NH_4I-CATALYZED FORMAL [4+2] CYCLOADDITION OF α,β-UNSATURATED *O*-ACETYL OXIME WITH ALKYL PYRUVATE FOR RAPID SUBSTITUTED PYRIDINE FORMATION

Cheng Dong, Xiangzhen Meng*, Shuailu Wang, Xuan Zhao and Jingwen Chen

College of chemistry and materials engineering, Chaohu College, Chaohu Anhui, People's Republic of China.

E-mail: mxzcd79@163.com

Context

Typical procedure for the preparation of substituted pyridines

Ketoxime-enoates **1** (3.0 mmol), ester pyruvates **2** (6.0 mmol), NH_4I (0.22 g, 0.15 mmol) and $NaHSO_3$ (0.31 g, 3.0 mmol) were loaded into a 20 mL tube under a N_2 atmosphere. The solvent toluene (15 mL) was added into the tube by syringe. The reaction mixture was stirred at 100 ℃ for 12 h. Upon completion of the reaction, the mixture was then allowed to cool down to room temperature and flushed through a short column of silica gel with EtOAc (15 mL). After rotary evaporation, the residue was purified by column chromatography on silica gel (Petroleum Ether/ EtOAc) to give the product.

Diethyl 6-phenylpyridine-2,4-dicarboxylate (3a) White solid; 72% yield; mp: 99-102 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.54 (s, 1H), 8.47 (s, 1H), 8.14–8.13 (m, 2H), 7.53–7.47 (m, 3H), 4.54–4.47 (m, 4H), 1.50–1.44 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.9, 164.7, 158.7, 149.4, 139.8, 137.7, 130.0, 129.0, 127.3, 122.7, 122.4, 62.2, 62.2, 14.4, 14.3; IR (film) 2979, 2906, 1742, 1721, 1603, 1556, 1251, 1223, 1025, 757. ESI-HRMS $C_{17}H_{18}NO_4$ ($[M+H]^+$): calcd 300.1231, found 300.1241.

4-Ethyl 2-methyl 6-phenylpyridine-2,4-dicarboxylate (3b) White solid; 65% yield; mp: 107-110 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.47 (s, 1H), 8.12–8.11 (m, 2H), 7.53–7.47 (m, 3H), 4.48 (q, J = 7.2 Hz, 2H), 4.06 (s, 3H), 1.47–1.45 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4, 164.6, 158.8, 149.0, 139.9, 137.7, 130.0, 129.0, 127.3, 122.9, 122.5, 62.2, 53.1, 14.3; IR (film) 3072, 2946, 1746, 1716, 1597, 1566, 1339, 1232, 754; ESI-HRMS $C_{16}H_{16}NO_4$ ($[M+H]^+$): calcd 286.1074, found 286.1077.

Diethyl 6-(p-tolyl)pyridine-2,4-dicarboxylate (3c) White solid; 62% yield; mp: 105-107 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.44 (s, 1H), 8.04 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 4.52–4.47 (m, 4H), 2.42 (s, 3H), 1.49–1.44 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.0, 164.7, 158.7, 149.2, 140.2, 139.7, 134.9, 129.7, 127.2, 122.4, 122.1, 62.2, 62.1, 21.4, 14.4, 14.3; IR (film) 2985, 2912, 1738, 1721, 1604, 1563, 1337, 1232, 759; ESI-HRMS $C_{18}H_{20}NO_4$ ($[M+H]^+$): calcd 314.1387, found 314.1385.

Diethyl 6-(4-methoxyphenyl)pyridine-2,4-dicarboxylate (3d) White solid; 56%

yield; mp: 76-77 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.47 (s, 1H), 8.40 (s, 1H), 8.12–8.10 (m, 2H), 7.03–7.02 (m, 2H), 4.53–4.46 (m, 4H), 3.88 (s, 3H), 1.49–1.44 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.0, 164.8, 161.2, 158.3, 149.2, 139.7, 130.3, 128.7, 121.9, 121.6, 114.3, 62.1, 62.1, 55.4, 14.3, 14.3; IR (film) 2991, 1836, 1740, 1719, 1605, 1514, 1337, 1263, 759; ESI-HRMS $C_{18}H_{20}NO_5$ ($[M+H]^+$): calcd 300.1336, found 300.1339.

Diethyl 6-(2-methoxyphenyl)pyridine-2,4-dicarboxylate (3e) White solid; 47% yield; mp: 109-110 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.60 (s, 1H), 8.53 (s, 1H), 7.92–7.91 (m, 1H), 7.43–7.40 (m, 1H), 7.12–7.10 (m, 1H), 7.02–7.01 (m, 1H), 4.53–4.44 (m, 4H), 3.89 (s, 3H), 1.48–1.43 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.0, 164.9, 157.5, 157.3, 149.0, 138.6, 131.6, 130.9, 127.7, 127.6, 122.1, 121.3, 111.4, 62.0, 62.0, 55.7, 14.4, 14.3; IR (film) 3097, 2974, 1721, 1608, 1437, 1254, 1237, 1027, 757; ESI-HRMS $C_{18}H_{20}NO_5$ ($[M+H]^+$): calcd 300.1336, found 300.1343.

Diethyl 6-(4-fluorophenyl)pyridine-2,4-dicarboxylate (3f) White solid; 78% yield; mp: 139-140 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.53–8.53 (m, 1H), 8.42–8.41 (m, 1H), 8.15–8.13 (m, 2H), 7.21–7.18 (m, 2H), 4.54–4.47 (m, 4H), 1.49–1.45 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.3 ($J_{C\text{-}F}$ = 187.8 Hz), 164.8, 164.5, 157.6, 149.4, 139.9, 133.9 ($J_{C\text{-}F}$ = 3.9 Hz), 129.3, 129.2, 122.3, 115.9 ($J_{C\text{-}F}$ = 21.5 Hz), 62.3, 62.2, 14.3, 14.3; IR (film) 2982, 2906, 1743, 1725, 1604, 1511, 1231, 1163, 763; ESI-HRMS $C_{17}H_{17}FNO_4$ ($[M+H]^+$): calcd 318.1137, found 318.1132.

Diethyl 6-(4-chlorophenyl)pyridine-2,4-dicarboxylate (3g) White solid; 74% yield; mp: 107-108 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.54 (s, 1H), 8.43 (s, 1H), 8.09 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 4.54–4.47 (m, 4H), 1.50–1.45 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.7, 164.5, 157.4, 149.4, 140.0, 136.2, 136.1, 129.2, 128.6, 122.6, 122.4, 62.3, 62.2, 14.3, 14.3; IR (film) 2982, 2904, 1746, 1723, 1603, 1560, 1369, 1336, 1243, 762; ESI-HRMS $C_{17}H_{17}ClNO_4$ ($[M+H]^+$): calcd 334.0841, found 334.0849.

Diethyl 6-(3-chlorophenyl)pyridine-2,4-dicarboxylate (3h) Light yellow solid; 70% yield; mp: 72-73 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.43 (s, 1H), 8.14 (s, 1H), 8.01–8.00 (m, 1H), 7.45–7.44 (m, 2H), 4.55–4.47 (m, 4H), 1.50–1.45 (m, 6H);

^{13}C NMR (125 MHz, $CDCl_3$): δ 164.7, 164.4, 157.2, 149.5, 140.1, 139.5, 135.1, 130.2, 129.9, 127.5, 125.4, 122.9, 122.7, 62.3, 62.3, 14.3, 14.3; IR (film) 2982, 2940, 1726, 1558, 1442, 1181, 1029, 760; ESI-HRMS $C_{17}H_{17}ClNO_4$ ($[M+H]^+$): calcd 334.0841, found 334.0843.

Diethyl 6-(naphthalen-2-yl)pyridine-2,4-dicarboxylate (3i) White solid; 64% yield; mp: 88-89 ℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.63–8.61 (m, 2H), 8.56 (s, 1H), 8.29–8.28 (m, 1H), 8.00–7.97 (m, 2H), 7.89–7.88 (m, 1H), 7.55–7.53 (m, 2H), 4.57–4.49 (m, 4H), 1.52–1.47 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.9, 164.7, 158.6, 149.5, 139.9, 135.0, 134.1, 133.4, 129.0, 128.8, 127.7, 127.1, 127.1, 126.5, 124.5, 122.9, 122.4, 62.3, 62.2, 14.4, 14.3; IR (film) 2984, 2904, 1743, 1726, 1597, 1254, 1230, 1023, 760; ESI-HRMS $C_{21}H_{20}NO_4$ ($[M+H]^+$): calcd 350.1387, found 350.1383.

Ethyl 4,6-diphenylpicolinate (4a) White solid; 46% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 8.16–8.10 (m, 3H), 7.76–7.75 (m, 2H), 7.56–7.47 (m, 6H), 4.55 (q, J = 6.0 Hz, 2H), 1.51 (t, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.3, 150.4, 149.0, 138.7, 137.7, 129.5, 129.3, 128.9, 127.4, 127.2, 121.5, 121.5, 62.0, 14.4.

Methyl 4-phenyl-6-(p-tolyl)picolinate (4b) White solid; 42% yield; mp: 96-98℃; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.32–8.32 (m, 1H), 8.11–8.10 (m, 3H), 7.76–7.75 (m, 2H), 7.55–7.46 (m, 6H), 4.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 158.5, 150.5, 148.6, 138.7, 137.6, 129.5, 129.5, 129.3, 128.9, 127.4, 127.2, 121.7, 121.6, 53.0; IR (film) 2951, 1738, 1715, 1600, 1260, 1235, 1150, 768; ESI-HRMS $C_{19}H_{16}NO_2$ ($[M+H]^+$): calcd 290.1176, found 290.1172.

Ethyl 6-(4-methoxyphenyl)-4-phenylpicolinate (4c) White solid; 38% yield; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.21 (s, 1H), 8.10–8.09 (m, 2H), 8.02 (s, 1H), 7.73–7.72 (m, 2H), 7.53–7.47 (m, 3H), 7.02–7.01 (m, 2H), 4.51 (q, J = 7.2 Hz, 2H), 3.87 (s, 3H), 1.48 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7, 160.9, 157.9, 150.3, 148.8, 137.9, 131.3, 129.4, 129.2, 128.7, 127.2, 120.9, 120.7, 114.2, 61.9, 55.4, 14.4.

Ethyl 6-(4-chlorophenyl)-4-phenylpicolinate (4d) White solid; 55% yield; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.29 (s, 1H), 8.08–8.05 (m, 3H), 7.74–7.73 (m, 2H), 7.55–7.47

(m, 5H), 4.52 (q, J = 7.2 Hz, 2H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4, 157.1, 150.7, 149.0, 137.6, 137.1, 135.7, 129.6, 129.3, 129.1, 128.6, 127.2, 121.8, 121.2, 62.1, 14.4.

Ethyl 4-phenyl-6-(p-tolyl)picolinate (4e) White solid; 35% yield; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.26–8.25 (m, 1H), 8.07–8.02 (m, 3H), 7.75–7.74 (m, 2H), 7.54–7.49 (m, 3H), 7.32–7.30 (m, 2H), 4.52 (q, J = 7.2 Hz, 2H), 2.42 (s, 3H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7, 158.3, 150.3, 148.9, 139.6, 137.9, 135.9, 129.6, 129.4, 129.2, 127.2, 127.2, 121.3, 121.2, 61.9, 21.4, 14.4.

Ethyl 6-phenyl-4-(p-tolyl)picolinate (4f) White solid; 59% yield; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.27 (s, 1H), 8.12–8.07 (m, 3H), 7.66–7.65 (m, 2H), 7.52–7.49 (m, 3H), 7.34–7.33 (m, 2H), 4.52 (q, J = 7.2 Hz, 2H), 2.44 (s, 3H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7, 158.3, 150.3, 148.9, 139.7, 138.8, 134.8, 130.0, 129.4, 128.8, 127.4, 127.0, 121.3, 121.2, 61.9, 21.3, 14.4.

Ethyl 4-(4-chlorophenyl)-6-phenylpicolinate (4g) White solid; 43% yield; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.25 (s, 1H), 8.11 (d, J = 7.8 Hz, 2H), 8.05 (s, 1H), 7.69–7.68 (m, 2H), 7.52–7.45 (m, 5H), 4.53 (q, J = 7.2 Hz, 2H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.5, 158.5, 149.2, 149.1, 138.4, 136.2, 135.8, 129.7, 129.5, 128.9, 128.5, 127.4, 121.3, 62.1, 14.4.

Ethyl (E)-4-phenyl-6-styrylpicolinate (4h) White solid; 32% yield; mp: 82-85 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.86 (s, 1H), 8.74–7.70 (m, 3H), 7.63–7.62 (m, 2H), 7.55–7.50 (m, 3H), 7.44–7.39 (m, 3H), 7.34–7.33(m, 1H), 4.54 (q, J = 7.2 Hz, 2H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3, 156.7, 150.3, 148.6, 137.5, 136.3, 134.6, 129.6, 129.3, 128.8, 128.8, 127.5, 127.4, 127.2, 122.1, 121.6, 62.2, 14.4; IR (film) 3056, 2982, 1712, 1591, 1445, 1254, 1145, 757; ESI-HRMS $C_{21}H_{18}NO_2$ ($[M+H]^+$): calcd 316.1333, found 316.1331.

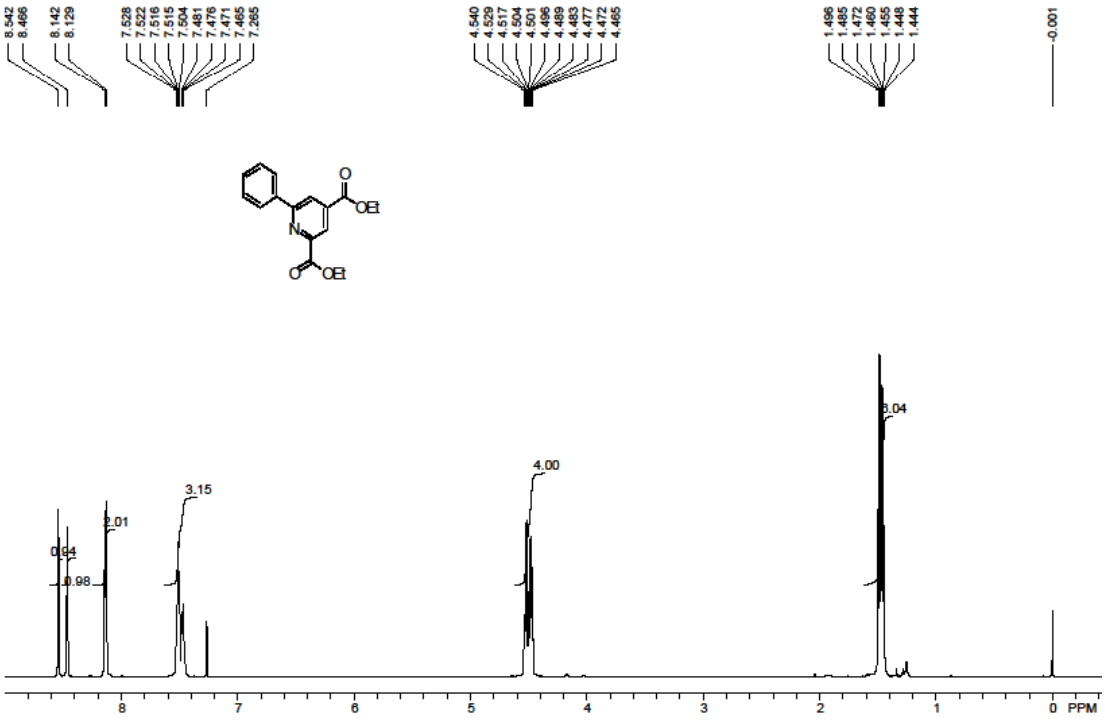
2,4,6-Triphenylpyridine (4A) White solid; 14% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (d, J = 7.8 Hz, 4H), 7.89 (s, 2H), 7.75 (d, J =7.8 Hz, 2H), 7.55–7.44 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 150.3, 139.5, 139.1, 129.2, 129.1, 129.0, 128.8, 127.2, 127.2, 117.2.

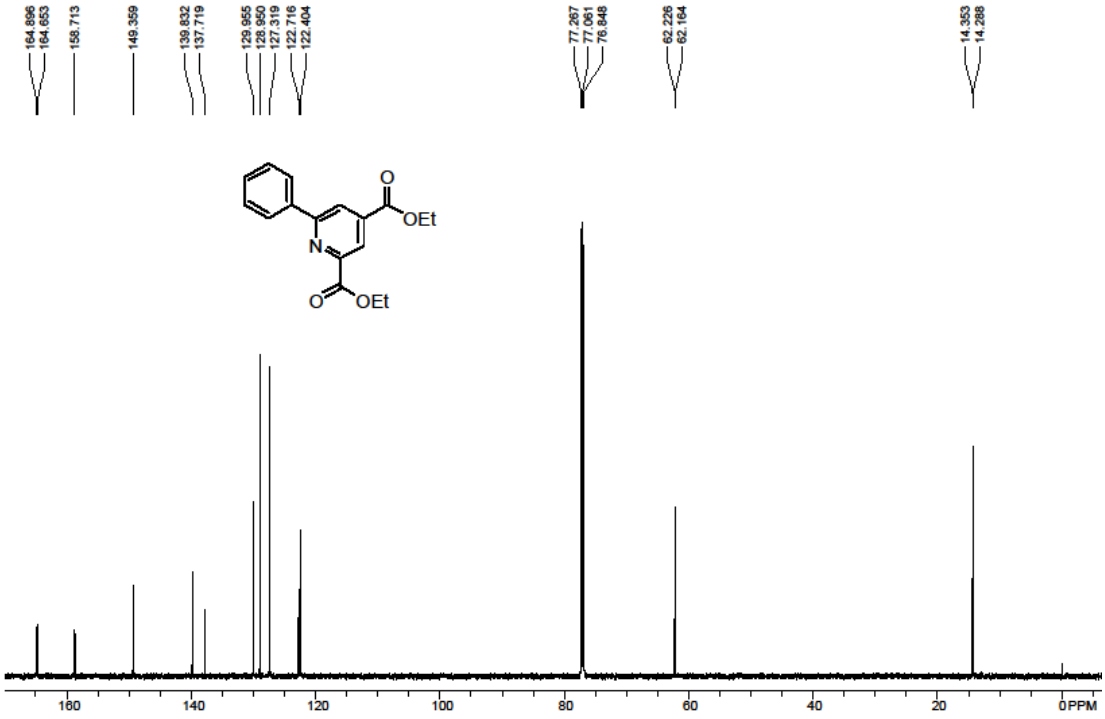
2,6-Bis(4-methoxyphenyl)-4-phenylpyridine (4B) White solid; 15% yield; ^{1}H NMR

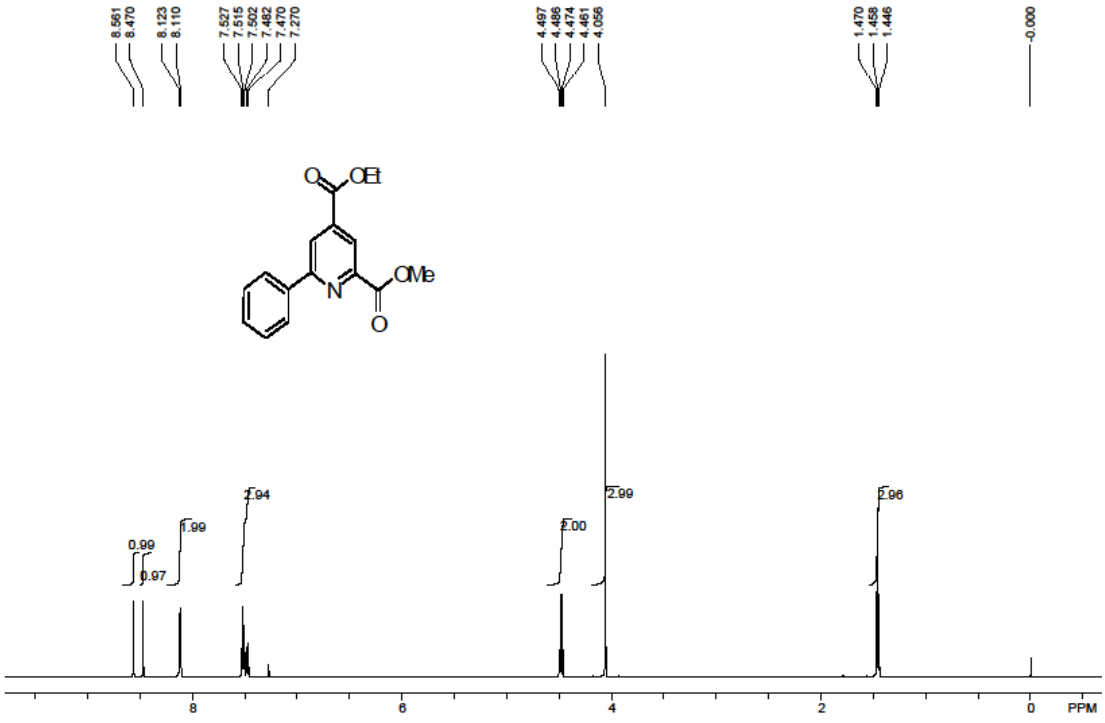
(600 MHz, $CDCl_3$) δ 8.15 (d, J = 8.4 Hz, 4H), 7.77 (s, 2H), 7.73–7.72 (m, 2H), 7.53–7.50 (m, 2H), 7.47–7.45 (m, 1H), 7.04–7.02 (m, 4H), 3.88 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 156.9, 150.1, 139.3, 132.2, 129.1, 128.9, 128.4, 127.2, 115.8, 114.0, 55.4.

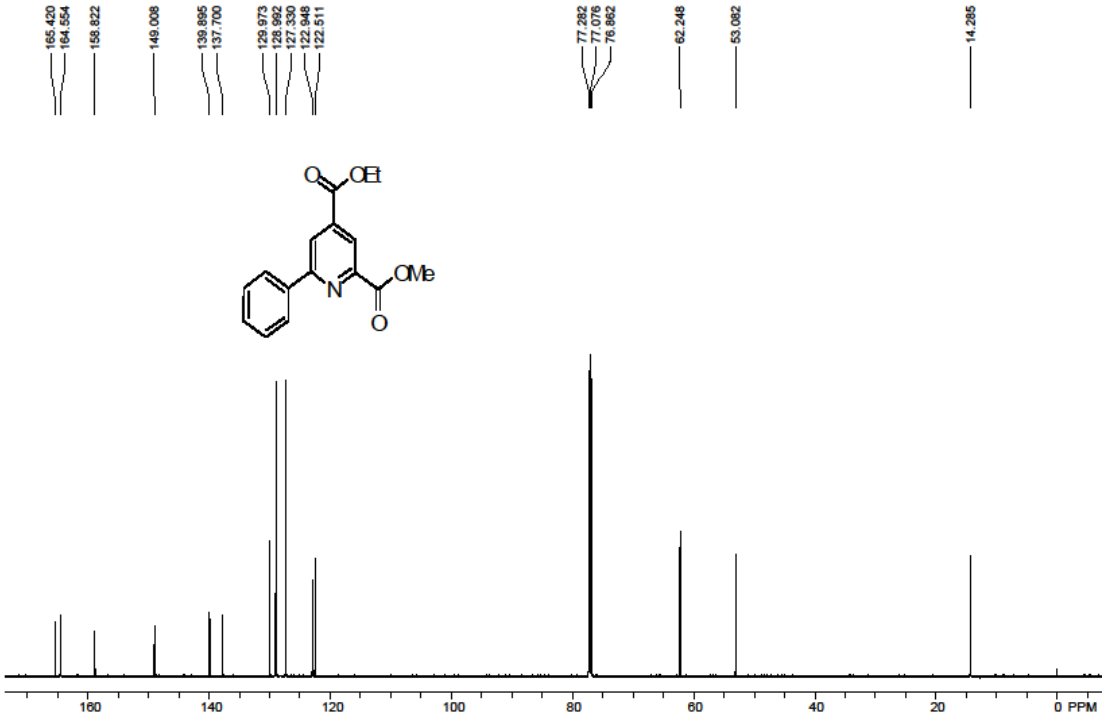
2,6-Diphenyl-4-(p-tolyl)pyridine (4C) White solid; 18% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, J = 7.8 Hz, 4H), 7.88 (s, 2H), 7.66 (d, J =7.8 Hz, 2H), 7.53–7.50 (m, 4H), 7.46–7.44 (m, 2H), 7.33 (d, J =7.8 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 150.2, 139.6, 139.2, 136.1, 129.9, 129.1, 128.7, 127.2, 127.1, 117.0, 21.3.

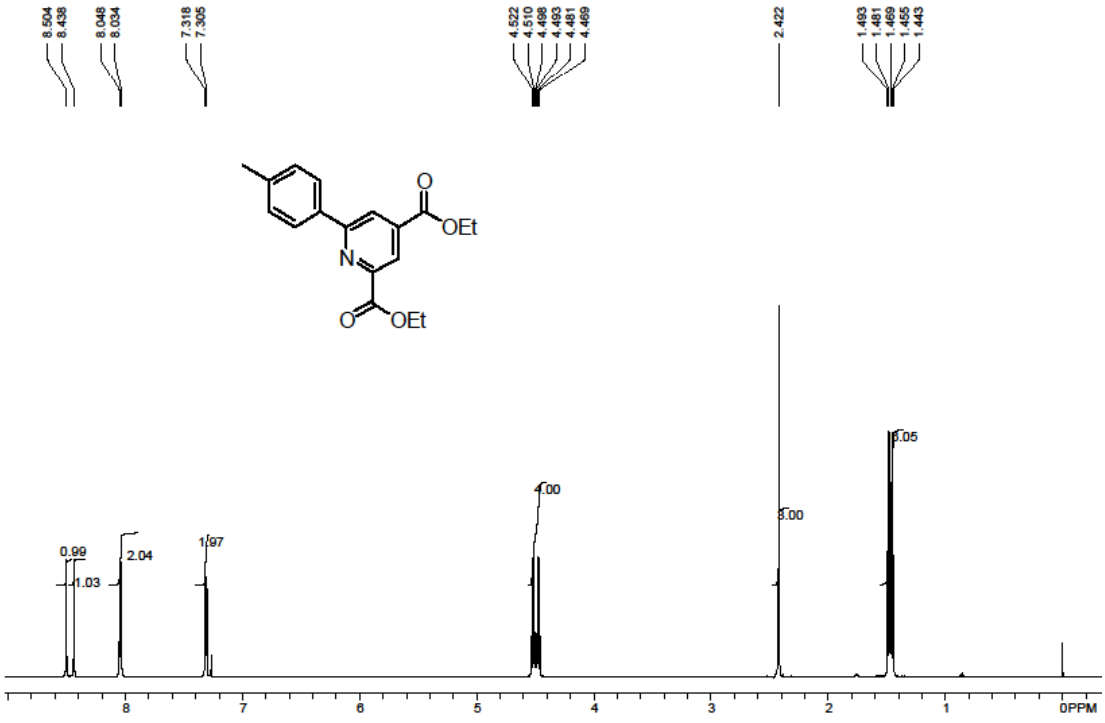
4-(4-Chlorophenyl)-2,6-diphenylpyridine (4D) White solid; 12% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (d, J = 7.8 Hz, 4H), 7.83 (s, 2H), 7.67 (d, J =8.4 Hz, 2H), 7.53–7.44 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 149.0, 139.3, 137.5, 135.3, 129.4, 129.2, 128.8, 128.5, 127.2, 116.9.

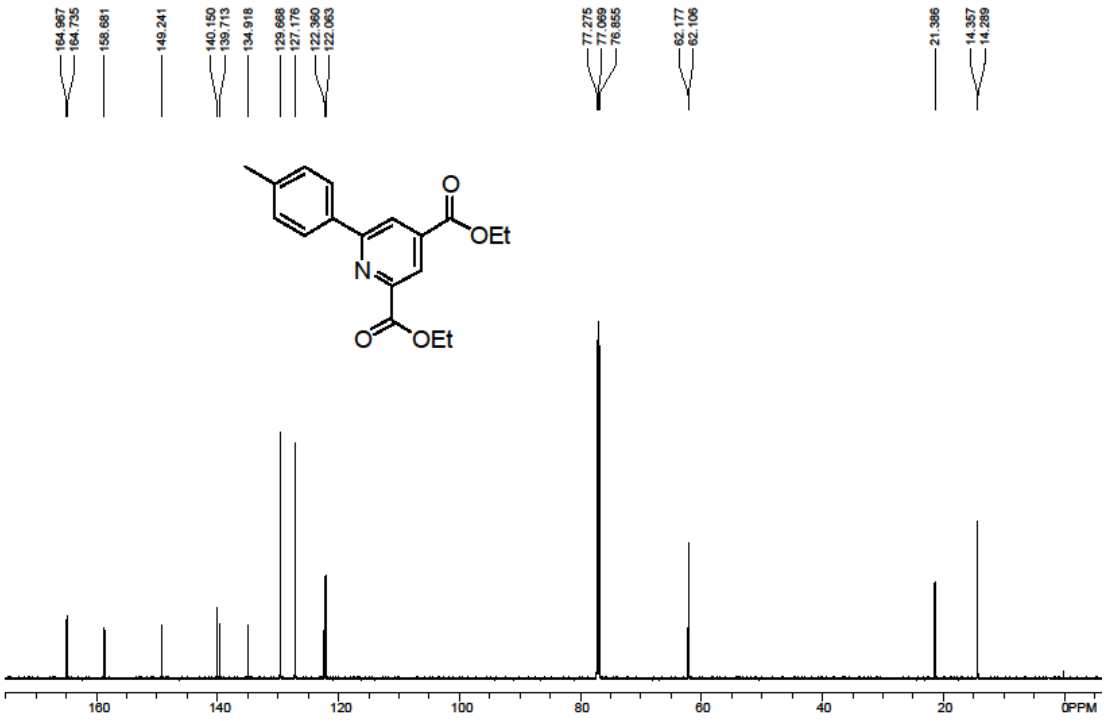

8.542
8.466
8.142
8.129
7.528
7.522
7.516
7.515
7.504
7.481
7.476
7.471
7.465
7.265
4.540
4.529
4.517
4.504
4.501
4.496
4.489
4.483
4.477
4.472
4.465
1.496
1.485
1.472
1.460
1.455
1.448
1.444
-0.001
O
OEt
N
O
OEt
0.84
0.98
2.01
3.15
4.00
3.04
8
7
6
5
4
3
2
1
0 PPM

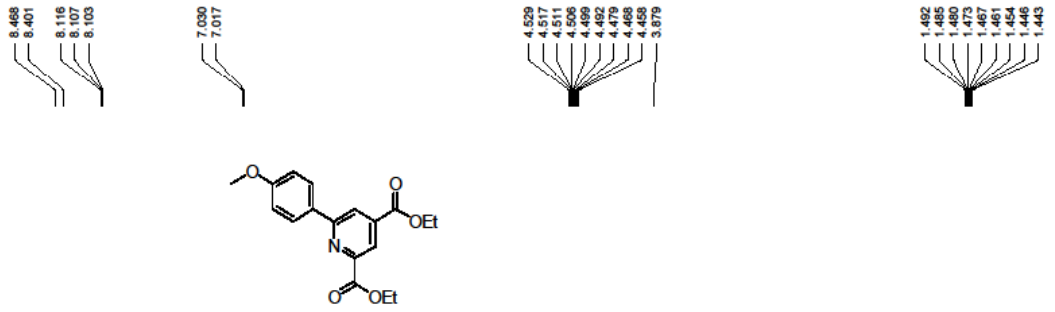

164.896
164.653
158.713
149.359
139.832
137.719
129.955
128.950
127.319
122.716
122.404
77.267
77.061
76.848
62.226
62.164
14.353
14.288
O
OEt
N
O
OEt
160
140
120
100
80
60
40
20
0 PPM


8.561
8.470
8.123
8.110
7.527
7.515
7.502
7.482
7.470
7.270
4.497
4.486
4.474
4.461
4.056
1.470
1.458
1.446
-0.000
O
OEt
N
OMe
O
0.99
0.97
1.99
2.94
2.00
2.99
2.96
8
6
4
2
0
PPM

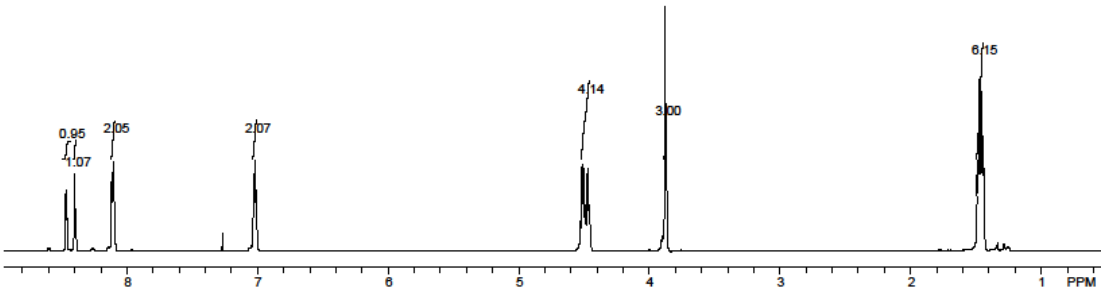

165.420
164.554
158.822
149.008
139.895
137.700
129.973
128.992
127.330
122.948
122.511
77.282
77.076
76.862
62.248
53.082
14.285
O
OEt
N
OMe
O
160
140
120
100
80
60
40
20
0 PPM

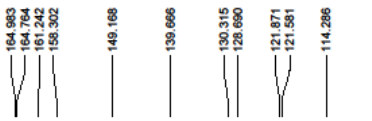

8.504
8.438
8.048
8.034
7.318
7.305
4.522
4.510
4.498
4.493
4.481
4.469
2.422
1.493
1.481
1.469
1.455
1.443
O
OEt
N
O
OEt
0.99
1.03
2.04
1.97
4.00
3.00
6.05
8
7
6
5
4
3
2
1
0PPM

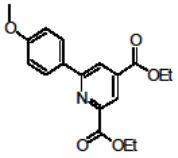

164.967
164.735
158.681
149.241
140.150
139.713
134.918
129.668
127.176
122.360
122.063
77.275
77.069
76.855
62.177
62.106
21.386
14.357
14.289
O
OEt
N
O
OEt
160
140
120
100
80
60
40
20
0PPM

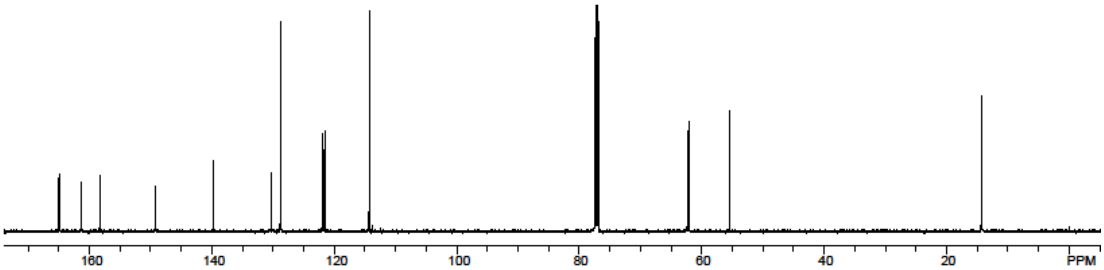

8.468
8.401
8.116
8.107
8.103
7.030
7.017
4.529
4.517
4.511
4.506
4.499
4.492
4.479
4.468
4.458
3.879
1.492
1.485
1.480
1.473
1.467
1.461
1.454
1.446
1.443

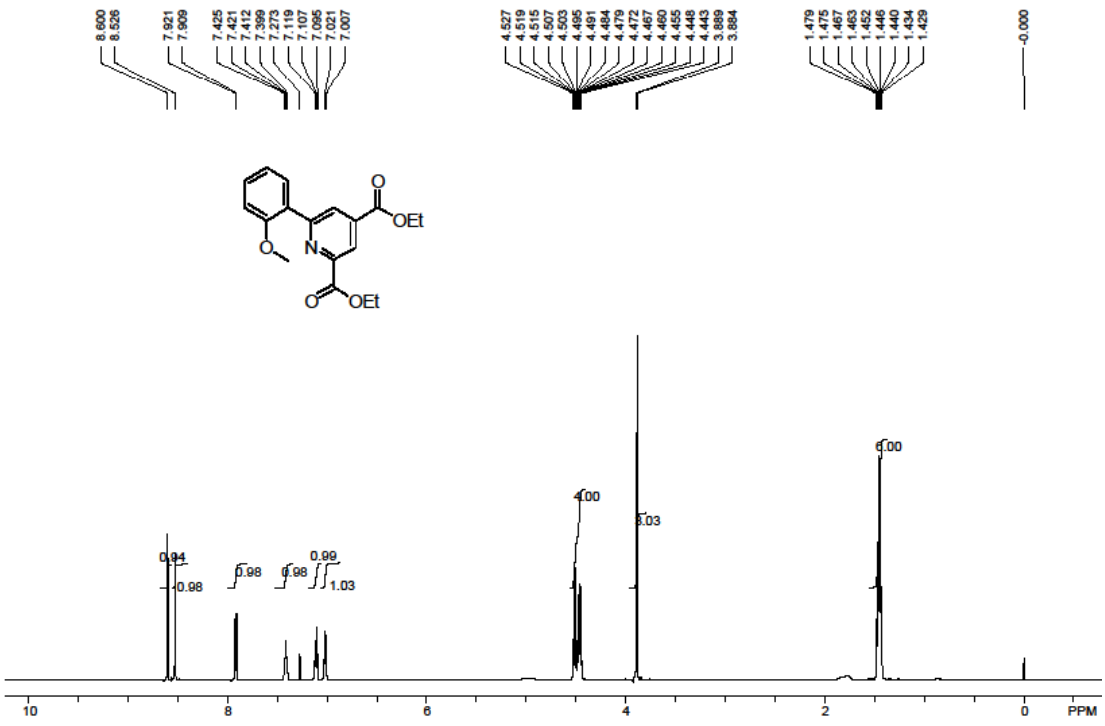
O
O
OEt
N
O
OEt

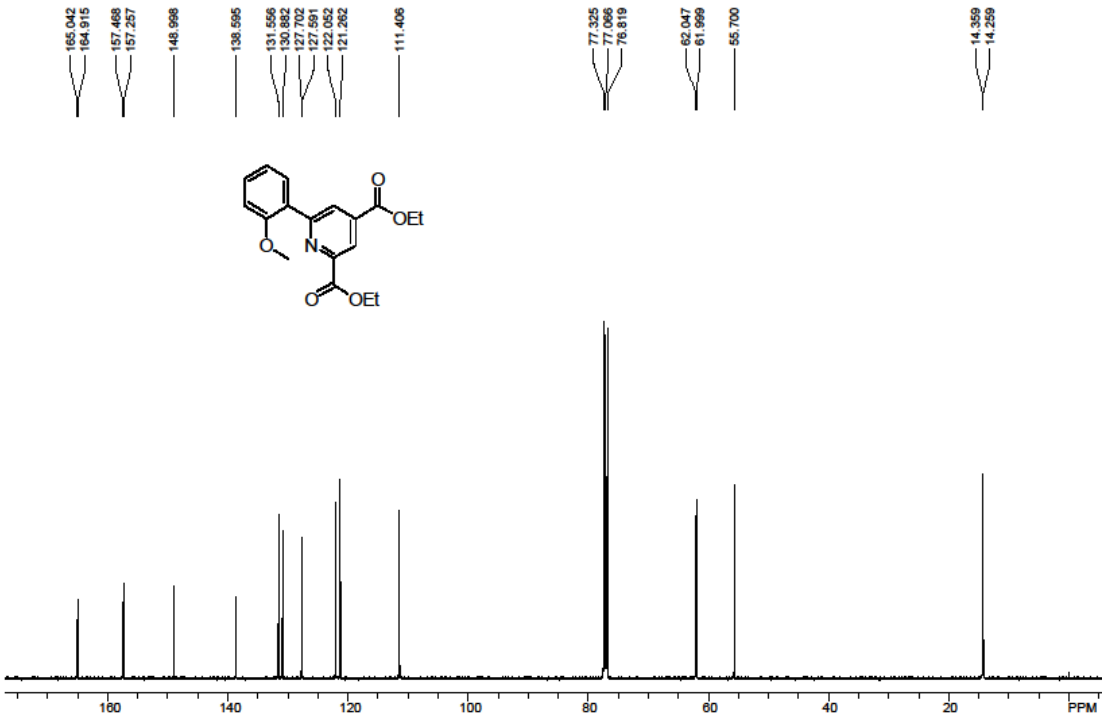

0.95
1.07
2.05
2.07
4.14
3.00
6.15
8
7
6
5
4
3
2
1
PPM

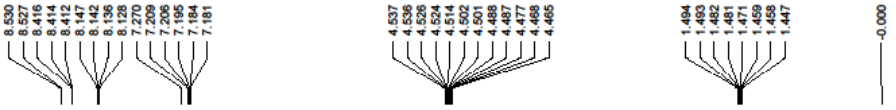

164.983
164.764
161.242
158.302
149.168
139.666
130.315
128.690
121.871
121.581
114.286
77.322
77.062
76.803
62.127
62.056
55.399
14.339
14.274

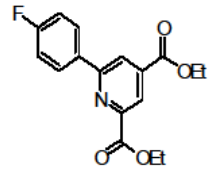

O
O
OEt
N
O
OEt

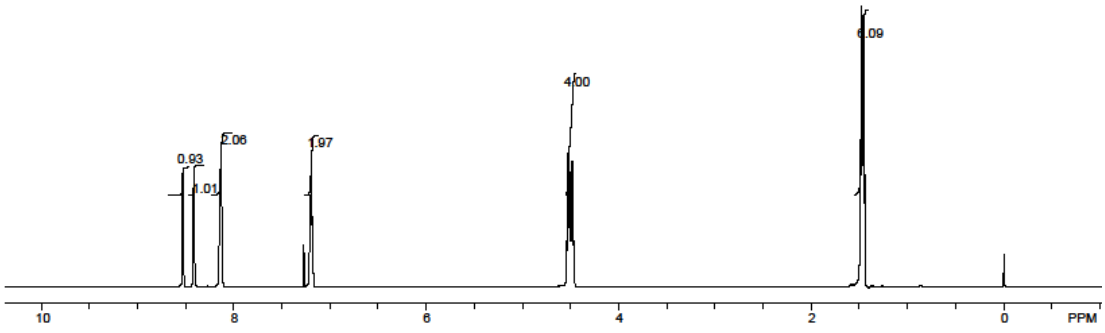

160
140
120
100
80
60
40
20
PPM

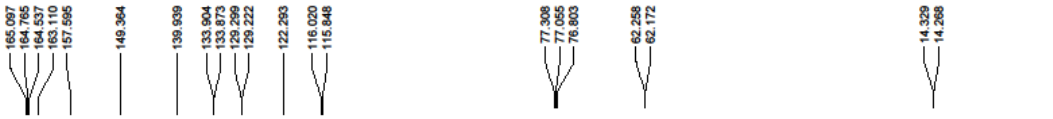

8.600
8.526
7.921
7.909
7.425
7.421
7.412
7.399
7.273
7.119
7.107
7.095
7.021
7.007
4.527
4.519
4.515
4.507
4.503
4.495
4.491
4.484
4.479
4.472
4.467
4.460
4.455
4.448
4.443
3.889
3.884
1.479
1.475
1.467
1.463
1.452
1.446
1.440
1.434
1.429
-0.000
O
OEt
N
O
O
OEt
0.94
0.98
0.98
0.98
0.99
1.03
4.00
3.03
6.00
10
8
6
4
2
0
PPM

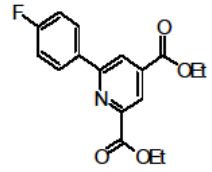

165.042
164.915
157.468
157.257
148.998
138.595
131.556
130.882
127.702
127.591
122.052
121.262
111.406
77.325
77.066
76.819
62.047
61.999
55.700
14.359
14.259
O
OEt
N
O
O
OEt
160
140
120
100
80
60
40
20
PPM

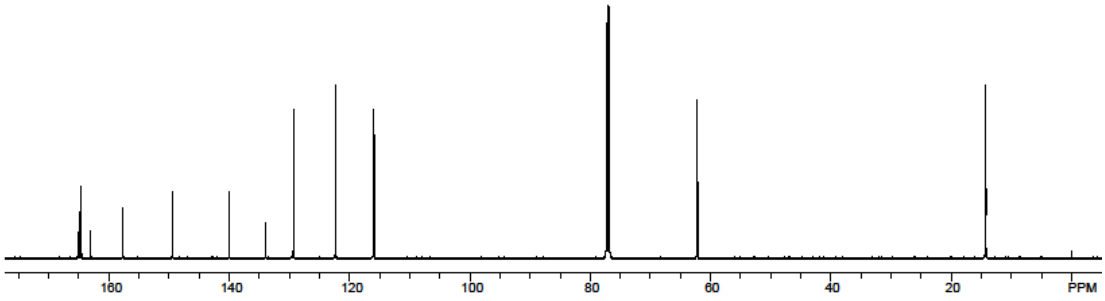

8.530
8.527
8.416
8.414
8.412
8.147
8.142
8.136
8.128
7.270
7.209
7.206
7.195
7.184
7.181
4.537
4.536
4.526
4.524
4.514
4.502
4.501
4.488
4.487
4.477
4.468
4.465
1.494
1.493
1.482
1.481
1.471
1.459
1.458
1.447
-0.000

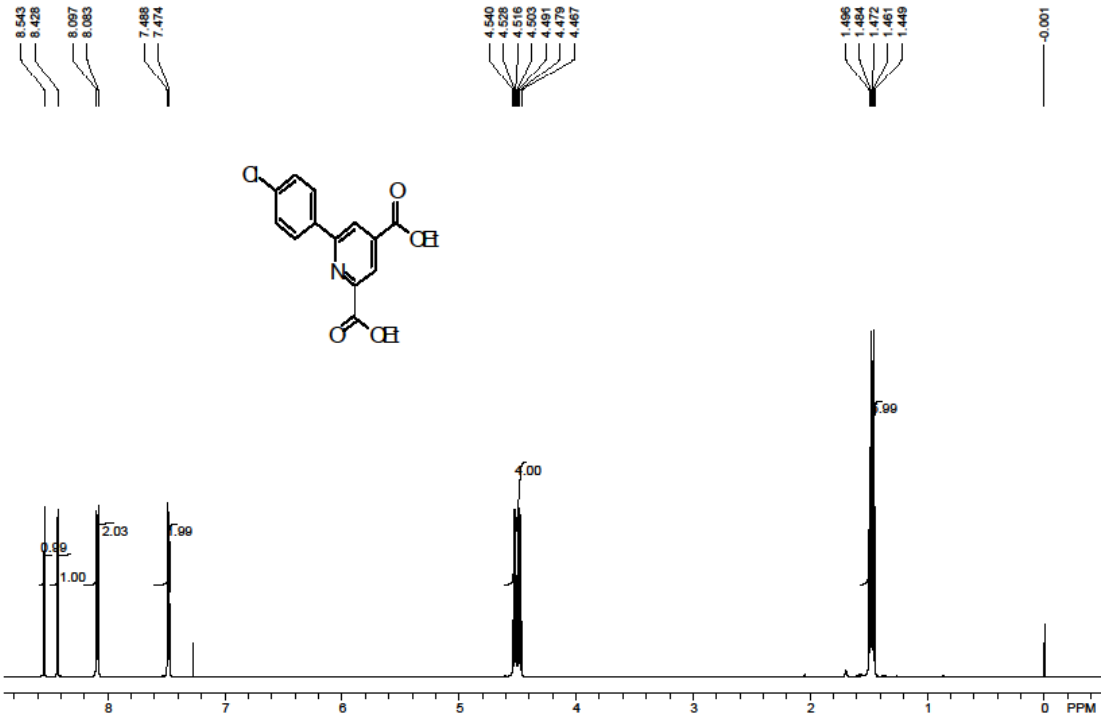

F
O
OEt
N
O
OEt

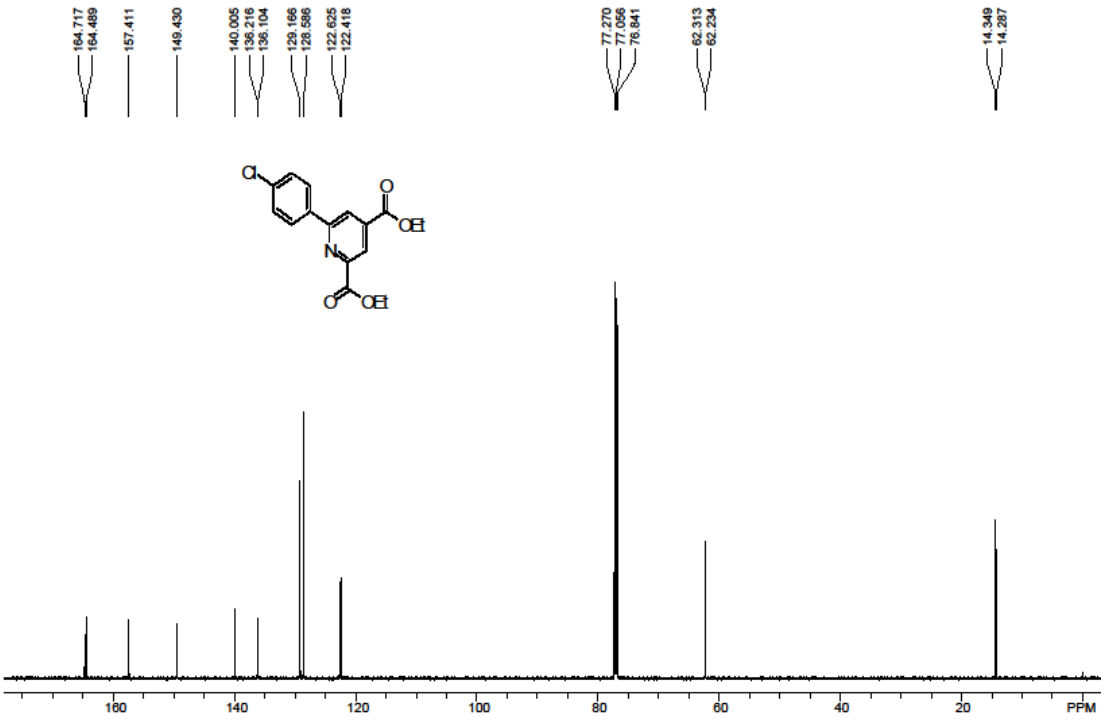

6.09
4.00
2.06
1.97
0.93
1.01
10
8
6
4
2
0
PPM

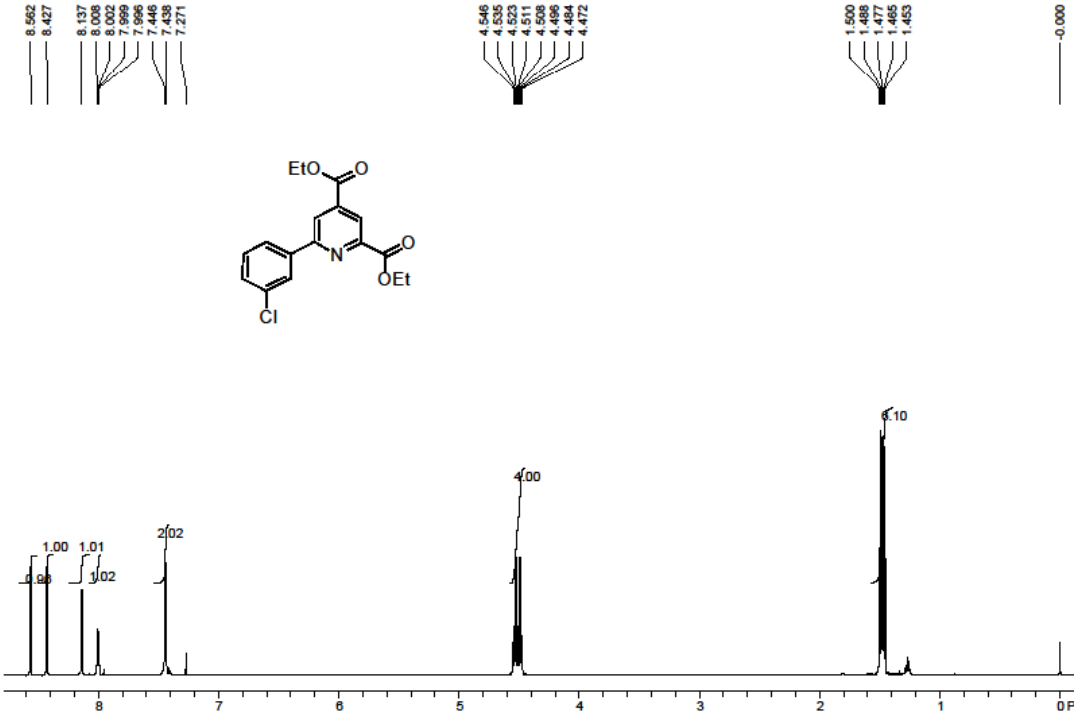

165.097
164.785
164.537
163.110
157.595
149.364
139.939
133.904
133.873
129.299
129.222
122.293
116.020
115.848
77.308
77.055
76.803
62.258
62.172
14.329
14.268

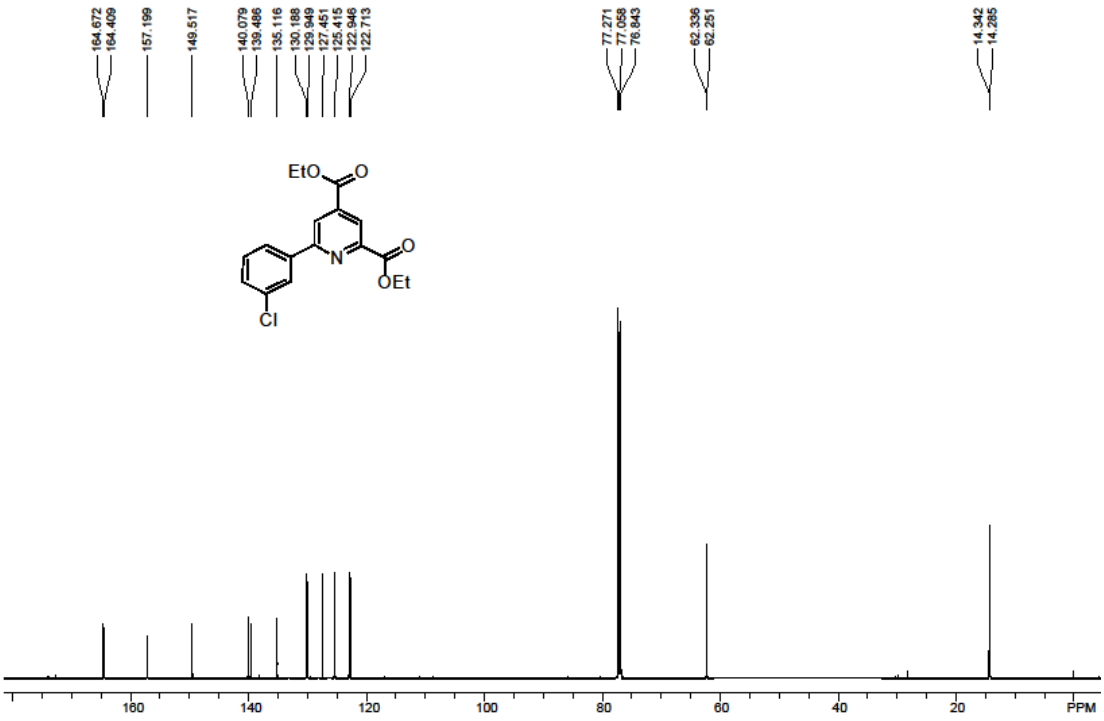

F
O
OEt
N
O
OEt

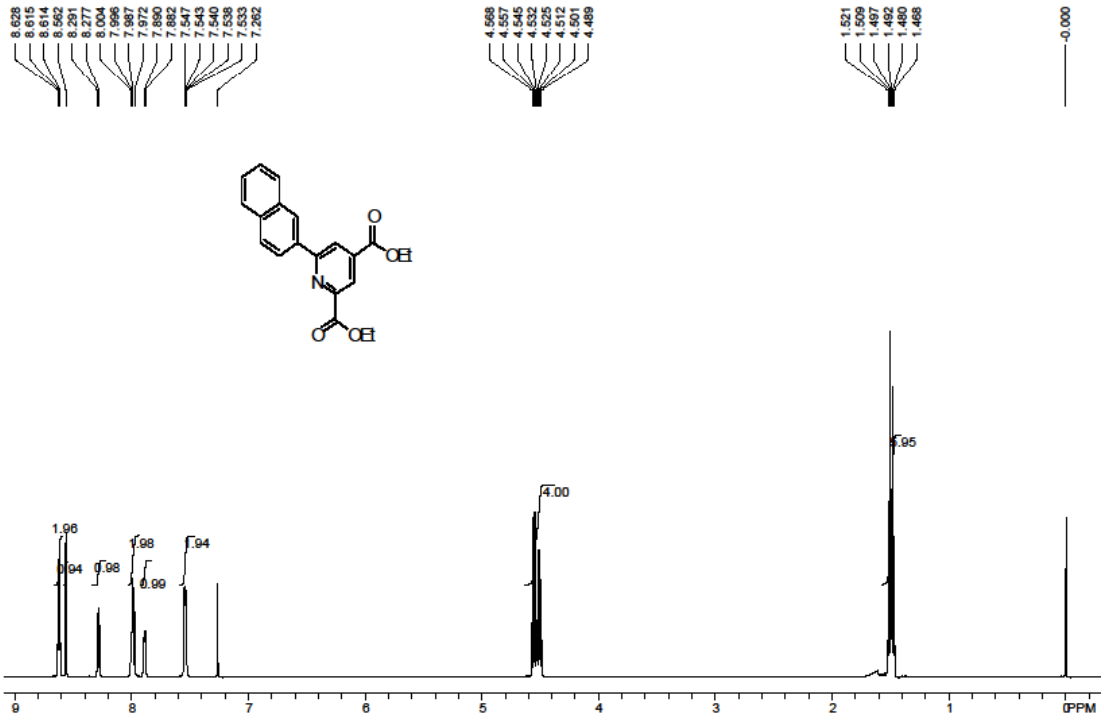

160
140
120
100
80
60
40
20
PPM

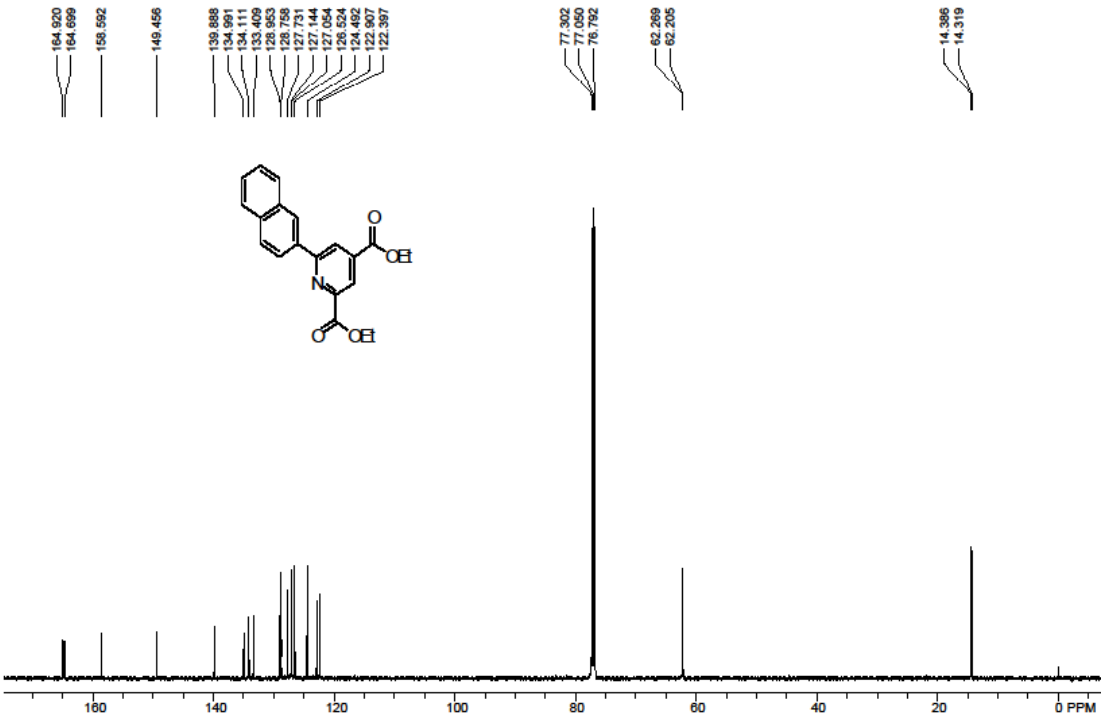

8.543
8.428
8.097
8.083
7.488
7.474
4.540
4.528
4.516
4.503
4.491
4.479
4.467
1.496
1.484
1.472
1.461
1.449
-0.001
Cl
O
OEt
N
O
OEt
0.99
1.00
2.03
1.99
4.00
7.99
8
7
6
5
4
3
2
1
0
PPM

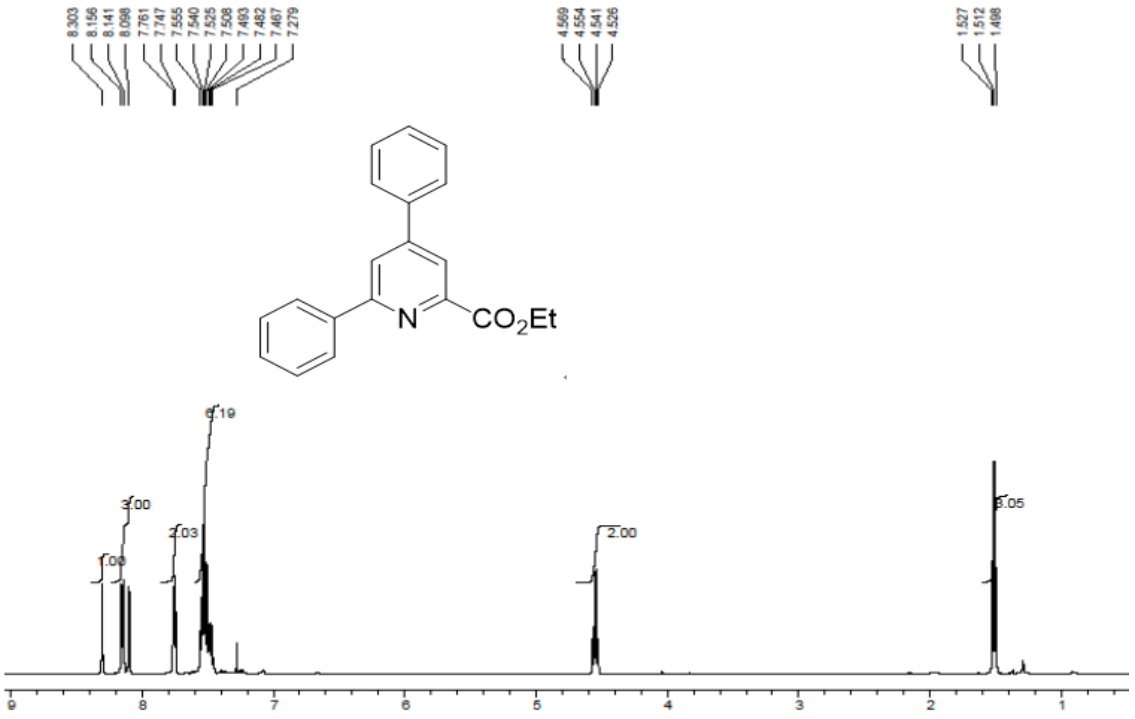

164.717
164.489
157.411
149.430
140.005
136.216
136.104
129.166
128.586
122.625
122.418
77.270
77.056
76.841
62.313
62.234
14.349
14.287
Cl
O
OEt
N
O
OEt
160
140
120
100
80
60
40
20
PPM

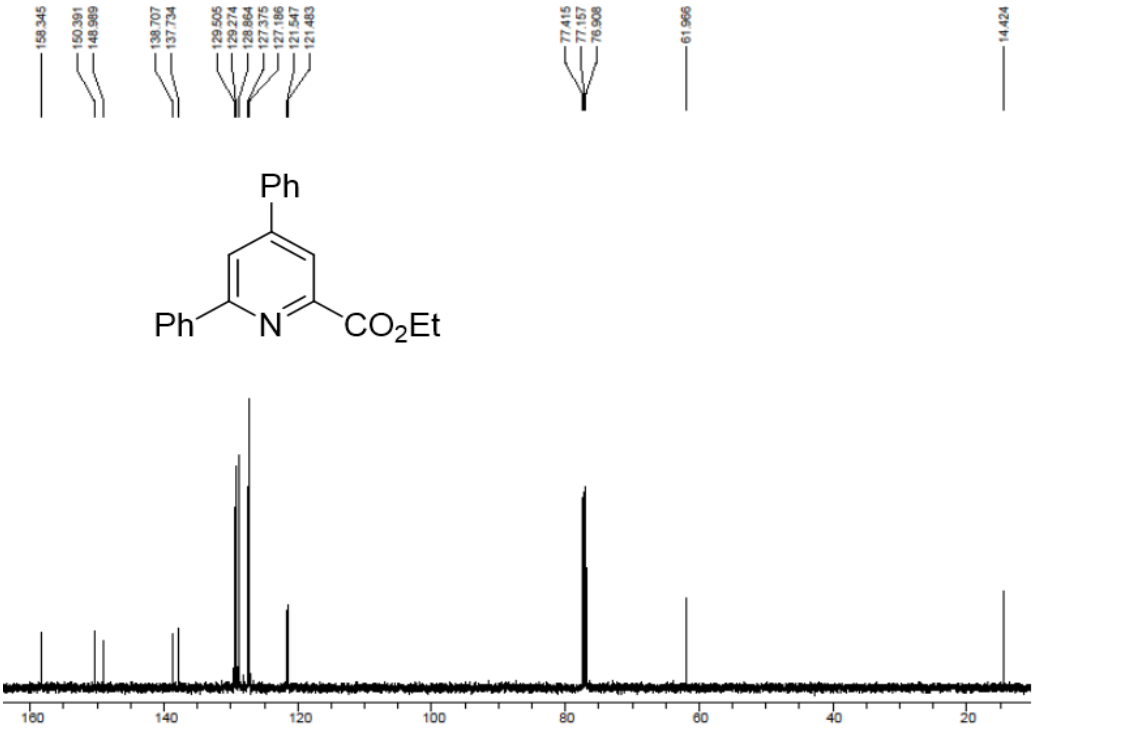

8.562
8.427
8.137
8.008
8.002
7.999
7.996
7.446
7.438
7.271
4.546
4.535
4.523
4.511
4.508
4.496
4.484
4.472
1.500
1.488
1.477
1.465
1.453
-0.000
EtO
O
N
O
OEt
Cl
1.00
1.01
0.98
1.02
2.02
4.00
6.10
8
7
6
5
4
3
2
1
0 PPM

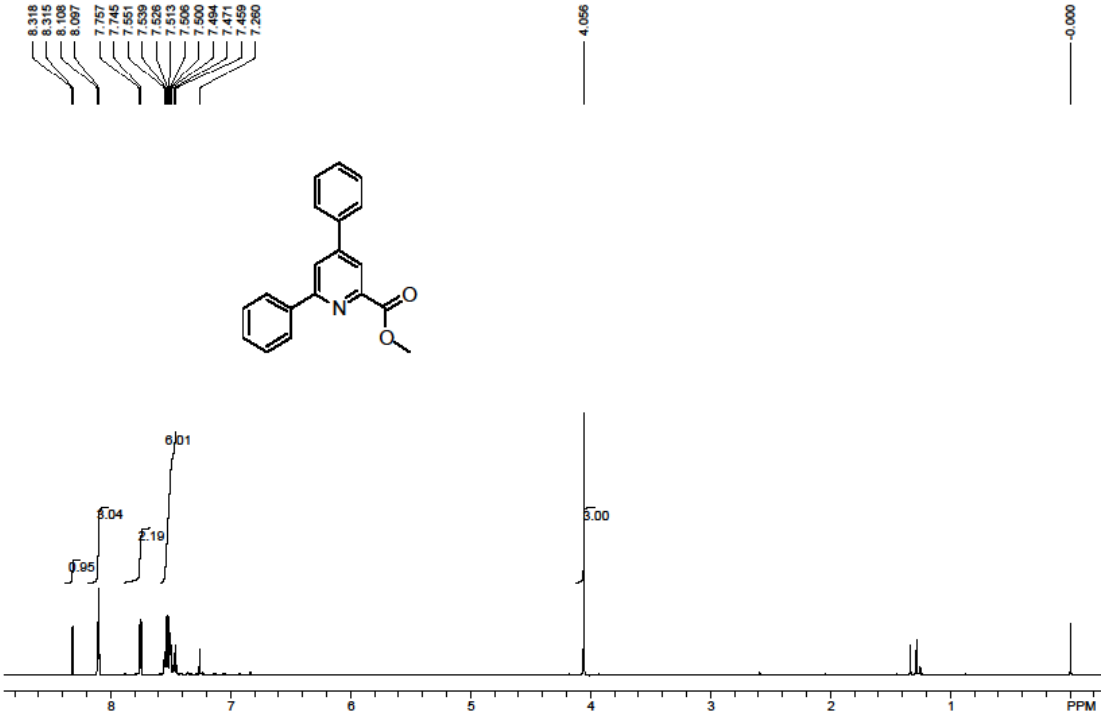

164.672
164.409
157.199
149.517
140.079
139.486
135.116
130.188
129.949
127.451
125.415
122.946
122.713
77.271
77.058
76.843
62.336
62.251
14.342
14.285
EtO
O
N
O
OEt
Cl
160
140
120
100
80
60
40
20
PPM

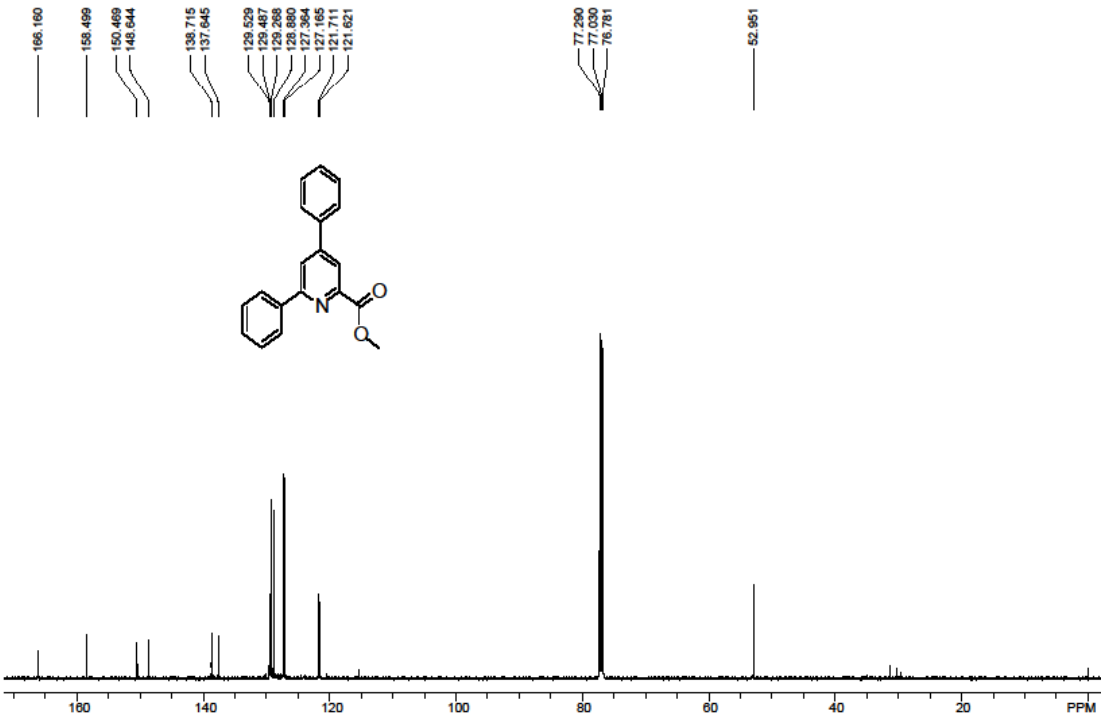

8.628
8.615
8.614
8.562
8.291
8.277
8.004
7.996
7.987
7.972
7.890
7.882
7.547
7.543
7.540
7.538
7.533
7.262
4.568
4.557
4.545
4.532
4.525
4.512
4.501
4.489
1.521
1.509
1.497
1.492
1.480
1.468
0.000
O
OEt
N
O
OEt
1.96
0.94
0.98
1.98
0.99
1.94
4.00
5.95
9
8
7
6
5
4
3
2
1
0PPM

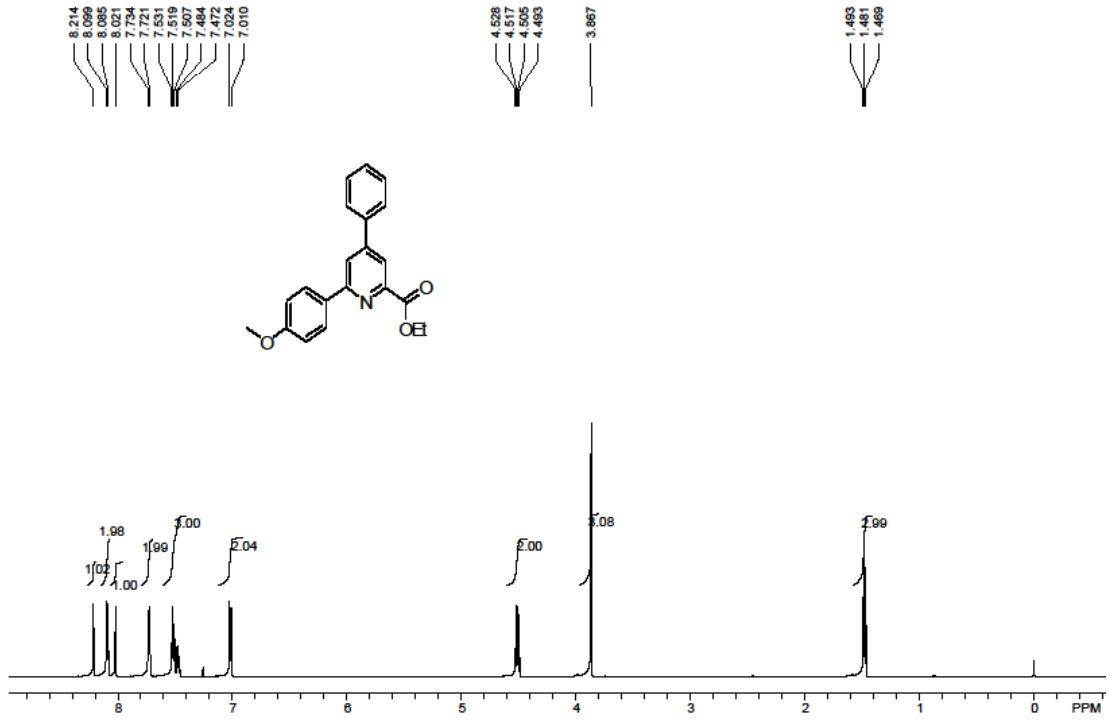

164.920
164.699
158.592
149.456
139.888
134.991
134.111
133.406
128.953
128.758
127.731
127.144
127.054
126.524
124.492
123.977
122.397
77.302
77.050
76.792
62.269
62.205
14.386
14.319
O
OEt
N
O
OEt
160
140
120
100
80
60
40
20
0 PPM

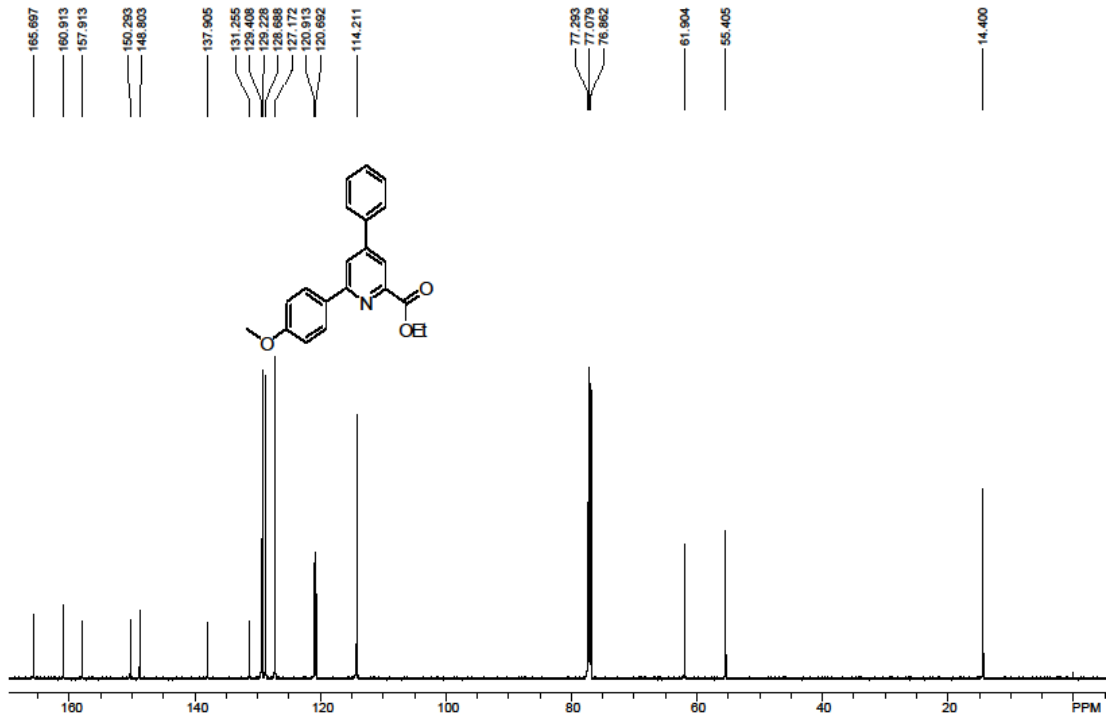

8.303
8.156
8.141
8.098
7.761
7.747
7.555
7.540
7.525
7.508
7.493
7.482
7.467
7.279
4.569
4.554
4.541
4.526
1.527
1.512
1.498
N
CO2Et
6.19
3.00
2.03
1.00
2.00
3.05

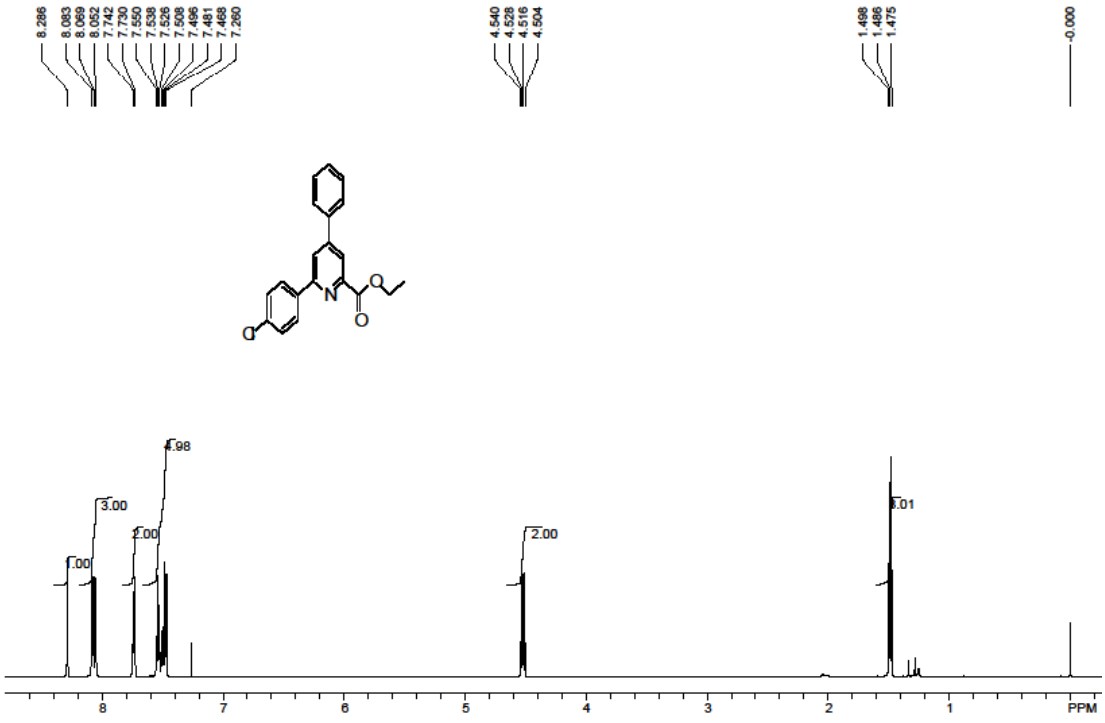

158.345
150.391
148.989
138.707
137.734
129.505
129.274
128.864
127.375
127.186
121.547
121.483
77.415
77.157
76.908
61.966
14.424
Ph
Ph
N
CO2Et

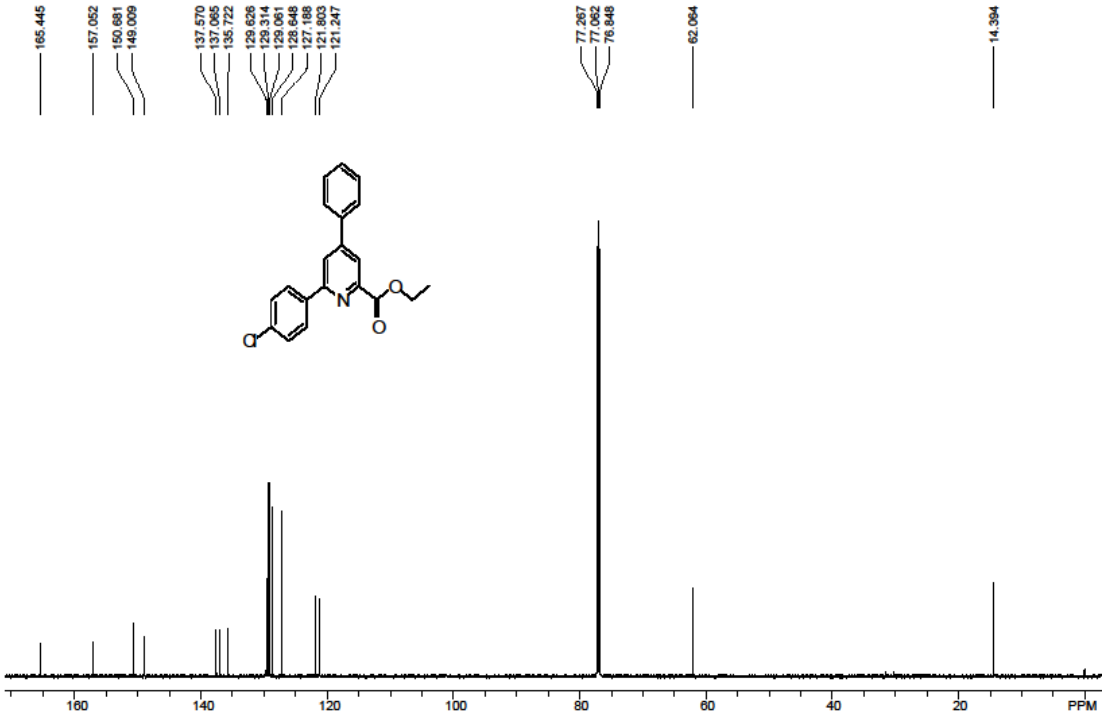

8.318
8.315
8.109
8.097
7.757
7.745
7.551
7.539
7.526
7.513
7.506
7.500
7.494
7.471
7.459
7.260
4.056
0.000
N
O
O
6.01
4.04
2.19
0.95
3.00
8
7
6
5
4
3
2
1
PPM

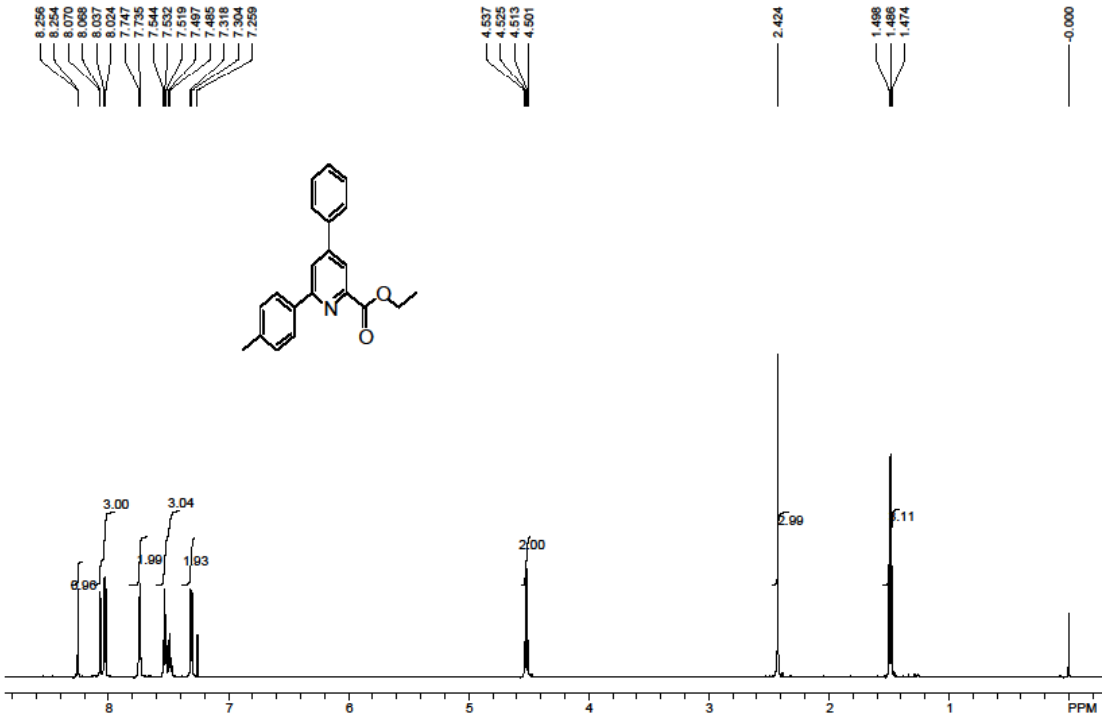

166.160
158.499
150.469
148.644
138.715
137.645
129.529
129.487
129.268
128.880
127.364
127.165
121.711
121.621
77.290
77.030
76.781
52.951
N
O
O
160
140
120
100
80
60
40
20
PPM

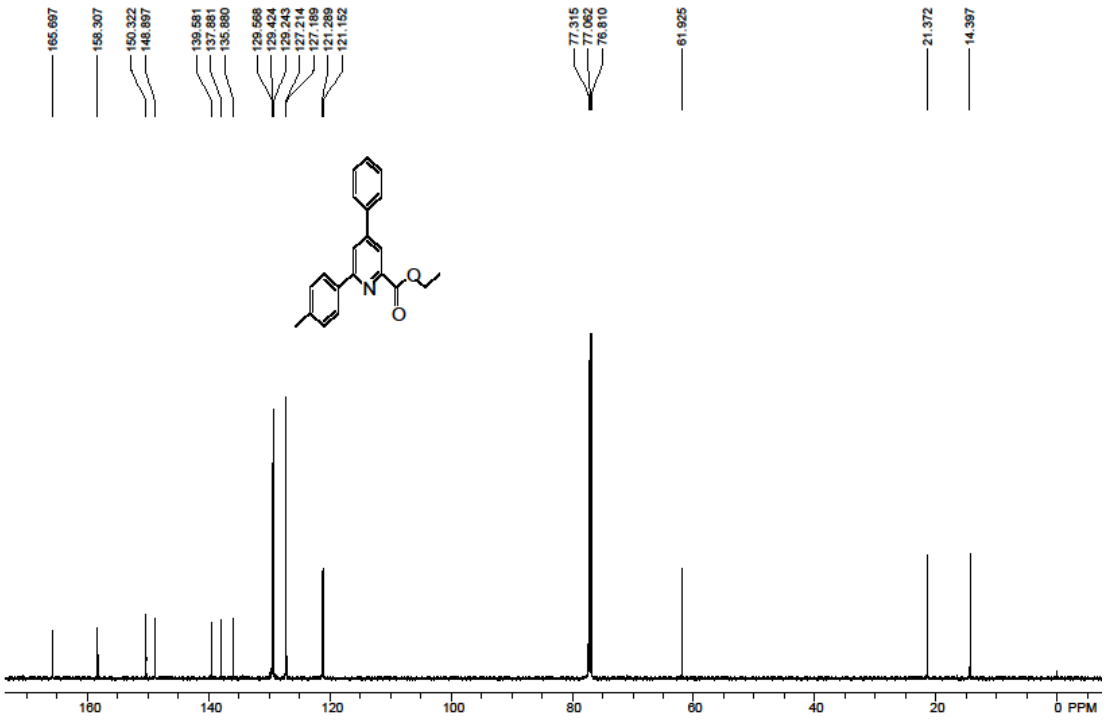

8.214
8.099
8.085
8.021
7.734
7.721
7.531
7.519
7.507
7.484
7.472
7.024
7.010
4.528
4.517
4.505
4.493
3.867
1.493
1.481
1.469
O
N
O
OEt
1.98
1.02
1.00
1.99
3.00
2.04
2.00
3.08
2.99
8
7
6
5
4
3
2
1
0
PPM

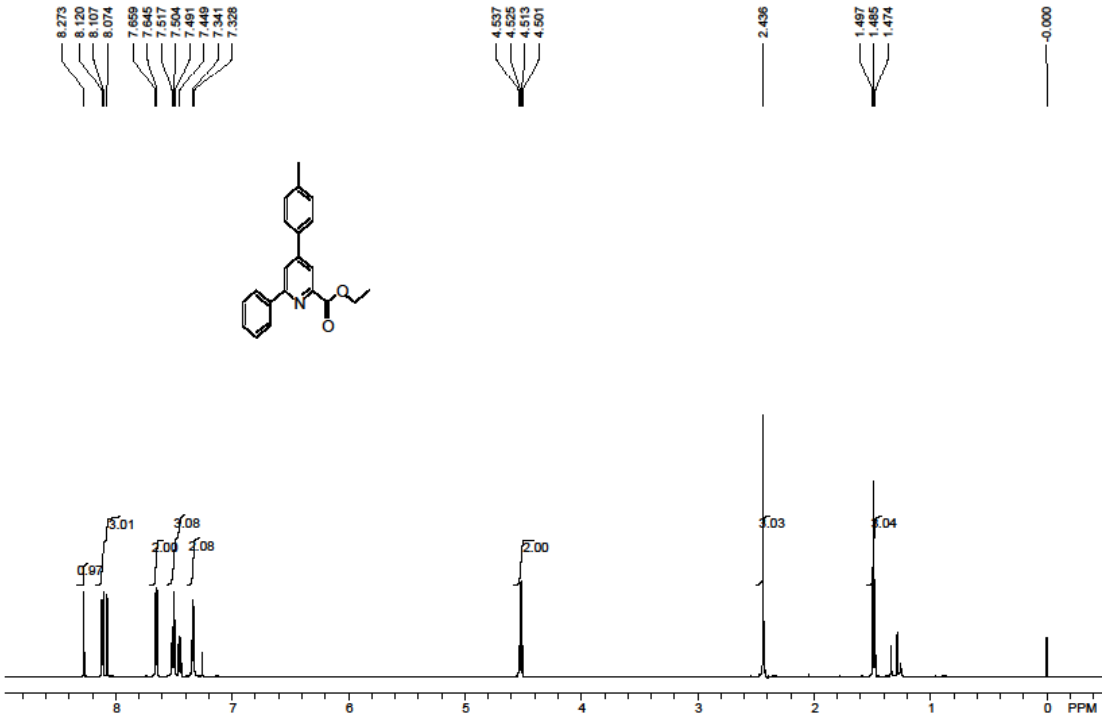

165.697
160.913
157.913
150.293
148.803
137.905
131.255
129.408
129.228
128.688
127.172
120.913
120.692
114.211
77.293
77.079
76.862
61.904
55.405
14.400
O
N
O
OEt
160
140
120
100
80
60
40
20
PPM

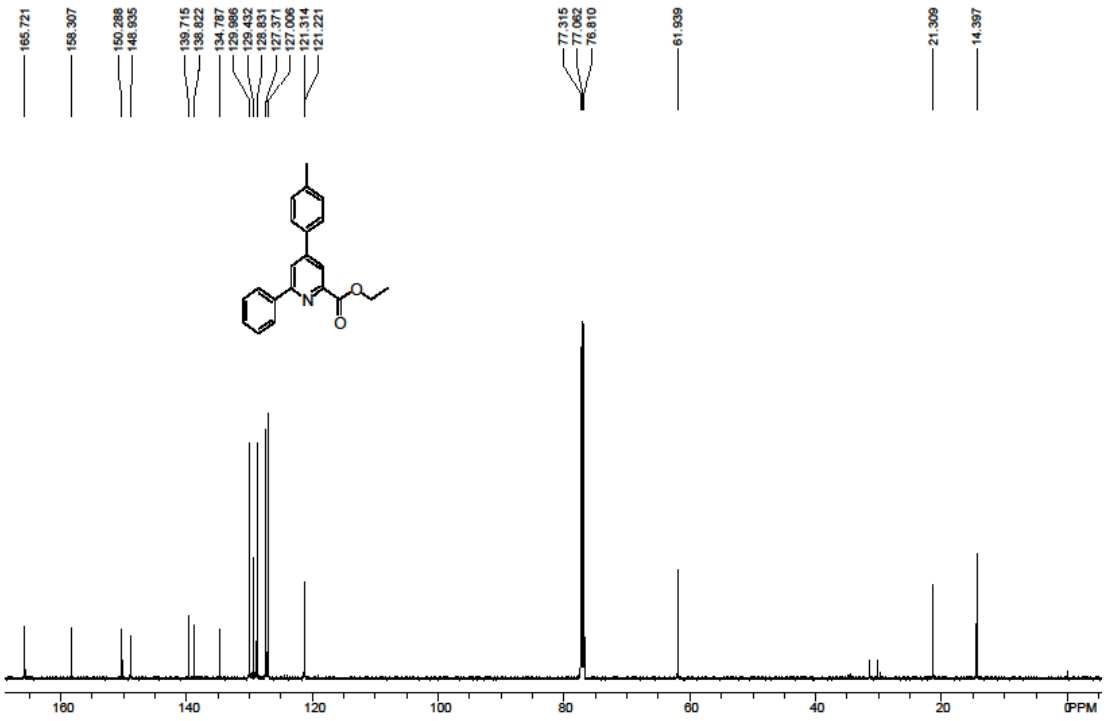

8.286
8.083
8.069
8.052
7.742
7.730
7.550
7.538
7.526
7.508
7.496
7.481
7.468
7.260
4.540
4.528
4.516
4.504
1.498
1.486
1.475
0.000
Cl
N
O
O
4.98
3.00
2.00
1.00
2.00
3.01
8
7
6
5
4
3
2
1
PPM

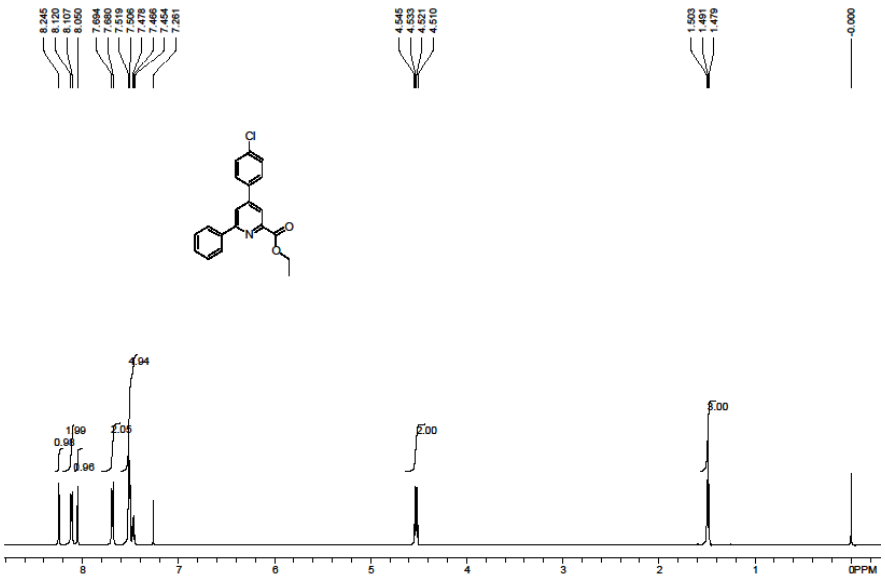

165.445
157.052
150.681
149.009
137.570
137.065
135.722
129.626
129.314
129.061
128.648
127.188
121.803
121.247
77.267
77.052
76.848
62.064
14.394
Cl
N
O
O
160
140
120
100
80
60
40
20
PPM

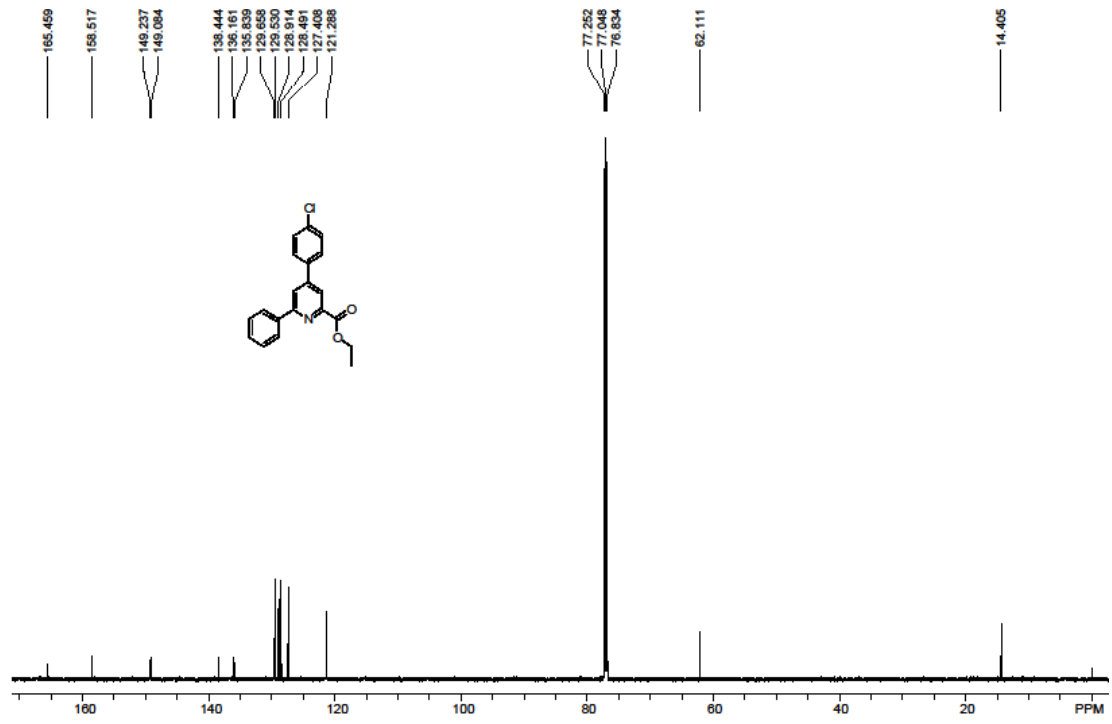

8.256
8.254
8.070
8.068
8.037
8.024
7.747
7.735
7.544
7.532
7.519
7.497
7.485
7.318
7.304
7.259
4.537
4.525
4.513
4.501
2.424
1.498
1.486
1.474
0.000
N
O
O
3.00
3.04
1.99
1.93
6.98
2.00
2.99
3.11
8
7
6
5
4
3
2
1
PPM


165.697
158.307
150.322
148.897
139.581
137.881
135.880
129.568
129.424
129.243
127.214
127.189
121.289
121.152
77.315
77.062
76.810
61.925
21.372
14.397
N
O
O
160
140
120
100
80
60
40
20
0 PPM

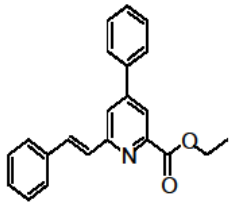

8.273
8.120
8.107
8.074
7.659
7.645
7.517
7.504
7.491
7.449
7.341
7.328
4.537
4.525
4.513
4.501
2.436
1.497
1.485
1.474
0.000
3.01
3.08
2.00
2.08
0.97
2.00
3.03
3.04
8
7
6
5
4
3
2
1
0
PPM

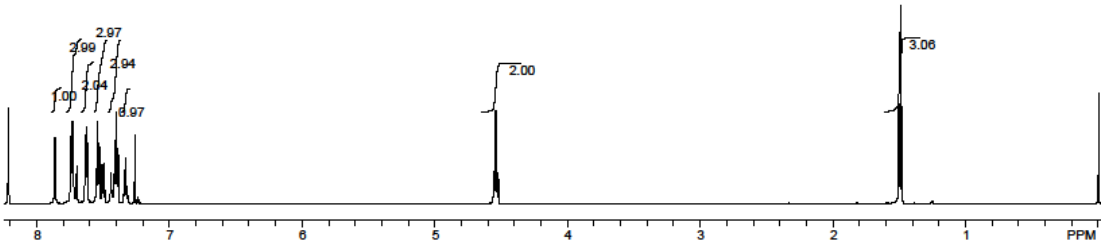

165.721
158.307
150.288
148.935
139.715
138.822
134.787
129.986
129.432
128.831
127.371
127.006
121.314
121.221
77.315
77.062
76.810
61.939
21.309
14.397
160
140
120
100
80
60
40
20
0
PPM

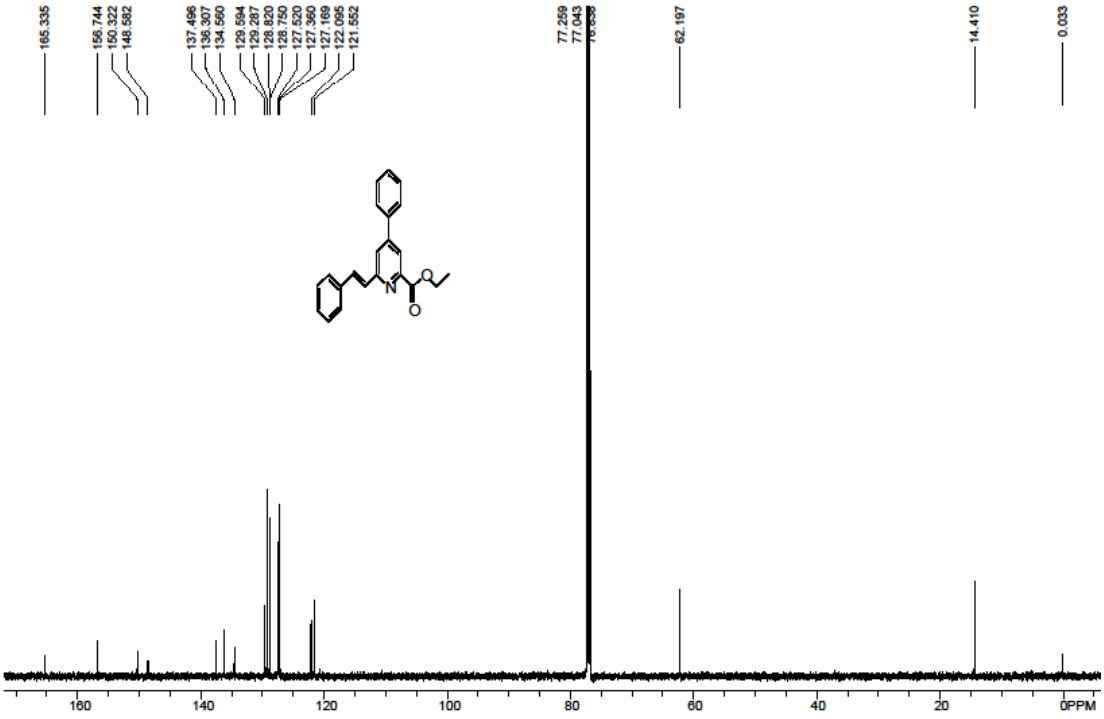

8.245
8.239
8.107
8.050
7.694
7.680
7.519
7.506
7.478
7.466
7.454
7.261
4.545
4.533
4.521
4.510
1.503
1.491
1.479
0.000
Cl
N
O
O
4.04
1.99
0.98
2.05
0.96
2.00
3.00
8
7
6
5
4
3
2
1
0PPM


165.459
158.517
149.237
149.084
138.444
136.161
135.839
129.658
129.530
128.914
128.491
127.408
121.288
77.252
77.048
76.834
62.111
14.405
Cl
N
O
O
160
140
120
100
80
60
40
20
PPM

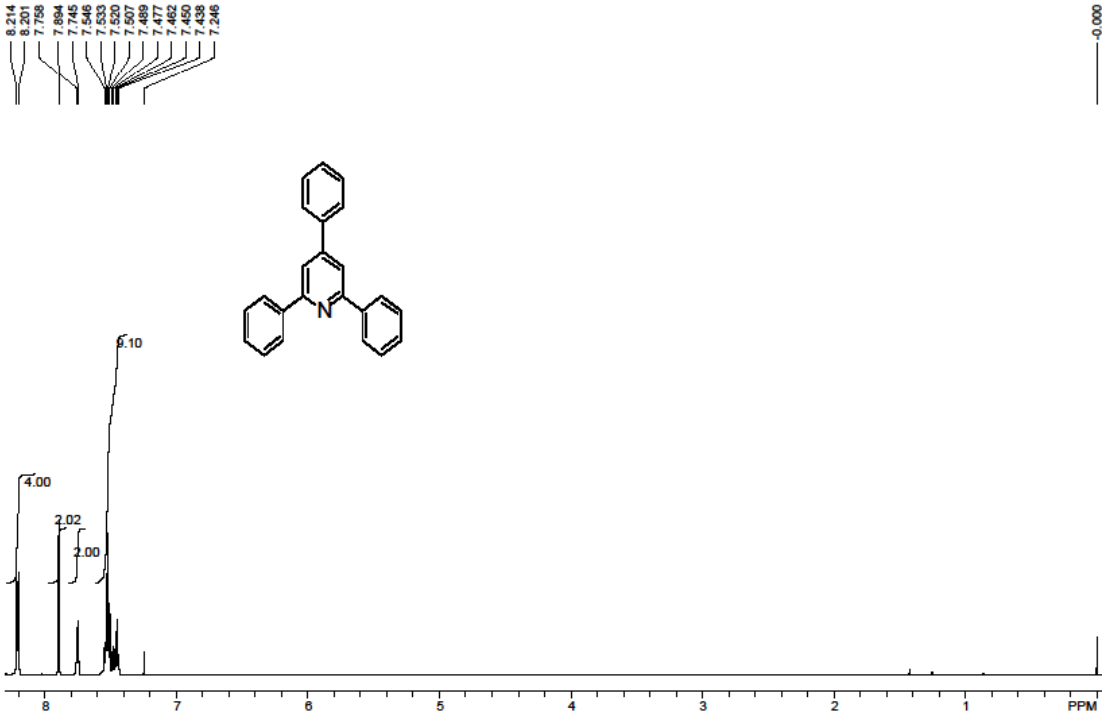

8.213
7.743
7.730
7.633
7.620
7.551
7.539
7.526
7.506
7.495
7.440
7.411
7.398
7.386
7.340
7.328
7.261
4.556
4.544
4.533
4.520
1.504
1.492
1.480
0.000

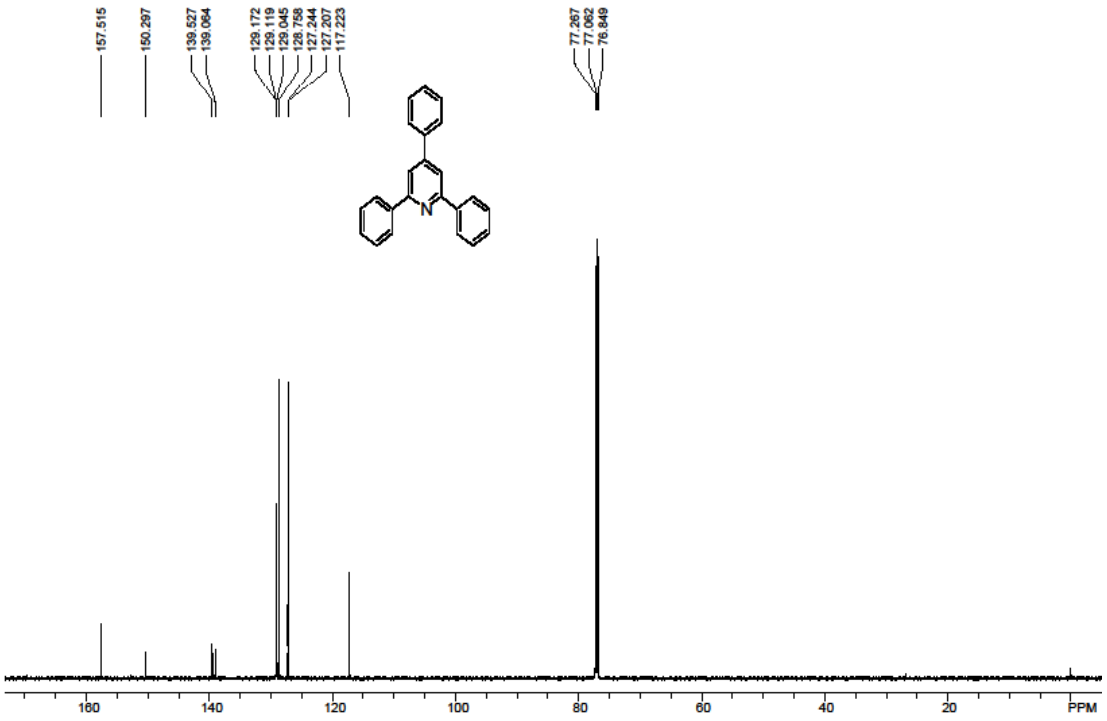

N
O
O

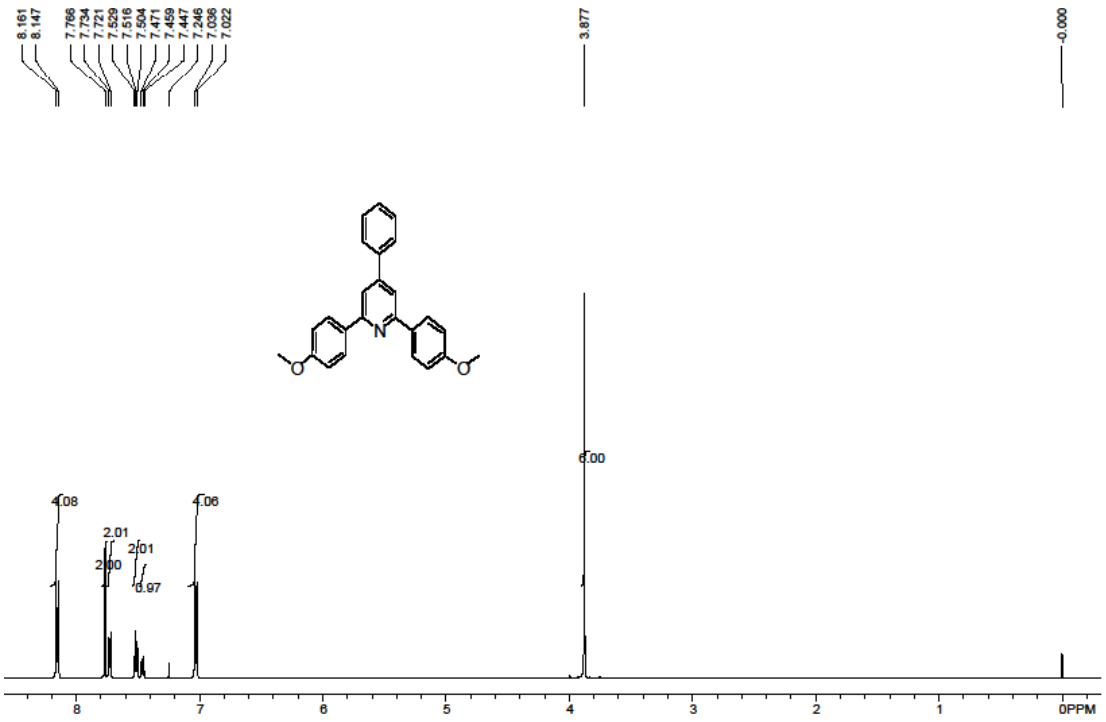

2.97
2.99
2.94
2.04
1.00
6.97
2.00
3.06
8
7
6
5
4
3
2
1
PPM

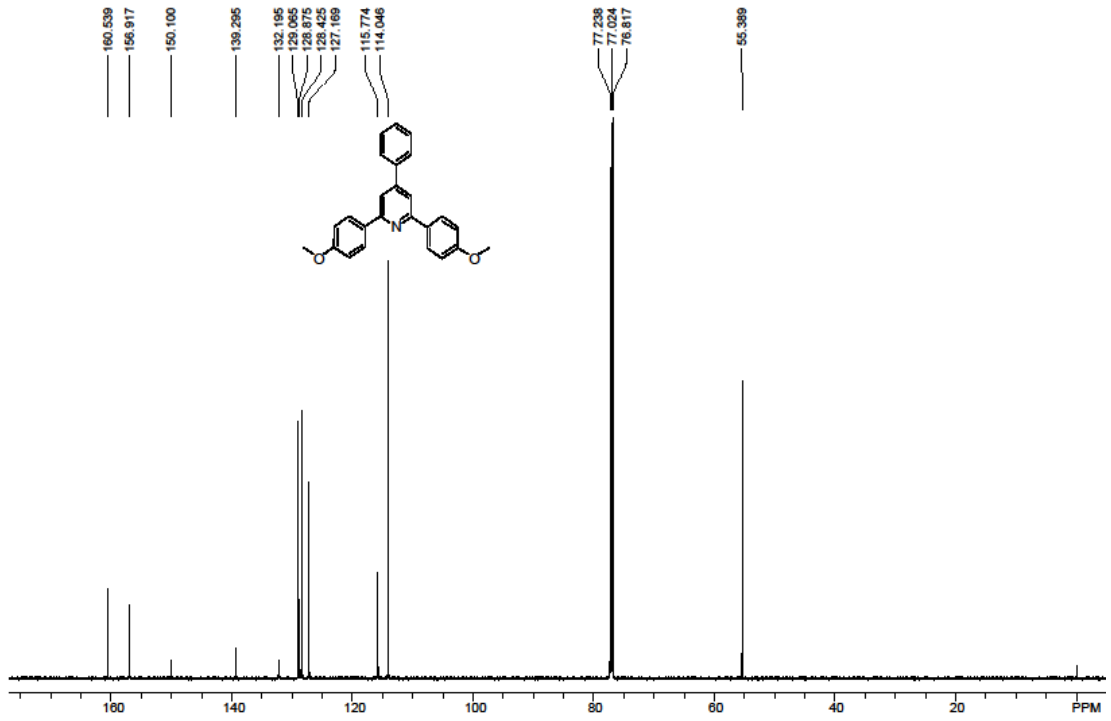

165.335
156.744
150.322
148.582
137.496
136.307
134.560
129.594
129.287
128.820
128.750
127.520
127.360
127.169
122.095
121.552
77.259
77.043
62.197
14.410
0.033
160
140
120
100
80
60
40
20
0PPM

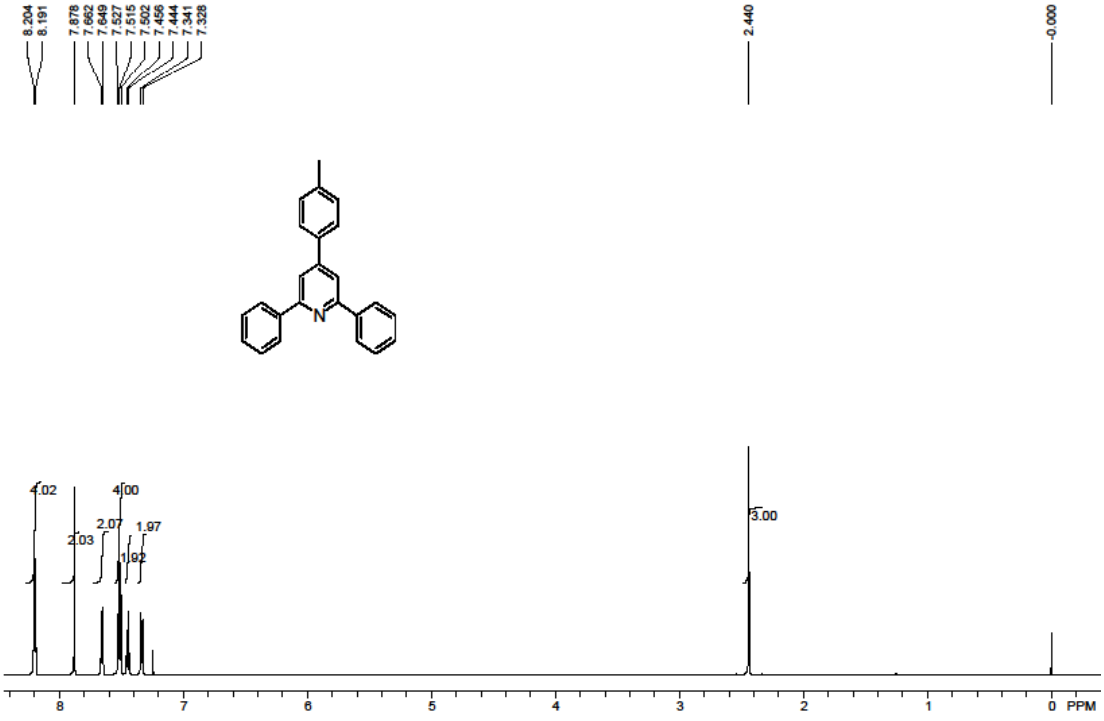
N
O
O

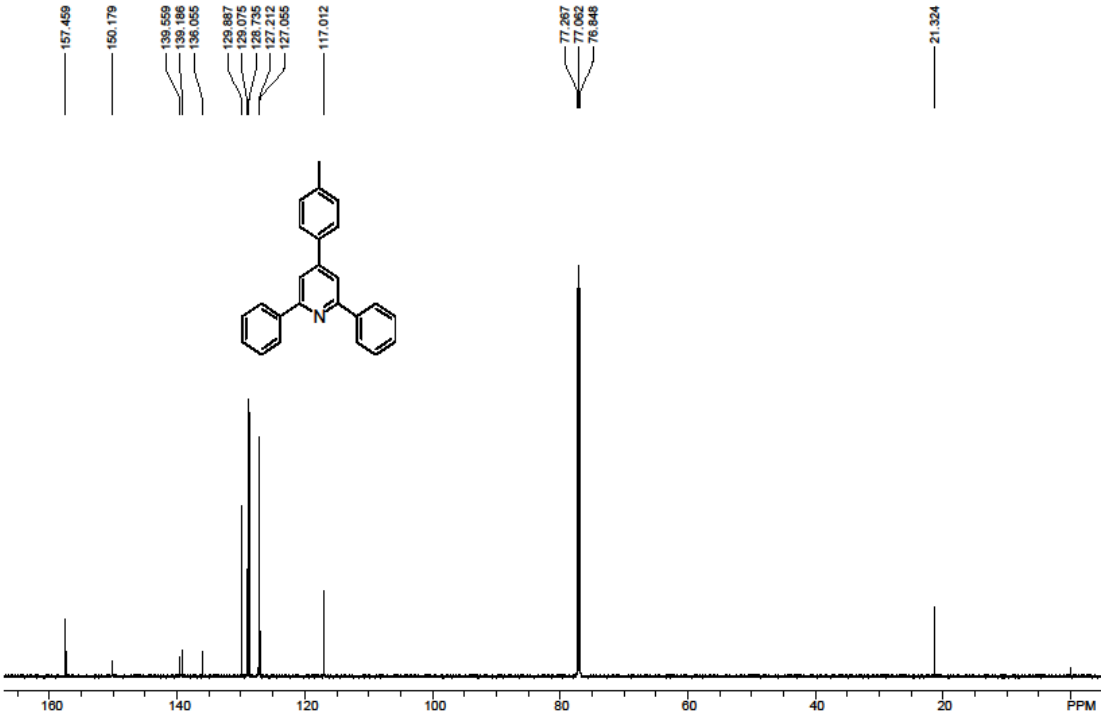

8.214
8.201
7.758
7.894
7.745
7.546
7.533
7.520
7.507
7.489
7.477
7.462
7.450
7.438
7.246
-0.000
N
9.10
4.00
2.02
2.00
8
7
6
5
4
3
2
1
PPM

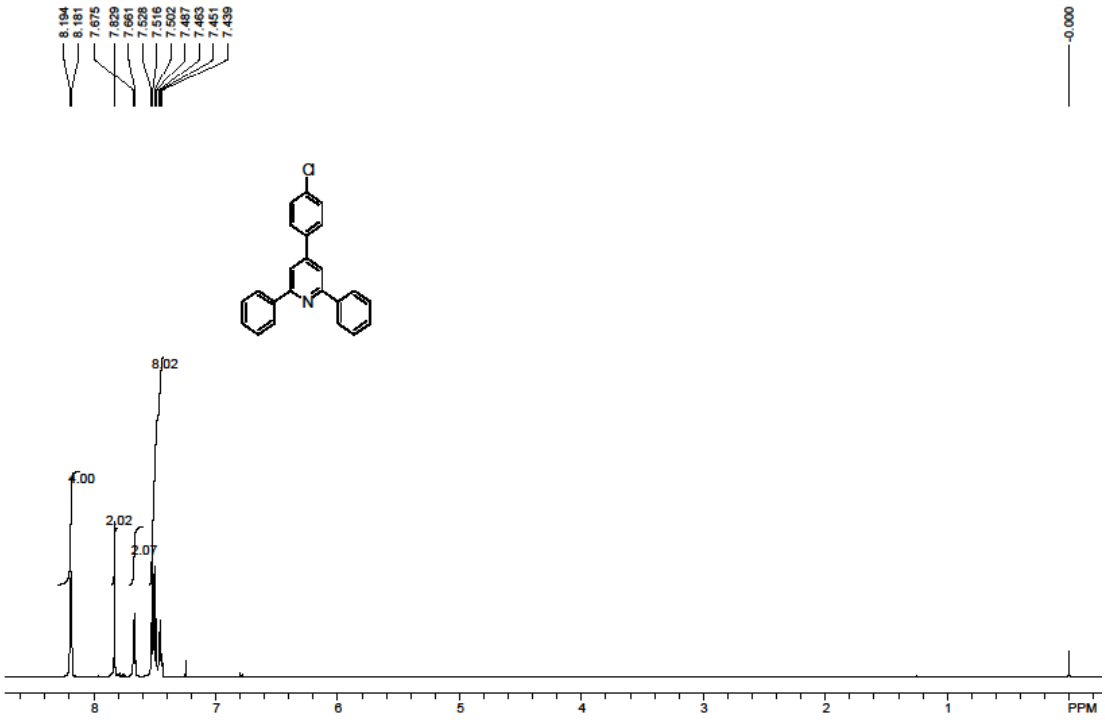

157.515
150.297
139.527
139.064
129.172
129.119
129.045
128.758
127.244
127.207
117.223
77.267
77.062
76.849
N
160
140
120
100
80
60
40
20
PPM

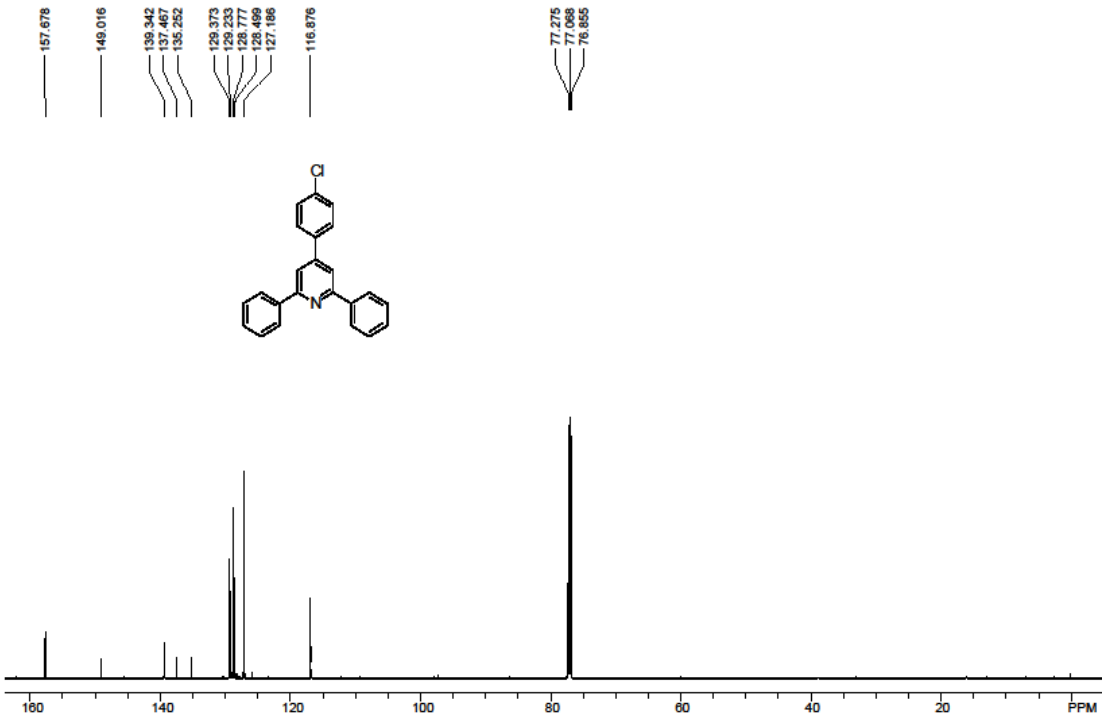

8.161
8.147
7.766
7.734
7.721
7.529
7.516
7.504
7.471
7.459
7.447
7.246
7.038
7.022
3.877
-0.000
6.00
4.08
4.06
2.01
2.00
2.01
0.97
8
7
6
5
4
3
2
1
0PPM


160.539
156.917
150.100
139.295
132.196
129.065
128.875
128.425
127.169
115.774
114.046
77.238
77.024
76.817
55.389
160
140
120
100
80
60
40
20
PPM

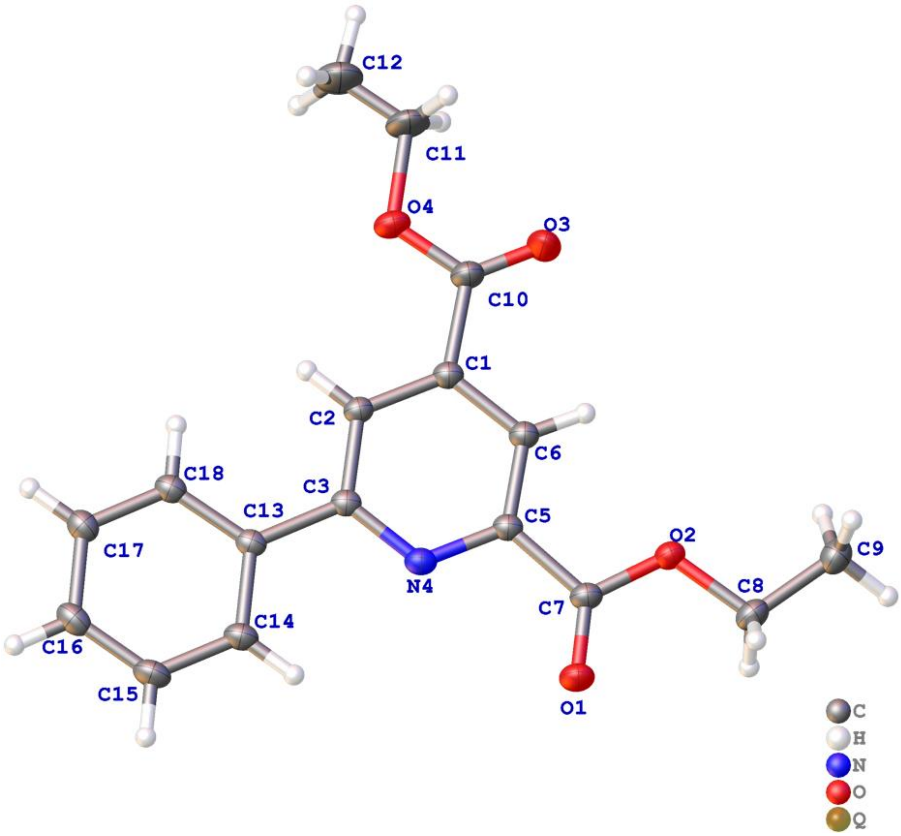

8.204
8.191
7.878
7.662
7.649
7.527
7.515
7.502
7.456
7.444
7.341
7.328
2.440
-0.000
4.02
2.03
2.07
4.00
1.92
1.97
3.00
8
7
6
5
4
3
2
1
0
PPM


157.459
150.179
139.559
139.186
136.055
129.887
129.075
128.735
127.212
127.055
117.012
77.267
77.062
76.848
21.324
160
140
120
100
80
60
40
20
PPM


8.194
8.181
7.675
7.829
7.661
7.528
7.516
7.502
7.487
7.463
7.451
7.439
0.000
Cl
N
8.02
4.00
2.02
2.07
8
7
6
5
4
3
2
1
PPM


157.678
149.016
139.342
137.467
135.252
129.373
129.233
128.777
128.499
127.186
116.876
77.275
77.068
76.855
Cl
N
160
140
120
100
80
60
40
20
PPM

3a X-Ray:



3a X-Ray: