Metal-free Michael Addition Initiated Multicomponent Oxidative Cyclodehydration Route to Polysubstituted Pyridines from 1,3 Dicarbonyls

Supporting Information

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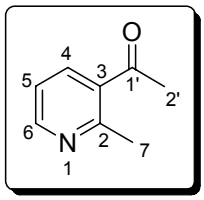
General Information : Melting points (mp) were determined with a Büchi Melting-point B-450 apparatus and were not corrected. ^{1}H and ^{13}C NMR spectra were recorded in solution respectively at 300.13 MHz and 75.47 MHz on a Bruker AC 300 spectrometer. NMR data were collected at ambient temperature, and chemical shifts were given in ppm referenced to the appropriate solvent peak. Data for ^{1}H NMR are reported as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quadruplet, dd = doublet of doublets, m = multiplet). Infrared (IR) spectra were recorded on a Perkin-Elmer 1600 Series FTIR spectrometer. Low and high-resolution mass spectra were recorded on an API 111 Plus Triple Quadrupole spectrometer (Sciex), and on a Bruker-Daltonics MALDI-ToF Autoflex spectrometer. Analytical thin layer chromatography was performed using 0.20 mm silica gel 60 plates. Flash chromatography was performed using 70-230 mesh silica gel 60 (Merck).

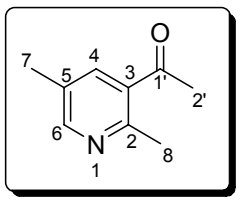
Typical Procedure : To a 50 mL two-necked round bottomed flask, equipped with a magnetic stirring bar and a reflux condenser, were added toluene freshly distilled over CaH_2 (25 mL), 4Å MS (6 g), substrate **1** (200 mg, 1.0 equiv.), freshly distilled acrolein **2** (1.5 equiv.), and ammonium acetate **3** (2.0 equiv.). The heterogeneous mixture was stirred at reflux for 24h. The solution was filtered through a short pad of Celite, which was thoroughly washed with toluene. The solvent was evaporated under reduced pressure to afford crude compound **4** with acceptable chemical purity. Pure product was isolated by flash chromatography over silica gel.

Description of pyridines



1-(2-Methyl-pyridin-3-yl)-ethanone 4a

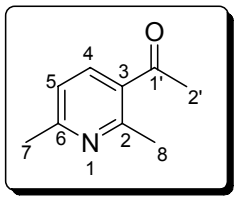
Yellow gum, 52% yield; R_f = 0.42 (AcOEt); **IR** (KBr, cm^{-1}) : 3051, 2957, 2926, 1691, 1583, 1435, 1357, 1277; **MS** (ESI) m/z (relative intensities (%)) : 136 $[M+H]^+$ (100), 153 $[M+NH_4]^+$ (22), 158 $[M+Na]^+$ (6); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 2.53 ($3H_{2'}$, s), 2.68 ($3H_7$, s), 7.17 ($1H_5$, dd, J = 7.8 Hz, J = 4.8 Hz), 7.90 ($1H_4$, dd, J = 8 Hz, J = 1.6 Hz)), 8.52 ($1H_6$, dd, J = 5 Hz, J = 1.6 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 24.6 (C_7), 29.2 ($C_{2'}$), 120.7 (C_5), 132.7 (C_3), 136.6 (C_4), 151.1 (C_6), 157.9 (C_2), 200.3 ($C_{1'}$).



1-(2,5-Dimethyl-pyridin-3-yl)-ethanone 4b

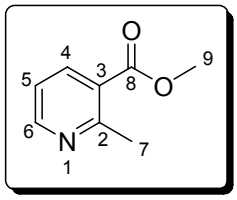
Orange oil, 65% yield; R_f = 0.29 (AcOEt/Hexanes 1/1); **IR** (KBr, cm^{-1}) : 2973, 2929, 1688, 1556, 1455, 1354, 1293, 1197; **MS** (ESI) m/z (relative intensities (%)) : 150 $[M+H]^+$ (100), 167 $[M+NH_4]^+$ (29), 172 $[M+Na]^+$ (7); **^{1}H NMR** ($CDCl_3$,

300.13 MHz) : 2.32 ($3H_7$, s), 2.54 ($3H_8$, s), 2.65 ($3H_{2'}$, s), 7.71 ($1H_4$, d, J = 2.1 Hz), 8.37 ($1H_6$, d, J = 1.8 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 17.8 (C_7), 24.0 (C_8), 29.3 ($C_{2'}$), 130.2 (C_5), 132.3 (C_3), 137.1 (C_4), 151.5 (C_6), 154.8 (C_2), 200.6 ($C_{1'}$).



1-(2,6-Dimethyl-pyridin-3-yl)-ethanone 4c

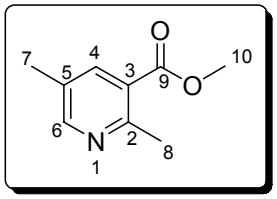
Beige gum; 62% yield; R_f = 0.45 (AcOEt/Hexanes 1/1); **IR** (KBr, cm^{-1}) : 2915, 1686, 1588, 1561, 1433, 1256; **MS** (ESI) m/z (relative intensities(%)) : 150 $[M+H]^+$ (100), 167 $[M+NH_4]^+$ (20), 172 $[M+Na]^+$ (5); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 2.57 ($3H_7$+$3H_8$, s), 2.73 ($3H_{2'}$, s), 7.07 ($1H_5$, d, J = 7.8 Hz), 7.88 ($1H_4$, d, J = 7.8 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 24.3 (C_8), 24.5 (C_7), 28.9 ($C_{2'}$), 120.1 (C_5), 129.6 (C_3), 137.2 (C_4), 157.6 (C_6), 160.5 (C_2), 199.7 ($C_{1'}$).



2-Methyl-nicotinic acid methyl ester 4d

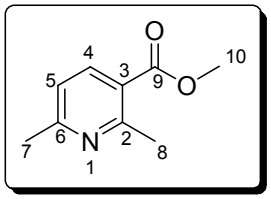
Yellow oil; 56% yield; R_f = 0.39 (AcOEt/Hexanes 1/1); **IR** (KBr, cm^{-1}) : 2953, 1724, 1435, 1281, 1258, 1088; **MS** (ESI) m/z (relative intensity (%)) : 152 $[M+H]^+$ (100), 174 $[M+Na]^+$ (69), 190 $[M+K]^+$ (4); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 2.83

($3H_7$, s), 3.91 ($3H_9$, s), 7.20 ($1H_5$, dd, J = 8.1 Hz, J = 4.8 Hz), 8.18 ($1H_4$, dd, J = 7.8 Hz, J = 1.8 Hz), 8.60 ($1H_6$, dd, J = 4.8 Hz, J = 1.8 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 24.6 (C_7), 52.0 (C_9), 120.7 (C_5), 125.1 (C_3), 138.2 (C_4), 151.6 (C_6), 159.7 (C_2), 166.7 (C_8).



2,5-Dimethyl-nicotinic acid methyl ester 4e

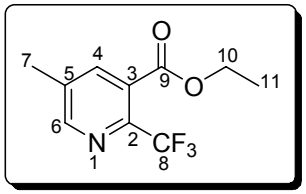
Yellow oil; 44% yield; R_f = 0.42 (AcOEt/Hexanes 1/1); **IR** (KBr, cm^{-1}) : 2952, 1723, 1459, 1436, 1297, 1256, 1205, 1089; **MS** (ESI) m/z (relative intensities (%)) : 166 $[M+H]^+$ (100), 188 $[M+Na]^+$ (74), 204 $[M+K]^+$ (7); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 2.21 ($3H_7$, s), 2.65 ($3H_8$, s), 3.78 ($3H_{10}$, s), 7.86 ($1H_4$, d, J = 1.8 Hz), 8.30 ($1H_6$, d, J = 1.8 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 17.4 (C_7), 23.9 (C_8), 51.8 (C_{10}), 124.4 (C_3), 130.0 (C_5), 138.4 (C_4), 151.9 (C_6), 156.5 (C_2), 166.7 (C_9).



2,6-Dimethyl-nicotinic acid methyl ester 4f

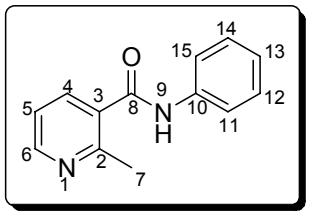
Yellow oil; 65% yield; R_f = 0.34(AcOEt/Hexanes 1/3); **IR** (KBr, cm^{-1}) : 3052, 2952, 1724, 1669, 1593, 1435, 1278, 1264, 1086; **MS** (ESI) m/z (relative intensities (%)) : 166 $[M+H]^+$ (100), 188 $[M+Na]^+$ (62), 204 $[M+K]^+$ (9); **^{1}H NMR**

($CDCl_3$, 300.13 MHz) : 2.49 ($3H_7$, s), 2.73 ($3H_8$, s), 3.82 ($3H_{10}$, s), 6.97 ($1H_5$, d, J = 8.1 Hz), 8.01 ($1H_4$, d, J = 8.1 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 24.5 (C_7), 24.7 (C_8), 51.9 (C_{10}), 120.3 (C_5), 122.2 (C_3), 138.6 (C_4), 159.4 (C_6), 161.2 (C_2), 166.9 (C_9).



2-trifluoromethyl-5-methyl-nicotinic acid ethyl ester 4g

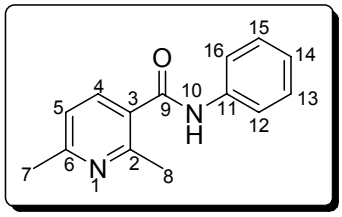
Yellow oil; 70% yield; R_f = 0.21(AcOEt/Hexanes 1/3); **IR** (KBr, cm^{-1}) : 3029, 2964, 2285, 1576, 1411, 1346, 1255, 1068, 1031; **MS** (ESI) m/z (relative intensities (%)) : 256 $[M+Na]^+$ (100), 234 $[M+H]^+$ (1); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 1.35 ($3H_{11}$, t, J = 7.8 Hz), 2.41 ($3H_7$, s), 4.36 ($2H_{10}$, q, J = 7.1 Hz), 7.85 ($1H_4$, s), 8.55 ($1H_6$, s); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 13.7 (C_{11}), 18.0 (C_7), 62.4 (C_{10}), 121.2 (C_8, q, J = 273 Hz), 127.5 (C_3), 136.6 (C_5), 138.3 (C_4), 142.8 (C_2, q, J = 35 Hz), 151.0 (C_6), 165.6 (C_9); **^{19}F NMR** ($CDCl_3$, 282.40 MHz) : -64.5 ($3F_8$, s).



2-Methyl-N-phenyl-nicotinamide 4h

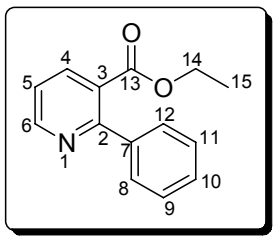
Beige solid (Pf = 111-112°C); 61% yield; R_f = 0.27 (AcOEt); **IR** (KBr, cm^{-1}) : 3294, 3054, 2986, 1677, 1599, 1523, 1442, 1265 ; **MS** (ESI) m/z (relative intensities (%)) : 213 $[M+H]^+$ (100), 230 $[M+NH_4]^+$ (68), 235 $[M+Na]^+$ (39),

251 $[M+K]^+$ (17); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 2.66 ($3H_7$, s), 7.12-7.19 ($2H_{13and5}$, m), 7.36 ($2H_{12and14}$, t, J = 7.8 Hz), 7.60 ($2H_{11and15}$, d, J = 7.8 Hz), 7.71 ($1H_4$, d, J = 6.6 Hz), 7.97 ($1H_9$, br s), 8.52 ($1H_6$, dd, J = 4.8 Hz, J = 1.8 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 22.9 (C_7), 120.0 (C_5), 120.8 ($2C_{12and14}$), 124.9 (C_{13}), 129.1 ($2C_{11and15}$), 131.9 (C_3), 134.6 (C_4), 137.6 (C_{10}), 150.3 (C_6), 156.2 (C_2), 166.6 (C_8).



2,6-Dimethyl-N-phenyl-nicotinamide 4i

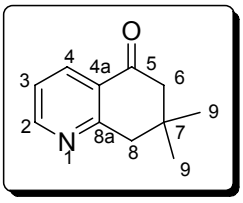
Beige gum; 42% yield; R_f = 0.39 (AcOEt); **IR** (KBr, cm^{-1}) : 3295, 3054, 2963, 2927, 1656, 1596, 1441, 1322; **MS** (ESI) m/z (relative intensities (%)) : 227 $[M+H]^+$ (100), 244 $[M+NH_4]^+$ (65), 249 $[M+Na]^+$ (31), 265 $[M+K]^+$ (14); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 2.55 ($3H_8$, s), 2.68 ($3H_7$, s), 7.03 ($1H_5$, d, 7.8 Hz), 7.16 ($1H_{14}$, t, J = 7.2 Hz), 7.36 ($2H_{13and15}$, t, J = 7.5 Hz), 7.59-7.67 (4H, m); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 23.0 (C_8), 24.5 (C_7), 120.0 (C_5), 120.3 ($2C_{13and15}$), 124.8 (C_{14}), 128.9 (C_3), 129.1 ($2C_{12and16}$), 135.1 (C_4), 137.7 (C_{11}), 155.7 ($2C_{2and6}$), 159.7 (C_9).



2-Phenyl-nicotinic acid ethyl ester 4j

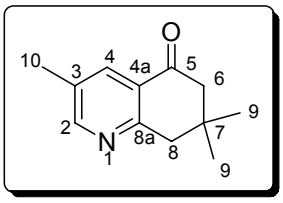
Yellow oil; 48% yield; R_f = 0.36 (AcOEt/Hexanes 1/3); **IR** (KBr, cm^{-1}) : 3061, 2981, 2937, 1723, 1582, 1561, 1430, 1282; **MS** (ESI) m/z (relative

intensities(%)) : 228 $[M+H]^+$, 245 $[M+NH_4]^+$, 250 $[M+Na]^+$, 266 $[M+K]^+$; **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 1.03 ($3H_{15}$, t, J = 7.1 Hz), 4.14 ($2H_{14}$, q, J = 7.2 Hz), 7.33 ($1H_5$, dd, J = 7.8 Hz, J = 4.8 Hz), 7.40-7.54 ($5H_{8to12}$, m), , 8.09 ($1H_4$, dd, J = 7.8 Hz, J = 2 Hz), 8.76 ($1H_6$, dd, J = 4.8 Hz, J = 1.8 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 13.5 (C_{15}), 61.4 (C_{14}), 121.5 (C_5), 127.3 (C_3), 128.0 (C_{9and11}), 128.4 (C_{8and12}), 128.5 (C_{10}), 137.8 (C_4), 140.1 (C_7), 151.1 (C_6), 158.8 (C_2), 168.1 (C_{13}).



7,7-Dimethyl-7,8-dihydro-6H-quinolin-5-one 4k

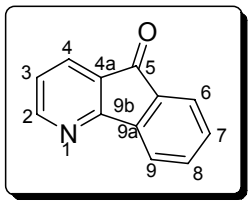
Orange oil; 51% yield; R_f = 0.22 (AcOEt/Hexanes 1/3); **IR** (KBr, cm^{-1}) : 3053, 2957, 2871, 1691, 1583, 1459, 1432, 1425, 1302, 1284; **MS** (ESI) m/z (relative intensities(%)) : 176 $[M+H]^+$ (100), 193 $[M+NH_4]^+$ (23), 198 $[M+Na]^+$ (16); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 1.09 ($6H_9$, s), 2.53 ($2H_6$, s), 3.02 ($2H_8$, s), 7.26 ($1H_3$, dd, J = 4.3 Hz, J = 7.6 Hz), 8.23 ($1H_4$, dd, J = 7.8 Hz, J = 1.5 Hz), 8.67 ($1H_2$, dd, J = 4.8 Hz, J = 1.5 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 28.0 ($2C_9$), 32.7 (C_7), 46.1 (C_8), 51.8 (C_6), 122.0 (C_3), 127.0 (C_{4a}), 134.3 (C_4), 153.6 (C_2), 162.0 (C_{8a}),197.8 (C_5).



3,7,7-Trimethyl-7,8-dihydro-6H-quinolin-5-one 4l

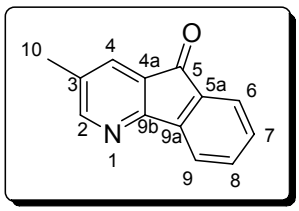
Yellow oil; 44% yield; R_f = 0.20 (AcOEt/Hexanes 1/3); **IR** (KBr, cm^{-1}) :

2958, 2868, 1690, 1647, 1465, 1302, 1283, 1217, 1195; **MS** (ESI) m/z (relative intensities(%)) : 190 $[M+H]^+$ (100), 207 $[M+NH_4]^+$ (27), 212 $[M+Na]^+$ (12), 228 $[M+K]^+$ (4); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 1.06 ($6H_9$, s), 2.33 ($3H_{10}$, s), 2.48 ($2H_6$, s), 2.95 ($2H_8$, s), 8.01 ($1H_4$, d, J = 1.6Hz), 8.48 ($1H_2$, d, J = 1.6Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 17.9 (C_{10}), 28.1 ($2C_9$), 32.9 (C_7), 45.8 (C_8), 52.0 (C_6), 126.5 (C_3), 131.7 (C_{4a}), 134.5 (C_4), 154.3 (C_2), 159.2 (C_{8a}), 198.3 (C_5).



Indeno[1,2-b]pyridin-5-one 4m

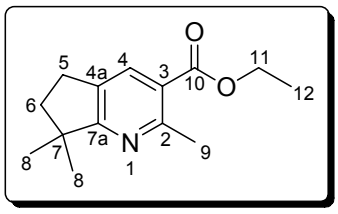
Red solid (Pf = 128-130°C, *litt* 132-136°C); 50% yield; R_f = 0.5 (AcOEt/Hexanes 1/1); **IR** (KBr, cm^{-1}) : 3051, 2917, 2844, 1710, 1591, 1569, 1403; **MS** (ESI) m/z (relative intensities (%)) : 182 $[M+H]^+$ (100), 199 $[M+NH_4]^+$ (38), 204 $[M+Na]^+$ (24), 220 $[M+K]^+$ (12); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 7.21 ($1H_3$, t, J = 5.1 Hz), 7.44 ($1H_7$, t, J = 7.5 Hz), 7.61 ($1H_8$, t, J = 7.5 Hz), 7.73 ($1H_4$, d, J = 7.5 Hz), 7.84-7.91 ($2H_{6and9}$, m), 8.61 ($1H_2$, d, J = 5.1 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 121.0 (C_9), 123.3 (C_3), 124.2 (C_6), 128.4 (C_{4a}), 131.0 (C_4), 131.4 (C_7), 134.8 (C_{5a}), 135.4 (C_8), 143.5 (C_{9a}), 154.0 (C_2), 165.1 (C_{9b}), 191.8 (C_5).



3-methyl-indeno[1,2-b]pyridin-5-one 4n

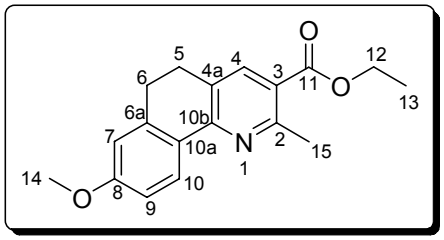
Orange solid (Pf = 122-124°C); 72% yield; R_f = 0.32 (AcOEt/Hexanes

1/3); **IR** (KBr, cm^{-1}) : 3054, 2926, 2841, 1711, 1587, 1569, 1405; **MS** (ESI) m/z (relative intensities (%)) : 196 $[M+H]^+$ (100), 213 $[M+NH_4]^+$ (44), 218 $[M+Na]^+$ (29), 234 $[M+K]^+$ (11); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 2.37 ($3H_{10}$, s), 7.38 ($1H_7$, dt, J = 7.5 Hz, J = 0.9 Hz), 7.55 ($1H_8$, dd, J = 7.4 Hz, J = 1.1 Hz), 7.59 ($1H_4$, d, J = 1.2 Hz), 7.68 ($1H_6$, d, J = 6.3 Hz), 7.79 ($1H_9$, d, 7.5 Hz), 8.42 ($1H_2$, d, J = 1.5 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 18.5 (C_{10}), 120.4 (C_7), 123.9 (C_9), 128.1 (C_3), 130.4 (C_6), 131.8 (C_{4a}), 133.2 (C_8), 134.8 (C_{5a}), 135.2 (C_4), 143.5 (C_{9a}), 154.1 (C_2), 162.5 (C_{9b}),191.9 (C_5).



2,7,7-Trimethyl-6,7-dihydro-5H-[1]pyrindine-3-carboxylic acid ethyl ester 4o

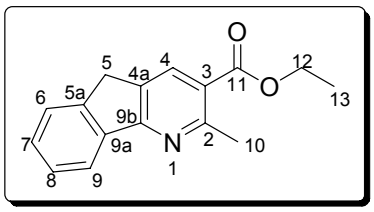
Colorless oil; 83% yield; R_f = 0.6 (AcOEt/Hexanes 1/5); **IR** (KBr, cm^{-1}) : 2957, 2864, 1723, 1604, 1562, 1265, 1237; **MS** (ESI) m/z (relative intensities(%)) : 234 $[M+H]^+$ (100), 251 $[M+NH_4]^+$ (74), 256 $[M+Na]^+$ (54), 272 $[M+K]^+$ (32); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 1.28 ($6H_8$, s),1.38 ($3H_{12}$, t, J = 6.9 Hz), 1.97 ($2H_6$, t, J = 7.2 Hz), 2.79 ($3H_9$, s), 2.84 ($2H_5$, t, J = 7.2 Hz), 4.34 ($2H_{11}$, q, J = 6.9 Hz), 7.94 ($1H_4$, s); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 14.3 (C_{12}), 24.8 (C_9), 26.8 ($2C_8$), 39.7 (C_{5and6}), 44.1 (C_7), 60.9 (C_{11}), 123.2 (C_3), 132.7 (C_{4a}), 134.2 (C_4), 158.4 (C_2), 167.3 (C_{7a}), 174.0 (C_{10}).



8-Methoxy-2-methyl-5,6-dihydro-benzo[h]quinoline-3-carboxylic acid ethyl ester 4p

White solid (Pf = 119-120°C); 55% yield; R_f = 0.41

(AcOEt/EP 1/7); **IR** (KBr, cm^{-1}) : 2980, 2938, 2828, 1705, 1595, 1503, 1440, 1305, 1256, 1233; **MS** (ESI) m/z (relative intensities(%)) : 298 $[M+H]^+$ (100), 315 $[M+NH_4]^+$ (69), 320 $[M+Na]^+$ (51), 336 $[M+K]^+$ (22); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 1.41 ($3H_{13}$, t, J = 7.2 Hz), 2.86 ($3H_{15}$, s), 2.92 ($4H_{5et6}$, s), 3.86 ($3H_{14}$, s), 4.37 ($2H_{12}$, q, J = 7.2 Hz), 6.76 ($1H_7$, d, J = 2.0 Hz), 6. 90 ($1H_9$, dd, J = 8.7 Hz, J = 2.0 Hz), 7.98 ($1H_4$, s); 8.32 ($1H_{10}$, d, J = 8.7 Hz); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 14.3 (C_{13}), 24.9 (C_{15}), 27.3 (C_6), 28.4 (C_5), 55.3 (C_{14}), 60.9 (C_{12}), 112.7 (C_7), 113.1 (C_9), 122.5 (C_{4a}), 126.9 (C_3), 127.4 (C_4), 127.5 (C_{6a}), 137.6 (C_{10}), 140.7 (C_{10a}), 154.3 (C_8), 158.0 (C_2), 161.0 (C_{10b}), 166.8 (C_{11}).

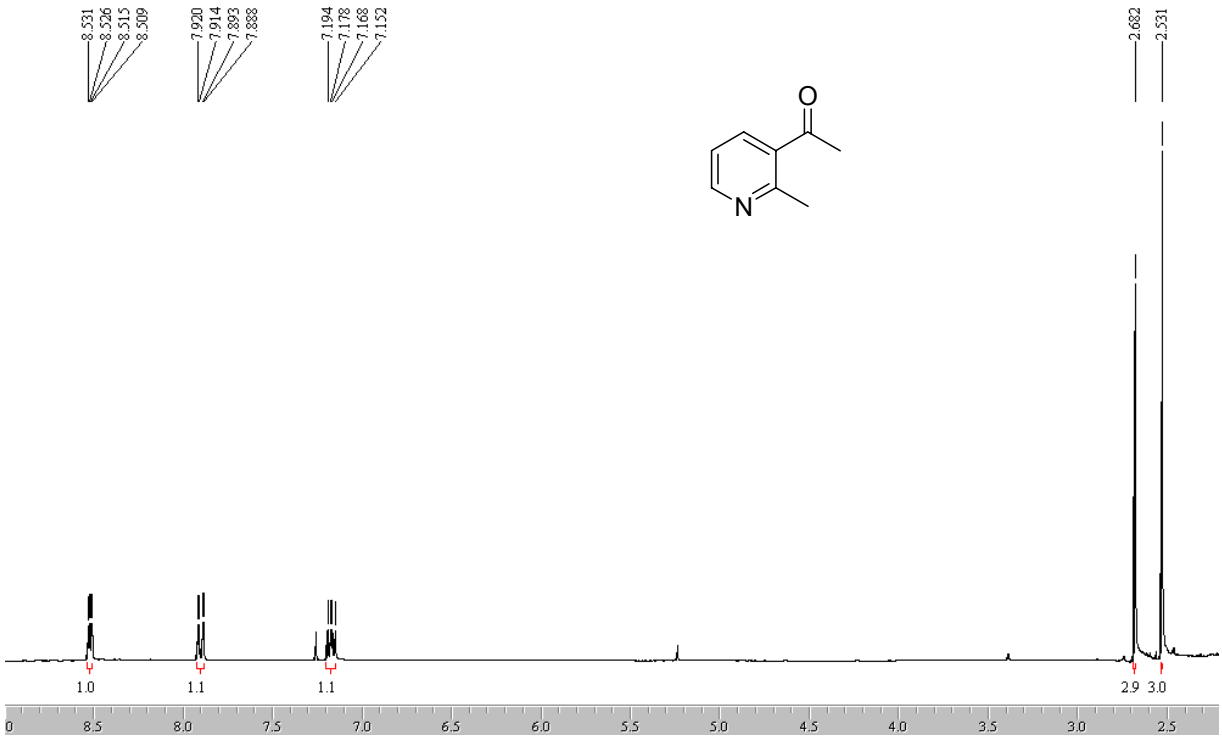


2-Methyl-5H-indeno[1,2-b]pyridine-3-carboxylic acid ethyl ester 4q

Yellow solid (Pf = 88-90°C); 58% yield; R_f = 0.32 (AcOEt/Hexanes 1/3); **IR** (KBr, cm^{-1}) : 2978, 2926, 1719, 1603, 1394, 1289, 1240, 1100, 1077; **MS** (ESI) m/z (relative intensities(%)) : 254 $[M+H]^+$ (100), 271 $[M+NH_4]^+$ (44), 276 $[M+Na]^+$ (41), 292 $[M+K]^+$ (16); **^{1}H NMR** ($CDCl_3$, 300.13 MHz) : 1.43 ($3H_{13}$, t, J = 7.2 Hz), 2.94 ($3H_{10}$, s), 3.88 ($2H_5$, s), 4.40 ($2H_{12}$, q, J = 7.2 Hz), 7.45-7.47 ($2H_{7and8}$, m), 7.57-7.60 ($1H_6$, m), 8.13-8.16 ($1H_9$, m), 8.32 ($1H_4$, s); **^{13}C NMR** ($CDCl_3$, 75.47 MHz) : 14.3 (C_{13}), 25.2 (C_{10}), 34.1 (C_5), 61.1 (C_{12}), 121.7 (C_9), 122.8 (C_{4a}), 125.3 (C_6), 127.4 (C_8), 129.5 (C_7), 133.6 (C_3), 134.4 (C_4), 140.2 (C_{5a}), 145.1 (C_{9a}), 159.5 (C_2), 162.6 (C_{9b}), 167.1 (C_{11}).

NMR data

Compound 4a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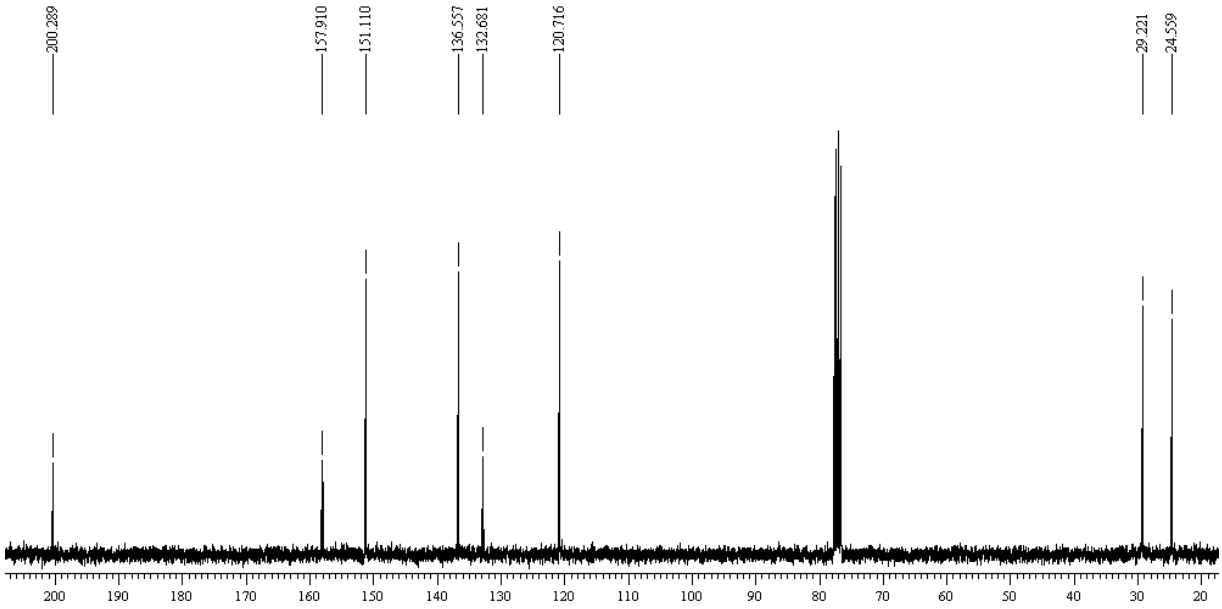
8.515
8.509
7.920
7.914
7.893
7.888
7.194
7.178
7.168
7.152
2.682
2.531
O
N
1.0
1.1
1.1
2.9
3.0
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5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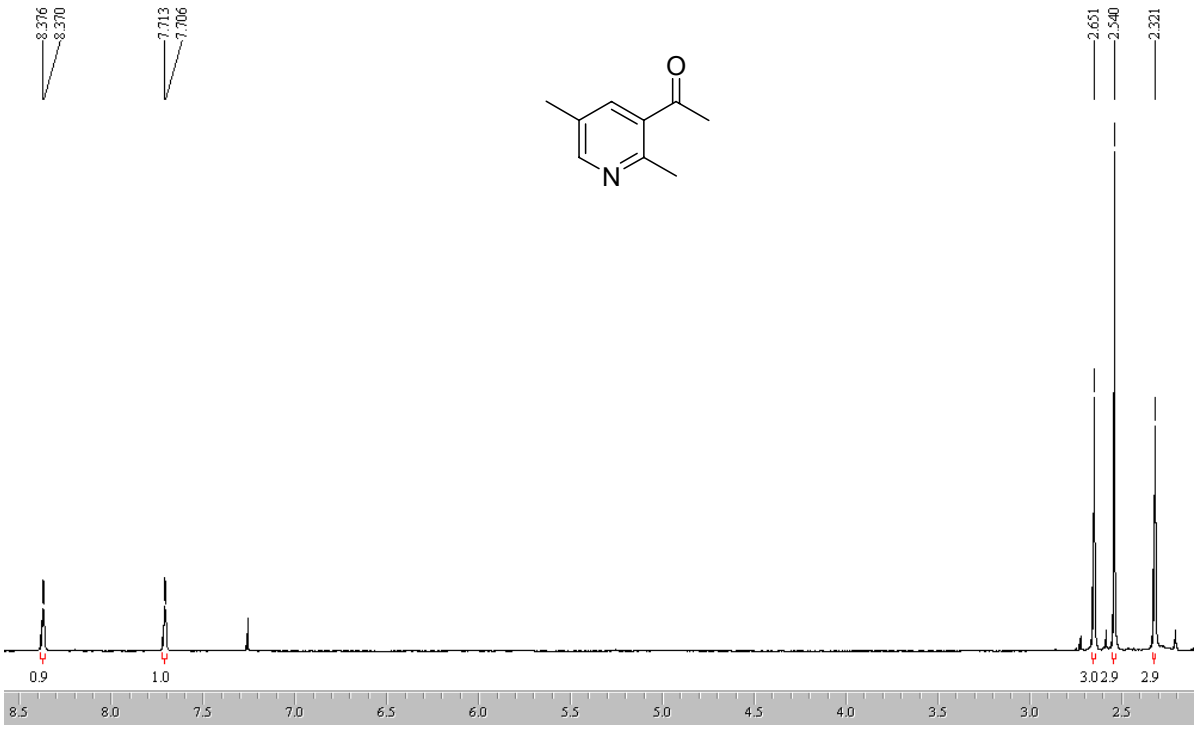
157.910
151.110
136.557
132.681
120.716
29.221
24.559
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

Compound 4b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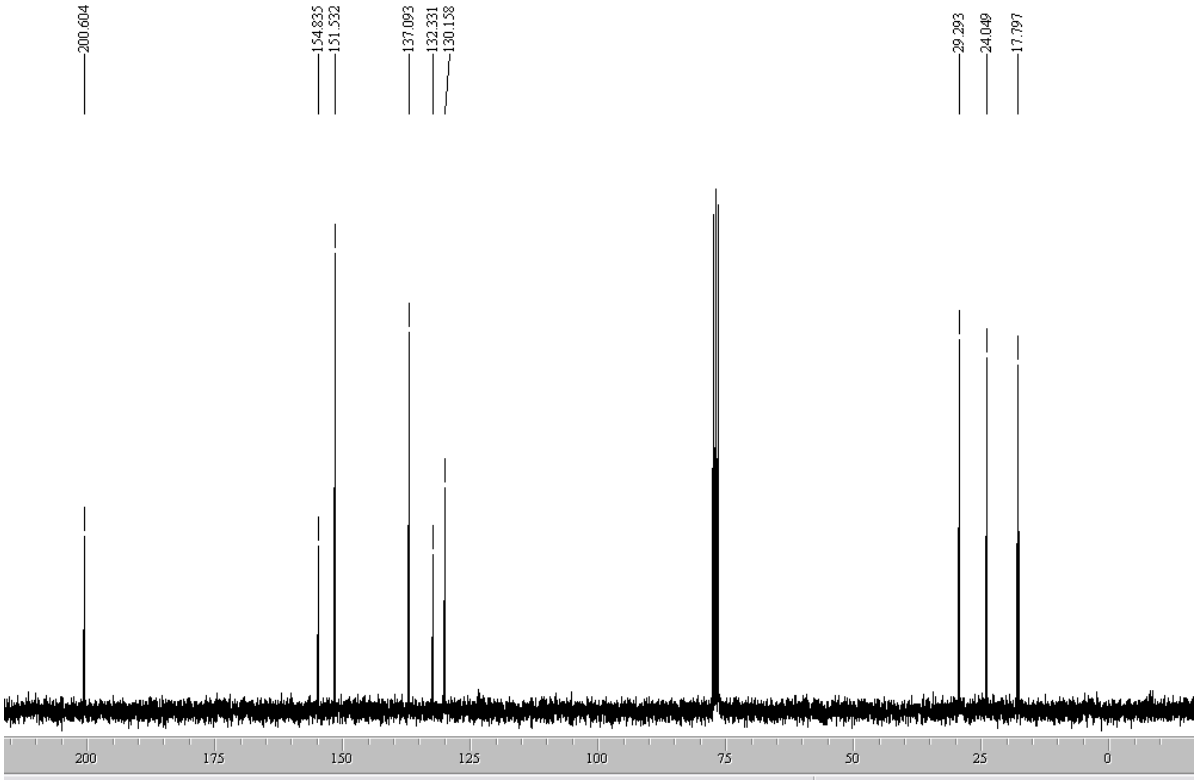
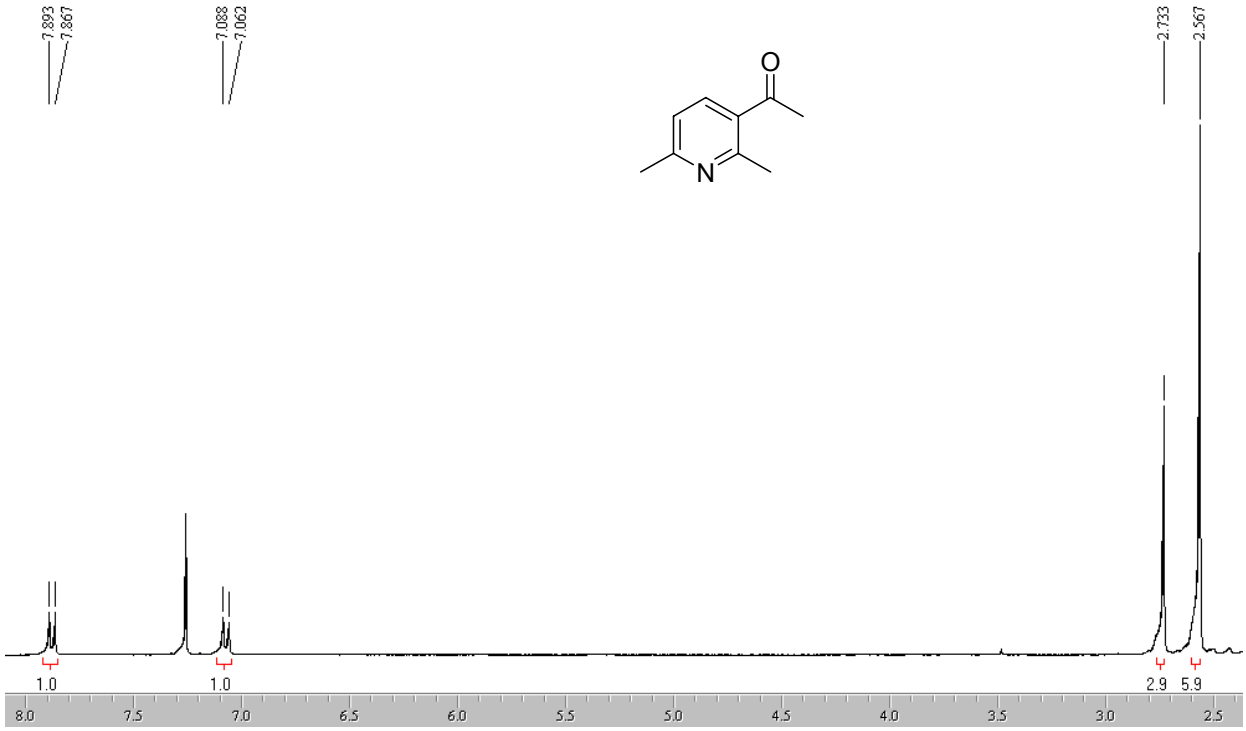
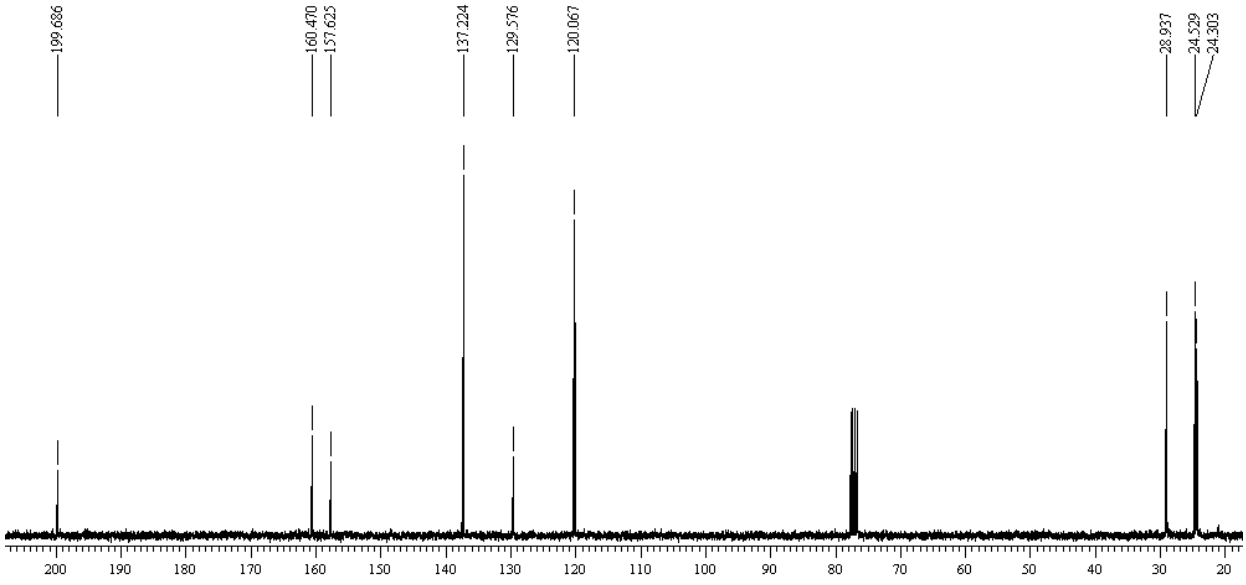
8.370
7.713
7.706
2.651
2.540
2.321
O
N
0.9
1.0
3.0
2.9
2.9
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5

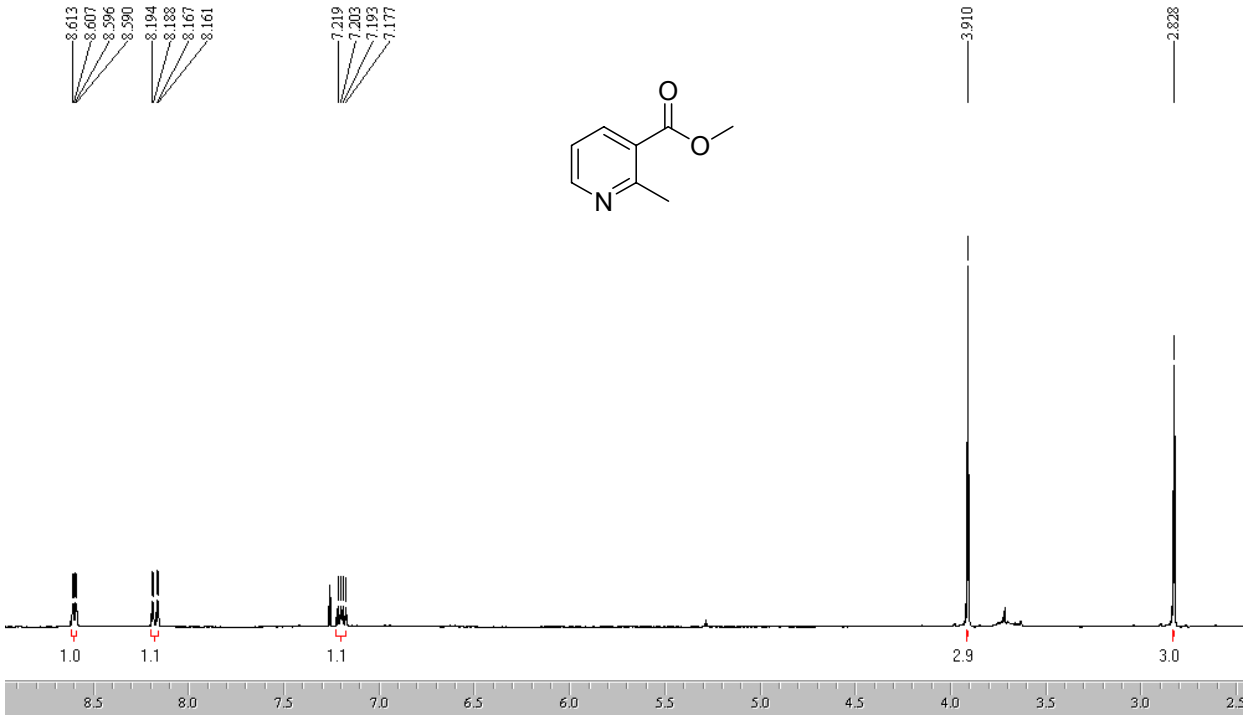

200.604
154.835
151.532
137.093
132.331
130.158
29.293
24.049
17.797
200
175
150
125
100
75
50
25
0

Compound 4c


7.893
7.867
7.088
7.062
2.733
2.567
O
N
1.0
1.0
2.9
5.9
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5


199.686
160.470
157.625
137.224
129.576
120.067
28.937
24.529
24.303
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

Compound 4d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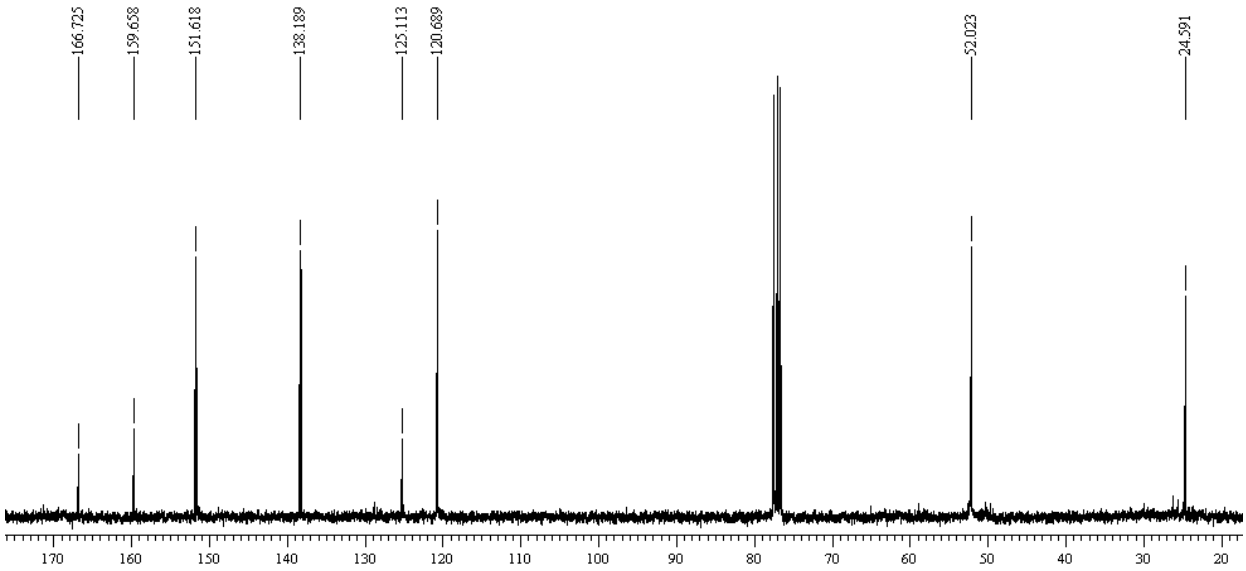
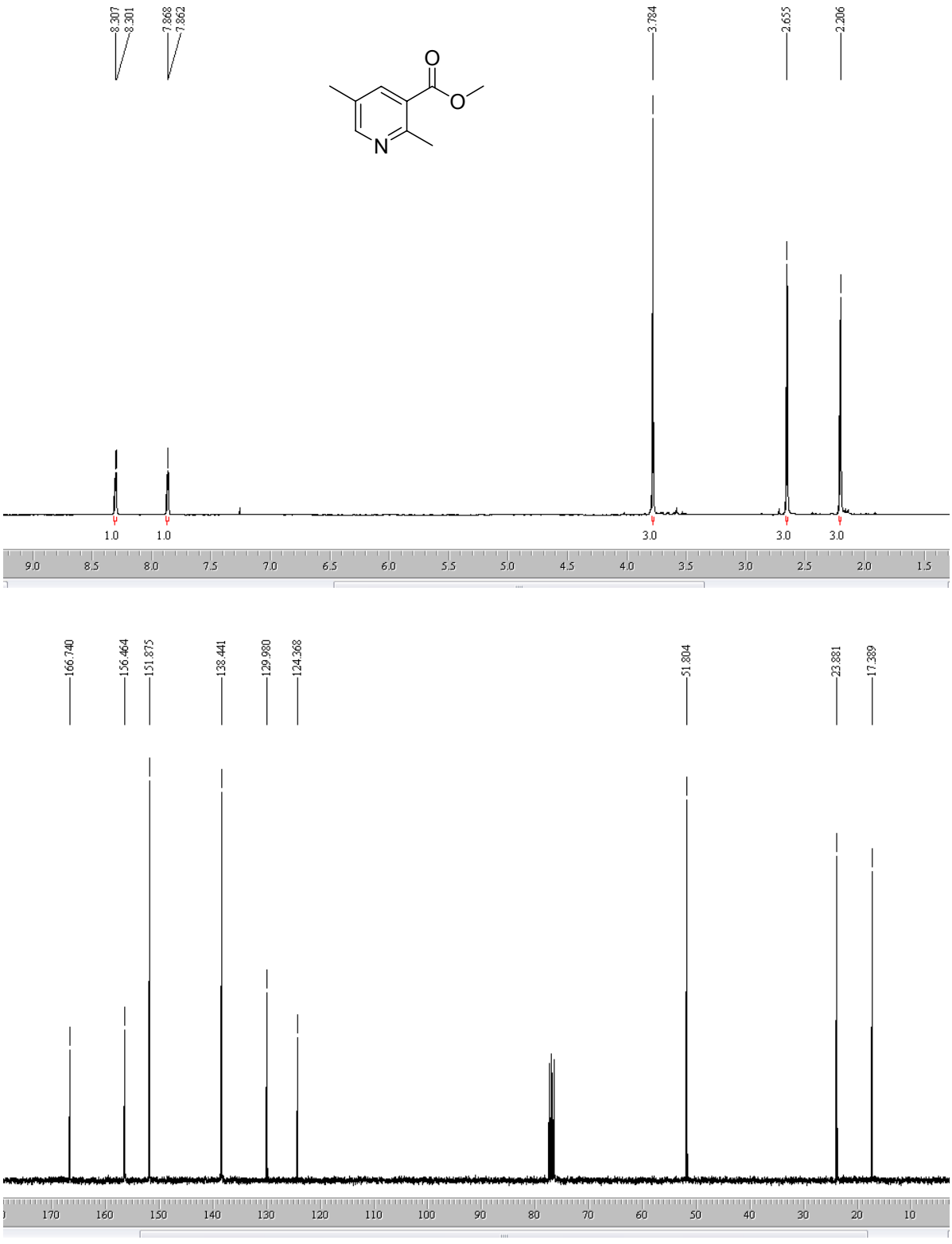
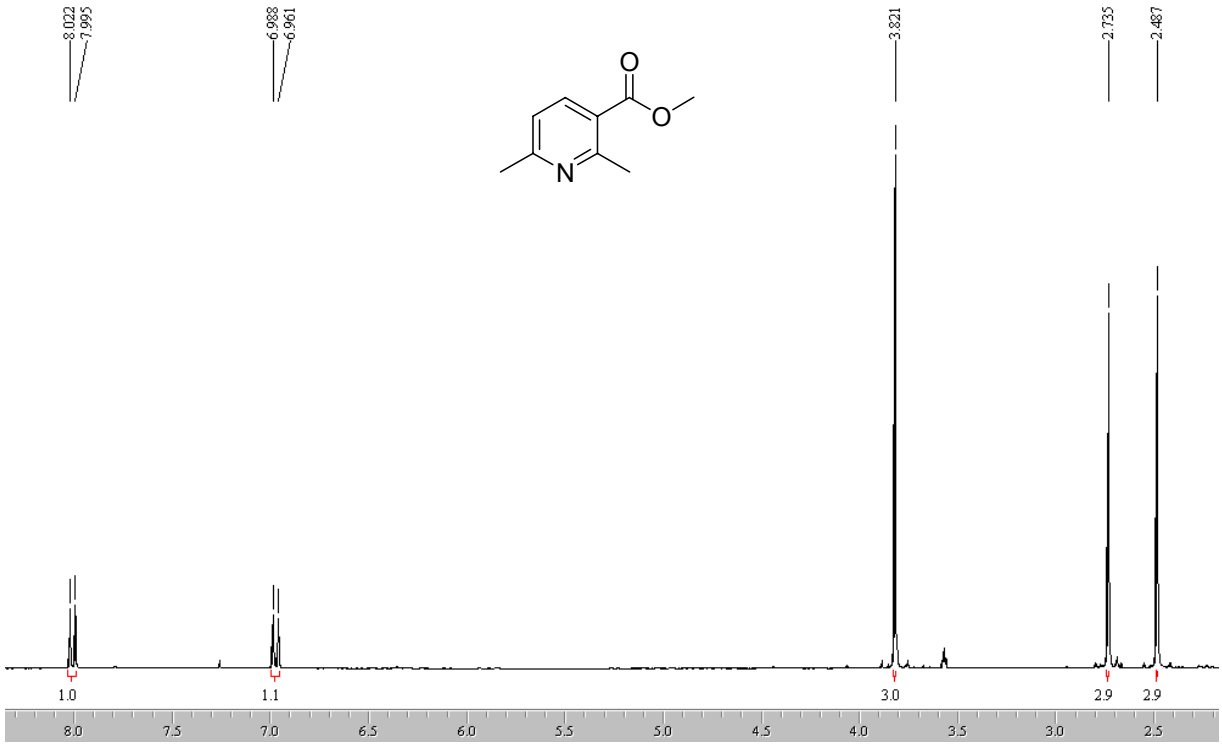
8.607
8.596
8.590
8.194
8.188
8.167
8.161
7.219
7.203
7.193
7.177
3.910
2.828
O
O
N
1.0
1.1
1.1
2.9
3.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0

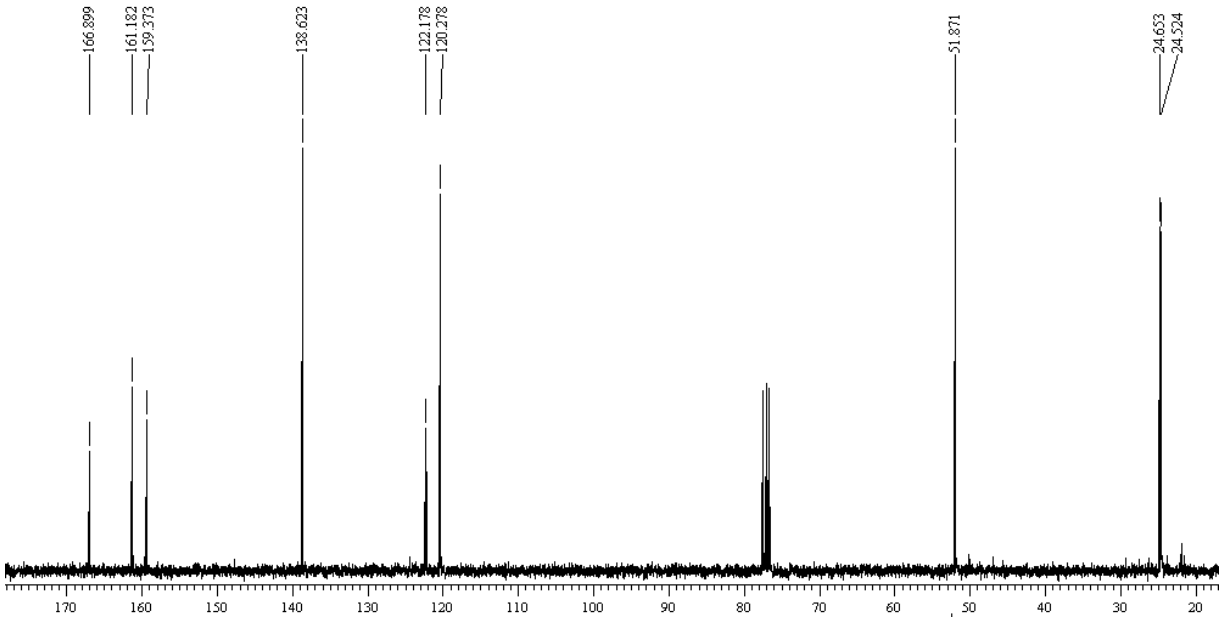

166.725
159.658
151.618
138.189
125.113
120.689
52.023
24.591
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

Compound 4e

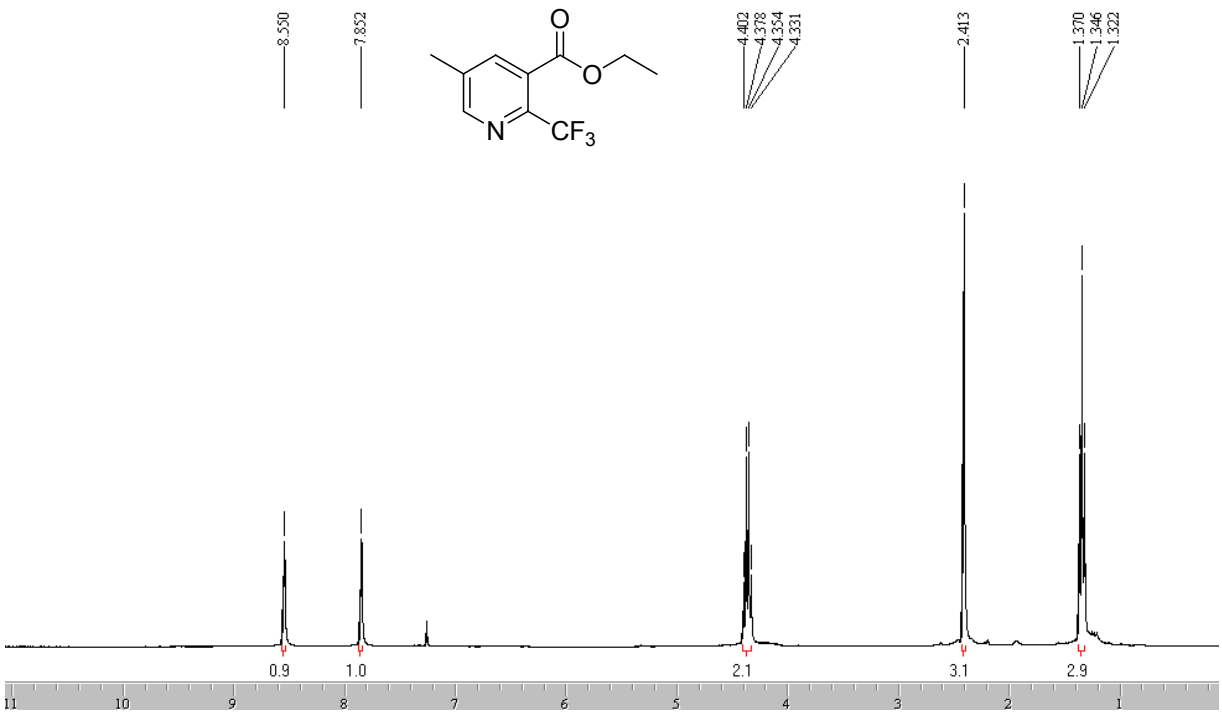

8.307
8.301
7.868
7.862
3.784
2.655
2.206
O
O
N
1.0
1.0
3.0
3.0
3.0
166.740
156.464
151.875
138.441
129.980
124.368
51.804
23.881
17.389

Compound 4f


8.022
7.995
6.988
6.961
3.821
2.735
2.487
O
O
N
1.0
1.1
3.0
2.9
2.9
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5


166.899
161.182
159.373
138.623
122.178
120.278
51.871
24.653
24.524
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

Compound 4g


8.550
7.852
4.402
4.378
4.354
4.331
2.413
1.370
1.346
1.322
O
O
N
CF3
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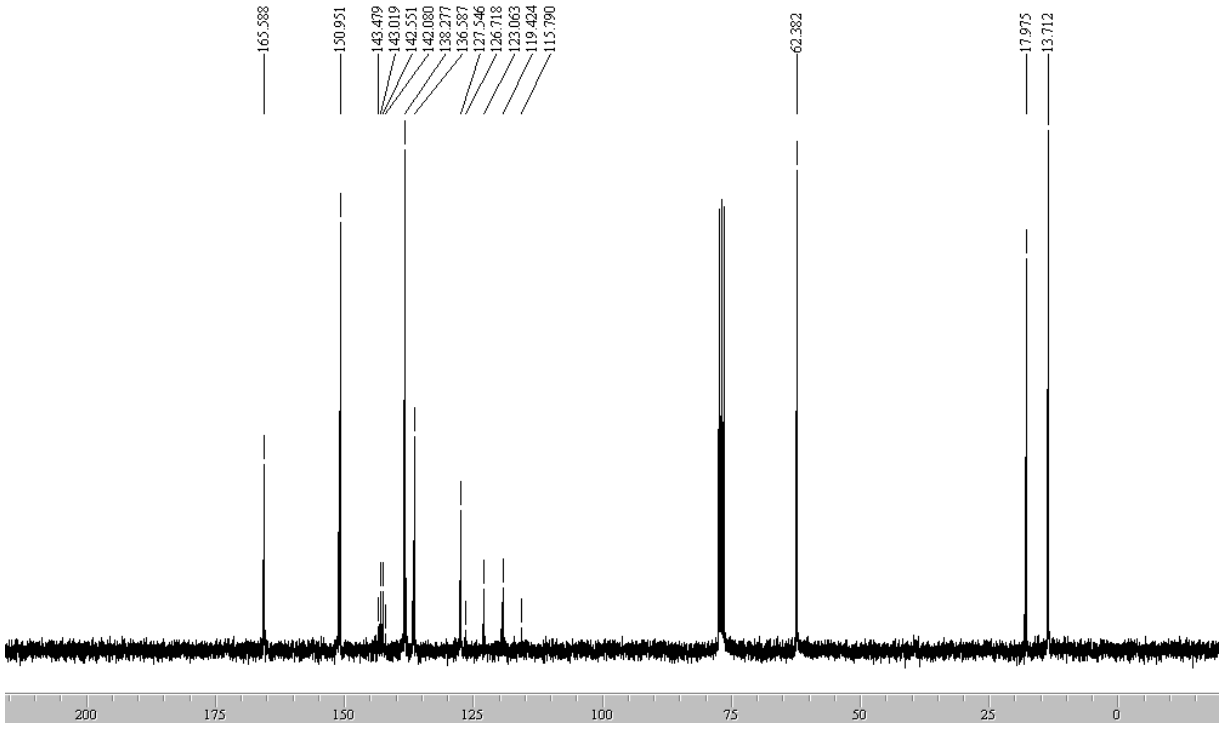
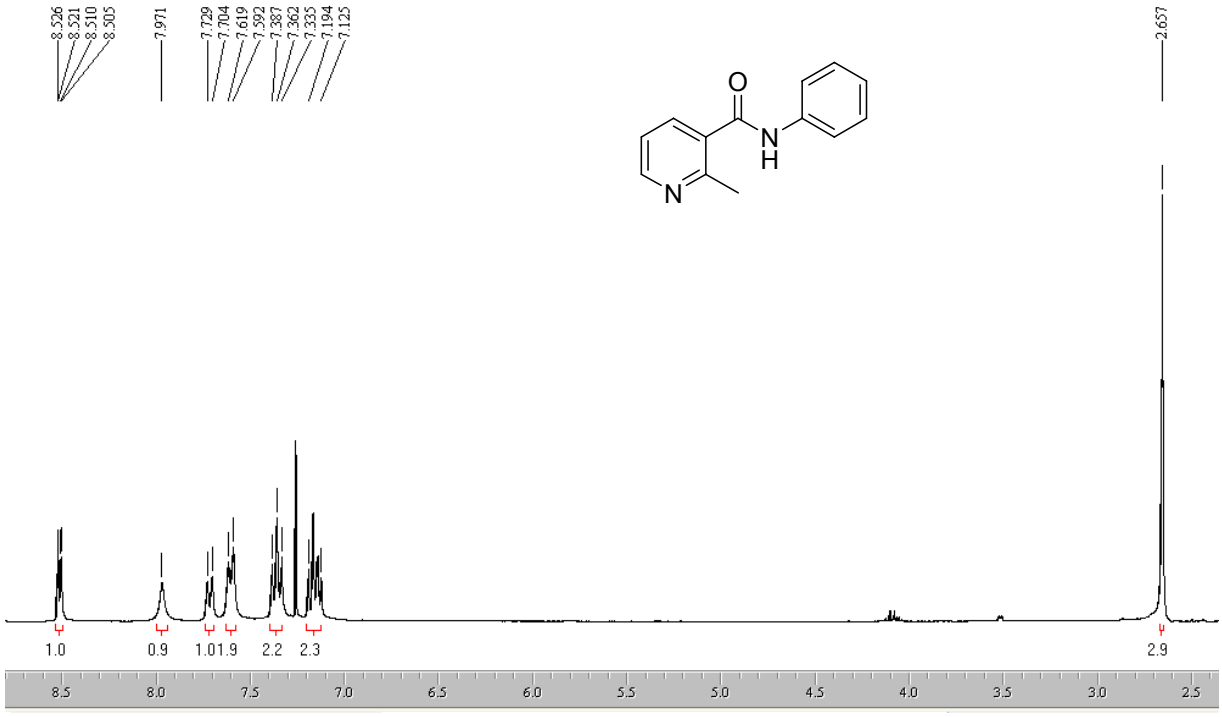
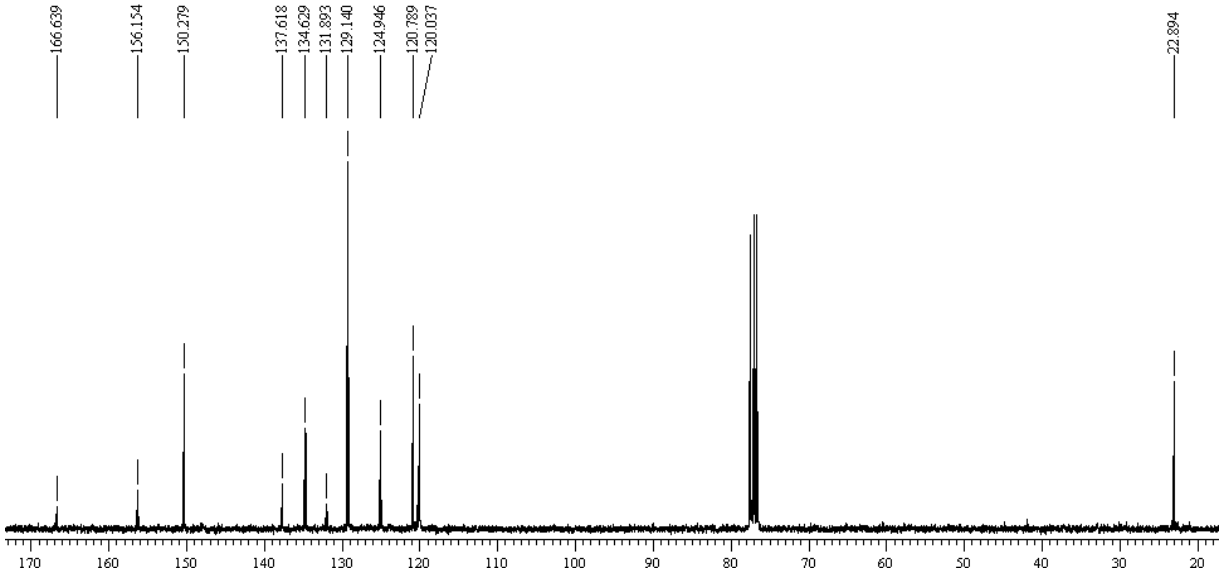
1.0
2.1
3.1
2.9
11
10
9
8
7
6
5
4
3
2
1

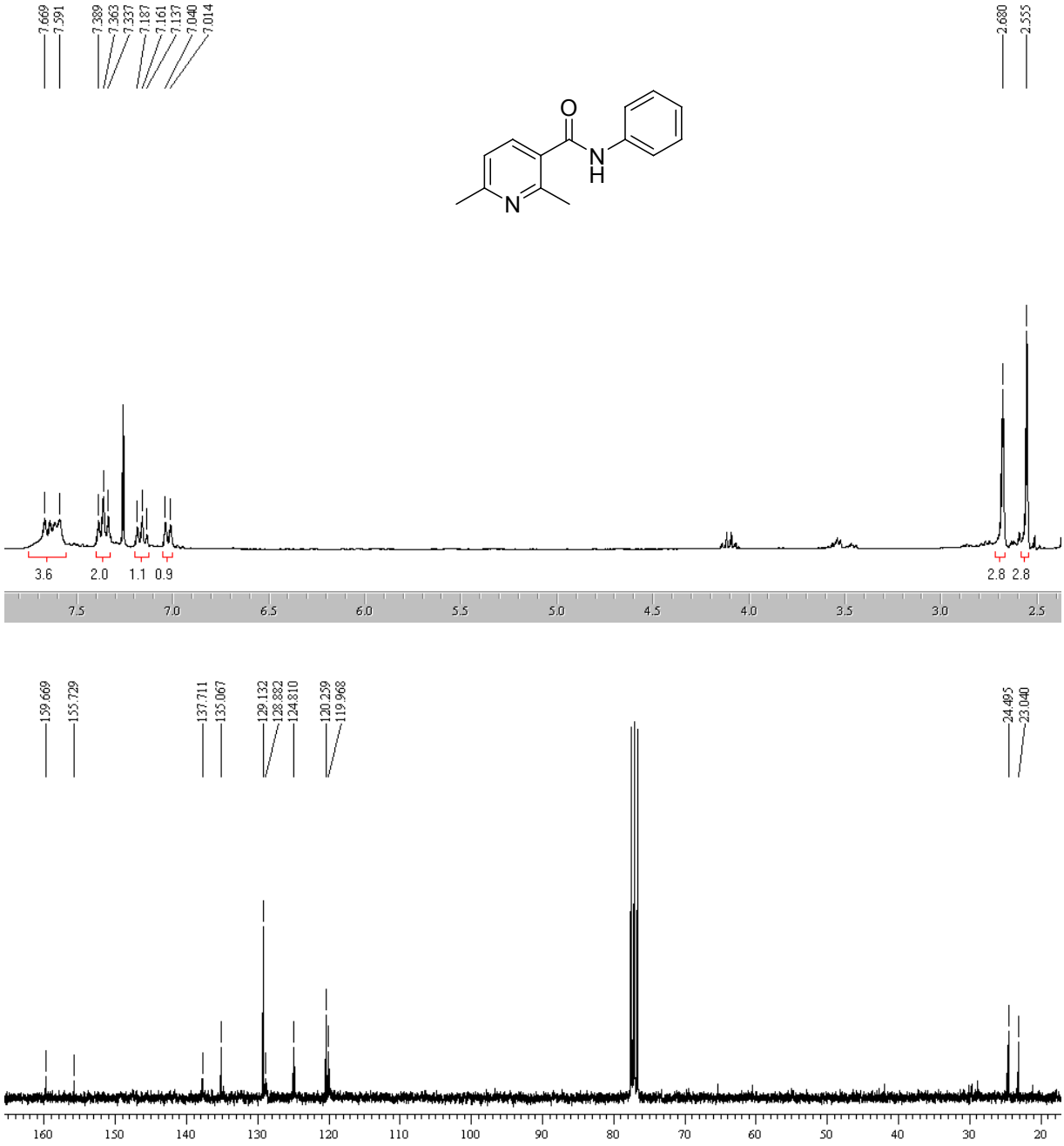

165.588
150.951
143.479
143.019
142.551
142.080
138.277
136.587
127.546
126.718
123.063
119.424
115.790
62.382
17.975
13.712
200
175
150
125
100
75
50
25
0

Compound 4h


8.526
8.521
8.510
8.505
7.971
7.729
7.704
7.619
7.592
7.387
7.362
7.335
7.194
7.125
2.657
O
N
H
N
1.0
0.9
1.01.9
2.2
2.3
2.9
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5


166.639
156.154
150.279
137.618
134.629
131.893
129.140
124.946
120.789
120.037
22.894
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

Compound 4i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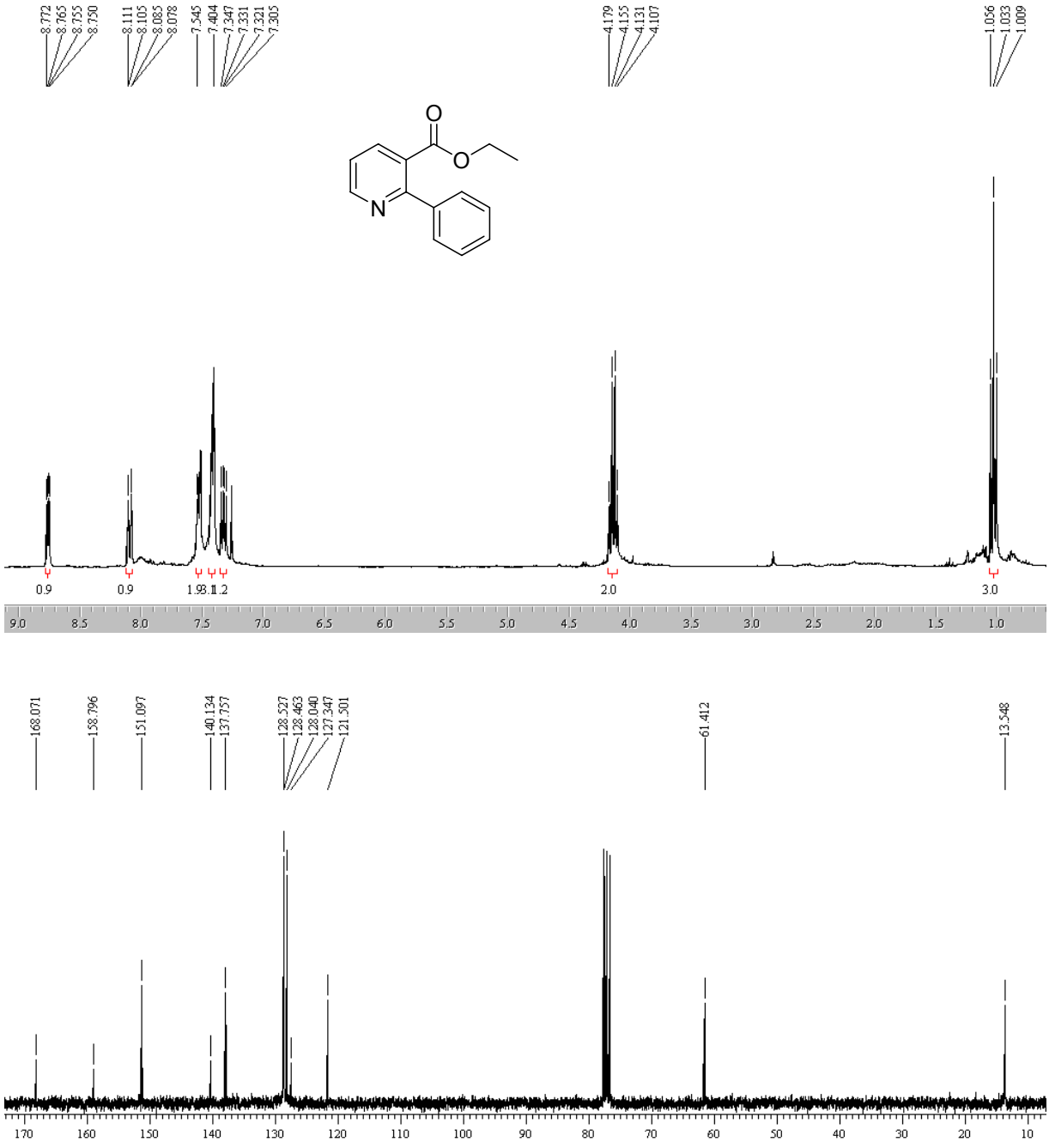
7.591
7.389
7.363
7.337
7.187
7.161
7.137
7.040
7.014
2.680
2.555
O
N
H
N
3.6
2.0
1.1
0.9
2.8
2.8
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
159.669
155.729
137.711
135.067
129.132
128.882
124.810
120.259
119.968
24.495
23.040
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

Compound 4j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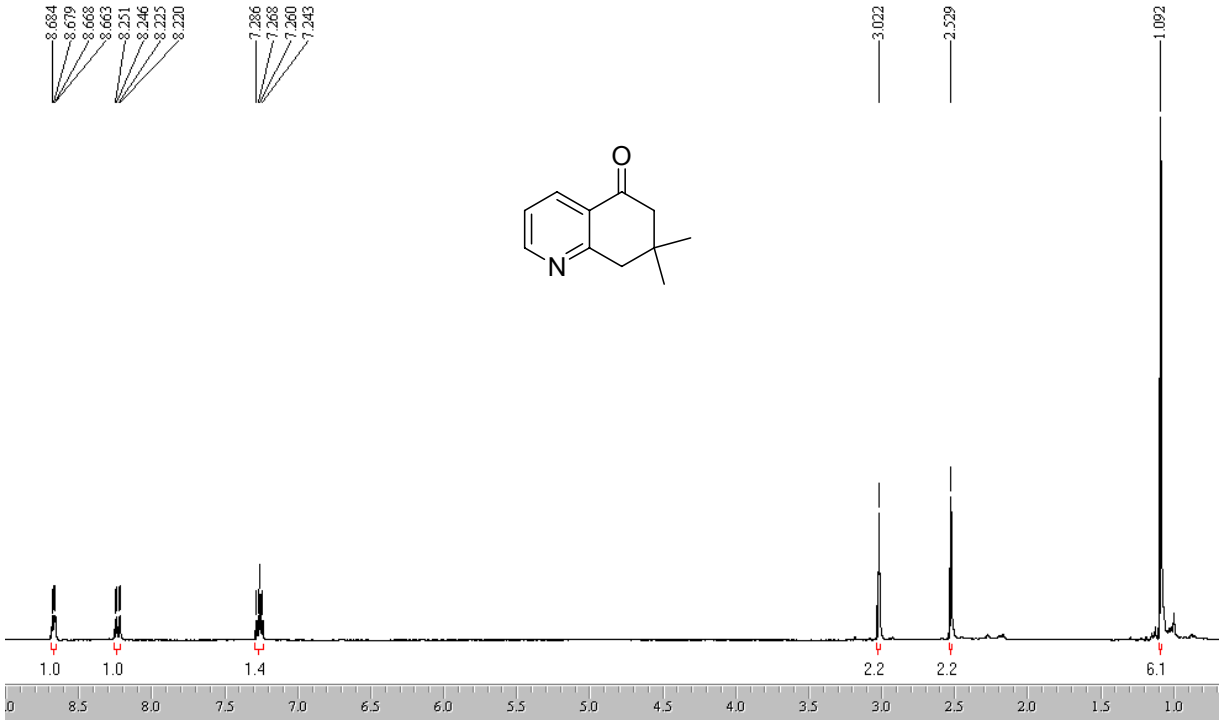
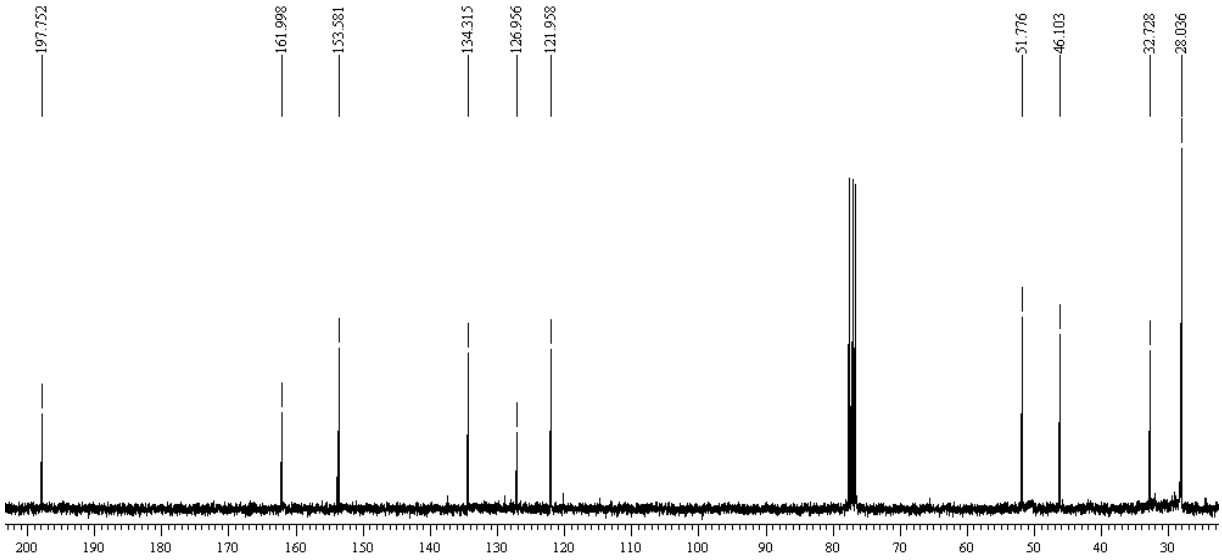
8.765
8.755
8.750
8.111
8.105
8.085
8.078
7.545
7.404
7.347
7.331
7.321
7.305
4.179
4.155
4.131
4.107
1.056
1.033
1.009
O
O
N
0.9
0.9
1.93
1.1.2
2.0
3.0
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
168.071
158.796
151.097
140.134
137.757
128.527
128.463
128.040
127.347
121.501
61.412
13.548
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

Compound 4k


8.684
8.679
8.668
8.663
8.251
8.246
8.225
8.220
7.286
7.268
7.260
7.243
3.022
2.529
1.092
O
N
1.0
1.0
1.4
2.2
2.2
6.1


197.752
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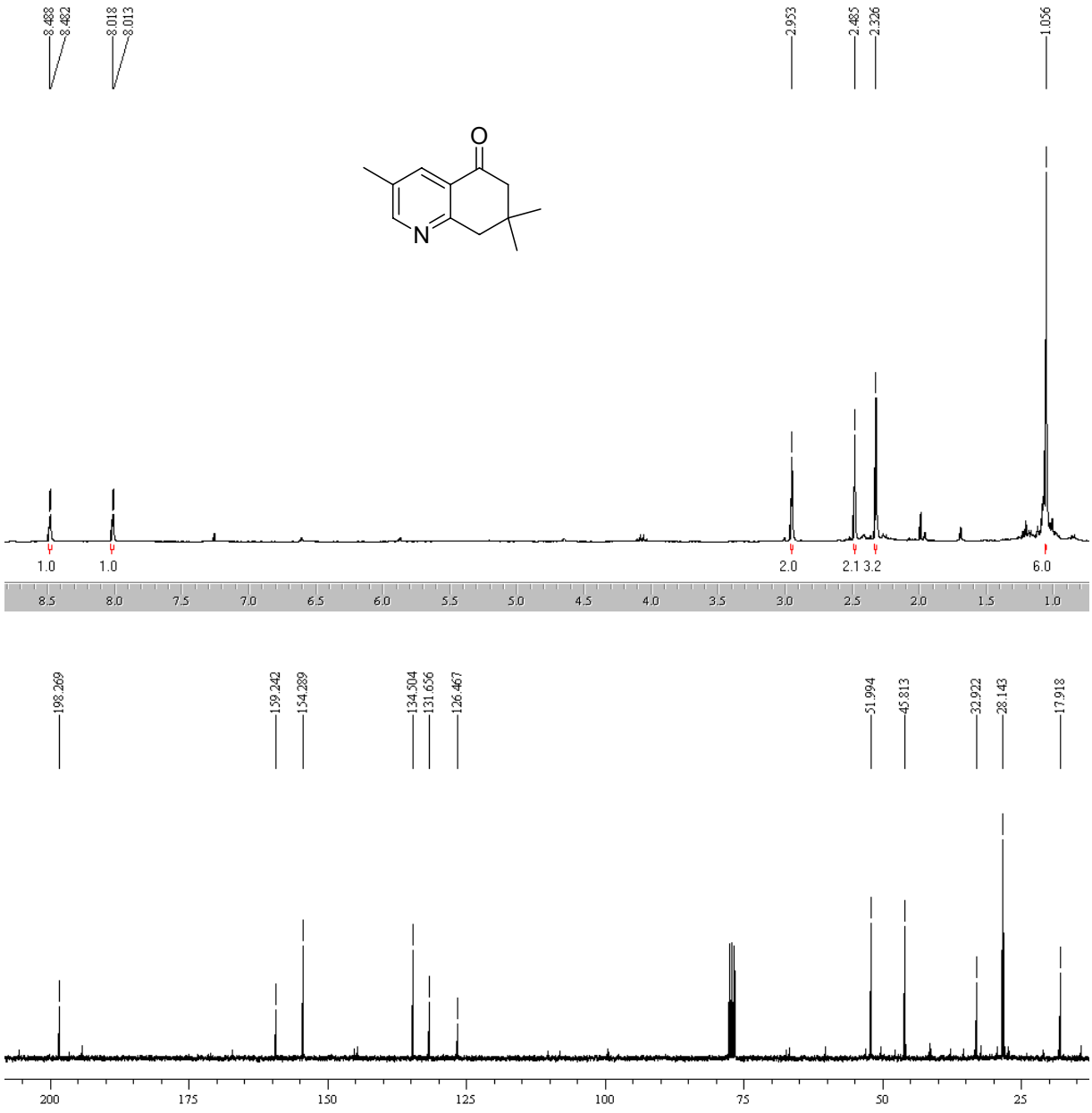
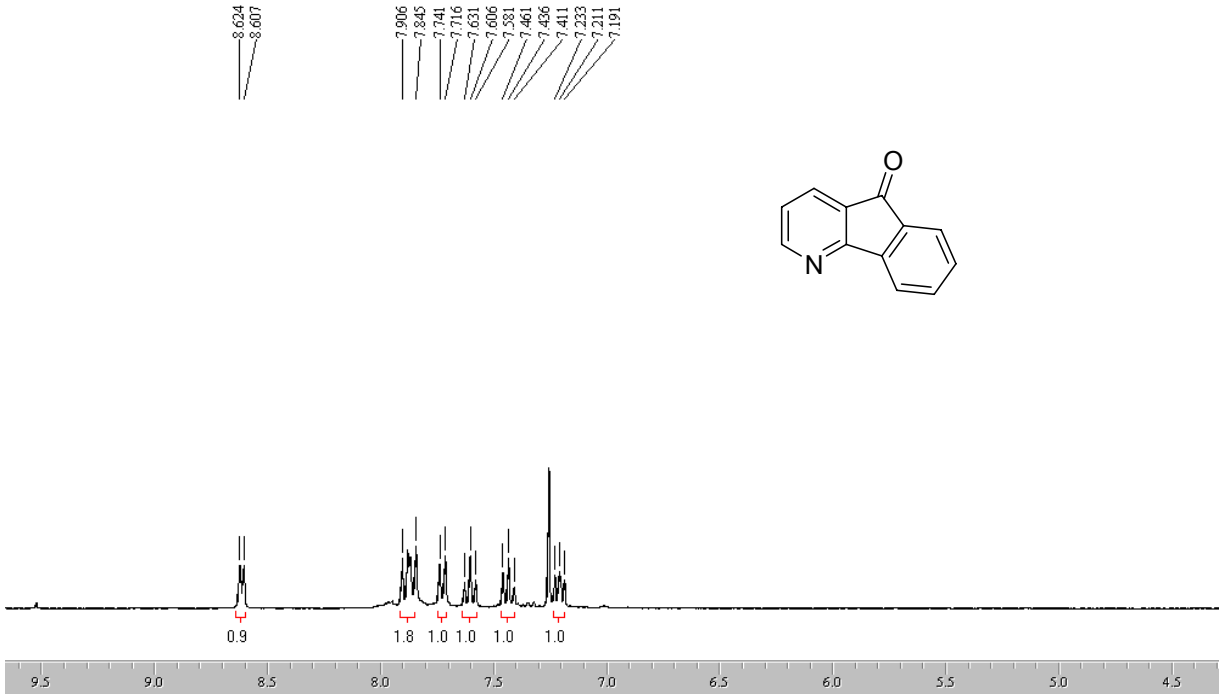
134.315
126.956
121.958
51.776
46.103
32.728
28.036

Compound 4l


8.488
8.482
8.018
8.013
2.953
2.485
2.326
1.056
O
N
1.0
1.0
2.0
2.1
3.2
6.0
198.269
159.242
154.289
134.504
131.656
126.467
51.994
45.813
32.922
28.143
17.918

Compound 4m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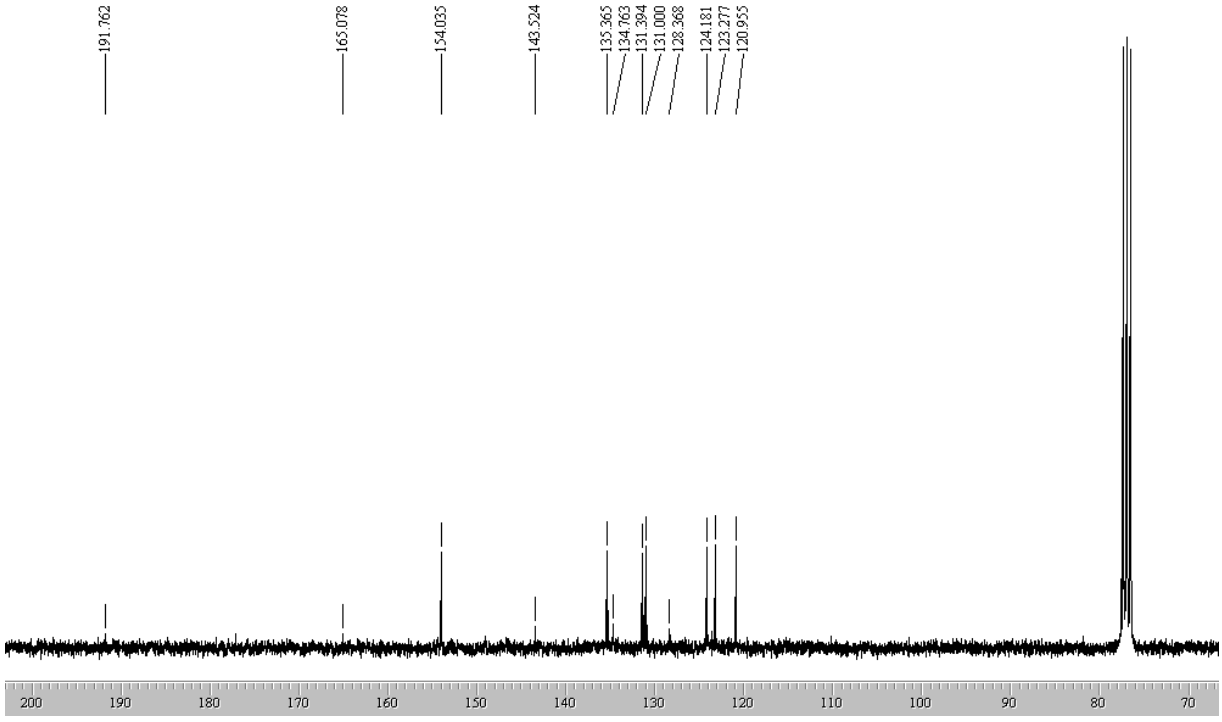
8.607
7.906
7.845
7.741
7.716
7.631
7.606
7.581
7.461
7.436
7.411
7.233
7.211
7.191
O
N
0.9
1.8
1.0
1.0
1.0
1.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5


191.762
165.078
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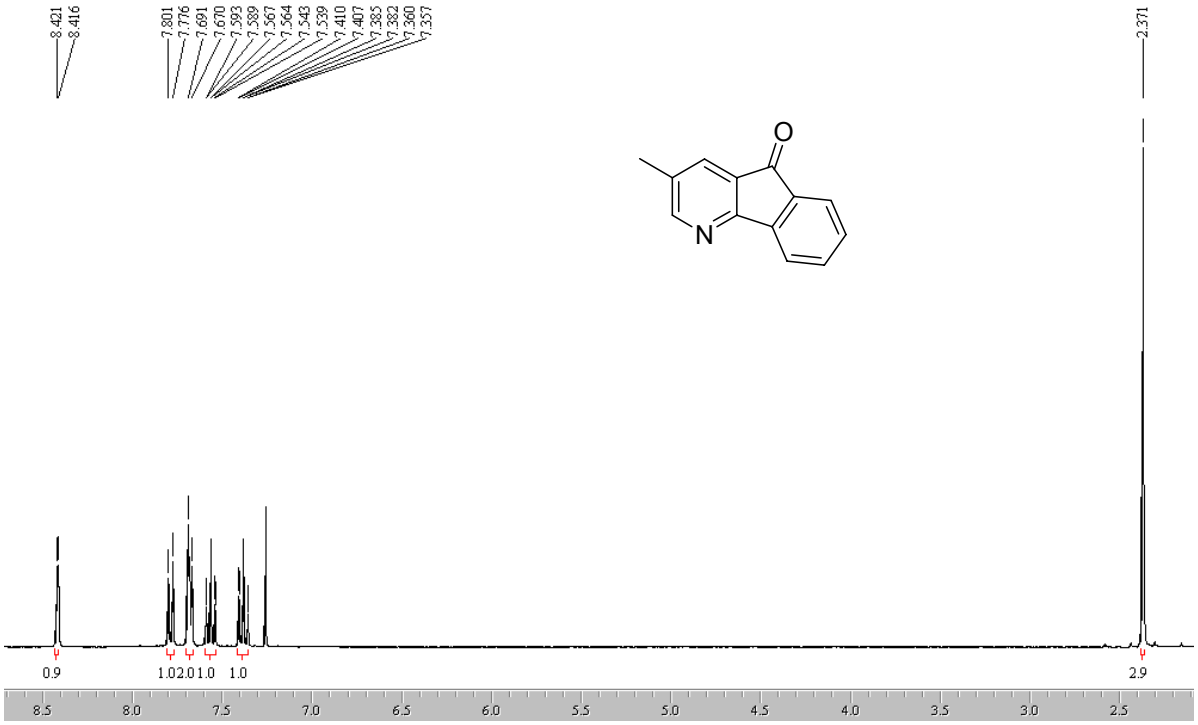
143.524
135.365
134.763
131.394
131.000
128.368
124.181
123.277
120.955
200
190
180
170
160
150
140
130
120
110
100
90
80
70

Compound 4n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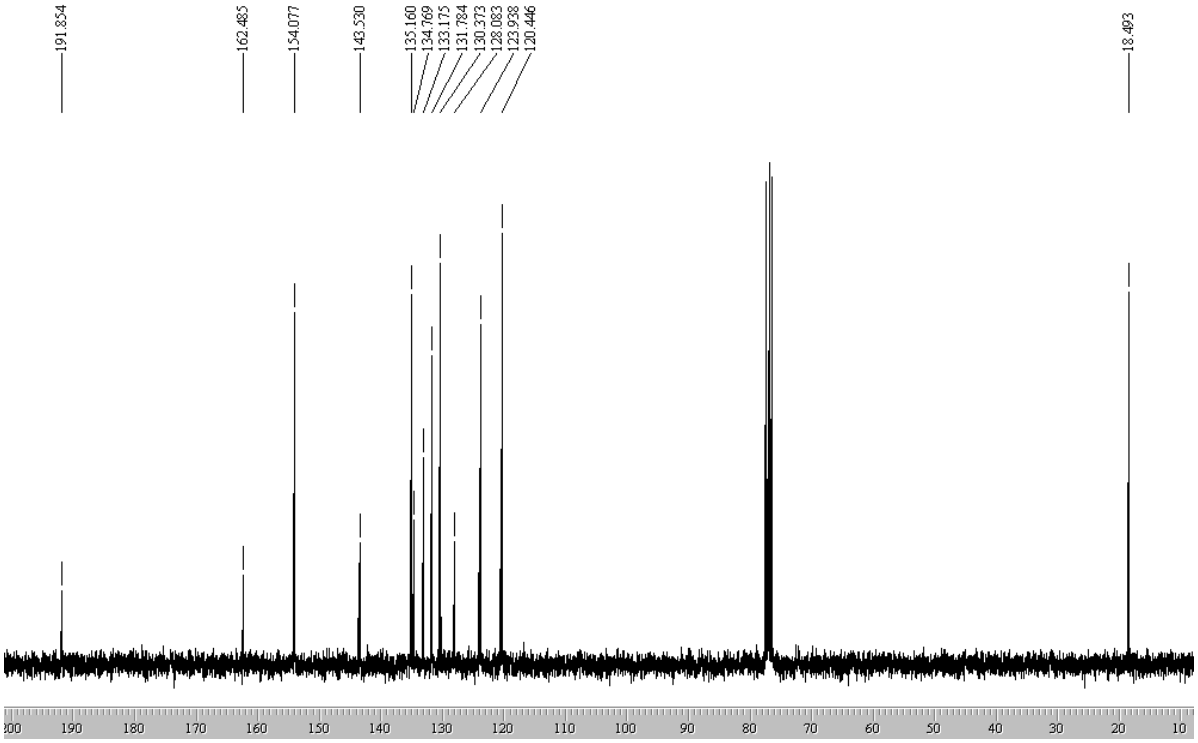
7.801
7.776
7.691
7.670
7.593
7.589
7.567
7.564
7.543
7.539
7.410
7.407
7.385
7.382
7.360
7.357
2.371
O
N
0.9
1.0
2.0
1.0
1.0
2.9
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5


191.834
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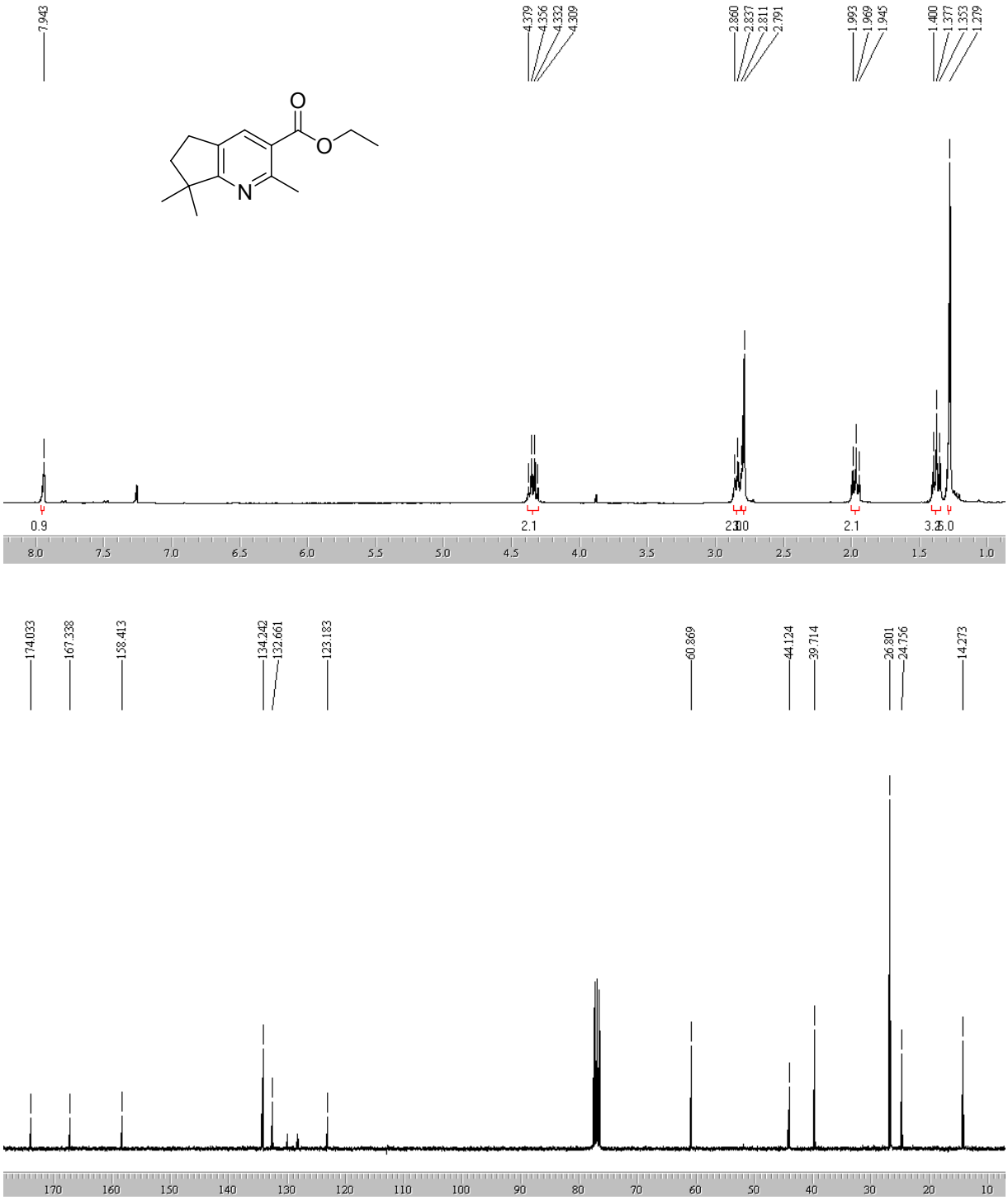
154.077
143.530
135.160
134.769
133.175
131.784
130.373
128.083
123.938
120.446
18.493
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

Compound 4o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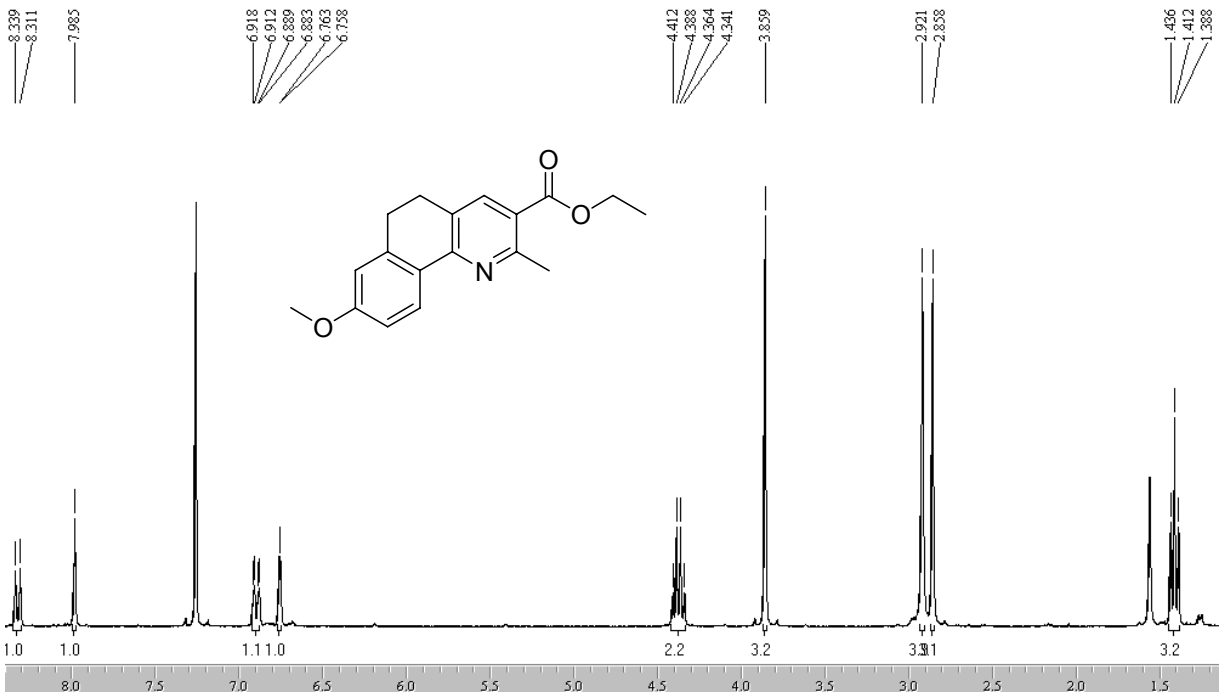
4.356
4.332
4.309
2.860
2.837
2.811
2.791
1.993
1.969
1.945
1.400
1.377
1.333
1.279
O
O
N
0.9
2.1
2.1
3.2
5.0
174.033
167.338
158.413
134.242
132.661
123.183
60.869
44.124
39.714
26.801
24.756
14.273

Compound 4p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6.889
6.883
6.763
6.758
4.412
4.388
4.364
4.341
3.859
2.921
2.858
1.436
1.412
1.388
O
O
N
O
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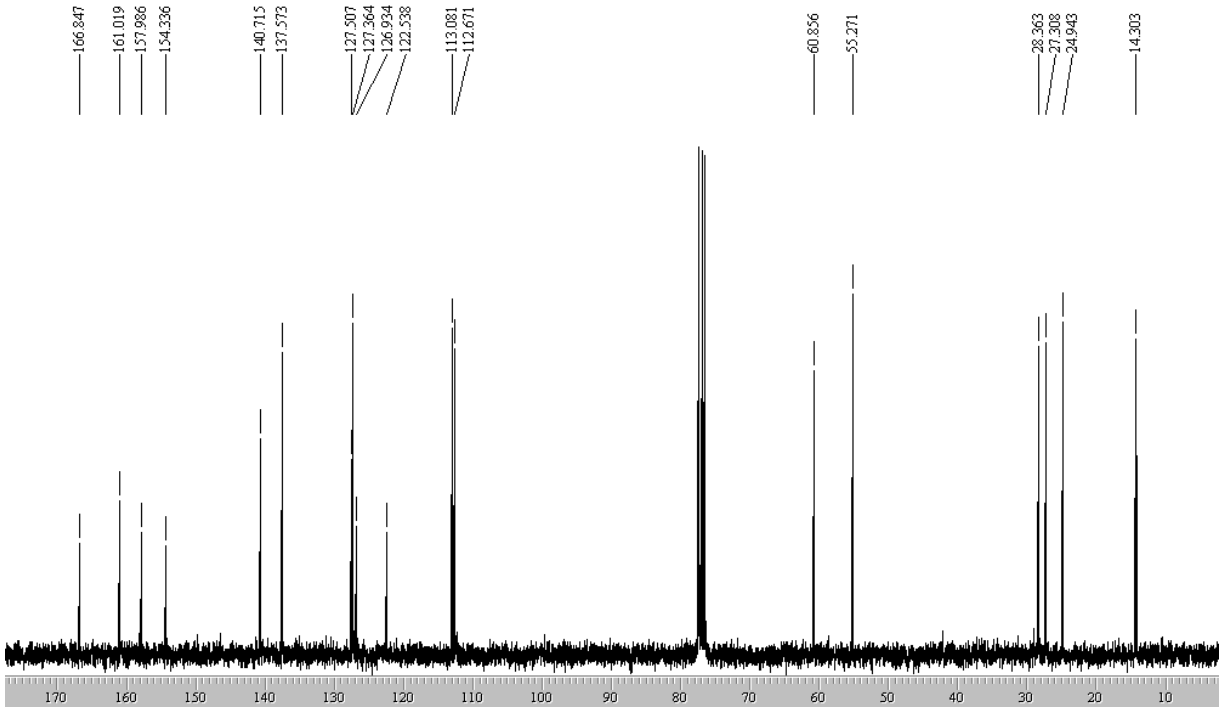
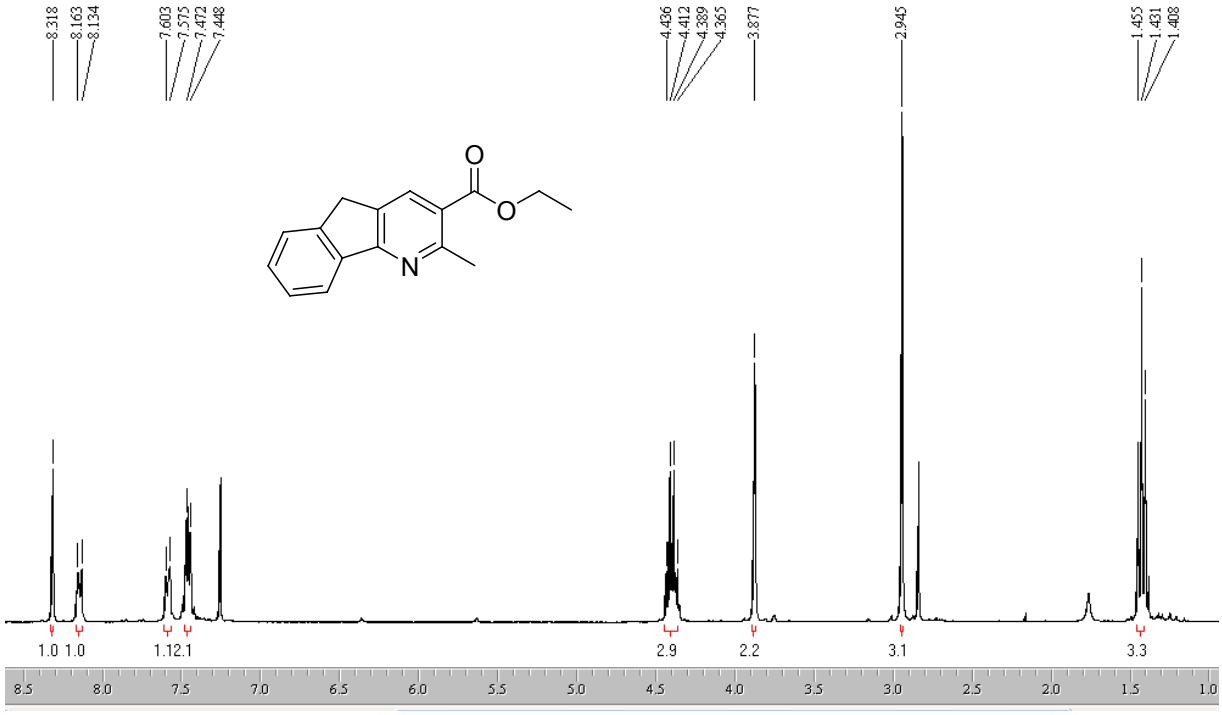
1.0
1.1
1.0
2.2
3.2
3.2


166.847
161.019
157.986
154.336
140.715
137.573
127.507
127.364
126.934
122.538
113.081
112.671
60.856
55.271
28.363
27.308
24.943
14.303

Compound 4q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8.163
8.134
7.603
7.575
7.472
7.448
4.436
4.412
4.389
4.365
3.877
2.945
1.455
1.431
1.408
O
O
N
1.0 1.0
1.12.1
2.9
2.2
3.1
3.3
8.5
8.0
7.5
7.0
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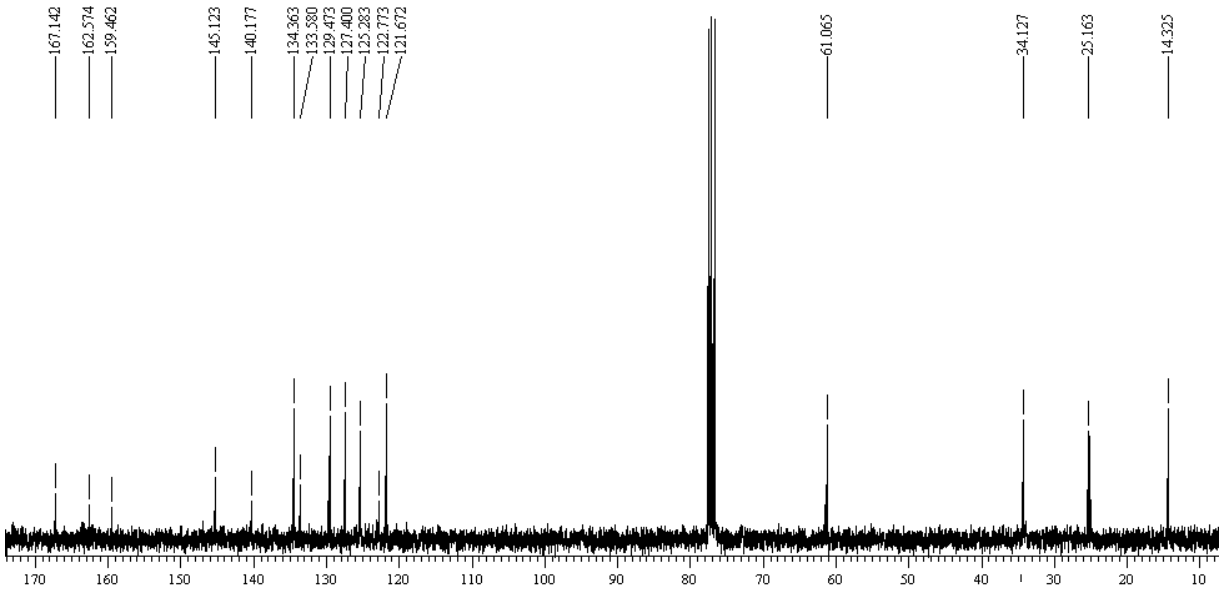
1.0


167.142
162.574
159.462
145.123
140.177
134.363
133.580
129.473
127.400
125.283
122.773
121.672
61.065
34.127
25.163
14.325
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10