Supporting Information

Picolinate Directed Arene *meta*-C-H Amination via $FeCl_3$ Catalysis

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Materials and Methods

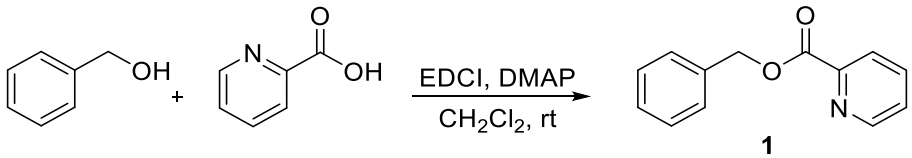
Proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were obtained on a Varian Inova 400 spectrometer at 400 MHz and 101 MHz, respectively, or a Varian Inova 500 at 500 MHz and 126 MHz, respectively, in $CDCl_3$, unless otherwise stated. The ^{1}H and ^{13}C NMR chemical shifts were measured relative to residual $CHCl_3$ as the internal reference (^{1}H: δ = 7.26 ppm; ^{13}C: δ = 77.00 ppm), unless otherwise stated. ^{1}H NMR data are reported as chemical shift (ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, app q = apparent quartet, qn = quintet, m = multiplet), and coupling constant (Hz). High resolution mass spectra (HRMS) were obtained using a TripleTOF®6600 Quadrupole mass spectrometer. Melting points were measured using an OptiMelt (Stanford Research Systems) and are uncorrected. Analytical thin layer chromatography (TLC) used EMD Chemicals TLC silica gel 60 F_{254} plates (0.040-0.063 mm) with visualization by UV light and/or $KMNO_4$, phosphomolybdic acid (PMA) and/or ninhydrin solution(s) followed by heating. Chromatographic purifications utilized preparative thin layer chromatography (PTLC) or flash chromatography using pre-packed SiO_2 columns on a medium pressure automated chromatograph. Unless otherwise noted, yields refer to isolated, purified material whose spectral data were consistent with assigned structures or, if known, were in agreement with literature values. All reactions were conducted under an argon atmosphere in oven-dried glassware with magnetic stirring, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification. Reaction solvents were purified via passage through activated, neutral alumina columns and stored under argon. $CsOH{\cdot}H_2O$ and pyridine were purchased from Aldrich Chem. Co. and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) was purchased from Oakwood Chemicals and used without purification.

Experimental Procedures and Analytical Data

General Procedure: Synthesis of Picolinate Esters

A mixture of alcohol (1 equiv), picolinic acid (1.2 equiv), EDCI (1.2 equiv) and DMAP (0.1 equiv) in CH_2Cl_2 (0.5 M) was stirred at 0 °C for 1 h, then warmed to room temperature for 12-24 h. All volatiles were removed *in vacuo*. The residue was purified using a commercial pre-packed SiO_2 on a medium pressure, automated chromatograph using EtOAc/hexanes to furnish the picolinate ester(s) in the indicated yield.

Benzyl picolinate (1)



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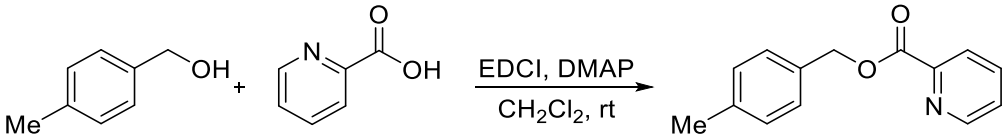
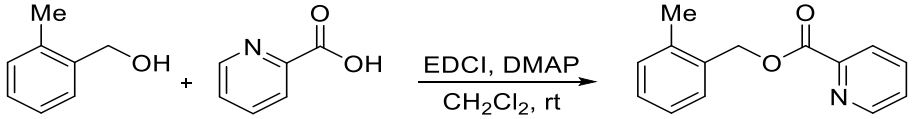
Following the general picolinate ester procedure, benzyl alcohol (500 mg, 4.627 mmol), picolinic acid (683 mg, 5.552 mmol), EDCI (1.06 g, 5.552 mmol) and DMAP (56 mg, 0.462 mmol) were stirred at rt in CH_2Cl_2 (20 mL) for 16 h. Chromatographic purification of the crude product afforded benzyl picolinate (**1**) (818 mg, 83%) as an oil whose spectral data were in agreement with literature values.[1] TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes).

4-Methylbenzyl picolinate



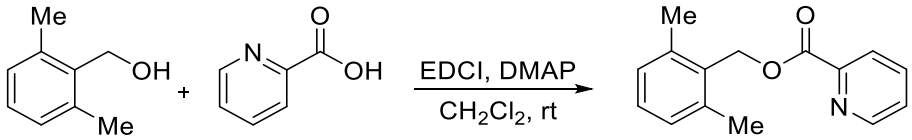
Following the general picolinate ester procedure, 4-methylbenzyl alcohol (200 mg, 1.638 mmol), picolinic acid (241 mg, 1.966 mmol), EDCI (376 mg, 1.966 mmol) and DMAP (20 mg, 0.163 mmol) were stirred at rt in in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 4-methylbenzyl picolinate (331 mg, 89%) as an oil. TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.2 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.79 (td, *J* = 7.7, 1.5 Hz, 1H), 7.45–7.41 (m, 1H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.16 (d, *J* = 7.7 Hz, 2H), 5.40 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.08, 149.96, 148.11, 138.31, 136.99, 132.68, 129.30, 128.82, 126.93, 125.28, 67.52, 21.28. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{13}NO_2+H]^+$ 228.1024, Found 228.1030.

2-Methylbenzyl picolinate



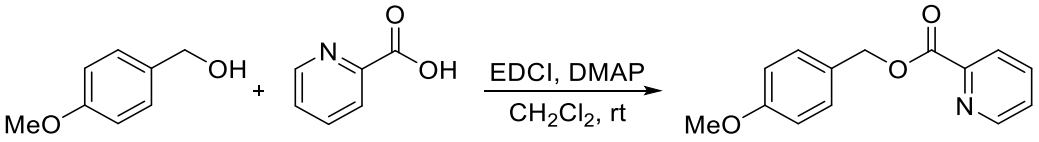
Following the general picolinate ester procedure, 2-methylbenzyl alcohol (200 mg, 1.638 mmol), picolinic acid (241 mg, 1.966 mmol), EDCI (376 mg, 1.966 mmol) and DMAP (20 mg, 0.163 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 2-methylbenzyl picolinate (290 mg, 78%) as a solid, mp 60-62 °C. TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.6 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.81 (tt, *J* = 7.8, 1.9 Hz, 1H), 7.48–7.40 (m, 2H), 7.28–7.18 (m, 3H), 5.46 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.05, 150.11, 148.08, 137.18, 137.04, 133.64, 130.50, 129.54, 128.73, 126.99, 126.14, 125.29, 66.02, 19.18. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{13}NO_2+H]^+$ 228.1025, Found 228.1031.

2,6-Dimethylbenzyl picolinate



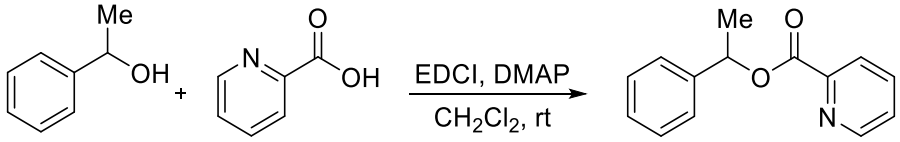
Following the general picolinate ester procedure, 2,6-dimethylbenzyl alcohol (200 mg, 1.470 mmol), picolinic acid (217 mg, 1.764 mmol), EDCI (338 mg, 1.764 mmol) and DMAP (17 mg, 0.147 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 2,6-dimethylbenzyl picolinate (276 mg, 78%) as a solid, mp 80-82 °C. TLC: $R_f \approx 0.4$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.7 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.79 (tt, *J* = 7.8, 1.9 Hz, 1H), 7.47–7.41 (m, 1H), 7.18–7.13 (m, 1H), 7.06 (d, *J* = 7.6 Hz, 2H), 5.51 (s, 2H), 2.45 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.26, 150.15, 148.09, 138.65, 137.01, 131.74, 128.94, 128.45, 126.92, 125.26, 62.72, 19.91. HRMS (ESI$^+$) Calcd. for $[C_{15}H_{15}NO_2+H]^+$ 242.1181, Found 242.1182.

4-Methoxybenzyl picolinate



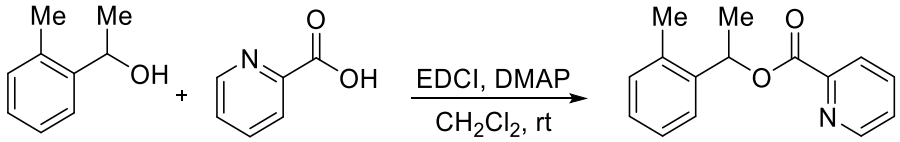
Following the general picolinate ester procedure, 4-methoxybenzyl alcohol (200 mg, 1.449 mmol), picolinic acid (213 mg, 1.739 mmol), EDCI (333 mg, 1.739 mmol) and DMAP (17 mg, 0.144 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 4-methoxybenzyl picolinate (302 mg, 86%) as an oil whose spectral data were in agreement with literature values.[2] TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes).

1-Phenylethyl picolinate



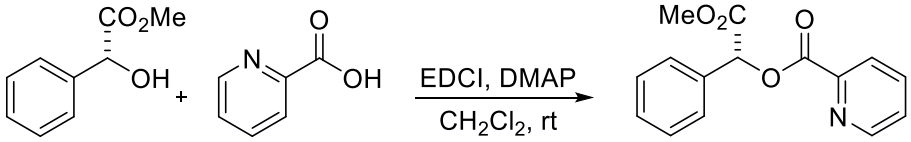
Following the general picolinate ester procedure, 1-phenylethan-1-ol (200 mg, 1.638 mmol), picolinic acid (241 mg, 1.966 mmol), EDCI (376 mg, 1.966 mmol) and DMAP (20 mg, 0.163 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 1-phenylethyl picolinate (319 mg, 86%) as an oil whose spectral data were in agreement with literature values.[3] TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes).

1-(*o*-Tolyl)ethyl picolinate



Following the general picolinate ester procedure, 1-(*o*-tolyl)ethan-1-ol (200 mg, 1.470 mmol), picolinic acid (217 mg, 1.764 mmol), EDCI (338 mg, 1.764 mmol) and DMAP (17 mg, 0.147 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 1-(*o*-tolyl)ethyl picolinate (265 mg, 75%) as an oil. TLC: $R_f \approx 0.4$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.7 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.8, 1.6 Hz, 1H), 7.57–7.51 (m, 1H), 7.48–7.40 (m, 1H), 7.25–7.10 (m, 3H), 6.38 (q, *J* = 6.6 Hz, 1H), 2.45 (s, 3H), 1.70 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.51, 150.06, 148.38, 139.81, 136.98, 134.96, 130.52, 127.85, 126.86, 126.44, 125.48, 125.22, 71.02, 21.50, 19.23. HRMS (ESI^+) Calcd. for $[C_{15}H_{15}NO_2+H]^+$ 242.1181, Found 242.1186.

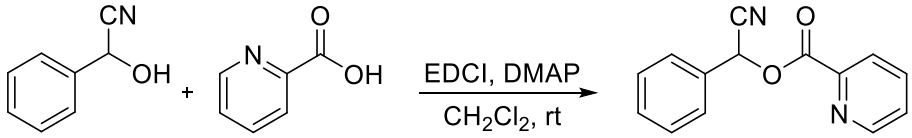
(*R*)-2-Methoxy-2-oxo-1-phenylethyl picolinate



Following the general picolinate ester procedure, methyl (*R*)-2-hydroxy-2-phenylacetate[4] (200 mg, 1.204 mmol), picolinic acid (177 mg, 1.445 mmol), EDCI (277 mg, 1.445 mmol) and DMAP (14 mg, 0.120 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 24 h. Chromatographic purification of the crude product afforded (*R*)-2-methoxy-2-oxo-1-phenylethyl picolinate (283 mg, 87%) as an oil. TLC: $R_f \approx 0.4$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.0 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.84 (td, *J* = 7.8, 1.3 Hz, 1H), 7.59 (dd, *J* = 7.4, 2.3 Hz, 2H), 7.51–7.46

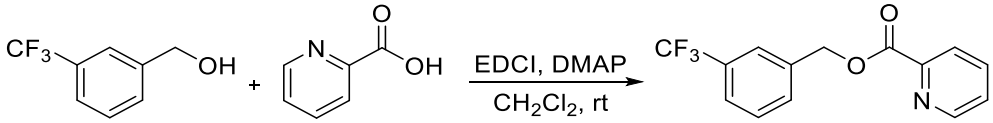
(m, 1H), 7.46–7.35 (m, 3H), 6.24 (s, 1H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.08, 164.38, 150.32, 147.34, 137.09, 133.65, 129.52, 129.02, 127.93, 127.32, 125.68, 75.52, 52.89. HRMS (ESI^+) Calcd. for $[C_{15}H_{13}NO_4+H]^+$ 272.0923, Found 272.0918.

Cyano(phenyl)methyl picolinate



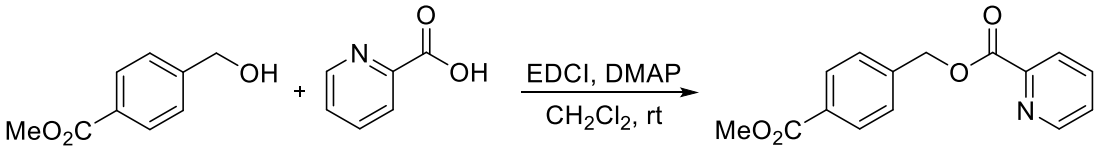
Following the general picolinate ester procedure, cyano(phenyl)methyl alcohol (200 mg, 1.503 mmol), picolinic acid (221 mg, 1.804 mmol), EDCI (345 mg, 1.804 mmol) and DMAP (18 mg, 0.150 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 24 h. Chromatographic purification of the crude product afforded cyano(phenyl)methyl picolinate (249 mg, 70%) as a viscous oil. TLC: R_f ≈ 0.4 (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.0 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.87 (td, *J* = 7.8, 1.6 Hz, 1H), 7.69–7.60 (m, 2H), 7.55–7.49 (m, 1H), 7.49–7.38 (m, 3H), 6.74 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.35, 150.42, 146.37, 137.30, 131.49, 130.66, 129.42, 128.24, 127.85, 126.00, 115.93, 64.13. HRMS (ESI^+) Calcd. for $[C_{14}H_{10}N_2O_2+H]^+$ 239.0820, Found 239.0822.

Synthesis of 3-(trifluoromethyl)benzyl picolinate



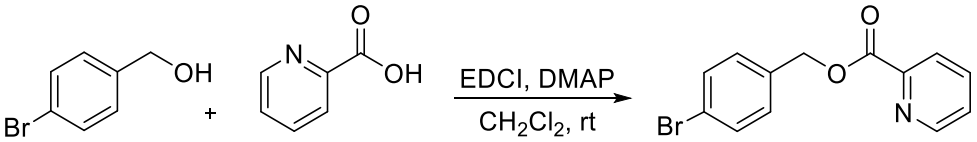
Following the general picolinate ester procedure, 3-(trifluoromethyl)benzyl alcohol (200 mg, 1.136 mmol), picolinic acid (167 mg, 1.363 mmol), EDCI (260 mg, 1.363 mmol) and DMAP (13 mg, 0.113 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 24 h. Chromatographic purification of the crude product afforded 3-(trifluoromethyl)benzyl picolinate (271 mg, 85%) as a solid, mp 61-63 °C. TLC: R_f ≈ 0.4 (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.7 Hz, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.85 (tt, *J* = 7.8, 2.0 Hz, 1H), 7.74 (s, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 7.7 Hz, 1H), 7.53–7.46 (m, 2H), 5.49 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.04, 150.14, 147.77, 137.22, 136.67, 132.01, 131.62, 131.30, 130.97, 130.65, 129.29, 128.65, 128.11, 127.29, 125.52, 125.49, 125.45, 125.42, 125.38, 125.35, 122.69, 119.98, 66.74. HRMS (ESI^+) Calcd. for $[C_{14}H_{10}F_3NO_2+H]^+$ 282.0742, Found 282.0750.

4-(Methoxycarbonyl)benzyl picolinate



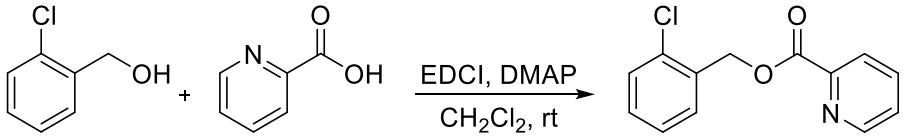
Following the general picolinate ester procedure, 4-(methoxycarbonyl)benzyl alcohol (200 mg, 1.204 mmol), picolinic acid (177 mg, 1.445 mmol), EDCI (277 mg, 1.445 mmol) and DMAP (14 mg, 0.120 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded (286 mg, 88%) as a solid, mp 57-59 °C, whose spectral data were in agreement with literature values.[5] TLC: R_f ≈ 0.4 (50% EtOAc/hexanes).

4-Bromobenzyl picolinate



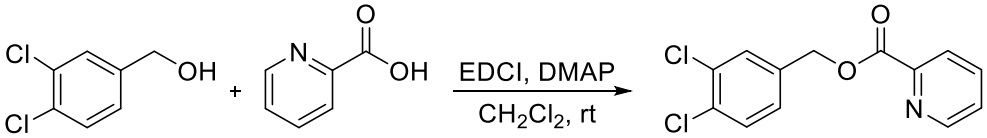
Following the general picolinate ester procedure, 4-bromobenzyl alcohol (200 mg, 1.075 mmol), picolinic acid (158 mg, 1.290 mmol), EDCI (247 mg, 1.290 mmol) and DMAP (13 mg, 0.107 mmol) were stirred at rt in in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 4-bromobenzyl picolinate (266 mg, 85%) as a solid, mp 48-50 °C. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 5.4 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.84 (td, *J* = 7.8, 1.6 Hz, 1H), 7.54–7.44 (m, 3H), 7.36 (d, *J* = 8.3 Hz, 2H), 5.40 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.93, 149.95, 147.75, 137.05, 134.60, 131.75, 130.29, 127.08, 125.32, 122.51, 66.70. HRMS (ESI$^+$) Calcd. for $[C_{13}H_{10}BrNO_2+H]^+$ 291.9973, Found 291.9982.

2-Chlorobenzyl picolinate



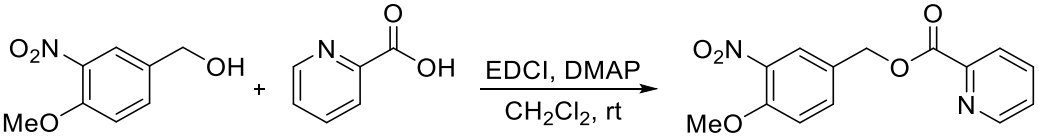
Following the general picolinate ester procedure, 2-chlorobenzyl alcohol (200 mg, 1.408 mmol), picolinic acid (207 mg, 1.690 mmol), EDCI (323 mg, 1.690 mmol) and DMAP (17 mg, 0.140 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 2-chlorobenzyl picolinate (288 mg, 83%) as a solid, mp 50-52 °C, whose spectral data were in agreement with literature values.[6,7] TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes).

3,4-Dichlorobenzyl picolinate



Following the general picolinate ester procedure, 3,4-dichlorobenzyl alcohol (200 mg, 0.961 mmol), picolinic acid (141 mg, 1.153 mmol), EDCI (220 mg, 1.153 mmol) and DMAP (11 mg, 0.096 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 3,4-dichlorobenzyl picolinate (246 mg, 82%) as a solid whose spectral data were in agreement with literature values.[5] TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes).

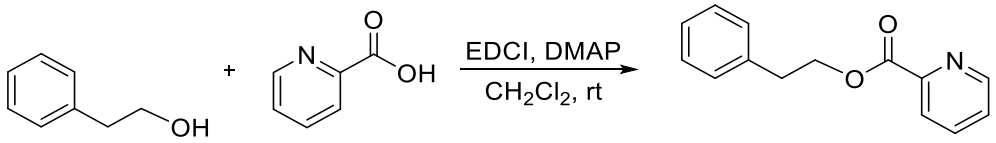
4-Methoxy-3-nitrobenzyl picolinate



Following the general picolinate ester procedure, (4-methoxy-3-nitrophenyl)methanol (200 mg, 1.092 mmol), picolinic acid (161 mg, 1.311 mmol), EDCI (250 mg, 1.311 mmol) and DMAP (13 mg, 0.109 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 4-methoxy-3-nitrobenzyl picolinate (257 mg 82% yield) as a solid, mp 119-120 °C. TLC: $R_f \approx 0.4$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.1 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 1.8 Hz, 1H), 7.85 (t, *J* = 1.4 Hz, 1H), 7.69 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.55–7.44 (m, 1H), 7.09 (d, *J* = 8.7 Hz, 1H), 5.41 (s, 2H), 3.96 (s, 3H); ^{13}C NMR

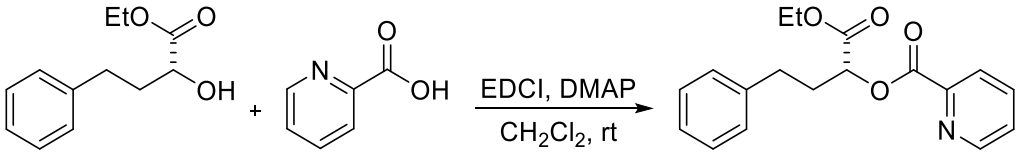
(101 MHz, $CDCl_3$) δ 164.93, 153.00, 149.99, 147.57, 139.45, 137.09, 134.81, 128.02, 127.19, 126.33, 125.38, 113.64, 65.90, 56.64. HRMS (ESI^+) Calcd. for $[C_{14}H_{12}N_2O_5+H]^+$ 289.0824, Found 289.0819.

Phenethyl picolinate



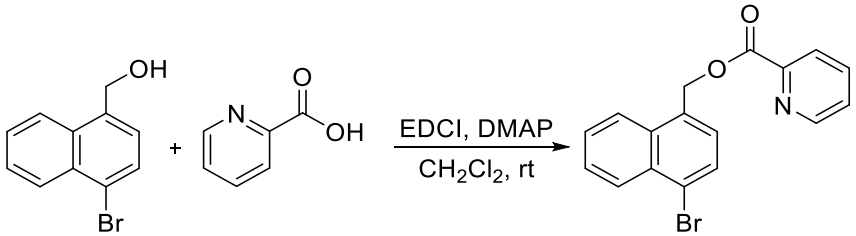
EDCI (943 mg, 4.917 mmol) was added to a 0 °C solution of 2-phenylethanol (0.5 g, 4.098 mmol), and picolinic acid (555 mg, 4.508 mmol) in CH_2Cl_2 (20 mL) followed by DMAP (50 mg, 0.409 mmol). After stirring at rt for 24 h, the reaction mixture was concentrated in *vacuo*. The residue was purified using a commercial pre-packed SiO_2 (1g column) on a medium pressure, automated chromatograph using 40% EtOAc/hexanes to give phenethyl picolinate as viscous oil (790 mg, 85%) whose spectral data were in agreement with literature values.[8] TLC: $R_f \approx 0.4$ (60% EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 8.81–8.74 (m, 1H), 8.12–8.06 (m, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.52–7.45 (m, 1H), 7.36–7.21 (m, 5H), 4.62 (t, *J* = 7.5 Hz, 2H), 3.14 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.05, 149.92, 148.06, 137.36, 136.99, 128.99, 128.57, 126.88, 126.67, 125.13, 66.34, 35.16.

(*R*)-1-Ethoxy-1-oxo-4-phenylbutan-2-yl picolinate



Following the general picolinate ester procedure, ethyl (*R*)-2-hydroxy-4-phenylbutanoate (200 mg, 0.961 mmol), picolinic acid (141 mg, 1.153 mmol), EDCI (200 mg, 1.153 mmol) and DMAP (11 mg, 0.096 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded (*R*)-1-ethoxy-1-oxo-4-phenylbutan-2-yl picolinate (219 mg, 73%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 8.82–8.87 (m, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.8, 1.7 Hz, 1H), 7.52–7.47 (m, 1H), 7.31–7.24 (m, 2H), 7.23–7.15 (m, 3H), 5.31 (dd, *J* = 8.0, 5.1 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.89–2.79 (m, 2H), 2.39–2.35 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.80, 164.61, 150.24, 147.51, 140.45, 137.08, 128.64, 128.57, 127.23, 126.34, 125.57, 72.96, 61.67, 32.76, 31.58, 14.25. HRMS (ESI^+) Calcd. for $[C_{18}H_{19}NO_4+H]^+$ 314.1392, Found 314.1393.

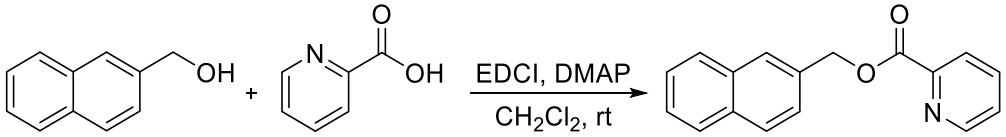
(4-Bromonaphthalen-1-yl)methyl picolinate



Following the general picolinate ester procedure, (4-bromonaphthalen-1-yl)methanol (200 mg, 0.851 mmol), picolinic acid (125 mg, 1.021 mmol), EDCI (195 mg, 1.021 mmol) and DMAP (10 mg, 0.085 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of

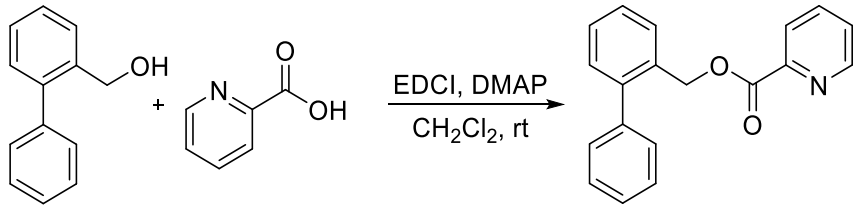
the crude product afforded (4-bromonaphthalen-1-yl)methyl picolinate (220 mg, 76%) as a solid, mp 106-108 °C. TLC: $R_f \approx 0.4$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72–8.69 (m, 1H), 8.30–8.23 (m, 1H), 8.12–8.07 (m, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.78–7.70 (m, 2H), 7.62–7.54 (m, 2H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.43–7.37 (m, 1H), 5.83 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.90, 150.03, 147.74, 136.99, 132.73, 132.09, 131.17, 129.41, 127.99, 127.51, 127.37, 127.02, 125.30, 124.23, 123.95, 65.25. HRMS (ESI$^+$) Calcd. for $[C_{17}H_{12}BrNO_2+H]^+$ 342.0130, Found 342.0127.

Naphthalen-2-ylmethyl picolinate



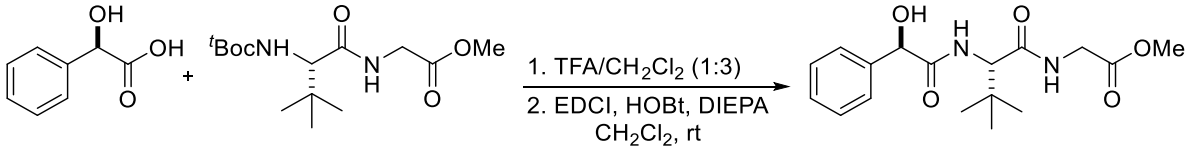
Following the general picolinate ester procedure, napthalen-2-ylmethyl alcohol (200 mg, 1.265 mmol), picolinic acid (186 mg, 1.518 mmol), EDCI (291 mg, 1.518 mmol) and DMAP (15 mg, 0.126 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded naphthalen-2-ylmethyl picolinate (258 mg, 78%) as a solid whose spectral data were in agreement with literature values.[9] TLC: $R_f \approx 0.5$ (50% EtOAc/hexanes).

[1,1'-Biphenyl]-2-ylmethyl picolinate



Following the general picolinate ester procedure, [1,1'-biphenyl]-2-ylmethanol (200 mg, 1.086 mmol), picolinic acid (160 mg, 1.304 mmol), EDCI (249 mg, 1.304 mmol) and DMAP (13 mg, 0.108 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 24 h. Chromatographic purification of the crude product afforded [1,1'-biphenyl]-2-ylmethyl picolinate (232 mg, 74%) as an oil. TLC: $R_f \approx$ 0.4 (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.7 Hz, 1H), 8.04 (d, *J* = 7.9 Hz, 1H), 7.84–7.78 (m, 1H), 7.63–7.56 (m, 1H), 7.49–7.43 (m, 1H), 7.43–7.30 (m, 8H), 5.38 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.88, 150.14, 148.11, 142.50, 140.48, 137.03, 133.05, 130.32, 129.62, 129.28, 128.49, 128.39, 127.79, 127.48, 126.98, 125.28, 65.72. HRMS (ESI$^+$) Calcd. for $[C_{19}H_{15}NO_2+H]^+$ 290.1181, Found 290.1188.

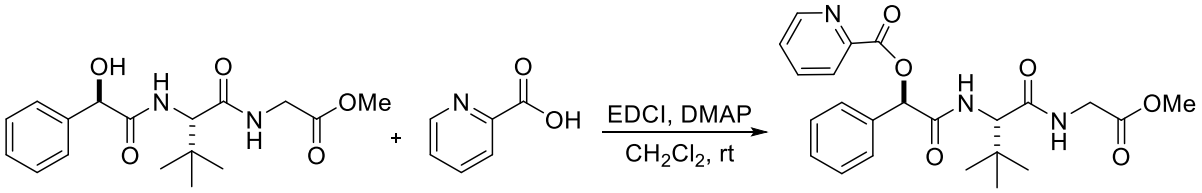
Methyl ((*S*)-2-((*R*)-2-hydroxy-2-phenylacetamido)-3,3-dimethylbutanoyl)glycinate



N-[(1,1-Dimethylethoxy)carbonyl]-3-methyl-L-valyl-glycine methyl ester[10] (500 mg, 1.655 mmol) in TFA/CH_2Cl_2 (5 mL, 1:3) was stirred at 0 °C under argon. After 4 h, the reaction mixture was concentrated in *vacuo*. The crude product (372 mg, 1.177 mmol) was dissolved in CH_2Cl_2 (10 mL) and (*R*)-mandelic acid (214 mg, 1.412 mmol), EDCI (247 mg, 1.294 mmol), HOBt (174 mg, 1.294 mmol) and DIEPA (0.6 mL, 3.531) were added sequentially. After stirring at rt for 24 h, water (15 mL) was added and the resulting aqueous layer was separated and extracted with CH_2Cl_2

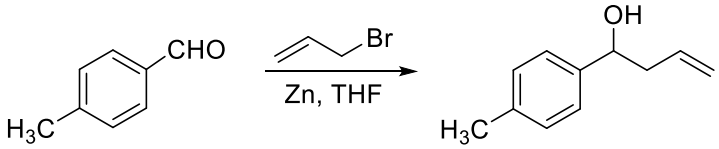
(3 × 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified using a commercial, pre-packed SiO_2 column on a medium pressure, automated chromatograph using 60% EtOAc/hexanes to furnish the title amide (416 mg, 68%) as a solid, mp 73-75 °C. TLC: $R_f \approx 0.5$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.28 (m, 4H), 7.12 (d, *J* = 9.6 Hz, 1H), 5.05 (s, 1H), 4.48 (d, *J* = 9.7 Hz, 1H), 4.35 (br s, 1H), 3.94 (dd, *J* = 18.0, 6.1 Hz, 1H), 3.69 (s, 3H), 3.47 (dd, *J* = 18.0, 4.3 Hz, 1H), 0.90 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.17, 170.56, 169.99, 139.70, 128.73, 128.55, 126.90, 74.20, 60.14, 52.23, 40.82, 35.07, 26.34. HRMS (ESI^+) Calcd. for $[C_{17}H_{24}N_2O_5+H]^+$ 337.1763, Found 337.1768.

(*R*)-2-(*S*)-1-(2-methoxy-2-oxoethyl)amino)-3,3-dimethyl-1-oxobutan-2-yl)amino)-2-oxo-1-phenylethyl picolinate



Following the general picolinate ester procedure, methyl (*S*)-2-(*R*)-2-hydroxy-2-phenylacetamido)-3,3-dimethylbutanoyl)glycinate (200 mg, 0.595 mmol), picolinic acid (87 mg, 0.714 mmol), EDCI (136 mg, 0.714 mmol) and DMAP (7 mg, 0.059 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 18 h. Chromatographic purification of the crude product afforded (*R*)-2-(*S*)-1-((2-methoxy-2-oxoethyl)amino)-3,3-dimethyl-1-oxobutan-2-yl)amino)-2-oxo-1-phenylethyl picolinate (225 mg, 86%) as a viscous oil. TLC: $R_f \approx 0.4$ (30% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.4 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.8, 1.7 Hz, 1H), 7.59–7.41 (m, 4H), 7.31–7.28 (m, 2H), 6.33 (s, 1H), 4.58 (d, *J* = 9.5 Hz, 1H), 3.94 (dd, *J* = 17.7, 6.2 Hz, 1H), 3.64 (s, 3H), 3.36 (dd, *J* = 17.7, 5.0 Hz, 1H), 3.07 (brs, 1H), 0.93 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.53, 169.99, 168.37, 163.68, 150.19, 147.20, 137.16, 135.24, 129.22, 128.83, 127.96, 127.42, 125.29, 76.31, 60.02, 52.04, 40.85, 35.07, 26.43. HRMS (ESI^+) Calcd. for $[C_{23}H_{27}N_3O_6+H]^+$ 442.1978, Found 442.1975.

1-(*p*-Tolyl)but-3-en-1-ol

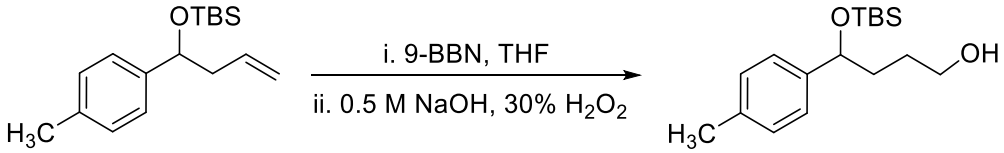


Allyl bromide (2.15 mL, 24.968 mmol) was added dropwise to a 0 °C solution of zinc powder (1.08 g, 16.645 mmol) in dry THF (20 mL). After stirring for 15 min at 0 °C, a solution of *p*-tolualdehyde (1.0 g, 8.322 mmol) in dry THF (5 mL) was added and then the reaction mixture was warmed to rt. After 25 h, the reaction mixture was filtered through a diatomaceous earth pad and the filter cake was washed with EtOAc (20 mL). The combined filtrates were concentrated in *vacuo* and the residue was purified on a commercial pre-packed SiO_2 column using a medium pressure, automated chromatograph using 10% EtOAc/hexanes to give 1-(*p*-tolyl)but-3-en-1-ol as a viscous oil (1.2 g, 89%) whose spectral data were in agreement with literature values.[11] TLC: $R_f \approx 0.4$ (20% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.3 Hz, 2H), 7.20 (d, *J* = 7.5 Hz, 2H), 5.91–5.77 (m, 1H), 5.24–5.12 (m, 2H), 4.74 (dd, *J* = 7.5, 5.5 Hz, 1H), 2.59–2.49 (m, 2H), 2.38 (s, 3H).

tert-Butyldimethyl ((1-(_p_-tolyl)but-3-en-1-yl)oxy)silane

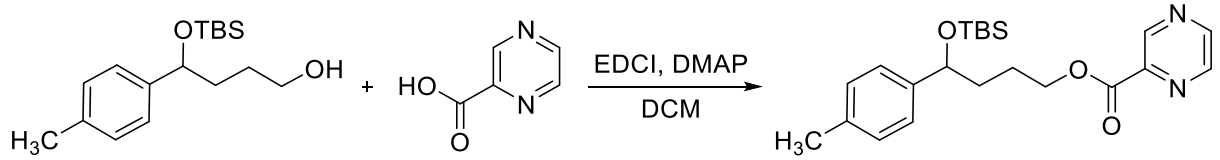
tert-Butyldimethylchlorosilane (TBSCl) (1.34 g, 8.888 mmol) was added portion wise to a stirring, rt solution of 1-(*p*-tolyl)but-3-en-1-ol (1.2 g, 7.407 mmol) and imidazole (755 mg, 11.111 mmol) in dry CH_2Cl_2 (35 mL). After 20 h, water (20 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The extracts and organic layer were combined, washed with brine (15 mL), dried with Na_2SO_4, and concentrated in *vacuo*. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using 5% EtOAc/hexanes to obtain *tert*-butyldimethyl ((1-(*p*-tolyl)but-3-en-1-yl)oxy)silane as a colorless oil (1.8 g, 89%). TLC: $R_f \approx 0.6$ (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 5.86–5.69 (m, 1H), 5.05–4.97 (m, 2H), 4.64 (dd, *J* = 7.3, 5.2 Hz, 1H), 2.53–2.28 (m, 5H), 0.87 (s, 9H), 0.02 (s, 3H), -0.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.15, 136.37, 135.43, 128.64, 125.76, 116.70, 74.80, 45.57, 25.83, 21.13, 18.25, -4.62, -4.92. HRMS (ESI^+) Calcd. for $[C_{17}H_{28}OSi]^+$ 276.1909, Found 276.1900.

4-((_tert_-Butyldimethylsilyl)oxy)-4-(_p_-tolyl)butan-1-ol



A solution of 9-BBN (14.2 mL, 7.174 mmol, 0.5 M in THF) was added to a 0 °C solution of the above *tert*-butyldimethyl ((1-(*p*-tolyl)but-3-en-1-yl)oxy)silane (1.8 g, 6,522 mmol) in dry THF (30 mL) at 0 °C and then stirred at room temperature. After 18 h, 0.5 M aq. NaOH (12 mL) and 30% H_2O_2 (12 mL) were added sequentially. After 4 h, the reaction mixture was diluted with EtOAc (15 mL), the organic phase was separated, and the aq. phase was extracted with EtOAc (3 × 15 mL). The extracts and the organic layer were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using 25% EtOAc/hexanes to obtain 4-((*tert*-butyldimethylsilyl)oxy)-4-(*p*-tolyl)butan-1-ol as a viscous oil (1 g, 55%). TLC: $R_f \approx 0.5$ (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 4.75–4.65 (m, 1H), 3.68–3.54 (m, 2H), 2.33 (s, 3H), 1.83–1.68 (m, 2H), 1.66–1.54 (m, 3H), 0.89 (s, 9H), 0.02 (s, 3H), -0.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.11, 136.37, 128.69, 125.74, 74.61, 63.05, 37.22, 28.60, 25.85, 21.11, 18.23, -4.62, -5.01. HRMS (ESI^+) Calcd. for $[C_{17}H_{30}O_2Si]^+$ 294.2015, Found 294.2015.

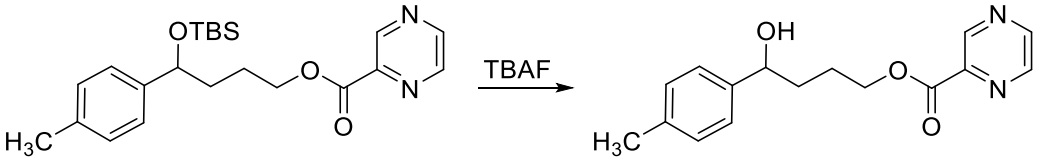
4-((_tert_-Butyldimethylsilyl)oxy)-4-(_p_-tolyl)butyl pyrazine-2-carboxylate



EDCI (1.02 g, 5.357 mmol) was added to a 0 °C solution of 4-((*tert*-butyldimethylsilyl)oxy)-4-(*p*-tolyl)butan-1-ol (1 g, 3.571 mmol), and pyrazine-2-carboxylic acid (658 mg, 5.357 mmol) in

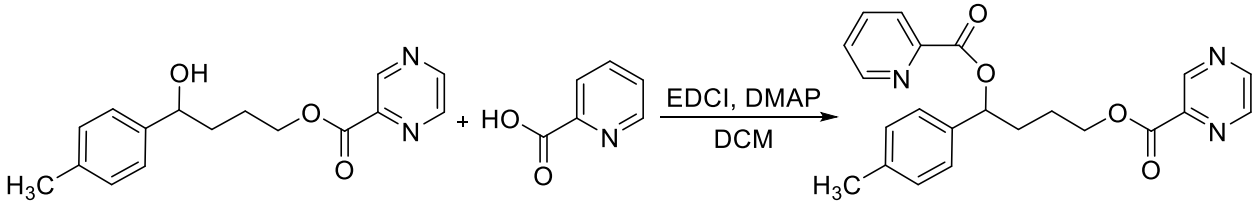
CH_2Cl_2 (30 mL) followed by DMAP (43 mg, 0.357 mmol). After stirring at rt for 18 h, the reaction mixture was concentrated in *vacuo*. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using 40% EtOAc/hexanes to give 4-((*tert*-butyldimethylsilyl)oxy)-4-(*p*-tolyl)butyl pyrazine-2-carboxylate as a viscous oil (1.1 g, 82%). TLC: $R_f \approx 0.4$ (60% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (d, *J* = 1.4 Hz, 1H), 8.75 (d, *J* = 2.4 Hz, 1H), 8.72 (dd, *J* = 2.4, 1.4 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 4.70 (t, *J* = 5.4 Hz, 1H), 4.48–4.38 (m, 2H), 2.32 (s, 3H), 1.91–1.74 (m, 4H), 0.88 (s, 9H), 0.02 (s, 3H), -0.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.87, 147.53, 146.23, 144.43, 143.55, 142.00, 136.54, 128.76, 125.71, 74.20, 36.99, 25.83, 24.67, 21.11, 18.19, -4.61, -4.99. HRMS (ESI$^+$) Calcd. for $[C_{22}H_{32}N_2O_3Si+H]^+$ 401.2260, Found 401.2199.

4-Hydroxy-4-(*p*-tolyl)butyl pyrazine-2-carboxylate



To a solution of 4-((*tert*-butyldimethylsilyl)oxy)-4-(*p*-tolyl)butyl pyrazine-2-carboxylate (800 mg, 2.072 mmol) in THF (20 mL) cooled to 0 °C was added TBAF (2.5 mL, 2.487 mmol, 1.0 M in THF). After stirring for 3 h at rt, the mixture was diluted with saturated aqueous NH_4Cl (10 mL). Two layers were separated and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layer and organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using 60% EtOAc/hexanes to give 4-hydroxy-4-(*p*-tolyl)butyl pyrazine-2-carboxylate as a viscous oil (450 mg, 80%). TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (d, *J* = 1.3 Hz, 1H), 8.74 (d, *J* = 2.4 Hz, 1H), 8.69 (dd, *J* = 2.6, 1.3 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 4.71 (t, *J* = 6.0 Hz, 1H), 4.53–4.38 (m, 2H), 2.33 (s, 3H), 2.21 (br s, 1H), 1.99–1.82 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.86, 147.59, 146.21, 144.41, 143.44, 141.36, 137.42, 129.21, 125.77, 73.81, 66.23, 35.20, 25.08, 21.10. HRMS (ESI$^+$) Calcd. for $[C_{16}H_{18}N_2O_3+H]^+$ 287.1396, Found 287.1393.

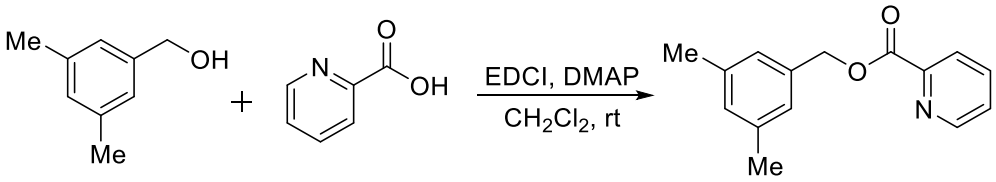
Synthesis of 4-(picolinoyloxy)4-(*p*-tolyl)butyl pyrazine-2-carboxylate



EDCI (317 mg, 1.654 mmol) was added to a 0 °C solution of 4-hydroxy-4-(*p*-tolyl)butyl pyrazine-2-carboxylate (0.3 g, 1.103 mmol) and picolinic acid (202 mg, 1.654 mmol) in CH_2Cl_2 (15 mL) followed by DMAP (13 mg, 0.111 mmol). After stirring at rt for 14 h, the reaction mixture was concentrated in *vacuo*. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using 80% EtOAc/hexanes to give 4-(picolinoyloxy)4-(*p*-tolyl)butyl pyrazine-2-carboxylate as a viscous oil (260 mg, 62%). TLC: $R_f \approx$ 0.4 (100% EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (s, 1H), 8.81–8.64 (m, 3H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.8, 1.8 Hz, 1H), 7.48–7.41 (m, 1H), 7.36 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 6.09 (t, *J* = 6.9 Hz, 1H), 4.47 (td, *J* = 6.7, 2.2 Hz, 2H), 2.31 (s, 4H), 2.17–2.08 (m,

1H), 2.04–1.94 (m, 1H), 1.90–1.83 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.46, 163.83, 149.96, 148.14, 147.63, 146.25, 144.43, 143.36, 138.07, 136.89, 136.68, 129.28, 126.84, 126.65, 125.22, 76.92, 65.78, 32.56, 25.00, 21.16. HRMS (ESI$^+$) Calcd. for $[C_{22}H_{21}N_4O_4+H]^+$ 392.1610, Found 392.1614.

Synthesis of 3,5-dimethylbenzyl picolinate

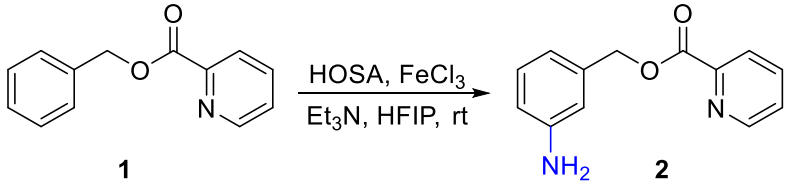


Following the general picolinate ester procedure, (3,5-dimethylphenyl)methanol (250 mg, 1.835 mmol), picolinic acid (271 mg, 2.205 mmol), EDCI (422 mg, 2.205 mmol) and DMAP (22 mg, 0.183 mmol) were stirred at rt in CH_2Cl_2 (10 mL) for 16 h. Chromatographic purification of the crude product afforded 3,5-dimethylbenzyl picolinate (390 mg, 88%) as a viscous oil. TLC: $R_f \approx$ 0.5 (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.7 Hz, 1H), 8.14 (d, *J* = 7.7 Hz, 1H), 7.83 (td, *J* = 7.7, 1.8 Hz, 1H), 7.50–7.43 (m, 1H), 7.10 (s, 2H), 6.97 (s, 1H), 5.39 (s, 2H), 2.32 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.03, 149.92, 148.06, 138.17, 136.96, 135.38, 130.06, 126.87, 126.47, 125.27, 67.65, 21.22.

General Procedure: Amination of Picolinate Esters

To a stirring, 0 °C solution of HOSA (0.4 mmol, 2 equiv) in 1,1,1,3,3,3-hexafluoroisopropanol (2 mL) was added Et_3N (0.4 mmol, 2 equiv) under an argon atmosphere. After 15 min, the picolinate ester (0.2 mmol, 1 equiv) and anhydrous $FeCl_3$ (5 mol%; n.b., deliquescent) were added sequentially while maintaining an inert atmosphere. After complete consumption of the picolinate ester (6-24 h, monitored by TLC), the reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with saturated aqueous Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified on a commercial pre-packed SiO_2 column using a medium pressure, automated chromatograph equipped with a UV detector and eluted with MeOH/CH_2Cl_2 or EtOAc/hexanes to furnish aminated picolinate(s) in the indicated yield (Table 2). Variations in reaction conditions are noted in the legend of Table 2 for select substrates.

3-Aminobenzyl picolinate (2)



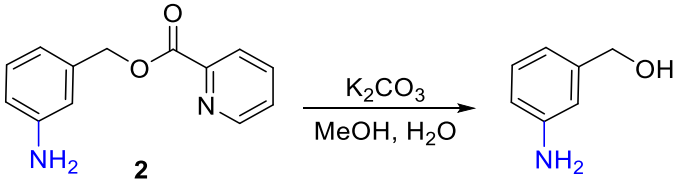
1 **2**

Following the general amination procedure, benzyl picolinate (**1**) (50 mg, 0.234 mmol), $FeCl_3$ (1.8 mg, 0.011 mmol), Et_3N (65 µL, 0.469 mmol), and HOSA (53 mg, 0.469 mmol) were stirred at rt in HFIP (2.3 mL) for 10 h. Chromatographic purification of the crude product afforded 3-aminobenzyl picolinate (**2**) (33 mg, 72%) as an oil. TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.7 Hz, 1H), 8.12 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.81 (td, *J* = 7.7, 1.8 Hz, 1H), 7.48–7.42 (m, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.79 (t, *J* = 1.9 Hz, 1H), 6.63 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.35 (s, 2H), 3.71 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

165.10, 150.01, 148.11, 146.78, 137.07, 136.82, 129.61, 127.01, 125.37, 118.66, 115.17, 115.07, 67.63. HRMS (ESI$^+$) Calcd. for $[C_{13}H_{12}N_2O_2+H]^+$ 229.0971, Found 229.0982.

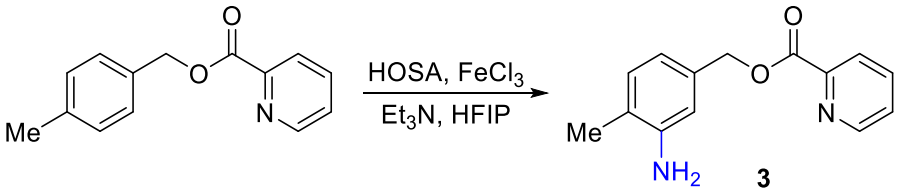
5 mmol scale: 1 (1.1 g, 5.164 mmol), $FeCl_3$ (41.8 mg, 0.2582 mmol), Et_3N (1.43 mL, 10.328 mmol), and HOSA (1.16 g, 10.328 mmol) were stirred at rt in HFIP (50 mL) for 15 h. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using a gradient of 1-3% MeOH/CH_2Cl_2 to obtain 3-aminobenzyl picolinate (**2**) (763 mg, 65%) as an oil and unreacted **1** (55 mg, 5%) as an oil.

Hydrolysis of 2 to 3-Aminobenzyl alcohol



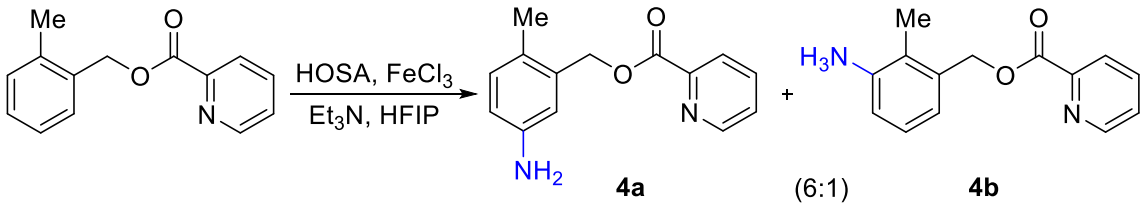
K_2CO_3 (121 mg, 0.877 mmol) was added portionwise to a 0 °C solution of 3-aminobenzyl picolinate (**2**) (100 mg, 0.438 mmol) in MeOH/H_2O (10:1, 6.6 mL). After stirring at rt for 21 h, the reaction mixture was concentrated in *vacuo* and the residue was diluted with H_2O (5 mL) and EtOAc (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The organic layer and the organic extracts were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using 3% MeOH/CH_2Cl_2 to give 3-aminobenzyl alcohol as a white solid (43 mg, 81%) whose spectral data were in agreement with literature values.[12]. TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.95 (t, J = 7.7 Hz, 1H), 6.56 (t, J = 1.9 Hz, 1H), 6.50–6.37 (m, 2H), 5.05–4.91 (m, 3H), 4.35 (d, J = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 148.47, 143.17, 128.54, 114.08, 112.39, 112.15, 63.29.

3-Amino-4-methylbenzyl picolinate (3)



Following the general amination procedure, 4-methylbenzyl picolinate (50 mg, 0.220 mmol), $FeCl_3$ (1.7 mg, 0.011 mmol), Et_3N (61 µL, 0.440 mmol), and HOSA (49 mg, 0.440 mmol) were stirred at rt in HFIP (2.2 mL) for 16 h. Chromatographic purification of the crude product afforded 3-amino-4-methylbenzyl picolinate (**3**) (37 mg, 70%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 4.7 Hz, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.81 (td, J = 7.8, 1.8 Hz, 1H), 7.48–7.42 (m, 1H), 7.03 (d, J = 7.5 Hz, 1H), 6.81 (d, J = 6.8 Hz, 2H), 5.34 (s, 2H), 3.64 (s, 2H), 2.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.15, 150.01, 148.22, 144.84, 137.04, 134.49, 130.69, 126.97, 125.36, 122.69, 118.97, 115.15, 67.70, 17.28. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{14}N_2O_2+H]^+$ 243.1128, Found 243.1128.

5-Amino-2-methylbenzyl picolinate (4a) and 3-amino-2-methylbenzyl picolinate (4b)

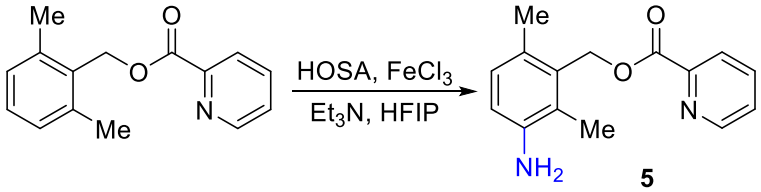


Following the general amination procedure, 2-methylbenzyl picolinate (50 mg, 0.220 mmol), $FeCl_3$ (1.7 mg, 0.011 mmol), Et_3N (61 µL, 0.440 mmol), and HOSA (49 mg, 0.440 mmol) were stirred at rt in HFIP (2.2 mL) for 16 h. Chromatographic purification of the crude product afforded 5-amino-2-methylbenzyl picolinate (**4a**) (34 mg) as an oil and 5-amino-2-methylbenzyl picolinate (**4b**) (5 mg) as an oil for a 75% combined yield.

5-Amino-2-methylbenzyl picolinate (4a): TLC: $R_f \approx 0.5$ (70% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.3 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.7, 1.7 Hz, 1H), 7.49–7.41 (m, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 2.6 Hz, 1H), 6.58 (dd, *J* = 8.1, 2.5 Hz, 1H), 5.36 (s, 2H), 3.60 (br s, 2H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.04, 150.07, 148.10, 144.57, 137.05, 134.35, 131.25, 126.98, 126.65, 125.30, 116.36, 115.36, 65.98, 18.17. HRMS (ESI^+) Calcd. for $[C_{14}H_{14}N_2O_2+H]^+$ 243.1128, Found 243.1128.

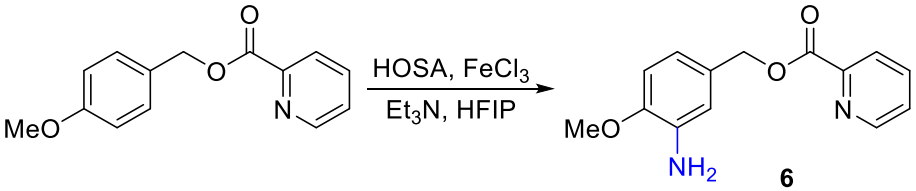
3-Amino-2-methylbenzyl picolinate (4b): TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.3 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.82 (td, *J* = 7.8, 1.8 Hz, 1H), 7.49–7.49 (m, 1H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.91 (d, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 5.45 (s, 2H), 3.68 (br s, 2H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07, 150.16, 148.20, 145.14, 137.07, 134.28, 126.99, 126.59, 125.35, 121.64, 120.75, 116.01, 66.75, 12.77. HRMS (ESI^+) Calcd. for $[C_{14}H_{14}N_2O_2+H]^+$ 243.1128, Found 243.1132.

3-Amino-2,6-dimethylbenzyl picolinate (5)



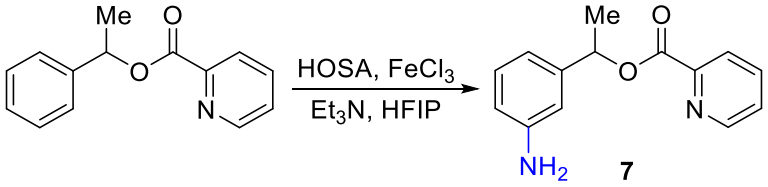
Following the general amination procedure, 2,6-dimethylbenzyl picolinate (50 mg, 0.207 mmol), $FeCl_3$ (1.6 mg, 0.010 mmol), Et_3N (57 µL, 0.414 mmol), and HOSA (46 mg, 0.414 mmol) were stirred at rt in HFIP (2 mL) for 16 h. Chromatographic purification of the crude product afforded 3-amino-2,6-dimethylbenzyl picolinate (**5**) (41 mg, 78%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.7 Hz, 1H), 8.04 (d, *J* = 7.9 Hz, 1H), 7.77 (tt, *J* = 7.8, 1.9 Hz, 1H), 7.46–7.39 (m, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 5.49 (s, 2H), 3.53 (br s, 2H), 2.35 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.14, 150.07, 148.05, 143.07, 136.94, 131.94, 128.48, 128.40, 126.84, 125.20, 123.29, 116.09, 62.91, 19.46, 13.23. HRMS (ESI^+) Calcd. for $[C_{15}H_{16}N_2O_2+H]^+$ 257.1284, Found 257.1283.

3-Amino-4-methoxybenzyl picolinate (6)



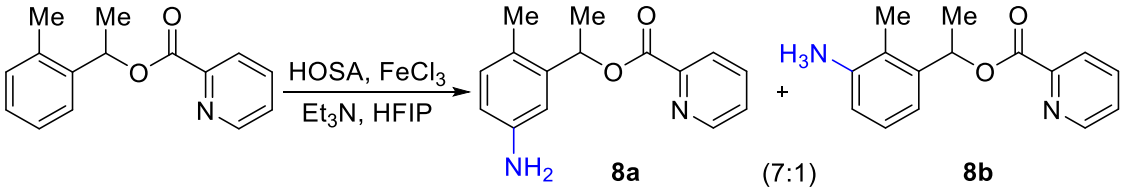
Following the general amination procedure, 4-methoxybenzyl picolinate (50 mg, 0.205 mmol), $FeCl_3$ (1.6 mg, 0.010 mmol), Et_3N (57 µL, 0.411 mmol), and HOSA (46 mg, 0.411 mmol) were stirred at rt in HFIP (2 mL) for 6 h. Chromatographic purification of the crude product afforded 3-amino-4-methoxybenzyl picolinate (**6**) (37 mg, 71%) as an oil. TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.6 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.7, 1.8 Hz, 1H), 7.50–7.39 (m, 1H), 6.85 (s, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 5.32 (s, 2H), 3.82 (s, 3H), 3.82–3.79 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.19, 149.98, 148.27, 147.57, 137.02, 136.35, 128.35, 126.92, 125.32, 119.40, 115.64, 110.19, 67.82, 55.61. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{14}N_2O_3+H]^+$ 281.0896, Found 281.0900.

1-(3-Aminophenyl)ethyl picolinate (7)



Following the general amination procedure, 1-phenylethyl picolinate (50 mg, 0.220 mmol), $FeCl_3$ (1.7 mg, 0.011 mmol), Et_3N (61 µL, 0.440 mmol), and HOSA (49 mg, 0.440 mmol) were stirred at rt in HFIP (2.2 mL) for 16 h. Chromatographic purification of the crude product afforded 1-(3-aminophenyl)ethyl picolinate (**7**) (36 mg, 68%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.6 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.8, 1.7 Hz, 1H), 7.45 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.80 (t, *J* = 1.9 Hz, 1H), 6.61 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.11 (q, *J* = 6.6 Hz, 1H), 3.71 (br s, 2H), 1.69 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.57, 150.07, 148.50, 146.70, 142.67, 137.02, 129.62, 126.89, 125.35, 116.49, 114.87, 112.96, 74.05, 22.32. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{14}N_2O_2+H]^+$ 265.0947, Found 265.0952.

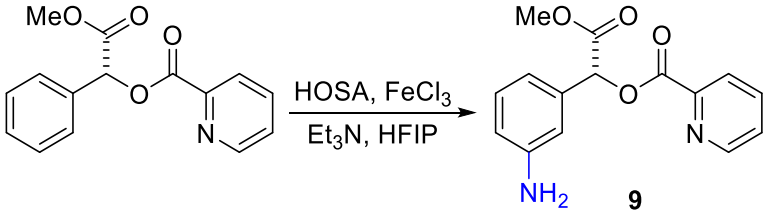
1-(5-Amino-2-methylphenyl)ethyl picolinate (8a) and 1-(3-amino-2-methylphenyl)ethyl picolinate (8b)



Following the general amination procedure, 1-(*o*-tolyl)ethyl picolinate (50 mg, 0.207 mmol), $FeCl_3$ (1.6 mg, 0.010 mmol), Et_3N (57 µL, 0.414 mmol), and HOSA (46 mg, 0.414 mmol) were stirred at rt in HFIP (2 mL) for 16 h. Chromatographic purification of the crude product afforded 1-(5-amino-2-methylphenyl)ethyl picolinate (**8a**) (35 mg) as an oil and 1-(3-amino-2-methylphenyl)ethyl picolinate (**8b**) (4 mg) as an oil for a 75% combined yield.

1-(5-Amino-2-methylphenyl)ethyl picolinate (**8a**): TLC: $R_f \approx 0.5$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.7 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.82 (td, *J* = 7.8, 1.8 Hz, 1H), 7.49–7.44 (m, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 2.4 Hz, 1H), 6.54 (dd, *J* = 8.0, 2.5 Hz, 1H), 6.29 (q, *J* = 6.6 Hz, 1H), 3.60 (br s, 2H), 2.32 (s, 3H), 1.66 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.58, 150.08, 148.55, 144.79, 140.74, 137.04, 131.39, 126.90, 125.36, 124.82, 114.93, 112.45, 71.20, 21.61, 18.35. HRMS (ESI$^+$) Calcd. for $[C_{15}H_{16}N_2O_2+H]^+$ 257.1284, Found 257.1287.
1-(3-Amino-2-methylphenyl)ethyl picolinate (**8b**): TLC: $R_f \approx 0.6$ (70% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, *J* = 4.4 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.7, 1.4 Hz, 1H), 7.53–7.44 (m, 1H), 7.08 (t, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.68 (d, *J* = 7.5 Hz, 1H), 6.45 (q, *J* = 6.5 Hz, 1H), 3.66 (br s, 2H), 2.24 (s, 3H), 1.72 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.57, 150.15, 148.53, 144.90, 140.47, 137.03, 126.89, 126.81, 125.30, 119.56, 116.24, 114.95, 71.62, 21.69, 12.47. HRMS (ESI$^+$) Calcd. for $[C_{15}H_{16}N_2O_2+H]^+$ 257.1284, Found 257.1284.

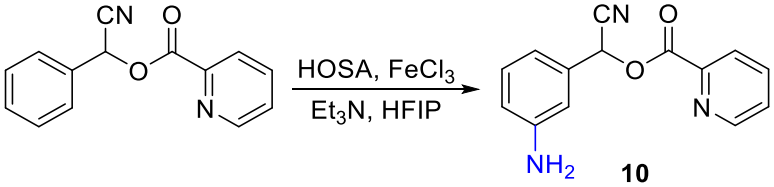
(*R*)-1-(3-Aminophenyl)-2-methoxy-2-oxoethyl picolinate (9)



9

Following the general amination procedure, (*R*)-2-methoxy-2-oxo-1-phenylethyl picolinate (50 mg, 0.184 mmol), $FeCl_3$ (1.4 mg, 0.009 mmol), Et_3N (51 µL, 0.368 mmol), and HOSA (41 mg, 0.368 mmol) were stirred at 40 °C in HFIP (1.8 mL) for 24 h. Chromatographic purification of the crude product afforded (*R*)-1-(3-aminophenyl)-2-methoxy-2-oxoethyl picolinate (**9**) (36 mg, 71%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.2 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.84 (td, *J* = 7.8, 1.6 Hz, 1H), 7.51–7.46 (m, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.90 (s, 1H), 6.70 (d, *J* = 7.9 Hz, 1H), 6.13 (s, 1H), 3.79 (br s, 2H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.20, 164.44, 150.29, 147.40, 147.06, 137.09, 134.60, 129.95, 127.31, 125.72, 118.10, 116.19, 114.20, 75.60, 52.90. HRMS (ESI$^+$) Calcd. for $[C_{15}H_{14}N_2O_4+H]^+$ 287.1026, Found 287.1029.

(3-Aminophenyl)(cyano)methyl picolinate (10)

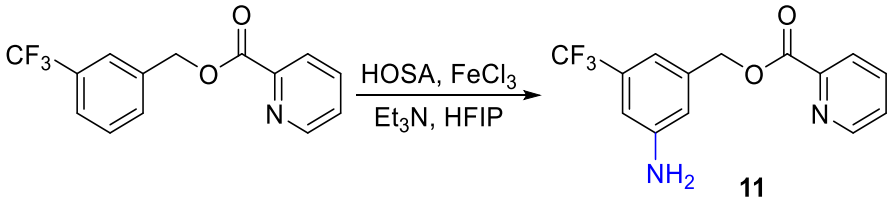


10

Following the general amination procedure, cyano(phenyl)methyl picolinate (50 mg, 0.210 mmol), $FeCl_3$ (1.7 mg, 0.010 mmol), Et_3N (117 µL, 0.840 mmol), and HOSA (94 mg, 0.840 mmol) were stirred at 0 ˚C in HFIP (2.1 mL) for 8 h. Chromatographic purification of the crude product afforded (3-aminophenyl)(cyano)methyl picolinate (**10**) (21 mg, 41%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.4 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.92–7.81 (m, 1H), 7.58–7.47 (m, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H),

6.94 (s, 1H), 6.78–6.70 (d, *J* = 7.8 Hz, 1H), 6.65 (s, 1H), 3.85 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.41, 150.47, 147.39, 146.53, 137.32, 132.52, 130.39, 127.84, 126.05, 118.08, 117.09, 116.07, 114.26, 64.18. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{11}N_3O_2+H]^+$ 254.0924, Found 254.0925.

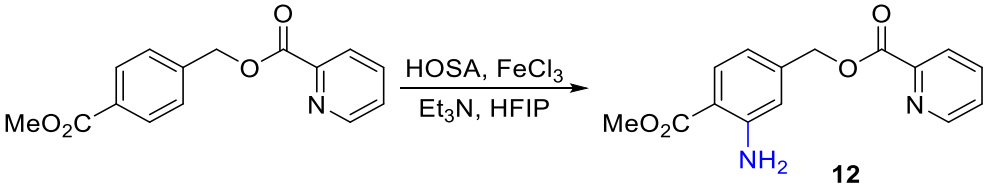
3-Amino-5-(trifluoromethyl)benzyl picolinate (11)



11

Following the general amination procedure, 3-(trifluoromethyl)benzyl picolinate (50 mg, 0.177 mmol), $FeCl_3$ (1.4 mg, 0.008 mmol), Et_3N (49 µL, 0.355 mmol), and HOSA (40 mg, 0.355 mmol) were stirred at 40 °C in HFIP (1.7 mL) for 24 h. Chromatographic purification of the crude product afforded 3-amino-5-(trifluoromethyl)benzyl picolinate (**11**) (36 mg, 71%) as an solid, mp 77-78 °C. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.3 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.84 (tt, *J* = 7.8, 1.8 Hz, 1H), 7.51–7.41 (m, 1H), 7.06 (s, 1H), 6.92 (s, 1H), 6.83 (s, 1H), 5.37 (s, 2H), 3.94 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.03, 150.07, 147.80, 147.28, 137.73, 137.21, 132.51, 132.19, 131.87, 131.55, 128.10, 127.24, 125.49, 125.39, 122.68, 119.97, 117.80, 117.78, 114.94, 114.90, 114.86, 114.83, 111.47, 111.43, 111.40, 111.36, 66.86. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{11}F_3N_2O_2+H]^+$ 297.0841, Found 297.0845.

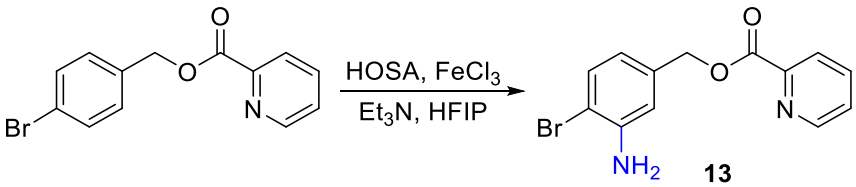
3-Amino-4-(methoxycarbonyl)benzyl picolinate (12)



12

Following the general amination procedure, 4-(methoxycarbonyl)benzyl picolinate (50 mg, 0.184 mmol), $FeCl_3$ (1.4 mg, 0.009 mmol), Et_3N (51 µL, 0.368 mmol), and HOSA (41 mg, 0.368 mmol) were stirred at 40 °C in HFIP (1.8 mL) for 24 h. Chromatographic purification of the crude product afforded 3-amino-4-(methoxycarbonyl)benzyl picolinate (**12**) (26 mg, 51%) as an oil. TLC: $R_f \approx$ 0.4 (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.7 Hz, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.91–7.79 (m, 2H), 7.52–7.46 (m, 1H), 6.76 (s, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 5.77 (br s, 2H), 5.36 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.41, 165.03, 150.67, 150.12, 147.92, 141.94, 137.18, 131.83, 127.21, 125.49, 115.82, 115.76, 110.56, 66.83, 51.71. HRMS (ESI$^+$) Calcd. for $[C_{15}H_{14}N_2O_4+H]^+$ 287.1026, Found 287.1024.

3-Amino-4-bromobenzyl picolinate (13)

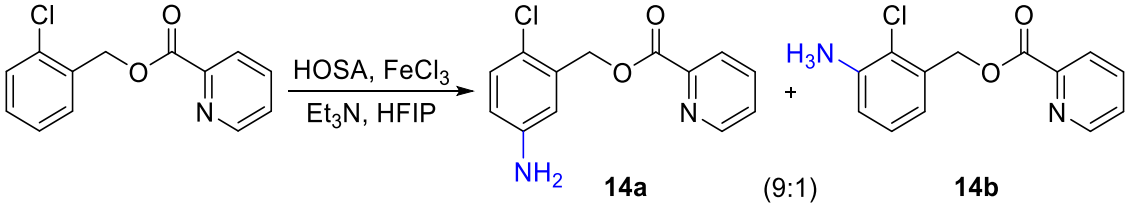


13

Following the general amination procedure, 4-bromobenzyl picolinate (50 mg, 0.171 mmol), $FeCl_3$ (1.3 mg, 0.008 mmol), Et_3N (47 µL, 0.343 mmol), and HOSA (38 mg, 0.343 mmol) were stirred

at 40 °C in HFIP (1.7 mL) for 24 h. Chromatographic purification of the crude product afforded 3-amino-4-bromobenzyl picolinate (**13**) (38 mg, 74%) as a solid, mp 79-80 °C. TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.6 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.83 (td, *J* = 7.8, 1.8 Hz, 1H), 7.51–7.43 (m, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 6.88 (d, *J* = 2.0 Hz, 1H), 6.71 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.31 (s, 2H), 3.83 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.08, 150.06, 147.98, 144.34, 137.14, 136.20, 132.84, 127.14, 125.43, 119.47, 115.69, 109.27, 67.02. HRMS (ESI$^+$) Calcd. for $[C_{13}H_{11}BrN_2O_2+H]^+$ 307.0076, Found 307.0079.

5-Amino-2-chlorobenzyl picolinate (14a) and 3-Amino-2-chlorobenzyl picolinate (14b)

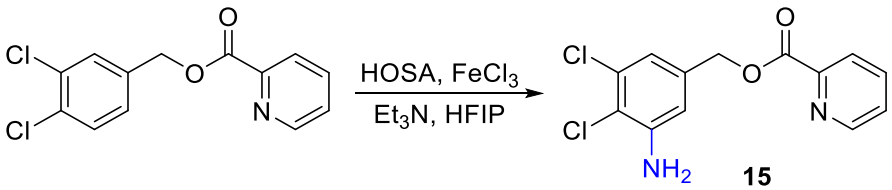


Following the general amination procedure, 2-chlorobenzyl picolinate (50 mg, 0.202 mmol), $FeCl_3$ (1.6 mg, 0.010 mmol), Et_3N (56 µL, 0.404 mmol), and HOSA (45 mg, 0.404 mmol) were stirred at 40 °C in HFIP (2 mL) for 16 h. Chromatographic purification of the crude product afforded 5-amino-2-chlorobenzyl picolinate (**14a**) (36 mg) as an oil and 3-amino-2-chlorobenzyl picolinate (**14b**) (4 mg) as an oil for a 76% combined yield.

5-Amino-2-chlorobenzyl picolinate (**14a**): TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.1 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.85 (td, *J* = 7.8, 1.6 Hz, 1H), 7.53–7.45 (m, 1H), 7.15 (d, *J* = 8.5 Hz, 1H), 6.84 (d, *J* = 2.8 Hz, 1H), 6.58 (dd, *J* = 8.5, 2.8 Hz, 1H), 5.47 (s, 2H), 3.60 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.94, 150.15, 148.00, 145.47, 137.17, 133.93, 130.25, 127.15, 125.53, 122.50, 116.38, 116.20, 64.93. HRMS (ESI$^+$) Calcd. for $[C_{13}H_{11}ClN_2O_2+H]^+$ 263.0581, Found 263.0584.

3-Amino-2-chlorobenzyl picolinate (**14b**): TLC: $R_f \approx 0.6$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.6 Hz, 1H), 8.15 (d, *J* = 7.6 Hz, 1H), 7.84 (t, *J* = 7.7 Hz, 1H), 7.53–7.43 (m, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 5.52 (s, 2H), 4.13 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.93, 150.18, 148.03, 143.49, 137.14, 134.00, 127.36, 127.10, 125.49, 119.50, 118.76, 115.98, 65.41. HRMS (ESI$^+$) Calcd. for $[C_{13}H_{11}ClN_2O_2+H]^+$ 263.0581, Found 263.0583.

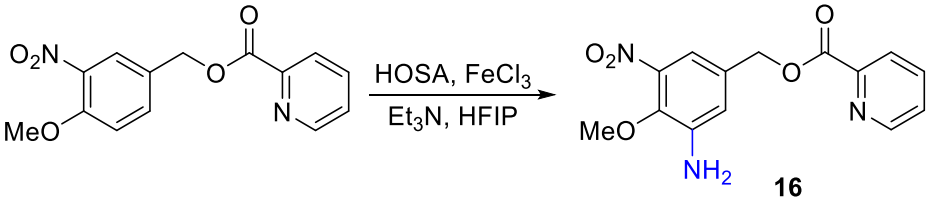
3-Amino-4,5-dichlorobenzyl picolinate (15)



Following the general amination procedure, 3,4-dichlorobenzyl picolinate (50 mg, 0.159 mmol), $FeCl_3$ (1.2 mg, 0.007 mmol), Et_3N (88 µL, 0.638 mmol), and HOSA (72 mg, 0.638 mmol) were stirred at rt in HFIP (1.5 mL) for 24 h. Chromatographic purification of the crude product afforded 3-amino-4,5-dichlorobenzyl picolinate (**15**) (22 mg, 43%) as an oil. TLC: $R_f \approx 0.3$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84–8.71 (m, 1H), 8.14 (d, *J* = 9.0 Hz, 1H), 7.85 (t, *J* = 7.7 Hz, 1H), 7.53–7.46 (m, 1H), 6.96 (s, 1H), 6.78 (s, 1H), 5.29 (s, 2H), 4.24 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.03, 150.13, 147.82, 144.72, 137.22, 135.64, 133.35, 127.28,

125.52, 119.39, 117.47, 113.58, 66.45. HRMS (ESI$^+$) Calcd. for $[C_{13}H_{10}Cl_2N_2O_2+H]^+$ 297.0192, Found 297.0196.

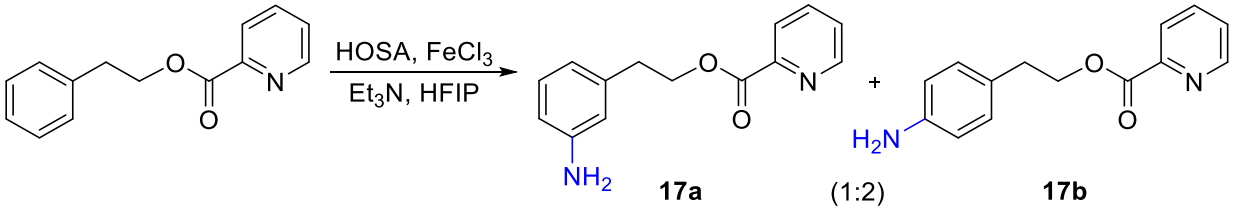
3-Amino-4-methoxy-5-nitrobenzyl picolinate (16)



16

Following the general amination procedure, 4-methoxy-3-nitrobenzyl picolinate (50 mg, 0.173 mmol), $FeCl_3$ (1.4 mg, 0.008 mmol), Et_3N (48 µL, 0.347 mmol), and HOSA (39 mg, 0.347 mmol) were stirred at 40 ºC in HFIP (1.7 mL) for 24 h. Chromatographic purification of the crude product afforded 3-amino-4-methoxy-5-nitrobenzyl picolinate (**16**) (7 mg, 15%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.7 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.86 (td, *J* = 7.8, 1.7 Hz, 1H), 7.52–7.47 (m, 1H), 7.31 (d, *J* = 2.0 Hz, 1H), 7.07 (d, *J* = 2.0 Hz, 1H), 5.34 (s, 2H), 4.14 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.03, 150.15, 147.72, 143.98, 142.53, 140.33, 137.26, 132.33, 127.35, 125.56, 119.60, 114.18, 66.31, 61.18. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{13}N_3O_5+H]^+$ 304.0928, Found 304.0928.

3-Aminophenethyl picolinate (17a) and 4-aminophenethyl picolinate (17b)



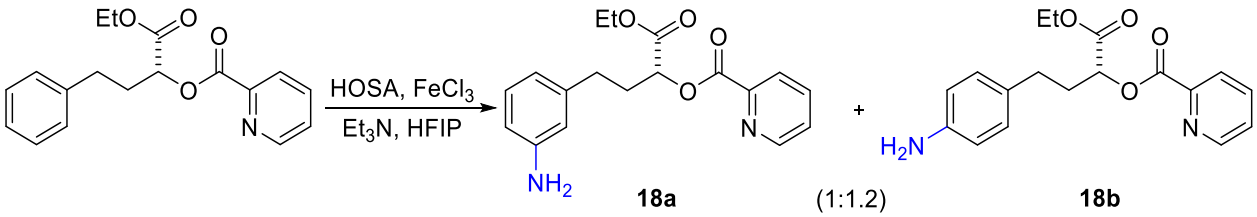
17a (1:2) **17b**

Following the general amination procedure, phenethyl picolinate (50 mg, 0.221 mmol), $FeCl_3$ (1.8 mg, 0.011 mmol), Et_3N (123 µL, 0.881 mmol), and HOSA (99 mg, 0.881 mmol) were stirred at rt in HFIP (2.2 mL) for 18 h. Chromatographic purification of the crude product afforded 3-aminophenethyl picolinate (**17a**) (11 mg) as an oil and 3-aminophenethyl picolinate (**17b**) (22 mg) as an oil (33 mg) for a 64% combined yield.

3-Aminophenethyl picolinate (**17a**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82–8.71 (m, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.90–7.76 (m, 1H), 7.48 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.09 (t, *J* = 7.7 Hz, 1H), 6.68 (d, *J* = 7.5 Hz, 1H), 6.62 (t, *J* = 1.8 Hz, 1H), 6.57 (d, *J* = 7.8 Hz, 1H), 4.59 (t, *J* = 7.6 Hz, 2H), 3.66 (br s, 2H), 3.04 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07, 149.89, 148.09, 146.57, 138.51, 137.00, 129.49, 126.87, 125.15, 119.23, 115.66, 113.47, 66.36, 35.12. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{14}N_2O_2+H]^+$ 243.1133, Found 243.1139.

4-Aminophenethyl picolinate (**17b**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.1 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.83 (td, *J* = 7.8, 1.7 Hz, 1H), 7.50–7.45 (m, 1H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.64 (d, *J* = 8.3 Hz, 2H), 4.54 (t, *J* = 7.6 Hz, 2H), 3.64 (br s, 2H), 3.02 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07, 149.88, 148.13, 144.97, 136.98, 129.83, 127.17, 126.84, 125.12, 115.33, 66.73, 34.30. HRMS (ESI$^+$) Calcd. for $[C_{14}H_{14}N_2O_2+H]^+$ 243.1133, Found 243.1134.

(*R*)-4-(3-Aminophenyl)-1-ethoxy-1-oxobutan-2-yl picolinate (18a) and ((*R*)-4-(4-Aminophenyl)-1-ethoxy-1-oxobutan-2-yl picolinate (18b)

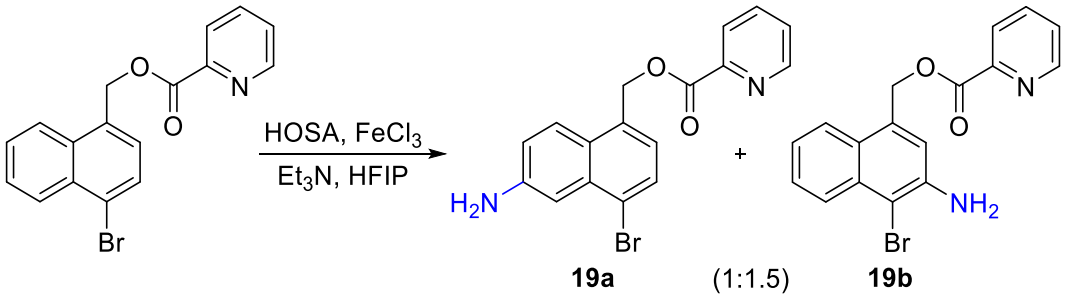


Following the general amination procedure, (*R*)-1-ethoxy-1-oxo-4-phenylbutan-2-yl picolinate (50 mg, 0.159 mmol), $FeCl_3$ (1.2 mg, 0.007 mmol), Et_3N (88 µL, 0.638 mmol), and HOSA (72 mg, 0.638 mmol) were stirred at 40 ºC in HFIP (1.5 mL) for 24 h. Chromatographic purification of the crude product afforded (*R*)-4-(3-aminophenyl)-1-ethoxy-1-oxobutan-2-yl)oxy)carbonyl)pyridin-4-ylium (**18a**) (15 mg) as an oil and ((*R*)-4-(4-aminophenyl)-1-ethoxy-1-oxobutan-2-yl picolinate (**18b**) (19 mg) as an oil for a 66% combined yield.

(*R*)-4-(3-Aminophenyl)-1-ethoxy-1-oxobutan-2-yl picolinate (**18a**): TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 7.2 Hz, 1H), 8.13 (d, *J* = 9.8 Hz, 1H), 7.86 (td, *J* = 7.7, 1.8 Hz, 1H), 7.53–7.48 (m, 1H), 7.07 (t, *J* = 7.7 Hz, 1H), 6.61 (d, *J* = 7.7 Hz, 1H), 6.56–6.50 (m, 2H), 5.32 (dd, *J* = 8.0, 5.1 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.61 (br s, 2H), 2.79–2.69 (m, 2H), 2.41–2.29 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.91, 164.65, 150.28, 147.61, 146.69, 141.77, 137.12, 129.61, 127.26, 125.62, 118.91, 115.39, 113.23, 73.07, 61.70, 32.73, 31.61, 14.31. HRMS (ESI$^+$) Calcd. for $[C_{18}H_{20}N_2O_4+H]^+$ 329.1495, Found 329.1501.

((*R*)-4-(4-Aminophenyl)-1-ethoxy-1-oxobutan-2-yl picolinate (**18b**): TLC: $R_f \approx 0.5$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 4.3 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.86 (tt, *J* = 7.8, 2.0 Hz, 1H), 7.53–7.46 (m, 1H), 6.99 (dd, *J* = 8.4, 2.2 Hz, 2H), 6.62 (dd, *J* = 8.4, 2.1 Hz, 2H), 5.33–5.25 (m, 1H), 4.21 (qd, *J* = 7.1, 2.0 Hz, 2H), 3.51 (br s, 2H), 2.81–2.64 (m, 1H), 2.38–2.22 (m, 1H), 1.26 (td, *J* = 7.1, 2.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.99, 164.65, 150.24, 147.59, 144.72, 137.09, 130.38, 129.46, 129.41, 127.22, 125.59, 115.47, 73.01, 61.63, 33.12, 30.72, 14.27. HRMS (ESI$^+$) Calcd. for $[C_{18}H_{20}N_2O_4+H]^+$ 329.1495, Found 329.1509.

(6-Amino-4-bromonaphthalen-1-yl)methyl picolinate (19a) and (3-amino-4-bromonaphthalen-1-yl)methyl picolinate (19b)



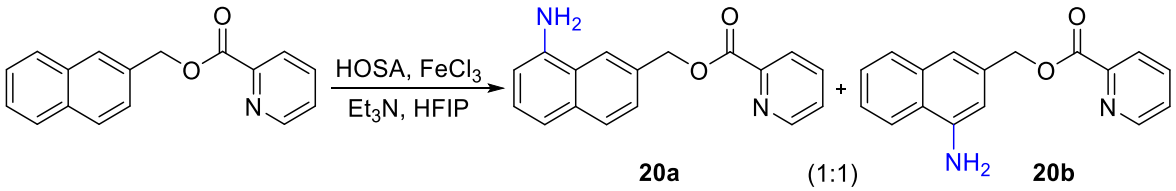
Following the general amination procedure, (3-amino-4-bromonaphthalen-1-yl)methyl picolinate (50 mg, 0.146 mmol), $FeCl_3$ (1.1 mg, 0.007 mmol), Et_3N (40 µL, 0.293 mmol), and HOSA (33 mg, 0.293 mmol) were stirred at 0 °C in HFIP (1.4 mL) for 10 h. Chromatographic purification of the crude product afforded (6-amino-4-bromonaphthalen-1-yl)methyl picolinate (**19a**) (13 mg) as an oil and (3-amino-4-bromonaphthalen-1-yl)methyl picolinate (**19b**) (19 mg) as an oil for a 62% combined yield.

(6-Amino-4-bromonaphthalen-1-yl)methyl picolinate (**19a**): TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.6 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 9.0

Hz, 1H), 7.82 (td, *J* = 7.8, 1.8 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.50–7.45 (m, 1H), 7.44 (d, *J* = 2.4 Hz, 1H), 7.28 (s, 1H), 5.81 (s, 2H), 4.08 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07, 150.17, 147.98, 145.73, 137.13, 133.97, 131.15, 129.99, 127.12, 126.97, 125.69, 125.45, 124.69, 122.10, 119.38, 108.72, 65.62. HRMS (ESI$^+$) Calcd. for $[C_{17}H_{13}BrN_2O_2+H]^+$ 357.0233, Found 357.0220.

(3-Amino-4-bromonaphthalen-1-yl)methyl picolinate (**19b**): TLC: $R_f \approx 0.5$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.3 Hz, 1H), 8.14–8.05 (m, 2H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.51–7.43 (m, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.23 (s, 1H), 5.81 (s, 2H), 4.41 (brs, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.02, 150.15, 147.89, 141.67, 137.16, 133.49, 131.92, 127.88, 127.18, 126.70, 125.86, 125.82, 125.48, 123.80, 123.66, 119.50, 104.88, 65.21. HRMS (ESI$^+$) Calcd. for $[C_{17}H_{13}BrN_2O_2+H]^+$ 357.0233, Found 357.0227.

(8-Aminonaphthalen-2-yl)methyl picolinate (20a) and (4-aminonaphthalen-2-yl)methyl picolinate (20b)

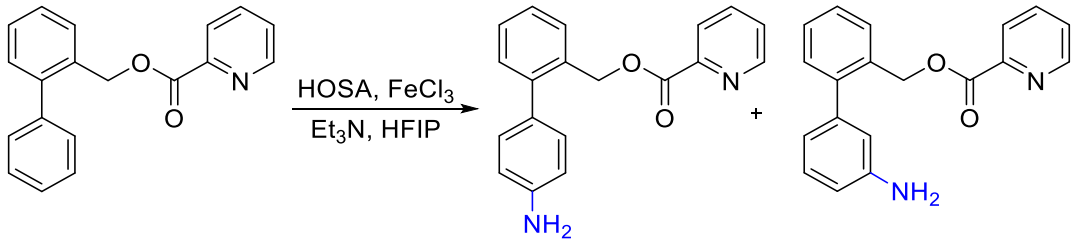


Following the general amination procedure, naphthalen-2-ylmethyl picolinate (50 mg, 0.190 mmol), $FeCl_3$ (1.5 mg, 0.009 mmol), Et_3N (52 µL, 0.380 mmol), and HOSA (42 mg, 0.380 mmol) were stirred at rt in HFIP (1.9 mL) for 16 h. Chromatographic purification of the crude product afforded (8-aminonaphthalen-2-yl)methyl picolinate (**20a**) (19 mg) as an oil and (4-aminonaphthalen-2-yl)methyl picolinate (**20b**) (19 mg) as an oil for a 66% combined yield.

(8-Aminonaphthalen-2-yl)methyl picolinate (**20a**): TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.2 Hz, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.96 (s, 1H), 7.83 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.80 (d, *J* = 6.6 Hz, 1H), 7.58 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.49–7.45 (m, 1H), 7.30 (s, 1H), 7.29 (d, *J* = 1.7 Hz, 1H), 6.79 (dd, *J* = 5.0, 3.4 Hz, 1H), 5.62 (s, 2H), 4.23 (br s, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 165.20, 150.06, 148.12, 142.43, 137.16, 134.34, 132.00, 129.20, 127.12, 127.05, 126.54, 125.45, 123.47, 121.66, 118.84, 110.27, 68.17. HRMS (ESI$^+$) Calcd. for $[C_{17}H_{14}N_2O_2+H]^+$ 279.1128, Found 279.1125.

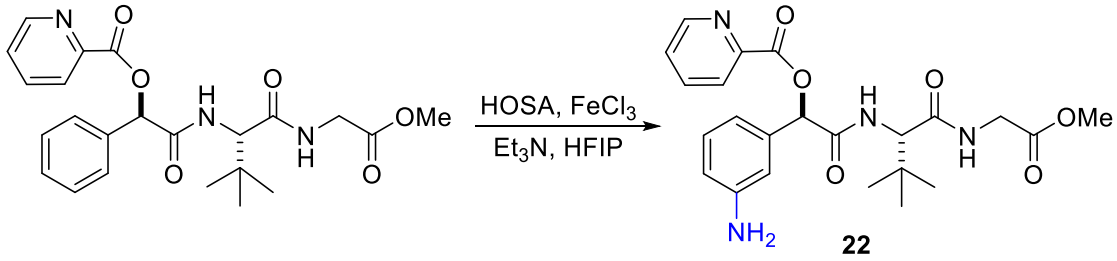
(4-Aminonaphthalen-2-yl)methyl picolinate (**20b**): TLC: $R_f \approx 0.5$ (70% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.7 Hz, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 7.88–7.75 (m, 4H), 7.52–7.43 (m, 3H), 6.90 (d, *J* = 1.5 Hz, 1H), 5.53 (s, 2H), 4.23 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.24, 150.10, 148.21, 142.68, 137.14, 134.34, 133.75, 128.89, 127.08, 126.44, 125.47, 123.66, 120.83, 119.01, 109.64, 68.03. HRMS (ESI$^+$) Calcd. for $[C_{17}H_{14}N_2O_2+H]^+$ 279.1128, Found 279.1130.

(4'-Amino-[1,1'-biphenyl]-2-yl)methyl picolinate (21a) and (3'-Amino-[1,1'-biphenyl]-2-yl)methyl picolinate (21b)



Following the general amination procedure, (1,1'-biphenyl)-2-ylmethyl picolinate (50 mg, 0.172 mmol), $FeCl_3$ (1.3 mg, 0.008 mmol), Et_3N (48 µL, 0.345 mmol), and HOSA (39 mg, 0.345 mmol) were stirred at rt in HFIP (1.7 mL) for 16 h. Chromatographic purification of the crude product afforded (4'-amino-[1,1'-biphenyl]-2-yl)methyl picolinate (**21a**) (24 mg) as an oil and (3'-amino-[1,1'-biphenyl]-2-yl)methyl picolinate (**21b**) (7 mg) as an oil for a 61% combined yield.
(4'-Amino-[1,1'-biphenyl]-2-yl)methyl picolinate (**21a**): TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.3 Hz, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.82 (td, *J* = 7.7, 1.6 Hz, 1H), 7.57 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.49–7.43 (m, 1H), 7.40–7.28 (m, 3H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 5.40 (s, 2H), 3.79 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.92, 150.10, 148.16, 145.84, 142.62, 137.06, 133.05, 130.61, 130.40, 130.26, 129.59, 128.43, 127.18, 126.97, 125.28, 114.97, 65.94. HRMS (ESI$^+$) Calcd. for $[C_{19}H_{16}N_2O_2+H]^+$ 305.1284, Found 305.1292.
(3'-Amino-[1,1'-biphenyl]-2-yl)methyl picolinate (**21b**): TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.0 Hz, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.82 (td, *J* = 7.7, 1.7 Hz, 1H), 7.61–7.54 (m, 1H), 7.49–7.44 (m, 1H), 7.38–7.27 (m, 3H), 7.17 (t, *J* = 7.7 Hz, 1H), 6.76 (dt, *J* = 7.5, 1.2 Hz, 1H), 6.73 (t, *J* = 2.0 Hz, 1H), 6.66 (ddd, *J* = 7.9, 2.4, 0.9 Hz, 1H), 5.39 (s, 2H), 3.73 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.94, 150.12, 148.22, 146.36, 142.72, 141.57, 137.09, 133.02, 130.10, 129.46, 129.29, 128.38, 127.65, 127.00, 125.33, 119.69, 116.16, 114.23, 65.81. HRMS (ESI$^+$) Calcd. for $[C_{19}H_{16}N_2O_2+H]^+$ 305.1284, Found 305.1287.

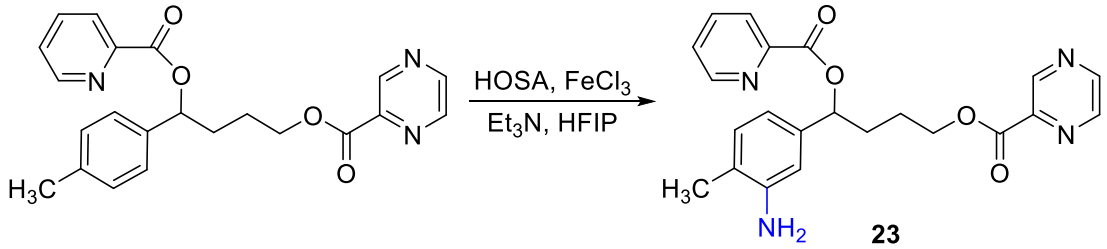
(*R*)-1-(3-Aminophenyl)-2-(*S*)-1-((2-methoxy-2-oxoethyl)amino)-3,3-dimethyl-1-oxobutan-2-yl)amino)-2-oxoethyl picolinate (22)



Following the general amination procedure, (*R*)-2-(*S*)-1-((2-methoxy-2-oxoethyl)amino)-3,3-dimethyl-1-oxobutan-2-yl)amino)-2-oxo-1-phenylethyl picolinate (50 mg, 0.113 mmol), $FeCl_3$ (0.9 mg, 0.005 mmol), Et_3N (31 µL, 0.226 mmol), and HOSA (25 mg, 0.226 mmol) were stirred at 40 °C in HFIP (1.1 mL) for 24 h. Chromatographic purification of the crude product afforded (*R*)-1-(3-aminophenyl)-2-(*S*)-1-(2-methoxy-2-oxoethyl)amino)-3,3-dimethyl-1-oxobutan-2-yl)amino)-2-oxoethyl picolinate (**22**) (36 mg, 72%) as an oil. TLC: $R_f \approx 0.4$ (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.2 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.84 (td, *J* = 7.8, 1.7 Hz, 1H), 7.53–7.46 (m, 1H), 7.45 (br s, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.07 (br s, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 6.86 (t, *J* = 2.0 Hz, 1H), 6.63 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.29 (s, 1H), 4.49 (d, *J* = 9.5 Hz, 1H), 3.95 (dd, *J* = 17.9, 6.0 Hz, 1H), 3.87 (br s, 2H), 3.71 (s, 3H), 3.66 (dd, *J* = 17.9, 6.0

Hz, 1H), 0.97 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.58, 170.24, 168.55, 163.77, 150.20, 147.42, 147.29, 137.25, 136.20, 129.82, 127.49, 125.44, 118.28, 116.01, 114.14, 76.53, 60.34, 52.32, 41.01, 34.99, 26.55. HRMS (ESI$^+$) Calcd. for $[C_{23}H_{28}N_4O_6+H]^+$ 457.2081, Found 457.2073.

4-(3-Amino-4-methylphenyl)-4-(picolinoyloxy)butyl pyrazine-2-carboxylate (23)

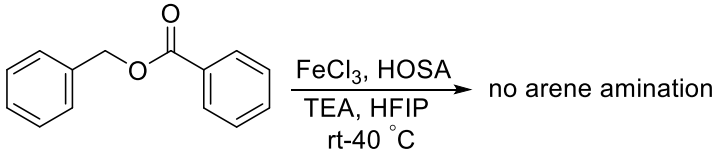


23

Following the general amination procedure, 4-(picolinoyloxy)4-(*p*-tolyl)butyl pyrazine-2-carboxylate (50 mg, 0.133 mmol), $FeCl_3$ (1.1 mg, 0.007 mmol), TEA (74 µL, 0.265 mmol), and HOSA (60 mg, 0.531 mmol) were stirred at rt in HFIP (1.5 mL) for 16 h. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using a gradient of 3-7% MeOH/CH_2Cl_2 to afforded 4-(3-Amino-4-methylphenyl)-4-(picolinoyloxy)butyl pyrazine-2-carboxylate (**23**) (30 mg, 56%) as a viscous oil. TLC: $R_f \approx 0.5$ (10% MeOH/CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.31 (d, *J* = 1.4 Hz, 1H), 8.81–8.77 (m, 2H), 8.74 (t, *J* = 1.9 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.84 (td, *J* = 7.8, 1.7 Hz, 1H), 7.50–7.46 (m, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.84–6.82 (m, 2H), 6.08–6.00 (m, 1H), 4.53–4.48 (m, 2H), 3.70 (br s, 2H), 2.33–2.27 (m, 1H), 2.17–2.11 (m, 4H), 2.04–1.98 (m, 1H), 1.94–1.88 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.47, 163.83, 149.91, 148.20, 147.61, 146.26, 144.68, 144.43, 143.40, 138.50, 136.90, 130.61, 126.82, 125.26, 122.41, 116.84, 113.06, 65.85, 32.50, 25.01, 17.13. HRMS (ESI+) Calcd. for $[C_{22}H_{22}N_2O_4+H]$+ 407.1719, Found 407.1728.

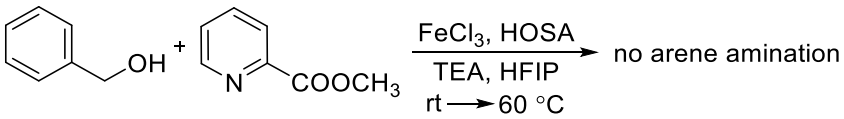
Control Experiments

Benzyl benzoate as substrate



Following the general amination procedure, benzyl benzoate (50 mg, 0.235 mmol), $FeCl_3$ (1.9 mg, 0.011 mmol), TEA (65 µL, 0.471 mmol), and HOSA (53 mg, 0.471 mmol) were stirred at rt in HFIP (2.3 mL). After stirring for 12 h, the reaction was warmed to 40 °C for 12 h. No amination product was observed by TLC or NMR.

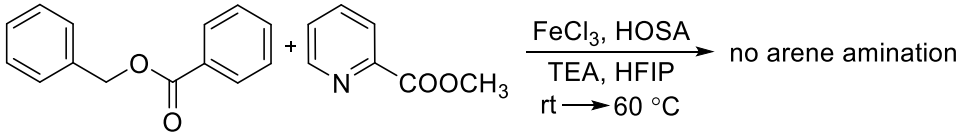
Benzyl alcohol plus methyl picolinate as substrates



Following the general amination procedure, benzyl alcohol (50 mg, 0.462 mmol), methyl picolinate (63 mg, 0.463 mmol), $FeCl_3$ (3.7 mg, 0.023 mmol), TEA (129 µL, 0.926 mmol), and HOSA (105 mg, 0.926 mmol) were stirred at rt in HFIP (4.5 mL). After stirring for 12 h, the

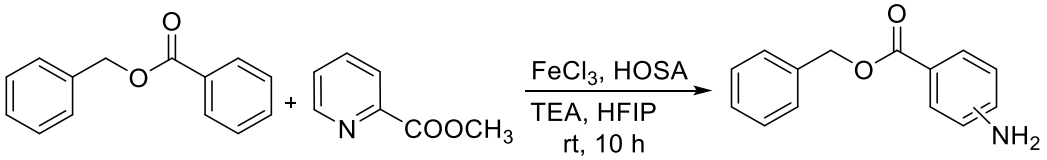
reaction was warmed to 40 °C for 5 h, and then to 60 °C for additional 5 h. No amination product was observed by TLC or NMR.

Benzyl benzoate plus methyl picolinate (1 equiv) as substrates



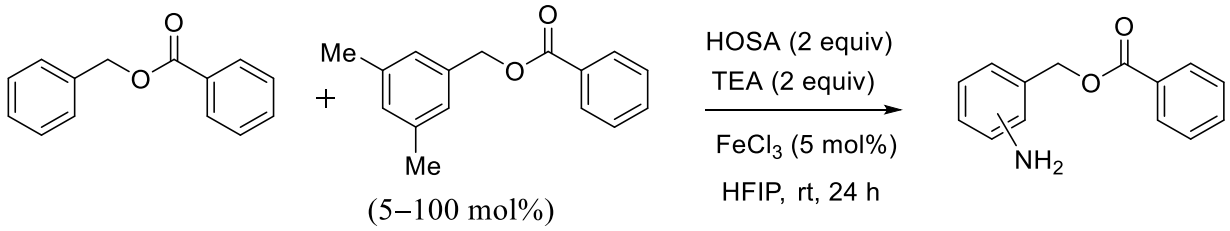
Following the general amination procedure, benzyl benzoate (50 mg, 0.237 mmol), methyl picolinate (32 mg, 0.237 mmol), $FeCl_3$ (1.9 mg, 0.012 mmol), TEA (66 µL, 0.474 mmol), and HOSA (54 mg, 0.474 mmol) were stirred at rt in HFIP (2.5 mL). After stirring for 12 h, the reaction was warmed to 40 °C for 5 h, and then to 60 °C for additional 5 h. No amination product was observed by TLC or NMR.

Benzyl benzoate plus methyl picolinate (5 mol%) as substrates



Following the general amination procedure, benzyl benzoate (50 mg, 0.237 mmol), methyl picolinate (1.6 mg, 0.012 mmol), $FeCl_3$ (1.9 mg, 0.012 mmol), TEA (66 µL, 0.474 mmol), and HOSA (54 mg, 0.474 mmol) were stirred at rt in HFIP (2.5 mL) for 10 h. Chromatographic purification of the crude product afforded mixed aminobenzyl benzoates (6 mg, 11%) along with recovered benzyl benzoate (39 mg, 78%), both as viscous oils.

Benzyl benzoate plus dimethylbenzyl picolinate (5 – 100 mol%) as substrates

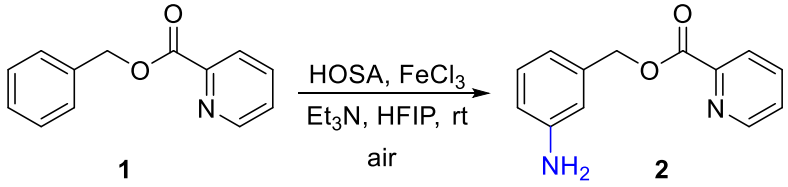


Following the general amination procedure, benzyl benzoate (50 mg, 0.207 mmol), $FeCl_3$ (1.7 mg, 0.010 mmol), Et_3N (58 µL, 0.414 mmol), HOSA (47 mg, 0.414 mmol) and either 5 mol%, 50 mol%, or 100 mol% of 3,5-dimethylbenzyl picolinate (2.2 mg, 22 mg, or 44 mg, respectively, in separate reactions) were stirred at rt in HFIP (2 mL) for 24 h.

Entry	Benzyl benzoate	3,5-Dimethylbenzyl benzoate	Yield mixed aminobenzyl benzoate
01	1 equiv	5 mol%	≤5%

02	1 equiv	50 mol%	0
03	1 equiv	100 mol%	0

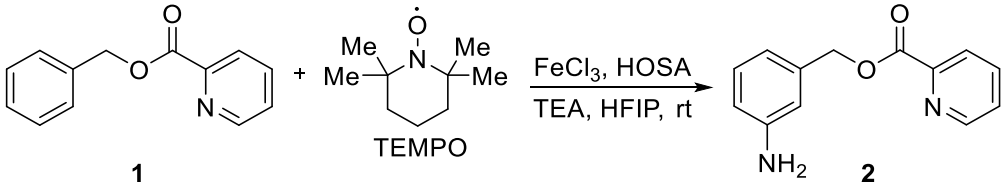
Amination in presence of air



1 2

Following the general amination procedure, benzyl picolinate (**1**) (50 mg, 0.234 mmol), $FeCl_3$ (1.8 mg, 0.011 mmol), Et_3N (65 µL, 0.469 mmol), and HOSA (53 mg, 0.469 mmol) were stirred in presence of air (using drying tube filled with $CaSO_4$) at rt in HFIP (2.3 mL) for 10 h. Chromatographic purification of the crude product afforded 3-aminobenzyl picolinate (**2**) (29 mg, 54%) as an oil and unreacted **1** (3 mg, 6%) as an oil.

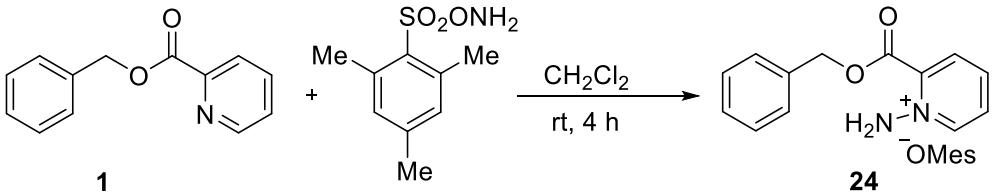
Amination in presence of TEMPO (free radical inhibitor)



1 2

Following the general amination procedure, benzyl picolinate (**1**) (50 mg, 0.234 mmol), TEMPO (36.6 mg, 0.234 mmol), $FeCl_3$ (1.9 mg, 0.012 mmol), TEA (65 µL, 0.469 mmol), and HOSA (53 mg, 0.469 mmol) were stirred at rt in HFIP (2.3 mL) for 23 h. Chromatographic purification of the crude product afforded *meta*-aminated **2** (22 mg, 41%) along with unreacted **1** (20 mg) as viscous oils.

1-Amino-2-((benzyloxy)carbonyl)pyridin-1-ium 2,4,6-trimethylbenzenesulfonate



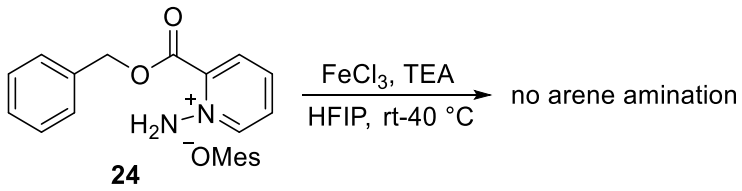
1 24

Following literature procedure,[13] *O*-mesitylenesulphonylhydroxylamine[14] (Mes-*O*-NH_2) (100 mg, 0.469 mmol) was added to a stirring, 0 °C solution of benzyl picolinate (**1**) (100 mg, 0.469 mmol) in CH_2Cl_2 (4.6 mL). The solution was warmed to rt and stirred. After 4 h, the reaction mixture was diluted with Et_2O and the resulting precipitate was collected by filtration and dried *in vacuo* to give 1-amino-2-((benzyloxy)carbonyl)pyridin-1-ium 2,4,6-trimethylbenzenesulfonate (**24**) (176 mg, 88%) as a white solid, mp 123-124 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (br s, 2H), 8.90 (d, J = 6.2 Hz, 1H), 8.47 (d, J = 9.3 Hz, 1H), 8.32 (t, J = 7.8 Hz, 1H), 8.19–8.12 (m, 1H), 7.53 (d, J = 6.7 Hz, 2H), 7.45–7.34 (m, 3H), 6.72 (s, 2H), 5.48 (s, 2H), 2.48 (s, 6H), 2.15 (s, 3H); ^{13}C NMR

(101 MHz, DMSO-d_6) δ 159.50, 142.74, 139.93, 139.91, 136.24, 135.87, 135.48, 134.41, 130.68, 129.88, 129.85, 128.71, 128.60, 128.58, 68.85, 22.78, 20.30. Efforts to obtain a HRMS of **24** failed.

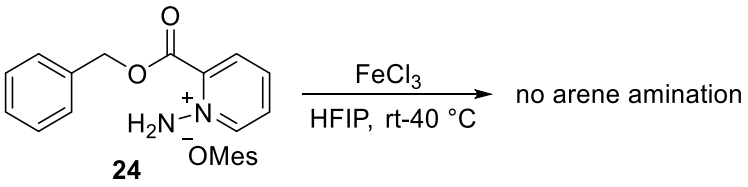
The $^{1}H/^{13}C$ spectral values of the picolinate moiety of **24** were comparable with the aromatic portion of 1-amino-2-(ethoxycarbonyl)pyridinium 2,4,6-trimethylbenzenesulfonate[13] prepared from ethyl picolinate.

1-Amino-2-((benzyloxy)carbonyl)pyridin-1-ium 2,4,6-trimethylbenzenesulfonate as substrate



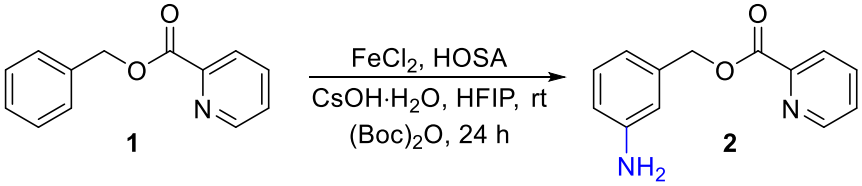
To a stirring, homogeneous, 0 °C solution of 1-amino-2-((benzyloxy)carbonyl)pyridin-1-ium 2,4,6-trimethylbenzenesulfonate (**24**) (50 mg, 0.116 mmol) in 1,1,1,3,3,3-hexafluoroisopropanol (1.1 mL) were added Et_3N (16 µL, 0.116 mmol) and $FeCl_3$ (0.9 mg, 0.005 mmol). After stirring for 12 h, the reaction was warmed to 40 °C for 12 h. No amination product was observed by TLC or NMR.

1-Amino-2-((benzyloxy)carbonyl)pyridin-1-ium 2,4,6-trimethylbenzenesulfonate as substrate in absence of base



To a stirring, homogeneous, 0 °C solution of 1-amino-2-((benzyloxy)carbonyl)pyridin-1-ium 2,4,6-trimethylbenzenesulfonate (**24**) (50 mg, 0.116 mmol) in 1,1,1,3,3,3-hexafluoroisopropanol (1.1 mL) was added $FeCl_3$ (0.9 mg, 0.005 mmol). After stirring for 12 h, the reaction was warmed to 40 °C for 12 h. No amination product was observed by TLC or NMR.

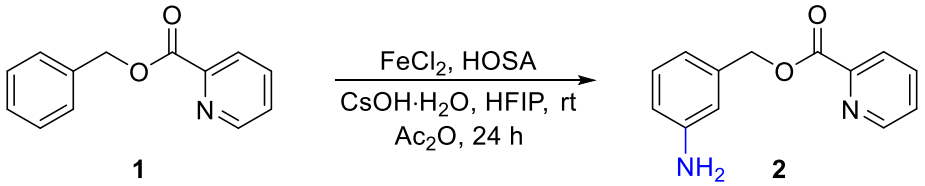
Attempted $(Boc)_2O$ *in situ* protection of aniline



Benzyl picolinate (1) (50 mg, 0.234 mmol), $(Boc)_2O$ (51 mg, 0.234 mmol), $FeCl_2$ (2.9 mg, 0.023 mmol), $CsOH·H_2O$ (79 mg, 0.469 mmol), and HOSA (53 mg, 0.469 mmol) were stirred at rt in

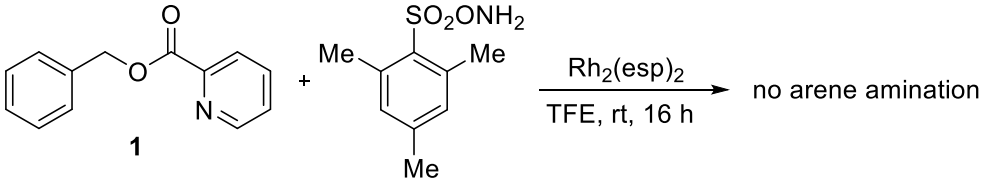
HFIP (2.3 mL) for 24 h. Chromatographic purification of the crude product afforded *meta*-product (**2**) without N-Boc protection (16 mg, 30%) along with unreacted **1** (26 mg) as viscous oils.

Attempted acetic anhydride *in situ* protection of aniline



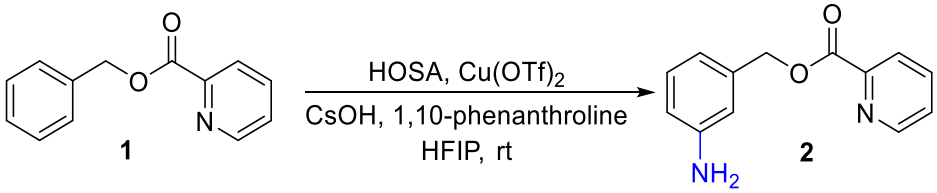
Benzyl picolinate (**1**) (50 mg, 0.234 mmol), Ac_2O (22 µL, 0.234 mmol), $FeCl_2$ (2.9 mg, 0.023 mmol), $CsOH{\cdot}H_2O$ (79 mg, 0.469 mmol), and HOSA (53 mg, 0.469 mmol) were stirred at rt in HFIP (2.3 mL) for 24 h. Chromatographic purification of the crude product afforded *meta*-product (**2**) without *N*-acetyl protection (16 mg, 30%) along with unreacted **1** (24 mg) as viscous oils.

Benzyl picolinate as a substrate using $Rh_2(esp)_2$



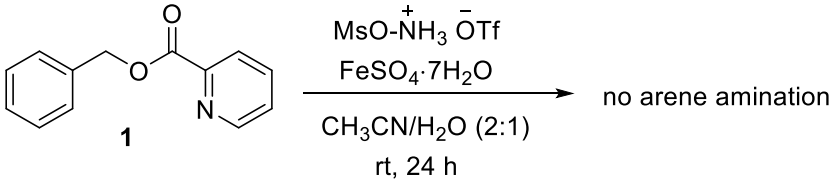
Following literature procedure,[20] benzyl picolinate (**1**) (50 mg, 0.234 mmol), $Rh_2(esp)_2$ (3.5 mg, 0.004 mmol), *O*-mesitylenesulphonylhydroxylamine[14] (Mes-*O*-NH_2) (100 mg, 0.469 mmol) were stirred at rt in TFE (2 mL) for 16 h. No amination product was observed by TLC or NMR.

Benzyl picolinate as a substrate using $Cu(OTf)_2$



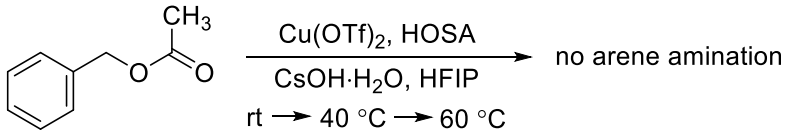
Following literature procedure,[10] benzyl picolinate (**1**) (50 mg, 0.234 mmol), $Cu(OTf)_2$ (8.3 mg, 0.023 mmol), $CsOH{\cdot}H_2O$ (59 mg, 0.352 mmol), 1,10-phenanthroline (4.1 mg, 0.023 mmol), and HOSA (39 mg, 0.352 mmol) were stirred at rt in HFIP (2 mL) for 16 h. Chromatographic purification of the crude product afforded **2** (2 mg, 5%) along with unreacted **1** (38 mg, 76%) as viscous oils.

Benzyl picolinate as a substrate using $FeSO_4{\cdot}7H_2O$



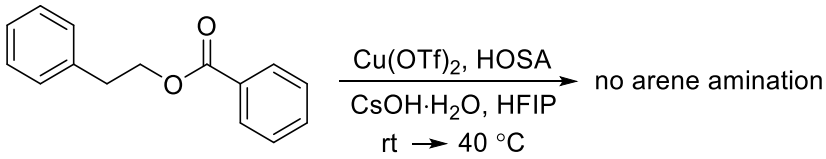
Following literature procedure,[21] benzyl picolinate (50 mg, 0.220 mmol), MsO-NH_3OTf (70 mg, 0.330 mmol), and $FeSO_4 \cdot 7H_2O$ (3 mg, 0.011 mmol) were stirred in CH_3CN/H_2O (0.75 mL, 2:1 ratio) at rt for 24 h. No arene amination was noted by TLC or NMR.

Benzyl acetate as substrate using $Cu(OTf)_2$



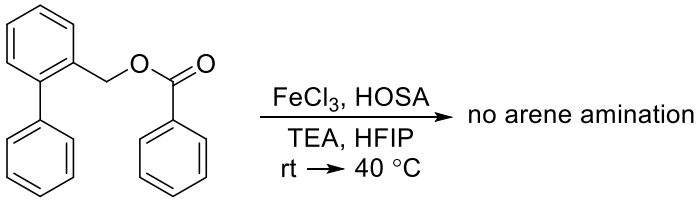
To a stirring, rt solution of phenethyl acetate[15] (50 mg, 0.333 mmol) in 1,1,1,3,3,3-hexafluoroisopropanol (3 mL) was added $Cu(OTf)_2$ (12 mg, 0.033 mmol). After 30 min, the reaction mixture was cooled to 0 °C and HOSA (75 mg, 0.666 mmol) and $CsOH \cdot H_2O$ (112 mg, 0.666 mmol) were added sequentially. After stirring at rt for 12 h, the reaction was warmed at 40 °C for 5 h, and then at 60 °C for additional 5 h. No amination product was observed by TLC or NMR.

Phenethyl benzoate as substrate using $Cu(OTf)_2$



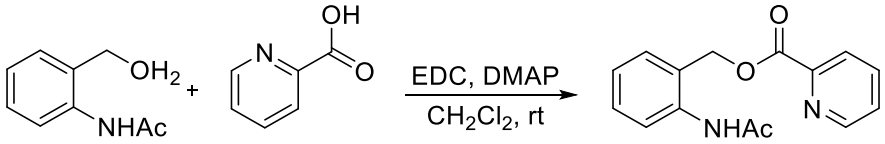
To a stirring, rt solution of phenethyl benzoate[16] (50 mg, 0.221 mmol) in 1,1,1,3,3,3-hexafluoroisopropanol (2.2 mL) was added $Cu(OTf)_2$ (7.9 mg, 0.022 mmol). After 30 min, the reaction mixture was cooled to 0 °C and HOSA (100 mg, 0.882 mmol) and $CsOH \cdot H_2O$ (148 mg, 0.882 mmol) were added sequentially. After stirring at rt for 12 h, the reaction was warmed at 40 °C for 12 h. No amination product was observed by TLC or NMR.

(1,1'-Biphenyl)-2-ylmethyl benzoate as subsrate



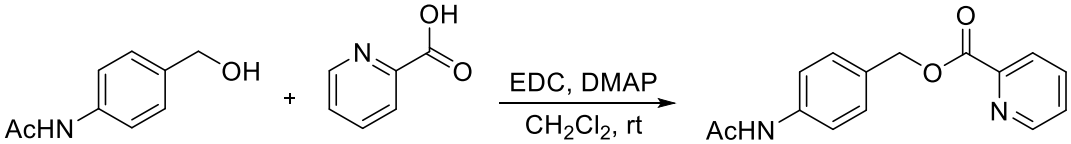
Following the general amination procedure, (1,1'-biphenyl)-2-ylmethyl benzoate[17] (50 mg, 0.173 mmol), $FeCl_3$ (1.4 mg, 0.008 mmol), TEA (48 µL, 0.347 mmol), and HOSA (39 mg, 0.347 mmol) were stirred at rt in HFIP (1.7 mL). After 12 h, the reaction was warmed to 40 °C for another 5 h. No amination product was observed by TLC or NMR.

2-Acetamidobenzyl picolinate standard



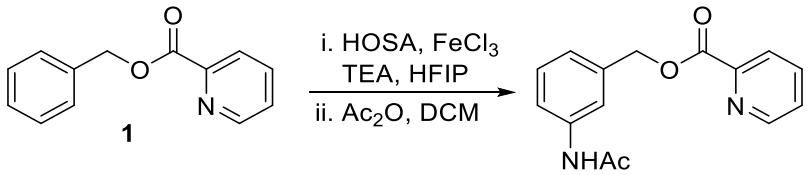
Following the general picolinate ester procedure, *N*-(2-(hydroxymethyl)phenyl)acetamide[18] (40 mg, 0.242 mmol), picolinic acid (35 mg, 0.290 mmol), EDCI (55 mg, 0.290 mmol) and DMAP (2.9 mg, 0.0242 mmol) were stirred at rt in CH_2Cl_2 (5 mL) for 16 h. Chromatographic purification of the crude product afforded 2-acetamidobenzyl picolinate (57 mg, 89%) as a solid, mp 112-113 °C. TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (br s, 1H), 8.74 (d, *J* = 5.4 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.52–7.48 (m, 1H), 7.46 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.39–7.33 (m, 1H), 7.14 (td, *J* = 7.5, 1.2 Hz, 1H), 5.44 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.12, 165.92, 150.04, 147.46, 137.28, 137.02, 131.53, 130.12, 127.51, 125.88, 125.53, 124.97, 124.36, 65.20, 24.50. HRMS (ESI^+) Calcd. for $[C_{15}H_{14}N_2O_3+H]^+$ 271.1077, Found 271.1085.

4-Acetamidobenzyl picolinate standard



Following the general picolinate ester procedure, *N*-(4-(hydroxymethyl)phenyl)acetamide[19] (50 mg, 0.303 mmol), picolinic acid (44 mg, 0.363 mmol), EDCI (69 mg, 0.363 mmol) and DMAP (3.6 mg, 0.0303 mmol) were stirred at rt in CH_2Cl_2 (6 mL) for 16 h. Chromatographic purification of the crude product afforded 4-acetamidobenzyl picolinate (70 mg, 85%) as a solid, mp 136-137 °C. TLC: $R_f \approx 0.5$ (70% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.6 Hz, 1H), 8.13 (d, *J* = 7.7 Hz, 2H), 7.83 (td, *J* = 7.8, 1.7 Hz, 1H), 7.52–7.44 (m, 3H), 7.36 (d, *J* = 8.5 Hz, 2H), 5.37 (s, 2H), 2.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.95, 165.04, 149.77, 147.91, 138.68, 137.29, 130.87, 129.62, 127.22, 125.44, 119.86, 67.40, 24.48. HRMS (ESI^+) Calcd. for $[C_{15}H_{14}N_2O_3+H]^+$ 271.1077, Found 271.1083.

3-Acetamidobenzyl picolinate standard

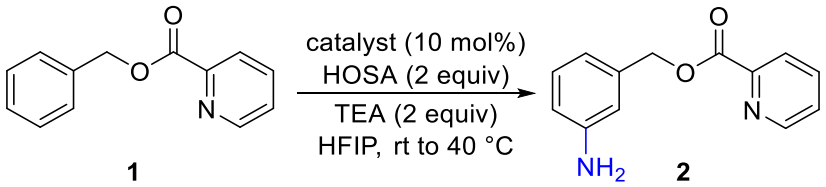


Following the general amination procedure, benzyl picolinate **1** (50 mg, 0.234 mmol), $FeCl_3$ (1.9 mg, 0.012 mmol), TEA (65 µL, 0.469 mmol), and HOSA (53 mg, 0.469 mmol) were stirred at rt in HFIP (2.3 mL) for 10 h. After isolation, the residue (55 mg) was acetylated without purification.

Acetic anhydride (0.22 mL, 2.412 mmol) was added to stirring solution of the above crude **1** (55 mg, 0.241 mmol) in dry CH_2Cl_2 (5 mL). After 15 h, all volatiles were removed *in vacuo* and the crude residue was used for the HPLC study described below.

An analytical sample of N-acetyl **2** was prepared via TLC to afford a solid, mp 121-122 °C. TLC: $R_f \approx 0.4$ (100% EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.1 Hz, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 7.85 (td, *J* = 7.7, 1.7 Hz, 1H), 7.59–7.51 (m, 2H), 7.51–7.41 (m, 2H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 5.41 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.57, 164.88, 149.72, 147.76, 138.40, 137.15, 136.11, 129.17, 127.09, 125.36, 124.06, 119.86, 119.71, 67.39, 24.46. HRMS (ESI$^+$) Calcd. for $[C_{15}H_{14}N_2O_3+H]^+$ 271.1077, Found 271.1082.

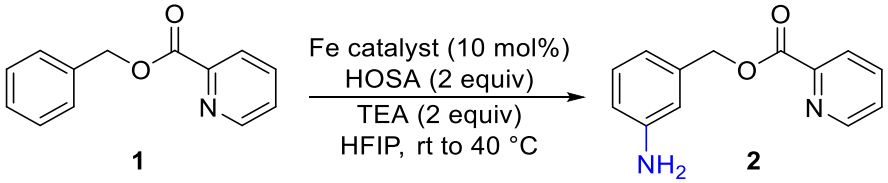
Catalyst Screen



1 **2**

Under standardized reaction conditions, yields of ≤5% of *meta*-amine **2** from **1** were realized using CuOAc, $CuCl_2$, $Cu(OTf)_2$, CuTC, $Cu(OAc)_2$, $CoBr_2$, $Rh_2(esp)_2$, $Pd(OAc)_2$, and $Ni(OAc)_2$.

Fe Catalyst Screen

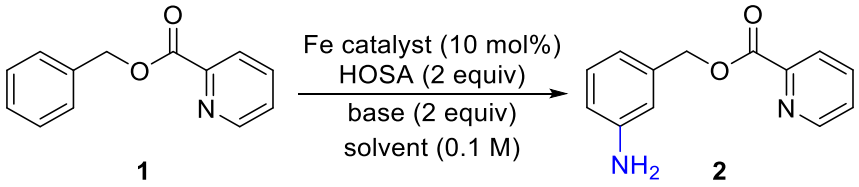


1 **2**

Under standardized reaction conditions, yields of 30-56% of amine **2** from **1** were realized using $Fe(acac)_3$, $Fe(OTf)_3$, $Fe_2(SO_4)_3 \cdot xH_2O$, $FeCl_3 \cdot 6H_2O$, $Fe(BF_4)_2 \cdot 6H_2O$, $Fe(NO_3)_3 \cdot 9H_2O$, $Fe(ClO_4)_3 \cdot H_2O$, $FeBr_3$, and FeF_2.

Reaction Optimization Studies

Table S1



1 **2**

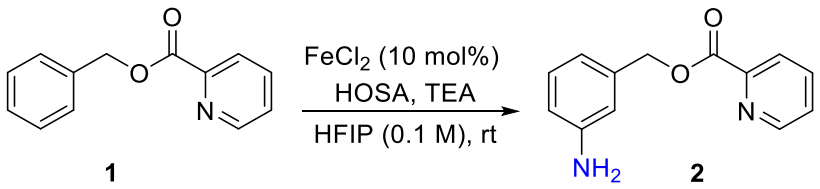
Entry	Catalyst	Base	Temp (˚C)/Time (h)	Solvent	Yield (%)
1	$FeCl_2$	Et_3N	23/16	HFIP	66
2	$FeCl_2$	$^i Pr_2NEt$	23/17	HFIP	58
3	$FeCl_2$	imidazole	23/40	HFIP	25
4	$FeCl_2$	Et_2NH	23/40	HFIP	30
5	$FeCl_2$	pyridine	23/26	HFIP	40
6	$FeCl_2$	$CsOH \cdot H_2O$	23/26	HFIP	15
7	$FeCl_2$	DBU	23/26	HFIP	25
8	$FeCl_2$	DABCO	23/26	HFIP	30
9	$FeCl_2$	quiniclidine	23/22	HFIP	64
10	$FeCl_2$	DMAP	23/26	HFIP	40

11	$FeCl_2$	1,2,2,6,6-pentamethylpiperidine	23/26	HFIP	30
12	$FeCl_2$	*N*-methylmorpholine	23/26	HFIP	26
13	$FeCl_2$	LiOH	23/26	HFIP	30
14	$FeCl_2$	NaOH	23/26	HFIP	no reaction
15	$FeCl_2$	Na_2CO_3	23/26	HFIP	no reaction
16	$FeCl_2$	K_2CO_3	23/26	HFIP	20
17	$FeCl_3$	-	23/24	HFIP	<10
18	-	Et_3N	23/24	HFIP	no reaction
19	$FeCl_3$	Et_3N	40/24	TFE	20
20	$FeCl_3$	Et_3N	40/24	$PhCF_3$	0
21	$FeCl_3$	Et_3N	40/24	DME	0
22	$FeCl_3$	Et_3N	40/24	THF	0
23	$FeCl_3$	Et_3N	40/24	CH_2Cl_2:HFIP (1:2)	33
24	$FeCl_3$	Et_3N	23/16	$CHCl_3$:HFIP (1:2)	41
25	$FeCl_3$	Et_3N	23/16	THF:HFIP (1:2)	0
26	$FeCl_3$	Et_3N	23/16	MeOH:HFIP (1:2)	<5
27	$FeCl_3$	Et_3N	23/16	DMI:HFIP (1:2)	0
28	$FeCl_3$	Et_3N	23/6	HFIP	61
29	**$FeCl_3$ (5 mol%)**	**Et_3N**	**23/10**	**HFIP**	**72**
30	$FeCl_3$ (3 mol%)	Et_3N	23/33	HFIP	60
31	$FeCl_2$	CsOH	23/10	HFIP + HOAc (1 to 4 equiv)	32
32	$Fe(OAc)_2$	Et_3N	23/24	HFIP	43
33	$Fe(acac)_3$	Et_3N	23/24	HFIP	51

DMI =1,3-dimethyl-2-imidazolidinone

HOSA and TEA Screen

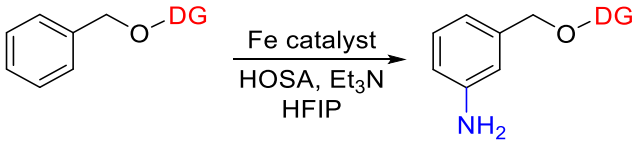
Table S2



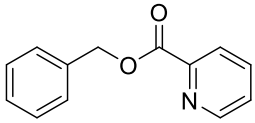
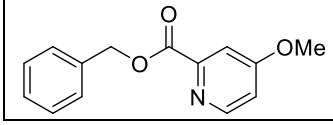
1 **2**

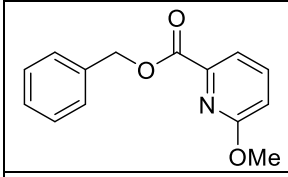
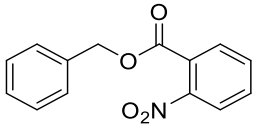
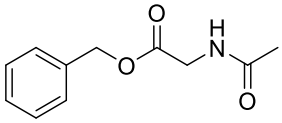
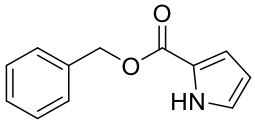
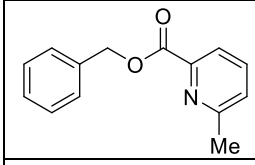
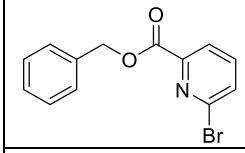
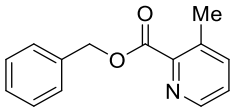
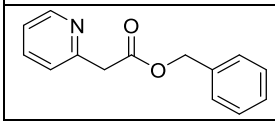
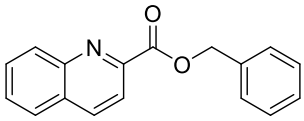
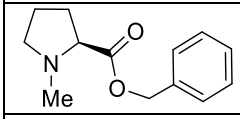
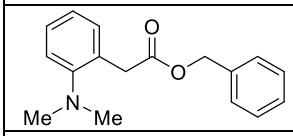
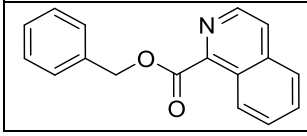
Entry	TEA (equiv)	HOSA (equiv)	Time (h)	Yield (%)
01	1.1	1.1	30	40
02	1.5	1.5	30	50
03	1	2	30	33
04	2	3	26	45
05	3	2	26	50
06	2	2	16	66

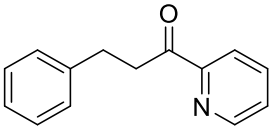
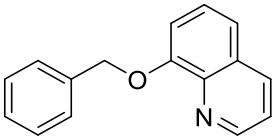
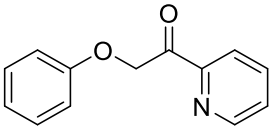
Directing Group Screen
Table S3



To a stirring, 0 °C solution of HOSA (0.4 mmol, 2 equiv) in 1,1,1,3,3,3-hexafluoroisopropanol (2 mL) was added Et_3N (0.4 mmol, 2 equiv). After 15 min, the selected benzyl ester (0.2 mmol, 1 equiv) and anhydrous $FeCl_3$ (5-10 mol%) were added sequentially. Guided by TLC monitoring, reactions were continued until complete consumption of ester or the reaction appeared to have stopped (10-24 h). Then, the reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with saturated aqueous Na_2CO_3 (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified on a commercial pre-packed SiO_2 column using a medium pressure, automated chromatograph equipped with a UV detector and eluted with MeOH/CH_2Cl_2 or EtOAc/hexanes to furnish *meta*-aminobenzyl ester in the indicated yield. No other regioisomeric aminobenzyl adducts were detected.

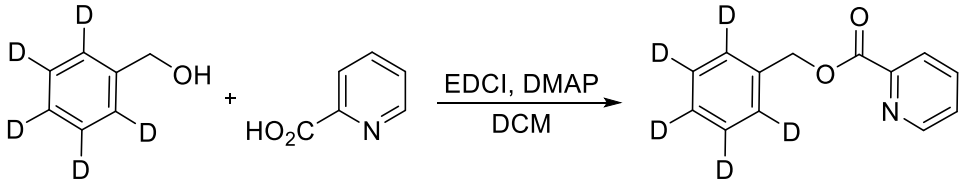
Directing Group	Catalyst (mol%)	Conditions	Yield (%) *meta*-NH_2
	**$FeCl_3$ (5 mol%)**	**rt, 10 h**	**72**
	$FeCl_3$ (10 mol%)	40 ˚C, 24 h	30

	$FeCl_3$ (10 mol%)	40 ˚C, 24 h	35
	$FeCl_3$ (10 mol%)	rt, 3 h	ester hydrolysis
	$FeCl_2$ (10 mol%)	40 ˚C, 24 h	no reaction
	$FeCl_3$ (10 mol%)	40 ˚C, 24 h	no reaction
	$FeCl_3$ (10 mol%)	rt, 24 h	13
	$FeCl_3$ (10 mol%)	40 ˚C, 24 h	5
	$FeCl_3$ (10 mol%)	rt, 26 h	35
	$FeCl_2$ (10 mol%)	40 °C, 24 h	no reaction
	$FeCl_3$ (10 mol%)	rt, 24 h	10
	$FeCl_3$ (10 mol%)	40 °C, 24 h	no reaction
	$FeCl_3$ (10 mol%)	40 °C, 24 h	no reaction
	$FeCl_3$ (5 mol%)	rt, 24 h	72

 *Prep: J. Org. Chem.* **2014**, *79*, 5852−5857	$FeCl_3$ (5 mol%)	rt, 24 h	<10 mixture of products
 *Prep: J. Med. Chem.* **2017**, *60*, 4693−4713	$FeCl_3$ (5 mol%)	rt, 24 h	ether cleavage
 *Prep: Chem. Med. Chem* **2014**, *9*, 177–188.	$FeCl_3$ (5 mol%)	rt, 24 h	<10 mixture of products

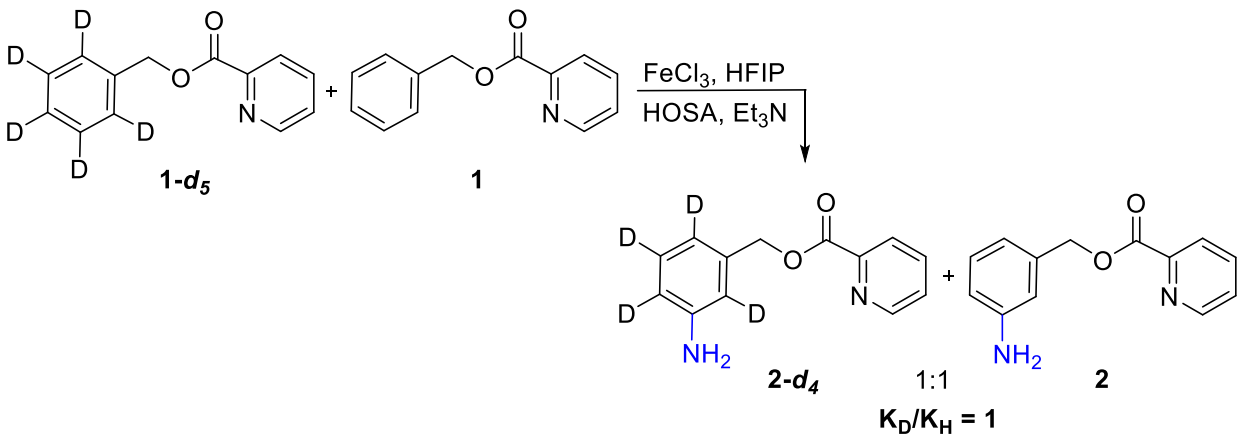
Kinetic Isotope Study

Preparation of 2,3,4,5,6-benzyl-d_5 picolinate



EDCI (203 mg, 1.062 mmol) was added to a 0 °C solution of benzyl alcohol-d_5 (0.1 g, 0.885 mmol, 98 atom % D) and picolinic acid (119 mg, 0.973 mmol) in CH_2Cl_2 (10 mL) followed by DMAP (11 mg, 0.088 mmol). After stirring at rt for 20 h, the reaction mixture was concentrated in *vacuo*. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using 40% EtOAc/hexanes to give benzyl picolinate-d_5 as a viscous oil (160 mg, 83%). TLC: $R_f \approx 0.4$ (70% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 4.6 Hz, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.82 (td, J = 7.8, 1.7 Hz, 1H), 7.52–7.43 (m, 1H), 5.46 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.99, 149.92, 147.96, 136.94, 135.39, 128.34 (d), 128.09 (d), 127.85 (d), 126.91, 125.24, 77.32, 77.00, 76.68, 67.43. HRMS (ESI^+) Calcd. for $[C_{13}H_6D_5NO_2+H]^+$ 219.1182, Found 219.1190.

Kinetic isotope study of *meta*-amination reaction



Following the general amination procedure, benzyl picolinate (**1**) (50 mg, 0.234 mmol), benzyl picolinate-d_5 (**1-*d*$_5$**)(51 mg, 0.234 mmol), $FeCl_3$ (1.9 mg, 0.011 mmol), TEA (32.7 µL, 0.234 mmol), and HOSA (27 mg, 0.234 mmol) were stirred at rt in HFIP (2.3 mL) for 9 h. The residue was purified using a commercial pre-packed SiO_2 column on a medium pressure, automated chromatograph using a gradient of 1-3% MeOH/CH_2Cl_2 to obtain *meta*-products **2** and **2-*d*$_4$** (22 mg, 20%, K_H/K_D 1:1 ratio) with unreacted **1** and **1-d$_5$** (64 mg) as viscous oils. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.9 Hz, 2H), 8.19–8.07 (m, 2H), 7.82 (td, *J* = 7.8, 1.8 Hz, 2H), 7.50–7.42 (m, 2H), 7.14 (t, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.81–6.76 (m, 1H), 6.66–6.60 (m, 1H), 5.39–5.31 (s, 4H), 3.72 (br s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.01, 149.91, 148.01, 146.67, 146.54, 136.98, 136.73, 136.56, 132.12, 132.02, 129.52, 129.46, 128.85, 128.56, 128.44, 126.92, 125.28, 118.60, 115.21, 115.09, 114.99, 114.71, 114.47, 67.54, 67.47. HRMS (ESI$^+$) Calcd. for $[C_{13}H_8D_4N_2O_2+H]^+$ 233.1228, Found 233.1224.

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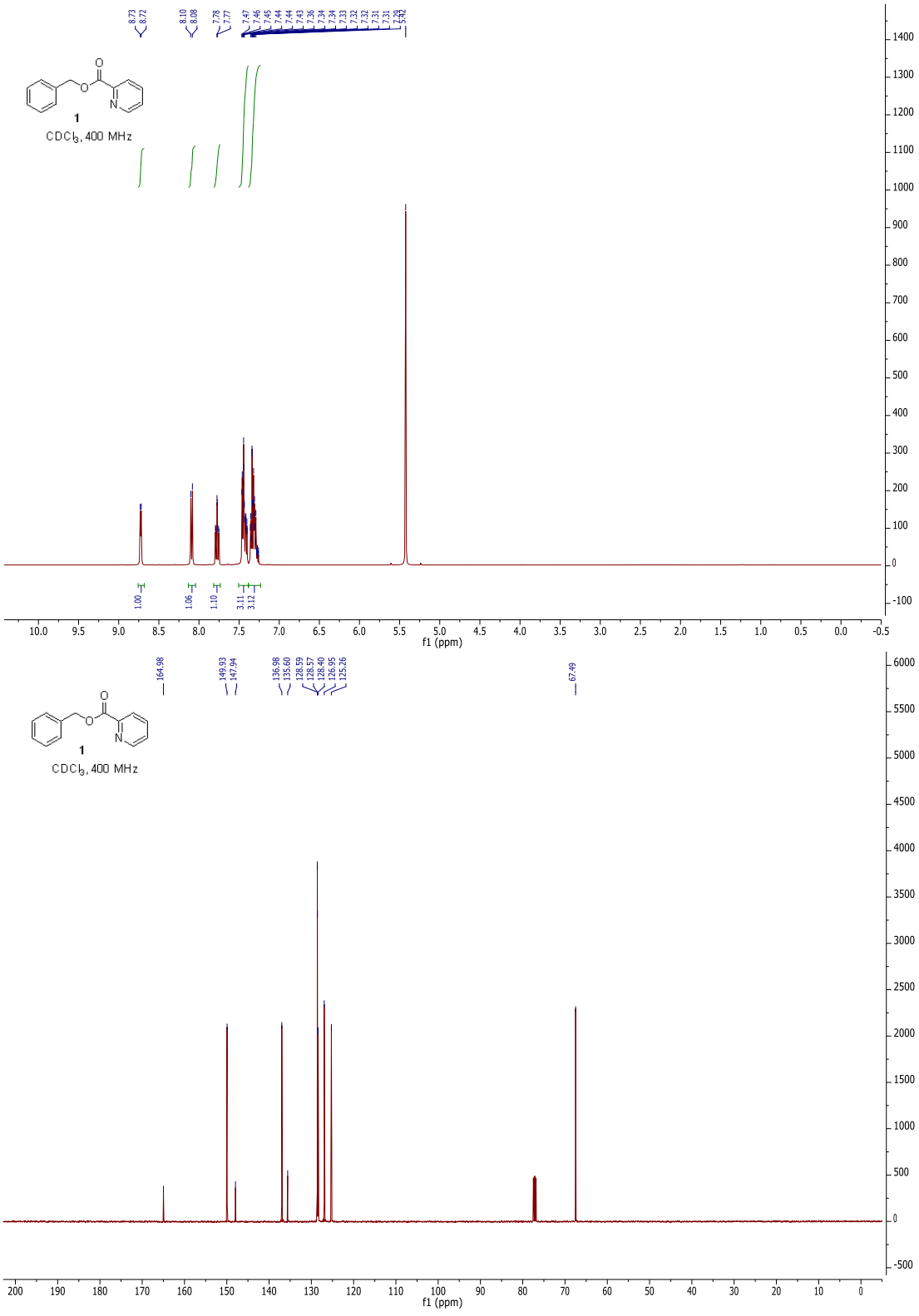
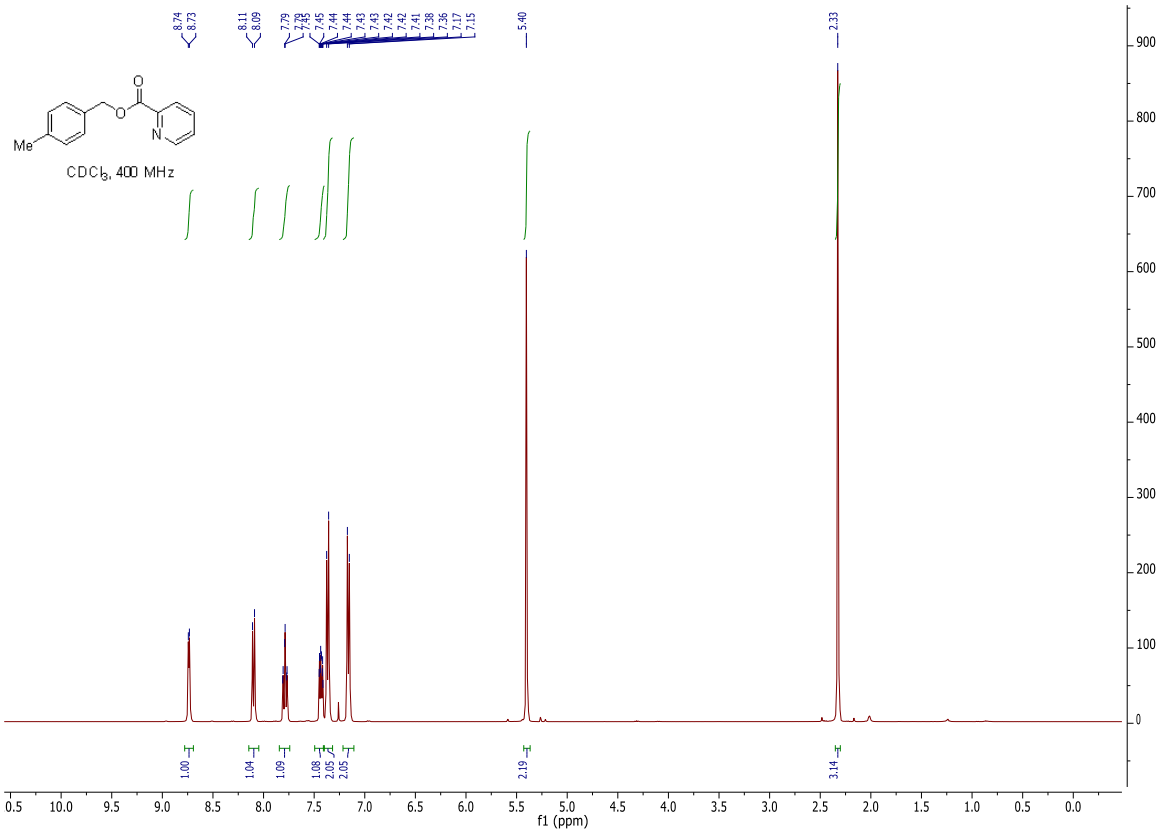
$^{1}H/^{13}C$ NMR Spectra

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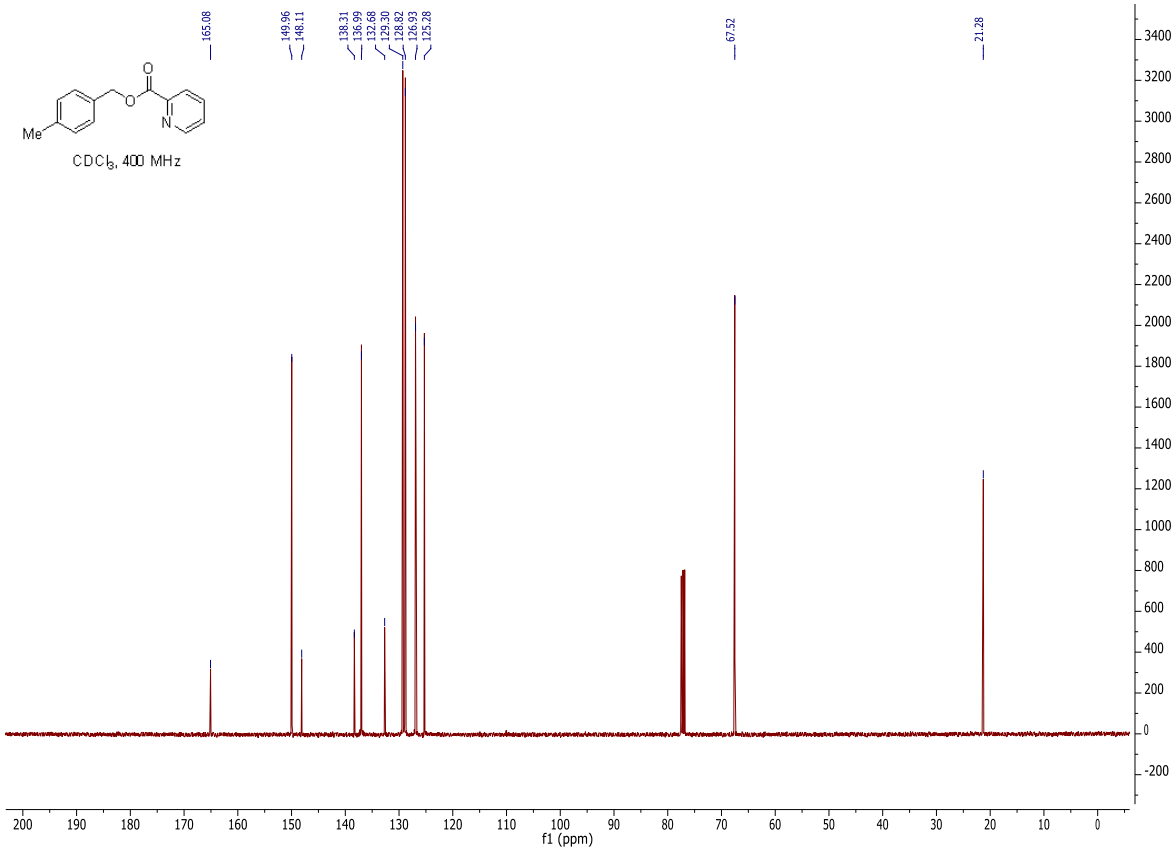
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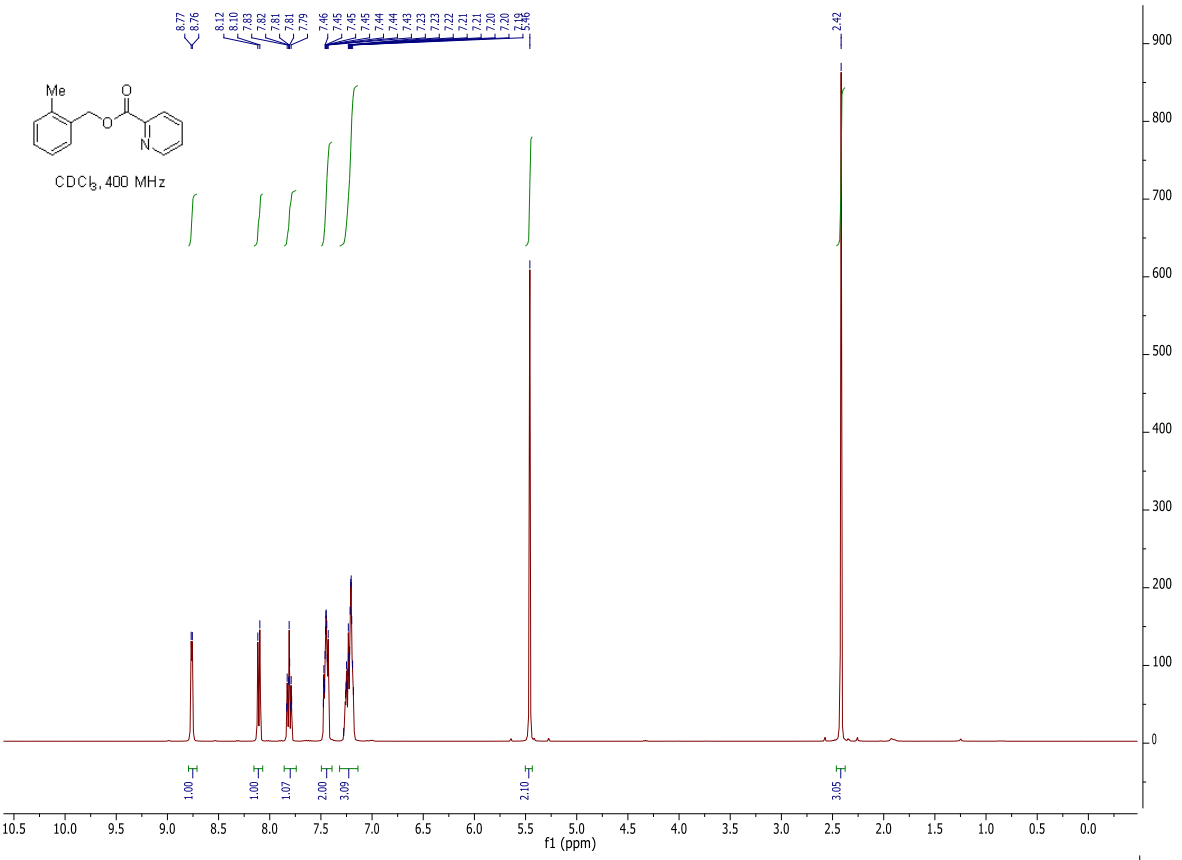
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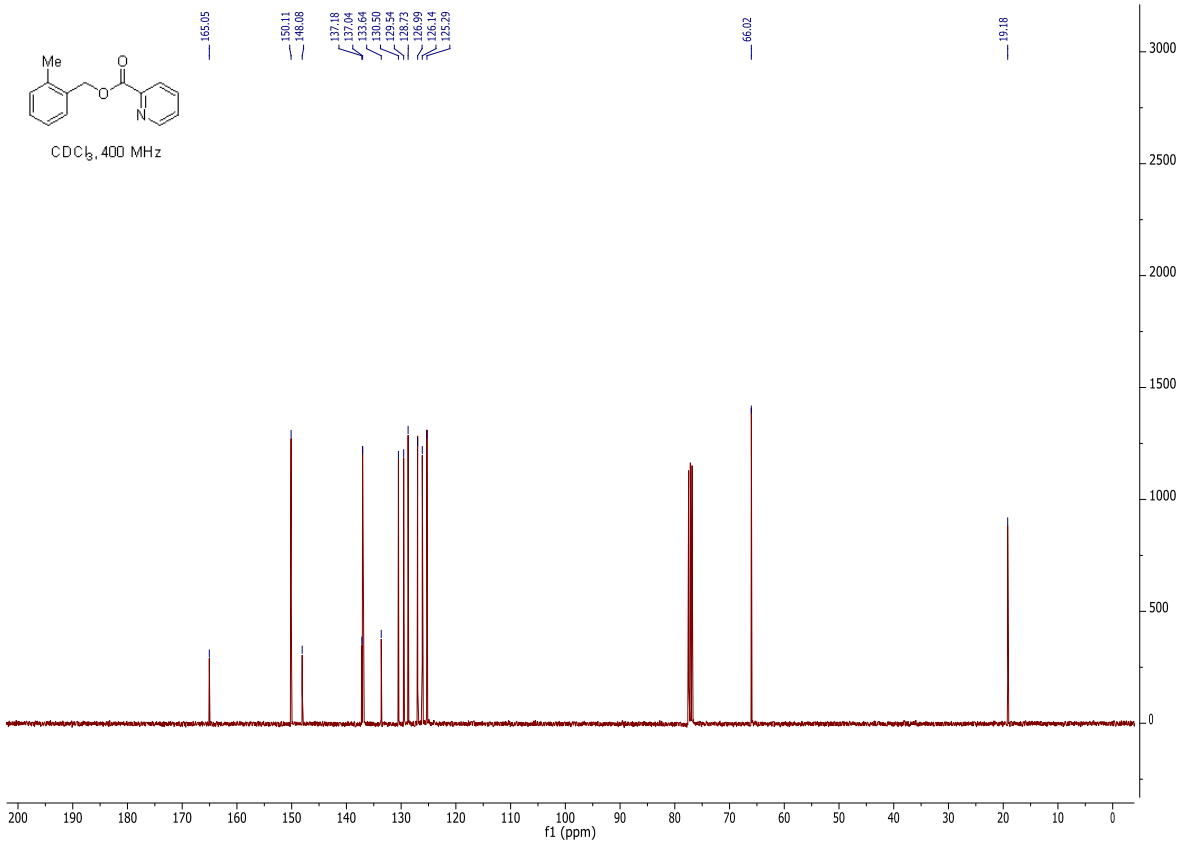
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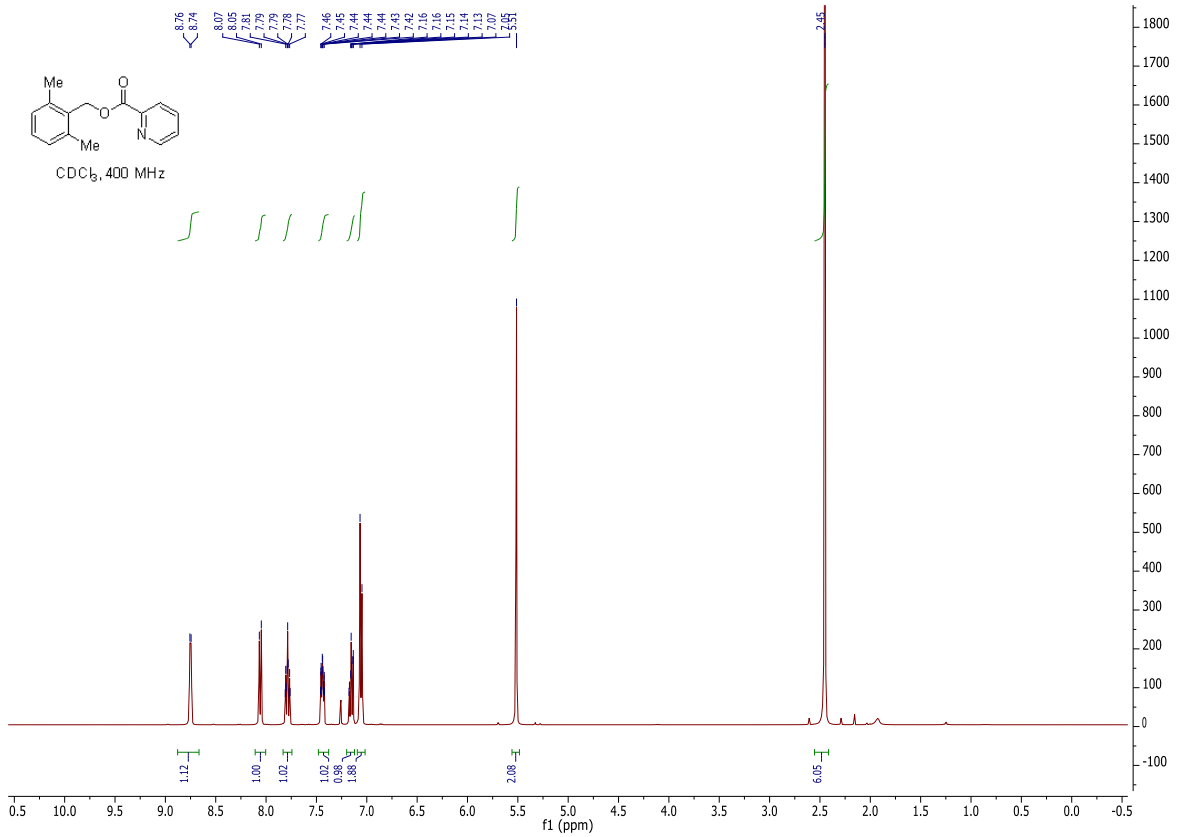
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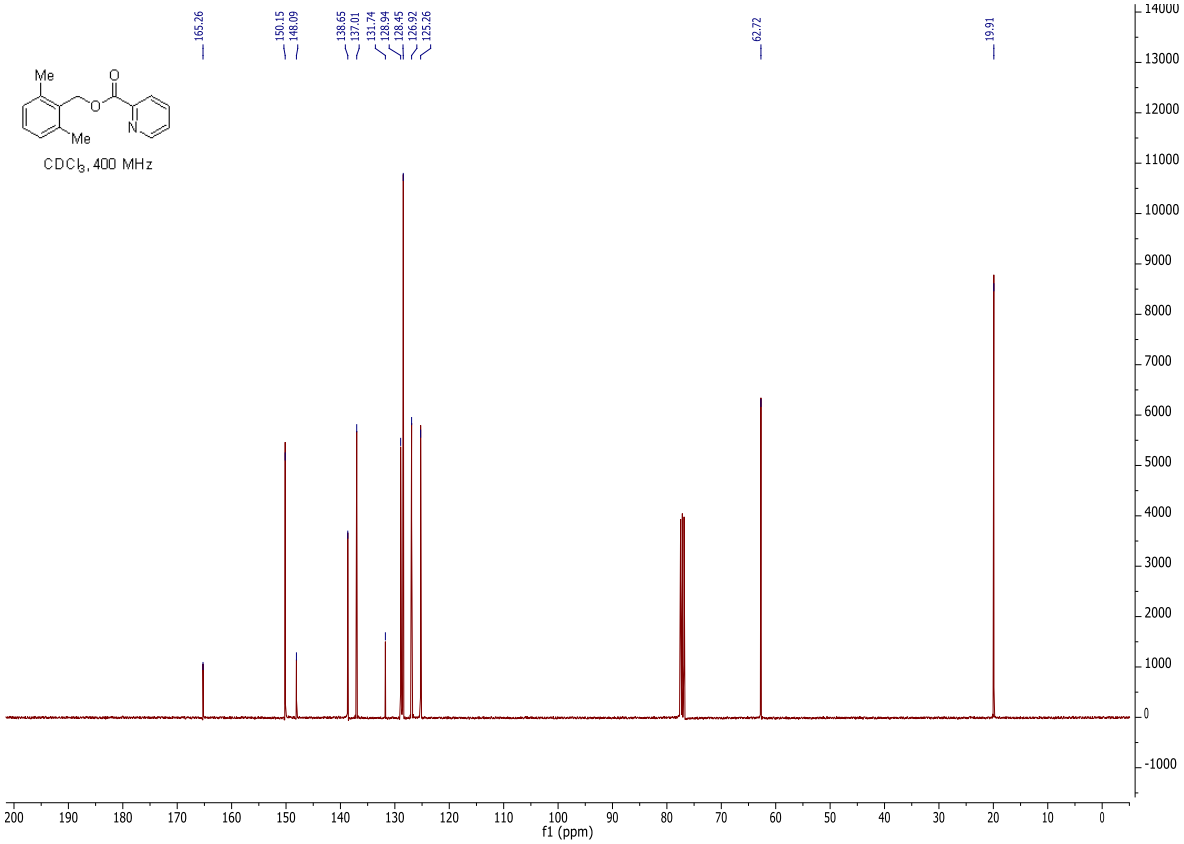
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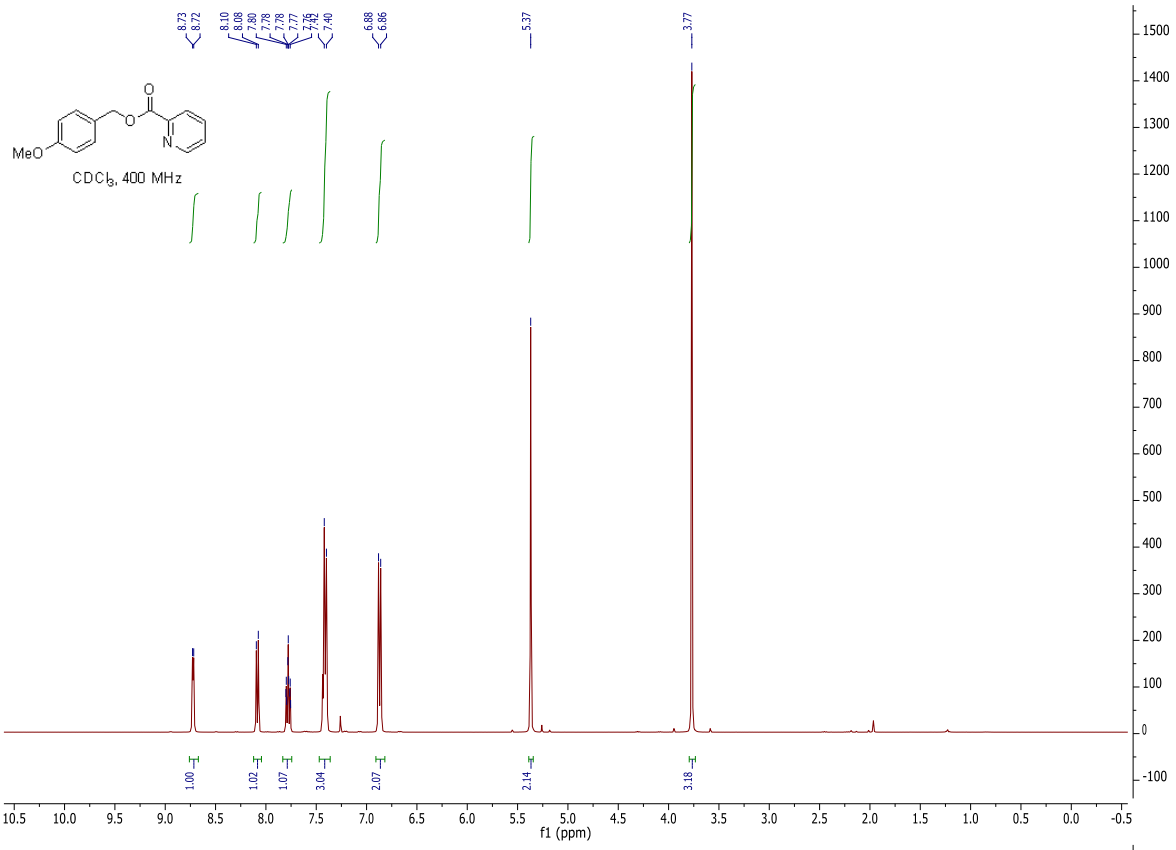
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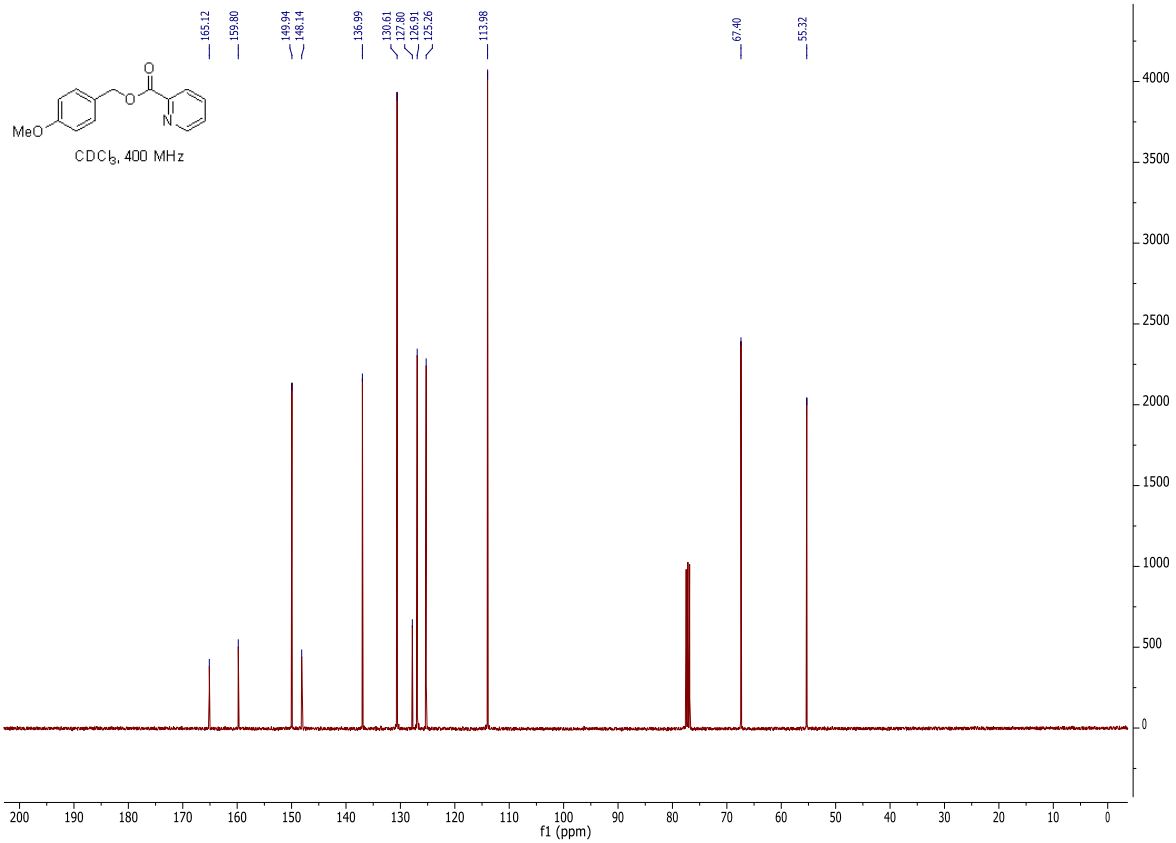
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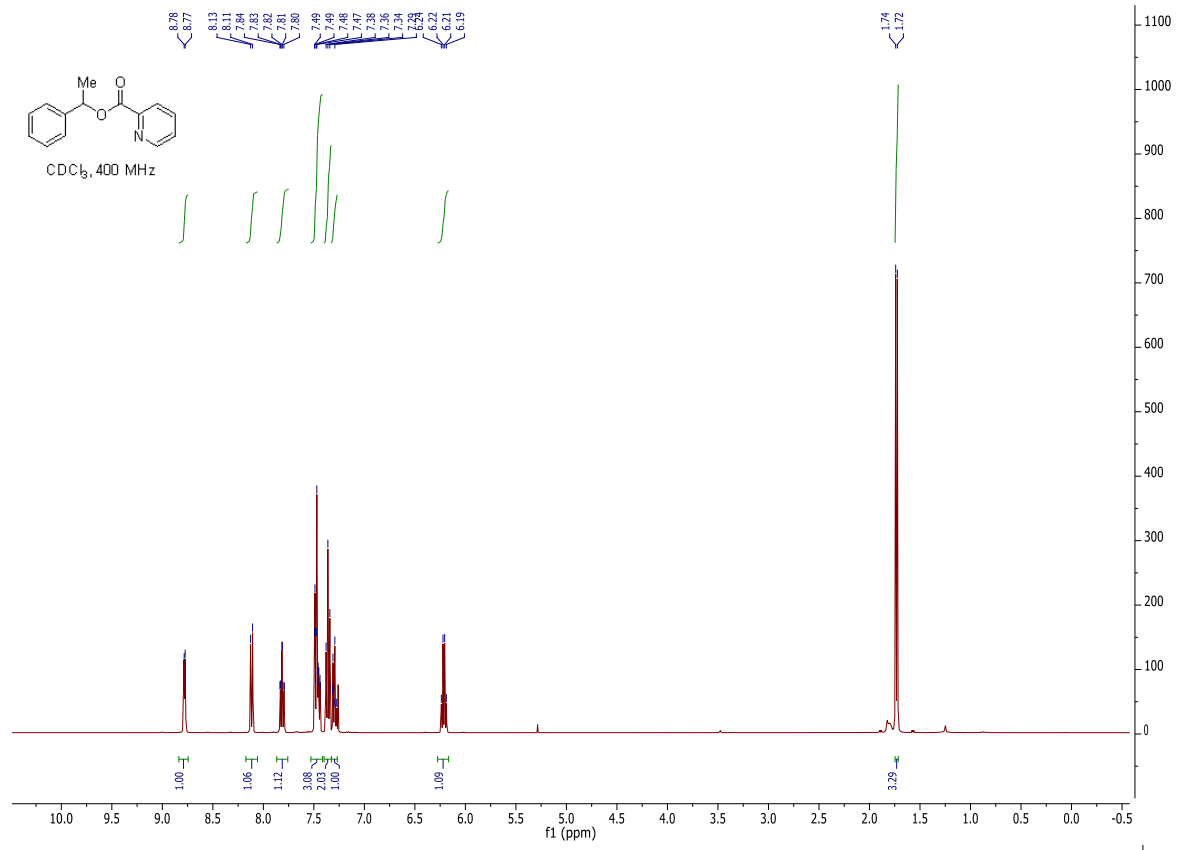
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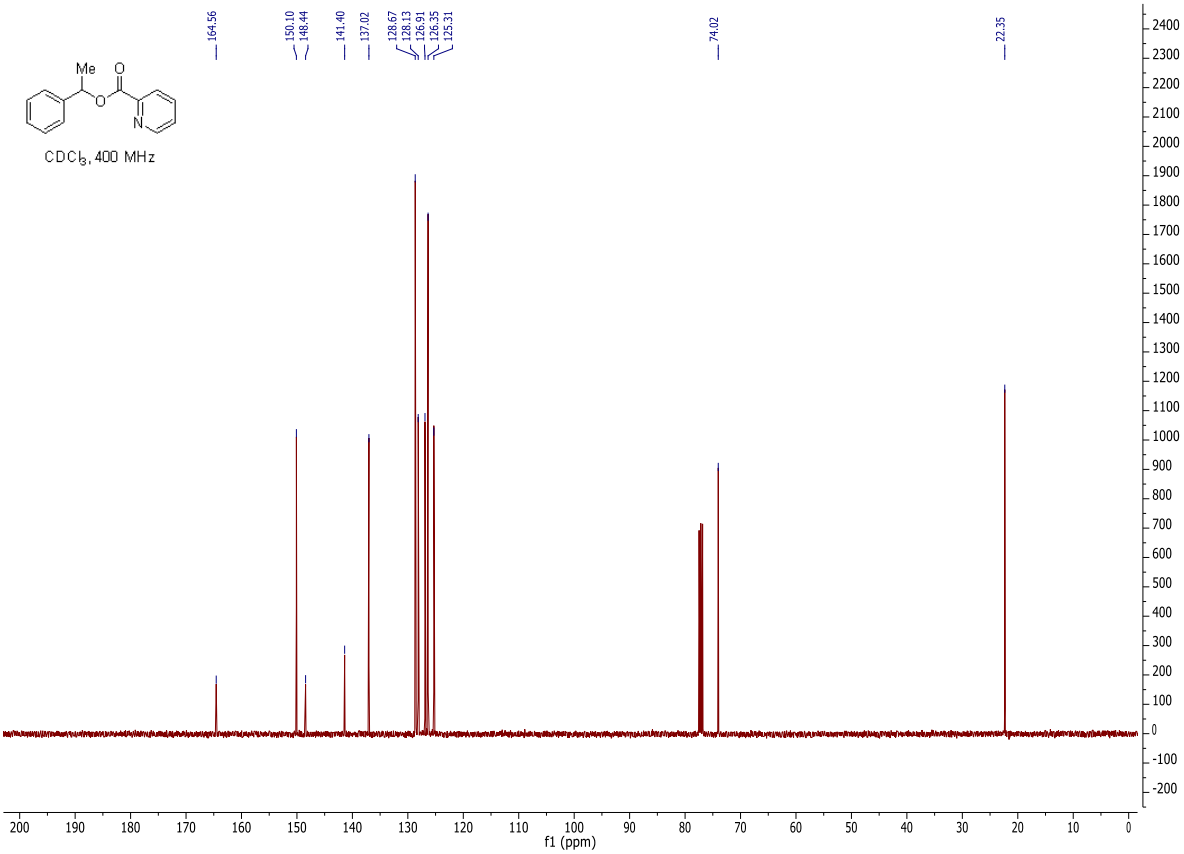
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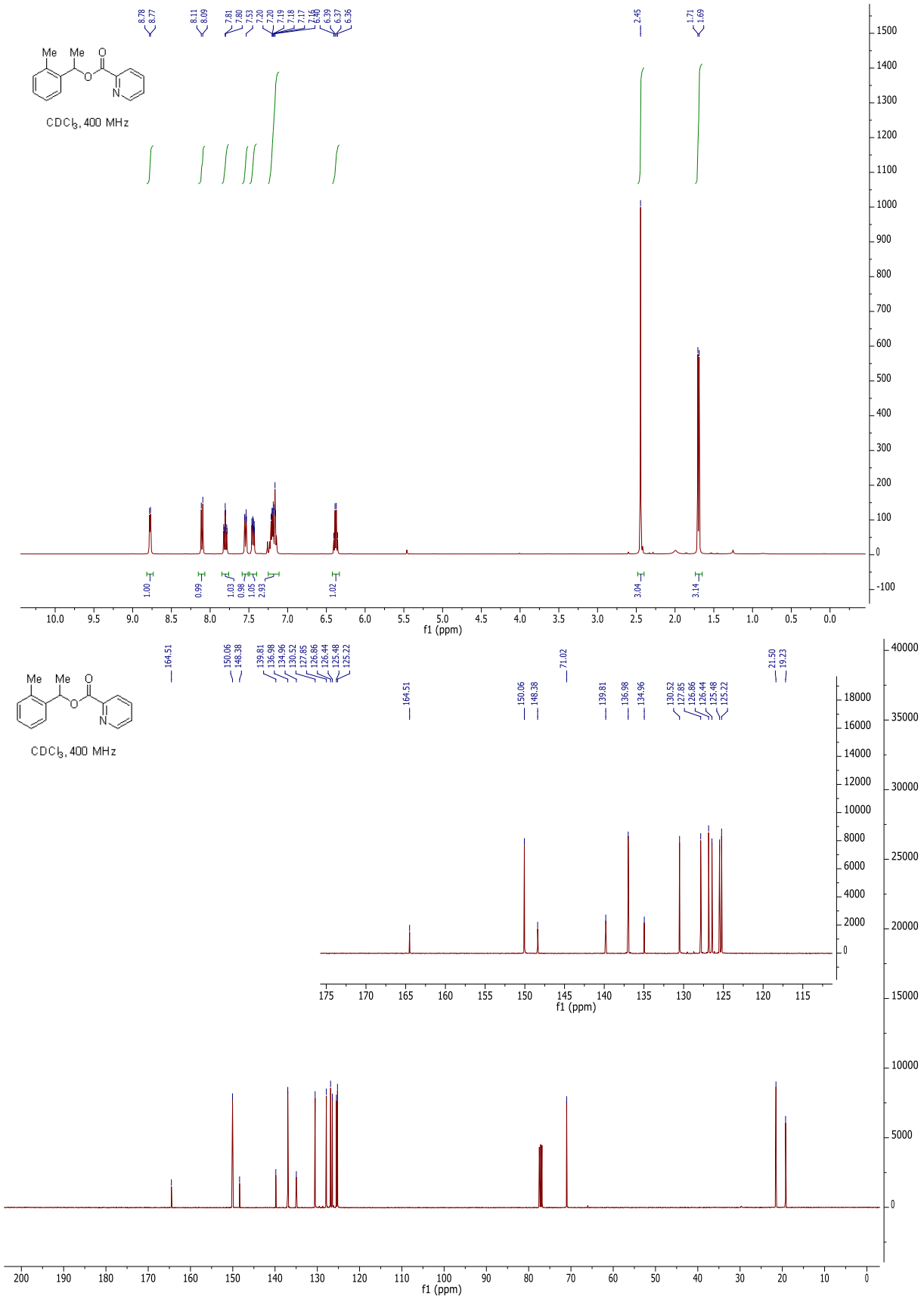
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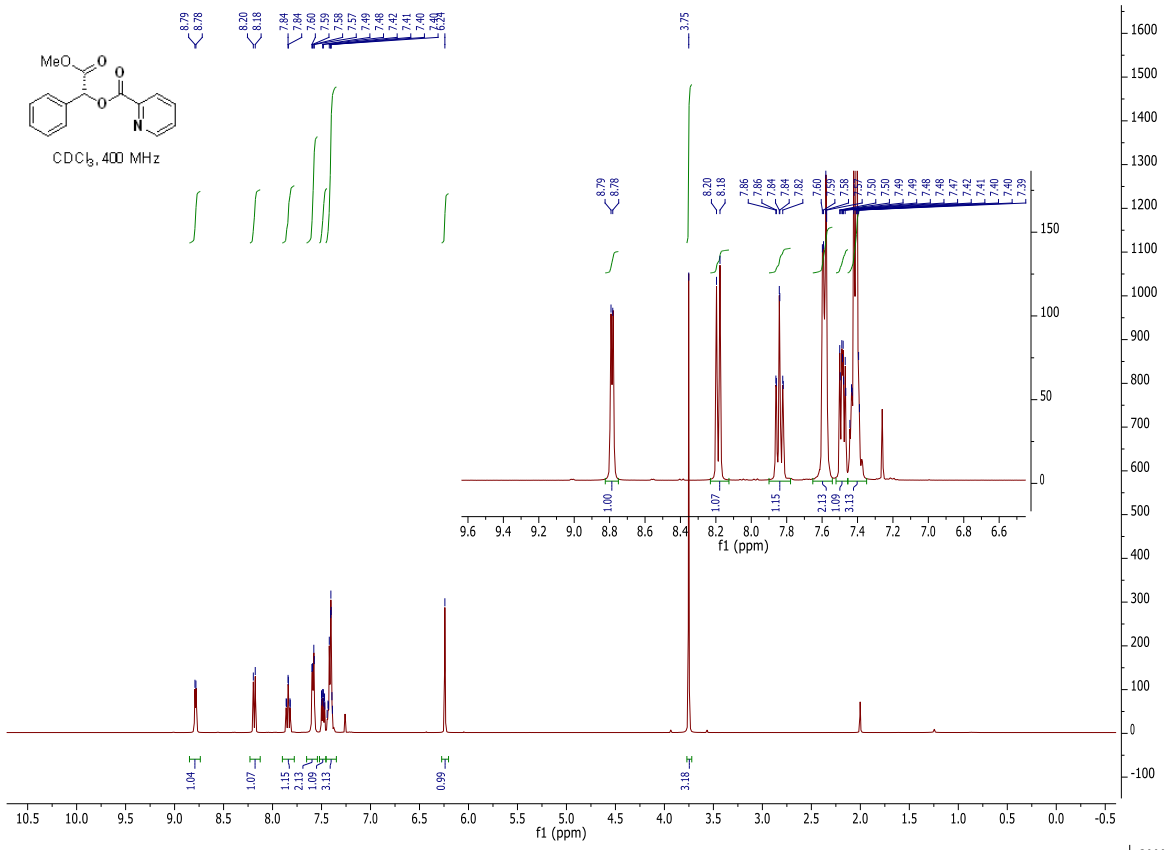
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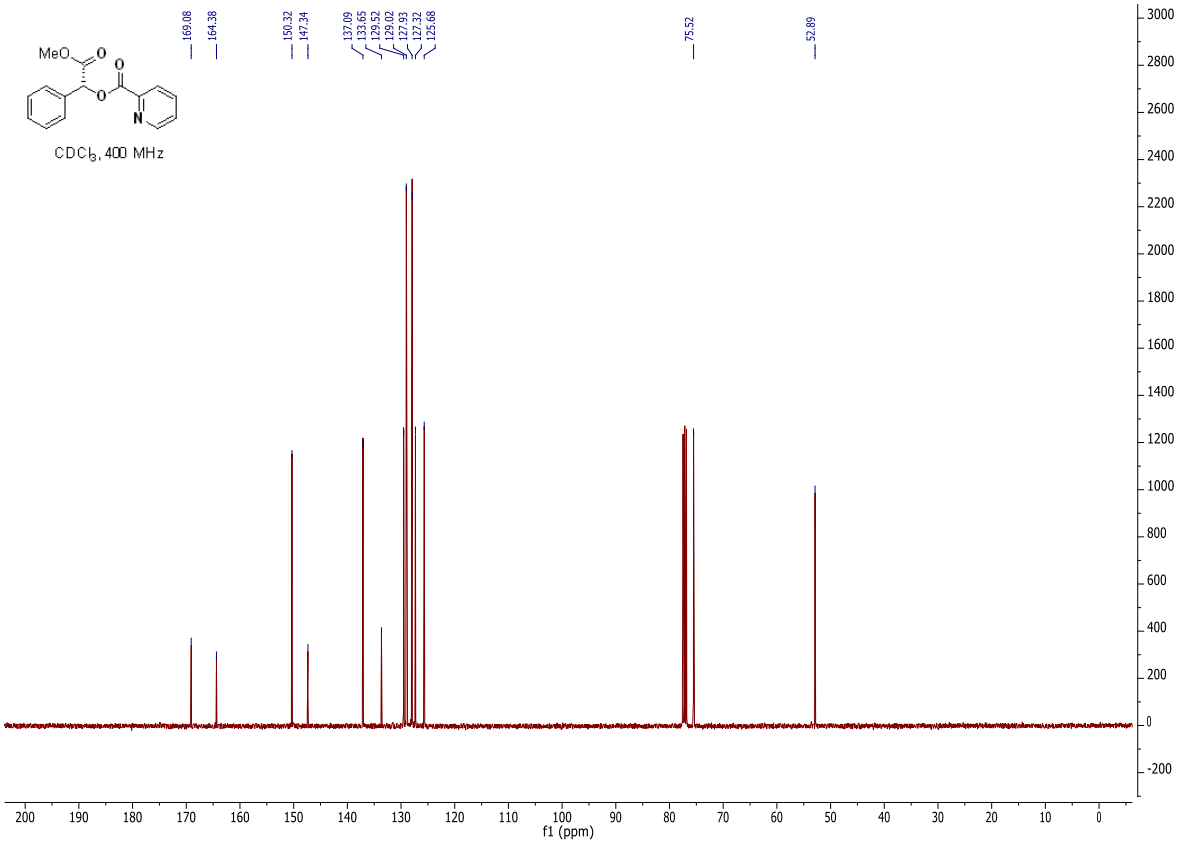
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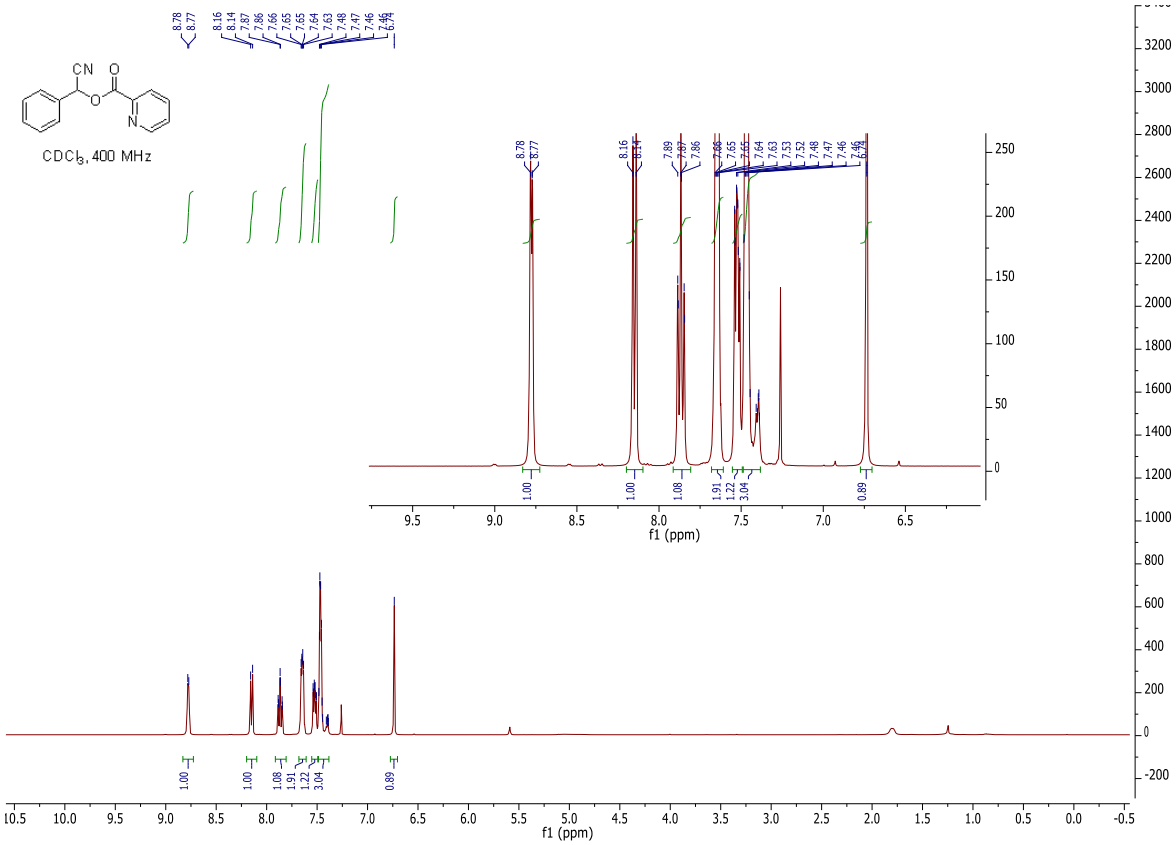
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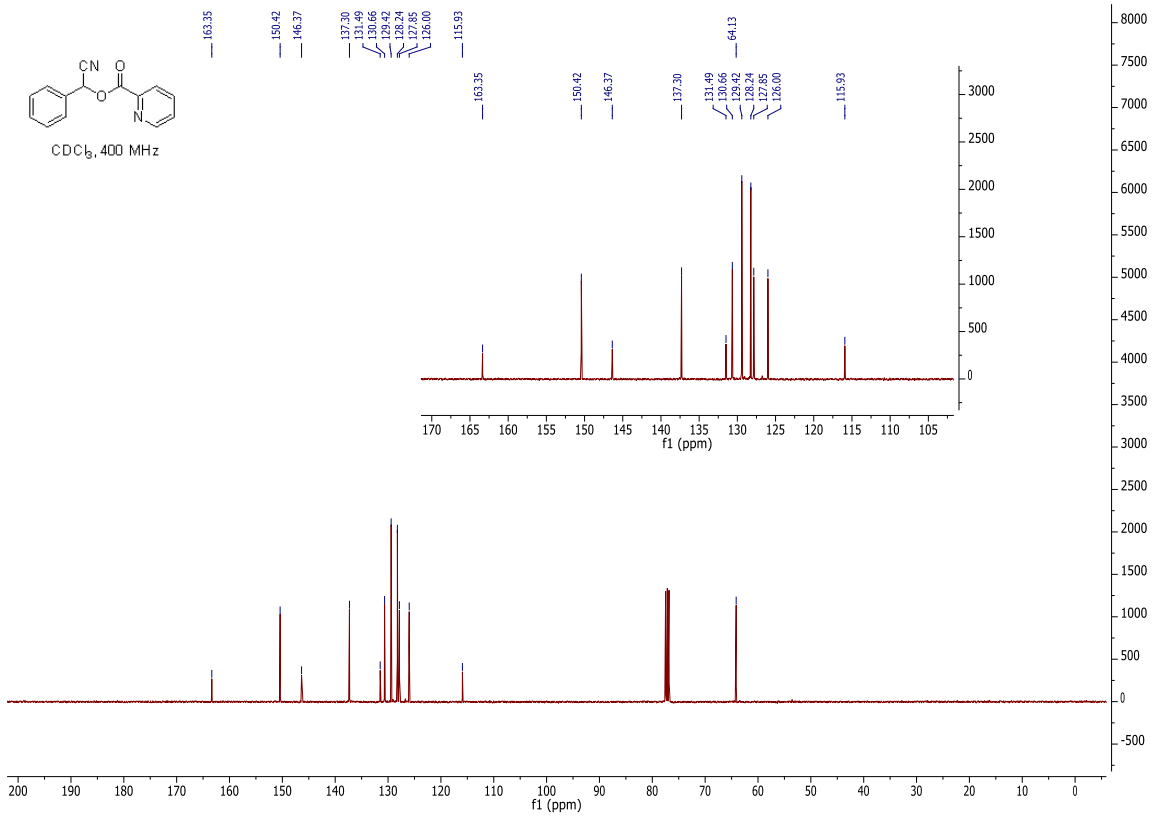
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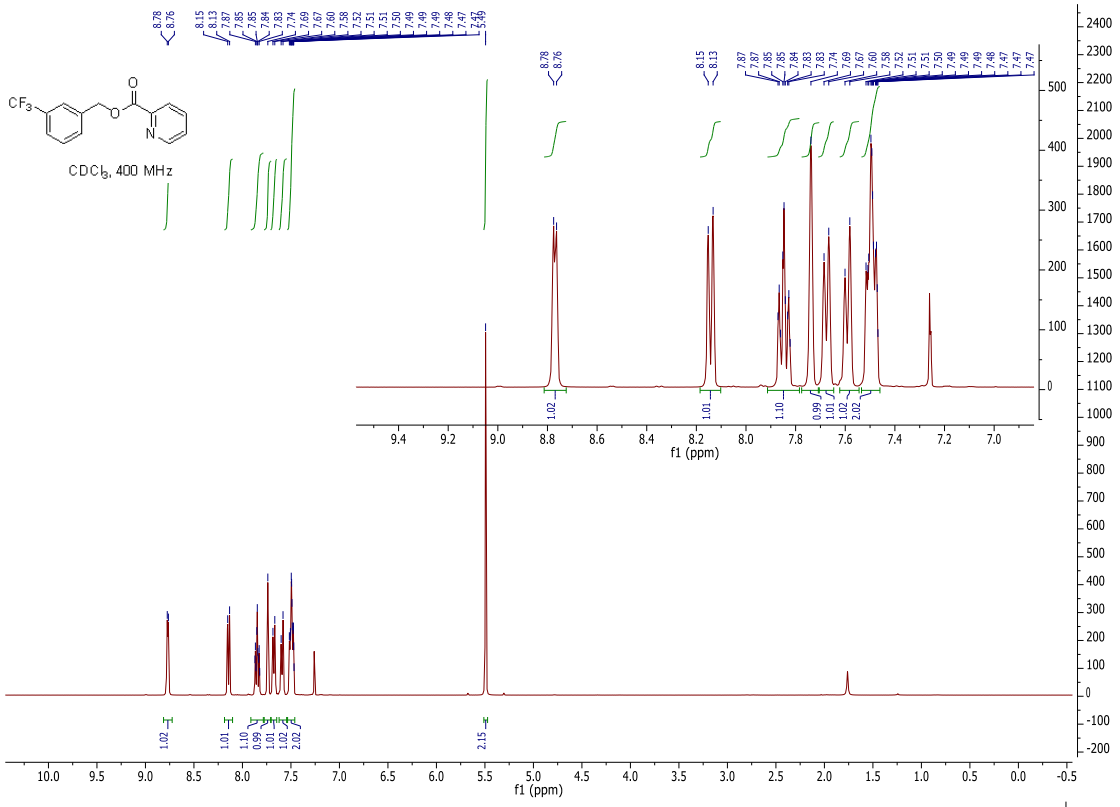
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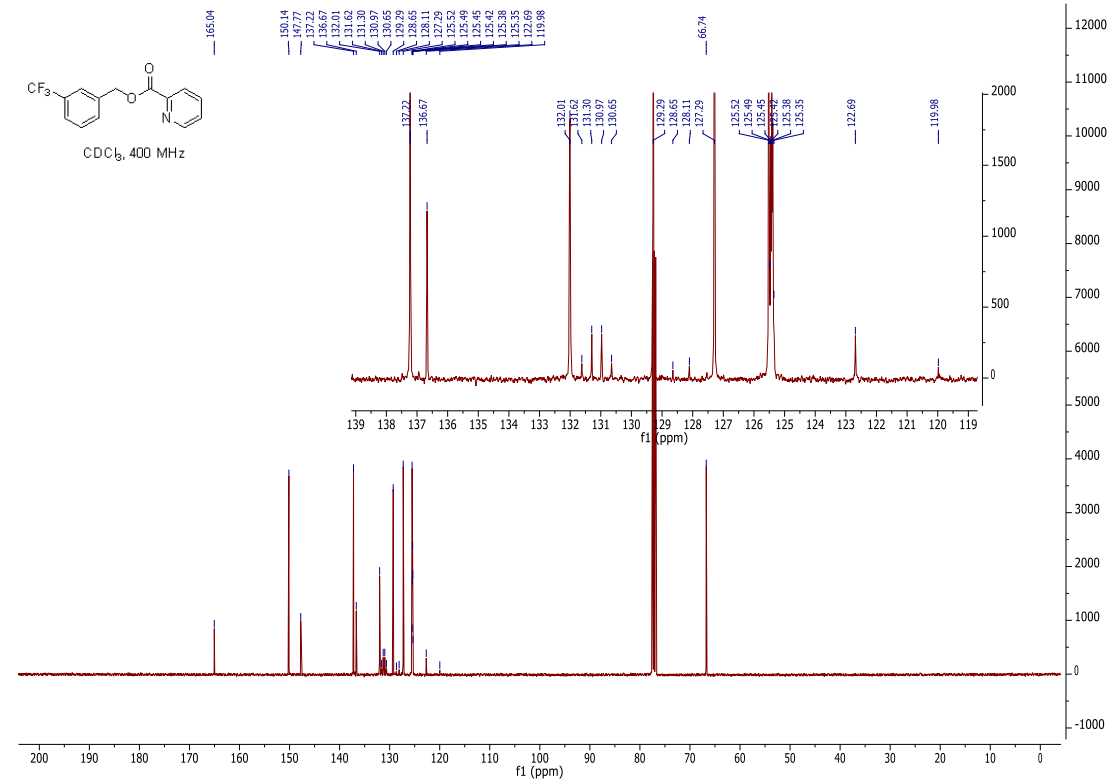
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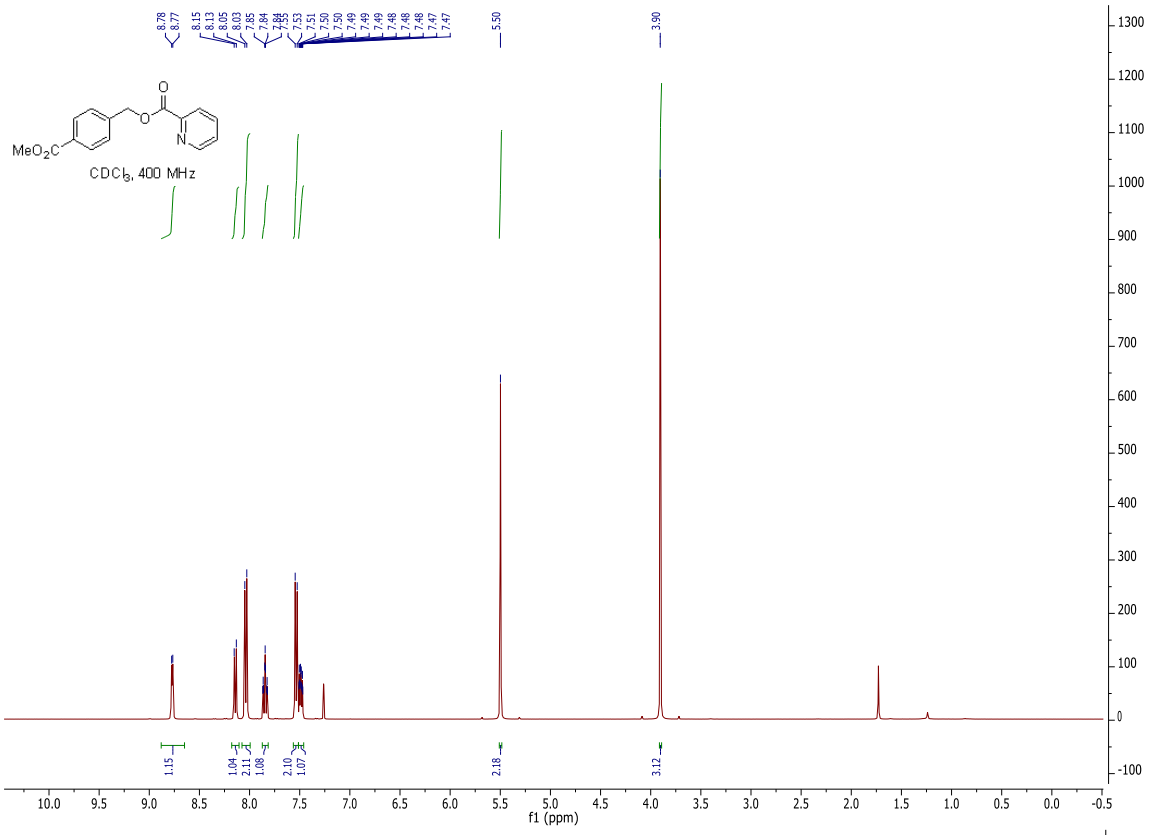
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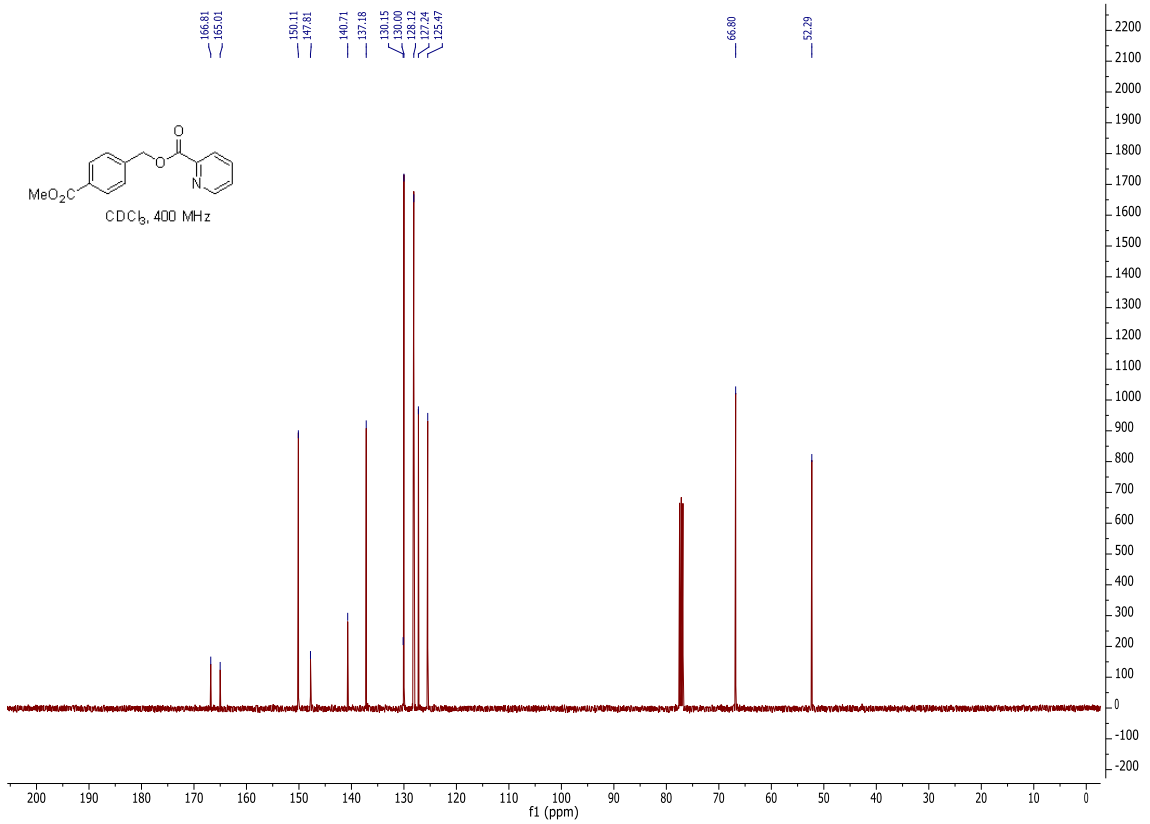
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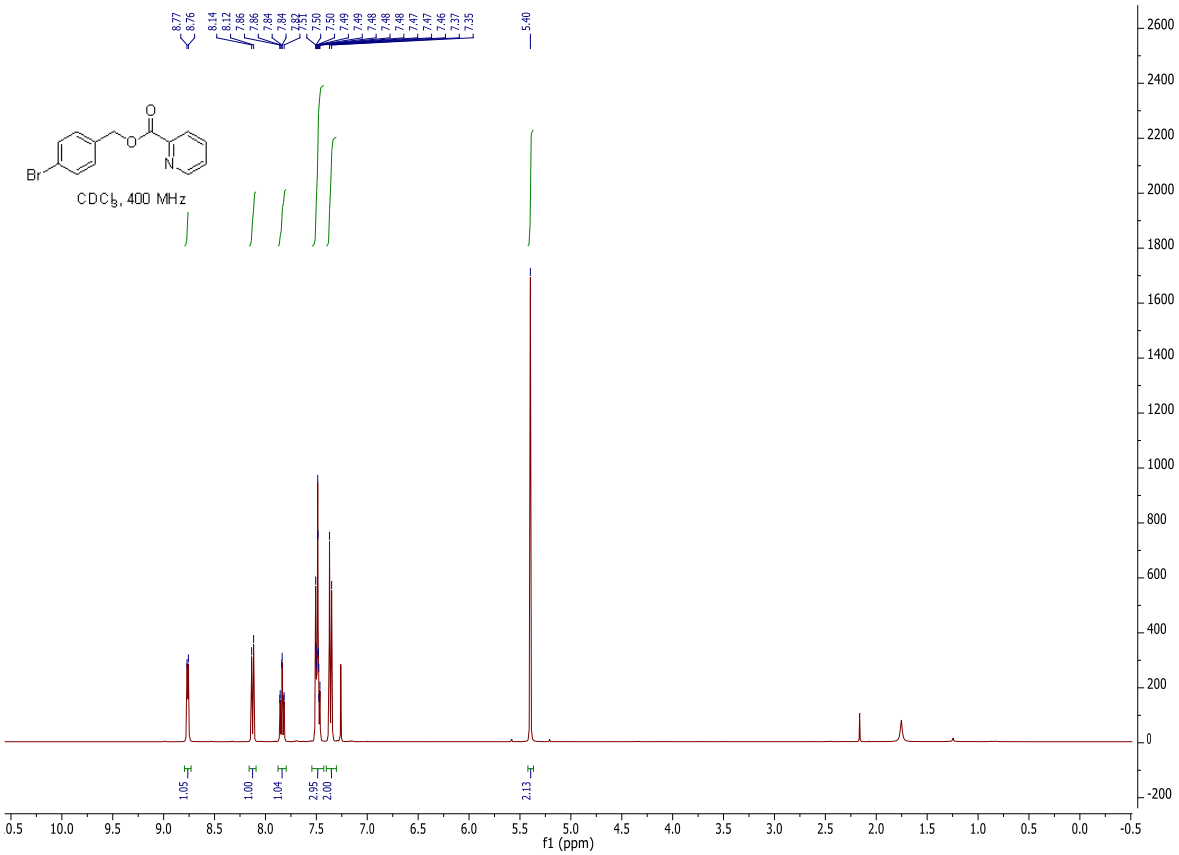
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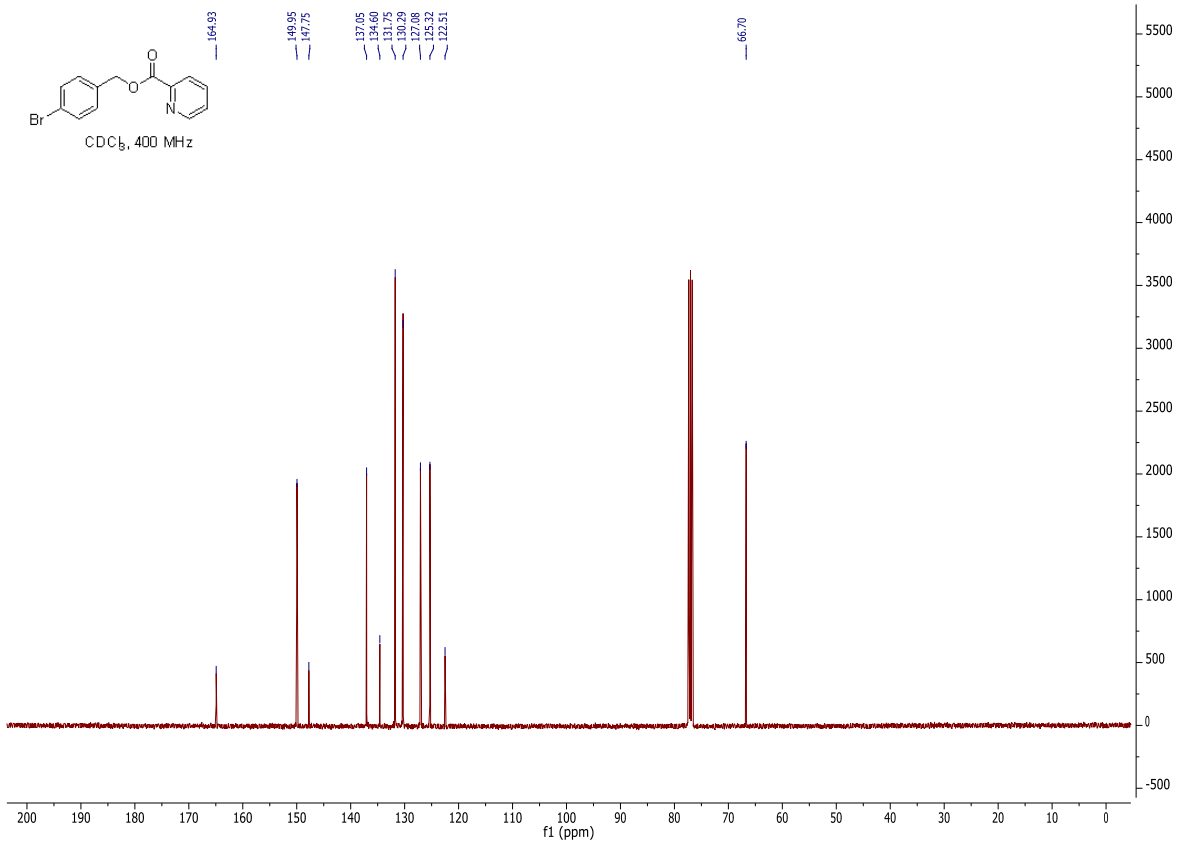
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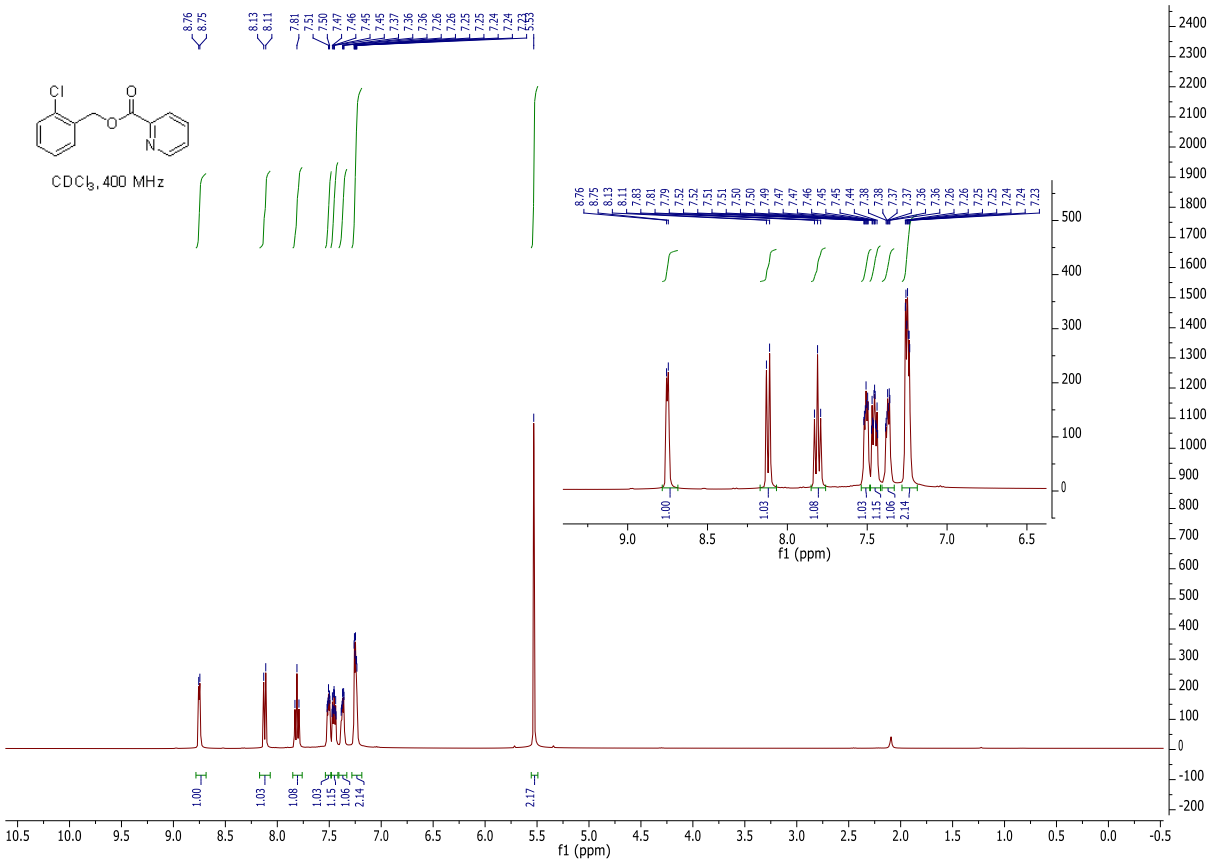
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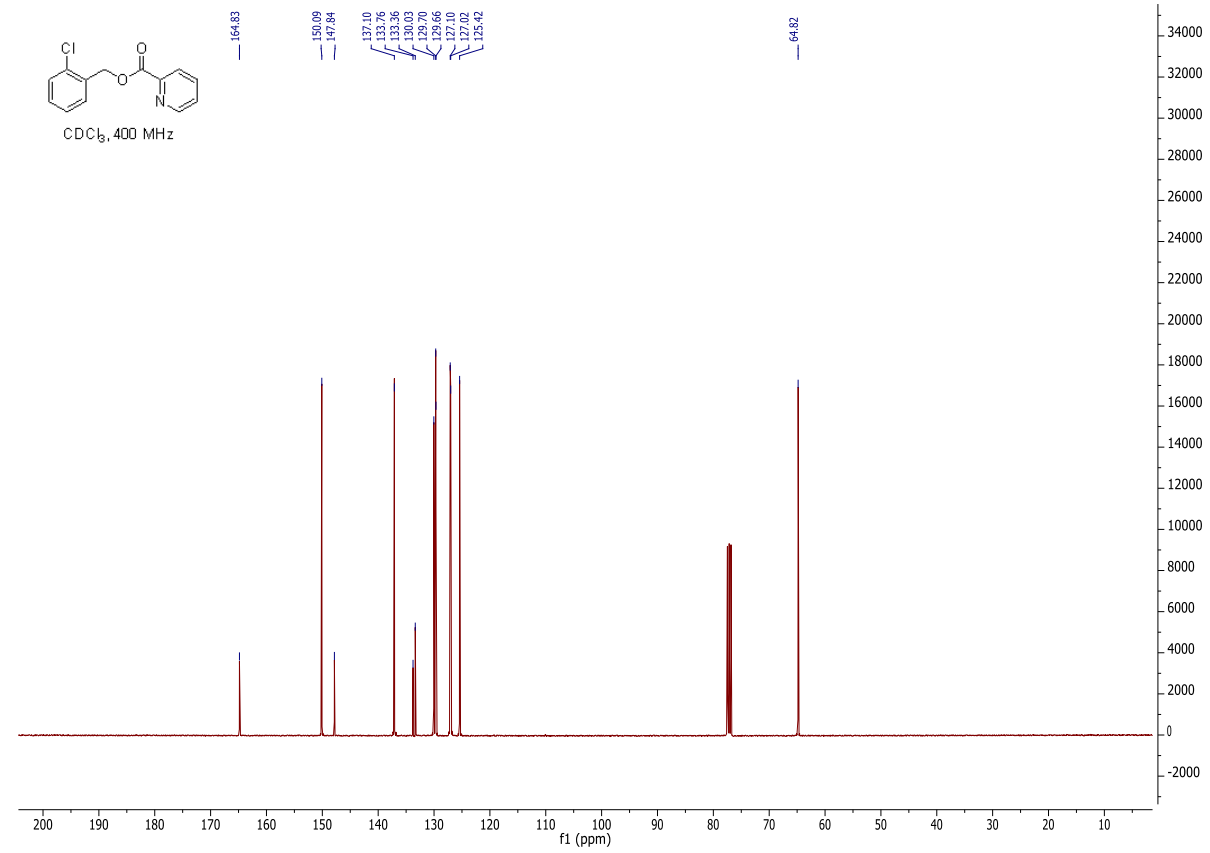
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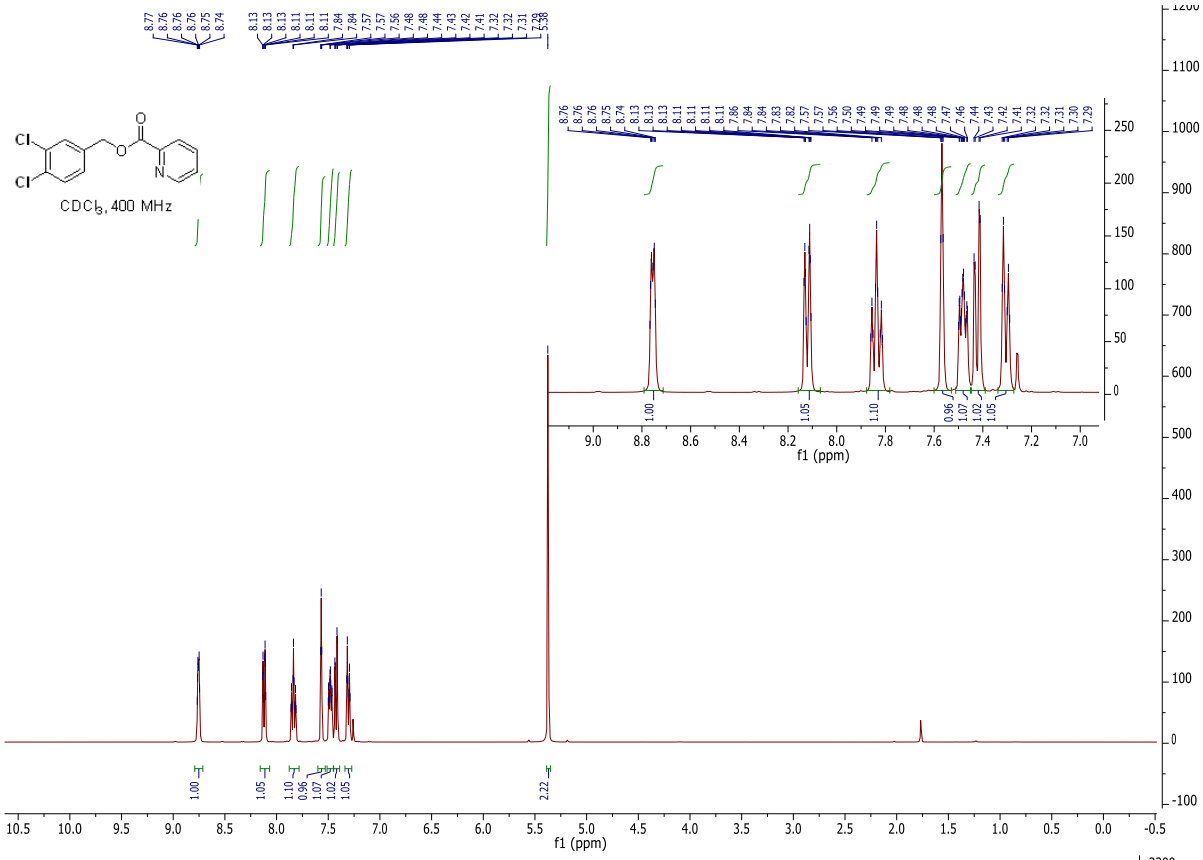
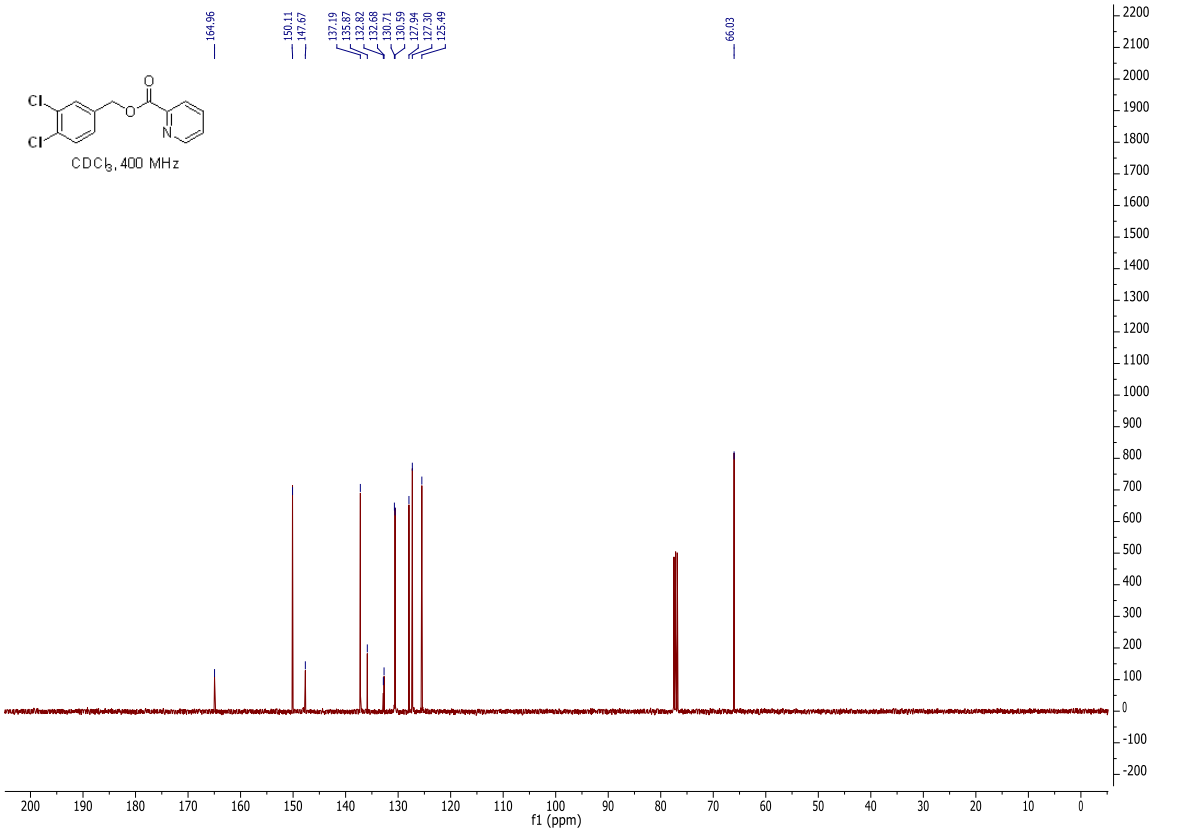
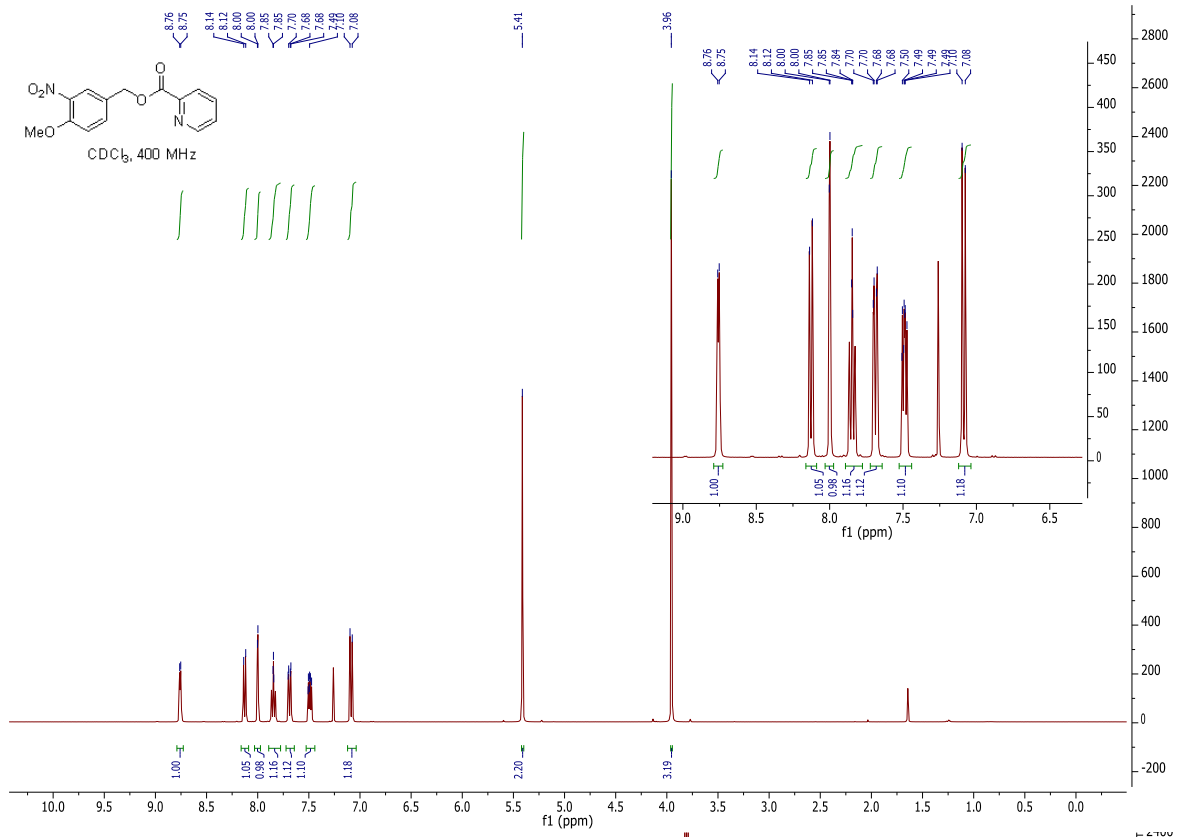
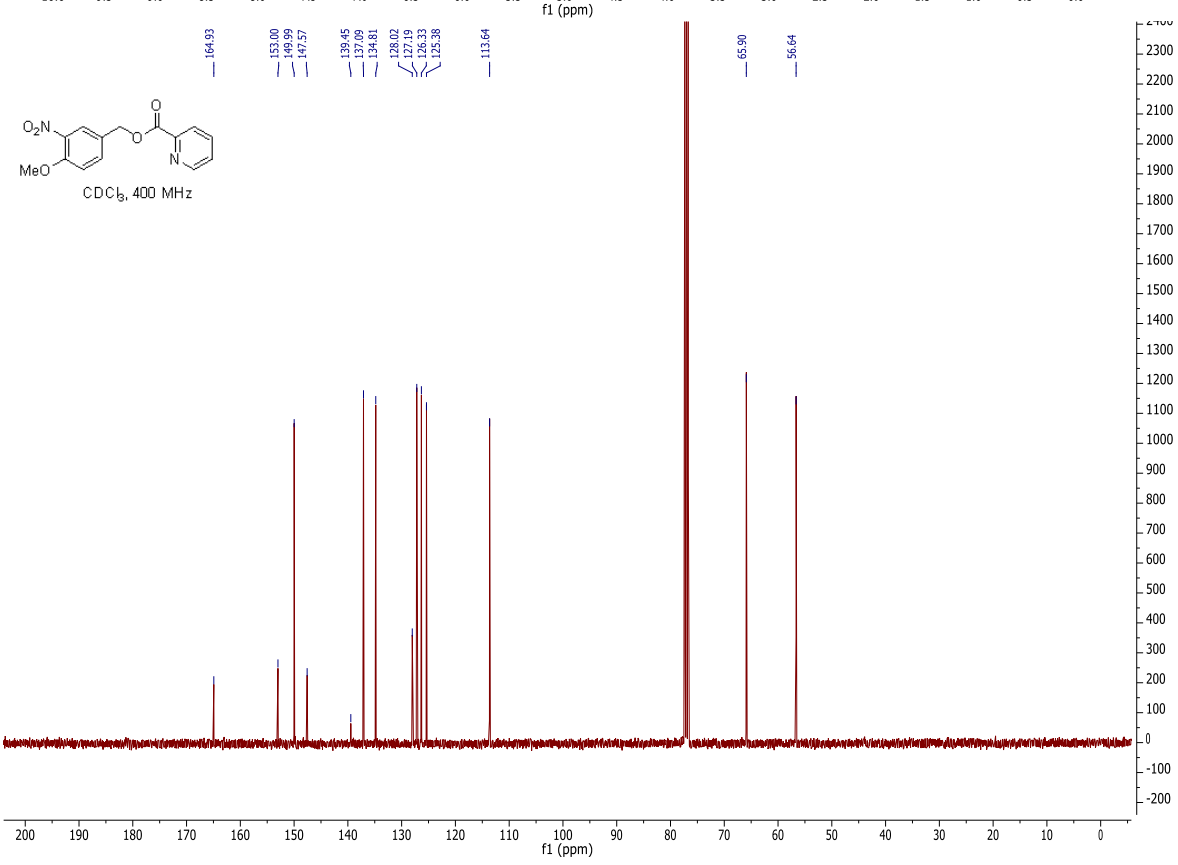
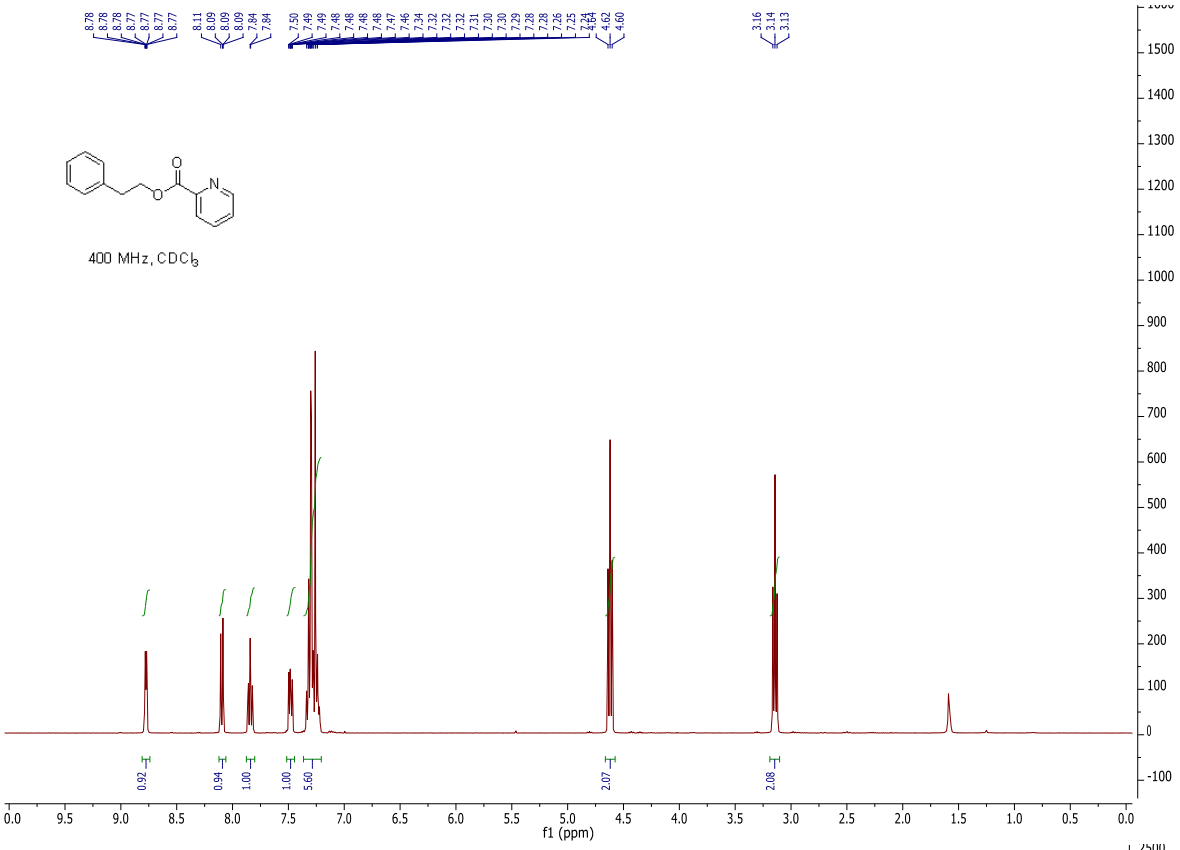
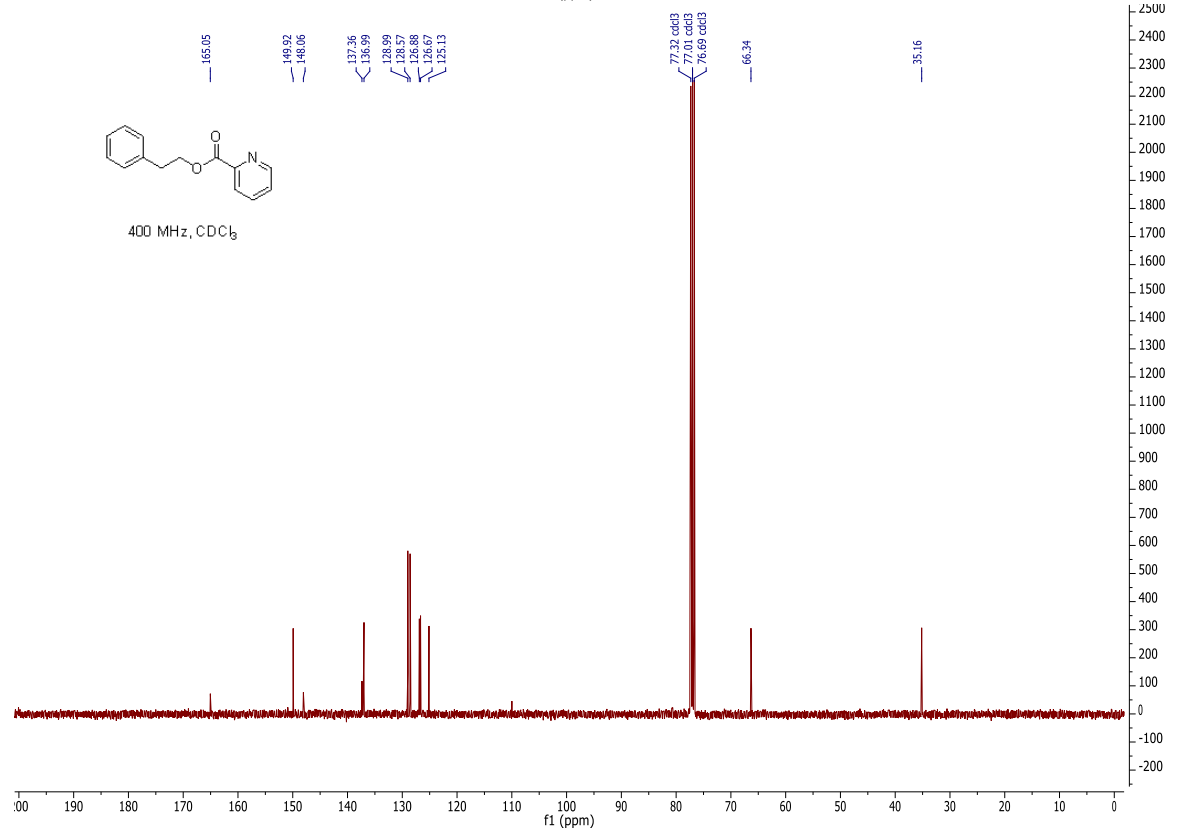

CDCl3, 400 MHz
f1 (ppm)

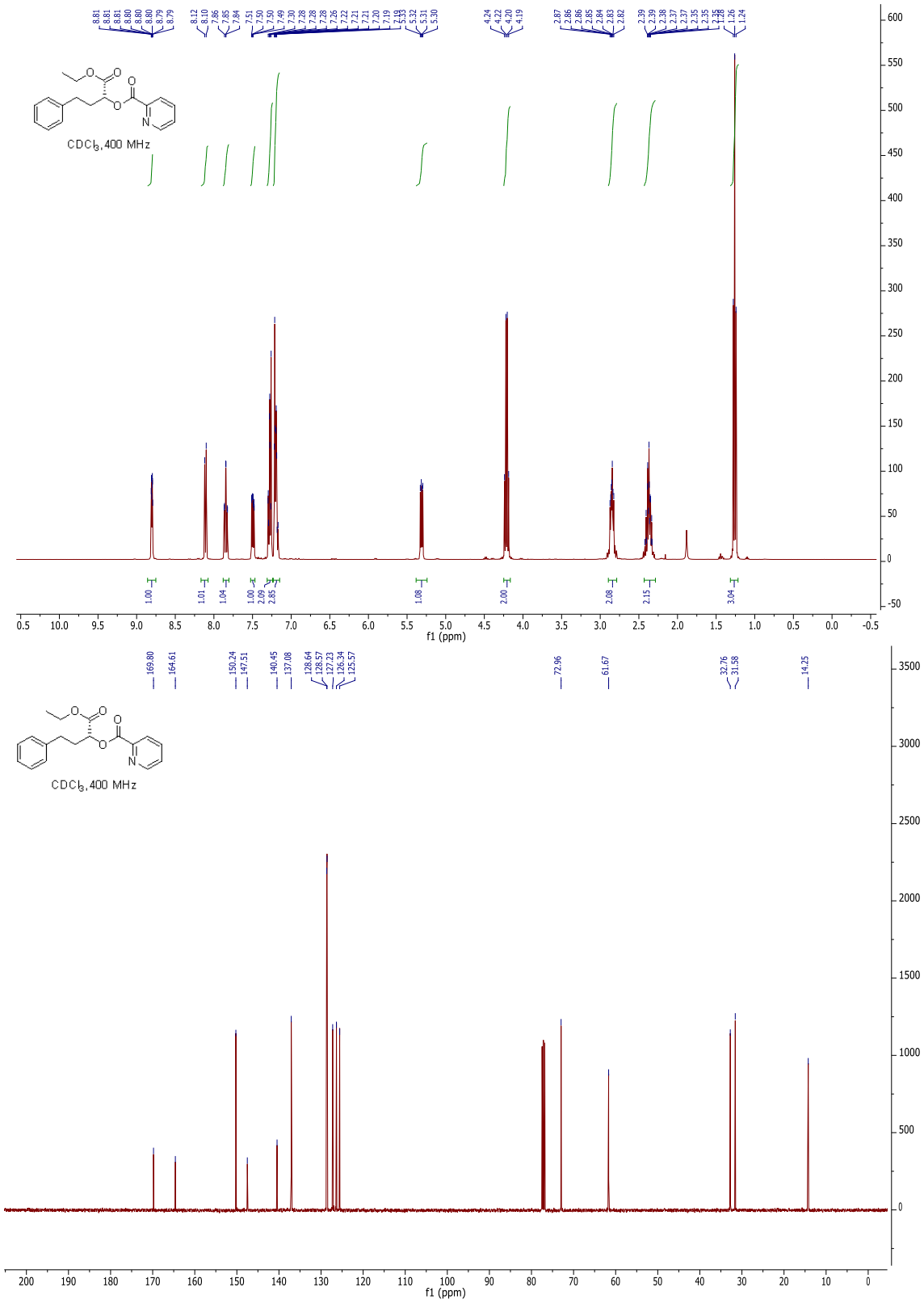

CDCl3, 400 MHz
f1 (ppm)

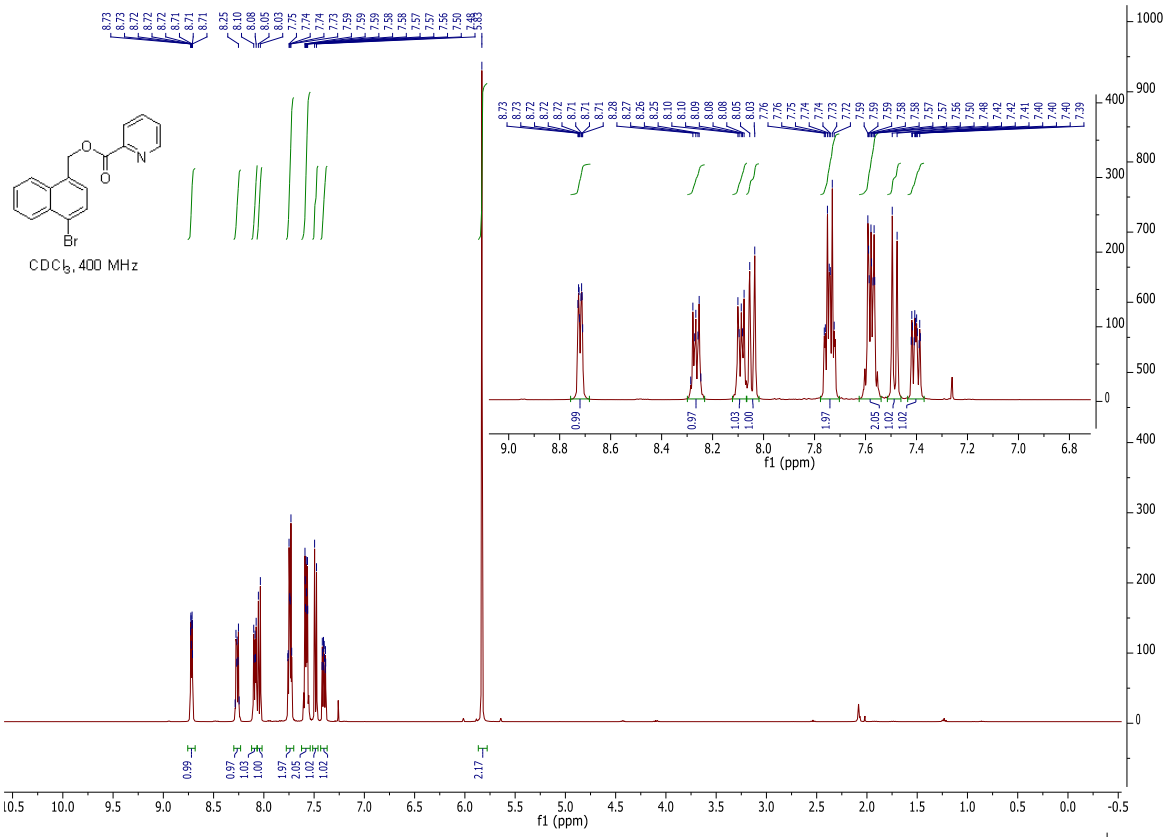

8.76
8.75
8.14
8.12
8.00
8.00
7.85
7.70
7.68
7.68
7.49
7.10
7.08
5.41
3.96
O2N
MeO
O
O
N
CDCl3, 400 MHz
1.00
1.05
0.98
1.16
1.12
1.10
1.18
2.20
3.19
f1 (ppm)

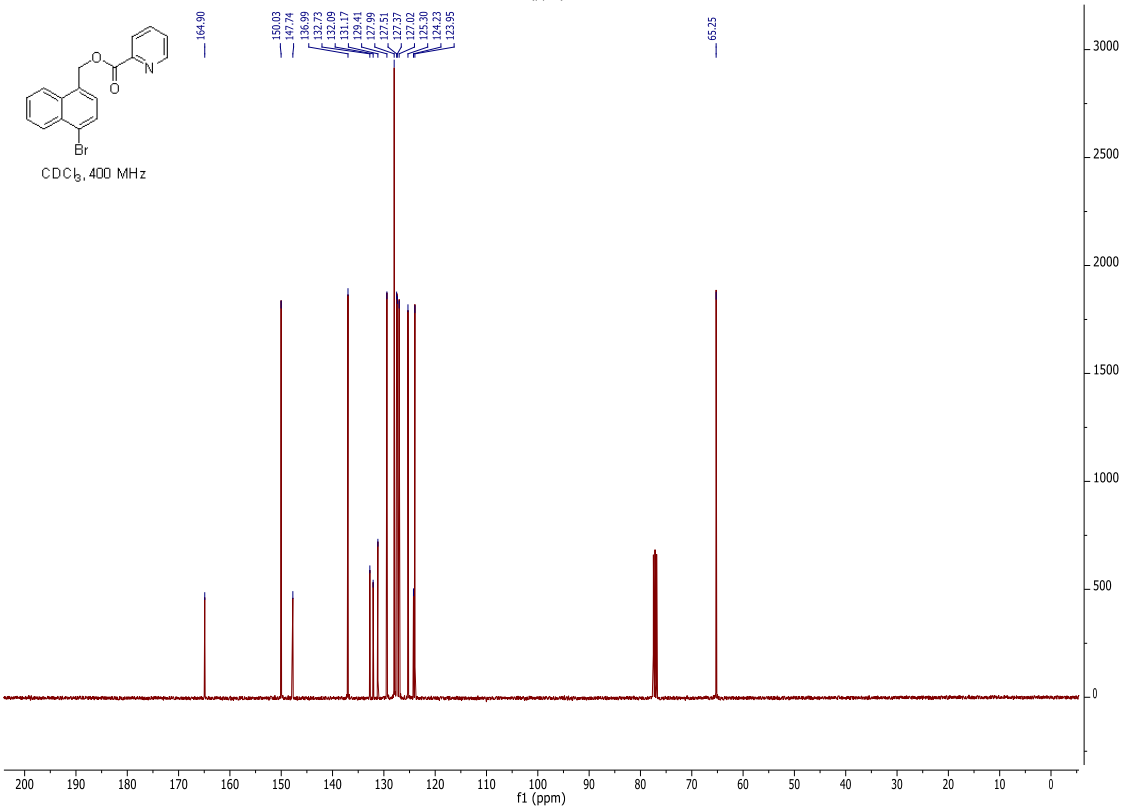

164.93
153.00
149.99
147.57
139.45
137.09
134.81
128.02
127.19
126.33
125.38
113.64
65.90
56.64
O2N
MeO
O
O
N
CDCl3, 400 MHz
f1 (ppm)

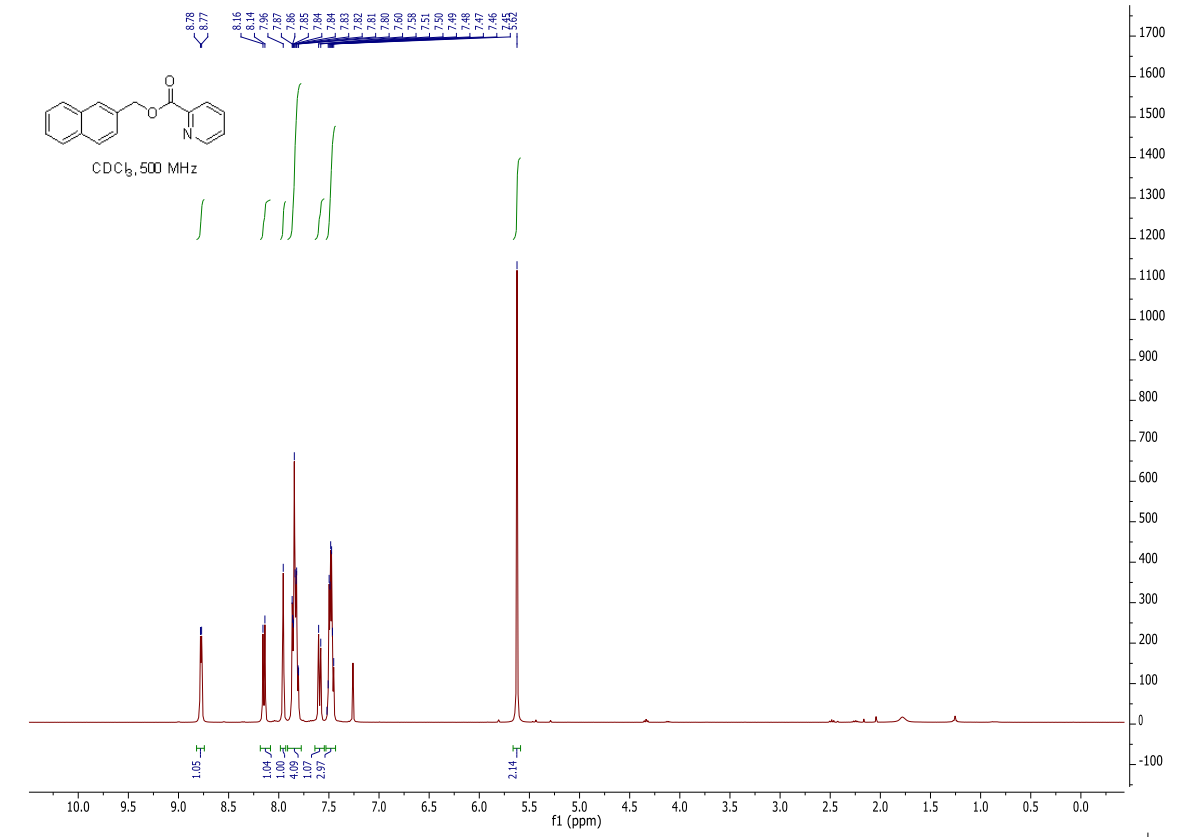

8.78
8.78
8.78
8.77
8.77
8.77
8.77
8.11
8.09
8.09
8.09
7.84
7.84
7.50
7.49
7.49
7.48
7.48
7.48
7.48
7.47
7.46
7.34
7.32
7.32
7.32
7.31
7.30
7.30
7.29
7.28
7.28
7.26
7.25
4.64
4.62
4.60
3.16
3.14
3.13
O
O
N
400 MHz, CDCl3
0.92
0.94
1.00
1.00
5.60
2.07
2.08
f1 (ppm)

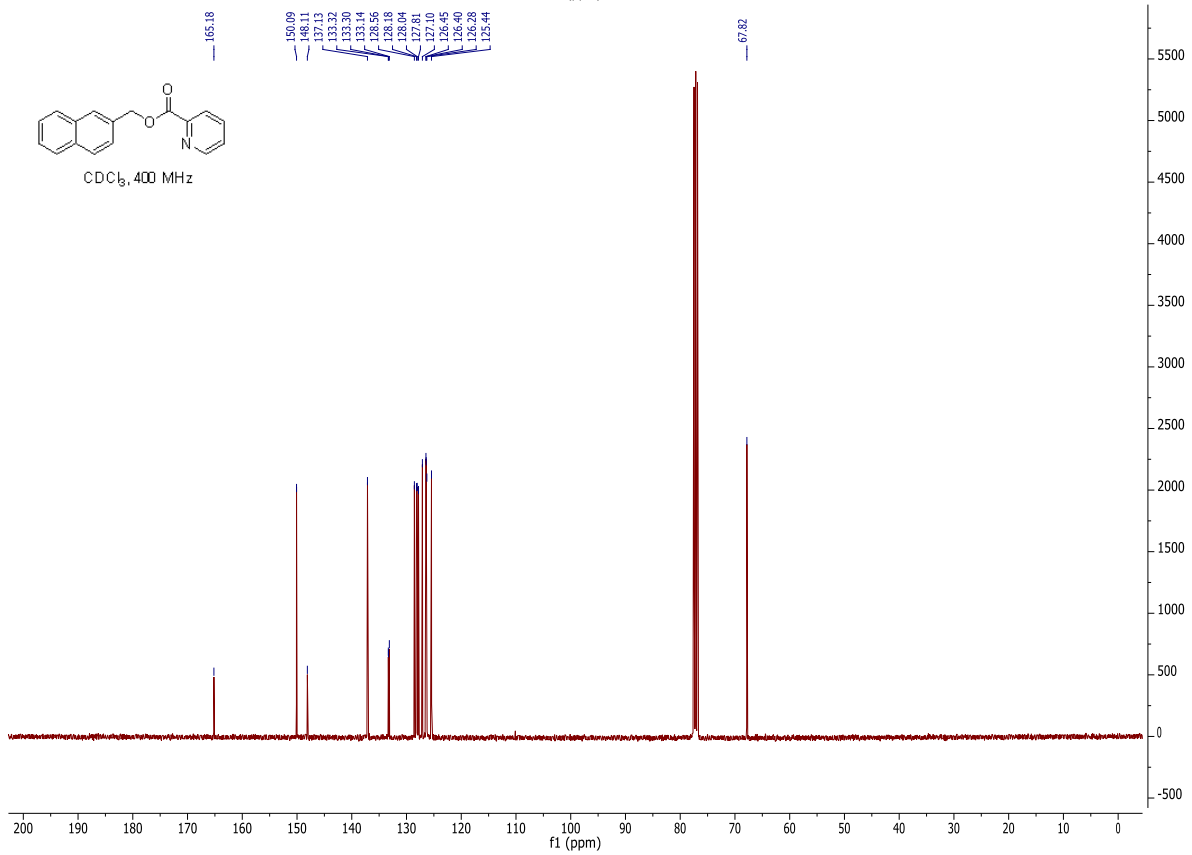

165.05
149.92
148.06
137.36
136.99
128.99
128.57
126.88
126.67
125.13
77.32 cdcl3
77.01 cdcl3
76.69 cdcl3
66.34
35.16
O
O
N
400 MHz, CDCl3
f1 (ppm)

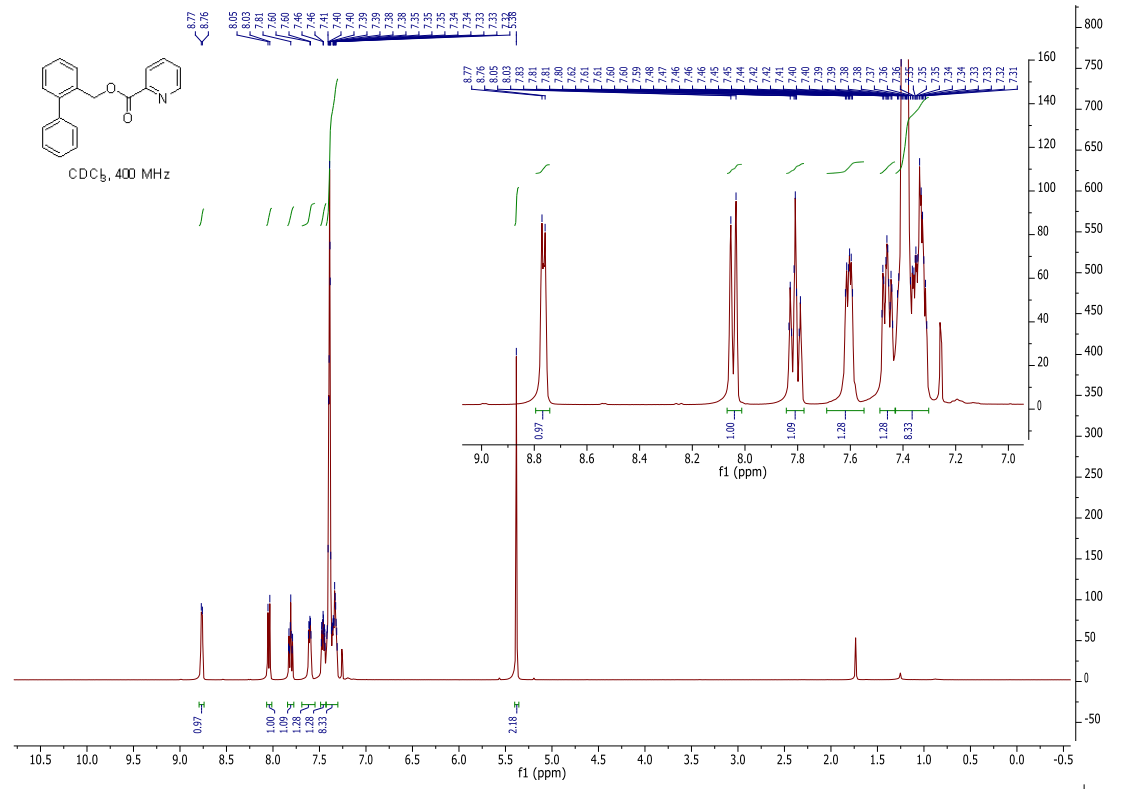

CDCl3, 400 MHz
f1 (ppm)
CDCl3, 400 MHz
f1 (ppm)

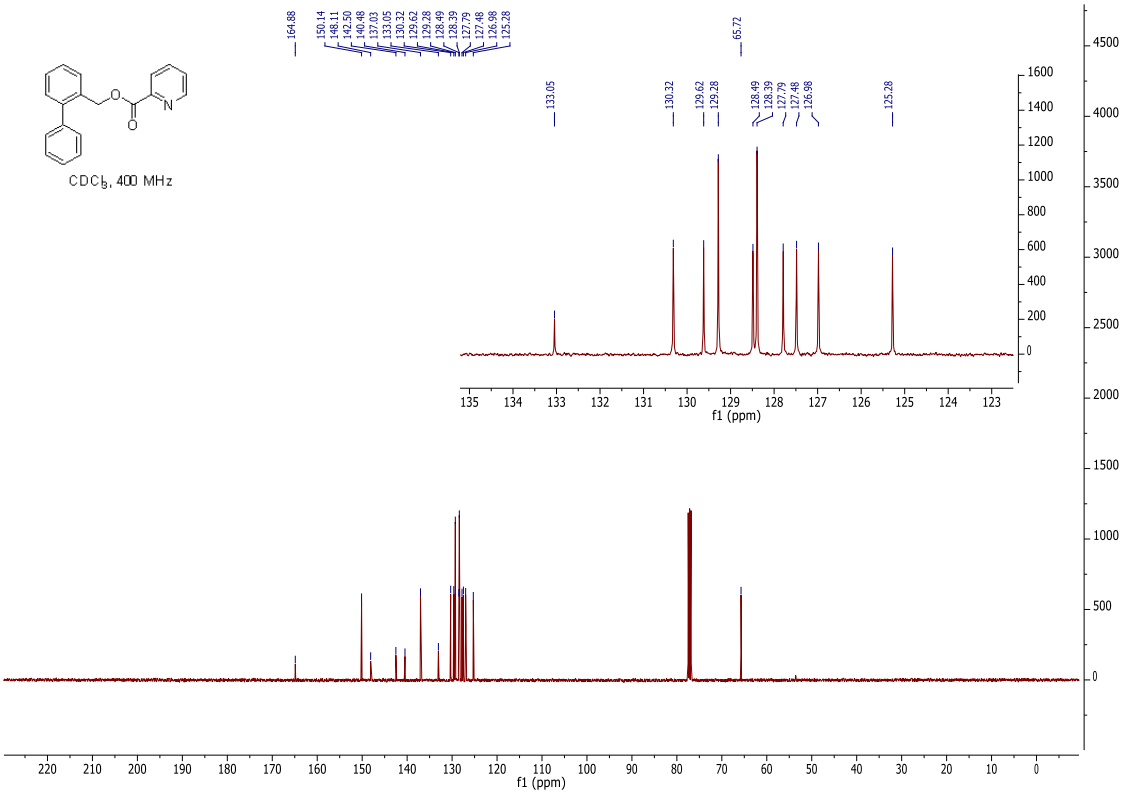

CDCl3, 400 MHz
f1 (ppm)

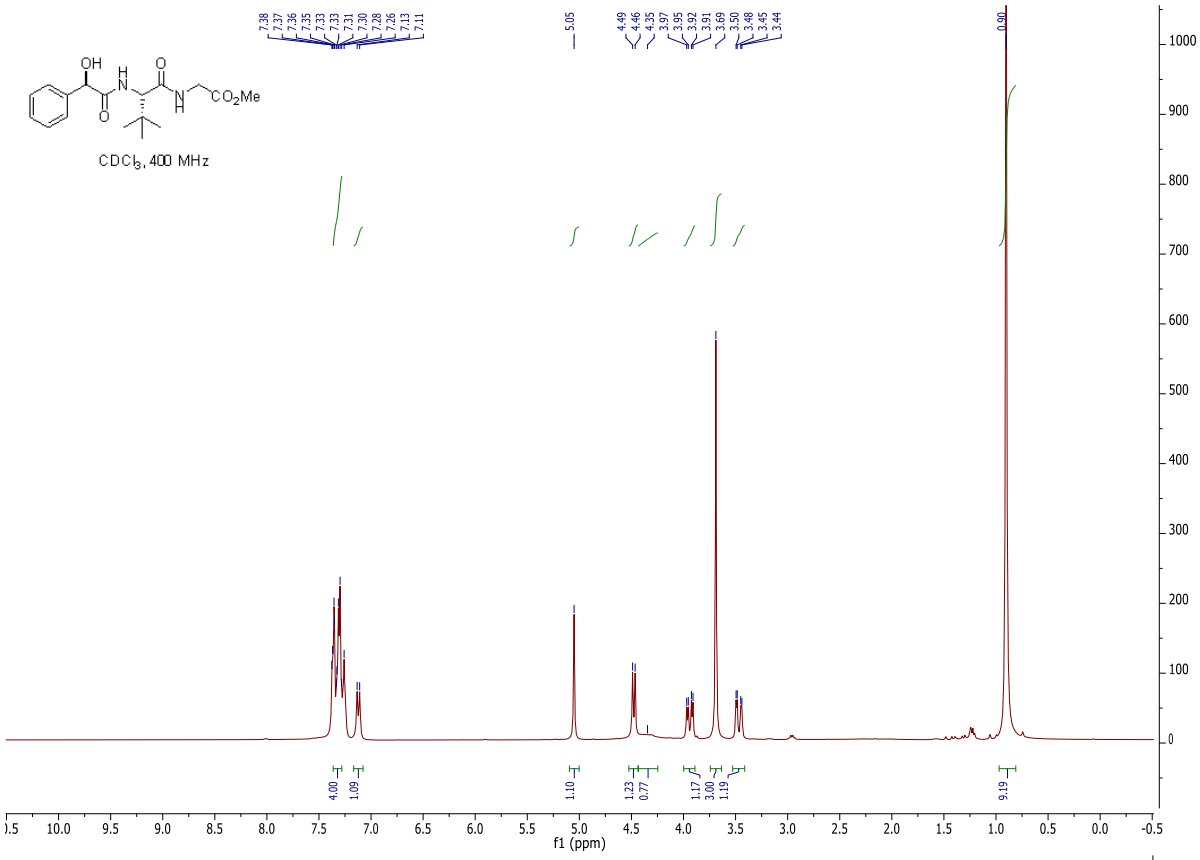

CDCl3, 400 MHz
f1 (ppm)

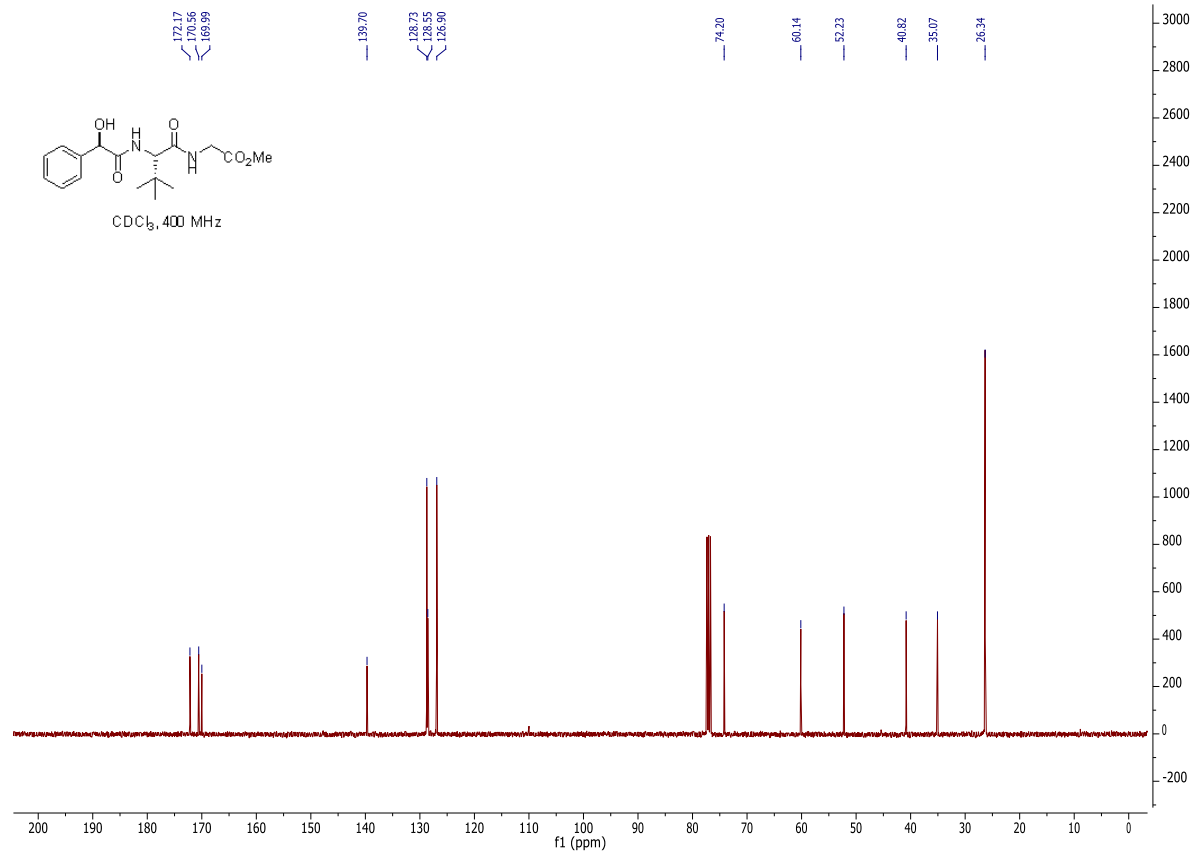

8.78
8.77
8.16
8.14
7.96
7.87
7.86
7.85
7.84
7.84
7.83
7.82
7.81
7.80
7.60
7.58
7.51
7.50
7.49
7.48
7.47
7.46
7.45
7.45
5.402
CDCl3, 500 MHz
1.05
1.04
1.00
4.09
1.07
2.97
2.14
f1 (ppm)

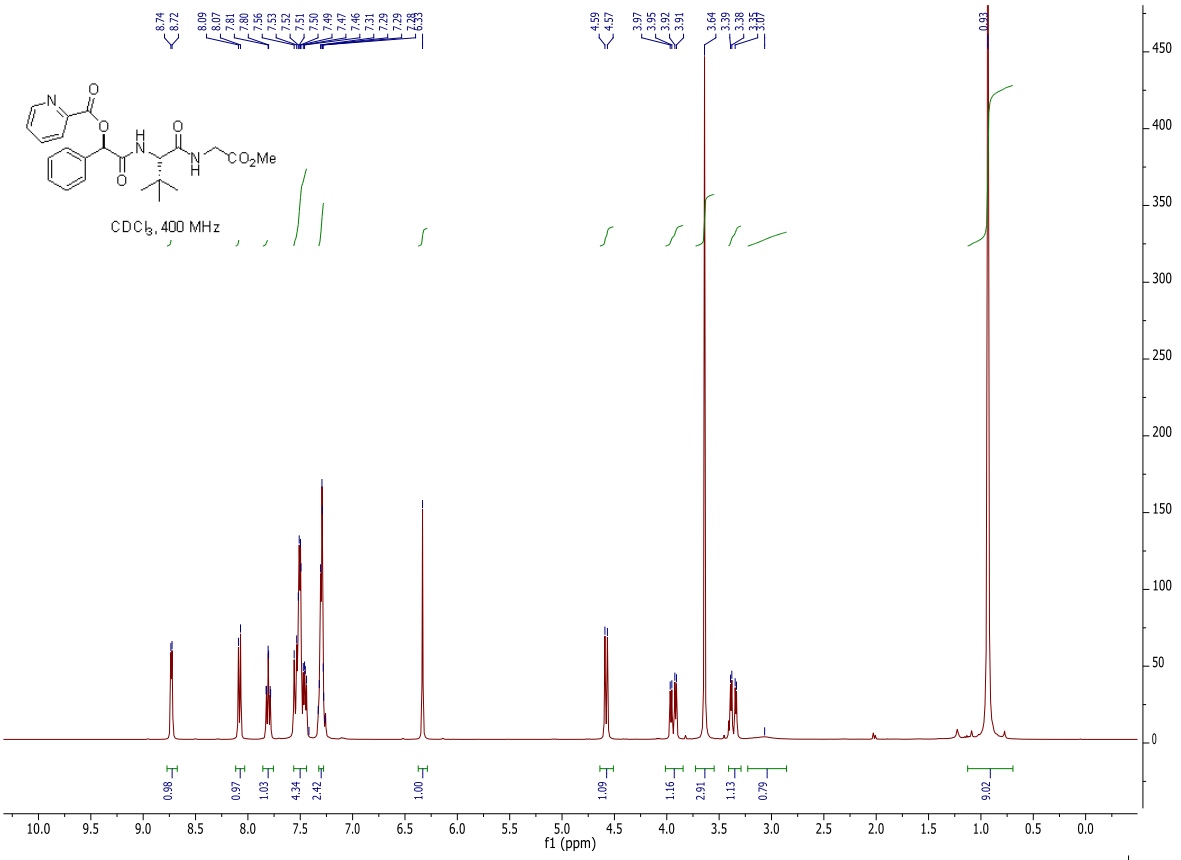

165.18
150.09
148.11
137.13
133.32
133.30
133.14
128.56
128.18
128.04
127.81
127.10
126.45
126.40
126.28
125.44
67.82
CDCl3, 400 MHz
f1 (ppm)

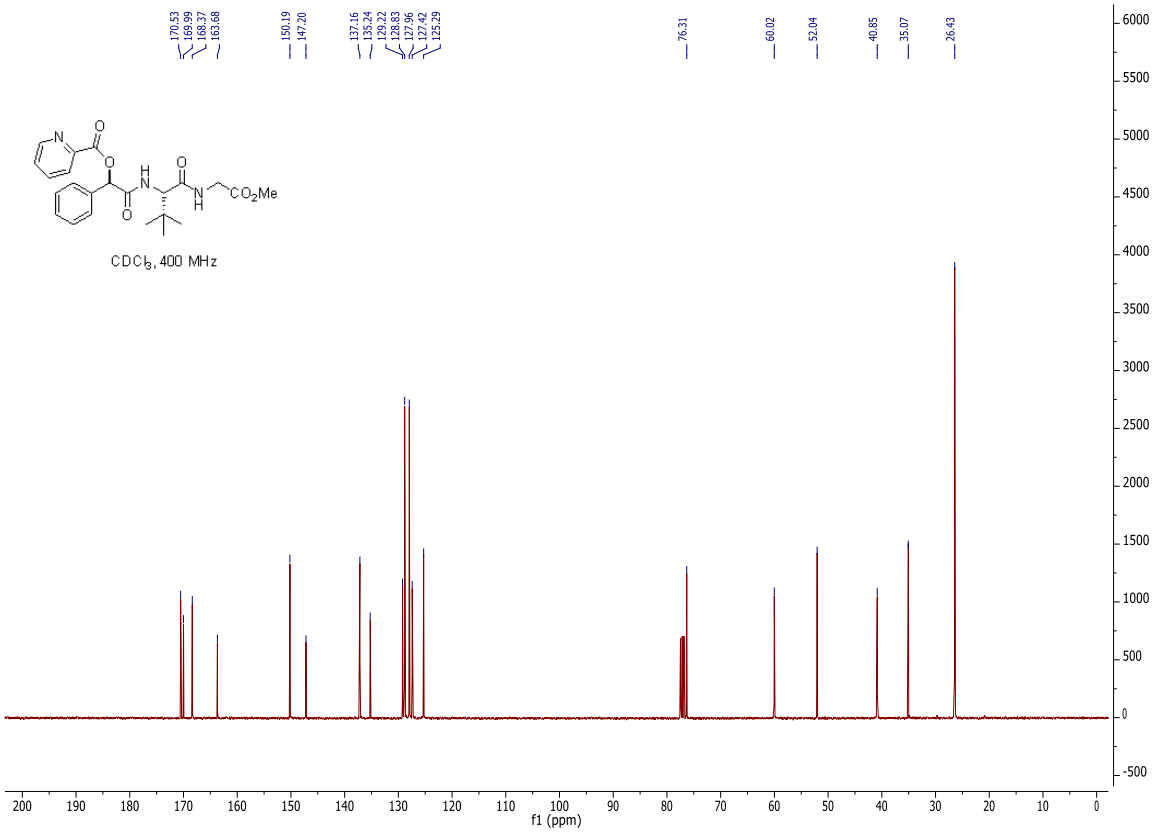

CDCl3, 400 MHz
f1 (ppm)

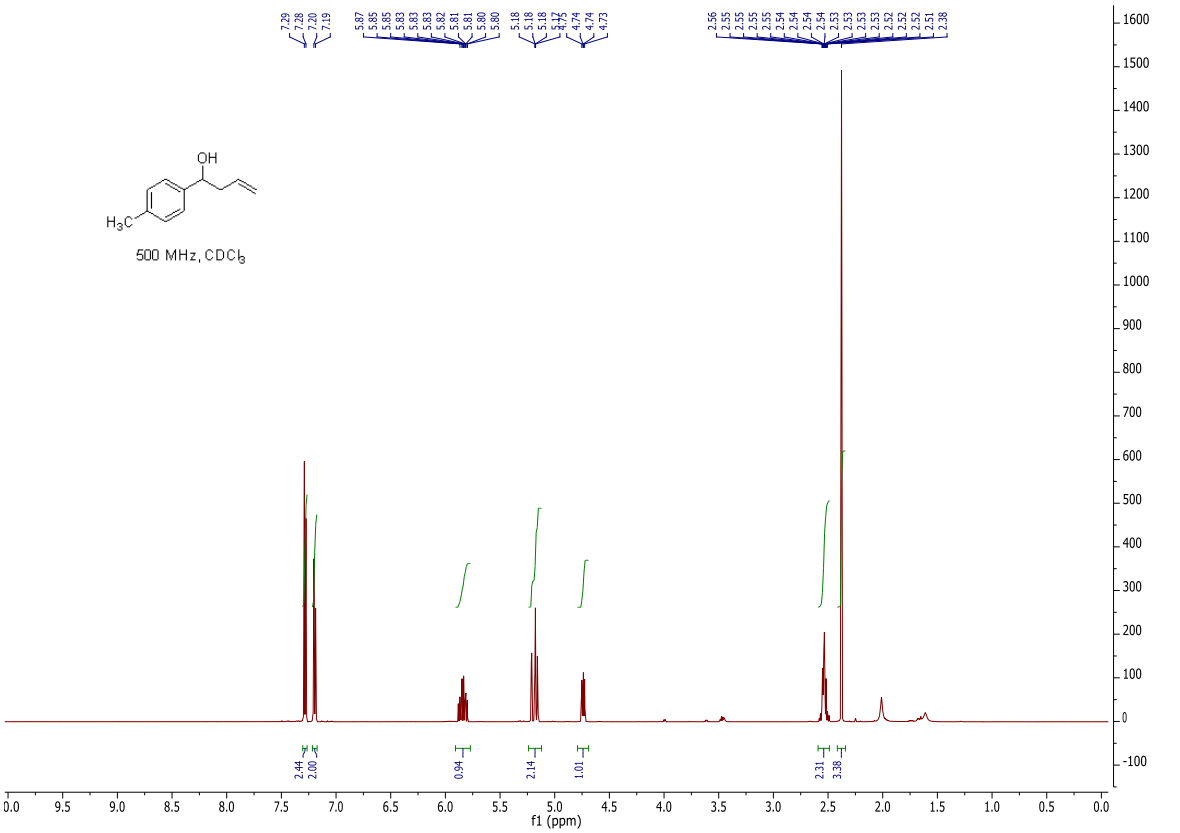

CDCl3, 400 MHz
f1 (ppm)

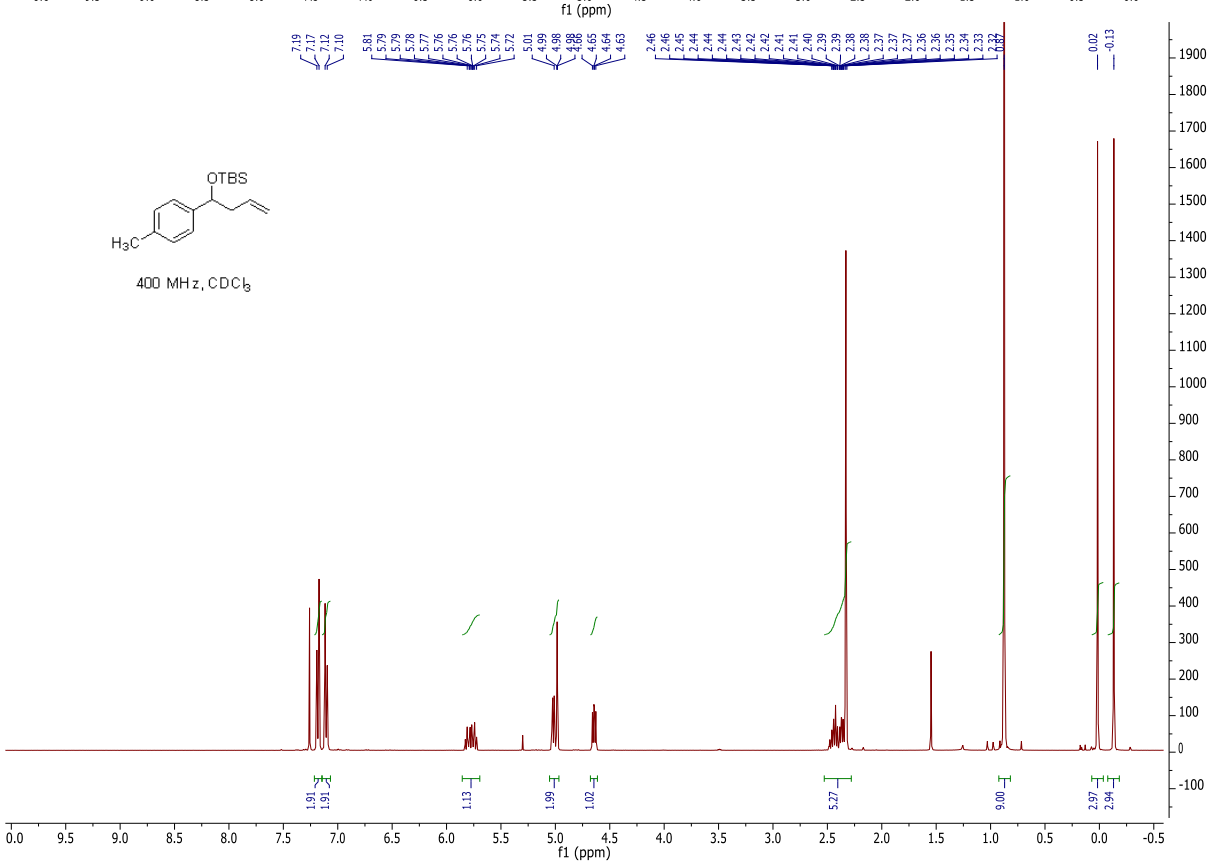

OH
H
N
O
O
N
H
O
CO2Me
CDCl3, 400 MHz
7.38
7.37
7.36
7.35
7.33
7.33
7.31
7.30
7.28
7.26
7.13
7.11
5.05
4.49
4.46
4.35
3.97
3.95
3.92
3.91
3.69
3.50
3.48
3.45
3.44
0.90
4.00
1.09
1.10
1.23
0.77
1.17
3.00
1.19
9.19
f1 (ppm)

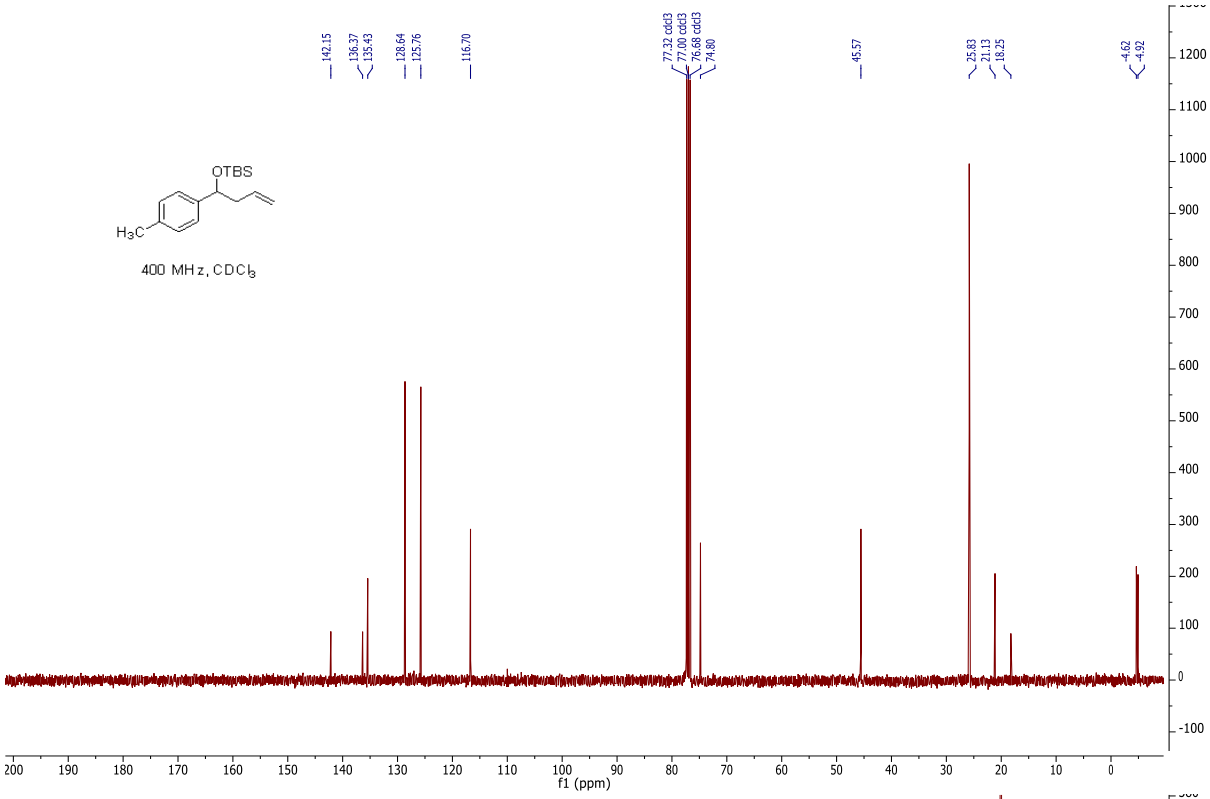

OH
H
N
O
O
N
H
O
CO2Me
CDCl3, 400 MHz
172.17
170.56
169.99
139.70
128.73
128.55
126.90
74.20
60.14
52.23
40.82
35.07
26.34
f1 (ppm)

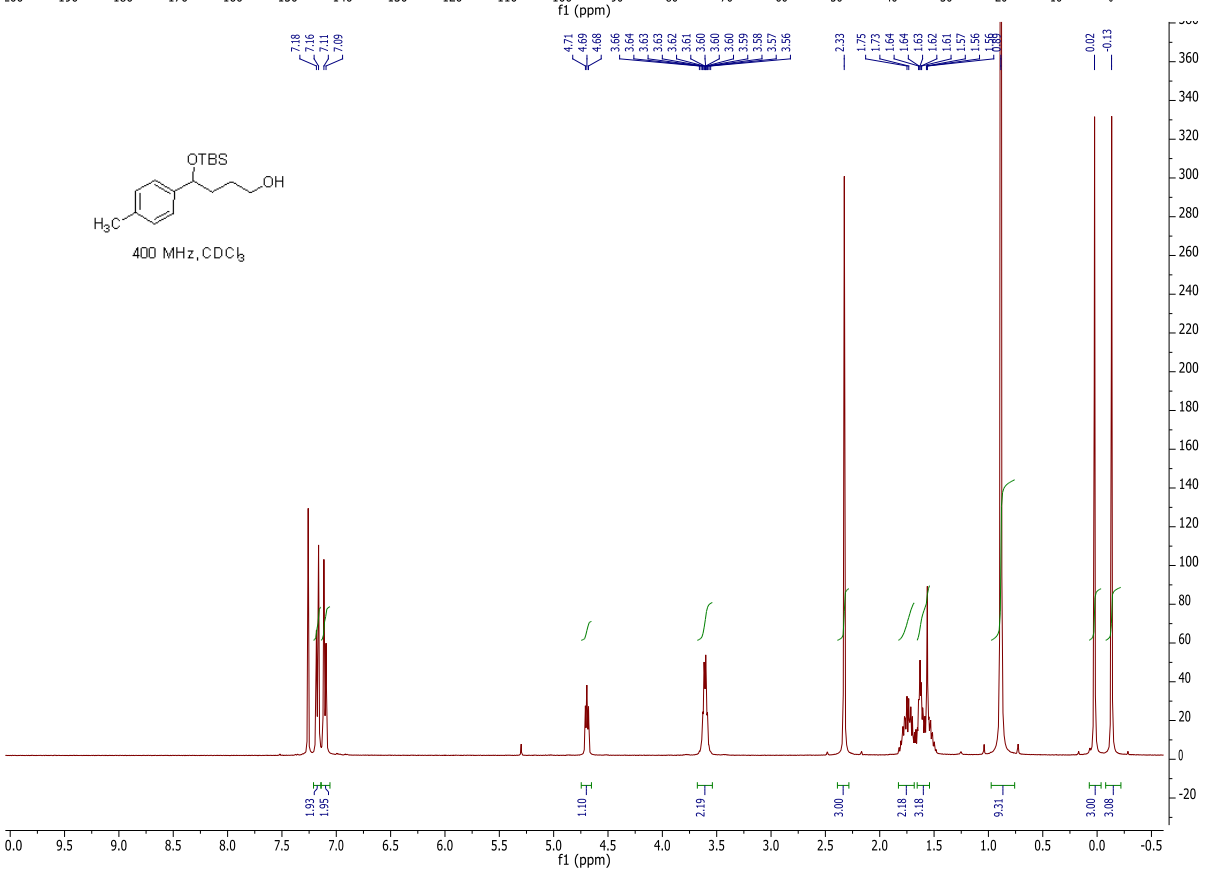

8.74
8.72
8.09
8.07
7.81
7.80
7.56
7.53
7.52
7.51
7.50
7.49
7.47
7.46
7.31
7.29
7.29
7.28
6.33
4.59
4.57
3.97
3.95
3.92
3.91
3.64
3.39
3.38
3.35
3.07
0.93
CO2Me
CDCl3, 400 MHz
0.98
0.97
1.03
4.34
2.42
1.00
1.09
1.16
2.91
1.13
0.79
9.02
f1 (ppm)

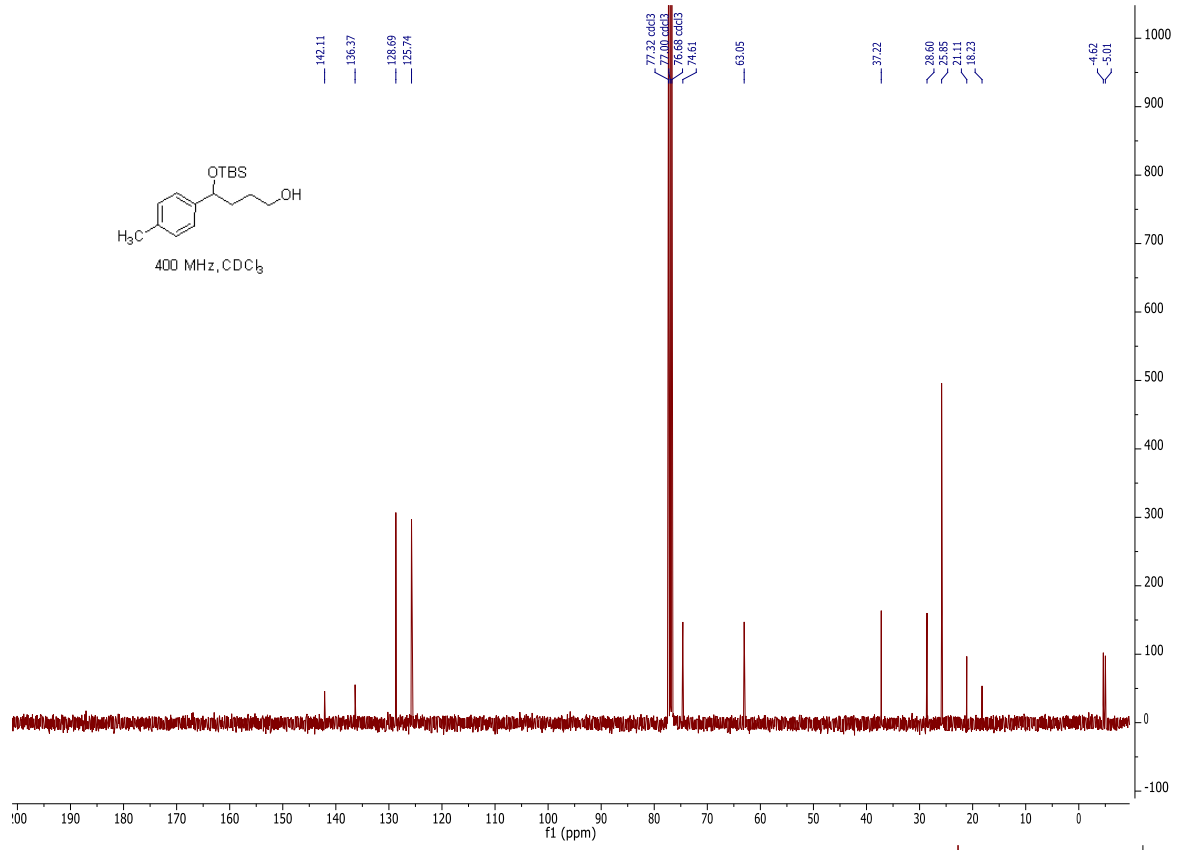

170.53
169.99
168.37
163.68
150.19
147.20
137.16
135.24
129.22
128.83
127.96
127.42
125.29
76.31
60.02
52.04
40.85
35.07
26.43
CO2Me
CDCl3, 400 MHz
f1 (ppm)

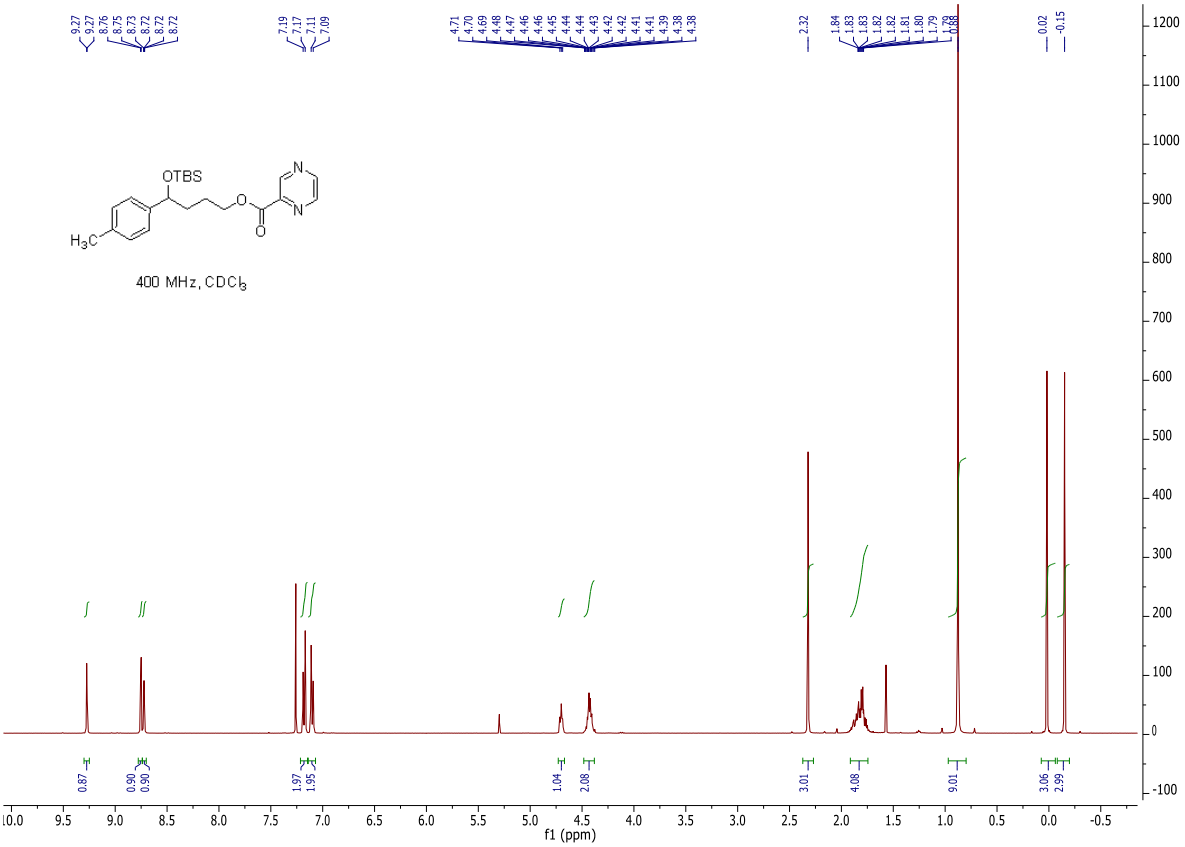

OH
H3C
500 MHz, CDCl3
f1 (ppm)

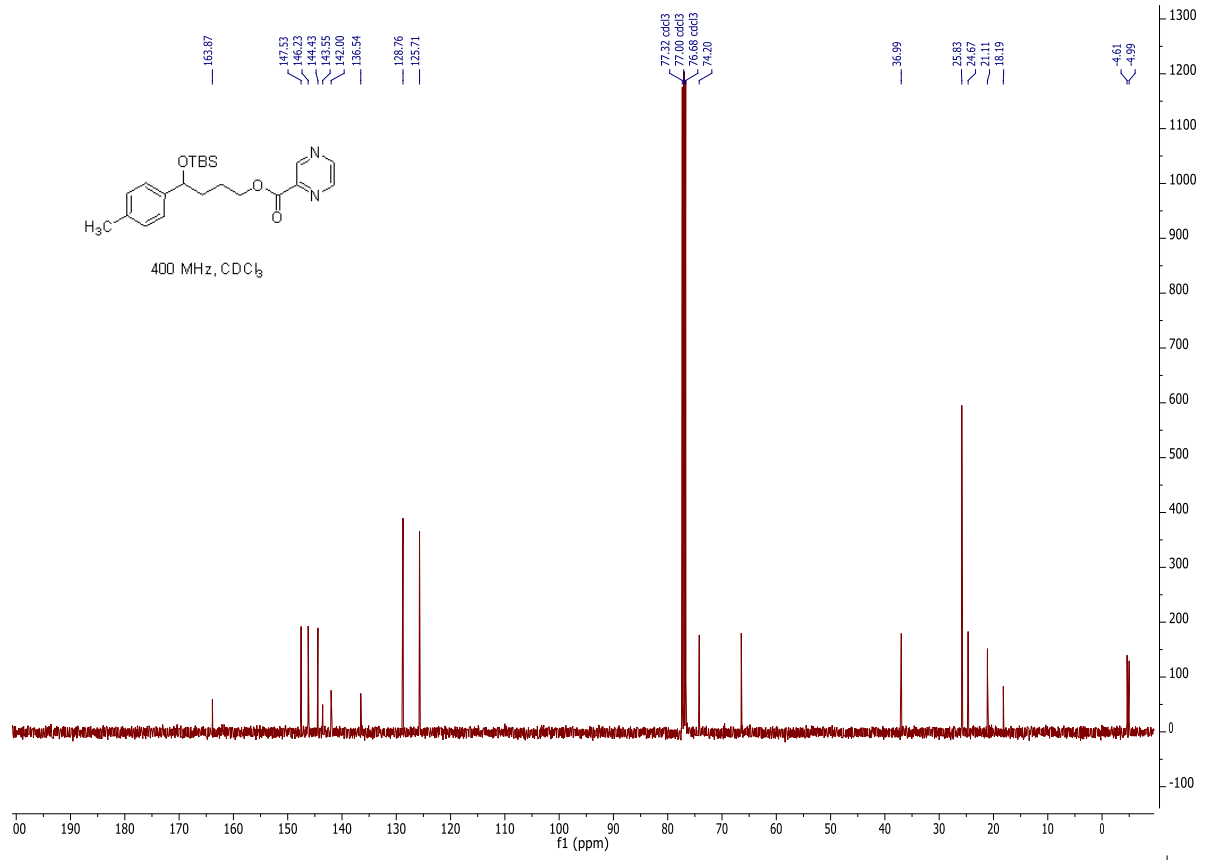

OTBS
H3C
400 MHz, CDCl3
f1 (ppm)

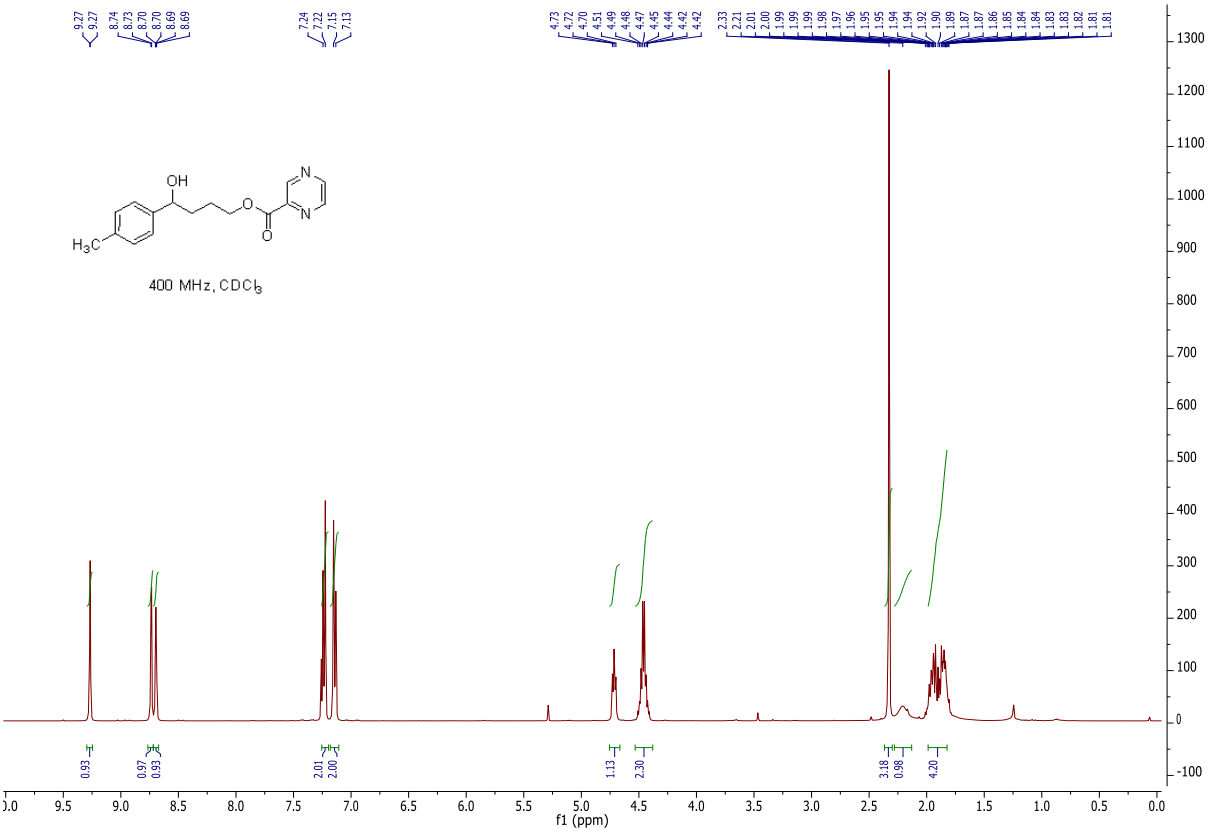

OTBS
H3C
400 MHz, CDCl3
142.15
136.37
135.43
128.64
125.76
116.70
77.32 cdcl3
77.00 cdcl3
76.68 cdcl3
74.80
45.57
25.83
21.13
18.25
-4.62
-4.92
f1 (ppm)

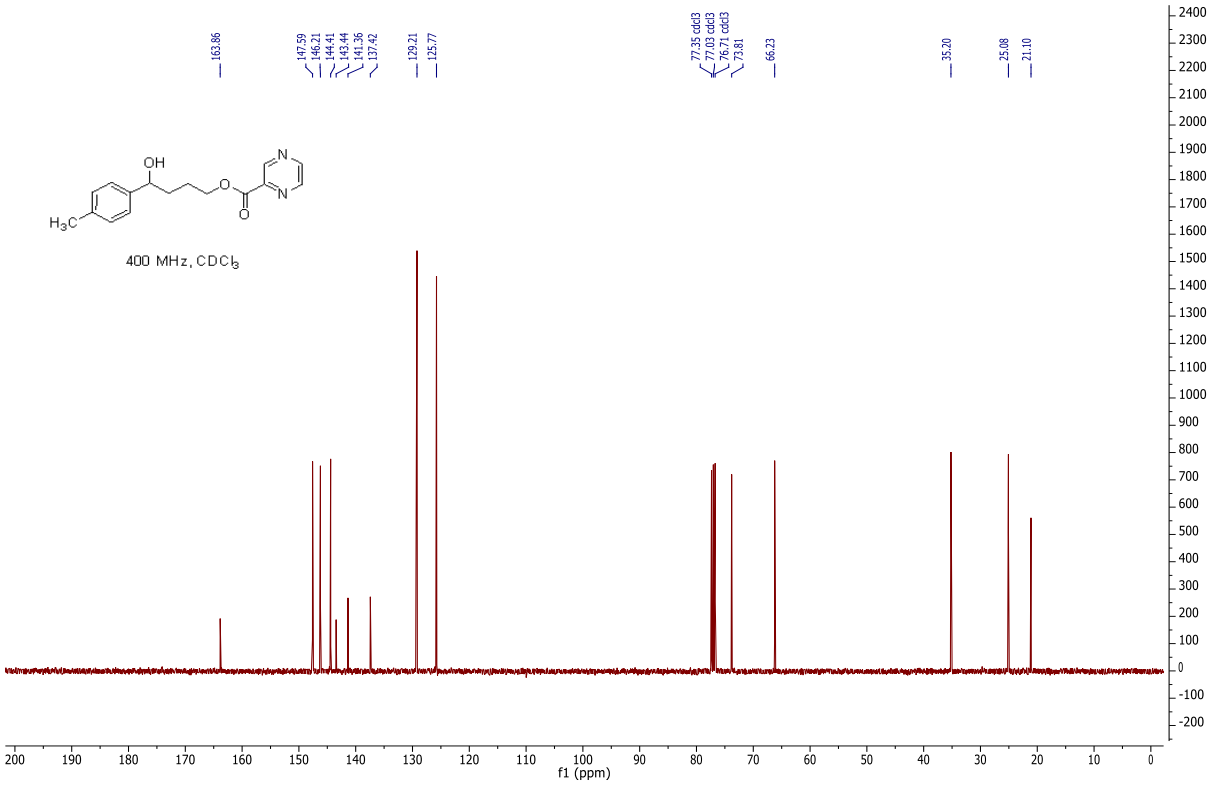

OTBS
OH
H3C
400 MHz, CDCl3
7.18
7.16
7.11
7.09
4.71
4.69
4.68
3.66
3.64
3.63
3.63
3.62
3.61
3.60
3.60
3.60
3.59
3.58
3.57
3.56
2.33
1.75
1.73
1.64
1.64
1.63
1.62
1.61
1.57
1.56
0.02
-0.13
1.93
1.95
1.10
2.19
3.00
2.18
3.18
9.31
3.00
3.08
f1 (ppm)

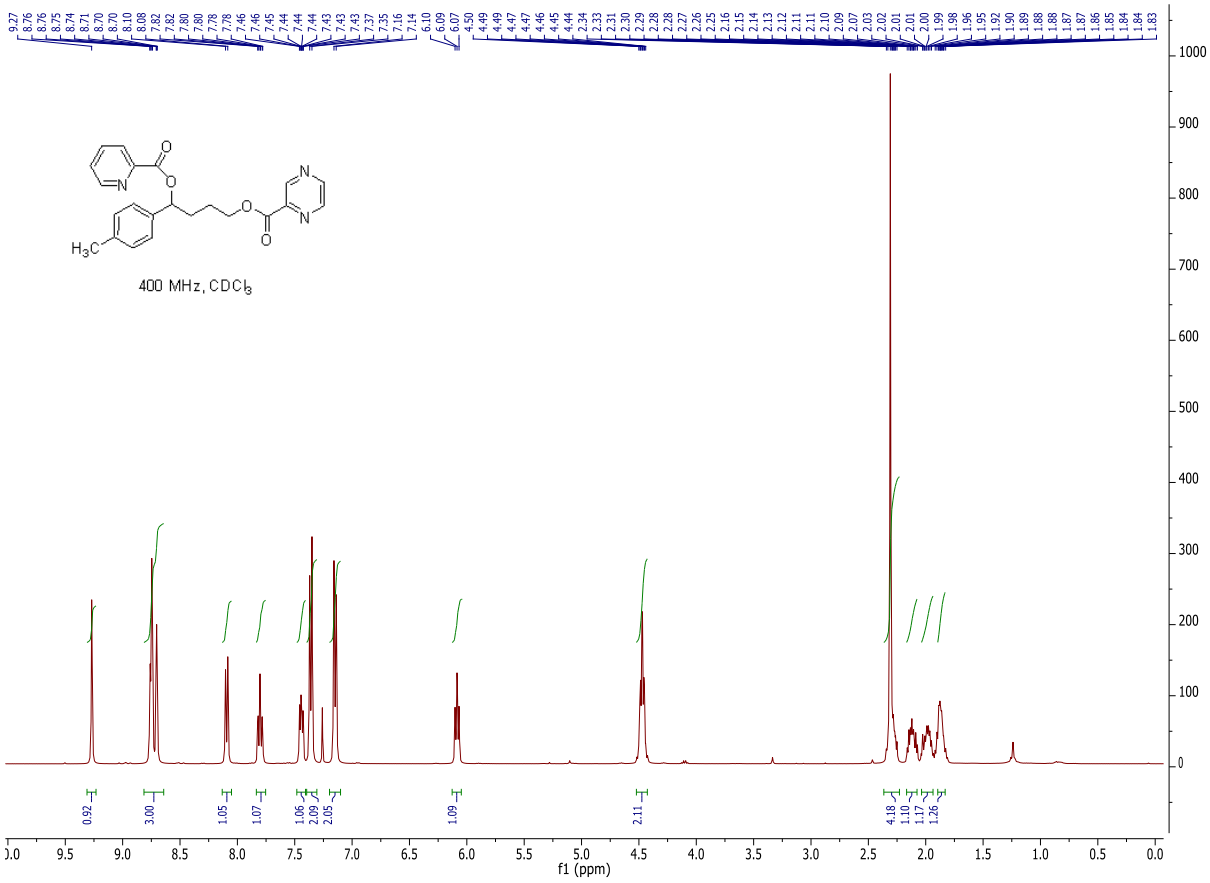

OTBS
OH
H3C
400 MHz, CDCl3
142.11
136.37
128.69
125.74
77.32 cdcl3
77.00 cdcl3
76.68 cdcl3
74.61
63.05
37.22
28.60
25.85
21.11
18.23
-4.62
-5.01
f1 (ppm)

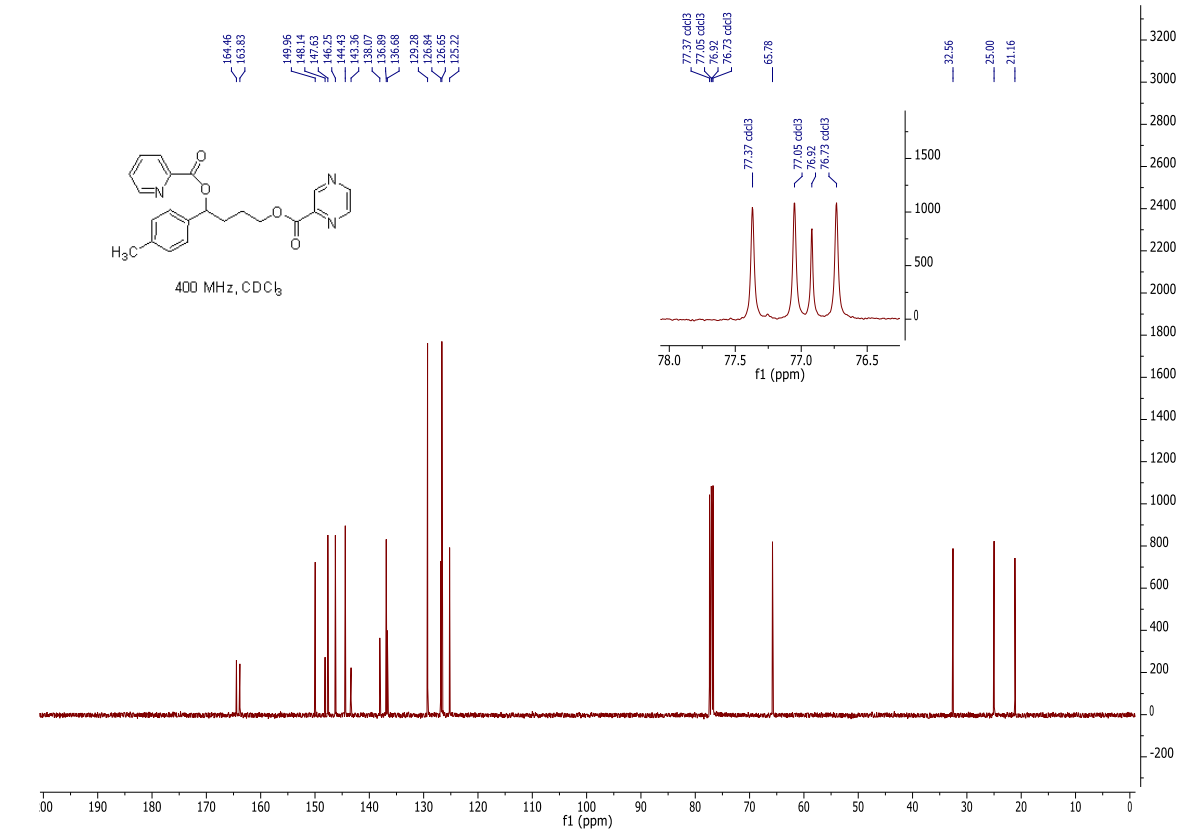

OTBS
N
O
O
H3C
400 MHz, CDCl3
9.27
8.76
8.75
8.73
8.72
7.19
7.17
7.11
7.09
4.71
4.70
4.69
4.48
4.47
4.46
4.45
4.44
4.43
4.42
4.41
4.39
4.38
2.32
1.84
1.83
1.82
1.81
1.80
1.79
0.88
0.02
-0.15
0.87
0.90
0.90
1.97
1.95
1.04
2.08
3.01
4.08
9.01
3.06
2.99
f1 (ppm)

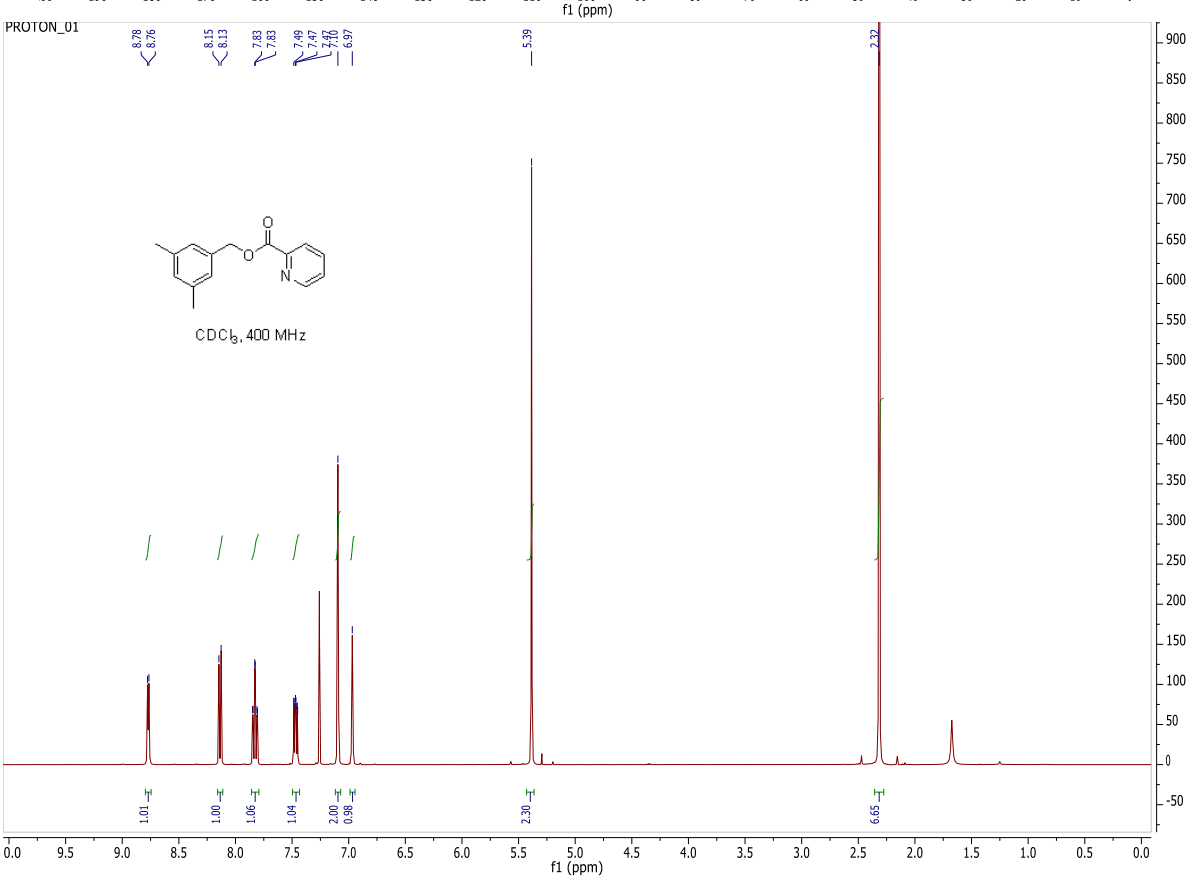

OTBS
H_3C
N
N
O
O
400 MHz, $CDCl_3$
163.87
147.53
146.23
144.43
143.55
142.00
136.54
128.76
125.71
77.32 cdcl3
77.00 cdcl3
76.68 cdcl3
74.20
36.99
25.83
24.67
21.11
18.19
-4.61
-4.99
f1 (ppm)

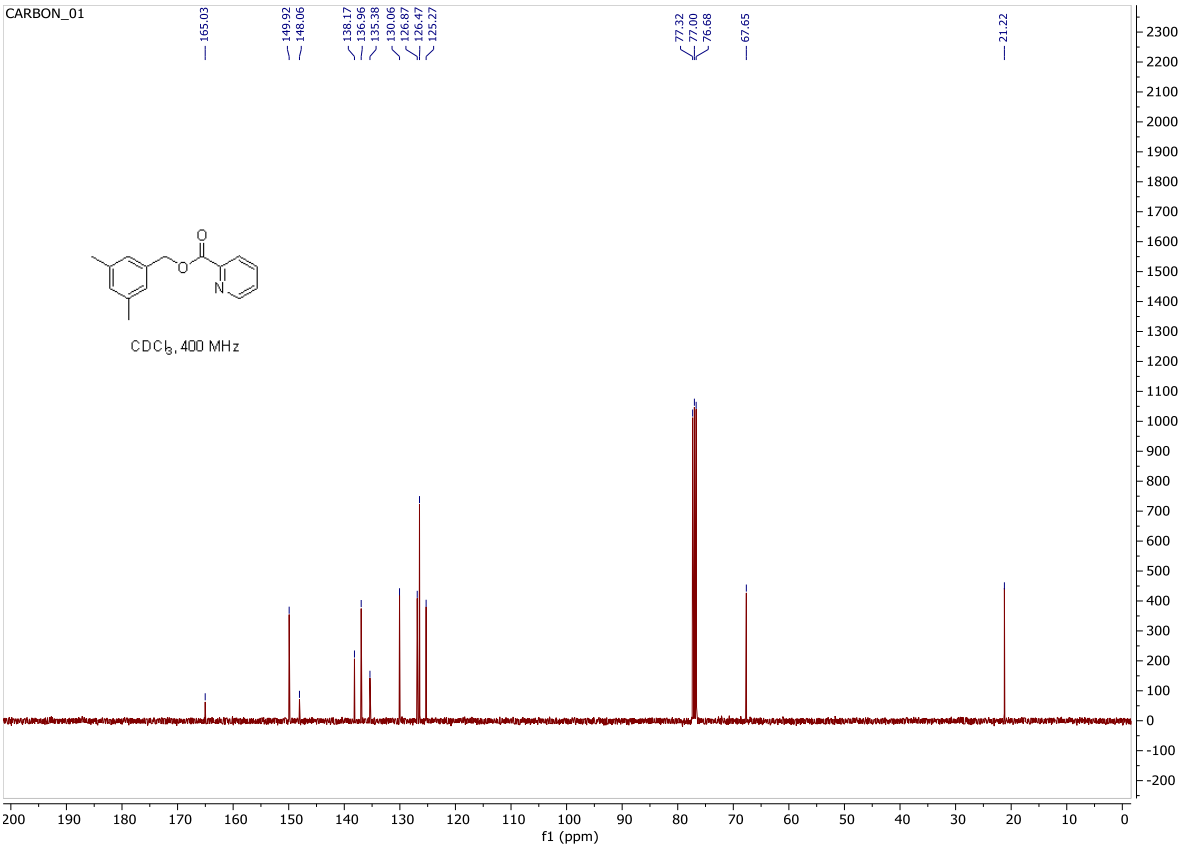

OH
H_3C
N
N
O
O
400 MHz, $CDCl_3$
9.27
9.27
8.74
8.73
8.70
8.70
8.69
8.69
7.24
7.22
7.15
7.13
4.73
4.72
4.70
4.51
4.49
4.48
4.47
4.45
4.44
4.42
4.42
2.33
2.21
2.01
2.00
1.99
1.99
1.98
1.97
1.96
1.95
1.95
1.94
1.94
1.92
1.90
1.89
1.87
1.87
1.86
1.85
1.84
1.84
1.83
1.83
1.82
1.81
1.81
0.93
0.97
0.93
2.01
2.00
1.13
2.30
3.18
0.98
4.20
f1 (ppm)

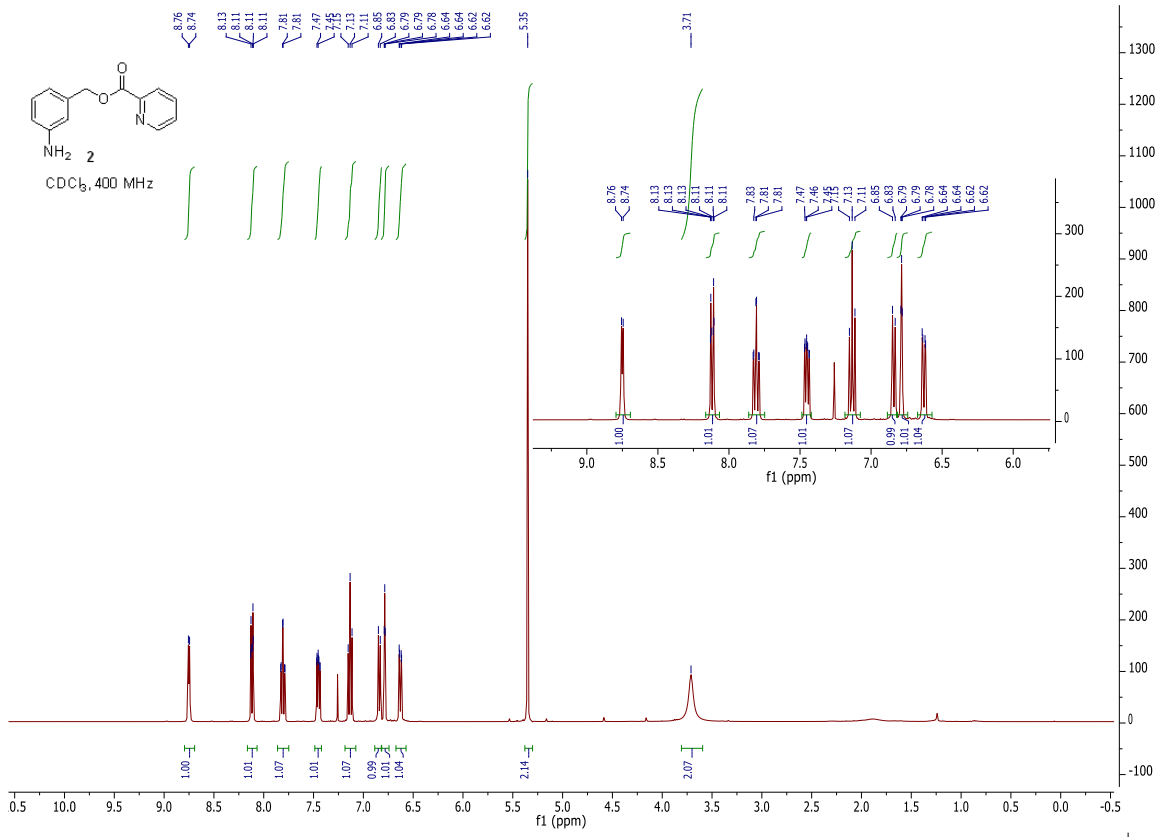

163.86
147.59
146.21
144.41
143.44
141.36
137.42
129.21
125.77
77.35 cdcl3
77.03 cdcl3
76.71 cdcl3
73.81
66.23
35.20
25.08
21.10
OH
O
N
N
O
H3C
400 MHz, CDCl3
f1 (ppm)

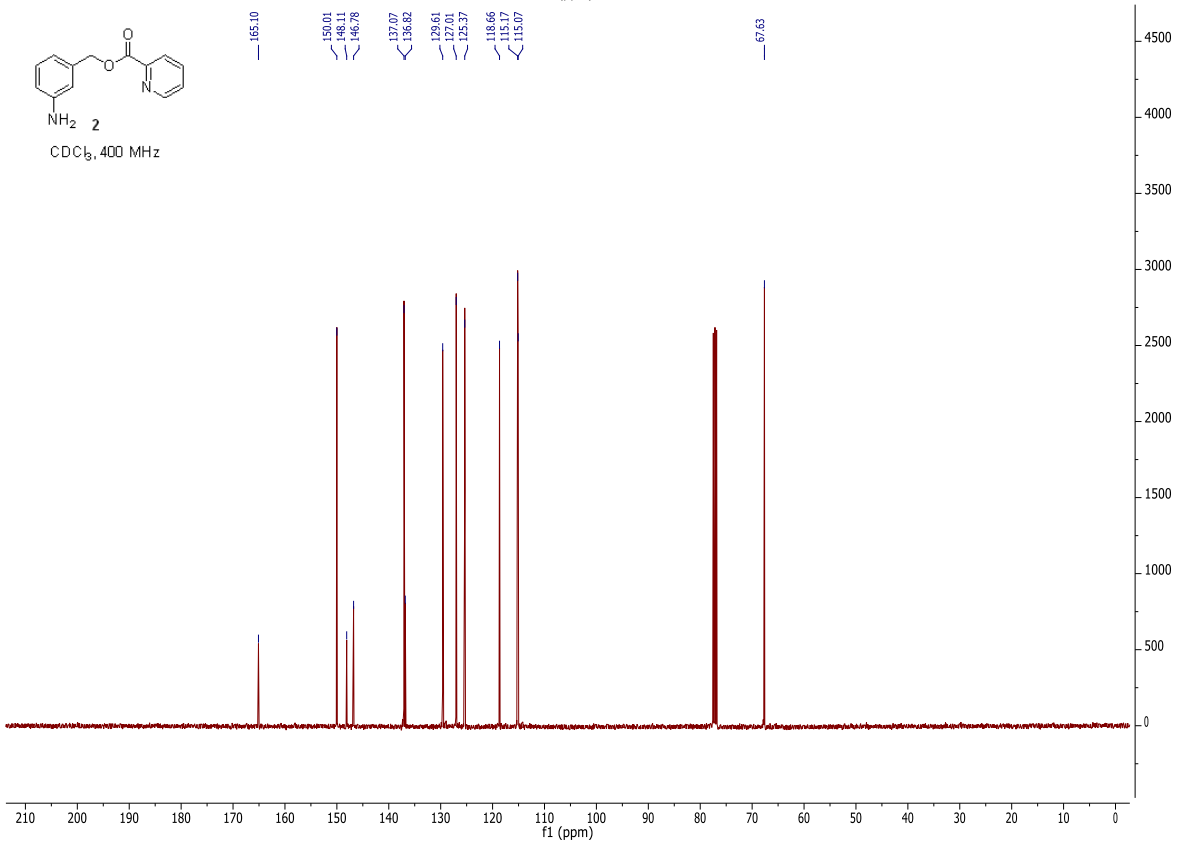

O
N
O
O
N
N
O
H3C
400 MHz, CDCl3
0.92
3.00
1.05
1.07
1.06
2.09
2.05
1.09
2.11
4.18
1.10
1.17
1.26
f1 (ppm)

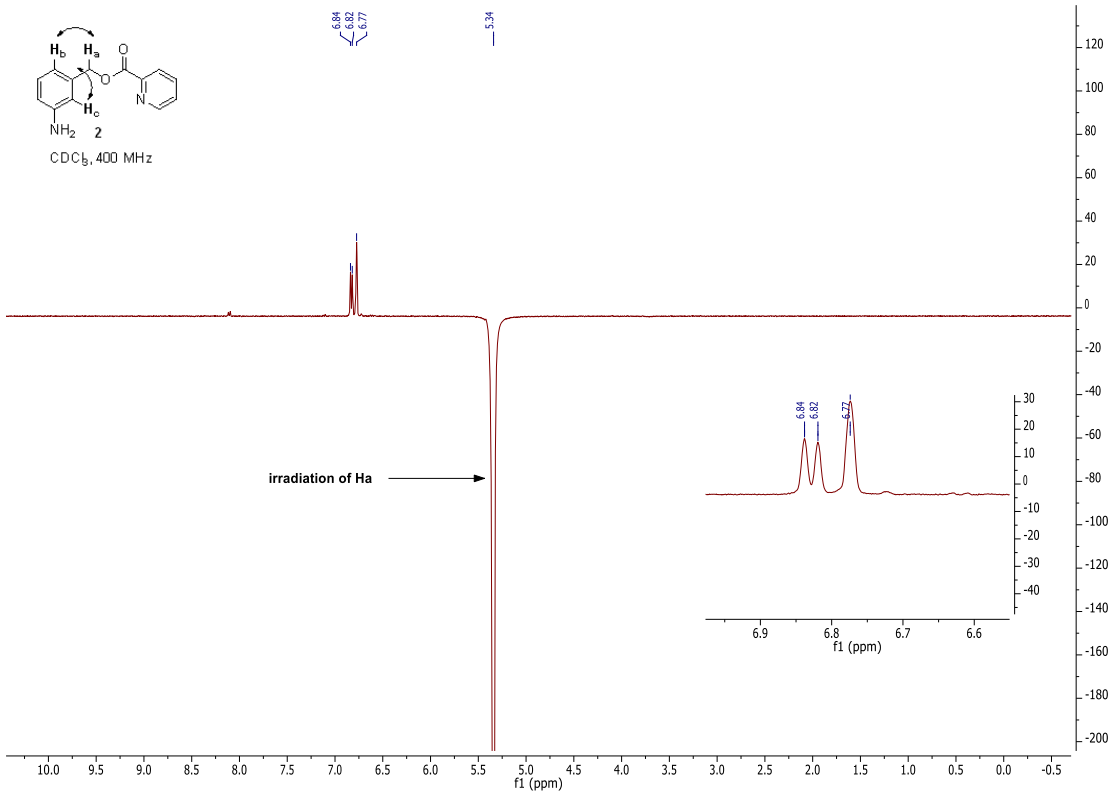

164.46
163.83
149.96
149.14
147.63
146.25
144.43
143.36
138.07
136.89
136.68
129.28
126.84
126.65
125.22
77.37 cdcl3
77.05 cdcl3
76.92
76.73 cdcl3
65.78
32.56
25.00
21.16
400 MHz, CDCl3
f1 (ppm)

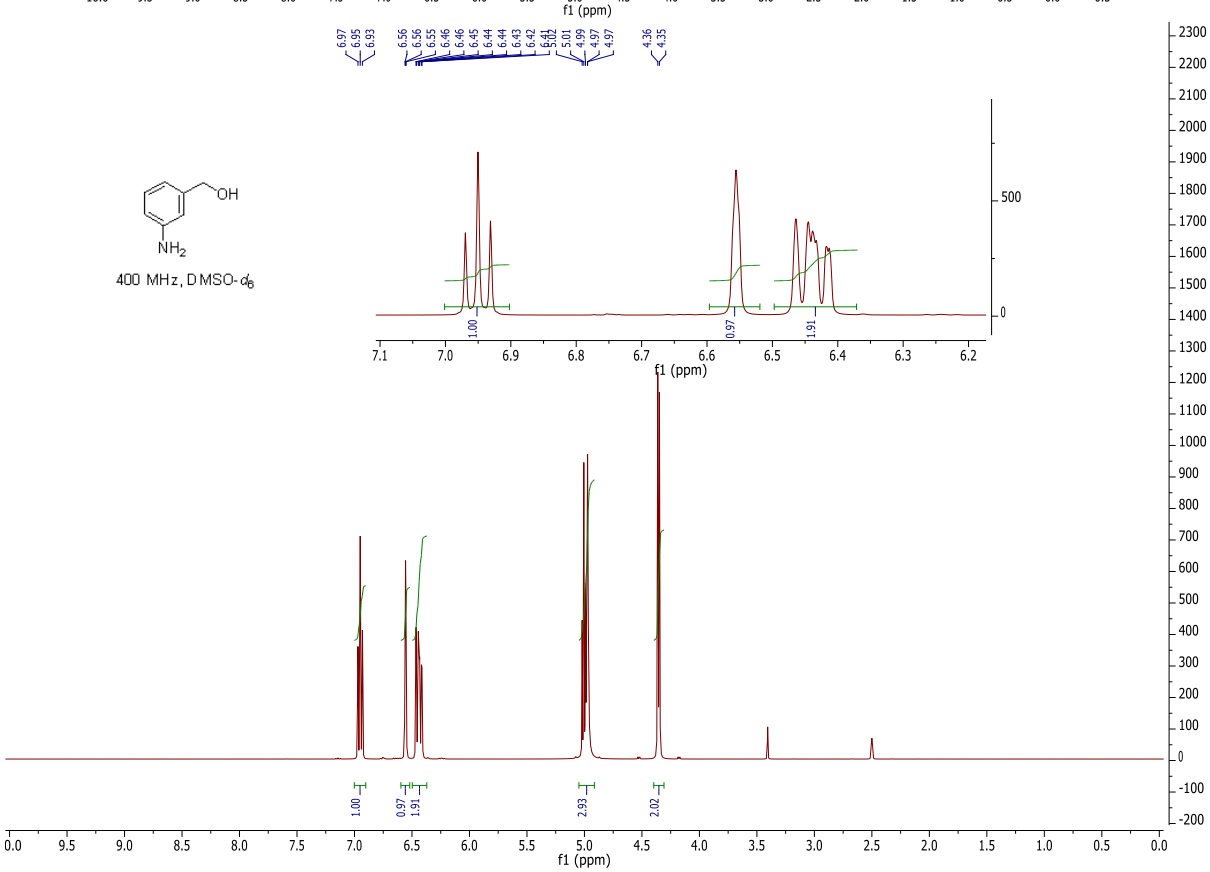

PROTON_01
8.78
8.76
8.15
8.13
7.83
7.83
7.49
7.47
7.47
7.10
6.97
5.39
2.32
CDCl3, 400 MHz
1.01
1.00
1.06
1.04
2.00
0.98
2.30
6.65
f1 (ppm)

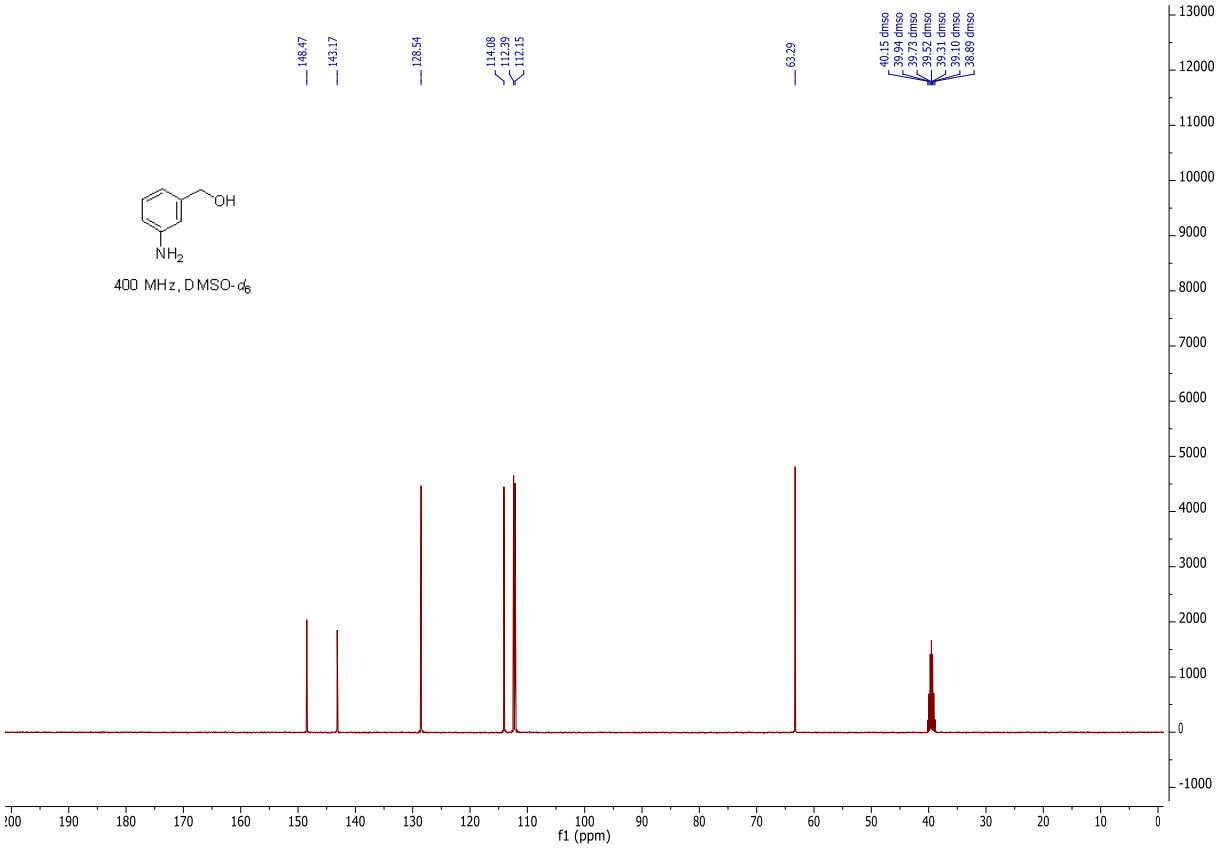

CARBON_01
165.03
149.92
148.06
138.17
136.96
135.38
130.06
126.87
126.47
125.27
77.32
77.00
76.68
67.65
21.22
O
O
N
CDCl3, 400 MHz
f1 (ppm)

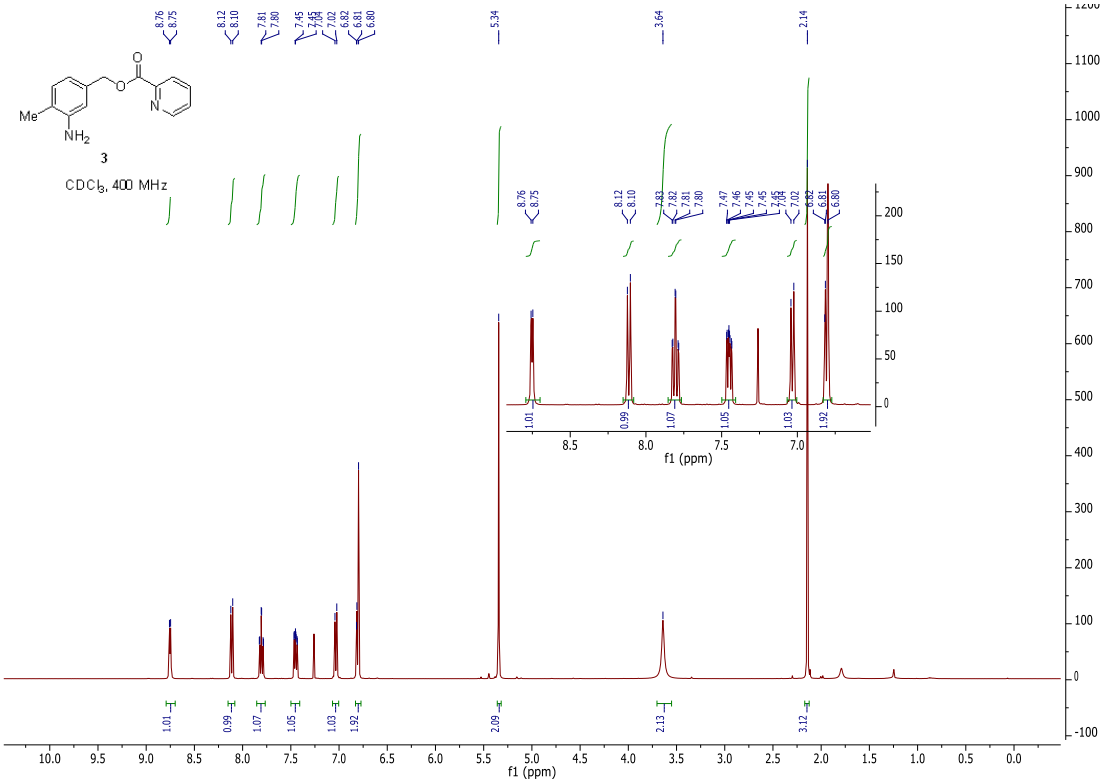

NH2 2
CDCl3, 400 MHz
f1 (ppm)

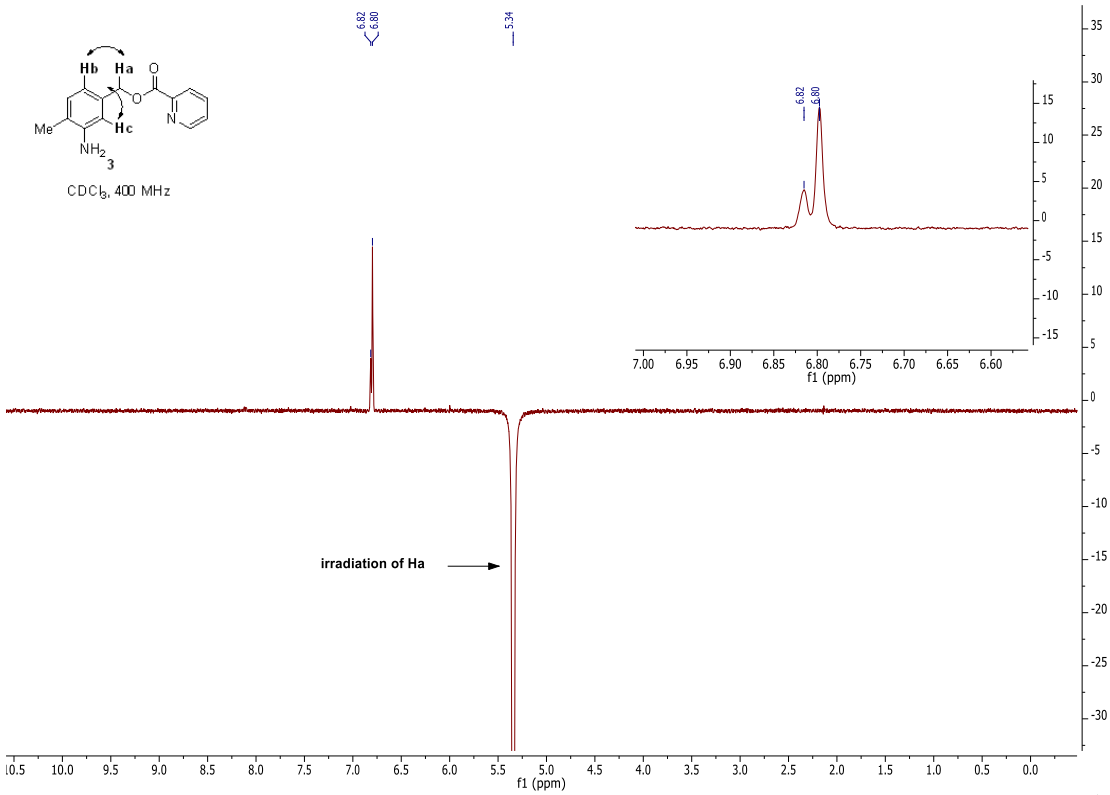

NH2 2
CDCl3, 400 MHz
f1 (ppm)

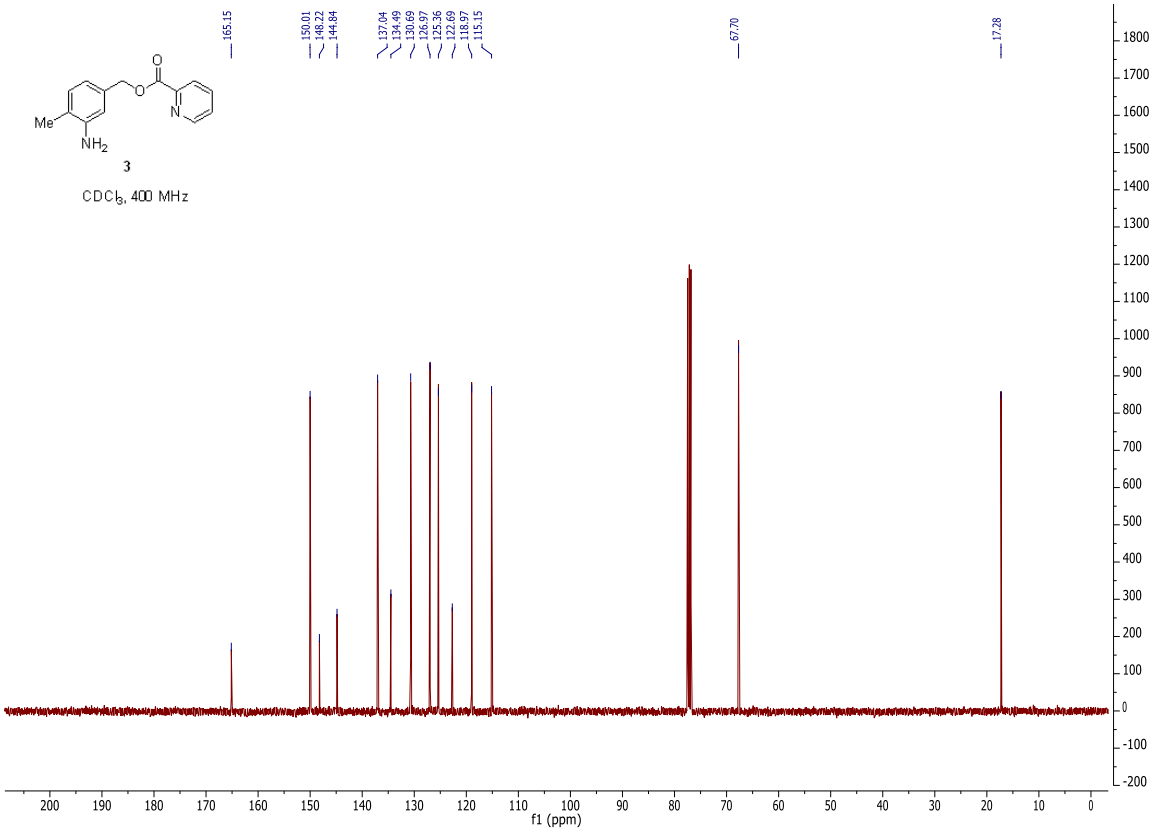

6.84
6.82
6.77
5.34
Hb
Ha
Hc
O
O
N
NH2
2
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

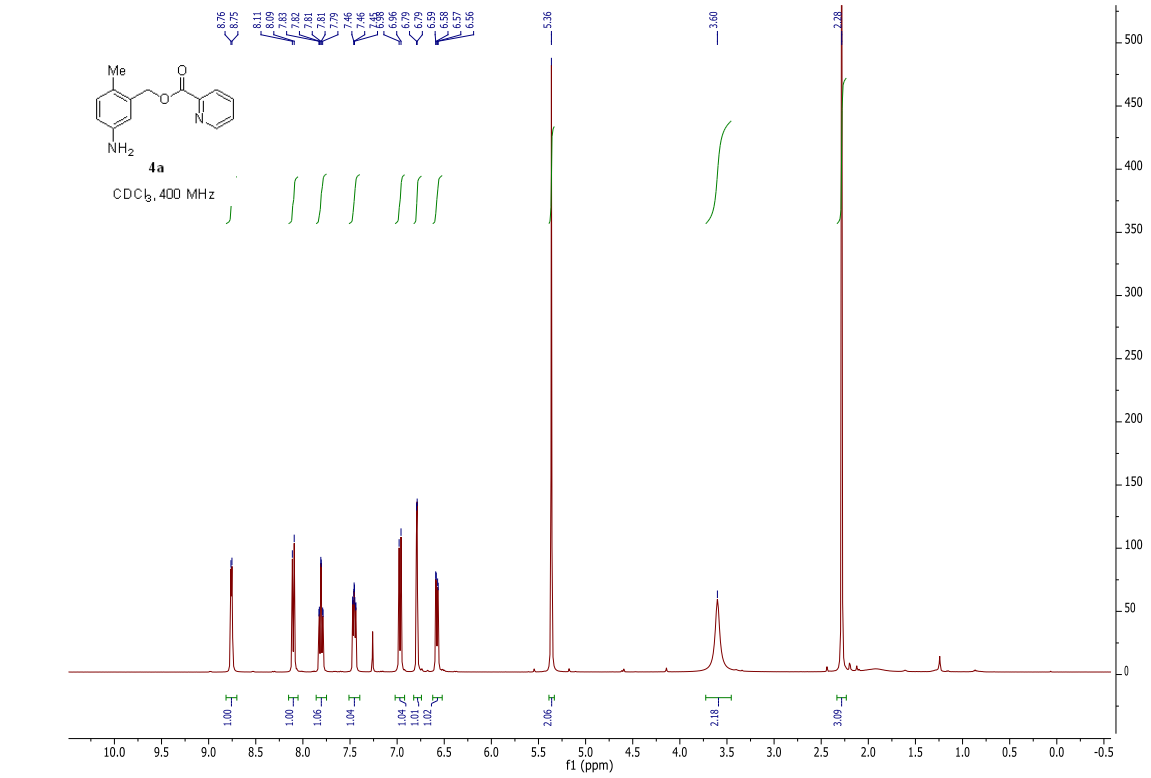

6.97
6.95
6.93
6.56
6.56
6.55
6.46
6.46
6.45
6.44
6.44
6.43
6.42
6.41
5.01
4.99
4.97
4.97
4.36
4.35
OH
NH2
400 MHz, DMSO-d6
1.00
0.97
1.91
2.93
2.02
f1 (ppm)

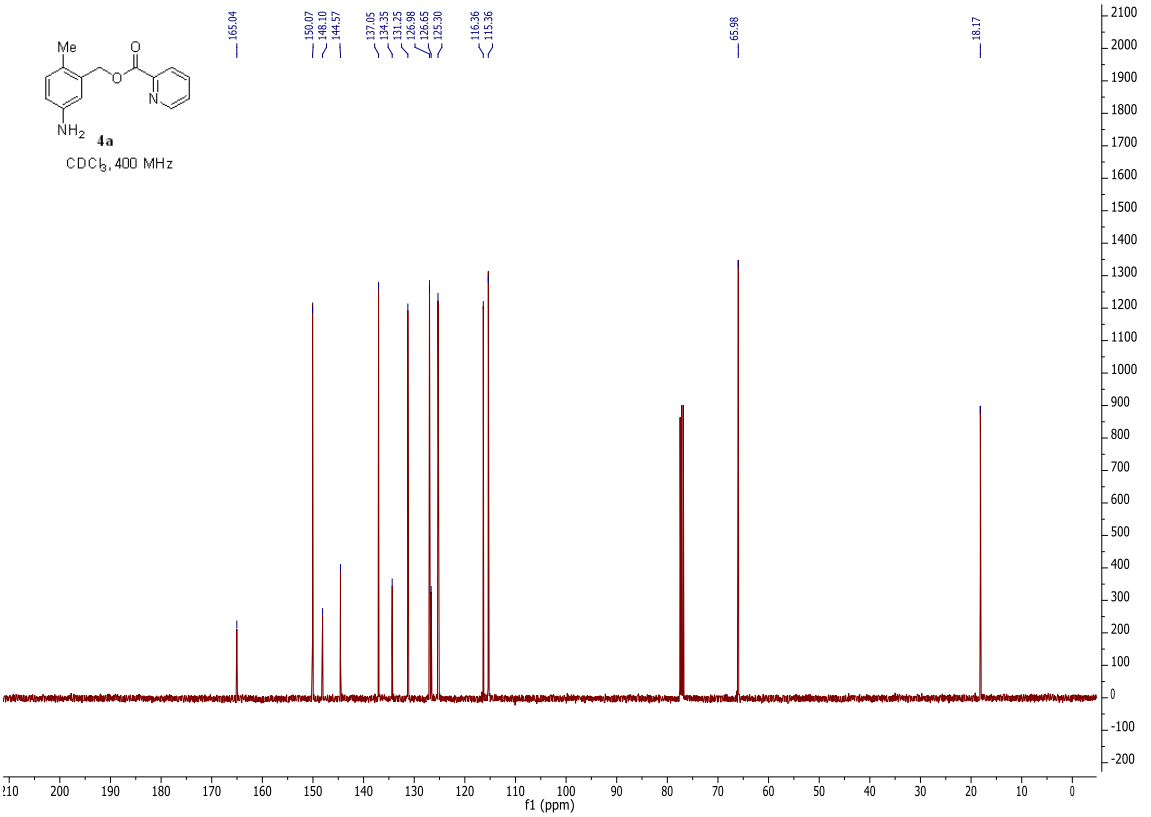

148.47
143.17
128.54
114.08
112.39
112.15
63.29
40.15 dmso
39.94 dmso
39.73 dmso
39.52 dmso
39.31 dmso
39.10 dmso
38.89 dmso
OH
NH2
400 MHz, DMSO-d6
f1 (ppm)

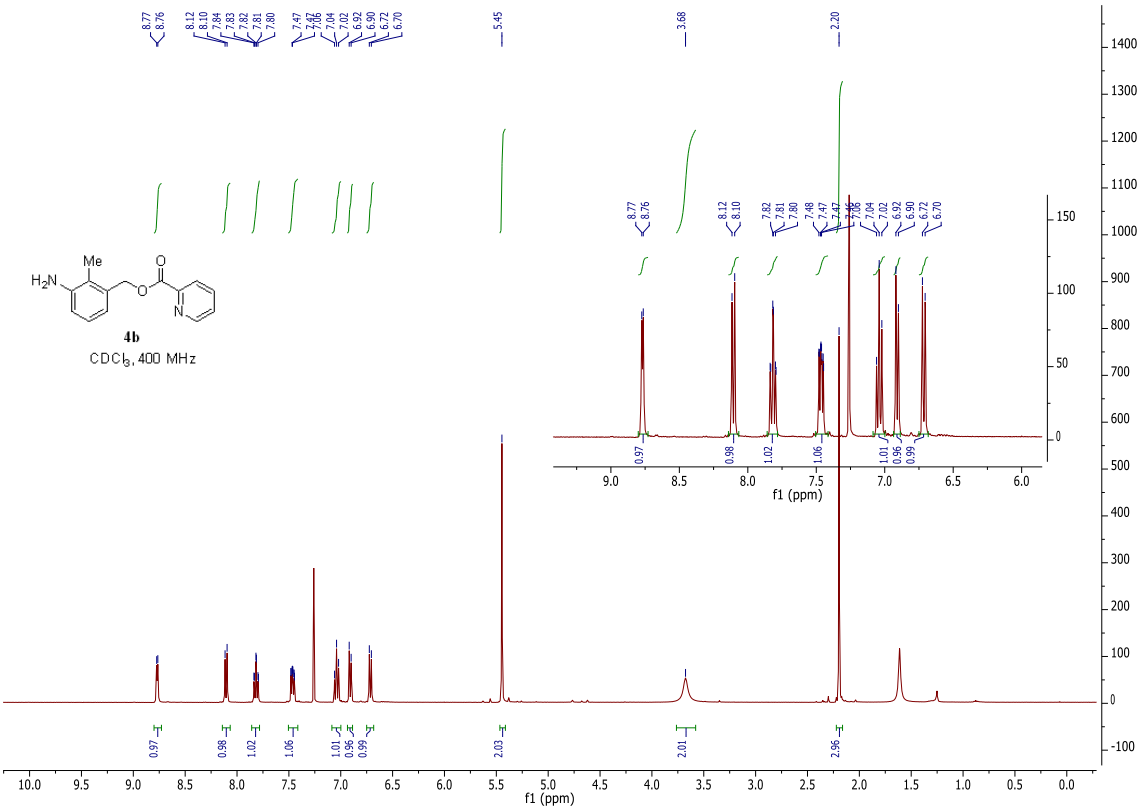

8.76
8.75
8.12
8.10
7.81
7.80
7.45
7.04
7.02
6.82
6.81
6.80
5.34
3.64
2.14
Me
NH2
3
CDCl3, 400 MHz
1.01
0.99
1.07
1.05
1.03
1.92
2.09
2.13
3.12
f1 (ppm)

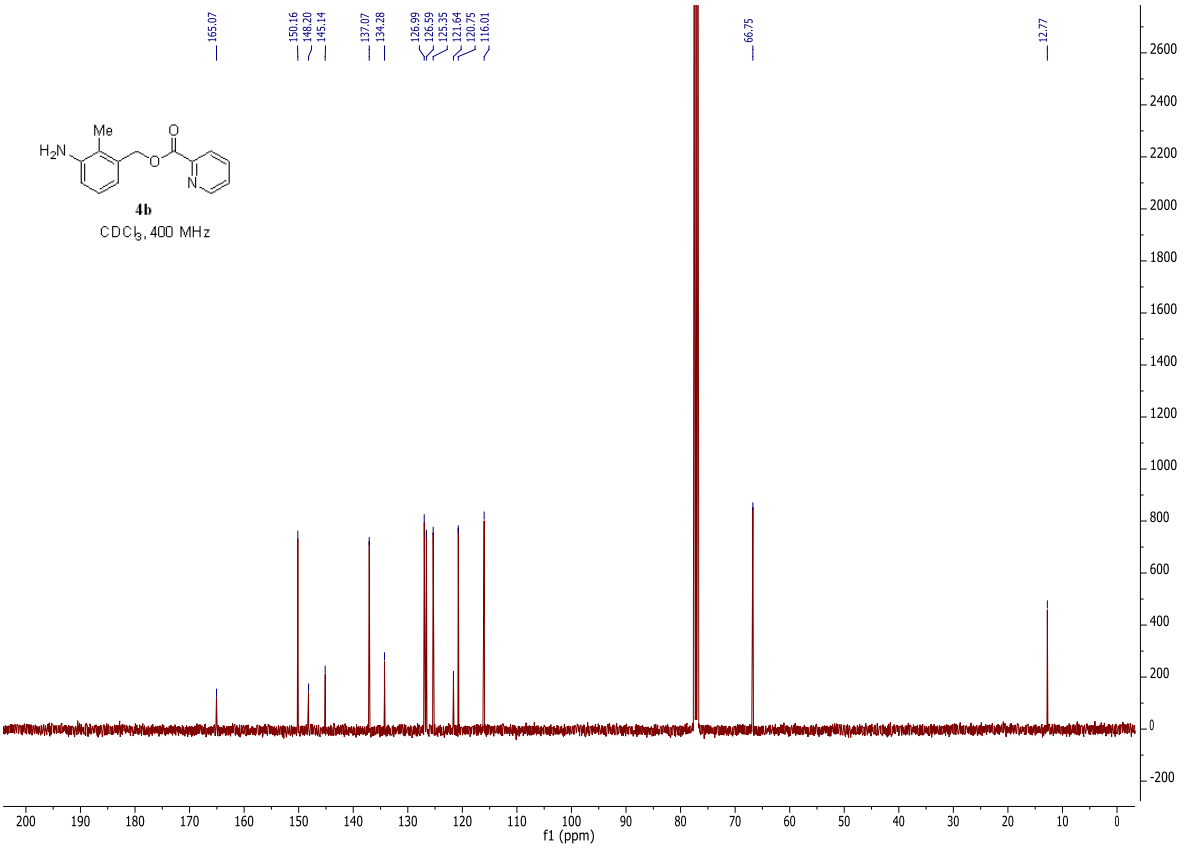

Hb
Ha
Hc
Me
NH2
3
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

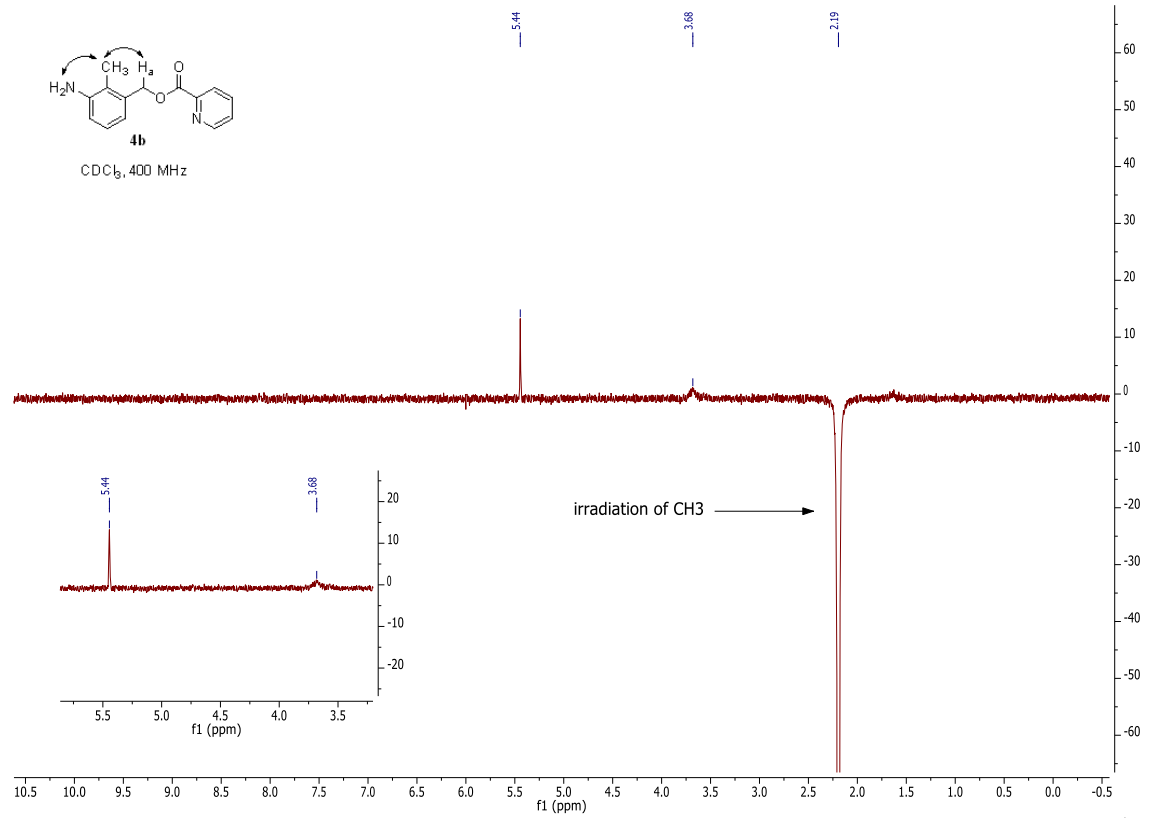

Me
NH2
3
CDCl3, 400 MHz
f1 (ppm)

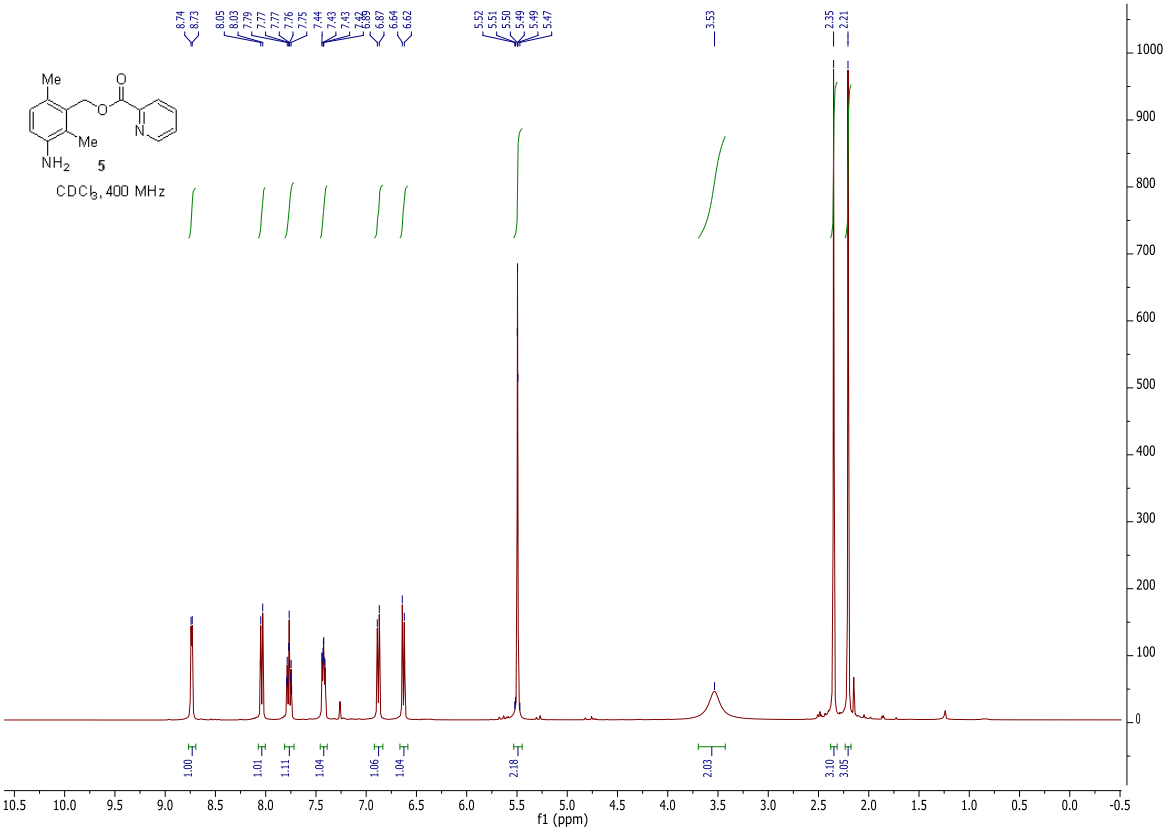

Me
O
O
N
NH2
4a
CDCl3, 400 MHz
8.76
8.75
8.11
8.09
7.83
7.82
7.81
7.81
7.79
7.46
7.46
6.96
6.79
6.79
6.59
6.58
6.57
6.56
5.36
3.60
2.28
1.00
1.00
1.06
1.04
1.04
1.01
1.02
2.06
2.18
3.09
f1 (ppm)

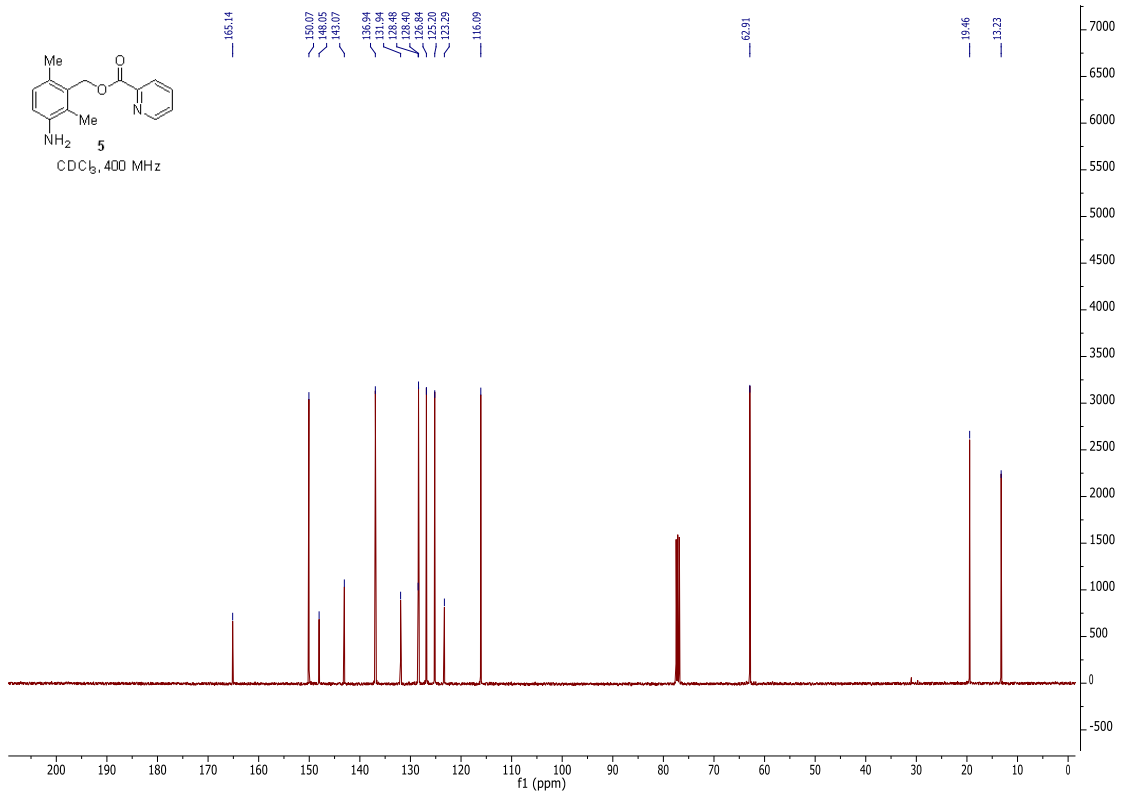

Me
O
O
N
NH2
4a
CDCl3, 400 MHz
165.04
150.07
148.10
144.57
137.05
134.35
131.25
126.98
126.65
125.30
116.36
115.36
65.98
18.17
f1 (ppm)

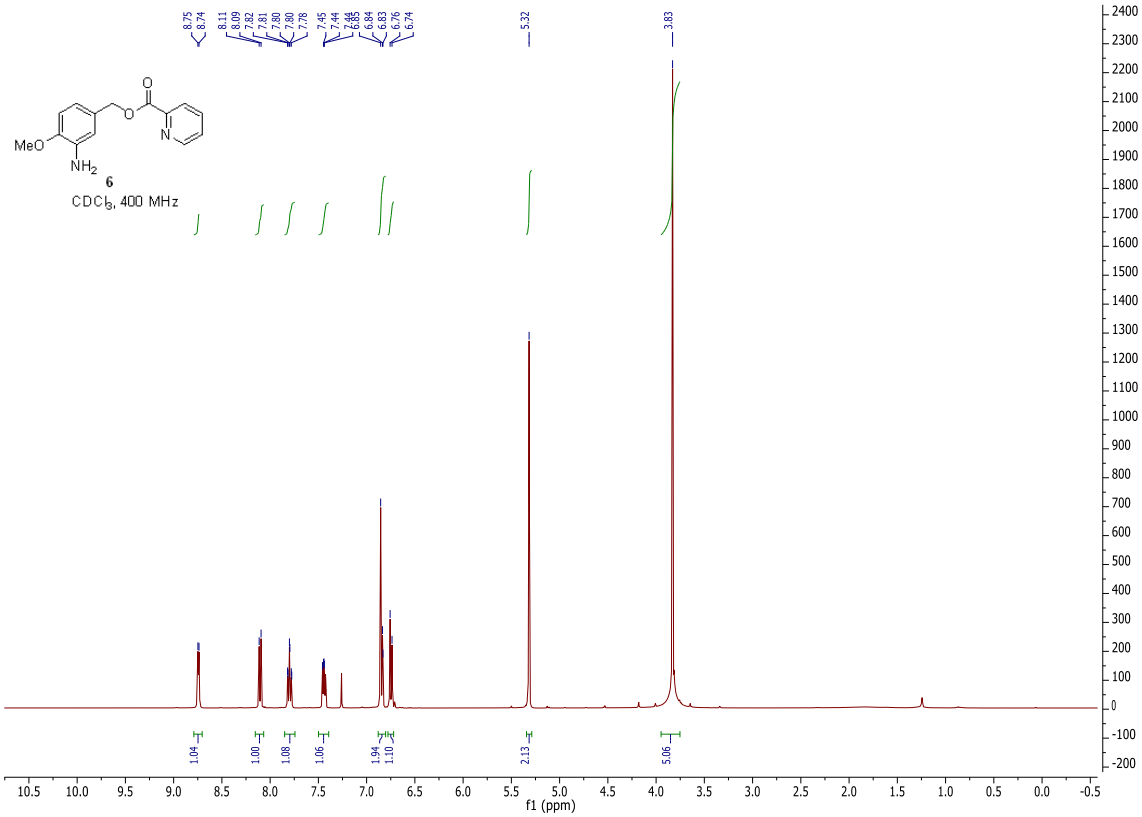

4b
CDCl3, 400 MHz
f1 (ppm)

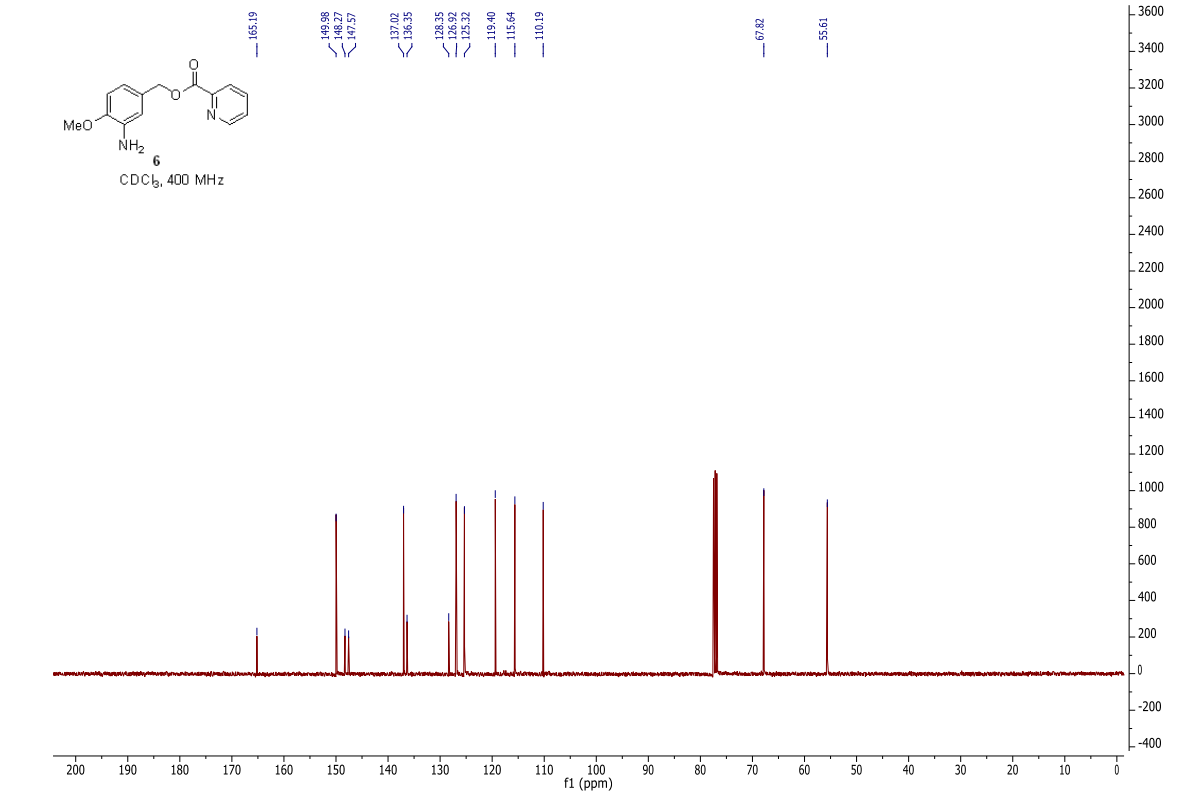

4b
CDCl3, 400 MHz
f1 (ppm)

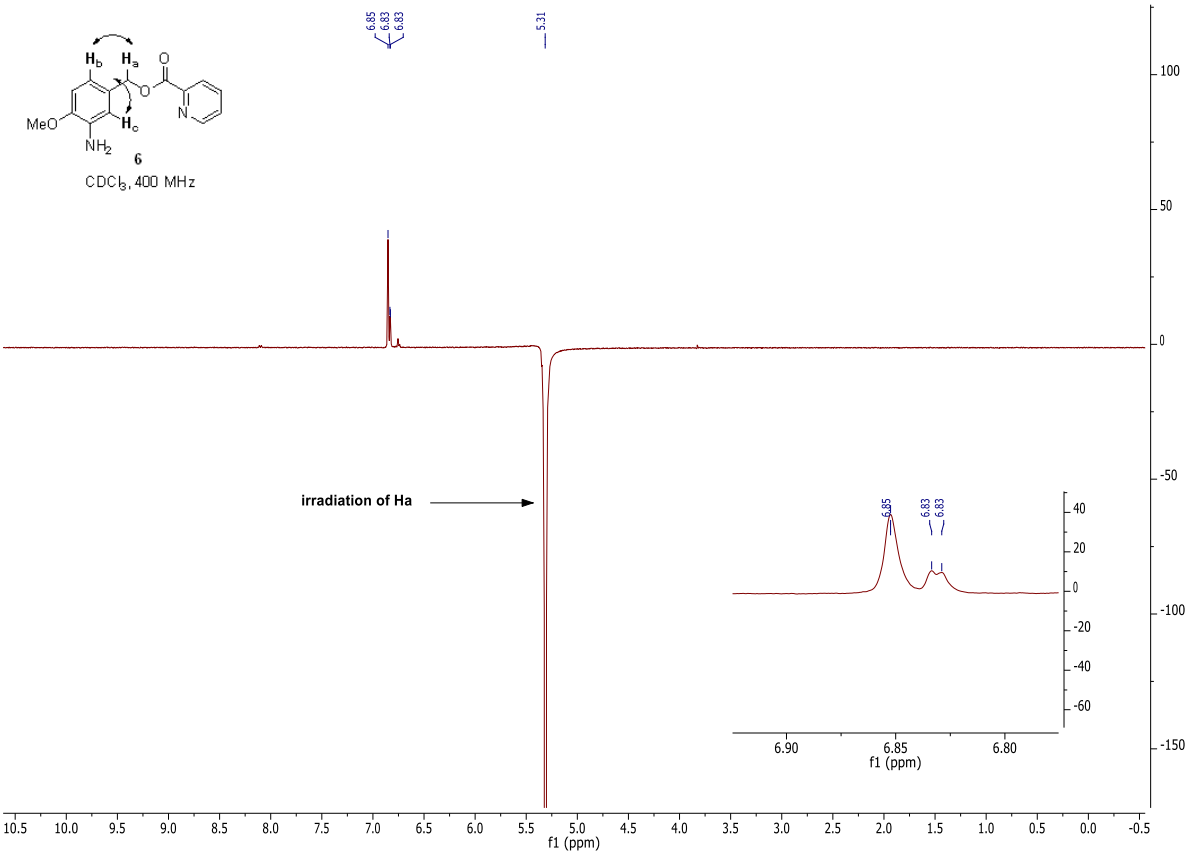

4b
CDCl3, 400 MHz
irradiation of CH3
f1 (ppm)

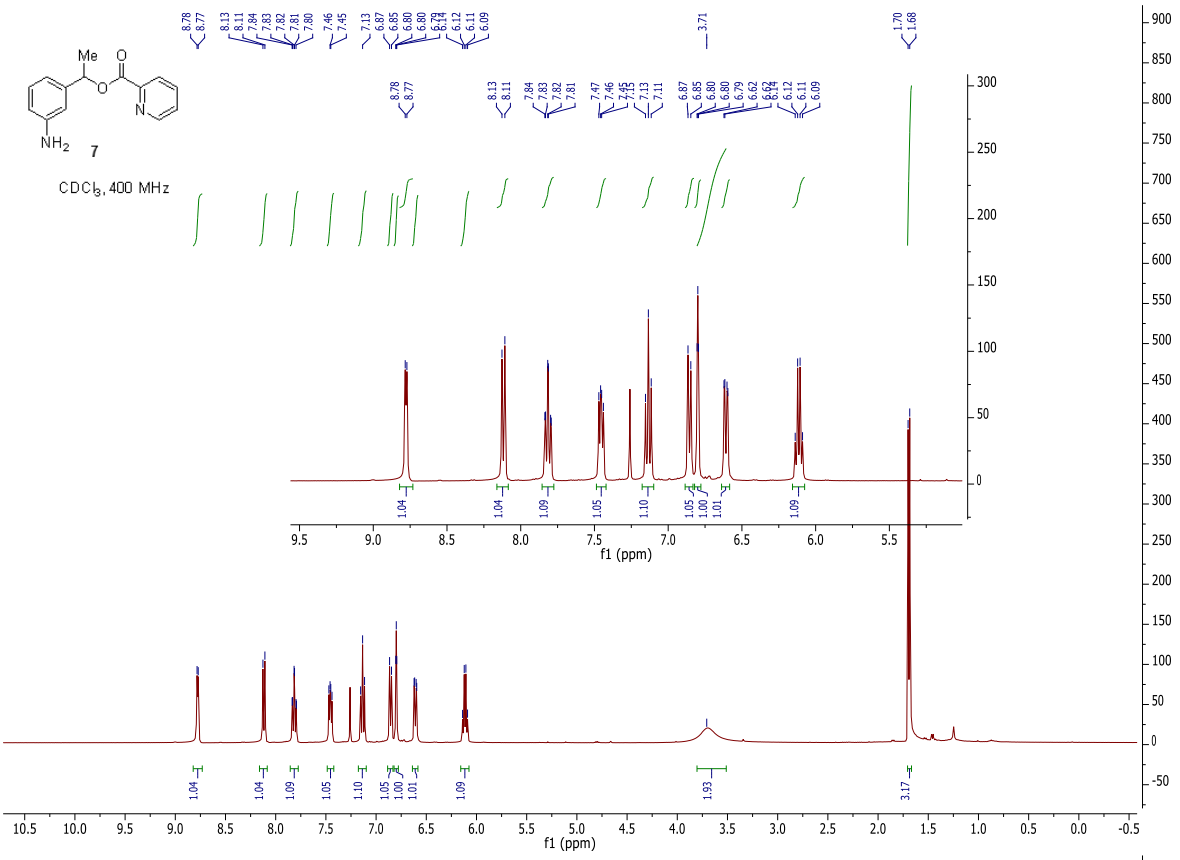

5
CDCl3, 400 MHz
f1 (ppm)

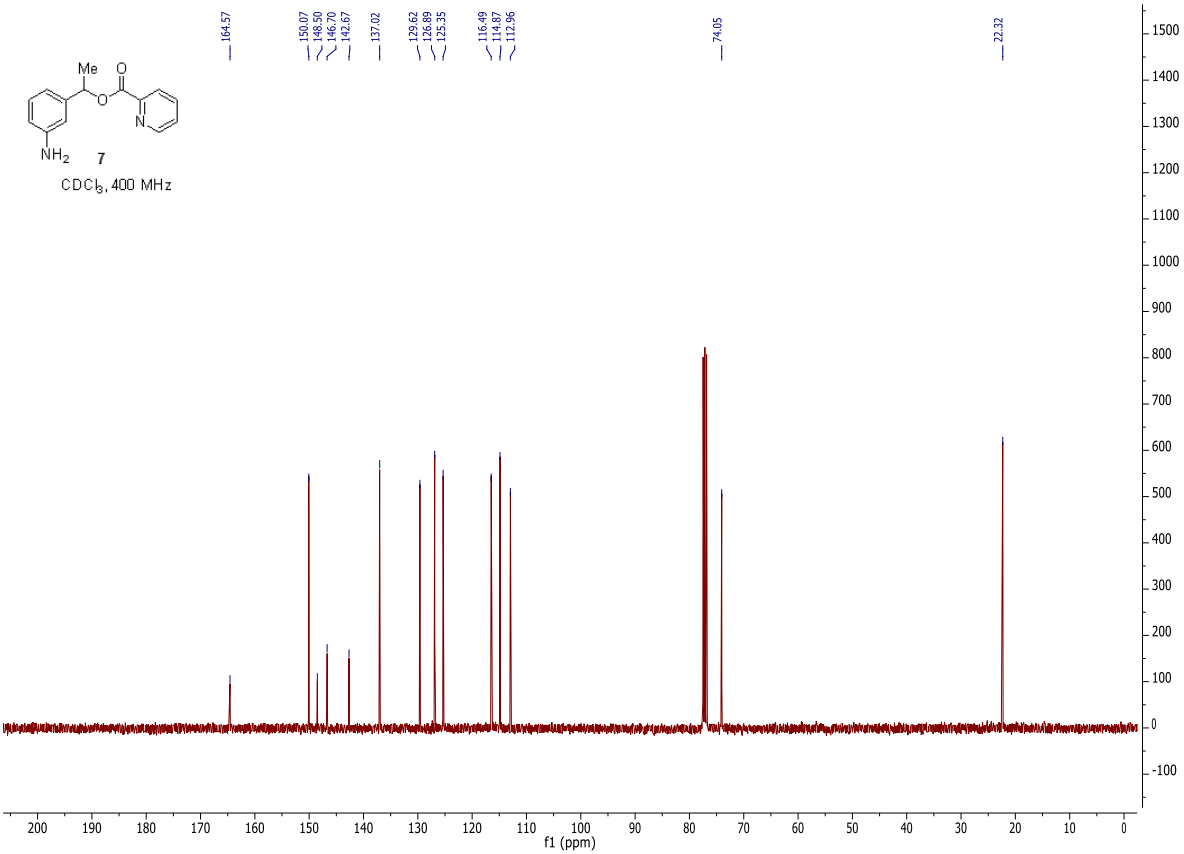

Me
O
O
N
Me
NH2
5
CDCl3, 400 MHz
165.14
150.07
148.05
143.07
136.94
131.94
128.48
128.40
126.84
125.20
123.29
116.09
62.91
19.46
13.23
f1 (ppm)

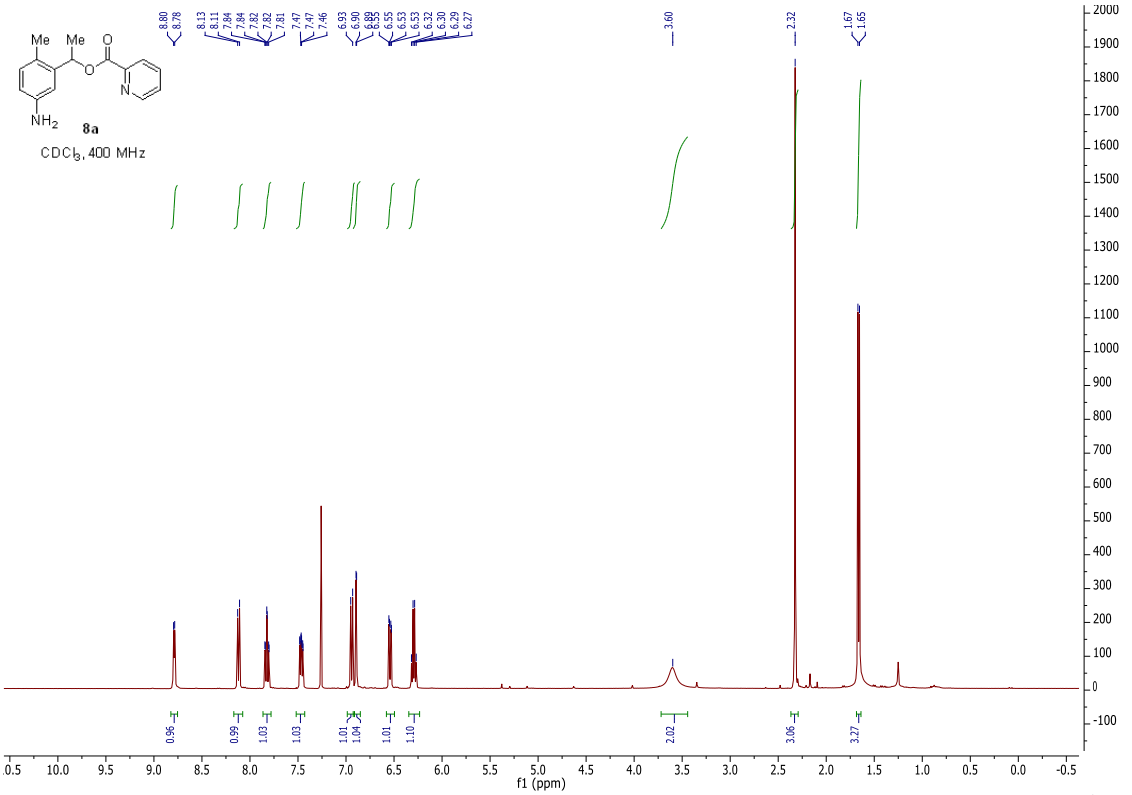

8.75
8.74
8.11
8.09
7.82
7.81
7.80
7.80
7.78
7.45
7.44
6.85
6.84
6.83
6.76
6.74
5.32
3.83
O
O
N
MeO
NH2
6
CDCl3, 400 MHz
1.04
1.00
1.08
1.06
1.94
1.10
2.13
5.06
f1 (ppm)

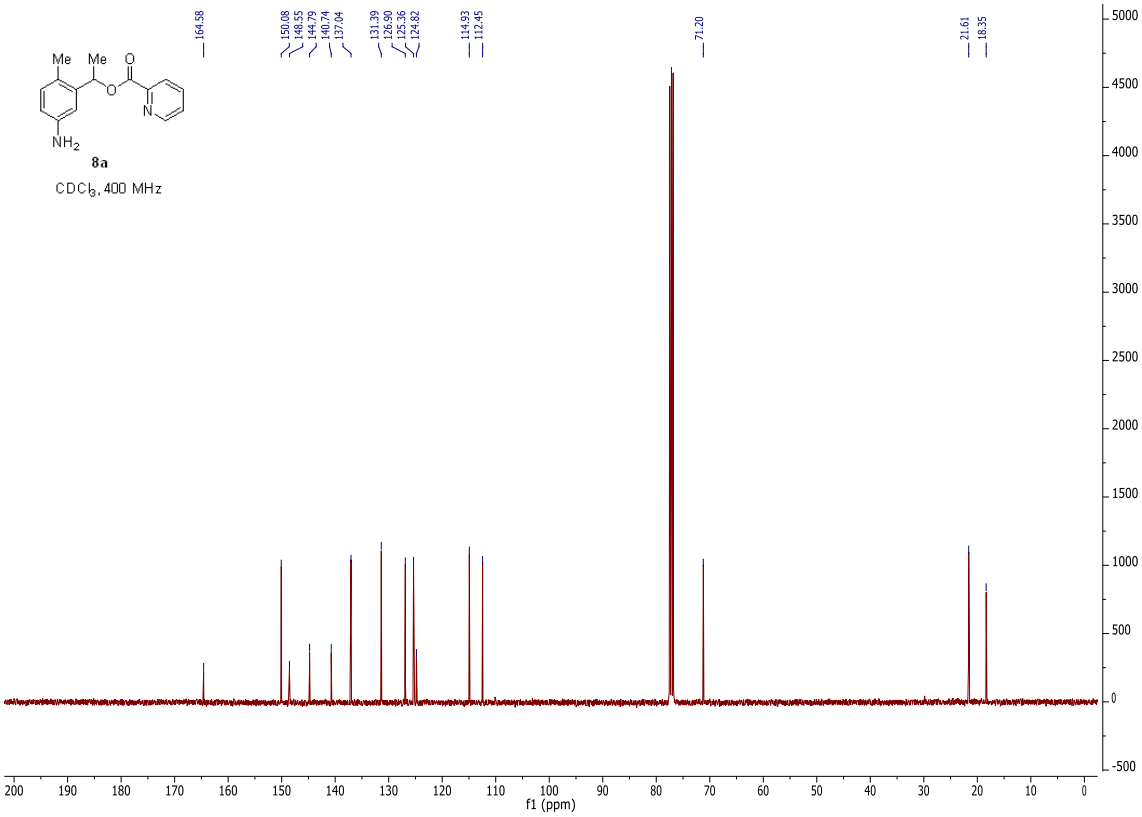

165.19
149.98
148.27
147.57
137.02
136.35
128.35
126.92
125.32
119.40
115.64
110.19
67.82
55.61
MeO
NH2
6
CDCl3, 400 MHz
f1 (ppm)

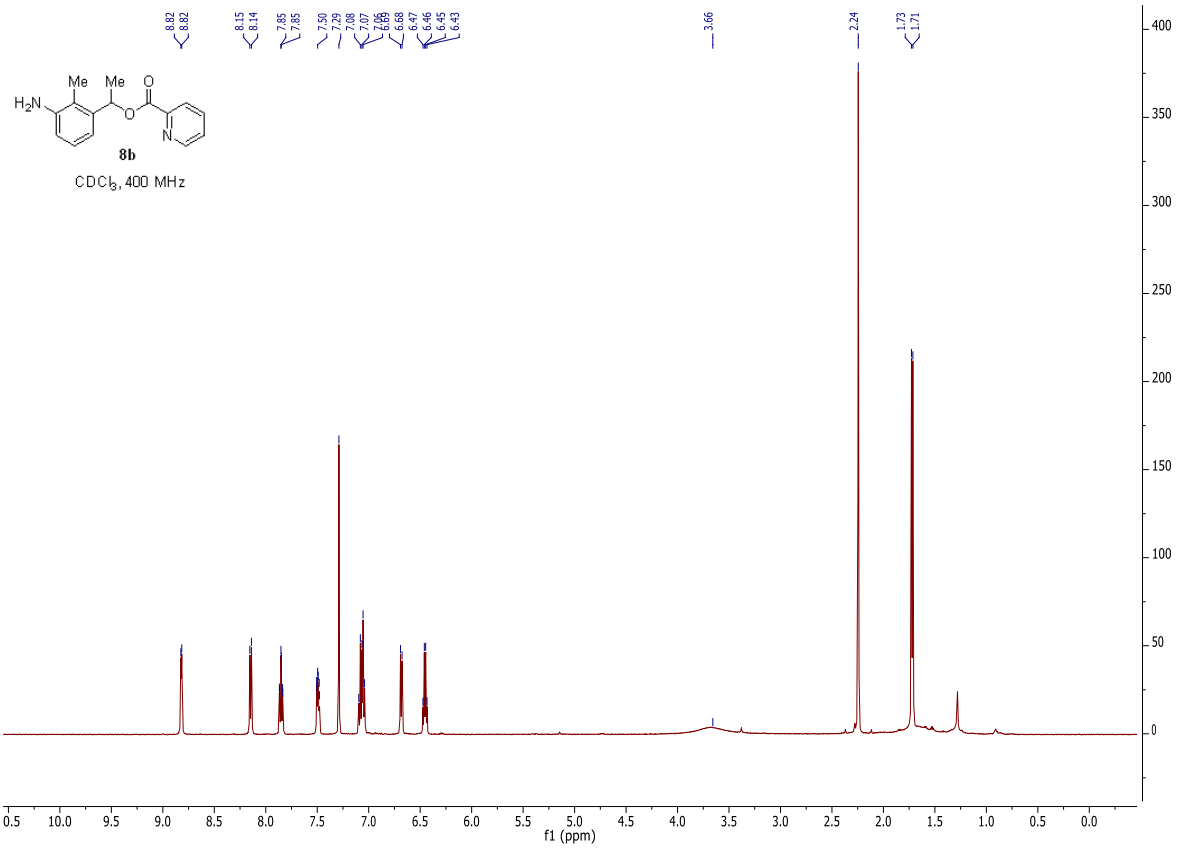

6.85
6.83
6.83
5.31
Hb
Ha
Hc
MeO
NH2
6
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

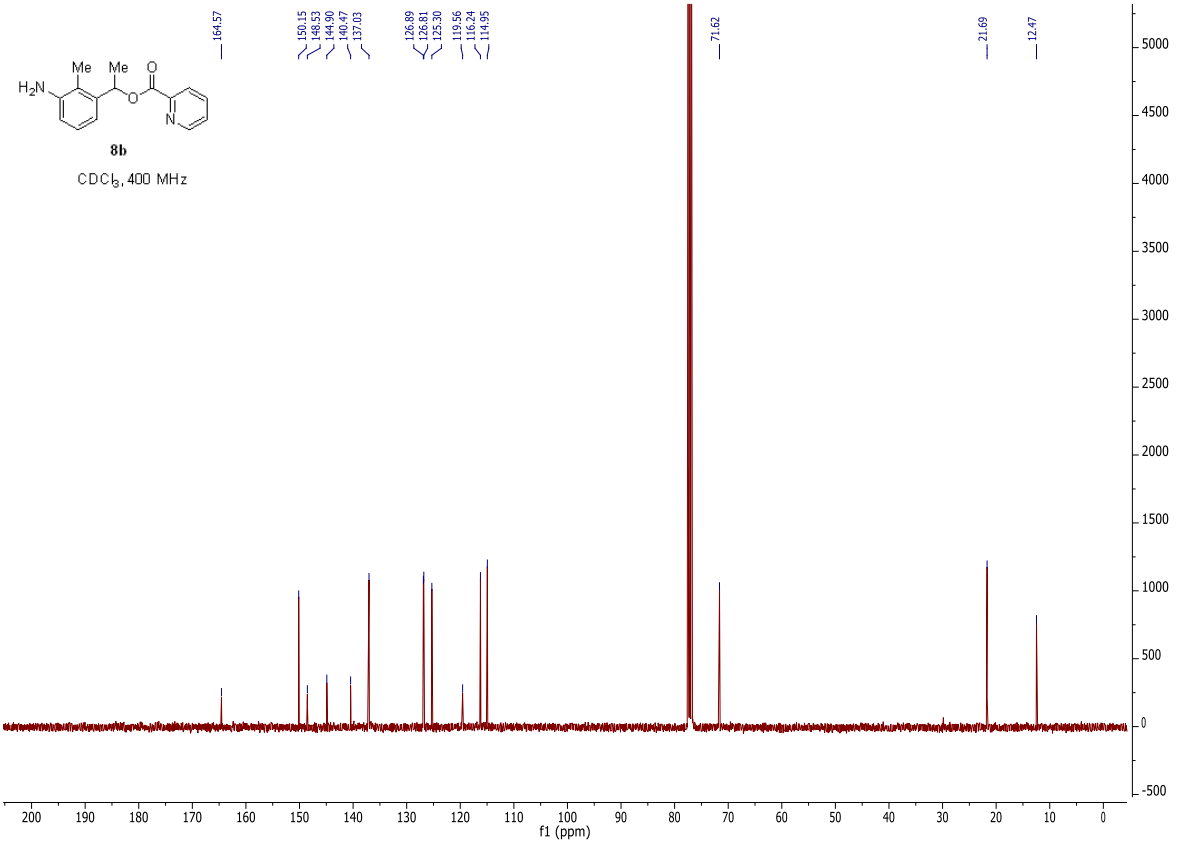

Me
O
O
N
NH2
7
CDCl3, 400 MHz
f1 (ppm)

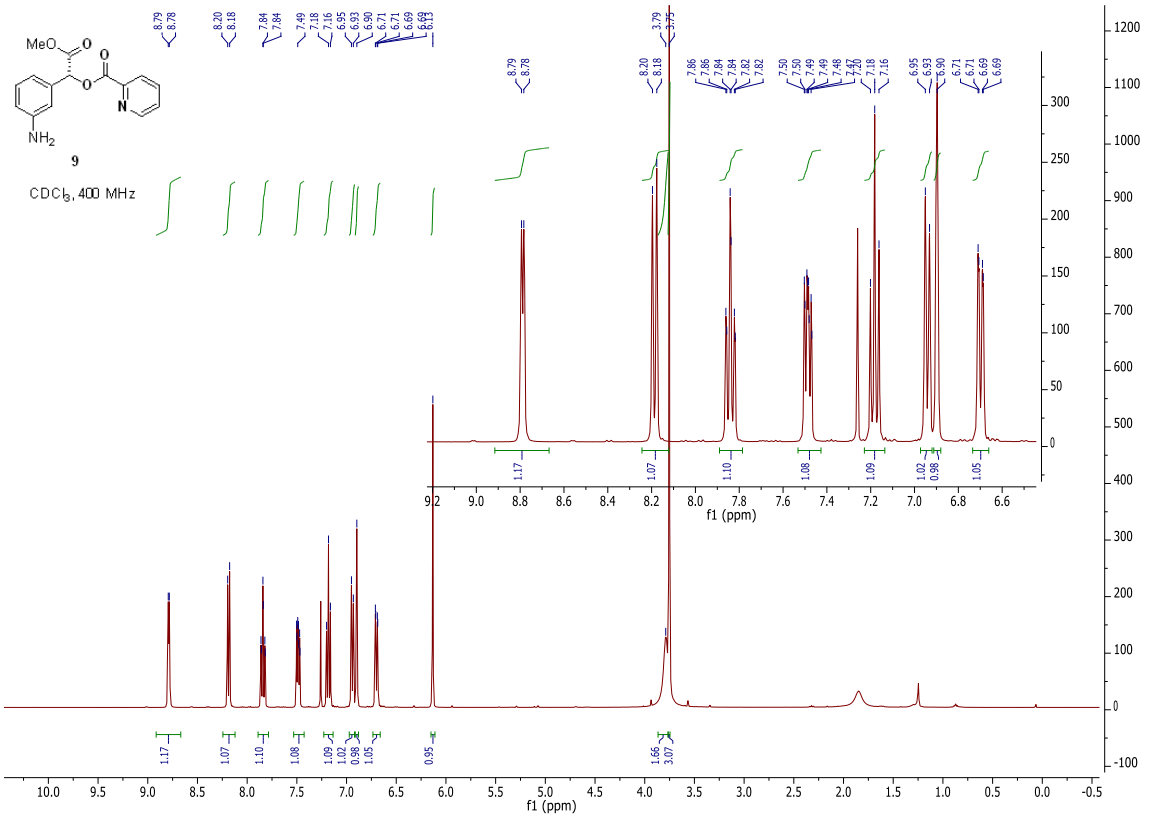

Me
O
O
N
NH2
7
CDCl3, 400 MHz
f1 (ppm)

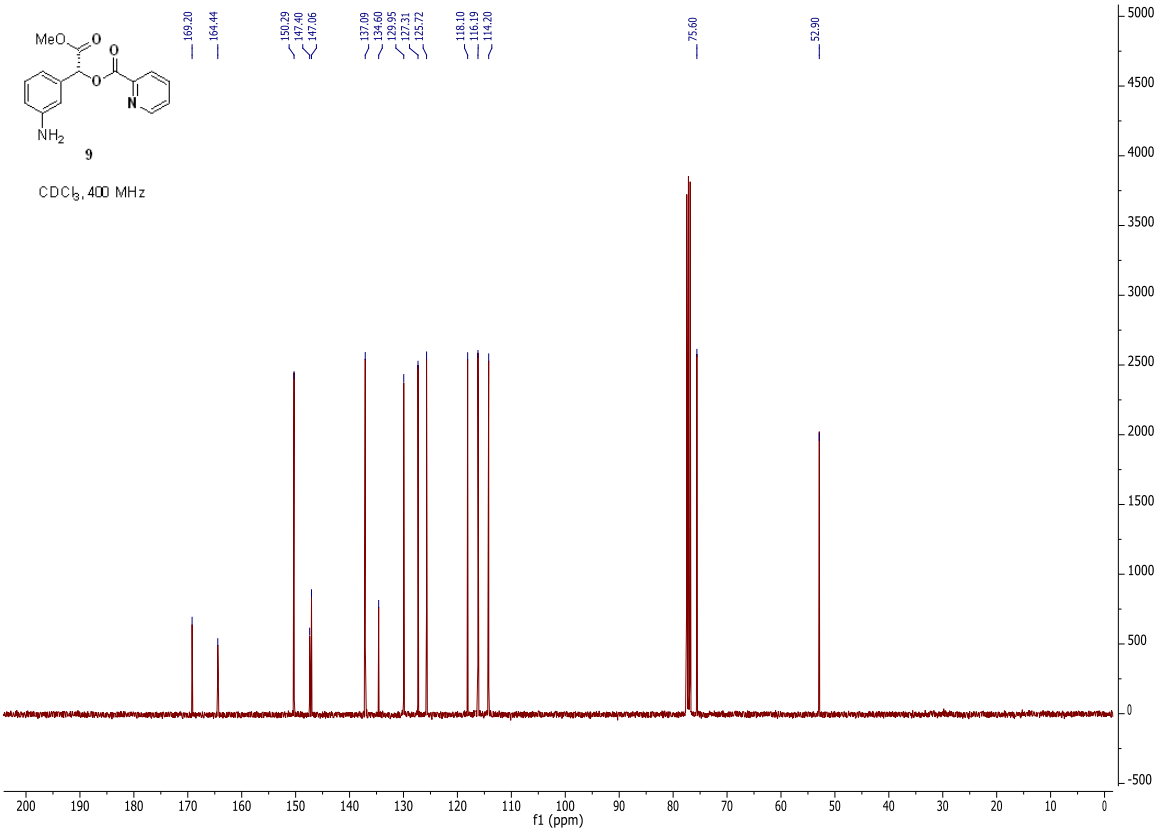

8a
CDCl3, 400 MHz
f1 (ppm)

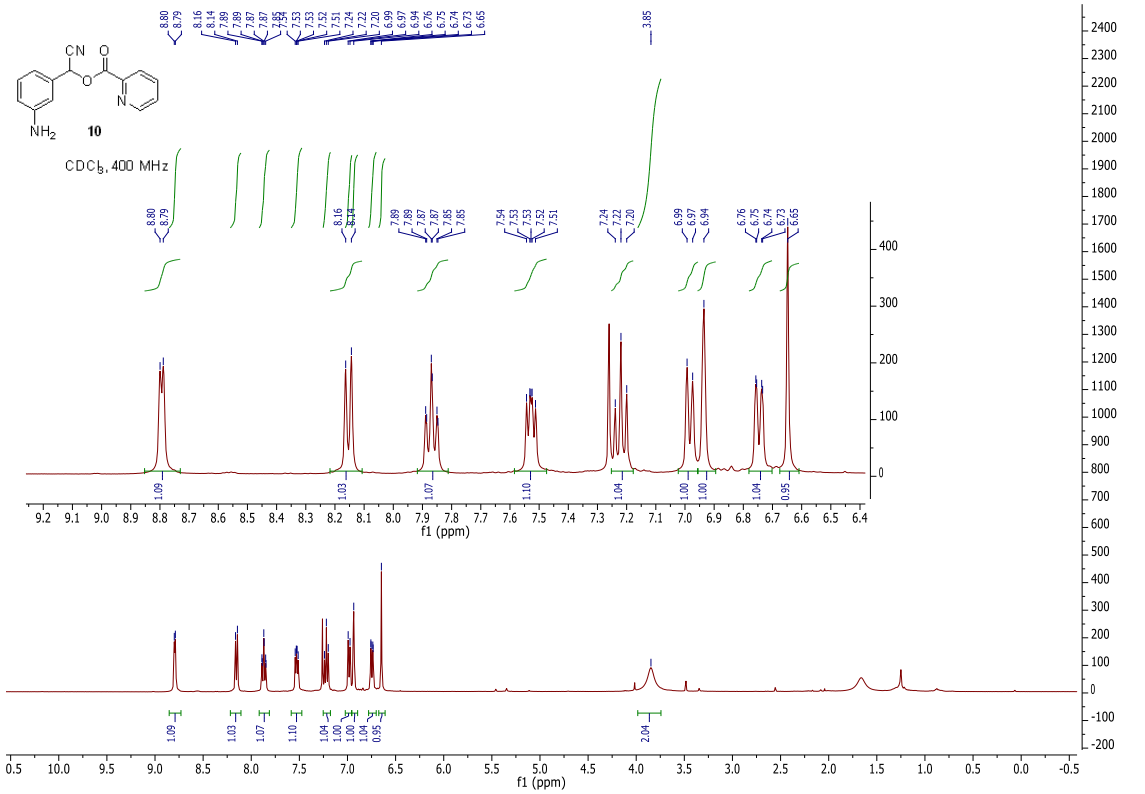

8a
CDCl3, 400 MHz
f1 (ppm)

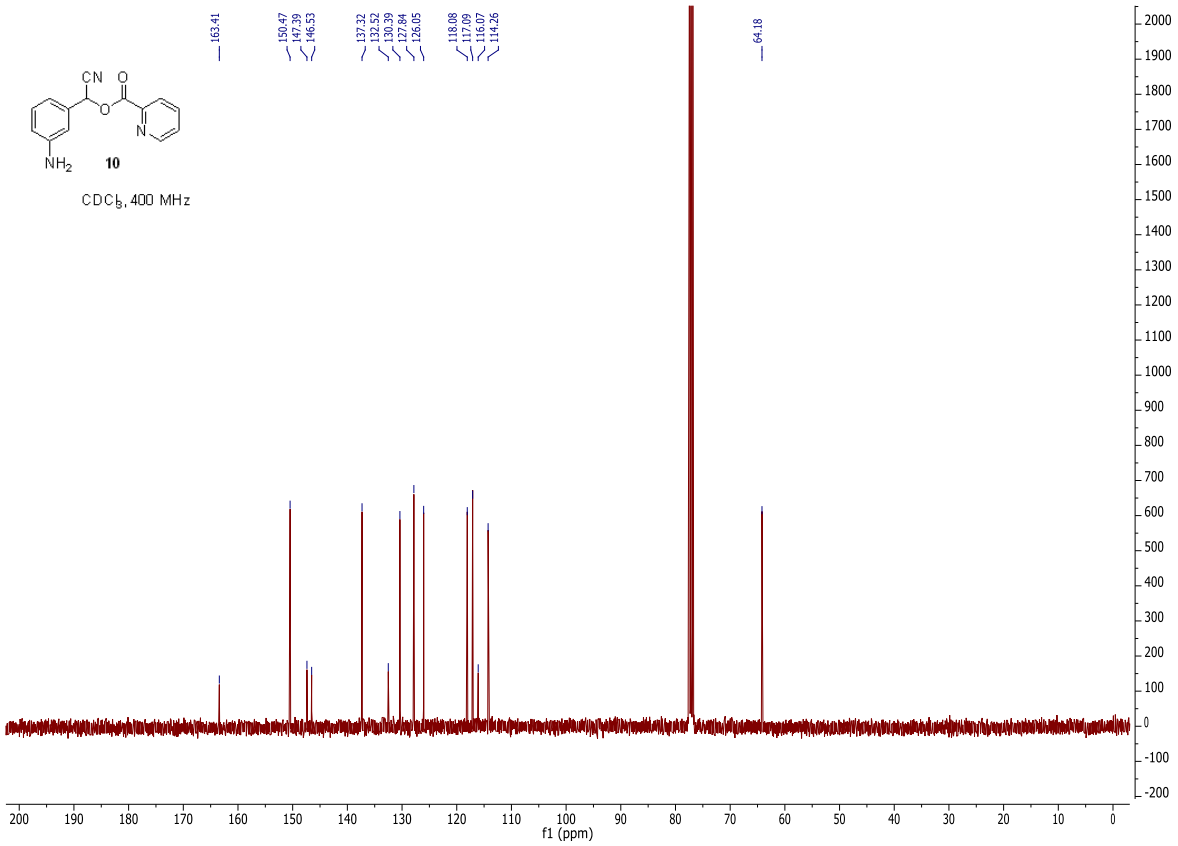

8.82
8.82
8.15
8.14
7.85
7.85
7.50
7.29
7.08
7.07
7.05
6.69
6.68
6.47
6.46
6.45
6.43
3.66
2.24
1.73
1.71
Me
Me
O
H2N
O
N
8b
CDCl3, 400 MHz
f1 (ppm)

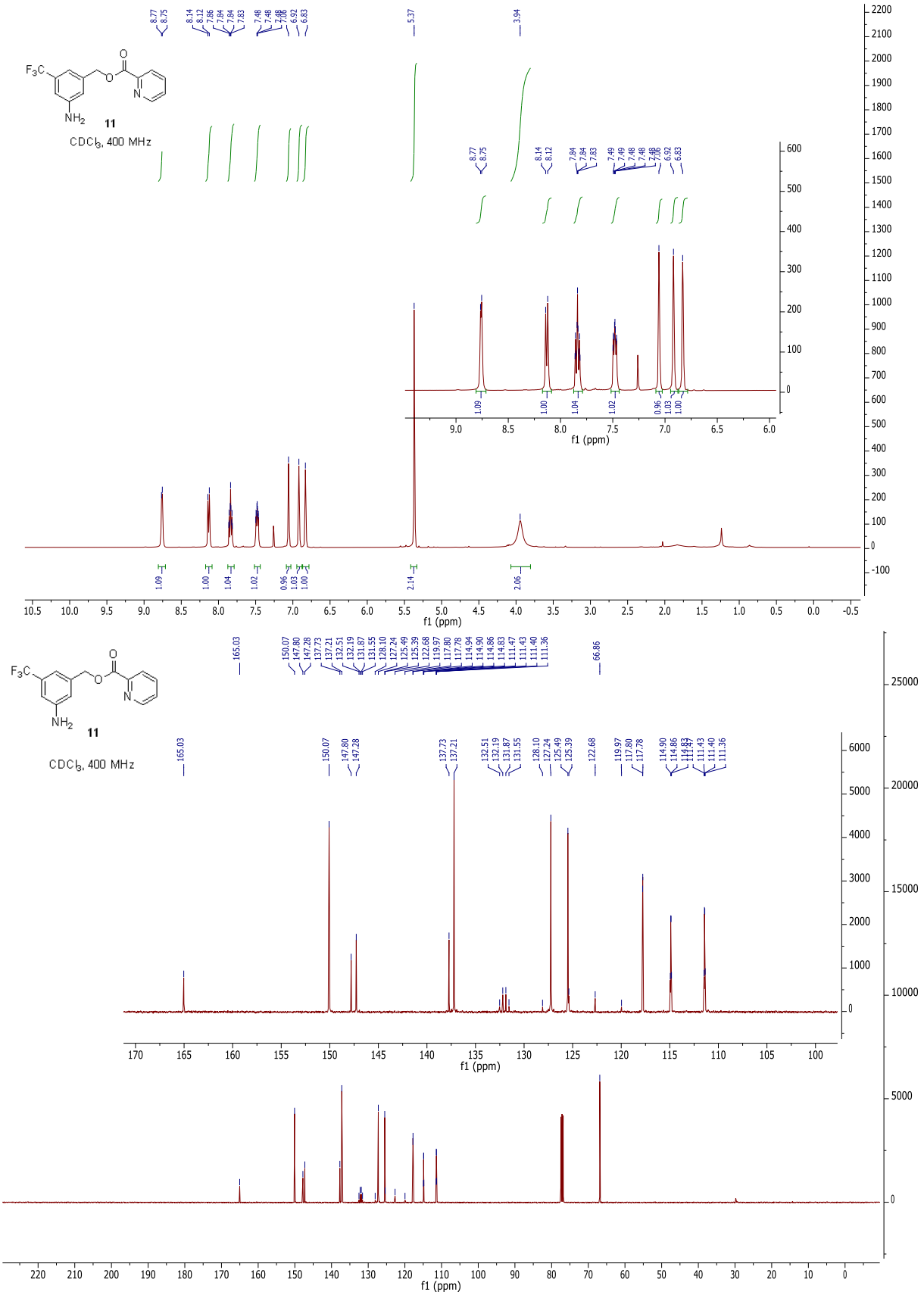

164.57
150.15
148.53
144.90
140.47
137.03
126.89
126.81
125.30
119.56
116.24
114.95
71.62
21.69
12.47
Me
Me
O
H2N
O
N
8b
CDCl3, 400 MHz
f1 (ppm)

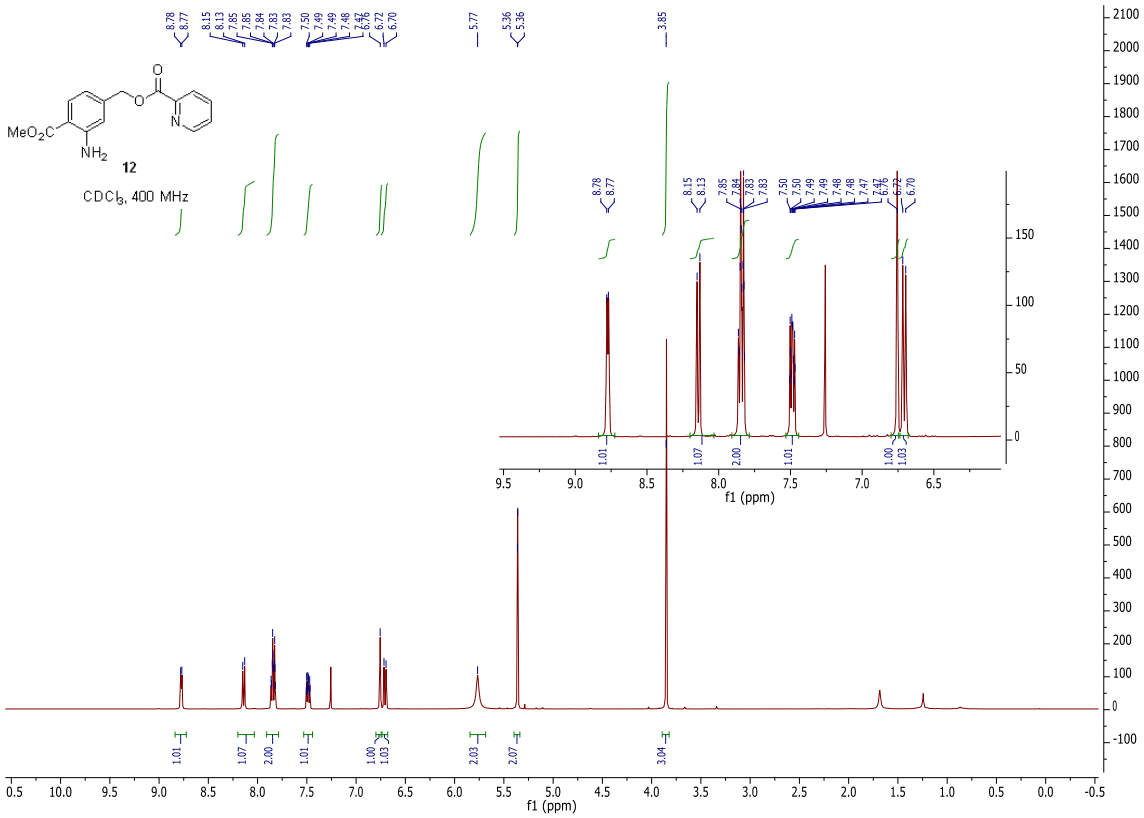

MeO
O
O
O
N
NH2
9
CDCl3, 400 MHz
f1 (ppm)

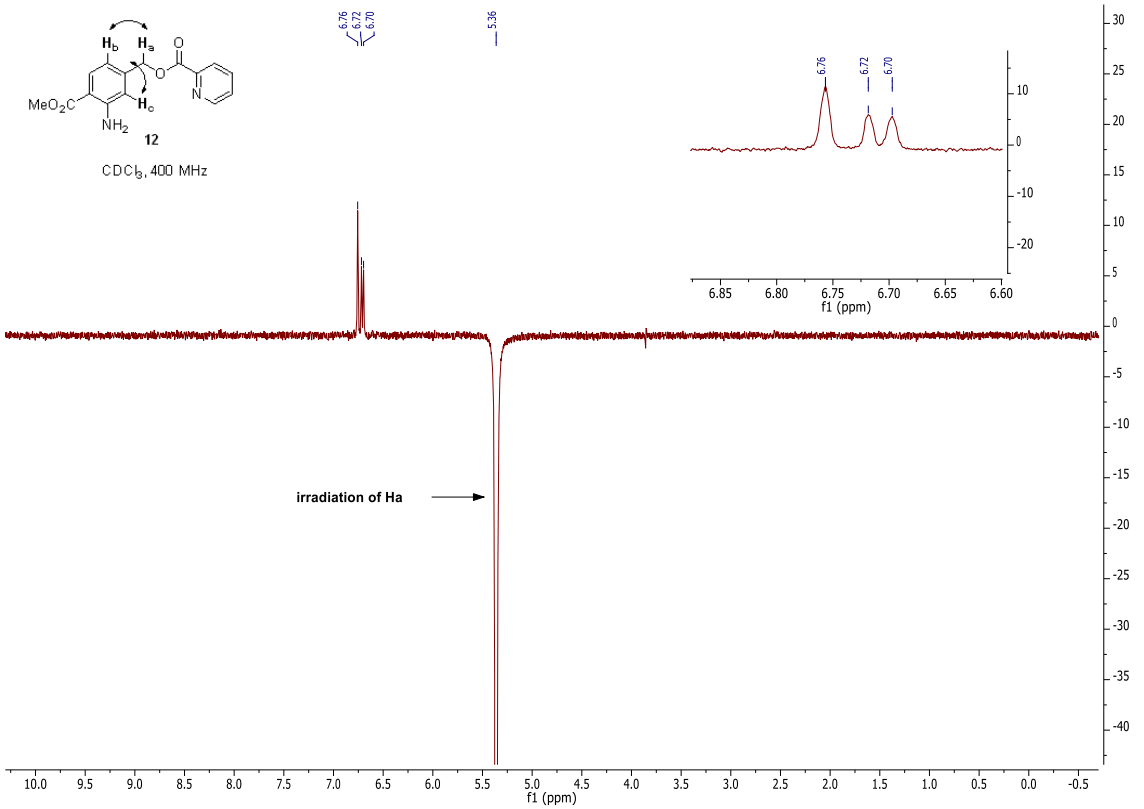

MeO
O
O
O
N
NH2
9
CDCl3, 400 MHz
f1 (ppm)

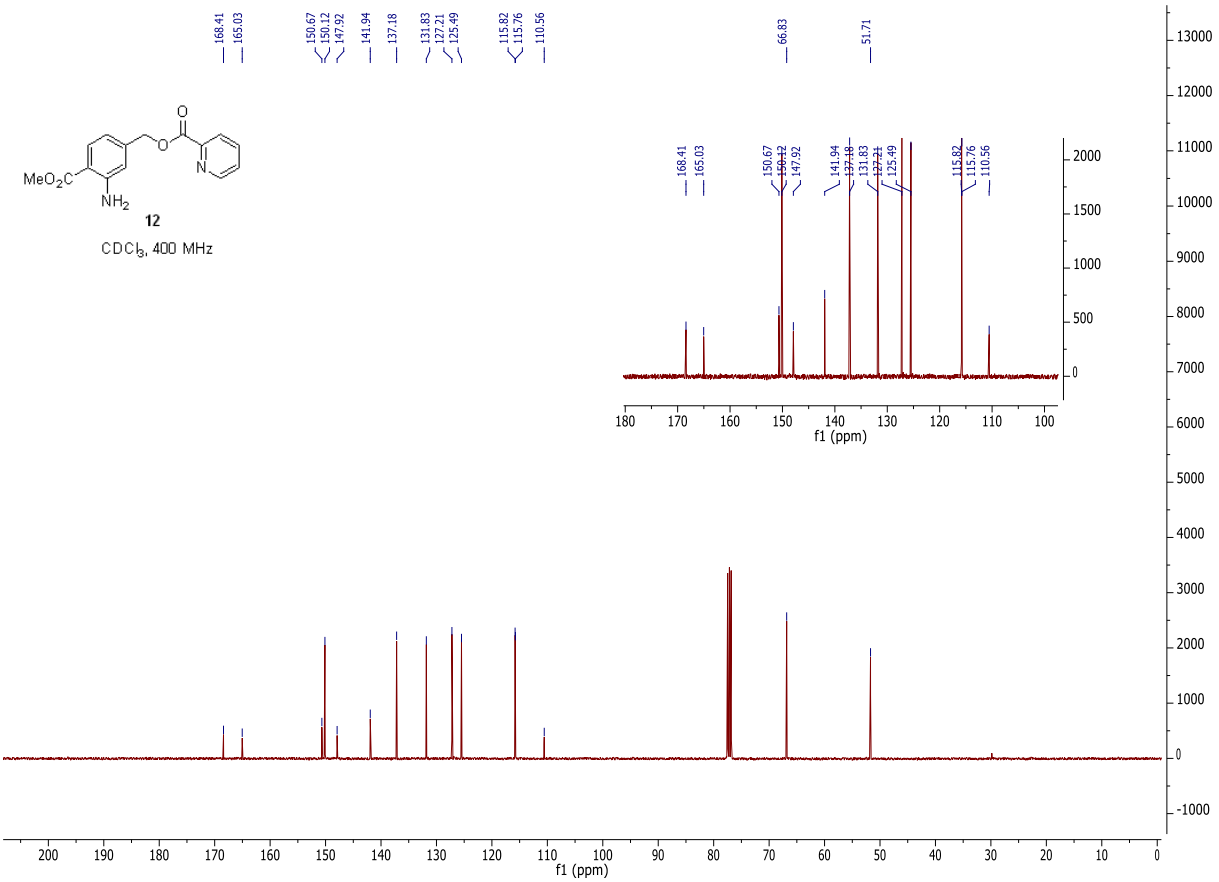

CN
O
O
N
NH2
10
CDCl3, 400 MHz
f1 (ppm)

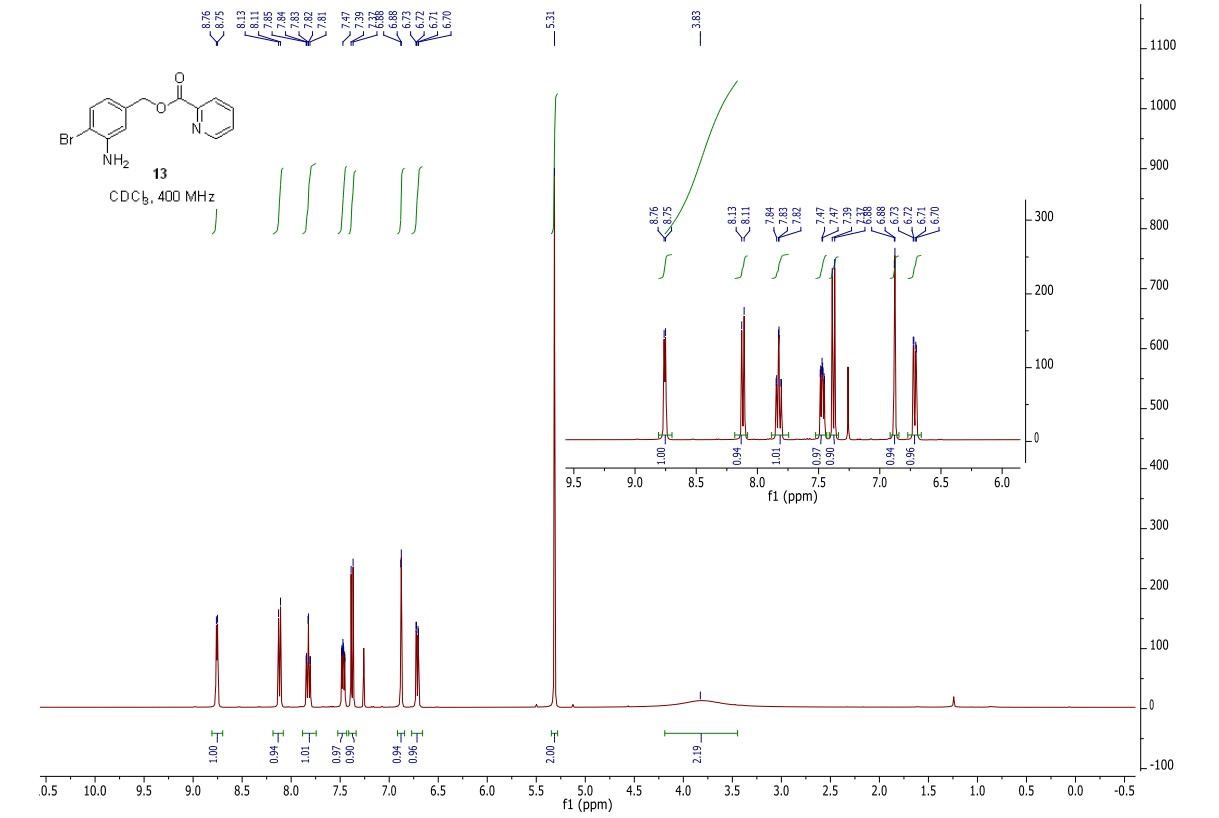

CN
O
O
N
NH2
10
CDCl3, 400 MHz
f1 (ppm)

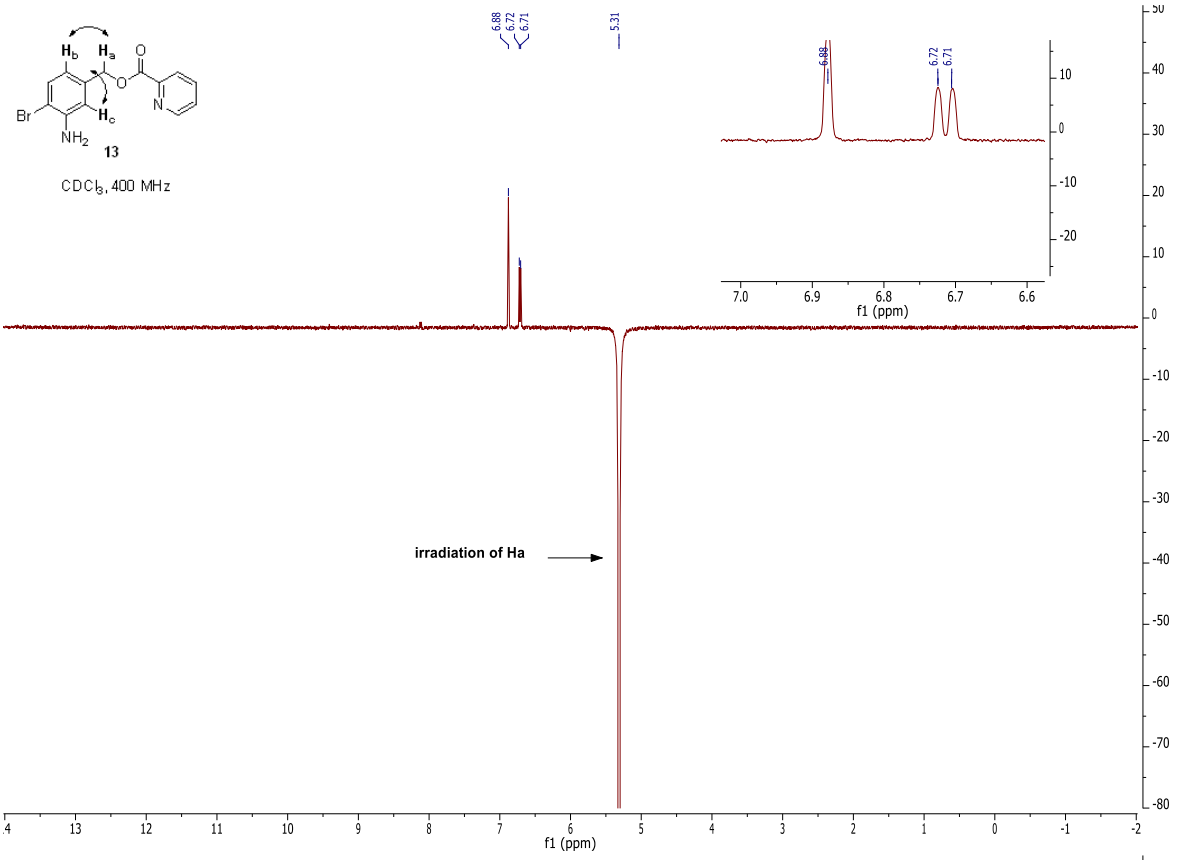

11
CDCl3, 400 MHz
f1 (ppm)
11
CDCl3, 400 MHz
f1 (ppm)

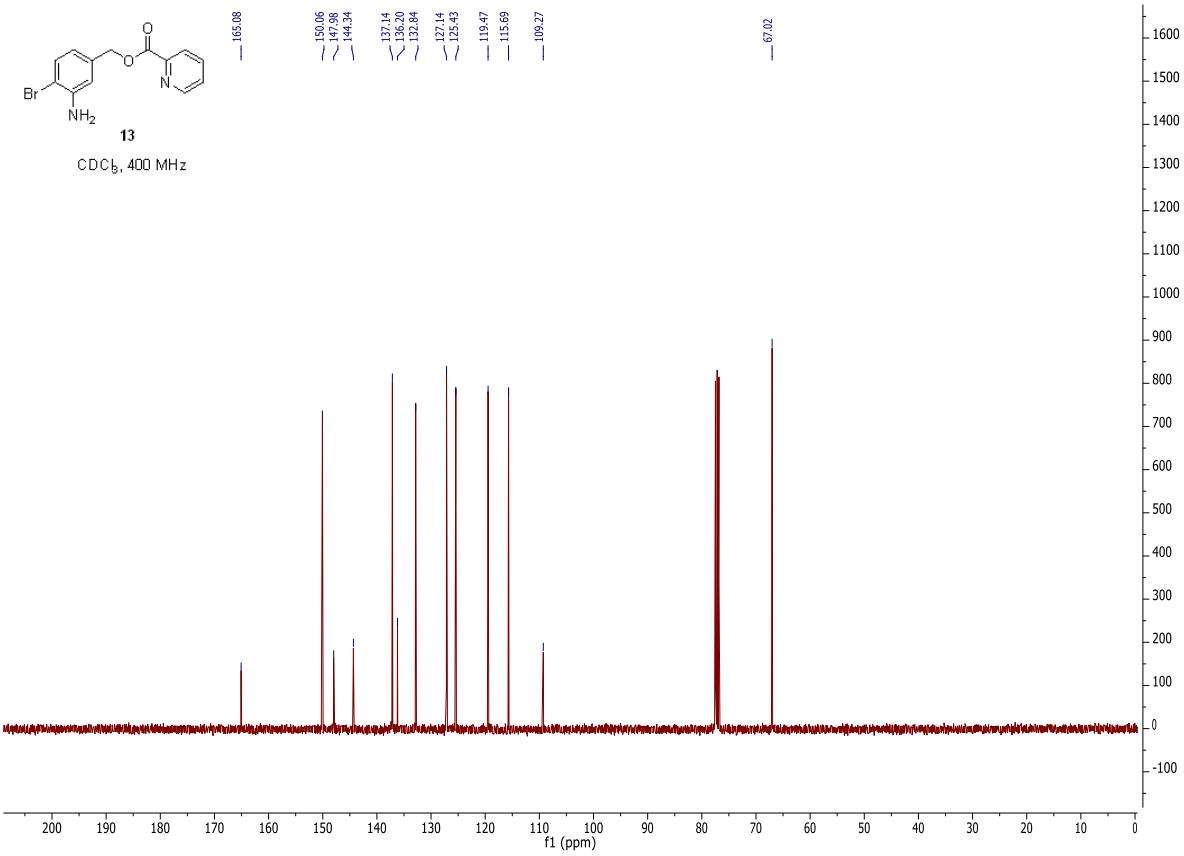

MeO2C
NH2
12
CDCl3, 400 MHz
f1 (ppm)

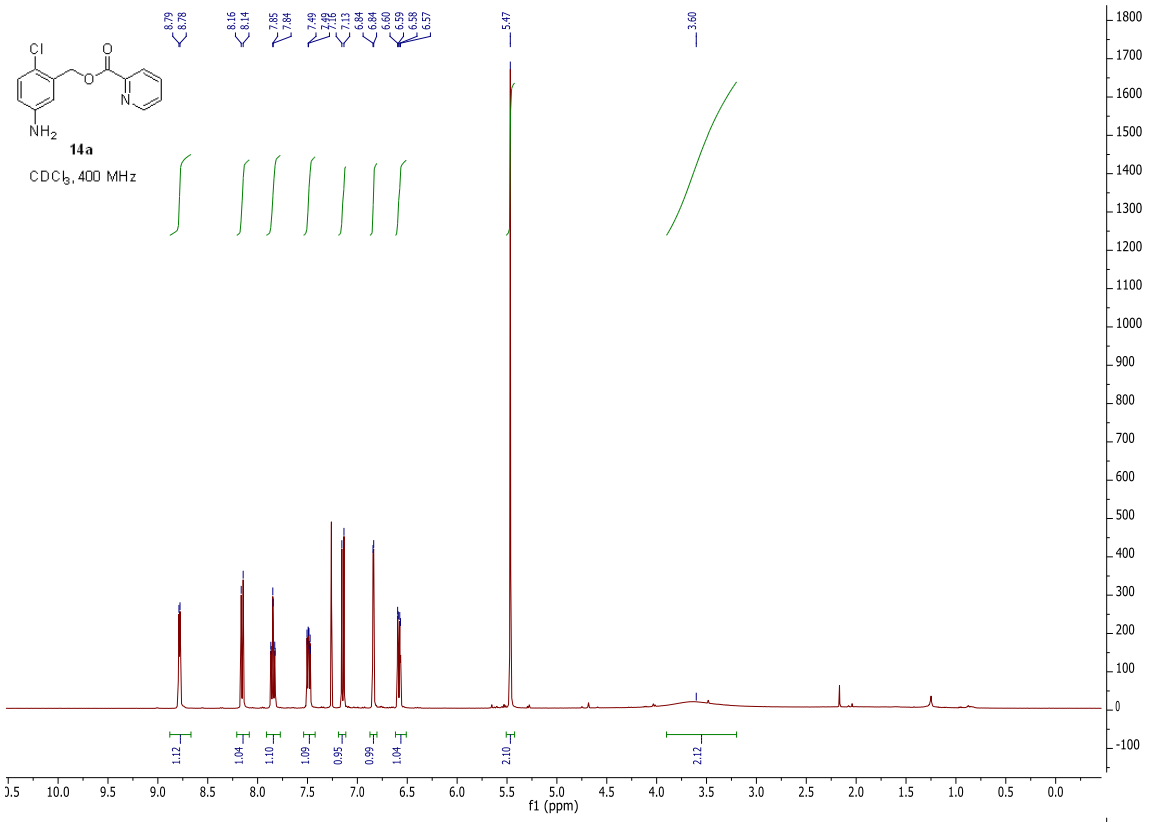

Hb
Ha
Hc
MeO2C
NH2
12
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

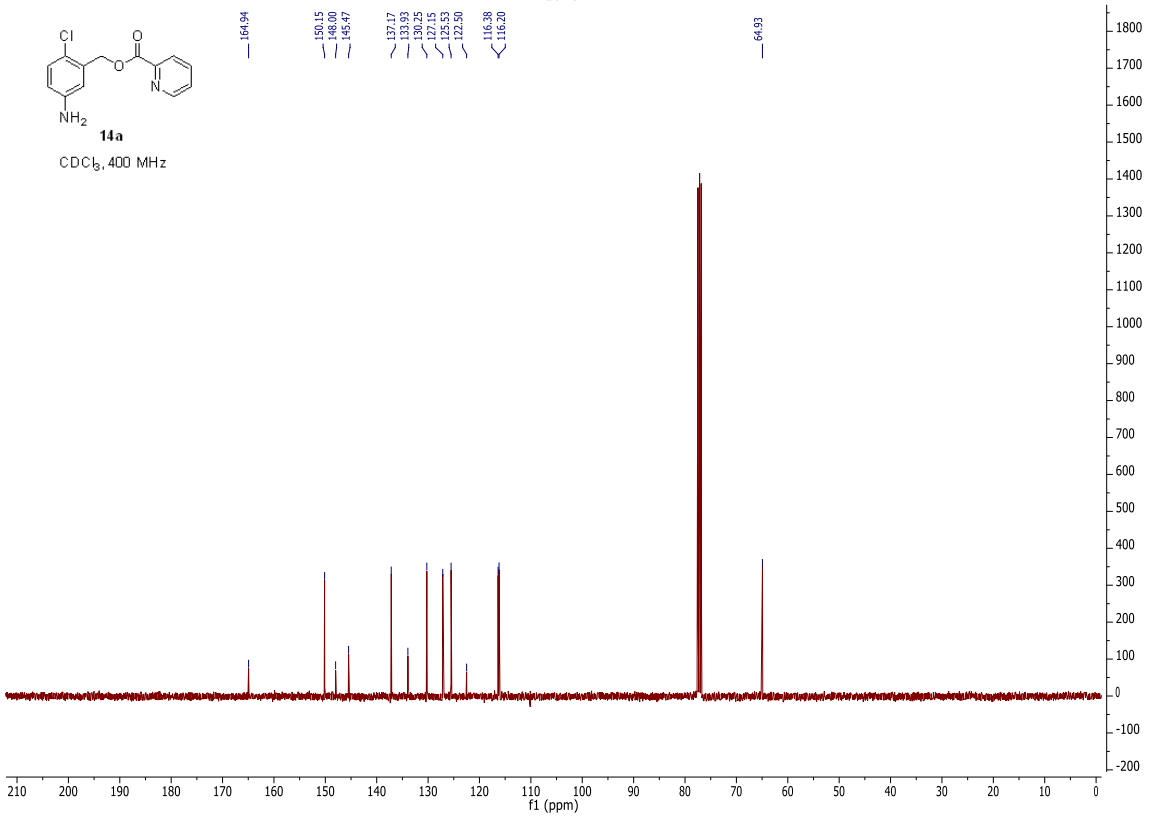

168.41
165.03
150.67
150.12
147.92
141.94
137.18
131.83
127.21
125.49
115.82
115.76
110.56
66.83
51.71
MeO2C
NH2
12
CDCl3, 400 MHz
f1 (ppm)

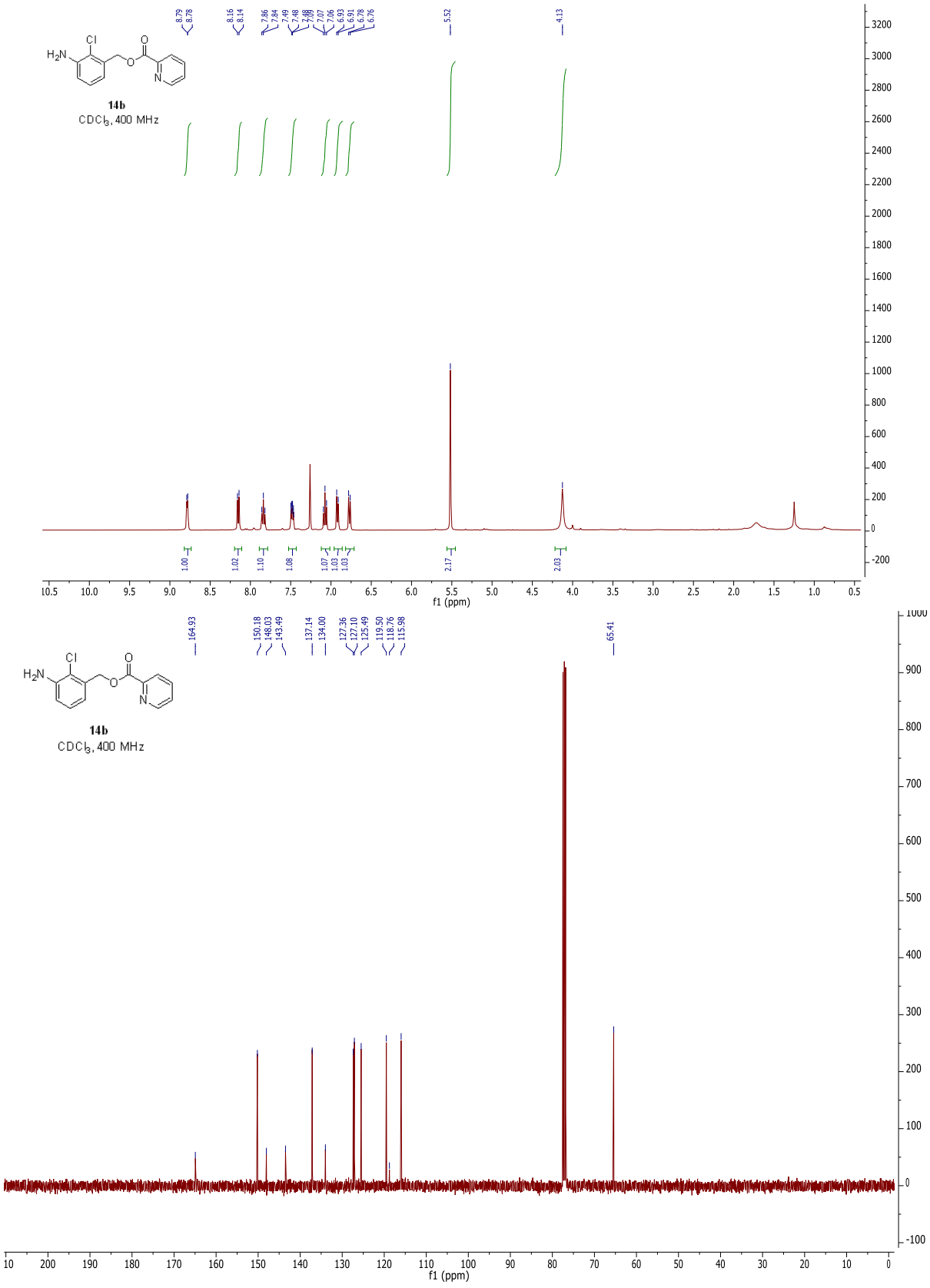

8.76
6.75
8.13
8.11
7.85
7.84
7.83
7.82
7.81
7.47
7.39
7.38
6.88
6.73
6.72
6.71
6.70
5.31
3.83
Br
NH2
13
CDCl3, 400 MHz
1.00
0.94
1.01
0.97
0.90
0.94
0.96
2.00
2.19
f1 (ppm)

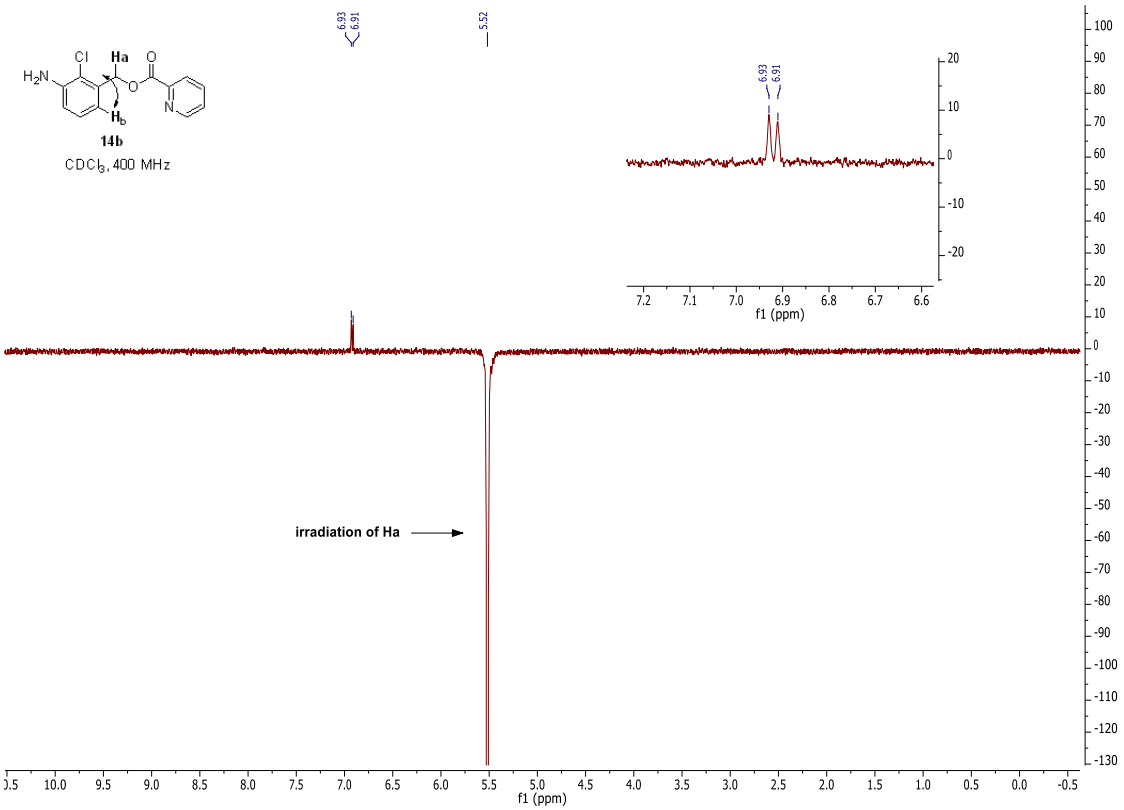

13
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

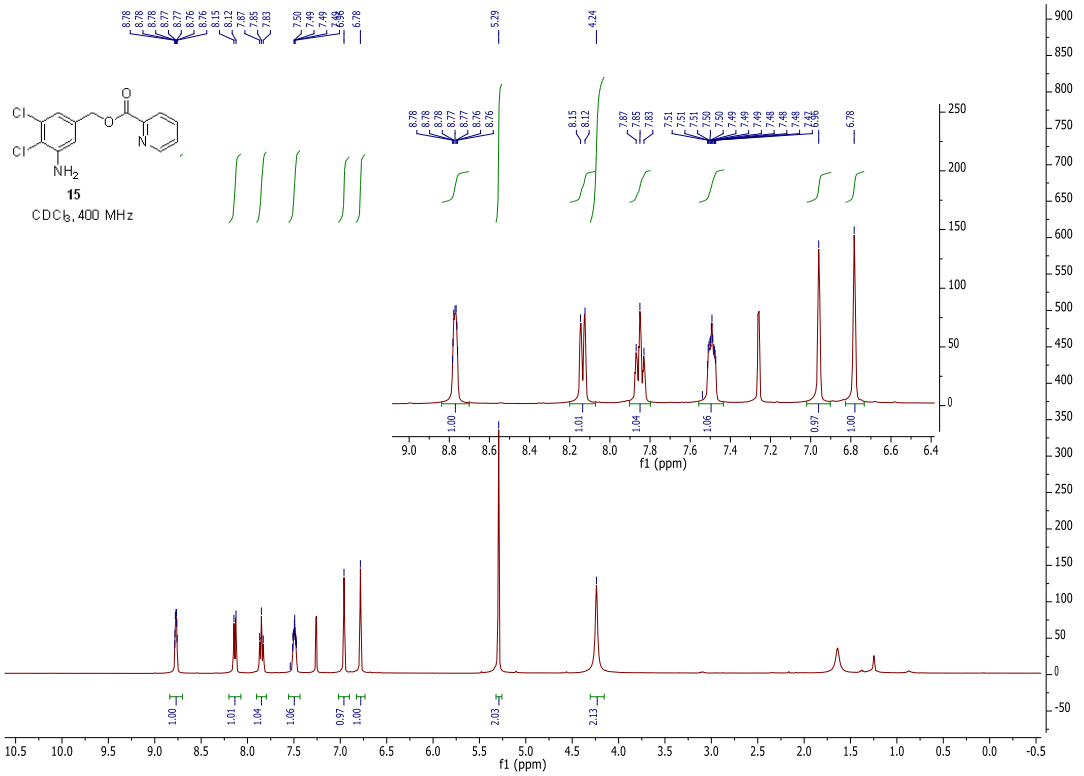

13
CDCl3, 400 MHz
f1 (ppm)

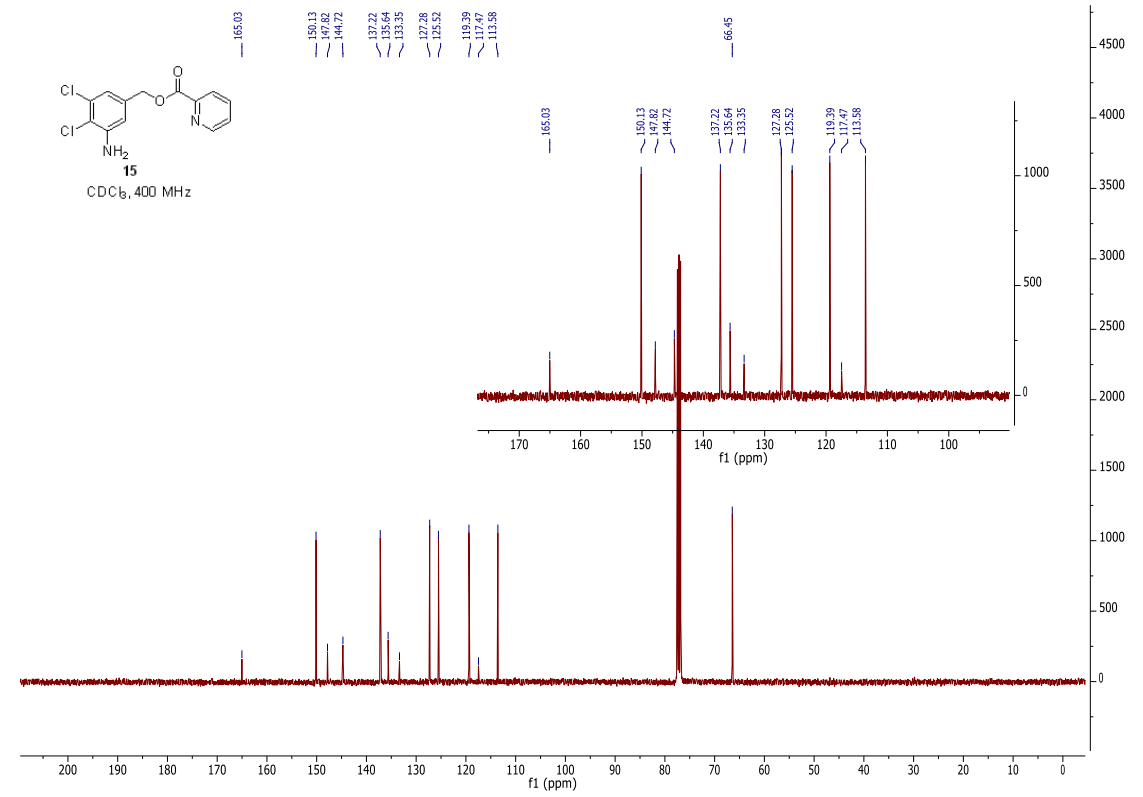

8.79
8.78
8.16
8.14
7.85
7.84
7.49
7.48
7.13
6.84
6.84
6.60
6.59
6.58
6.57
5.47
3.60
Cl
O
O
N
NH2
14a
CDCl3, 400 MHz
1.12
1.04
1.10
1.09
0.95
0.99
1.04
2.10
2.12
f1 (ppm)

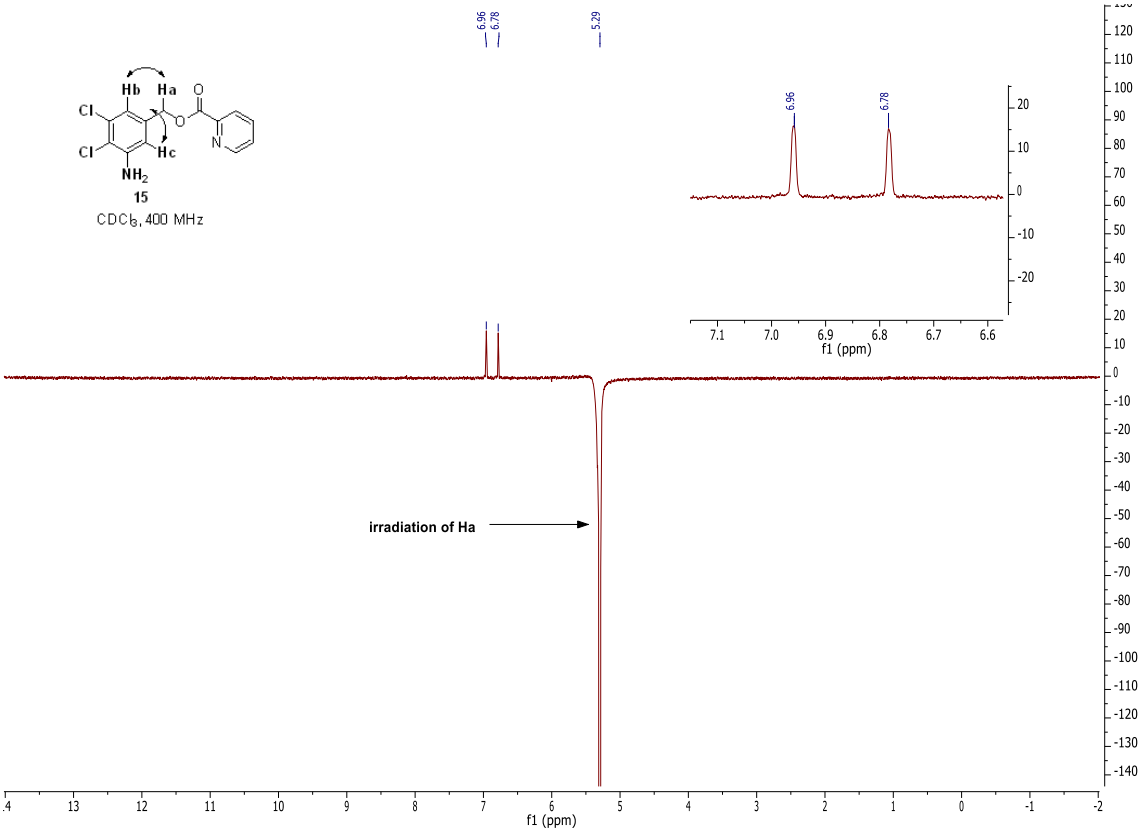

164.94
150.15
148.00
145.47
137.17
133.93
130.25
127.15
125.53
122.50
116.38
116.20
64.93
Cl
O
O
N
NH2
14a
CDCl3, 400 MHz
f1 (ppm)

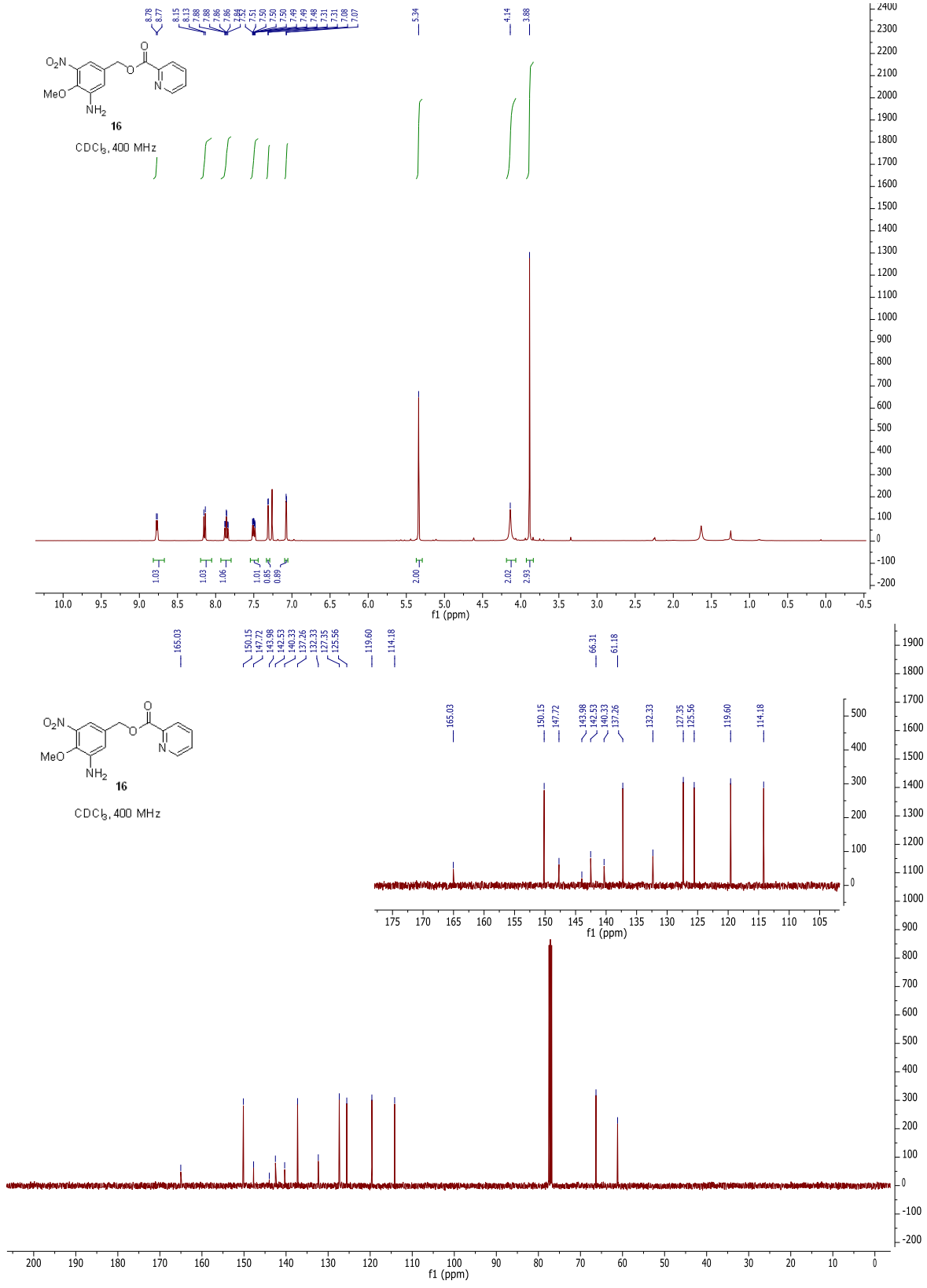

14b
CDCl3, 400 MHz
f1 (ppm)
14b
CDCl3, 400 MHz
f1 (ppm)

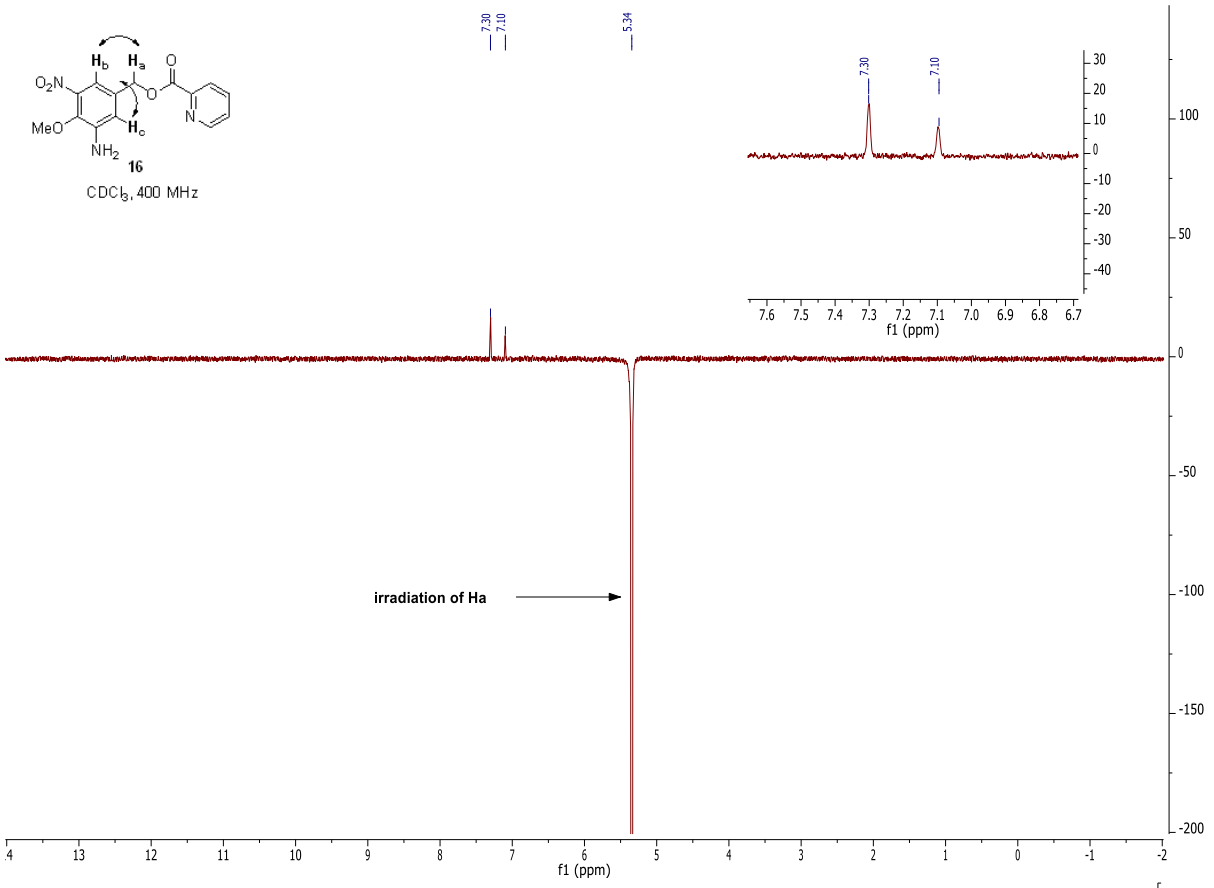

14b
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

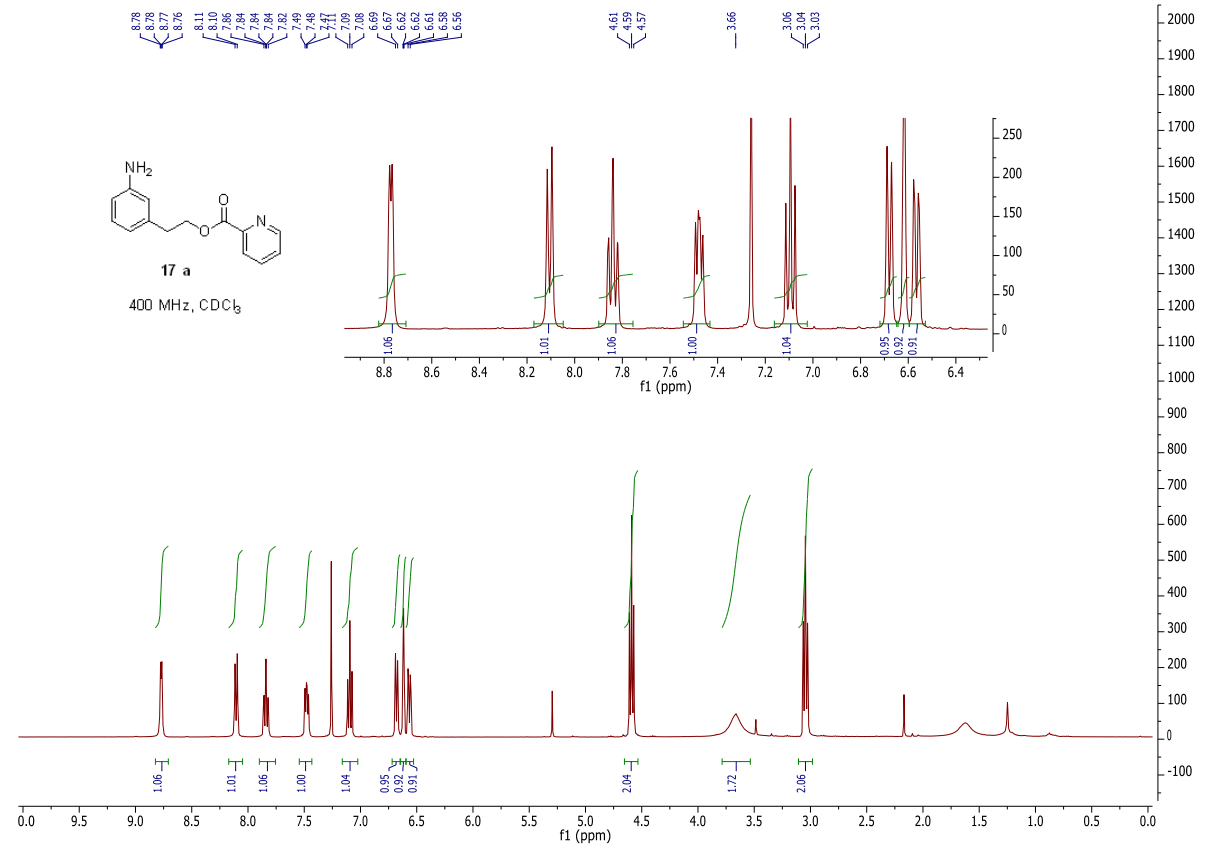

15
CDCl3, 400 MHz
f1 (ppm)

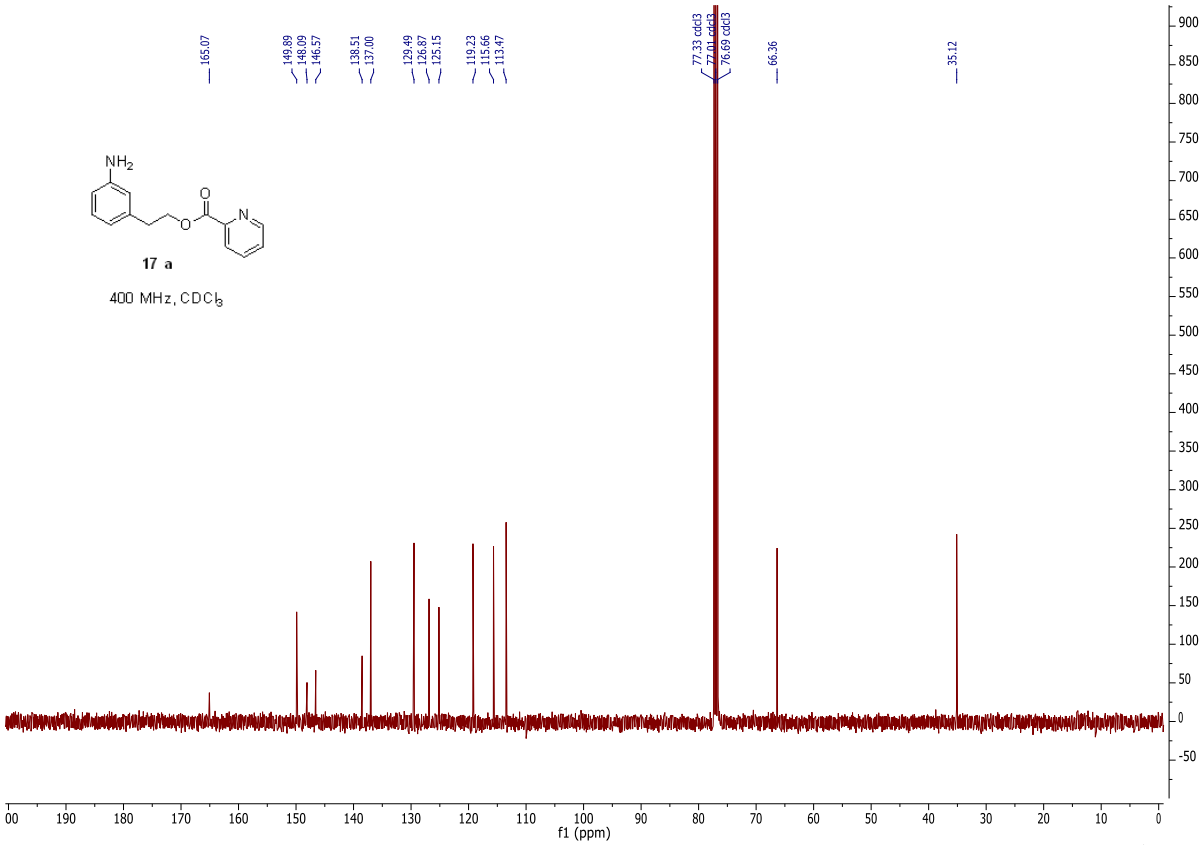

165.03
150.13
147.82
144.72
137.22
135.64
133.35
127.28
125.52
119.39
117.47
113.58
66.45
Cl
Cl
NH2
O
N
15
CDCl3, 400 MHz
f1 (ppm)

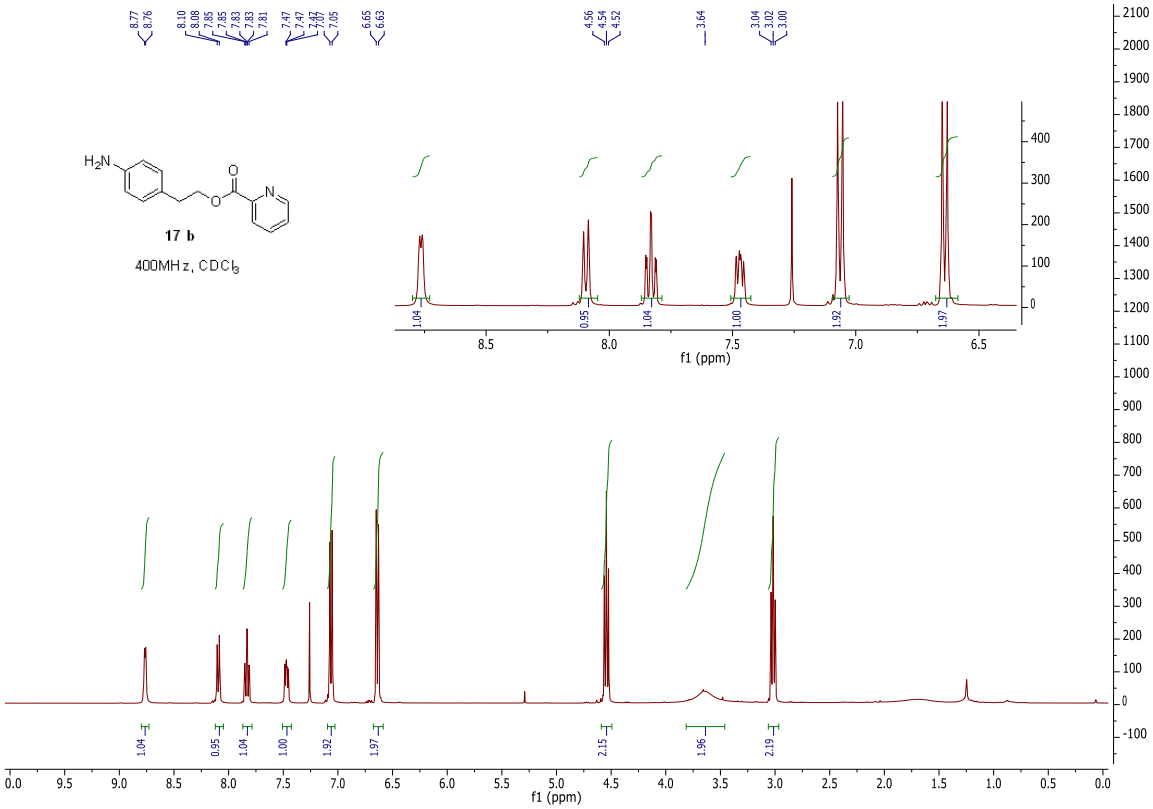

6.96
6.78
5.29
Hb
Ha
Hc
Cl
Cl
NH2
O
N
15
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

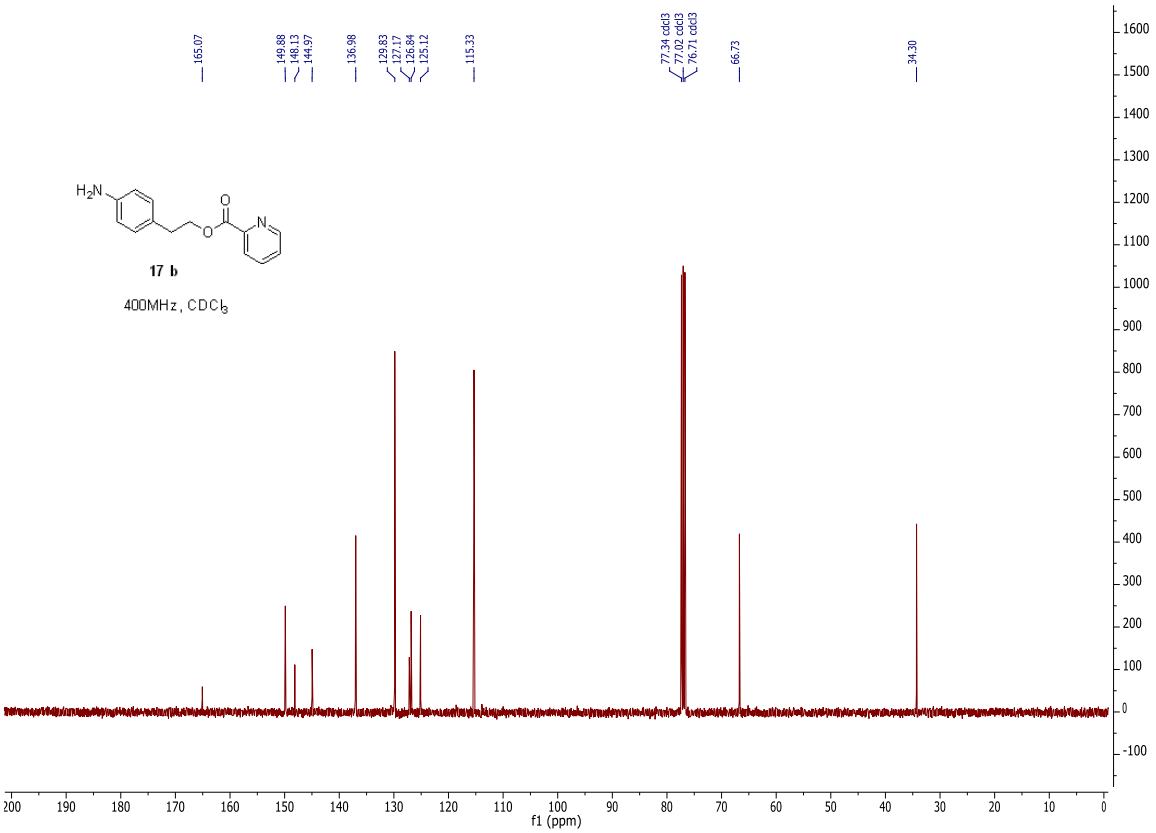

16
CDCl3, 400 MHz
f1 (ppm)
16
CDCl3, 400 MHz
f1 (ppm)

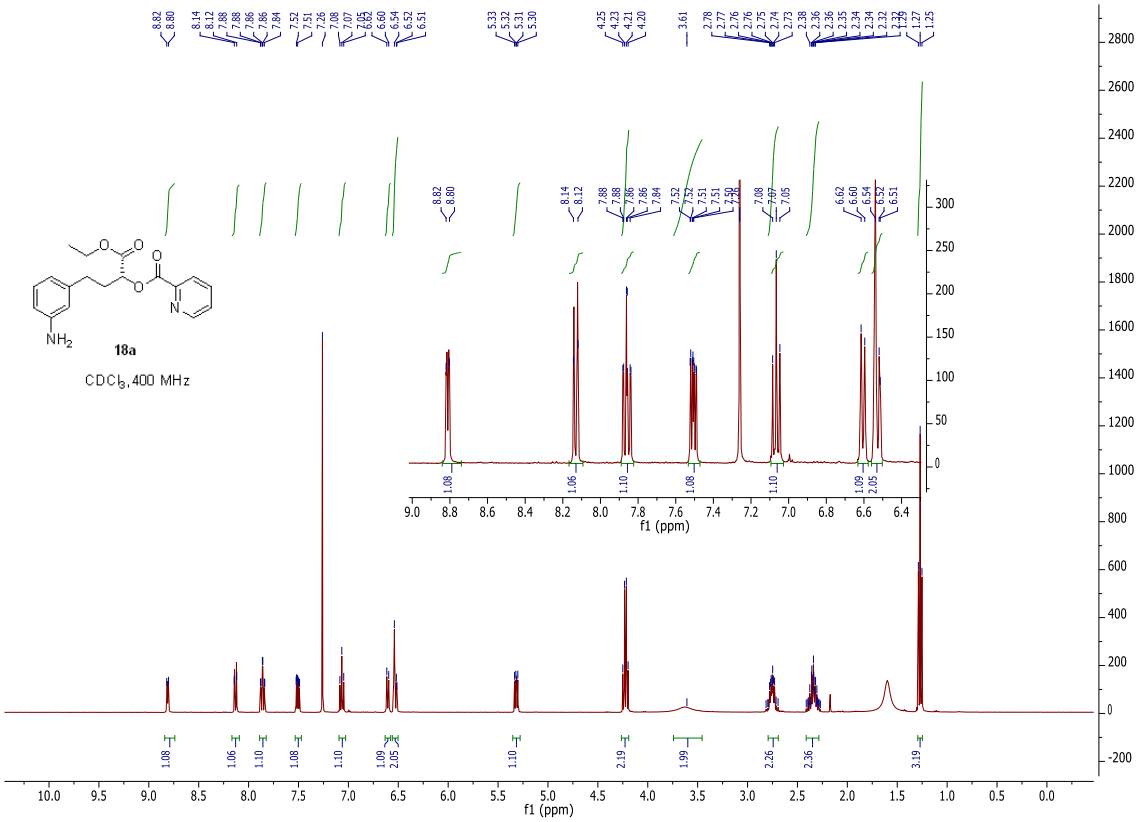

16
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

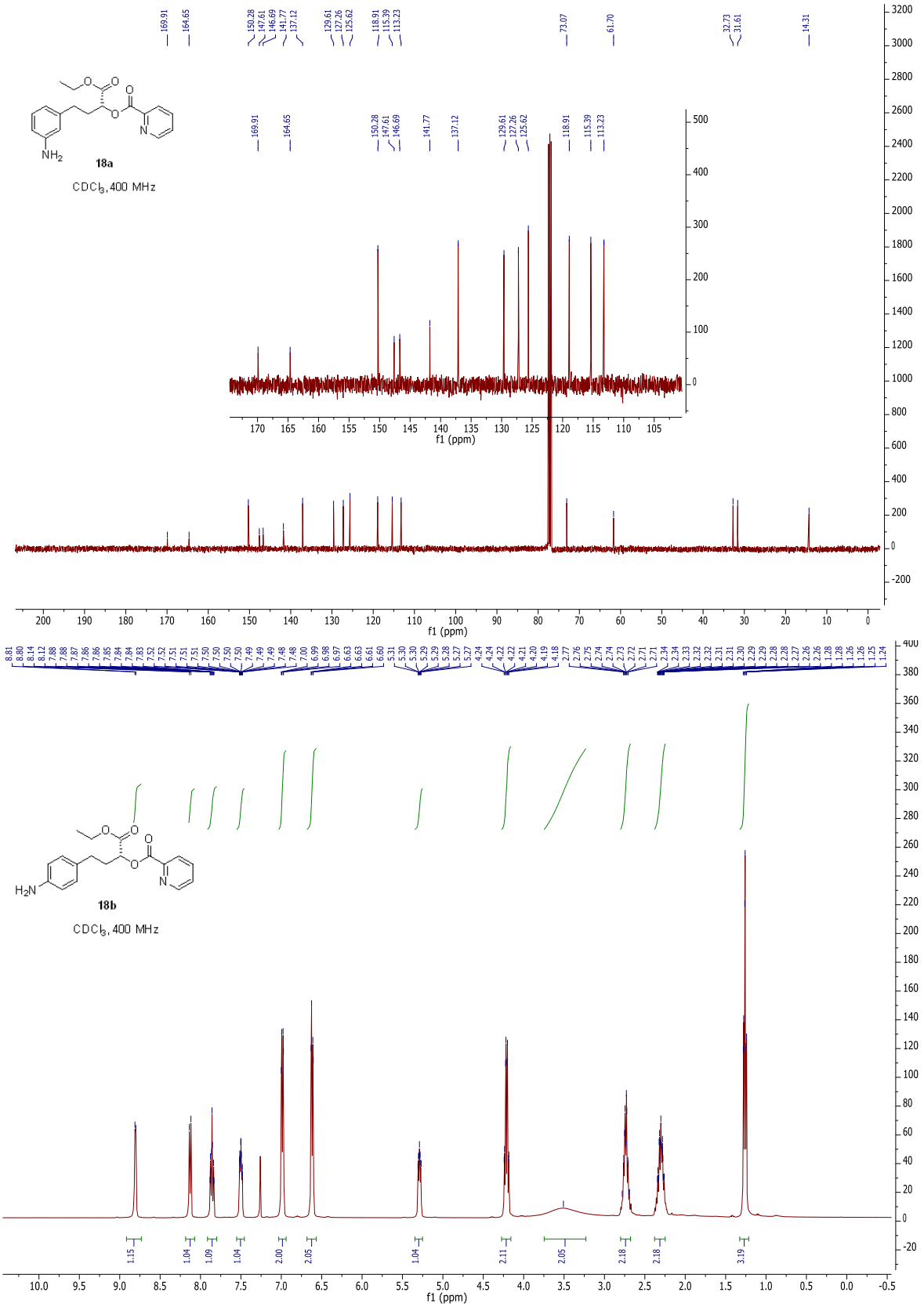

17 a
400 MHz, CDCl3
f1 (ppm)

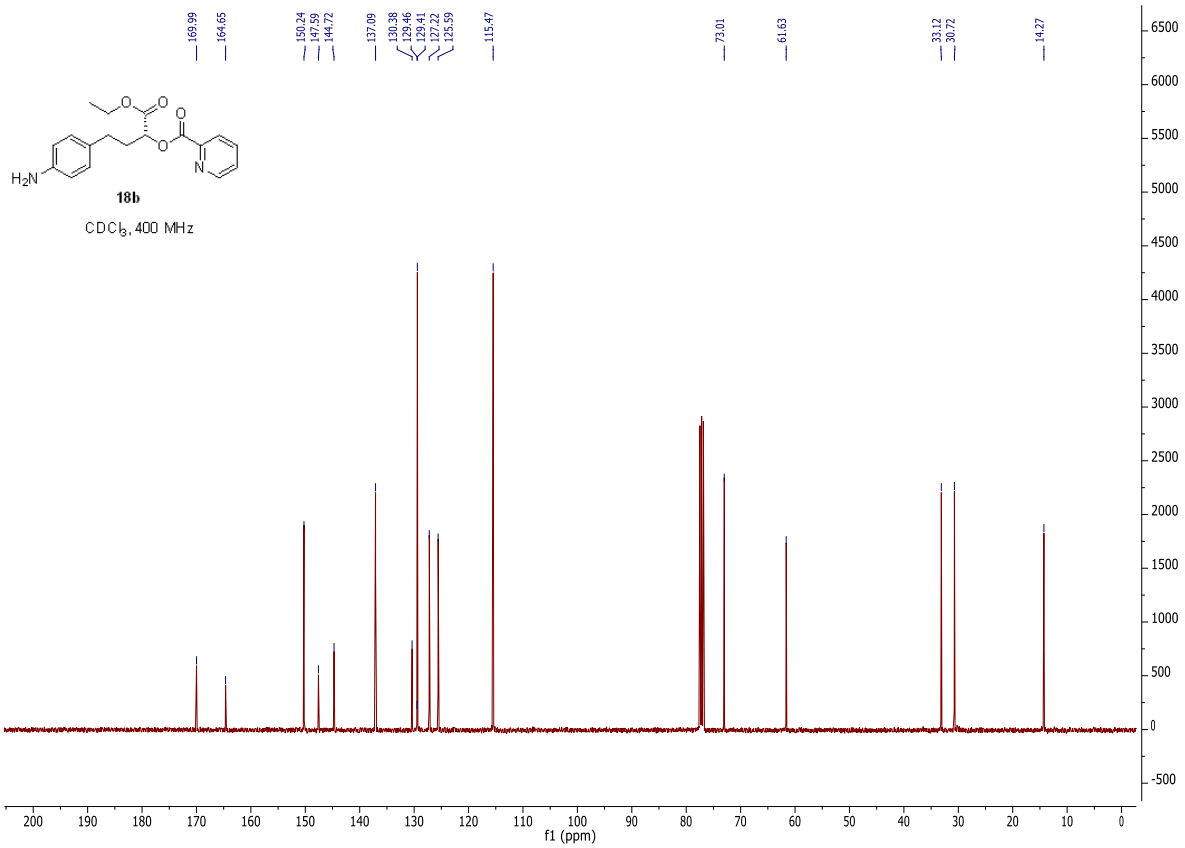

165.07
149.89
148.09
146.57
138.51
137.00
129.49
126.87
125.15
119.23
115.66
113.47
77.33 cdcl3
77.01 cdcl3
76.69 cdcl3
66.36
35.12
NH2
O
O
N
17 a
400 MHz, CDCl3
f1 (ppm)

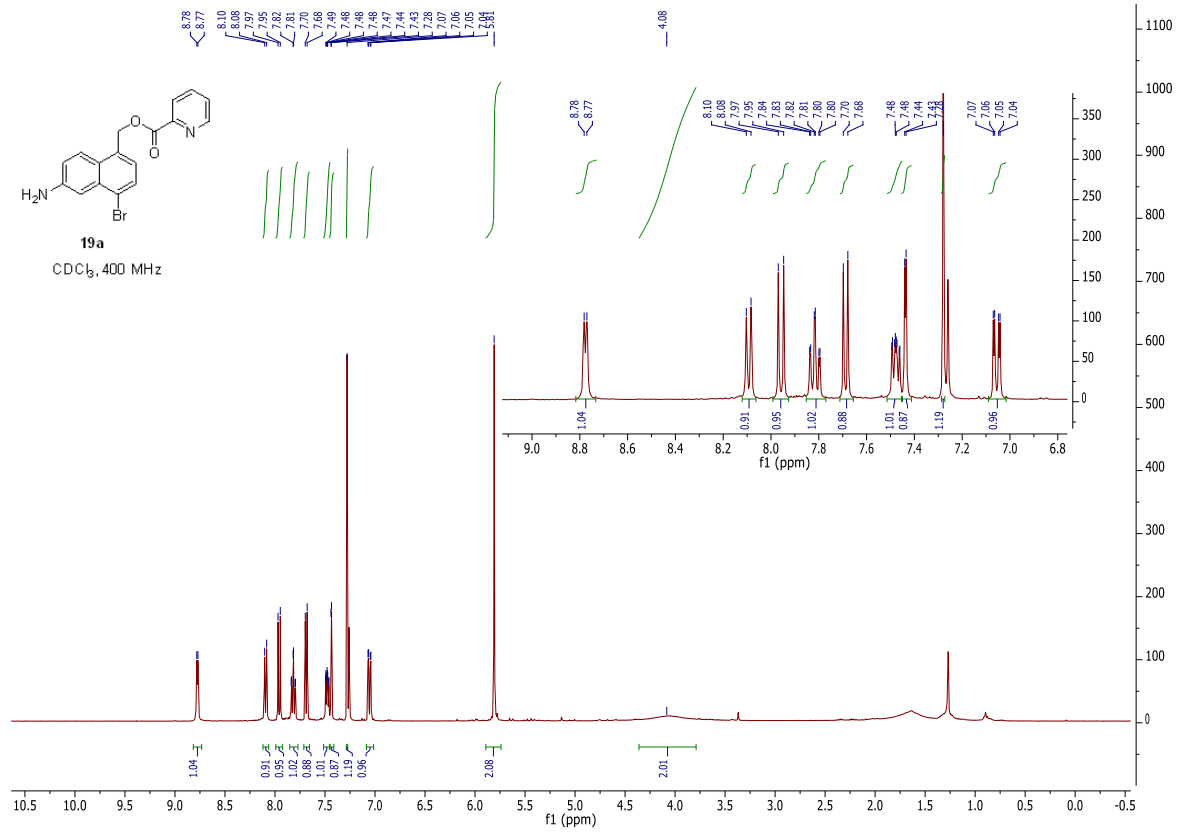

8.77
8.76
8.10
8.08
7.85
7.85
7.83
7.83
7.81
7.47
7.47
7.47
7.47
7.05
6.65
6.63
4.56
4.54
4.52
3.64
3.04
3.02
3.00
H2N
O
O
N
17 b
400MHz, CDCl3
1.04
0.95
1.04
1.00
1.92
1.97
2.15
1.96
2.19
f1 (ppm)

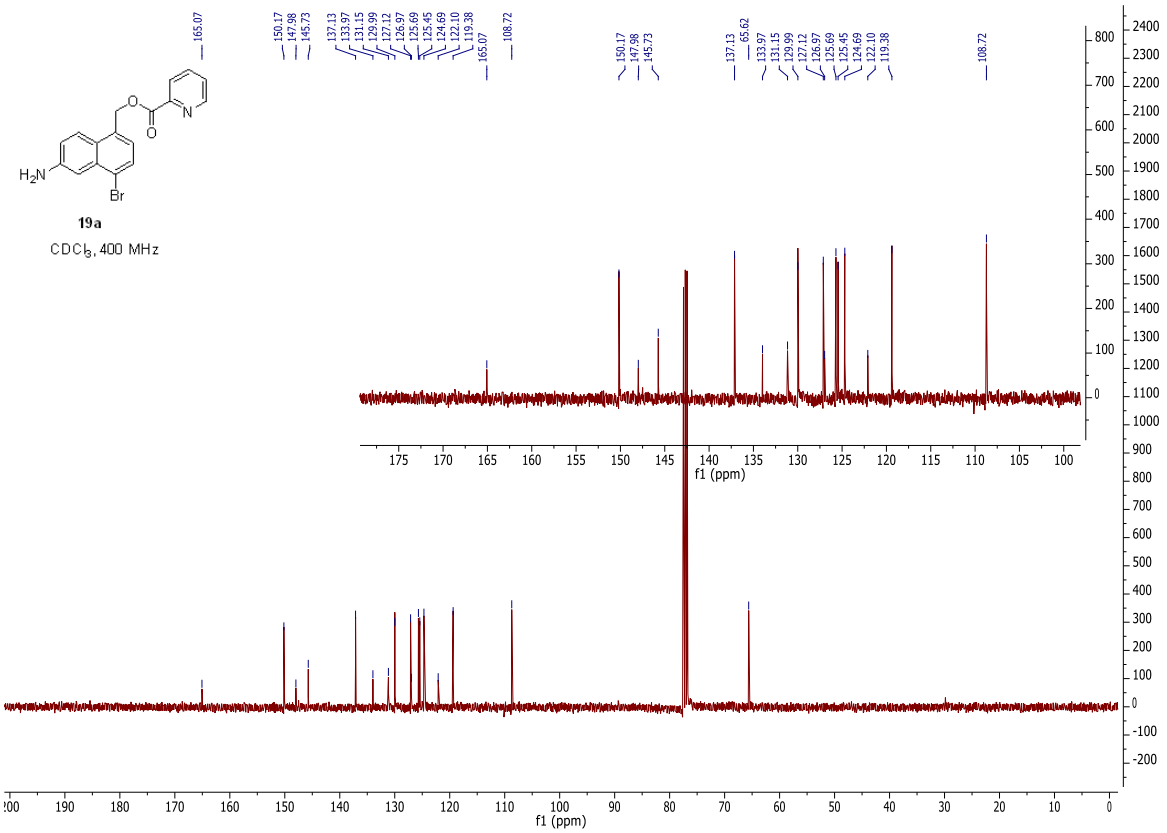

165.07
149.88
148.13
144.97
136.98
129.83
127.17
126.84
125.12
115.33
77.34 cdcl3
77.02 cdcl3
76.71 cdcl3
66.73
34.30
17 b
400MHz, CDCl3
f1 (ppm)

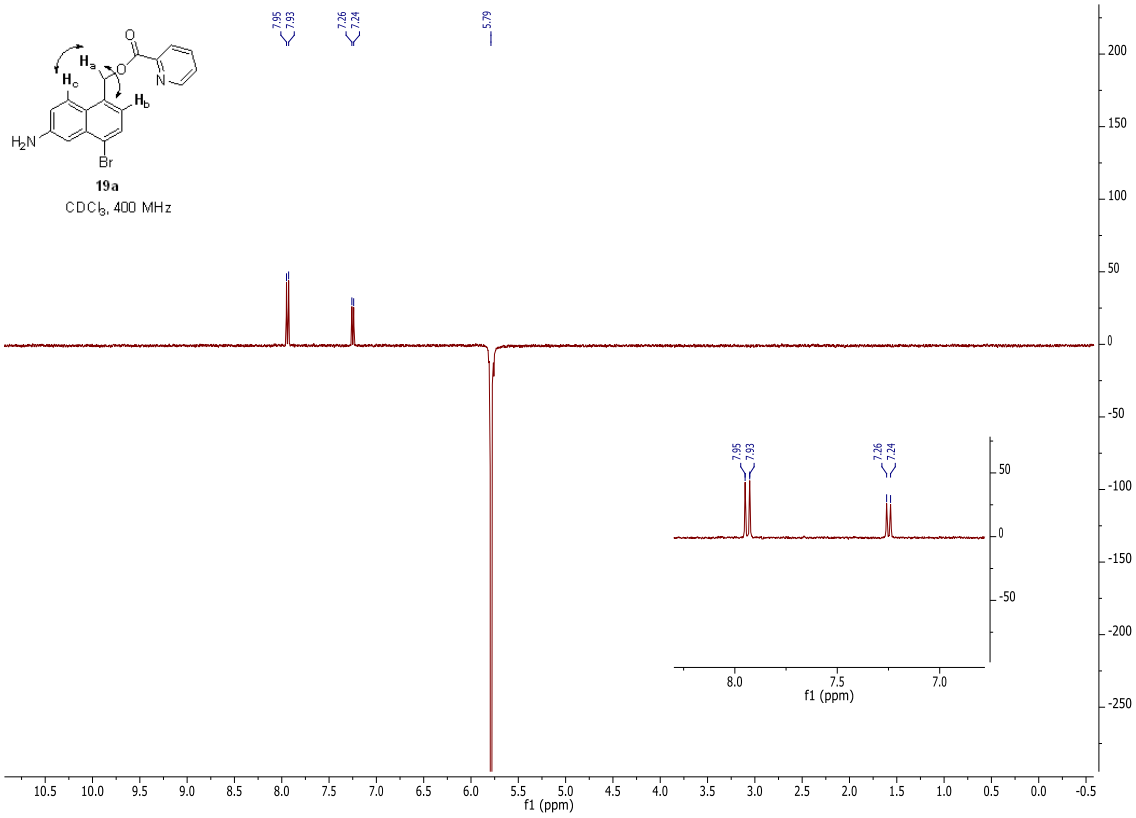

18a
CDCl3, 400 MHz
f1 (ppm)

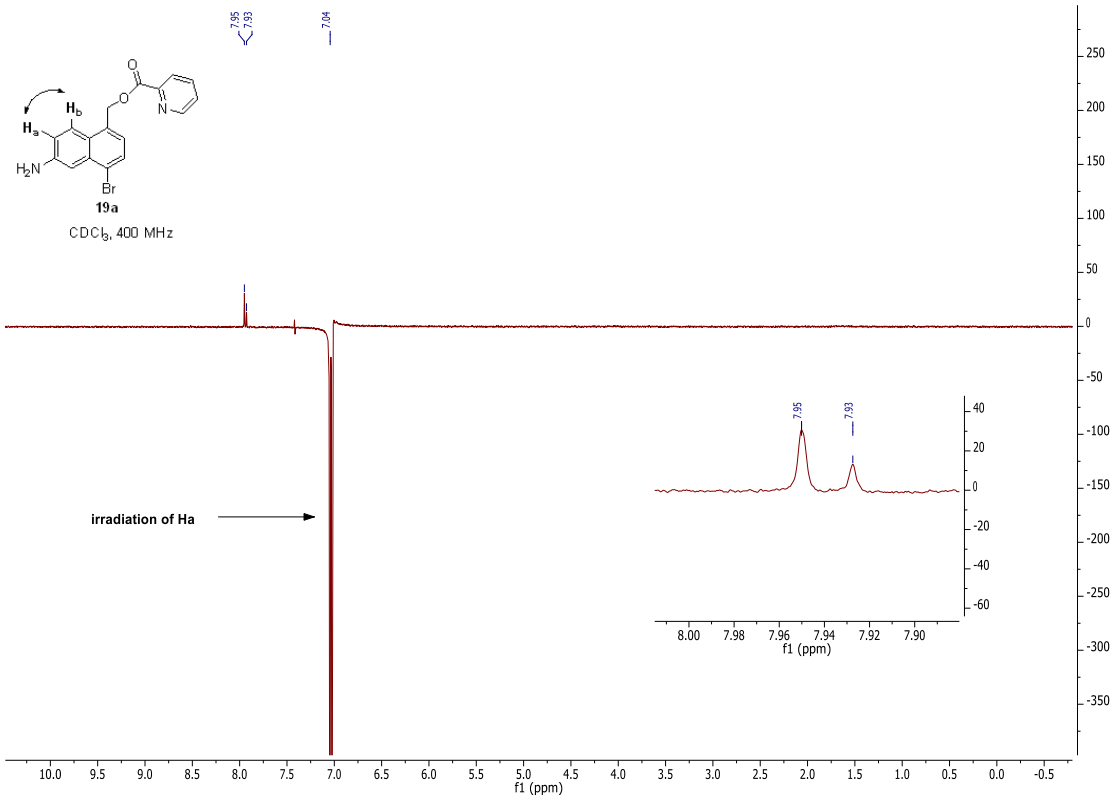

18a
CDCl3, 400 MHz
18b
CDCl3, 400 MHz
f1 (ppm)

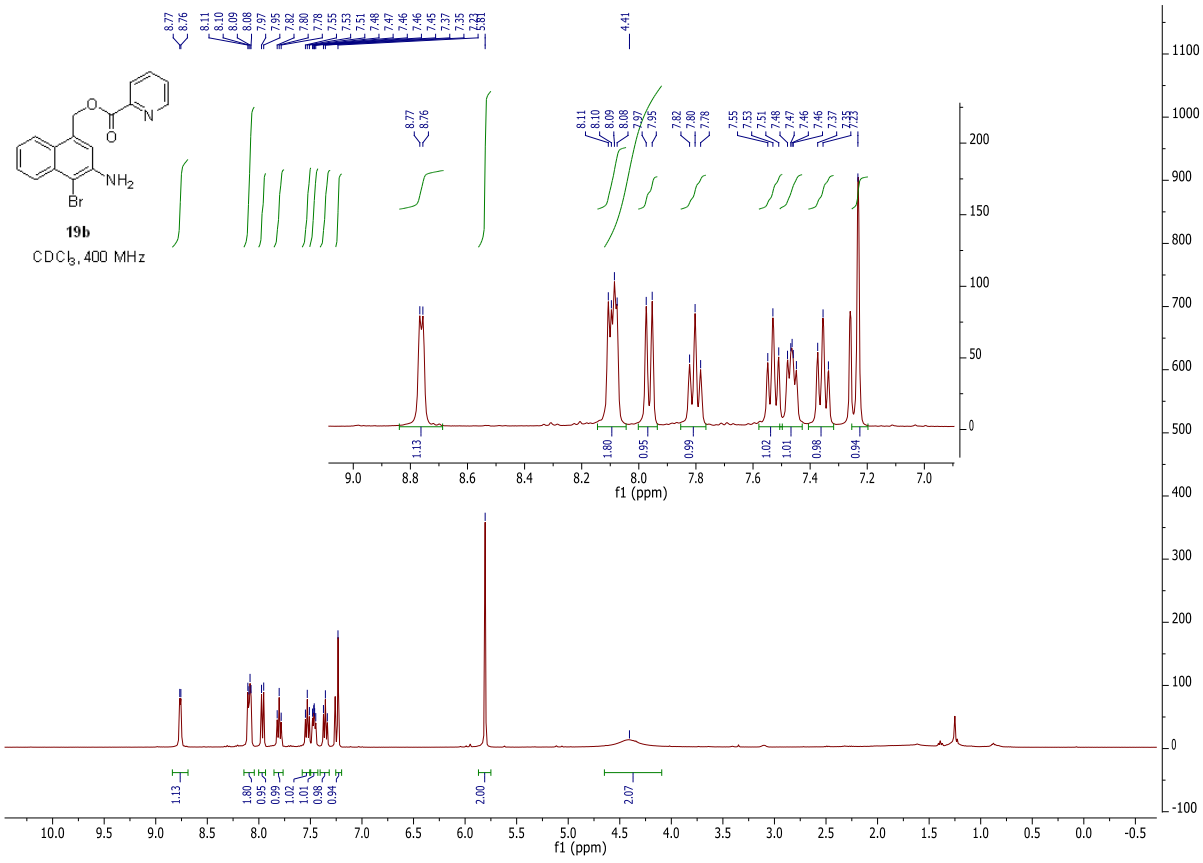

169.99
164.65
150.24
147.59
144.72
137.09
130.38
129.46
129.41
127.22
125.59
115.47
73.01
61.63
33.12
30.72
14.27
18b
CDCl3, 400 MHz
f1 (ppm)

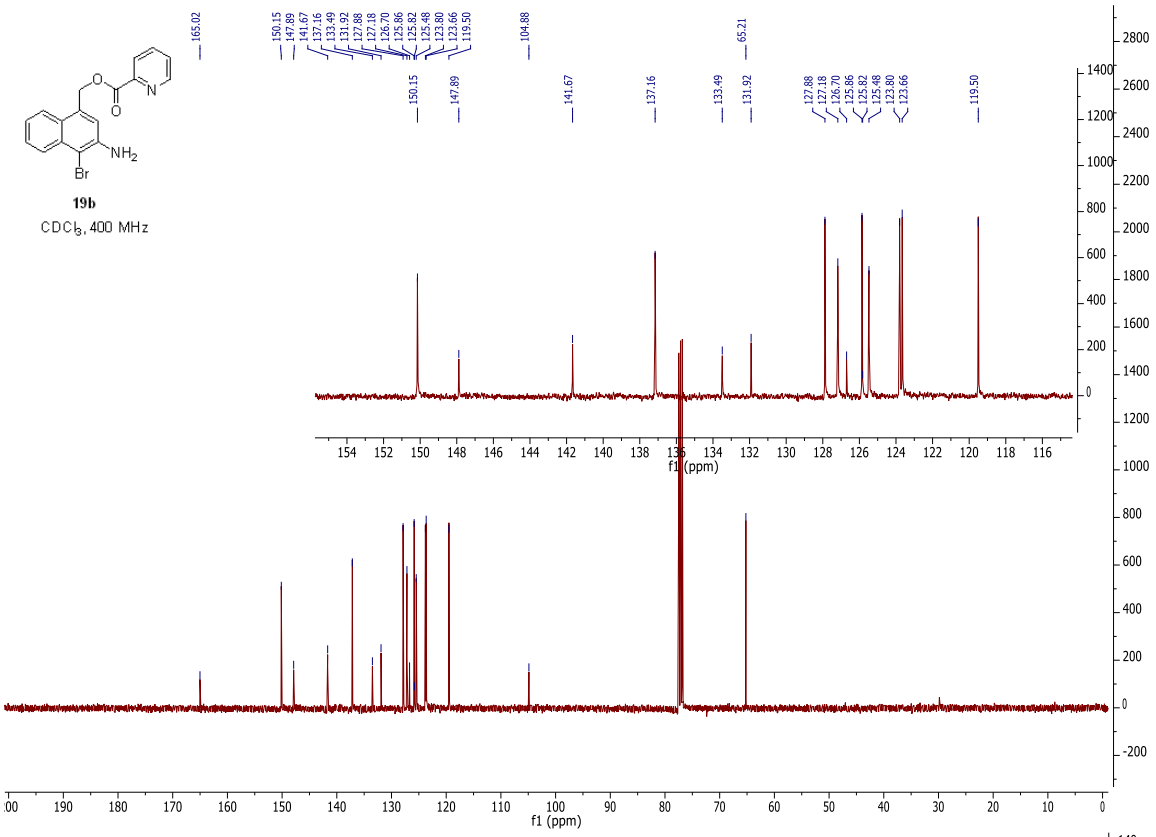

4.08
19a
CDCl3, 400 MHz
f1 (ppm)

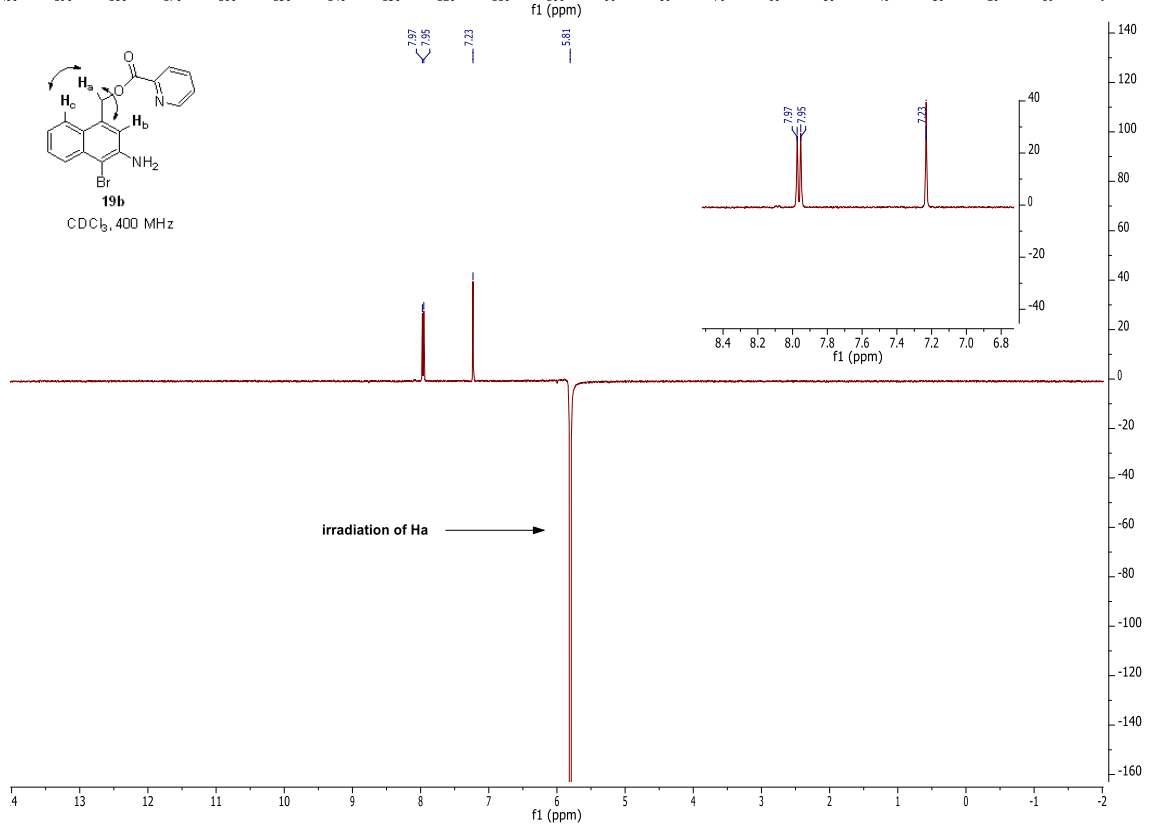

19a
CDCl3, 400 MHz
f1 (ppm)

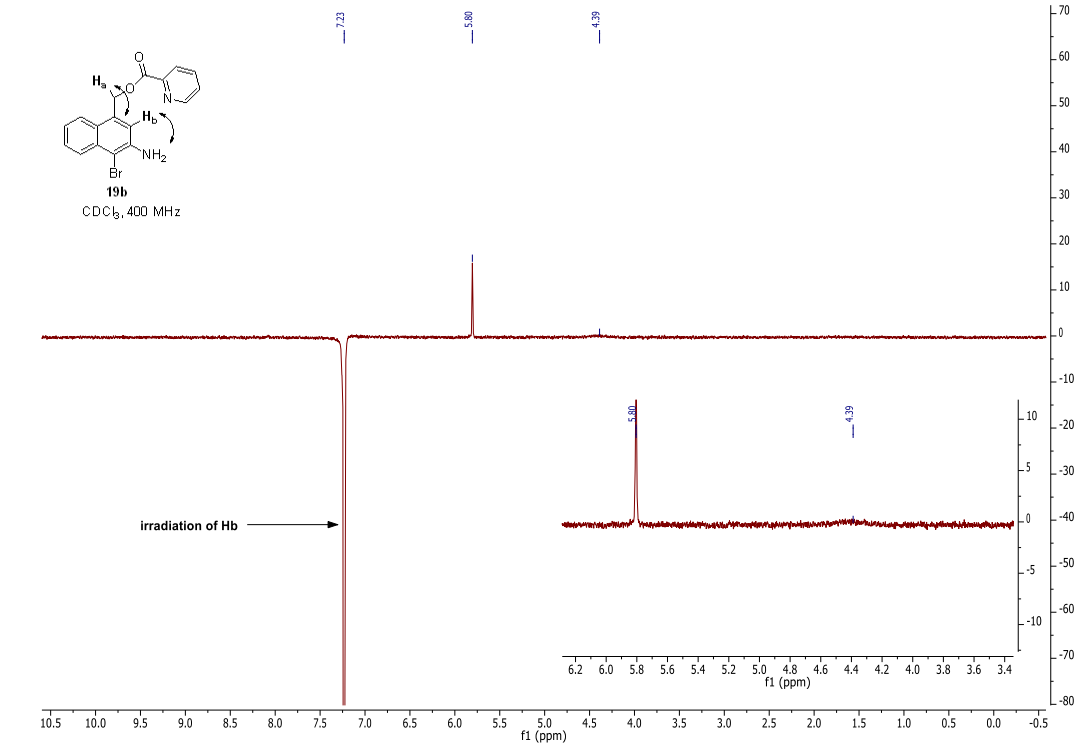

19a
CDCl3, 400 MHz
f1 (ppm)

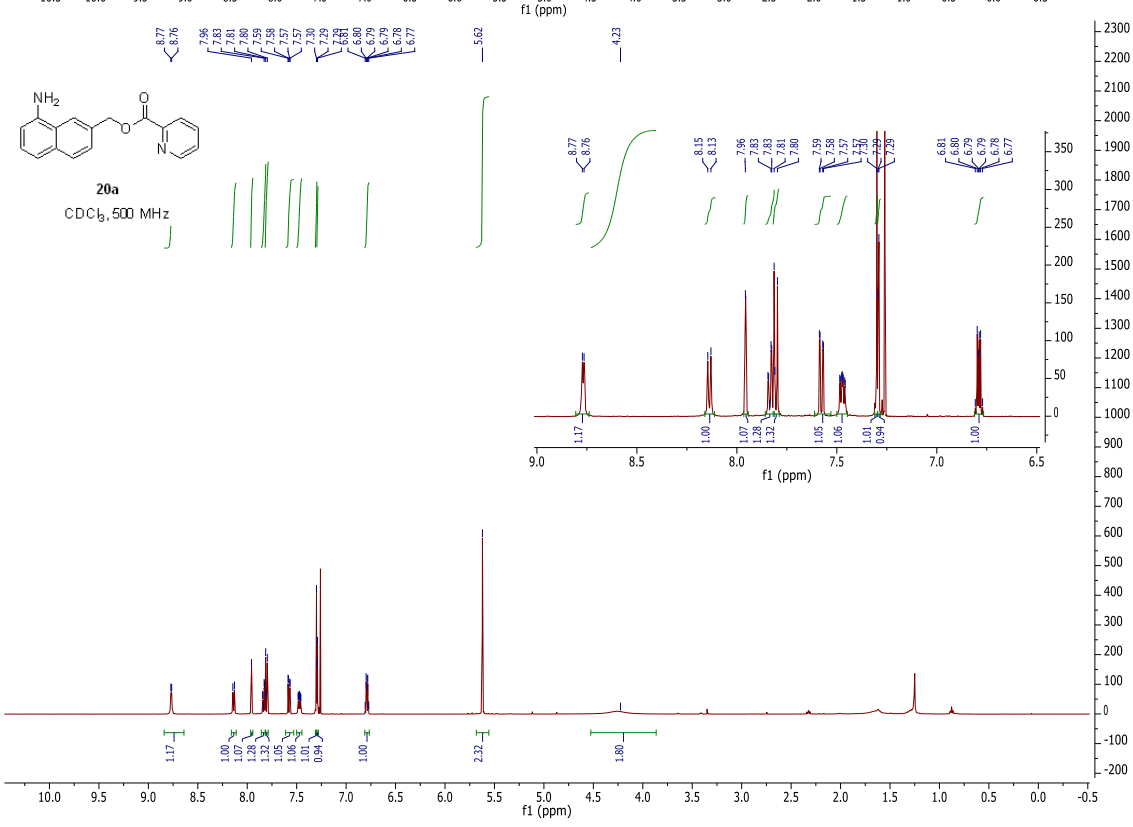

19a
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

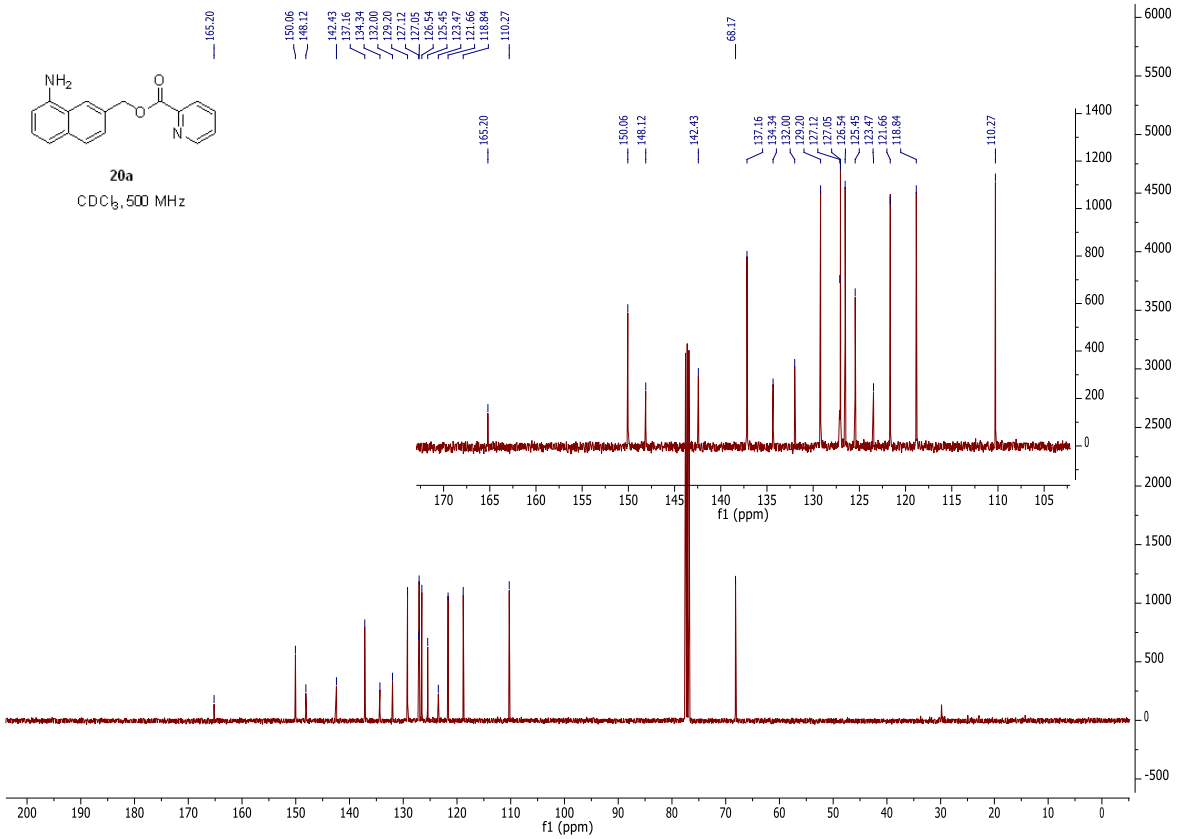

19b
CDCl3, 400 MHz
f1 (ppm)

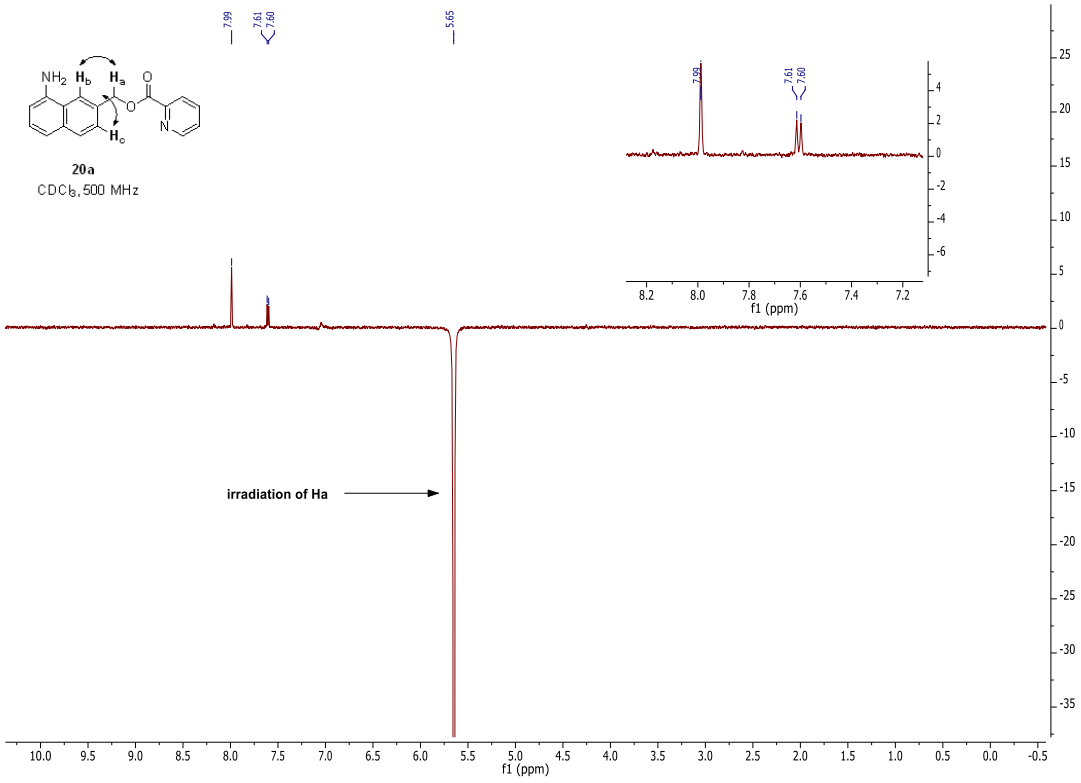

19b
CDCl3, 400 MHz
f1 (ppm)

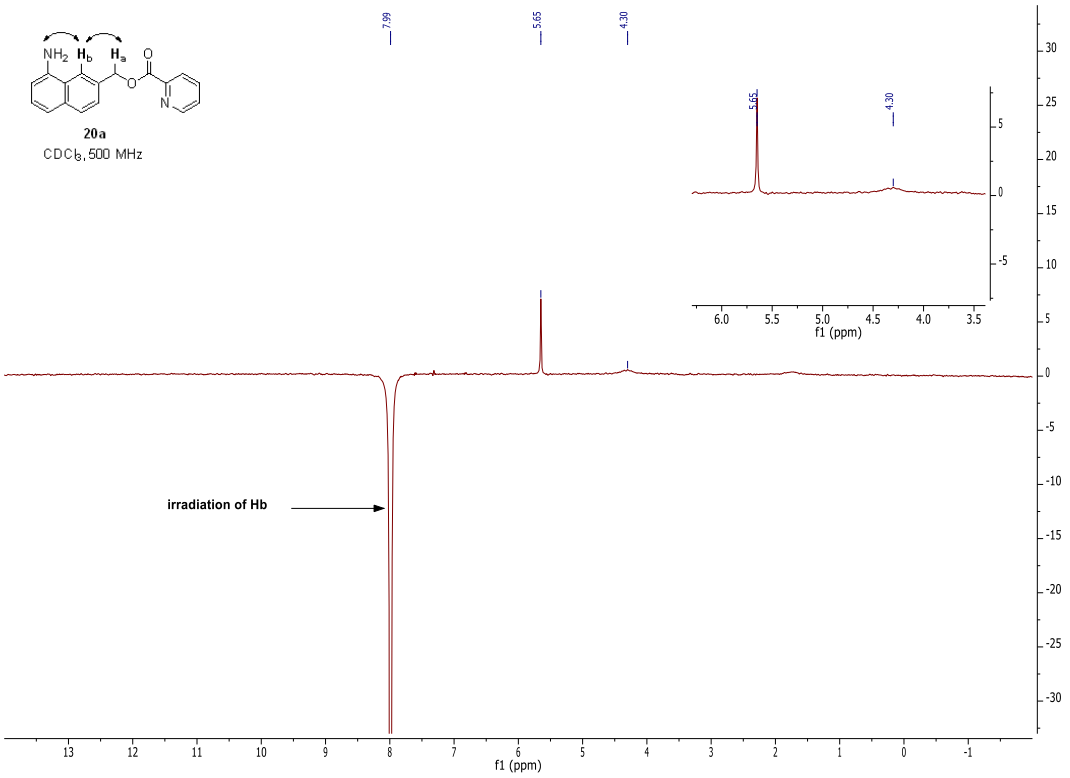

19b
CDCl3, 400 MHz
irradiation of Ha
f1 (ppm)

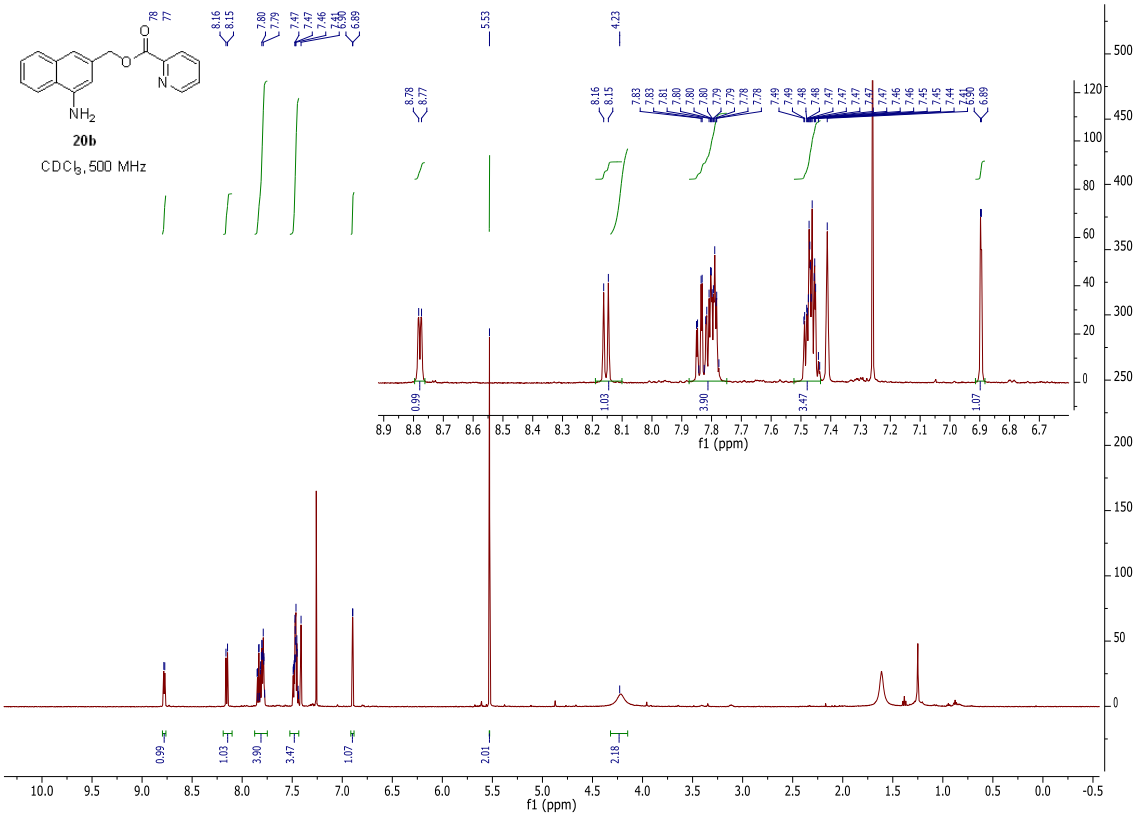

19b
CDCl3, 400 MHz
irradiation of Hb
f1 (ppm)

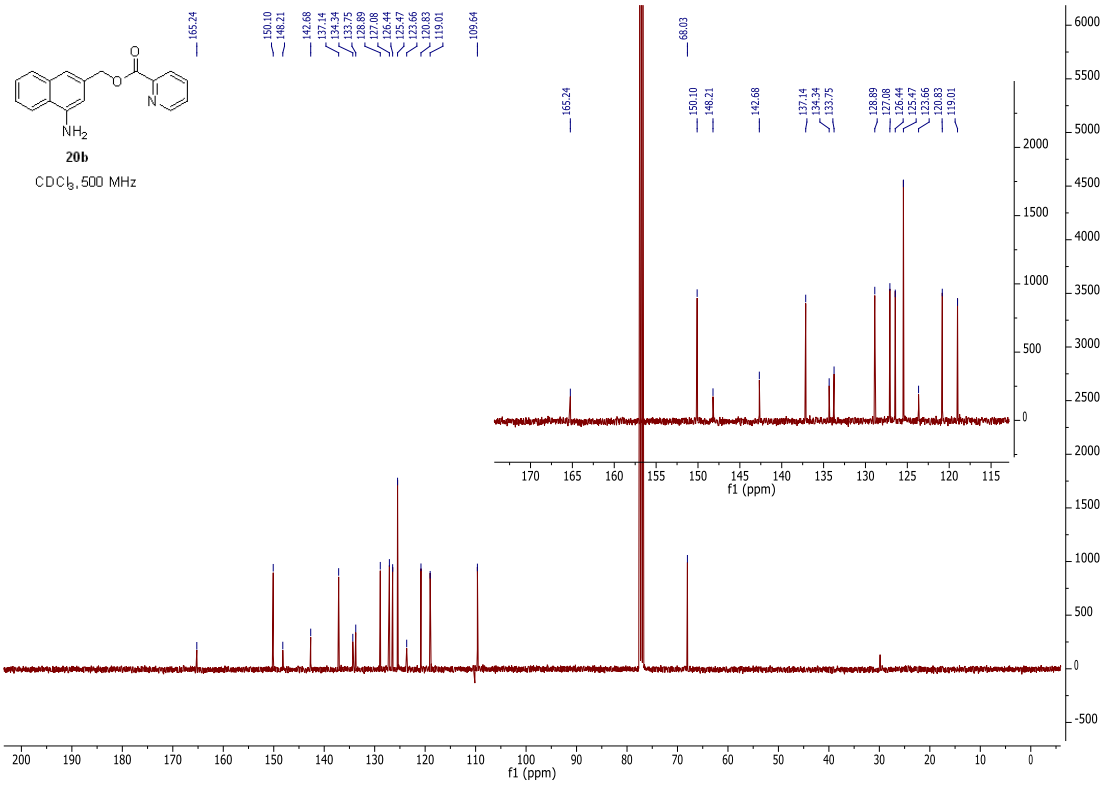

20a
CDCl3, 500 MHz
f1 (ppm)

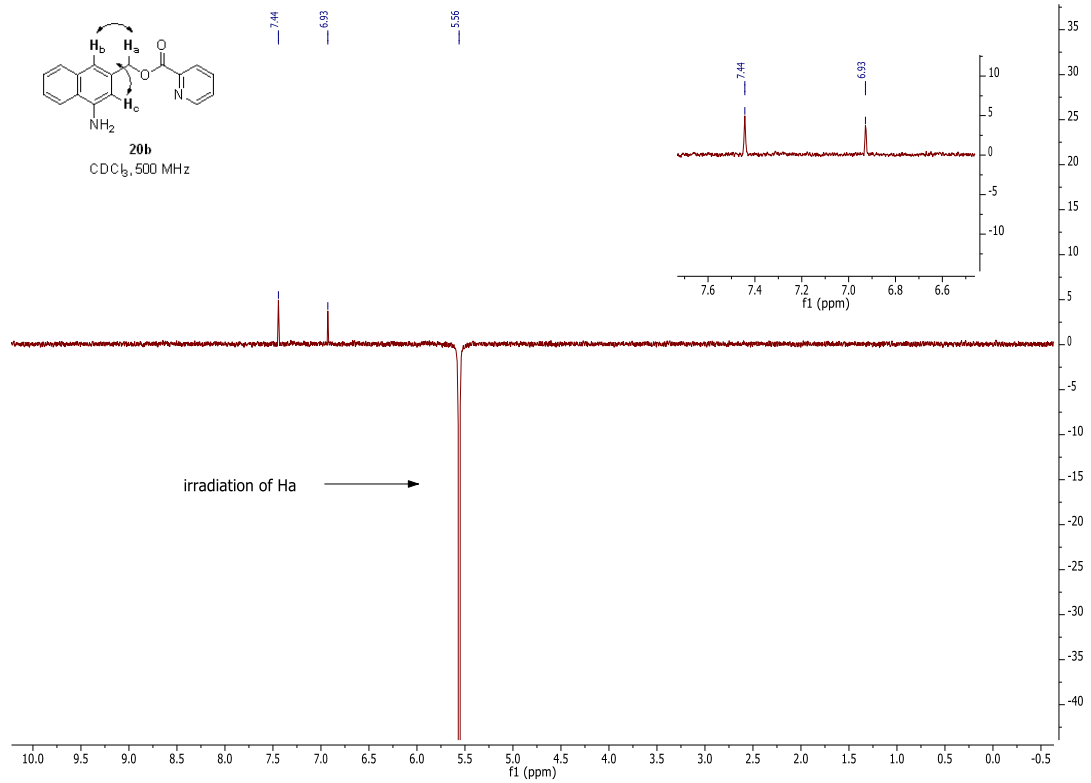

165.20
150.06
148.12
142.43
137.16
134.34
132.00
129.20
127.12
127.05
126.54
125.45
123.47
121.66
118.84
110.27
68.17
NH2
O
N
20a
CDCl3, 500 MHz
f1 (ppm)

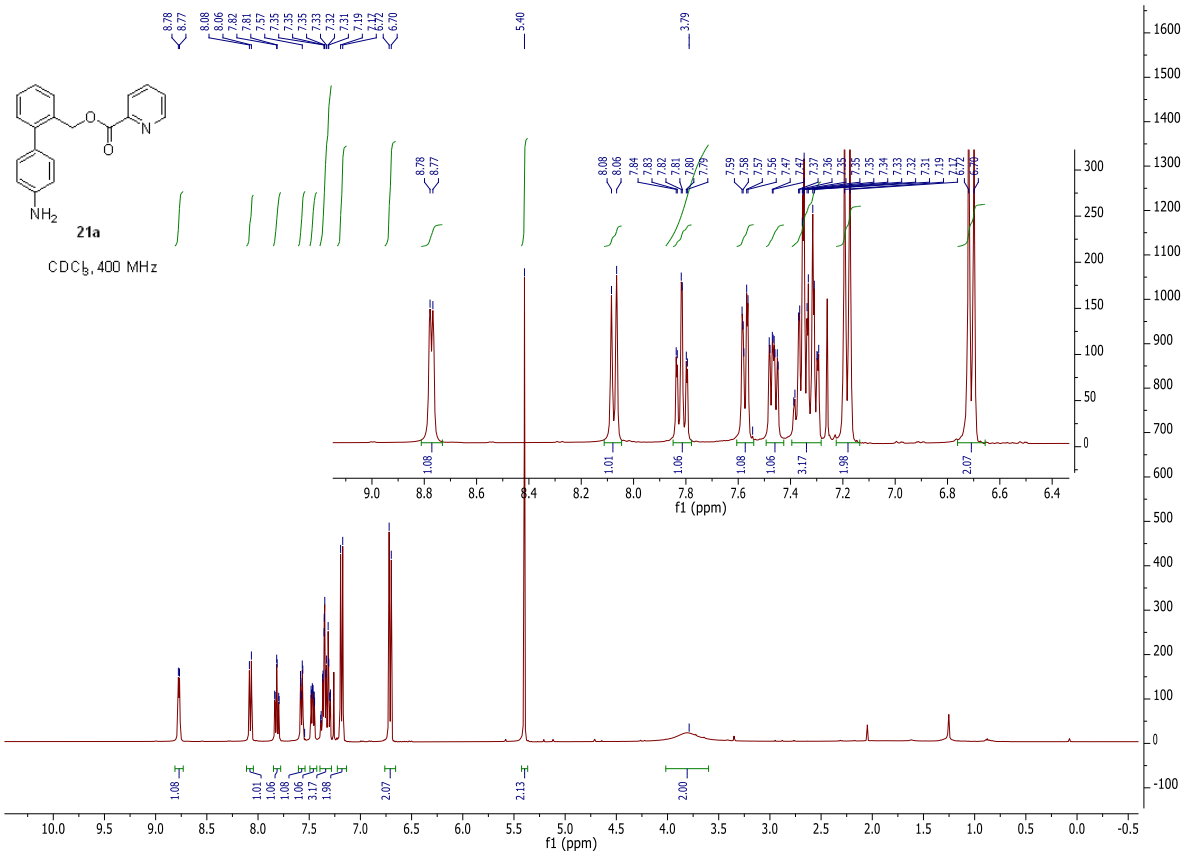

7.99
7.61
7.60
5.65
NH2
Hb
Ha
Hc
O
N
20a
CDCl3, 500 MHz
irradiation of Ha
f1 (ppm)

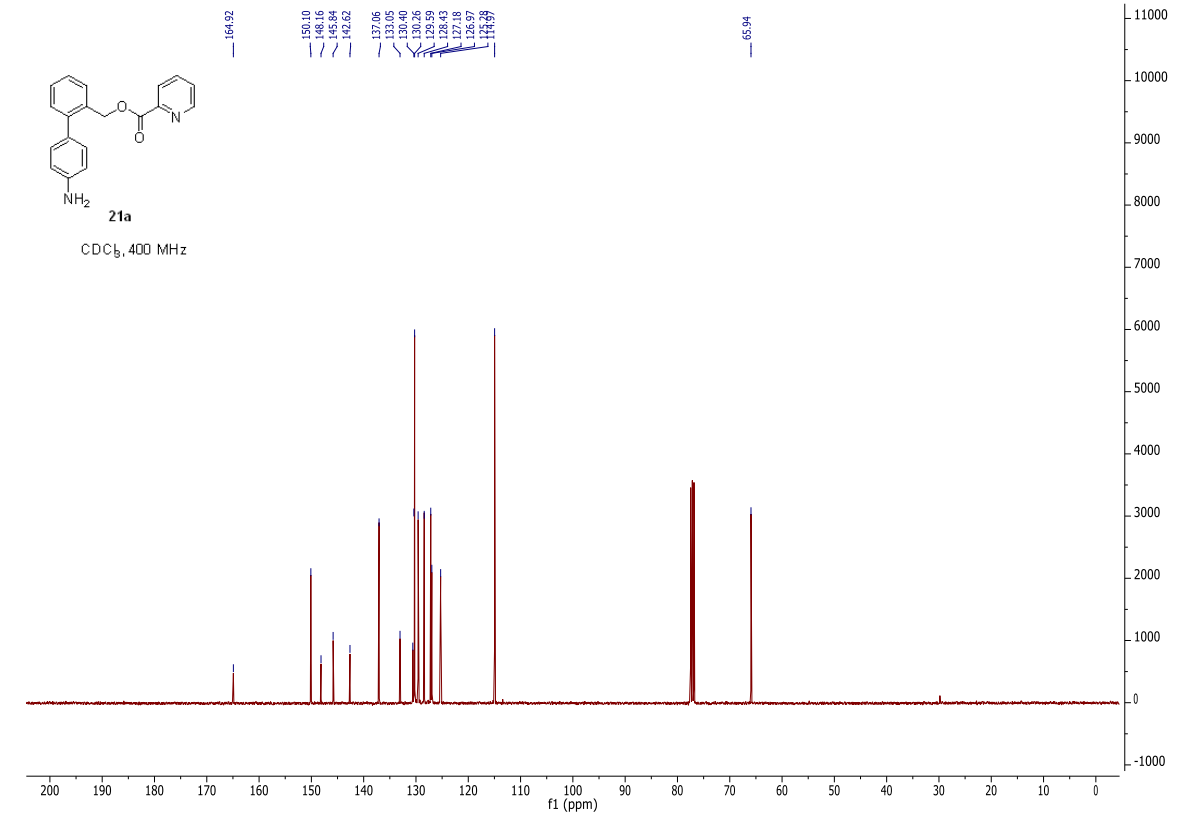

20a
CDCl3, 500 MHz
irradiation of Hb
f1 (ppm)

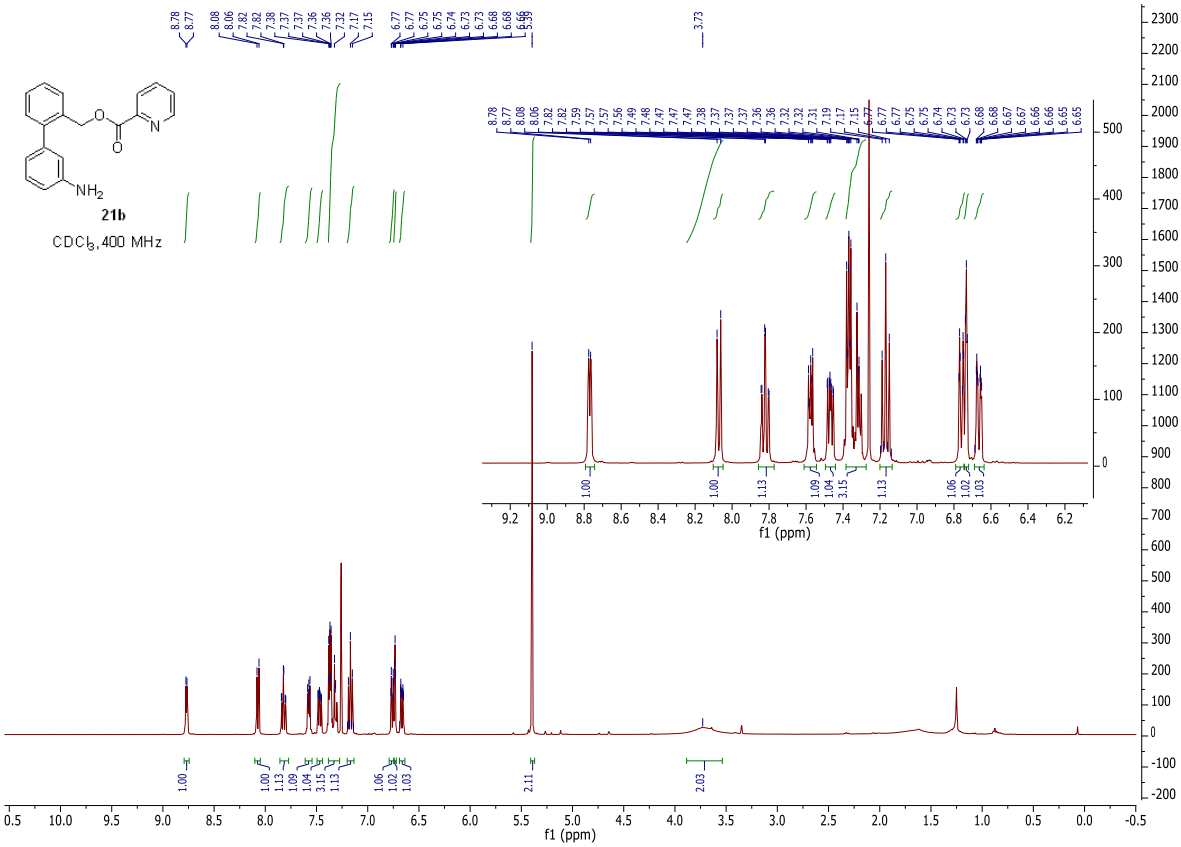

20b
CDCl3, 500 MHz
f1 (ppm)

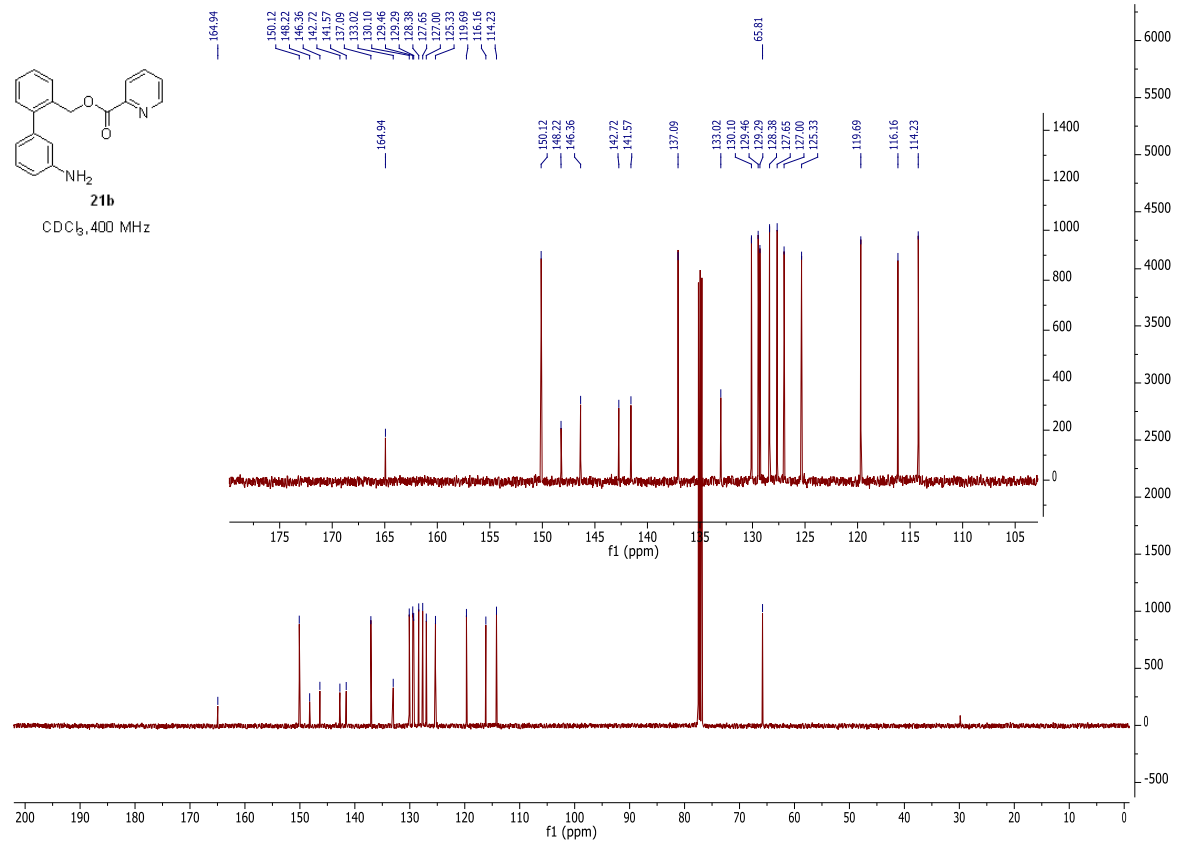

20b
CDCl3, 500 MHz
f1 (ppm)

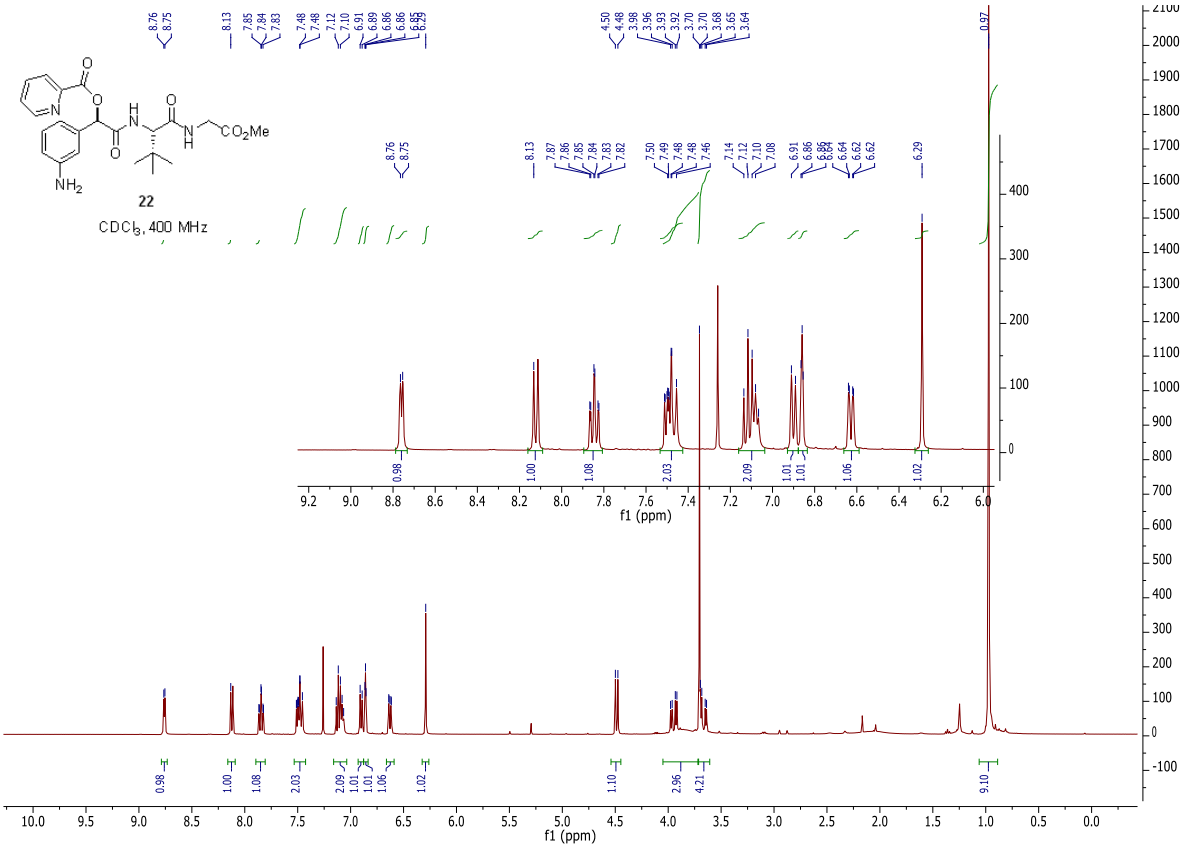

20b
CDCl3, 500 MHz
irradiation of Ha
f1 (ppm)

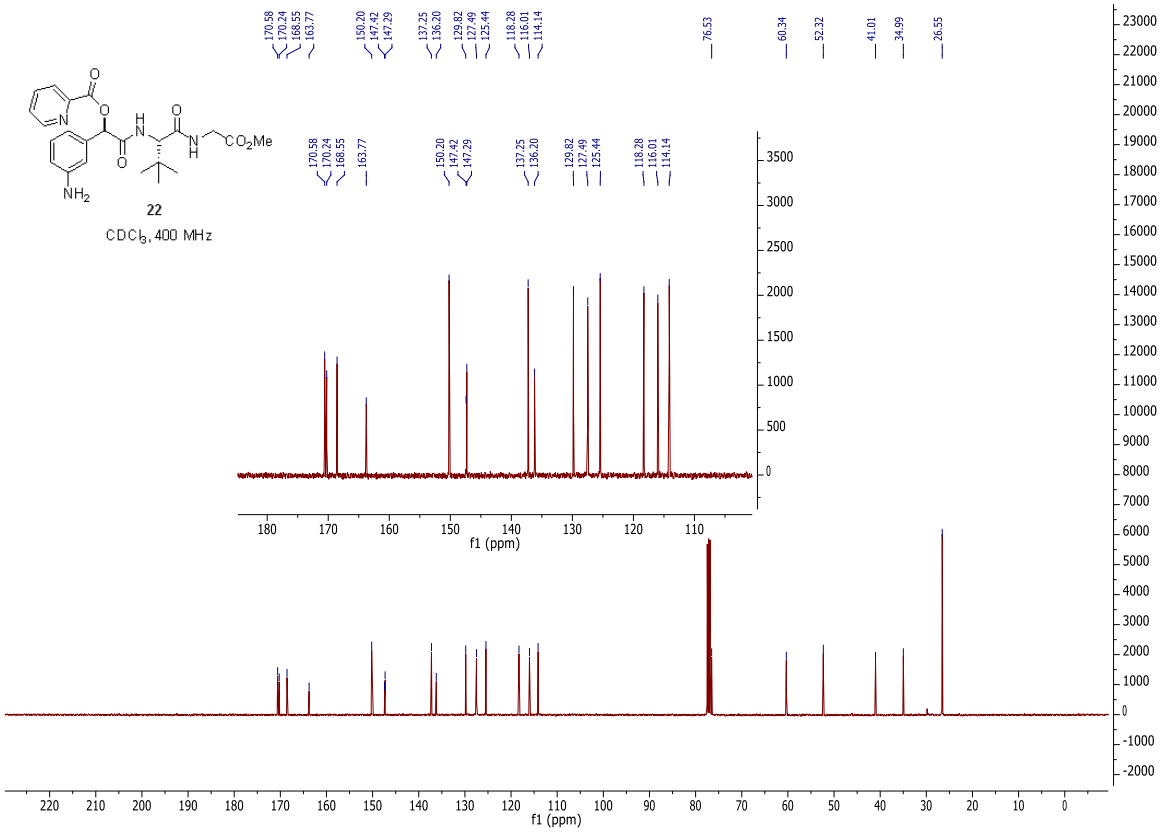

21a
CDCl3, 400 MHz
f1 (ppm)

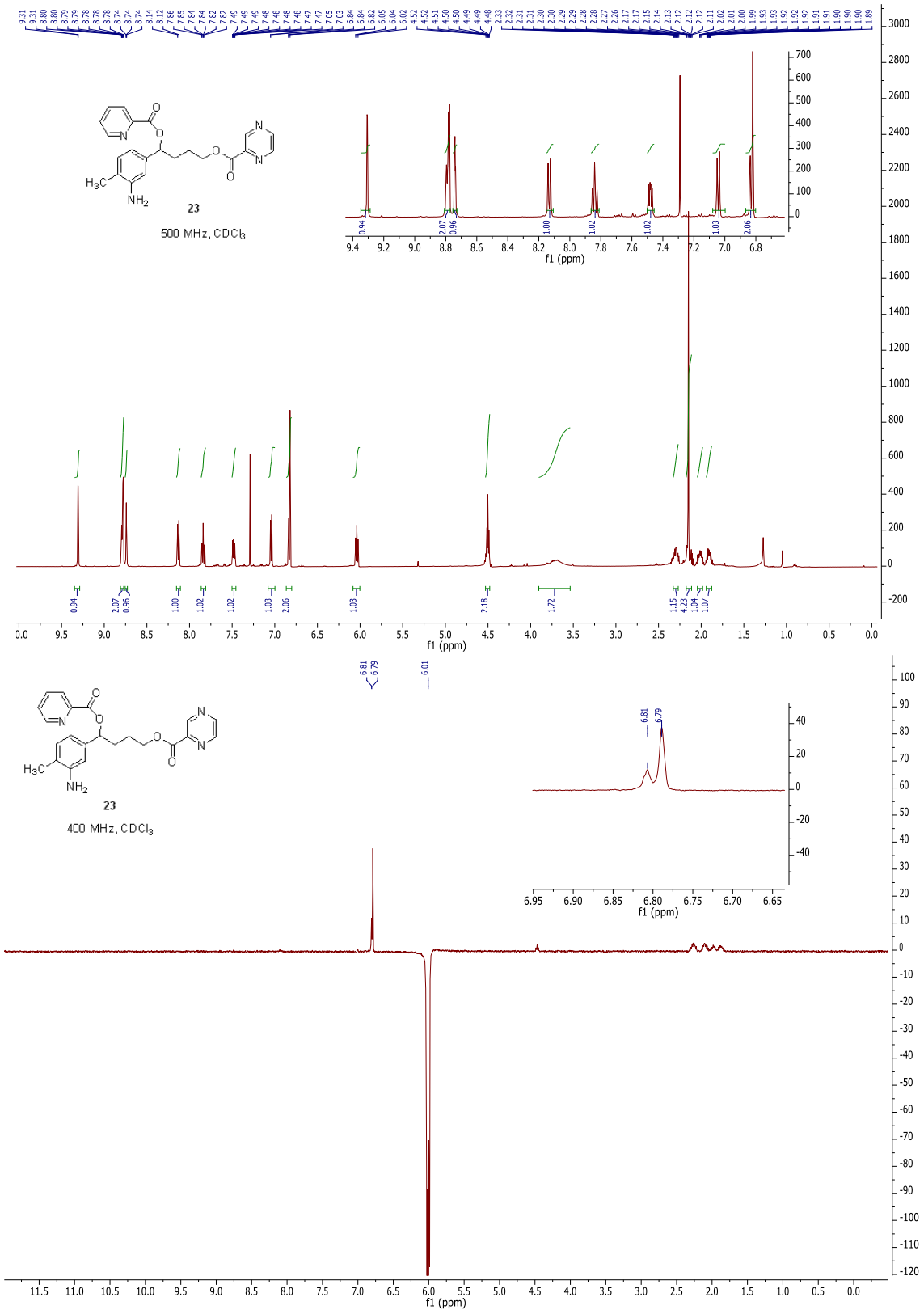

21a
CDCl3, 400 MHz
f1 (ppm)

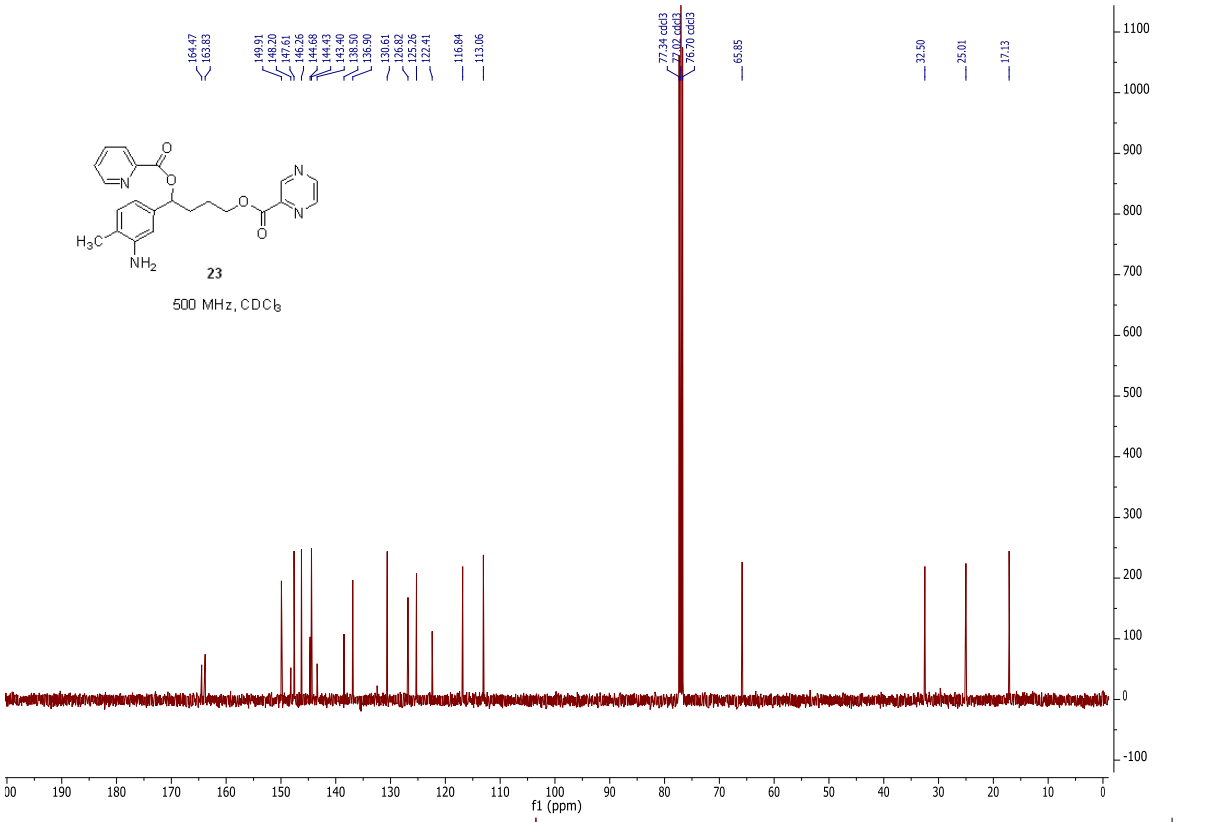

21b
CDCl3, 400 MHz
f1 (ppm)

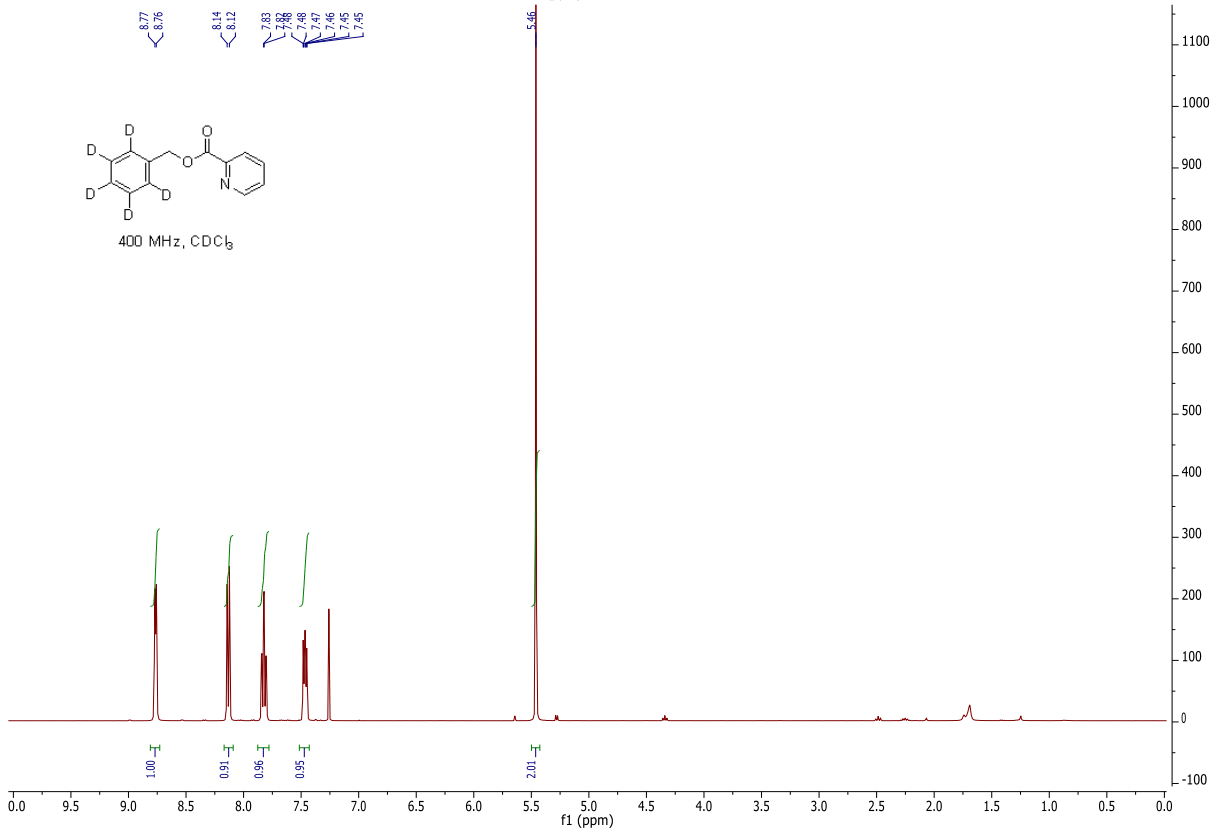

21b
CDCl3, 400 MHz
f1 (ppm)

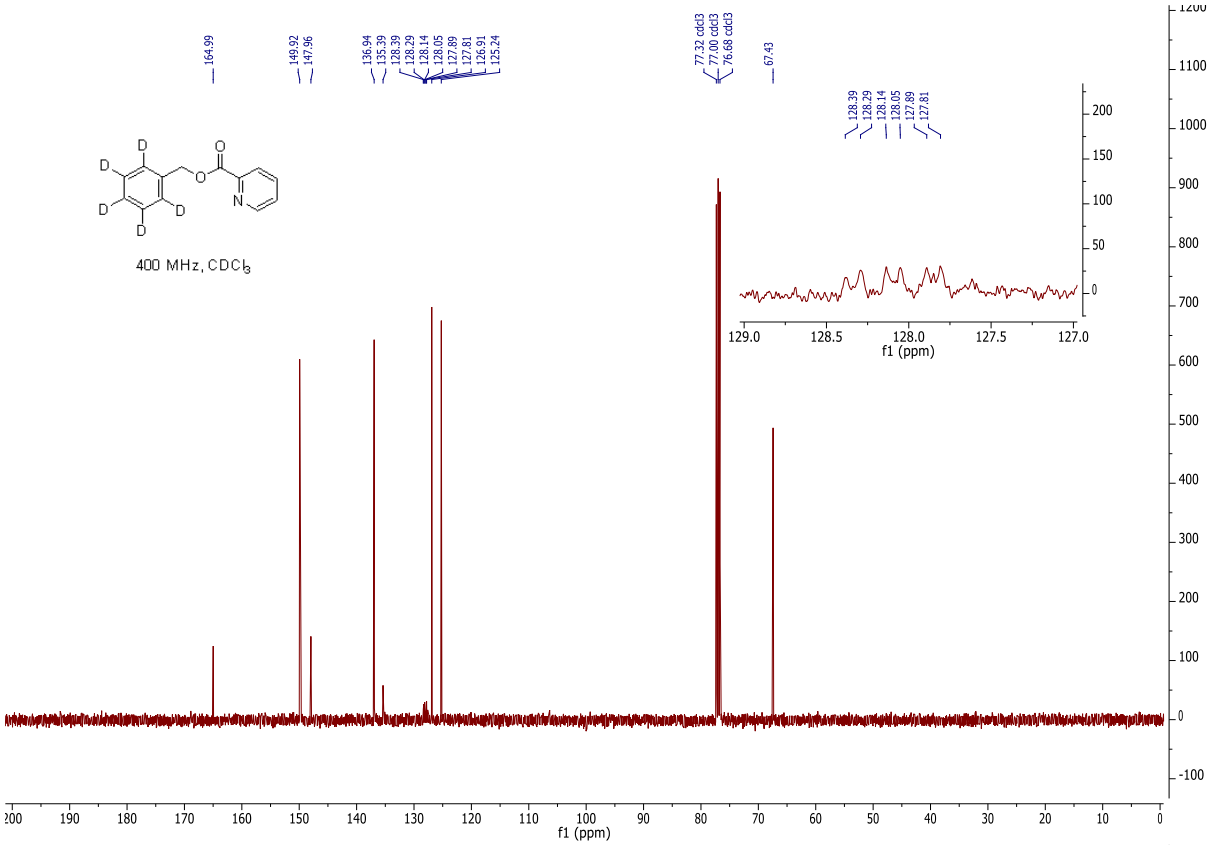

22
CDCl3, 400 MHz
f1 (ppm)

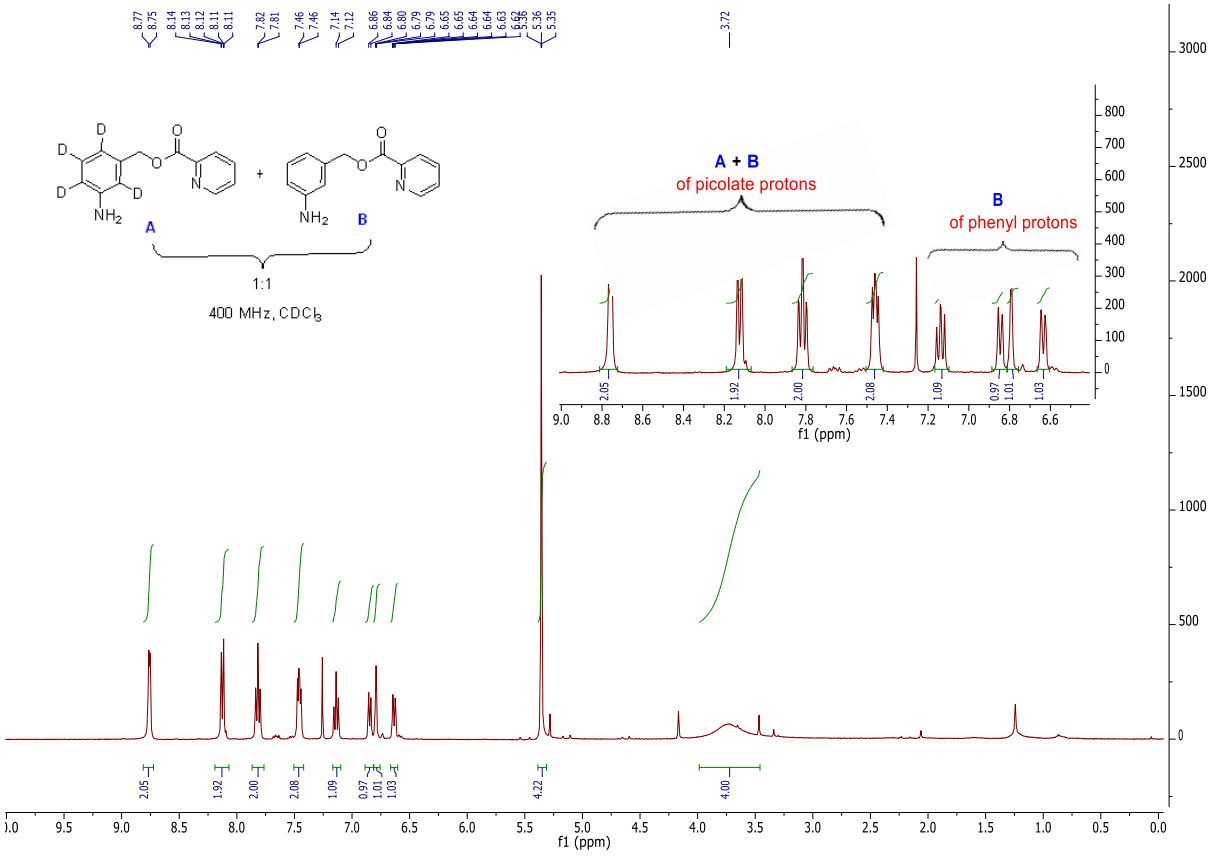

22
CDCl3, 400 MHz
f1 (ppm)

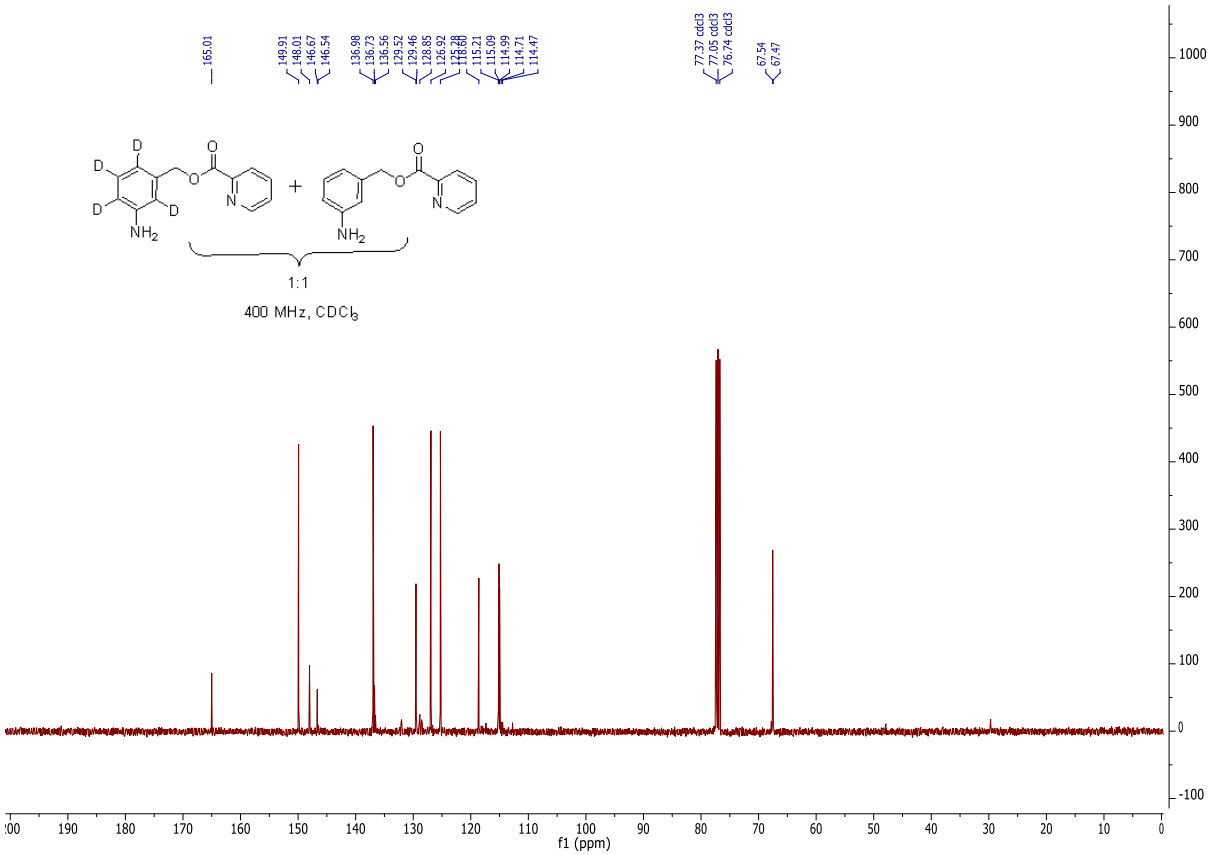

23
500 MHz, CDCl3
f1 (ppm)
23
400 MHz, CDCl3
f1 (ppm)

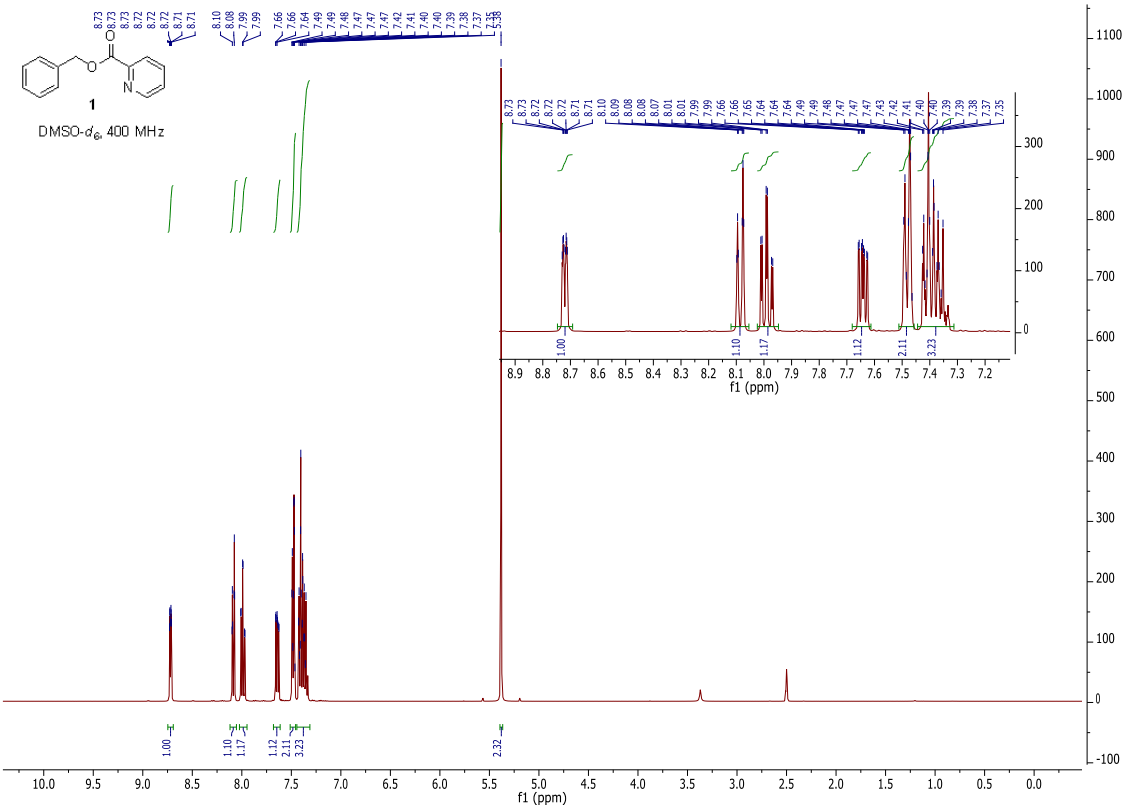

164.47
163.83
149.91
149.20
147.61
146.26
144.68
144.43
143.40
138.50
136.90
130.61
126.82
125.26
122.41
116.84
113.06
77.34 cdcl3
77.02 cdcl3
76.70 cdcl3
65.85
32.50
25.01
17.13
23
500 MHz, CDCl3
f1 (ppm)

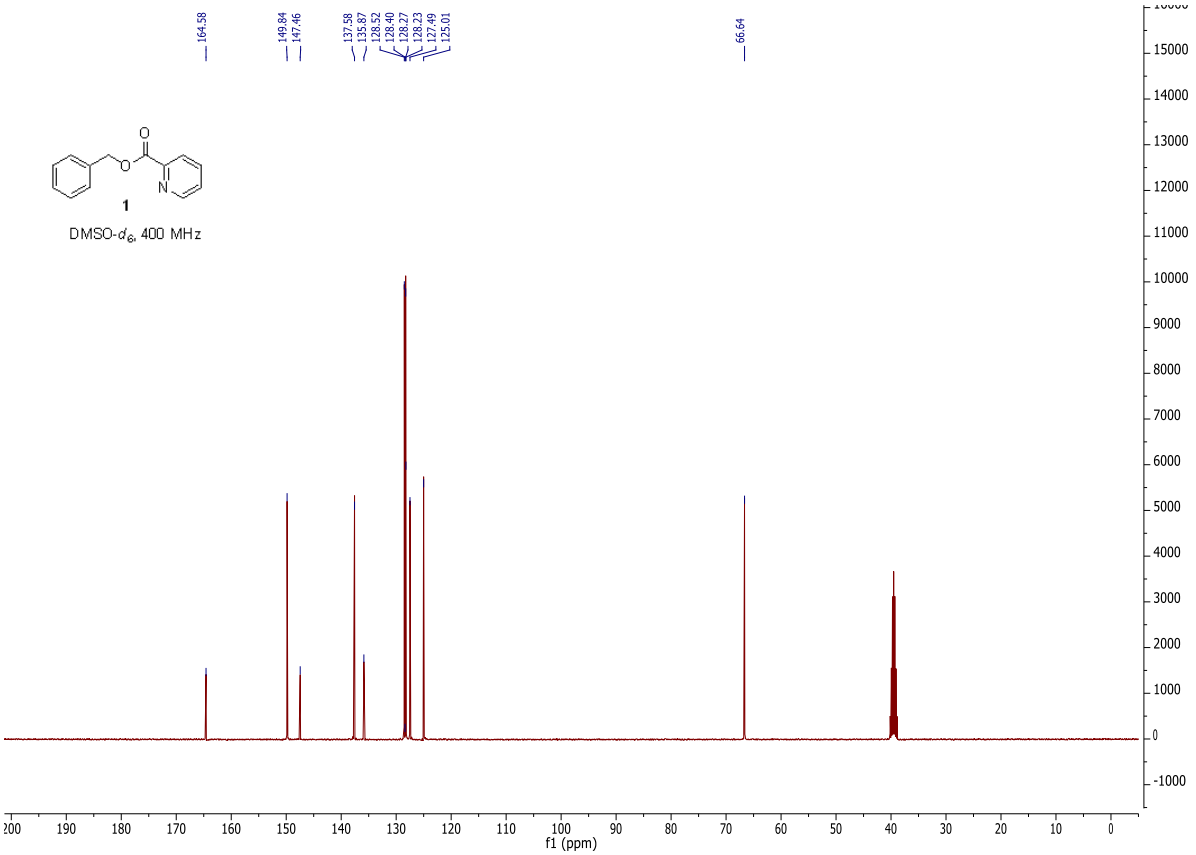

8.77
8.76
8.14
8.12
7.83
7.48
7.47
7.46
7.45
5.46
400 MHz, CDCl3
1.00
0.91
0.96
0.95
2.01
f1 (ppm)

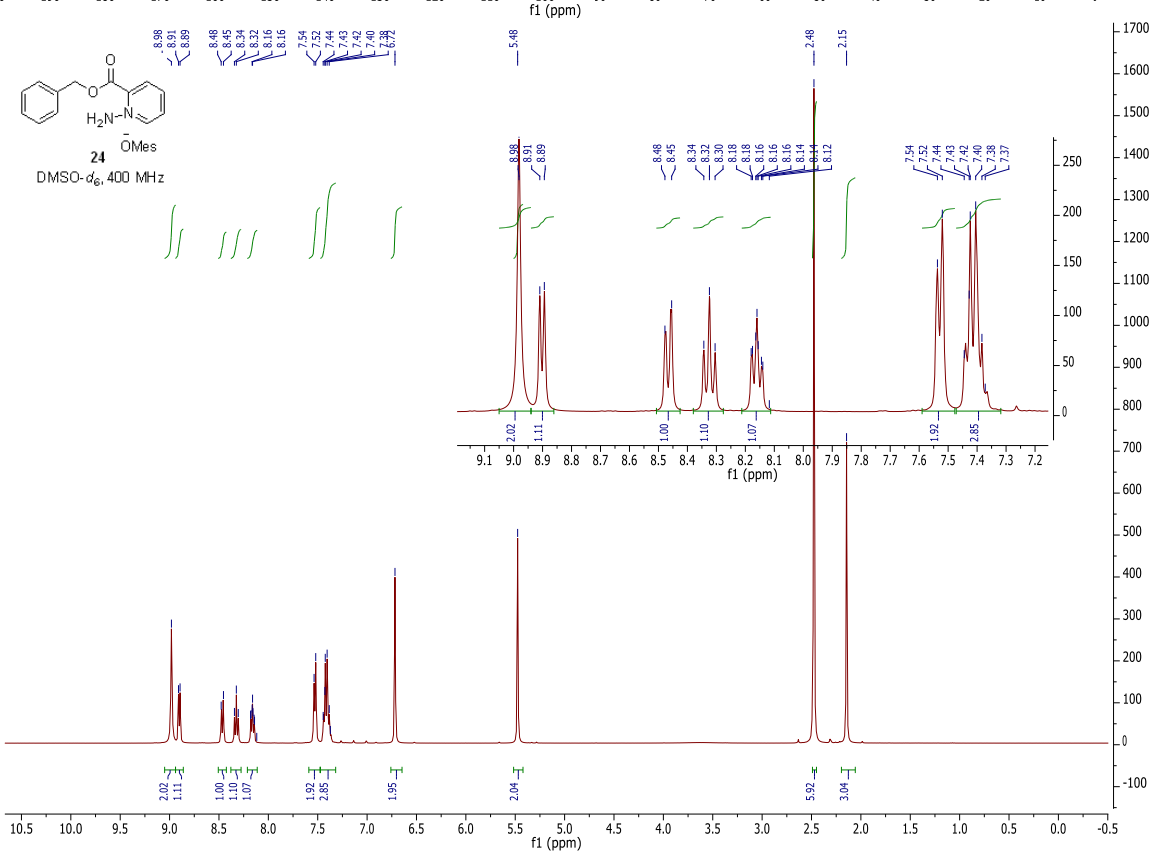

400 MHz, CDCl3
f1 (ppm)

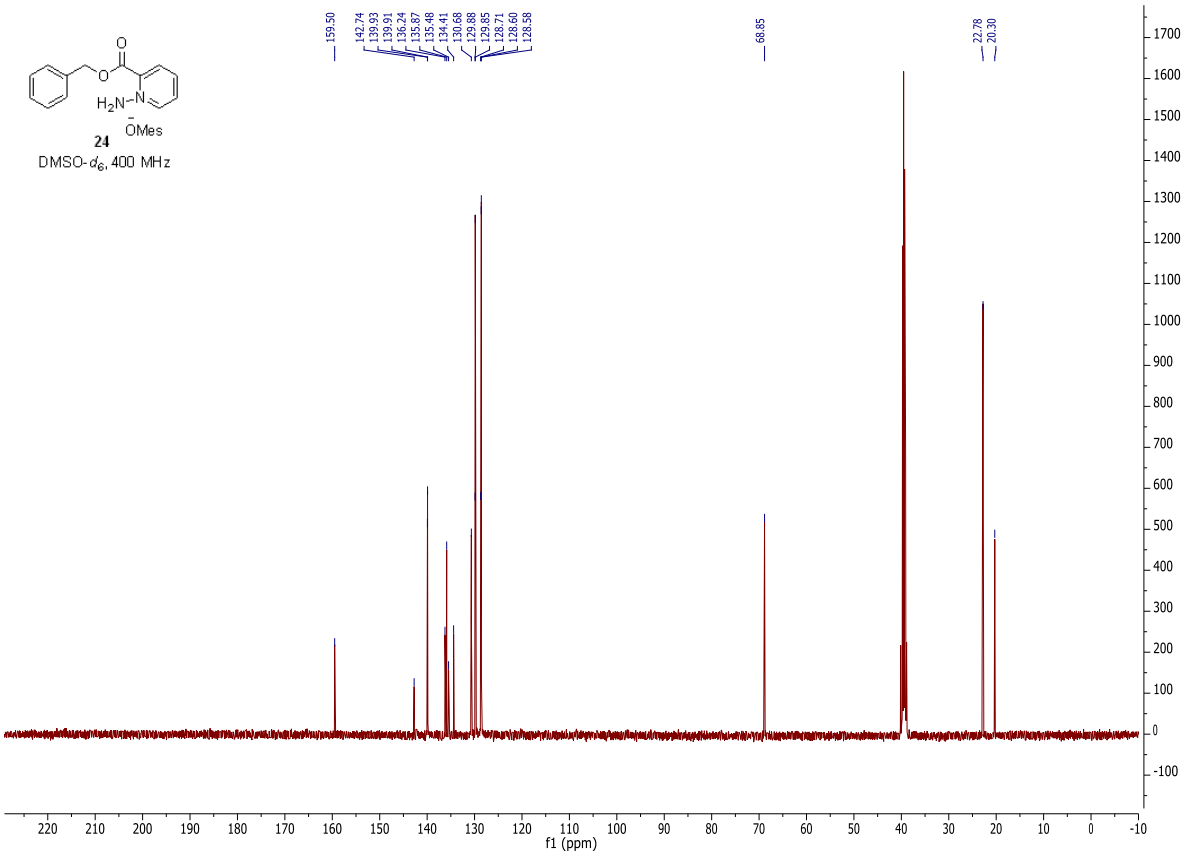

A
B
1:1
400 MHz, CDCl3
A + B
of picolate protons
B
of phenyl protons
f1 (ppm)

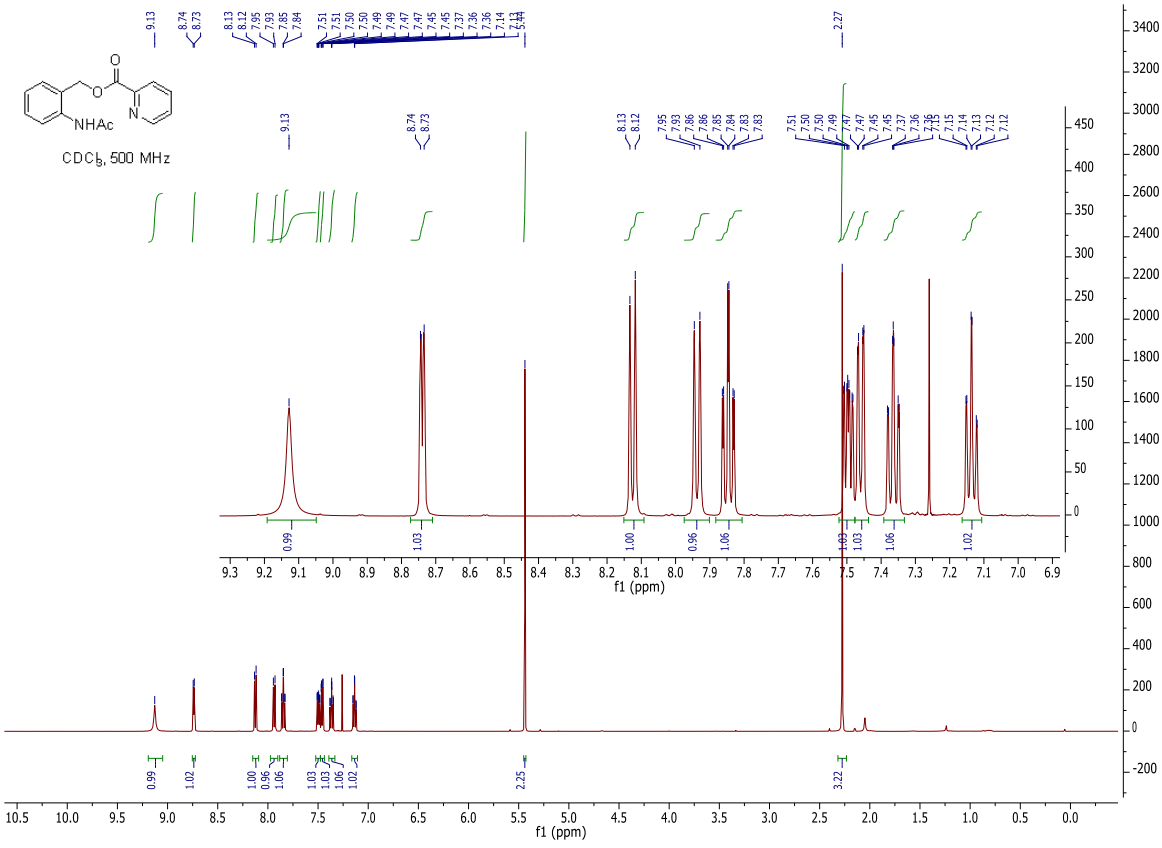

1:1
400 MHz, CDCl3
f1 (ppm)

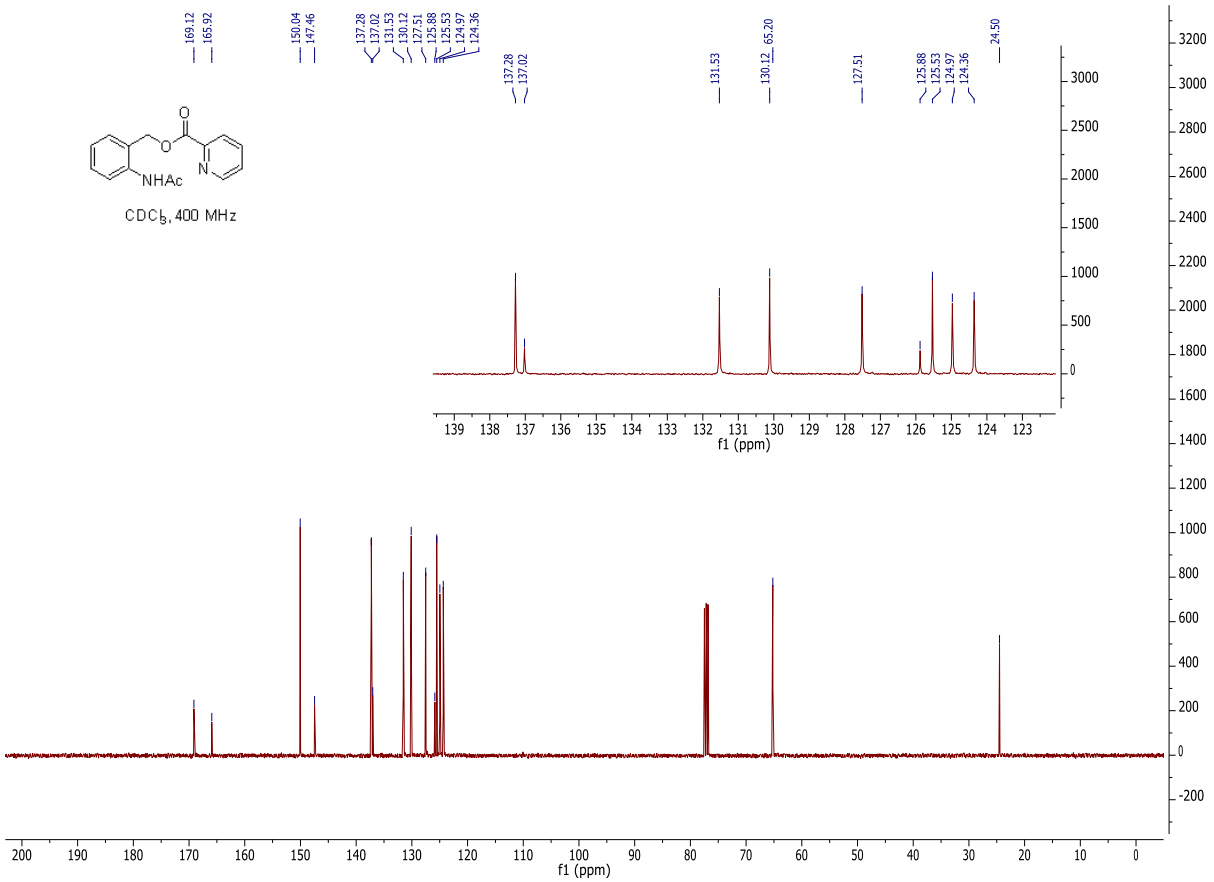

1
DMSO-d6, 400 MHz
f1 (ppm)

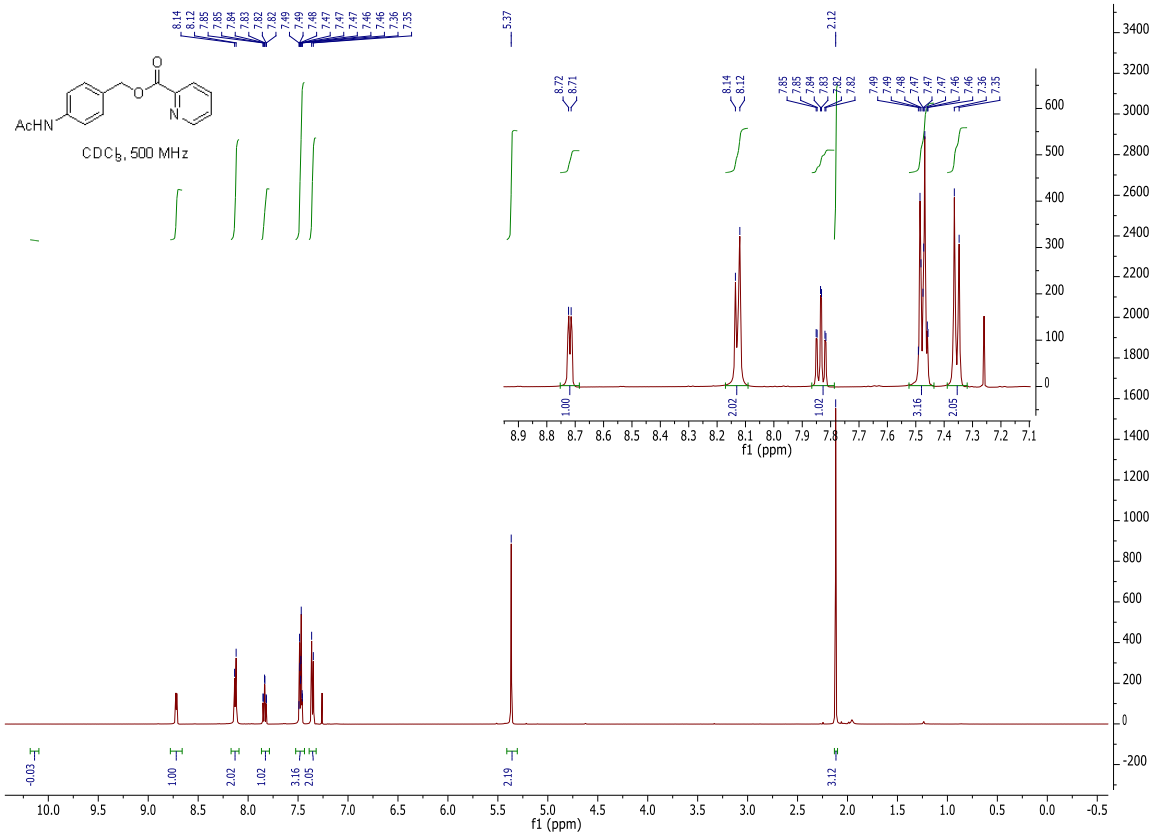

164.58
149.84
147.46
137.58
135.87
128.52
128.40
128.27
128.23
127.49
125.01
66.64
1
DMSO-d_6, 400 MHz
f1 (ppm)

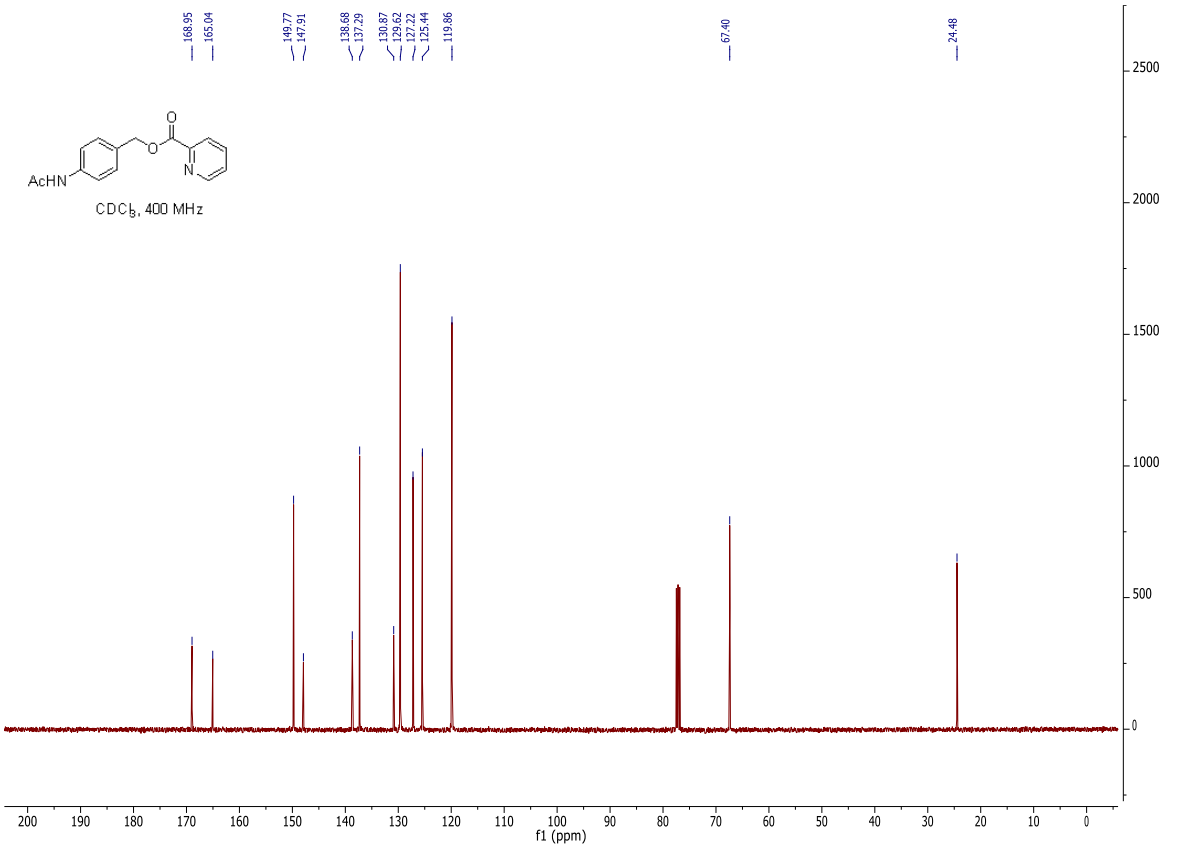

8.98
8.91
8.89
8.48
8.45
8.34
8.32
8.16
8.16
7.54
7.52
7.44
7.43
7.42
7.40
5.48
2.48
2.15
24
DMSO-d_6, 400 MHz
f1 (ppm)

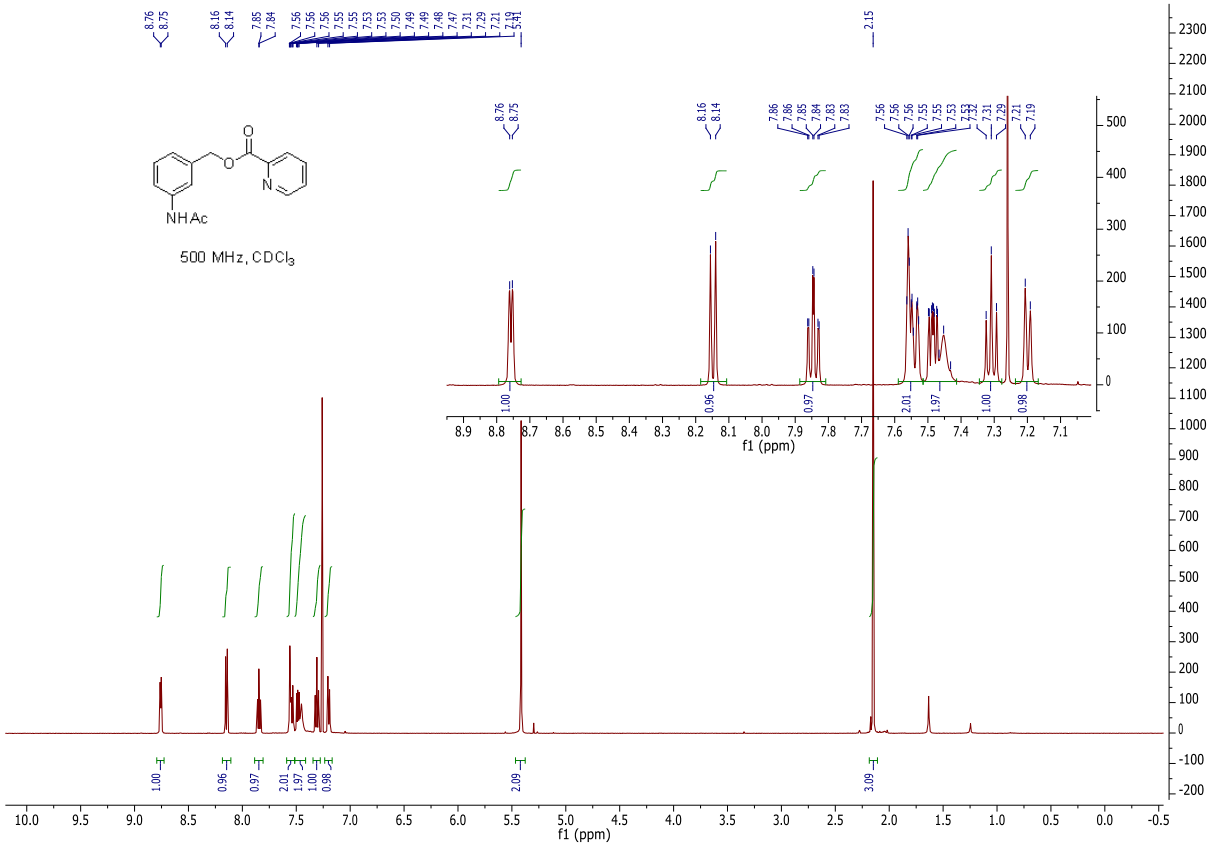

24
DMSO-d_6, 400 MHz
159.50
142.74
139.93
139.91
136.24
135.87
135.48
134.41
130.68
129.88
129.85
128.71
128.60
128.58
68.85
22.78
20.30
f1 (ppm)

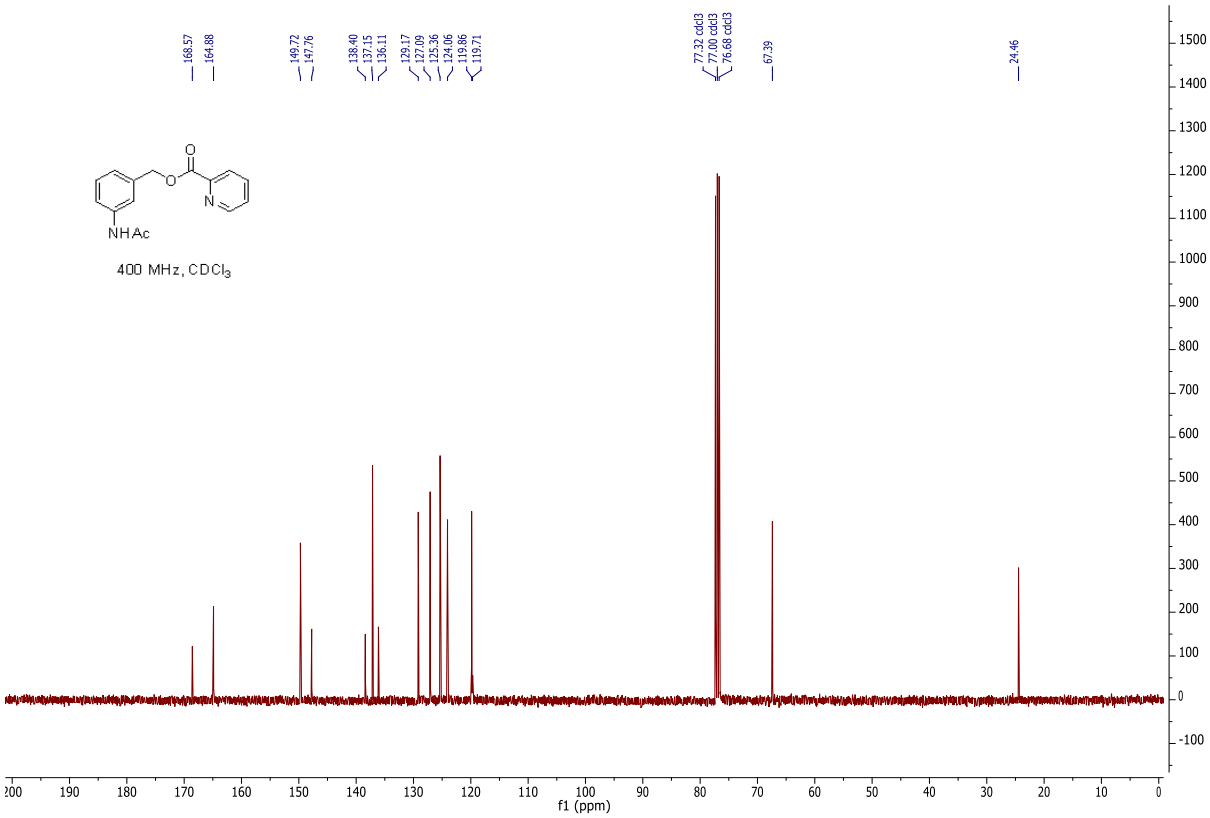

NHAc
$CDCl_3$, 500 MHz
9.13
8.74
8.73
8.13
8.12
7.95
7.93
7.86
7.85
7.84
7.83
7.51
7.50
7.49
7.47
7.45
7.37
7.36
7.15
7.14
7.13
7.12
2.27
f1 (ppm)


169.12
165.92
150.04
147.46
137.28
137.02
131.53
130.12
127.51
125.88
125.53
124.97
124.36
24.50
NHAc
CDCl3, 400 MHz
f1 (ppm)


8.14
8.12
7.85
7.84
7.83
7.82
7.49
7.48
7.47
7.46
7.36
7.35
5.37
2.12
AcHN
CDCl3, 500 MHz
f1 (ppm)


168.95
165.04
149.77
147.91
138.68
137.29
130.87
129.62
127.22
125.44
119.86
67.40
24.48
AcHN
CDCl3, 400 MHz
f1 (ppm)


8.76
8.75
8.16
8.14
7.85
7.84
2.15
NHAc
500 MHz, CDCl3
f1 (ppm)

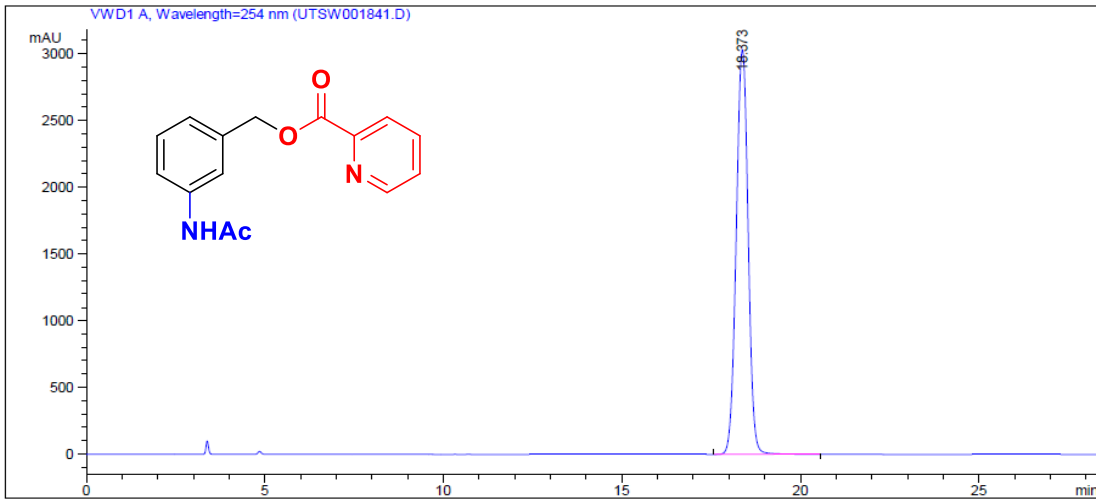

168.57
164.88
149.72
147.76
138.40
137.15
136.11
129.17
127.09
125.36
124.06
119.86
119.71
77.32 cdcl3
77.00 cdcl3
76.68 cdcl3
67.39
24.46
O
O
N
NHAc
400 MHz, CDCl3
f1 (ppm)

HPLC Chromatograms
Analysis conditions:
Column: Agilent Extend-C18, Column size: 4.6 × 250 mm, 5 µm

Mobile phase: 20% CH_3CN/H_2O, Flow rate: 1.0 mL/min.

```
Data File D:\CHEM32\1\DATA\UTSW001841.D
Sample Name: SAI-VII-241-MetaPure-2

======================================================================
Acq. Operator   : Sailu
Acq. Instrument : Instrument 1                    Location : Vial 41
Injection Date  : 11/7/2019 10:20:32 AM
                                                  Inj Volume : 10 µl
Acq. Method     : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/7/2019 10:09:39 AM by Sailu
                  (modified after loading)
Analysis Method : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/8/2019 11:15:18 AM by Sailu
                  (modified after loading)
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.373 BB    0.3619 7.02322e4  3033.01147 100.0000

Totals :                  7.02322e4  3033.01147
```

Figure S1a. Regioselectivity studies –HPLC of analytically pure *N*-Ac **2** standard

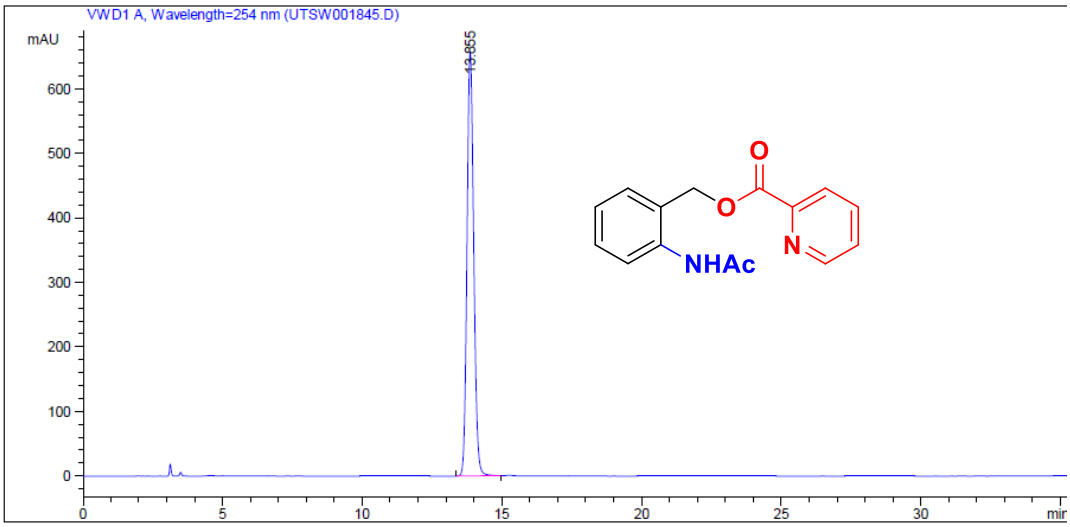
HPLC analysis conditions:

Column: Agilent Extend-C18, Column size: 4.6 × 250 mm, 5 µm

Mobile phase: 20% CH_3CN/H_2O, Flow rate: 1.0 mL/min.

```
Data File D:\CHEM32\1\DATA\UTSW001845.D
Sample Name: SAI-VII-241-Ortho-Pure-1

======================================================================
Acq. Operator   : Sailu
Acq. Instrument : Instrument 1                    Location : Vial 41
Injection Date  : 11/7/2019 12:48:04 PM
                                                  Inj Volume : 10 µl
Acq. Method     : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/7/2019 12:45:43 PM by Sailu
                  (modified after loading)
Analysis Method : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/8/2019 11:15:18 AM by Sailu
                  (modified after loading)
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  13.855 BB    0.2599 1.10342e4   657.31812 100.0000

Totals :                 1.10342e4   657.31812
```

Figure S1b. Regioselectivity studies –HPLC of Analytically pure *ortho*-NHAc **1** standard

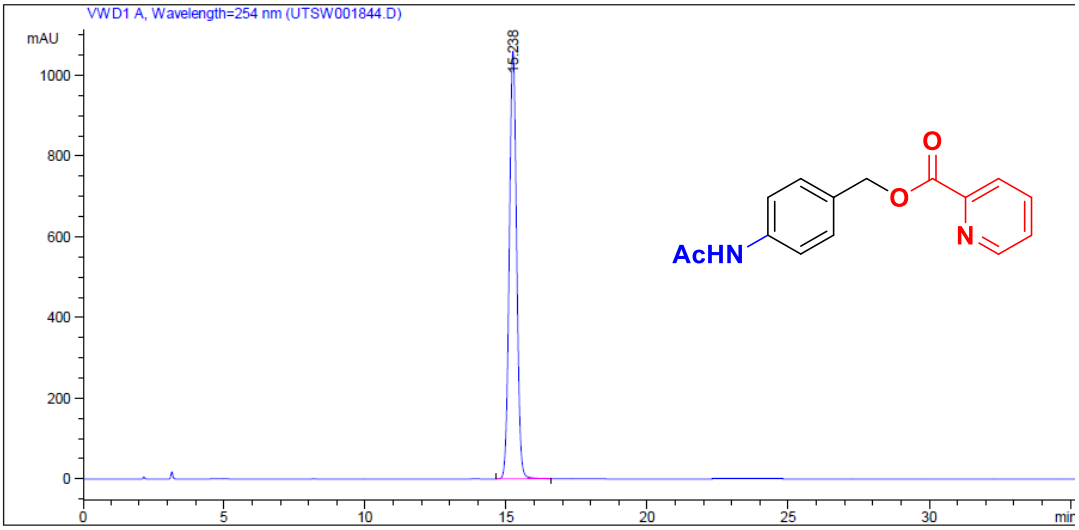
HPLC analysis conditions:

Column: Agilent Extend-C18, Column size: 4.6 × 250 mm, 5 µm

Mobile phase: 20% CH_3CN/H_2O, Flow rate: 1.0 mL/min.

```
Data File D:\CHEM32\1\DATA\UTSW001844.D
Sample Name: SAI-VII-241-Para-Pure-2

======================================================================
Acq. Operator   : Sailu
Acq. Instrument : Instrument 1                    Location : Vial 41
Injection Date  : 11/7/2019 12:10:09 PM
                                                  Inj Volume : 10 µl
Acq. Method     : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/7/2019 12:07:55 PM by Sailu
                  (modified after loading)
Analysis Method : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/8/2019 11:15:18 AM by Sailu
                  (modified after loading)
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  15.238 BB    0.2813 1.92083e4  1060.12476 100.0000

Totals :                  1.92083e4  1060.12476
```

Figure S1c. Regioselectivity studies –HPLC of analytically pure *para*-NHAc **1** standard

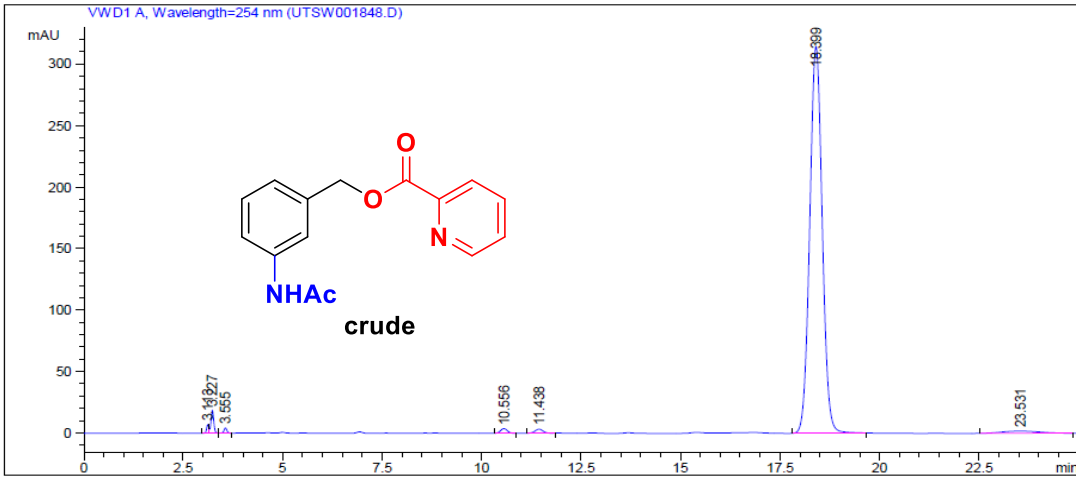
HPLC analysis conditions:

Column: Agilent Extend-C18, Column size: 4.6 × 250 mm, 5 µm

Mobile phase: 20% CH_3CN/H_2O, Flow rate: 1.0 mL/min.

```
Data File D:\CHEM32\1\DATA\UTSW001848.D
Sample Name: SAI-VII-241-CrudeMeta-2

=====================================================================
Acq. Operator   : Sailu
Acq. Instrument : Instrument 1                    Location : Vial 41
Injection Date  : 11/7/2019 4:56:22 PM
                                                  Inj Volume : 10 µl
Acq. Method     : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/7/2019 4:45:21 PM by Sailu
                  (modified after loading)
Analysis Method : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/8/2019 11:15:18 AM by Sailu
                  (modified after loading)
```




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   3.113 VV    0.0636   28.35105    6.94745   0.3925
   2   3.227 VV    0.0750   88.90837   18.50697   1.2309
   3   3.555 VB    0.0807   22.55161    4.25755   0.3122
   4  10.556 BB    0.1847   45.28659    3.82558   0.6270

   5  11.438 BB    0.2199   46.93131    3.29731   0.6497
   6  18.399 BB    0.3395 6871.08936  314.26385  95.1256
   7  23.531 BBA   0.8870  120.05857    1.81779   1.6621

Totals :                  7223.17686  352.91651
```

Figure S1d. Regioselectivity studies –HPLC of crude *N*-Ac **2** reaction mixture

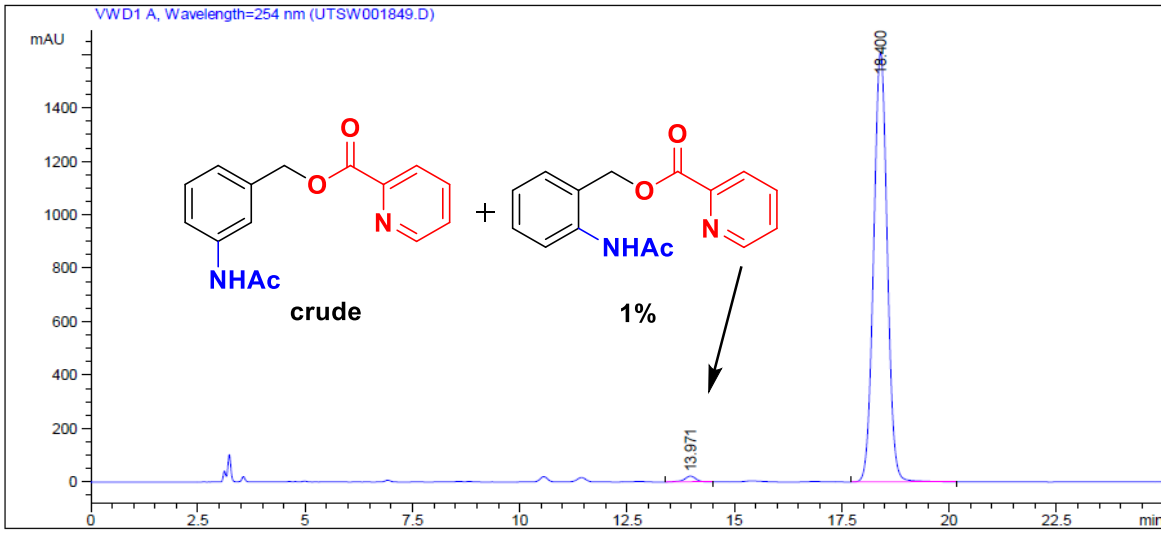
HPLC analysis conditions:

Column: Agilent Extend-C18, Column size: 4.6 × 250 mm, 5 µm

Mobile phase: 20% CH_3CN/H_2O, Flow rate: 1.0 mL/min

```
Data File D:\CHEM32\1\DATA\UTSW001849.D
Sample Name: SAI-VII-241-CrudeMetawith2%ortho-1

======================================================================
Acq. Operator    : Sailu
Acq. Instrument : Instrument 1                    Location : Vial 41
Injection Date  : 11/7/2019 5:33:50 PM
                                                  Inj Volume : 10 µl
Acq. Method     : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/7/2019 5:21:42 PM by Sailu
                  (modified after loading)
Analysis Method : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/8/2019 11:15:18 AM by Sailu
                  (modified after loading)
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  13.971 BB    0.2827  410.07385   21.88011   1.1432
   2  18.400 BB    0.3443 3.54604e4  1610.13428  98.8568

Totals :                  3.58705e4  1632.01439
```

Figure S1e. Regioselectivity studies – Stacked crude HPLC of *N*-Ac **2** spiked with 1% of analytically pure *ortho*-NHAc **1**

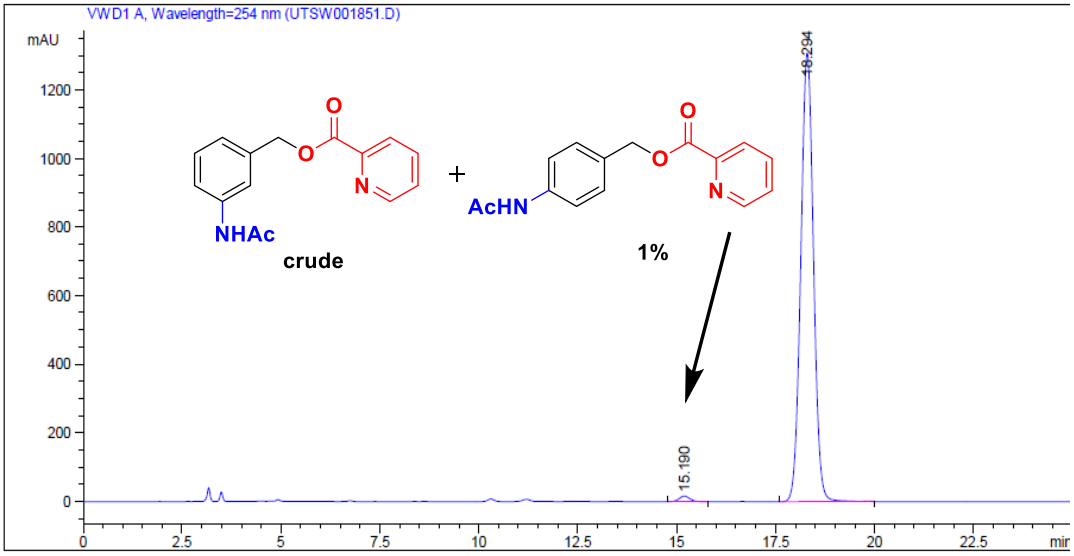
HPLC analysis conditions:

Column: Agilent Extend-C18, Column size: 4.6 × 250 mm, 5 µm

Mobile phase: 20% CH_3CN/H_2O, Flow rate: 1.0 mL/min

```
Data File D:\CHEM32\1\DATA\UTSW001851.D
Sample Name: SAI-VII-241-CrudeMetawith2%para-2

=====================================================================
Acq. Operator   : Sailu
Acq. Instrument : Instrument 1                    Location : Vial 41
Injection Date  : 11/8/2019 12:24:14 PM
                                                  Inj Volume : 10 µl
Method          : D:\CHEM32\1\METHODS\SAILU_METAPROJECT.M
Last changed    : 11/7/2019 6:59:53 PM by Sailu
```




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  15.190 BB    0.2977  313.20578   16.45988   1.0612
   2  18.294 BB    0.3478 2.92015e4  1308.22070  98.9388

Totals :                  2.95147e4  1324.68059
```

Figure S1f. Regioselectivity studies – Stacked crude HPLC of *N*-Ac **2** spiked with 1% of analytically pure *para*-NHAc **1**