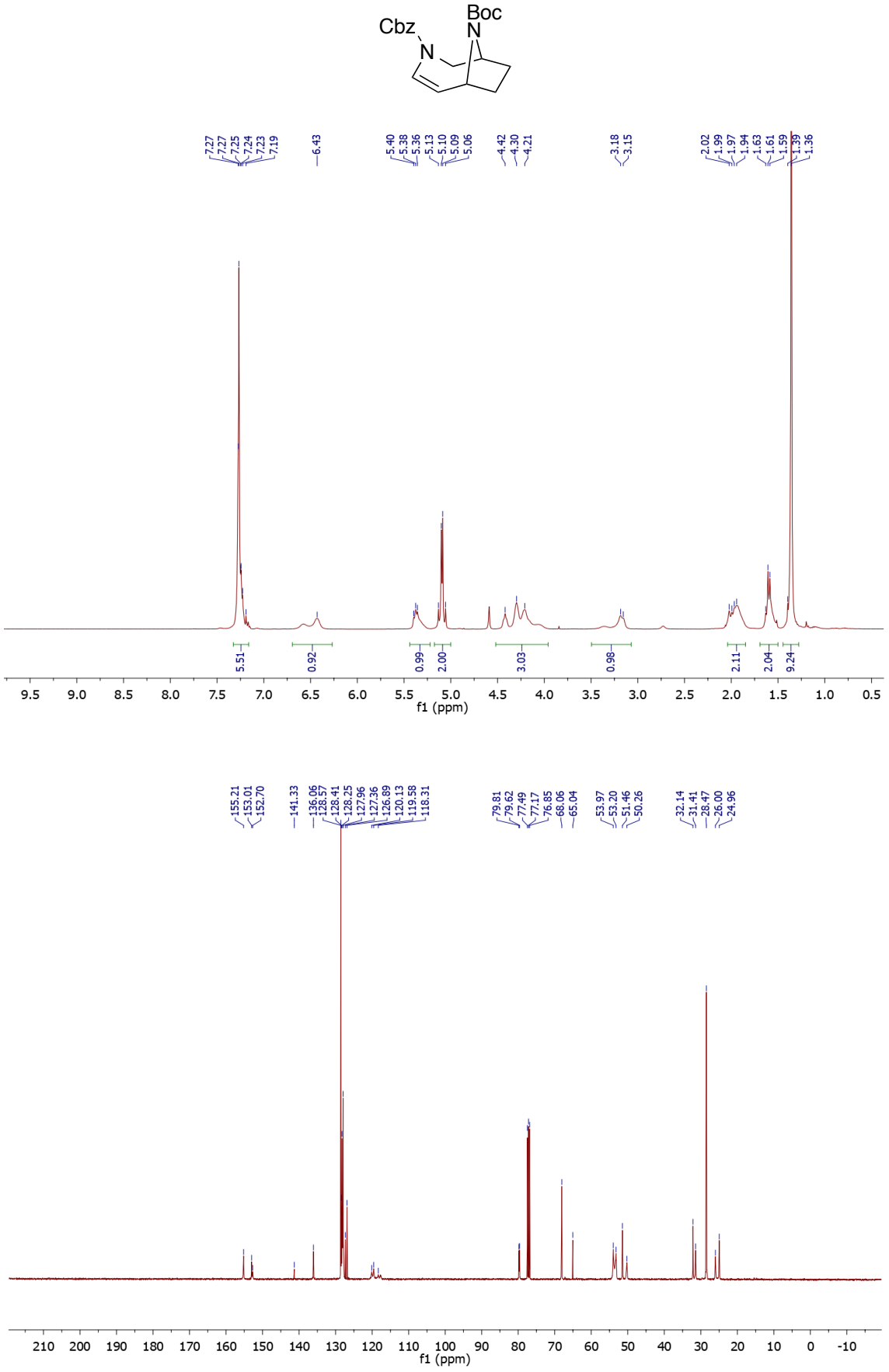
1-Benzyl 4-*tert*-butyl 2,3-dihydro-1H-1,4-diazepine-1,4(5H)-dicarboxylate



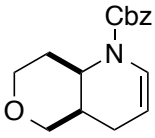


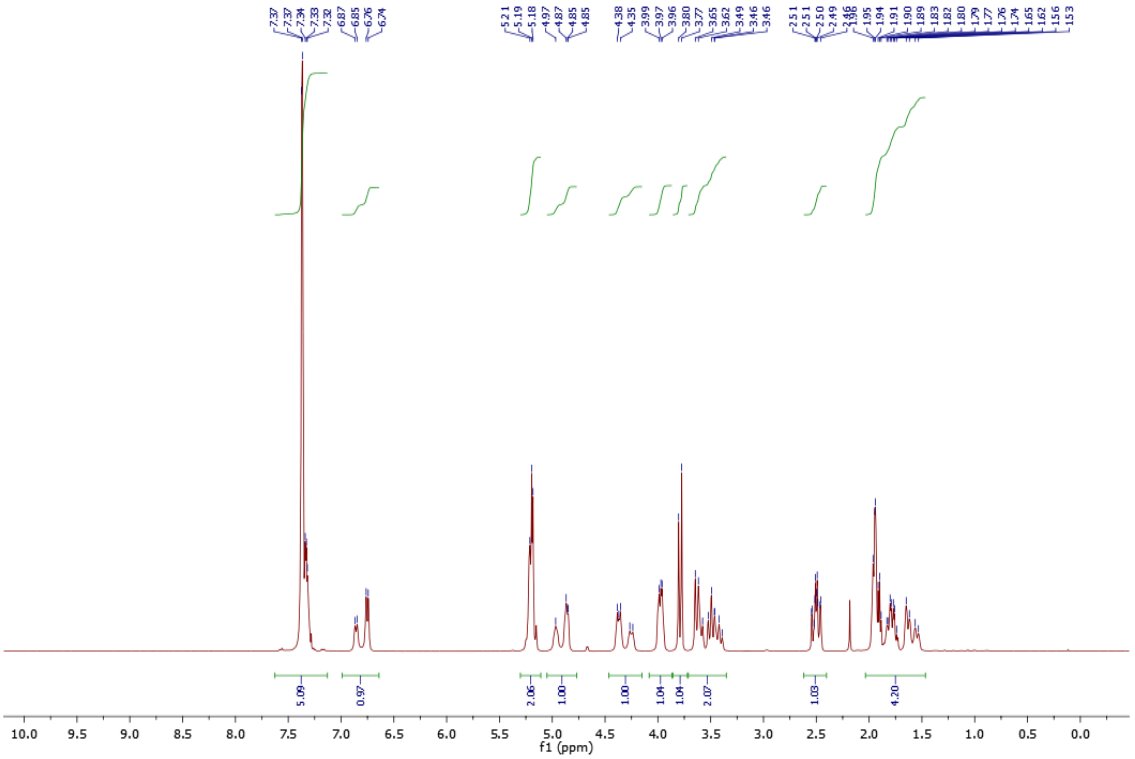


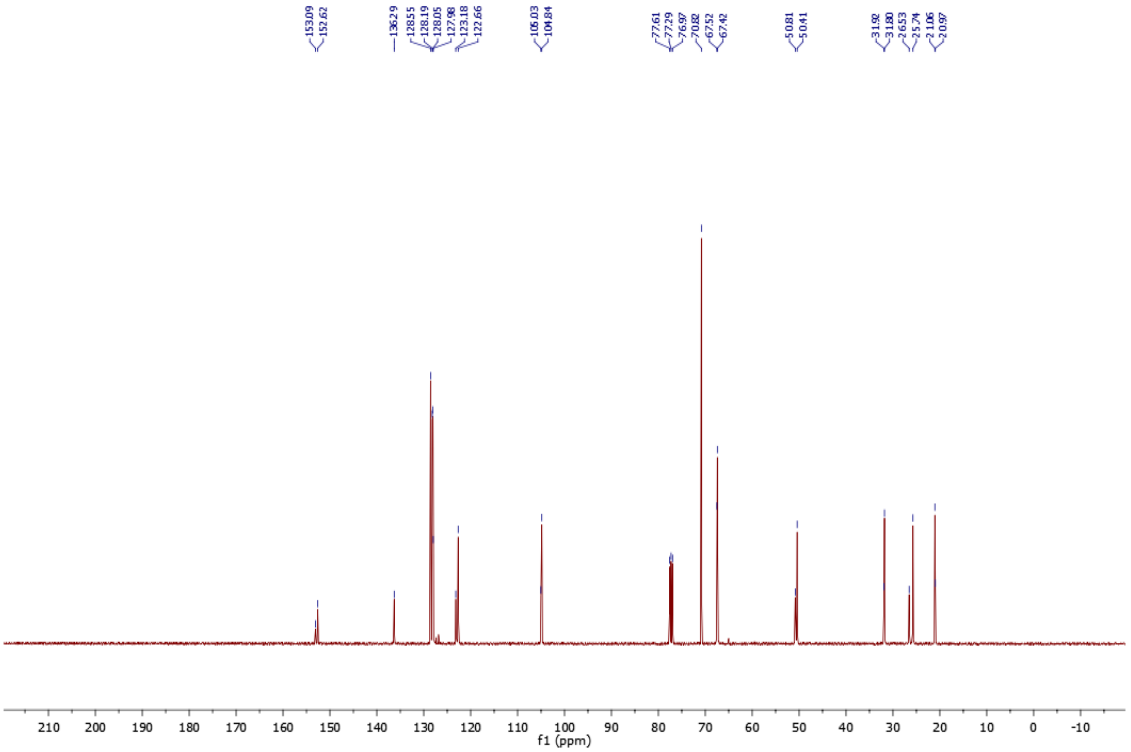
3-Benzyl 9-*tert*-butyl 3,9-diazabicyclo[4.2.1]non-4-ene-3,9-dicarboxylate



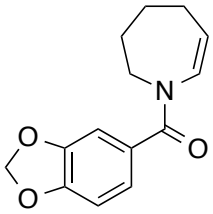
Benzyl 4,4a,5,7,8,8a-hexahydro-1H-pyrano[4,3-b]pyridine-1-carboxylate

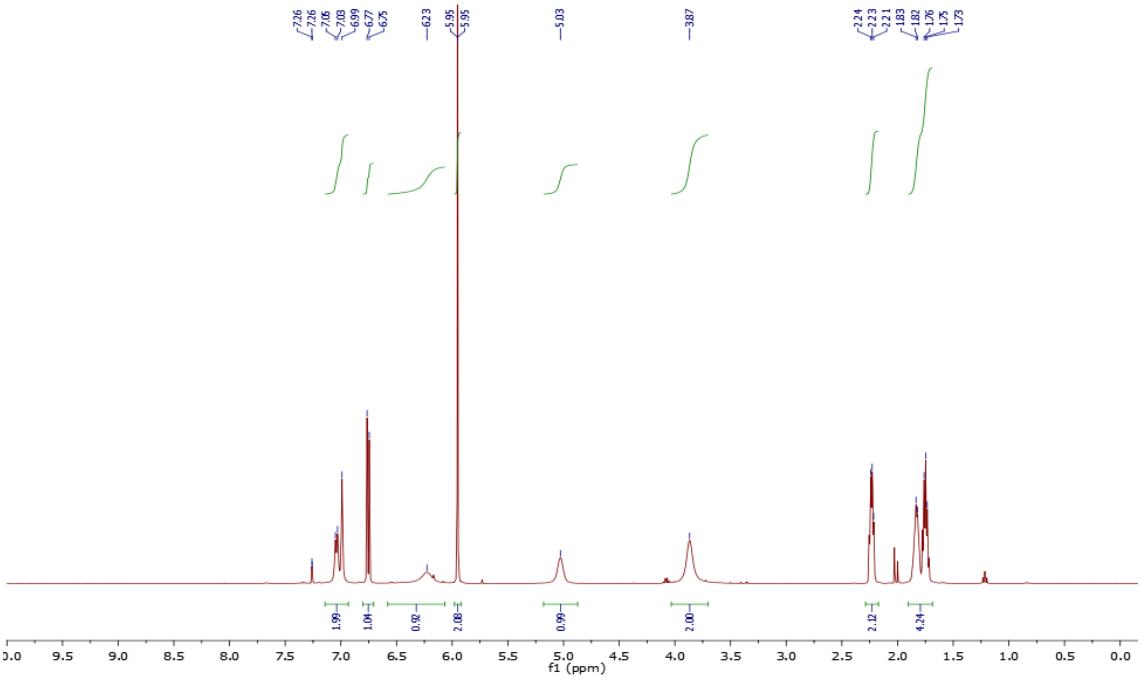


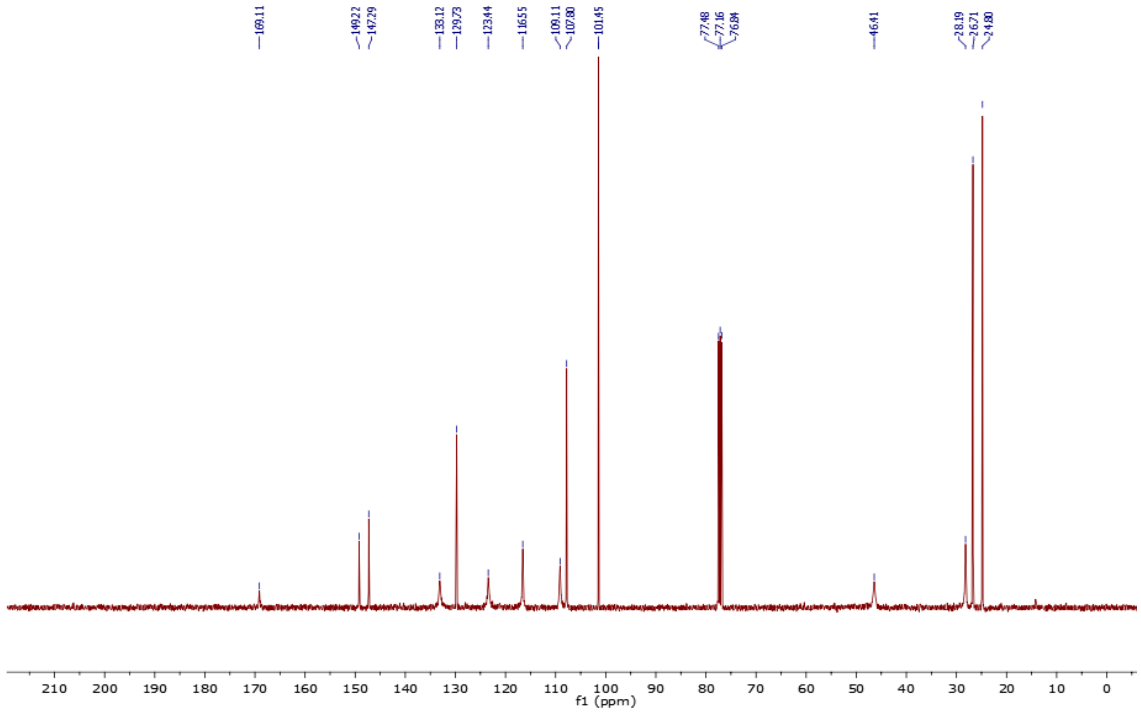




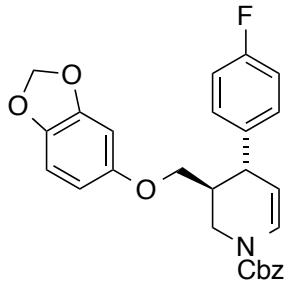
Benzo[d][1,3]dioxol-5-yl(2,3,4,5-tetrahydro-1H-azepin-1-yl)methanone (13)

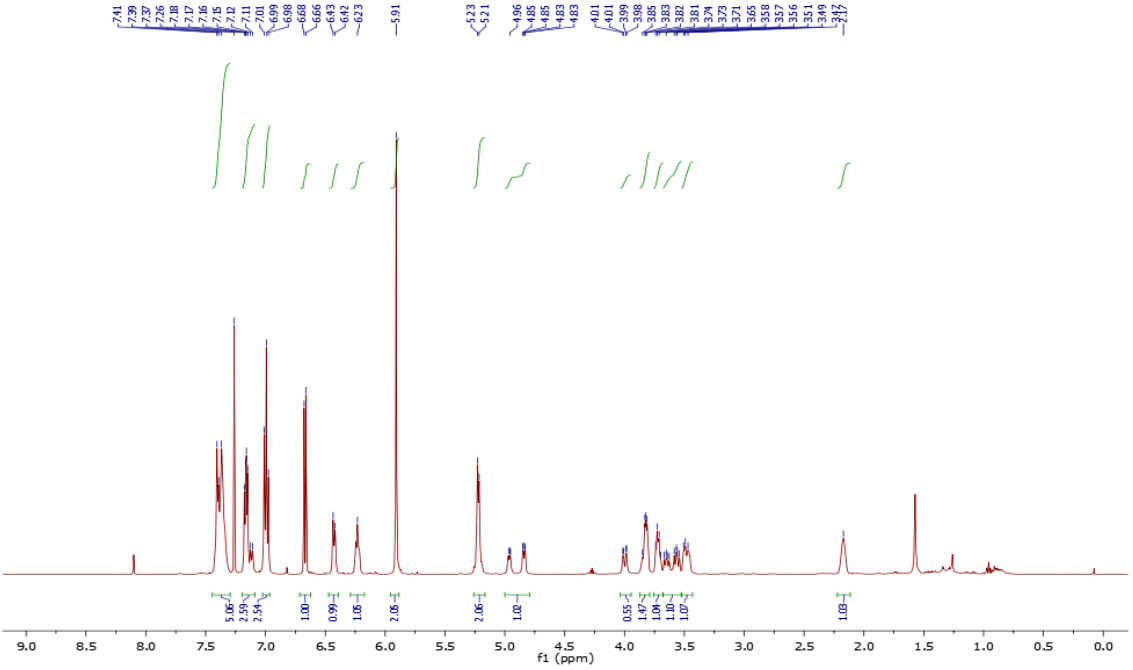


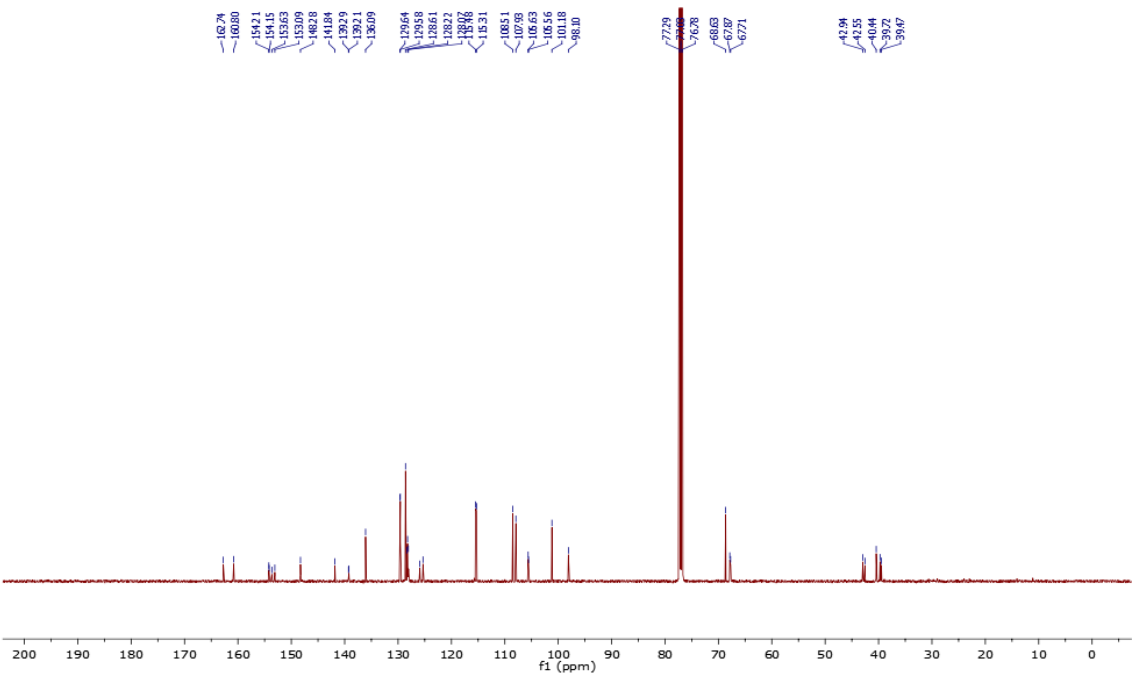




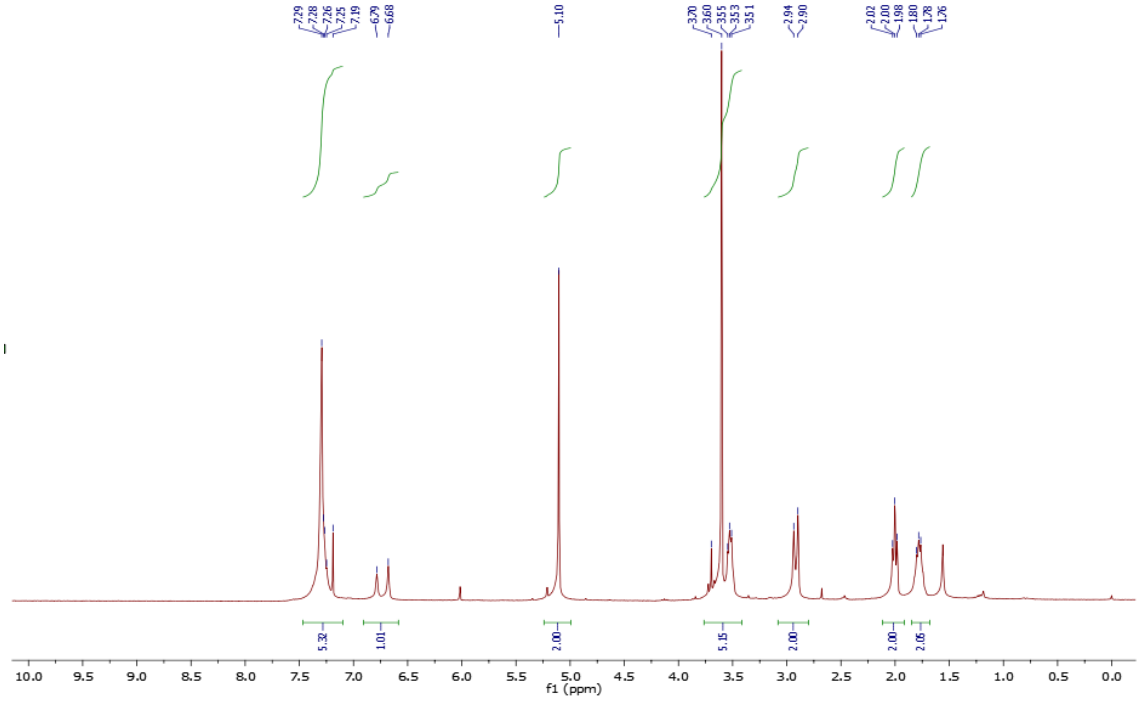
(3*S*,4*R*)-Benzyl 3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)-3,4-dihydropyridine-1(2H)-carboxylate (16)

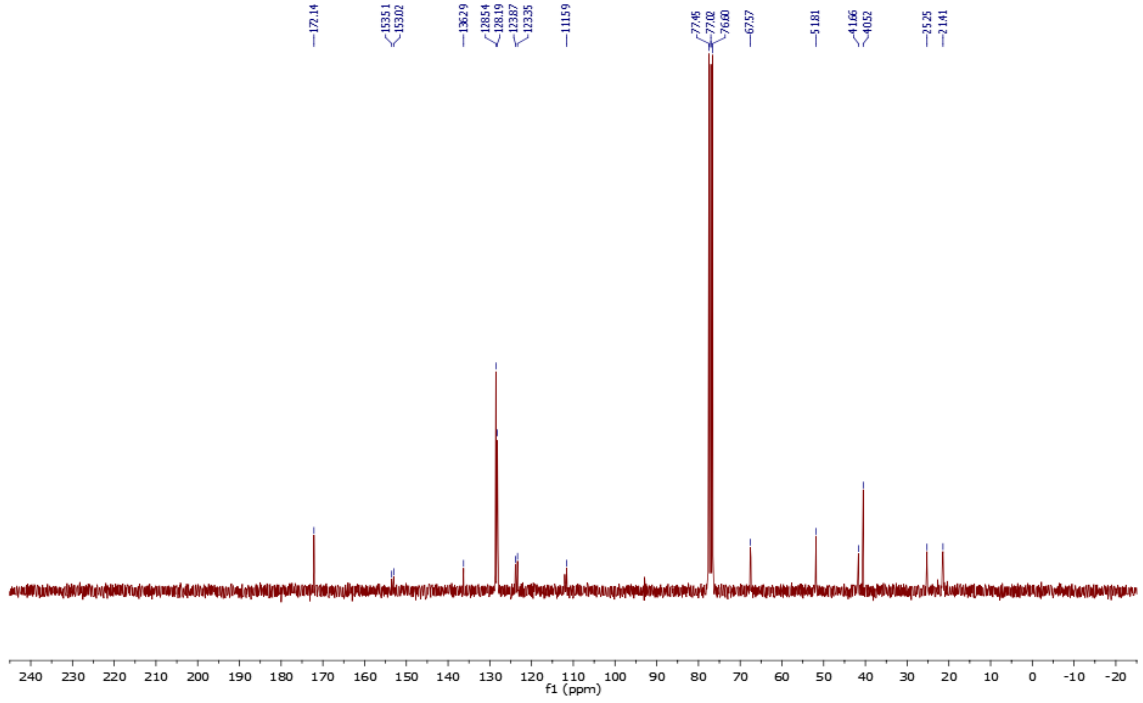




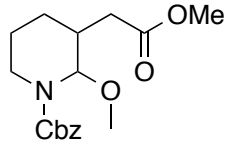


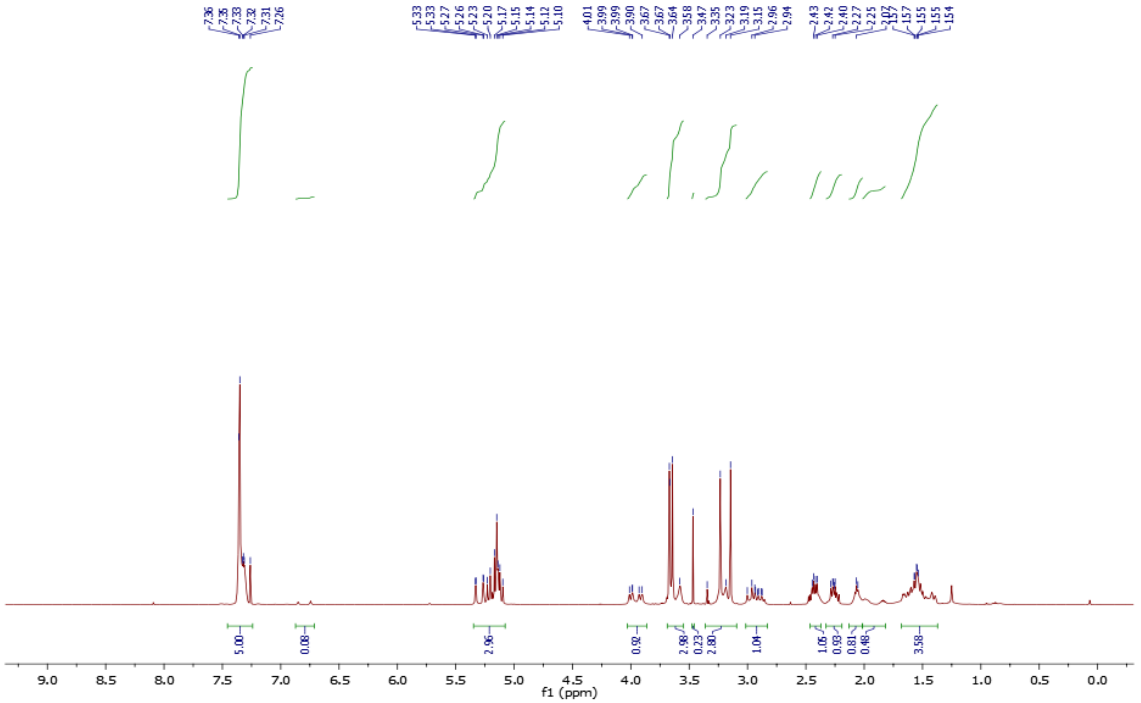
Benzyl 5-(2-methoxy-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate

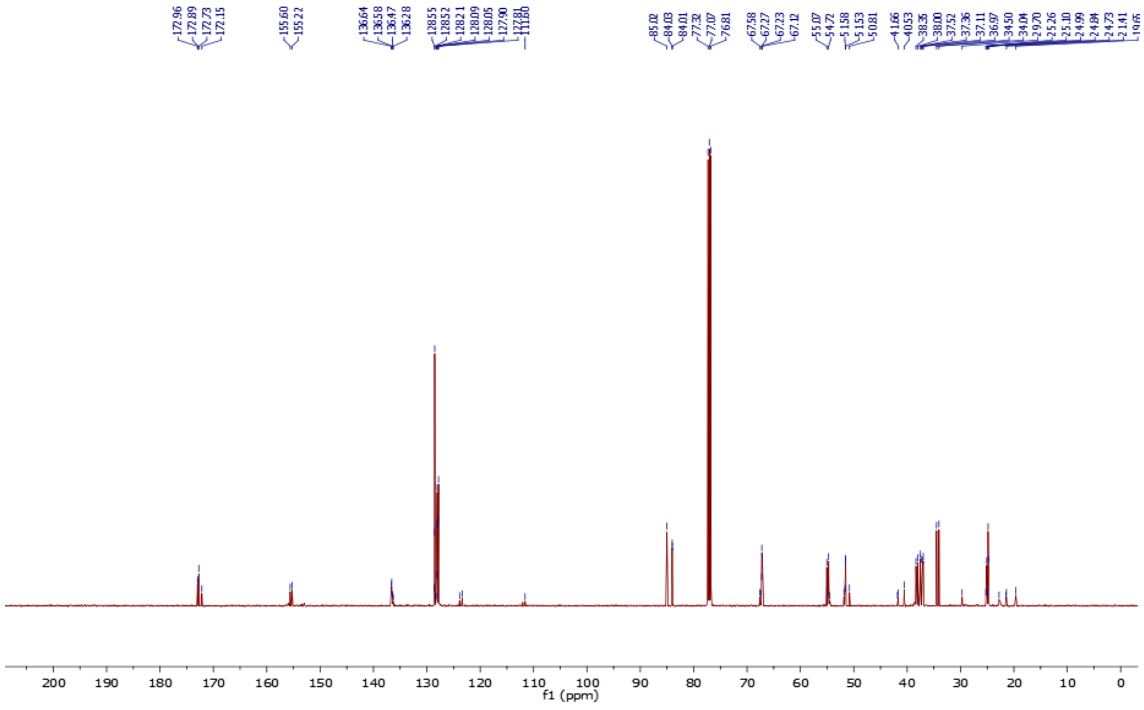




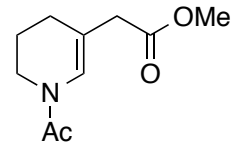
Benzyl 2-methoxy-3-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate (7a)

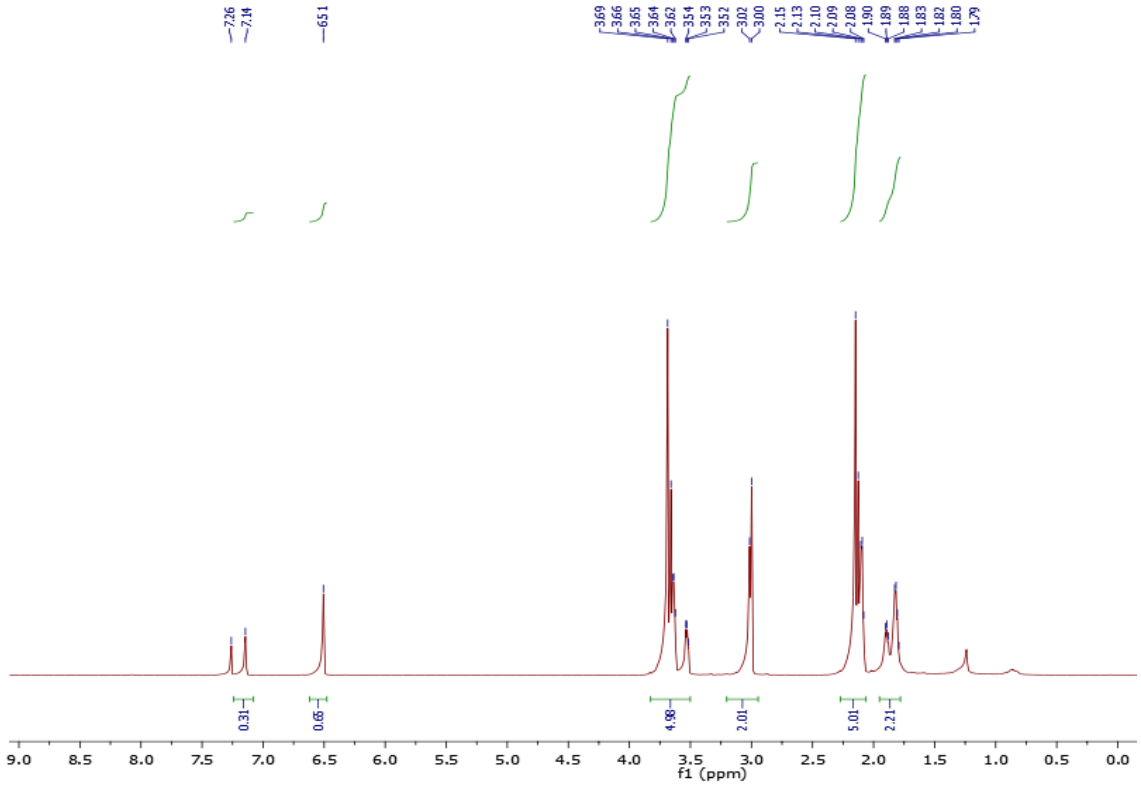


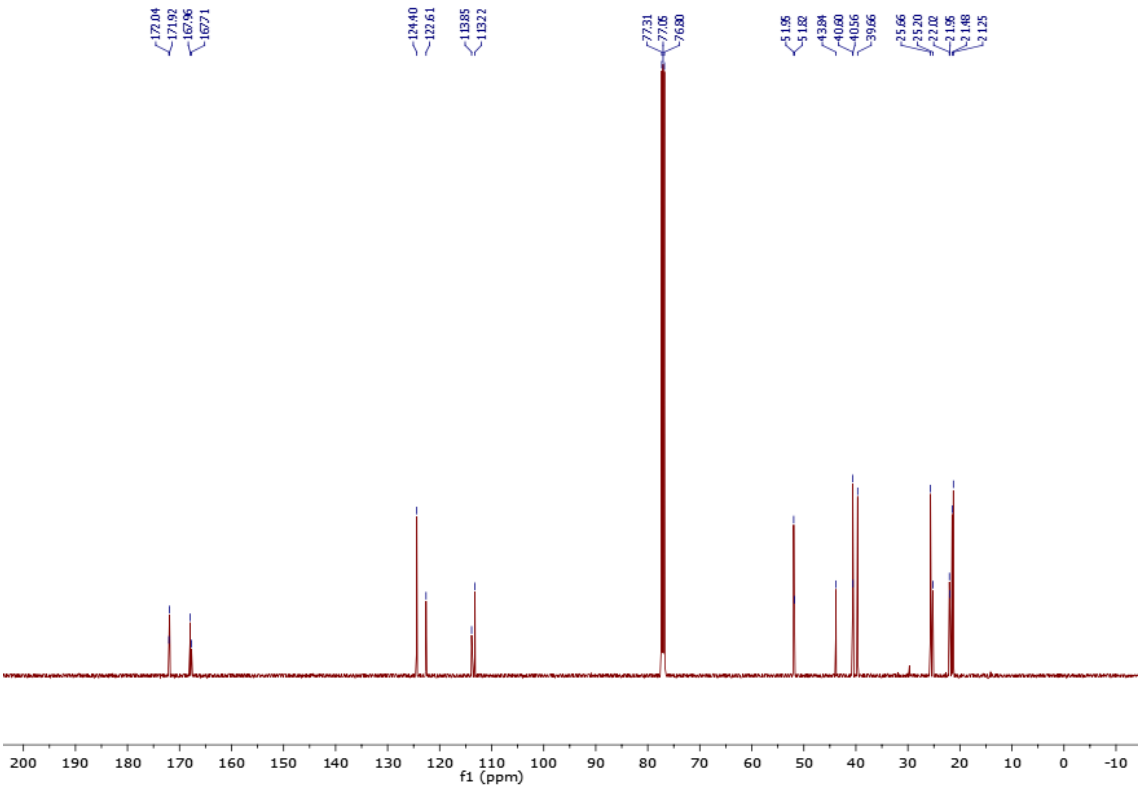




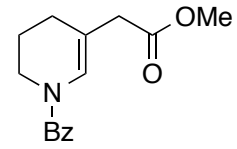
Methyl 2-(1-acetyl-1,4,5,6-tetrahydropyridin-3-yl)acetate

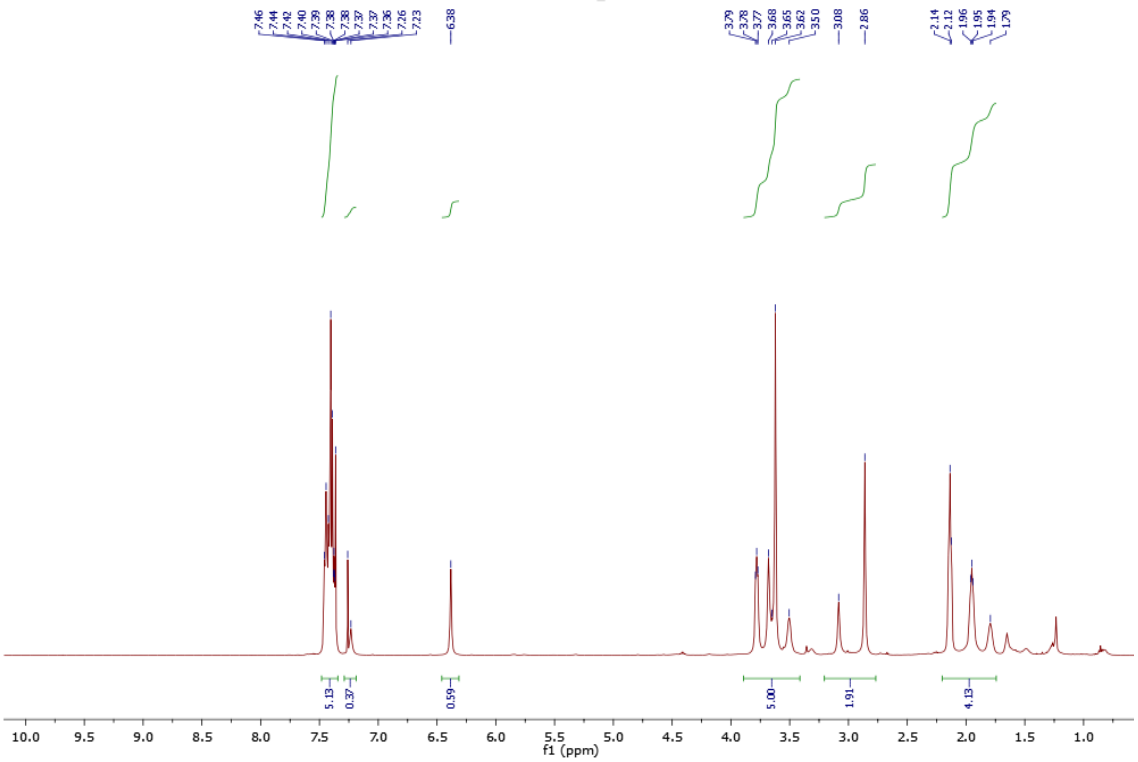


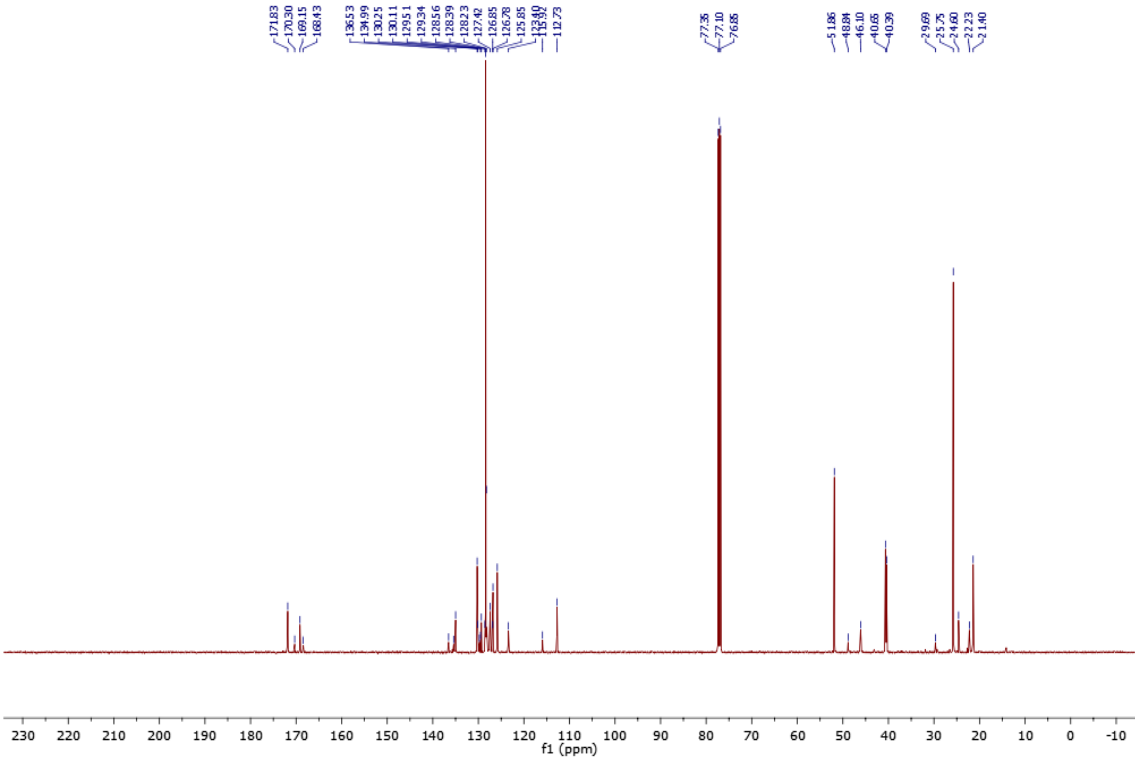




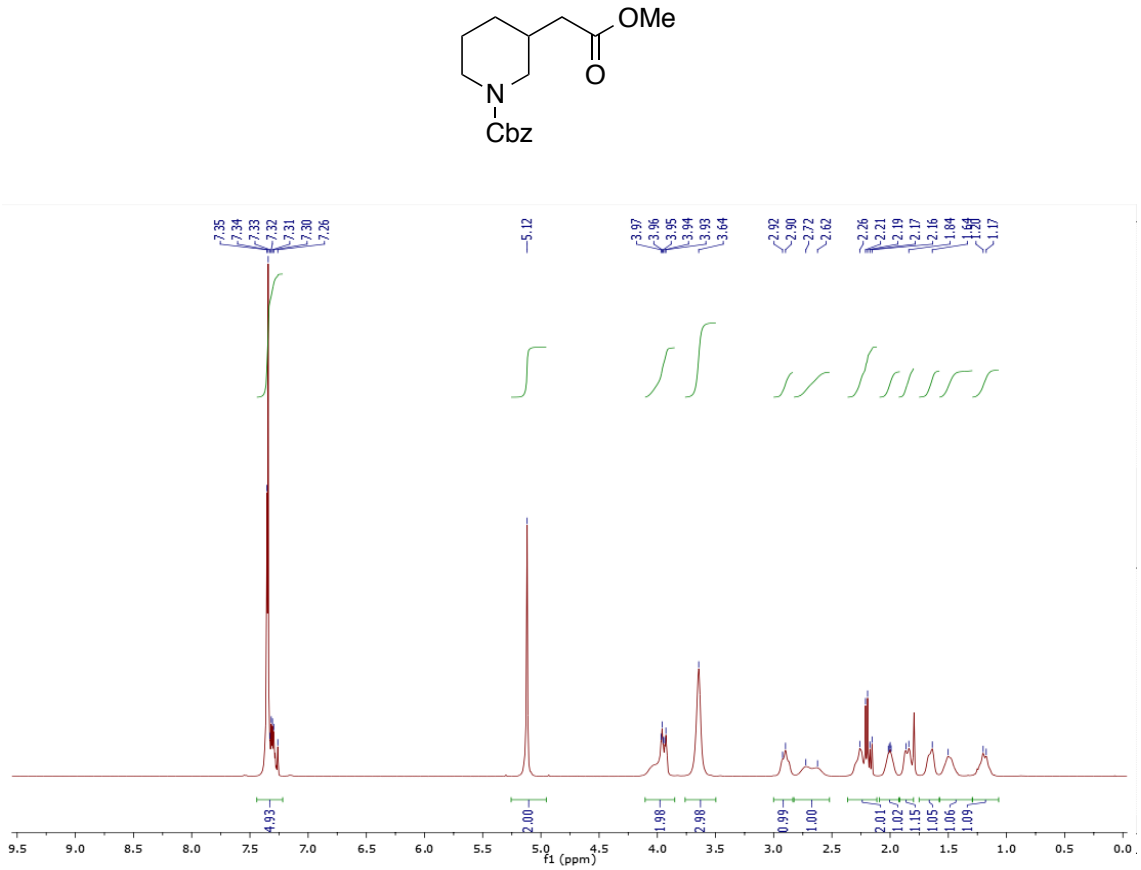
Methyl 2-(1-benzoyl-1,4,5,6-tetrahydropyridin-3-yl)acetate

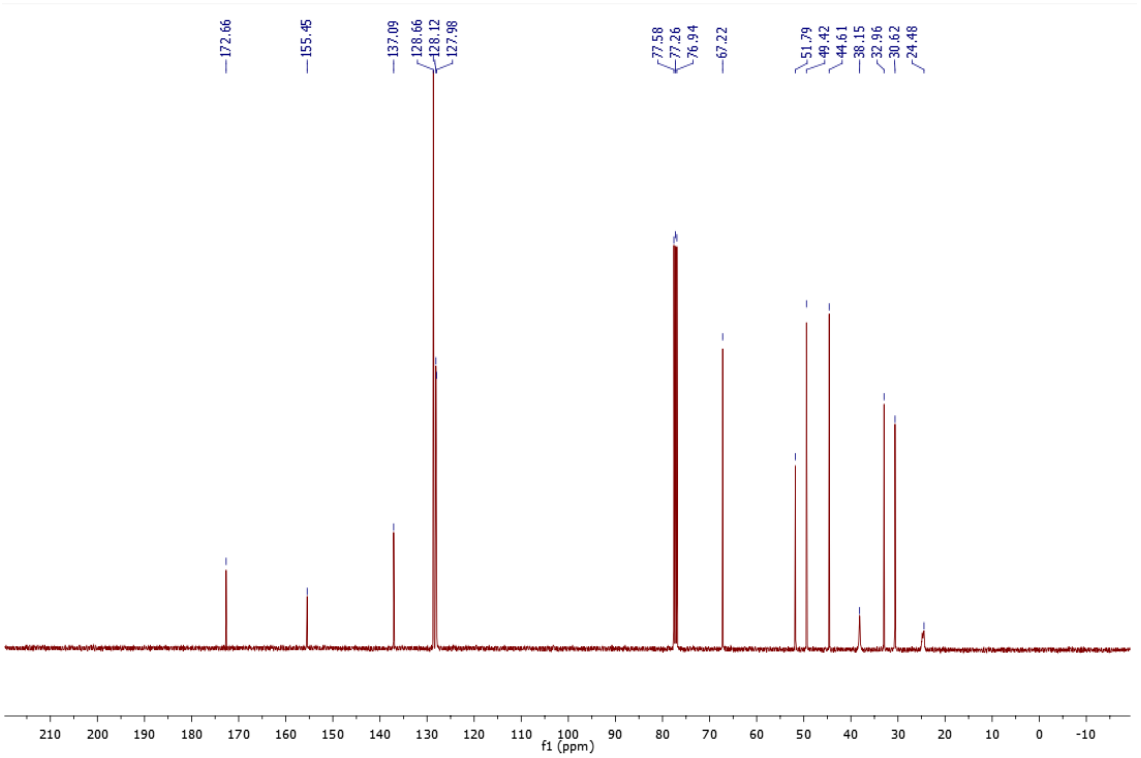




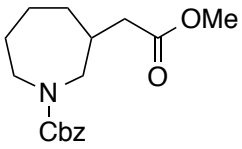


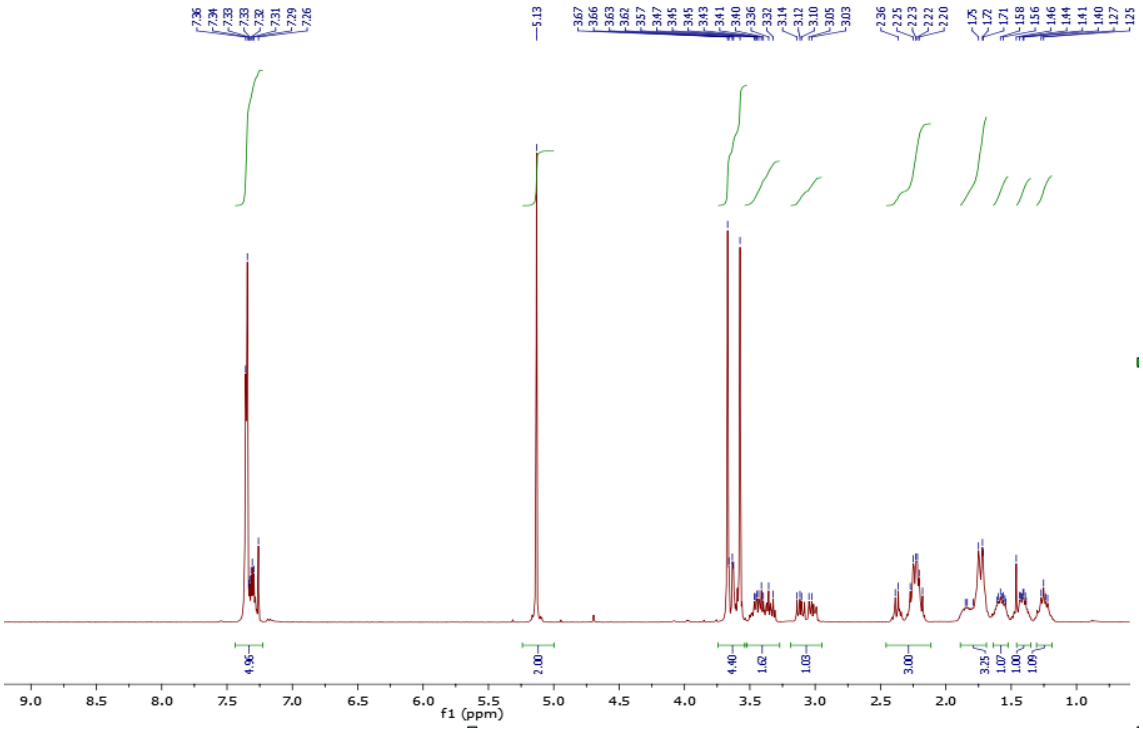
Benzyl 3-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate (8a)

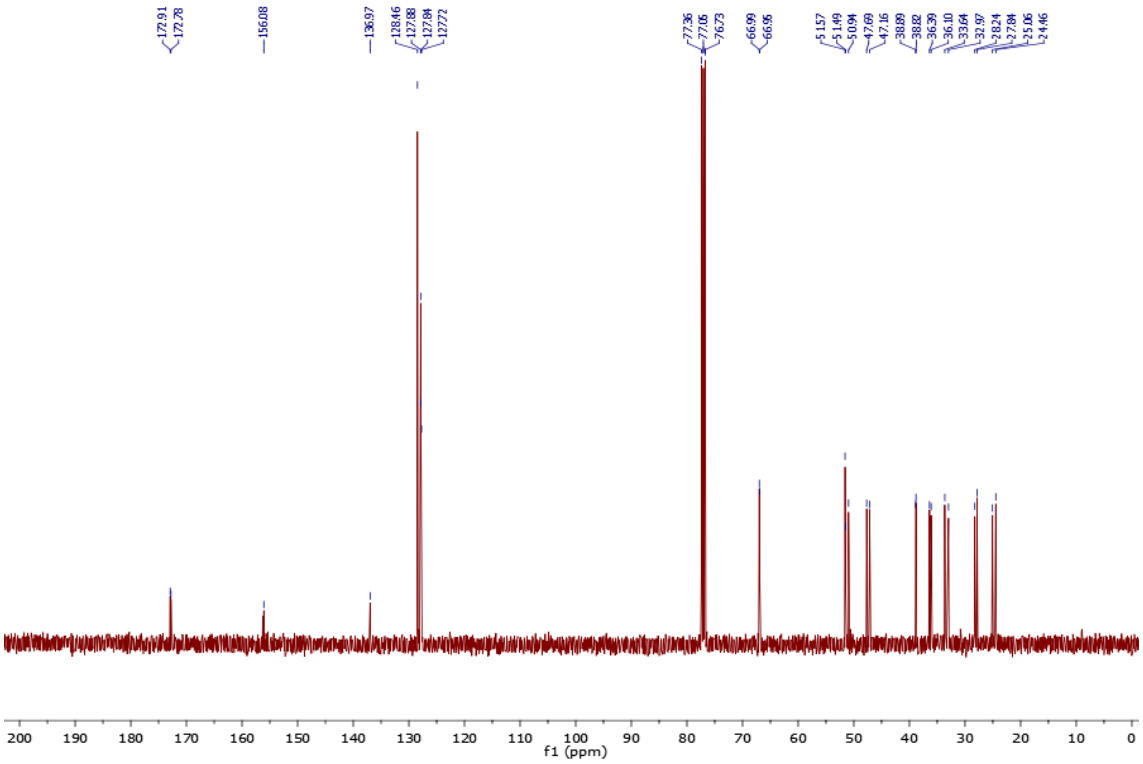




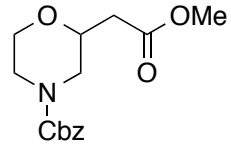
Benzyl 3-(2-methoxy-2-oxoethyl)azepane-1-carboxylate (8b)

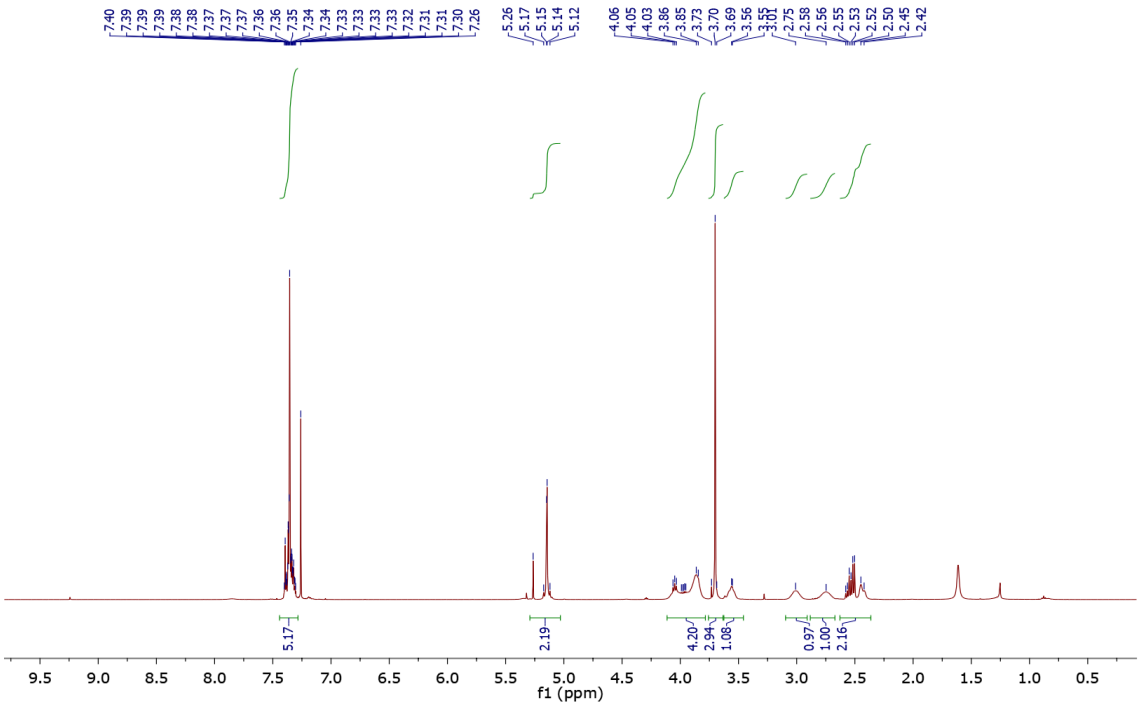


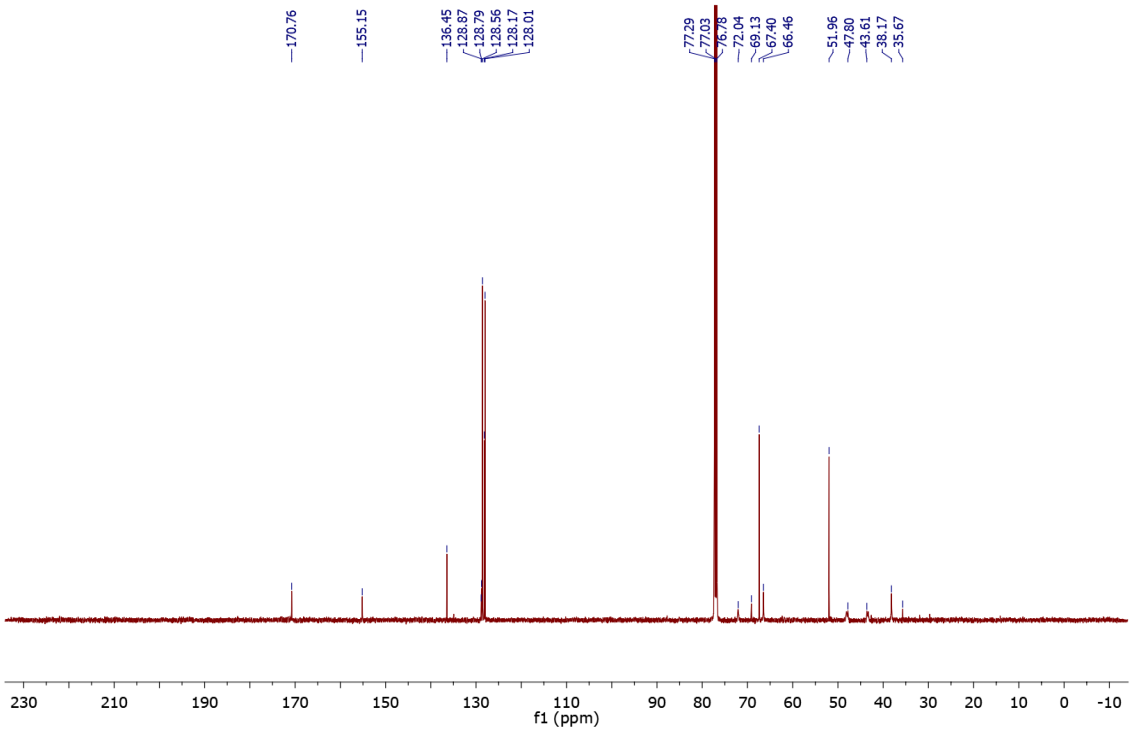




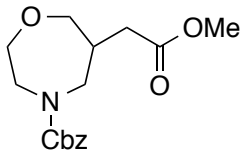
Benzyl 2-(2-methoxy-2-oxoethyl)morpholine-4-carboxylate (8c)

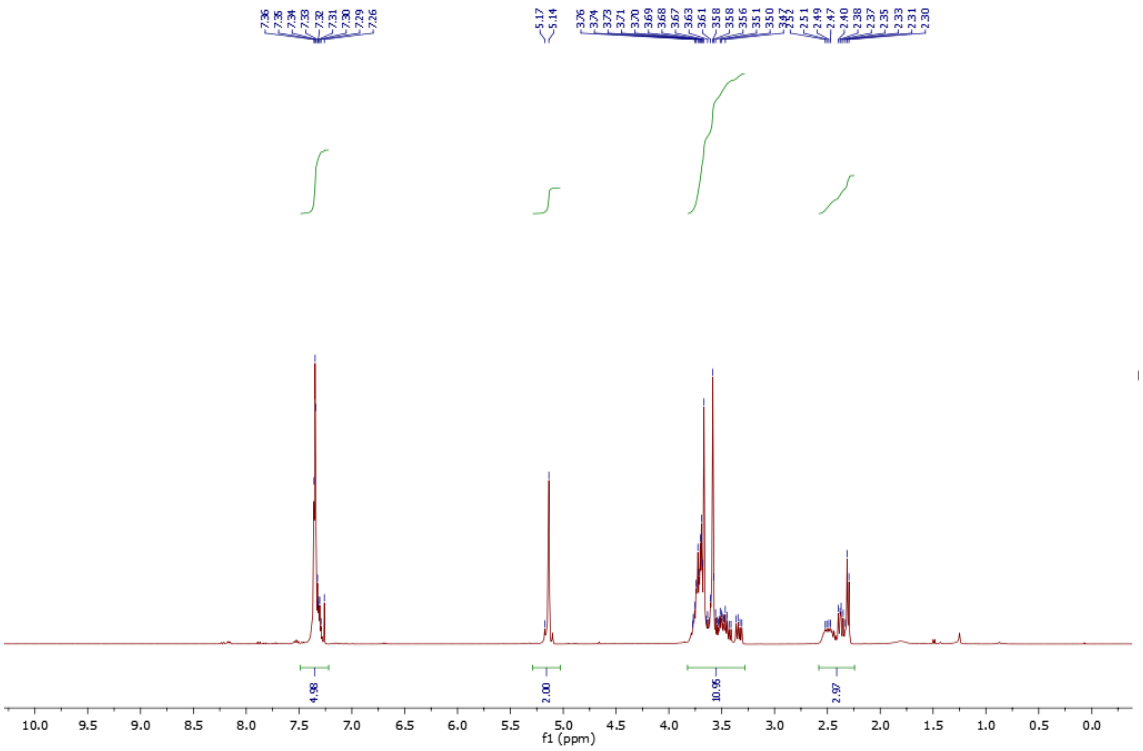


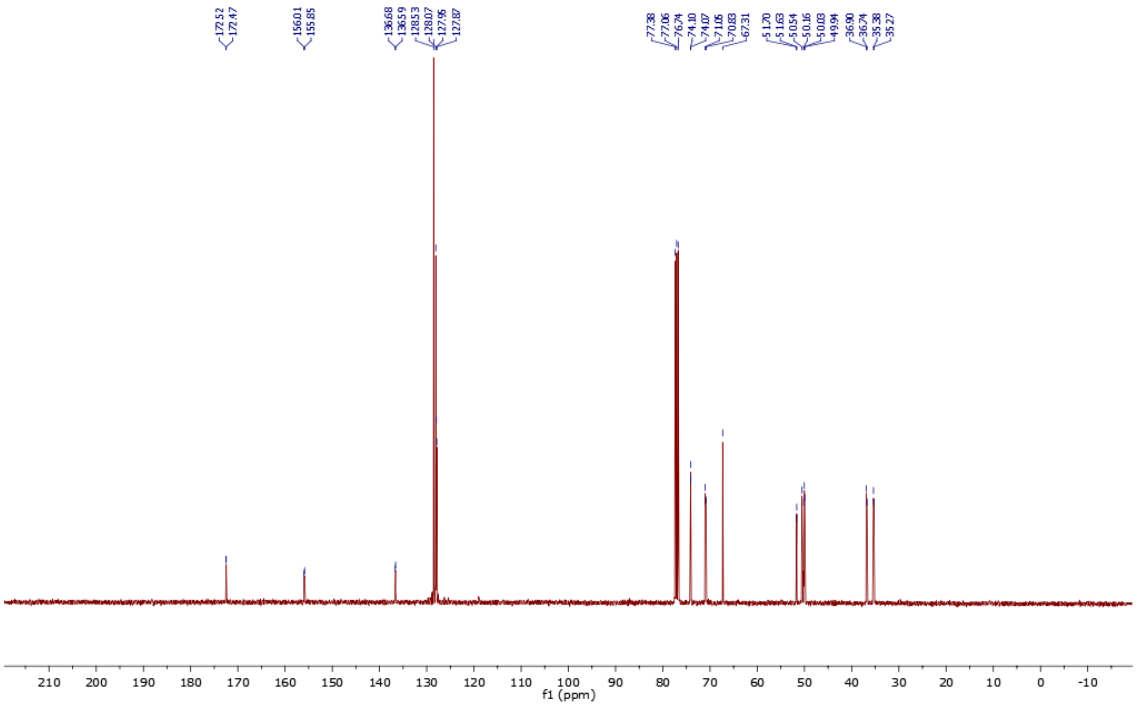




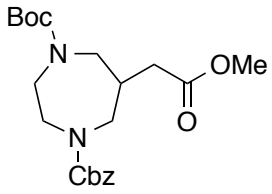
Benzyl 6-(2-methoxy-2-oxoethyl)-1,4-oxazepane-4-carboxylate (8d)

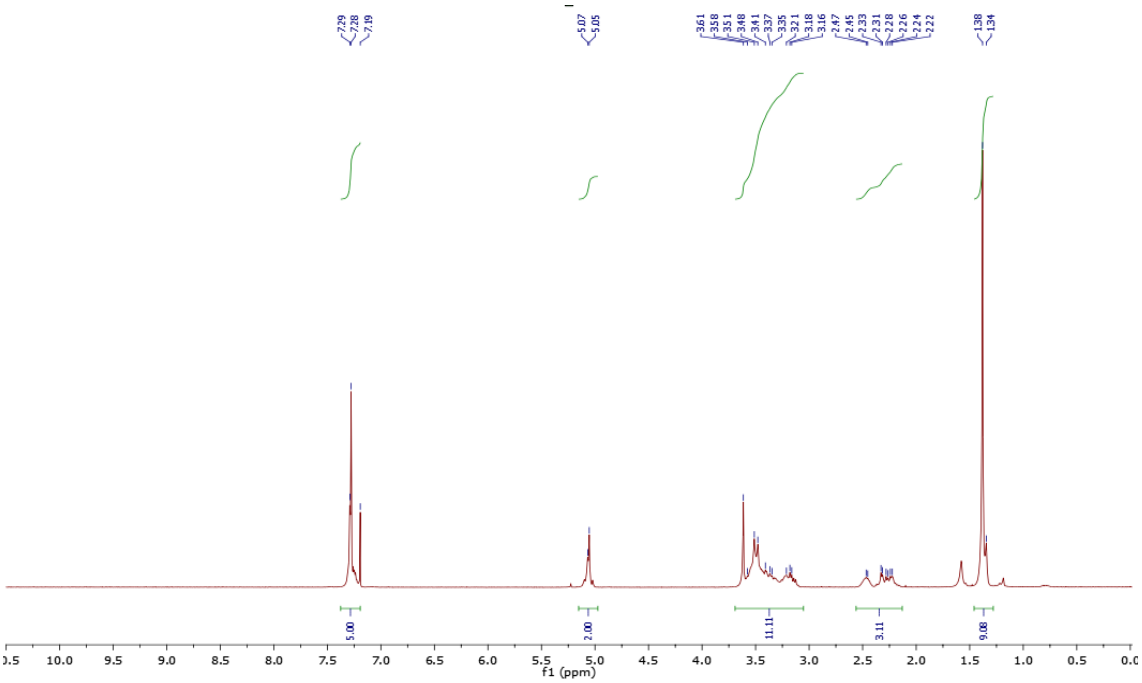


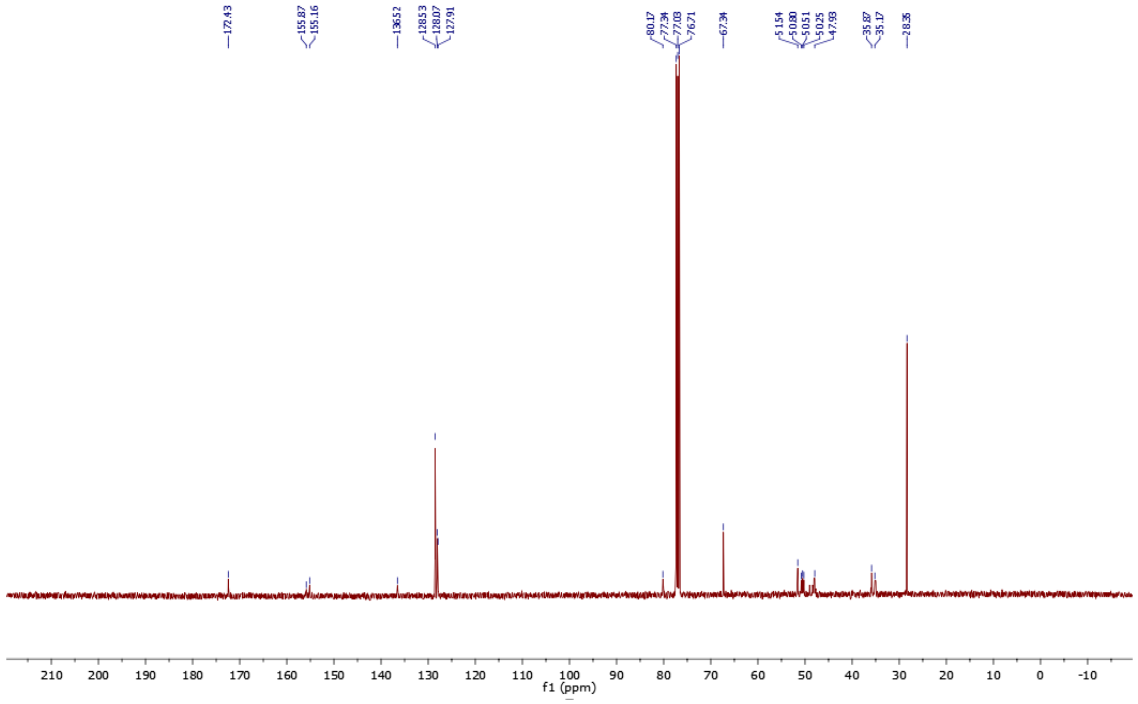




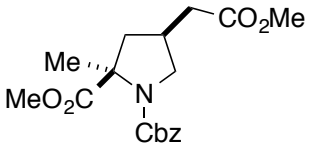
1-Benzyl 4-*tert* butyl 6-(2-methoxy-2-oxoethyl)-1,4-diazepane-1,4-dicarboxylate (8e)

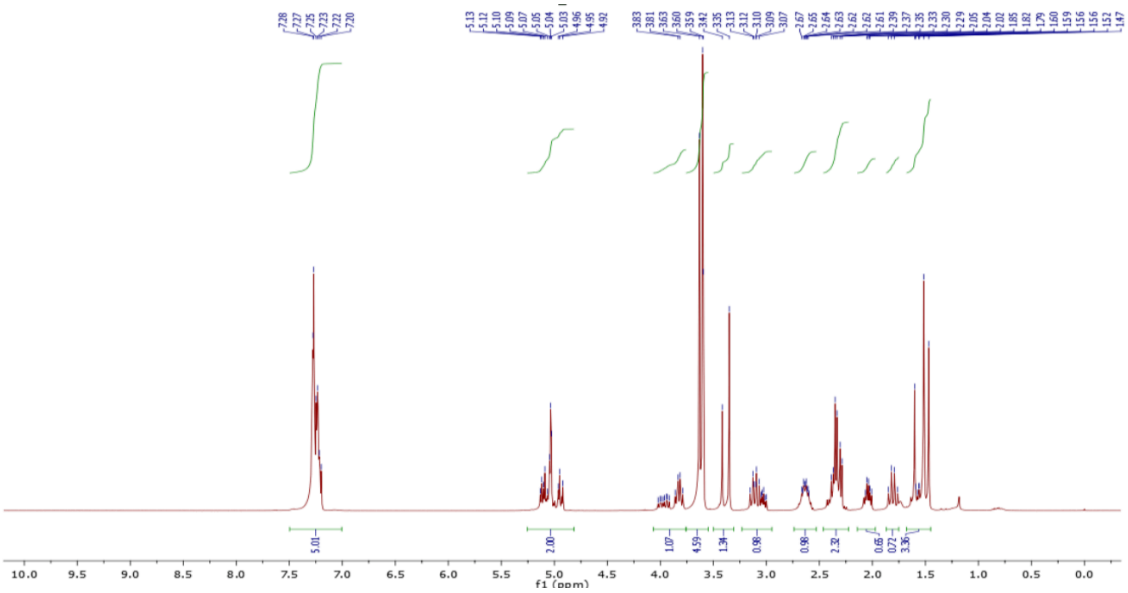


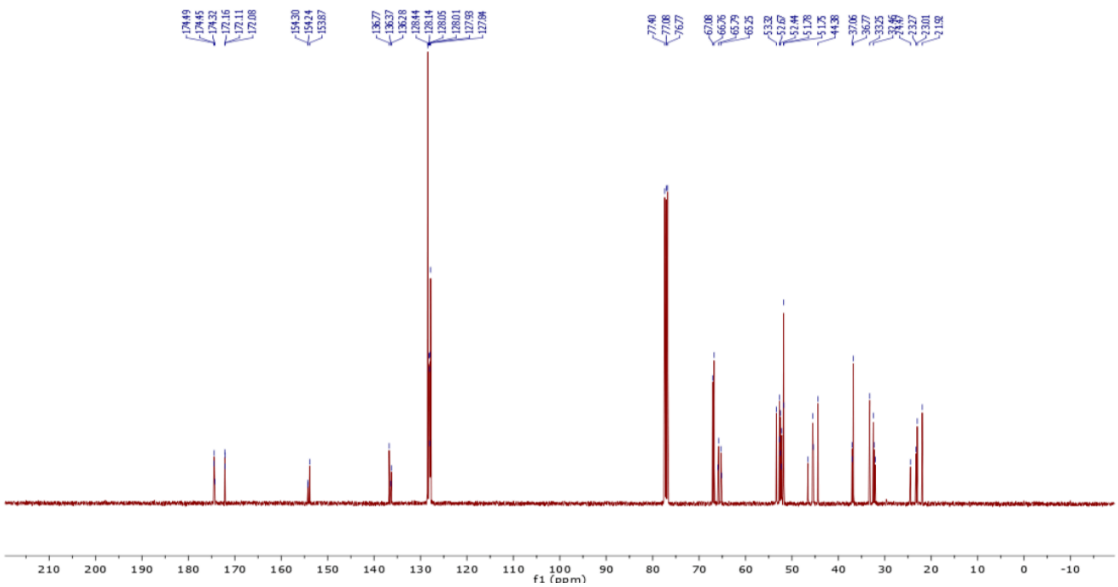




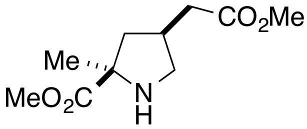
Methyl 4-(2-methoxy-2-oxoethyl)-2-methylpyrrolidine-2-carboxylate (8f)

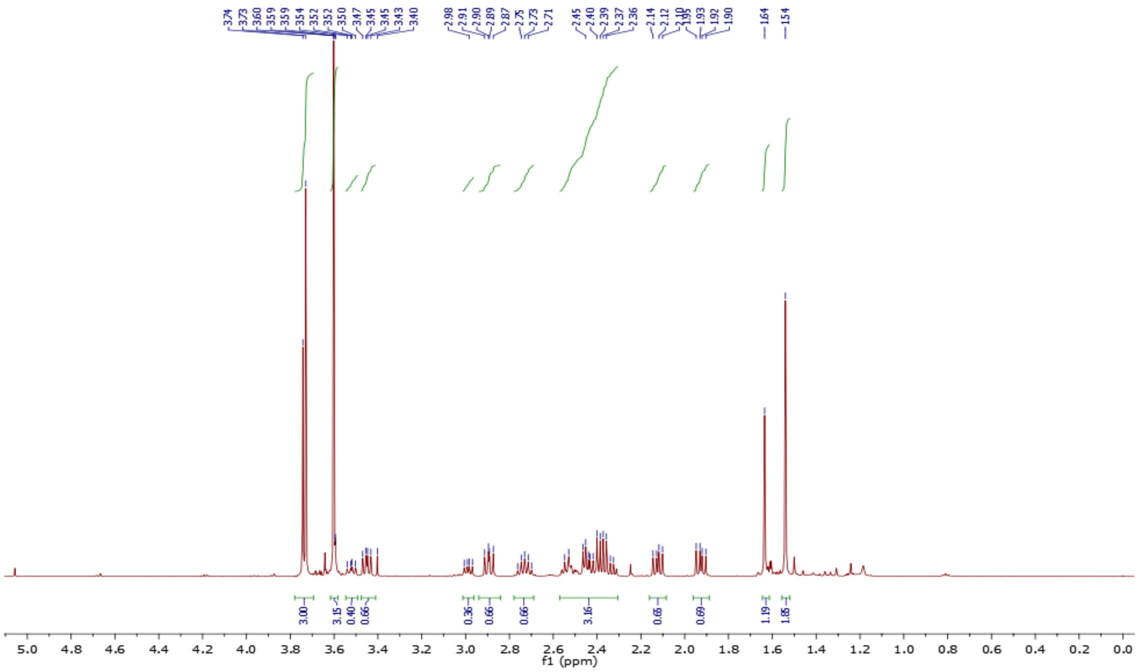


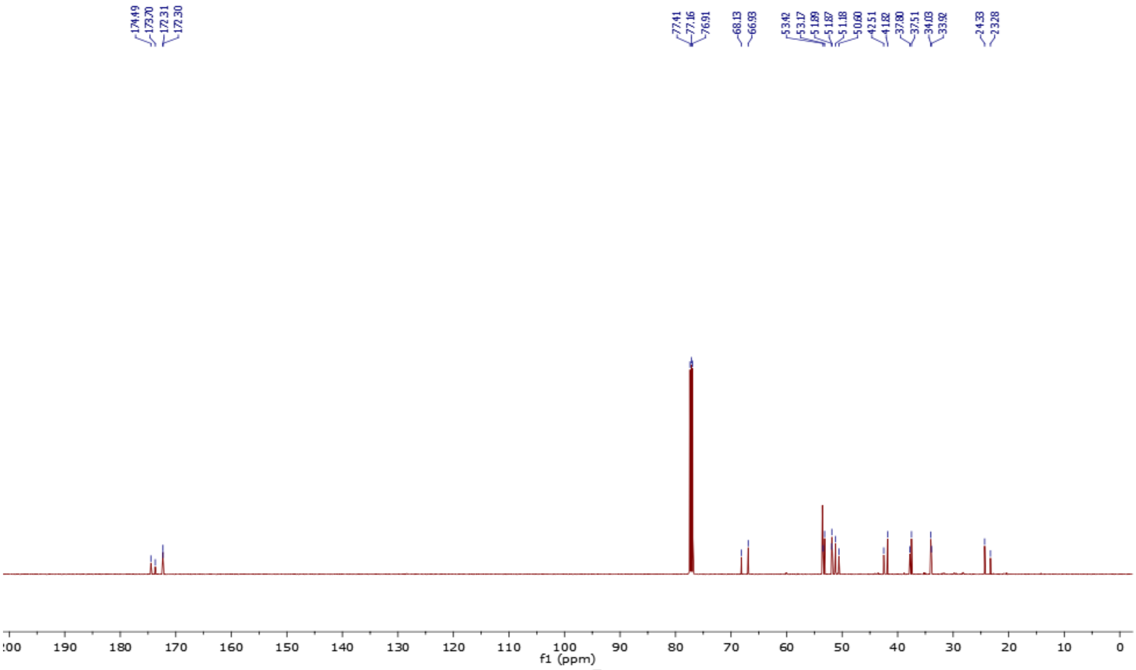


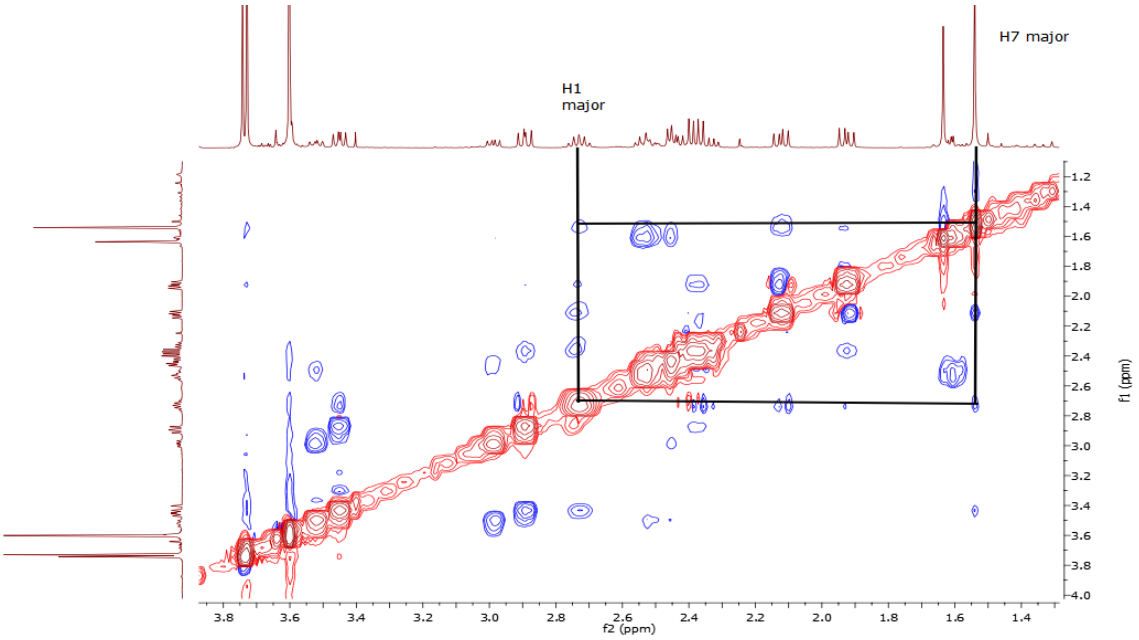


^{1}H, ^{13}C and nOe spectra for deprotected **8f**

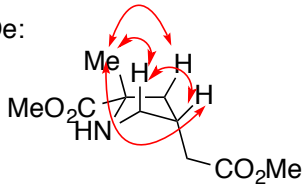




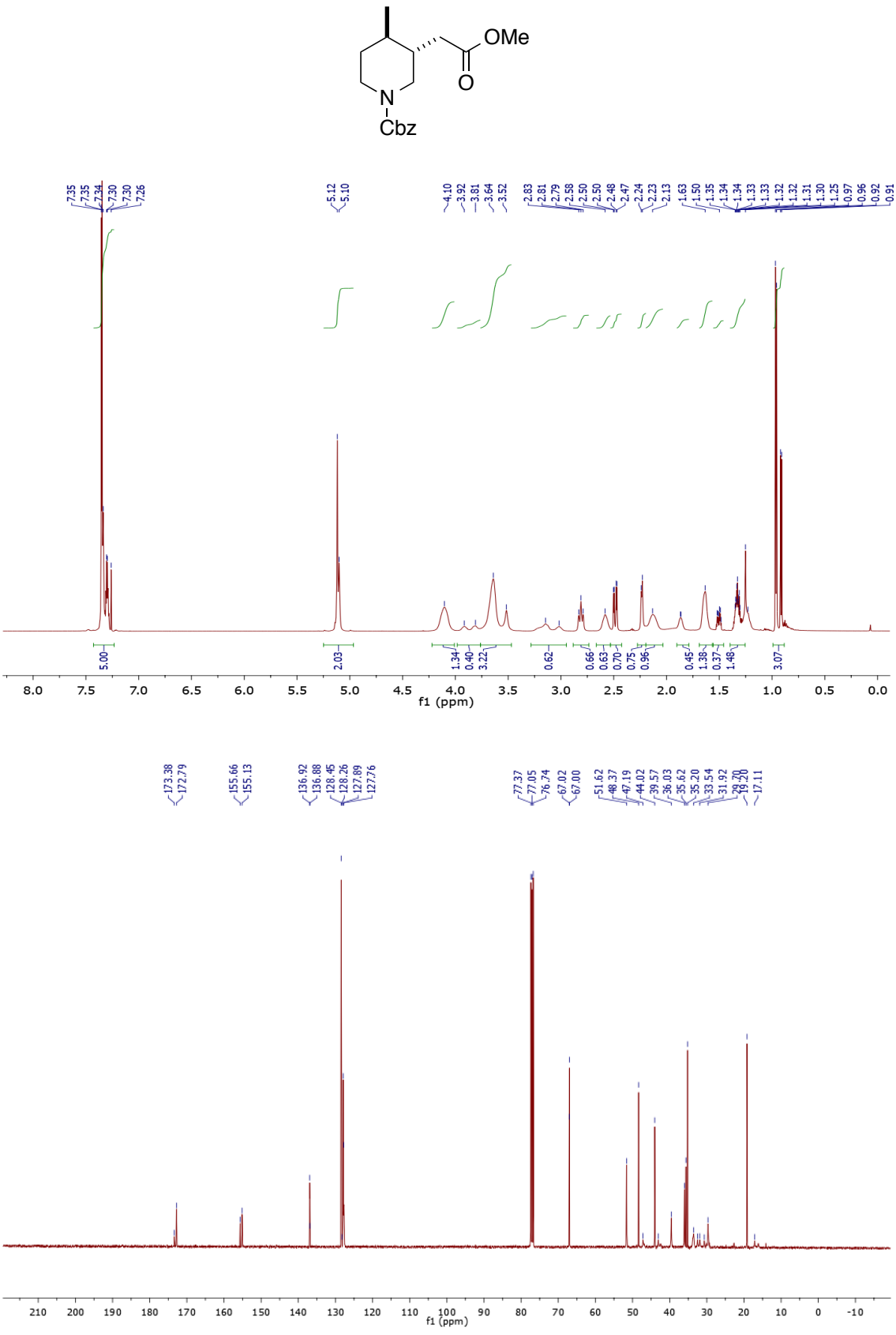


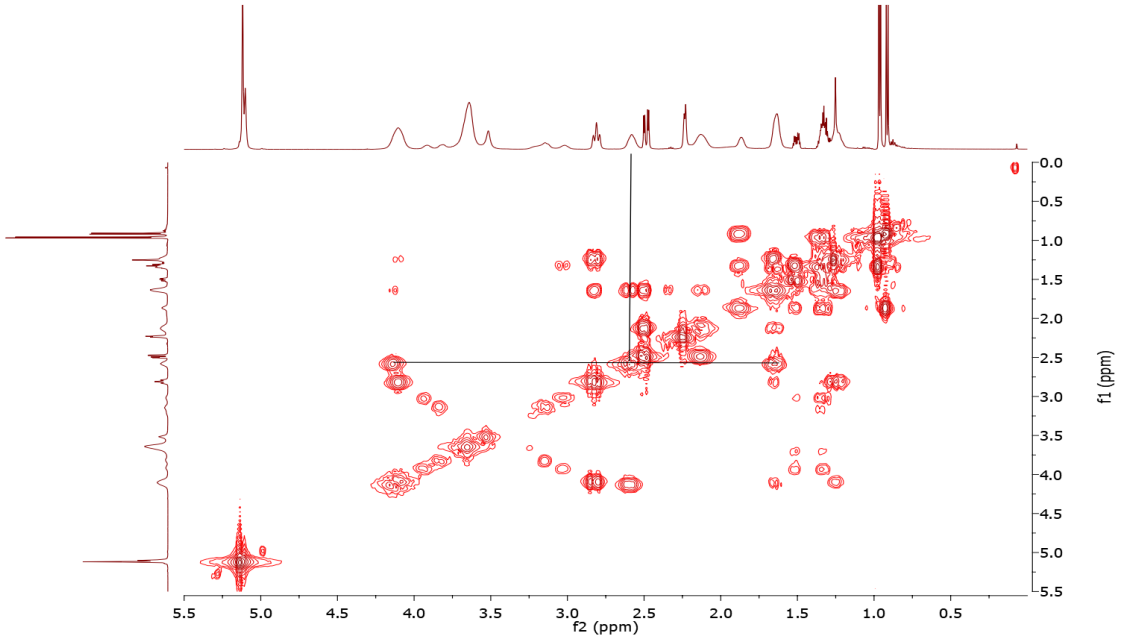


Diagnostic nOe:

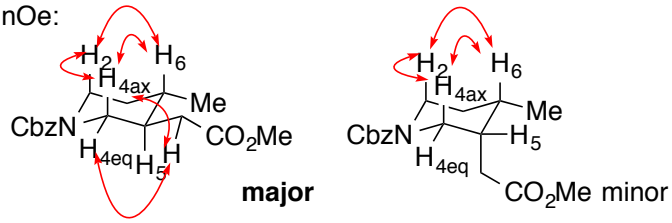


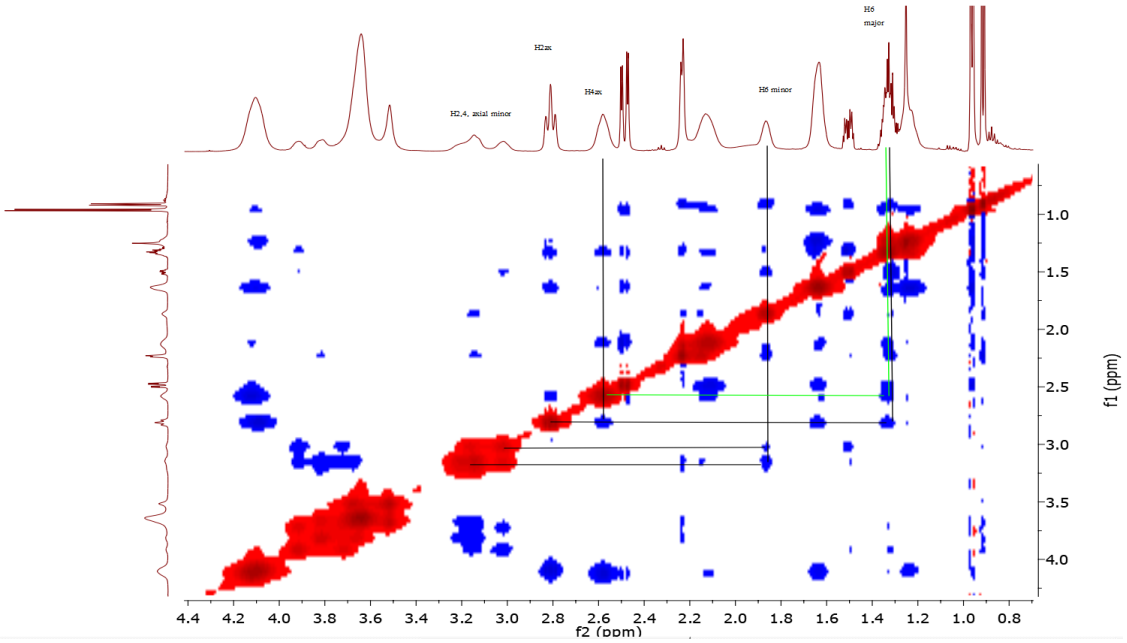
Benzyl 3-(2-methoxy-2-oxoethyl)-4-methylpiperidine-1-carboxylate (8g)



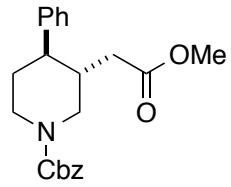


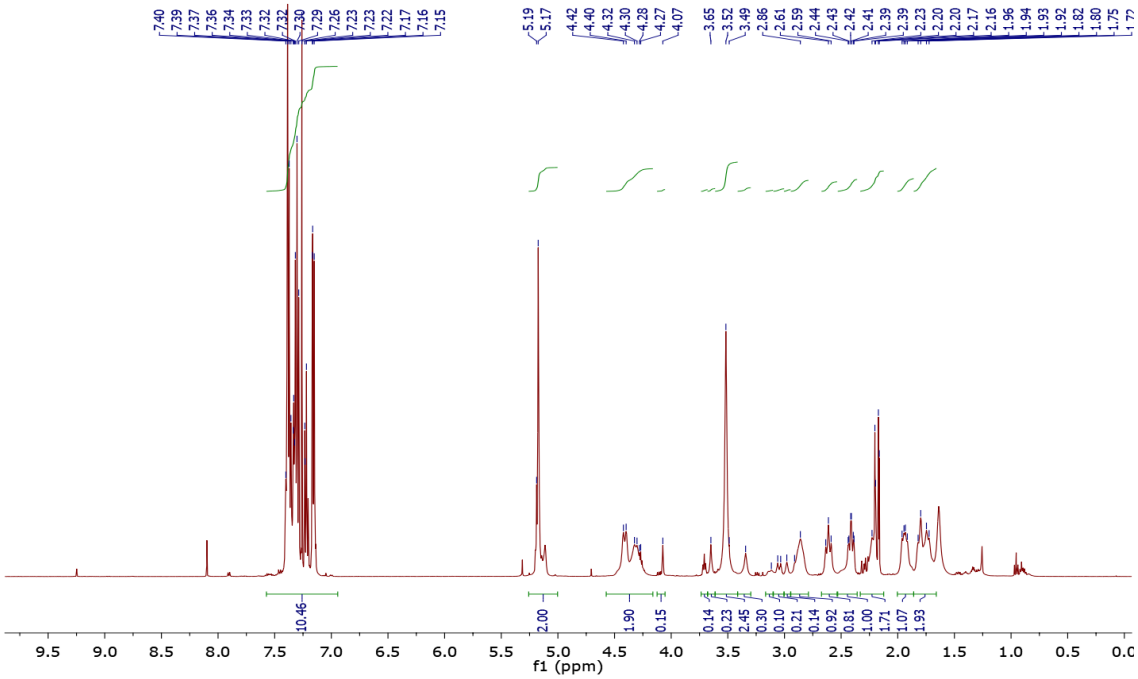
Diagnostic nOe:

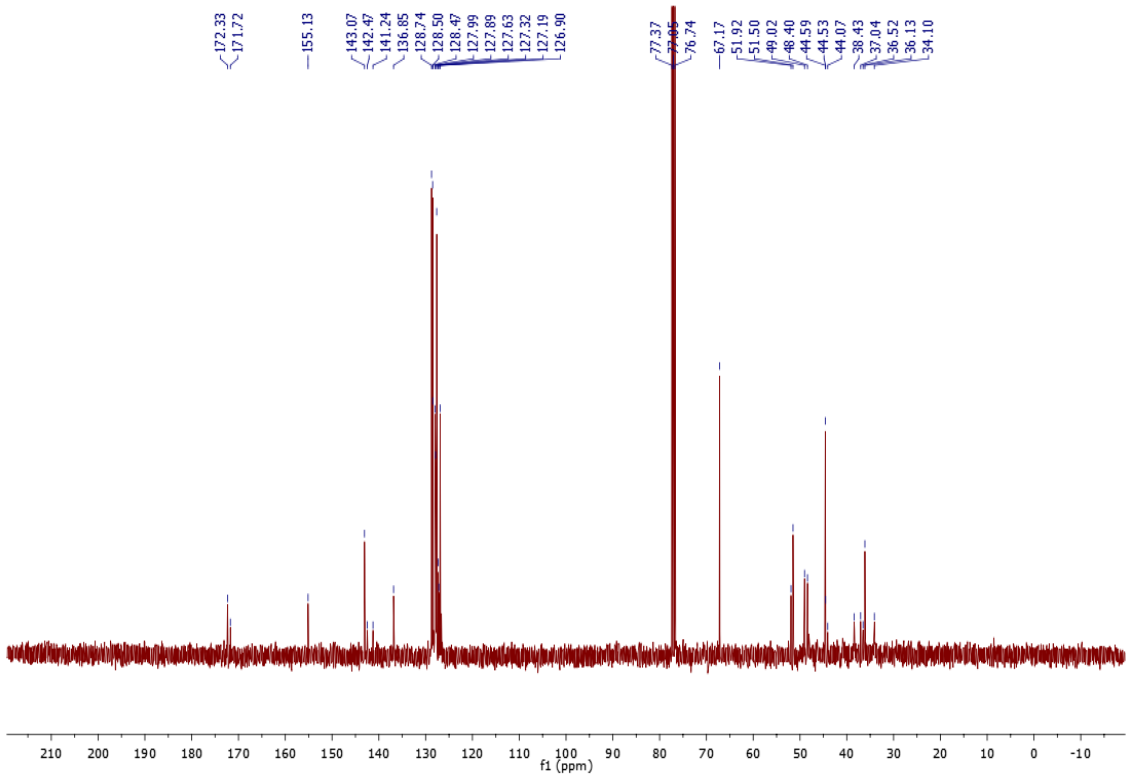


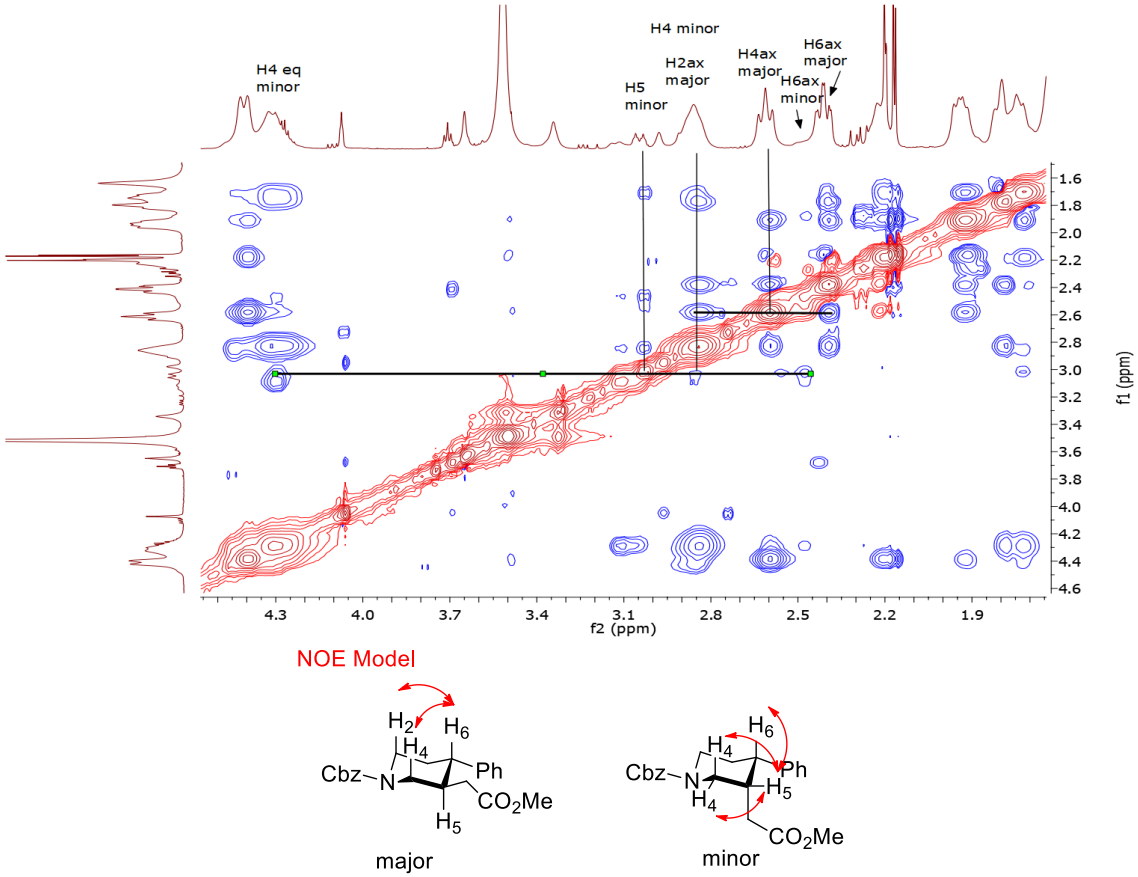


Benzyl 3-(2-methoxy-2-oxoethyl)-4-phenylpiperidine-1-carboxylate (8h)









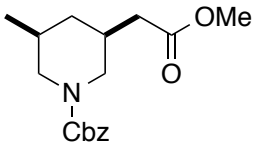
NOE Model

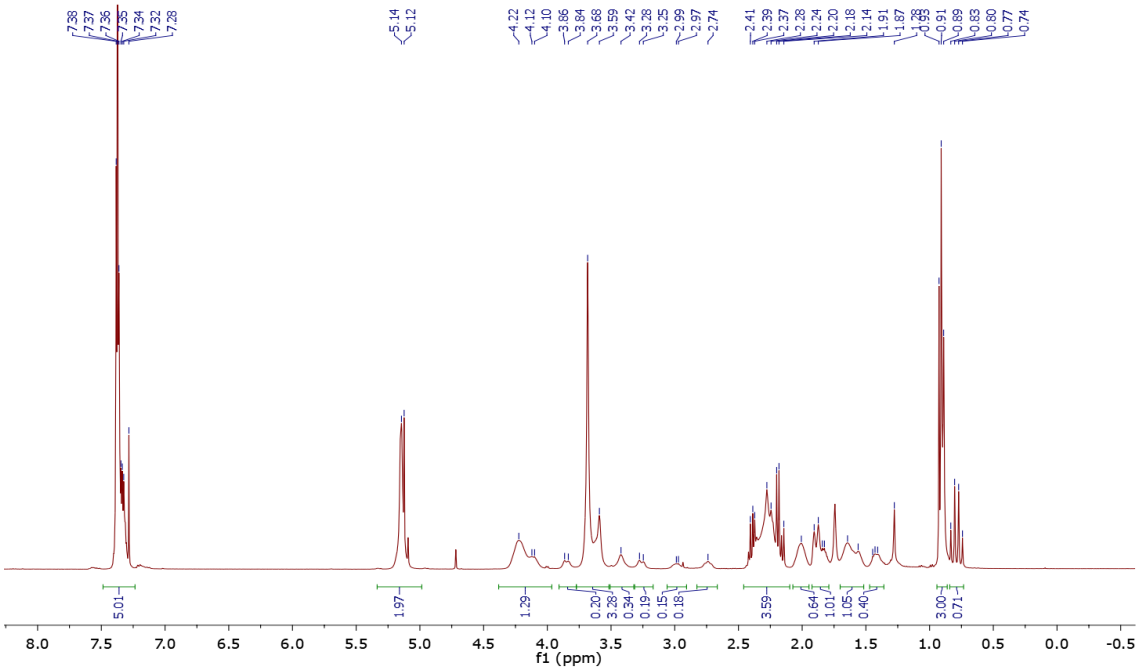
major

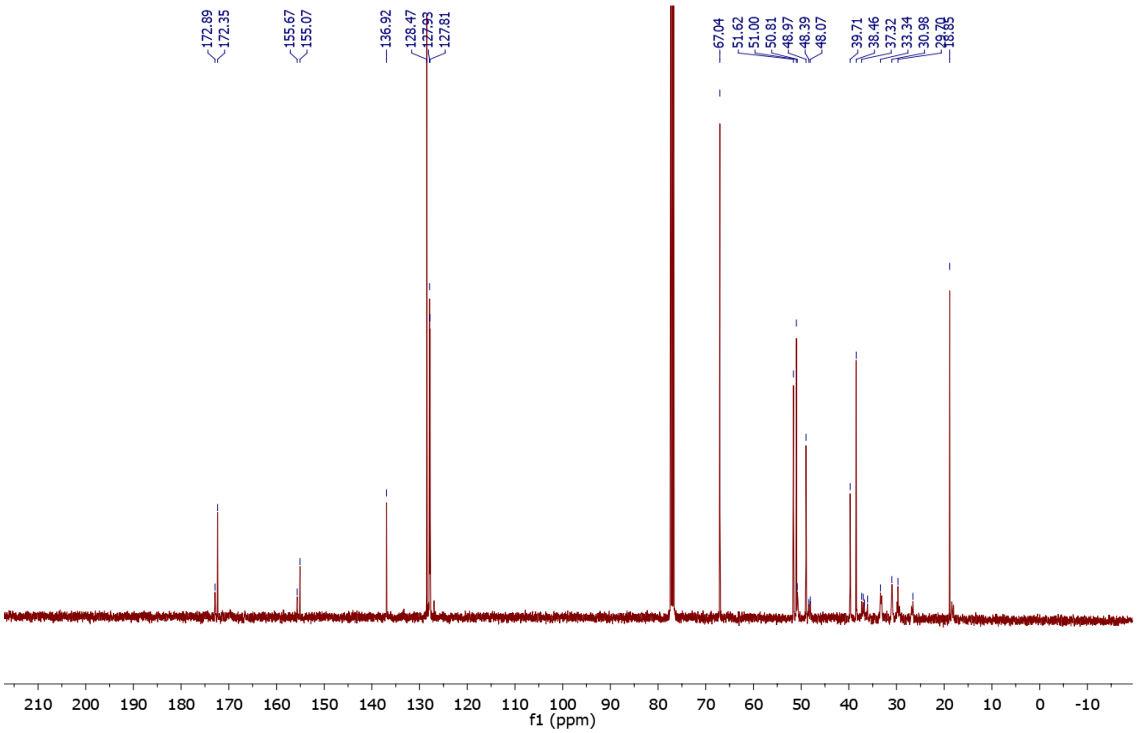
minor

Major diastereomer identified as *trans* on basis of two large (transdiaxial) *J* for H6; confirmed by nOe.

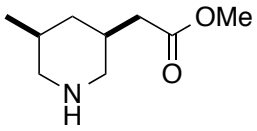
Benzyl 3-(2-methoxy-2-oxoethyl)-5-methylpiperidine-1-carboxylate (8i)

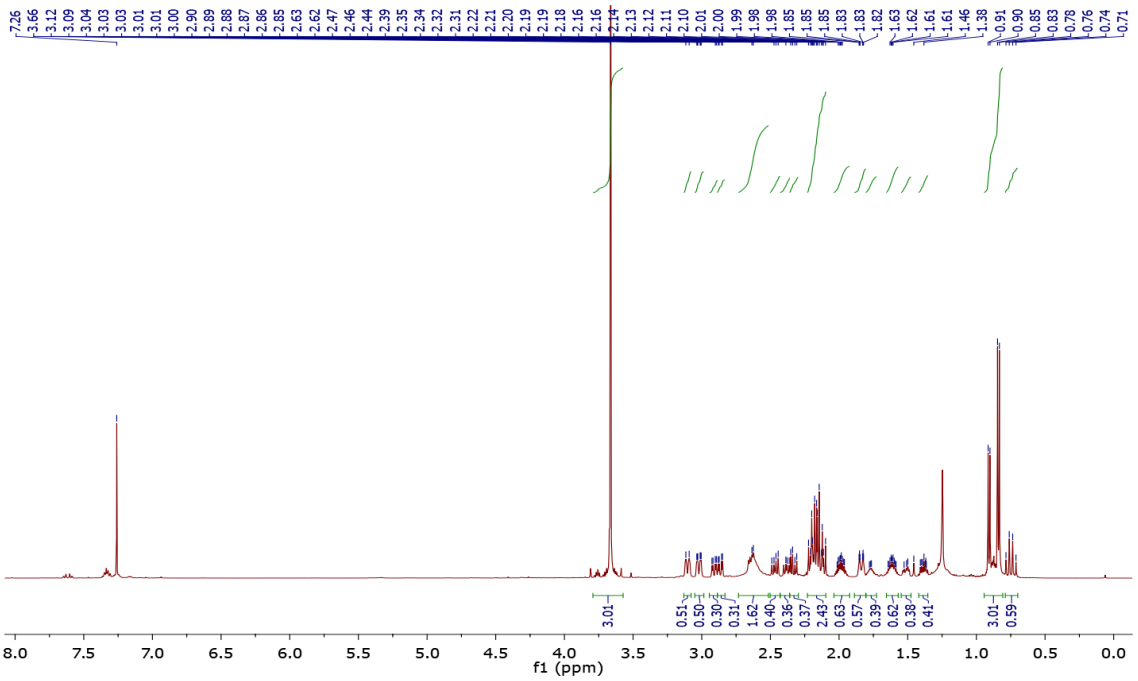


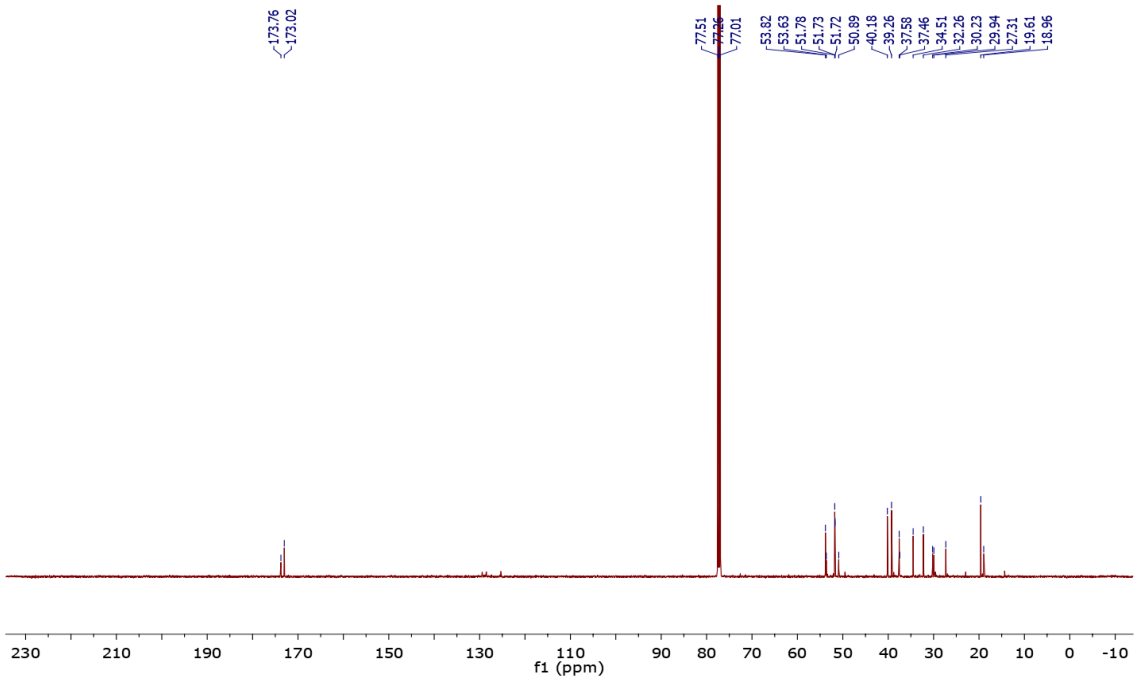


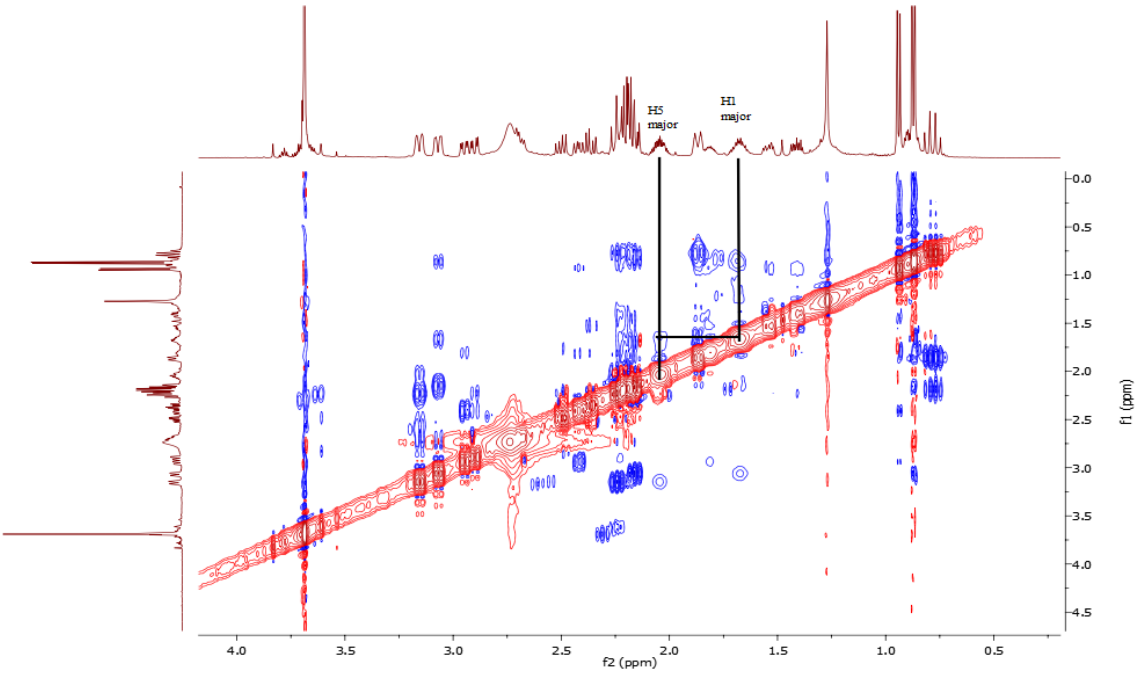


3-(2-Methoxy-2-oxoethyl)-5-methylpiperidine (for determination of stereochemistry)

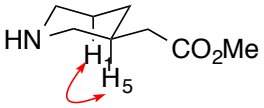




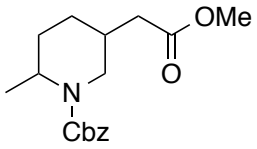


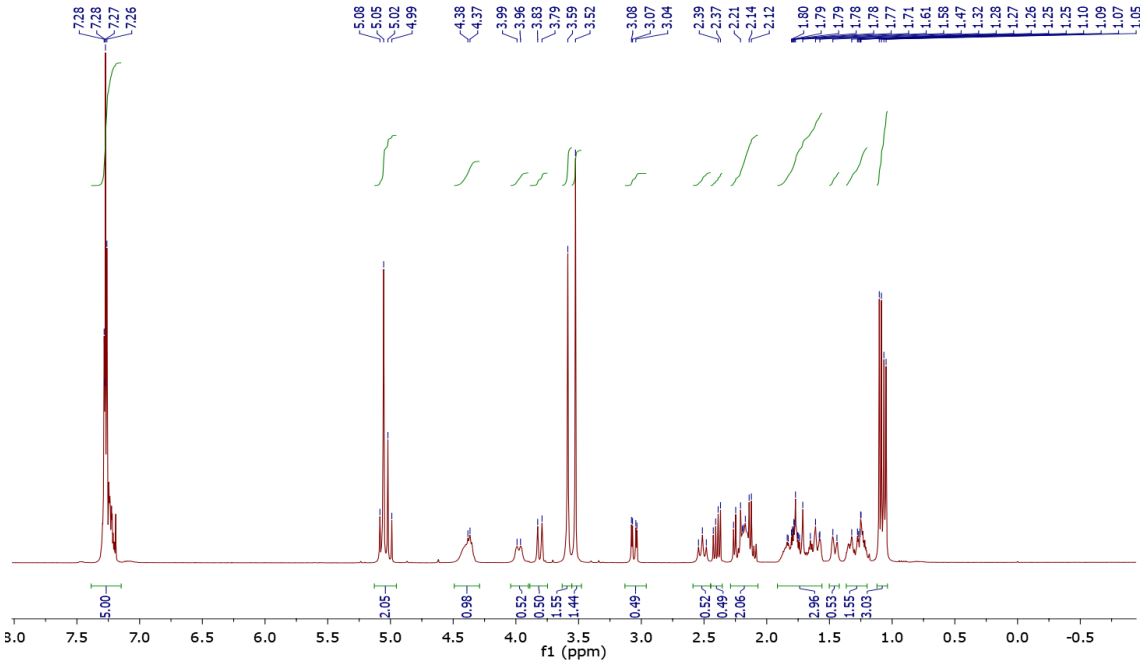


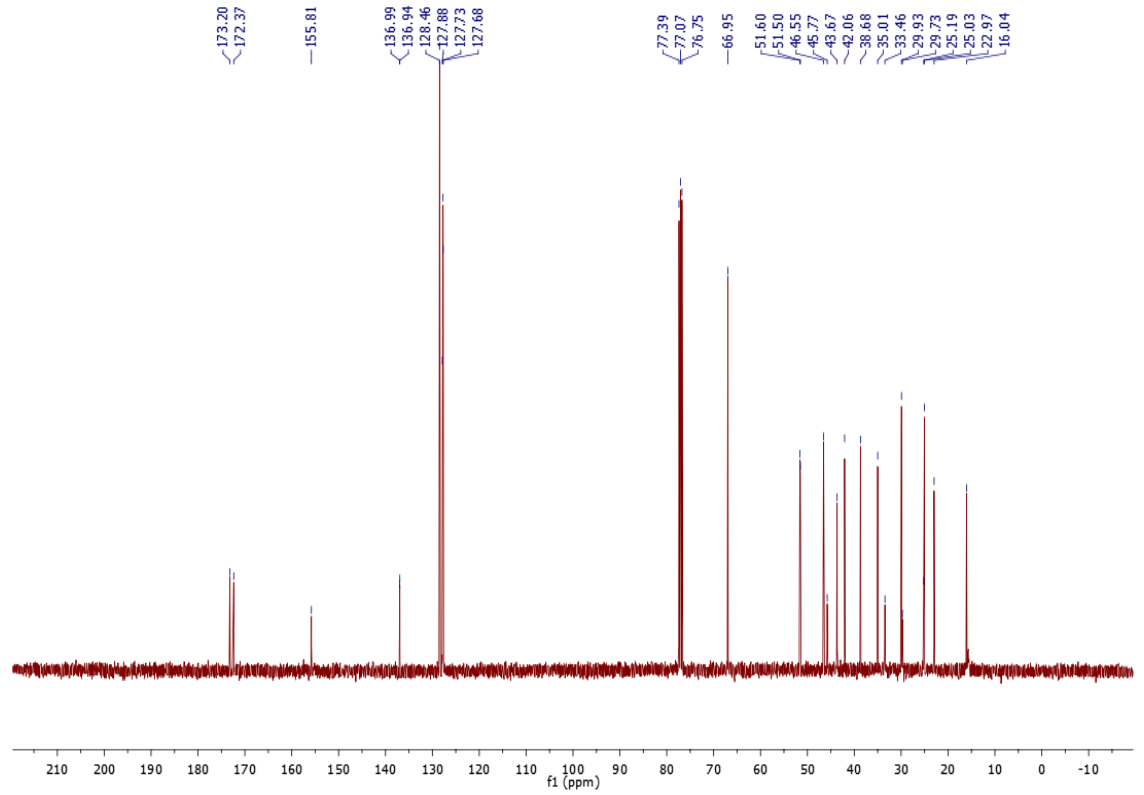
Diagnostic nOe:



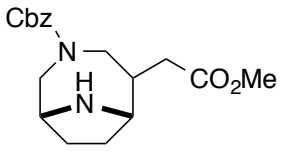
Benzyl 5-(2-methoxy-2-oxoethyl)-2-methylpiperidine-1-carboxylate (8j)

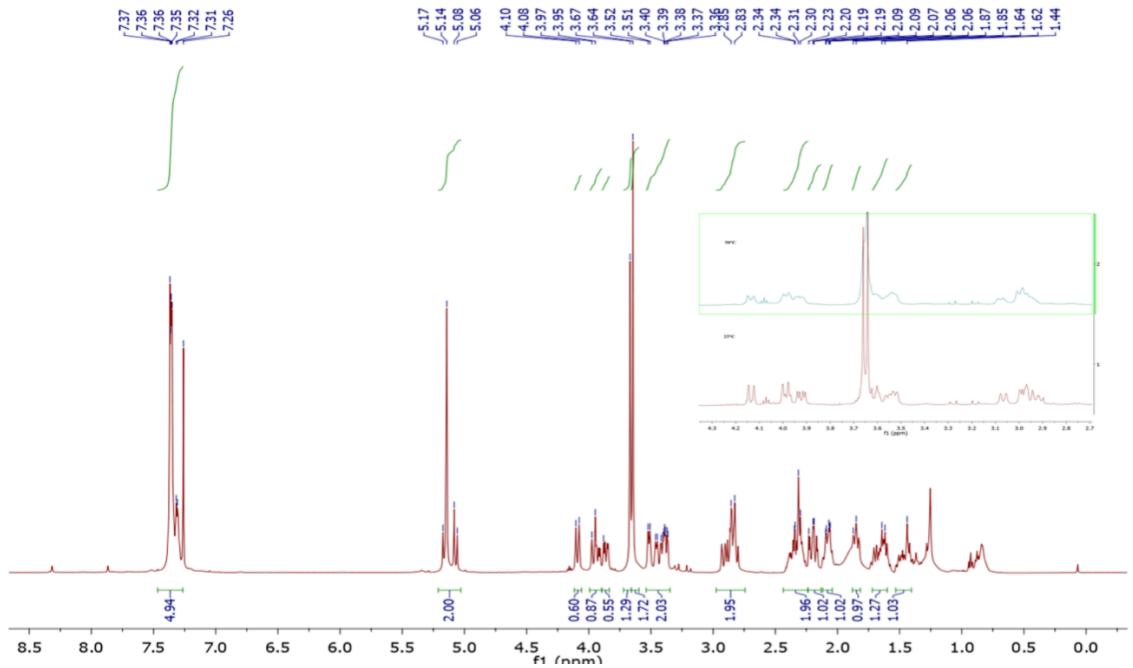


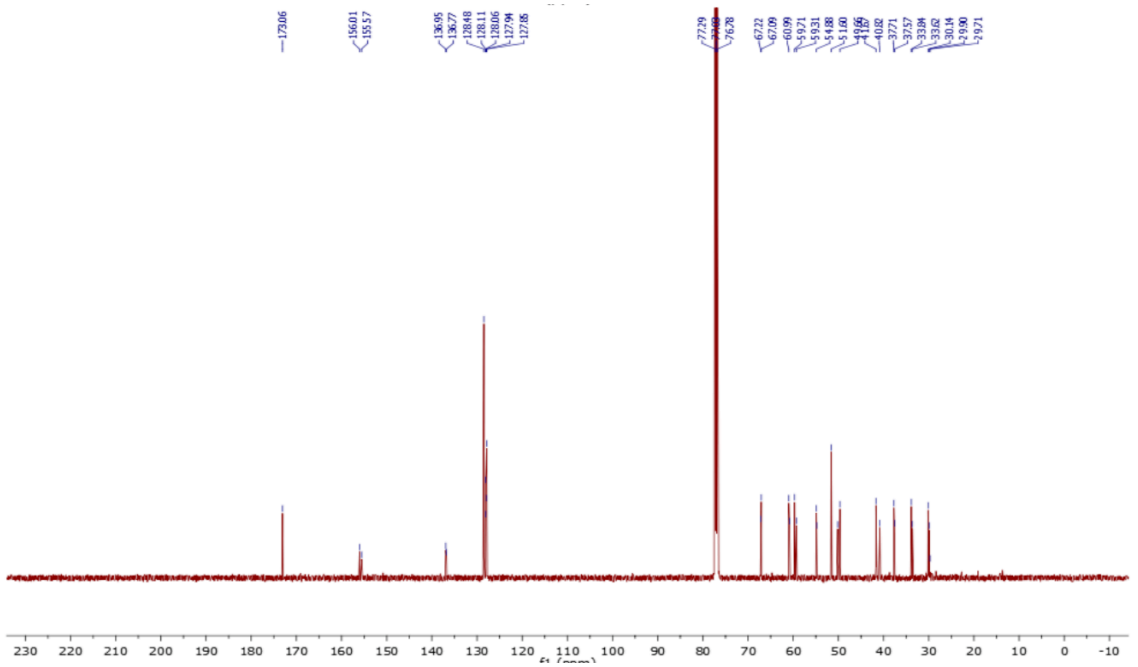




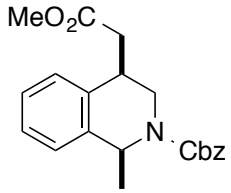
3-Benzyl 5-(2-methoxy-2-oxoethyl)-3,9-diazabicyclo[4.2.1]nonane-3-carboxylate (8k)

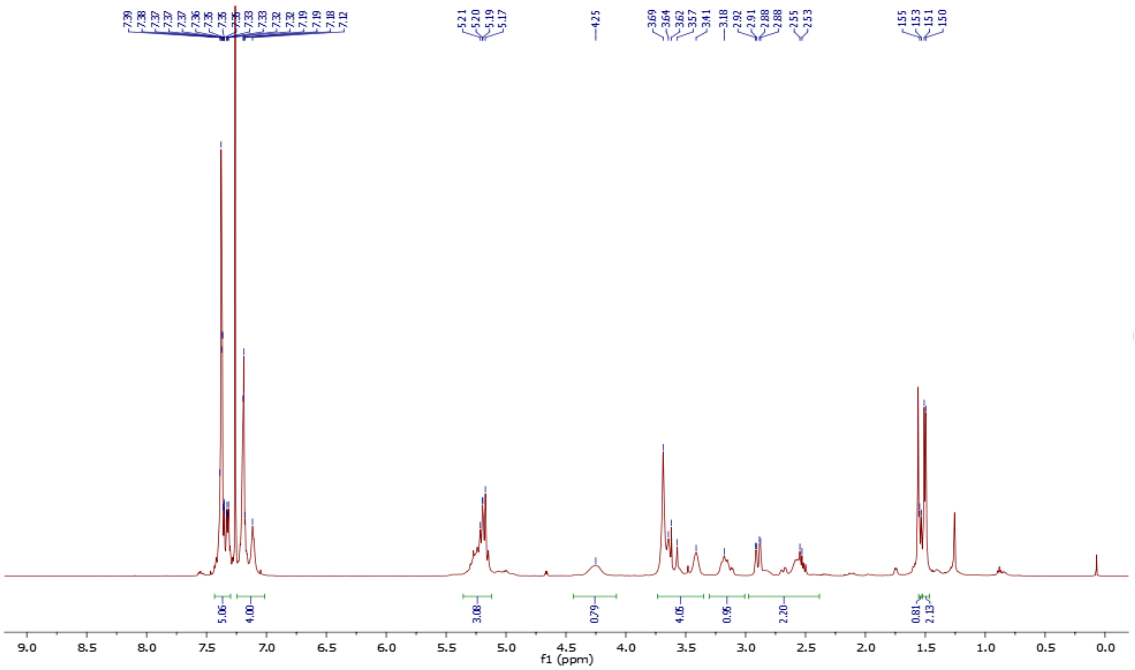


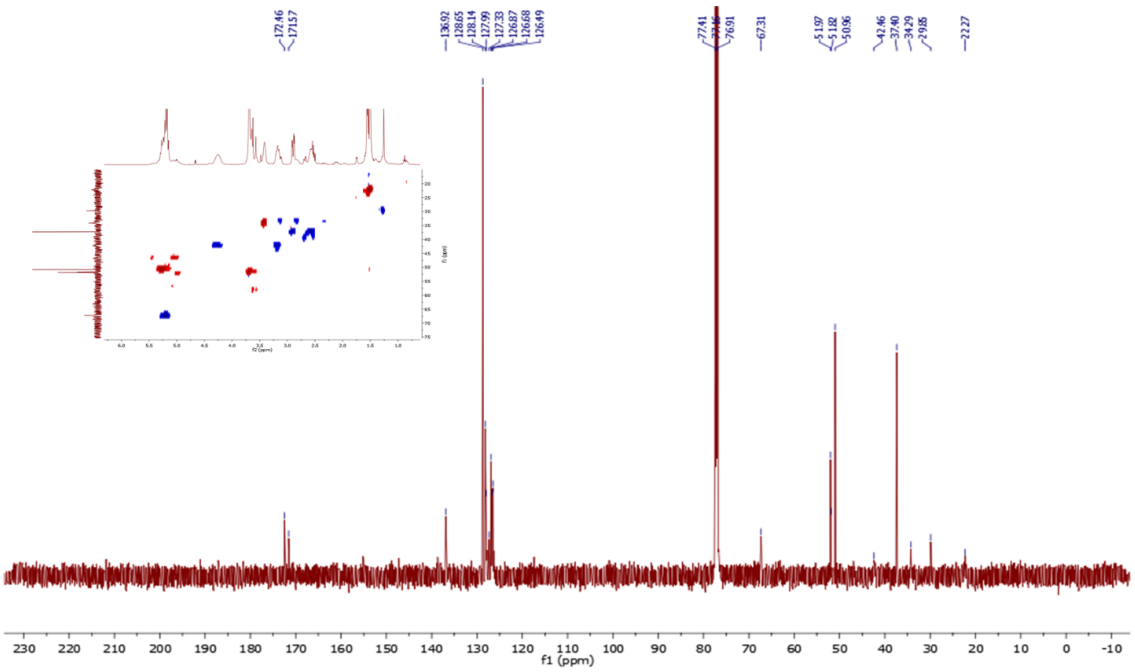


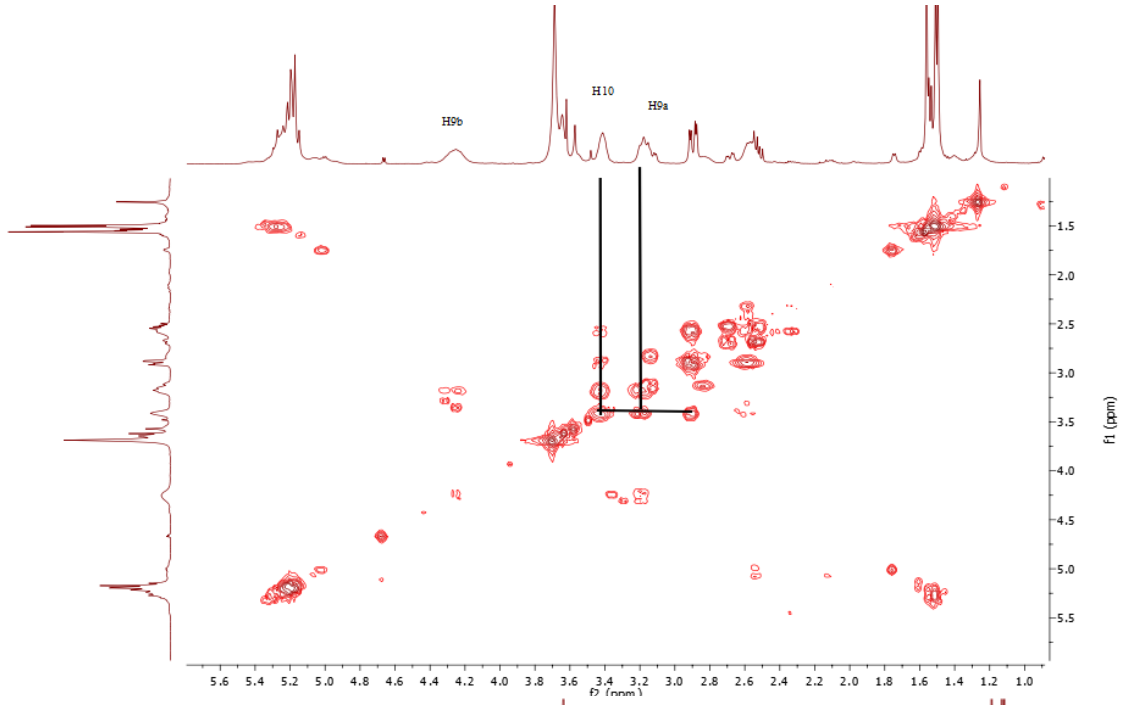


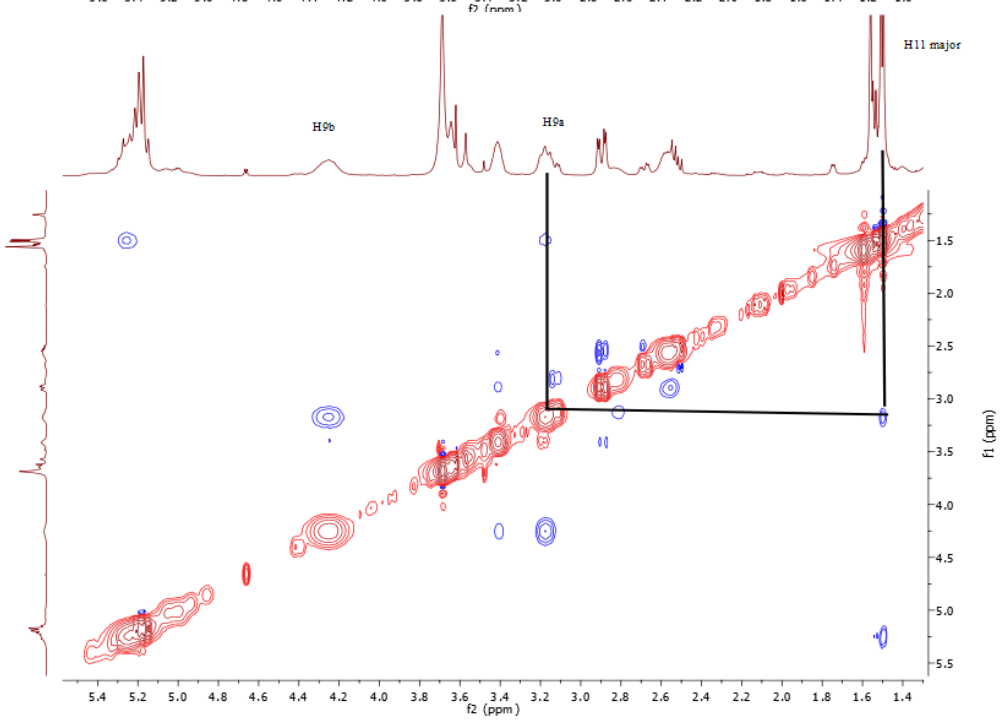
Benzyl 4-(2-methoxy-2-oxoethyl)-1-methyl-3,4-dihydroisoquinoline-2(1H)-carboxylate (8l)



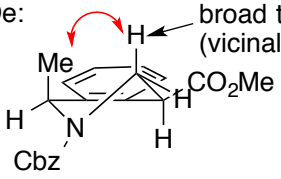








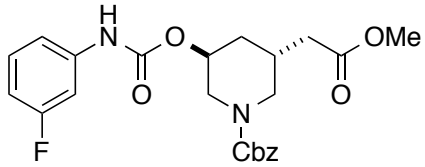
Diagnostic nOe:

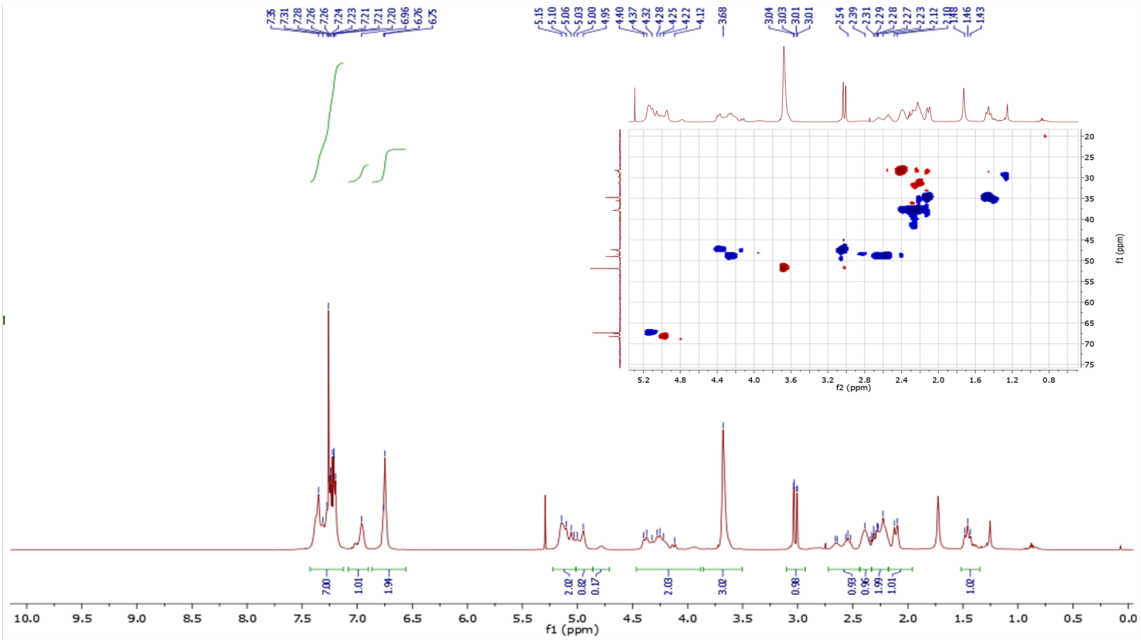


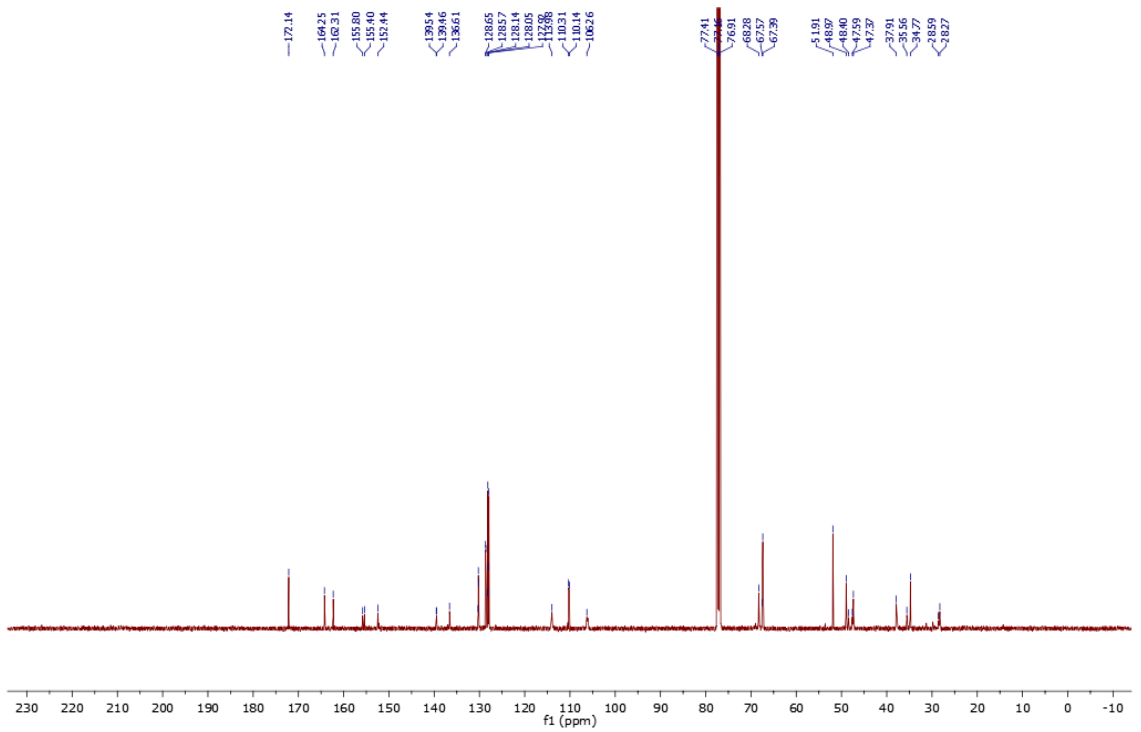
broad t with 2 large (vicinal/diaxial) *J* values

Benzyl 3-(((3-fluorophenyl)carbamoyl)oxy)-5-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate (8m)

Major isomer assigned as *trans*: axial H4 proton (1.46ppm) presents as br t – two large *J* values: one geminal, one vicinal diaxial).

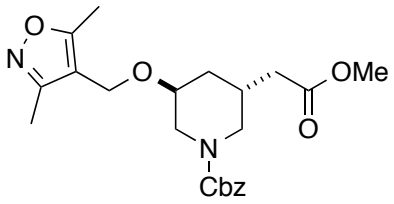


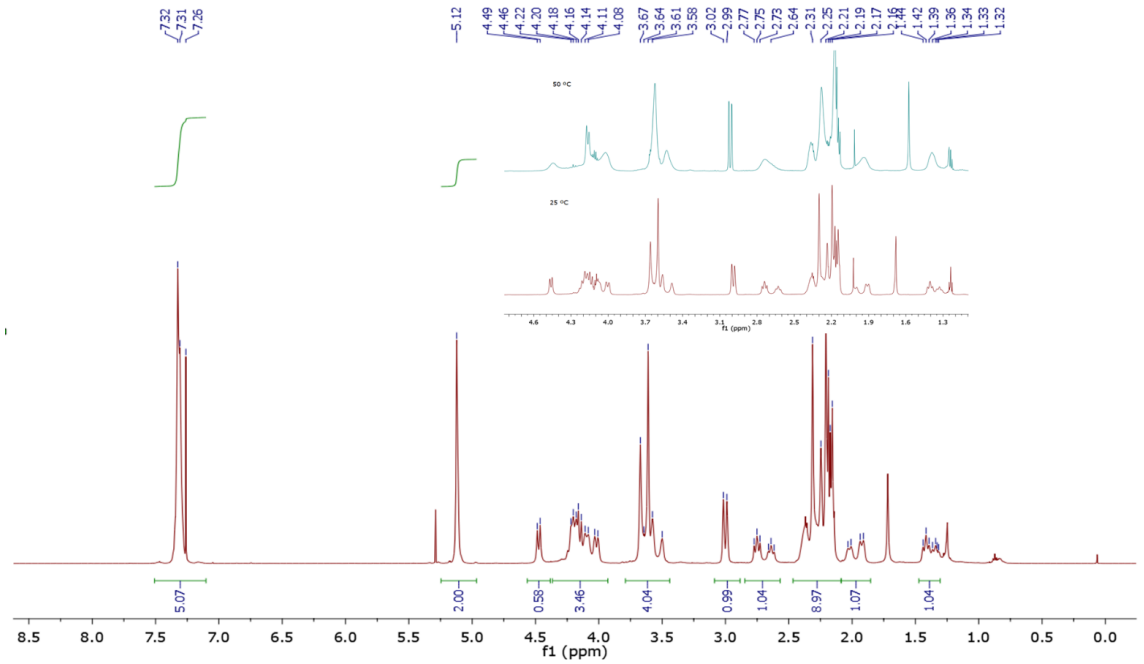


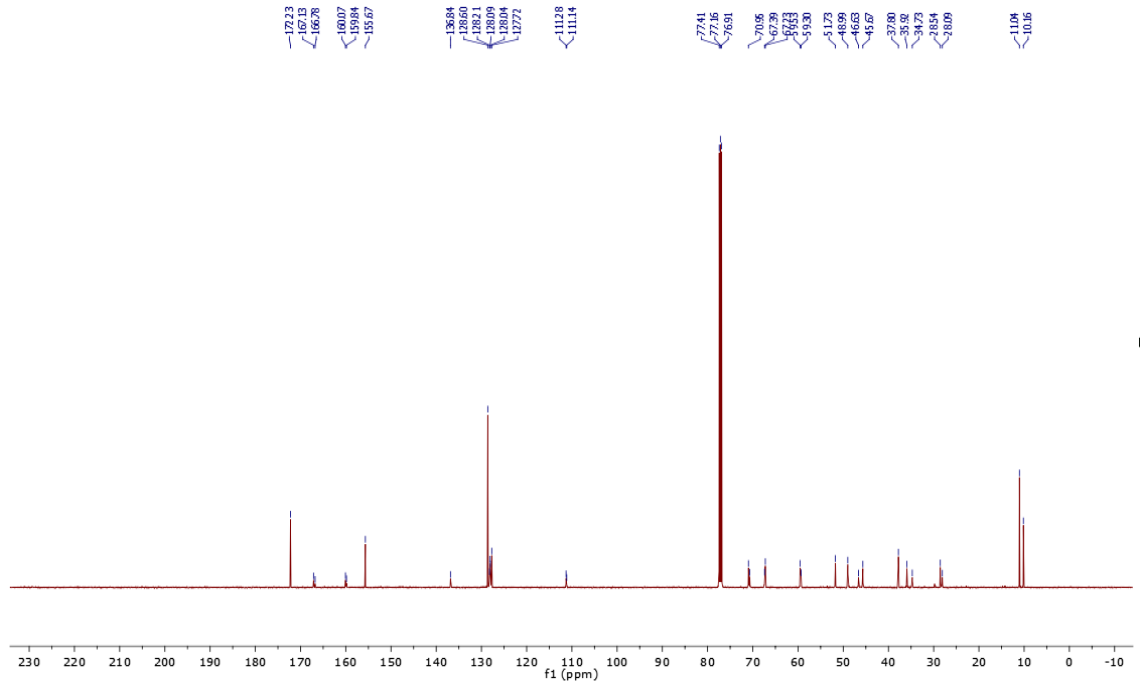


Benzyl 3-((3,5-dimethylisoxazol-4-yl)methoxy)-5-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate (8n)

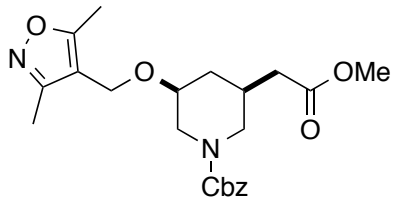
Major *trans* diastereomer (axial proton at C4 resolves to br t in VT – one large geminal, one large vicinal diaxial coupling)

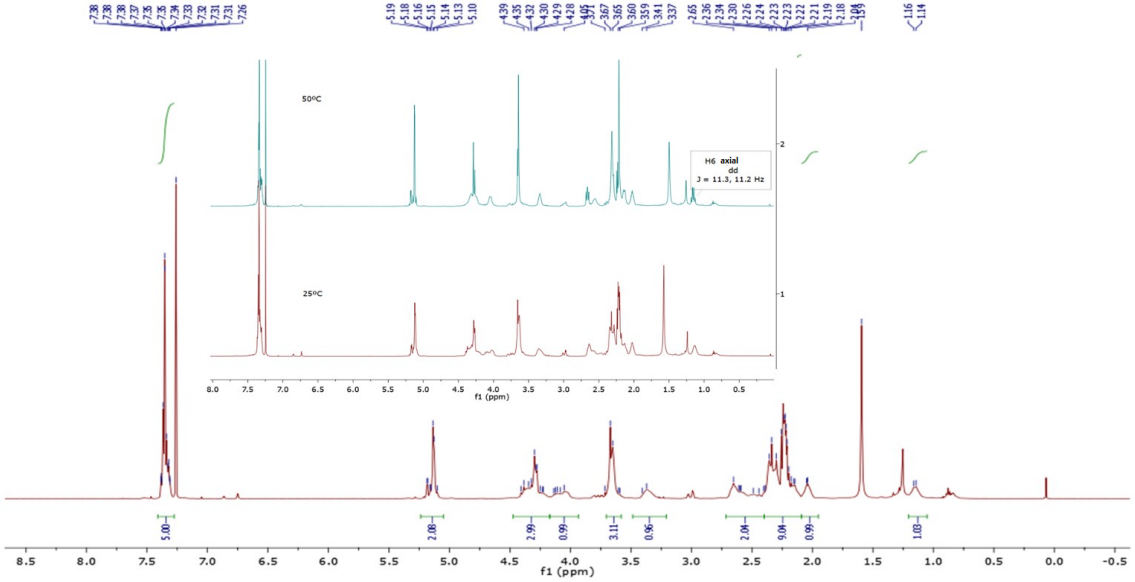


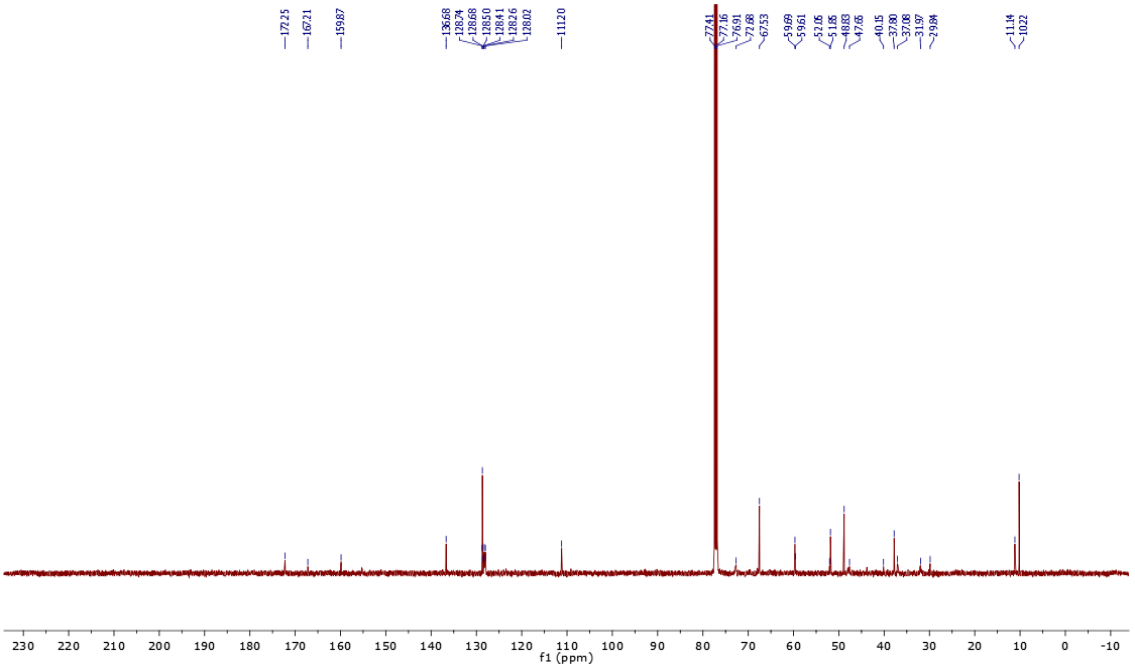




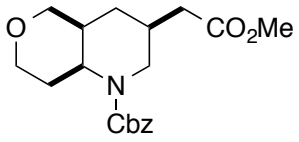
Minor *cis* diastereomer (axial proton at C4 resolves to br q in VT – one large vicinal, two large diaxial coupling)

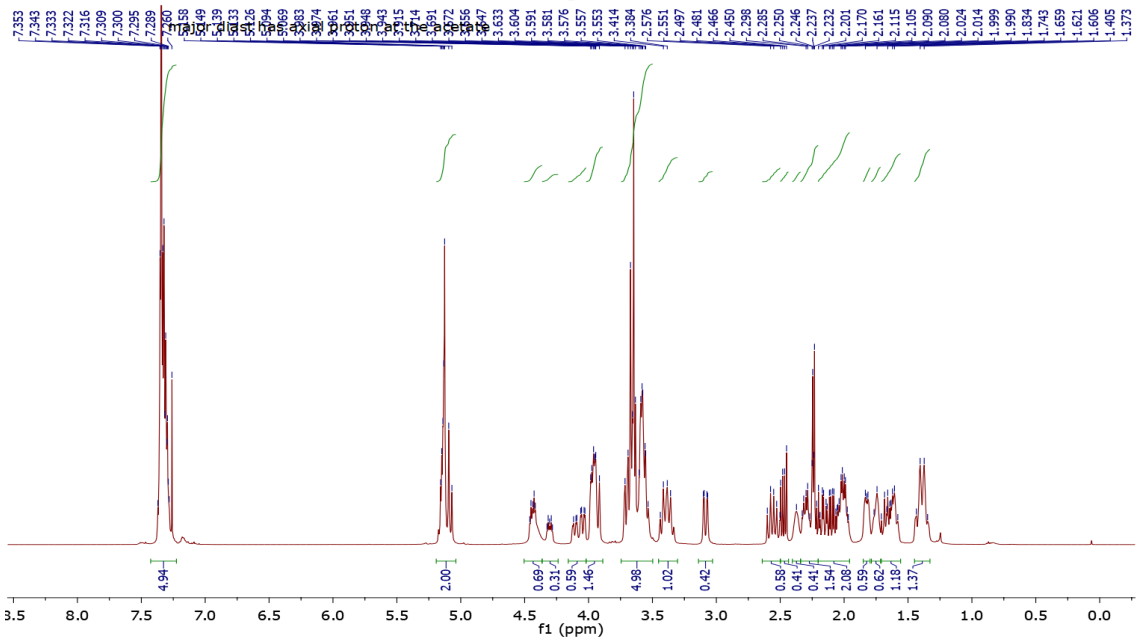


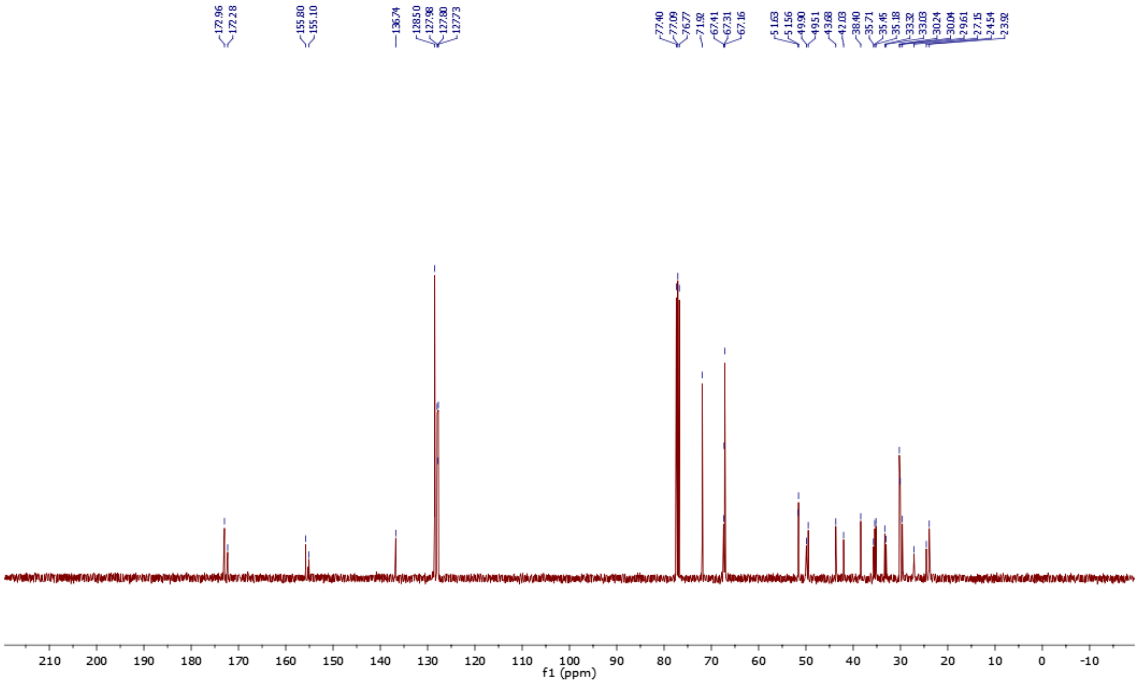


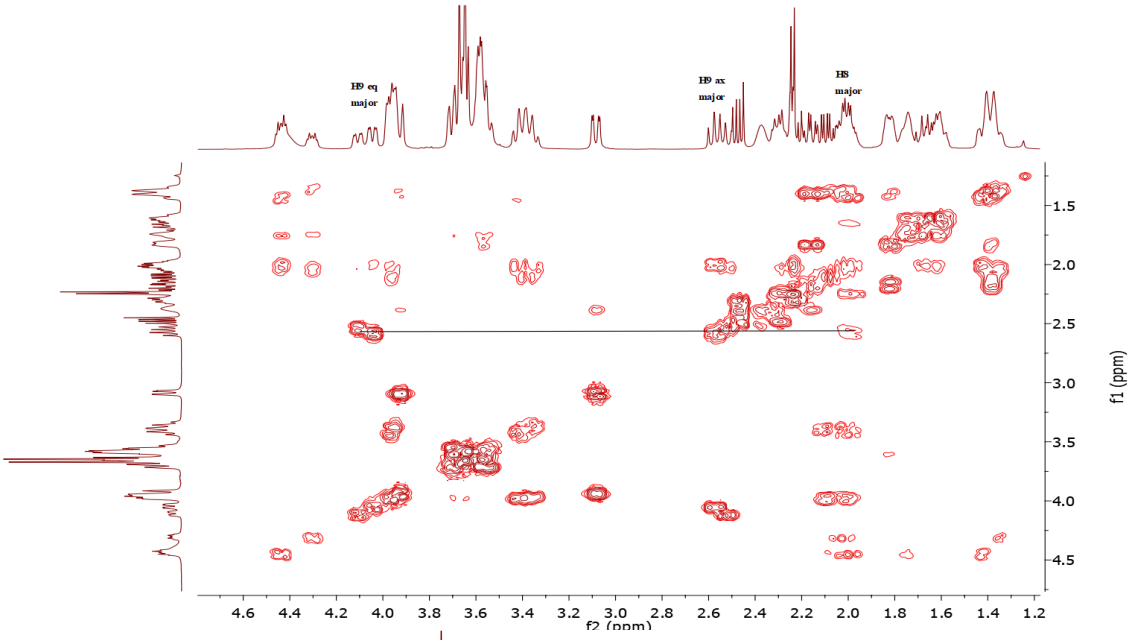


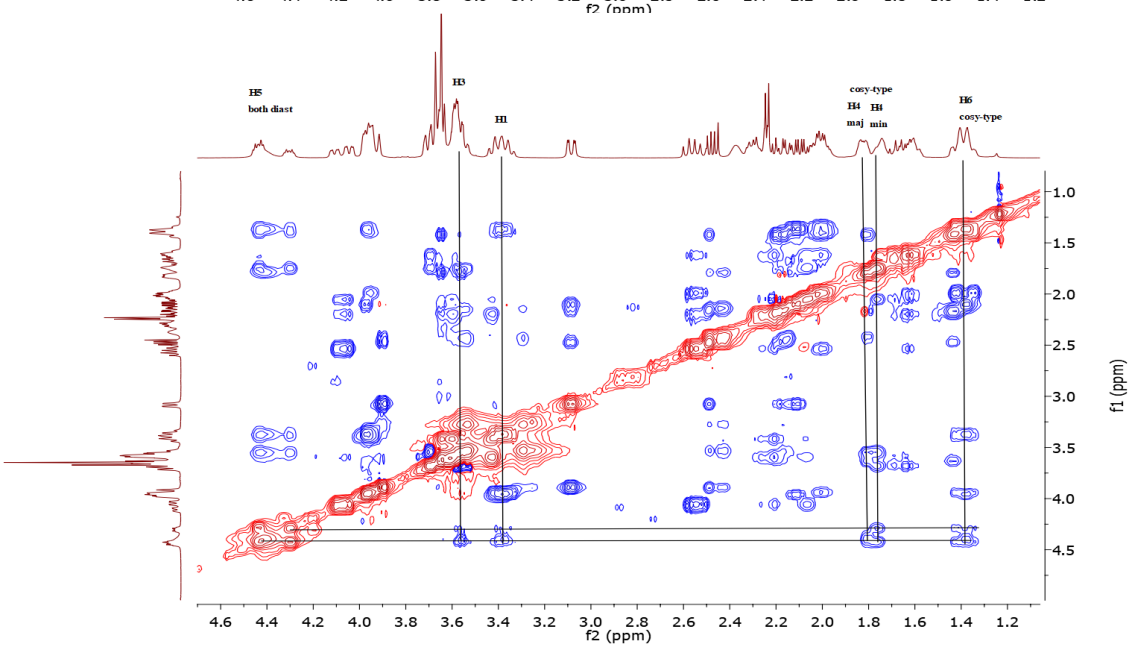
Benzyl 3-(2-methoxy-2-oxoethyl)octahydro-1H-pyrano[4,3-b]pyridine-1-carboxylate (8o)



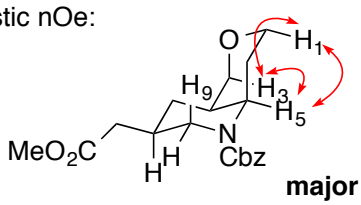




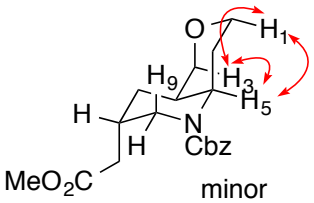




Diagnostic nOe:



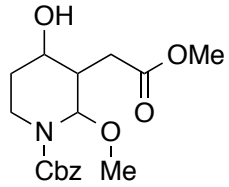
major

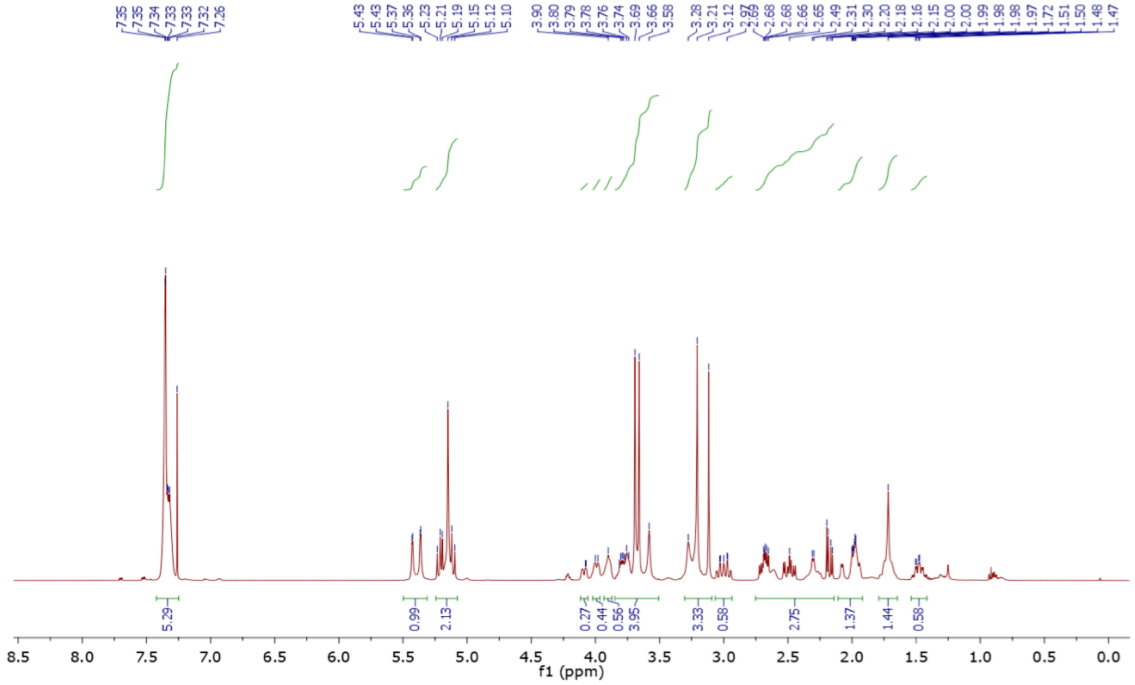


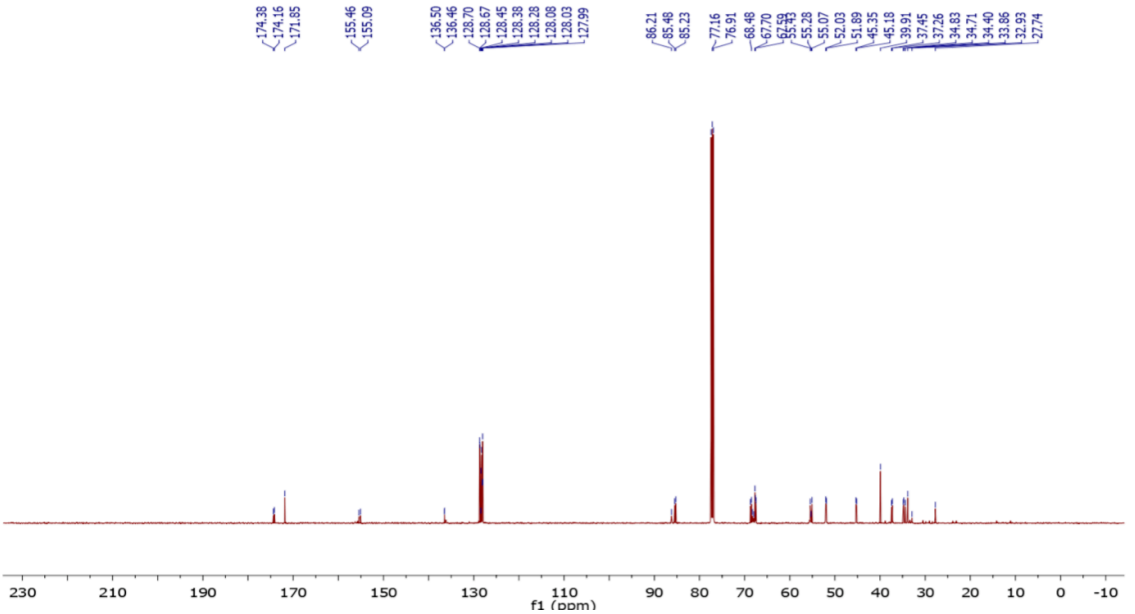
minor

nOe interactions confirm H5 equatorial in *cis*-oxazadecalin structure. One H9 signal for major isomer shows two large (geminal and vicinal transdiaxial) *J* values, only possible if carboxymethyl substituent is equatorial.

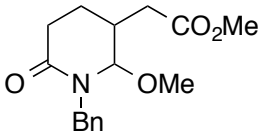
Benzyl 4-hydroxy-2-methoxy-3-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate

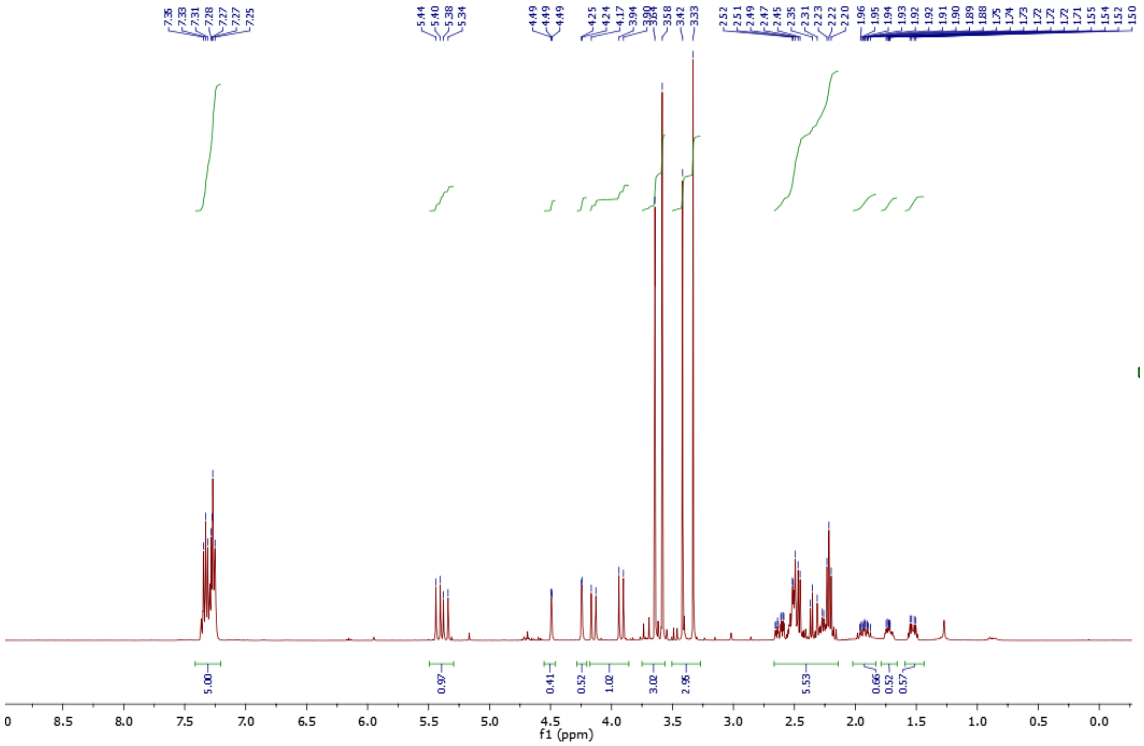


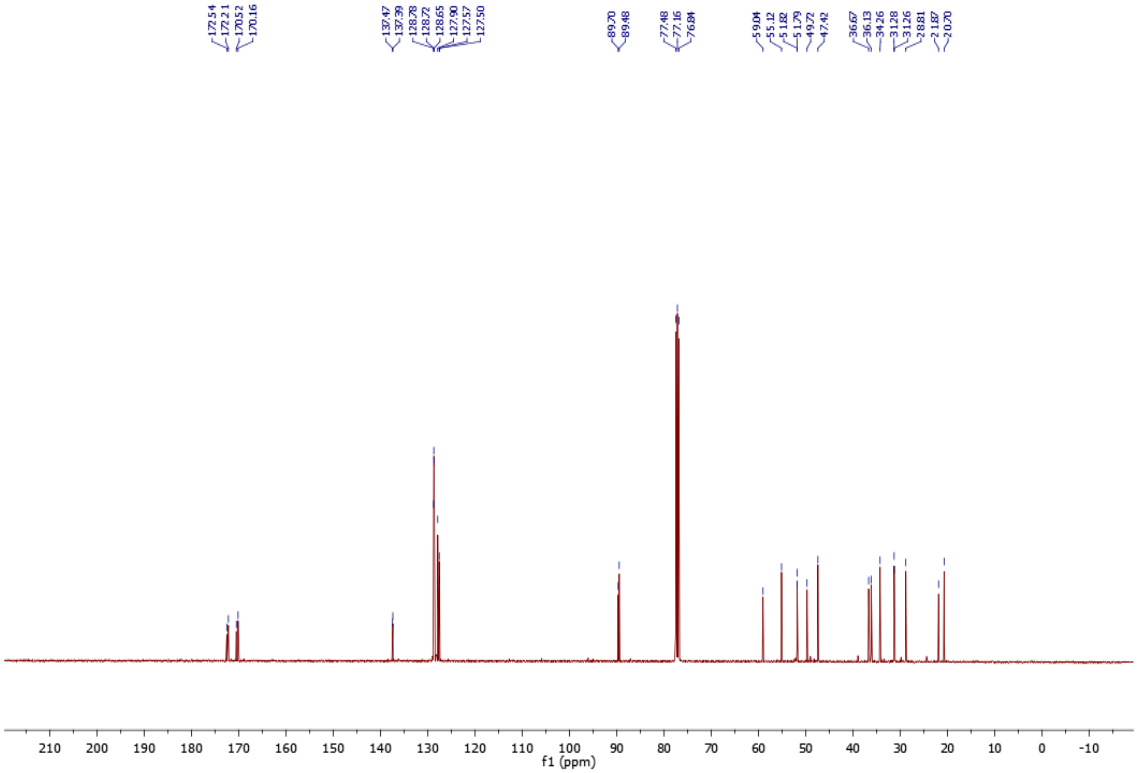




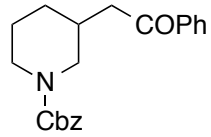
Methyl 2-(1-benzyl-2-methoxy-6-oxopiperidin-3-yl)acetate

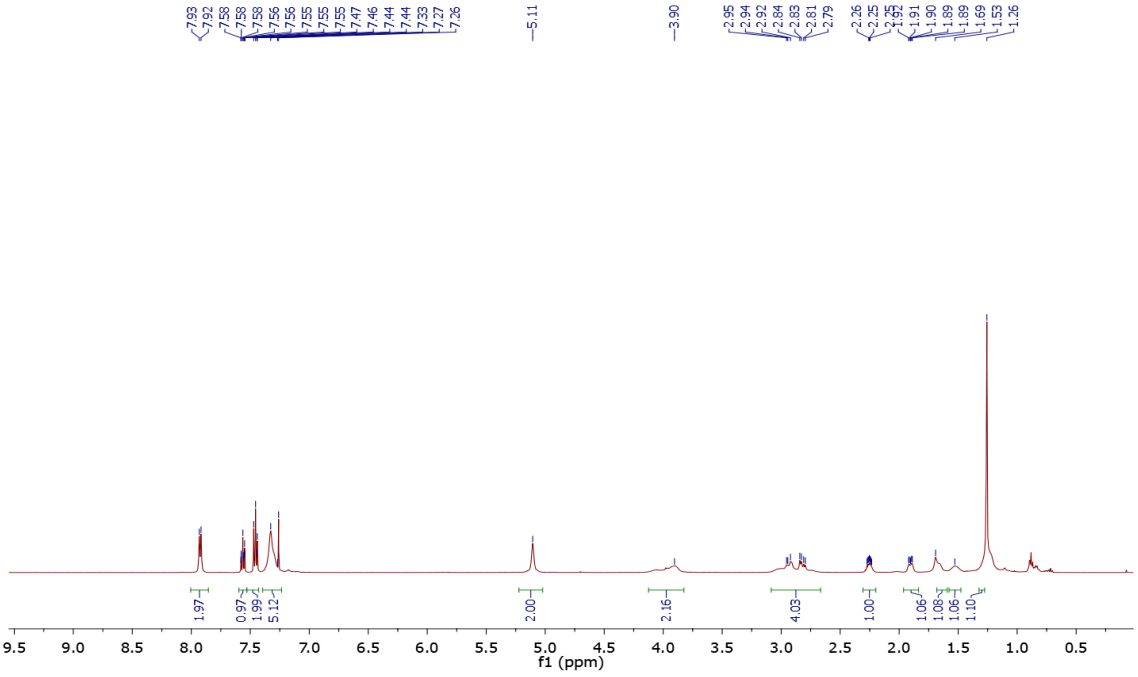


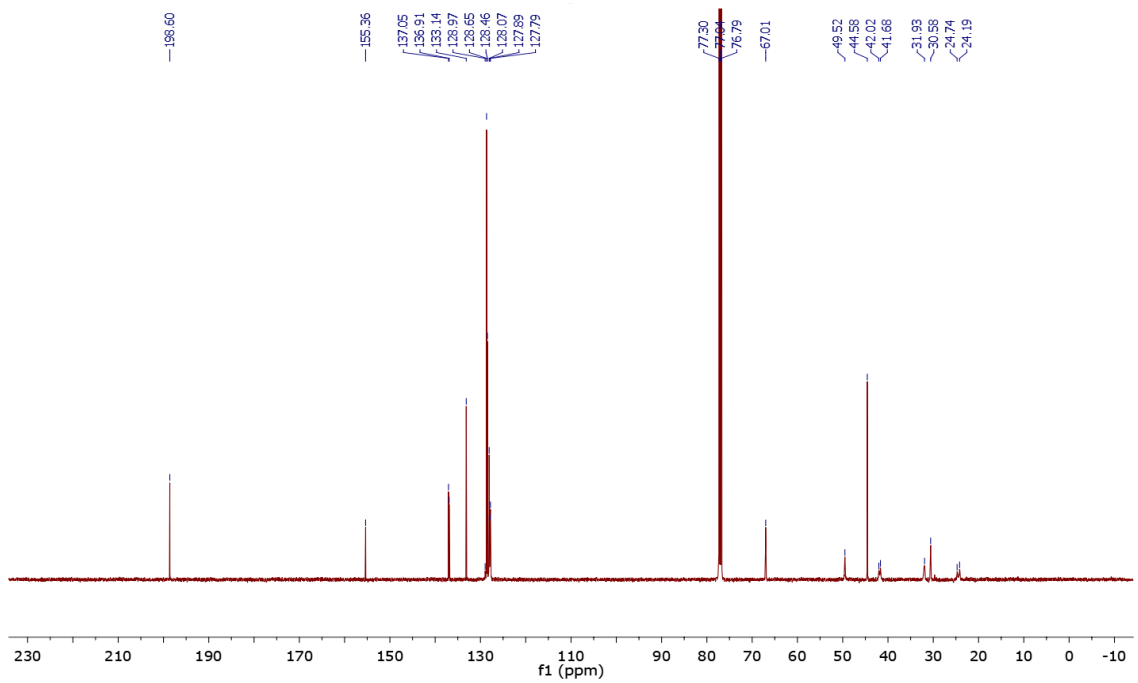




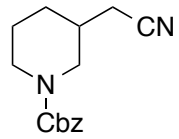
Benzyl 3-(2-oxo-2-phenylethyl)piperidine-1-carboxylate

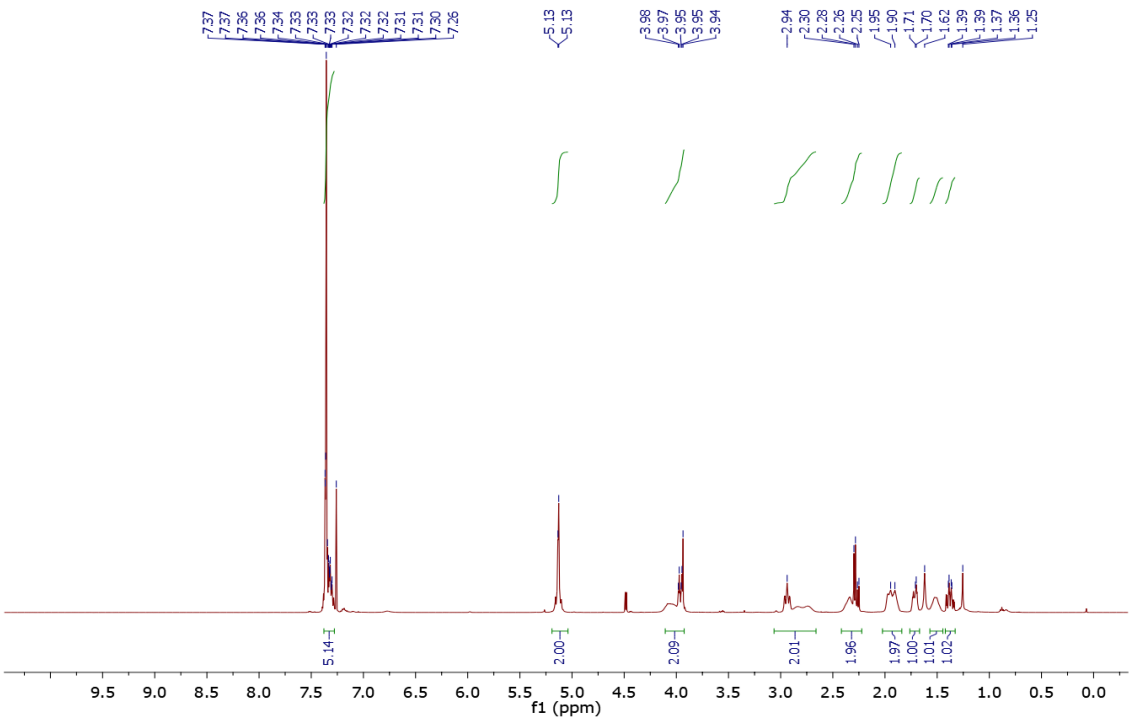


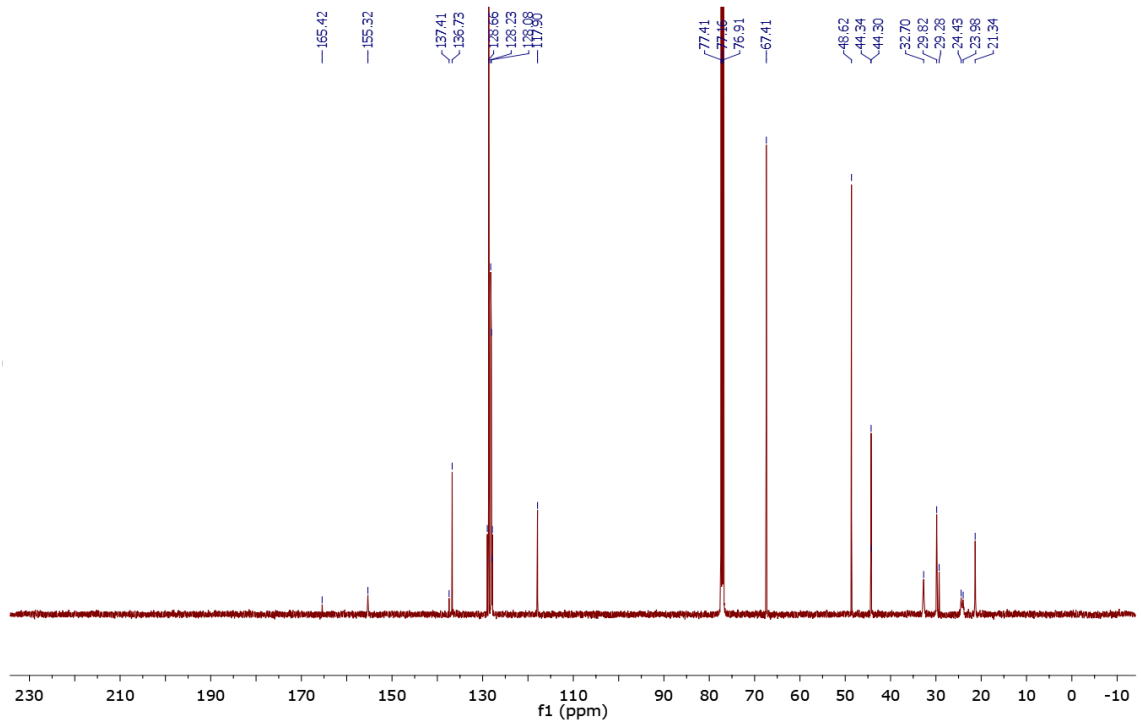




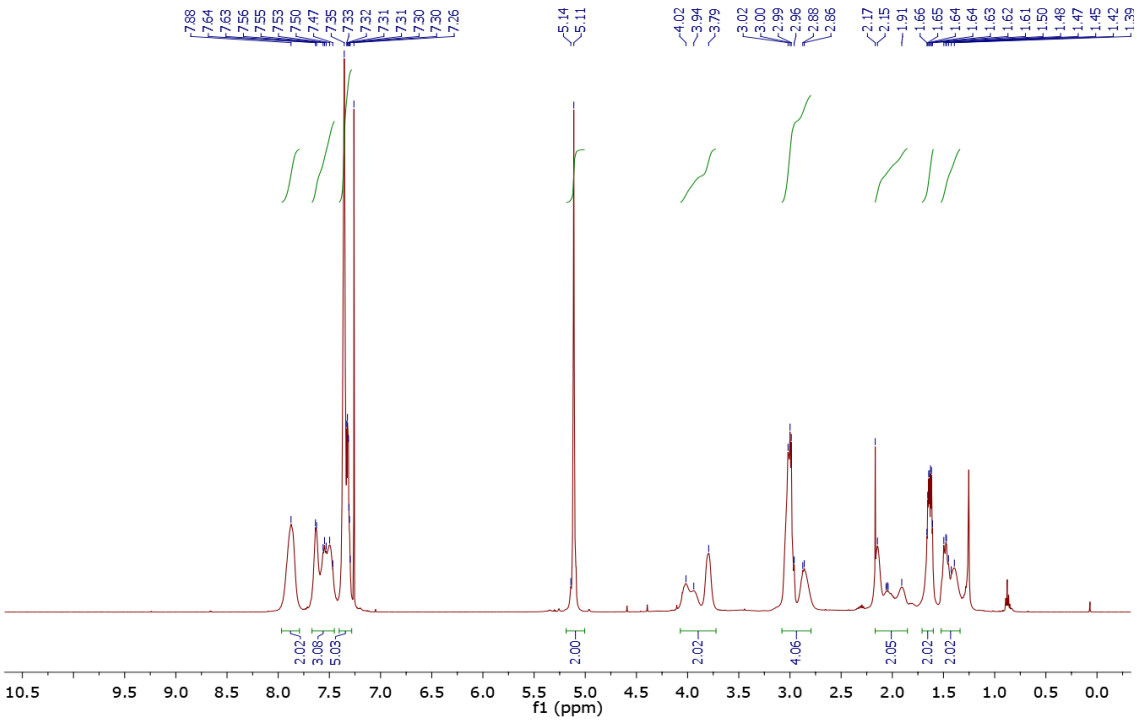
Benzyl 3-(cyanomethyl)piperidine-1-carboxylate

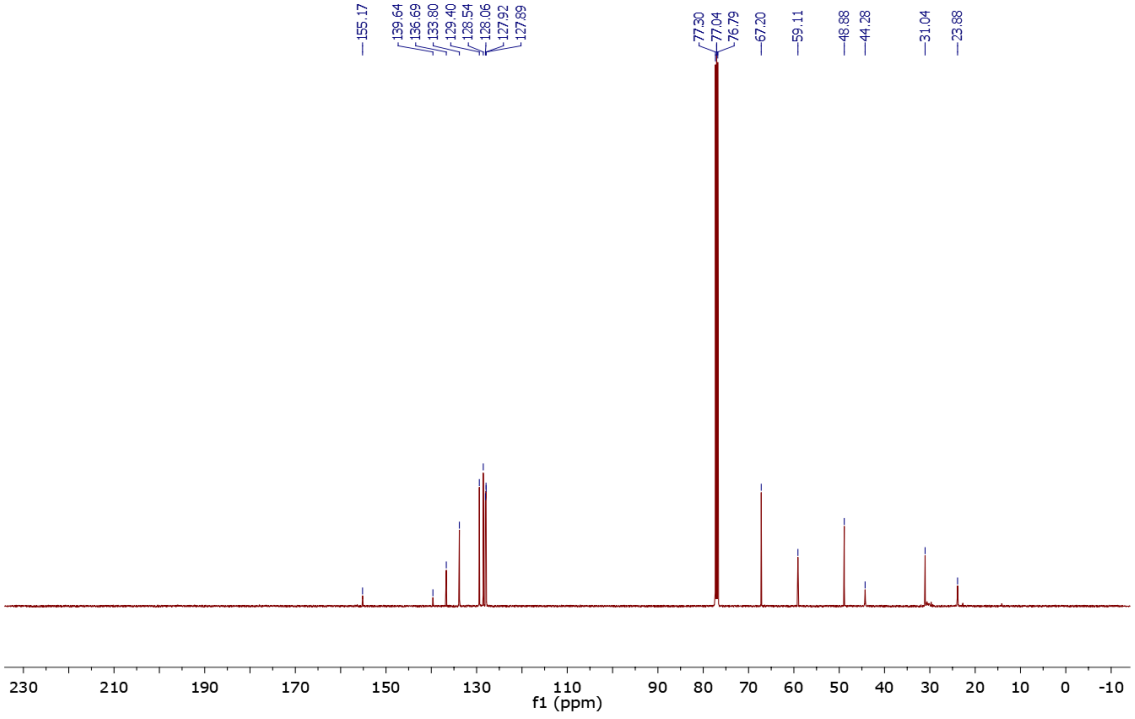




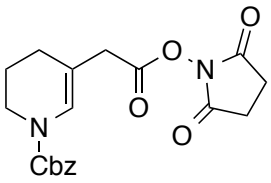


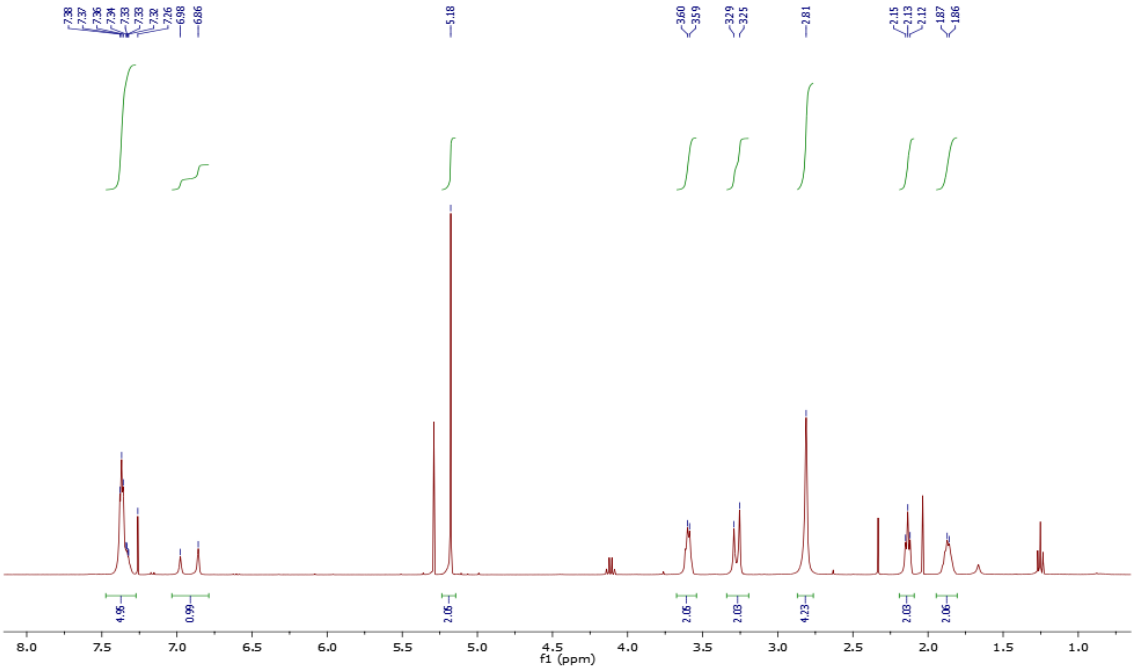
Benzyl 3-((phenylsulfonyl)methyl)piperidine-1-carboxylate

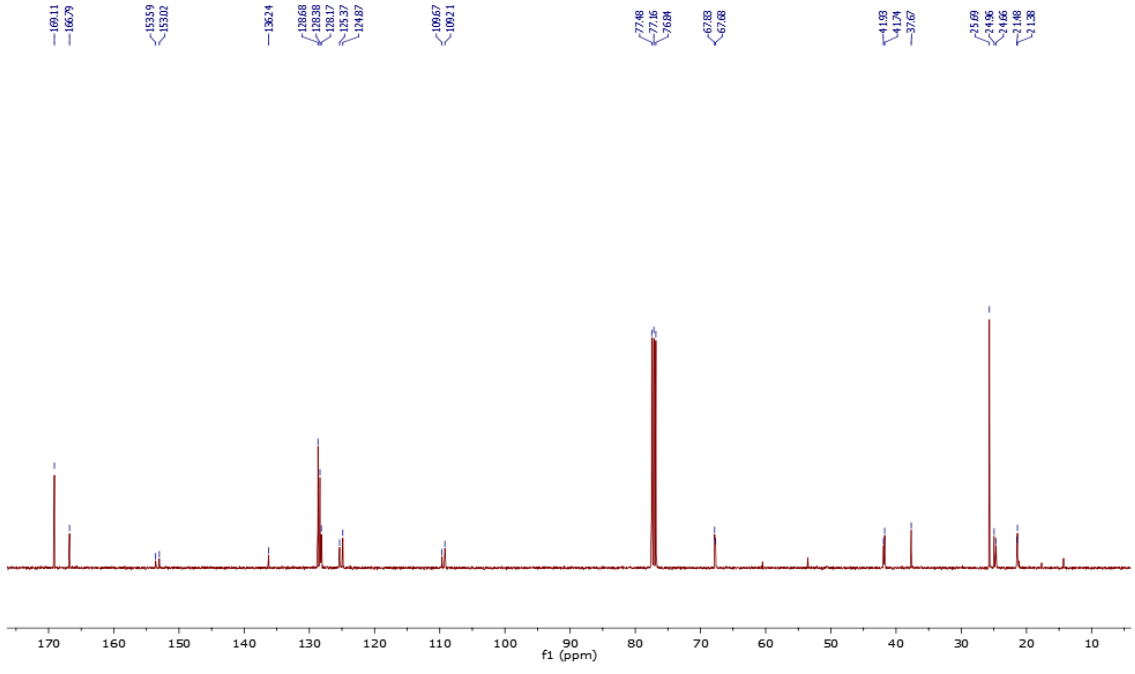




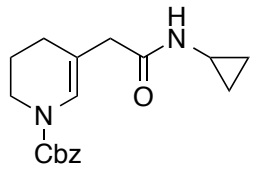
Benzyl 5-(2-((2,5-dioxopyrrolidin-1-yl)oxy)-2-oxoethyl)-3,4-dihydropyridine-1(2*H*)-carboxylate (10)

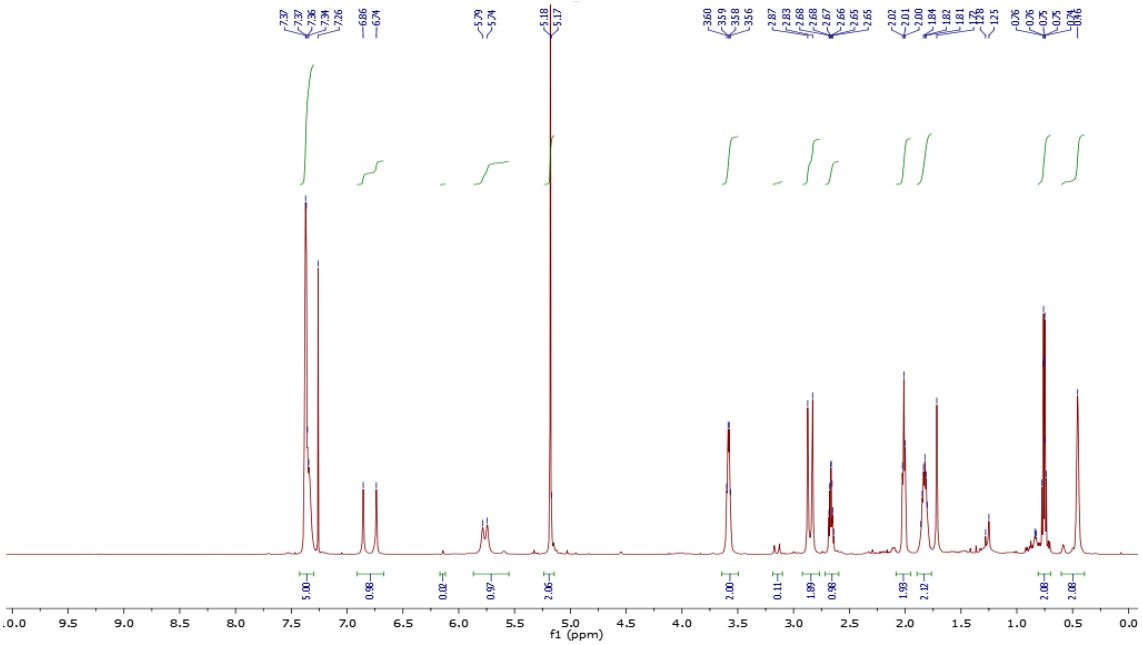


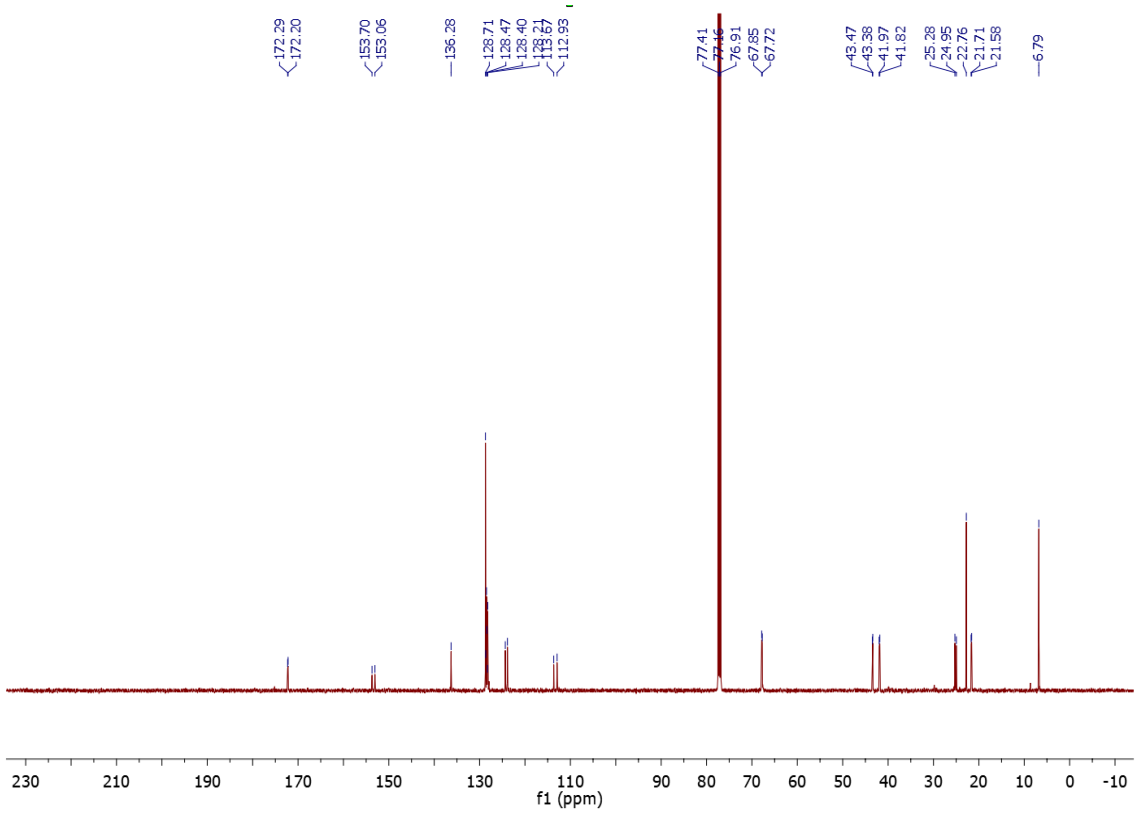




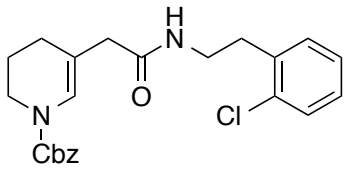
Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11a)

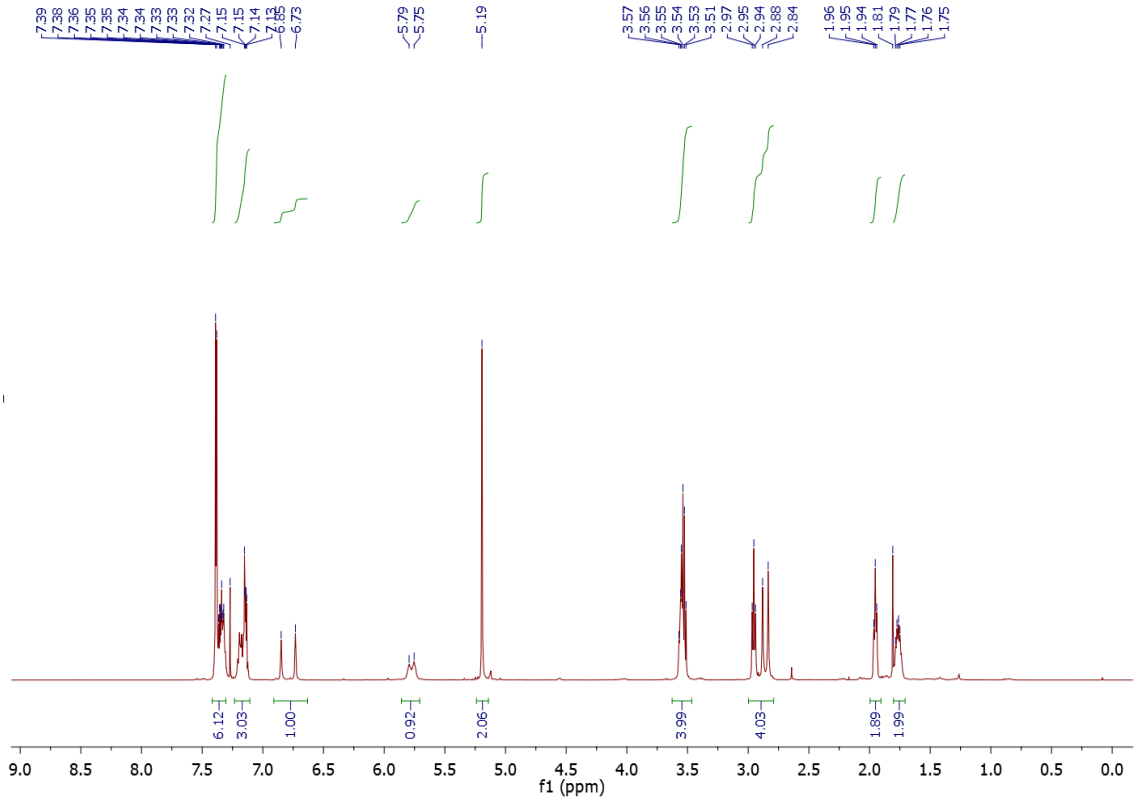


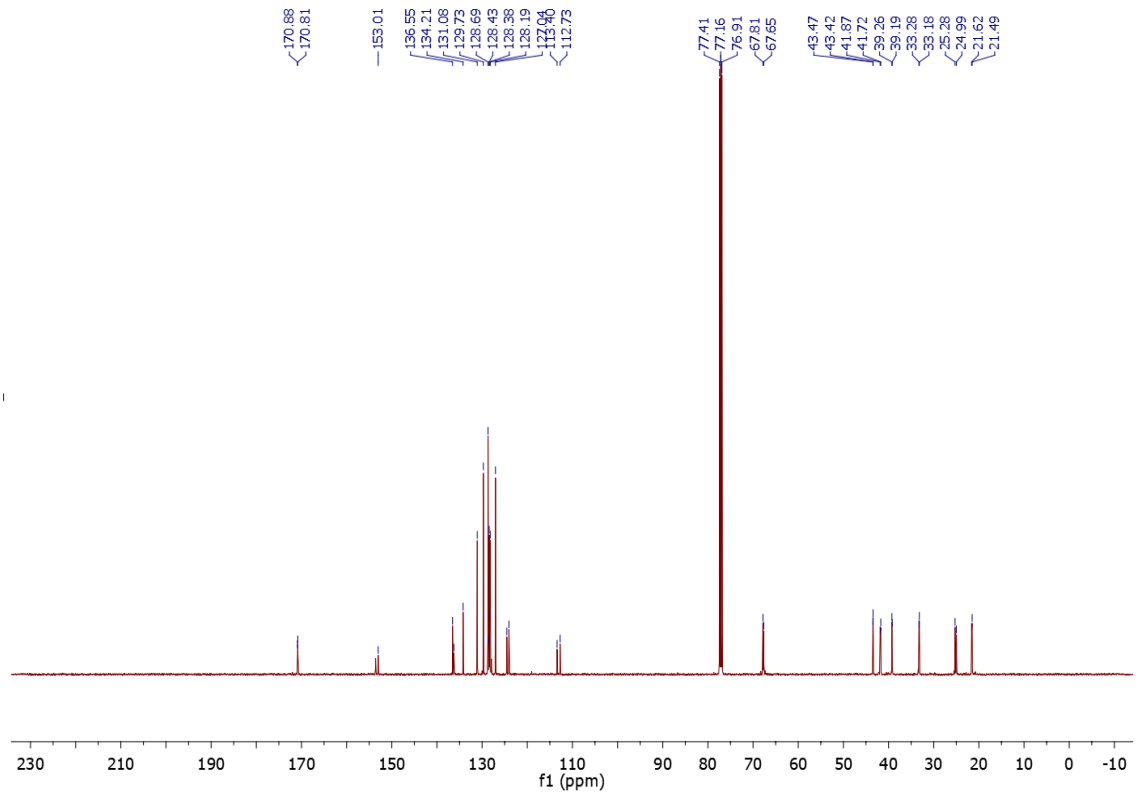




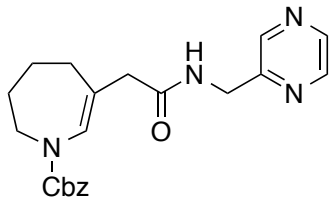
Benzyl 5-(2-((2-chlorophenethyl)amino)-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11b)

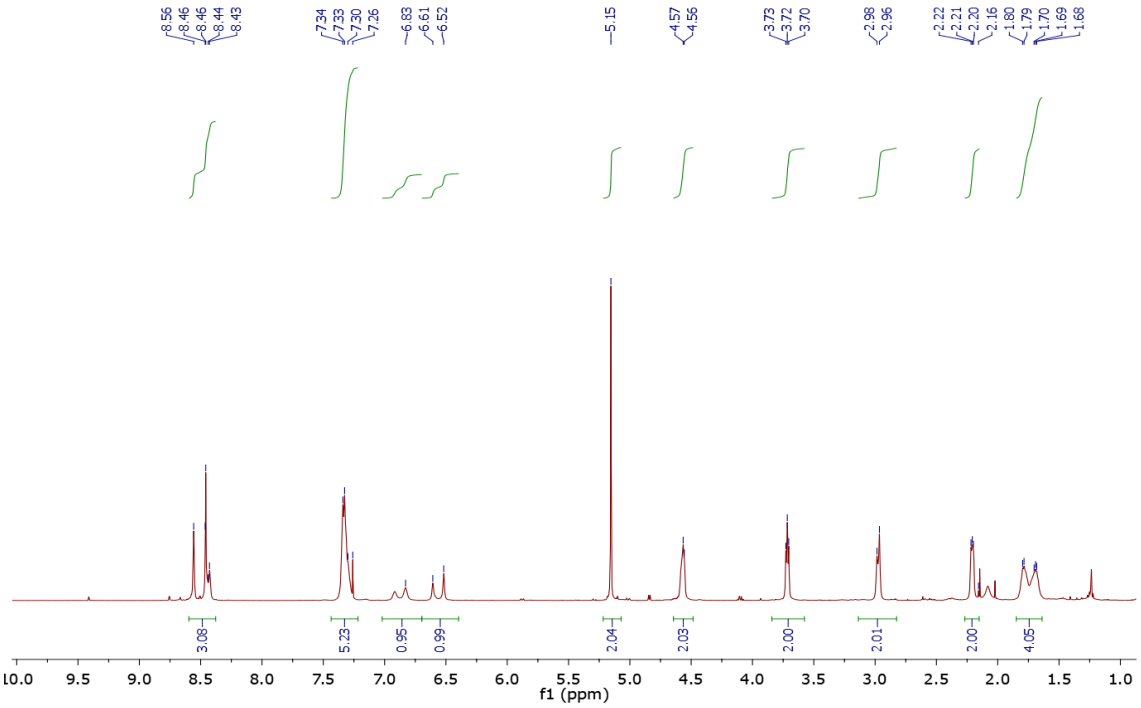


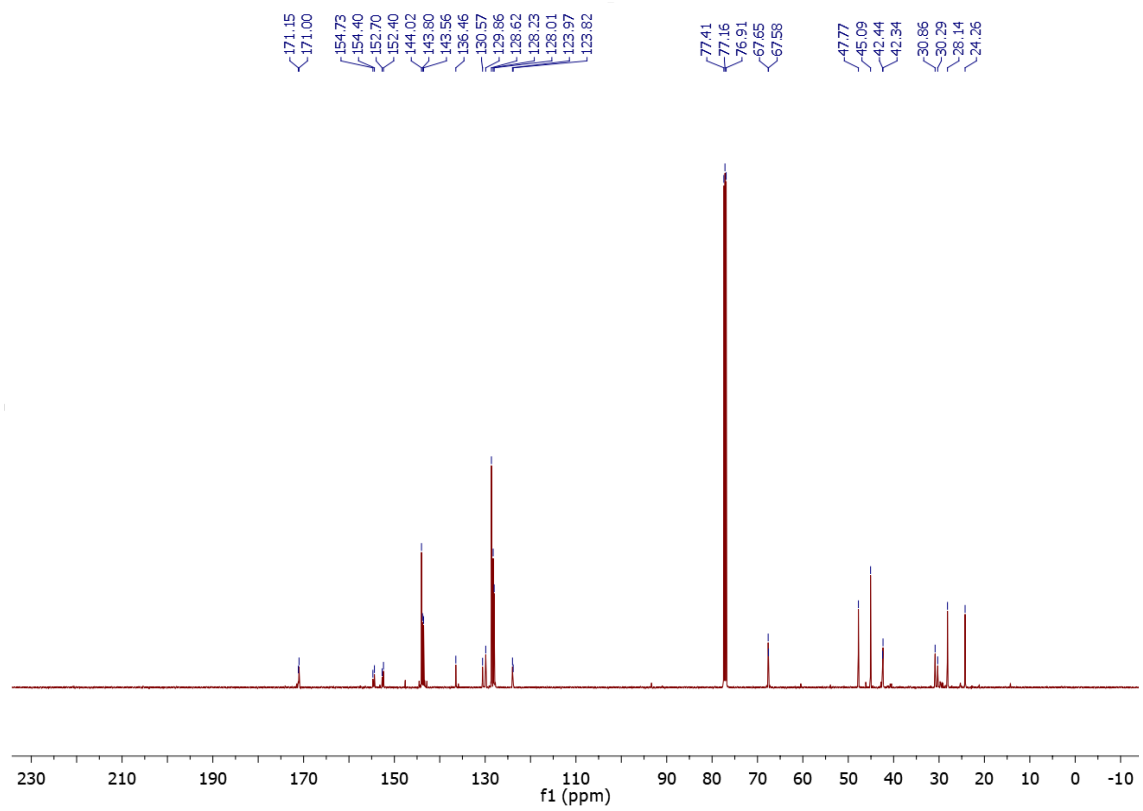




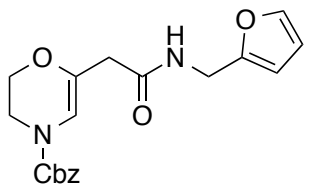
Benzyl 6-(2-oxo-2-((pyrazin-2-ylmethyl)amino)ethyl)-2,3,4,5-tetrahydro-1H-azepine-1-carboxylate (11c)

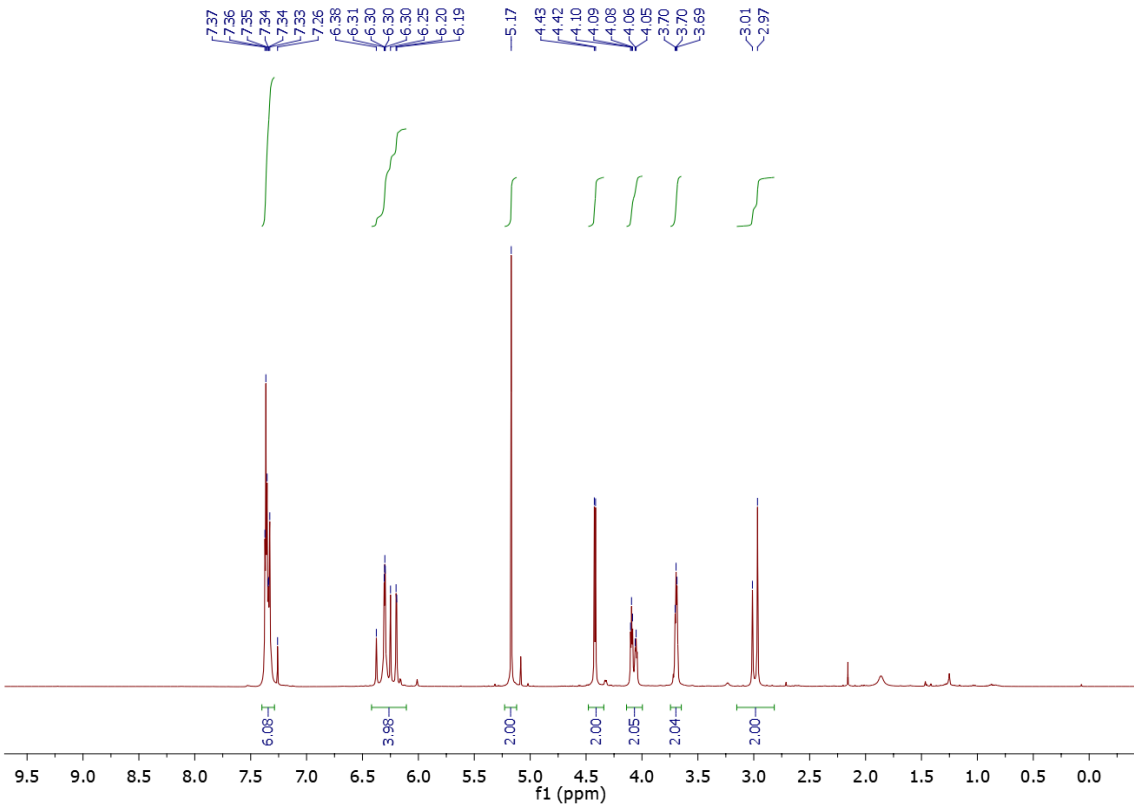


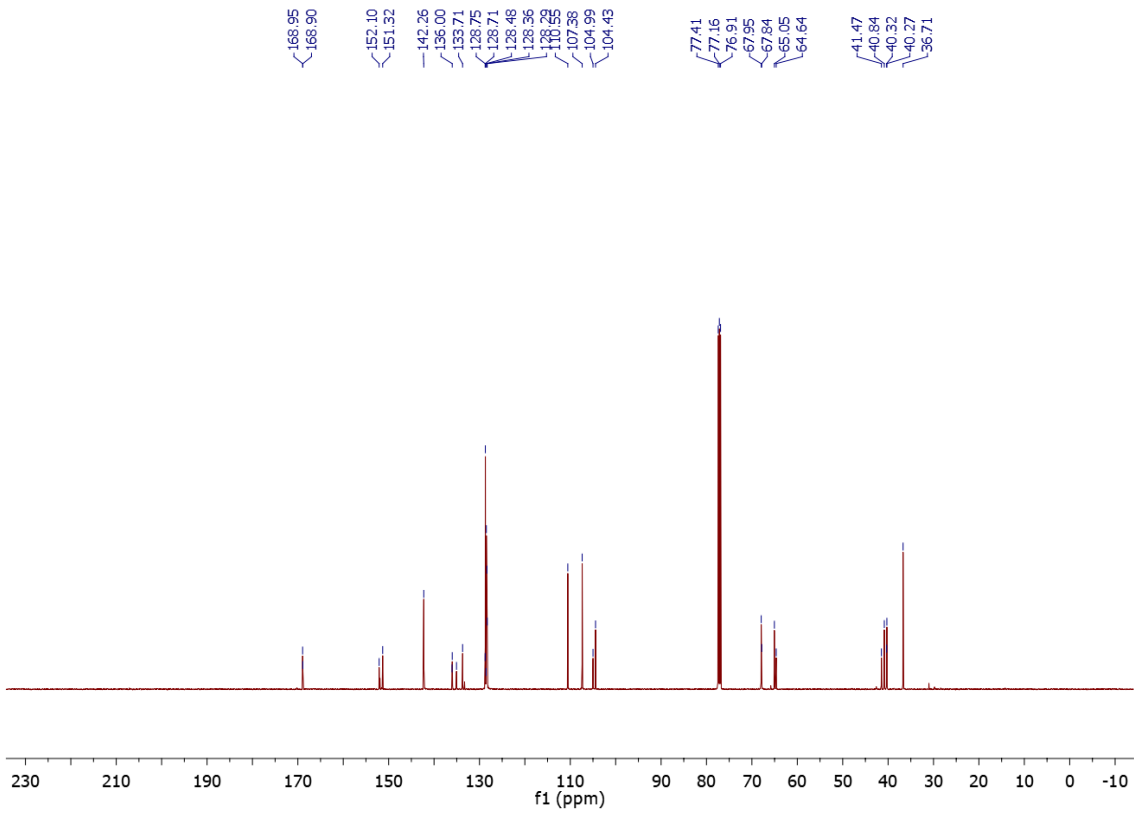




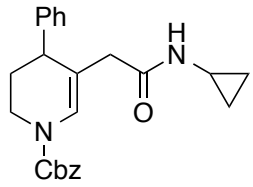
Benzyl 6-(2-((furan-2-ylmethyl)amino)-2-oxoethyl)-2H-1,4-oxazine-4(3H)-carboxylate (11d)

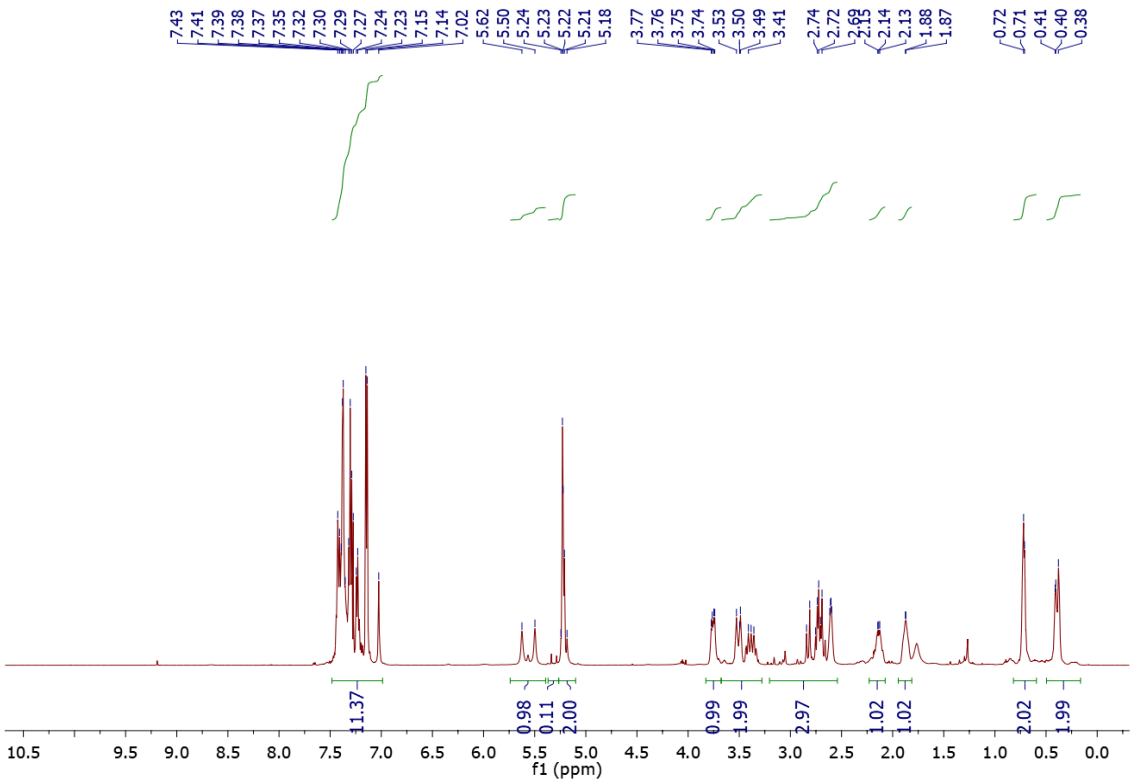


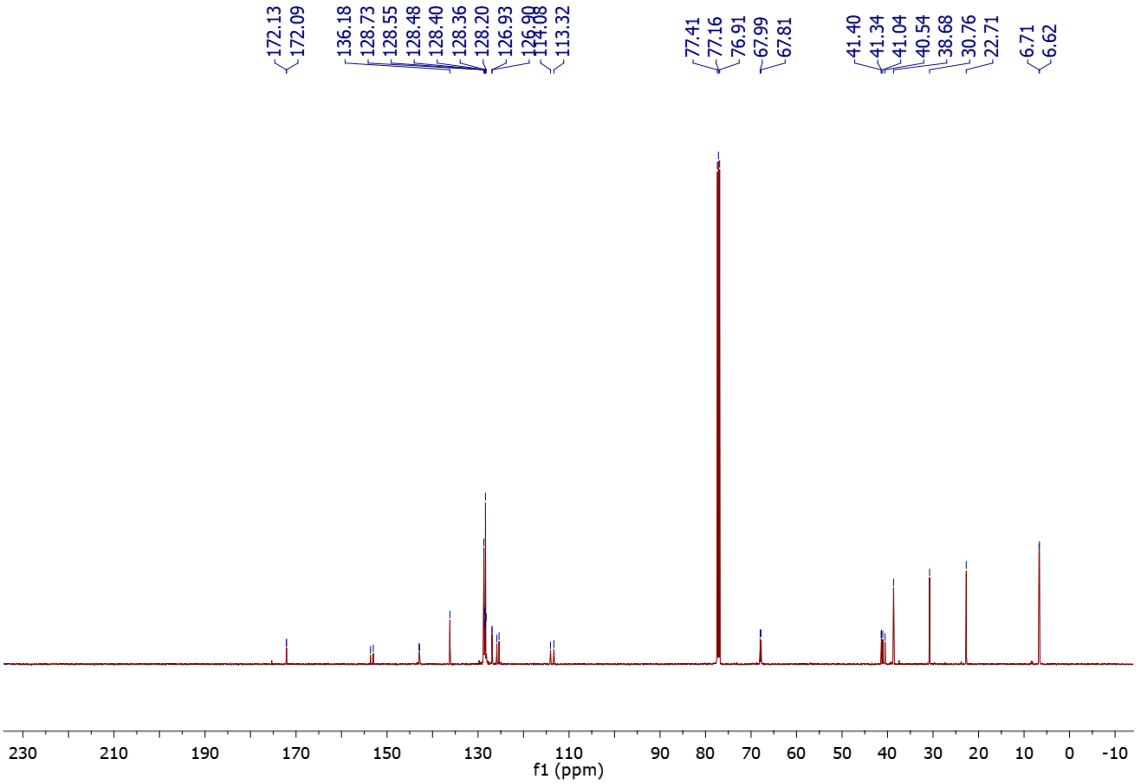




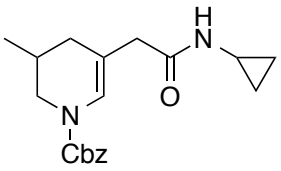
Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-4-phenyl-3,4-dihydropyridine-1(2H)-carboxylate (11e)

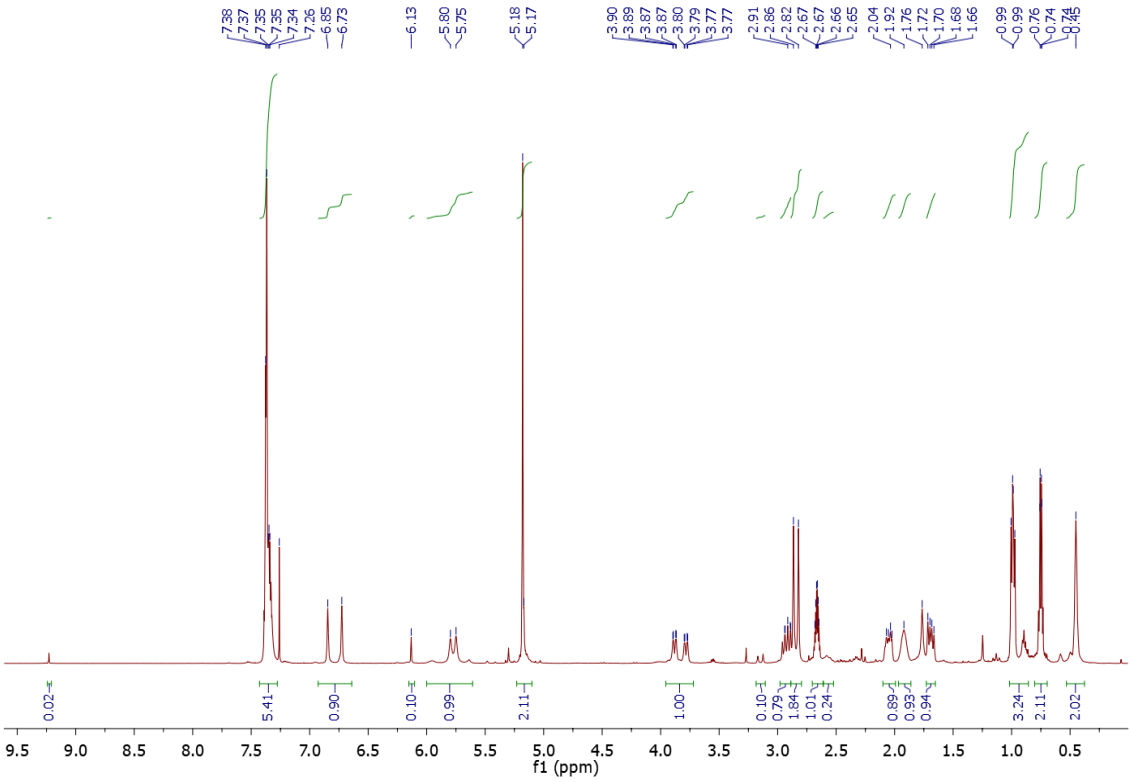


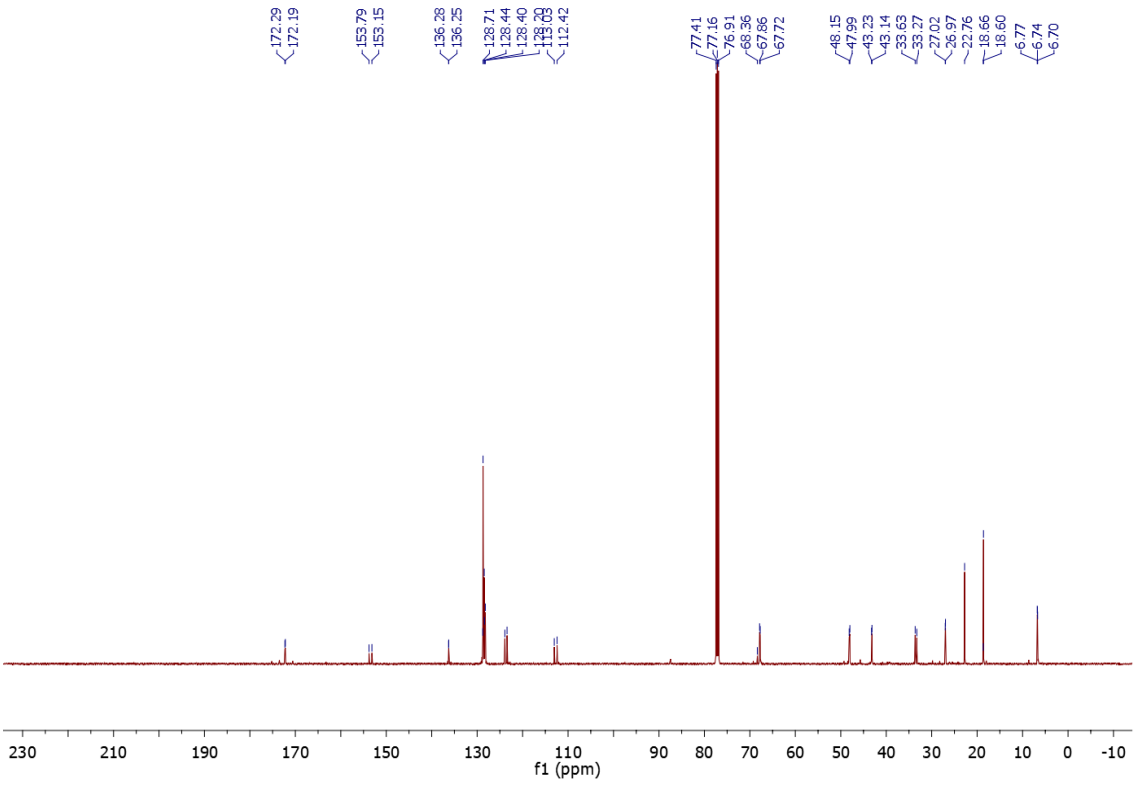




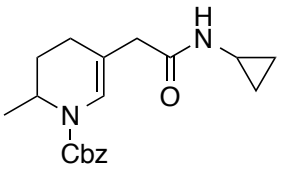
Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-3-methyl-3,4-dihydropyridine-1(2H)-carboxylate (11f)

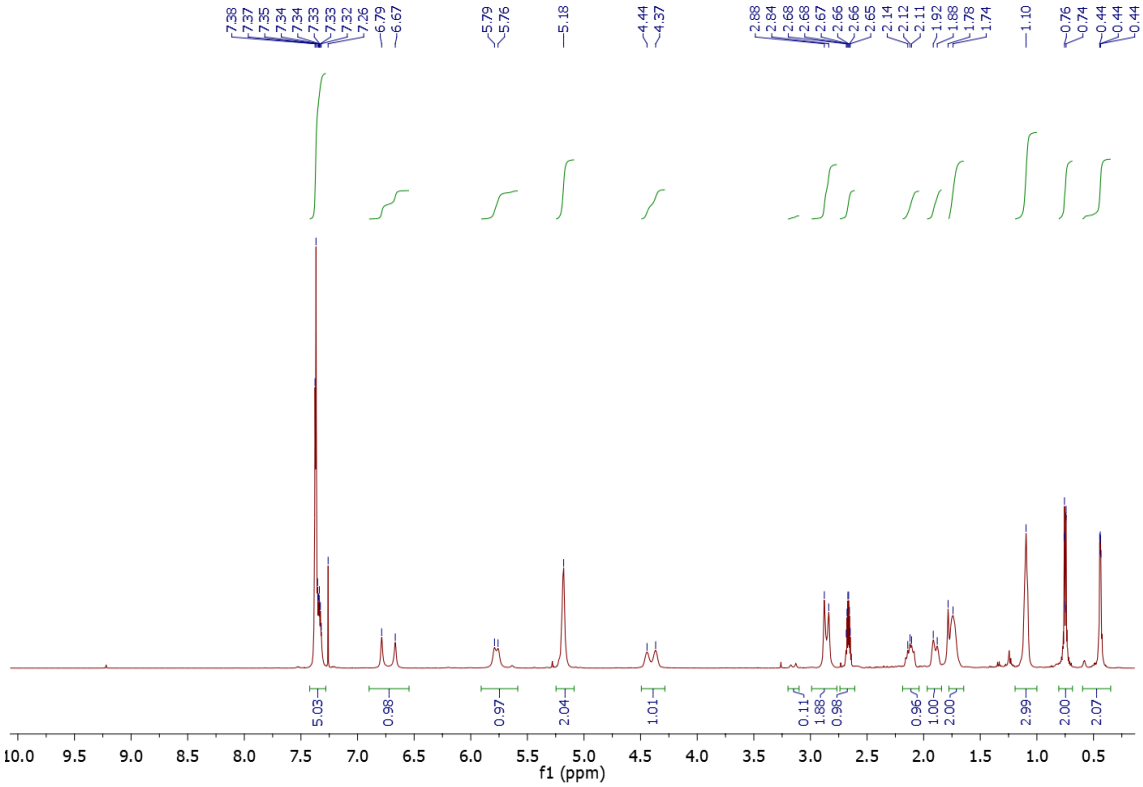


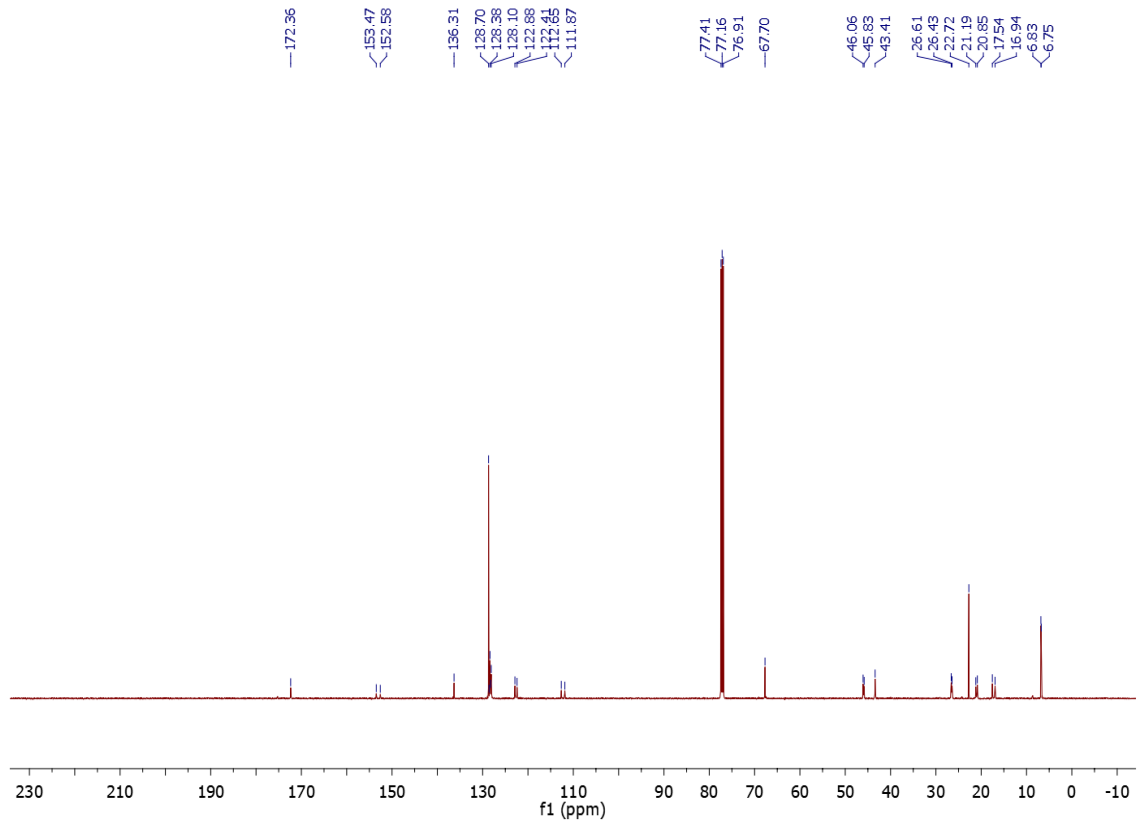




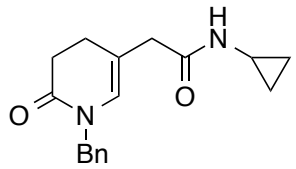
Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-2-methyl-3,4-dihydropyridine-1(2H)-carboxylate (11g)

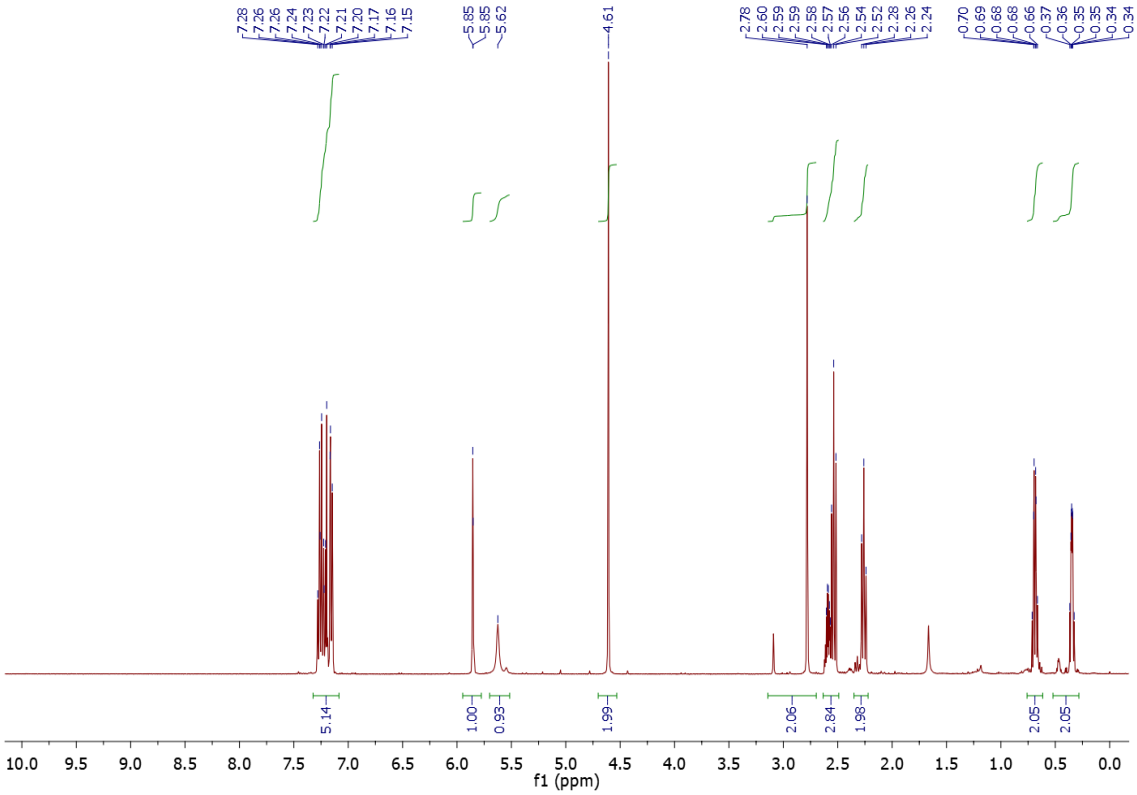


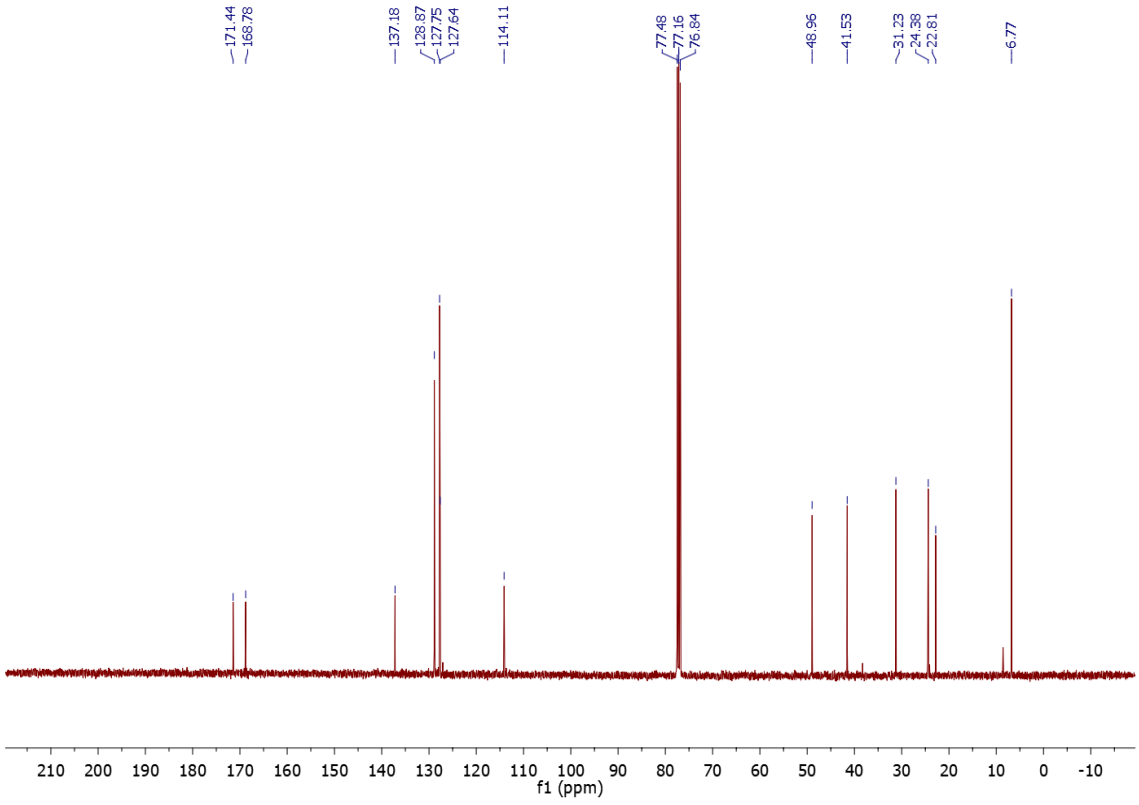




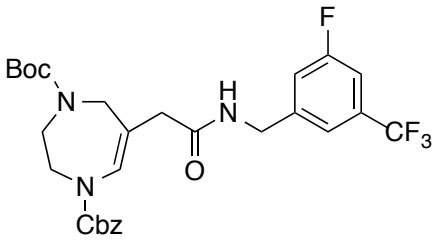
2-(1-Benzyl-6-oxo-1,4,5,6-tetrahydropyridin-3-yl)-*N*-cyclopropylacetamide (11h)

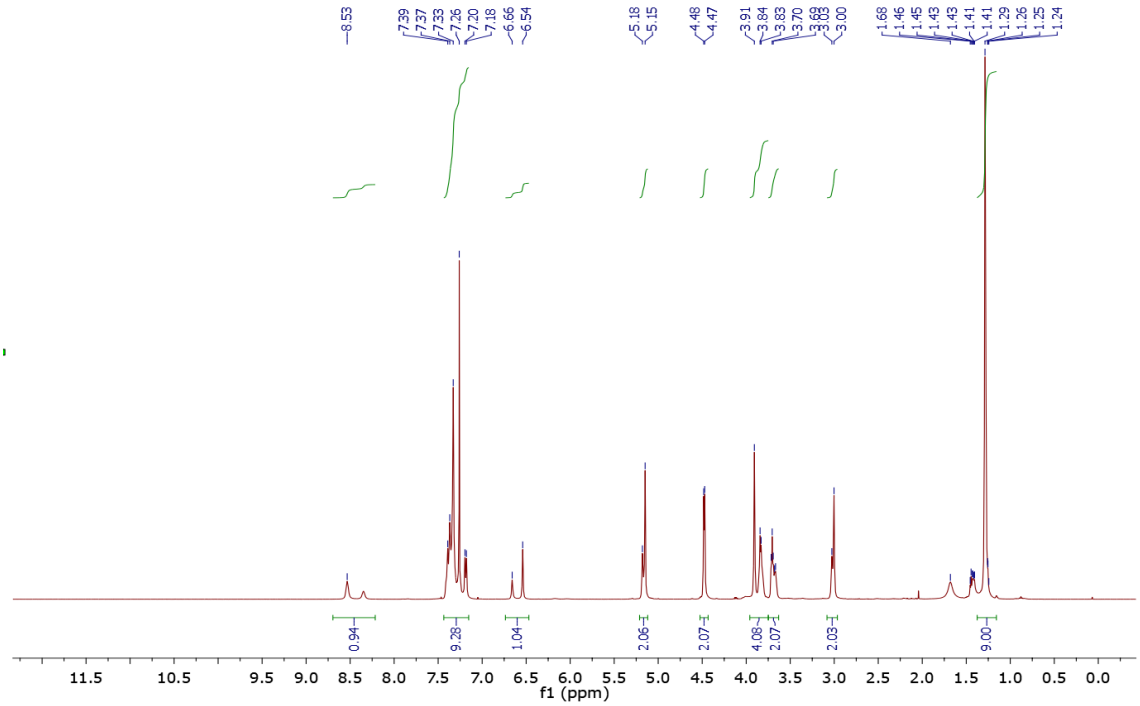


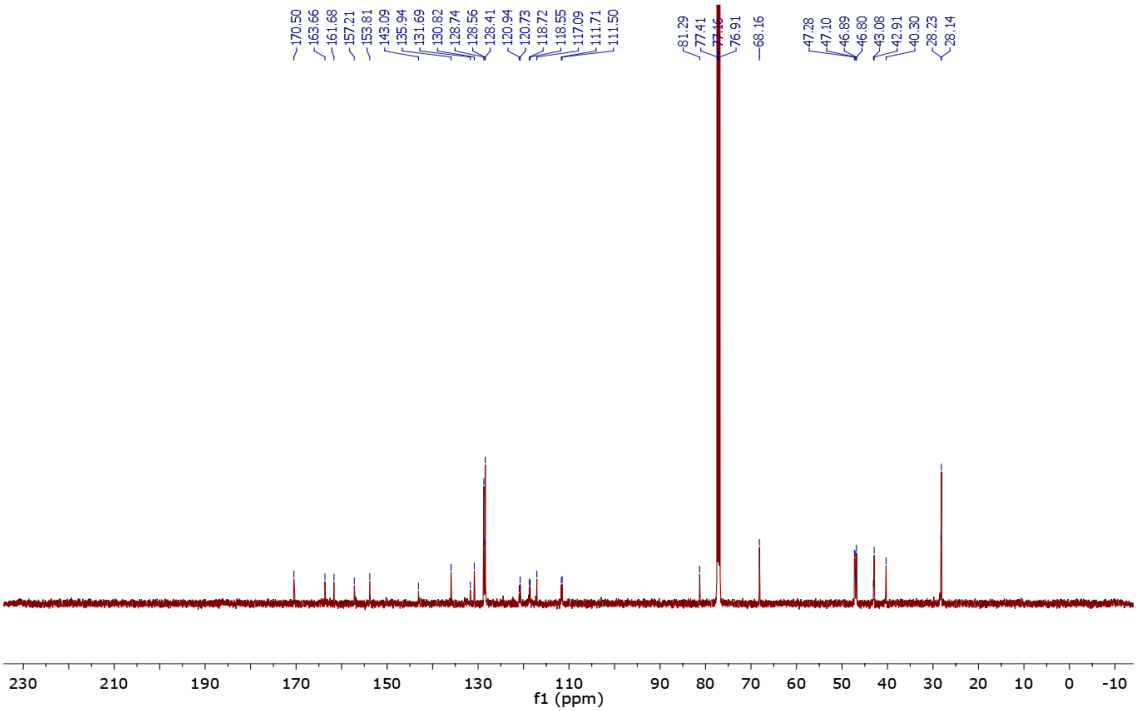




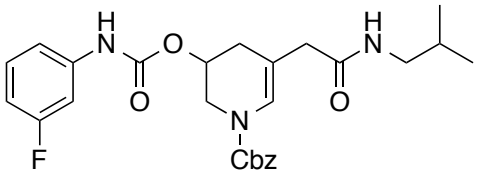
1-Benzyl 4-*tert*-butyl 6-(2-((3-fluoro-5-(trifluoromethyl)benzyl)amino)-2-oxoethyl)-2,3-dihydro-1H-1,4-diazepine-1,4(5H)-dicarboxylate (11i)

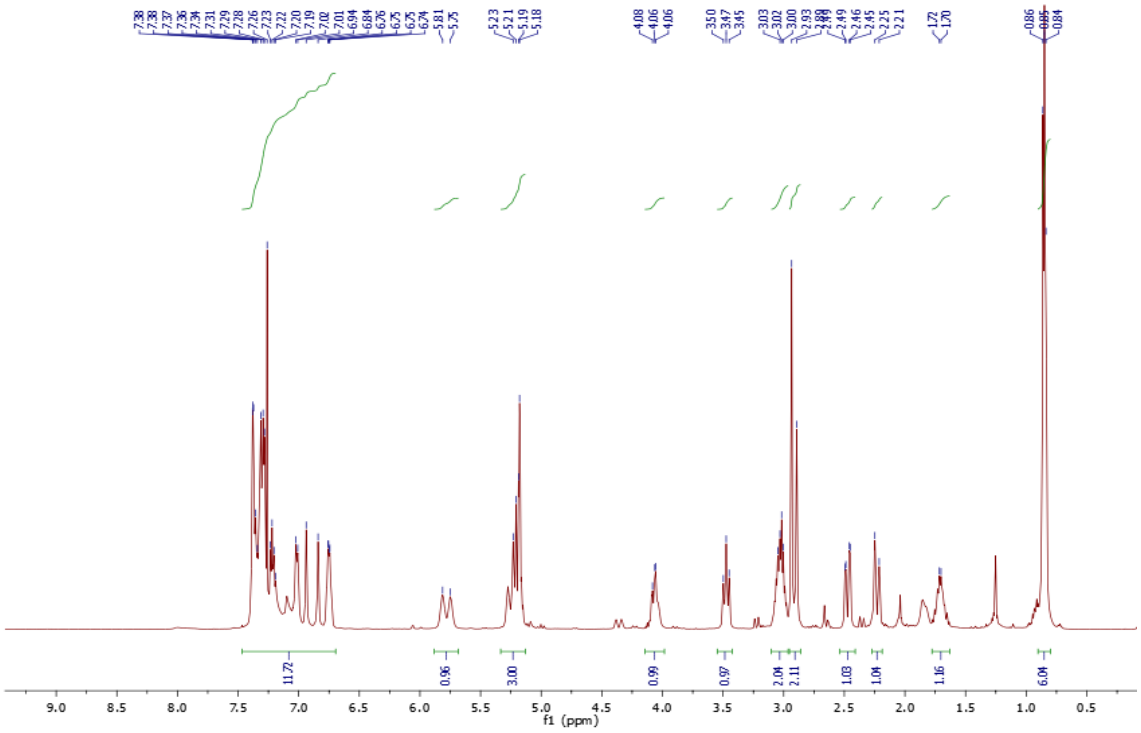


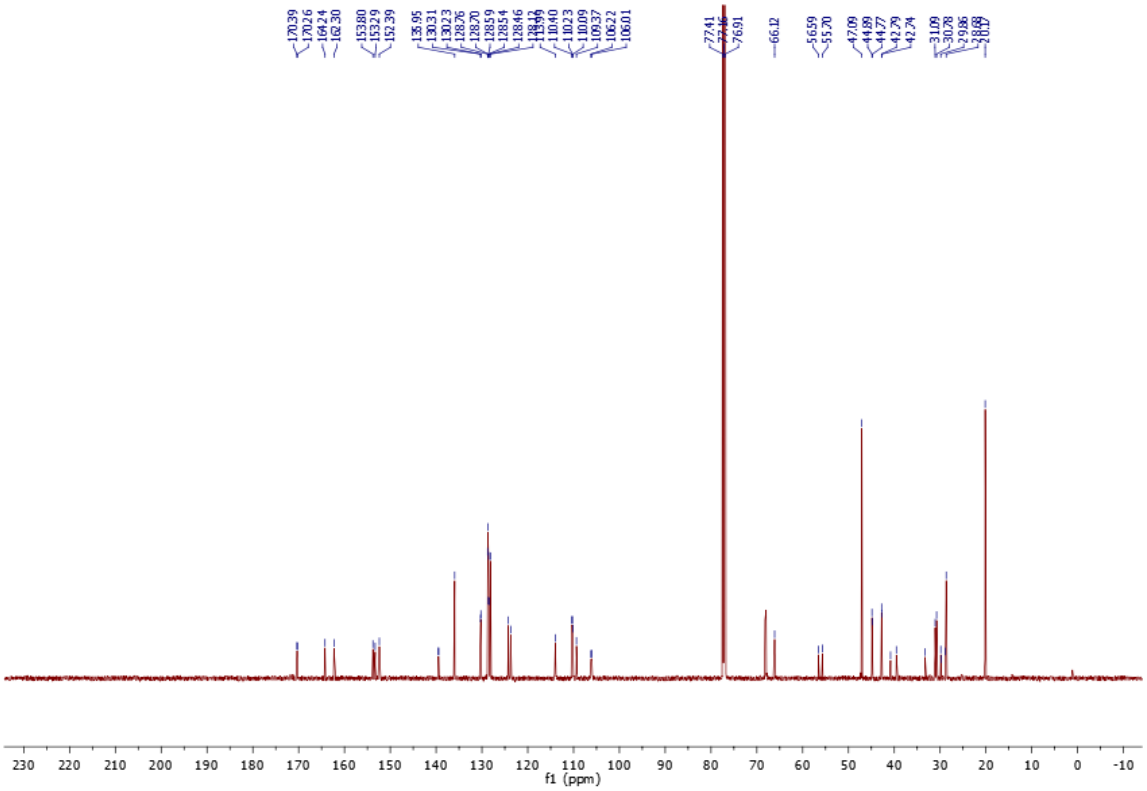




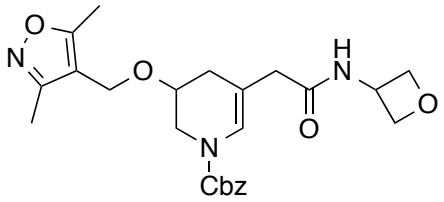
Benzyl 3-(((3-fluorophenyl)carbamoyl)oxy)-5-(2-(isobutylamino)-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11j)

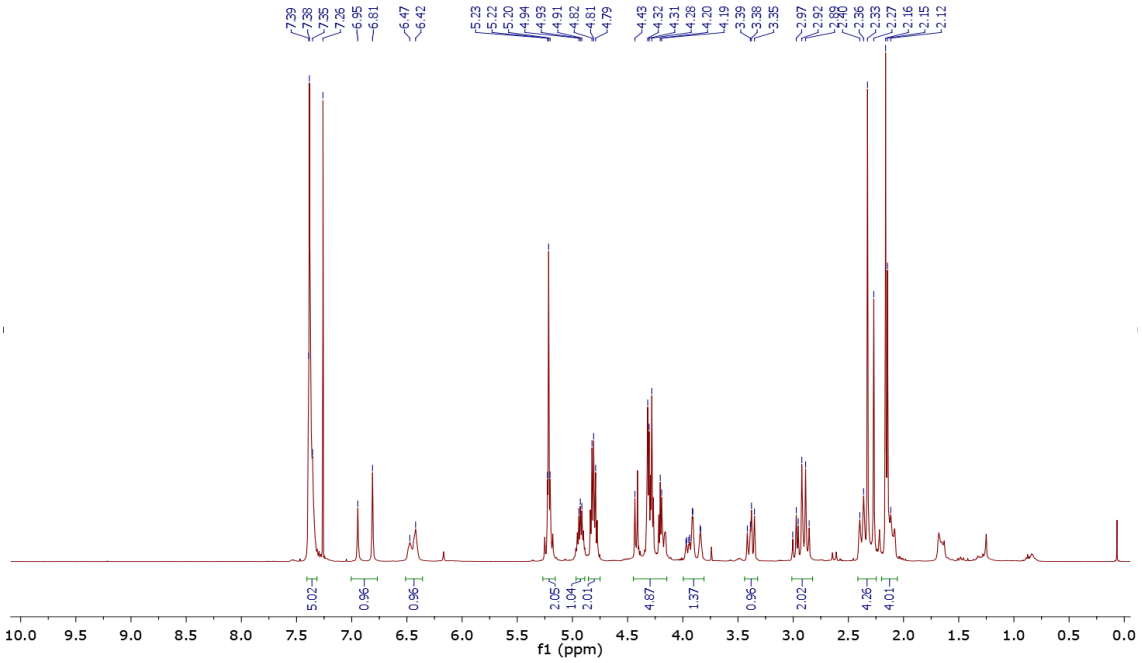


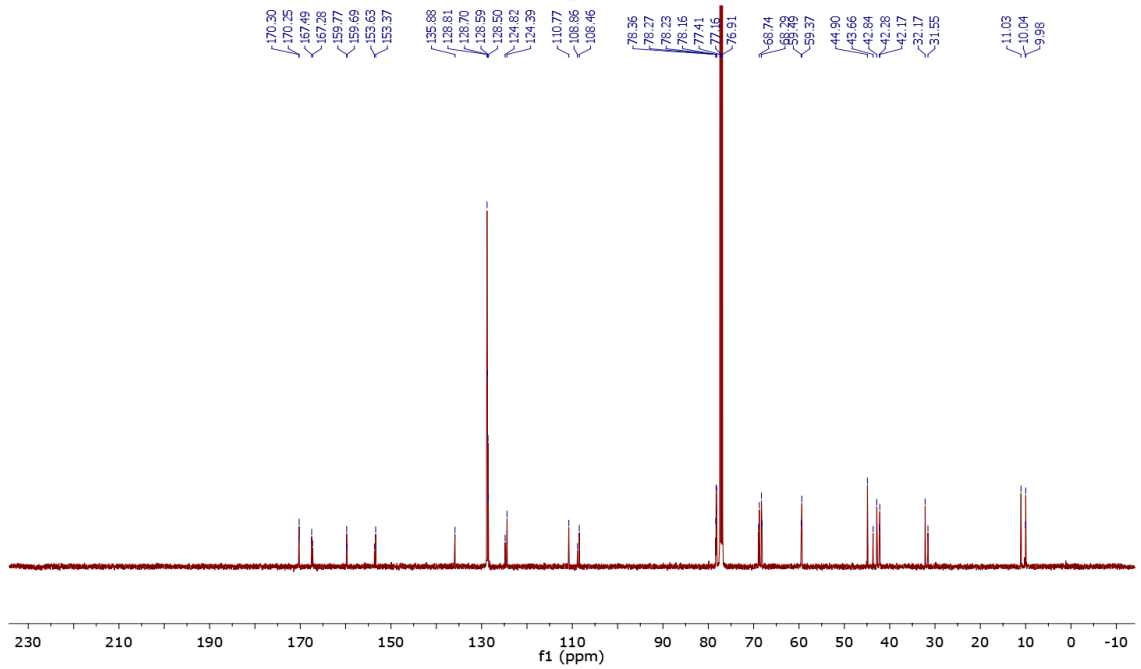




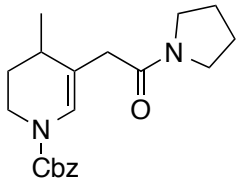
Benzyl 3-((3,5-dimethylisoxazol-4-yl)methoxy)-5-(2-(3-oxetanyl)amino-2-oxoethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11k)

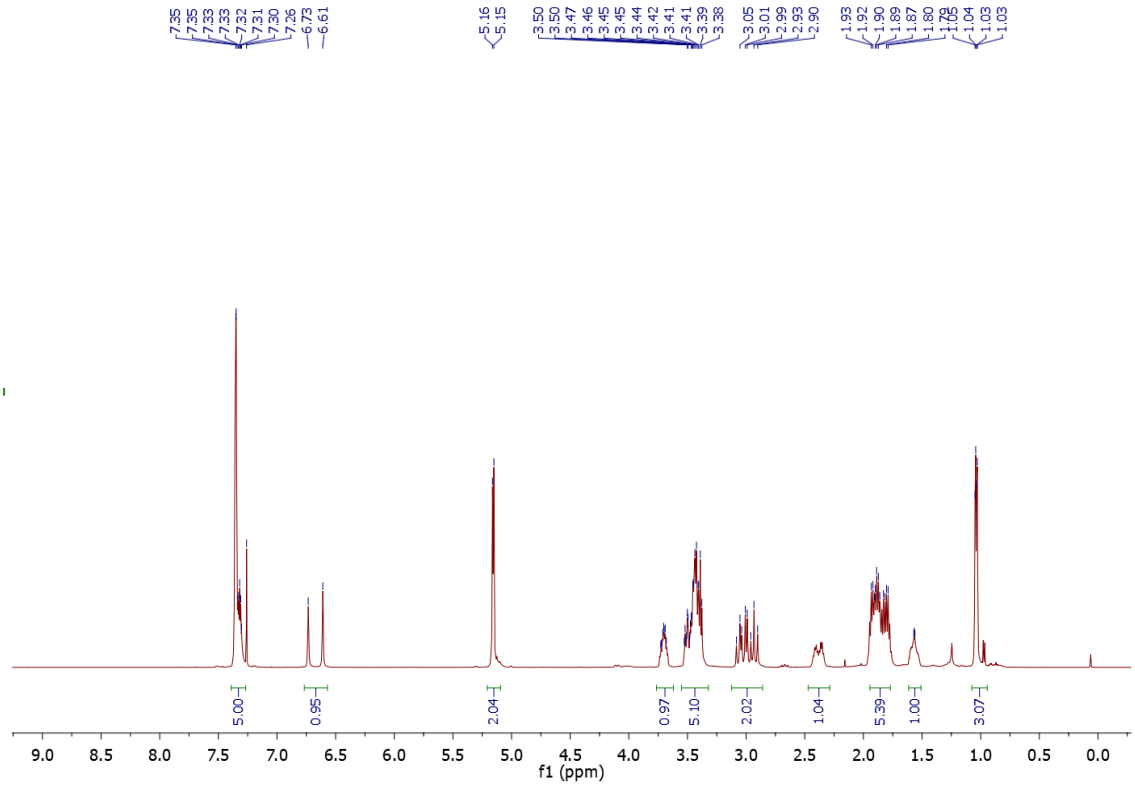


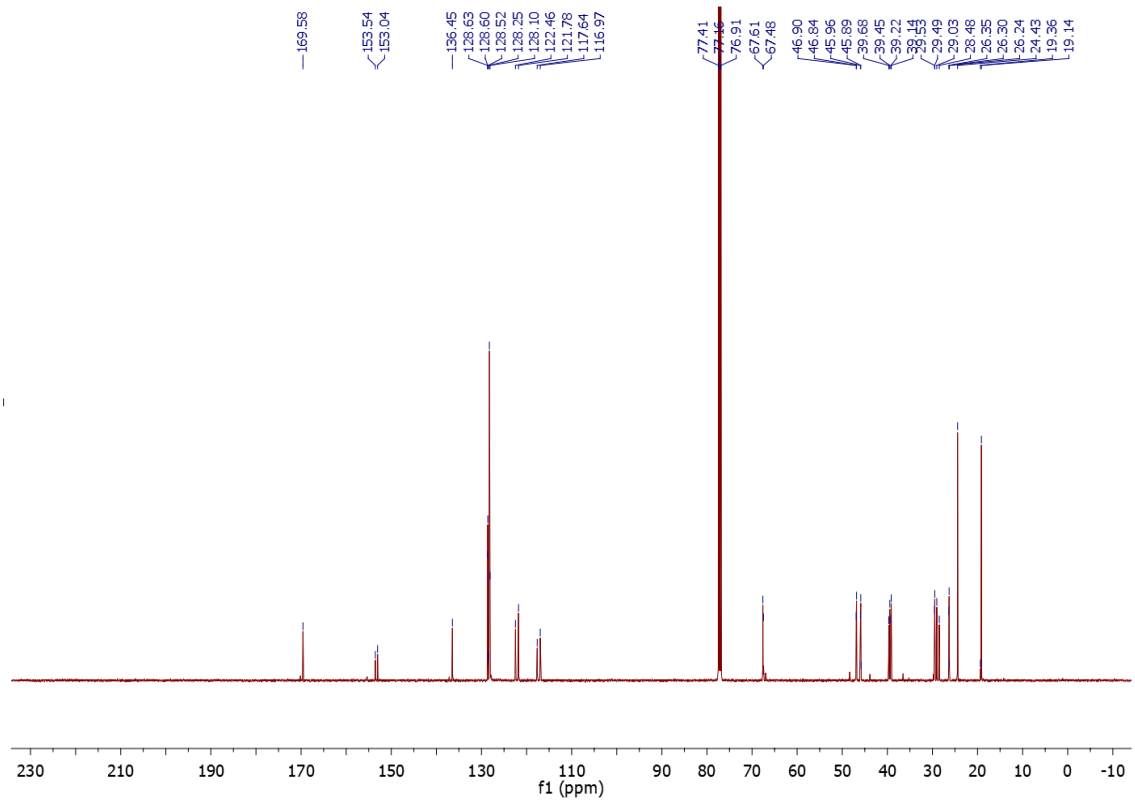




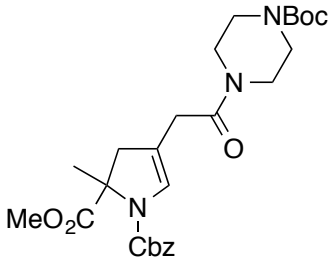
Benzyl 4-methyl-5-(2-oxo-2-(pyrrolidin-1-yl)ethyl)-3,4-dihydropyridine-1(2H)-carboxylate (11l)

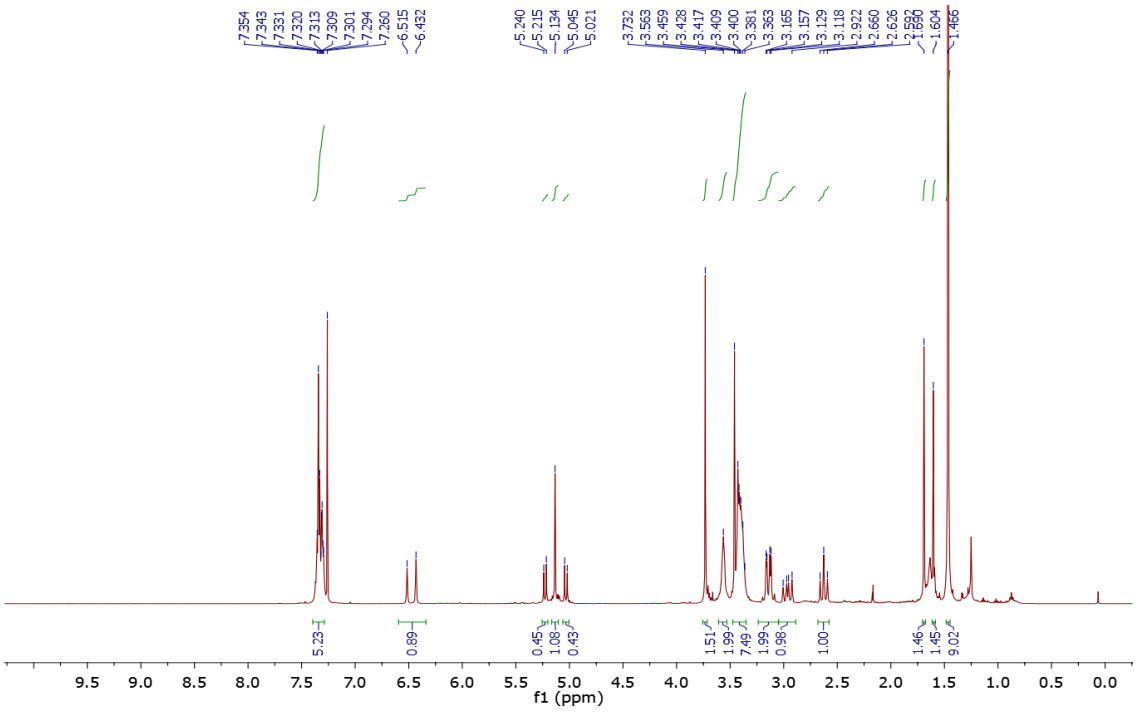


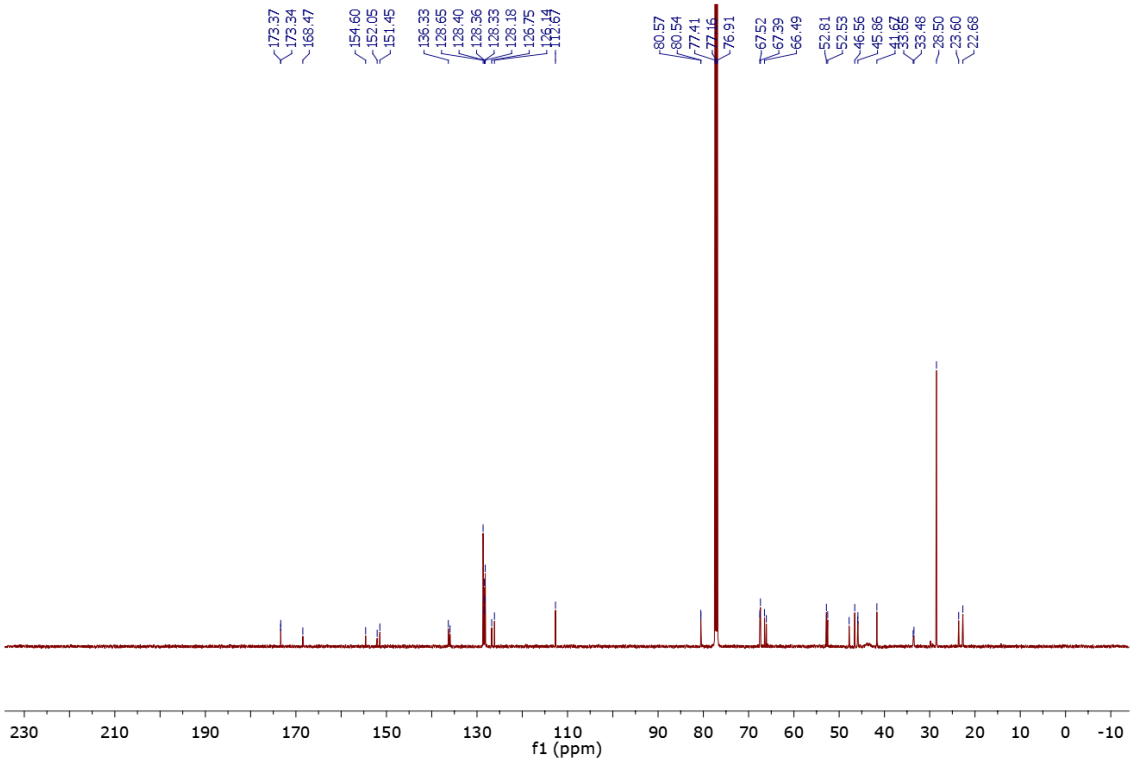




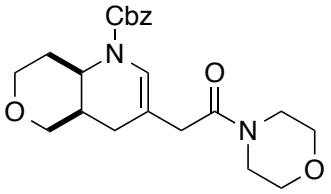
1-Benzyl 2-methyl 4-(2-(4-(*tert*-butoxycarbonyl)piperazin-1-yl)-2-oxoethyl)-2-methyl-2,3-dihydro-1H-pyrrole-1,2-dicarboxylate (11m)

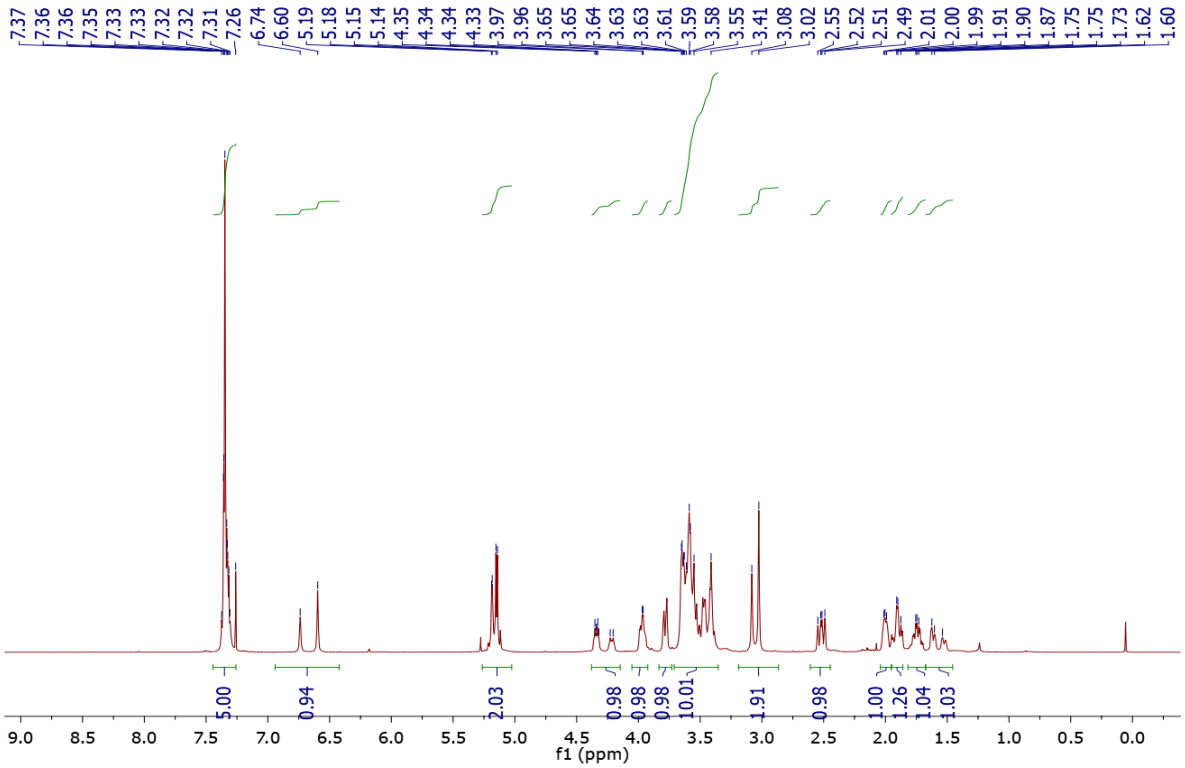


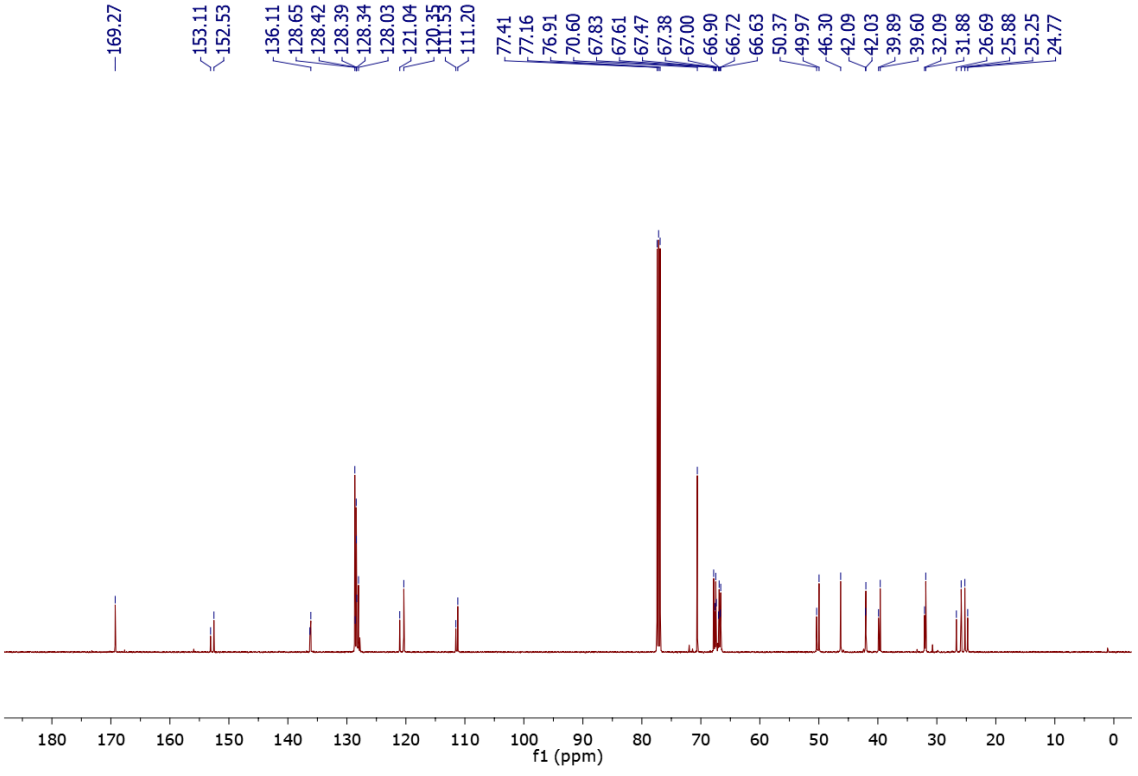




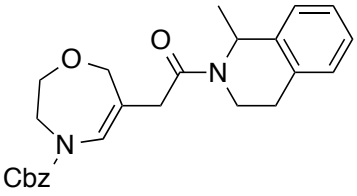
Benzyl 3-(2-morpholino-2-oxoethyl)-4,4a,5,7,8,8a-hexahydro-1H-pyrano[4,3-b]pyridine-1-carboxylate (11n)

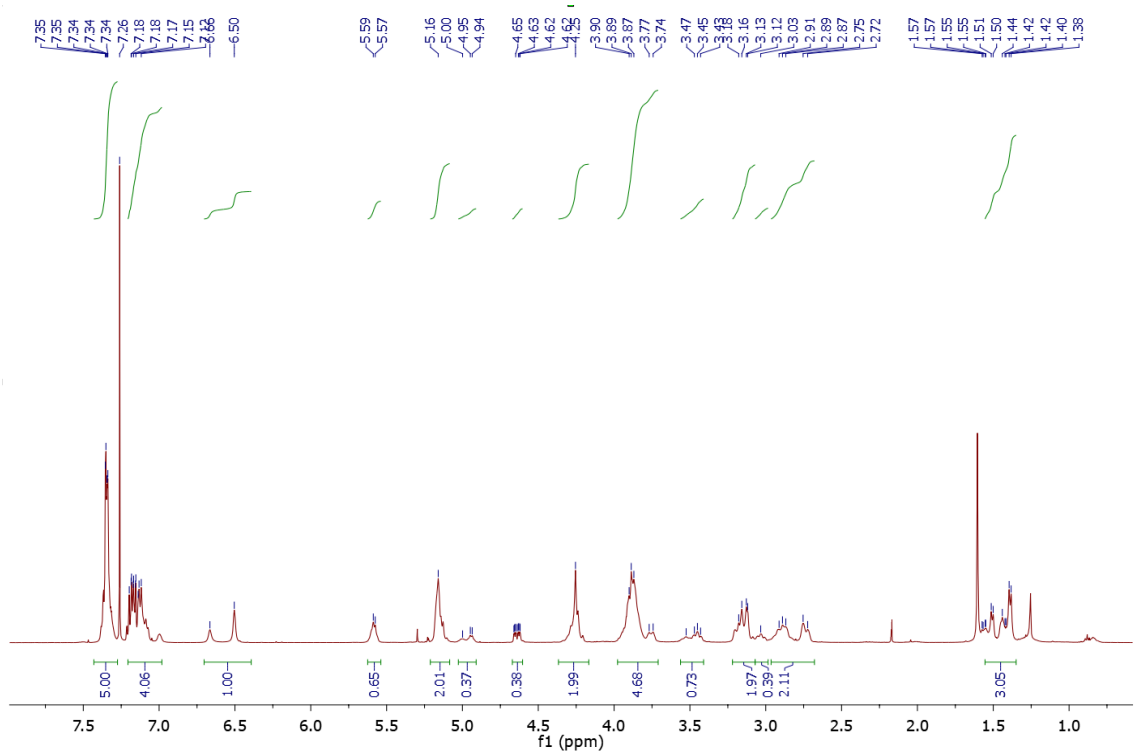


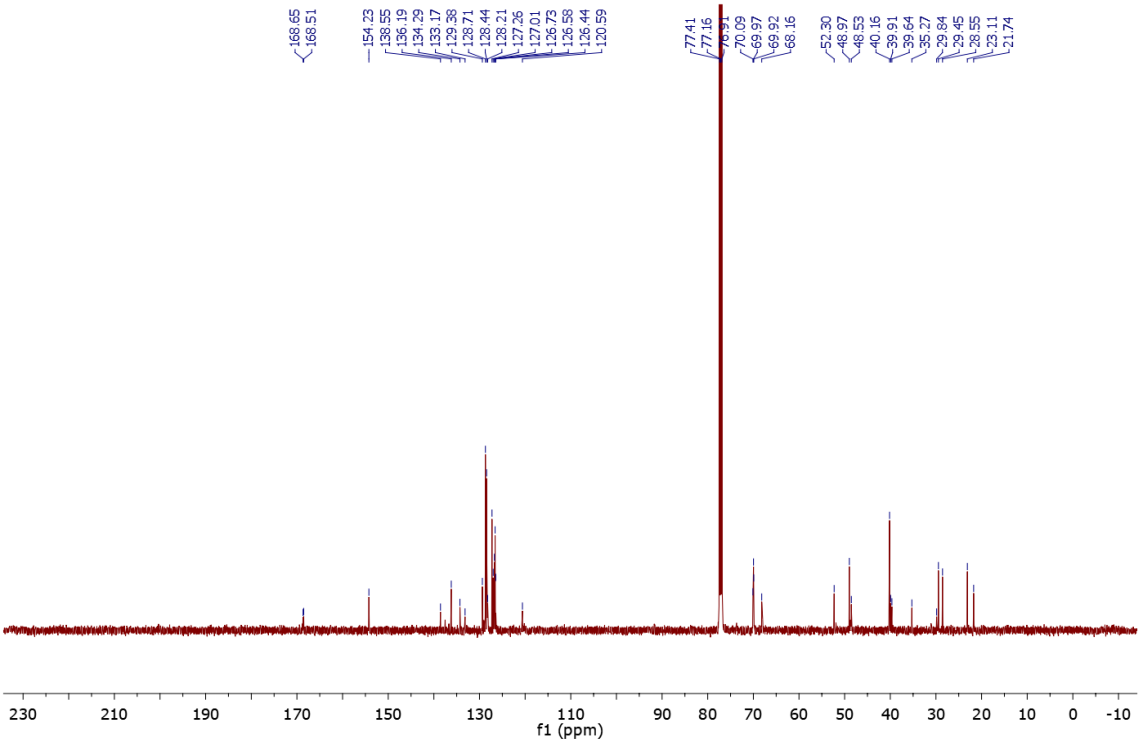




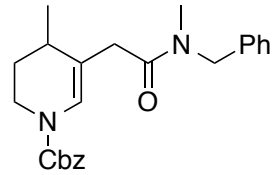
Benzyl 6-(2-(1-methyl-3,4-dihydroisoquinolin-2(1H)-yl)-2-oxoethyl)-2,3-dihydro-1,4-oxazepine-4(7H)-carboxylate (11o)

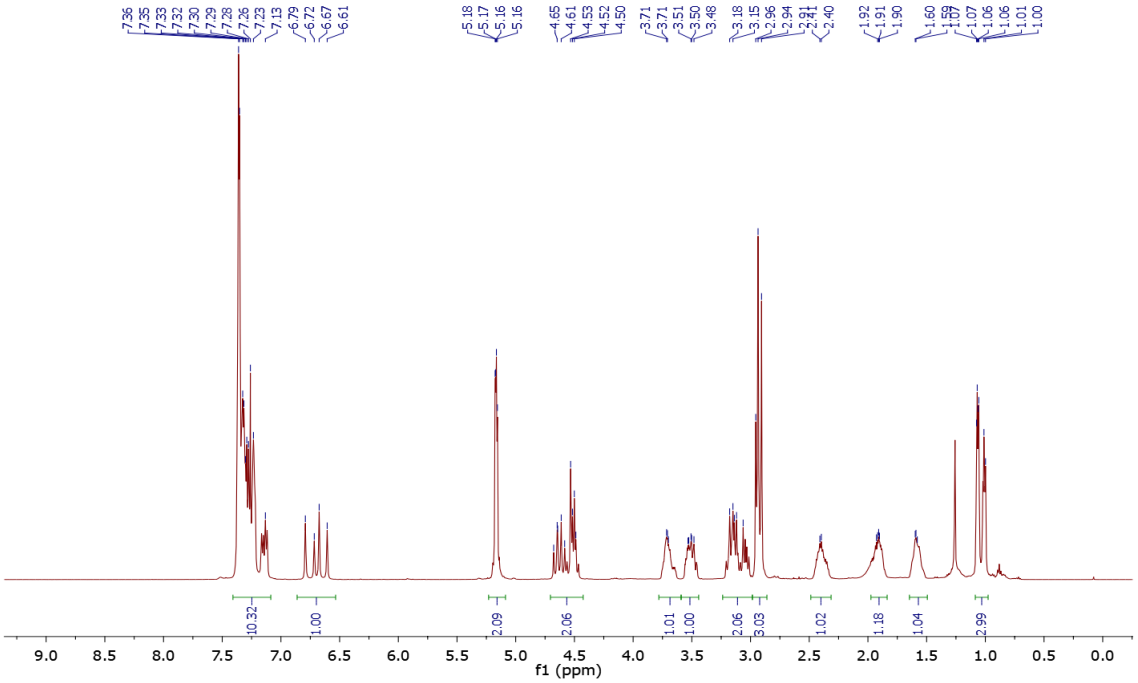


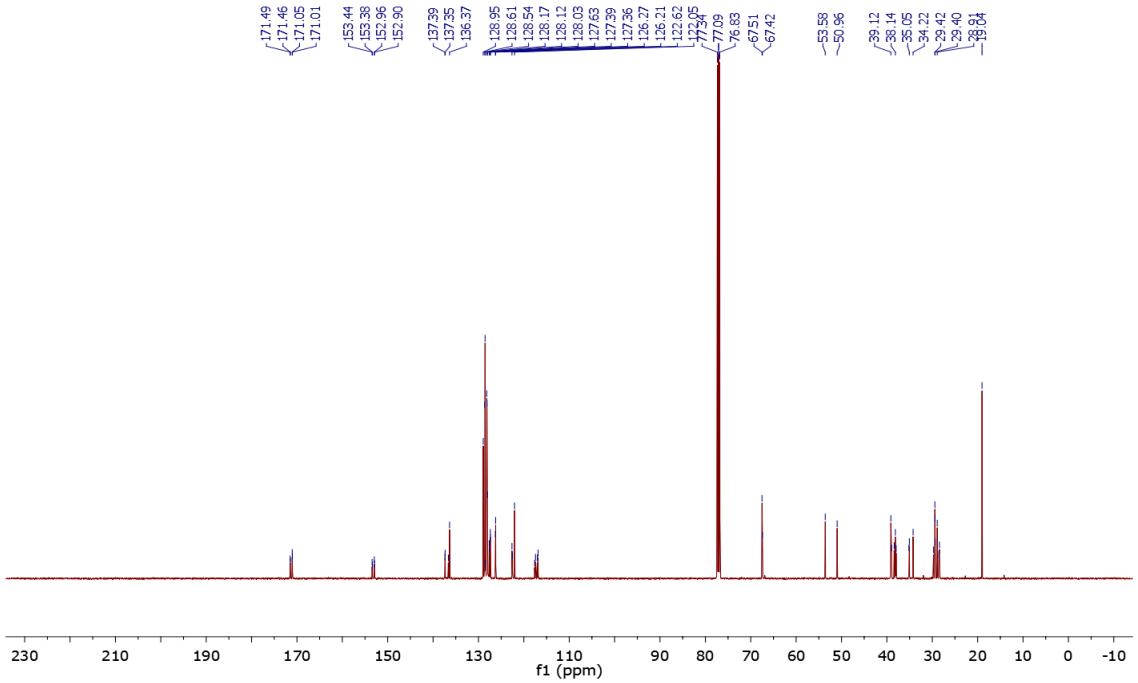




Benzyl 5-(2-(benzyl(methyl)amino)-2-oxoethyl)-4-methyl-3,4-dihydropyridine-1(2H)-carboxylate (11p)

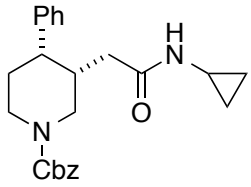


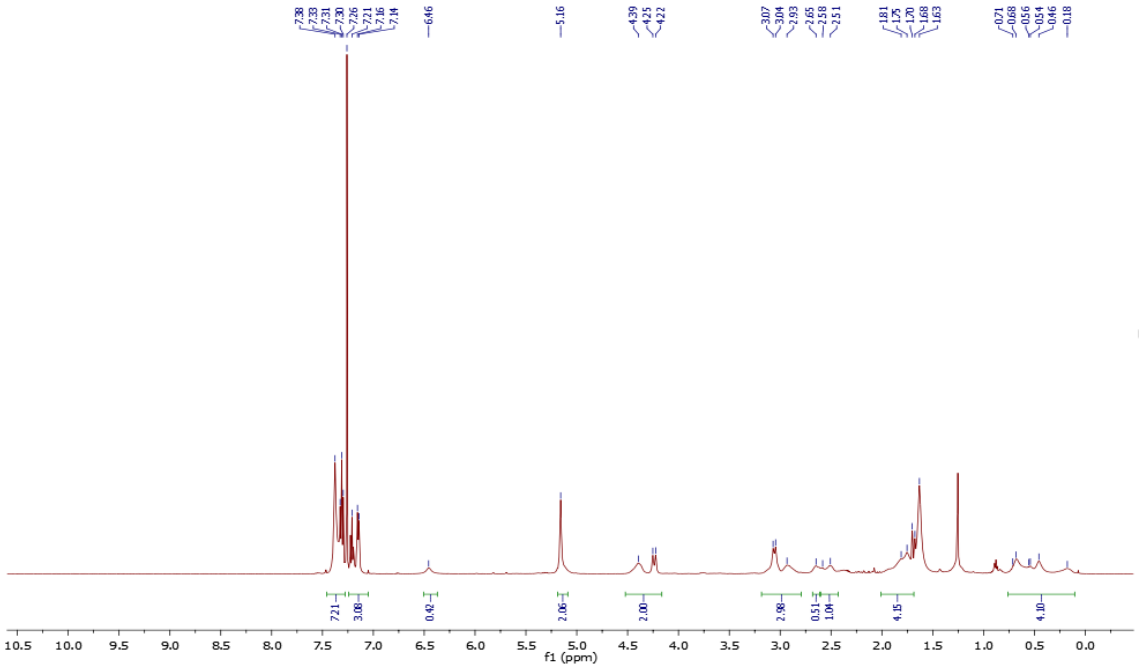


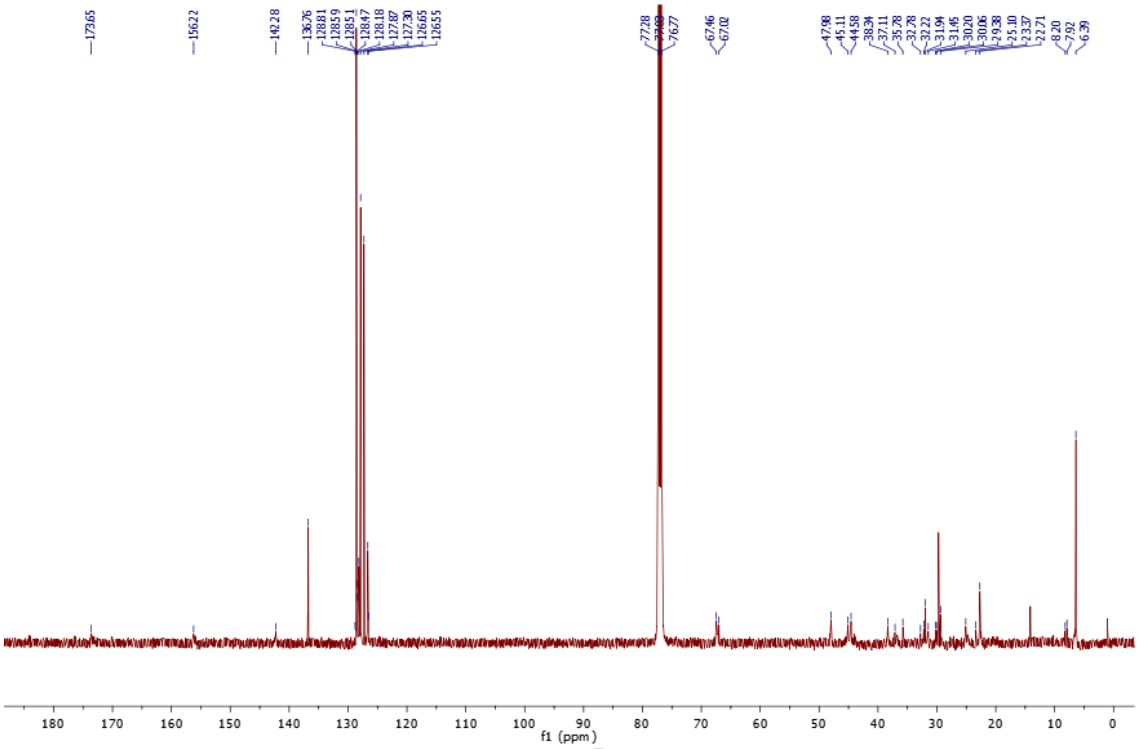


Benzyl 3-(2-(cyclopropylamino)-2-oxoethyl)-4-phenylpiperidine-1-carboxylate (12a)

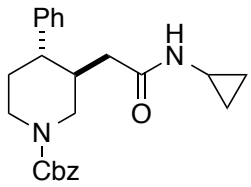
Major diastereomer

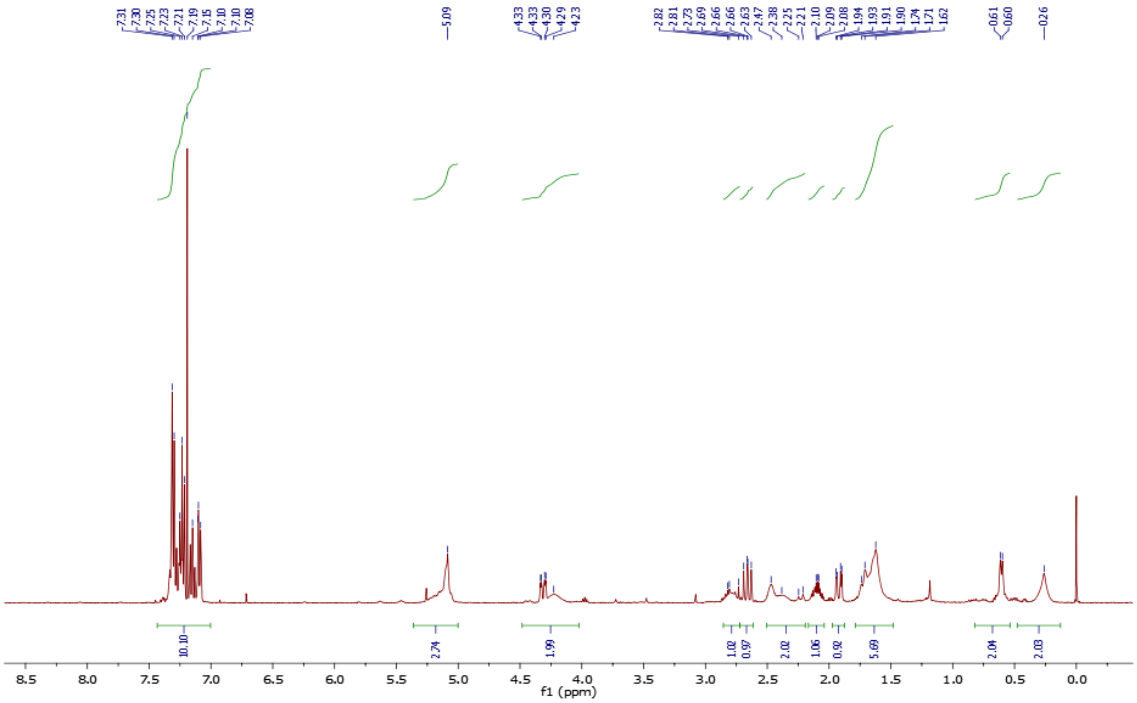


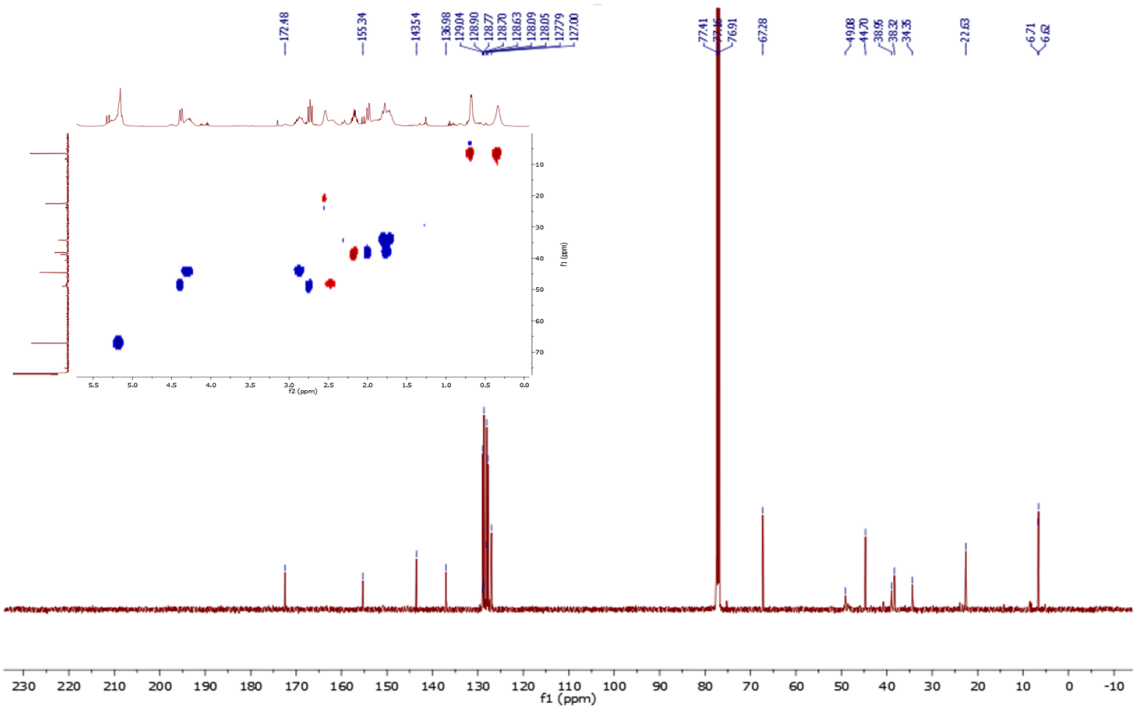


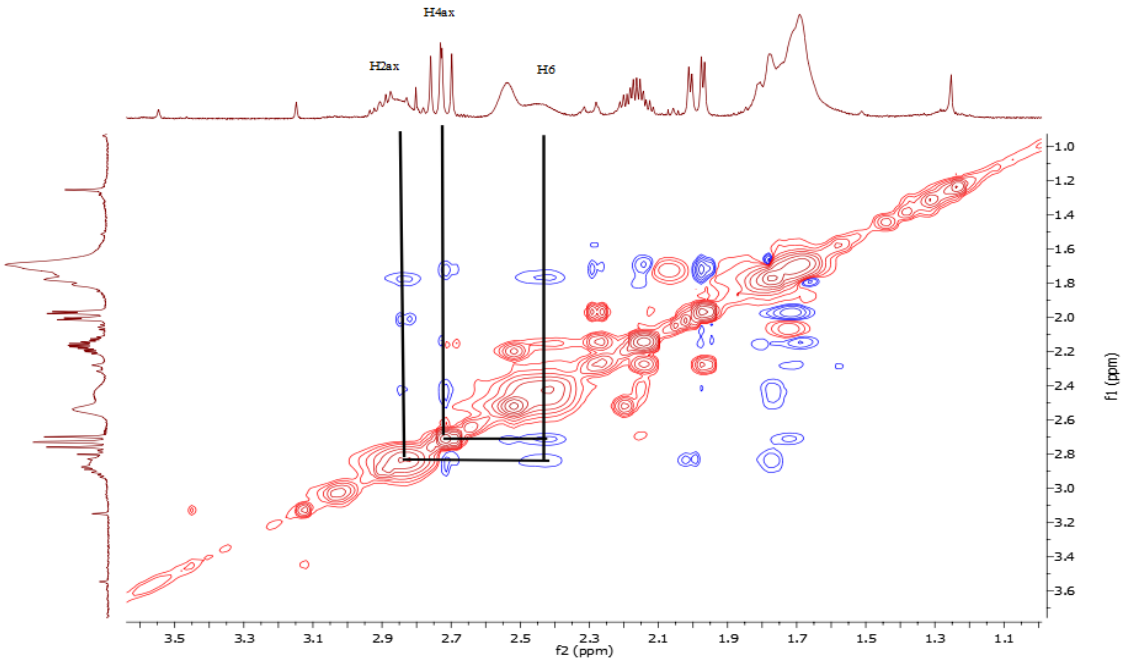


Minor diastereomer

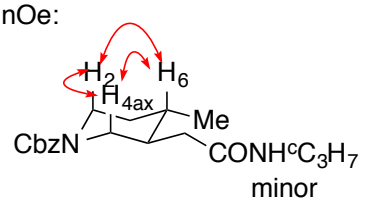






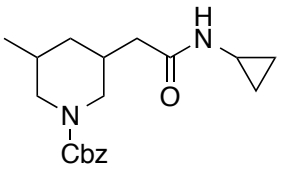


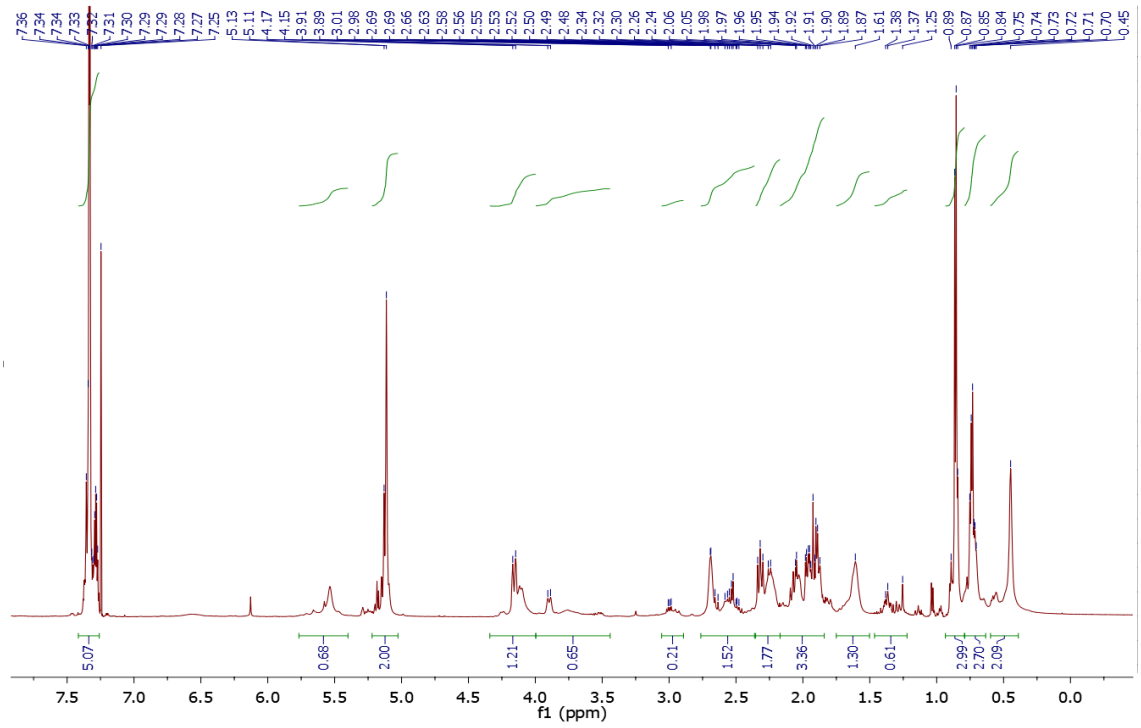
Diagnostic nOe:

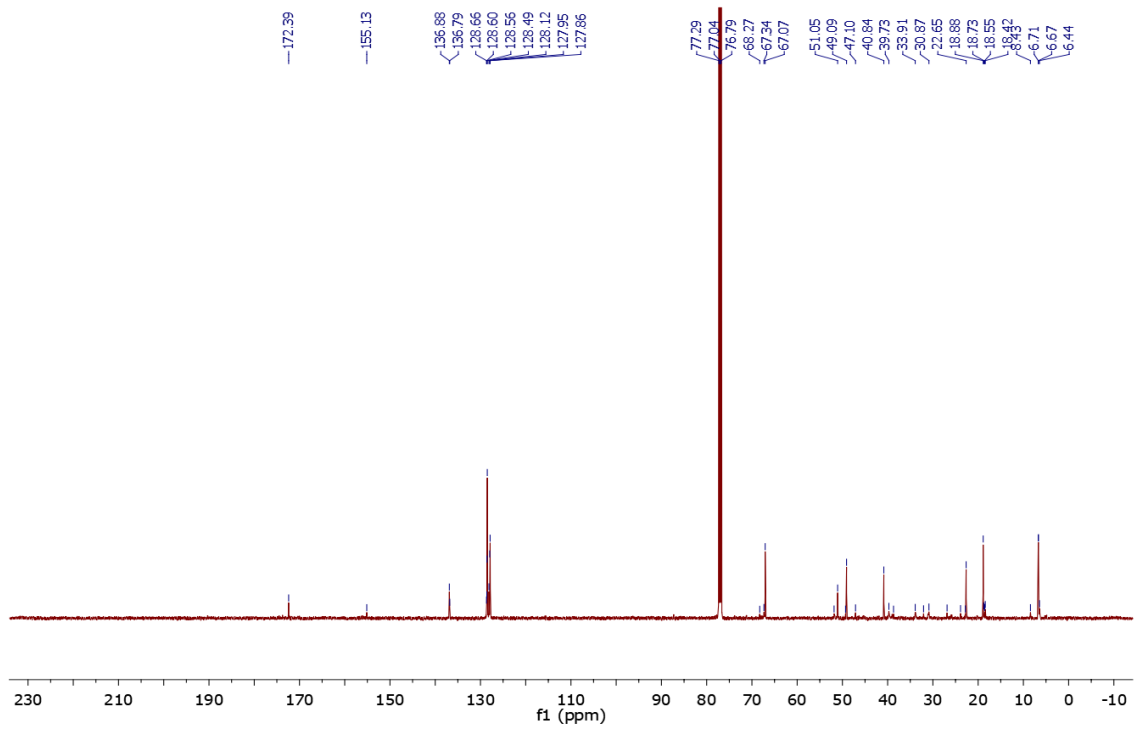


$H4_{ax}$ presents with two large *J* values (one geminal, one vicinal diaxial) which fixes the carboxymethyl group as equatorial.

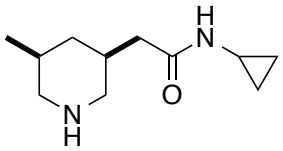
Benzyl 3-(2-(cyclopropylamino)-2-oxoethyl)-5-methylpiperidine-1-carboxylate (12b)



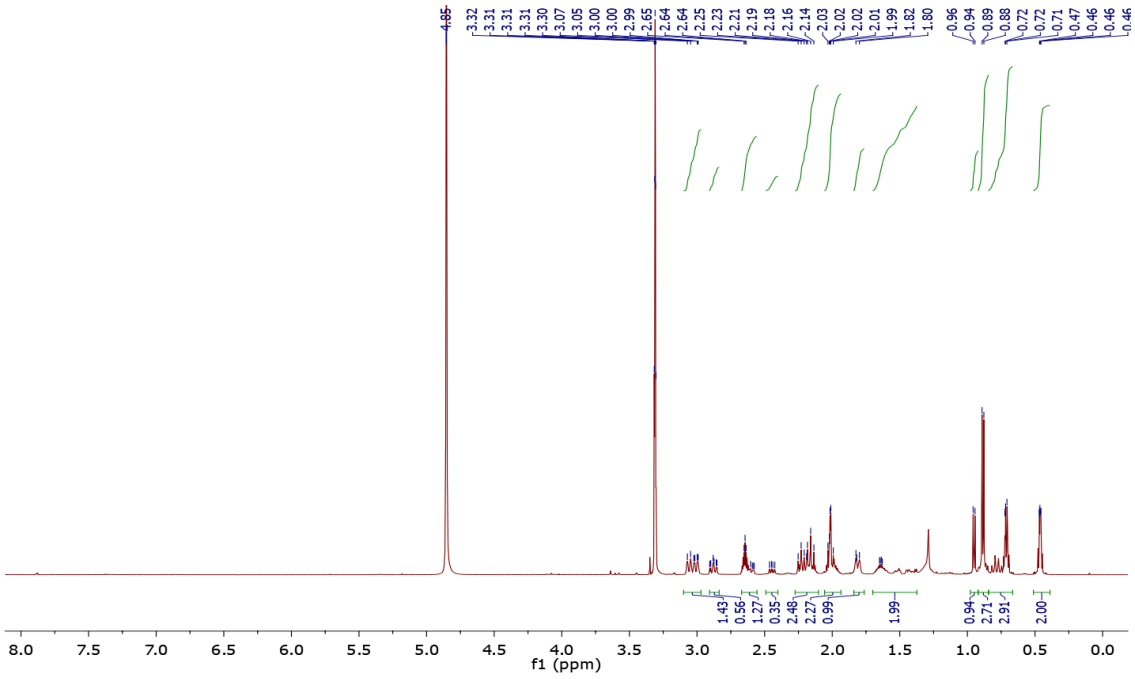


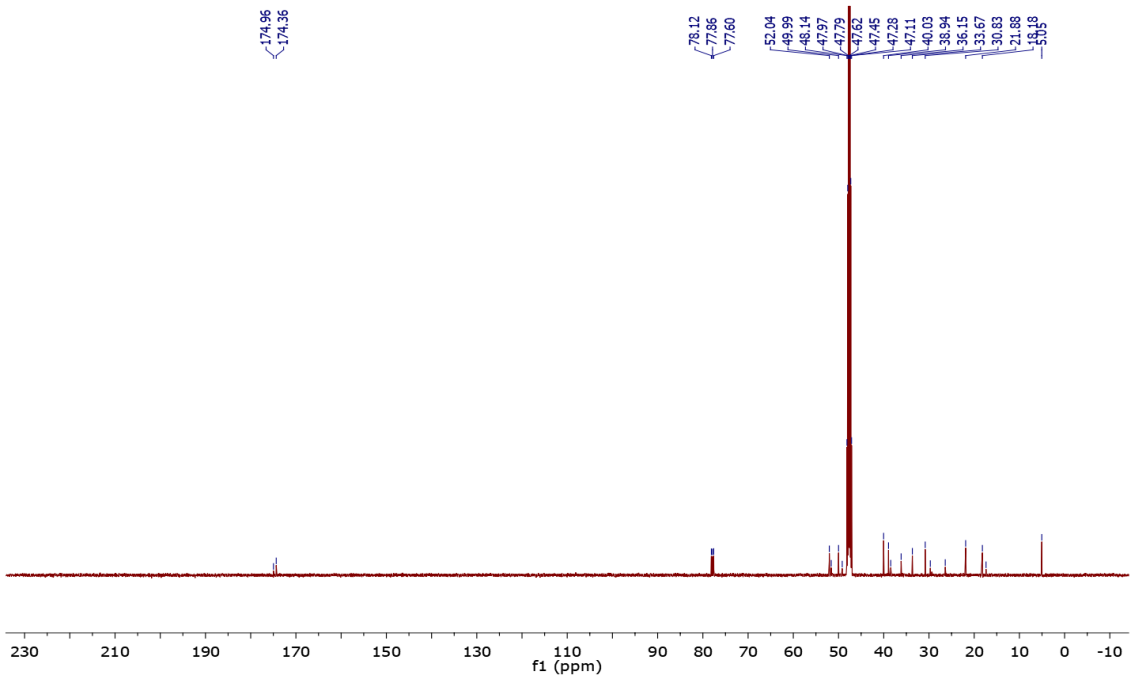


***N*-cyclopropyl-2-(5-methylpiperidin-3-yl)acetamide**

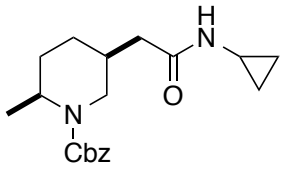


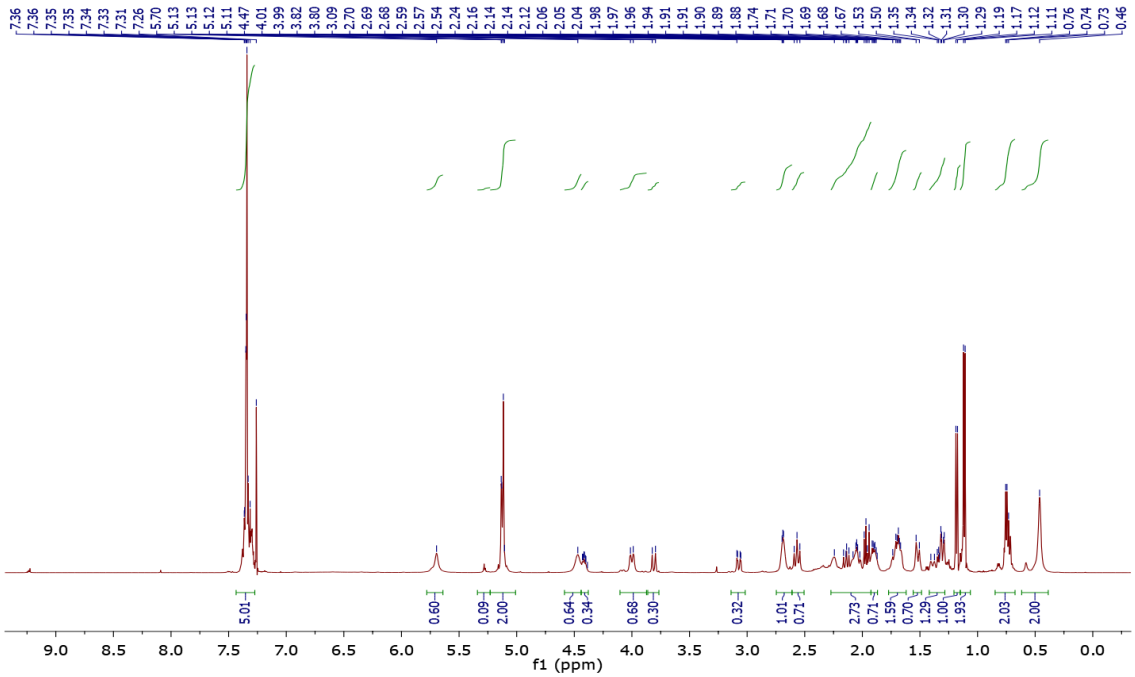
(*cis* product identified as major diastereomer – axial C4 proton presents as q with 3 large *J* values)

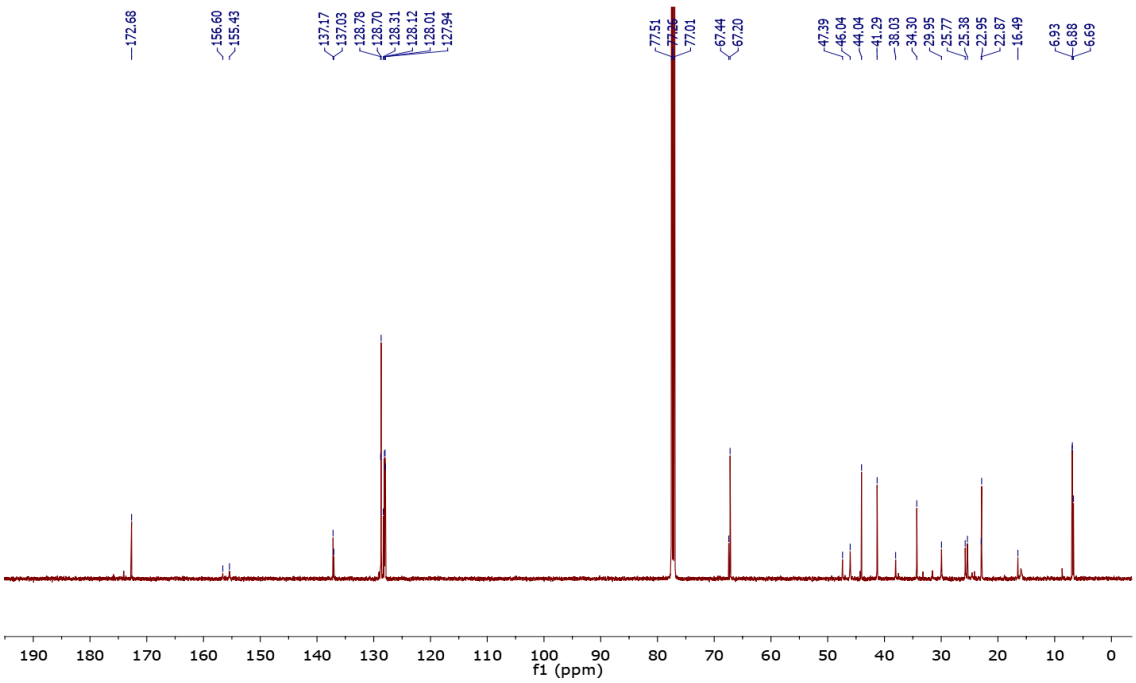


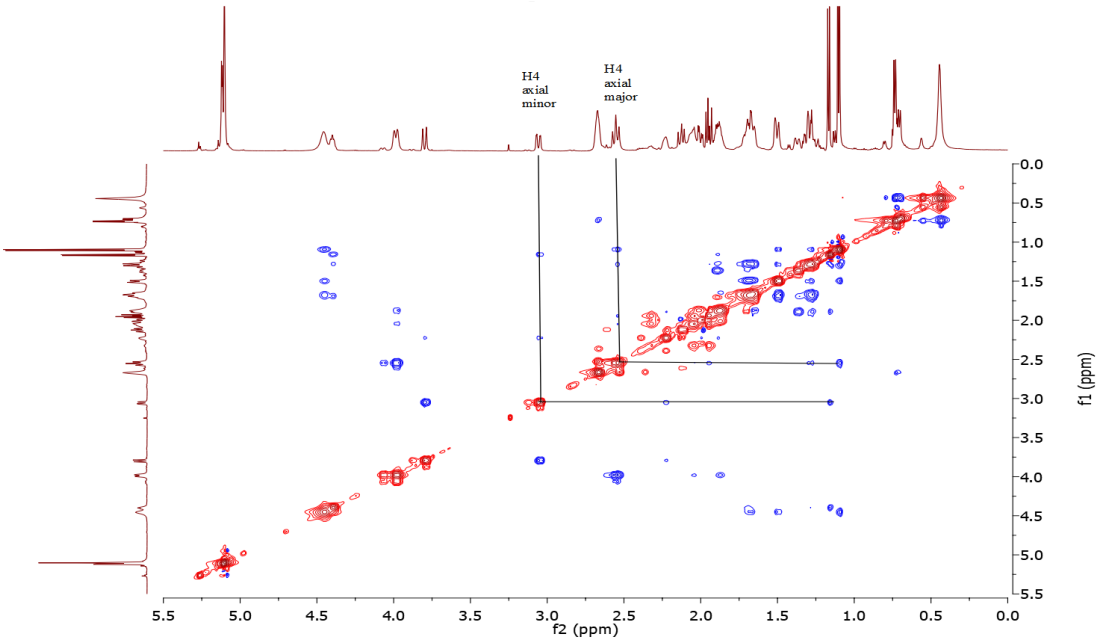


Benzyl 5-(2-(cyclopropylamino)-2-oxoethyl)-2-methylpiperidine-1-carboxylate (12c)

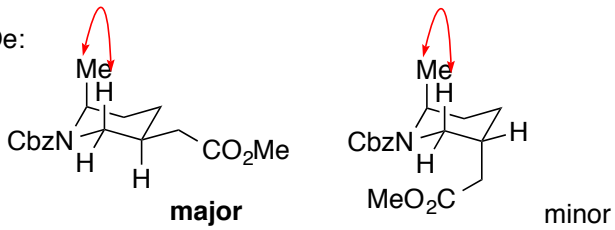






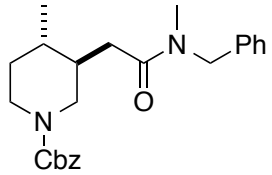


Diagnostic nOe:

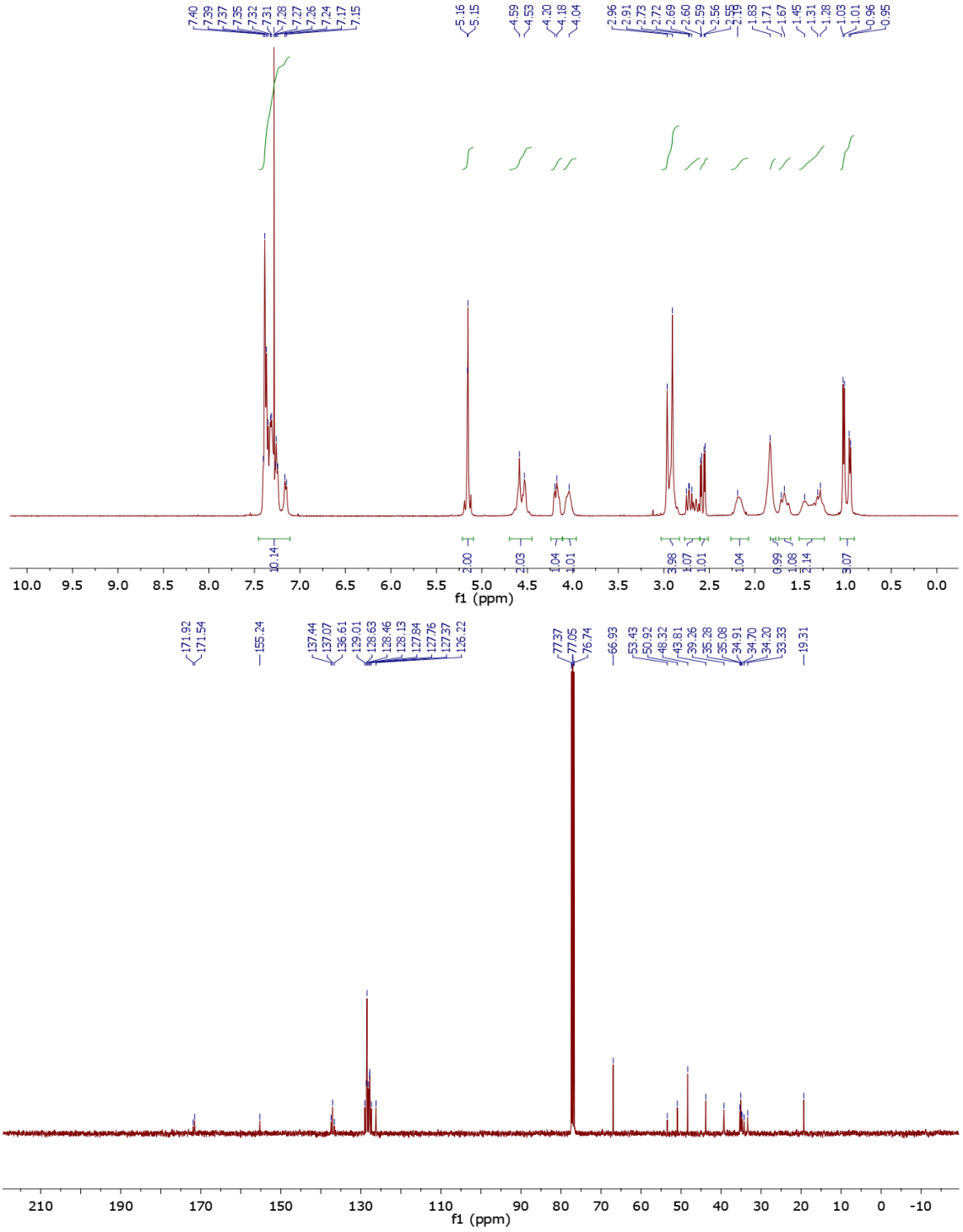


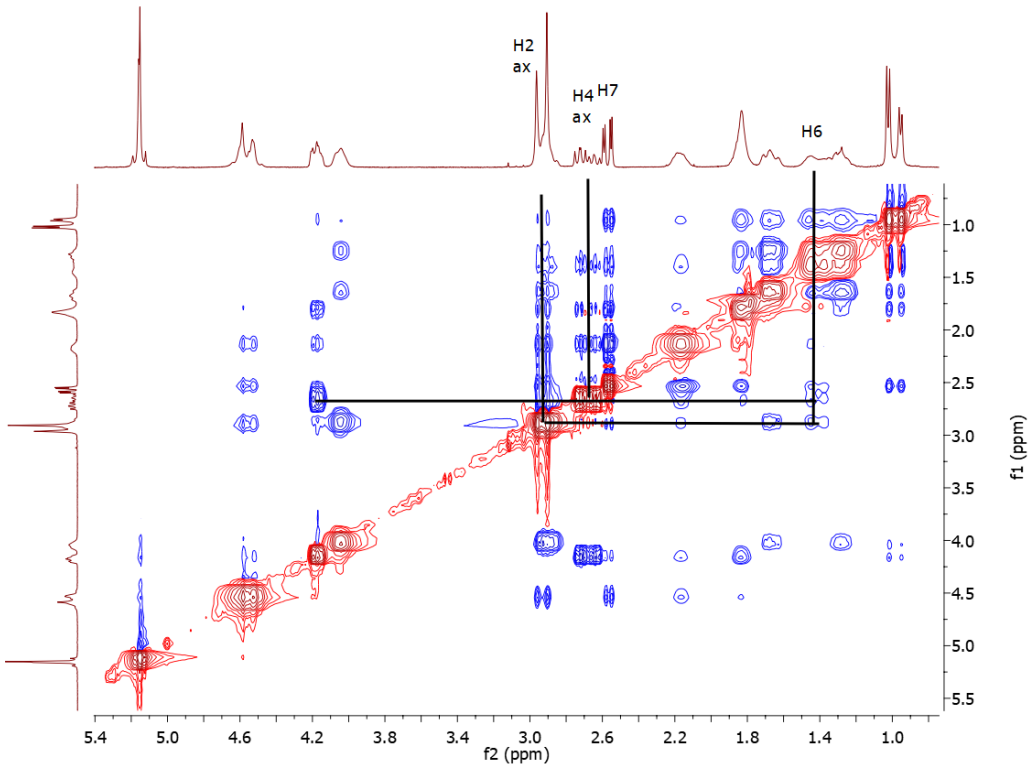
Axial C6 proton presents as triplet with two large *J* values (one geminal and one vicinal trans-diaxial coupling) which fixes carboxymethyl group equatorial; in the minor isomer it presents as a doublet of doublets (one large geminal coupling, one small vicinal axial/equatorial coupling).

Benzyl 3-(2-(benzyl(methyl)amino)-2-oxoethyl)-4-methylpiperidine-1-carboxylate (12d)

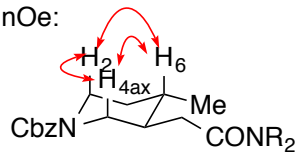


(major diastereomer)

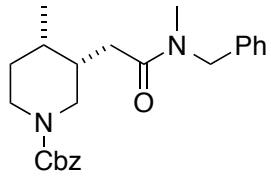




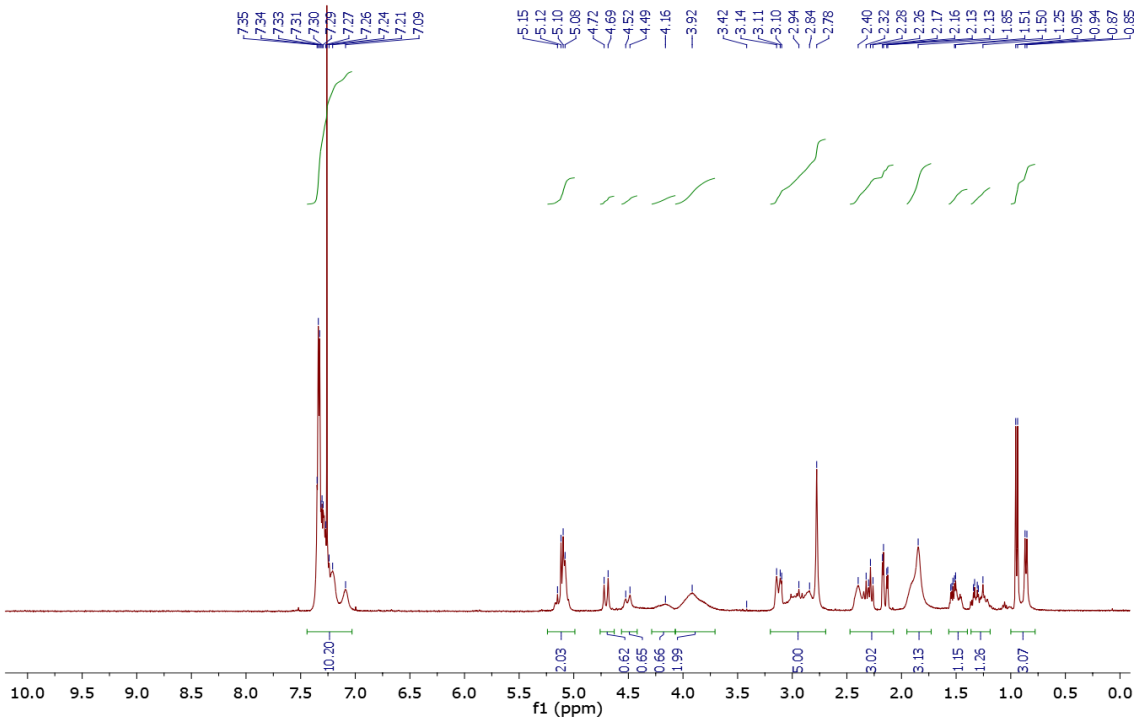
Diagnostic nOe:

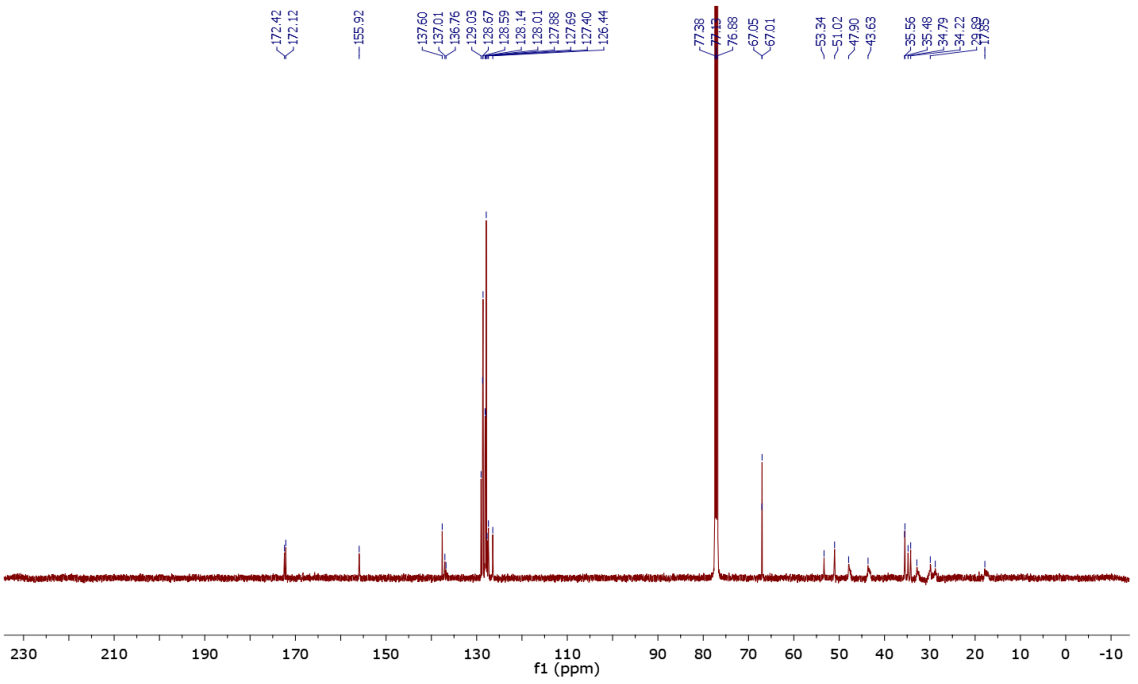


The axial proton at C2 (labelled $H4_{ax}$ above) presents as a doublet of doublets with two large *J* values (one geminal, one vicinal diaxial) which fixes the carboxymethyl group as equatorial.

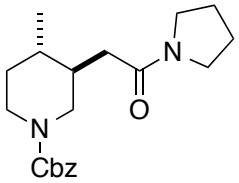


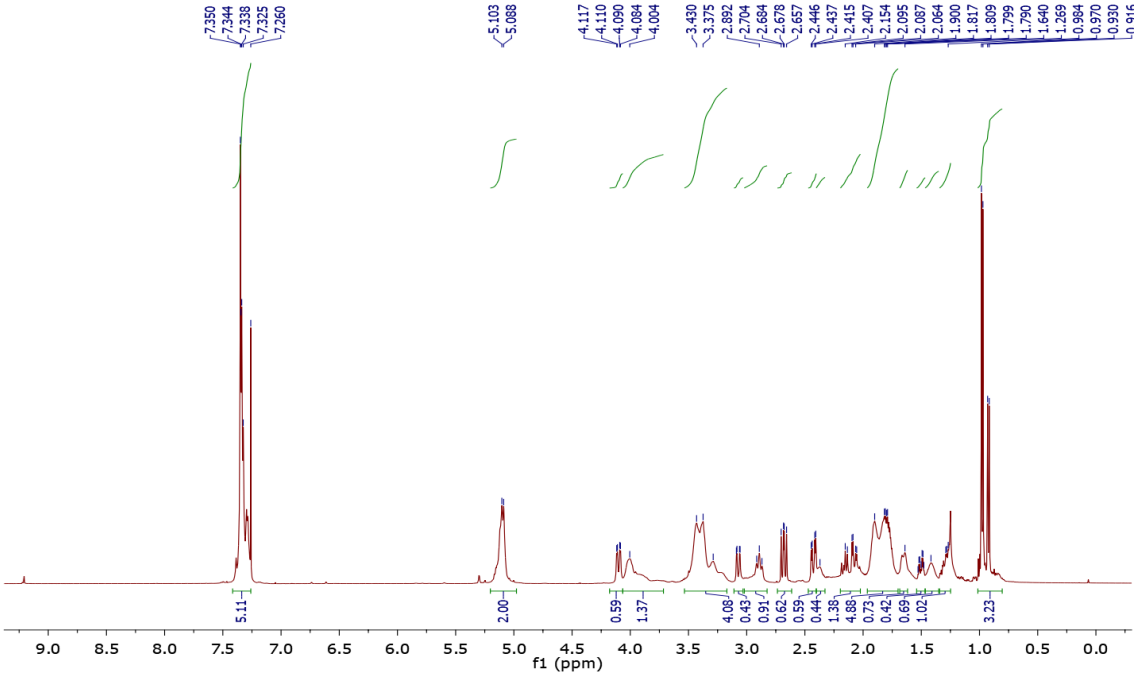
(minor diastereomer)

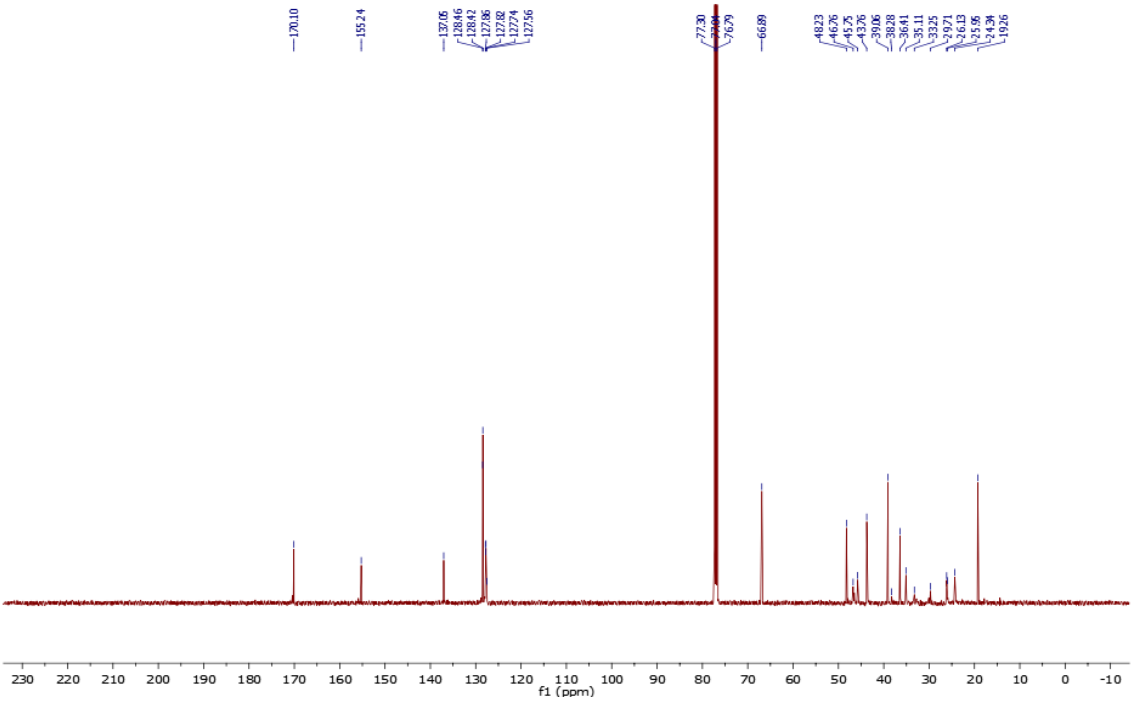


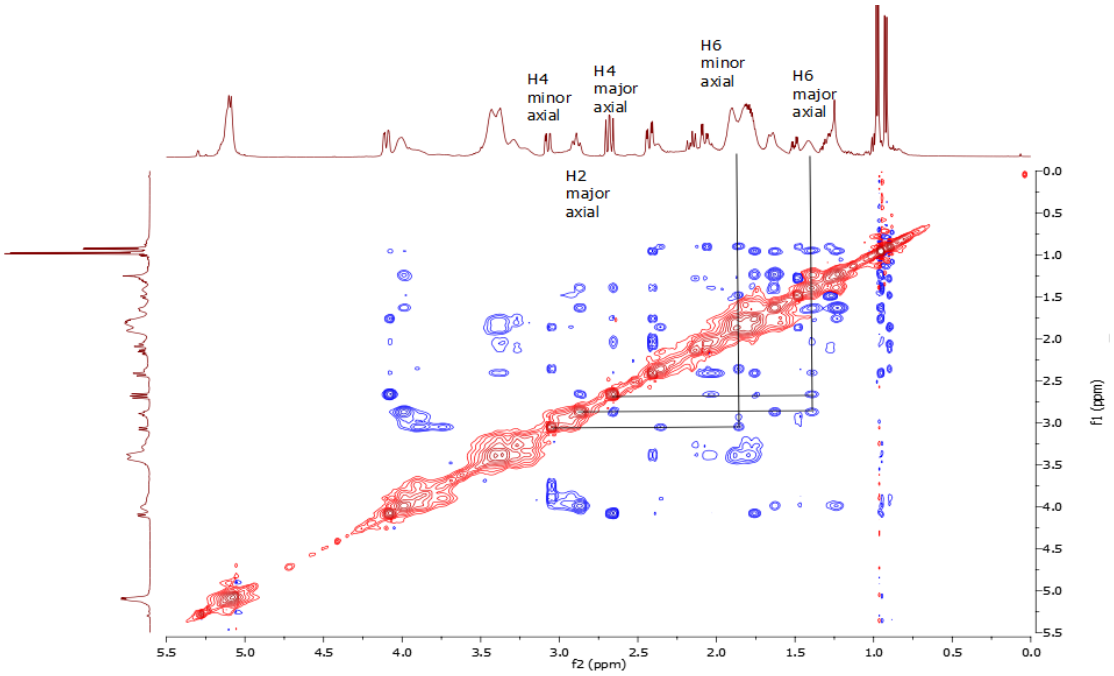


Benzyl 4-methyl-3-(2-oxo-2-(pyrrolidin-1-yl)ethyl)piperidine-1-carboxylate (12e)

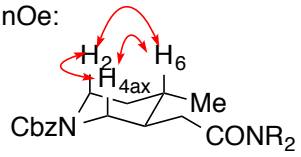








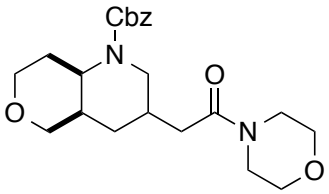
Diagnostic nOe:

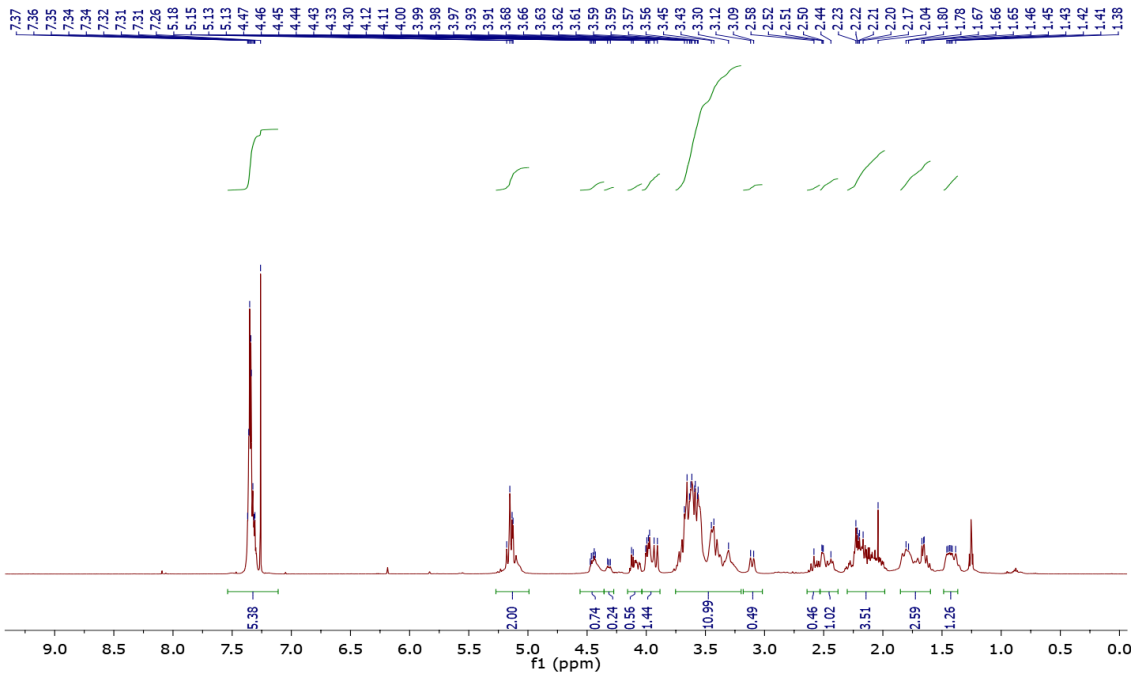


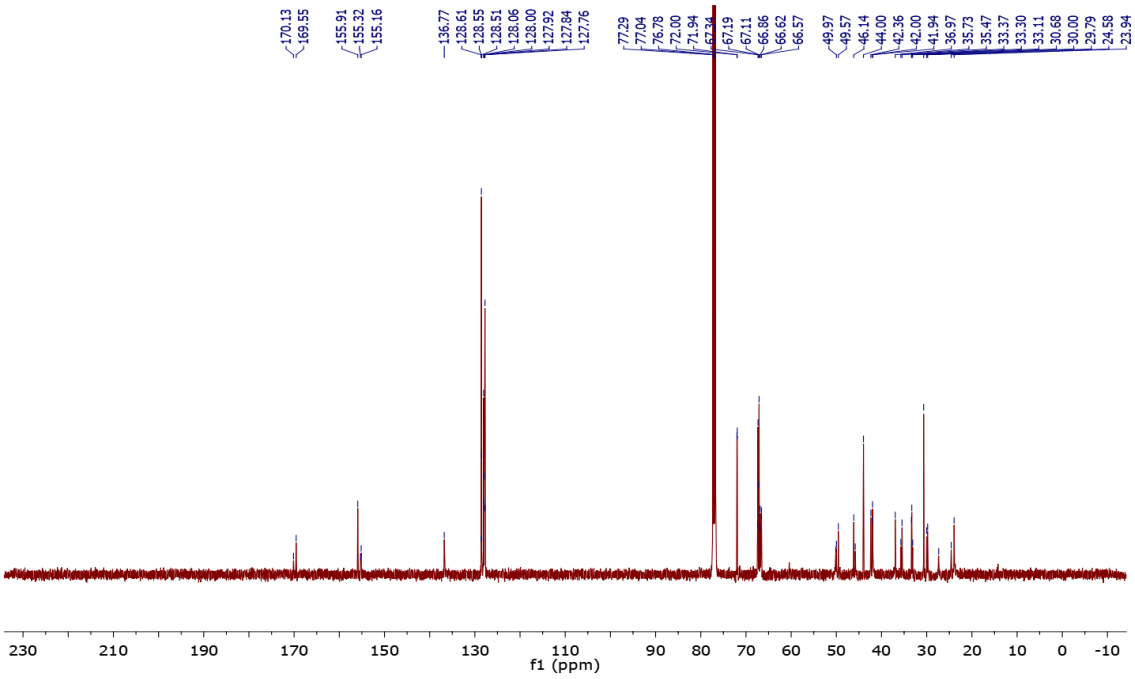
major

The axial proton at C2 (labelled $H4_{ax}$ above) presents as a doublet of doublets with two large *J* values (one geminal, one vicinal diaxial) which fixes the carboxymethyl group as equatorial; the corresponding proton in the minor isomer presents as a doublet of doublets with one large (geminal) *J* value and one small (vicinal axial/equatorial) one.

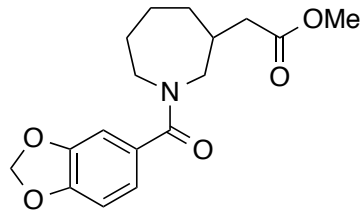
(4a*R,8a*R**)-Benzyl 3-(2-morpholino-2-oxoethyl)octahydro-1H-pyrano[4,3-b]pyridine-1-carboxylate (12f)**

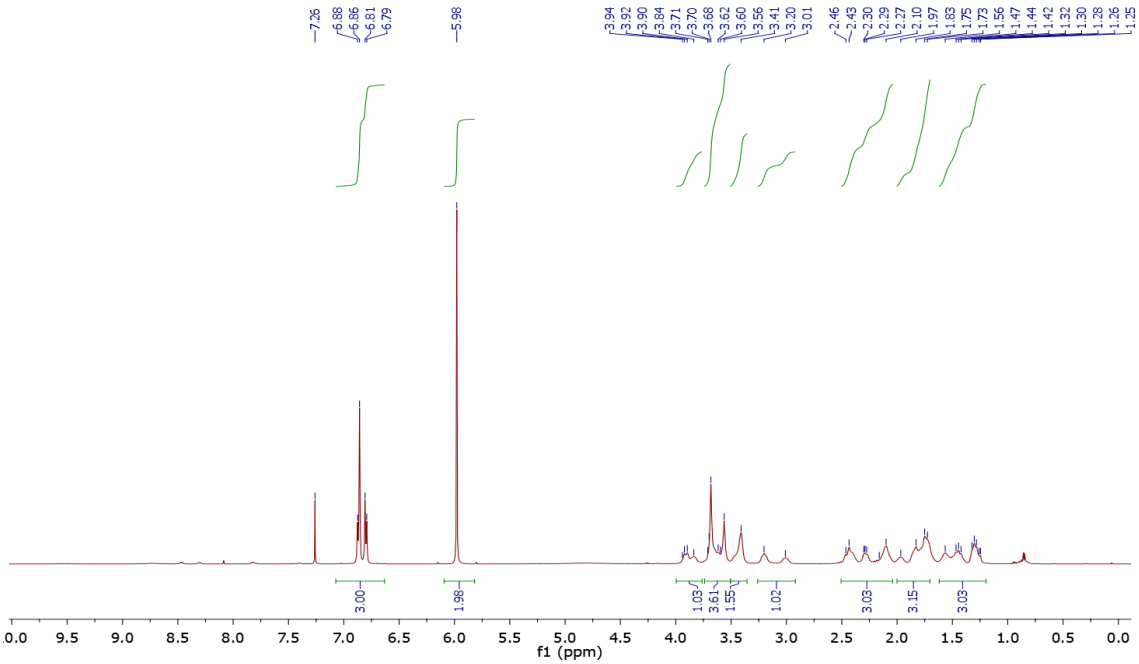


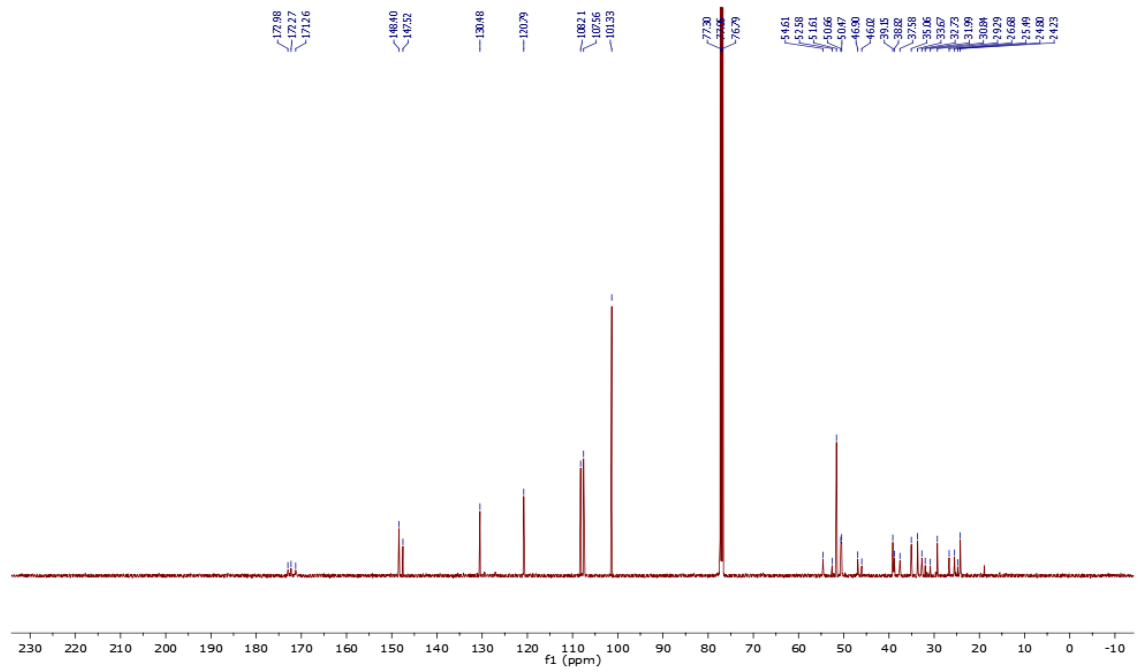




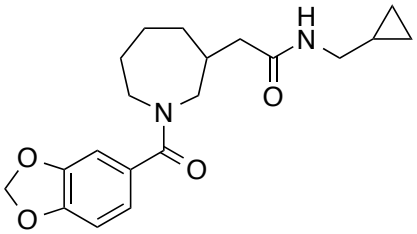
Methyl 2-(1-(benzo[d][1,3]dioxole-5-carbonyl)azepan-3-yl)acetate (14)

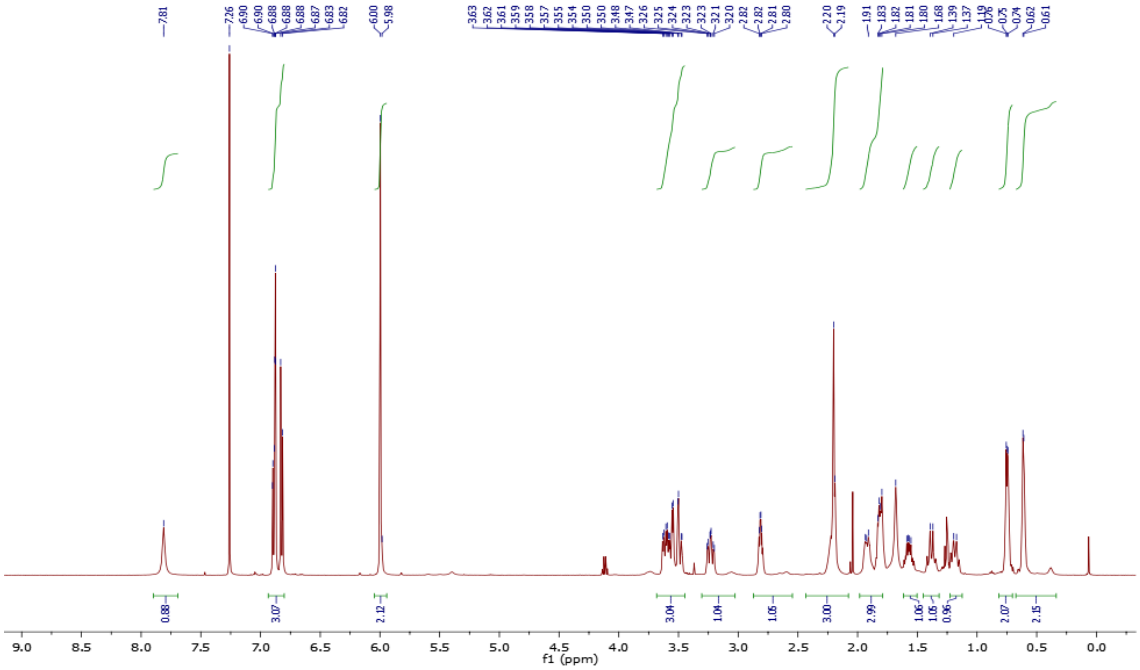


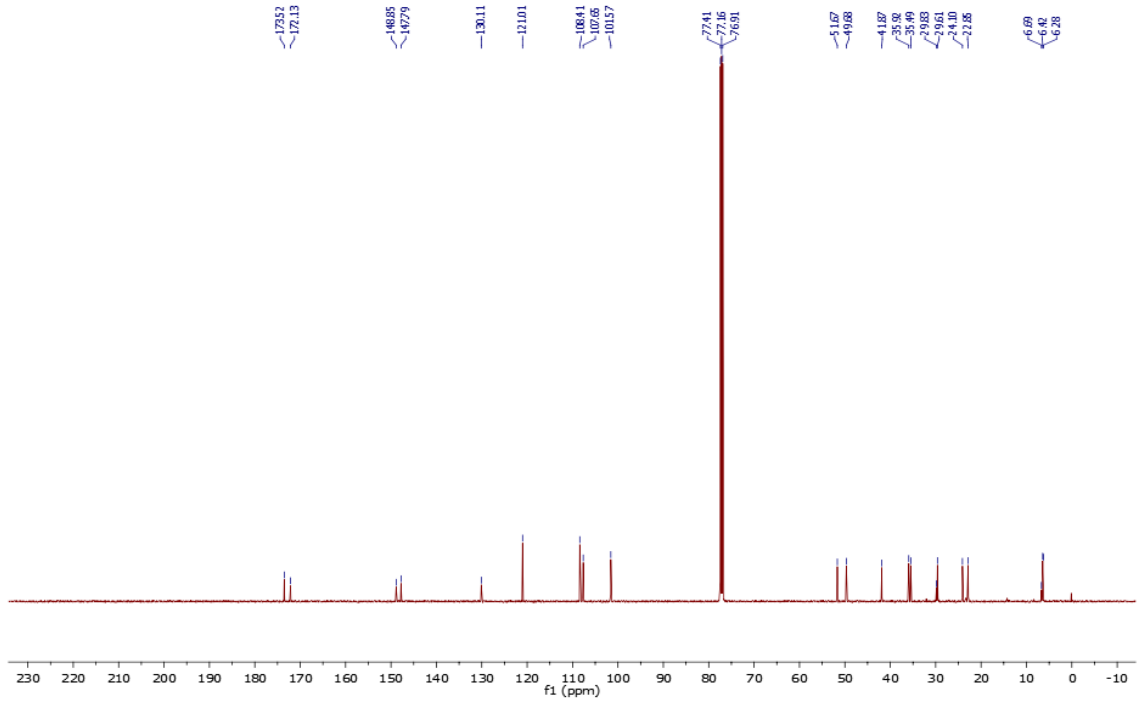




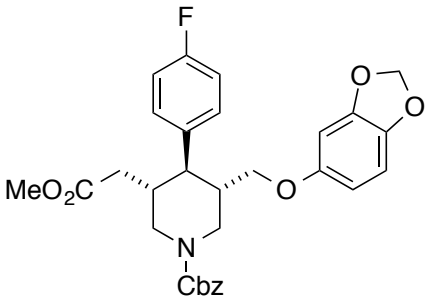
2-(1-(Benzo[d][1,3]dioxole-5-carbonyl)azepan-3-yl)-N-cyclopropylacetamide (15)



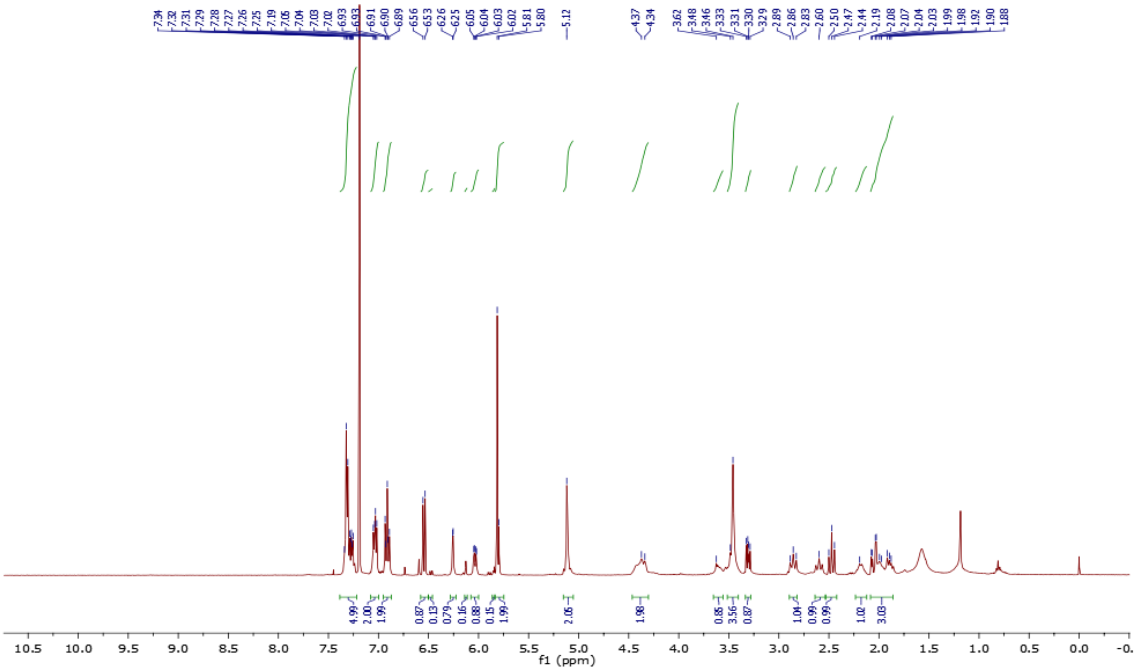


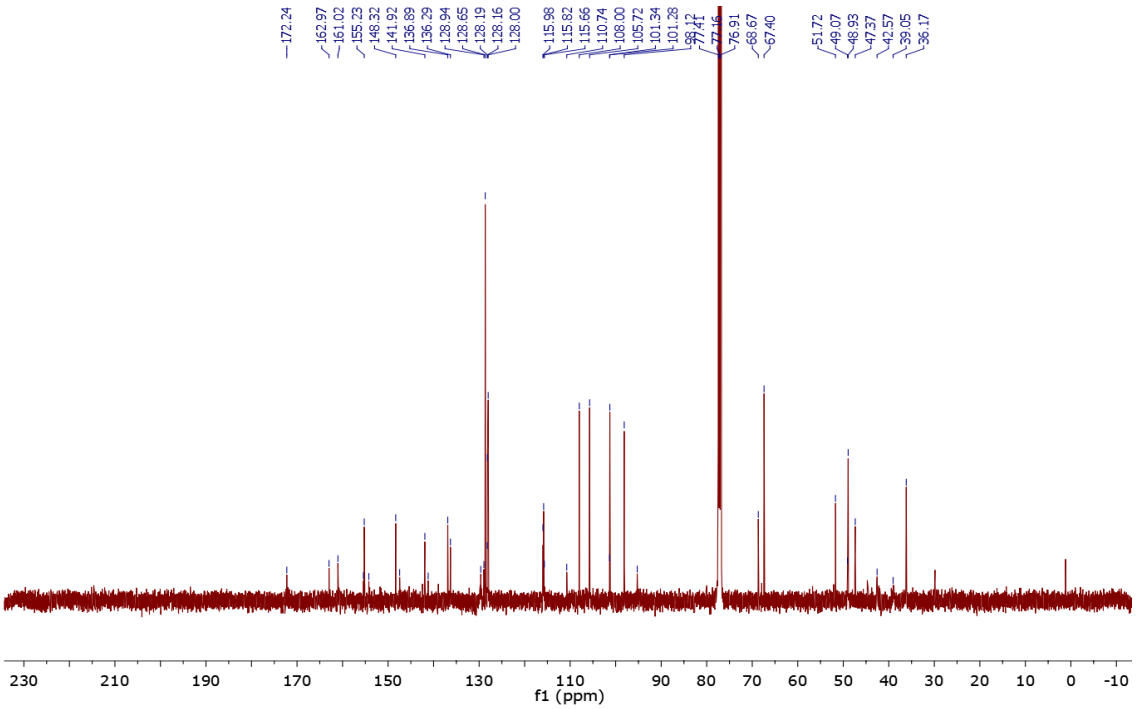


3-(3*S*,4*R*,5*R*)-benzyl 3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)-5-(2-methoxy-2-oxoethyl)piperidine-1-carboxylate (17)



Stereochemistry assigned as *trans,trans*-since H4 (2.47ppm) presents as a triplet (*J* = 11.3Hz) which must correspond to two diaxial vicinal couplings.





Benzyl 3-((benzo[d][1,3]dioxol-5-yloxy)methyl)-5-(2-(cyclopropylamino)-2-oxoethyl)-4-(4-fluorophenyl)-3,4-dihydropyridine-1(2H)-carboxylate