

## A metal-free decarboxylative cyclization from natural $\alpha$ -amino acids to construct pyridine derivatives

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### General

All reagents used in this reaction were prepared free of water.

$^1\text{H}$  NMR (300 MHz) and  $^{13}\text{C}$  NMR (75 MHz) were registered on 300 M spectrometers with  $\text{CDCl}_3$  as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the  $^1\text{H}$  spectrum as 0.00 ppm and  $\text{CDCl}_3$  resonance in the  $^{13}\text{C}$  spectrum as 77.16 ppm. All coupling constants (J values) were reported in Hertz (Hz). Column chromatography was performed on silica gel 200-300 mesh.

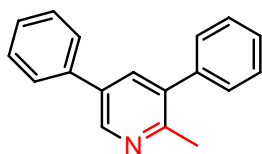
### Typical Procedure for the decarboxylative cyclization between Ala and phenylacetaldehyde

$\text{I}_2$  (0.1 mmol) was dissolved in 2 mL DMA, powder 4Å MS (200 mg), L-Ala (0.32 mmol) phenylacetaldehyde (0.4 mmol), TBHP (0.4 mmol) were added. The system was stirred under nitrogen, temperature was slowly raised from room temperature to 70 °C in 20 minutes, and kept this temperature for 1.5 h. Reaction was monitored by TLC. Cooled to room temperature, the system was extracted by ethyl acetate (3 × 40 ml), then the organic layer were washed with brine

(2 × 20 mL), dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed and purified by flash column chromatography (petroleum ether : ethyl acetate = 10 : 1) to give yellow oil.

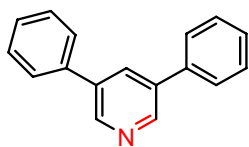
**Analytical and spectral data for the compounds.**

**2-methyl-3,5-diphenylpyridine(C1):**



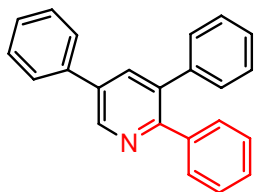
Purified by column chromatography (petroleum ether : ethyl acetate = 10 : 1) to give light yellow oil, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.74 (d, *J* = 1.8 Hz, 1H), 7.74 (d, *J* = 1.8 Hz, 1H), 7.61 (m, 2H), 7.48-7.36 (m, 8H), 2.86 (s, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 154.66, 146.14, 139.84, 137.64, 136.95, 135.76, 134.15, 129.09, 128.53, 127.96, 127.66, 127.04, 23.05. HRMS calcd 245.1204, Found 245.1208. IR (cm<sup>-1</sup>) ν 3058, 3030, 2924, 1433, 762, 699.

**3,5-diphenylpyridine(C2)**



Purified by column chromatography (petroleum ether : ethyl acetate = 12 : 1) to give light yellow solid, melting point: 135-136 °C, (lit<sup>1</sup>. mp 137-138 °C). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.82 (s, 2H), 8.07 (s, 1H), 7.66-7.63 (m, 4H), 7.53-7.36 (m, 6H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 146.96, 137.75, 136.68, 132.97, 129.17, 128.29, 127.30. HRMS calcd 231.1048, Found 231.1053. IR (cm<sup>-1</sup>) ν 3073, 3037, 2915, 1435, 762, 699.

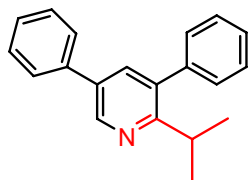
**2,3,5-triphenylpyridine(C3)<sup>2</sup>**



Purified by column chromatography (petroleum ether : ethyl acetate = 15 : 1) to give light yellow solid, melting point: 119-121 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.93 (d, *J* = 2.1 Hz, 1H), 7.93 (d, *J* = 2.1 Hz, 1H), 7.69-7.66 (m, 2H), 7.53-7.38 (m, 5H), 7.32-7.23 (m, 8H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 155.91, 146.72, 139.92, 139.87, 137.43, 136.99, 136.00, 135.04,

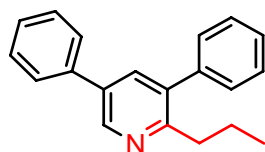
129.96, 129.64, 129.20, 128.46, 128.23, 127.98, 127.90, 127.41, 127.18. **HRMS calcd** 307.1361, **Found** 307.1363. **IR (cm<sup>-1</sup>)**  $\nu$  3083, 3057, 2925, 1428, 760, 697.

#### 2-isopropyl-3,5-diphenylpyridine (C4)



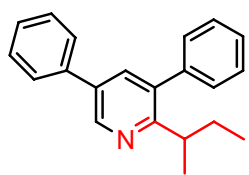
Purified by column chromatography (petroleum ether : ethyl acetate = 10 : 1) to give light yellow oil, **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)**  $\delta$  8.85 (d,  $J$  = 2.4Hz, 2H), 7.69 (d,  $J$  = 2.4Hz, 1H), 7.62-7.59 (m, 2H), 7.48-7.33 (m, 8H), 3.26 (m, 1H), 1.27-1.25 (d, 6H). **<sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)**  $\delta$  163.07, 146.79, 140.04, 137.78, 135.94, 133.55, 129.17, 129.08, 128.44, 127.88, 127.52, 127.05, 31.27, 22.70. **HRMS calcd** 273.1517, **Found** 273.1516. **IR (cm<sup>-1</sup>)**  $\nu$  2961, 1431, 1396, 759, 697.

#### 3,5-diphenyl-2-propylpyridine(C5)



Purified by column chromatography (petroleum ether : ethyl acetate = 10 : 1) to give light yellow oil, **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)**  $\delta$  8.80 (d,  $J$  = 2.4Hz, 1H), 7.74 (d,  $J$  = 2.4Hz, 1H), 7.62-7.59 (m, 2H), 7.49-7.34 (m, 8H), 2.82-2.77 (m, 2H), 1.78-1.65 (m, 2H), 0.90-0.85 (m, 3H). **<sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)**  $\delta$  158.42, 146.37, 139.96, 137.69, 136.92, 135.91, 133.76, 129.15, 128.43, 128.17, 127.91, 127.54, 127.03, 37.14, 23.09, 14.12. **HRMS calcd** 273.1517, **Found** 273.1519. **IR (cm<sup>-1</sup>)**  $\nu$  3029, 2961, 1453, 1432, 761, 699.

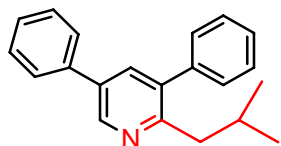
#### 2-sec-butyl-3,5-diphenylpyridine(C6)



Purified by column chromatography (petroleum ether : ethyl acetate = 10 : 1) to give light yellow oil, **<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)**  $\delta$  8.64 (d,  $J$  = 2.4Hz, 1H), 7.69 (d,  $J$  = 2.4Hz, 1H), 7.62-7.59 (m, 2H), 7.48-7.31 (m, 8H), 3.01 (m, 1H), 1.89 (m, 1H), 1.63 (m, 1H), 1.26 (d,  $J$  =

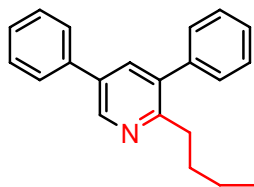
6.9, 3H), 0.74 (m, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  162.36, 146.90, 140.16, 137.79, 136.92, 135.67, 133.28, 129.29, 129.07, 128.39, 127.86, 127.44, 127.04, 38.26, 29.89, 21.00, 12.36. HRMS calcd 287.1674, Found 287.1678. IR ( $\text{cm}^{-1}$ )  $\nu$  2963, 2907, 1448, 1431, 1261, 1030, 864, 800, 700.

#### 2-isobutyl-3,5-diphenylpyridine(C7)



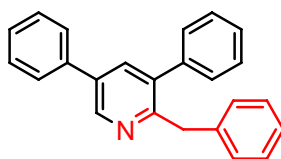
Purified by column chromatography (petroleum ether : ethyl acetate = 10 : 1) to give light yellow oil,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  8.81 (d,  $J$  = 1.8Hz, 1H), 7.71 (d,  $J$  = 1.8Hz, 1H), 7.62-7.60 (m, 2H), 7.48-7.25 (m, 8H), 7.73 (d,  $J$  = 7.2Hz, 2H), 2.13 (m, 1H), 0.81 (d,  $J$  = 6.6Hz, 6H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  157.86, 146.36, 140.09, 137.68, 137.38, 135.81, 133.57, 129.35, 129.08, 128.38, 127.91, 127.46, 127.03, 43.72, 29.03, 22.51. HRMS calcd 287.1674, Found 287.1679. IR ( $\text{cm}^{-1}$ )  $\nu$  3030, 2955, 2867, 1452, 760, 698.

#### 2-butyl-3,5-diphenylpyridine (C8)



Purified by column chromatography (petroleum ether : ethyl acetate = 10 : 1) to give light yellow oil,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  8.79 (d,  $J$  = 2.4Hz, 1H), 7.71 (d,  $J$  = 2.4Hz, 1H), 7.61-7.59 (d,  $J$  = 7.8Hz, 2H), 7.48-7.34 (m, 8H), 2.83 (m, 2H), 1.71 (m, 2H), 1.34 (m, 2H), 0.85 (m, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  158.69, 146.47, 139.99, 137.75, 136.81, 135.83, 133.70, 129.15, 129.05, 128.40, 127.87, 127.52, 127.03, 34.91, 32.03, 22.69, 13.88. HRMS calcd 287.1674, Found 287.1680. IR ( $\text{cm}^{-1}$ )  $\nu$  3030, 2957, 2929, 2859, 1453, 1432, 761, 699.

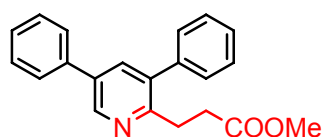
#### 2-benzyl-3,5-diphenylpyridine(C9)



Purified by column chromatography (petroleum ether : ethyl acetate =

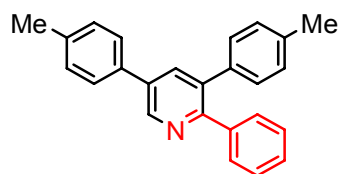
10 : 1) to give light yellow oil,  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  8.83 (d,  $J = 2.4\text{Hz}$ , 1H), 7.75 (d,  $J = 2.4\text{Hz}$ , 1H), 7.62-7.61 (d,  $J = 1.2\text{Hz}$ , 2H), 7.59 (d,  $J = 2.4\text{Hz}$ , 2H), 7.46-7.13 (m, 12H), 7.05 (d,  $J = 6.9\text{Hz}$ , 2H), 4.19 (s, 2H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  156.70, 146.76, 140.06, 139.63, 137.56, 137.48, 136.30, 134.37, 129.33, 129.16, 128.91, 128.51, 128.35, 128.10, 127.79, 127.14, 126.08, 41.33. **HRMS calcd** 321.1517, **Found** 321.1513. **IR** ( $\text{cm}^{-1}$ )  $\nu$  3059, 3028, 2926, 1451, 1433, 761, 698.

**methyl 3-(3,5-diphenylpyridin-2-yl)propanoate (C10)**



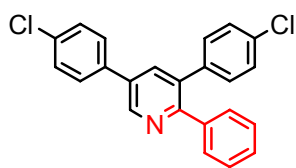
Purified by column chromatography (petroleum ether : ethyl acetate = 10 : 1) to give light yellow oil,  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  8.77 (d,  $J = 2.4\text{Hz}$ , 1H), 7.72 (d,  $J = 2.4\text{Hz}$ , 1H), 7.61 (d,  $J = 1.2\text{Hz}$ , 2H), 7.49-7.36 (m, 8H), 3.64 (s, 3H), 3.15 (m, 2H), 2.83 (m, 2H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  173.78, 155.86, 146.33, 139.43, 137.60, 136.96, 135.81, 134.17, 129.79, 129.11, 129.07, 128.58, 127.97, 127.74, 127.05, 51.56, 32.59, 29.86. **HRMS calcd** 317.1416, **Found** 317.1410 **IR** ( $\text{cm}^{-1}$ )  $\nu$  3029, 2949, 1737, 1434, 1172, 762, 699.

**2-phenyl-3,5-dip-tolylpyridine (C11)**



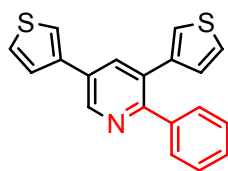
Purified by column chromatography (petroleum ether : ethyl acetate = 15 : 1) to give light yellow oil,  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  8.80 (d,  $J = 2.4\text{Hz}$ , 1H), 7.78 (d,  $J = 2.4\text{Hz}$ , 1H), 7.47 (s, 1H), 7.44 (s, 1H), 7.33-7.28 (m, 2H), 7.20-7.12 (m, 5H), 7.04-6.97 (m, 4H), 2.30 (s, 3H), 2.23 (s, 3H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  155.55, 146.31, 140.03, 138.15, 137.14, 136.99, 136.81, 135.96, 134.99, 134.56, 129.93, 129.51, 129.18, 127.97, 127.79, 127.00, 21.25. **HRMS calcd** 335.1674, **Found** 335.1680. **IR** ( $\text{cm}^{-1}$ )  $\nu$  3130, 2865, 2217, 1906, 1514, 821.

**3,5-bis(4-chlorophenyl)-2-phenylpyridine (C12)**



Purified by column chromatography (petroleum ether : ethyl acetate = 15 : 1) to give light yellow solid, melting point: 197-198.5 °C.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  8.90 (d,  $J = 2.4\text{Hz}$ , 1H), 7.85 (d,  $J = 2.4\text{Hz}$ , 1H), 7.61 (d,  $J = 8.7\text{Hz}$ , 2H), 7.49 (d,  $J = 8.4\text{Hz}$ , 2H), 7.39-7.36 (m, 2H), 7.29-7.25 (m, 5H), 7.17 (d,  $J = 8.4\text{Hz}$ , 2H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  156.23, 146.78, 139.39, 138.21, 136.65, 135.71, 134.93, 134.64, 134.04, 133.75, 130.93, 129.93, 129.49, 128.80, 128.43, 128.23. HRMS calcd 375.0582, Found 375.0589. IR ( $\text{cm}^{-1}$ )  $\nu$  3030, 1490, 1446, 1089, 824.

#### 2-phenyl-3,5-di(thiophen-3-yl)pyridine(C13)



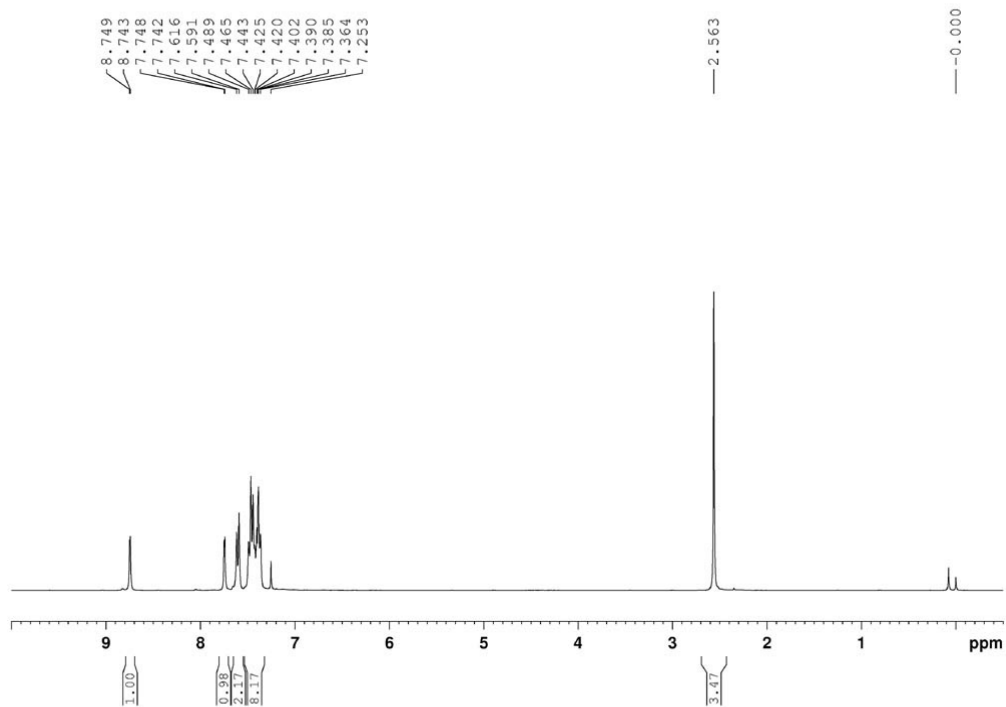
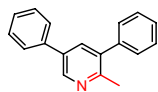
Purified by column chromatography (petroleum ether : ethyl acetate = 12 : 1) to give light yellow solid, melting point: 137-139 °C.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  8.83 (d,  $J = 2.1\text{Hz}$ , 1H), 7.87 (d,  $J = 2.1\text{Hz}$ , 1H), 7.52-7.50 (m, 1H), 7.38-7.33 (m, 4H), 7.23-7.21 (m, 3H), 7.17-7.09 (m, 2H), 6.72-6.71 (m, 1H).  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  155.66, 146.00, 140.16, 139.91, 138.37, 135.80, 131.07, 130.19, 129.59, 128.75, 128.17, 127.16, 126.04, 125.69, 123.84, 121.70, HRMS calcd 319.0489, Found 319.0496. IR ( $\text{cm}^{-1}$ )  $\nu$  3102, 2960, 2926, 1446, 1427, 1018, 778, 698, 640.

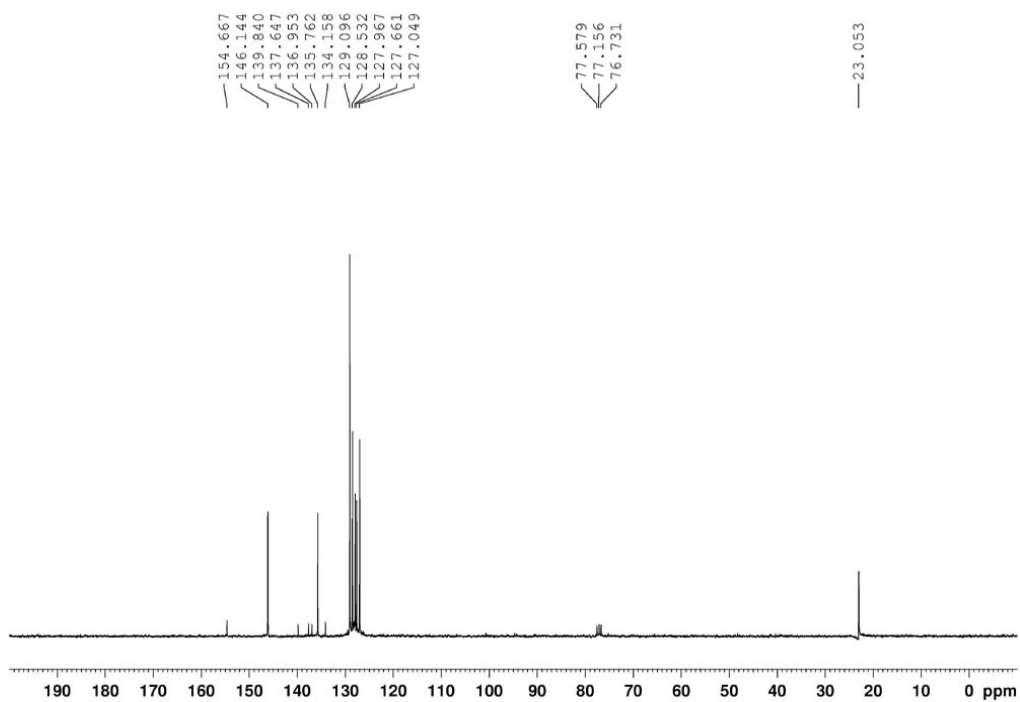
#### Reference:

1. T.-H. Chuang, Y.-C. Chen and S. Pola, *J. Org. Chem.*, 2010, **75**, 6625.
2. J. L. Papparín, Crevisy, R. Greand and L. Toupet, *J. Heterocyclic chem.*, 2000, **37**, 411.

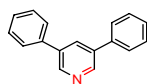
#### $^1\text{H NMR}$ and $^{13}\text{C NMR}$ spectrogram

**2-methyl-3,5-diphenylpyridine(C1)**

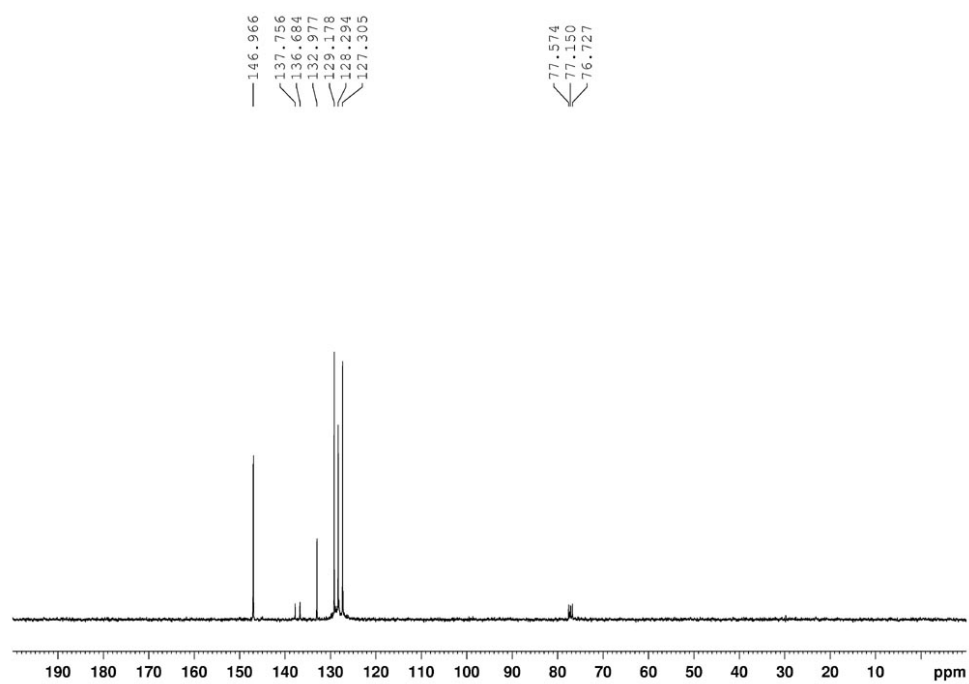
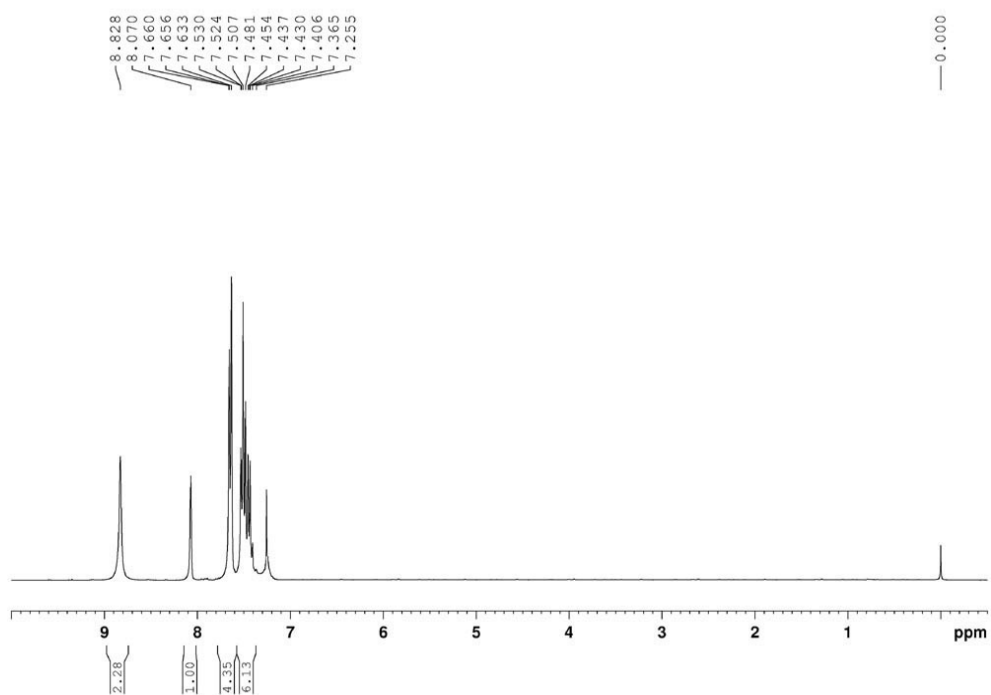




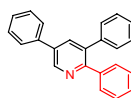
**3,5-diphenylpyridine(C2)**

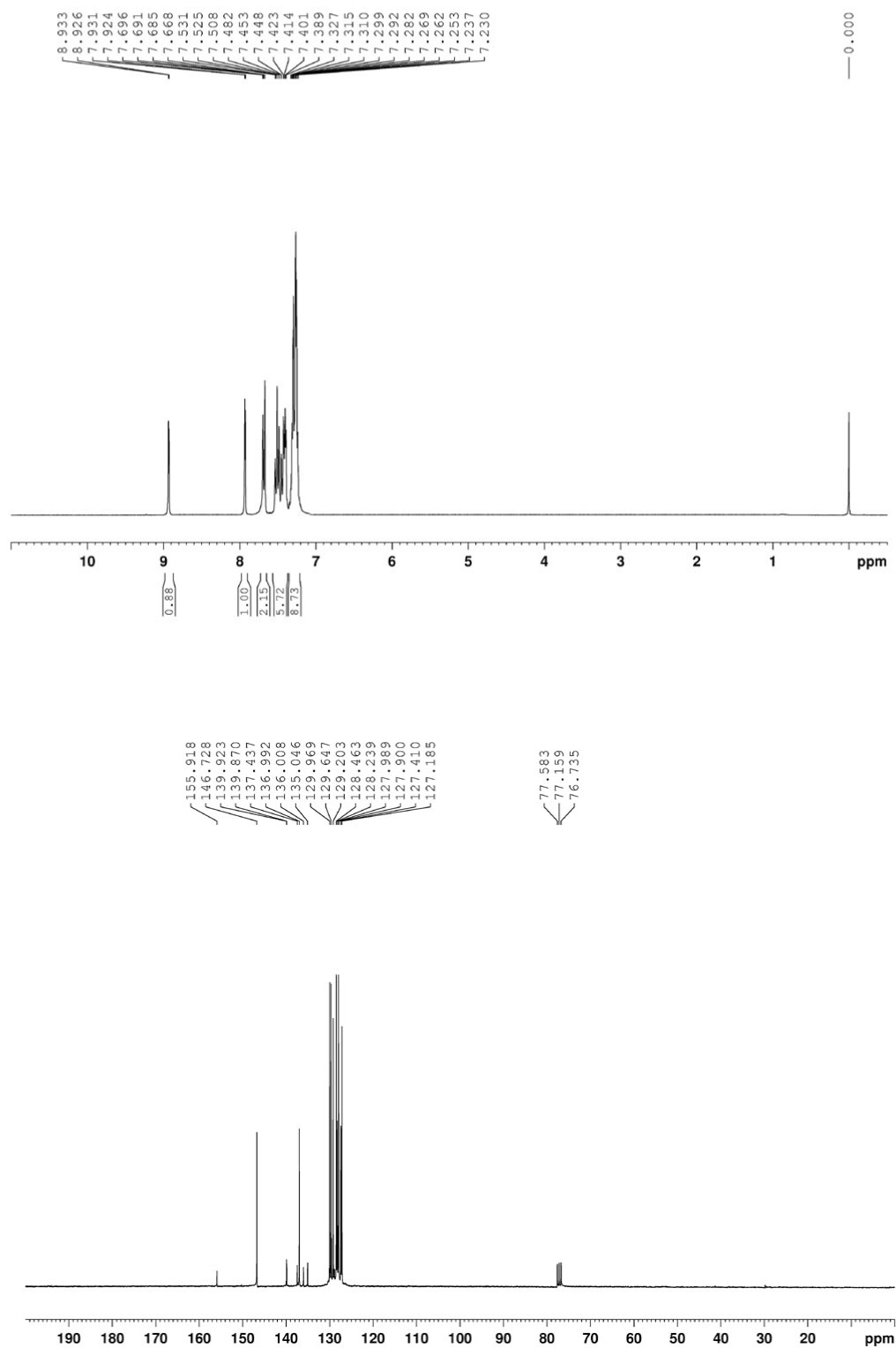




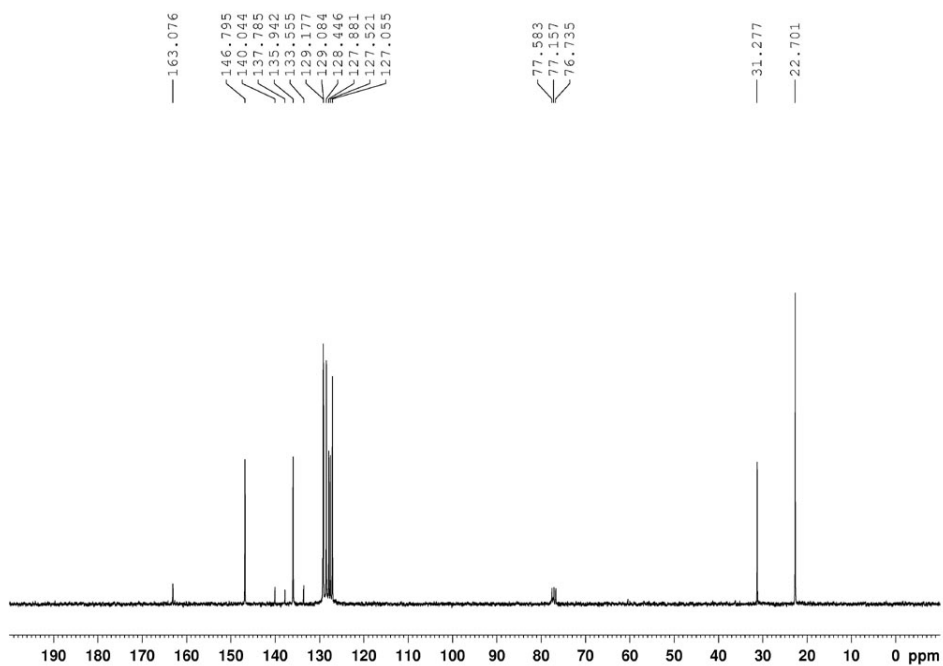
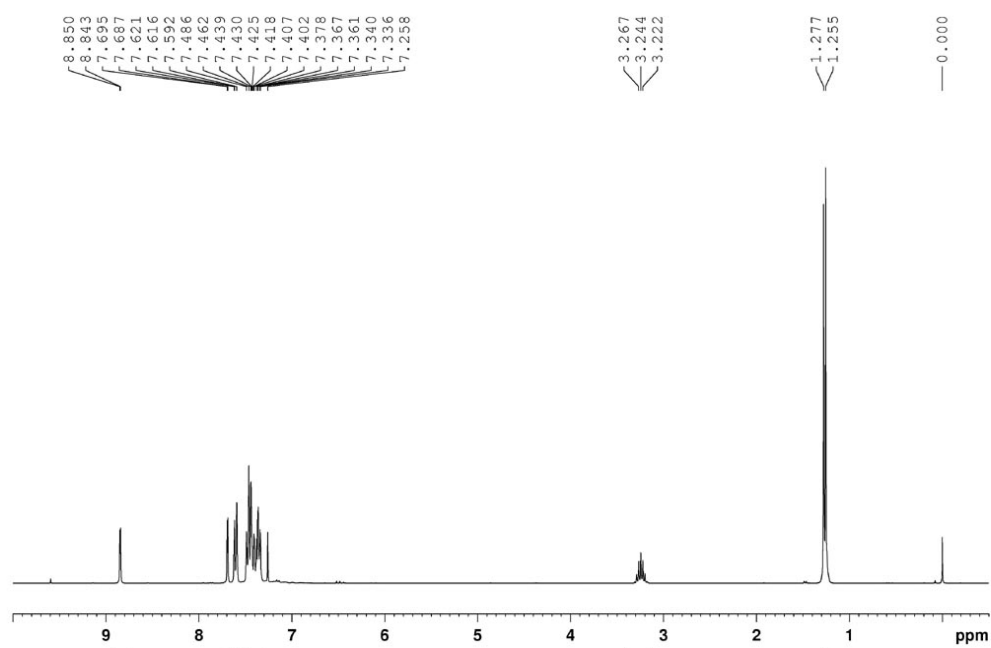
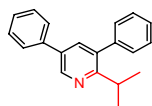


### 2,3,5-triphenylpyridine(C3)

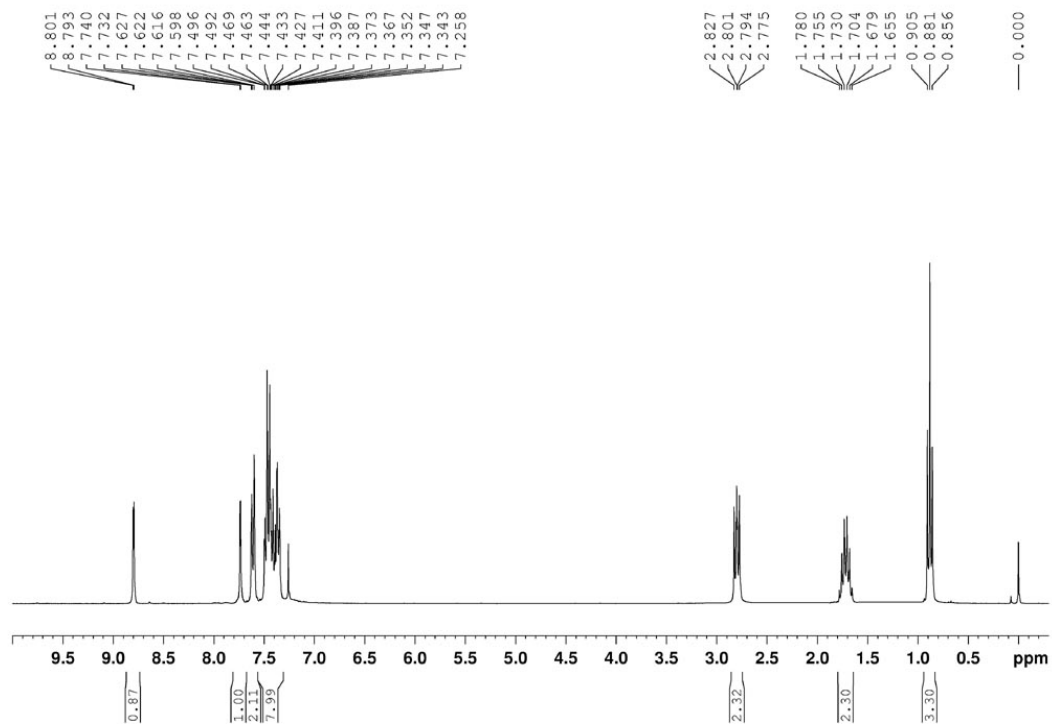
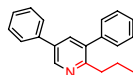


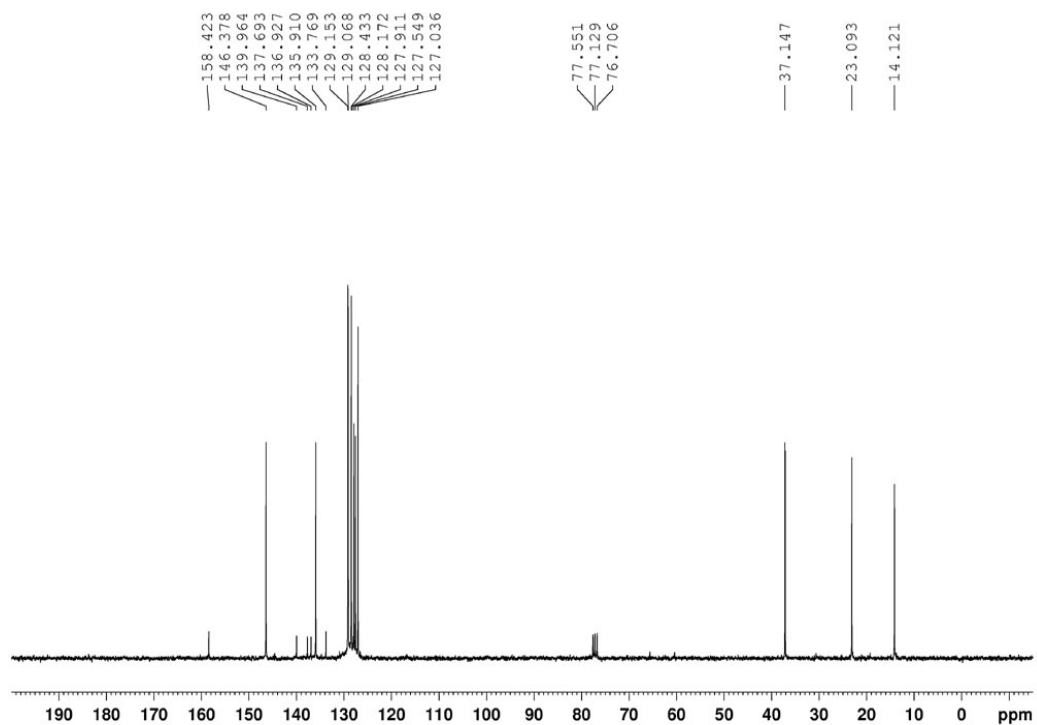


2-isopropyl-3,5-diphenylpyridine(C4)

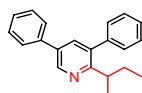


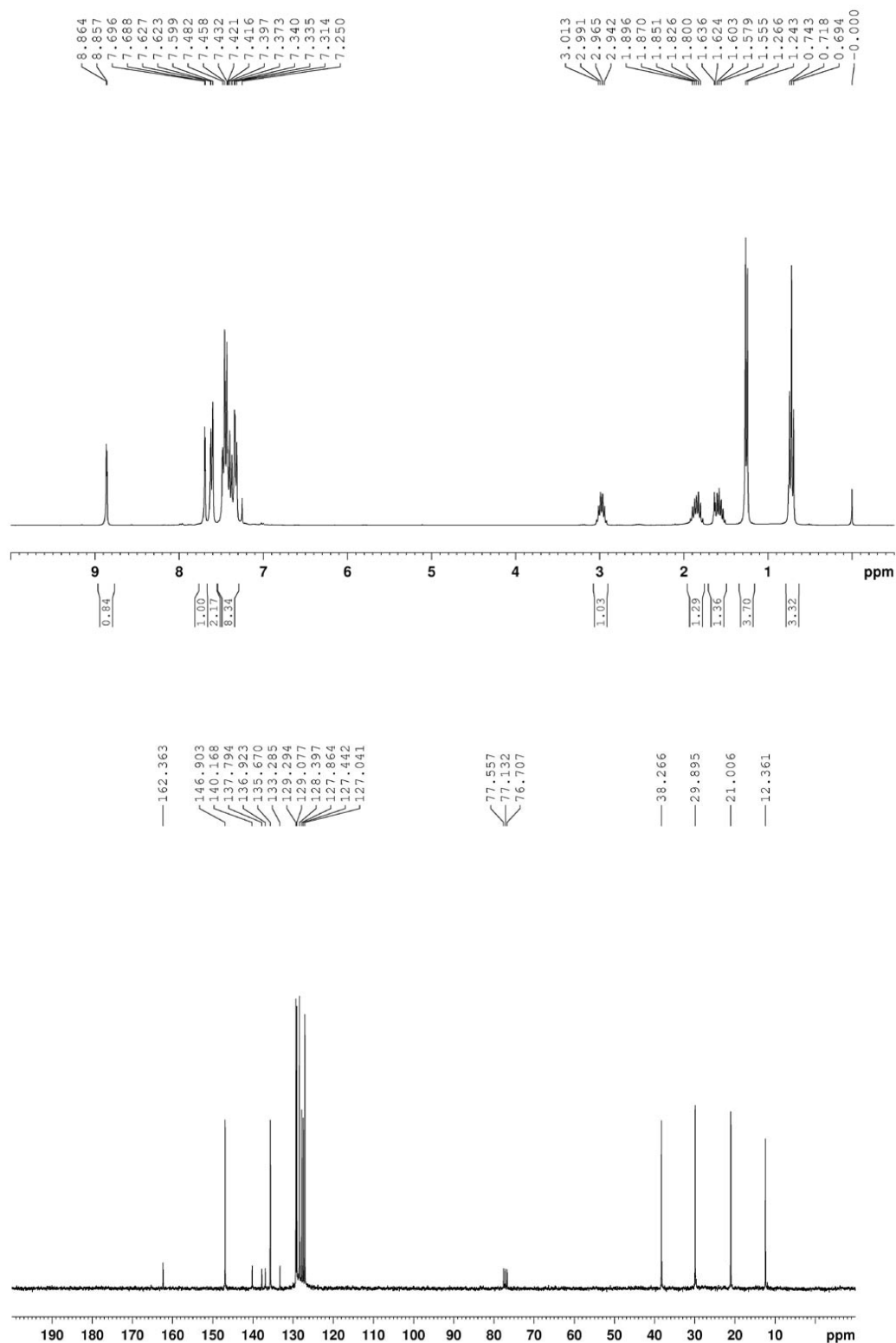
### 3,5-diphenyl-2-propylpyridine(C5)



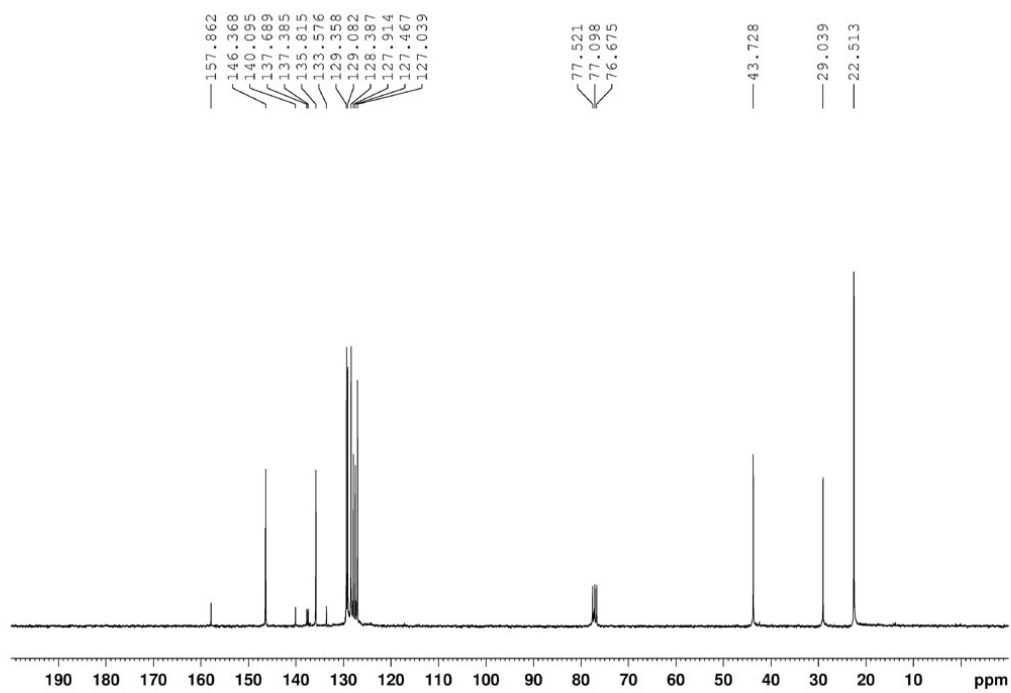
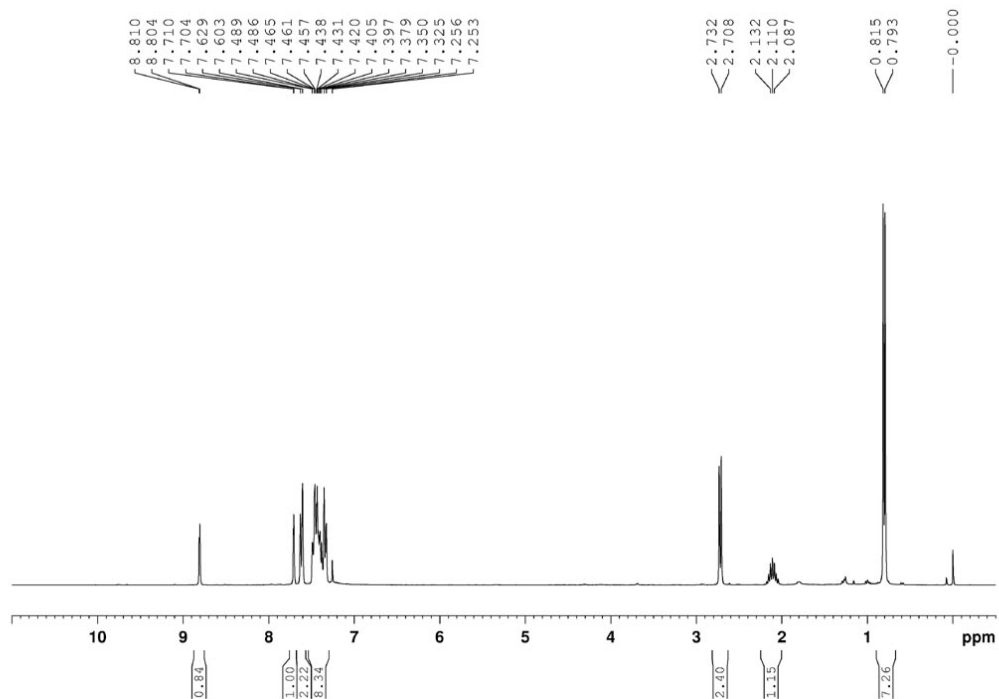
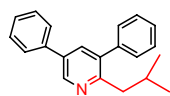


**2-sec-butyl-3,5-diphenylpyridine (C6)**

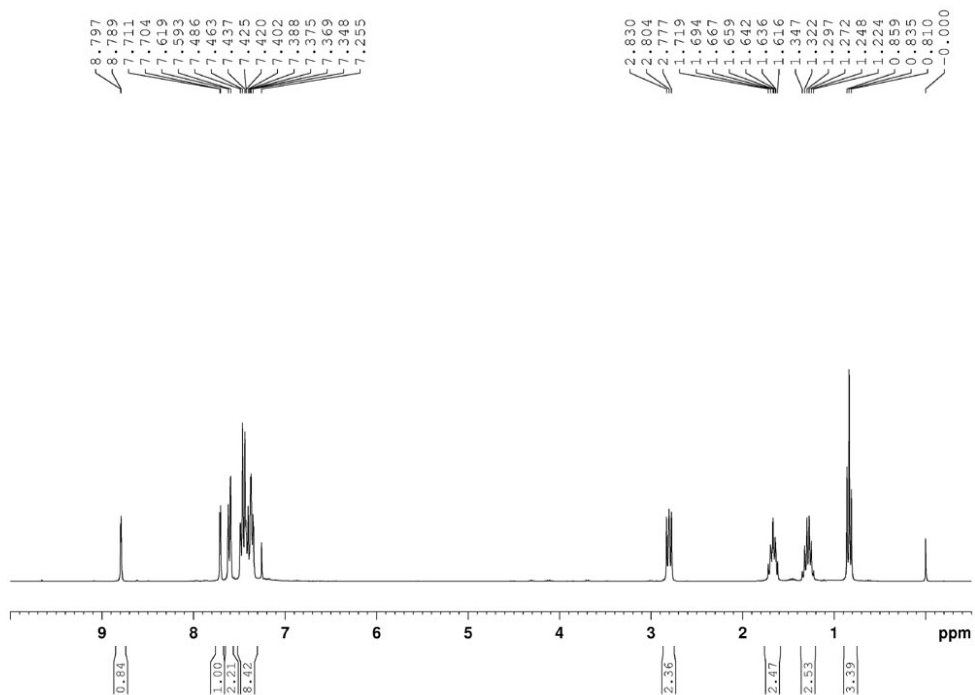
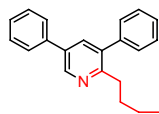




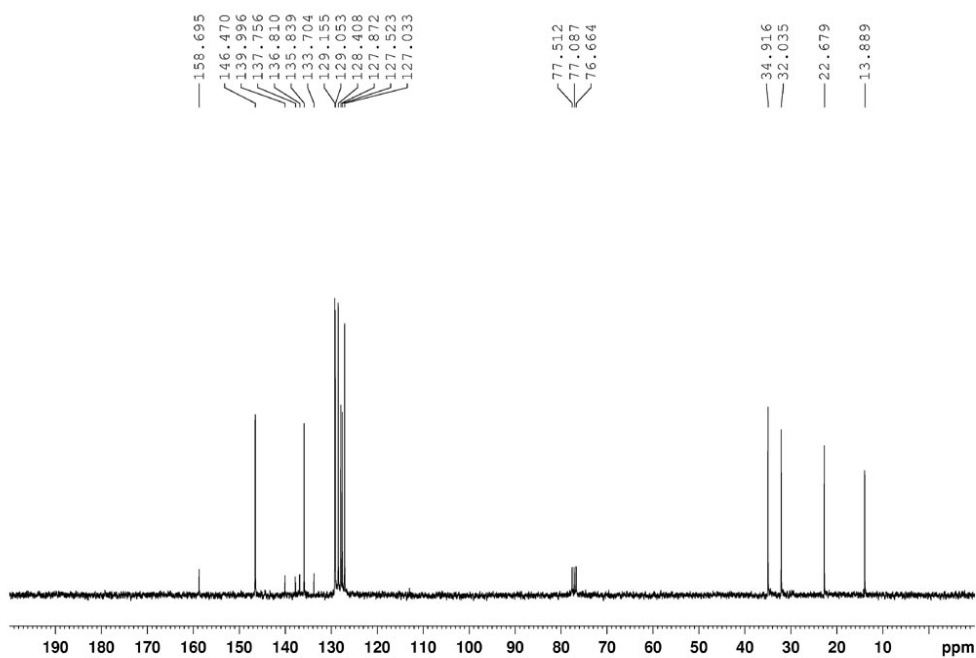
2-isobutyl-3,5-diphenylpyridine (C7)



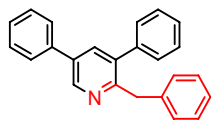
2-butyl-3,5-diphenylpyridine(C8)

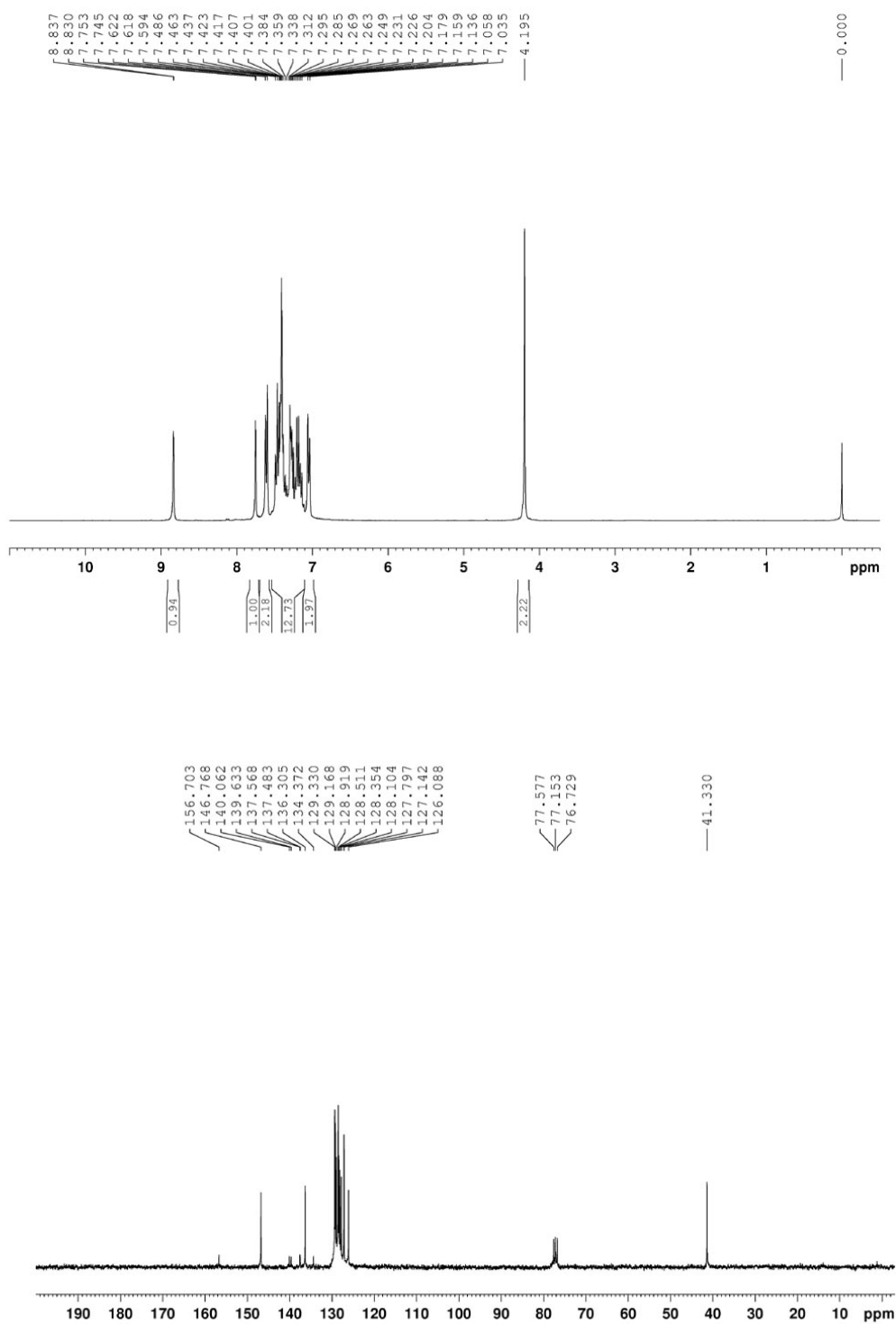




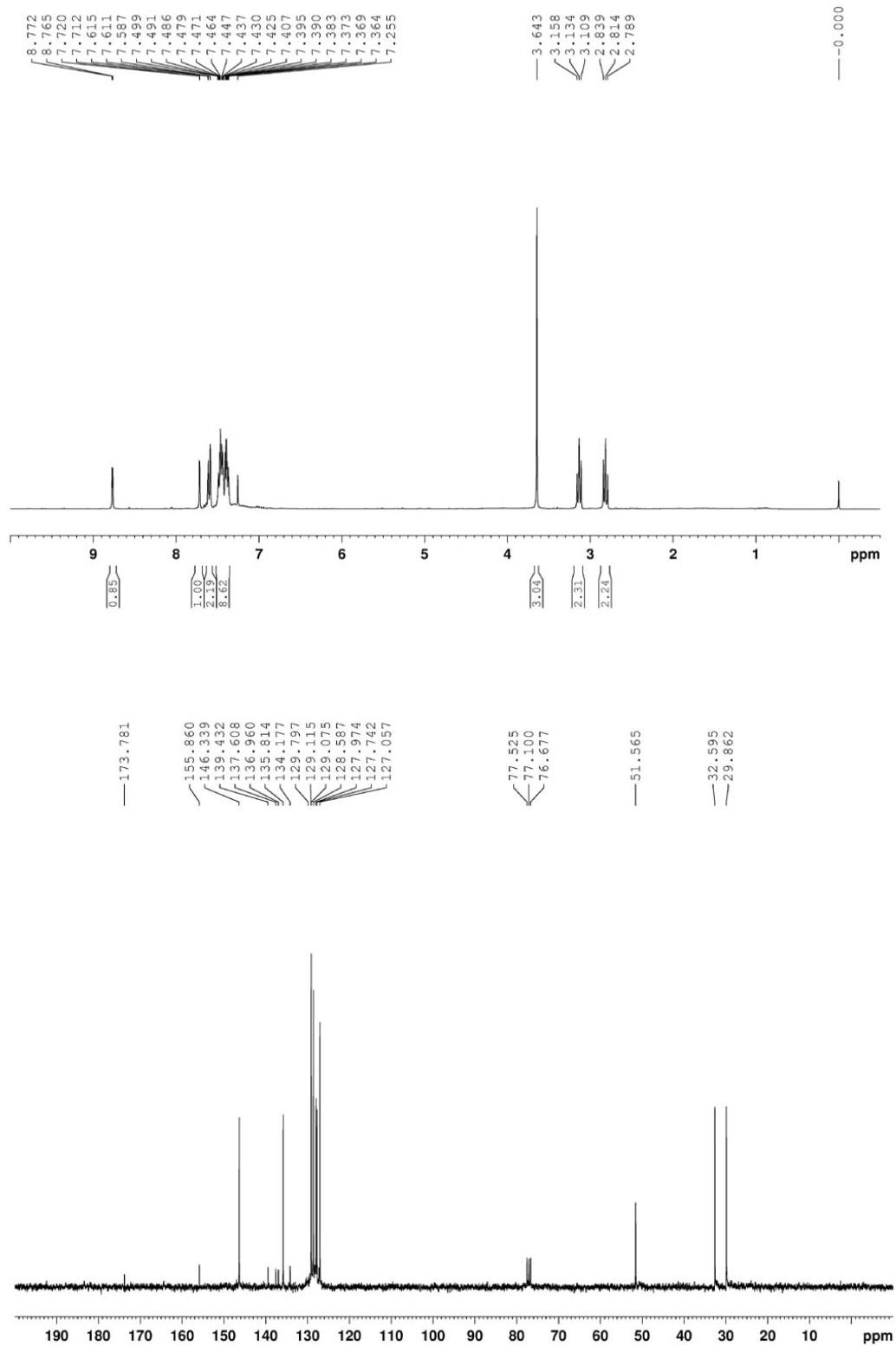
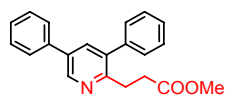


**2-benzyl-3,5-diphenylpyridine(C9)**

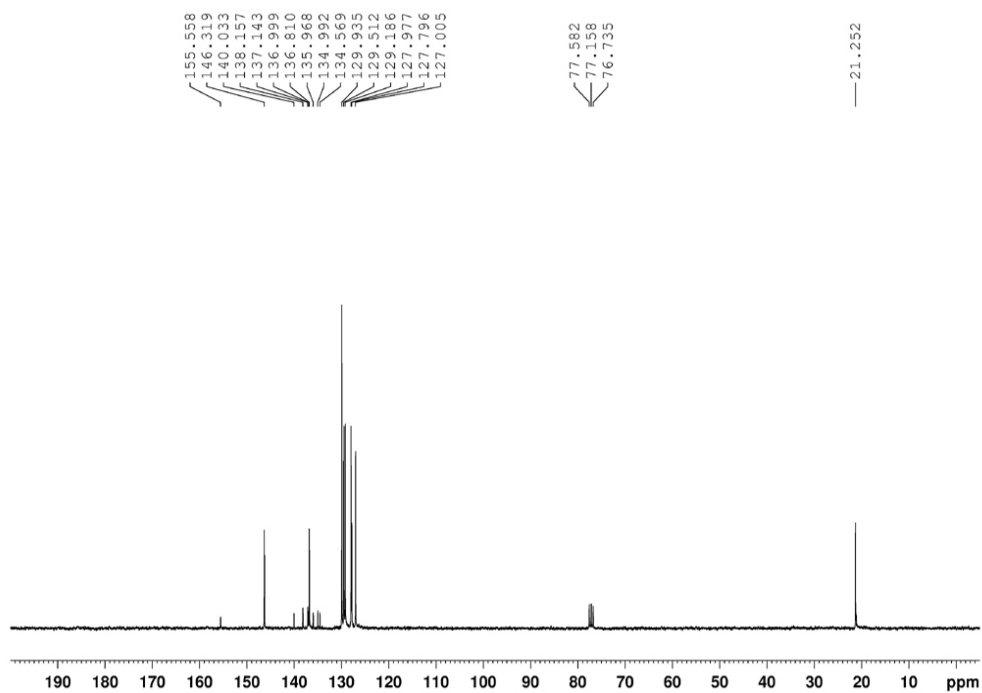
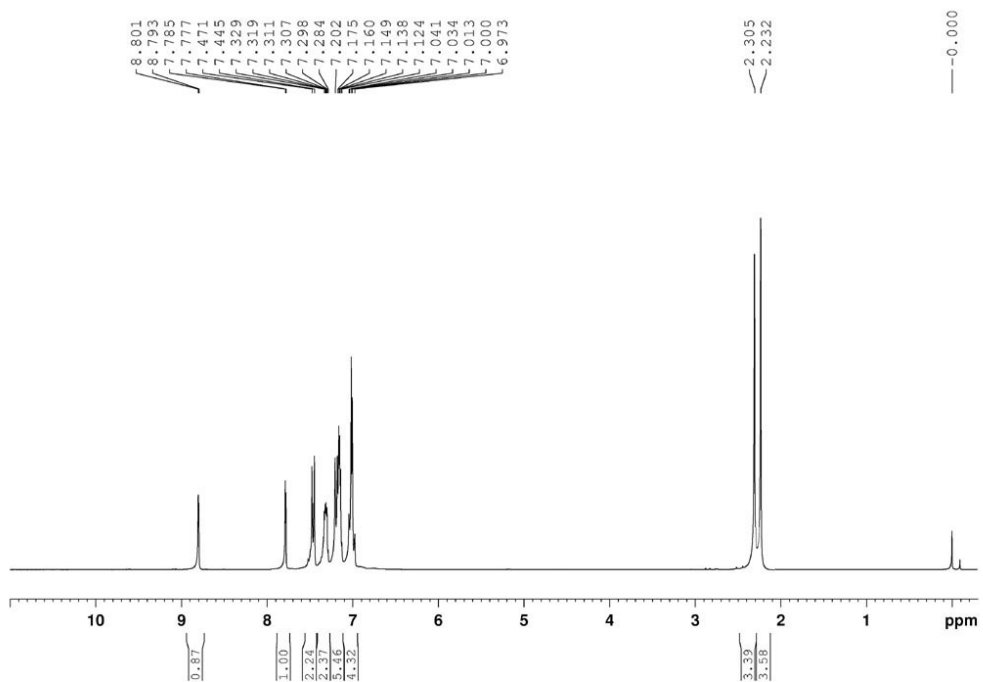
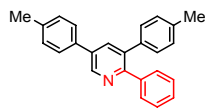




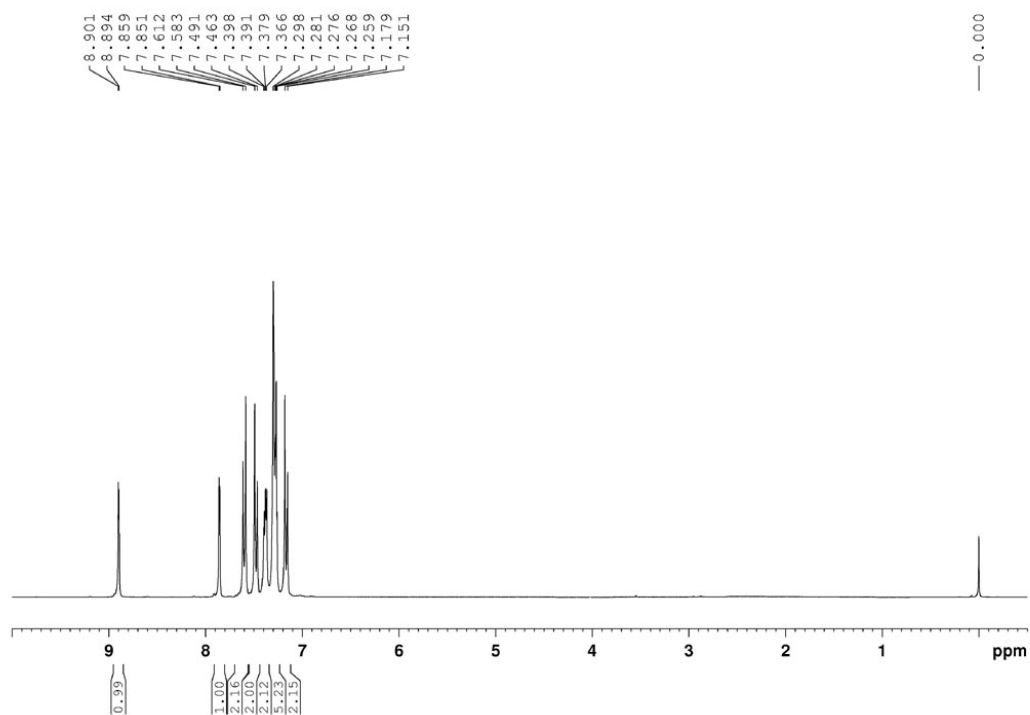
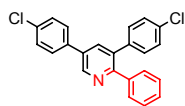
methyl 3-(3,5-diphenylpyridin-2-yl)propanoate (C10)

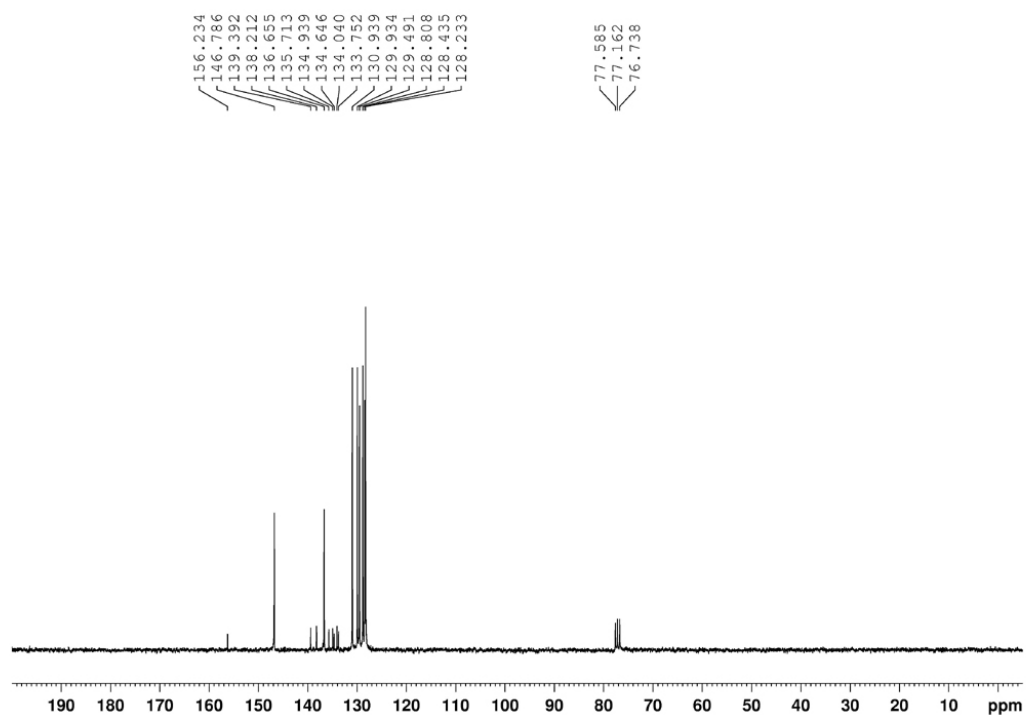


### 2-phenyl-3,5-dip-tolylpyridine (C11)



**3,5-bis(4-chlorophenyl)-2-phenylpyridine(C12)**





**2-phenyl-3,5-di(thiophen-3-yl)pyridine(C13)**

