Supporting Information

Synthesis of 3-Hydroxymethyl Isoindolinones via Cobalt Catalyzed C(sp^2)-H Carbonylation of Phenylglycinol Derivatives

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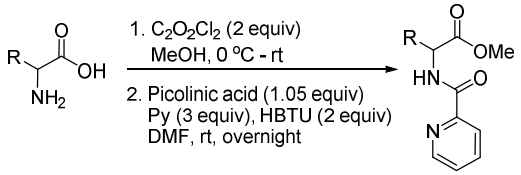
General considerations

Reactions were performed using standard glassware or were run in 4 mL vials with PTFE/Liner screw caps and 30 mL vials using w/polyseal screw caps. Reactions were heated using Chemglass aluminum reaction blocks. Column chromatography was performed using Kieselgel silicagel (35 -70 and 60 - 200 μm). Thin layer chromatography (TLC) was performed on silica gel using Merck TLC Silica gel 60 F254 Aluminum sheets and was visualized by UV lamp, staining with $KMnO_4$. ^{1}H, ^{13}C, ^{19}F and 2D-NMR spectra were recorded on 400 MHz Bruker spectrometer using residual solvent peak as a reference. Compounds for HRMS were analyzed by positive mode electrospray ionization (ESI) using Waters Synapt G2-Si mass spectrometer. HPLC data were obtained using Waters Alliance 2695 HPLC system with a Phenomenex Lux Amylose (4.6 x 150 mm) column (conditions specified on attached HPLC chromatograms). IR spectra were obtained using a Shimadzu IR Prestige-21 FT-IR spectrometer. Optical rotations were measured at 20 °C on a Rudolph Research Analytical Autopol VI Polarimeter, cell lenght 50 mm, using solvent and concentration stated, at 589 nm. All procedures were performed under ambient air unless otherwise noted. Reagents and starting materials were obtained from commercial sources and used without further purification unless otherwise noted.

1. Substrate synthesis

1.1 Synthesis and characterization of methyl-2-aryl-2-(picolinamido)acetates

Corresponding methyl-2-aryl-2-(picolinamido)acetates were synthesized in two steps from commercially available amino acids according to procedure A (Scheme S1).



Scheme S1. Synthesis of methyl-2-aryl-2-(picolinamido)acetates

Procedure A

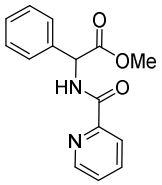
Synthesis of methyl 2-phenyl-2-(picolinamido)acetate is representative.

Step 1: 2-Amino-2-phenylacetic acid (6.00 g, 39.69 mmol, 1 equiv) was suspended in MeOH (48 mL) under an argon atmosphere. The solution was cooled to 0 °C and oxalyl chloride (6.9 mL, 79.38 mmol, 2 equiv) was slowly added dropwise. The reaction mixture was stirred overnight at

room temperature. Solvent was evaporated under vacuum to obtain crude product as a pale solid. Crude product was used in the next step without further purification.

Step 2: Under an argon atmosphere methyl 2-amino-2-phenylacetate hydrogen chloride (39.69 mmol, 1 equiv), picolinic acid (5.12 g, 41.58 mmol, 1.05 equiv) and *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (30.03 g, 79.38 mmol, 2 equiv) were dissolved in DMF (48 mL). Pyridine (9.6 mL, 119.07 mmol, 3 equiv) was added to the solution directly. Reaction mixture was stirred at room temperature overnight. Then reaction mixture was diluted with EtOAc (60 mL) and H_2O (40 mL), filtered. Organic phase was separated and aqueous phase was extracted with EtOAc (50 mL), combined organic phase was washed with dist. H_2O (20 mL), brine (20 mL) and dried over Na_2SO_4, filtered. Solvent was evaporated under reduced pressure to afford the crude product, which was further purified by flash chromatography on silica gel using petroleum ether/EtOAc (3/1) as an eluent to give corresponding product 8.07 g (75%) as a white solid.

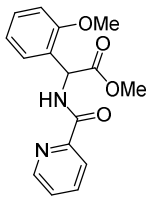
Methyl 2-phenyl-2-(picolinamido)acetate



This compound is known.[1]

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.94 (d, *J* = 6.9 Hz, 1H), 8.59 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.16 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.51 – 7.46 (m, 2H), 7.46 – 7.30 (m, 4H), 5.78 (d, *J* = 7.6 Hz, 1H), 3.77 (s, 3H).

Methyl 2-(2-methoxyphenyl)-2-(picolinamido)acetate



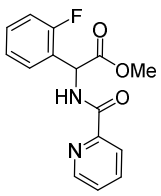
Procedure A. Step 1: (2-Methoxyphenyl)glycine (1.28 g, 7.10 mmol, 1 equiv), $C_2O_2Cl_2$ (1.2 mL, 14.20 mmol, 2 equiv), MeOH (12 mL).

Step 2: Crude reaction mixture from Step 1, picolinic acid (873 mg, 7.10 mmol, 1 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (5.38 g, 14.20 mmol, 2 equiv), DMF (15 mL), pyridine (1.7 mL, 21.30 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 900 mg (42%) of product was obtained as a colorless oil.

This compound is known.[1]

^{1}H-NMR (400 MHz, Chloroform-d) δ 8.98 (d, *J* = 8.4 Hz, 1H), 8.56 (d, *J* = 4.1 Hz, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.7, 1.7 Hz, 1H), 7.48 – 7.35 (m, 2H), 7.35 – 7.27 (m, 1H), 7.05 – 6.81 (m, 2H), 6.00 (d, *J* = 8.6 Hz, 1H), 3.89 (s, 3H), 3.73 (s, 3H).

Methyl 2-(2-fluorophenyl)-2-(picolinamido)acetate



Procedure A. Step 1: (2-Fluorophenyl)glycine hydrochloride (1.84 g, 9.00 mmol, 1 equiv), $C_2O_2Cl_2$ (1.6 mL, 18.00 mmol, 2 equiv), MeOH (10 mL).

Step 2: Crude reaction mixture from Step 1, picolinic acid (1.16 g, 9.50 mmol, 1.04 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (6.80 g, 18.00 mmol, 2 equiv), DMF (18 mL), pyridine (2.2 mL, 27.00 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 1.50 g (58%) of product was obtained as a colorless oil. R_f = 0.36 (petroleum ether/EtOAc 2:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.98 (d, *J* = 7.4 Hz, 1H), 8.58 (d, *J* = 4.7 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.82 (td, *J* = 7.7, 1.6 Hz, 1H), 7.52 – 7.38 (m, 2H), 7.39 – 7.27 (m, 1H), 7.20 – 7.05 (m, 2H), 6.02 (d, *J* = 7.9 Hz, 1H), 3.78 (s, 3H).

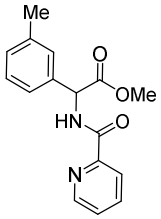
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.6, 163.9, 160.7 (d, J_{C-F} = 248.5 Hz), 149.3, 148.5, 137.4, 130.5 (d, J_{C-F} = 8.3 Hz), 129.9 (d, J_{C-F} = 3.5 Hz), 126.6, 124.7 (d, J_{C-F} = 3.6 Hz), 124.4 (d, J_{C-F} = 14.3 Hz), 122.5, 116.1 (d, J_{C-F} = 21.3 Hz), 53.1, 51.5 (d, J_{C-F} = 2.6 Hz).

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -117.06.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}H_{14}N_2O_3F$ 289.0988; found: 289.0999.

FT-IR (thin film, cm^{-1}) υ 3387, 2955, 1750, 1683, 1510, 1233.

Methyl 2-(3-methylphenyl)-2-(picolinamido)acetate



Synthesized from commercially available methyl amino(3-methylphenyl)acetate hydrochloride using **Procedure A**, Step 2: Amino(3-methylphenyl)acetate hydrochloride (1.0 g, 4.6 mmol), picolinic acid (599 mg, 4.8 mmol, 1.05 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (3.52 g, 9.20 mmol, 2 equiv), DMF (10 mL), pyridine (1.1 mL, 13.80 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 1.00 g (76%) of product was obtained as a colorless oil. R_f = 0.59 (petroleum ether/EtOAc 1:1).

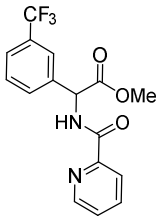
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.93 (d, *J* = 7.0 Hz, 1H), 8.60 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.18 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.32 – 7.23 (m, 3H), 7.20 – 7.11 (m, 1H), 5.75 (d, *J* = 7.5 Hz, 1H), 3.79 (s, 3H), 2.38 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 171.3, 163.9, 149.4, 148.4, 138.9, 137.4, 136.5, 129.5, 129.0, 128.2, 126.5, 124.6, 122.5, 56.7, 52.9, 21.5.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{17}N_2O_3$ 285.1239; found: 285.1250.

FT-IR (thin film, cm^{-1}) υ 3388, 2953, 1744, 1685, 1512, 1437, 1202.

Methyl 2-(3-trifluoromethylphenyl)-2-(picolinamido)acetate



Procedure A. Step 1: 2-(3-Trifluoromethylphenyl)glycine (1.21 g, 5.50 mmol, 1 equiv), $C_2O_2Cl_2$ (0.95 mL, 11.00 mmol, 2 equiv), MeOH (12 mL).

Step 2: Crude reaction mixture from Step 1, picolinic acid (679 mg, 5.50 mmol, 1 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (4.18 g, 11.00 mmol, 2 equiv), DMF (15 mL), pyridine (1.34 mL, 16.50 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 1.12 g (59%) of product was obtained as a colorless oil. R_f = 0.22 (petroleum ether/EtOAc 3:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 9.07 (d, *J* = 7.0 Hz, 1H), 8.62 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 8.15 (d, *J* = 7.8, 1.0 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.73 (s, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.43 (m, 2H), 5.84 (d, *J* = 7.4 Hz, 1H), 3.80 (s, 3H).

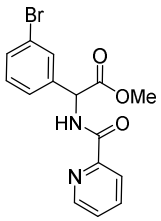
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.6, 164.0, 149.2, 148.5, 137.9, 137.5, 131.5 (q, J_{C-F} = 32.4 Hz), 130.9 (q, J_{C-F} = 1.2 Hz), 129.6, 126.8, 125.6 (q, J_{C-F} = 3.6 Hz), 124.3 (q, J_{C-F} = 3.7 Hz), 124.0 (q, J_{C-F} = 272.5 Hz), 122.5, 56.4, 53.3.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -62.60.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{14}N_2O_3F_3$ 339.0957; found: 339.0957.

FT-IR (thin film, cm^{-1}) υ 2957, 1748, 1684, 1330, 1168, 1127.

Methyl 2-(3-bromophenyl)-2-(picolinamido)acetate



Procedure A. Step 1: 2-(3-Bromophenyl)glycine (1.59 g, 6.0 mmol, 1 equiv), $C_2O_2Cl_2$ (1.6 mL, 18.0 mmol, 3 equiv), MeOH (10 mL).

Step 2: Crude reaction mixture from Step 1, picolinic acid (775 mg, 6.3 mmol, 1.05 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (4.55 g, 12.0 mmol, 2 equiv), DMF (12 mL), pyridine (1.5 mL, 18.0 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 990 mg (47%) of product was obtained as a colorless oil. R_f = 0.63 (eluent petroleum ether/EtOAc = 1/1).

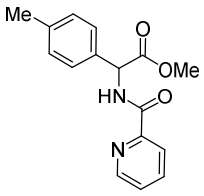
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.99 (d, *J* = 7.0 Hz, 1H), 8.60 (d, *J* = 4.1 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.61 (t, *J* = 1.8 Hz, 1H), 7.49 – 7.38 (m, 3H), 7.24 (t, *J* = 7.9 Hz, 1H), 5.74 (d, *J* = 7.5 Hz, 1H), 3.78 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.6, 163.9, 149.2, 148.5, 138.9, 137.5, 131.8, 130.6, 130.5, 126.7, 126.2, 123.1, 122.5, 56.2, 53.2.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}H_{14}N_2O_3Br$ 349.0188; found: 349.0192.

FT-IR (thin film, cm^{-1}) υ 3384, 2954, 1743, 1686, 1512, 1505, 1435, 1343, 1213.

Methyl 2-(4-methylphenyl)-2-(picolinamido)acetate



Procedure A. Step 1: (4-Methylphenyl)glycine hydrochloride (1.4 g, 7.0 mmol, 1 equiv), $C_2O_2Cl_2$ (1.2 mL, 14.0 mmol, 2 equiv), MeOH (8 mL).

Step 2: Crude reaction mixture from Step 1, picolinic acid (903 mg, 7.3 mmol, 1.04 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (5.30 g, 14.0 mmol, 2 equiv), DMF (14 mL), pyridine (1.7 mL, 21.0 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 750 mg (38%) of product was obtained as a colorless oil. R_f = 0.40 (petroleum ether/EtOAc 2:1).

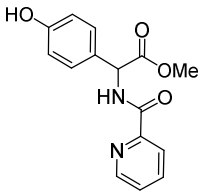
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.90 (d, *J* = 6.8 Hz, 1H), 8.62 – 8.45 (m, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.82 (td, *J* = 7.7, 1.7 Hz, 1H), 7.50 – 7.37 (m, 1H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 5.73 (d, *J* = 7.5 Hz, 1H), 3.76 (s, 3H), 2.34 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 171.4, 163.9, 149.5, 148.4, 138.6, 137.4, 133.7, 129.8, 127.4, 126.5, 122.5, 56.5, 52.9, 21.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{17}N_2O_3$ 285.1239; found: 285.1243.

FT-IR (thin film, cm^{-1}) υ 3388, 2951, 1743, 1684, 1507, 1437, 1180.

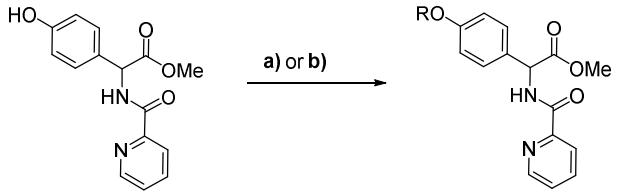
Methyl 2-(4-hydroxyphenyl)-2-(picolinamido)acetate



Procedure A. Step 1: 4-Hydroxyphenylglycine (1.50 g, 9.0 mmol, 1 equiv), $C_2O_2Cl_2$ (1.6 mL, 18.0 mmol, 2 equiv), MeOH (10 mL).

Step 2: Crude reaction mixture from Step 1, picolinic acid (1.16 g, 9.45 mmol, 1.05 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (6.80 g, 18.0 mmol, 2 equiv), DMF (18 mL), pyridine (2.2 mL, 27.0 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 1.2 g (47%) of product was obtained as a colorless oil. This compound is known.[1]

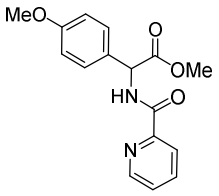
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.97 (d, *J* = 7.2 Hz, 1H), 8.59 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.16 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.30 – 7.21 (m, 2H), 6.79 – 6.67 (m, 2H), 5.67 (d, *J* = 7.3 Hz, 1H), 3.76 (s, 3H).



a) R = Me; MeI (1.3 equiv), 60% NaH dispersion in mineral oil (1.5 equiv), DMF, 0 °C - rt
b) R = MOM; MOMCl (1.3 equiv), 60% NaH dispersion in mineral oil (1.5 equiv), DMF, 0 °C - rt

Scheme S2. Protection of hydroxylgroup

Methyl 2-(4-methoxyphenyl)-2-(picolinamido)acetate



Synthesized according to Scheme S2, a). To a solution of methyl 2-(4-hydroxyphenyl)-2-(picolinamido)acetate (500 mg, 1.75 mmol) in DMF (8 mL), NaH (60% dispersion in mineral oil, 105 mg, 2.62 mmol, 1.5 equiv) was added at 0 °C temperature. The reaction was stirred at the same temperature for 5 min and then MeI (142 µL, 2.27 mmol 1.3 equiv) was added and further stirred for 30 min at the same temperature. The reaction mixture was quenched with ice water and then extracted with ethyl acetate (3 x 20 mL). The combined organic phase was washed with dist. H_2O (20 mL), brine (20 mL) and then dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 270 mg (52%) of product was obtained as a colorless oil. R_f = 0.25 (petroleum ether/EtOAc 2:1).

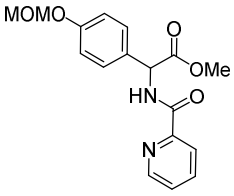
^{1}H-NMR (400 MHz, $C_2D_2Cl_4$, ppm) δ 8.86 (d, *J* = 7.4 Hz, 1H), 8.61 (d, *J* = 4.1 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.87 (td, *J* = 7.7, 1.7 Hz, 1H), 7.48 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.45 – 7.32 (m, 2H), 6.96 – 6.89 (m, 2H), 5.68 (d, *J* = 7.4 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 171.5, 163.9, 159.9, 149.5, 148.4, 137.4, 128.8, 128.7, 126.5, 122.5, 114.5, 56.2, 55.5, 52.9.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+Na]^+$: $C_{16}H_{16}N_2O_4Na$ 323.1008; found: 323.1015.

FT-IR (thin film, cm^{-1}) υ 3385, 3007, 2954, 1745, 1682, 1513, 1259, 1179.

Methyl 2-(4-(methoxymethoxy)phenyl)-2-(picolinamido)acetate



Synthesized according to Scheme S2, b). To a solution of methyl 2-(4-hydroxyphenyl)-2-(picolinamido)acetate (1.0 g, 3.49 mmol) in DMF (15 mL), NaH (60% dispersion in mineral oil, 210 mg, 5.24 mmol, 1.5 equiv) was added at 0 °C temperature. The reaction was stirred at the same temperature for 5 min and then MOMCl (0.35 mL, 4.54 mmol 1.3 equiv) was added and further stirred for 30 min at the same temperature. The reaction mixture was quenched with ice water and then extracted with ethyl acetate (3 x 20 mL). The combined organic phase was washed with dist. H_2O (20 mL), brine (20 mL) and then dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 550 mg (48%) of product was obtained as a colorless oil. R_f = 0.33 (petroleum ether/EtOAc 2:1).

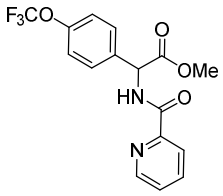
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.88 (d, *J* = 7.1 Hz, 1H), 8.58 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.15 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 – 7.37 (m, 3H), 7.06 – 7.01 (m, 2H), 5.71 (d, *J* = 7.4 Hz, 1H), 5.16 (s, 2H), 3.77 (s, 3H), 3.46 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 171.4, 163.9, 157.5, 149.4, 148.4, 137.4, 129.9, 128.8, 126.6, 122.5, 116.8, 94.5, 56.2, 56.1, 52.9.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+Na]^+$: $C_{17}H_{18}N_2O_5Na$ 335.1113; found: 335.1117.

FT-IR (thin film, cm^{-1}) υ 3386, 2954, 1751, 1683, 1508, 1236, 1153.

Methyl 2-(4-trifluoromethoxyphenyl)-2-(picolinamido)acetate



Procedure A. Step 1: (4-Trifluoromethoxyphenyl)glycine (1.0 g, 4.3 mmol, 1 equiv), $C_2O_2Cl_2$ (0.74 mL, 8.6 mmol, 2 equiv), MeOH (5 mL).

Step 2: Crude reaction mixture from Step 1, picolinic acid (550 mg, 4.5 mmol, 1.05 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (3.23 g, 8.6 mmol, 2 equiv), DMF (8 mL), pyridine (1.0 mL, 12.9 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 1.3 g (82%) of product was obtained as a colorless oil. R_f = 0.42 (petroleum ether/EtOAc 2:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 9.01 (d, *J* = 7.2 Hz, 1H), 8.60 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 8.14 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.45 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.25 – 7.17 (m, 2H), 5.79 (d, *J* = 7.5 Hz, 1H), 3.79 (s, 3H).

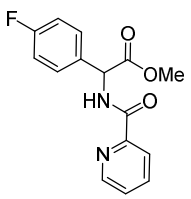
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.8, 164.0, 149.4 (q, J_{C-F} = 1.6 Hz), 149.2, 148.5, 137.5, 135.4, 129.0, 126.7, 122.5, 121.5, 120.5 (q, J_{C-F} = 257.6 Hz), 56.0, 53.2.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -57.84.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{14}N_2O_4F_3$ 355.0906; found: 355.0906.

FT-IR (thin film, cm^{-1}) υ 3384, 2957, 1743, 1675, 1505, 1436, 1261, 1221, 1162.

Methyl 2-(4-fluorophenyl)-2-(picolinamido)acetate



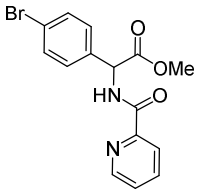
Procedure A. Step 1: 2-(4-Fluorophenyl)glycine (1.0 g, 5.9 mmol, 1 equiv), $C_2O_2Cl_2$ (1.5 mL, 17.7 mmol, 3 equiv), MeOH (9 mL).

Step 2: Crude reaction mixture from Step 1, picolinic acid (762 mg, 6.2 mmol, 1.05 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (4.48 g, 11.8 mmol, 2 equiv), DMF (12 mL), pyridine (1.4 mL, 17.7 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 1.3 g (76%) of product was obtained as a colorless oil. R_f = 0.37 (eluent petroleum ether/EtOAc = 2/1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.96 (d, *J* = 6.8 Hz, 1H), 8.65 – 8.54 (m, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.89 – 7.76 (m, 1H), 7.50 – 7.40 (m, 3H), 7.12 – 7.00 (m, 2H), 5.75 (d, *J* = 7.4 Hz, 1H), 3.77 (s, 3H).

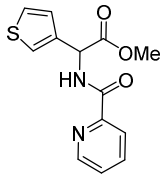
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 171.1, 163.9, 162.9 (d, J_{C-F} = 247.4 Hz), 149.3, 148.5, 137.5, 132.6 (d, J_{C-F} = 3.3 Hz), 129.3 (d, J_{C-F} = 8.4 Hz), 126.7, 122.5, 116.1 (d, J_{C-F} = 21.8 Hz), 56.0, 53.1.
^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -113.28.
HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}FH_{14}N_2O_3$ 289.0988; found: 289.1002.
FT-IR (thin film, cm^{-1}) υ 3386, 2955, 1744, 1683, 1507, 1437, 1225, 1161.

Methyl 2-(4-bromophenyl)-2-(picolinamido)acetate



Procedure A. Step 1: 2-(4-Bromophenyl)glycine (1.59 g, 6.0 mmol, 1 equiv), $C_2O_2Cl_2$ (1.6 mL, 18.0 mmol, 3 equiv), MeOH (10 mL).
Step 2: Crude reaction mixture from Step 1, picolinic acid (775 mg, 6.3 mmol, 1.05 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (4.55 g, 12.0 mmol, 2 equiv), DMF (12 mL), pyridine (1.5 mL, 18.0 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 700 mg (33%) of product was obtained as a colorless oil. R_f = 0.40 (eluent petroleum ether/EtOAc = 2/1).
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.99 (d, *J* = 7.0 Hz, 1H), 8.60 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.14 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.45 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.38 – 7.33 (m, 2H), 5.73 (d, *J* = 7.4 Hz, 1H), 3.77 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.8, 163.9, 149.2, 148.4, 137.5, 135.8, 132.3, 129.2, 126.7, 122.8, 122.5, 56.2, 53.1.
HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}BrH_{14}N_2O_3$ 349.0188; found: 349.0190.
FT-IR (thin film, cm^{-1}) υ 3378, 2954, 1748, 1680, 1507, 1173.

Methyl 2-(picolinamido)-2-(thiophen-3-yl)acetate



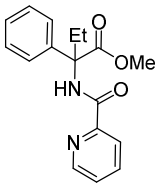
Procedure A. Step 1: 2-Amino-2-(thiophen-3-yl)acetic acid hydrochloride (1.23 g, 7.8 mmol, 1 equiv), $C_2O_2Cl_2$ (1.36 mL, 15.6 mmol, 2 equiv), MeOH (15 mL).
Step 2: Crude reaction mixture from Step 1, picolinic acid (965 mg, 7.8 mmol, 1.0 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (5.95 g, 15.6 mmol, 2 equiv), DMF (24 mL), pyridine (1.89 mL, 23.4 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 2:1) 280 mg (13%) of product was obtained as a colorless oil. R_f = 0.51 (eluent petroleum ether/EtOAc = 1/1).
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.84 (d, *J* = 7.2 Hz, 1H), 8.58 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.17 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.44 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.41 – 7.36 (m, 1H), 7.33 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.17 (dd, *J* = 5.0, 1.3 Hz, 1H), 5.92 (d, *J* = 7.9 Hz, 1H), 3.80 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.9, 164.0, 149.4, 148.4, 137.4, 136.6, 126.9, 126.6, 126.5, 123.5, 122.5, 53.0, 52.5.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{13}H_{13}N_2O_3S$ 277.0647; found: 277.0655.

FT-IR (thin film, cm^{-1}) υ 3387, 3098, 2954, 1752, 1679, 1514, 1212, 1164.

Methyl 2-phenyl-2-(picolinamido)butanoate



Step 1: 2-Amino-2-phenylbutanoic acid (1.00 g, 5.6 mmol, 1 equiv) was dissolved in MeOH (22 mL), cooled to 0 °C and thionyl chloride (10.12 mL, 140.0 mmol, 25 equiv) was added. The reaction was then warmed to room temperature and heated to reflux for 40h. The reaction was then cooled to room temperature and concentrated in vacuo. To remove inorganic salts, reaction mixture was dissolved in EtOH (20 mL) and filtrated through cotton. The filtrate was concentrated under reduced pressure to afford crude product, which was used in the next step without further purification

Procedure A Step 2: Crude reaction mixture from Step 1, picolinic acid (726 mg, 5.9 mmol, 1.05 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluoro-phosphate (4.25 g, 11.2 mmol, 2 equiv), DMF (5 mL), pyridine (1.4 mL, 16.8 mmol, 3 equiv). After column chromatography (gradient hexanes/EtOAc from 3:1 to 1:1) 585 mg (35%) of product was obtained as a colorless oil. R_f = 0.72 (eluent petroleum ether/EtOAc = 1/1).

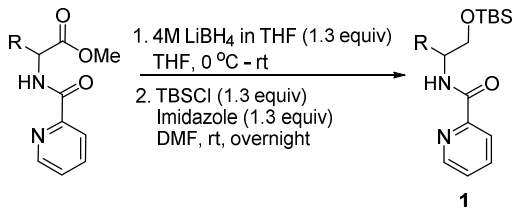
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 9.46 (s, 1H), 8.55 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.01 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.73 (td, *J* = 7.7, 1.7 Hz, 1H), 7.44 (d, *J* = 9.7 Hz, 2H), 7.35 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.22 – 7.17 (m, 1H), 3.65 (s, 3H), 2.96 – 2.84 (m, 1H), 2.61 – 2.49 (m, 1H), 0.81 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 173.3, 162.9, 150.1, 148.4, 139.8, 137.3, 128.7, 127.9, 126.3, 126.1, 122.0, 66.4, 53.3, 26.2, 8.8.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{17}H_{19}N_2O_3$ 299.1396; found: 299.1396.

FT-IR (thin film, cm^{-1}) υ 3386, 2954, 2928, 2857, 1682, 1511, 1464, 1257, 1102.

1.2. Synthesis and characterization of picolinamides 1



Scheme S3. Synthesis of picolinamides **1**

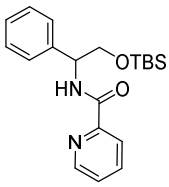
Procedure B

Synthesis of N-(2-((tert-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide is representative.

Step 1: Methyl 2-phenyl-2-(picolinamido)acetate (1.50 g, 5.55 mmol, 1 equiv) was dissolved in THF (20 mL) under an argon atmosphere. The solution was cooled in water/ice bath to 0 °C and lithium borohydride (4 M in THF, 1.8 mL, 7.21 mmol, 1.3 equiv.) was added slowly dropwise, then reaction mixture was stirred at room temperature for 3 h. The reaction was monitored by TLC to achieve full conversion, then cooled in water/ice bath and quenched by 15% citric acid solution in water. Organic solvent was evaporated in vacuum and water phase was extracted by DCM (2 x 30 mL). Combined organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure to afford the crude product, which was used in next step without further purification.

Step 2: To the solution of *N*-(2-hydroxy-1-phenylethyl)picolinamide (5.55 mmol, 1 equiv) in DMF (18 mL) under an argon atmosphere imidazole (1.10 g, 7.21 mmol, 1.3 equiv) and *tert*-butyldimethylsilyl chloride (491 mg, 7.21 mmol, 1.3 equiv) were added. The reaction mixture was stirred at room temperature to achieve full conversion, then was diluted with EtOAc (30 mL) and H_2O (20 mL). Organic phase was separated and water phase was extracted with EtOAc (20 mL), combined organic phase was washed with dist. H_2O (20 mL) and brine (20 mL). Combined organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure to afford the crude product, which was further purified by flash chromatography on silica gel using petroleum ether/EtOAc (6/1) as an eluent to give corresponding product 1.6 g (81%) as colorless oil.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (1a)**



R_f = 0.34 (petroleum ether/EtOAc 4:1).

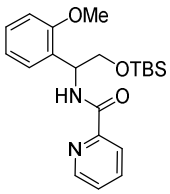
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.86 (d, *J* = 7.7 Hz, 1H), 8.58 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 8.18 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.36 – 7.29 (m, 2H), 7.28 – 7.22 (m, 1H), 5.22 (dt, *J* = 8.7, 4.6 Hz, 1H), 4.01 (dd, *J* = 10.2, 4.6 Hz, 1H), 3.94 (dd, *J* = 10.2, 4.6 Hz, 1H), 0.87 (s, 9H), -0.01 (s, 3H), -0.05 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.9, 150.1, 148.2, 140.3, 137.4, 128.5, 127.5, 127.2, 126.3, 122.4, 66.4, 54.9, 25.9, 18.4, -5.4, -5.5.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{20}H_{29}N_2O_2Si$ 357.1998; found: 357.2007.

FT-IR (thin film, cm^{-1}) υ 3386, 2954, 2927, 2856, 1681, 1517, 1254, 1107.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(2-methoxyphenyl)ethyl)picolinamide (1f)**



Procedure B. Step 1: Methyl 2-(2-methoxyphenyl)-2-(picolinamido)acetate (0.90 g, 2.99 mmol, 1 equiv), $LiBH_4$ (4 M in THF 0.97 mL, 3.89 mmol, 1.3 equiv), THF (24 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (265 mg, 3.89 mmol, 1.3 equiv), TBSCl (587 mg, 3.89 mmol, 1.3 equiv), DMF (12 mL). After column chromatography (hexanes/EtOAc 6:1) 627 mg (54%) of product was obtained as a colorless oil. R_f = 0.38 (petroleum ether/EtOAc 3:1).

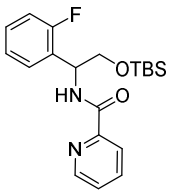
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 9.02 (d, *J* = 8.6 Hz, 1H), 8.59 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.18 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.82 (td, *J* = 7.7, 1.7 Hz, 1H), 7.41 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.22 (td, *J* = 7.9, 1.7 Hz, 1H), 6.94 – 6.85 (m, 2H), 5.53 (dt, *J* = 9.0, 5.1 Hz, 1H), 3.98 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.94 – 3.86 (m, 4H), 0.83 (s, 9H), -0.06 (s, 3H), -0.10 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.7, 157.1, 150.5, 148.3, 137.3, 128.8, 128.5, 127.9, 126.1, 122.4, 120.6, 110.7, 64.9, 55.6, 51.4, 25.9, 18.4, -5.47, -5.48.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{21}H_{31}N_2O_3Si$ 387.2104; found: 387.2108.

FT-IR (thin film, cm^{-1}) υ 3394, 2930, 2856, 1694, 1508, 1256, 1110.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(2-fluorophenyl)ethyl)picolinamide (1g)**



Procedure B. Step 1: Methyl 2-(2-fluorophenyl)-2-(picolinamido)acetate (1.40 g, 4.86 mmol, 1 equiv), $LiBH_4$ (4 M in THF 1.58 mL, 6.32 mmol, 1.3 equiv), THF (24 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (430 mg, 6.32 mmol, 1.3 equiv), TBSCl (952 mg, 6.32 mmol, 1.3 equiv), DMF (10 mL). After column chromatography (hexanes/EtOAc 6:1) 1.30 g (71%) of product was obtained as a colorless oil. R_f = 0.38 (petroleum ether/EtOAc 4:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.91 (d, *J* = 8.2 Hz, 1H), 8.59 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.17 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.83 (td, *J* = 7.6, 1.7 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.37 (td, *J* = 7.6, 1.7 Hz, 1H), 7.26 – 7.18 (m, 1H), 7.11 – 7.01 (m, 2H), 5.52 (dt, *J* = 8.9, 4.8 Hz, 1H), 4.01 (dd, *J* = 10.1, 4.8 Hz, 1H), 3.95 (dd, *J* = 10.1, 4.8 Hz, 1H), 0.84 (s, 9H), -0.03 (s, 3H), -0.09 (s, 3H).

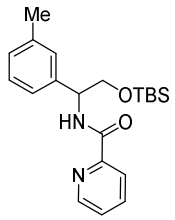
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.9, 160.7 (d, J_{C-F} = 245.5 Hz), 150.0, 148.3, 137.4, 129.1 (d, J_{C-F} = 4.5 Hz), 129.0 (d, J_{C-F} = 8.3 Hz), 127.1 (d, J_{C-F} = 13.4 Hz), 126.3, 124.0 (d, J_{C-F} = 3.4 Hz), 122.4, 115.5 (d, J_{C-F} = 21.8 Hz), 65.2 (d, J_{C-F} = 1.2 Hz), 50.0 (d, J_{C-F} = 1.4 Hz), 25.9, 18.3, -5.5, -5.6.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -118.54.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{20}H_{28}N_2O_2SiF$ 375.1904; found: 375.1916.

FT-IR (thin film, cm^{-1}) υ 3388, 2955, 2928, 1685, 1514, 1107.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(3-methylphenyl)ethyl)picolinamide (1h)**



Procedure B. Step 1: Methyl 2-(3-methylphenyl)-2-(picolinamido)acetate (1.00 g, 3.52 mmol, 1 equiv), $LiBH_4$ (4 M in THF 1.07 mL, 4.26 mmol, 1.2 equiv), THF (17 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (312 mg, 4.58 mmol, 1.3 equiv), TBSCl (690 mg, 4.58 mmol, 1.3 equiv), DMF (15 mL). After column chromatography (petroleum ether/EtOAc 6:1) 441 mg (34%) of product was obtained as a colorless oil. R_f = 0.37 (petroleum ether/EtOAc 5:1).

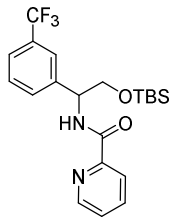
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.82 (d, *J* = 7.7 Hz, 1H), 8.58 (ddd, *J* = 4.7, 1.5, 0.8 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.24 – 7.16 (m, 3H), 7.10 – 7.01 (m, 1H), 5.22 – 5.10 (m, 1H), 3.99 (dd, *J* = 10.2, 4.6 Hz, 1H), 3.92 (dd, *J* = 10.2, 4.6 Hz, 1H), 2.33 (s, 3H), 0.88 (s, 9H), 0.00 (s, 3H), -0.04 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 164.0, 150.2, 148.3, 140.3, 138.0, 137.3, 128.4, 128.2, 128.0, 126.2, 124.2, 122.3, 66.4, 54.9, 25.9, 21.6, 18.4, -5.4.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{21}H_{31}N_2O_2Si$ 371.2155; found: 371.2159.

FT-IR (thin film, cm^{-1}) υ 3397, 2954, 2927, 2857, 1684, 1512, 1101.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(3-trifluoromethylphenyl)ethyl)picolinamide (1i)**



Procedure B. Step 1: Methyl 2-(3-trifluoromethylphenyl)-2-(picolinamido)acetate (1.12 g, 3.30 mmol, 1 equiv), $LiBH_4$ (4 M in THF 1.07 mL, 4.29 mmol, 1.3 equiv), THF (30 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (292 mg, 4.29 mmol, 1.3 equiv), TBSCl (647 mg, 4.29 mmol, 1.3 equiv), DMF (12 mL). After column chromatography (hexanes/EtOAc 6:1) 1.40 g (60%) of product was obtained as a colorless oil. R_f = 0.37 (petroleum ether/EtOAc 3:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.94 (d, *J* = 7.9 Hz, 1H), 8.59 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.17 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.69 (s, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.49 – 7.32 (m, 2H), 5.26 (dt, *J* = 8.2, 4.1 Hz, 1H), 4.04 (dd, *J* = 10.2, 4.4 Hz, 1H), 3.94 (dd, *J* = 10.2, 3.8 Hz, 1H), 0.88 (s, 9H), 0.01 (s, 3H), -0.05 (s, 3H).

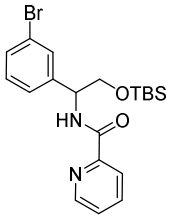
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 164.1, 149.8, 148.4, 141.7, 138.5, 130.8, 130.8 (q, J_{C-F} = 32.1 Hz), 128.9, 126.4, 124.4 (q, J_{C-F} = 3.8 Hz), 124.1 (q, J_{C-F} = 3.8 Hz), 124.3 (q, J_{C-F} = 272.4 Hz), 122.4, 66.2, 54.4, 25.8, 18.3, -5.5, -5.6.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -62.54.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{21}H_{28}N_2O_2SiF_3$ 425.1872; found: 425.1881.

FT-IR (thin film, cm^{-1}) υ 3386, 2955, 2930, 2859, 1683, 1508, 1329, 1126.

_N_-(2-((_Tert_-butyldimethylsilyl)oxy)-1-(3-bromophenyl)ethyl)picolinamide (1j)



Procedure B. Step 1: Methyl 2-(3-bromophenyl)-2-(picolinamido)-acetate (1.17 g, 3.34 mmol, 1 equiv), $LiBH_4$ (4 M in THF 1.08 mL, 4.34 mmol, 1.3 equiv), THF (25 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (295 mg, 4.34 mmol, 1.3 equiv), TBSCl (654 mg, 4.34 mmol, 1.3 equiv), DMF (20 mL). After column chromatography (hexanes/EtOAc 6:1) 938 g (65%) of product was obtained as a colorless oil. R_f = 0.40 (petroleum ether/EtOAc 4:1).

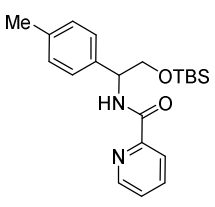
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.87 (d, J = 7.7 Hz, 1H), 8.62 – 8.55 (m, 1H), 8.17 (d, J = 7.8 Hz, 1H), 7.84 (td, J = 7.7, 1.7 Hz, 1H), 7.56 (t, J = 1.7 Hz, 1H), 7.44 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H), 7.38 (ddd, J = 7.9, 1.9, 1.0 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 5.21 – 5.12 (m, 1H), 4.00 (dd, J = 10.2, 4.4 Hz, 1H), 3.91 (dd, J = 10.2, 4.2 Hz, 1H), 0.89 (s, 9H), 0.01 (s, 3H), -0.04 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 164.0, 149.9, 148.3, 142.9, 137.4, 130.6, 130.3, 130.0, 126.4, 126.0, 122.6, 122.4, 66.2, 54.3, 25.9, 18.4, -5.5.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{20}BrH_{28}N_2O_2Si$ 435.1103; found: 435.1106.

FT-IR (thin film, cm^{-1}) υ 2955, 2928, 2857, 1682, 1511, 1464, 1434, 1257, 1102.

_N_-(2-((_Tert_-butyldimethylsilyl)oxy)-1-(4-methylphenyl)ethyl)picolinamide (1k)



Procedure B. Step 1: Methyl 2-(4-methylphenyl)-2-(picolinamido)acetate (668 mg, 2.35 mmol, 1 equiv), $LiBH_4$ (4 M in THF 0.76 mL, 3.05 mmol, 1.3 equiv), THF (15 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (208 mg, 3.05 mmol, 1.3 equiv), TBSCl (460 mg, 3.05 mmol, 1.3 equiv), DMF (8 mL). After column chromatography (hexanes/EtOAc 6:1) 514 mg (59%) of product was obtained as a colorless oil. R_f = 0.46 (petroleum ether/EtOAc 4:1).

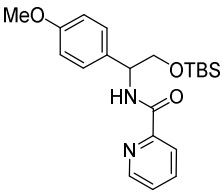
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.79 (d, *J* = 7.8 Hz, 1H), 8.56 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 8.17 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.82 (td, *J* = 7.7, 1.7 Hz, 1H), 7.41 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 5.17 (dt, *J* = 8.7, 4.7 Hz, 1H), 3.99 (dd, *J* = 10.2, 4.7 Hz, 1H), 3.92 (dd, *J* = 10.2, 4.9 Hz, 1H), 2.32 (s, 3H), 0.88 (s, 9H), 0.01 (s, 3H), -0.02 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.9, 150.2, 148.2, 137.4, 137.3, 137.0, 129.2, 127.1, 126.2, 122.3, 66.4, 54.7, 25.9, 21.2, 18.4, -5.38, -5.42.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{21}H_{31}N_2O_2Si$ 371.2155; found: 371.2164.

FT-IR (thin film, cm^{-1}) υ 3389, 2952, 2859, 1679, 1518, 1257, 1115.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-methoxyphenyl)ethyl)picolinamide (1l)**



Procedure B. Step 1: Methyl 2-(4-methoxyphenyl)-2-(picolinamido)acetate (260 mg, 0.87 mmol, 1 equiv), $LiBH_4$ (4 M in THF 0.28 mL, 1.12 mmol, 1.3 equiv), THF (5 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (77 mg, 1.12 mmol, 1.3 equiv), TBSCl (170 mg, 1.12 mmol, 1.3 equiv), DMF (4 mL). After column chromatography (hexanes/EtOAc 6:1) 180 mg (54%) of product was obtained as a colorless oil. R_f = 0.33 (petroleum ether/EtOAc 4:1).

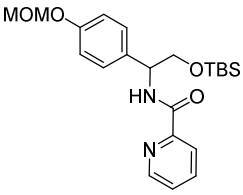
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.79 (d, *J* = 7.8 Hz, 1H), 8.56 (d, *J* = 4.1 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.82 (td, *J* = 7.7, 1.6 Hz, 1H), 7.45 – 7.37 (m, 1H), 7.37 – 7.29 (m, 2H), 6.94 – 6.80 (m, 2H), 5.16 (dt, *J* = 8.7, 4.6 Hz, 1H), 3.98 (dd, *J* = 10.2, 4.7 Hz, 1H), 3.91 (dd, *J* = 10.2, 4.7 Hz, 1H), 3.78 (s, 3H), 0.88 (s, 9H), 0.01 (s, 3H), -0.02 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.9, 159.0, 150.1, 148.2, 137.4, 132.6, 128.3, 126.2, 122.3, 113.9, 66.4, 55.4, 54.3, 25.9, 18.3, -5.4.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+Na]^+$: $C_{21}H_{30}N_2O_3NaSi$ 409.1923; found: 409.1926.

FT-IR (thin film, cm^{-1}) υ 3389, 3058, 2952, 2929, 2857, 1688, 1505, 1249, 1109.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-methoxymethoxyphenyl)ethyl)picolinamide (1m)**



Procedure B. Step 1: Methyl 2-(4-methoxymethoxyphenyl)-2-(picolinamido)-acetate (514 mg, 1.56 mmol, 1 equiv), $LiBH_4$ (4 M in THF 0.51 mL, 2.02 mmol, 1.3 equiv), THF (10 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (138 mg, 2.02 mmol, 1.3 equiv), TBSCl (305 mg, 2.02 mmol, 1.3 equiv), DMF (5 mL). After column chromatography (hexanes/EtOAc 6:1) 370 mg (57%) of product was obtained as a colorless oil. R_f = 0.20 (petroleum ether/EtOAc 4:1).

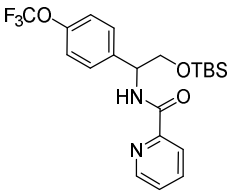
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.78 (d, *J* = 7.9 Hz, 1H), 8.56 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 8.17 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.41 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.38 – 7.30 (m, 2H), 7.03 – 6.95 (m, 2H), 5.23 – 5.08 (m, 3H), 3.98 (dd, *J* = 10.2, 4.7 Hz, 1H), 3.91 (dd, *J* = 10.2, 4.7 Hz, 1H), 3.46 (s, 3H), 0.88 (s, 9H), 0.01 (s, 3H), -0.02 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.9, 156.3, 150.2, 148.3, 137.4, 133.9, 128.4, 126.2, 122.3, 116.3, 94.6, 66.4, 56.1, 54.3, 25.9, 18.4, -5.37, -5.41.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{22}H_{33}N_2O_4Si$ 417.2210; found: 417.2206.

FT-IR (thin film, cm^{-1}) υ 3388, 2930, 1512, 1153, 1108, 1080, 1006.

_N_-(2-((_Tert_-butyldimethylsilyl)oxy)-1-(4-trifluoromethoxyphenyl)ethyl)picolinamide (1n)



Procedure B. Step 1: Methyl 2-(4-trifluoromethoxyphenyl)-2-(picolinamido)-acetate (1.16 g, 3.27 mmol, 1 equiv), $LiBH_4$ (4 M in THF 1.06 mL, 4.26 mmol, 1.3 equiv), THF (24 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (290 mg, 4.26 mmol, 1.3 equiv), TBSCl (642 mg, 4.26 mmol, 1.3 equiv), DMF (10 mL). After column chromatography (hexanes/EtOAc 6:1) 1.00 g (69%) of product was obtained as a colorless oil. R_f = 0.34 (petroleum ether/EtOAc 4:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.88 (d, *J* = 7.9 Hz, 1H), 8.58 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.17 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.48 – 7.40 (m, 3H), 7.21 – 7.12 (m, 2H), 5.21 (dt, *J* = 8.3, 4.3 Hz, 1H), 4.01 (dd, *J* = 10.2, 4.5 Hz, 1H), 3.92 (dd, *J* = 10.2, 4.2 Hz, 1H), 0.87 (s, 9H), 0.01 (s, 3H), -0.05 (s, 3H).

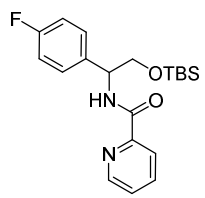
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 164.1, 149.9, 148.6 (q, J_{C-F} = 1.8 Hz), 148.3, 139.3, 137.5, 128.6, 126.4, 122.4, 121.0, 120.6 (q, J_{C-F} = 256.8 Hz), 66.3, 54.2, 25.9, 18.3, -5.47, -5.48.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -57.19.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{21}H_{28}N_2O_3SiF_3$ 441.1821; found: 441.1828.

FT-IR (thin film, cm^{-1}) υ 3386, 2955, 2931, 2858, 1686, 1507, 1260, 1224, 1165, 1109.

_N_-(2-((_Tert_-butyldimethylsilyl)oxy)-1-(4-fluorophenyl)ethyl)picolinamide (1o)



Procedure B. Step 1: Methyl 2-(4-fluorophenyl)-2-(picolinamido)-acetate (742 mg, 2.57 mmol, 1 equiv), $LiBH_4$ (4 M in THF 0.84 mL, 3.34 mmol, 1.3 equiv), THF (20 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (228 mg, 3.34 mmol, 1.3

equiv), TBSCl (504 mg, 3.34 mmol, 1.3 equiv), DMF (10 mL). After column chromatography (petroleum ether/EtOAc 6:1) 590 g (61%) of product was obtained as a colorless oil. R_f = 0.32 (petroleum ether/EtOAc 5:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.85 (d, *J* = 7.7 Hz, 1H), 8.57 (ddd, *J* = 4.8, 1.6, 0.9 Hz, 1H), 8.17 (dt, *J* = 7.8, 0.9 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.46 – 7.33 (m, 3H), 7.05 – 6.94 (m, 2H), 5.18 (dt, *J* = 8.4, 4.4 Hz, 1H), 3.99 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.91 (dd, *J* = 10.1, 4.3 Hz, 1H), 0.88 (s, 9H), 0.01 (s, 3H), -0.04 (s, 3H).

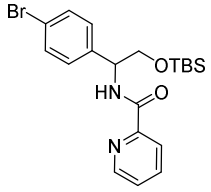
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 164.0, 162.2 (d, J_{C-F} = 245.0 Hz), 150.0, 148.3, 137.4, 136.3 (d, J_{C-F} = 3.1 Hz), 128.8 (d, J_{C-F} = 8.1 Hz), 126.3, 122.4, 115.3 (d, J_{C-F} = 21.4 Hz), 66.3, 54.2, 25.9, 18.4, -5.4, -5.5.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -115.67.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{20}FH_{28}N_2O_2Si$ 375.1904; found: 375.1910.

FT-IR (thin film, cm^{-1}) υ 3388, 2954, 2929, 2858, 1687, 1514, 1258, 1223, 1103.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-bromophenyl)ethyl)picolinamide (1p)**



Procedure B. Step 1: Methyl 2-(4-bromophenyl)-2-(picolinamido)-acetate (335 mg, 0.96 mmol, 1 equiv), $LiBH_4$ (4 M in THF 0.31 mL, 1.24 mmol, 1.3 equiv), THF (20 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (85 mg, 1.24 mmol, 1.3 equiv), TBSCl (188 mg, 1.24 mmol, 1.3 equiv), DMF (10 mL). After column chromatography (hexanes/EtOAc 6:1) 222 mg (53%) of product was obtained as a colorless oil. R_f = 0.33 (petroleum ether/EtOAc 5:1).

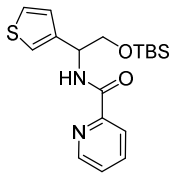
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.85 (d, *J* = 7.7 Hz, 1H), 8.61 – 8.49 (m, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.51 – 7.40 (m, 3H), 7.33 – 7.27 (m, 2H), 5.15 (dt, *J* = 8.3, 4.3 Hz, 1H), 3.99 (dd, *J* = 10.2, 4.5 Hz, 1H), 3.90 (dd, *J* = 10.2, 4.2 Hz, 1H), 0.88 (s, 9H), 0.01 (s, 3H), -0.03 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 164.0, 150.0, 148.3, 136.6, 137.4, 131.5, 129.0, 126.4, 122.4, 121.3, 66.1, 54.3, 25.9, 18.4, -5.4, -5.5.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{20}BrH_{28}N_2O_2Si$ 435.1103; found: 435.1102.

FT-IR (thin film, cm^{-1}) υ 2954, 2928, 2856, 1684, 1515, 1255, 1107.

***N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(thiophen-3-yl)ethyl)picolinamide (1q)**



Procedure B. Step 1: Methyl 2-(picolinamido)-2-(thiophen-3-yl)acetate (280 mg, 1.01 mmol, 1 equiv), $LiBH_4$ (4 M in THF 0.33 mL, 1.31 mmol, 1.3 equiv), THF (10 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (89 mg, 1.31 mmol, 1.3 equiv), TBSCl (197 mg, 1.31 mmol, 1.3 equiv), DMF (5 mL). After column chromatography (petroleum ether/EtOAc 6:1) 233 mg (64%) of product was obtained as a colorless oil. R_f = 0.36 (petroleum ether/EtOAc 5:1).

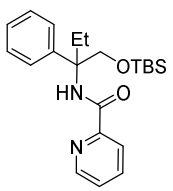
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.72 (d, *J* = 8.4 Hz, 1H), 8.55 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.20 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.32 – 7.23 (m, 2H), 7.16 (dd, *J* = 4.9, 1.4 Hz, 1H), 5.36 (dt, *J* = 8.5, 4.2 Hz, 1H), 4.07 – 3.93 (m, 2H), 0.89 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.8, 150.1, 148.3, 141.3, 137.4, 127.1, 126.3, 125.7, 122.4, 122.0, 65.8, 50.7, 25.9, 18.4, -5.4.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{18}H_{27}N_2O_2SiS$ 363.1563; found: 363.1573.

FT-IR (thin film, cm^{-1}) υ 2954, 2928, 1676, 1513, 1510, 1255, 1114.

***N*-(1-((*Tert*-butyldimethylsilyl)oxy)-2-phenylbutan-2-yl)picolinamide (1s)**



Procedure B. Step 1: Methyl 2-phenyl-2-(picolinamido)butanoate (2.00 g, 6.69 mmol, 1 equiv), $LiBH_4$ (4 M in THF 2.17 mL, 8.70 mmol, 1.3 equiv), THF (20 mL).

Step 2: Crude reaction mixture from Step 1, imidazole (592 mg, 8.70 mmol, 1.3 equiv), TBSCl (1.31 g, 8.70 mmol, 1.3 equiv), DMF (20 mL). After column chromatography (petroleum ether/EtOAc 6:1) 1.20 g (47%) of product was obtained as a colorless oil. R_f = 0.81 (petroleum ether/EtOAc 1:1).

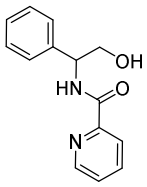
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.81 (s, 1H), 8.57 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.15 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.44 – 7.37 (m, 3H), 7.33 – 7.27 (m, 2H), 7.24 – 7.19 (m, 1H), 4.08 (d, *J* = 9.6 Hz, 1H), 4.01 (d, *J* = 9.6 Hz, 1H), 2.51 – 2.41 (m, 1H), 2.30 – 2.20 (m, 1H), 0.93 (t, *J* = 7.5 Hz, 3H), 0.85 (s, 9H), -0.03 (s, 3H), -0.12 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.5, 150.8, 148.1, 143.2, 137.4, 128.2, 126.8, 126.2, 126.1, 122.0, 67.8, 62.7, 28.6, 25.8, 18.2, 8.7, -5.5, -5.7.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{22}H_{33}N_2O_2Si$ 385.2311; found: 385.2315.

FT-IR (thin film, cm^{-1}) υ 3378, 2955, 2929, 2856, 1688, 1515, 1464, 1257, 1094.

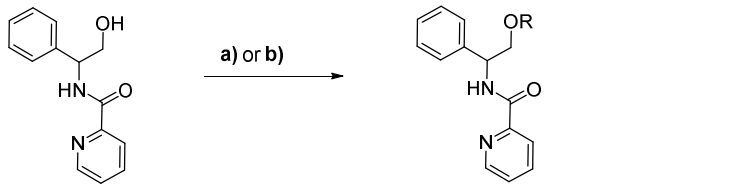
N-(2-Hydroxy-1-phenylethyl)picolinamide (1b)



Procedure B. Step 1: Methyl 2-phenyl-2-(picolinamido)acetate (1.10 g, 4.07 mmol, 1 equiv), $LiBH_4$ (4 M in THF 1.32 mL, 5.29 mmol, 1.3 equiv), THF (15 mL). After column chromatography (gradient hexanes/EtOAc from 1:1 to EtOAc) 880 mg (89%) of product was obtained as a colorless oil.

This compound is known.[2]

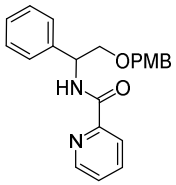
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.70 (d, *J* = 6.5 Hz, 1H), 8.63 – 8.48 (m, 1H), 8.23 – 8.09 (m, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.51 – 7.22 (m, 6H), 5.32 – 5.18 (m, 1H), 4.11 – 3.89 (m, 2H), 3.07 (s, 1H).



a) R = PMB; PMBCl (1.3 equiv), 60% NaH dispersion in mineral oil (1.5 equiv), DMF, 0 °C - rt
b) R = MOM; MOMCl (1.3 equiv), 60% NaH dispersion in mineral oil (1.5 equiv), DMF, 0 °C - rt

Scheme S4. Synthesis of picolinamides **1c**,**d**

N-(2-((4-Methoxybenzyl)oxy)-1-phenylethyl)picolinamide (1c)



Synthesized according to Scheme S4, a). To a solution of *N*-(2-hydroxy-1-phenylethyl)picolinamide (300 mg, 1.24 mmol) in DMF (4 mL), NaH (60% dispersion in mineral oil, 74 mg, 1.86 mmol, 1.5 equiv) was added at 0 °C. The reaction was stirred at the same temperature for 5 min and then PMBCl (0.22 mL, 1.61 mmol 1.3 equiv) was added and further stirred for 30 min at the same temperature. The reaction mixture was quenched with ice water and then extracted with ethyl acetate (3 x 10 mL). The combined organic phase was washed with dist. H_2O (10 mL), brine (10 mL) and then dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. After column chromatography (gradient hexanes/EtOAc from 5:1 to 3:1) 380 mg (85%) of product was obtained as a colorless oil. R_f = 0.10 (petroleum ether/EtOAc 4:1).

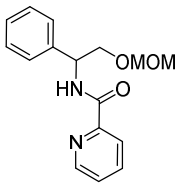
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.75 (d, *J* = 8.0 Hz, 1H), 8.58 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.18 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.46 – 7.38 (m, 3H), 7.38 – 7.30 (m, 2H), 7.31 – 7.23 (m, 1H), 7.24 – 7.18 (m, 2H), 6.87 – 6.81 (m, 2H), 5.39 (dt, *J* = 8.2, 5.2 Hz, 1H), 4.59 – 4.46 (m, 2H), 3.83 (d, *J* = 5.3 Hz, 2H), 3.79 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 164.0, 159.3, 150.0, 148.2, 139.9, 137.4, 130.1, 129.4, 128.6, 127.5, 127.1, 126.3, 122.4, 113.9, 72.8, 72.3, 53.3, 53.1.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+Na]^+$: $C_{22}H_{22}N_2O_3Na$ 385.1528; found: 385.1530.

FT-IR (thin film, cm^{-1}) υ 3393, 2862, 1683, 1512, 1250, 1096.

_N_-(2-(Methoxymethoxy)-1-phenylethyl)picolinamide (1d)



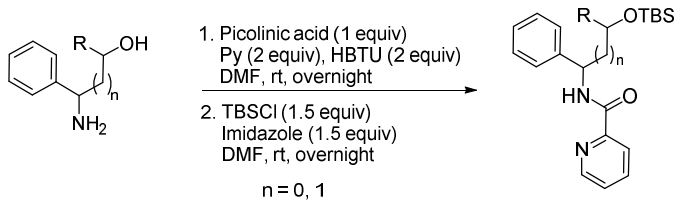
Synthesized according to Scheme S4, b). To a solution of *N*-(2-hydroxy-1-phenylethyl)picolinamide (300 mg, 1.24 mmol) in DMF (4 mL), NaH (60% dispersion in mineral oil, 74 mg, 1.86 mmol, 1.5 equiv) was added at 0 °C. The reaction was stirred at the same temperature for 5 min and then MOMCl (0.12 mL, 1.61 mmol 1.3 equiv) was added and further stirred for 30 min at the same temperature. The reaction mixture was quenched with ice water and then extracted with ethyl acetate (3 x 10 mL). The combined organic phase was washed with dist. H_2O (10 mL), brine (10 mL) and then dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. After column chromatography (gradient hexanes/EtOAc from 2:1 to 1:1) 185 mg (52%) of product was obtained as a colorless oil. R_f = 0.29 (petroleum ether/EtOAc 1:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.71 (d, *J* = 8.0 Hz, 1H), 8.53 – 8.42 (m, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.79 – 7.67 (m, 1H), 7.43 – 7.30 (m, 3H), 7.32 – 7.22 (m, 2H), 7.23 – 7.14 (m, 1H), 5.34 (dt, *J* = 8.5, 5.1 Hz, 1H), 4.63 – 4.52 (m, 2H), 3.92 – 3.82 (m, 2H), 3.20 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.9, 149.8, 148.1, 139.7, 137.3, 128.6, 127.5, 126.9, 126.3, 122.3, 96.5, 70.4, 55.4, 53.0.

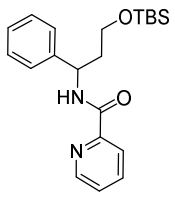
HR-MS (ESI-TOF) m/z: Calcd. for $[M+Na]^+$: $C_{16}H_{18}N_2O_3Na$ 309.1215; found: 309.1217.

FT-IR (thin film, cm^{-1}) υ 3390, 2932, 2887, 1680, 1518, 1151, 1041.



Scheme S5. Synthesis of picolinamides **1e**, **1r** and **(*S*)-1a**

***N*-(3-((*Tert*-butyldimethylsilyl)oxy)-1-phenylpropyl)picolinamide (1e)**



Synthesized according to Scheme S5. Step 1: Under an argon atmosphere 3-amino-3-phenylpropan-1-ol (700 mg, 4.62 mmol, 1 equiv), picolinic acid (570 mg, 4.62 mmol, 1 equiv) and *N,N,N',N'*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (3.51 g, 9.24 mmol, 2 equiv) were dissolved in DMF (15 mL). Pyridine (0.75 mL, 9.24 mmol, 2 equiv) was added to the solution directly. Reaction mixture was stirred at room temperature overnight. Reaction was monitored by TLC to achieve full conversion, and then was diluted with EtOAc (30 mL) and H_2O (30 mL), filtered. Organic phase was separated and aqueous phase was extracted with EtOAc (30 mL), combined organic phase was washed with dist. H_2O (20 mL), brine (20 mL) and dried over Na_2SO_4, filtered. Solvent was evaporated under reduced pressure to afford the crude product, which was used in next step without further purification.

Step 2: To the solution of crude reaction mixture from previous step in DMF (12 mL) under an argon atmosphere imidazole (471 mg, 6.93 mmol, 1.5 equiv) and *tert*-butyldimethylsilyl chloride (1.04 g, 6.93 mmol, 1.5 equiv) were added. The reaction mixture was stirred at room temperature to achieve full conversion, then was diluted with EtOAc (30 mL) and H_2O (20 mL). Organic phase was separated and water phase was extracted with EtOAc (20 mL), combined organic phase was washed with dist. H_2O (20 mL) and brine (20 mL). Combined organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure to afford the crude product, which was further purified by flash chromatography on silica gel using petroleum ether/EtOAc (5/1) as an eluent to give corresponding product 776 mg (68%) as colorless oil. R_f = 0.40 (petroleum ether/EtOAc 3:1).

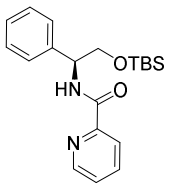
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 8.90 (d, *J* = 7.6 Hz, 1H), 8.56 – 8.42 (m, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.76 (td, *J* = 7.7, 1.7 Hz, 1H), 7.35 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.30 – 7.21 (m, 2H), 7.20 – 7.14 (m, 1H), 5.37 – 5.25 (m, 1H), 3.67 – 3.52 (m, 2H), 2.23 – 2.07 (m, 1H), 2.10 – 1.96 (m, 1H), 0.86 (s, 9H), -0.00 (s, 3H), -0.01 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.8, 150.3, 148.1, 142.1, 137.3, 128.6, 127.2, 126.7, 126.1, 122.4, 60.4, 51.9, 38.6, 26.1, 18.5, -5.30, -5.32.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{21}H_{31}N_2O_2Si$ 371.2155; found: 371.2155.

FT-IR (thin film, cm^{-1}) υ 3379, 2952, 2928, 2856, 1682, 1519, 1257, 1093.

(*S*)-*N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (*S*-1a)

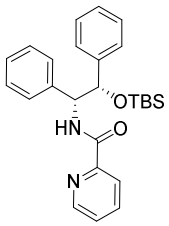


Synthesized according to Scheme S5. Step 1: (*S*)-2-Amino-2-phenylethanol (1.00 g, 7.29 mmol, 1 equiv), picolinic acid (942 mg, 7.65 mmol, 1.05 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluoro-phosphate (5.53 g, 14.58 mmol, 2 equiv), DMF (20 mL), pyridine (1.18 mL, 14.58 mmol, 2 equiv). Reaction mixture was filtered through short silicagel column.

Step 2: Reaction mixture from previous step, imidazole (645 mg, 9.48 mmol, 1.3 equiv), TBSCl (1.43 g, 9.48 mmol, 1.3 equiv), DMF (25 mL). After column chromatography (petroleum ether/EtOAc 6:1) 1.87 g (72%) of product was obtained as a colorless oil. R_f = 0.34 (petroleum ether/EtOAc 4:1). *ee* = 99.9% (see attached HPLC data). The NMR data matched to racemate.

$[\alpha]_D^{20}$ -27.2 (*c* = 0.993, $CHCl_3$).

***N*-((*1R,2S*)-2-((*tert*-butyldimethylsilyl)oxy)-1,2-diphenylethyl)picolinamide (1r)**



Synthesized according to Scheme S5. Step 1: (*1R,2S*)-(-)-2-Amino-1,2-diphenylethanol (800 mg, 3.75 mmol, 1 equiv), picolinic acid (462 mg, 3.75 mmol, 1.0 equiv), *N,N,N′,N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluoro-phosphate (2.85 g, 7.50 mmol, 2 equiv), DMF (10 mL), pyridine (0.9 mL, 11.25 mmol, 3 equiv). Reaction mixture was filtered through short silicagel column.

Step 2: Reaction mixture from previous step, imidazole (332 mg, 4.88 mmol, 1.3 equiv), TBSCl (735 mg, 4.88 mmol, 1.3 equiv), DMF (15 mL), 16 h at room temperature and additional 12 h at 60 °C. After column chromatography (petroleum ether/EtOAc 6:1) 726 mg (45%) of product was obtained as a colorless oil. R_f = 0.43 (petroleum ether/EtOAc 4:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 9.01 (d, *J* = 8.9 Hz, 1H), 8.58 (ddd, *J* = 4.7, 1.6, 0.9 Hz, 1H), 8.16 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.82 (td, *J* = 7.7, 1.7 Hz, 1H), 7.42 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 7.22 – 7.14 (m, 6H), 7.14 – 7.08 (m, 2H), 7.08 – 7.00 (m, 2H), 5.27 (dd, *J* = 9.1, 3.9 Hz, 1H), 5.20 (d, *J* = 3.9 Hz, 1H), 0.95 (s, 9H), 0.03 (s, 3H), -0.21 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 163.4, 150.1, 148.2, 141.0, 137.6, 137.4, 128.8, 127.8, 127.7, 127.5, 127.4, 126.8, 126.2, 122.3, 77.4, 59.8, 26.0, 18.3, -4.6, -5.2.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+Na]^+$: $C_{26}H_{32}N_2O_2SiNa$ 455.2131; found: 455.2129.

FT-IR (thin film, cm^{-1}) υ 3402, 2955, 2928, 2857, 1683, 1514, 1257, 1097.

2. Cobalt-catalyzed C(sp^2)-H carbonylation

Reactions were heated using Chemglass aluminium reaction blocks.

2.1. Optimization of cobalt-catalyzed C(sp^2)-H carbonylation

Under the cobalt catalyzed carbonylation conditions reported for benzylamines[3] carbonylation of phenylglycinol derivative **1a** gave 13% of product **2a**.

Conditions: *N*-(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (35.6 mg, 0.1 mmol), $Co(OAc)_2 \cdot 4\ H_2O$ (5 mg, 0.02 mmol, 20 mol%), Ag_2CO_3 (55 mg, 2 equiv), PivOH (10 mg, 0.1 mmol, 1 equiv), DEAD (31 μL, 0.2 mmol, 2 equiv), CF_3CH_2OH (1 mL), air, 24h at 120 °C.

2.1.1. Oxidant

General procedure for oxidant optimization experiments.

A 4 mL vial with a screw cap (PTFE/Liner) was charged with *N*-(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (35.6 mg, 0.1 mmol), oxidant (0.2 mmol, 2 equiv), NaOPiv (24.8 mg, 0.2 mmol, 2 equiv), $Co(dpm)_2$ (8.6 mg, 0.02 mmol, 20 mol%), DEAD (31 μL, 0.2 mmol, 2 equiv), and DCE (1.0 mL). Resulting mixture was heated at 100 °C for 16 h, cooled to room temperature and analyzed by TLC (hexanes/EtOAc 2:1). To reaction mixture Ph_3CH (24.4 mg, 0.1 mmol, 1 equiv) was added, mixture was diluted with dist. H_2O (1.5 mL) and extracted with EtOAc (3 x 1.5 mL). Combined organic phase was separated, dried over anh. Na_2SO_4, filtered, evaporated. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR spectroscopy.

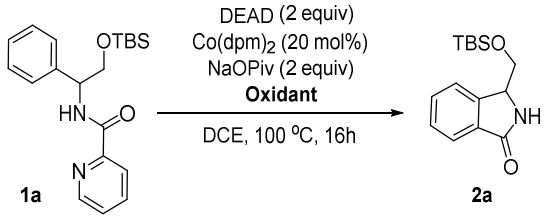


Table S1

Entry	Oxidant	Substrate : Product ratio	NMR yield, %[a]
1	$Mn(OAc)_3 \cdot 2H_2O$	4:1	20
2	AgOAc	19:1	<5%
3	**Ag_2CO_3**	**1.1:1**	**45**
4	w/o oxidant (air)	5.7:1	15

[a] NMR yield using triphenylmethane as an internal standard.

2.1.2. Additive

General procedure for additive optimization experiments.

A 4 mL vial with a screw cap (PTFE/Liner) was charged with *N*-(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (35.6 mg, 0.1 mmol), Ag_2CO_3 (55 mg, 2 equiv), additive (0.05 - 0.2 mmol, 0.5 - 2 equiv), $Co(dpm)_2$ (8.6 mg, 0.02 mmol, 20 mol%), DEAD (31 μL, 0.2 mmol, 2 equiv), and DCE (1.0 mL). Vial was heated at 100 °C for 16 h, cooled to room temperature and analyzed by TLC (hexanes/EtOAc 2:1). To reaction mixture Ph_3CH (24.4 mg, 0.1 mmol, 1 equiv) was added, mixture was diluted with dist. H_2O (1.5 mL) and extracted with EtOAc (3 x 1.5 mL). Combined organic phase was separated, dried over anh. Na_2SO_4, filtered, evaporated. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR spectroscopy.

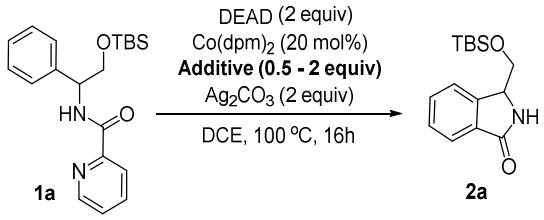


Table S2

Entry	Additive (equiv)	Substrate : Product ratio	NMR yield, %[a]
1	NaOPiv (2)	1.1:1	45
2	NaOAc (2)	1.7:1	35
3	NH_4OPiv (2)	1:1.5	60
4	AcOH (2)	4.3:1	15
5	PivOH (2)	1:3	75
6[b]	**PivOH (1)**	**1:49**	**98**
7[b]	PivOH (0.5)	1:2.7	65
8	w/o additive	1:4.7	62

[a] NMR yield using triphenylmethane as an internal standard. [b] DIAD used as "CO" surrogate.

2.1.3. Solvent

General procedure for solvent optimization experiments.

A 4 mL vial with a screw cap (PTFE/Liner) was charged with *N*-(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (35.6 mg, 0.1 mmol), Ag_2CO_3 (55 mg, 2 equiv), PivOH (10 mg, 0.1 mmol, 1 equiv), $Co(dpm)_2$ (8.6 mg, 0.02 mmol, 20 mol%), DIAD (40 μL, 0.2 mmol, 2 equiv), and solvent (1.0 mL). Vial was heated at 100 °C for 16 h, cooled to room temperature and analyzed by TLC (hexanes/EtOAc 4:1). To reaction mixture Ph_3CH (24.4 mg, 0.1 mmol, 1 equiv) was added,

mixture was diluted with dist. H_2O (1.5 mL) and extracted with EtOAc (3 x 1.5 mL). Combined organic phase was separated, dried over anh. Na_2SO_4, filtered, evaporated. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR spectroscopy.

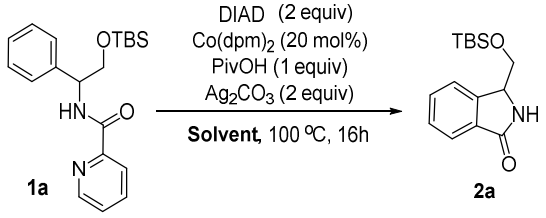


Table S3

Entry	Solvent	Substrate : Product ratio	NMR yield, %[a]
1	**DCE**	**1:49**	**98**
2	Toluene	1.6:1	25
3	CF_3CH_2OH	>19:1	<5%
4	1,4-Dioxane	4:1	11

[a] NMR yield using triphenylmethane as an internal standard.

2.1.4. Catalyst

General procedure for catalyst optimization experiments.

A 4 mL vial with a screw cap (PTFE/Liner) was charged with *N*-(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (35.6 mg, 0.1 mmol), Ag_2CO_3 (55 mg, 2 equiv), PivOH (10 mg, 0.1 mmol, 1 equiv), cobalt catalyst (0.02 mmol, 20 mol%), DIAD (40 μL, 0.2 mmol, 2 equiv), and solvent (1.0 mL). Vial was heated at 100 °C for 16 h, cooled to room temperature and analyzed by TLC (hexanes/EtOAc 4:1). To reaction mixture Ph_3CH (24.4 mg, 0.1 mmol, 1 equiv) was added, mixture was diluted with dist. H_2O (1.5 mL) and extracted with EtOAc (3 x 1.5 mL). Combined organic phase was separated, dried over anh. Na_2SO_4, filtered, evaporated. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR spectroscopy.

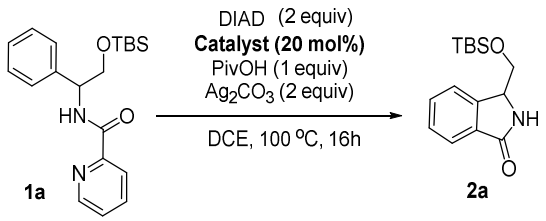


Table S4

Entry	Catalyst	Substrate : Product ratio	NMR yield, %[a]
1	**$Co(dpm)_2$**	**1:49**	**98**
2	$Co(OAc)_2 \cdot 4H_2O$	3.5:1	18
3	$Co(acac)_2$	7.2:1	11
4	$Co(acac)_3$	3.9:1	15
5	w/o catalyst	>99:0	0

[a] NMR yield using triphenylmethane as an internal standard.

Note! Bis(2,2,6,6-tetramethyl-3,5-heptanedionato)cobalt(II) ($Co(dpm)_2$) can be used commercial (Alfa Aesar, CAS: 13986-53-3) or self-made (by procedure written below).

Bis(2,2,6,6-tetramethyl-3,5-heptanedionato)cobalt(II)

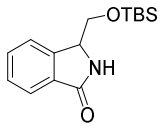
$Co(NO_3)_2 \cdot 6\ H_2O$ (1.61 g, 5.53 mmol, 1 equiv) and 2,2,6,6-tetramethyl-3,5-heptanedione (2.36 mL, 11.29 mmol, 2.04 equiv) were dissolved in MeOH (15 mL), then 2 M $NaOH_{aq}$ (443 mg, 11.07 mmol, 15 mL dist. H_2O) was added dropwise (formation of pink precipitate) and the resulting mixture was heated at 80 °C for 2 h. Mixture was cooled to room temperature, the pink precipitate was filtered off. Then precipitate was dissolved in Et_2O (10 mL), filtered, filtrate was evaporated and dried under reduced pressure to give 1.5 g (64%) of bis(2,2,6,6-tetramethyl-3,5-heptanedionato)cobalt(II) as a pink powder, mp 142-144 °C (Et_2O).

2.2. Cobalt-catalyzed C(sp^2)-H carbonylation and characterization of products

General procedure for cobalt-catalyzed C(sp^2)-H carbonylation.

A 30 mL vial equipped with a magnetic stir bar was charged with picolinamide (0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL). The reaction mixture was heated at 100 °C for indicated time (24 – 48 h). Reaction was monitored by TLC after 24 h to determine the completion time. The reaction mixture was cooled to room temperature. To the reaction mixture silica gel was added and solvent was evaporated. Product was purified by column chromatography on silica gel using appropriate eluent. After purification product was dried under reduced pressure.

3-(((*Tert*-butyldimethylsilyl)oxy)methyl)isoindolin-1-one (2a)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (178 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 116 mg (84%) of a colorless oil that slowly solidifies was obtained. R_f = 0.62 (petroleum ether/EtOAc 1:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.85 (d, *J* = 7.4 Hz, 1H), 7.59 – 7.52 (m, 1H), 7.52 – 7.40 (m, 2H), 6.92 (s, 1H), 4.68 (dd, *J* = 8.2, 5.0 Hz, 1H), 3.96 (dd, *J* = 9.9, 5.0 Hz, 1H), 3.54 (dd, *J* = 9.8, 8.4 Hz, 1H), 0.90 (s, 9H), 0.07 (d, *J* = 5.1 Hz, 6H).

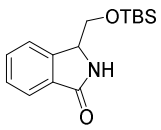
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.8, 144.3, 132.5, 131.8, 128.7, 124.1, 123.1, 66.2, 58.8, 25.9, 18.4, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}H_{24}NO_2Si$ 278.1576; found: 278.1581.

FT-IR (thin film, cm^{-1}) υ 3223, 2928, 2857, 1704, 1700, 1472, 1257, 1118.

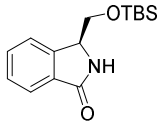
Procedure for 1 mmol scale synthesis

Synthesis of 3-(((*Tert*-butyldimethylsilyl)oxy)methyl)isoindolin-1-one (2a)



A 100 mL pressure tube equipped with a magnetic stir bar was charged with *N*-(2-((*tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (356 mg, 1.0 mmol), DIAD (0.4 mL, 2.0 mmol, 2 equiv), $Co(dpm)_2$ (85 mg, 0.20 mmol, 20 mol%), PivOH (100 mg, 1.0 mmol, 1 equiv), Ag_2CO_3 (550 mg, 2.0 mmol, 2 equiv), and DCE (10 mL). The reaction mixture was heated at 100 °C (oil bath) for 40h. The reaction mixture was cooled to room temperature. To the reaction mixture silica gel was added and solvent was evaporated. After column chromatography on silica gel (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 243 mg (88%) of a colorless oil that slowly solidifies was obtained.

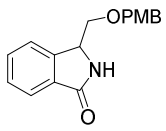
(*S*)-3-(((*Tert*-butyldimethylsilyl)oxy)methyl)isoindolin-1-one (*S*)-2a



(*S*)-*N*-(2-((*Tert*-butyldimethylsilyl)oxy)-1-phenylethyl)picolinamide (35.6 mg, 0.1 mmol), DIAD (40 μL, 0.2 mmol, 2 equiv), $Co(dpm)_2$ (8.5 mg, 0.02 mmol, 20 mol%), PivOH (10 mg, 0.1 mmol, 1 equiv), Ag_2CO_3 (55 mg, 0.2 mmol, 2 equiv), and DCE (1 mL), 24 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 25 mg (90%) of a colorless oil that slowly solidifies was obtained. R_f = 0.62 (petroleum ether/EtOAc 1:1). *ee* = > 99.9 % (see attached HPLC data). The NMR data matched to racemate.

$[\alpha]_D^{20}$ 33.6 (*c* = 1.000, $CHCl_3$).

3-(((4-Methoxybenzyl)oxy)methyl)isoindolin-1-one (2c)



N-(2-((4-Methoxybenzyl)oxy)-1-phenylethyl)picolinamide (181 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 51 mg (36%) of a colorless oil that slowly solidifies was obtained. R_f = 0.51 (EtOAc).

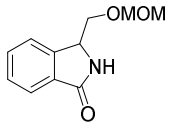
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.86 (d, *J* = 7.4 Hz, 1H), 7.54 (td, *J* = 7.4, 1.1 Hz, 1H), 7.51 – 7.42 (m, 2H), 7.29 (s, 1H), 7.28 – 7.24 (m, 2H), 6.93 – 6.81 (m, 2H), 4.78 (dd, *J* = 8.5, 4.6 Hz, 1H), 4.51 (s, 2H), 3.86 – 3.76 (m, 4H), 3.37 (t, *J* = 8.9 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.9, 159.5, 144.2, 132.4, 131.9, 129.6, 128.7, 124.1, 123.0, 114.0, 73.4, 72.6, 56.8, 55.4.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{17}H_{18}NO_3$ 284.1287; found: 284.1298.

FT-IR (thin film, cm^{-1}) υ 3228, 2934, 2861, 1699, 1694, 1613, 1514, 1250.

3-((Methoxymethoxy)methyl)isoindolin-1-one (2d)



N-(2-(Methoxymethoxy)-1-phenylethyl)picolinamide (143 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 59 mg (61%) of a colorless oil that slowly solidifies was obtained. R_f = 0.22 (EtOAc).

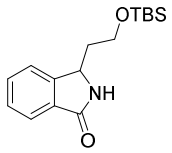
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.90 – 7.82 (m, 1H), 7.58 – 7.53 (m, 1H), 7.51 – 7.46 (m, 2H), 7.31 (s, 1H), 4.78 (dd, *J* = 8.4, 4.4 Hz, 1H), 4.71 – 4.64 (m, 2H), 3.97 (dd, *J* = 10.0, 4.4 Hz, 1H), 3.47 (dd, *J* = 10.0, 8.5 Hz, 1H), 3.37 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.9, 144.0, 132.5, 132.0, 128.8, 124.1, 122.9, 97.0, 70.8, 56.9, 55.7.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{11}H_{14}NO_3$ 208.0974; found: 208.0974.

FT-IR (thin film, cm^{-1}) υ 3238, 2932, 1709, 1470, 1152, 1115, 1037.

3-(2-((*Tert*-butyldimethylsilyl)oxy)ethyl)isoindolin-1-one (2e)



N-(3-((*Tert*-butyldimethylsilyl)oxy)-1-phenylpropyl)picolinamide (185 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 132 mg (91%) of a colorless oil that slowly solidifies was obtained. R_f = 0.53 (petroleum ether/EtOAc 1:1).

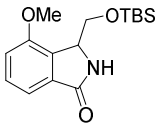
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ δ 7.89 – 7.81 (m, 1H), 7.56 (td, *J* = 7.5, 1.2 Hz, 1H), 7.51 – 7.38 (m, 2H), 6.59 (s, 1H), 4.70 (dd, *J* = 9.9, 2.9 Hz, 1H), 3.95 – 3.84 (m, 2H), 2.23 – 2.15 (m, 1H), 1.74 – 1.65 (m, 1H), 0.94 (s, 9H), 0.11 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.4, 147.9, 132.0, 131.9, 128.3, 124.0, 122.5, 61.6, 55.8, 37.6, 26.1, 18.4, -5.2, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{26}NO_2Si$ 292.1733; found: 292.1740.

FT-IR (thin film, cm^{-1}) υ 3214, 2928, 2856, 1694, 1471, 1257, 1107.

4-Methoxy-3-(((*tert*-butyldimethylsilyl)oxy)methyl)isoindolin-1-one (2f)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(2-methoxyphenyl)ethyl)picolinamide (193 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 101 mg (66%) of a colorless oil that slowly solidifies was obtained. R_f = 0.67 (petroleum ether/EtOAc 1:1).

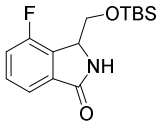
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.45 – 7.40 (m, 2H), 7.03 – 6.98 (m, 1H), 6.63 (s, 1H), 4.71 (dd, *J* = 8.8, 3.6 Hz, 1H), 4.38 (dd, *J* = 9.9, 3.3 Hz, 1H), 3.89 (s, 3H), 3.35 – 3.27 (m, 1H), 0.88 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.4, 155.2, 134.5, 131.1, 130.3, 116.1, 113.3, 64.7, 58.1, 55.6, 26.0, 18.3, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{26}NO_3Si$ 308.1682; found: 308.1685.

FT-IR (thin film, cm^{-1}) υ 3196, 2924, 2857, 1696, 1604, 1276, 1091.

4-Fluoro-3-(((*tert*-butyldimethylsilyl)oxy)methyl)isoindolin-1-one (2g)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(2-fluorophenyl)ethyl)picolinamide (187 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv),

and DCE (5 mL), 24 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 126 mg (85%) of a colorless oil that slowly solidifies was obtained. Rf = 0.62 (petroleum ether/EtOAc 1:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.66 (d, *J* = 7.5 Hz, 1H), 7.48 (td, *J* = 8.0, 4.8 Hz, 1H), 7.26 – 7.20 (m, 1H), 6.56 (s, 1H), 4.82 (dd, *J* = 9.0, 3.3 Hz, 1H), 4.28 (ddd, *J* = 10.0, 3.4, 1.5 Hz, 1H), 3.44 (dd, *J* = 9.8, 9.1 Hz, 1H), 0.89 (s, 9H), 0.07 (d, *J* = 13.0 Hz, 6H).

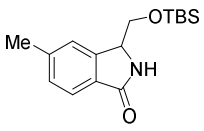
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 169.3, 158.0 (d, J_{C-F} = 250.7 Hz), 135.9 (d, J_{C-F} = 4.8 Hz), 130.9 (d, J_{C-F} = 6.5 Hz), 129.3 (d, J_{C-F} = 17.6 Hz), 120.1 (d, J_{C-F} = 3.7 Hz), 118.8 (d, J_{C-F} = 20.0 Hz), 64.8, 57.2 (d, J_{C-F} = 2.4 Hz), 25.9, 18.3, -5.3, -5.4.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -119.46.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}H_{23}NO_2SiF$ 296.1482; found: 296.1487.

FT-IR (thin film, cm^{-1}) υ 3196, 2929, 2858, 1706, 1695, 1243, 1125.

5-Methyl-3-(((*tert*-butyldimethylsilyl)oxy)methyl)isoindolin-1-one (2h)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(3-methylphenyl)ethyl)picolinamide (185 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 30 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 104 mg (71%) of a colorless oil that slowly solidifies was obtained. R_f = 0.51 (petroleum ether/EtOAc 1:1).

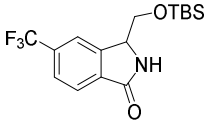
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.26 (s, 1H), 6.67 (s, 1H), 4.63 (dd, *J* = 8.6, 4.8 Hz, 1H), 3.96 (dd, *J* = 9.8, 4.8 Hz, 1H), 3.49 (dd, *J* = 9.8, 8.7 Hz, 1H), 2.45 (s, 3H), 0.91 (s, 9H), 0.07 (d, *J* = 4.9 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.8, 144.6, 142.6, 129.9, 129.7, 123.9, 123.5, 66.4, 58.6, 26.0, 22.0, 18.4, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{26}NO_2Si$ 292.1733; found: 292.1739.

FT-IR (thin film, cm^{-1}) υ 3216, 2927, 2856, 1702, 1622, 1361, 1254, 1107.

5-Trifluoromethyl-3-(((*tert*-butyldimethylsilyl)oxy)methyl)isoindolin-1-one (2i)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(3-trifluoromethylphenyl)ethyl)picolinamide (212 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg,

1.0 mmol, 2 equiv), and DCE (5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 140 mg (81%) of a colorless oil that slowly solidifies was obtained. R_f = 0.63 (petroleum ether/EtOAc 1:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.97 (d, *J* = 7.7 Hz, 1H), 7.82 – 7.73 (m, 2H), 6.87 (s, 1H), 4.79 – 4.71 (m, 1H), 3.91 (dd, *J* = 9.8, 5.5 Hz, 1H), 3.66 (dd, *J* = 9.8, 7.8 Hz, 1H), 0.90 (s, 9H), 0.07 (d, *J* = 4.5 Hz, 6H).

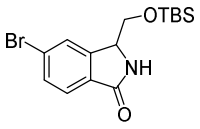
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 169.6, 145.2, 135.7, 133.8 (q, J_{C-F} = 32.4 Hz), 126.0 (q, J_{C-F} = 3.6 Hz), 124.6, 123.9 (q, J_{C-F} = 272.9 Hz), 120.7 (q, J_{C-F} = 3.8 Hz), 65.6, 58.6, 25.9, 18.3, -5.4.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -62.44.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{23}NO_2SiF_3$ 346.1450; found: 346.1467.

FT-IR (thin film, cm^{-1}) υ 3093, 2932, 2859, 1699, 1695, 1329, 1168, 1128.

5-Bromo-3-(((*tert*-butyldimethylsilyl)oxy)methyl)isoindolin-1-one (2j)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(3-bromophenyl)ethyl)picolinamide (218 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 24 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 160 mg (90%) of a colorless oil that slowly solidifies was obtained. R_f = 0.60 (petroleum ether/EtOAc 1:1).

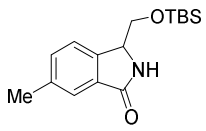
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.76 – 7.63 (m, 2H), 7.61 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.25 (s, 1H), 4.73 – 4.58 (m, 1H), 3.85 (dd, *J* = 9.8, 5.6 Hz, 1H), 3.63 (dd, *J* = 9.8, 7.8 Hz, 1H), 0.89 (s, 9H), 0.06 (d, *J* = 3.1 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.1, 146.4, 132.1, 131.4, 126.7, 126.6, 125.4, 65.8, 58.3, 25.9, 18.3, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}H_{23}NO_2SiBr$ 356.0681; found: 356.0691.

FT-IR (thin film, cm^{-1}) υ 3212, 3091, 2930, 2857, 1718, 1683, 1257, 1115.

3-(((*Tert*-butyldimethylsilyl)oxy)methyl)-6-methylisoindolin-1-one (2k)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-methylphenyl)ethyl)picolinamide (185 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 24 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 112 mg (77%) of a colorless oil that slowly solidifies was obtained. R_f = 0.58 (petroleum ether/EtOAc 1:1).

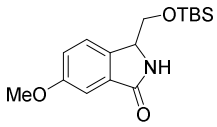
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.66 (s, 1H), 7.39 – 7.29 (m, 2H), 6.57 (s, 1H), 4.63 (dd, *J* = 8.6, 4.7 Hz, 1H), 3.96 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.46 (dd, *J* = 9.8, 8.8 Hz, 1H), 2.44 (s, 3H), 0.91 (s, 9H), 0.07 (d, *J* = 5.5 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.8, 141.3, 138.9, 132.9, 132.6, 124.4, 122.7, 66.5, 58.6, 26.0, 21.5, 18.4, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{26}NO_2Si$ 292.1733; found: 292.1739.

FT-IR (thin film, cm^{-1}) υ 3218, 2928, 2857, 1717, 1257, 1113.

3-(((*Tert*-butyldimethylsilyl)oxy)methyl)-6-methoxyisoindolin-1-one (2l)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-methoxyphenyl)ethyl)picolinamide (193 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 24 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 148 mg (96%) of a colorless oil that slowly solidifies was obtained. R_f = 0.42 (petroleum ether/EtOAc 1:1).

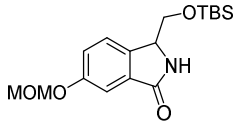
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.38 – 7.31 (m, 2H), 7.11 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.69 (s, 1H), 4.61 (dd, *J* = 8.5, 4.8 Hz, 1H), 3.94 (dd, *J* = 9.9, 4.9 Hz, 1H), 3.86 (s, 3H), 3.47 (dd, *J* = 9.8, 8.6 Hz, 1H), 0.91 (s, 9H), 0.07 (d, *J* = 5.0 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.7, 160.6, 136.4, 133.8, 123.9, 120.3, 106.8, 66.5, 58.4, 55.8, 26.0, 18.4, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{26}NO_3Si$ 308.1682; found: 308.1687.

FT-IR (thin film, cm^{-1}) υ 3222, 2929, 2856, 1717, 1495, 1253, 1111.

3-(((*Tert*-butyldimethylsilyl)oxy)methyl)-6-(methoxymethoxy)isoindolin-1-one (2m)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-methoxymethoxyphenyl)ethyl)picolinamide (208 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 48 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 121 mg (72%) of a colorless oil that slowly solidifies was obtained. R_f = 0.46 (petroleum ether/EtOAc 1:1).

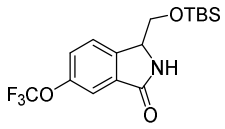
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.52 (d, *J* = 2.2 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.22 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.47 (s, 1H), 5.21 (s, 2H), 4.62 (dd, *J* = 8.8, 4.7 Hz, 1H), 3.96 (dd, *J* = 9.8, 4.7 Hz, 1H), 3.48 (s, 3H), 3.44 (dd, *J* = 9.8, 8.8 Hz, 1H), 0.92 (s, 9H), 0.08 (d, *J* = 5.5 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.6, 158.0, 137.6, 133.8, 124.0, 121.1, 110.8, 94.8, 66.3, 58.4, 56.2, 25.9, 18.4, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{17}H_{28}NO_4Si$ 338.1788; found: 338.1795.

FT-IR (thin film, cm^{-1}) υ 3212, 2928, 2857, 1704, 1490, 1246, 1116, 1067, 1006.

3-(((*Tert*-butyldimethylsilyl)oxy)methyl)-6-trifluoromethoxyisoindolin-1-one (2n)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-trifluoromethoxyphenyl)ethyl)picolinamide (220 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 48 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 135 mg (75%) of a colorless oil that slowly solidifies was obtained. R_f = 0.72 (petroleum ether/EtOAc 1:1).

^{1}H-NMR (400 MHz, $C_2D_2Cl_4$, ppm) δ 7.70 (s, 1H), 7.53 (d, *J* = 8.3 Hz, 1H), 7.42 (dd, *J* = 8.1, 1.8 Hz, 1H), 6.56 (s, 1H), 4.69 (dd, *J* = 8.1, 4.9 Hz, 1H), 3.95 (dd, *J* = 9.9, 4.9 Hz, 1H), 3.54 (dd, *J* = 9.8, 8.3 Hz, 1H), 0.90 (s, 9H), 0.08 (d, *J* = 5.7 Hz, 6H).

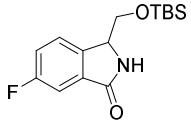
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 169.4, 149.8 (q, J_{C-F} = 1.8 Hz), 142.6, 134.4, 124.9, 124.7, 120.5 (q, J_{C-F} = 258.1 Hz), 116.6, 65.8, 58.5, 25.9, 18.3, -5.3.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -58.06.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{16}H_{23}NO_3SiF_3$ 362.1399; found: 362.1404.

FT-IR (thin film, cm^{-1}) υ 3218, 2929, 2859, 1695, 1251, 1218, 1167, 1112.

3-(((*Tert*-butyldimethylsilyl)oxy)methyl)-6-fluoroisoindolin-1-one (2o)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-fluorophenyl)ethyl)picolinamide (187 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 24 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 139 mg (94%) of a colorless oil that slowly solidifies was obtained. R_f = 0.63 (petroleum ether/EtOAc 1:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.51 (dd, *J* = 7.6, 2.4 Hz, 1H), 7.44 (dd, *J* = 8.3, 4.5 Hz, 1H), 7.25 (td, *J* = 8.7, 2.5 Hz, 1H), 6.86 (s, 1H), 4.65 (dd, *J* = 7.5, 5.2 Hz, 1H), 3.91 (dd, *J* = 9.8, 5.1 Hz, 1H), 3.54 (dd, *J* = 9.8, 8.2 Hz, 1H), 0.90 (s, 9H), 0.07 (d, *J* = 4.2 Hz, 6H).

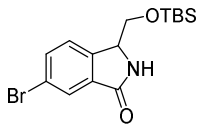
^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 169.6, 163.3 (d, J_{C-F} = 247.9 Hz), 139.8 (d, J_{C-F} = 2.3 Hz), 134.6 (d, J_{C-F} = 8.5 Hz), 124.6 (d, J_{C-F} = 8.3 Hz), 119.4 (d, J_{C-F} = 23.6 Hz), 110.9 (d, J_{C-F} = 23.4 Hz), 66.1, 58.4, 25.9, 18.4, -5.3.

^{19}F-NMR (376 MHz, $CDCl_3$, ppm) δ -112.39.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}H_{23}NO_2SiF$ 296.1482; found: 296.1485.

FT-IR (thin film, cm^{-1}) υ 3212, 2930, 2858, 1724, 1488, 1263, 1112.

3-(((*Tert*-butyldimethylsilyl)oxy)methyl)-6-bromoisoindolin-1-one (2p)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(4-bromophenyl)ethyl)picolinamide (218 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 163 mg (91%) of a colorless oil that slowly solidifies was obtained. R_f = 0.55 (petroleum ether/EtOAc 1:1).

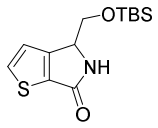
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.98 (d, *J* = 1.7 Hz, 1H), 7.67 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 6.76 (s, 1H), 4.63 (dd, *J* = 8.1, 5.2 Hz, 1H), 3.90 (dd, *J* = 9.8, 5.2 Hz, 1H), 3.55 (dd, *J* = 9.8, 8.1 Hz, 1H), 0.90 (s, 9H), 0.07 (d, *J* = 3.7 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 169.1, 143.0, 134.9, 134.5, 127.4, 124.7, 122.9, 65.9, 58.5, 25.9, 18.4, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{15}H_{23}NO_2SiBr$ 356.0681; found: 356.0689.

FT-IR (thin film, cm^{-1}) υ 3195, 2928, 2859, 1722, 1681, 1258, 1111.

4-(((*Tert*-butyldimethylsilyl)oxy)methyl)-4,5-dihydro-6H-thieno[2,3-c]pyrrol-6-one (2q)



N-(2-((*Tert*-butyldimethylsilyl)oxy)-1-(thiophen-3-yl)ethyl)picolinamide (181 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (42.5 mg, 0.10 mmol, 20 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 73 mg (52%) of a colorless oil that slowly solidifies was isolated as major regioisomer. R_f = 0.56 (petroleum ether/EtOAc 1:1).

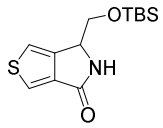
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.66 (dd, *J* = 4.8, 1.0 Hz, 1H), 7.04 (d, *J* = 4.8 Hz, 1H), 6.33 (s, 1H), 4.61 (ddd, *J* = 8.4, 5.2, 0.9 Hz, 1H), 3.89 (dd, *J* = 9.8, 5.3 Hz, 1H), 3.55 (dd, *J* = 9.7, 8.4 Hz, 1H), 0.91 (s, 9H), 0.08 (d, *J* = 2.7 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 166.4, 155.0, 135.7, 121.1, 116.3, 65.6, 58.1, 26.0, 18.4, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{13}H_{22}NO_2SiS$ 284.1141; found: 284.1142.

FT-IR (thin film, cm^{-1}) υ 3086, 2928, 2857, 1700, 1258, 1111.

6-(((*Tert*-butyldimethylsilyl)oxy)methyl)-5,6-dihydro-4H-thieno[3,4-c]pyrrol-4-one (2q')



After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 21 mg (15%) of a colorless oil that slowly solidifies was isolated as minor regioisomer. R_f = 0.46 (petroleum ether/EtOAc 1:1).

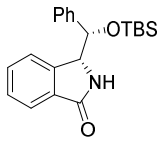
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.75 (d, *J* = 2.3 Hz, 1H), 7.11 (dd, *J* = 2.3, 1.1 Hz, 1H), 6.72 (s, 1H), 4.57 (dd, *J* = 8.2, 5.3 Hz, 1H), 3.83 (dd, *J* = 9.8, 5.3 Hz, 1H), 3.56 (dd, *J* = 9.8, 8.3 Hz, 1H), 0.90 (s, 9H), 0.07 (d, *J* = 2.9 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 165.1, 145.1, 138.2, 122.7, 117.1, 66.2, 56.3, 25.9, 18.4, -5.3.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{13}H_{22}NO_2SiS$ 284.1141; found: 284.1146.

FT-IR (thin film, cm^{-1}) υ 3238, 2928, 2857, 1699, 1257, 1113.

(*R*)-3-((*S*)-((*tert*-butyldimethylsilyl)oxy)(phenyl)methyl)isoindolin-1-one (2r)



N-((*1R*,*2S*)-2-((*tert*-butyldimethylsilyl)oxy)-1,2-diphenylethyl)picolinamide (152 mg, 0.35 mmol), DIAD (0.14 mL, 0.70 mmol, 2 equiv), $Co(dpm)_2$ (45 mg, 0.10 mmol, 30 mol%), PivOH (36 mg, 0.35 mmol, 1 equiv), Ag_2CO_3 (194 mg, 0.70 mmol, 2 equiv), and DCE (3.5 mL), 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 49 mg (40%) of a colorless oil that slowly solidifies was obtained. Isolated as single diastereomer. R_f = 0.55 (petroleum ether/EtOAc 1:1).

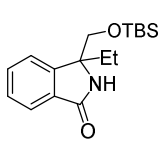
^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.75 (d, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.52 (td, *J* = 7.5, 1.1 Hz, 1H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.32 – 7.20 (m, 5H), 6.09 (s, 1H), 4.72 (d, *J* = 6.7 Hz, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 0.89 (s, 9H), -0.02 (s, 3H), -0.24 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.5, 145.0, 140.6, 132.4, 131.4, 128.6, 128.4, 127.1, 124.6, 123.8, 77.5, 62.9, 26.0, 18.2, -4.4, -4.7.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{21}H_{28}NO_2Si$ 354.1889; found: 354.1896.

FT-IR (thin film, cm^{-1}) υ 2928, 2857, 1703, 1258, 1107.

3-(((*Tert*-butyldimethylsilyl)oxy)methyl)-3-ethylisoindolin-1-one (2s)



N-(1-((*Tert*-butyldimethylsilyl)oxy)-2-phenylbutan-2-yl)picolinamide (192 mg, 0.5 mmol), DIAD (0.2 mL, 1.0 mmol, 2 equiv), $Co(dpm)_2$ (63.8 mg, 0.15 mmol, 30 mol%), PivOH (51 mg, 0.5 mmol, 1 equiv), Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv), and DCE (5 mL), (after 24h additional amount of $Co(dpm)_2$ (63.8 mg, 0.15 mmol, and Ag_2CO_3 (276 mg, 1.0 mmol, 2 equiv) were added) 40 h at 100 °C. After column chromatography (gradient petroleum ether/EtOAc from 6:1 to 4:1, then 2:1), 61 mg (40%) of a colorless oil that slowly solidifies was obtained. R_f = 0.70 (petroleum ether/EtOAc 1:1).

^{1}H-NMR (400 MHz, $CDCl_3$, ppm) δ 7.83 (dt, *J* = 7.4, 0.9 Hz, 1H), 7.54 (td, *J* = 7.5, 1.2 Hz, 1H), 7.46 (td, *J* = 7.5, 1.0 Hz, 1H), 7.36 (dt, *J* = 7.6, 0.9 Hz, 1H), 6.31 (s, 1H), 3.76 (d, *J* = 9.6 Hz, 1H), 3.55 (d, *J* = 9.6 Hz, 1H), 2.15 – 2.05 (m, 1H), 1.95 – 1.86 (m, 1H), 0.89 (s, 9H), 0.67 (t, *J* = 7.4 Hz, 3H), 0.03 (d, *J* = 6.9 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, ppm) δ 170.3, 148.0, 132.6, 131.9, 128.6, 124.1, 122.1, 69.0, 66.3, 27.3, 25.9, 18.4, 7.7, -5.4.

HR-MS (ESI-TOF) m/z: Calcd. for $[M+H]^+$: $C_{17}H_{28}NO_2Si$ 306.1889; found: 306.1892.

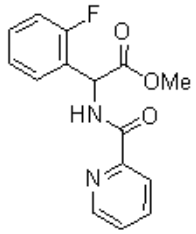
FT-IR (thin film, cm^{-1}) υ 2928, 2857, 1708, 1700, 1475, 1258, 1098.

3. References

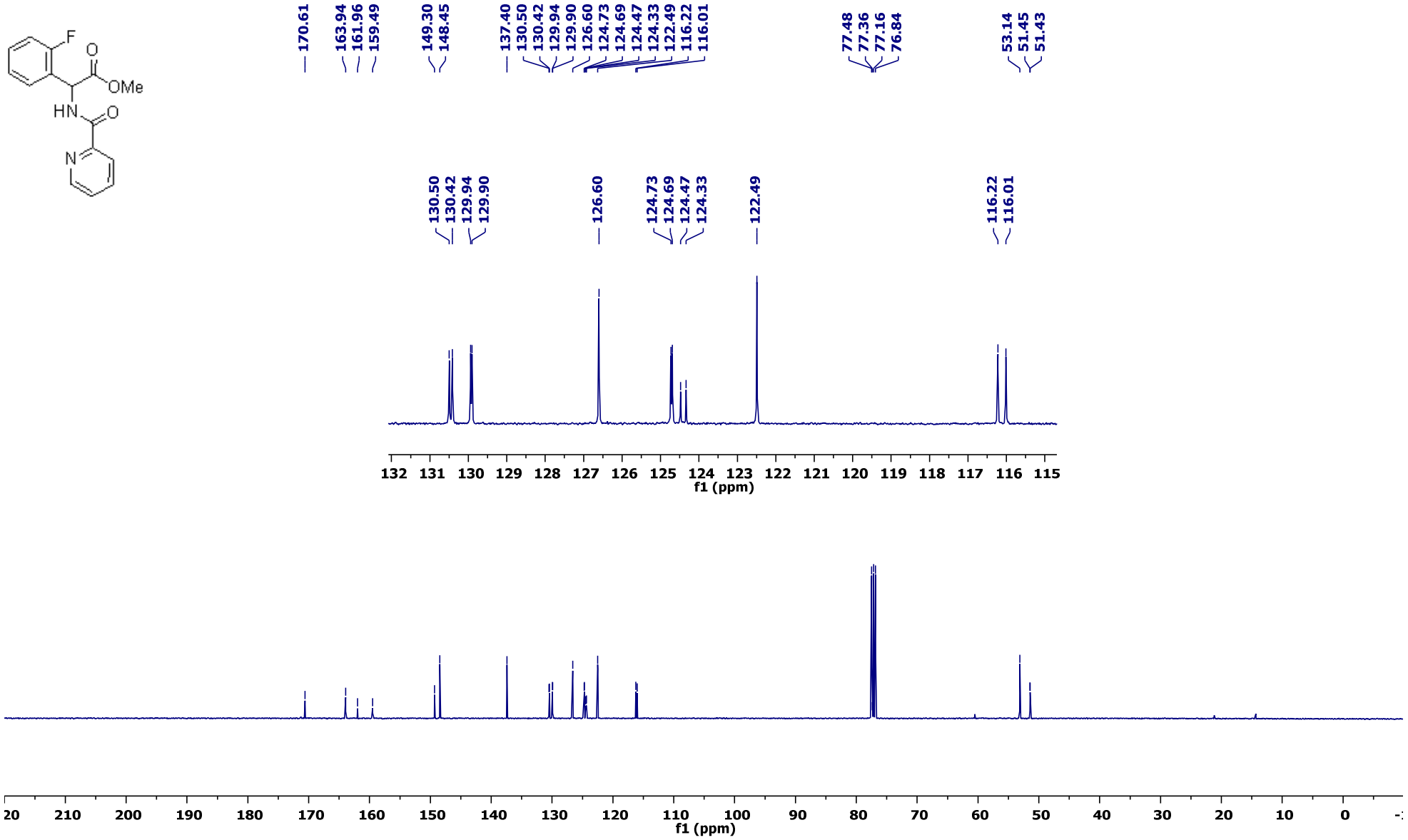
1. Zeng, W.; Nukeyeva, M.; Wang, Q.; Jiang, C. *Org. Biomol. Chem.*, **2018**, *16*, 598.
2. Malkov, A. V.; Gouriou, L.; Lloyd-Jones, G. C.; Starý, I.; Langer, V.; Sapoor, P.; Vinader, V.; Kočovskỳ, P. *Chem. Eur. J.* **2006**, *12*, 6910.
3. Ling, F.; Ai, C.; Lv, Y.; Zhong, W. *Adv. Synth. Catal.* **2017**, *359*, 3707-3712.

4. NMR spectra

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



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



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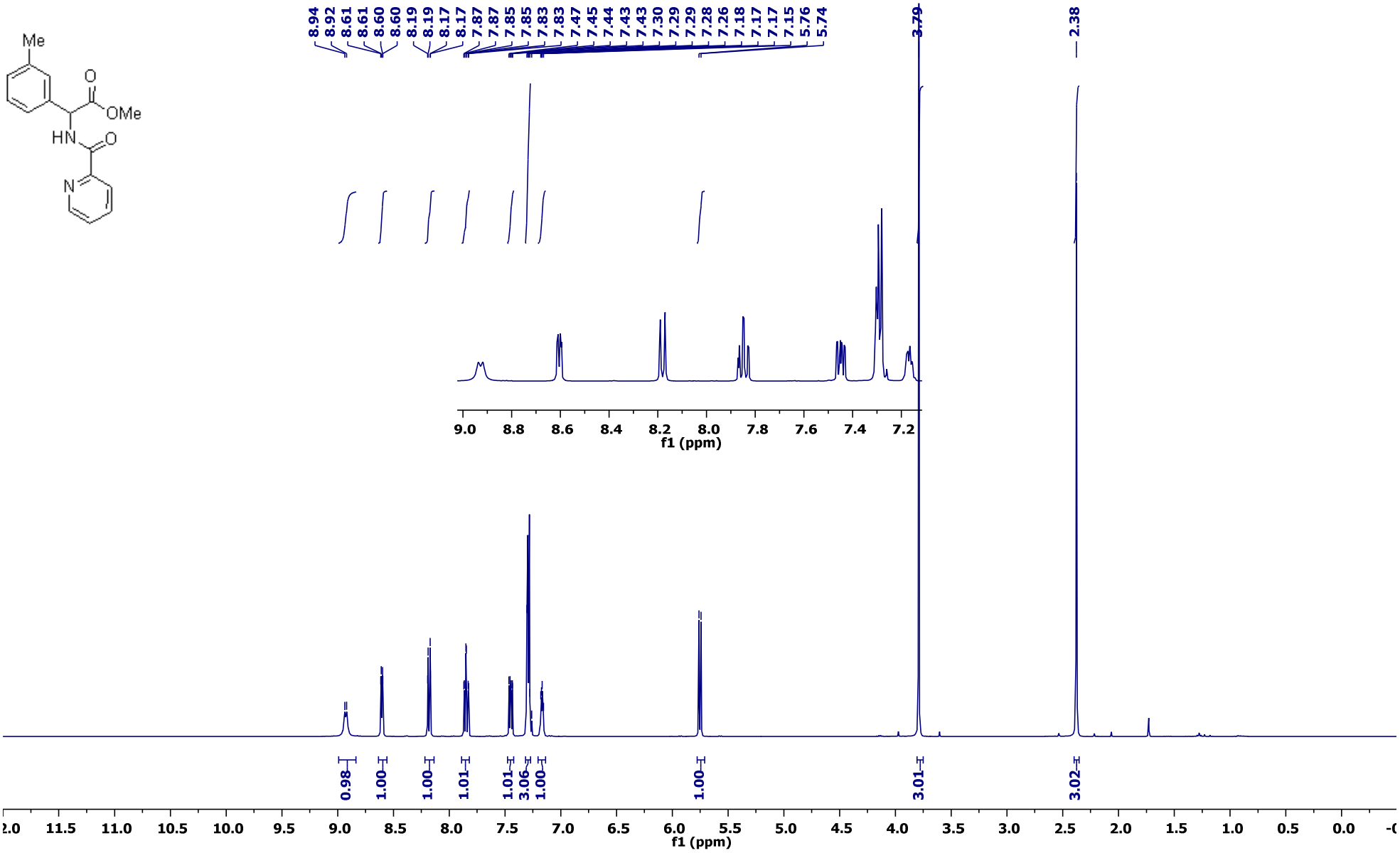

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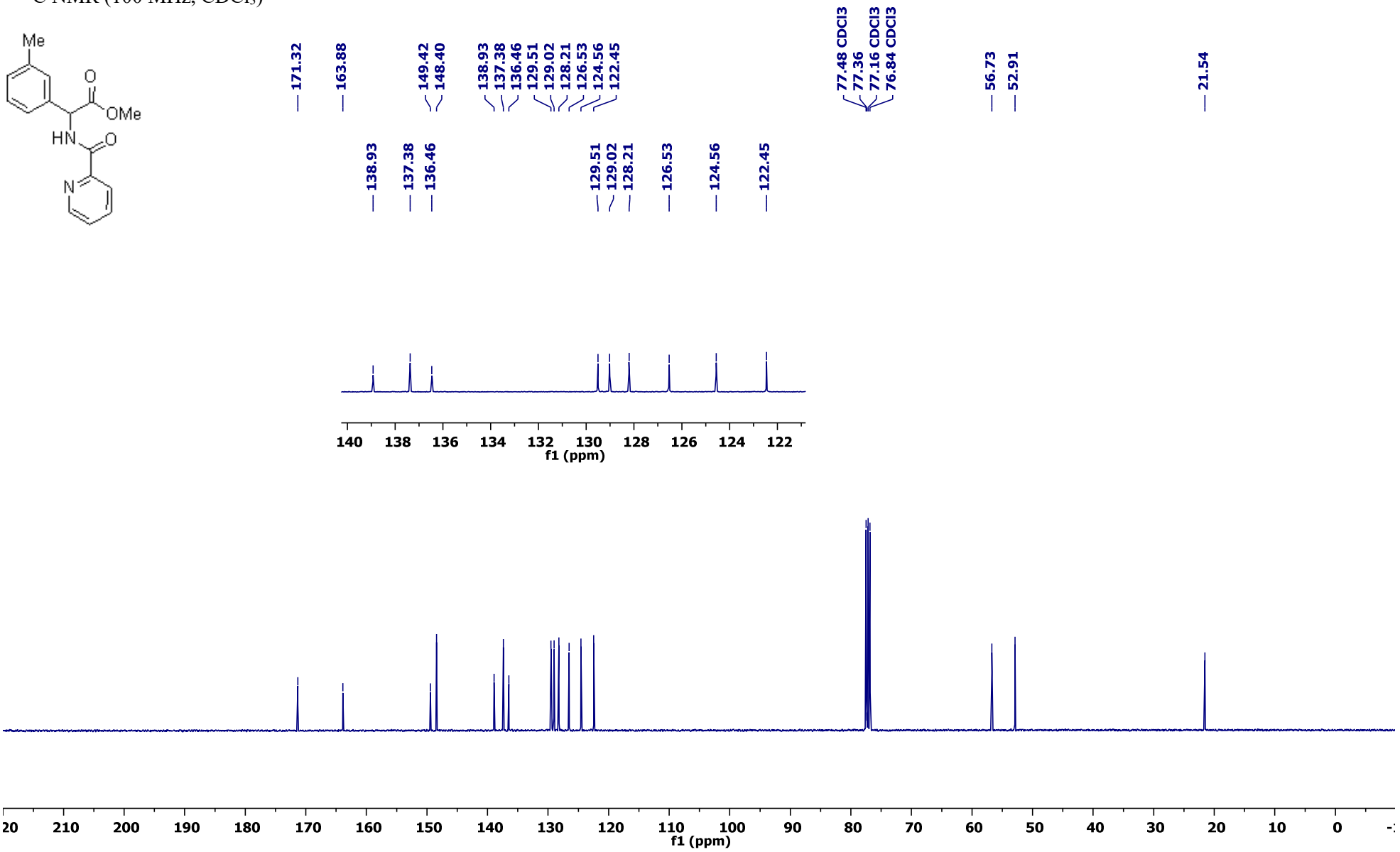

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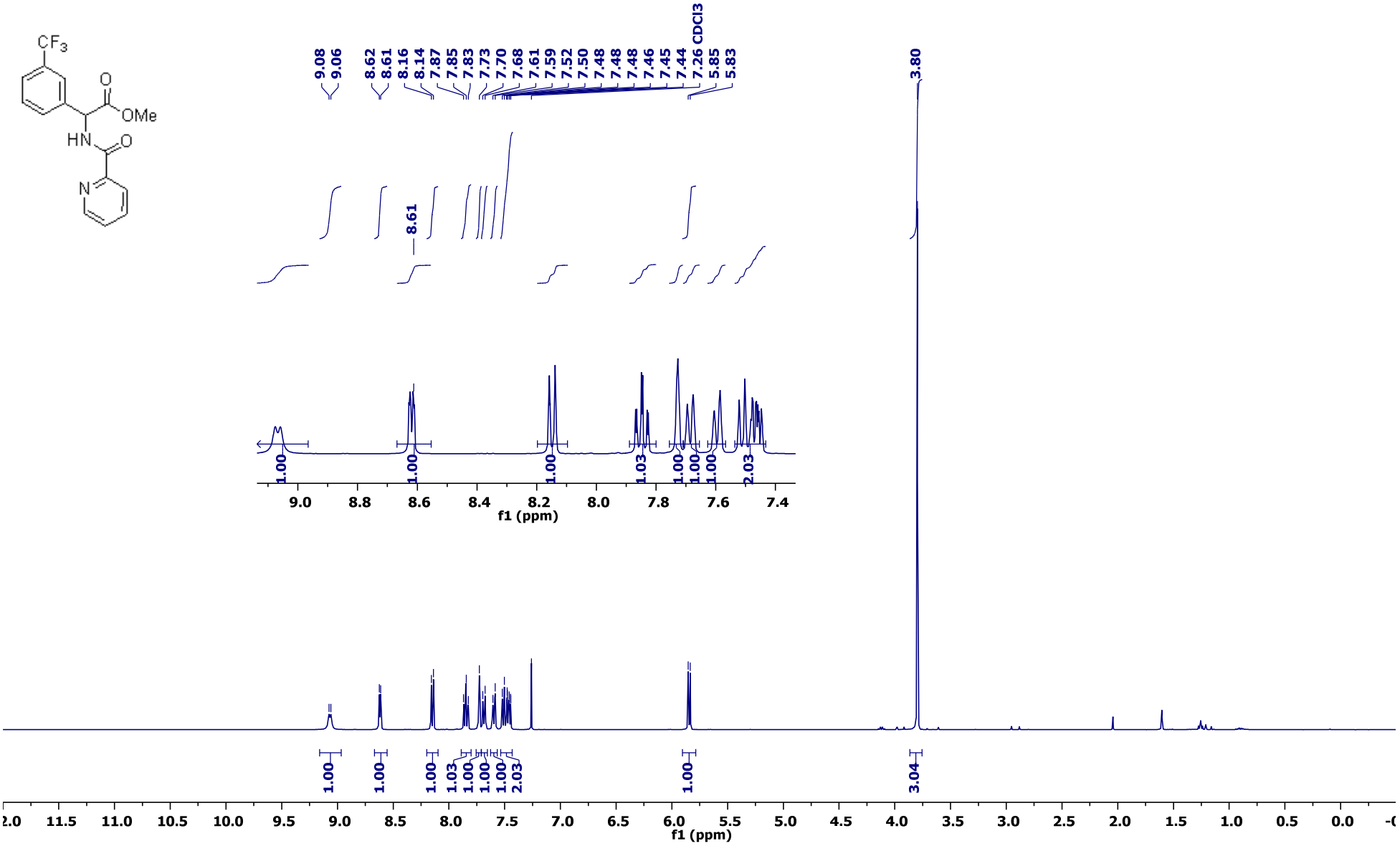

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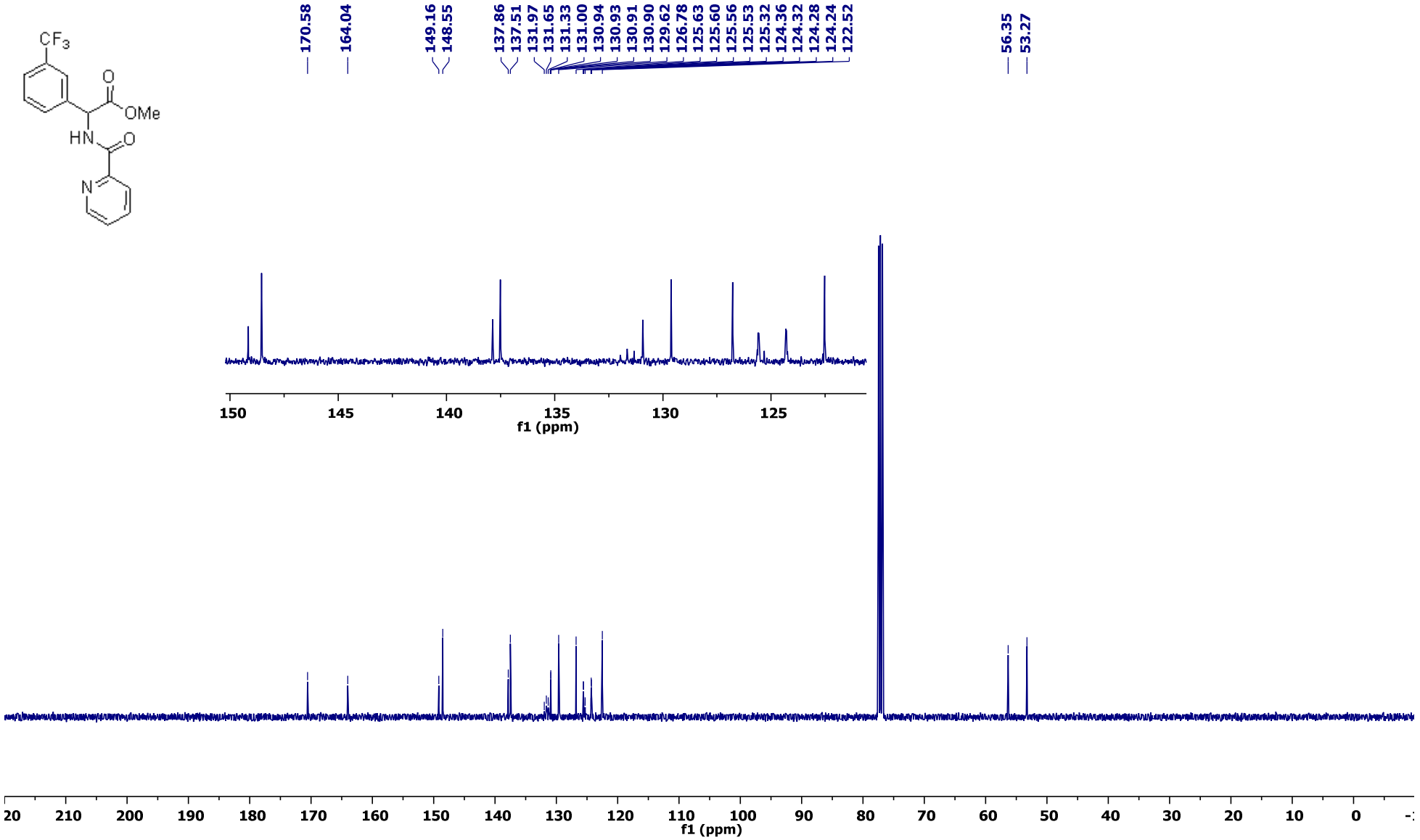

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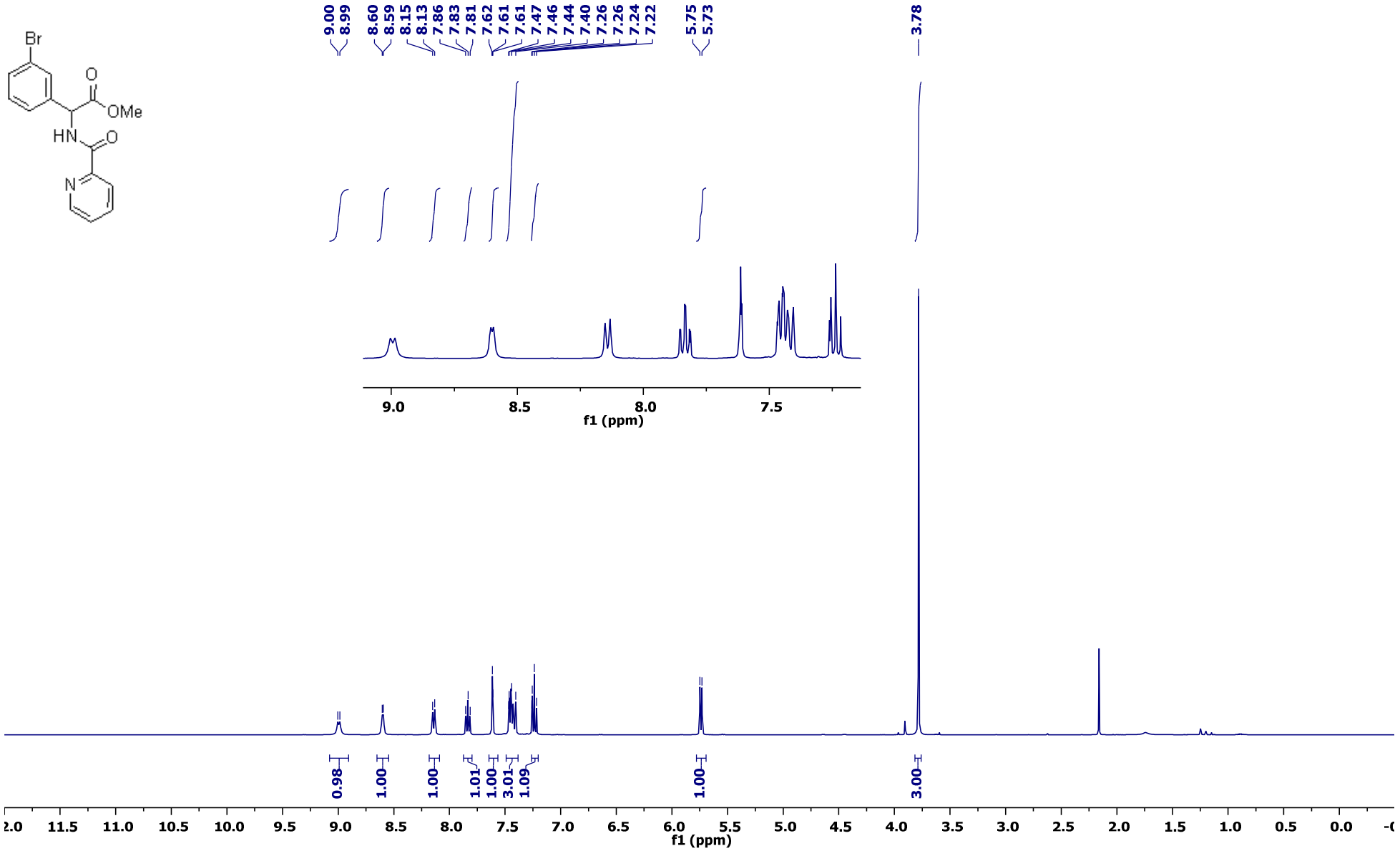
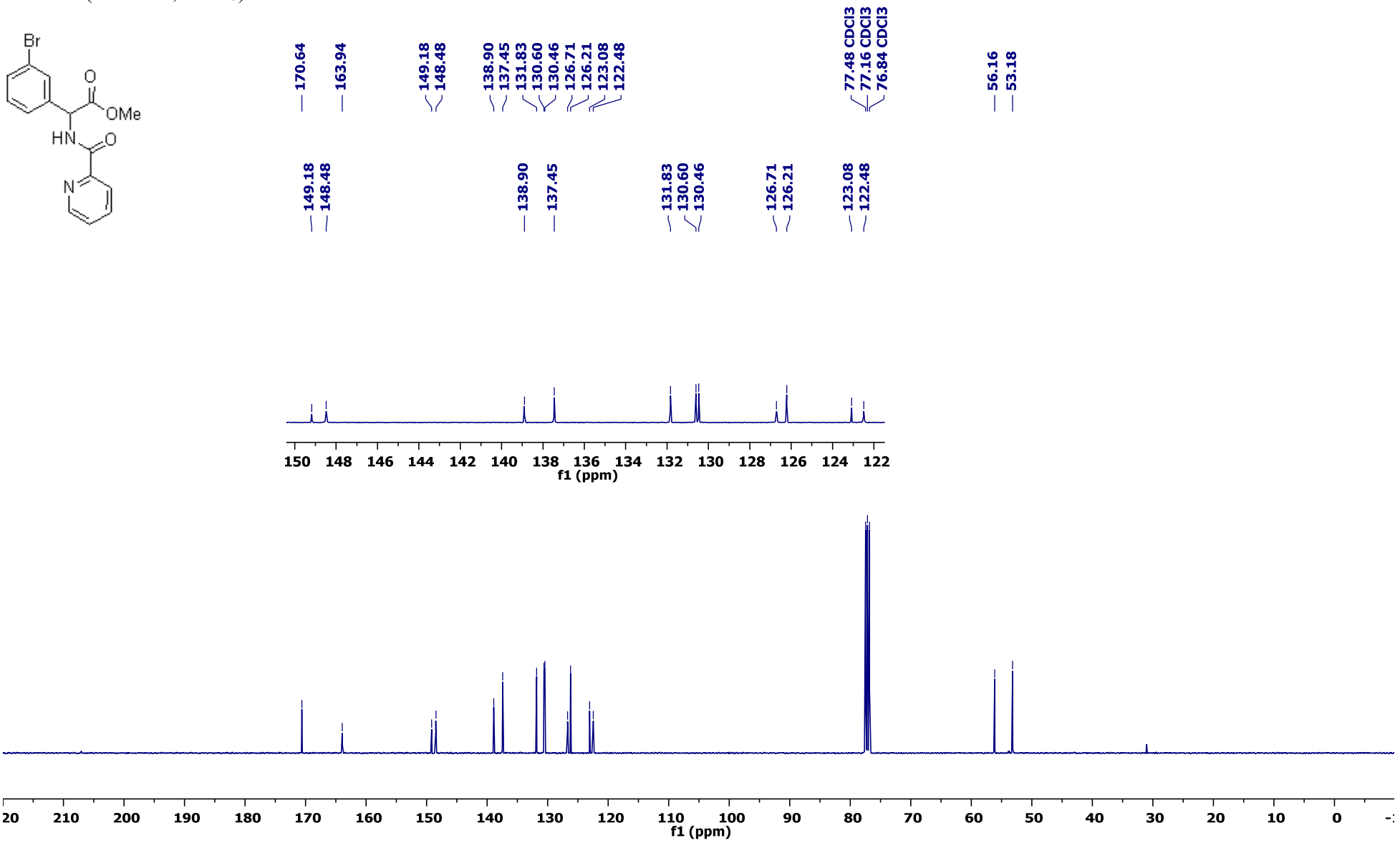
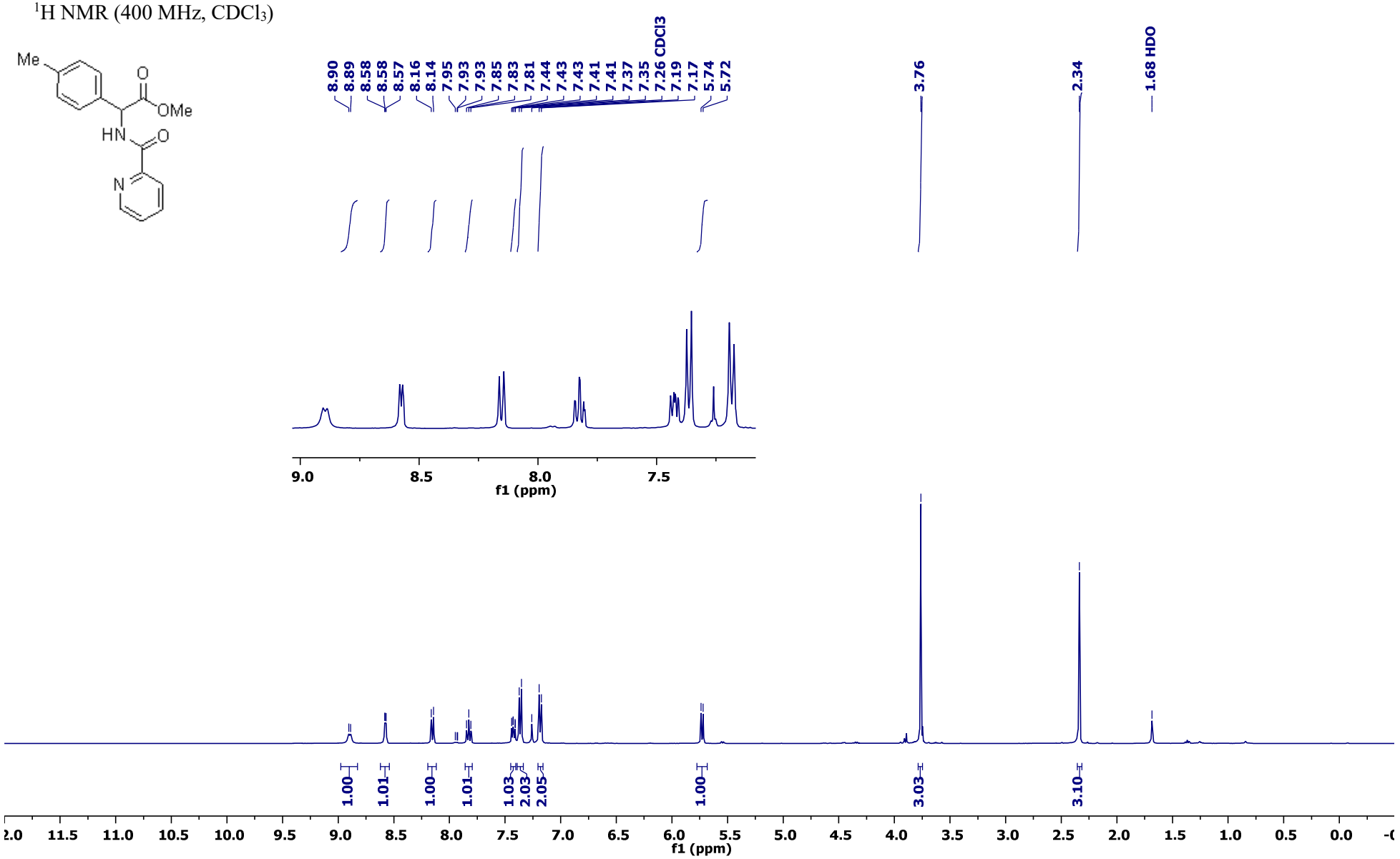


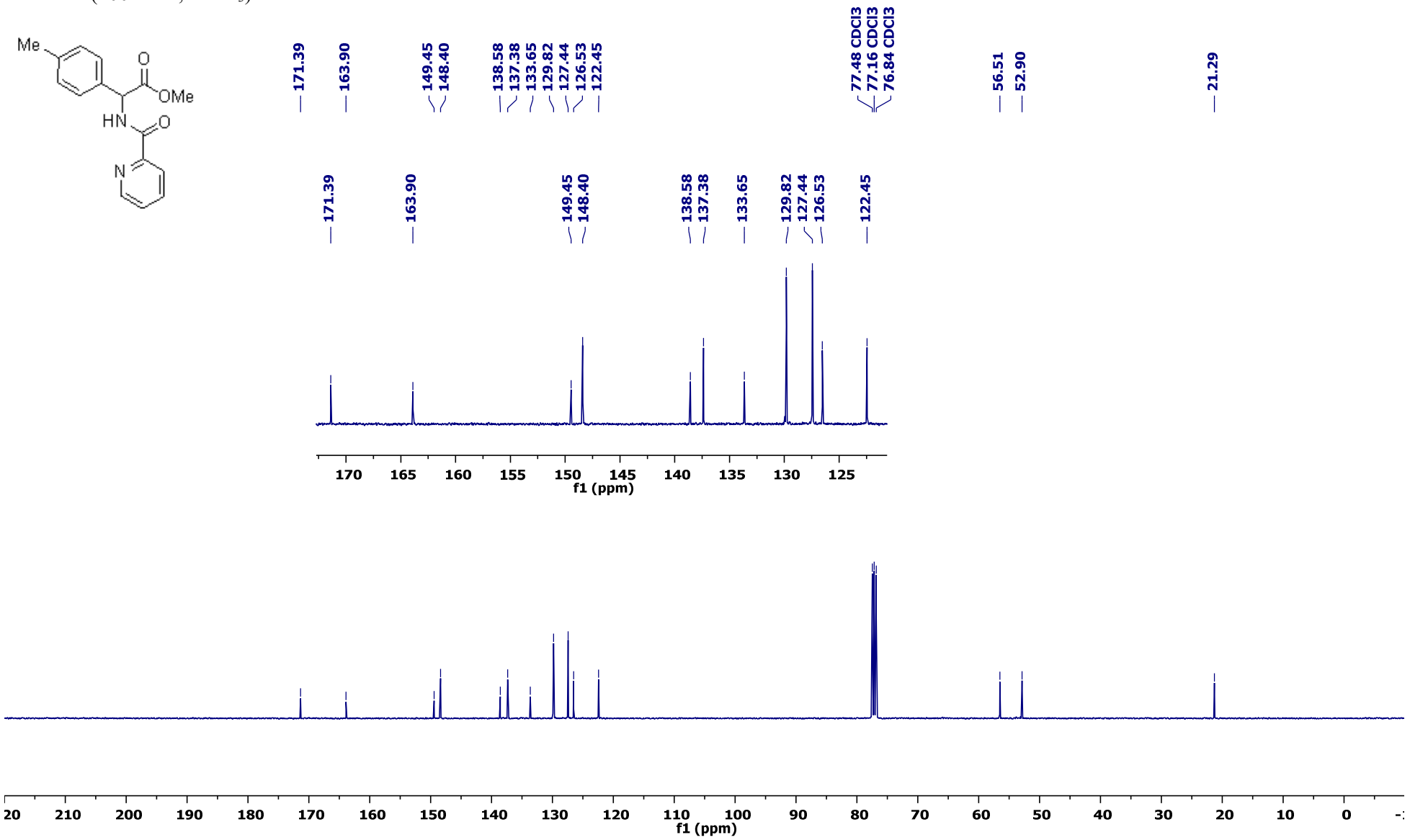
^{13}C NMR (100 MHz, $CDCl_3$)



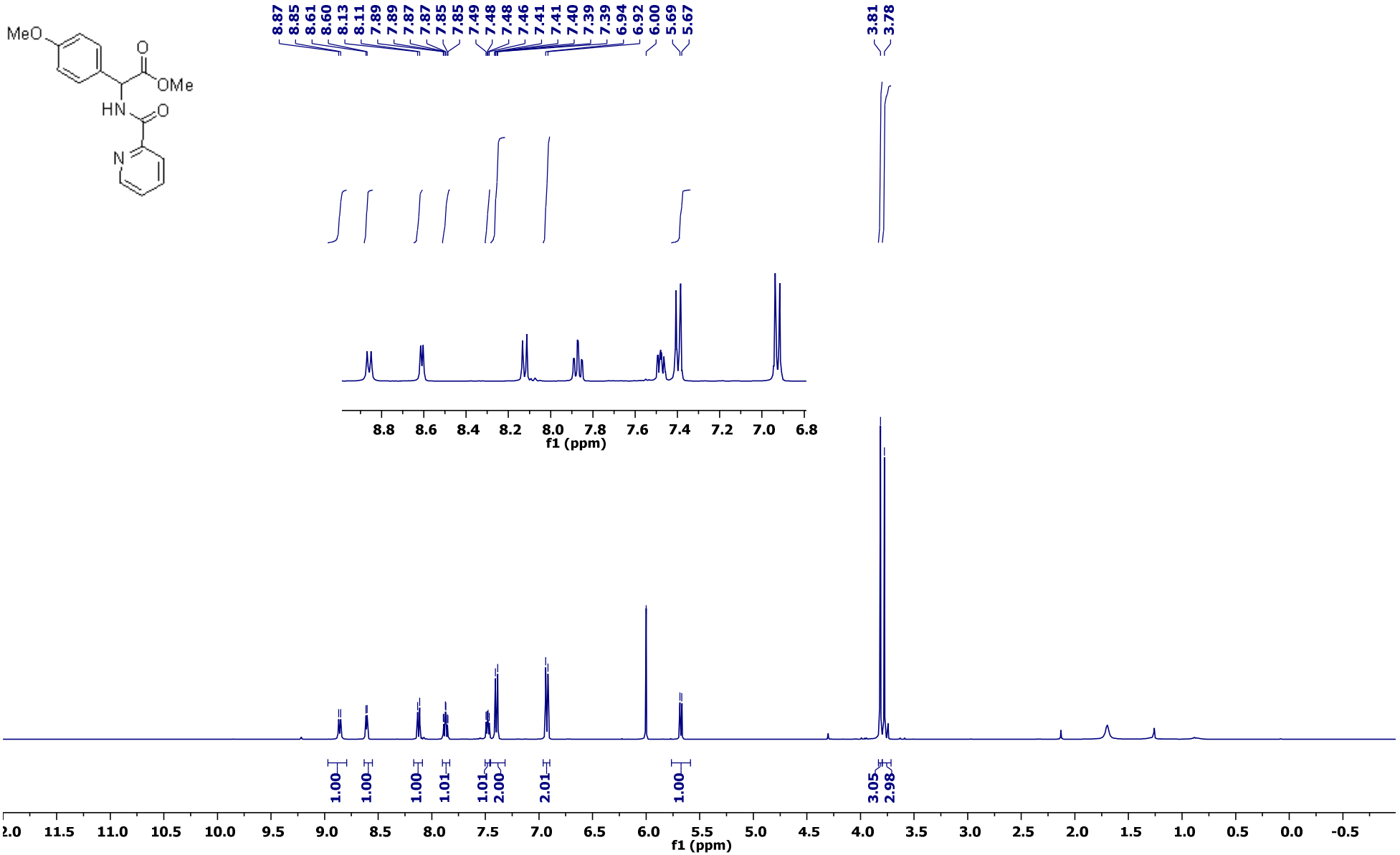
^{1}H NMR (400 MHz, $CDCl_3$)



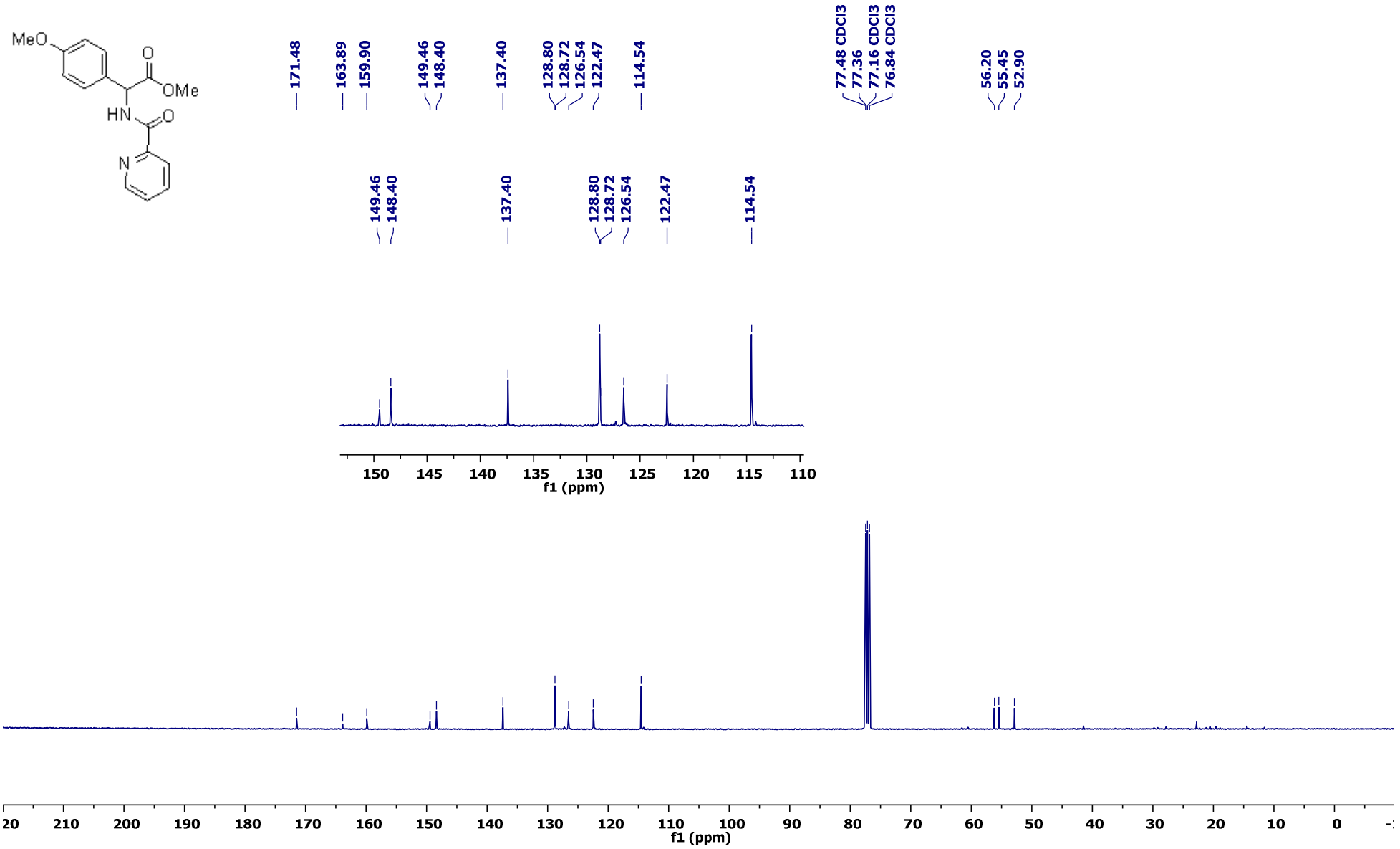
^{13}C NMR (100 MHz, $CDCl_3$)



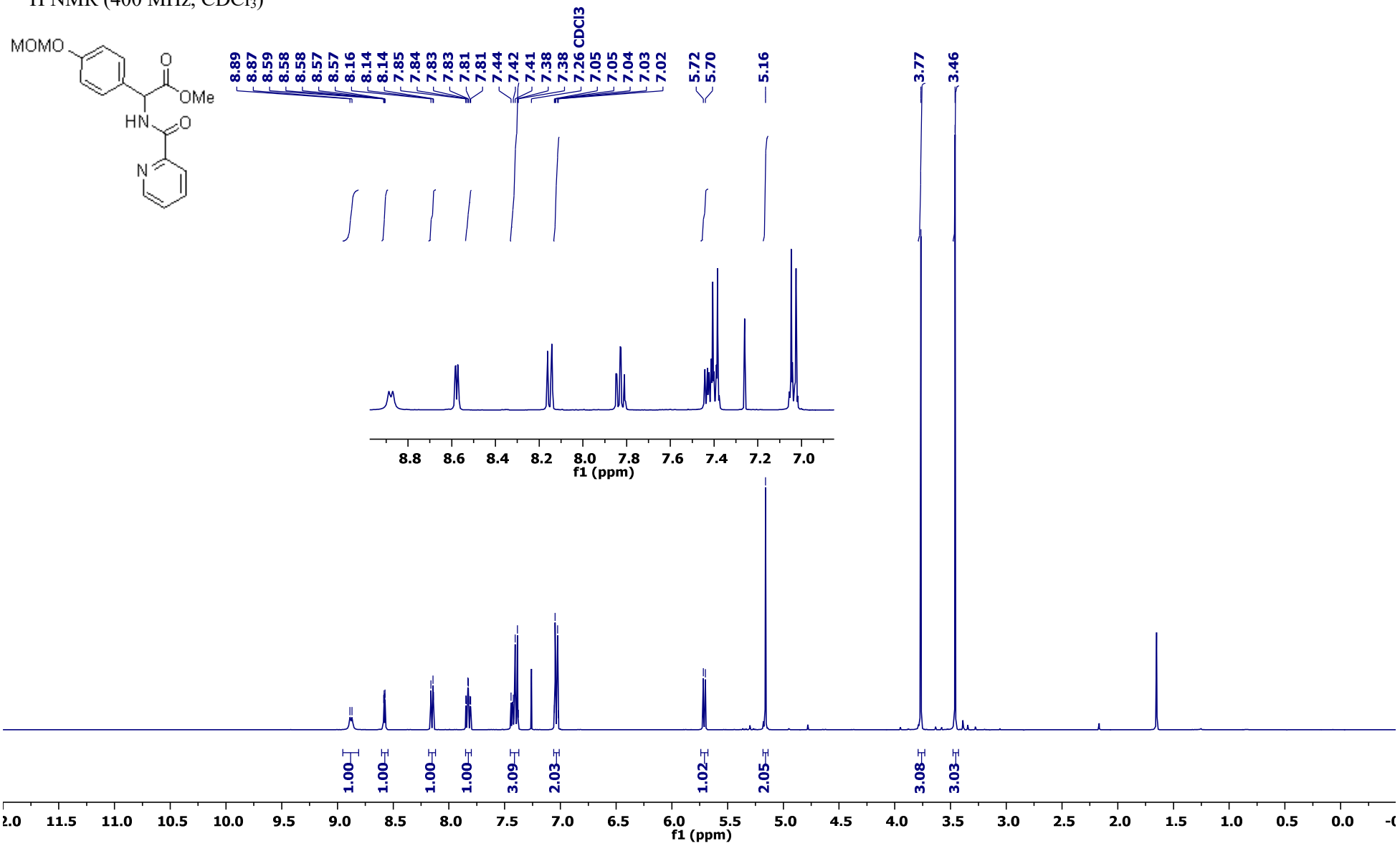
^{1}H NMR (400 MHz, $C_2D_2Cl_4$)



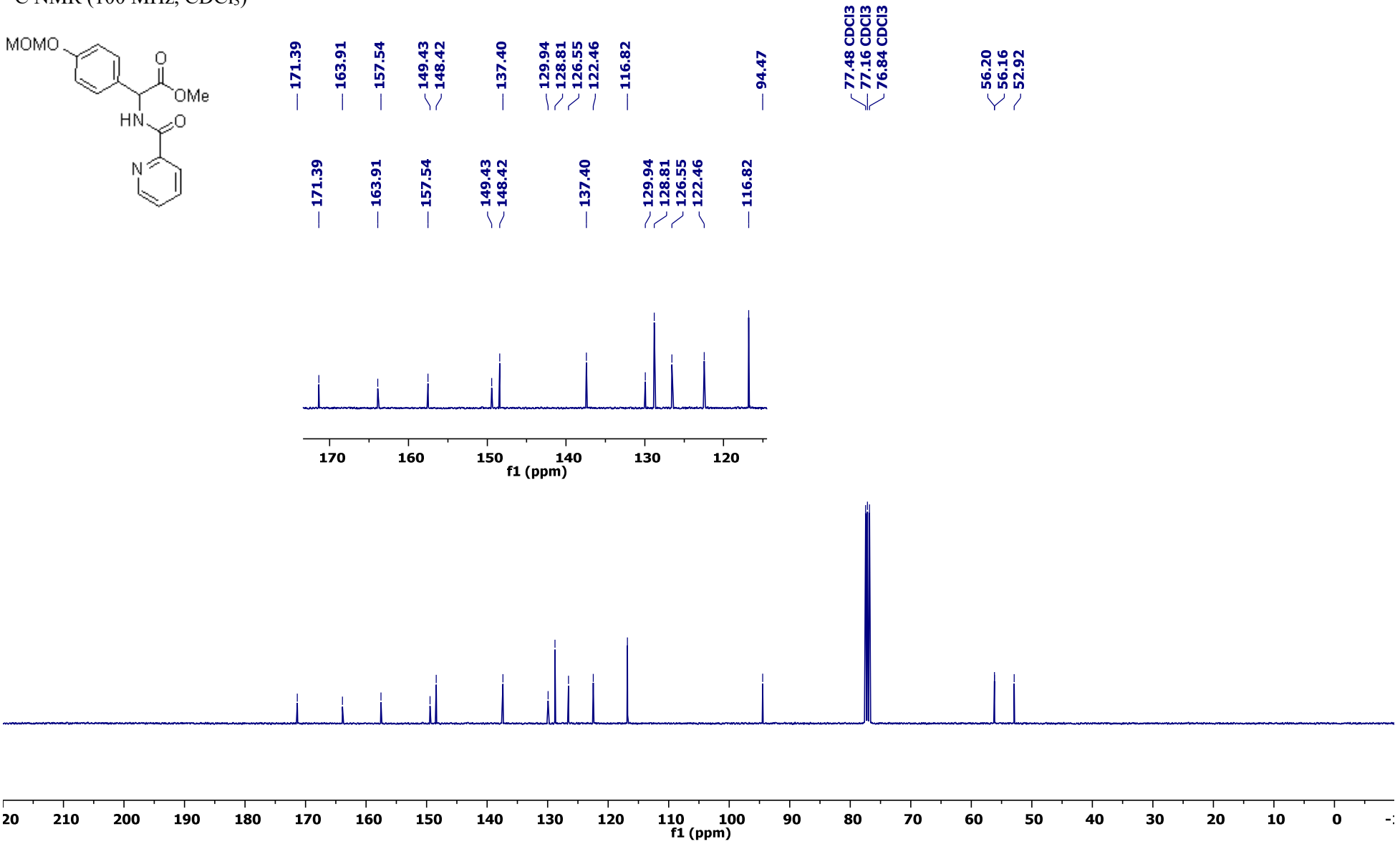
^{13}C NMR (100 MHz, $CDCl_3$)



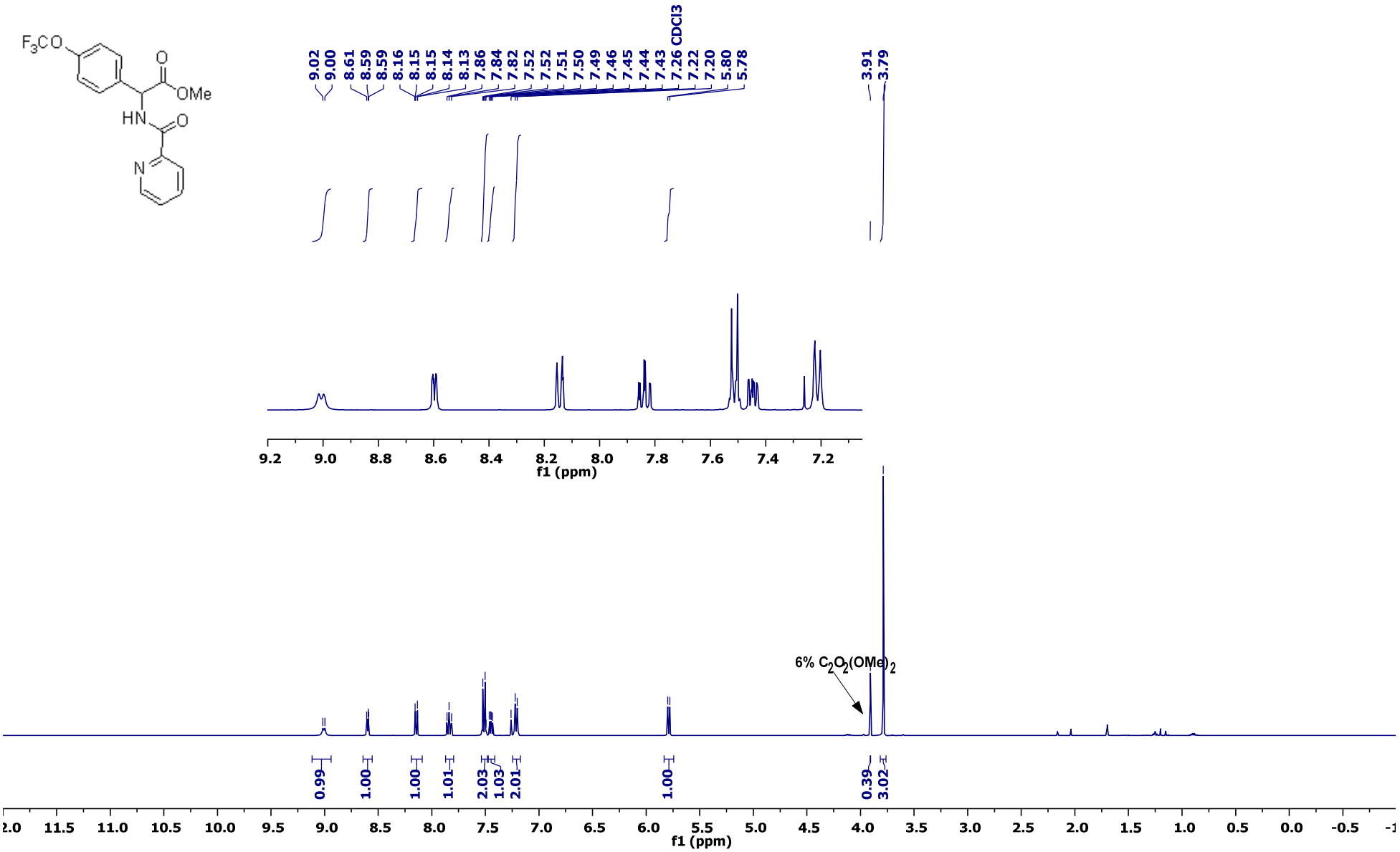
^{1}H NMR (400 MHz, $CDCl_3$)



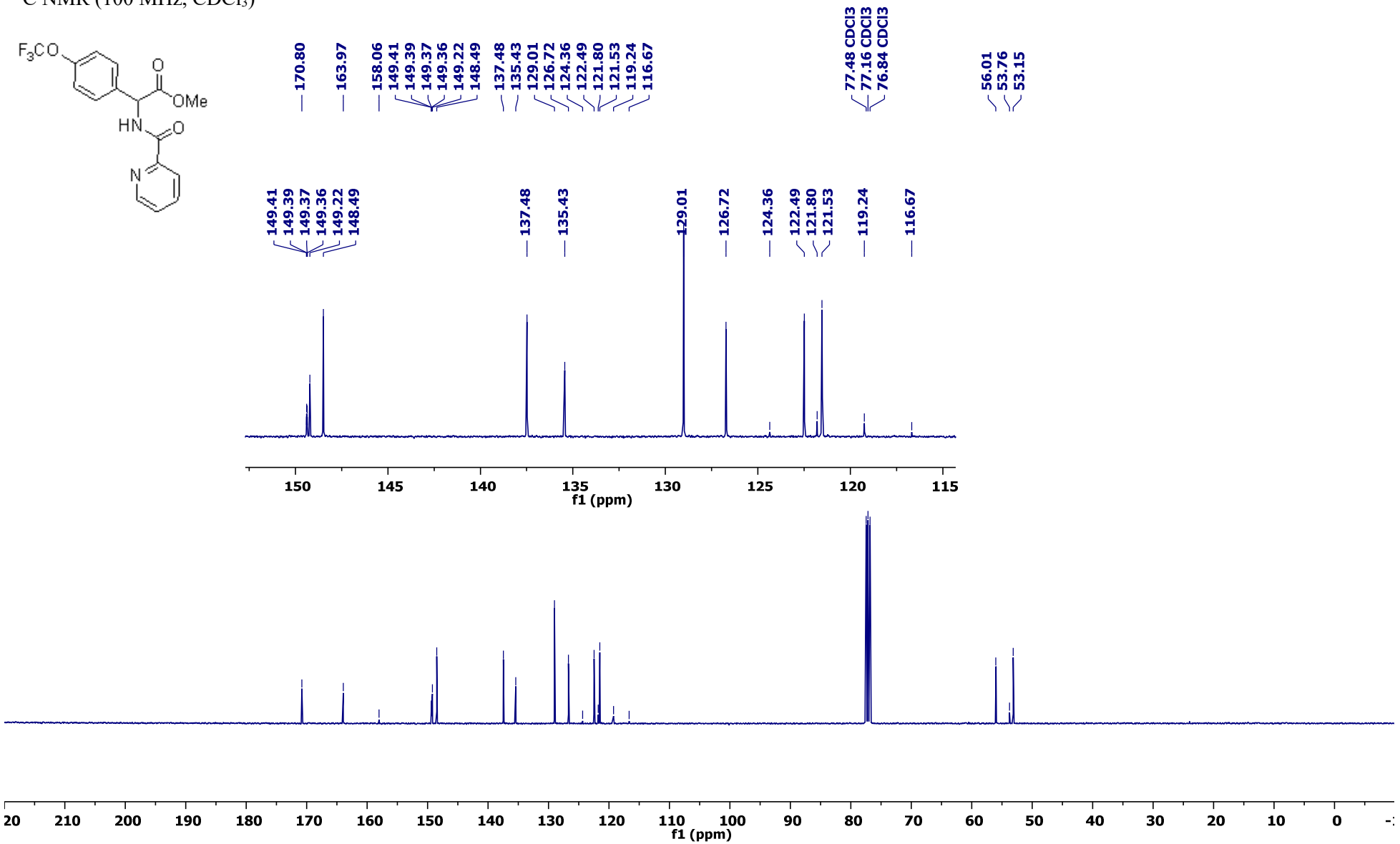
^{13}C NMR (100 MHz, $CDCl_3$)



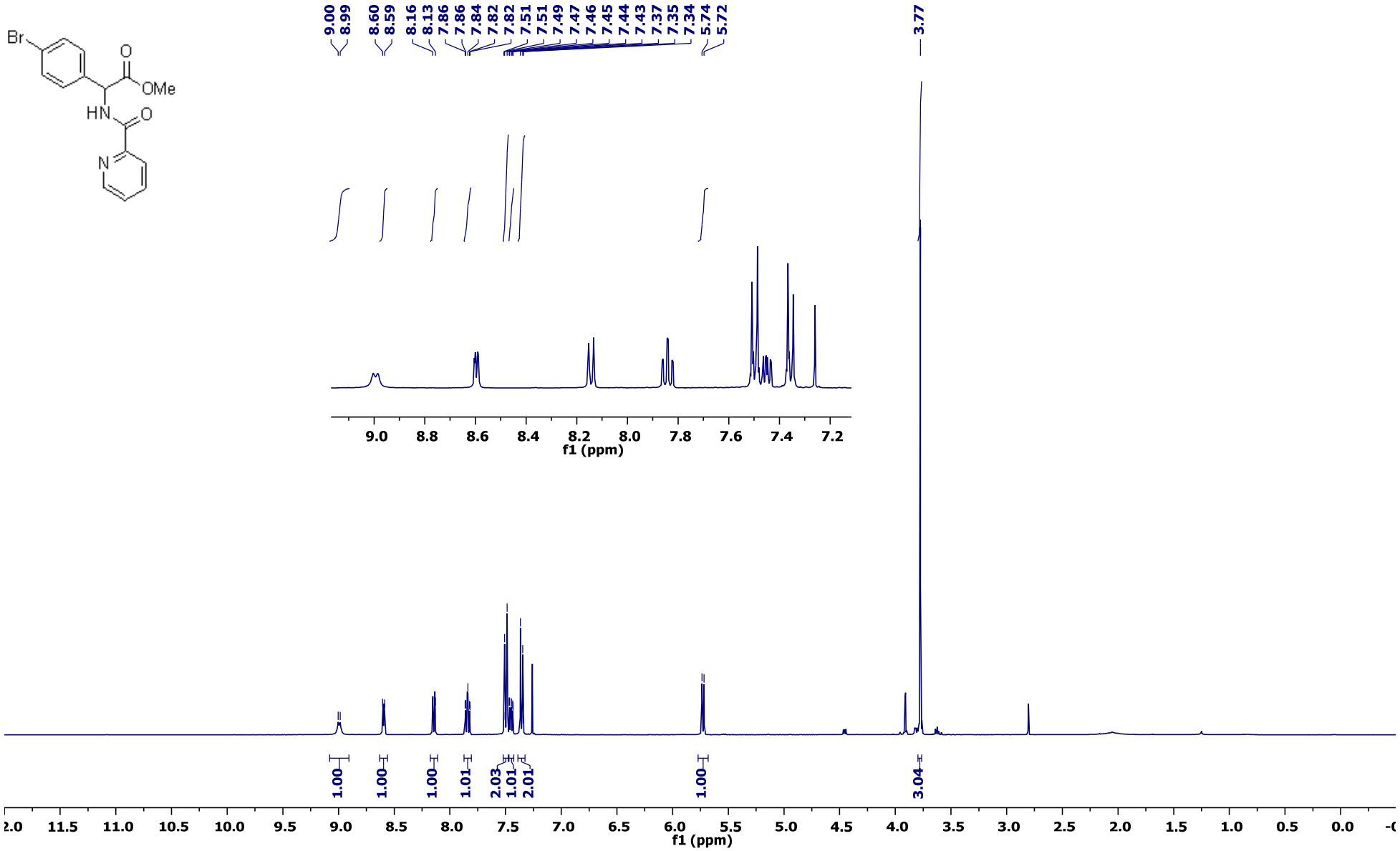
^{1}H NMR (400 MHz, $CDCl_3$)



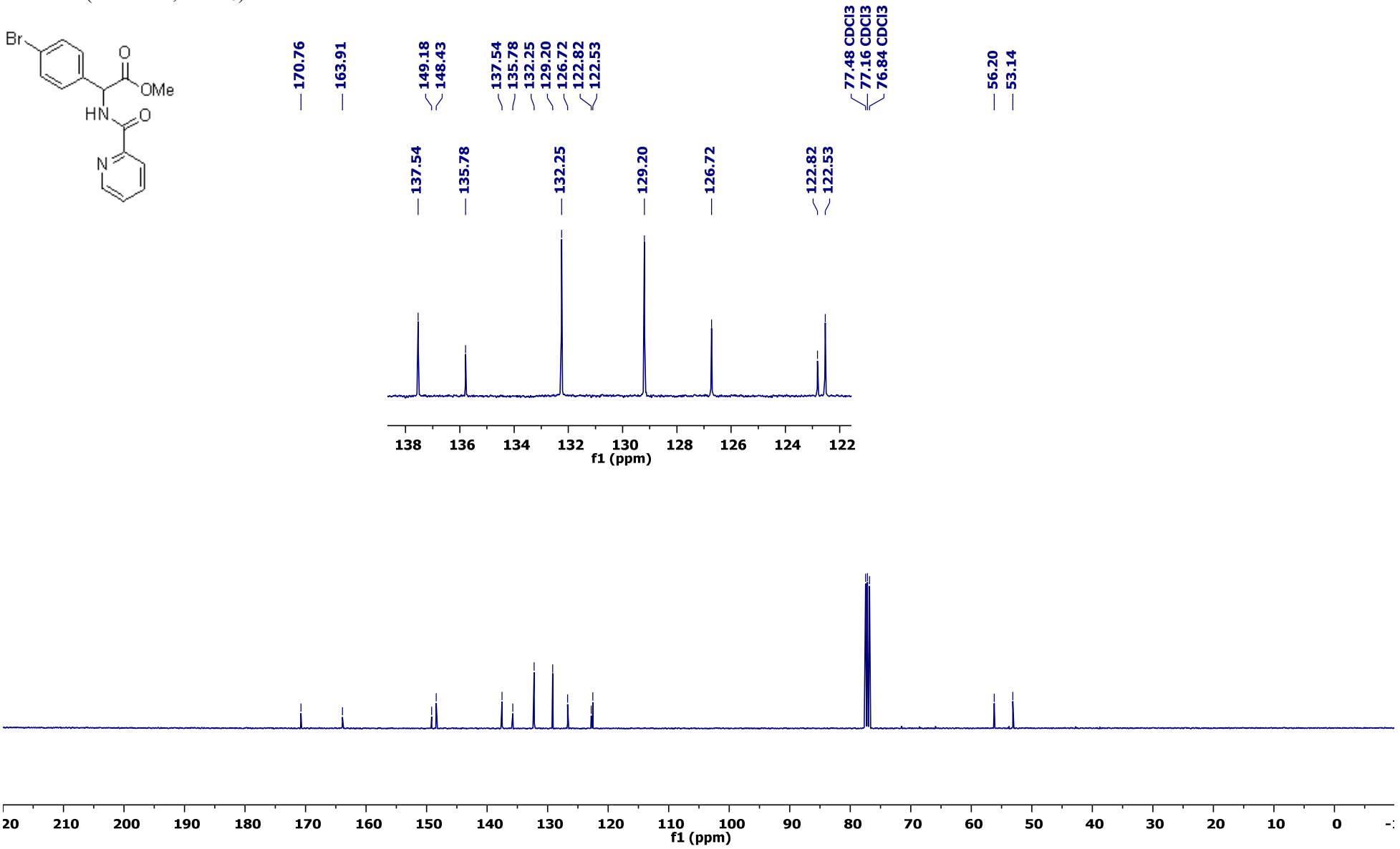
^{13}C NMR (100 MHz, $CDCl_3$)



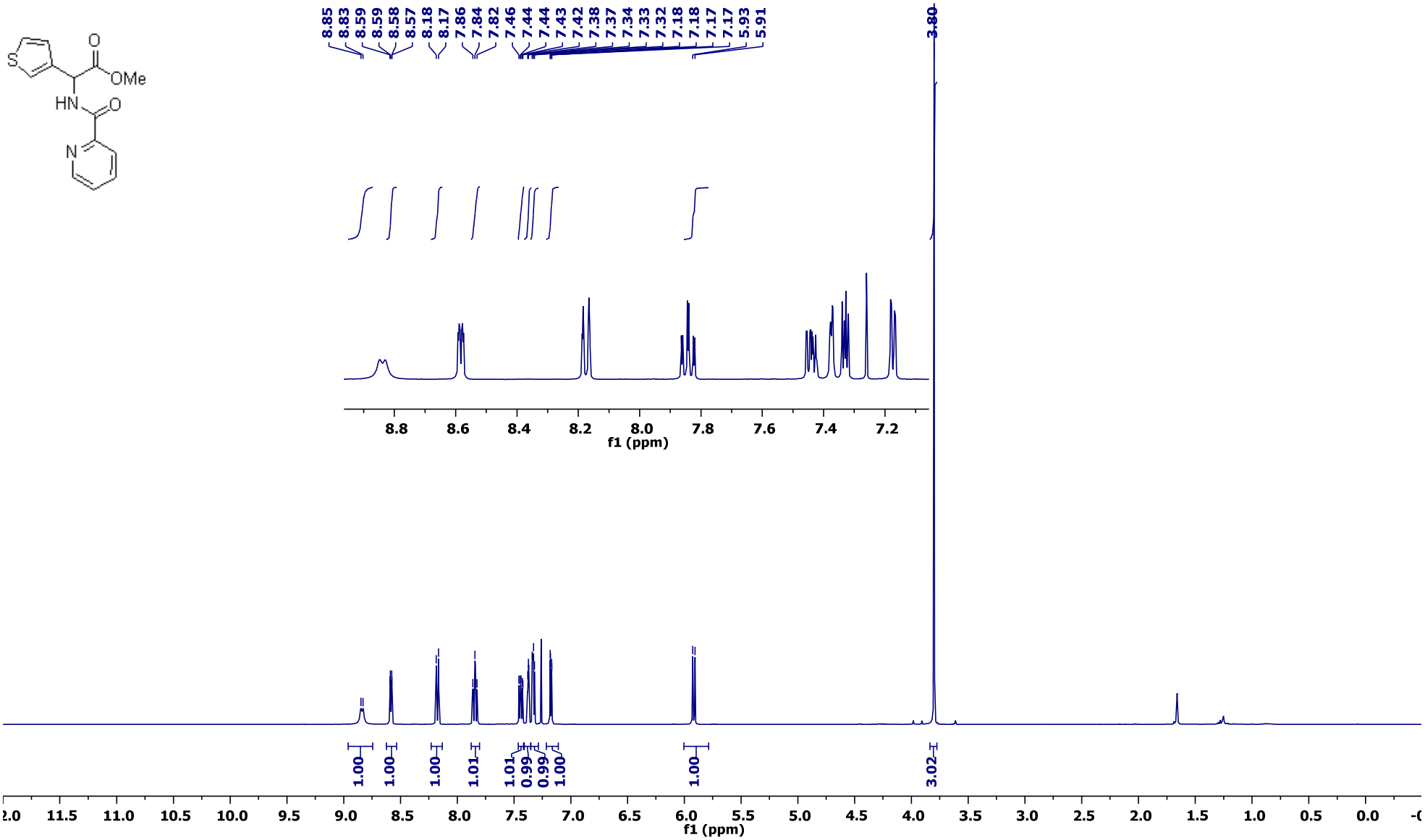
^{1}H NMR (400 MHz, $CDCl_3$)



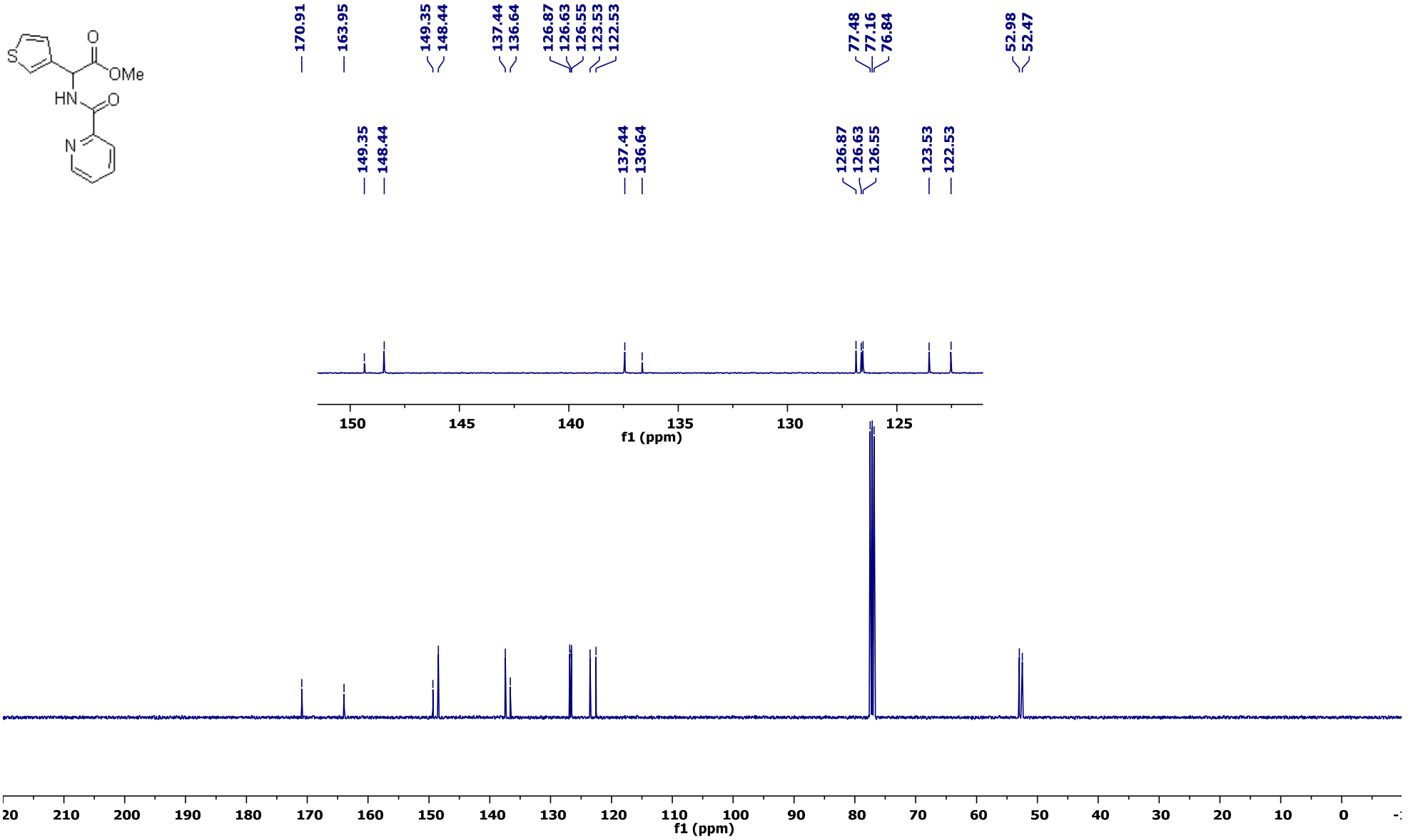
^{13}C NMR (100 MHz, $CDCl_3$)



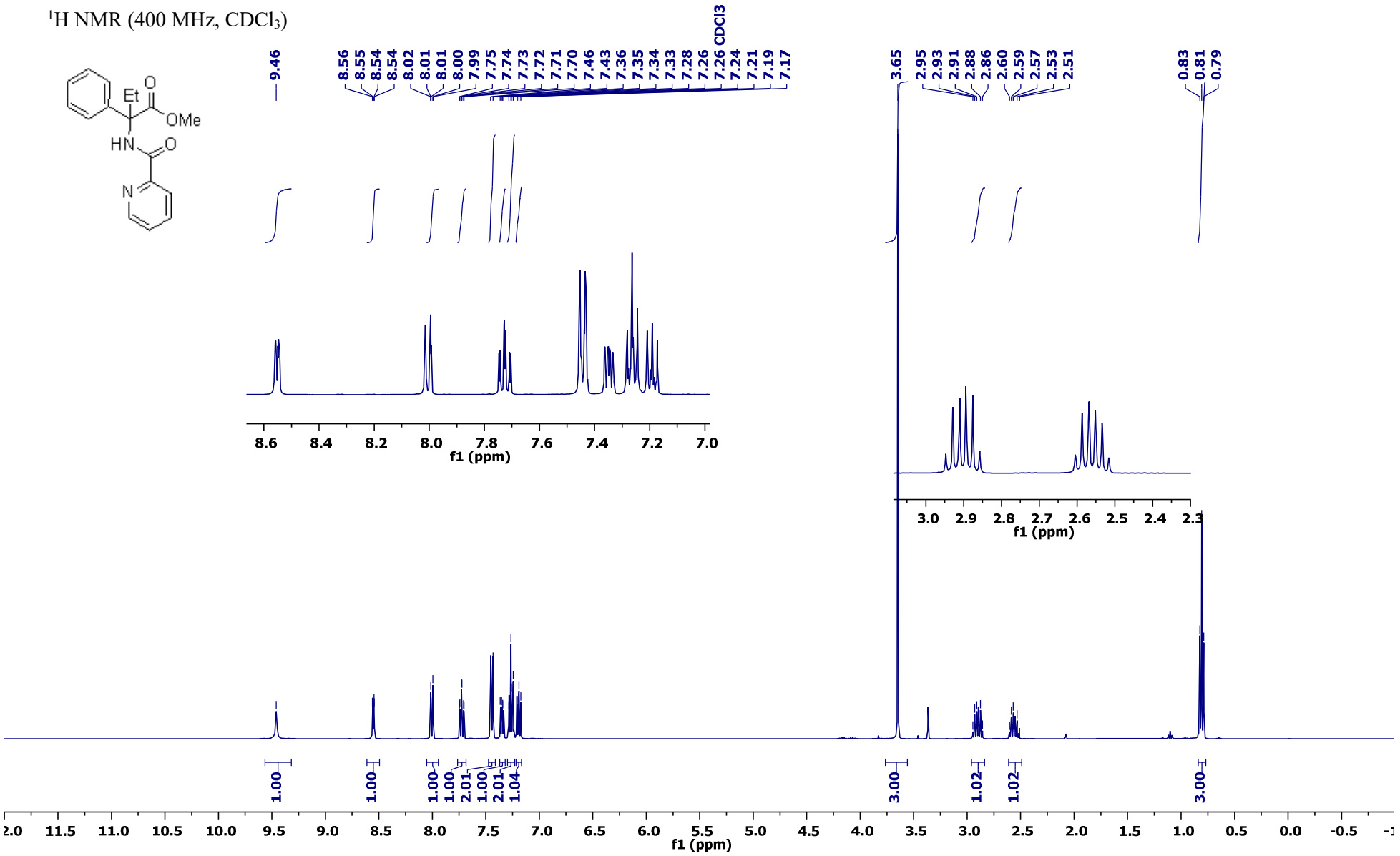
^{1}H NMR (400 MHz, $CDCl_3$)



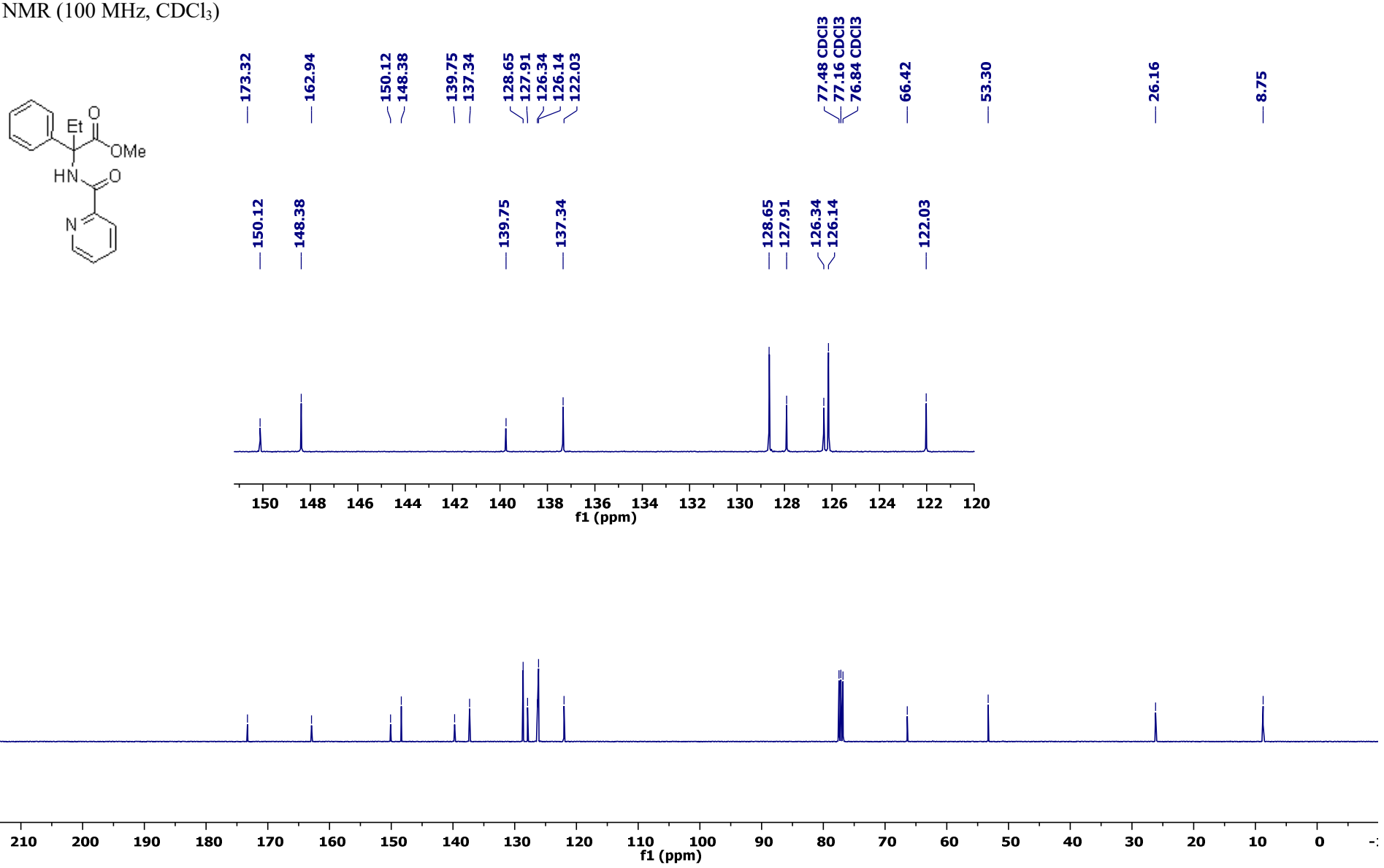
^{13}C NMR (100 MHz, $CDCl_3$)



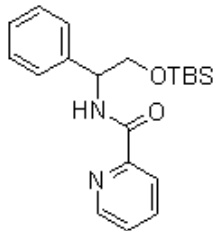
^{1}H NMR (400 MHz, $CDCl_3$)



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

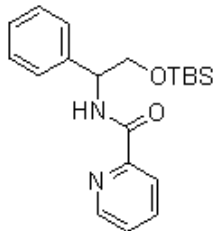


^{1}H NMR (400 MHz, $CDCl_3$)



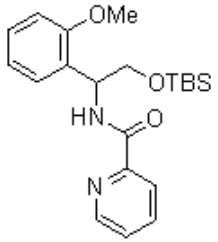
(1a)

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



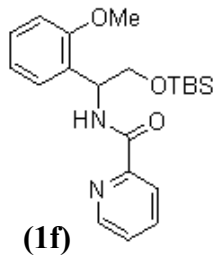
(1a)

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



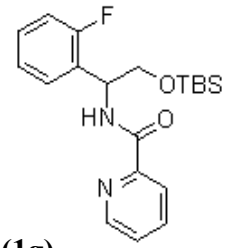
(1f)

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



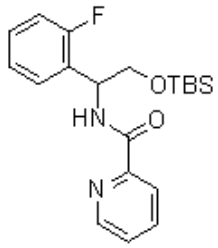
(1f)

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



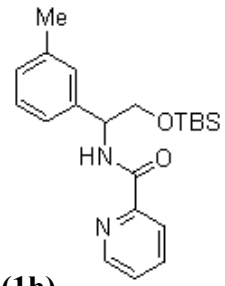
(1g)

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



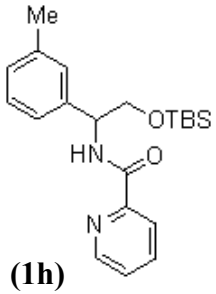
(1g)

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



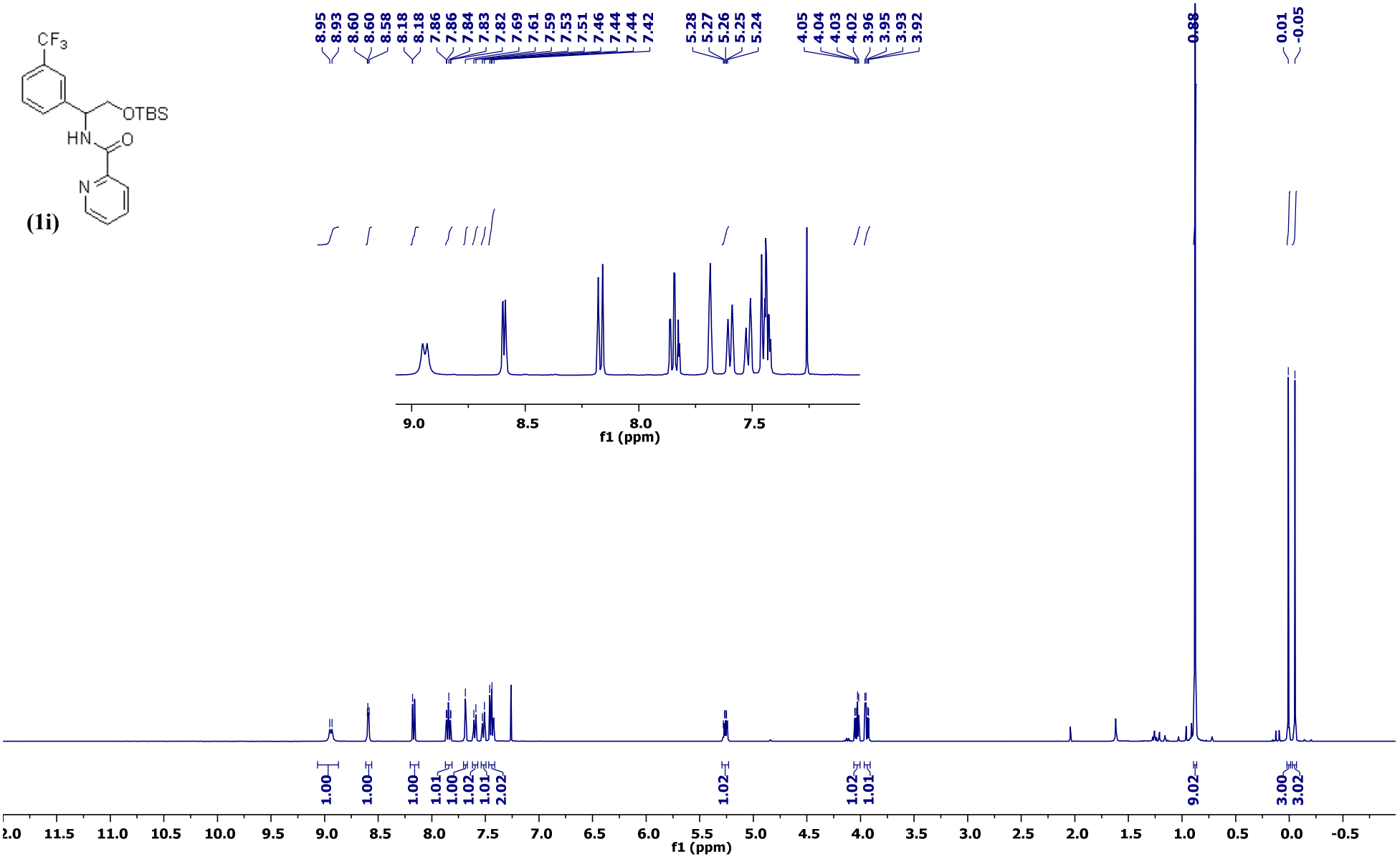
(1h)

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

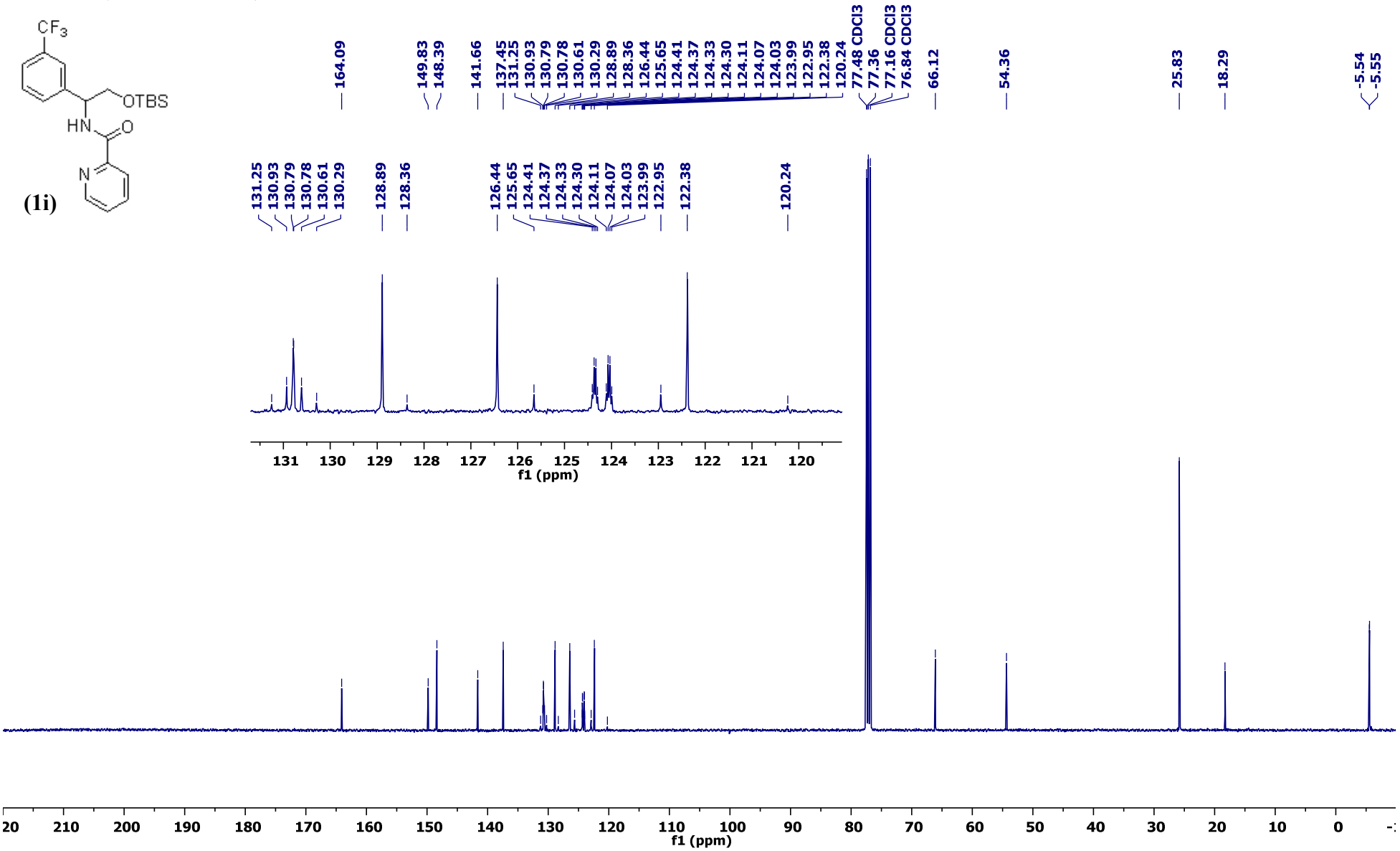


(1h)

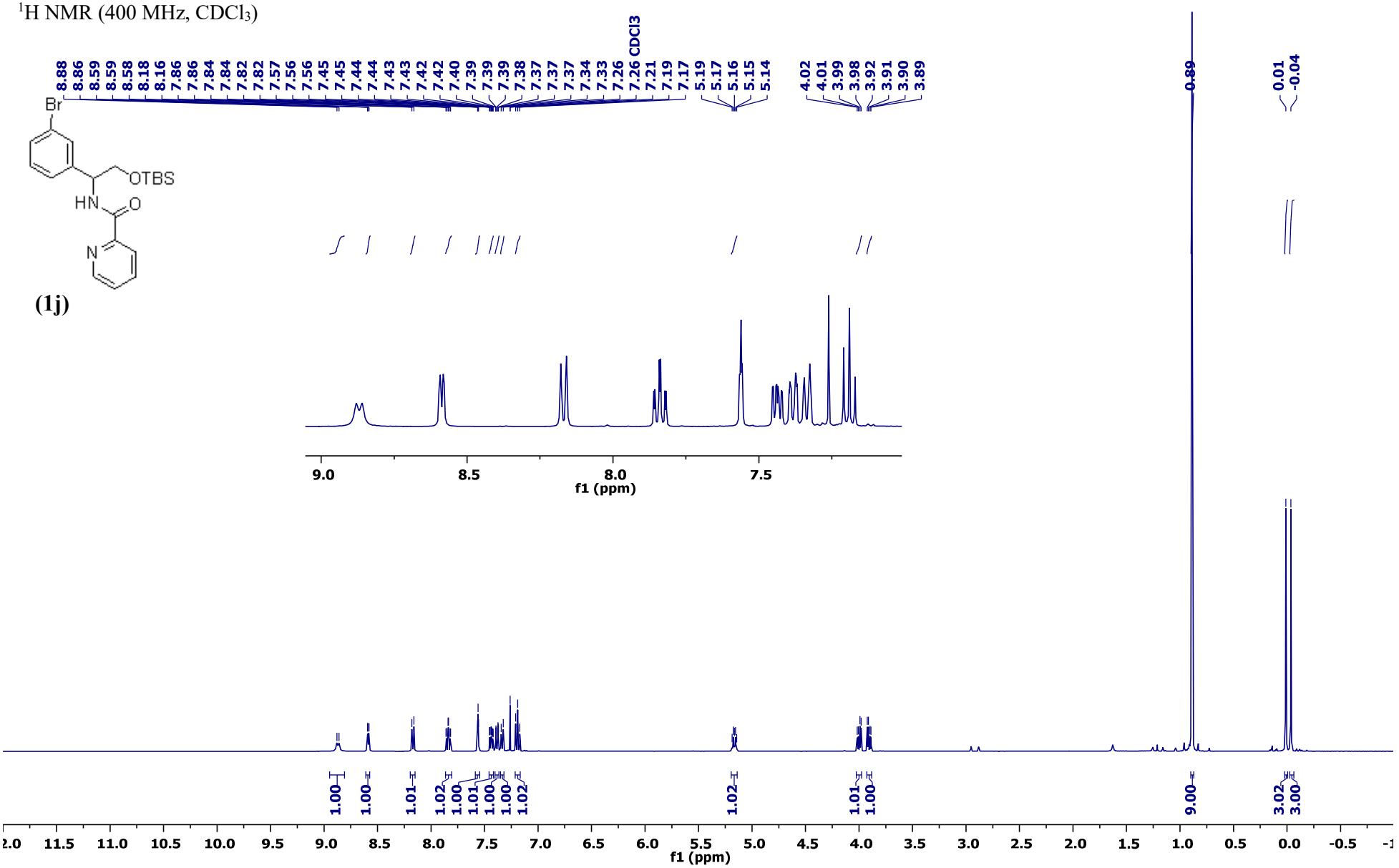
^{1}H NMR (400 MHz, $CDCl_3$)



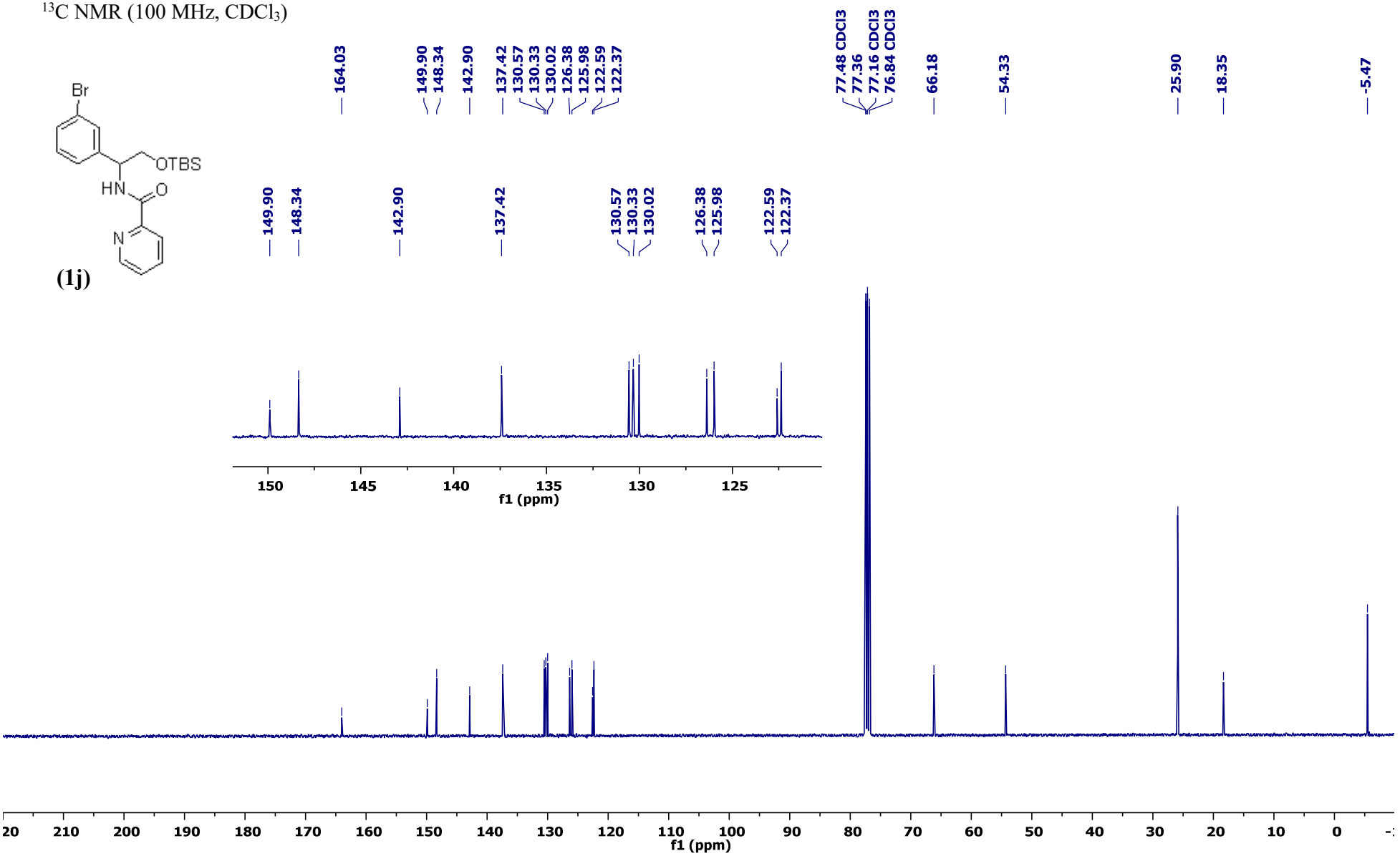
^{13}C NMR (100 MHz, $CDCl_3$)



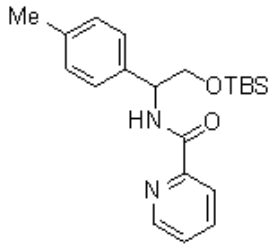
^{1}H NMR (400 MHz, $CDCl_3$)



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

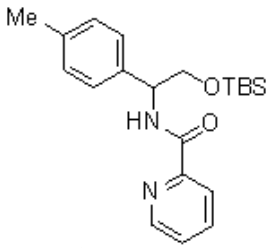


^{1}H NMR (400 MHz, $CDCl_3$)



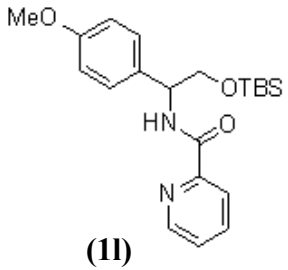
(1k)

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



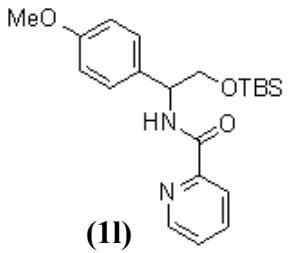
(1k)

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



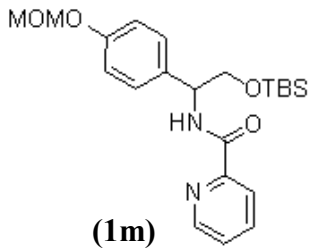
(1l)

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



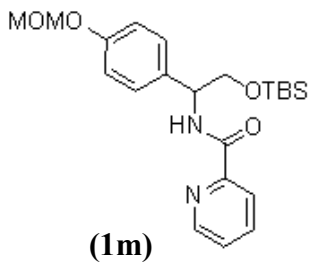
(1l)

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



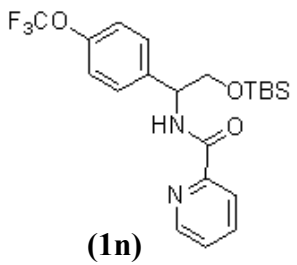
(1m)

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



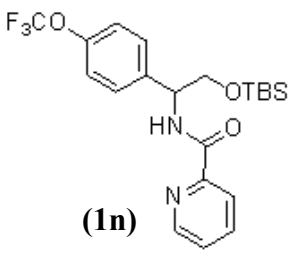
(1m)

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



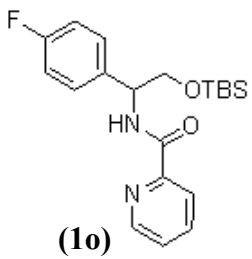
(1n)

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



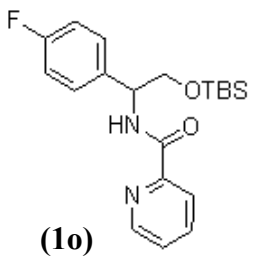
(1n)

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



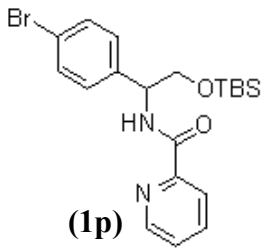
(1o)

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



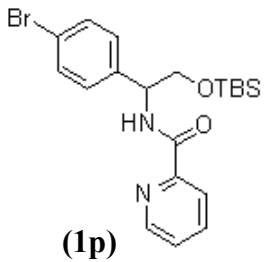
(1o)

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



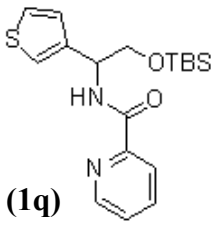
(1p)

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



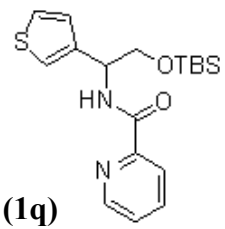
(1p)

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



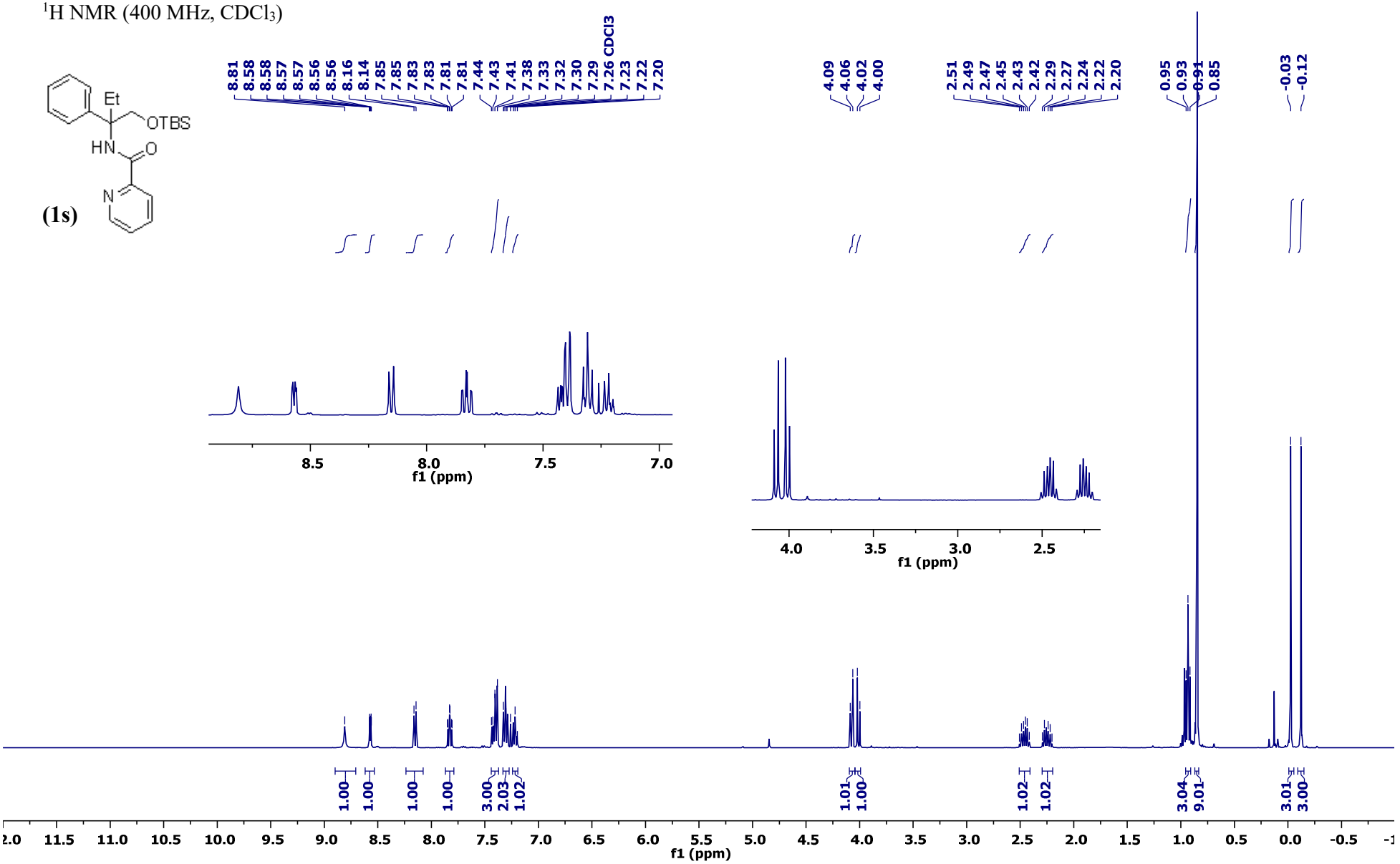
(1q)

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

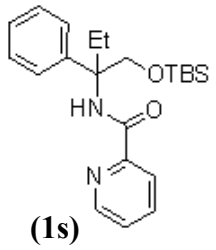


(1q)

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

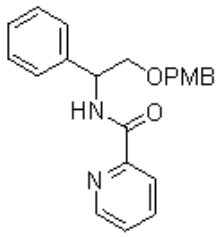


^{13}C NMR (100 MHz, $CDCl_3$)



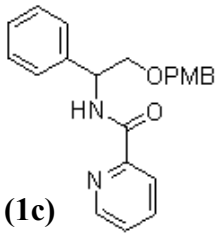
(1s)

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



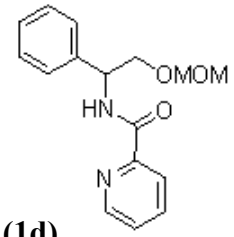
(1c)

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



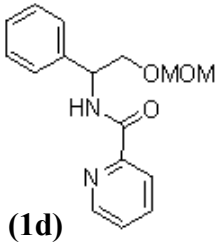
(1c)

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



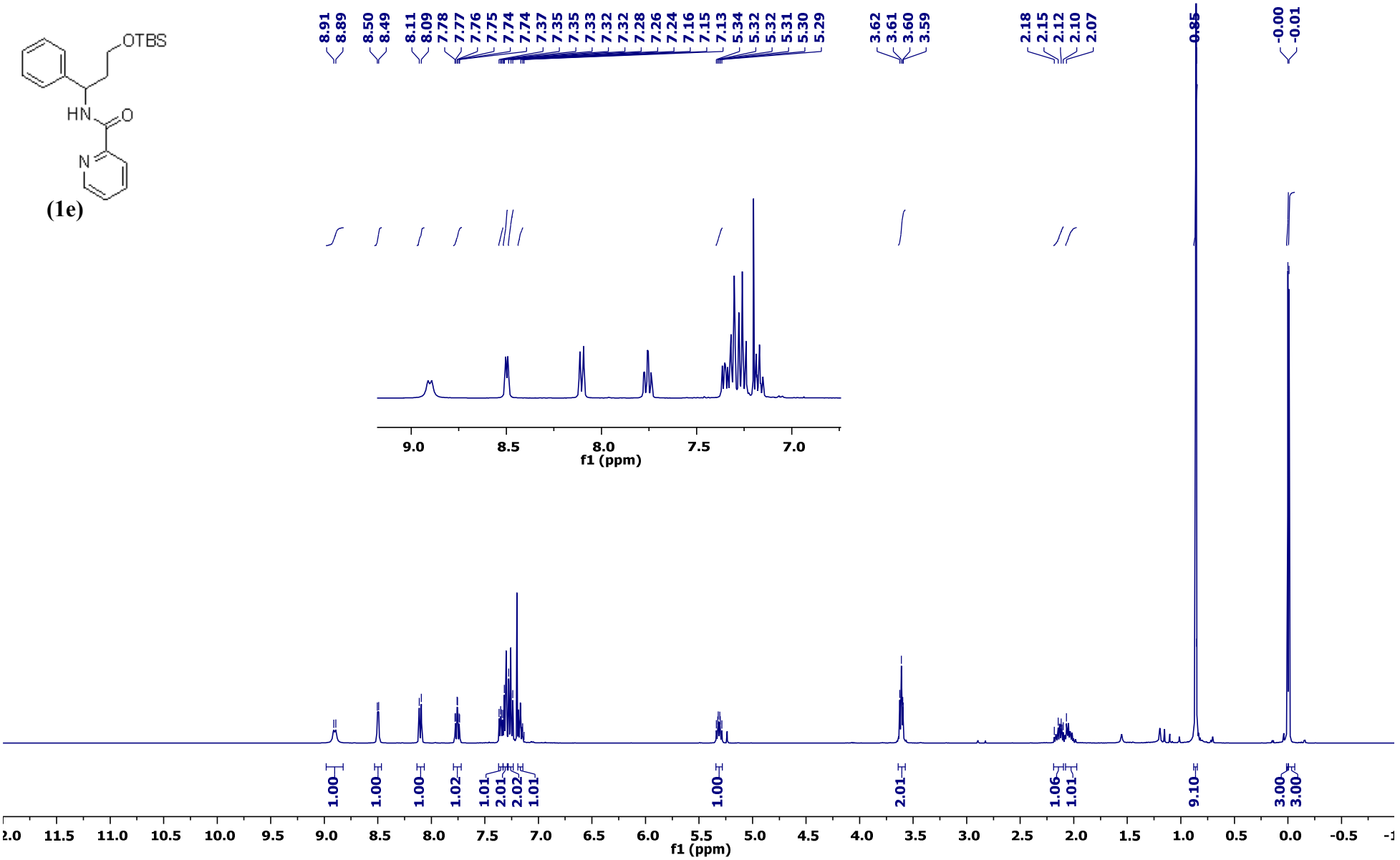
(1d)

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

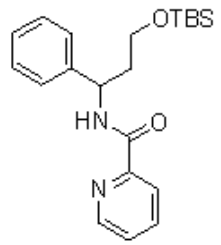


(1d)

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

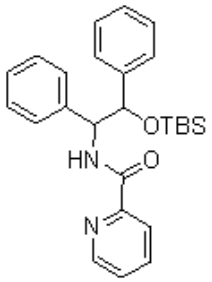


^{13}C NMR (100 MHz, $CDCl_3$)



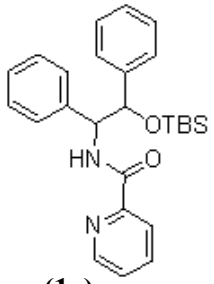
(1e)

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



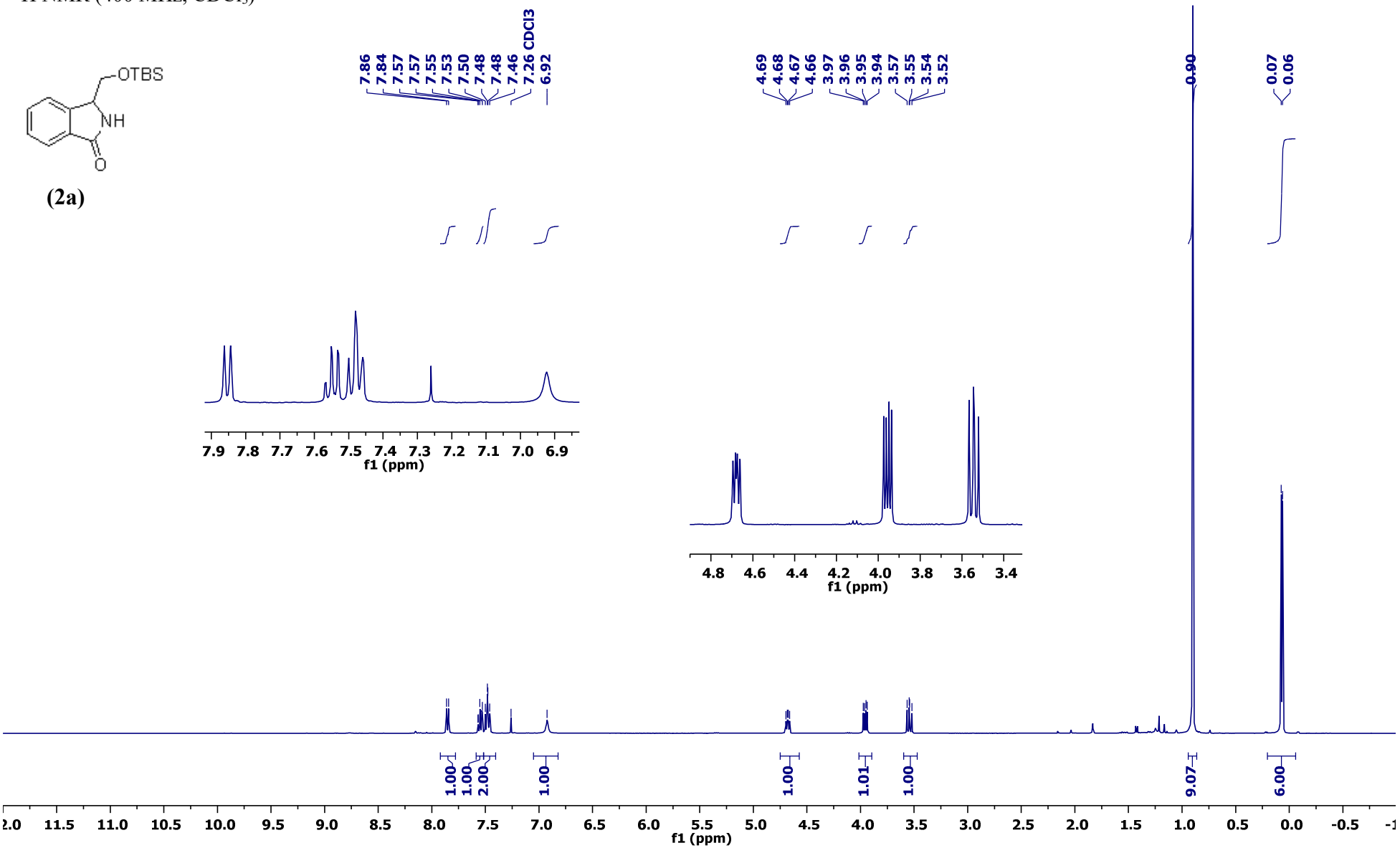
(1r)

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



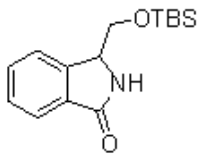
(1r)

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



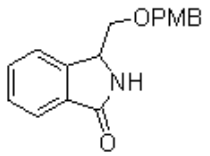
(2a)

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



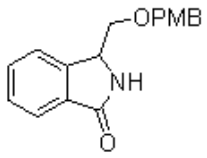
(2a)

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



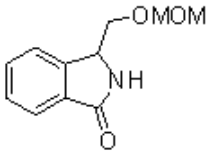
(2c)

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



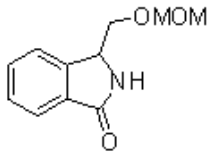
(2c)

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



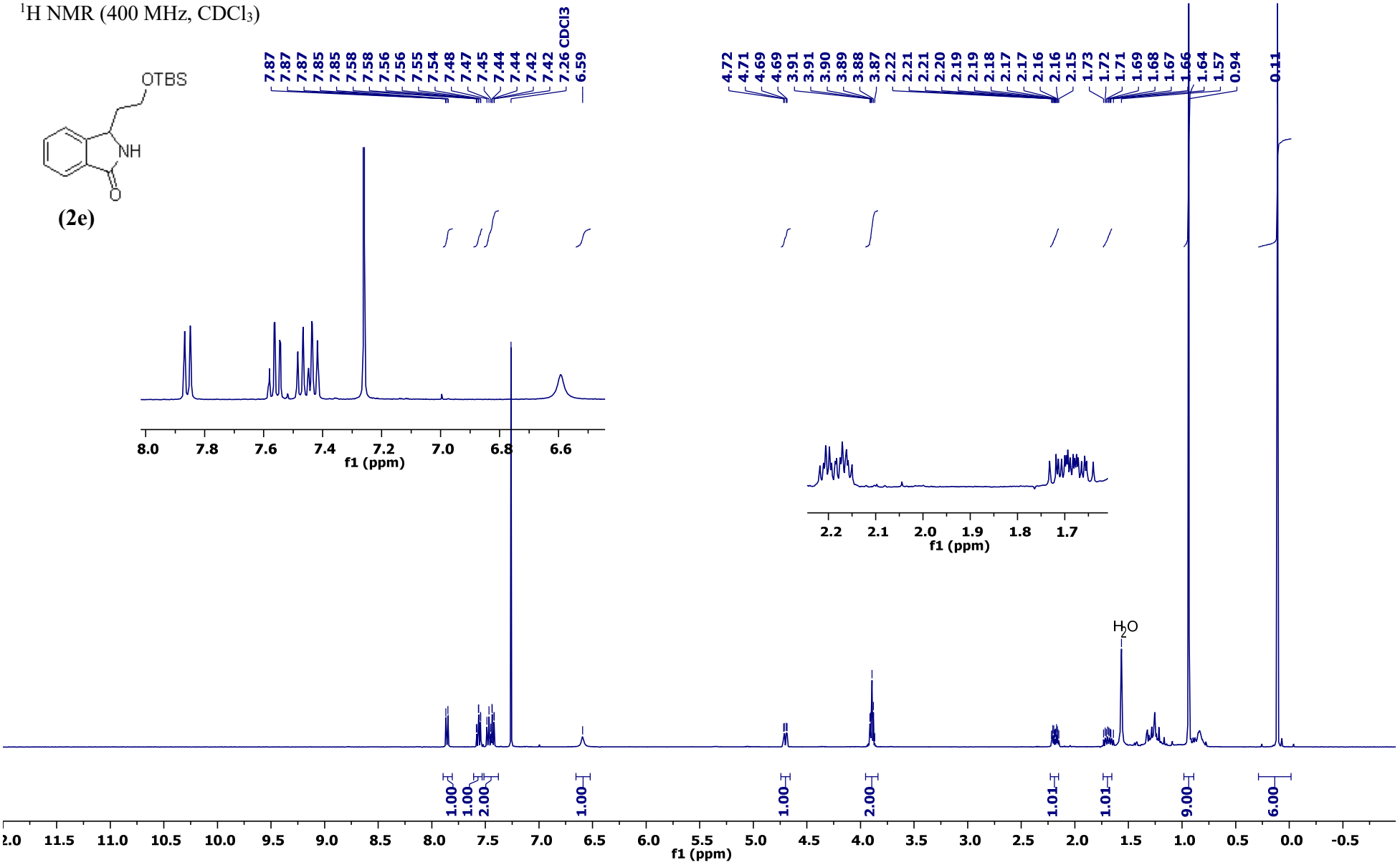
(2d)

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

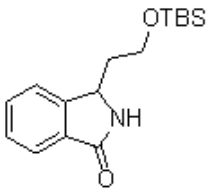


(2d)

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

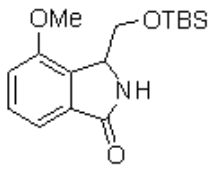


^{13}C NMR (100 MHz, $CDCl_3$)



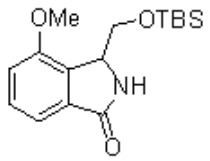
(2e)

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



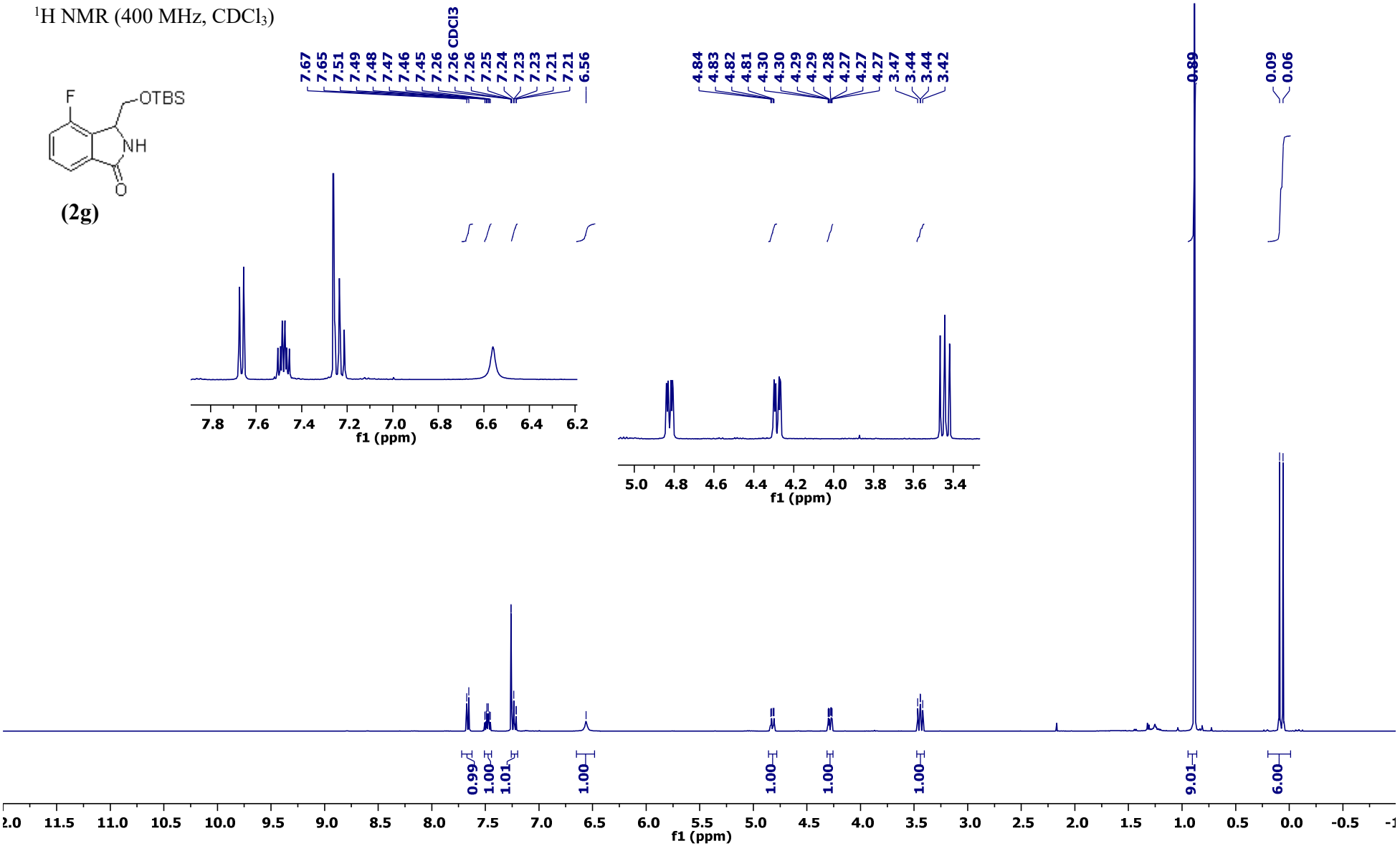
(2f)

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

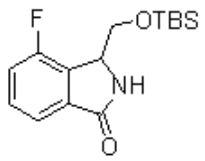


(2f)

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

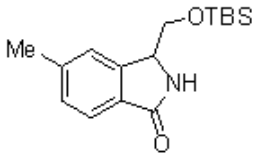


^{13}C NMR (100 MHz, $CDCl_3$)



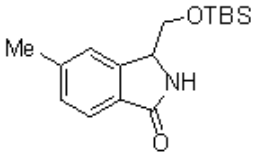
(2g)

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



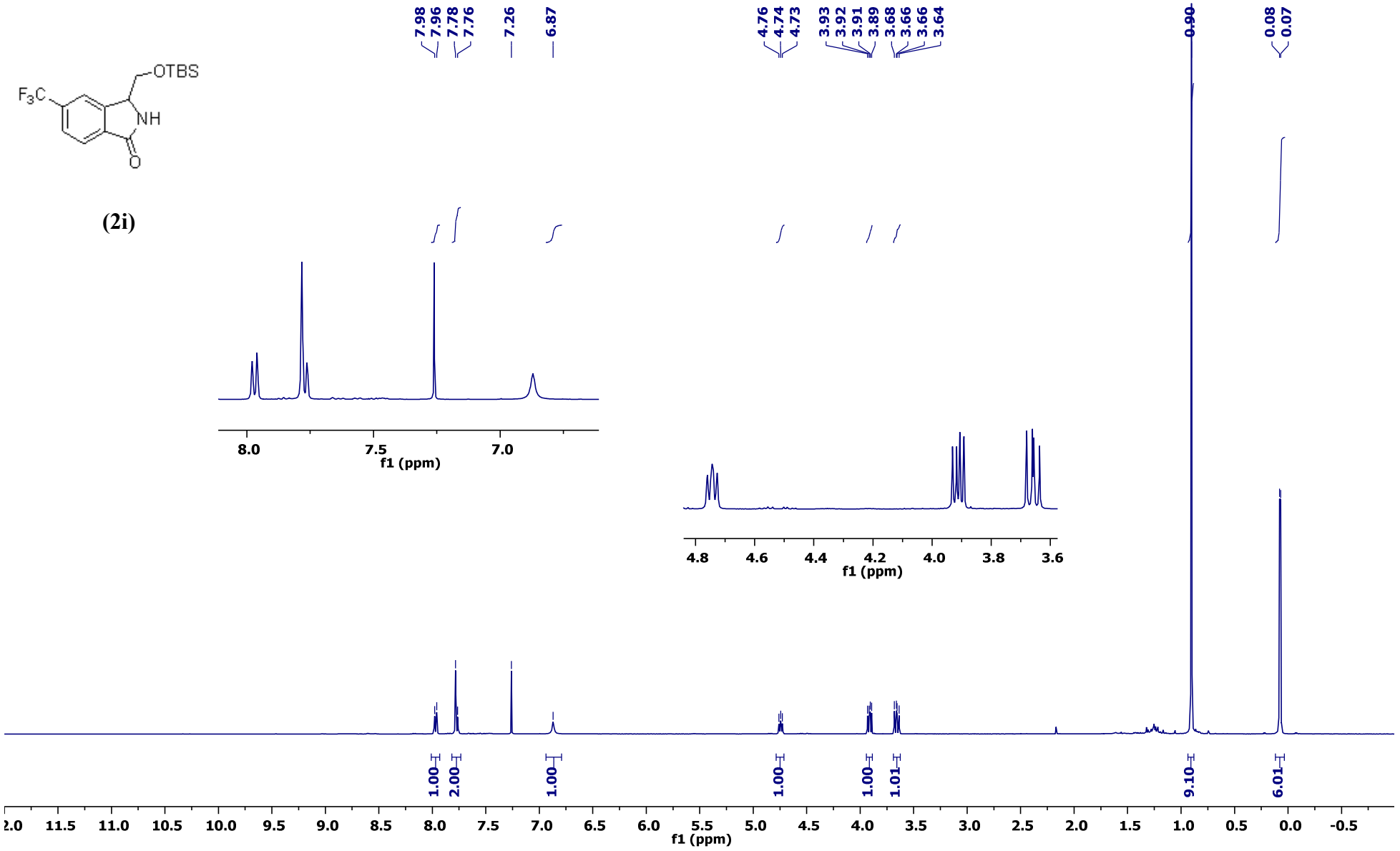
(2h)

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

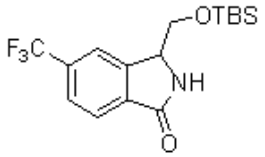


(2h)

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

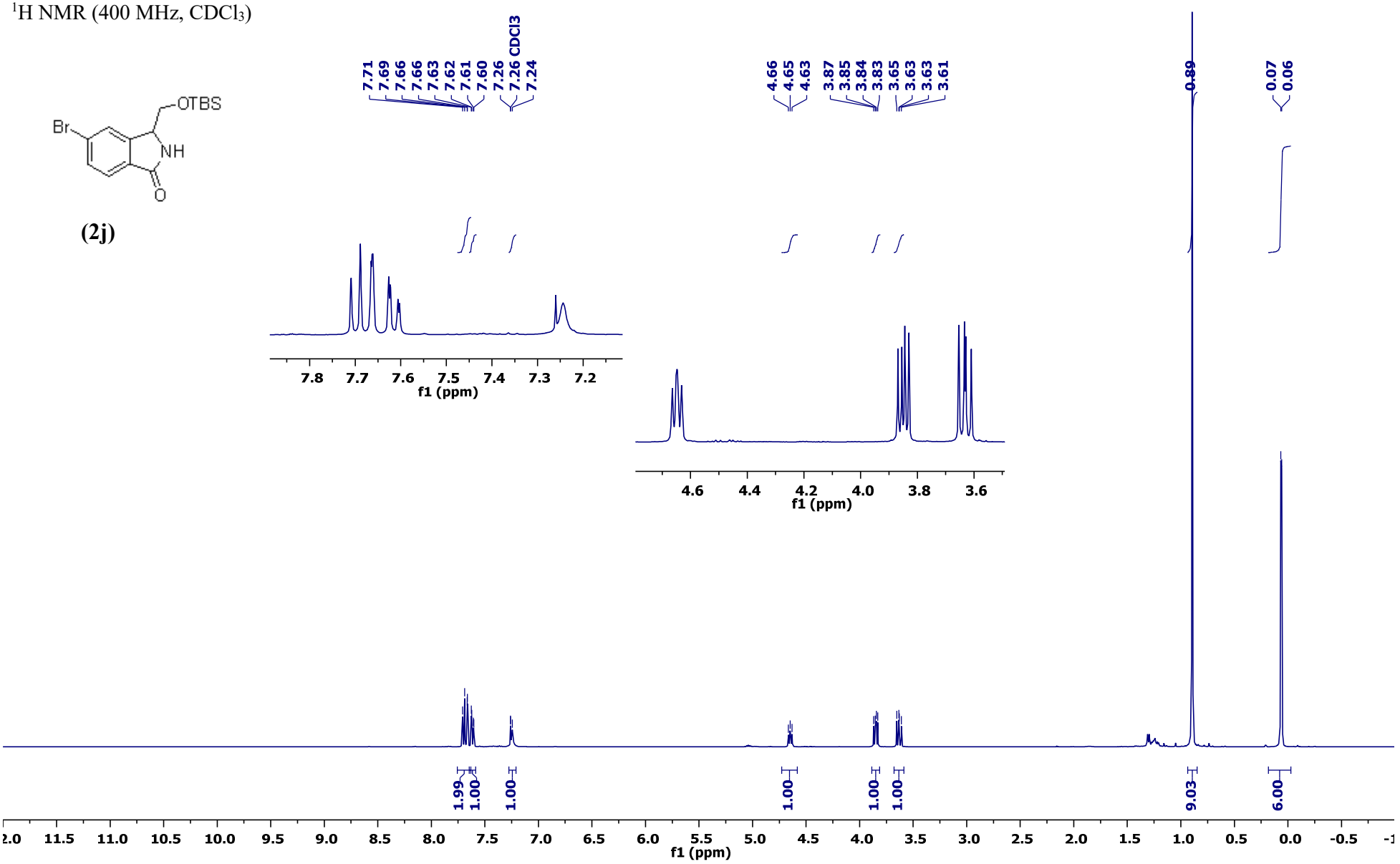


^{13}C NMR (100 MHz, $CDCl_3$)

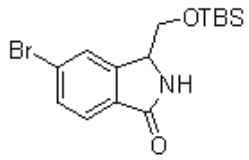


(2i)

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

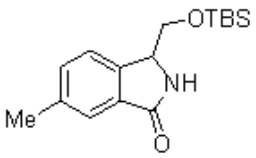


^{13}C NMR (100 MHz, $CDCl_3$)



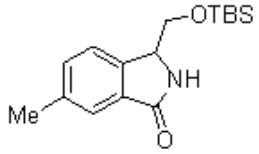
(2j)

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



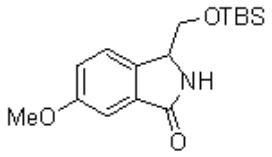
(2k)

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



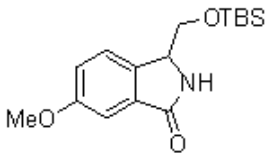
(2k)

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



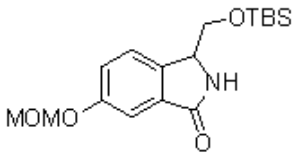
(2l)

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



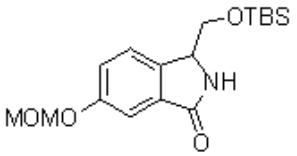
(2l)

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



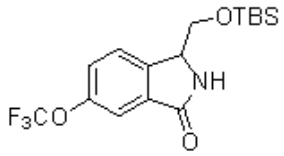
(2m)

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



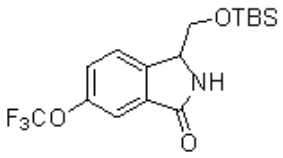
(2m)

^{1}H NMR (400 MHz, $C_2D_2Cl_4$)



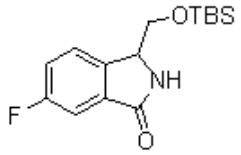
(2n)

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



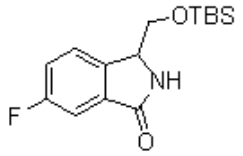
(2n)

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



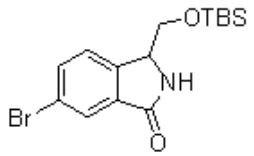
(2o)

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



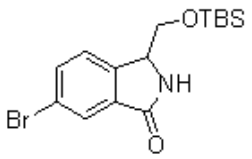
(2o)

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



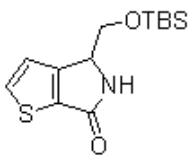
(2p)

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



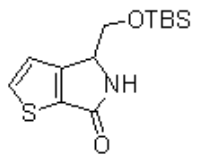
(2p)

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



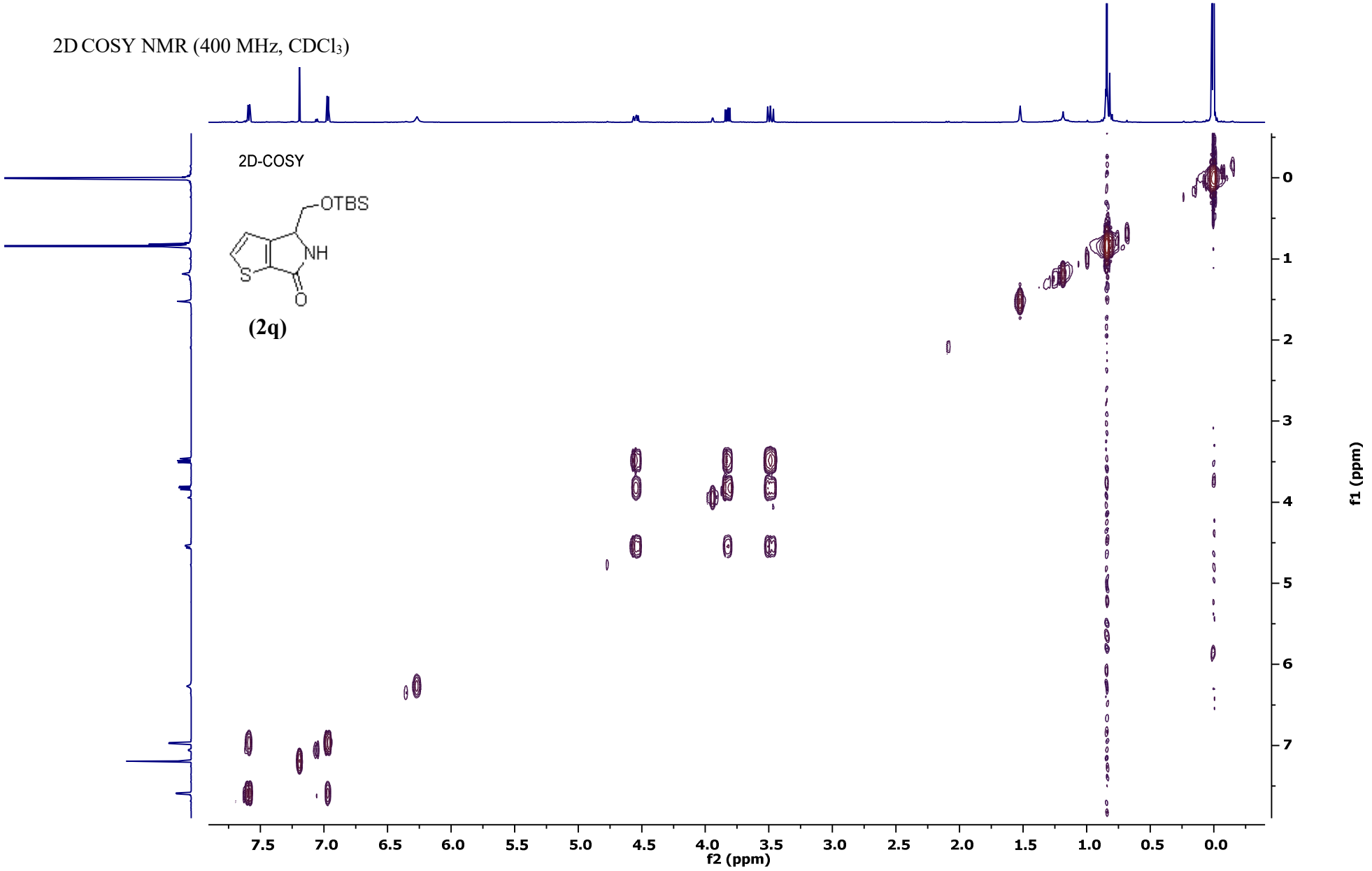
(2q)

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

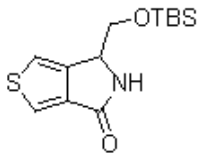


(2q)

2D COSY NMR (400 MHz, $CDCl_3$)

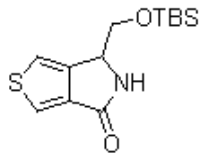


^{1}H NMR (400 MHz, $CDCl_3$)



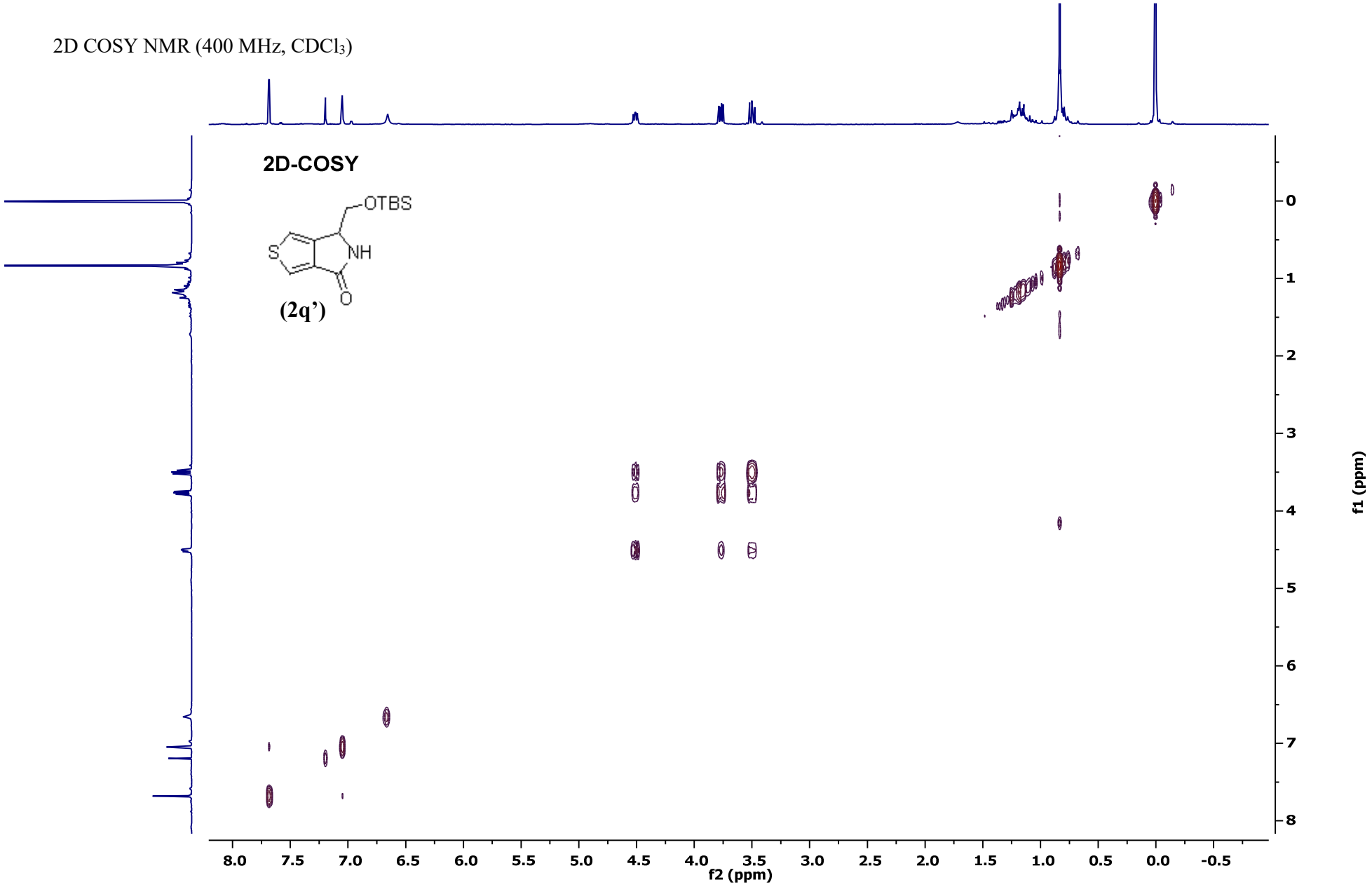
(2q')

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

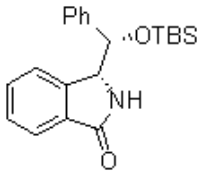


(2q')

2D COSY NMR (400 MHz, $CDCl_3$)

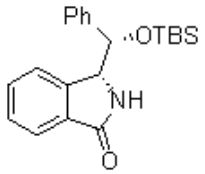


^{1}H NMR (400 MHz, $CDCl_3$)



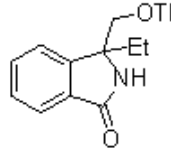
(2r)

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



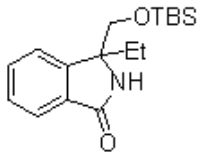
(2r)

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



(2s)

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



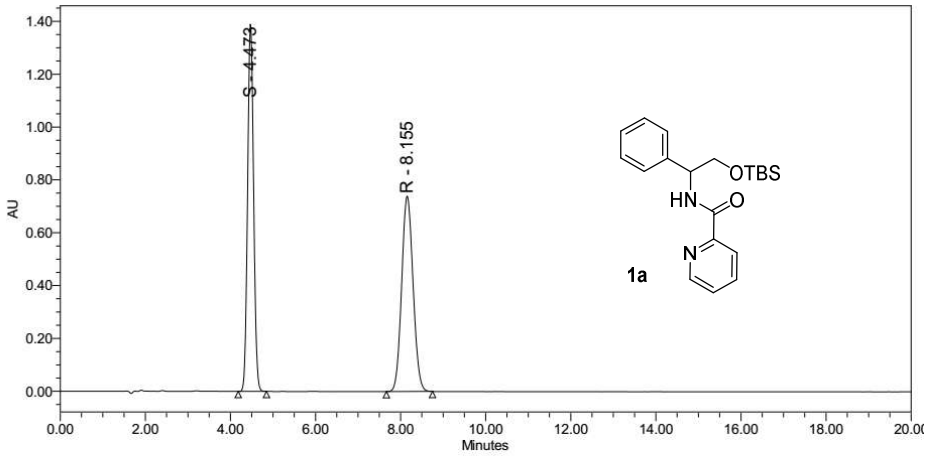
(2s)

5. HPLC data

SAMPLE INFORMATION

Sample Name:	#876-Ch-276-JB-656 rac		
Sample Type:	Unknown	Sample Set Name:	260819
Vial:	38	Acq. Method Set:	Iz_210_254_F1_90%A_10%B
Injection #:	1	Processing Method	Ch_276 LA1
Injection Volume:	10.00 ul	Channel Name:	W2489 ChA
Run Time:	20.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 210nm
Date Acquired:	8/26/2019 4:38:42 PM EEST	Acquired By:	System
Date Processed:	8/27/2019 9:06:34 AM EEST		

Lux Amylose-1 (4.6x150 mm)
10% IPA + Hex; F=1 mL/min; T=25oC



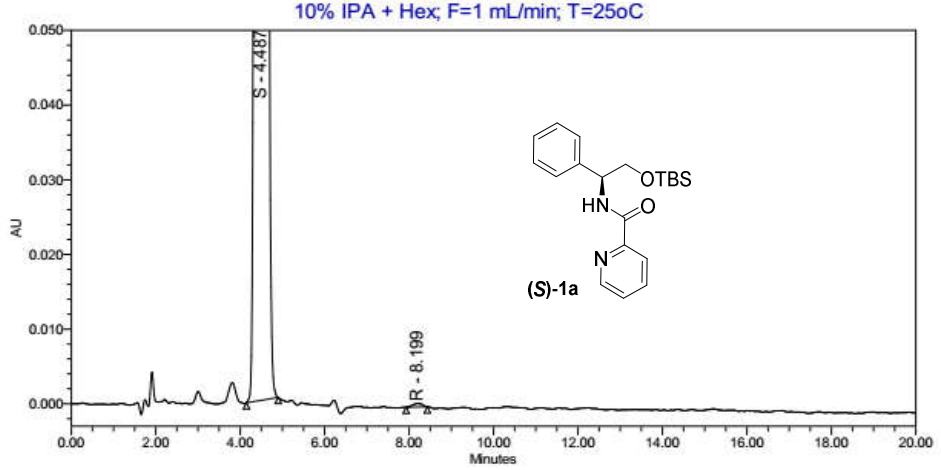
C = 1 mg/mL (10%IPA+Hex)

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	S	4.473	13651802	49.77	1393305	4726			0.153	1.678
2	R	8.155	13777447	50.23	739801	4383	9.807	2.314	0.290	3.883

SAMPLE INFORMATION

Sample Name:	#876-Ch-276-JB-663		
Sample Type:	Unknown	Sample Set Name:	260819
Vial:	39	Acq. Method Set:	Iz_210_254_F1_90%A_10%B
Injection #:	1	Processing Method	Ch_276 LA1
Injection Volume:	10.00 ul	Channel Name:	W2489 ChA
Run Time:	20.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 210nm
Date Acquired:	8/26/2019 4:59:32 PM EEST	Acquired By:	System
Date Processed:	8/27/2019 9:06:58 AM EEST		

Lux Amylose-1 (4.6x150 mm)
10% IPA + Hex; F=1 mL/min; T=25oC



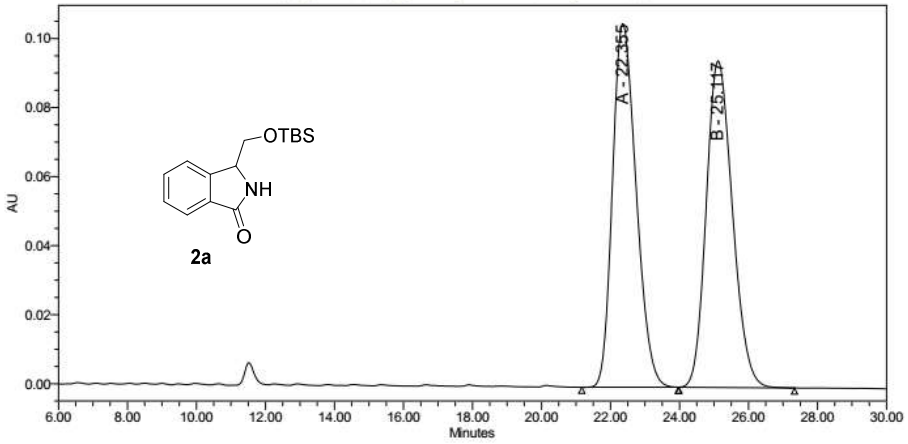
C = 1 mg/mL (10%IPA+Hex)

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime
1	S	4.487	32120072	99.98	2974539	3778			0.172	1.687
2	R	8.199	7615	0.02	472	4846	9.756	2.318	0.277	3.910

SAMPLE INFORMATION

Sample Name:	164-Ch-303-LL-5-53-5		
Sample Type:	Unknown	Sample Set Name:	11022020
Vial:	29	Acq. Method Set:	Iz_210_254_F1_70A_30B
Injection #:	1	Processing Method	LA1
Injection Volume:	10.00 ul	Channel Name:	W2489 ChA
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 210nm
Date Acquired:	2/11/2020 2:24:03 PM EET	Acquired By:	System
Date Processed:	2/11/2020 3:57:34 PM EET		

Lux Amylose 1(2)(4.6x150 mm)
Iz. 30% IPA / 70%HEX; F=1 mL/min; T=25oC



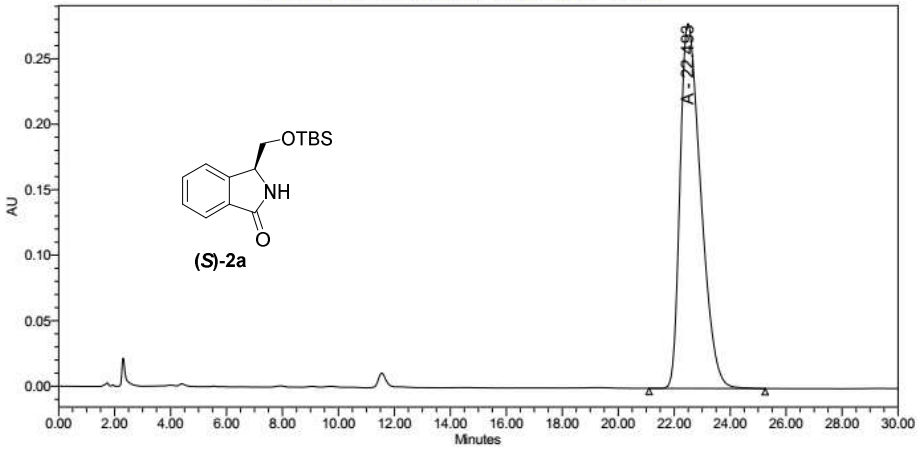
c~1 mg/ml diluent (10%IPA+Hex)

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Resolution	Selectivity	Width @ 50%	K Prime	RRT
1	A	22.355	5011655	50.08	105343	5004			0.744	12.800	
2	B	25.117	4996029	49.92	94570	5181	2.082	1.133	0.821	14.504	1.124

SAMPLE INFORMATION

Sample Name:	164-Ch-303-LL-5-53-4		
Sample Type:	Unknown	Sample Set Name:	11022020
Vial:	30	Acq. Method Set:	Iz_210_254_F1_70A_30B
Injection #:	1	Processing Method	LA1_
Injection Volume:	10.00 ul	Channel Name:	W2489 ChA
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	W2489 ChA 210nm
Date Acquired:	2/11/2020 2:56:14 PM EET	Acquired By:	System
Date Processed:	2/11/2020 4:01:39 PM EET		

Lux Amylose 1(2)(4.6x150 mm)
Iz. 30% IPA / 70%HEX; F=1 mL/min; T=25oC



c~1 mg/ml diluent (10%IPA+Hex)

	Peak Name	RT	Area	% Area	Height	EP Plate Count	Width @ 50%	K Prime
1	A	22.493	14351854	100.00	278290	4341	0.804	12.885