Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Copper/Amine-Catalyzed Formal Regioselective [3+2] Cycloaddition of α,β-unsaturated *O*-acetyl Oxime with Enals

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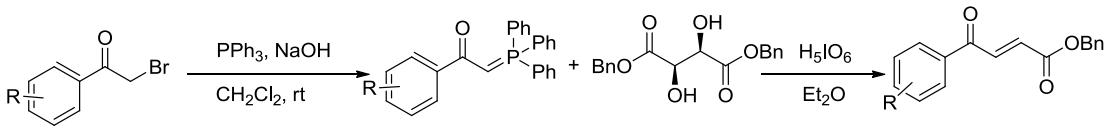
Part I. Experimental section

1.1. General information

All reactions were carried out in flame-dried sealed tubes with magnetic stirring. Unless otherwise noted, all experiments were performed under argon atmosphere. All reagents were purchased from TCI, Acros or Strem. Solvents were treated with 4 Å molecular sieves or sodium and distilled prior to use. Purifications of reaction products were carried out by flash chromatography using Qingdao Haiyang Chemical Co. Ltd silica gel (40-63 mm). Infrared spectra (IR) were recorded on a Brucker TENSOR 27 FTIR spectrophotometer and are reported as wavelength numbers (cm^{-1}). Infrared spectra were recorded by preparing a KBr pellet containing the title compound. ^{1}H NMR and ^{13}C NMR spectra were recorded with tetramethylsilane (TMS) as internal standard at ambient temperature unless otherwise indicated on a Bruker Avance DPX 600 fourier Transform spectrometer operating at 600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR. Chemical shifts are reported in parts per million (ppm) and coupling constants are reported as Hertz (Hz). Splitting patterns are designated as singlet (s), broad singlet (bs), doublet (d), triplet (t). Splitting patterns that could not be interpreted or easily visualized are designated as multiple (m). High resolution mass spectra (HRMS) were recorded on an IF-TOF spectrometer (Micromass).

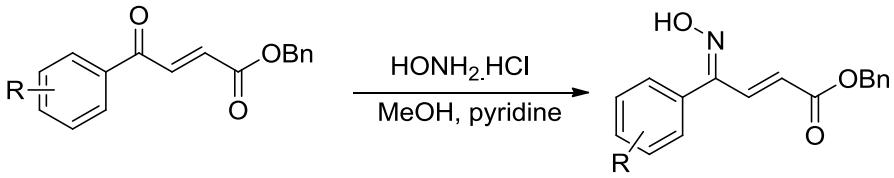
1.2. General procedure for the synthesis of oxime-enoate



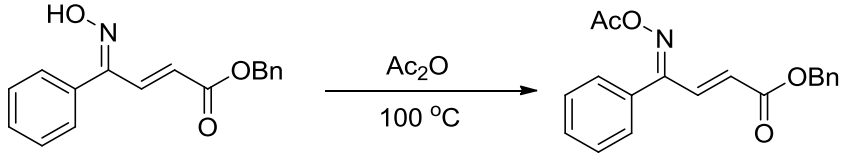
To a solution of 2-bromo-1-phenylethanone (1 equiv) in CH_2Cl_2 (0.5 M) at rt was added triphenylphosphine (1 equiv) and the solution was allowed to stir for 4 h. before being concentrated in vacuo. The residue was dissolved in CH_2Cl_2:H_2O (40:60) and 2 M NaOH (2 equiv) was added. The reaction mixture was stirred at rt for 1 h before being extracted with CH_2Cl_2. The combine organic fraction were washed with brine, dried, filtered and concentrated in vacuo to give the crude reaction mixture. The mixture was not purified

To a solution of dibenzyl L-tartrate (1 equiv) in Et_2O (0.45 M) at rt was added periodic acid (1 equiv) and the solution was allowed to stir for 1 h. The reaction was filtrated and the solids washed with THF. The organic fraction was dried and filtered. The above reside was added and

the reaction mixture was stirred at rt for 2 h before being concentrated in vacuo to give the crude reaction mixture. Products purified by column chromatography.[1]

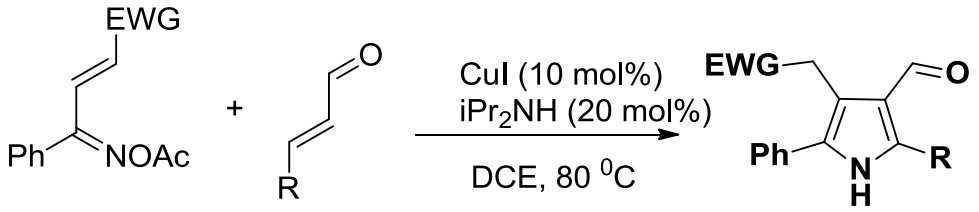


2.66 g (10 mmol) of benzyl 4-oxo-4-phenylbut-2-enoate, 0.69 g (10 mmol) of powdered hydroxylamine hydrochloride and 0.79 g (10 mmol) of pyridine dissolved in 50 mL of methanol was stirred at rt for overnight. The mixture was concentrated and resulting oil was purified by column chromatography on silical gel using 30% ethy acetate in petroleum ether as eluent to affording product.[2]



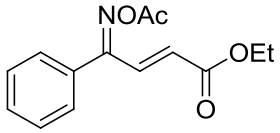
The mixture of benzyl 4-(hydroxyimino)-4-phenylbut-2-enoate (1 equiv), anhydride (2 equiv) was stirred at 100 ℃ for 3 h. Upon completion of the reaction as indicated by TLC, The reaction mixture was diluted with EA, washed with H_2O. Neutralization with $NaHCO_3$ and dried over anhydrous Na_2SO_4 and evaporated in vacuo. The crude residue was purified by column chromatography on silical gel using 20% ethy acetate in petroleum ether as eluent to affording product.[3]

1.3. General procedure for synthesis of polysubstituted pyrrole derivatives (3a – 3r)



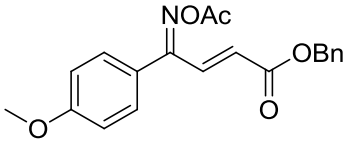
A 15 mL of reaction tube was charged with CuI (2.0 mg, 10 mol %), i-Pr_2NH (20 mmol%) oxime-enoate (0.10 mmol), cinnamaldehyde (0.15 mmol) and DCE (2.0 mL) under argon atmosphere at 80℃ for 24 h. The corresponding reaction mixture was cooled to room temperature concentrated under reduced pressure. The residue was purified by flash chromatography on silical gel using 25% (v/v) ethyl acetate in petroleum ether as eluent to afford the desired product **.**

1.4. Characterization Data of products



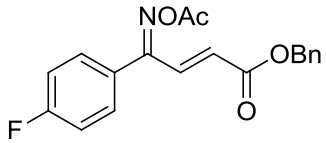
1a

Ethyl 4-(acetoxyimino)-4-phenylbut-2-enoate: oil in 78 % yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 16.2 Hz, 1H), 7.54 – 7.52 (m, 2H), 7.48 (dd, *J* = 6.3, 0.9 Hz, 3H), 6.19 – 6.13 (d, *J*= 16.2 Hz, 1H), 4.27 (q, *J*= 7.1 Hz, 2H), 2.29 (s, 3H), 1.34 – 1.30 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.11, 165.55, 160.98, 139.96, 131.91, 131.45, 130.72, 130.65, 129.85, 129.34, 128.69, 128.54, 127.91, 61.41, 61.10, 19.69, 14.15, 14.12. HR-MS (ESI) calcd for $[M + H]^+$: $C_{14}H_{16}NO_4$ 261.1074.1438, found: 261.1070; IR (KBr): 1771, 1614, 1183, 1053, 838 cm^{-1}.



1b

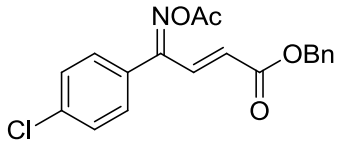
(2E)-Benzyl 4-(acetoxyimino)-4-(4-methoxyphenyl)but-2-enoate: oil in 81 % yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 16.2 Hz, 1H), 7.49 (d, *J* = 8.7 Hz, 2H), 7.38 (d, *J* = 3.7 Hz, 4H), 7.21 – 7.19 (m, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.22 (d, *J* = 16.2 Hz, 1H), 5.25 (s, 2H), 3.83 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.11, 165.39, 161.76, 160.44, 140.82, 135.27, 133.08, 130.82, 129.86, 128.67, 128.64, 128.47, 124.32, 121.74, 114.14, 67.13, 55.41, 19.70. HR-MS (ESI) calcd for $[M + H]^+$: $C_{20}H_{20}NO_5$ 354.1336, found: 354.1335; IR (KBr): 2839, 1776, 1609, 1176, 836 cm^{-1}.



1c

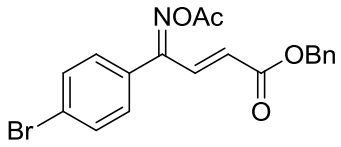
(2E)-Benzyl 4-(acetoxyimino)-4-(4-fluorophenyl)but-2-enoate: oil in 64 % yield.. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, *J* = 16.2 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.38 (d, *J* = 4.1 Hz, 5H), 7.12 (t, *J* = 8.5 Hz, 2H), 6.18 (d, *J* = 16.2 Hz, 1H), 5.25 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) 167.84, 165.22, 159.90, 140.29, 135.16, 132.40, 131.42, 131.37, 130.98, 130.28, 130.18,

130.13, 128.69, 128.66, 128.64, 128.53, 128.46, 116.02, 115.87, 67.26, 19.62. HR-MS (ESI) calcd for $[M + H]^+$: $C_{19}H_{17}FNO_4$ 342.1136, found: 342.1134; IR (KBr): 1778, 1729, 1500, 1231, 1053, 918 cm^{-1}.



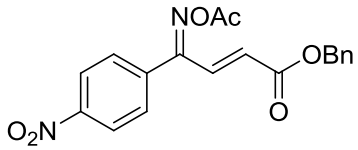
1d

(2E)-Benzyl 4-(acetoxyimino)-4-(4-chlorophenyl)but-2-enoate: oil in 68 % yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 16.3 Hz, 1H), 7.40 (dd, *J* = 11.5, 8.5 Hz, 3H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 4.1 Hz, 4H), 6.10 (d, *J* = 16.3 Hz, 1H), 5.18 (s, 2H), 2.22 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.78, 165.19, 159.85, 140.05, 137.17, 135.15, 132.18, 131.03, 130.63, 129.39, 129.08, 129.01, 128.71, 128.68, 128.67, 128.55, 128.48, 67.30, 19.66. HR-MS (ESI) calcd for $[M + H]^+$: $C_{19}H_{17}ClNO_4$ 358.0841, found: 358.0840; IR (KBr): 1776, 1720, 1506, 1181, 914 cm^{-1}.



1e

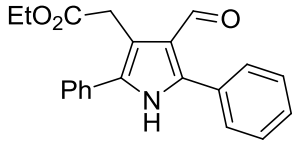
(2E)-Benzyl 4-(acetoxyimino)-4-(4-bromophenyl)but-2-enoate: oil in 75 % yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 16.3 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.38 (t, *J* = 4.2 Hz, 3H), 6.18 (d, *J*= 16.3 Hz, 1H), 5.25 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.80, 167.77, 165.17, 161.88, 159.92, 139.97, 135.15, 132.04, 131.96, 131.05, 130.82, 130.41, 129.57, 128.71, 128.68, 128.66, 128.54, 128.48, 125.49, 124.41, 67.30, 19.64. HR-MS (ESI) calcd for $[M]^+$: $C_{19}H_{17}BrNO_4$ 402.0335, found: 402.0334; IR (KBr): 1775, 1720, 1549, 1105, 914cm^{-1}.



1f

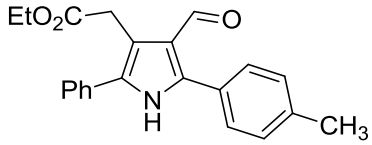
(2E)-Benzyl 4-(acetoxyimino)-4-(4-nitrophenyl)but-2-enoate: oil in 60 % yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 5.3, 3.5 Hz, 2H), 8.01 (d, *J* = 16.3 Hz, 1H), 7.75 – 7.72 (m, 2H), 7.39 – 7.37 (m, 5H), 6.15 (d, *J* = 16.3 Hz, 1H), 5.26 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.38, 164.89, 160.87, 158.94, 149.18, 139.19, 138.24, 131.38, 131.36, 130.71, 130.42,

129.09, 128.72, 128.68, 128.63, 128.58, 128.50, 123.96, 123.90, 67.45, 19.55. HR-MS (ESI) calcd for $[M + H]^+$: $C_{19}H_{17}N_2O_6$ 369.1081, found: 369.1080; IR (KBr): 1780, 1716, 1517, 1186, 855 cm^{-1}.



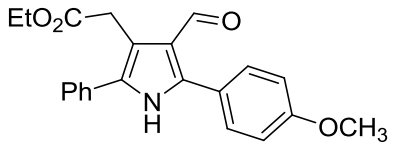
3a

Ethyl 2-(4-formyl-2,5-diphenyl-1H-pyrrol-3-yl)acetate : Yellow oil; 28.3 mg, 85 % yield; ^1H NMR (600 MHz, $CDCl_3$) δ 9.82 – 9.79 (m, 1H), 9.14 (s, H), 7.49 – 7.41 (m, 9H), 7.35 (dt, *J* = 10.6, 4.2 Hz, 1H), 4.23 – 4.18 (m, 2H), 3.89 (s, 2H), 1.31 – 1.29 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.50, 172.49, 142.49, 132.44, 131.06, 130.09, 129.05, 128.93, 127.92, 127.81, 121.26, 114.18, 60.77, 31.53, 14.28. HR-MS (ESI) calcd for $[M + H]^+$: $C_{21}H_{20}NO_3$ 334.1438, found: 334.1435; IR (KBr): 3134, 1732, 1637, 1330, 1178, 767, 696 cm^{-1}.



3b

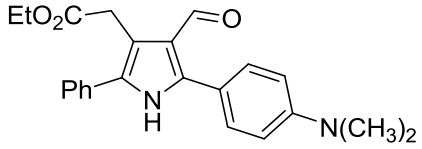
Ethyl 2-(4-formyl-2-phenyl-5-(p-tolyl)-1H-pyrrol-3-yl)acetate: Yellow solid; 31.2 mg, 90 % yield; m.p. 163.4-164.6 ℃; ^1H NMR (600 MHz, $CDCl_3$) δ 9.76 (d, *J* = 4.2 Hz, 1H), 9.18 (s, 1H), 7.42 – 7.28 (m, 7H), 7.22 (d, *J* = 7.6 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 2H), 2.38 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.54, 172.49, 142.81, 139.06, 132.22, 131.17, 129.59, 128.93, 128.89, 127.81, 127.24, 121.07, 114.06, 60.72, 31.52, 21.28, 14.25. HR-MS (ESI) calcd for $[M + H]^+$: $C_{22}H_{22}NO_3$ 348.1594, found: 348.1593; IR (KBr): 2919, 1730, 1635, 1448, 1173, 785 cm^{-1}.



3c

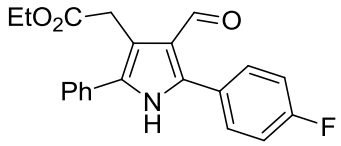
Ethyl 2-(4-formyl-5-(4-methoxyphenyl)-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 34.5 mg, 95 % yield; m.p. 158.1-159.2 ℃; ^1H NMR (600 MHz, $CDCl_3$) δ 9.75 (s, 1H), 9.20 (s, 1H), 7.44 – 7.37 (m, 6H), 7.35 – 7.31 (m, 1H), 6.97 – 6.95 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.87 (s,

2H), 3.85 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.47, 172.54, 160.26, 142.78, 132.05, 131.17, 130.36, 128.89, 127.77, 122.53, 120.88, 114.35, 113.92, 60.75, 55.39, 31.53, 14.27. HR-MS (ESI) calcd for $[M + H]^+$: $C_{22}H_{22}NO_3$ 364.1543, found: 364.1591; IR (KBr): 2924, 1735, 1626, 1372, 1182, 702 cm^{-1}.



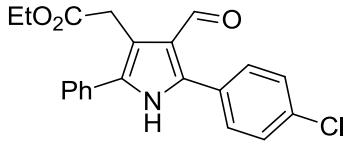
3d

Ethyl 2-(5-(4-(dimethylamino)phenyl)-4-formyl-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 35.3 mg, 94 % yield; m.p. 61.5-66.4 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.88 (s, 1H), 7.45 – 7.38 (m, 6H), 7.34 (dd, *J* = 9.2, 4.4 Hz, 1H), 6.83 (s, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 2H), 3.00 (s, 6H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.51, 172.54, 131.64, 131.39, 129.95, 128.93, 127.77, 120.61, 113.96, 112.56, 60.69, 40.53, 31.59, 14.28. HR-MS (ESI) calcd for $[M + H]^+$: $C_{23}H_{25}N_2O_3$ 377.1860, found: 377.1858; IR (KBr): 2807, 1729, 1610, 1374, 1029, 820 cm^{-1}.



3e

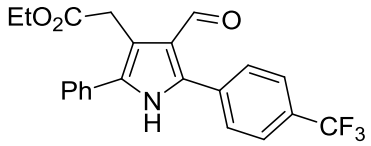
Ethyl 2-(5-(4-fluorophenyl)-4-formyl-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 26.3 mg, 75 % yield; m.p.154.3-155.9 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (s, 1H), 9.26 (s, 1H), 7.47 – 7.39 (m, 6H), 7.35 (td, *J* = 8.5, 4.3 Hz, 1H), 7.17 – 7.12 (m, 2H), 4.21 – 4.17 (m, 2H), 3.86 (s, 2H), 1.29 (t, *J* = 9.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.15, 172.49, 163.17 (d, J = 249.9 Hz), 141.38, 132.49, 130.91, 130.85, 128.94, 127.97, 127.78, 126.22 (d, *J* = 3.3 Hz), 121.25, 116.11, 115.97, 114.13, 60.83, 31.45, 14.26. HR-MS (ESI) calcd for $[M + H]^+$: $C_{21}H_{19}FNO_3$ 352.1343, found: 352.1341; IR (KBr): 3135, 1733, 1637, 1467, 1185, 775 cm^{-1}.



3f

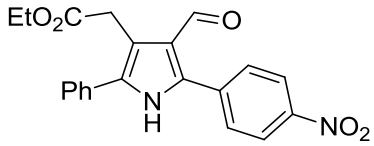
Ethyl 2-(5-(4-chlorophenyl)-4-formyl-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 29.4 mg, 80 % yield; m.p. 148.9-149.8 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.70 (s, 1H), 9.42 (s, 1H),

7.47-7.29 (s, 9H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.09, 172.48, 140.96, 135.18, 132.80, 130.87, 130.21, 129.16, 128.96, 128.52, 128.04, 127.84, 121.42, 114.37, 60.85, 31.46, 14.26. HR-MS (ESI) calcd for $[M + H]^+$: $C_{21}H_{19}ClNO_3$ 368.1048, found: 368.1045; IR (KBr): 3069, 1732, 1636, 1468, 1177, 824 cm^{-1}.



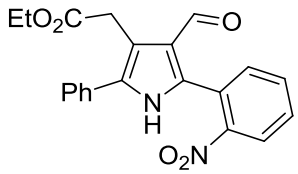
3g

Ethyl 2-(4-formyl-2-phenyl-5-(4-(trifluoromethyl)phenyl)-1H-pyrrol-3-yl)acetate: Yellow solid; 28.0mg, 70 % yield; m.p. 163.6-164.9 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.95 (s, 1H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.43 (m, 4H), 7.41-7.34 (m, 1H), 4.20 (q, *J* = 7.0 Hz, 2H), 3.87 (s, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.81, 172.23, 133.61, 133.25, 130.73, 129.20, 129.11, 128.36, 127.92, 125.99 (q, J = 3.6 Hz), 122.04, 114.90, 60.88, 31.41, 26.92, 14.27. HR-MS (ESI) calcd for $[M + H]^+$: $C_{22}H_{19}F_3NO_3$ 401.1312, found: 401.1310; IR (KBr): 3337, 1737, 1631, 1329, 1067, 828, 773 cm^{-1}.



3h

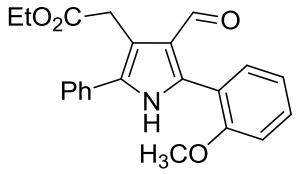
Ethyl 2-(4-formyl-5-(4-nitrophenyl)-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 25.7 mg, 68 % yield; m.p. 83.6-84.9 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.76 (s, 1H), 9.64 (s, 1H), 8.23 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.44-7.28 (m, 5H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.71, 172.44, 147.49, 138.63, 136.25, 134.23, 130.45, 129.47, 129.00, 128.37, 127.94, 124.09, 122.40, 115.28, 61.03, 31.44, 14.24. HR-MS (ESI) calcd for $[M + H]^+$: $C_{21}H_{19}N_2O_5$ 379.1288, found: 379.1285; IR (KBr): 2246, 1723, 1633, 1345, 854 cm^{-1}.



3i

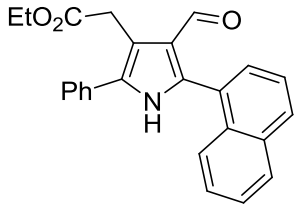
Ethyl 2-(4-formyl-5-(2-nitrophenyl)-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 24.5 mg,

65 % yield; m.p. 145.2-146.2 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.75 (s, 1H), 9.20 (s, 1H), 7.44 – 7.37 (m, 6H), 7.33 (ddd, *J* = 15.7, 6.3, 4.4 Hz, 1H), 6.97 – 6.95 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 2H), 3.85 (s, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.47, 172.54, 160.26, 142.78, 132.05, 131.17, 130.36, 128.89, 127.77, 122.53, 120.88, 114.35, 113.92, 60.75, 55.39, 31.53, 14.27 HR-MS (ESI) calcd for $[M + H]^+$: $C_{21}H_{19}N_2O_5$ 379.1288, found: 379.1285; IR (KBr): 1729, 1108, 1105, 850 cm^{-1}.



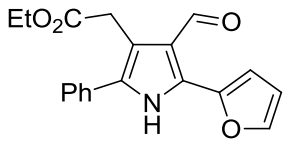
3j

Ethyl 2-(4-formyl-5-(2-methoxyphenyl)-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 31.2 mg, 86 % yield; m.p. 55.3-56.9 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.78 (s, 1H), 9.10 (s, 1H), 7.39 – 7.34 (m, 5H), 7.34 – 7.25 (m, 2H), 6.99 – 6.93 (m, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 2H), 3.80 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.63, 172.38, 156.65, 138.38, 132.54, 131.81, 131.43, 130.33, 128.98, 127.87, 127.82, 121.95, 121.05, 118.40, 113.70, 111.40, 60.67, 55.81, 31.54, 14.30. HR-MS (ESI) calcd for $[M + H]^+$: $C_{22}H_{22}NO_4$ 364.1543, found: 364.1541; IR (KBr): 3274, 1640, 1469, 1245, 1095, 756 cm^{-1}.



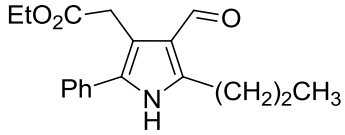
3k

Ethyl 2-(4-formyl-5-(naphthalen-1-yl)-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 33.3 mg, 87 % yield; m.p. 72.4-73.5 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 1H), 9.31 (s, 1H), 7.83 (d, *J* = 11.1 Hz, 3H), 7.76 (s, 1H), 7.52 (dd, *J* = 15.1, 6.2 Hz, 3H), 7.41 (d, *J* = 7.0 Hz, 2H), 7.37 (d, *J* = 7.1 Hz, 2H), 7.31 (d, *J* = 6.5 Hz, 1H), 4.21 – 4.15 (m, 2H), 3.88 (s, 2H), 1.27 (d, *J* = 4.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.64, 172.60, 142.43, 133.14, 133.12, 132.73, 131.08, 128.94, 128.70, 128.57, 128.27, 127.92, 127.83, 127.79, 127.38, 126.93, 126.16, 121.56, 114.33, 60.82, 31.58, 14.29. HR-MS (ESI) calcd for $[M + H]^+$: $C_{25}H_{22}NO_3$ 384.1594, found: 384.1593; IR (KBr): 2923, 1728, 1465, 1336, 1175, 820 cm^{-1}.



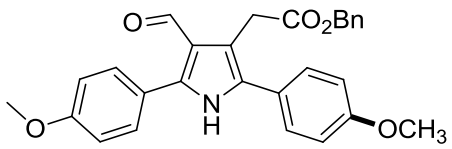
3l

Ethyl 2-(4-formyl-5-(furan-2-yl)-2-phenyl-1H-pyrrol-3-yl)acetate: Yellow solid; 29.0 mg, 72 % yield; m.p. 62.2-62.3 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.20 (s, 1H), 9.20 (s, 1H), 7.51 (d, *J* = 1.4 Hz, 1H), 7.42 (d, *J* = 4.3 Hz, 4H), 7.38 – 7.35 (m, 1H), 6.94 (d, *J* = 3.4 Hz, 1H), 6.54 (dt, *J* = 6.3, 3.2 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 2H), 1.32 (t, *J* = 5.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.14, 172.24, 145.27, 142.77, 132.26, 130.80, 130.44, 128.97, 128.31, 128.02, 127.75, 120.51, 114.67, 112.18, 109.80, 60.93, 31.35, 14.27. HR-MS (ESI) calcd for $[M + H]^+$: $C_{19}H_{18}NO_4$ 323.1231, found: 323.1229; IR (KBr): 2923, 1735, 1626, 1372, 1182, 804 cm^{-1}.



3m

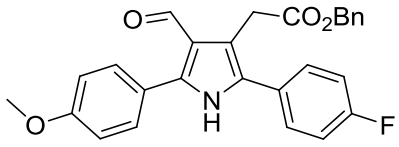
Ethyl 2-(4-formyl-2-phenyl-5-propyl-1H-pyrrol-3-yl)acetate: Yellow oil; 17.0 mg, 51 % yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.86 (d, 2H), 7.54 – 7.46 (m, 3H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 2H), 2.91 (t, *J* = 7.7 Hz, 2H), 1.76 (dd, *J* = 15.0, 7.5 Hz, 2H), 1.03 (t, *J* = 7.4 Hz, 3H). 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 185.50, 179.50, 169.20, 136.56, 131.39, 131.06, 128.93, 128.88, 127.66, 127.59, 125.97, 120.86, 113.29, 60.74, 43.06, 40.44, 33.12, 31.18, 23.50, 14.26, 11.56. HR-MS (ESI) calcd for $[M + H]^+$: $C_{18}H_{22}NO_3$ 300.1594, found: 300.1602; IR (KBr): 2931, 1780, 1656, 1175, 697 cm^{-1}.



3n

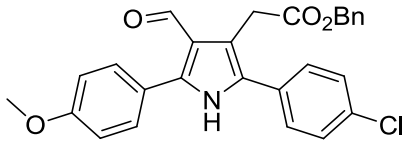
Benzyl 2-(4-formyl-2,5-bis(4-methoxyphenyl)-1H-pyrrol-3-yl)acetate: Yellow solid; 41.4 mg, 91 % yield; m.p. 61.3-62.2 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.75 (d, *J* = 3.3 Hz, 1H), 9.02 (s, 1H), 7.39 – 7.32 (m, 6H), 7.31 – 7.26 (m, 3H), 6.92 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.16 (s, 2H), 3.89 (s, 2H), 3.81 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.41, 171.48, 159.21, 158.29, 141.36, 135.26, 131.00, 129.29, 128.10, 127.42, 127.10, 126.96, 126.89,

122.53, 121.58, 119.80, 113.32, 111.97, 65.43, 54.35, 54.26, 30.46. HR-MS (ESI) calcd for [M + H]$^+$: $C_{28}H_{26}NO_5$ 356.1805, found: 358.1806; IR (KBr): 3272, 1732, 1508, 1250, 1029, 833 cm^{-1}.



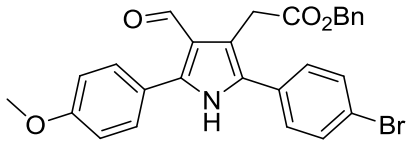
3o

Benzyl 2-(2-(4-fluorophenyl)-4-formyl-5-(4-methoxyphenyl)-1H-pyrrol-3-yl)acetate: Yellow solid; 31.9 mg, 72 % yield; m.p. 154.2-155.4 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (s, 1H), 9.16 (s, 1H), 7.34 (dd, *J* = 20.9, 14.2 Hz, 9H), 7.02 (d, *J* = 7.6 Hz, 2H), 6.93 (d, *J* = 7.1 Hz, 2H), 5.17 (s, 2H), 3.88 (s, 2H), 3.82 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.47, 172.42, 162.38 (d, *J* = 248.0 Hz), 160.37, 142.80, 136.18, 131.19, 130.34, 129.60 (d, J = 8.2 Hz), 128.50, 128.17, 128.10, 127.94, 127.22, 122.38, 120.81, 116.01, 115.86, 114.41, 113.73, 66.58, 55.40, 31.43. HR-MS (ESI) calcd for [M + H]$^+$: $C_{27}H_{23}FNO_4$ 444.1606, found: 444.1605; IR (KBr): 3210, 1734, 1625, 1506, 1252, 837 cm^{-1}.



3p

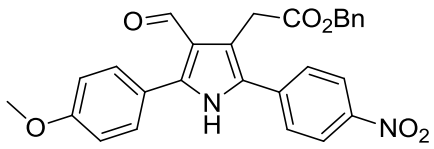
Benzyl 2-(2-(4-chlorophenyl)-4-formyl-5-(4-methoxyphenyl)-1H-pyrrol-3-yl)acetate: Yellow solid; 36.3 mg, 79 % yield; m.p. 144.2-143.3 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.68 (s, 1H), 9.32 (s, 1H), 7.36 (d, *J* = 9.6 Hz, 4H), 7.31 (d, *J* = 7.6 Hz, 3H), 7.24 (d, *J* = 9.3 Hz, 4H), 6.92 (d, *J* = 7.3 Hz, 2H), 5.18 (s, 2H), 3.88 (s, 2H), 3.82 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.40, 171.42, 159.36, 141.99, 135.10, 132.67, 129.89, 129.31, 128.47, 128.03, 127.81, 127.48, 127.11, 121.23, 119.83, 113.35, 113.04, 65.59, 54.37, 30.42. HR-MS (ESI) calcd for [M + H]$^+$: $C_{27}H_{23}ClNO_4$ 460.1310, found: 460.1307; IR (KBr): 2927, 1741, 1604, 1231, 1053, 853 cm^{-1}.



3q

Benzyl 2-(2-(4-bromophenyl)-4-formyl-5-(4-methoxyphenyl)-1H-pyrrol-3-yl)acetate: Yellow solid; 39.3 mg, 78 % yield; m.p. 145.2-146.3 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (s, 1H), 9.03 (s, 1H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.41 – 7.31 (m, 7H), 7.18 (d, *J* = 8.3 Hz, 2H), 6.94 (d, *J* = 8.6 Hz,

2H), 5.19 (s, 2H), 3.90 (s, 2H), 3.84 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.33, 171.37, 159.39, 141.92, 135.09, 131.04, 129.83, 129.28, 128.89, 128.03, 127.49, 127.12, 127.10, 121.19, 120.89, 119.89, 113.41, 113.14, 65.61, 54.40, 30.40. HR-MS (ESI) calcd for $[M]^+$: $C_{27}H_{22}BrNO_4$ 504.0805, found: 504.0801; IR (KBr): 3220, 1533, 1306, 1096, 1007, 969 cm^{-1}.

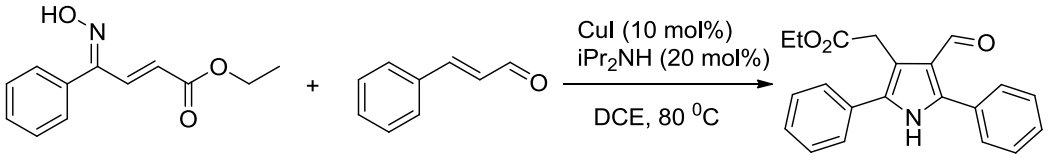


3r

Benzyl 2-(4-formyl-5-(4-methoxyphenyl)-2-(4-nitrophenyl)-1H-pyrrol-3-yl)acetate: Yellow solid; 33.0 mg, 70 % yield; m.p. 139.2-140.3 ℃; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.74 (s, 1H), 9.28 (s, 1H), 8.08 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.34 (dd, *J* = 6.6, 4.7 Hz, 3H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.28 – 7.25 (m, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.15 (s, 2H), 3.92 (s, 2H), 3.78 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 186.28, 170.92, 159.66, 145.62, 143.01, 136.42, 134.94, 129.43, 128.68, 127.62, 127.54, 127.42, 127.23, 127.17, 126.72, 123.22, 120.79, 120.30, 115.47, 113.50, 65.81, 54.43, 30.48. HR-MS (ESI) calcd for $[M + H]^+$: $C_{27}H_{23}N_6O_6$ 471.1551, found: 471.1543; IR (KBr): 2925, 1726, 1597, 1338, 1250, 838 cm^{-1}.

Preliminary mechanistic studies

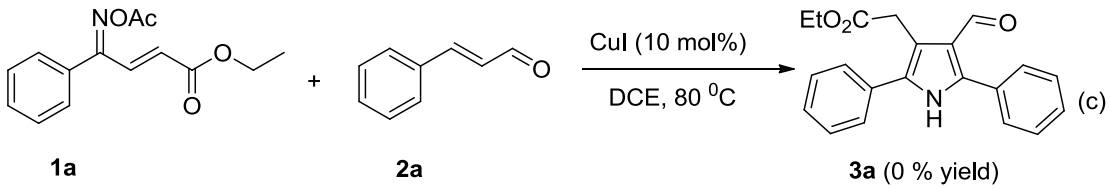
The effect of substrate of on the [3+2] cycloaddition reaction



1 **2a** **3a** (0 % yield)

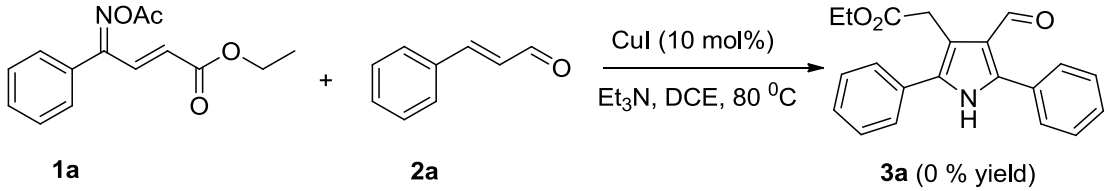
A mixture of ethyl 4-(hydroxyimino)-4-phenylbut-2-enoate **1** (22.0 mg, 0.1 mmol, 1.0 equiv), CuI (2.0 mg, 0.01 mmol, 0.1 equiv) and cinnamaldehyde (20 mg, 0.15 mmol, 1.5 equiv), and iPr_2NH (20 mol%) in DCE (2 mL) in a 25 mL reaction tube was stirred at 80 ℃ for 24 hours. The desired **3a** was not observed under these conditions.

The effect of amine on the [3+2] cycloaddition reaction of α,β-unsaturated *O*-acetyl oxime (1a) and cinnamaldehyde (2a)



1a **2a** **3a** (0 % yield)

To the solution of α,β-unsaturated *O*-acetyl oxime **1a** (0.1 mmol) in DCE (2 mL) were added CuI (10%), cinnamaldehyde (0.15 mmol) under Ar atmosphere, and then the corresponding reaction mixture was stirred in a sealed tube at 80 ℃ for 24 h. The desired **3a** was not observed under these conditions.



1a **2a** **3a** (0 % yield)

To the solution of α,β-unsaturated *O*-acetyl oxime **1a** (0.1 mmol) in DCE (2 mL) were added CuI (10%), cinnamaldehyde (0.15 mmol) and Et_3N (20 mol%) under Ar atmosphere, and then the corresponding reaction mixture was stirred in a sealed tube at 80 ℃ for 24 h. The desired **3a** was not observed under these conditions.

References

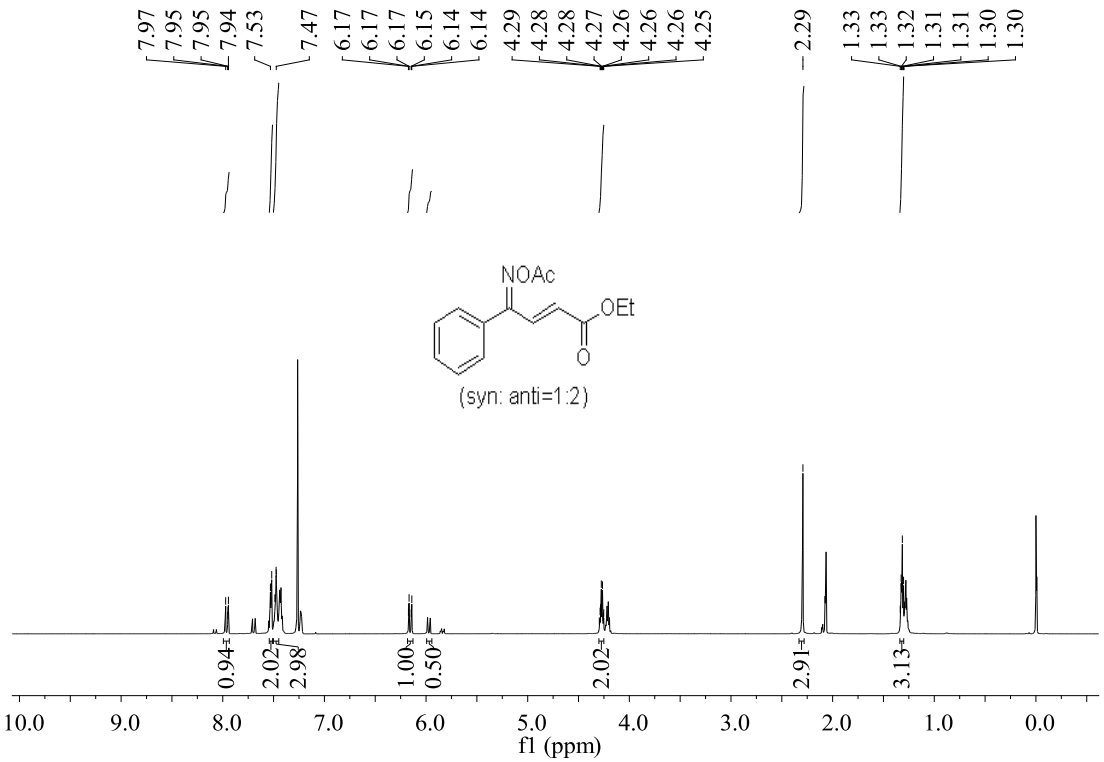
(1) Stark, D. G.; Morrill, L. C.; Yeh, P. P.; Slawin, A. M. Z.; O'Riordan, T. J. C.; Smith, A. D. *Angew. Chem. Int. Ed.* **2013**, *52*, 11642.

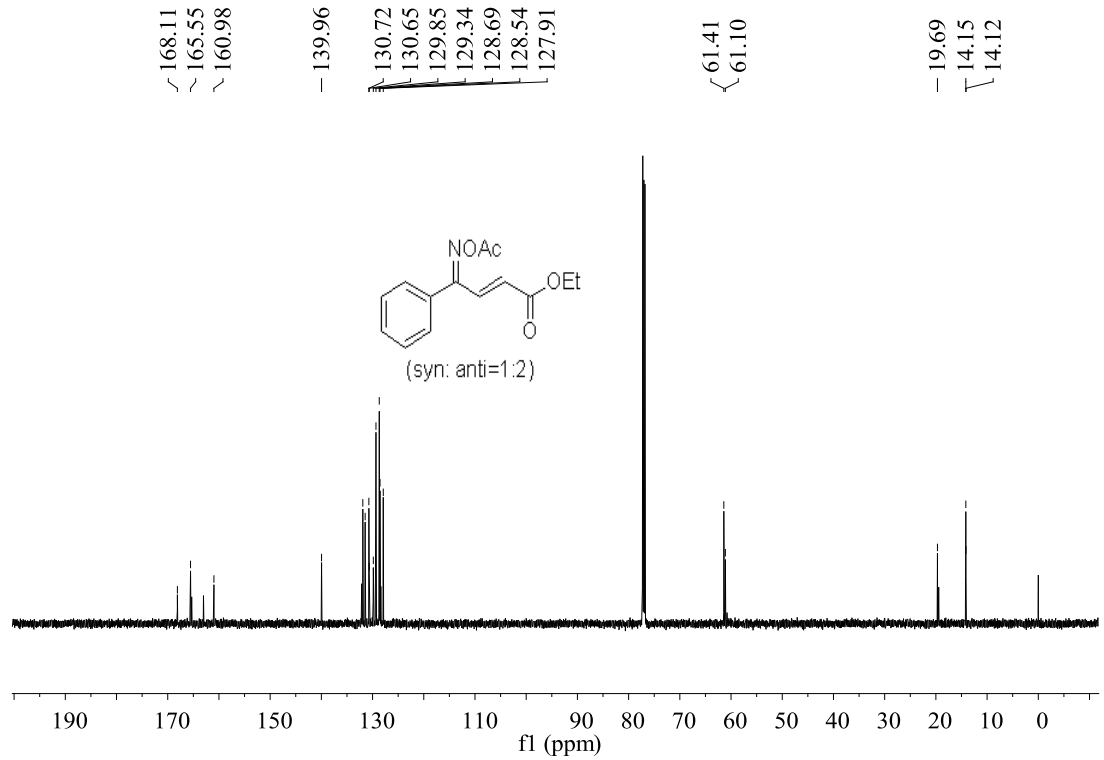
(2) Senadi, G. C.; Mutra, M. R.; Lu, T.-Y.; Wang, J. J. *Green. Chem.* **2017**, *19*, 4272.

(3) Zhu, Z. Z.; Tang, X. D.; Li, J. X.; Li, X.; Wu, W. Q.; Deng, G. J.; Jiang, H. F. *Org. Lett.* **2017**, *19*, 1370.

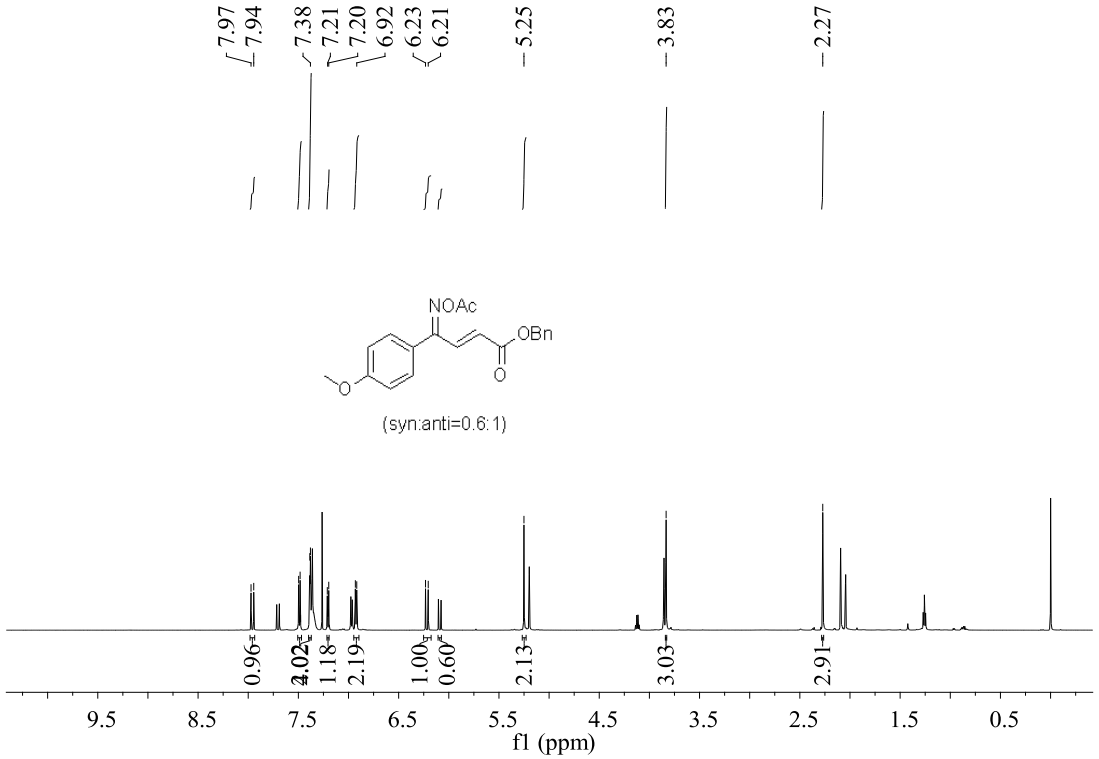
Part II. ^{1}H NMR and ^{13}C NMR spectrum for products

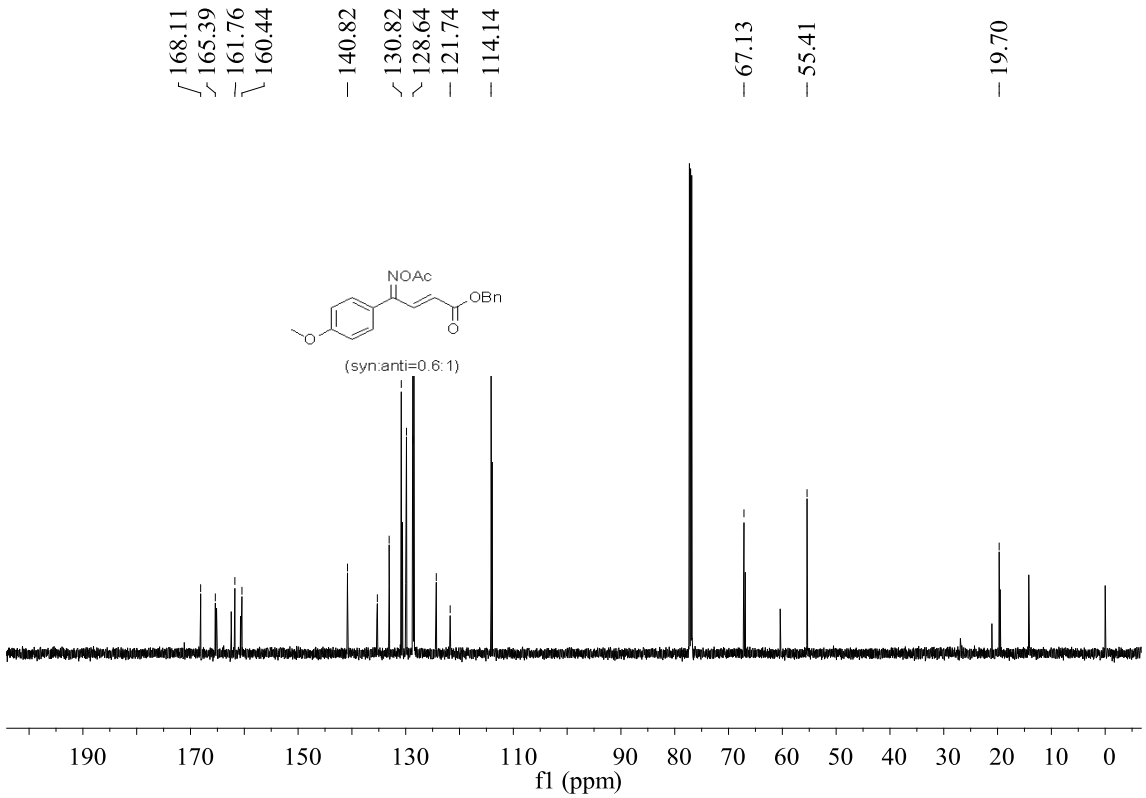
(2E)-ethyl 4-(acetoxyimino)-4-phenylbut-2-enoate (**1a**) (Using $CDCl_3$ as solvent)



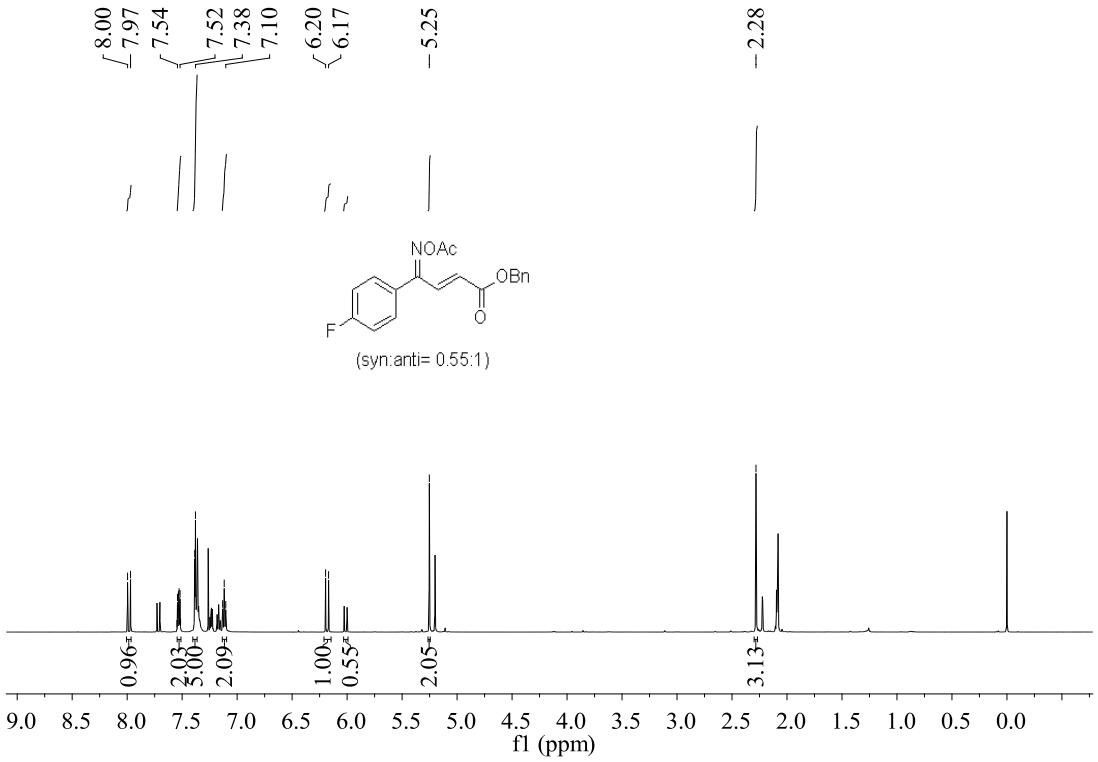


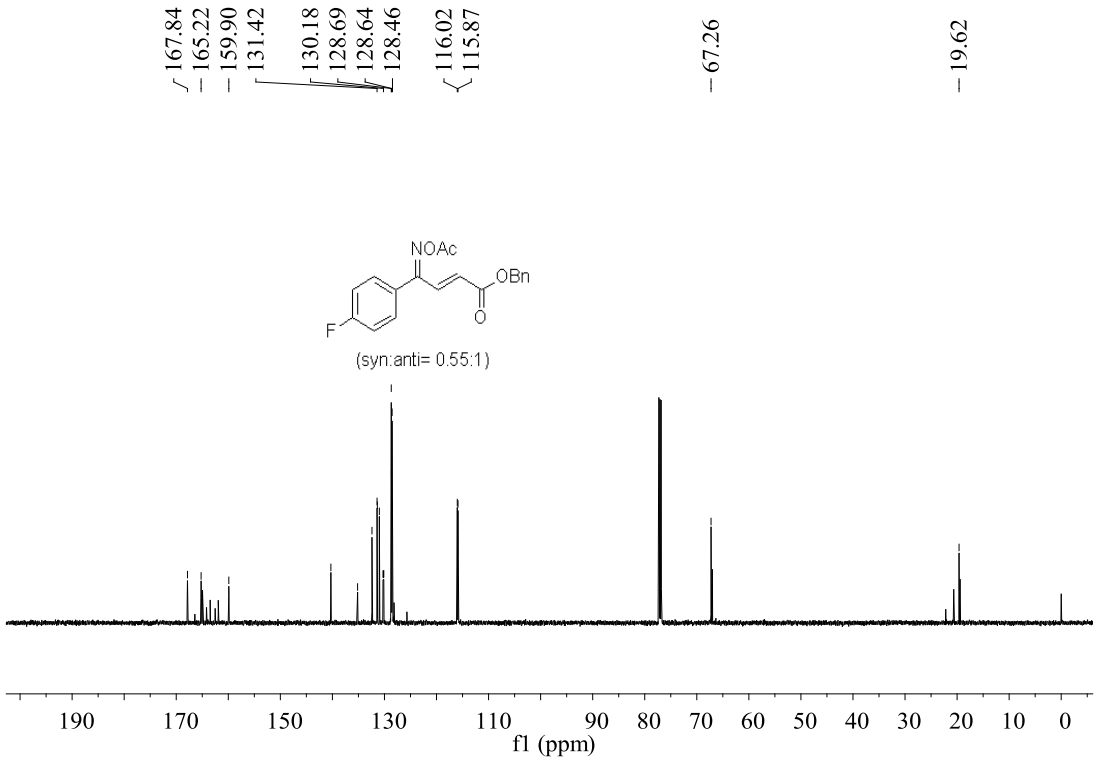
(2E)-benzyl 4-(acetoxyimino)-4-(4-methoxyphenyl)but-2-enoate (**1b**) (Using $CDCl_3$ as solvent)



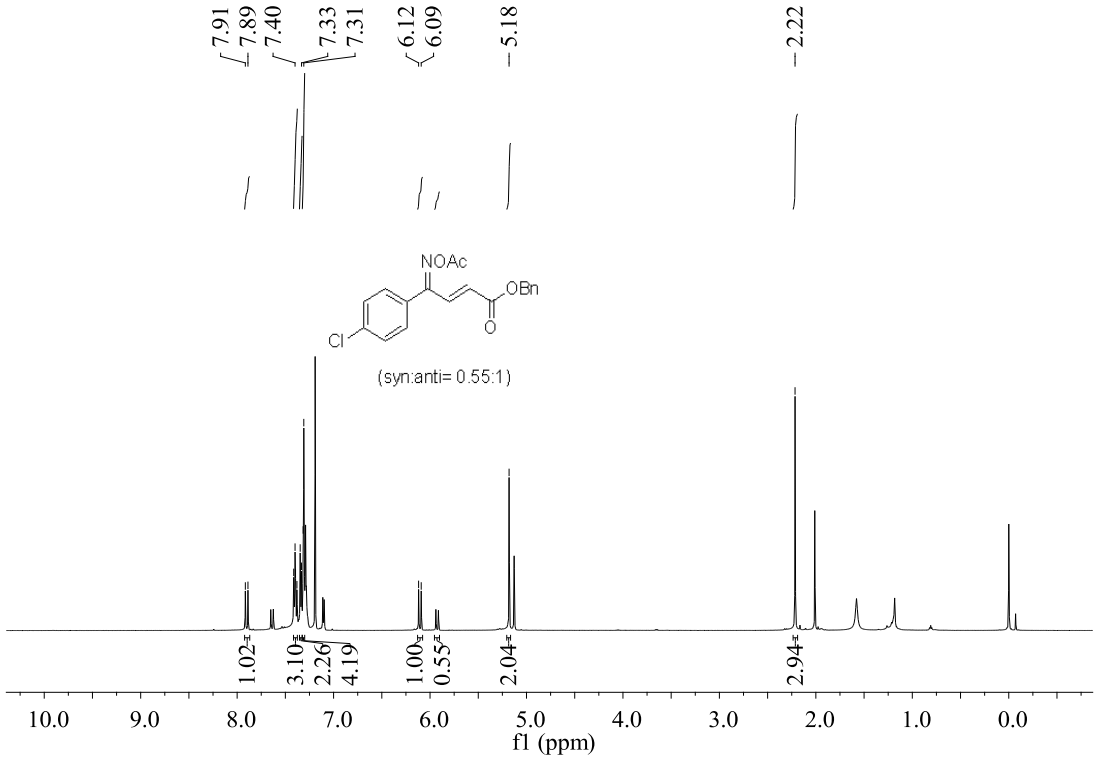


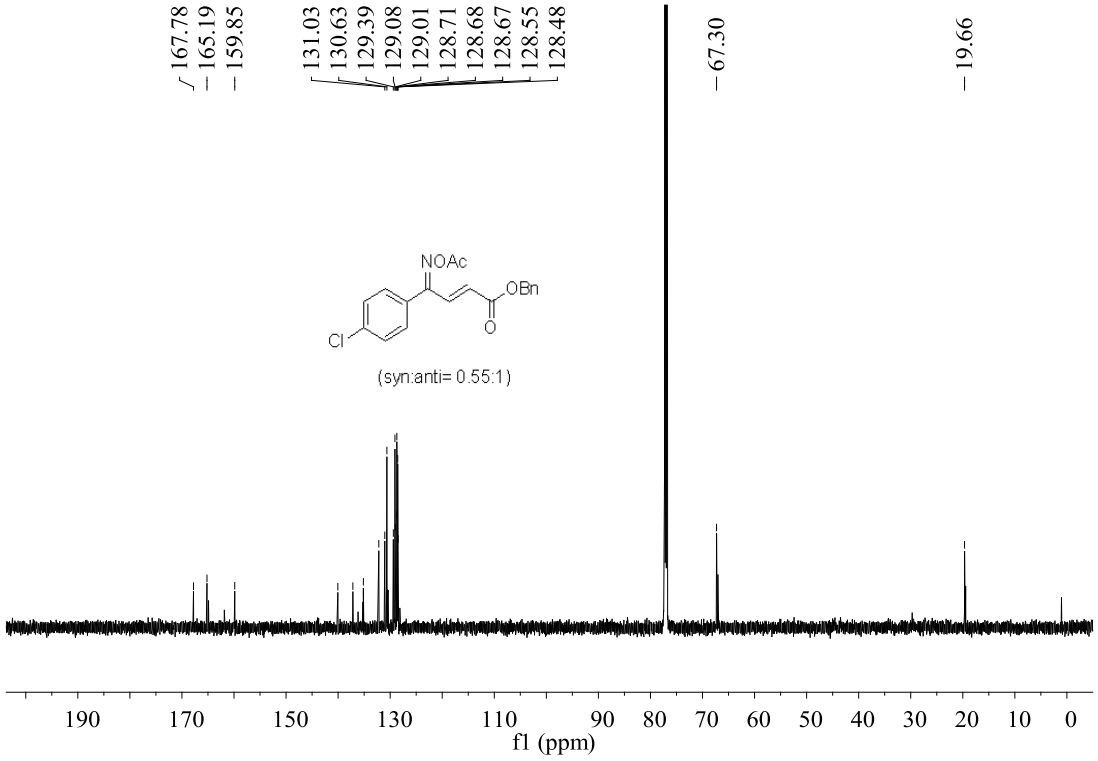
(2E)-benzyl 4-(acetoxyimino)-4-(4-fluorophenyl)but-2-enoate (**1c**) (Using $CDCl_3$ as solvent)



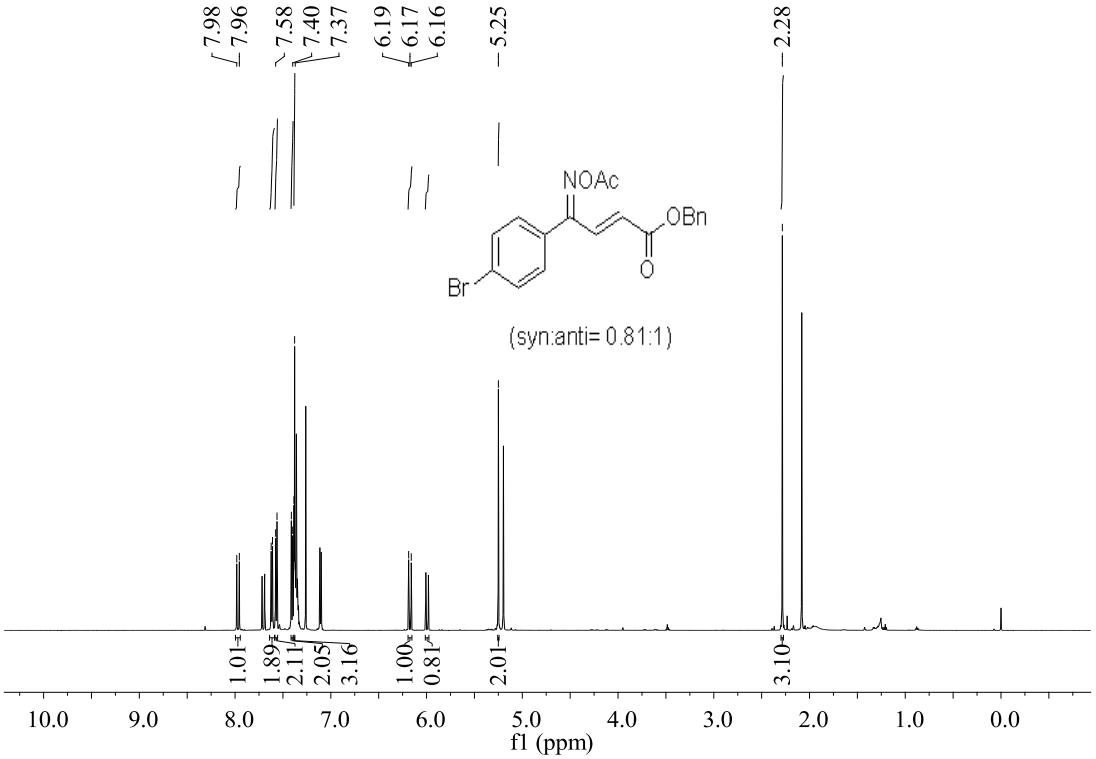


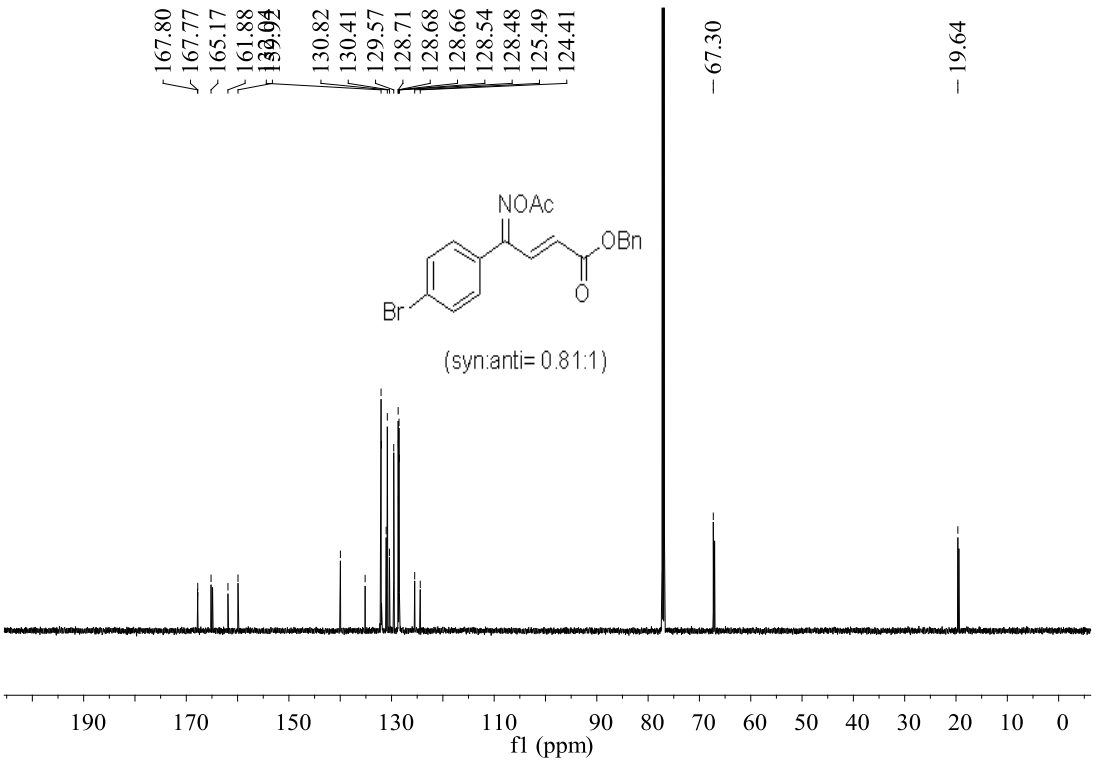
(2E)-benzyl 4-(acetoxyimino)-4-(4-chlorophenyl)but-2-enoate (**1d**) (Using $CDCl_3$ as solvent)



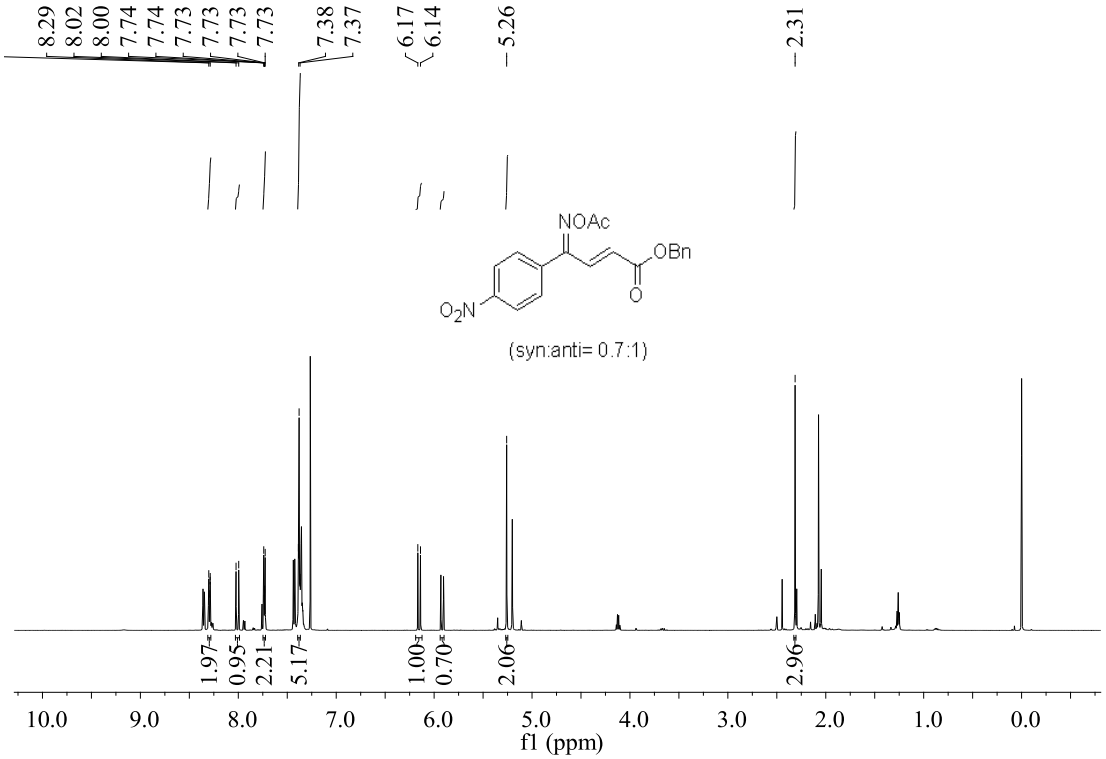


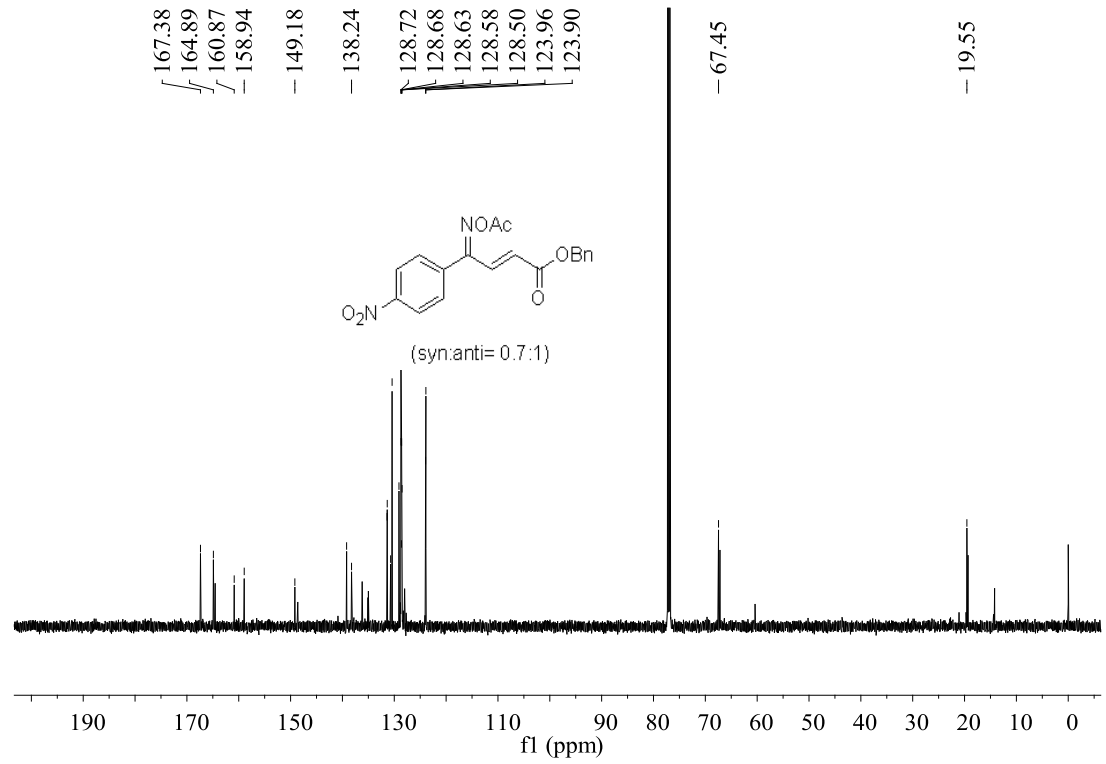
(2E)-benzyl 4-(acetoxyimino)-4-(4-bromophenyl)but-2-enoate (**1e**) (Using $CDCl_3$ as solvent)



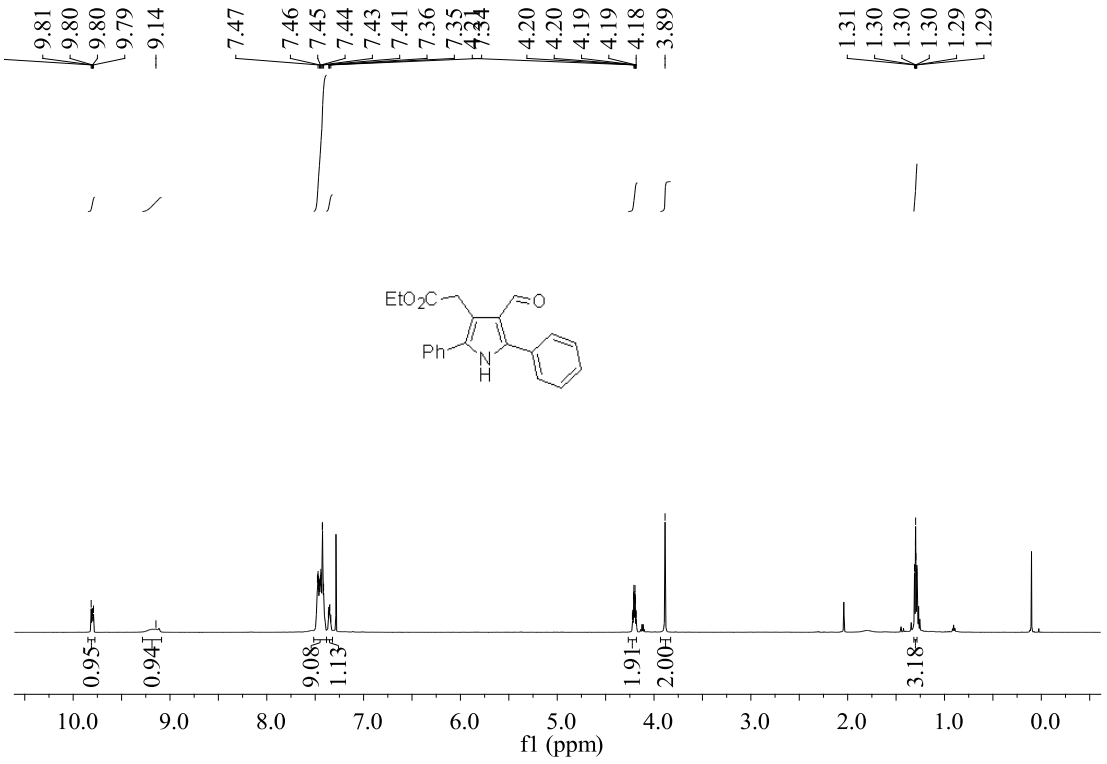


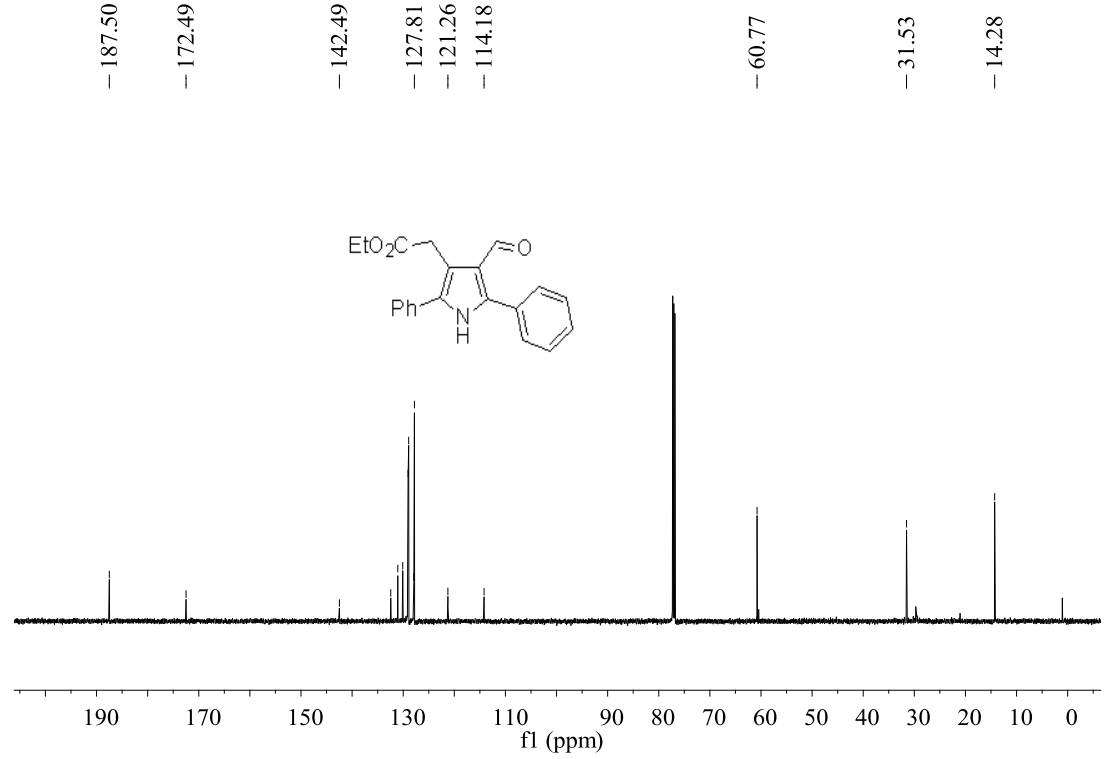
(2E)-benzyl 4-(acetoxyimino)-4-(4-nitrophenyl)but-2-enoate (**1f**) (Using $CDCl_3$ as solvent)



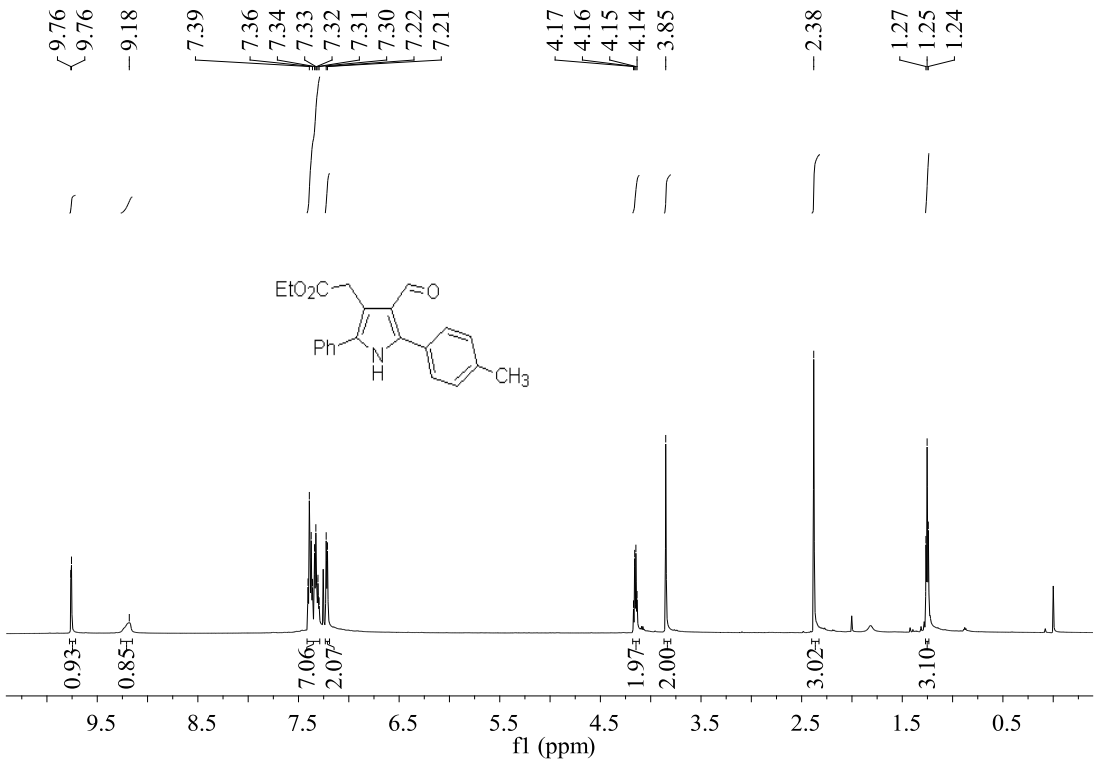


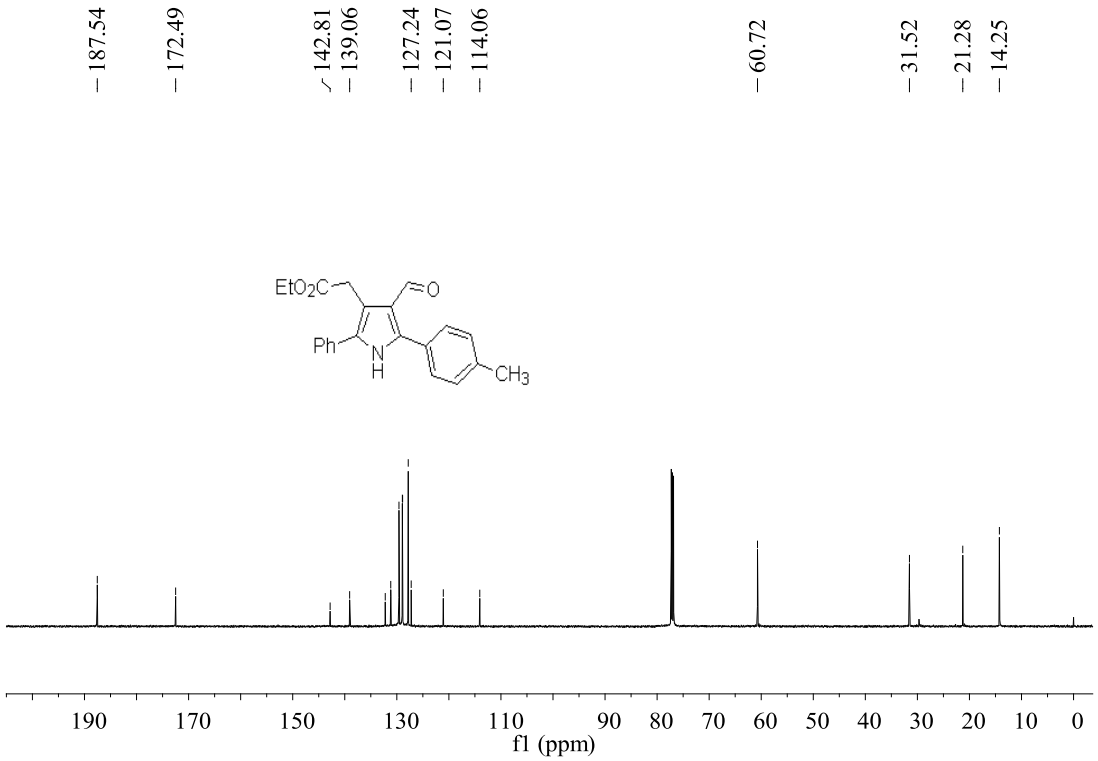
Ethyl 2-(4-formyl-2,5-diphenyl-1H-pyrrol-3-yl)acetate (**3a**) (Using $CDCl_3$ as solvent)



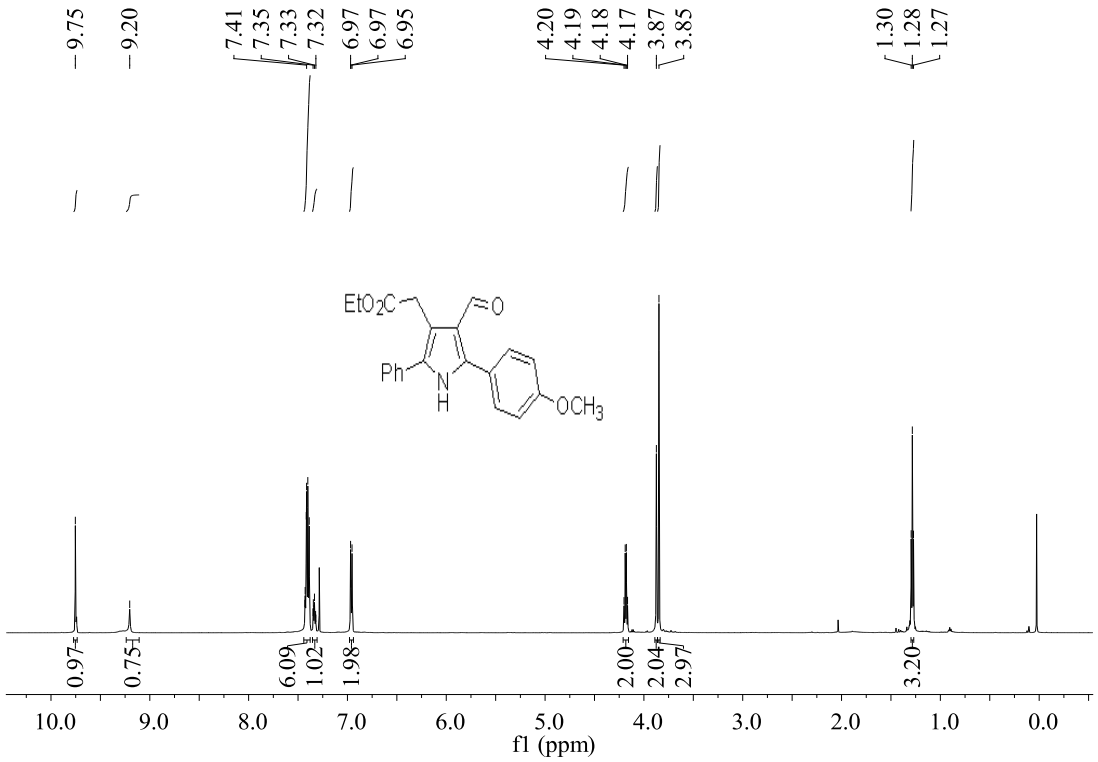


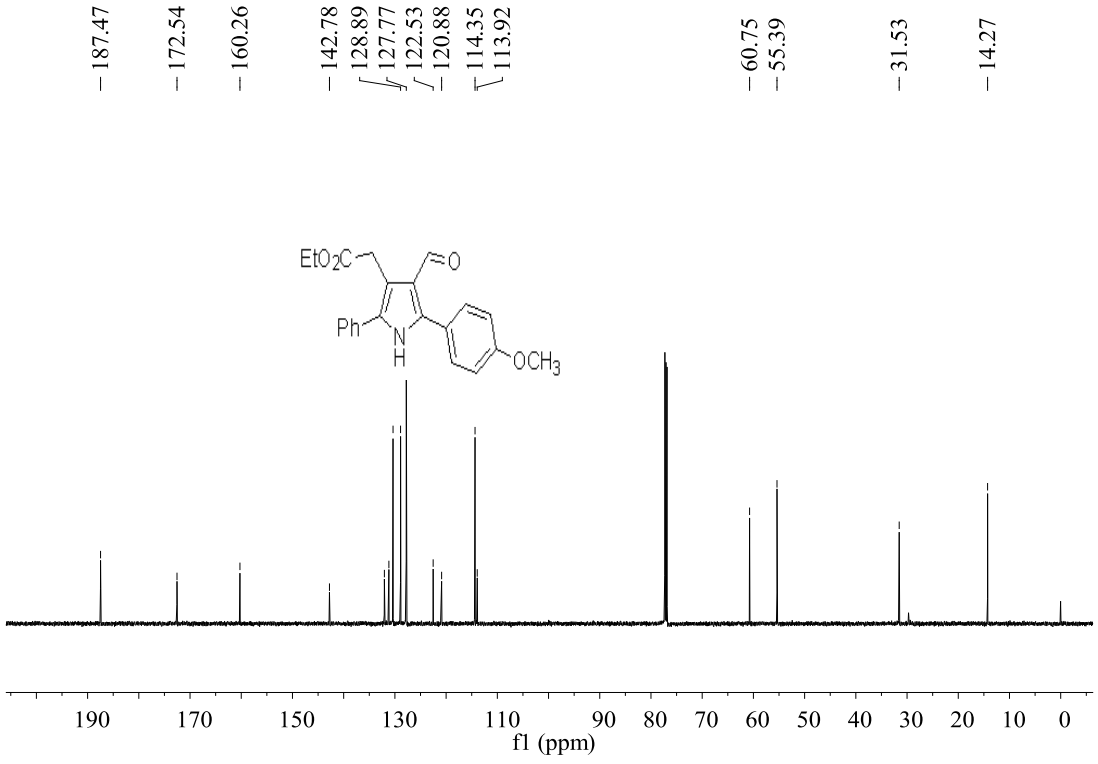
Ethyl 2-(4-formyl-2-phenyl-5-(p-tolyl)-1H-pyrrol-3-yl)acetate (**3b**) (Using $CDCl_3$ as solvent)



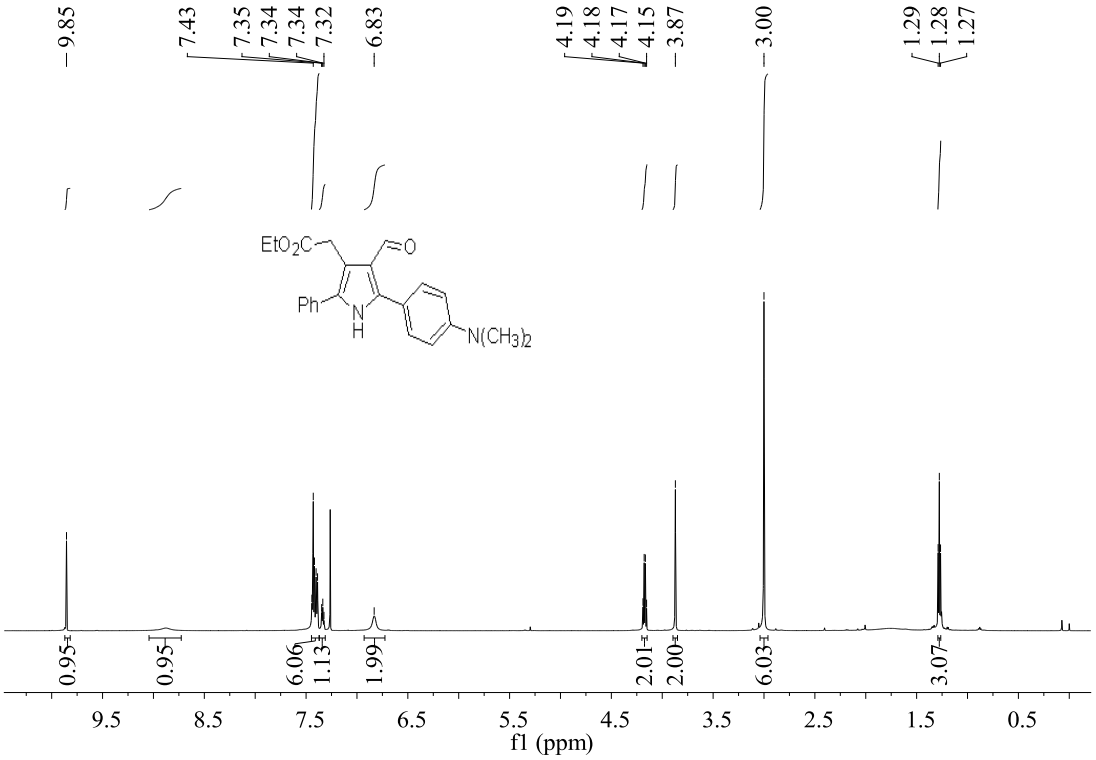


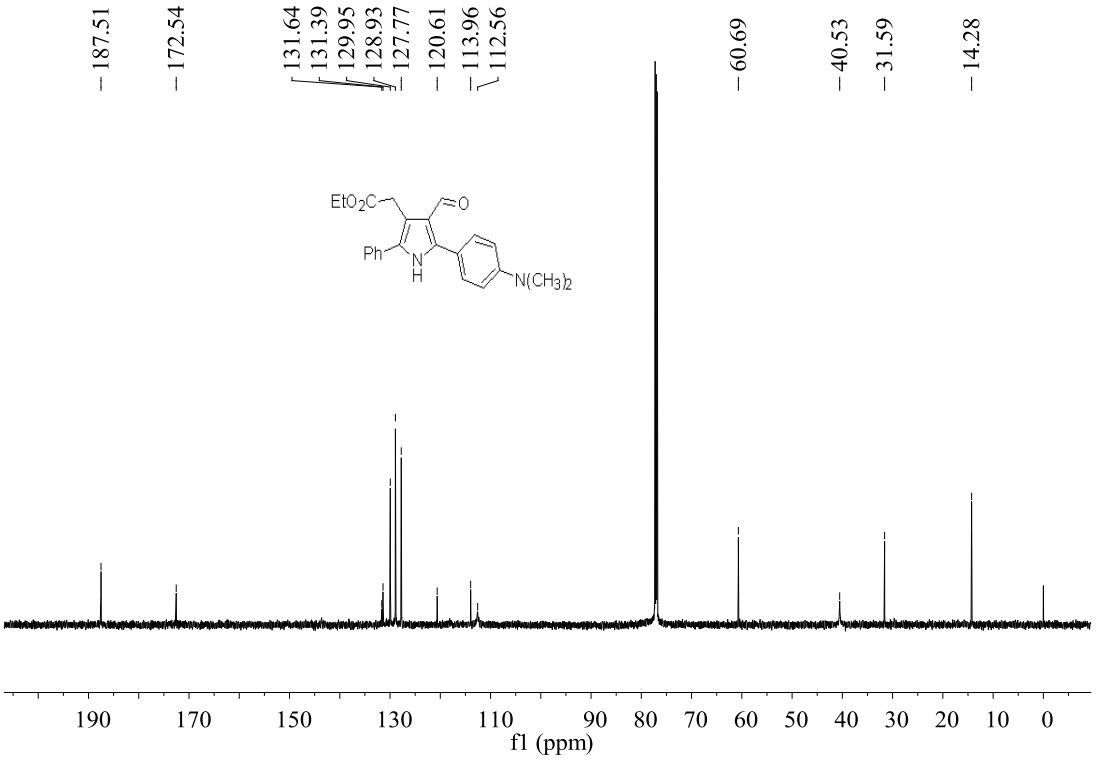
Ethyl 2-(4-formyl-5-(4-methoxyphenyl)-2-phenyl-1H-pyrrol-3-yl)acetate (**3c**) (Using $CDCl_3$ as solvent)



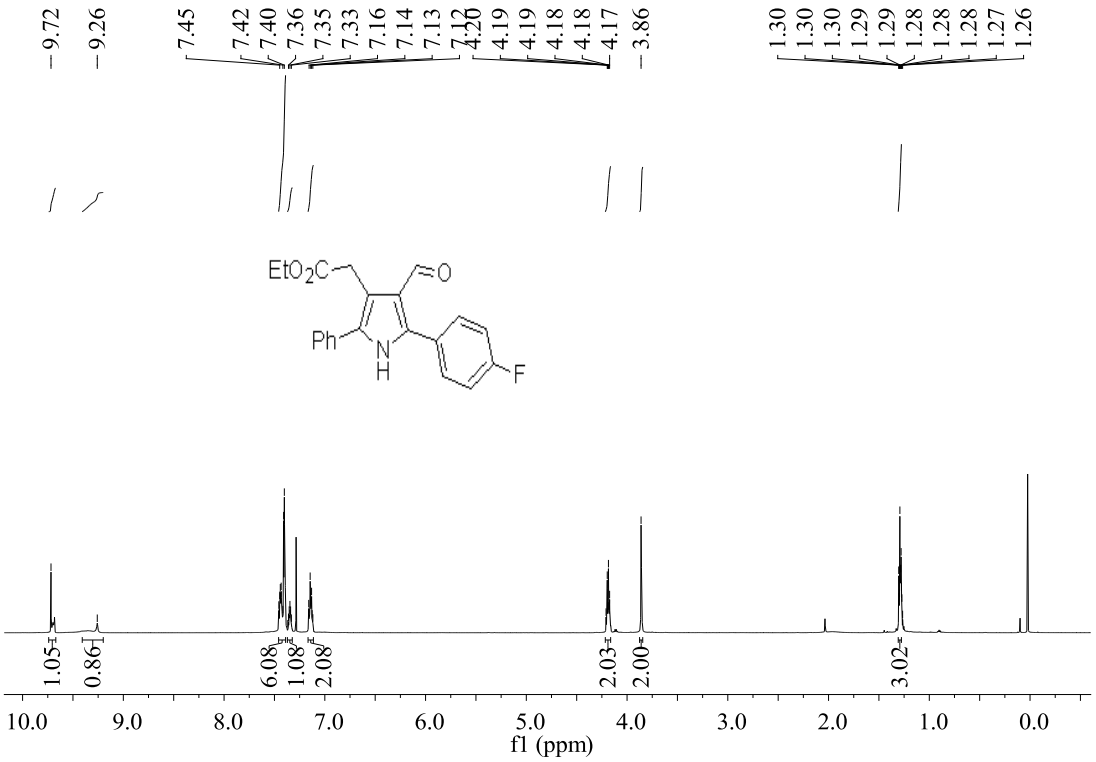


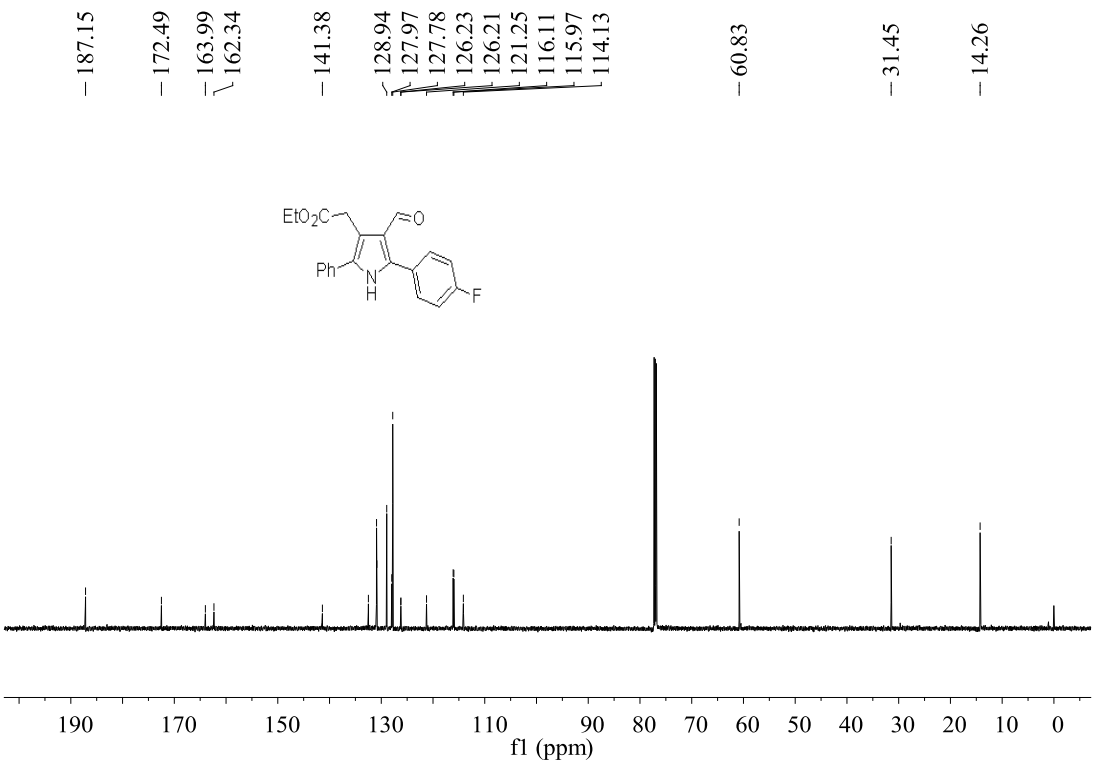
Ethyl 2-(5-(4-(dimethylamino)phenyl)-4-formyl-2-phenyl-1H-pyrrol-3-yl)acetate (**3d**) (Using $CDCl_3$ as solvent)



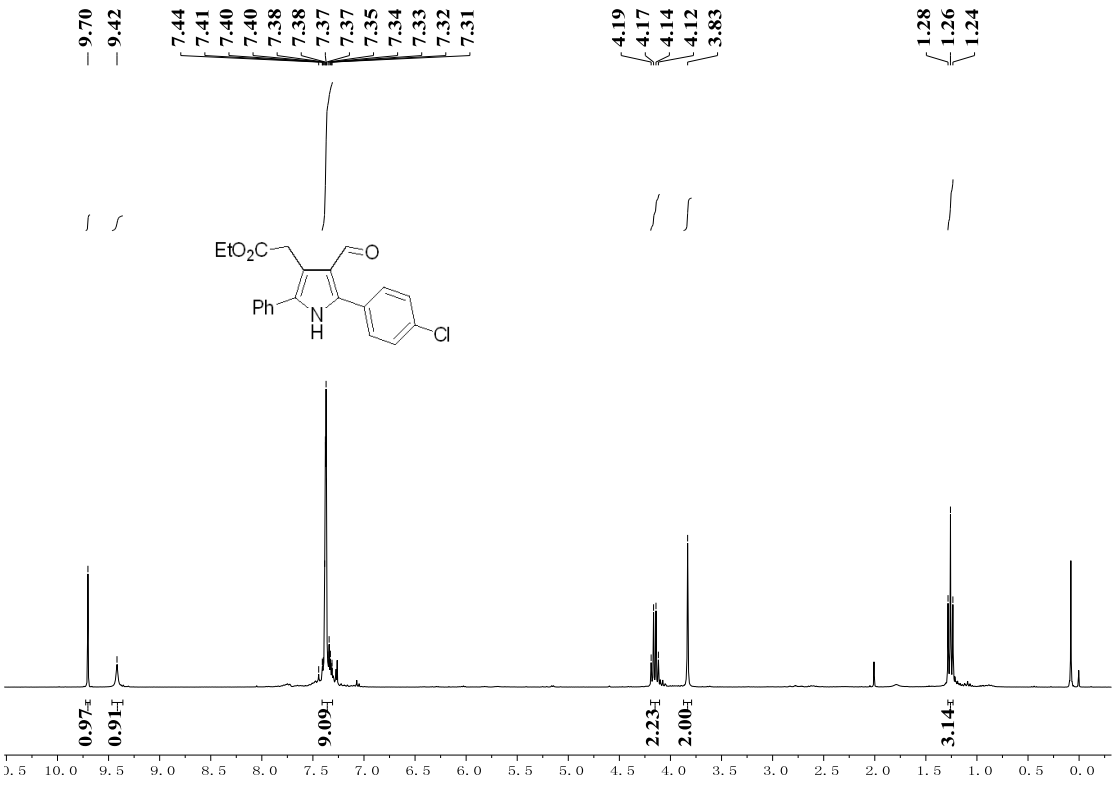


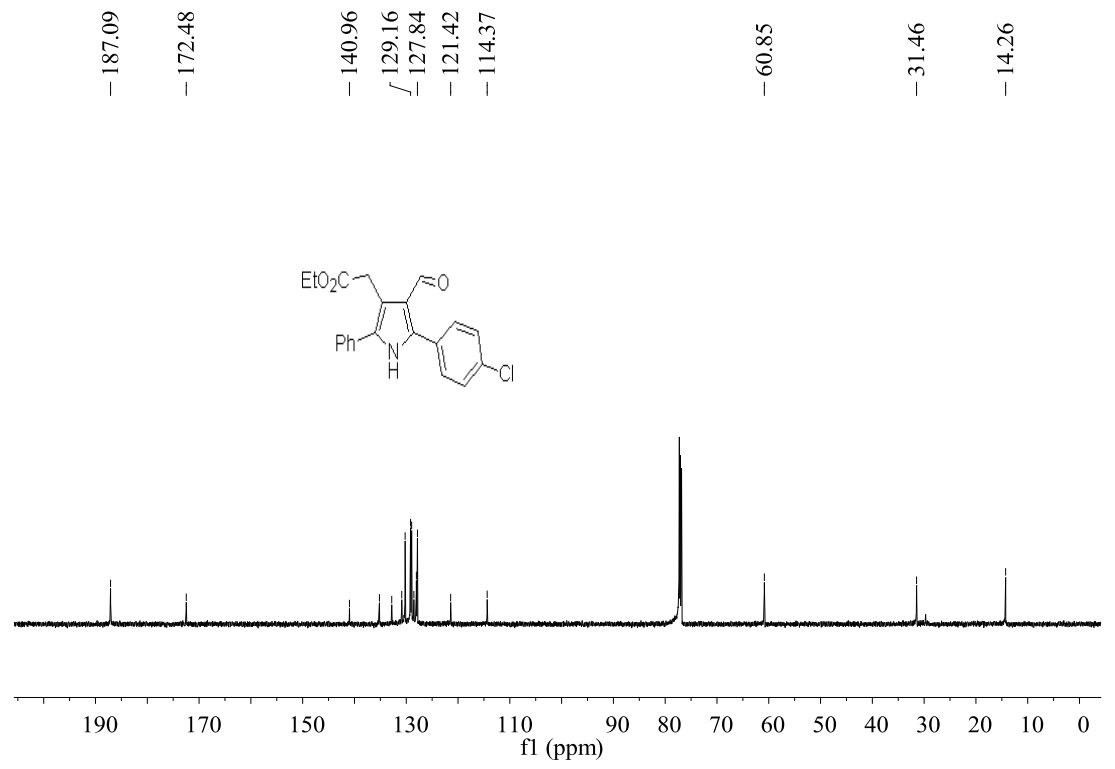
Ethyl 2-(5-(4-fluorophenyl)-4-formyl-2-phenyl-1H-pyrrol-3-yl)acetate (**3e**) (Using $CDCl_3$ as solvent)



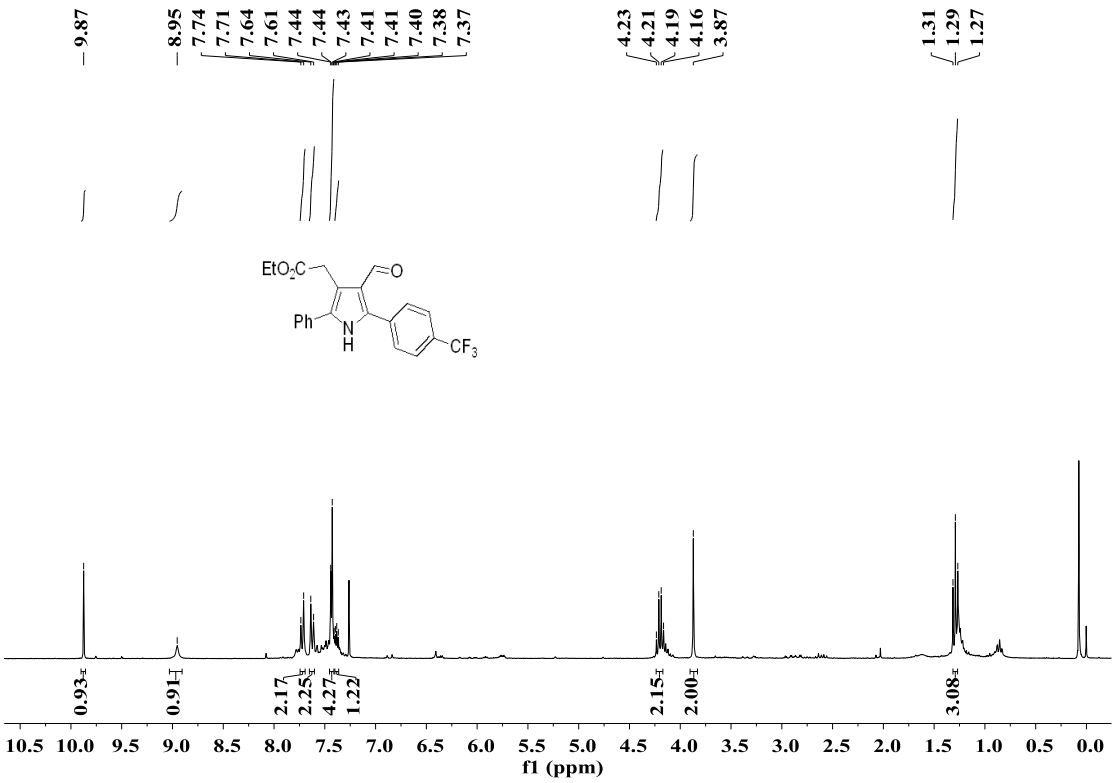


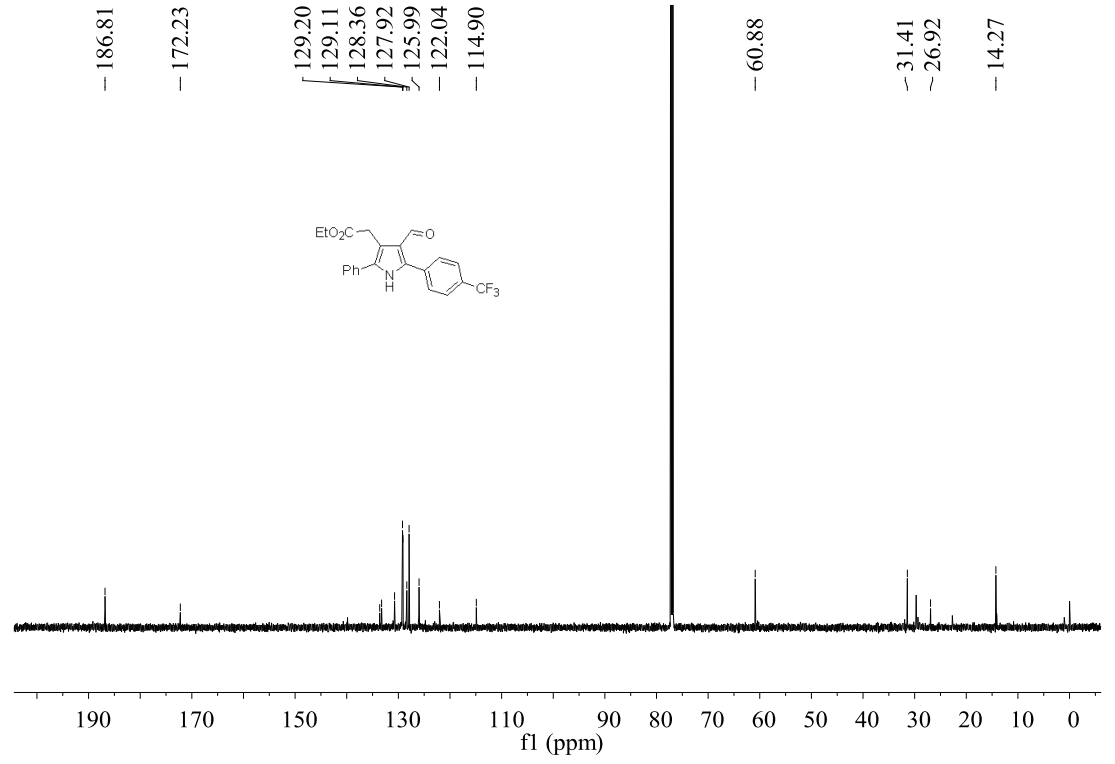
Ethyl 2-(5-(4-chlorophenyl)-4-formyl-2-phenyl-1H-pyrrol-3-yl)acetate (**3f**) (Using $CDCl_3$ as solvent)



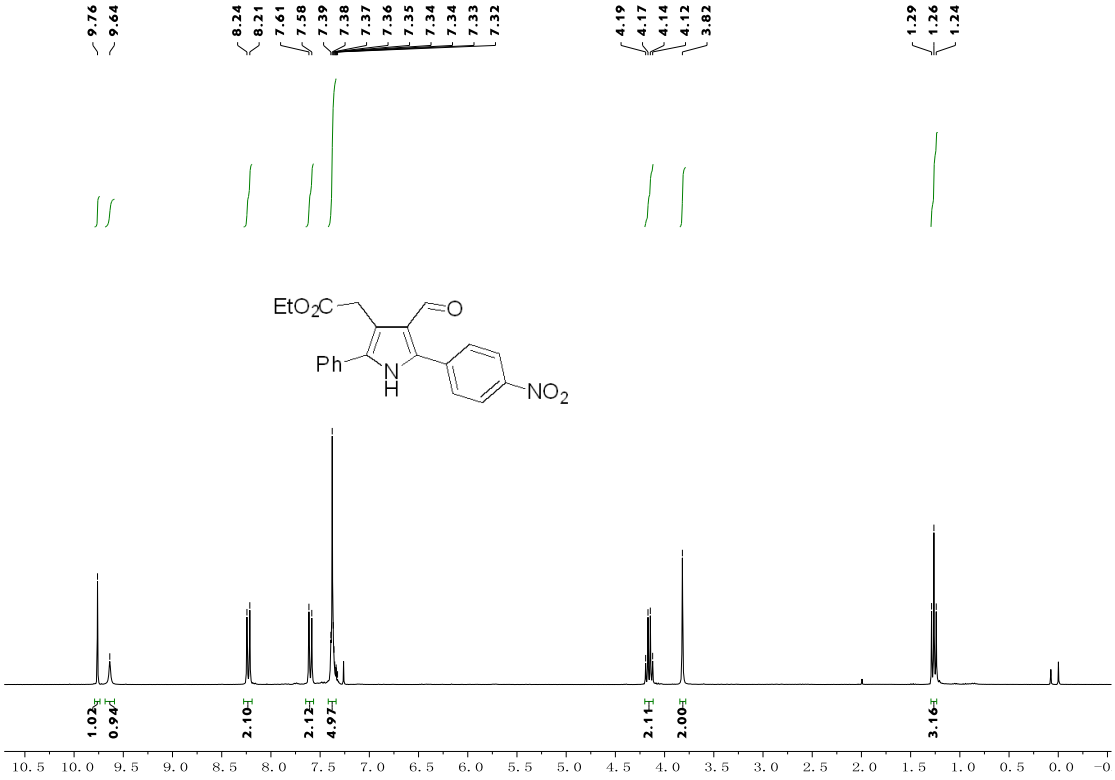


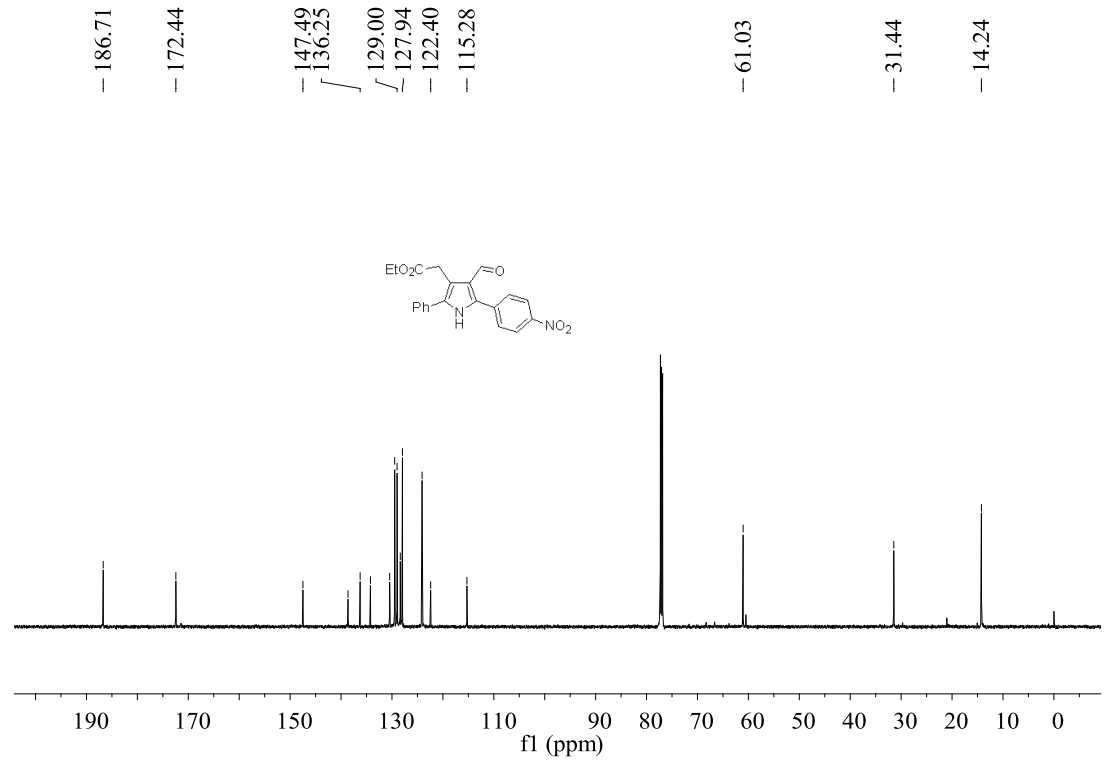
ethyl 2-(4-formyl-2-phenyl-5-(4-(trifluoromethyl)phenyl)-1H-pyrrol-3-yl)acetate (**3g**) (Using $CDCl_3$ as solvent)

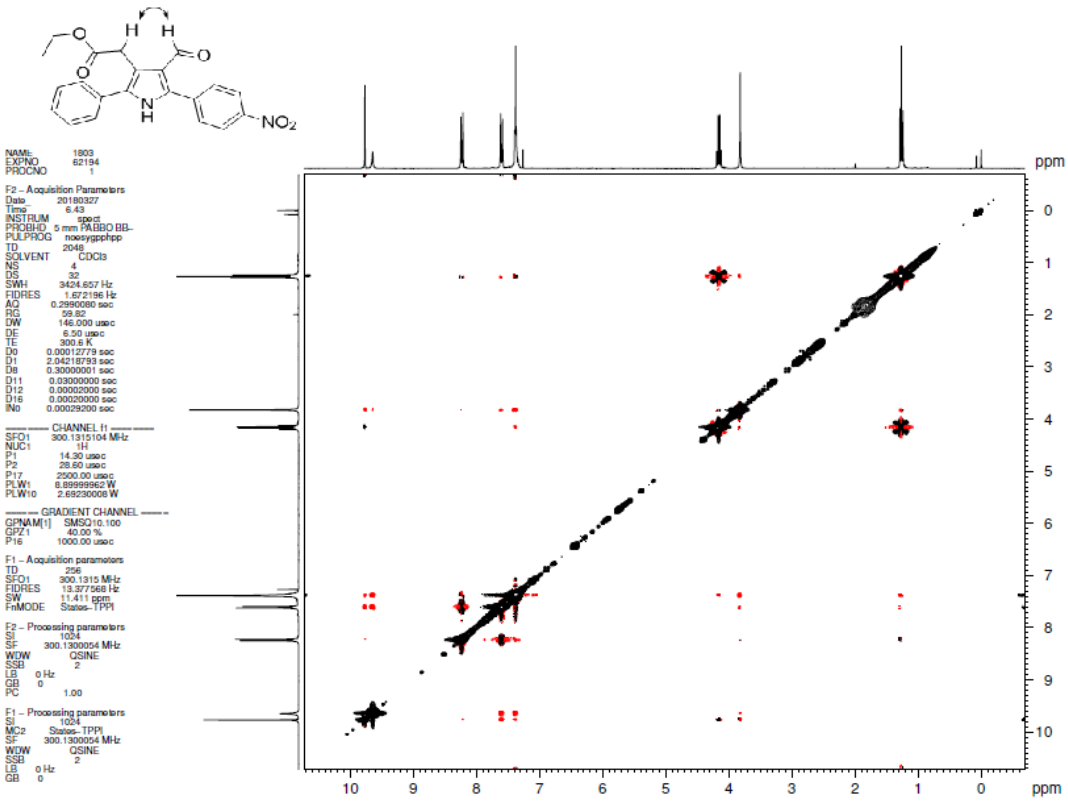




Ethyl 2-(4-formyl-5-(4-nitrophenyl)-2-phenyl-1H-pyrrol-3-yl)acetate (**3h**) (Using $CDCl_3$ as solvent)



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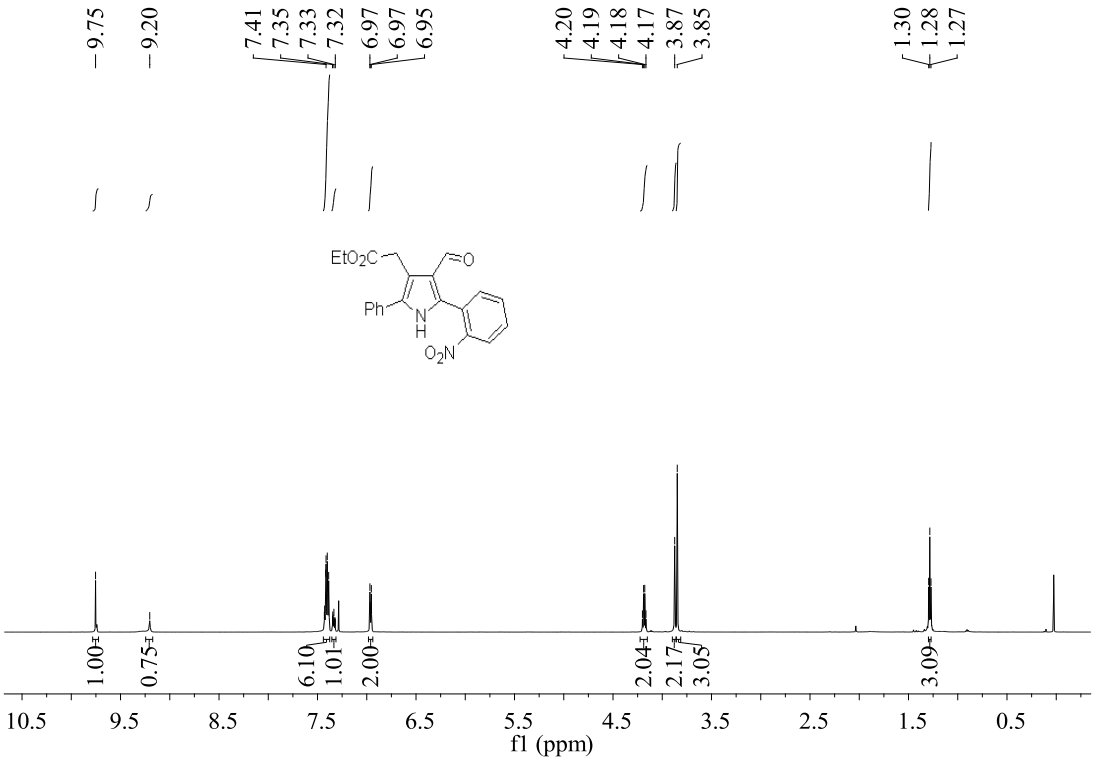
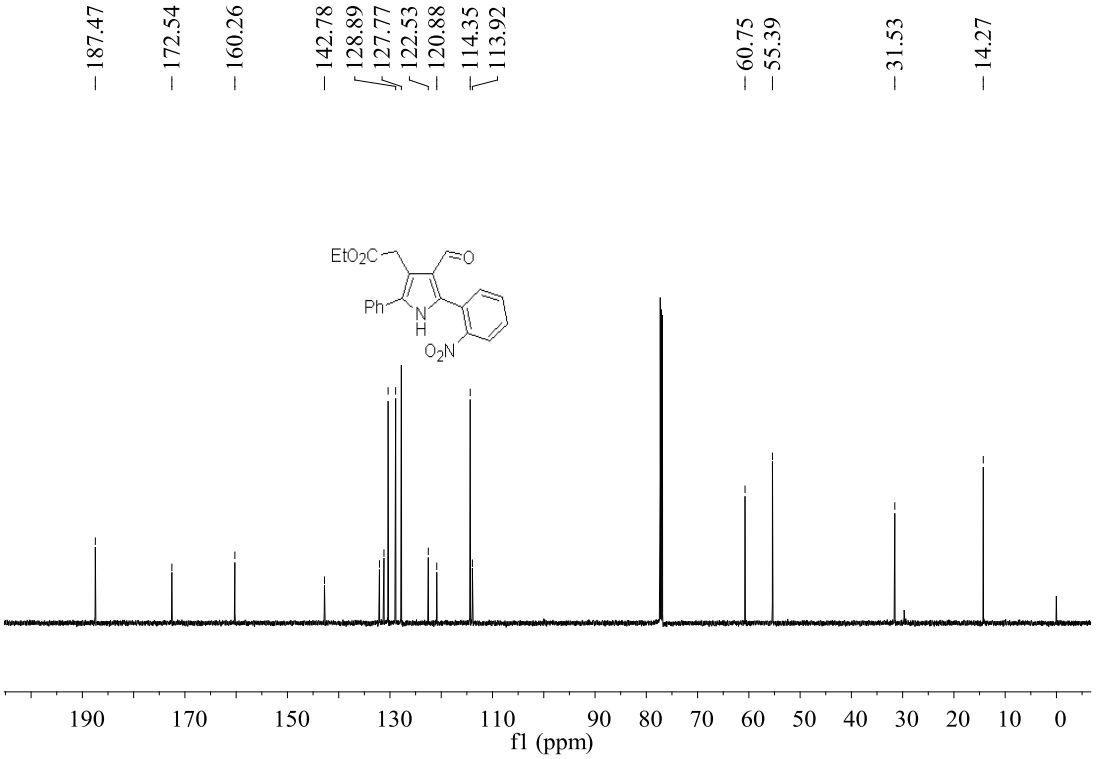
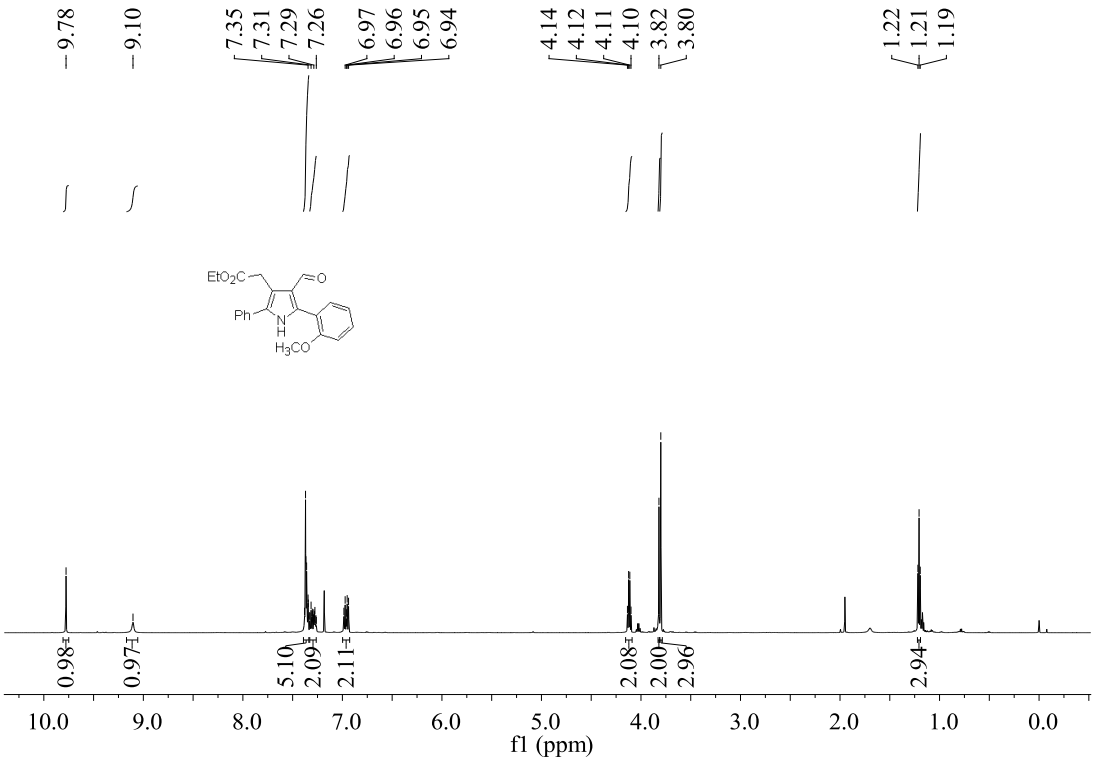
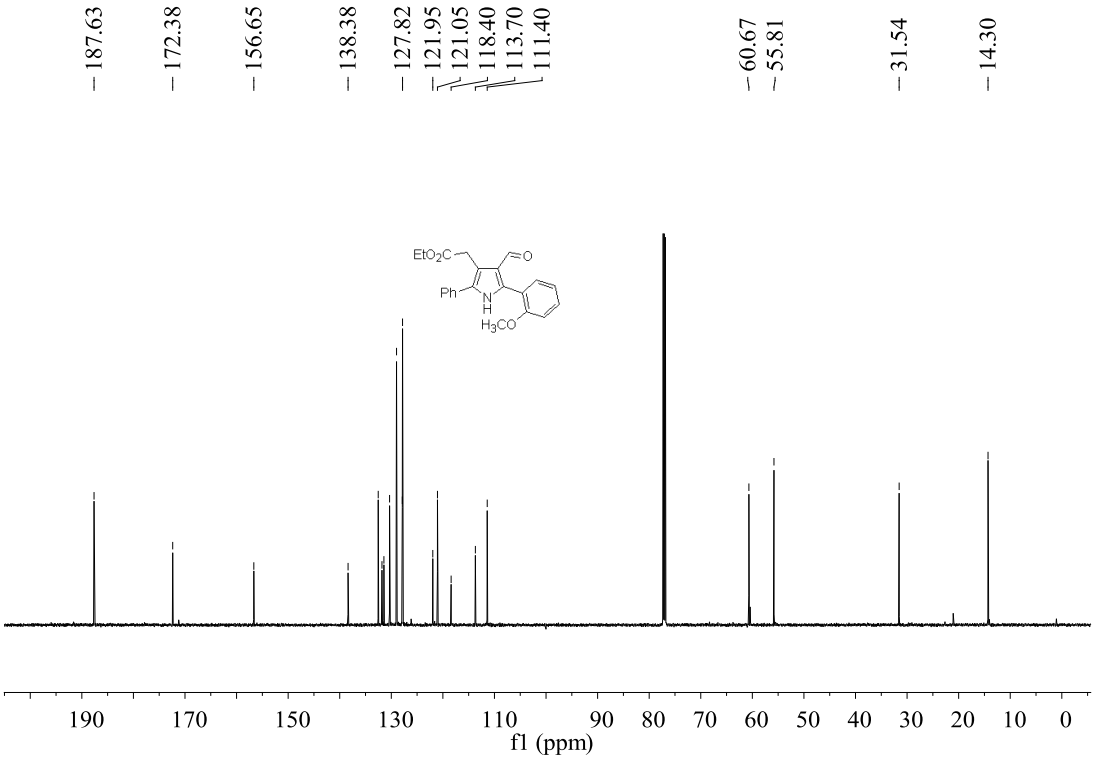
Ethyl 2-(4-formyl-5-(2-nitrophenyl)-2-phenyl-1H-pyrrol-3-yl)acetate (**3i**) (Using $CDCl_3$ as solvent)



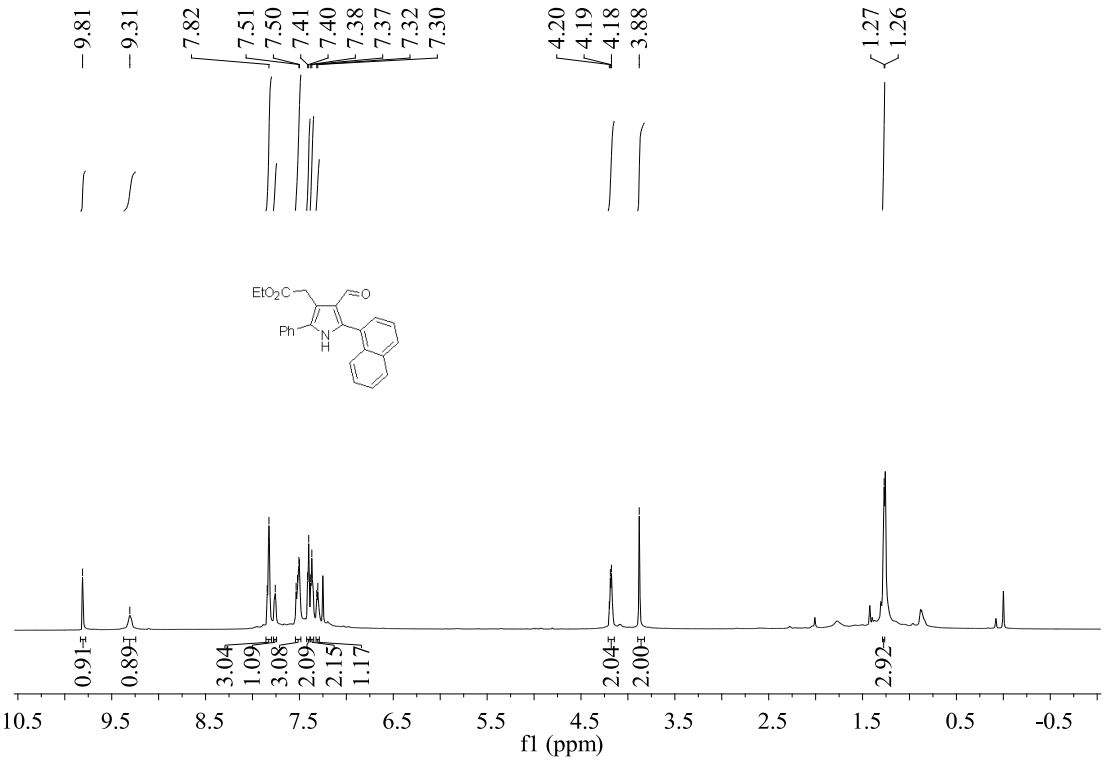


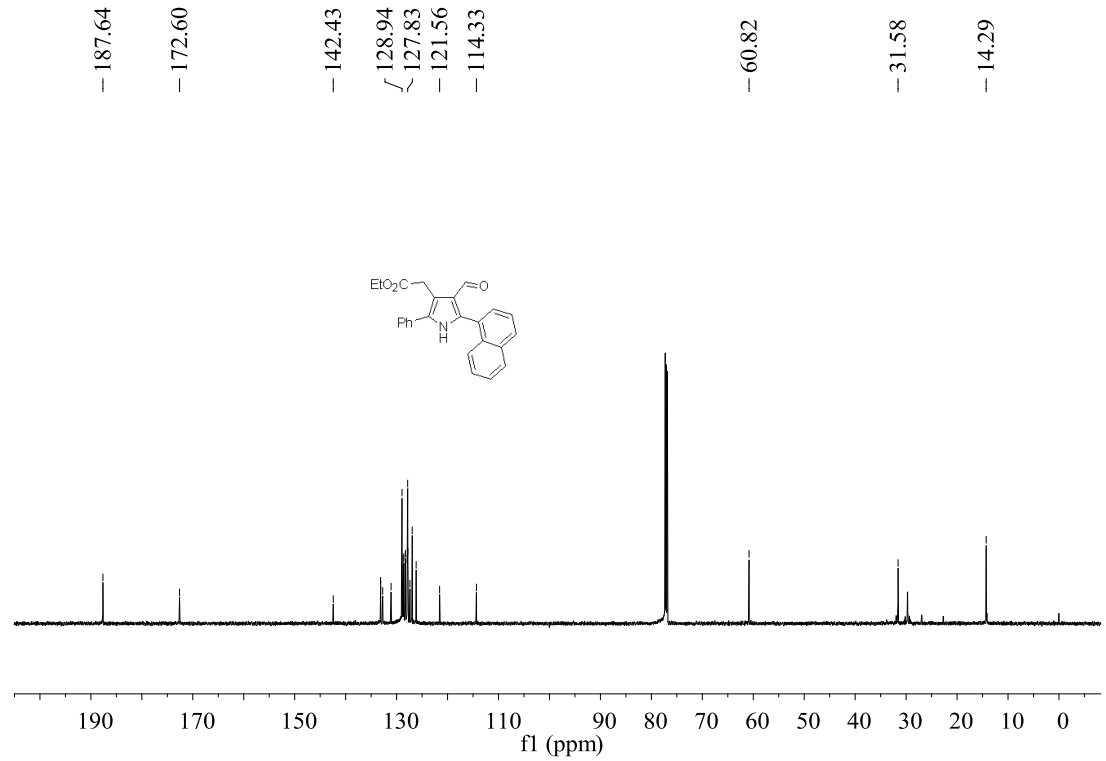
Ethyl 2-(4-formyl-5-(2-methoxyphenyl)-2-phenyl-1H-pyrrol-3-yl)acetate (**3j**) (Using $CDCl_3$ as solvent)



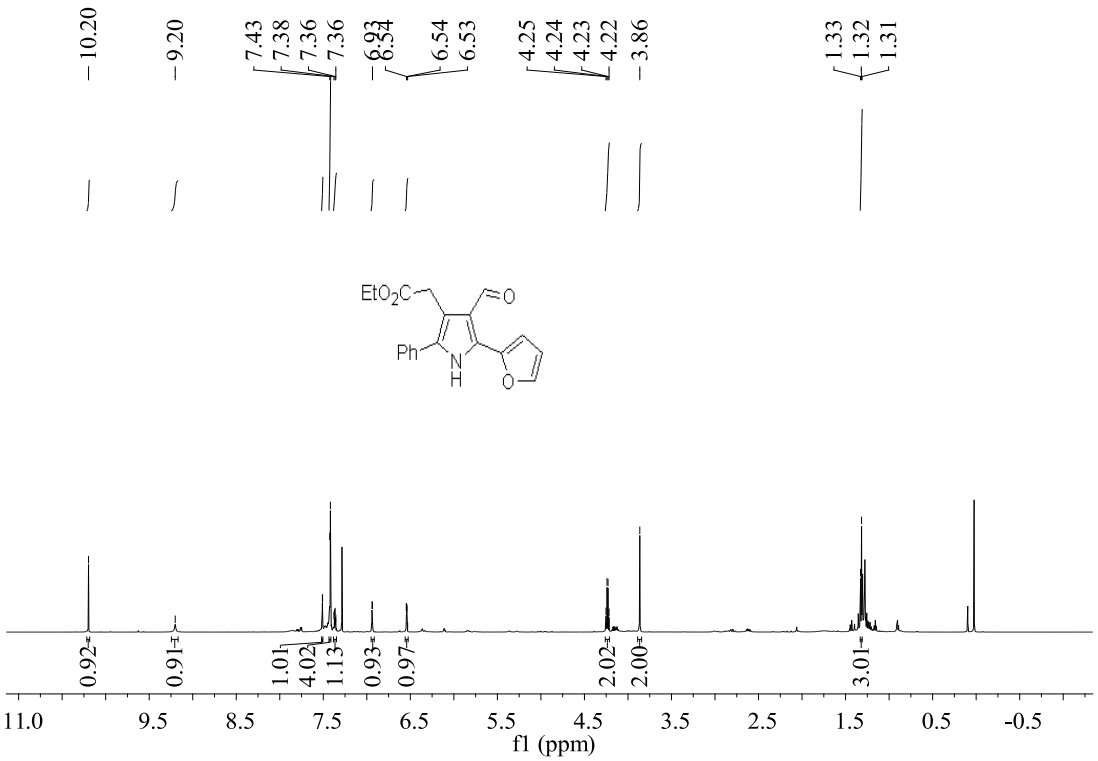


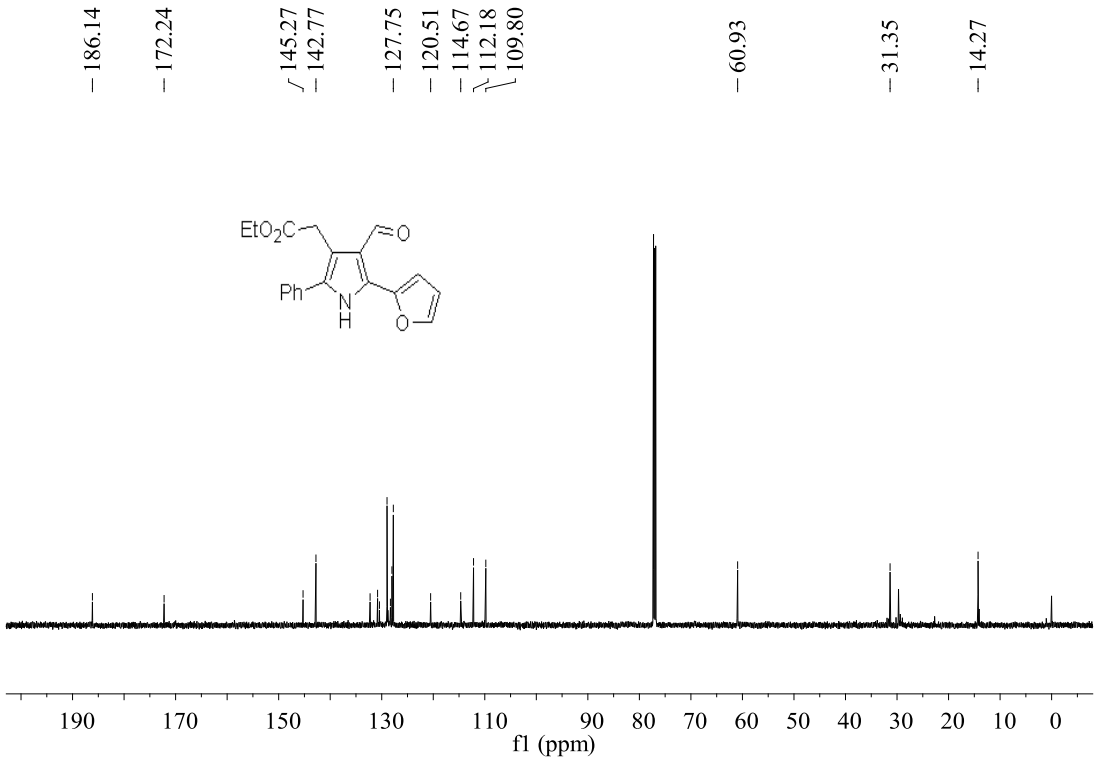
Ethyl 2-(4-formyl-5-(naphthalen-1-yl)-2-phenyl-1H-pyrrol-3-yl)acetate (**3k**) (Using $CDCl_3$ as solvent)



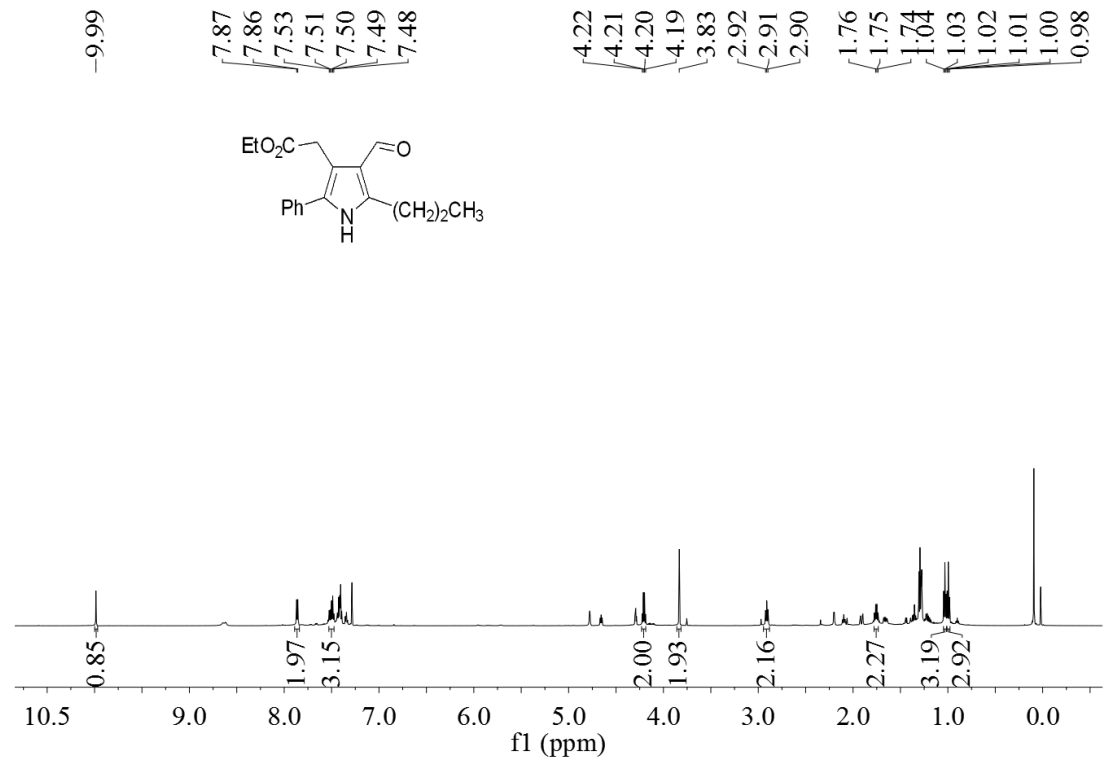


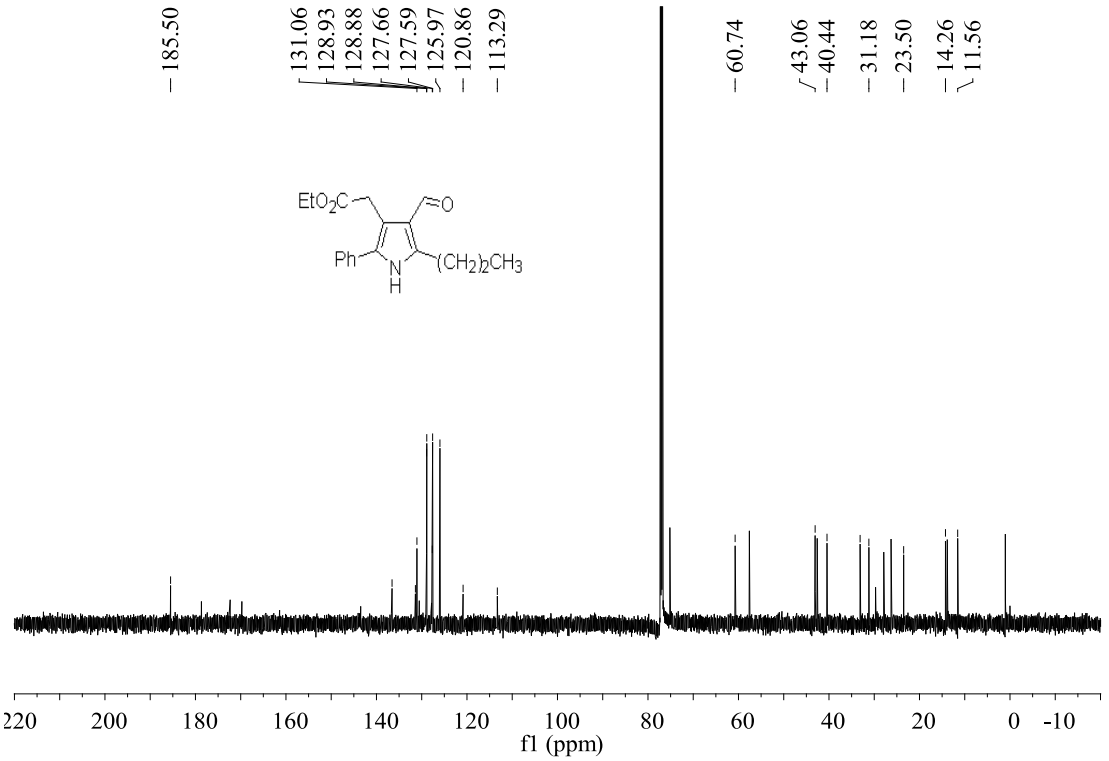
Ethyl 2-(4-formyl-5-(furan-2-yl)-2-phenyl-1H-pyrrol-3-yl)acetate (**3l**) (Using $CDCl_3$ as solvent)



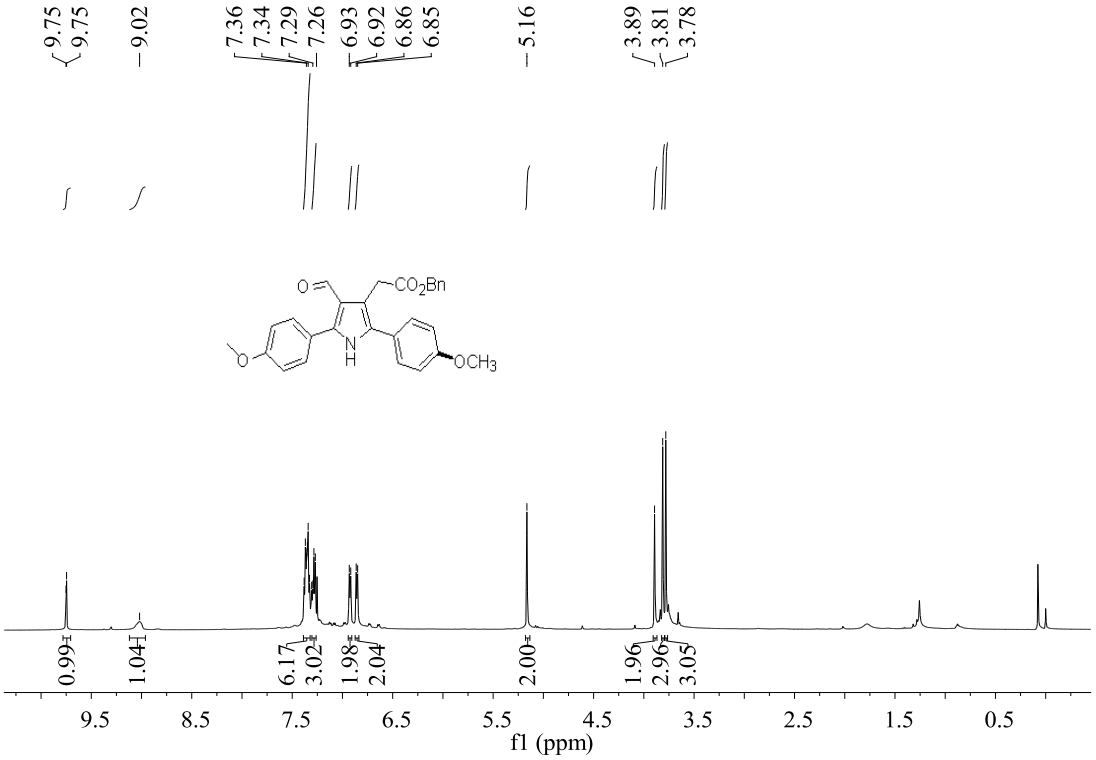


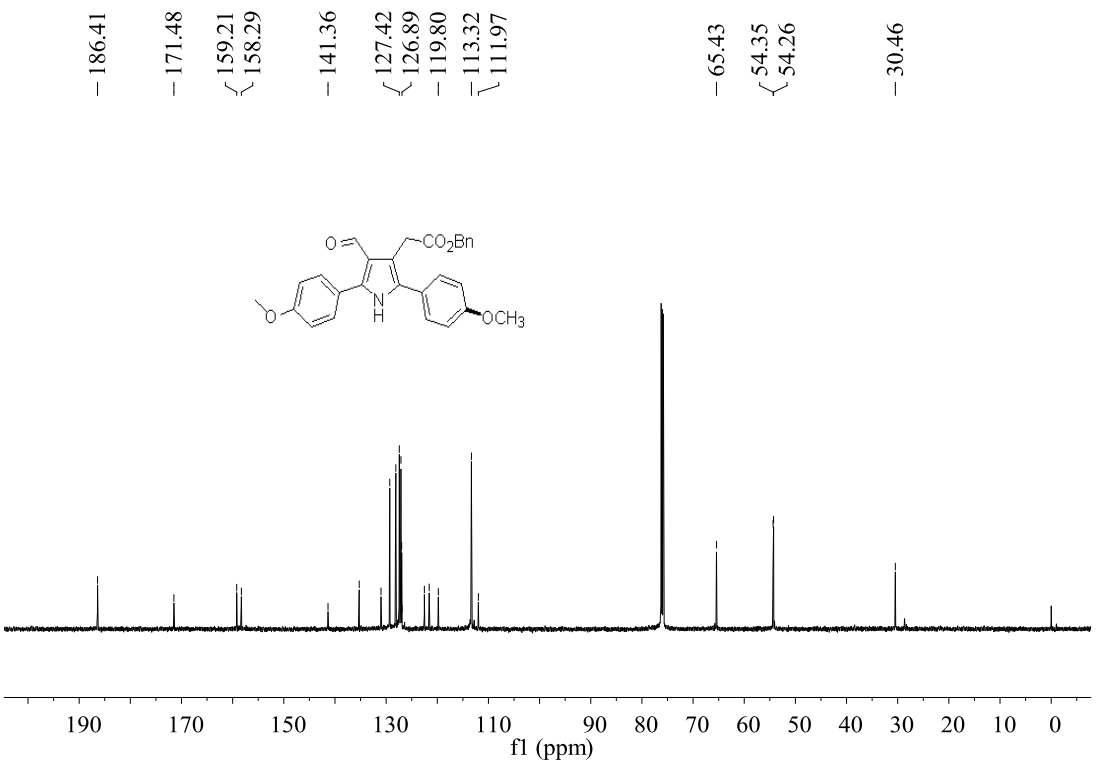
Ethyl 2-(4-formyl-2-phenyl-5-propyl-1H-pyrrol-3-yl)acetate (**3m**) (Using $CDCl_3$ as solvent)



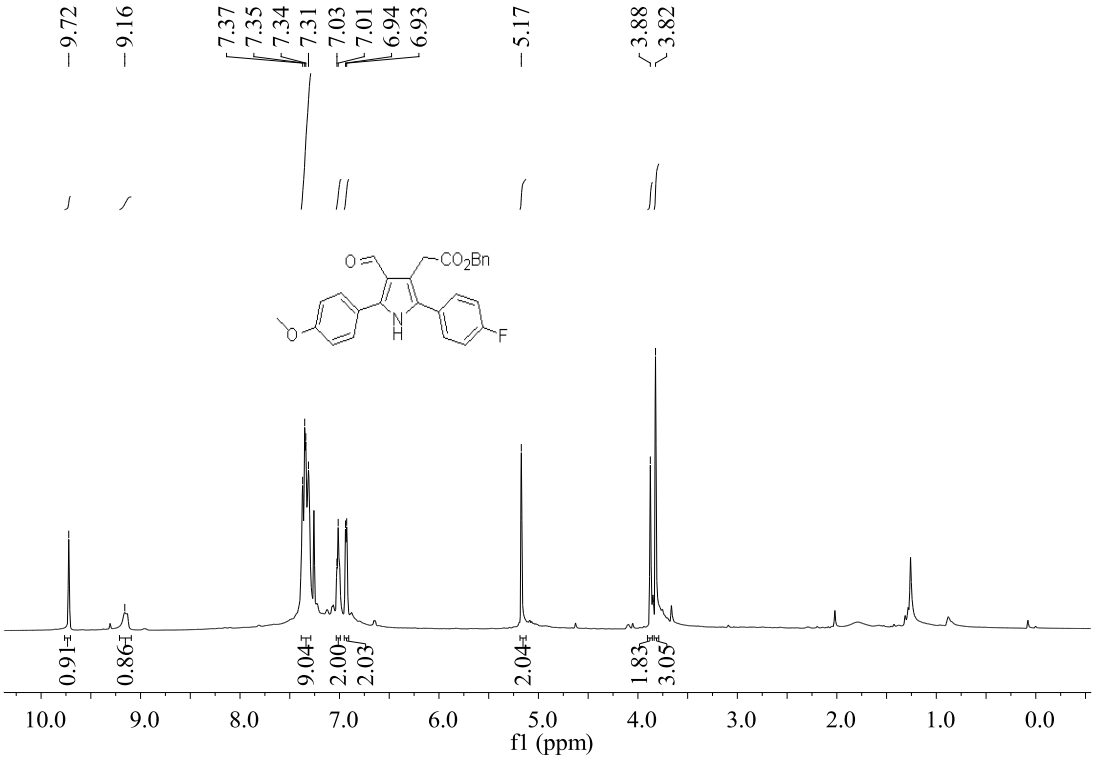


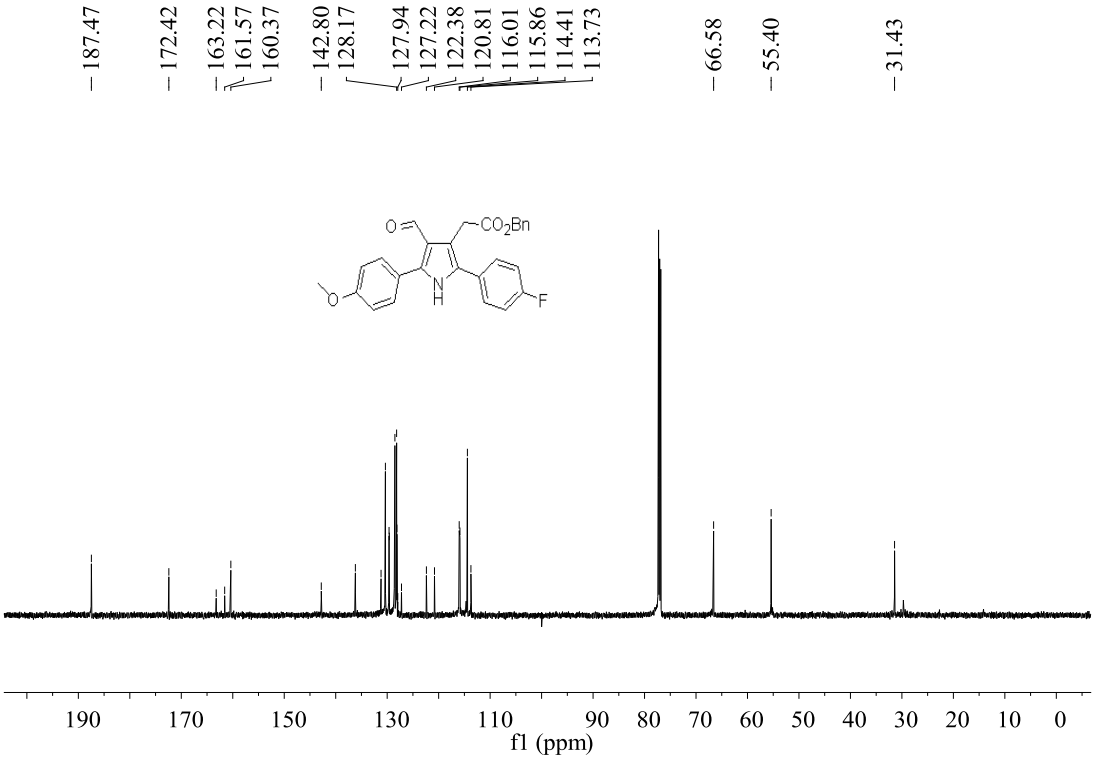
Benzyl 2-(4-formyl-2,5-bis(4-methoxyphenyl)-1H-pyrrol-3-yl)acetate (**3n**) (Using $CDCl_3$ as solvent)



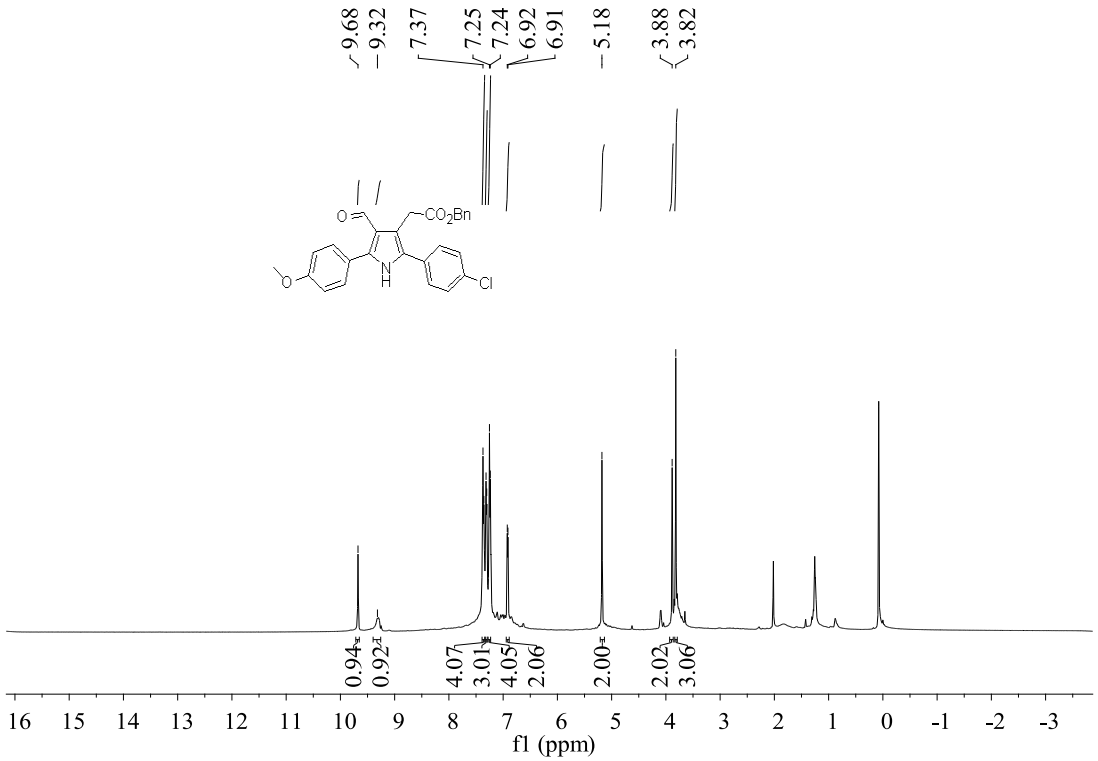


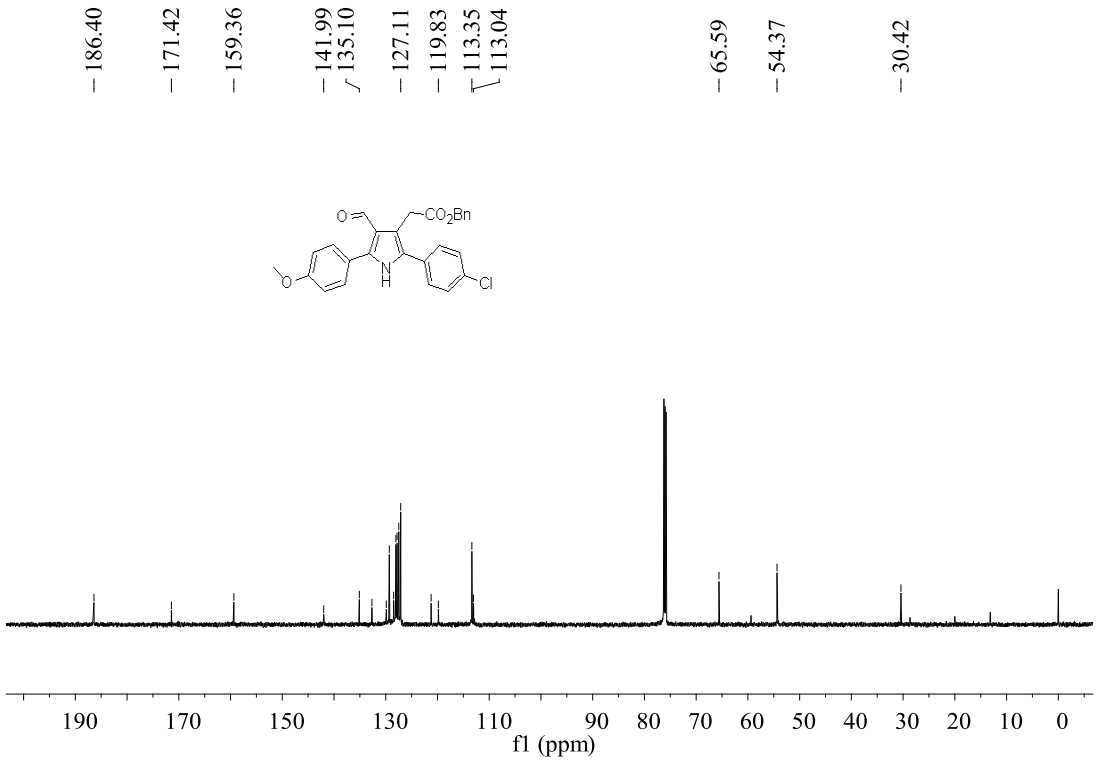
Benzyl 2-(2-(4-fluorophenyl)-4-formyl-5-(4-methoxyphenyl)-1H-pyrrol-3-yl)acetate (**3o**) (Using $CDCl_3$ as solvent)



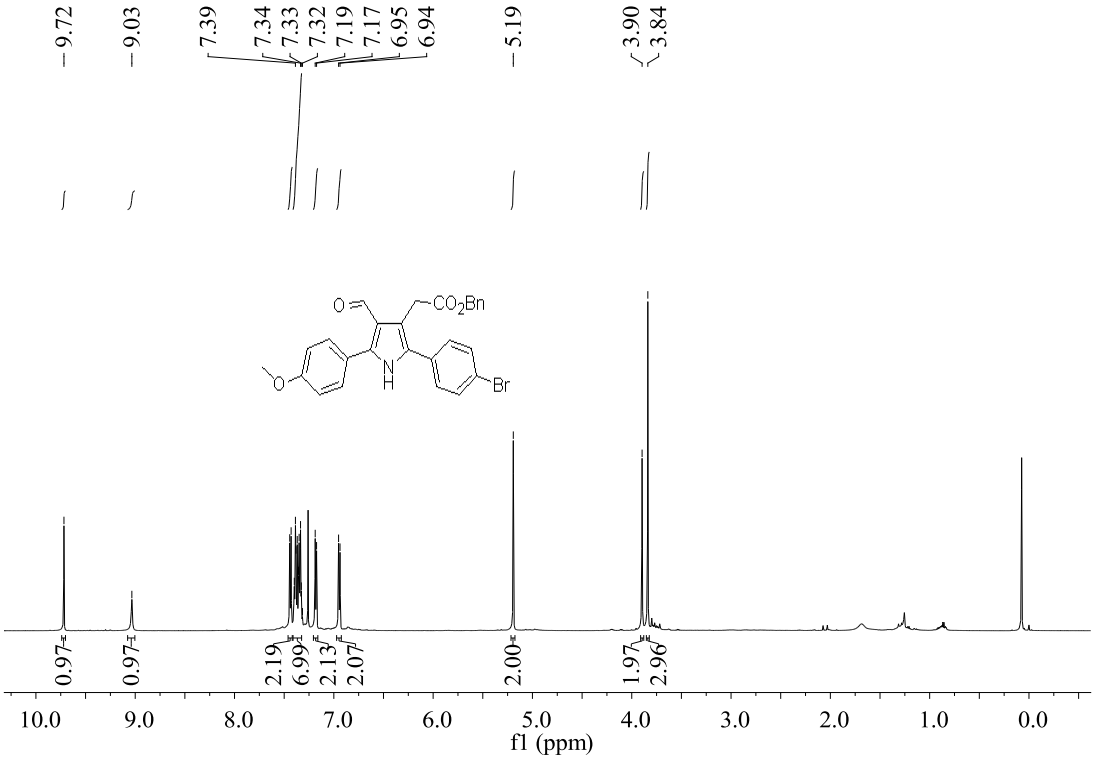


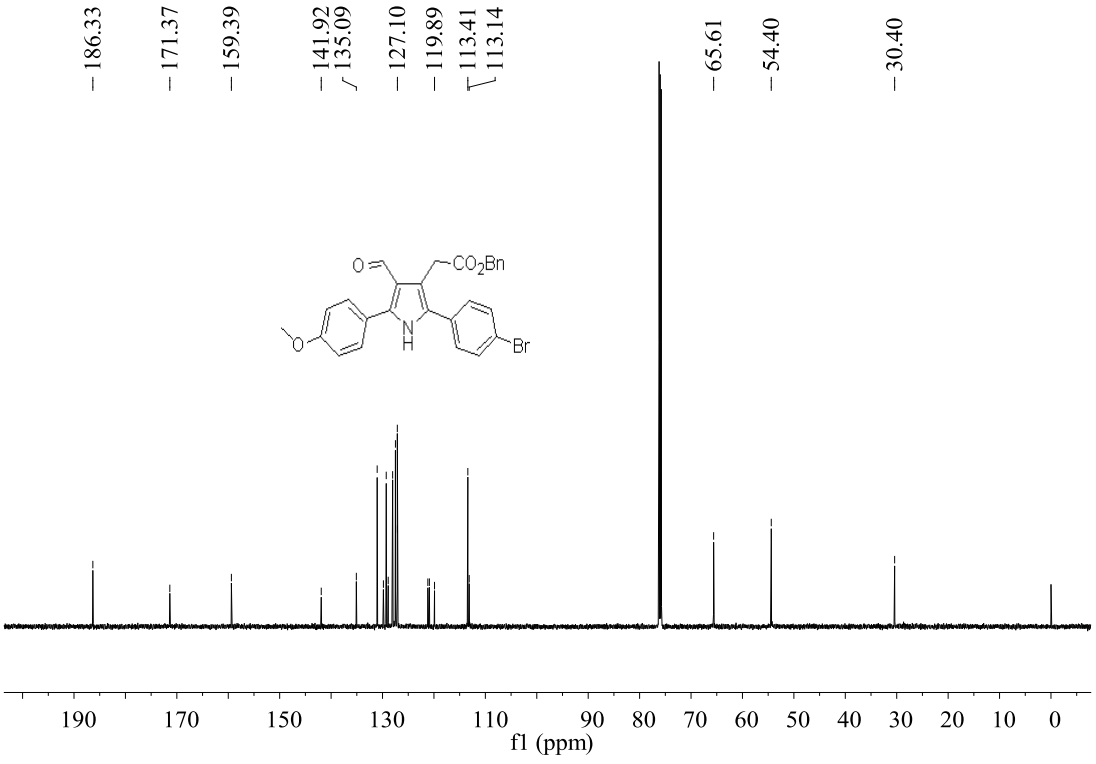
Benzyl 2-(2-(4-chlorophenyl)-4-formyl-5-(4-methoxyphenyl)-1H-pyrrol-3-yl)acetate (**3p**) (Using $CDCl_3$ as solvent)





Benzyl 2-(2-(4-bromophenyl)-4-formyl-5-(4-methoxyphenyl)-1H-pyrrol-3-yl)acetate (**3q**) (Using $CDCl_3$ as solvent)





Benzyl 2-(4-formyl-5-(4-methoxyphenyl)-2-(4-nitrophenyl)-1H-pyrrol-3-yl)acetate (**3r**) (Using $CDCl_3$ as solvent)