Supporting Information

Metal and additive-free synthesis of 2,4-disubstituted oxazoles via thiourea-mediated cyclization reaction

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Contents

1. General remarks

All non-aqueous reactions and manipulations were performed in N_2 atmosphere. The reactions were monitored by GC and LC-MS. The ^1H NMR and ^{13}C NMR spectra were recorded on a Brucker ADVANCE III spectrometer at 400 MHz and 100 MHz, respectively, and chemical shifts were reported in parts per million (ppm). Flash column chromatography was performed using silica gel 300-400 μm. LC-MS results were recorded on LC-MS JINDAO804, and GC analysis was performed on GC 7820A. Carboxylic acid compounds, substituted 2-bromo-benzyl ketones were purchased from Energy Chemical, dried by standard methods before using.

HRMS: Thermal Orbitrap Exploris 120

Ion Source Type = H-ESI

Spray Voltage: Positive Ion (V) = 3500

2. General experimental procedure for the synthesis of 2,4-disubstituted oxazoles

A 25 ml Schlenk-type tube equipped with a magnetic stir bar was charged with substrate **1a-1z4** (0.2 mmol), thiourea **2a** (0.24 mmol), base (0.2 mmol). The reaction tube was evacuated and back-filled with N_2. 1,4-dioxane (2 mL) were added at room temperature under N_2 atmosphere, then the reaction mixture was stirred at 150 ºC for 12 h. The reaction was monitored by GC or LC-MS. After completion of the reaction, the resulting solution was cooled to room temperature, and neutralized with saturated solution of NaCl. The product was extracted with EtOAc, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel to give analytically pure product.

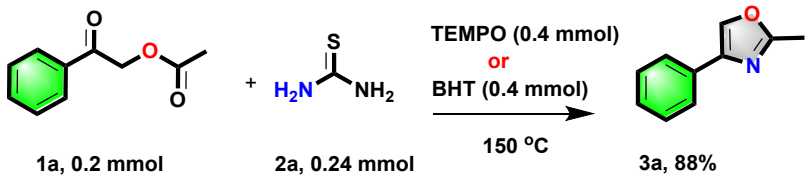
3. The synthesis of raw materials

A 500 mL three-neck flask equipped with a magnetic stir bar was charged with substrate 2-bromobenzoylacetone (100 mmol), acetic acid (150 mmol), K_2CO_3 (200

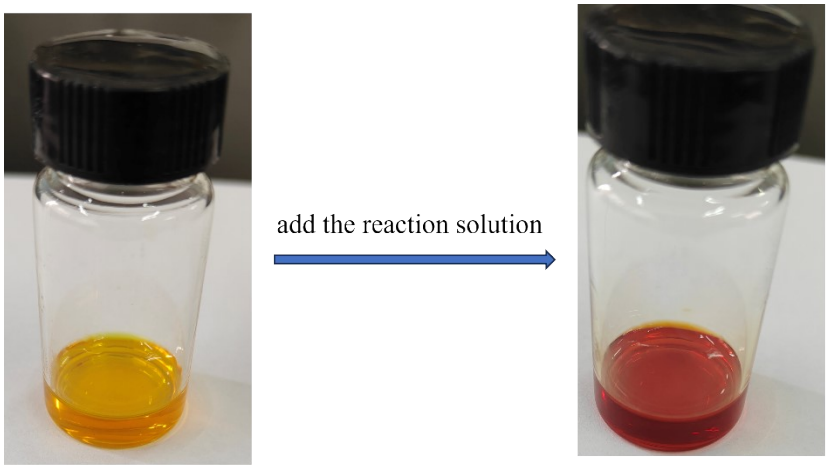
mmol), and 1,4-dioxane (300 mL) at room temperature. The reaction mixture was stirred at 25 °C for 48 h and monitored by GC or LC-MS. Upon completion, the mixture was neutralized with a saturated NaCl solution. The product was extracted with EtOAc, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product, obtained in pure form, was used directly in the next step without further purification. Other substrates were prepared following an analogous procedure.

4. The reaction mechanism

When radical scavengers such as 2,2,6,6-tetramethylpiperidinyloxy (TEMPO, 2 equiv) or butylated hydroxytoluene (BHT, 2 equiv) were added to the reaction mixture, the desired product 3a was still obtained in 88% yield. This result suggests that a radical pathway is unlikely to be involved in this transformation.



To demonstrate that the reaction follows the proposed mechanism, $SC(NH_2)_2$ is initially heated, decomposing into NH_3 and SCN^-. The presence of SCN^- ions in the system is confirmed using Fe^{3+} ions. After completion of the reaction, when the mixture is added dropwise to a $FeCl_3$ solution, the yellow solution immediately turns red.

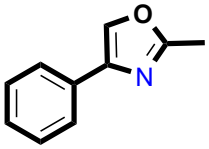


$FeCl_3$ solution

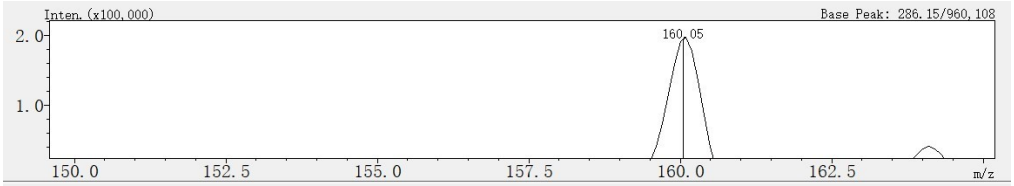
$FeCl_3$ solution + reaction mixture

5. ^{1}H NMR, ^{13}C NMR and LC-MS data of products

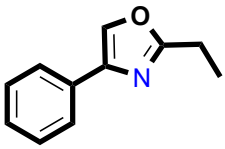
2-Methyl-4-phenyloxazole (3a)[1]



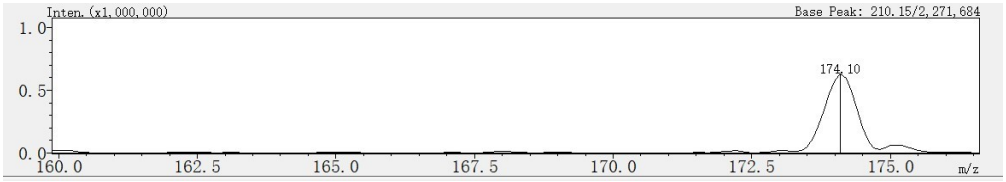
Following the general procedure (EtOAc/Petroleum ether 1:25), 3a was obtained as pale-yellow solid, isolated yield: 92%, m.p. 68-70℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.71 (d, J = 7.2 Hz, 2H), 7.38 (t, J = 7.6 Hz, 2H), 7.28 (d, J = 7.6 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 140.7, 133.1, 131.2, 128.7, 127.9, 125.4, 14.0. m/z = 159.07, LC-MS spectrum (+): m/z = 160.05.



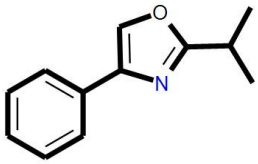
2-Ethyl-4-phenyloxazole (3b)[2]



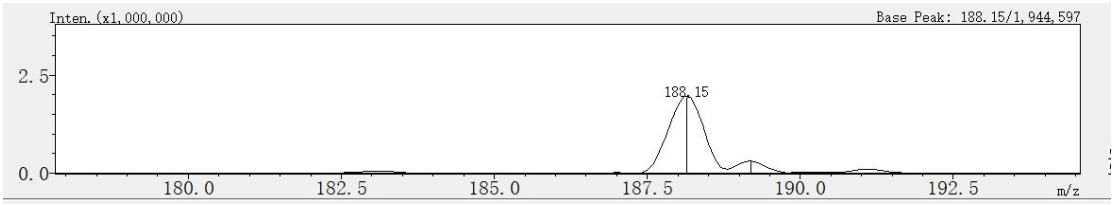
Following the general procedure (EtOAc/Petroleum ether 1:25), 3b was obtained as yellow oil liquid, isolated yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.72 (d, J = 7.2 Hz, 2H), 7.37 (t, J = 7.6 Hz, 2H), 7.29 (d, J = 7.4 Hz, 1H), 2.83 (q, J = 7.6 Hz 2H), 1.36 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 140.5, 132.9, 131.3, 128.6, 127.8, 125.4, 21.7, 11.1. LC-MS: m/z = 207.11.6. m/z = 173.08, LC-MS spectrum (+): m/z = 174.10.



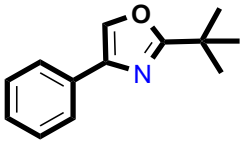
2-Isopropyl-4-phenyloxazole (3c)[2]



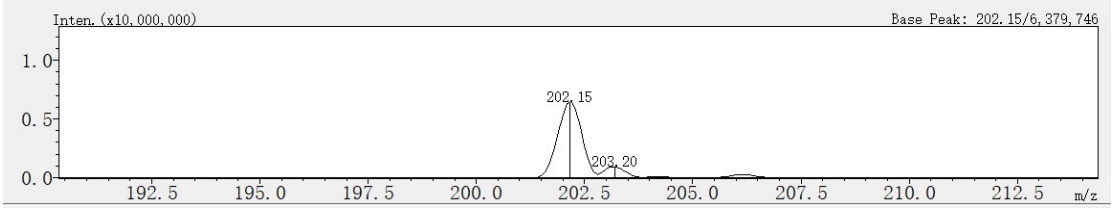
Following the general procedure (EtOAc/Petroleum ether 1:25), 3c was obtained as yellow oil liquid, isolated yield: 89%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.73 (d, *J* = 6.8 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 3.19-3.09 (m, 1H), 1.39 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 140.4, 132.8, 131.4, 128.7, 127.8, 125.5, 28.6, 20.5. m/z = 187.10, LC-MS spectrum (+): m/z = 188.15.



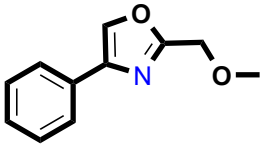
2-(Tert-butyl)-4-phenyloxazole (3d)[2]



Following the general procedure (EtOAc/Petroleum ether 1:25), 3d was obtained as yellow oil liquid, isolated yield: 91%, m.p. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.73 (d, *J* = 6.8 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 140.3, 132.8, 131.6, 128.6, 127.7, 125.6, 33.8, 28.6. m/z = 201.12, LC-MS spectrum (+): m/z = 202.15.

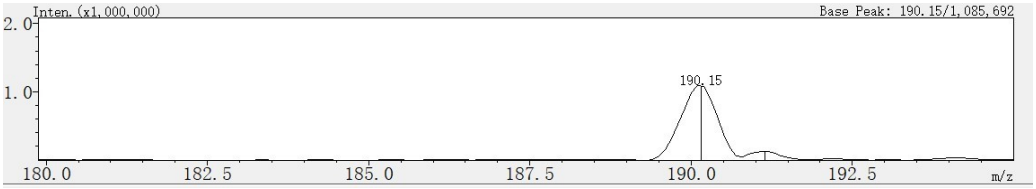


2-(Methoxymethyl)-4-phenyloxazole (3e)

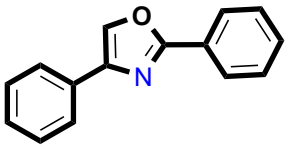


Following the general procedure (EtOAc/Petroleum ether 1:25), 3e was

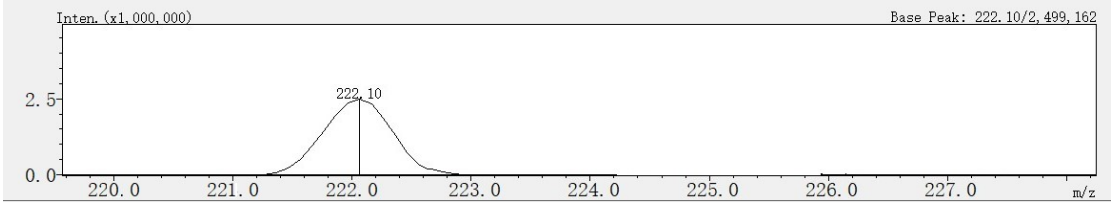
obtained as light yellow semi-solid, isolated yield: 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.74 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 4.57 (s, 2H), 3.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 140.9, 134.1, 130.8, 128.7, 128.1, 125.5, 66.4, 58.8. m/z = 189.08, LC-MS spectrum (+): m/z = 190.15, HRMS (ESI+): Calculated for $C_{11}H_{11}NO2$ $[M+H]^+$: 190.0868, Found $[M+H]^+$: 190.0872.



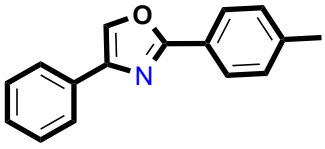
2,4-Diphenyloxazole (3f)[2]



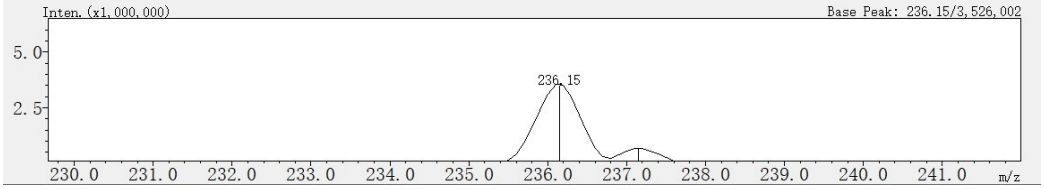
Following the general procedure (EtOAc/Petroleum ether 1:25), 3f was obtained as a yellow solid, isolated yield: 90%, m.p. 72-75 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.0 Hz, 2H), 7.95 (s, 1H), 7.81 (t, *J* = 6.8 Hz, 2H), 7.47-7.40 (m, 5H), 7.32 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 142.1, 133.4, 131.2, 130.4, 128.8, 128.1, 127.6, 126.5, 125.7. m/z = 221.08, LC-MS spectrum (+): m/z = 222.10.



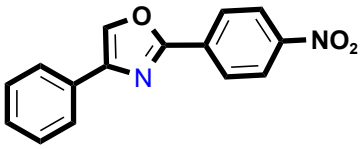
4-Phenyl-2-(p-tolyl)oxazole (3g)[1]



Following the general procedure (EtOAc/Petroleum ether 1:25), 3g was obtained as a yellow solid, isolated yield: 89%, m.p. 110-112 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.92 (s, 1H), 7.82 (d, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 141.9, 140.7, 133.1, 131.3, 129.5, 128.7, 128.1, 126.5, 126.7, 125.7, 124.9, 21.6. m/z = 235.10, LC-MS spectrum (+): m/z = 236.15

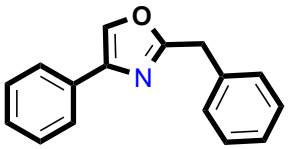


2-(4-Nitrophenyl)-4-phenyloxazole (3h)[1]

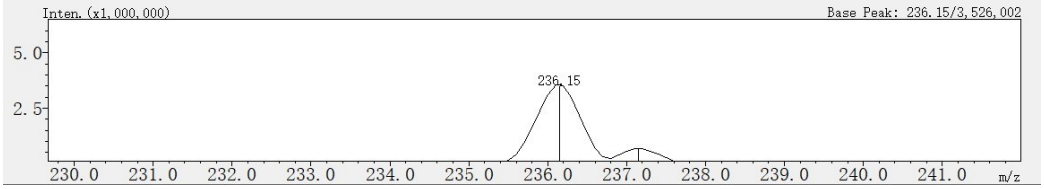


Following the general procedure (EtOAc/Petroleum ether 1:20), 3h was obtained as a yellow solid, isolated yield: 87%, m.p. 130-132 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (q, *J* = 8.8 Hz, 4H), 8.05 (s, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 148.8, 143.1, 134.8, 132.9, 130.5, 128.9, 128.7, 127.3, 125.8, 124.2. m/z = 266.07, LC-MS spectrum (+): m/z = 267.

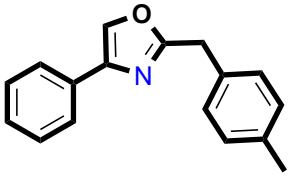
2-Benzyl-4-phenyloxazole (3i)[2]



Following the general procedure (EtOAc/Petroleum ether 1:25), 3i was obtained as a yellow solid, isolated yield: 86%, m.p. 94-96 ℃. ^{1}H NMR (400 MHz, CDCl3): δ 7.79 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.40-7.23 (m, 8H), 4.17 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 140.8, 135.5, 133.7, 131.7, 128.8, 128.7, 128.0, 127.1, 125.6, 34.8. m/z = 235.10, LC-MS spectrum (+): m/z = 236.15.

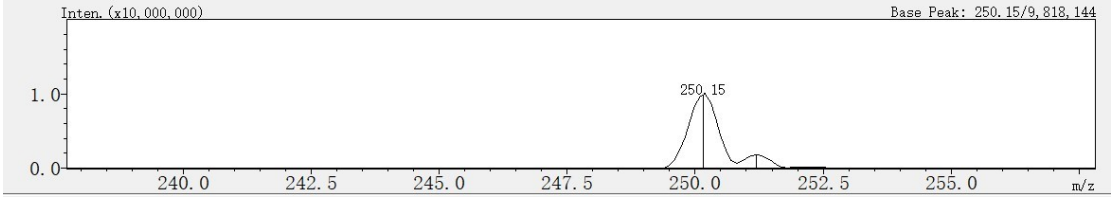


2-(4-Methylbenzyl)-4-phenyloxazole (3j)[4]

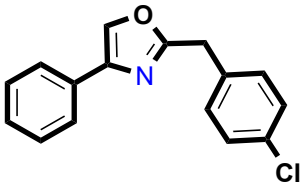


Following the general procedure (EtOAc/Petroleum ether 1:25), 3j was obtained as a yellow solid, isolated yield: 88%, m.p. 90-92 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.69 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 7.6 Hz, 2H), 4.12 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 140.8, 136.7,

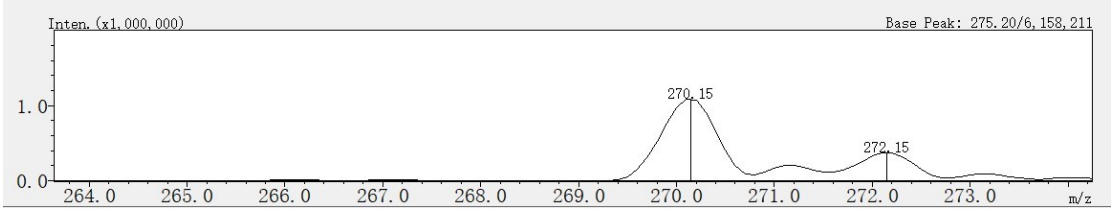
133.7, 132.4, 131.2, 129.4, 128.69, 128.68, 127.9 125.5, 34.4, 21.0. LC-MS: m/z = 249.12. LC-MS spectrum (+): m/z = 250.15.



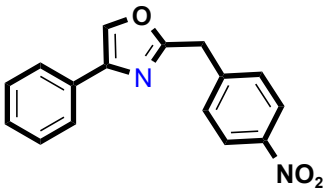
2-(4-Chlorobenzyl)-4-phenyloxazole (3k)[4]



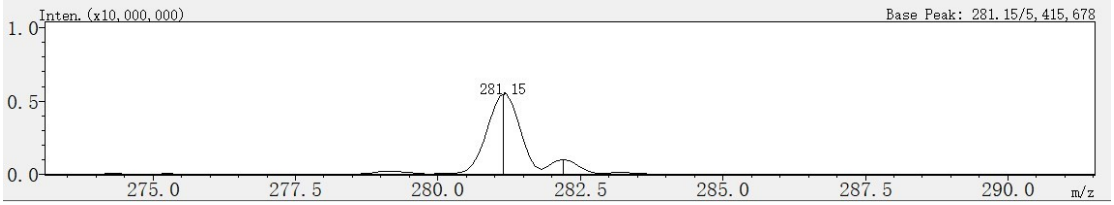
Following the general procedure (EtOAc/Petroleum ether 1:25), 3k was obtained as light yellow semi-solid, isolated yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.31-7.25(m, 5H), 4.13 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 140.9, 133.9, 133.8, 131.0, 128.9, 128.8, 128.1, 125.5, 34.1. LC-MS: m/z = 207.11.6. m/z = 269.06, LC-MS spectrum (+): m/z = 270.15.



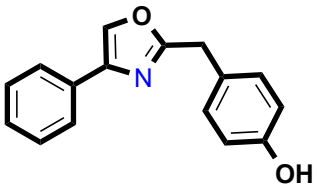
2-(4-Nitrobenzyl)-4-phenyloxazole (3l)[4]



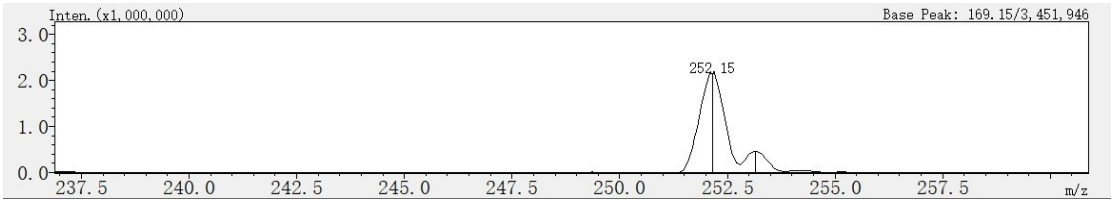
Following the general procedure (EtOAc/Petroleum ether 1:20), 3l was obtained as yellow solid, isolated yield: 89%, m.p. 123-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.8 Hz, 2H), 7.85 (s, 1H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 4.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 147.2, 142.8, 141.2, 134.0, 130.8, 129.8, 128.8, 128.2, 125.5, 123.9, 34.5. m/z = 280.08, LC-MS spectrum (+): m/z = 281.15.



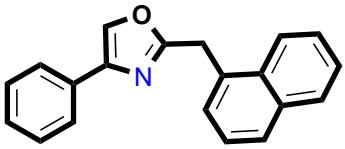
4-((4-Phenyloxazol-2-yl)methyl)phenol (3m)



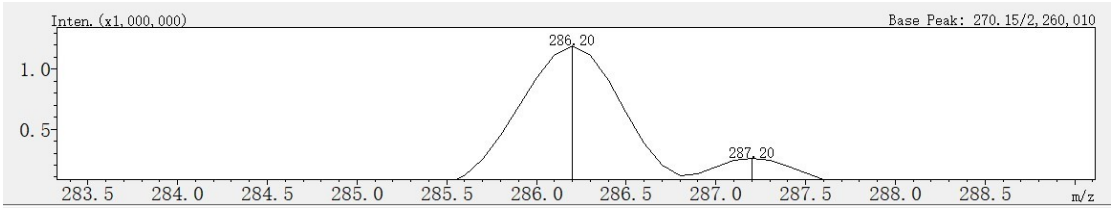
Following the general procedure (EtOAc/Petroleum ether 1:15), 3m was obtained as yellow solid, isolated yield: 86%, m.p. 133-135 ℃. ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.37 (s, 1H), 8.45 (s, 1H), 7.76 (d, J = 7.2 Hz, 2H), 7.40 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 7.2 Hz, 1H), 7.13 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 4.05 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 156.7, 140.2, 135.4, 131.4, 130.2, 129.2, 128.3, 126.3, 125.6, 115.9, 33.4. m/z = 251.09, LC-MS spectrum (+): m/z = 252.15, HRMS (ESI+): calculated for $C_{16}H_{13}NO_2$ $[M+H]^+$: 252.1024, Found $[M+H]^+$: 252.1016.



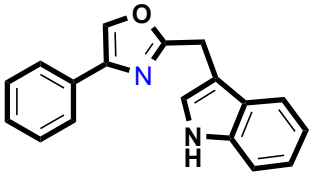
2-(naphthalen-1-ylmethyl)-4-phenyloxazole (3n)



Following the general procedure (EtOAc/Petroleum ether 1:25), 3n was obtained as yellow oil liquid, isolated yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.77 (m, 5H), 7.72 (d, J = 6.8 Hz, 2H), 7.47-7.45 (m, 3H), 7.44 (t, J = 7.6 Hz, 2H), 7.37 (t, J = 5.6 Hz, 1H), 4.33 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 140.9, 133.8, 133.5, 132.9, 132.5, 131.1, 128.8,128.5, 128.0, 127.7, 127.5, 126.9, 126.3, 125.9,125.6, 35.0. m/z = 285.12, LC-MS spectrum (+): m/z = 286.20, HRMS (ESI+): calculated for $C_{20}H_{15}NO$ $[M+H]^+$: 286.1232, Found $[M+H]^+$: 286.1224.

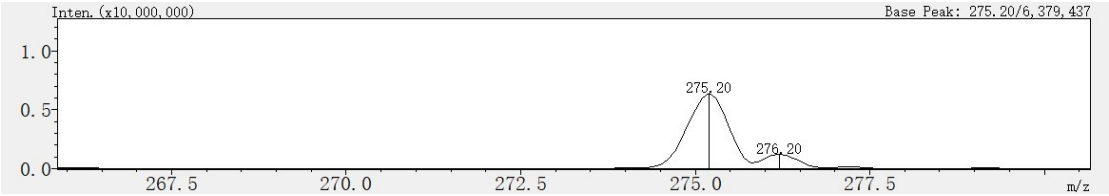


2-((3a,7a-Dihydro-1H-indol-3-yl)methyl)-4-phenyloxazole (3o)

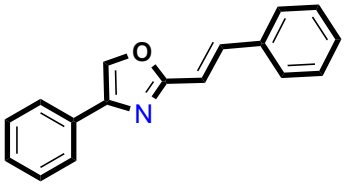


Following the general procedure (EtOAc/Petroleum ether 1:20), 3o was

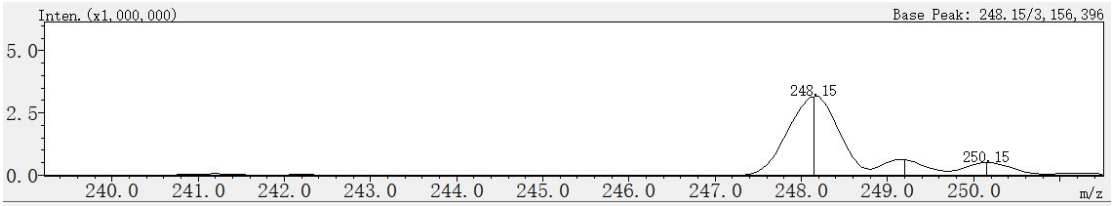
obtained as yellow oil liquid, isolated yield: 86. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 7.77 (s, 1H), 7.71 (d, *J* = 7.2 Hz, 2H), 7.66 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.18-7.09 (m, 4H), 7.05 (s,1H), 4.29 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 140.6, 136.2, 133.54 131.1, 128.7, 127.9, 125.5, 123.0, 122.2, 119.6, 118.9, 111.3, 109.6, 25.0 m/z = 274.11, LC-MS spectrum (+): m/z = 275.20, HRMS (ESI+): calculated for $C_{18}H_{14}N_2O$ $[M+H]^+$:275.1184, Found $[M+H]^+$: 275.1176.



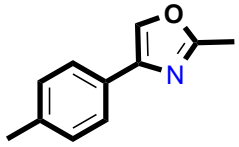
(*E*)-4-Phenyl-2-styryloxazole (3p)



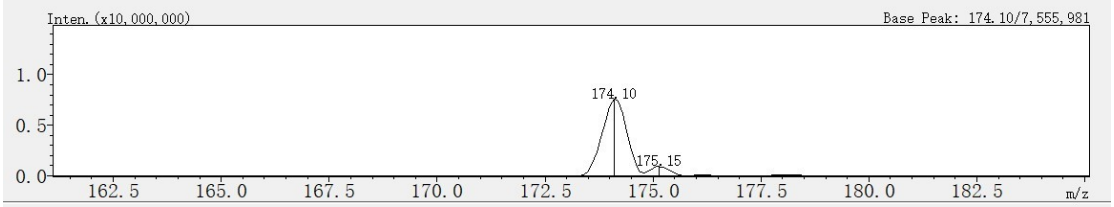
Following the general procedure (EtOAc/Petroleum ether 1:25), 3p was obtained as yellow solid, isolated yield: 88%, m.p. 128-129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.77 (d, *J* = 7.6 Hz, 2H), 7.54-7.52 (m, 3H), 7.43-7.31(m, 6H), 7.02 (d, *J* = 16.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 136.4, 135.5, 133.2, 131.0, 129.2, 128.9, 128.8, 128.2, 127.2, 125.6, 113.9. m/z = 247.10, LC-MS spectrum (+): m/z = 248.15, HRMS (ESI+): calculated for $C_{17}H_{13}NO$ $[M+H]^+$: 248.1075, Found $[M+H]^+$: 248.1069.



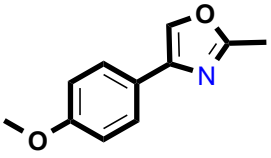
2-Methyl-4-(p-tolyl) oxazole (3q)[1]



Following the general procedure (EtOAc/Petroleum ether 1:25), 3q was obtained as light yellow semi-solid, isolated yield: 90. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 7.6 Hz, 2H), 2.50 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 140.7, 137.7, 132.7, 129.4, 128.4, 125.3, 21.3, 14.0. m/z = 173.08, LC-MS spectrum (+): m/z = 174.10.

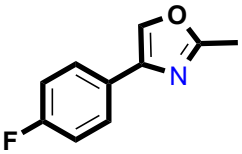


4-(4-Methoxyphenyl)-2-methyloxazole (3r)[3]

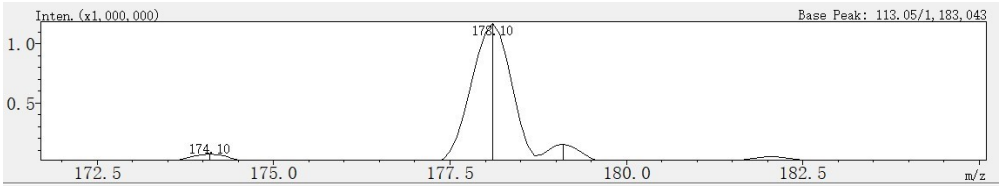


Following the general procedure (EtOAc/Petroleum ether 1:25), 3r was obtained as light yellow semi-solid, isolated yield: 92. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.63 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 159.4, 140.5, 132.1, 126.7, 123.9, 114.2, 55.3, 14.0. m/z = 189.08, MS: m/z = 207.

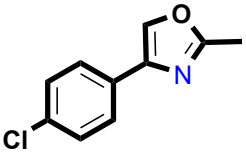
4-(4-Fluorophenyl)-2-methyl-1,3-oxazol (3s)[3]



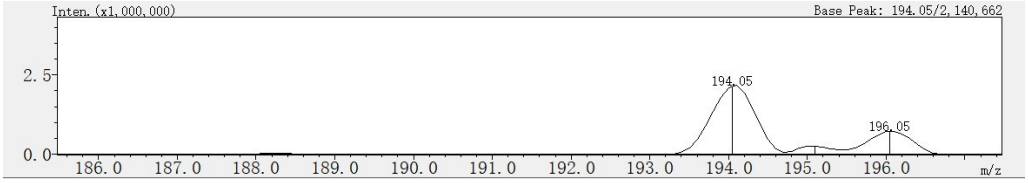
Following the general procedure (EtOAc/Petroleum ether 1:25), 3s was obtained as light yellow semi-solid, isolated yield: 89%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.68 (q, J = 5.2 Hz, 2H), 7.07 (t, J = 8.8 Hz, 2H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 161.9, 161.3, 139.9, 132.8 (d, $J_{c\text{-}f}$ = 2.0 Hz), 127.4 (q, $J_{c\text{-}f}$ = 3.0 Hz), 115.6 (d, $J_{c\text{-}f}$ = 22.0 Hz), 13.9. m/z = 177.06, LC-MS spectrum (+): m/z = 178.10.



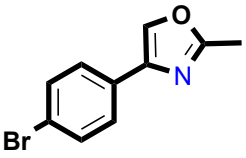
4-(4-Chlorophenyl)-2-methyloxazole (3t)[3]



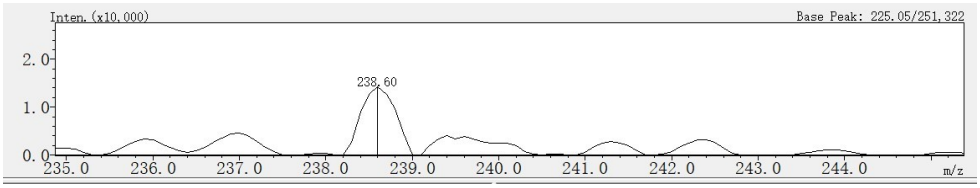
Following the general procedure (EtOAc/Petroleum ether 1:25), 3t was obtained as yellow solid, isolated yield: 91%, m.p. 73-75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 139.8, 133.6, 133.3, 129.7, 128.9, 126.7, 13.9. m/z = 193.03, LC-MS spectrum (+): m/z = 194.05.



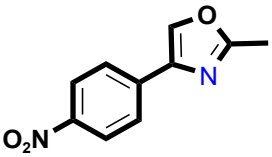
4-(4-Bromophenyl)-2-methyloxazole (3u)[3]



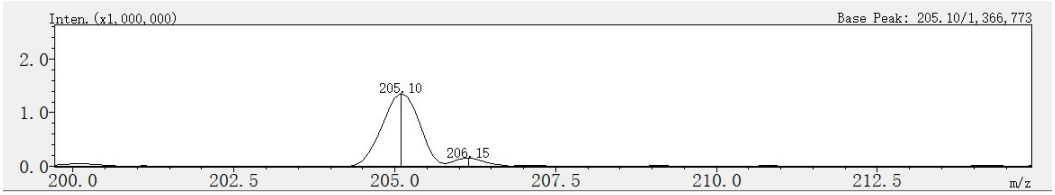
Following the general procedure (EtOAc/Petroleum ether 1:25), 3u was obtained as light yellow semi-solid, isolated yield: 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.58 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 139.8, 133.4, 131.9, 130.2, 127.0, 121.7, 13.9. m/z = 236.98, LC-MS spectrum (+): m/z = 238.60.



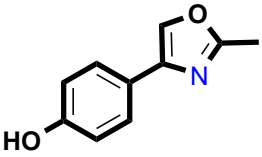
2-Methyl-4-(4-nitrophenyl) oxazole (3v)



Following the general procedure (EtOAc/Petroleum ether 1:25), 3v was obtained as yellow solid, isolated yield: 86%, m.p. 133-135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 8.8 Hz, 2H), 7.96 (s, 1H), 7.88 (d, *J* = 8.8 Hz, 2H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7, 147.2, 139.1, 137.6, 135.4, 125.9, 124.2, 14.0. m/z = 204.05, LC-MS spectrum (+): m/z = 205.10, calculated for $C_{10}H_8N_2O_3$ $[M+H]^+$: 205.0613, Found $[M+H]^+$: 205.0616.

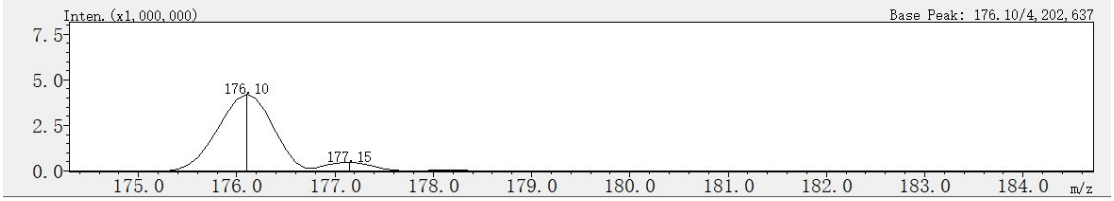


4-(2-Methyloxazol-4-yl) phenol (3w)

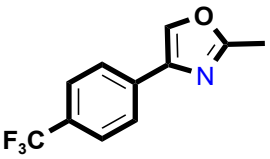


Following the general procedure (EtOAc/Petroleum ether 1:25), 3w was obtained as yellow solid, isolated yield: 80%, m.p. 115-118 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.56 (s, 1H), 8.22 (s, 1H), 7.57 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.0, 157.2, 139.9, 132.7, 126.5 122.1, 115.5, 13.5. m/z = 175.06, LC-MS spectrum

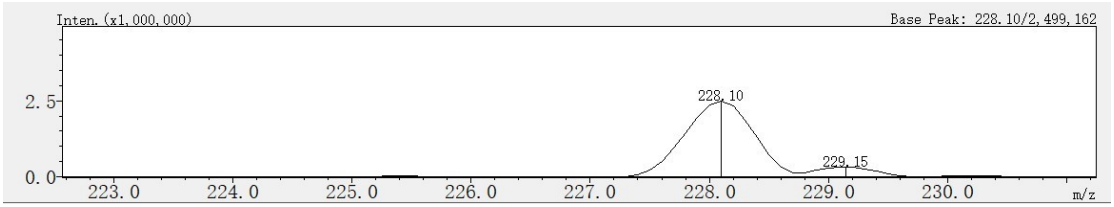
(+): m/z = 176.10, calculated for $C_{10}H_9NO_2$ $[M+H]^+$: 176.0711, Found $[M+H]^+$: 176.0717.



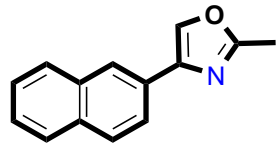
2-Methyl-4-(4-(trifluoromethyl) phenyl) oxazole (3x)[3]



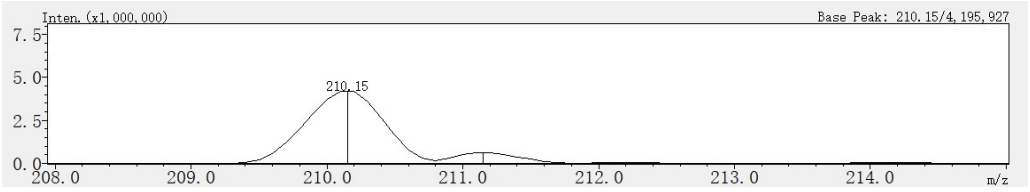
Following the general procedure (EtOAc/Petroleum ether 1:25), 3x was obtained as yellow solid, isolated yield: 81%, m.p. 98-110 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 139.6, 134.7, 134.3, 130.2 (q, $J_{c\text{-}f}$ = 33.0 Hz), 125.7, 125.6, 125.5, 13.9. m/z = 227.06, LC-MS spectrum (+): m/z = 228.10.



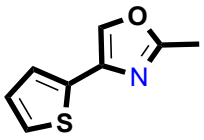
2-Methyl-4-(naphthalen-2-yl)oxazole (3y)[3]



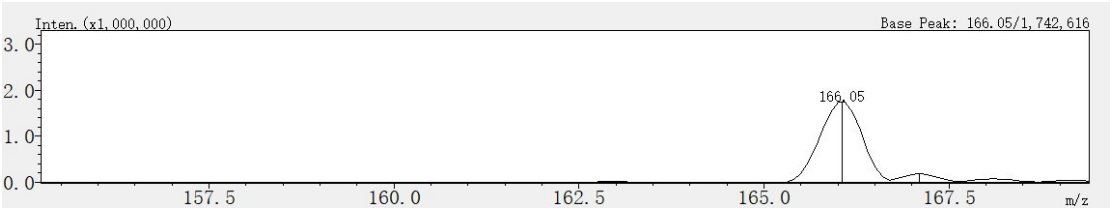
Following the general procedure (EtOAc/Petroleum ether 1:25), 3y was obtained as yellow solid, isolated yield: 88%, m.p. 93-95 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.90 (s, 1H), 7.86-7.80 (m, 3H), 7.73 (d, *J* = 6.8 Hz, 1H), 7.49-7.43 (m, 2H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 140.8, 133.7, 133.6, 133.1, 128.5, 128.4, 128.2, 127.7, 126.4, 126.0, 124.2, 123.4, 14.0. m/z = 209.08, LC-MS spectrum (+): m/z = 210.15.



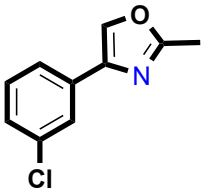
2-Methyl-4-(thiophen-2-yl)oxazole (3z)[3]



Following the general procedure (EtOAc/Petroleum ether 1:25), 3z was obtained as light yellow semi-solid, isolated yield: 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.30-7.25 (m, 2H), 7.04 (d, *J* = 3.6 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 135.8, 133.9, 132.4, 127.6, 124.7, 123.7,13.4. m/z = 165.02, LC-MS spectrum (+): m/z = 166.05.

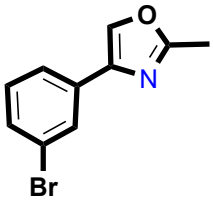


4-(3-Chlorophenyl)-2-methyloxazole (3z1)[3]



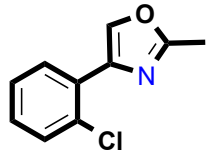
Following the general procedure (EtOAc/Petroleum ether 1:25), 3z1 was obtained as light yellow semi-solid, isolated yield: 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.71 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.33-7.26 (m, 2H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 139.6, 134.8, 133.7, 133.0, 130.0, 127.9, 125.5, 123.5, 14.0. m/z = 193.03, LC-MS spectrum (+): m/z = 194.05.

4-(3-Bromophenyl)-2-methyloxazole (3z2)[3]



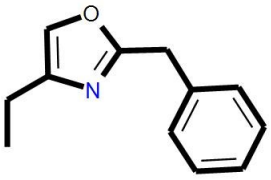
Following the general procedure (EtOAc/Petroleum ether 1:25), 3z2 was obtained as light yellow semi-solid, isolated yield: 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (s, 1H), 7.80 (s, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 6.0 Hz, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 139.5, 133.7, 133.2, 130.8, 130.2, 128.4, 123.9, 122.9, 13.9. m/z = 236.98, LC-MS spectrum (+): m/z = 238.60.

4-(2-Chlorophenyl)-2-methyloxazole (3z3)[3]

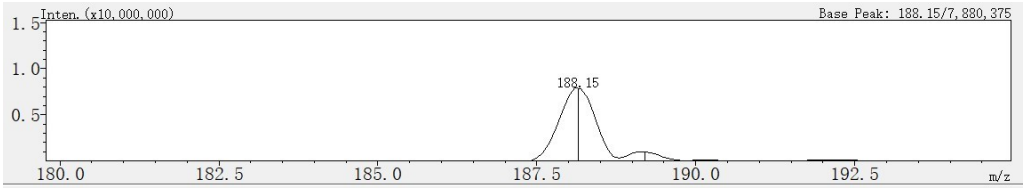


Following the general procedure (EtOAc/Petroleum ether 1:25), 3z3 was obtained as light yellow semi-solid, isolated yield: 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6, 137.0, 136.8, 131.4, 130.2, 129.9, 129.6, 128.4, 126.9, 13.8. m/z = 193.03, LC-MS spectrum (+): m/z =194.05

2-Benzyl-4-ethyloxazole (3z4)[5]



Following the general procedure (EtOAc/Petroleum ether 1:25), 3az4 was obtained as yellow oil solid, isolated yield: 71%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.65 (s, 1H), 7.33-7.21 (m, 5H), 4.06 (s, 2H), 2.43 (q, J = 7.6 Hz, 2H), 1.12 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.3, 142.0, 136.1, 134.1, 128.8, 128.6, 126.8, 33.8, 19.2, 12.6. m/z = 187.10, LC-MS spectrum (+): m/z = 188.15, HRMS (ESI+): Calculated for $C_{12}H_{13}NO$ [M+H]+: 188.1076, Found [M+H]+: 188.1069.



6. Reference

(1) P. F. Carneiro, B. Gutmann, R. O. M. A. de Souza and C. O. Kappe, ACS Sustainable Chem. Eng., 2015, 3, 3445–3453.

(2) Takuma Yagyu, Yusuke Takemoto, Akira Yoshimura, Viktor V. Zhdankin, and Akio Saito, Org. Lett. 2017, 19, 2506−2509

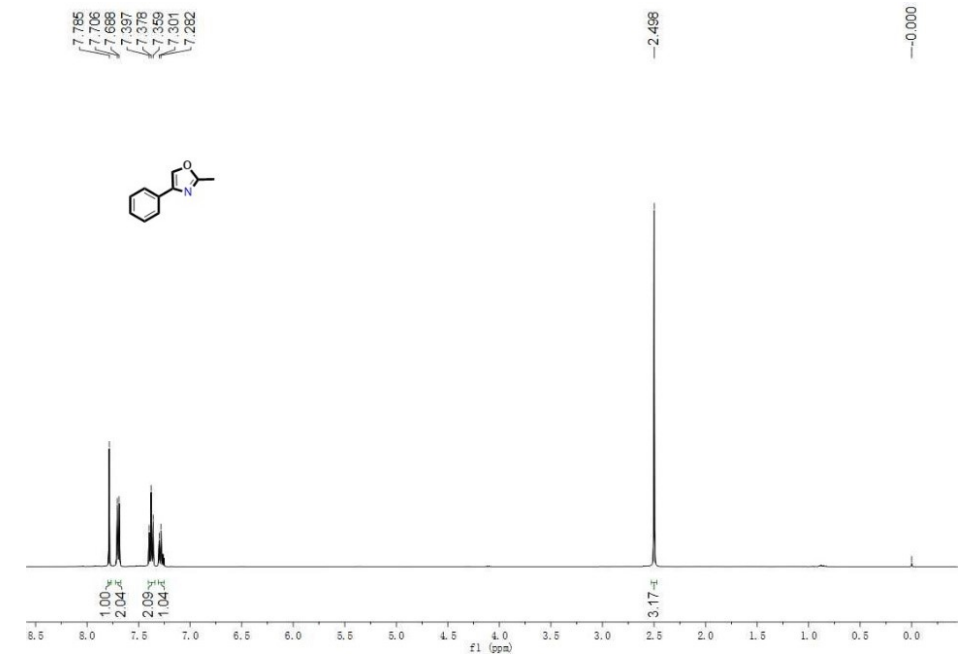
(3) Kang Xu, Ruiqi Yang, Shuang Yang, Cheng Jiang, Zhenhua Ding, Org. Biomol. Chem., 2019, 17, 8977.

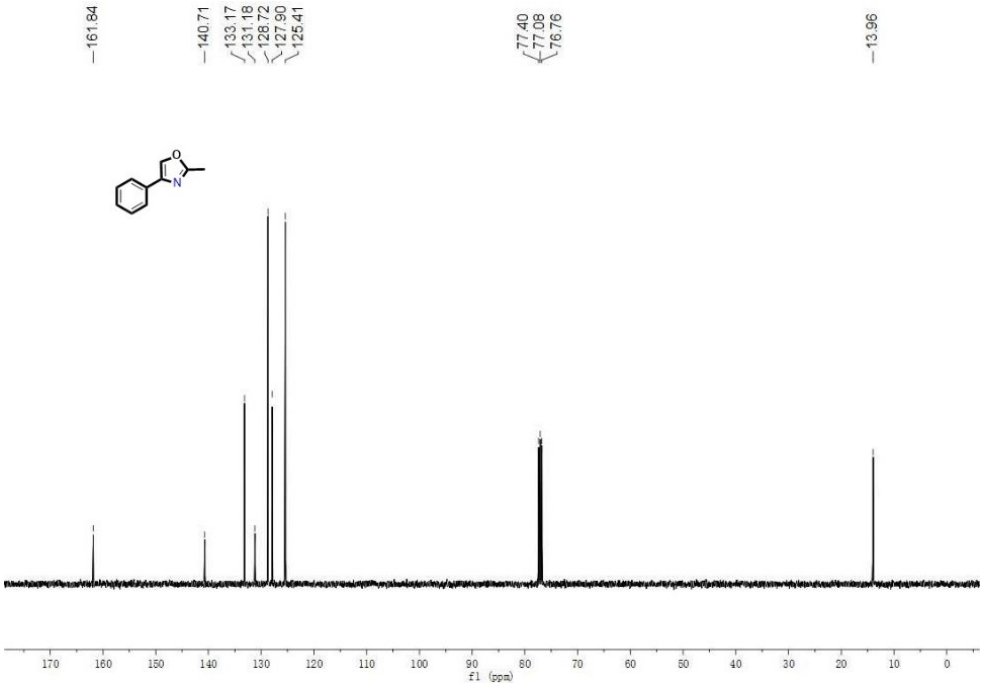
(4) Hiroki Yoneyama, Naoki Oka, Yoshihide Usami, Shinya Harusawa, Tetrahedron Letters 61 (2020) 151983.

(5) M. Ramana Reddy, G. Niranjan Reddy, Umer Mehmood, Ibnelwaleed A. Hussein, S. U. Rahman, Khalil Harrabi, Basireddy V. Subba Reddy, Synthesis 2015, 47, 3315–3320

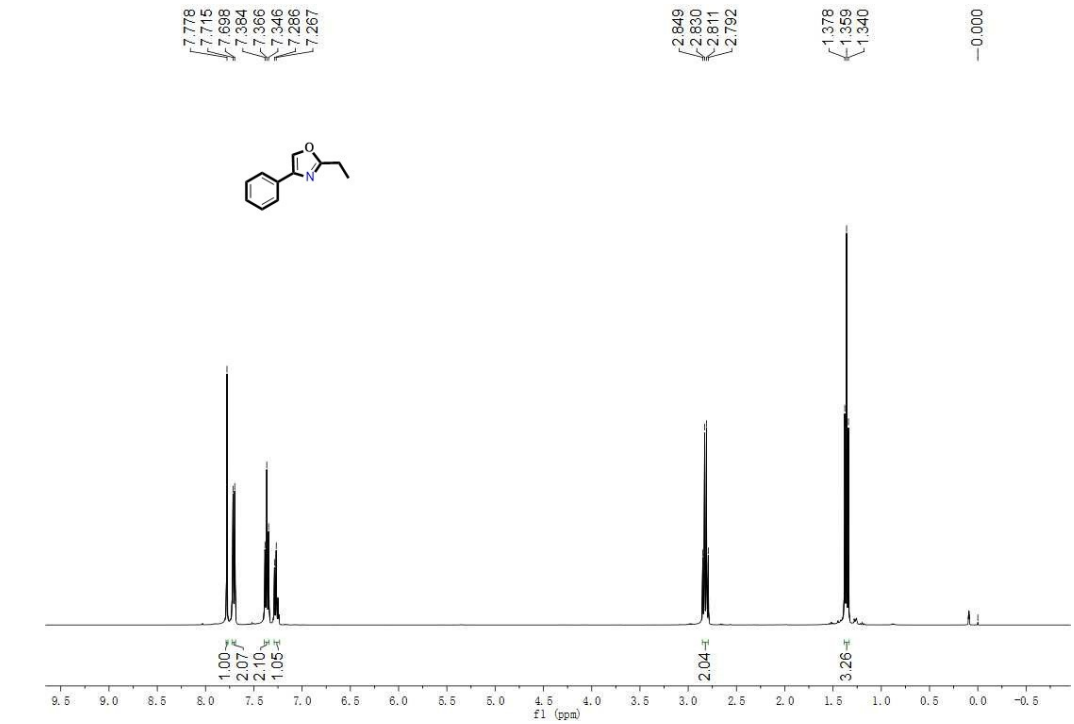
7. Copies of ^{1}H NMR and ^{13}C NMR spectrum

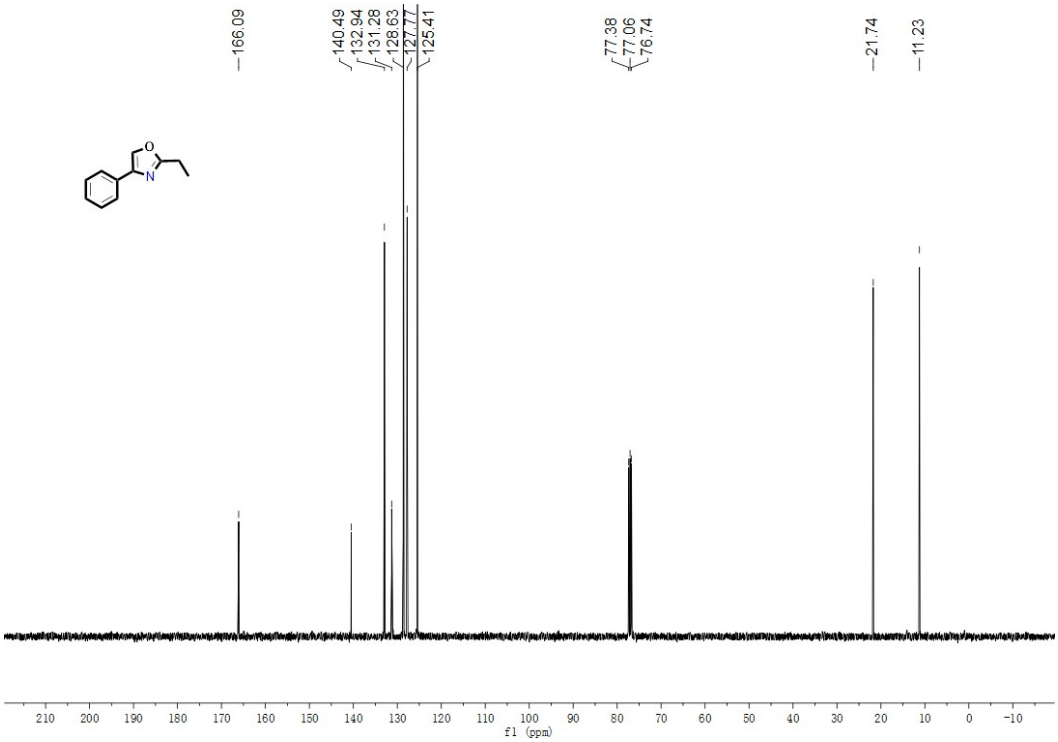
3a ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



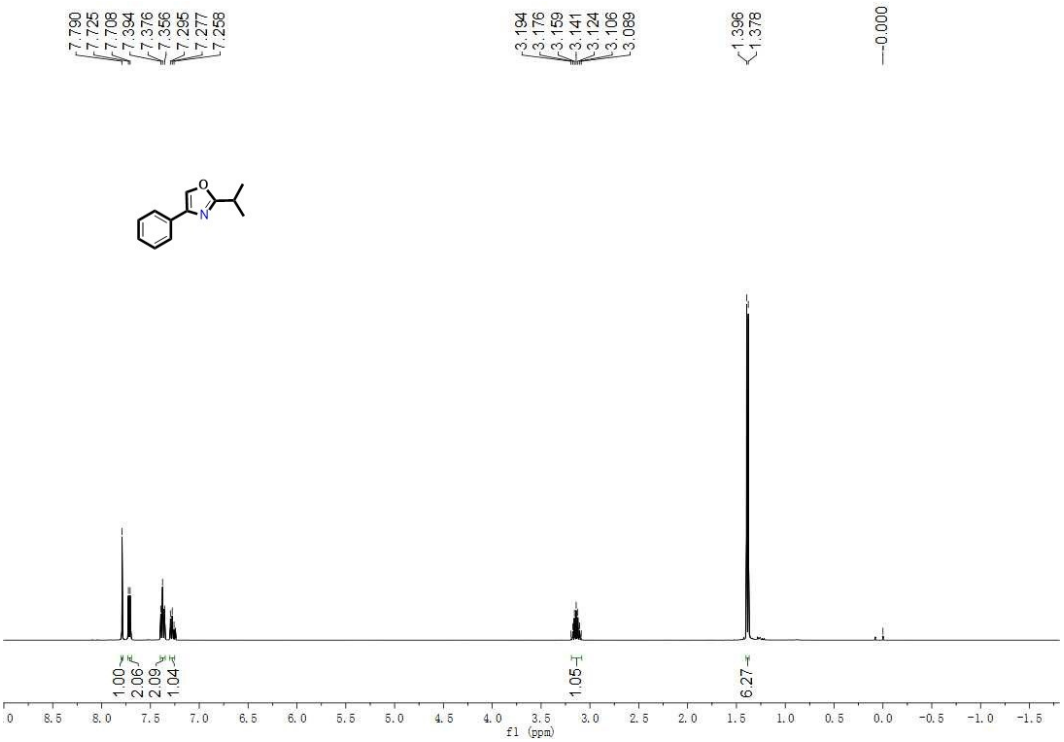


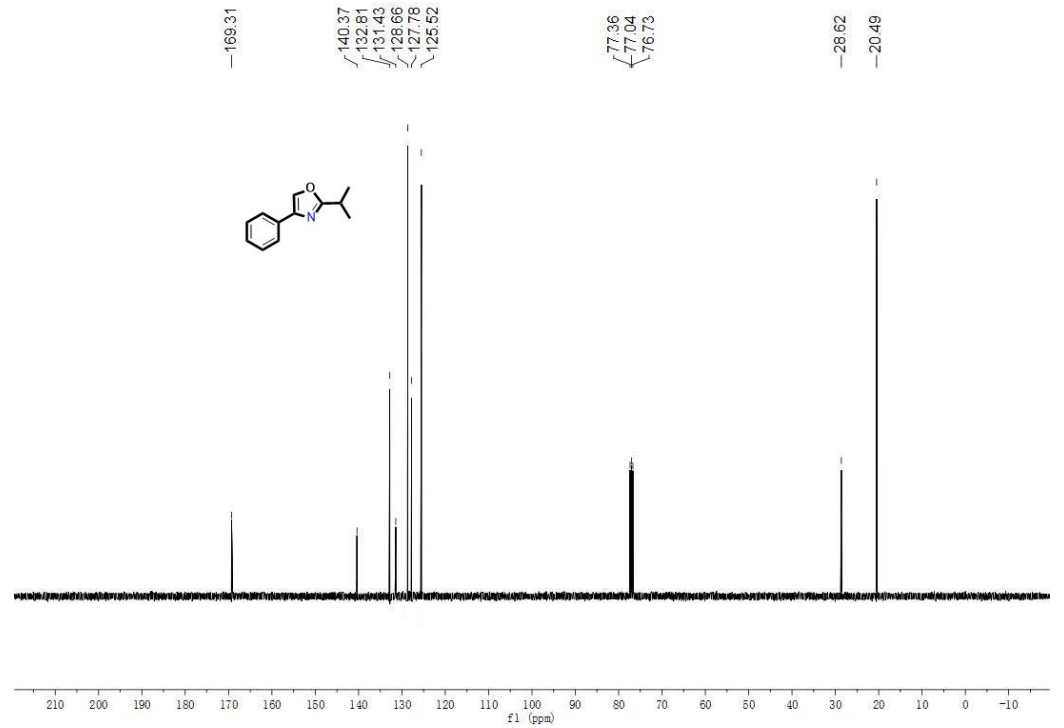
3b ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



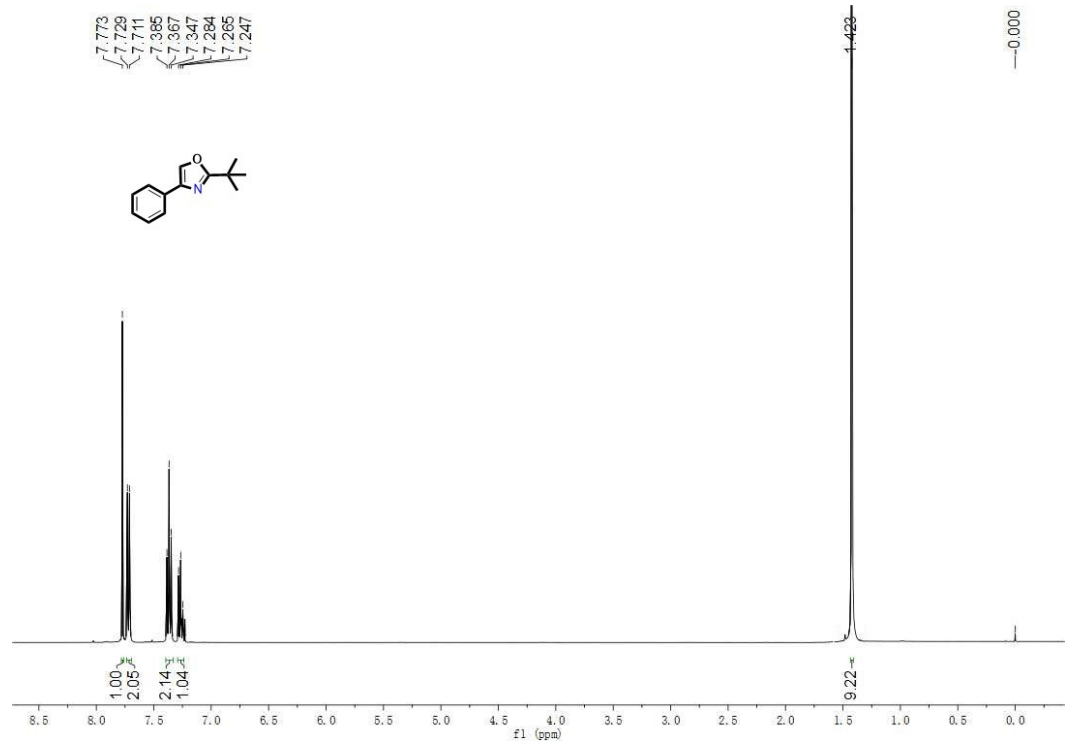


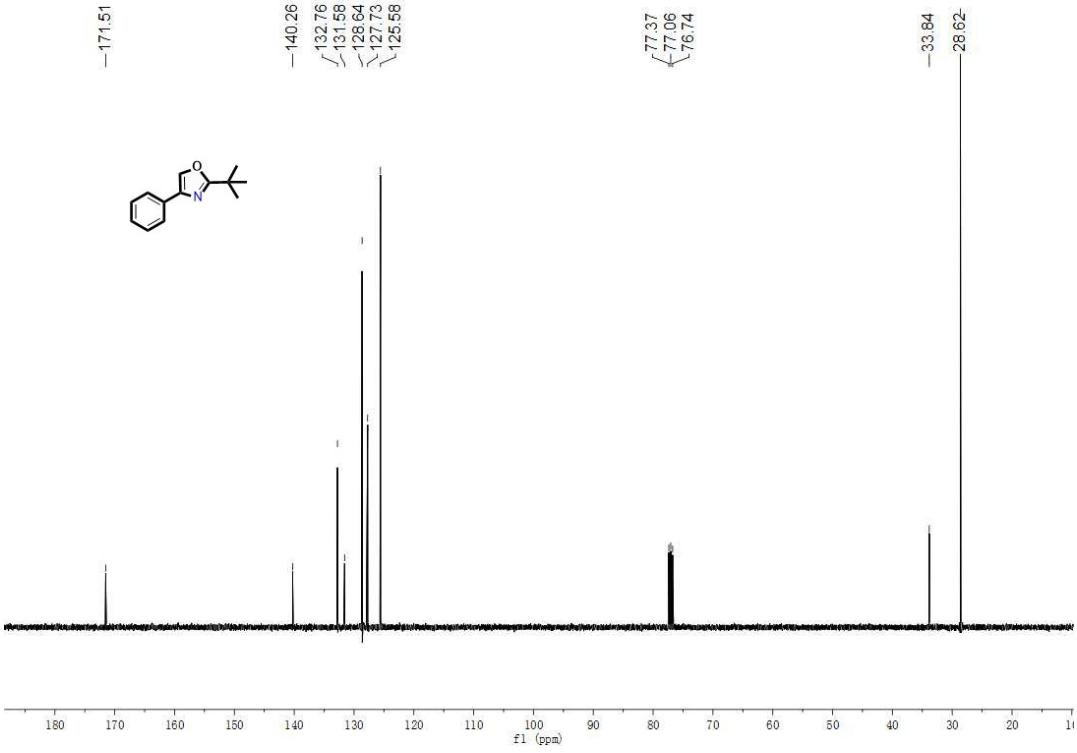
3c ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



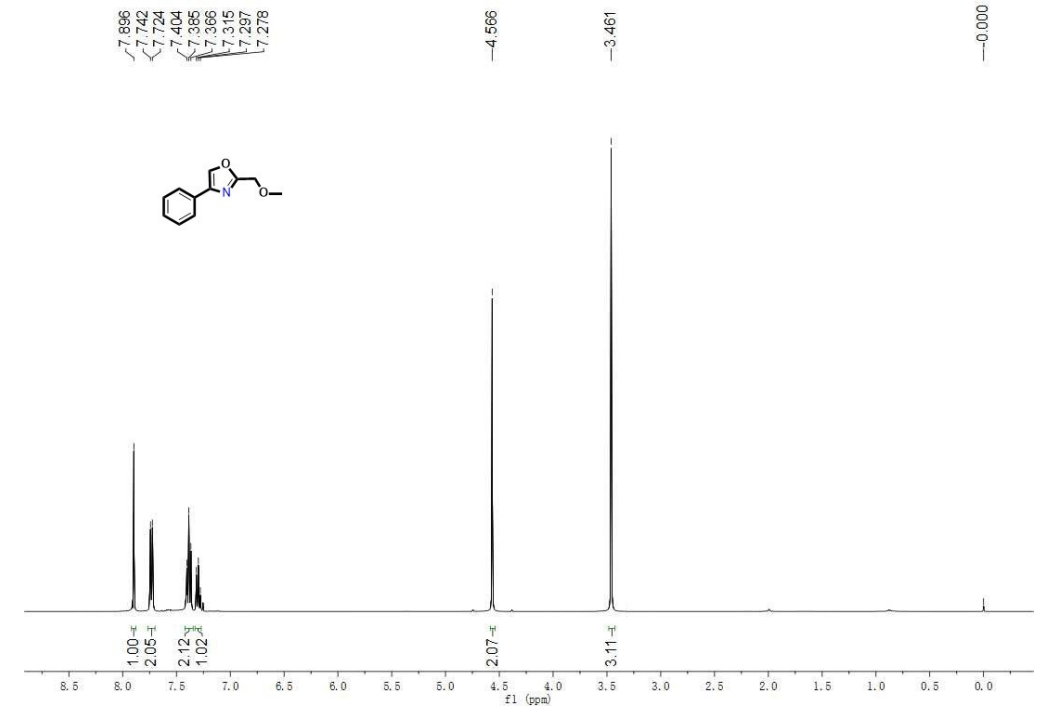


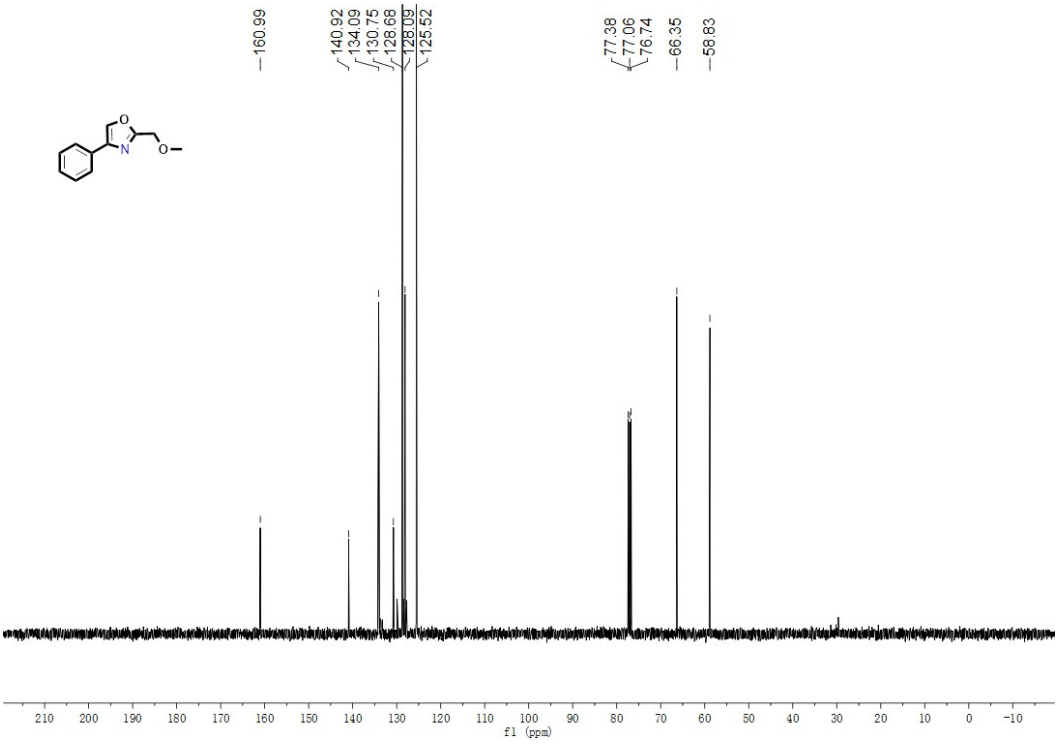
3d ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



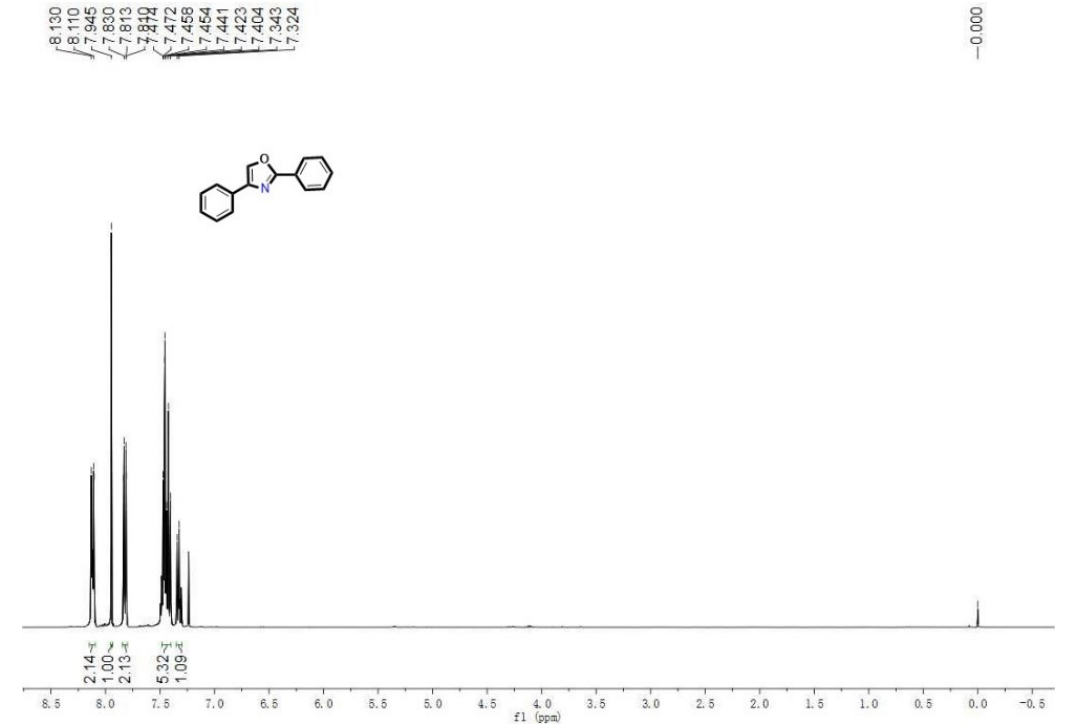


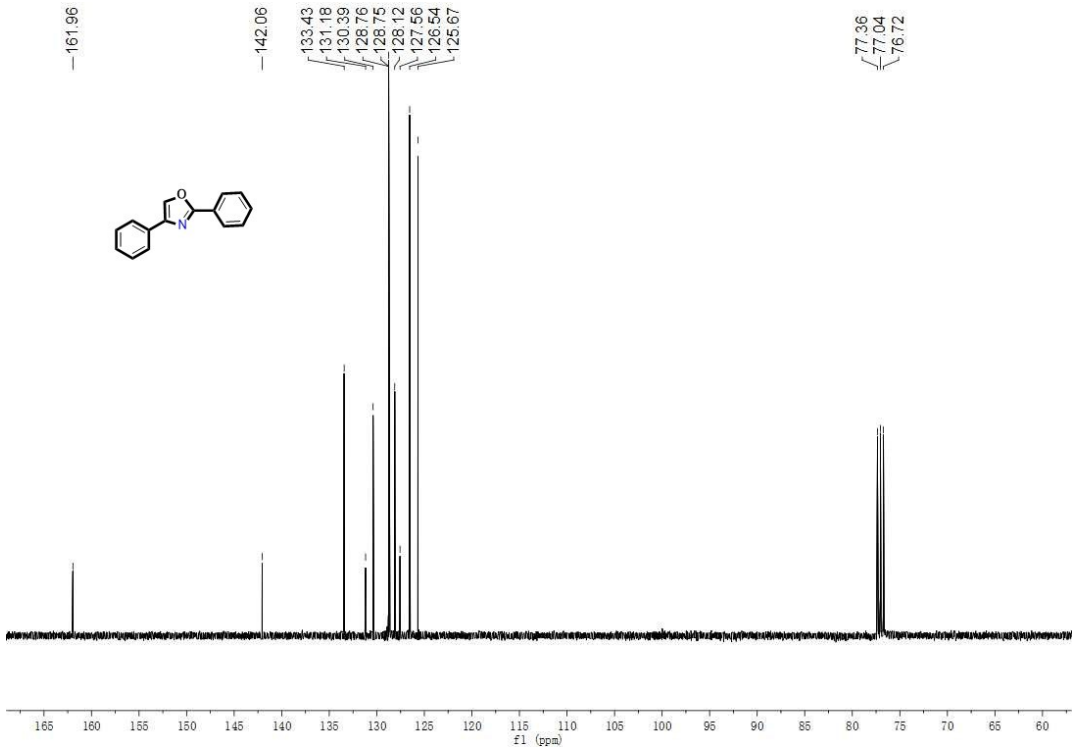
3e ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



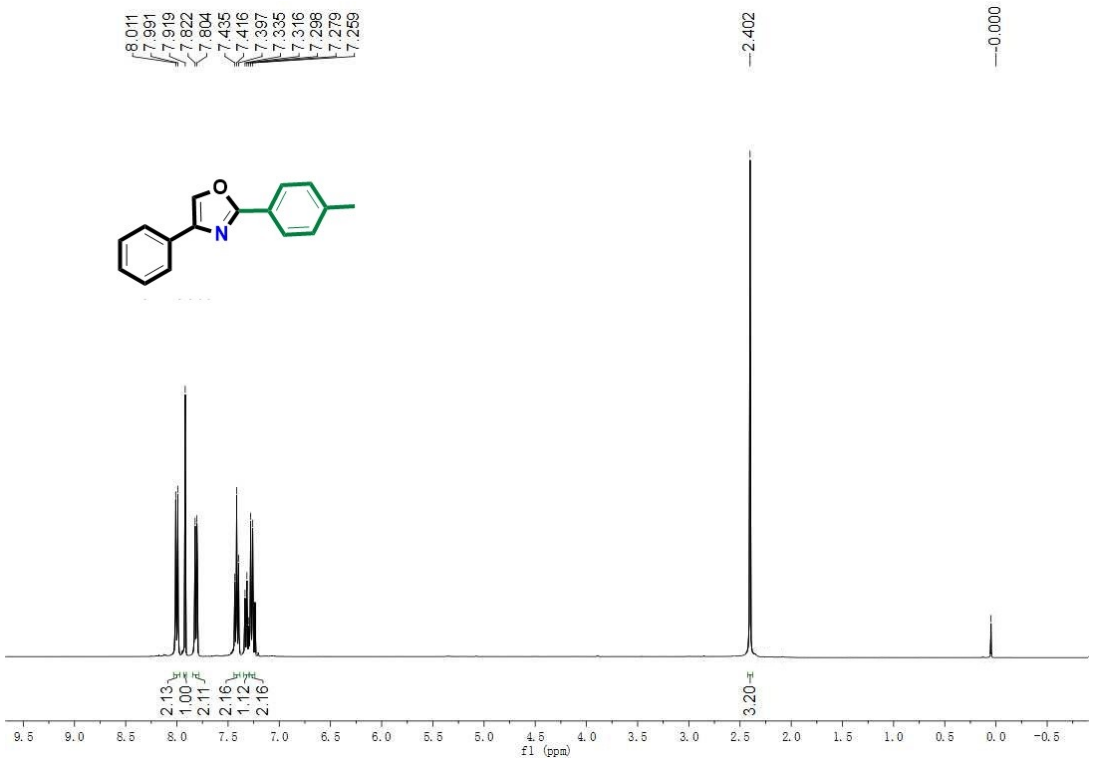


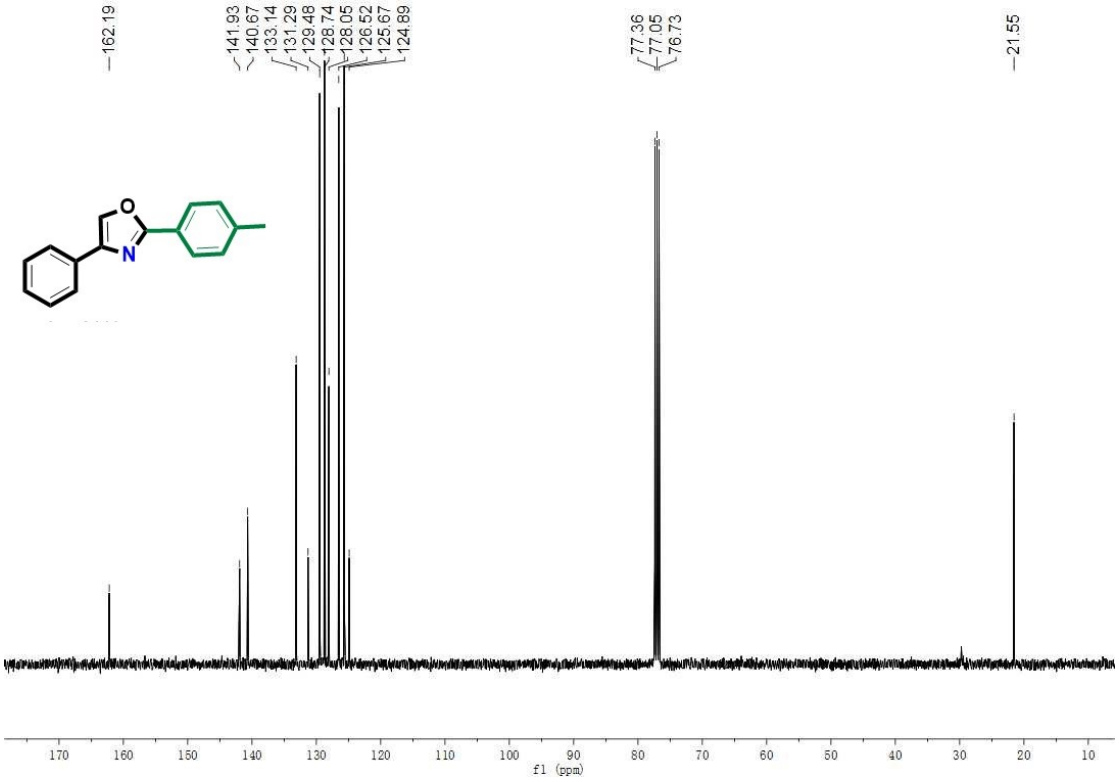
3f ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



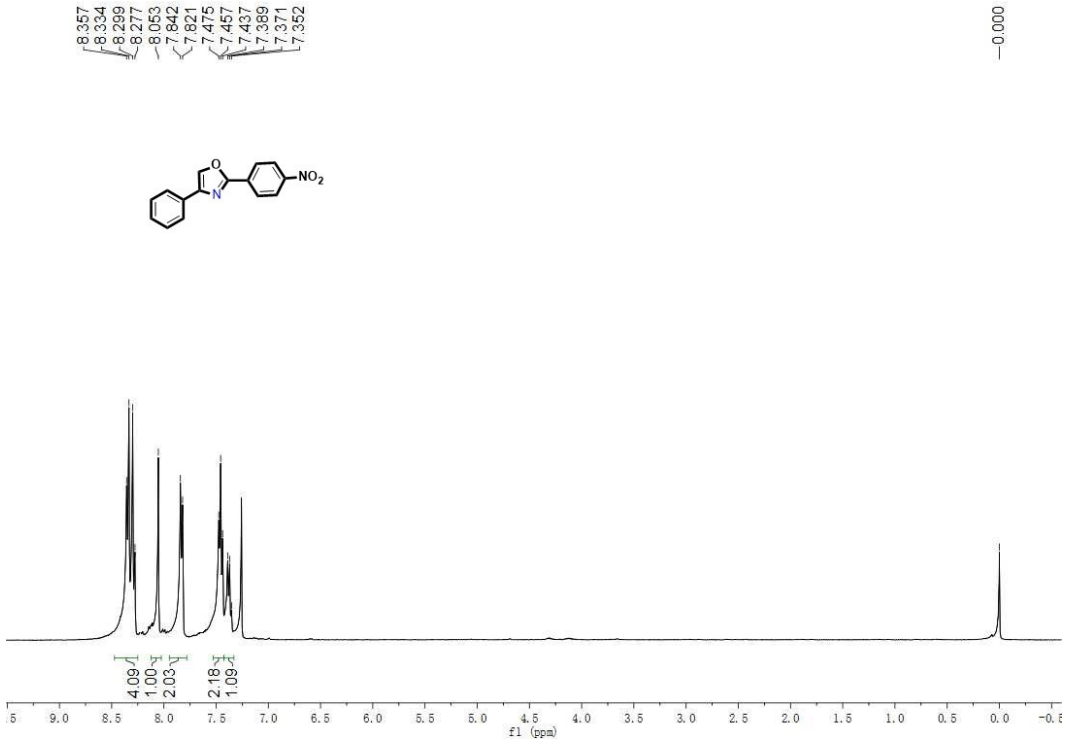


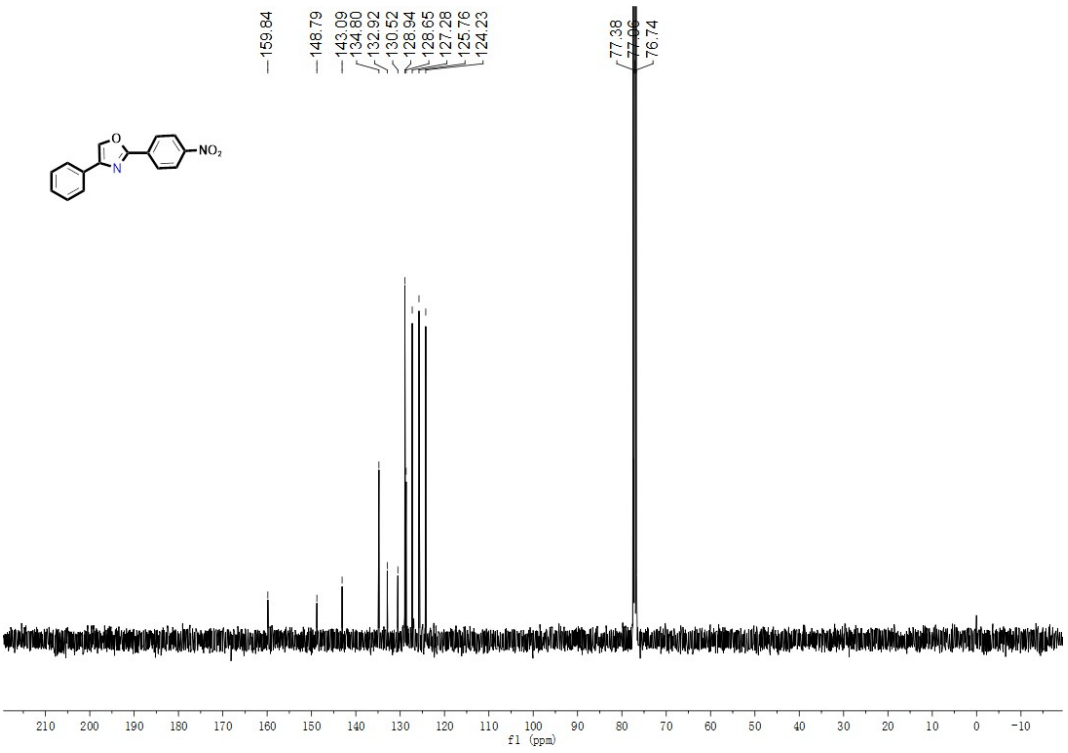
3g ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



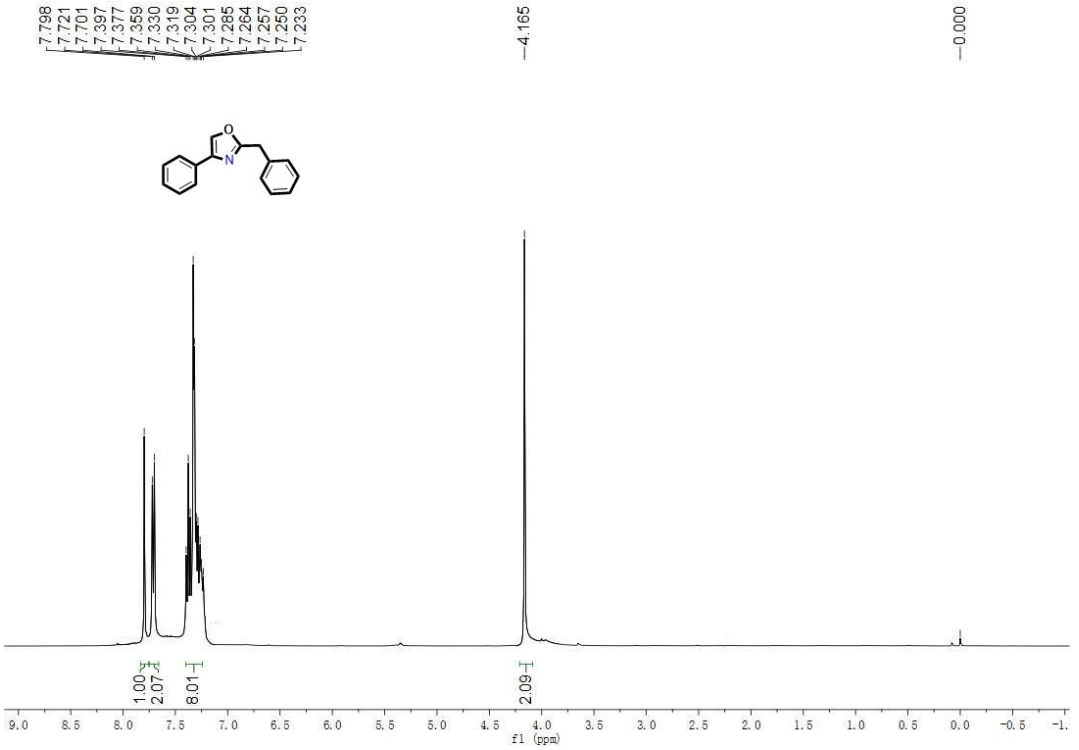


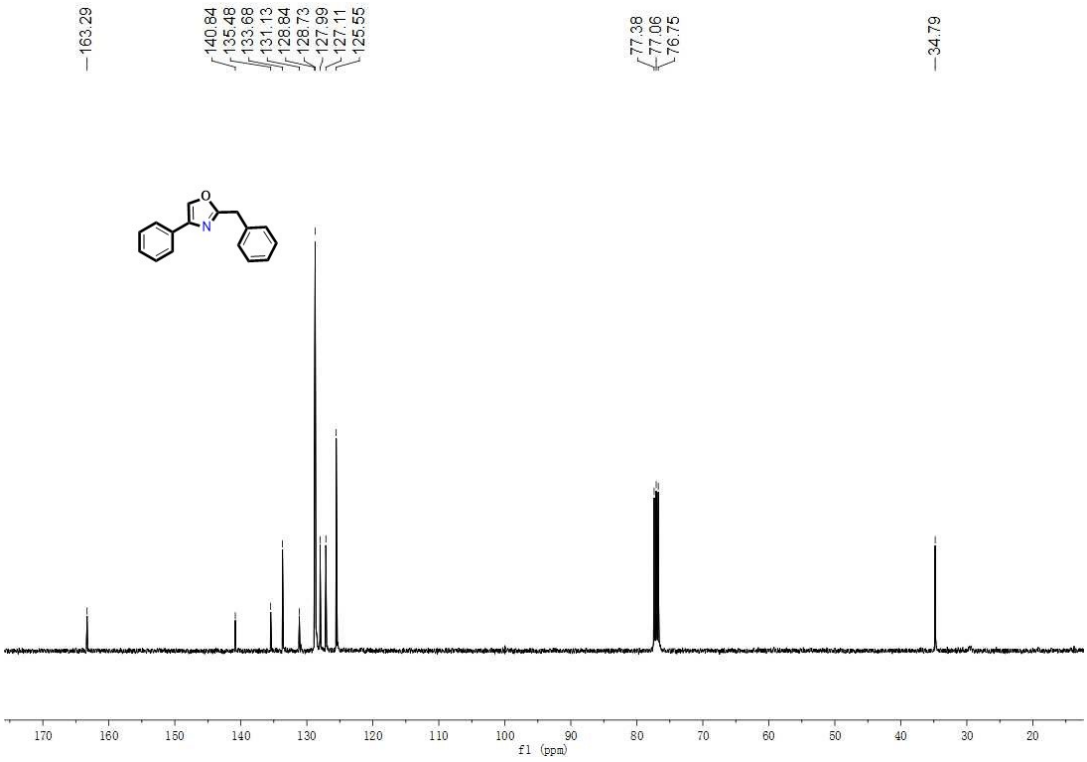
3h ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



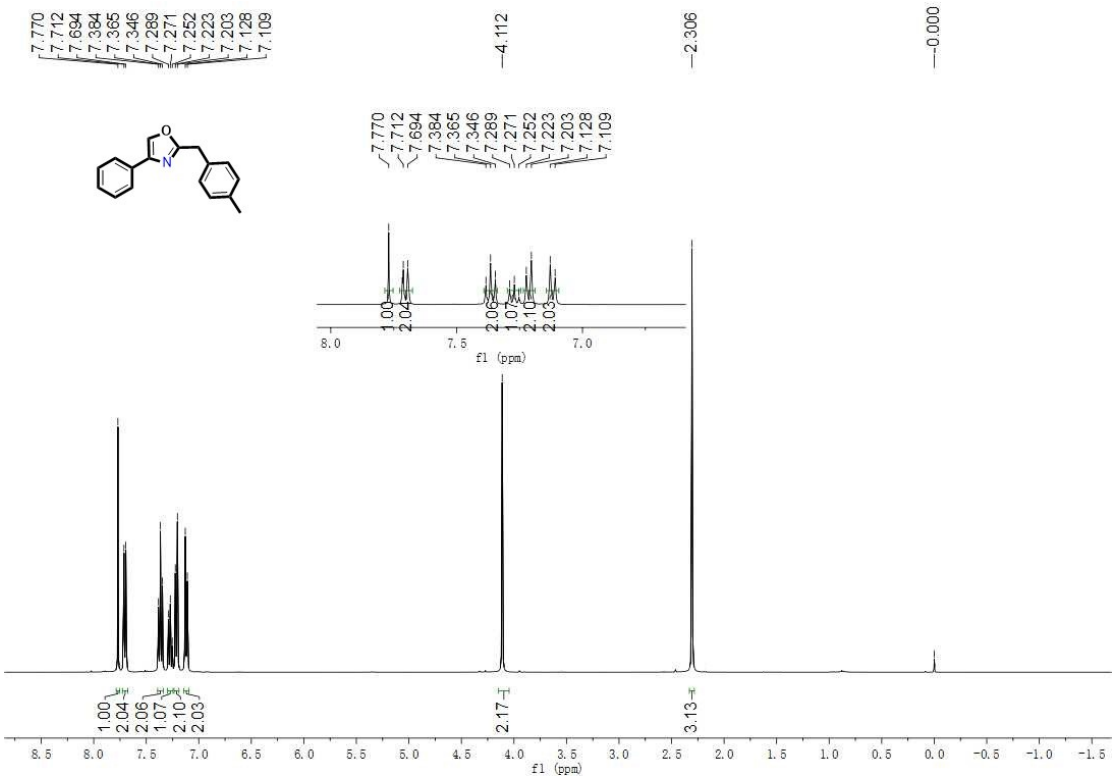


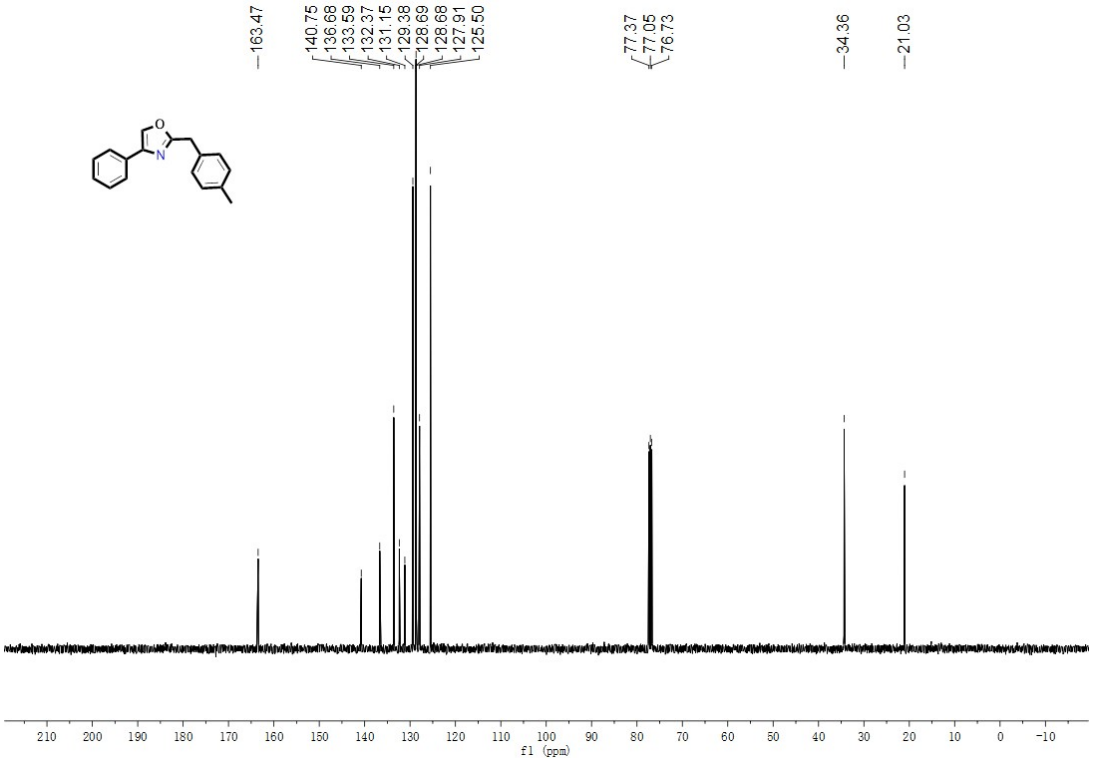
3i ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



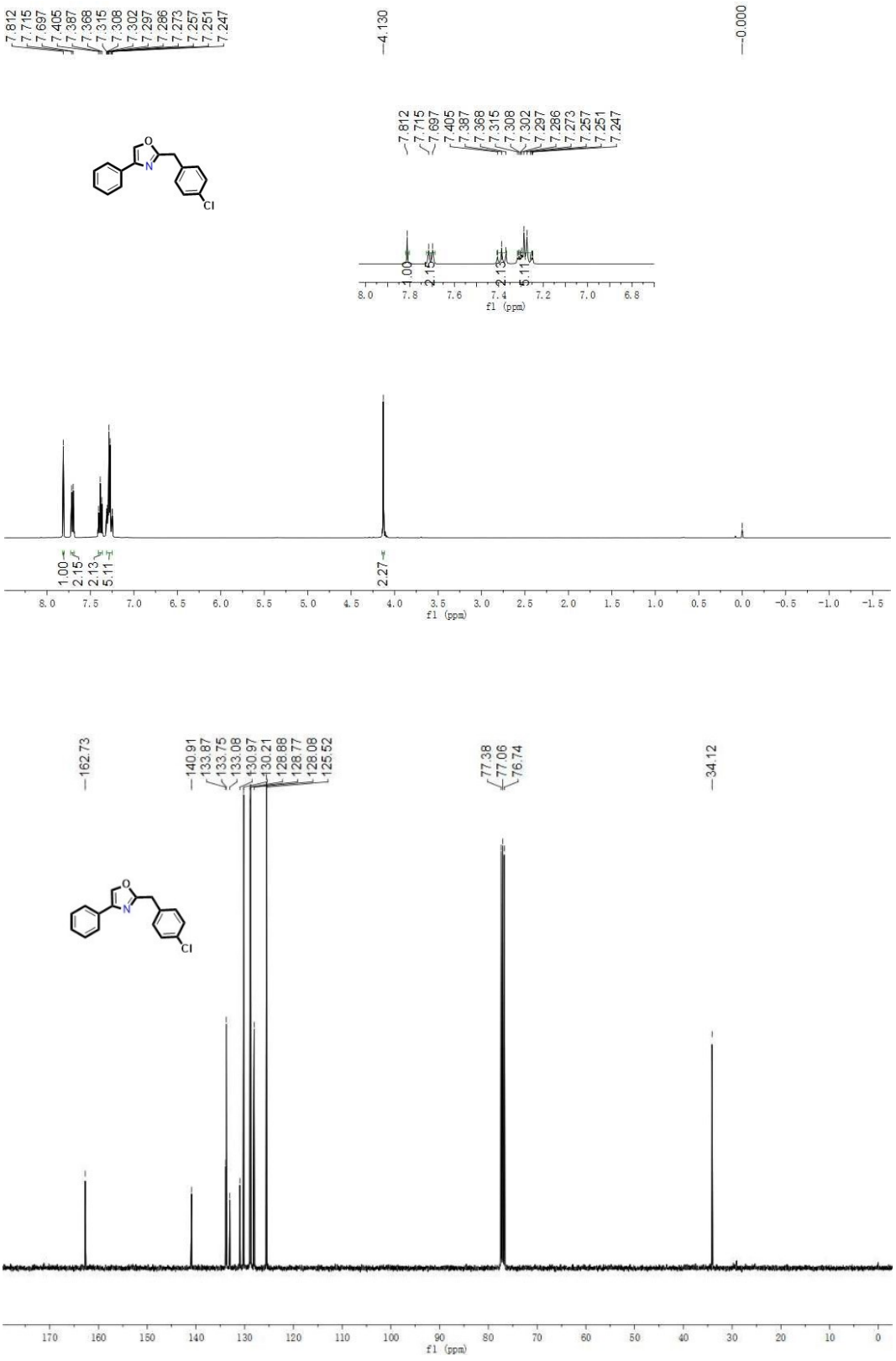


3j ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)

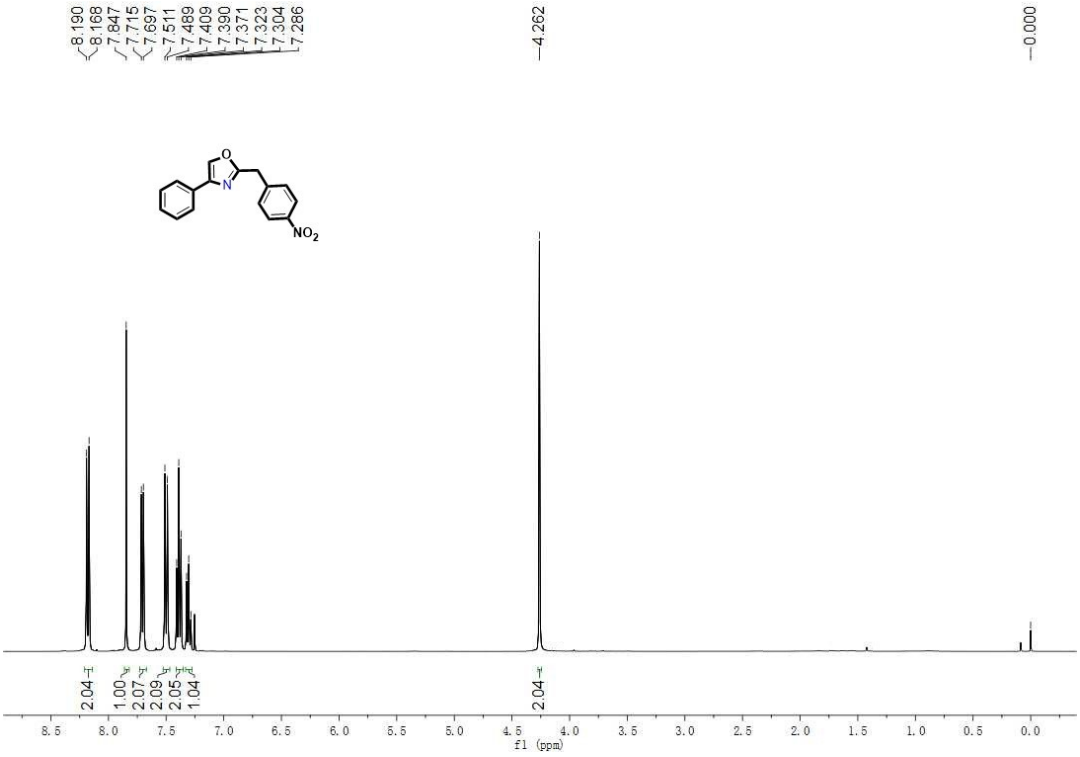


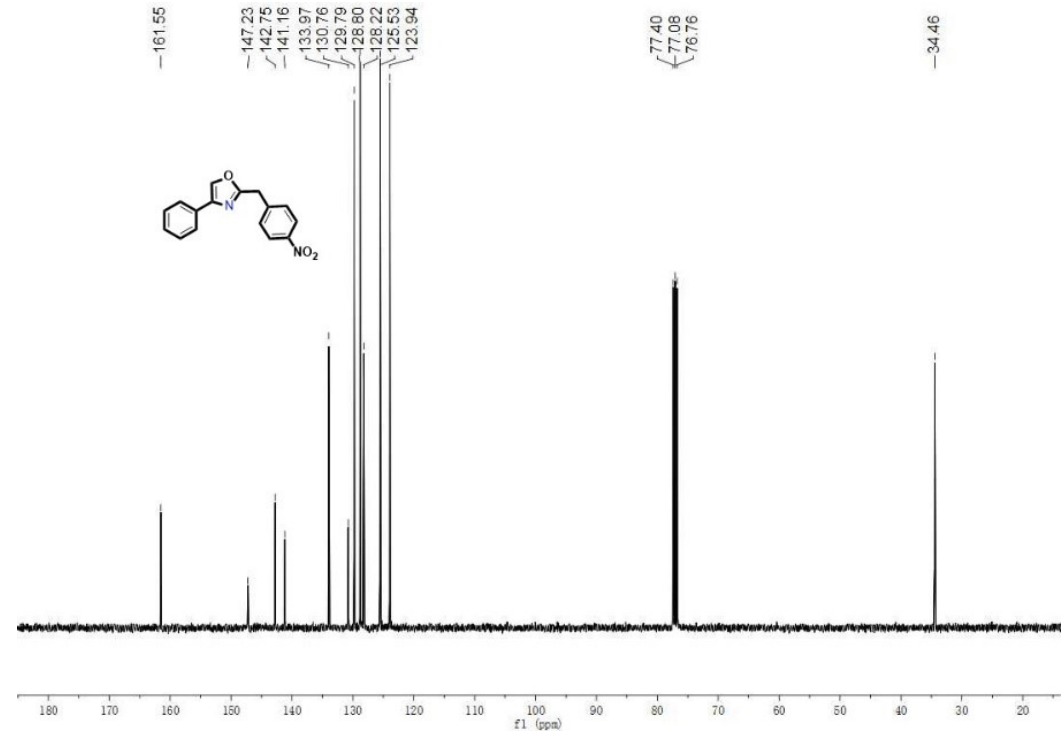


3k ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)

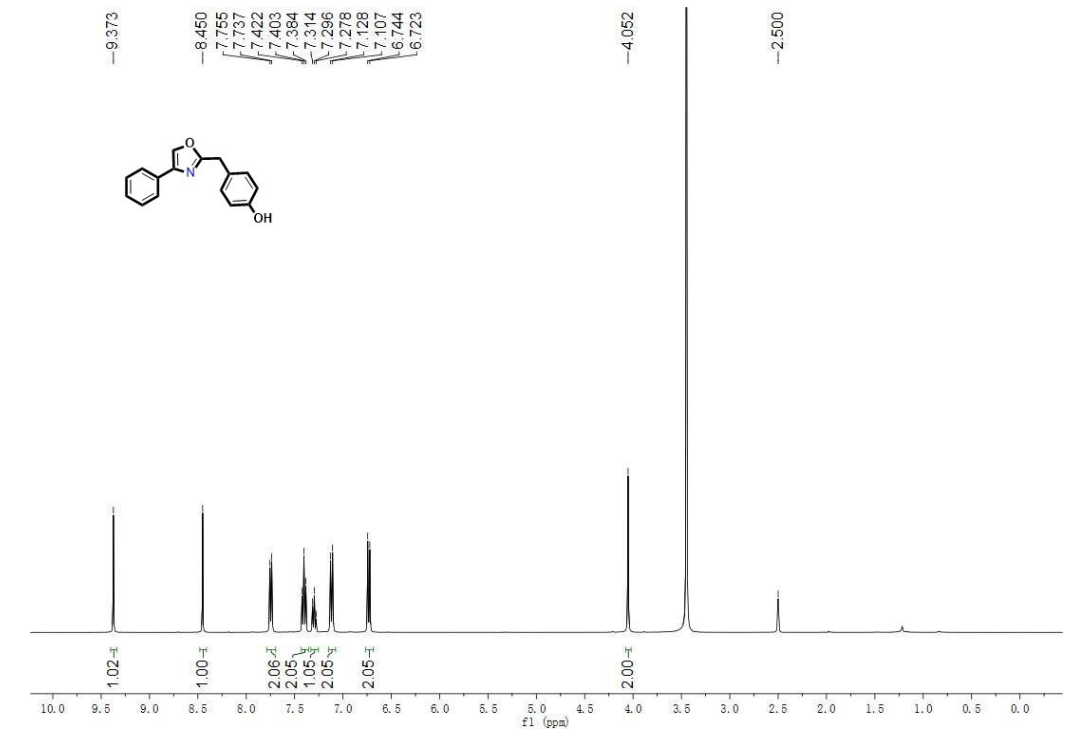


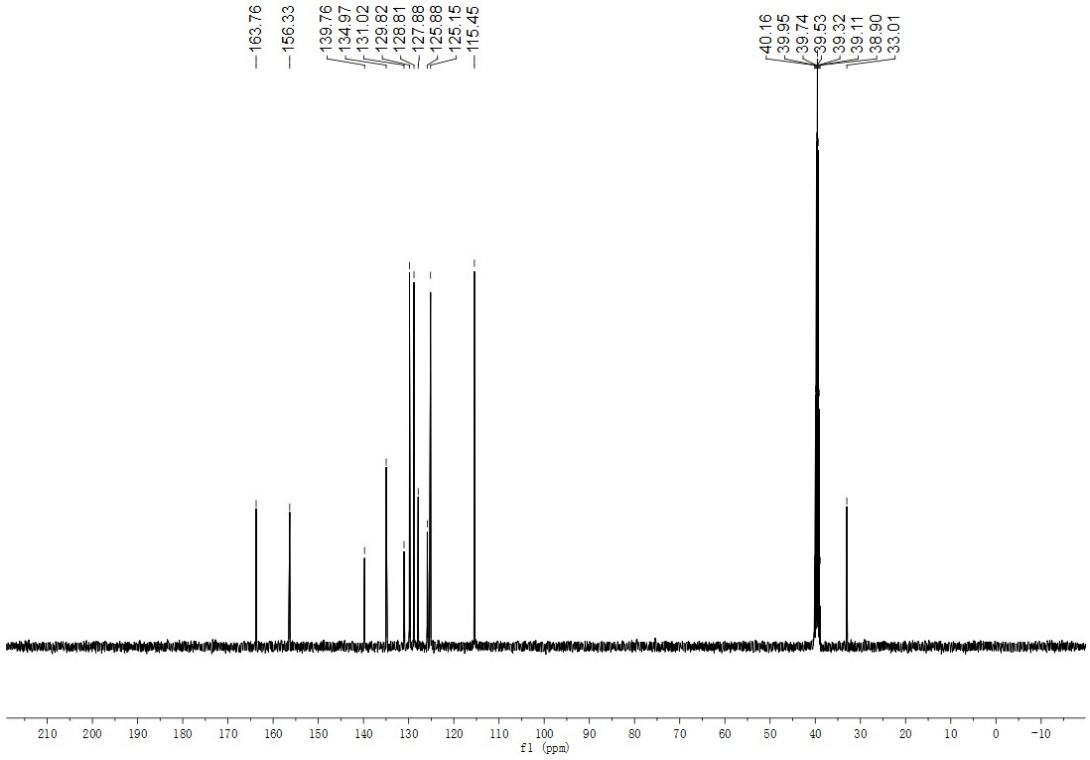
3l ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



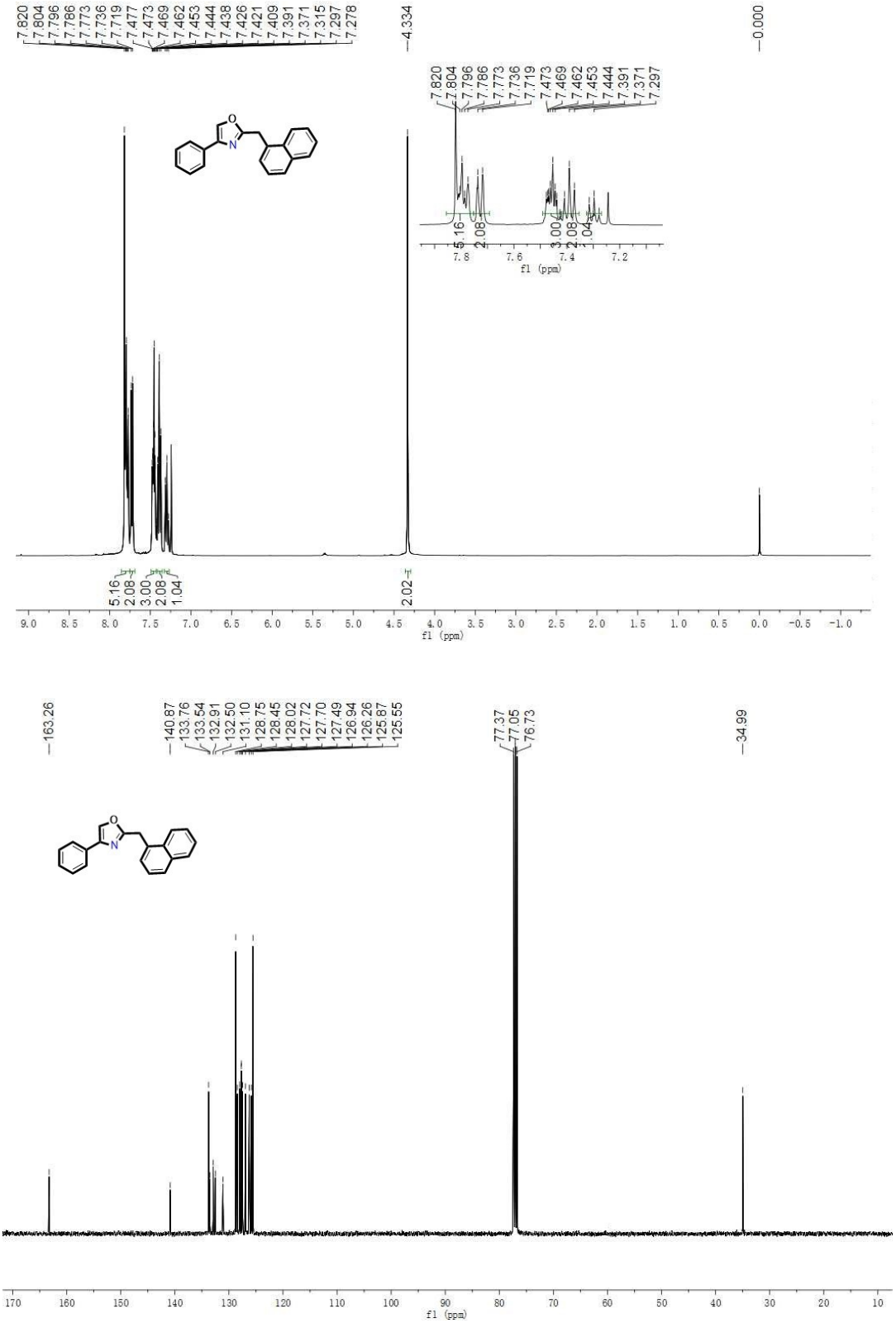


3m ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)

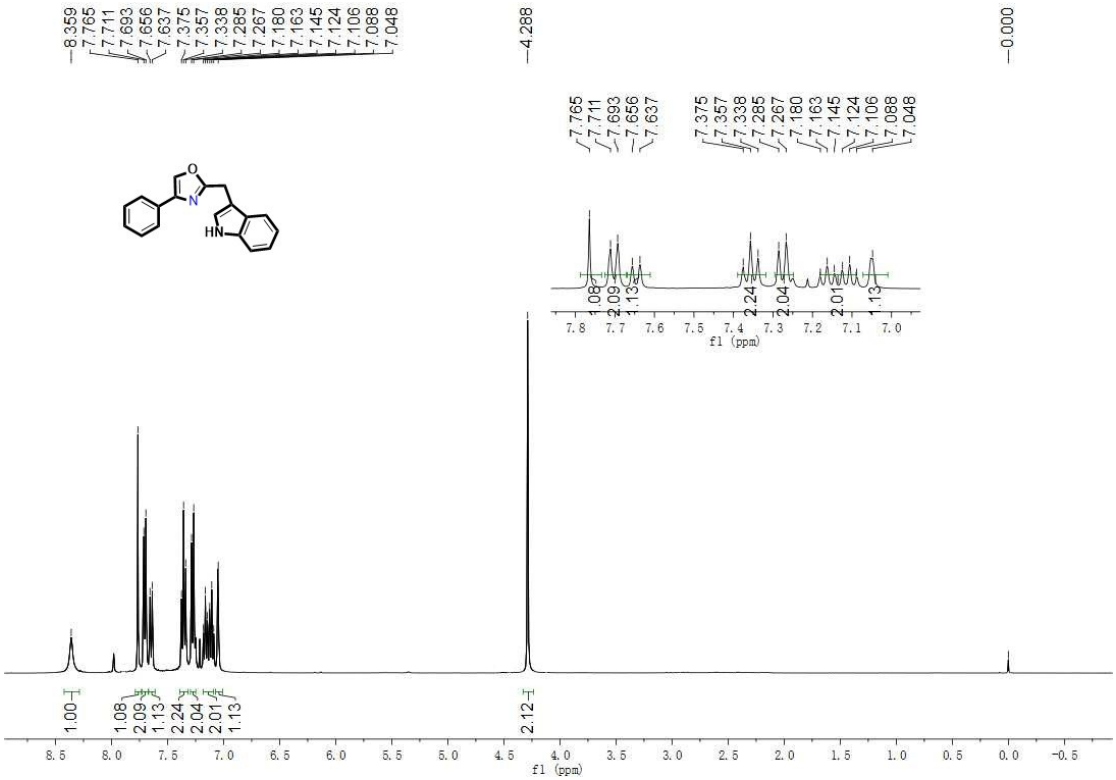


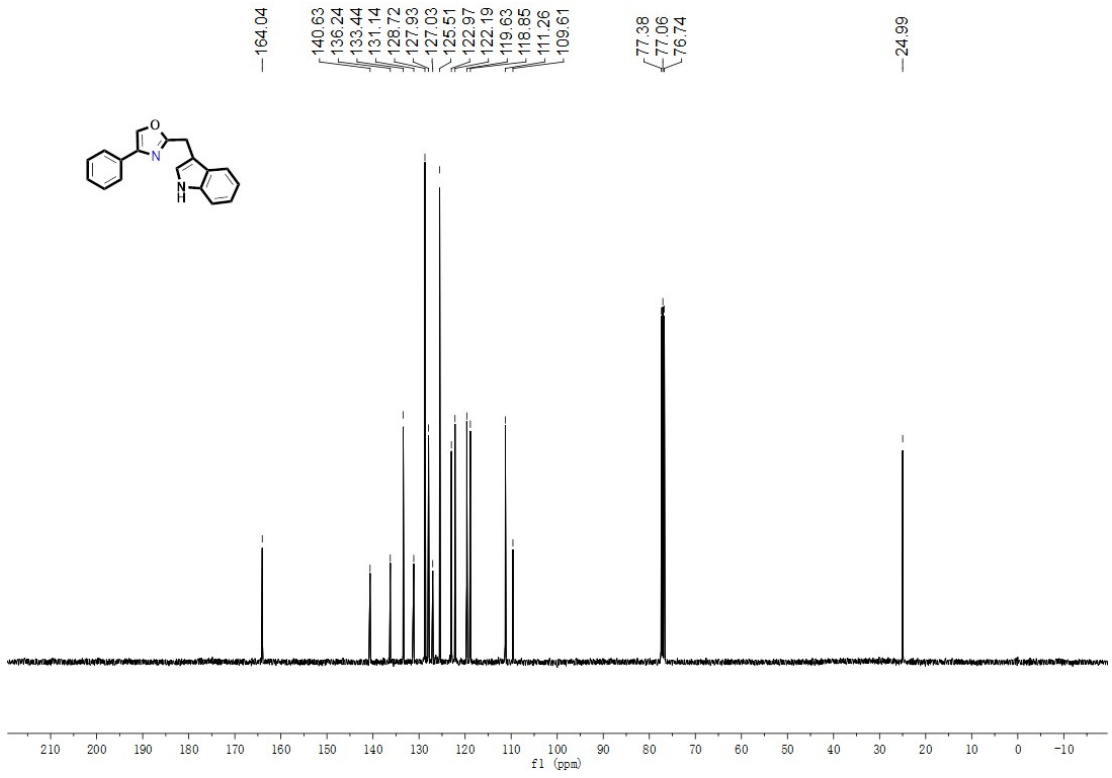


3n ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)

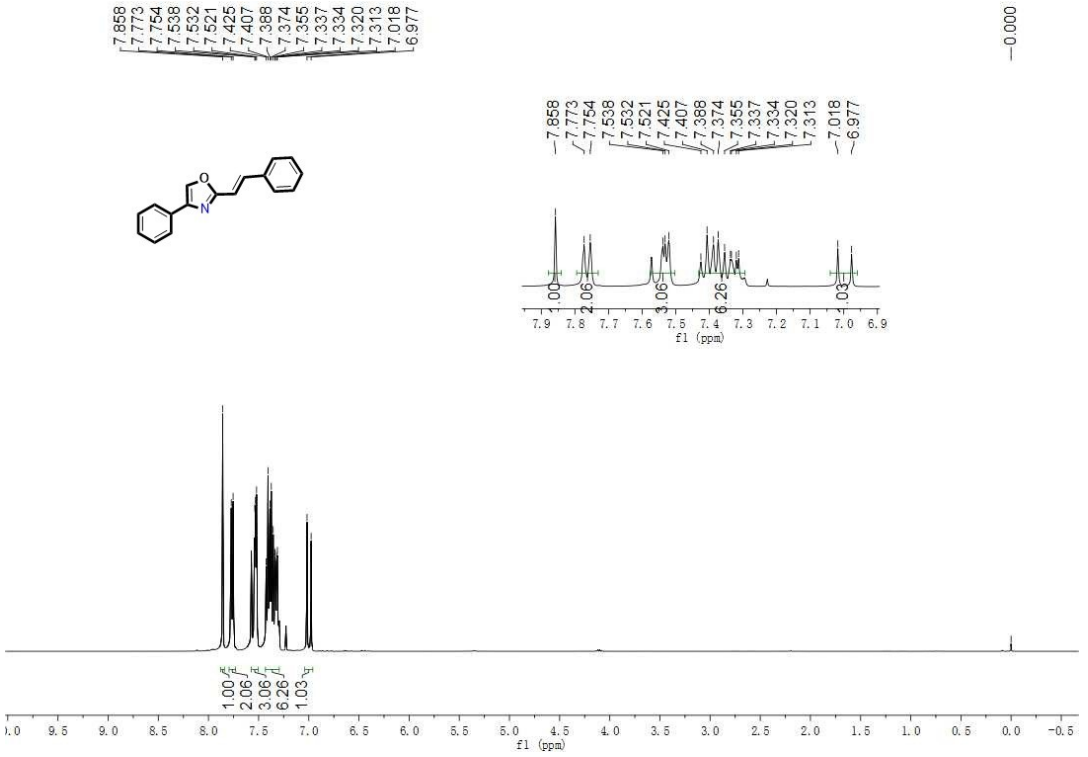


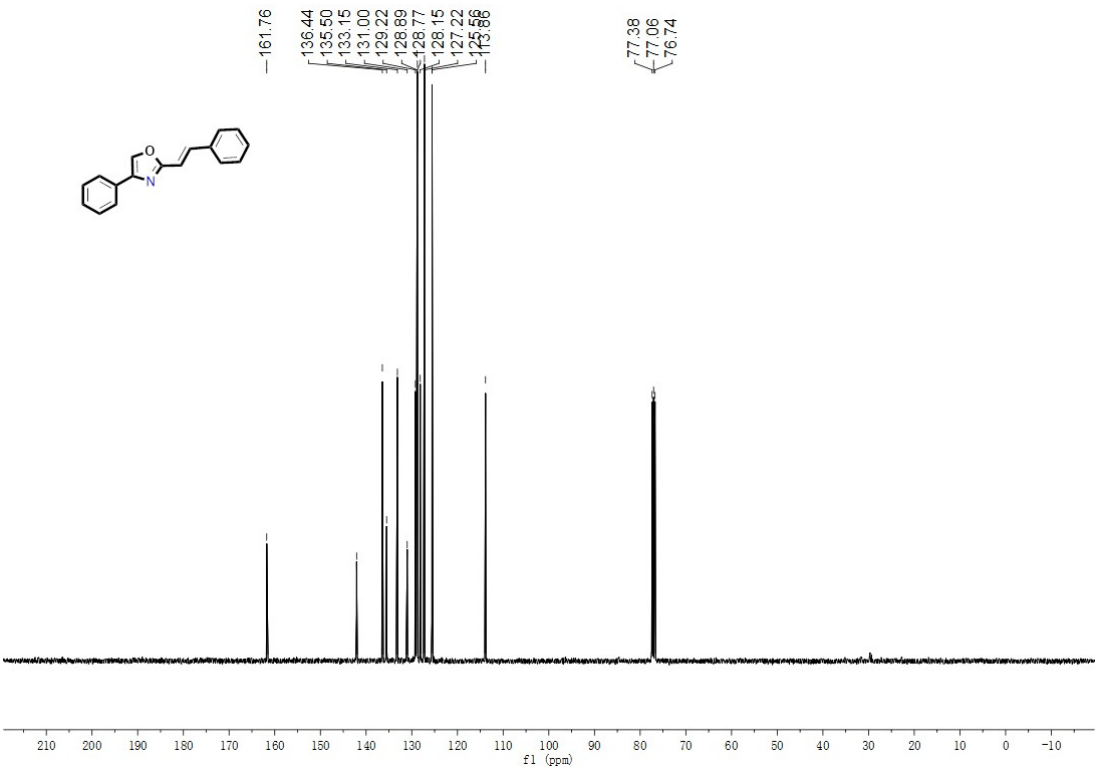
3o ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



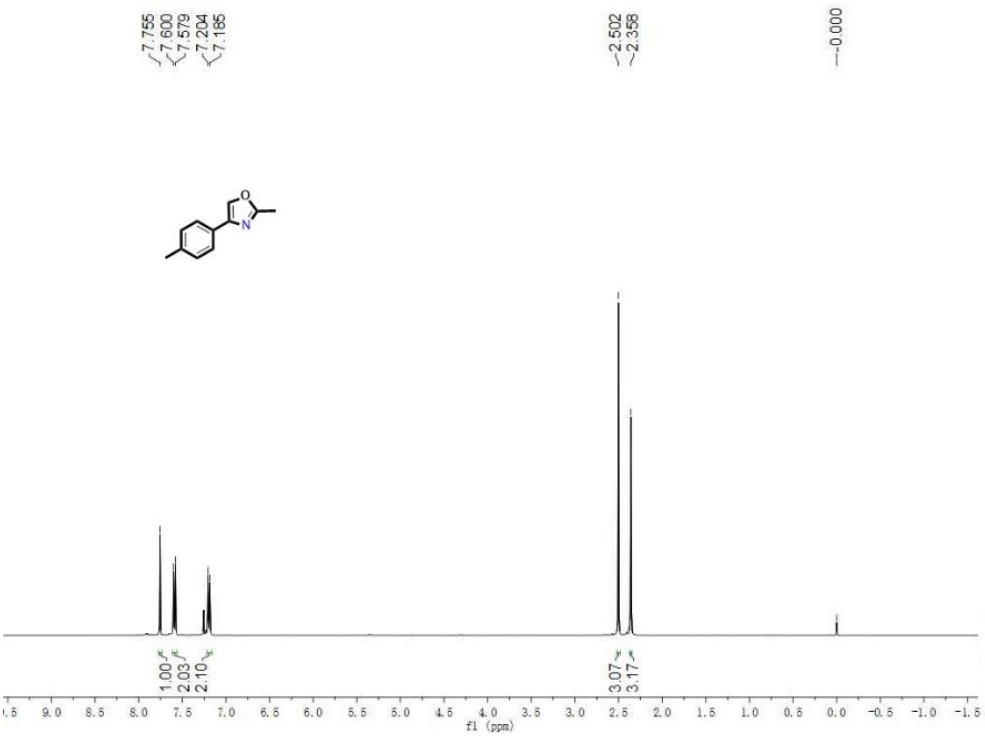


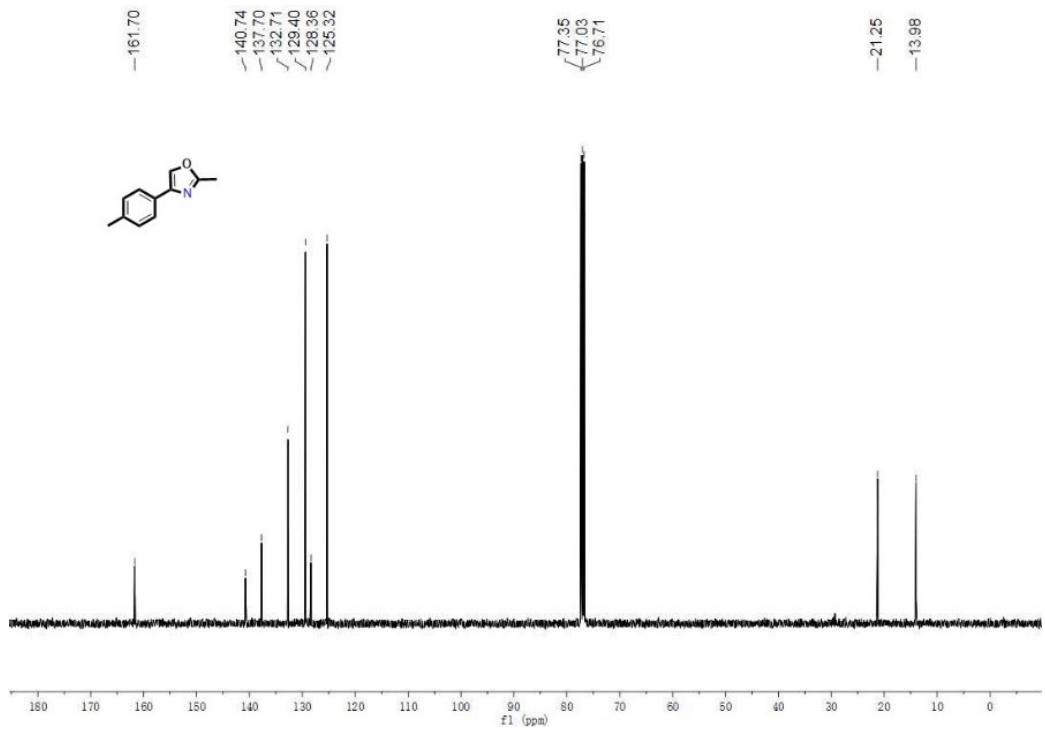
3p ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



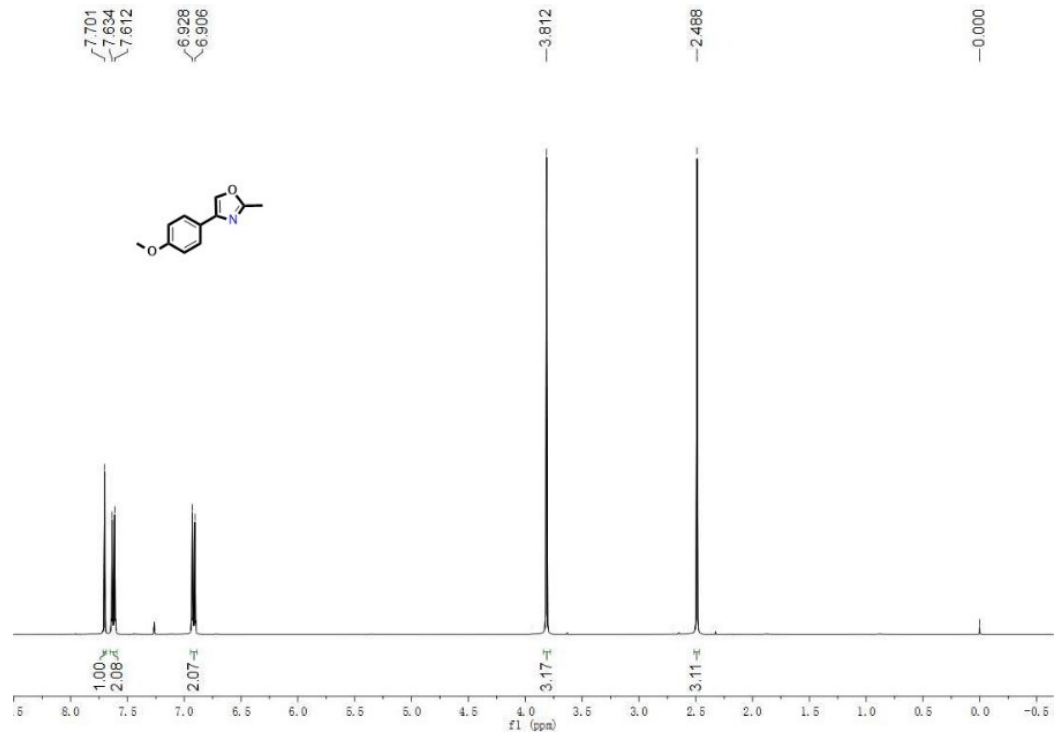


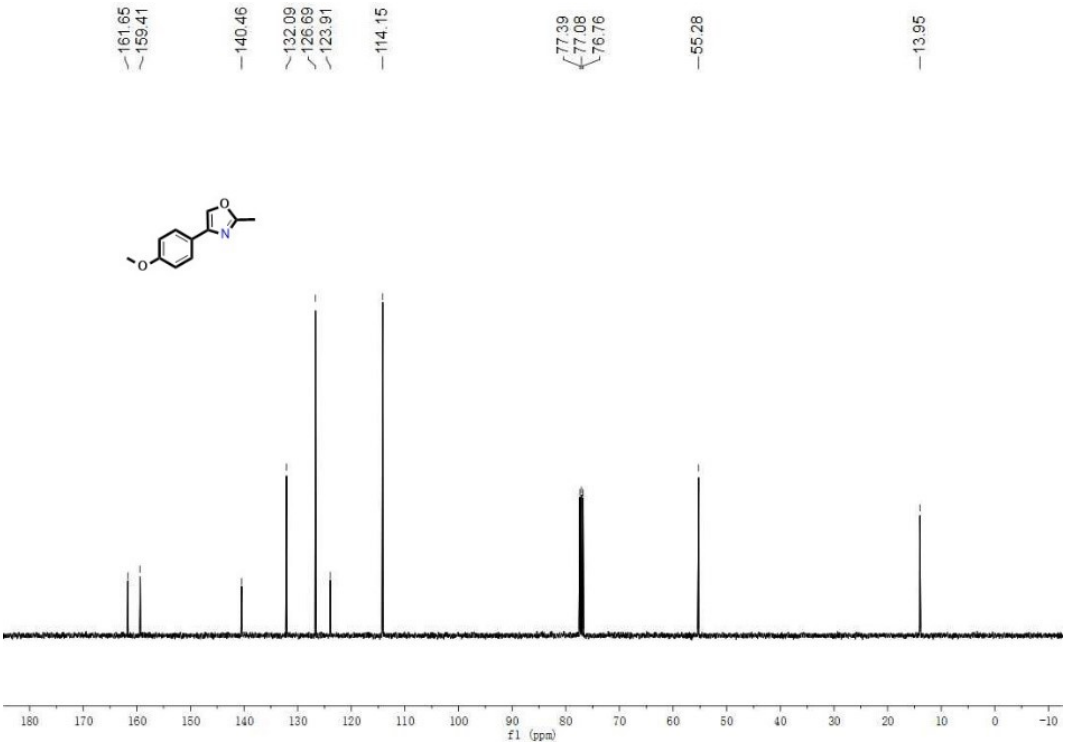
3q ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



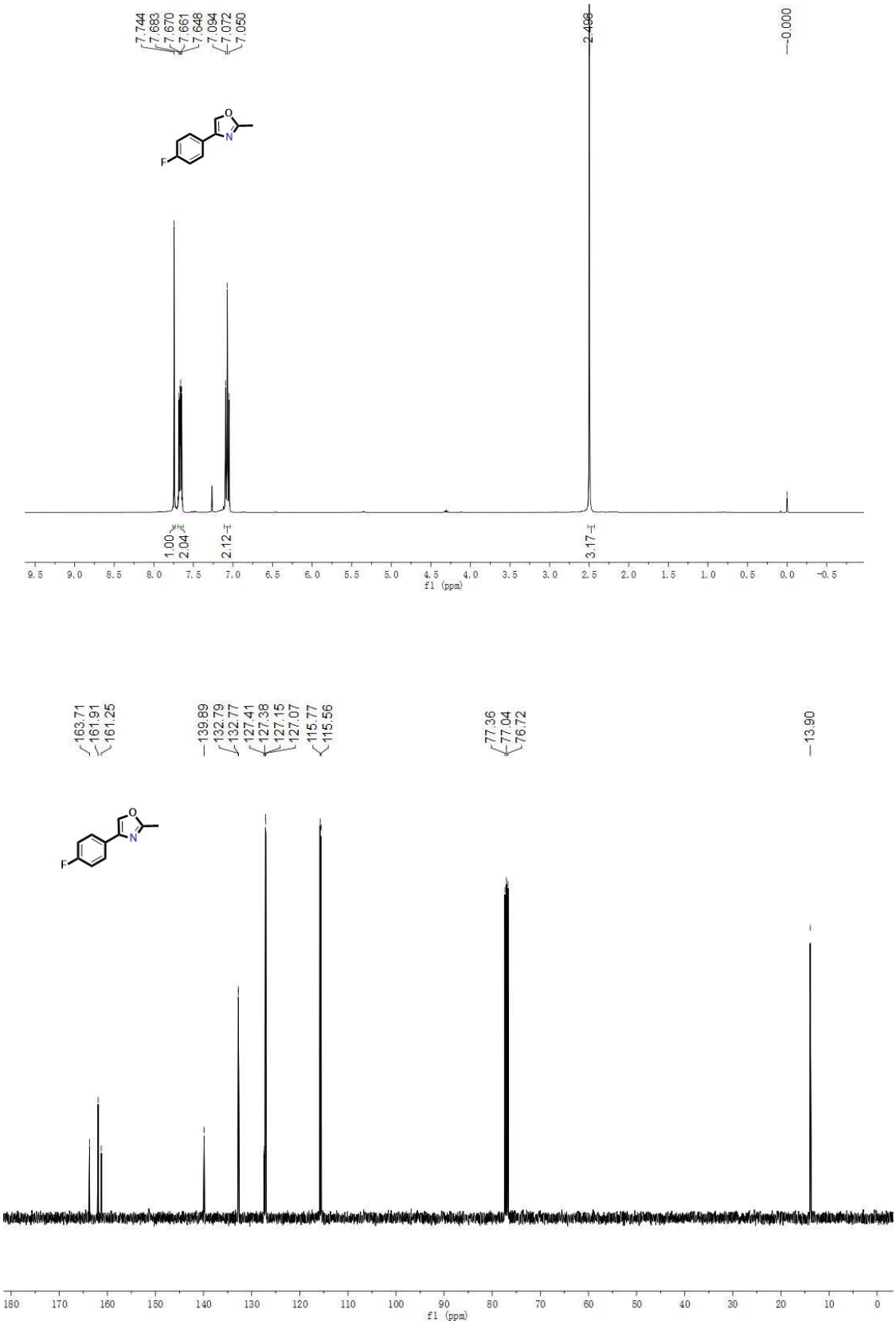


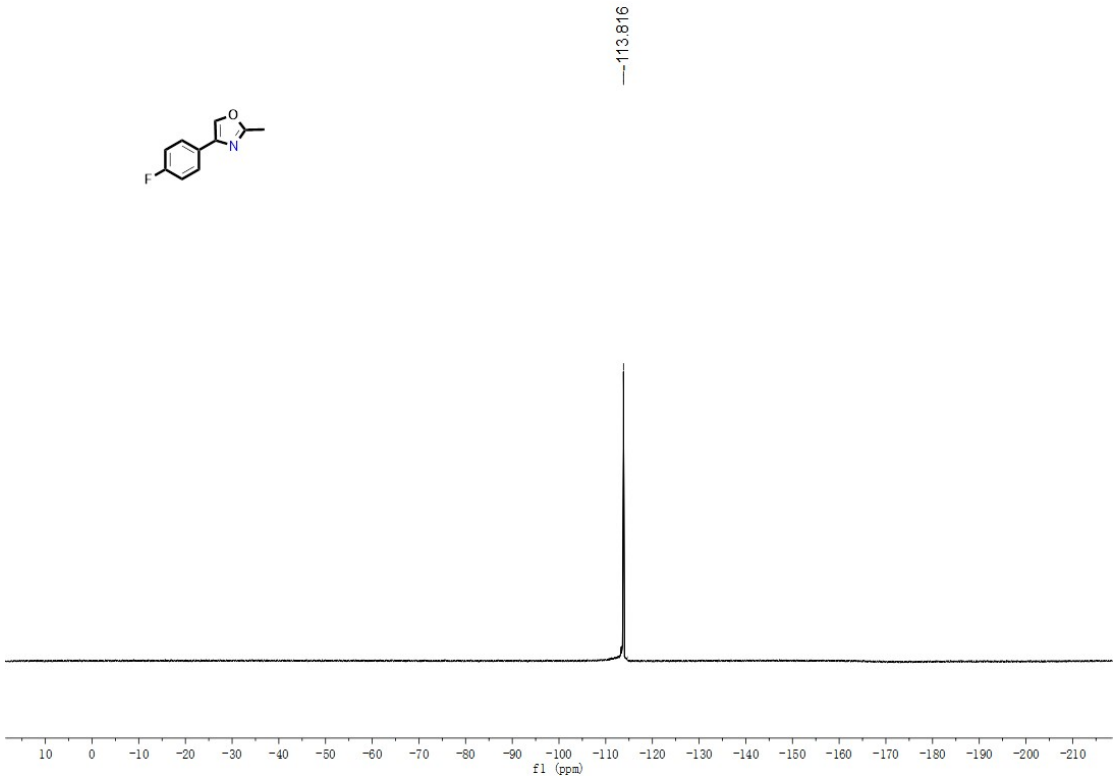
3r ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



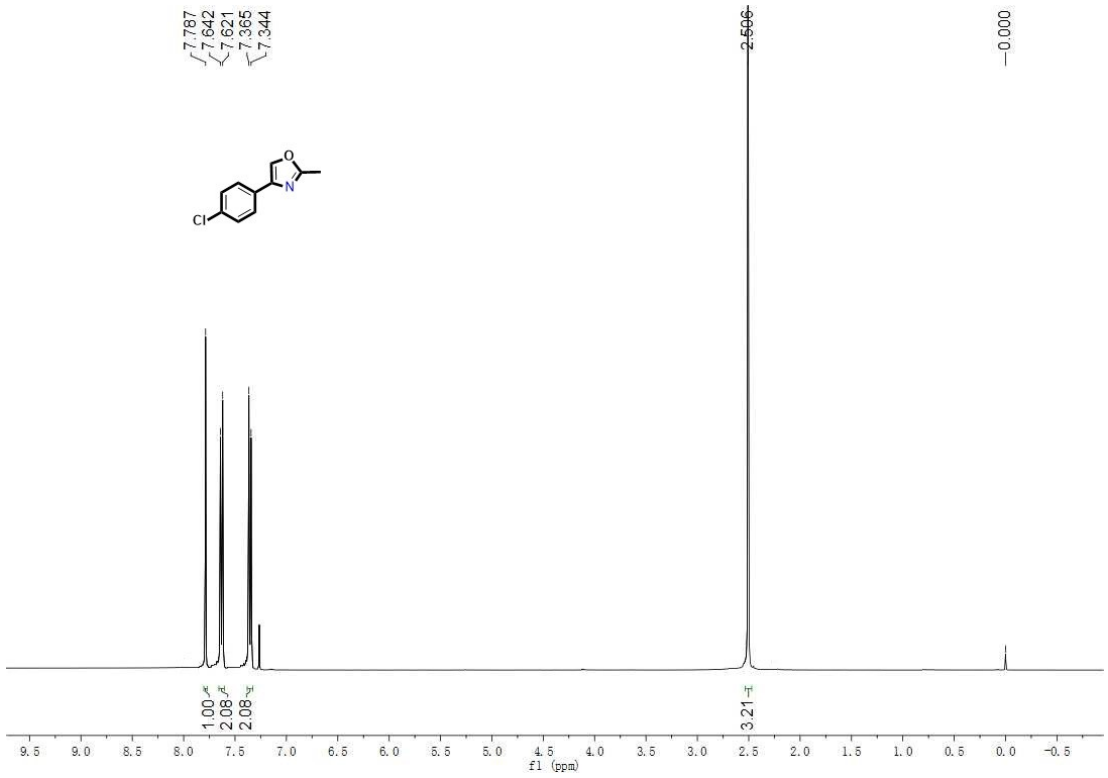


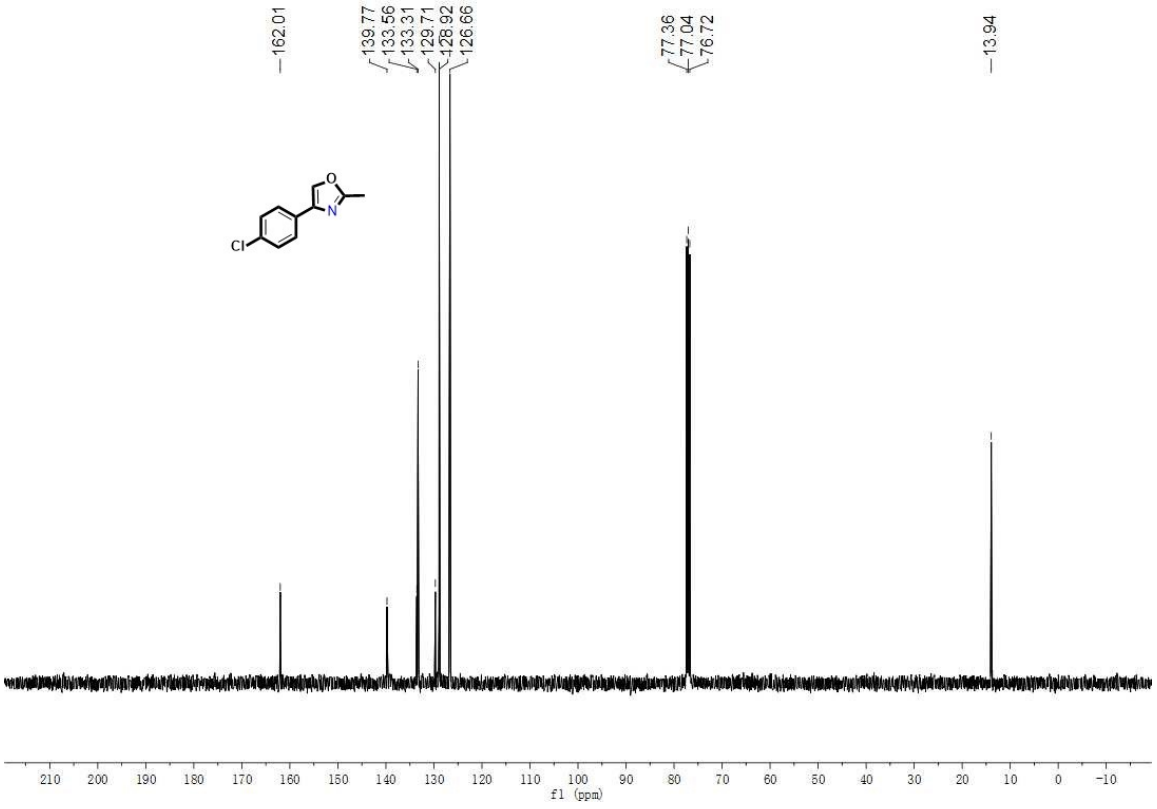
3s ^{1}H NMR (400 MHz), ^{19}F NMR (400 MHz) and ^{13}C NMR (100 MHz)



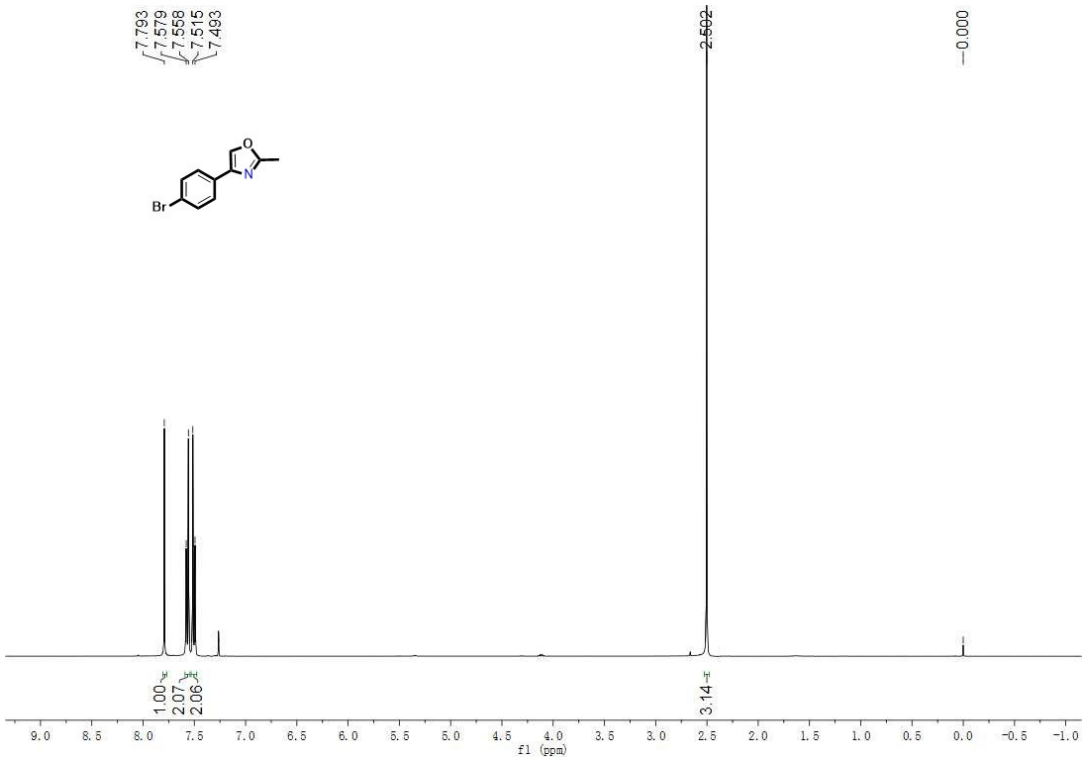

-113.816
O
N
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

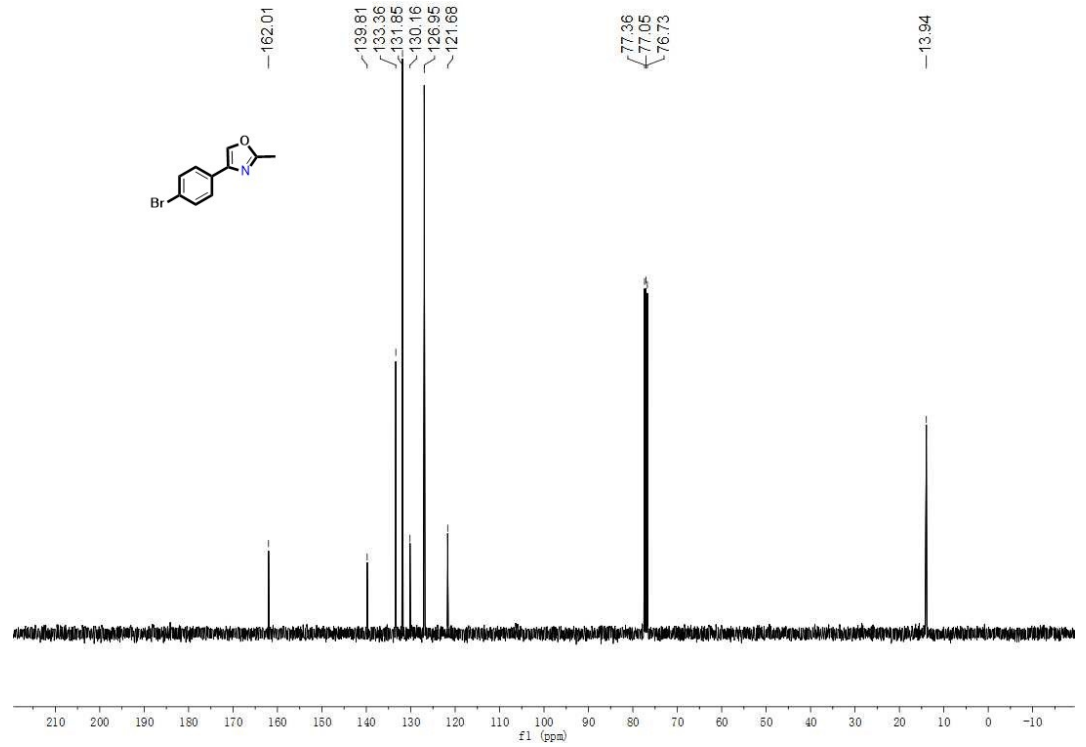
3t ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



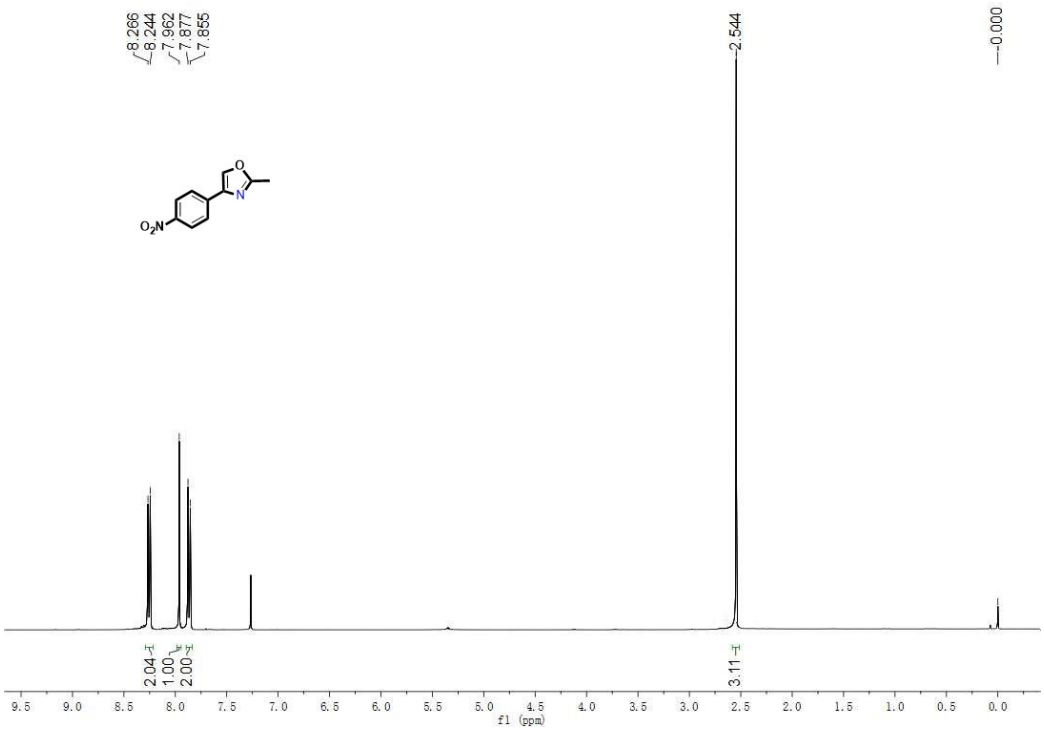


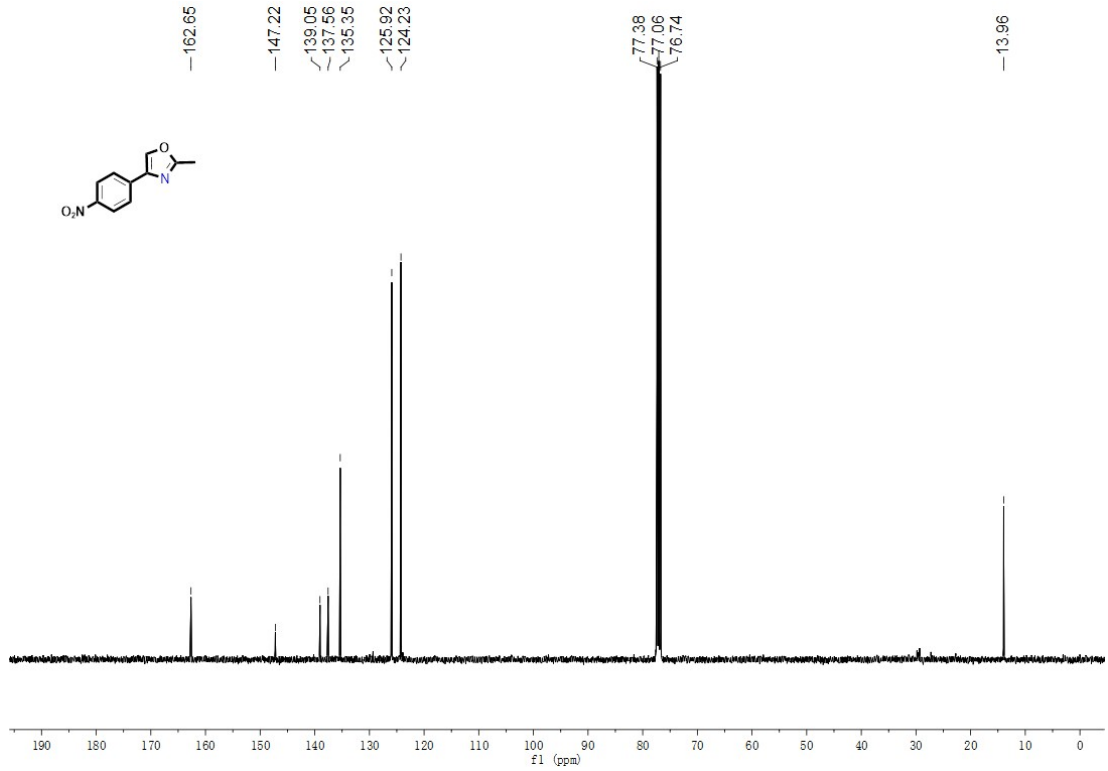
3u ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



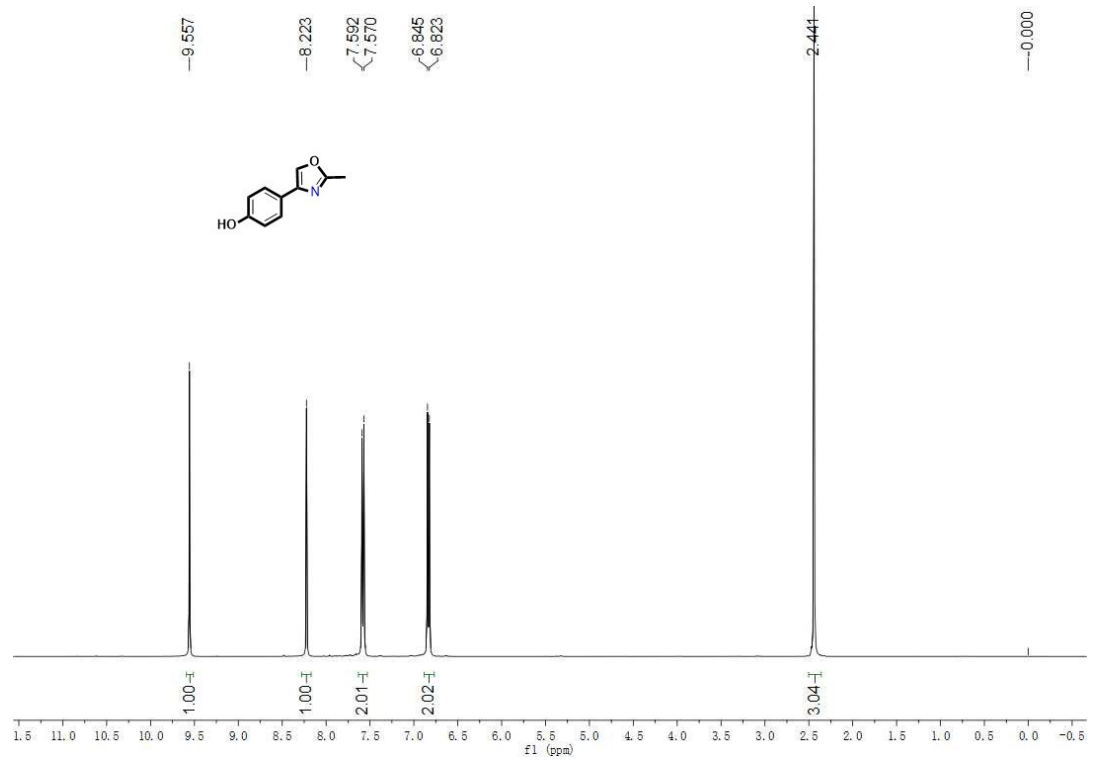


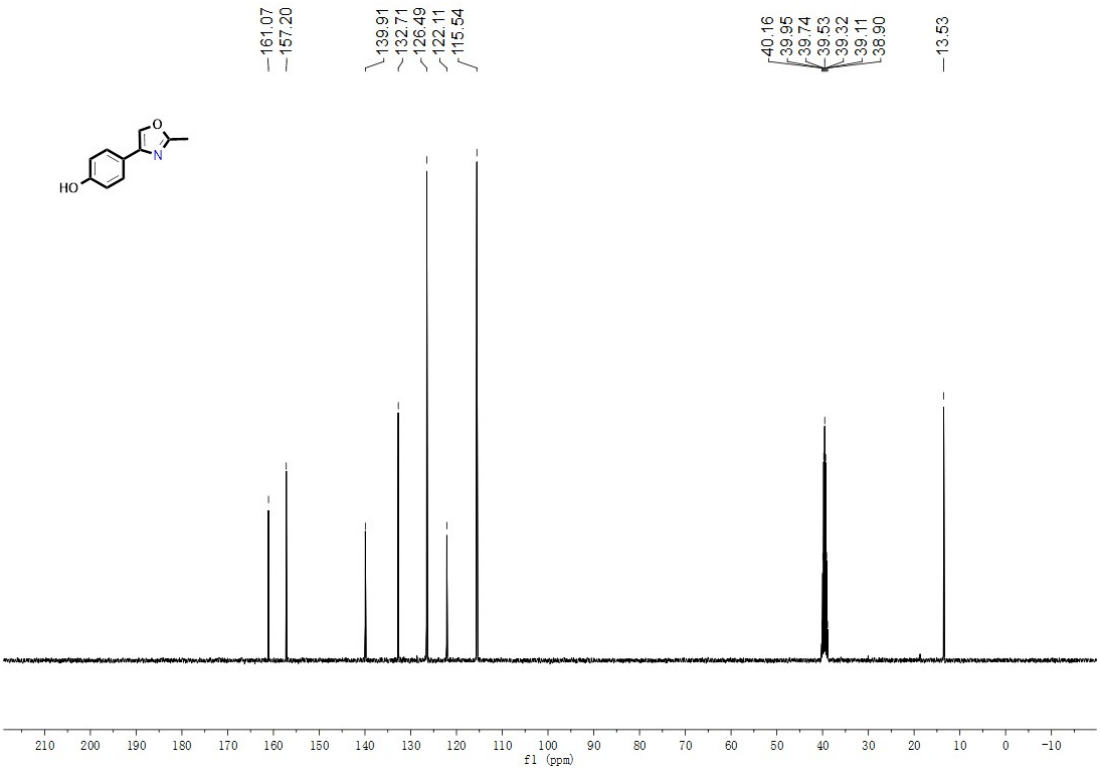
3v ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



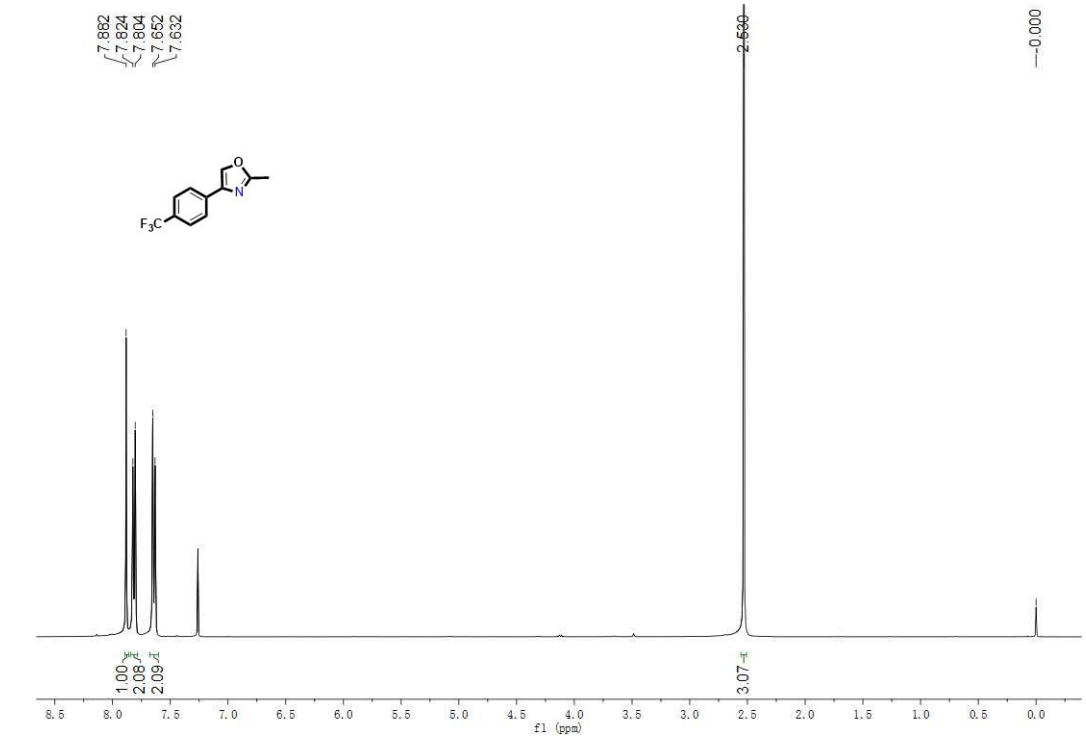


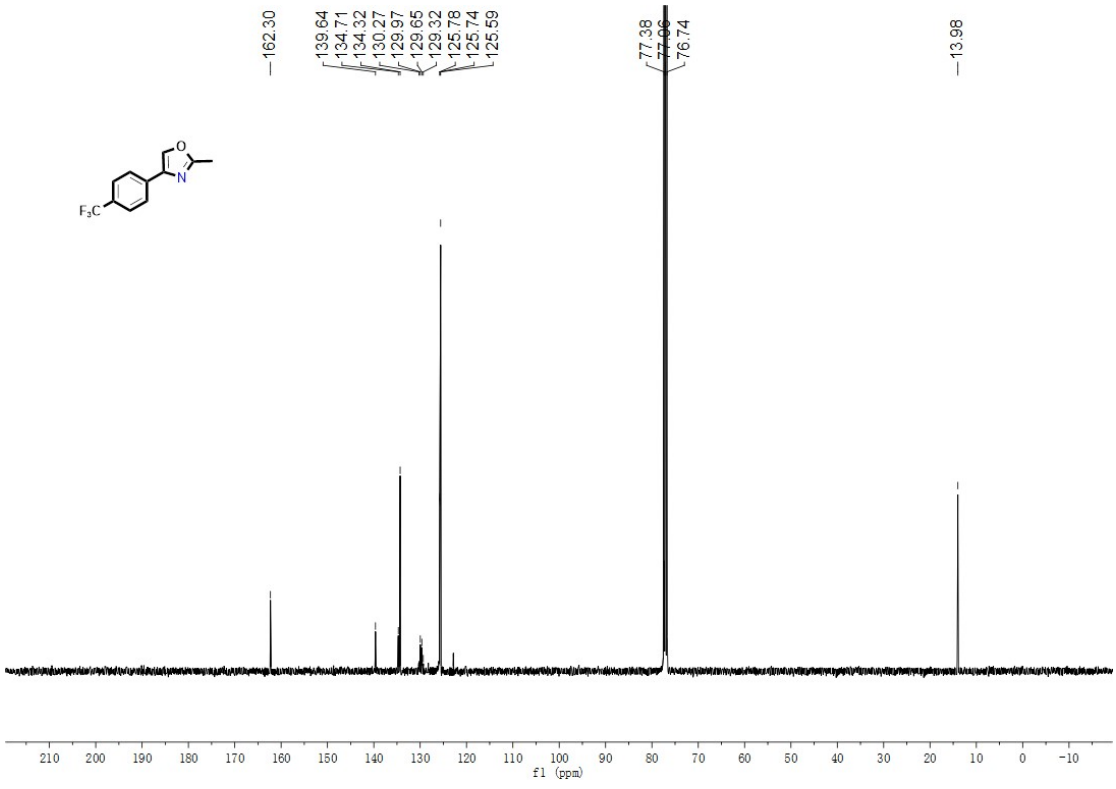
3w ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)

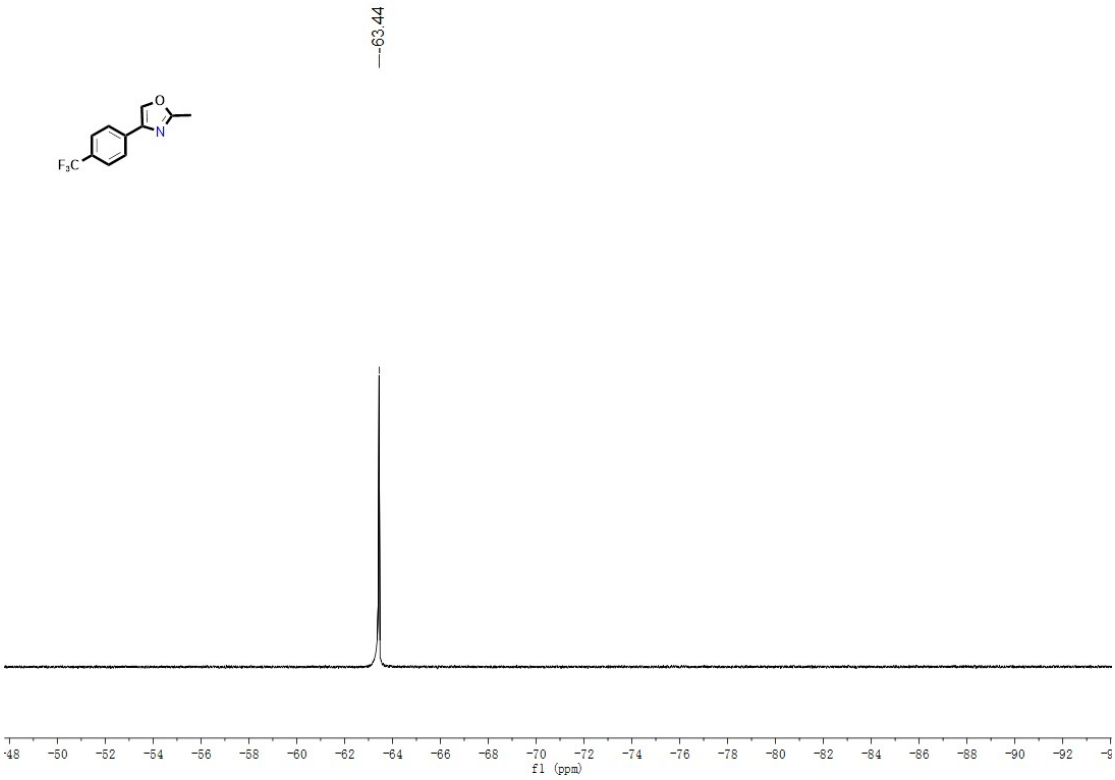




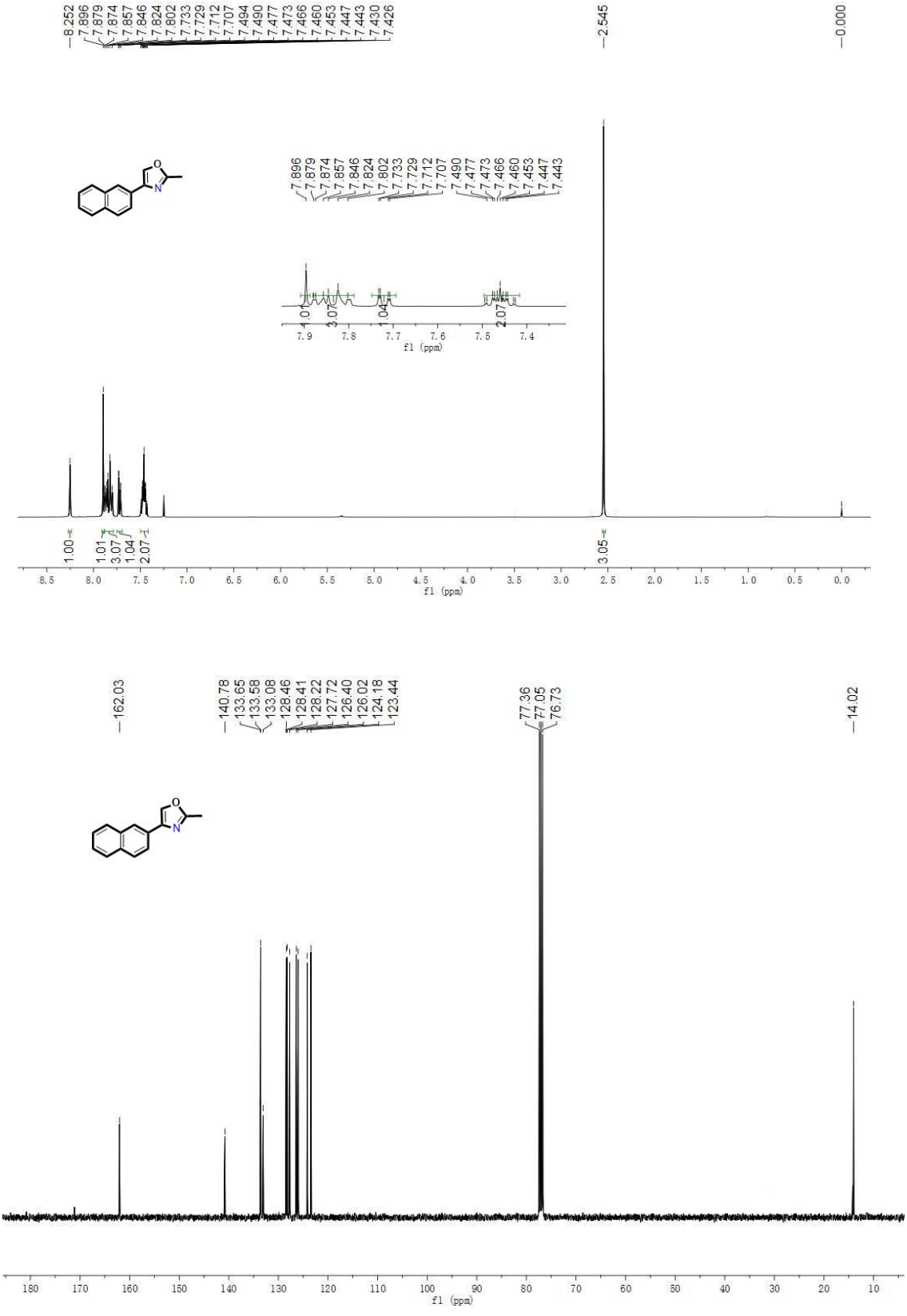
3x ^{1}H NMR (400 MHz), ^{19}F NMR (400 MHz) and ^{13}C NMR (100 MHz)



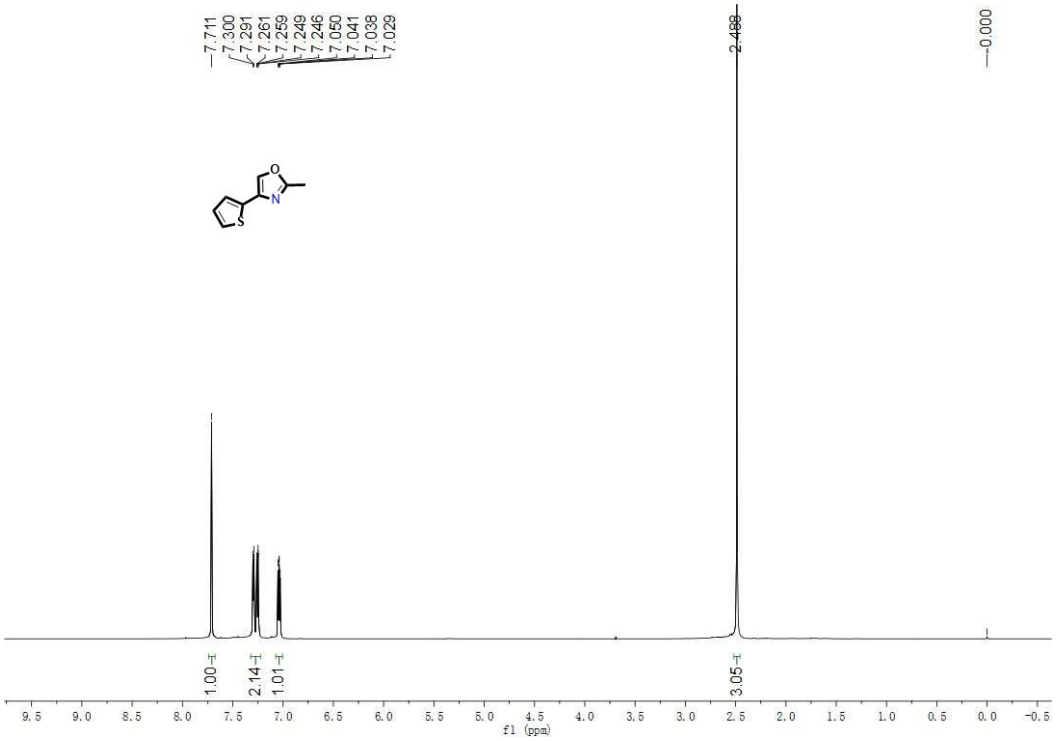


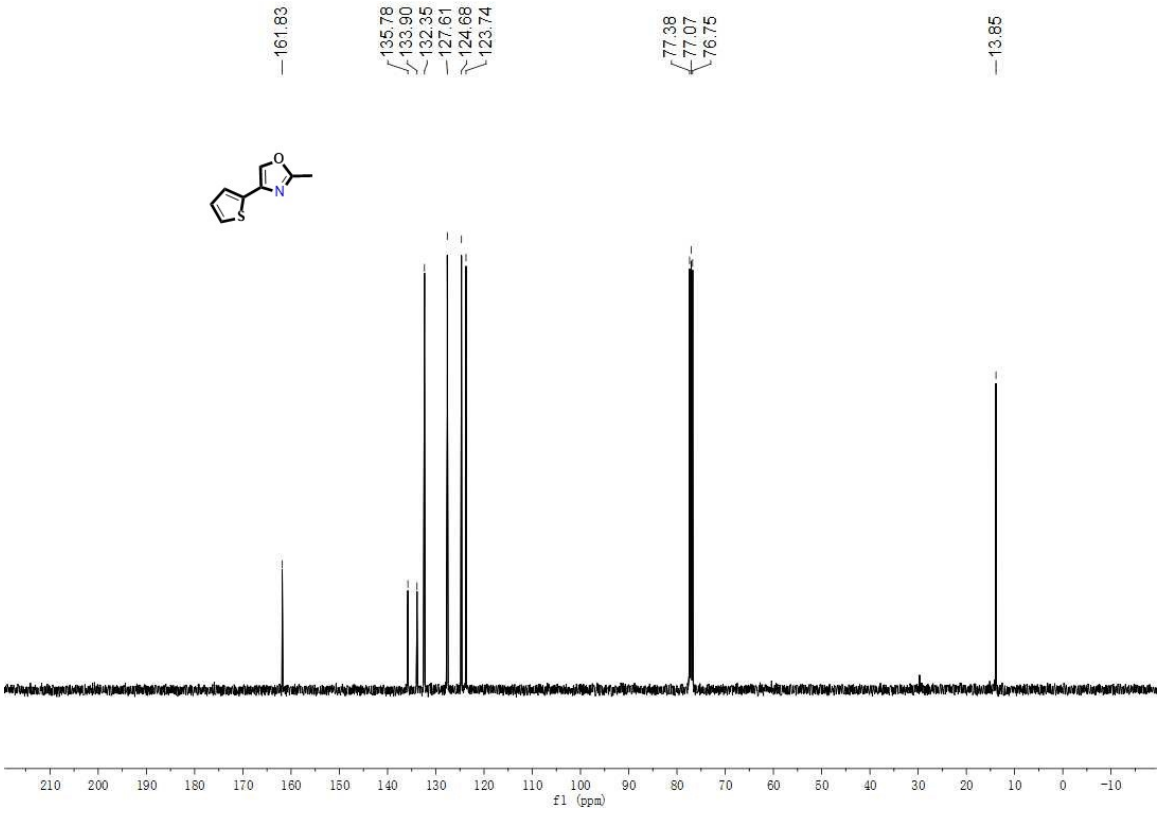

-63.44
O
N
F3C
-48 -50 -52 -54 -56 -58 -60 -62 -64 -66 -68 -70 -72 -74 -76 -78 -80 -82 -84 -86 -88 -90 -92
f1 (ppm)

3y ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)

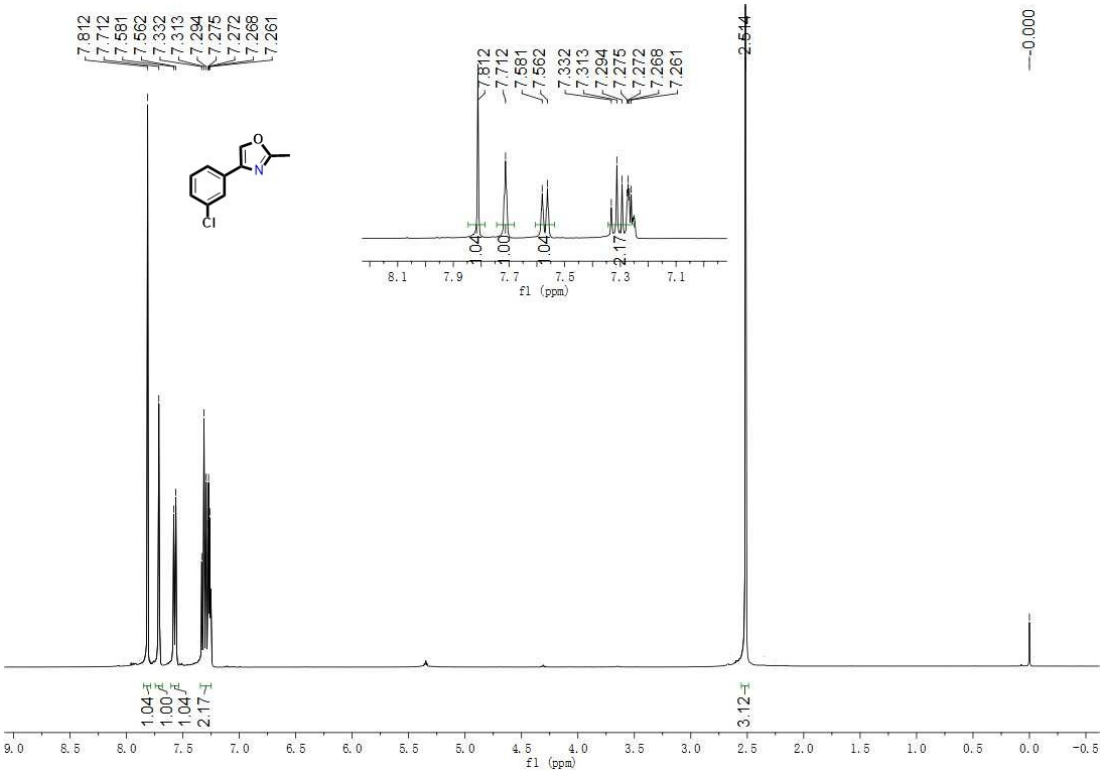


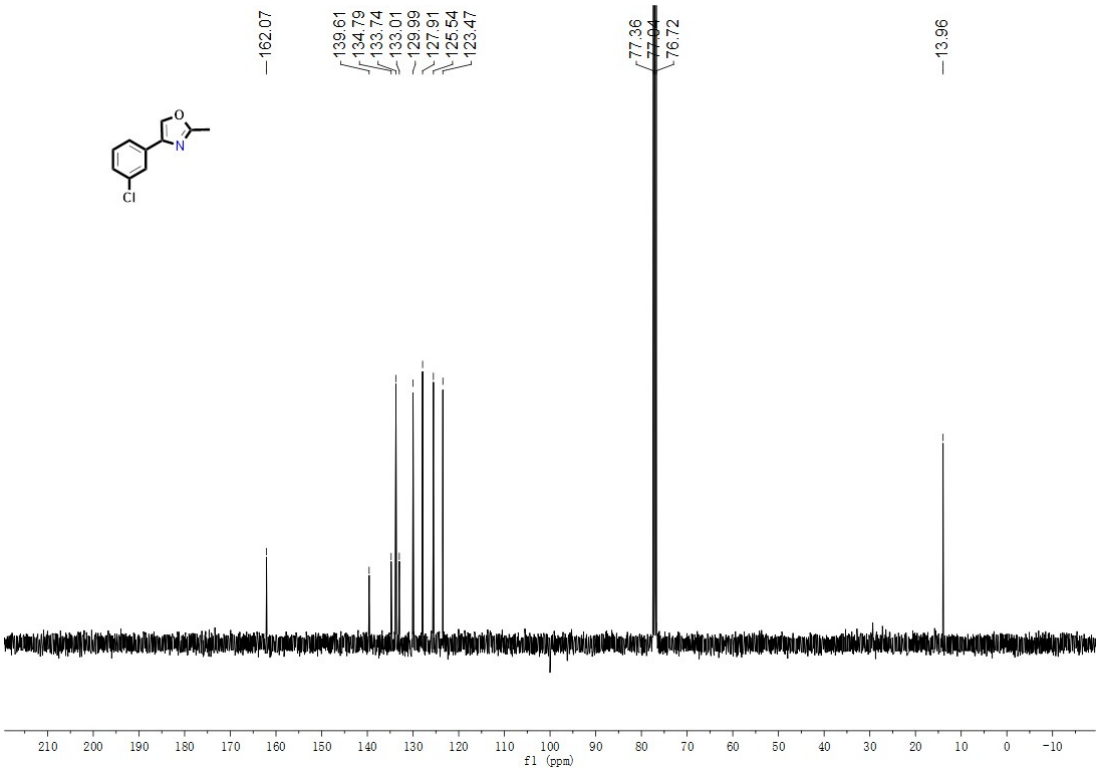
3z ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



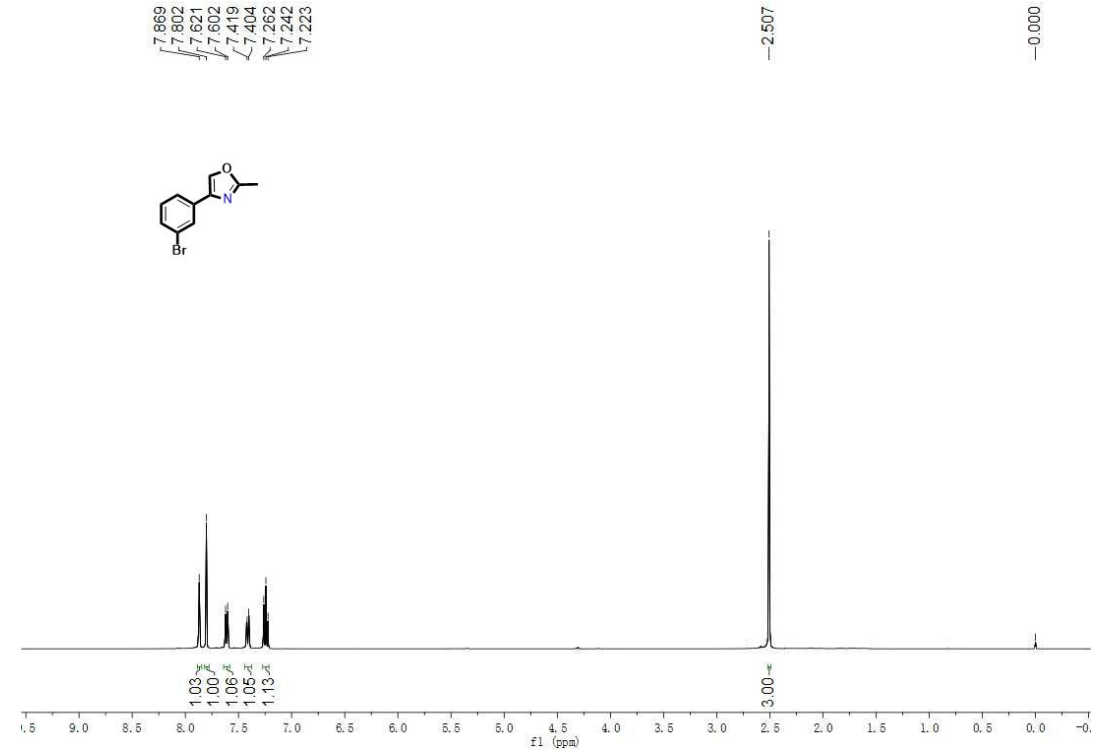


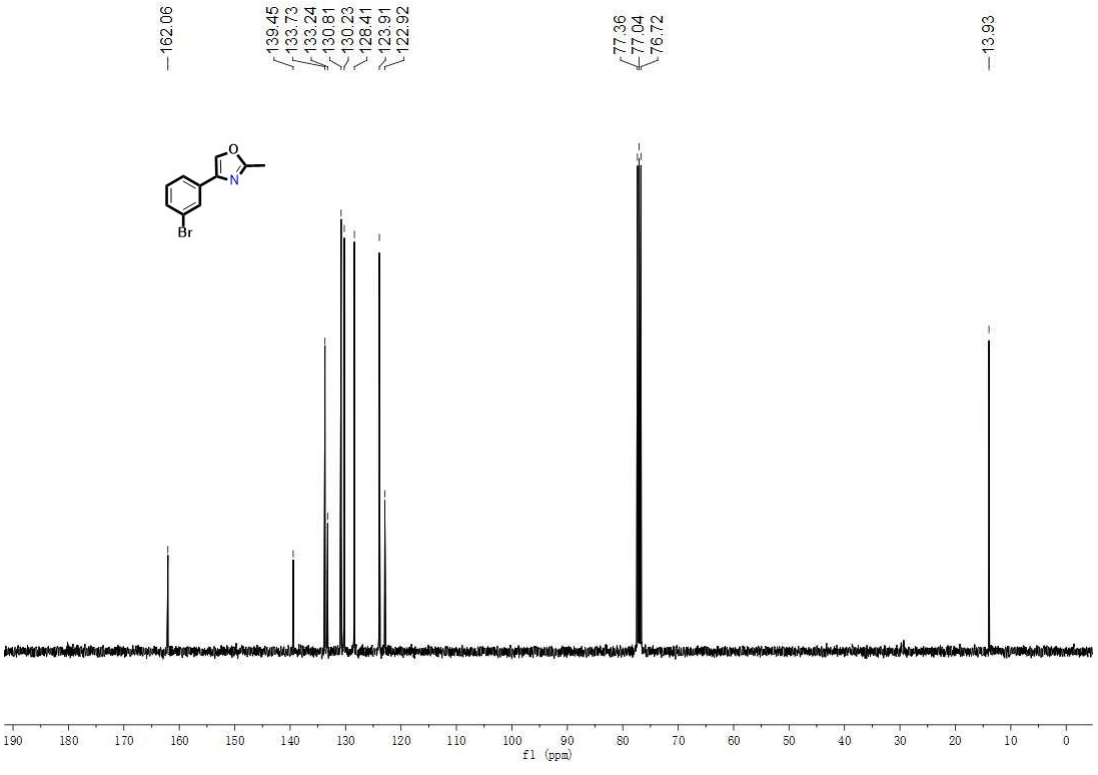
3z1 ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)



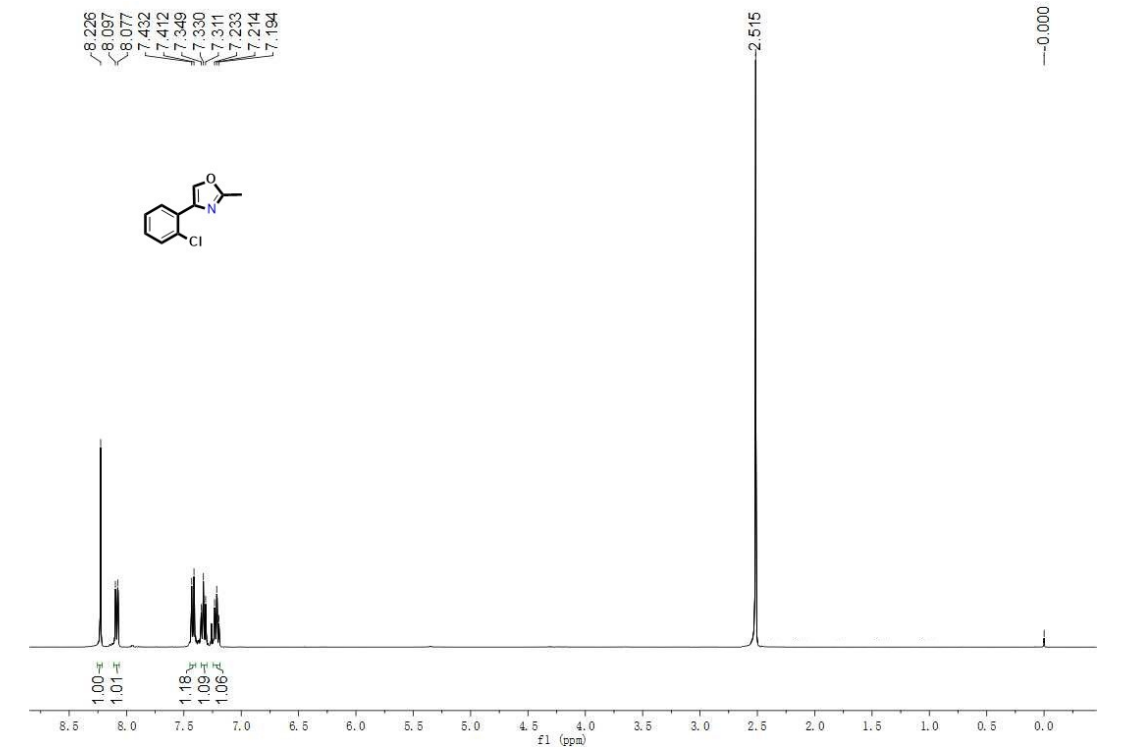


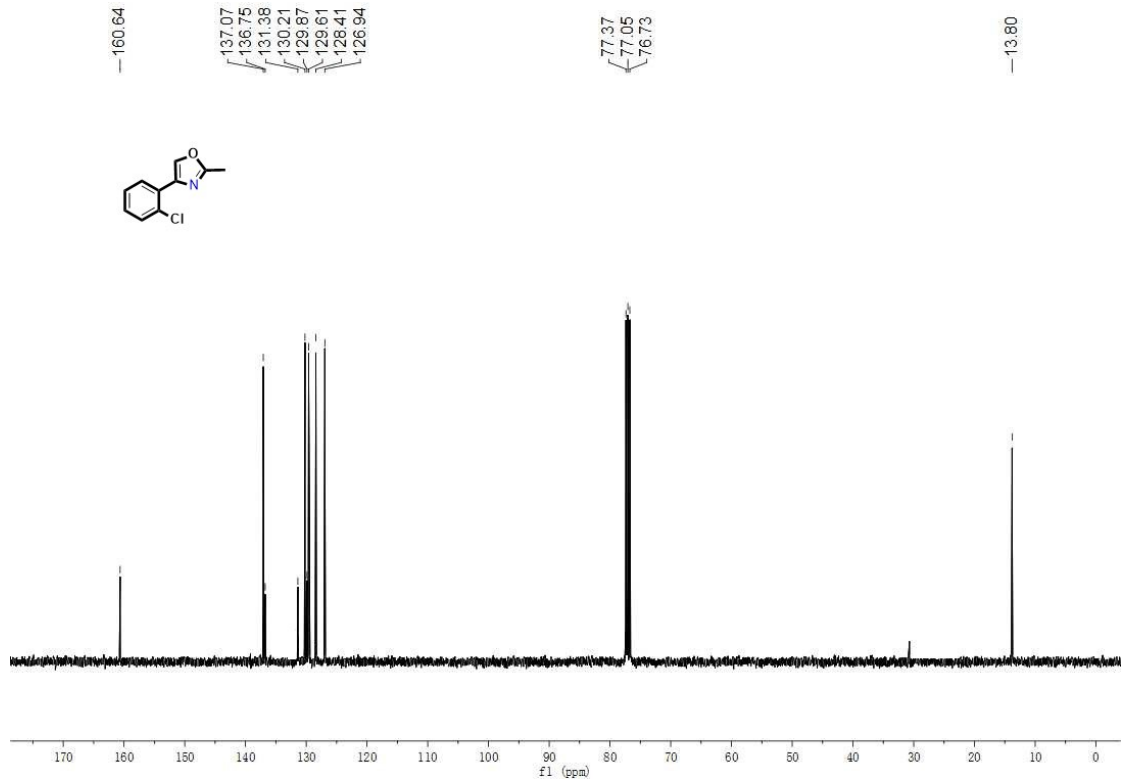
3z2 ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)





3z3 ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)





3z4 ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)