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Supporting Information

Interrupted Pyridine Hydrogenation: Asymmetric Synthesis of δ-Lactams

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Table of Contents

1. General Information

Unless otherwise noted, all reactions for starting material synthesis were carried out under an atmosphere of argon in oven-dried glassware. Catalytic hydrogenation reactions were prepared under air without further care of excluding moisture. Reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. The solvents used for starting material synthesis were purified by distillation over the drying agents indicated in parentheses and were transferred under argon: toluene (CaH_2), dichloromethane (CaH_2), and THF (Na-benzophenone). Ethanol (4 Å) and methanol (3 Å) were purchased as dry solvents from commercial suppliers and stored over molecular sieves. Solvents for hydrogenation reactions (methanol, THF) were purchased as reagent grade solvents (>99%) and used as received. All hydrogenation reactions were carried out in Berghof High Pressure Reactors using hydrogen gas.

Commercially available chemicals were obtained from Acros Organics, Aldrich Chemical Co., Strem Chemicals, Alfa Aesar, ABCR, Combi-Blocks, Chempur and TCI Europe and used as received. Heterogeneous catalysts were obtained from Johnson Matthey (Rh/C, 5 wt%, Ru/C, 5 wt%), Sigma Aldrich ($Pd(OH)_2$/C, 20 wt%) Evonik Industries (Pd/C, 10 wt%), Acros Organics (PtO_2) or Alfa Aesar (Rh/Al_2O_3, 5 wt%) and used as received. Catalytic hydrogenations were conducted using 5 wt% Pd/C from Evonik Industries (PMPC SP1010 D, eggshell reduced).

Analytical thin layer chromatography (TLC) was performed on silica gel 60 F254 aluminum plates (Merck). TLC plates were visualized by exposure to short wave ultraviolet light (254 nm, 366 nm) and were dipped into a solution of $KMnO_4$. Flash chromatography was performed on Acros Organics silica gel (35-70 mesh) under a positive pressure of argon, eluting with the specified solvent system. GC-MS spectra were recorded on an Agilent Technologies 7890A GC-system with an Agilent 5975C VL MSD or an Agilent 5975 inert Mass Selective Detector (EI) and a HP-5MS column (0.25 mm x 30 m, film: 0.25 µm). ESI mass spectra were recorded on a Bruker Daltonics MicroTof spectrometer. ^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker Avance II300 or Avance II400, AgilentDD2 500 or AgilentDD2 600 in the indicated solvents. Chemical shifts (δ) are given in ppm relative to TMS. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm; CD_3OD: δ_H = 3.31 ppm, δ_C = 49.0 ppm. ^{19}F NMR spectra are referenced according to the proton resonance of TMS as the primary reference for the unified chemical shift scale (IUPAC recommendation 2001). Broadband ^{19}F-decoupled ^{13}C spectra were recorded using the WURST decoupling method.

2. Synthesis of Starting Materials

General Procedure 1 for oxazolidinone-coupling from bromopyridines (GP1):

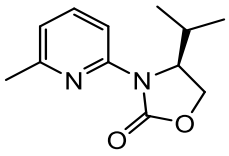
Oxazolidinone-substituted pyridines were prepared based on a literature procedure reported by Buchwald and coworkers.[1] An oven-dried Schlenk tube was charged with the corresponding 2-brominated pyridine (1.0 equiv.), the corresponding 2-oxazolidinone (1.0 equiv.), K_2CO_3 (1.3 equiv.), CuI (5 mol%) and 1,10-phenanthroline (10 mol%) and was put under an argon atmosphere. Dry toluene (0.5 M) was added to the solids and the mixture was stirred at 140 °C for 16 h. After cooling to room temperature, the reaction mixture was filtered through a silica pad and concentrated in *vacuo*. The residue was purified by column chromatography on silica gel.

General Procedure 2 for oxazolidinone coupling starting from chloropyridines (GP2):

Oxazolidinone-substituted pyridines were prepared based on a literature procedure reported by Buchwald and coworkers.[1] An oven-dried Schlenk tube was charged with the corresponding 2-chlorinated pyridine (1.0 equiv.), the corresponding 2-oxazolidinone (1.2 equiv.), K_2CO_3 (2.0 equiv.) and CuI (50 mol%) and was put under an argon atmosphere. Dry toluene (0.5 M) and *N,N'*-dimethylehtylenediamine (50 mol%) were added to the solids and the mixture was stirred at 140 °C for 16 h. After cooling to room temperature, the reaction mixture was filtered through a silica pad and concentrated in *vacuo*. The residue was purified by column chromatography on silica gel.

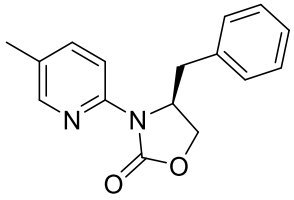
General Procedure 3 for Suzuki coupling (GP3):

An oven-dried Schlenk tube was charged with the corresponding halogenated pyridine (1.0 equiv.), arylboronic acid (1.2 equiv.), K_2CO_3 (4.8 equiv.) and $Pd(PPh_3)_4$ (5 mol%). THF and H_2O were added and the mixture was stirred at the indicated temperature for 16 h. After cooling to room temperature, H_2O was added and the aqueous layer extracted using CH_2Cl_2 (3×). The combined organics were dried over $MgSO_4$ and concentrated in *vacuo*. The residue was purified by column chromatography on silica gel.



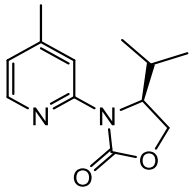
(*S*)-4-Isopropyl-3-(6-methylpyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-6-methylpyridine (460 µL, 4.0 mmol, 1.0 equiv.), (*S*)-4-isopropyloxazolidin-2-one (517 mg, 4.0 mmol, 1.0 equiv.), CuI (38.1 mg, 0.2 mmol, 5 mol%), 1,10-phenanthrolin (72.0 mg, 0.4 mmol, 10 mol%) and K_2CO_3 (719 mg, 5.2 mmol, 1.3 equiv.) in toluene (4 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 6:1, later 4:1) as white solid (780 mg, 3.5 mmol, 89%).

^{1}H NMR (400 MHz, Chloroform-*d*) 7.92 (d, *J* = 8.3 Hz, 1H), 7.58 (t, *J* = 7.9 Hz, 1H), 6.87 (d, *J* = 7.4 Hz, 1H), 4.90 (dt, *J* = 8.8, 3.7 Hz, 1H), 4.36 (t, *J* = 8.8 Hz, 1H), 4.27 (dd, *J* = 8.9, 3.8 Hz, 1H), 2.53 – 2.43 (m, 1H), 2.45 (s, 3H), 0.93 (d, *J* = 7.1 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 156.7, 155.7, 149.9, 138.3, 118.7, 111.3, 63.1, 59.0, 27.9, 24.4, 18.1, 14.6. **HRMS** (ESI) m/z calculated for [$C_{12}H_{16}N_2O_2Na$] ([M+Na$^+$]) 243.1104, found 243.1097.



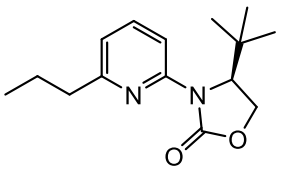
(*S*)-4-Benzyl-3-(5-methylpyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-5-methylpyridine (585 mg, 3.4 mmol, 1.0 equiv.), (*S*)-4-benzyl-2-oxazolidinone (602 mg, 3.4 mmol, 1.0 equiv.), CuI (32.4 mg, 0.17 mmol, 5 mol%), 1,10-phenanthrolin (61.3 mg, 0.34 mmol, 10 mol%) and K_2CO_3 (608 mg, 4.4 mmol, 1.3 equiv.) in toluene (4 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 4:1) as white solid (839 mg, 3.1 mmol, 91%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.23 (d, *J* = 2.3 Hz, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.56 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.29 – 7.20 (m, 3H), 5.09 (ddt, *J* = 9.2, 8.0, 3.4 Hz, 1H), 4.36 – 4.18 (m, 2H), 3.40 (dd, *J* = 13.4, 3.2 Hz, 1H), 2.83 (dd, *J* = 13.4, 9.3 Hz, 1H), 2.33 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 155.1, 148.4, 147.8, 138.8, 136.3, 129.6, 128.9, 128.7, 127.1, 113.6, 66.2, 56.1, 37.9, 17.9. **HRMS** (ESI) m/z calculated for [$C_{16}H_{16}N_2O_2Na$] ([M+Na$^+$]) 291.1104, found 291.1099.



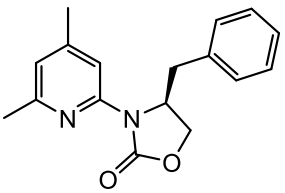
(*S*)-4-Isopropyl-3-(4-methylpyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-4-methylpyridine (450 µL, 4.0 mmol, 1.0 equiv.), (*S*)-4-isopropyloxazolidin-2-one (517 mg, 4.0 mmol, 1.0 equiv.), CuI (38.1 mg, 0.2 mmol, 5 mol%), 1,10-phenanthrolin (72.0 mg, 0.4 mmol, 10 mol%) and K_2CO_3 (719 mg, 5.2 mmol, 1.3 equiv.) in toluene (4 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 6:1, later 4:1) as colorless oil (839 mg, 3.8 mmol, 95%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.17 (d, *J* = 5.1 Hz, 1H), 7.98 (s, 1H), 6.85 (dd, *J* = 5.1, 0.6 Hz, 1H), 4.86 (dt, *J* = 8.8, 3.8 Hz, 1H), 4.36 (t, *J* = 8.8 Hz, 1H), 4.27 (dd, *J* = 8.9, 3.8 Hz, 1H), 2.46 (heptd, *J* = 7.2, 3.9 Hz, 1H), 2.36 (s, 3H), 0.92 (d, *J* = 7.1 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 155.6, 150.7, 149.6, 147.2, 120.8, 115.1, 63.0, 59.1, 27.8, 21.5, 18.1, 14.5. **HRMS** (ESI) m/z calculated for [$C_{12}H_{16}N_2O_2Na$] ([M+Na$^+$]) 243.1104, found 243.1096.



(*S*)-4-(*tert*-Butyl)-3-(6-propylpyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to a modified version of GP1 from 2-allyl-6-bromopyridine (2.64 g, 13.3 mmol, 1.00 equiv.), (*S*)-4-*tert*-butyloxazolidin-2-one (2.0 g, 14.0 mmol, 1.05 equiv.), CuI (190.5 mg, 1.0 mmol, 7.5 mol%), *N,N'*-dimethylehtylenediamine (212.0 µl, 2.0 mmol, 15 mol%) and K_2CO_3 (2.75 g, 26.6 mmol, 2.0 equiv.) in toluene (6 mL) at 140 °C. (*S*)-3-(6-allylpyridin-2-yl)-4-(*tert*-butyl)oxazolidin-2-one was isolated after column chromatography (eluent: *n*-pentane/EtOAc 6:1, later 4:1) as yellow solid (2.6 g). The compound was dissolved in EtOH (40 ml), Pd/C (200 mg) was added and the mixture was stirred under an atmosphere of hydrogen gas (10 bar) for 16 h. The desired product was obtained after recrystallization from *n*-hexanes / ethyl acetate as white solid (2.4 g, 9.2 mmol, 69%).

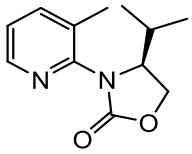
^{1}H NMR (400 MHz, Chloroform-*d*) 7.73 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.61 (dd, *J* = 8.2, 7.4 Hz, 1H), 6.88 (dd, *J* = 7.4, 0.9 Hz, 1H), 5.04 (dd, *J* = 8.2, 2.5 Hz, 1H), 4.44 – 4.33 (m, 2H), 2.74 – 2.59 (m, 2H), 1.82 – 1.64 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.86 (s, 9H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 160.3, 156.6, 151.1, 138.3, 119.1, 113.4, 65.2, 61.5, 40.1, 36.0, 26.0, 22.8, 14.0. **HRMS** (ESI) m/z calculated for [$C_{15}H_{22}N_2O_2Na$] ([M+Na$^+$]) 300.1319, found 300.1315.



(*S*)-4-Benzyl-3-(4,6-dimethylpyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP2 from 2-chloro-4,6-dimethylpyridine (636 µL, 5.0 mmol, 1.0 equiv.),

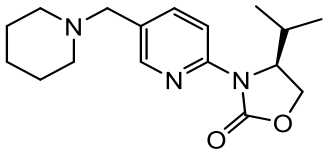
(*S*)-4-benzyloxazolidin-2-one (1.06 g, 6.0 mmol, 1.2 equiv.), CuI (476 mg, 2.5 mmol, 50 mol%), *N*,*N*'-dimethylethylenediamine (269 µl, 2.5 mmol, 50 mol%) and K_2CO_3 (1.38 g, 10.0 mmol, 2.0 equiv.) in toluene (5 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 4:1) as white solid (1.23 g, 4.4 mmol, 87%).

^{1}H NMR (400 MHz, Chloroform-*d*) 7.77 (s, 1H), 7.29 – 7.23 (m, 2H), 7.22 – 7.15 (m, 3H), 6.69 (s, 1H), 5.08 – 4.99 (m, 1H), 4.21 (t, *J* = 8.4 Hz, 1H), 4.14 (dd, *J* = 8.8, 3.3 Hz, 1H), 3.38 (dd, *J* = 13.3, 3.2 Hz, 1H), 2.70 (dd, *J* = 13.3, 9.5 Hz, 1H), 2.42 (s, 3H), 2.27 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 156.4, 155.0, 149.8, 136.7, 129.5, 128.9, 127.1, 119.9, 111.3, 66.3, 56.4, 38.1, 24.3, 21.4 (one carbon overlapping). **HRMS** (ESI) m/z calculated for [$C_{17}H_{18}N_2O_2Na$] ([M+Na$^+$]) 305.1261, found 305.1256.



(*S*)-4-Isopropyl-3-(3-methylpyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-3-methylpyridine (334 µL, 3.0 mmol, 1.0 equiv.), (*S*)-4-isopropyloxazolidin-2-one (387 mg, 3.0 mmol, 1.0 equiv.), CuI (29.0 mg, 0.15 mmol, 5 mol%), 1,10-phenanthrolin (54.0 mg, 0.3 mmol, 10 mol%) and K_2CO_3 (539 mg, 3.9 mmol, 1.3 equiv.) in toluene (3 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 4:1) as white solid (548 mg, 2.5 mmol, 83%).

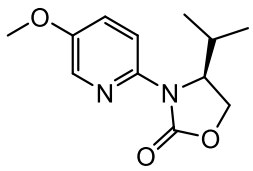
^{1}H NMR (400 MHz, Chloroform-*d*) 8.28 – 8.25 (m, 1H), 7.61 – 7.57 (m, 1H), 7.13 (dd, *J* = 7.6, 4.7 Hz, 1H), 4.89 (td, *J* = 8.8, 4.8 Hz, 1H), 4.48 (t, *J* = 8.8 Hz, 1H), 4.22 (t, *J* = 8.7 Hz, 1H), 2.37 (s, 3H), 1.96 (heptd, *J* = 6.9, 4.7 Hz, 1H), 0.83 (d, *J* = 0.9 Hz, 3H), 0.81 (d, *J* = 0.6 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 156.3, 149.5, 145.9, 140.4, 130.5, 122.5, 64.6, 60.8, 28.9, 18.1, 18.1, 15.7. **HRMS** (ESI) m/z calculated for [$C_{12}H_{16}N_2O_2Na$] ([M+Na$^+$]) 243.1104, found 243.1098.



(*S*)-4-Isopropyl-3-(5-(piperidin-1-ylmethyl)pyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP2 from 2-chloro-5-(piperidin-1-ylmethyl)pyridine[2] (3.16 g, 15.0 mmol, 1.0 equiv.), (*S*)-4-isopropyloxazolidin-2-one (1.97 g, 15.0 mmol, 1.0 equiv.), CuI (214 mg, 1.13 mmol, 7.5 mol%), 1,10-phenanthrolin (240 µl, 2.25 mmol, 15 mol%) and K_2CO_3 (3.1 g, 30.0 mmol, 2.0 equiv.) in toluene (7 mL) at 130 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 2:1) as white solid (3.6 g, 11.9 mmol, 79%).

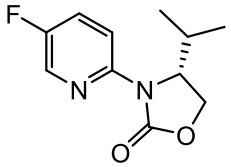
^{1}H NMR (400 MHz, Chloroform-*d*) 8.21 (d, *J* = 2.3 Hz, 1H), 8.09 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.68 (dd, *J* = 8.6, 2.4 Hz, 1H), 4.85 (dt, *J* = 8.9, 3.8 Hz, 1H), 4.40 – 4.25 (m, 2H), 3.43 (s, 2H), 2.56 – 2.44 (m, 1H),

2.41 – 2.31 (m, 4H), 1.60 – 1.52 (m, 4H), 1.47 – 1.39 (m, 2H), 0.93 (d, *J* = 7.1 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H}** NMR (101 MHz, Chloroform-*d*) 155.6, 149.6, 148.0, 139.1, 129.7, 114.0, 63.0, 60.6, 59.1, 54.5, 27.7, 26.1, 24.4, 18.1, 14.4. **HRMS** (ESI) m/z calculated for [$C_{17}H_{25}N_3O_2Na$] ([M+Na$^+$]) 326.1839, found 326.1835.



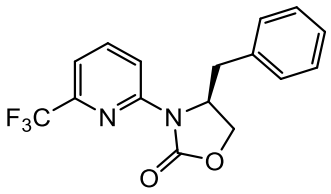
(*S*)-4-Isopropyl-3-(5-methoxypyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-5-methoxypyridine (248 µL, 2.0 mmol, 1.0 equiv.), (*S*)-4-isopropyloxazolidin-2-one (258 mg, 2.0 mmol, 1.0 equiv.), CuI (19.0 mg, 0.1 mmol, 5 mol%), 1,10-phenanthrolin (36.0 mg, 0.2 mmol, 10 mol%) and K_2CO_3 (359 mg, 2.6 mmol, 1.3 equiv.) in toluene (2 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 4:1) as colorless oil (467 mg, 2.0 mmol, 99%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.05 – 7.98 (m, 2H), 7.27 (dd, *J* = 9.0, 3.1 Hz, 1H), 4.81 (dt, *J* = 8.9, 4.0 Hz, 1H), 4.37 (t, *J* = 8.9 Hz, 1H), 4.25 (dd, *J* = 8.9, 4.1 Hz, 1H), 3.84 (s, 3H), 2.41 (heptd, *J* = 7.0, 3.7 Hz, 1H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 155.8, 152.7, 144.1, 134.0, 123.6, 115.5, 63.0, 59.2, 56.0, 27.8, 18.0, 14.5. **HRMS** (ESI) m/z calculated for [$C_{12}H_{16}N_2O_3Na$] ([M+Na$^+$]) 259.1053, found 259.1046.



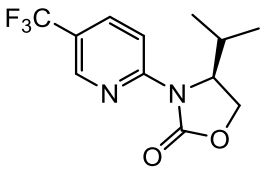
(*R*)-3-(5-Fluoropyridin-2-yl)-4-isopropyloxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-5-fluoropyridine (889 mg, 5.0 mmol, 1.0 equiv.), (*R*)-4-isopropyloxazolidin-2-one (646 mg, 5.0 mmol, 1.0 equiv.), CuI (48 mg, 0.25 mmol, 5 mol%), 1,10-phenanthrolin (90 mg, 0.5 mmol, 10 mol%) and K_2CO_3 (898 mg, 6.5 mmol, 1.3 equiv.) in toluene (5 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 9:1) as white solid (1.01 g, 4.5 mmol, 90%).

^{1}H NMR (500 MHz, Chloroform-*d*) 8.19 – 8.14 (m, 2H), 7.46 – 7.41 (m, 1H), 4.81 (dt, *J* = 8.8, 3.8 Hz, 1H), 4.37 (t, *J* = 8.9 Hz, 1H), 4.27 (dd, *J* = 8.9, 3.9 Hz, 1H), 2.45 (heptd, *J* = 7.0, 3.7 Hz, 1H), 0.92 (d, *J* = 7.1 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H} NMR** (126 MHz, Chloroform-*d*) 156.4 (d, *J* = 251.5 Hz), 155.5, 146.7 (d, *J* = 2.3 Hz), 135.0 (d, *J* = 25.3 Hz), 125.3 (d, *J* = 19.8 Hz), 115.4 (d, *J* = 4.3 Hz), 63.0, 59.2, 27.7, 18.0, 14.4. **^{19}F-NMR (**470 MHz**,** Chloroform-*d***)** –113.5 (dd, *J* = 7.7, 4.0 Hz). **HRMS** (ESI) m/z calculated for [$C_{11}H_{13}N_2O_2FNa$] ([M+Na$^+$]) 247.0853, found 247.0850.



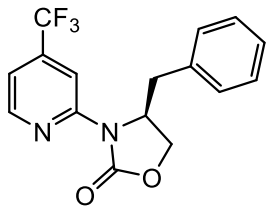
(*S*)-4-Benzyl-3-(6-(trifluoromethyl)pyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-6-(trifluoromethyl)pyridine (457 mg, 2.0 mmol, 1.0 equiv.), (*S*)-4-benzyloxazolidin-2-one (354 mg, 2.0 mmol, 1.0 equiv.), CuI (19.0 mg, 0.1 mmol, 5 mol%), 1,10-phenanthrolin (36.0 mg, 0.2 mmol, 10 mol%) and K_2CO_3 (359 mg, 2.6 mmol, 1.3 equiv.) in toluene (2 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 4:1) as colorless oil (443 mg, 1.4 mmol, 69%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.47 (d, *J* = 8.6 Hz, 1H), 7.96 – 7.87 (m, 1H), 7.45 (d, *J* = 7.3 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.31 – 7.24 (m, 3H), 5.07 (dddd, *J* = 9.9, 6.9, 4.0, 3.0 Hz, 1H), 4.36 – 4.27 (m, 2H), 3.51 (dd, *J* = 13.2, 3.1 Hz, 1H), 2.79 (dd, *J* = 13.2, 9.8 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 154.7, 150.7, 146.3 (q, *J* = 35.3 Hz), 139.6, 136.1, 129.5, 129.1, 127.4, 121.4 (q, *J* = 274.2 Hz), 116.5, 115.9 – 115.2 (m), 66.7, 56.6, 37.9. **^{19}F{^{1}H} NMR** (376 MHz, Chloroform-*d*) –68.4. **HRMS** (ESI) m/z calculated for [$C_{16}H_{13}N_2O_2F_3Na$] ([M+Na$^+$]) 345.0821, found 345.0818.



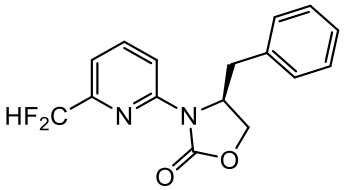
(*S*)-4-Isopropyl-3-(5-(trifluoromethyl)pyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-5-(trifluoromethyl)pyridine (457 mg, 2.0 mmol, 1.0 equiv.), (*S*)-4-isopropyloxazolidin-2-one (258 mg, 2.0 mmol, 1.0 equiv.), CuI (19.0 mg, 0.1 mmol, 5 mol%), 1,10-phenanthrolin (36.0 mg, 0.2 mmol, 10 mol%) and K_2CO_3 (359 mg, 2.6 mmol, 1.3 equiv.) in toluene (2 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 6:1) as yellow oil (464 mg, 1.7 mmol, 85%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.59 – 8.57 (m, 1H), 8.37 (d, *J* = 8.9 Hz, 1H), 7.91 (dd, *J* = 8.9, 2.3 Hz, 1H), 4.87 (dt, *J* = 8.6, 3.5 Hz, 1H), 4.40 (t, *J* = 8.8 Hz, 1H), 4.33 (dd, *J* = 9.0, 3.5 Hz, 1H), 2.55 (heptd, *J* = 7.0, 3.7 Hz, 1H), 0.96 (d, *J* = 7.1 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 155.2, 153.3, 145.1 (q, *J* = 4.3 Hz), 135.3 (q, *J* = 3.3 Hz), 123.8 (q, *J* = 271.5 Hz), 122.0 (q, *J* = 33.3 Hz), 113.4, 63.2, 59.3, 27.7, 18.1, 14.4. **^{19}F{^{1}H} NMR** (376 MHz, Chloroform-*d*) –61.9. **HRMS** (ESI) m/z calculated for [$C_{12}H_{13}N_2O_2F_3Na$] ([M+Na$^+$]) 297.0821, found 297.0816.



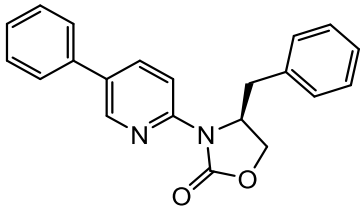
(*S*)-4-Benzyl-3-(4-(trifluoromethyl)pyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP2 from 2-chloro-4-(trifluoromethyl)pyridine (386 µL, 3.0 mmol, 1.0 equiv.), (*S*)-4-benzyl-2-oxazolidinone (638 mg, 3.6 mmol, 1.2 equiv.), CuI (286 mg, 1.5 mmol, 50 mol%), *N*,*N*'-dimethylethylenediamine (161 µl, 1.5 mmol, 50 mol%) and K_2CO_3 (829 mg, 6.0 mmol, 2.0 equiv.) in toluene (3 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 9:1) as white solid (171 mg, 0.53 mmol, 18%).

^{1}H NMR (500 MHz, Chloroform-*d*) 8.57 (dd, *J* = 5.2, 0.7 Hz, 1H), 8.55 – 8.54 (m, 1H), 7.34 (tt, *J* = 6.8, 1.0 Hz, 2H), 7.30 – 7.27 (m, 2H), 7.25 – 7.22 (m, 2H), 5.11 (ddt, *J* = 9.5, 7.9, 3.3 Hz, 1H), 4.36 – 4.26 (m, 2H), 3.45 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.83 (dd, *J* = 13.4, 9.5 Hz, 1H). **^{13}C{^{1}H} NMR** (126 MHz, Chloroform-*d*) 154.7, 151.5, 149.0, 140.6 (q, *J* = 34.1 Hz), 135.9, 129.5, 129.1, 127.4, 122.7 (d, *J* = 273.4 Hz), 114.8 (q, *J* = 3.3 Hz), 109.9 (q, *J* = 4.0 Hz), 66.5, 56.3, 37.9. **^{19}F-NMR (**470 MHz, Chloroform-*d***)** –64.8. **HRMS** (ESI) m/z calculated for [$C_{16}H_{13}N_2O_3F_3Na$] ([M+Na$^+$]) 345.0821, found 345.0819.



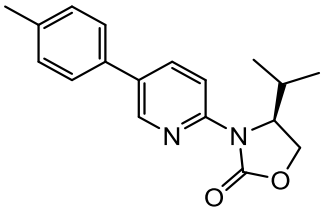
(*S*)-4-Benzyl-3-(6-(difluoromethyl)pyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP1 from 2-bromo-6-(difluoromethyl)pyridine (184 µL, 1.5 mmol, 1.0 equiv.), (*S*)-4-benzyl-2-oxazolidinone (266 mg, 1.5 mmol, 1.0 equiv.), CuI (14.0 mg, 0.075 mmol, 5 mol%), 1,10-phenanthrolin (27.0 mg, 0.15 mmol, 10 mol%) and K_2CO_3 (370 mg, 2.0 mmol, 1.3 equiv.) in toluene (2 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 9:1) as colorless oil (449 mg, 1.48 mmol, 98%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.37 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.88 (dd, *J* = 8.5, 7.5 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.30 – 7.25 (m, 1H), 7.25 – 7.21 (m, 2H), 6.59 (t, *J* = 55.6 Hz, 1H), 5.09 (ddt, *J* = 9.5, 7.7, 3.3 Hz, 1H), 4.42 – 4.23 (m, 2H), 3.46 (dd, *J* = 13.3, 3.2 Hz, 1H), 2.82 (dd, *J* = 13.3, 9.5 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 154.8, 150.9 (t, *J* = 25.7 Hz), 150.4, 139.5, 136.1, 129.5, 129.1, 127.3, 115.5 (t, *J* = 1.7 Hz), 115.4 (t, *J* = 3.6 Hz), 113.5 (t, *J* = 240.7 Hz), 66.6, 56.4, 38.0. **^{19}F-NMR (**377 MHz, Chloroform-*d***)** –116.5 (d, *J* = 57.4 Hz). **HRMS** (ESI) m/z calculated for [$C_{16}H_{14}N_2O_4F_2Na$] ([M+Na$^+$]) 327.0916, found 327.0912.



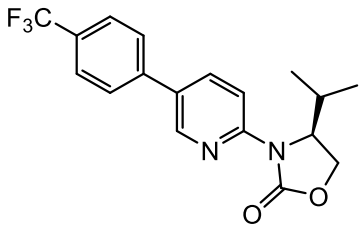
(*S*)-4-Benzyl-3-(5-phenylpyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP3 from 2-bromo-5-phenylpyridine (468 mg, 2.0 mmol, 1.0 equiv.), (*S*)-4-benzyl-2-oxazolidinone (354 mg, 2.0 mmol, 1.0 equiv.), CuI (19.1 mg, 0.1 mmol, 5 mol%), 1,10-phenanthrolin (36.0 mg, 0.2 mmol, 10 mol%) and K_2CO_3 (359 mg, 2.6 mmol, 1.3 equiv.) in toluene (2 mL) at 140 °C. The product was isolated after column chromatography (pentane:EtOAc = 9:1) as white solid (651 mg, 1.97 mmol, 99%).

^{1}H NMR (300 MHz, Chloroform-*d*) 8.65 (dd, *J* = 2.5, 0.8 Hz, 1H), 8.30 (dd, *J* = 8.7, 0.8 Hz, 1H), 7.96 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.53 – 7.45 (m, 2H), 7.44 – 7.23 (m, 6H), 5.16 (ddt, *J* = 9.3, 7.9, 3.3 Hz, 1H), 4.44 – 4.22 (m, 2H), 3.49 (dd, *J* = 13.4, 3.3 Hz, 1H), 2.88 (dd, *J* = 13.4, 9.3 Hz, 1H). **^{13}C{^{1}H} NMR** (75 MHz, Chloroform-*d*) 155.0, 149.7, 146.0, 137.6, 136.7, 136.2, 132.4, 129.6, 129.2, 129.0, 128.0, 127.2, 127.0, 113.8, 66.4, 56.2, 38.0. **HRMS** (ESI) m/z calculated for [$C_{21}H_{18}N_2O_2Na$] ([M+Na$^+$]) 353.1261, found 353.1261.



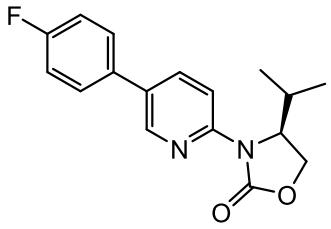
(*S*)-4-Isopropyl-3-(5-(p-tolyl)pyridin-2-yl)oxazolidin-2-one: The title compound was prepared according to GP3 from (*S*)-3-(5-chloropyridin-2-yl)-4-isopropyloxazolidin-2-one (963 mg, 4.0 mmol, 1.0 equiv.), *p*-tolylboronic acid (653 mg, 4.8 mmol, 1.2 equiv.), tetrakis(triphenylphosphin)palladium (231 mg, 0.2 mmol, 5 mol%), and K_2CO_3 (2.65 g, 19.2 mmol, 4.8 equiv.) in 1,4-dioxane (11 mL) and H_2O (8 mL) at 110 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 12:1, later 9:1, 7:1) as white solid (277 mg, 0.9 mmol, 23%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.54 (dd, *J* = 2.6, 0.8 Hz, 1H), 8.23 (dd, *J* = 8.7, 0.8 Hz, 1H), 7.91 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.30 – 7.27 (m, 2H), 4.92 (dt, *J* = 8.8, 3.7 Hz, 1H), 4.41 (t, *J* = 8.8 Hz, 1H), 4.31 (dd, *J* = 8.9, 3.8 Hz, 1H), 2.59 – 2.51 (m, 1H), 2.41 (s, 3H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 155.6, 149.5, 145.6, 137.9, 136.5, 134.6, 132.5, 129.9, 126.8, 114.3, 63.1, 59.2, 27.8, 21.3, 18.1, 14.5. **HRMS** (ESI) m/z calculated for [$C_{18}H_{20}N_2O_2Na$] ([M+Na$^+$]) 319.1417, found 319.1414.



(*S*)-4-Isopropyl-3-(5-(4-(trifluoromethyl)phenyl)pyridine-2-yl)oxazolidin-2-one: The title compound was prepared according to GP3 from (*S*)-3-(5-chloropyridin-2-yl)-4-isopropyloxazolidin-2-one (963 mg, 4.0 mmol, 1.0 equiv.), (4-(trifluoromethyl)phenyl)boronic acid (912 mg, 4.8 mmol, 1.2 equiv.), tetrakis(triphenylphosphin)palladium (231 mg, 0.2 mmol, 5 mol%), and K_2CO_3 (2.65 g, 19.2 mmol, 4.8 equiv.) in 1,4-dioxane (11 mL) and H_2O (8 mL) at 110 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 12:1, later 9:1, 7:1) as white solid (526 mg, 1.5 mmol, 38%).

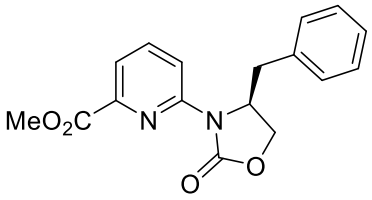
^{1}H NMR (400 MHz, Chloroform-*d*) 8.57 (dd, *J* = 2.6, 0.8 Hz, 1H), 8.31 (dd, *J* = 8.7, 0.8 Hz, 1H), 7.93 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.75 – 7.64 (m, 4H), 4.91 (dt, *J* = 8.7, 3.7 Hz, 1H), 4.42 (t, *J* = 8.8 Hz, 1H), 4.33 (dd, *J* = 9.0, 3.7 Hz, 1H), 2.58 (heptd, *J* = 7.0, 3.7 Hz, 1H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 155.4, 150.4, 145.8, 141.0 (d, *J* = 1.4 Hz), 136.6, 130.8, 129.9 (q, *J* = 32.6 Hz), 127.1, 126.1 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 272.0 Hz), 114.1, 63.0, 59.1, 27.7, 18.0, 14.3. **^{19}F{^{1}H} NMR** (376 MHz, Chloroform-*d*) –62.5. **HRMS** (ESI) m/z calculated for [$C_{18}H_{17}N_2O_2F_3Na$] ([M+Na$^+$]) 373.1134, found 373.1131.



(*S*)-3-(5-(4-Fluorophenyl)pyridin-2-yl)-4-isopropyloxazolidin-2-one: The title compound was prepared according to GP3 from (*S*)-3-(5-chloropyridin-2-yl)-4-isopropyloxazolidin-2-one (963 mg, 4.0 mmol, 1.0 equiv.), (4-fluorophenyl)boronic acid (672 mg, 4.8 mmol, 1.2 equiv.), tetrakis(triphenylphosphin)palladium (231 mg, 0.2 mmol, 5 mol%), and K_2CO_3 (2.65 g, 19.2 mmol, 4.8 equiv.) in 1,4-dioxane (11 mL) and H_2O (8 mL) at 110 °C. The reaction time was extended to 72 h. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 9:1, later 4:1, 3:1) as white solid (629 mg, 2.1 mmol, 52%).

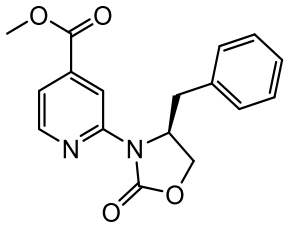
^{1}H NMR (400 MHz, Chloroform-*d*) 8.49 (dd, *J* = 2.5, 0.9 Hz, 1H), 8.24 (dd, *J* = 8.8, 0.9 Hz, 1H), 7.86 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.19 – 7.11 (m, 2H), 4.90 (dt, *J* = 8.7, 3.7 Hz, 1H), 4.40 (t, *J* = 8.8 Hz, 1H), 4.31 (dd, *J* = 8.9, 3.8 Hz, 1H), 2.55 (heptd, *J* = 6.9, 3.7 Hz, 1H), 0.96 (d, *J* = 7.1 Hz, 3H), 0.86 (d, *J* = 7.0 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 162.8 (d, *J* = 247.4 Hz), 155.5, 149.8, 145.6, 136.4, 133.7 (d, *J* = 3.3 Hz), 131.5, 128.5 (d, *J* = 8.1 Hz), 116.1 (d, *J* = 21.6 Hz), 114.2, 63.1,

59.2, 27.8, 18.1, 14.4. **$^{19}F\{^{1}H\}$ NMR** (376 MHz, Chloroform-*d*) –114.6. **HRMS** (ESI) m/z calculated for [$C_{17}H_{17}N_2O_2FNa$] ([M+Na$^+$]) 323.1166, found 323.1162.



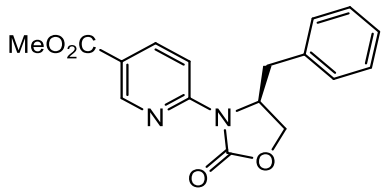
Methyl (*S*)-6-(4-benzyl-2-oxooxazolidin-3-yl)picolinate: The title compound was prepared according to GP1 from methyl 6-bromopicolinate (648 mg, 3.0 mmol, 1.0 equiv.), (*S*)-4-benzyl-2-oxazolidinone (532 mg, 3.0 mmol, 1.0 equiv.), CuI (29.0 mg, 0.15 mmol, 5 mol%), 1,10-phenanthrolin (54.0 mg, 0.3 mmol, 10 mol%) and K_2CO_3 (539 mg, 2.6 mmol, 1.3 equiv.) in toluene (3 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 9:1, later 4:1) as white solid (853 mg, 2.7 mmol, 90%).

^{1}H NMR (599 MHz, Chloroform-*d*) 8.46 – 8.42 (m, 1H), 7.88 (dd, *J* = 4.7, 0.9 Hz, 2H), 7.38 – 7.33 (m, 4H), 7.29 – 7.26 (m, 1H), 5.13 (ddt, *J* = 9.8, 7.6, 3.2 Hz, 1H), 4.37 – 4.27 (m, 2H), 4.03 (s, 2H), 3.57 (dd, *J* = 13.1, 3.0 Hz, 1H), 2.78 (dd, *J* = 13.1, 9.8 Hz, 1H). **$^{13}C\{^{1}H\}$ NMR** (151 MHz, Chloroform-*d*) 165.5, 154.9, 150.4, 146.0, 139.2, 136.5, 129.6, 129.0, 127.2, 120.6, 117.2, 66.8, 56.9, 52.8, 38.0. **HRMS** (ESI) m/z calculated for [$C_{17}H_{16}N_2O_4Na$] ([M+Na$^+$]) 335.1002, found 335.0998.



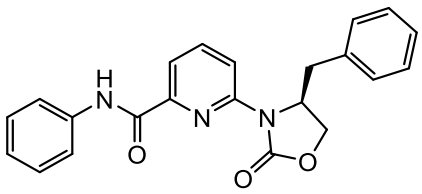
Methyl (*S*)-2-(4-benzyl-2-oxooxazolidin-3-yl)isonicotinate: The title compound was prepared according to GP1 from methyl 2-bromoisonicotinate (648 mg, 3.0 mmol, 1.0 equiv.), (*S*)-4-benzyloxazolidin-2-one (531 mg, 3.0 mmol, 1.0 equiv.), CuI (29.0 mg, 0.15 mmol, 5 mol%), 1,10-phenanthrolin (54.0 mg, 0.3 mmol, 10 mol%) and K_2CO_3 (539 mg, 2.6 mmol, 1.3 equiv.) in toluene (3 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 2:1) as colorless oil (948 mg, 3.0 mmol, 99%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.81 – 8.76 (m, 1H), 8.56 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.66 (dd, *J* = 5.1, 1.4 Hz, 1H), 7.39 – 7.33 (m, 2H), 7.33 – 7.22 (m, 3H), 5.21 – 5.08 (m, 1H), 4.39 – 4.33 (m, 1H), 4.29 (dd, *J* = 8.9, 3.3 Hz, 1H), 3.99 (s, 3H), 3.45 (dd, *J* = 13.4, 3.3 Hz, 1H), 2.86 (dd, *J* = 13.4, 9.3 Hz, 1H). **$^{13}C\{^{1}H\}$ NMR** (101 MHz, Chloroform-*d*) 165.6, 154.8, 151.4, 148.6, 139.8, 136.0, 129.5, 129.0, 127.3, 118.6, 113.5, 66.4, 56.3, 52.9, 37.9. **HRMS** (ESI) m/z calculated for [$C_{17}H_{16}N_2O_4Na$] ([M+Na$^+$]) 335.1002, found 335.0997.



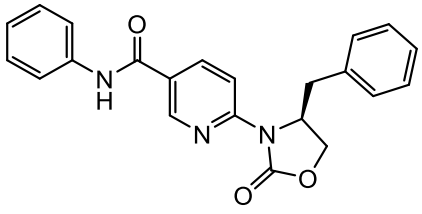
Methyl (*S*)-6-(4-benzyl-2-oxooxazolidin-3-yl)picolinate: The title compound was prepared according to GP1 from methyl 6-bromonicotinate (648 mg, 3.0 mmol, 1.0 equiv), (*S*)-4-benzyl-2-oxazolidinone (532 mg, 3.0 mmol, 1.0 equiv.), CuI (29.0 mg, 0.15 mmol, 5 mol%), 1,10-phenanthrolin (54.0 mg, 0.3 mmol, 10 mol%) and K_2CO_3 (539 mg, 2.6 mmol, 1.3 equiv.) in toluene (3 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 9:1, later 4:1) as white solid (853 mg, 2.7 mmol, 90%).

^{1}H NMR (599 MHz, Chloroform-*d*) 8.46 – 8.42 (m, 1H), 7.88 (dd, *J* = 4.7, 0.9 Hz, 2H), 7.38 – 7.33 (m, 4H), 7.29 – 7.26 (m, 1H), 5.13 (ddt, *J* = 9.8, 7.6, 3.2 Hz, 1H), 4.37 – 4.27 (m, 2H), 4.03 (s, 2H), 3.57 (dd, *J* = 13.1, 3.0 Hz, 1H), 2.78 (dd, *J* = 13.1, 9.8 Hz, 1H). **^{13}C{^{1}H} NMR** (151 MHz, Chloroform-*d*) 165.5, 154.9, 150.4, 146.0, 139.2, 136.5, 129.6, 129.0, 127.2, 120.6, 117.2, 66.8, 56.9, 52.8, 38.0. **HRMS** (ESI) m/z calculated for [$C_{17}H_{16}N_2O_4Na$] ([M+Na$^+$]) 335.1002, found 335.0998.



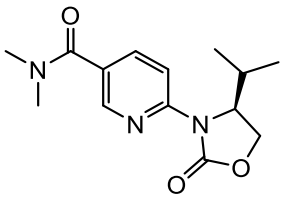
(*S*)-2-(4-Benzyl-2-oxooxazolidin-3-yl)-*N*-phenylisonicotinamide: The title compound was prepared according to GP1 from 6-bromo-*N*-phenylpicolinamide (554 mg, 2.0 mmol, 1.0 equiv.), (*S*)-4-benzyloxazolidin-2-one (354 mg, 2.0 mmol, 1.0 equiv.), CuI (19.1 mg, 0.1 mmol, 5 mol%), 1,10-phenanthrolin (36.0 mg, 0.2 mmol, 10 mol%) and K_2CO_3 (359 mg, 2.6 mmol, 1.3 equiv.) in toluene (2 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 2:1) as white solid (595 mg, 1.6 mmol, 80%).

^{1}H NMR (300 MHz, Chloroform-*d*) 9.44 (s, 1H), 8.32 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.93 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.82 (dd, *J* = 8.4, 7.5 Hz, 1H), 7.62 – 7.54 (m, 2H), 7.33 – 7.00 (m, 8H), 5.11 (ddt, *J* = 9.3, 7.9, 3.3 Hz, 1H), 4.41 – 4.31 (m, 1H), 4.24 (dd, *J* = 8.9, 3.3 Hz, 1H), 3.34 (dd, *J* = 13.8, 3.5 Hz, 1H), 2.85 (dd, *J* = 13.8, 9.2 Hz, 1H). **^{13}C{^{1}H} NMR** (75 MHz, Chloroform-*d*) 161.5, 154.6, 149.1, 147.8, 140.1, 137.5, 135.6, 129.2, 129.2, 129.0, 127.5, 124.6, 119.6, 118.1, 117.0, 66.7, 55.9, 38.2. **HRMS** (ESI) m/z calculated for [$C_{22}H_{19}N_3O_4Na$] ([M+Na$^+$]) 396.1319, found 396.1319.



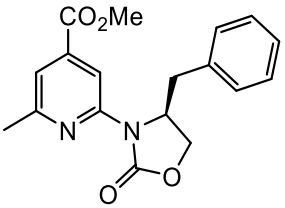
(*S*)-6-(4-Benzyl-2-oxooxazolidin-3-yl)-*N*-phenylnicotinamide: The title compound was prepared according to GP2 from 6-chloro-*N*-phenylnicotinamide (465 mg, 2.0 mmol, 1.0 equiv.), (*S*)-4-benzyl-2-oxazolidinone (425 mg, 2.4 mmol, 1.2 equiv.), CuI (77 mg, 0.4 mmol, 20 mol%), *N*,*N*'-dimethylethylenediamine (43 µl, 0.4 mmol, 20 mol%) and K_2CO_3 (564 mg, 4.0 mmol, 2.0 equiv.) in toluene (2 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 2:1) as white solid (489 mg, 1.3 mmol, 66%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.97 (dd, *J* = 2.5, 0.8 Hz, 1H), 8.35 (dd, *J* = 8.8, 0.8 Hz, 1H), 8.22 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.94 (s, 1H), 7.70 – 7.65 (m, 2H), 7.42 – 7.16 (m, 8H), 5.14 (ddt, *J* = 9.2, 7.8, 3.2 Hz, 1H), 4.38 – 4.26 (m, 2H), 3.44 (dd, *J* = 13.5, 3.2 Hz, 1H), 2.87 (dd, *J* = 13.4, 9.3 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 163.6, 154.8, 152.8, 147.6, 137.8, 137.0, 135.9, 129.6, 129.3, 129.1, 127.4, 126.0, 125.0, 120.5, 113.0, 66.5, 56.3, 37.9. **HRMS** (ESI) m/z calculated for [$C_{22}H_{19}N_3O_4Na$] ([M+Na$^+$]) 396.1319, found 396.1318.



(*S*)-6-(4-Isopropyl-2-oxooxazolidin-3-yl)-*N*,*N*-dimethylnicotinamide: The title compound was prepared according to GP2 from 6-chloro-*N*,*N*-dimethylnicotinamide (3.03 g, 16.4 mmol, 1.00 equiv.), (*S*)-4-isopropyl-2-oxazolidinone (2.23 g, 17.2 mmol, 1.05 equiv.), CuI (235 mg, 1.23 mmol, 7.5 mol%), *N*,*N*'-dimethylethylenediamine (262 µl, 2.46 mmol, 15 mol%) and K_2CO_3 (3.39 mg, 32.85 mmol, 2.0 equiv.) in toluene (8 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 1:1) as white solid (2.40 g, 8.65 mmol, 53%).

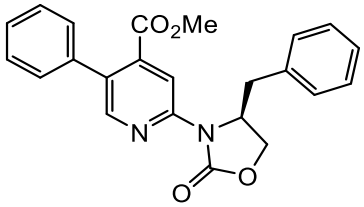
^{1}H NMR (400 MHz, Chloroform-*d*) 8.43 (dd, *J* = 2.4, 0.9 Hz, 1H), 8.22 (dd, *J* = 8.7, 0.8 Hz, 1H), 7.77 (dd, *J* = 8.7, 2.4 Hz, 1H), 4.86 (dt, *J* = 8.7, 3.7 Hz, 1H), 4.43 – 4.27 (m, 2H), 3.11 (s, 3H), 3.04 (s, 3H), 2.58 – 2.45 (m, 1H), 0.94 (d, *J* = 7.1 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 169.0, 155.4, 151.3, 146.8, 137.3, 127.4, 113.4, 63.1, 59.1, 39.8, 35.7, 27.6, 18.1, 14.3. **HRMS** (ESI) m/z calculated for [$C_{14}H_{19}N_3O_3Na$] ([M+Na$^+$]) 300.1319, found 300.1315.



Methyl (*S*)-2-(4-benzyl-2-oxooxazolidin-3-yl)-6-methylisonicotinate: The title compound was prepared according to GP2 from methyl 2-chloro-6-methylisonicotinate (557 mg,

3.0 mmol, 1.0 equiv.), (*S*)-4-benzyl-2-oxazolidinone (3.6 mmol, 638 mg, 1.2 equiv.) CuI (286 mg, 1.5 mmol, 50 mol%), *N*,*N*'-dimethylethylenediamine (161 µl, 1.5 mmol, 50 mol%) and K_2CO_3 (829 mg, 6.0 mmol, 2.0 equiv.) in toluene (3 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 9:1) as white solid (360 mg, 1.1 mmol, 37%).

^{1}H NMR (400 MHz, Chloroform-*d*) 8.54 (d, *J* = 0.6 Hz, 1H), 7.49 (d, *J* = 0.6 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.29 – 7.22 (m, 3H), 5.10 (ddt, *J* = 9.5, 7.8, 3.2 Hz, 1H), 4.38 – 4.22 (m, 2H), 3.95 (s, 3H), 3.45 (dd, *J* = 13.3, 3.3 Hz, 1H), 2.80 (dd, *J* = 13.3, 9.4 Hz, 1H), 2.61 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 165.9, 157.9, 154.8, 150.6, 140.1, 136.3, 129.5, 129.0, 127.3, 117.9, 110.3, 66.4, 56.5, 52.8, 38.0, 24.5. **HRMS** (ESI) m/z calculated for [$C_{18}H_{18}N_2O_4Na$] ([M+Na$^+$]) 349.1159, found 349.1156.



Methyl (*S*)-2-(4-benzyl-2-oxooxazolidin-3-yl)-5-phenylisonicotinate: The title compound was prepared according to GP2 from methyl 2-chloro-5-phenylisonicotinate (495 mg, 2.0 mmol, 1.0 equiv.), (*S*)-4-benzyl-2-oxazolidinone (2.4 mmol, 425 mg, 1.2 equiv.), CuI (190 mg, 1.0 mmol, 50 mol%), *N*,*N*'-dimethylethylenediamine (108 µl, 1.0 mmol, 50 mol%) and K_2CO_3 (553 mg, 4.0 mmol, 2.0 equiv.) in toluene (2 mL) at 140 °C. The product was isolated after column chromatography (eluent: *n*-pentane/EtOAc 4:1) as colorless oil (469 mg, 1.2 mmol, 60%).

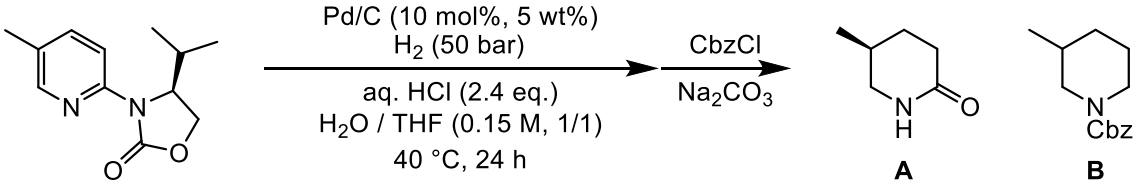
^{1}H NMR (400 MHz, Chloroform-*d*) 8.56 (d, *J* = 0.8 Hz, 1H), 8.47 (d, *J* = 0.8 Hz, 1H), 7.49 – 7.40 (m, 3H), 7.38 – 7.30 (m, 4H), 7.31 – 7.23 (m, 3H), 5.14 (ddt, *J* = 9.4, 7.9, 3.3 Hz, 1H), 4.41 – 4.25 (m, 2H), 3.75 (s, 3H), 3.46 (dd, *J* = 13.4, 3.3 Hz, 1H), 2.86 (dd, *J* = 13.4, 9.3 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 167.4, 154.8, 150.0, 149.2, 140.5, 136.9, 136.0, 131.7, 129.6, 129.0, 128.7, 128.6, 128.1, 127.3, 112.6, 66.4, 56.2, 52.8, 37.9. **HRMS** (ESI) m/z calculated for [$C_{23}H_{20}N_2O_4Na$] ([M+Na$^+$]) 411.1315, found 411.1319.

3. Investigation of Reaction Parameters

General Procedure for the hydrogenation of oxazolidinone-substituted pyridines:

A 4 ml glass vial (screw-cap) equipped with a stir bar was charged with 5 wt% Pd/C (32 mg, 0.015 mmol, 10 mol%) and solid oxazolidinone-substituted pyridine (0.15 mmol, 1.0 equiv). THF (0.5 mL) and H_2O (0.5 mL) were added (1 mL / 0.15 M in total) followed by the addition of liquid oxazolidinone-substituted pyridine (0.15 mmol, 1.0 equiv) and concentrated aqueous HCl (30 µl, 2.4 equiv). The glass vial was placed in a 150 ml stainless steel autoclave under air. The autoclave was pressurized and depressurized four times with hydrogen gas before the final hydrogen pressure was set to 50 bar. If not otherwise stated, the reaction mixture was stirred at 40 °C for 24 h. After the autoclave was carefully depressurized, Na_2CO_3 (64 mg, 4.0 equiv) was added and the mixture was filtered over celite using CH_2Cl_2. Mesitylene (20.9 µl) was added as internal standard and the product yield was determined using GC-FID. Enantiomeric excess of the product was determined using HPLC-UV analysis.

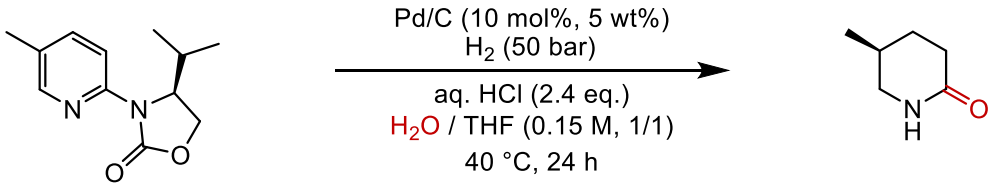
Table S1: Investigation of reaction parameters.[a]



entry	deviation	conversion	yield A	yield B
1	none	>95%	91%	<5%
2	H_2O/MeOH (1/1)	>95%	79%	5%
3	H_2O/MeCN (1/1)	36%	<5%	<5%
4	H_2O/dioxane (1/1)	>95%	29%	6%
5	H_2O only	>95%	84%	17%
6	THF only[b]	41%	19%[b]	<5%
7	formic acid instead HCl	>95%	<5%	>95%

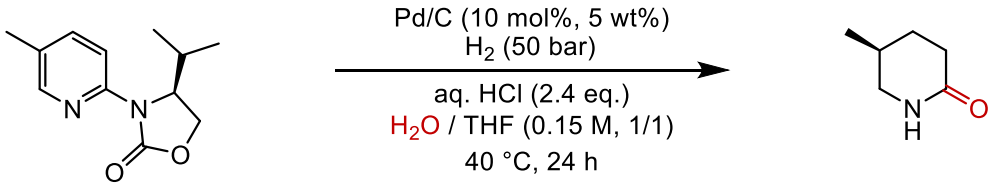
[a] After the autoclave was carefully depressurized, Na_2CO_3 (95 mg, 6.0 equiv) and CbzCl (63 µl. 3.0 equiv) were added, the mixture was stirred for 1 h at room temperature and filtered over celite using CH_2Cl_2. Mesitylene (20.9 µl) was added as internal standard and the product yield was determined using GC-FID.[b]H_2O is still present in the reaction mixture. Hydrochloric acid is added as aqueous solution and the Pd/C catalyst contains small amounts of water.

Table S2: Investigation of reaction parameters.



entry	deviation	yield	e.r.
1	none	91%	97:3
2	Pd/C (10 wt%)	57%	96:4
3	Pd/Rh/C (4.5 wt%, 0.5 wt%)	85%	96:4
4	Pd/Al_2O_3 (5 wt%)	65%	95:5
5	Pd/SiO_2	82%	94:6
6	$Pd(OH)_2/C$ (20 wt%)	92%	96:4
7	PtO_2	0%	n.d.
8	Ru/C (5 wt%)	19%	n.d.
9	Rh/C (5 wt%)	19%	97:3
10	(*S*)-4-benzyloxazolidin-2-one	90%	98:2
11	(*S*)-4-phenyloxazolidin-2-one	79%	95:5
12	(4*S*,5*R*)-5-methyl-4-phenyloxazolidin-2-one	88%	96:4
13	p = 25 bar	92%	95:5

4. Reaction-Condition-Based Sensitivity Assessment



Following a procedure recently developed by our group,[3] a reaction-condition-based sensitivity screen was conducted. Key reaction parameters were varied in a systematic manner and the reaction results were compared to the standard reaction conditions. Table S3 gives an overview of the experimental results.

Preparation of the stock solution: (*S*)-4-Isopropyl-3-(5-methylpyridin-2-yl)oxazolidin-2-one (991 mg, 4.5 mmol, 1.0 equiv.) was dissolved in THF (13.5 ml, 0.33 M).

Standard reaction conditions: n = 0.30 mmol, c = 0.15 M, V = 2 mL, T = 40 °C, $p(H_2)$ = 50 bar.

Standard reaction procedure: A 4 ml glass vial (screw-cap) equipped with a stir bar was charged with 5 wt% Pd/C (64 mg, 0.03 mmol, 10 mol%), stock solution (0.9 ml), THF (0.1 ml), H_2O (1.0 ml, total concentration c = 0.15 M, total volume V = 2 mL) and concentrated aqueous HCl (60 µl, 2.4 equiv.). The glass vial was placed in a 150 ml stainless steel autoclave under air. The autoclave was pressurized and depressurized four times with hydrogen gas before the final hydrogen pressure was set to 50 bar. The reaction mixture was stirred at 40 °C for 24 h. After the autoclave was carefully depressurized, Na_2CO_3 (212 mg, 4.0 equiv) was added and the mixture was filtered over celite using CH_2Cl_2. Mesitylene (20.9 µl) was added as internal standard and the product yield was determined using GC-FID. Enantiomeric excess of the product was determined using HPLC-UV analysis.

Big scale conditions: n = 8.05 mmol, c = 0.15 M, V = 54 mL, air atmosphere, T = 40 °C, $p(H_2)$ = 50 bar. (*S*)-4-Isopropyl-3-(6-propylpyridin-2-yl)oxazolidin-2-one was used. The reaction outcome was compared to the synthesis of compound **4**.

Analysis: By systematic variation we determined the influence of the reaction parameters of concentration, temperature, hydrogen pressure and oxygen content on the reaction outcome. Interestingly, small changes in these reaction parameters show only minor effects on the reaction yield. It is worth mentioning that the reaction shows minimal deviation when tap water is used as solvent instead of demineralized water.

Table S3: Investigation of the reaction-condition-based sensitivity.

entry	experiment	deviation	yield	yield dev.	e.r.	e.r. dev.
1	standard	none	91%	-	97:3	-
2	high *c*	no extra THF, 1.0 ml H_2O	99%	+9%	97:3	±0%
3	low *c*	+0.1 ml THF, +0.1 ml H_2O	85%	–7%	98:2	+1%
4	tap H_2O	1.0 ml tap H_2O	99%	+9%	97:3	±0%
5	low O_2	degassed solvent, setup under Argon	98%	+8%	97:3	±0%
6	high O_2	autoclave was not flushing	87%	–4%	97:3	±0%
7	low *T*	*T* = 30 °C	92%	+1%	98:2	+1%
8	high *T*	*T* = 50 °C	96%	+5%	97:3	±0%
9	low *p*	*p* = 40 bar	99%	+9%	97:3	±0%
10	high *p*	*p* = 60 bar	97%	+7%	97:3	±0%
11	big scale	*n*(substrate) = 8.05 mmol	78%*	–7%	97:3	–4%

* (*S*)-4-Isopropyl-3-(6-propylpyridin-2-yl)oxazolidin-2-one was used and the reaction outcome was compared to the synthesis of compound **4**.

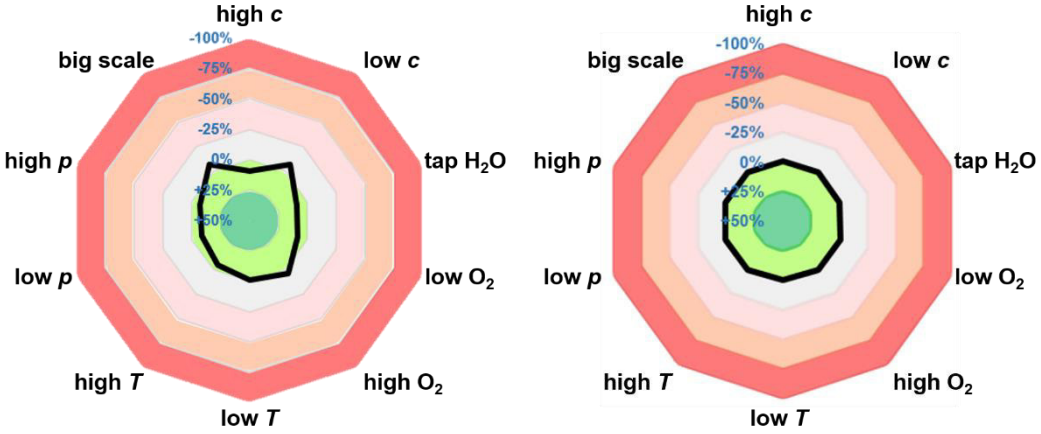
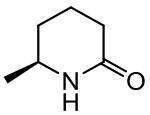


Figure S1: Radar diagrams of the reaction-condition-based sensitivity assessment for reaction yield (left-hand side) and enantiomeric excess (right-hand side).

5. Catalytic Hydrogenation Reactions

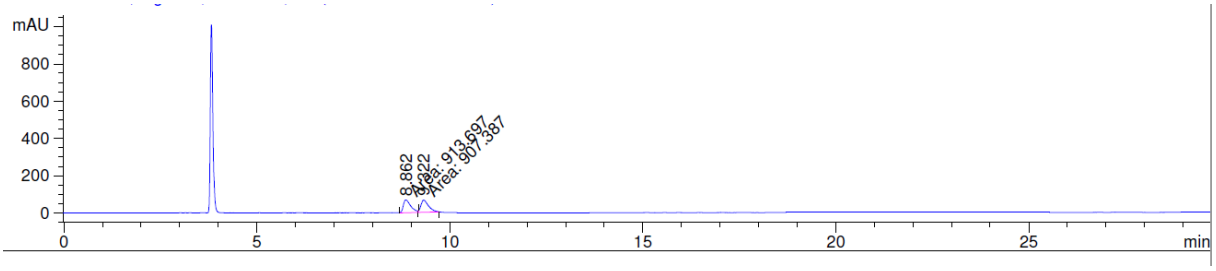
General Procedure for the hydrogenation of oxazolidinone-substituted pyridines:

A 4 ml glass vial (screw-cap) equipped with a stir bar was charged with 5 wt% Pd/C (64 mg, 0.03 mmol, 10 mol%) and solid oxazolidinone-substituted pyridine (0.3 mmol, 1.0 equiv.). THF (1 mL) and H_2O (1 mL) were added (2 mL / 0.15 M in total) followed by the addition of liquid oxazolidinone-substituted pyridine (0.3 mmol, 1.0 equiv.) and concentrated aqueous HCl (60 µl, 2.4 equiv.). The glass vial was placed in a 150 ml stainless steel autoclave under air. The autoclave was pressurized and depressurized four times with hydrogen gas before the final hydrogen pressure was set to 50 bar. If not otherwise stated, the reaction mixture was stirred at 40 °C for 24 h. After the autoclave was carefully depressurized, Na_2CO_3 (127 mg, 4.0 equiv) was added and the mixture was filtered over celite using CH_2Cl_2. The solvent was removed *in vacuo* and the product was purified using column chromatography on silica gel. The diastereoselectivities were determined by GC-MS analysis of the basified reaction mixture. Enantiomeric excess of the product was determined after column chromatography using HPLC-UV or GC-FID analysis. The racemic products were prepared by hydrogenation of pyridines with unsubstituted oxazolidinone.



(*S*)-6-Methylpiperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(6-methylpyridin-2-yl)oxazolidin-2-one (66 mg, 0.30 mmol, 1.0 equiv.). The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (30 mg, 0.27 mmol, 89%, 98:2 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 88:12, flow rate = 1 mL/min, λ = 210 nm, retention time: 9.0 min (minor), 9.3 min (major).

^{1}H NMR (400 MHz, Chloroform-*d*) 6.66 (s, 1H), 3.54 – 3.41 (m, 1H), 2.40 – 2.16 (m, 2H), 1.92 – 1.80 (m, 2H), 1.74 – 1.58 (m, 1H), 1.36 – 1.24 (m, 1H), 1.16 (d, *J* = 6.4 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.6, 48.8, 31.1, 30.5, 22.8, 19.9. **HRMS** (ESI) m/z calculated for [$C_6H_{11}NONa$] ([M+Na^+]) 136.0733, found 136.0730.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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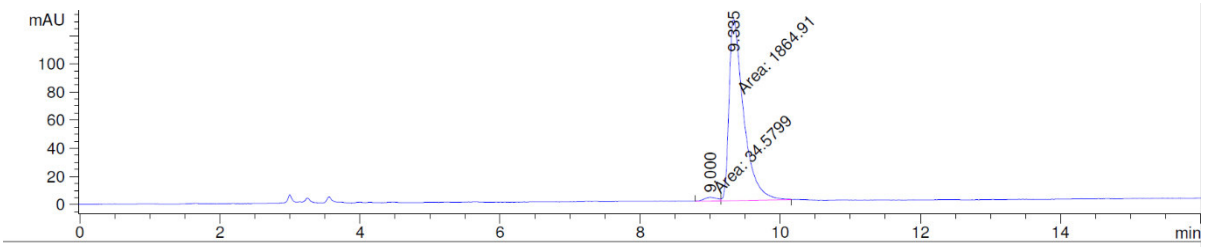
2	9.322	MM	0.2299	907.38702	65.77692	49.8267



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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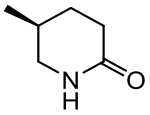
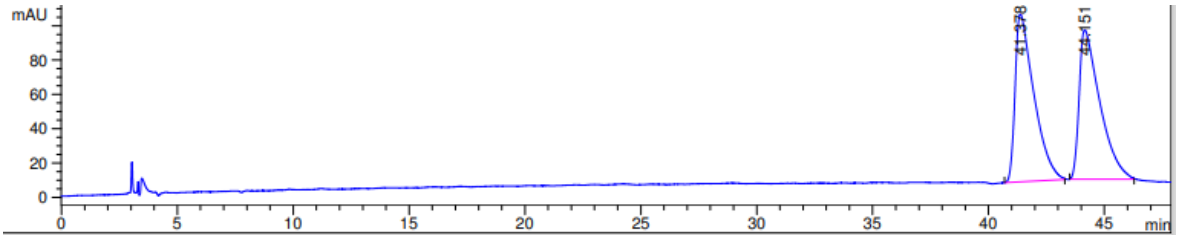
2	9.335	FM	0.2415	1864.90796	128.68031	98.1795

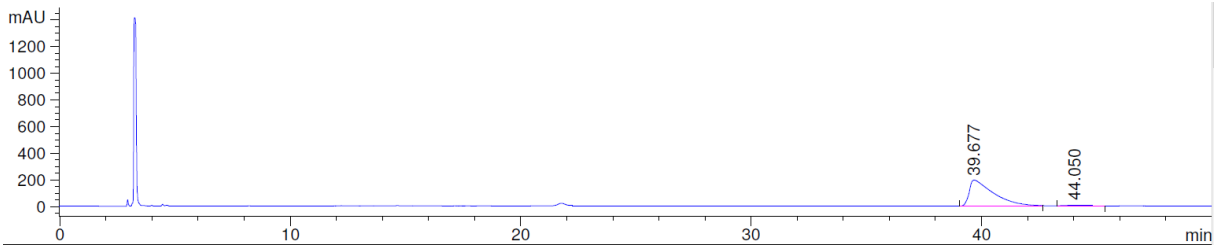


(*S*)-5-Methylpiperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(5-methylpyridin-2-yl)oxazolidin-2-one (66 mg, 0.30 mmol, 1.0 equiv.). The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as colorless liquid (31 mg, 0.27 mmol, 90%, 98:2 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 97:3, flow rate = 1 mL/min, λ = 210 nm, retention time: 39.7 min (major), 44.1 min (minor).

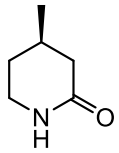
^{1}H NMR (400 MHz, Chloroform-*d*) 6.40 (s, 1H), 3.33 – 3.23 (m, 1H), 2.96 – 2.84 (m, 1H), 2.47 – 2.26 (m, 2H), 1.98 – 1.78 (m, 2H), 1.54 – 1.39 (m, 1H), 1.00 (d, *J* = 6.6 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.5, 49.3, 30.9, 29.2, 28.3, 18.5. **HRMS** (ESI) m/z calculated for [$C_6H_{11}NONa$] ([M+Na$^+$]) 136.0733, found 136.0732.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.378	BB	0.7286	5521.03076	97.80560	50.5098
2	44.151	BB	0.7318	5409.58691	87.07893	49.4902

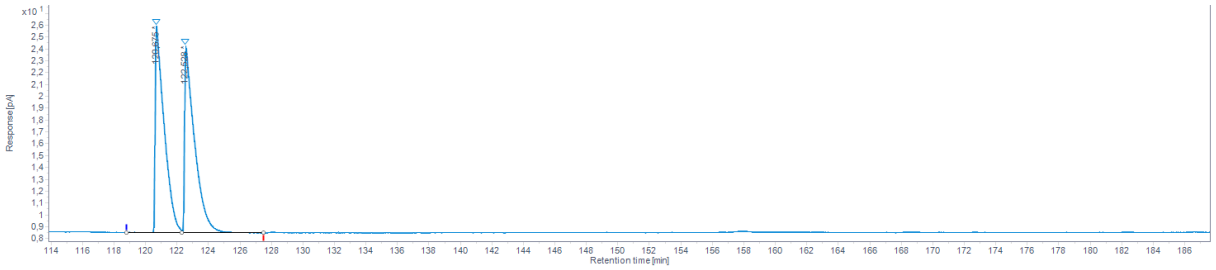


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.677	BB	0.9066	1.39387e4	193.22797	98.3977
2	44.050	BB	0.6088	226.97058	4.39307	1.6023

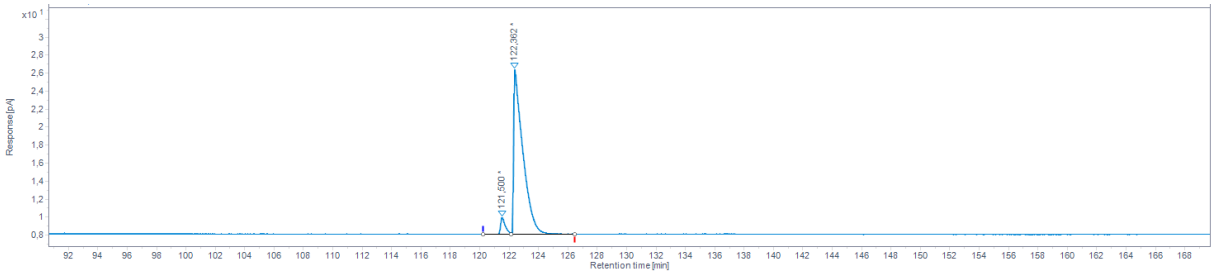


(*R*)-4-Methylpiperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(4-methylpyridin-2-yl)oxazolidin-2-one (66 mg, 0.30 mmol, 1.0 equiv.). The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (30 mg, 0.26 mmol, 87%, 95:5 e.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 5 °C/min to 80 °C, then 0.5 °C/min to 220 °C).

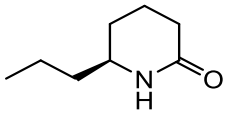
^{1}H NMR (400 MHz, Chloroform-*d*) 6.28 (s, 1H), 3.39 – 3.25 (m, 2H), 2.50 – 237 (m, 1H), 2.00 – 1.89 (m, 2H), 1.86 – 1.77 (m, 1H), 1.48 – 1.35 (m, 1H), 1.02 (d, *J* = 6.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.6, 41.4, 39.8, 30.2, 27.7, 21.2. **HRMS** (ESI) m/z calculated for [$C_6H_{11}NONa$] ([M+Na$^+$]) 136.0733, found 136.0731.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	120,675	686,749	49,943	17,382	52,46			118,775	122,313
2		FID1A	122,528	688,317	50,057	15,750	47,54			122,313	127,472

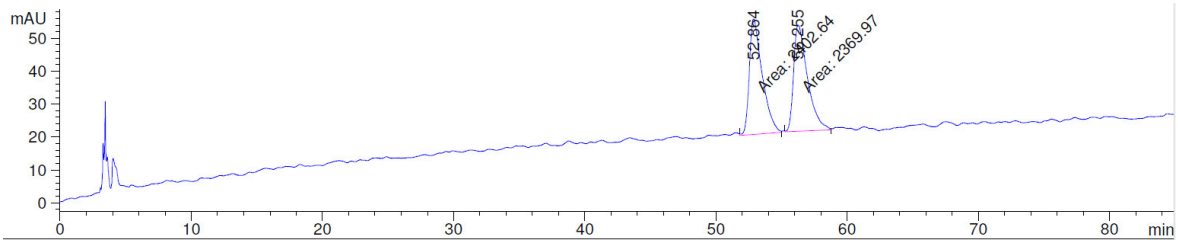


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	121,500	39,752	4,799	1,844	9,17			120,250	122,158
2		FID1A	122,362	788,583	95,201	18,269	90,83			122,158	126,448

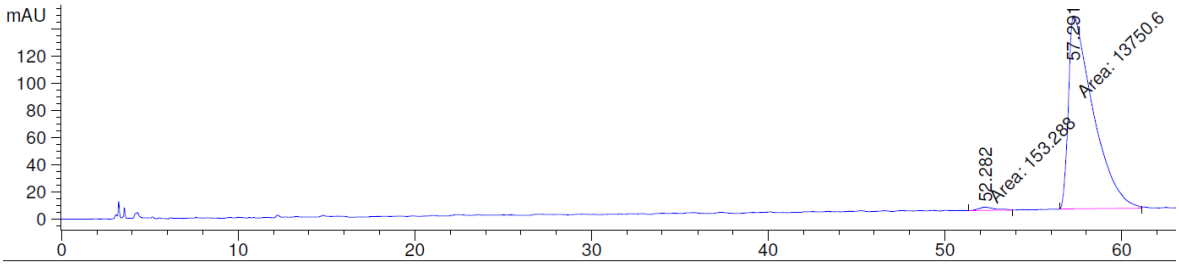


(*S*)-6-Propylpiperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-(*tert*-butyl)-3-(6-propylpyridin-2-yl)oxazolidin-2-one (79 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (32 mg, 0.25 mmol, 84%, 99:1 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 98:2, flow rate = 1 mL/min, λ = 210 nm, retention time: 52.3 min (minor), 57.3 min (major).

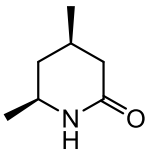
^{1}H NMR (400 MHz, Chloroform-*d*) 5.93 (s, 1H), 3.40 – 3.28 (m, 1H), 2.46 – 2.32 (m, 1H), 2.32 – 2.21 (m, 1H), 1.95 – 1.83 (m, 2H), 1.75 – 1.60 (m, 1H), 1.49 – 1.27 (m, 5H), 0.93 (t, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.4, 53.1, 39.3, 31.5, 28.6, 20.0, 18.6, 14.0. **HRMS** (ESI) m/z calculated for [$C_8H_{15}NONa$] ([M+Na$^+$]) 164.1046, found 164.1042.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	52.864	MM	1.1407	2402.63818	35.10623	50.3423
2	56.255	MM	1.2262	2369.96851	32.21357	49.6577

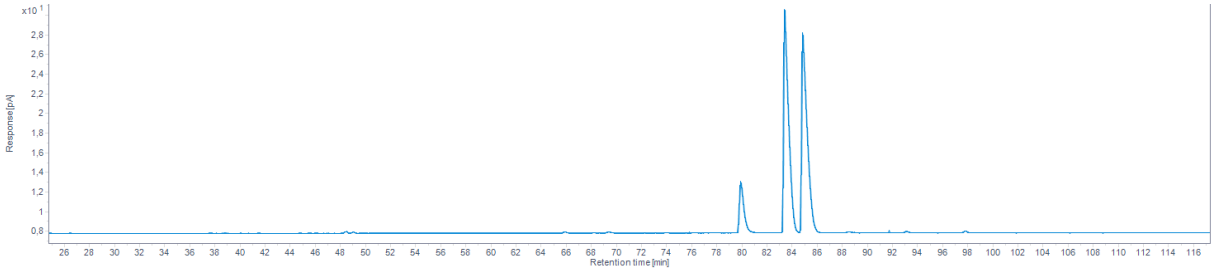


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	52.282	MM	1.0781	153.28813	2.36983	1.1025
2	57.291	MM	1.6157	1.37506e4	141.84796	98.8975

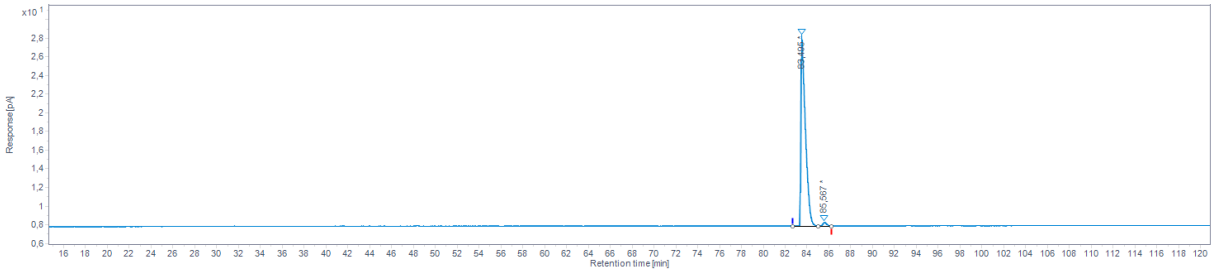


(4*R*,6*S*)-4,6-Dimethylpiperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-benzyl-3-(4,6-dimethylpyridin-2-yl)oxazolidin-2-one (85 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (25 mg, 0.20 mmol, 66%, 98:2 e.r., >95:5 d.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 5 °C/min to 100 °C, then 0.5 °C/min to 150 °C, and 5 °C to 220 °C).

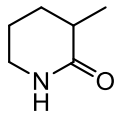
^{1}H NMR (400 MHz, Chloroform-*d*) 6.21 (s, 1H), 3.48 (tt, *J* = 10.4, 6.3 Hz, 1H), 2.47 – 2.33 (m, 1H), 1.98 – 1.78 (m, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.07 – 0.96 (m, 1H), 0.99 (d, *J* = 6.1 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.5, 48.8, 39.7, 27.9, 22.9, 21.6. **HRMS** (ESI) m/z calculated for [$C_7H_{13}NONa$] ([M+Na^+]) 150.0900, found 150.0889.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	83,372	613,566	50,086	22,781	52,86			83,036	84,558
2		FID1A	84,817	611,449	49,914	20,317	47,14			84,558	86,607

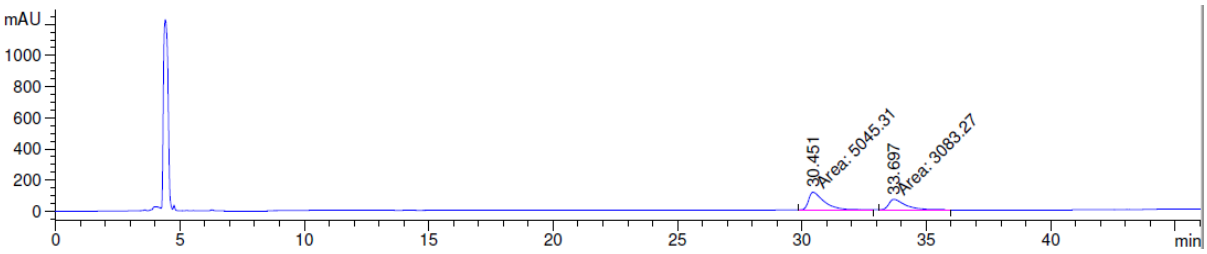


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	83,495	572,553	98,304	20,437	98,11			82,642	84,983
2		FID1A	85,567	9,876	1,696	0,394	1,89			84,983	86,191

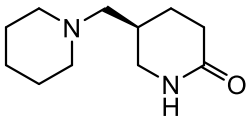


3-Methylpiperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(3-methylpyridin-2-yl)oxazolidin-2-one (66 mg, 0.30 mmol, 1.0 equiv.). The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as colorless liquid (14 mg, 0.12 mmol, 40%, 62:38 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 97:3, flow rate = 1 mL/min, λ = 210 nm, retention time: 30.5 min (major), 33.7 min (minor). Due to problems in the preparation of a racemic reference sample only the HPLC trace of the product is given. The diminished enantiomeric ratio of the product might be caused by steric repulsion of the pyridine and oxazolidinone substituents. Therefore, the formation of a stable conformer upon protonation is hampered if the pyridine 3-position is substituted (see page S51–S52 for further details).

^{1}H NMR (400 MHz, Chloroform-*d*) 5.98 (s, 1H), 3.33 – 3.27 (m, 2H), 2.44 – 2.32 (m, 1H), 2.02 – 1.92 (m, 1H), 1.91 – 1.81 (m, 1H), 1.80 – 1.68 (m, 1H), 1.55 – 1.44 (m, 1H), 1.24 (d, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 175.8, 42.9, 36.2, 29.4, 21.6, 17.6. **HRMS** (ESI) m/z calculated for [$C_6H_{11}NONa$] ([M+Na^+]) 136.0733, found 136.0732.

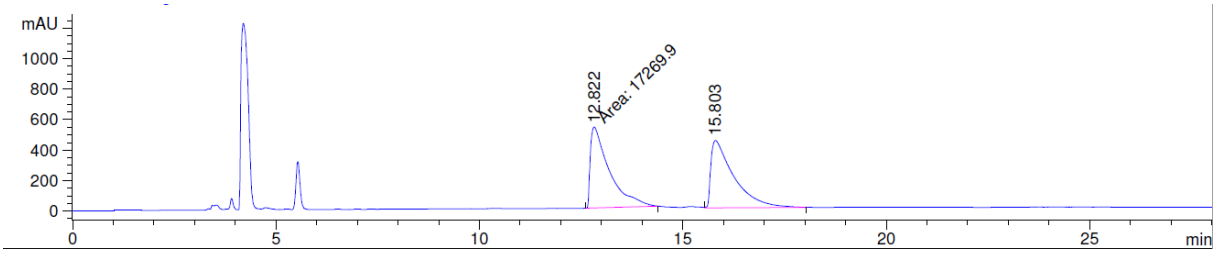


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.451	MM	0.7362	5045.30859	114.22527	62.0687
2	33.697	MM	0.7634	3083.27295	67.31745	37.9313

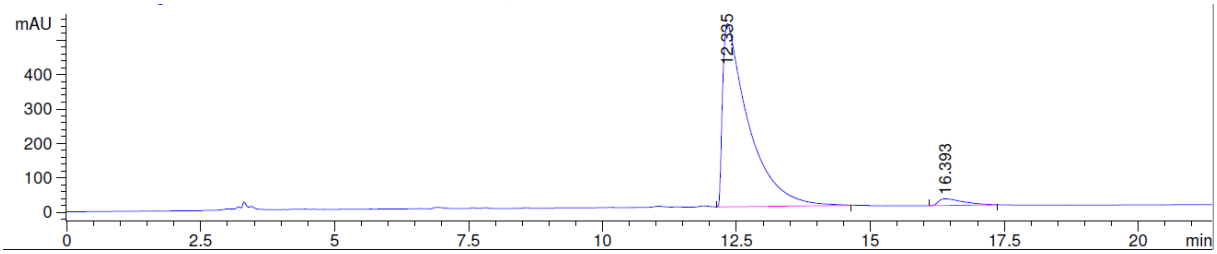


(*S*)-5-(Piperidin-1-ylmethyl)piperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(5-(piperidin-1-ylmethyl)pyridin-2-yl)oxazolidin-2-one (91 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 95:5, 90:10, 80:20) as off-white solid (38 mg, 0.19 mmol, 65%, 97:3 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK AD-H, *n*-hexane:2-propanol = 90:10, flow rate = 1 mL/min, λ = 210 nm, retention time: 12.3 min (major), 16.4 min (minor).

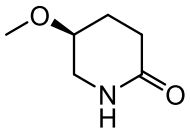
^{1}H NMR (400 MHz, Chloroform-*d*) 6.18 (s, 1H), 3.48 – 3.38 (m, 1H), 3.05 – 2.92 (m, 1H), 2.51 – 2.21 (m, 8H), 2.12 – 1.98 (m, 1H), 1.94 – 1.85 (m, 1H), 1.65 – 1.38 (m, 7H). **^{13}C{^{1}H}-NMR (101 MHz, $CDCl_3$):** 172.5, 62.1, 55.2, 46.6, 30.8, 30.6, 25.9, 25.7, 24.4. **HRMS** (ESI) m/z calculated for [$C_{11}H_{10}N_2ONa$] ([M+Na$^+$]) 219.1479, found 219.1466.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.822	MM	0.5403	1.72699e4	532.73193	50.0875
2	15.803	VB	0.5221	1.72096e4	442.18750	49.9125

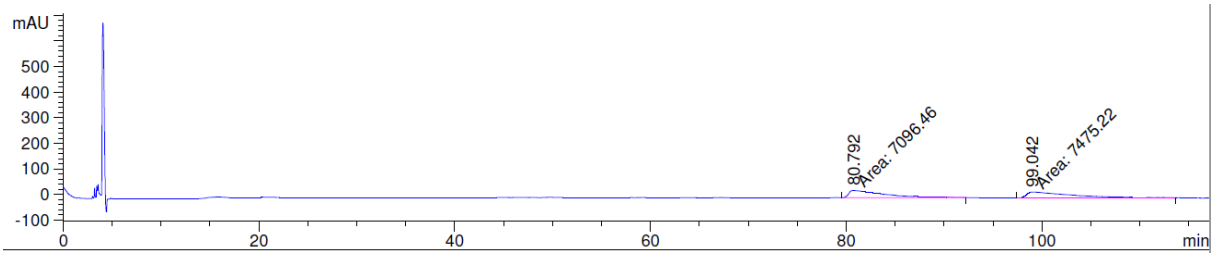


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.335	VB	0.4482	1.78498e4	532.32013	96.5402
2	16.393	BB	0.3895	639.69379	19.51378	3.4598

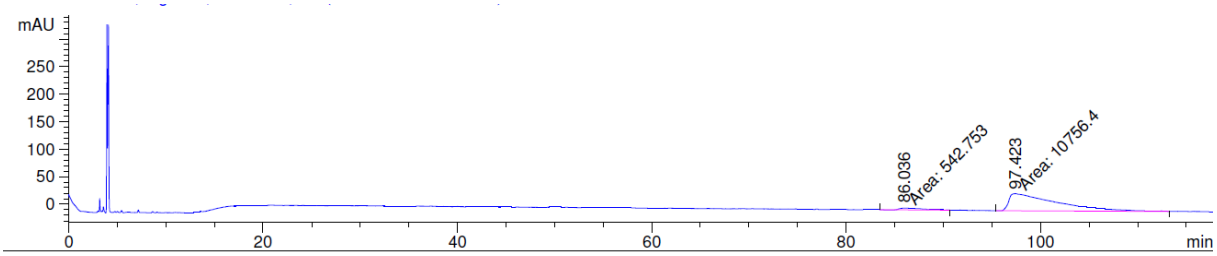


(*S*)-5-Methoxypiperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-benzyl-3-(5-methoxypyridin-2-yl)oxazolidin-2-one (71 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as colorless liquid (32 mg, 0.30 mmol, 99%, 95:5 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 97:3, flow rate = 1 mL/min, λ = 210 nm, retention time: 86.0 min (minor), 97.4 min (major).

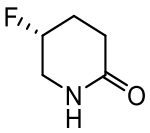
^{1}H NMR (400 MHz, Chloroform-*d*) 7.01 (s, 1H), 3.57 (ddd, *J* = 6.7, 5.5, 3.6 Hz, 1H), 3.43 – 3.25 (m, 1H), 3.33 (s, 3H), 2.46 (ddd, *J* = 17.7, 9.3, 6.4 Hz, 1H), 2.26 (dt, *J* = 17.8, 6.0 Hz, 1H), 2.03 – 1.82 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.3, 71.8, 56.2, 45.6, 27.4, 24.9. **HRMS** (ESI) m/z calculated for [$C_6H_{11}NO_2Na$] ([M+Na$^+$]) 152.0682, found 152.0678.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	80.792	MM	4.1233	7096.45654	28.68446	48.7003
2	99.042	MM	5.4963	7475.21973	22.66737	51.2997

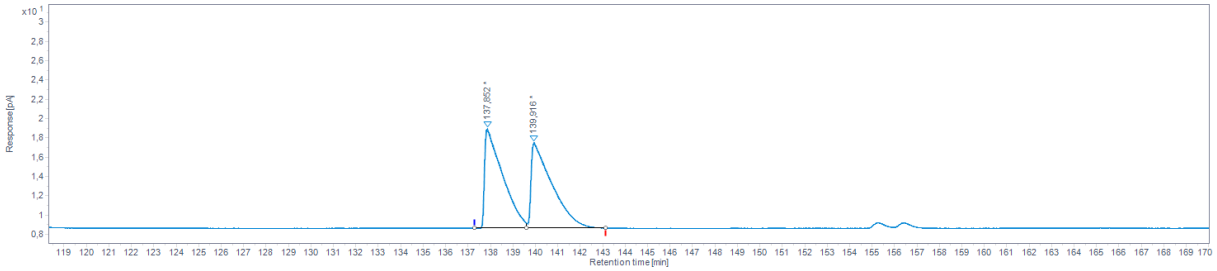


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	86.036	MM	2.7654	542.75256	3.27108	4.8035
2	97.423	MM	5.7950	1.07564e4	30.93561	95.1965

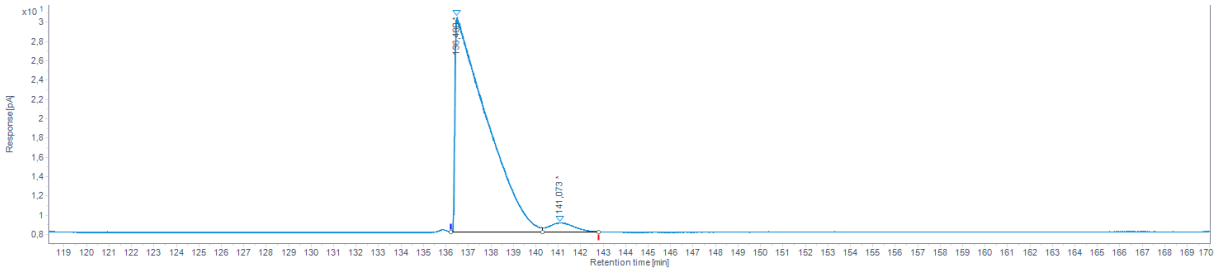


(*R*)-5-Fluoropiperidin-2-one: The title compound was prepared following a modification of the General Procedure using (*R*)-3-(5-fluoropyridin-2-yl)-4-isopropyloxazolidin-2-one (112 mg, 0.50 mmol, 1.0 equiv.), 20 wt% $Pd(OH)_2/C$ (17.6 mg, 5 mol%), aq. HCl (100 µl, 2.4 equiv., 12 M) in H_2O/THF (0.5 M, 1/1). The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3, 95:5) as off-white solid (37 mg, 0.32 mmol, 64%, 97:3 e.r.) accompanied with traces of defluorinated piperidone. The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 5 °C/min to 80 °C, then 0.5 °C/min to 120 °C, hold for 10 min, 0.5 °C/min to 125 °C, hold for 10 min, 0.5 °C/min to 130 °C, hold for 10 min, 0.5 °C/min to 135 °C, hold for 10 min, 0.5 °C/min to 140 °C, hold for 10 min, 0.5 °C/min to 160 °C, and 5 °C/min to 220 °C.

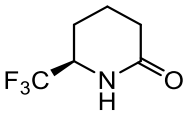
^{1}H NMR (400 MHz, Chloroform-*d*) 7.33 (s, 1H), 4.94 (dm, *J* = 48.0 Hz, 1H), 3.61 – 3.36 (m, 2H), 2.58 – 2.45 (m, 1H), 2.37 – 2.26 (m, 1H), 2.25 – 2.13 (m, 1H), 2.03 – 1.80 (m, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 171.7, 84.1 (d, *J* = 173.4 Hz), 46.6 (d, *J* = 23.2 Hz), 26.1 (d, *J* = 5.3 Hz), 25.6 (d, *J* = 21.2 Hz). **^{19}F NMR** (376 MHz, Chloroform-*d*) –187.1. **HRMS** (ESI) m/z calculated for [C_5H_8NOFNa] ([M+Na$^+$]) 140.0482, found 140.0482.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	137,852	572,392	50,054	10,277	53,77			137,264	139,616
2		FID1A	139,916	571,153	49,946	8,834	46,23			139,616	143,107

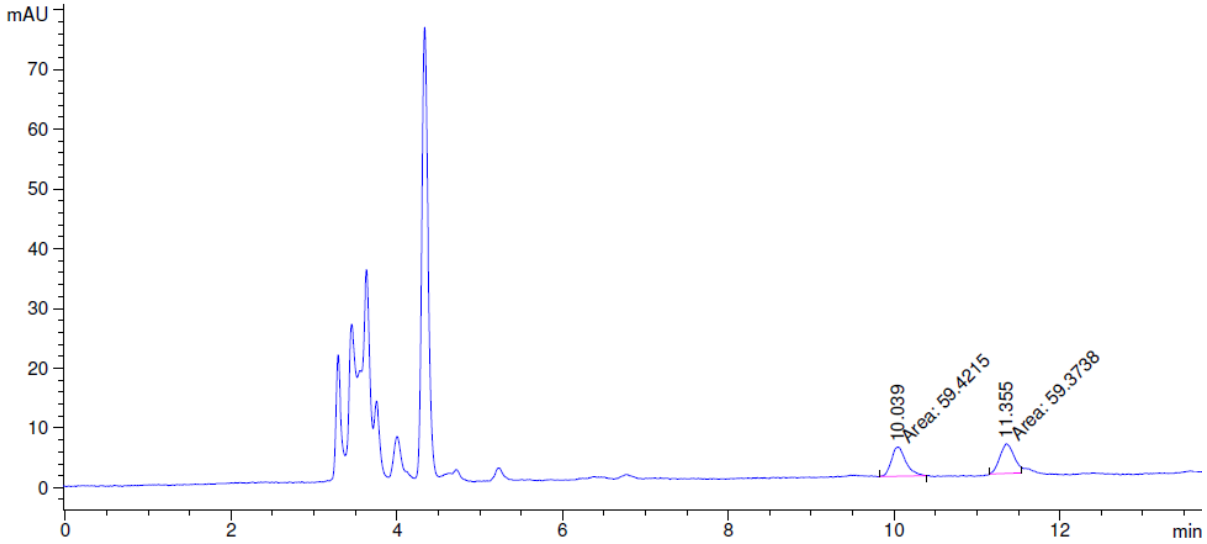


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	136,480	2162,445	96,702	22,241	95,92			136,198	140,277
2		FID1A	141,073	73,750	3,298	0,946	4,08			140,277	142,776

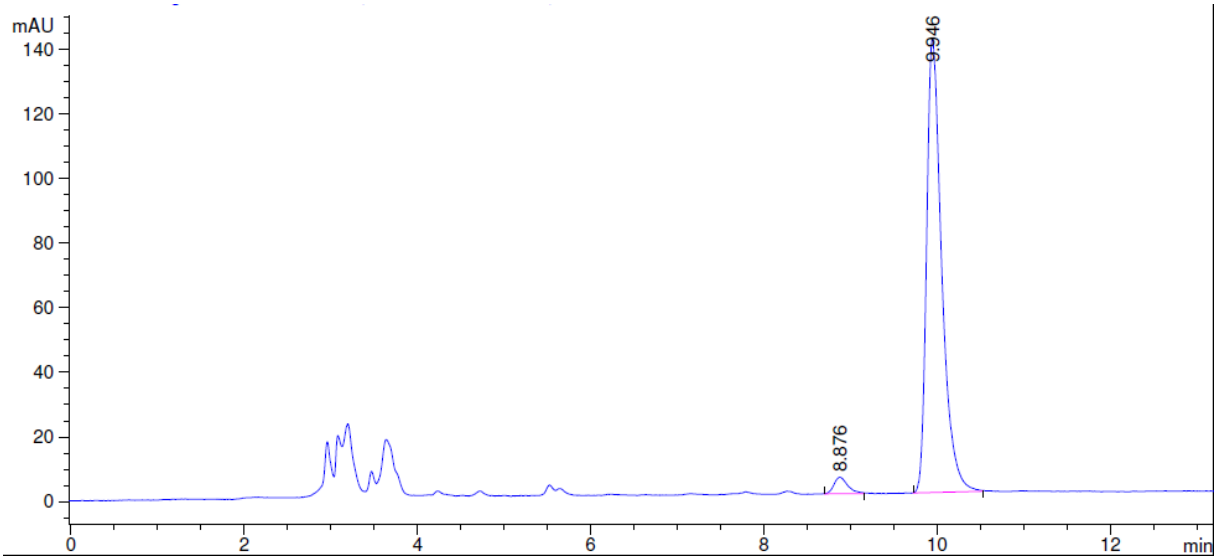


(*R*)-6-(Trifluoromethyl)piperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-benzyl-3-(6-(trifluoromethyl)pyridin-2-yl)oxazolidin-2-one (97 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3, 95:5) as white solid (16 mg, 0.10 mmol, 32%, 97:3 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 97:3, flow rate = 1 mL/min, λ = 210 nm, retention time: 8.9 min (minor), 9.9 min (major).

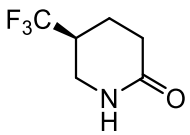
^{1}H NMR (400 MHz, Chloroform-*d*) 6.43 (s, 1H), 3.99 – 3.85 (m, 1H), 2.50 – 2.29 (m, 2H), 2.13 – 1.95 (m, 2H), 1.92 – 1.69 (m, 2H), 1.30 – 1.18 (m, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.2, 124.7 (q, J = 281.0 Hz), 54.1 (q, J = 30.9 Hz), 31.3, 21.2 (q, J = 1.9 Hz), 18.4. **^{19}F NMR** (376 MHz, Chloroform-*d*) –78.0. **HRMS** (ESI) m/z calculated for [$C_6H_8NOF_3Na$] ([M+Na$^+$]) 190.0450, found 190.0450.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.039	MM	0.2041	59.42149	4.85253	50.0201
2	11.355	MM	0.1986	59.37382	4.98265	49.9799

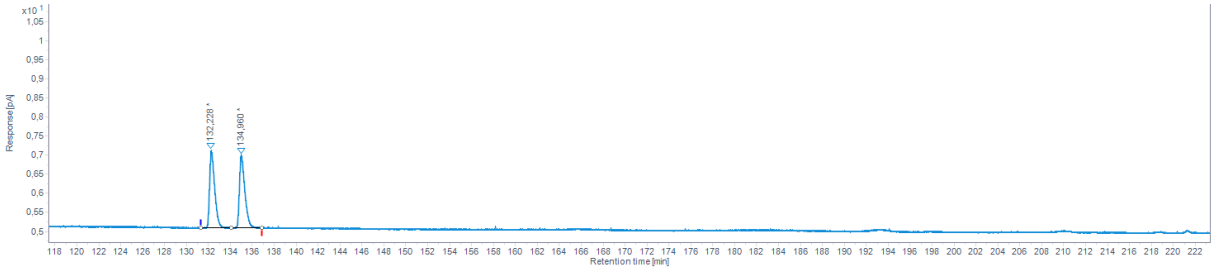


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.876	BB	0.1516	55.62970	5.04680	3.1631
2	9.946	BB	0.1826	1703.10596	140.34044	96.8369

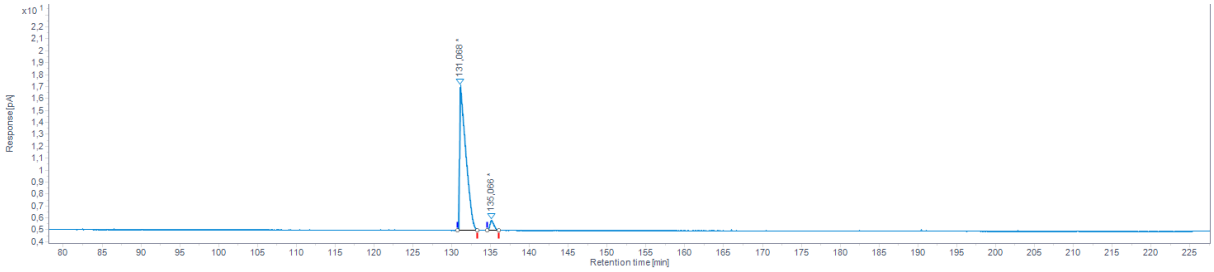


(*S*)-5-(Trifluoromethyl)piperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(5-(trifluoromethyl)pyridin-2-yl)oxazolidin-2-one (82 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3, 95:5) as off-white solid (33 mg, 0.20 mmol, 66%, 96:4 e.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 0.5 °C/min).

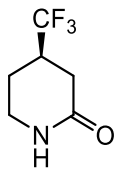
^{1}H NMR (400 MHz, Chloroform-*d*) 7.30 (s, 1H), 3.56 – 3.45 (m, 1H), 3.34 (t, *J* = 11.4 Hz, 1H), 2.63 – 2.45 (m, 2H), 2.36 (ddd, *J* = 18.0, 11.5, 6.6 Hz, 1H), 2.16 – 2.06 (m, 1H), 1.86 (dtd, *J* = 13.5, 11.5, 6.1 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 171.6, 126.5 (q, *J* = 278.5 Hz), 40.6 (q, *J* = 3.3 Hz), 38.0 (q, *J* = 27.9 Hz), 29.6, 20.3 (d, *J* = 2.5 Hz). **^{19}F NMR** (376 MHz, Chloroform-*d*) –72.2. **HRMS** (ESI) m/z calculated for [$C_6H_8NOF_3Na$] ([M+Na$^+$]) 190.0450, found 190.0449.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	132,228	64,287	49,650	2,038	51,47			131,333	134,043
2		FID1A	134,960	65,192	50,350	1,921	48,53			134,043	136,829



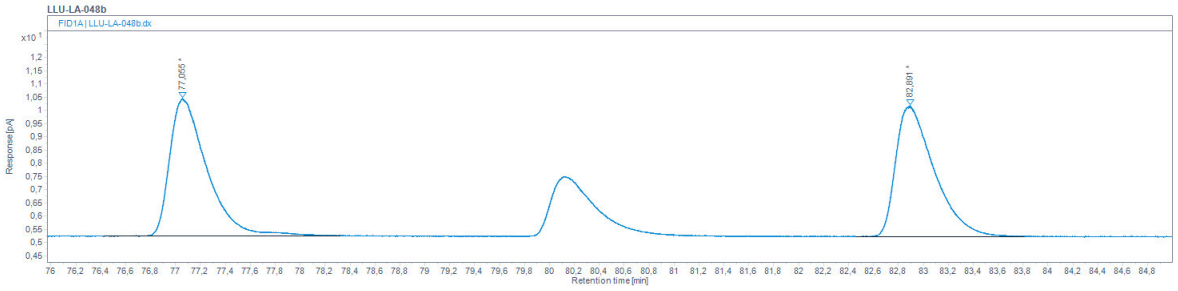
#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	131,068	667,395	95,917	12,138	93,64			130,708	133,318
2		FID1A	135,066	28,407	4,083	0,824	6,36			134,593	136,034



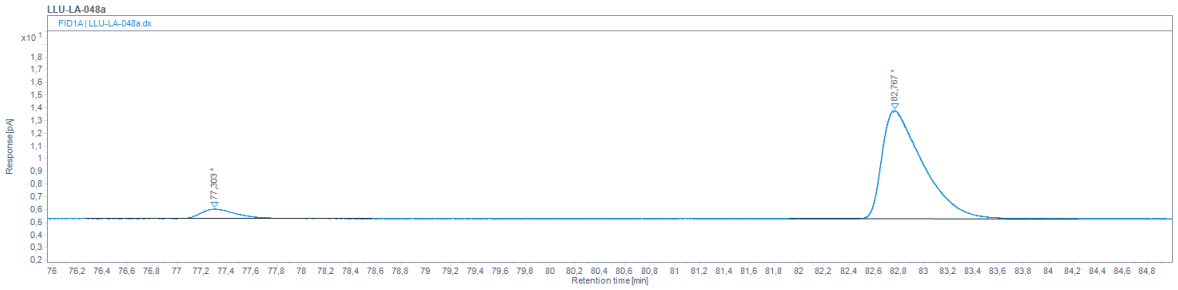
(*R*)-4-(Trifluoromethyl)piperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-benzyl-3-(4-(trifluoromethyl)pyridin-2-yl)oxazolidin-2-one (97 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent:

CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3, 95:5) as off-white solid (33 mg, 0.20 mmol, 66%, 93:7 e.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 0.5 °C/min to 220 °C).

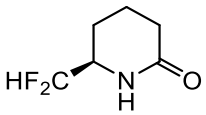
^{1}H NMR (400 MHz, Chloroform-*d*) 6.69 (s, 1H), 3.50 – 3.40 (m, 1H), 3.39 – 3.28 (m, 1H), 2.67 – 2.52 (m, 2H), 2.45 – 2.33 (m, 1H), 2.17 – 2.06 (m, 1H), 1.85 – 1.72 (m, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 169.6, 126.6 (q, *J* = 278.3 Hz), 40.4, 37.8 (q, *J* = 28.7 Hz), 30.5 (q, *J* = 2.5 Hz), 21.7 (q, *J* = 2.8 Hz). **^{19}F NMR** (376 MHz, Chloroform-*d*) –74.0. **HRMS** (ESI) m/z calculated for [$C_6H_8NOF_3Na$] ([M+Na$^+$]) 190.0450, found 190.0449.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	77,055	108,228	50,565	5,202	51,28			76,426	78,317
2		FID1A	82,891	105,810	49,435	4,942	48,72			82,457	83,811

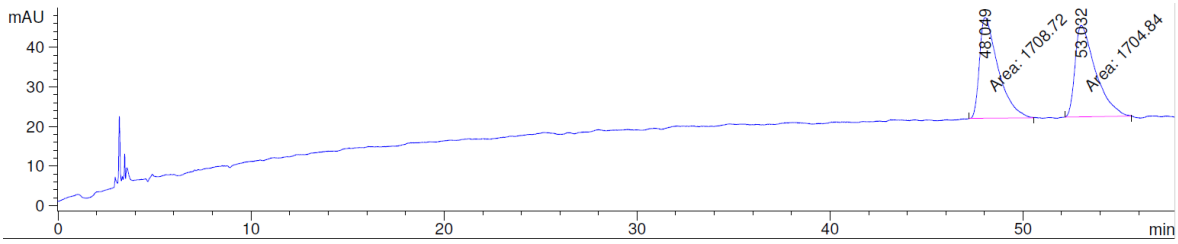


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	77,303	14,418	6,928	0,757	8,15			76,255	78,573
2		FID1A	82,767	193,686	93,072	8,533	91,85			81,922	84,240

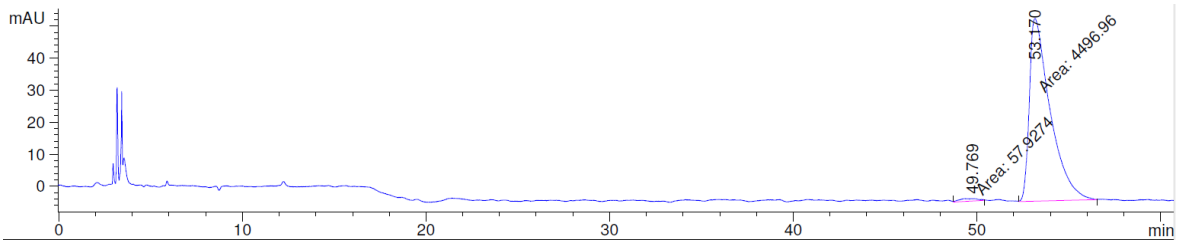


(*R*)-6-(Difluoromethyl)piperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-benzyl-3-(6-(difluoromethyl)pyridin-2-yl)oxazolidin-2-one (91 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3, 95:5) as white solid (33 mg, 0.22 mmol, 73%, 99:1 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 97:3, flow rate = 1 mL/min, λ = 210 nm, retention time: 49.8 min (minor), 53.2 min (major).

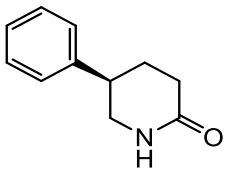
^{1}H NMR (400 MHz, Chloroform-*d*) 6.10 (s, 1H), 5.61 (ddd, *J* = 56.5, 55.3, 5.3 Hz, 1H), 3.76 – 3.58 (m, 1H), 2.51 – 2.28 (m, 2H), 2.07 – 1.89 (m, 2H), 1.84 – 1.60 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.1, 115.7 (t, *J* = 244.6 Hz), 54.5 (dd, *J* = 25.8, 20.7 Hz), 31.5, 22.1 (dd, *J* = 4.7, 2.7 Hz), 18.9. **^{19}F NMR** (376 MHz, Chloroform-*d*) –125.8 (d, *J* = 288.0 Hz), -128.0 (d, *J* = 287.9 Hz). **HRMS** (ESI) m/z calculated for [$C_6H_9NOF_2Na$] ([M+Na$^+$]) 172.0544, found 172.0541.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.049	MM	1.1187	1708.71570	25.45671	50.0567
2	53.032	MM	1.2330	1704.84497	23.04412	49.9433

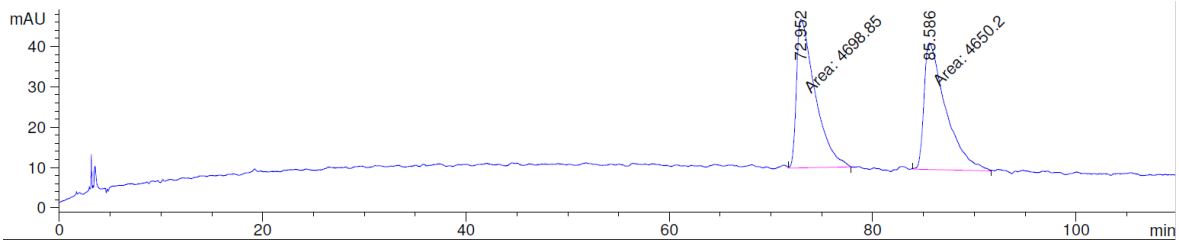


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	49.769	MM	1.2831	57.92736	7.52429e-1	1.2718
2	53.170	MM	1.3129	4496.96436	57.08585	98.7282

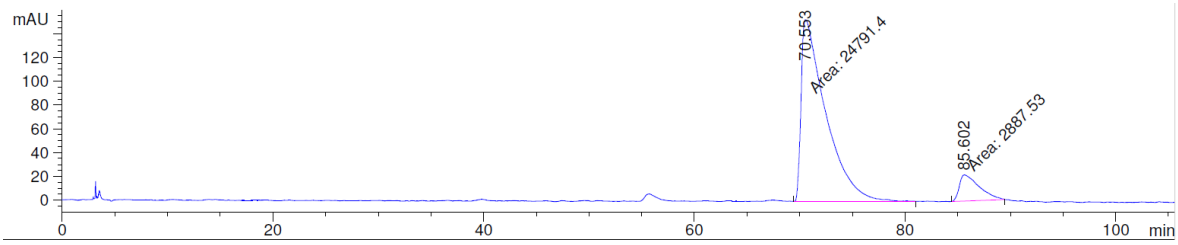


(*R*)-5-Phenylpiperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-benzyl-3-(5-phenylpyridin-2-yl)oxazolidin-2-one (99 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3, 95:5) as off-white solid (39 mg, 0.22 mmol, 74%, 90:10 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 97:3, flow rate = 1 mL/min, λ = 210 nm, retention time: 70.6 min (major), 85.6 min (minor).

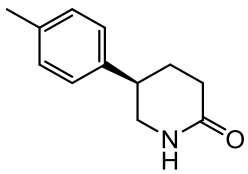
^{1}H NMR (400 MHz, Chloroform-*d*) 7.30 – 7.24 (m, 2H), 7.23 – 7.16 (m, 3H), 6.29 (s, 1H), 3.47 – 3.40 (m, 1H), 3.35 – 3.27 (m, 1H), 3.04 – 2.93 (m, 1H), 2.54 – 2.37 (m, 2H), 2.09 – 1.93 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.0, 141.9, 128.9, 127.3, 127.1, 48.8, 39.7, 31.4, 27.9. **HRMS** (ESI) m/z calculated for [$C_{11}H_{13}NONa$] ([M+Na$^+$]) 198.0889, found 198.0887.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	72.952	MM	2.1268	4698.85156	36.82318	50.2602
2	85.586	MM	2.4694	4650.19727	31.38603	49.7398



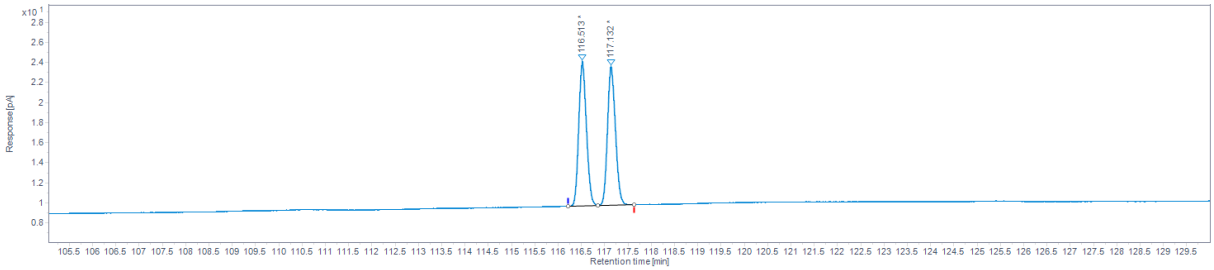
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	70.553	MM	2.7016	2.47914e4	152.94334	89.5678
2	85.602	MM	2.1833	2887.53003	22.04277	10.4322



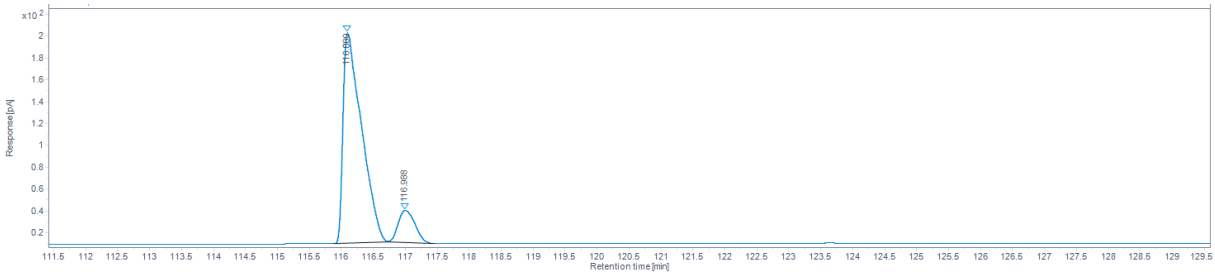
(*R*)-5-(*p*-Tolyl)piperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(5-(*p*-tolyl)pyridin-2-yl)oxazolidin-2-one (89 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (37 mg, 0.19 mmol, 65%, 88:12 e.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 5 °C/min to 120 °C, then 1 °C/min to 220 °C).

^{1}H NMR (400 MHz, Chloroform-*d*) 7.23 – 6.93 (m, 5H), 3.47 – 3.35 (m, 1H), 3.34 – 3.21 (m, 1H), 2.94 (ddt, *J* = 15.8, 10.7, 5.4 Hz, 1H), 2.44 (dtd, *J* = 13.3, 10.2, 8.3, 4.2 Hz, 2H), 2.31 – 2.20 (m, 3H), 2.06 –

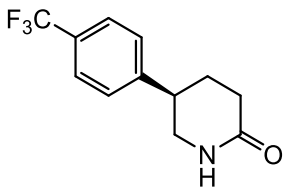
1.90 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.3, 138.8, 136.7, 129.4, 126.8, 48.6, 39.1, 31.3, 27.9, 21.0. **HRMS** (ESI) m/z calculated for [$C_{12}H_{15}NONa$] ([M+Na$^+$]) 212.1046, found 212.1043.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	116.513	163.462	50.113	14.394	50.98			116.223	116.861
2		FID1A	117.132	162.725	49.887	13.842	49.02			116.861	117.624



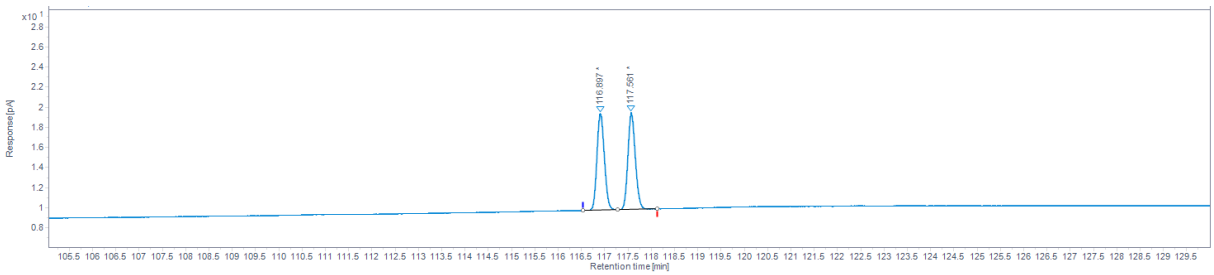
#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	116.089	3869.753	88.038	192.552	86.82			115.873	116.728
2		FID1A	116.988	525.810	11.962	29.233	13.18			116.730	117.452



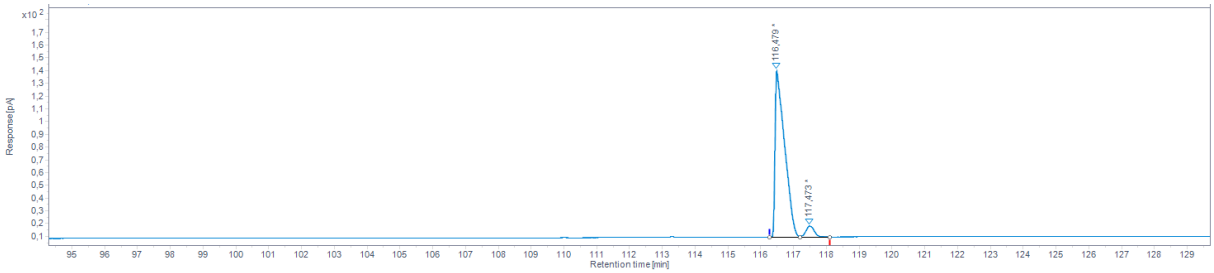
(*R*)-5-(4-(Trifluoromethyl)phenyl)piperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(5-(4-(trifluoromethyl)phenyl)pyridin-2-yl)oxazolidin-2-one (105 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (63 mg, 0.26 mmol, 87%, 95:5 e.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 5 °C/min to 120 °C, then 1 °C/min to 220 °C).

^{1}H NMR (400 MHz, Chloroform-*d*) 7.58 (d, *J* = 8.1 Hz, 2H), 7.42 (s, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 3.55 – 3.45 (m, 1H), 3.37 (t, *J* = 11.3 Hz, 1H), 3.10 (tt, *J* = 10.2, 4.7 Hz, 1H), 2.58 – 2.41 (m, 2H), 2.15 – 1.99 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.2, 145.9 (d, *J* = 1.4 Hz), 129.5 (q, *J* = 32.5 Hz), 127.5, 125.8 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 271.9 Hz), 48.2, 39.4, 31.1, 27.7. **^{19}F{^{1}H} NMR** (377 MHz,

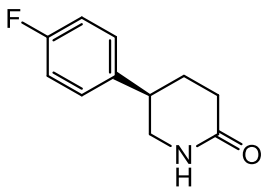
Chloroform-*d*) –62.5. **HRMS** (ESI) m/z calculated for [$C_{12}H_{12}NOF_3Na$] ([M+Na^+]) 266.0763, found 266.0760.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	116.897	106.134	49.985	9.630	50.03			116.525	117.269
2		FID1A	117.561	106.198	50.015	9.617	49.97			117.269	118.120

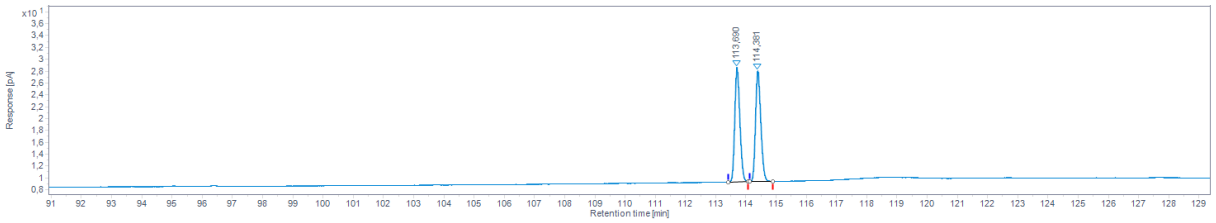


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	116,479	2637,808	94,607	131,294	93,85			116,271	117,188
2		FID1A	117,473	150,377	5,393	8,605	6,15			117,188	118,105

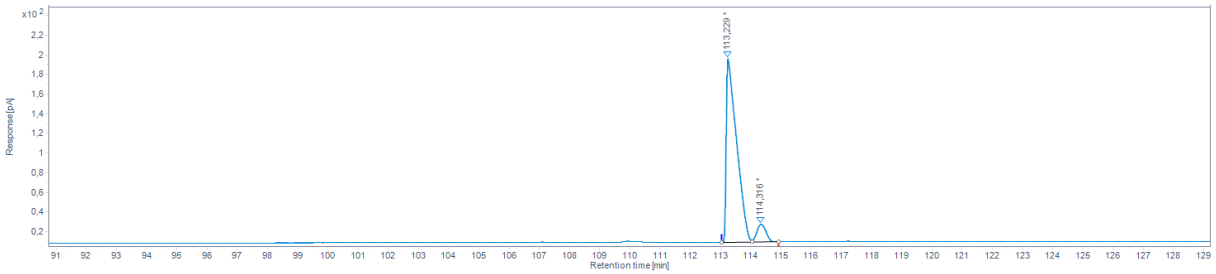


(*R*)-5-(4-fluorophenyl)piperidin-2-one: The title compound was prepared following the General Procedure using (*S*)-4-isopropyl-3-(5-(4-fluorophenyl)pyridin-2-yl)oxazolidin-2-one (90 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (44 mg, 0.23 mmol, 76%, 92:8 e.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 5 °C/min to 120 °C, then 1 °C/min to 220 °C.)

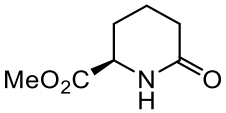
^{1}H NMR (400 MHz, Chloroform-*d*) 7.22 (s, 1H), 7.21 – 7.16 (m, 2H), 7.04 – 6.95 (m, 2H), 3.50 – 3.42 (m, 1H), 3.30 (t, *J* = 11.4 Hz, 1H), 3.06 – 2.96 (m, 1H), 2.56 – 2.39 (m, 2H), 2.11 – 1.93 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.2, 161.9 (d, *J* = 245.3 Hz), 137.6 (d, *J* = 3.3 Hz), 128.5 (d, *J* = 8.0 Hz), 115.6 (d, *J* = 21.3 Hz), 48.7 (d, *J* = 1.1 Hz), 38.9, 31.2, 27.9. **^{19}F{^{1}H} NMR** (377 MHz, Chloroform-*d*) –115.6. **HRMS** (ESI) m/z calculated for [$C_{11}H_{12}NOFNa$] ([M+Na^+]) 216.0795, found 216.0793.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	113,690	225,238	49,969	19,332	50,95			113,410	114,063
2		FID1A	114,381	225,513	50,031	18,610	49,05			114,118	114,900

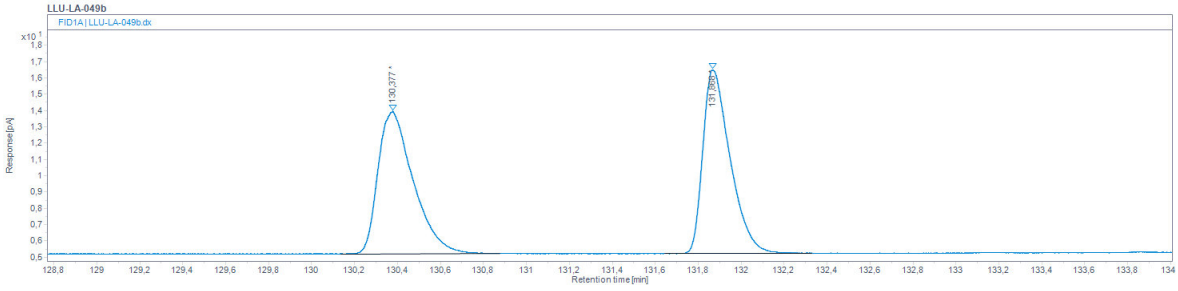


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	113,229	4431,741	92,133	186,488	91,10			113,043	114,033
2		FID1A	114,316	378,429	7,867	18,226	8,90			114,033	114,935

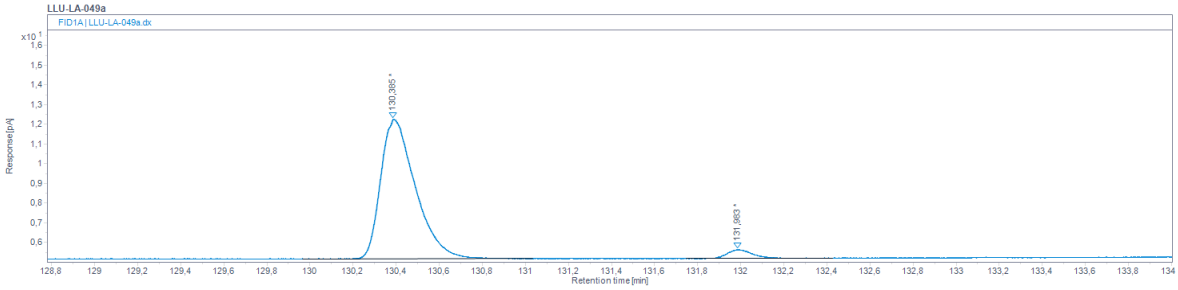


Methyl (*R*)-6-oxopiperidine-2-carboxylate: The title compound was prepared following the General Procedure using (*S*)-6-(4-benzyl-2-oxooxazolidin-3-yl)picolinate (94 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as yellow oil (42 mg, 0.27 mmol, 89%, 96:4 e.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 0.5 °C/min to 220 °C).

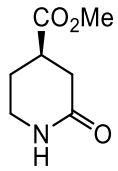
^{1}H NMR (400 MHz, Chloroform-*d*) 6.29 (s, 1H), 4.12 – 4.06 (m, 1H), 3.77 (s, 3H), 2.45 – 2.29 (m, 2H), 2.23 – 2.14 (m, 1H), 1.94 – 1.73 (m, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 171.7, 171.4, 54.9, 52.8, 31.2, 25.5, 19.6. **HRMS** (ESI) m/z calculated for [$C_7H_{11}NO_3Na$] ([M+Na$^+$]) 180.0631, found 180.0628.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	130,377	99,388	50,025	8,729	43,72			130,137	130,879
2		FID1A	131,868	99,287	49,975	11,238	56,28			131,643	132,329

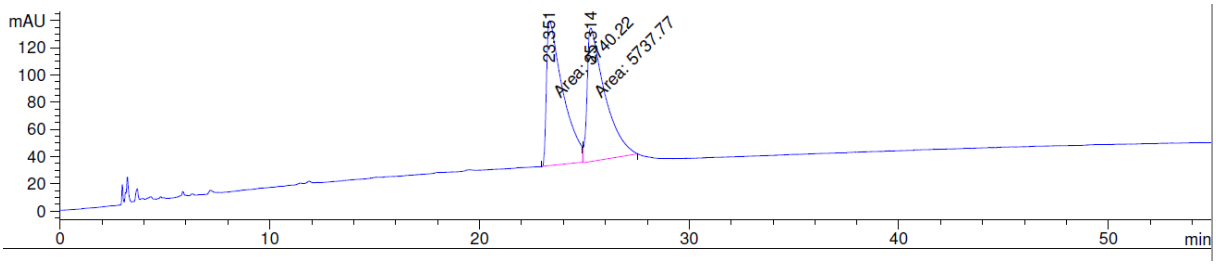


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	130,385	79,614	95,871	7,084	94,16			129,966	131,035
2		FID1A	131,983	3,429	4,129	0,439	5,84			131,748	132,425

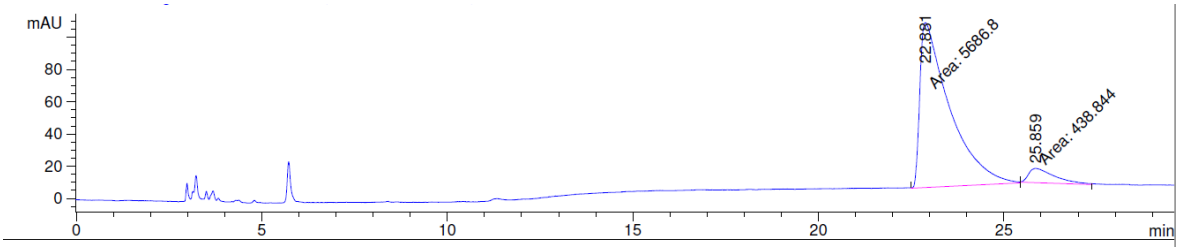


Methyl (*R*)-6-oxopiperidine-4-carboxylate: The title compound was prepared following the General Procedure using methyl (*S*)-2-(4-benzyl-2-oxooxazolidin-3-yl)isonicotinate (94 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (25 mg, 0.16 mmol, 53%, 93:7 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 90:10, flow rate = 1 mL/min, λ = 210 nm, retention time: 22.9 min (major), 25.9 min (minor).

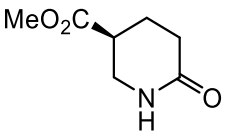
^{1}H NMR (400 MHz, Chloroform-*d*) 6.80 (s, 1H), 3.71 (s, 3H), 3.43 – 3.26 (m, 2H), 2.88 – 2.78 (m, 1H), 2.63 – 2.49 (m, 2H), 2.16 – 2.06 (m, 1H), 1.97 – 1.83 (m, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 173.8, 52.3, 40.7, 38.0, 33.5, 25.1. **HRMS** (ESI) m/z calculated for [$C_7H_{11}NO_3Na$] ([M+Na^+]) 180.0631, found 180.0629.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.351	MM	0.9006	5740.22168	106.22820	50.0107
2	25.314	MM	0.9754	5737.77197	98.03738	49.9893

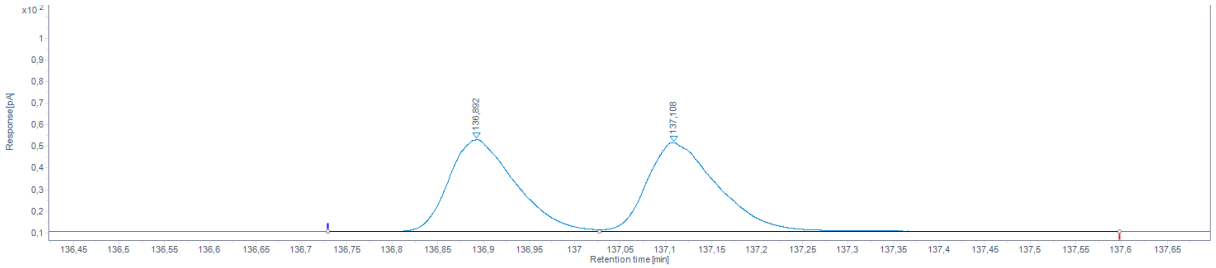


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.881	MM	0.9274	5686.79639	102.19711	92.8359
2	25.859	MM	0.8235	438.84436	8.88208	7.1641

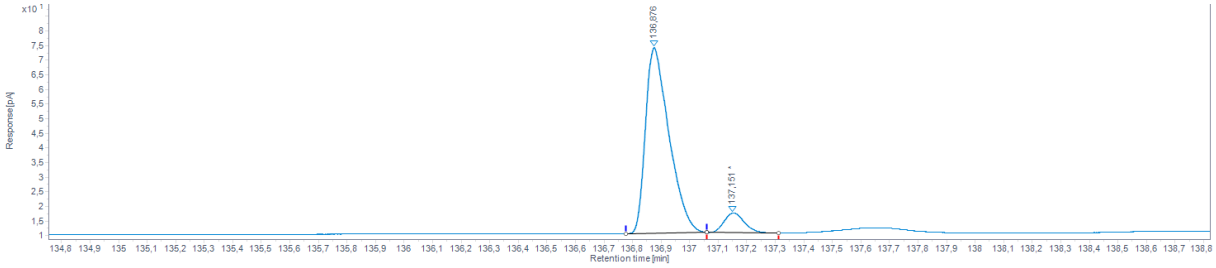


Methyl (*S*)-6-oxopiperidine-3-carboxylate: The title compound was prepared following the General Procedure using methyl (*S*)-6-(4-benzyl-2-oxooxazolidin-3-yl)nicotinate (94 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (39 mg, 0.26 mmol, 86%, 93:7 e.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 0.5 °C/min to 220 °C).

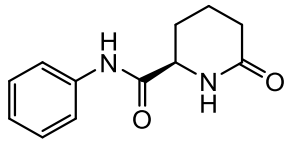
^{1}H NMR (400 MHz, Chloroform-*d*) 6.49 (s, 1H), 3.72 (s, 3H), 3.54 – 3.49 (m, 2H), 2.83 – 2.73 (m, 1H), 2.53 – 2.31 (m, 2H), 2.20 – 2.10 (m, 1H), 2.07 – 1.94 (m, 1H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.8, 171.5, 52.3, 43.5, 38.5, 30.0, 23.7. **HRMS** (ESI) m/z calculated for [$C_7H_{11}NO_3Na$] ([M+Na^+]) 180.0631, found 180.0628.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	136,892	215,627	49,190	42,592	50,84			136,729	137,027
2		FID1A	137,108	222,729	50,810	41,188	49,16			137,027	137,598

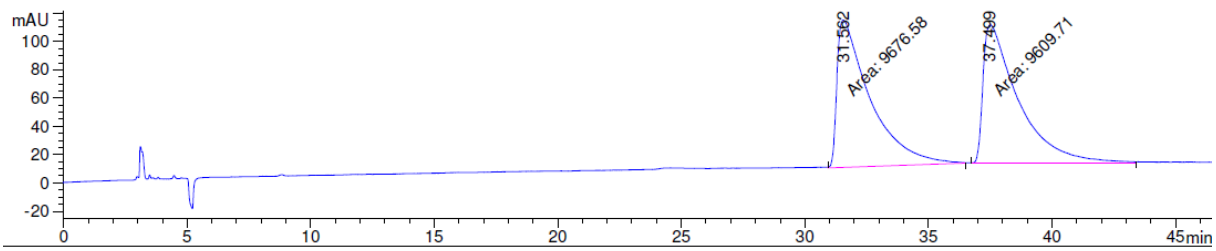


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	136,876	402,548	93,262	64,945	91,18			136,772	137,071
2		FID1A	137,151	29,082	6,738	6,285	8,82			137,090	137,288

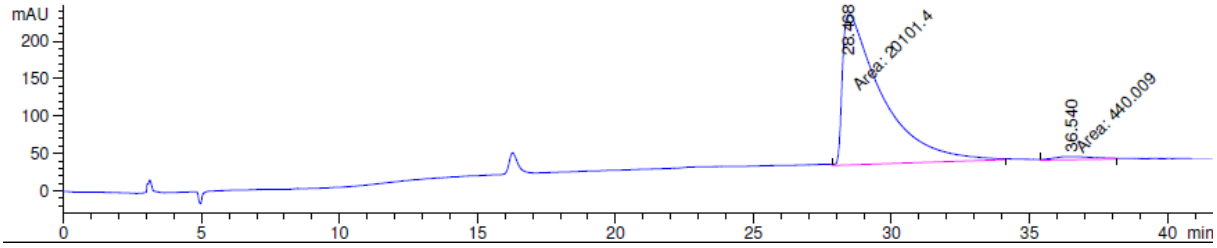


(*R*)-6-Oxo-*N*-phenylpiperidine-2-carboxamide: The title compound was prepared following the General Procedure using (*S*)-6-(4-benzyl-2-oxooxazolidin-3-yl)-*N*-phenylpicolinamide (112 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 97:3, 95:5, 90:10) as white solid (40 mg, 0.19 mmol, 62%, 98:2 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 90:10, flow rate = 1 mL/min, λ = 210 nm, retention time: 28.5 min (major), 36.5 min (minor).

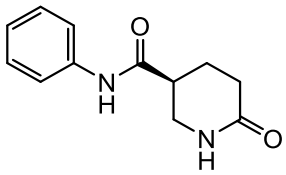
^{1}H NMR (400 MHz, Methanol-d_4) 175.3, 172.5, 139.4, 129.8, 125.5, 121.5, 57.5, 31.8, 27.3, 19.7. **^{13}C{^{1}H} NMR** (101 MHz, Methanol-d_4) 175.3, 172.5, 139.4, 129.8, 125.5, 121.5, 57.5, 31.8, 27.3, 19.7. **HRMS** (ESI) m/z calculated for [$C_{12}H_{14}N_2O_2Na$] ([M+Na$^+$]) 241.0948, found, 241.0945.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.562	MM	1.5494	9676.57715	104.08638	50.1734
2	37.499	MM	1.6449	9609.70508	97.36959	49.8266

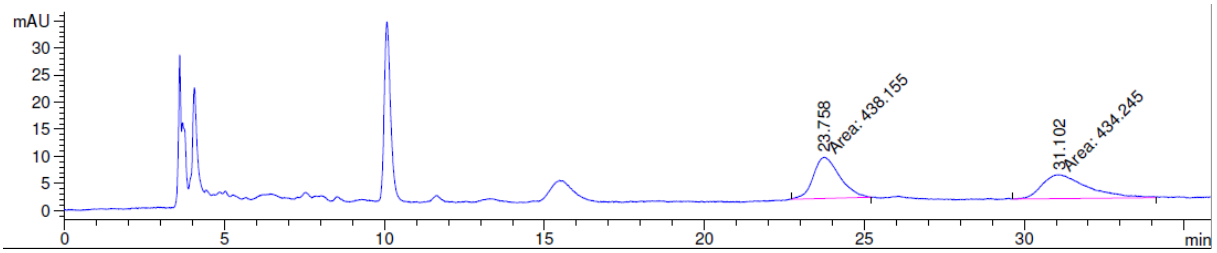


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.468	MM	1.6653	2.01014e4	201.17468	97.8579
2	36.540	MM	1.7382	440.00916	4.21896	2.1421

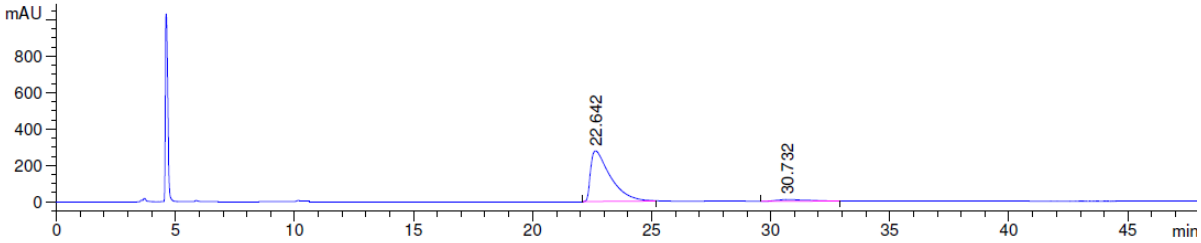


(*S*)-6-Oxo-*N*-phenylpiperidine-3-carboxamide: The title compound was prepared following the General Procedure using (*S*)-6-(4-benzyl-2-oxooxazolidin-3-yl)-*N*-phenylnicotinamide (112 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 97:3, 95:5, 90:10) as white solid (54 mg, 0.25 mmol, 83%, 95:5 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK OJ-H, *n*-hexane:2-propanol = 90:10, flow rate = 1 mL/min, λ = 210 nm, retention time: 22.6 min (major), 30.7 min (minor).

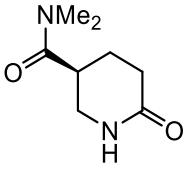
^{1}H NMR (400 MHz, Methanol-d_4) 7.55 (d, J = 7.6 Hz, 2H), 7.30 (t, J = 8.0 Hz, 2H), 7.09 (t, J = 7.4 Hz, 1H), 3.54 – 3.43 (m, 2H), 2.91 – 2.81 (m, 1H), 2.52 – 2.33 (m, 2H), 2.17 – 1.98 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Methanol-d_4) 174.1, 173.4, 139.7, 129.8, 125.3, 121.3, 44.7, 41.7, 30.9, 25.6. **HRMS** (ESI) m/z calculated for [$C_{12}H_{14}N_2O_2Na$] ([M+Na$^+$]) 241.0948, found, 241.0945.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.758	MM	0.9567	438.15472	7.63299	50.2241
2	31.102	MM	1.6312	434.24542	4.43685	49.7759

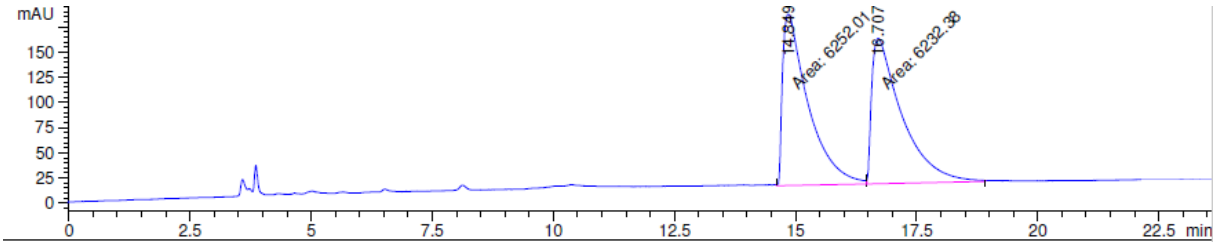


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.642	BB	0.7602	1.59574e4	277.80270	94.9515
2	30.732	BB	0.9936	848.45166	10.01311	5.0485

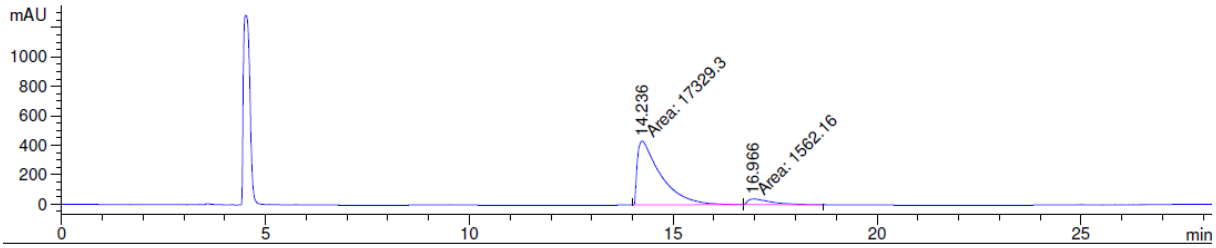


(*S*)-*N*,*N*-Dimethyl-6-oxopiperidine-3-carboxamide: The title compound was prepared following the General Procedure using (*S*)-6-(4-isopropyl-2-oxooxazolidin-3-yl)-*N*,*N*-dimethylnicotinamide (83 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 95:5, 90:10) as white solid (32 mg, 0.19 mmol, 63%, 92:8 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK OJ-H, *n*-hexane:2-propanol = 80:20, flow rate = 1 mL/min, λ = 210 nm, retention time: 14.2min (major), 17.0 min (minor).

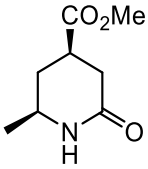
^{1}H NMR (400 MHz, Chloroform-*d*) 6.41 (s, 1H), 3.61 – 3.52 (m, 1H), 3.37 – 3.29 (m, 1H), 3.08 (s, 3H), 3.01 – 2.89 (m, 4H), 2.56 – 2.47 (m, 1H), 2.43 – 2.32 (m, 1H), 2.06 – 1.95 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.1, 171.5, 44.2, 37.3, 36.6, 35.8, 30.6, 24.4. **HRMS** (ESI) m/z calculated for [$C_8H_{14}N_2O_2Na$] ([M+Na$^+$]) 193.0948, found, 193.0944.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.849	MF	0.6119	6252.00732	170.29579	50.0786
2	16.707	FM	0.7195	6232.37842	144.37550	49.9214

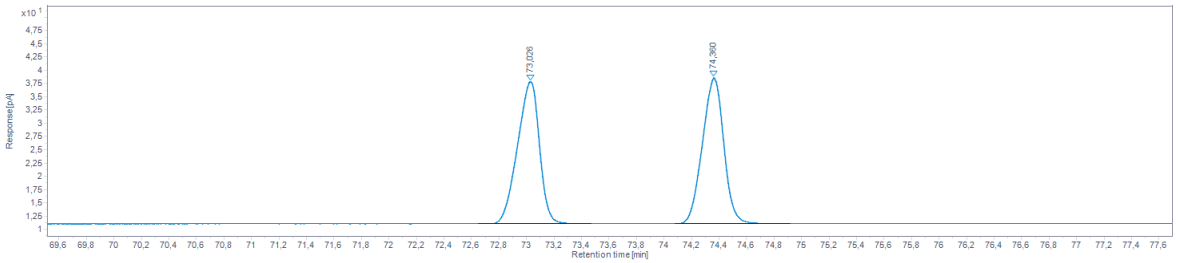


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.236	MM	0.6664	1.73293e4	433.37759	91.7309
2	16.966	MM	0.6644	1562.16052	39.18980	8.2691

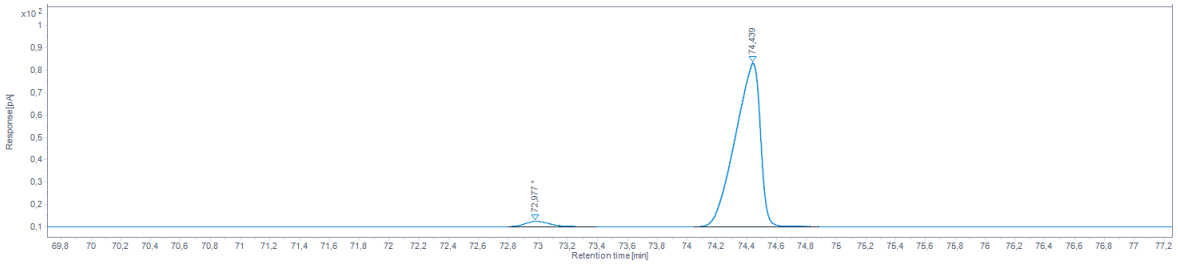


Methyl (2*S*,4*R*)-2-methyl-6-oxopiperidine-4-carboxylate: The title compound was prepared following the General Procedure using methyl 2-(4-benzyl-2-oxooxazolidin-3-yl)-6-methylisonicotinate (98 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (41 mg, 0.24 mmol, 80%, 97:3 e.r., >95:5 d.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 5 °C/min to 120 °C, then 1 °C/min to 220 °C).

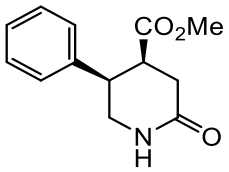
^{1}H NMR (400 MHz, Chloroform-*d*) 6.31 (s, 1H), 3.71 (s, 3H), 3.58 – 3.46 (m, 1H), 2.86 – 2.74 (m, 1H), 2.69 – 2.56 (m, 1H), 2.52 – 2.40 (m, 1H), 2.24 – 2.15 (m, 1H), 1.52 – 1.38 (m, 1H), 1.22 (d, *J* = 6.4 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 173.8, 170.7, 52.3, 48.3, 38.3, 33.8, 33.2, 22.7. **HRMS** (ESI) m/z calculated for [$C_8H_{13}NO_3Na$] ([M+Na^+]) 194.0788, found 194.0785.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	72,264	282,615	50,073	60,771	43,51			72,111	72,542
2		FID1A	72,739	281,791	49,927	78,908	56,49			72,615	72,963

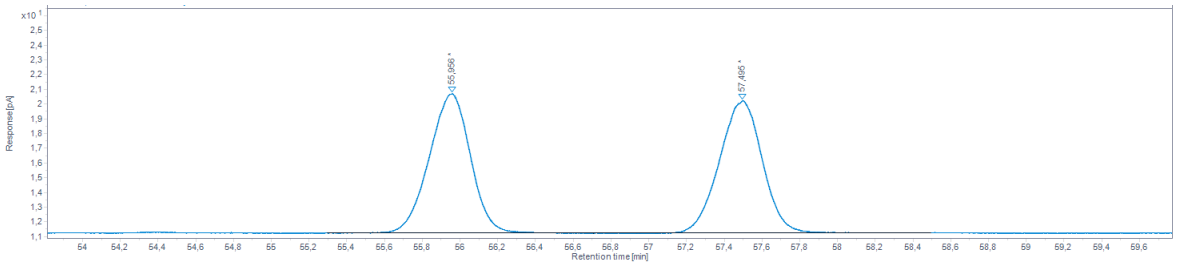


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	72,977	26,180	2,989	2,332	3,09			72,799	73,393
2		FID1A	74,439	849,855	97,011	73,157	96,91			74,040	74,883

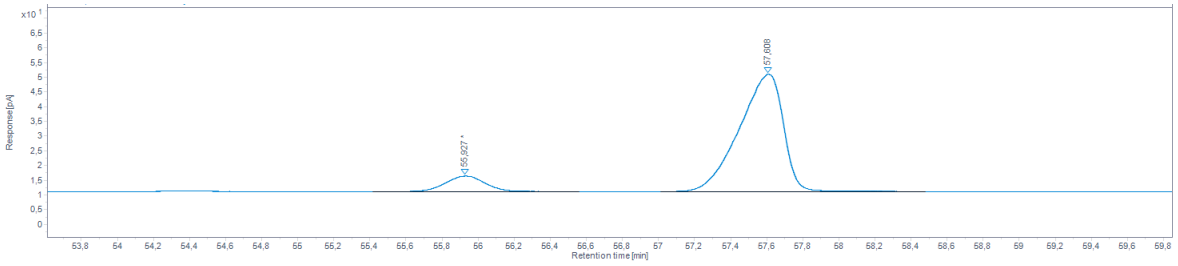


Methyl (4*S*,5*R*)-2-oxo-5-phenylpiperidine-4-carboxylate: The title compound was prepared following the General Procedure using methyl 2-(4-benzyl-2-oxooxazolidin-3-yl)-5-phenylisonicotinate (117 mg, 0.30 mmol, 1.0 equiv.) The product was isolated after column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) as white solid (21 mg, 0.09 mmol, 30%, 89:11 e.r., >95:5 d.r.). The enantiomeric ratio of the product was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 20 °C/min to 180 °C, then 1 °C/min to 220 °C and hold for 30 min).

^{1}H NMR (400 MHz, Chloroform-*d*) 7.35 – 7.26 (m, 3H), 7.23 – 7.17 (m, 2H), 6.56 (s, 1H), 3.90 – 3.83 (m, 1H), 3.72 – 3.64 (m, 1H), 3.61 (s, 3H), 3.58 – 3.51 (m, 1H), 3.25 – 3.17 (m, 1H), 2.67 – 2.58 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*)172.6, 170.7, 138.9, 128.9, 127.8, 127.6, 51.9, 45.1, 43.3, 39.7, 31.8. **HRMS** (ESI) m/z calculated for [$C_{13}H_{15}NO_3Na$] ([M+Na$^+$]) 256.0944, found 256.0941.

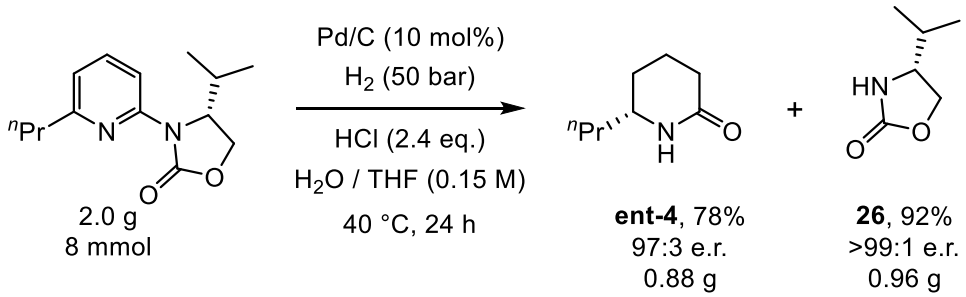


#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	55,956	142,968	50,227	9,441	51,22			55,297	56,705
2		FID1A	57,495	141,673	49,773	8,990	48,78			56,705	58,495



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	55,927	80,653	10,632	5,269	11,64			55,414	56,559
2		FID1A	57,608	677,939	89,368	39,992	88,36			57,013	58,480

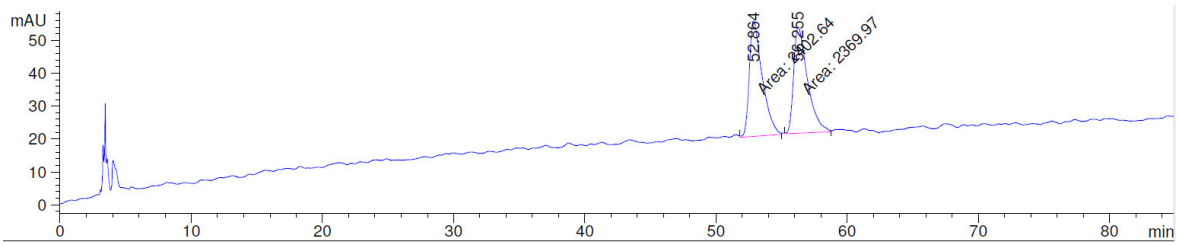
6. Gram-Scale Hydrogenation and Hydrolytic Ring Opening of δ-Lactams



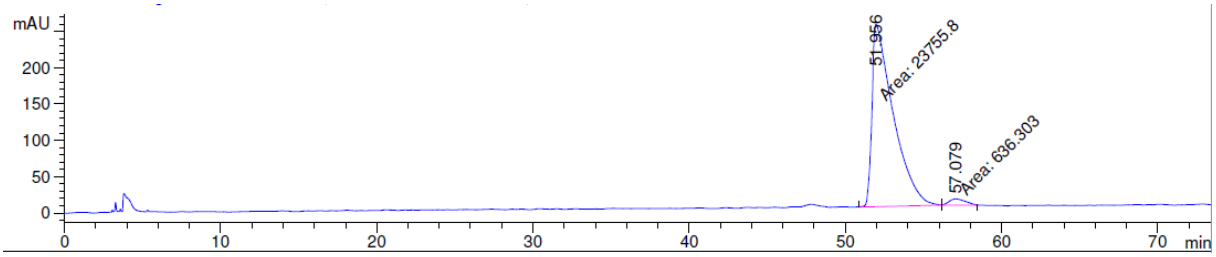
Experimental Procedure: The reaction was performed according to the general procedure from the previous chapter using (*R*)-4-isopropyl-3-(6-propylpyridin-2-yl)oxazolidin-2-one (2.00 g, 8.05 mmol, 1.0 equiv.), 5 wt% Pd/C (1.71 g, 0.805 mmol, 10 mol%), and aqueous HCl (1.61 ml, 19.32 mmol, 2.4 equiv., 12 M) in H_2O (27 ml) and THF (27 ml). The crude mixture was purified using column chromatography (eluent: CH_2Cl_2, later CH_2Cl_2/MeOH 99:1, 98:2, 97:3) to give **ent-4** as white solid (884 mg, 6.26 mmol, 78%, 97:3 e.r.) and **26** as white solid (959 mg, 7.42 mmol, 92%, >99:1 e.r.). The enantiomeric ratio of **ent-4** was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 90:10, flow rate = 1 mL/min, λ = 210 nm, retention time: 52.0 min (major), 57.1 min (minor). The enantiomeric ratio of **26** was determined after purification using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 0.5 °C/min to 220 °C).

Analytical data **ent-4**:

^{1}H NMR (500 MHz, Chloroform-*d*) 5.85 (s, 1H), 3.39 – 3.30 (m, 1H), 2.43 – 2.33 (m, 1H), 2.32 – 2.22 (m, 1H), 1.93 – 1.84 (m, 2H), 1.73 – 1.62 (m, 1H), 1.48 – 1.40 (m, 2H), 1.40 – 1.28 (m, 3H), 0.93 (t, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (126 MHz, Chloroform-*d*) 172.5, 53.1, 39.3, 31.5, 28.6, 20.0, 18.6, 14.0.



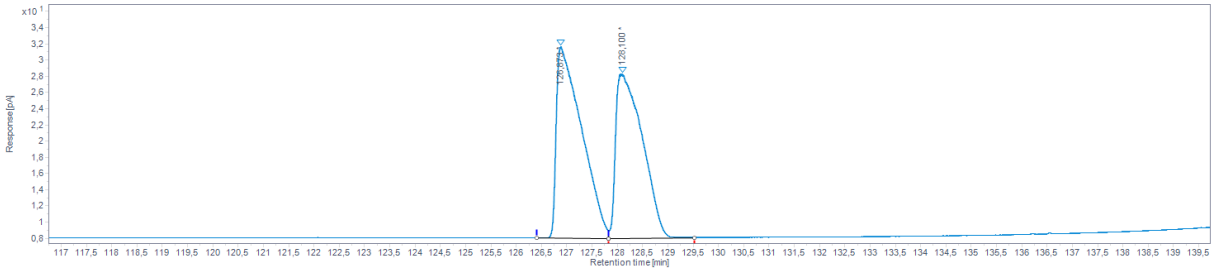
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	52.864	MM	1.1407	2402.63818	35.10623	50.3423
2	56.255	MM	1.2262	2369.96851	32.21357	49.6577



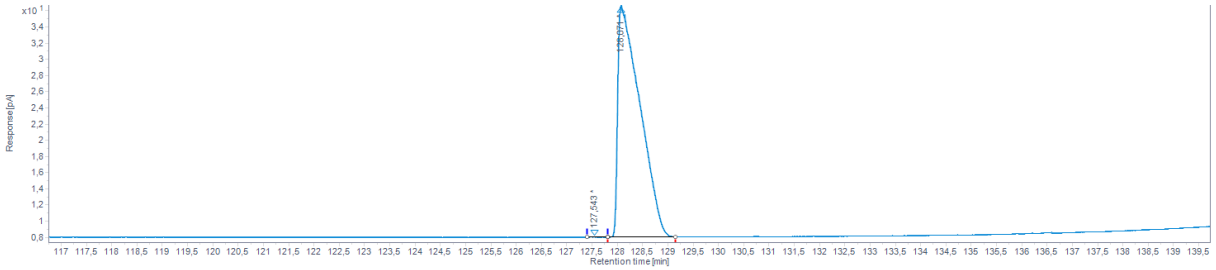
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	51.956	MM	1.5756	2.37558e4	251.28220	97.3914
2	57.079	MM	1.2116	636.30286	8.75269	2.6086

Analytical data **26**:

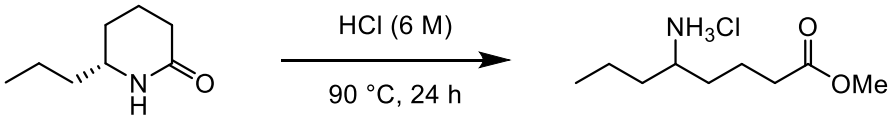
^{1}H NMR (400 MHz, Chloroform-*d*) 7.10 (s, 1H), 4.40 (t, *J* = 8.7 Hz, 1H), 4.06 (dd, *J* = 8.7, 6.3 Hz, 1H), 3.64 – 3.54 (m, 1H), 1.76 – 1.62 (m, *J* = 6.8 Hz, 1H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H).
^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) 160.8, 68.7, 58.5, 32.8, 18.0, 17.7.



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	126,873	818,902	52,453	23,601	53,79			126,409	127,833
2		FID1A	128,100	742,319	47,547	20,272	46,21			127,833	129,519



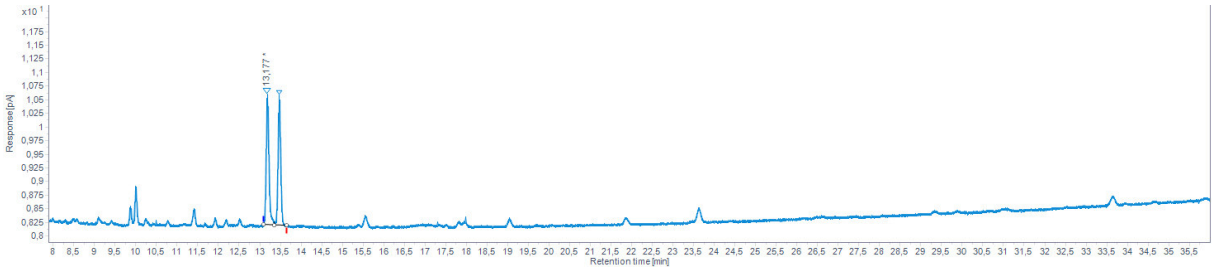
#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	127,543	0,079	0,009	0,015	0,05			127,393	127,817
2		FID1A	128,071	869,621	99,991	28,578	99,95			127,817	129,156



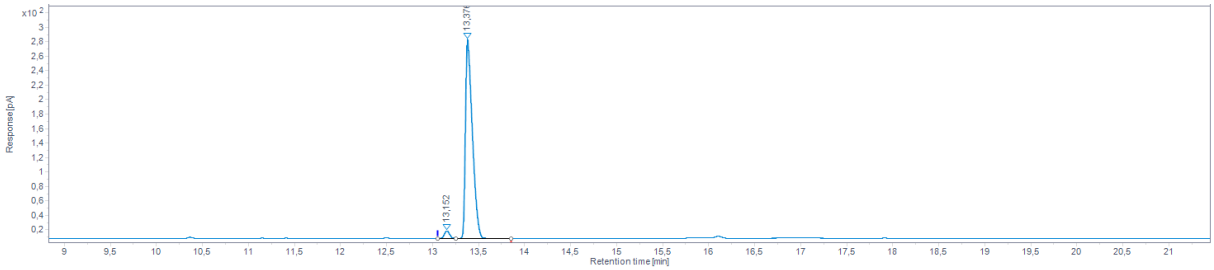
ent-4 **27,** 99%

Experimental Procedure: The reaction was performed following a procedure from Zacharie and co-workers.[4] In a schlenk flask equipped with a stir bar, δ-Lactam **ent-4** (141 mg, 1.0 mmol, 1.0 equiv.) was dissolved in 6 M HCl (10 ml, 0.1 M) and the mixture was stirred at 90 °C for 24 h. After having reached room temperature, hydrochloric acid was removed under reduced pressure. The oily residue was diluted in methanol and transferred to a 20 ml vial. The solvent was removed under reduced pressure and the product was dried under high vacuum to give amino acid methyl ester **28** (208 mg, 1.0 mmol, 99%, 97:3 e.r.) as white solid. The enantiomeric ratio of the product was determined after purification and deprotonation with NEt_3 using gas chromatography (HYDRODEX β-6TBDM column, 25 m, 0.25 mm ID; carrier gas: H_2; injection temperature 230 °C; oven temperature 50 °C, heating rate: 20 °C/min to 180 °C, then 1 °C/min to 220 °C).

^{1}H NMR (400 MHz, DMSO-d_6) 8.07 (s, 3H), 3.57 (s, 3H), 3.09 – 2.96 (m, 1H), 2.36 – 2.25 (m, 2H), 1.63 – 1.42 (m, 6H), 1.38 – 1.25 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H).**^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) 173.2, 51.4, 50.3, 34.1, 33.1, 31.3, 20.2, 17.9, 13.9. **HRMS** (ESI) m/z calculated for [$C_9H_{20}NO_2$] ([M+H$^+$]) 174.1489, found 174.1487.



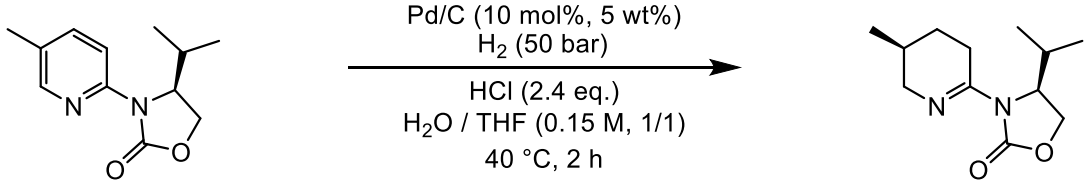
#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	13,177	9,789	50,339	2,339	50,02			13,100	13,287
2		FID1A	13,463	9,657	49,661	2,338	49,98			13,383	13,659



#	Name	Signal description	RT (min)	Area	Area%	Height	Height%	Amount	Concentration	Start time (min)	End time (min)
1		FID1A	13,152	40,496	2,772	10,479	3,67			13,053	13,249
2		FID1A	13,376	1420,395	97,228	274,721	96,33			13,249	13,850

7. Mechanistic Investigation

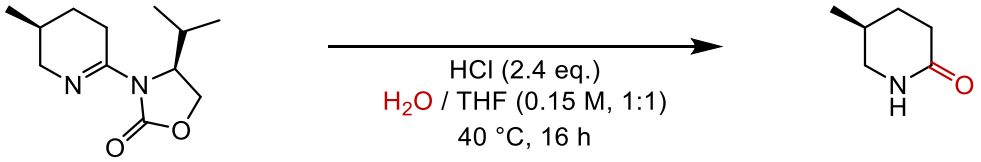
Isolation of imine intermediate:



Experimental Procedure: A 60 ml glass vial equipped with a stir bar was charged with 5 wt% Pd/C (639 mg, 0.3 mmol, 10 mol%) and (*S*)-4-isopropyl-3-(5-methylpyridin-2-yl)oxazolidin-2-one (661 mg, 3.0 mmol, 1.0 equiv.). THF (10 ml) and H_2O (10 ml) were added (20 ml / 0.15 M in total) followed by the addition of concentrated aqueous HCl (0.60 ml, 2.4 equiv.). The glass vial was placed in a 150 ml stainless steel autoclave under air. The autoclave was pressurized and depressurized four times with hydrogen gas before the final hydrogen pressure was set to 50 bar. The reaction mixture was stirred at 40 °C for 2 h. After the autoclave was carefully depressurized, Na_2CO_3 (1.27 g, 4.0 equiv.) was added and the mixture was filtered over celite using CH_2Cl_2. The solvent was removed *in vacuo* and the product was isolated after column chromatography on silica gel (eluent: *n*-pentane/EtOAc 4:1) as white solid (36 mg, 0.16 mmol, 5%).

^{1}H NMR (400 MHz, Chloroform-*d*) 4.48 (dt, *J* = 8.5, 3.6 Hz, 1H), 4.28 – 4.11 (m, 2H), 3.75 – 3.64 (m, 1H), 3.25 – 3.15 (m, 1H), 3.06 – 2.93 (m, 1H), 2.60 – 2.42 (m, 2H), 1.90 – 1.79 (m, 1H), 1.69 – 1.55 (m, 1H), 1.35 – 1.21 (m, 2H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 7.1 Hz, 3H), 0.83 (d, *J* = 7.0 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 155.6, 154.5, 62.9, 59.3, 55.3, 28.1, 27.5, 27.2, 26.3, 18.9, 18.2, 14.6. **HRMS** (ESI) m/z calculated for [$C_{12}H_{20}N_2O_2Na$] ([M+Na$^+$]) 247.1417, found 247.1416.

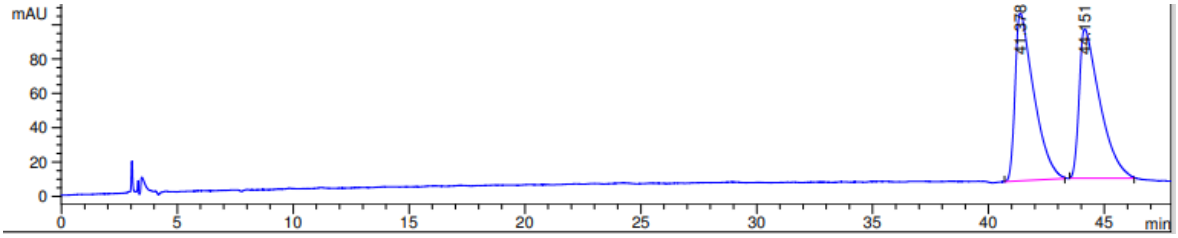
Hydrolysis of imine intermediate:



Experimental Procedure: A 4 mL glass vial (screw cap) equipped with a stir bar was charged with (*S*)-4-isopropyl-3-((*S*)-5-methyl-3,4,5,6-tetrahydropyridin-2-yl)oxazolidin-2-one (34 mg, 0.15 mmol, 1.0 equiv.). THF (0.5 ml) and H_2O (0.5 ml) were added (1.0 ml / 0.15 M in total) followed by the addition of concentrated aqueous HCl (30 µl, 2.4 equiv.). The reaction mixture was stirred at 40 °C for 2 h. Na_2CO_3 (64 mg, 4.0 equiv.) was added and the mixture was filtered over celite using CH_2Cl_2. The solvent was removed *in vacuo* and the product was isolated after

column chromatography on silica gel (eluent: CH_2Cl_2/MeOH 98:2) as colourless liquid (16 mg, 0.14 mmol, 94%, 98:2 e.r.). The enantiomeric ratio of the product was determined after purification using HPLC Daicel CHIRALPAK IA-3, *n*-hexane:2-propanol = 97:3, flow rate = 1 mL/min, λ = 210 nm, retention time: 43.7 min (major), 48.5 min (minor).

^{1}H NMR (400 MHz, Chloroform-*d*) 6.40 (s, 1H), 3.33 – 3.23 (m, 1H), 2.96 – 2.84 (m, 1H), 2.47 – 2.26 (m, 2H), 1.98 – 1.78 (m, 2H), 1.54 – 1.39 (m, 1H), 1.00 (d, *J* = 6.6 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) 172.5, 49.3, 30.9, 29.2, 28.3, 18.5.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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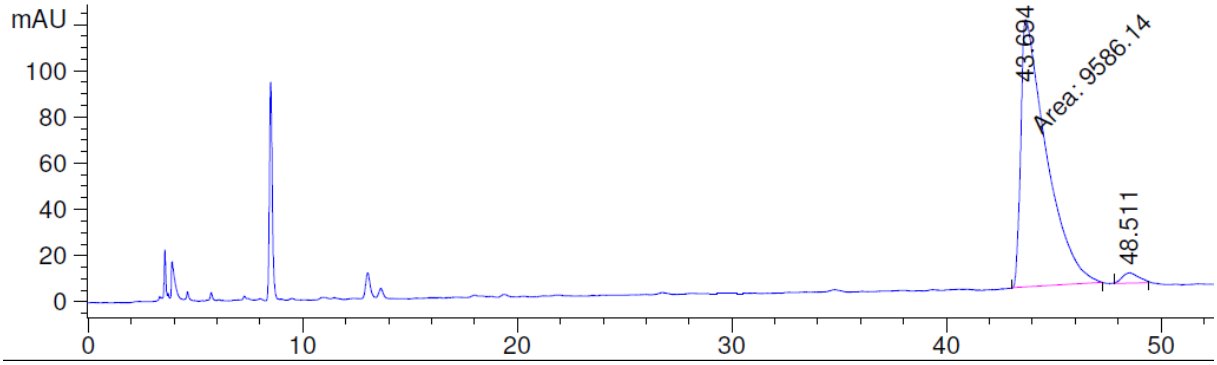
2	44.151	BB	0.7318	5409.58691	87.07893	49.4902



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	43.694	MM	1.3794	9586.13574	115.82081	97.5784
2	48.511	BB	0.6324	237.89856	4.44477	2.4216

Deuteration experiment:

A 4 ml glass vial (screw-cap) equipped with a stir bar was charged with 5 wt% Pd/C (32 mg, 0.015 mmol, 10 mol%) and (*S*)-4-isopropyl-3-(5-methylpyridin-2-yl)oxazolidin-2-one (0.15 mmol, 33 mg, 1.0 equiv). THF (0.5 mL) and D_2O (0.5 mL) were added (1 mL / 0.15 M in total) followed by the addition of DCl in D_2O (30 µl, 35 wt%, 2.4 equiv). The glass vial was placed in a 150 ml stainless steel autoclave under air. The autoclave was pressurized and depressurized four times with deuterium gas before the final hydrogen pressure was set to 30 bar. The reaction mixture was stirred at 40 °C for 24 h. After the autoclave was carefully depressurized, Na_2CO_3 (63 mg, 4.0 equiv) was added and the mixture was filtered over celite using CH_2Cl_2. The solvent was removed *in vacuo* and the product was purified using column chromatography on silica gel and analyzed by ^1H and ^2H NMR spectroscopy.

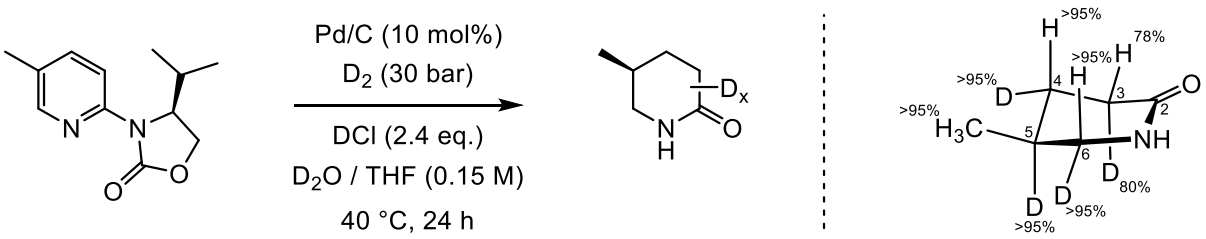


Figure S2: Deuteration experiment and product analysis. Note: Deuterium on the nitrogen is exchanged during silica gel work-up.

Based on the Horiuti-Polanyi mechanism,[5] hydrogen is added exclusively to the metal surface coordinating side of a π-bond in a heterogeneous hydrogenation. In the case of arene hydrogenation, the reduction of each double bond occurs iteratively and mainly from one side (Scheme S1). This deuteration experiment confirms a selective addition of deuterium to only one face of the pyridine. Positions 4–6 of the lactam product exhibit deuterium and hydrogen, respectively, with >95% selectivity (Figure S2). The 3-position of the lactam exhibits diminished selectivity for deuterium in the pseudo-axial position (80%) and hydrogen in the pseudo-equatorial position (78%). This may be due to tautomerization of the imine intermediate to the corresponding enamine (Figure S3).

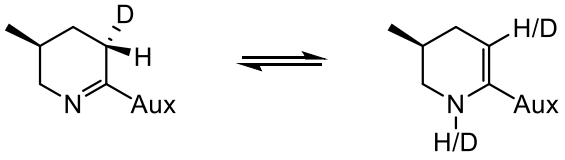
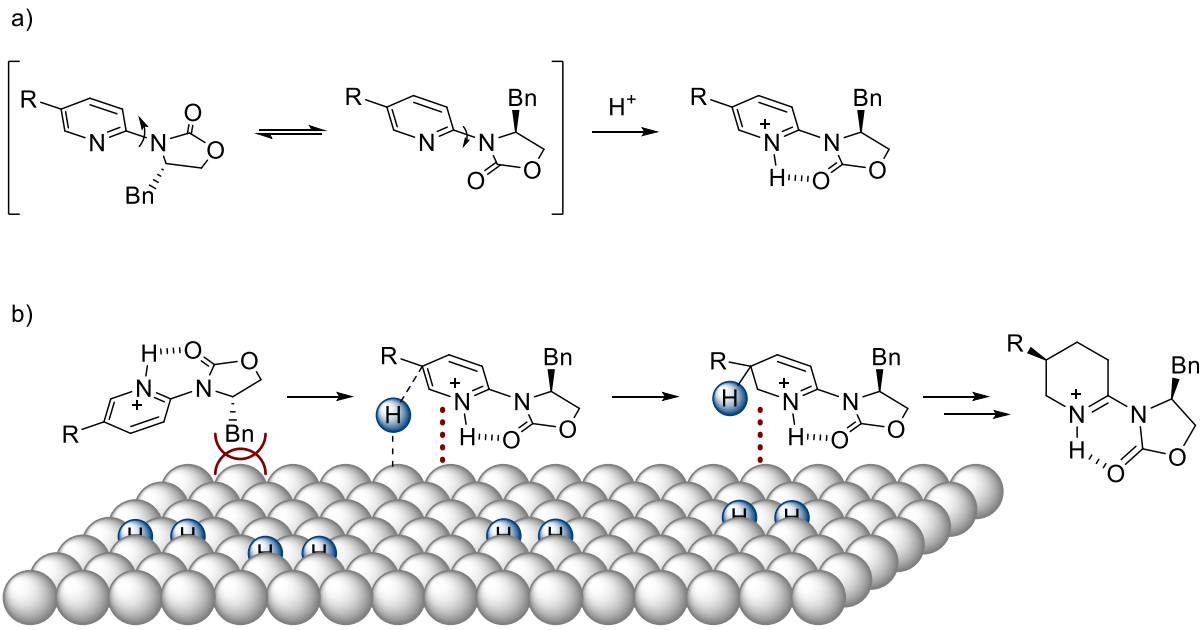


Figure S3: Tautomerization of the imine intermediate.



Scheme S1: a) Formation of a rigid conformer upon protonation. b) Diastereoselective addition of hydrogen to the non-hindered diastereotopic face of the pyridine substrate.

8. X-Ray Data

X-Ray diffraction: Data sets for compounds **1** and **10** were collected with a Bruker D8 Venture PHOTON III diffractometer. Programs used: data collection: APEX3 V2016.1-0[6] (Bruker AXS Inc., **2016**); cell refinement: SAINT V8.37A[7] (Bruker AXS Inc., **2015**); data reduction: SAINT V8.37A[7] (Bruker AXS Inc., **2015**); absorption correction, SADABS V2014/7[8] (Bruker AXS Inc., **2014**); structure solution *SHELXT-2015*[9]; structure refinement *SHELXL-2015*[10] and graphics, *XP*[11] (Version 5.1, Bruker AXS Inc., Madison, Wisconsin, USA, **1998**). *R*-values are given for observed reflections, and *w*R^2 values are given for all reflections.

X-ray crystal structure analysis of 1: A colorless plate-like specimen of $C_6H_{11}NO$, approximate dimensions 0.065 mm x 0.100 mm x 0.154 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker D8 Venture PHOTON III Diffractometer system equipped with a micro focus tube Cu Ims (CuK_α, λ = 1.54178 Å) and a MX mirror monochromator. A total of 954 frames were collected. The total exposure time was 13.22 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 5232 reflections to a maximum θ angle of 68.28° (0.83 Å resolution), of which 1160 were independent (average redundancy 4.510, completeness = 98.4%, R_{int} = 3.01%, R_{sig} = 2.48%) and 1127 (97.16%) were greater than $2\sigma(F^2)$. The final cell constants of a = 7.6609(2) Å, b = 9.1064(2) Å, c = 9.1822(2) Å, volume = 640.58(3) $Å^3$, are based upon the refinement of the XYZ-centroids of 3922 reflections above 20 σ(I) with 15.06° < 2θ < 136.5°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.907. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9080 and 0.9600. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P2_12_12_1$, with Z = 4 for the formula unit, $C_6H_{11}NO$. The final anisotropic full-matrix least-squares refinement on F^2 with 78 variables converged at R1 = 2.46%, for the observed data and wR2 = 6.56% for all data. The goodness-of-fit was 1.064. The largest peak in the final difference electron density synthesis was 0.116 $e^-/Å^3$ and the largest hole was -0.100 $e^-/Å^3$ with an RMS deviation of 0.024 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.173 g/cm^3 and F(000), 248 e^-. Flack parameter was refined to -0.07(10). Hydrogen at N1 atom was refined freely. CCDC Nr.: 2043968.

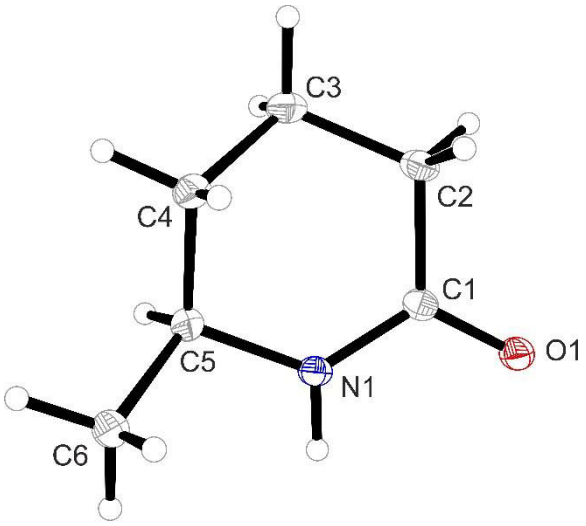


Figure S4: Crystal structure of compound **1**. Thermal ellipsoids are shown at 30% probability.

X-ray crystal structure analysis of 10: A colorless prism-like specimen of $C_6H_8F_3NO$, approximate dimensions 0.039 mm x 0.047 mm x 0.071 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker D8 Venture PHOTON III Diffractometer system equipped with a micro focus tube Cu Ims (CuK_α, λ = 1.54178 Å) and a MX mirror monochromator. A total of 926 frames were collected. The total exposure time was 15.33 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 6121 reflections to a maximum θ angle of 68.24° (0.83 Å resolution), of which 1279 were independent (average redundancy 4.786, completeness = 99.0%, R_{int} = 5.74%, R_{sig} = 4.16%) and 1120 (87.57%) were greater than $2\sigma(F^2)$. The final cell constants of a = 6.8779(2) Å, b = 10.0589(3) Å, c = 10.2256(3) Å, volume = 707.45(4) $Å^3$, are based upon the refinement of the XYZ-centroids of 2113 reflections above 20 σ(I) with 12.34° < 2θ < 136.4°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.895. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9060 and 0.9470. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P2_12_12_1$, with Z = 4 for the formula unit, $C_6H_8F_3NO$. The final anisotropic full-matrix least-squares refinement on F^2 with 104 variables converged at R1 = 3.05%, for the observed data and wR2 = 6.74% for all data. The goodness-of-fit was 1.051. The largest peak in the final difference electron density synthesis was 0.168 $e^-/Å^3$ and the largest hole was -0.159 $e^-/Å^3$ with an RMS deviation of 0.041 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.569 g/cm^3 and F(000), 344 e^-. Flack parameter was refined to -0.10(14). Hydrogen at N1 atom was refined freely. CCDC Nr.: 2043969.

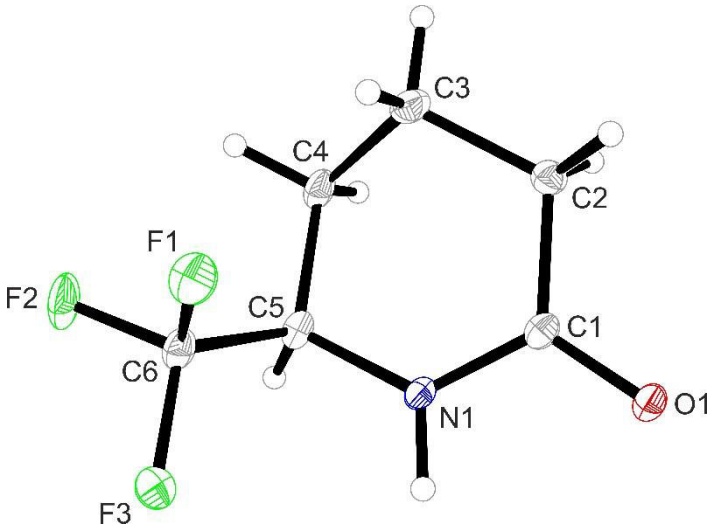


Figure S5: Crystal structure of compound **10**. Thermal ellipsoids are shown at 30% probability.

9. Literature

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[2] B. Latli, K. D'Amour, J. E. Casida, *J. Med. Chem.* **1999**, *42*, 2227–2234.

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[4] B. Zacharie, S. D. Abbott, C. B. Baigent, C. Doyle, R. S. Yalagala, *Eur. J. Org. Chem.* **2018**, 6486–6493.

[5] I. Horiuti, M. Polanyi, *Trans. Faraday Soc.* **1934**, *30*, 1164–1172.

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[7] SAINT (2015), Bruker AXS Inc., Madison, Wisconsin, USA.

[8] SADABS (2015), Bruker AXS Inc., Madison, Wisconsin, USA.

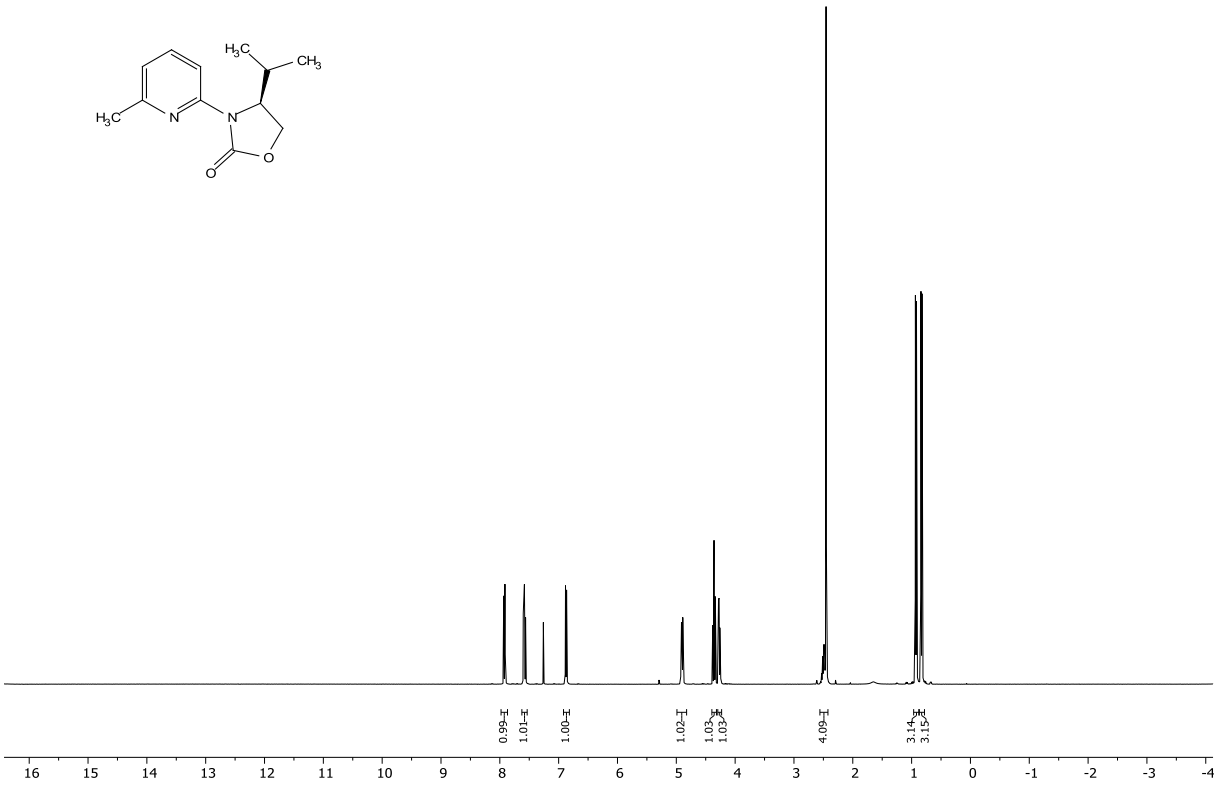
[9] G. M. Sheldrick, *Acta. Cryst.* **2015**, *C71*, 3–8.

[10] G. M. Sheldrick, *Acta. Cryst.* **2015**, *A71*, 3–8.

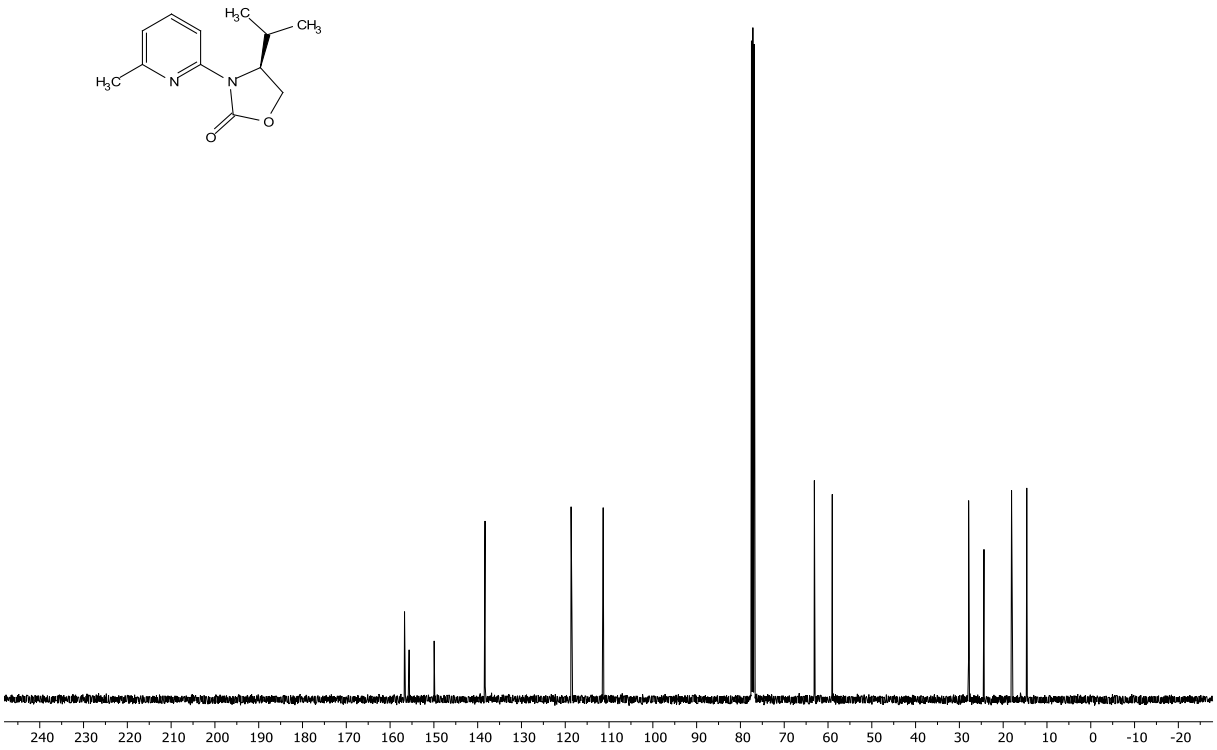
[11] XP – Interactive molecular graphics, Version 5.1, Bruker AXS Inc., Madison, Wisconsin, USA, 1998.

10. NMR Data

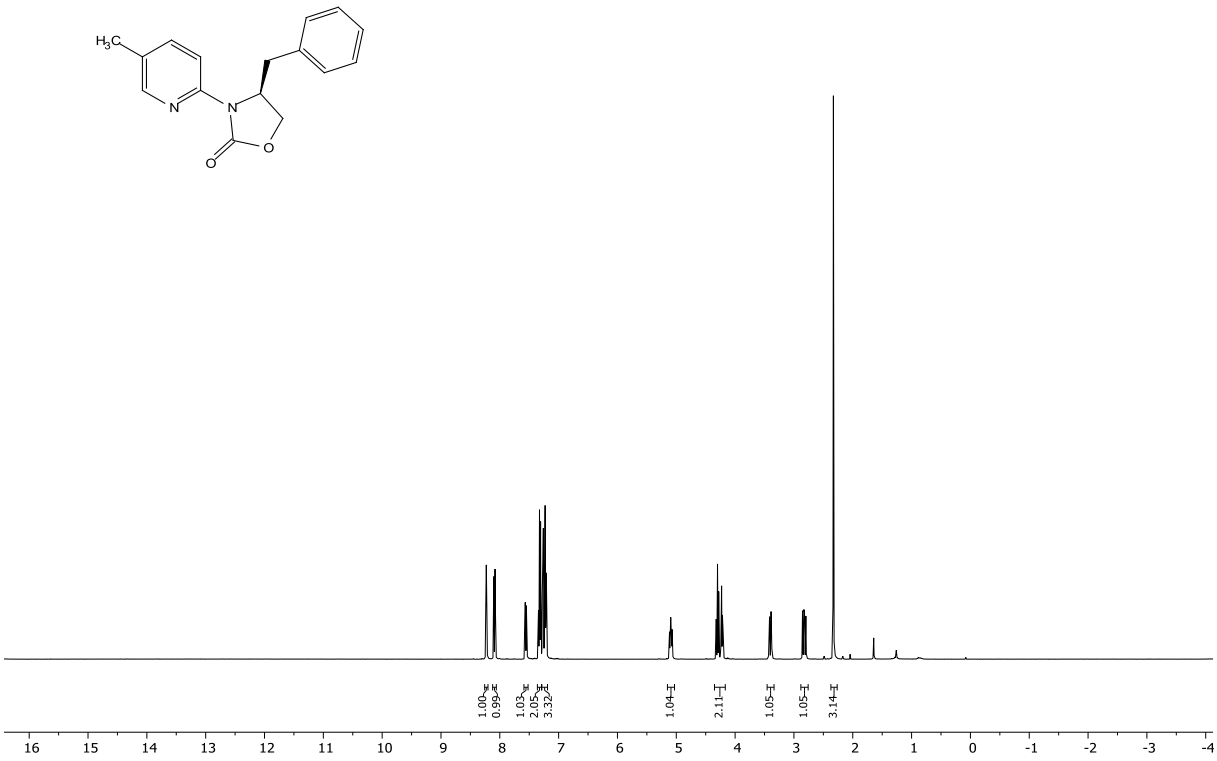
1H NMR(400 MHz, Chloroform-*d*)



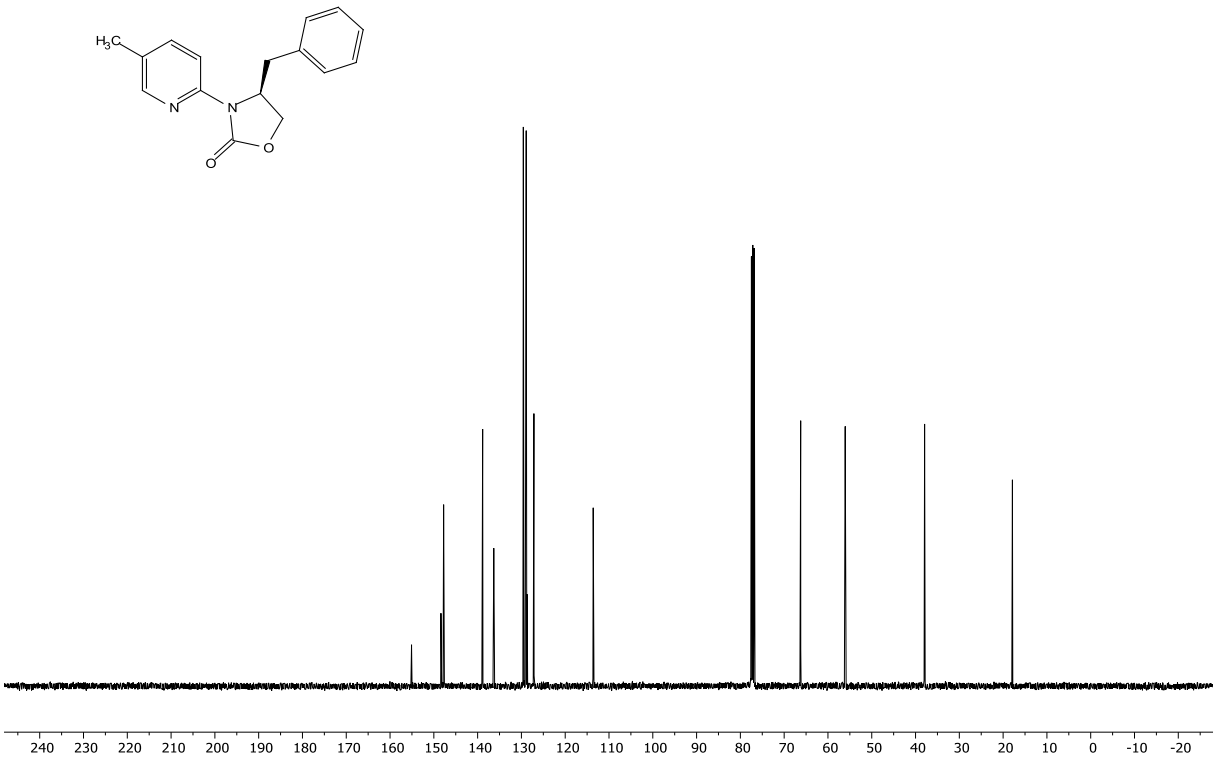
13C{1H} NMR(101 MHz, Chloroform-*d*)



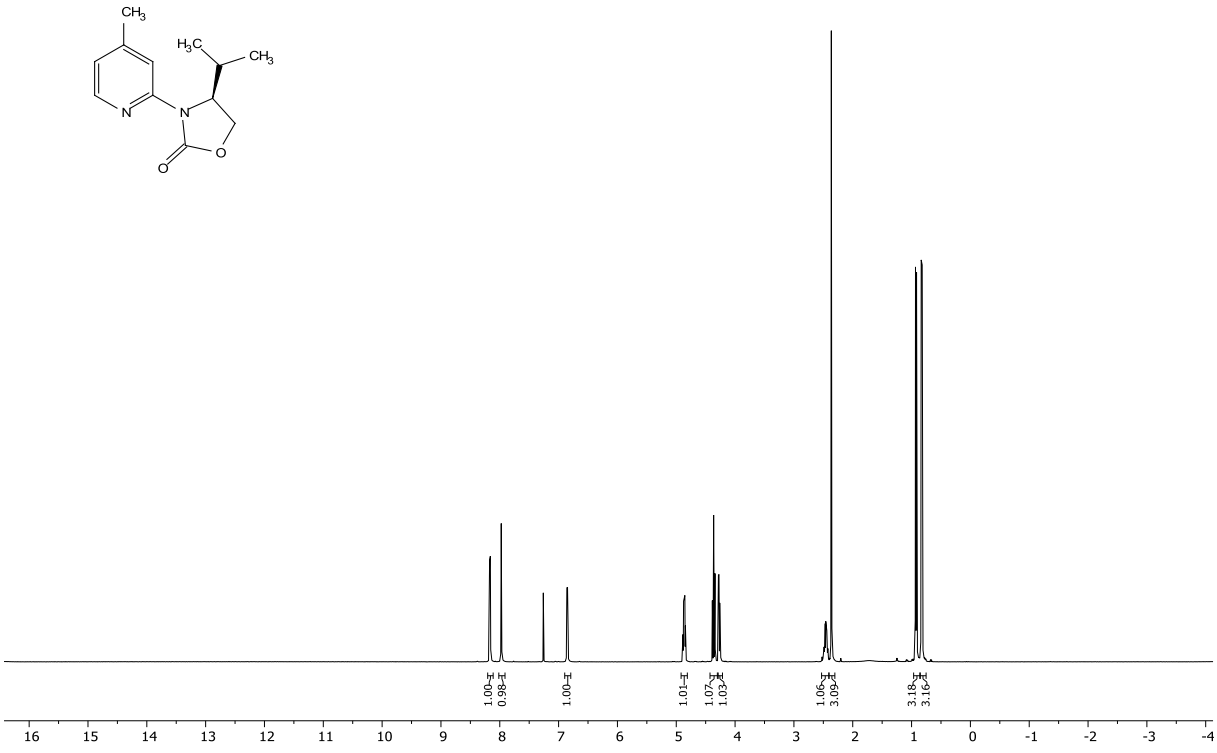
^{1}H NMR(400 MHz, Chloroform-*d*)



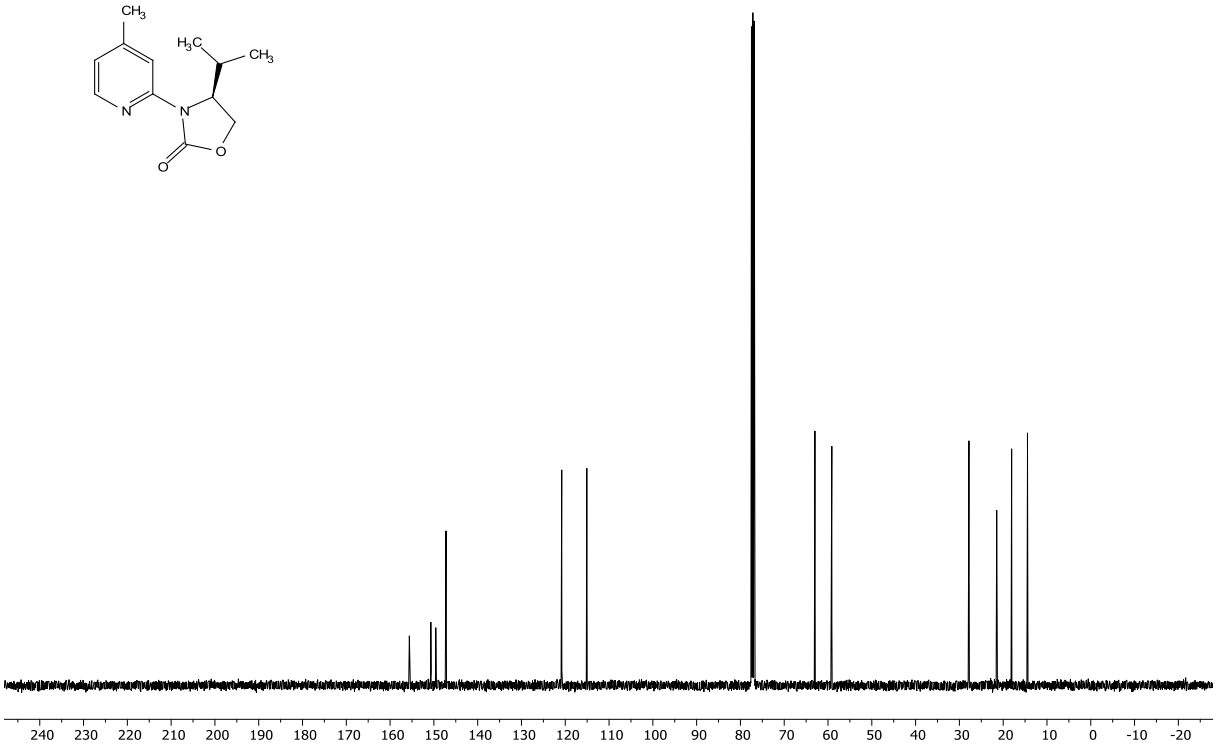
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



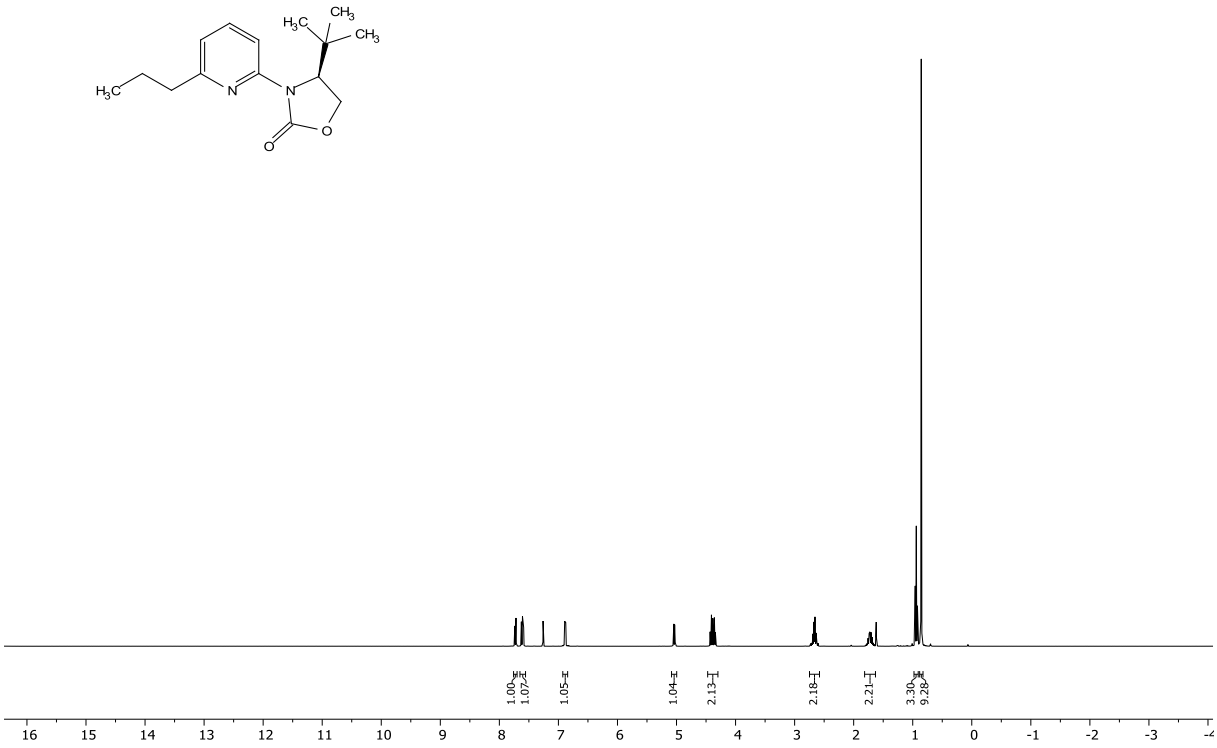
^{1}H NMR(400 MHz, Chloroform-*d*)



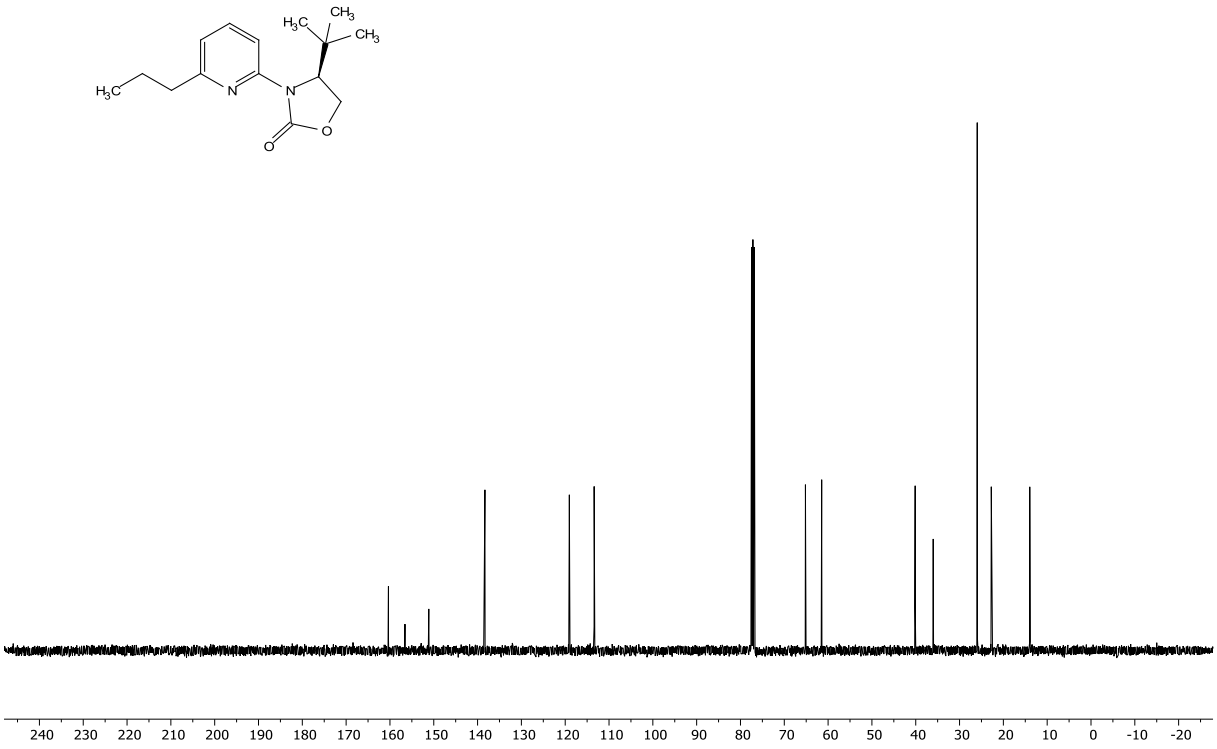
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



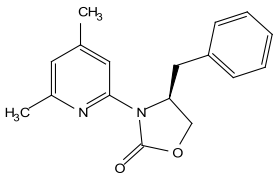
^{1}H NMR(400 MHz, Chloroform-*d*)



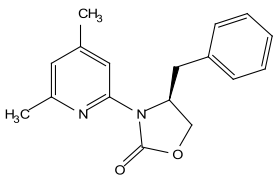
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



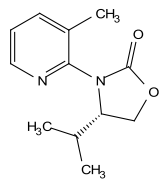
^{1}H NMR(400 MHz, Chloroform-*d*)



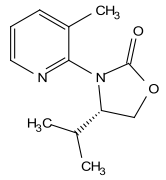
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



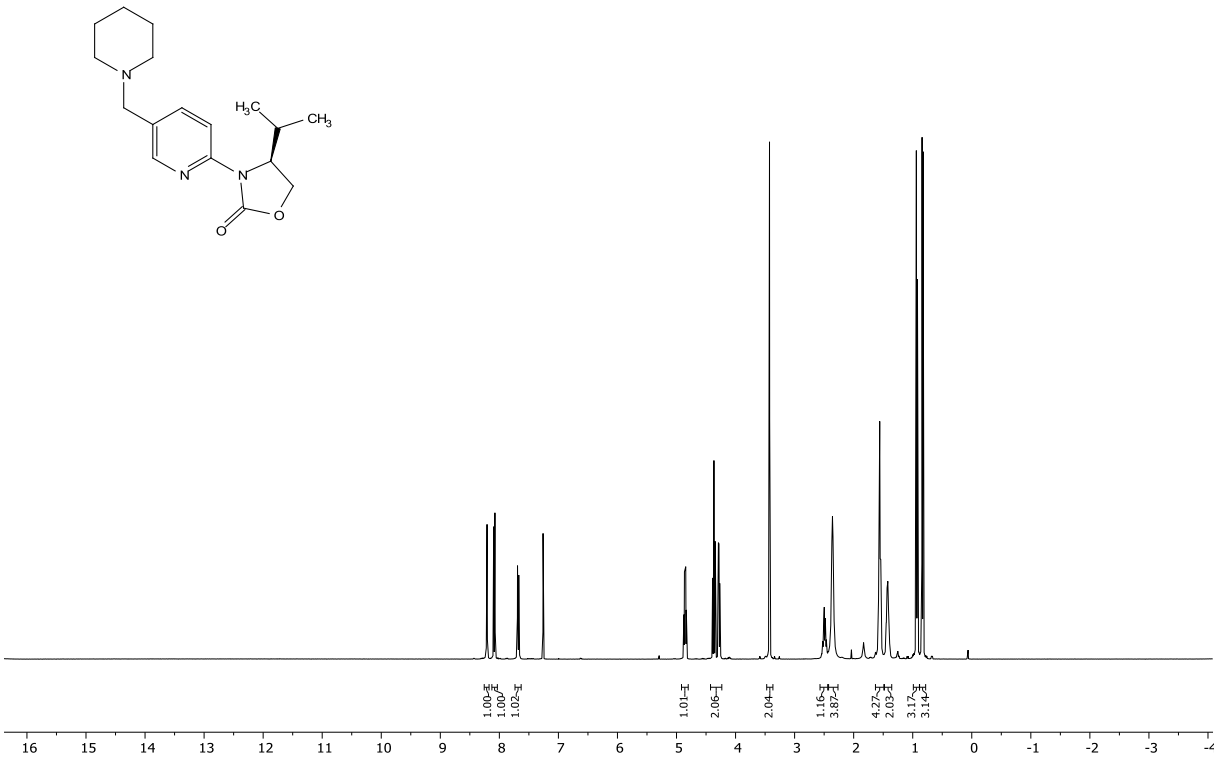
1H NMR(400 MHz, Chloroform-*d*)



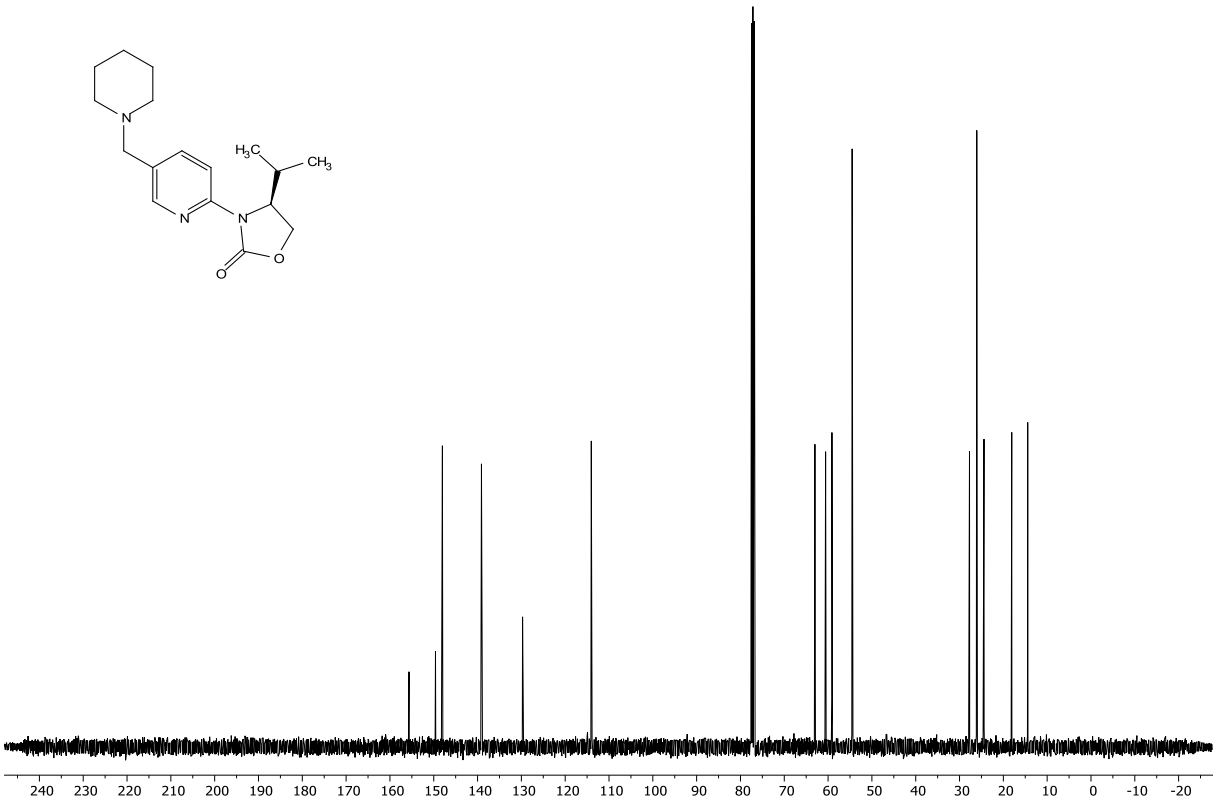
13C{1H} NMR(101 MHz, Chloroform-*d*)



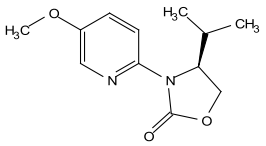
1H NMR(400 MHz, Chloroform-*d*)



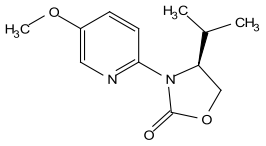
13C{1H} NMR(101 MHz, Chloroform-*d*)

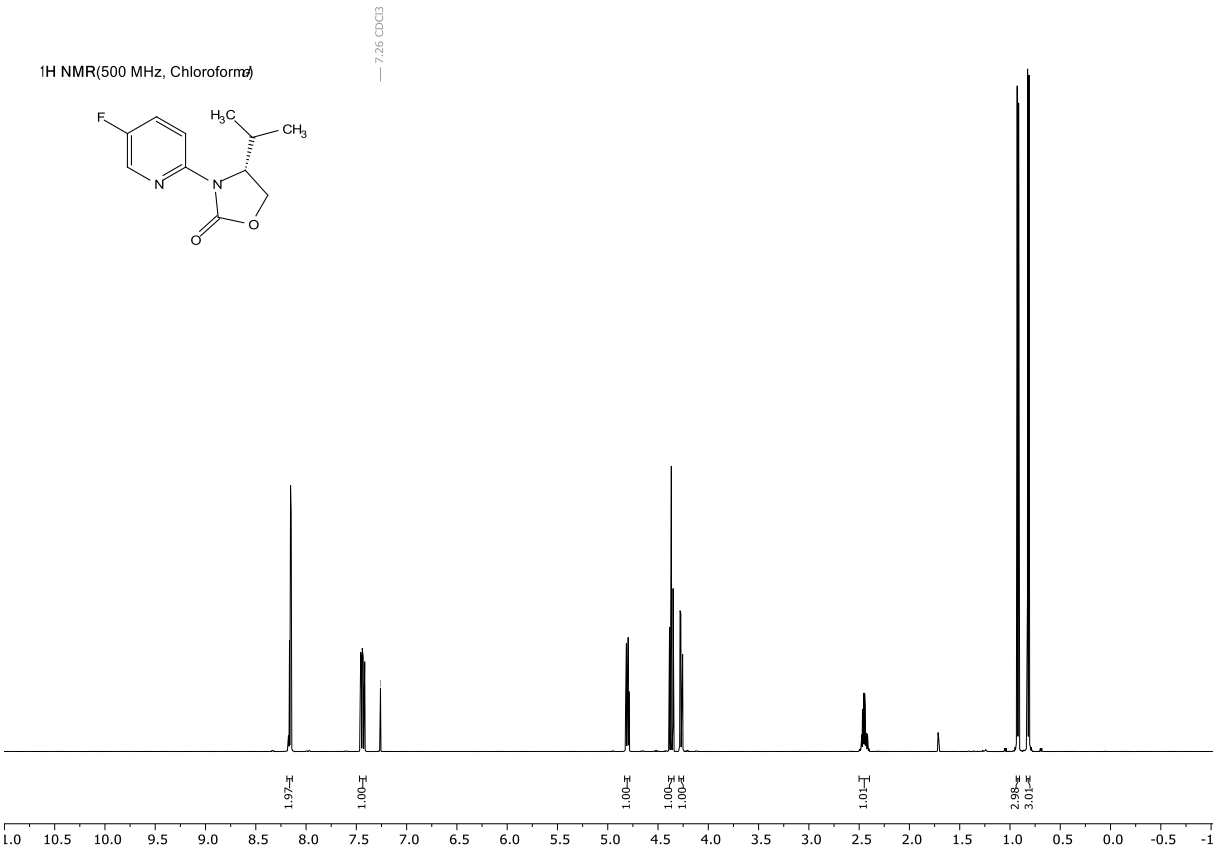


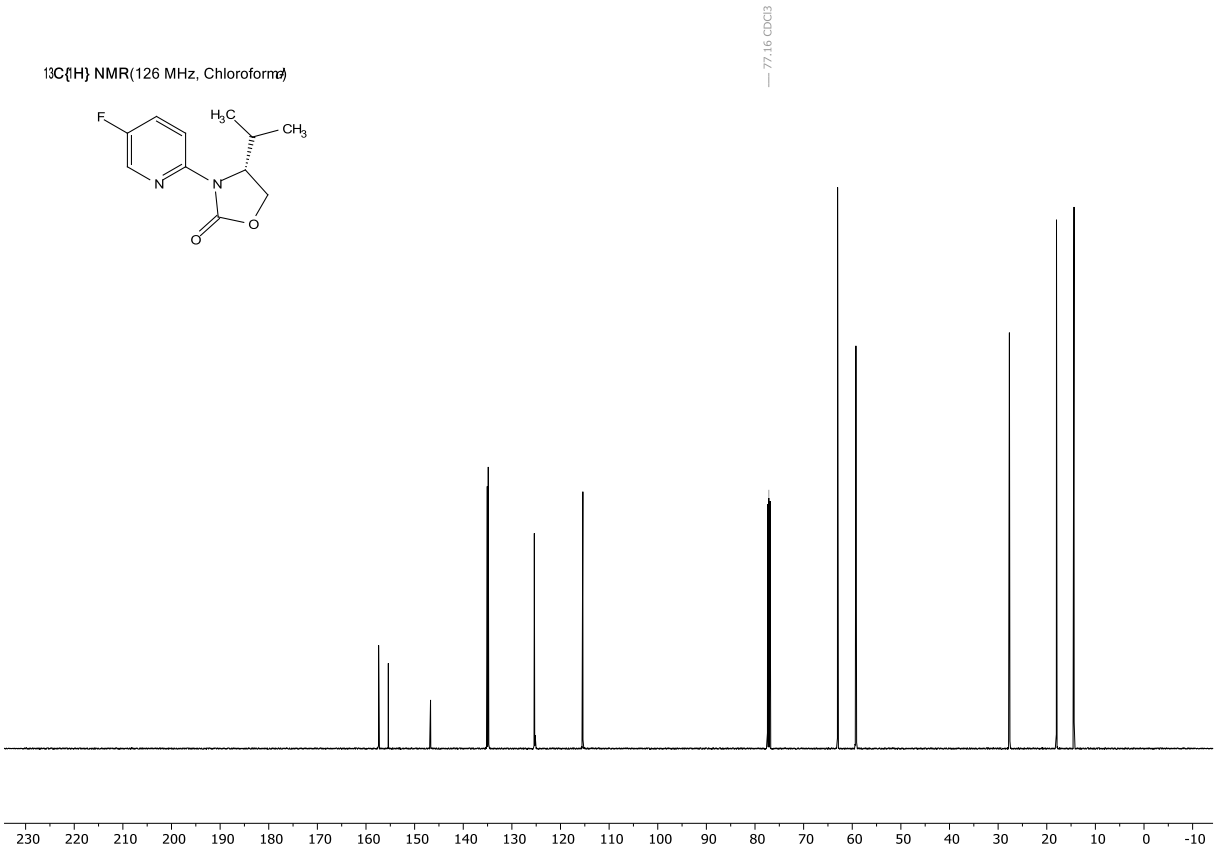
1H NMR(400 MHz, Chloroform-*d*)



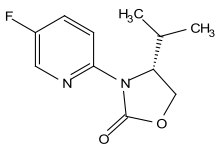
13C{1H} NMR(101 MHz, Chloroform-*d*)

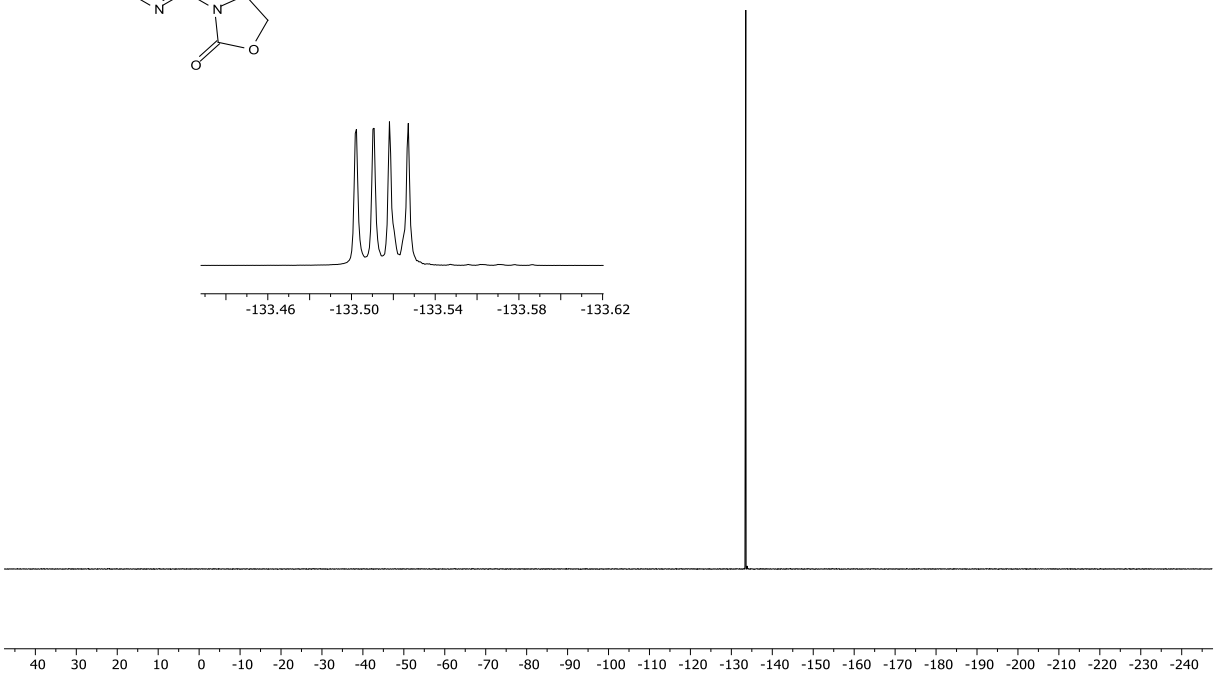



1H NMR(500 MHz, Chloroform-d)
7.26 CDCl3
F
H3C
CH3
N
N
O
O
1.97
1.00
1.00
1.00
1.00
1.01
2.98
3.01
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

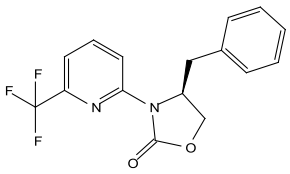

13C{1H} NMR(126 MHz, Chloroform-d)
77.16 CDCl3
F
H3C
CH3
N
N
O
O
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

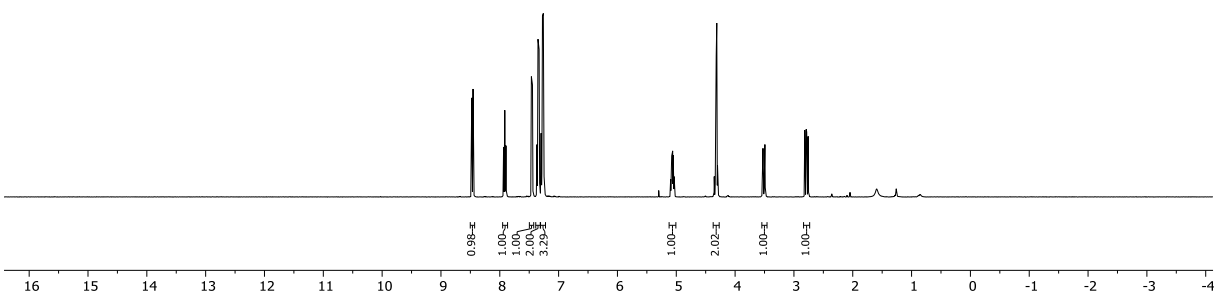
^{19}F-NMR (470 MHz, Chloroform-*d*)



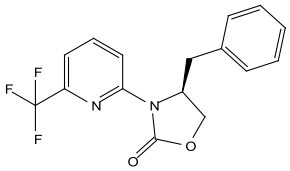


^{1}H NMR (400 MHz, Chloroform-*d*)

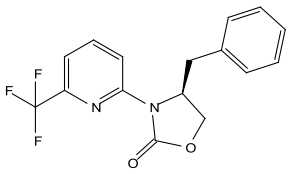




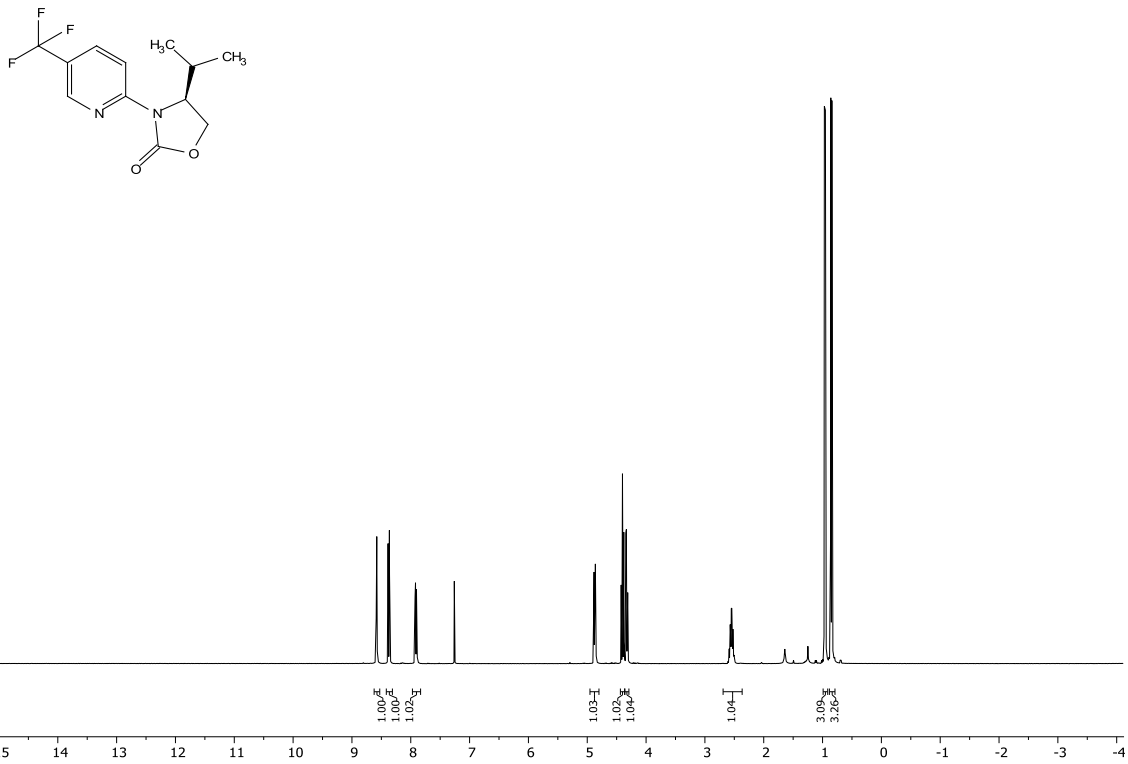
$^{13}C\{^{1}H\}$ NMR(101 MHz, Chloroform-*d*)



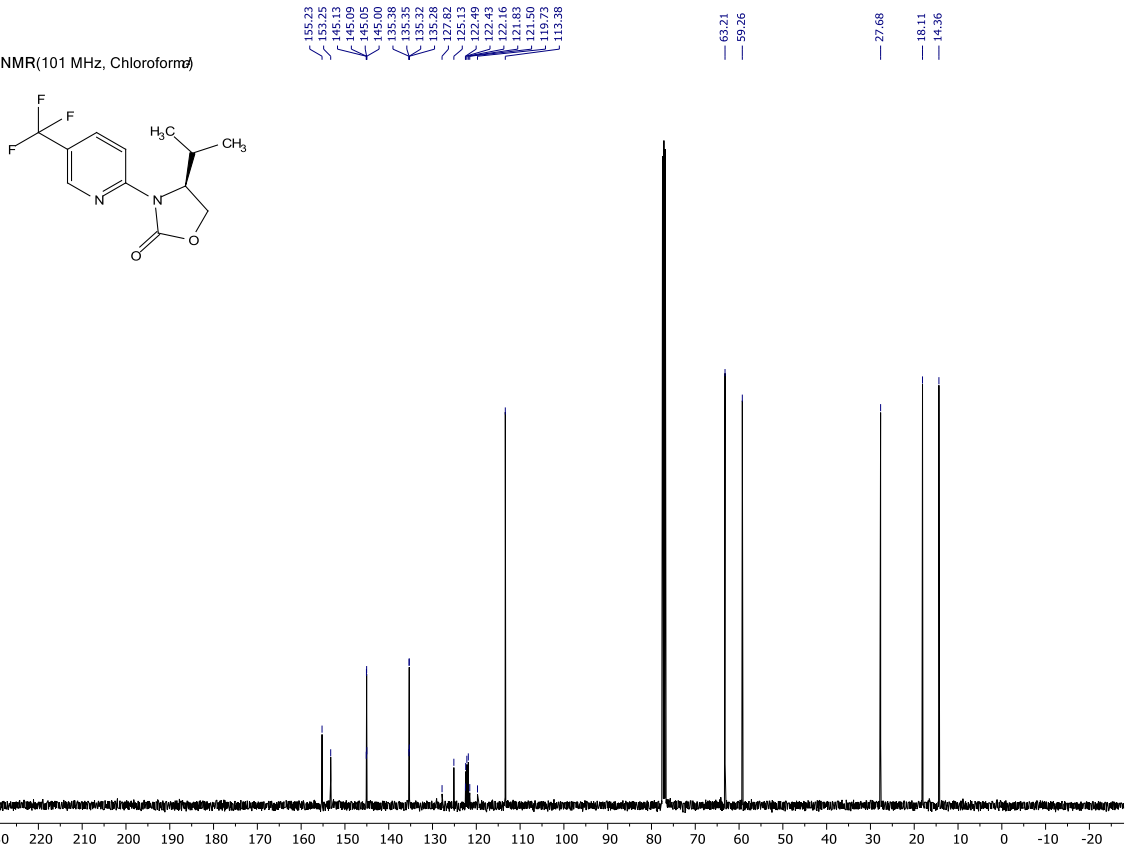
$^{19}F\{^{1}H\}$ NMR(376 MHz, Chloroform-*d*)



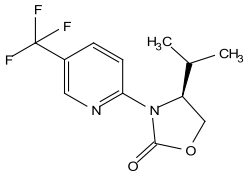
1H NMR(400 MHz, Chloroform-*d*)

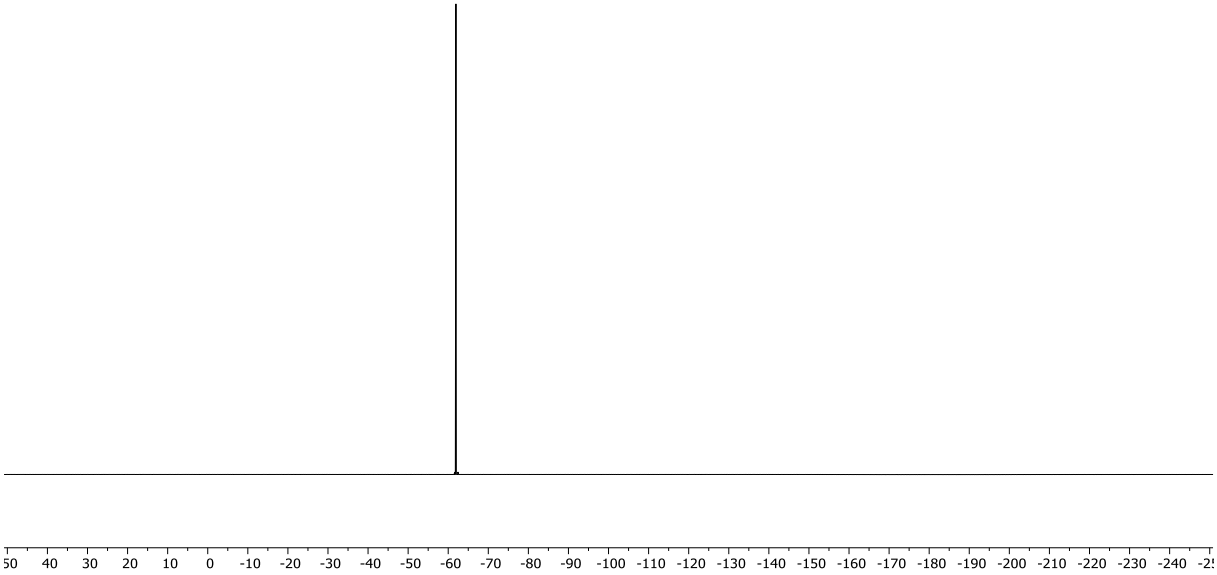


13C{1H} NMR(101 MHz, Chloroform-*d*)

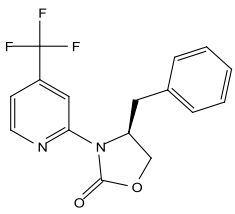


$^{19}F\{^{1}H\}$ NMR(376 MHz, Chloroform-*d*)

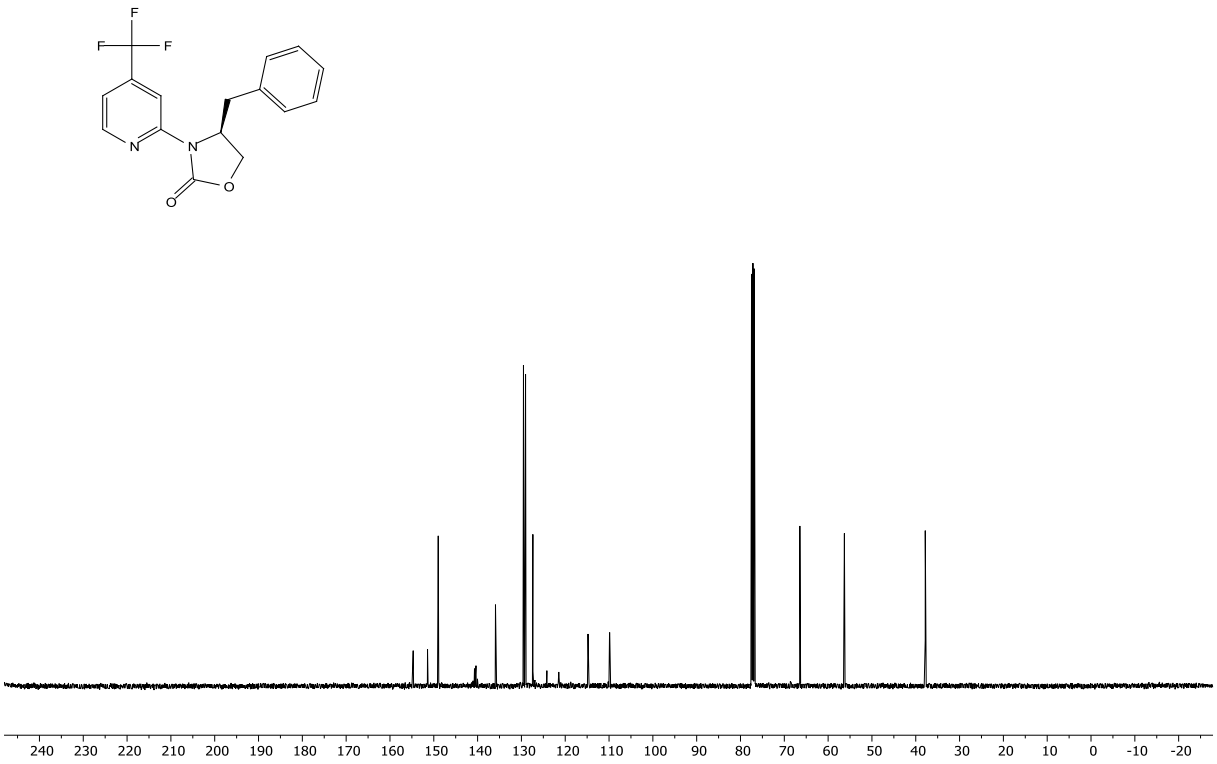




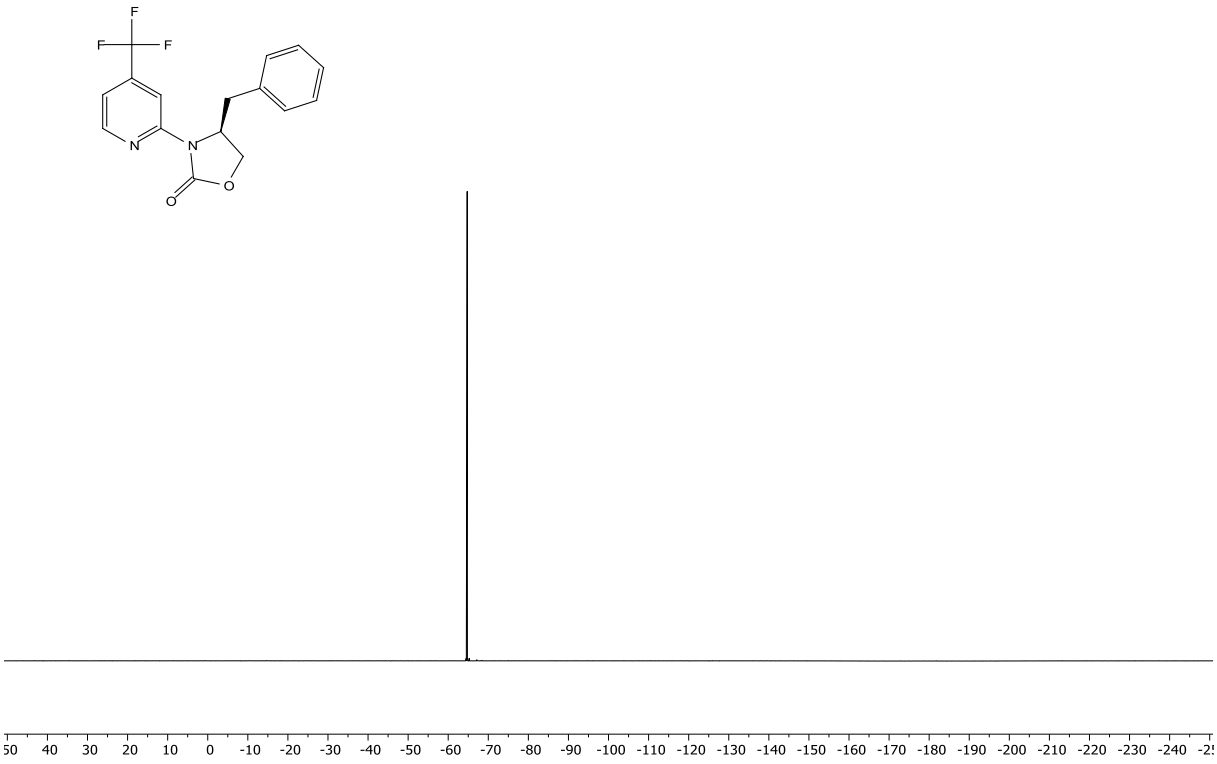
^{1}H NMR(400 MHz, Chloroform-*d*)



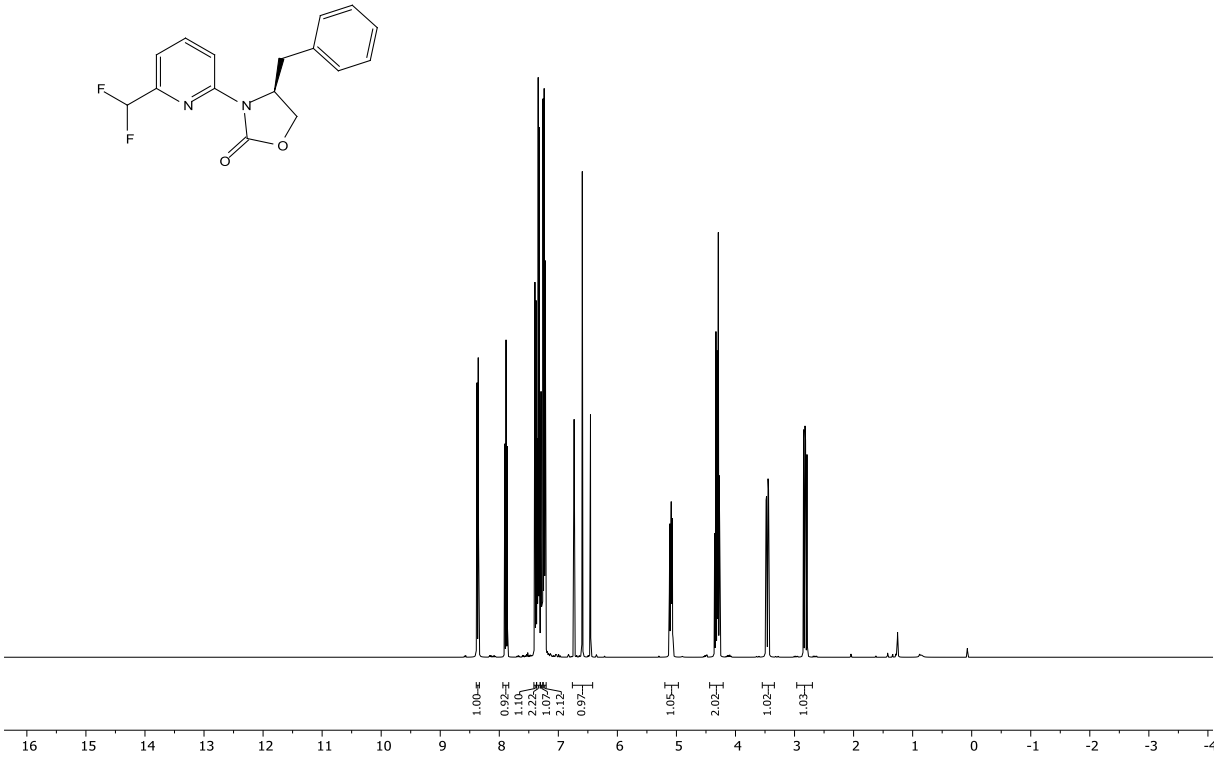
$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*)



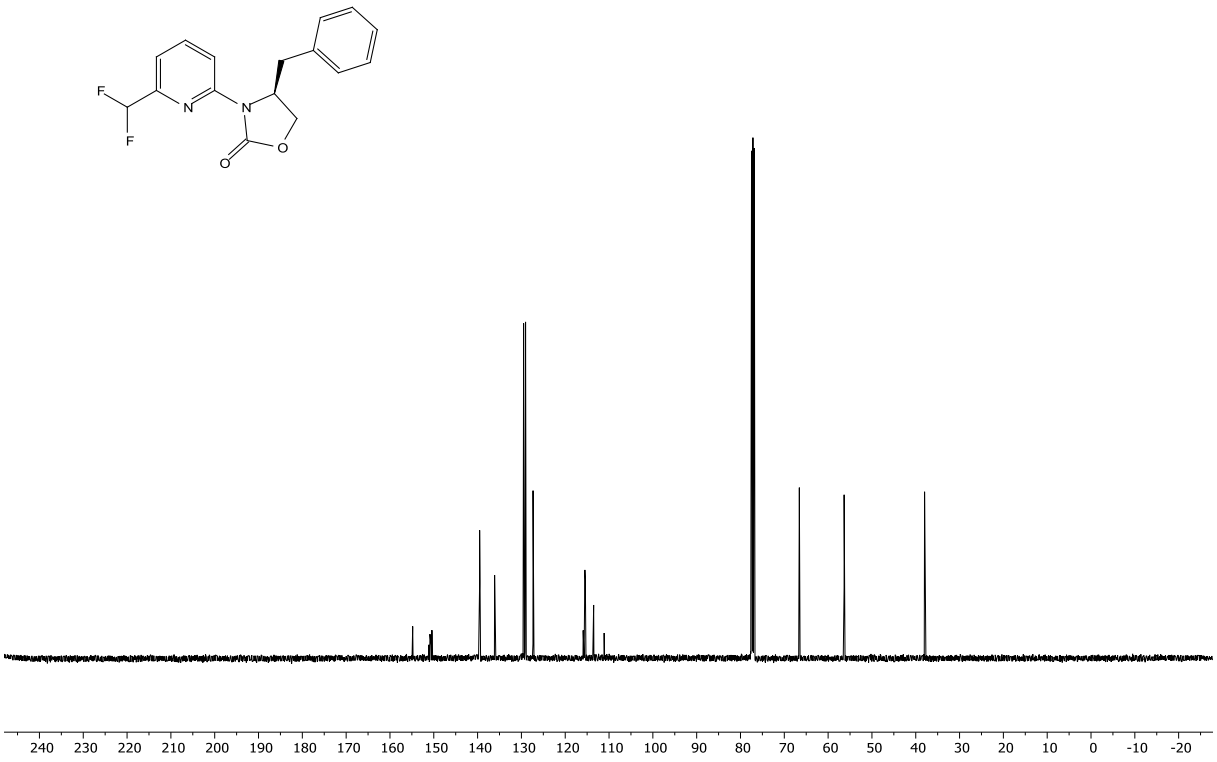
^{19}F NMR (376 MHz, Chloroform-*d*)



^{1}H NMR(400 MHz, Chloroform-*d*)

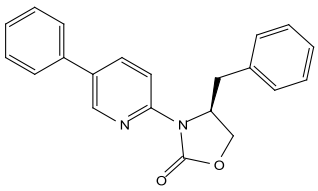


^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)

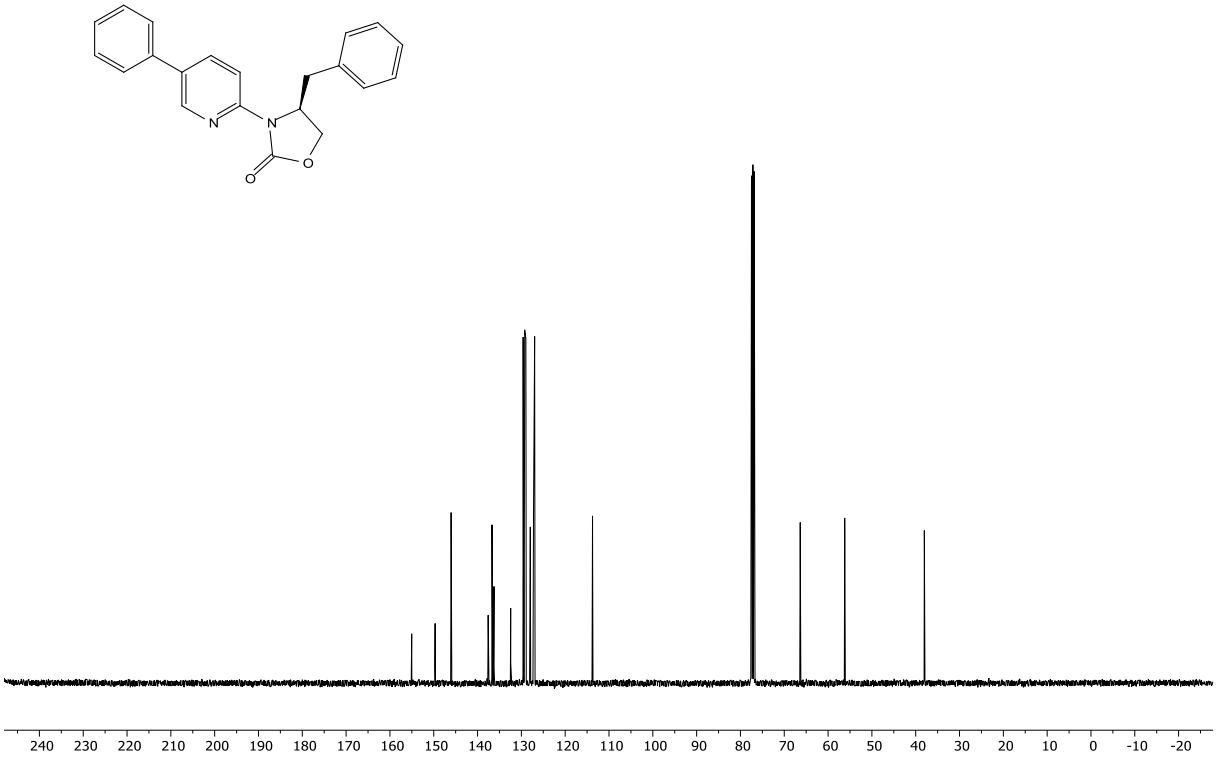


^{19}F-NMR(377 MHz, Chloroform-*d*)

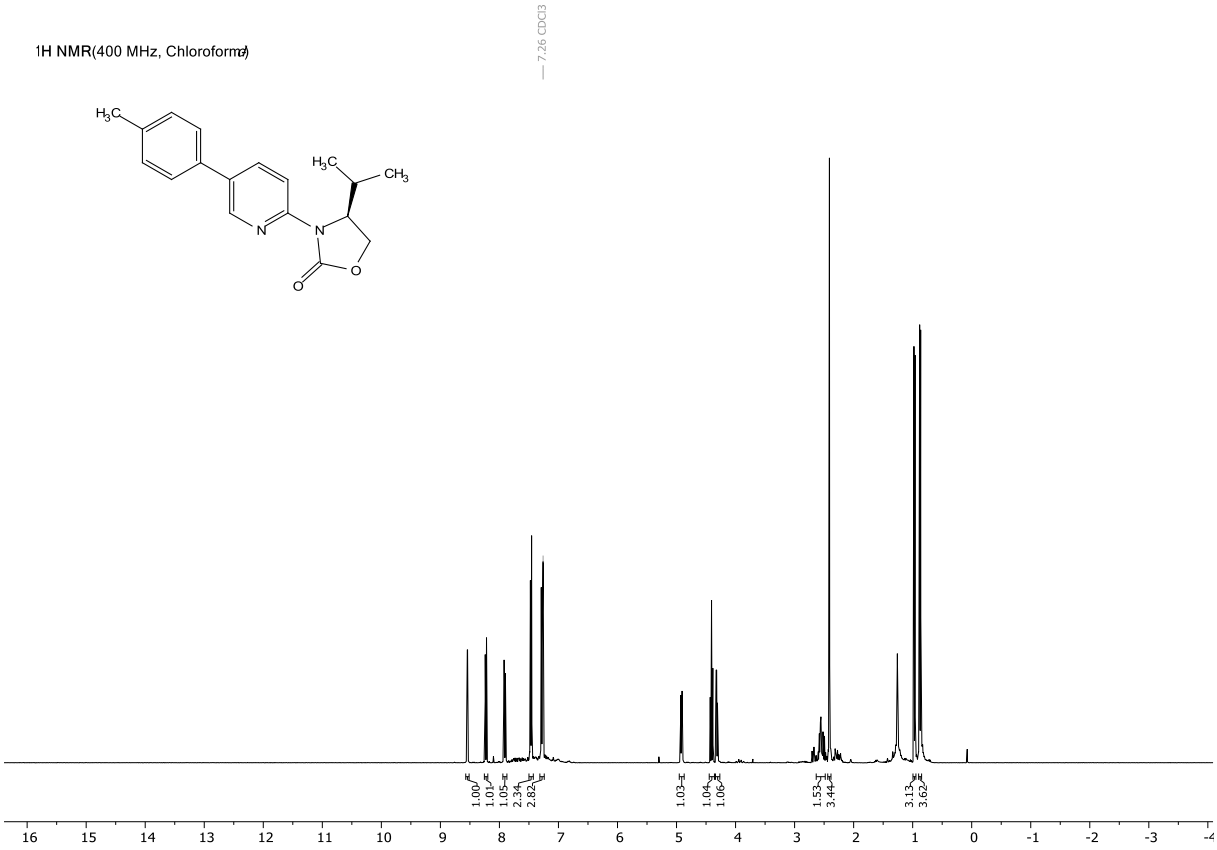
^{1}H NMR(300 MHz, Chloroform-*d*)

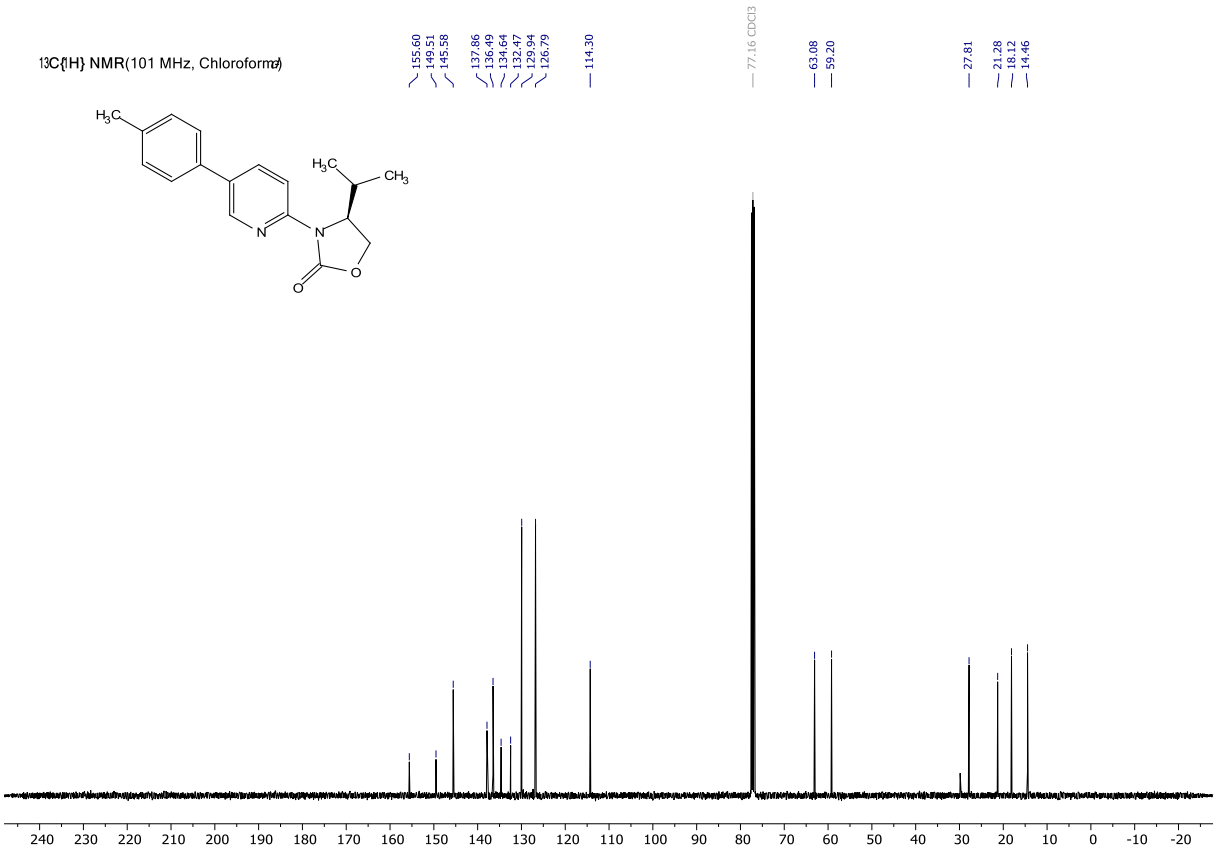


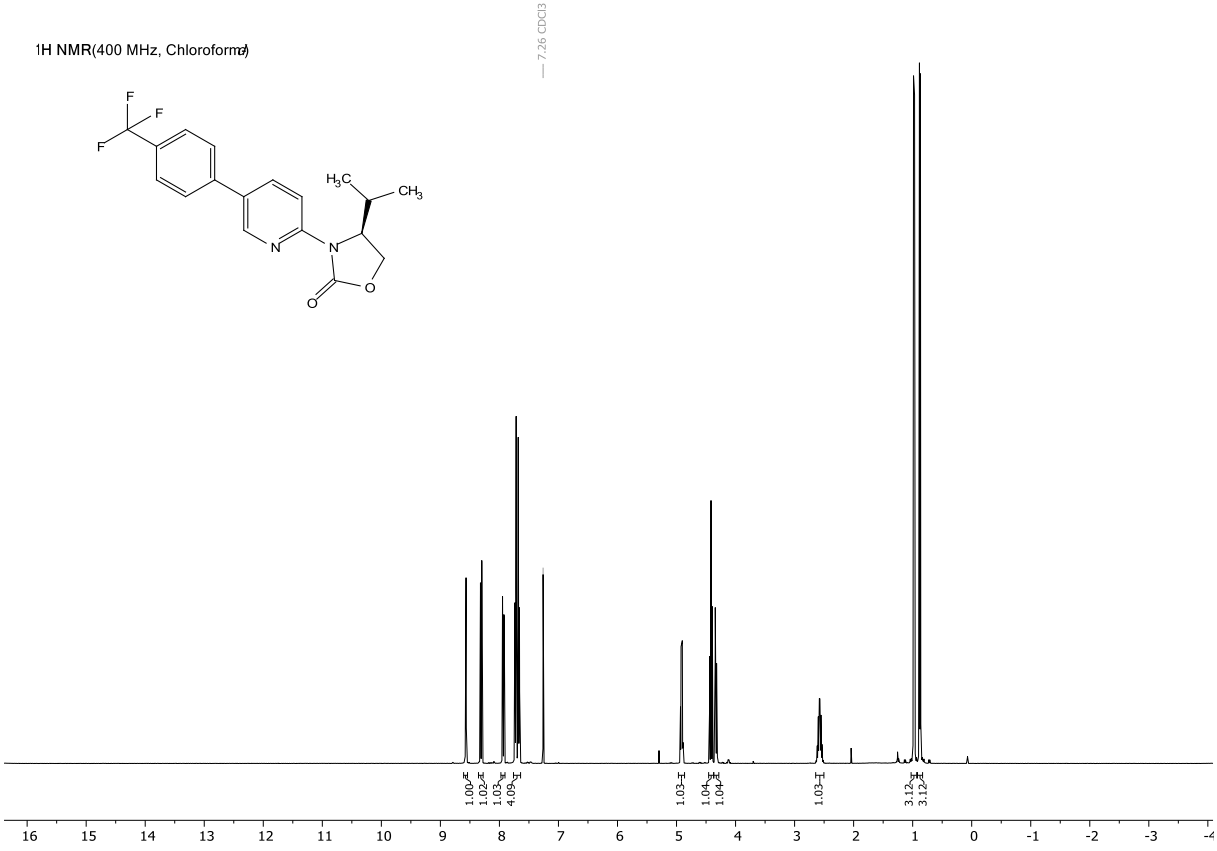
$^{13}C\{^1H\}$ NMR(75 MHz, Chloroform-*d*)



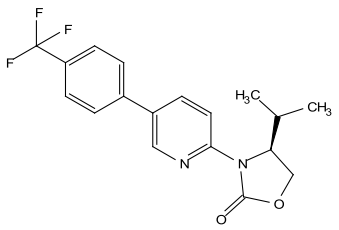
^1H NMR(400 MHz, Chloroform-*d*)



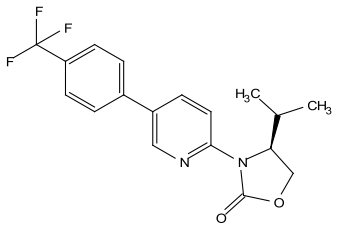

13C{1H} NMR(101 MHz, Chloroform-d)
155.60
149.51
145.58
137.86
136.49
134.64
132.47
129.94
126.79
114.30
77.16 CDCl3
63.08
59.20
27.81
21.28
18.12
14.46
H3C
CH3
N
N
O
O
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

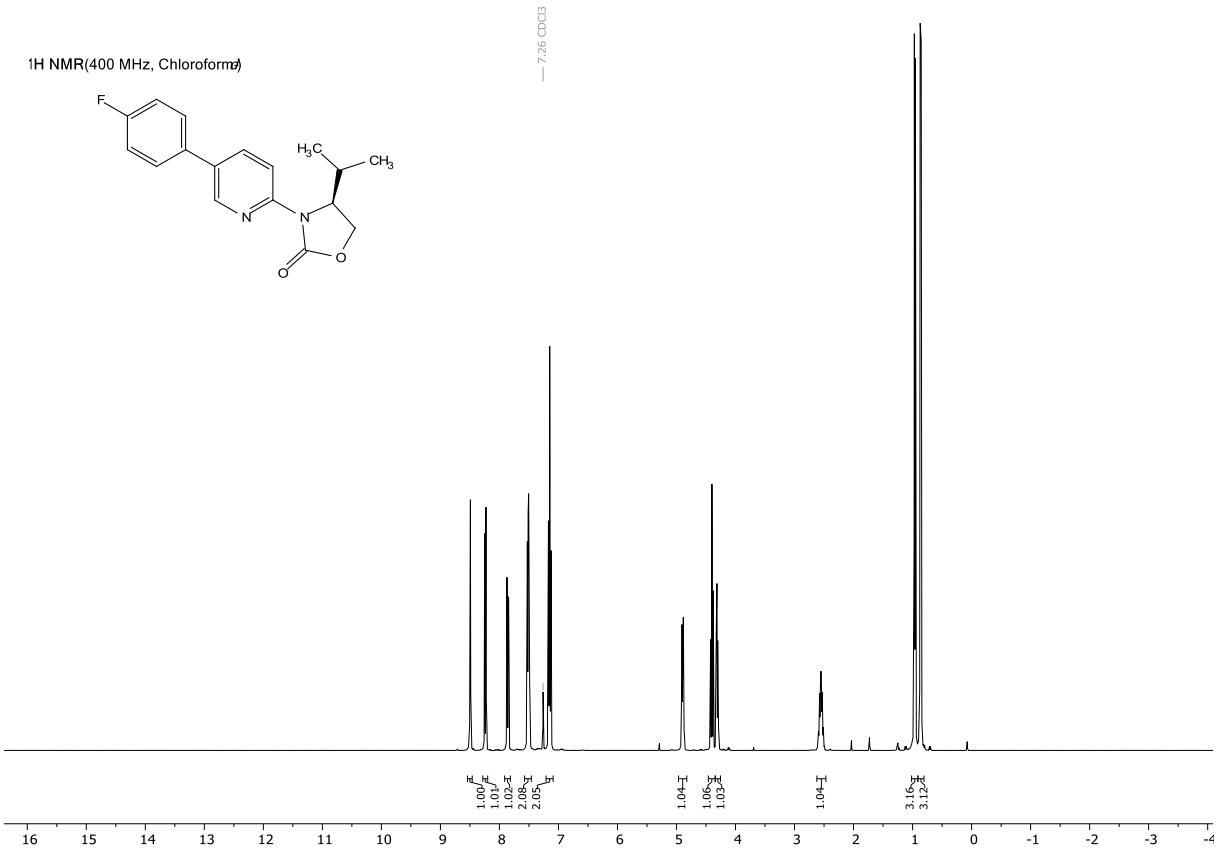

1H NMR(400 MHz, Chloroform-d)
7.26 CDCl3
F
F
F
H3C
CH3
N
N
O
O
1.00
1.02
1.03
4.09
1.03
1.04
1.04
1.03
3.12
3.12
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3

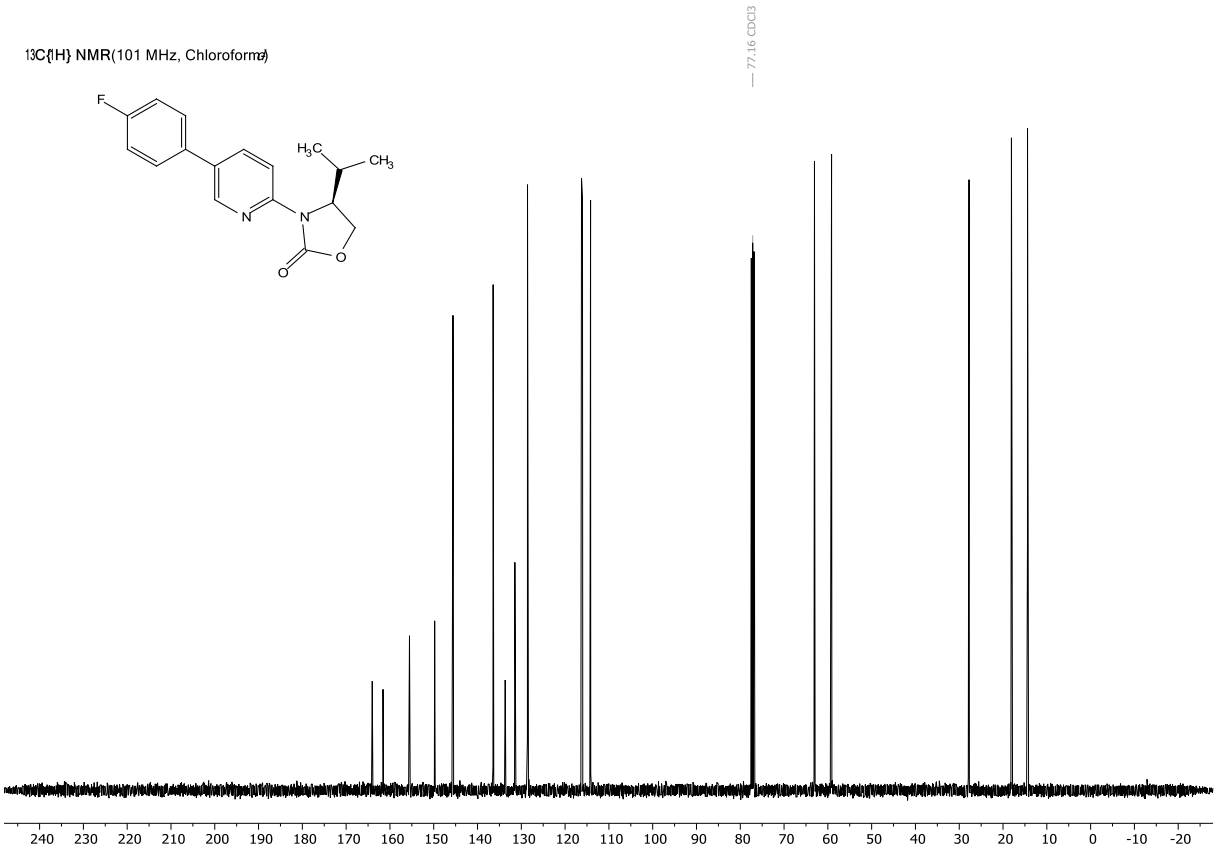
$^{13}C\{^{1}H\}$ NMR(101 MHz, Chloroform-*d*)



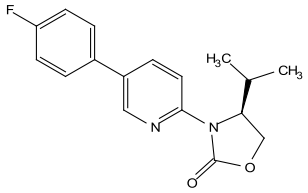
$^{19}F\{^{1}H\}$ NMR(376 MHz, Chloroform-*d*)



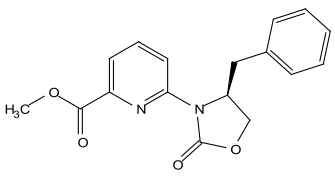

1H NMR(400 MHz, Chloroform-d)
7.26 CDCl3
1.00
1.01
1.02
2.08
2.05
1.04
1.06
1.03
1.04
3.16
3.12


13C{1H} NMR(101 MHz, Chloroform-d)
77.16 CDCl3

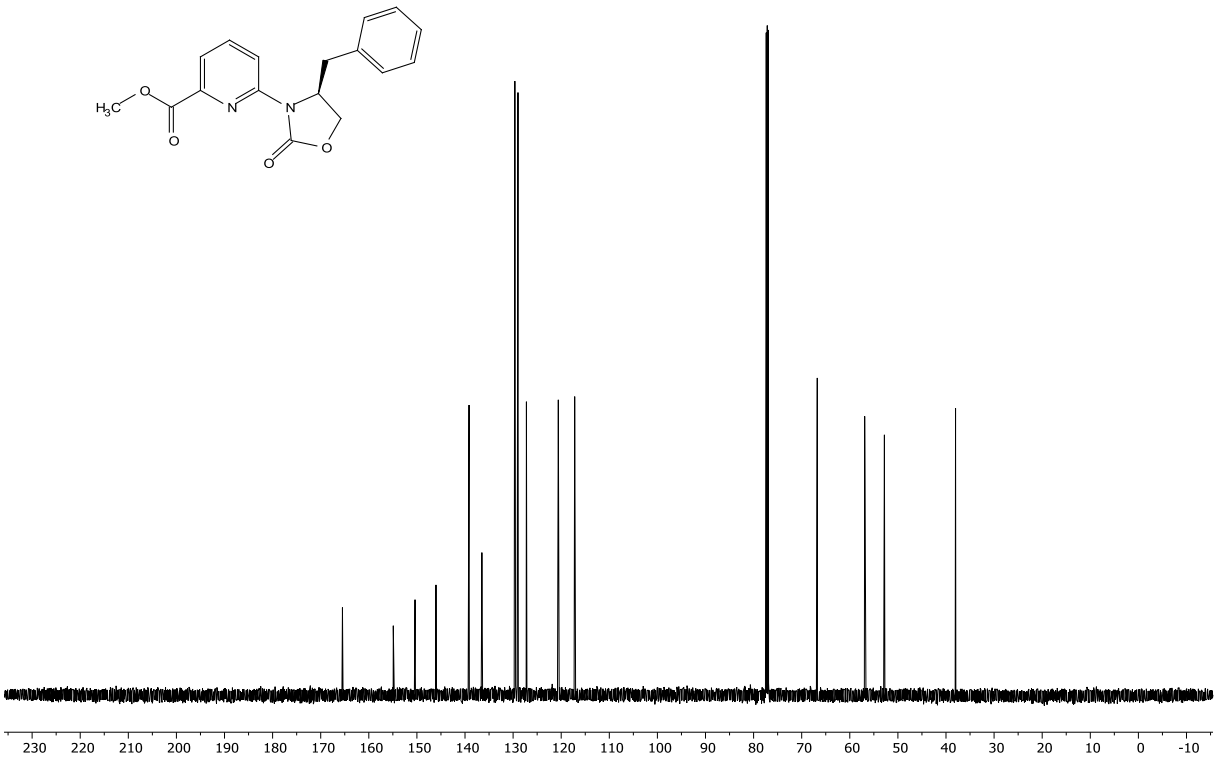
$^{19}F\{^{1}H\}$ NMR(376 MHz, Chloroform-*d*)



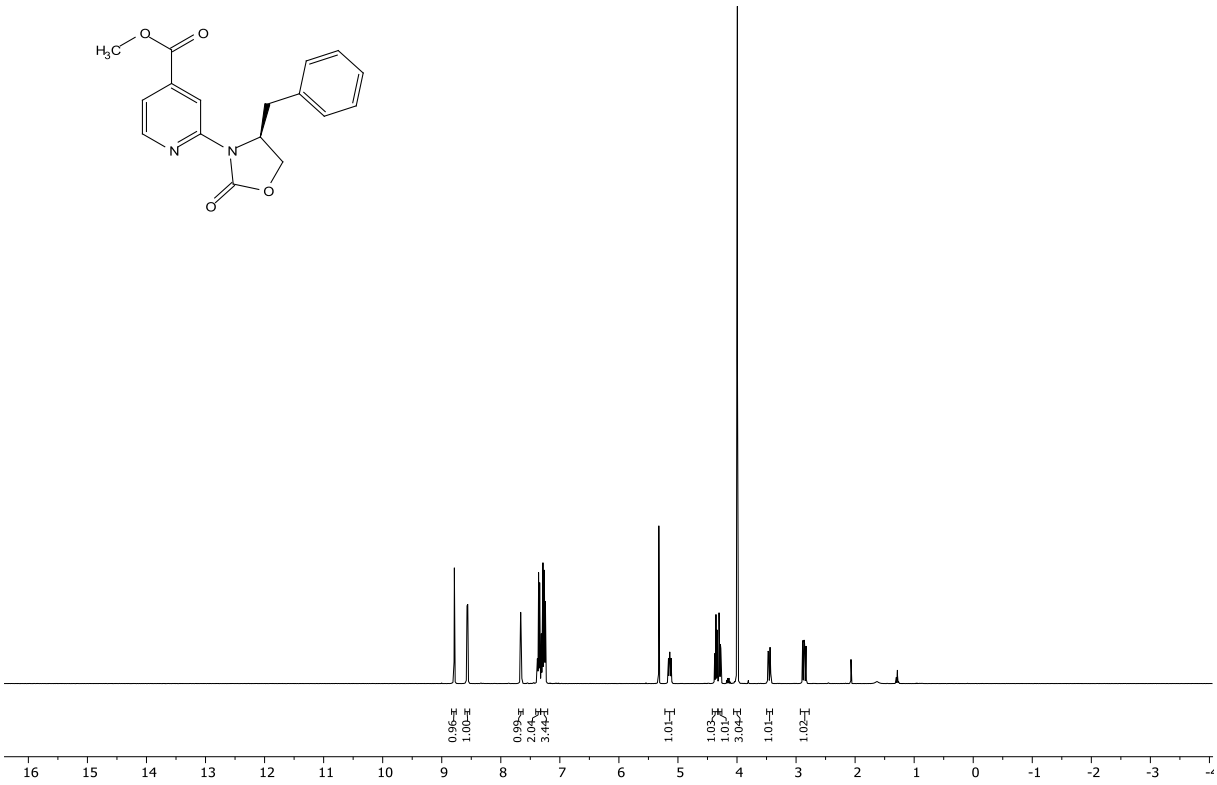
^{1}H NMR(400 MHz, Chloroform-*d*)



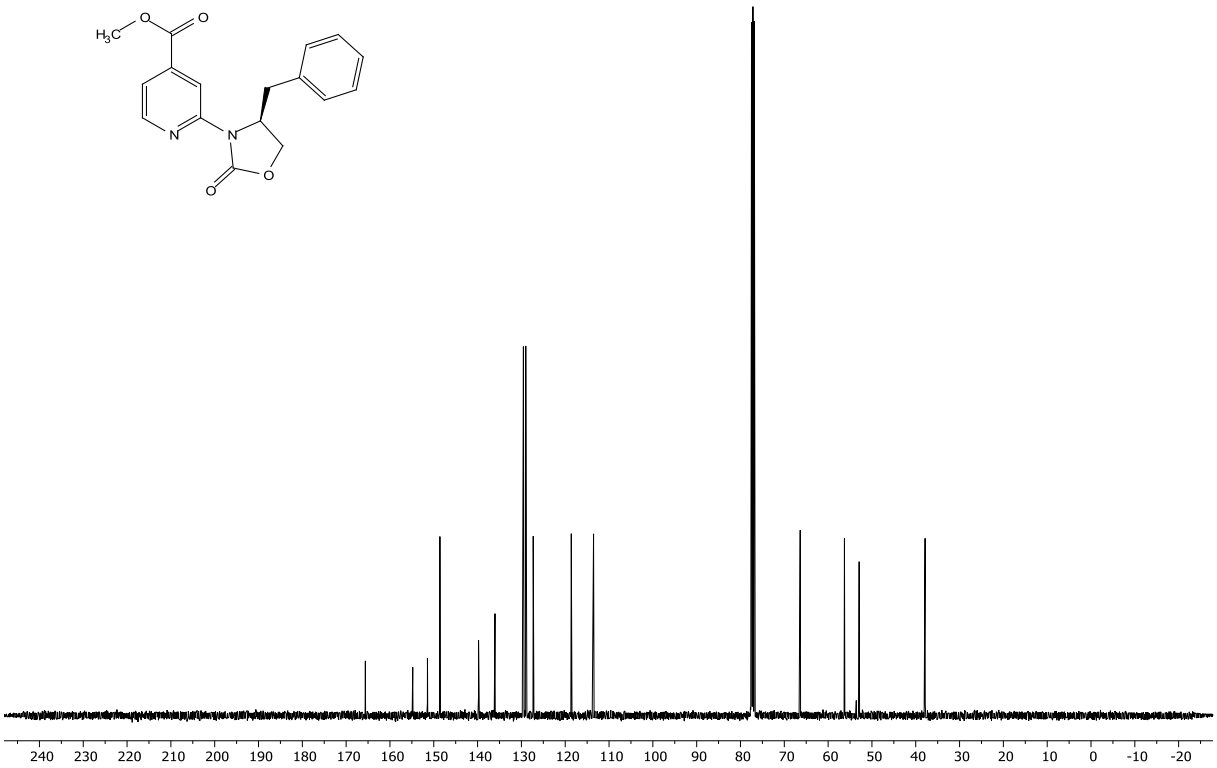
13C{1H} NMR(101 MHz, Chloroform-*d*)



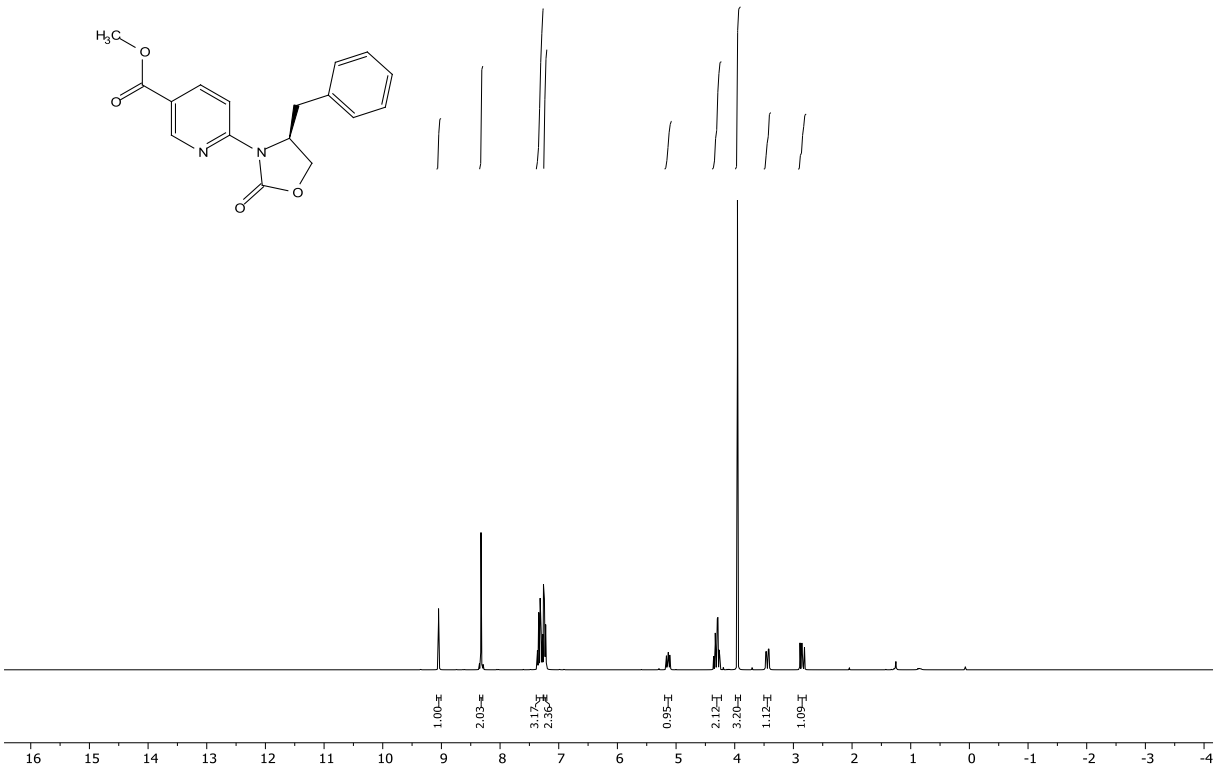
1H NMR(400 MHz, Chloroform-*d*)



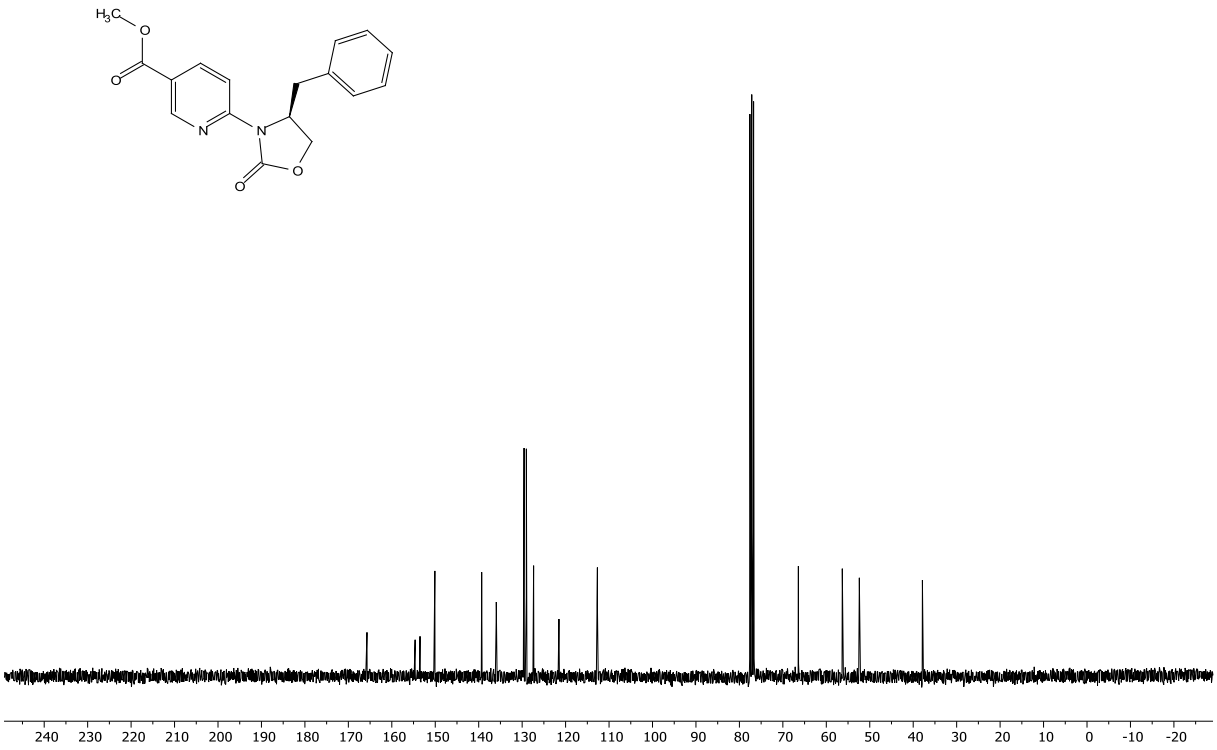
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



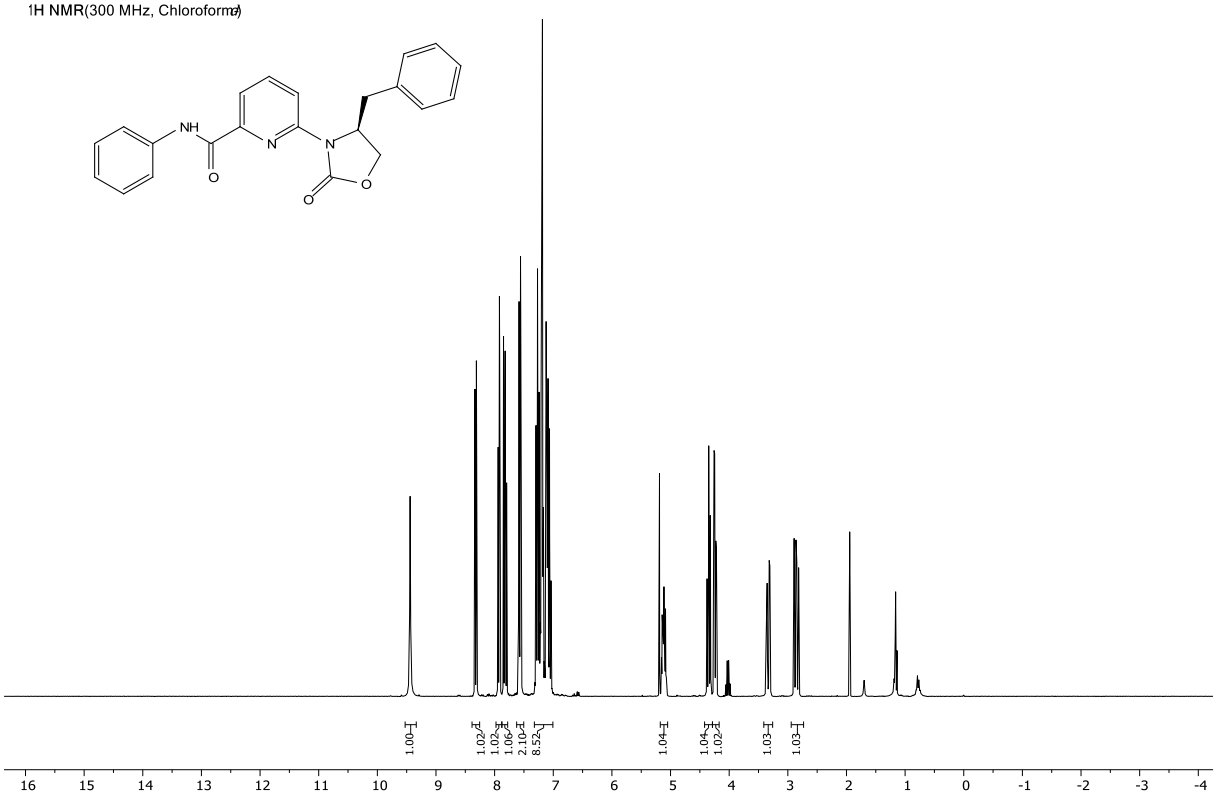
^1H NMR(400 MHz, Chloroform-*d*)

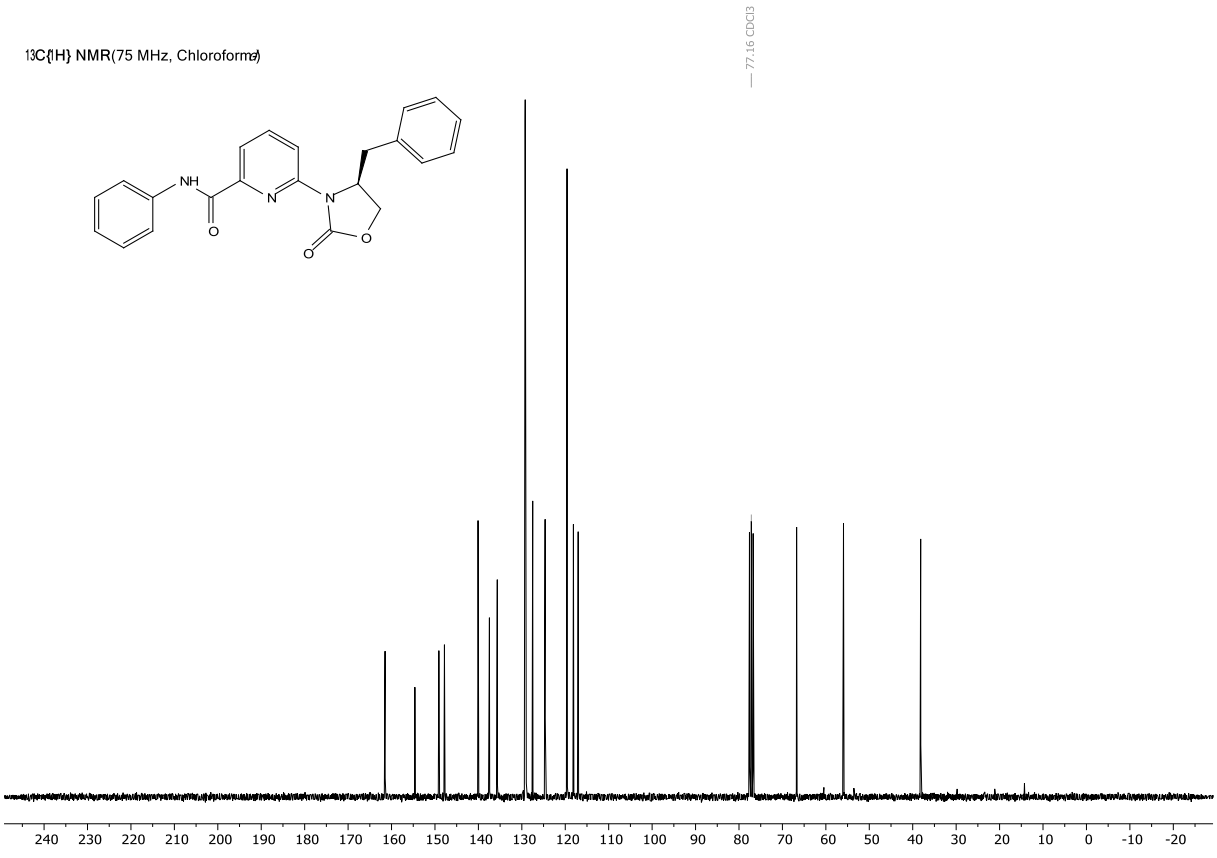


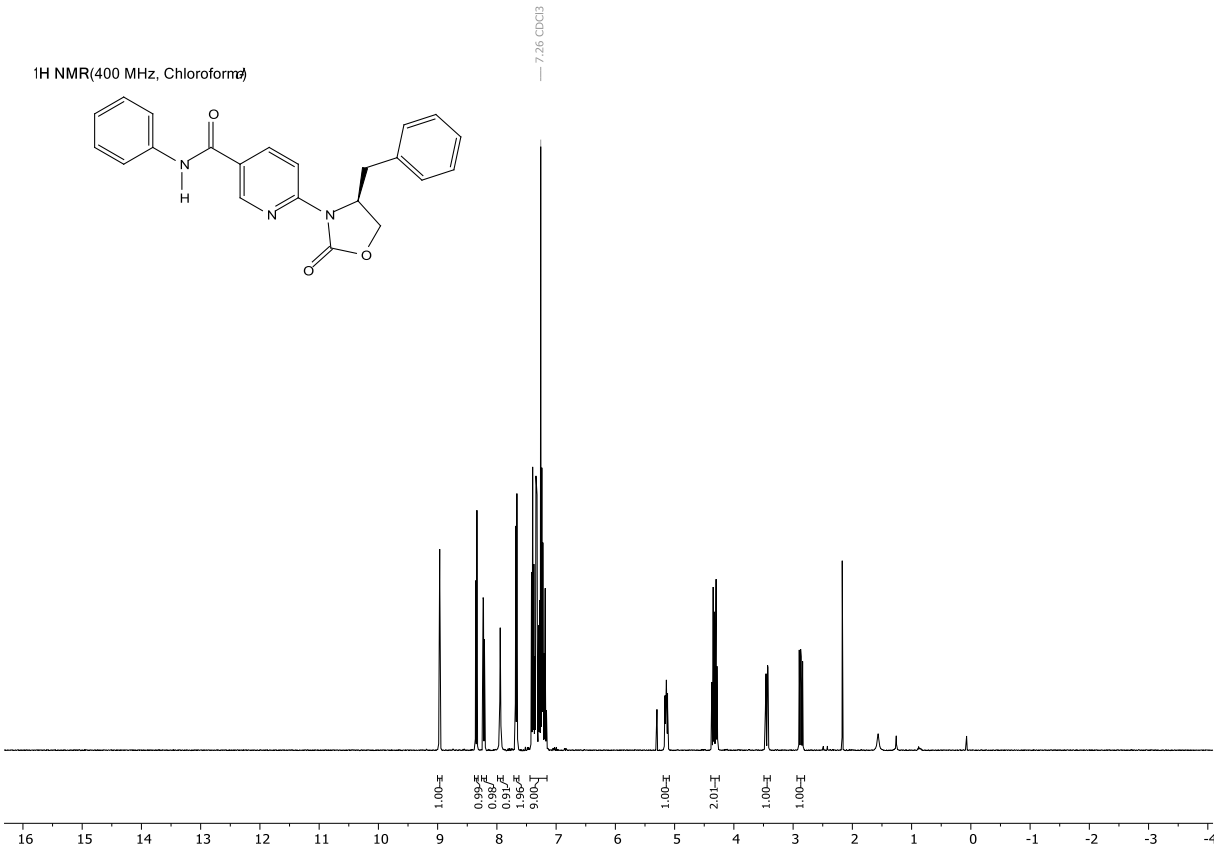
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



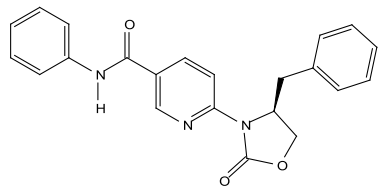
^1H NMR(300 MHz, Chloroform-*d*)



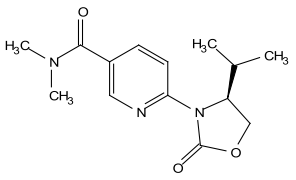

13C{1H} NMR(75 MHz, Chloroform-d)
77.16 CDCl3
NH
N
N
O
O
O
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

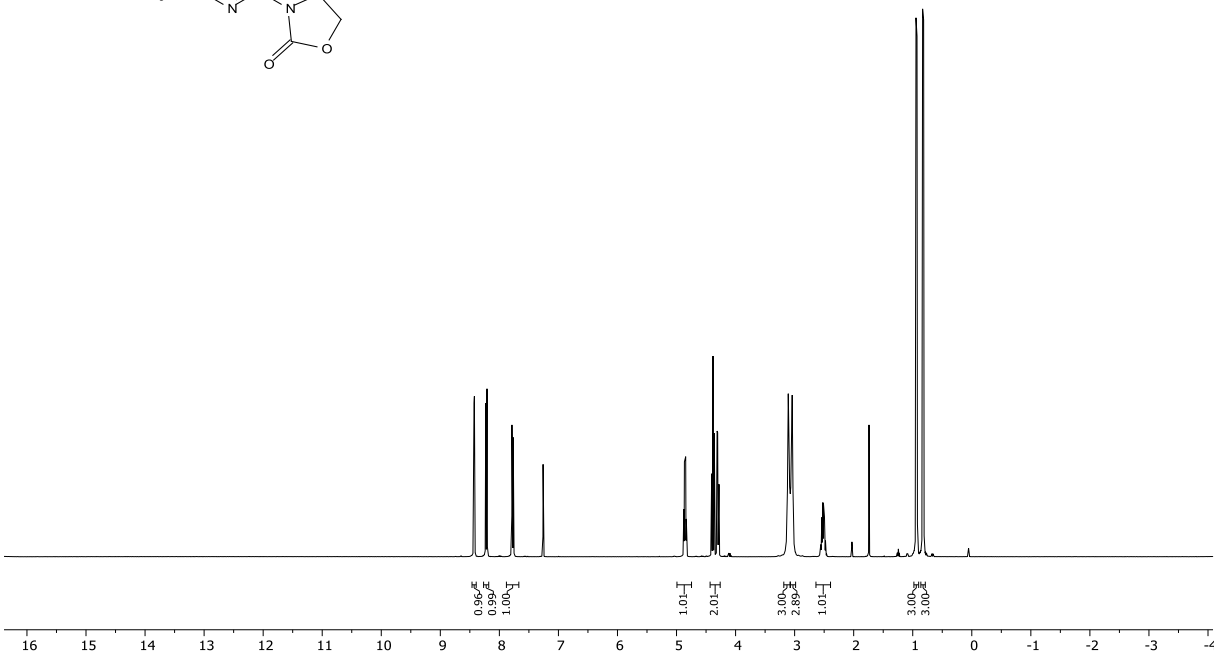

1H NMR(400 MHz, Chloroform-d)
7.26 CDCl3
O
N
H
N
N
O
O
1.00
0.99
0.98
0.97
2.96
6.00
1.00
2.01
1.00
1.00
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3

$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)

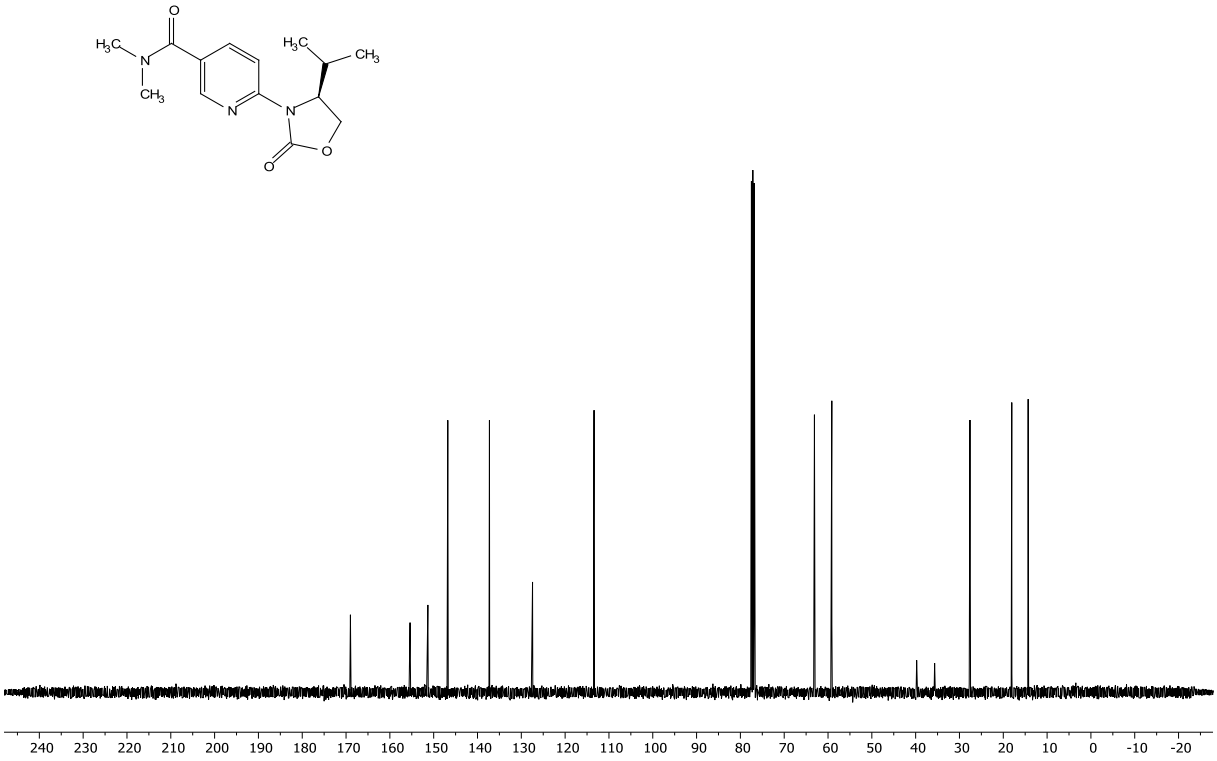


^1H NMR(400 MHz, Chloroform-*d*)

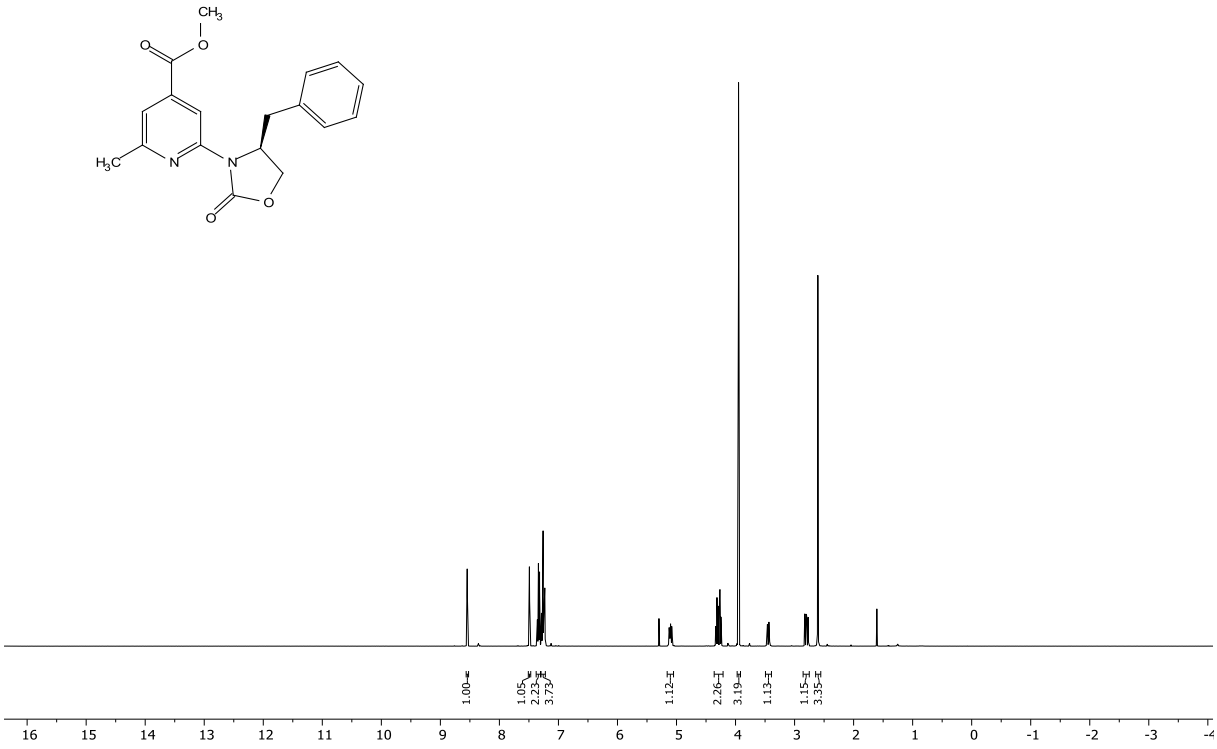




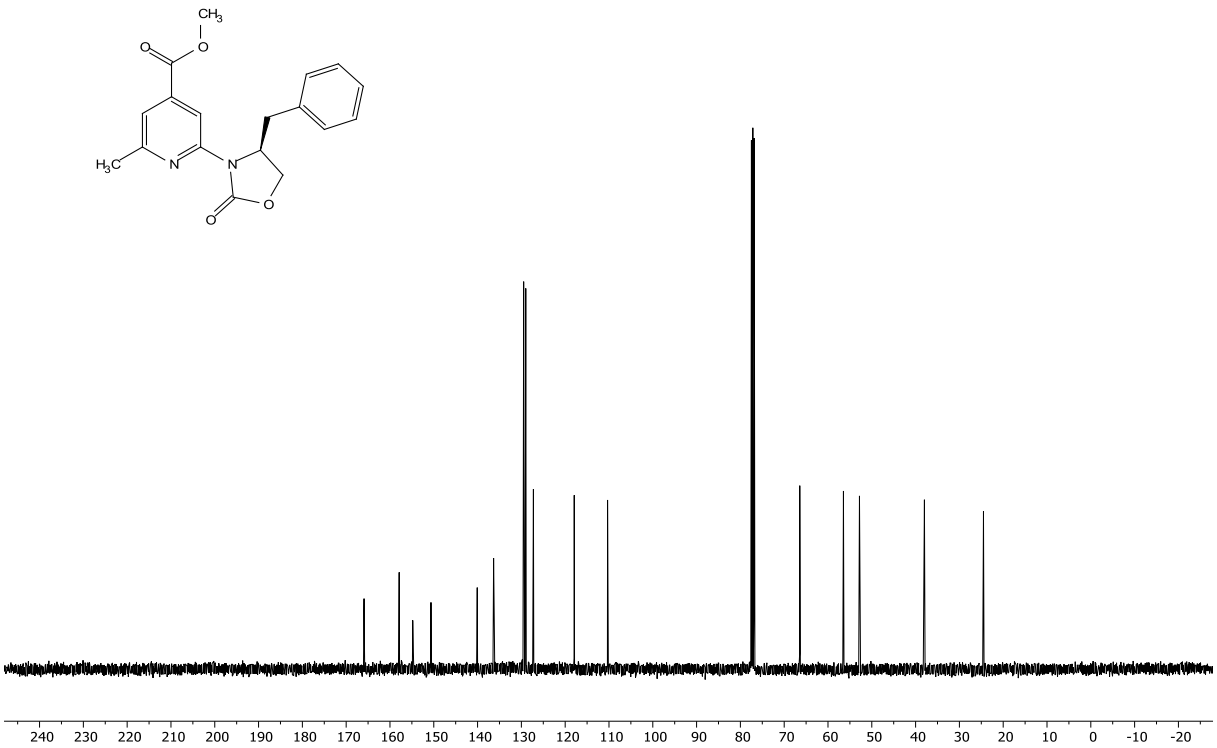
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



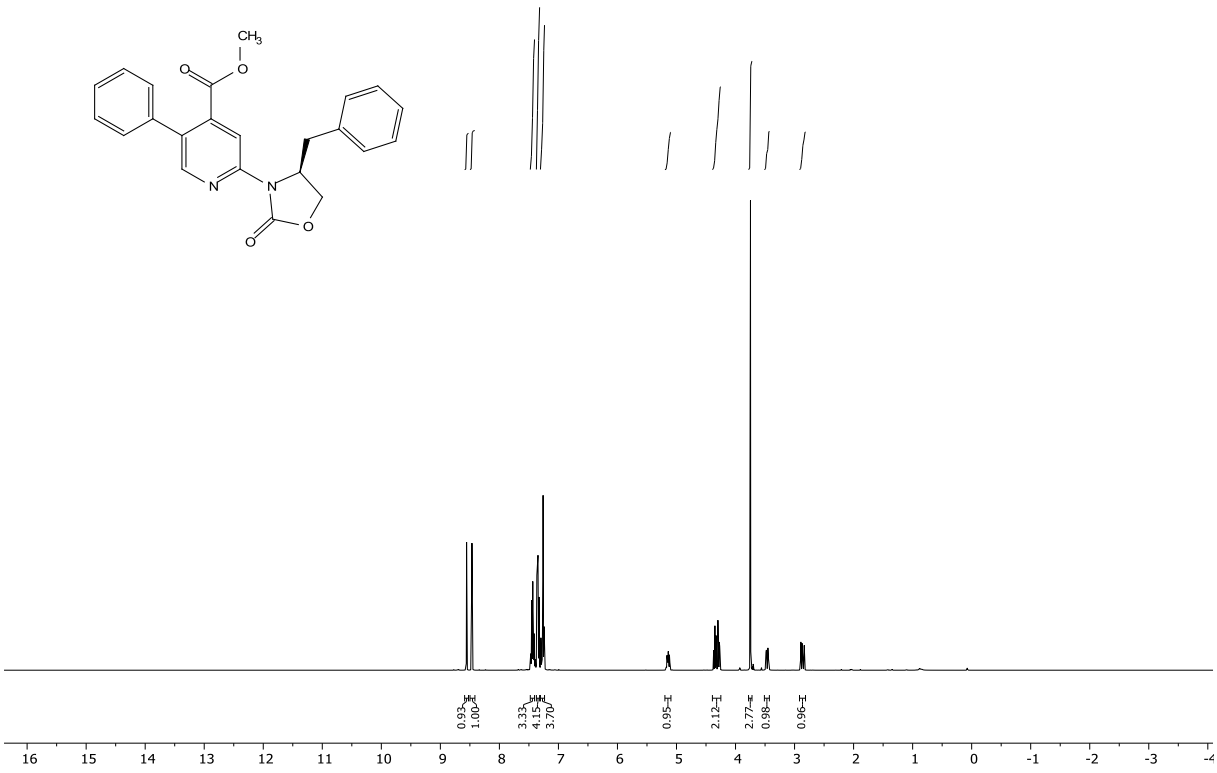
^1H NMR(400 MHz, Chloroform-*d*)



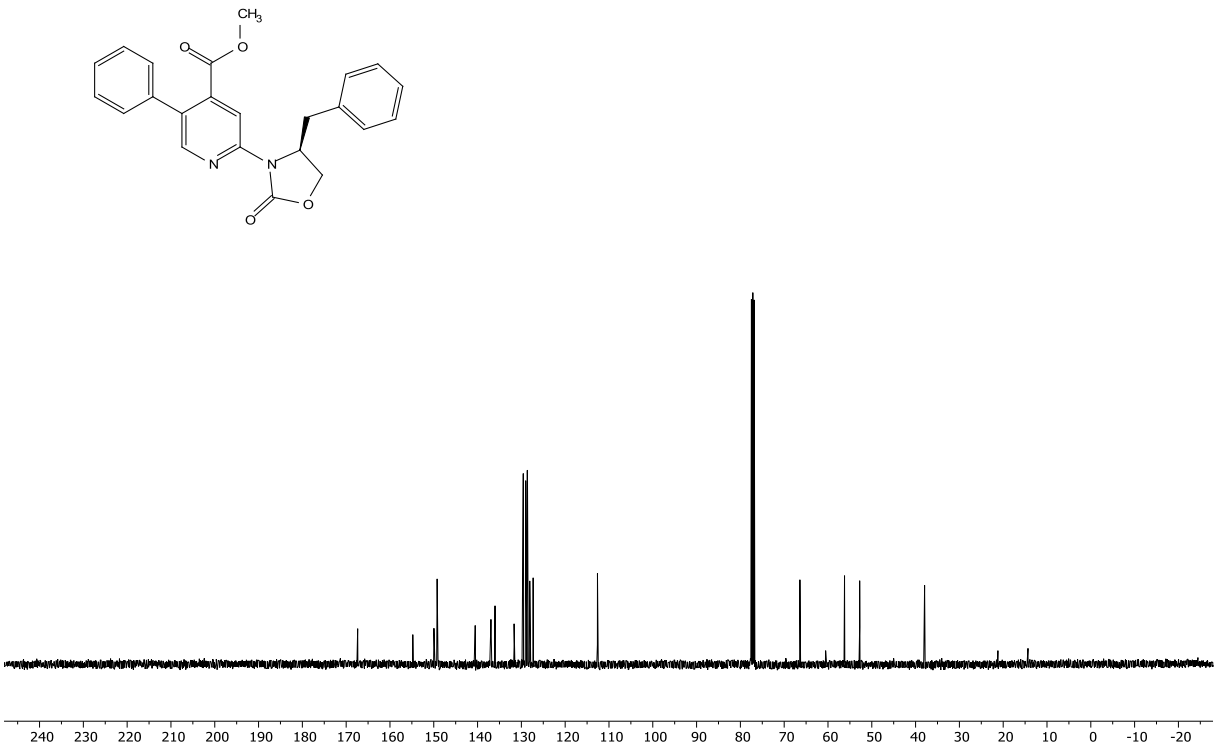
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



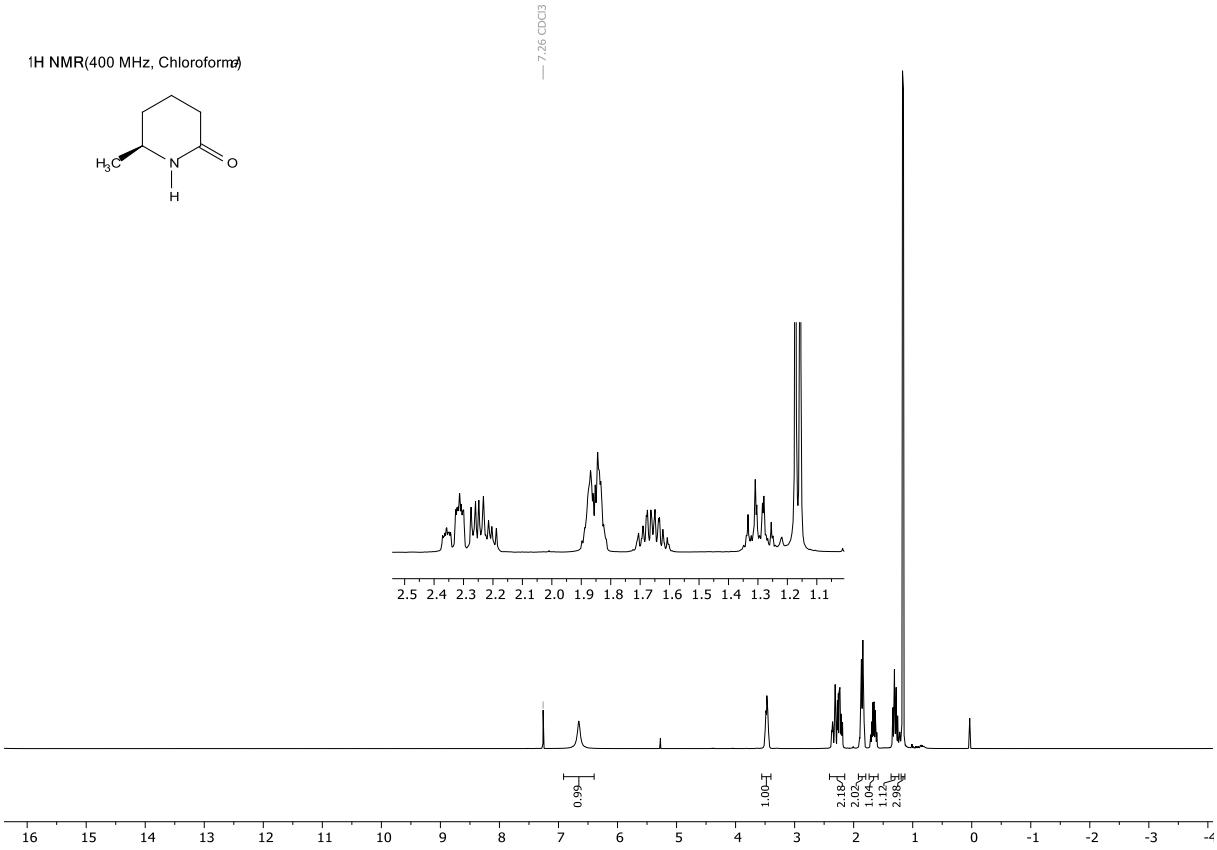
^1H NMR(400 MHz, Chloroform-*d*)

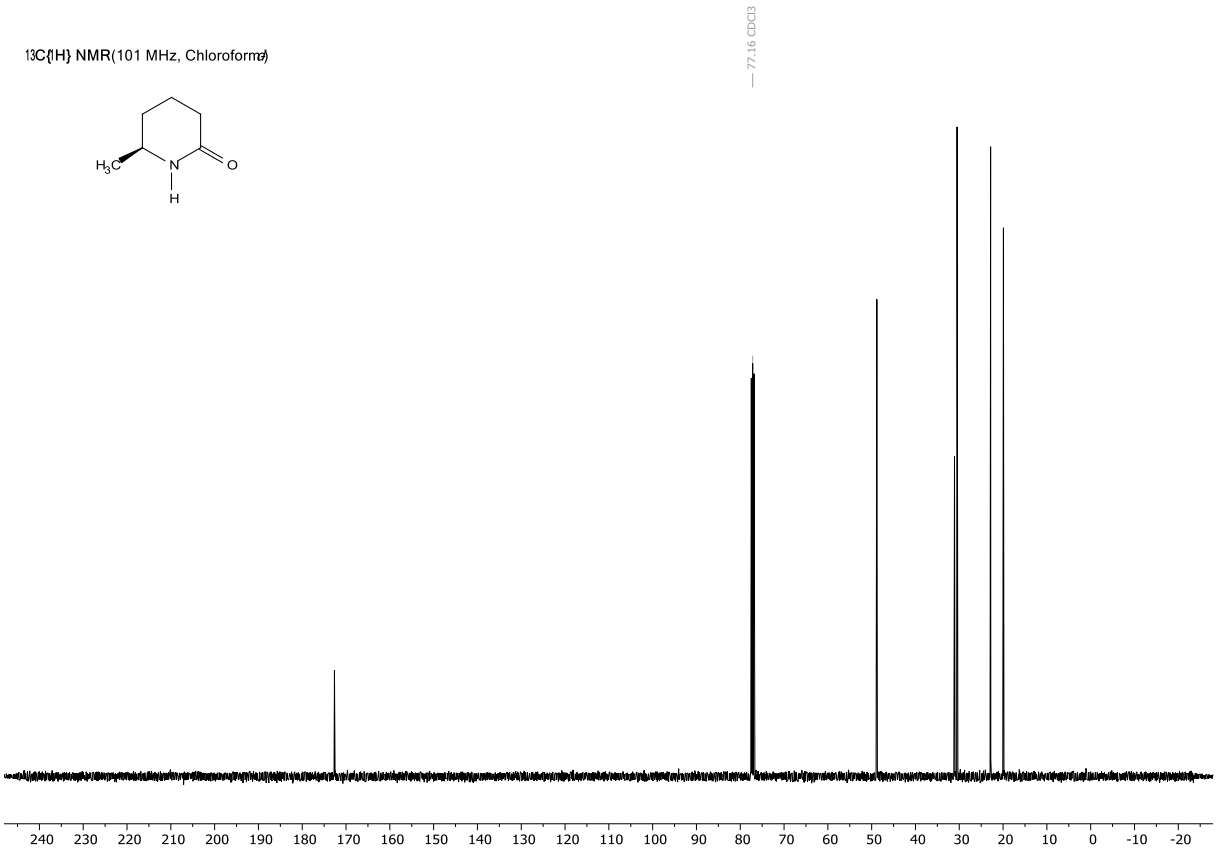


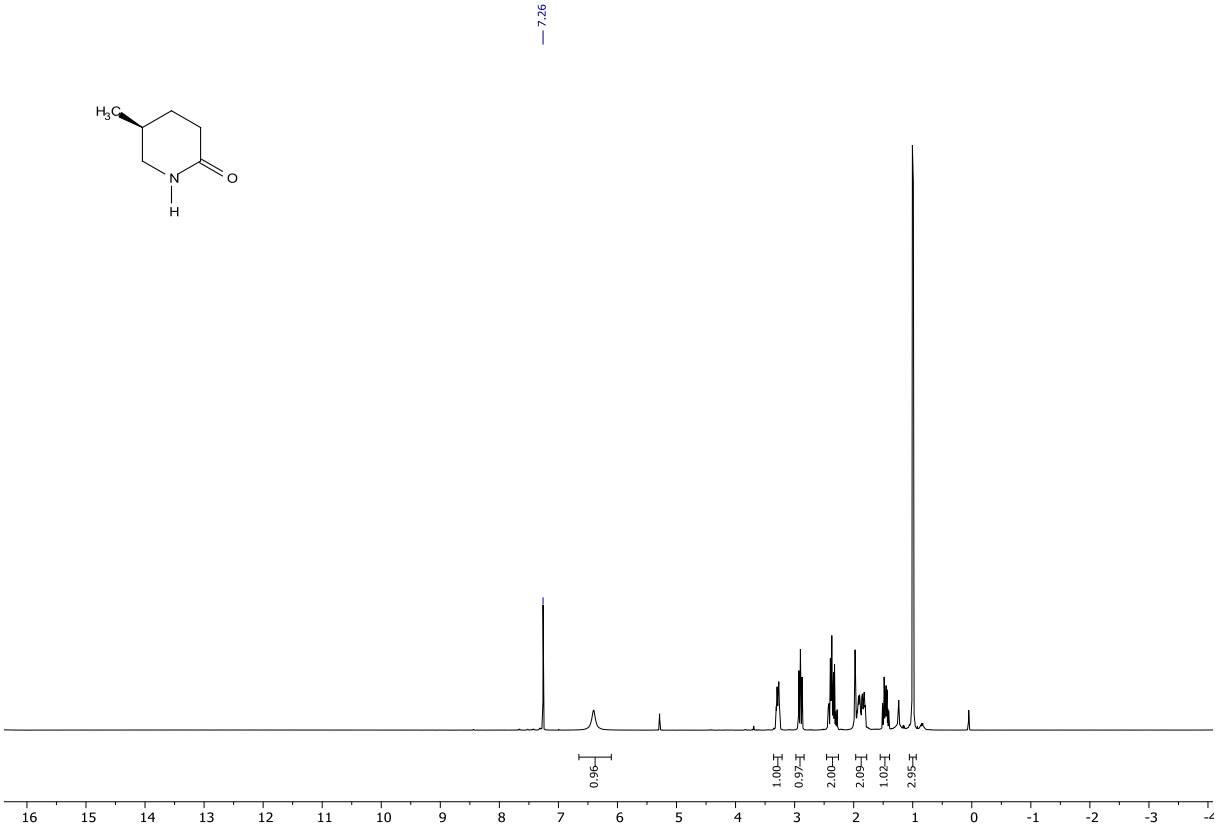
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



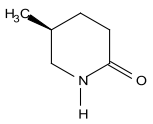
^1H NMR(400 MHz, Chloroform-*d*)

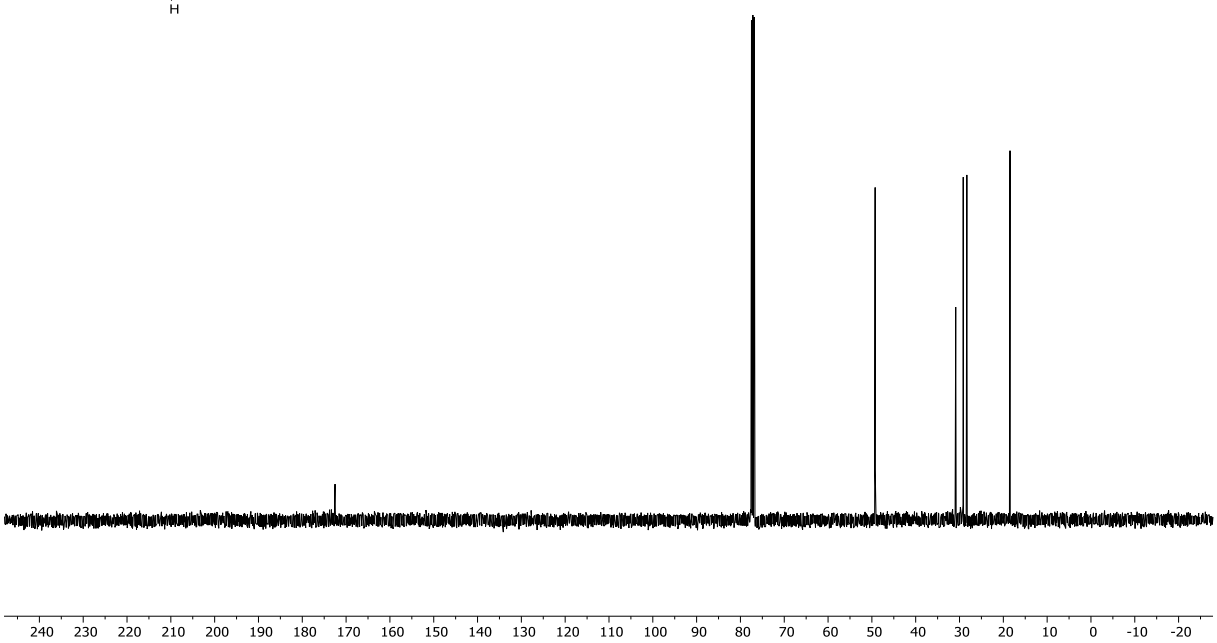



13C{1H} NMR(101 MHz, Chloroform-d)
77.16 CDCl3
H3C
N
H
O
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

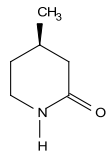

7.26
H3C
N
H
O
0.96
1.00
0.97
2.00
2.09
1.02
2.95
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3

$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)

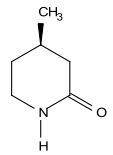




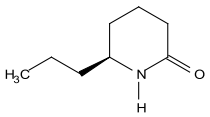
^1H NMR(400 MHz, Chloroform-*d*)



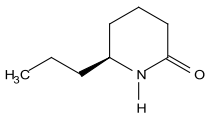
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)

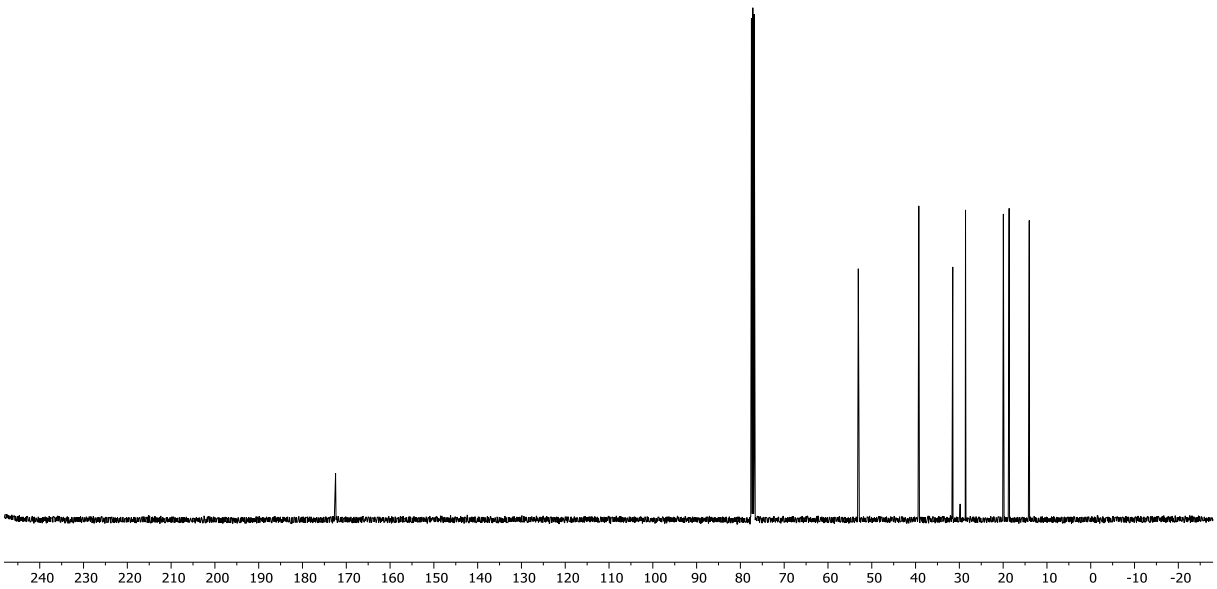


^1H NMR(400 MHz, Chloroform-*d*)

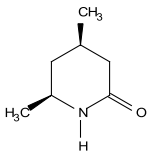


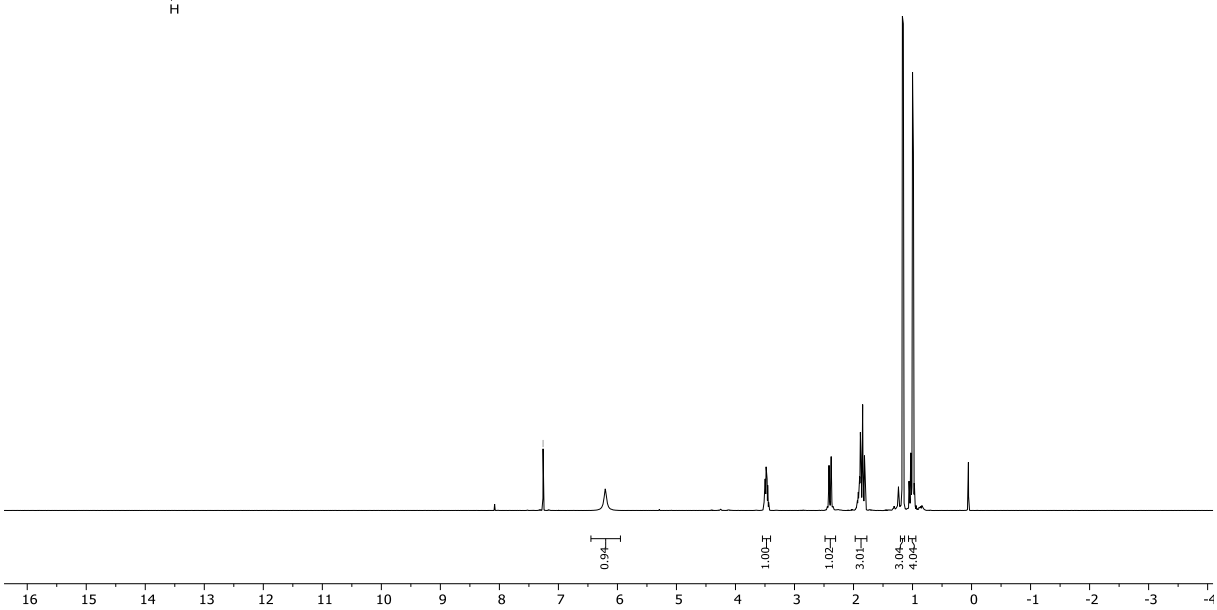
13C{1H} NMR(101 MHz, Chloroform-*d*)



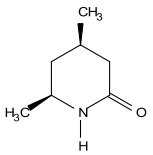


1H NMR(400 MHz, Chloroform-*d*)

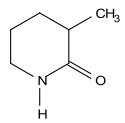




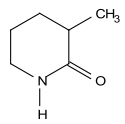
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



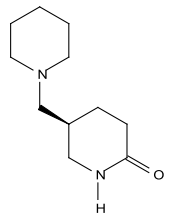
^1H NMR(400 MHz, Chloroform-*d*)

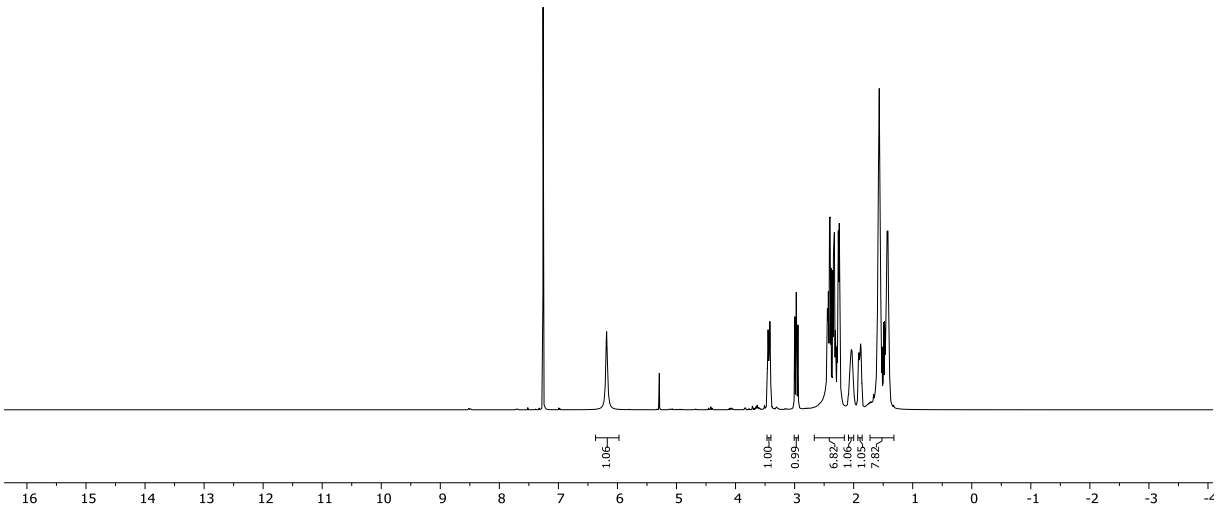


$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)

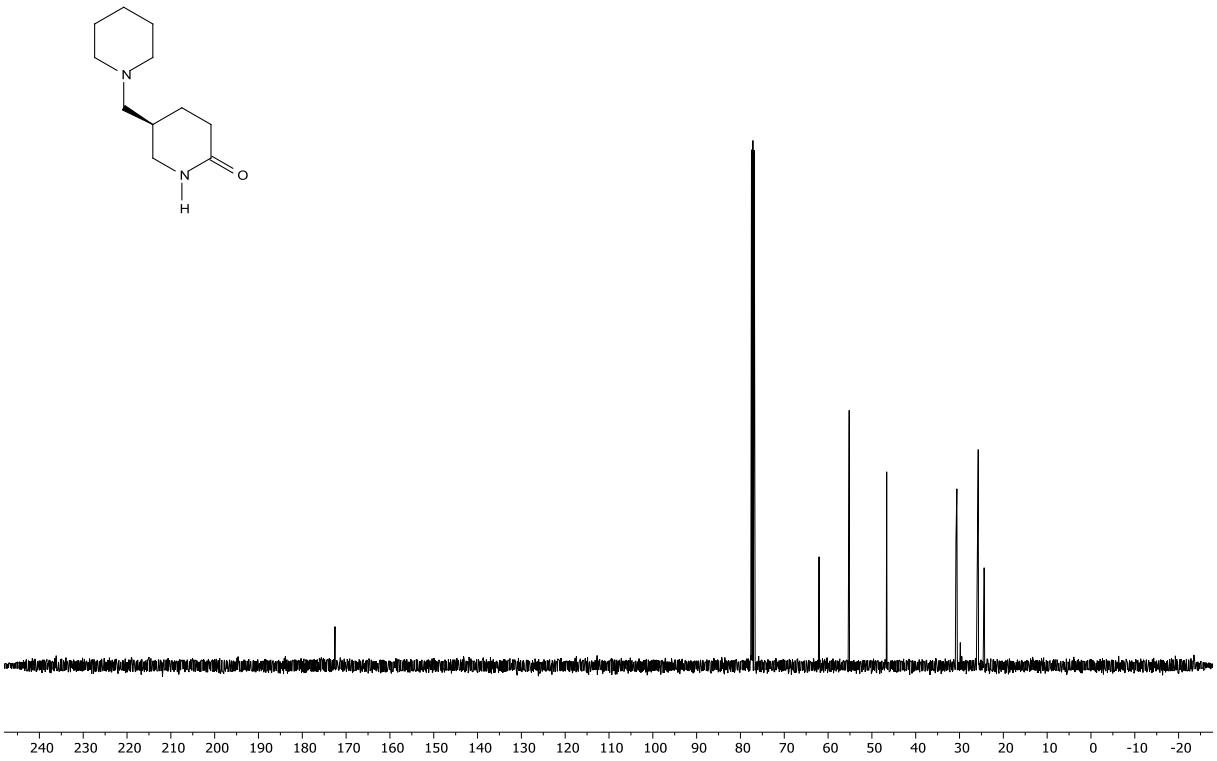


^1H NMR(400 MHz, Chloroform-*d*)

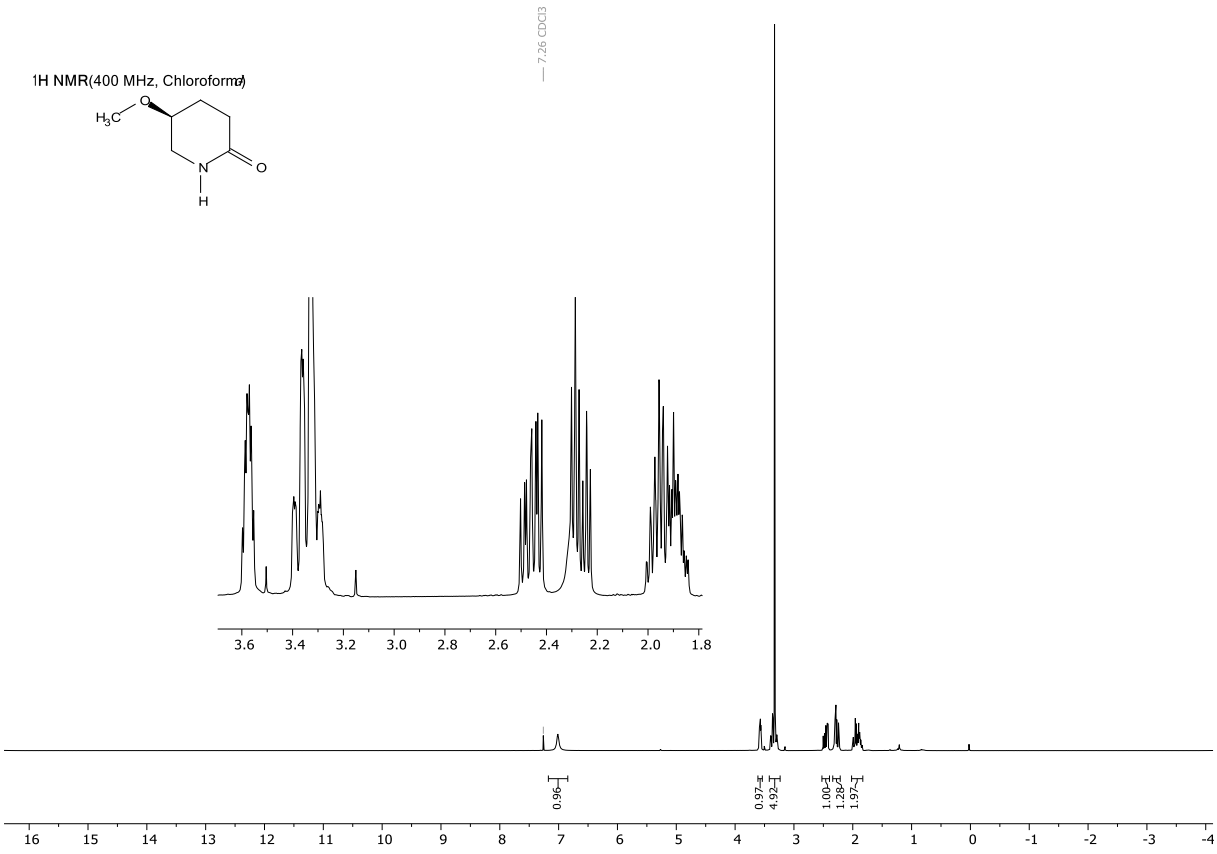




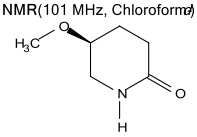
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



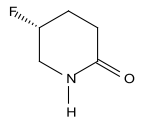
^1H NMR(400 MHz, Chloroform-*d*)



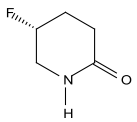
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



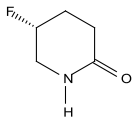
^1H NMR(400 MHz, Chloroform-*d*)



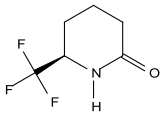
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



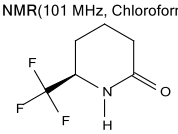
$^{19}F\{^1H\}$ NMR(376 MHz, Chloroform-*d*)



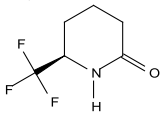
1H NMR(400 MHz, Chloroform-*d*)



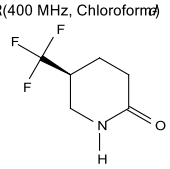
13C{1H} NMR(101 MHz, Chloroform-*d*)



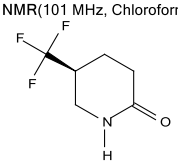
$^{19}F\{^1H\}$ NMR(376 MHz, Chloroform-*d*)



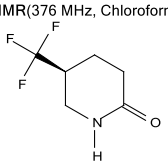
^1H NMR(400 MHz, Chloroform-*d*)

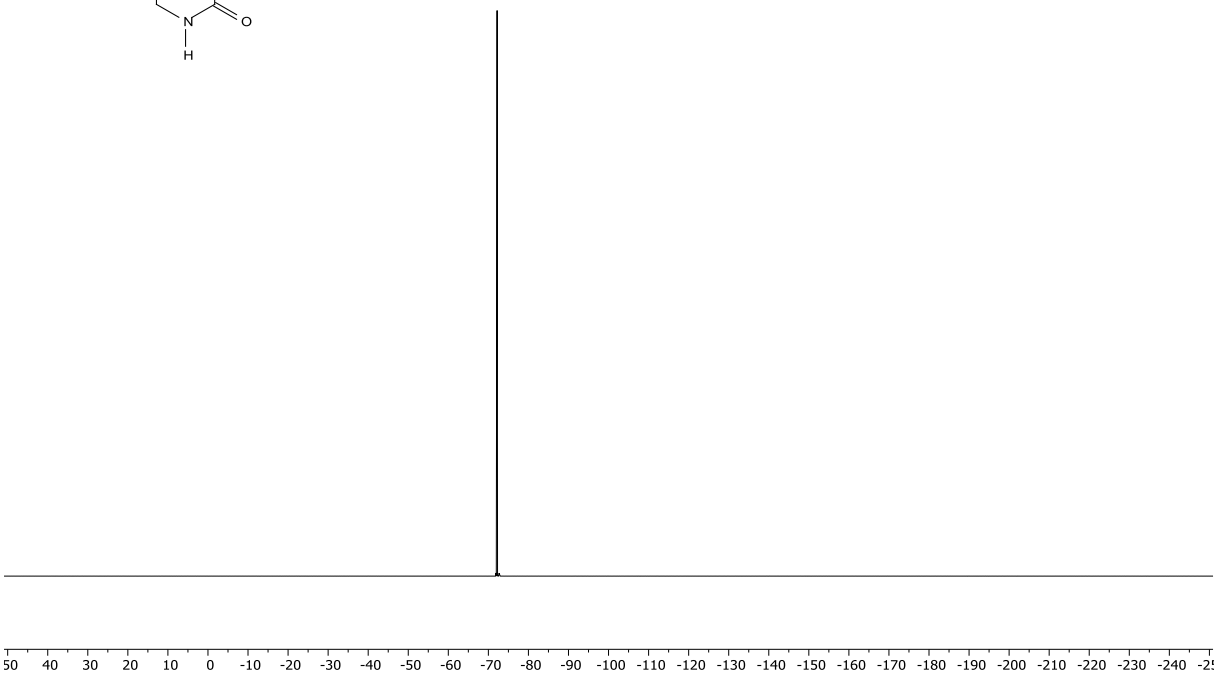


$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)

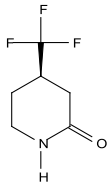


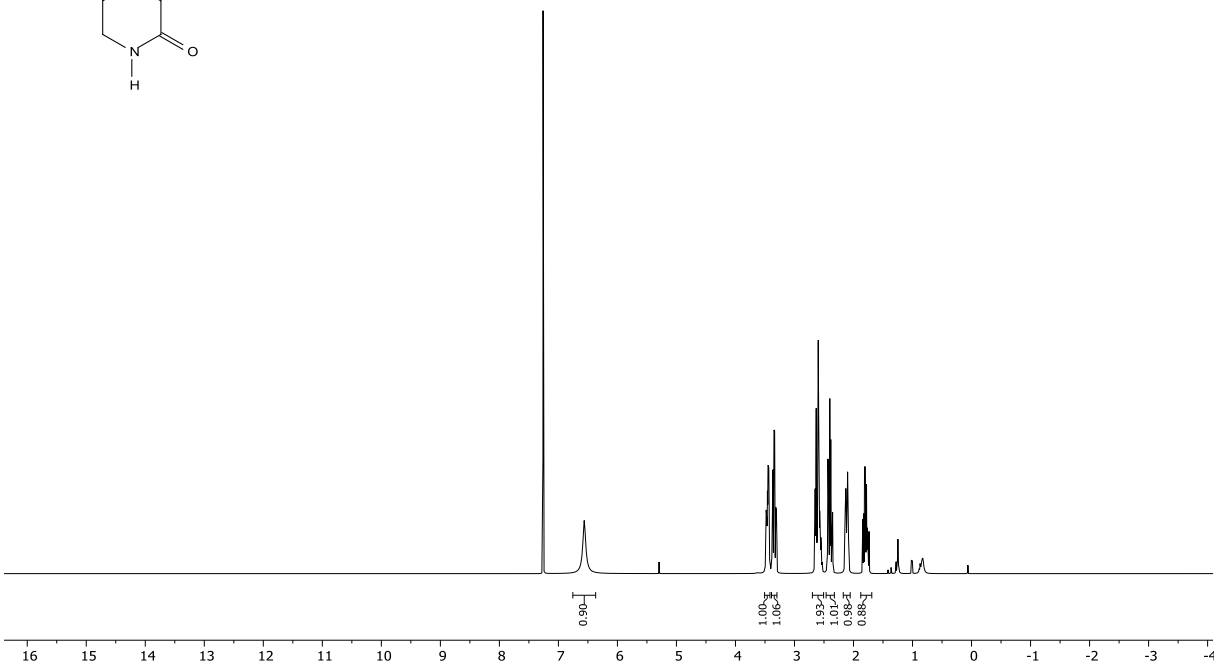
$^{19}F\{^1H\}$ NMR(376 MHz, Chloroform-*d*)



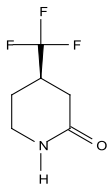


^{1}H NMR(400 MHz, Chloroform-*d*)

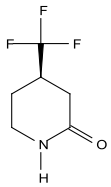


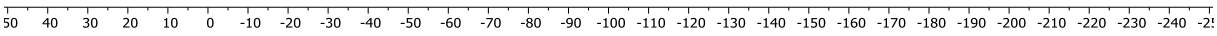


^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)

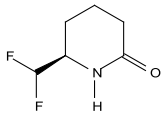


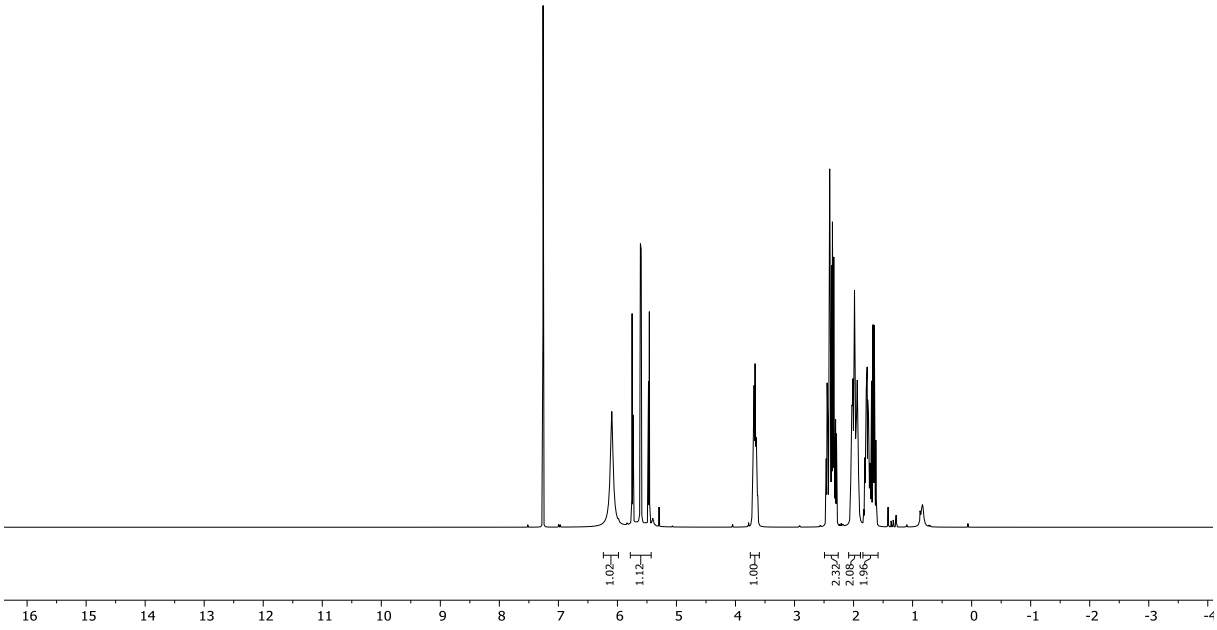
^{19}F NMR(376 MHz, Chloroform-*d*)



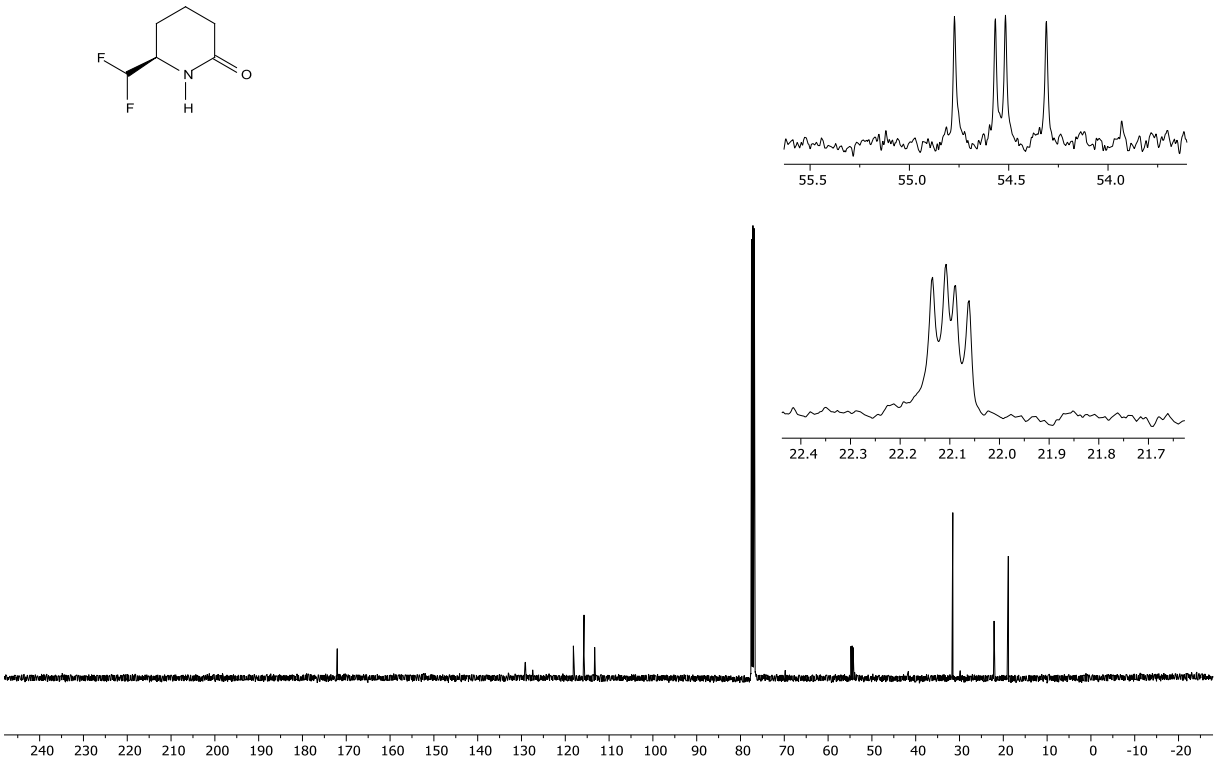


^{1}H NMR(400 MHz, Chloroform-*d*)

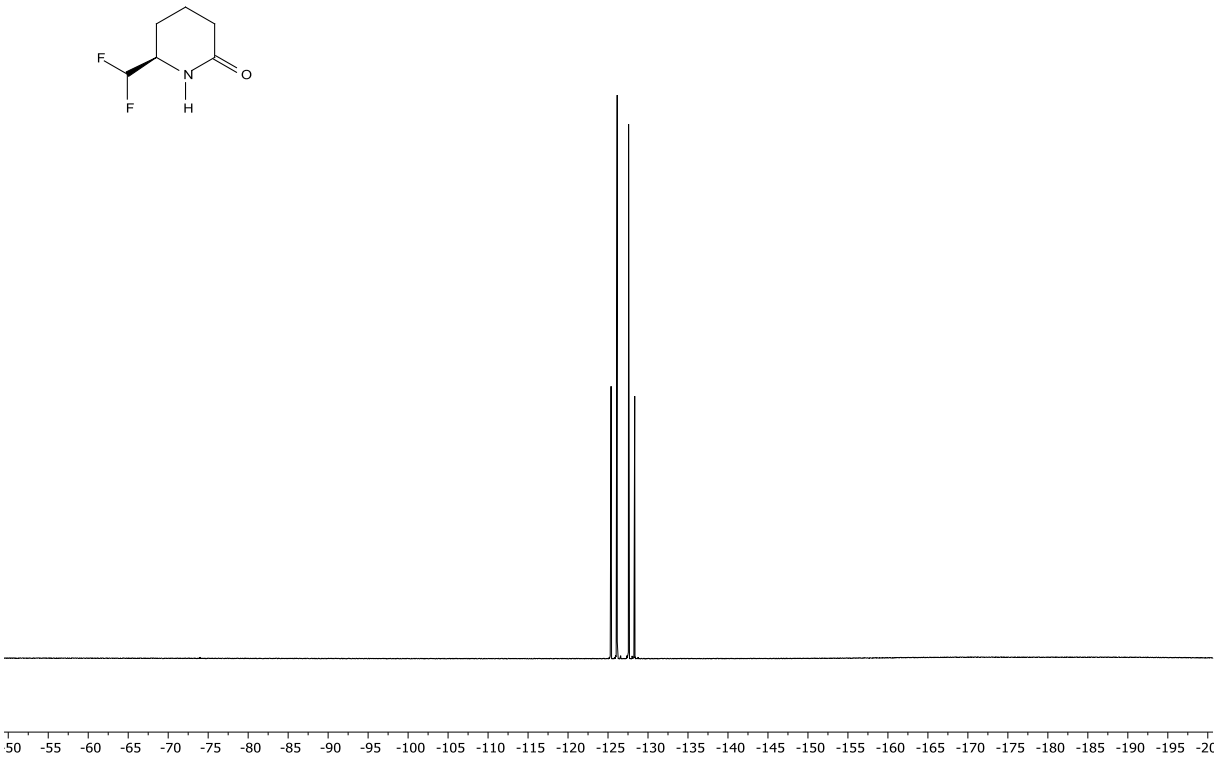




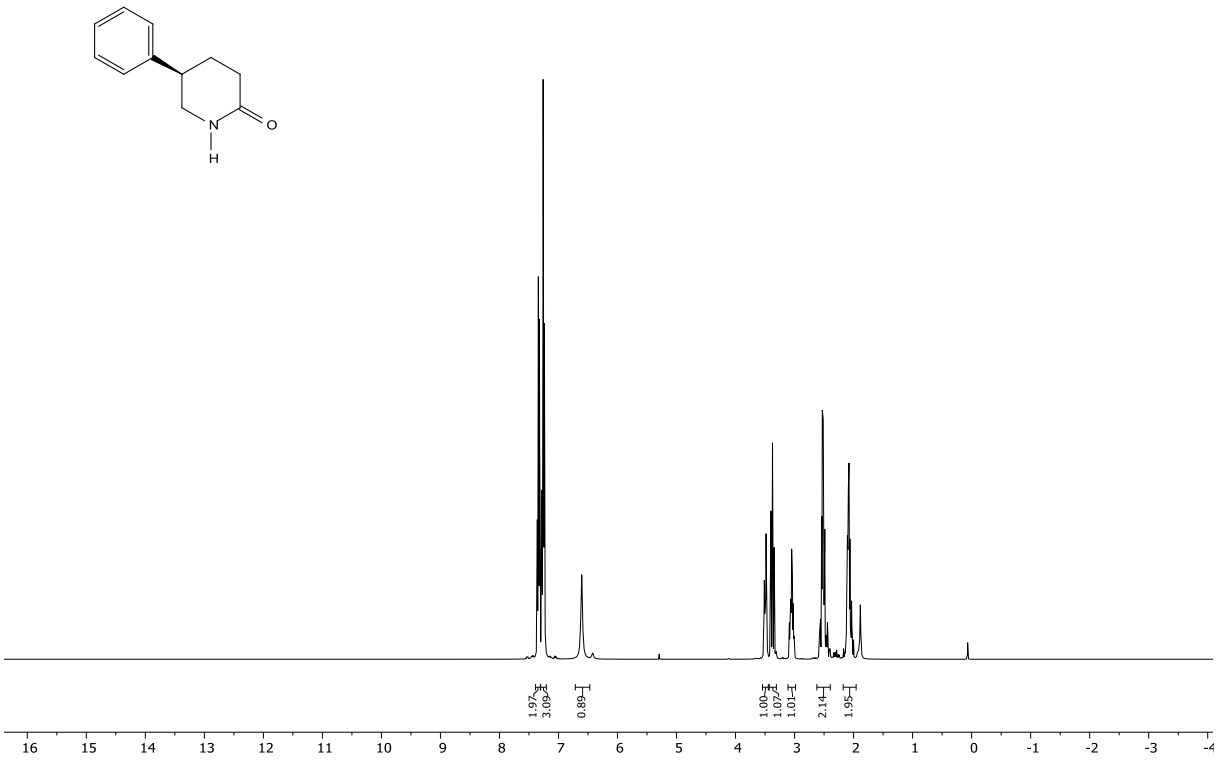
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)



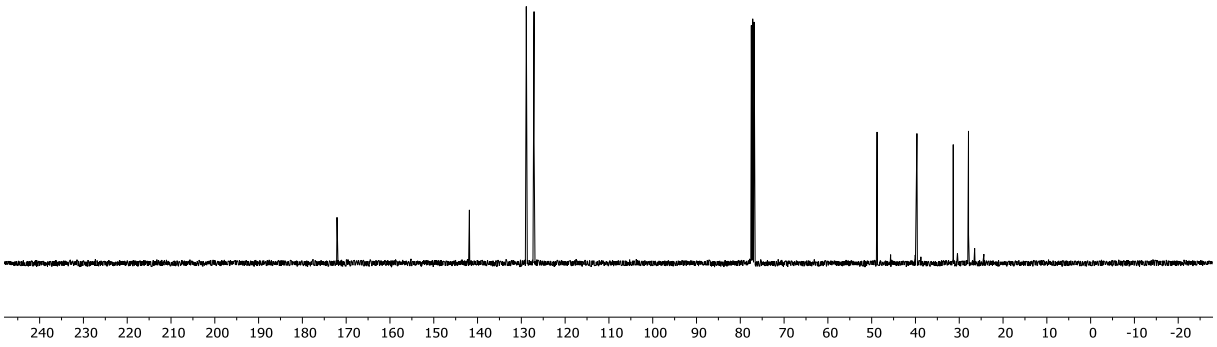
^{19}F NMR(376 MHz, Chloroform-*d*)



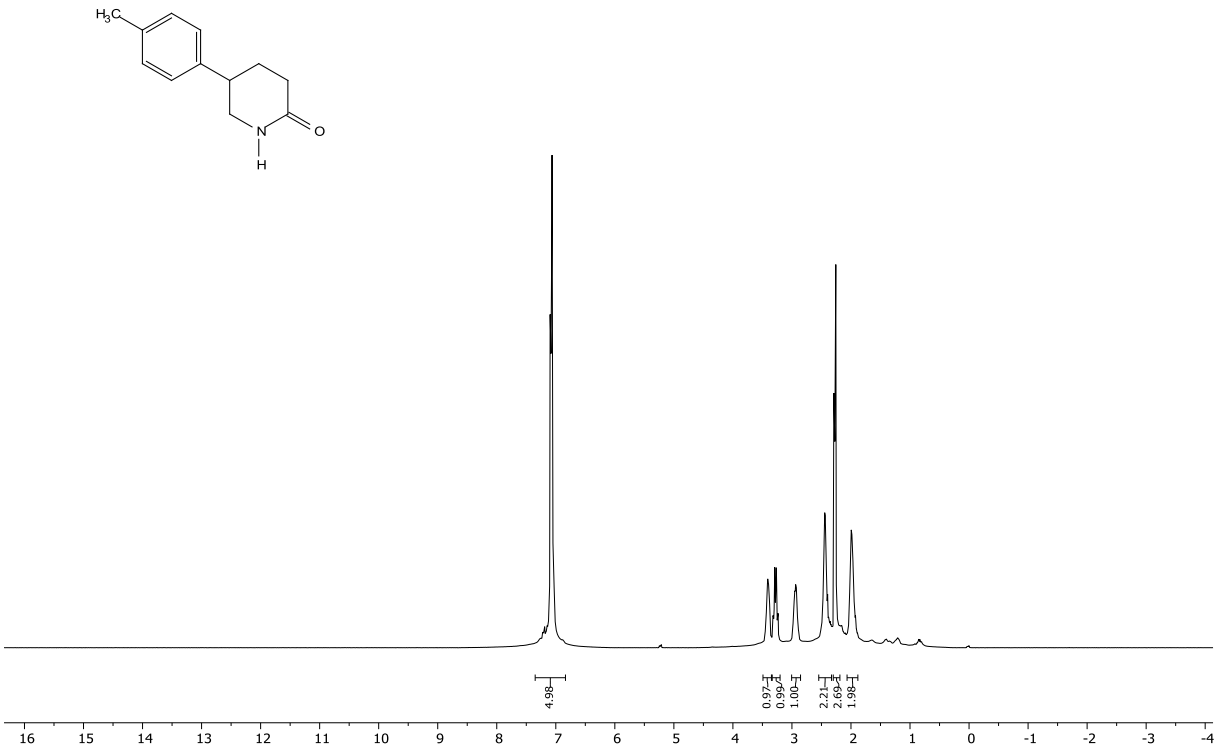
^{1}H NMR(400 MHz, Chloroform-*d*)



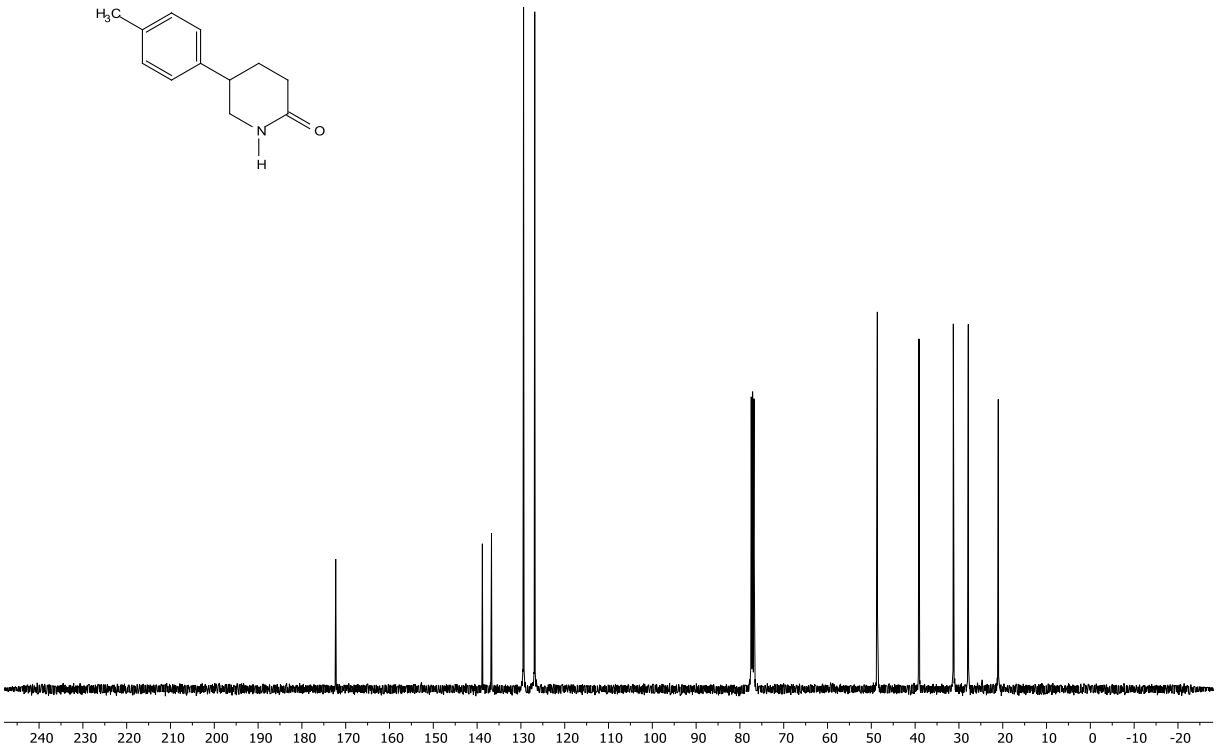
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



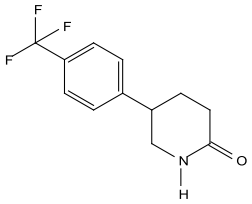
^{1}H NMR(400 MHz, Chloroform-*d*)



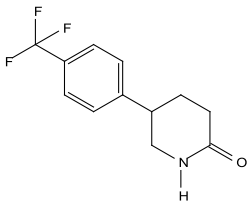
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



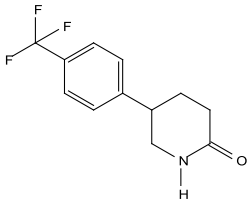
^{1}H NMR(400 MHz, Chloroform-*d*)

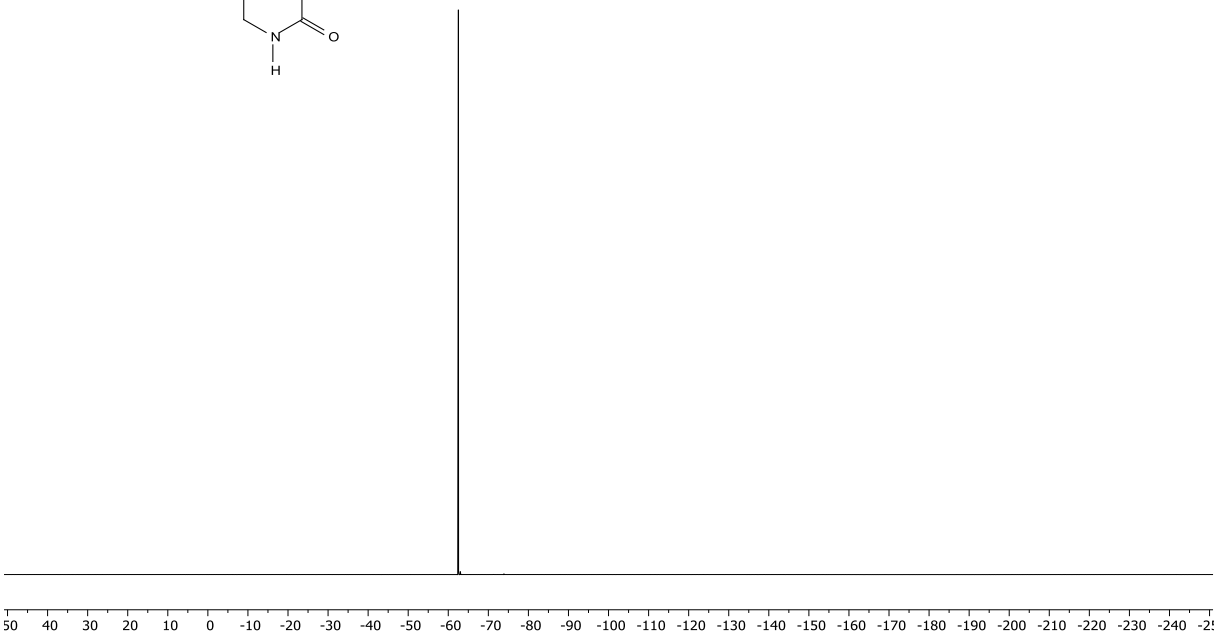


^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)

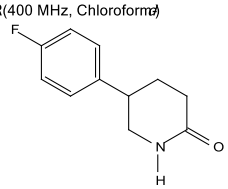


^{19}F{^{1}H} NMR(376 MHz, Chloroform-*d*)

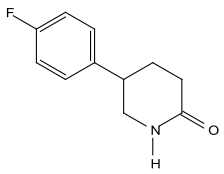




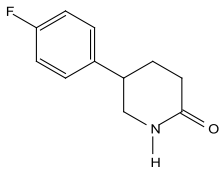
^{1}H NMR(400 MHz, Chloroform-*d*)



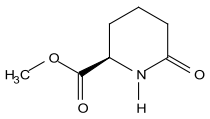
$^{13}C\{^1H\}$ NMR(101 MHz, Chloroform-*d*)

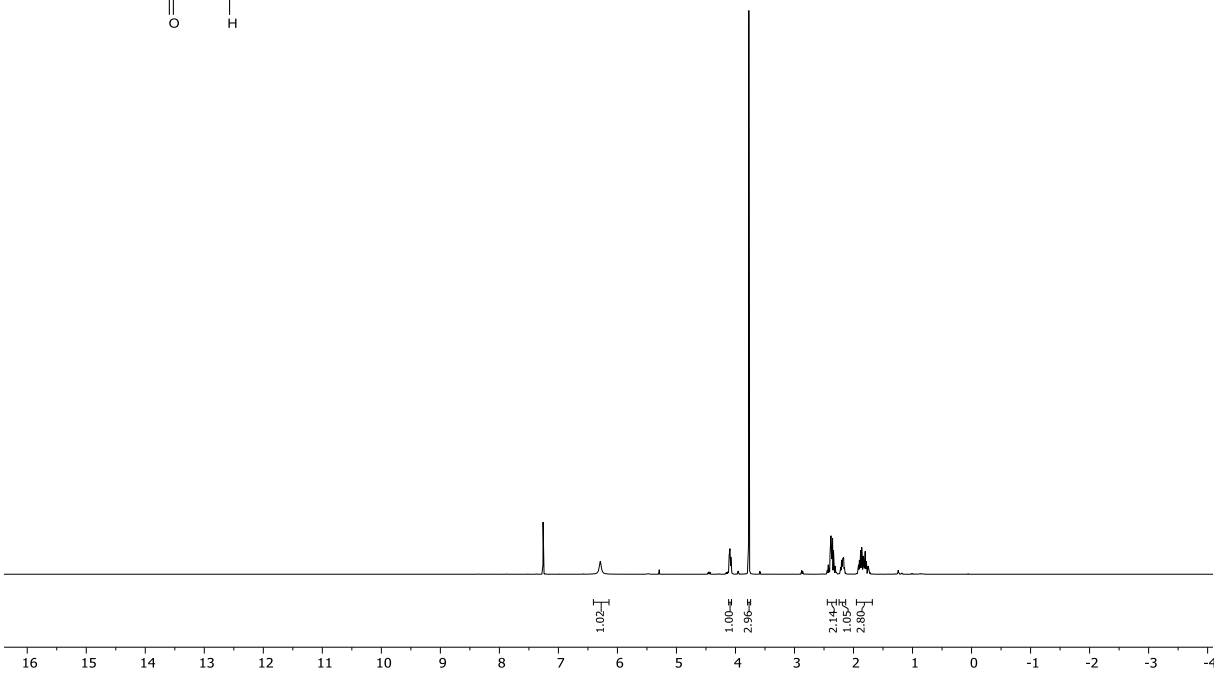


$^{19}F\{^1H\}$ NMR(376 MHz, Chloroform-*d*)

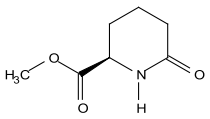


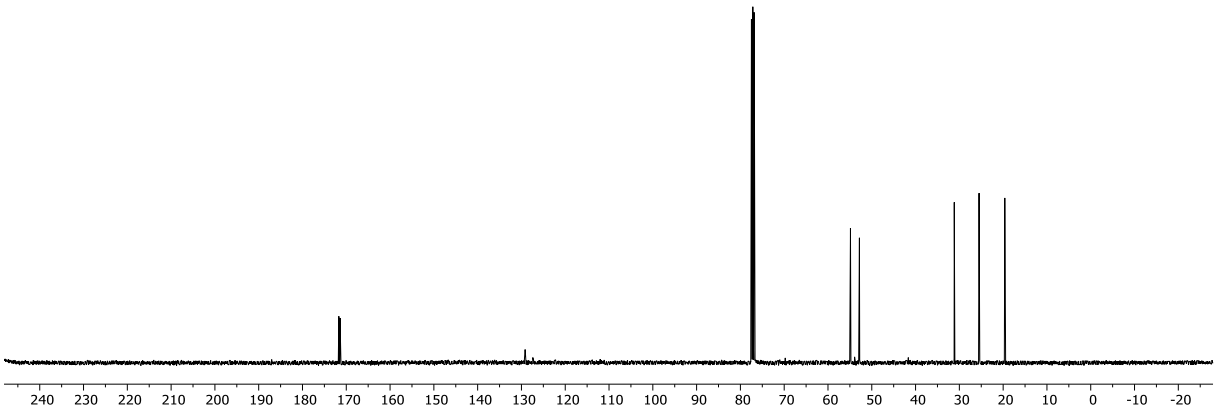
1H NMR(400 MHz, Chloroform-*d*)



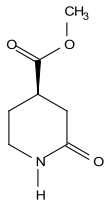


13C{1H} NMR(101 MHz, Chloroform-*d*)

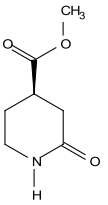




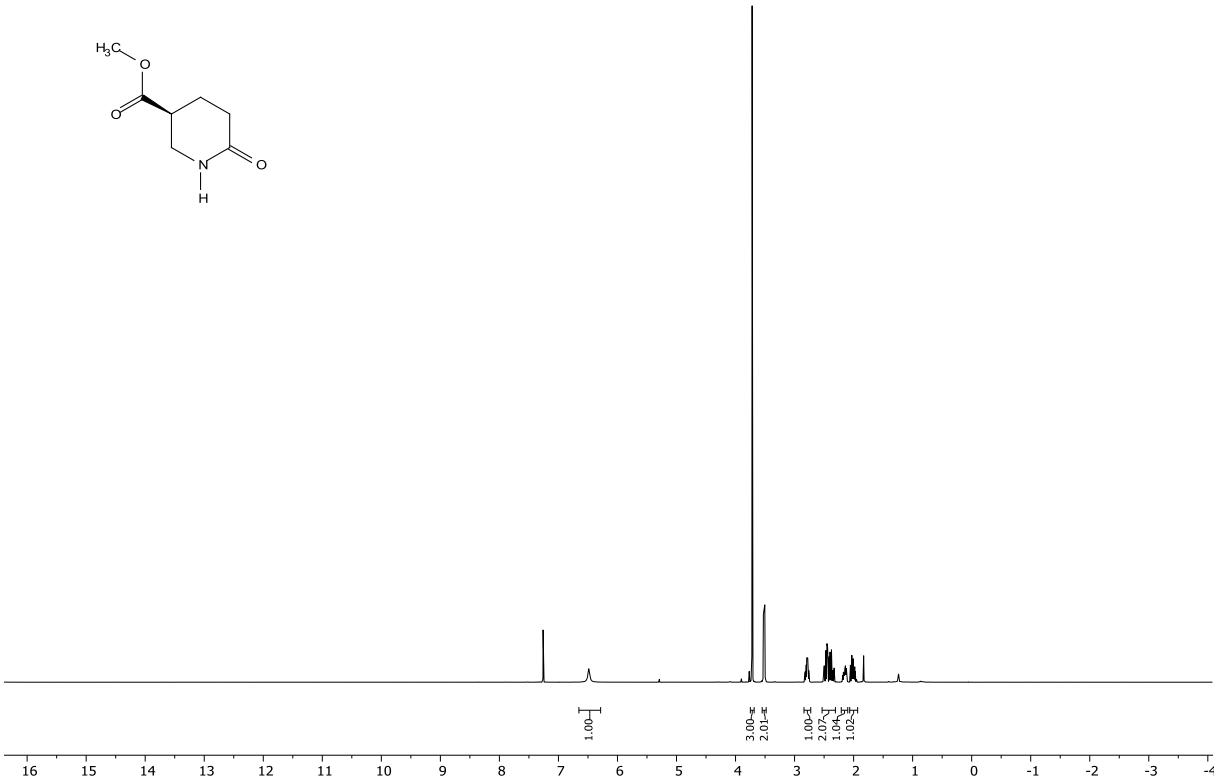
^{1}H NMR(400 MHz, Chloroform-*d*)



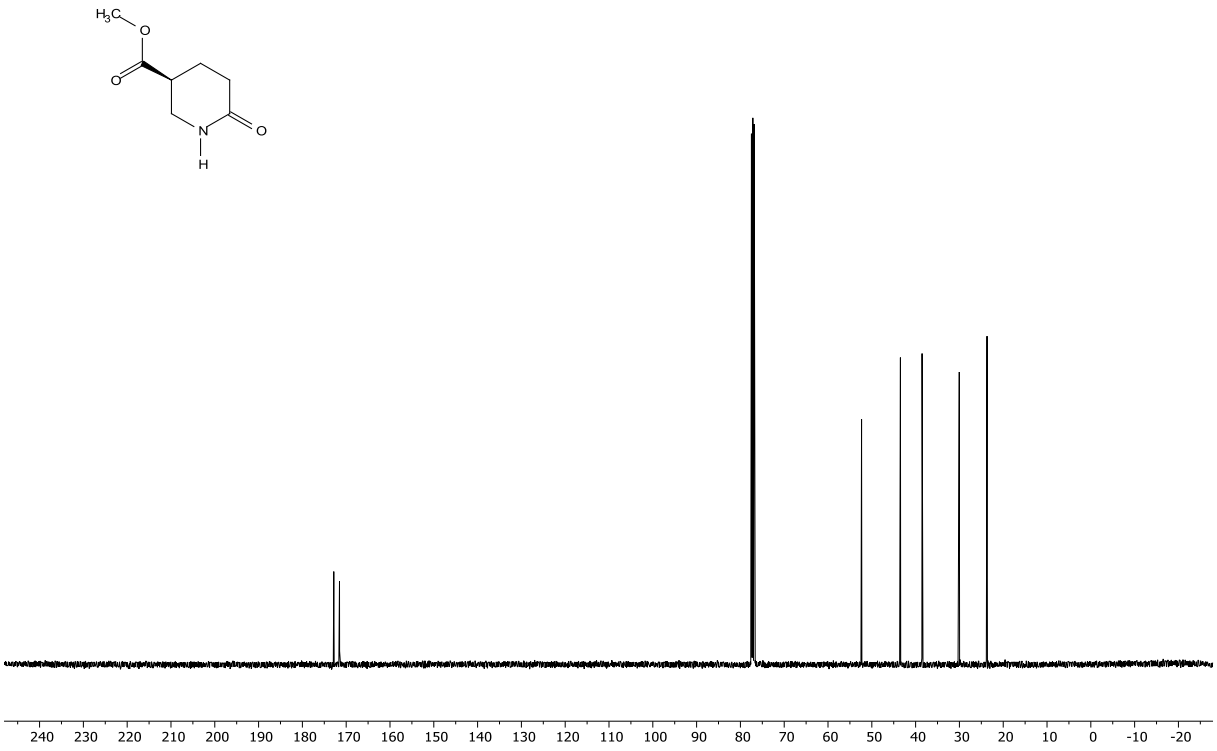
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



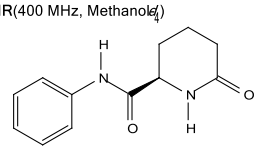
^{1}H NMR(400 MHz, Chloroform-*d*)



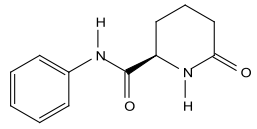
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)

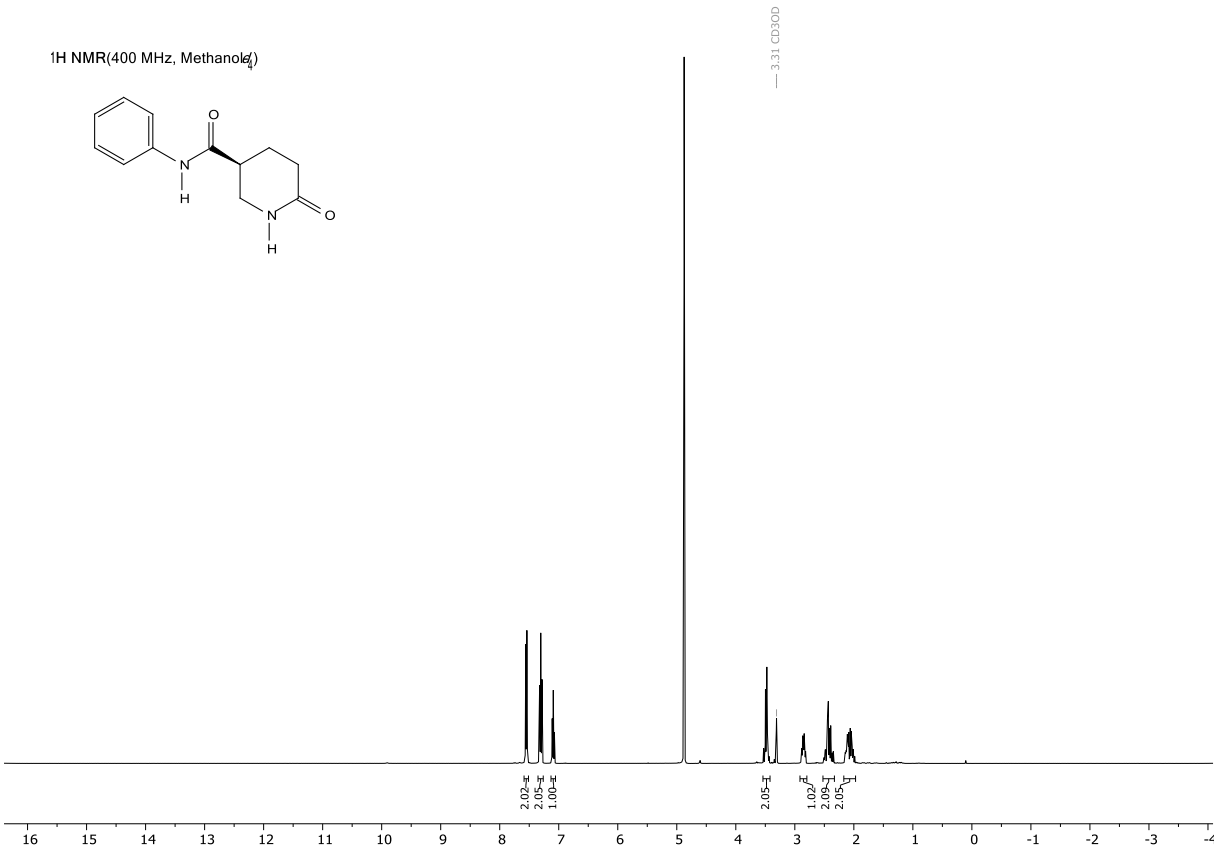


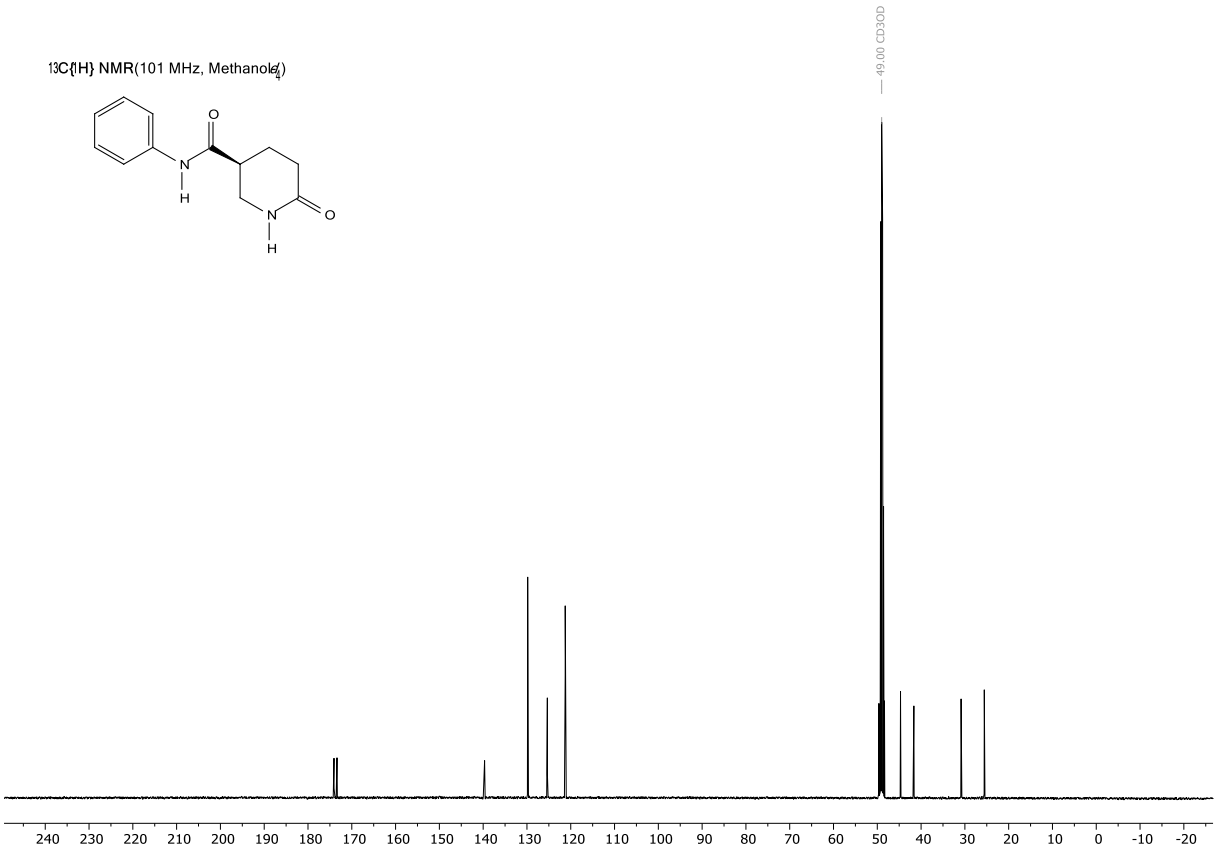
^{1}H NMR(400 MHz, Methanol-d_4)



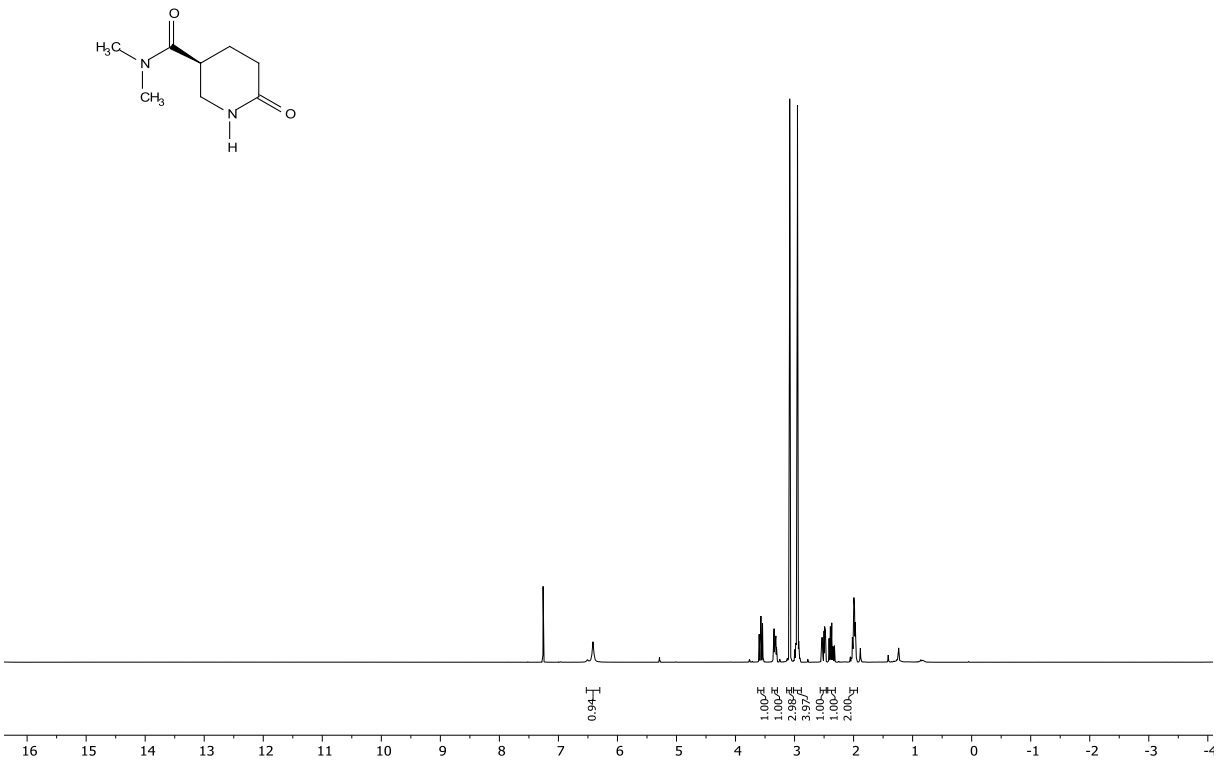
^{13}C{^{1}H} NMR(101 MHz, Methanol-d_4)



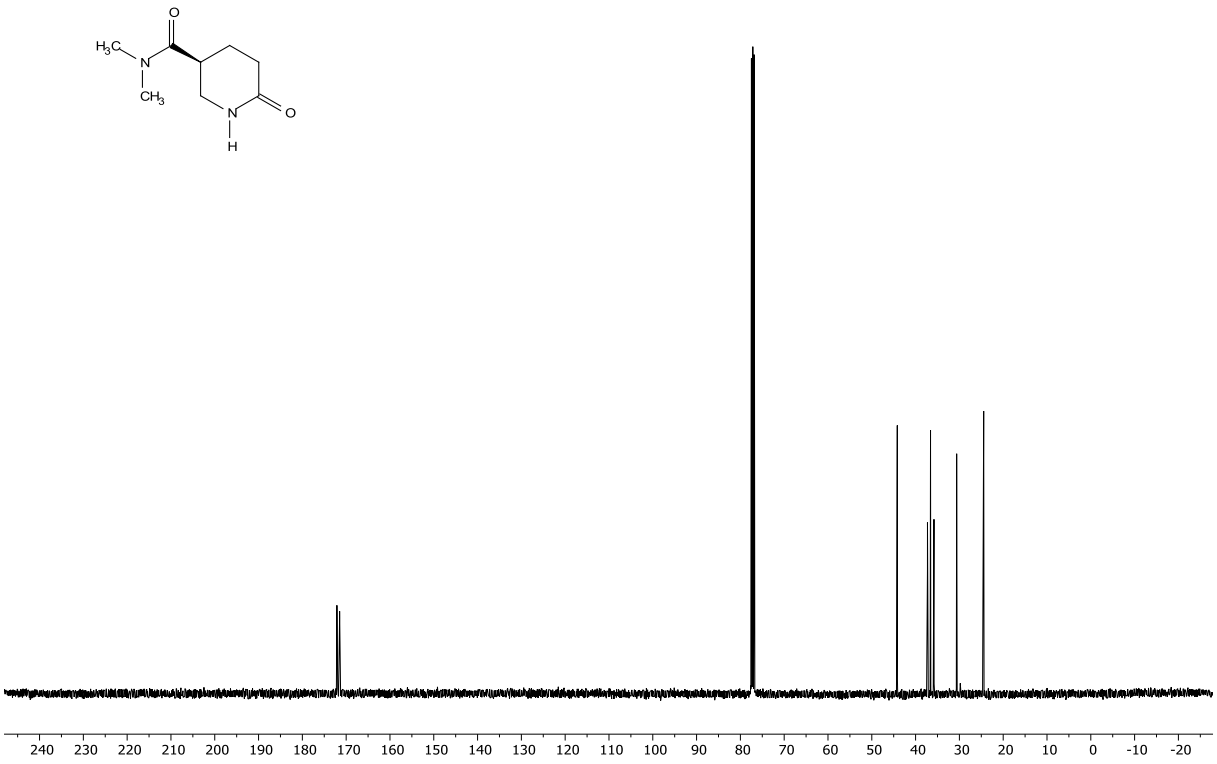

1H NMR(400 MHz, Methanol-d4)
3.31 CD3OD
2.02
2.05
1.00
2.05
1.02
2.09
2.05


13C{1H} NMR(101 MHz, Methanol-d4)
49.00 CD3OD

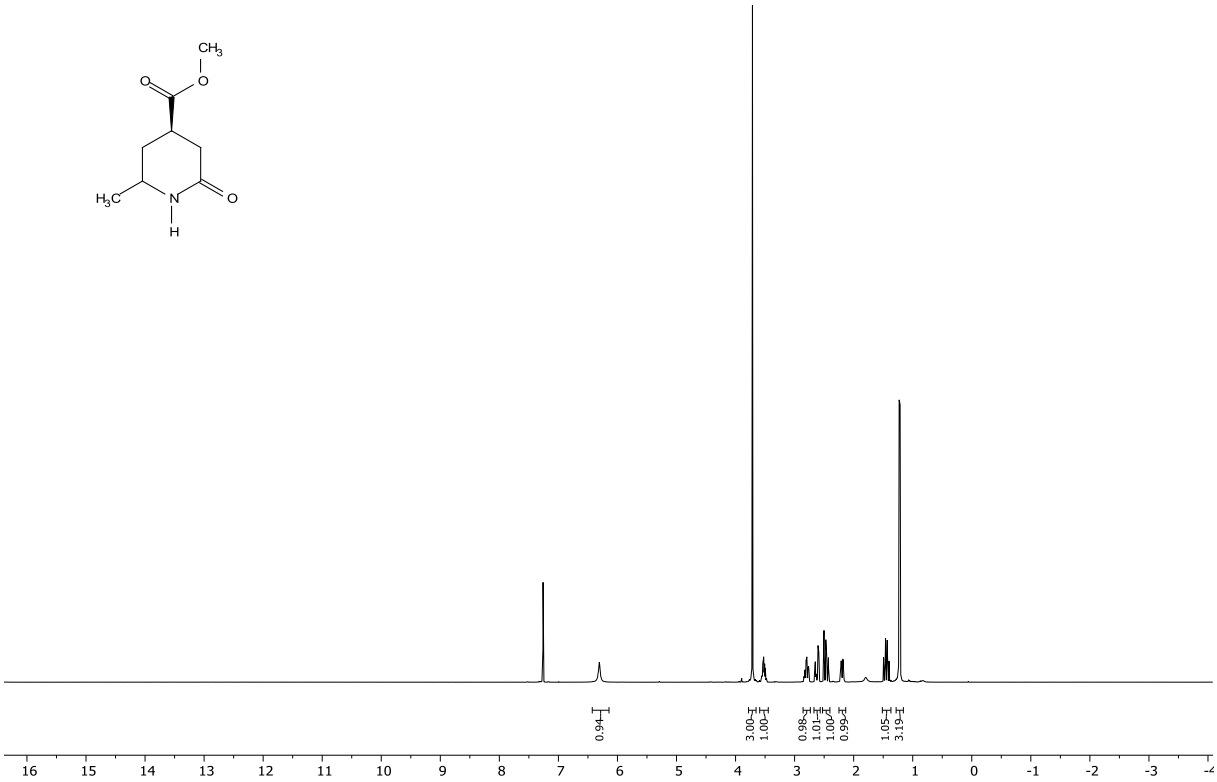
^{1}H NMR(400 MHz, Chloroform-*d*)



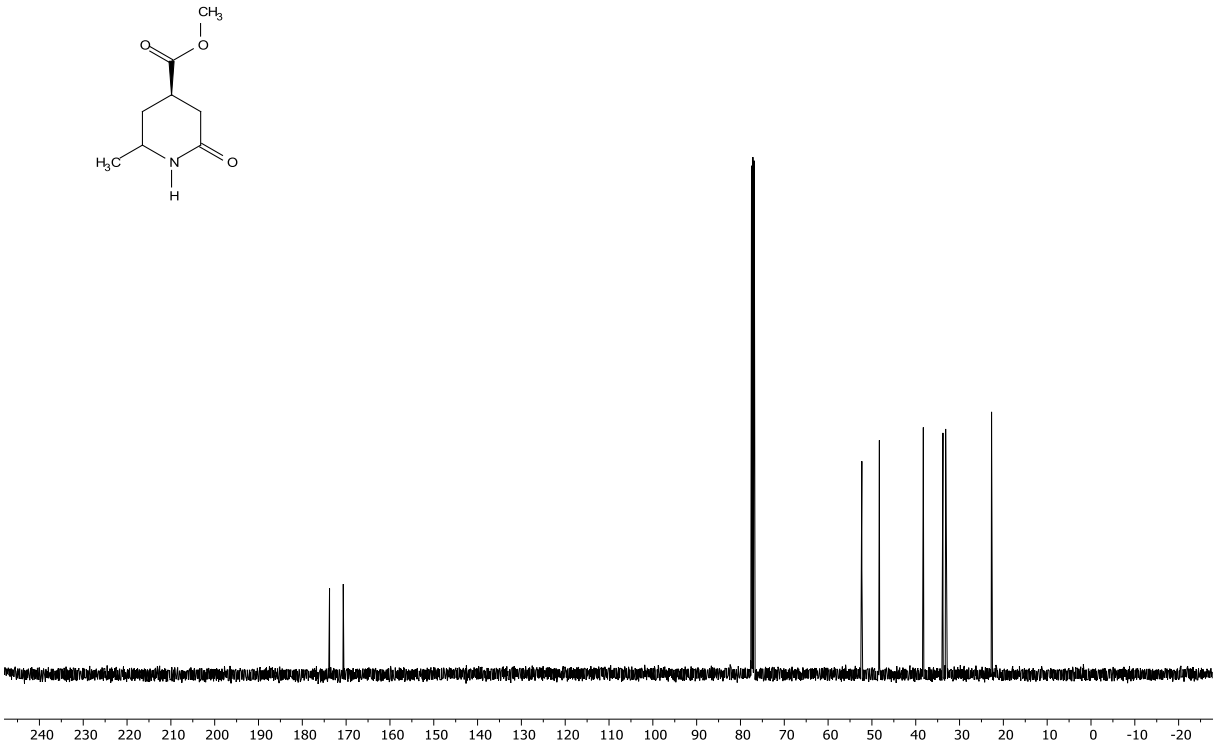
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



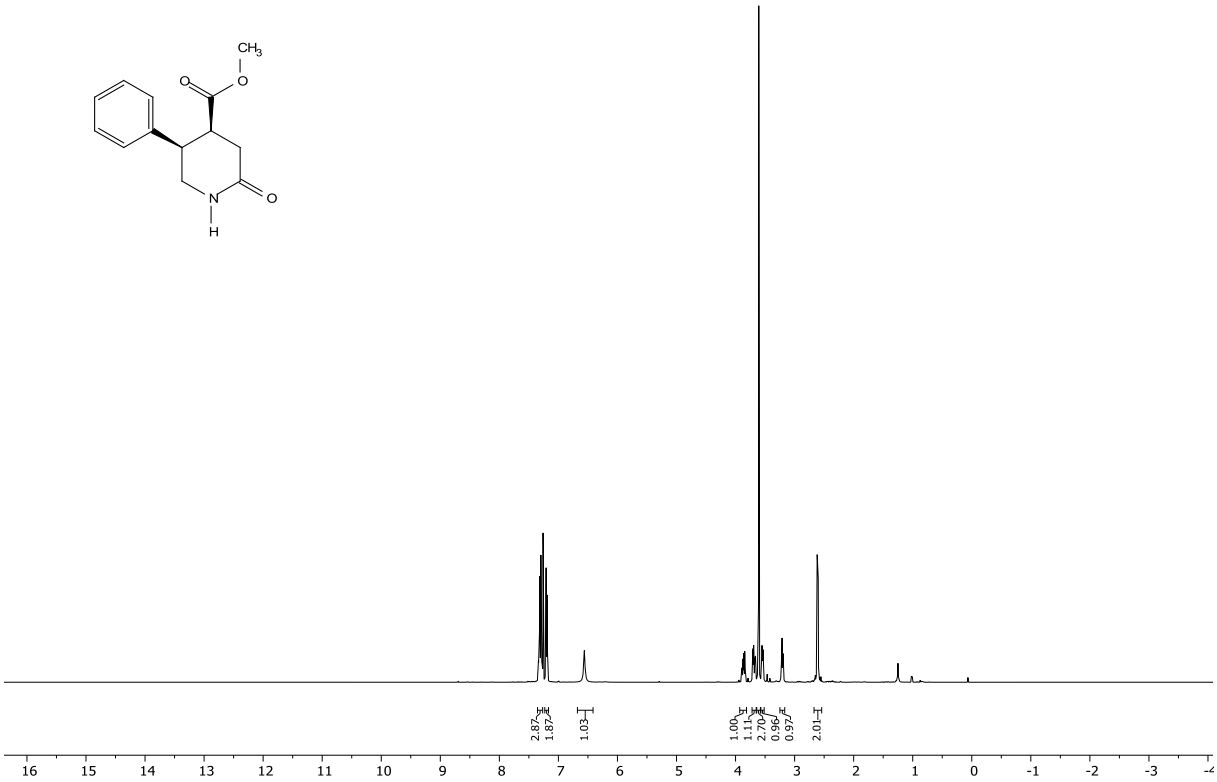
^{1}H NMR(400 MHz, Chloroform-*d*)



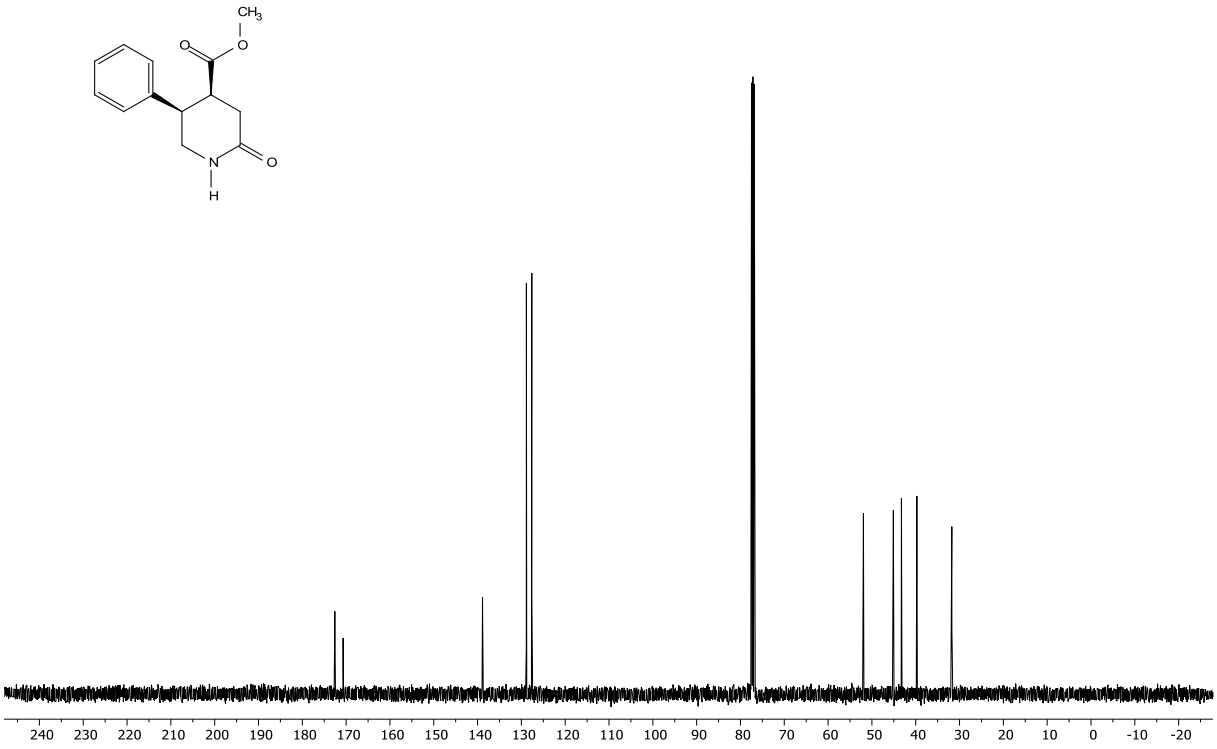
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)

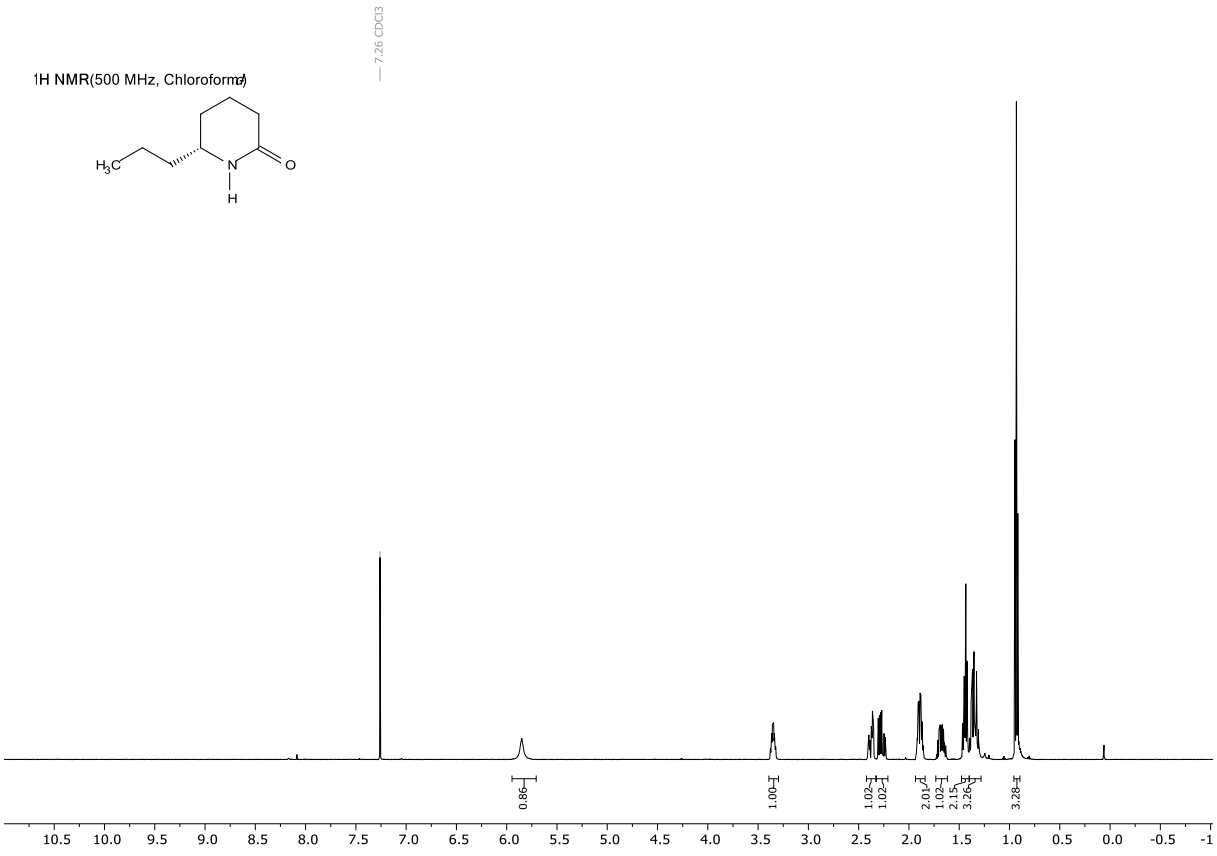


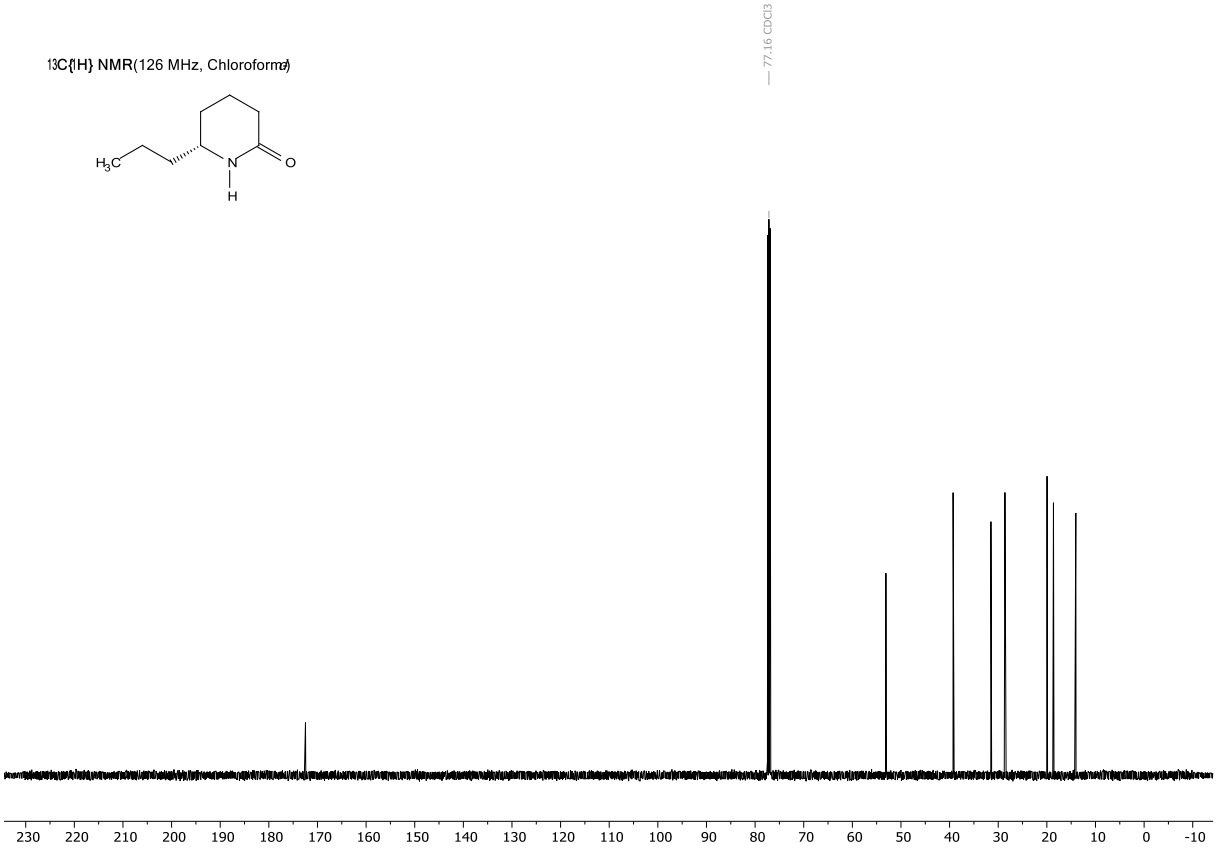
^{1}H NMR(400 MHz, Chloroform-*d*)

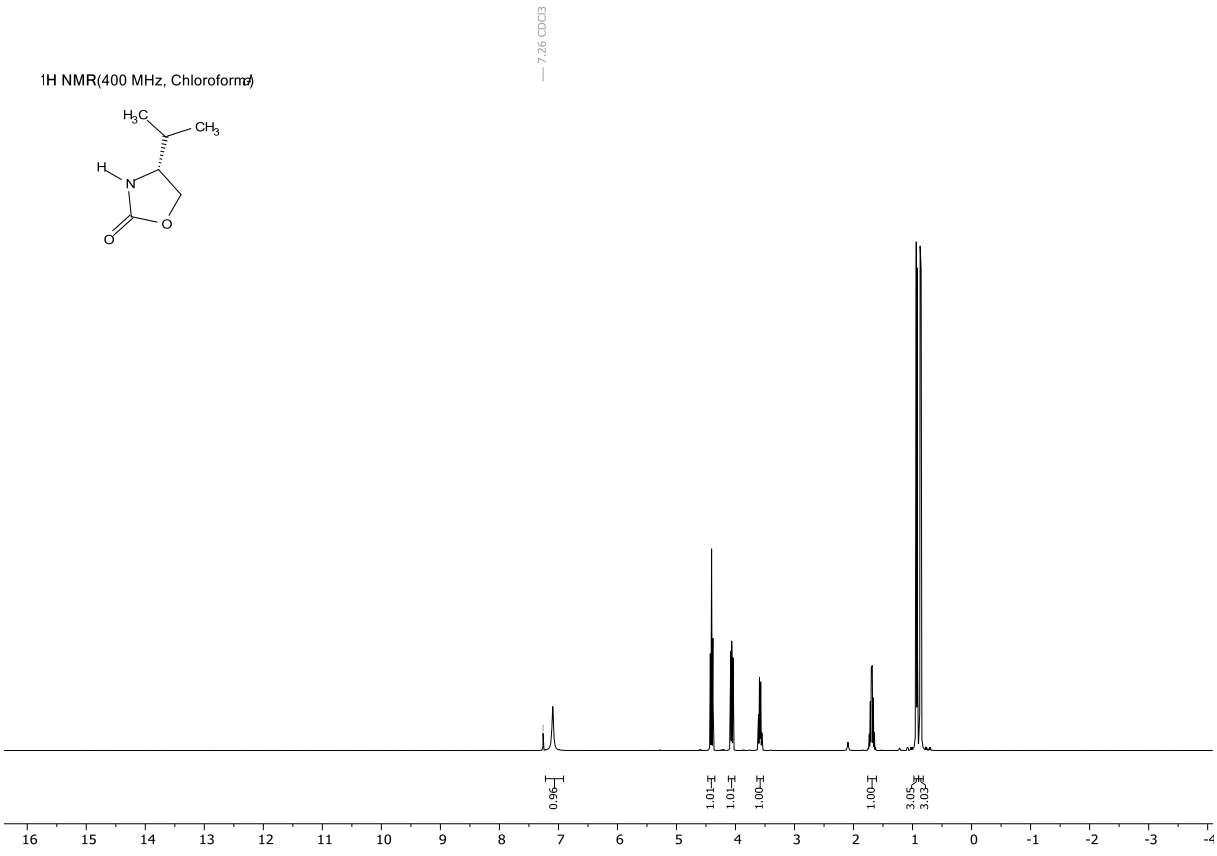


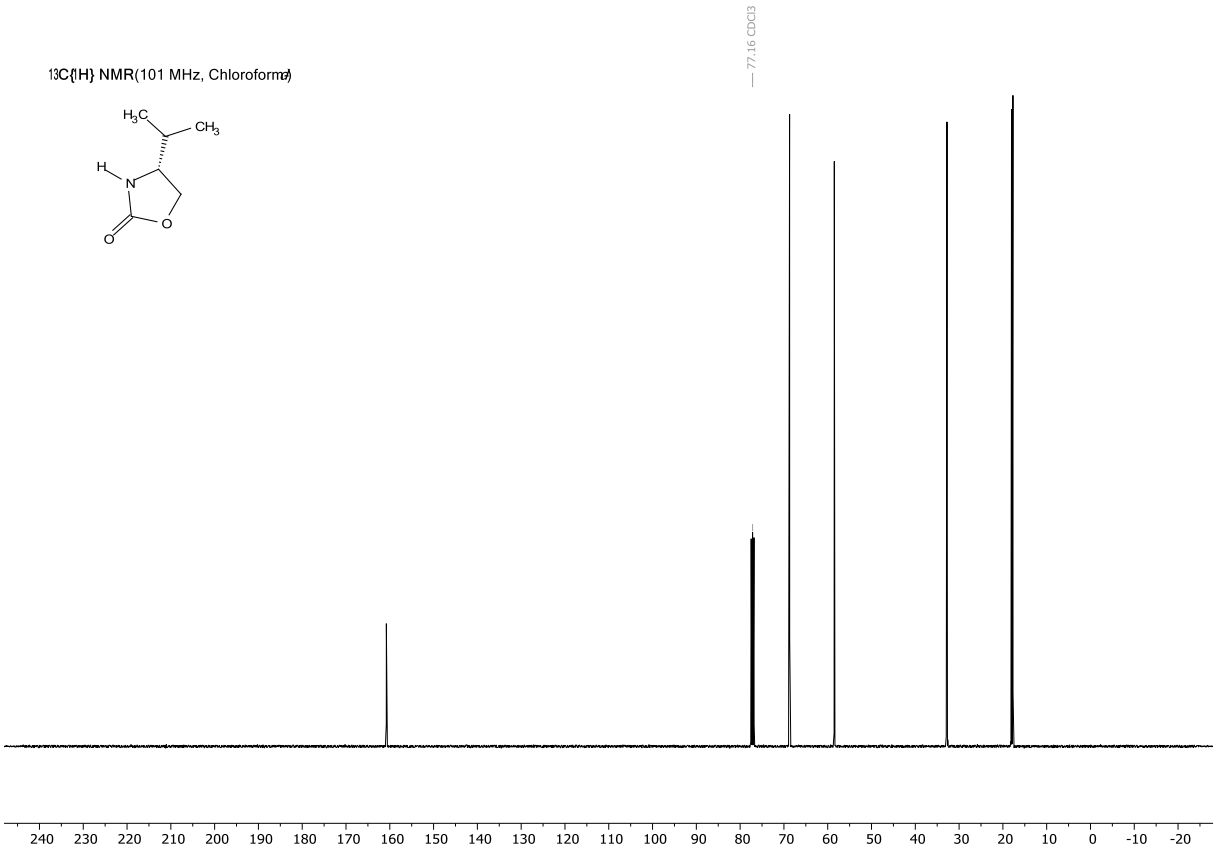
^{13}C{^{1}H} NMR(101 MHz, Chloroform-*d*)



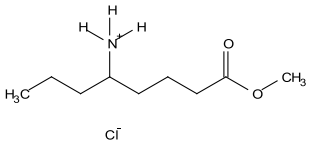

1H NMR(500 MHz, Chloroform-d)
7.26 CDCl3
0.86
1.00
1.02
1.02
2.01
1.02
2.15
3.26
3.28
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1


13C{1H} NMR(126 MHz, Chloroform-d)
77.16 CDCl3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

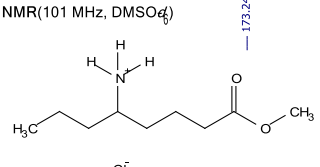

1H NMR(400 MHz, Chloroform-d)
7.26 CDCl3
0.96
1.01
1.01
1.00
1.00
3.05
3.03


13C{1H} NMR(101 MHz, Chloroform-d)
77.16 CDCl3

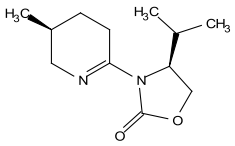
^{1}H NMR(400 MHz, DMSO-d_6)

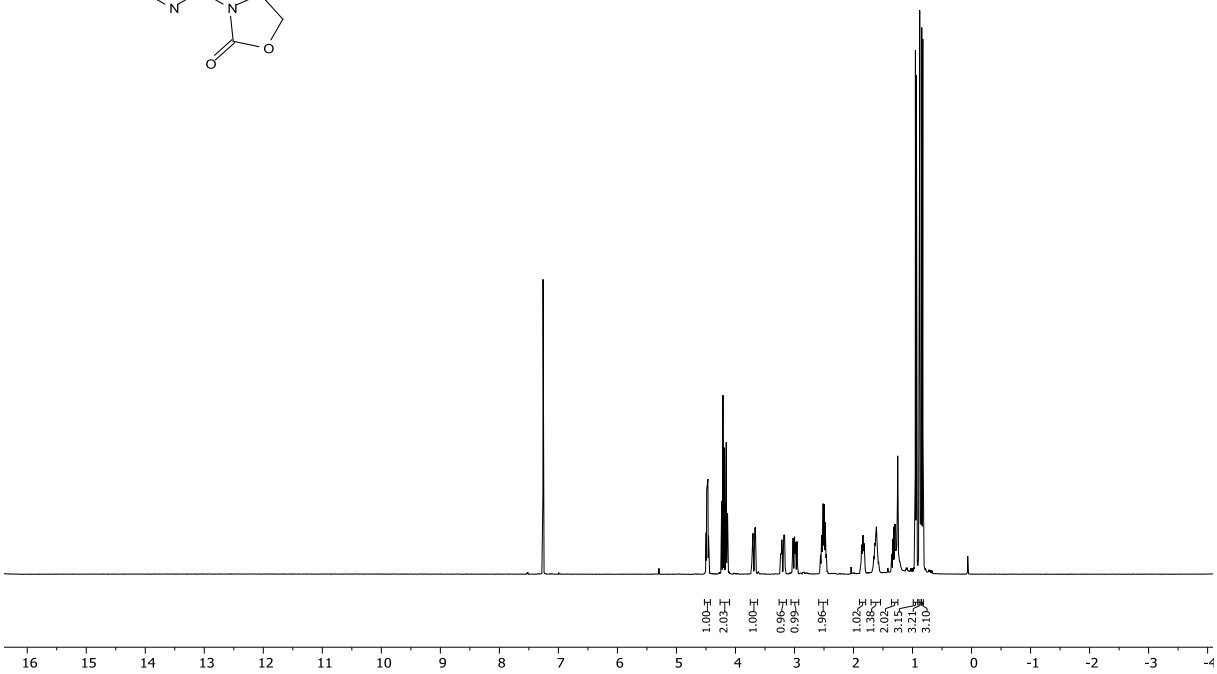


^{13}C{^{1}H} NMR(101 MHz, DMSO-d_6)



1H NMR(400 MHz, Chloroform-*d*)





13C{1H} NMR(101 MHz, Chloroform-*d*)