# Supporting Information

# Decarboxylative Arylation and Alkoxylation of Pyridine-2-carboxylic acid *N*-oxide derivatives via Electrophilic Carbene: Access to Lucidimine E and Australine

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**1. General Information:**

All reagents and solvents were used as received from commercial sources unless and otherwise noted. Anhydrous solvents were distilled prior to use. Benzene, DCM, MeOH, and THF were dried prior to use. Air and moisture-sensitive reactions were performed under an argon atmosphere. Precoated plates (silica gel 60 PF254, 0.25 mm or 0.5 mm) were utilized for Thin Layer Chromatography (TLC), which was visualized with UV light at 254 nm. Column chromatographic purifications were carried out on flash silica-gel (230-400 mesh) using petroleum ether and ethyl acetate as eluents. The $^{1}H$ and $^{13}C$ NMR spectra were recorded on Brucker 400/500 MHz and 101/126 MHz NMR spectrometer respectively in $CDCl_3$/DMSO-$d_6$/$CD_3OD$. Chemical shifts were reported as $\delta$ values from standard peaks. The multiplicities of signals are designated by the following abbreviations: s (singlet), d (doublet), dd (doublet of doublet), t (triplet) etc. Splitting patterns that could not be interpreted or easily visualized are designated as m (multiplet). Coupling constants ($J$) are reported in hertz. High-resolution mass spectrometry (HRMS) was performed on QTOF/ESITOF mass spectrometer. LC-Mass spectra were recorded with ES ionization in a single quadrupole mass spectrometer.

## 2. Experimental procedures, plausible mechanism and data:

### 2.1 General procedures for syntheses of 2-picolinic acid, quinaldic acid and isoquinoline-1-carboxylic acid *N*-oxides:

**General Procedure A:**[1]

2-Picolinic acids, or quinaldic acid (1.0 equiv) were dissolved in trifluoroacetic acid (TFA, 0.4 M) and then 30% $H_2O_2$ (26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated in vacuo, and the concentrate was diluted with water (30 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the solid product.

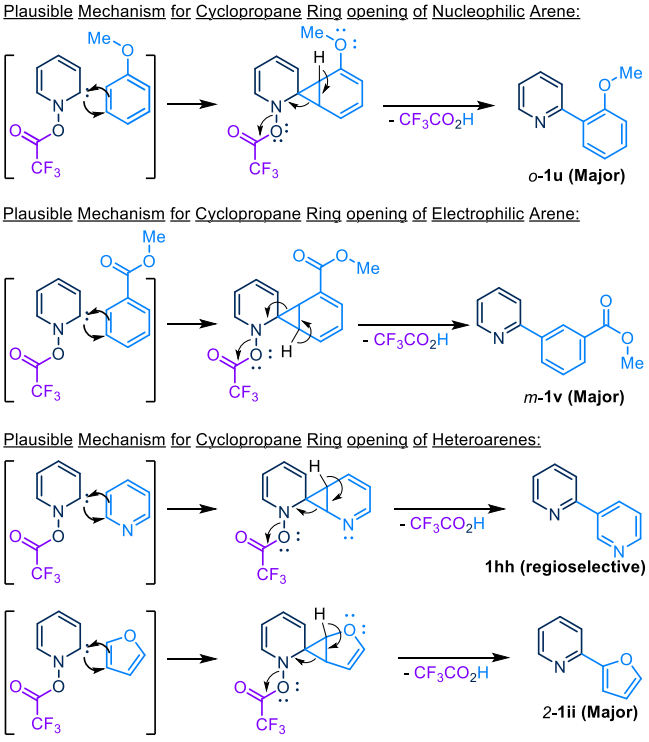
**General Procedure B:**[2]

A mixture of 2-picolinic acids (1.0 equiv) and *m*-CPBA (3.0 equiv) in DCM (0.12 M) was stirred overnight at 40 °C. After evaporation of solvents, the crude product was purified by column chromatography to give the title compound.

**General Procedure C:**[3]

Isoquinoline-1-carboxylic acid (1.0 equiv) and UHP (2.0 equiv) was dissolved in anhydrous DCM (0.3 M). The mixture was cooled to 0 °C and trifluoroacetic anhydride (2 equiv) was added dropwise. After 30 min at 0 °C, the mixture was allowed to warm to room temperature and stirred for an additional hour. A saturated $Na_2S_2O_8$ aqueous solution was added. The aqueous layer was extracted with DCM (3x). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure.

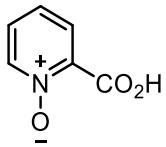
**Plausible Mechanism**:




The observed regioselectivity is likely governed by the relative stability and mode of ring opening of the transient cyclopropane intermediates, which are strongly influenced by the electronic properties and resonance effects of the substituents present on the arene or heteroarene coupling partners, which affects the acidity of the proton present on the cyclopropane ring.

**Synthesis of N-oxides:**

**2-Picolinic acid *N*-oxide (2a)[4]:** Compound **2a** was prepared from 2-picolinic acid according to the general procedure A. 2-Picolinic acid (500 mg, 4.06 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 10.15 mL) and then 30% $H_2O_2$ (3.23 mL, 105.56 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2a** as white solid (511 mg, 90%) without the need for column chromatography.

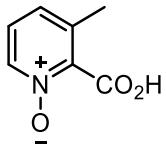


mp. 158 – 162 $^oC$; $R_f$: 0.4 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400 MHz, DMSO-$d_6$)**: $\delta$ 8.80 - 8.66 (*m*, 1H), 8.37 - 8.27 (*m*, 1H), 7.99 - 7.83 (*m*, 2H).

**LCMS-ESI** (m/z) calcd for $(C_6H_5NO_3 + H)^+$: 140.0, found: 139.9697.

**3-Methylpicolinic acid *N*-oxide (2b):** Compound **2b** was prepared from 3-methylpicolinic acid according to the general procedure B. A mixture of 3-methylpicolinic acid (500 mg, 3.64 mmol, 1.0 equiv) and *m*-CPBA (1887mg, 10.93 mmol, 3.0 equiv) in DCM (30 ml) was stirred overnight at 40 °C. After evaporation of solvents, the crude product was purified by column chromatography to give the product **2b** as off-white solid (193.6 mg, 35%).



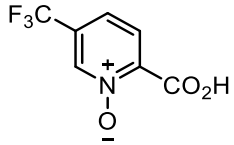
mp. 130 – 134 $^oC$; $R_f$: 0.3 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400 MHz, DMSO-$d_6$)**: $\delta$ 8.44 - 8.37 (m, 1 H), 7.61 - 7.55 (m, 2 H), 2.48 (s, 3 H).

**$^{13}$C NMR (101 MHz, DMSO-$d_6$)**: $\delta$ 162.3, 138.6, 137.7, 136.9, 132.3, 126.8, 19.3.

**HRMS-ESI** (m/z) calcd for $(C_7H_7NO_3 + H)^+$: 154.0504, found: 154.0499.

**5-Trifluoromethylpicolinic acid *N*-oxide (2c):** Compound **2c** was prepared from 5-trifluoromethylpicolinic acid according to the general procedure A. 5-Trifluoromethylpicolinic acid (500 mg, 2.61 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 6.54 mL) and then 30% $H_2O_2$ (2.1 mL, 68.02 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2c** as light brown solid (440.6 mg, 81%) without the need for column chromatography.



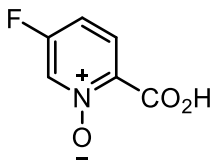
mp. 73 – 77 °C; $R_f$: 0.2 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400 MHz, DMSO-*d*$_6$)**: $\delta$ 9.38 (s, 1 H), 8.42 (d, $J$ = 8.3 Hz, 1 H), 8.23 (d, $J$ = 8.3 Hz, 1 H)

**$^{13}$C NMR (101 MHz, DMSO-*d*$_6$)**: $\delta$ 160.2, 139.5, 137.5 (q, $J_{C,F}$ = 4.1 Hz), 130.62 (q, $J_{C,F}$ = 35.1 Hz), 129.2, 128.2 (q, $J_{C,F}$ = 3.6 Hz), 121.4 (q, $J_{C,F}$ = 273.6 Hz)

**HRMS-ESI** (m/z) calcd for $(C_7H_4F_3NO_3 + H)^+$: 208.0211, found: 208.0216.

**5-Fluoropicolinic acid *N*-oxide (2d):** Compound **2d** was prepared from 5-fluoropicolinic acid according to the general procedure A. 5-fluoropicolinic acid (500 mg, 3.54 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 8.85 mL) and then 30% $H_2O_2$ (2.82 mL, 92.13 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2d** as light yellow solid (511.9 mg, 92%) without the need for column chromatography.

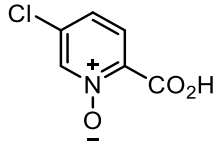


mp. 146 – 149 °C; $R_f$: 0.3 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400 MHz, DMSO-*d*$_6$)**: $\delta$ 9.16 (dd, $J$ = 2.3, 4.3 Hz, 1 H), 8.35 (dd, $J$ = 6.9, 9.1 Hz, 1 H), 7.91 (m, 1 H)

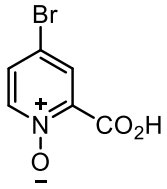
**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 161.07 (d, $J_{C,F}$ = 256.35 Hz), 160.2, 133.8 (d, $J_{C,F}$ = 4.6 Hz), 130.2 (d, $J_{C,F}$ = 9.9 Hz), 129.75 (d, $J_{C,F}$ = 9.9 Hz), 120.0 (d, $J_{C,F}$ = 19.8 Hz).
**HRMS-ESI** (m/z) calcd for $(C_6H_4FNO_3 + H)^+$: 158.0247, found: 158.0248.

**5-Chloropicolinic acid *N*-oxide (2e)[3]:** Compound **2e** was prepared from 5-chloropicolinic acid according to the general procedure A. 5-Chloropicolinic acid (500 mg, 3.17 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 7.93 mL) and then 30% $H_2O_2$ (2.82 mL, 82.51 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2e** as off-white solid (505.3 mg, 92%) without the need for column chromatography.




mp. 150 – 152 $^o$C; R$_f$: 0.4 (1 : 9, methanol : dichloromethane)
**$^1$H NMR (400 MHz, DMSO-*d*$_6$)**: $\delta$ 9.14 (br. s., 1 H), 8.25 (d, $J$ = 8.5 Hz, 1 H), 8.02 (d, $J$ = 8.6 Hz, 1 H)
**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 160.4, 138.5, 135.6, 135.3, 132.1, 128.8
**LCMS-ESI** (m/z) calcd for $(C_6H_4ClNO_3 + H)^+$: 174.0, found: 173.9303.

**4-Bromopicolinic acid *N*-oxide (2f):** Compound **2f** was prepared from 4-bromopicolinic acid according to the general procedure A. 4-Bromopicolinic acid (500 mg, 2.47 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 6.18 mL) and then 30% $H_2O_2$ (1.97 mL, 64.35 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2f** as light yellow solid (496.9 mg, 92%) without the need for column chromatography.



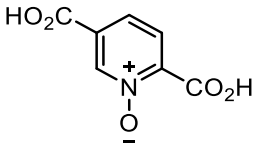

mp. 143 – 147 $^o$C; R$_f$: 0.4 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400 MHz, DMSO-$d_6$)**: $\delta$ 8.65 (d, $J$ = 6.6 Hz, 1 H), 8.39 (br. s., 1 H), 8.16 (d, $J$ = 4.8 Hz, 1 H)

**$^{13}$C NMR (101MHz, DMSO-$d_6$)**: $\delta$ 160.0, 140.1, 137.0, 132.7, 131.0, 125.7

**HRMS-ESI** (m/z) calcd for $(C6H4Br^{79}NO3 + H)^+$: 217.9448, found: 217.9447.

**Pyridine-2,5-dicarboxylic acid *N*-oxide (2g):** Compound **2g** was prepared from pyridine-2,5-dicarboxylic acid according to the general procedure A. Pyridine-2,5-dicarboxylic acid (500 mg, 2.99 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 7.47 mL) and then 30% $H_2O_2$ (2.38 mL, 77.79 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2g** as white solid (521.8 mg, 95%) without the need for column chromatography.



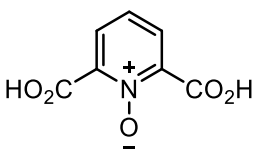
mp. 251 – 255 °C; $R_f$: 0.2 (5 : 5, methanol : dichloromethane)

**$^1$H NMR (400MHz, DMSO-$d_6$)**: $\delta$ 14.36 (br. s., 1 H), 8.92 (s, 1 H), 8.38 (d, $J$ = 8.3 Hz, 1 H), 8.25 (d, $J$ = 8.3 Hz, 1 H)

**$^{13}$C NMR (101MHz, DMSO-$d_6$)**: $\delta$ 163.1, 160.5, 139.5, 138.5, 132.9, 132.1, 128.8

**HRMS-ESI** (m/z) calcd for $(C_7H_5NO_5 + H)^+$: 184.0242, found: 184.0240.

**Pyridine-2,6-dicarboxylic acid *N*-oxide (2h)[5]:** Compound **2h** was prepared from pyridine-2,6-dicarboxylic acid according to the general procedure A. Pyridine-2,6-dicarboxylic acid (500 mg, 2.99 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 7.47 mL) and then 30% $H_2O_2$ (2.38 mL, 77.79 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2h** as light yellow solid (434.8 mg, 79%) without the need for column chromatography.



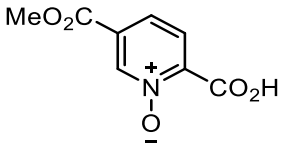
mp. 155 – 157 °C; $R_f$: 0.3 (5 : 5, methanol : dichloromethane)

**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 8.18 (d, *J* = 7.9 Hz, 2 H), 7.97 - 7.90 (m, 1 H)

**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 161.0, 139.9, 132.6, 128.5

**LCMS-ESI** (m/z) calcd for $(C_7H_5NO_5 + H)^+$: 184.0, found: 183.9709.

**5-(Methoxycarbonyl)picolinic acid *N*-oxide (2i):** Compound **2i** was prepared from 5-(methoxycarbonyl)picolinic acid according to the general procedure B. A mixture of 5-(methoxycarbonyl)picolinic acid (500 mg, 2.76 mmol, 1.0 equiv) and *m*-CPBA (1429 mg, 8.28 mmol, 3.0 equiv) in DCM (23 ml) was stirred overnight at 40 °C. After evaporation of solvents, the crude product was purified by column chromatography to give the white solid product **2i** (420.4 mg, 77%).



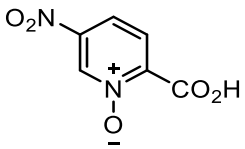
mp. 149 – 154 °C; $R_f$: 0.3 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 8.99 (d, *J* = 1.1 Hz, 1 H), 8.39 (d, *J* = 8.3 Hz, 1 H), 8.27 (dd, *J* = 1.5, 8.3 Hz, 1 H), 3.95 (s, 3 H)

**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 162.2, 160.4, 139.5, 138.9, 131.8, 131.5, 128.8, 53.4

**HRMS-ESI** (m/z) calcd for $(C_8H_7NO_5 + H)^+$: 198.0396, found: 198.0397.

**5-Nitropicolinic acid *N*-oxide (2j):** Compound **2j** was prepared from 5-nitropicolinic acid according to the general procedure A. 5-Nitropicolinic acid (500 mg, 2.97 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 7.43 mL) and then 30% $H_2O_2$ (2.36 mL, 77.33 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2j** as light brown solid (383.8 mg, 70%) without the need for column chromatography.



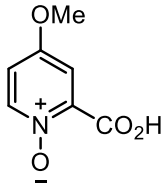
mp. 140 – 144 °C; $R_f$: 0.2 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 9.47 (br. s., 1 H), 8.49 (d, *J* = 7.5 Hz, 1 H), 8.36 (d, *J* = 8.6 Hz, 1 H)

**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 160.1, 147.2, 142.0, 136.2, 128.4, 125.3

**HRMS-ESI** (m/z) calcd for $(C_6H_4N_2O_5 + H)^+$: 185.0193, found: 185.0193.

**4-Methoxypicolinic acid *N*-oxide (2k):** Compound **2k** was prepared from 4-methoxypicolinic acid according to the general procedure B. A mixture of 4-methoxypicolinic acid (500 mg, 3.26 mmol, 1.0 equiv) and *m*-CPBA (1690 mg, 9.79 mmol, 3.0 equiv) in DCM (27 ml) was stirred overnight at 40 °C. After evaporation of solvents, the crude product was purified by column chromatography to give the white solid product **2k** (519.5 mg, 94%).



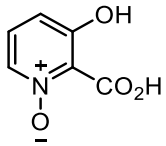

mp. 134 – 138 °C; $R_f$: 0.5 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400MHz, DMSO-$d_6$)**: $\delta$ 8.68 (d, $J$ = 7.3 Hz, 1 H), 7.76 (d, $J$ = 3.5 Hz, 1 H), 7.50 (dd, $J$ = 3.6, 7.3 Hz, 1 H), 4.00 (s, 3 H)

**$^{13}$C NMR (101MHz, DMSO-$d_6$)**: $\delta$ 162.4, 160.9, 139.7, 137.0, 115.8, 112.8, 57.3

**HRMS-ESI** (m/z) calcd for $(C_7H_7NO_4 + H)^+$: 170.0448, found: 170.0448.

**3-Hydroxypicolinic acid *N*-oxide (2l):** Compound **2l** was prepared from 3-hydroxypicolinic acid according to the general procedure A. 3-Hydroxypicolinic acid (500 mg, 3.59 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 8.98 mL) and then 30% $H_2O_2$ (2.86 mL, 93.45 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2l** as white solid (366.2 mg, 66%) without the need for column chromatography.



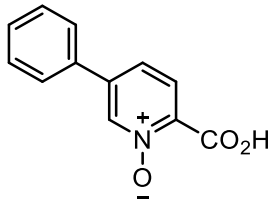

mp. 173 – 177 °C; $R_f$: 0.6 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400MHz, DMSO-$d_6$)**: $\delta$ 12.77 (br. s., 1 H), 8.44 (d, $J$ = 6.3 Hz, 1 H), 7.78 (dd, $J$ = 6.4, 8.7 Hz, 1 H), 7.61 (d, $J$ = 8.8 Hz, 1 H)

**$^{13}$C NMR (101MHz, DMSO-$d_6$)**: $\delta$ 167.1, 159.5, 129.9, 129.0, 123.9, 121.6

**HRMS-ESI** (m/z) calcd for $(C_6H_5NO_4 + H)^+$: 156.0287, found: 156.0291.

**5-Phenylpicolinic acid *N*-oxide (2m):** Compound **2m** was prepared from 5-phenylpicolinic acid according to the general procedure B. A mixture of 5-phenylpicolinic acid (200 mg, 1.00 mmol, 1.0 equiv) and *m*-CPBA (520 mg, 3.01 mmol, 3.0 equiv) in DCM (8.3 ml) was stirred overnight at 40 °C. After evaporation of solvents, the crude product was purified by column chromatography to give the white solid product **2m** (210.4 mg, 97%).



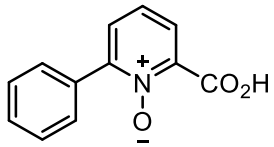
mp. 174 – 178 °C; $R_f$: 0.6 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 8.35 (dd, *J* = 2.2, 7.8 Hz, 1 H), 8.04 (dd, *J* = 2.3, 8.0 Hz, 1 H), 7.97 (t, *J* = 7.9 Hz, 1 H), 7.82 - 7.78 (m, 2 H), 7.59 - 7.54 (m, 3 H)

**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 161.2, 148.3, 136.4, 132.2, 131.5, 130.7, 130.3, 129.7, 128.3, 127.9

**HRMS-ESI** (m/z) calcd for $(C_{12}H_9NO_3 + H)^+$: 216.0654, found: 216.0655.

**6-Phenylpicolinic acid *N*-oxide (2n):** Compound **2n** was prepared from 6-phenylpicolinic acid according to the general procedure B. A mixture of 6-phenylpicolinic acid (300 mg, 1.50 mmol, 1.0 equiv) and *m*-CPBA (780 mg, 4.52 mmol, 3.0 equiv) in DCM (12.5 ml) was stirred overnight at 40 °C. After evaporation of solvents, the crude product was purified by column chromatography to give the white solid product **2n** (219.2 mg, 68%).



mp. 123 – 128 °C; $R_f$: 0.6 (1 : 9, methanol : dichloromethane)

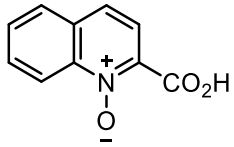
**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 8.35 (dd, *J* = 2.0, 7.8 Hz, 1 H), 8.04 (dd, *J* = 2.1, 7.9 Hz, 1 H), 7.97 (t, *J* = 7.9 Hz, 1 H), 7.80 (dd, *J* = 2.9, 6.6 Hz, 2 H), 7.58 - 7.54 (m, 3 H)

**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 161.2, 148.3, 136.4, 132.2, 131.5, 130.7, 130.3, 129.7, 128.3, 127.9

**HRMS-ESI** (m/z) calcd for $(C_{12}H_9NO_3 + H)^+$: 216.0666, found: 216.0655.

**Quinaldic acid *N*-oxide (2o)[4]:** Compound **2o** was prepared from quinaldic acid according to the general procedure A. Quinaldic acid (500 mg, 2.89 mmol, 1.0 equiv) was dissolved in

trifluoroacetic acid (TFA, 7.22 mL) and then 30% $H_2O_2$ (2.30 mL, 75.07 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (10 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2o** as white solid (474.3 mg, 86%) without the need for column chromatography.

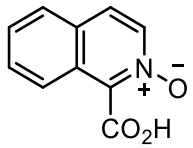


mp. 167 – 170 °C; $R_f$: 0.6 (1 : 9, methanol : dichloromethane)

**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 8.66 (d, *J* = 8.9 Hz, 1 H), 8.47 (d, *J* = 8.8 Hz, 1 H), 8.28 (t, *J* = 8.1 Hz, 2 H), 8.12 - 8.04 (m, 1 H), 8.02 - 7.91 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{10}H_7NO_3 + H)^+$: 190.0, found: 189.9903.

**Isoquinoline-1-carboxylic acid *N*-oxide (2p)**[3]**:** Isoquinoline-1-carboxylic acid (500 mg, 2.88 mmol, 1.0 equiv) and UHP (543 mg, 5.77 mmol, 2.0 equiv) were dissolved in anhydrous DCM (9.6 mL). The mixture was cooled to 0 °C and trifluoroacetic anhydride (0.8 mL, 5.77 mmol, 2 equiv) was added dropwise. After 30 min at 0 °C, the mixture was allowed to warm to room temperature and stirred for an additional hour. A saturated $Na_2S_2O_8$ aqueous solution (20 mL) was added. The aqueous layer was extracted with DCM (20 mL x 3). The combined organic layers were dried over $Na_2SO_4$, and the solvent was removed under reduced pressure. The desired product **2p** was obtained as a white solid (433.8 g, 79%) after trituration in $Et_2O$ and filtration.



mp. 121 – 125 °C; $R_f$: 0.3 (5 : 5, methanol : dichloromethane)

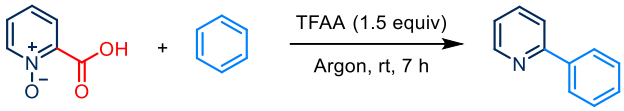
**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 9.83 (d, *J* = 8.6 Hz, 1 H), 8.29 (d, *J* = 6.9 Hz, 1 H), 7.99 (d, *J* = 6.9 Hz, 1 H), 7.94 - 7.81 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{10}H_7NO_3 + H)^+$: 190.0, found: 190.0052.

## 2.2 General procedure for decarboxylative arylation and alkoxylation of 2-picolinic acid *N*-oxides, quinaldic acid *N*-oxide and isoquinoline-1-carboxylic acid *N*-oxide with arenes and cyclic ethers

Several permutations and combinations were screened (see Table 1 below) to optimize the protocol using the general procedure provided below. Addition of solvent was need in the case of solid arenes.

**Table 1: Optimization of the Decarboxylative Arylation Protocol**[a]




| Entry | TFAA (equiv) | Benzene (mL) | Additive | Temperature | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | 1.0 | 1.0 | - | rt | 61 |
| **2** | **1.5** | **1.0** | **-** | **rt** | **74** |
| 3 | 2.0 | 1.0 | - | rt | 72 |
| 4 | 2.5 | 1.0 | - | rt | 73 |
| 5 | 1.5 | 0.5 | - | rt | 64 |
| 6 | 1.5 | 2.0 | - | rt | 70 |
| 7 | 1.5 | 3.0 | - | rt | 66 |
| 8 | 1.5 | 1.0 | - | 40 °C | 55 |
| 9 | 1.5 | 1.0 | - | 50 °C | 51 |
| 10 | 1.5 | 1.0 | - | 60 °C | 45 |
| 11[c] | 1.5 | 1.0 | $K_2CO_3$ (2.0 equiv) | 0 °C to rt | 57 |
| 12[c] | 1.5 | 1.0 | $K_2CO_3$ (0.5 equiv) | 0 °C to rt | 73 |
| 13[c] | 1.5 | 1.0 | $Cs_2CO_3$ (0.5 equiv) | 0 °C to rt | 69 |
| 14[c] | 1.5 | 1.0 | $Na_2CO_3$ (0.5 equiv) | 0 °C to rt | 70 |
| 15[c] | 1.5 | 1.0 | $NEt_3$ (1.0 equiv) | 0 °C to rt | 72 |
| 16[c] | 1.5 | 1.0 | DABCO (1.0 equiv) | 0 °C to rt | 68 |
| 17[c] | 1.5 | 1.0 | DBU (1.0 equiv) | 0 °C to rt | 67 |
| 18[d] | 1.5 | 0.5 | Cyclohexane (0.5 mL) | rt | 51 |
| 19[d] | 1.5 | 0.5 | Methanol (0.5 mL) | rt | NR |
| 20 | 1.5 | 1.0 | 4 Å molecular sieves | rt | 71 |

[a]**Reaction conditions: 2a** (0.359 mmol), TFAA (0.539 mmol), and **3a** (1 mL) under Argon at room temperature for 7 h, [b]Isolated yield, [c]Reactions were cooled to 0 °C prior to addition of bases and subsequently warmed to rt. [d]Solvent mixture composed of **3a** (0.5 mL) and co-solvent (0.5 mL).

To explore the feasibility of our approach, we began by investigating the decarboxylative arylation between 2-picolinic acid *N*-oxide (PANO, **2a**) and benzene (**3a**, precaution) as the model reaction partners (Table 1). Systematic variation of the amounts of TFAA and benzene revealed that the desired product, 2-phenylpyridine (**1a**), was obtained in 74% yield when 1.5 equiv of TFAA was employed at room temperature. After that, we tried various inorganic and organic bases. The addition of base to the reaction mixture led to an exothermic reaction; therefore, the temperature was maintained at 0 °C during the addition of base, and then it was allowed to rise to room temperature, but no improvement in yield was observed. Later, we examined some co-solvents. When cyclohexane was used, a sudden decrease in the yield was observed, and when methanol was used, no product was observed in the reaction mixture. When 4Å molecular sieves were added to the reaction mixture, no significant change in the yield was observed.

**General procedure**: An oven dried schlenk tube containing a stirrer bar, 2-picolinic acid *N*-oxide or quinaldic acid *N*-oxide or isoquinoline-1-carboxylic acid *N*-oxide was evacuated well, flushed and refilled with argon. Arene/cyclic ether was added *via* syringe and the reaction mixture was stirred at room temperature for 2 min. Then, trifluoroacetic anhydride was added slowly to the reaction mixture *via* syringe and the reaction mixture was stirred at room temperature for 7 h. After completion of reaction, the mixture was diluted with ethyl acetate and washed with saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with ethyl acetate three times and the combined organic phase was dried over anhydrous $Na_2SO_4$. The solvent was evaporated under reduced pressure and the crude product was purified by silica gel column chromatography using ethyl acetate and petroleum ether as eluents to obtain the products **1a-1jj, 5a** & **5b** in moderate to excellent yields.

For entries **1g**, **1h**, and **1l**, after completion of reaction, the mixture was diluted with ethyl acetate and the pH of the aqueous solution was adjusted to 6-7 with saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with ethyl acetate three times and the combined organic phase was dried over anhydrous $Na_2SO_4$. The solvent was evaporated under reduced pressure and the crude product was purified by silica gel column chromatography using ethyl acetate and petroleum ether as eluents to obtain the products.

Decarboxylative coupling of picolinic acid *N*-oxide with cyclic ethers was complete within 2 h, yielding products **5a** and **5b** which are having stability upto 2-3 hours.

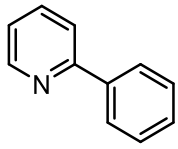
The solid arenes **3h, 3j, 3k, 3l, 3m,** and **3q** (500 mg of each) were dissolved in 0.5 mL of $CCl_4$.

**Typical experimental procedure for the synthesis of representative compound 1a:** An oven-dried Schlenk tube containing a stir bar, 2-picolinic acid *N*-oxide (50 mg, 0.36 mmol, 1 equiv) was evacuated well, flushed and refilled with argon. Benzene (1mL, precaution: Benzene is a volatile and carcinogenic compound and it should be handled only in a well-ventilated fume hood with appropriate PPE and strict safety precautions.) was added *via* syringe and the reaction mixture was stirred at room temperature for 2 min. Then, trifluoroacetic anhydride (75.34 μL, 0.54 mmol, 1.5 eq.) was added slowly to the reaction mixture *via* syringe and the reaction mixture was stirred at room temperature for 7 h. After completion of reaction, the mixture was diluted with ethyl acetate (10 mL) and washed with saturated aqueous $NaHCO_3$ solution (10 mL). The aqueous phase was extracted with ethyl acetate (10 mL) three times and the combined organic phase was dried over anhydrous $Na_2SO_4$. The solvent was evaporated under reduced pressure and the crude product was purified by silica gel column chromatography using ethyl acetate and petroleum ether as eluents (gradient 0 – 10% EtOAc/petroleum ether) to obtain the compound **1a** in 74% yield (41.2 mg).

**Characterization Data of Products 1 & 5:**

The spectroscopic data of all the products are presented. All the known compounds were in accordance with the data reported in the literature.

**2-Phenylpyridine (1a)**[6]

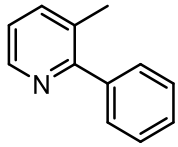


74% (41.2 mg) Colourless oil, $R_f$: 0.4 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.71 (d, *J* = 4.9 Hz, 1 H), 8.03 - 7.99 (m, 2 H), 7.79 - 7.72 (m, 2 H), 7.51 - 7.47 (m, 2 H), 7.45 - 7.41 (m, 1 H), 7.24 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_9N + H)^+$: 156.0, found: 156.0276.

**3-Methyl-2-phenylpyridine (1b)**[6]

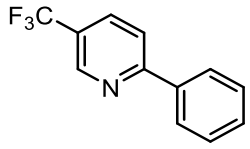


72% (39.8 mg) Colourless oil, $R_f$: 0.2 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.54 (d, *J* = 4.8 Hz, 1 H), 7.59 (d, *J* = 7.6 Hz, 1 H), 7.56 - 7.50 (m, 2 H), 7.49 - 7.43 (m, 2 H), 7.42 - 7.37 (m, 1 H), 7.19 (dd, *J* = 4.8, 7.7 Hz, 1 H), 2.37 (s, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_{11}N + H)^+$: 170.0, found: 170.0164.

**2-Phenyl-5-(trifluoromethyl)pyridine (1c)**[7]

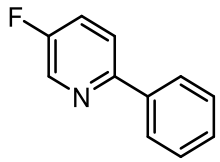


53% (28.3 mg) White solid, mp. 62 – 65 $^o$C; $R_f$: 0.7 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.97 (br. s., 1 H), 8.10 - 7.97 (m, 3 H), 7.86 (d, *J* = 8.0 Hz, 1 H), 7.57 - 7.46 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_8F_3N + H)^+$: 224.0, found: 224.0157.

**5-Fluoro-2-phenylpyridine (1d)**[8]

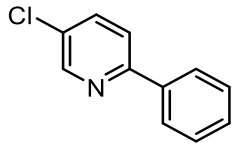


59% (32.3 mg) Pale yellow soid, mp. 41 – 44 ºC; $R_f$: 0.5 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.56 (d, *J* = 2.9 Hz, 1 H), 7.97 - 7.93 (m, 2 H), 7.73 (dd, *J* = 4.3, 8.8 Hz, 1 H), 7.51 - 7.40 (m, 4 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_8FN + H)^+$: 174.0, found: 174.0275.

**5-Chloro-2-phenylpyridine (1e)**[8]

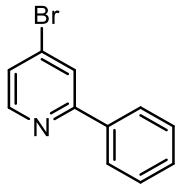


70% (38.3 mg) White solid, mp. 53 – 55 ºC; $R_f$: 0.6 (1 : 9, ethyl acetate : petroleum ether), m.p.= 63.7–64.8°C

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.65 (d, *J* = 1.9 Hz, 1 H), 7.97 (d, *J* = 7.1 Hz, 2 H), 7.77 - 7.65 (m, 2 H), 7.53 - 7.41 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_8ClN + H)^+$: 190.0, found: 189.9782.

**4-Bromo-2-phenylpyridine (1f)**[6]

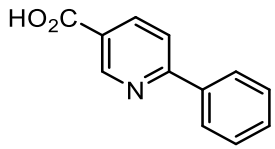


71% (38.2 mg); Colourless oil; $R_f$: 0.5 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.52 (d, *J* = 5.3 Hz, 1 H), 7.98 (dd, *J* = 1.4, 8.0 Hz, 2 H), 7.91 (d, *J* = 1.6 Hz, 1 H), 7.54 - 7.39 (m, 4 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_8BrN + H)^+$: 234.0, found: 233.9733.

**6-Phenylnicotinic acid (1g)**[9]

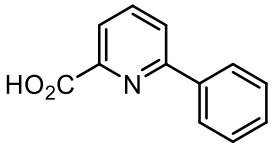


76% (41.5 mg); White solid; mp. 226 – 230 ºC; $R_f$: 0.2 (10 : 0, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 13.36 (br. s., 1 H), 9.21 - 9.10 (m, 1 H), 8.33 (dd, *J* = 2.0, 8.3 Hz, 1 H), 8.19 - 8.09 (m, 3 H), 7.56 - 7.48 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_9NO_2 + H)^+$: 200.1, found: 200.0012.

**6-Phenylpicolinic acid (1h)**[10]

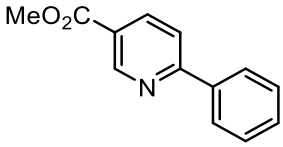


61% (33.1 mg); White solid; mp. 98 – 102 ºC; $R_f$: 0.3 (10 : 0, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, DMSO-*d*$_6$):** $\delta$ 13.01 (br. s., 1 H), 8.24 - 8.15 (m, 3 H), 8.06 (t, *J* = 7.6 Hz, 1 H), 8.00 (d, *J* = 7.4 Hz, 1 H), 7.57 - 7.45 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_9NO_2 + H)^+$: 200.1, found: 200.0015.

**Methyl 6-phenylnicotinate (1i)**[6]

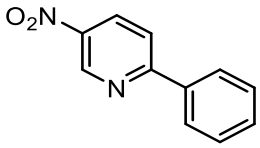


61% (32.9 mg); White solid; mp. 110 – 113 ºC; $R_f$: 0.2 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 9.29 (d, *J* = 1.9 Hz, 1 H), 8.36 (dd, *J* = 2.1, 8.4 Hz, 1 H), 8.07 (dd, *J* = 1.4, 7.9 Hz, 2 H), 7.82 (d, *J* = 8.3 Hz, 1 H), 7.58 - 7.41 (m, 3 H), 3.98 (s, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{13}H_{11}NO_2 + H)^+$: 214.1, found: 214.0124.

**5-Nitro-2-phenylpyridine (1j)**[6]

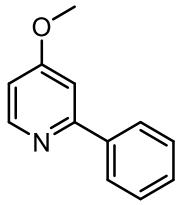


46% (25.0 mg); White solid; mp. 118 – 120 ºC; $R_f$: 0.4 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*):** $\delta$ 9.51 (d, *J* = 2.3 Hz, 1 H), 8.54 (dd, *J* = 2.7, 8.8 Hz, 1 H), 8.12 - 8.09 (m, 2 H), 7.94 - 7.91 (m, 1 H), 7.56 - 7.52 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_8N_2O_2 + H)^+$: 201.1, found: 200.9759.

**4-Methoxy-2-phenylpyridine (1k)**[7]

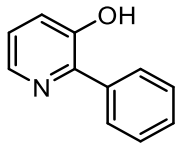


56% (30.5 mg); Colourless oil; $R_f$: 0.4 (3 : 7, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*):** $\delta$ 8.53 (d, *J* = 5.6 Hz, 1 H), 7.97 (d, *J* = 7.8 Hz, 2 H), 7.50 - 7.40 (m, 3 H), 7.24 (s, 1 H), 6.80 - 6.77 (m, 1 H), 3.91 (s, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_{11}NO + H)^+$: 186.1, found: 186.0617.

**2-Phenylpyridin-3-ol (1l)**[11]

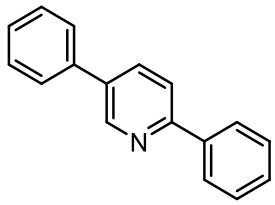


50% (27.5 mg); White solid; mp. 209 – 212 ºC; $R_f$: 0.3 (3 : 7, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, DMSO-*d*$_6$):** $\delta$ 10.11 (br. s., 1 H), 8.15 (br. s., 1 H), 8.00 (d, *J* = 6.1 Hz, 2 H), 7.42 (br. s., 2 H), 7.38 - 7.30 (m, 2 H), 7.19 (br. s., 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_9NO + H)^+$: 172.1, found: 172.0329.

**2,5-Diphenylpyridine (1m)**[6]

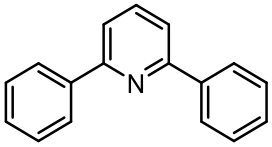


56% (30.1 mg); White solid; mp. 165 – 169 ºC; $R_f$: 0.5 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.96 (d, *J* = 2.0 Hz, 1 H), 8.08 - 8.04 (m, 2 H), 7.98 (dd, *J* = 2.4, 8.3 Hz, 1 H), 7.85 - 7.81 (m, 1 H), 7.68 - 7.64 (m, 2 H), 7.54 - 7.48 (m, 4 H), 7.47 - 7.41 (m, 2 H)

**LCMS-ESI** (m/z) calcd for $(C_{17}H_{13}N + H)^+$: 232.1, found: 232.0658.

**2,6-Diphenylpyridine (1n)**[12]

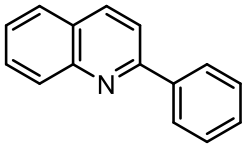


51% (27.5 mg); White solid; mp. 63 – 66 ºC; $R_f$: 0.6 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.22 - 8.15 (m, 4 H), 7.83 (dd, *J* = 7.3, 8.4 Hz, 1 H), 7.71 (d, *J* = 7.6 Hz, 2 H), 7.56 - 7.50 (m, 4 H), 7.49 - 7.41 (m, 2 H)

**LCMS-ESI** (m/z) calcd for $(C_{17}H_{13}N + H)^+$: 232.1, found: 232.0711.

**2-Phenylquinoline (1o)**[6]

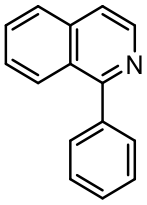


59% (32.0 mg); Yellow solid; mp. 80 – 83 ºC; $R_f$: 0.5 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.24 (d, *J* = 8.6 Hz, 1 H), 8.22 - 8.16 (m, 3 H), 7.89 (d, *J* = 8.6 Hz, 1 H), 7.84 (d, *J* = 8.0 Hz, 1 H), 7.77 - 7.72 (m, 1 H), 7.57 - 7.52 (m, 3 H), 7.51 - 7.46 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{15}H_{11}N + H)^+$: 206.1, found: 206.0499.

**1-Phenylisoquinoline (1p)**[6]

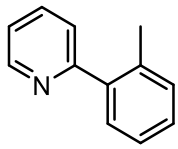


43% (23.4 mg); Pale yellow solid; mp. 94 – 97 ºC; $R_f$: 0.2 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*):** $\delta$ 8.63 (d, *J* = 5.8 Hz, 1 H), 8.12 (d, *J* = 8.5 Hz, 1 H), 7.90 (d, *J* = 8.3 Hz, 1 H), 7.73 - 7.68 (m, 3 H), 7.66 (d, *J* = 5.6 Hz, 1 H), 7.57 - 7.49 (m, 4 H)

**LCMS-ESI** (m/z) calcd for $(C_{15}H_{11}N + H)^+$: 206.1, found: 206.0176.

**2-(*o*-Tolyl)pyridine (*o*-1r)**[13]

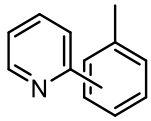


23% (14.2 mg); Colourless oil; $R_f$: 0.2 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.73 - 8.69 (m, 1 H), 7.75 (m, 1 H), 7.41 (d, *J* = 7.9 Hz, 2 H), 7.33 - 7.27 (m, 3 H), 7.27 - 7.23 (m, 1 H), 2.38 (s, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_{11}N + H)^+$: 170.1, found: 170.0745.

**2-(*m*-Tolyl)pyridine (*m*-1r)**[13] **and 2-(*p*-tolyl)pyridine (*p*-1r)**[13]



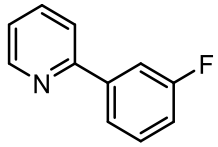
36% (21.7 mg); Colourless oil; $R_f$: 0.4 (1 : 9, ethyl acetate : petroleum ether)

*m*-3ab : *p*-3ab = 1.14 : 1.0 (detected by $^1$H NMR).

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.73 - 8.66 (m, 1 H), 7.93 - 7.69 (m, 4 H), 7.40 - 7.19 (m, 3 H), 2.44 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_{11}N + H)^+$: 170.1, found: 170.0954.

**2-(3-Fluorophenyl)pyridine (*m*-1s)**[14]

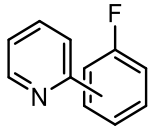


11% (7.1 mg); pale yellow oil; $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*):** $\delta$ 8.71 (d, *J* = 4.6 Hz, 1 H), 7.81 - 7.70 (m, 4 H), 7.44 (m, 1 H), 7.29 - 7.25 (m, 1 H), 7.12 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_8FN + H)^+$: 174.1, found: 174.0001.

**2-(2-Fluorophenyl)pyridine (*o*-1s)**[15] **and 2-(4-fluorophenyl)pyridine (*p*-1s)**[15]



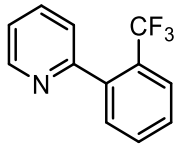
40% (25.1 mg); pale yellow oil; $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

*o*-3ab : *p*-3ab = 1.28 : 1.0 (detected by $^1$H NMR).

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.77 - 8.65 (m, 1 H), 8.07 - 7.33 (m, 4 H), 7.30 - 7.12 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_8FN + H)^+$: 174.1, found: 174.0275.

**2-(2-(tri-Fluoromethyl)phenyl)pyridine (*o*-1t)**[16]

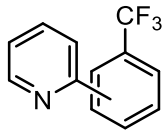



13% (10.8 mg) Colourless oil, $R_f$: 0.2 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.70 (d, *J* = 4.6 Hz, 1 H), 7.80 - 7.74 (m, 2 H), 7.66 - 7.60 (m, 1 H), 7.56 - 7.49 (m, 2 H), 7.44 (d, *J* = 7.9 Hz, 1 H), 7.35 - 7.30 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_8F_3N + H)^+$: 224.1, found: 224.0403.

**2-(3-(tri-Fluoromethyl)phenyl)pyridine (*m*-1t)**[17] **and 2-(4-(trifluoromethyl)phenyl)pyridine (*p*-1t)**[17]



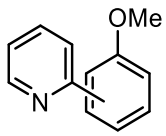

31% (24.9 mg) Colourless oil, $R_f$: 0.4 (1 : 9, ethyl acetate : petroleum ether)

*m*-3ab : *p*-3ab = 3.7 : 1.0 (detected by $^1$H NMR).

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.74 (d, *J* = 4.5 Hz, 1 H), 8.30 - 8.11 (m, 2 H), 7.83 - 7.58 (m, 4 H), 7.31 – 7.29 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_8F_3N + H)^+$: 224.1, found: 223.9911.

**2-(2-Methoxyphenyl)pyridine (*o*-1u)**[18]**, 2-(3-methoxyphenyl)pyridine (*m*-1u)**[18]**, and 2-(4-methoxyphenyl)pyridine (*p*-1u)**[18]



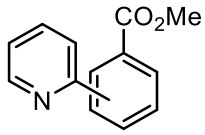

54% (36.0 mg); pale yellow oil; $R_f$: 0.2 (1 : 9, ethyl acetate : petroleum ether)

*o*-3ae : *m*-3ae : *p*-3ae = 3.31 : 1.0 : 2.62 (detected by $^1$H NMR).

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.78 - 8.59 (m, 1 H), 7.99 - 7.35 (m, 4 H), 7.25 - 6.97 (m, 3 H), 3.91 - 3.85 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_{11}NO + H)^+$: 186.1, found: 186.0520.

**Methyl 2-(pyridin-2-yl)benzoate (*o*-1v)[19], methyl 3-(pyridin-2-yl)benzoate (*m*-1v)[19], and methyl 4-(pyridin-2-yl)benzoate (*p*-1v)[19]**



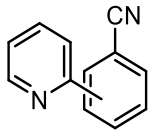

28% (21.3 mg); pale yellow oil; $R_f$: 0.5 (3 : 7, ethyl acetate : petroleum ether)

*o*-3ae : *m*-3ae : *p*-3ae = 1.70 : 2.31 : 1.0 (detected by $^1$H NMR).

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.75 - 8.06 (m, 3 H), 7.86 - 7.71 (m, 2 H), 7.62 - 7.21 (m, 3 H), 3.97 - 3.68 (m, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{13}H_{11}NO_2 + H)^+$: 214.1, found: 214.0131.

**2-(Pyridin-2-yl)benzonitrile (*o*-1w)[20], 3-(pyridin-2-yl)benzonitrile (*m*-1w)[21], and 4-(pyridin-2-yl)benzonitrile (*p*-1w)[21]**



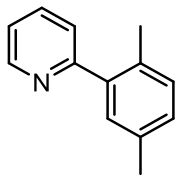

21% (13.6 mg); Colourless oil; $R_f$: 0.4 (3 : 7, ethyl acetate : petroleum ether)

*o*-3ae : *m*-3ae : *p*-3ae = 1.0 : 2.69 : 2.11 (detected by $^1$H NMR).

**$^1$H NMR (400MHz, CHLOROFORM-*d*):** $\delta$ 8.77 - 8.68 (m, 1 H), 8.34 - 8.11 (m, 2 H), 7.84 -7.55 (m, 4 H), 7.35 - 7.28 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_8N_2 + H)^+$: 181.1, found: 181.0473.

**2-(2,5-Dimethylphenyl)pyridine (1x)[6]**

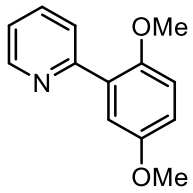



44% (28.8 mg); Colourless oil, $R_f$: 0.4 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.73 - 8.68 (m, 1 H), 7.74 (m, 1 H), 7.41 (m, 1 H), 7.26 - 7.22 (m, 2 H), 7.18 (d, *J* = 7.8 Hz, 1 H), 7.15 - 7.11 (m, 1 H), 2.37 (s, 3 H), 2.33 (s, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{13}H_{13}N + H)^+$: 184.1, found: 184.0385.

**2-(2,5-Dimethoxyphenyl)pyridine (1y)**



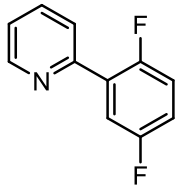

38% (29.1 mg); Colourless oil; $R_f$: 0.1 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.71 (d, *J* = 4.1 Hz, 1 H), 7.85 (d, *J* = 8.0 Hz, 1 H), 7.70 (m, 1 H), 7.39 (d, *J* = 2.3 Hz, 1 H), 7.21 (m, 1 H), 6.96 - 6.91 (m, 2 H), 3.84 (s, 3 H), 3.81 (s, 3 H)

**$^{13}$C NMR (101MHz, CHLOROFORM-*d*)** $\delta$ 155.8, 153.9, 151.2, 149.3, 135.6, 129.7, 125.1, 121.7, 115.7, 115.6, 113.0, 56.3, 55.8

**HRMS-ESI** (m/z) calcd for $(C_{13}H_{13}NO_2 + H)^+$: 216.1014, found: 216.1019.

**2-(2,5-Difluorophenyl)pyridine (1z)**[6]

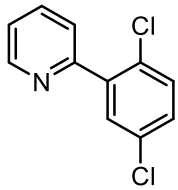



34% (23.1 mg); White solid; mp. 30 – 33 $^o$C; $R_f$: 0.5 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.74 (d, *J* = 4.8 Hz, 1 H), 7.85 - 7.82 (m, 1 H), 7.80 - 7.73 (m, 2 H), 7.30 (m, 1 H), 7.17 - 7.03 (m, 2 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_7F_2N + H)^+$: 192.1, found: 192.0178.

**2-(2,5-Dichlorophenyl)pyridine (1aa)**[22]

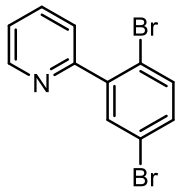



14% (11.4 mg); White solid; mp. 89 – 92 $^o$C; $R_f$: 0.5 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.73 (d, *J* = 4.3 Hz, 1 H), 7.79 (m, 1 H), 7.70 - 7.60 (m, 2 H), 7.44 - 7.39 (m, 1 H), 7.34 - 7.30 (m, 2 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_7Cl_2N + H)^+$: 224.0, found: 223.9300.

**2-(2,5-Dibromophenyl)pyridine (1bb)**[23]

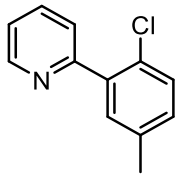



3% (3.2 mg); White solid; mp. 75 – 80 ºC; $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.73 (d, *J* = 4.3 Hz, 1 H), 7.79 (m, 1 H), 7.70 (d, *J* = 2.4 Hz, 1 H), 7.61 (d, *J* = 7.8 Hz, 1 H), 7.54 (d, *J* = 8.5 Hz, 1 H), 7.39 (dd, *J* = 2.4, 8.5 Hz, 1 H), 7.33 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_7Br_2N + H)^+$: 311.9, found: 311.8870.

**2-(2-Chloro-5-methylphenyl)pyridine (*o*-1cc)**[24]

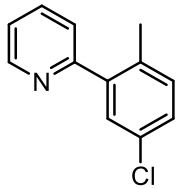



26% (19.1 mg); Pale yellow oil; $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.73 (d, *J* = 4.8 Hz, 1 H), 7.76 (t, *J* = 7.7 Hz, 1 H), 7.66 (d, *J* = 7.8 Hz, 1 H), 7.43 (s, 1 H), 7.36 (d, *J* = 8.1 Hz, 1 H), 7.31 - 7.26 (m, 1 H), 7.15 (d, *J* = 8.1 Hz, 1 H), 2.38 (s, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_{10}ClN + H)^+$: 204.1, found: 203.9680.

**2-(5-Chloro-2-methylphenyl)pyridine (*m*-1cc)**[25]

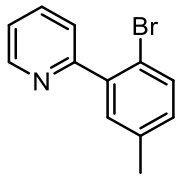



20% (14.5 mg); Pale yellow oil; $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.71 (d, *J* = 4.8 Hz, 1 H), 7.83 - 7.74 (m, 1 H), 7.48 - 7.34 (m, 2 H), 7.31 - 7.26 (m, 2 H), 7.24 - 7.19 (m, 1 H), 2.33 (s, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_{10}ClN + H)^+$: 204.1, found: 203.9652.

**2-(2-Bromo-5-methylphenyl)pyridine (*o*-1dd)**[26]

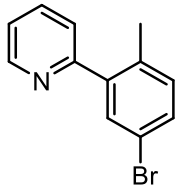



22% (19.8 mg) Colourless oil, $R_f$: 0.2 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.71 (d, *J* = 4.9 Hz, 1 H), 7.76 (m, 1 H), 7.61 (d, *J* = 7.9 Hz, 1 H), 7.55 (d, *J* = 8.1 Hz, 1 H), 7.39 - 7.35 (m, 1 H), 7.31 - 7.27 (m, 1 H), 7.07 (dd, *J* = 2.1, 8.1 Hz, 1 H), 2.36 (s, 3 H)

**LCMS-ESI** (m/z) calcd for $(C_{12}H_{10}BrN + H)^+$: 248.0, found: 247.9539.

**2-(5-Bromo-2-methylphenyl)pyridine (*m*-1dd)**



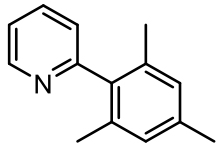

14% (12.3 mg) Colourless oil, $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.70 (d, *J* = 4.3 Hz, 1 H), 7.76 (m, 1 H), 7.55 (d, *J* = 2.1 Hz, 1 H), 7.44 - 7.37 (m, 2 H), 7.30 - 7.25 (m, 1 H), 7.16 (d, *J* = 8.1 Hz, 1 H), 2.31 (s, 3 H)

**$^{13}$C NMR (101MHz, CHLOROFORM-*d*)**: $\delta$ 158.5, 149.3, 142.2, 136.3, 134.7, 132.3 (2C), 131.1, 124.0, 122.1, 119.3, 19.8

**HRMS-ESI** (m/z) calcd for $(C_{12}H_{10}Br^{79}N + H)^+$: 248.0071, found: 248.0069.

**2-Mesitylpyridine (1ee)**[27]

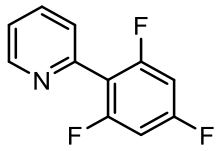



46% (32.3 mg); Pale yellow oil; $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.74 - 8.69 (m, 1 H), 7.75 (m, 1 H), 7.27 - 7.21 (m, 2 H), 6.94 (s, 2 H), 2.33 (s, 3 H), 2.03 (s, 6 H)

**LCMS-ESI** (m/z) calcd for $(C_{14}H_{15}N + H)^+$: 198.1, found: 198.0566.

**2-(2,4,6-tri-Fluorophenyl)pyridine (1ff)**[28]

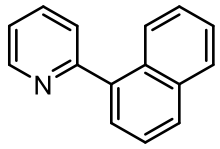


21% (16.0 mg) Colourless oil, $R_f$: 0.4 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.77 (d, *J* = 4.0 Hz, 1 H), 7.87 - 7.75 (m, 1 H), 7.47 (d, *J* = 7.8 Hz, 1 H), 7.34 (dd, *J* = 5.5, 6.9 Hz, 1 H), 6.79 (t, *J* = 8.1 Hz, 2 H)

**LCMS-ESI** (m/z) calcd for $(C_{11}H_6F_3N + H)^+$: 210.0, found: 210.0121.

**2-(Naphthalen-1-yl)pyridine ($\alpha$-1gg)**[18]

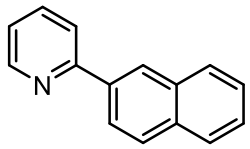


28% (20.4 mg); Yellow oil; $R_f$: 0.2 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.82 (d, *J* = 4.8 Hz, 1 H), 8.10 (d, *J* = 7.8 Hz, 1 H), 7.93 (d, *J* = 8.1 Hz, 2 H), 7.84 (m, 1 H), 7.66 - 7.45 (m, 5 H), 7.39 - 7.31 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{15}H_{11}N + H)^+$: 206.1, found: 206.0238.

**2-(Naphthalen-2-yl)pyridine ($\beta$-1gg)**[18]

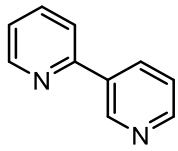


21% (15.5 mg); Yellow solid; mp. 76 – 78 $^o$C; $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.77 (d, *J* = 4.5 Hz, 1 H), 8.50 (s, 1 H), 8.20 - 8.13 (m, 1 H), 7.96 (d, *J* = 7.8 Hz, 2 H), 7.89 (d, *J* = 7.1 Hz, 2 H), 7.84 - 7.77 (m, 1 H), 7.58 - 7.48 (m, 2 H), 7.29 – 7.26 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{15}H_{11}N + H)^+$: 206.1, found: 206.0344.

**2,3'-Bipyridine (1hh)**[29]

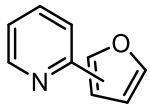


20% (11.3 mg); Yellow oil; $R_f$: 0.4 (10 : 0, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 9.21 (s, 1 H), 8.74 (d, *J* = 4.6 Hz, 1 H), 8.67 (d, *J* = 4.5 Hz, 1 H), 8.34 (d, *J* = 8.0 Hz, 1 H), 7.84 - 7.75 (m, 2 H), 7.42 (dd, *J* = 4.9, 7.9 Hz, 1 H), 7.36 - 7.28 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_{10}H_8N_2 + H)^+$: 157.1, found: 157.0038.

**2-(Furan-2-yl)pyridine (*2*-1ii)**[27] **and 2-(furan-3-yl)pyridine (*3*-1ii)**[30]



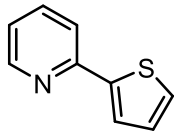
76% (39.5 mg) Colourless oil, $R_f$: 0.8 (1 : 9, ethyl acetate : petroleum ether)

*2*-1ii : *3*-31ii = 3.83 : 1.0 (detected by $^1$H NMR).

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.63 - 8.55 (m, 1 H), 7.88 - 7.64 (m, 2 H), 7.54 - 7.43 (m, 1 H), 7.16 - 7.12 (m, 1 H), 7.07 - 6.98 (m, 1 H), 6.54 – 6.52 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_9H_7NO + H)^+$: 146.1, found: 146.0257.

**2-(Thiophen-2-yl)pyridine (*2*-1jj)**[31]

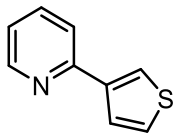


55% (31.9 mg); White solid; mp. 59 – 60 $^o$C; $R_f$: 0.2 (0.5 : 9.5, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.57 (d, *J* = 4.8 Hz, 1 H), 7.70 - 7.64 (m, 2 H), 7.60 - 7.57 (m, 1 H), 7.40 (dd, *J* = 0.9, 5.1 Hz, 1 H), 7.16 - 7.10 (m, 2 H)

**LCMS-ESI** (m/z) calcd for $(C_9H_7NS + H)^+$: 162.0, found: 161.9718.

**2-(Thiophen-3-yl)pyridine (*3*-1jj)**[32]

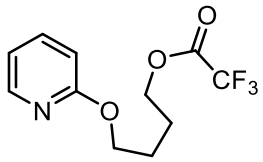


25% (14.3 mg); Pale yellow oil; $R_f$: 0.2 (0.5 : 9.5, ethyl acetate : petroleum ether)

**$^{1}$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.63 (d, *J* = 4.5 Hz, 1 H), 7.91 (dd, *J* = 1.1, 3.0 Hz, 1 H), 7.74 - 7.61 (m, 3 H), 7.41 (dd, *J* = 3.0, 5.0 Hz, 1 H), 7.18 (m, 1 H)

**LCMS-ESI** (m/z) calcd for $(C_9H_7NS + H)^+$: 162.0, found: 161.9719.

**4-(Pyridin-2-yloxy)butyl 2,2,2-trifluoroacetate (5a)**



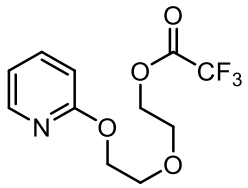
60% (57.1 mg); Pale yellow oil; $R_f$: 0.3 (1 : 9, ethyl acetate : petroleum ether)

**$^{1}$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.20 - 8.09 (m, 1 H), 7.59 - 7.54 (m, 1 H), 6.89 - 6.84 (m, 1 H), 6.72 (d, *J* = 8.4 Hz, 1 H), 4.44 (t, *J* = 6.3 Hz, 2 H), 4.34 (t, *J* = 6.0 Hz, 2 H), 1.99 - 1.85 (m, 4 H)

**$^{13}$C NMR (101MHz, CHLOROFORM-*d*)**: $\delta$ 163.7, 157.5 (q, $J_{C,F}$ = 42.21 Hz), 146.8, 138.6, 116.7, 114.5 (q, $J_{C,F}$ = 285.59 Hz), 111.0, 67.9, 64.7, 25.2, 25.1

**HRMS-ESI** (m/z) calcd for $(C_{11}H_{12}F_3NO_3 + H)^+$: 264.0842, found: 264.0842.

**2-(2-(Pyridin-2-yloxy)ethoxy)ethyl 2,2,2-trifluoroacetate (5b)**



70% (70.5 mg); Colourless oil; $R_f$: 0.5 (3 : 7, ethyl acetate : petroleum ether)

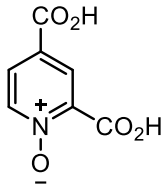
**$^{1}$H NMR (400MHz, CHLOROFORM-*d*)**: $\delta$ 8.13 (dd, *J* = 1.3, 5.0 Hz, 1 H), 7.60 - 7.55 (m, 1 H), 6.87 (m, 1 H), 6.77 (d, *J* = 8.4 Hz, 1 H), 4.53 - 4.50 (m, 2 H), 4.50 - 4.47 (m, 2 H), 3.88 - 3.84 (m, 4 H)

**$^{13}$C NMR (101MHz, CHLOROFORM-*d*)**: $\delta$ 163.4, 157.5 (q, $J_{C,F}$ = 42.47 Hz), 146.7, 138.6, 116.9, 114.5 (q, $J_{C,F}$ = 285.59 Hz), 111.2, 69.9, 68.1, 66.9, 64.8

**HRMS-ESI** (m/z) calcd for $(C_{11}H_{12}F_3NO_4 + H)^+$: 280.0792, found: 280.0791.

**2.3) Total synthesis of Lucidimine E and Australine (Experimental procedures and Data)**

**Pyridine-2,4-dicarboxylic acid *N*-oxide (2q):** Compound **2g** was prepared from pyridine-2,4-dicarboxylic acid according to the general procedure A. Pyridine-2,4-dicarboxylic acid (500 mg, 2.99 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (TFA, 7.47 mL) and then 30% $H_2O_2$ (2.38 mL, 77.79 mmol, 26.0 equiv) was added dropwise with caution. The reaction mixture was heated at 80 °C for 12 h. The solution was concentrated *in vacuo*, and the concentrate was diluted with water (30 mL), which resulted in the immediate formation of a precipitate. The precipitate was vacuum-filtered and dried to afford the desired product **2q** as white solid (467.1 mg, 85%) without the need for column chromatography.



mp. 256 – 262 ºC; $R_f$: 0.3 (3 : 7, methanol : dichloromethane)

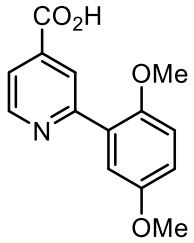
**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 14.24 (br. s., 1 H), 8.77 (d, *J* = 6.6 Hz, 1 H), 8.51 (d, *J* = 2.5 Hz, 1 H), 8.17 (dd, *J* = 2.6, 6.7 Hz, 1 H)

**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 163.8, 160.5, 140.2, 137.0, 132.7, 129.1, 127.9

**HRMS-ESI** (m/z) calcd for $(C_7H_5NO_5 + H)^+$: 184.0240, found: 184.0240.

**2-(2,5-Dimethoxyphenyl)isonicotinic acid (6)**

An oven-dried Schlenk tube containing a stir bar, pyridine-2,4-dicarboxylic acid *N*-oxide (50mg, 0.27 mmol, 1eq.) and 1,4-Dimethoxybenzene (500 mg) was evacuated well, flushed and refilled with argon. $CCl_4$ (1.0 mL) was added *via* syringe and the reaction mixture was stirred at room temperature for 2 min. Then, trifluoroacetic anhydride (57.23 μL, 0.41 mmol, 1.5 eq.) was added slowly to the reaction mixture *via* syringe and the reaction mixture was stirred at room temperature for 7 h. After completion of reaction, the mixture was diluted with ethyl acetate (10 mL) the pH of the aqueous solution was adjusted to 6-7 with saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with ethyl acetate (10 mL) three times and the combined organic phase was dried over anhydrous $Na_2SO_4$. The solvent was evaporated under reduced pressure and the crude product was purified by silica gel column chromatography using ethyl acetate and petroleum ether as eluents (gradient 60 – 100% EtOAc/petroleum ether) to obtain the desired product **6** as pale yellow solid (24.5 mg, 35%).




mp. 207 – 210 ºC; $R_f$: 0.5 (1 : 9, methanol : dichloromethane)

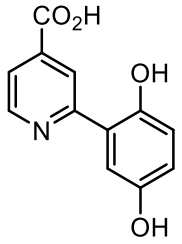
**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 13.62 (br. s., 1 H), 8.83 (br. s., 1 H), 8.33 (br. s., 1 H), 7.74 (br. s., 1 H), 7.37 (br. s., 1 H), 7.16 - 6.96 (m, 2 H), 3.80 (br. s., 3 H), 3.76 (br. s., 3 H)

**$^{13}$C NMR (101MHz, DMSO-*d*$_6$)**: $\delta$ 166.5, 155.8, 153.3, 151.1, 150.3, 138.4, 128.1, 123.7, 121.0, 115.8, 115.5, 113.5, 56.3, 55.5

**HRMS-ESI** (m/z) calcd for $(C_{14}H_{13}NO_4 + H)^+$: 260.0918, found: 260.0917.

**2-(2,5-Dihydroxyphenyl)isonicotinic acid (7)**

2-(2,5-Dimethoxyphenyl)isonicotinic acid (**6**, 90 mg, 0.35 mmol, 1.0 equiv) was dissolved in DCM (3.0 mL) and then $BBr_3$ (133.79 µL, 1.39 mmol, 4.0 equiv) was added dropwise with caution under argon atmosphere. The reaction mixture was stirred at room temperature for overnight under argon. The reaction mixture was then slowly quenched with ice-cold water, and extracted with ethyl acetate (10 mL) three times and the combined organic phase was dried over anhydrous $Na_2SO_4$. The solvent was evaporated under reduced pressure to obtain the compound **7** as yellow solid (74.2 mg, 92 %).




mp. 284 – 288 ºC; $R_f$: 0.6 (3 : 7, methanol : dichloromethane)

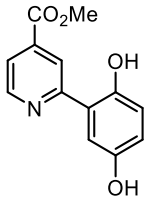
**$^1$H NMR (400MHz, DMSO-*d*$_6$)**: $\delta$ 13.79 (br. s., 1 H), 12.34 (br. s., 1 H), 8.95 (br. s., 1 H), 8.83 - 8.74 (m, 1 H), 8.39 (br. s., 1 H), 7.84 - 7.69 (m, 1 H), 7.36 (br. s., 1 H), 6.79 (br. s., 2 H)

**$^{13}$C NMR (126MHz, DMSO-*d*$_6$)**: $\delta$ 166.0, 157.4, 151.1, 149.8, 148.2, 139.9, 120.8, 119.5, 119.5, 119.3, 118.4, 112.6

**HRMS-ESI** (m/z) calcd for $(C_{12}H_9NO_4 + H)^+$: 232.0605, found: 232.0604.

**Lucidimine E (8)**[33]

Thionyl chloride (18.94 µL, 0.26 mmol, 2.0 equiv.) was added dropwise to a stirred suspension of 2-(2,5-dihydroxyphenyl)isonicotinic acid (30 mg, 0.13 mmol, 1.0 equiv.) in anhydrous methanol (2 mL) at 0 °C. The reaction mixture was warmed to room temperature and refluxed for 3 h. After completion, the solvent was evaporated under reduced pressure to afford Lucidimine E (**8**, 27.9 mg, 88%) as yellow solid.




mp. 186 – 188 ºC; $R_f$: 0.36 (3 : 7, ethyl acetate : petroleum ether)

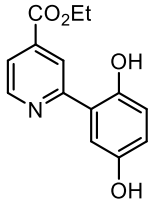
**$^1$H NMR (400MHz, METHANOL-*d*$_4$)**: $\delta$ 8.70 (d, *J* = 5.1 Hz, 1 H), 8.42 (s, 1 H), 7.80 (dd, *J* = 1.0, 5.1 Hz, 1 H), 7.31 (d, *J* = 2.1 Hz, 1 H), 6.86 - 6.75 (m, 2 H), 4.00 (s, 3 H)

**$^{13}$C NMR (101MHz, METHANOL-*d*$_4$)**: $\delta$ 166.7, 160.1, 153.7, 151.3, 148.8, 140.6, 121.8, 120.9, 120.3, 120.3, 120.0, 113.4, 53.6

**HRMS-ESI** (m/z) calcd for $(C_{13}H_{11}NO_4 + H)^+$: 246.0761, found: 246.0761.

**Australine (9)**[34]

Thionyl chloride (18.94 µL, 0.26 mmol, 2.0 equiv.) was added dropwise to a stirred suspension of 2-(2,5-dihydroxyphenyl)isonicotinic acid (30 mg, 0.13 mmol, 1.0 equiv.) in anhydrous ethanol (2 mL) at 0 °C. The reaction mixture was warmed to room temperature and refluxed for 5 h. After completion, the solvent was evaporated under reduced pressure to afford Australine (**9**, 28.6 mg, 85%) as yellow solid.




mp. 158 – 161 ºC; $R_f$: 0.44 (3 : 7, ethyl acetate : petroleum ether)

**$^1$H NMR (400MHz, METHANOL-*d*$_4$)**: $\delta$ 8.65 (d, *J* = 5.1 Hz, 1 H), 8.36 (s, 1 H), 7.76 (dd, *J* = 1.0, 5.1 Hz, 1 H), 7.27 (d, *J* = 2.4 Hz, 1 H), 6.86 - 6.74 (m, 2 H), 4.43 (q, *J* = 7.1 Hz, 2 H), 1.43 (t, *J* = 7.1 Hz, 3 H)

**$^{13}$C NMR (101MHz, METHANOL-*d*$_4$)**: $\delta$ 166.2, 159.9, 153.7, 151.2, 148.7, 140.8, 121.8, 120.9, 120.2, 120.1, 120.0, 113.2, 63.4, 14.6

**HRMS-ESI** (m/z) calcd for $(C_{14}H_{13}NO_4 + H)^+$: 260.0918, found: 260.0917.

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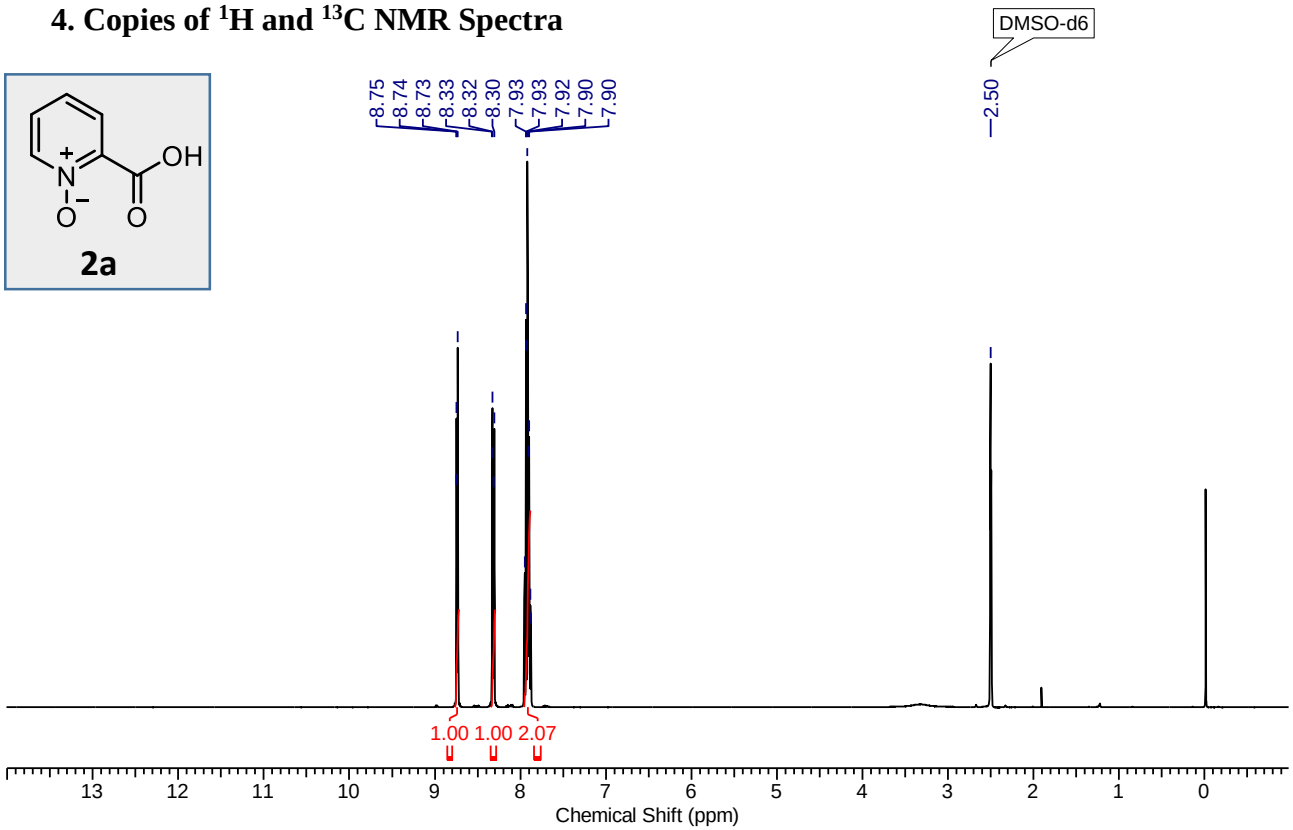
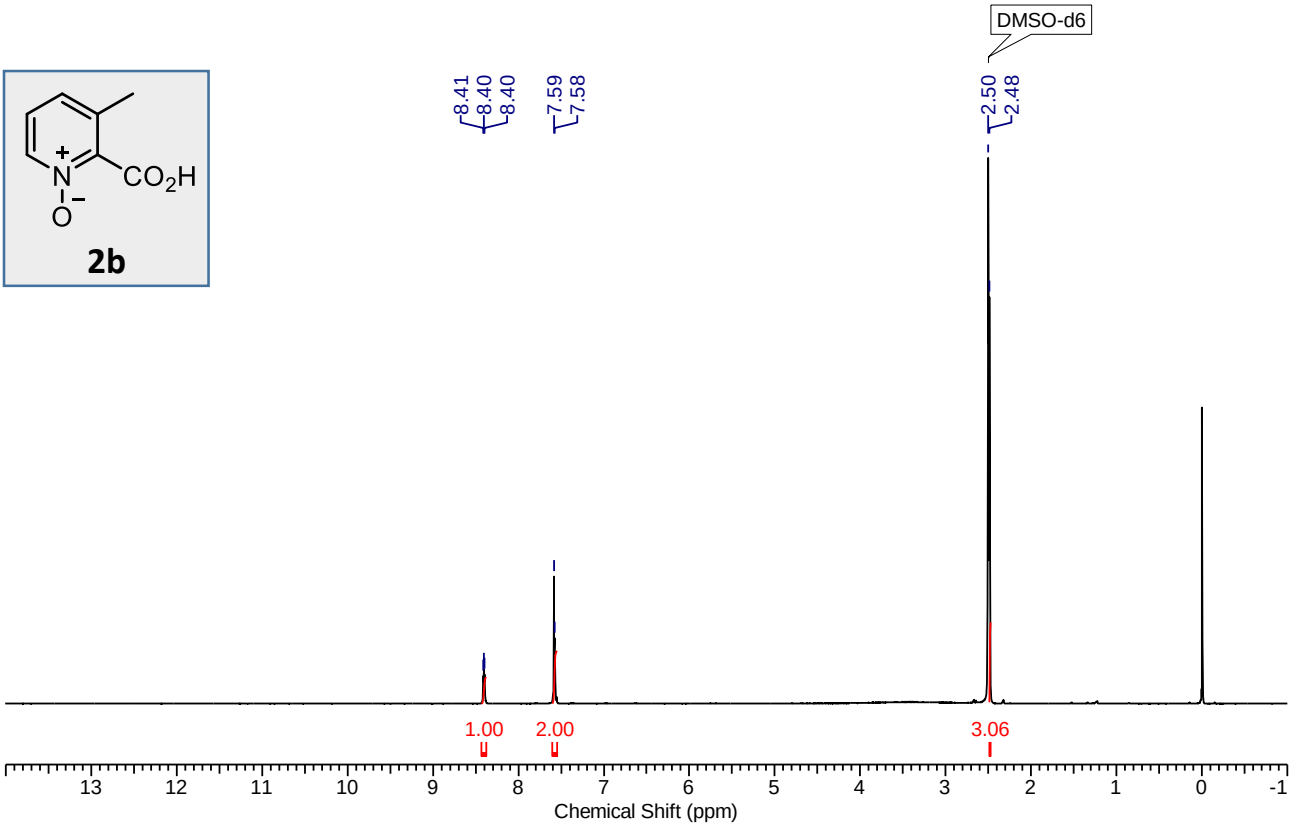
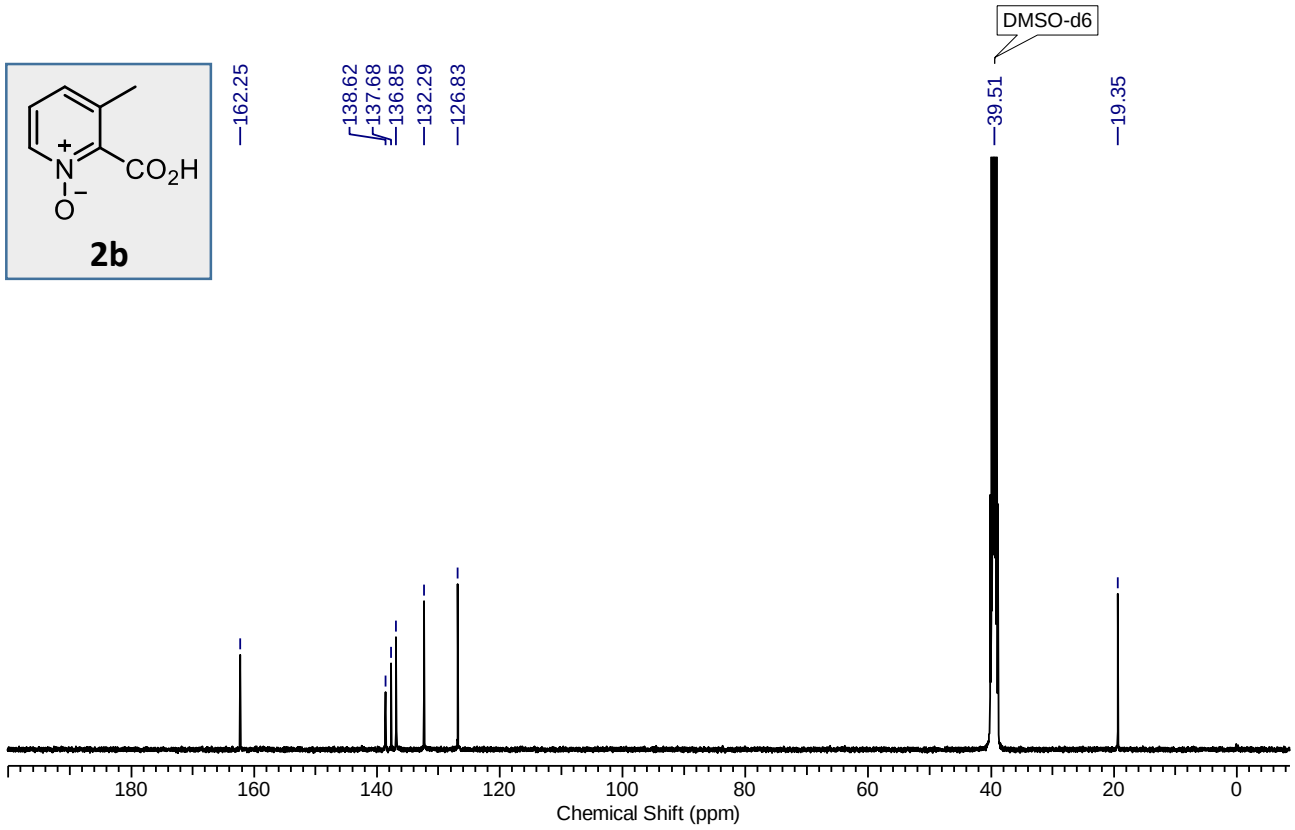
## 4. Copies of $^{1}H$ and $^{13}C$ NMR Spectra



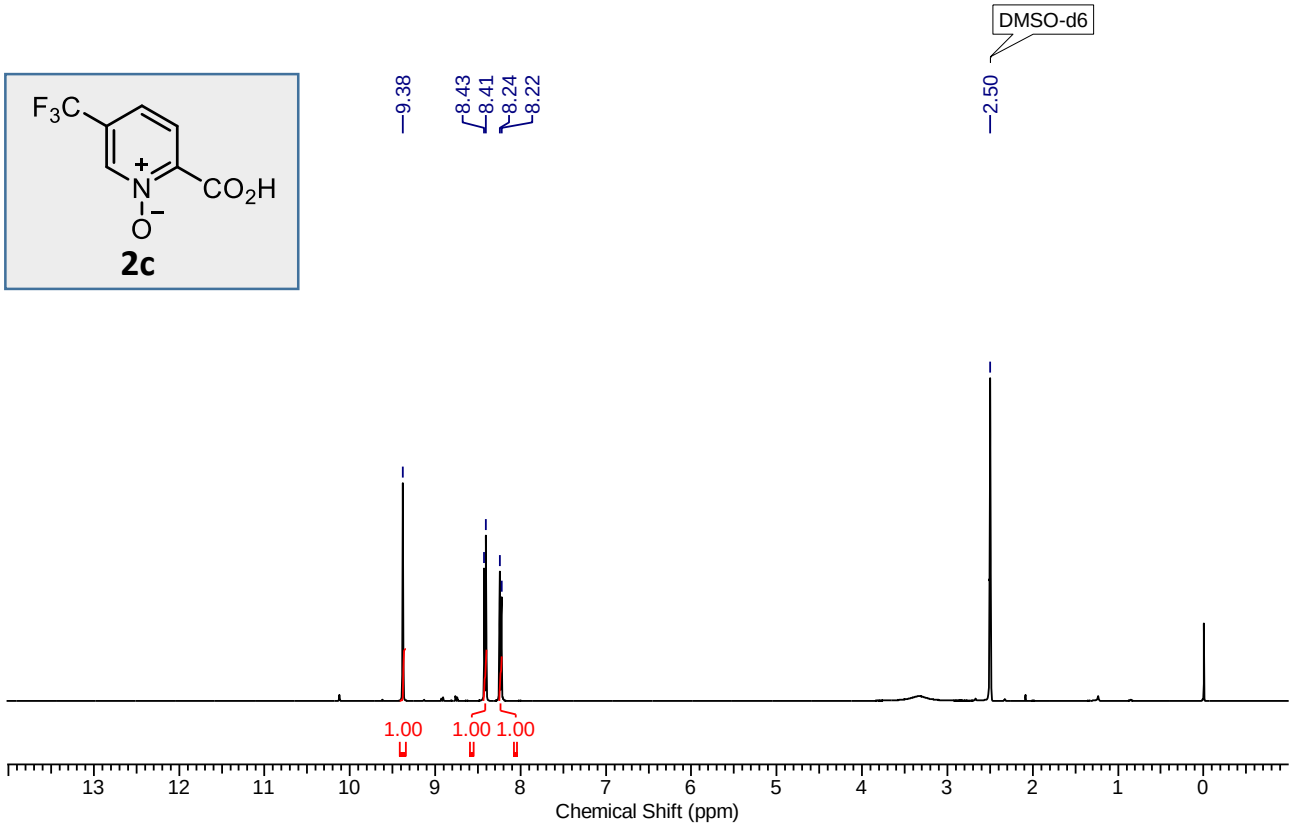

**$^{1}H$ NMR (400 MHz, DMSO-$d_6$) of compound 2a**



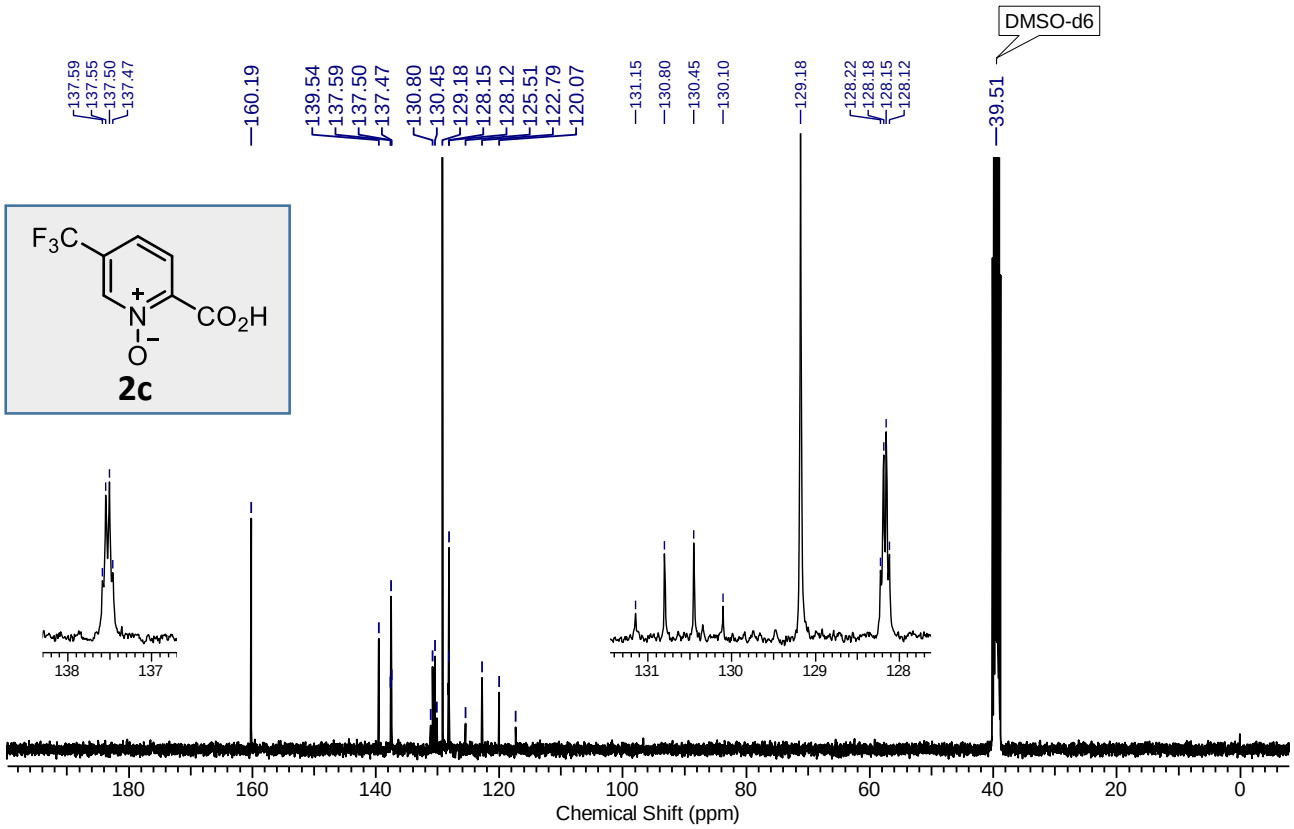

**$^{1}H$ NMR (400 MHz, DMSO-$d_6$) of compound 2b**



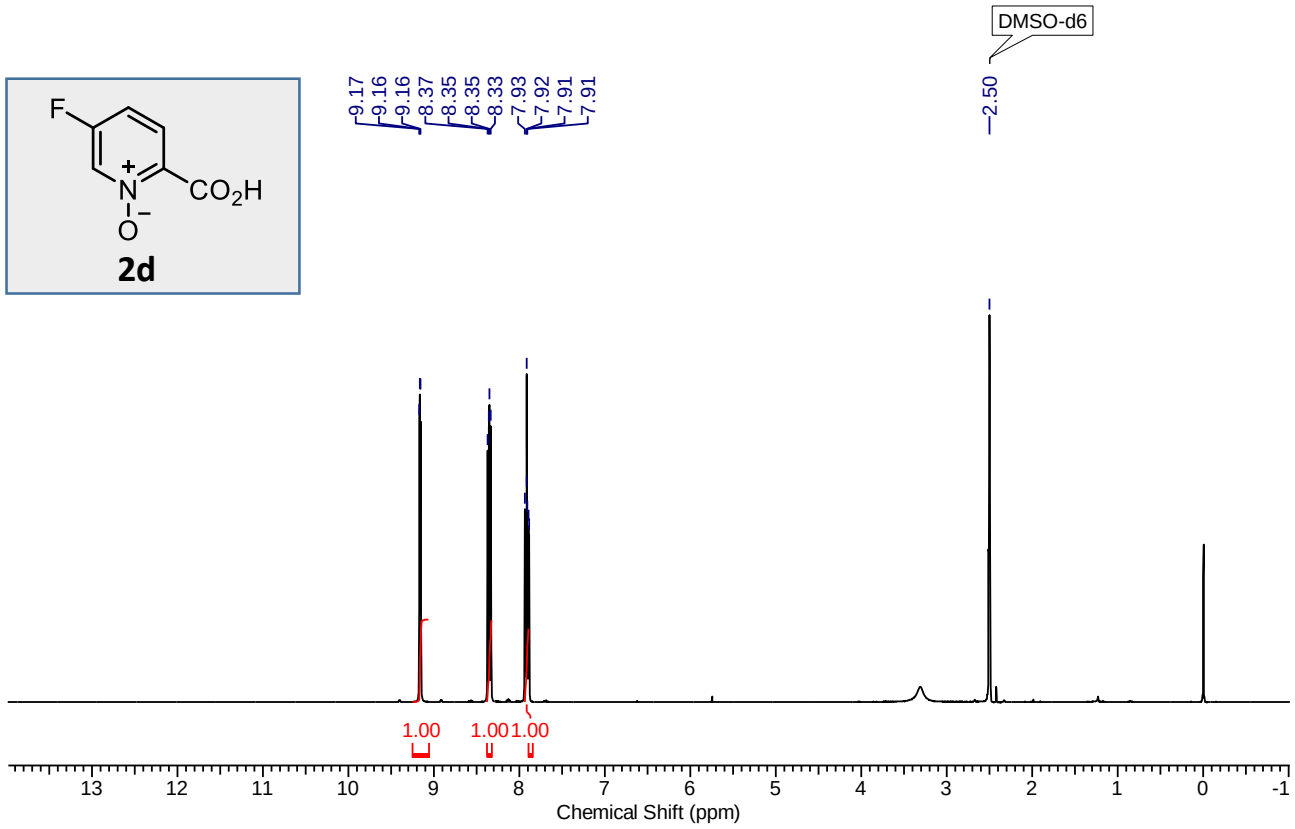

**$^{13}$C NMR (101 MHz, DMSO-d$_6$) of compound 2b**



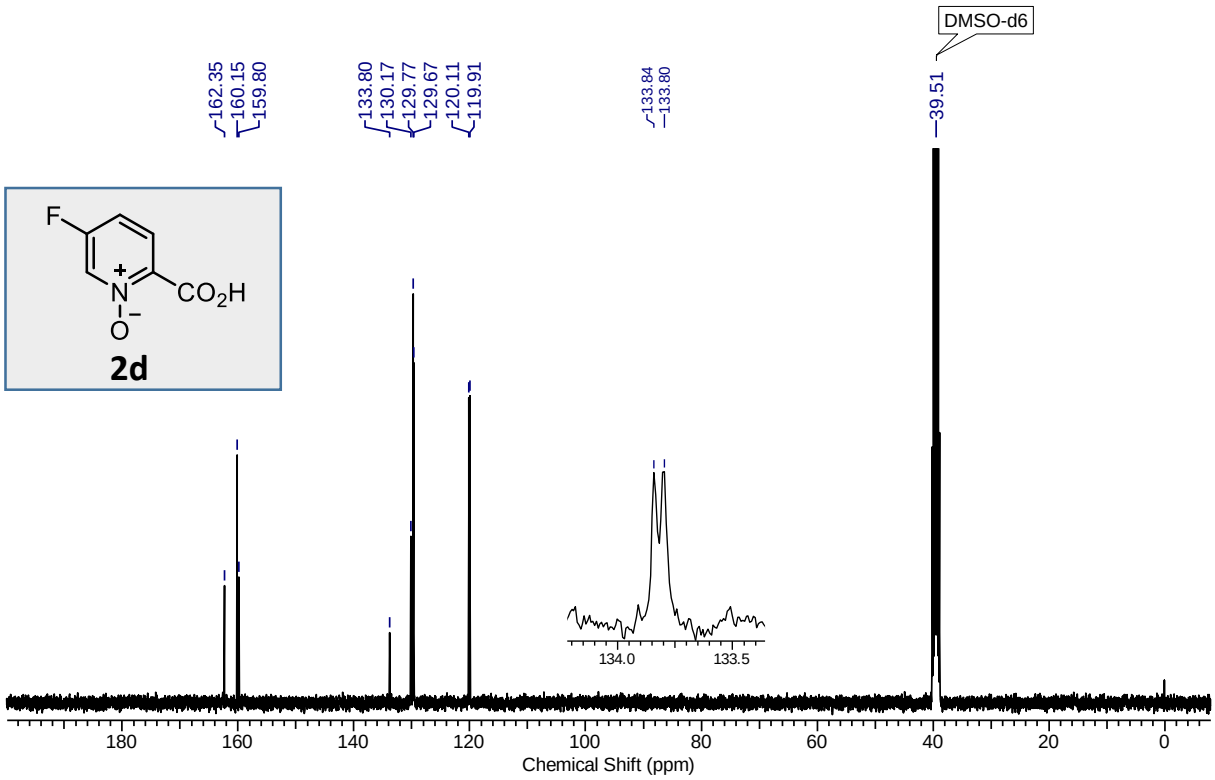

**$^{1}$H NMR (400 MHz, DMSO-d$_6$) of compound 2c**



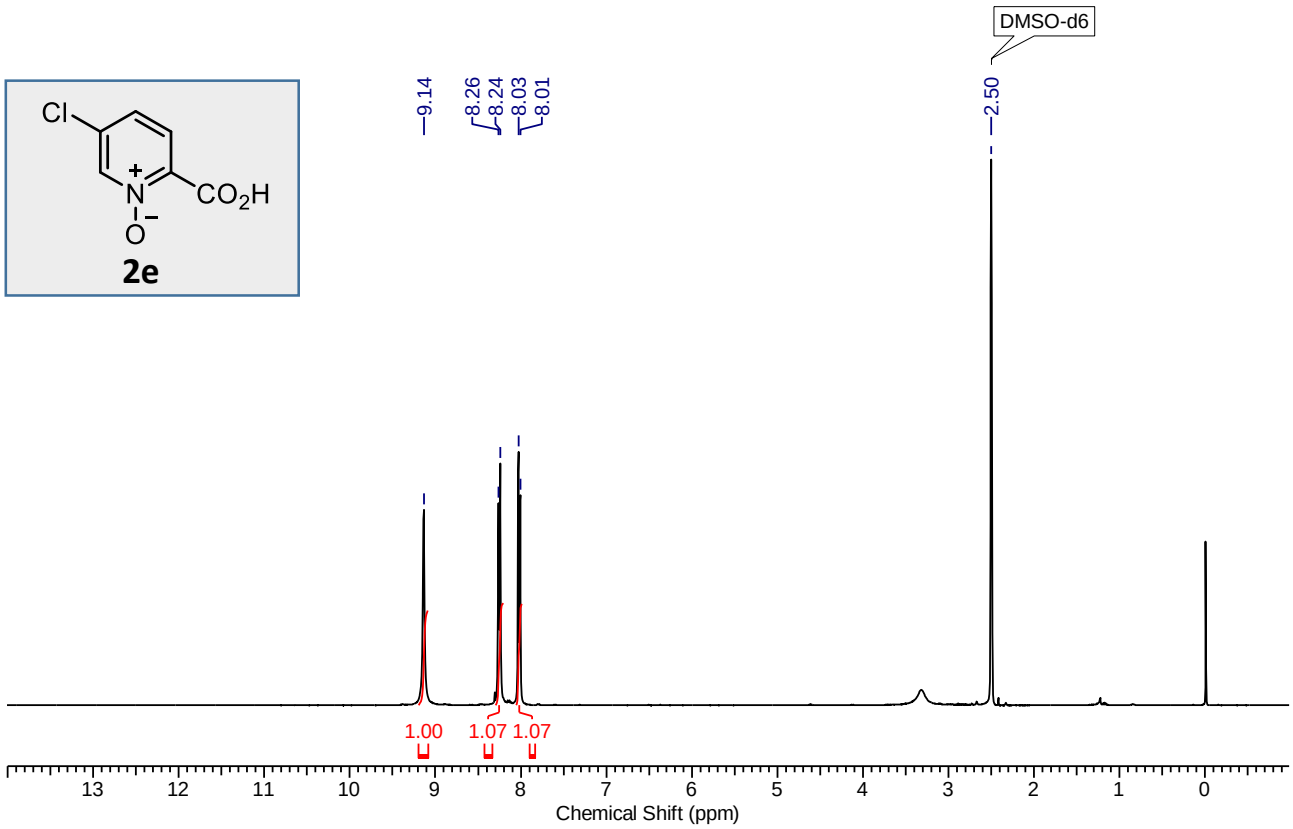

**$^{13}$C NMR (101 MHz, DMSO-$d_6$) of compound 2c**



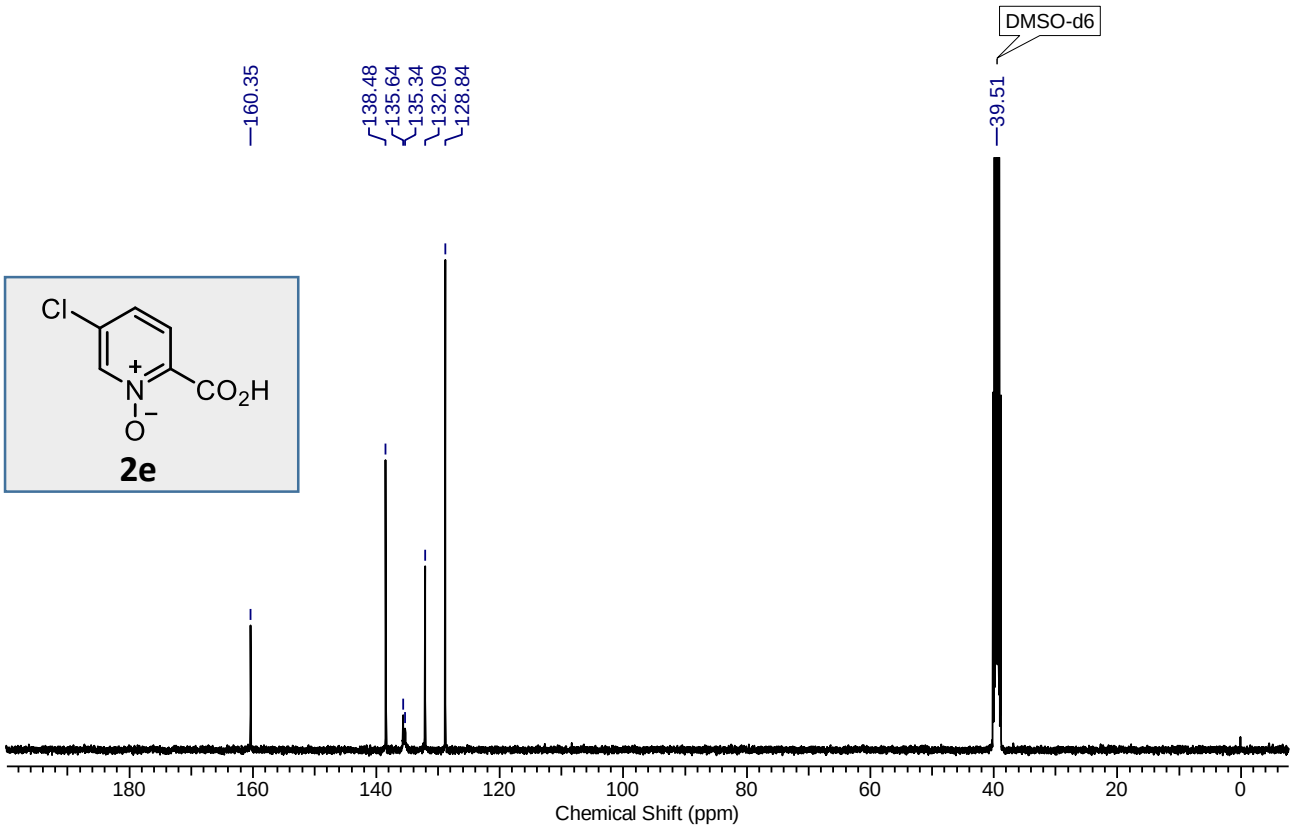

**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 2d**



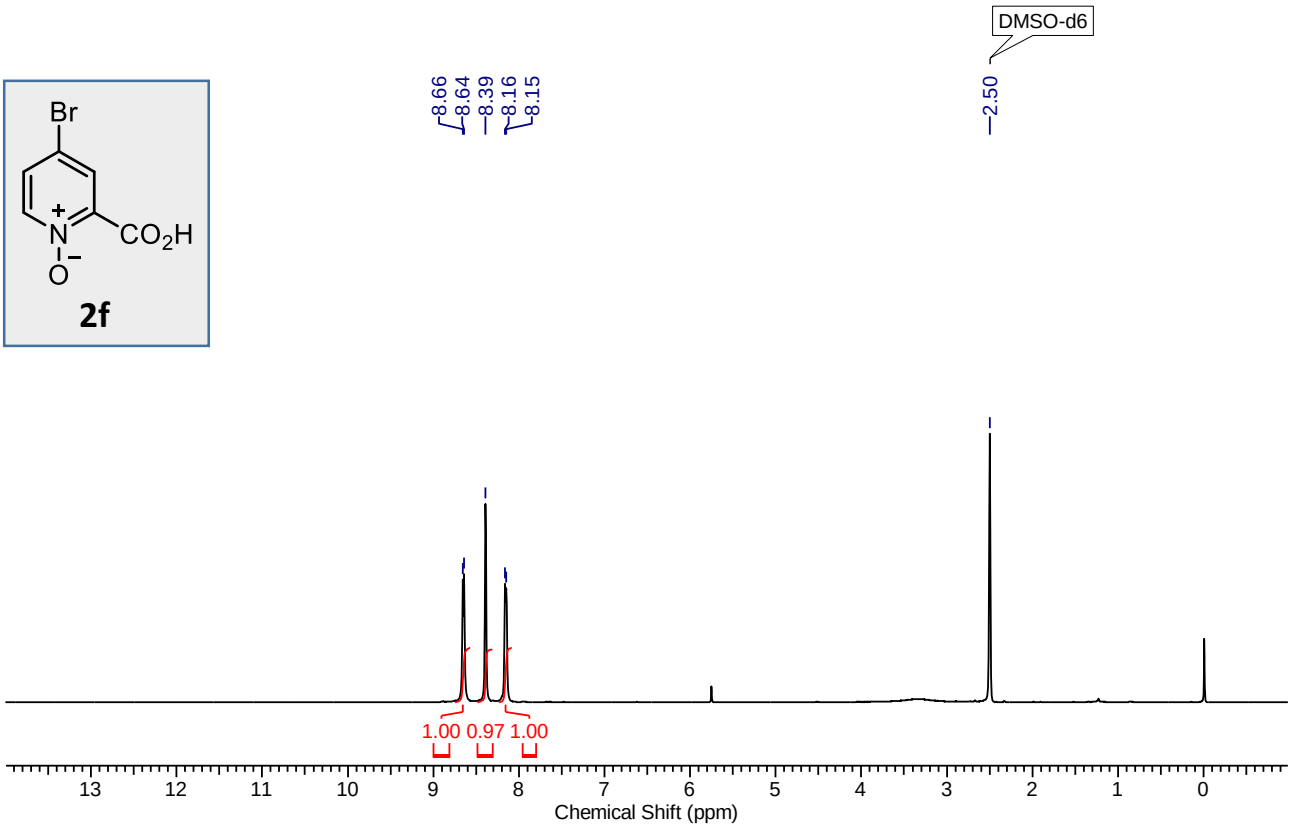

**$^{13}$C NMR (101 MHz, DMSO-$d_6$) of compound 2d**



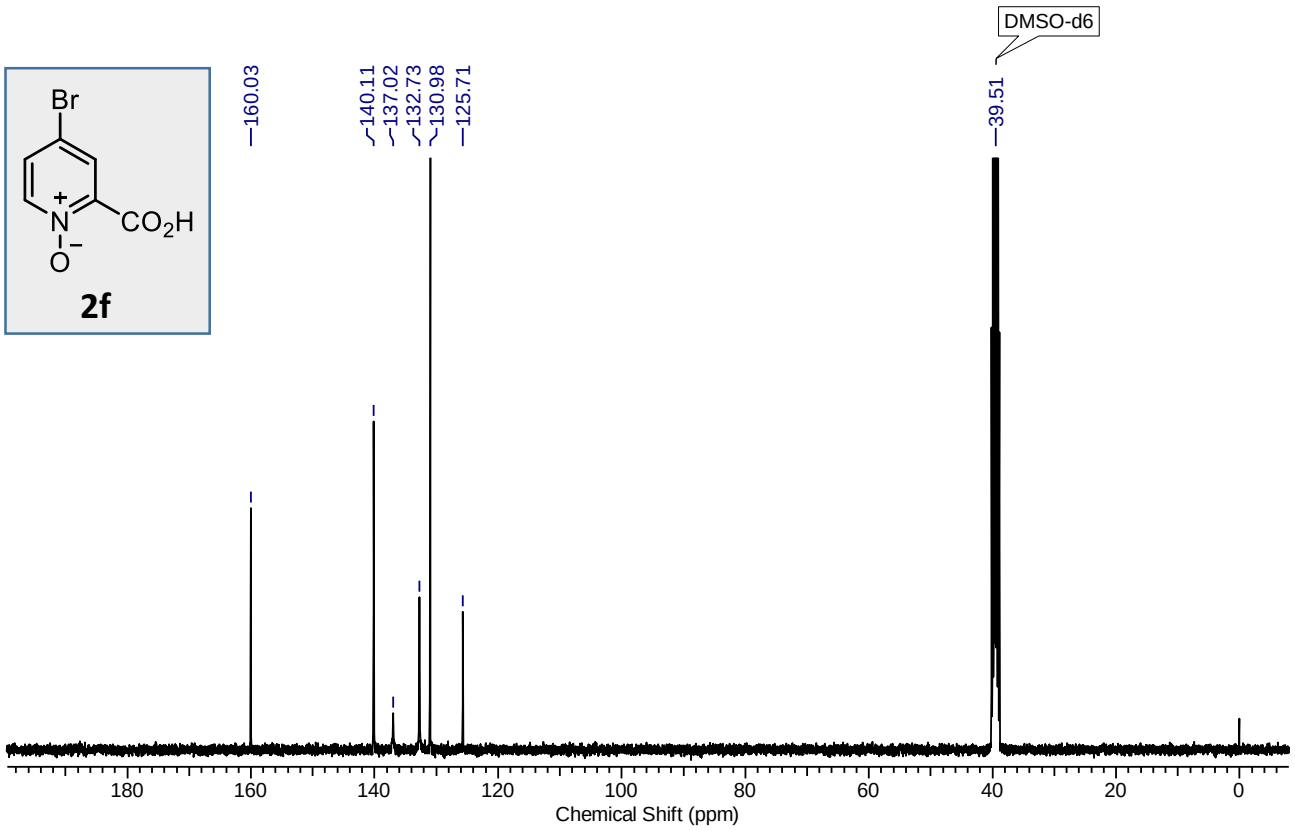

**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 2e**




**$^{13}$C NMR (101 MHz, DMSO-$d_6$) of compound 2e**




**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 2f**

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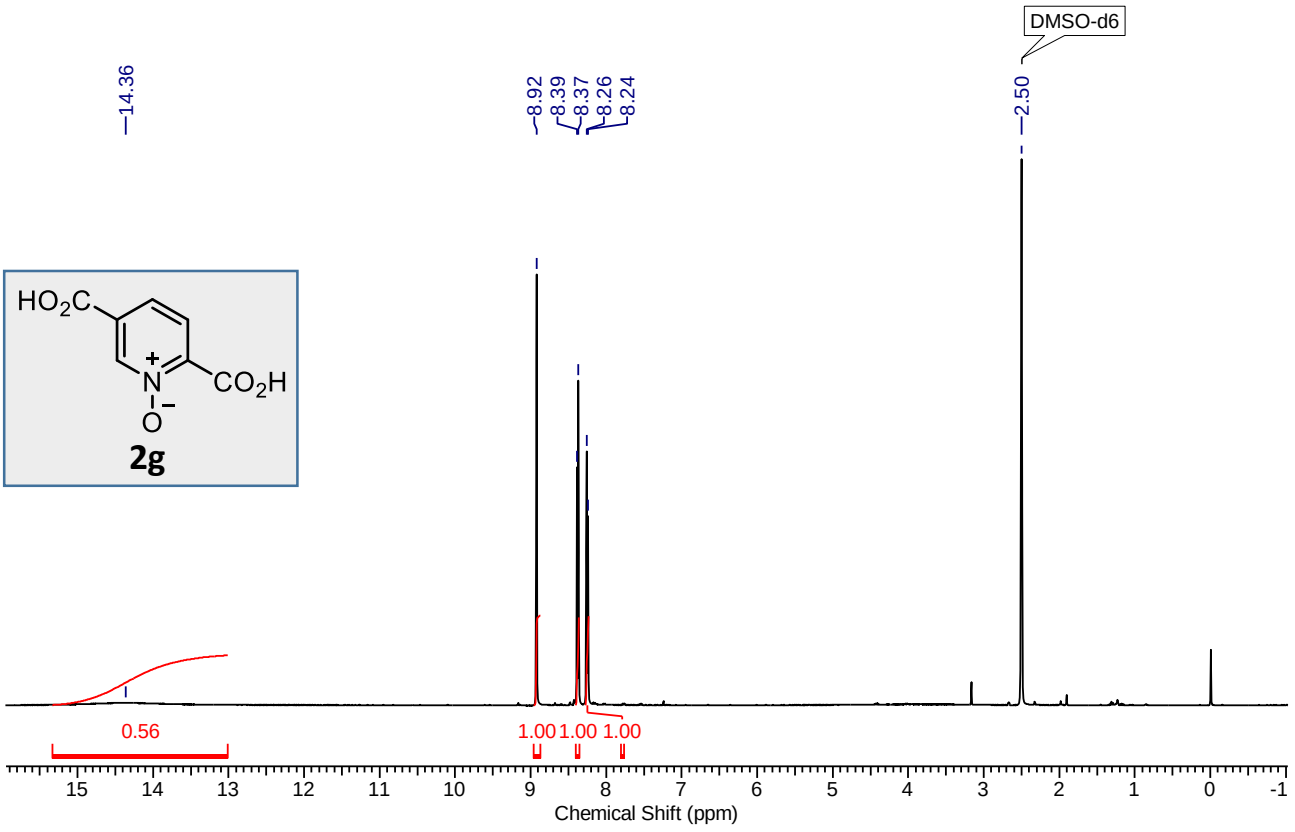


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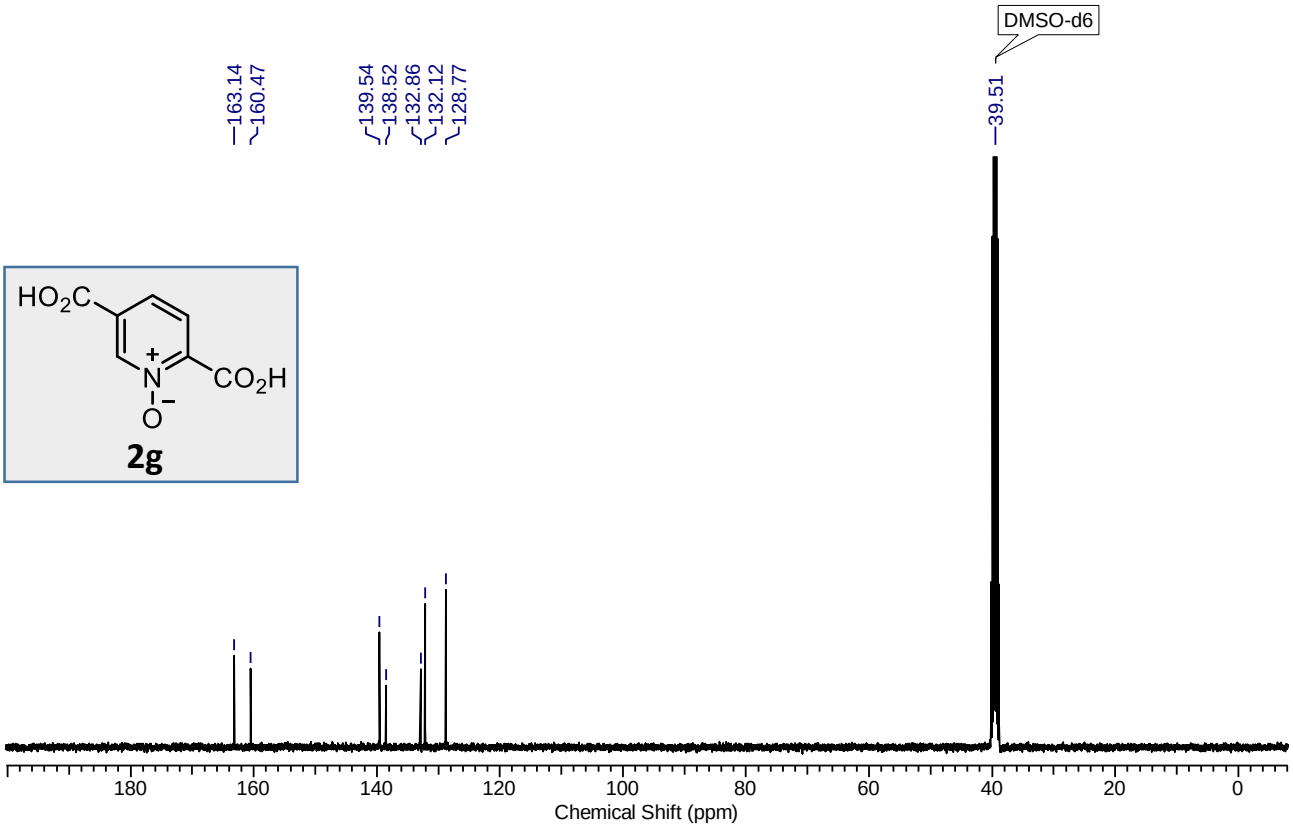


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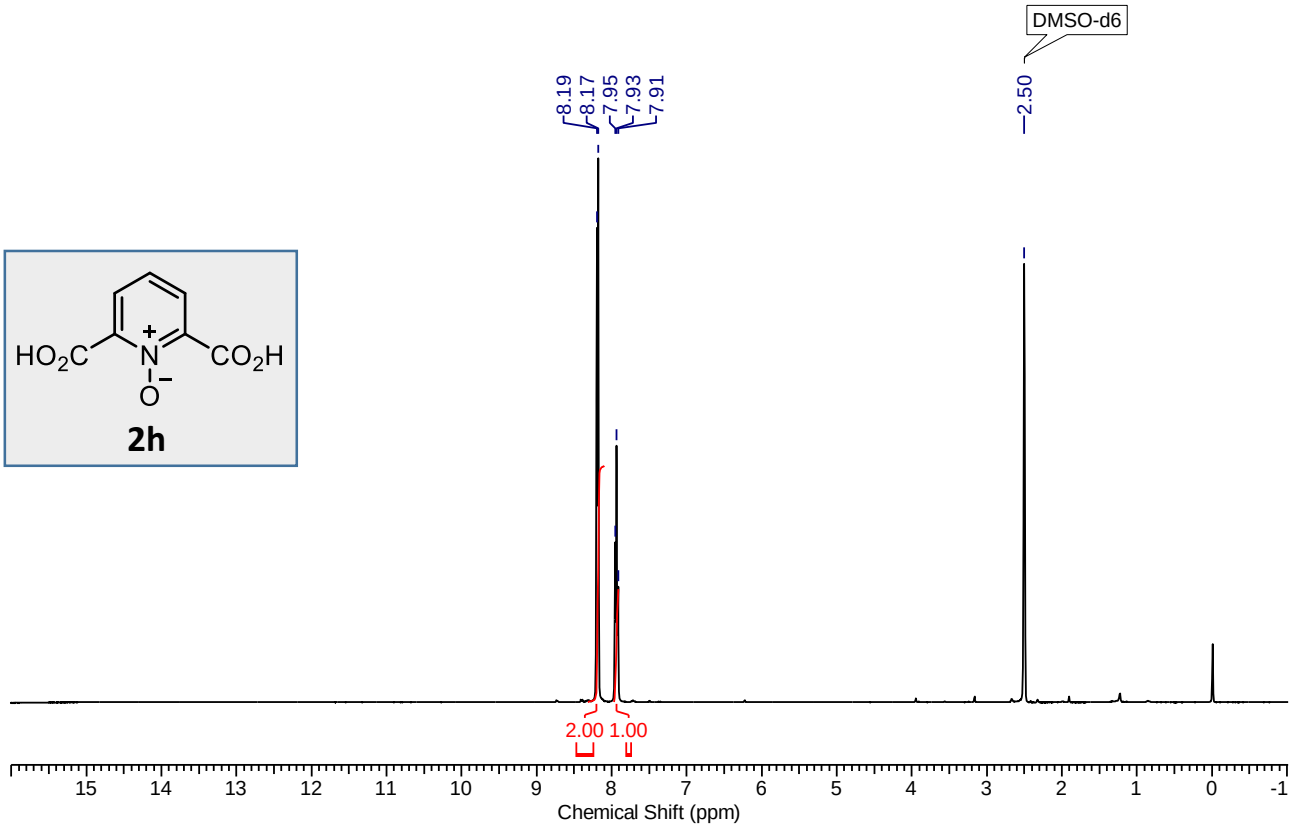
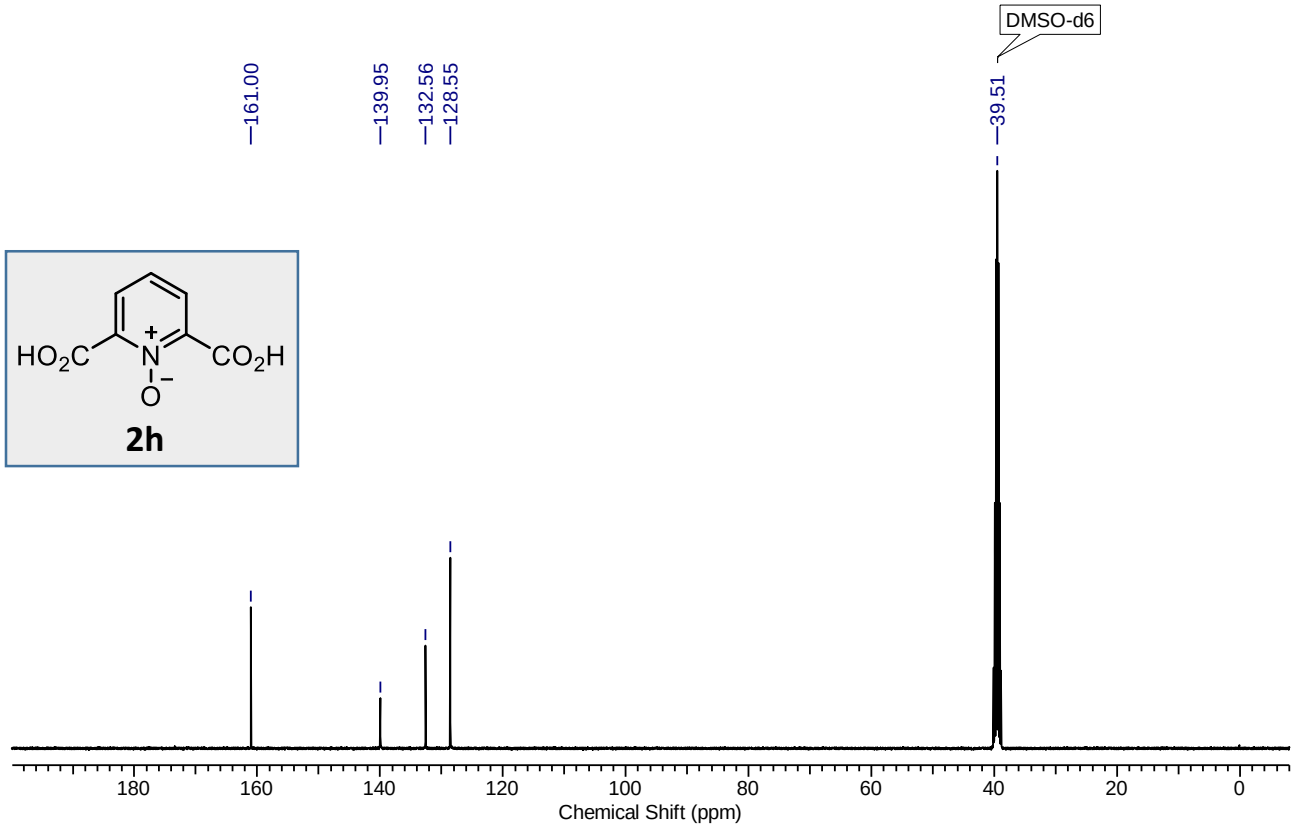



**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 2h**

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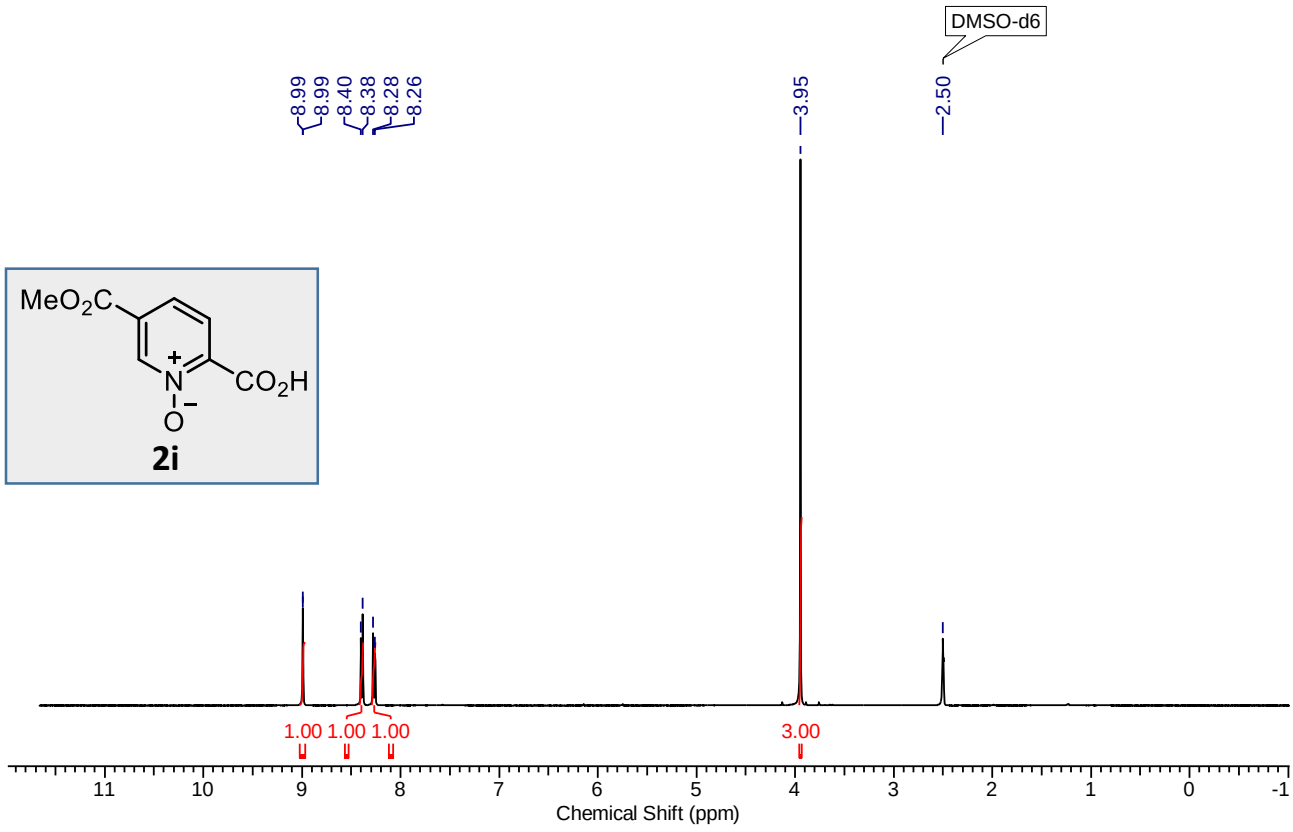


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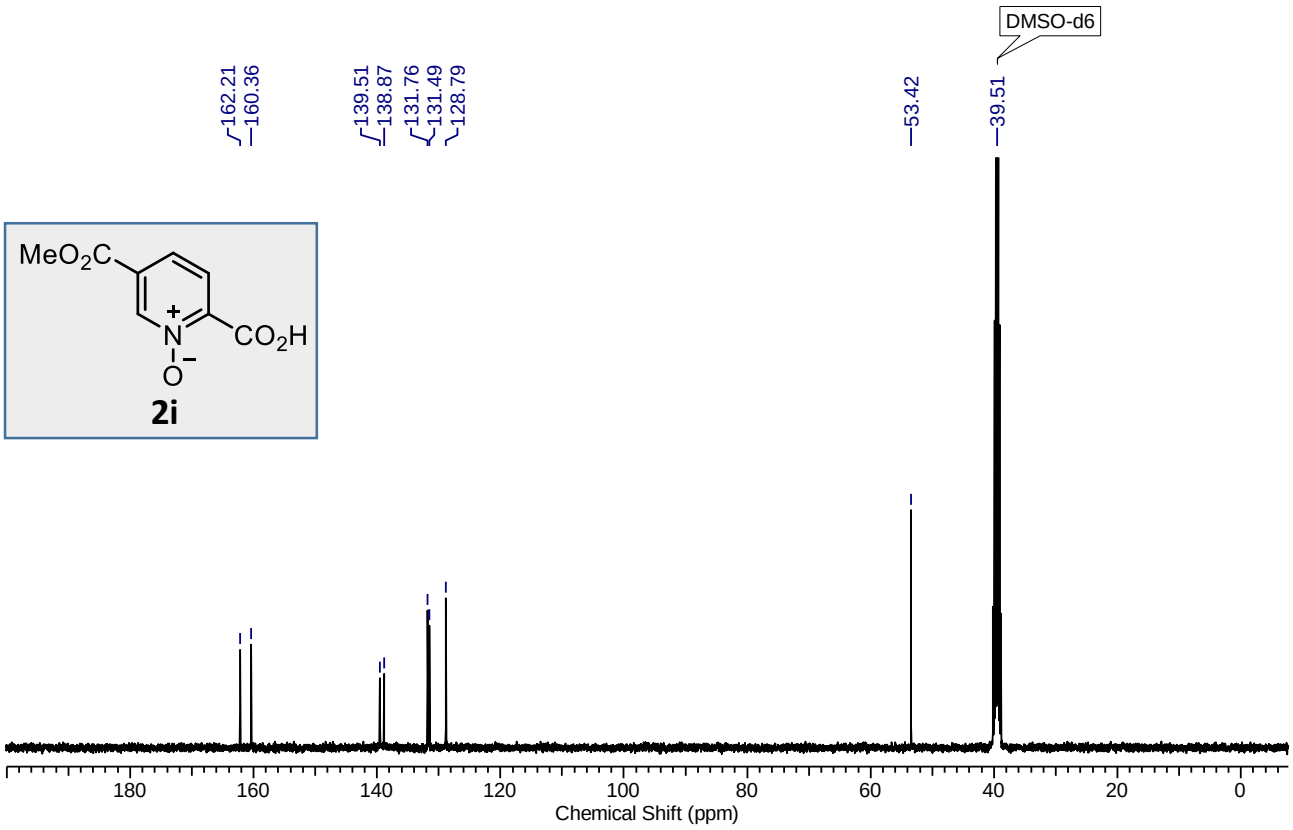


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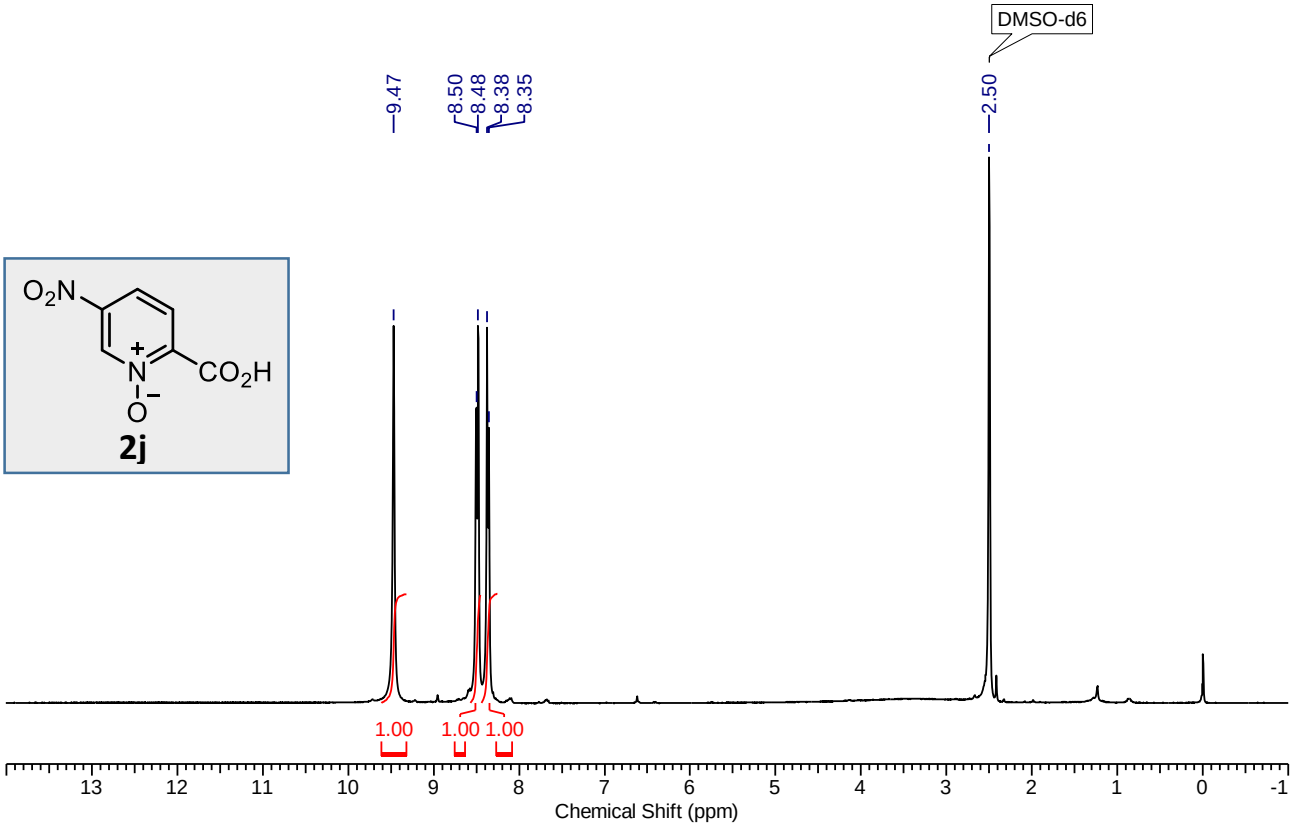


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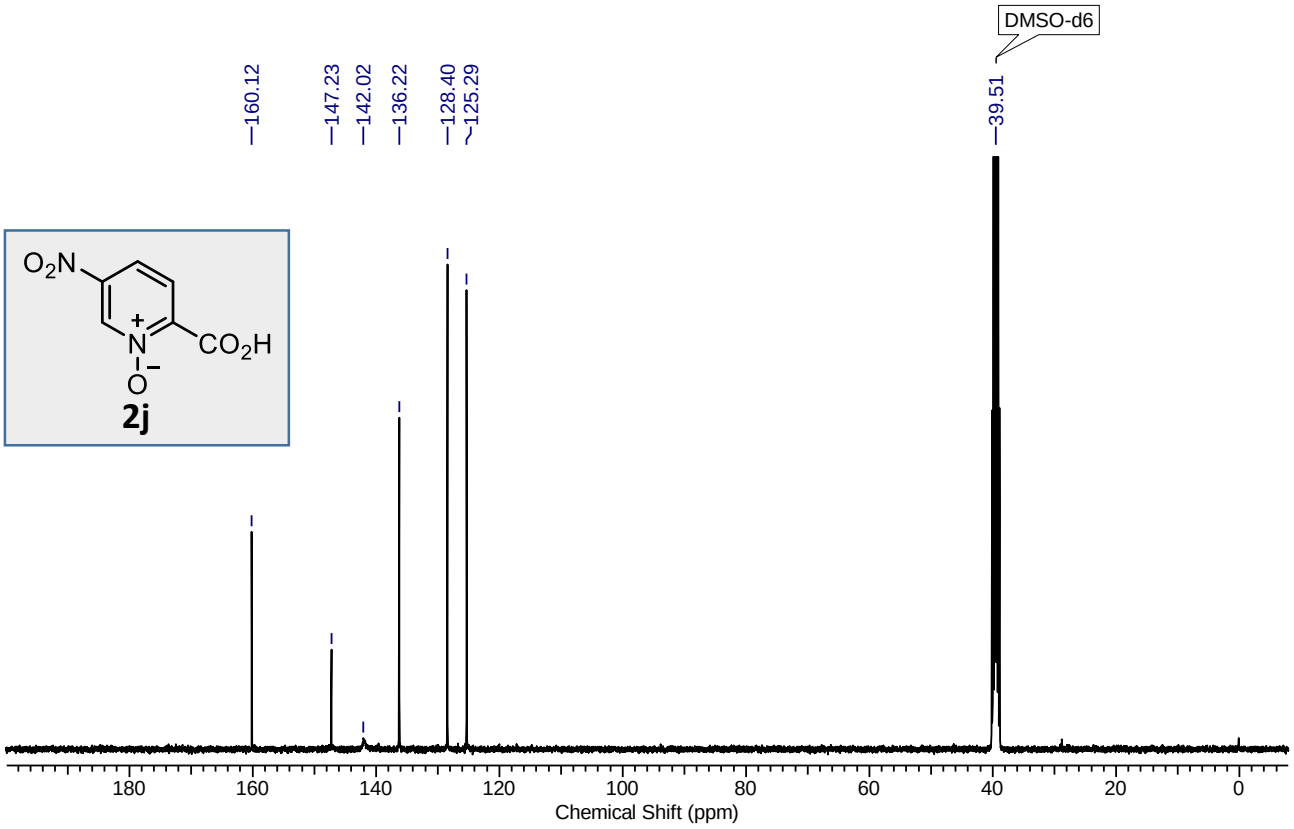


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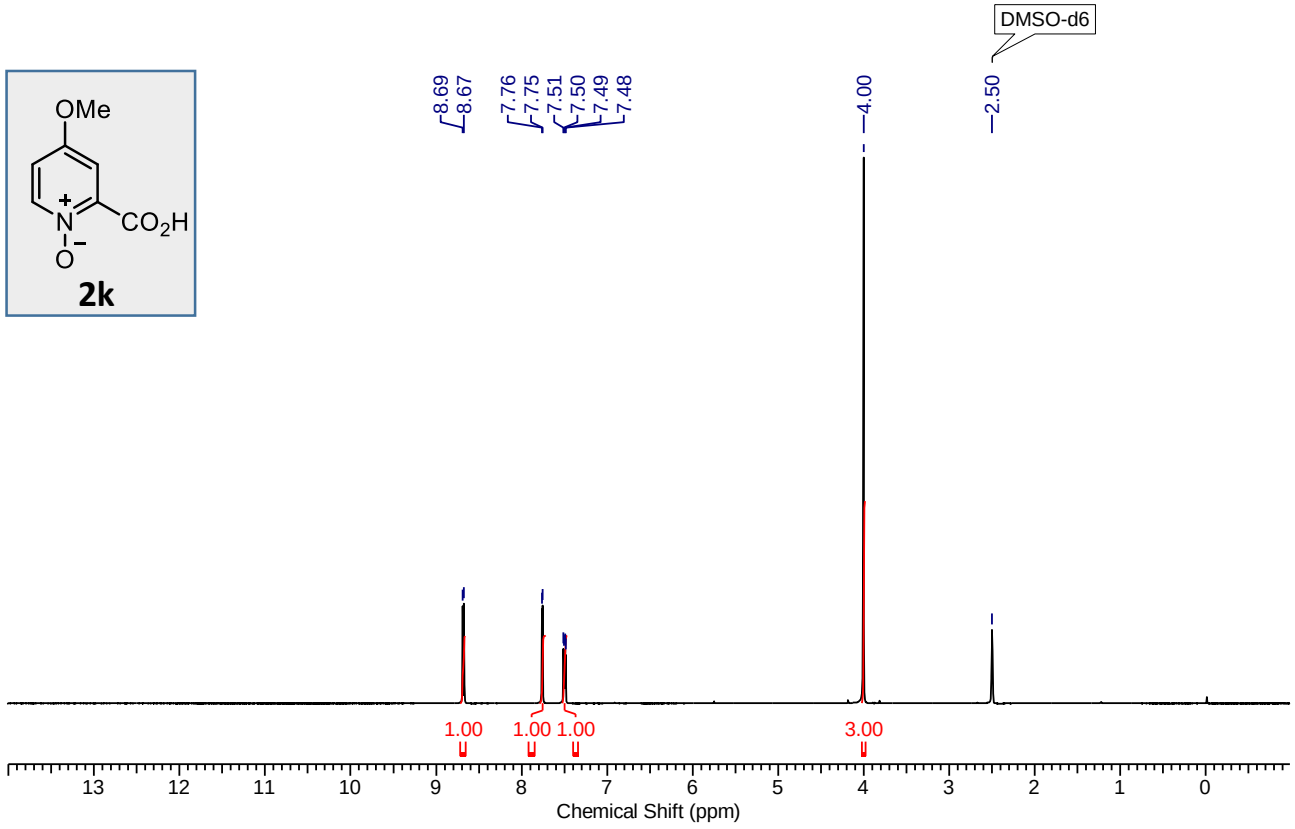


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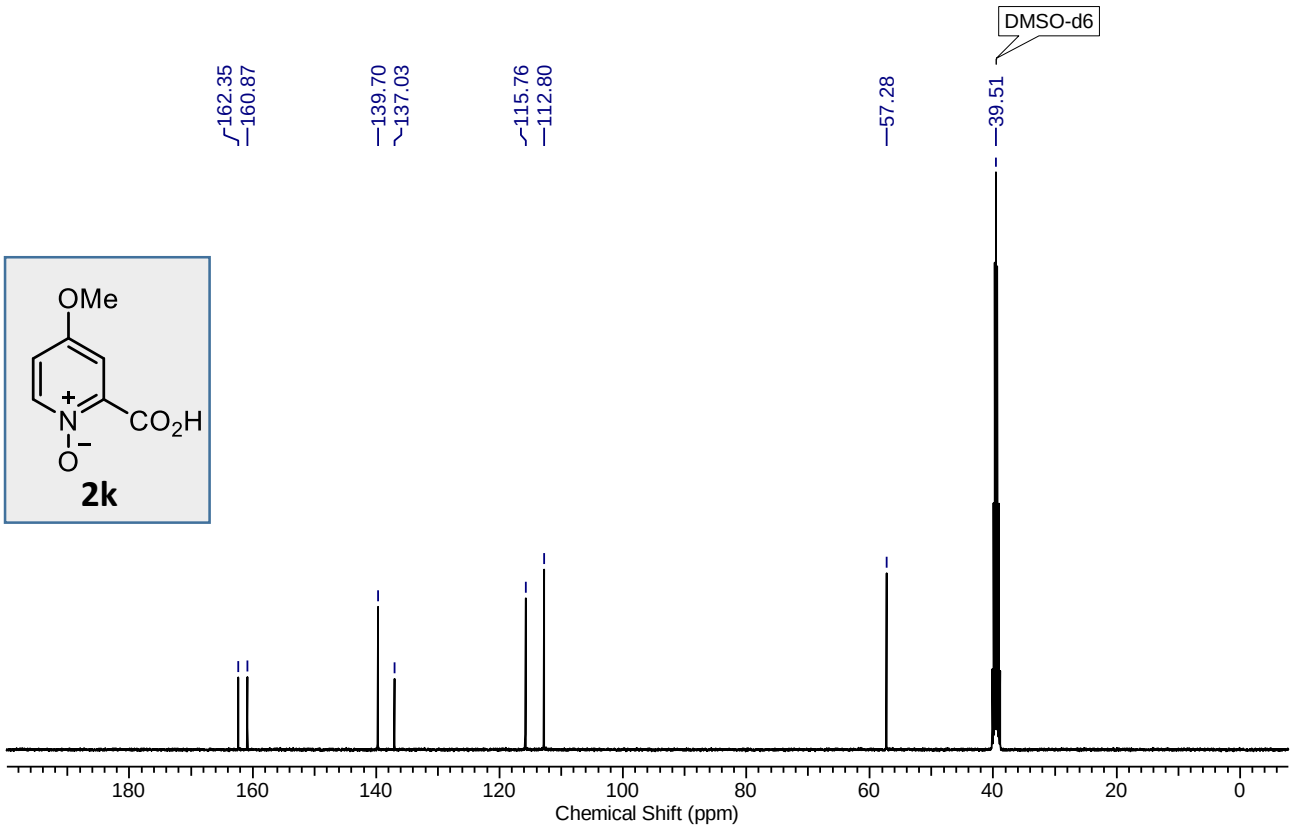


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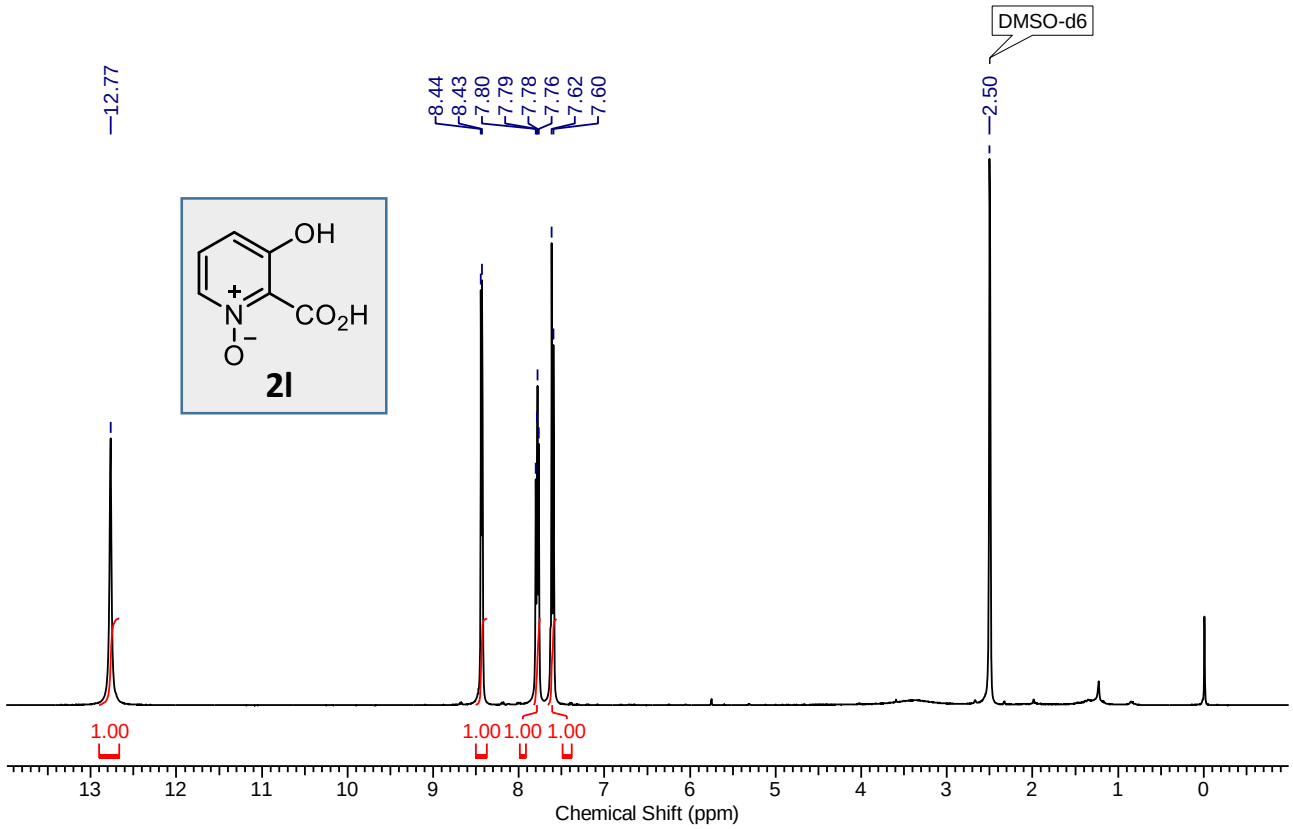


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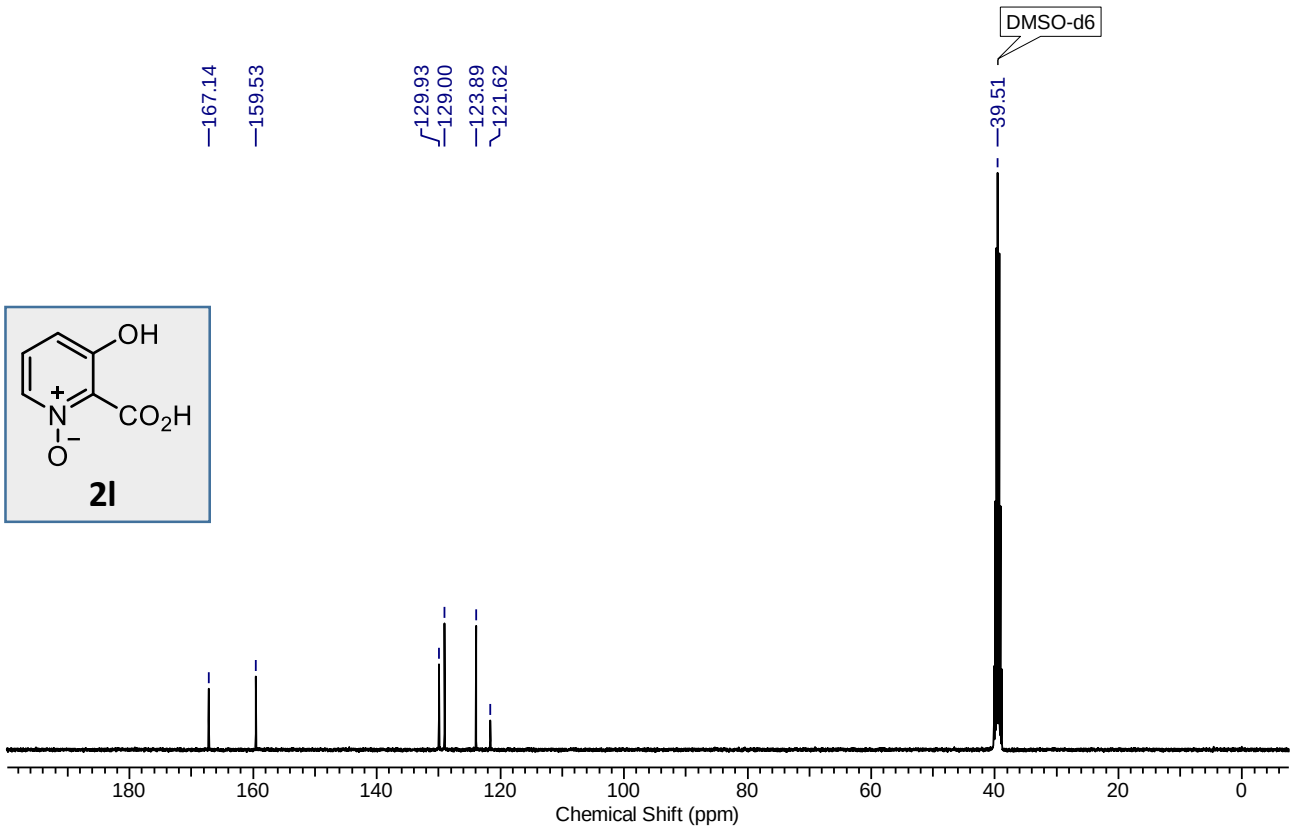


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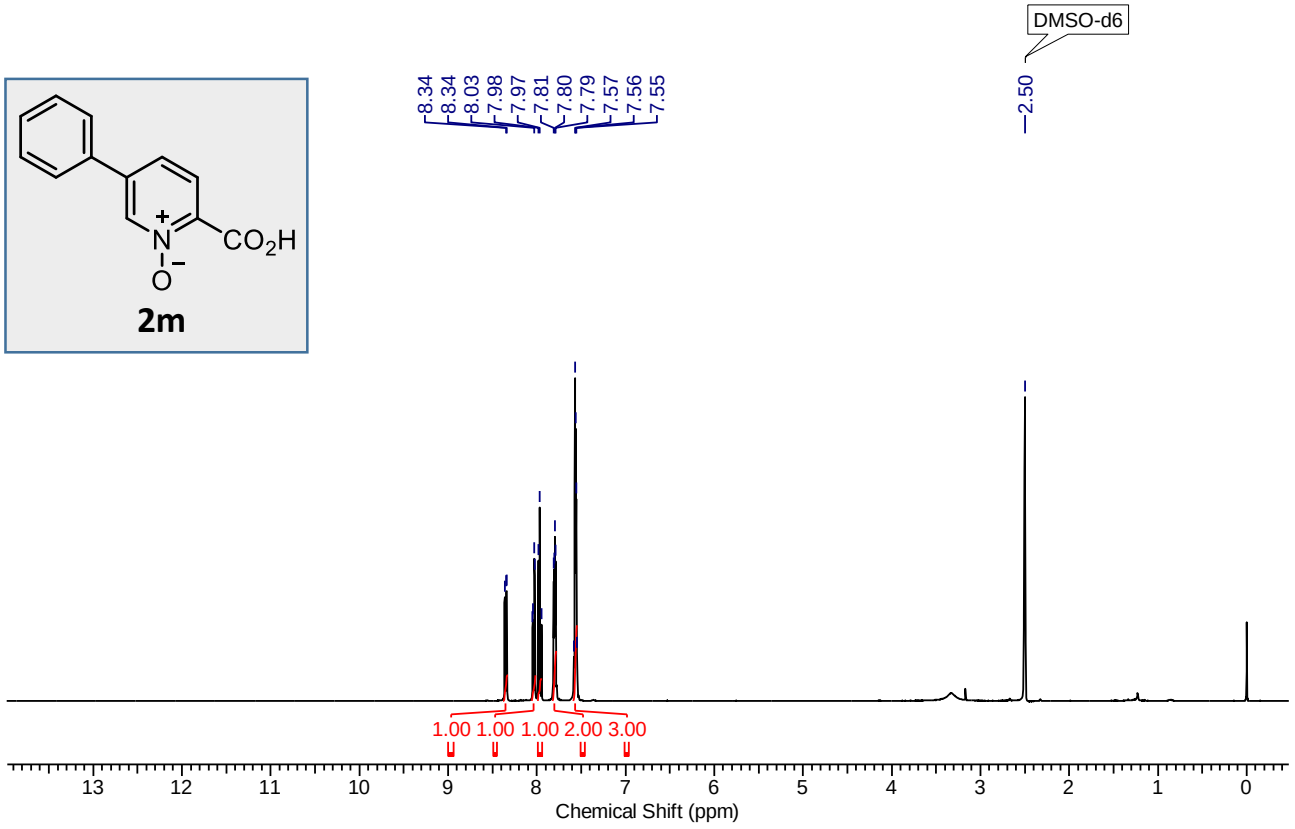


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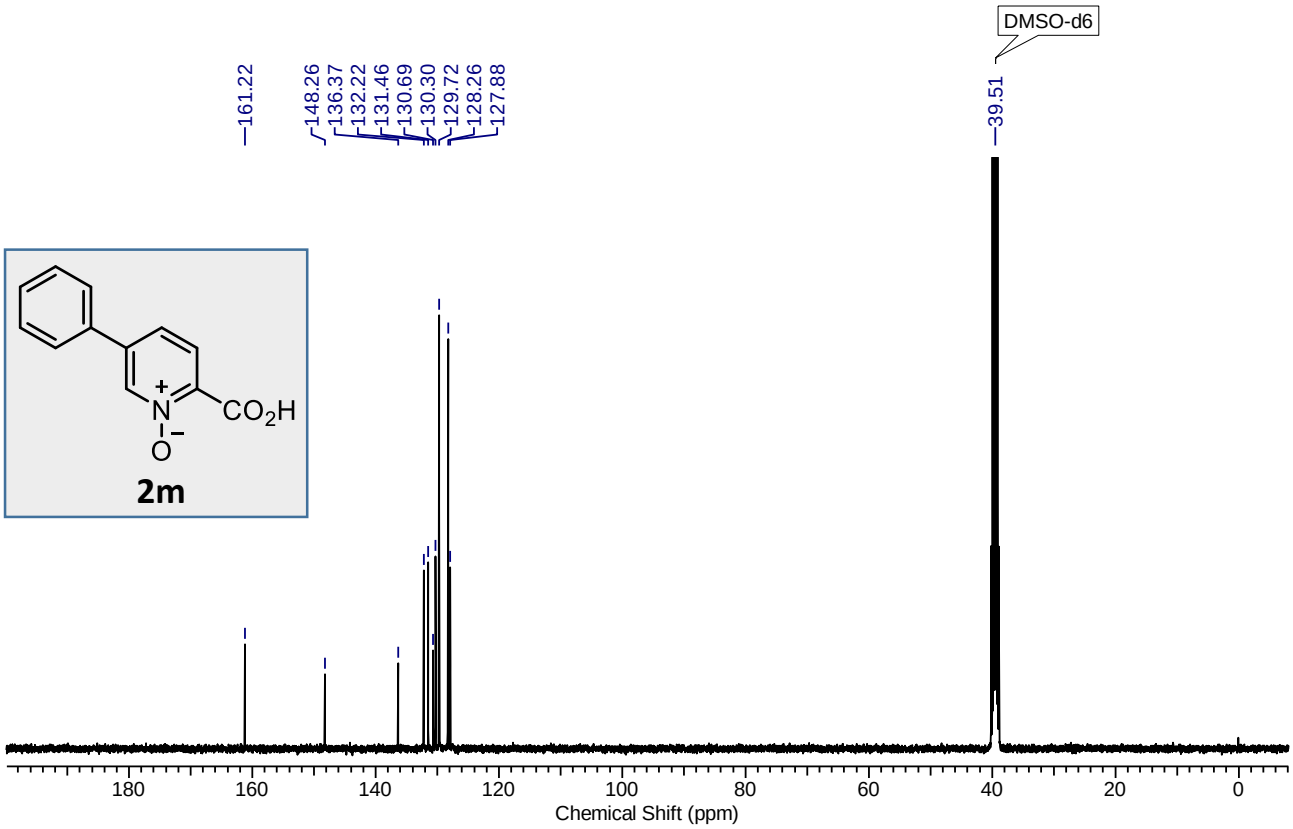


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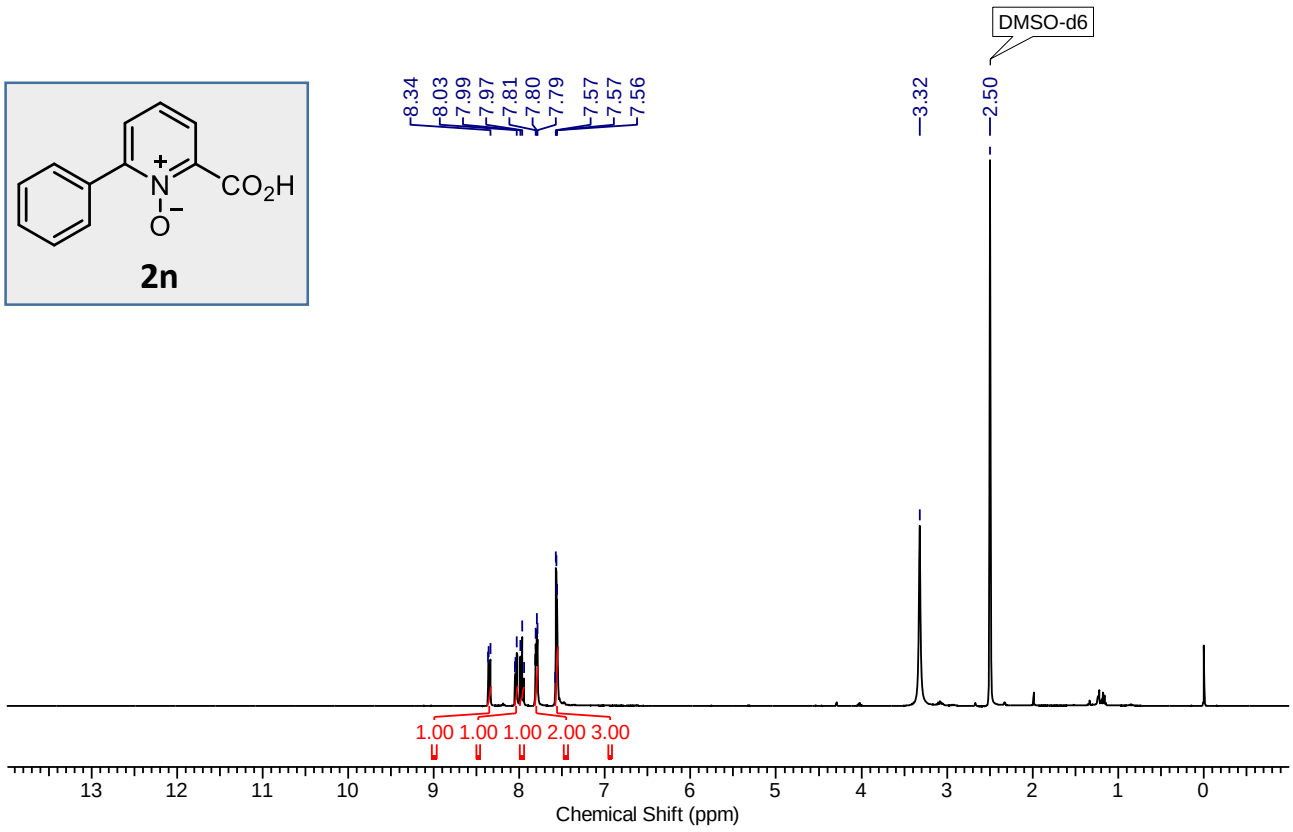


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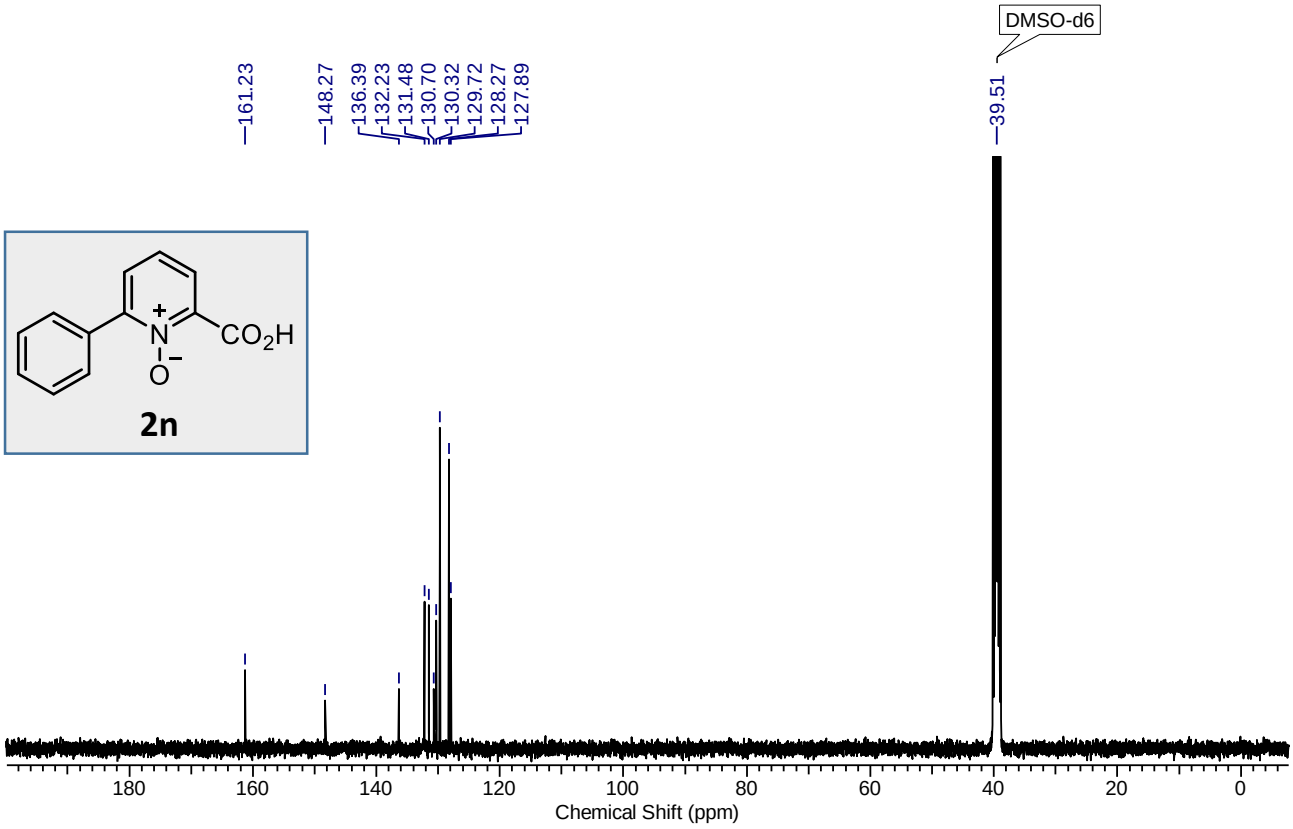


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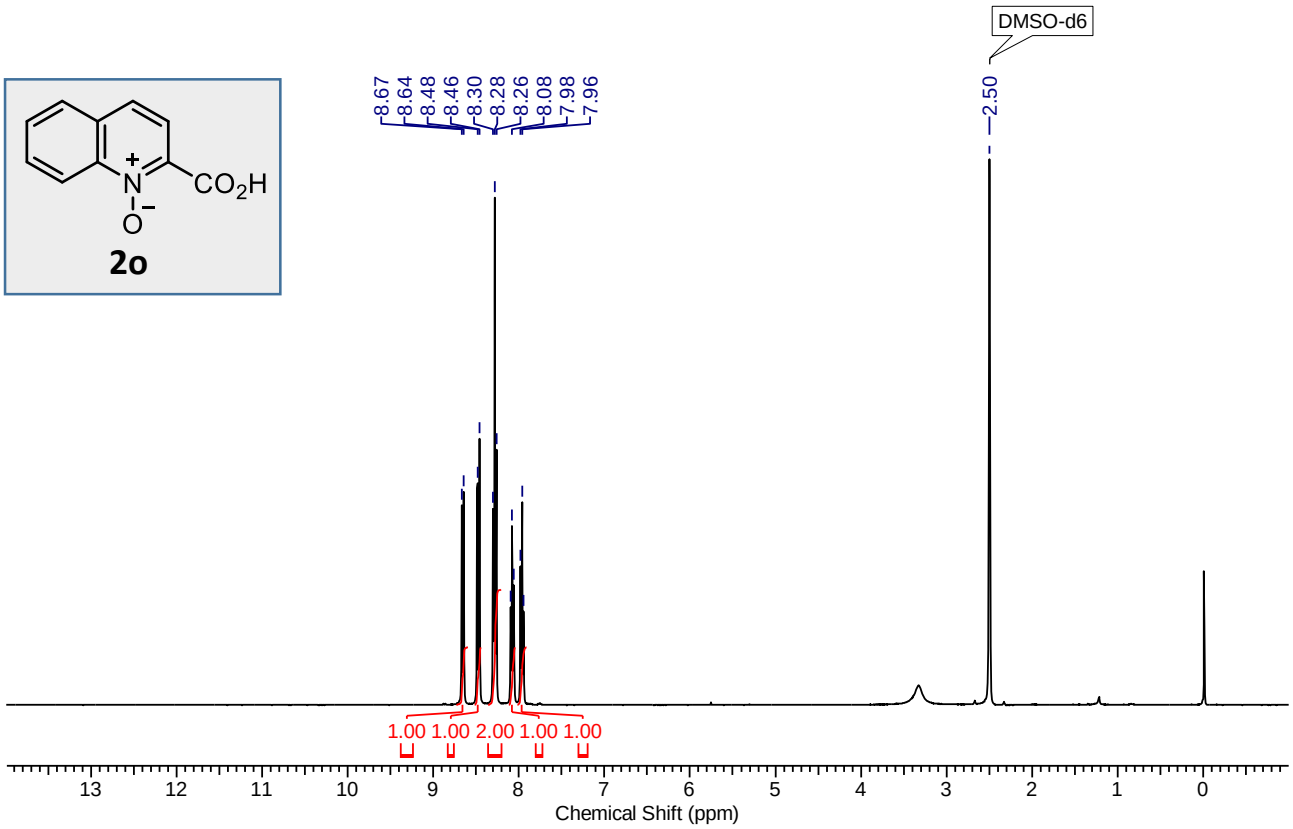
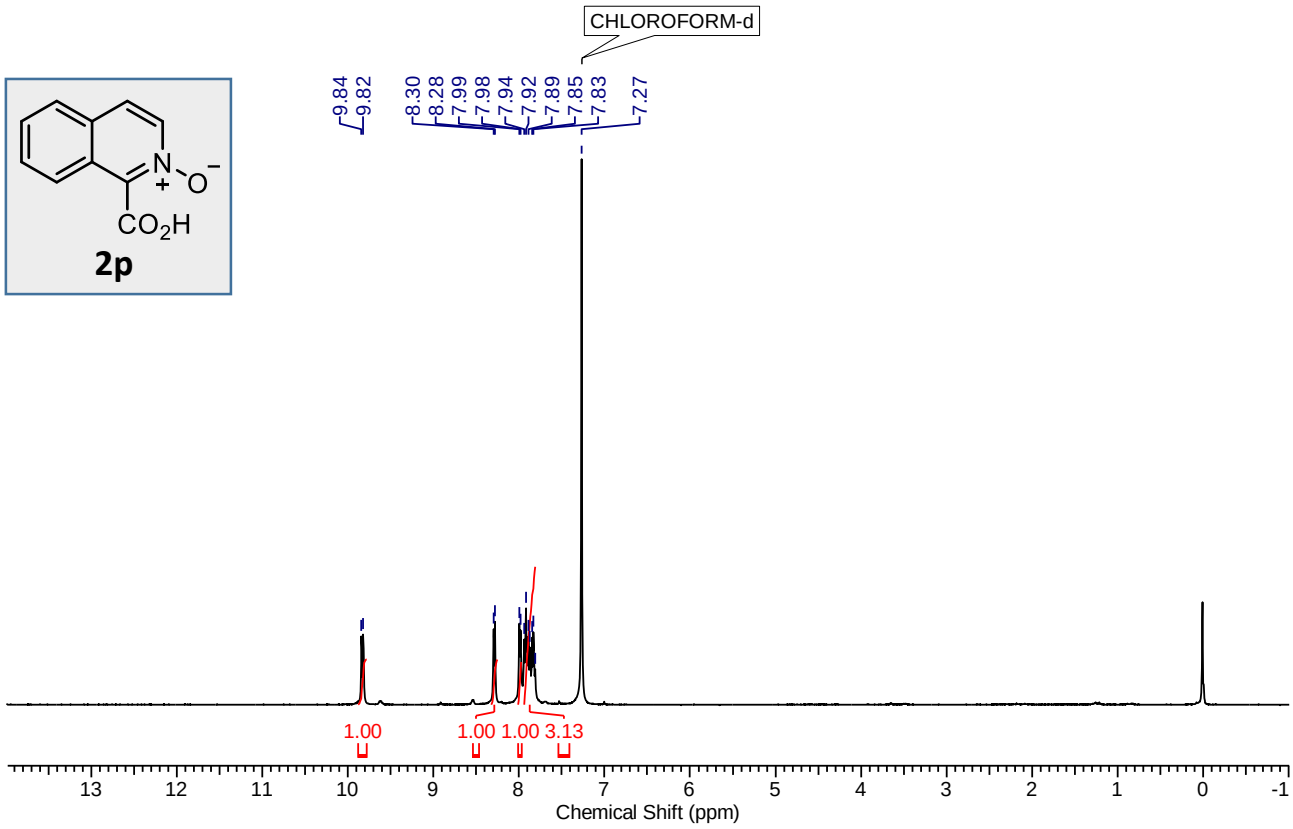
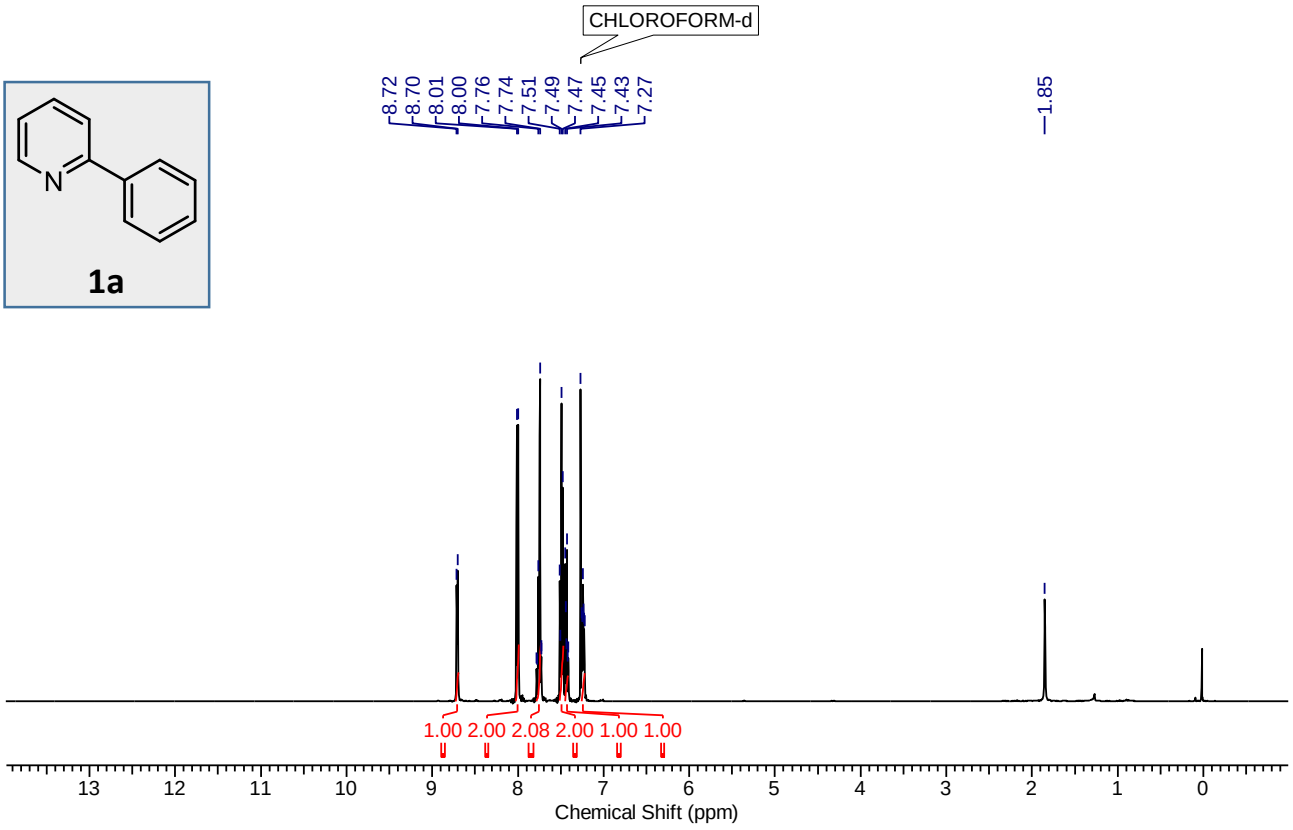


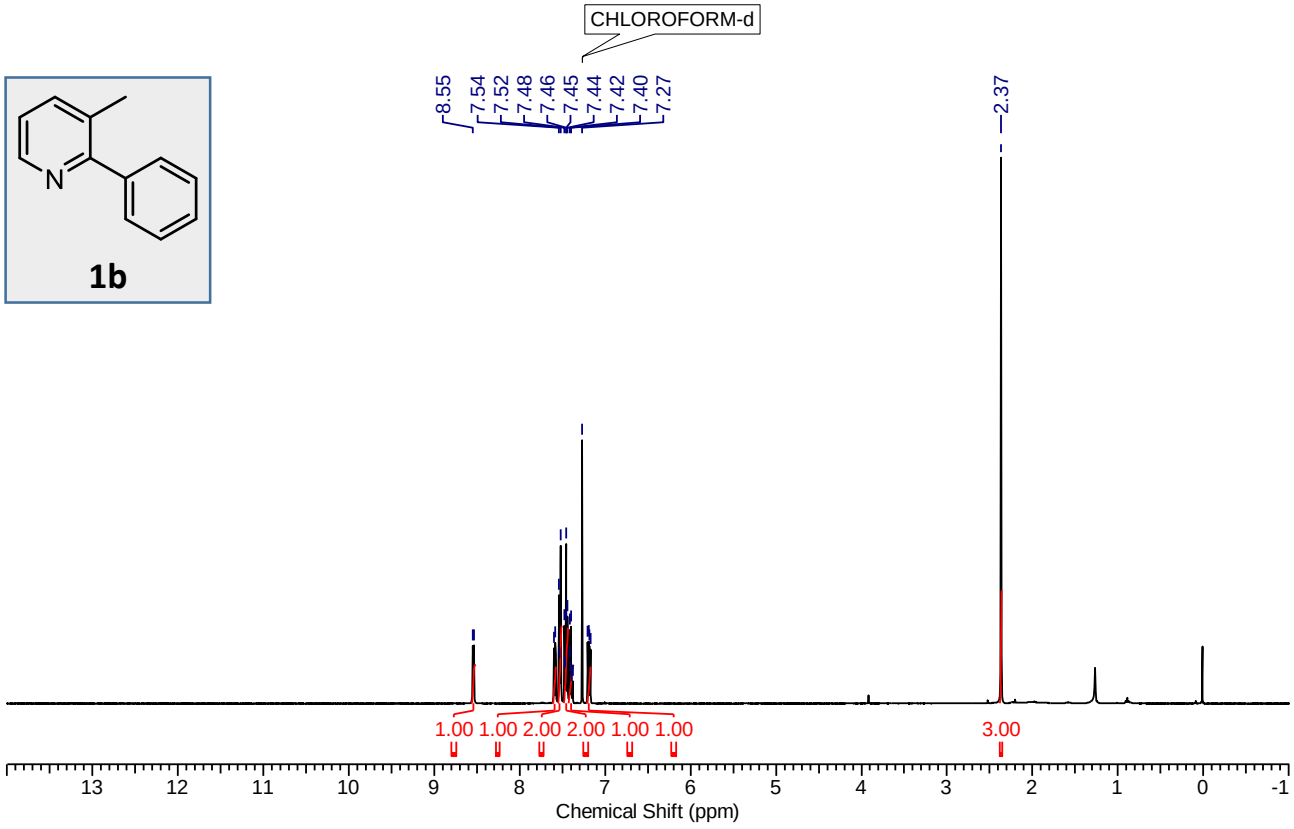

**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 2o**



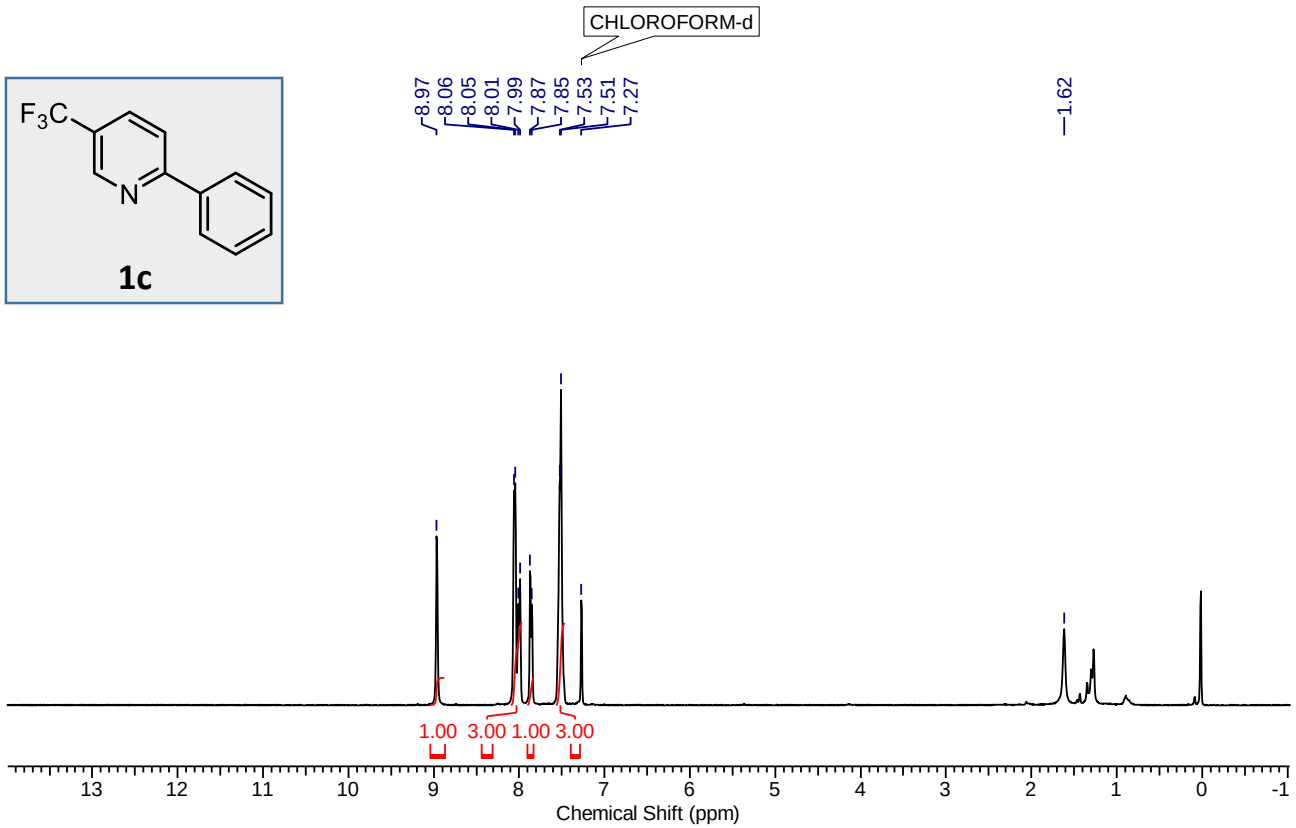

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 2p**




**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1a**




**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1b**

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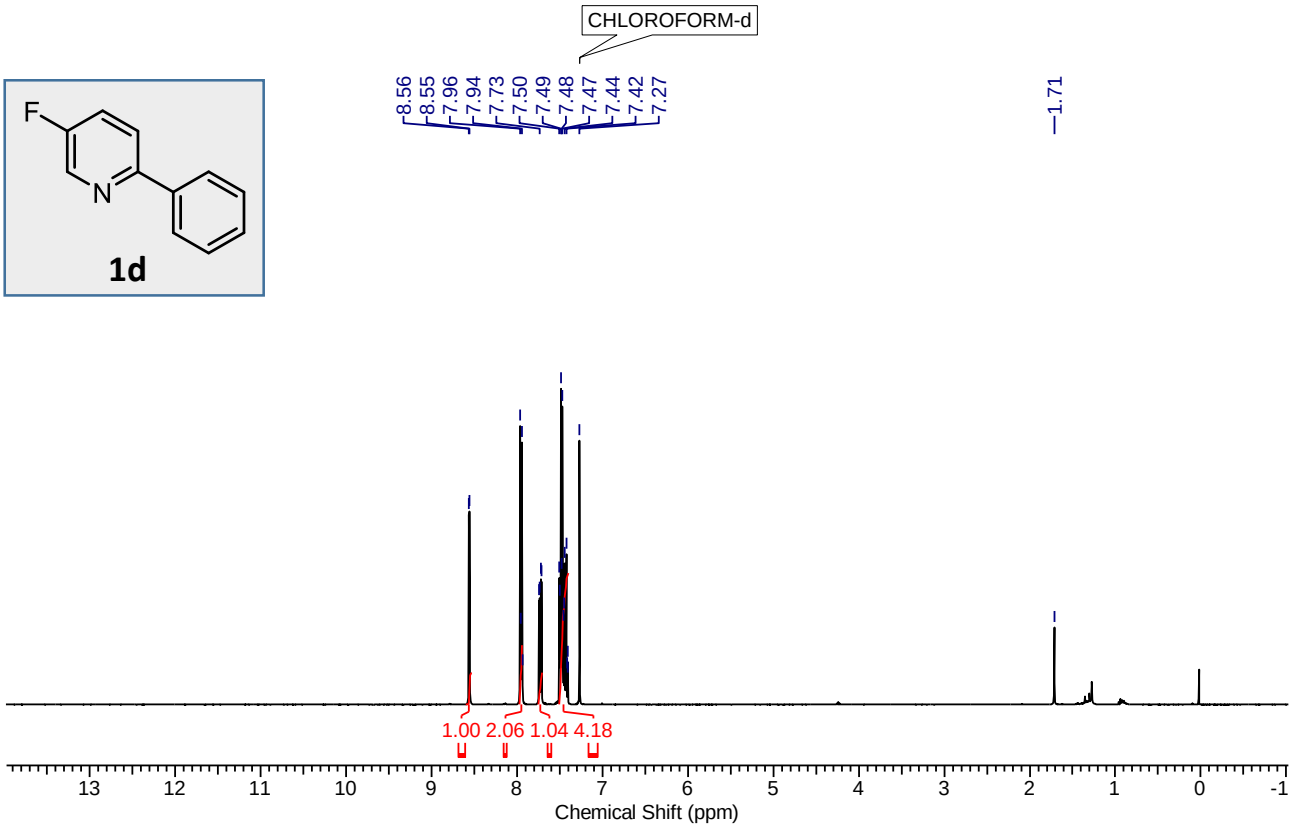


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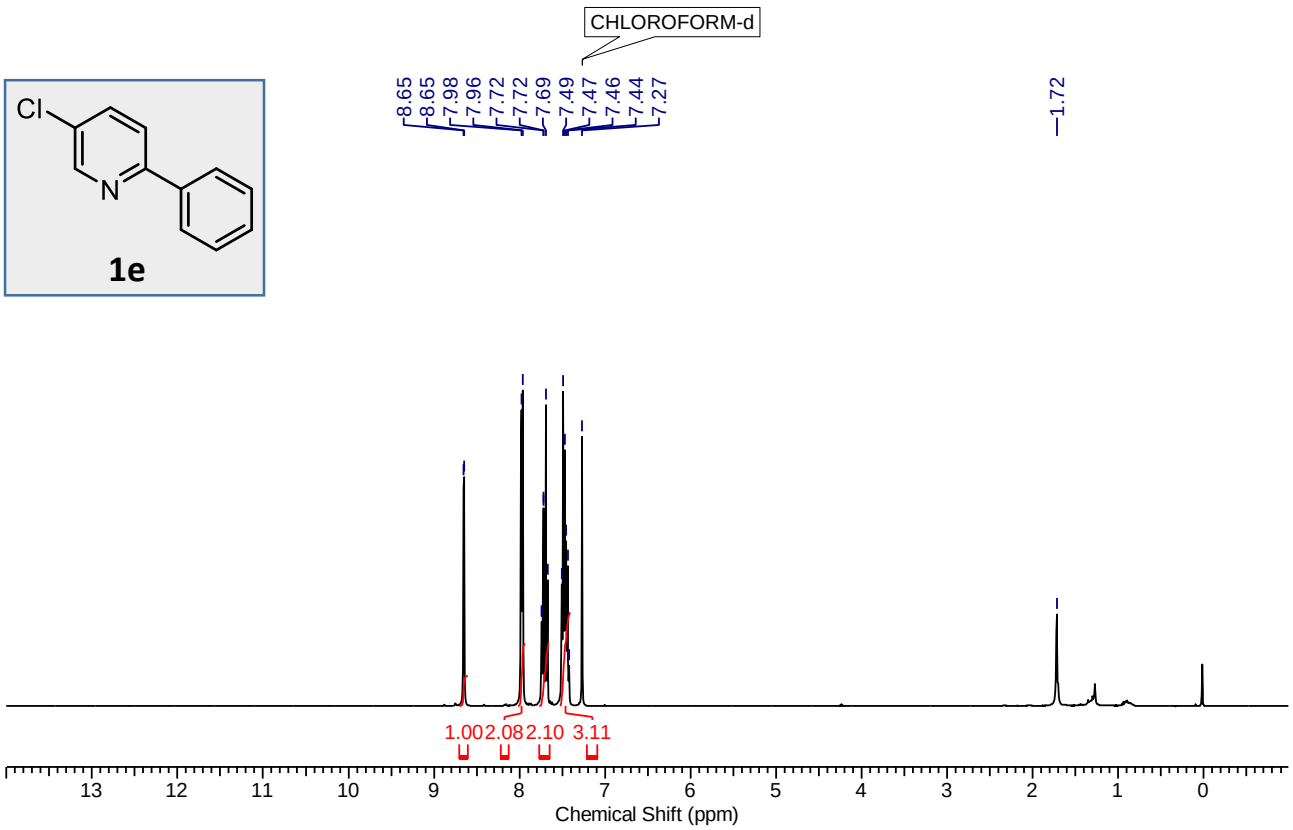


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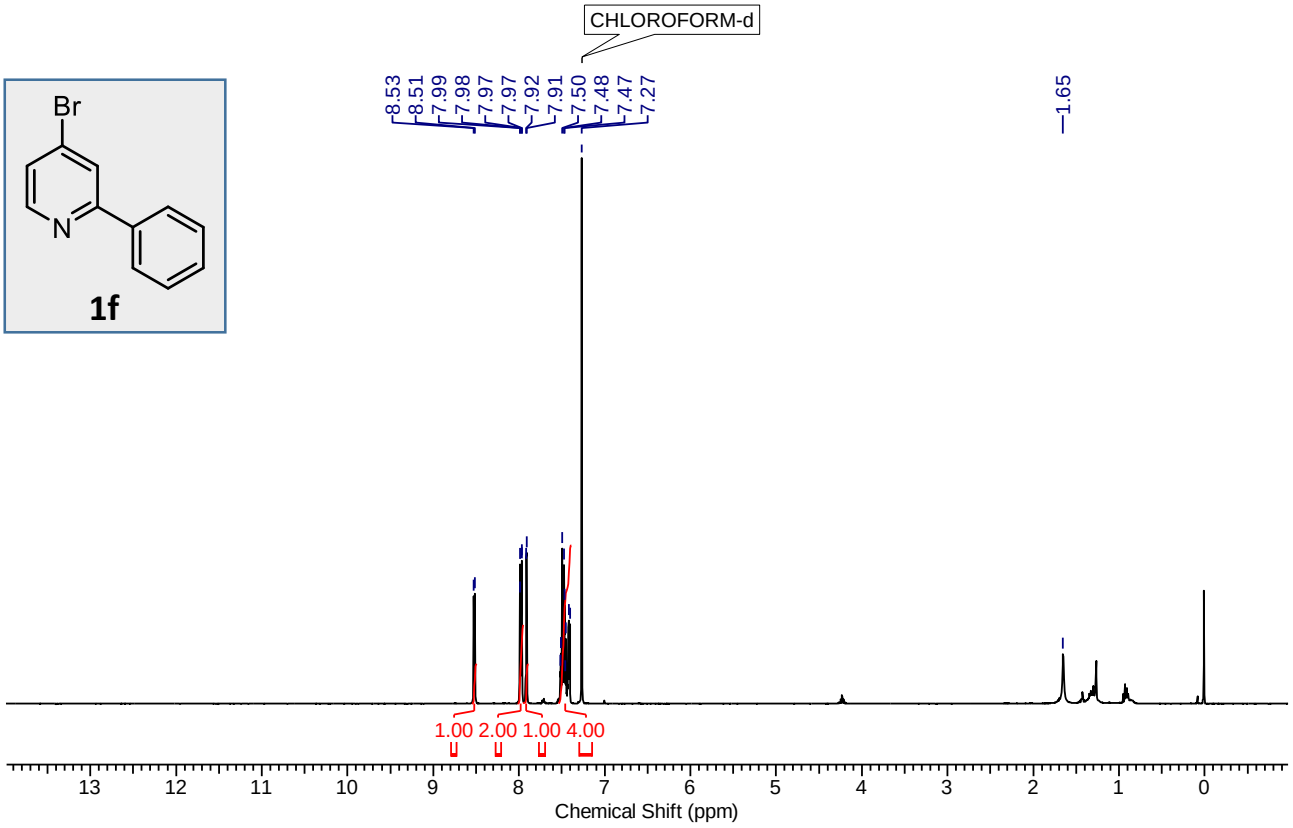


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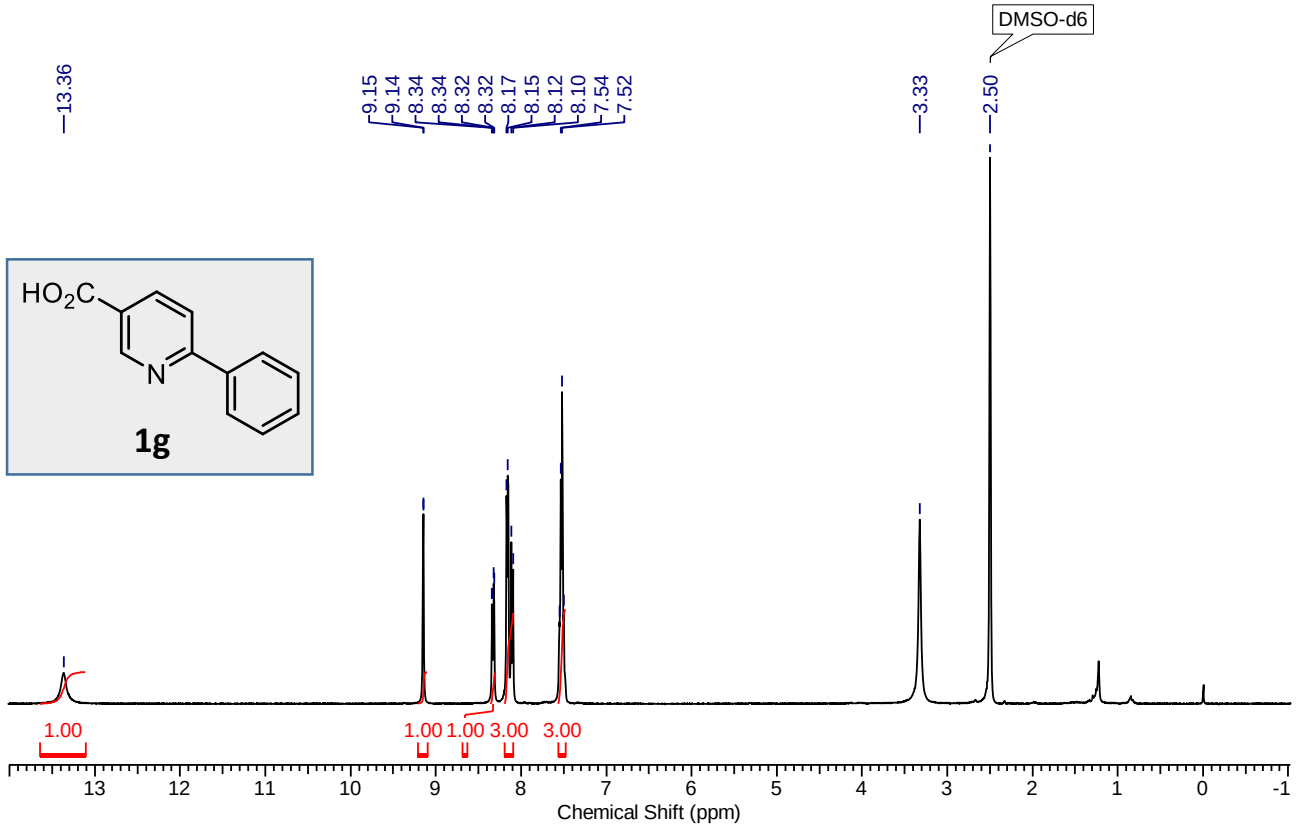
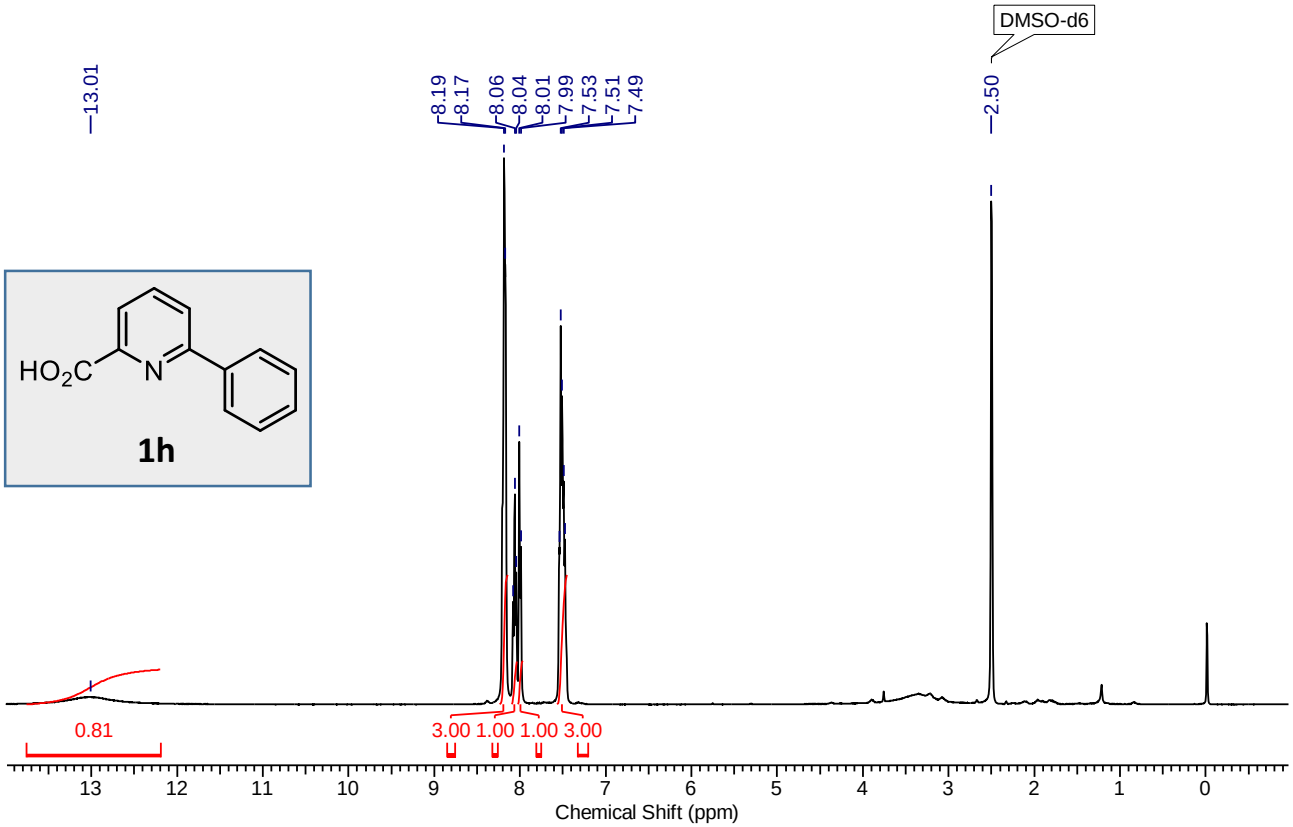
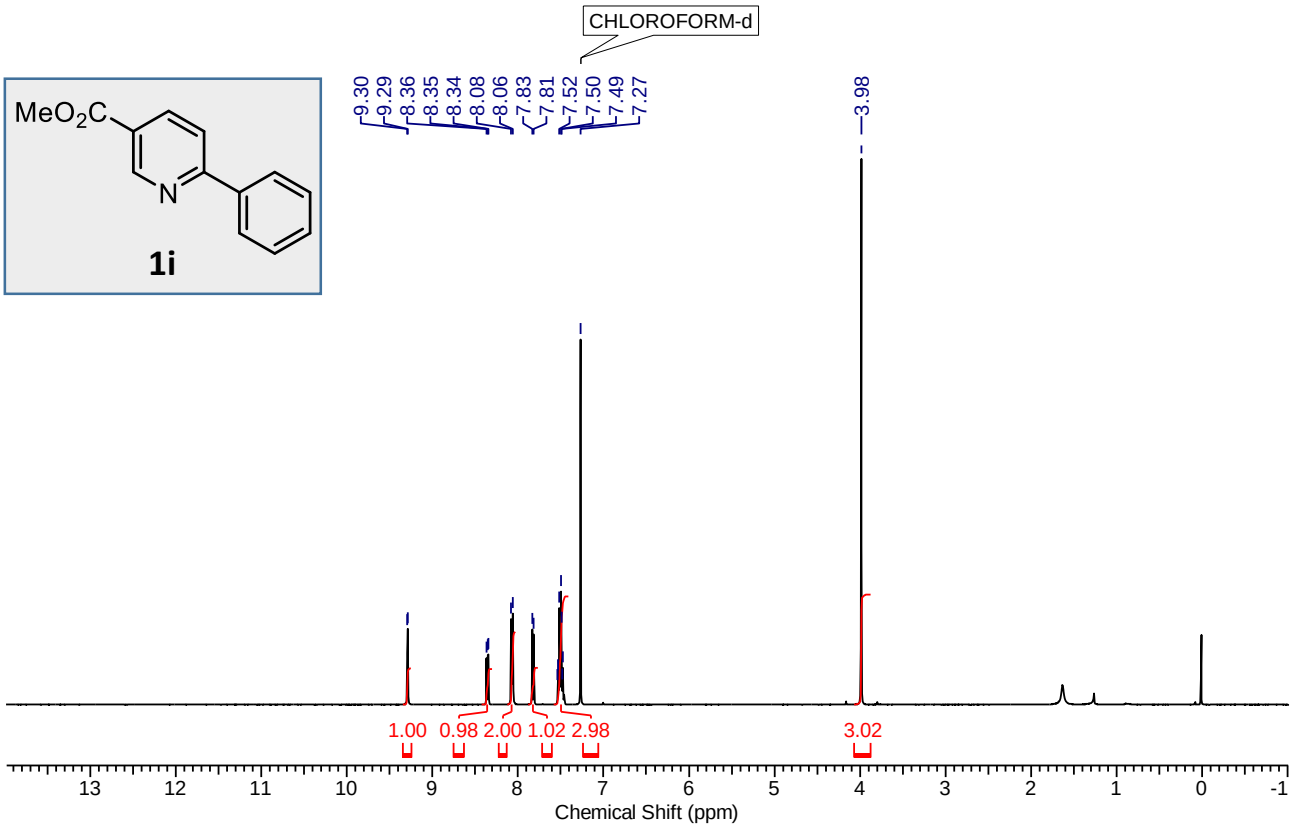



**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 1g**




**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 1h**

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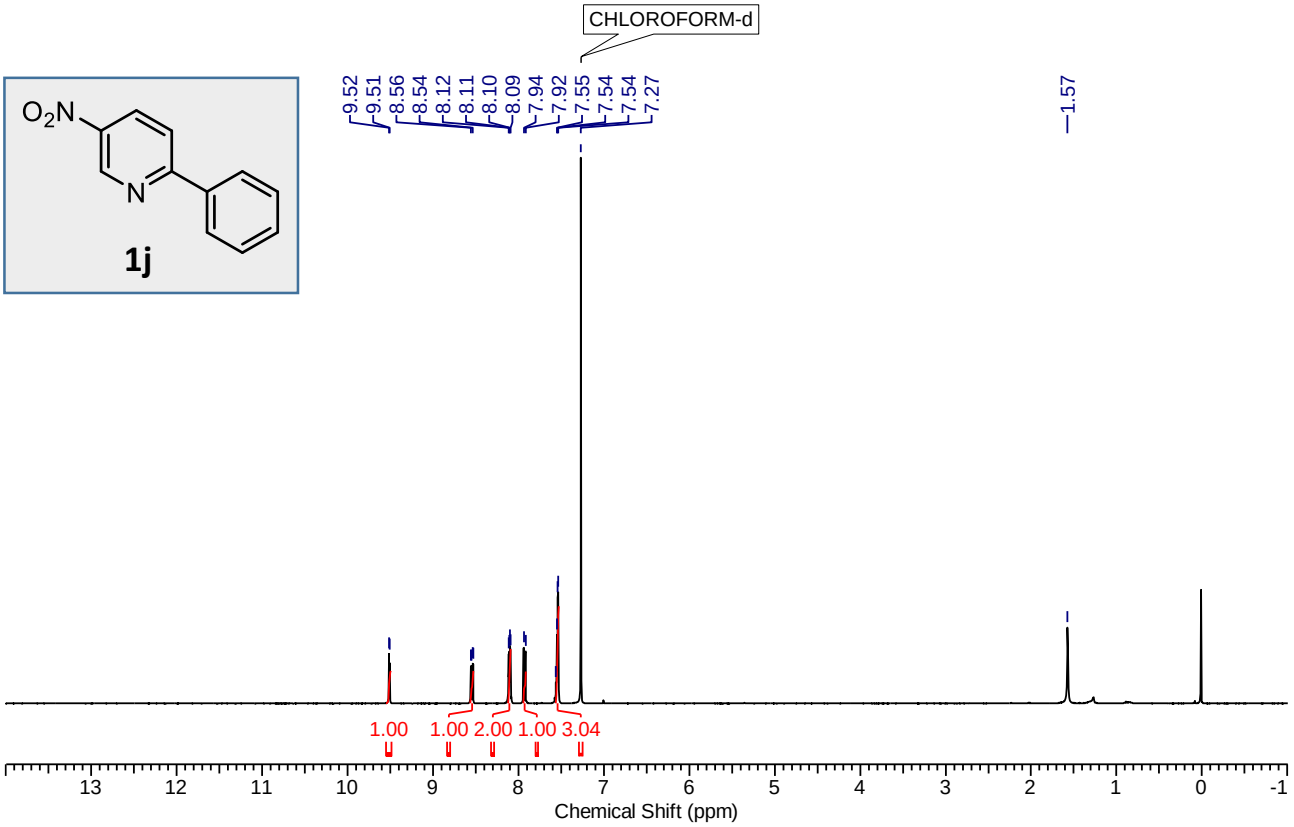


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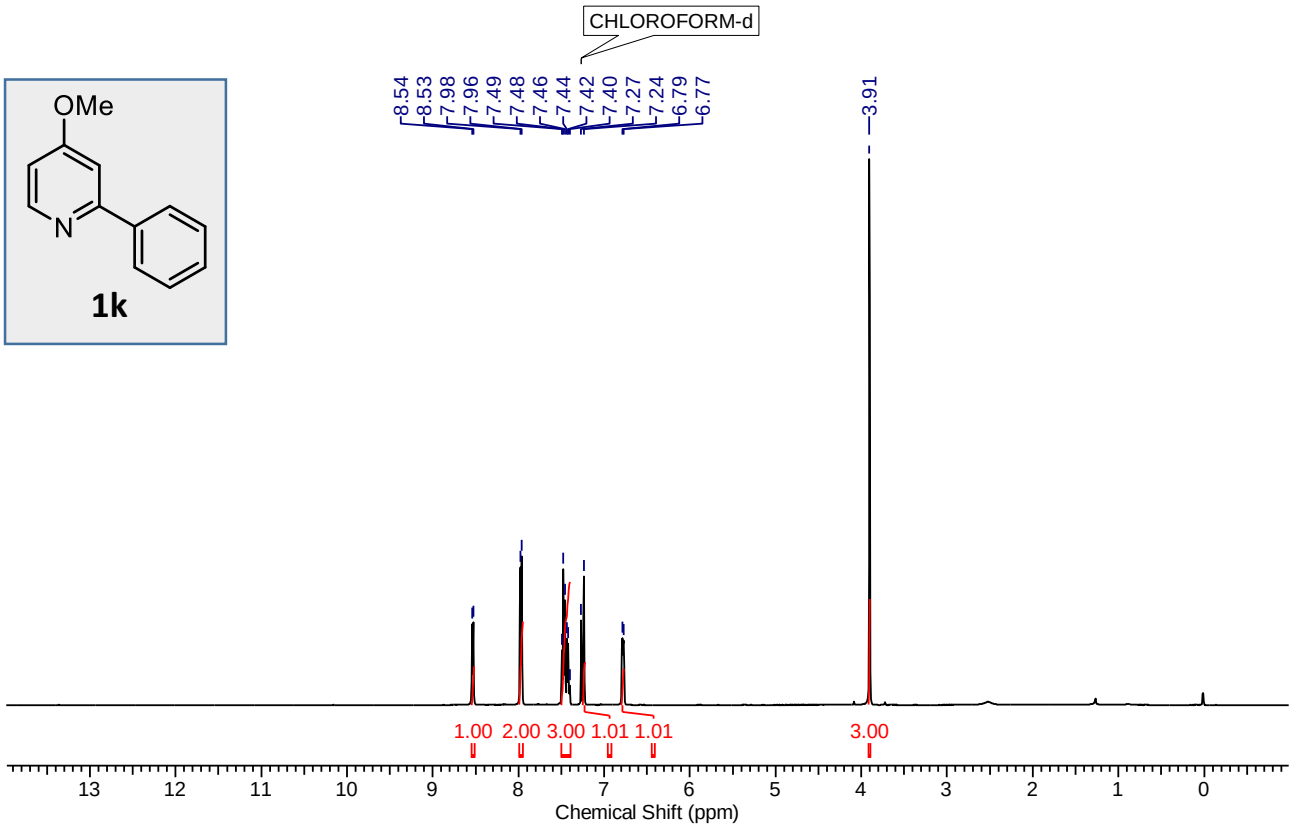


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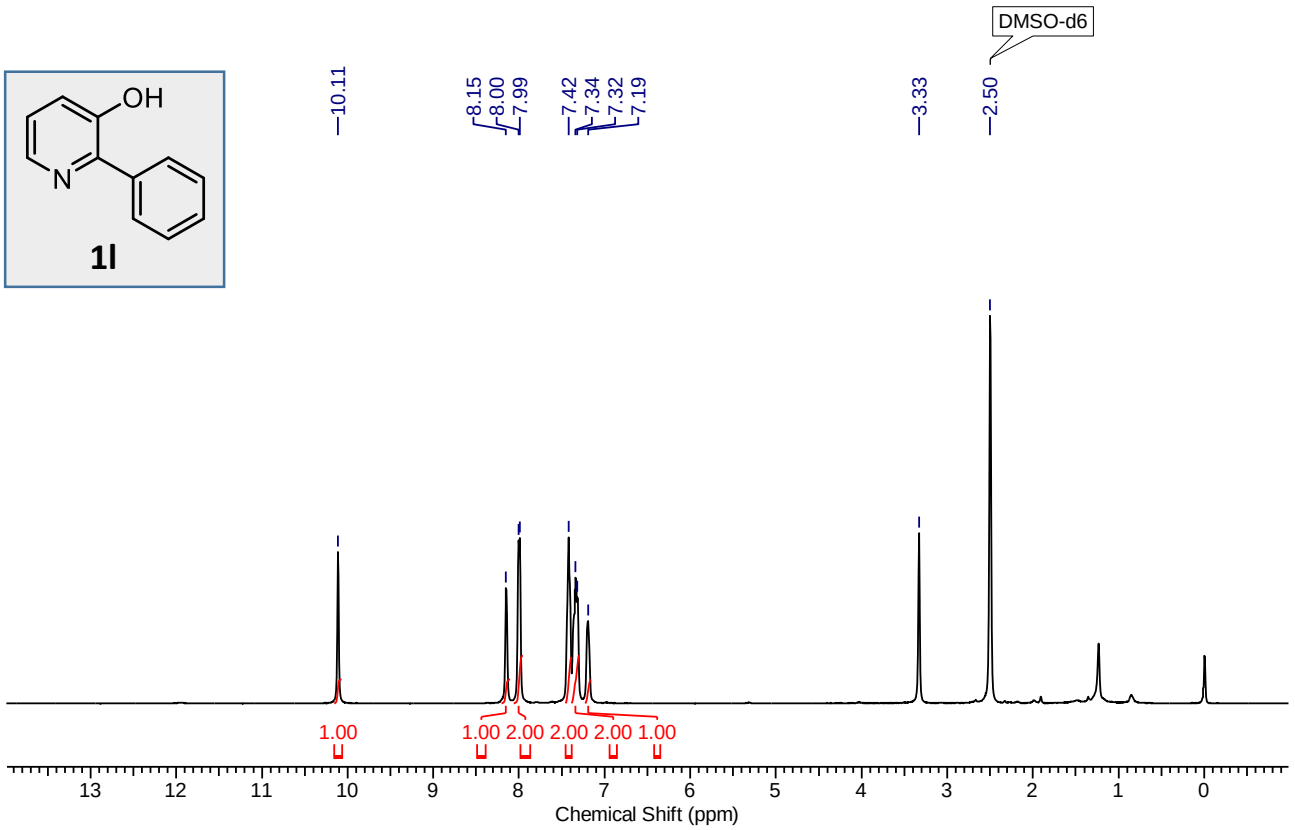


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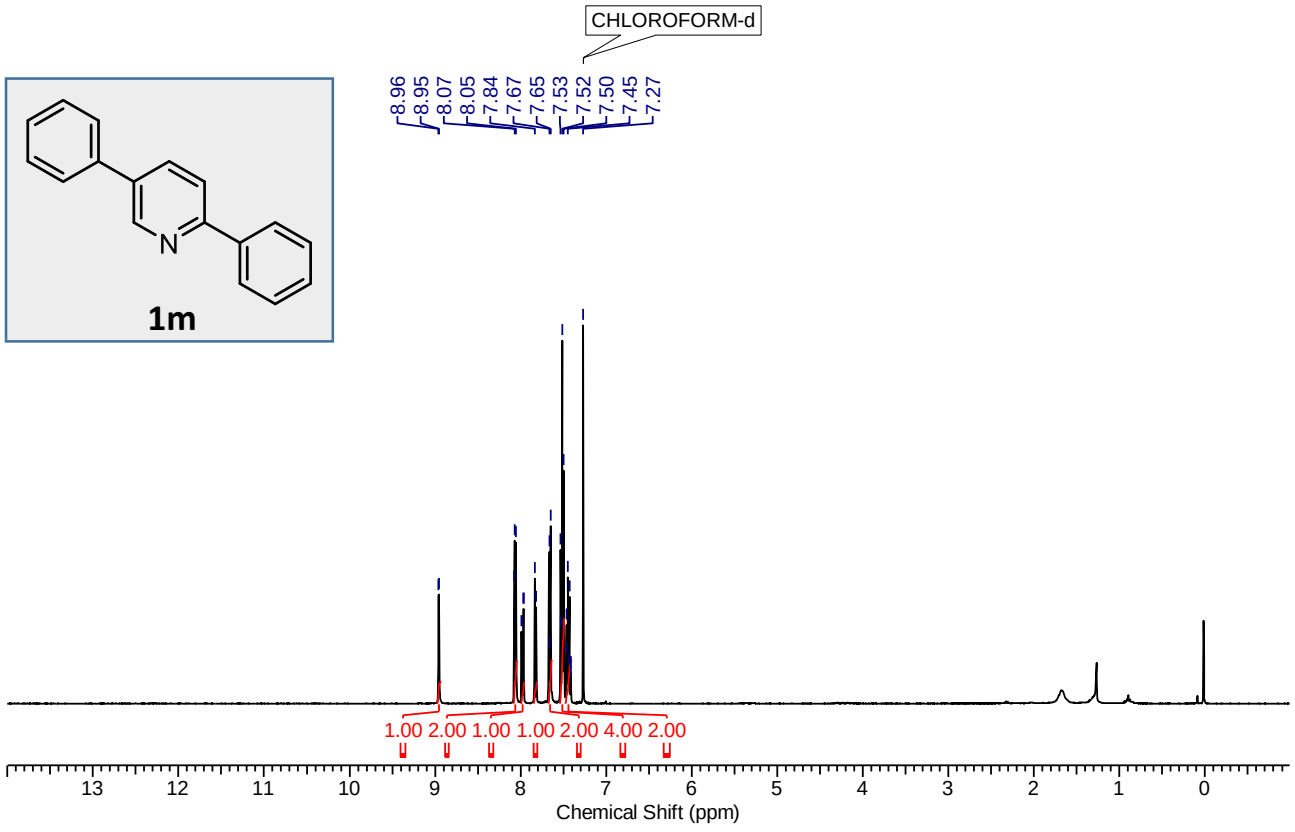


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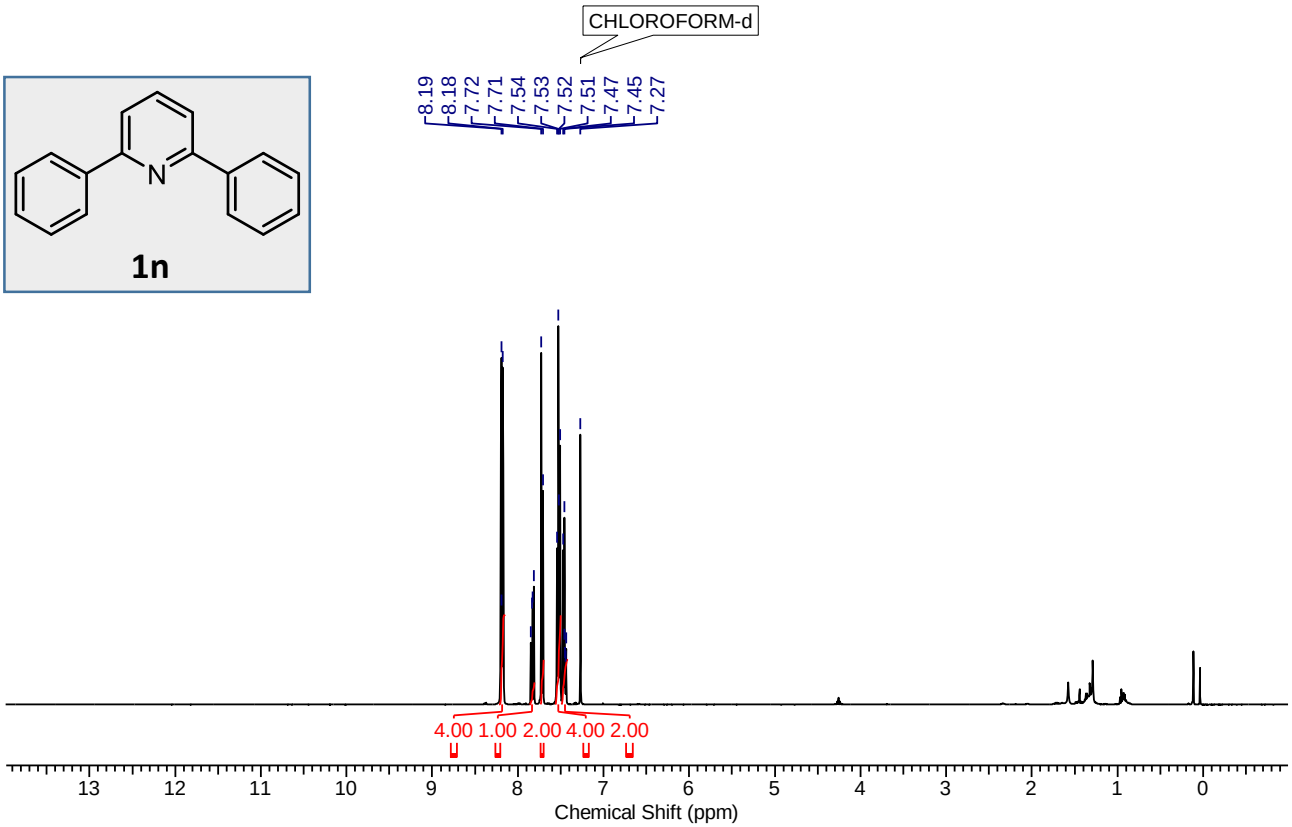


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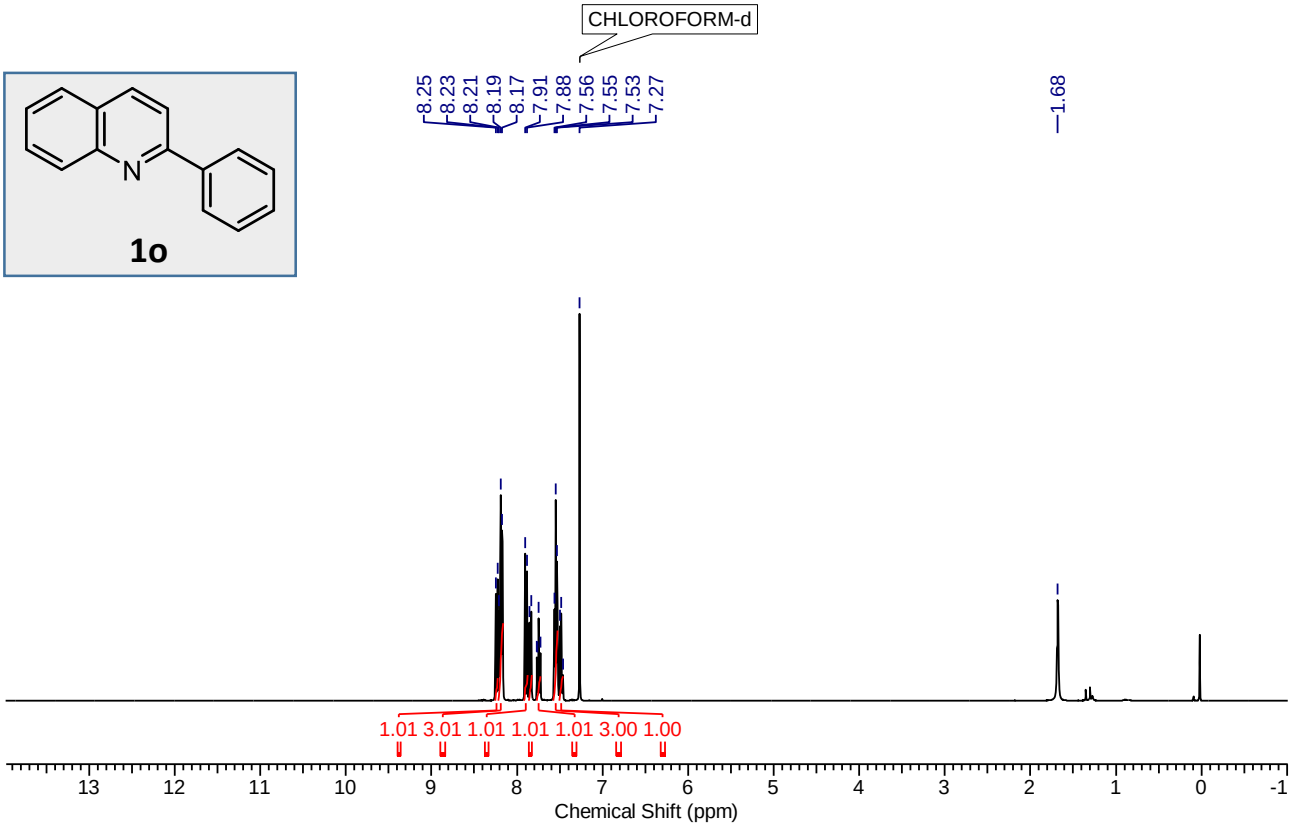


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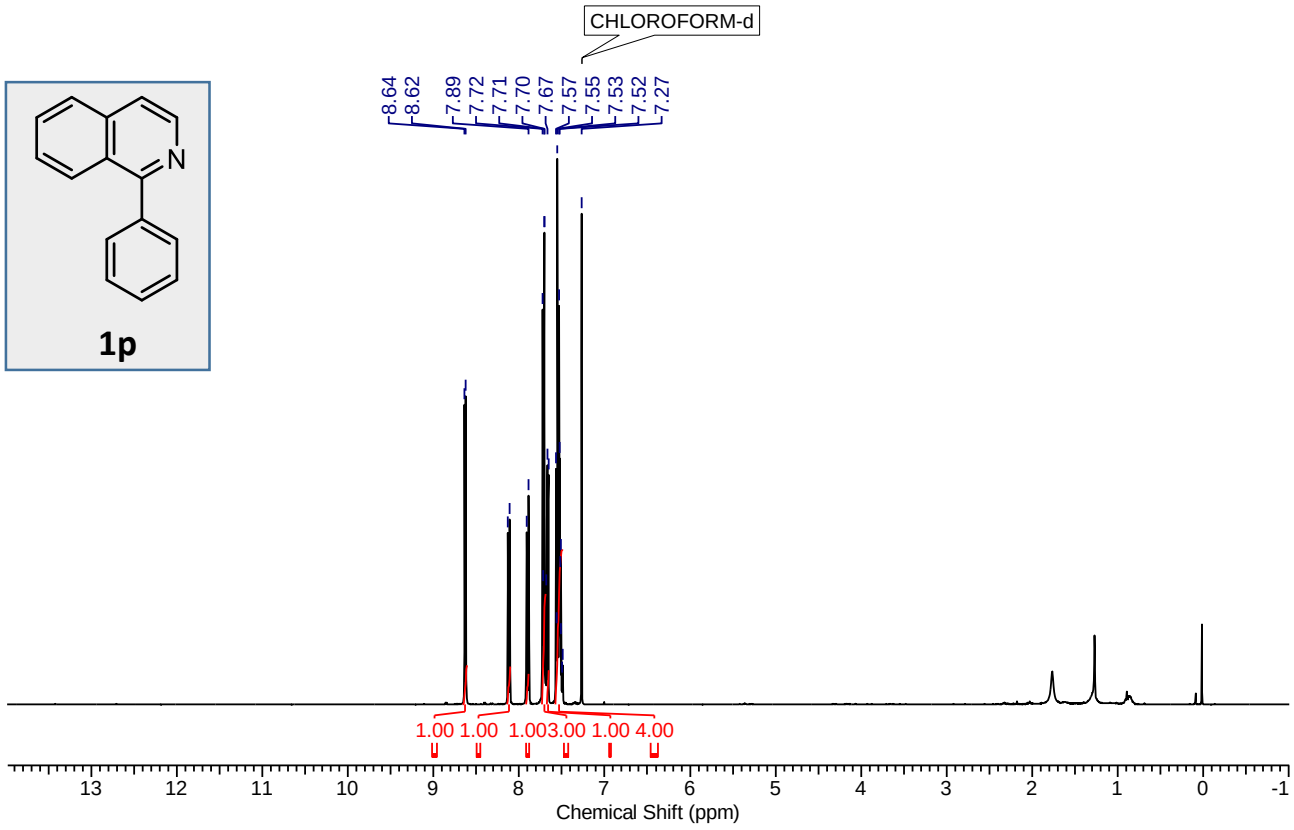
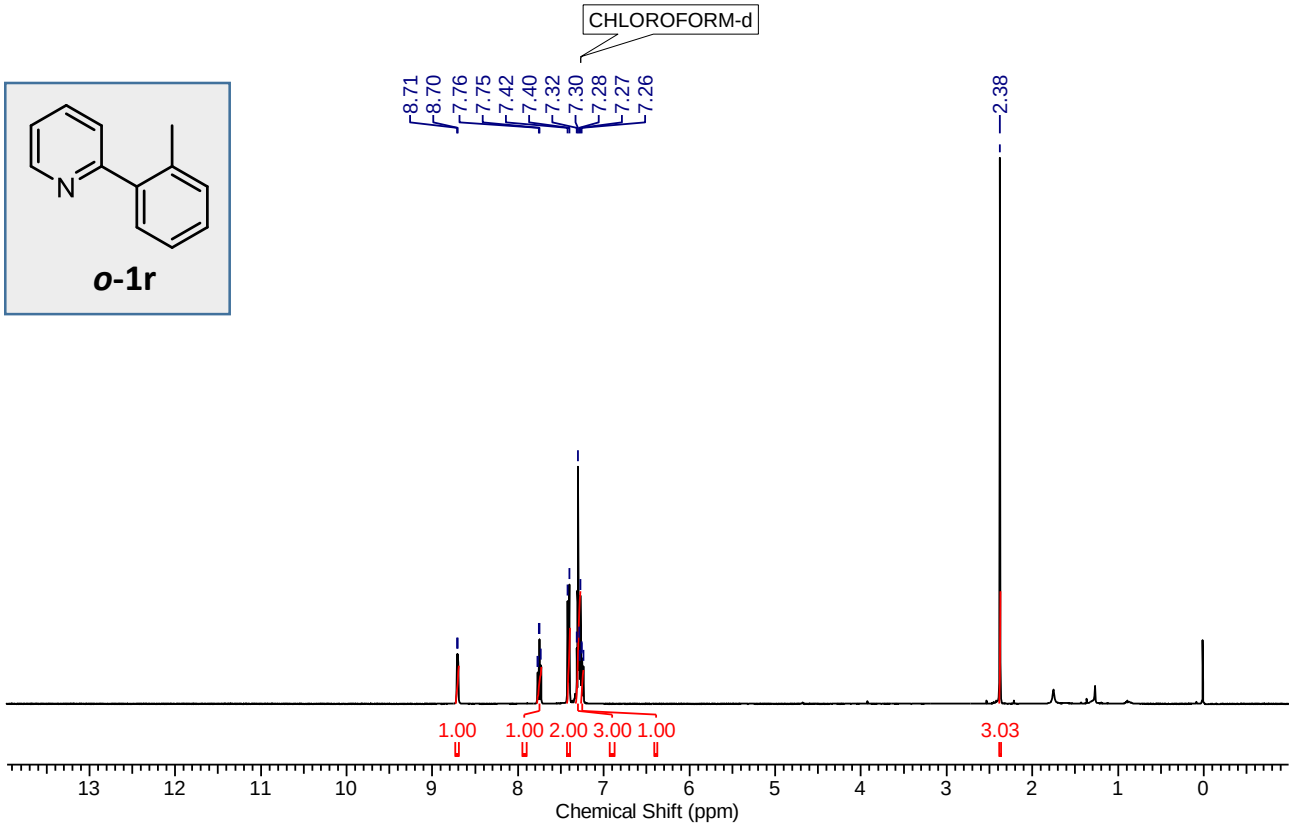



**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1p**

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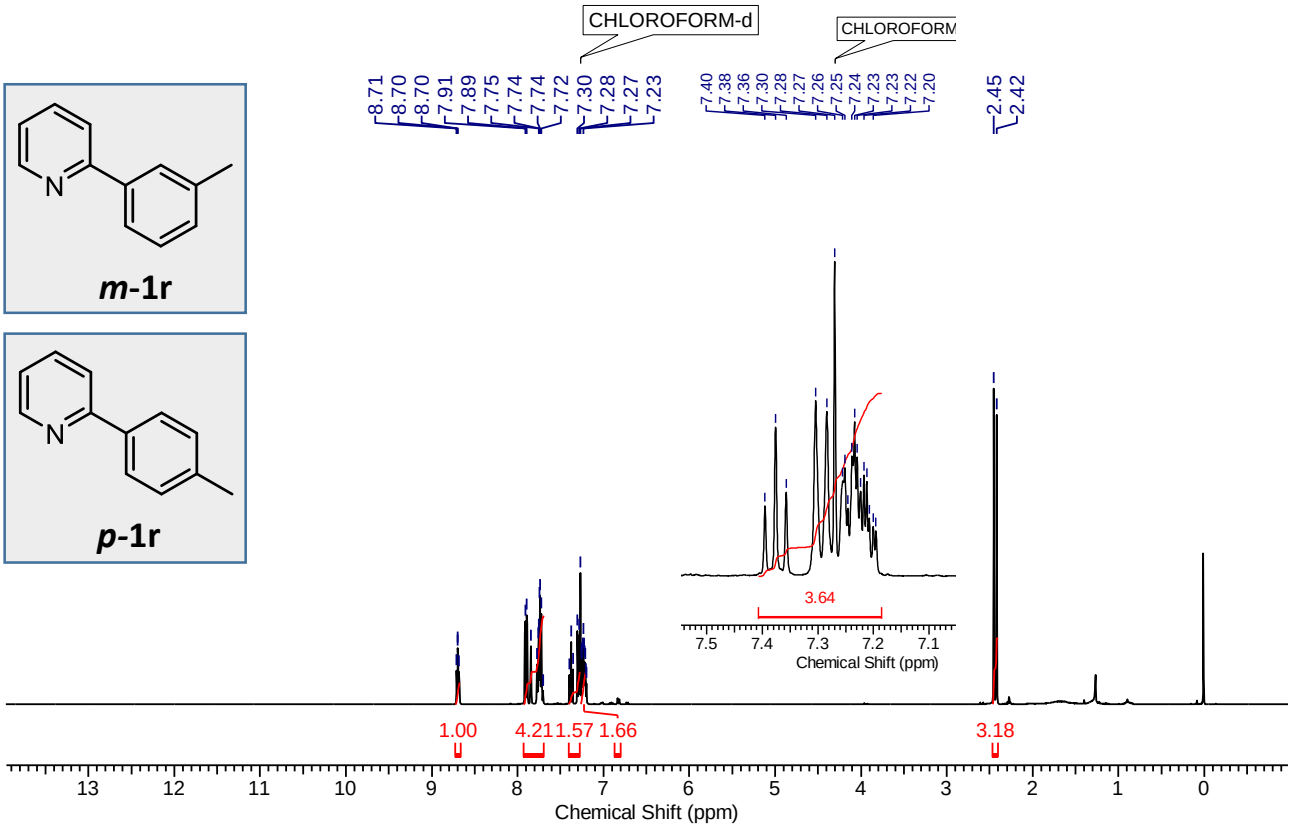
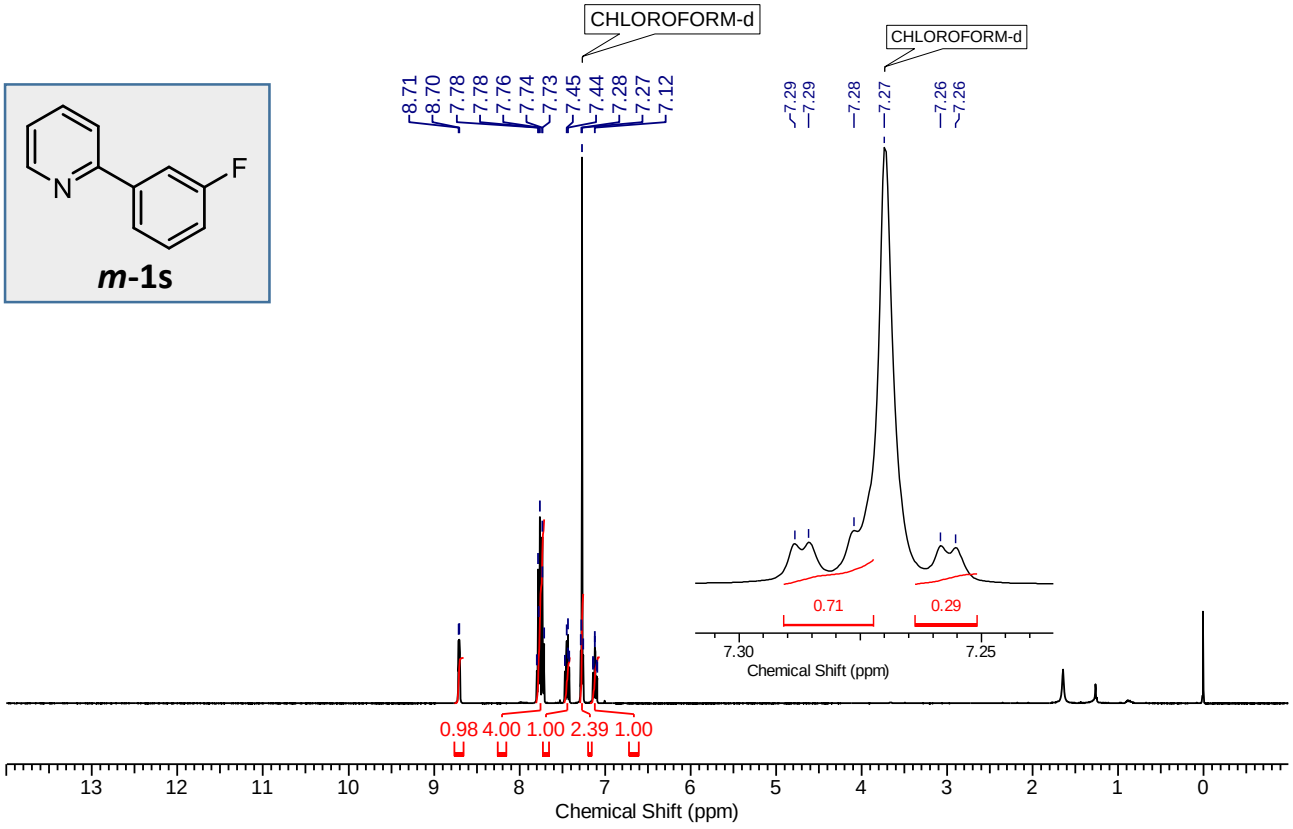



**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *m*-1r & *p*-1r**

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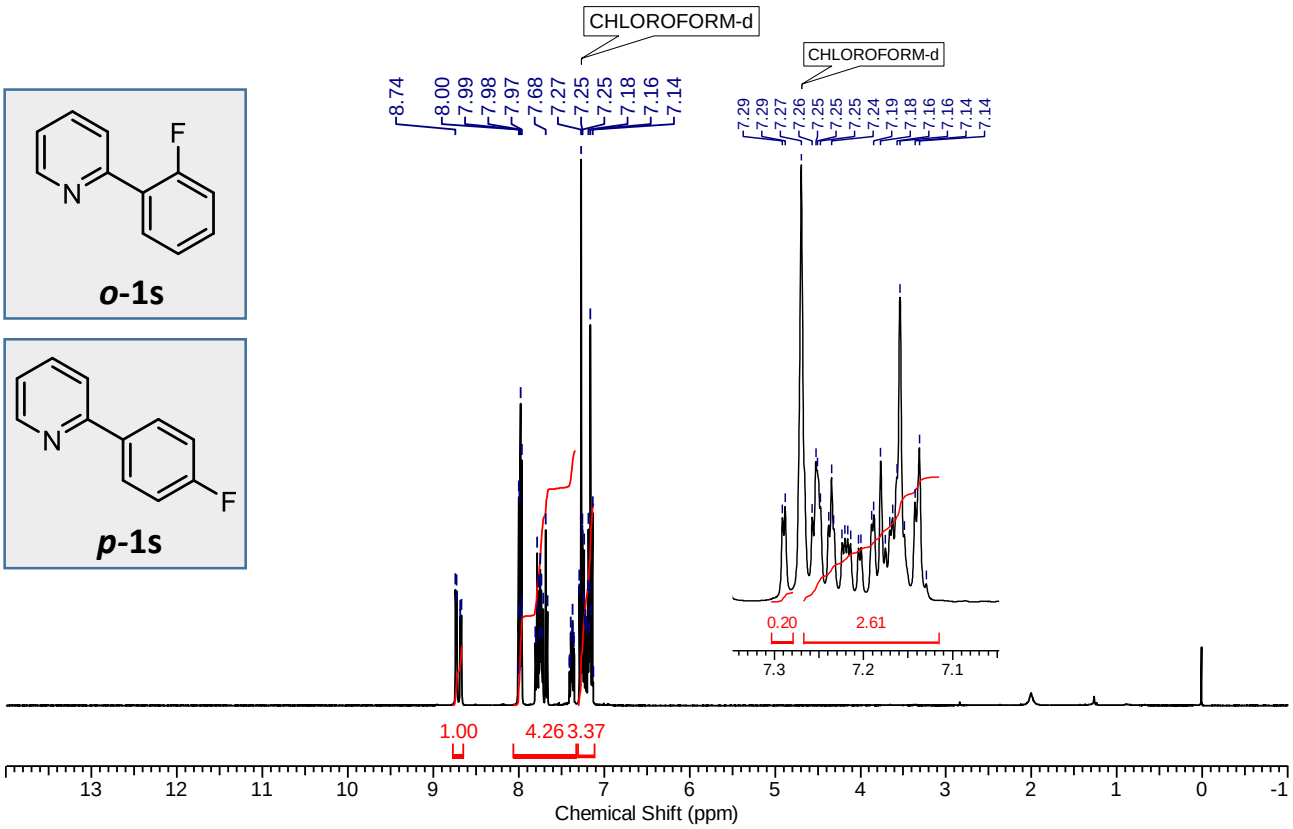
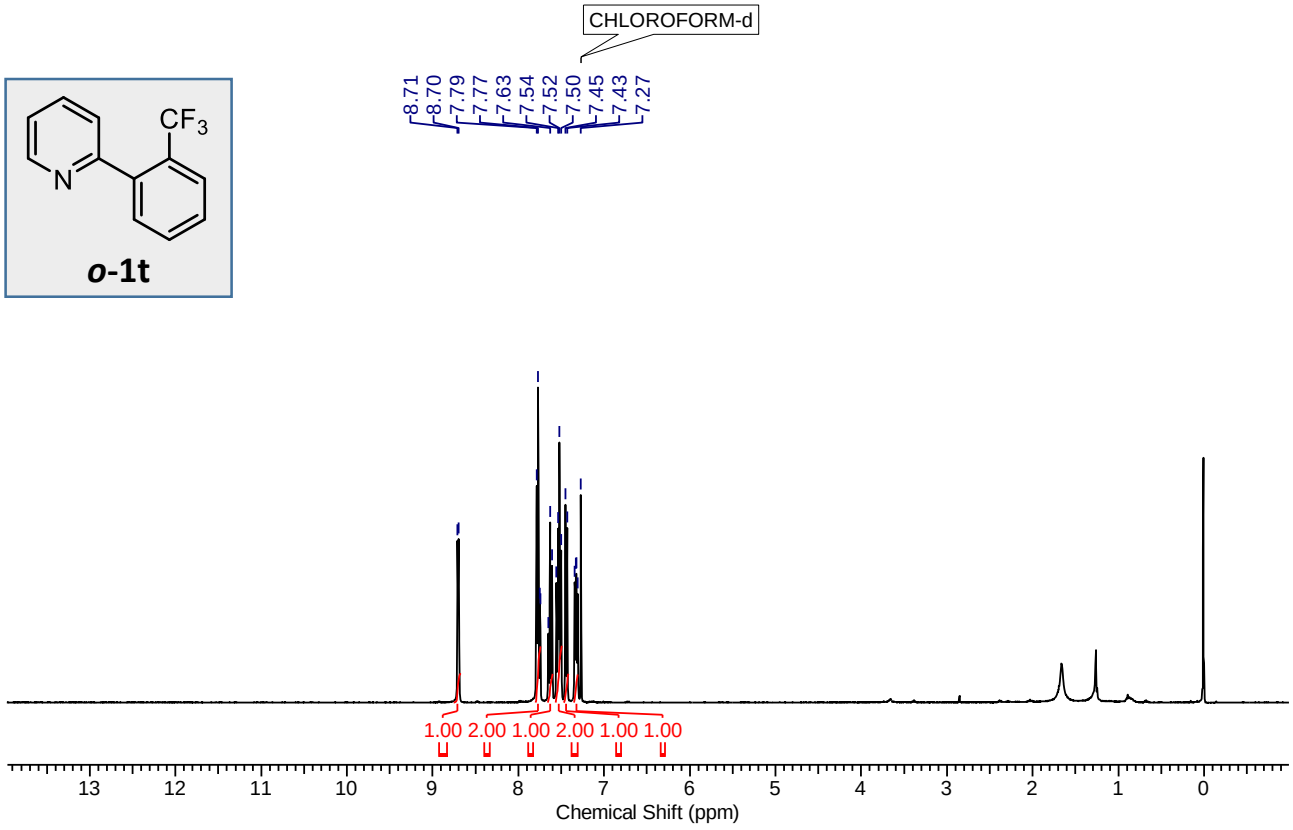
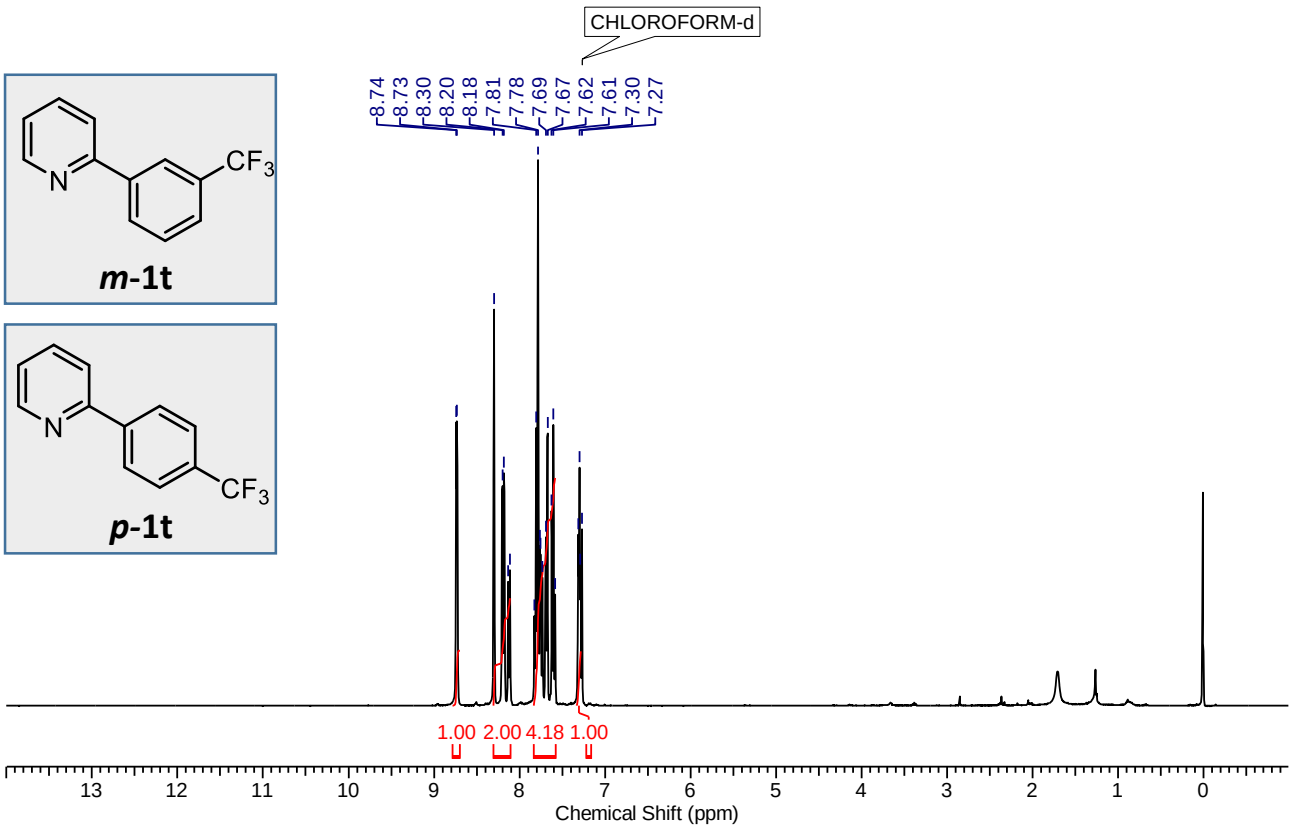


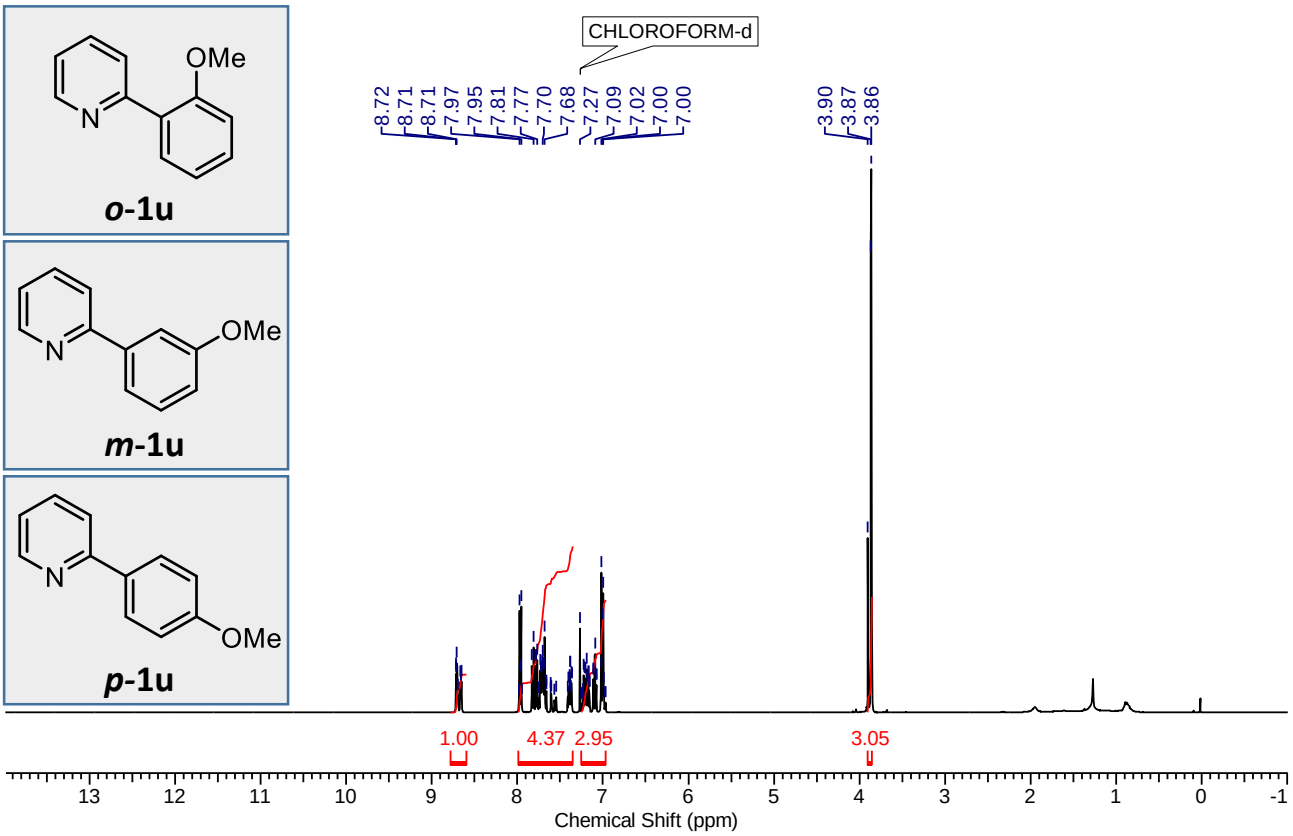

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *o*-1s & *p*-1s**



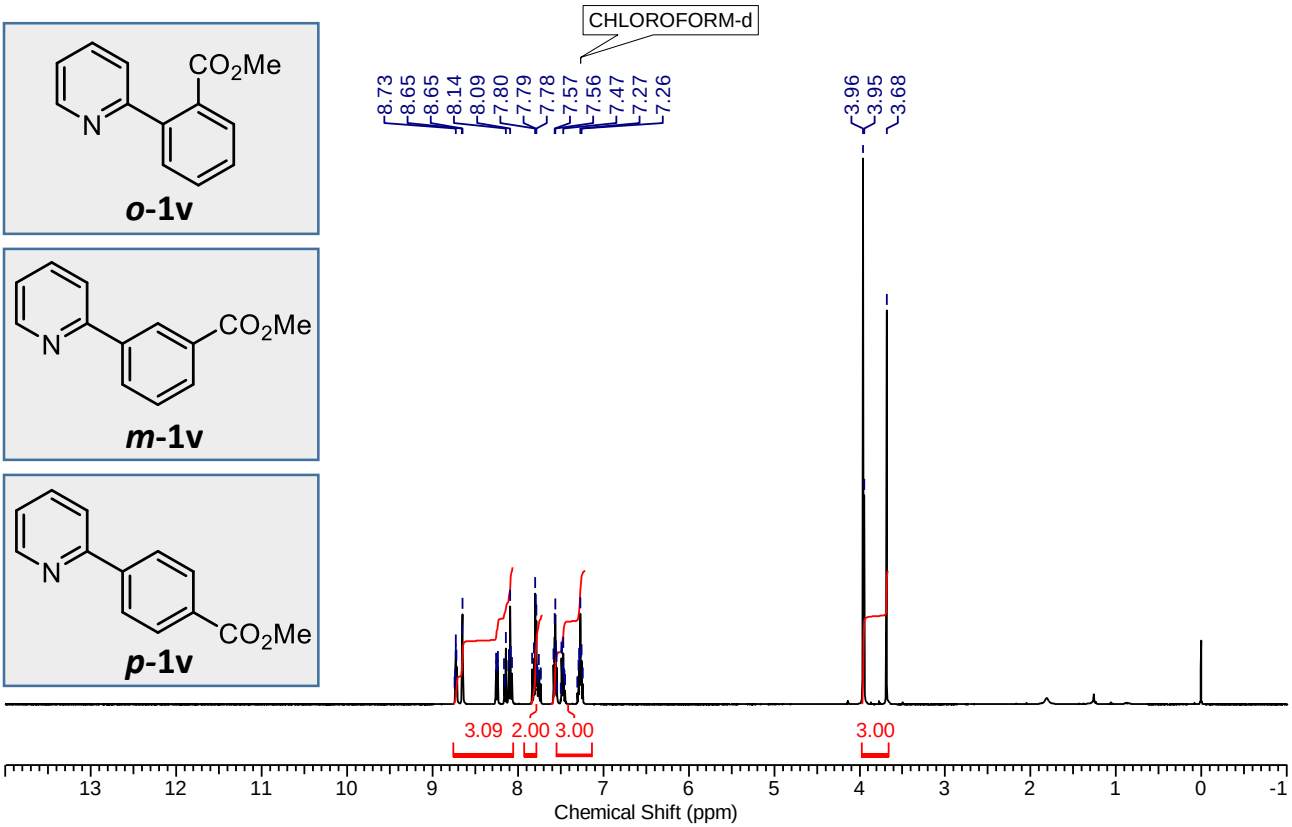

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *o*-1t**



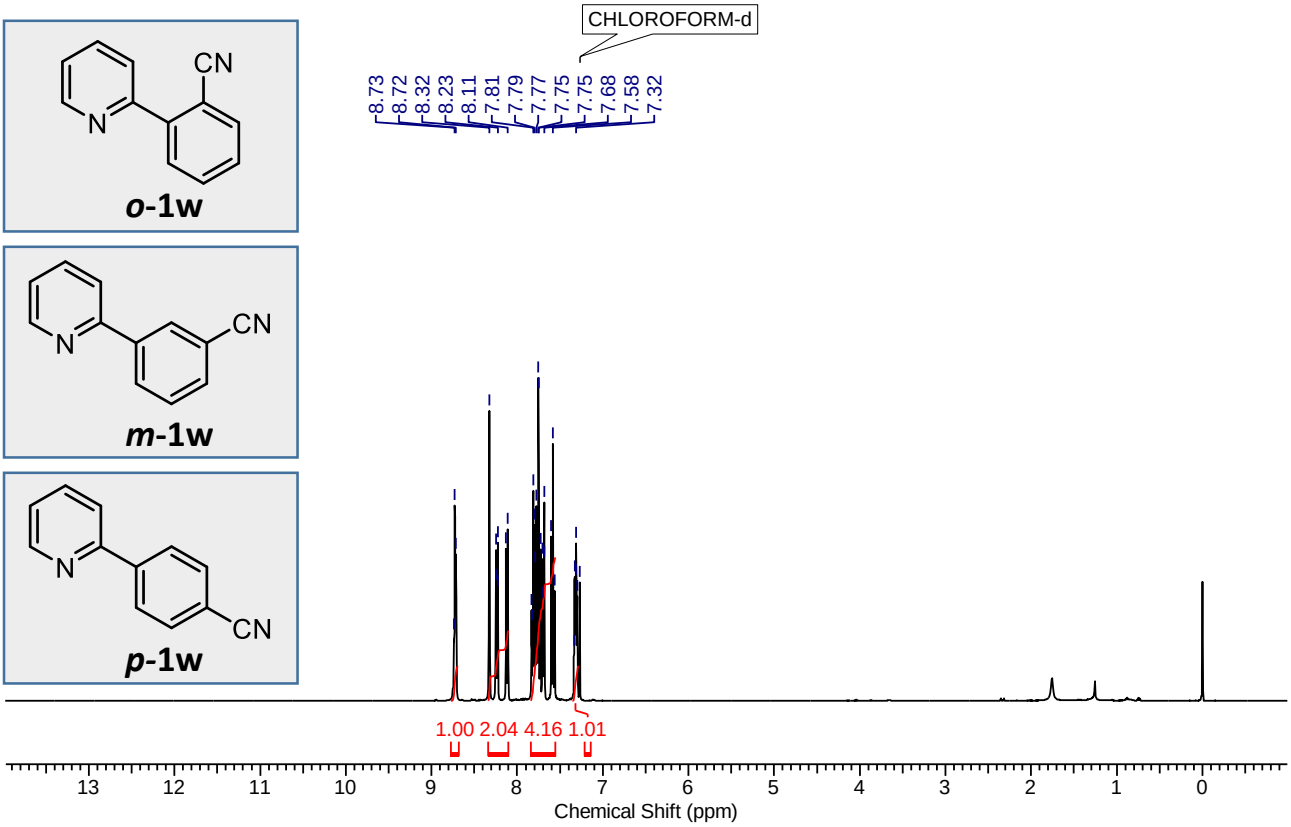

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *m*-1t & *p*-1t**



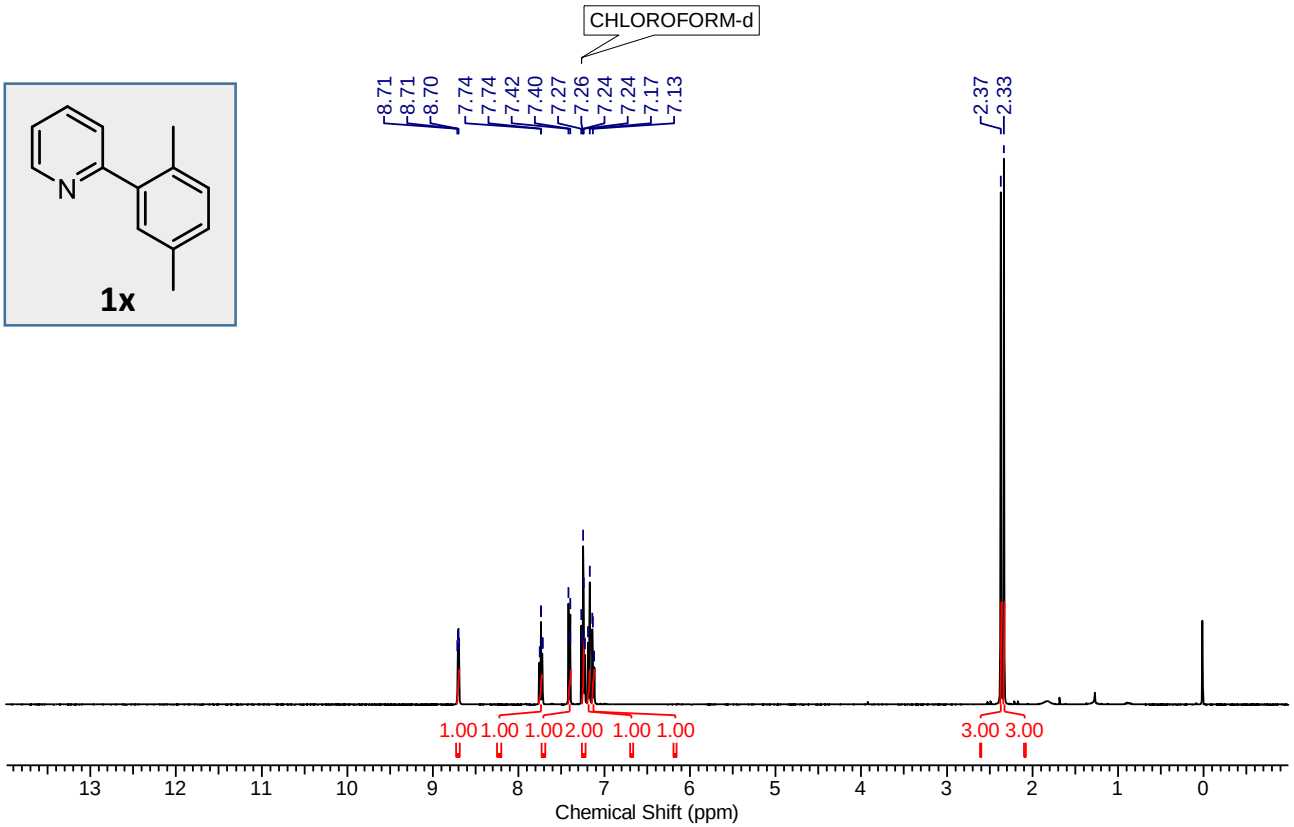

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *o*-1u, *m*-1u & *p*-1u**



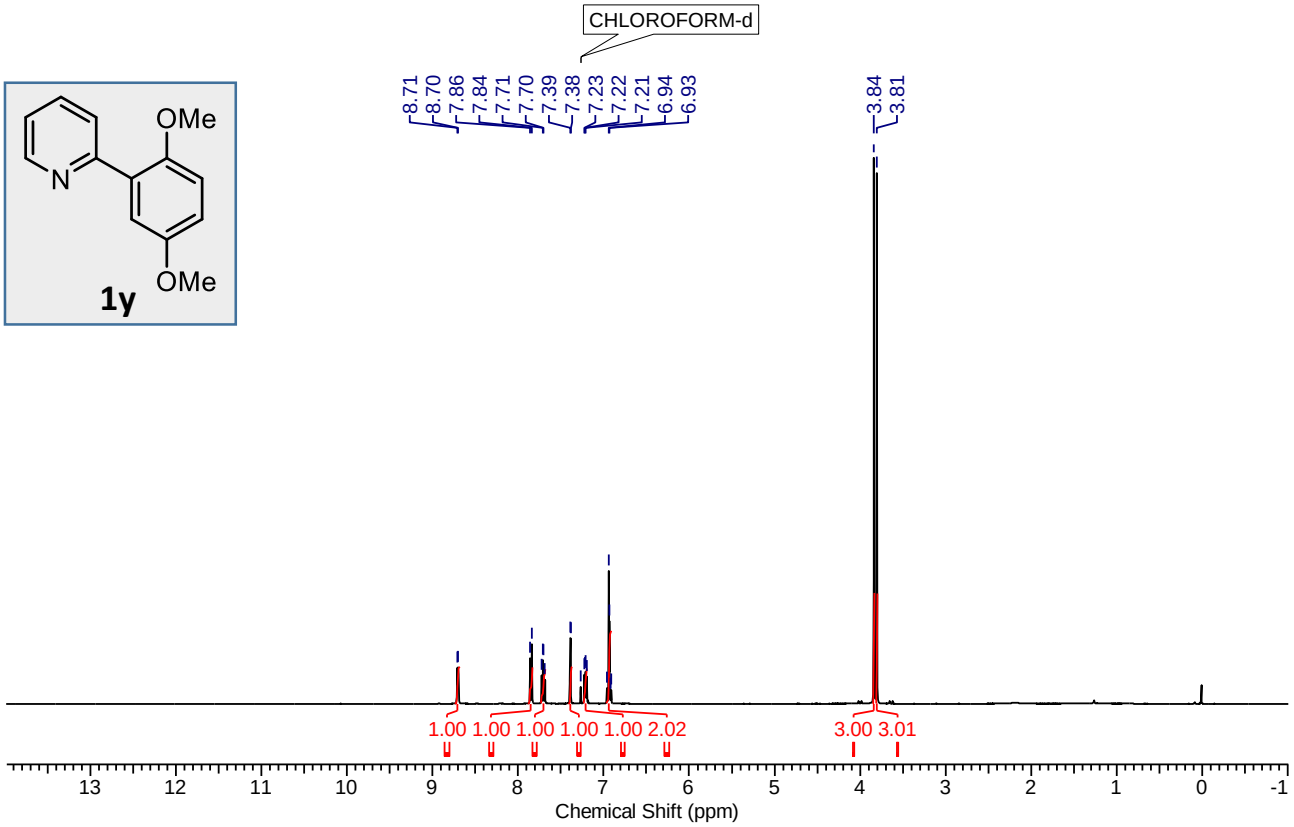

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *o*-1v, *m*-1v & *p*-1v**



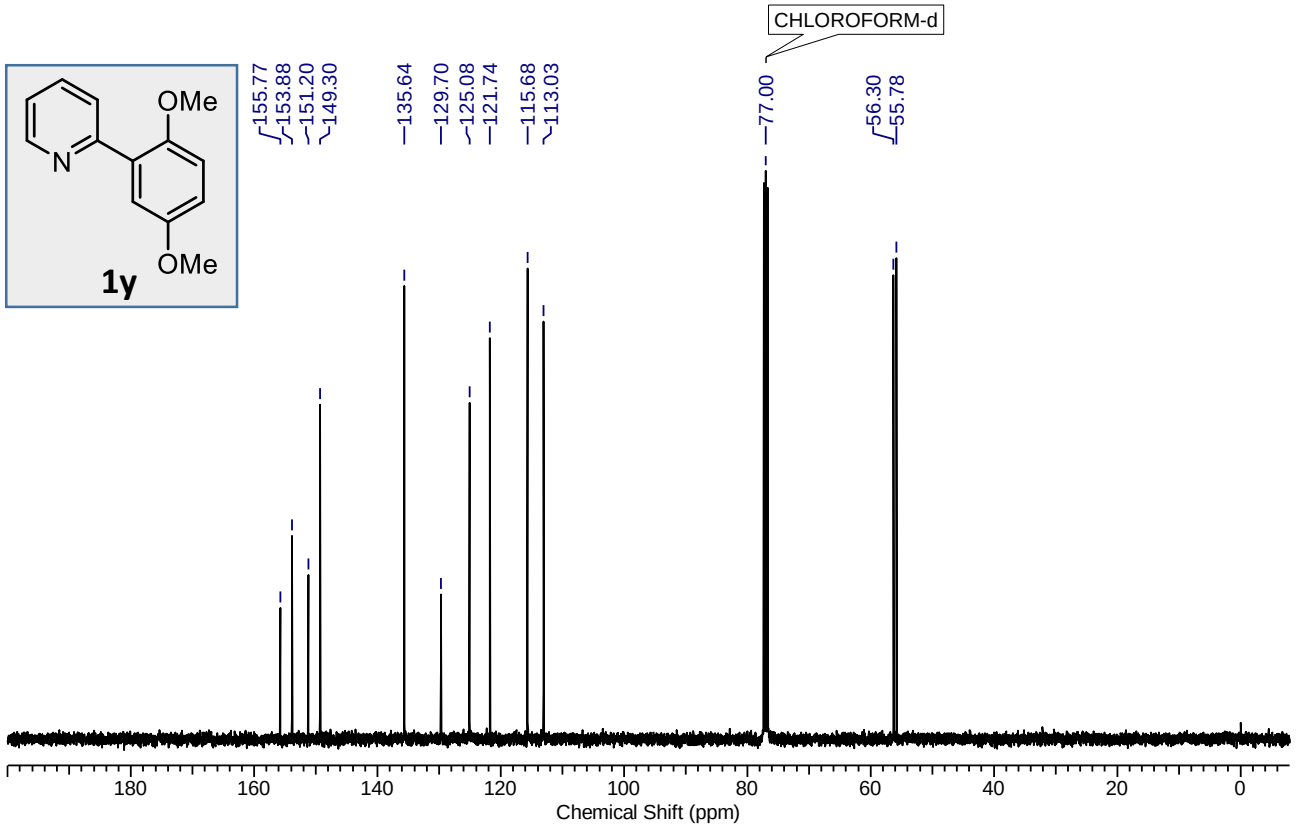

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *o*-1w, *m*-1w & *p*-1w**



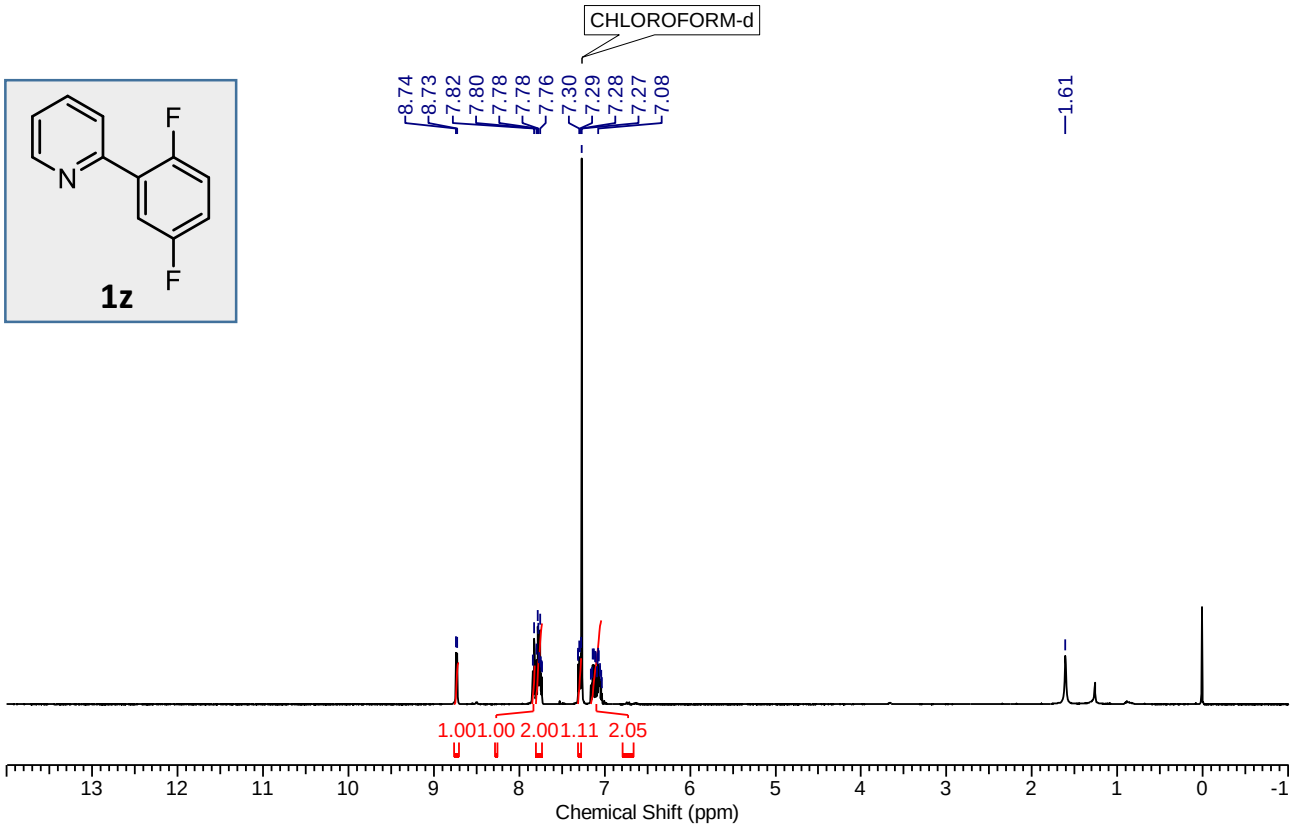

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1x**



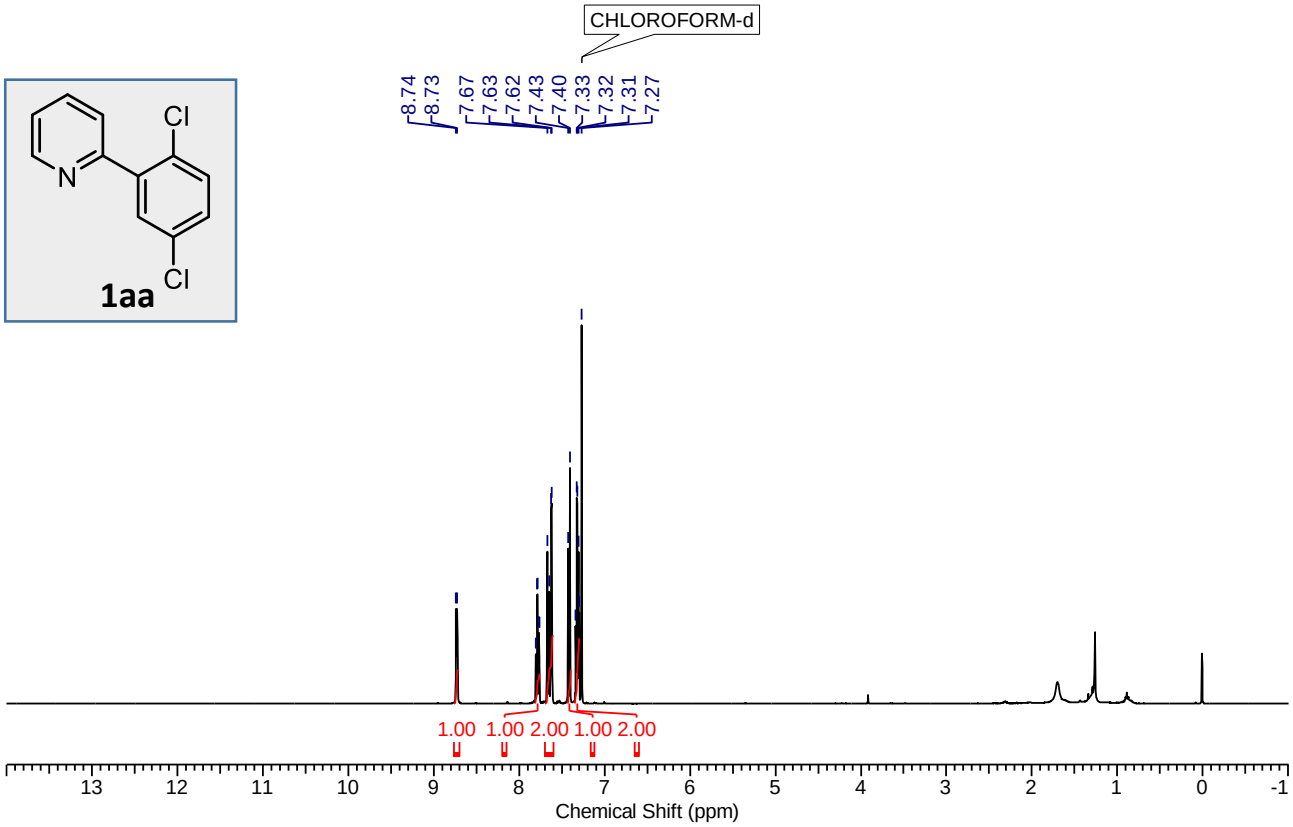

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1y**



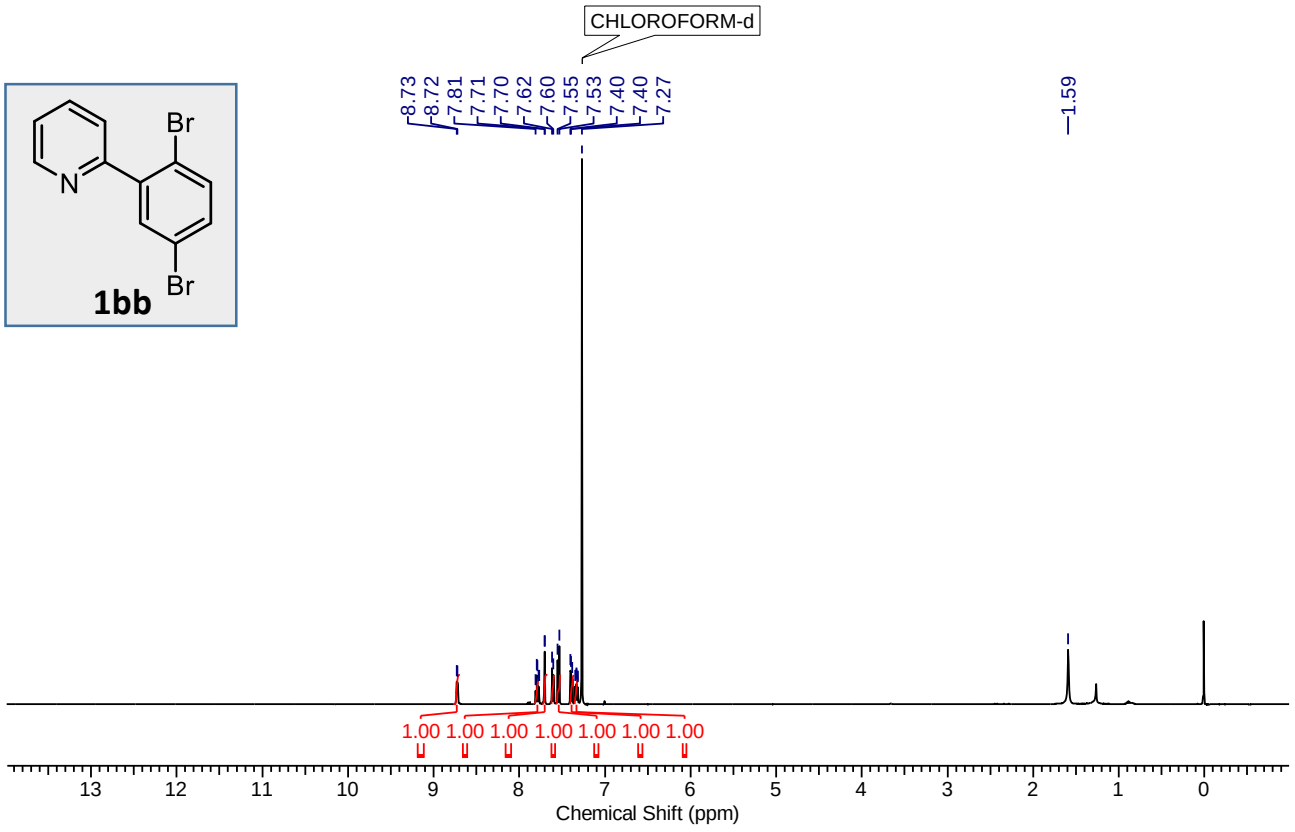

**$^{13}$C NMR (101 MHz, $CDCl_3$) of compound 1y**



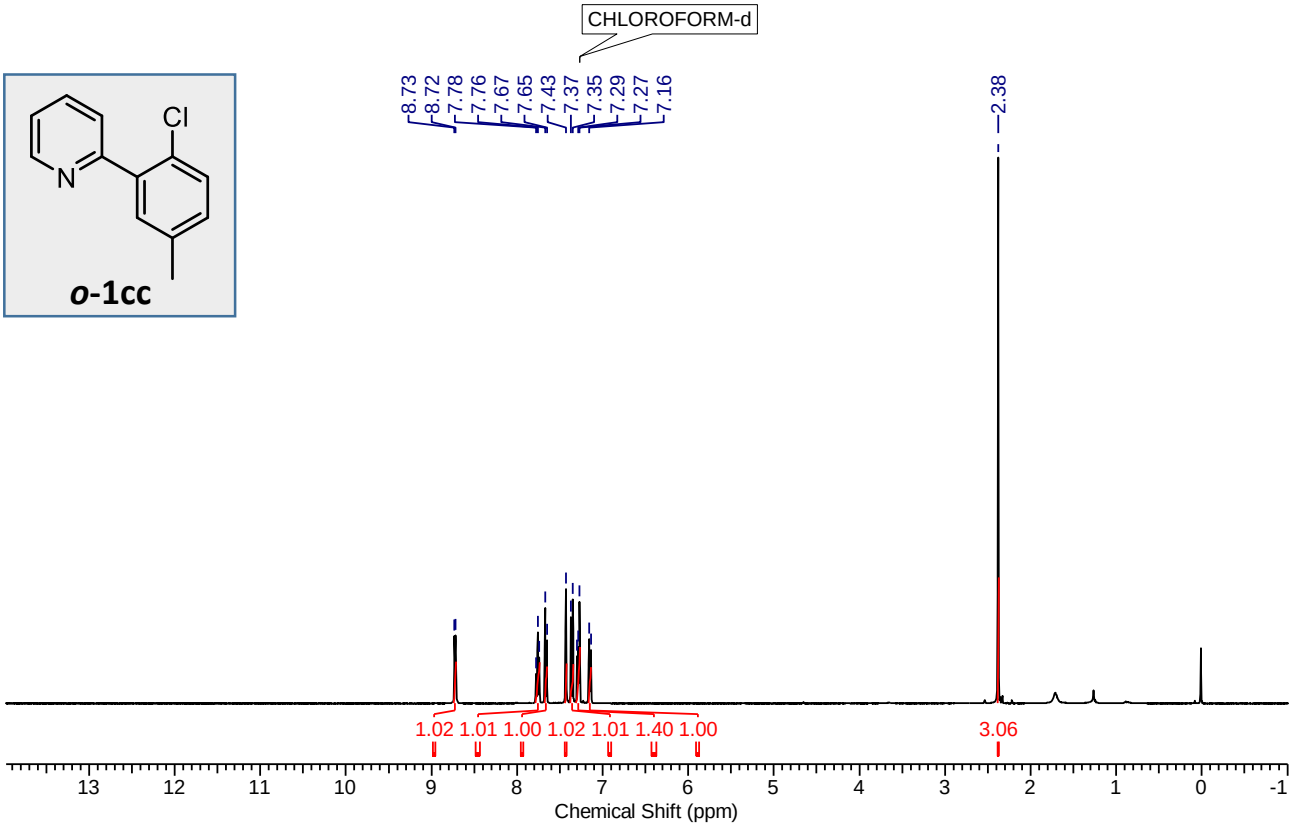

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1z**



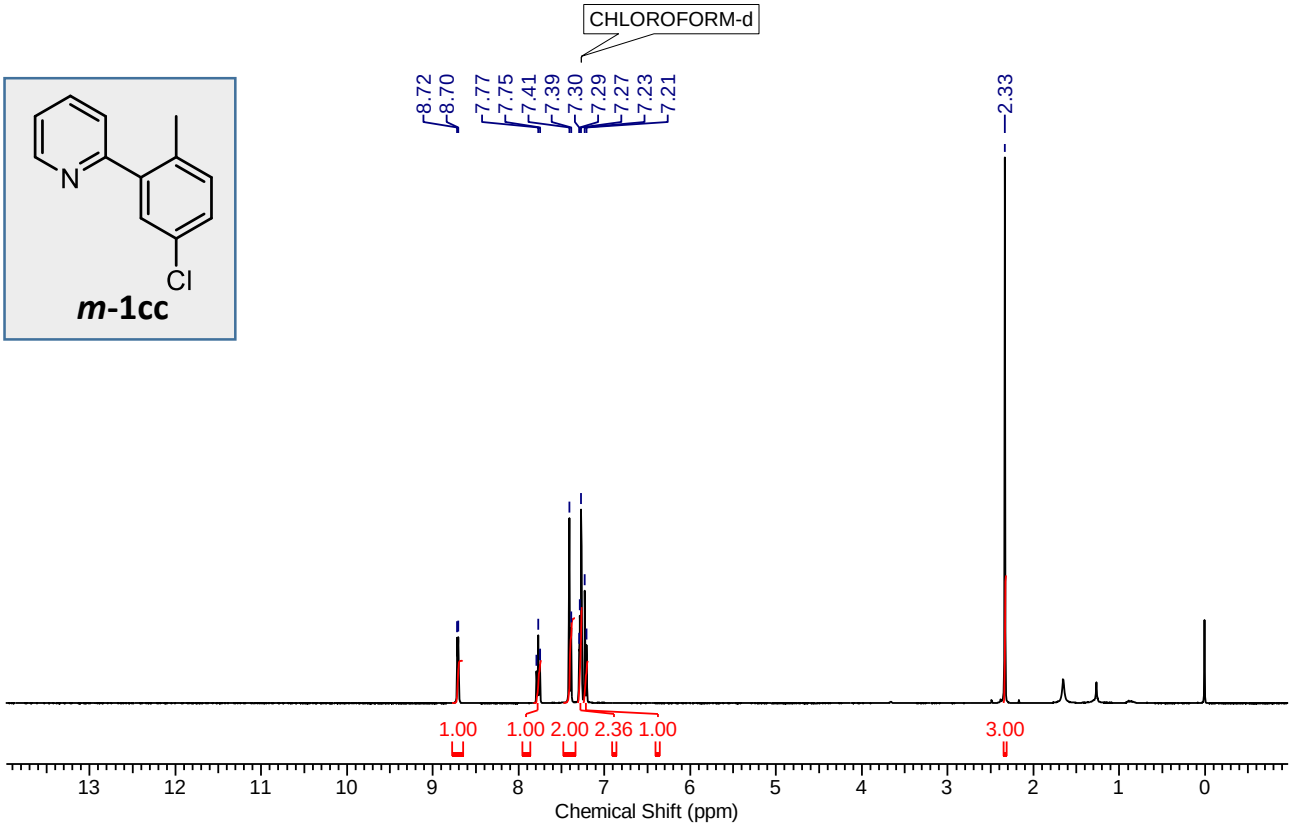

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1aa**



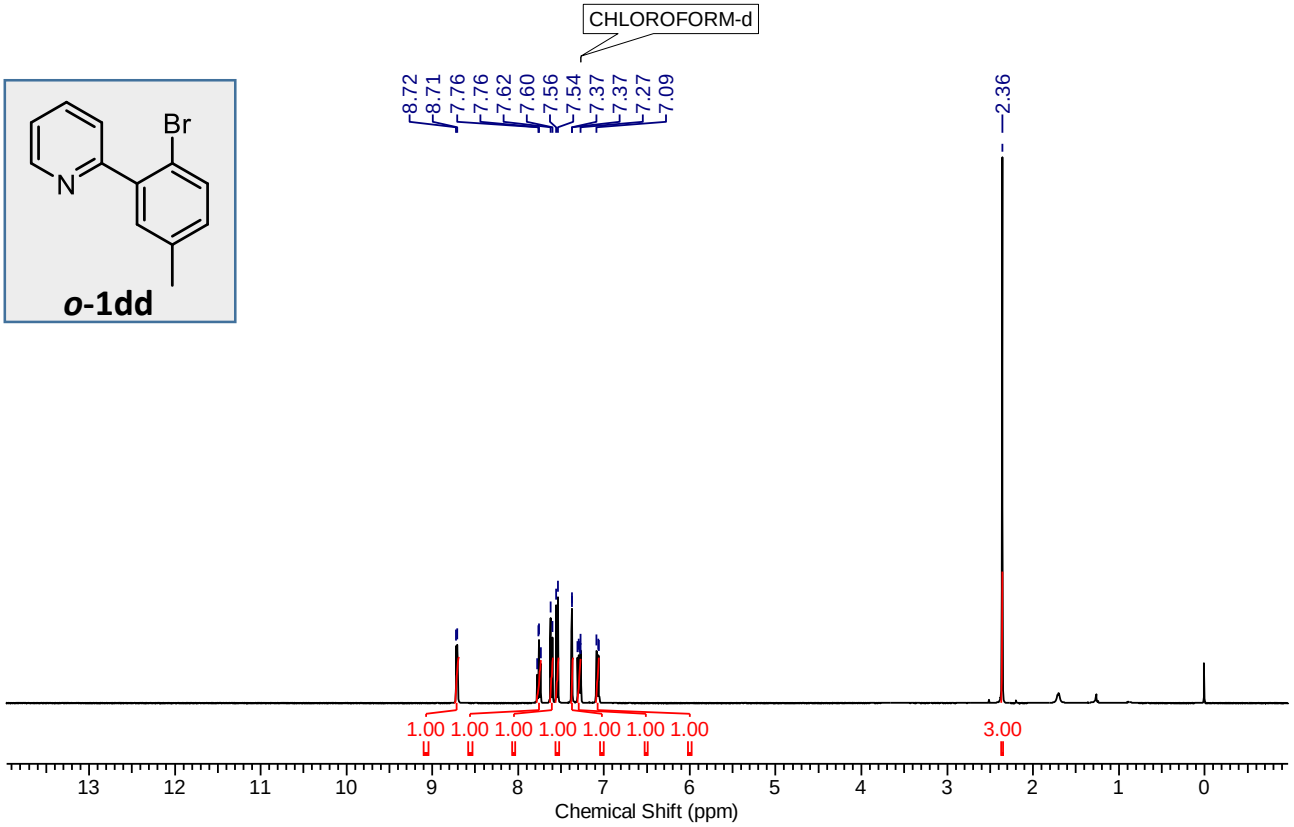

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1bb**



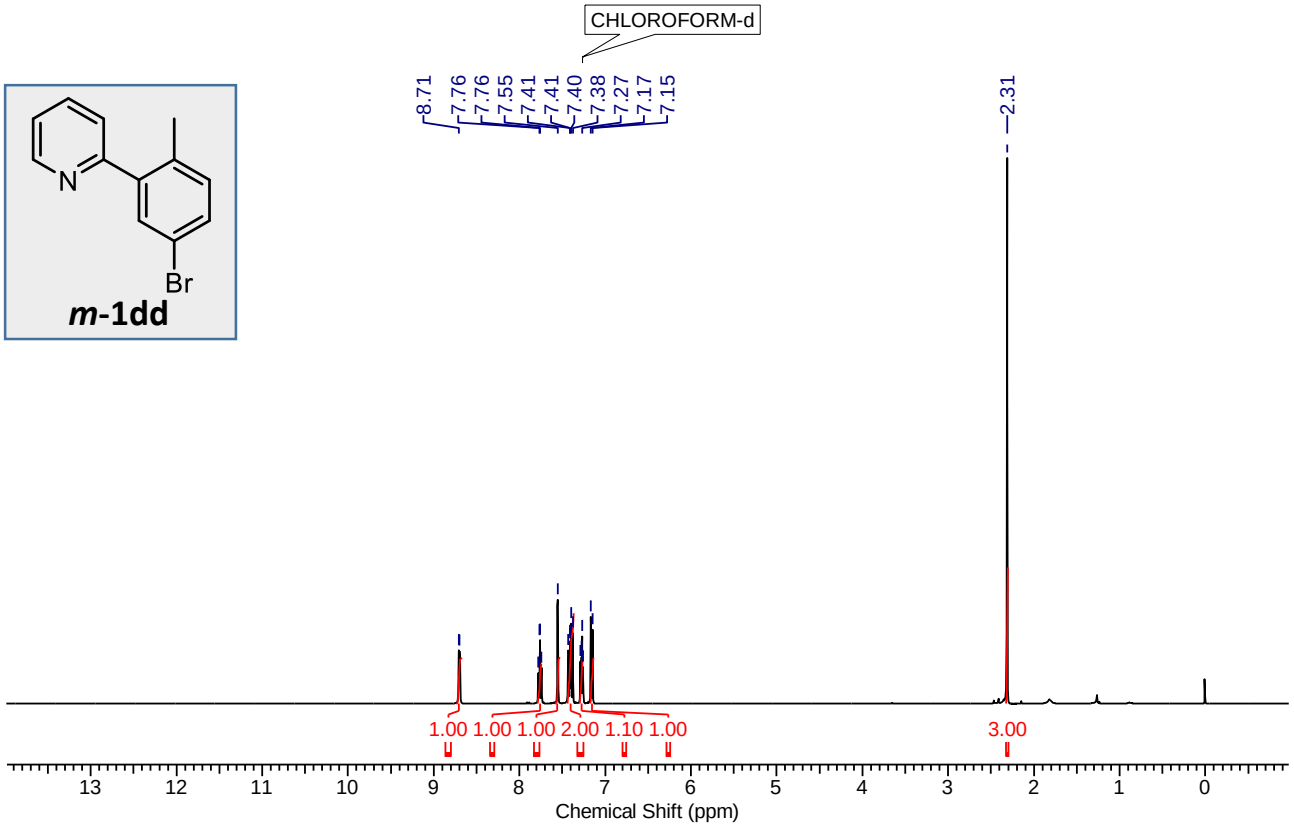

**$^1$H NMR (400 MHz, $CDCl_3$) of compound *o*-1cc**



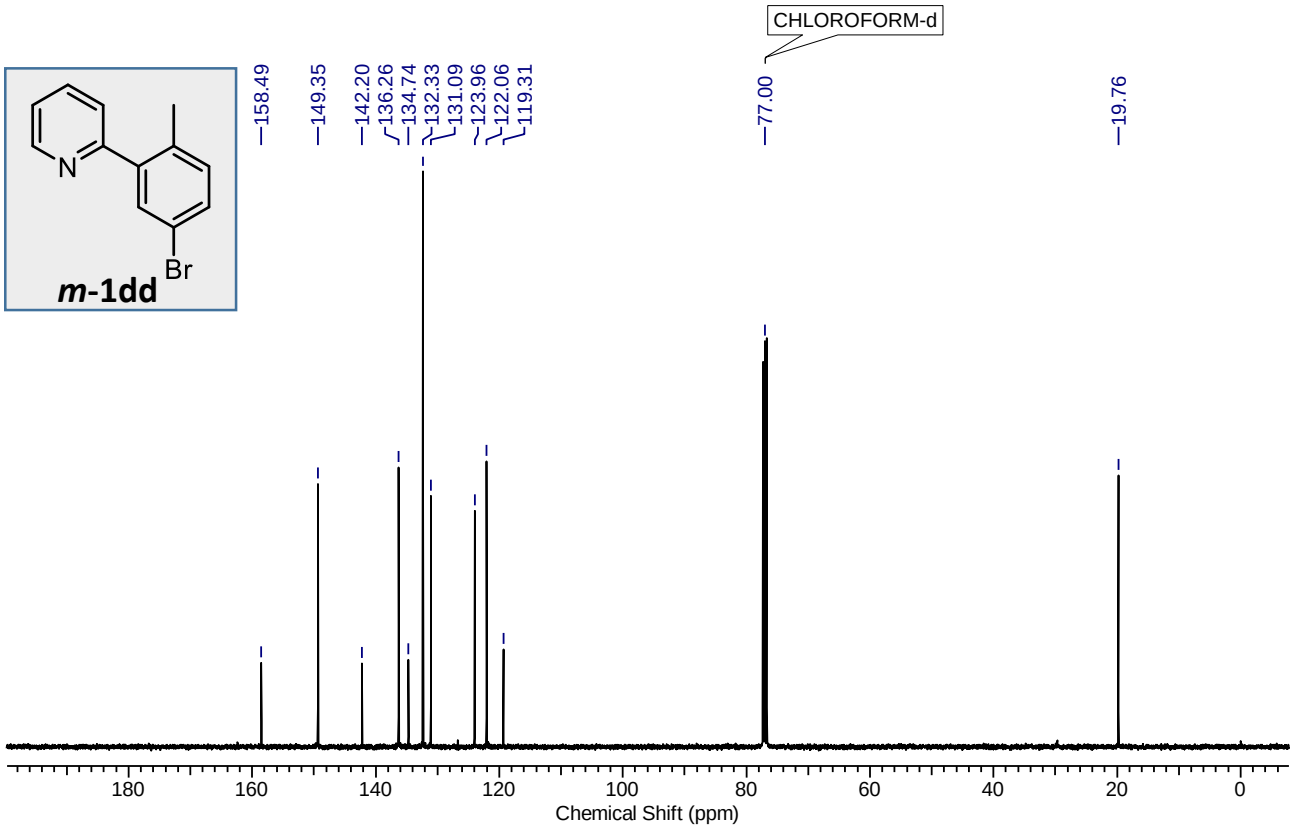

**$^1$H NMR (400 MHz, $CDCl_3$) of compound *m*-1cc**



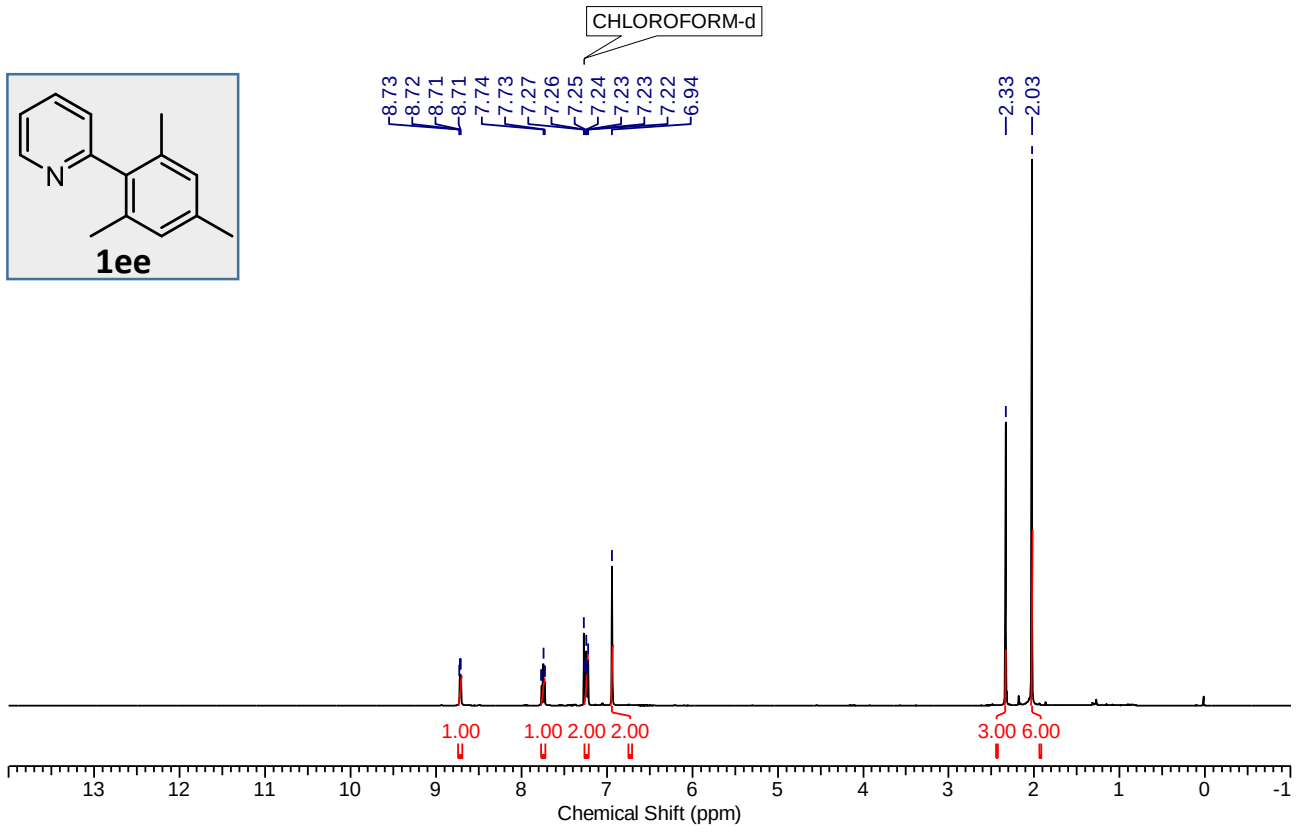

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *o*-1dd**



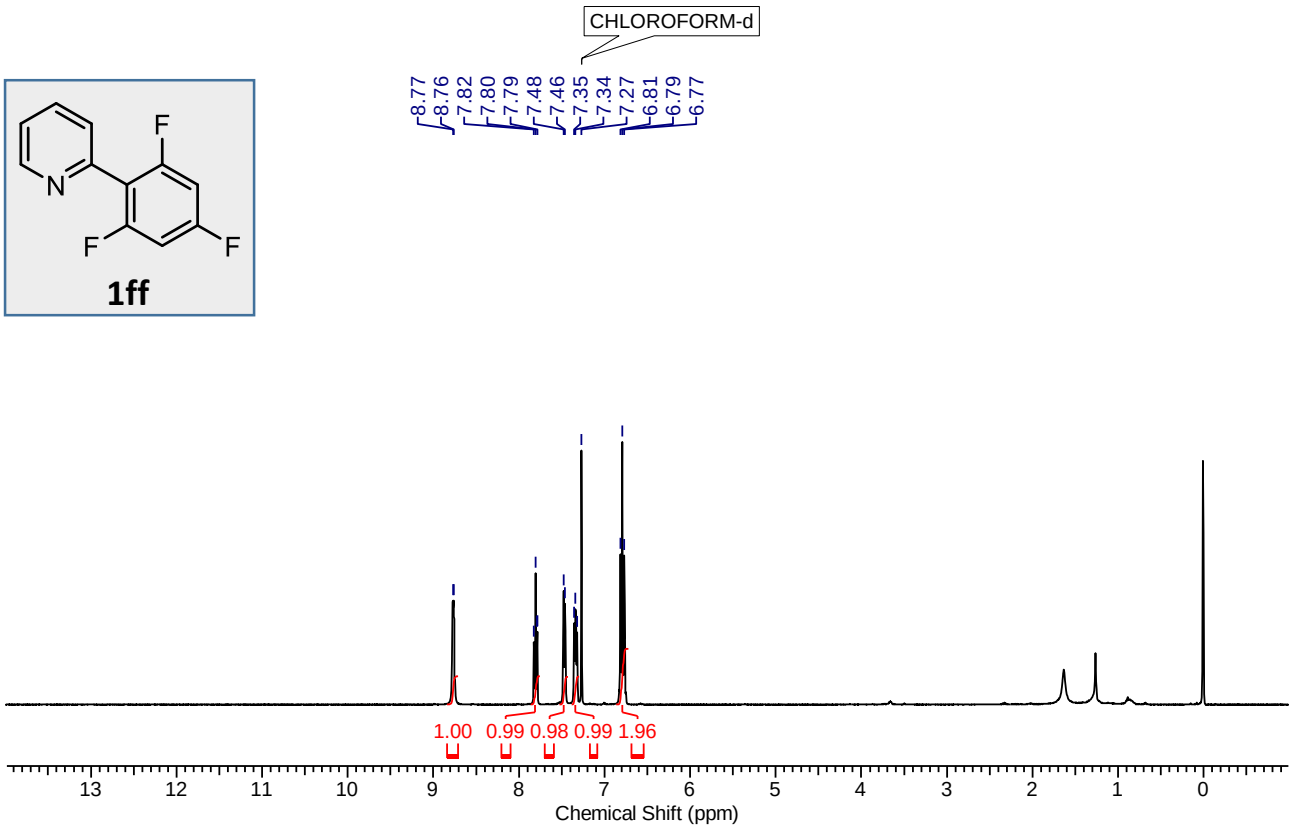

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *m*-1dd**



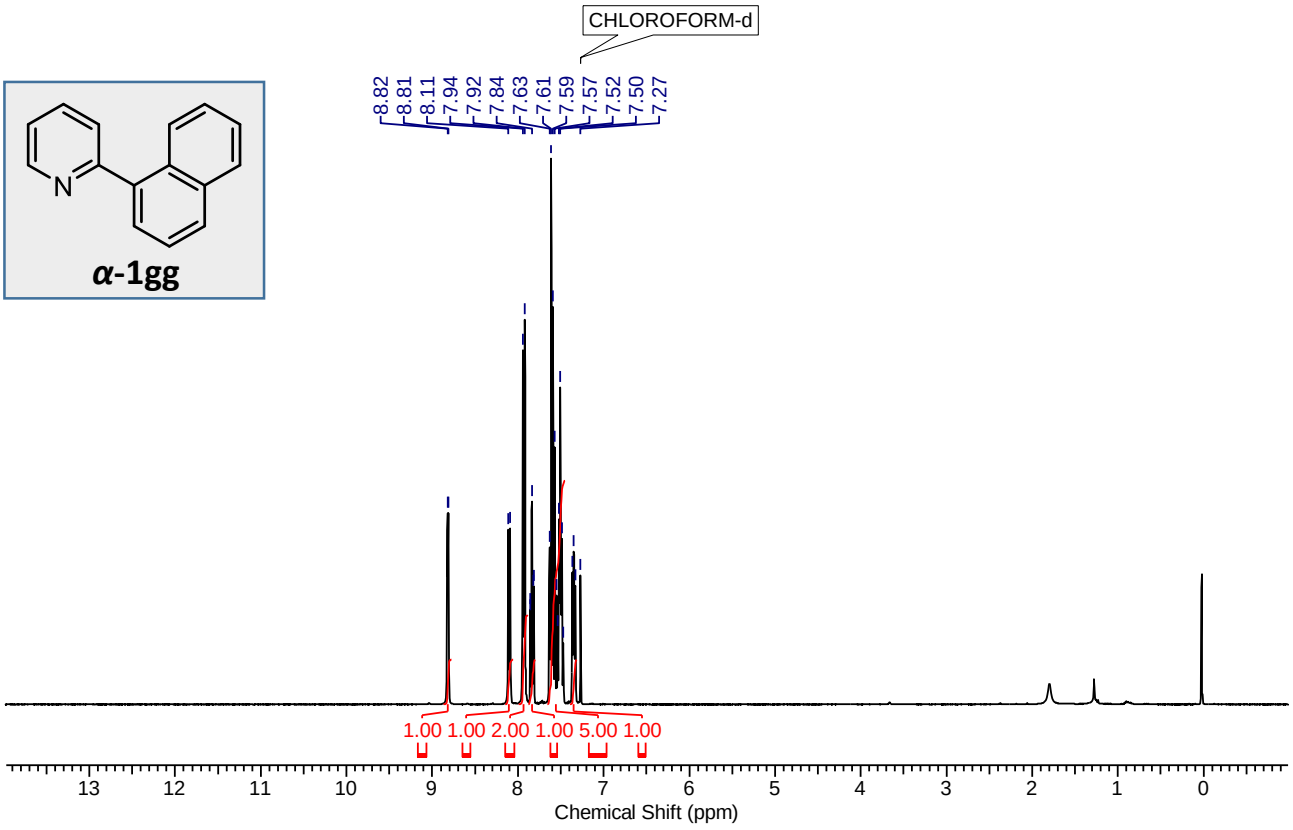

**$^{13}$C NMR (101 MHz, $CDCl_3$) of compound *m*-1dd**



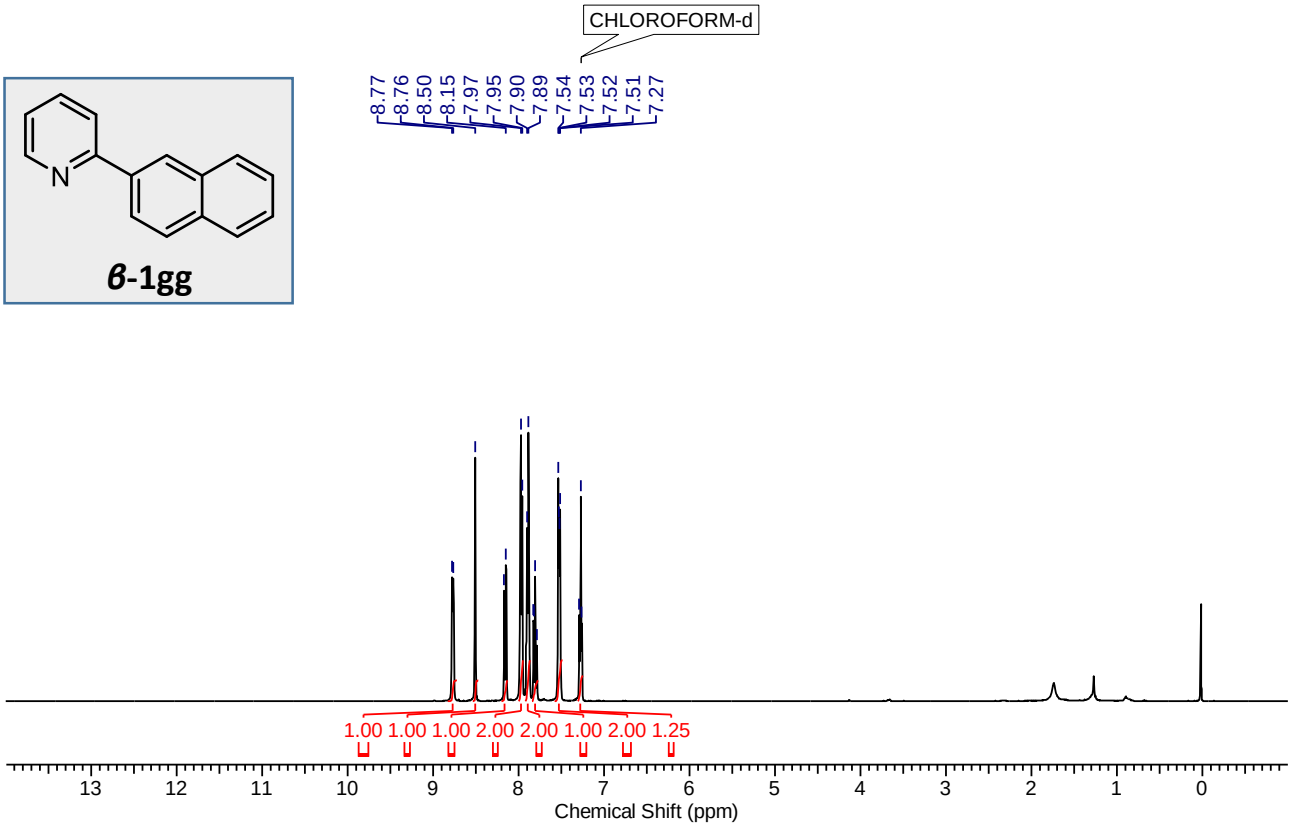

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1ee**



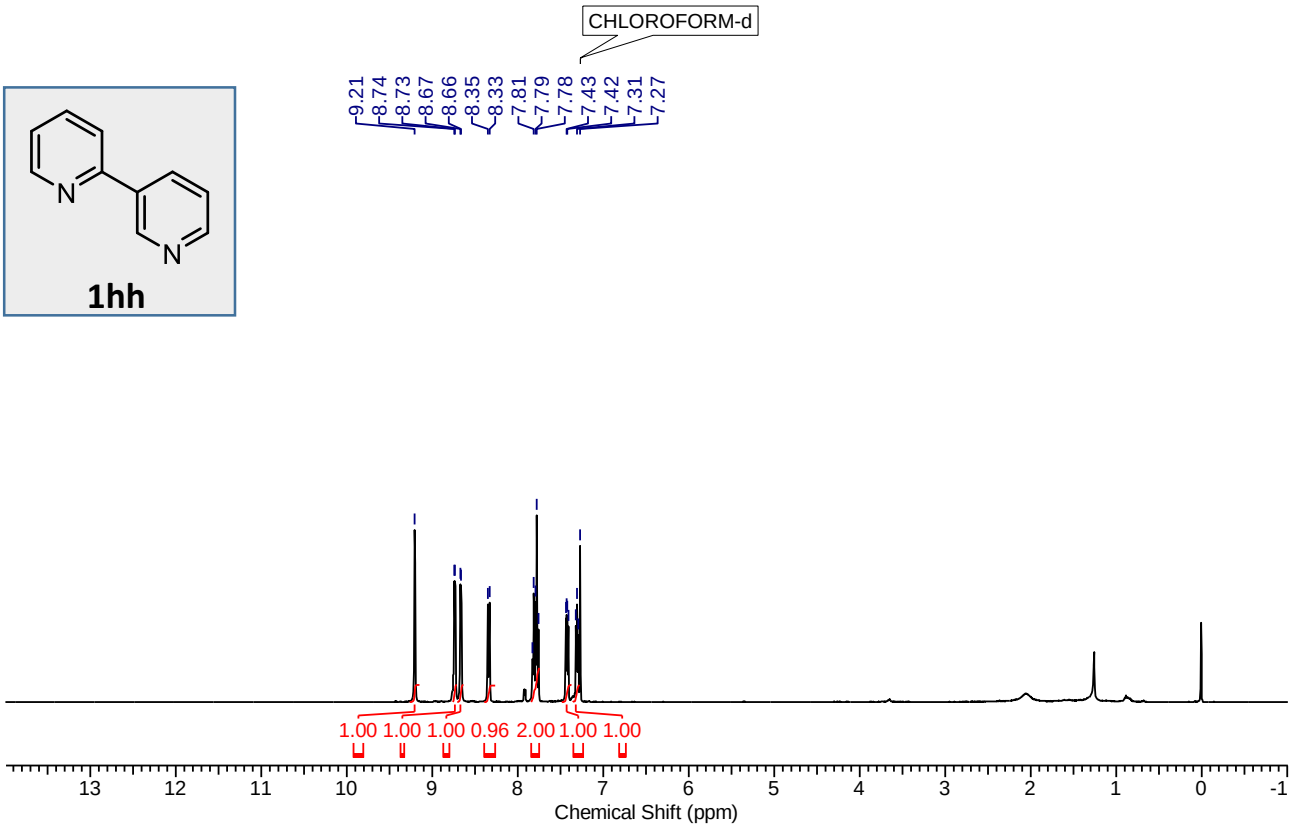

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1ff**



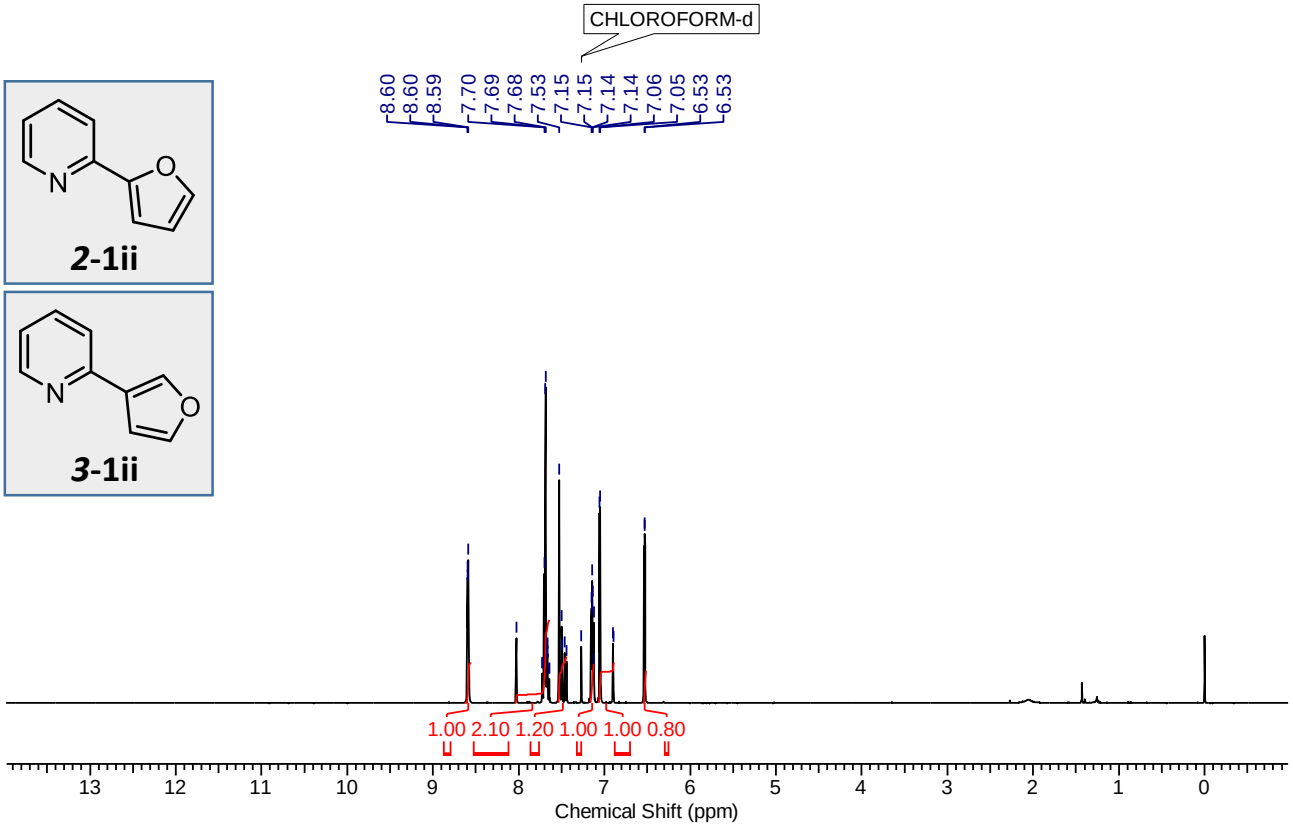

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *α*-1gg**



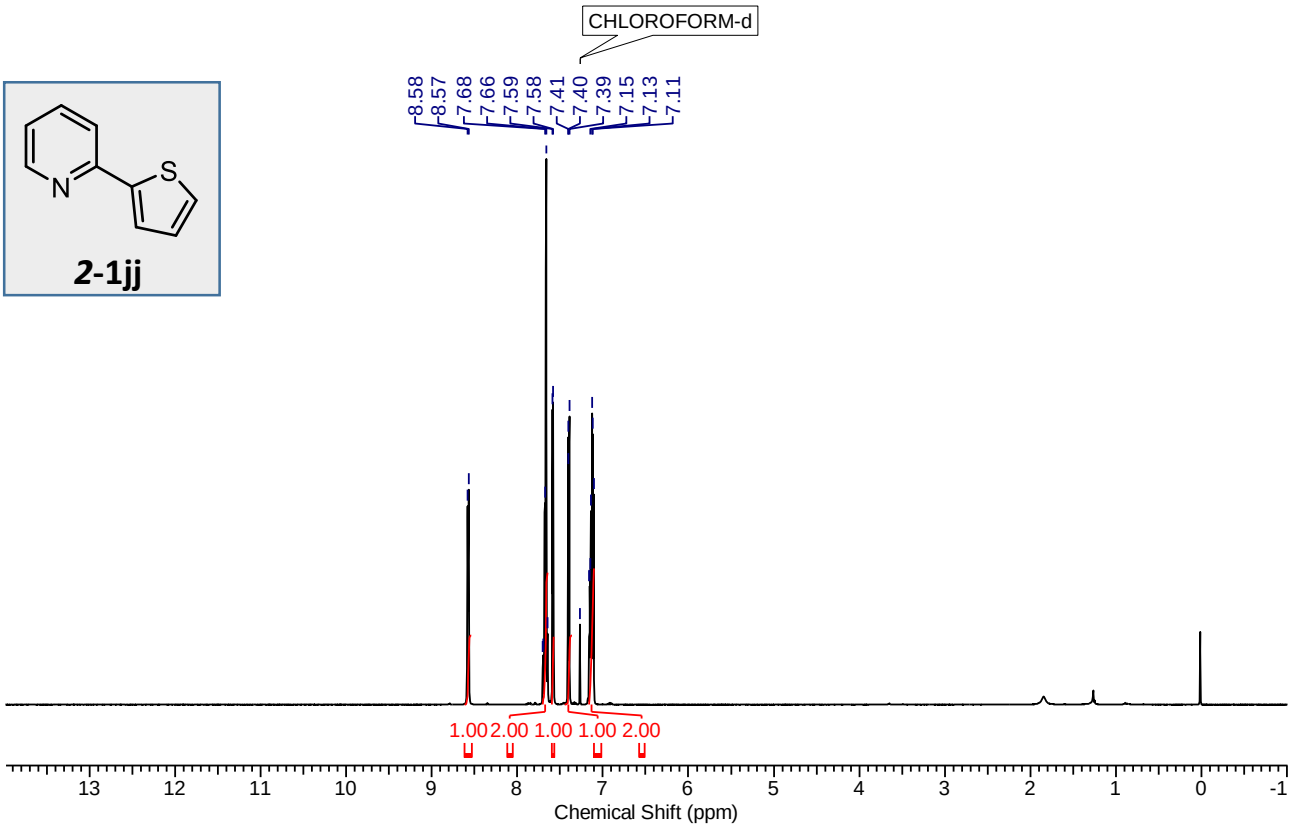

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *β*-1gg**



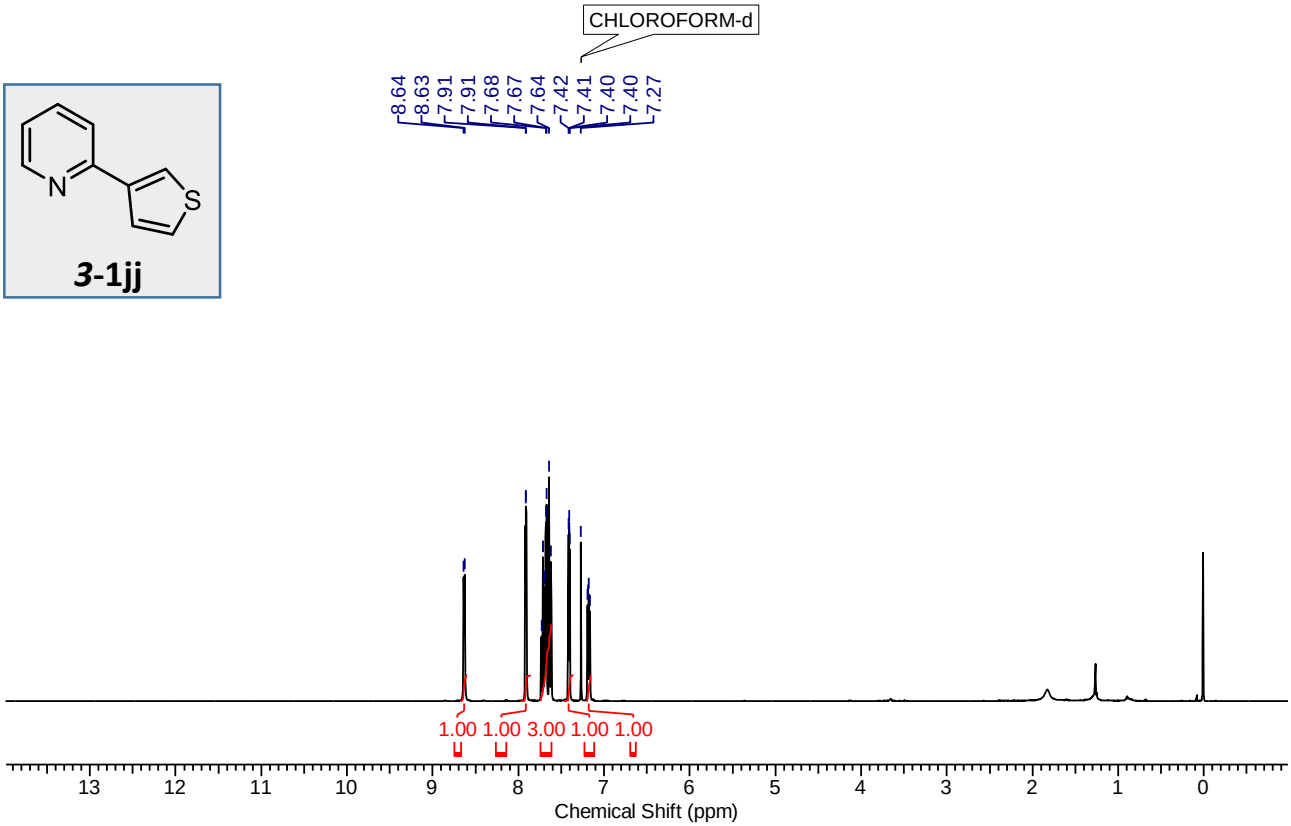

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 1hh**



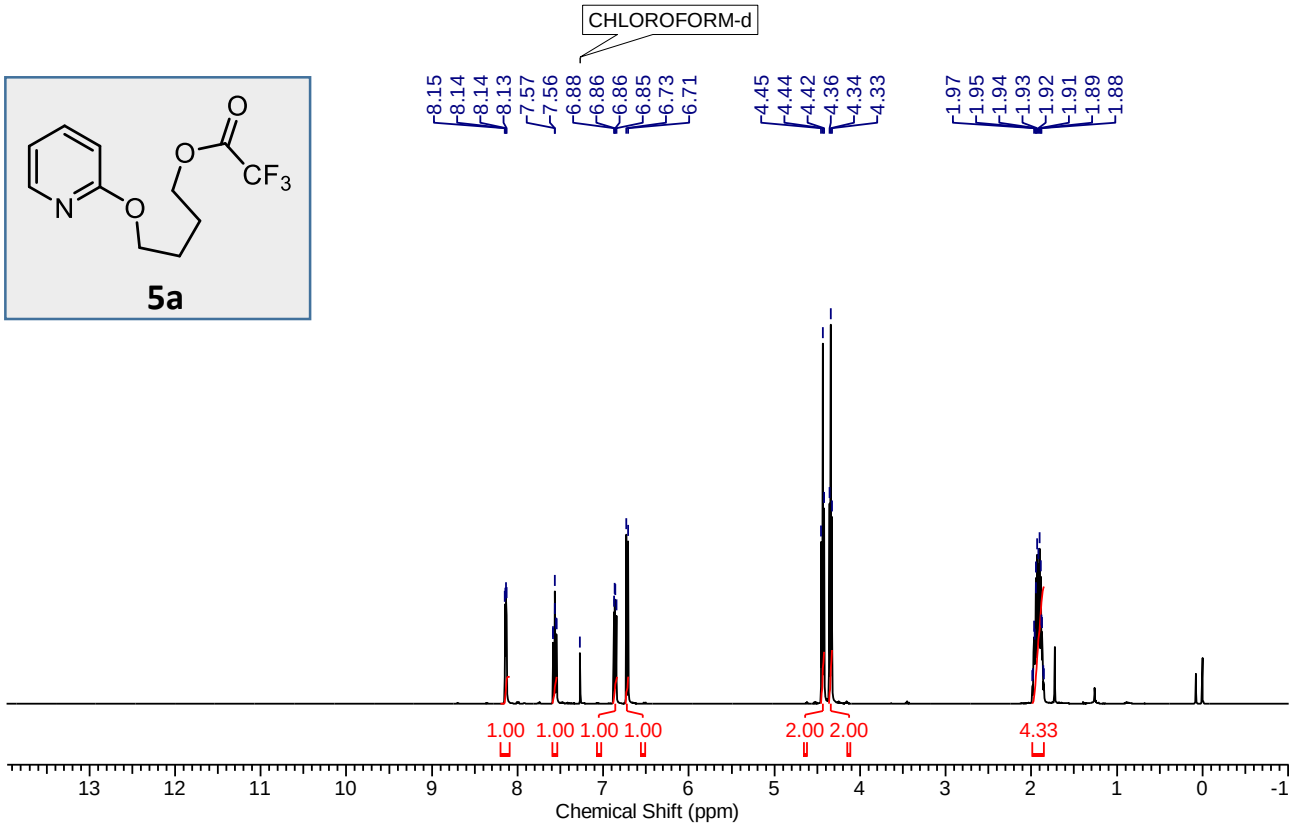

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *2*-1ii & *3*-1ii**



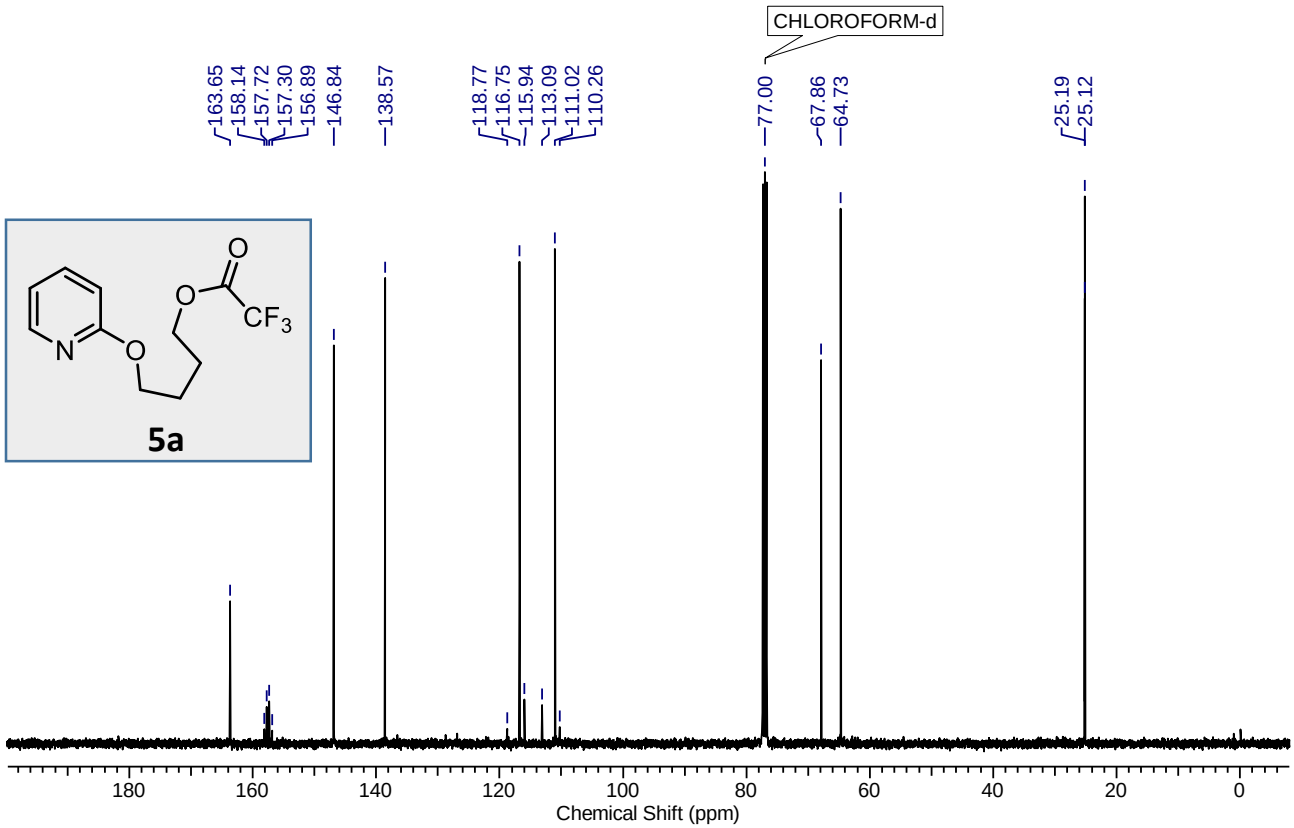

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound *2*-1jj**



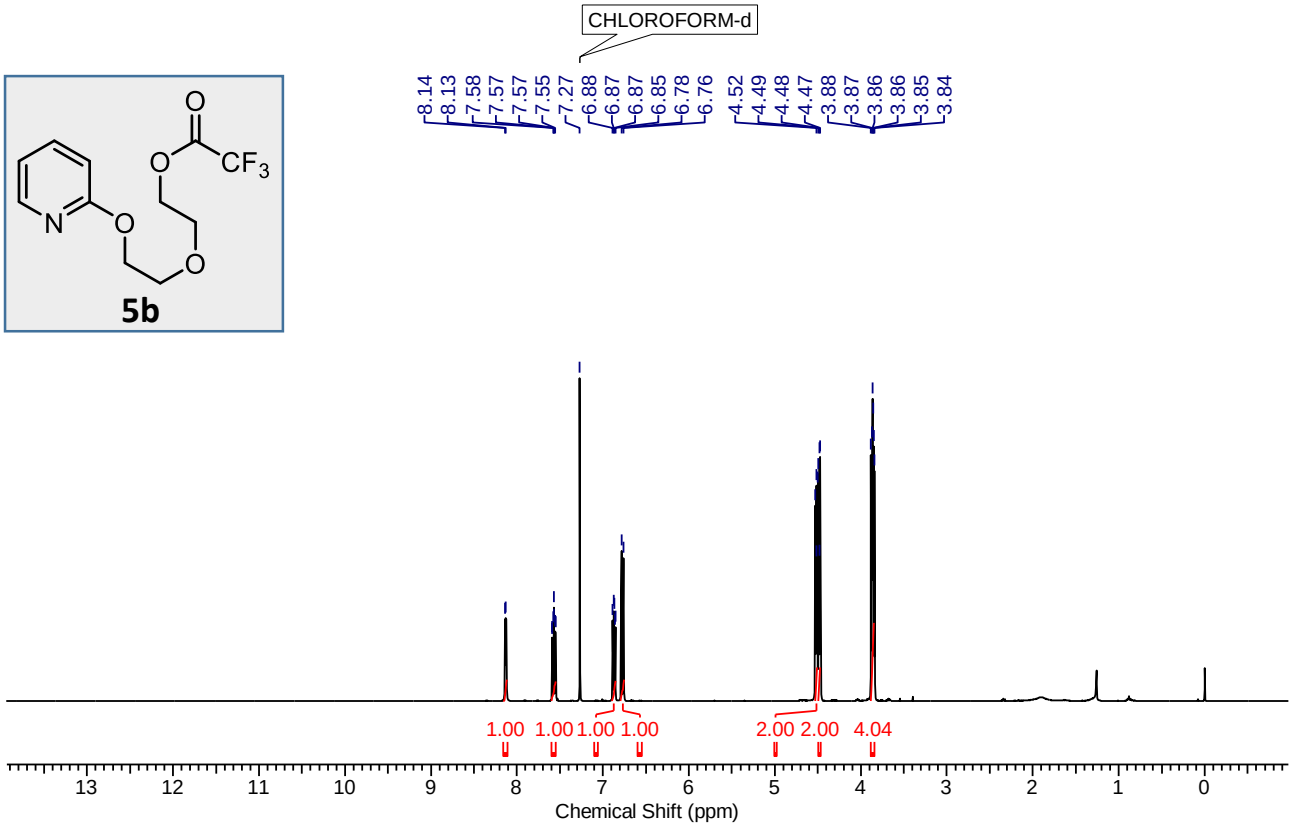

**$^1$H NMR (400 MHz, $CDCl_3$) of compound *3*-1jj**



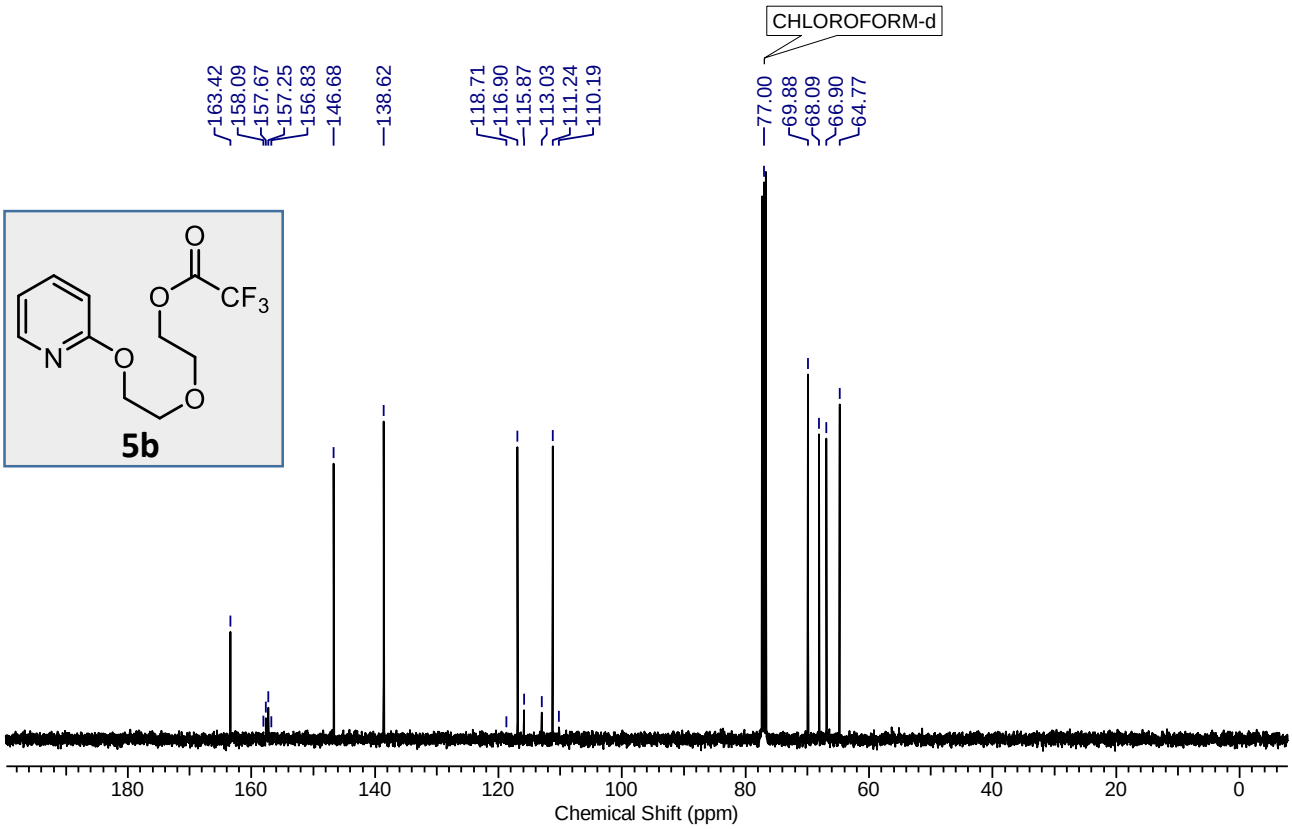

**$^1$H NMR (400 MHz, $CDCl_3$) of compound 5a**



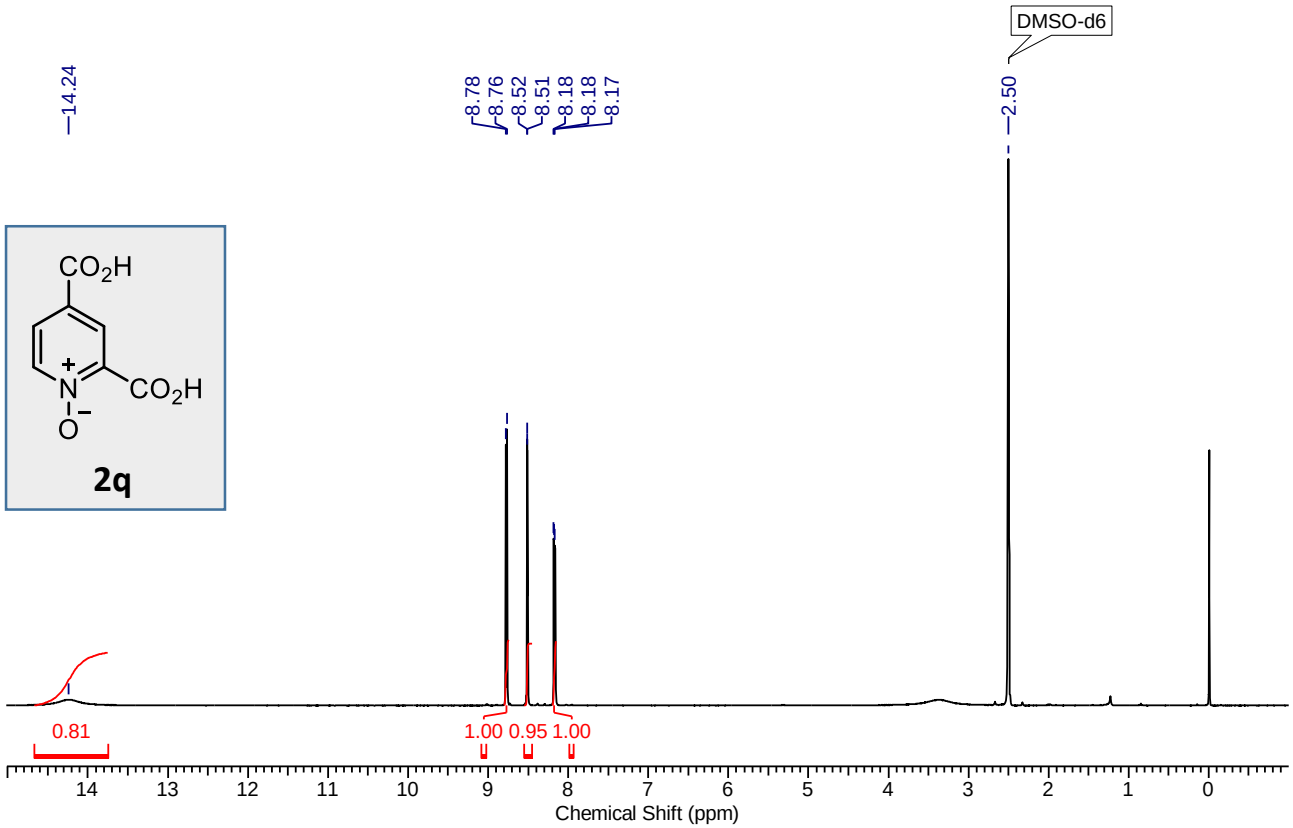

**$^{13}$C NMR (101 MHz, $CDCl_3$) of compound 5a**



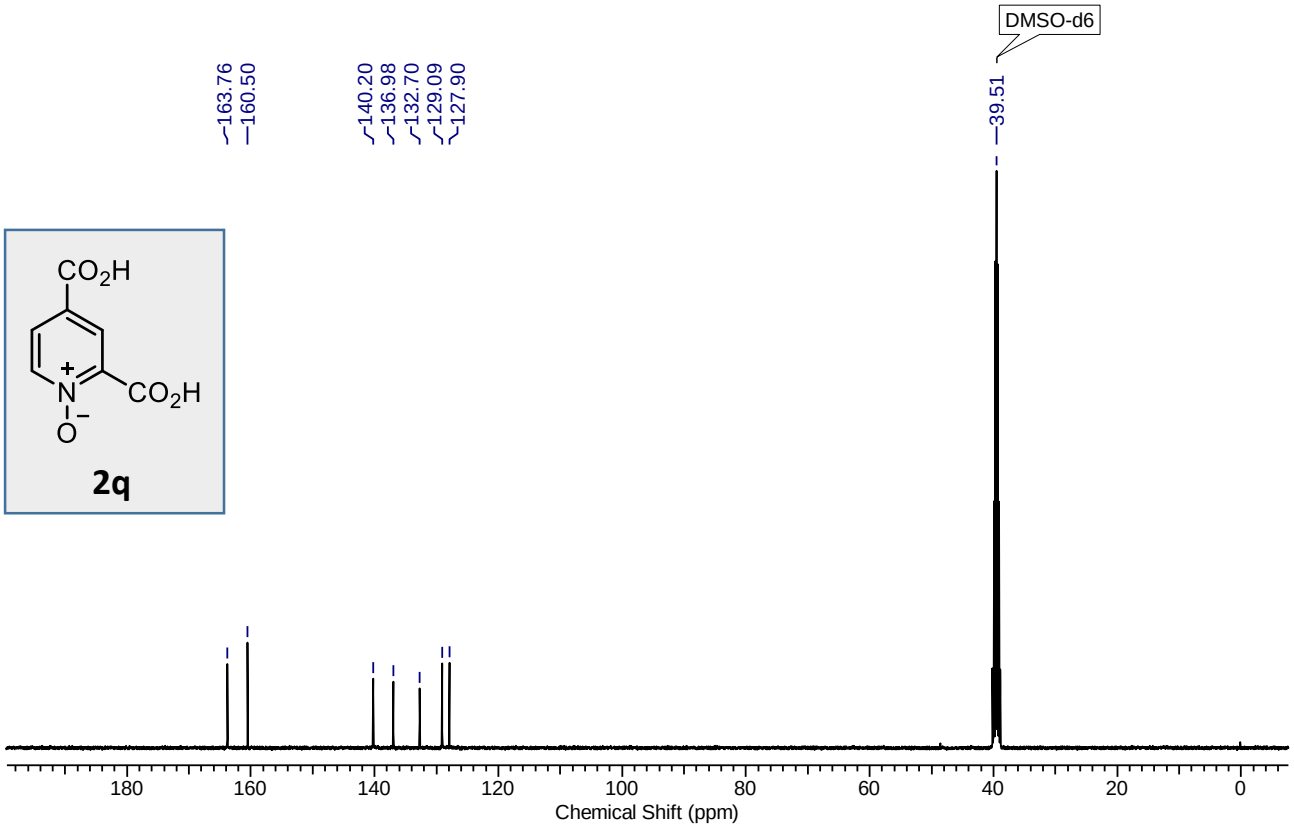

**$^{1}$H NMR (400 MHz, $CDCl_3$) of compound 5b**



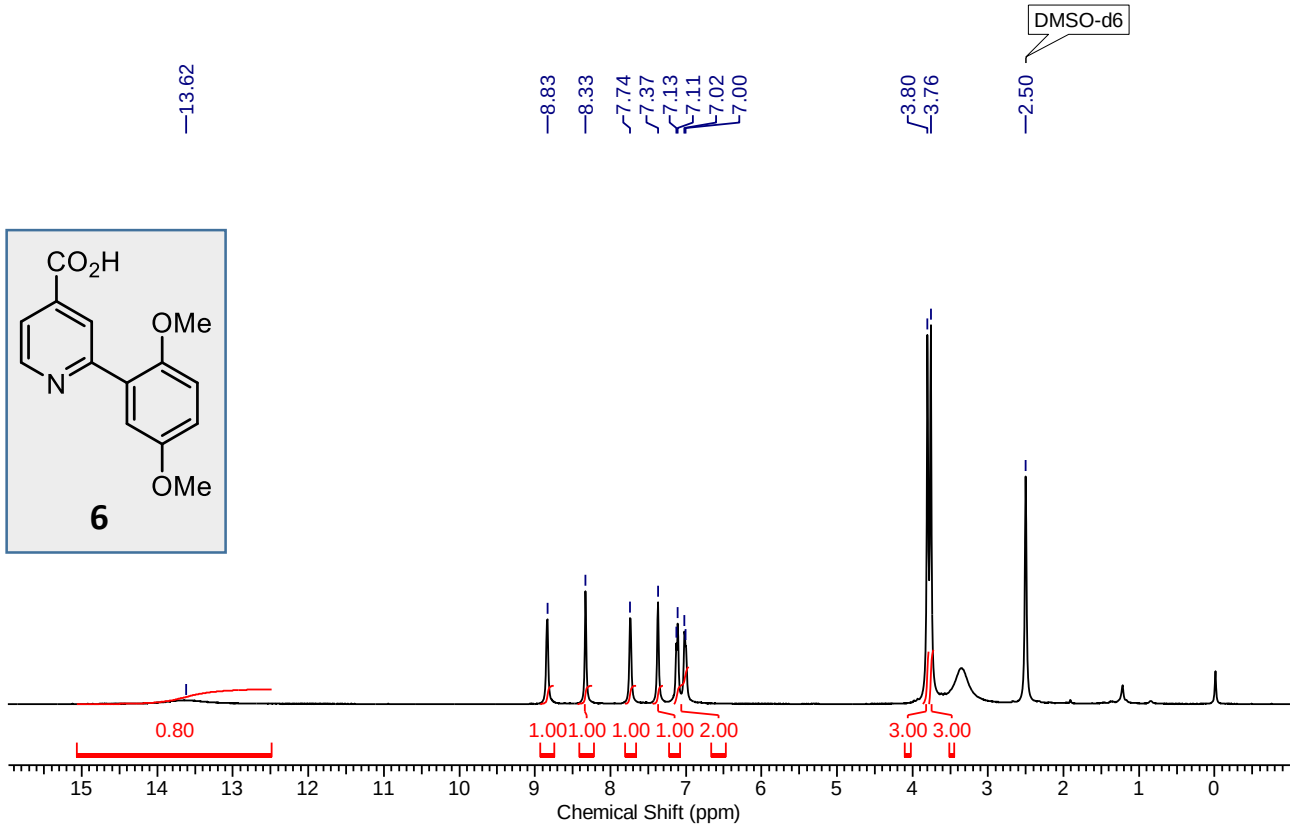

**$^{13}$C NMR (101 MHz, $CDCl_3$) of compound 5b**



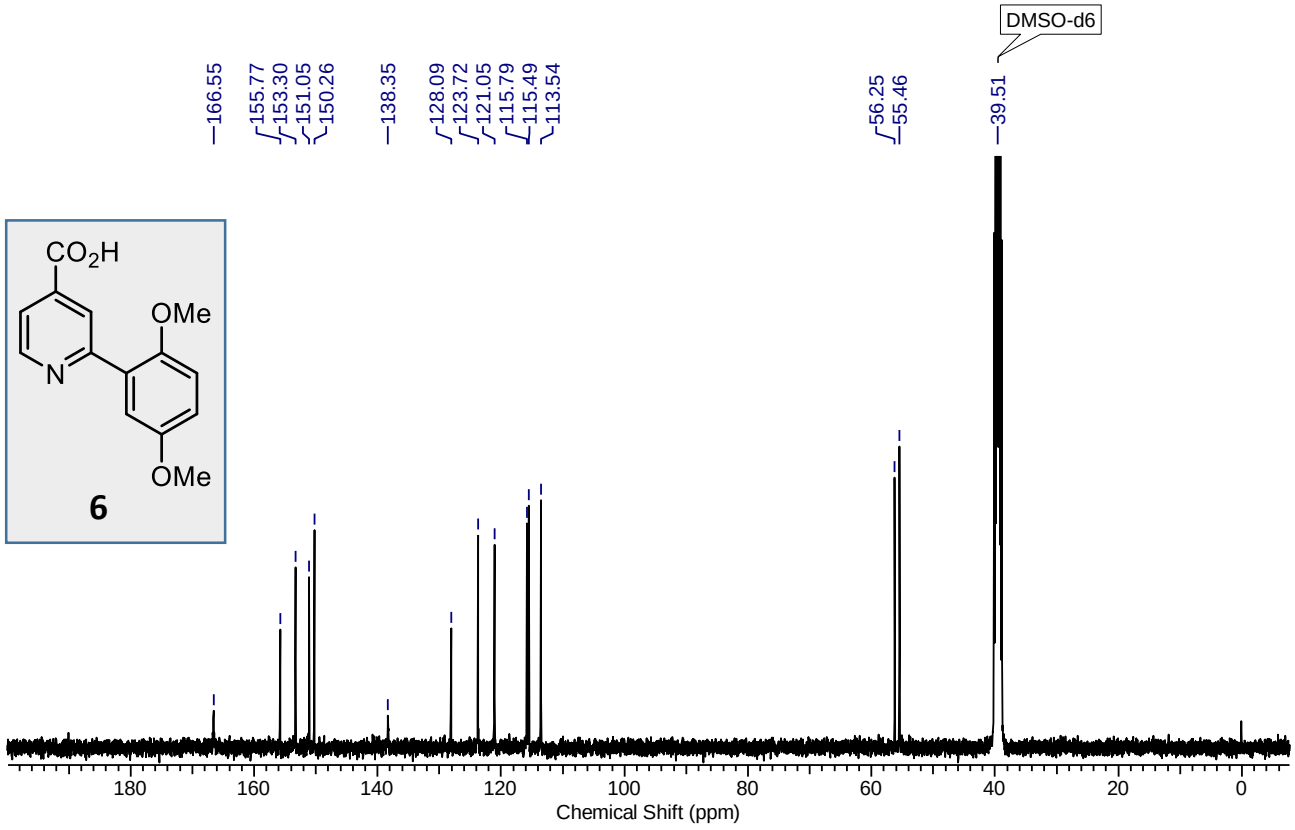

**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 2q**



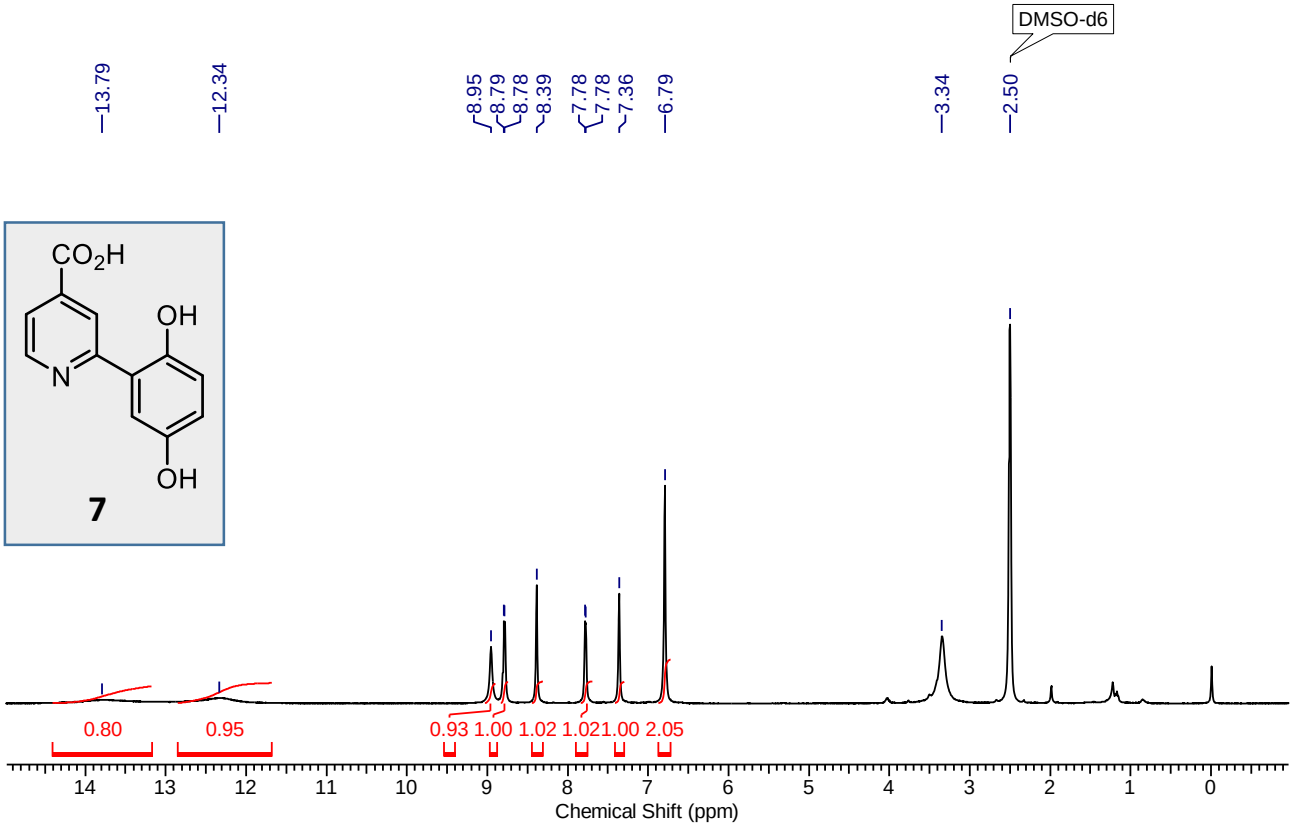

**$^{13}$C NMR (101 MHz, DMSO-$d_6$) of compound 2q**



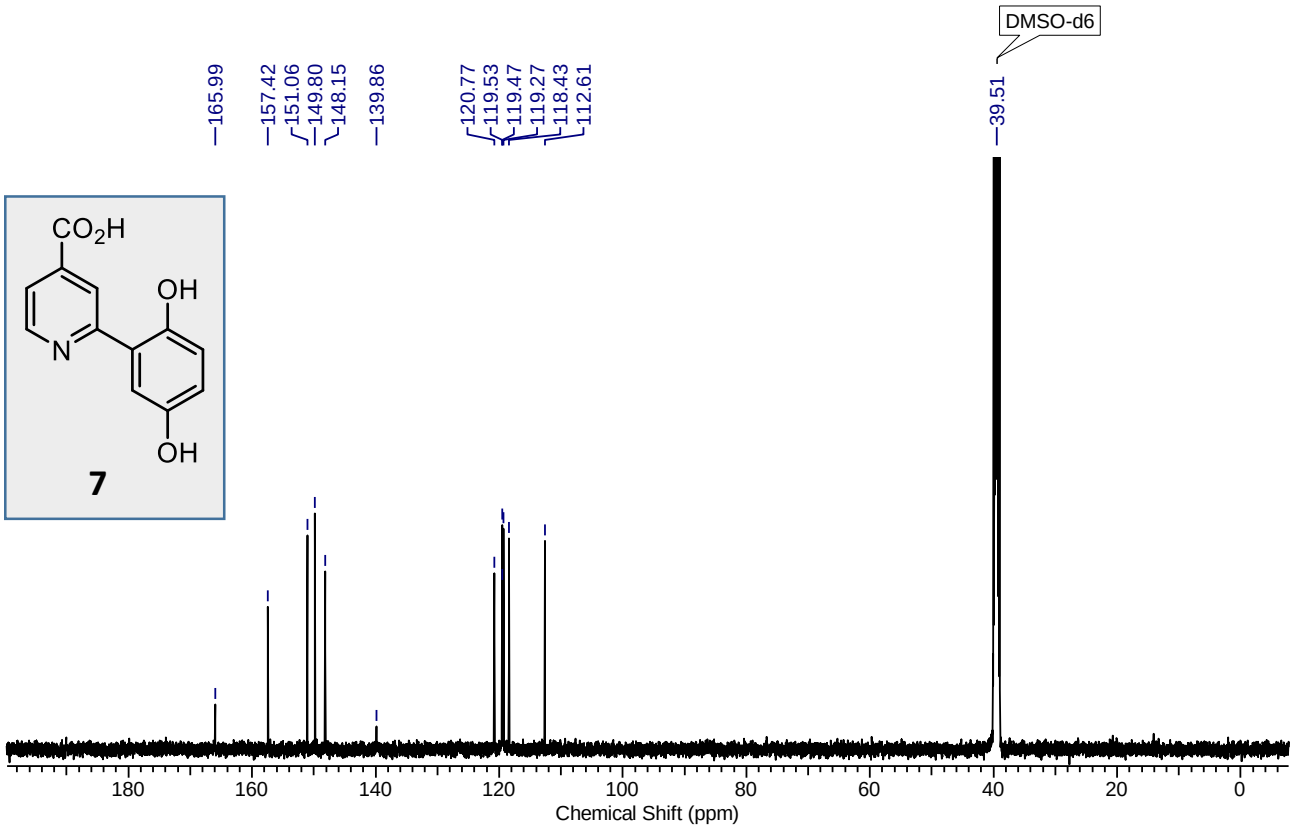

**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 6**



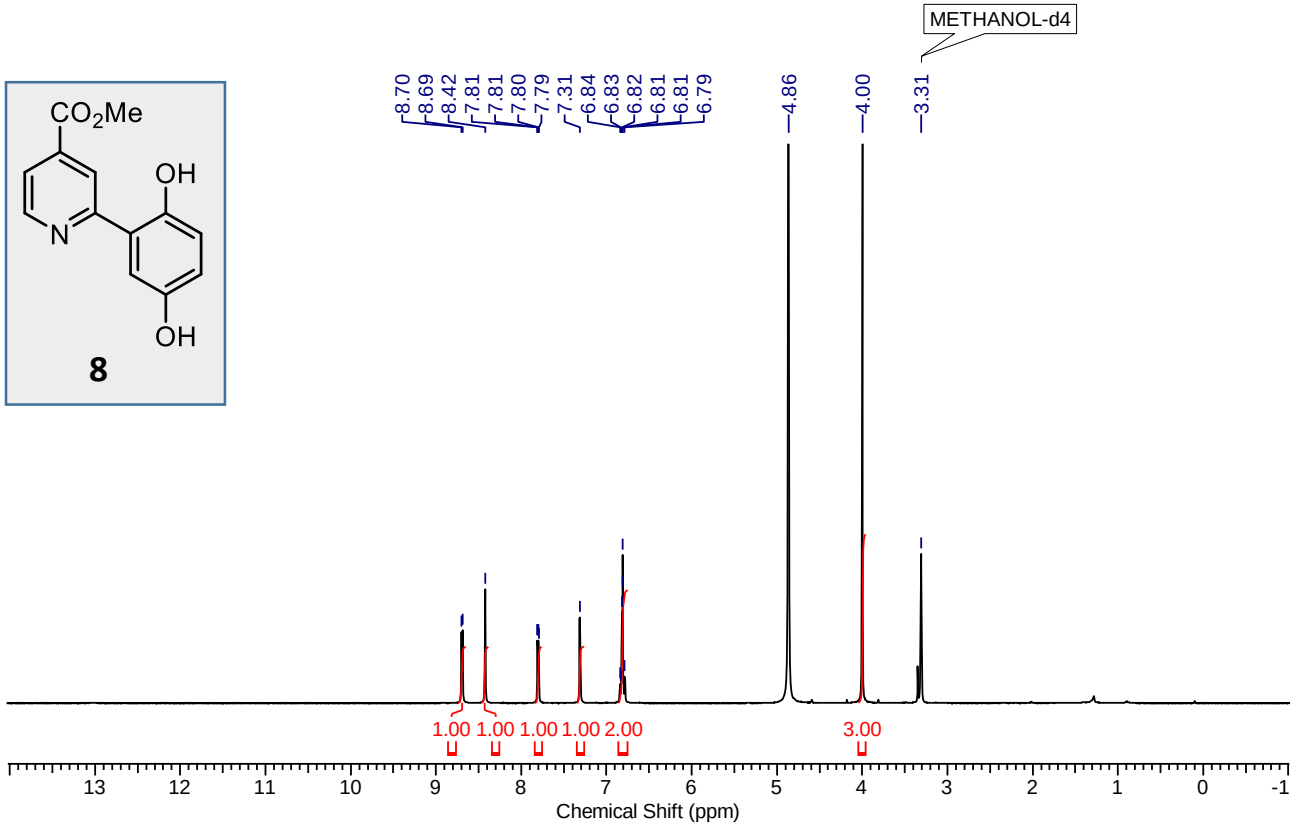

**$^{13}$C NMR (101 MHz, DMSO-$d_6$) of compound 6**



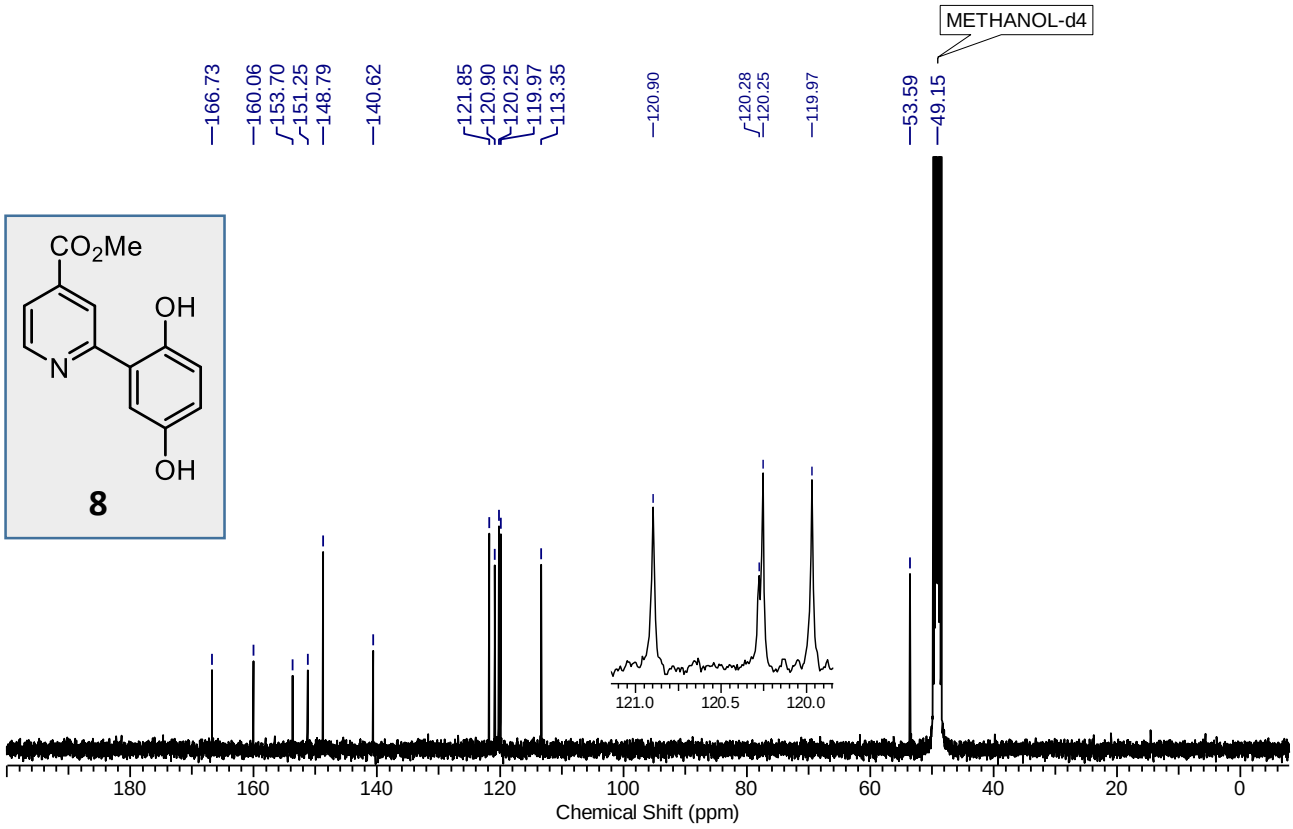

**$^{1}$H NMR (400 MHz, DMSO-$d_6$) of compound 7**



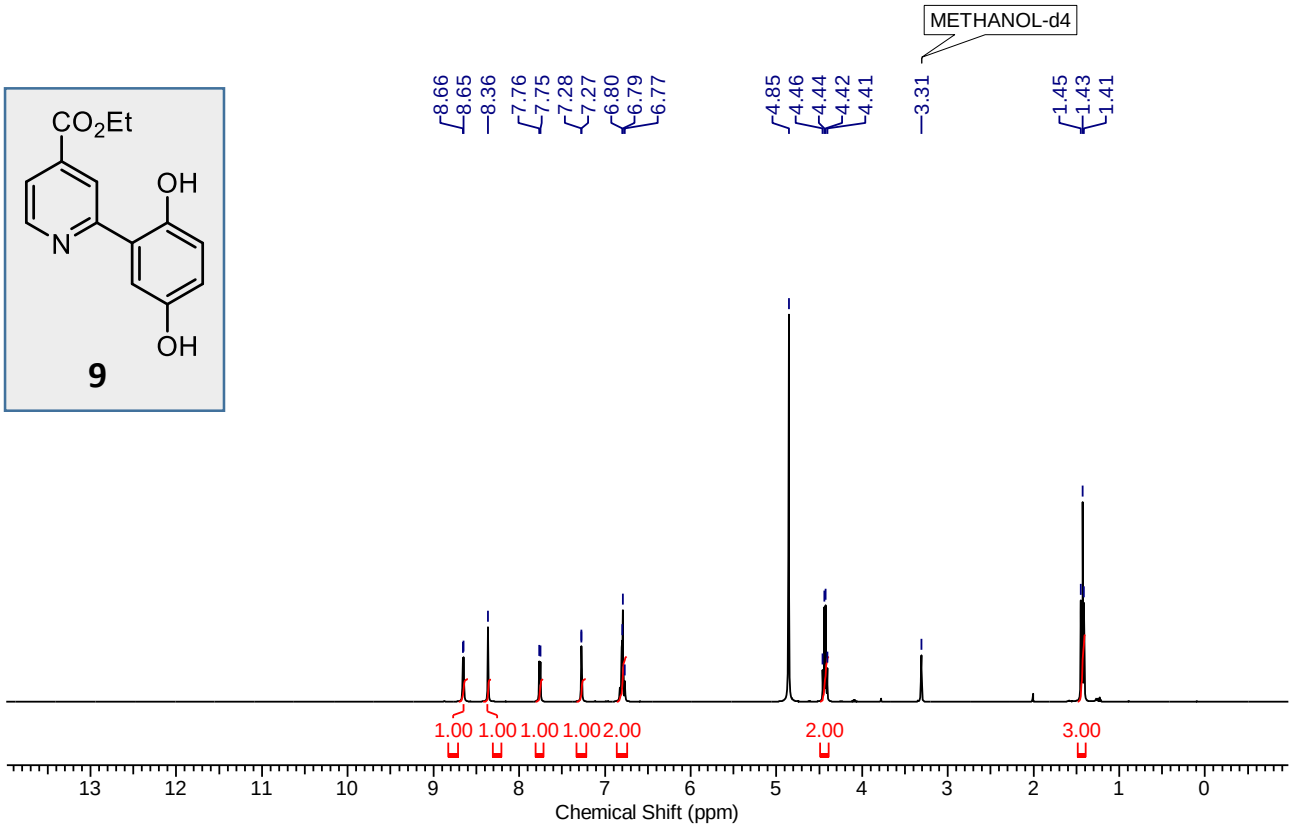

**$^{13}$C NMR (126 MHz, DMSO-$d_6$) of compound 7**



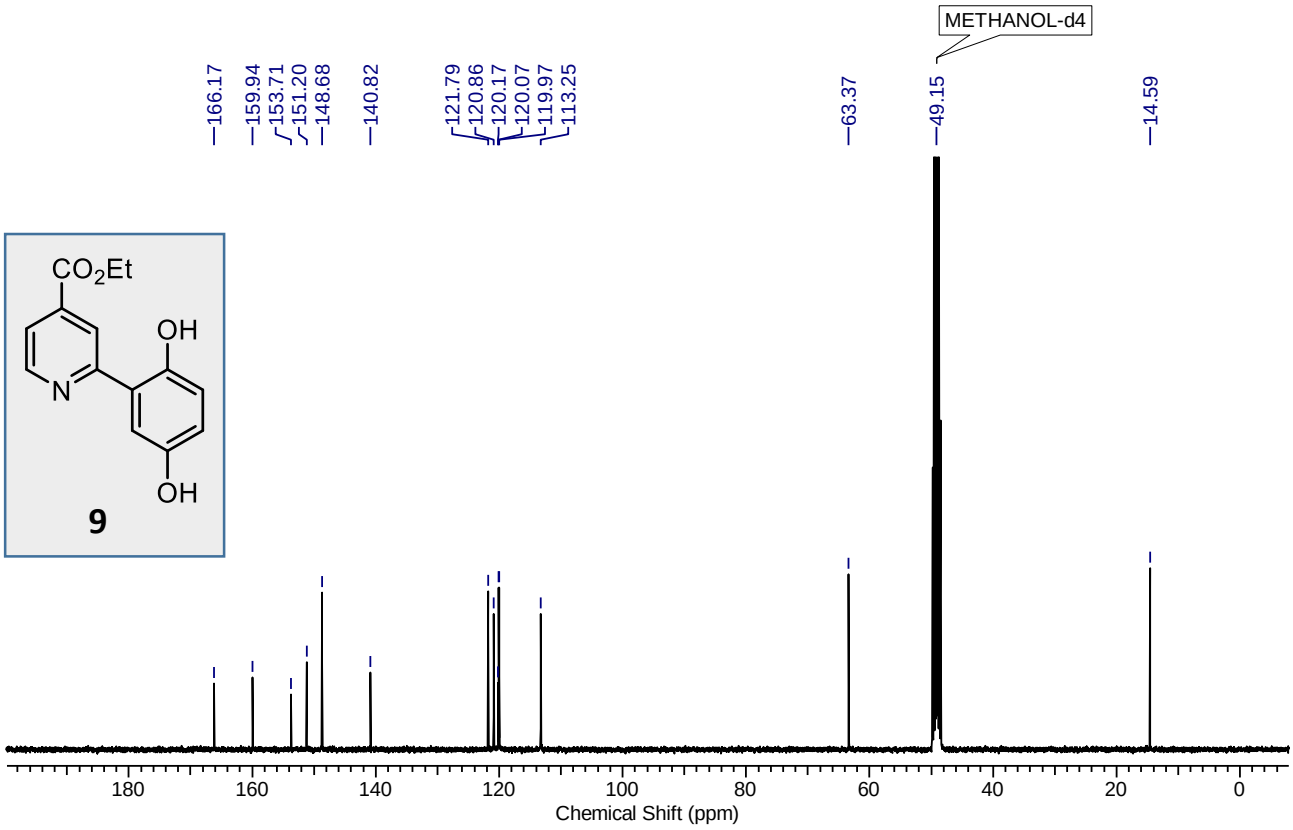

**$^{1}$H NMR (400 MHz, METHANOL-$d_4$) of compound 8**




**$^{13}$C NMR (101 MHz, METHANOL-*d*$_4$) of compound 8**




**$^{1}$H NMR (400 MHz, METHANOL-*d*$_4$) of compound 9**




**$^{13}$C NMR (101 MHz, METHANOL-$d_4$) of compound 9**