

Supporting Information

Direct C-H Heteroarylation of Azoles with 1,2-Di(pyrimidin-2-yl)disulfides through C-S Cleavage of Disulfides

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1. General

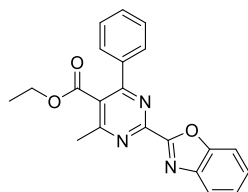
¹H NMR and ¹³C NMR data analyses were performed with a Varian Mercury plus-400 instrument and plus-600 instrument unless otherwise specified. Dual-beam infrared spectrophotometer CDCl₃ as solvent and tetramethylsilane (TMS) as the internal standard were employed. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the ¹H NMR spectrum as 0.00 ppm. The data of ¹H NMR was reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and br = broad), coupling constant (J values) in Hz and integration. Chemical shift for ¹³C NMR spectrawere recorded in ppm from TMS using the central peak of CDCl₃ (77.0ppm) as the internal standard. Flash chromatography was performed using 200-300 mesh silica gel with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on pre-coated, glass-backed silica gel plates. Melting points were measured with an XT-4 apparatus. High-resolution mass spectra (HRMS) (ESI) were obtained with a Bruker Daltonics APEX II 47e and Orbitrap Elite mass spectrometer. Column chromatography was generally performed on silica gel (200–300 mesh) and TLC analyses were conducted on silica gel GF254 plates.

2. Experimental details and characterization data for all compounds.

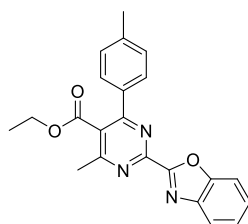
2.1 General procedure for the synthesis of 3aa. Under an atmosphere of nitrogen, disulfide 1a (1 mmol, 0.546g), benzoxazole 2a (3 mmol, 0.357g), Pd(OAc)₂ (0.05mmol, 0.011g), CuTC (2.0mmol, 0.382g) dppp (0.1mmol, 0.041) and Cs₂CO₃ (3mmol, 0.978g) were added to an oven-dried Schlenk tube. The tube was stoppered and degassed with nitrogen three times. Water-free dioxane (3 mL) was added by syringe and the mixture was stirred for 18 h at 120°C and the reaction was monitored by TLC analysis. Then, 2mL diluted hydrochloric acid were added to the mixture to quench the reaction and extracted with ethyl acetate (3×100 mL). The combined organic layers were washed with aqueous NaHCO₃ and brine, dried over MgSO₄, filtered, and the volatiles were removed in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/ petroleum ether 1:30) to give the corresponding products.

2.2 General procedure for the synthesis of 5aa. Under an atmosphere of nitrogen, disulfide 1a (1 mmol, 0.546g), benzothiazole 4a (3 mmol, 0.456g), Pd(OAc)₂ (0.05mmol, 0.011g), CuTC (2.0mmol, 0.382g) PCy₃ (0.1mmol, 0.028) and ^tBuOK (3mmol, 0.337g) were added to an oven-dried Schlenk tube. The tube was stoppered and degassed with nitrogen three times. Water-free DMA (3 mL) was added by syringe and the mixture was stirred for 18h at 140°C and the reaction was monitored by TLC analysis. Then, 2mL diluted hydrochloric acid were added to the mixture to quench the reaction and extracted with ethyl acetate (3×100 mL). The combined organic layers were washed with aqueous NaHCO₃ and brine, dried over MgSO₄, filtered, and the volatiles were removed in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/ petroleum ether 1:30) to give the corresponding products.

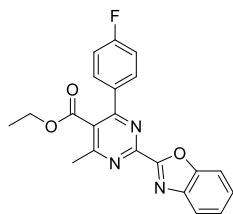
2.2 Characterization Data for the Isolated Products.



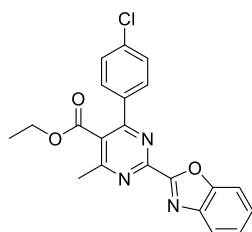
Ethyl 2-(benzo[d]oxazol-2-yl)-4-methyl-6-phenylpyrimidine-5-carboxylate (3aa). Yellow solid, m.p. = 166-167 °C. ¹H NMR (600 MHz, CDCl₃): δ 7.94 (d, *J* = 7.8 Hz, 1H), 7.78-7.76 (m, 2H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.46 (m, 4H), 7.43 (t, *J* = 7.2 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 2.80 (s, 3H), 1.10 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 167.30, 166.59, 164.59, 159.40, 141.79, 136.98, 130.47, 128.69, 128.55, 126.99, 126.26, 125.25, 123.32, 121.65, 111.60, 109.99, 62.22, 22.83, 13.63; HRMS (ESI⁺) *m/z*: Calcd for C₂₁H₁₈N₃O₃ [M+H]⁺ 360.1343, Found 360.1347.



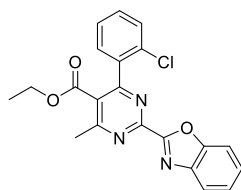
Ethyl 2-(benzo[d]oxazol-2-yl)-4-methyl-6-(p-tolyl)pyrimidine-5-carboxylate (3ba). Yellow solid, m.p. = 165-166 °C. ¹H NMR (600 MHz, CDCl₃): δ 7.91 (d, *J* = 7.8 Hz, 1H), 7.68 – 7.67 (m, 3H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 2H), 4.25 (q, *J* = 7.2 Hz, 2H), 2.76 (s, 3H), 2.39 (s, 3H), 1.13 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 167.51, 166.34, 164.33, 159.54, 154.19, 151.28, 141.71, 140.91, 134.03, 129.40, 128.55, 126.91, 125.99, 125.71, 125.19, 121.58, 111.56, 62.18, 22.78, 21.42, 13.70; HRMS (ESI⁺) *m/z*: Calcd for C₂₂H₂₀N₃O₃ [M+H]⁺ 374.1499, Found 374.1492.



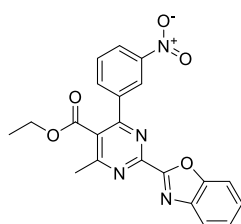
Ethyl 2-(benzo[d]oxazol-2-yl)-4-(4-fluorophenyl)-6-methylpyrimidine-5-carboxylate (3ca). Yellow solid, m.p. = 179-180 °C. ¹H NMR (600 MHz, CDCl₃): δ 7.94 (d, *J* = 7.8 Hz, 1H), 7.81 – 7.79 (m, 2H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.19 (t, *J* = 8.4 Hz, 2H), 4.28 (q, *J* = 7.2 Hz, 2H), 2.79 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 167.24, 166.71, 165.11, 163.44, 163.29, 159.34, 154.26, 151.31, 141.70, 130.82, 130.76, 127.07, 126.08, 125.31, 121.66, 115.97, 115.82, 111.59, 62.34, 22.84, 13.74; HRMS (ESI⁺) *m/z*: Calcd for C₂₁H₁₇FN₃O₃ [M+H]⁺ 378.1248, Found 378.1254.



Ethyl 2-(benzo[d]oxazol-2-yl)-4-(4-chlorophenyl)-6-methylpyrimidine-5-carboxylate (3da). Yellow solid, m.p. = 147-148 °C. ¹H NMR (600 MHz, CDCl₃): δ 7.92 (d, *J* = 7.2 Hz, 1H), 7.69 (m, 3H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 2H), 4.26 (q, *J* = 7.2 Hz, 2H), 2.77 (s, 3H), 1.14 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 167.52, 166.34, 164.35, 159.55, 154.20, 151.29, 141.73, 140.91, 134.04, 129.40, 128.55, 126.91, 126.00, 125.20, 121.60, 111.57, 62.18, 22.79, 13.71; HRMS (ESI⁺) *m/z*: Calcd for C₂₁H₁₇ClN₃O₃ [M+H]⁺ 394.0953, Found 394.0951.

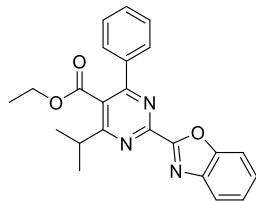


Ethyl 2-(benzo[d]oxazol-2-yl)-4-(2-chlorophenyl)-6-methylpyrimidine-5-carboxylate (3ea). Yellow solid, m.p. = 195-197 °C. ¹H NMR (600 MHz, CDCl₃): δ 7.92 (d, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.47-7.36 (m, 6H), 4.13 (q, *J* = 7.2 Hz, 2H), 2.88 (s, 3H), 0.97 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 167.64, 165.61, 164.50, 159.22, 154.31, 151.35, 141.71, 136.59, 132.36, 130.64, 130.24, 129.58, 128.65, 127.12, 126.76, 125.31, 121.68, 111.67, 61.98, 23.52, 13.44; HRMS (ESI⁺) *m/z*: Calcd for C₂₁H₁₇ClN₃O₃ [M+H]⁺ 394.0953, Found 394.0948.

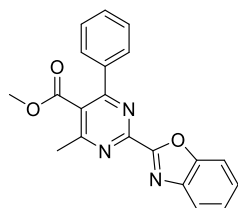


Ethyl 2-(benzo[d]oxazol-2-yl)-4-methyl-6-(3-nitrophenyl)pyrimidine-5-carboxylate (3fa). Yellow solid, m.p. = 153-154 °C. ¹H NMR (600 MHz, CDCl₃): δ 8.65 (s, 1H), 8.39 (d, *J* = 8.4 Hz, 1H), 8.15 (d, *J*

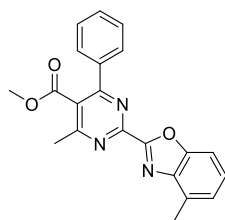
= 7.8 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.74-7.70 (m, 2H), 7.49 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.2 Hz, 1H), 4.33 (q, J = 7.2 Hz, 2H), 2.84 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 167.41, 166.59, 161.92, 154.52, 148.36, 141.66, 138.43, 134.63, 129.95, 127.31, 126.34, 125.44, 125.12, 123.64, 121.74, 111.64, 62.71, 23.02, 13.77; HRMS (ESI⁺) m/z : Calcd for $\text{C}_{21}\text{H}_{17}\text{N}_4\text{O}_5$ [M+H]⁺ 405.1193, Found 405.1191.



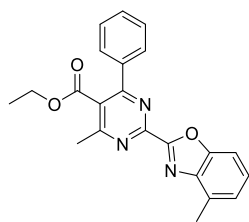
Ethyl 2-(benzo[d]oxazol-2-yl)-4-isopropyl-6-phenylpyrimidine-5-carboxylate (3ga). Yellow solid, m.p. = 150-152 °C. ^1H NMR (600 MHz, CDCl_3): δ 7.95 (d, J = 7.8 Hz, 1H), 7.77 (d, J = 5.4 Hz, 2H), 7.71 (d, J = 7.8 Hz, 1H), 7.50-7.44 (m, 4H), 7.41 (t, J = 7.8 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.33-3.30 (m, 1H), 1.47 (d, J = 6.6 Hz, 6H), 1.09 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 174.17, 167.49, 164.49, 159.81, 154.77, 151.28, 141.85, 137.21, 130.28, 128.63, 128.56, 127.51, 126.76, 125.74, 125.57, 125.06, 121.65, 121.49, 111.52, 62.15, 33.79, 21.72, 13.64; HRMS (ESI⁺) m/z : Calcd for $\text{C}_{23}\text{H}_{22}\text{N}_3\text{O}_3$ [M+H]⁺ 388.1656, Found 388.1652.



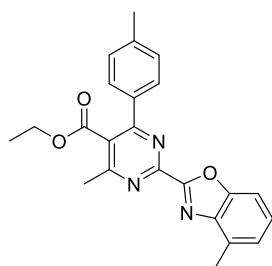
Methyl 2-(benzo[d]oxazol-2-yl)-4-methyl-6-phenylpyrimidine-5-carboxylate (3ha). White solid, m.p. = 167-168 °C. ^1H NMR (600 MHz, CDCl_3): δ 7.93 (d, J = 7.8 Hz, 1H), 7.77 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 7.8 Hz, 1H), 7.50 – 7.40 (m, 5H), 3.75 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 167.88, 166.67, 164.44, 159.43, 154.37, 151.32, 141.72, 136.85, 130.61, 128.79, 128.46, 127.01, 125.89, 125.26, 121.64, 111.59, 52.86, 22.87; HRMS (ESI⁺) m/z : Calcd for $\text{C}_{20}\text{H}_{16}\text{N}_3\text{O}_3$ [M+H]⁺ 346.1186, Found 346.1188.



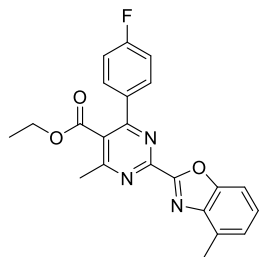
Methyl 4-methyl-2-(4-methylbenzo[d]oxazol-2-yl)-6-phenylpyrimidine-5-carboxylate (3hb). Yellow solid, m.p. = 154-155 °C. ^1H NMR (600 MHz, CDCl_3): δ 7.77 (d, J = 4.8 Hz, 2H), 7.70 (s, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.51 (s, 3H), 7.27 (d, J = 8.4 Hz, 1H), 3.76 (s, 3H), 2.78 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 167.92, 166.63, 164.43, 159.48, 154.45, 149.51, 141.95, 136.91, 135.24, 130.58, 128.78, 128.46, 128.38, 125.79, 121.29, 110.95, 52.85, 22.88, 21.54; HRMS (ESI⁺) m/z : Calcd for $\text{C}_{21}\text{H}_{18}\text{N}_3\text{O}_3$ [M+H]⁺ 360.1343, Found 360.1341.



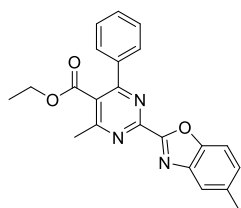
Ethyl 4-methyl-2-(4-phenylbenzo[d]oxazol-2-yl)-6-phenylpyrimidine-5-carboxylate (3ab). Light yellow oil. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.80 – 7.75 (m, 3H), 7.50-7.49 (m, 4H), 7.24 (d, $J = 8.4$ Hz, 1H), 4.24 (q, $J = 7.2$ Hz, 2H), 2.79 (s, 3H), 2.53 (s, 3H), 1.10 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 167.34, 166.51, 164.55, 159.02, 154.35, 151.66, 139.62, 137.79, 137.04, 130.42, 128.67, 128.55, 126.73, 126.07, 120.95, 111.55, 62.18, 22.82, 22.01, 13.62; HRMS (ESI^+) m/z : Calcd for $\text{C}_{22}\text{H}_{20}\text{N}_3\text{O}_3$ [$\text{M}+\text{H}$] $^+$ 374.1499, Found 374.1496.



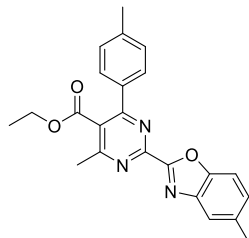
Ethyl 4-methyl-2-(4-methylbenzo[d]oxazol-2-yl)-6-(p-tolyl)pyrimidine-5-carboxylate (3bb). Grey solid, m.p. = 154-156 °C. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.62 (d, $J = 8.0$ Hz, 3H), 7.51 (d, $J = 8.4$ Hz, 1H), 7.20 (d, $J = 9.2$ Hz, 3H), 4.21 (q, $J = 7.2$ Hz, 2H), 2.71 (s, 3H), 2.44 (s, 3H), 2.36 (s, 3H), 1.09 (t, $J = 7.2$ Hz, 3H). $^{13}\text{C NMR}$ (600 MHz, CDCl_3): δ 167.81, 166.56, 164.60, 159.85, 154.53, 149.84, 142.21, 141.12, 135.41, 134.34, 129.64, 128.79, 128.52, 126.15, 121.51, 111.18, 62.41, 23.04, 21.78, 19.38, 13.96. HRMS (ESI^+) m/z : Calcd for $\text{C}_{23}\text{H}_{22}\text{N}_3\text{O}_3$ [$\text{M}+\text{H}$] $^+$ 388.1656, Found 388.1655.



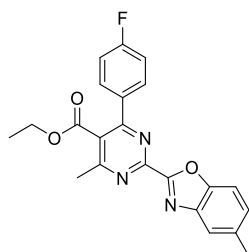
Ethyl 4-(4-fluorophenyl)-6-methyl-2-(4-methylbenzo[d]oxazol-2-yl)pyrimidine-5-carboxylate (3cb). Grey solid, m.p. = 137-139 °C. $^1\text{H NMR}$ (600 MHz, CDCl_3): δ 7.79-7.77 (m, 2H), 7.69 (s, 1H), 7.57 (d, $J = 8.4$ Hz, 1H), 7.27 (d, $J = 9.0$ Hz, 1H), 7.18 (t, $J = 8.4$ Hz, 2H), 4.26 (q, $J = 6.6$ Hz, 2H), 2.78 (s, 3H), 2.50 (s, 3H), 1.15 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3): δ 167.26, 166.65, 165.08, 163.42, 163.26, 159.38, 154.33, 149.59, 141.92, 135.28, 130.74, 128.43, 125.96, 121.30, 115.94, 110.94, 62.30, 22.83, 21.53, 13.73; HRMS (ESI^+) m/z : Calcd for $\text{C}_{22}\text{H}_{19}\text{FN}_3\text{O}_3$ [$\text{M}+\text{H}$] $^+$ 392.1405, Found 392.1407.



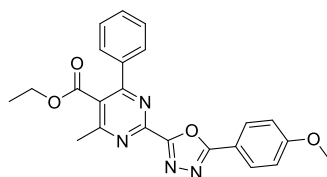
Ethyl 4-methyl-2-(5-methylbenzo[d]oxazol-2-yl)-6-phenylpyrimidine-5-carboxylate (3ac). Light yellow oil. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.78 – 7.76 (m, 2H), 7.71 (s, 1H), 7.59 (d, $J = 8.8$ Hz, 1H), 7.51–7.50 (m, 3H), 7.28 (d, $J = 10.0$ Hz, 1H), 4.25 (q, $J = 7.2$ Hz, 2H), 2.80 (s, 3H), 2.51 (s, 3H), 1.11 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 167.33, 166.54, 164.57, 159.52, 154.33, 149.61, 141.95, 137.02, 135.23, 130.43, 128.68, 128.55, 128.35, 126.15, 121.29, 110.96, 62.20, 22.82, 21.53, 13.63; HRMS (ESI $^+$) m/z : Calcd for $\text{C}_{22}\text{H}_{20}\text{N}_3\text{O}_3$ [M+H] $^+$ 374.1499, Found 374.1506.



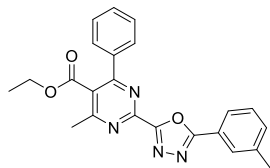
Ethyl 4-methyl-2-(5-methylbenzo[d]oxazol-2-yl)-6-(p-tolyl)pyrimidine-5-carboxylate (3bc). Yellow solid, m.p. = 146–148 °C. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.72 (d, $J = 12$ Hz, 1H), 7.62 (d, $J = 12$ Hz, 2H), 7.42 (s, 1H), 7.26 – 7.13 (m, 3H), 4.20 (q, $J = 10.8$ Hz, 2H), 2.70 (s, 3H), 2.46 (s, 3H), 2.35 (s, 3H), 1.09 (t, $J = 10.8$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 167.83, 166.53, 164.58, 159.35, 154.54, 151.89, 141.10, 139.87, 137.95, 134.35, 129.63, 128.79, 126.93, 126.07, 121.16, 111.78, 62.40, 23.04, 22.25, 21.67, 13.96; HRMS (ESI $^+$) m/z : Calcd for $\text{C}_{23}\text{H}_{22}\text{N}_3\text{O}_3$ [M+H] $^+$ 388.1656, Found 388.1653.



Ethyl 4-(4-fluorophenyl)-6-methyl-2-(5-methylbenzo[d]oxazol-2-yl)pyrimidine-5-carboxylate (3cc). Yellow solid, m.p. = 153–155 °C. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.79 – 7.77 (m, 3H), 7.53 – 7.49 (m, 2H), 7.18 (t, $J = 8.4$ Hz, 2H), 4.26 (q, $J = 7.2$ Hz, 2H), 2.78 (s, 3H), 2.52 (s, 3H), 1.15 (t, $J = 7.2$ Hz, 3H). $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 167.28, 166.63, 163.25, 158.90, 151.65, 137.89, 132.35, 130.87, 130.74, 126.79, 120.97, 115.93, 111.53, 62.30, 22.02, 19.13, 13.73; HRMS (ESI $^+$) m/z : Calcd for $\text{C}_{22}\text{H}_{19}\text{FN}_3\text{O}_3$ [M+H] $^+$ 392.1405, Found 392.1407.

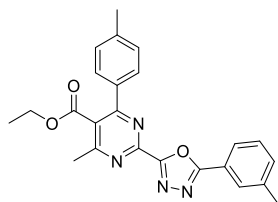


Ethyl 2-(5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl)-4-methyl-6-phenylpyrimidine-5-carboxylate (3ad). Light yellow oil. $^1\text{H NMR}$ (600 MHz, CDCl_3): δ 8.19 (d, $J = 8.4$ Hz, 2H), 7.77 (d, $J = 7.8$ Hz, 2H), 7.53 – 7.49 (m, 3H), 7.03 (d, $J = 9.0$ Hz, 2H), 4.26 (q, $J = 7.2$ Hz, 2H), 3.89 (s, 3H), 2.77 (s, 3H), 1.12 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3): δ 167.23, 166.71, 164.36, 162.78, 152.47, 136.75, 130.65, 129.43, 128.69, 128.61, 126.20, 115.89, 114.76, 114.49, 62.27, 55.48, 22.74, 13.64; HRMS (ESI $^+$) m/z : Calcd for $\text{C}_{23}\text{H}_{21}\text{N}_4\text{O}_4$ [M+H] $^+$ 417.1557, Found 417.1552.



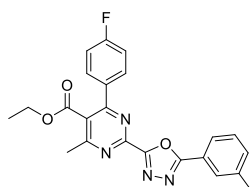
Ethyl 4-methyl-6-phenyl-2-(5-(m-tolyl)-1,3,4-oxadiazol-2-yl)pyrimidine-5-carboxylate (3ae).

Yellow solid, m.p. = 151-152 °C. ¹H NMR (600 MHz, CDCl₃): δ 8.08 (s, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 2H), 7.54-7.50 (m, 3H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 2.78 (s, 3H), 2.46 (s, 3H), 1.12 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (151 MHz, CDCl₃): δ 167.14, 166.76, 166.32, 164.41, 152.39, 138.99, 136.72, 133.09, 130.68, 128.94, 128.71, 128.61, 128.05, 124.75, 123.10, 114.95, 62.30, 22.75, 21.28, 13.64; HRMS (ESI⁺) *m/z*: Calcd for C₂₃H₂₁N₄O₃ [M+H]⁺ 401.1608, Found 401.1611.



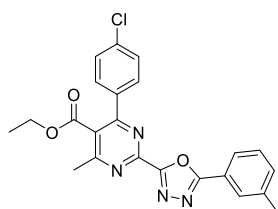
Ethyl 4-methyl-6-(p-tolyl)-2-(5-(m-tolyl)-1,3,4-oxadiazol-2-yl)pyrimidine-5-carboxylate (3be).

¹H NMR (600 MHz, CDCl₃): δ 8.08 (s, 1H), 8.04 (d, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 2H), 4.29 (q, *J* = 7.2 Hz, 2H), 2.76 (s, 3H), 2.46 (s, 3H), 2.44 (s, 3H), 1.17 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 167.10, 166.38, 164.33, 162.58, 152.38, 141.19, 139.09, 139.03, 133.05, 131.04, 129.44, 128.93, 128.62, 128.03, 124.73, 123.26, 62.26, 22.71, 21.45, 21.27, 13.72; HRMS (ESI⁺) *m/z*: Calcd for C₂₄H₂₃N₄O₃ [M+H]⁺ 415.1765, Found 415.1761.



Ethyl 4-(4-fluorophenyl)-6-methyl-2-(5-(m-tolyl)-1,3,4-oxadiazol-2-yl)pyrimidine-5-carboxylate (3ce).

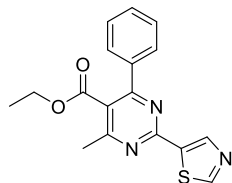
¹H NMR (600 MHz, CDCl₃) δ 8.07 (s, 1H), 8.03 (d, *J* = 7.2 Hz, 1H), 7.81-7.79 (m, 2H), 7.44 – 7.38 (m, 2H), 7.19 (t, *J* = 8.4 Hz, 2H), 4.29 (q, *J* = 7.2 Hz, 2H), 2.77 (s, 3H), 2.45 (s, 3H), 1.17 (t, *J* = 7.8 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃); δ 167.64, 166.86, 166.40, 165.21, 163.54, 162.42, 152.40, 139.00, 133.13, 130.88, 130.83, 128.95, 128.02, 126.15, 124.73, 123.22, 62.40, 22.74, 21.27, 13.74. HRMS (ESI⁺) *m/z*: Calcd for C₂₃H₂₀FN₄O₃ [M+H]⁺ 415.1765, Found 419.1514.



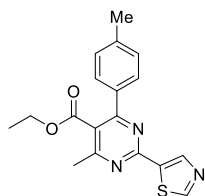
Ethyl 4-(4-chlorophenyl)-6-methyl-2-(5-(m-tolyl)-1,3,4-oxadiazol-2-yl)pyrimidine-5-carboxylate (3de).

Yellow solid, m.p. = 131-132 °C. ¹H NMR (600 MHz, CDCl₃): δ 8.07 (s, 1H), 8.04 (d, *J* = 7.2 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.45 – 7.39 (m, 2H), 4.30 (q, *J* = 7.1 Hz, 2H),

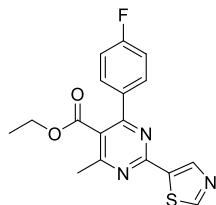
2.78 (s, 3H), 2.46 (s, 3H), 1.19 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3): δ 166.99, 166.34, 163.06, 162.37, 152.47, 139.02, 137.21, 135.07, 133.15, 130.03, 129.02, 128.97, 128.03, 126.18, 124.74, 123.21, 62.47, 22.77, 21.28, 13.75; HRMS (ESI⁺) m/z : Calcd for $\text{C}_{23}\text{H}_{20}\text{ClN}_4\text{O}_3$ $[\text{M}+\text{H}]^+$ 435.1218, Found 435.1213.



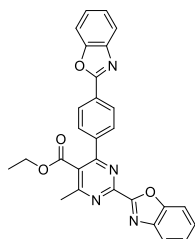
Ethyl 4-methyl-6-phenyl-2-(thiazol-2-yl)pyrimidine-5-carboxylate (3af). Yellow solid, m.p. = 126-128 °C. ^1H NMR (600 MHz, CDCl_3): δ 8.90 (s, 1H), 8.79 (s, 1H), 7.70 (d, $J = 6.6$ Hz, 2H), 7.50 – 7.46 (m, 3H), 4.20 (q, $J = 7.2$ Hz, 2H), 2.65 (s, 3H), 1.07 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3): δ 167.87, 165.88, 163.81, 159.31, 156.51, 145.41, 137.44, 130.26, 128.54, 128.39, 123.57, 61.91, 22.66, 13.62. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_3\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 326.0958, Found 326.0960.



Ethyl 4-methyl-2-(thiazol-2-yl)-6-(p-tolyl)pyrimidine-5-carboxylate (3bf). Yellow solid, m.p. = 126-128 °C. ^1H NMR (600 MHz, CDCl_3): δ 8.90 (s, 1H), 8.79 (s, 1H), 7.63 (d, $J = 7.8$ Hz, 2H), 7.28 (d, $J = 8.4$ Hz, 2H), 4.23 (q, $J = 7.2$ Hz, 2H), 2.63 (s, 3H), 2.42 (s, 3H), 1.13 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3): δ 168.09, 165.66, 163.61, 159.24, 156.41, 145.31, 140.67, 138.68, 134.54, 129.27, 128.38, 123.38, 61.88, 22.62, 21.40, 13.71. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_3\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 340.1114, Found 340.1112.

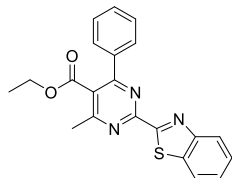


Ethyl 4-(4-fluorophenyl)-6-methyl-2-(thiazol-2-yl)pyrimidine-5-carboxylate (3cf). Light yellow oil. ^1H NMR (600 MHz, CDCl_3): δ 8.92 (s, 1H), 8.79 (s, 1H), 7.73 (t, $J = 8.4$ Hz, 2H), 7.17 (t, $J = 6.6$ Hz, 2H), 4.24 (q, $J = 7.2$ Hz, 2H), 2.65 (s, 3H), 1.14 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3): δ 167.81, 166.01, 162.53, 159.29, 156.60, 145.39, 130.59, 130.53, 123.42, 115.77, 115.62, 109.99, 62.01, 22.66, 13.73. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{17}\text{H}_{15}\text{FN}_3\text{O}_2\text{S}$ $[\text{M}+\text{H}]^+$ 344.0864, Found 344.0864.

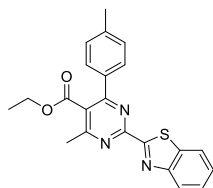


Ethyl 2-(benzo[d]oxazol-2-yl)-4-(4-(benzo[d]oxazol-2-yl)phenyl)-6-methylpyrimidine-5-carboxylate (3ja). Yellow solid, m.p. = 225-226 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.40 (d, $J =$

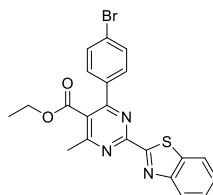
7.8 Hz, 2H), 7.96 (d, $J = 7.8$ Hz, 3H), 7.82 (d, $J = 5.4$ Hz, 1H), 7.74 (d, $J = 8.4$ Hz, 1H), 7.63 (d, $J = 5.4$ Hz, 1H), 7.50 – 7.39 (m, 4H), 4.28 (q, $J = 6.6$ Hz, 2H), 2.83 (s, 3H), 1.15 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 167.02, 163.52, 162.06, 159.29, 154.39, 151.34, 150.86, 142.03, 141.71, 139.68, 129.23, 128.99, 127.83, 127.14, 126.25, 125.60, 125.35, 124.84, 121.70, 120.24, 111.63, 110.72, 109.99, 62.46, 22.91, 13.73. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{28}\text{H}_{21}\text{N}_4\text{O}_4$ [M+H]⁺ 477.1557, Found 477.1559.



Ethyl 2-(benzo[d]thiazol-2-yl)-4-methyl-6-phenylpyrimidine-5-carboxylate (5aa). Yellow solid, m.p. = 149-150 °C ^1H NMR (600 MHz, CDCl_3): δ 8.29 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 7.8$ Hz, 1H), 7.78 (d, $J = 9.6$ Hz, 2H), 7.54 – 7.45 (m, 5H), 4.24 (q, $J = 7.2$ Hz, 2H), 2.78 (s, 3H), 1.10 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3): δ 167.56, 166.63, 164.01, 158.77, 154.43, 136.98, 136.86, 130.48, 128.61, 128.58, 126.54, 126.53, 125.60, 125.08, 121.82, 62.12, 22.83, 13.64. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{17}\text{H}_{14}\text{FN}_3\text{O}_2\text{S}$ [M+H]⁺ 343.0791, Found 343.0794. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{21}\text{H}_{18}\text{N}_3\text{O}_2\text{S}$ [M+H]⁺ 376.1114, Found 376.112



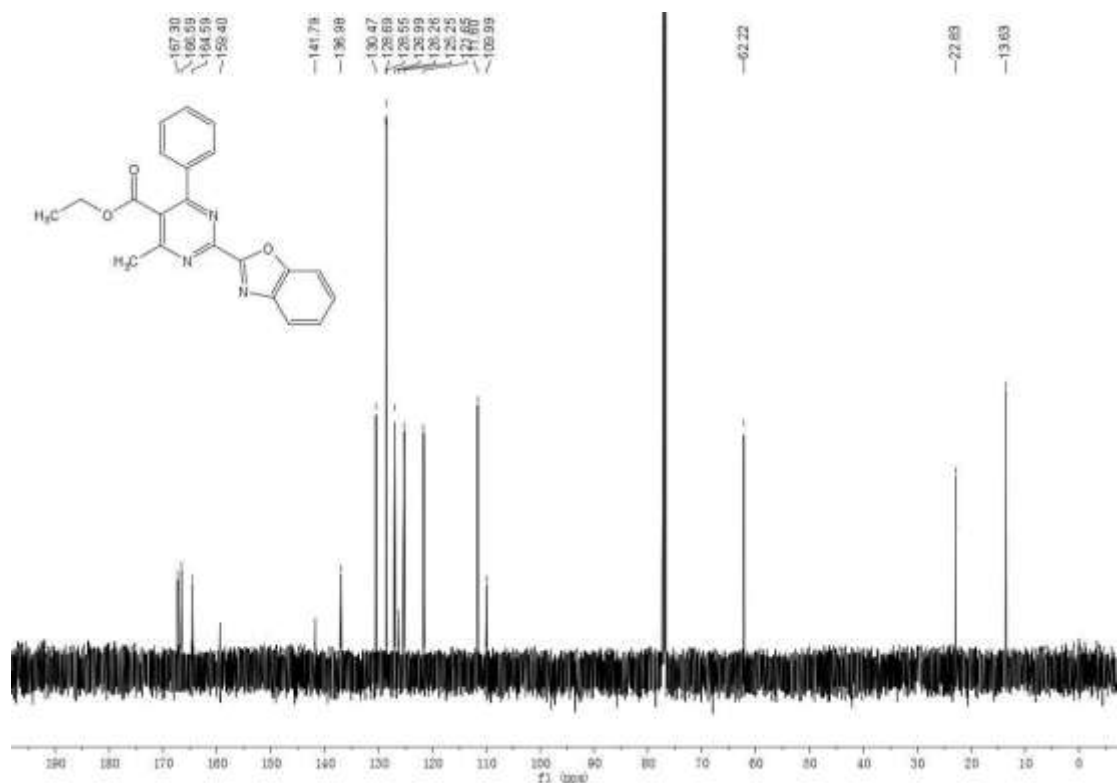
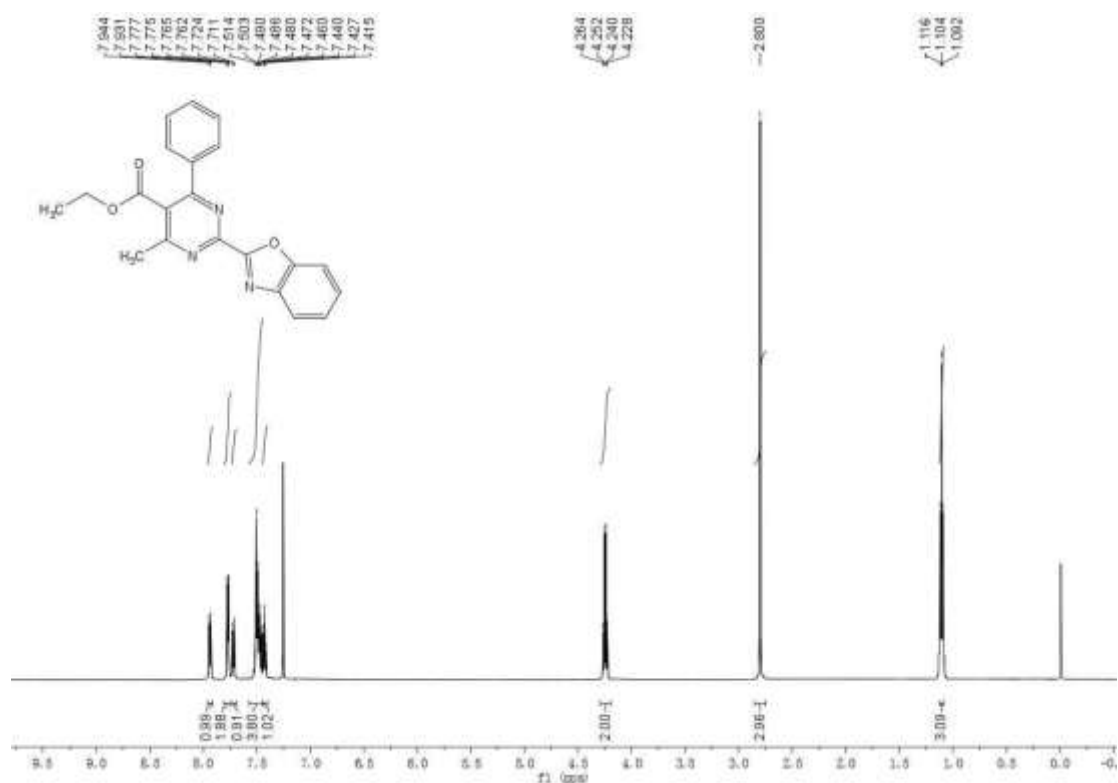
Ethyl 2-(benzo[d]thiazol-2-yl)-4-methyl-6-(p-tolyl)pyrimidine-5-carboxylate (5ba). Light yellow oil. ^1H NMR (600 MHz, CDCl_3) δ 8.29 (d, $J = 8.4$ Hz, 1H), 7.96 (d, $J = 7.8$ Hz, 1H), 7.71 (d, $J = 7.8$ Hz, 2H), 7.53 (t, $J = 7.2$ Hz, 1H), 7.47 (t, $J = 7.8$ Hz, 1H), 7.30 (d, $J = 8.4$ Hz, 2H), 4.27 (q, $J = 6.6$ Hz, 2H), 2.77 (s, 3H), 2.43 (s, 3H), 1.17 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 167.81, 166.80, 166.46, 163.77, 158.70, 154.44, 140.96, 136.86, 134.04, 129.36, 128.57, 126.51, 126.48, 125.35, 125.06, 121.82, 62.12, 22.82, 21.45, 13.73. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{17}\text{H}_{14}\text{FN}_3\text{O}_2\text{S}$ [M+H]⁺ 343.0791, Found 343.0794. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_2\text{S}$ [M+H]⁺ 379.1271, Found 390.1273.



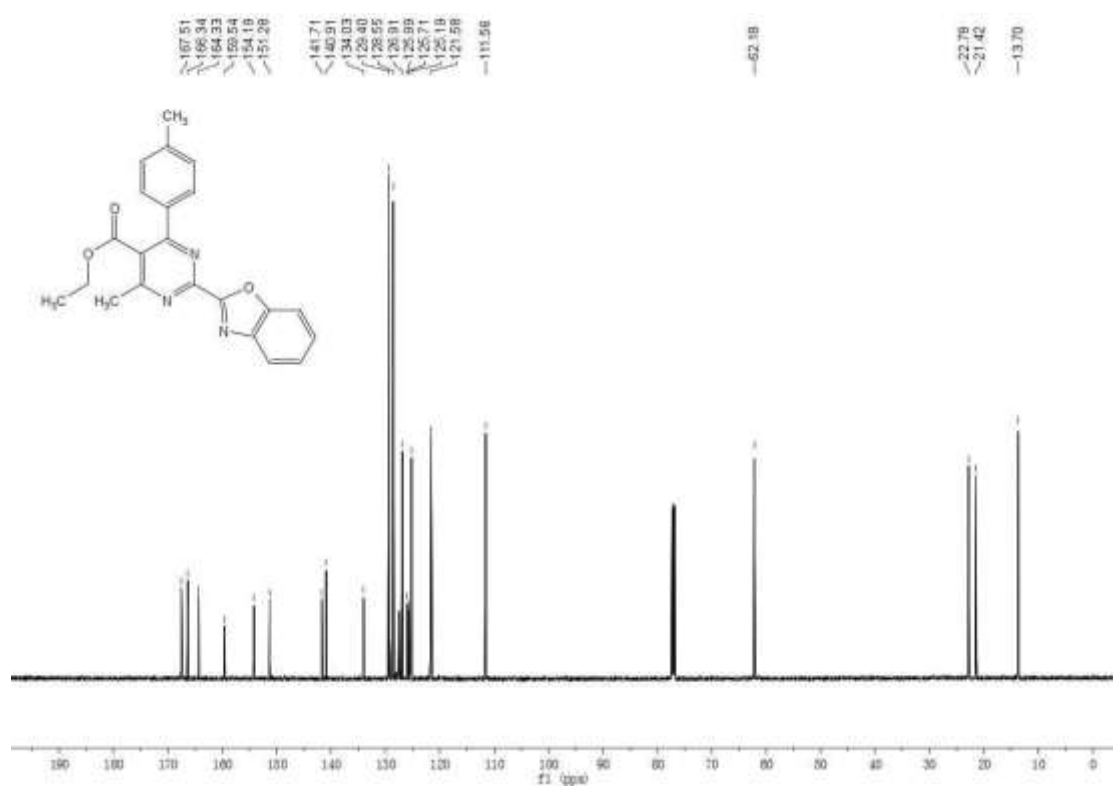
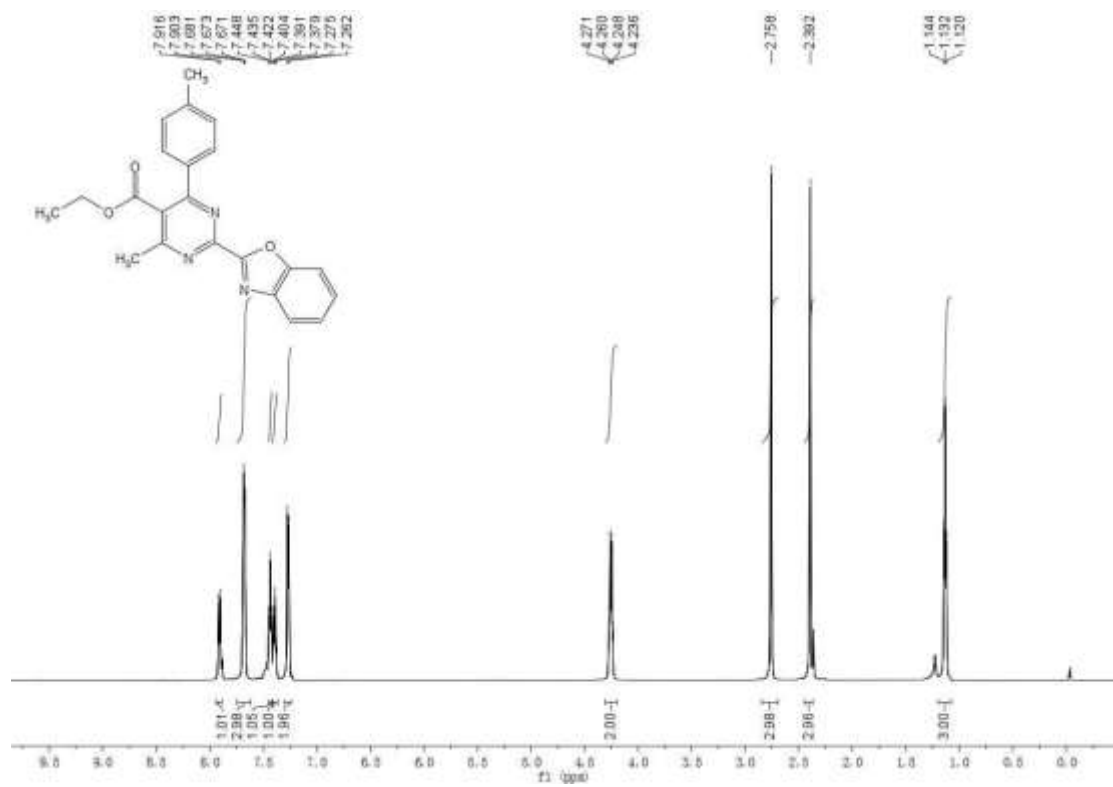
Ethyl 2-(benzo[d]thiazol-2-yl)-4-(4-bromophenyl)-6-methylpyrimidine-5-carboxylate (5da). Yellow solid, m.p. = 129-131 °C ^1H NMR (600 MHz, CDCl_3) δ 8.29 (d, $J = 8.4$ Hz, 1H), 7.97 (d, $J = 7.8$ Hz, 1H), 7.67 (d, $J = 8.4$ Hz, 2H), 7.64 (d, $J = 9.0$ Hz, 2H), 7.54 (t, $J = 7.2$ Hz, 1H), 7.48 (t, $J = 6.6$ Hz, 1H), 4.28 (q, $J = 7.2$ Hz, 2H), 2.78 (s, 3H), 1.18 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 167.36, 166.91, 166.35, 162.79, 158.85, 154.42, 136.84, 135.83, 131.89, 130.18, 126.64, 126.62, 125.41, 125.33, 125.12, 121.84, 62.32, 22.87, 13.75. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{17}\text{H}_{14}\text{FN}_3\text{O}_2\text{S}$ [M+H]⁺ 343.0791, Found 343.0794. HRMS (ESI⁺) m/z : Calcd for $\text{C}_{21}\text{H}_{17}\text{BrN}_3\text{O}_2\text{S}$ [M+H]⁺ 454.0219, Found 454.0218

3 Copies of the NMR Spectra for All Products.

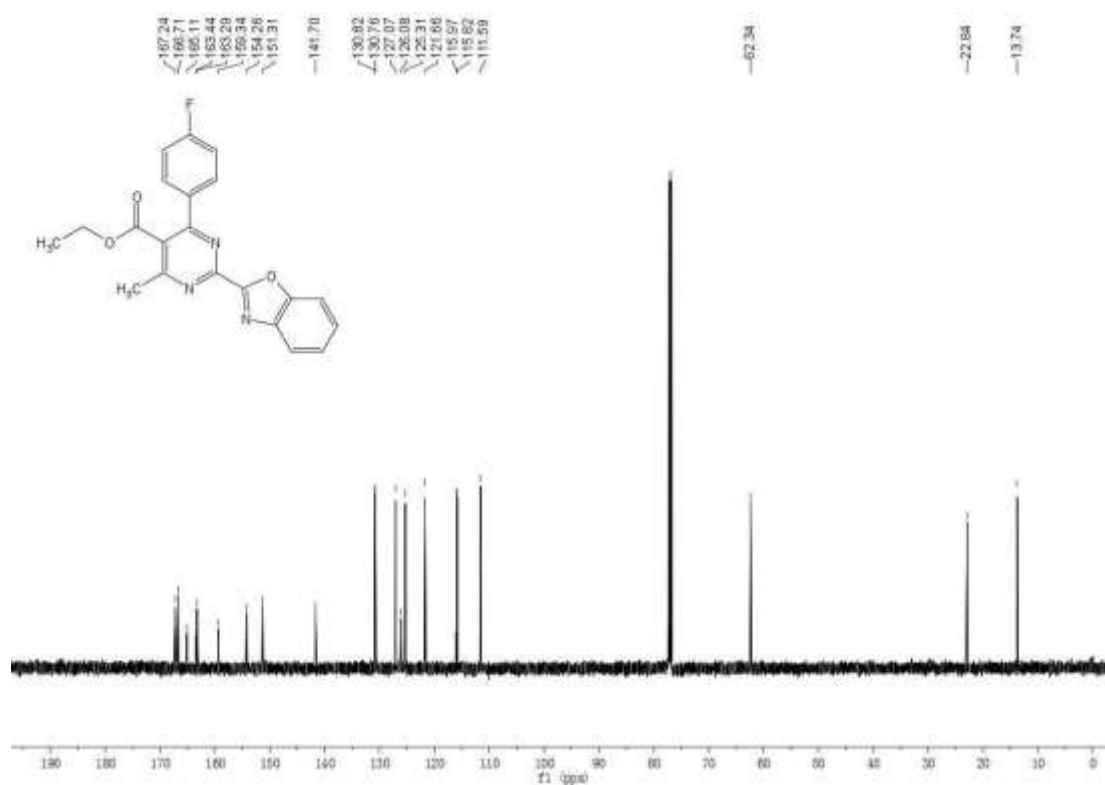
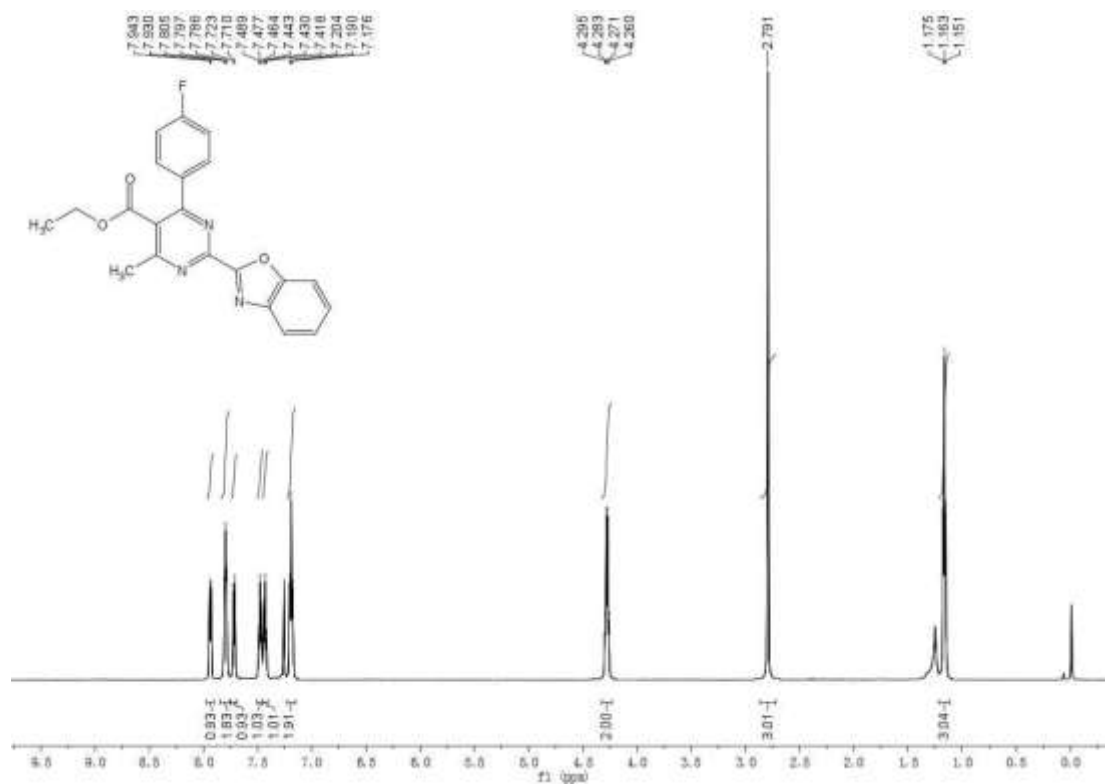
^1H and ^{13}C Spectra of compound 3aa (CDCl_3 , 600 MHz)



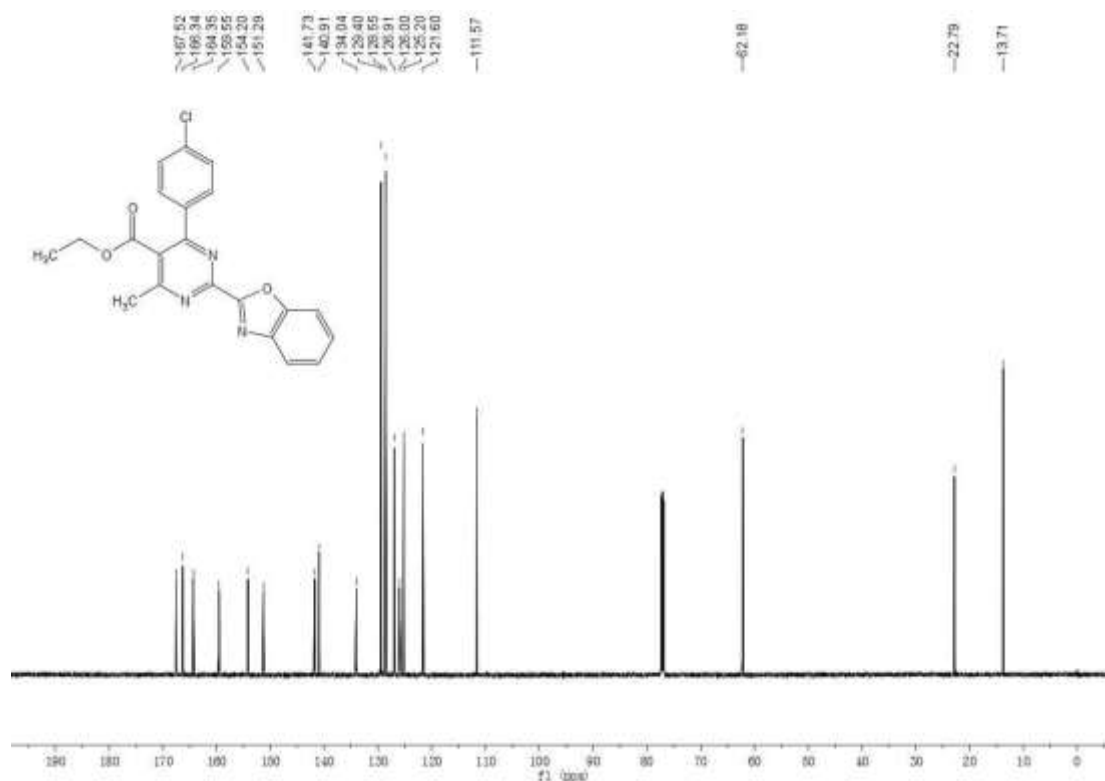
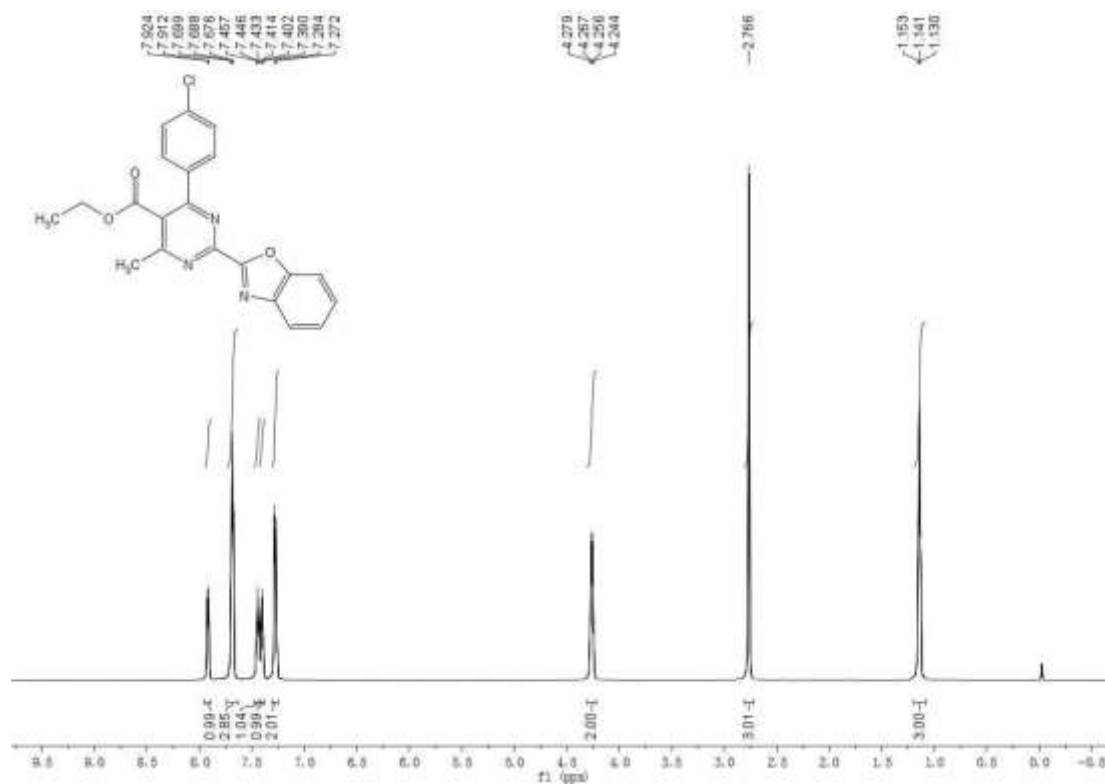
¹H and ¹³C Spectra of compound 3ba (CDCl₃, 600 MHz)



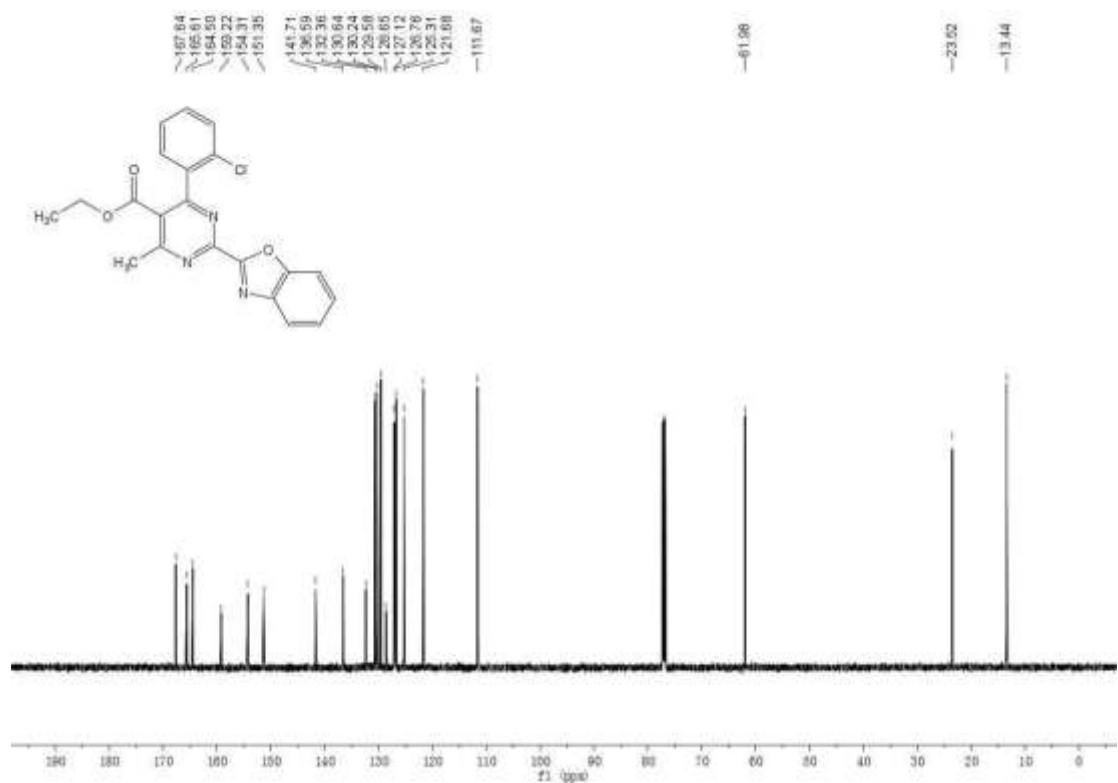
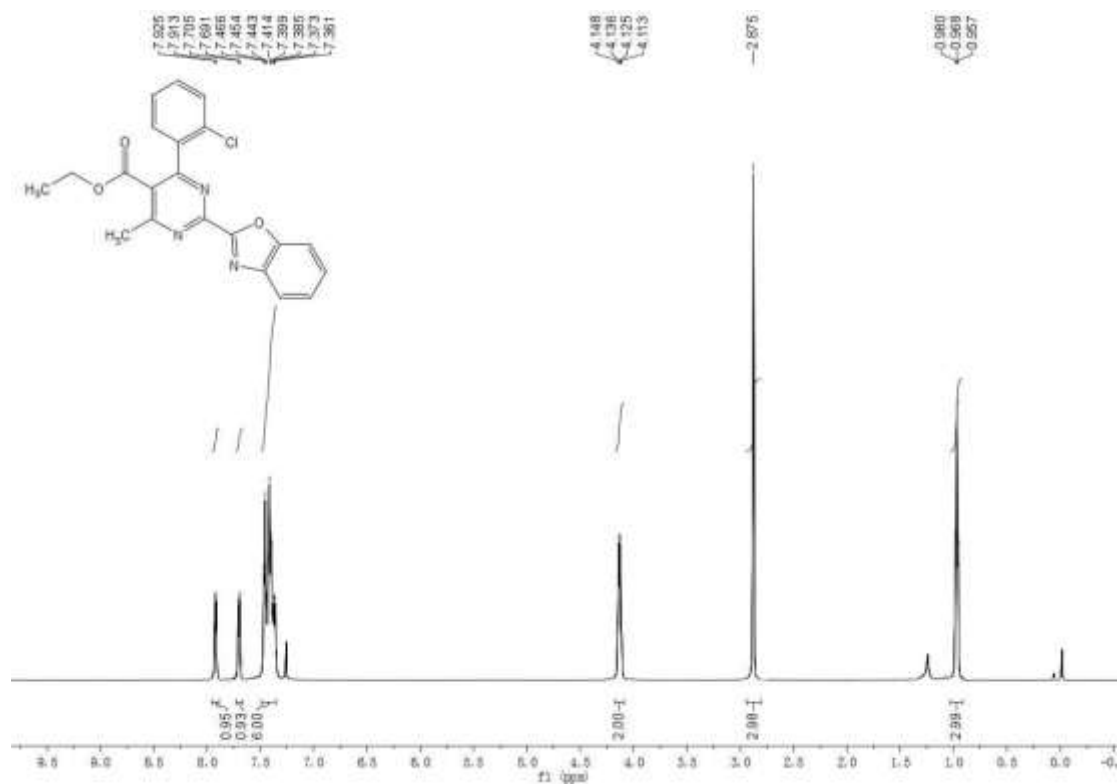
^1H and ^{13}C Spectra of compound 3ca (CDCl_3 , 600 MHz)



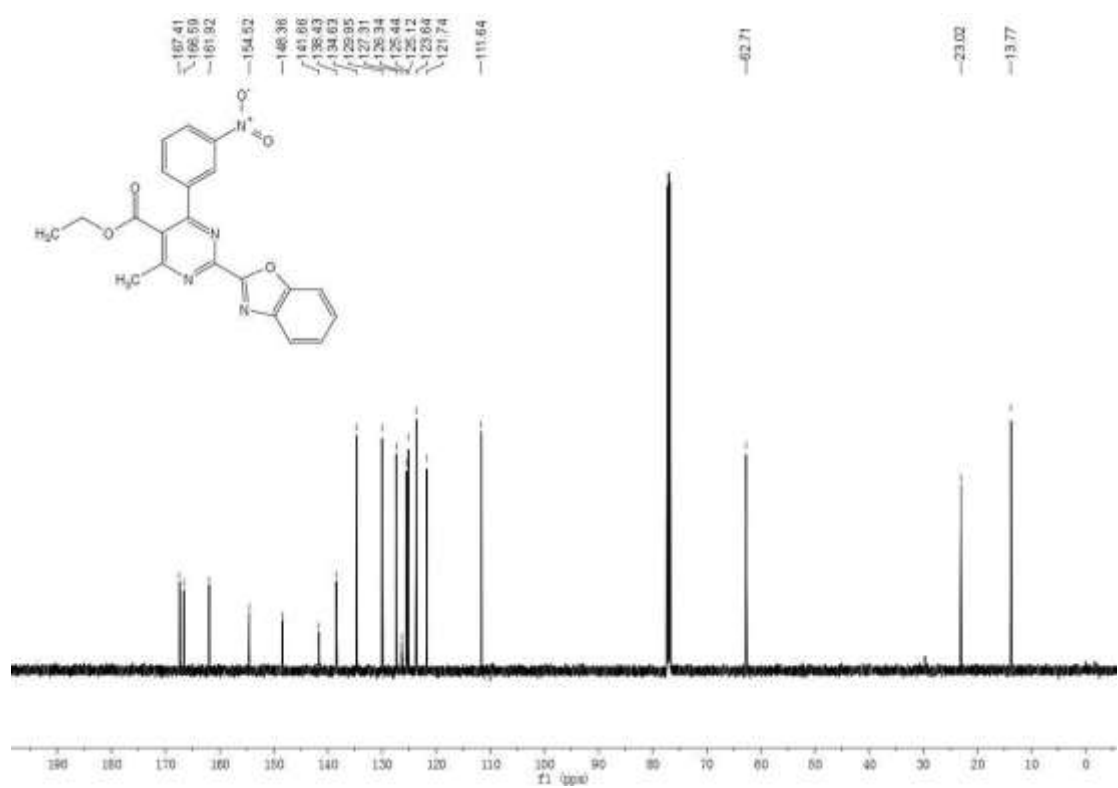
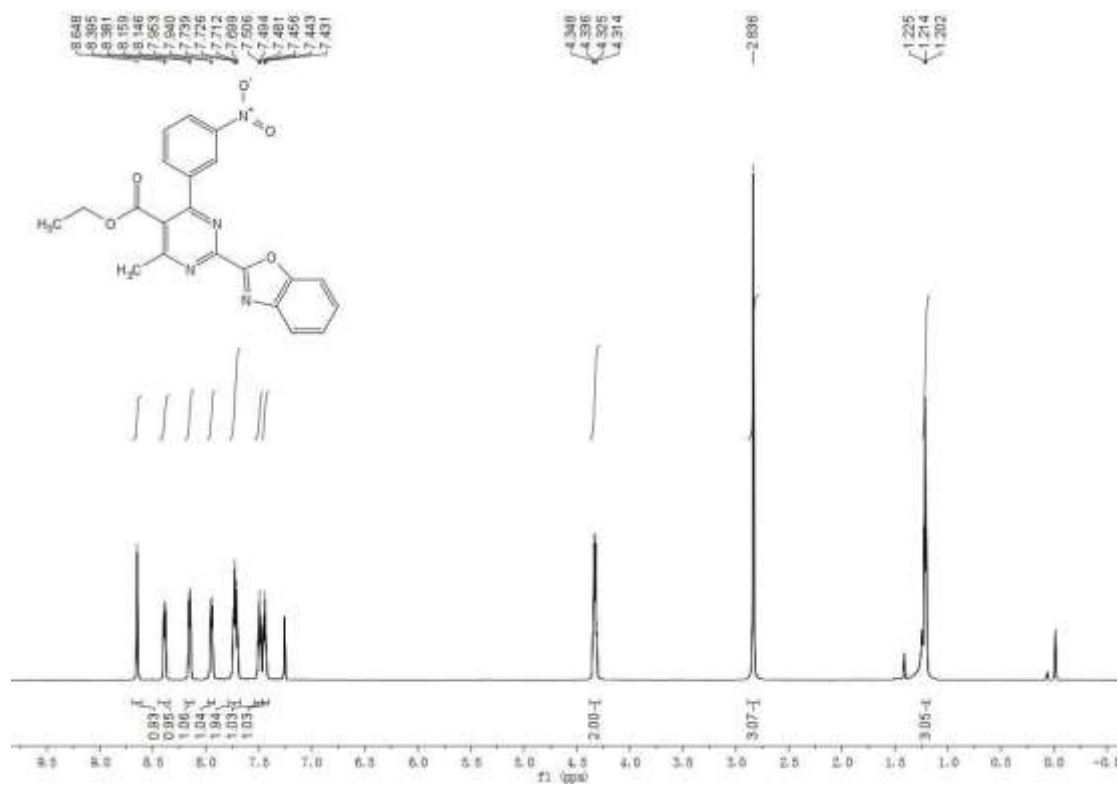
¹H and ¹³C Spectra of compound 3da (CDCl₃, 600 MHz)



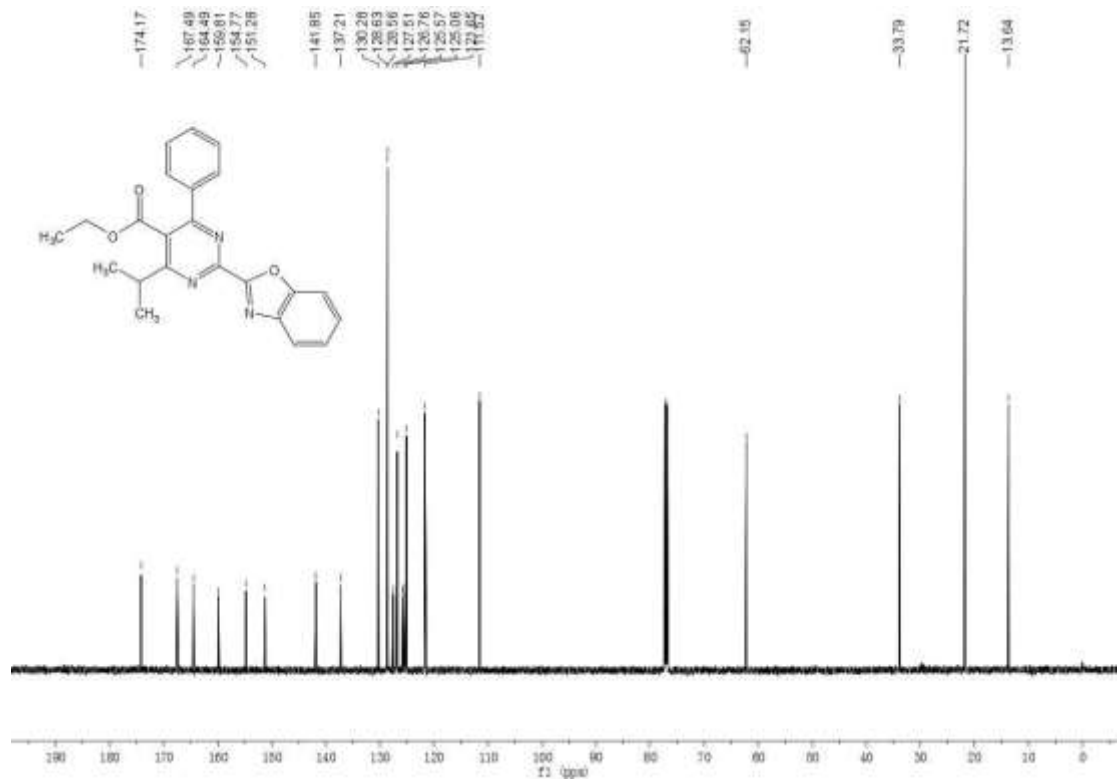
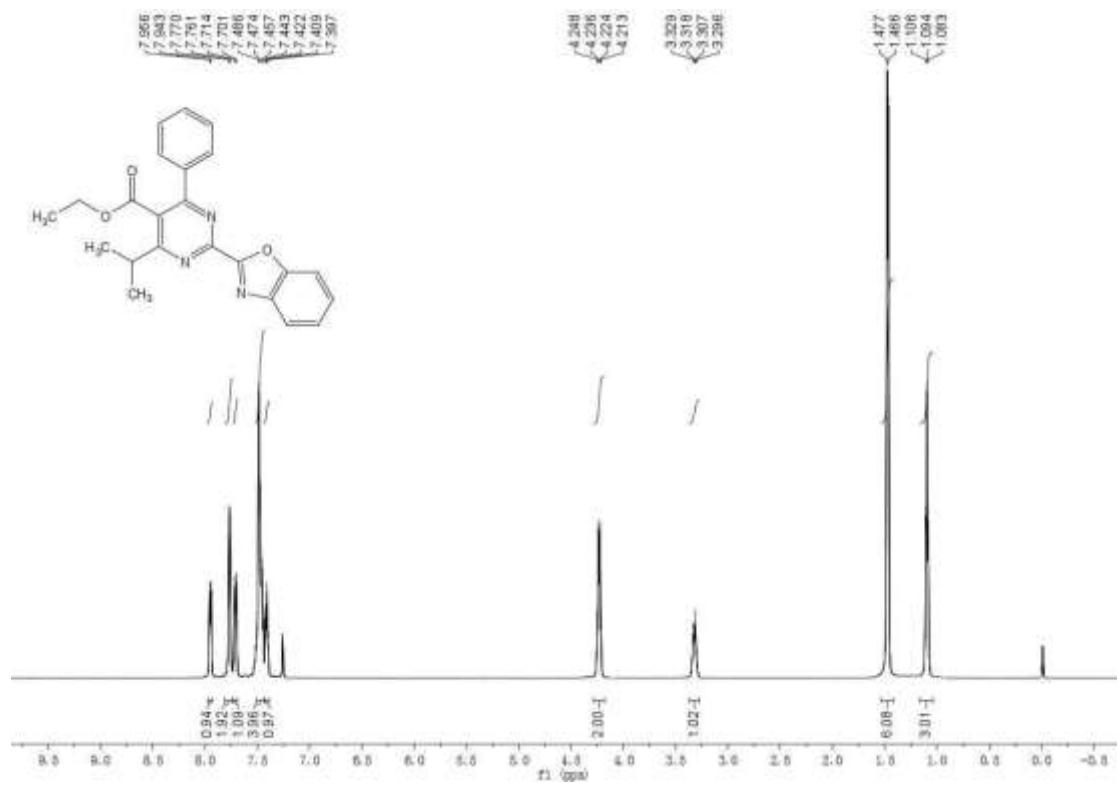
¹H and ¹³C Spectra of compound 3ea (CDCl₃, 600 MHz)



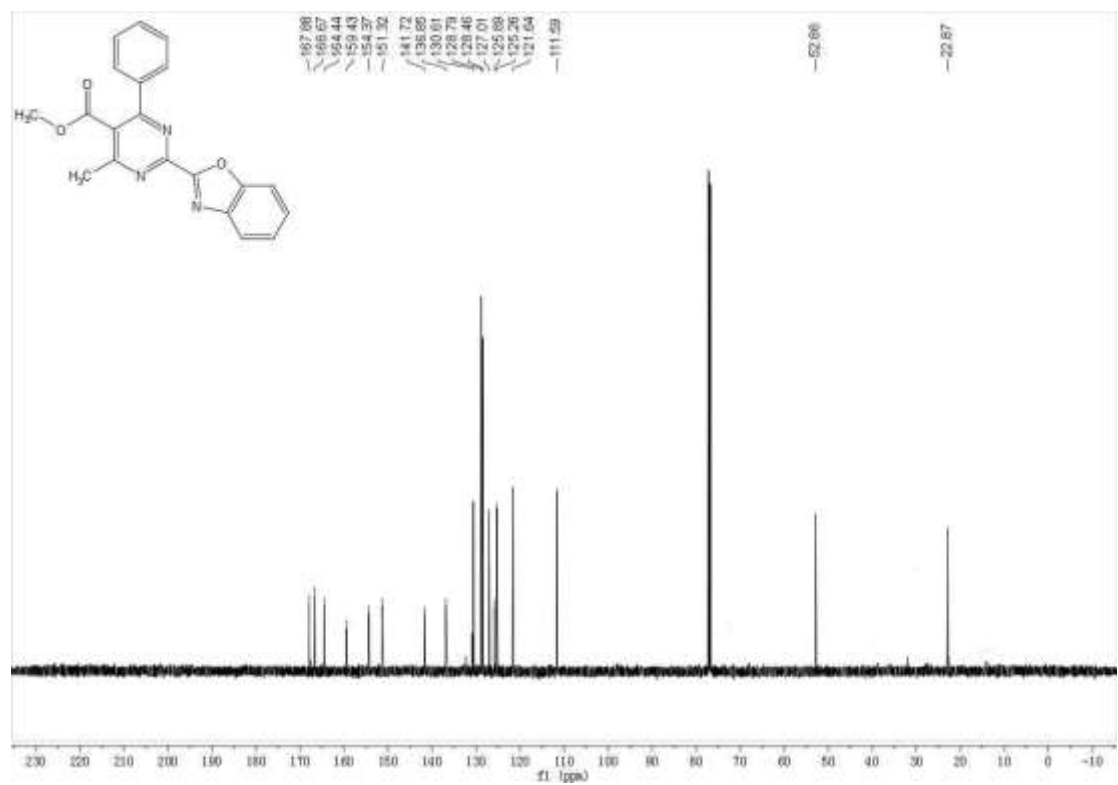
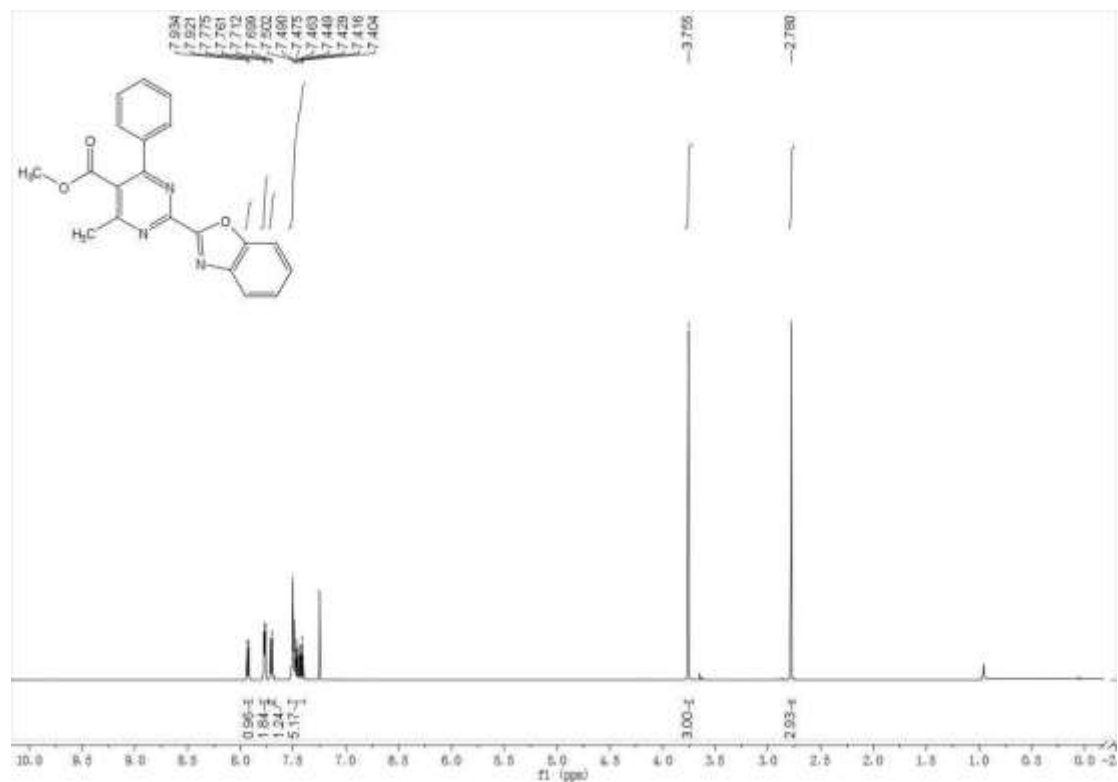
¹H and ¹³C Spectra of compound 3fa (CDCl₃, 600 MHz)



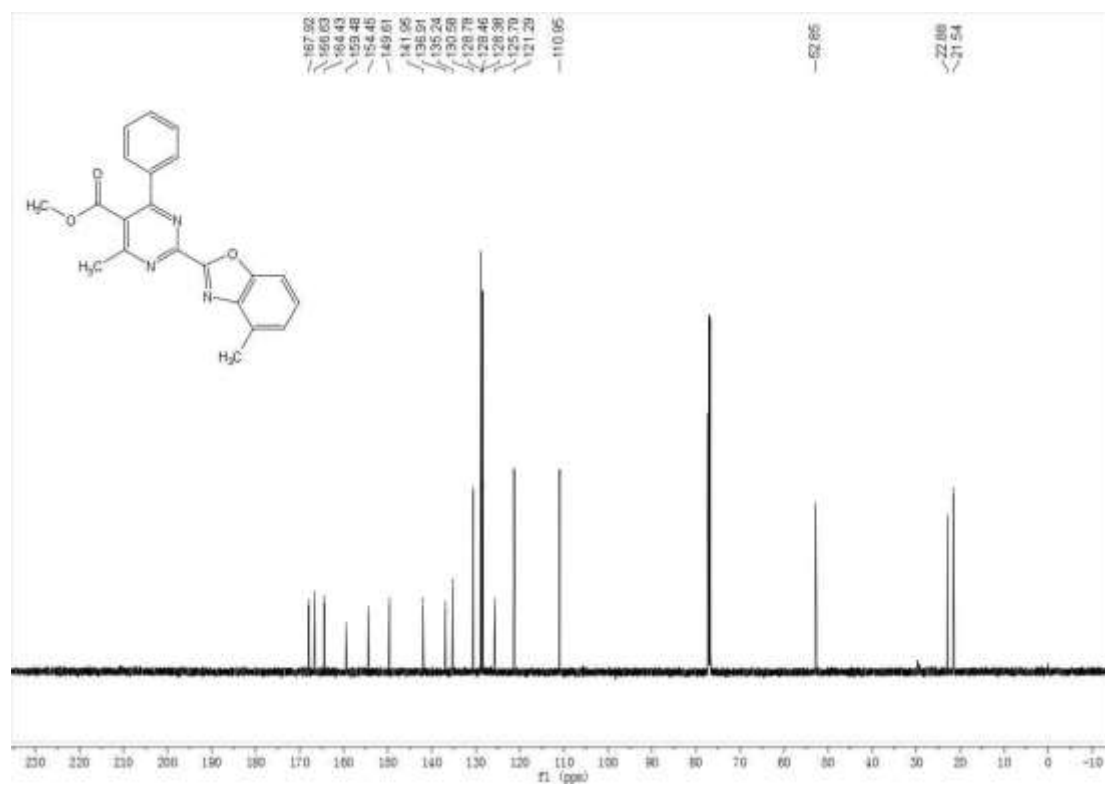
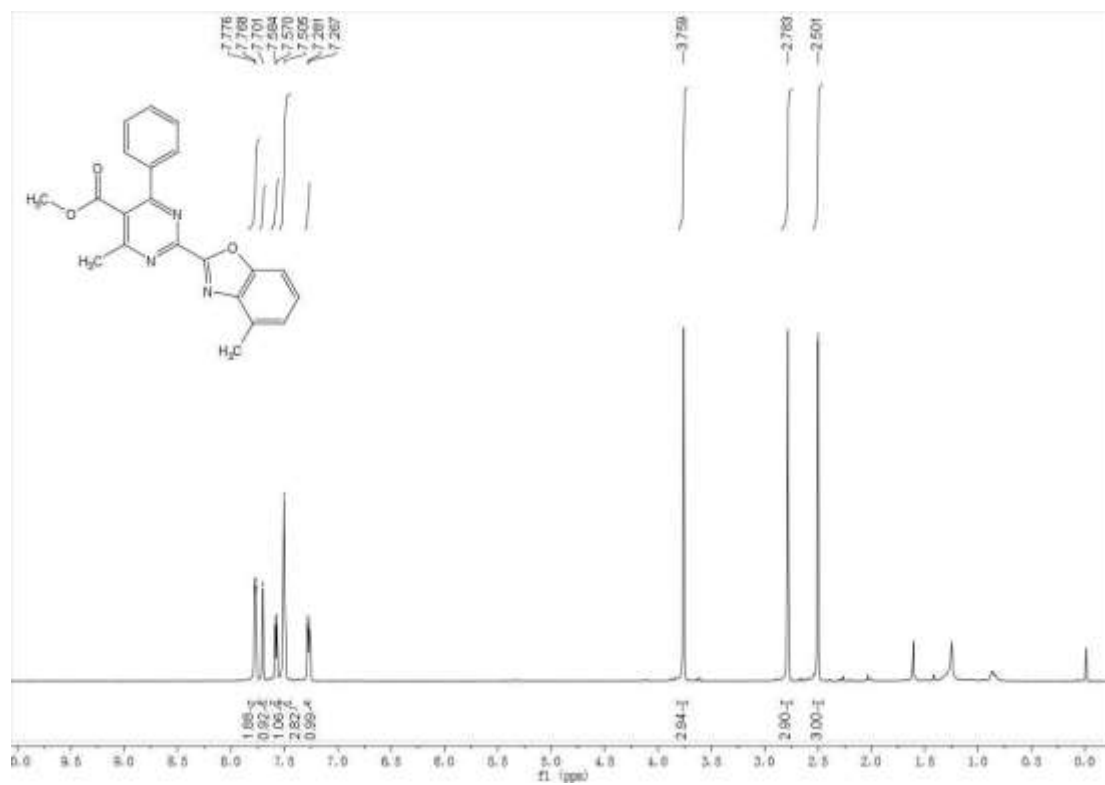
^1H and ^{13}C Spectra of compound 3ga (CDCl₃, 600 MHz)



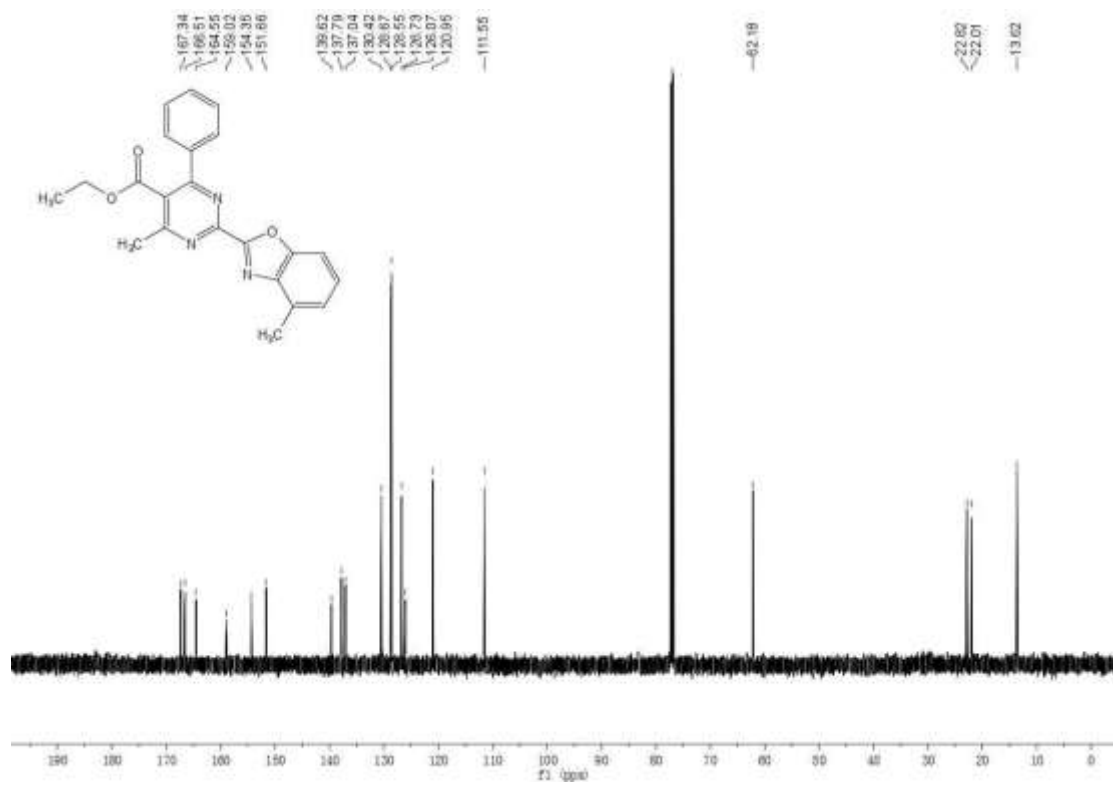
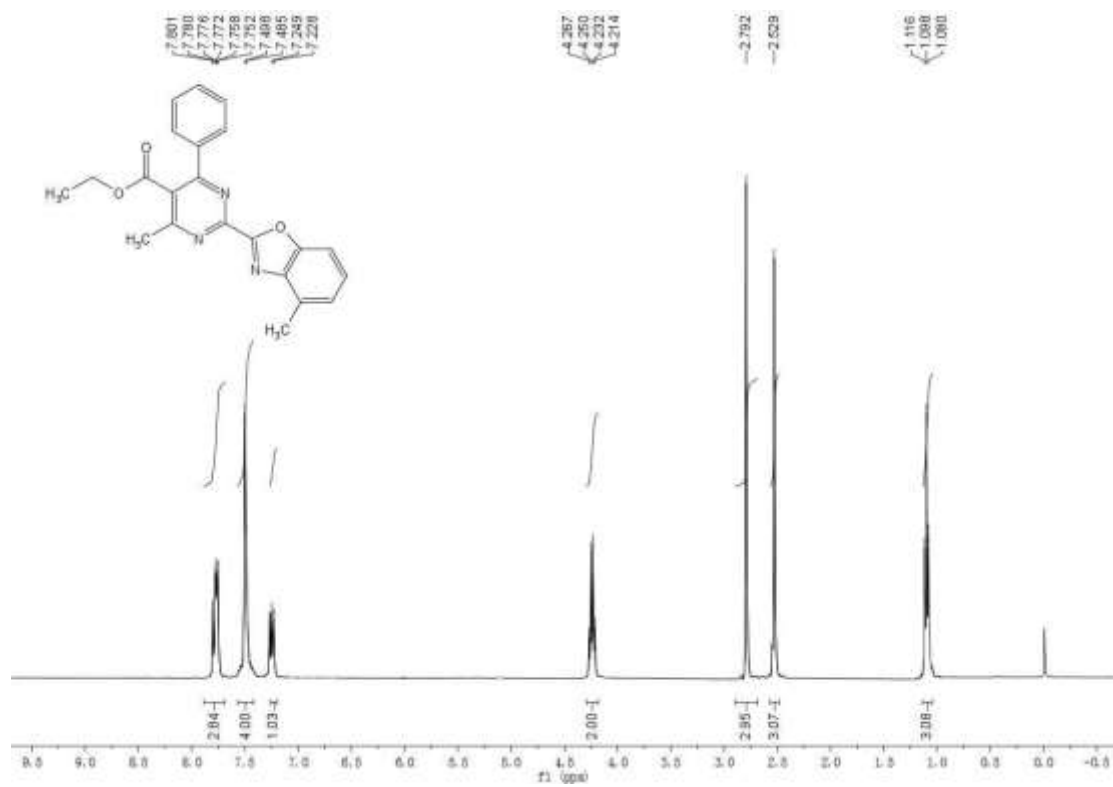
¹H and ¹³C Spectra of compound 3ha (CDCl₃, 600 MHz)



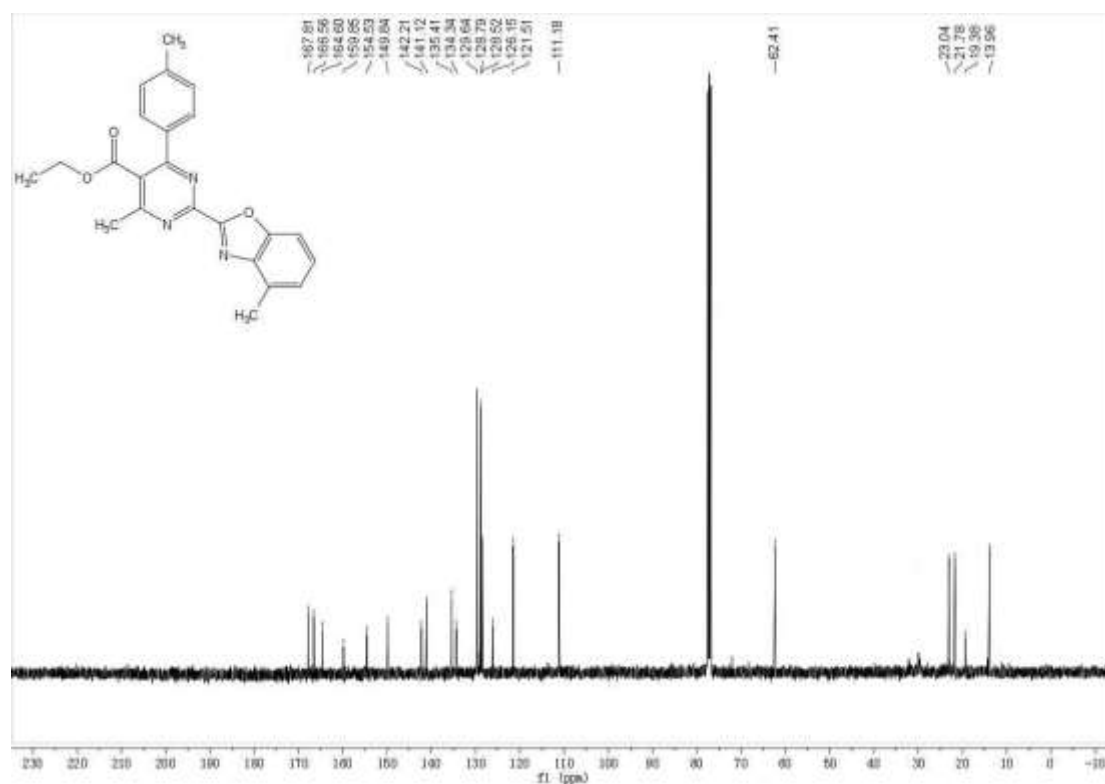
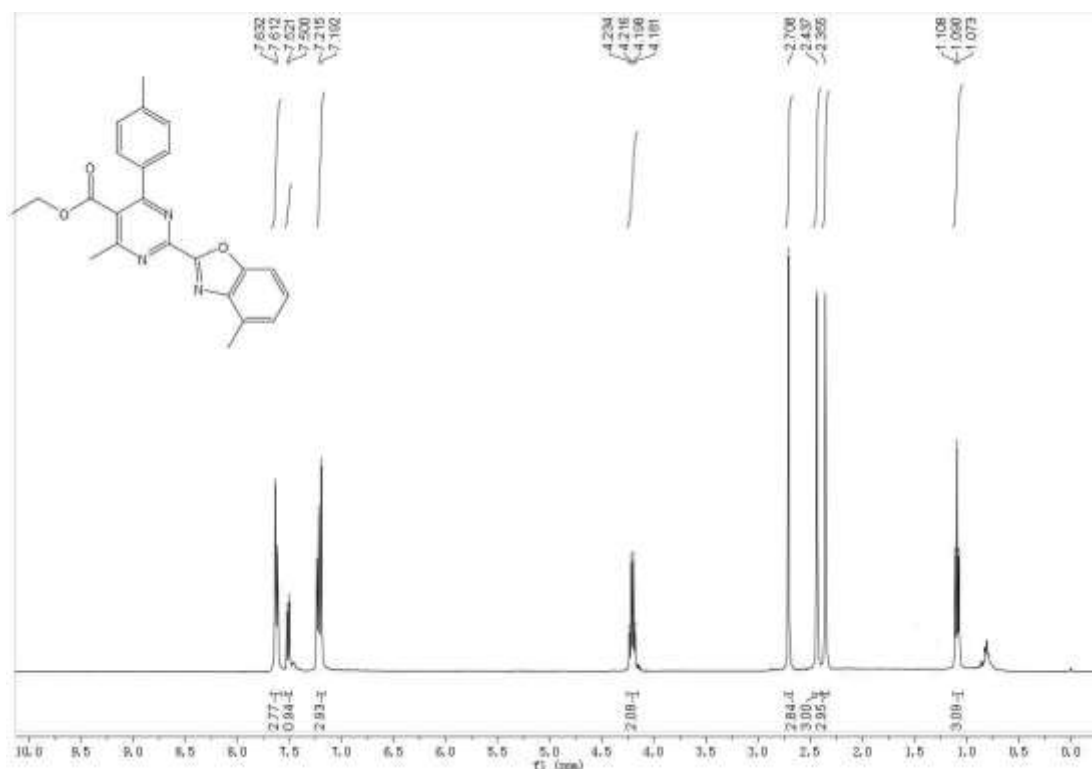
¹H and ¹³C Spectra of compound 3hb (CDCl₃, 600 MHz)



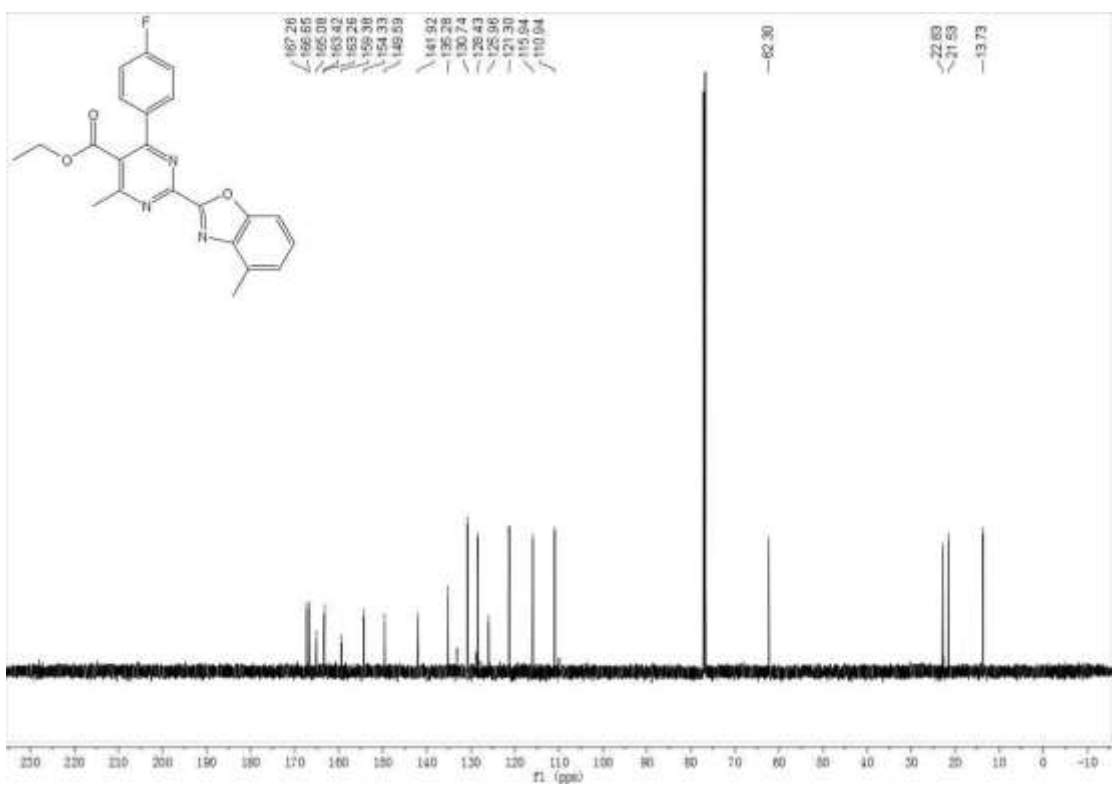
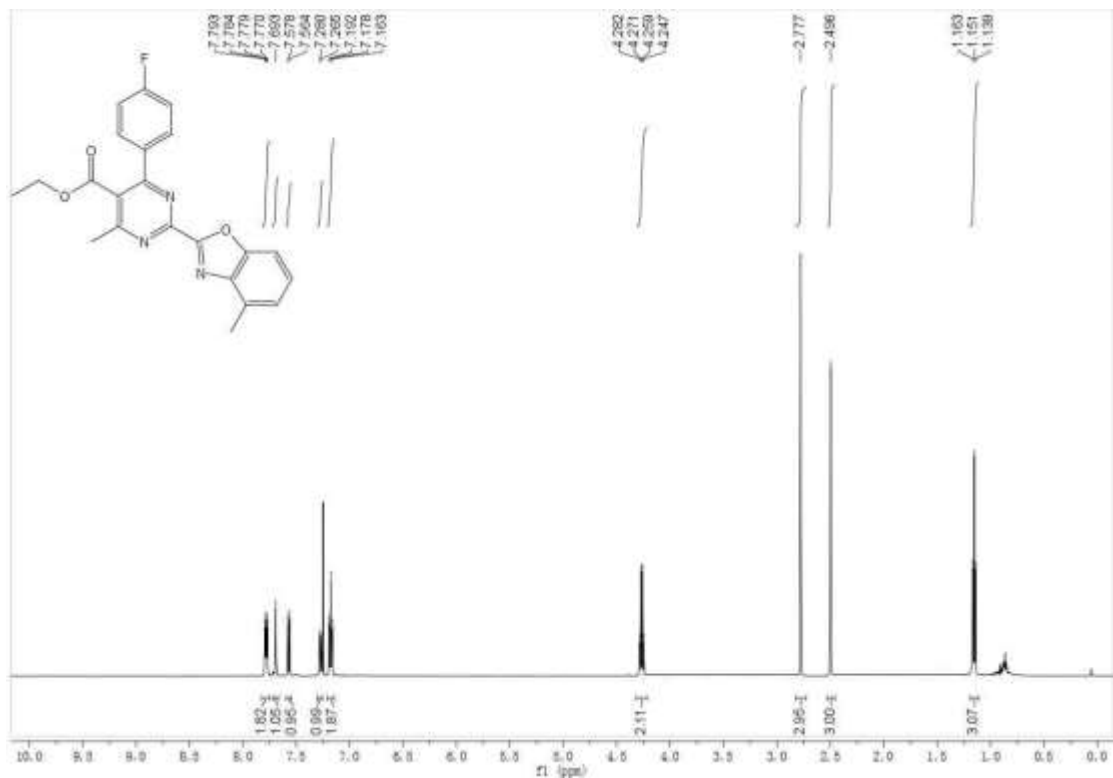
¹H and ¹³C Spectra of compound 3ab (CDCl₃, 600 MHz)



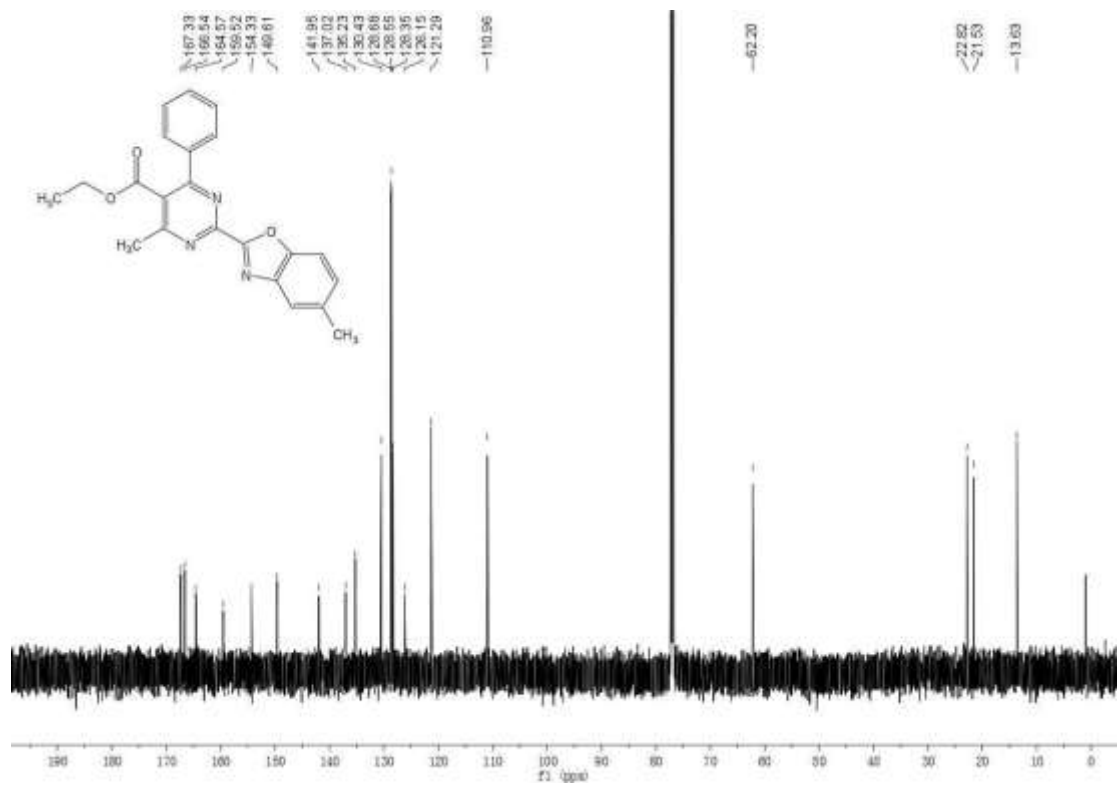
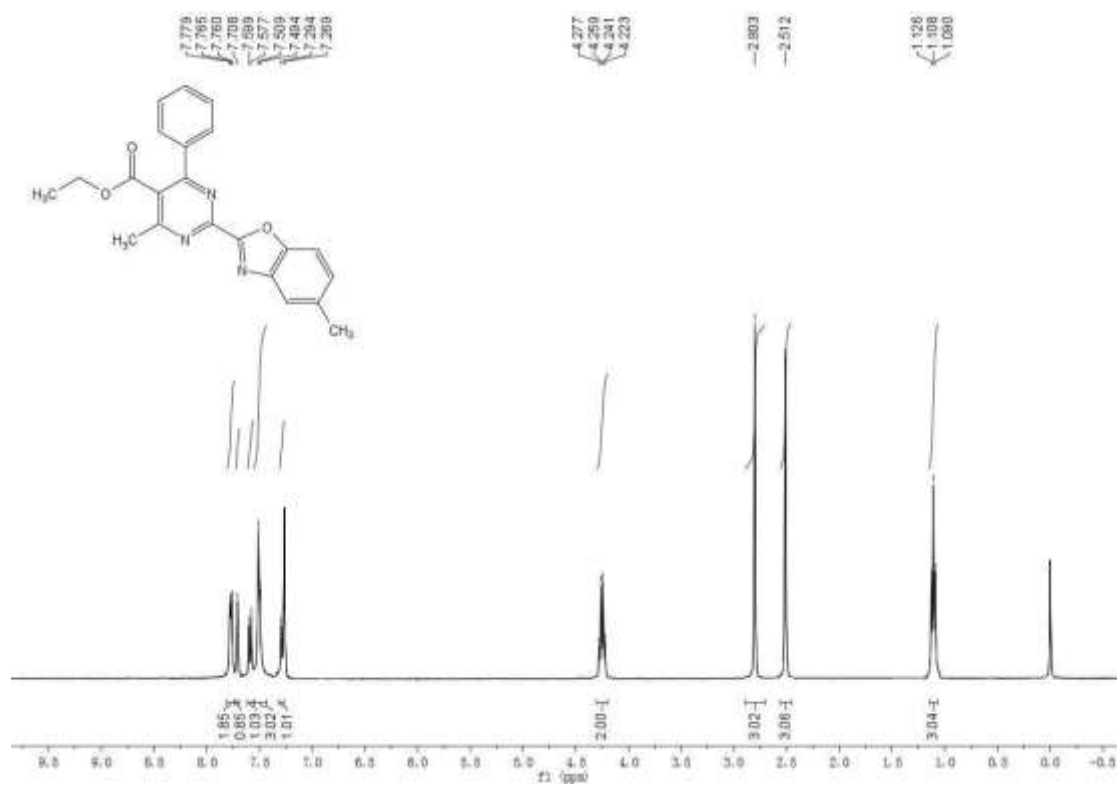
¹H and ¹³C Spectra of compound 3bb (CDCl₃, 600 MHz)



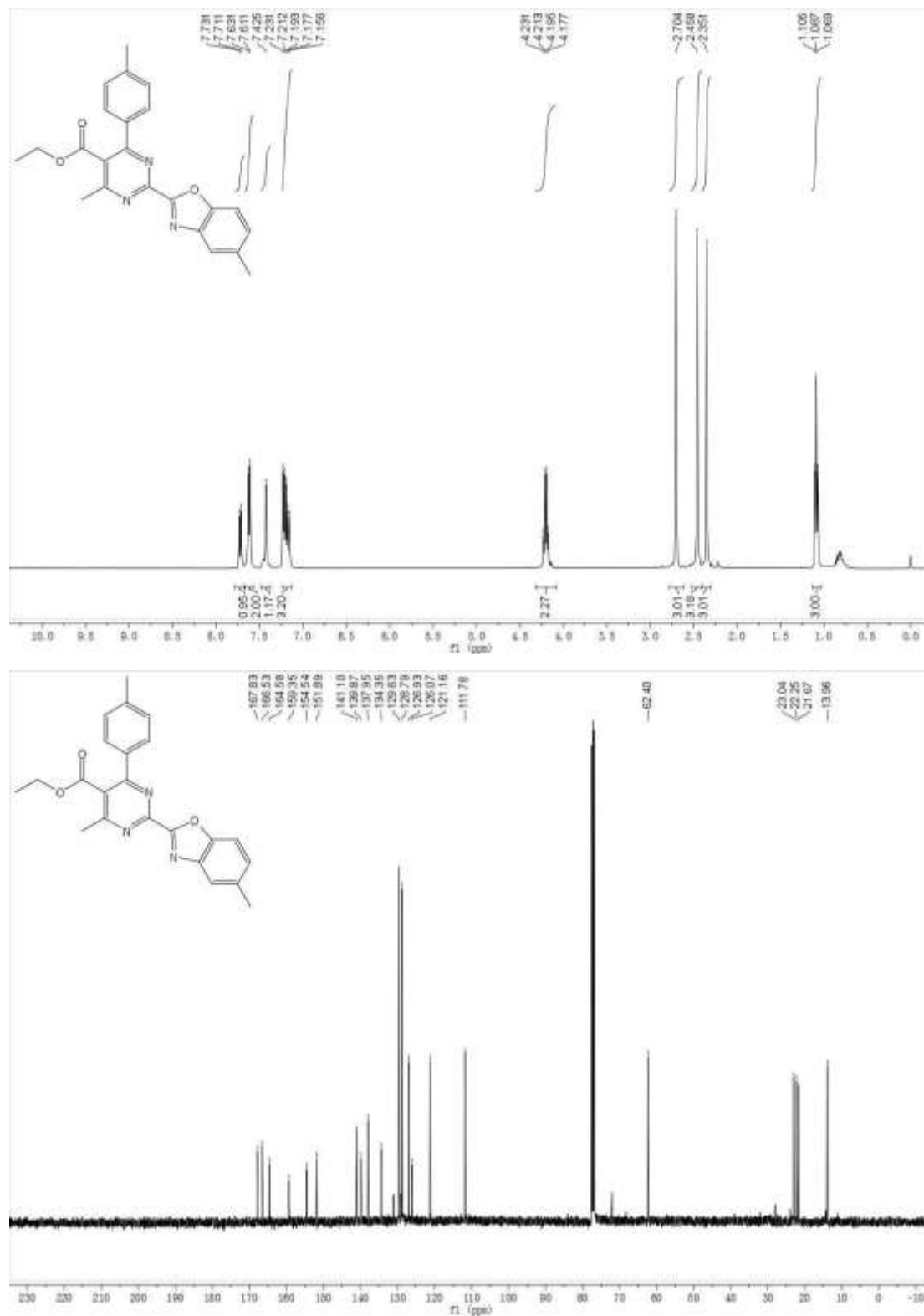
¹H and ¹³C Spectra of compound 3cb (CDCl₃, 600 MHz)



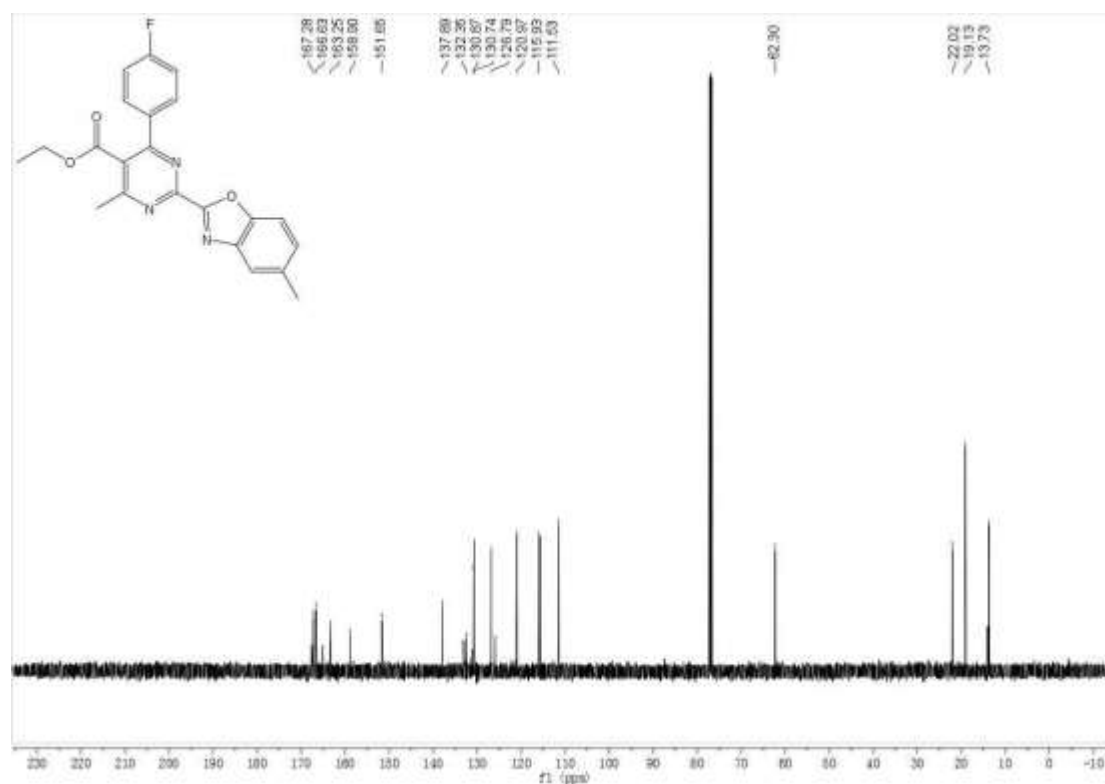
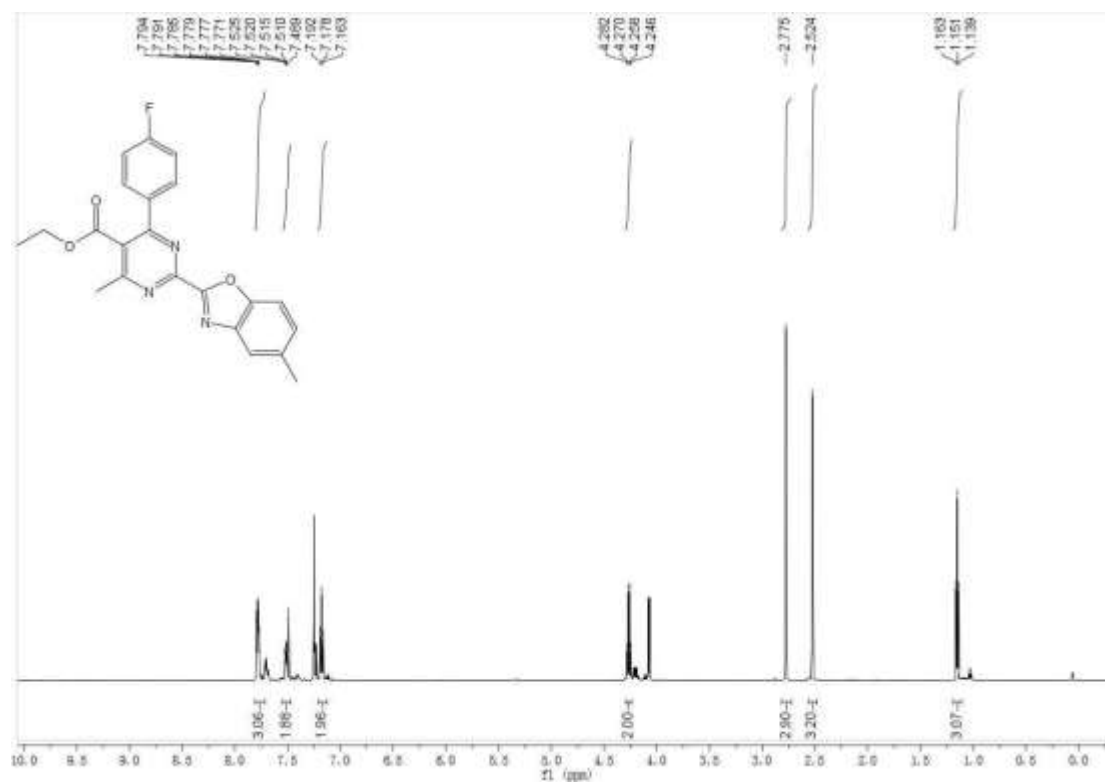
^1H and ^{13}C Spectra of compound 3ac (CDCl₃, 600 MHz)



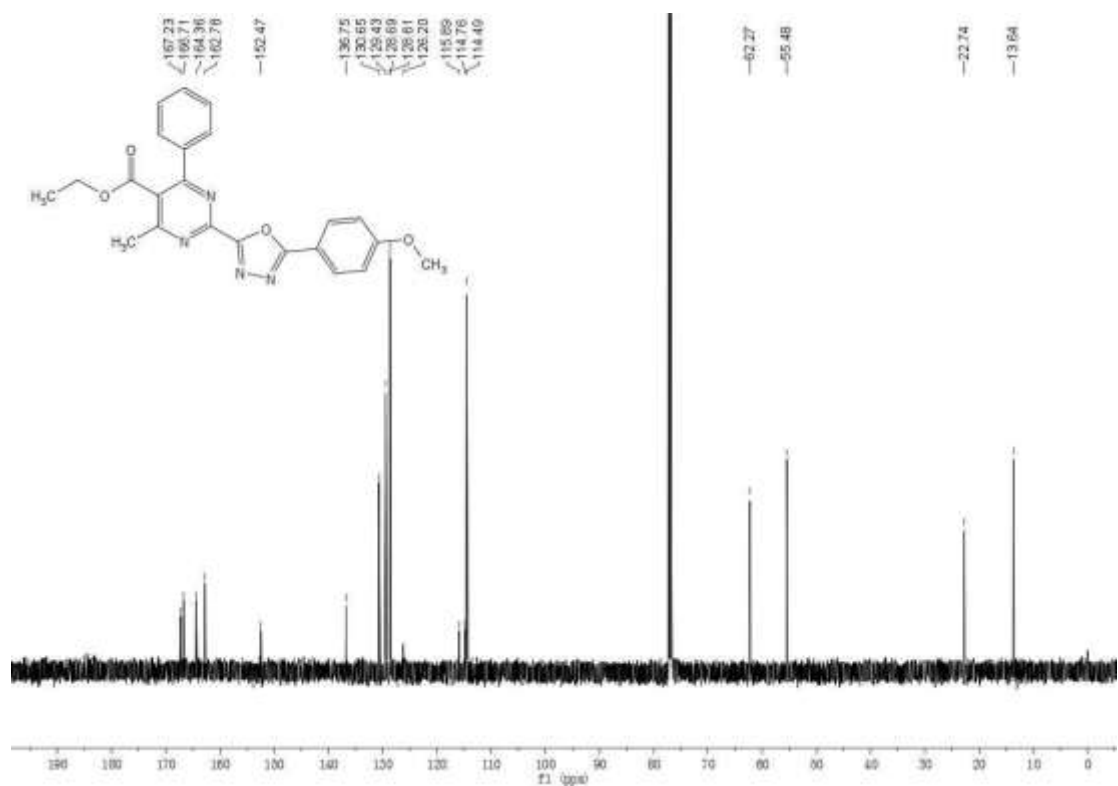
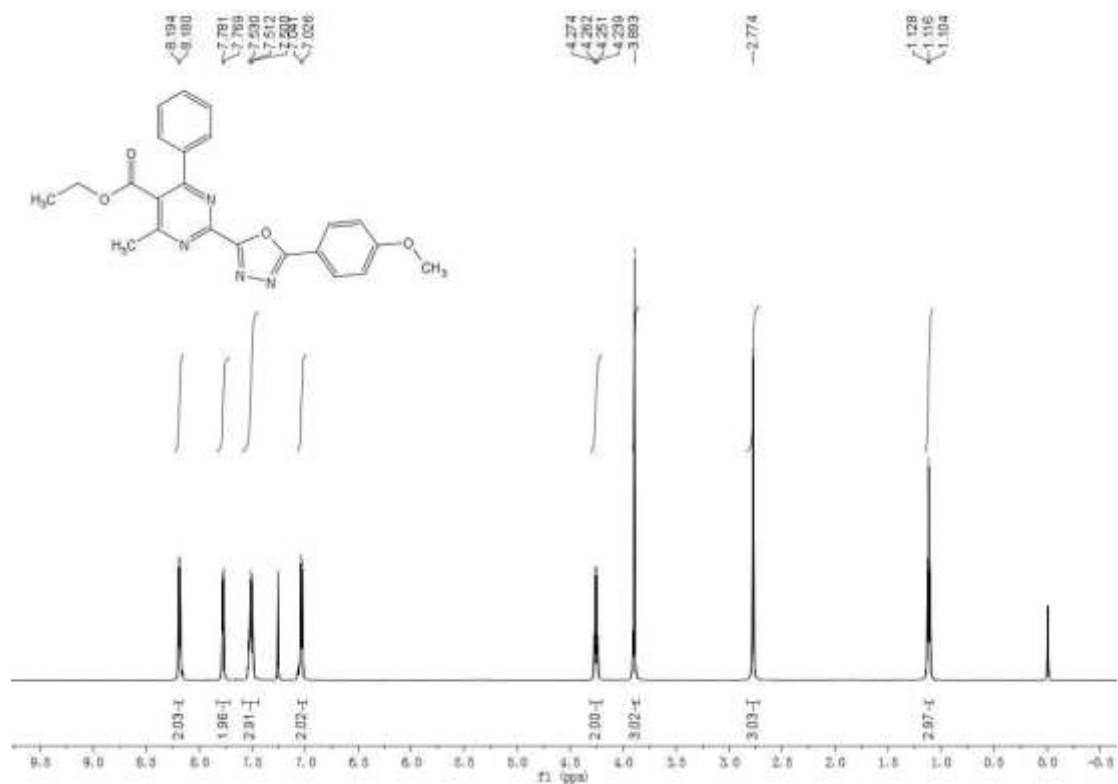
¹H and ¹³C Spectra of compound 3bc (CDCl₃, 600 MHz)



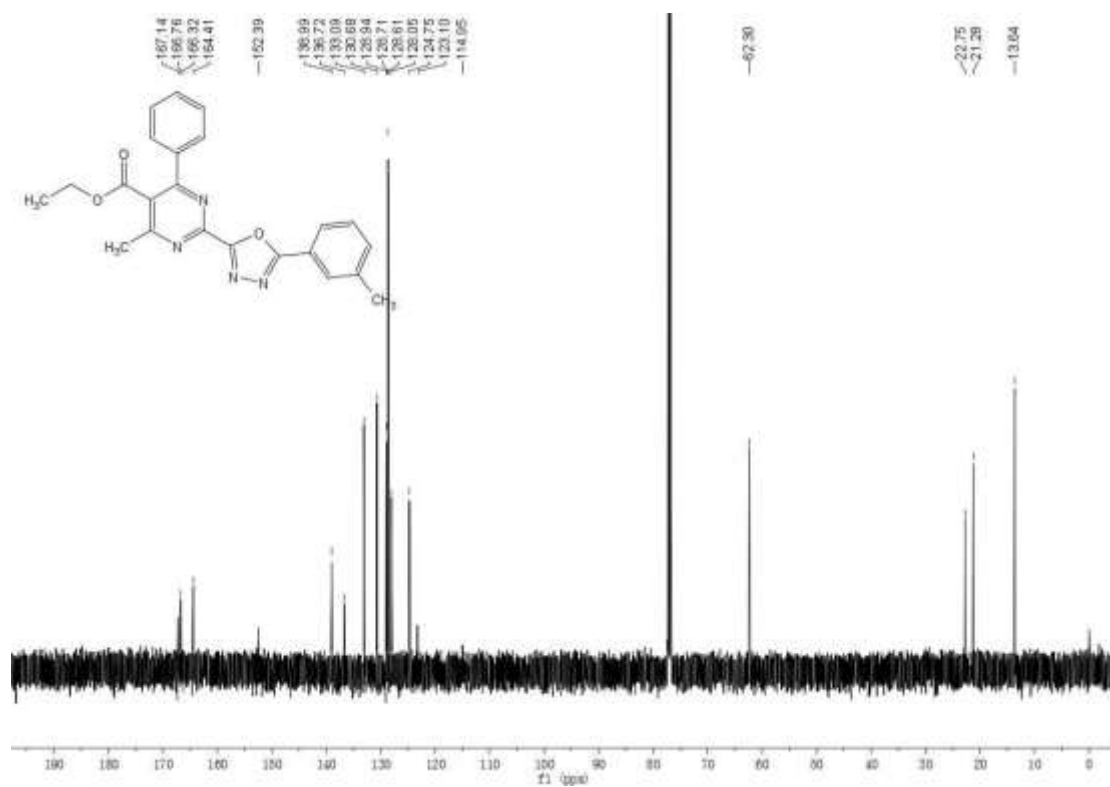
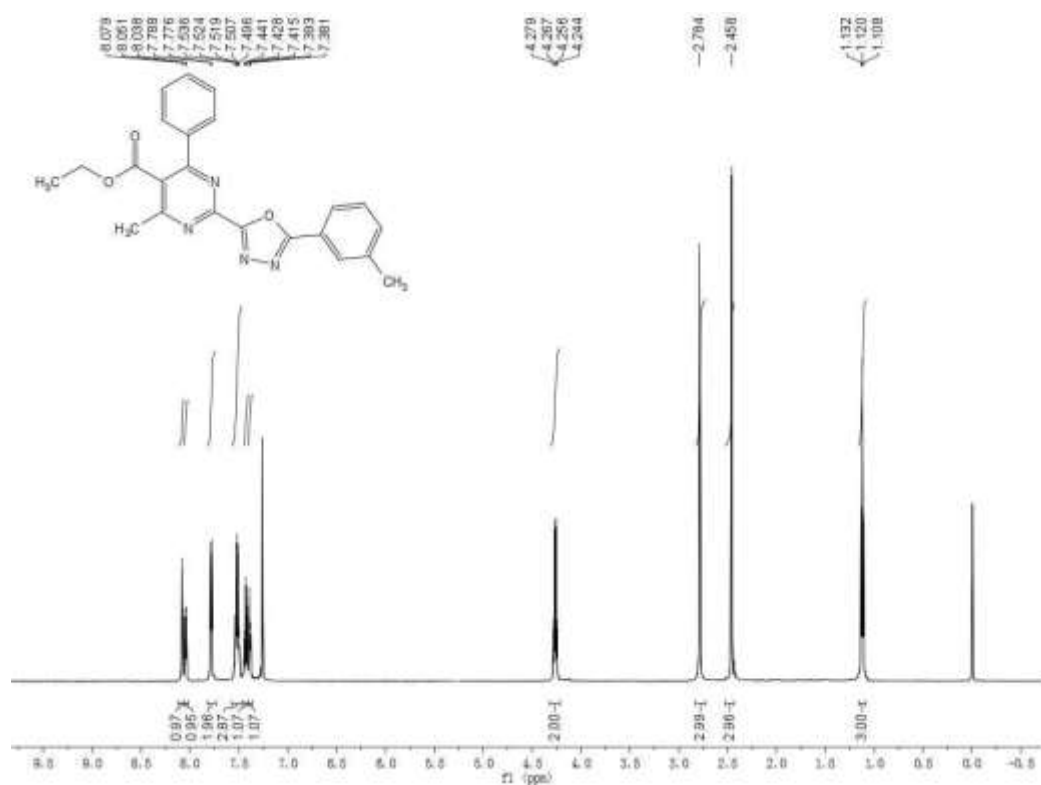
¹H and ¹³C Spectra of compound 3cc (CDCl₃, 600 MHz)



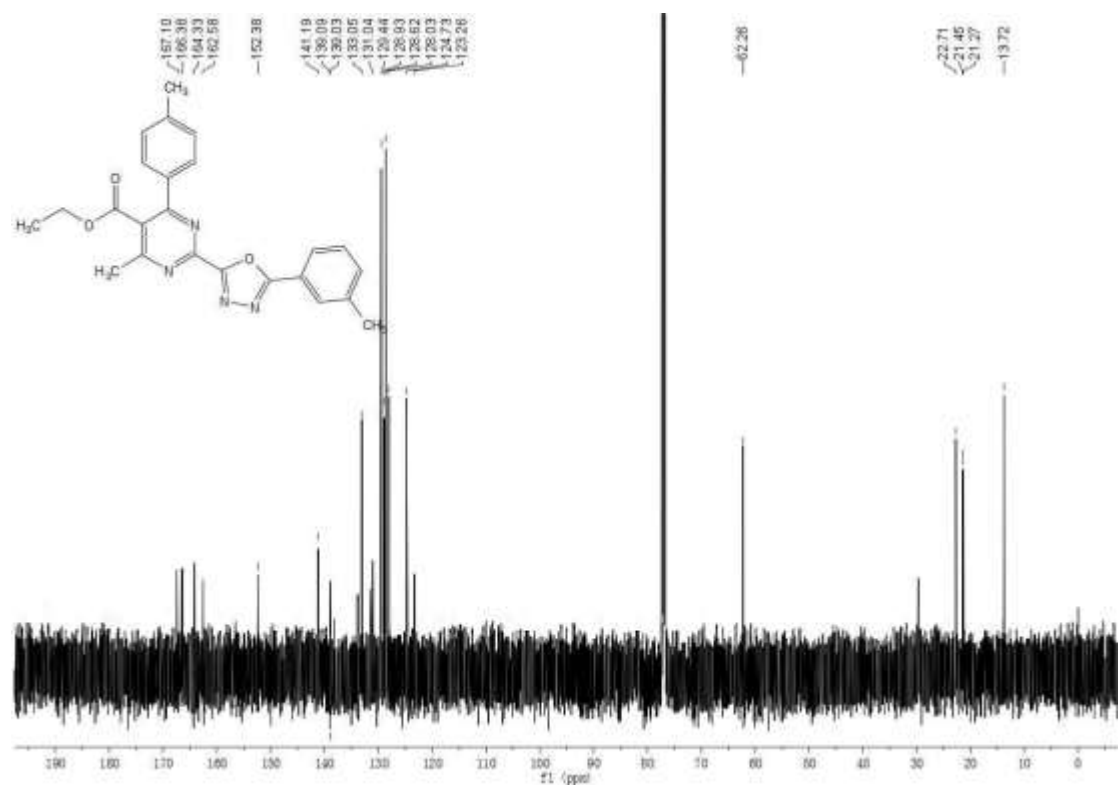
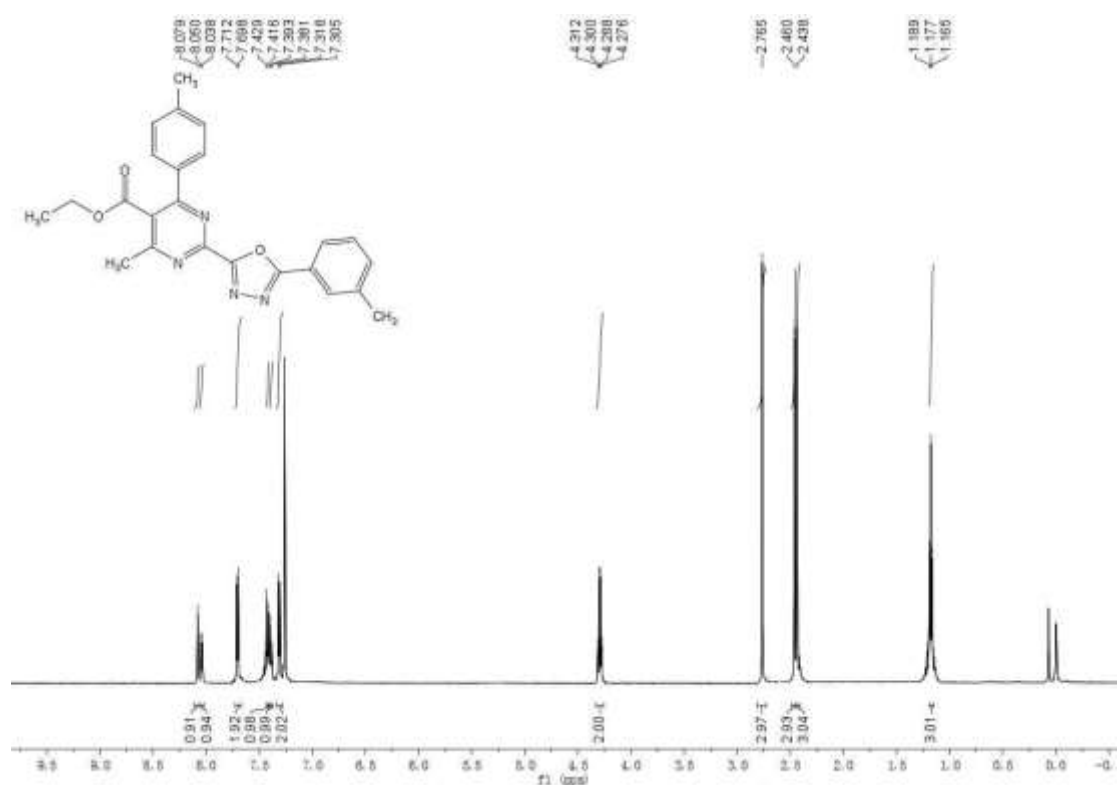
¹H and ¹³C Spectra of compound 3ad (CDCl₃, 600 MHz)



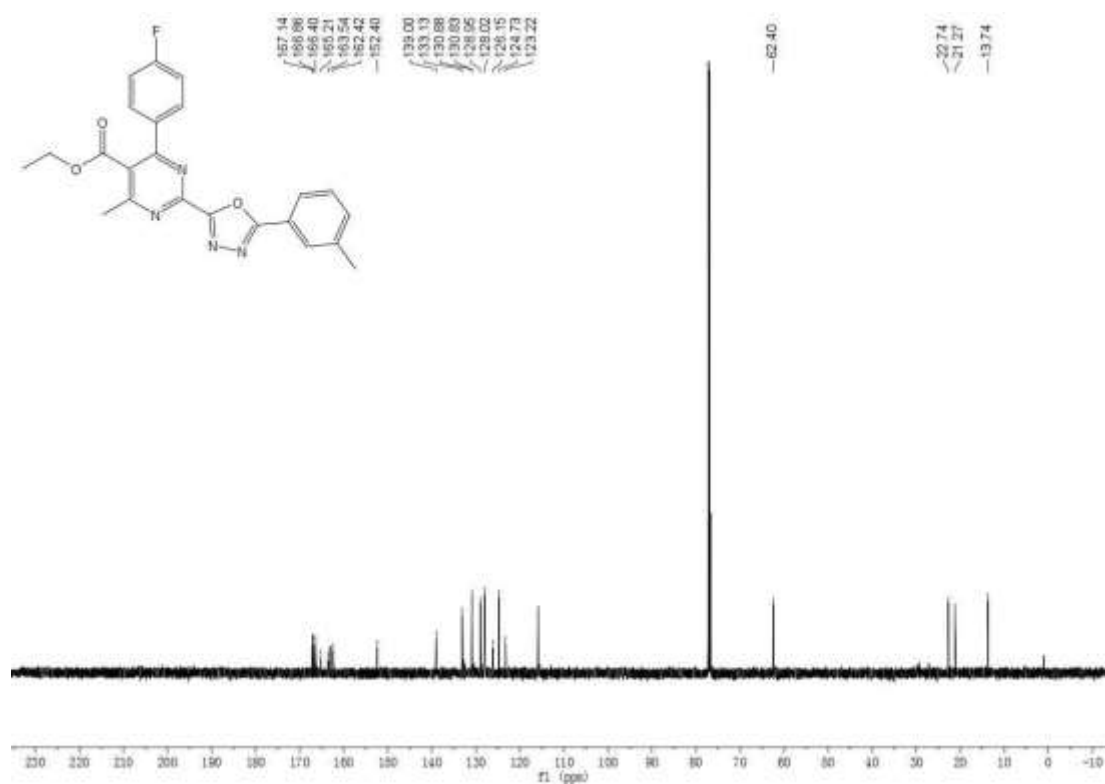
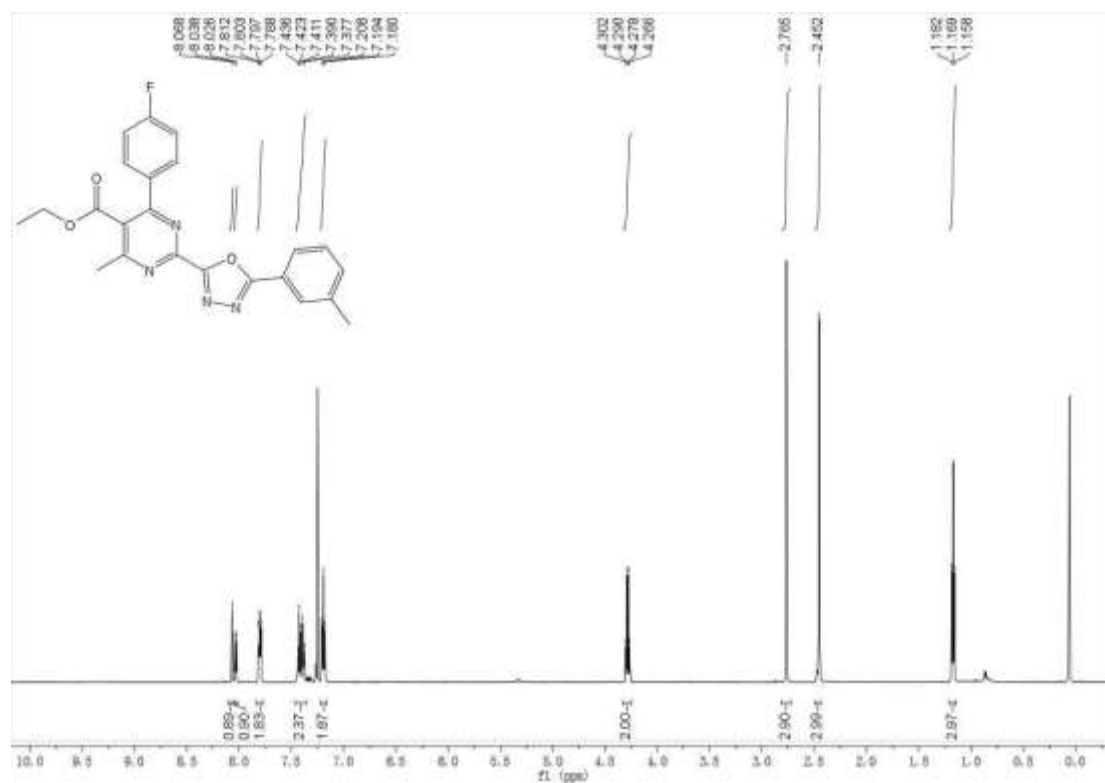
¹H and ¹³C Spectra of compound 3ae (CDCl₃, 600 MHz)



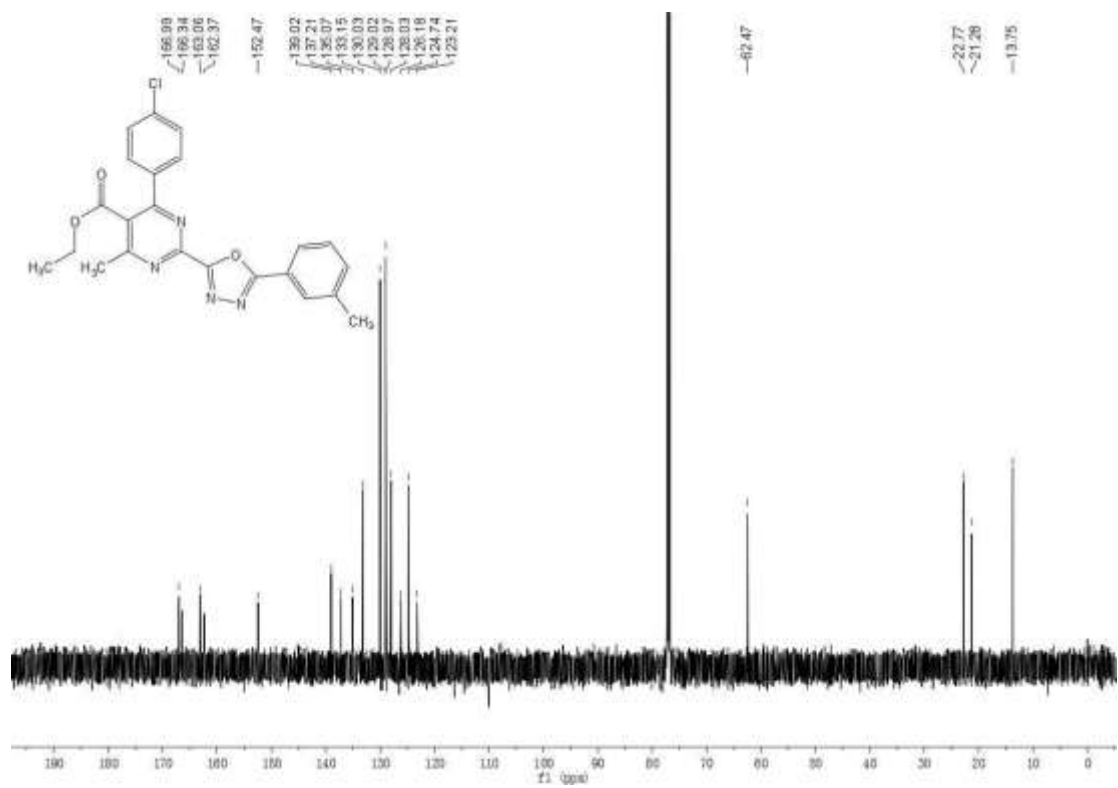
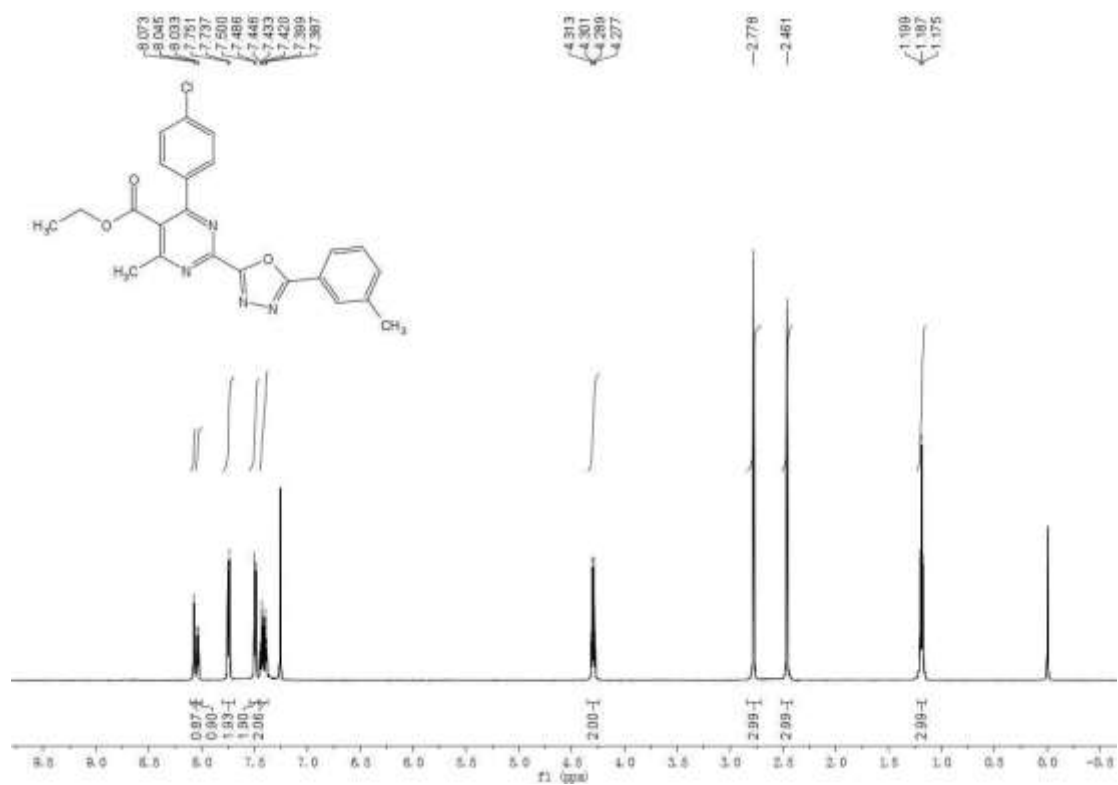
¹H and ¹³C Spectra of compound 3be (CDCl₃, 600 MHz)



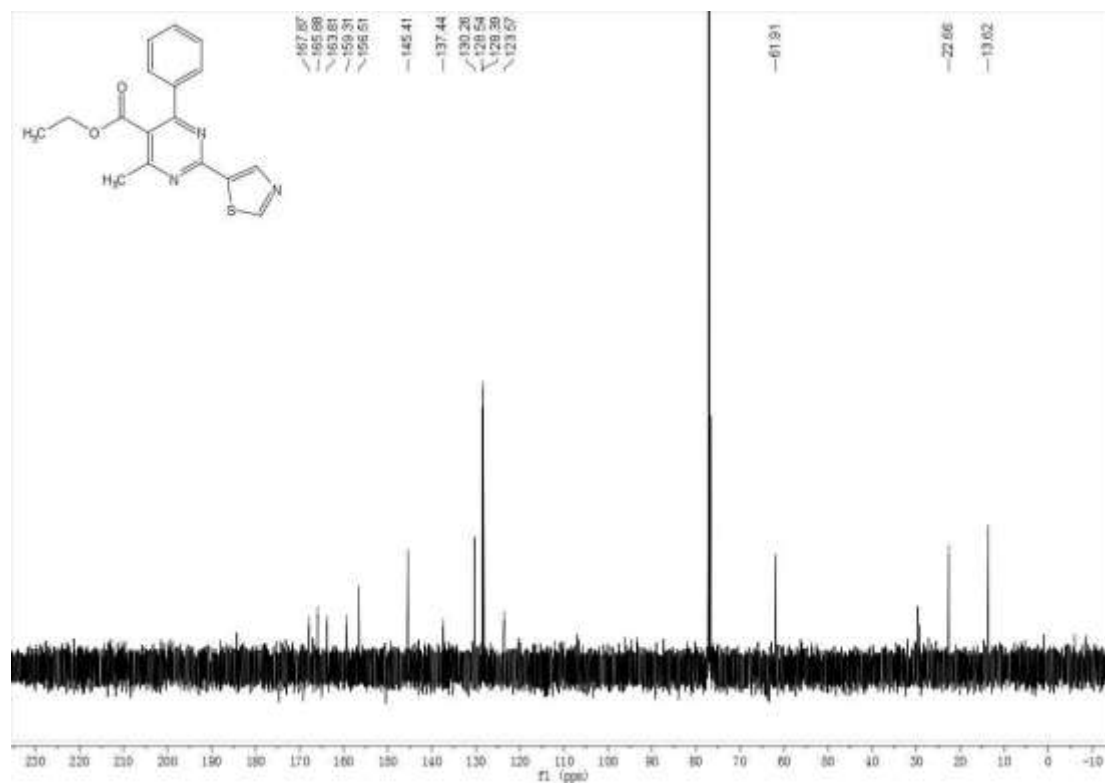
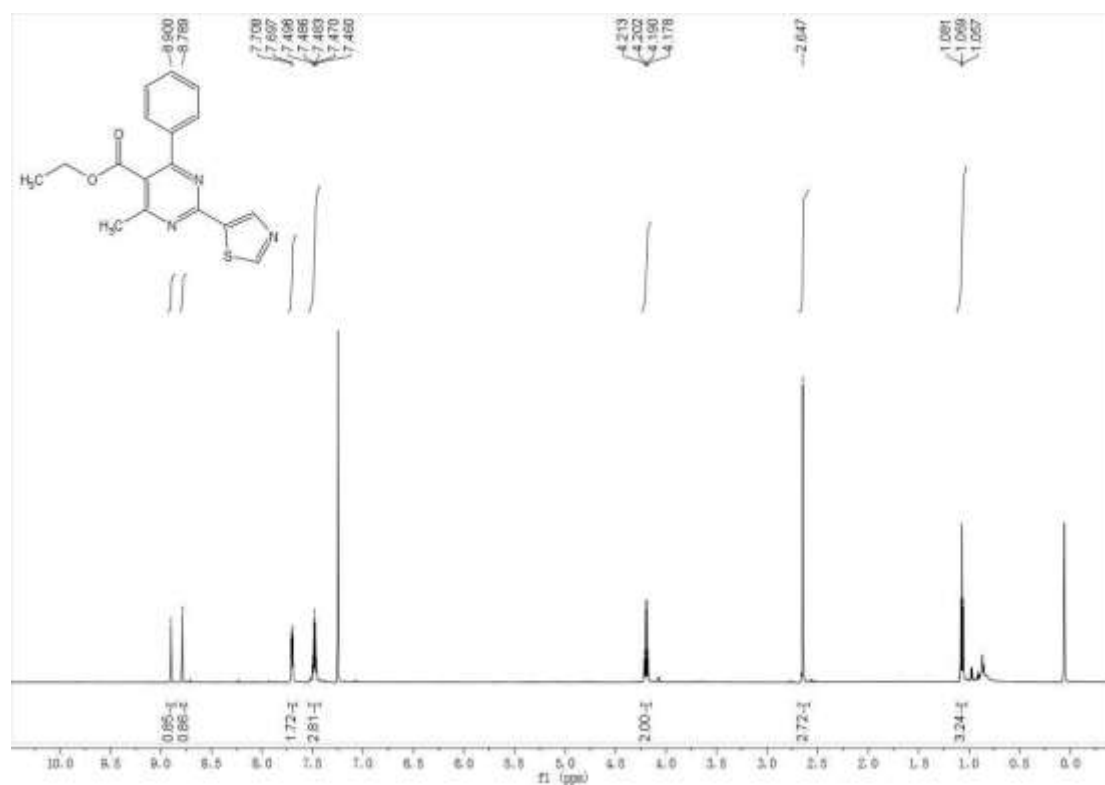
¹H and ¹³C Spectra of compound 3ce (CDCl₃, 600 MHz)



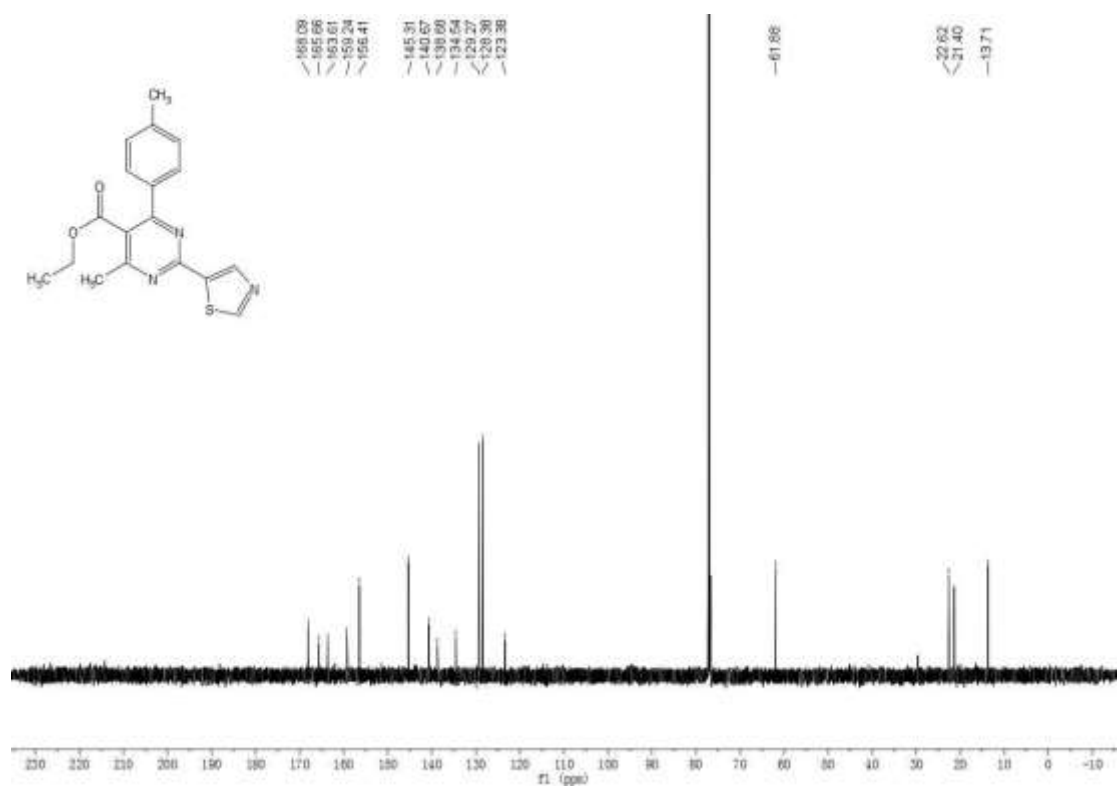
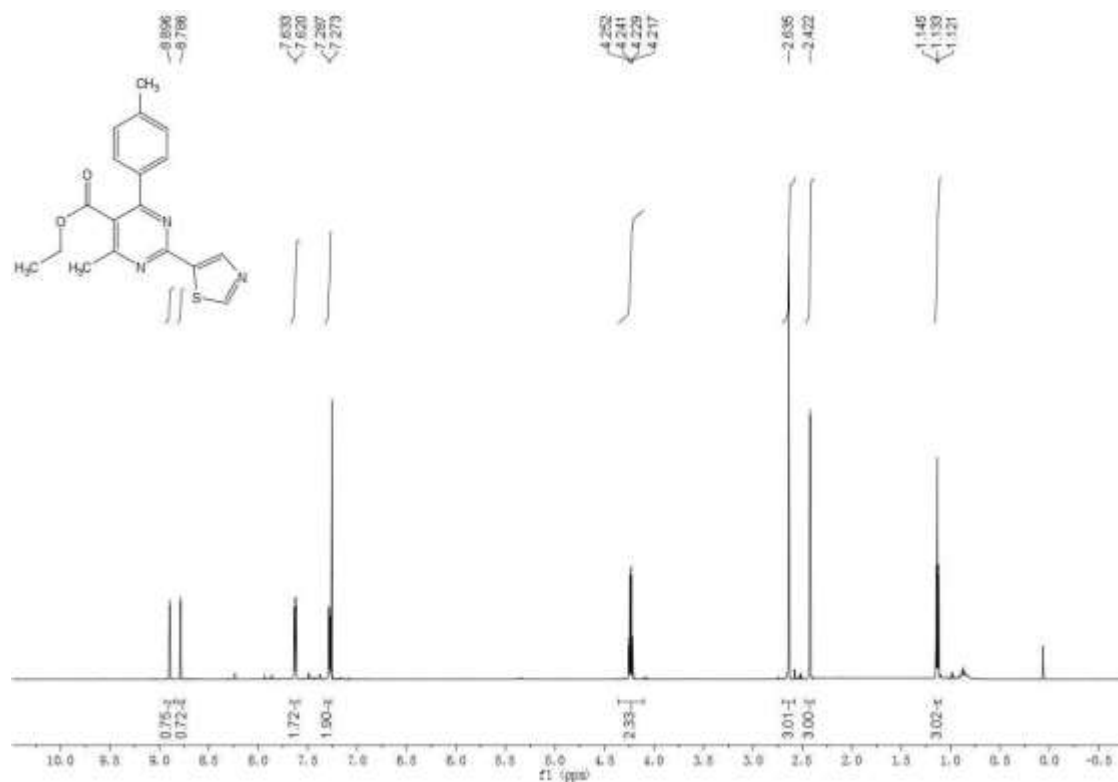
¹H and ¹³C Spectra of compound 3de (CDCl₃, 600 MHz)



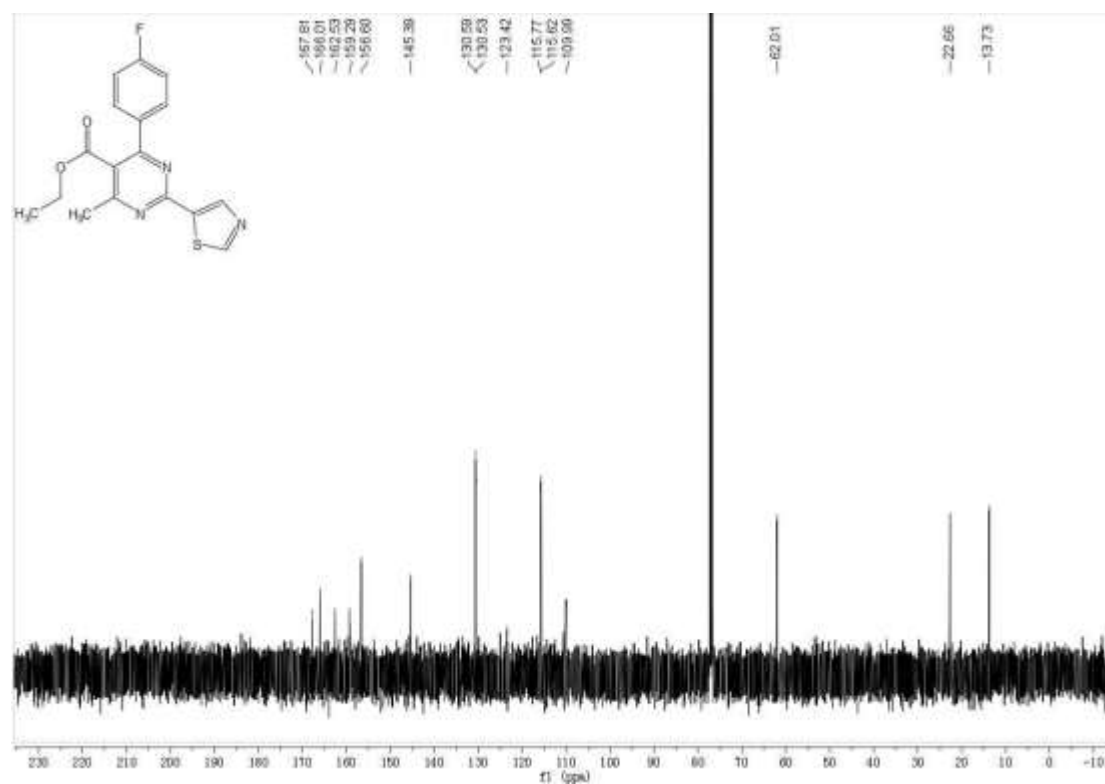
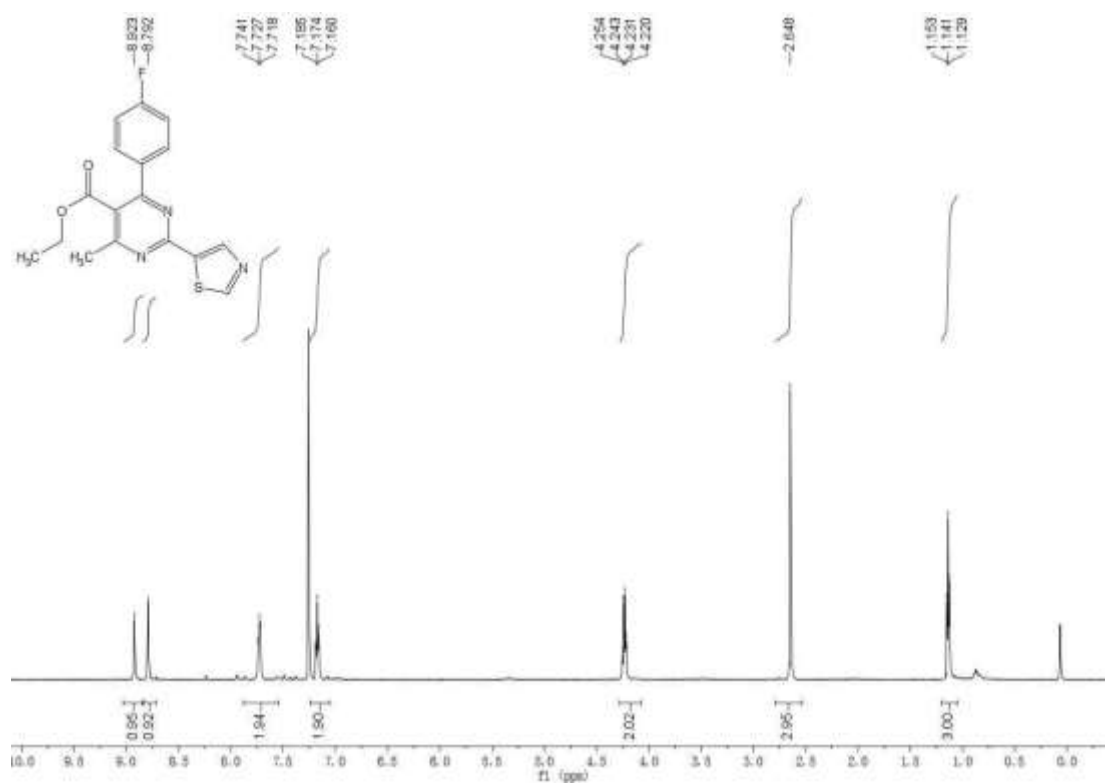
¹H and ¹³C Spectra of compound 3af (CDCl₃, 600 MHz)



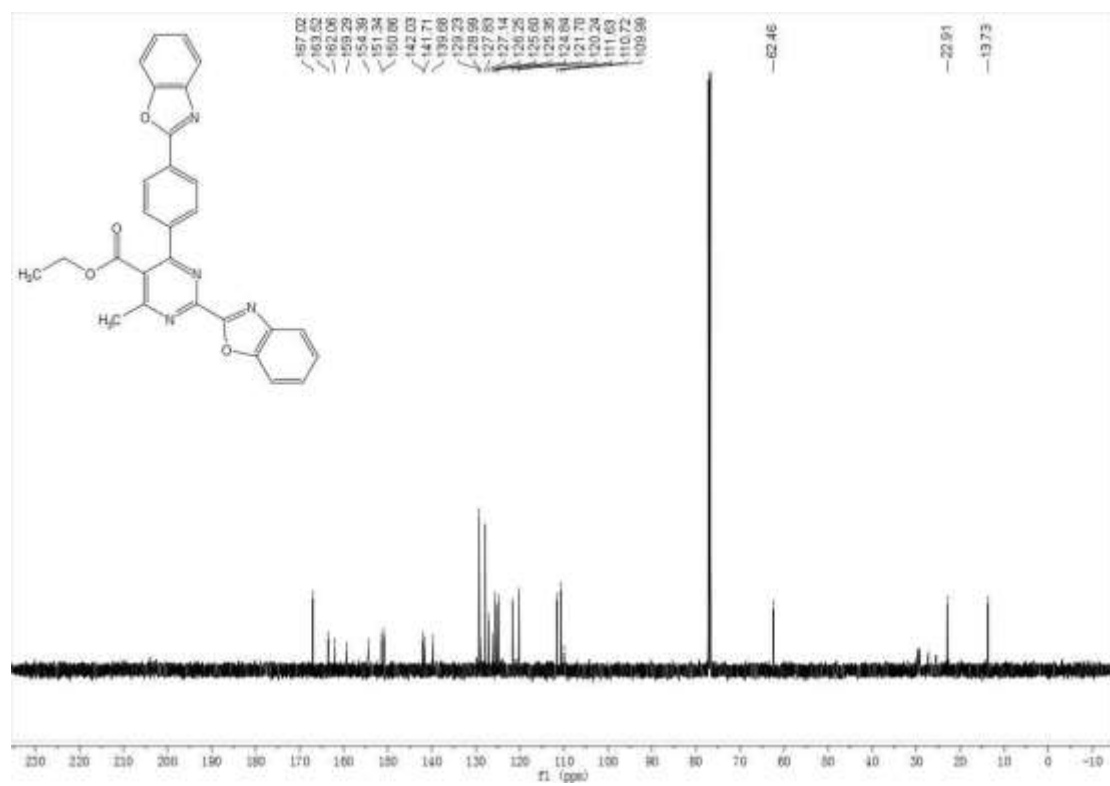
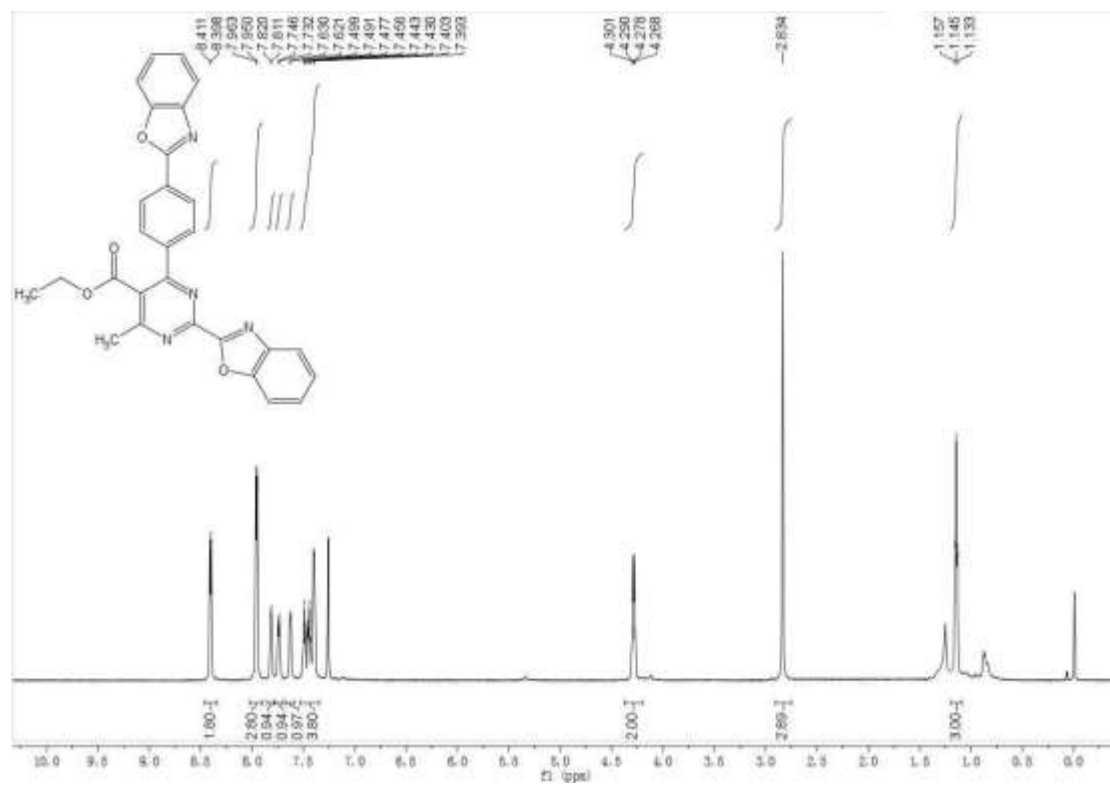
¹H and ¹³C Spectra of compound 3bf (CDCl₃, 600 MHz)



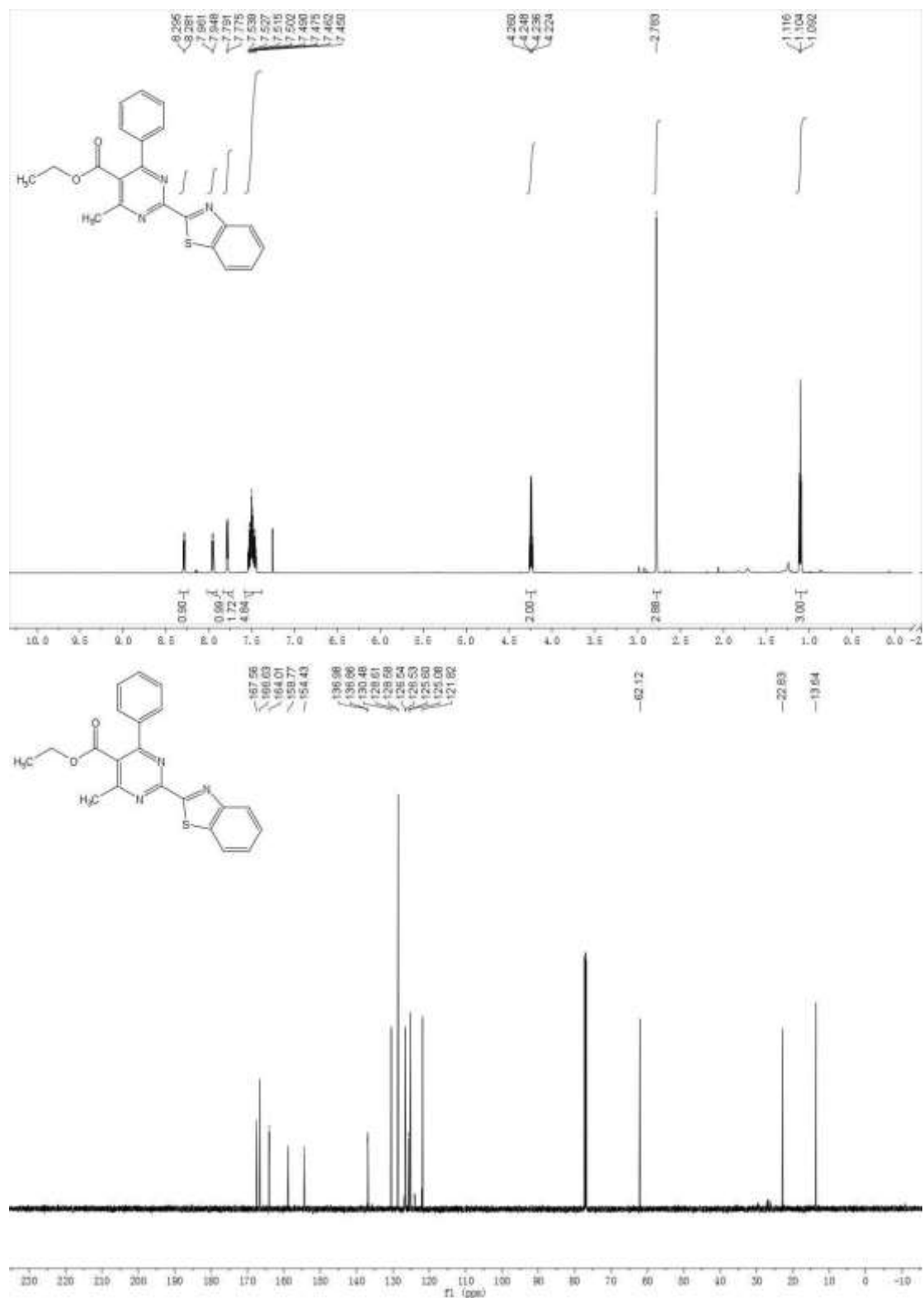
¹H and ¹³C Spectra of compound 3cf (CDCl₃, 600 MHz)



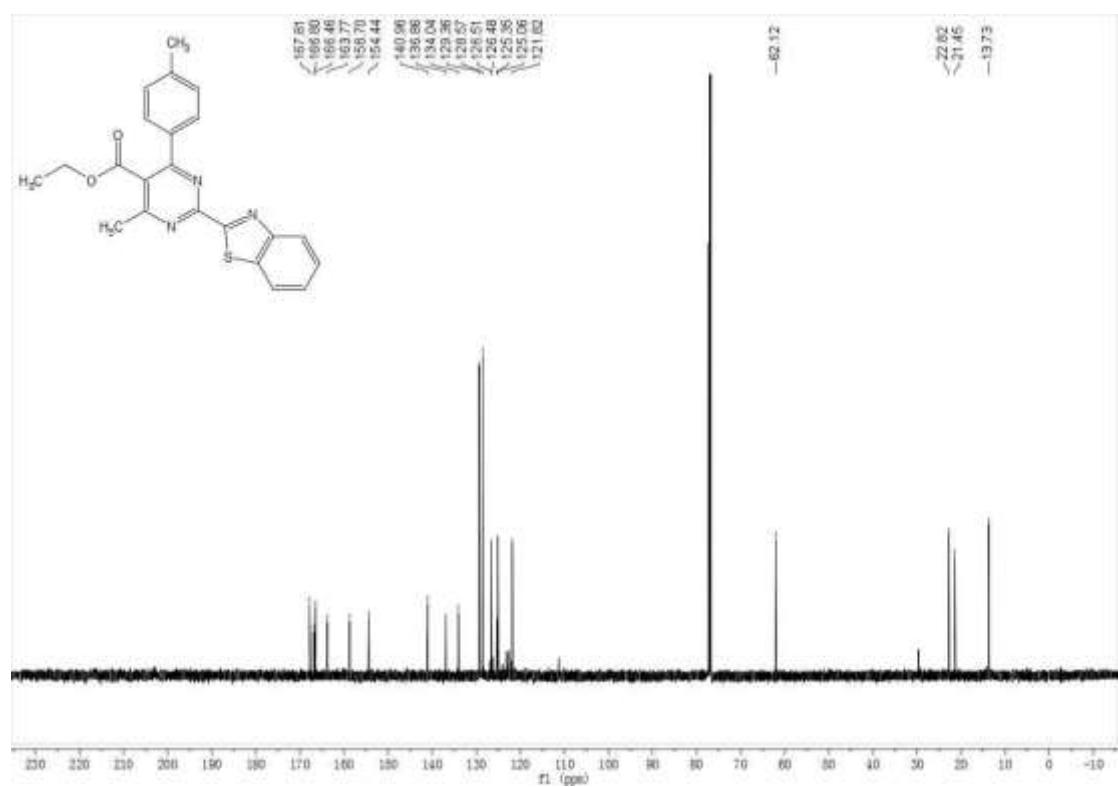
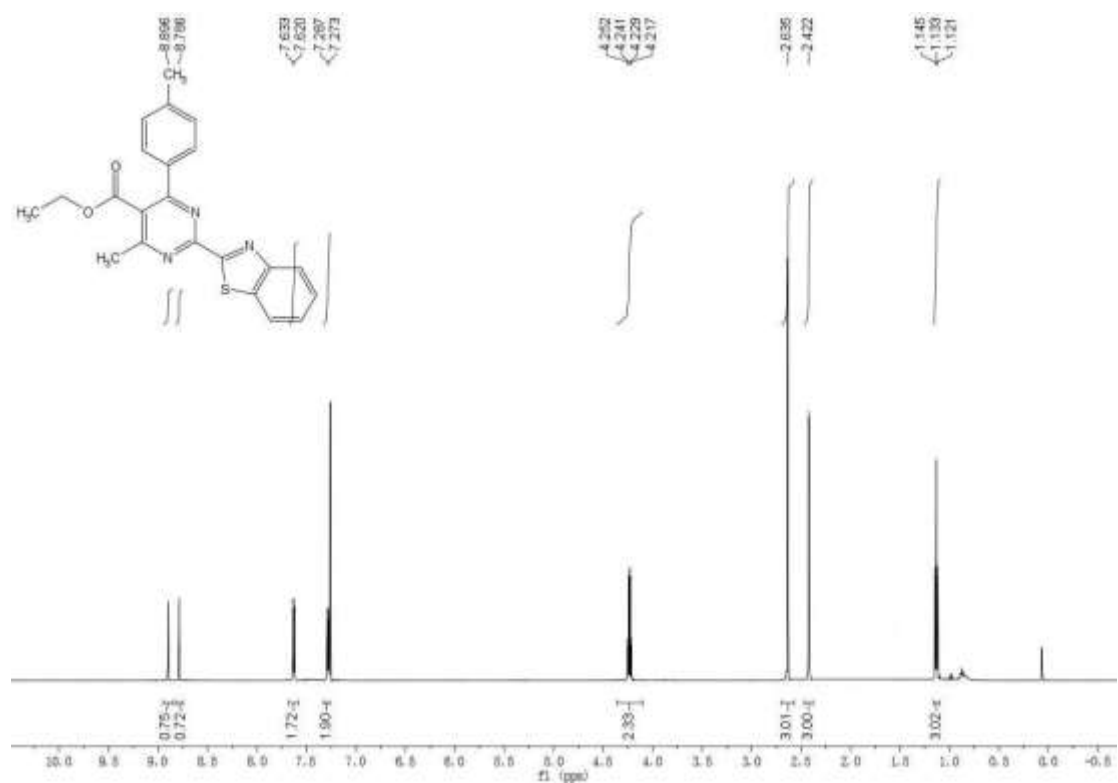
¹H and ¹³C Spectra of compound 3ja (CDCl₃, 600 MHz)



¹H and ¹³C Spectra of compound 5aa (CDCl₃, 600 MHz)



¹H and ¹³C Spectra of compound 5ba (CDCl₃, 600 MHz)



¹H and ¹³C Spectra of compound 5da (CDCl₃, 600 MHz)

