

## Supporting Information

### Highly Efficient One-Pot Synthesis of 2-Pyridones *via* Chemo- and Regioselective Tandem Blaise Reaction of Nitriles with Propiolates

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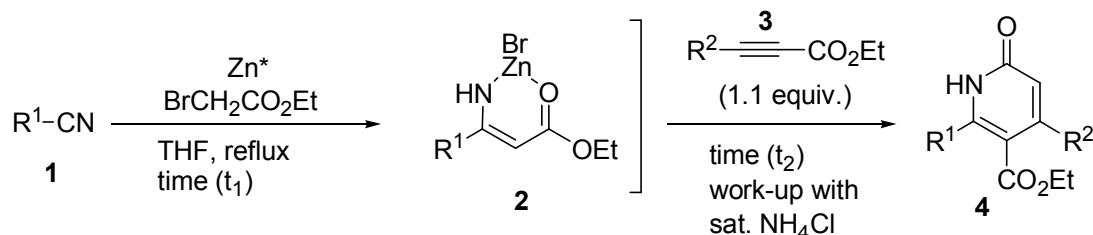
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#### Contents

|                                                                                                             |        |
|-------------------------------------------------------------------------------------------------------------|--------|
| General .....                                                                                               | S1     |
| General Procedure for the Tandem Blaise Reaction with Propiolate.....                                       | S1     |
| <sup>1</sup> H and <sup>13</sup> C NMR Spectral and HRMS Data of <b>4a</b> ~ <b>4q</b> , and <b>8</b> ..... | S2-S5  |
| Crystal data and structure refinement for <b>4k</b> .....                                                   | S6-S8  |
| <sup>1</sup> H and <sup>13</sup> C NMR Spectra of <b>4a</b> ~ <b>4q</b> , and <b>8</b> .....                | S9-S26 |

**General.** All reactions and manipulations were performed in a nitrogen atmosphere using standard Schlenk techniques. The reaction solvents were distilled prior to used (THF was distilled from sodium benzophenone ketyl). All purchased reagents were used without further purification. Anhydrous solvents were transferred by oven-dried syringe. Flasks were flames dried under a stream of nitrogen. The NMR spectra were recorded at 250 MHz (<sup>1</sup>H) and 62.9 MHz (<sup>13</sup>C). The chemical shifts were relative to TMS (as an internal reference) for <sup>1</sup>H NMR

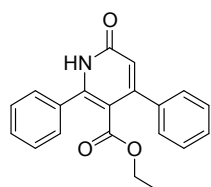
#### General Procedure for the Tandem Blaise Reaction with ethyl phenylpropiolate.



To a stirred suspension of commercial zinc dust (Aldrich, 10 μm, 1.0 g, 15.3 mmol) was added methanesulfonic acid (3.7 mg) in anhydrous THF (4.0 mL). After 10 min reflux, benzonitrile (0.8 mL, 7.6 mmol) was added all at one. While maintaining reflux temperature, ethyl bromoacetate (1.26 mL, 11.4 mmol) was added over 1h by using syringe pump

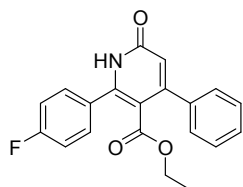
and the reaction mixture was further reflux for 1 h. To this reaction mixture, ethyl-phenylpropiolate (1.4 mL, 8.4 mmol) was added all at once. After stirring for 3h at reflux, the reaction mixture was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$ , at room temperature and, extracted with ethyl acetate (30 mL  $\times$  3). The combined organic layer was dried with anhydrous  $\text{MgSO}_4$ , filtered, and concentrated under reduced pressure. The residue was purified by silica chromatography to afford **4a** (98 %, 2.65 g).

**1,6-Dihydro-2,4-diphenyl -6-oxo-pyridine-3-carboxylic acid ethyl ester (4a).**



Yield: 98 %; Yellow solid; mp: 208-210 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.75 (t,  $J$  = 7.1 Hz, 3H), 3.80 (q,  $J$  = 7.2 Hz, 2H), 6.45 (s, 1H), 7.26 ~ 7.41 (m, 5H), 7.45 ~ 7.52 (m, 5H), 12.21 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.2, 61.2, 114.3, 118.5, 127.2, 128.2, 128.4, 128.7, 128.8, 130.3, 132.9, 138.1, 147.2, 154.0, 163.7, 166.7 ppm; IR (KBr pallet) 3441, 2893, 1967, 1651, 1280, 1010, 702; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{20}\text{H}_{18}\text{NO}_3$ : 320.1287. Found: 320.1285.

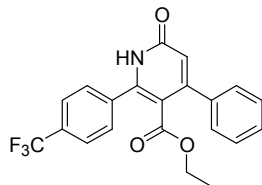
**2-(4-Fluoro-phenyl)-6-oxo-4-phenyl-1,6-dihydro-pyridine-3-carboxylic acid ethyl ester (4b).**



Yield: 97 %; Yellow solid; mp: 192-194 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.79 (t,  $J$  = 7.1 Hz, 3H), 3.82 (q,  $J$  = 7.1 Hz, 2H), 6.46 (s, 1H), 7.12 ~ 7.19 (m, 2H), 7.32 ~ 7.41 (m, 5H), 7.51 ~ 7.56 (m, 2H), 12.47 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.1, 61.1, 114.0, 115.5 (d,  $J$  = 22.1 Hz), 118.3, 127.0, 128.2, 128.6, 128.8, 130.4 (d,  $J$  = 8.6 Hz), 138.0, 146.3, 153.6, 163.9, 163.5 (d,  $J$  = 250.8 Hz), 166.6 ppm; IR (KBr pallet) 3433, 2989, 1720, 1658, 1280, 840, 705;

HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{20}\text{H}_{17}\text{FNO}_3$ : 338.1192. Found: 338.1184.

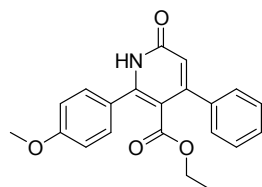
**1,6-Dihydro-2-(4-trifluoromethyl-phenyl)-6-oxo-4-phenyl-pyridine-3-carboxylic acid ethyl ester (4c)**



Yield: 95 %; Bright yellow solid; mp: 218-220 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.75 (t,  $J$  = 7.1 Hz, 3H), 3.81 (q,  $J$  = 7.2 Hz, 2H), 6.50 (s, 1H), 7.31 ~ 7.36 (m, 2H), 7.40 ~ 7.42 (m, 3H), 7.65-7.76 (m, 4H), 12.90 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.2, 61.4, 114.6, 119.2, 125.6 (q,  $J$  = 3.6/3.8 Hz), 127.2, 128.5, 128.9, 129.0, 131.6 (d,  $J$  = 33.0 Hz), 136.4,

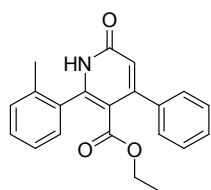
137.9, 145.9, 154.0, 164.0, 166.5 ppm; IR (KBr pallet) 3440, 1674, 1327, 1118, 848, 702; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{21}\text{H}_{17}\text{F}_3\text{NO}_3$ : 388.1161. Found: 388.1164.

**1,6-Dihydro-2-(4-methoxy-phenyl)-6-oxo-4-phenyl-pyridine-2-carboxylic acid ethyl ester (4d)**



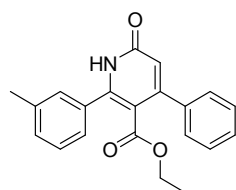
Yield: 95 %; Dark yellow solid; mp: 208-210 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.80 (t,  $J$  = 7.1 Hz, 3H), 3.83 (q,  $J$  = 7.1 Hz, 2H), 3.84 (s, 3H), 6.42 (s, 1H), 6.95 (d,  $J$  = 8.8 Hz, 2H), 7.31 ~ 7.40 (m, 5H), 7.47 (d,  $J$  = 8.8 Hz, 2H), 12.25 (brs, 1H)  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.3, 55.3, 61.2, 113.7, 114.2, 118.1, 125.3, 127.2, 128.4, 128.7, 129.7, 138.4, 146.9, 153.9, 161.1, 163.5, 167.0; IR (KBr pallet) 3437, 2935, 1720, 1647, 1249, 1107, 833, 702; HRMS Cal. for

$[\text{M}+\text{H}]^+$ :  $\text{C}_{21}\text{H}_{20}\text{NO}_4$ : 350.1392. Found: 350.1383.

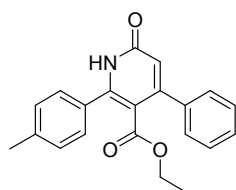
**1,6-Dihydro-2-(*o*-tolyl)-6-oxo-4-phenyl-pyridine-3-carboxylic acid ethyl ester (4e)**

Yield: 56 %; Yellow solid; mp: 182-188 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>) δ 0.65 (t, *J* = 7.1 Hz, 3H), 2.31 (s, 3H), 3.71 (q, *J* = 6.4 Hz, 2H), 6.37 (s, 1H), 7.17 ~ 7.30 (m, 3H), 7.32 ~ 7.40 (m, 6H), 12.08 (brs, 1H) ppm; <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>) δ 13.1, 19.5, 60.9, 114.1, 118.6, 125.5, 127.2, 128.3, 128.6, 128.7, 129.9, 130.2, 132.8, 136.5, 138.3, 147.8, 153.7, 163.5, 166.1 ppm; IR (KBr pallet) 3430, 2839, 1658, 1280, 1411, 1010, 779; HRMS Cal. for [M+H]<sup>+</sup>: C<sub>21</sub>H<sub>20</sub>NO<sub>3</sub>: 334.1443.

Found: 334.1456.

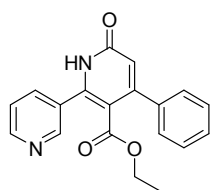
**1,6-Dihydro-2-(*m*-tolyl)-6-oxo-4-phenyl-pyridine-3-carboxylic acid ethyl ester (4f)**

Yield: 81 %; Yellow solid; mp: 210-212 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>) δ 0.78 (t, *J* = 7.1 Hz, 3H), 2.39 (s, 3H), 3.82 (q, *J* = 7.1 Hz, 2H), 6.45 (s, 1H), 7.30 ~ 7.41 (m, 9H), 11.44 (brs, 1H) ppm; <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>) δ 13.2, 21.3, 61.1, 113.7, 118.4, 125.3, 127.2, 128.3, 128.4, 128.6, 128.9, 130.9, 132.8, 138.2, 147.5, 153.6, 163.7, 166.9 ppm; IR (KBr pallet) 3417, 2947, 1651, 1280, 864, 702; HRMS Cal. for [M+H]<sup>+</sup>: C<sub>21</sub>H<sub>20</sub>NO<sub>3</sub>: 334.1443. Found: 334.1456.

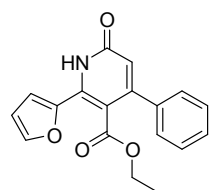
**1,6-Dihydro-2-(*p*-tolyl)-6-oxo-4-phenyl-pyridine-3-carboxylic acid ethyl ester (4g)**

Yield: 87 %; Yellow solid; mp: 218-220 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>) δ 0.78 (t, *J* = 7.1 Hz, 3H), 2.39 (s, 3H), 3.82 (q, *J* = 7.2 Hz, 2H), 6.47 (s, 1H), 7.25 (d, *J* = 7.1 Hz, 2H), 7.28 ~ 7.42 (m, 7H), 11.03 (brs, 1H) ppm; <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>) δ 13.3, 21.4, 61.2, 113.8, 118.3, 127.2, 128.1, 128.4, 128.6, 129.4, 130.1, 138.3, 140.4, 147.4, 153.8, 163.7, 167.0 ppm; IR (KBr pallet) 3425, 2908, 1658, 1280, 1110, 825, 779; HRMS Cal. for [M+H]<sup>+</sup>: C<sub>21</sub>H<sub>20</sub>NO<sub>3</sub>: 334.1443. Found:

334.1456.

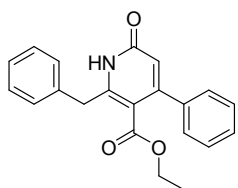
**1,6-Dihydro-6-oxo-4-phenyl-[2,3']bipyridinyl-3-carboxylic acid ethyl ester (4h)**

Yield: 83 %; Dark yellow solid; mp: 170-172 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>) δ 0.77 (t, *J* = 7.1 Hz, 3H), 3.83 (q, *J* = 7.1 Hz, 2H), 6.51 (s, 1H), 7.32 ~ 7.35 (m, 2H), 7.39 ~ 7.43 (m, 3H), 7.43 ~ 7.45 (m, 1H), 7.91-7.96 (m, 1H), 8.71 ~ 8.77 (m, 1H), 8.77 (d, *J* = 1.7 Hz, 1H), 13.37 (brs, 1H) ppm; <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>) δ 13.2, 61.4, 114.7, 119.0, 123.1, 127.1, 128.4, 128.8, 129.2, 136.1, 138.0, 144.5, 148.9, 150.8, 153.8, 164.0, 166.4 ppm; IR (KBr pallet) 3425, 2769, 1651, 1280, 1002, 709; HRMS Cal. for [M+H]<sup>+</sup>: C<sub>19</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub>: 321.1239. Found: 321.1253.

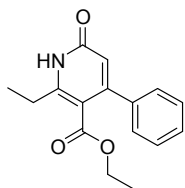
**1,6-Dihydro-2-(furan-2-yl)-6-oxo-4-phenyl-pyridine-3-carboxylic acid ethyl ester (4i)**

Yield: 90 %; Dark yellow solid; mp: 208-210 °C; <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>) δ 0.96 (t, *J* = 7.1 Hz, 3H), 4.03 (q, *J* = 7.1 Hz, 2H), 6.49 (s, 1H), 6.55 ~ 6.57 (m, 1H), 7.35 (d, *J* = 3.6 Hz, 1H), 7.37 ~ 7.43 (m, 5H), 7.54 (d, *J* = 1.2 Hz, 1H), 11.89 (brs, 1H) ppm; <sup>13</sup>C NMR (62.9 MHz, CDCl<sub>3</sub>) δ 13.6, 61.6, 111.6, 112.6, 113.7, 118.6, 127.4, 128.4, 128.8, 134.7, 137.9, 144.6, 144.9, 153.8, 163.2, 166.8; IR (KBr pallet) 3425, 2900, 1651, 1280, 1018, 771; HRMS Cal. for [M+H]<sup>+</sup>: C<sub>18</sub>H<sub>16</sub>NO<sub>4</sub>:

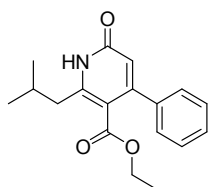
310.1079. Found: 310.1075.

**2-Benzyl-1,6-dihydro-6-oxo-4-phenyl-pyridine-3-carboxylic acid ethyl ester (4j)**

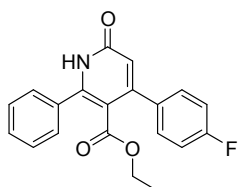
Yield: 92 %; Yellow solid; mp: 160-162 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.75 (t,  $J$  = 7.1 Hz, 3H), 3.86 (q,  $J$  = 7.2 Hz, 2H), 4.20 (s, 2H), 6.44 (s, 1H), 7.23 ~ 7.41 (m, 10H), 12.72 (brs, 1H);  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.3, 37.0, 61.1, 113.1, 117.6, 127.0, 127.1, 128.4, 128.5, 128.7, 129.0, 136.3, 139.1, 149.1, 154.6, 164.3, 167.0 ppm; IR (KBr pallet) 3456, 2777, 1658, 1265, 948, 702; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{21}\text{H}_{20}\text{NO}_3$ : 334.1443. Found: 334.1462.

**2-Ethyl-1,6-dihydro-6-oxo-4-phenyl-pyridine-3-carboxylic acid ethyl ester (4k)**

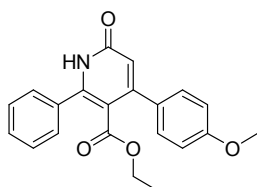
Yield: 92 %; Yellow solid; mp: 136-138 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.85 (t,  $J$  = 7.1 Hz, 3H), 1.39 (t,  $J$  = 7.5 Hz, 3H), 2.84 (q,  $J$  = 7.65 Hz, 2H), 3.95 (q,  $J$  = 7.1 Hz, 2H), 6.46 (s, 1H), 7.28 ~ 7.41 (m, 5H), 13.42 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.3, 14.3, 25.3, 61.0, 112.5, 116.9, 127.0, 128.3, 128.4, 139.0, 152.6, 154.7, 164.9, 166.9 ppm; IR (KBr pallet) 3433, 2985, 1651, 1265, 1018, 655; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{16}\text{H}_{18}\text{NO}_3$ : 272.1287. Found: 272.1297.

**1,6-Dihydro-2-isobutyl-6-oxo-4-phenyl-pyridine-3-carboxylic acid ethyl ester (4l)**

Yield: 88 %; Yellow solid; mp : 138-140 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.83 (t,  $J$  = 7.1 Hz, 3H), 0.99 (d,  $J$  = 6.6 Hz, 6H), 2.05 ~ 2.15 (m, 1H), 2.74 (d,  $J$  = 7.4 Hz, 2H), 3.92 (q,  $J$  = 7.2 Hz, 2H), 6.44 (s, 1H), 7.27 ~ 7.42 (m, 5H), 13.08 (s, 1H) ppm;  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.4, 22.2, 29.5, 39.9, 61.0, 113.4, 117.1, 127.0, 128.4, 128.5, 139.2, 150.6, 154.5, 164.5, 167.1 ppm; IR (KBr pallet) 3430, 2962, 1651, 1465, 1265, 987, 702; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{18}\text{H}_{22}\text{NO}_3$ : 300.1600. Found: 300.1611.

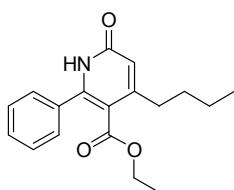
**1,6-Dihydro-4-(4-fluoro-phenyl)-6-oxo-2-phenyl-pyridine-3-carboxylic acid ethyl ester (4m)**

Yield: 92 %; Yellow solid; mp: 205-210 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.80 (t,  $J$  = 7.1 Hz, 3H), 3.83 (q,  $J$  = 7.1 Hz, 2H), 6.44 (s, 1H), 7.06 ~ 7.13 (m, 2H), 7.30 ~ 7.36 (m, 2H), 7.49 ~ 7.53 (m, 5H), 11.53 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.4, 61.4, 113.9, 115.5 (d,  $J$  = 21.7 Hz), 118.7, 128.2, 128.7, 129.2 (d,  $J$  = 8.2 Hz), 130.3, 133.0, 134.2 (d,  $J$  = 3.4 Hz), 147.5, 152.7, 163.3 (d,  $J$  = 248.6 Hz), 163.7, 166.8 ppm; IR (KBr pallet) 3437, 2900, 1724, 1647, 837; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{20}\text{H}_{17}\text{FNO}_3$ : 338.1192. Found: 338.1180.

**1,6-Dihydro-4-(4-methoxy-phenyl)-6-oxo-2-phenyl-pyridine-3-carboxylic acid ethyl ester (4n)**

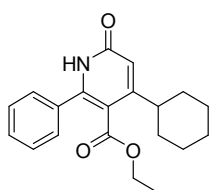
Yield: 94 %; Yellow solid; mp: 228-230 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.81 (t,  $J$  = 7.1 Hz, 3H), 3.84 (s, 3H), 3.85 (q,  $J$  = 7.1 Hz, 2H), 6.45 (s, 1H), 6.92 (d,  $J$  = 8.8 Hz, 2H), 7.28 (d,  $J$  = 8.8 Hz, 2H), 7.45 ~ 7.53 (m, 5H), 11.49 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  13.4, 55.3, 61.3, 113.9, 114.2, 118.1, 128.3, 128.6, 128.7, 130.2, 130.4, 133.1, 147.1, 153.4, 160.1, 163.9, 167.1 ppm; IR (KBr pallet) 3437, 2900, 1724, 1647, 837; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{21}\text{H}_{20}\text{NO}_4$ : 350.1392. Found: 350.1395.

#### 4-Butyl-1,6-dihydro-6-oxo-2-phenyl-pyridine-3-carboxylic acid ethyl ester (4o)



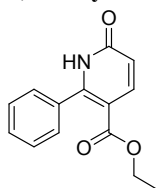
Yield: 90 %; Pale yellow solid; mp: 118-120 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.89 (t,  $J = 7.1$  Hz, 3H), 0.91 (t,  $J = 7.1$  Hz, 3H), 1.34 ~ 1.42 (m, 2H), 1.48 ~ 1.72 (m, 2H), 2.59 (t,  $J = 7.9$  Hz, 2H), 3.97 (q,  $J = 7.1$  Hz, 2H), 6.33 (s, 1H), 7.43 ~ 7.49 (m, 5H), 11.40 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9MHz,  $\text{CDCl}_3$ )  $\delta$  13.4, 13.8, 22.3, 31.5, 33.1, 61.1, 113.8, 117.4, 128.0, 128.4, 129.9, 133.6, 147.3, 155.1, 164.1, 167.3 ppm; IR (KBr pallet) 3428, 2958, 1720, 1643, 1276, 698; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{18}\text{H}_{22}\text{NO}_3$ : 300.1600. Found: 300.1613.

#### 4-Cyclohexyl-1,6-dihydro-6-oxo-2-phenyl-pyridine-3-carboxylic acid ethyl ester (4p)



Yield: 91 %; Pale yellow solid; mp: 210-212 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.91 (t,  $J = 7.1$  Hz, 3H), 1.15 ~ 1.40 (m, 5H), 1.71 ~ 1.89 (m, 5H), 2.52 ~ 2.71 (m, 1H), 3.98 (q,  $J = 7.1$  Hz, 2H), 6.39 (s, 1H), 7.44 ~ 7.46 (m, 5H), 11.54 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9MHz,  $\text{CDCl}_3$ )  $\delta$  13.5, 25.9, 26.5, 33.2, 40.8, 61.2, 114.2, 114.9, 128.2, 128.6, 129.9, 133.7, 146.7, 159.7, 164.7, 167.5 ppm; IR (KBr pallet) 3440, 2927, 1716, 1651, 1265, 702; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{20}\text{H}_{24}\text{NO}_3$ : 326.1756. Found: 326.1753.

#### 1,6-Dihydro-6-oxo-2-phenyl-pyridine-3-carboxylic acid ethyl ester (4q)



Yield: 35 %; Yellow solid; mp: 158-160 °C;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  1.01 (t,  $J = 7.1$  Hz, 3H), 4.06 (q,  $J = 7.2$  Hz, 2H), 6.45 (d,  $J = 9.6$  Hz, 1H), 7.37 ~ 7.50 (m, 5H), 7.98 (d,  $J = 9.7$  Hz, 1H), 11.13 (s, 1H) ppm;  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta$  13.7, 60.82, 109.2, 118.4, 128.2, 128.3, 130.1, 134.0, 142.1, 151.9, 163.7, 165.0 ppm; IR (KBr pallet): 3448, 1654, 1269, 702; HRMS Cal. for  $[\text{M}+\text{H}]^+$ :  $\text{C}_{14}\text{H}_{14}\text{NO}_3$ : 244.0974. Found: 244.0966.

#### 4-(Amino-phenyl-methylene)-3-phenyl-pent-2-enedionic acid diethyl ester (8)

To a stirred suspension of commercial zinc dust (Aldrich, 10  $\mu\text{m}$ , 1.0 g, 15.3 mmol) was added methanesulfonic acid (3.7 mg) in anhydrous THF (4.0 mL). After 10 min reflux, benzonitrile (0.8 mL, 7.6 mmol) was added all at one. While maintaining reflux temperature, ethyl bromoacetate (1.26 mL, 11.4 mmol) was added over 1h by using syringe pump and the reaction mixture was further reflux for 1h. The reaction mixture was cooled to room temperature and ethyl phenylpropionate (1.4 mL, 8.4 mmol) was added and stirred at 40 °C for 24 h. The reaction mixture was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$ , at room temperature and, extracted with ethyl acetate (30 mL  $\times$  3). The combined organic layer was dried with anhydrous  $\text{MgSO}_4$ , filtered, and concentrated under reduced pressure. The residue was purified by silica chromatography to afford **8**.

Yield: 45 %; Viscous yellowish liquid;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$  1.06 (t,  $J = 7.1$  Hz, 3H), 1.26 (t,  $J = 7.1$  Hz, 3H), 4.10 (q,  $J = 7.1$  Hz, 2H), 4.11 (q,  $J = 7.1$  Hz, 2H), 4.84 (brs, 1H), 6.02 (s, 1H), 7.09 ~ 7.22 (m, 10H), 8.86 (brs, 1H) ppm;  $^{13}\text{C}$  NMR (62.9MHz,  $\text{CDCl}_3$ )  $\delta$  14.0, 14.2, 59.1, 59.5, 96.3, 119.5, 127.2, 127.4, 127.6, 127.7, 128.1, 128.8, 137.8, 142.7, 153.1, 160.3, 166.1, 169.0 ppm.

## X-ray Crystallography

The diffraction data for **4k** were collected on a Bruker SMART AXS diffractometer using Mo K $\alpha$  ( $\lambda = 0.71073$  Å). The crystallographic data are listed in Table S1. The CIF deposition number: **CCDC 742379**

**Table S1.** Crystal data and structure refinement for **4k**.

|                                   |                                                  |                |
|-----------------------------------|--------------------------------------------------|----------------|
| Empirical formula                 | C <sub>16</sub> H <sub>17</sub> N O <sub>3</sub> |                |
| Formula weight                    | 271.31                                           |                |
| Temperature                       | 293(2) K                                         |                |
| Wavelength                        | 0.71073 Å                                        |                |
| Crystal system                    | Monoclinic                                       |                |
| Space group                       | P2 <sub>1</sub> /c                               |                |
| Unit cell dimensions              | a = 11.564(2) Å                                  | □ = 90.00°     |
|                                   | b = 16.918(3) Å                                  | □ = 109.86(3)° |
|                                   | c = 15.223(3) Å                                  | □ = 90.00°     |
| Volume                            | 2801.1(10) Å <sup>3</sup>                        |                |
| Z                                 | 8                                                |                |
| Density (calculated)              | 1.287 Mg/m <sup>3</sup>                          |                |
| Absorption coefficient            | 0.089 mm <sup>-1</sup>                           |                |
| F(000)                            | 1152                                             |                |
| Crystal size                      | 0.15 x 0.10 x 0.10 mm <sup>3</sup>               |                |
| θ range for data collection       | 1.86 to 26.00 °                                  |                |
| Index ranges                      | -13 ≤ h ≤ 14, -19 ≤ k ≤ 20, -18 ≤ l ≤ 18         |                |
| Reflections collected             | 15550                                            |                |
| Independent reflections           | 5490 [R(int) = 0.0551]                           |                |
| Completeness to theta = 26.00     | 99.7 %                                           |                |
| Refinement method                 | Full-matrix least-squares on F <sup>2</sup>      |                |
| Data / restraints / parameters    | 5490 / 0 / 373                                   |                |
| Goodness-of-fit on F <sup>2</sup> | 1.021                                            |                |
| Final R indices [I > 2σ(I)]       | R1 = 0.0511, wR2 = 0.1057                        |                |
| R indices (all data)              | R1 = 0.0979, wR2 = 0.1194                        |                |
| Largest diff. peak and hole       | 0.167 and -0.199 e.Å <sup>-3</sup>               |                |

**Table S2.** Selected Bond lengths [Å] and angles [°] for **4k**.

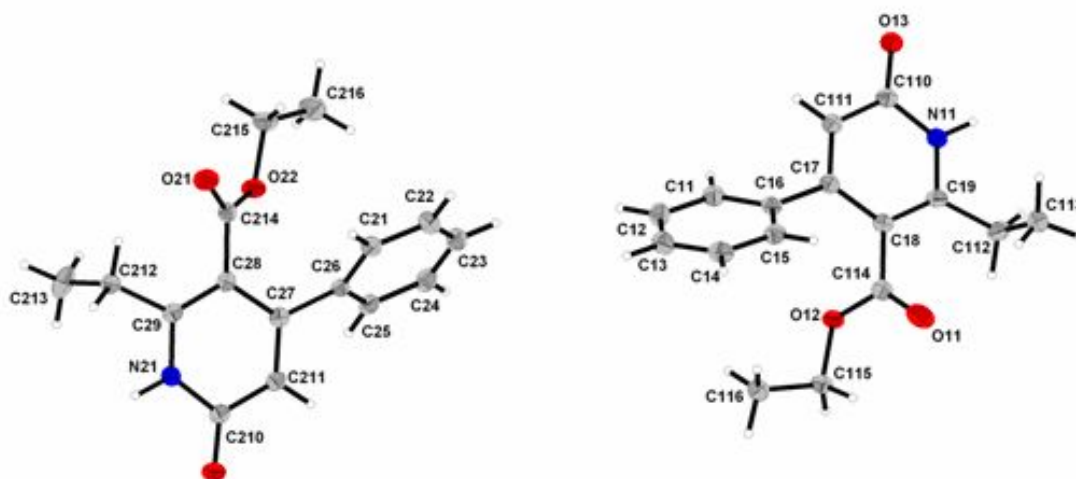
|                     |            |
|---------------------|------------|
| C(17)-C(111)        | 1.363(3)   |
| C(18)-C(19)         | 1.372(3)   |
| C(19)-N(11)         | 1.365(3)   |
| C(110)-O(13)        | 1.256(2)   |
| C(110)-N(11)        | 1.376(3)   |
| C(114)-O(11)        | 1.202(2)   |
| C(114)-O(12)        | 1.331(2)   |
| C(115)-O(12)        | 1.457(3)   |
| C(26)-C(27)         | 1.498(3)   |
| C(27)-C(211)        | 1.365(3)   |
| C(28)-C(29)         | 1.376(3)   |
| C(29)-N(21)         | 1.356(3)   |
| C(210)-O(23)        | 1.248(2)   |
| C(210)-N(21)        | 1.370(3)   |
| C(214)-O(21)        | 1.210(2)   |
| C(214)-O(22)        | 1.335(2)   |
| C(215)-O(22)        | 1.451(3)   |
| C(215)-C(216)       | 1.496(3)   |
| N(11)-H(11N)        | 0.89(2)    |
| N(21)-H(21N)        | 0.88(2)    |
|                     |            |
| N(11)-C(19)-C(18)   | 119.7(2)   |
| N(11)-C(19)-C(112)  | 114.18(19) |
| C(18)-C(19)-C(112)  | 126.1(2)   |
| O(13)-C(110)-N(11)  | 119.99(19) |
| O(13)-C(110)-C(111) | 124.6(2)   |
| N(11)-C(110)-C(111) | 115.4(2)   |
| C(17)-C(111)-C(110) | 122.4(2)   |
| O(11)-C(114)-O(12)  | 123.4(2)   |
| O(11)-C(114)-C(18)  | 125.5(2)   |
| O(12)-C(114)-C(18)  | 111.11(19) |
| O(12)-C(115)-C(116) | 109.60(18) |
| N(21)-C(29)-C(28)   | 119.35(19) |
| N(21)-C(29)-C(212)  | 114.12(18) |
| C(28)-C(29)-C(212)  | 126.5(2)   |
| O(23)-C(210)-N(21)  | 120.25(19) |

|                     |            |
|---------------------|------------|
| O(23)-C(210)-C(211) | 125.30(19) |
| N(21)-C(210)-C(211) | 114.4(2)   |
| C(27)-C(211)-C(210) | 122.19(19) |
| O(21)-C(214)-O(22)  | 122.6(2)   |
| O(21)-C(214)-C(28)  | 125.58(19) |
| O(22)-C(214)-C(28)  | 111.83(17) |
| O(22)-C(215)-C(216) | 107.56(19) |
| C(19)-N(11)-C(110)  | 124.49(19) |
| C(19)-N(11)-H(11N)  | 118.7(16)  |
| C(110)-N(11)-H(11N) | 116.8(16)  |
| C(29)-N(21)-C(210)  | 126.01(19) |
| C(29)-N(21)-H(21N)  | 118.7(15)  |
| C(210)-N(21)-H(21N) | 115.1(15)  |
| C(114)-O(12)-C(115) | 118.45(17) |
| C(214)-O(22)-C(215) | 117.09(17) |

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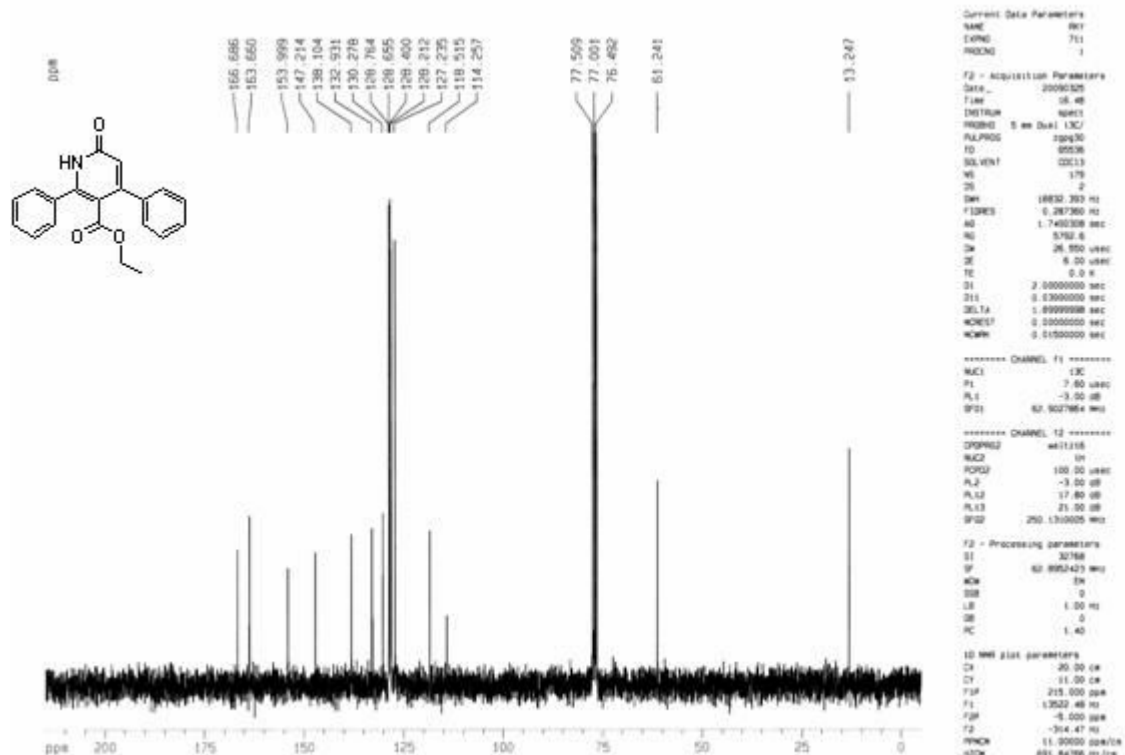
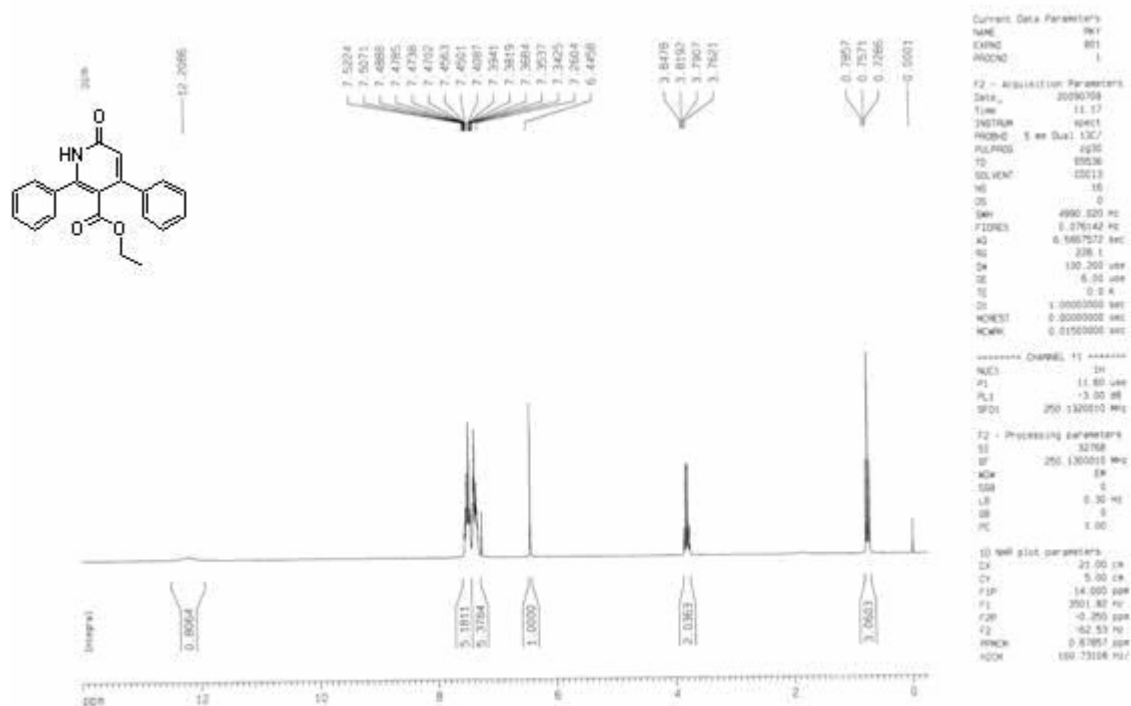
Symmetry transformations used to generate equivalent atoms:

**Figure S1.** X-Ray crystal structure of **4k**.





$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4a**



Chemical structure of the compound is shown at the top left. The structure is a substituted benzimidazole derivative with a fluorophenyl group, a benzyl group, and an ethyl ester group.

The <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) is displayed below the structure. The x-axis represents the chemical shift in ppm, ranging from 0 to 12. The spectrum shows several peaks, with the following chemical shifts (ppm) labeled above the peaks:

- 7.56528, 7.54450, 7.53045, 7.51750, 7.50980, 7.41369, 7.40030, 7.38761, 7.36498, 7.34911, 7.33830, 7.32373, 7.26081, 7.18079, 7.15398, 7.11949, 6.45933
- 3.85915, 3.83065, 3.80210, 3.77266
- 0.81451, 0.78597, 0.75747, 0.00060

The integration values for the peaks are shown below the baseline:

- 2.0005
- 2.0005
- 2.0005
- 1.0000
- 2.0083
- 3.0180

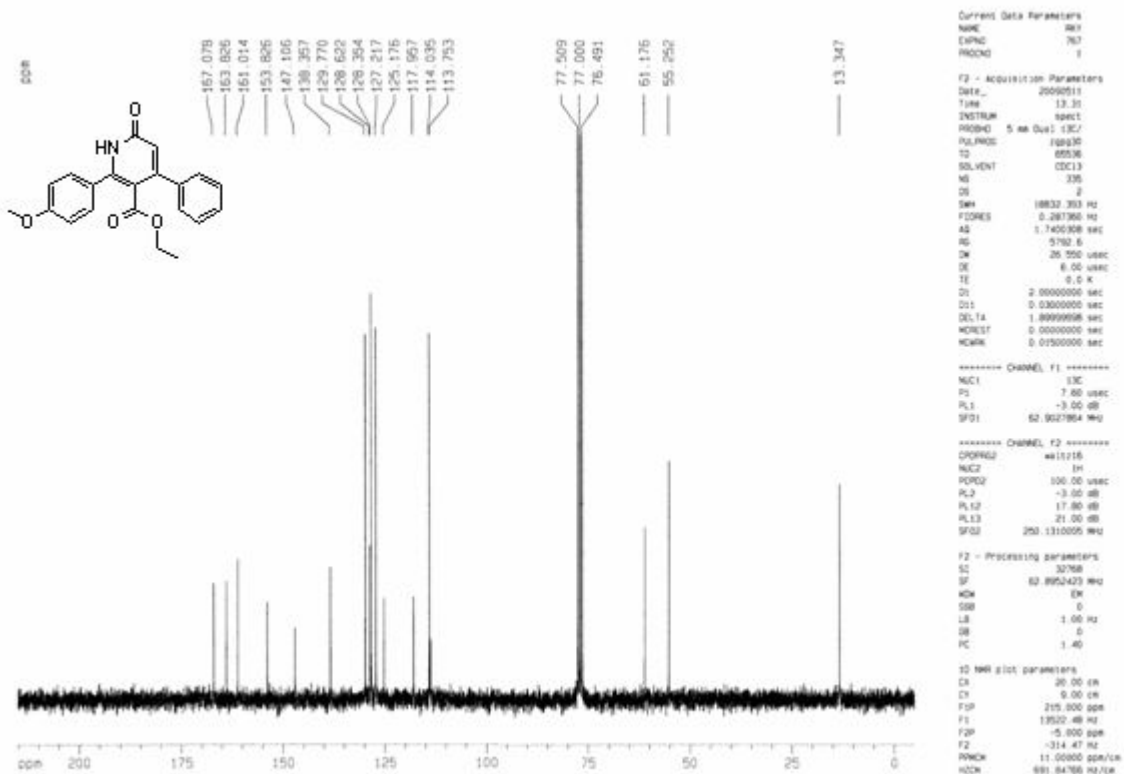
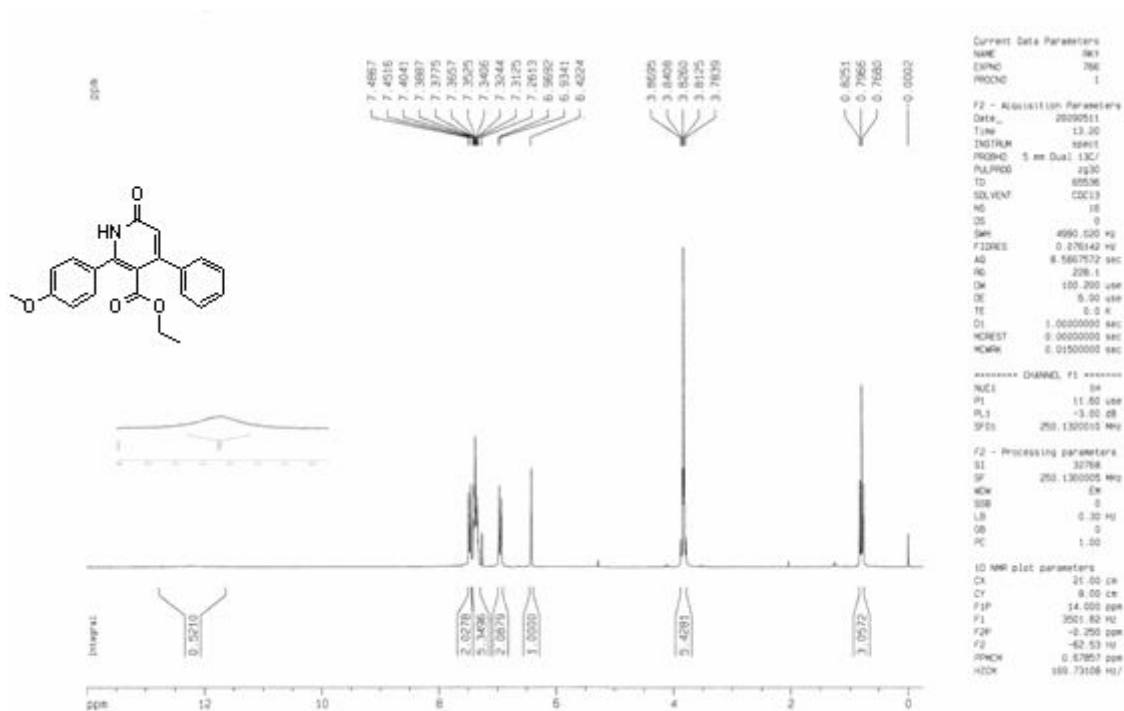
The spectrum is processed with the following parameters:

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- F2 - Acquisition Parameters: DATE\_: 20080331, TIME: 18.42, INSTRUM: spect, PROBHD: 5 mm QNP 13C/1, PULPROG: zgpg30, TO: 89936, SOLVENT: CDCl3, NS: 16, DS: 0, SWH: 4995.820 Hz, FIDRES: 0.278442 Hz, AQ: 8.5887572 sec, RG: 512, GW: 100.200 use, GU: 6.50 use, TE: 300.2 K, D1: 1.00000000 sec, DCREST: 0.00000000 sec, HCNMR: 0.01500000 sec
- CHANNEL f1 -----: NUC1: 13C, P1: 11.80 use, PL1: -3.00 dB, SFO1: 250.1300101 MHz
- F2 - Processing parameters: SI: 32768, SF: 250.1300104 MHz, WDW: EM, SSB: 0, LB: 0.30 Hz, GB: 0, PC: 1.00
- 13 AMX plot parameters: C1: 21.50 cm, CY: 4.50 cm, FIP: 14.000 gpm, FI: 3501.80 Hz, FIP: -0.250 gpm, F2: -52.93 Hz, F2MCK: 0.87857 gpm, H2OK: 100.73108 Hz

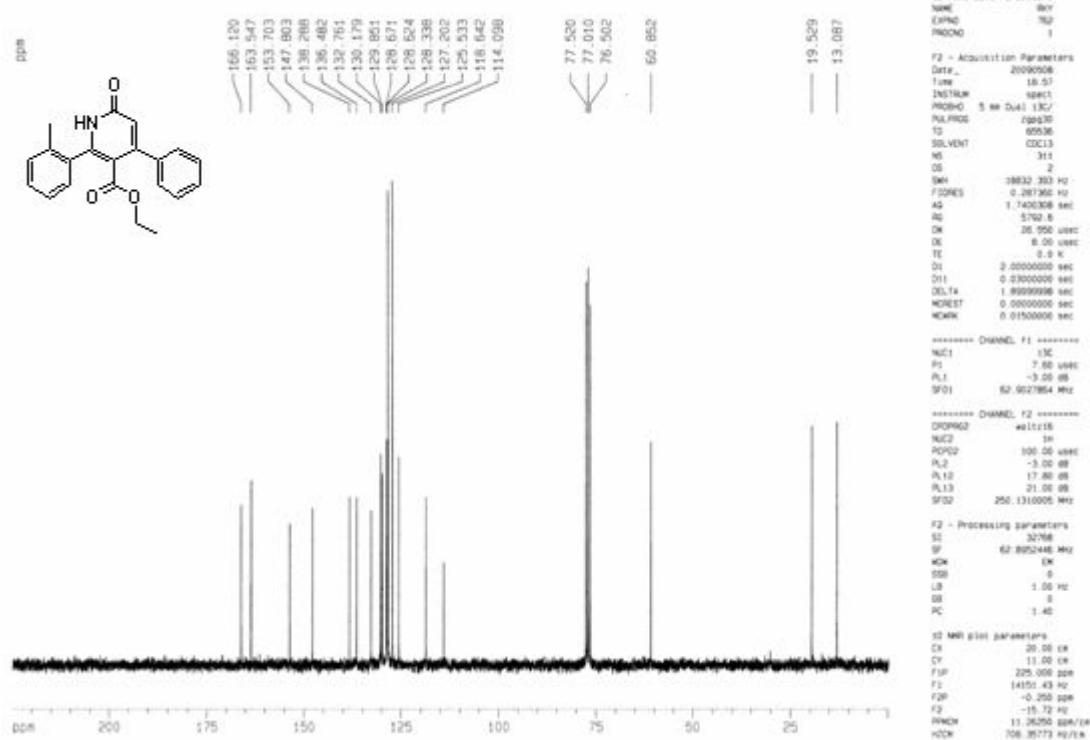
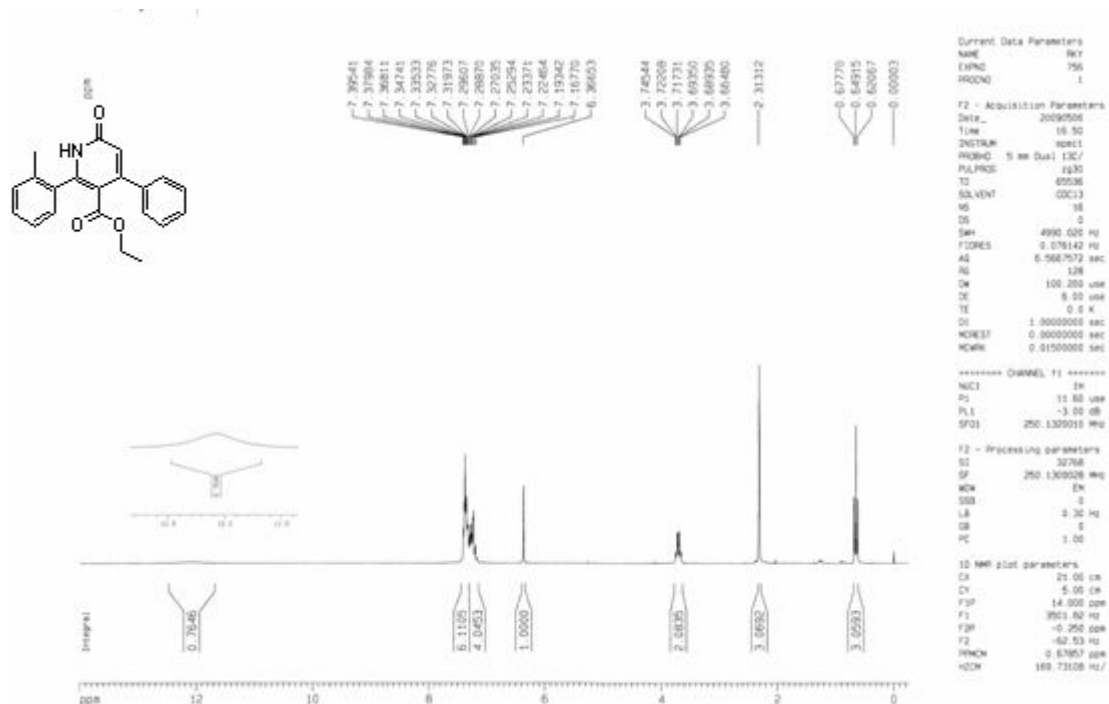




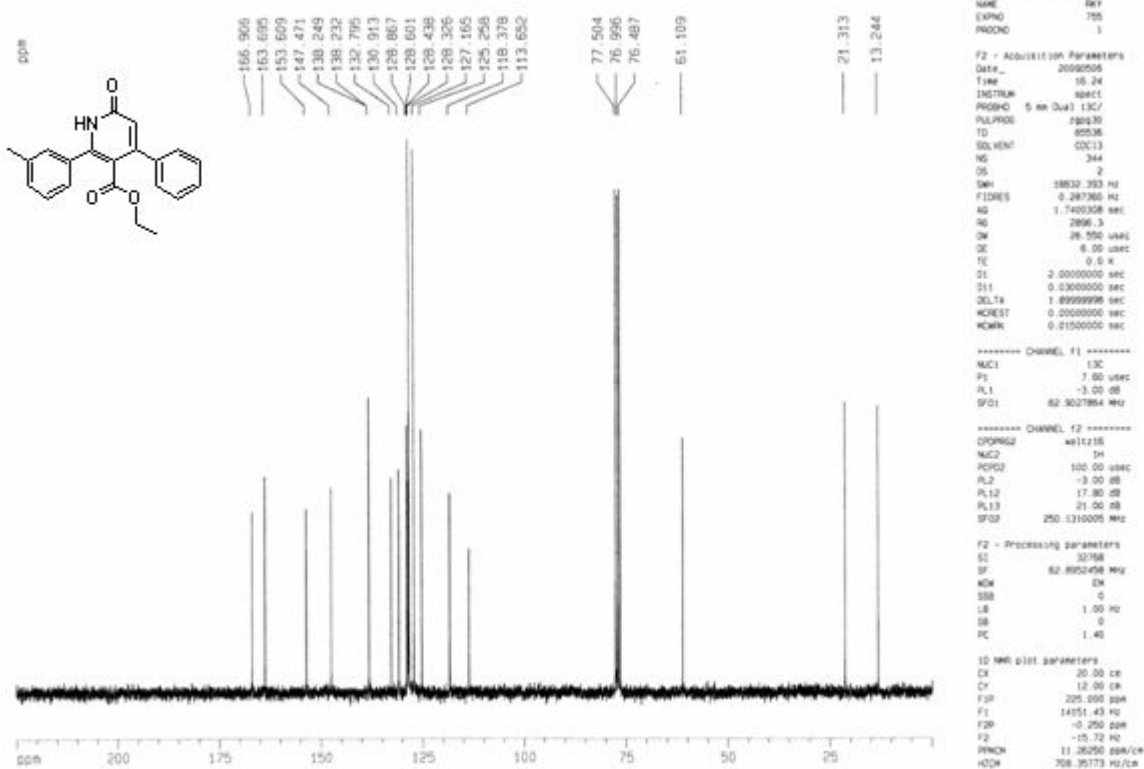
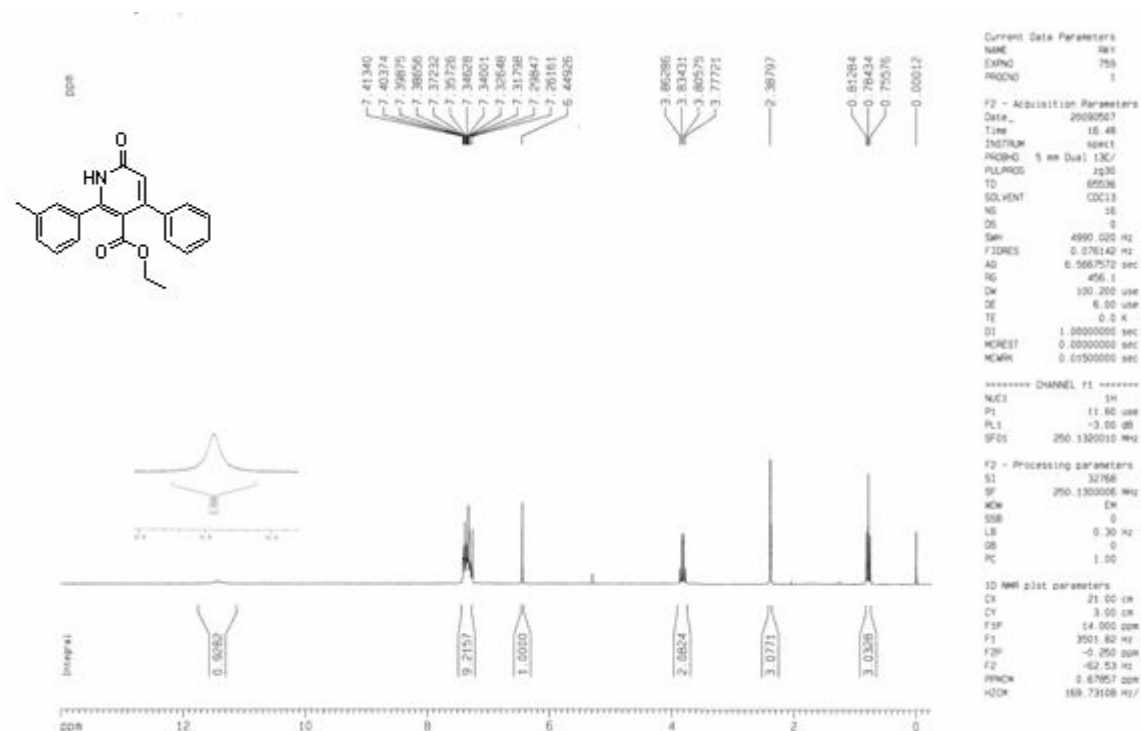
$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4d**



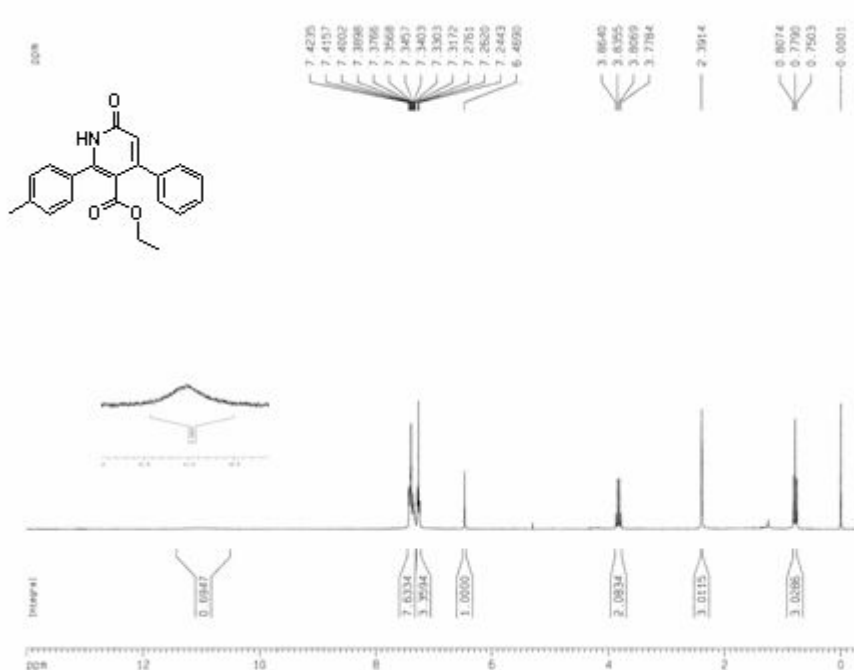
$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4e**



$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4f**



$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4g**



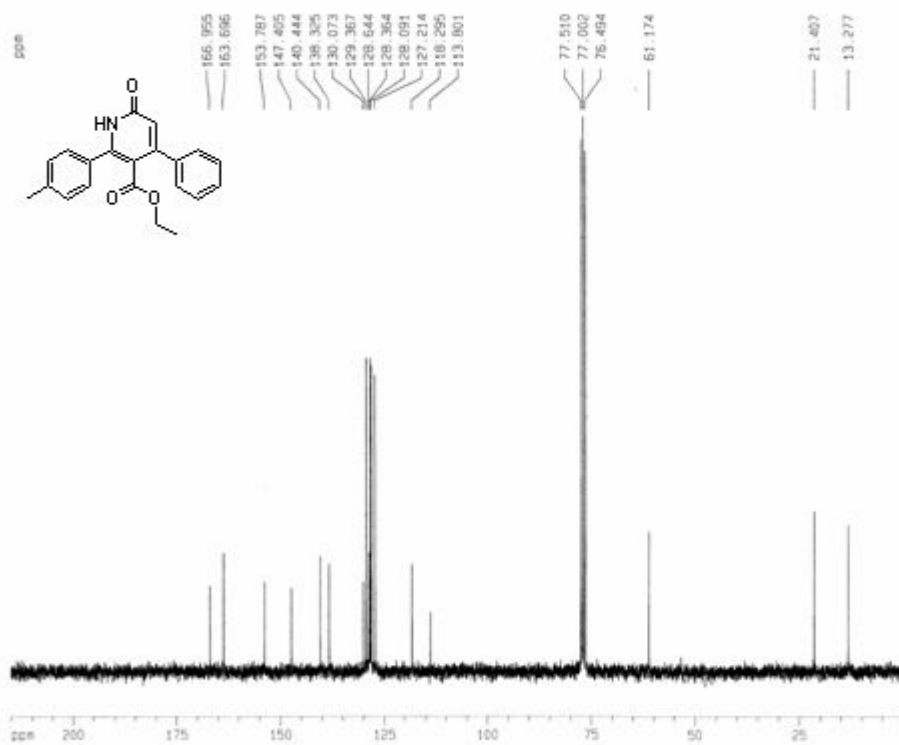
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PROCNO 1

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PULPROG zgpg30  
TD 65536  
SOLVENT CDCl3  
NS 30  
DS 2  
SWH 4990.020 Hz  
FIDRES 0.076142 Hz  
AQ 6.5867570 sec  
RG 724.1  
QW 100.000 use  
DE 6.00 use  
TE 300.2 K  
D1 1.00000000 sec  
MCHST 0.00000000 sec  
MCHW 0.01500000 sec

\*\*\*\*\* CHANNEL f1 \*\*\*\*\*  
NUC1 13C  
P1 11.00 use  
PL1 -3.00 dB  
SFO1 250.130010 MHz

F2 - Processing parameters  
SI 32768  
SF 250.130010 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

1D NMR plot parameters  
CX 21.00 cm  
CY 3.00 cm  
FSP 14.000 ppm  
F1 3501.82 Hz  
F2P -0.250 ppm  
F2 -62.53 Hz  
PPMH 0.67857 ppm  
H2CH 189.73108 Hz/



Current Data Parameters  
NAME 8k1  
EXPNO 731  
PROCNO 1

F2 - Acquisition Parameters  
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Time 17.20  
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PULPROG zgpg30  
TD 65536  
SOLVENT CDCl3  
NS 305  
DS 2  
SWH 18832.303 Hz  
FIDRES 0.287360 Hz  
AQ 1.7402358 sec  
RG 5160.6  
QW 26.000 use  
DE 6.00 use  
TE 300.2 K  
D1 2.00000000 sec  
D11 0.63000000 sec  
DELTA 1.80000000 sec  
MCHST 0.00000000 sec  
MCHW 0.01500000 sec

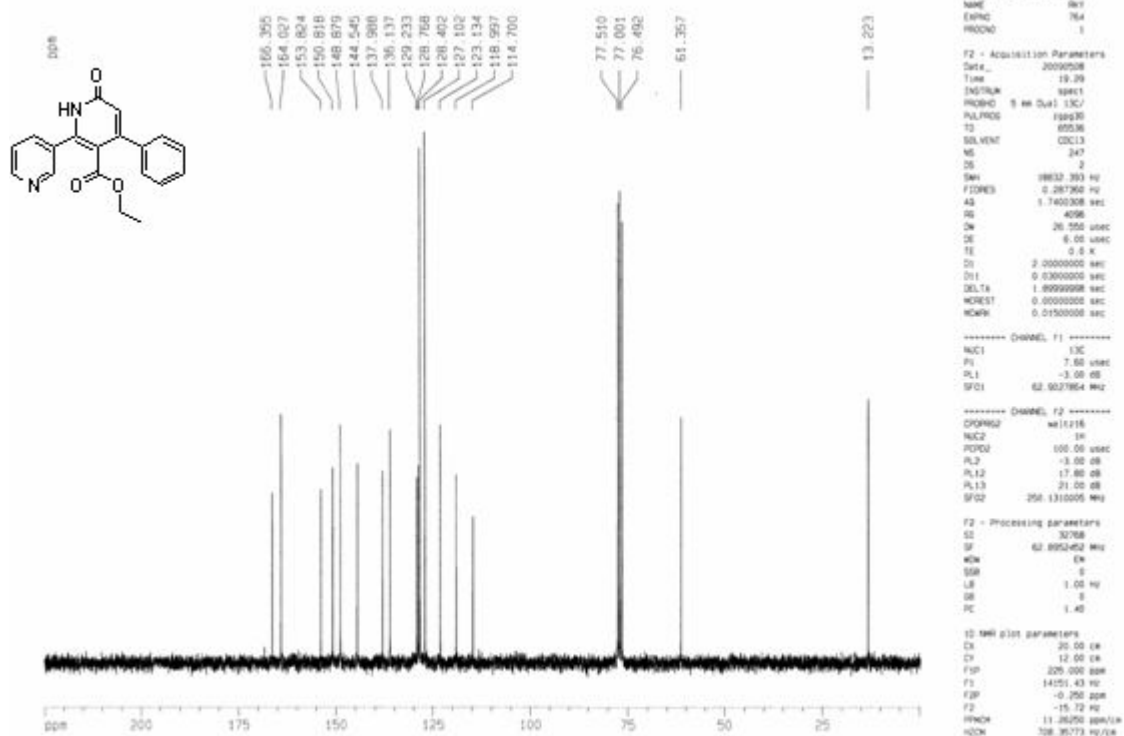
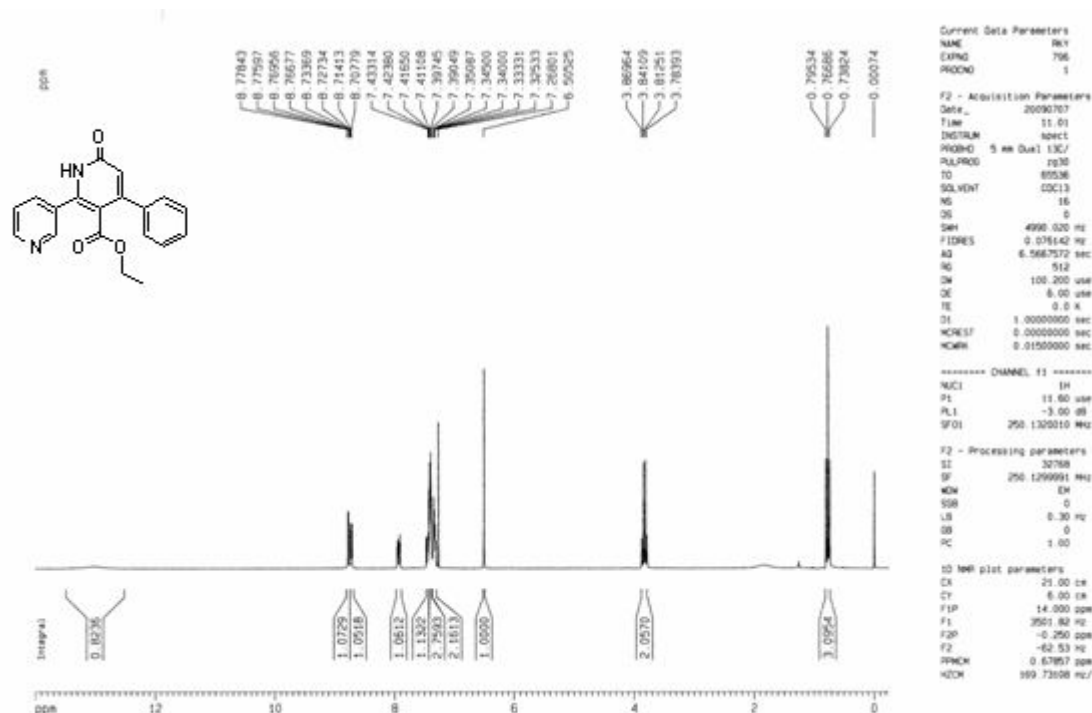
\*\*\*\*\* CHANNEL f1 \*\*\*\*\*  
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P1 7.50 use  
PL1 -3.00 dB  
SFO1 62.9027864 MHz

\*\*\*\*\* CHANNEL f2 \*\*\*\*\*  
EXPNO2 811118  
NUC2 1H  
P2 100.00 use  
PL2 -3.00 dB  
PL12 17.80 dB  
PL13 21.00 dB  
SFO2 250.1310005 MHz

F2 - Processing parameters  
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SF 62.9027864 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

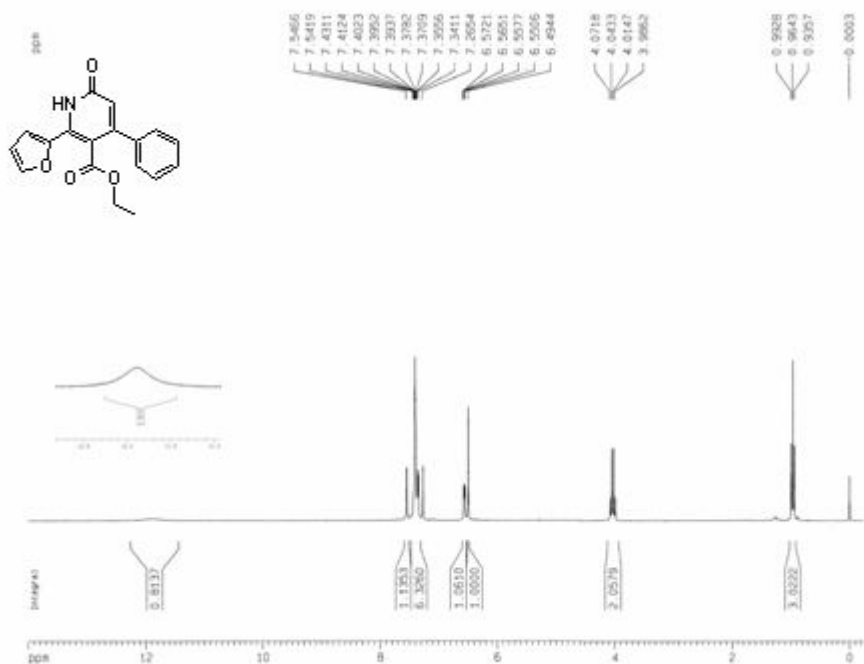
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CX 20.00 cm  
CY 7.00 cm  
FSP 215.000 ppm  
F1 3502.48 Hz  
F2P -1.52 Hz  
PPMH 30.75125 ppm/cx  
H2CH 676.20245 Hz/cx

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4h**





$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4i**



Current Data Parameters

|        |     |
|--------|-----|
| NAME   | 8K1 |
| EXPNO  | 729 |
| PROCNO | 1   |

F2 - Acquisition Parameters

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| PULPROG | zgpg30         |
| TD      | 65536          |
| SOLVENT | CDCl3          |
| NS      | 18             |
| DS      | 0              |
| SWH     | 4996.020 Hz    |
| FIDRES  | 0.076142 Hz    |
| AQ      | 6.5687572 sec  |
| RG      | 406.4          |
| DM      | 100.000 use    |
| DE      | 6.00 use       |
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| D1      | 1.0000000 sec  |
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| RGW     | 0.0150000 sec  |

===== CHANNEL f1 =====

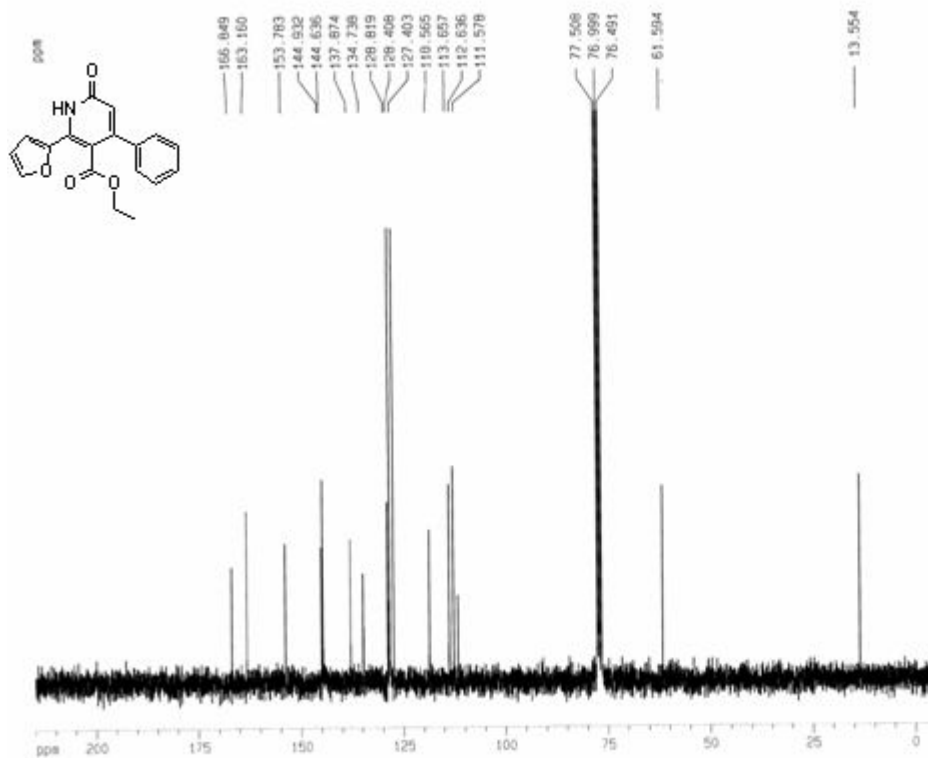
|      |                |
|------|----------------|
| NUC1 | $^1\text{H}$   |
| P1   | 11.80 use      |
| PL1  | -3.00 dB       |
| SFO1 | 250.130010 MHz |

F2 - Processing parameters

|     |                |
|-----|----------------|
| SF  | 32786          |
| SF  | 250.130005 MHz |
| WDW | EM             |
| SF8 | 0              |
| LB  | 0.30 Hz        |
| GB  | 0              |
| RC  | 1.00           |

1D NMR plot parameters

|      |               |
|------|---------------|
| CX   | 21.00 cm      |
| CY   | 4.00 cm       |
| F1P  | 14.000 ppm    |
| F1   | 2501.80 Hz    |
| F2P  | -0.250 ppm    |
| F2   | -62.53 Hz     |
| RGW  | 0.07857 ppm   |
| HZCN | 169.73108 Hz/ |



Current Data Parameters

|        |     |
|--------|-----|
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| EXPNO  | 729 |
| PROCNO | 1   |

F2 - Acquisition Parameters

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|---------|----------------|
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| PULPROG | zgpg30         |
| TD      | 65536          |
| SOLVENT | CDCl3          |
| NS      | 638            |
| DS      | 2              |
| SWH     | 18830.703 Hz   |
| FIDRES  | 0.267280 Hz    |
| AQ      | 1.7400308 sec  |
| RG      | 5792.6         |
| DM      | 28.550 usec    |
| DE      | 6.50 usec      |
| TE      | 0.3 K          |
| D1      | 2.0000000 sec  |
| D11     | 0.0300000 sec  |
| DELTA   | 1.8999999 sec  |
| RGW     | 0.0000000 sec  |
| RGW     | 0.0100000 sec  |

===== CHANNEL f1 =====

|      |                 |
|------|-----------------|
| NUC1 | $^{13}\text{C}$ |
| P1   | 7.00 usec       |
| PL1  | -3.00 dB        |
| SFO1 | 62.9027864 MHz  |

===== CHANNEL f2 =====

|      |                 |
|------|-----------------|
| NUC2 | $^1\text{H}$    |
| P2P2 | 100.00 usec     |
| PL2  | -3.00 dB        |
| PL12 | 17.80 dB        |
| PL13 | 21.00 dB        |
| SFO2 | 250.1310005 MHz |

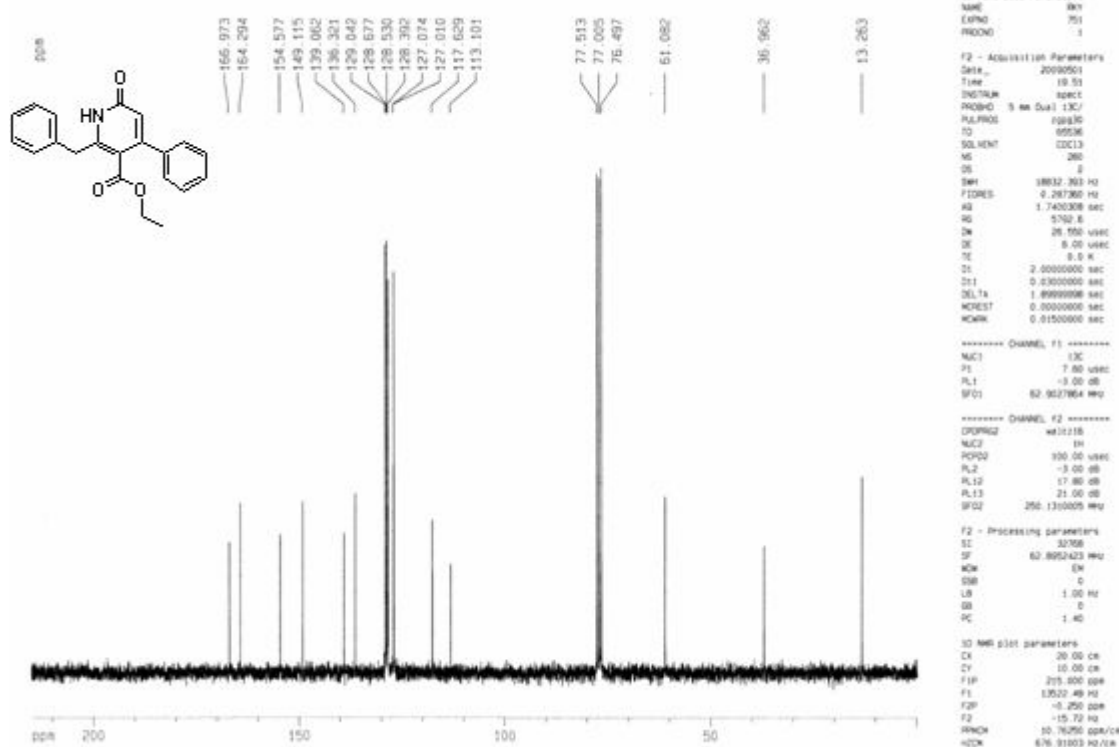
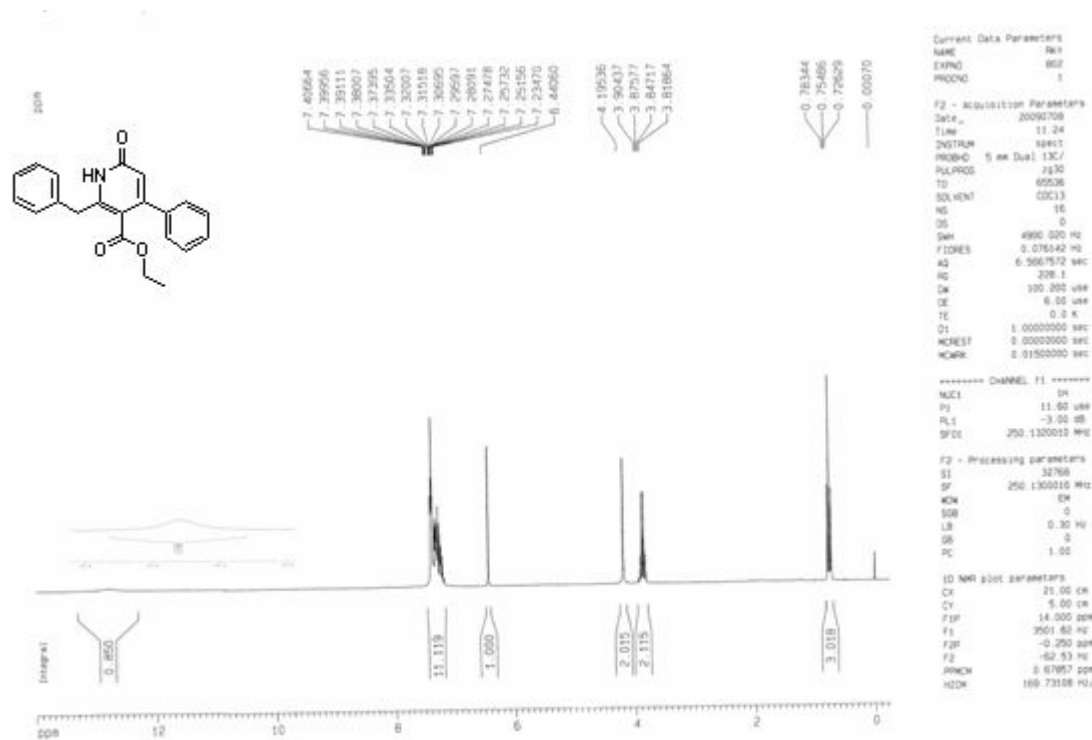
F2 - Processing parameters

|     |                |
|-----|----------------|
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| SF  | 62.9027864 MHz |
| WDW | EM             |
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| LB  | 1.00 Hz        |
| GB  | 0              |
| RC  | 1.40           |

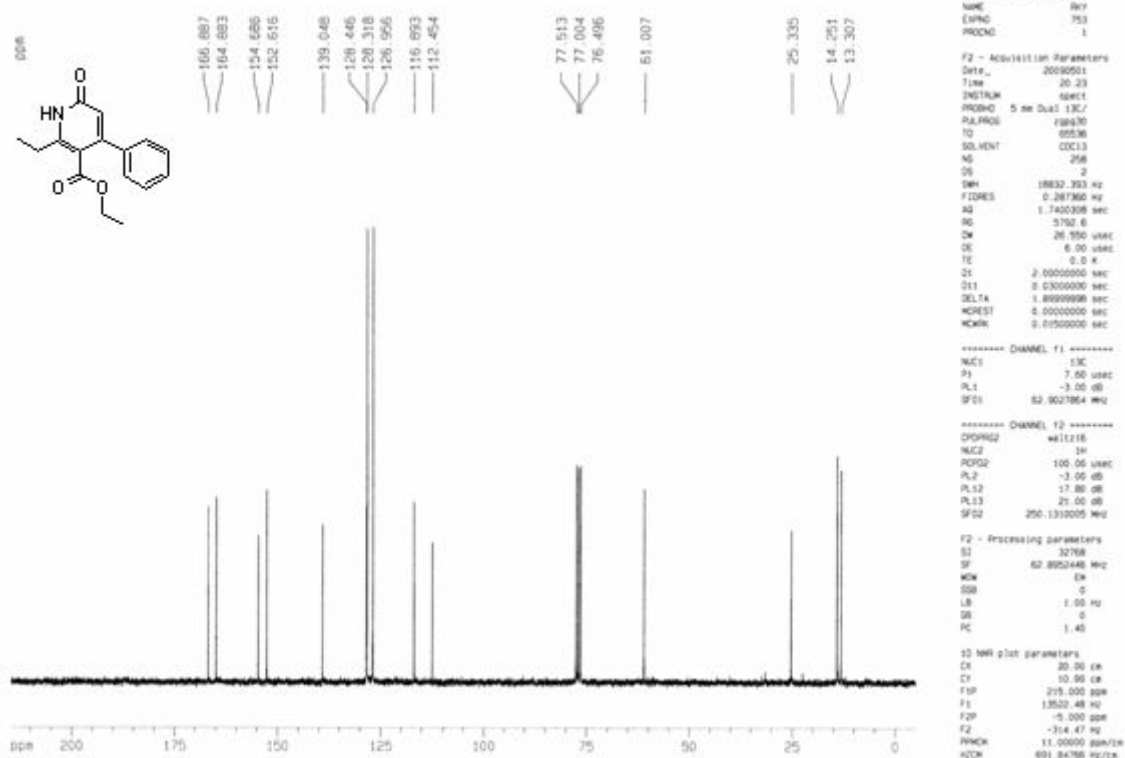
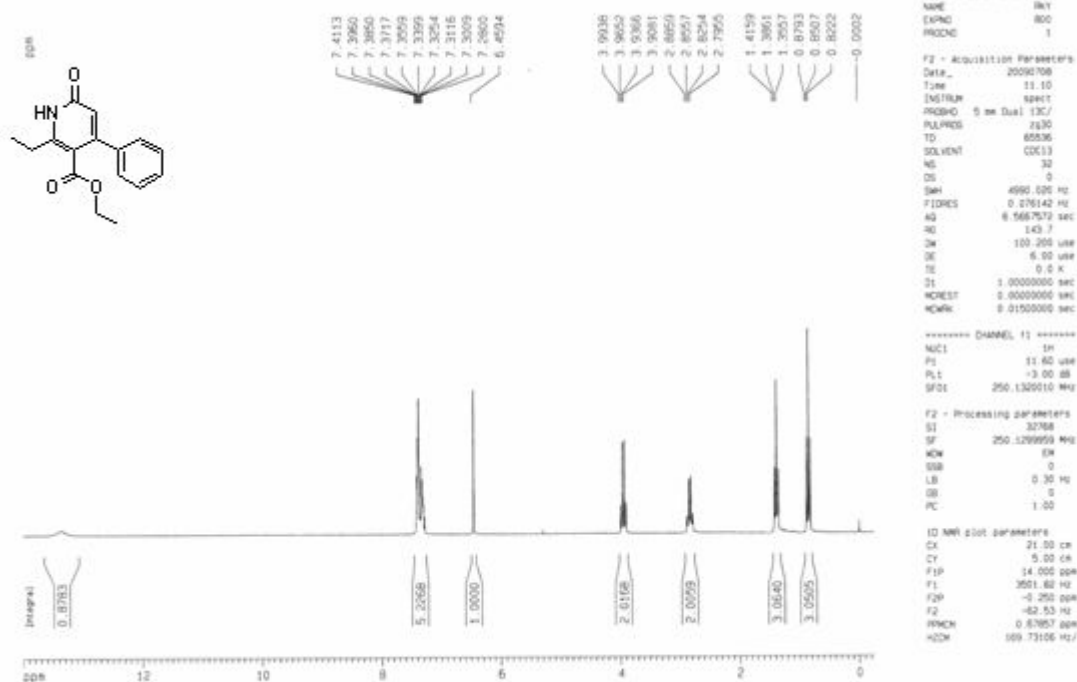
1D NMR plot parameters

|      |                 |
|------|-----------------|
| CX   | 20.00 cm        |
| CY   | 10.00 cm        |
| F1P  | 215.000 ppm     |
| F1   | 13522.48 Hz     |
| F2P  | -5.000 ppm      |
| F2   | -314.47 Hz      |
| RGW  | 11.00000 ppm/cm |
| HZCN | 681.84766 Hz/cm |

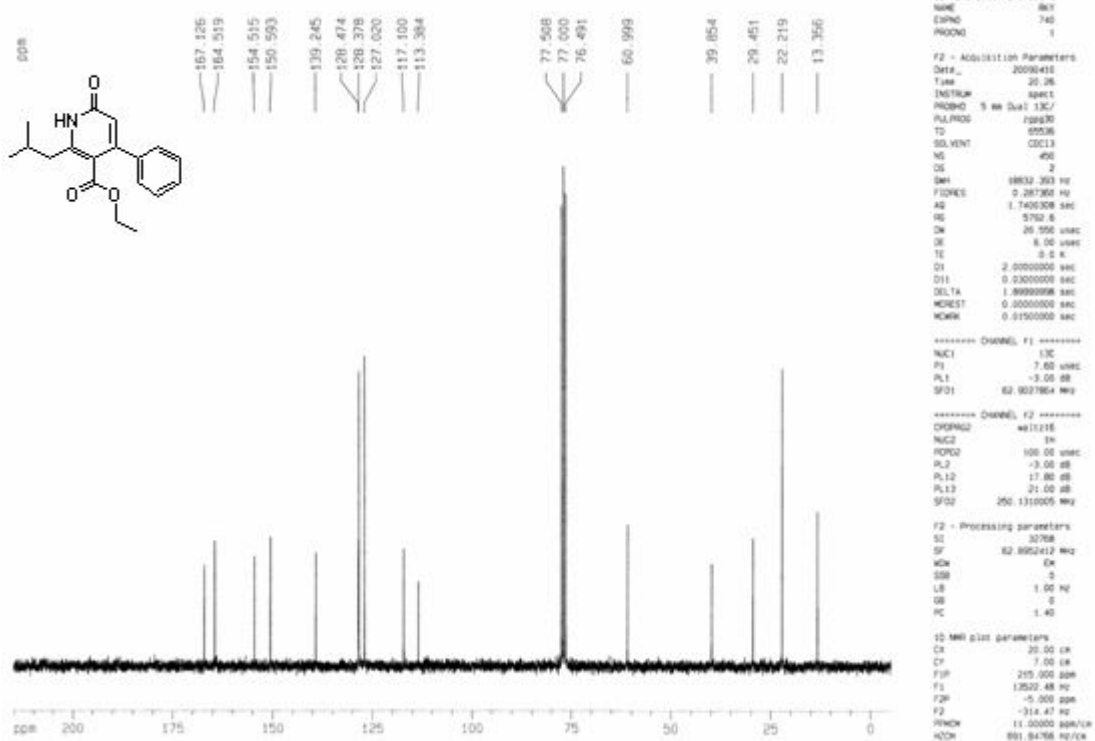
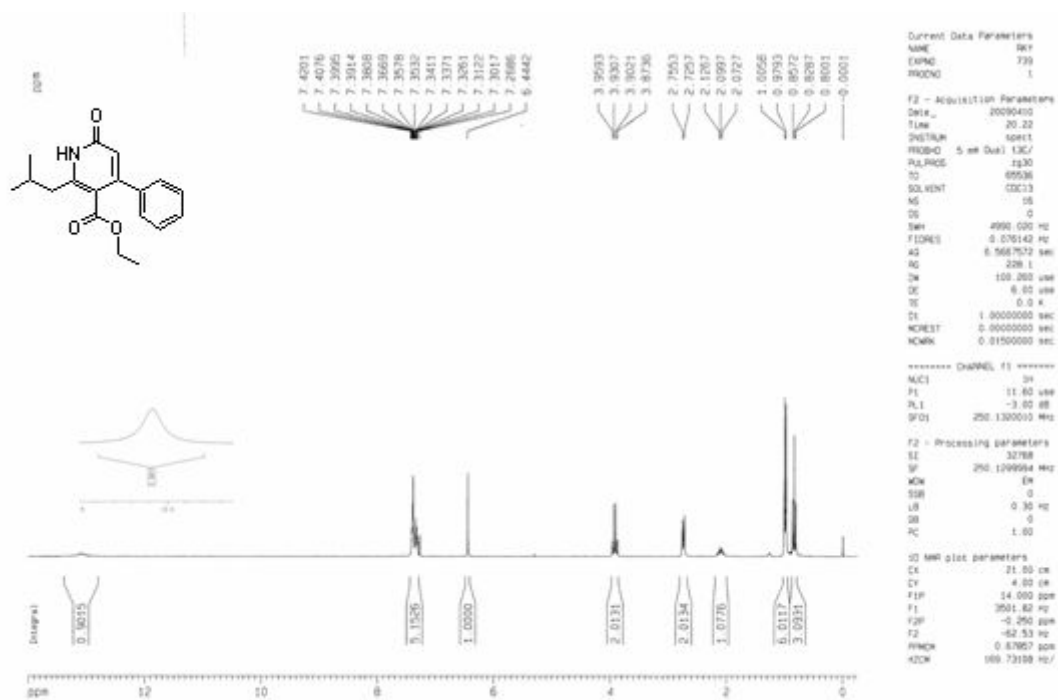
$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4j**



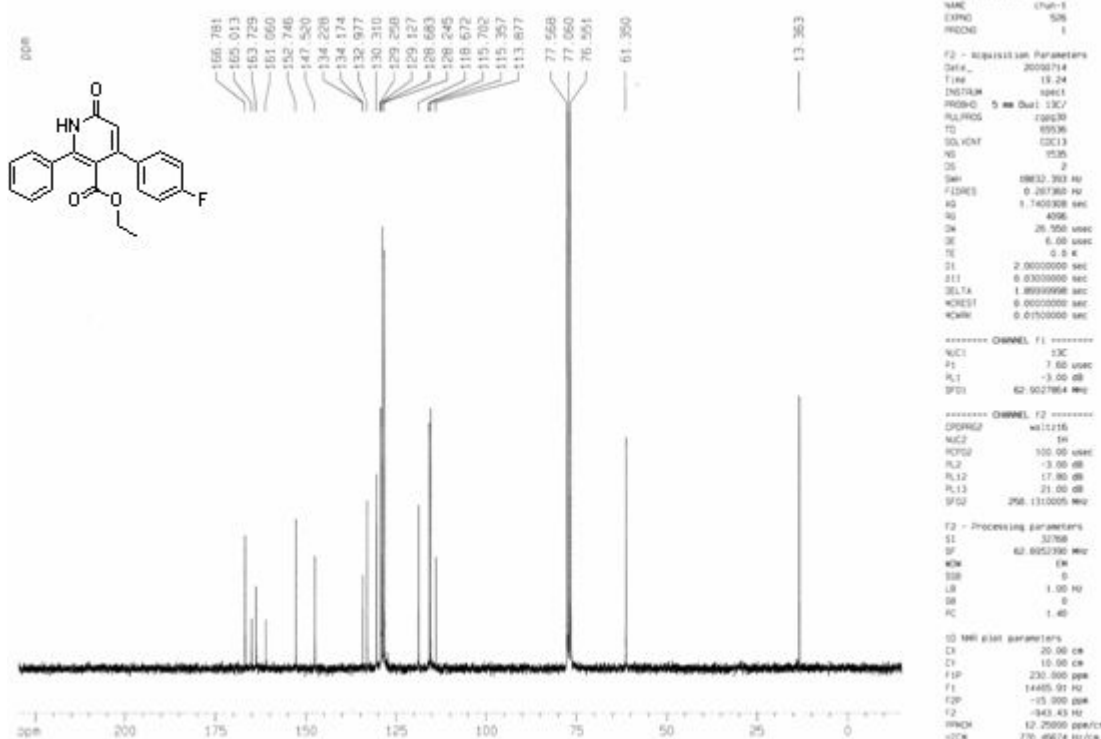
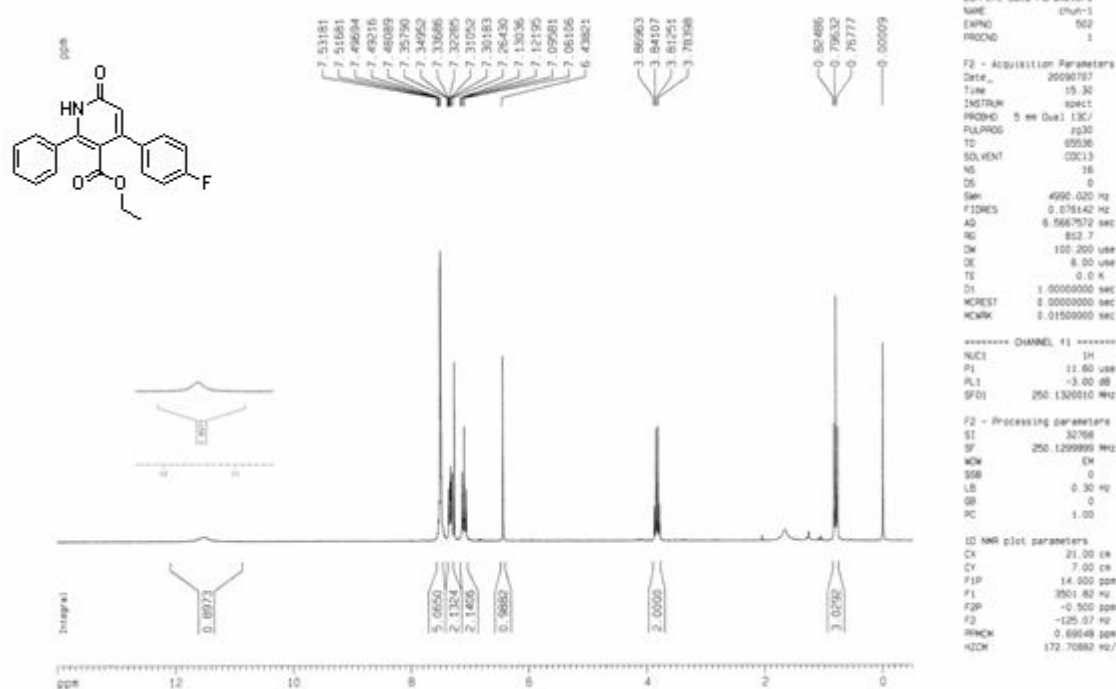
$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4k**



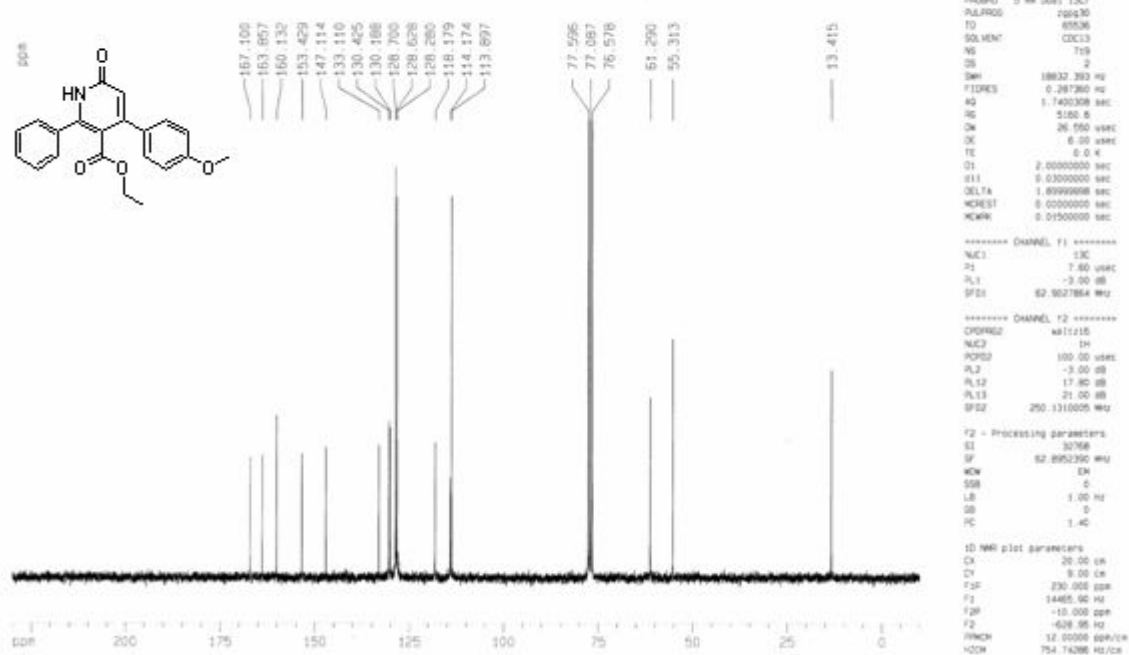
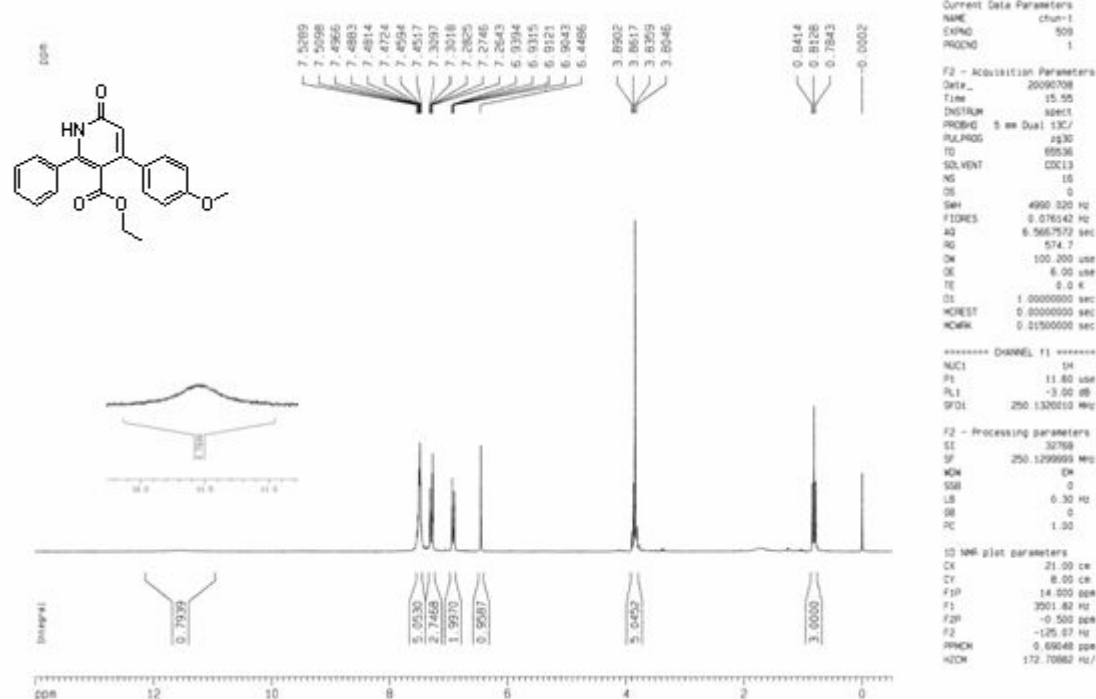
# <sup>1</sup>H and <sup>13</sup>C NMR spectra of **4I**



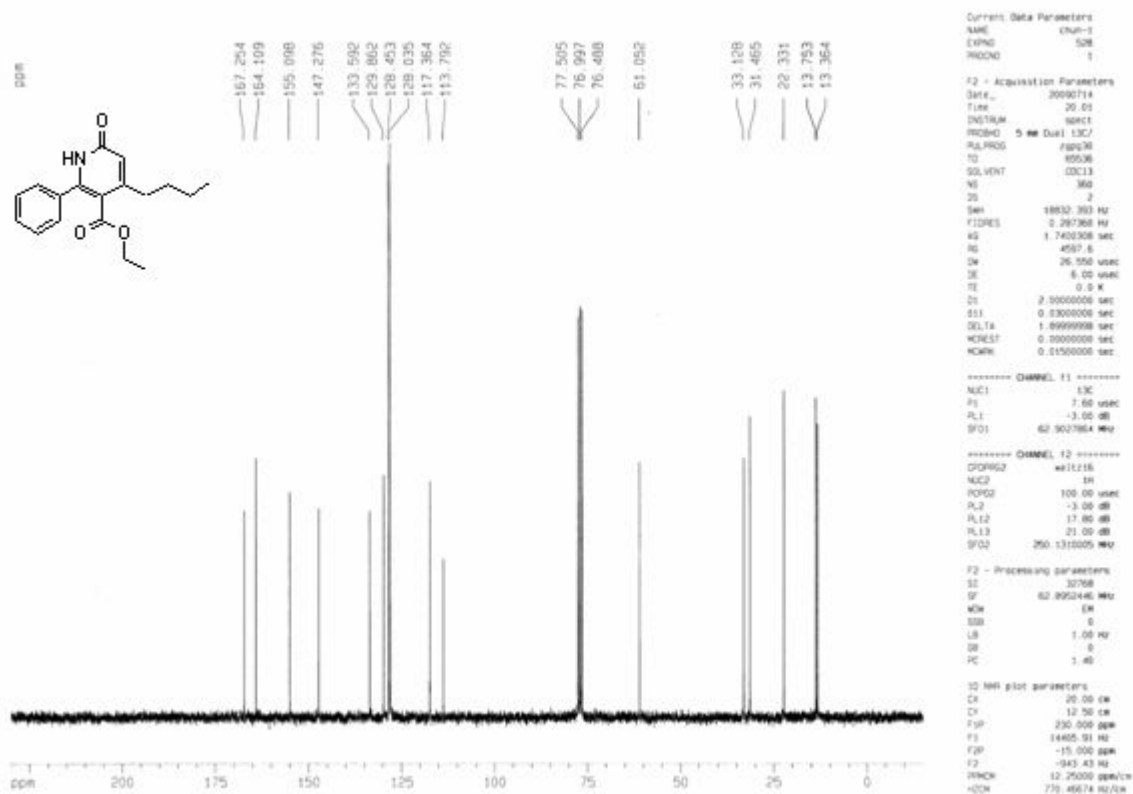
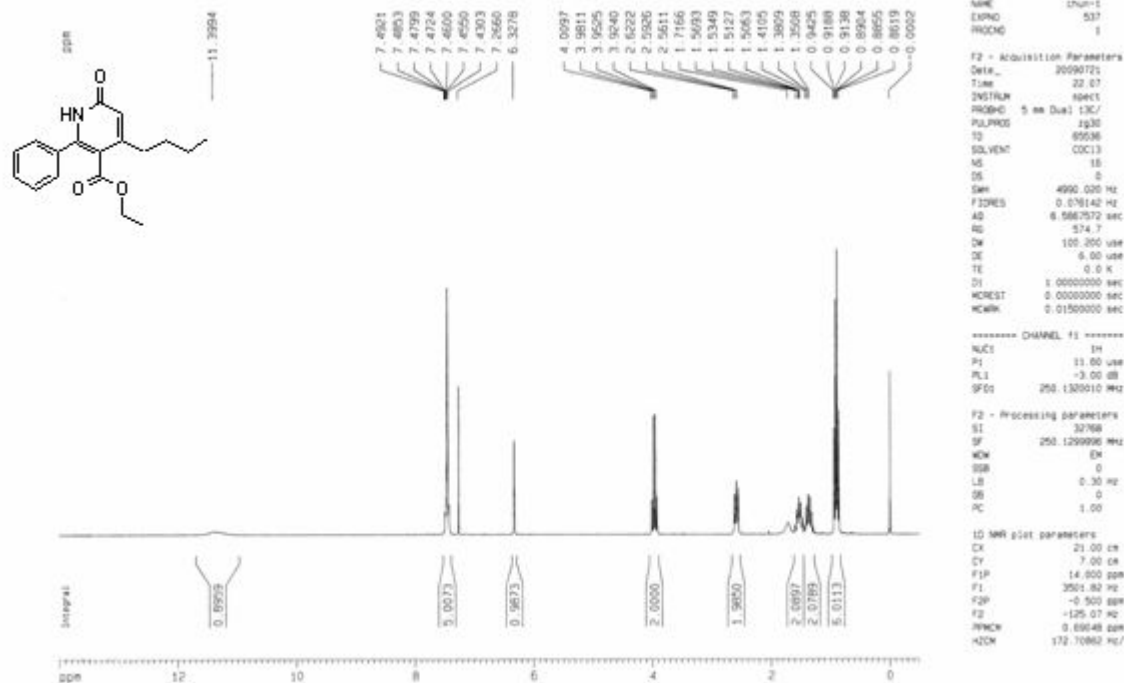
# <sup>1</sup>H and <sup>13</sup>C NMR spectra of **4m**



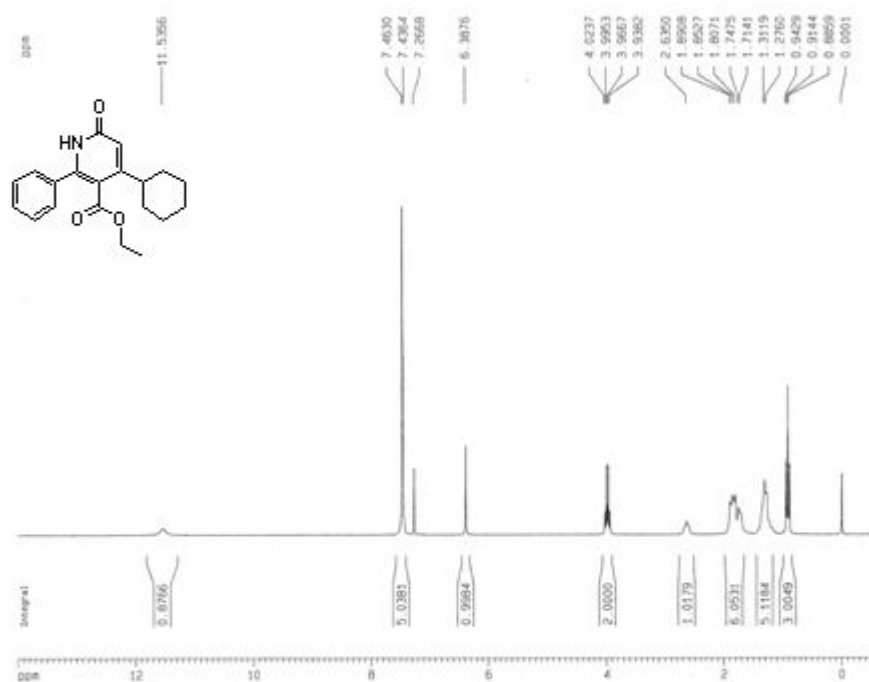
$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4n**



$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4o**



$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4p**



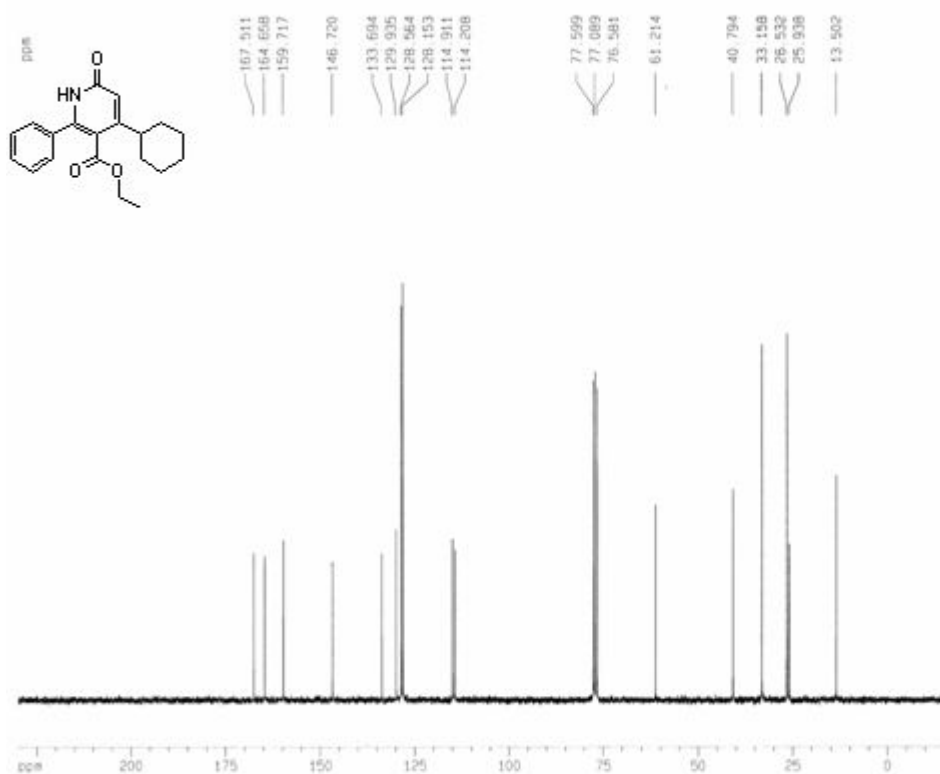
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PULPROG zg30  
TD 69536  
SOLVENT CDCl3  
NS 16  
DS 0  
SWH 4990.020 Hz  
FIDRES 0.076142 Hz  
AQ 0.5087572 sec  
RG 512  
SW 100.200 use  
DE 6.50 use  
TE 300.2 K  
D1 1.00000000 sec  
NOREST 0.00000000 sec  
NORM 0.01500000 sec

\*\*\*\*\* CHANNEL f1 \*\*\*\*\*  
NUC1 13C  
P1 11.00 use  
PL1 -3.00 dB  
SFO1 250.1300000 MHz

F2 - Processing parameters  
SI 32768  
SF 250.1299993 MHz  
WDW EM  
SSB 0  
LB 0.35 Hz  
GB 0  
PC 1.00

1D NMR plot parameters  
CX 21.90 cm  
CY 8.00 cm  
FIP 14.000 ppm  
F1 3601.82 Hz  
F2 -0.500 ppm  
F3 -129.67 Hz  
PRCK 0.00040 ppm  
HZCK 172.70882 Hz/



Current Data Parameters  
NAME chun-1  
EXPNO 525  
PROCNO 1

F2 - Acquisition Parameters  
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Time 16.07  
INSTRUM spect  
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PULPROG zgpg30  
TD 69536  
SOLVENT CDCl3  
NS 724  
DS 2  
SWH 18832.963 Hz  
FIDRES 0.287360 Hz  
AQ 1.7400308 sec  
RG 512.0  
SW 26.190 usec  
DE 6.50 usec  
TE 300.2 K  
D1 2.00000000 sec  
D11 0.03000000 sec  
DELTA 1.89999998 sec  
NOREST 0.00000000 sec  
NORM 0.01500000 sec

\*\*\*\*\* CHANNEL f1 \*\*\*\*\*  
NUC1 13C  
P1 7.00 usec  
PL1 -3.00 dB  
SFO1 62.9027864 MHz

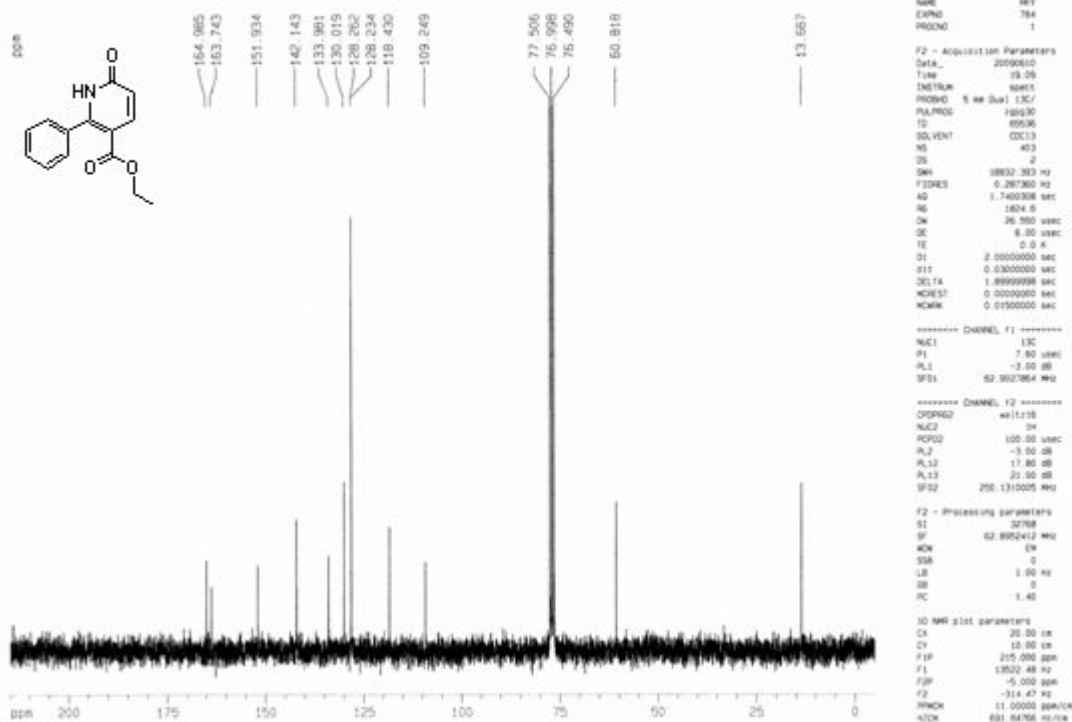
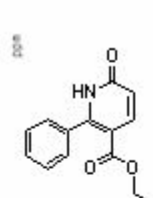
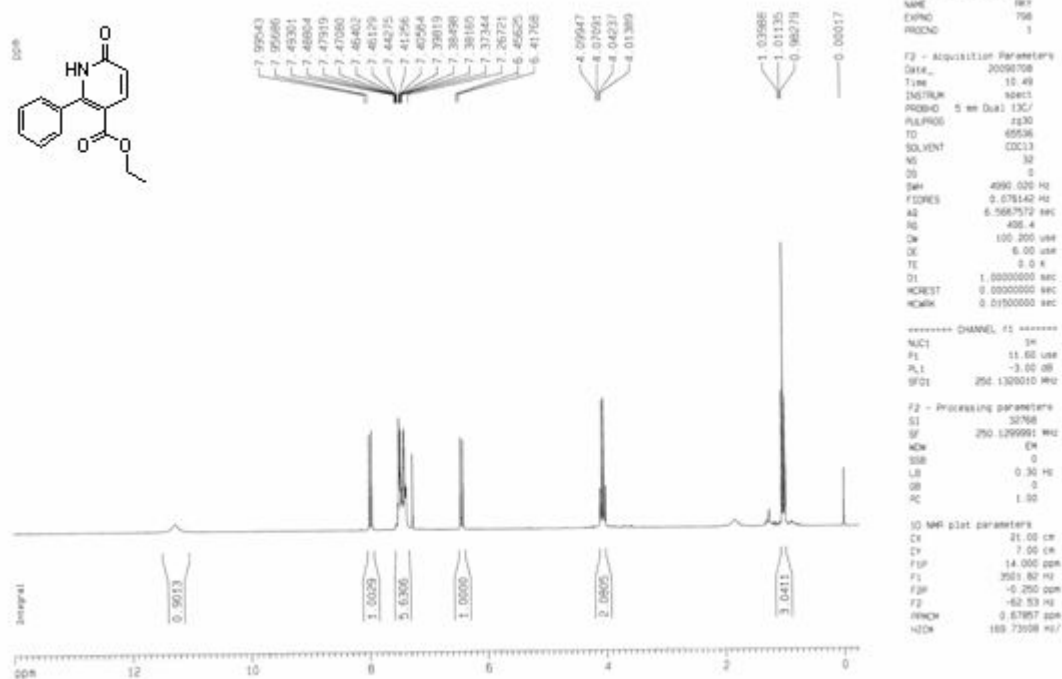
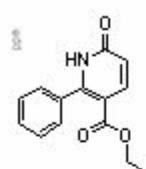
\*\*\*\*\* CHANNEL f2 \*\*\*\*\*  
CPROG2 waltz16  
NUC2 1H  
PCPS2 100.00 usec  
PL2 -3.00 dB  
PL12 17.80 dB  
PL13 21.00 dB  
SFO2 250.1300000 MHz

F2 - Processing parameters  
SI 32768  
SF 62.9027864 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

1D NMR plot parameters  
CX 20.00 cm  
CY 9.00 cm  
FIP 230.000 ppm  
F1 14485.95 Hz  
F2 -15.000 ppm  
F3 -843.43 Hz  
PRCK 12.25000 ppm/cm  
HZCK 770.46574 Hz/cm



# <sup>1</sup>H and <sup>13</sup>C NMR spectra of **4q**



# <sup>1</sup>H and <sup>13</sup>C NMR spectra of **8**

