Supplementary Materials: Practical $Pd(TFA)_2$-Catalyzed Aerobic [4+1] Annulation for the Synthesis of Pyrroles via "One-Pot" Cascade Reactions

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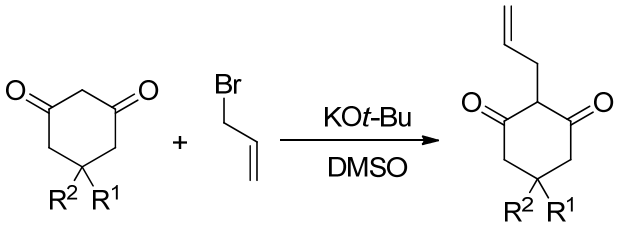
General Information

The reagents (chemicals) were purchased from commercial sources, and used without further purification. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15–0.2 mm thickness). All products were characterized by their NMR and MS SPECTRA. The NMR spectra were recorded on a Varian MERCURY plus-400 spectrometer with chemical shifts reported in ppm relative to the residual deuterated solvent. ^{1}H and ^{13}C NMR spectra were recorded in deuterchloroform ($CDCl_3$) on a 400 MHz instrument. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), multiple (m), and broad (br). Mass spectrometry analysis was carried out using an electrospray spectrometer Waters Micromass Q-TOF Premier Mass Spectrometer (Waters, Milford, MA, USA).

General Procedures for the Substrates Preparation

General procedure for the synthesis of 2-allylcyclohexane-1,3-dione and its derivatives (**5a**, **5b**, **5c**):



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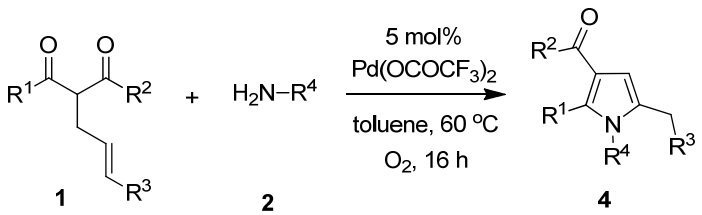
Under a nitrogen atmosphere, KO*t*-Bu (20 mmol) was dissolved in DMSO (100 mL) and substituted cyclohexane-1,3-dione (20 mmol) was added. After the solution was stirred at room temperature for 5 min, the allyl bromide (24 mmol, 1.2 eq) was added slowly and the reaction mixture was refluxed for 3 h. After completion of the reaction, ethyl acetate (400 mL) was added into the solution and washed with water (100 mL × 3). The organic layer was washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure. The crude reaction mixture was directly purified by column silica gel (hexane/EtOAc, *v*/*v*, 4/1), 30% isolated yield. The spectroscopic data were in accordance with those reported in literature [1,2].

Other substrates were prepared according to the literature [3].

General Procedures for the Synthesis of Substituted Pyrrole Derivatives



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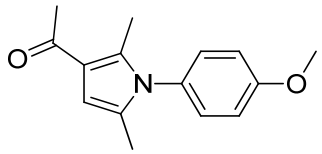
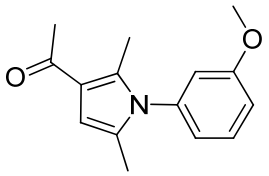
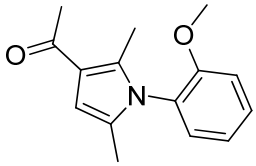
All the reactions were carried out under an aerobic atmosphere. To a solution of α-allyl diketones **1** (1.2 mmol) and amines **2** (0.6 mmol) in dry toluene (2 mL) was added $Pd(TFA)_2$ (0.03 mmol, 0.05 eq). The reaction mixture with an O_2 balloon was stirred at 60 °C for 16 h. The mixture was filtered through celite, washed with methanol (30 mL), the filtrate was concentrated, and the residue was purified by column chromatography, hexane/EtOAc (*v*/*v*, 20/1 then 10/1) as eluent, giving the desired pyrrole products as an oil.



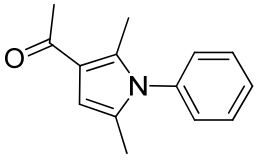
1-(1-(4-Methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone **4a**: Isolated yield 88%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08–7.06 (m, 2H), 6.98–6.96 (m, 2H), 6.26 (s, 1H), 3.84 (s, 3H), 2.39 (s, 3H), 2.28 (s, 3H), 1.95 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 159.5, 136.2, 130.2, 129.0, 128.9, 120.29, 114.9, 108.0, 55.6, 28.7, 13.0, 12.9 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{15}H17NNaO_2$: 266.1157, found: 266.1151.



1-(1-(3-Methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone **4b**: Isolated yield 86%, brown oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.37 (t, 1H, J = 8 Hz), 7.01–6.98 (dd, 1H, J_1 = 4 Hz, J_2 = 8 Hz), 6.77–6.75 (d, 1H, J = 8 Hz), 6.70–6.69 (t, 1H , J = 4 Hz), 6.31 (s, 1H), 3.83 (s, 3H), 2.42 (s, 3H), 2.32 (s, 3H), 2.00 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.0, 160.2, 138.3, 135.7, 130.0, 128.5, 120.3, 120.2, 114.2, 113.7, 107.9, 55.4, 28.6, 12.9, 12.6 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{15}H_{17}NNaO_2$: 266.1157, found: 266.1170.

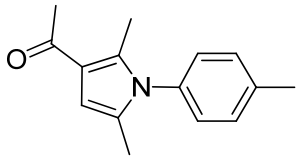


1-(1-(2-Methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone **4c**: Isolated yield 70%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.45 (m, 1H), 7.14–7.06 (m, 3H), 6.36 (s, 1H), 3.80 (s, 3H), 2.44 (s, 3H), 2.28 (s, 3H), 1.96 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.1, 155.5, 136.5, 130.4, 129.8, 128.9, 125.9, 120.9, 120.3, 112.1, 107.6, 55.7, 28.6, 12.6, 12.3 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{15}H_{17}NNaO_2$: 266.1157, found: 266.1163.

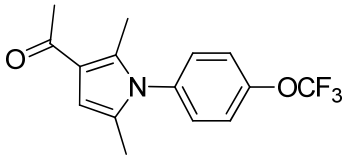


1-(2,5-Dimethyl-1-phenyl-1H-pyrrol-3-yl)ethanone **4d**: Isolated yield 77%, an oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.42 (m, 3H), 7.17–7.15 (m, 2H), 6.32 (s, 1H), 2.41 (s, 3H), 2.30 (s, 3H), 1.97 (s, 3H) ppm.

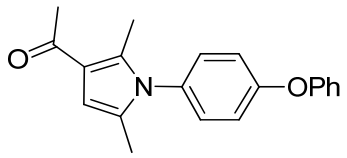
^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 137.2, 135.7, 129.3, 128.6, 128.5, 127.9, 120.3, 107.9, 28.5, 12.9, 12.6 ppm. HRMS (ESI) calcd for $C_{14}H_{15}NO$, 213.1154; found: 213.1144.



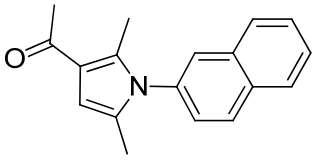
1-(2,5-Dimethyl-1-p-tolyl-1H-pyrrol-3-yl)ethanone **4e**: Isolated yield 82%, brown oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.26 (m, 2H), 7.05–7.02 (m, 2H), 6.30 (s, 1H), 2.42 (s, 3H), 2.41 (s, 3H), 2.29 (s, 3H), 1.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 138.5, 135.8, 134.6, 129.9, 128.6, 127.63, 120.2, 107.7, 28.5, 21.1, 12.8, 12.6 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{15}H_{17}NNaO$: 250.1208, found: 250.1187.



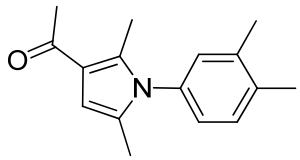
1-(2,5-Dimethyl-1-(4-(trifluoromethoxy)phenyl)-1H-pyrrol-3-yl)ethanone **4f**: Isolated yield 81%, an oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.34(d, 2H, J = 8 Hz), 7.26–7.20 (m, 2H), 6.33 (s, 1H), 2.42 (s, 3H), 2.30 (s, 3H), 1.99 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.1, 149.1, 135.8, 135.7, 129.7, 128.6, 121.8, 121.4, 120.7, 119.4, 108.3, 28.7, 12.9, 12.7 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{15}H_{14}F_3NNaO_2$: 320.0874, found: 320.0888.



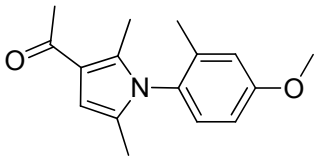
1-(2,5-Dimethyl-1-(4-phenoxyphenyl)-1H-pyrrol-3-yl)ethanone **4g**: Isolated yield 84%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.36 (m, 2H), 7.19–7.05 (m, 7H), 6.32 (s, 1H), 2.41 (s, 3H), 2.33 (s, 3H), 2.01 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.0, 157.9, 156.1, 135.9, 131.9, 130.1, 129.4, 128.8, 124.3, 120.5, 119.8, 118.7, 108.0, 28.7, 13.0, 12.7 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{20}H_{19}NNaO_2$: 328.1313, found: 328.1304.



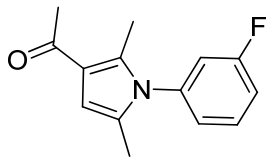
1-(2,5-Dimethyl-1-(naphthalen-2-yl)-1H-pyrrol-3-yl)ethanone **4h**: Isolated yield 84%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97–7.92 (m, 2H), 7.89–7.87 (m, 1H), 7.68–7.67 (m., 1H), 7.60–7.56 (m, 2H), 7.27–7.24 (dd, 1H, J_1 = 4 Hz, J_2 = 8 Hz), 6.38 (s, 1H), 2.46 (s, 3H), 2.36 (s, 3H), 2.03 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.0, 135.9, 134.6, 133.1, 132.7, 129.4, 128.7, 127.9, 127.8, 126.9, 126.7, 125.5, 120.4, 108.0, 28.6, 12.9, 12.7 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{18}H_{17}NNaO$: 286.1208, found: 286.1190.



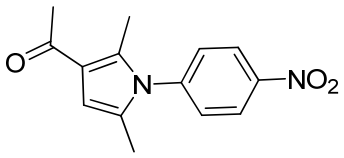
1-(1-(3,4-Dimethylphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone **4i**: Isolated yield 85%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23–7.21 (m, 1H), 6.93–6.87 (m, 2H), 6.30 (s, 1H), 2.41 (s, 3H), 2.32 (s, 3H), 2.30 (s, 6H), 1.97(s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.0, 137.9, 137.3, 135.9, 134.9, 130.5, 128.9, 128.7, 125.2, 120.3, 107.8, 28.6, 19.9, 19.5, 12.9, 12.7 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{16}H_{19}NNaO$: 264.1364, found: 264.1360.



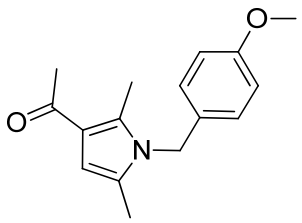
1-(1-(4-Methoxy-2-methylphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone **4j**: Isolated yield 74%, yellow oil, ^{1}H NMR (400 MHz,$CDCl_3$): δ 7.014–6.997 (d, 1H, J = 6.8 Hz), 6.863–6.858 (d, 1H, J = 2 Hz), 6.831–6.808 (dd, 1H, J_1 = 2 Hz, J_2 = 6.8 Hz), 6.32 (s, 1H), 3.84 (s, 3H), 2.41 (s, 3H), 2.22 (s, 3H), 1.89 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.1, 159.7, 137.7, 135.8, 129.3, 129.2, 128.4, 120.3, 116.0, 112.1, 107.7, 55.4, 28.5, 17.4, 12.5, 12.3 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{16}H_{19}NNaO_2$: 280.1313, found: 280.1290.



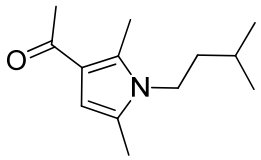
1-(1-(3-Fluorophenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone **4k**: 20 mmol % Catalyst was used, isolated yield 50%, ^{1}H NMR (500 MHz, $CDCl_3$) 7.51–7.46 (m, 1H), 7.21–7.17 (dt, 1H, J = 10 Hz), 7.00–6.99 (d, 1H, J = 5 Hz), 6.94–6.92 (dt, 1H, J_1 = 10 Hz, J_2 = 5 Hz), 6.33 (s,1H), 2.42 (s, 3H), 2.32 (s, 3H), 2.00 (s, 3H) ppm, ^{13}C NMR (125 MHz,$CDCl_3$) 195.0, 163.7, 161.7, 138.7, 138.6, 135.5, 130.6, 130.6, 128.4, 123.9, 123.9, 120.6, 115.9, 115.7, 115.7, 115.5, 108.2, 28.6, 12.7, 12.5 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{14}H_{14}FNONa$: 254.0957, found: 254.0956.



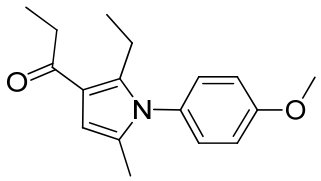
1-(2,5-Dimethyl-1-(4-nitrophenyl)-1H-pyrrol-3-yl)ethanone **4l**: 20 mmol % Catalyst was used, isolated yield 40%, ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40–8.38 (d, 2H, J = 10 Hz), 7.42–7.40 (d, 2H, J = 10 Hz), 6.37 (s, 1H), 2.42 (s, 3H), 2.33 (s, 3H), 2.03 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 195.0, 147.5, 142.9, 135.1, 129.1, 128.2, 124.8, 121.2, 109.1, 28.7, 12.8, 12.7 ppm; HRMS (ESI) calcd for $[M + Na]^+$ $C_{14}H_{14}N_2O_3Na$: 281.0902, found: 281.0903.



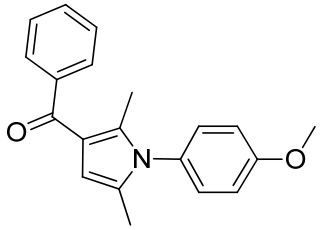
1-(1-(4-Methoxybenzyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone **4m**: Isolated yield 91%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.84–6.80 (m, 4H), 6.27 (s, 1H), 4.95 (s, 2H), 3.75 (s, 3H), 2.48 (s, 3H), 2.38 (s, 3H), 2.12 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 158.7, 134.9, 128.6, 127.7, 126.6, 120.0, 114.1, 108.2, 55.1, 45.9, 28.4, 12.0, 11.7 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{16}H_{19}NNaO_2$: 280.1313, found: 280.1331.



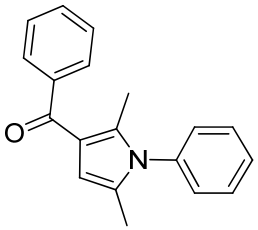
1-(1-Isopentyl-2,5-dimethyl-1H-pyrrol-3-yl)ethanone **4n**: Isolated yield 90%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.17 (s, 1H), 3.74–3.70 (t, 2H, J = 8 Hz), 2.52 (s, 3H), 2.32 (s, 3H), 2.19 (s, 3H), 1.70–1.60 (m, 1H), 1.49–1.43 (m, 2H), 0.96–0.95 (d, 6H, J = 4 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.8, 134.4, 127.0, 119.9, 108.2, 41.9, 39.4, 28.4, 26.3, 22.5, 12.2, 11.7 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{13}H_{21}NNaO$: 230.1521, found: 230.1508.



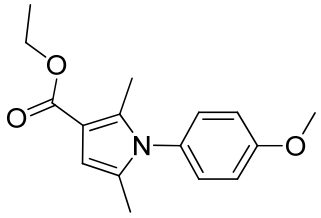
1-(2-Ethyl-1-(4-methoxyphenyl)-5-methyl-1H-pyrrol-3-yl)propan-1-one **4o**: Isolated yield 83%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13–7.09 (m, 2H), 7.00–6.96 (m, 2H), 6.30 (s, 1H), 3.87 (s, 3H), 2.82–2.77 (q, 2H, J = 8 Hz), 2.75–2.69 (q, 2H, J = 8 Hz), 1.95 (s, 3H), 1.20–1.16 (t, 3H, J = 8 Hz), 1.01–0.97 (t, 3H, J = 8 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 159.5, 142.3, 129.9, 129.2, 128.8, 118.8, 114.4, 107.1, 55.5, 33.4, 19.7, 14.0, 12.6, 8.6 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{17}H_{21}NNaO_2$: 294.1470, found: 294.1494.



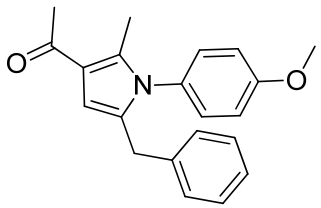
(1-(4-Methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)(phenyl)methanone **4p**: Isolated yield 78%, an oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84–7.82 (m, 2H), 7.51–7.42 (m, 3H), 7.16–7.12 (m, 2H), 7.02–6.98 (m, 2H), 6.18 (s, 1H), 3.86 (s, 3H), 2.33 (s, 3H), 1.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.3, 159.4, 140.9, 137.7, 130.8, 129.9, 128.9, 128.9, 128.6, 127.8, 119.3, 114.5, 109.5, 55.4, 13.0, 12.6 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{20}H_{19}NNaO2$: 328.1313, found: 328.1298.



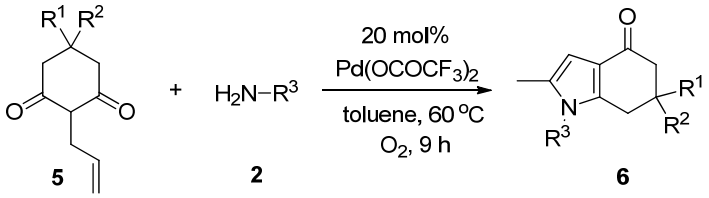
(2,5-Dimethyl-1-phenyl-1H-pyrrol-3-yl)(phenyl)methanone **4q**: Isolated yield 75%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87–7.84 (m, 2H), 7.54–7.43 (m, 6H), 7.27–7.21 (m, 2H), 6.21 (s, 1H), 2.34 (s, 3H), 1.99 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.3, 140.8, 137.4, 137.3, 130.9, 129.4, 128.9, 128.6, 128.3, 127.9, 127.8, 119.5, 109.8, 13.0, 12.6 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{19}H_{17}NNaO$: 298.1208, found: 298.1222.



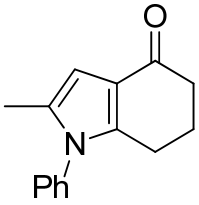
Ethyl 1-(4-methoxyphenyl)-2,5-dimethyl-1H-pyrrole-3-carboxylate **4r**: Isolated yield 85%, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09–7.07 (d, 2H, *J* = 8 Hz), 6.99–6.97 (d, 2H, *J* = 8 Hz), 6.34 (s, 1H), 4.29–4.24 (q, 2H, *J* = 8 Hz), 3.85 (s, 3H), 2.27 (s, 3H), 1.95 (s, 3H), 1.36–1.32 (t, 3H, *J* = 8 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 159.3, 136.4, 130.3, 129.0, 128.9, 114.4, 111.0, 107.1, 59.1, 55.4, 14.5, 12.5, 12.3 ppm. HRMS (ESI) calcd for $[M + Na]^+$ $C_{16}H_{19}NNaO_3$: 296.1236, found: 296.1238.



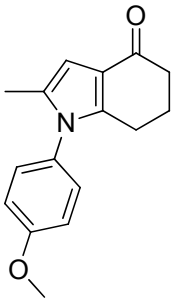
1-(5-Benzyl-1-(4-methoxyphenyl)-2-methyl-1H-pyrrol-3-yl)ethanone **4s**: Isolated yield 60%, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22–7.15 (m, 3H), 6.97–6.88 (m, 6H), 6.31 (s, 1H), 3.85 (s, 3H), 3.67 (s, 2H), 2.43 (s, 3H), 2.29 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.3, 159.6, 138.9, 136.5, 132.5, 132.2, 129.4, 128.6, 128.3, 126.2, 120.4, 114.4, 108.8, 55.5, 33.2, 28.6, 12.8. HRMS (ESI) calcd for $[M + H]^+$ $C_{21}H_{22}NO_2$: 320.1651, found: 320.1677.



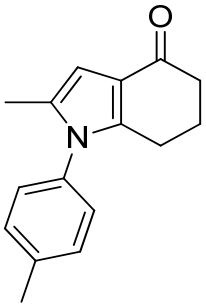
All the reactions were carried out under aerobic atmosphere. To a solution of α-allyl diketones **5** (1.2 mmol), and amines **2** (0.6 mmol) in dry toluene (2 mL) was added $Pd(TFA)_2$ (0.12 mmol, 0.2 eq). The reaction mixture with O_2 balloon was stirred at 60 °C for 9 h. The mixture was filtered through celite, washed with methanol (30 mL), the filtration was concentrated, and the residue was purified by column chromatography, hexane/EtOAc (*v*/*v*, 10/1 then 4/1) as eluent, giving the desired pyrrole products.



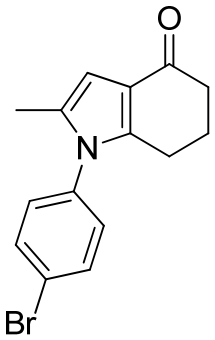
2-Methyl-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one **6a**: Isolated yield 71%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.52 (m, 3H), 7.22–7.24 (m, 2H), 6.38 (s, 1H), 2.47–2.54 (m, 4H), 2.07–2.17 (m, 2H), 2.07 (s, 3H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 194.4, 144.5, 137.1, 131.4, 129.5, 128.6, 127.6, 120.2, 103.5, 38.0, 23.9, 22.8, 12.6 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{15}H_{16}NO$: 226.1232, found: 226.1226.



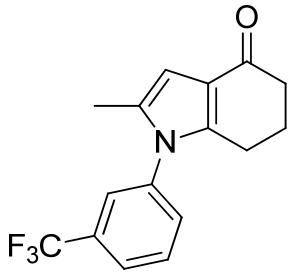
1-(4-Methoxyphenyl)-2-methyl-6,7-dihydro-1H-indol-4(5H)-one **6b**: Isolated yield 64%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (d, *J* = 8.8Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.38 (s, 1H), 2.47–2.54 (m, 4H), 1.97–2.02 (m, 2H), 1.95 (s, 3H) ppm; ^{13}C (100 MHz, $CDCl_3$) δ 194.6, 159.5, 145.0, 144.7, 131.4, 129.8, 128.6, 119.9, 114.6, 103.1, 55.2, 37.9, 23.8, 22.3, 12.3 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{16}H_{18}NO_2$: 256.1338, found: 256.1341.



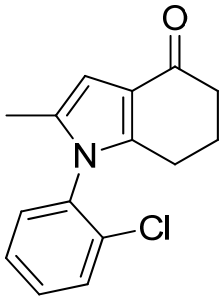
2-Methyl-1-(p-tolyl)-6,7-dihydro-1H-indol-4(5H)-one **6c**: Isolated yield 51%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.37 (s, 1H), 2.53–2.46 (m, 4H), 2.44 (s, 3H), 2.10–2.06 (m, 2H), 2.05 (s, 3H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 194.4, 144.7, 138.7, 134.5, 131.5, 130.1, 127.3, 120.0, 103.3, 37.9, 23.9, 22.8, 21.2 12.6 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{16}H_{18}NO$: 240.1388, found: 240.1389.



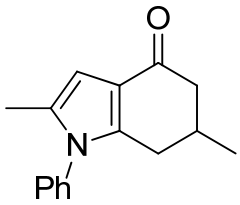
1-(4-Bromophenyl)-2-methyl-6,7-dihydro-1H-indol-4(5H)-one **6d**: Isolated yield 52%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.37 (s, 1H), 2.46–2.38 (m, 4H), 2.04–1.99 (m, 2H), 1.97 (s, 3H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 194.0, 144.0, 135.7, 132.8, 131.0, 129.0, 122.3, 120.0, 104.0, 37.7, 23.9, 22.8, 12.6 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{15}H_{15}NOBr$: 304.0337, found: 304.0338.



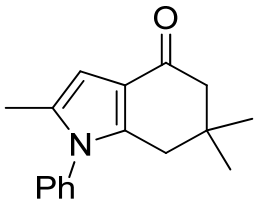
2-Methyl-1-(3-(trifluoromethyl)phenyl)-6,7-dihydro-1H-indol-4(5H)-one **6e**: Isolated yield 48%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 2H), 7.53 (bs, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 6.41 (s, 1H), 2.55–2.48 (m, 4H), 2.14–2.09 (m, 2H), 2.06 (s, 3H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 194.4, 144.3, 132.2 (q, $J_{C–F}$ = 32.8 Hz), 131.2, 131.0, 130.3, 125.5 (q, $J_{C–F}$ = 3.6 Hz), 124.7, 124.5 (q, $J_{C–F}$ = 3.7 Hz), 122.0, 120.7, 104.0, 37.8, 23.8, 22.7, 12.6 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{16}H_{15}NCF_3$: 294.1106, found: 294.1101.



1-(2-Chlorophenyl)-2-methyl-6,7-dihydro-1H-indol-4(5H)-one **6f**: Isolated yield 70%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (dd, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H), 7.05 (m, 2H), 7.37 (s, 1H), 7.24 (dd, J_1 = 7.2 Hz, J_2 = 2.0 Hz, 1H), 6.37 (s, 1H), 2.43–2.34 (m, 4H), 2.05–1.97 (m, 2H), 1.90 (s, 3H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 193.3, 143.7, 133.9, 132.4, 130.4, 129.5, 129.4, 129.0, 126.9, 119.4, 102.5, 36.7, 22.7, 21.2, 11.1 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{15}H_{15}NCl$: 260.0842, found: 260.0848.

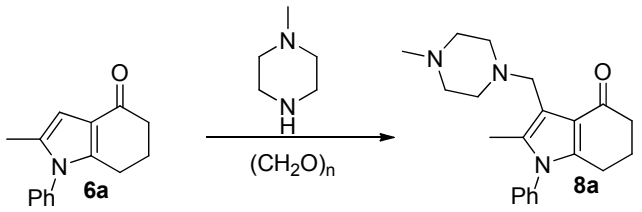


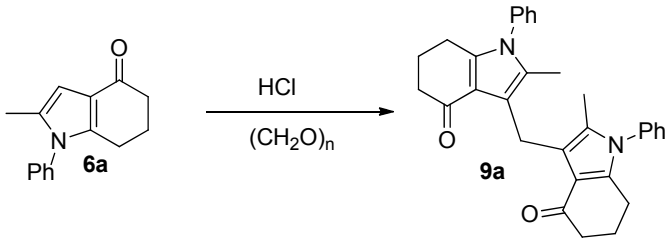
2,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one **6g**: Isolated yield 57%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (m, 3H), 7.15 (m, 2H), 6.30 (s, 1H), 2.48–2.38 (m, 2H), 2.25–2.12 (m, 3H), 1.97 (s, 3H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 194.1, 144.0, 137.0, 131.4, 129.5, 128.6, 127.6, 119.9, 103.5, 46.4, 31.9, 31.0, 21.3, 12.5 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{16}H_{18}NO$: 240.1388, found: 240.1393.



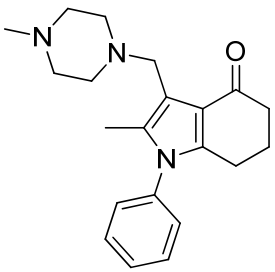
2,6,6-Trimethyl-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one **6h**: Isolated yield 65%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (m, 3H), 7.15 (m, 2H), 6.30 (s, 1H), 2.31 (s, 2H), 2.28 (s, 2H), 1.97 (s, 3H), 0.99 (s, 6H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 193.8, 143.4, 137.2, 131.5, 129.5, 128.6, 127.6, 119.0, 103.5, 51.9, 36.8, 35.5, 28.5, 12.5 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{17}H_{20}NO$: 254.1545, found: 254.1551.

Further Transformation of 6a



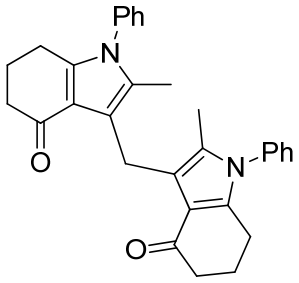


To a suspension of compound **6a** (45 mg, 0.2 mmol, 1.0 eq) and polyformaldehyde (18 mg, 0.6 mmol, 3.0 eq) in glacial acetic acid (0.4 mL) was added *N*-methyl piperazine (60 mg, 0.6 mmol, 3.0 eq) at 25 °C. The mixture was stirred at 25 °C overnight. Water (5 mL) was added, and pH was then adjusted to 8–9 with ammonium hydroxide. The reaction mixture was extracted with dichloromethane. The combined organic phases were washed with water (5 mL × 3), dried over $MgSO_4$, followed by concentration in vacuum, then washed with *n*-hexane, affording **8a** as a pink solid (55 mg, yield 82%).



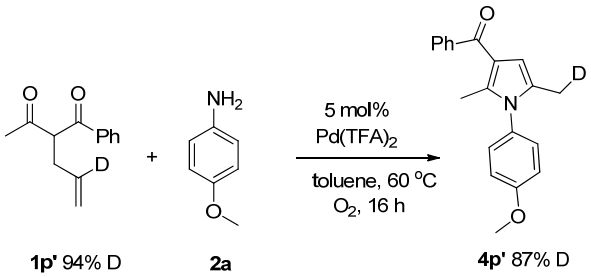
2-Methyl-3-((4-methylpiperazin-1-yl)methyl)-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one **8a**: Isolated yield 82%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (m, 3H), 7.15 (m, 2H), 3.90 (s, 2H), 2.65–2.43 (m, 12H), 2.26 (s, 3H), 2.07–2.02 (m, 2H), 2.01 (s, 3H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 194.7, 143.4, 137.3, 130.0, 129.5, 128.6, 127.7, 119.2, 114.0, 55.2, 52.0, 51.1, 46.1, 39.0, 23.7, 23.9, 10.7 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{21}H_{28}N_3O$: 338.2232, found: 338.2235.

A solution of **6a** (45 mg, 0.2 mmol, 1.0 eq) in dioxane (1.0 mL) was added polyformaldehyde (18 mg, 0.6 mmol, 3.0 eq) and HCl (conc., 1 mL). The mixture was stirred at 25 °C for 2 h. The solution was concentrated, the crude product was purified by column chromatography on silica gel (PE/EA = 5/1) to give the desired compound **9a** as a light yellow powder (36 mg, yield 78%).



3,3′-Methylenebis(2-methyl-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one) **9a**: Isolated yield 78%, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (m, 3H), 7.15 (m, 2H), 4.56 (s, 2H), 2.55–2.47 (m, 8H), 2.26 (s, 3H), 2.07–2.02 (m, 4H), 1.93 (s, 6H) ppm. ^{13}C (100 MHz, $CDCl_3$) δ 195.2, 142.6, 137.6, 129.2, 128.3, 128.2, 127.8, 118.7, 118.4, 39.1, 23.8, 23.1, 20.1, 10.2 ppm. HRMS (ESI) calcd for $[M + H]^+$ $C_{31}H_{31}N_2O_2$: 463.2386, found: 463.2381.

Deuterated Studies



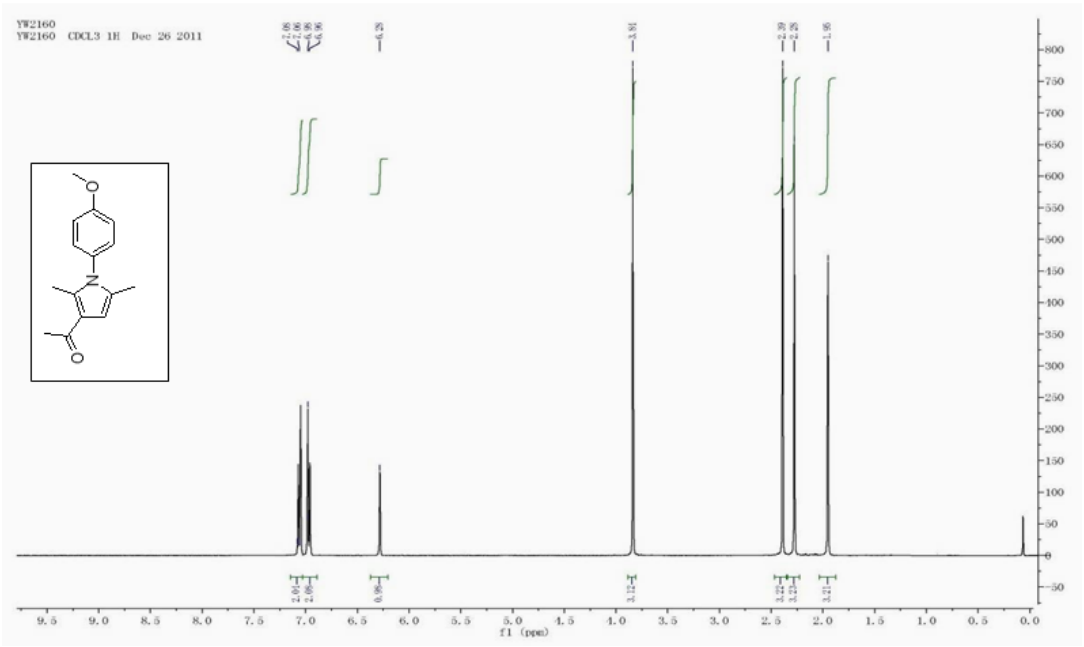
To a solution of deuterated 2-allyl-1-phenylbutane-1,3-dione **1p′** (1.2 mmol, 94% D) and amines **2a** (0.6 mmol) in dry toluene (2 mL) was added $Pd(TFA)_2$ (0.03 mmol, 0.05 eq). The reaction mixture with O_2 balloon was stirred at 60 °C for 16 h. The mixture was filtered through celite, washed with 30 mL methanol, the filtration was concentrated, and the residue was purified by column chromatography, hexane/EtOAc (*v*/*v*, 20/1 then 10/1) as eluent, giving the desired pyrrole products **4p′** (87% D).

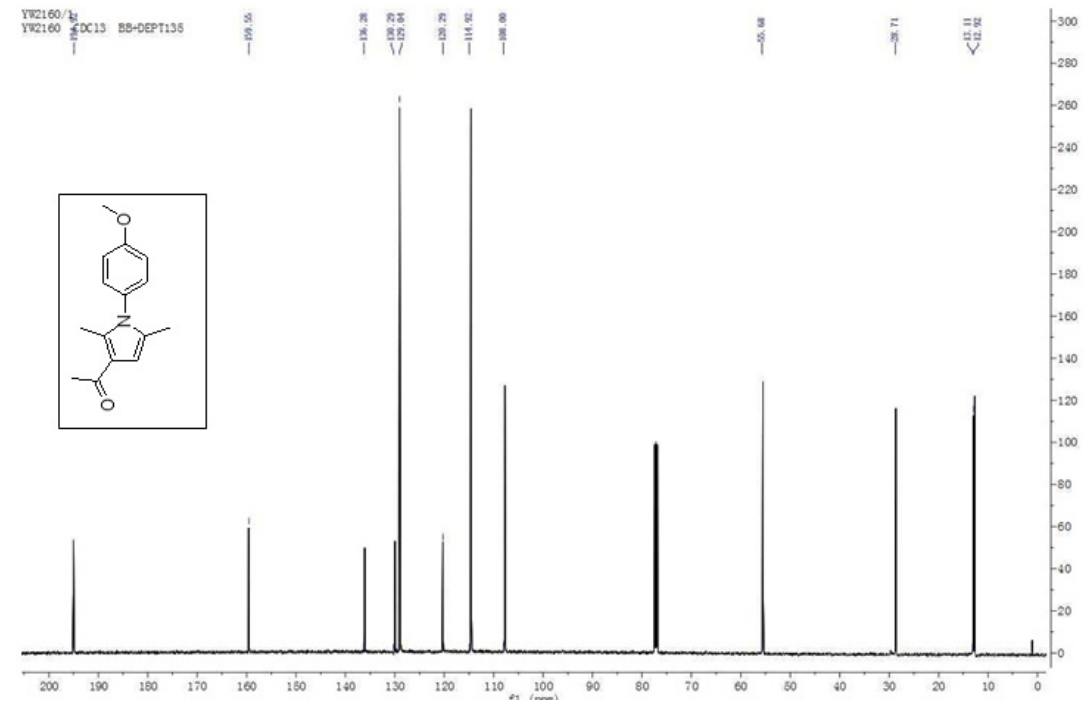
Deuterated-1-(1-(4-methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4p′

Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08–7.06 (m, 2H), 6.98–6.96 (m, 2H), 6.26 (s, 1H), 3.84 (s, 3H), 2.39 (s, 3H), 2.28 (s, 3H), 1.95 (s, 1.97H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 159.5, 136.2, 130.2, 129.0, 128.9, 120.29, 114.9, 108.0, 57.5, 15.0, 14.3 (t, $J_{C–D}$ = 20 Hz) ppm. ^{13}C (Dept-135): positive, 132.8, 130.8, 129.7, 116.4, 111.4, 57.3, 14.8; negative, 14.2 (t, $J_{C–D}$ = 20 Hz).

^{1}H and ^{13}C-NMR spectra data

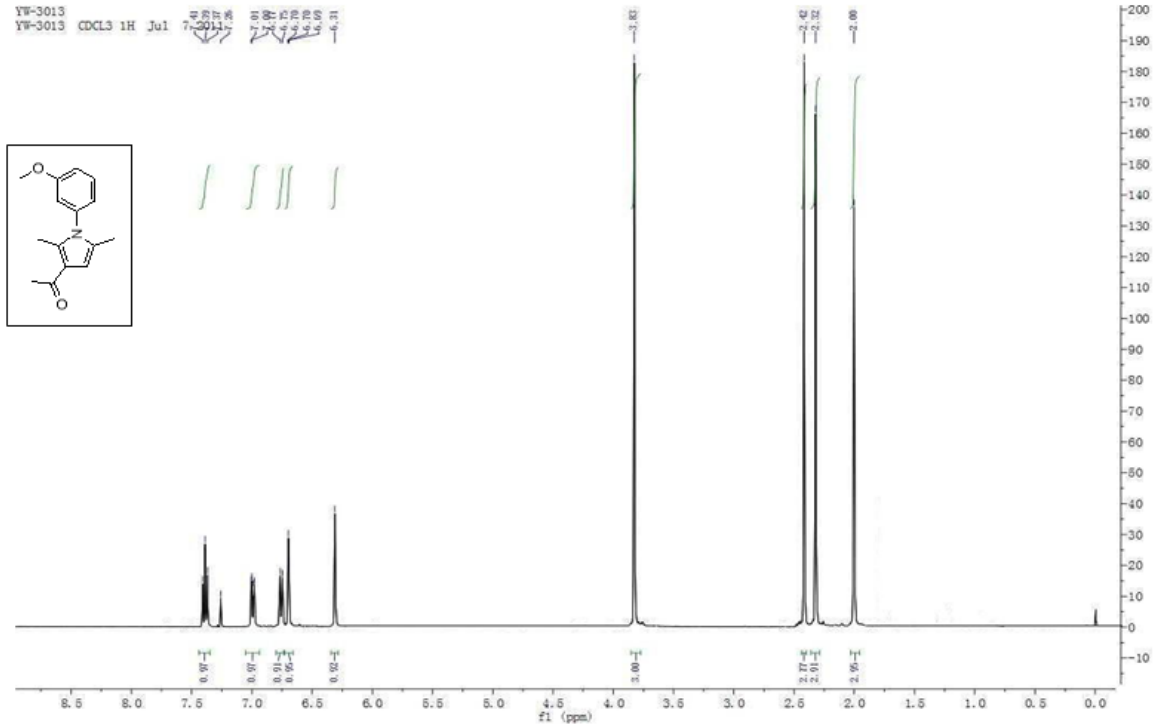
1-(1-(4-Methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4a

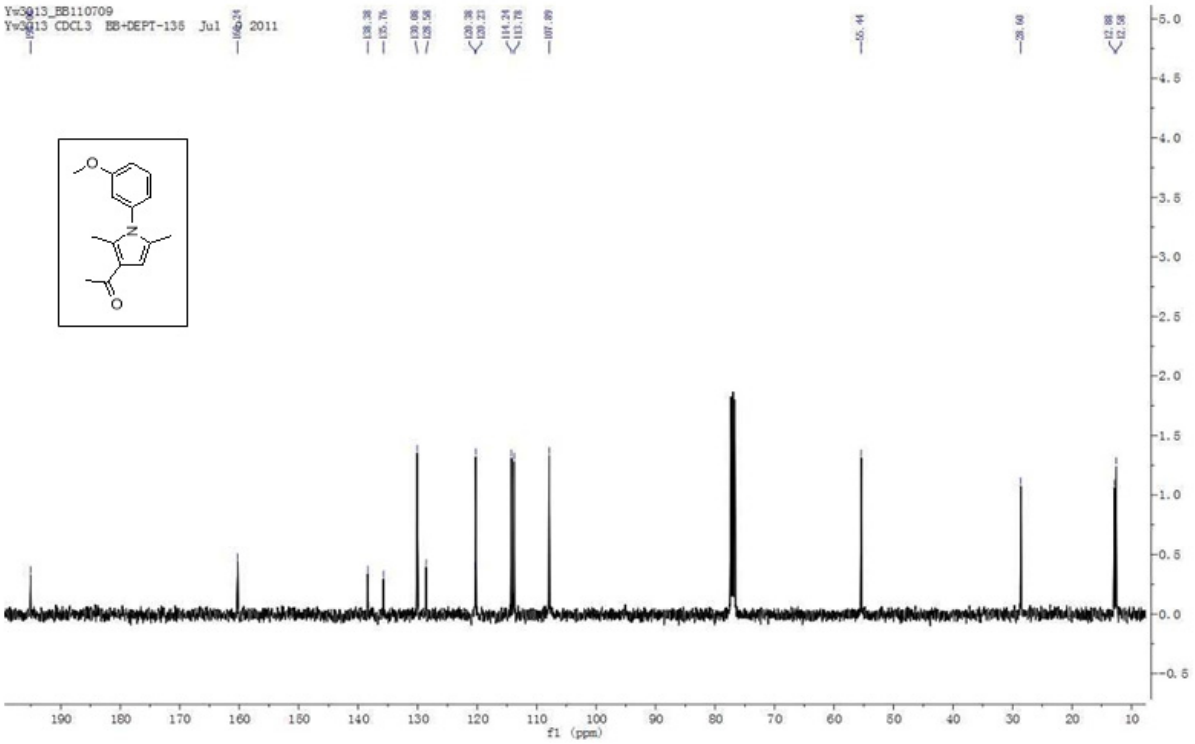




^{1}H and ^{13}C-NMR spectra data

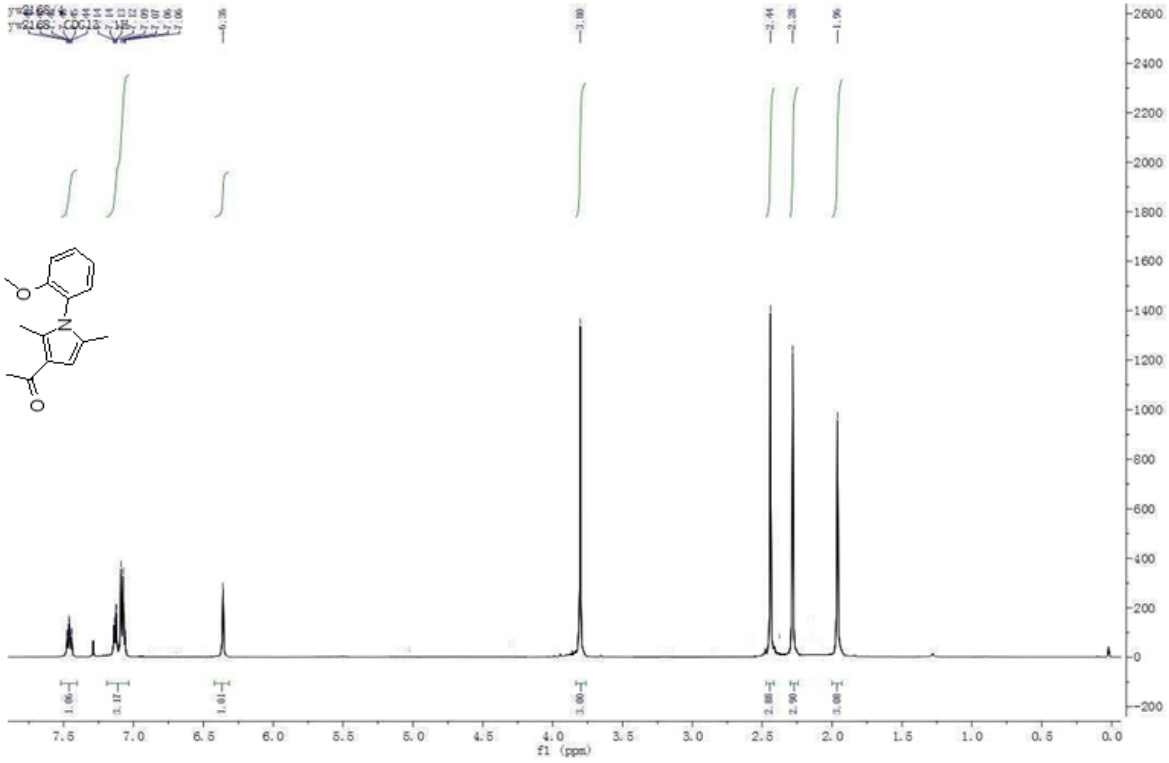
1-(1-(3-Methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4b

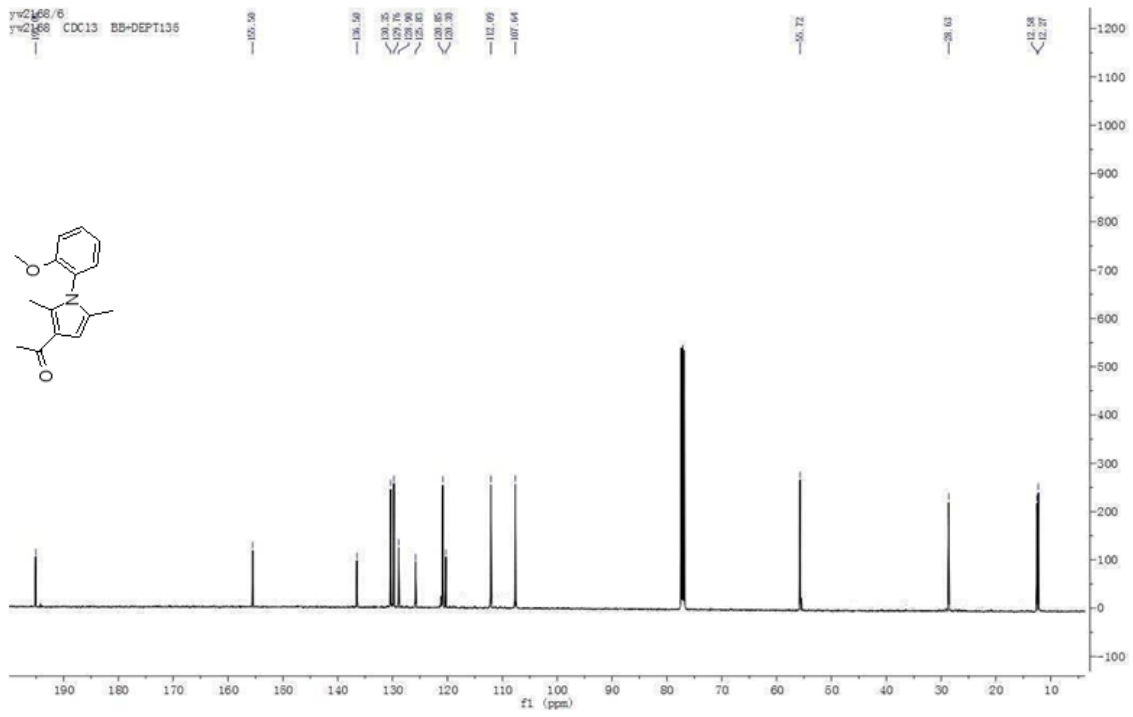




^{1}H and ^{13}C-NMR spectra data

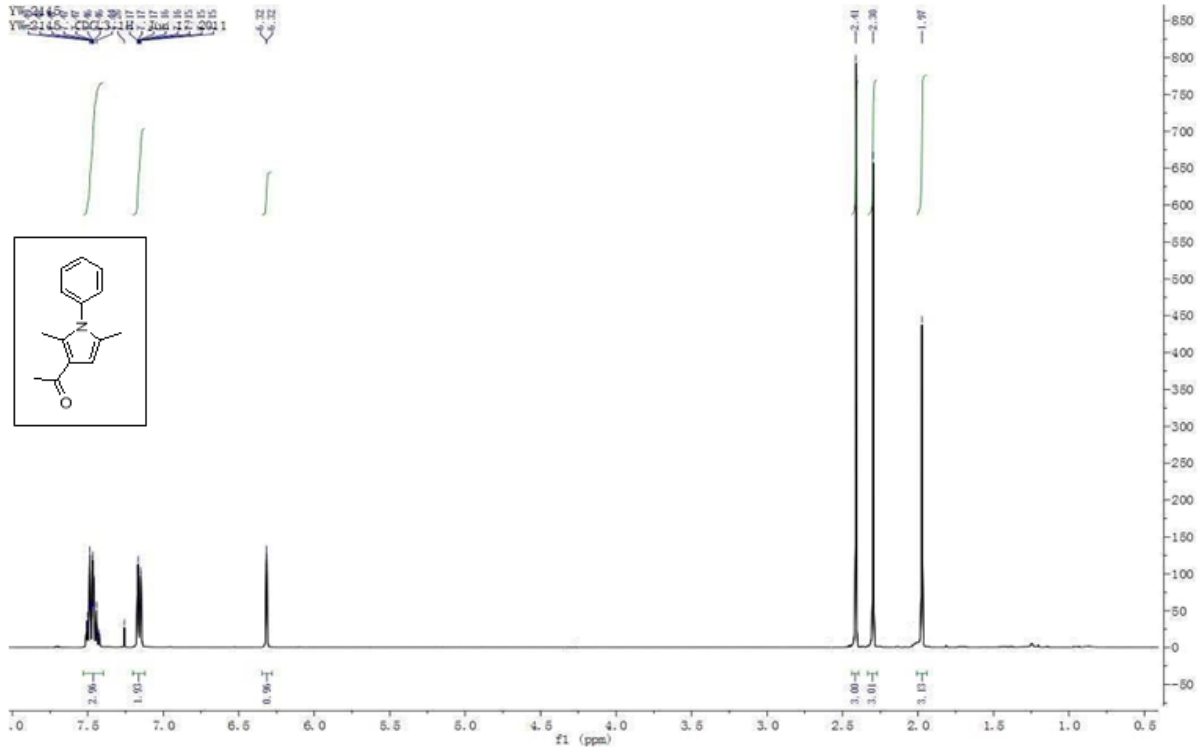
1-(1-(2-Methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4c

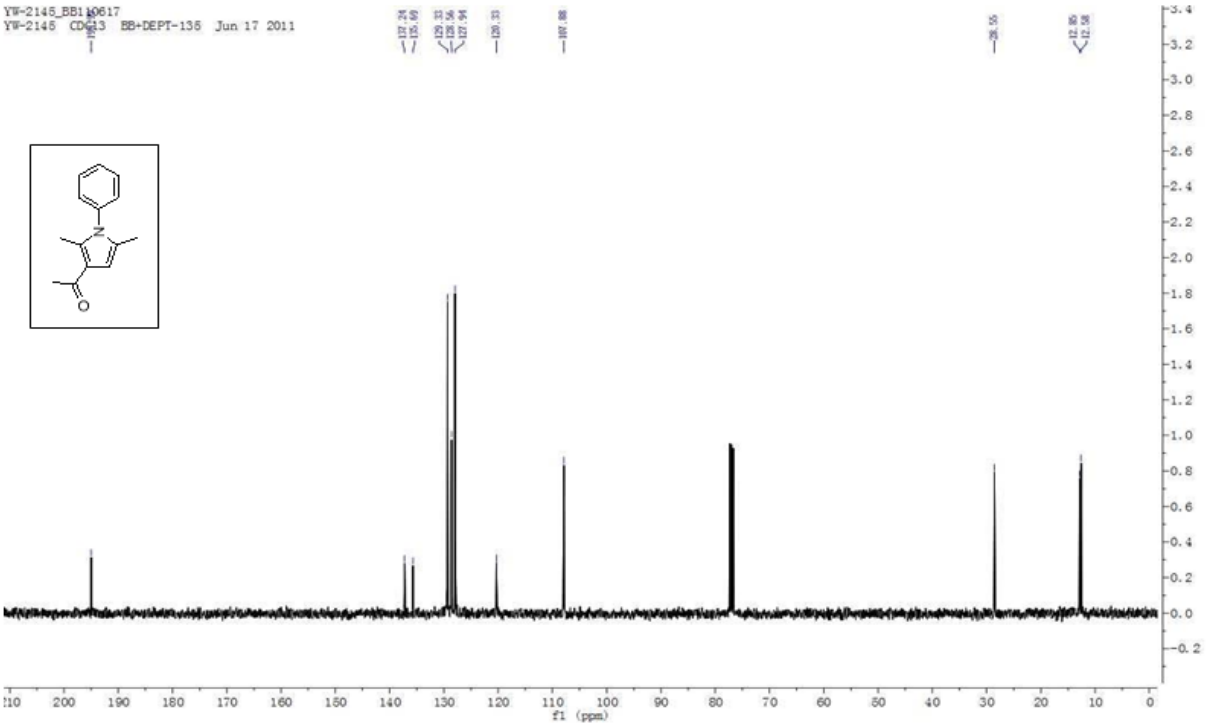




^{1}H and ^{13}C-NMR spectra data

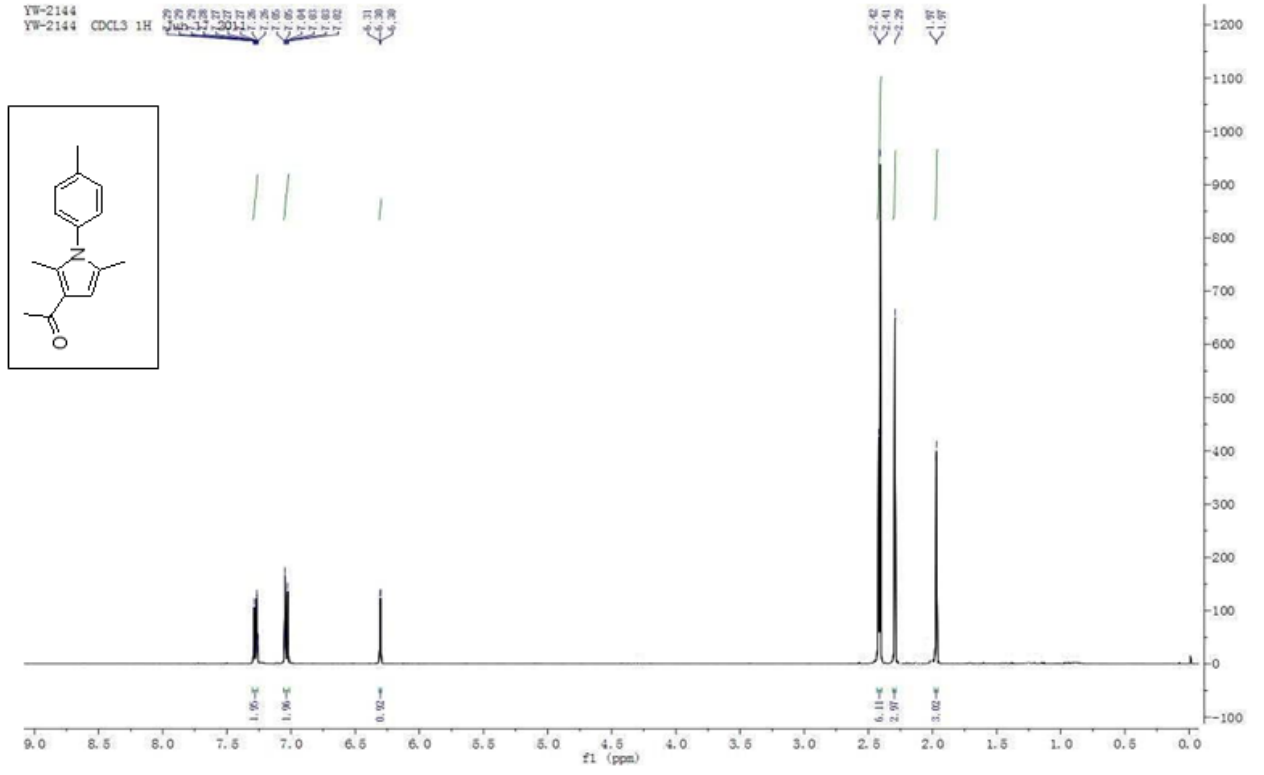
1-(2,5-Dimethyl-1-phenyl-1H-pyrrol-3-yl)ethanone 4d

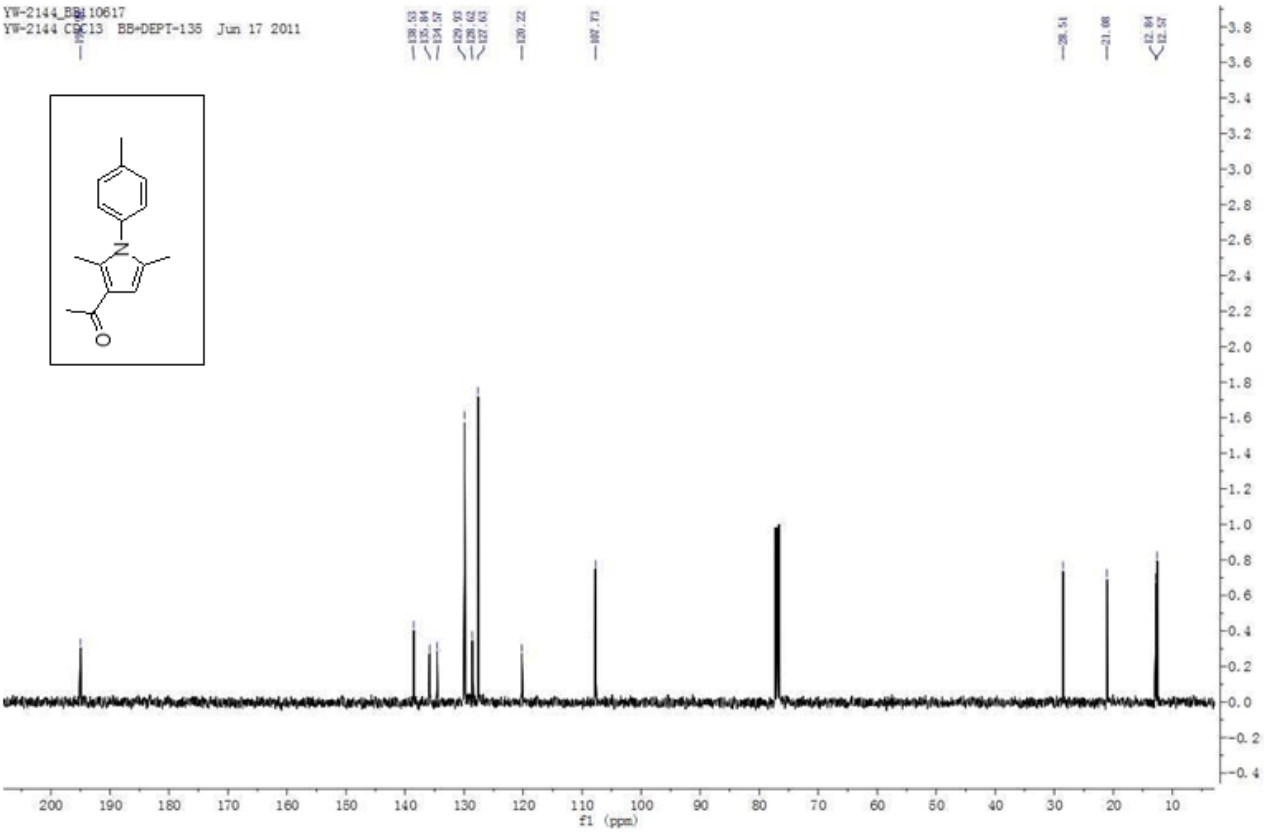




^{1}H and ^{13}C-NMR spectra data

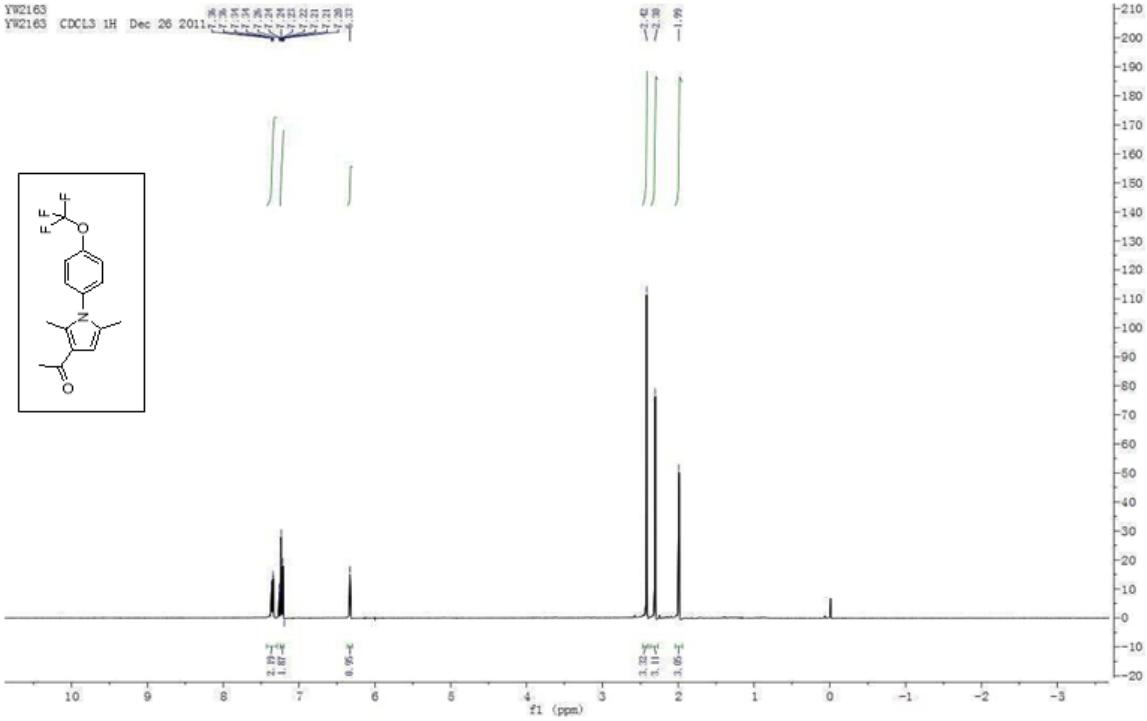
1-(2,5-Dimethyl-1-p-tolyl-1H-pyrrol-3-yl)ethanone 4e

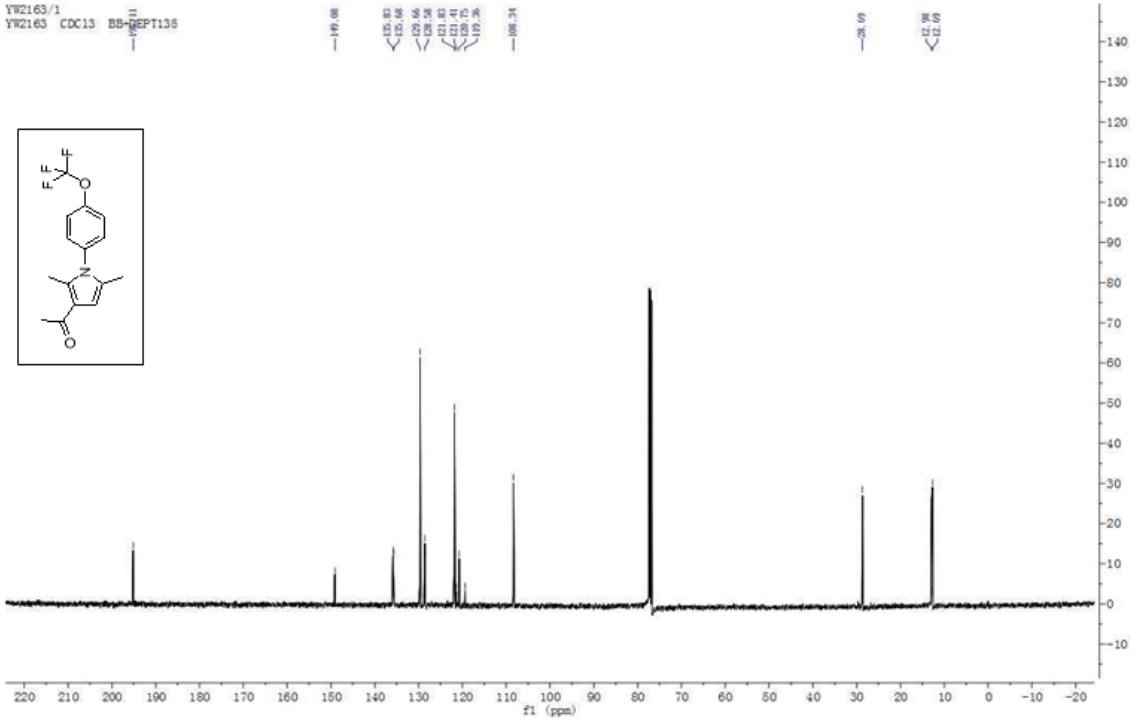




^{1}H and ^{13}C-NMR spectra data

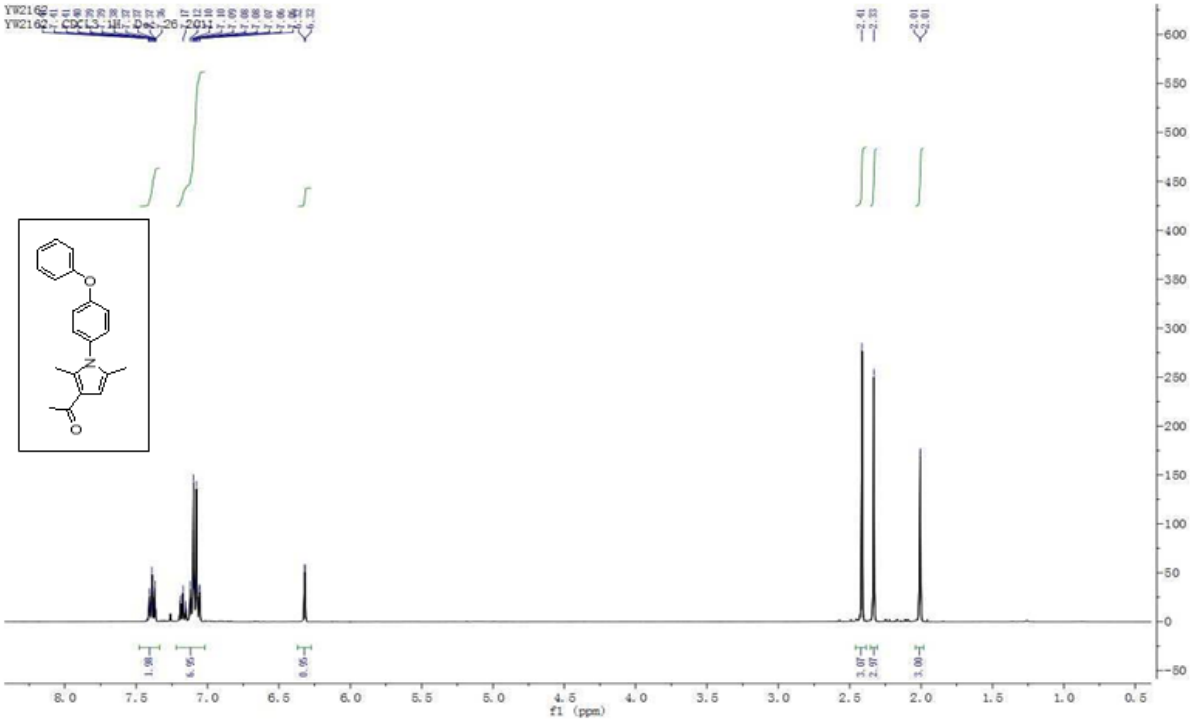
1-(2,5-Dimethyl-1-(4-(trifluoromethoxy)phenyl)-1H-pyrrol-3-yl)ethanone 4f

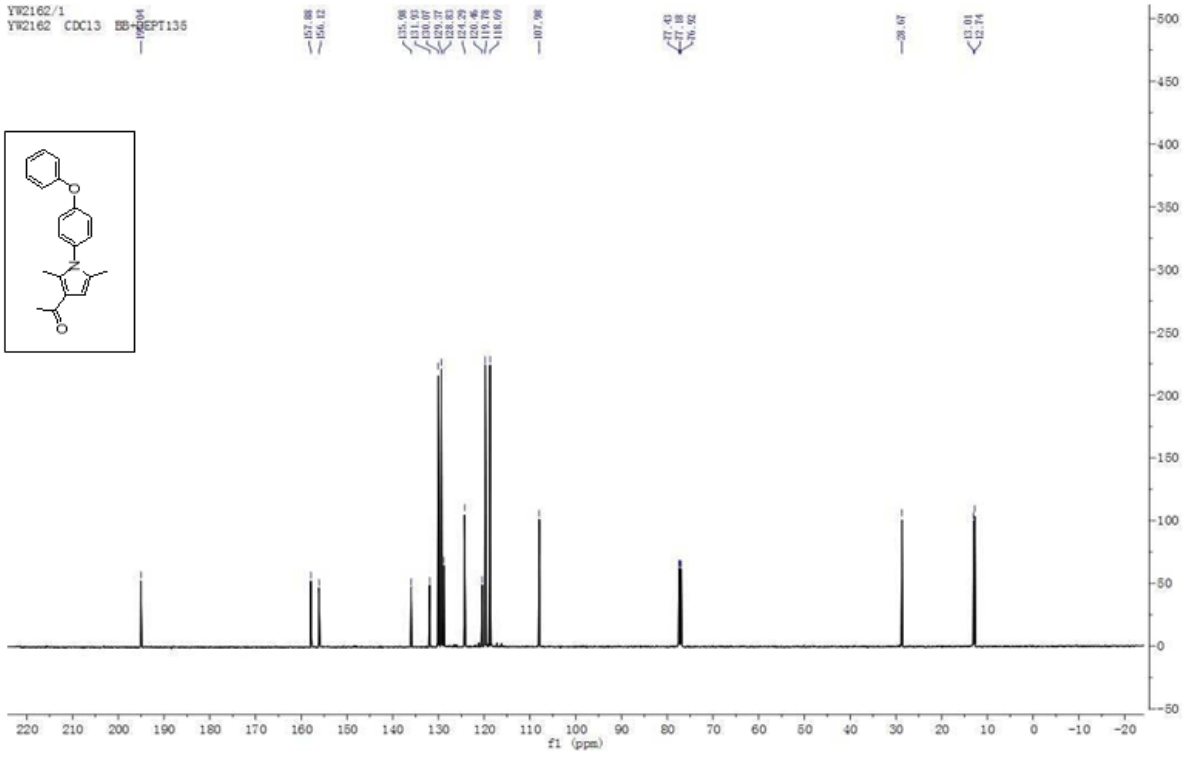




^{1}H and ^{13}C-NMR spectra data

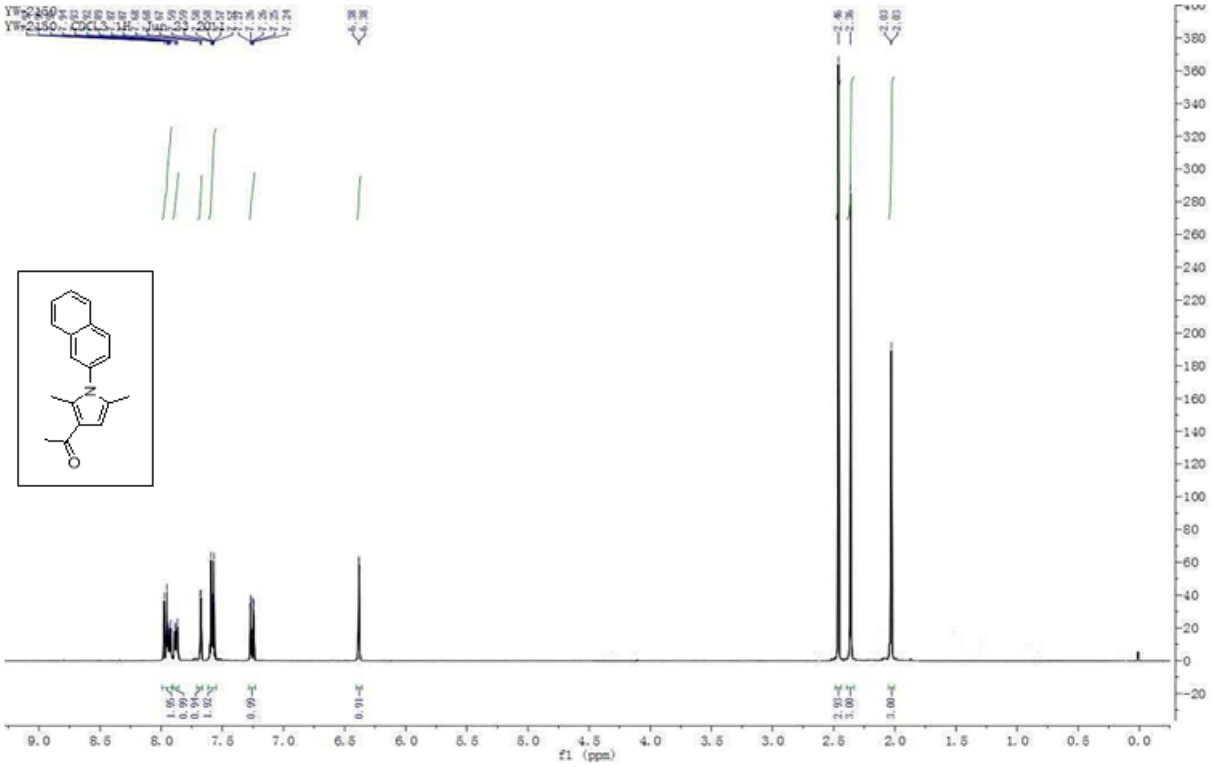
1-(2,5-Dimethyl-1-(4-phenoxyphenyl)-1H-pyrrol-3-yl)ethanone 4g

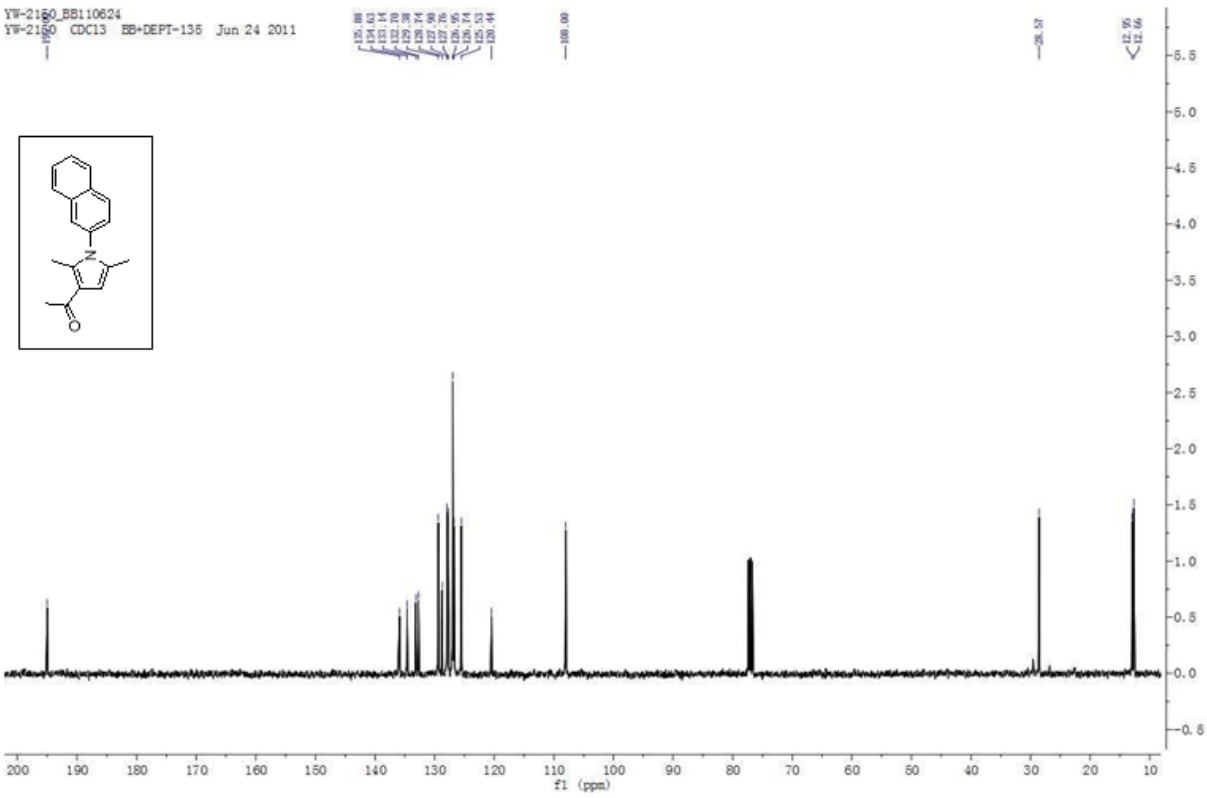




^{1}H and ^{13}C-NMR spectra data

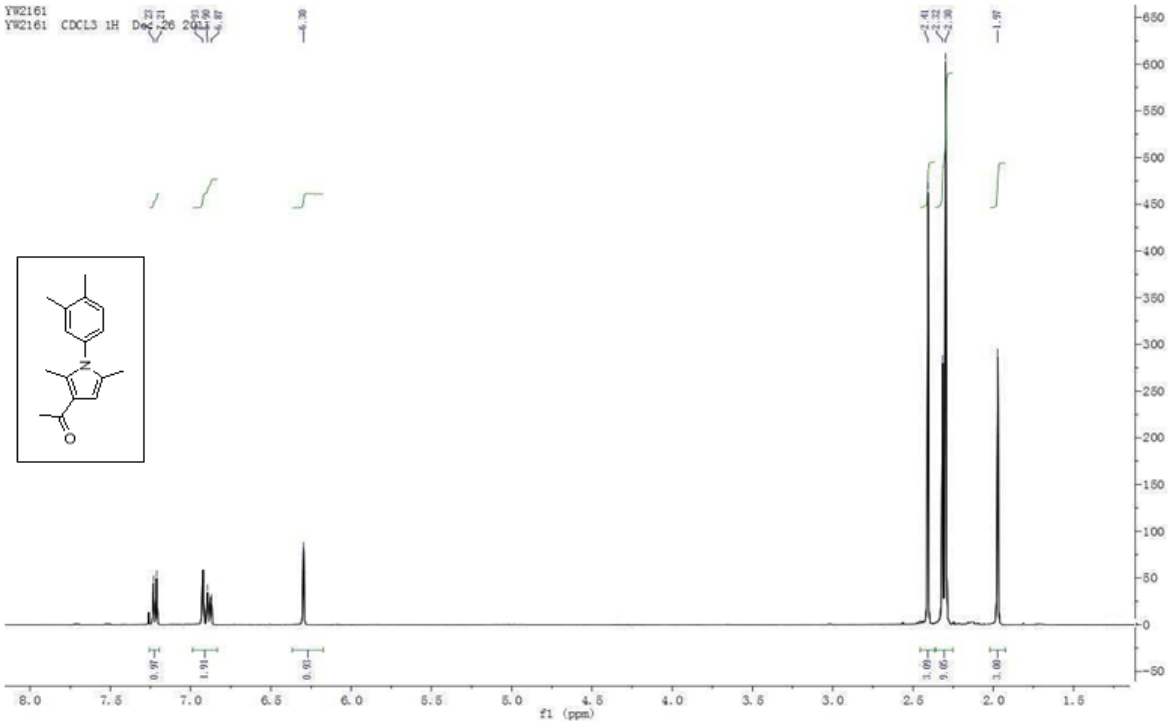
1-(2,5-Dimethyl-1-(naphthalen-2-yl)-1H-pyrrol-3-yl)ethanone 4h

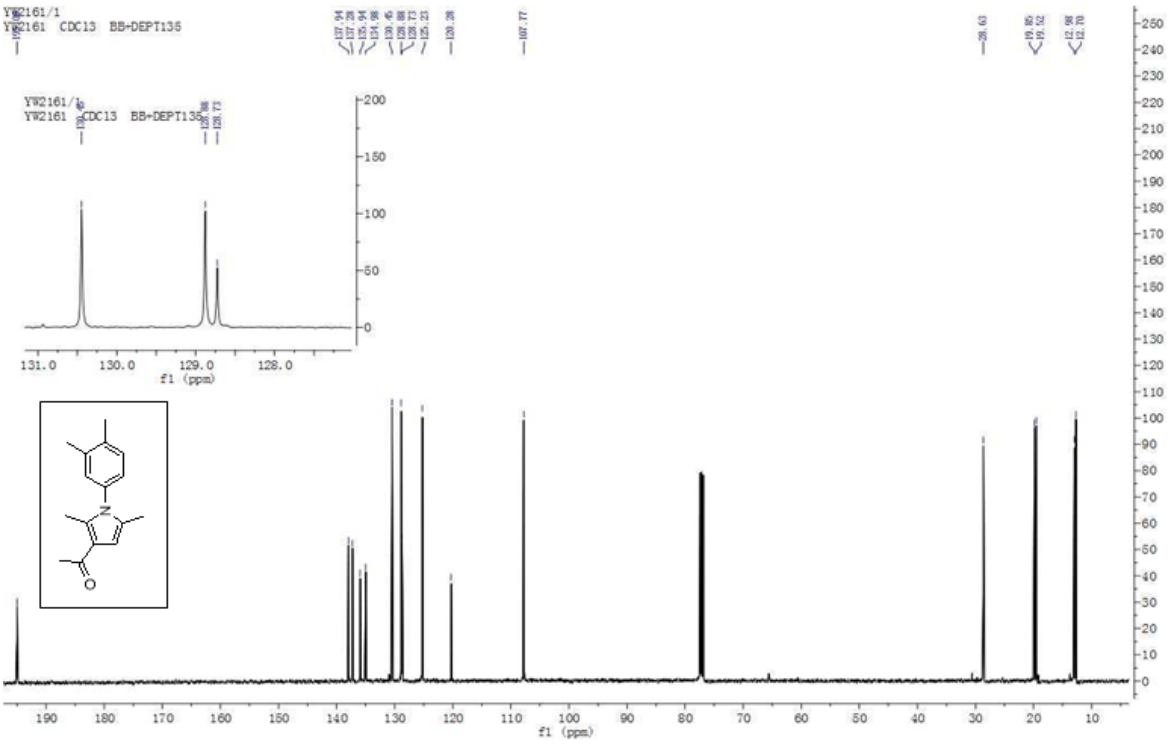




^{1}H and ^{13}C-NMR spectra data

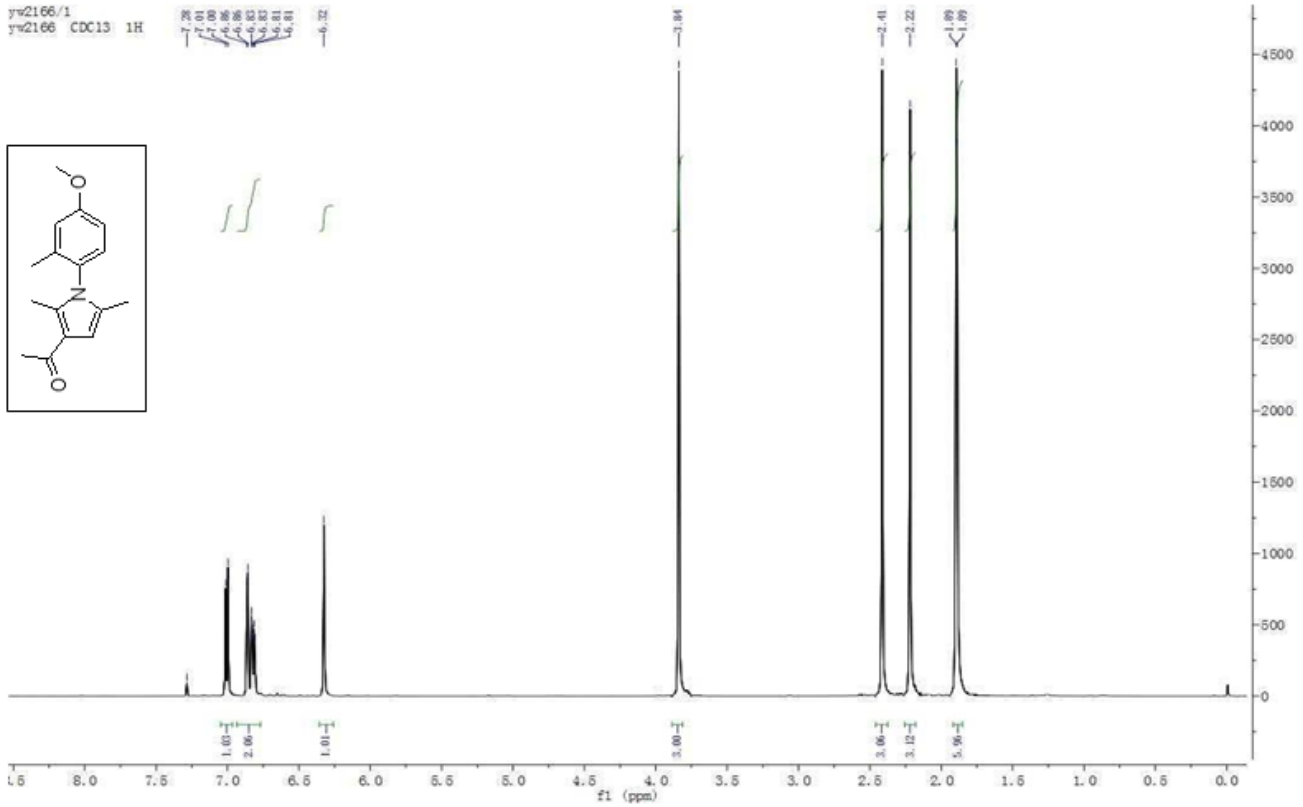
1-(1-(3,4-Dimethylphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4i

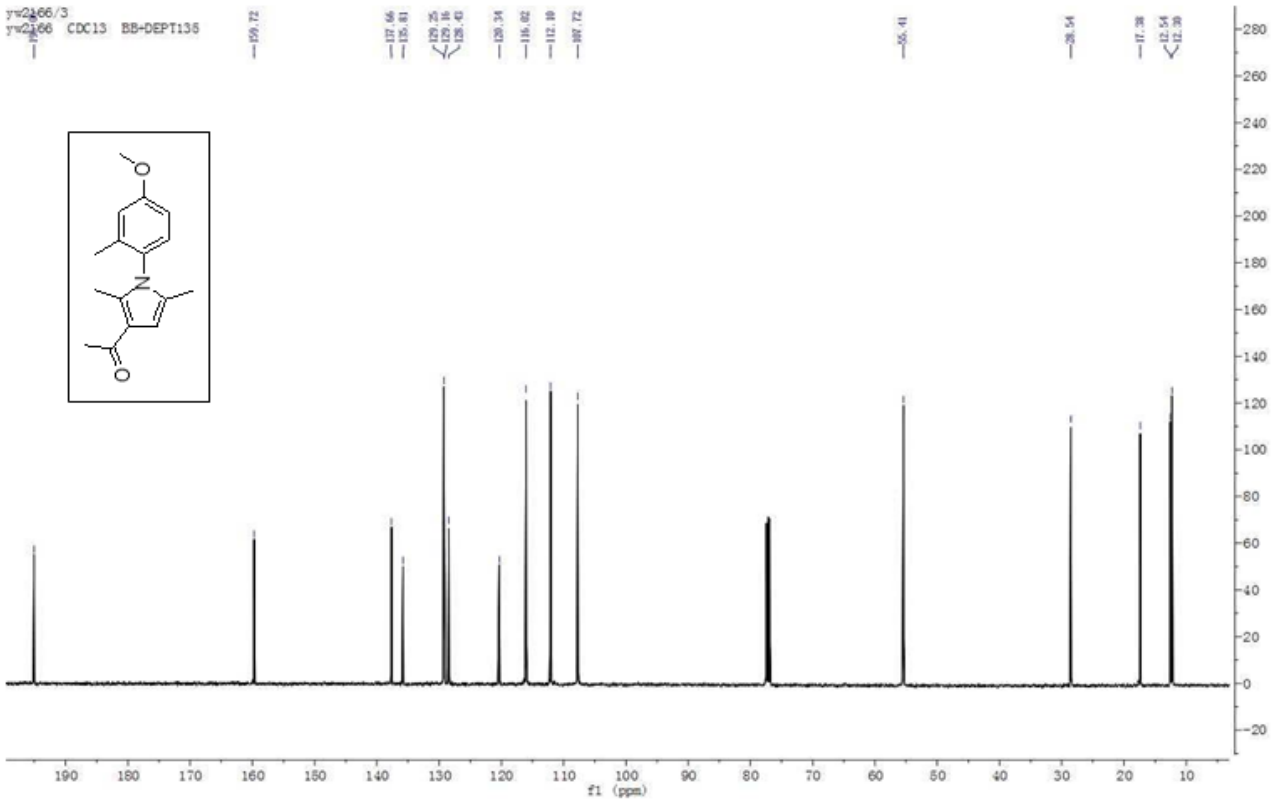




^{1}H and ^{13}C-NMR spectra data

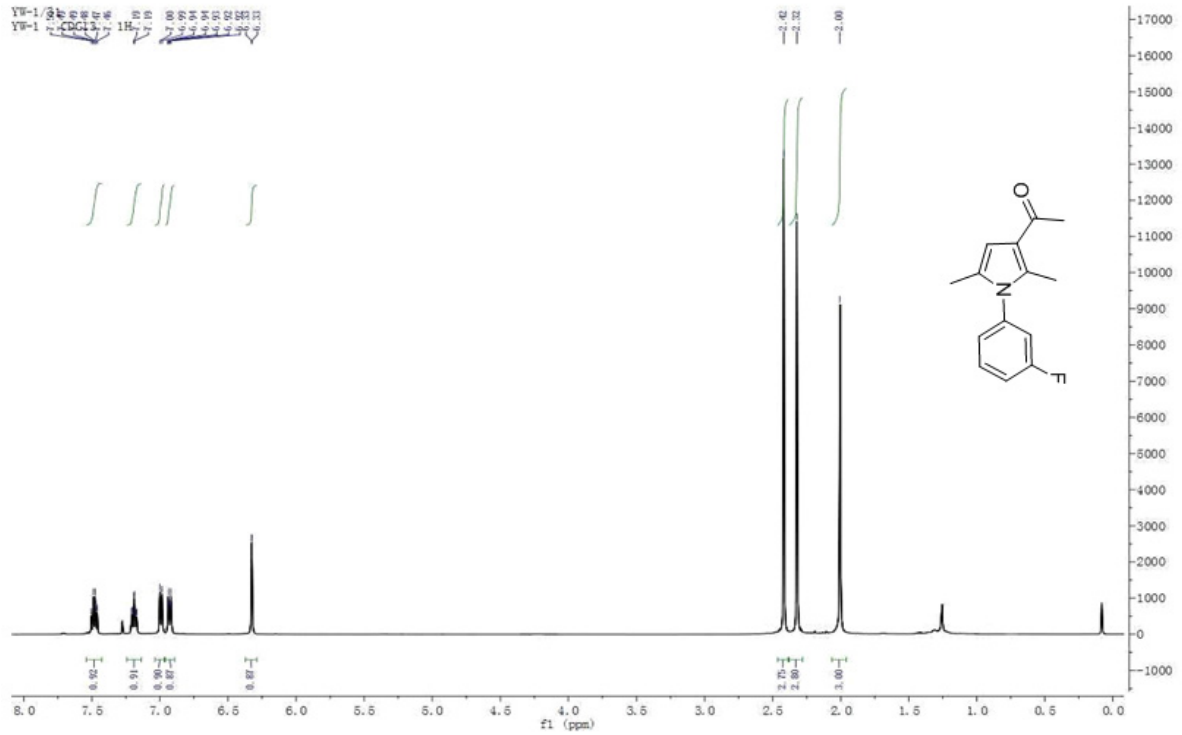
1-(1-(4-Methoxy-2-methylphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4j

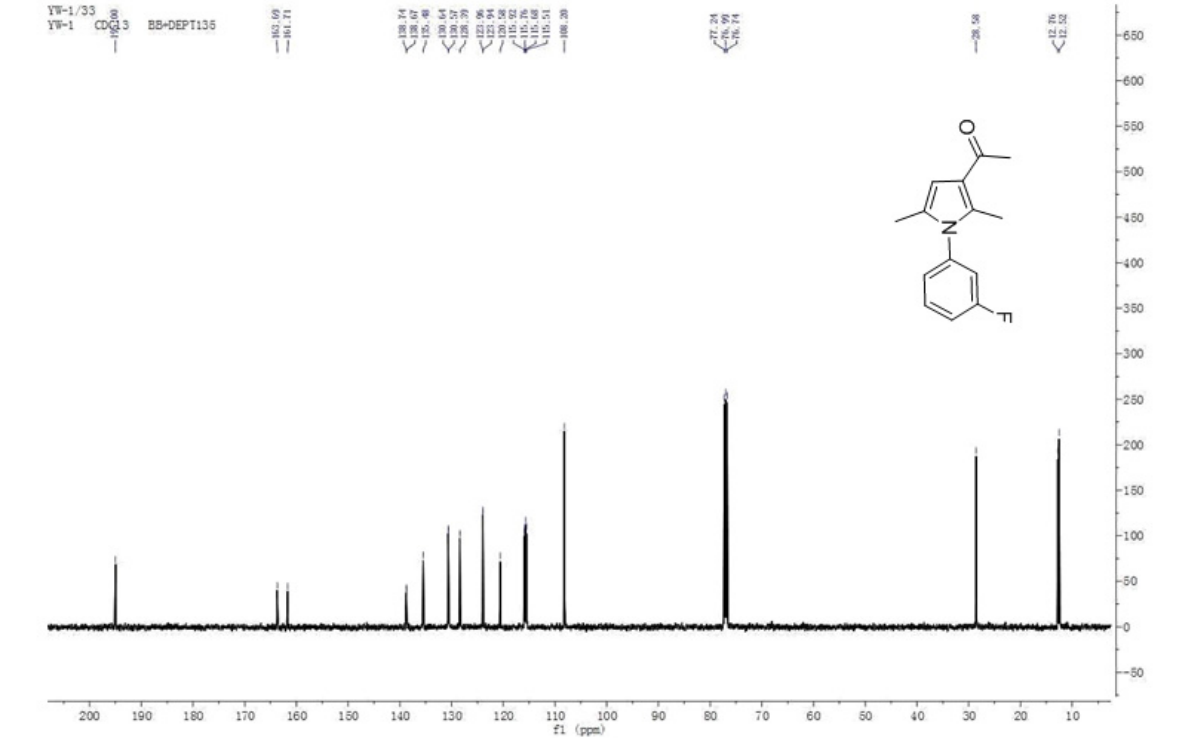




^{1}H and ^{13}C-NMR spectra data

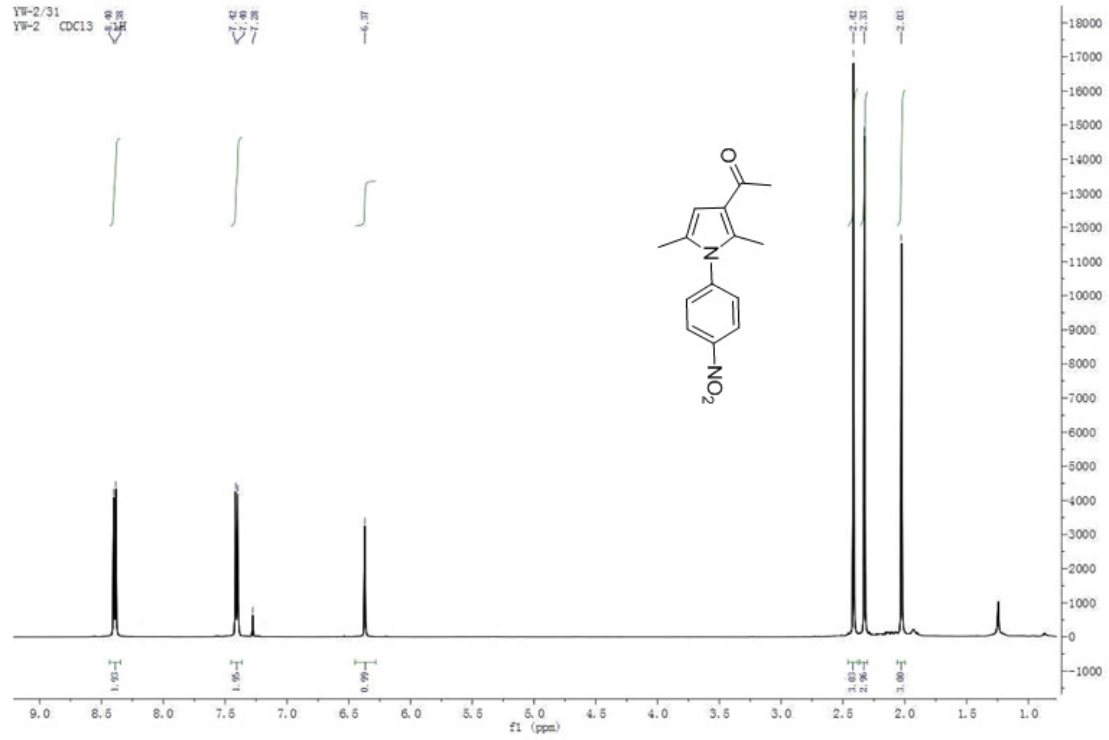
1-(1-(3-Fluorophenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4k

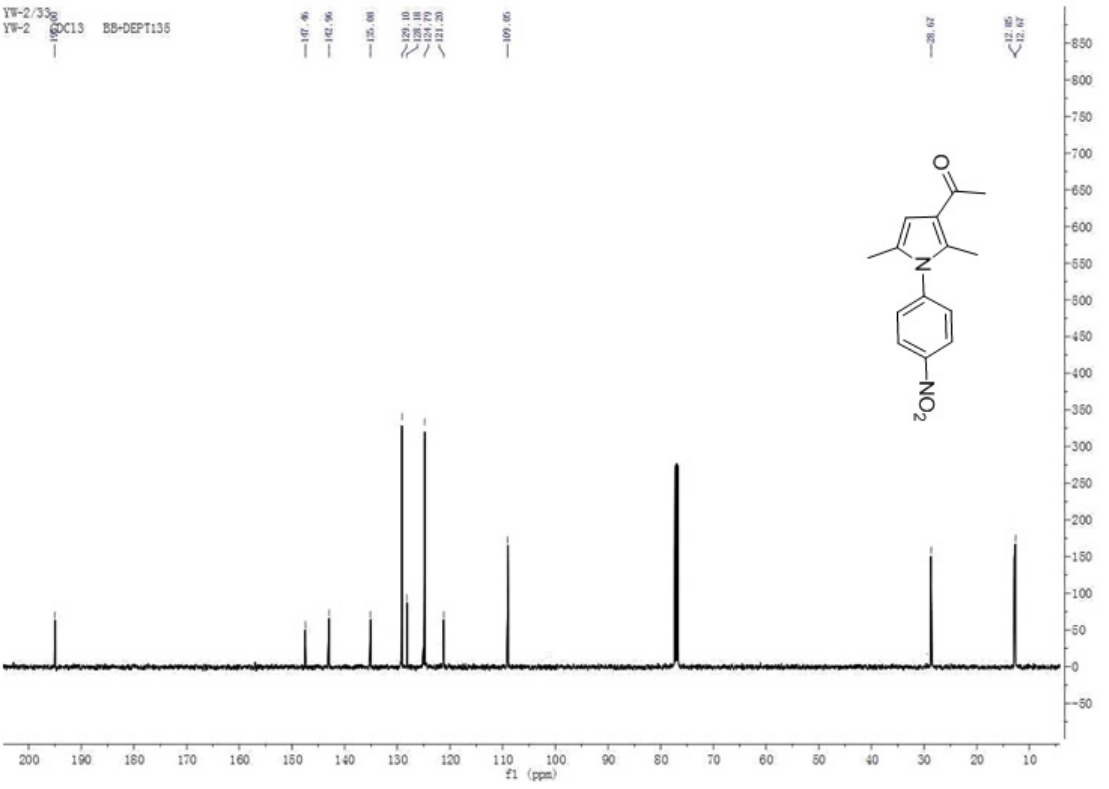




^{1}H and ^{13}C-NMR spectra data

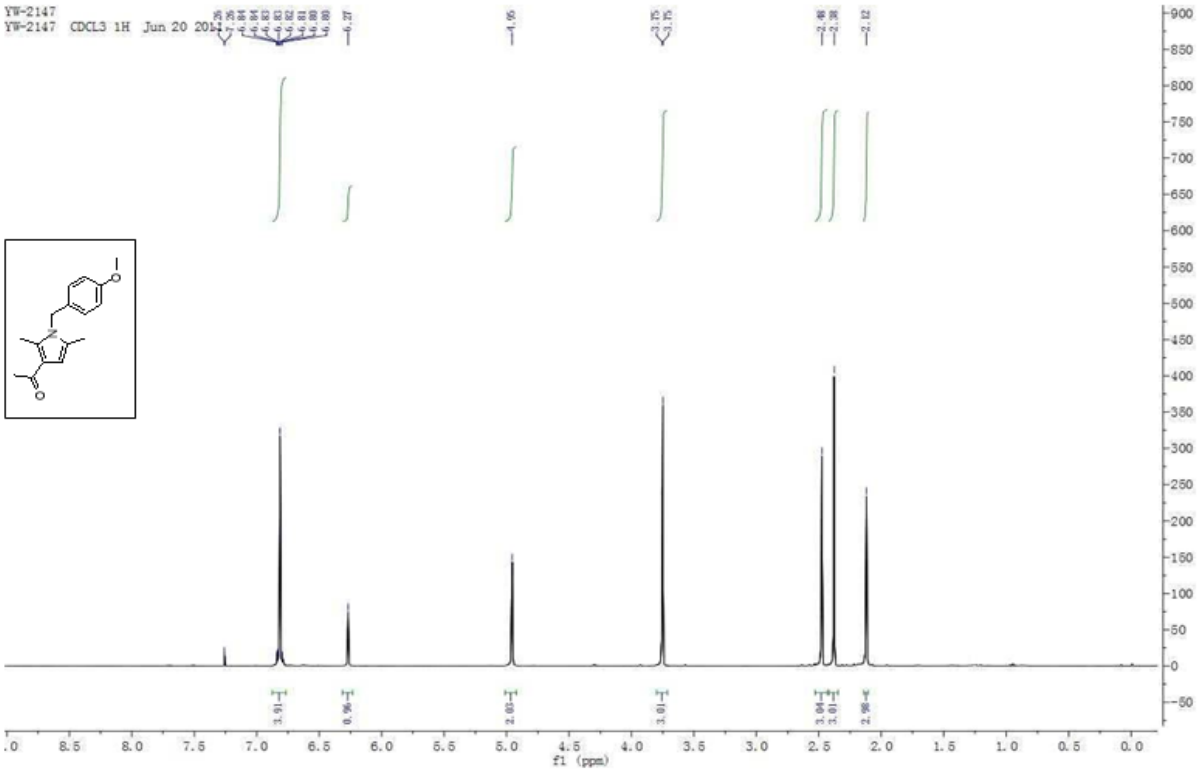
1-(2,5-Dimethyl-1-(4-nitrophenyl)-1H-pyrrol-3-yl)ethanone 4l

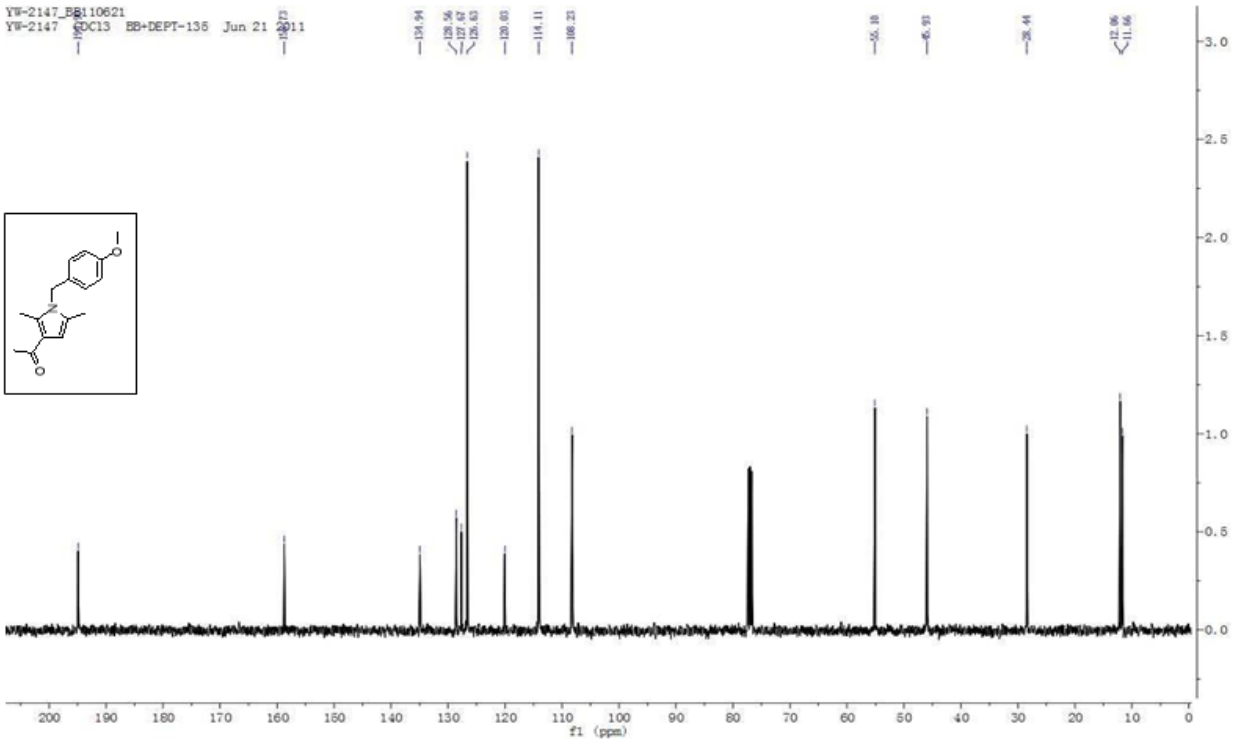




^{1}H and ^{13}C-NMR spectra data

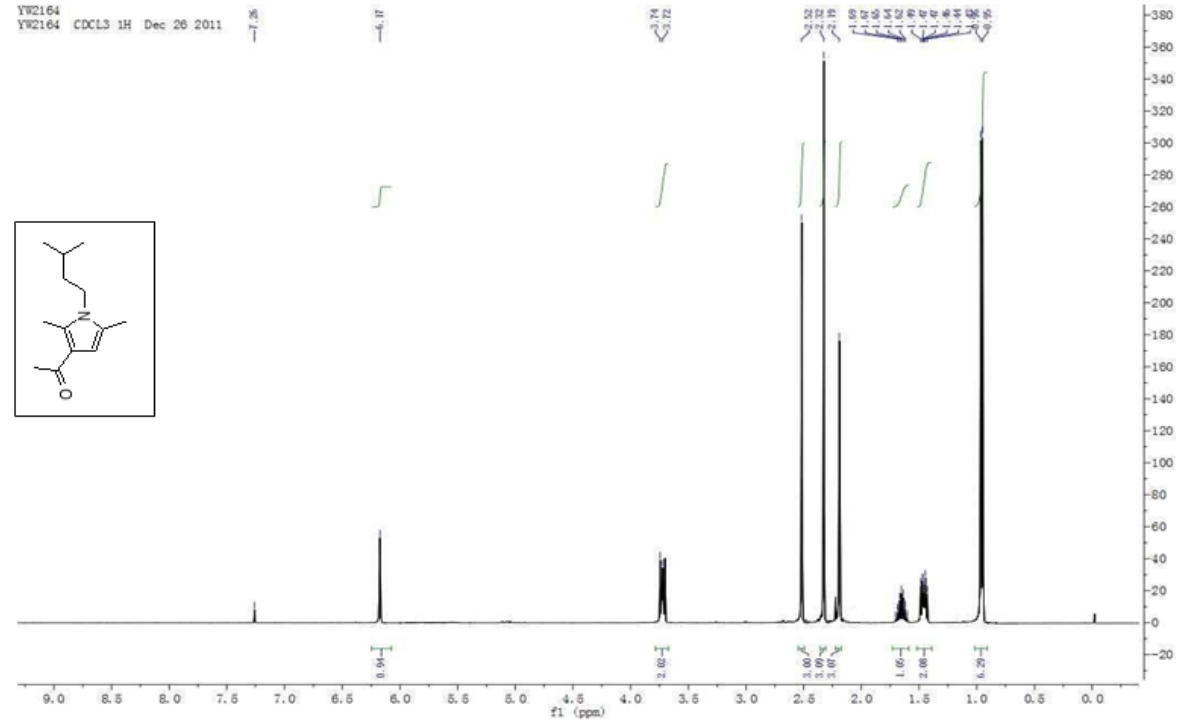
1-(1-(4-Methoxybenzyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4m

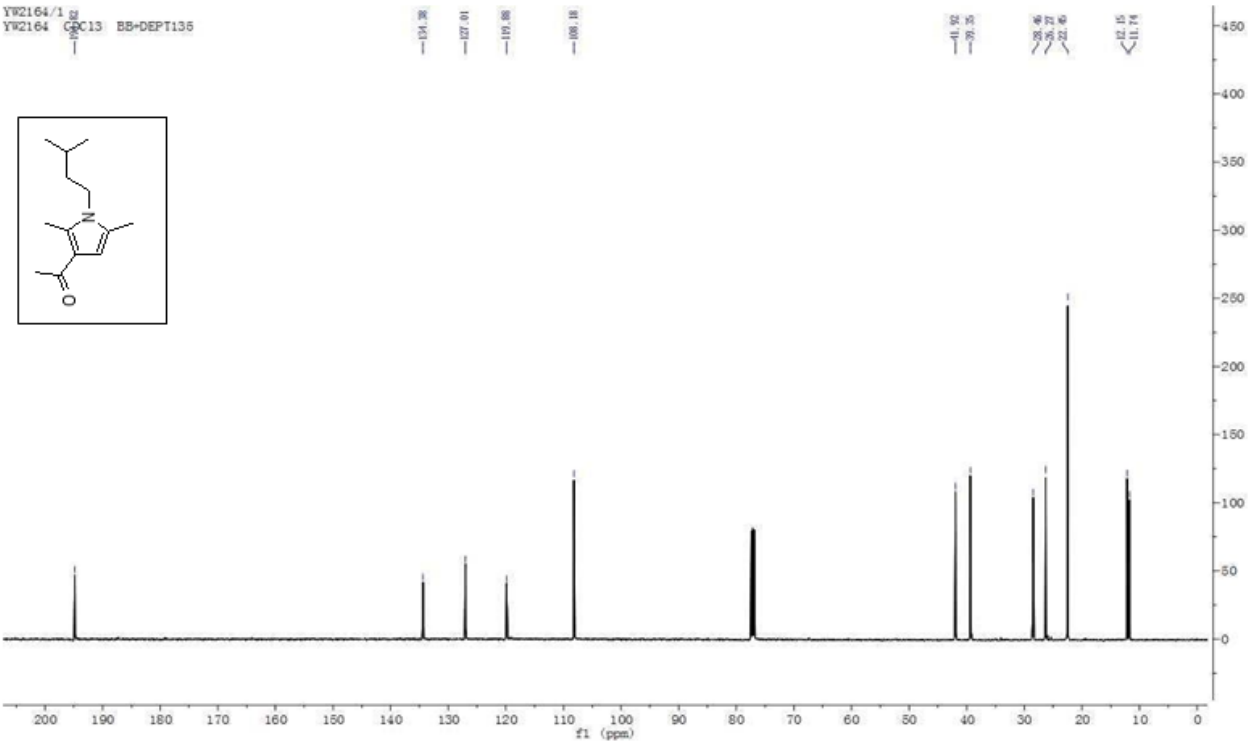




^{1}H and ^{13}C-NMR spectra data

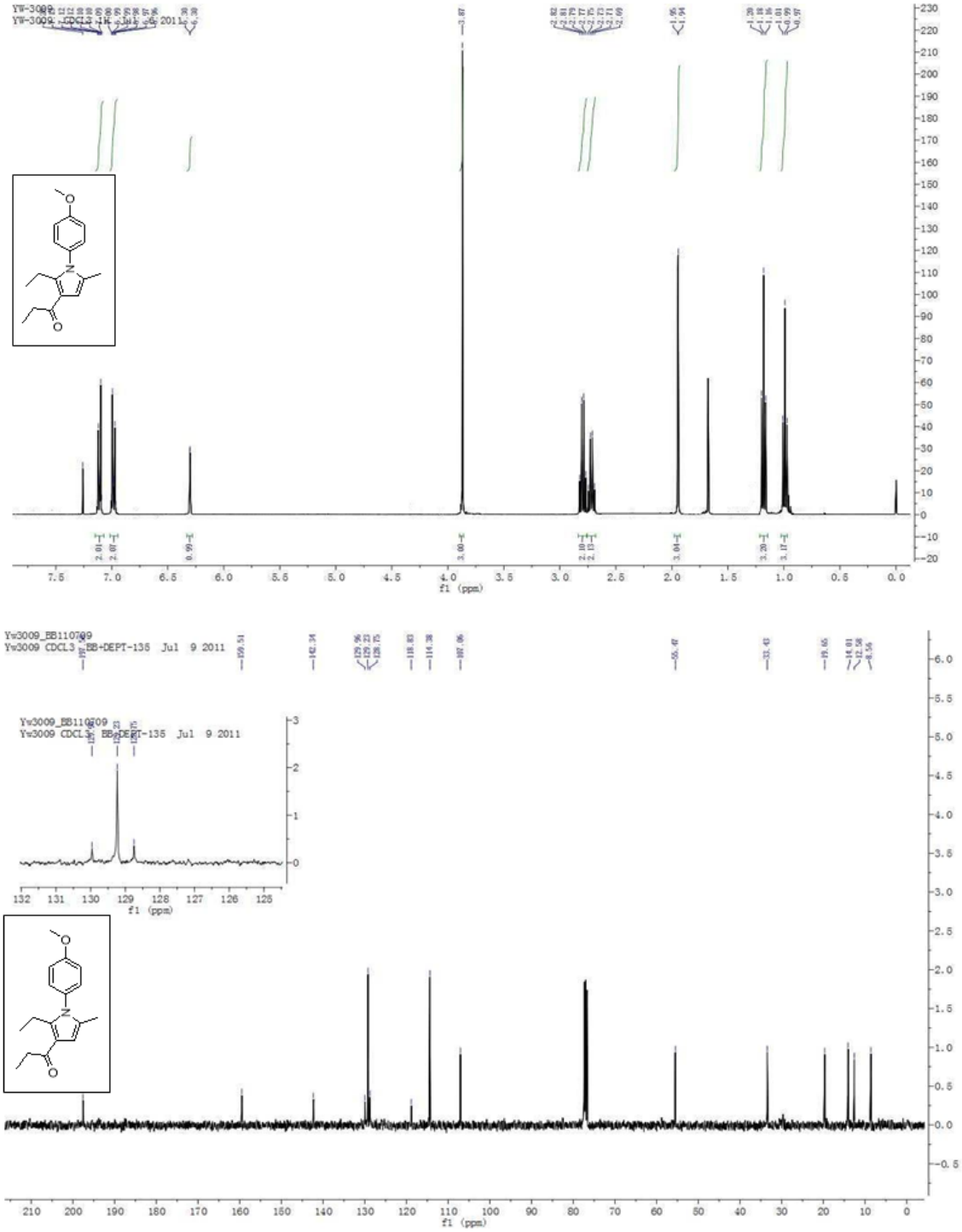
1-(1-Isopentyl-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4n





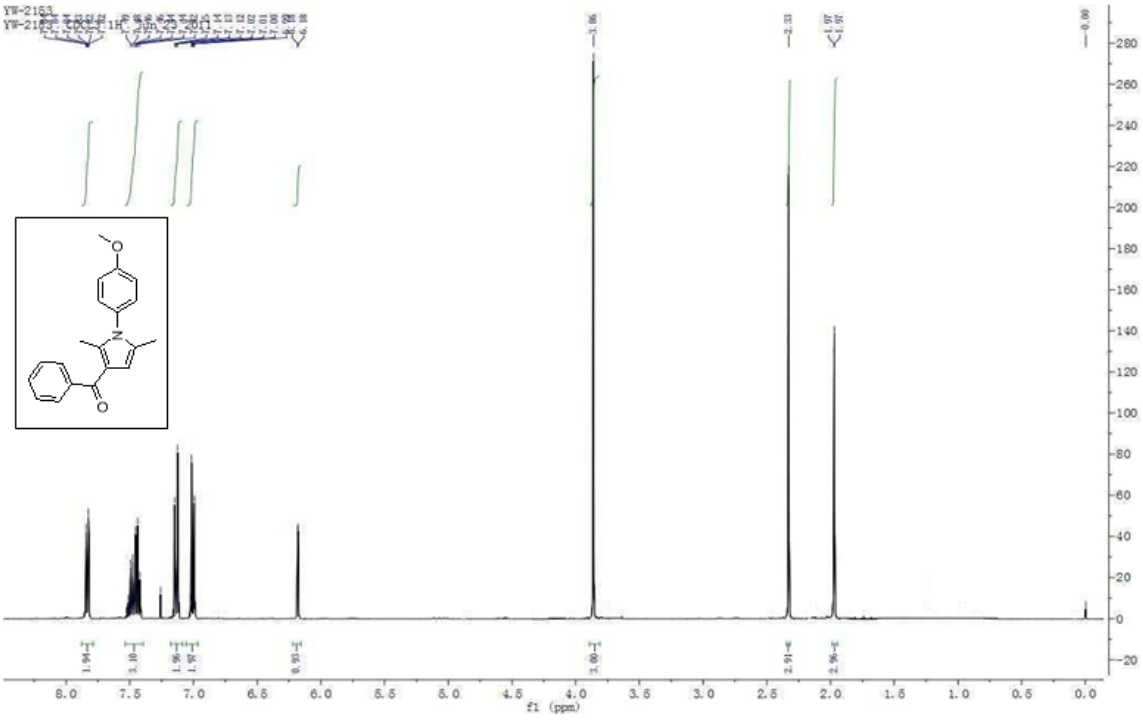
^{1}H and ^{13}C-NMR spectra data

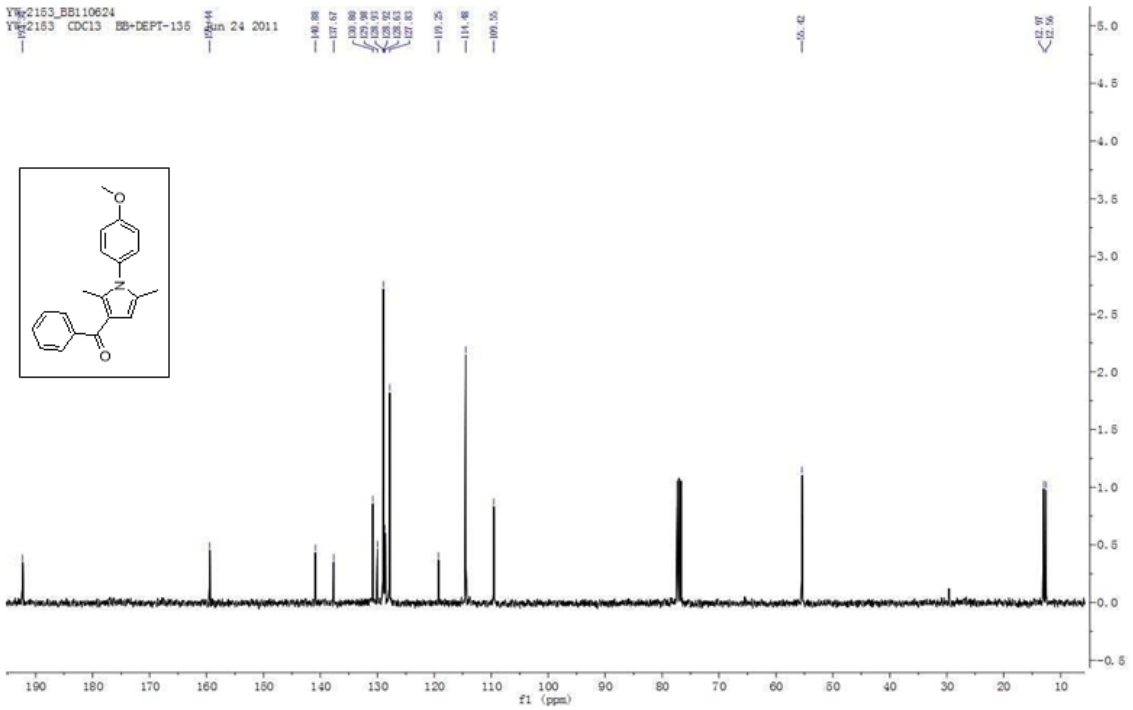
1-(2-Ethyl-1-(4-methoxyphenyl)-5-methyl-1H-pyrrol-3-yl)propan-1-one 4o



^{1}H and ^{13}C-NMR spectra data

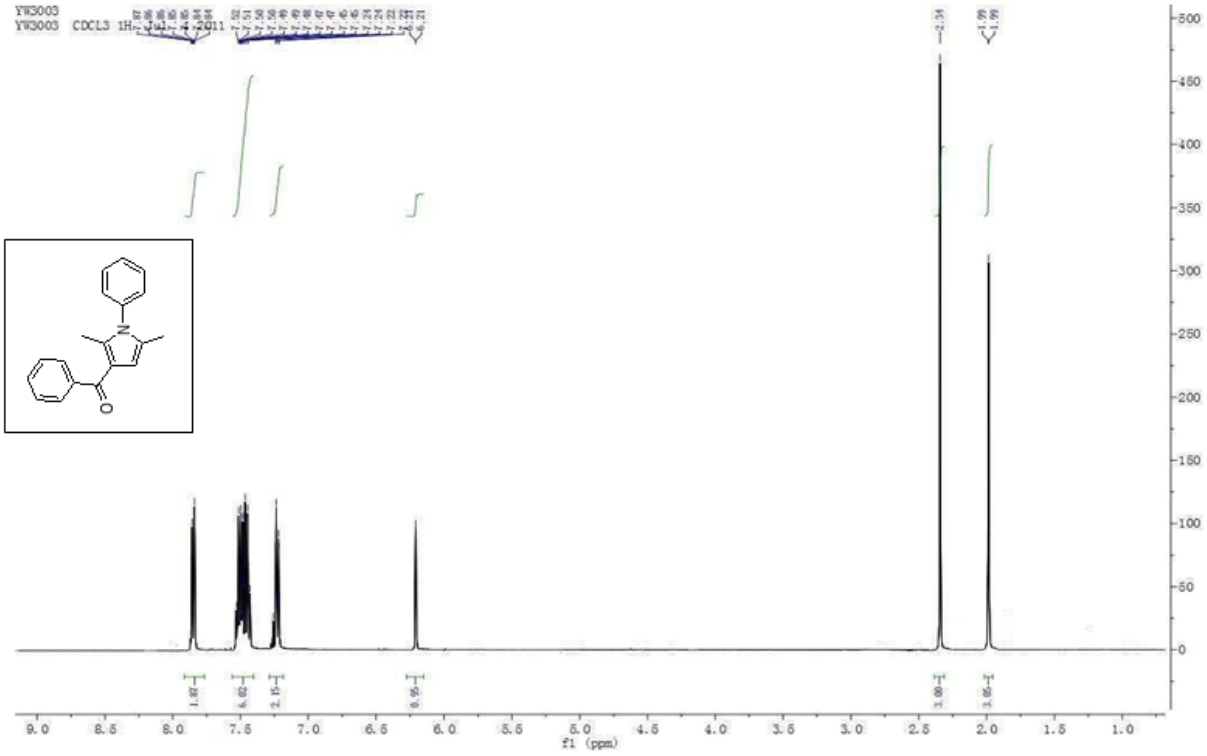
(1-(4-Methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)(phenyl)methanone 4p

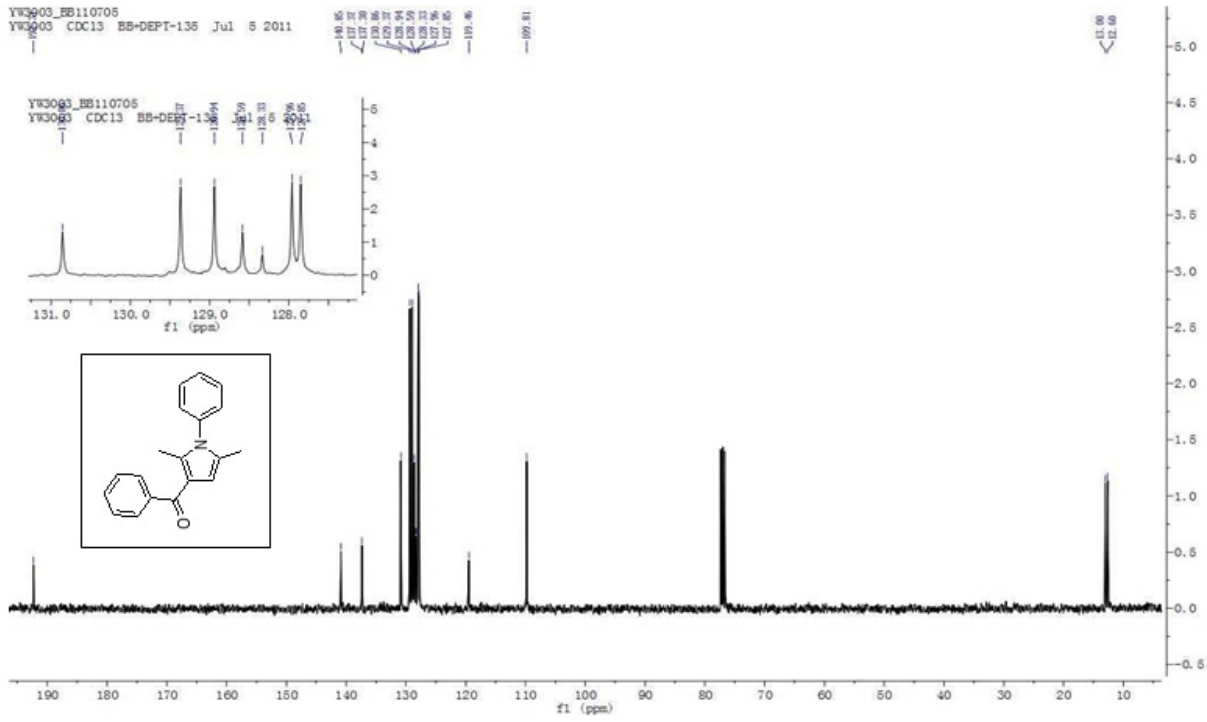




^{1}H and ^{13}C-NMR spectra data

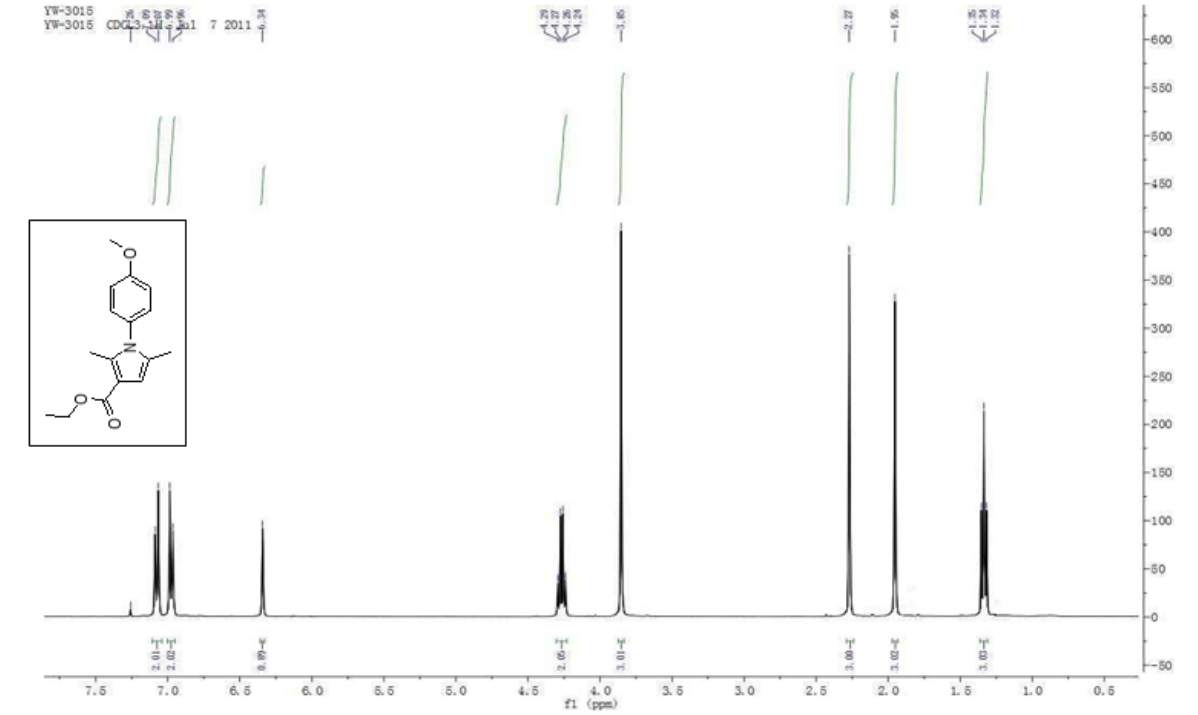
(2,5-Dimethyl-1-phenyl-1H-pyrrol-3-yl)(phenyl)methanone 4q

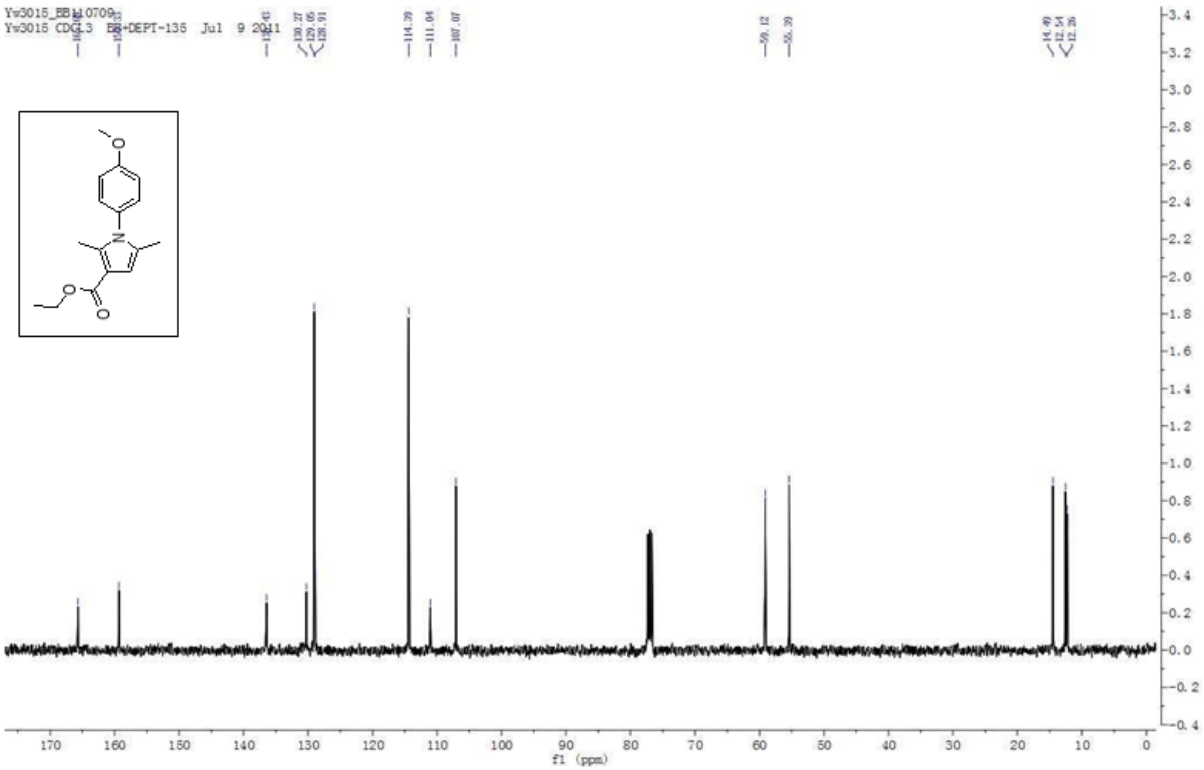




^{1}H and ^{13}C-NMR spectra data

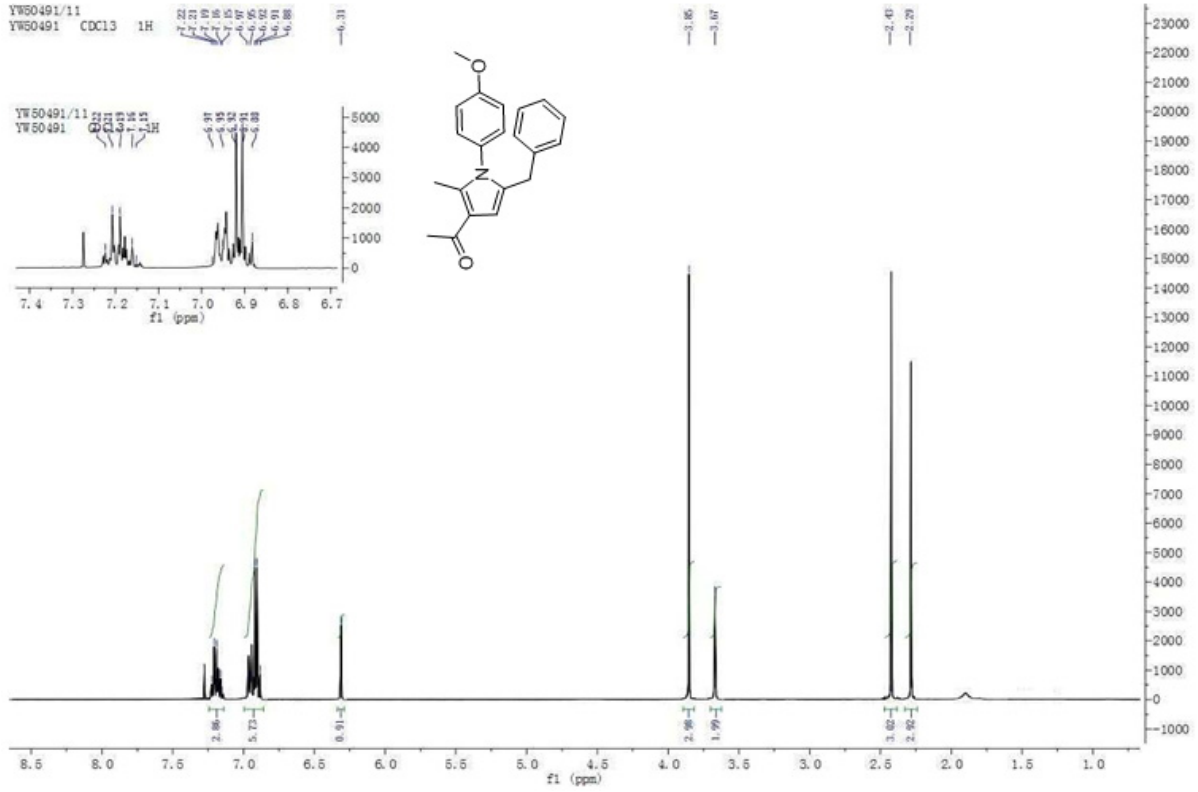
Ethyl 1-(4-methoxyphenyl)-2,5-dimethyl-1H-pyrrole-3-carboxylate 4r

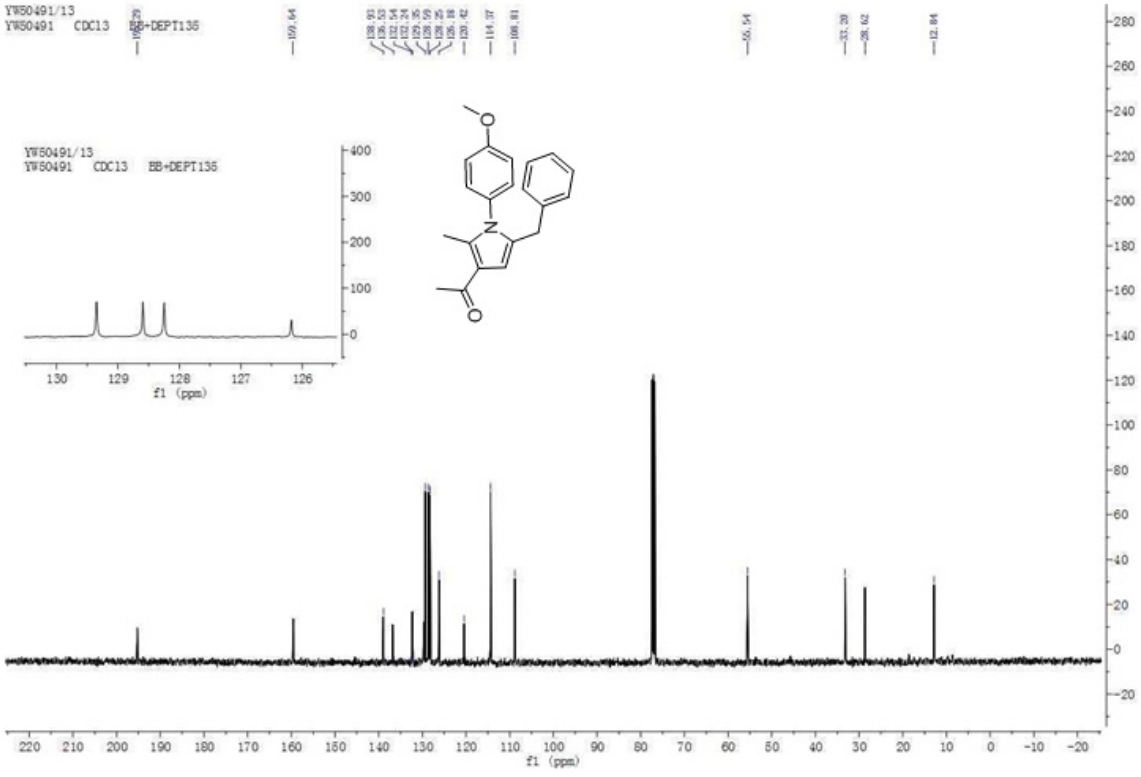




^{1}H and ^{13}C-NMR spectra data

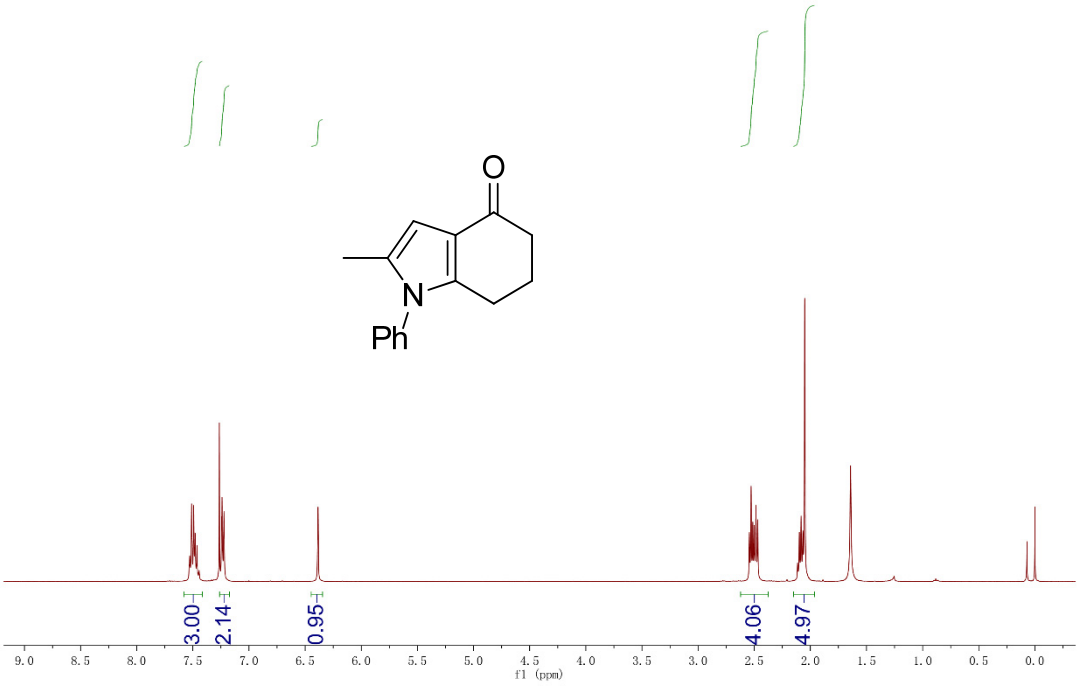
1-(5-Benzyl-1-(4-methoxyphenyl)-2-methyl-1H-pyrrol-3-yl)ethanone 4s

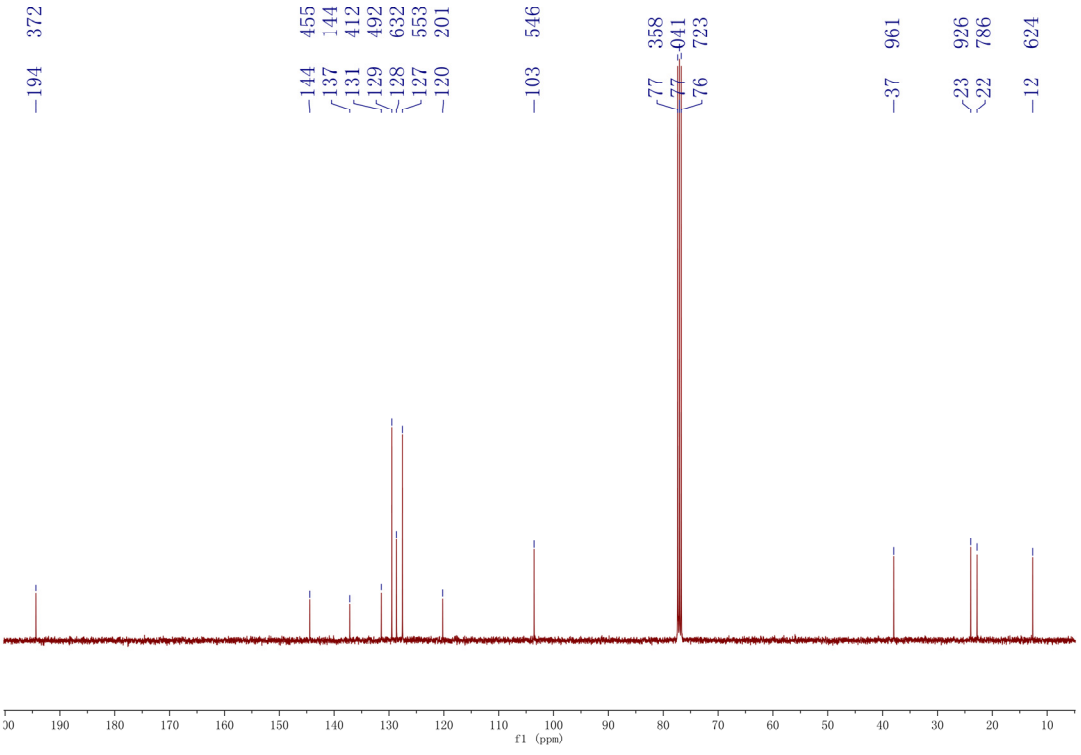




^{1}H and ^{13}C-NMR spectra data

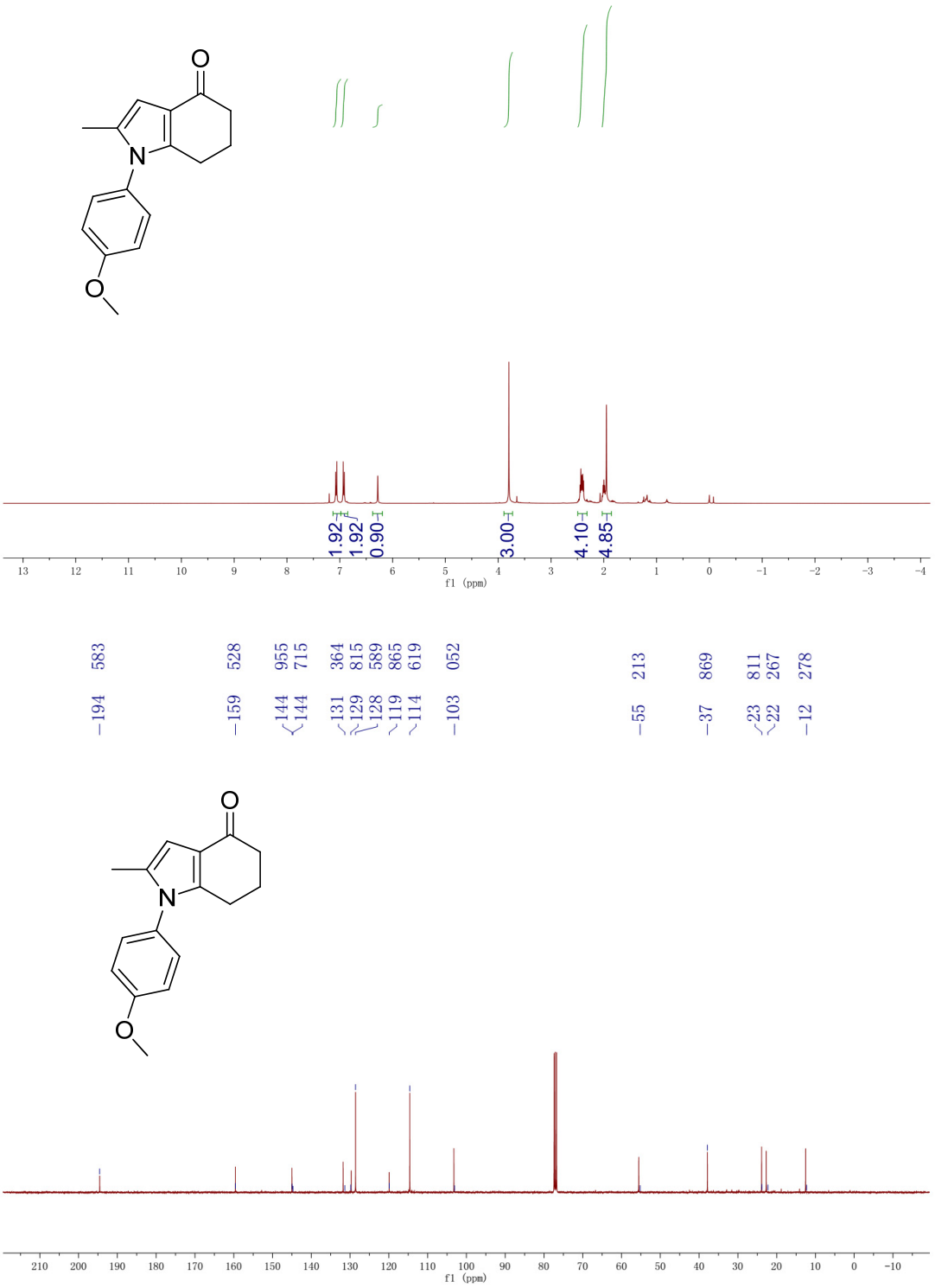
2-Methyl-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one 6a





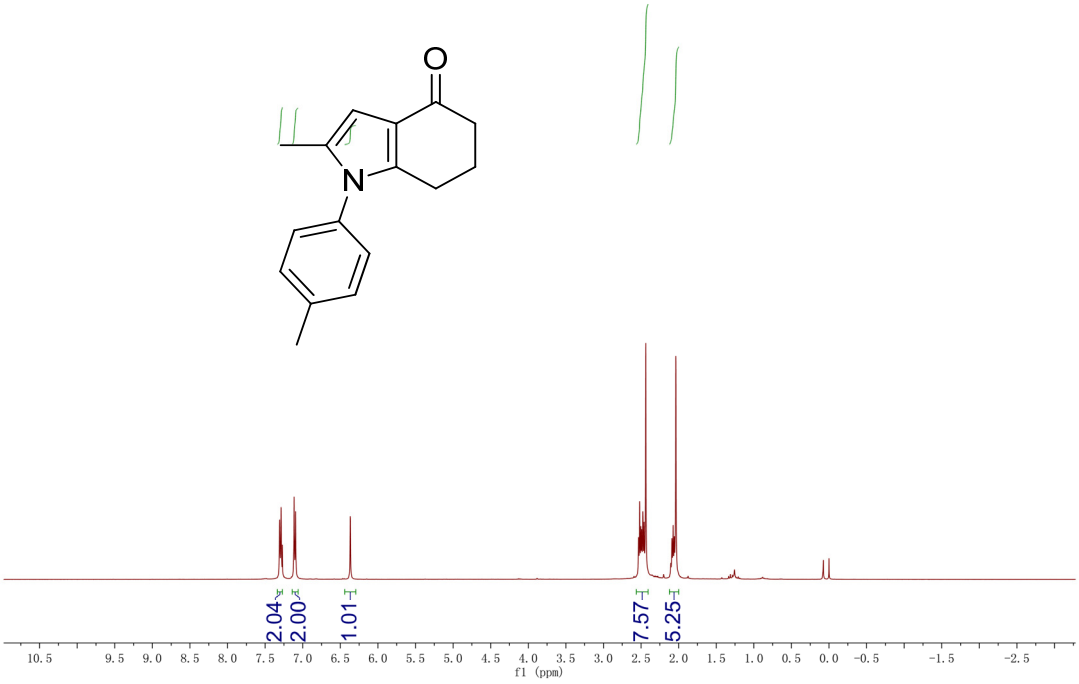
^{1}H and ^{13}C-NMR spectra data

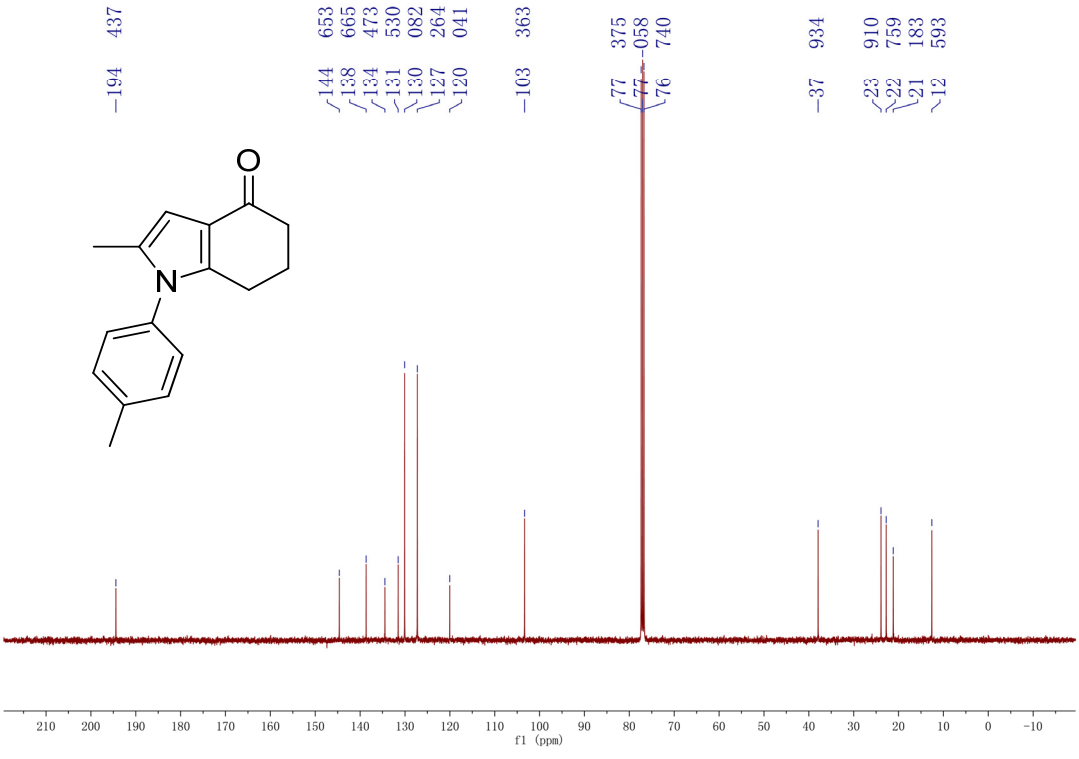
1-(4-Methoxyphenyl)-2-methyl-6,7-dihydro-1H-indol-4(5H)-one 6b



^{1}H and ^{13}C-NMR spectra data

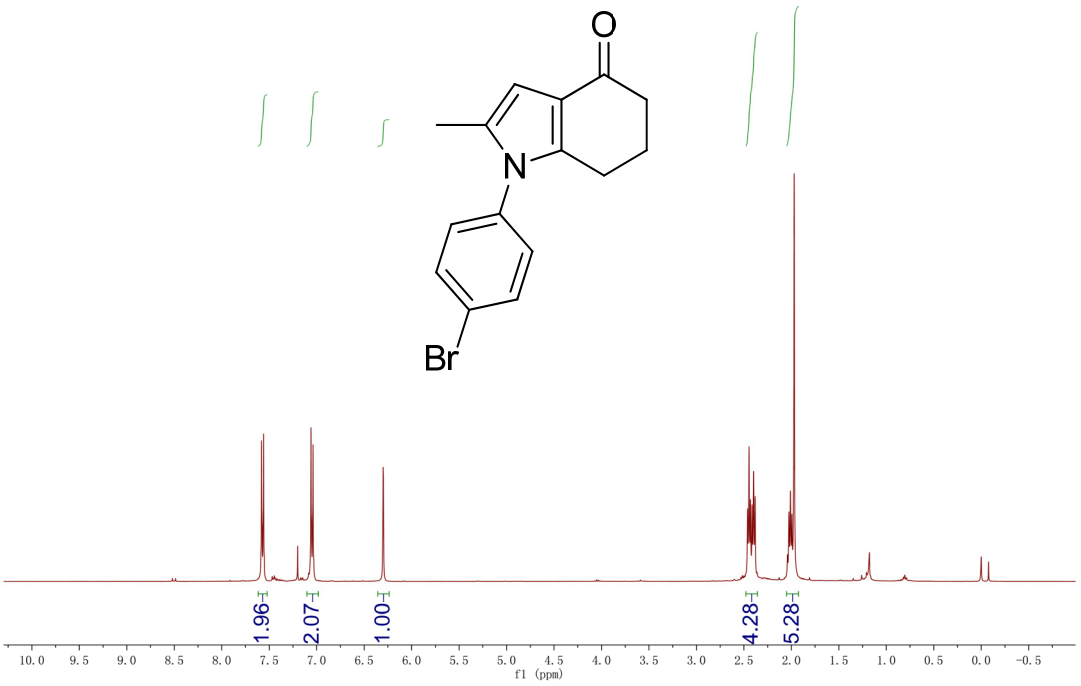
2-Methyl-1-(p-tolyl)-6,7-dihydro-1H-indol-4(5H)-one 6c

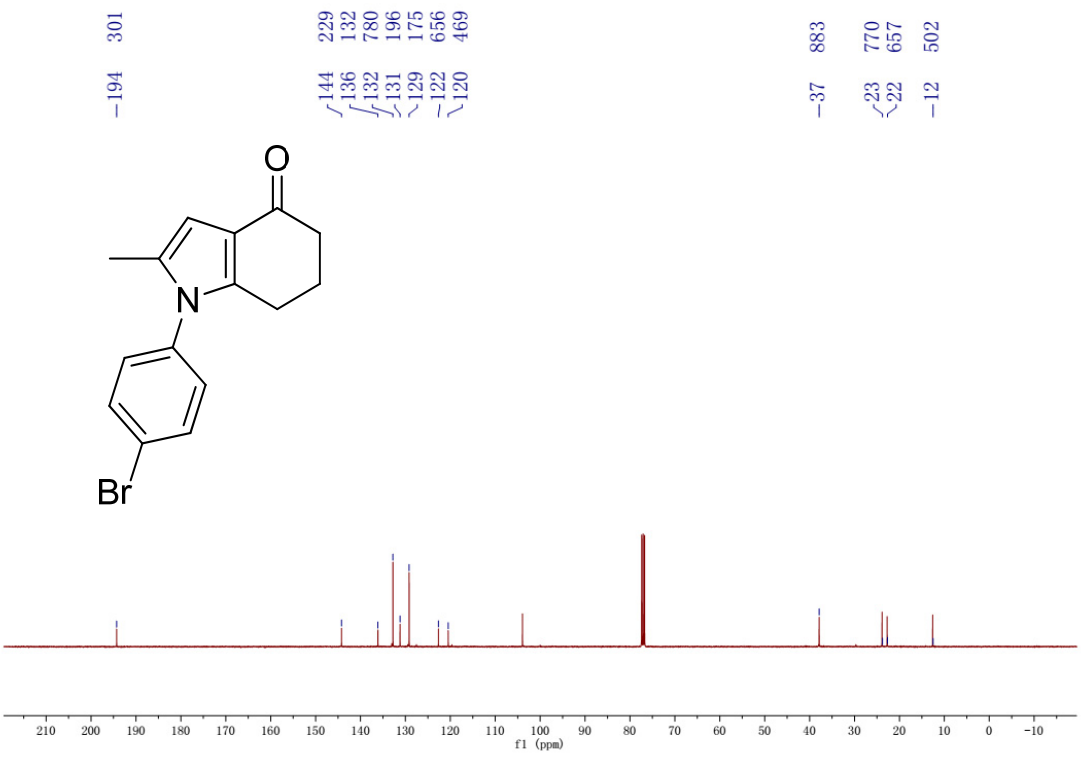




^{1}H and ^{13}C-NMR spectra data

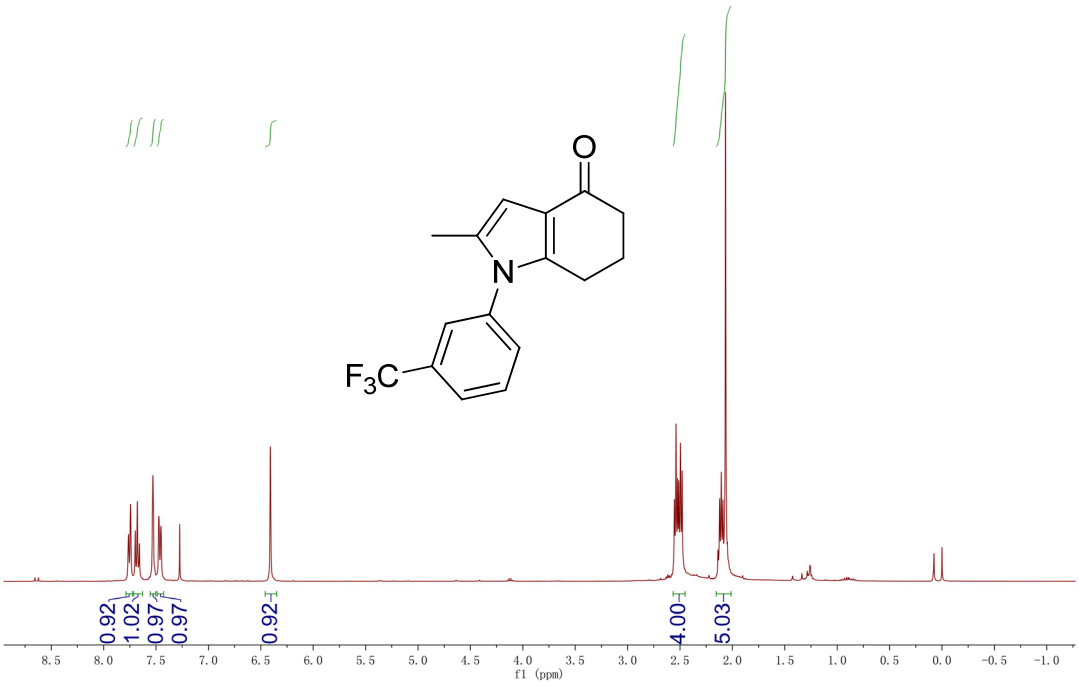
1-(4-Bromophenyl)-2-methyl-6,7-dihydro-1H-indol-4(5H)-one 6d

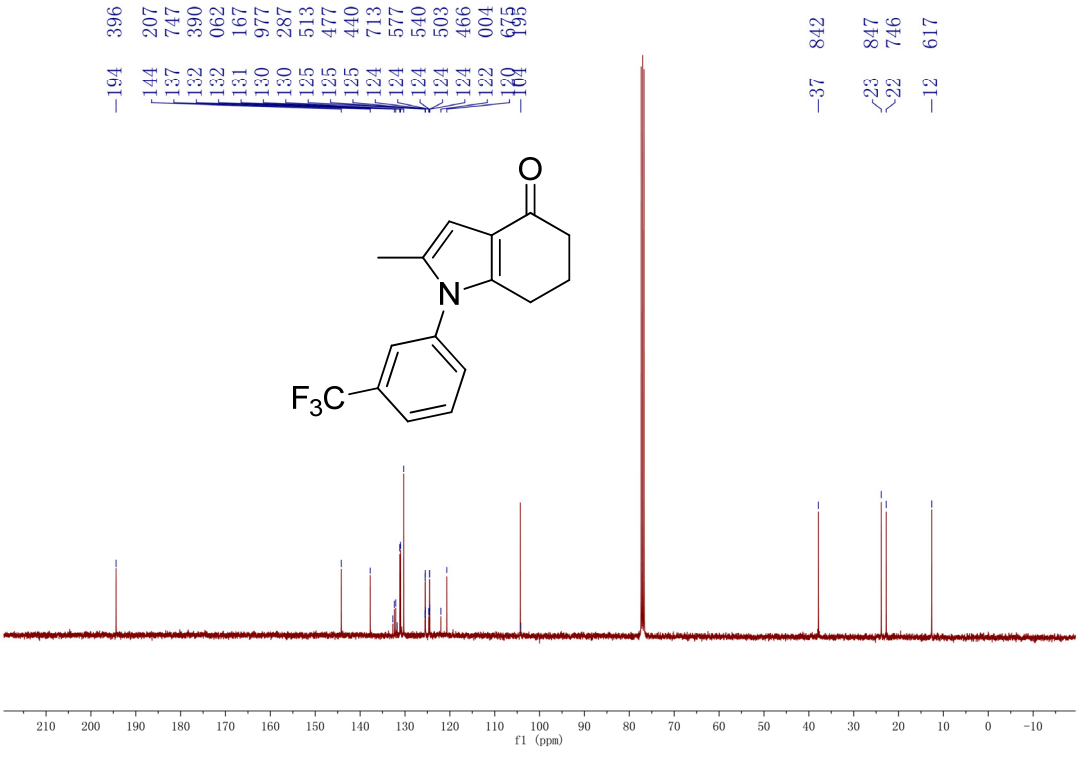




^{1}H and ^{13}C-NMR spectra data

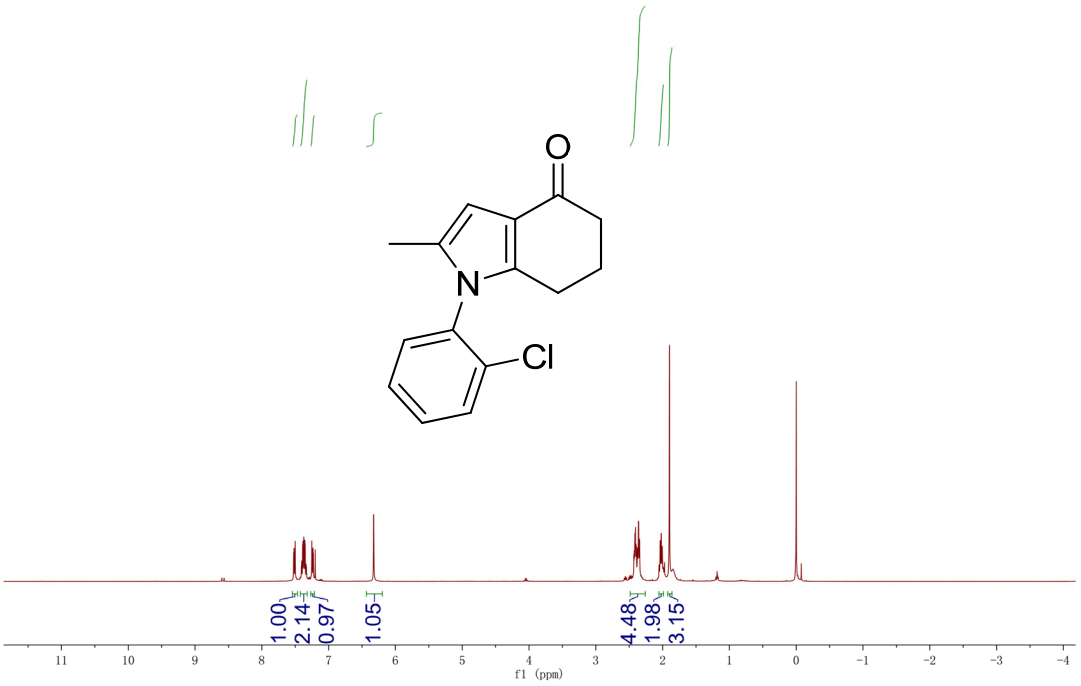
2-Methyl-1-(3-(trifluoromethyl)phenyl)-6,7-dihydro-1H-indol-4(5H)-one 6e

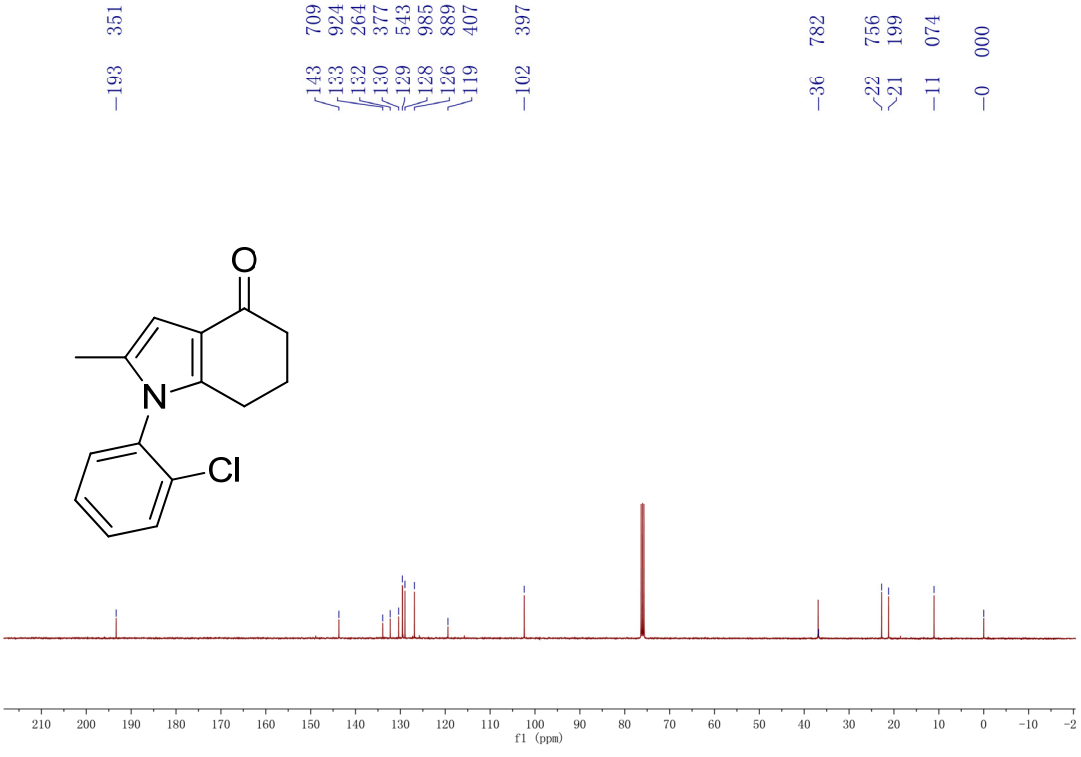




^{1}H and ^{13}C-NMR spectra data

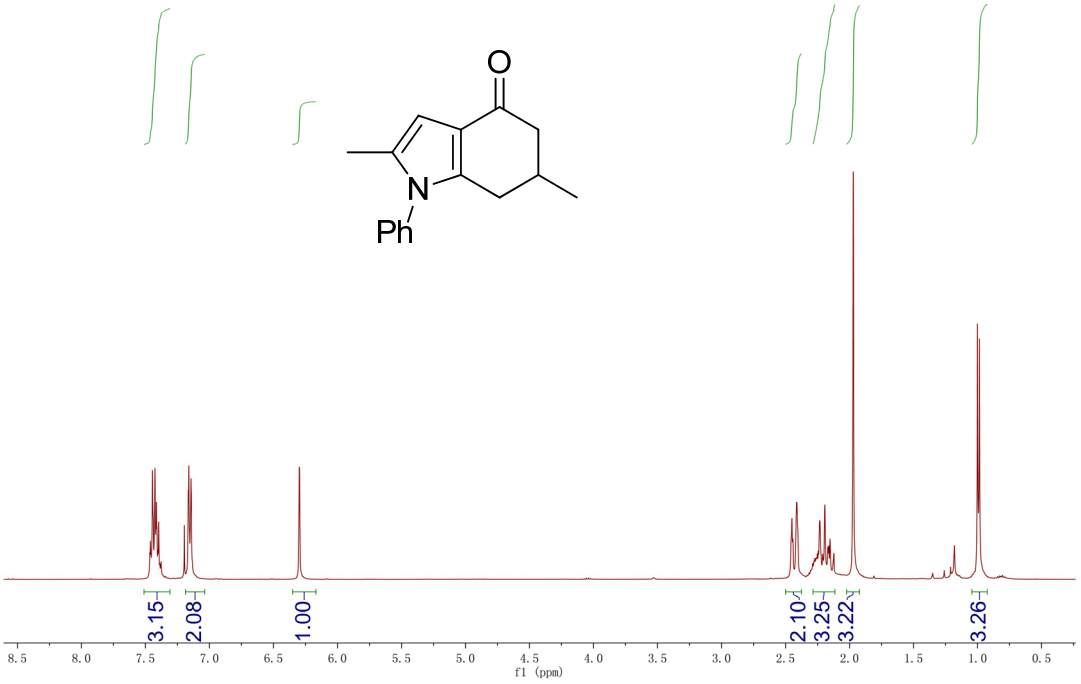
1-(2-Chlorophenyl)-2-methyl-6,7-dihydro-1H-indol-4(5H)-one 6f

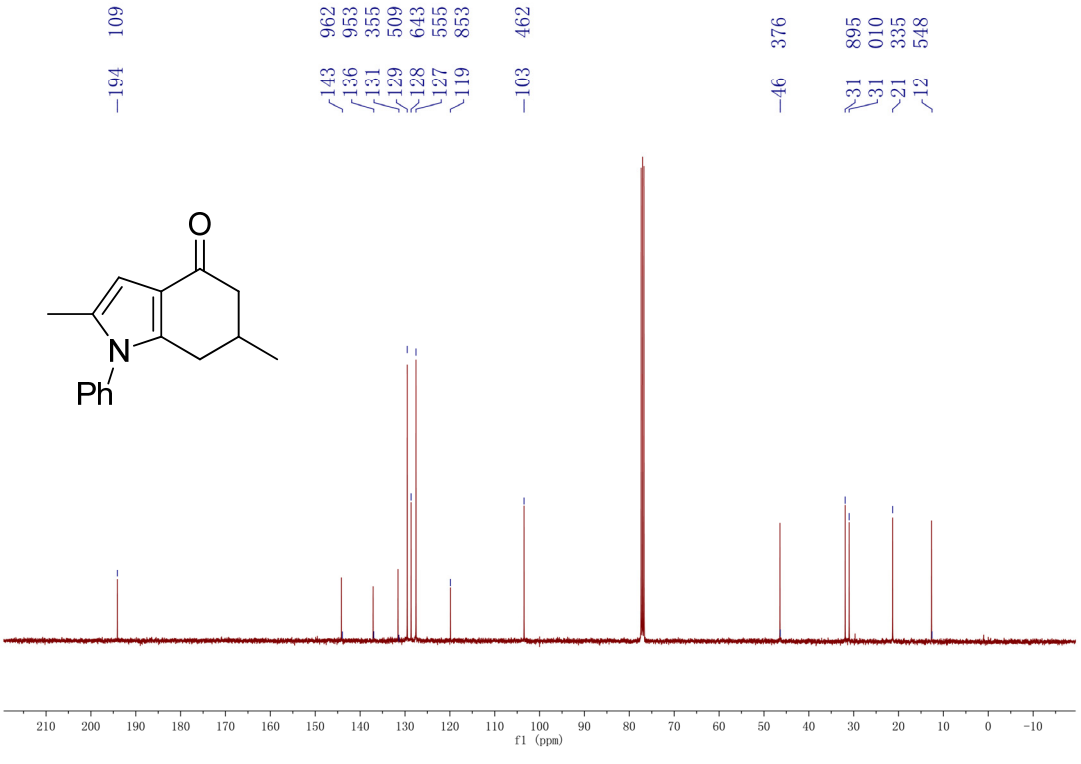




^{1}H and ^{13}C-NMR spectra data

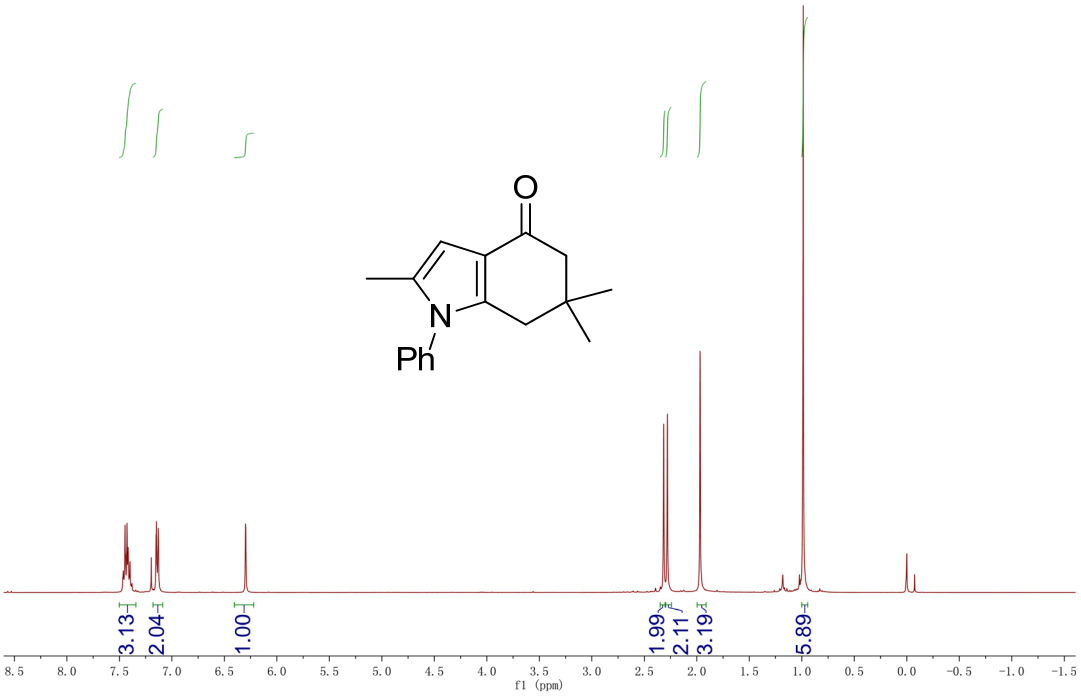
2,6-Dimethyl-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one 6g

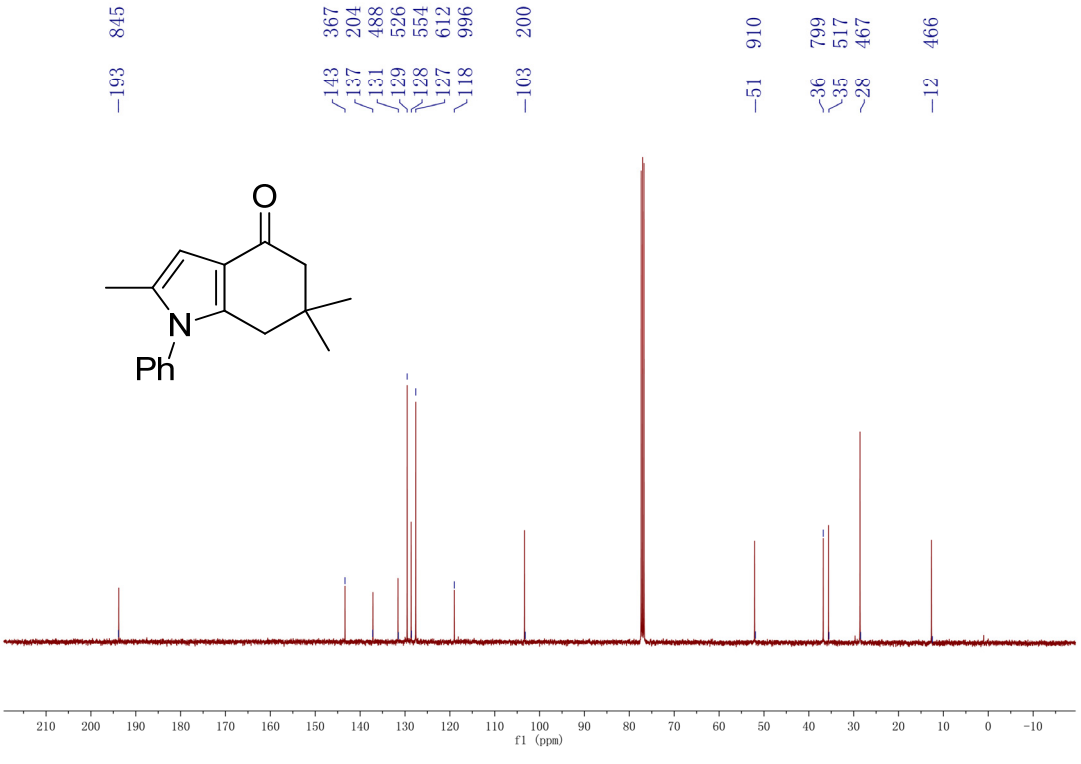




^{1}H and ^{13}C-NMR spectra data

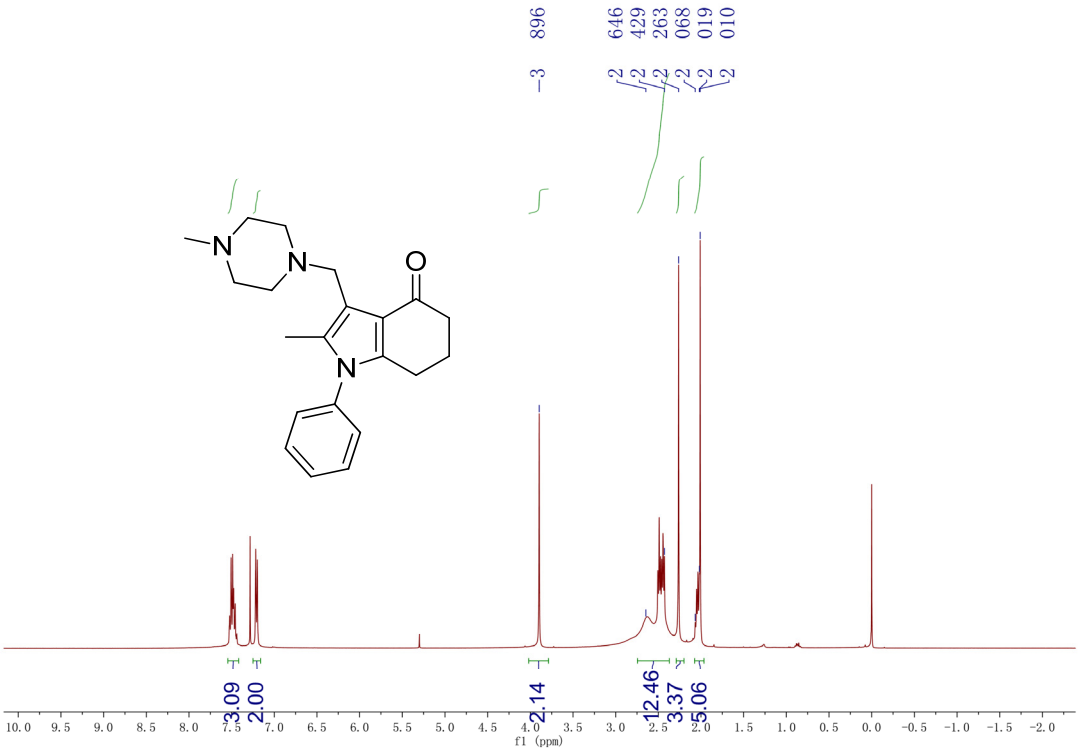
2,6,6-Trimethyl-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one 6h

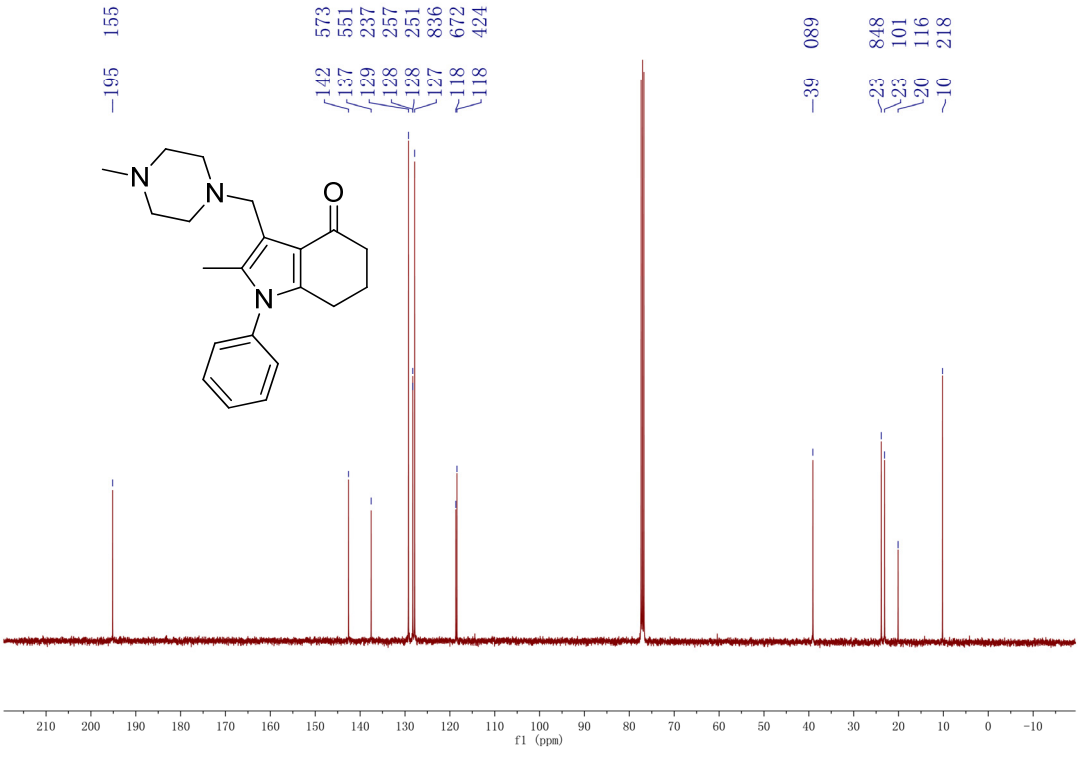




^{1}H and ^{13}C-NMR spectra data

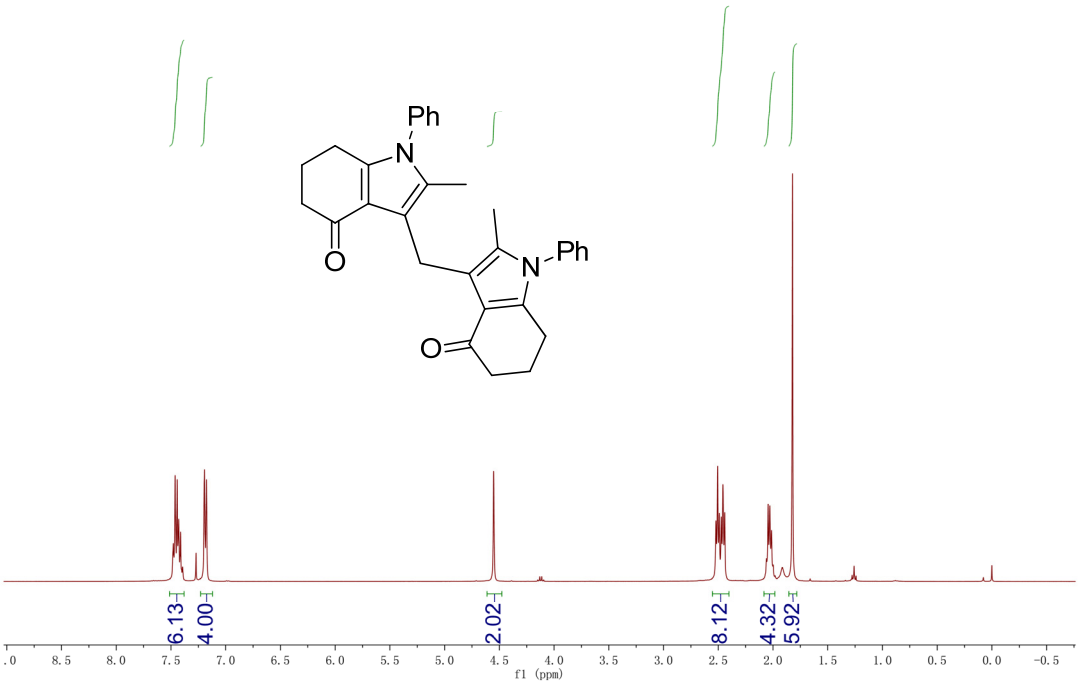
2-Methyl-3-((4-methylpiperazin-1-yl)methyl)-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one 8a

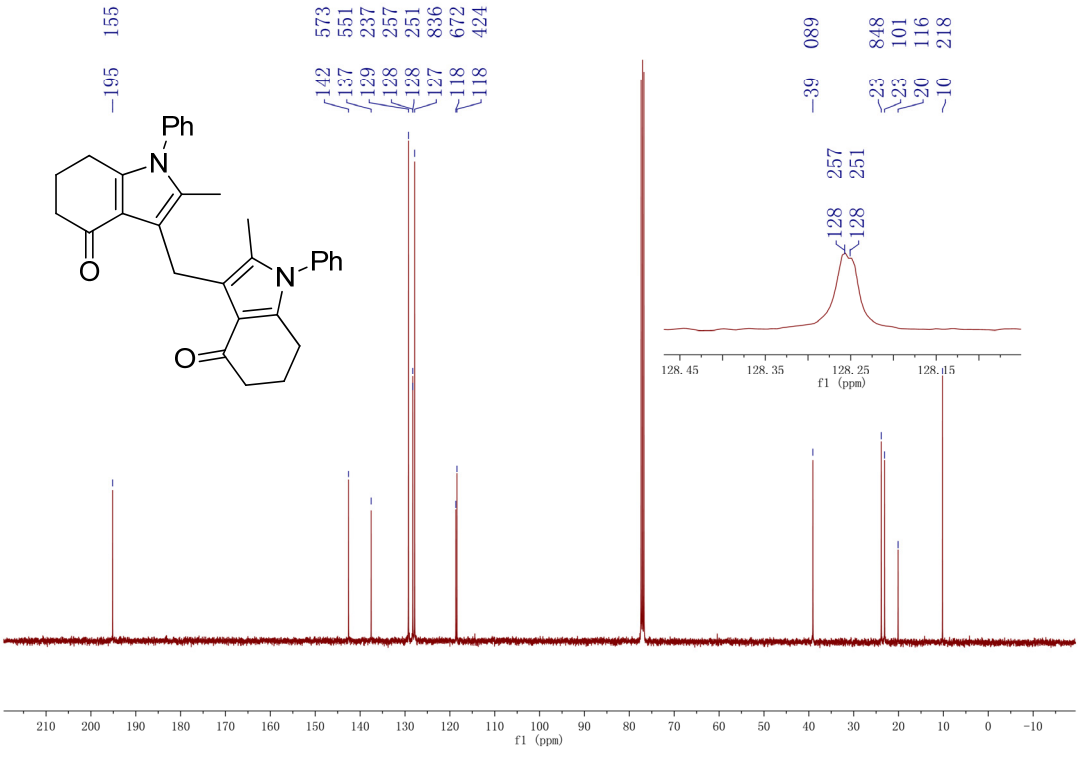




^{1}H and ^{13}C-NMR spectra data

3,3'-Methylenebis(2-methyl-1-phenyl-6,7-dihydro-1H-indol-4(5H)-one) 9a

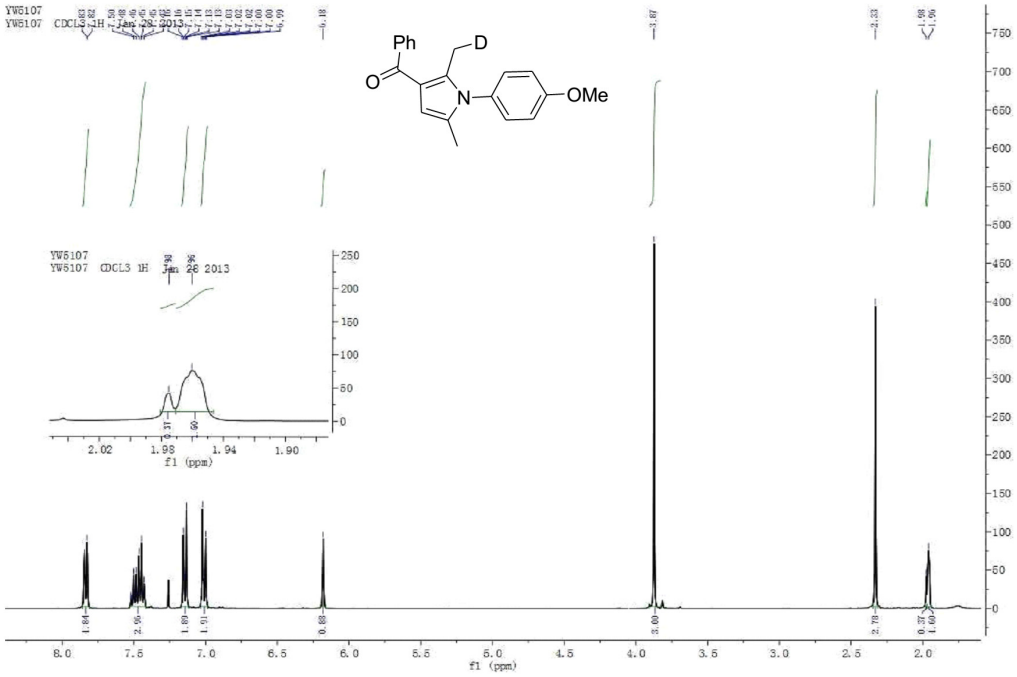




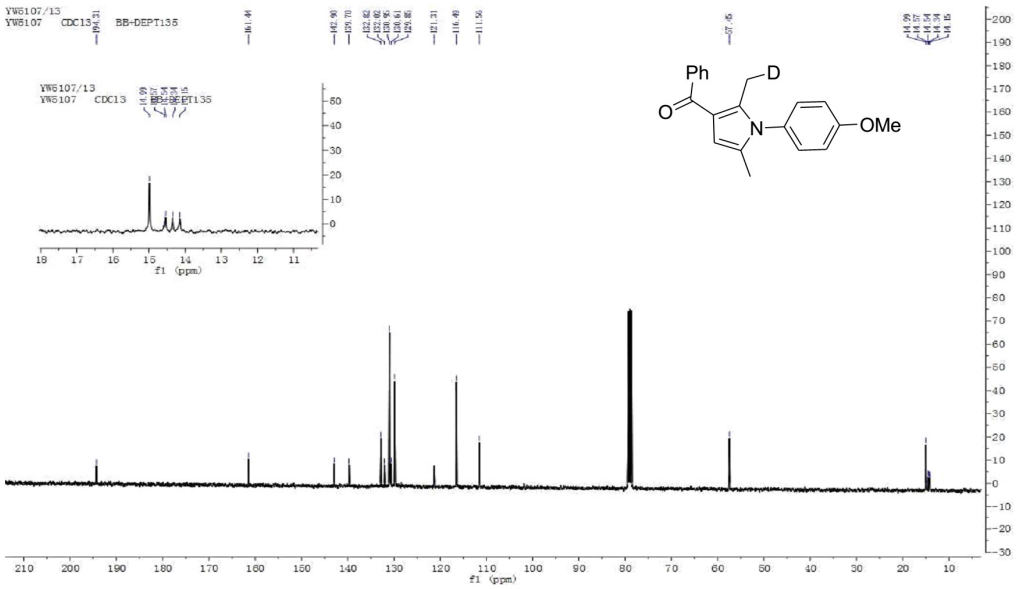
^{1}H and ^{13}C-NMR spectra data

Deuterated-1-(1-(4-methoxyphenyl)-2,5-dimethyl-1H-pyrrol-3-yl)ethanone 4p

^{1}H NMR



^{13}C NMR



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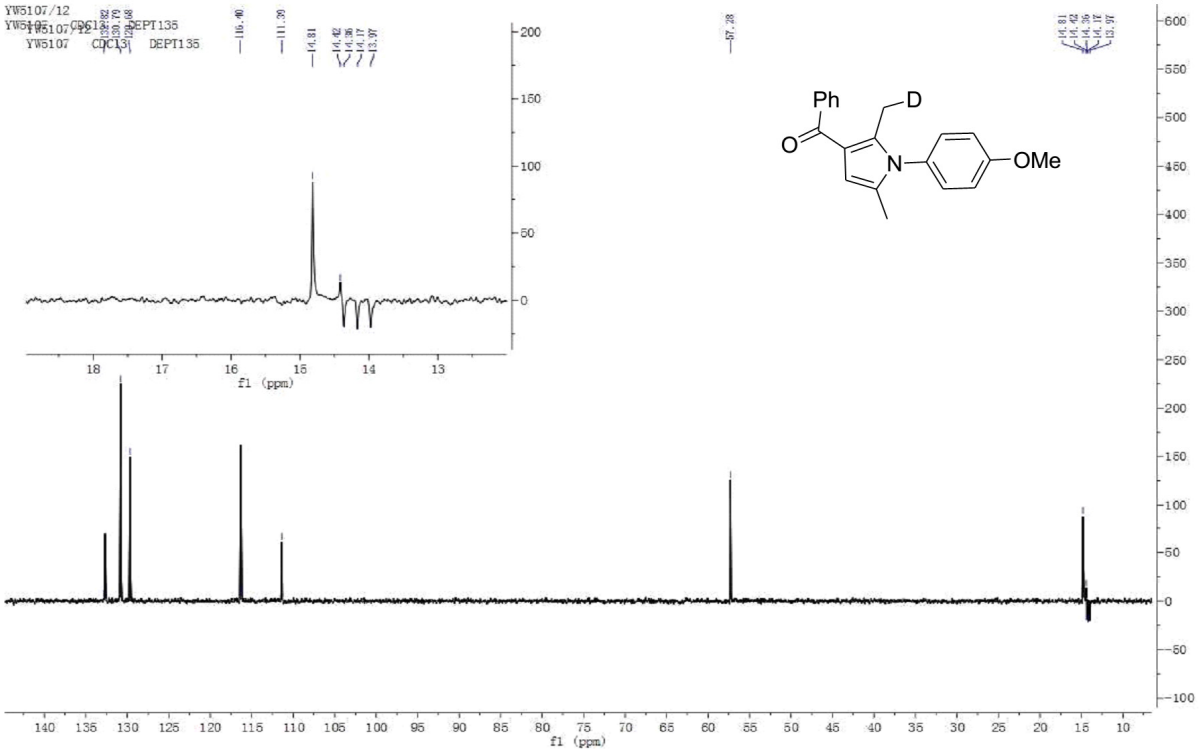

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1. Wu, Y.; Arenas, I.; Broomfield, L.M.; Martin, E.; Shafir, A. Hypervalent Activation as a Key Step for Dehydrogenative *ortho* C–C Coupling of Iodoarenes. *Chem. Eur. J.* **2015**, *21*, 18779–18784.
2. Zhao, Y.S.; Tang, X.Q.; Tao, J.C.; Tian, P.; Lin, G.Q. Efficient access to *cis*-decalinol frameworks: copper(I)-catalyzed borylative cyclization of allene cyclohexanediones. *Org. Biomol. Chem.* **2016**, *14*, 4400–4404.
3. Yang, W.; Huang, L.; Liu, H.; Wang, W.; Li, H. Efficient synthesis of highly substituted pyrroles through a Pd(OCOCF$_3$)$_2$-catalyzed cascade reaction of 2-alkenal-1,3-dicarbonyl compounds with primary amines. *Chem. Commun.* **2013**, *49*, 4667—4669.