Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

Palladium-Catalysed Aerobic Oxidative Heck-type Alkenylation of Csp^3-H for Pyrrole Synthesis

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General information

The reactions were conducted under oxygen atmosphere with a balloon fitted on a Schlenk tube,. All glassware was oven dried at 110 °C for hours and cooled down under vacuum. Toluene was purified by distillation with sodium and DMSO was purified by distillation with calcium hydride. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Imines were prepared following literature procedures. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 100-200 mesh silica gel in petroleum (bp. 60-90 °C). GC-MS spectra were recorded on a Varian GC-MS 3900-2100T. NMR spectra were recorded on a Bruker Advance III spectrometers at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR). Tetramethylsilane was used as an internal standard). All ^{1}H NMR spectra were reported in delta (δ) units, parts per million (ppm) downfield from the internal standard. Coupling constants (*J*) are reported in Hertz (Hz). High resolution mass spectra (HRMS) were measured with a Waters Micromass GCT instrument, accurate masses were reported for the molecular ion ($[M+H]^+$).

General procedure for the Pd-catalyzed aerobic oxidative intramolecular sp3 C-H Heck reaction

Method A: Firstly $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) with Bu_4NBr (161 mg, 0.5 mmol) was added in a Schlenk tube. Then the Schlenk tube was then sealed with septa and fitted with an oxygen balloon to make it filled with oxygen. After that Toluene (2 mL), DMSO (0.2 mL) and imine were injected in the tube via a syringe. At last the reaction was heated up to 35 °C. After stirring for 17 hours, it was quenched by water and extracted with ethyl ether (3 * 10 mL). The organic layers were combined and pure product was obtained by flash column chromatography on silica gel (petroleum: ethyl acetate = 40:1).

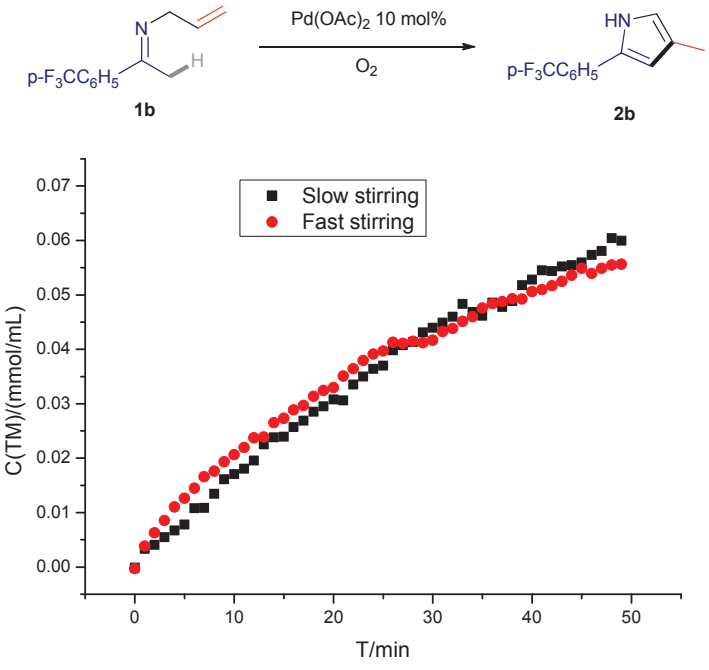
Method B: Firstly $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) with Bu_4NBr (161 mg, 0.5 mmol) was added in a Schlenk tube. Then the Schlenk tube was then sealed with septa and fitted with an oxygen balloon to make it filled with oxygen. After that Toluene (2 mL), DMSO (0.2 mL) and imine were injected in the tube via a syringe. At last the reaction was heated up to 35 °C. After stirring for 6 hours, it was quenched by water and extracted with ethyl ether (3 * 10 mL). The organic layers were combined and pure product was obtained by flash column chromatography on silica gel (petroleum: ethyl acetate = 40:1).

Method C: Firstly $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) with Bu_4NBr (161 mg, 0.5 mmol) was added in a Schlenk tube. Then the Schlenk tube was then sealed with septa and fitted with an oxygen balloon to make it filled with oxygen. After that Toluene (2 mL), DMSO (0.2 mL) and imine were injected in the tube via a syringe. At last the reaction was heated up to 90 °C. After stirring for 17 hours, it was quenched by water and extracted with ethyl ether (3 * 10 mL). The organic layers were combined and pure product was obtained by flash column chromatography on silica gel (petroleum: ethyl acetate = 40:1).

In-situ IR experiments

Procedure for the effect of stirring speed

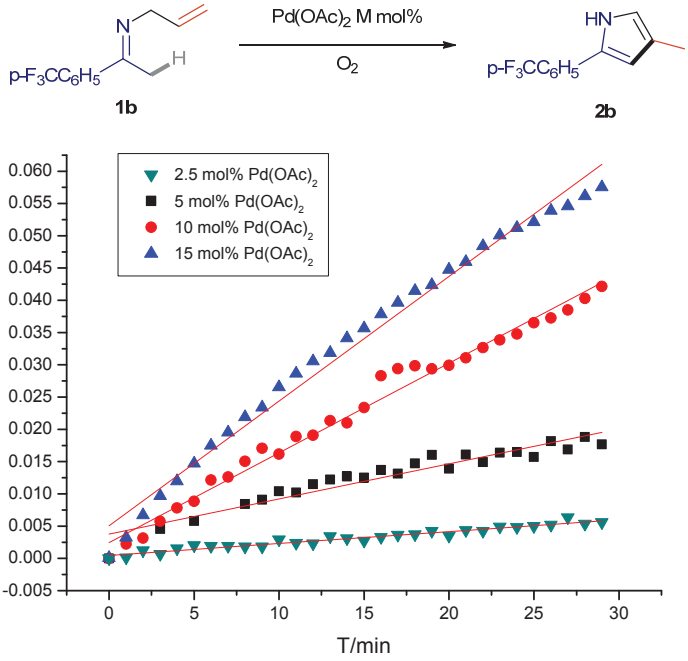
Firstly $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) with Bu_4NBr (161 mg, 0.5 mmol) was added in a Schlenk tube. Then the Schlenk tube was put onto in-situ IR, sealed with septa and fitted with an oxygen balloon to make it filled with oxygen. After that Toluene (2.5 mL), DMSO (0.25 mL) and imine **1b** (0.5 mmol) were injected in the tube via syringe. At last the reaction was heated up to 35 °C. The yield was determined by GC with biphenyl as internal standard.



Procedure for the effect of concentration of catalyst

Firstly $Pd(OAc)_2$ (m mg, n mmol) with Bu_4NBr (161 mg, 0.5 mmol) was added in a Schlenk tube. Then the Schlenk tube was put onto in-situ IR, sealed with septa and fitted with an oxygen balloon to make it filled with oxygen. After that Toluene (2.5 mL), DMSO (0.25 mL) and imine **1b** (0.5

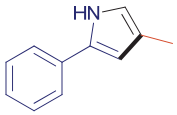
mmol) were injected in the tube via syringe. At last the reaction was heated up to 35 °C. The yield was determined by GC with biphenyl as internal standard.



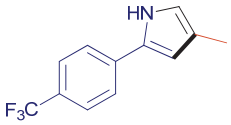
Procedure for the effect of concentration of substrate

Firstly $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) with Bu_4NBr (161 mg, 0.5 mmol) was added in a Schlenk tube. Then the Schlenk tube was put onto in-situ IR, sealed with septa and fitted with an oxygen balloon to make it filled with oxygen. After that Toluene (2.5 mL), DMSO (0.25 mL) and imine **1b** (n mmol) were injected in the tube via syringe. At last the reaction was heated up to 35 °C. The yield was detected by GC with biphenyl as internal standard.

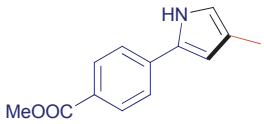
Detail descriptions for products



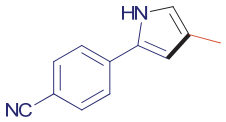
4-Methyl-2-phenyl-1H-pyrrole (**2a**)[1]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.49-7.47 (m, 2H), 7.39 (t, *J* = 8 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 6.65 (s, 1H), 6.43 (s, 1H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.9, 132.0, 128.8, 126.0, 123.7, 120.7, 116.8, 107.5, 12.0.



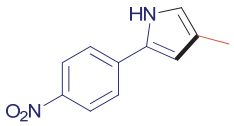
4-Methyl-2-(4-(trifluoromethyl)phenyl)-1H-pyrrole (**2b**)[1]: ^{1}H NMR (400 MHz, D-acetone) δ 10.43 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8 Hz, 2H), 6.74 (s, 1H), 6.55 (s, 1H), 2.12 (s, 3H). ^{13}C NMR (100 MHz, D-acetone) δ 137.1, 129.9, 125.6 (q, *J* = 3.9 Hz), 123.2, 120.1, 118.8, 118.6, 109.1, 109.0, 11.1. HRMS (ESI) calcd for $C_{12}H_{11}F_3N$ $[M+H]^+$: 226.0844; found: 226.0843



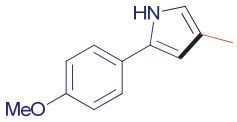
Methyl 4-(4-methyl-1H-pyrrol-2-yl)benzoate (**2c**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.02 (d, *J* = 7.1 Hz, 2H), 7.50 (d, *J* = 7.2 Hz, 2H), 6.70 (s, 1H), 6.52 (s, 1H), 3.94 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 136.9, 130.8, 130.3, 127.0, 122.9, 121.2, 118.3, 109.4, 52.0, 11.9. HRMS (ESI) calcd for $C_{13}H_{14}NO_2$ $[M+H]^+$: 216.1028; found: 216.1025.



4-(4-Methyl-1H-pyrrol-2-yl)benzonitrile (**2d**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.64-7.61 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H), 6.74 (s, 1H), 6.53 (s, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 132.8, 129.9, 123.4, 121.6, 119.3, 119.1, 110.1, 108.4, 11.8. HRMS (ESI) calcd for $C_{12}H_{11}N_2$ $[M+H]^+$: 183.0920; found: 183.0922.

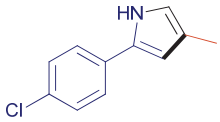


4-Methyl-2-(4-nitrophenyl)-1H-pyrrole (**2e**): ^{1}H NMR (400 MHz, D-acetone) δ 10.62 (s, 1H), 8.20-8.16 (m, 2H), 7.80-7.77 (m, 2H), 6.82 (s, 1H), 6.66 (s, 1H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, D-acetone) δ 144.7, 139.5, 129.5, 124.2, 123.0, 120.8, 120.5, 110.9, 11.1. HRMS (ESI) calcd for $C_{11}H_{11}N_2O_2$ $[M+H]^+$:203.0821; found: 203.0819

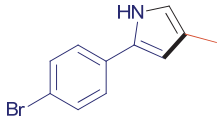


2-(4-Methoxyphenyl)-4-methyl-1H-pyrrole (**2f**)[1]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.39 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.61 (s, 1H), 6.29 (s, 1H), 3.85 (s, 3H), 2.19 (s,

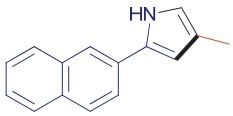
3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 132.1, 126.1, 125.1, 120.5, 116.0, 114.5, 106.5, 55.3, 12.0. . HRMS (ESI) calcd for $C_{12}H_{14}NO$ $[M+H]^+$: 188.1075; found: 188.1072.



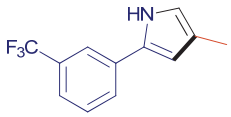
2-(4-Chlorophenyl)-4-methyl-1H-pyrrole (**2g**)[2]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.39-7.32 (m, 4H), 6.65 (s, 1H), 6.38 (s, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.5, 131.4, 130.9, 129.0, 124.8, 120.9, 117.2, 107.9, 11.9. HRMS (ESI) calcd for $C_{11}H_{11}ClN$ $[M+H]^+$: 192.0580; found: 192.0579.



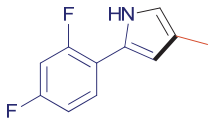
2-(4-Bromophenyl)-4-methyl-1H-pyrrole (**2h**)[1]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.50-7.47 (m, 2H), 7.33-7.30 (m, 2H), 6.66 (s, 1H), 6.39 (s, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz,$CDCl_3$) δ 131.9, 131.8, 130.9, 125.0, 120.9, 119.4, 117.2, 108.0, 11.9.



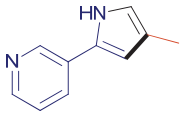
4-Methyl-2-(naphthalen-2-yl)-1H-pyrrole (**2i**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.86-7.82 (m, 4H), 7.67-7.65 (m, 1H), 7.52-7.43 (m, 2H), 6.70 (s, 1H), 6.55 (s, 1H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.8, 132.0(3), 132.0(2), 130.3, 128.5, 127.7(4), 127.6(6), 126.4, 125.3, 123.1, 120.9, 120.8, 117.2, 108.2, 12.0. HRMS (ESI) calcd for $C_{15}H_{14}N$ $[M+H]^+$: 208.1126; found: 208.1124.



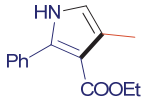
4-Methyl-2-(3-(trifluoromethyl)phenyl)-1H-pyrrole (**2j**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.68 (s, 1H), 7.62 (d, J = 7.4 Hz, 1H), 7.52 – 7.40 (m, 2H), 6.69 (s, 1H), 6.47 (s, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.6 , 131.4 , 131.1 , 130.5 , 129.3 , 126.6, 122.4 (q, J = 3.7 Hz), 121.1, 120.2 (q, J = 3.8 Hz), 117.7, 108.7, 11.8. HRMS (ESI) calcd for $C_{12}H_{11}F_3N$ $[M+H]^+$: 226.0845; found: 226.0844.



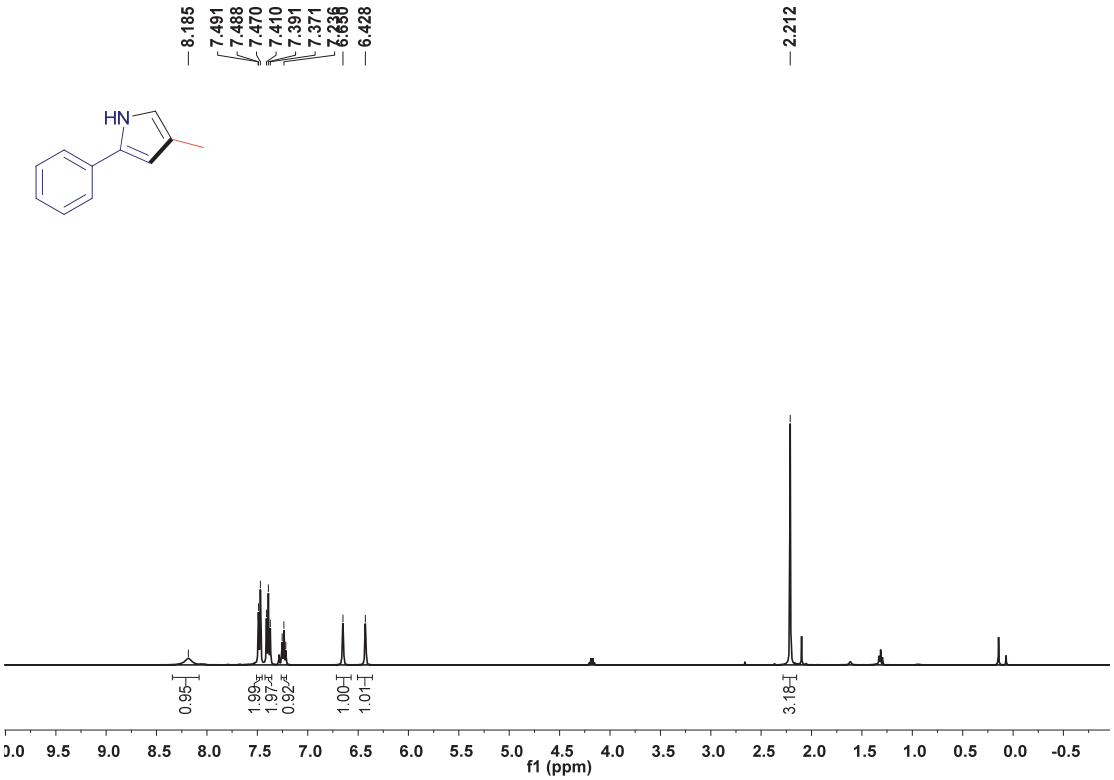
2-(2,4-Difluorophenyl)-4-methyl-1H-pyrrole (**2k**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.58-7.52 (m, 1H), 6.94-6.87 (m, 2H), 6.69 (s, 1H), 6.45 (s, 1H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9 (d, J = 12.6), 159.5 (dd, $J1$ = 4.2 Hz, $J2$ = 11.4 Hz), 157.1 (d, J = 11.3 Hz), 127.3 (q, J = 6.3 Hz), 125.8, 120.0, 117.1-116.9 (m), 112.0 (q, J = 3.3 Hz), 108.9, 104.5 (q, J = 25.4 Hz), 11.8. HRMS (ESI) calcd for $C_{11}H_{10}F_2N$ $[M+H]^+$: 194.0781; found: 194.0779.



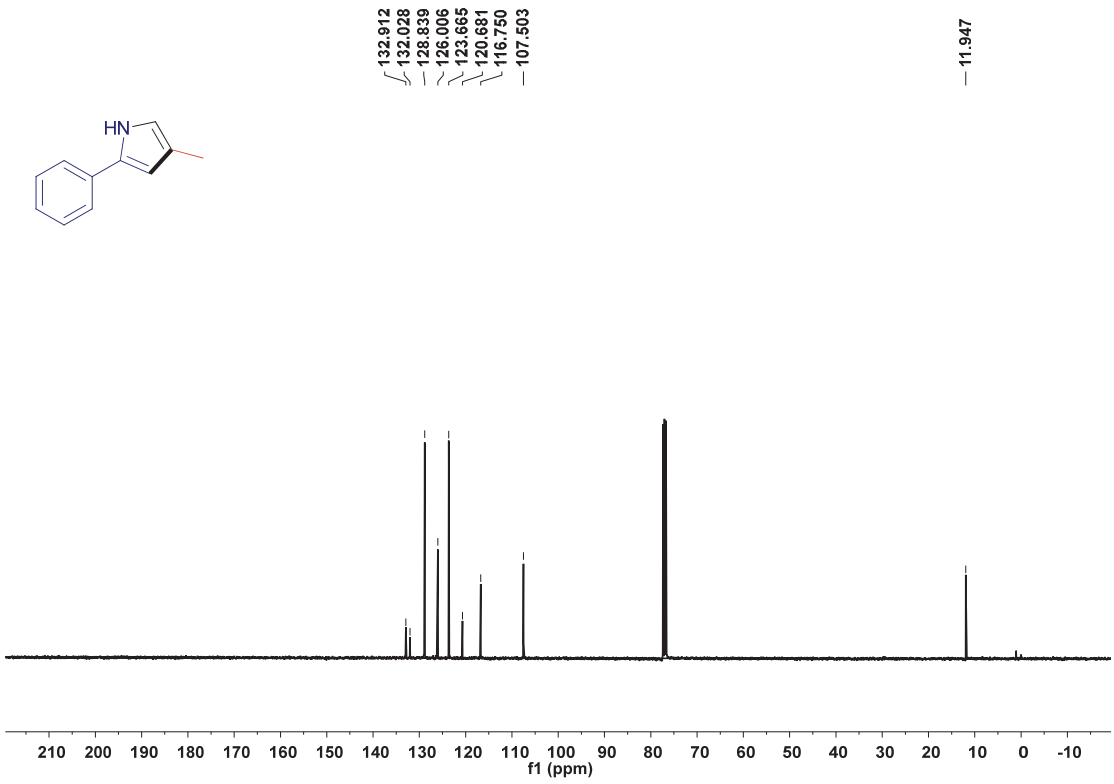
3-(4-Methyl-1H-pyrrol-2-yl)pyridine (**2l**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 1.8 Hz, 1H), 8.70 (s, 1H), 8.42 (m, 1H), 7.74 (m, 1H), 7.28 (s, 1H), 6.71 (s, 1H), 6.45 (s, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 145.1, 130.7, 128.9, 128.6, 123.7, 121.0, 118.0, 108.7, 11.8. HRMS (ESI) calcd for $C_{10}H_{11}N_2$ $[M+H]^+$: 159.0922; found: 159.0916.



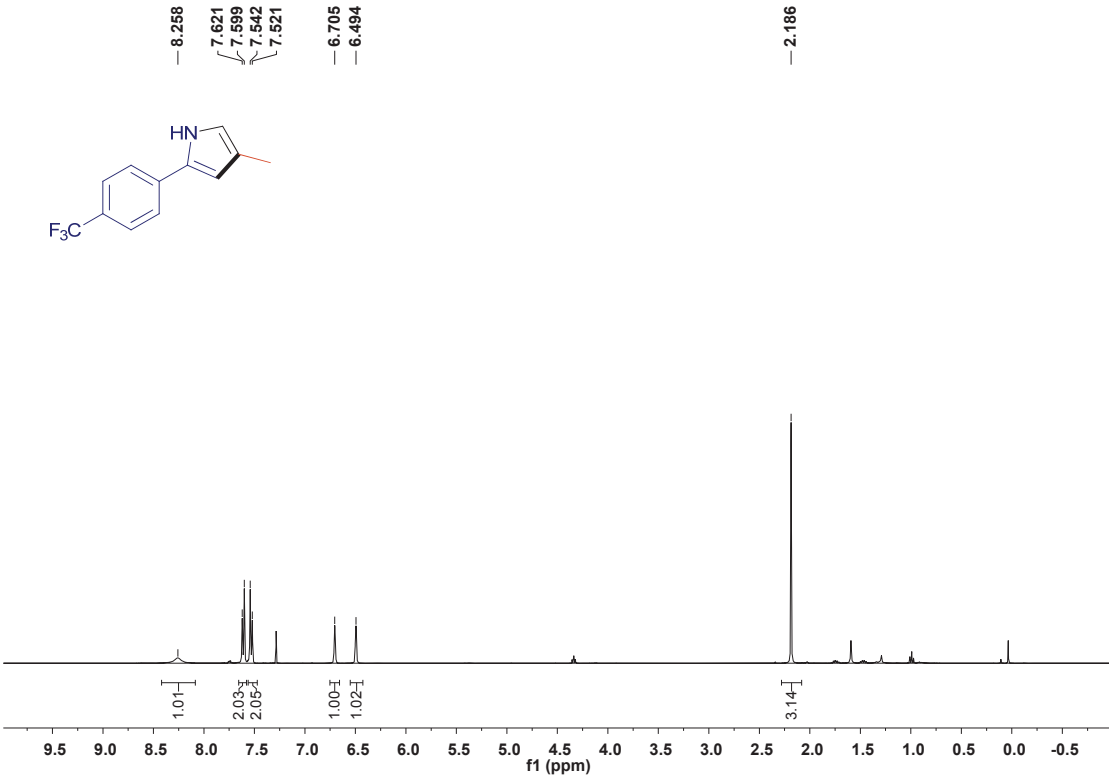
Ethyl 4-methyl-2-phenyl-1H-pyrrole-3-carboxylate (**4**)[1]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.51-7.49 (m, 2H), 7.40-7.37 (m, 3H), 6.57 (s, 1H), 4.18 (q, *J* = 6.8 Hz, 2H), 2.33 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz,$CDCl_3$) δ 165.8, 137.6, 133.0, 129.0, 128.0, 127.9, 122.6, 116.6, 111.4, 59.4, 14.1, 12.6.



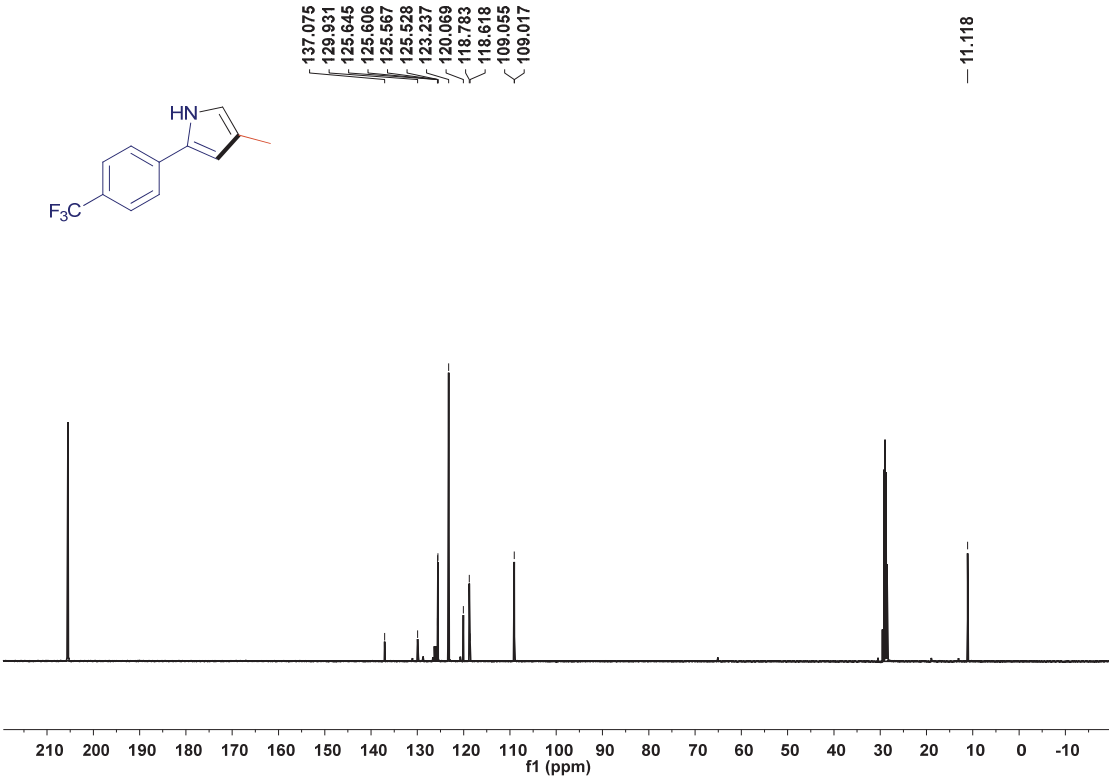
^{1}H NMR spectrum of 4-methyl-2-phenyl-1H-pyrrole 2a



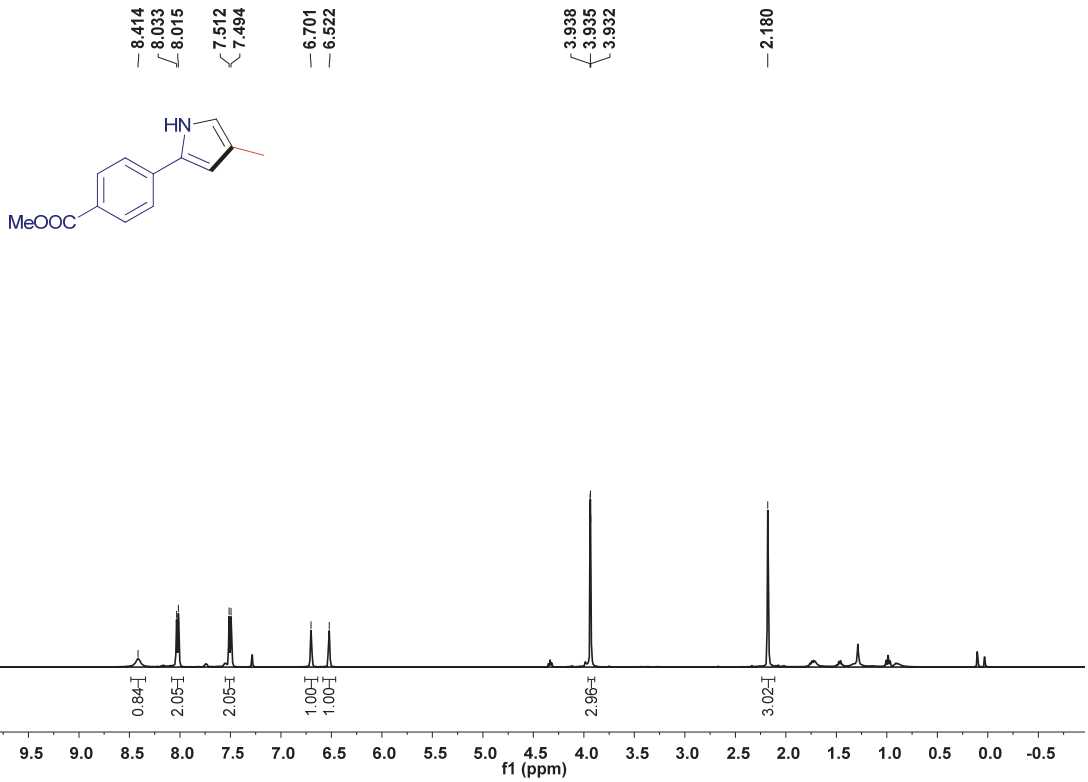
^{13}C NMR spectrum of 4-methyl-2-phenyl-1H-pyrrole 2a



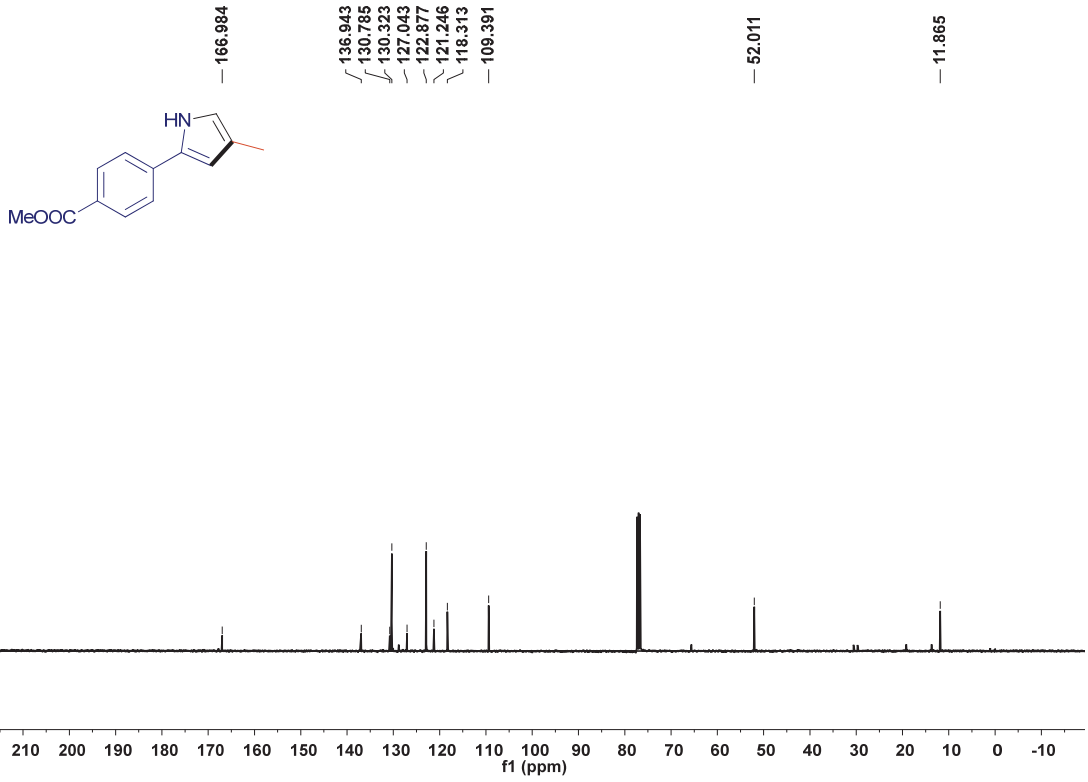
^{1}H NMR spectrum of 4-methyl-2-(4-(trifluoromethyl)phenyl)-1H-pyrrole 2b



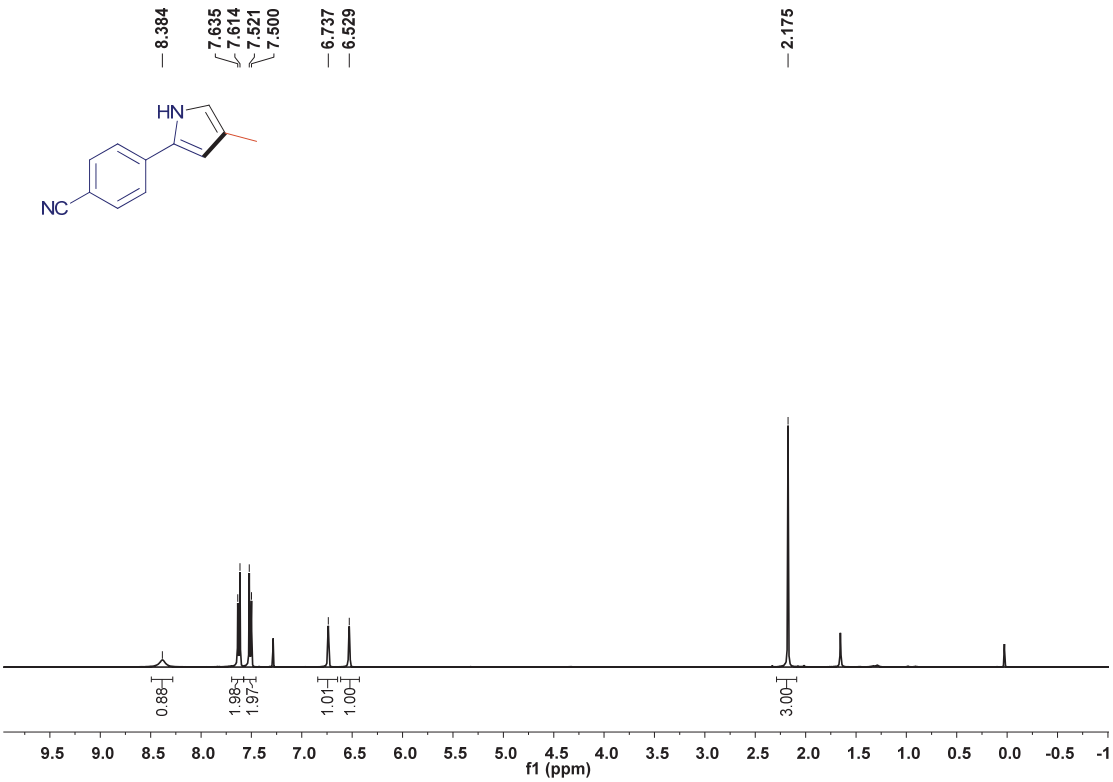
^{13}C NMR spectrum of 4-methyl-2-(4-(trifluoromethyl)phenyl)-1H-pyrrole 2b



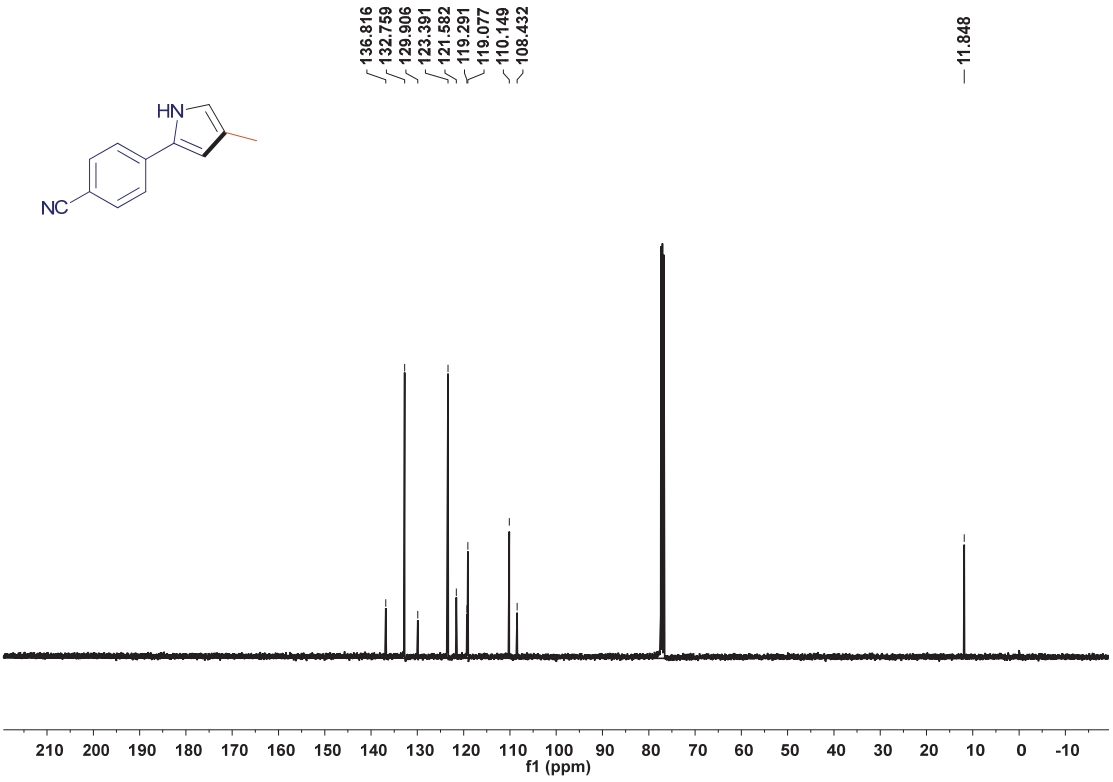
^{1}H NMR spectrum of methyl 4-(4-methyl-1H-pyrrol-2-yl)benzoate 2c



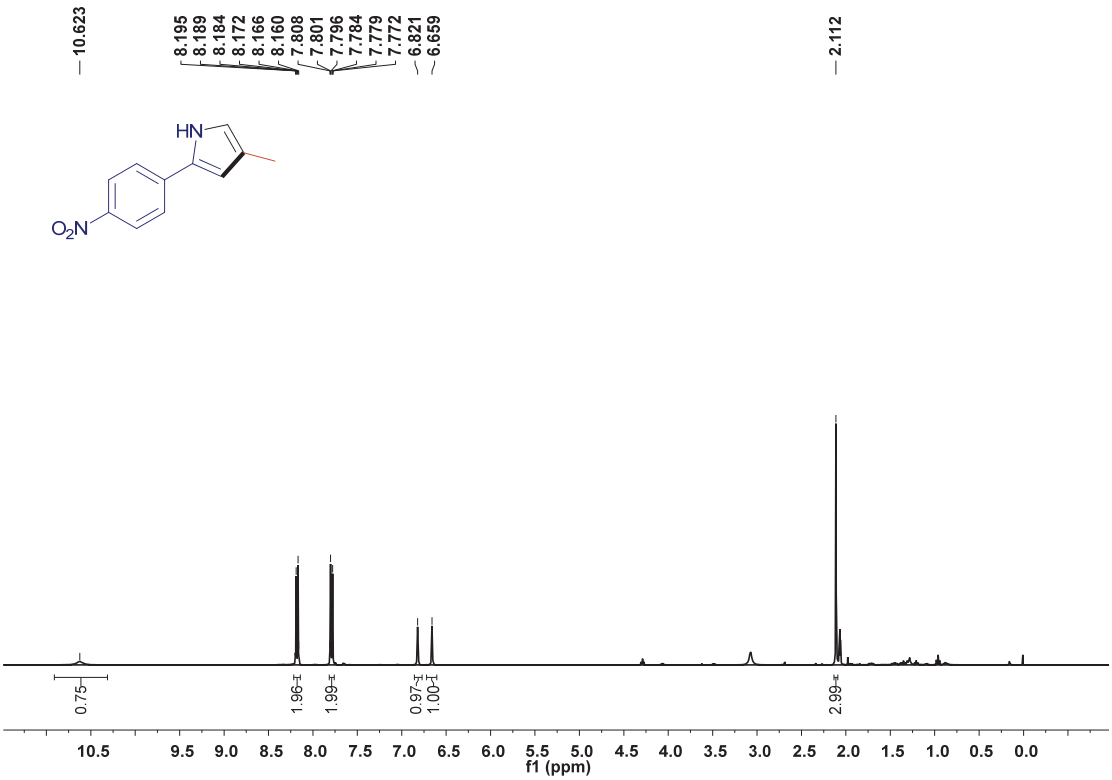
^{13}C NMR spectrum of methyl 4-(4-methyl-1H-pyrrol-2-yl)benzoate 2c



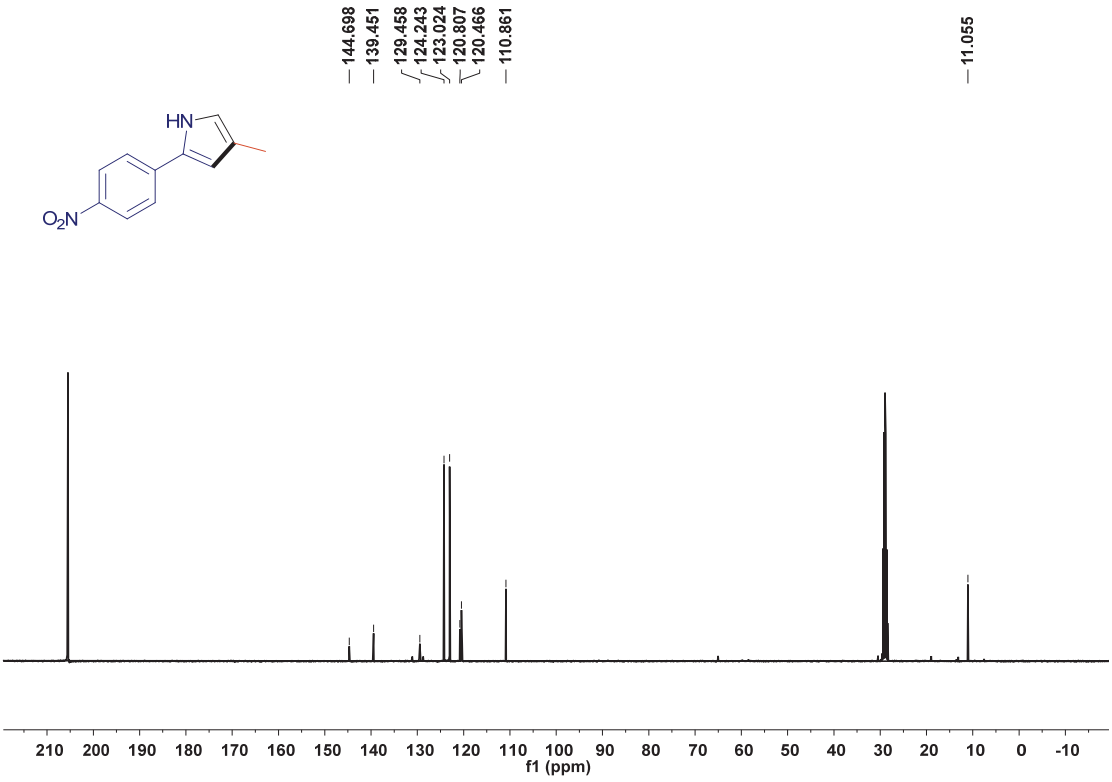
^{1}H NMR spectrum of 4-(4-methyl-1H-pyrrol-2-yl)benzonitrile 2d



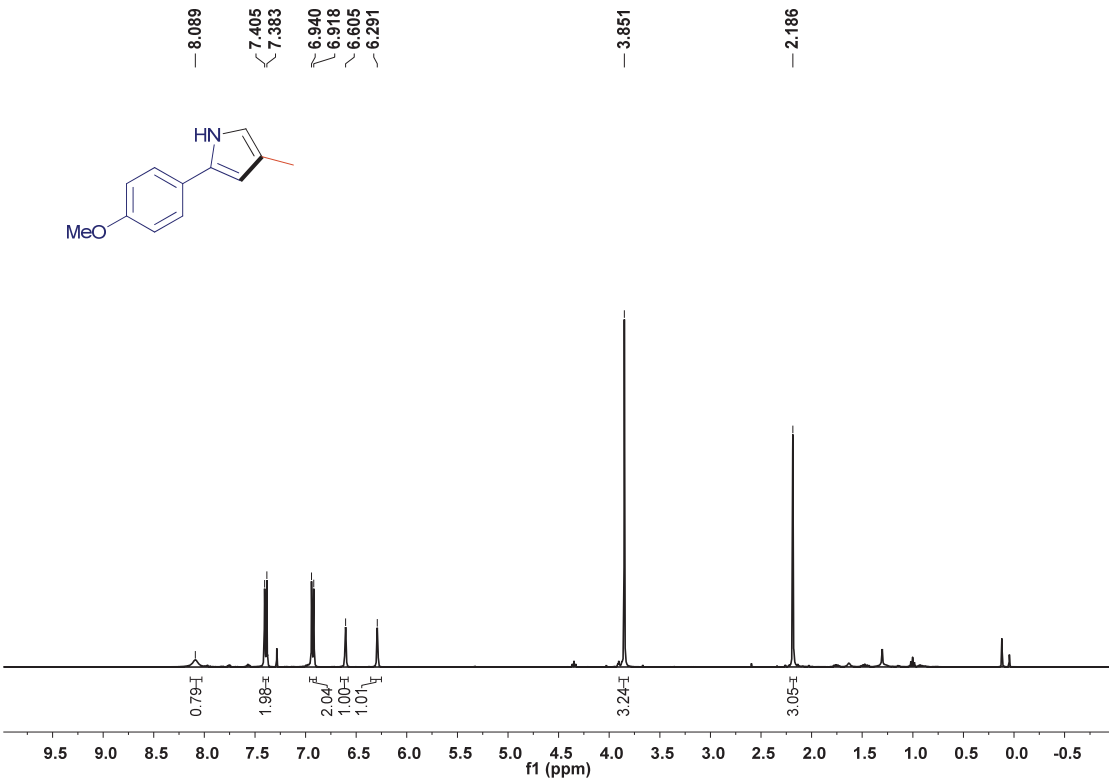
^{13}C NMR spectrum of 4-(4-methyl-1H-pyrrol-2-yl)benzonitrile 2d



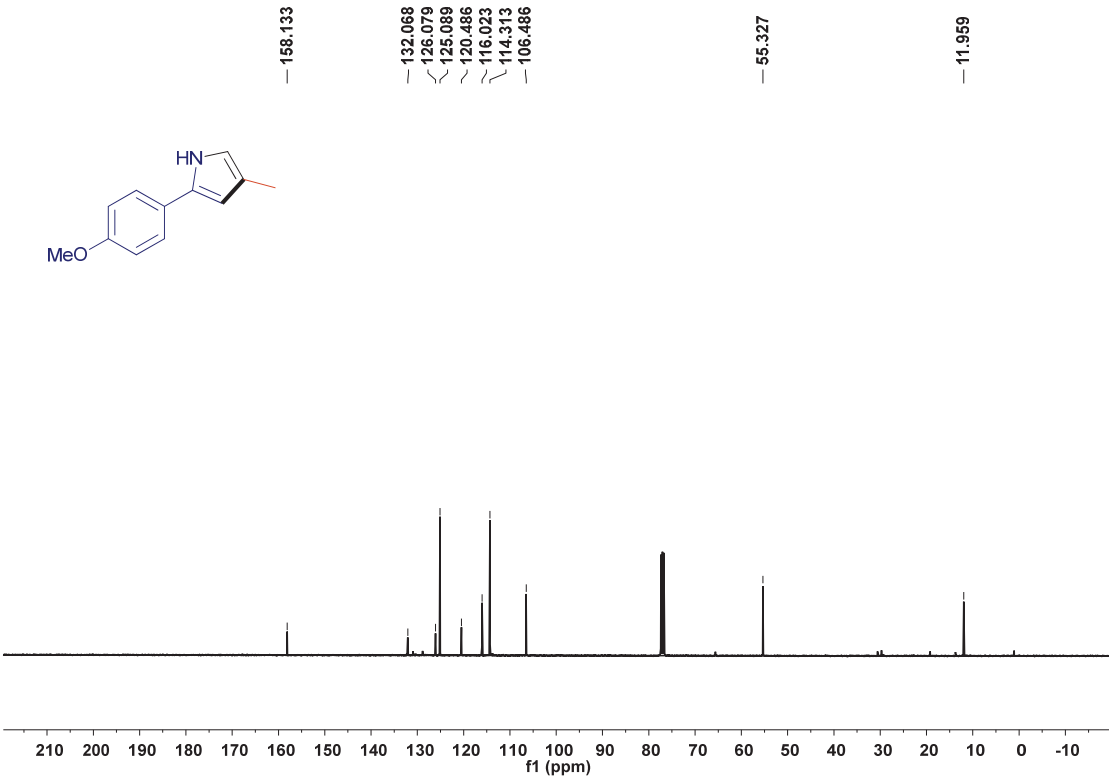
^{1}H NMR spectrum of 4-methyl-2-(4-nitrophenyl)-1H-pyrrole 2e



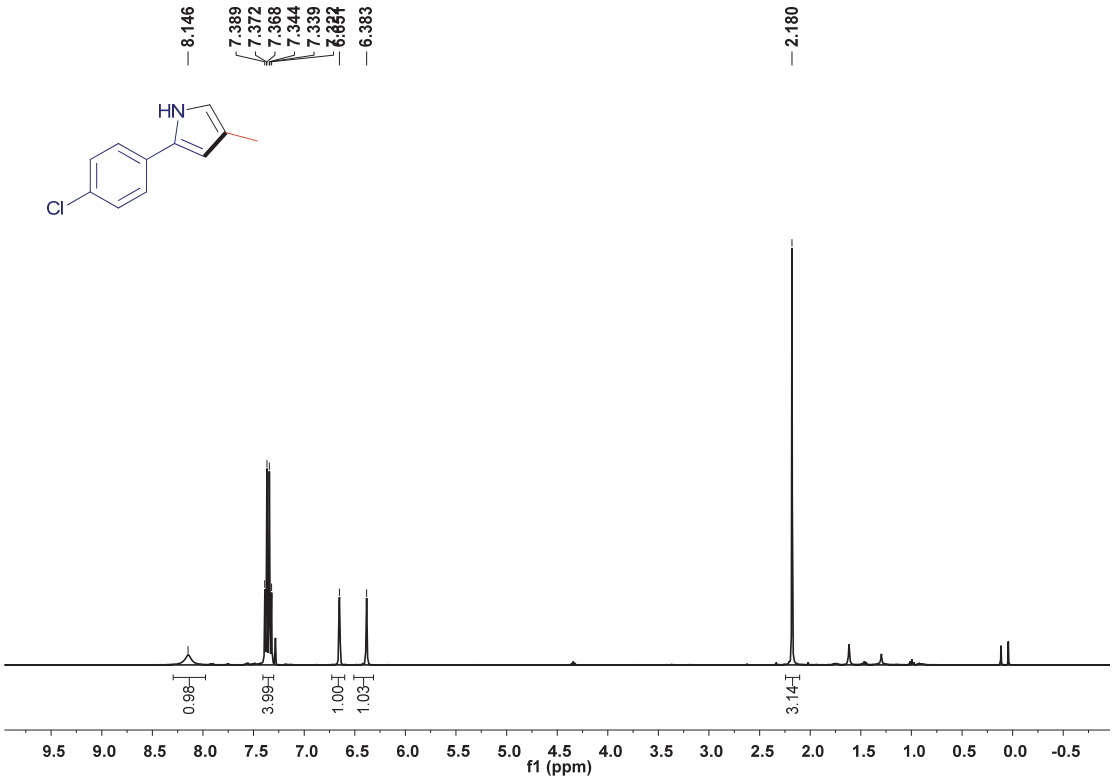
^{13}C NMR spectrum of 4-methyl-2-(4-nitrophenyl)-1H-pyrrole 2e



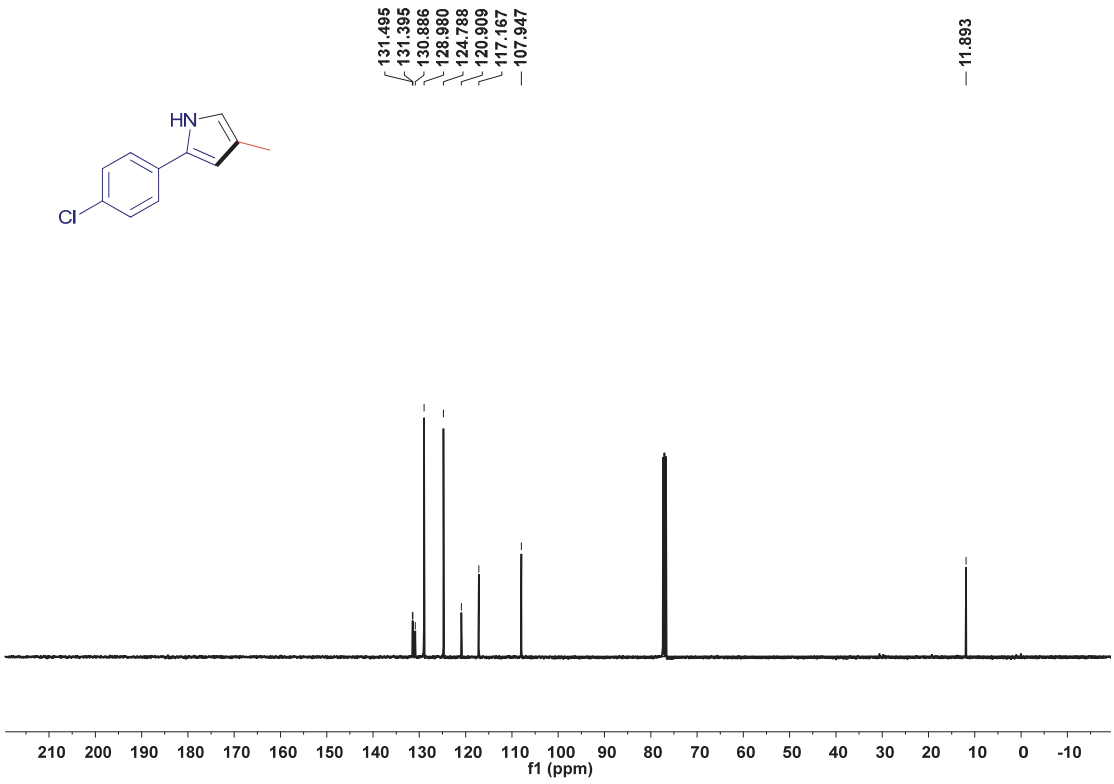
^{1}H NMR spectrum of 2-(4-methoxyphenyl)-4-methyl-1H-pyrrole 2f



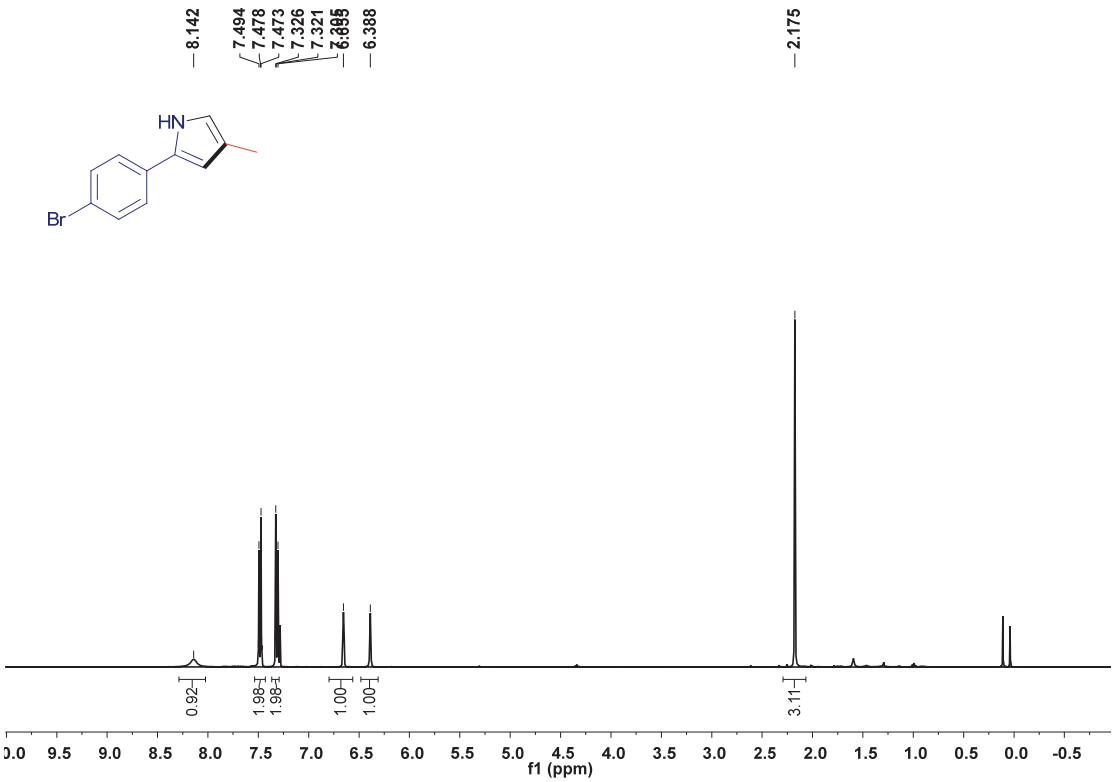
^{13}C NMR spectrum of 2-(4-methoxyphenyl)-4-methyl-1H-pyrrole 2f



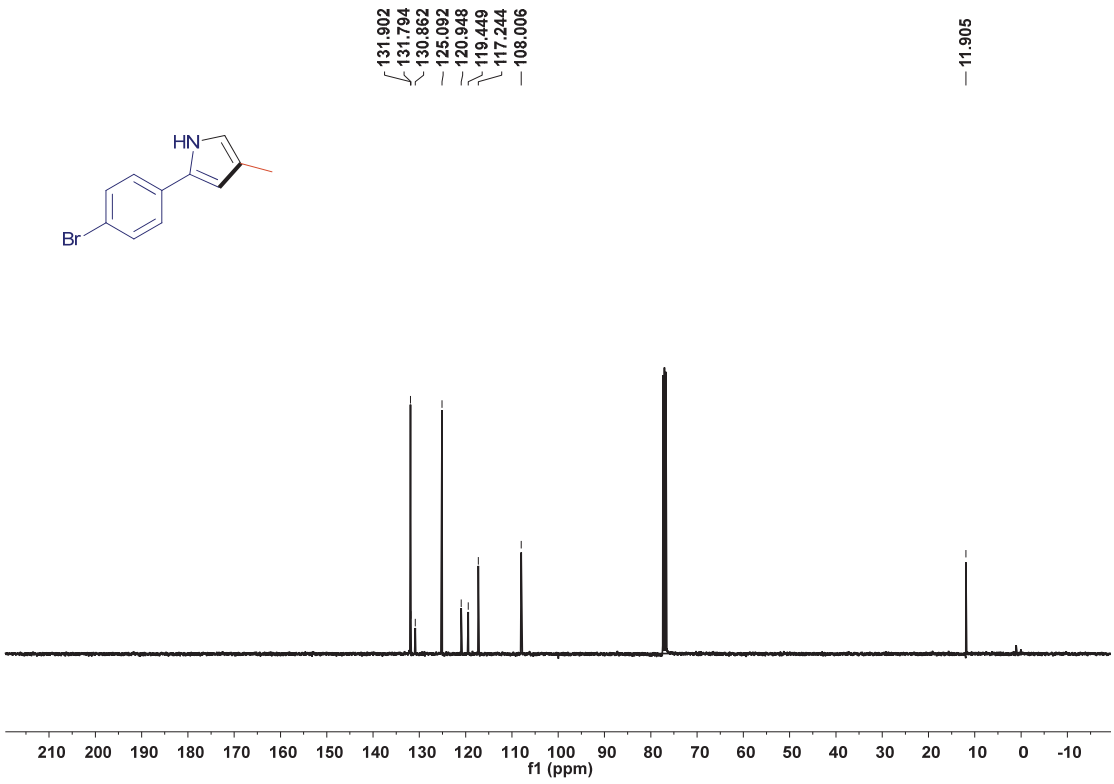
^{1}H NMR spectrum of 2-(4-chlorophenyl)-4-methyl-1H-pyrrole 2g



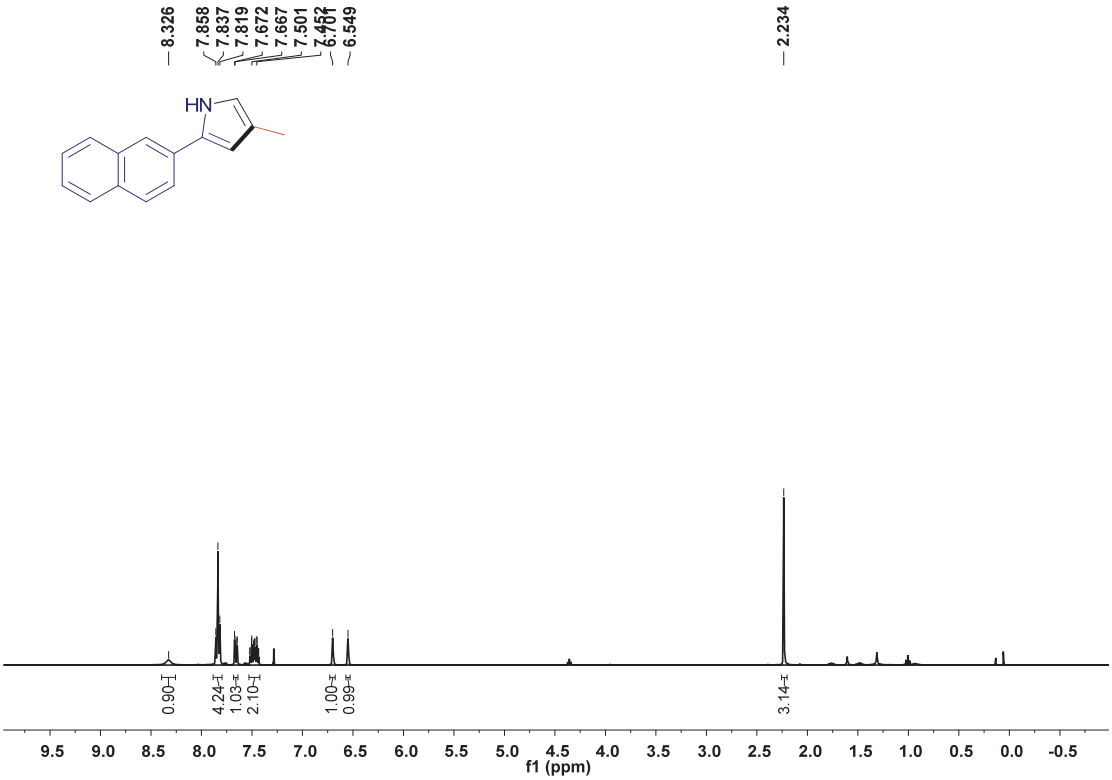
^{13}C NMR spectrum of 2-(4-chlorophenyl)-4-methyl-1H-pyrrole 2g



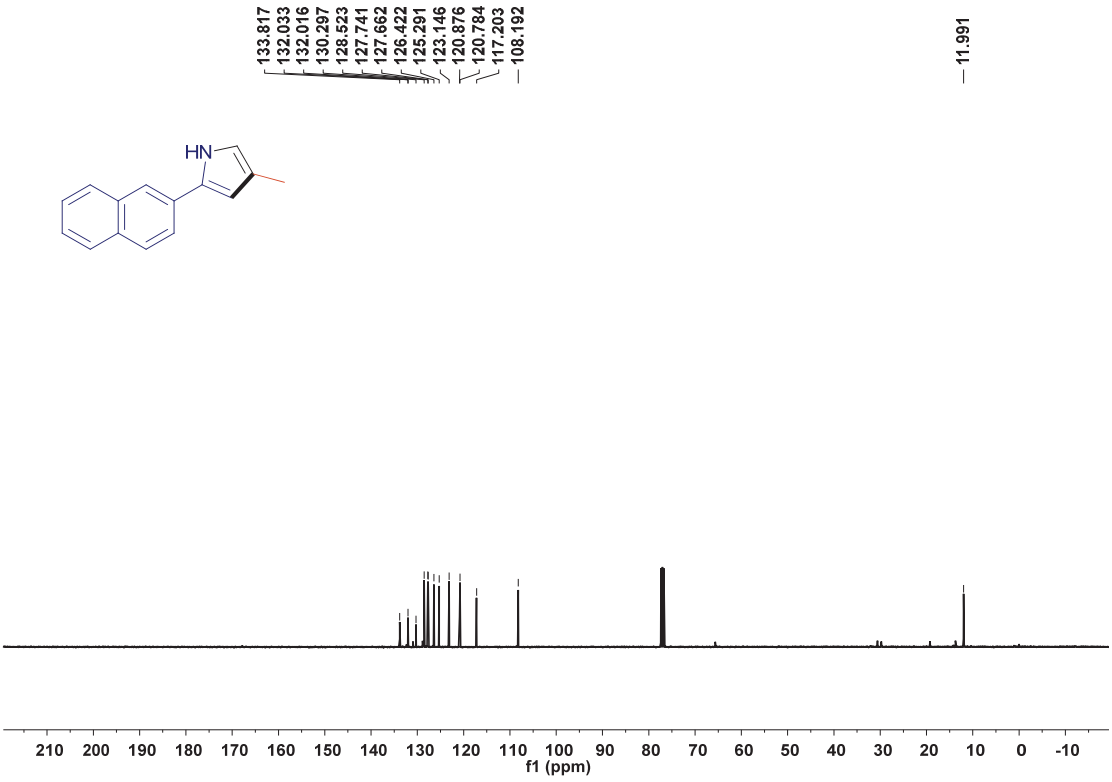
^{1}H NMR spectrum of 2-(4-bromophenyl)-4-methyl-1H-pyrrole 2h



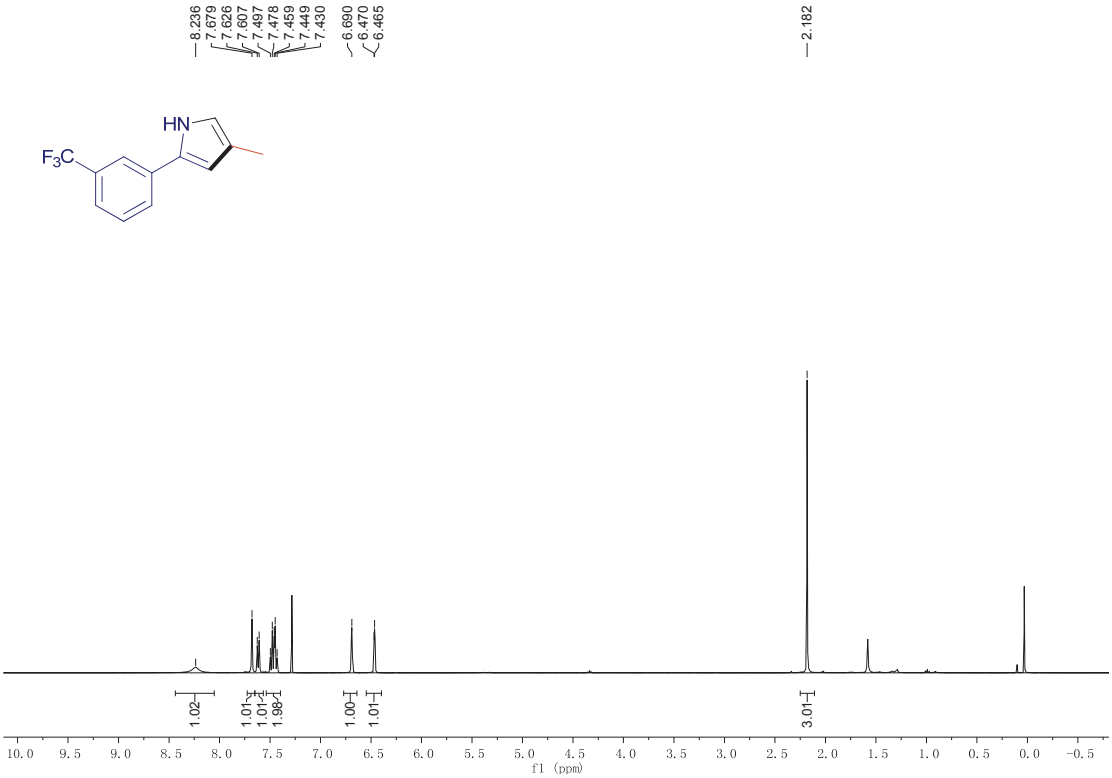
^{13}C NMR spectrum of 2-(4-bromophenyl)-4-methyl-1H-pyrrole 2h



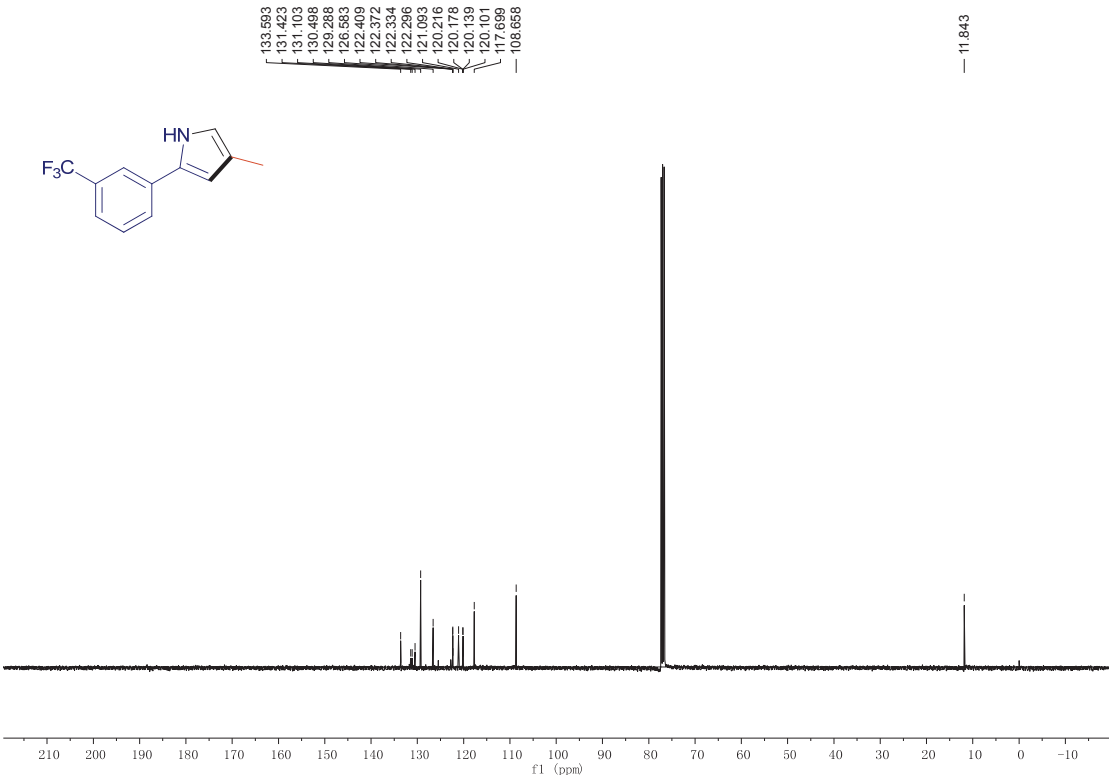
^{1}H NMR spectrum of 4-methyl-2-(naphthalen-2-yl)-1H-pyrrole 2i



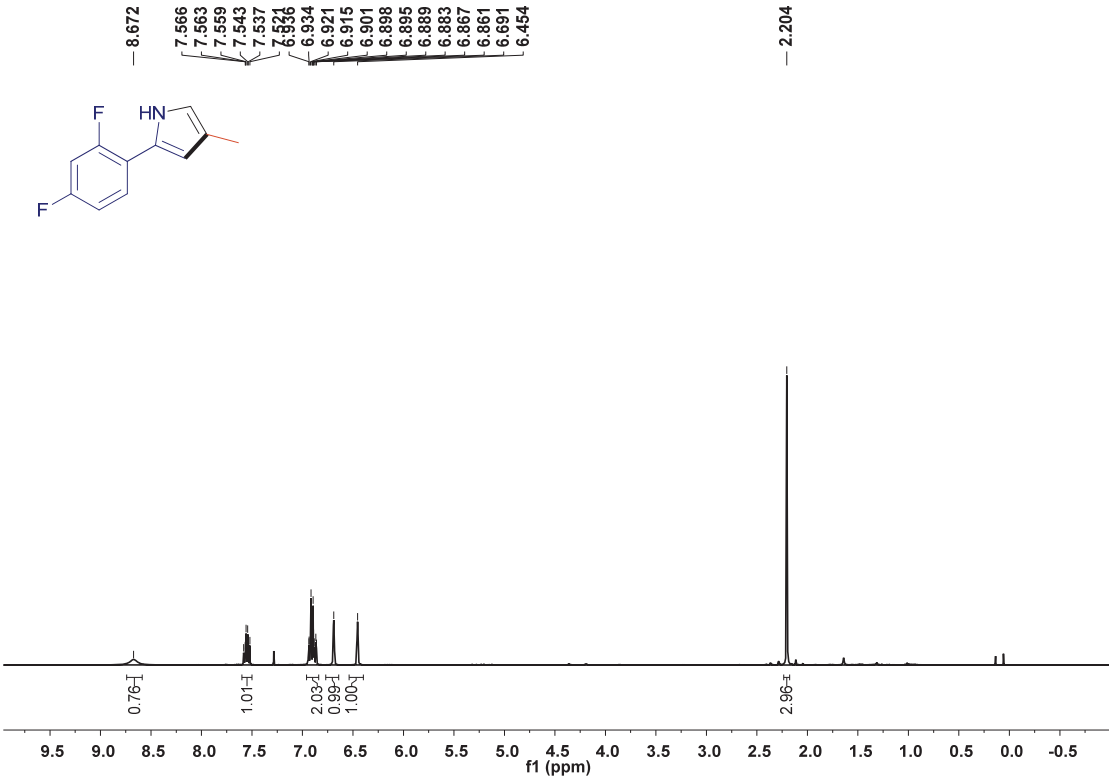
^{13}C NMR spectrum of 4-methyl-2-(naphthalen-2-yl)-1H-pyrrole 2i



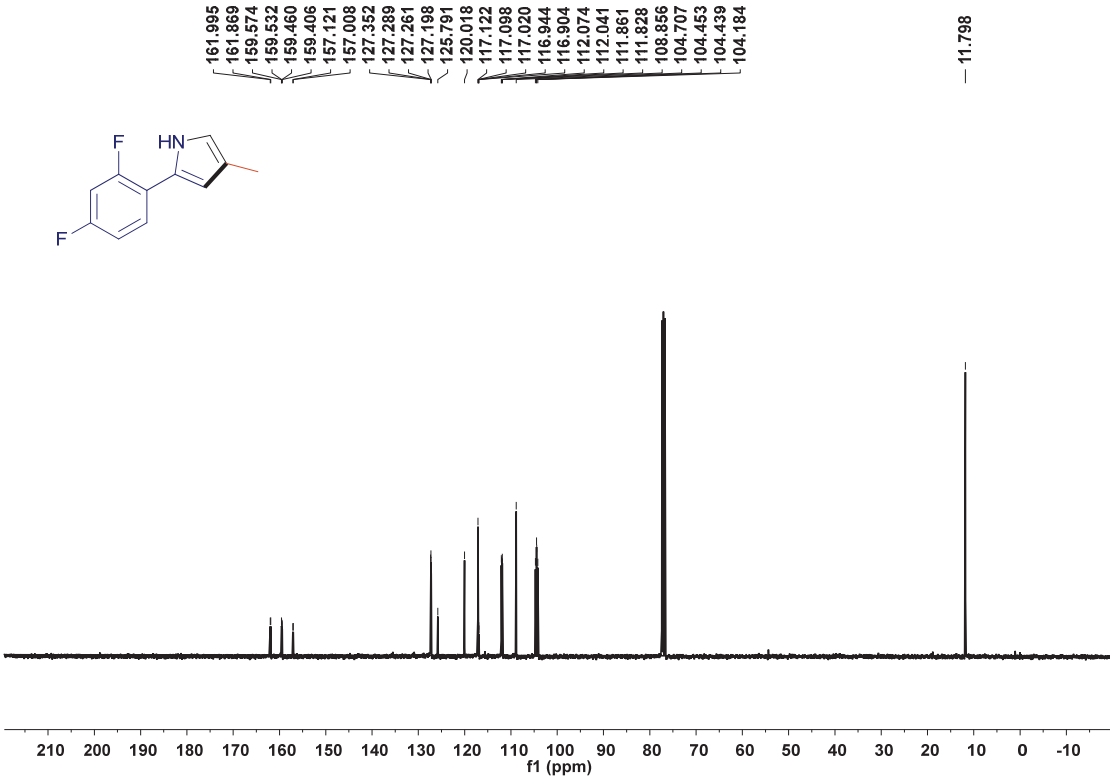
^{1}H NMR spectrum of 4-methyl-2-(3-(trifluoromethyl)phenyl)-1H-pyrrole 2j



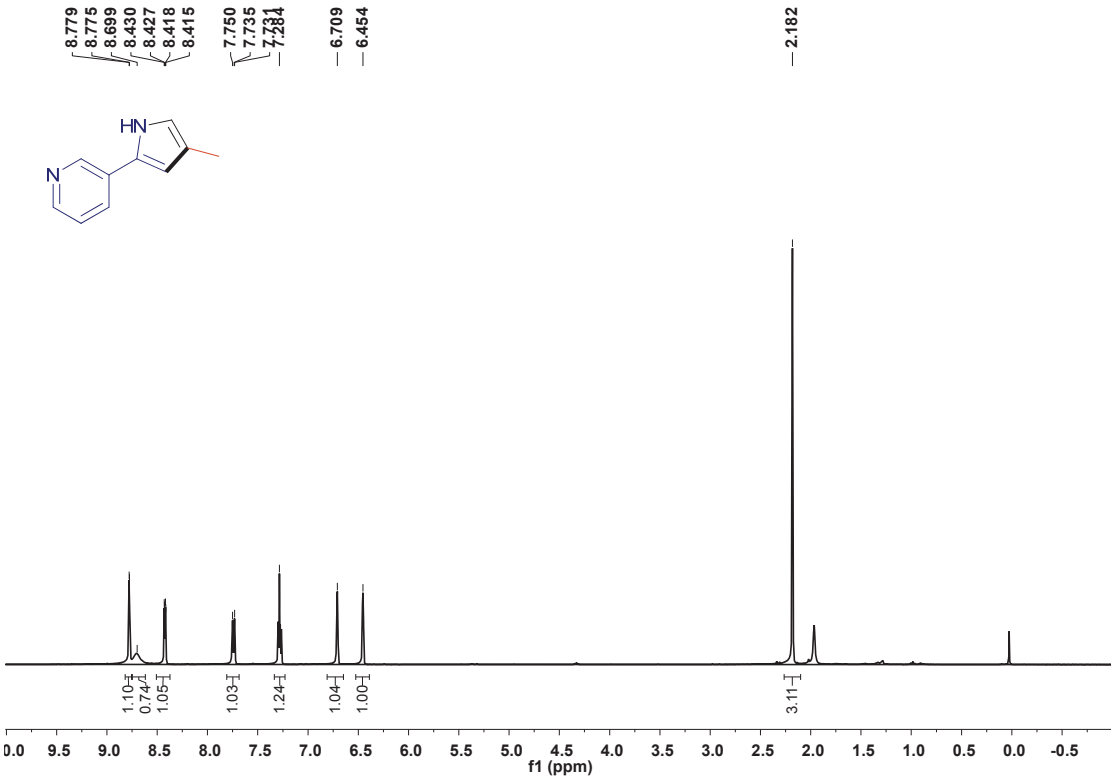
^{13}C NMR spectrum of 4-methyl-2-(3-(trifluoromethyl)phenyl)-1H-pyrrole 2j



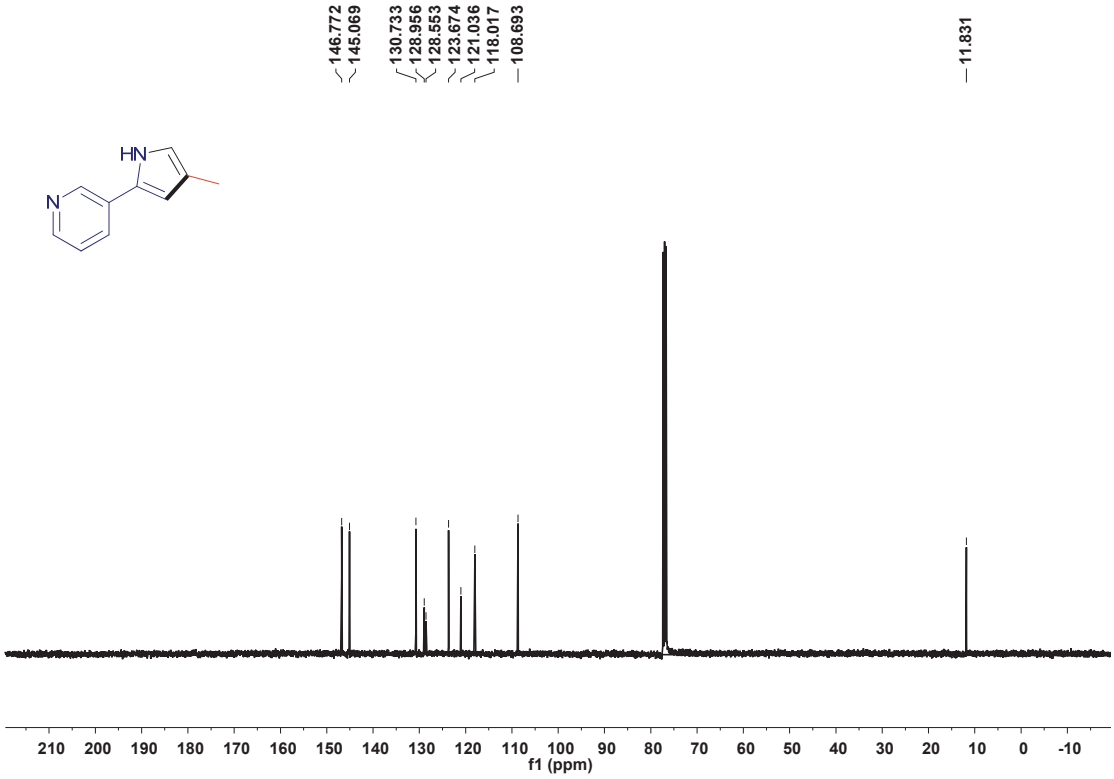
^{1}H NMR spectrum of 2-(2,4-difluorophenyl)-4-methyl-1H-pyrrole 2k



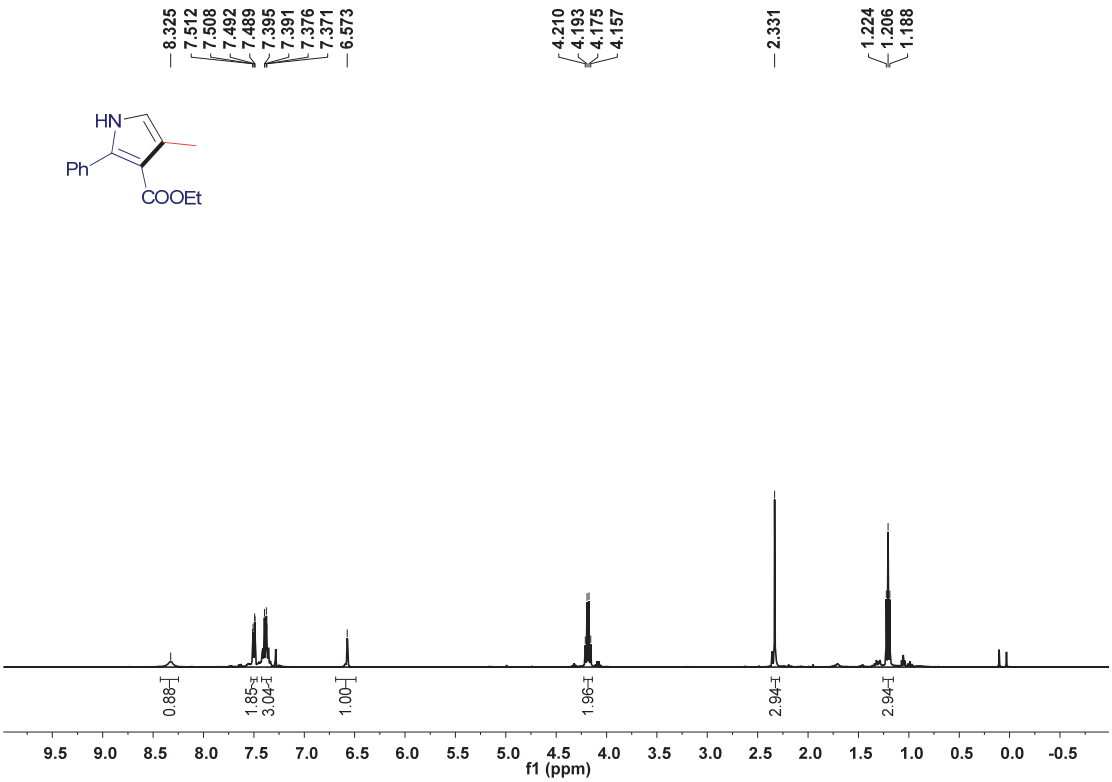
^{13}C NMR spectrum of 2-(2,4-difluorophenyl)-4-methyl-1H-pyrrole 2k



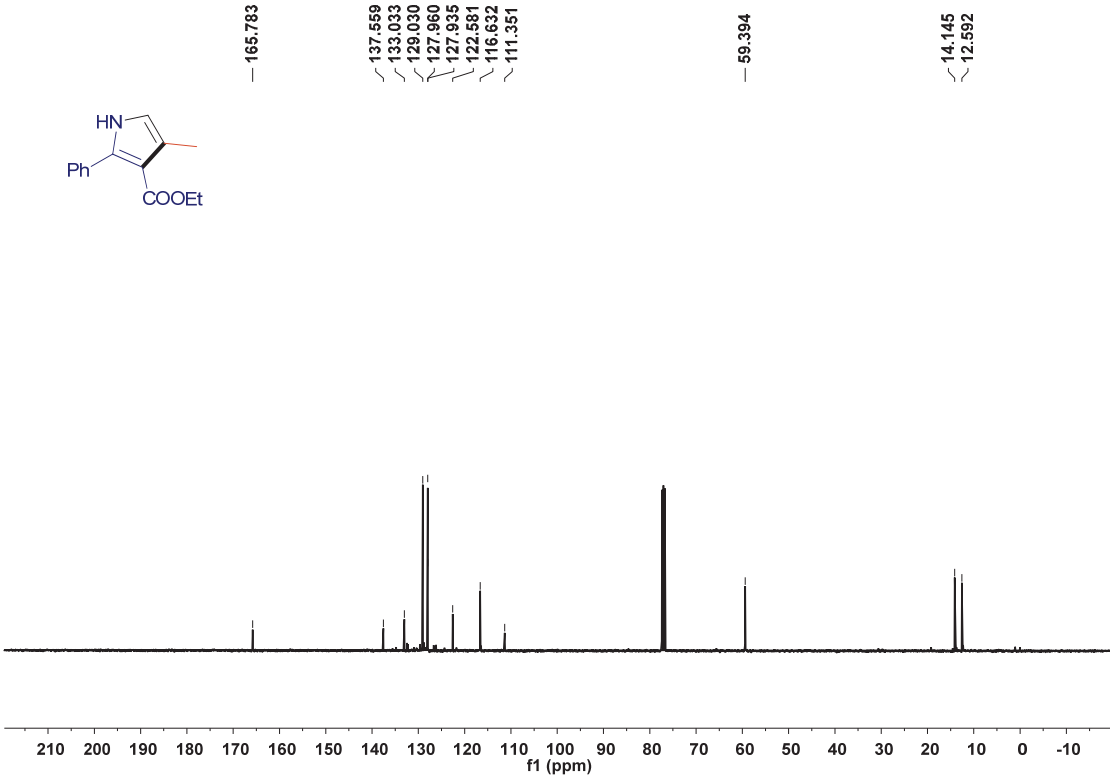
^{1}H NMR spectrum of 3-(4-methyl-1H-pyrrol-2-yl)pyridine 2l



^{13}C NMR spectrum of 3-(4-methyl-1H-pyrrol-2-yl)pyridine 2l



^{1}H NMR spectrum of ethyl 4-methyl-2-phenyl-1H-pyrrole-3-carboxylate 4



^{13}C NMR spectrum of ethyl 4-methyl-2-phenyl-1H-pyrrole-3-carboxylate 4

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2. D. Zhu, J. Zhao, Y. Wei and H. Zhou, *Synlett*, **2011**, 2185-2186.