Supporting Information

Efficient, Mild, and Completely Regioselective Synthesis of Substituted Pyridines

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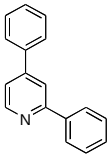
General Experimental

All reactions were carried out under an inert atmosphere with dry solvents under anhydrous conditions, unless otherwise stated. Tetrahydrofuran, THF, was distilled from sodium and benzophenone. TLC was performed on Silica Gel 60 F_{254} (Merck) with detection by UV light. Flash column chromatography (eluents given in brackets) was performed on silica gel (Matrex, 60 Å, 35-70 μm, Grace Amicon). The ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHZ Bruker DRX or 360 MHz Bruker DRX. Solutions in $CDCl_3$ [residual $CHCl_3$ (δ_H 7.26 ppm) or $CDCl_3$ (δ_C 77.0 ppm) as internal standard at 298 K. HRMS data were recorded with electron impact (EI^+) ionization on a Micromass Ultima Q-TOF hybrid quadrupole time of flight mass spectrometer operating in W-reflector mode.

Starting Materials

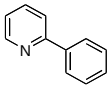
Pyridine *N*-oxide were either purchased from Sigma Aldrich or prepared according to a published procedure[1] and dried through Aluminum oxide activated followed by coevaporation with toluene. The Grignard reagents were purchased from Sigma Aldrich Titrated using I_2 in THF saturated with LiCl (0.5M) at rt.

(1) Campeau, L.-C.; Rousseaux, S.; Fagnou, K. *J. Am. Chem. Soc.* **2005**, *127*, 18020-18021.

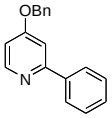


General procedure for the synthesis of , disubsituted pyridine 2a-2l. Exemplified with 2-4-diphenyl-pyridine, 2a.

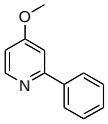
To a solution of 2-phenyl-pyridine-*N*-oxide (100 mg, 0.58 mmol) in 20 mL dried THF was added dropwise PhMgCl (0.35 mL, 0.7 mmol) at -78 ºC. The resulting red mixture was stired at -78 ºC for 10 minutes, whereupon MeOH (35µL, 0.87 mmol) was added and caused a change of color to yellow. After increase temperature to RT, trifluoroacetic anhydride (TFAA) was added and stirred 20 min at RT. The reaction was quenched with 3 mL of aq. 1M solution of NaOH solution, extracted twice with mixture of Heptane:diethylether: ethylacetate = 8:3:2 and one times with brine, dried (Na_2SO_4) and concentrated. Purified using column chromatography (ethylacetate:heptane 1:9) which after co-concentration from DCM gave **2a** as a yellowish oil (102 mg, 76%). Spectral data identical to previous reports.



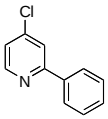
2-phenyl-pyridine, 2b. From **1b** (100mg, 0.5 mmol) was pyridine **2b** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (89 mg, 54%). Spectral data identical to previous reports.[2]



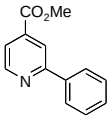
4-Benzyloxy-2-phenyl-pyridine, 2c. From **1c** (100mg, 0.5 mmol) was pyridine **2c** isolated by column chromatography (heptane:ethylacetate = 8:2) as white solid (89 mg, 68%). Spectral data identical to previous reports.[2]



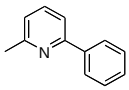
4-Methoxy-2-phenyl-pyridine, 2d. From **1d** (120mg, 0.59 mmol) was pyridine **2d** isolated by column chromatography (heptane:ethylacetate = 7:3) as white solid (72 mg, 66%).
IR(ν_{max}/cm^{-1}) 3050, 2940, 2840, 1590, 1564, 1455, 1411, 1306, 1218, 1021, 775.
^{1}H NMR (400 Mhz, $CDCl_3$) δ 8.55 (d, *J* = 5.7 Hz, 1H), 8.00-7.98 (m, 2H), 7.51-7.42 (m, 3H), 7.29-7.26 (m, 1H), 6.80 (dd, *J* = 5.7, 2.4 Hz, 1H), 3.91-3.90 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 159.2, 150.9, 139.4, 129.0, 128.6, 126.9, 108.1, 106.8, 55.1.
HRMS calcd for [M + H]$^+$ $C_{12}H_{12}NO^+$ 186.0913, obsd 186.0924.



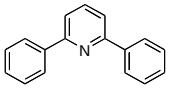
4-chloro-2-phenyl-pyridine, 2e. From **1e** (100mg, 0.5 mmol) was pyridine **2e** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (101 mg, 68%). Spectral data identical to previous reports.[2]



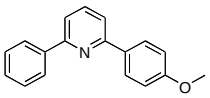
Methyl-2-phenyl-pyridine-4-carboxylate, 2f. From **1f** (100mg, 0.65 mmol) was pyridine **2f** isolated by column chromatography (heptane:ethylacetate = 8:2) as white solid (87 mg, 63%). Spectral data identical to previous reports.[3]



2-Methyl-6-phenyl-pyridine, 2g. From **1g** (115mg, 1,05 mmol) was pyridine **2g** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (103 mg, 62%). Spectral data identical to previous reports.[2]

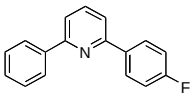


2-6-Diphenyl-pyridine, 2h. From **1h** (100mg, 0,58 mmol) was pyridine **2h** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (112 mg, 85%). Spectral data identical to previous reports.[4]



2-(4-Methoxyphenyl)-6-phenyl-pyridine, 2i. From **1h** (100mg, 0,58 mmol) was pyridine **2i** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (120 mg, 79%). Spectral data identical to previous reports.[5]

(2) Andersson, H.; Almqvist, F.; Olsson, R. *Org. Lett.* **2007**, *9*, 1335-1337.
(3) Craig, D.; Henry, G. D. *Tetrahedron Letters* **2005**, *46*, 2559-2562.
(4) Overberger, C. G.; Lombardino, J. G.; Hiskey, R. G. *J. Am. Chem. Soc.* **1957**, *79*, 6430-6435.
(5) Beaumard, F.; Dauban, P.; Dodd, R. H. *Organic Letters* **2009**, *11*, 1801-1804.



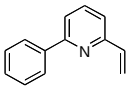
2-(4-Fluorophenyl)-6-phenyl-pyridine, 2j. From **1h** (100mg, 0,58 mmol) was pyridine **2j** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (115 mg, 79%).

IR(ν_{max}/cm^{-1}) 3051, 1598, 1565, 1509, 1444, 1225, 1154, 1092, 812, 762, 698.

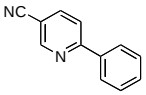
^{1}H NMR (400 Mhz, $CDCl_3$) δ 8.20-8.14 (m, 4H), 7.86-7.82 (m, 1H), 7.73-7.67 (m, 2H), 7.55-7.44 (m, 3H), 7.24-7.17 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (d, *J* = 248.1 Hz, 1C), 156.8, 155.8, 139.3, 137.5, 135.6 (d, *J* = 3.0 Hz, 1C), 129.0, 128.7 (d, *J* = 8.2 Hz, 1H), 128.7 (2C), 129.9 (2C), 118.4 (d, *J* = 29.9 Hz, 1H), 115.6, 115.4.

HRMS calcd for [M + H]$^+$ $C_{17}H_{13}FN^+$ 250.1027, obsd 250.1033



2-phenyl-6-vinyl-pyridine, 2k. From **1h** (100mg, 0,58 mmol) was pyridine **2k** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (81 mg, 77%). Spectral data identical to previous reports.[6]



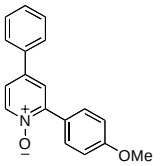
2-phenyl-5-cyano-pyridine, 2m. From **1j** (60 mg, 0,5 mmol) was pyridine **2m** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (54 mg, 60%).

IR(ν_{max}/cm^{-1}) 3051, 2237, 1598, 1550, 1473, 1444, 1374, 1028, 924, 839, 734.

^{1}H NMR (400 Mhz, $CDCl_3$) δ 9.05-8.92 (m, 1H), 8.10-8.02 (m, 3H), 7.89-7.87 (m, 1H), 7.58-7.51 (m, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 152.4, 139.9, 137.3, 130.6, 129.1, 127.4, 120.0, 117.7, 107.9.

HRMS calcd for [M + H]$^+$ $C_{12}H_9N_2^+$ 181.0760, obsd 181.0770



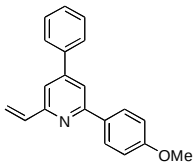
2-(4methoxyphenyl)-4-Phenyl-pyridine-*N*-oxide, 1k. To a solution of 4-phenyl-pyidine-*N*-oxide **1d** (500 mg, 2.82 mmol) in 100 mL dried THF was added dropwise 4-MeOPhMgCl (8.65 mL, 3.4 mmol) at -40 °C. The resulting red mixture was stired at -40 °C for 10 minutes, whereupon AcOH (250 μL, 4.23 mmol) was added and caused a change of color to yellow. 5 min latter we added Chloranil (1,45 mg, 5.64 mmol) and increase temperature at room temperature After 1 hour the mixture was directly concentrated and Purified using column chromatography (ethylacetate:MeOH 95:5) gave **1k** as a with solid (606 mg, 75%).

IR(ν_{max}/cm^{-1}) 3031, 3949, 2831, 1606, 1512, 1473, 1459, 1395, 1234, 1182, 1029, 828.

^{1}H NMR (400 Mhz, $CDCl_3$) δ 8.36 (d, *J* = 6.8 Hz, 1H), 7.91-7.88 (m, 2H), 7.65-7.62 (m, 3H), 7.52-7.40 (m, 4H), 7.03 (d, *J* = 8.8 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 148.8, 140.4, 138.5, 136.5, 130.8, 129.2, 128.9, 126.3, 124.9, 124.5, 121.5, 113.7, 55.3.

HRMS calcd for [M + H]$^+$ $C_{18}H_{16}NO_2^+$ 278.1176, obsd 278.1182



2-(4methoxyphenyl)-4-Phenyl-6vinyl-pyridine-*N*-oxide 2n. From **1k** (150 mg, 0,54 mmol) was pyridine **2n** isolated by column chromatography (heptane:ethylacetate = 9:1) as white solid (137 mg, 92 %) using general procedure presented above.

IR(ν_{max}/cm^{-1}) 3060, 3013, 2959, 2934, 2836, 1607, 1593, 1545,1 1503, 1497, 1387, 1253, 1176, 1034, 835.

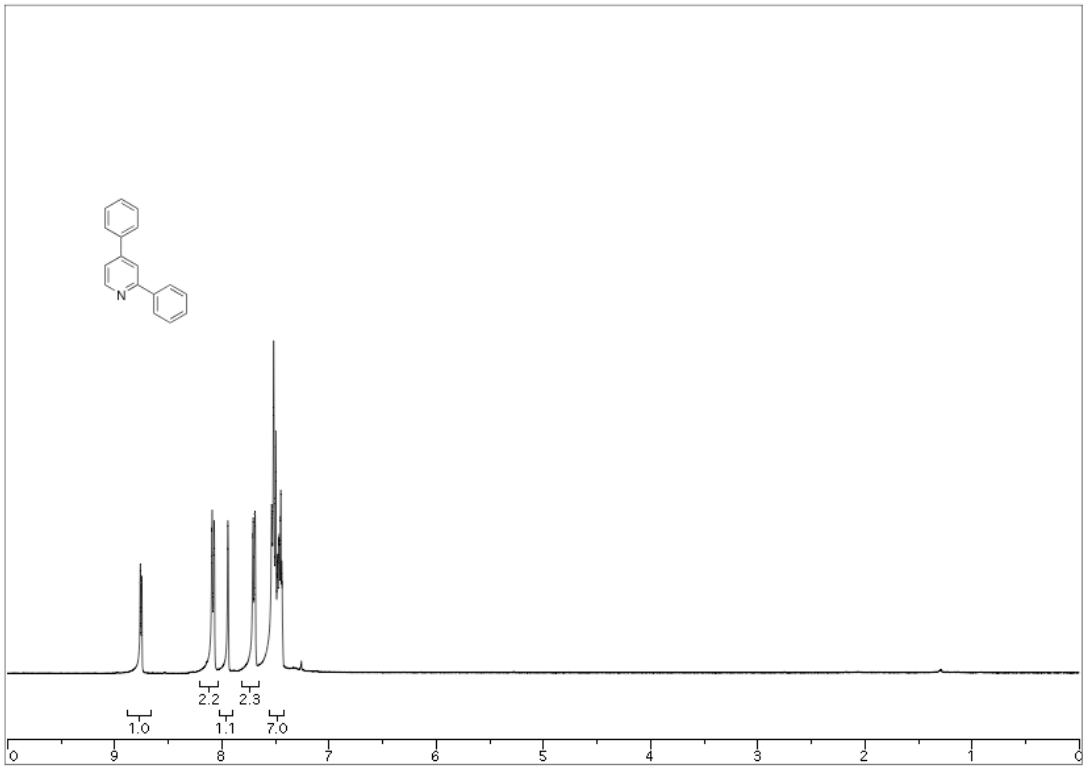
^{1}H NMR (400 Mhz, $CDCl_3$) δ 8.13 (d, *J* = 8.8 Hz, 2H), 7.80 (s, 1H), 7.73 (d, *J* = 7.0 Hz, 2H), 7.80-7.29 (m, 9H), 7.56-7.43 (m, 5H), 7.08-6.96 (m, 3H), 6.48 (dd, *J* = 17.3, 1.0 Hz, 1H), 5.61-5.58 (m, 1H), 3.91 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 157.1, 155.7, 149.7, 138.9, 137.2, 132.1, 129.0, 128.8, 128.3, 127.0, 118.3, 117.4, 116.7, 114.0, 55.3.

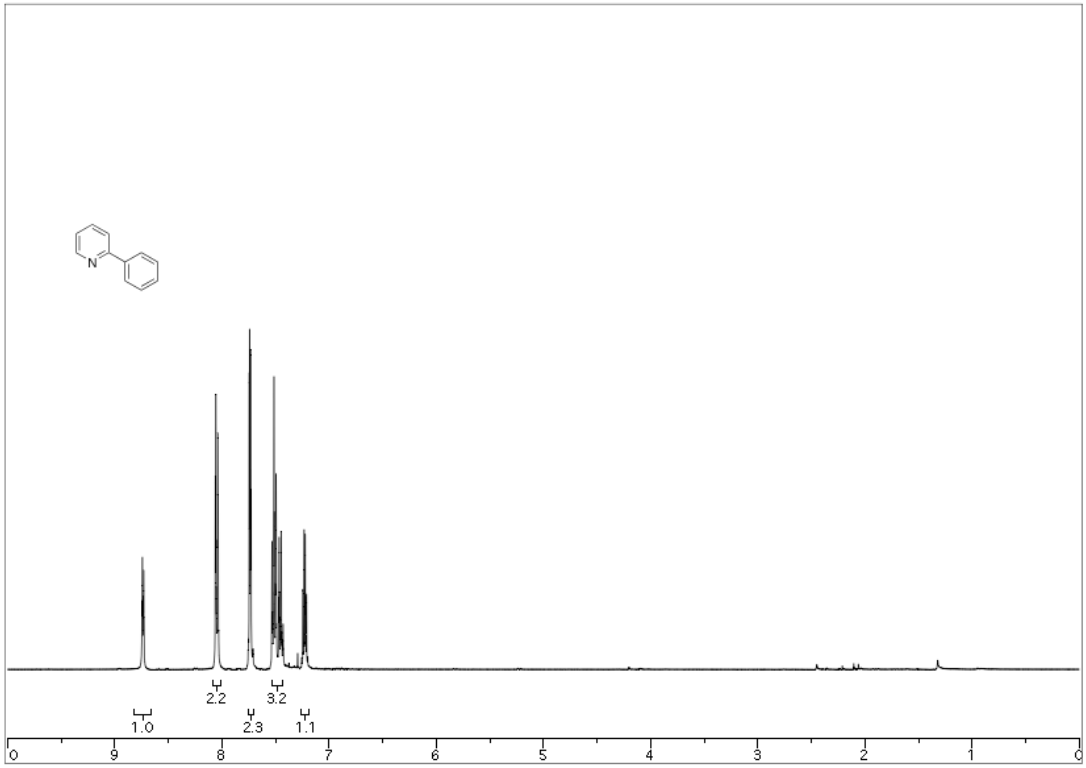
HRMS calcd for [M + H]$^+$ $C_{20}H_{18}NO^+$ 288.1383, obsd 288.1387

(5) Komanduri, V.; Grant, C. D.; Krische, M. J. *J Am. Chem. Soc.* **2008**, *130*, 12592-12593.

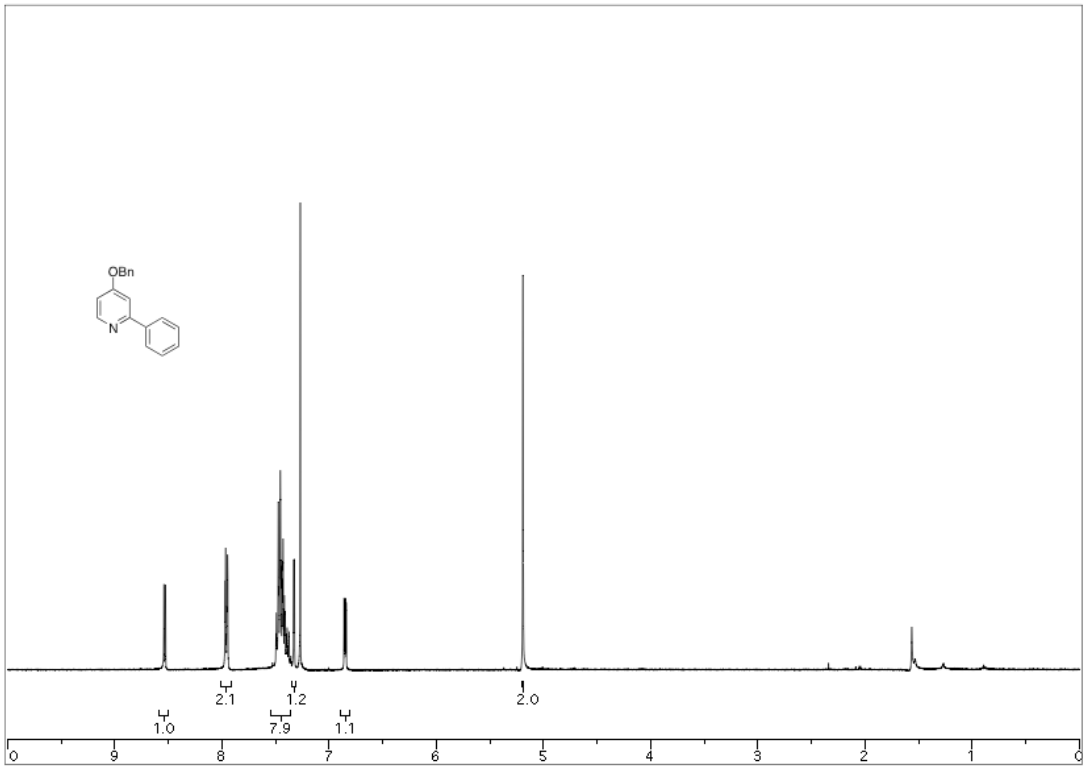
^{1}H spectra of compound **2a** in $CDCl_3$



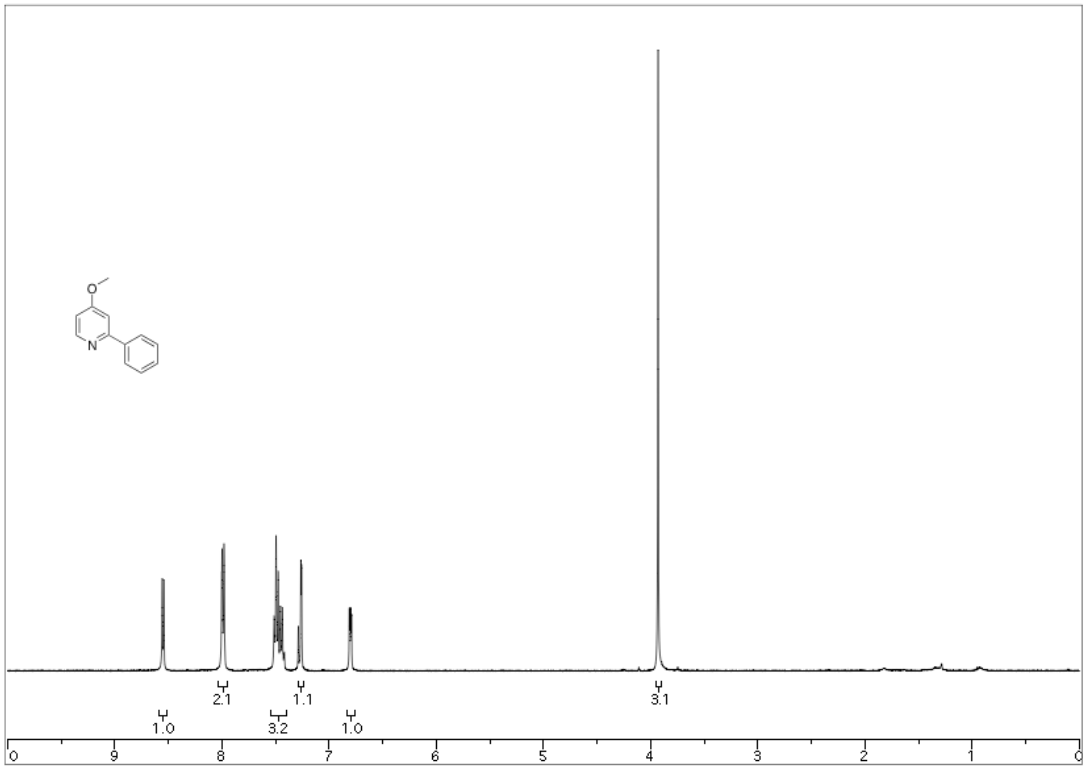
^{1}H spectra of compound **2b** in $CDCl_3$



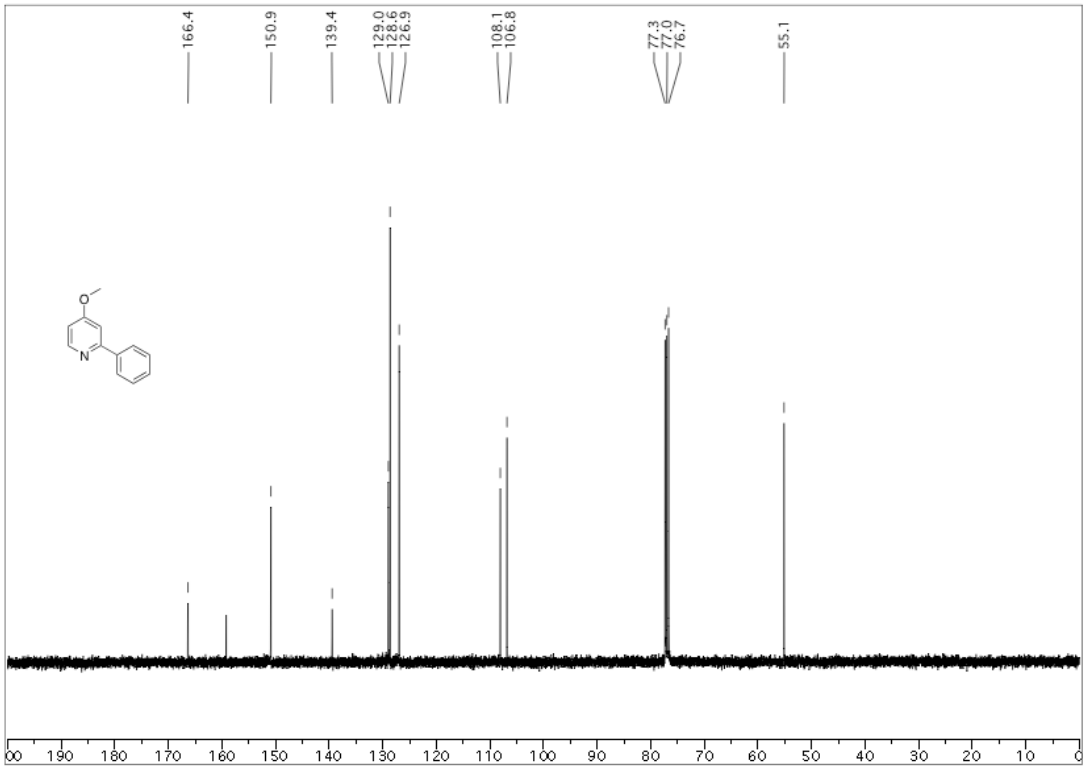
^{1}H spectra of compound **2c** in $CDCl_3$



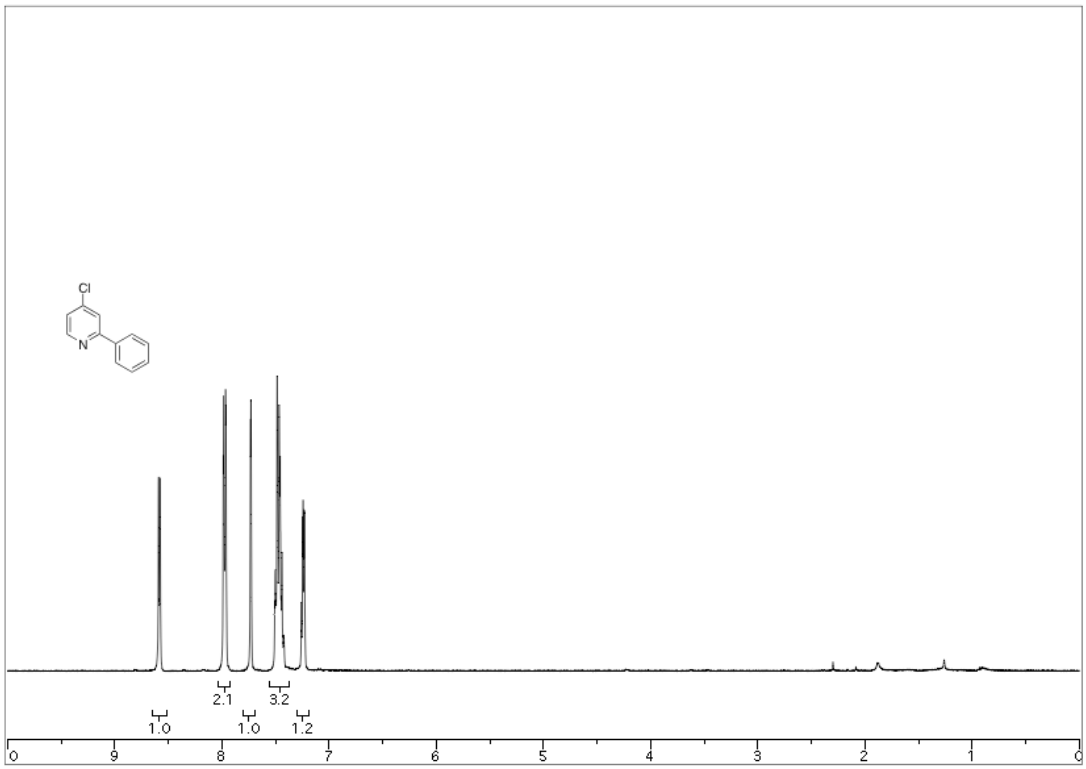
^{1}H spectra of compound **2d** in $CDCl_3$



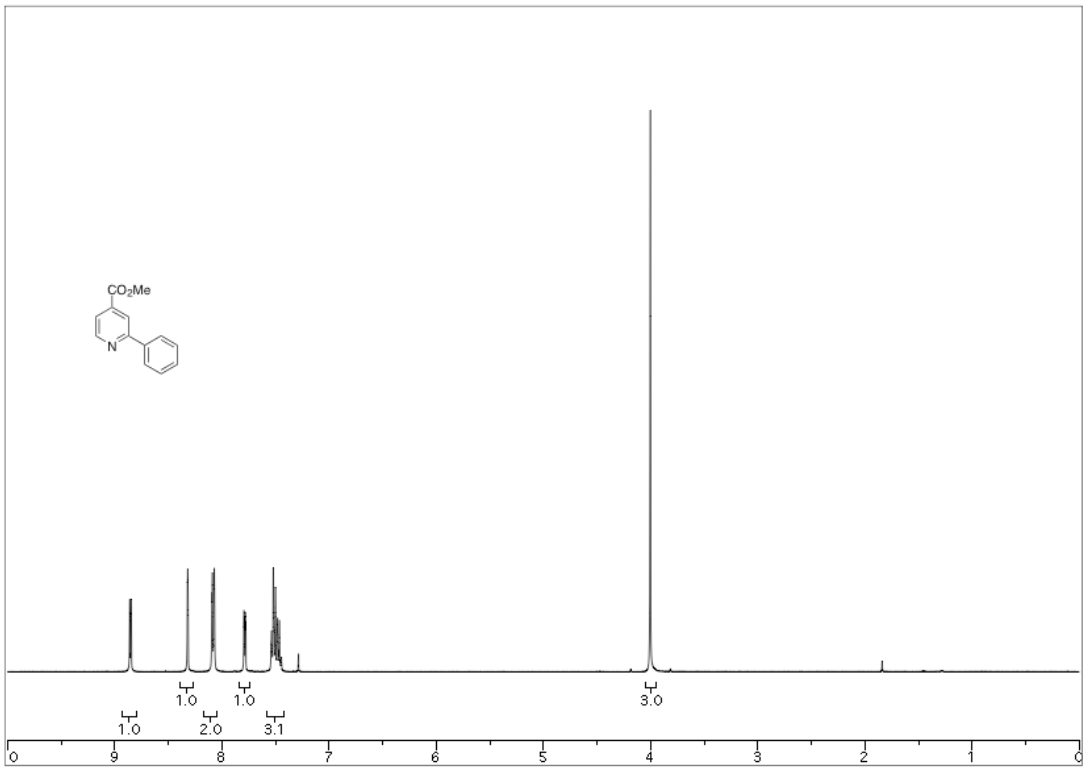
^{13}C spectra of compound **2d** in $CDCl_3$



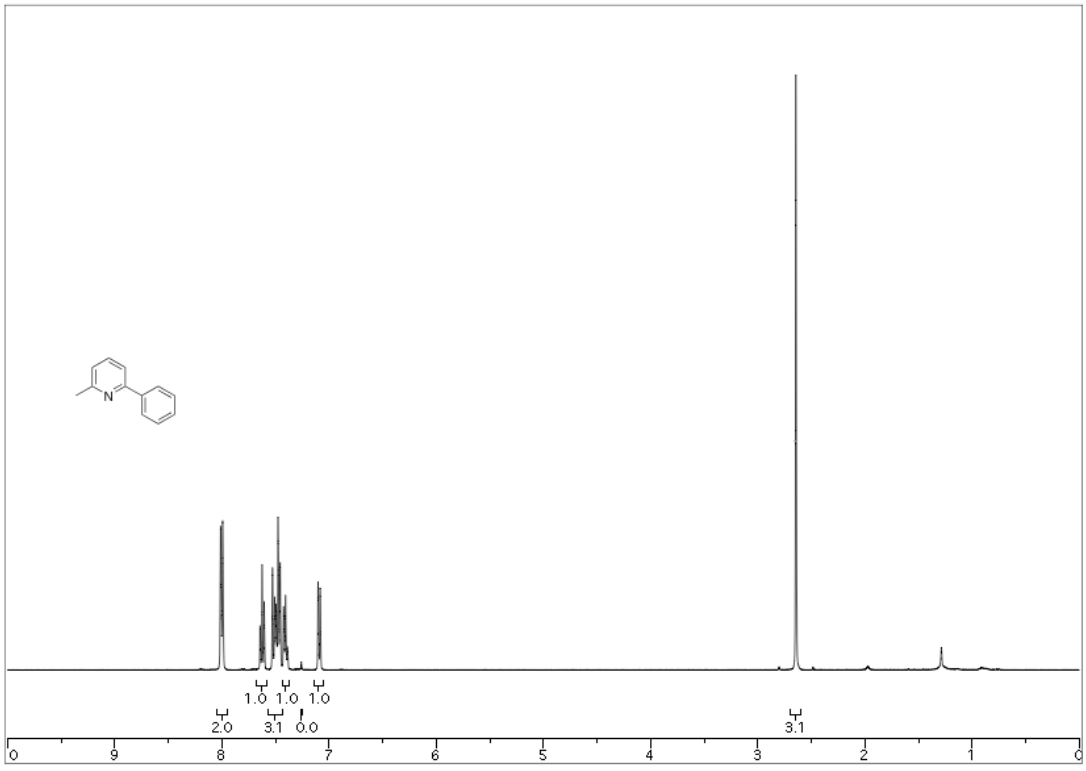
^{1}H spectra of compound **2e** in $CDCl_3$



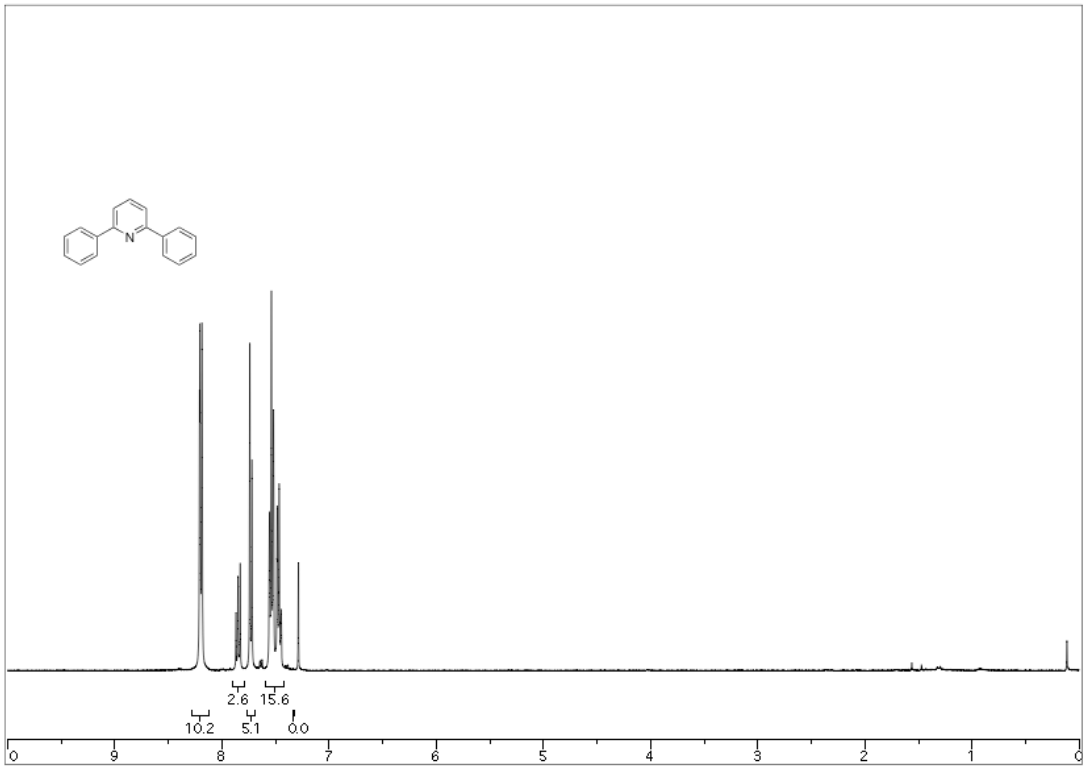
^{1}H spectra of compound **2f** in $CDCl_3$



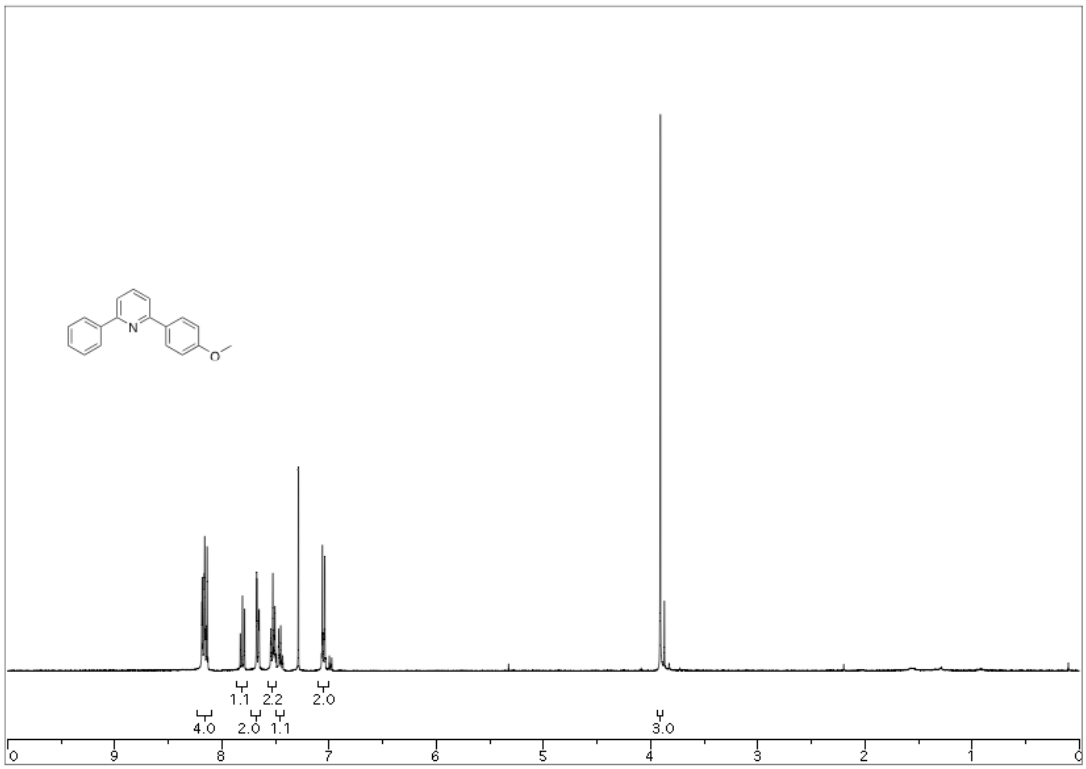
^{1}H spectra of compound **2g** in $CDCl_3$



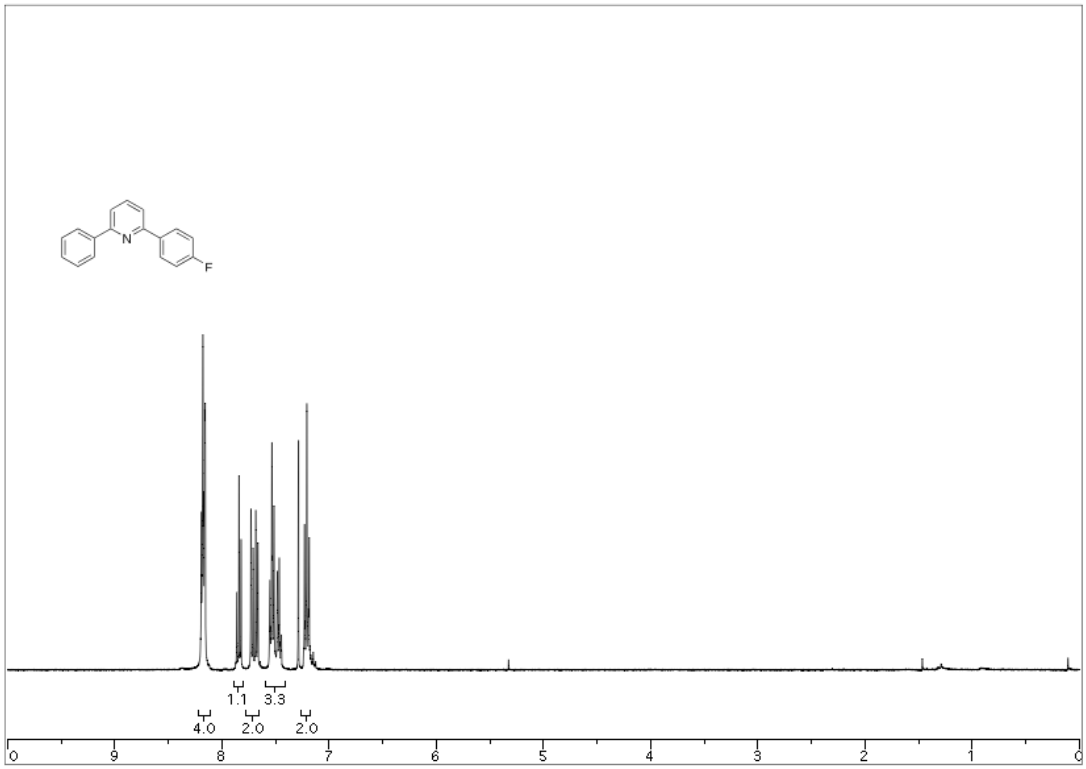
^{1}H spectra of compound **2h** in $CDCl_3$



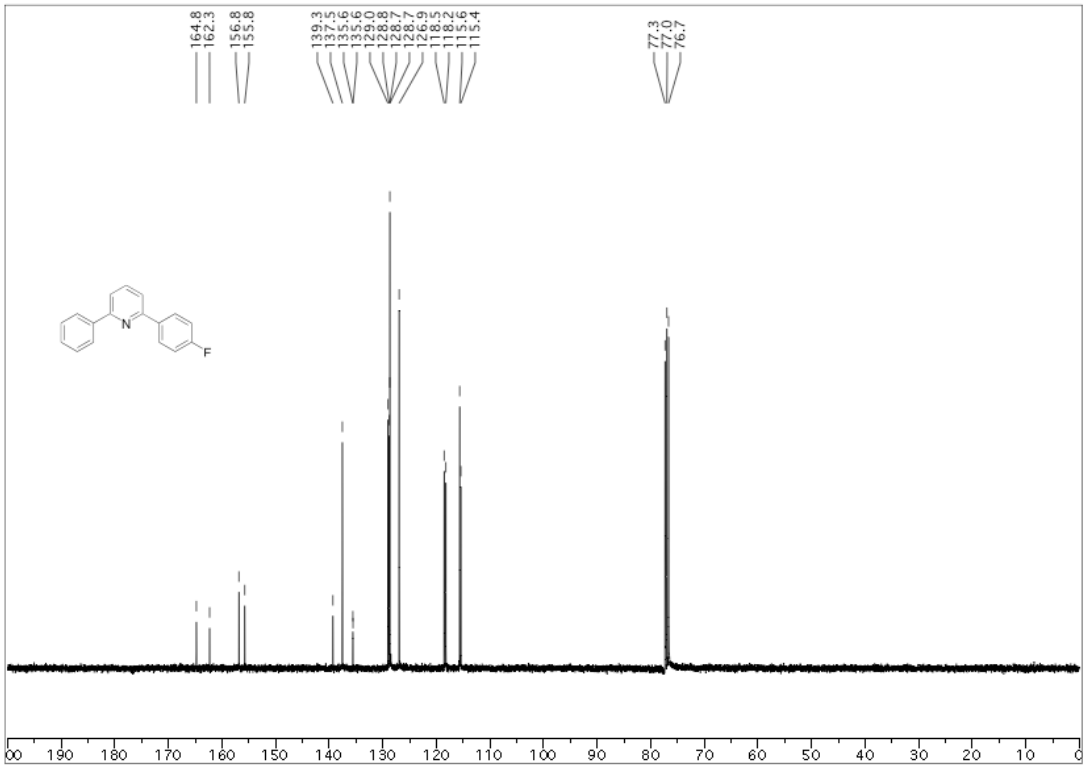
^{1}H spectra of compound **2i** in $CDCl_3$



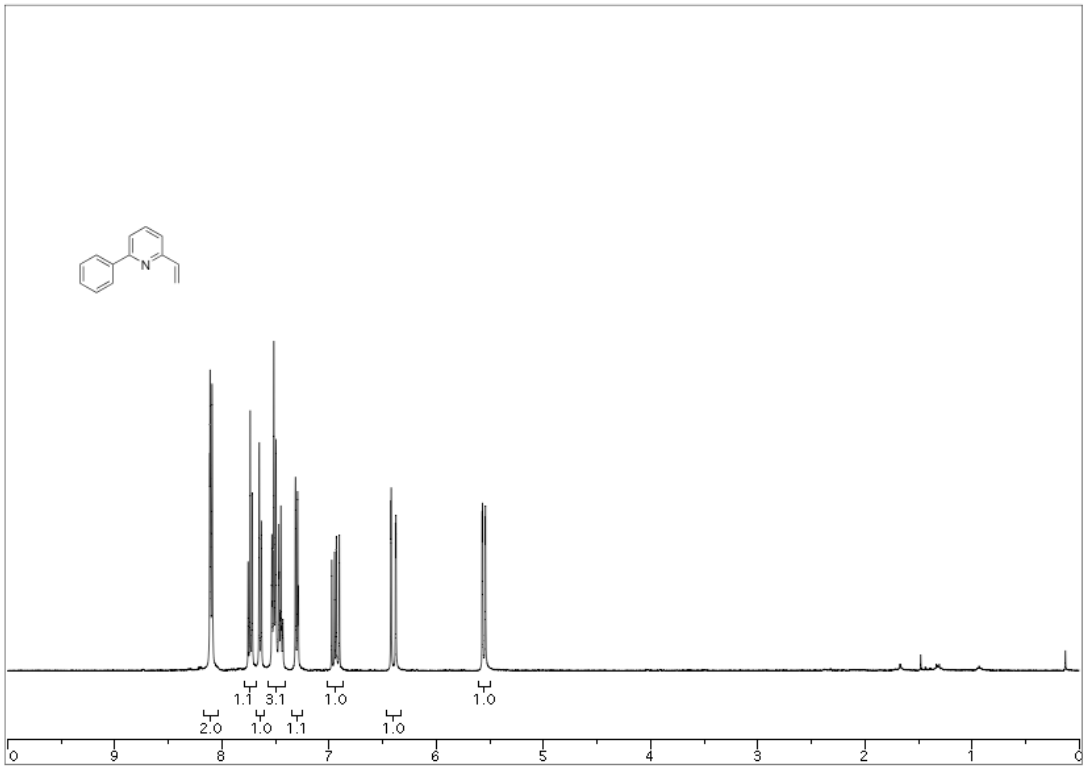
^{1}H spectra of compound **2j** in $CDCl_3$



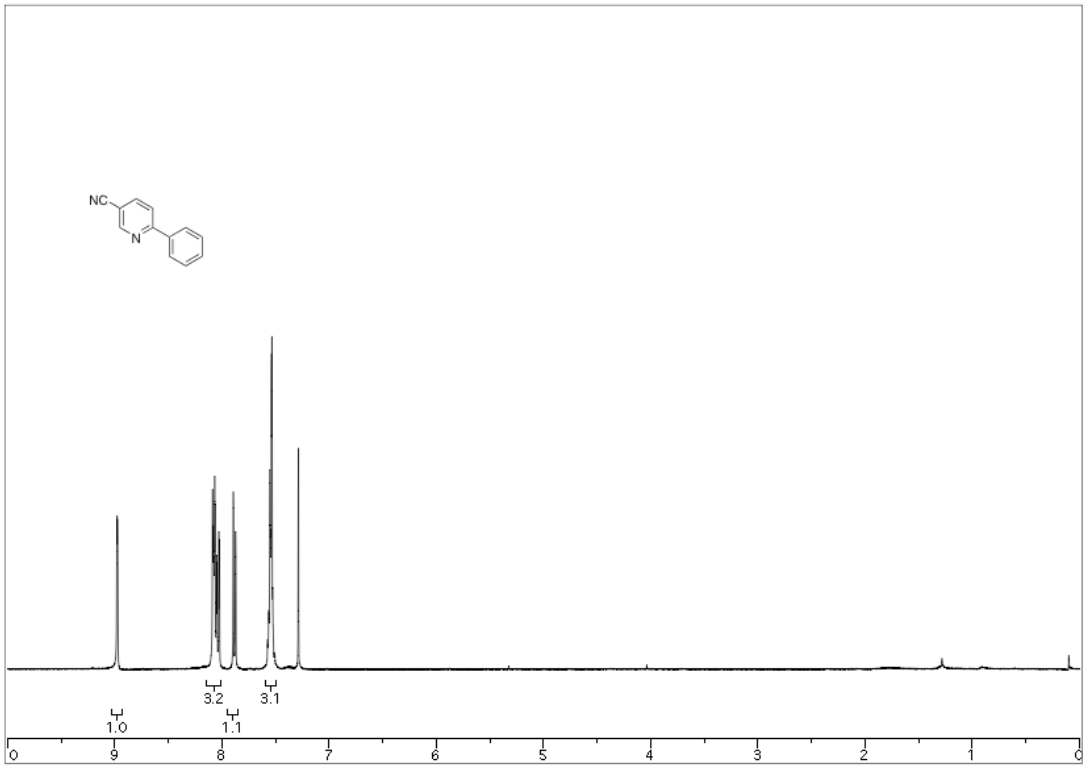
^{13}C spectra of compound **2j** in $CDCl_3$



^{1}H spectra of compound **2k** in $CDCl_3$



^{1}H spectra of compound **2m** in $CDCl_3$



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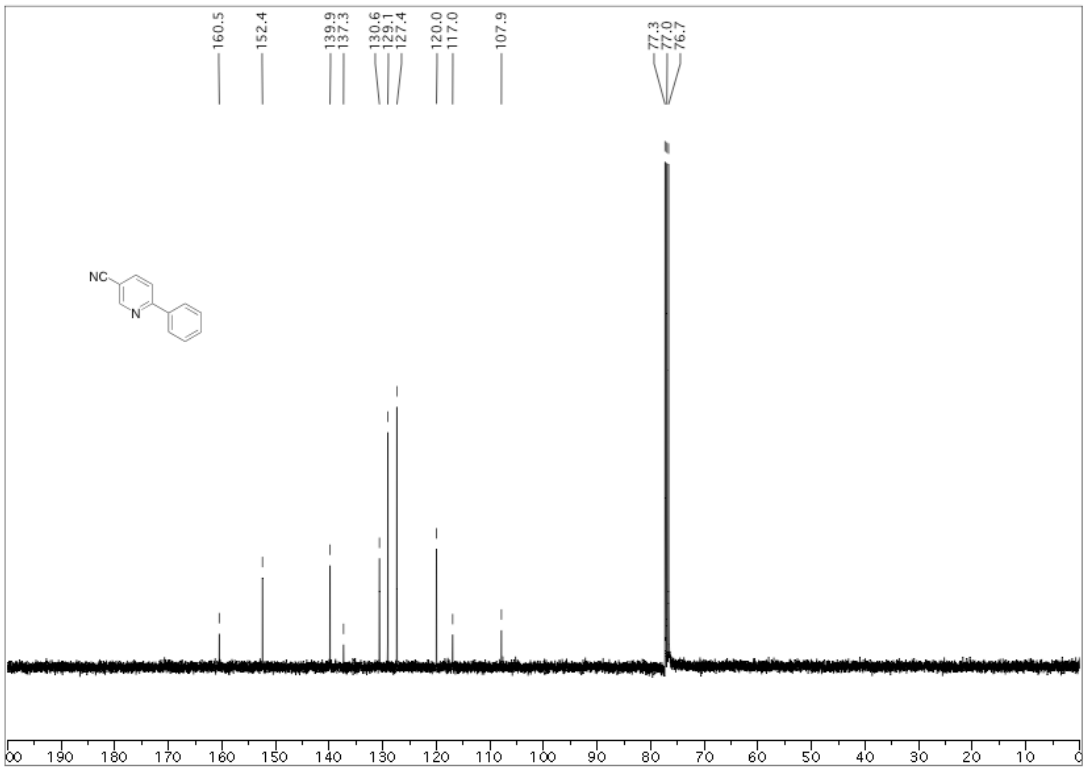
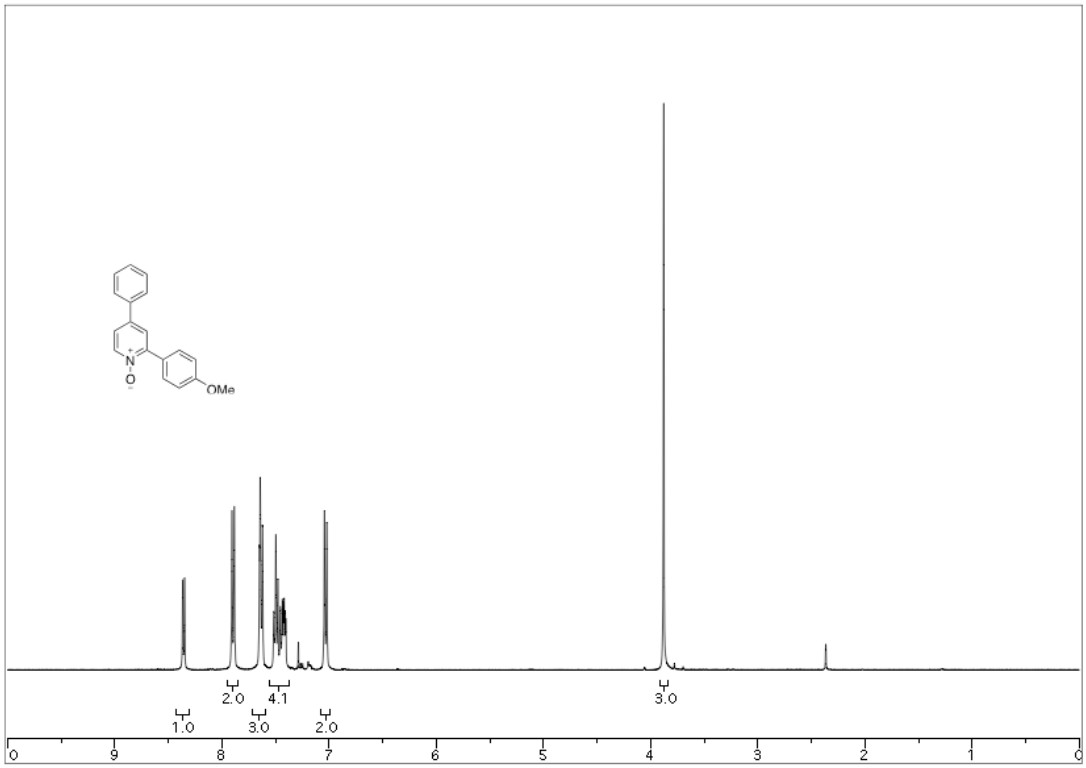
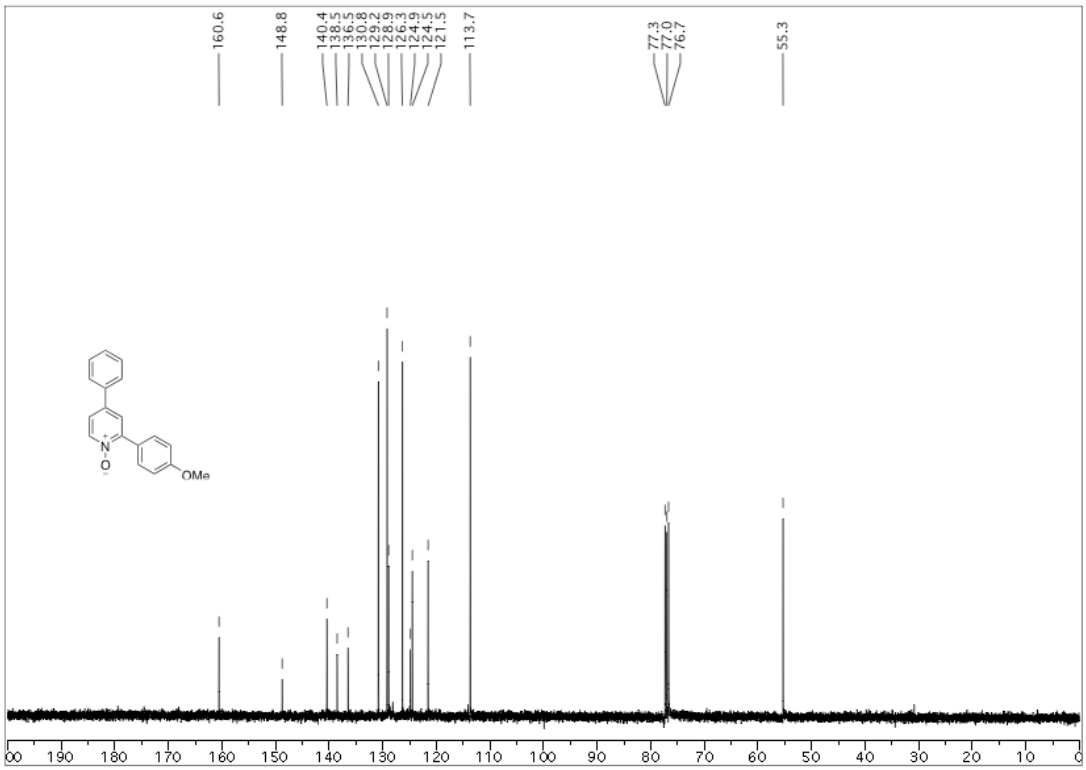


^{1}H spectra of compound **1k** in $CDCl_3$



^{13}C spectra of compound **1k** in $CDCl_3$



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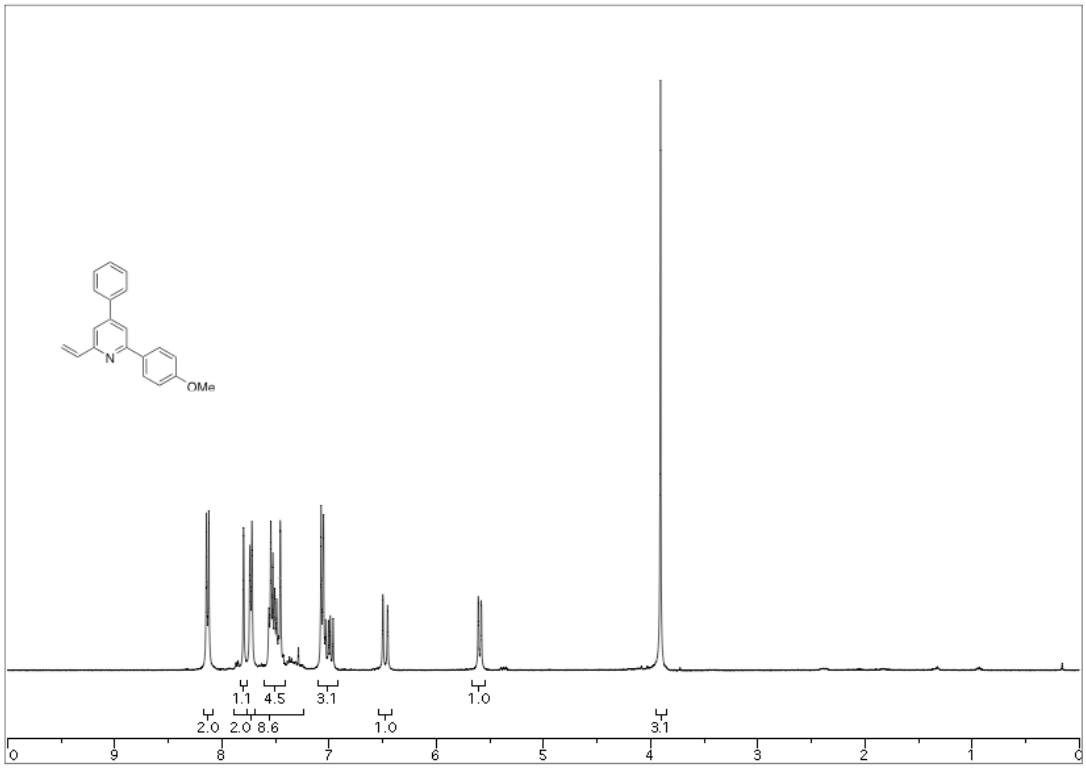

^{13}C spectra of compound **2n** in $CDCl_3$