Supporting Information For

Copper(I)-Catalyzed Tandem Synthesis of 4,5-Functionalized Oxazoles from Isocyanoacetate and Aldehydes

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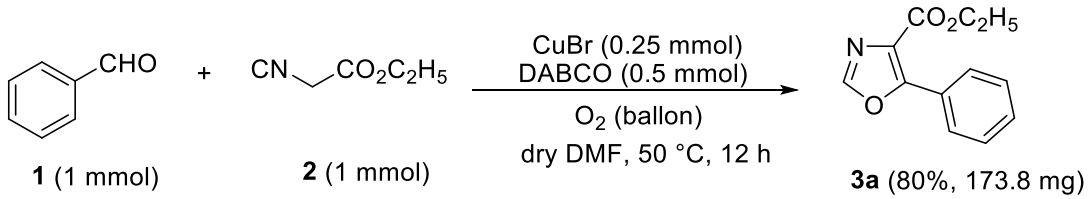
1. Supplementary Methods

All reactions were carried out under an atmosphere of dry oxygen. Anhydrous DMF was purchased from J&K and used as solvent without further purification. Unless otherwise stated, reagents were commercially available and used as purchased. Chemicals were obtained from Sigma-Aldrich, Acros, Innochem, Energy Chemical, TCI China or Alfa Aesar. The progress of the reactions was monitored by thin-layer chromatography using TLC plates and visualized by short-wave ultraviolet light. Flash chromatography was performed with Qingdao Haiyang flash silica gel (200–300 mesh). The NMR spectra were obtained using a Brüker 400 MHz Fourier-transform NMR spectrometer. Chemical shifts were reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants were reported in hertz. High resolution mass spectrometry (HRMS) data were obtained on a Waters LC-TOF mass spectrometer (Xevo G2-XS QTof) using electrospray ionization (ESI) in positive or negative mode. Melting points were measured using a WRS-1C Melt-Temp apparatus and were uncorrected.

2. General procedure for the cyclization.



1 (1 mmol) **2** (1 mmol) **3a** (80%, 173.8 mg)

Benzaldehyde (106.1 mg, 1 mmol, 1 equiv), DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv) was added in 50 mL glass tube with rubber stopper. A vacuum pump fitted with a hose and a needle was pierced through the rubber stopper and the glass tube subjected to vacuum and refilled with a balloon of O_2 fitted onto a hose and secured to a needle. This process was repeated two more times to remove as much air as possible. Next, the reaction glass tube was placed in an oil bath at 50 °C with stirring for 12 h. The resulting dark brown solution was removed from the oil bath, cooled to rt, quenched by addition of 5 drops water through the rubber stopper via syringe, and then the glass tube opened to air. After, the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (10 mL × 3). The combined organic layer was dried with anhydrous Na_2SO_4 and then filtered. The solvent was removed by rotary evaporator. The crude product was purified over a column of silica gel (eluant: EA:PE = 1:4) to afford the desired product **3a** with 80%

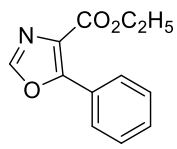
yield (173.8 mg).

Compounds **3b~3z** were synthesized according to the above procedure.

3. Spectral data

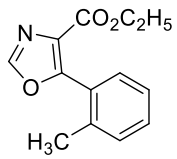
Ethyl 5-phenyloxazole-4-carboxylate (3a)

The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5



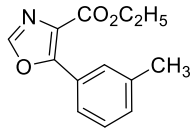
equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), benzaldehyde (**1a**) (106.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (173.8 mg, 80% yield) as a Light yellow liquid. R_f = 0.45 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[1].

Ethyl 5-(o-tolyl)oxazole-4-carboxylate (3b)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-methylbenzaldehyde (**1b**) (120.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (106.4 mg, 46% yield) as a light yellow liquid. R_f = 0.47 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[1].

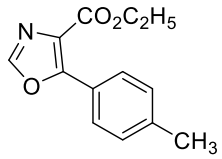
Ethyl 5-(m-tolyl)oxazole-4-carboxylate (3c)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), m-tolualdehyde (**1c**) (120.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (127.2 mg, 55% yield) as a light yellow liquid. R_f = 0.47 (petroleum ether: EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89(s, 1H), 7.86 (d, J = 6.2 Hz, 2H), 7.38-7.34 (m, 1H), 7.28 (s, 1H), 4.41 (q, J =

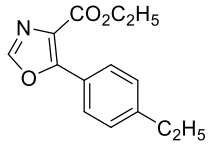
7.1 Hz, 2H), 2.42 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 161.94, 155.70, 148.96, 138.11, 131.28, 128.98, 128.32, 126.63, 126.51, 125.71, 61.38, 21.45, 14.25. HRMS (ESI): calcd for $C_{13}H_{14}NO_3$ $[M+H]^+$ 232.0974, found 232.0981.

Ethyl 5-(p-tolyl)oxazole-4-carboxylate (3d)



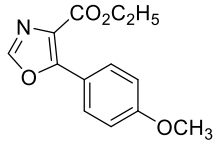
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), p-tolualdehyde (**1d**) (120.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (141.1 mg, 61% yield) as a white solid. m.p. 84-85 °C (EtOAc). R_f = 0.50 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[1].

Ethyl 5-(4-ethylphenyl)oxazole-4-carboxylate (3e)



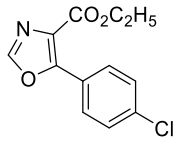
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-ethylbenzaldehyde (**1e**) (134.2 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with Petroleum ether:EtOAc = 4:1) to give the product (142.3 mg, 58% yield) as a white solid, m.p.39-40 °C (EtOAc). R_f = 0.50 (petroleum ether:EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.99 (d, *J* = 8.3 Hz, 2H), 7.88 (s, 1H), 7.31 (d, *J* = 8.3 Hz, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H), 1.26 (d, *J* = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 162.02, 155.85, 148.70, 147.11, 128.49, 127.94, 126.07, 124.09, 61.32, 28.82, 15.25, 14.24. HRMS (ESI): calcd for $C_{14}H_{16}NO_3$ $[M+H]^+$ 246.1130, found 246.1137.

Ethyl 5-(4-methoxyphenyl)oxazole-4-carboxylate (3f)



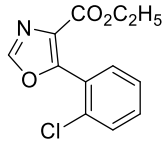
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), p-methoxybenzaldehyde (**1f**) (136.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (160.7 mg, 65% yield) as a white solid, m.p. 68-69 °C (EtOAc). R_f = 0.45 (petroleum ether:EtOAc = 4:1).The spectroscopic data for this product match the literature data[1].

thyl 5-(4-chlorophenyl)oxazole-4-carboxylate (3g)



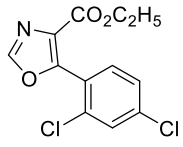
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-chlorobenzaldehyde (**1g**) (140.6 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (208.9 mg, 83% yield) as a white solid, m.p. 101-103 °C (EtOAc). R_f = 0.50 (petroleum ether:EtOAc = 4:1).The spectroscopic data for this product match the literature data[1].

Ethyl 5-(2-chlorophenyl)oxazole-4-carboxylate (3h)



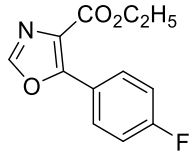
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-chlorobenzaldehyde (**1h**) (140.6 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (153.5 mg, 61% yield) as a light yellow liquid. R_f = 0.49 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[1].

Ethyl 5-(2,4-dichlorophenyl)oxazole-4-carboxylate (3i)



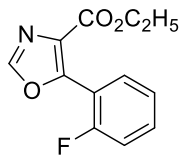
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2,4-dichlorobenzaldehyde (**1i**) (175.0 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (203.1 mg, 71% yield) as a white solid, m.p. 103-104 °C (EtOAc). R_f = 0.47 (petroleum ether:EtOAc = 4:1).The spectroscopic data for this product match the literature data[2].

Ethyl 5-(4-fluorophenyl)oxazole-4-carboxylate (3j)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), p-fluorobenzaldehyde (**1j**) (124.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (183.5 mg, 78% yield) as a Light yellow solid, m.p.45-46°C (EtOAc). R_f = 0.49 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[3].

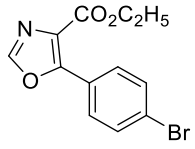
Ethyl 5-(2-fluorophenyl)oxazole-4-carboxylate (3k)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-fluorobenzaldehyde (**1k**) (124.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (148.2 mg, 63% yield) as a light yellow liquid. R_f = 0.50 (petroleum ether:EtOAc = 4:1).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.67-7.63 (m, 1H), 7.52-7.46 (m, 1H), 7.28 (d, J = 5.0 Hz, 1H), 7.19 (t, J = 9.2 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.24, 159.90 (d, J_{CF} = 253.9 Hz), 150.26, 132.47 (d, J_{CF} = 8.6 Hz) , 131.26, 131.25, 129.18, 123.92, 123.89, 116.05 (d, J_{CF} = 21.5 Hz) , 115.38(d, J_{CF}=13.7 HZ), 61.31, 14.03. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.93.

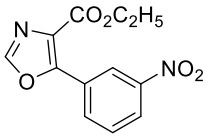
HRMS (ESI): calcd for $C_{12}H_{11}FNO_3$ $[M+H]^+$ 236.0723, found 236.0716.

Ethyl 5-(4-bromophenyl)oxazole-4-carboxylate (3l)



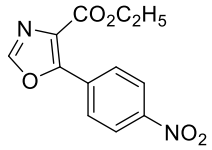
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-bromobenzaldehyde (**1l**) (185.0 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (219.1 mg, 74% yield) as a white solid, m.p. 110-111°C (EtOAc). R_f = 0.51 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[1].

Ethyl 5-(3-nitrophenyl)oxazole-4-carboxylate (3m)



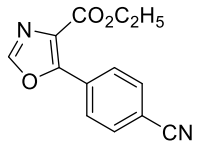
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 3-nitrobenzaldehyde (**1m**) (151.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (152.1 mg, 58% yield) as a white solid, m.p. 87-89°C (EtOAc). R_f = 0.50 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[2].

Ethyl 5-(4-nitrophenyl)oxazole-4-carboxylate (3n)



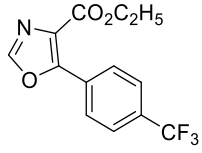
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-nitrobenzaldehyde (**1n**) (151.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (159.9 mg, 61% yield) as a Light yellow solid, m.p.119-120°C (EtOAc). R_f = 0.51 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[3].

Ethyl 5-(4-cyanophenyl)oxazole-4-carboxylate (3o)



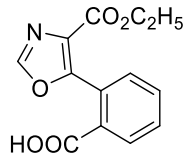
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-cyanobenzaldehyde (**1o**) (131.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (186.5 mg, 77% yield) as a white solid, m.p. 146-147°C (EtOAc). R_f = 0.52 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[4].

Ethyl 5-(4-(trifluoromethyl)phenyl)oxazole-4-carboxylate (3p)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-(trifluoromethyl)benzaldehyde (**1p**) (174.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (188.2 mg, 66% yield) as a light yellow solid, m.p.99-100°C (EtOAc). R_f = 0.55 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[1].

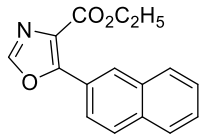
2-(4-(Ethoxycarbonyl)oxazol-5-yl)benzoic acid (3q)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-carboxybenzaldehyde (**1q**) (150.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 1:1) to give the product (175.0 mg, 67% yield) as a white solid. m.p.150-151°C (EtOAc). R_f = 0.51 (petroleum ether:EtOAc = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.51 (s, 1H), 8.43 (d, J = 8.0 Hz, 1H), 7.73-7.62 (m, 2H), 7.62-7.54 (m, 1H), 7.35 (s, 1H), 4.43 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ

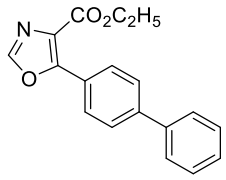
161.84, 161.63, 135.95, 132.92, 129.19, 128.16, 128.03, 127.79, 111.07, 62.46, 14.14, two resonance were not observed due to overlapping resonances. HRMS (ESI): calcd for $C_{13}H_{12}NO_5$ $[M+H]^+$ 262.0715, found 262.0713.

Ethyl 5-(naphthalen-2-yl)oxazole-4-carboxylate (3r)



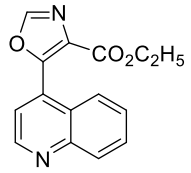
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-naphthaldehyde (**1r**) (156.2 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (195.1 mg, 73% yield) as a white solid, m.p.94-96°C (EtOAc). R_f = 0.53 (petroleum ether:EtOAc = 4:1). The spectroscopic data for this product match the literature data[1].

Ethyl 5-([1,1'-biphenyl]-4-yl)oxazole-4-carboxylate (3s)



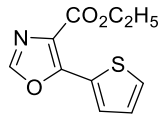
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-biphenylylcarboxaldehyde (**1s**) (182.2 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (164.2 mg, 56% yield) as a white solid, m.p.91-92°C (EtOAc). R_f = 0.49 (petroleum ether:EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.4 Hz, 2H), 7.93 (s, 1H), 7.71 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 7.4 Hz, 2H), 7.47 (t, J = 7.4 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 4.45 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.00, 155.35, 148.94, 143.13, 140.03, 128.88, 128.85, 127.92, 127.09, 127.04, 126.62, 125.50, 61.45, 14.25. HRMS (ESI): calcd for $C_{18}H_{16}NO_3$ $[M+H]^+$ 294.1130, found 294.1126.

Ethyl 5-(quinolin-4-yl)oxazole-4-carboxylate (3t)



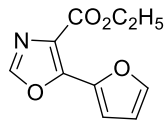
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-quinolinecarboxaldehyde (**1t**) (157.2 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (169.0 mg, 63% yield) as a light yellow liquid. R_f = 0.43 (petroleum ether:EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.02 (d, J = 4.4 Hz, 1H), 8.19 (d, J = 8.5 Hz, 1H), 8.12 (s, 1H), 7.79-7.68 (m, 2H), 7.62 (d, J = 4.4 Hz, 1H), 7.58-7.52 (m, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.10 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.71, 152.01, 150.86, 149.31, 148.35, 132.68, 130.41, 130.03, 129.81, 127.49, 125.54, 124.89, 122.90, 61.40, 13.73. HRMS (ESI): calcd for $C_{15}H_{13}N_2O_3$ $[M+H]^+$ 269.0926, found 269.0929

Ethyl 5-(thiophen-2-yl)oxazole-4-carboxylate (3u)



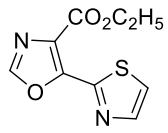
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-thiophenecarboxaldehyde (**1u**) (112.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 3:1) to give the product (122.8 mg, 55% yield) as a light yellow liquid. R_f = 0.51 (petroleum ether:EtOAc = 3:1). The spectroscopic data for this product match the literature data[1].

Ethyl 5-(furan-2-yl)oxazole-4-carboxylate (3v)



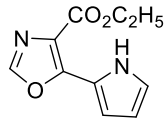
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-furaldehyde (**1v**) (96.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 3:1) to give the product (64.2 mg, 31% yield) as a white solid, m.p. 90-91°C (EtOAc). R_f = 0.50 (petroleum ether:EtOAc = 3:1). The spectroscopic data for this product match the literature data[2].

Ethyl 5-(thiazol-2-yl)oxazole-4-carboxylate (3w)



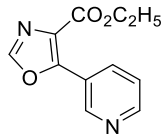
The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-thiazolecarboxaldehyde (**1w**) (113.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 4:1) to give the product (139.0 mg, 62% yield) as a white solid, m.p.171-172°C (EtOAc). R_f = 0.47 (petroleum ether:EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.05 (d, *J* = 3.0 Hz, 1H), 7.99 (s, 1H), 7.62 (d, *J* = 3.0 Hz, 1H), 4.49 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.54, 152.64, 149.92, 149.61, 143.92, 128.29, 123.11, 61.96, 14.23. HRMS (ESI): calcd for $C_9H_9N_2O_3S$ $[M+H]^+$ 225.0334, found 225.0335.

Ethyl 5-(1H-pyrrol-2-yl)oxazole-4-carboxylate (3x)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 2-pyrrolecarbaldehyde (**1x**) (95.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 3:1) to give the product (92.8 mg, 45% yield) as a light yellow liquid. R_f = 0.42 (petroleum ether:EtOAc = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.82 (s, 1H), 8.20 (s, 1H), 7.51 (d, *J* = 2.5 Hz, 1H), 7.01 – 6.91 (m, 1H), 6.74 (d, *J* = 3.8 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.08, 137.76, 130.58, 130.53, 117.78, 117.73, 113.35, 105.05, 61.41, 14.36. HRMS (ESI): calcd for $C_{10}H_{11}N_2O_3$ $[M+H]^+$ 207.0770, found 207.0774.

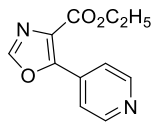
Ethyl 5-(pyridin-3-yl)oxazole-4-carboxylate (3y)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 3-pyridinecarboxaldehyde (**1y**)

(107.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 3:1) to give the product (100.4 mg, 46% yield) as a white solid, m.p. 66-67°C (EtOAc). R_f = 0.45 (petroleum ether:EtOAc = 3:1). The spectroscopic data for this product match the literature data[5].

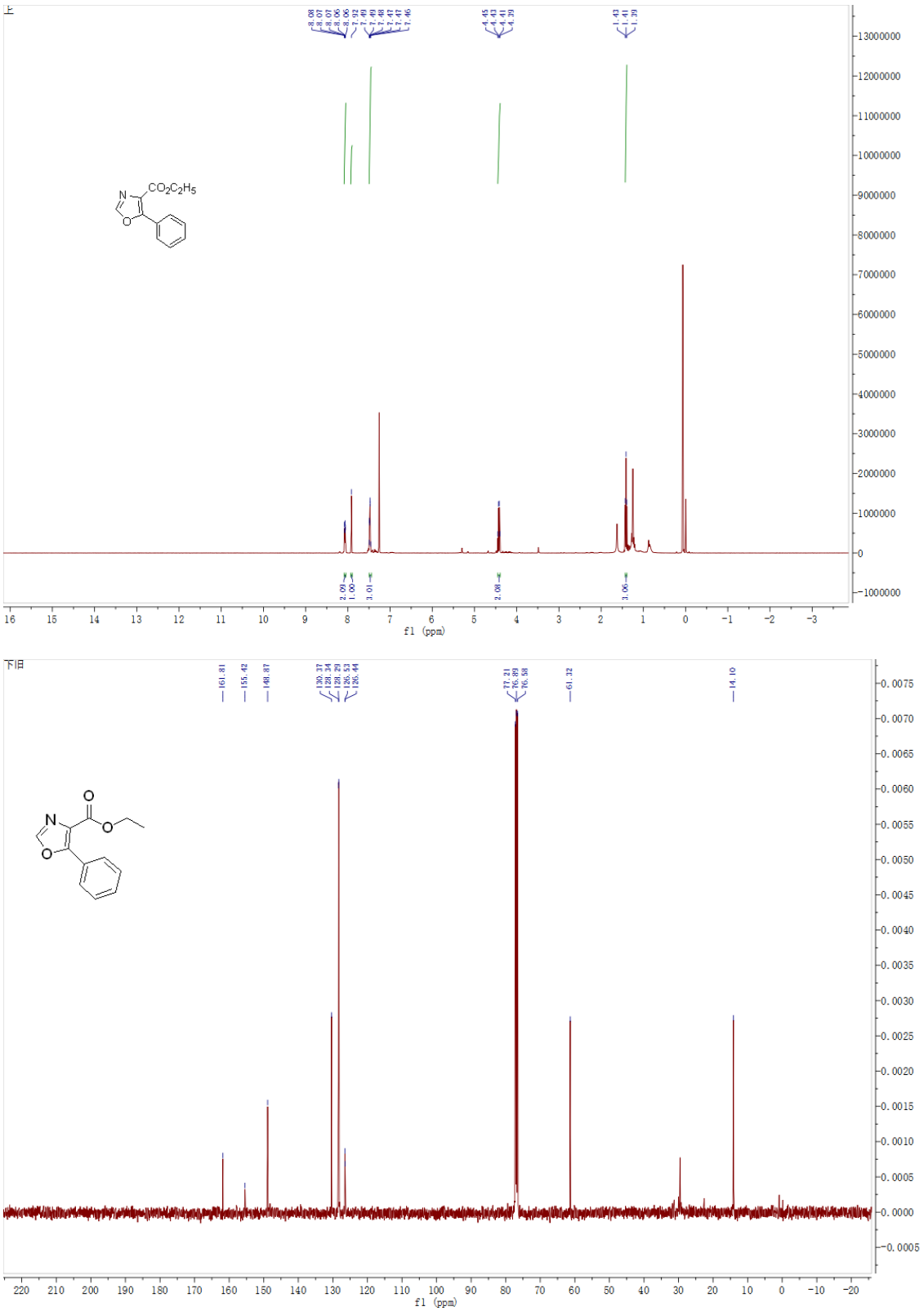
Ethyl 5-(pyridin-4-yl)oxazole-4-carboxylate (3z)



The reaction was performed following the General Procedure with DABCO (56.1 mg, 0.5 mmol, 0.5 equiv), CuBr (35.9 mg, 0.25 mmol, 0.25 equiv), dry DMF (2 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv), 4-pyridinecarboxaldehyde (**1z**) (107.1 mg, 1 mmol, 1 equiv) under a balloon pressure of O_2. The crude product was purified by flash chromatography on silica gel (eluted with petroleum ether:EtOAc = 3:1) to give the product (91.6 mg, 42% yield) as a white solid, m.p. 46-47°C (EtOAc). R_f = 0.46 (petroleum ether:EtOAc = 3:1). The spectroscopic data for this product match the literature data[1].

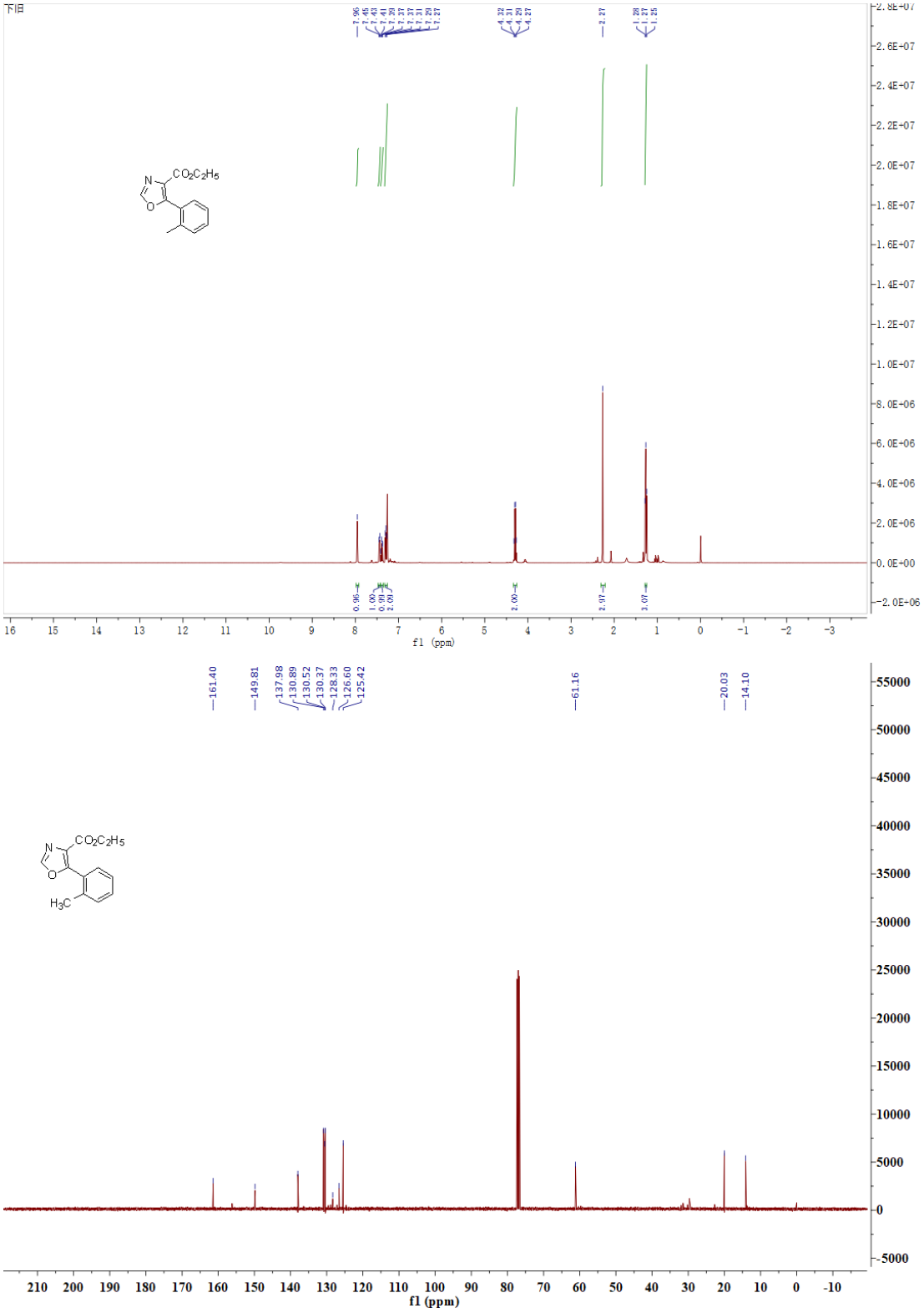
4.NMR spectra for 3

Ethyl 5-phenyloxazole-4-carboxylate (3a)



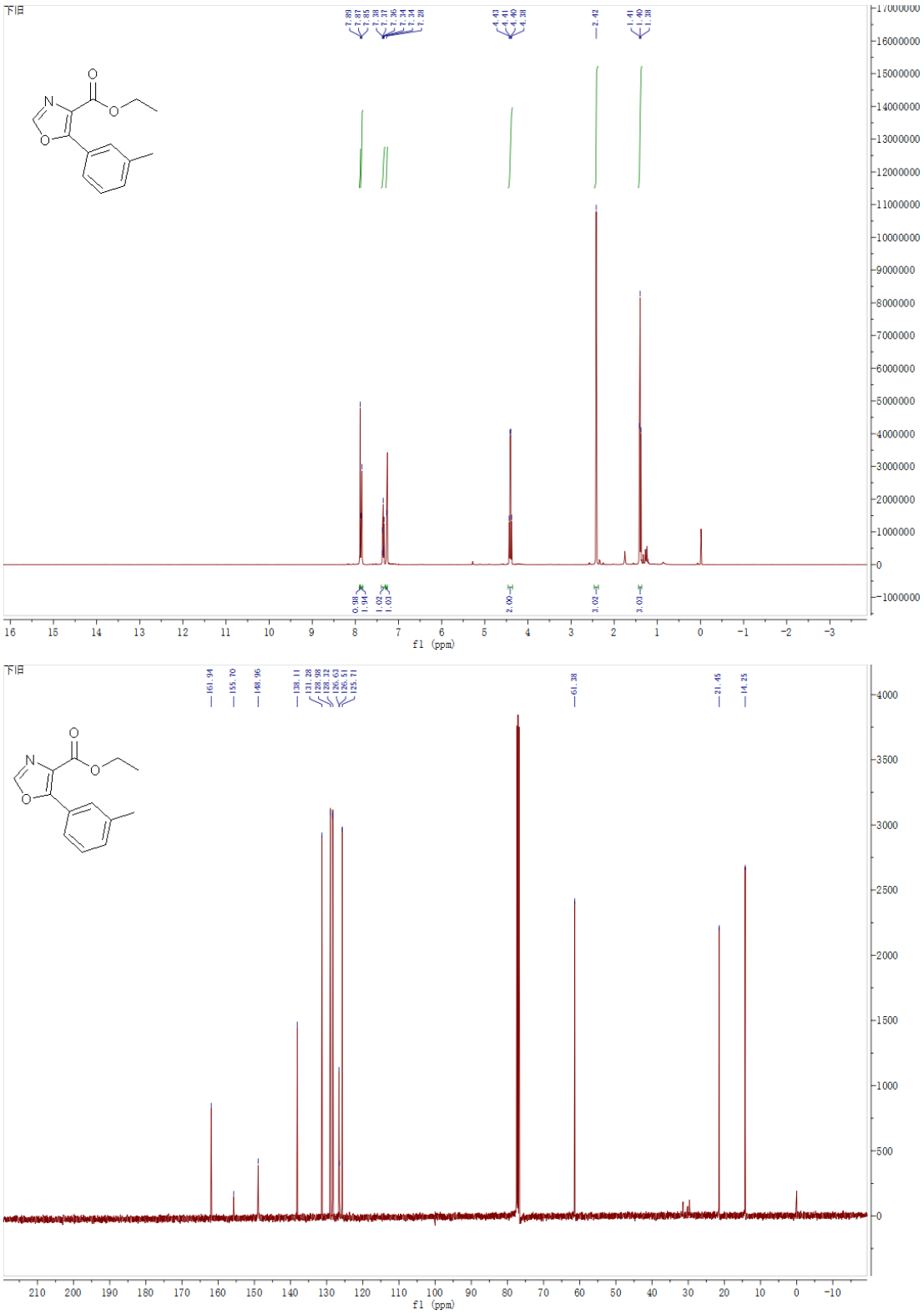
Supplementary Figure 1. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3a in $CDCl_3$

Ethyl 5-(o-tolyl)oxazole-4-carboxylate (3b)



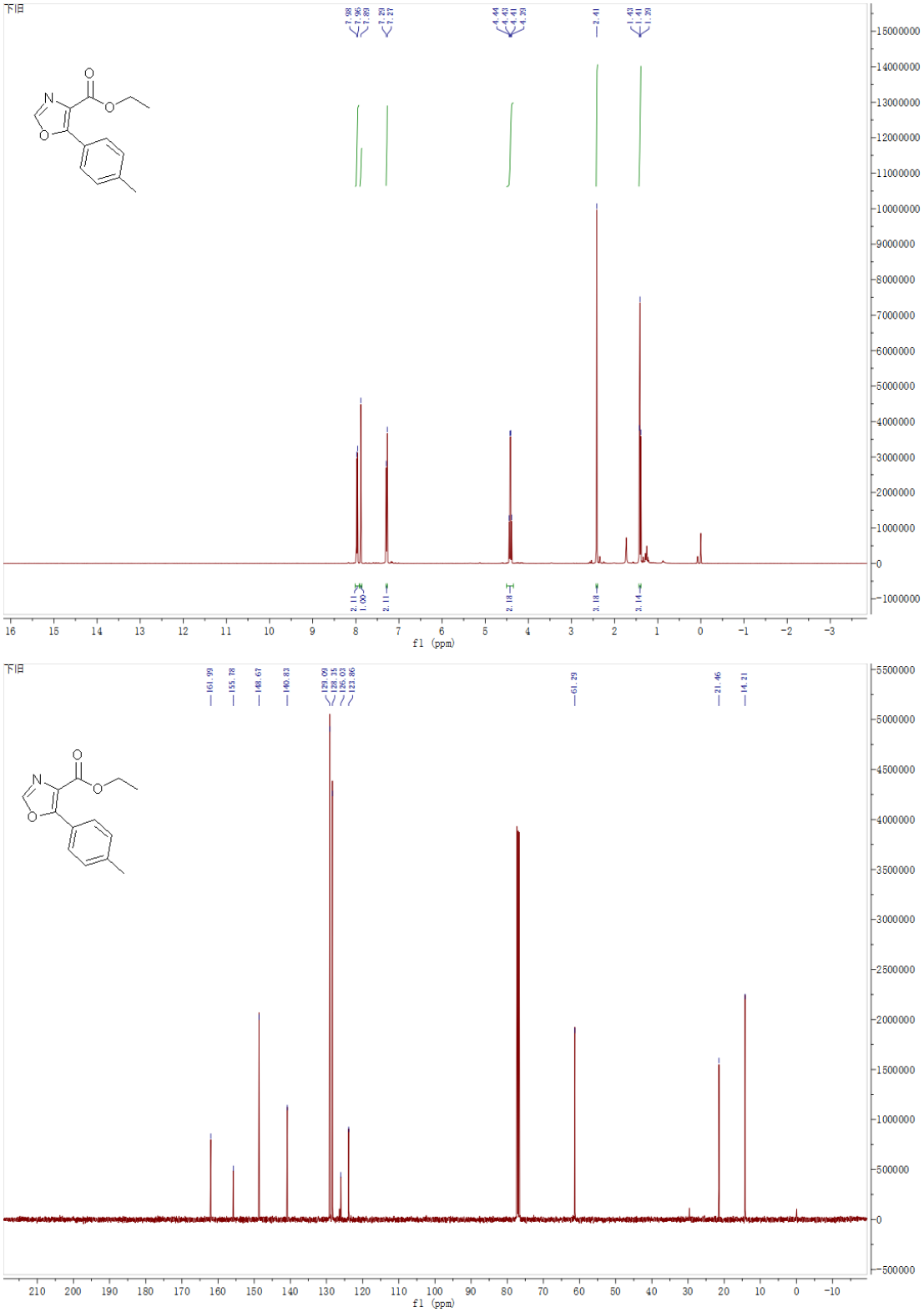
Supplementary Figure 2. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3b in $CDCl_3$

Ethyl 5-(m-tolyl)oxazole-4-carboxylate (3c)



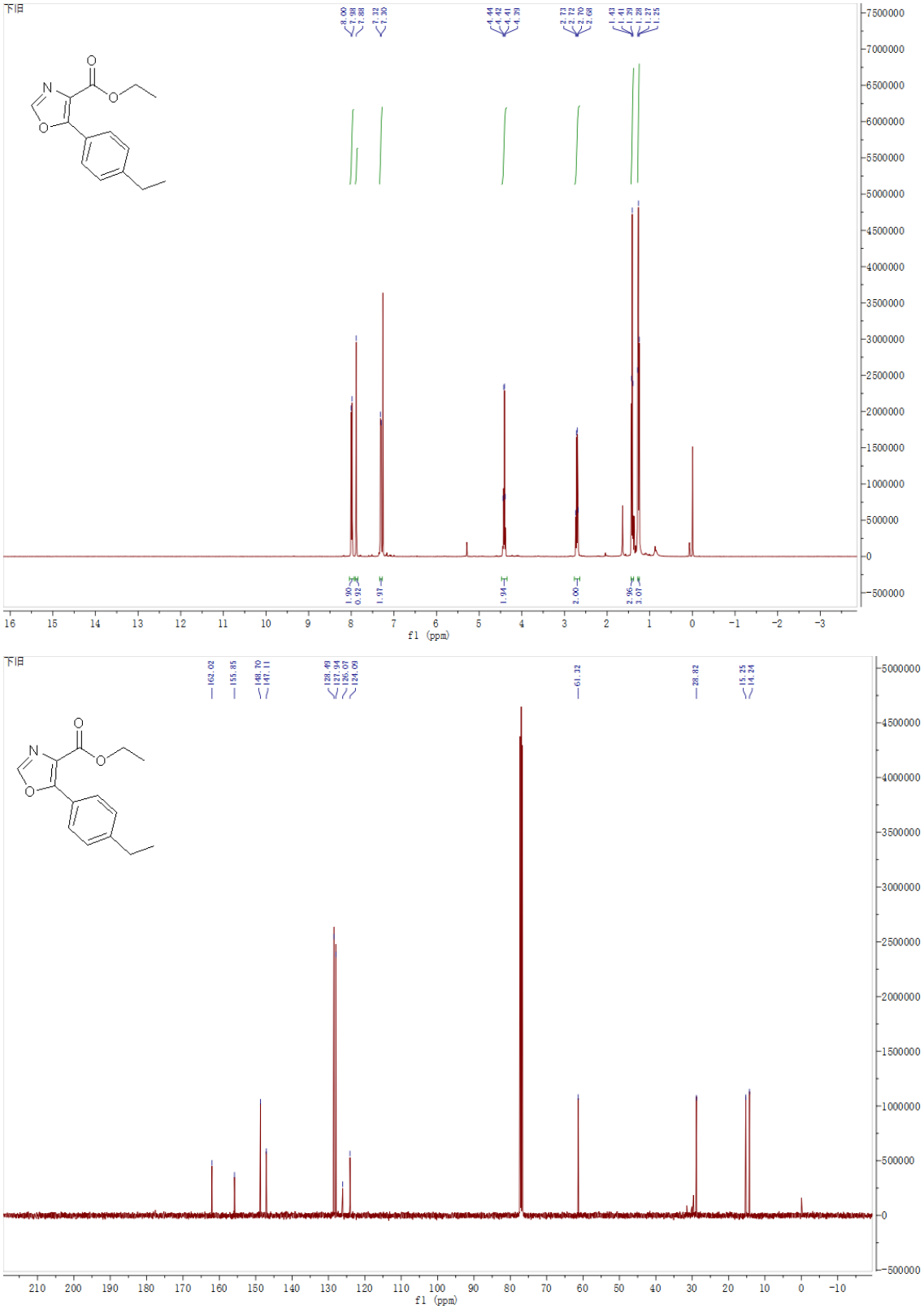
Supplementary Figure 3. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3c in $CDCl_3$

Ethyl 5-(p-tolyl)oxazole-4-carboxylate (3d)



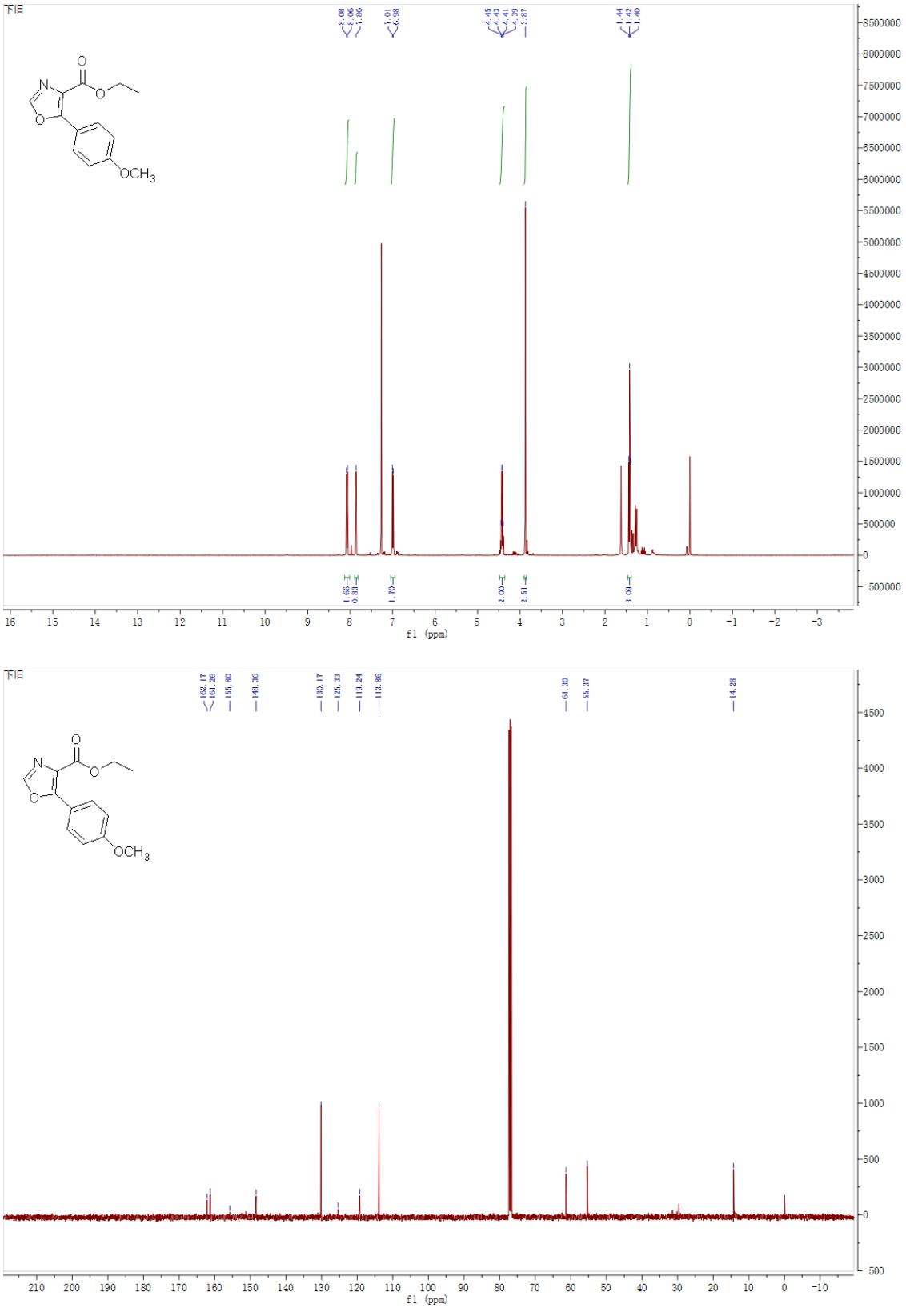
Supplementary Figure 4. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3d in $CDCl_3$

Ethyl 5-(4-ethylphenyl)oxazole-4-carboxylate (3e)



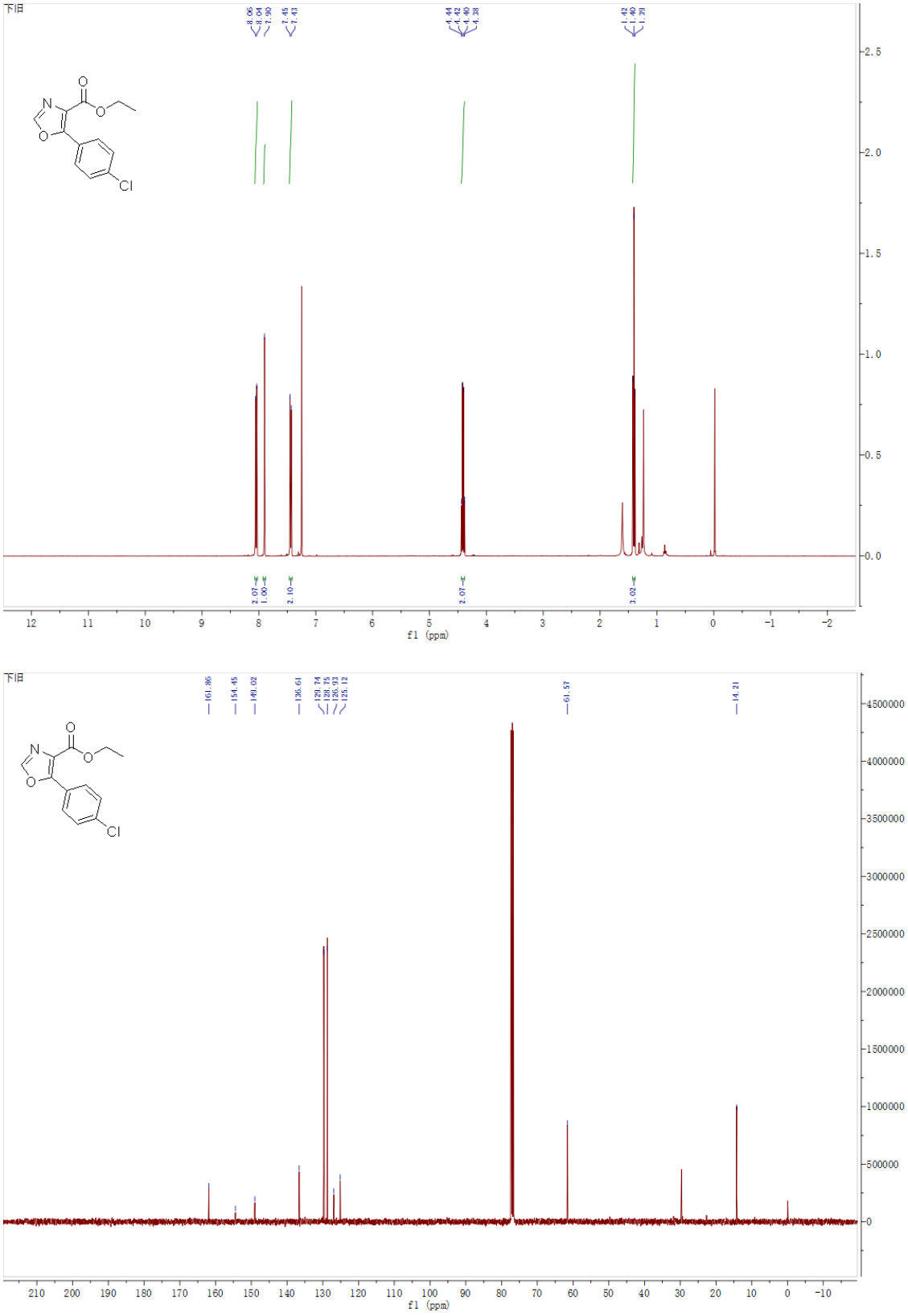
Supplementary Figure 5. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3e in $CDCl_3$

Ethyl 5-(4-methoxyphenyl)oxazole-4-carboxylate (3f)



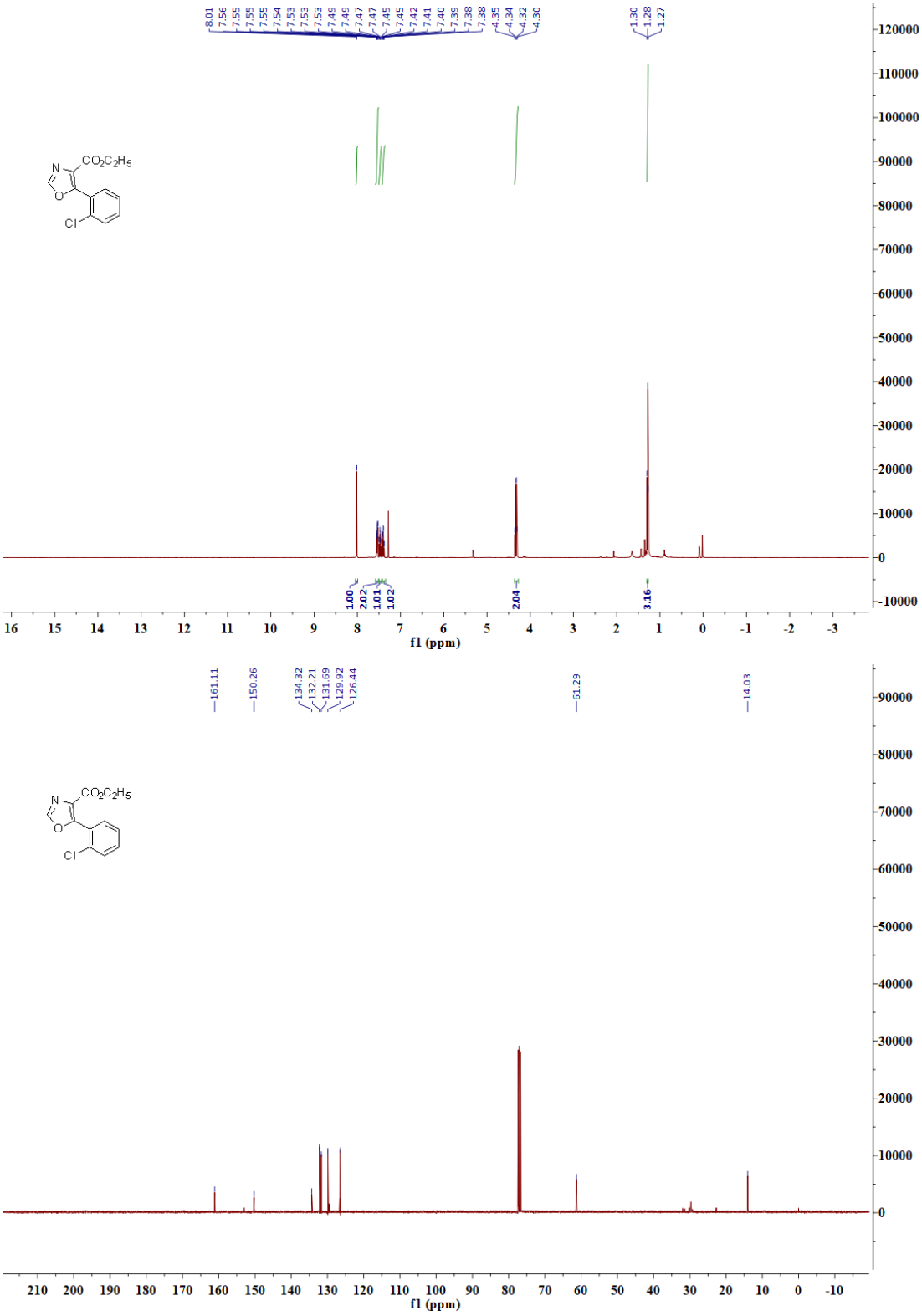
Supplementary Figure 6. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3f in $CDCl_3$

Ethyl 5-(4-chlorophenyl)oxazole-4-carboxylate (3g)



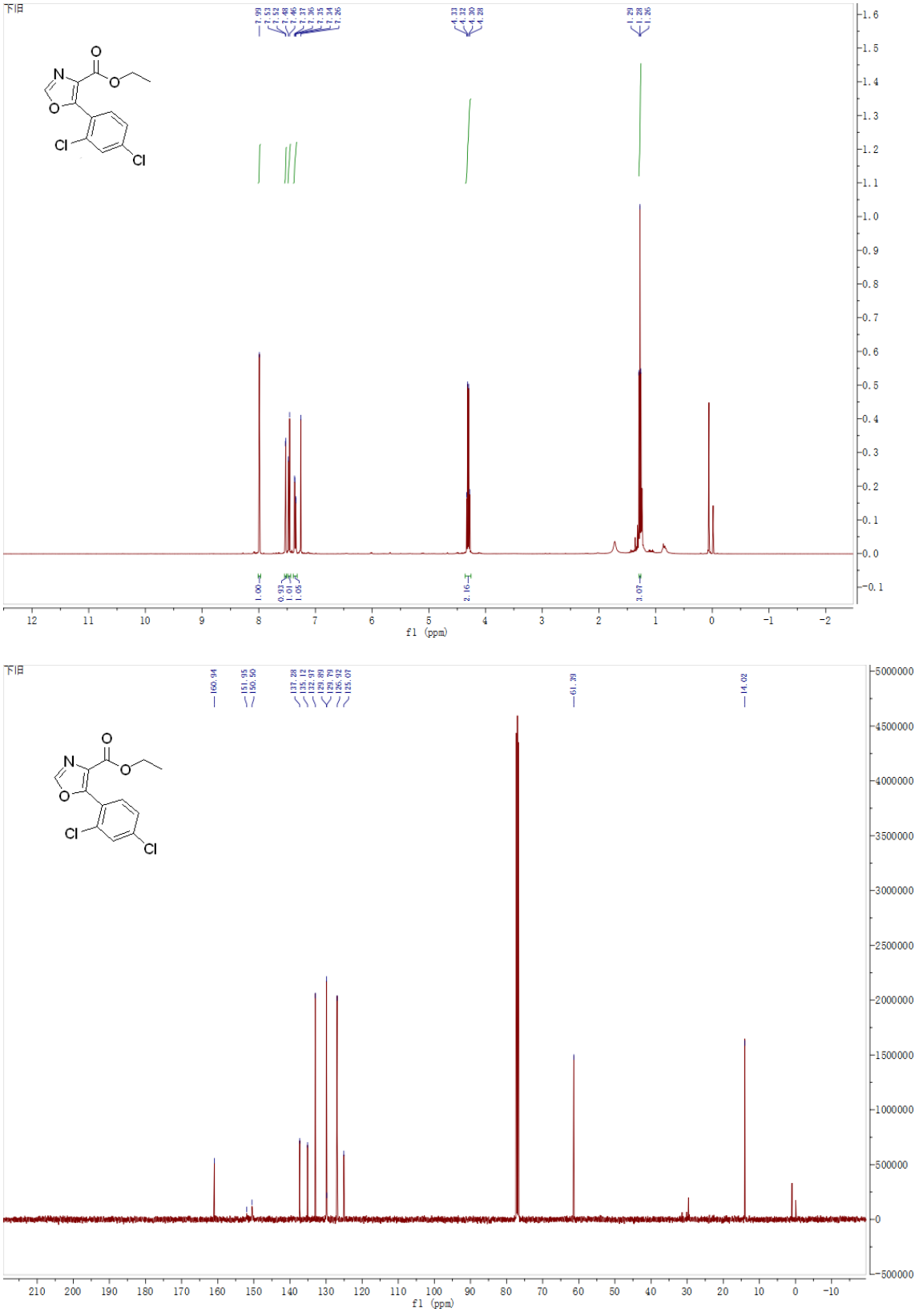
Supplementary Figure 7. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3g in $CDCl_3$

Ethyl 5-(2-chlorophenyl)oxazole-4-carboxylate (3h)



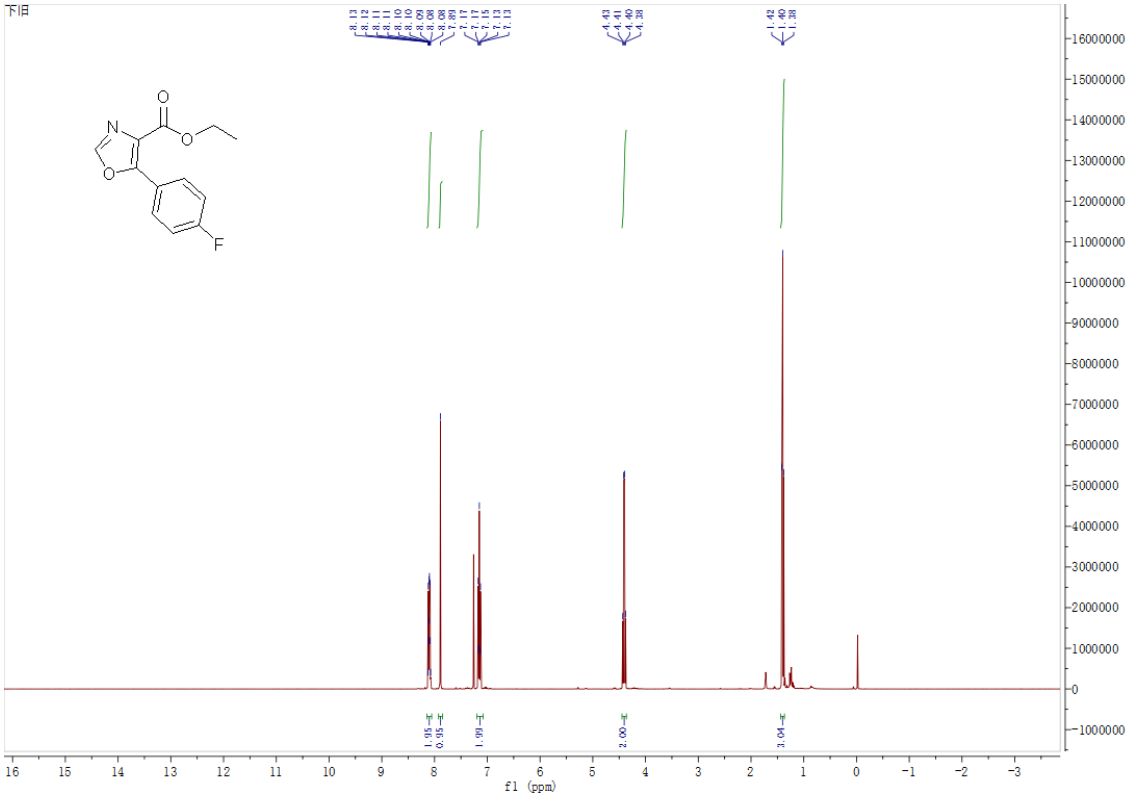
Supplementary Figure 8. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3h in $CDCl_3$

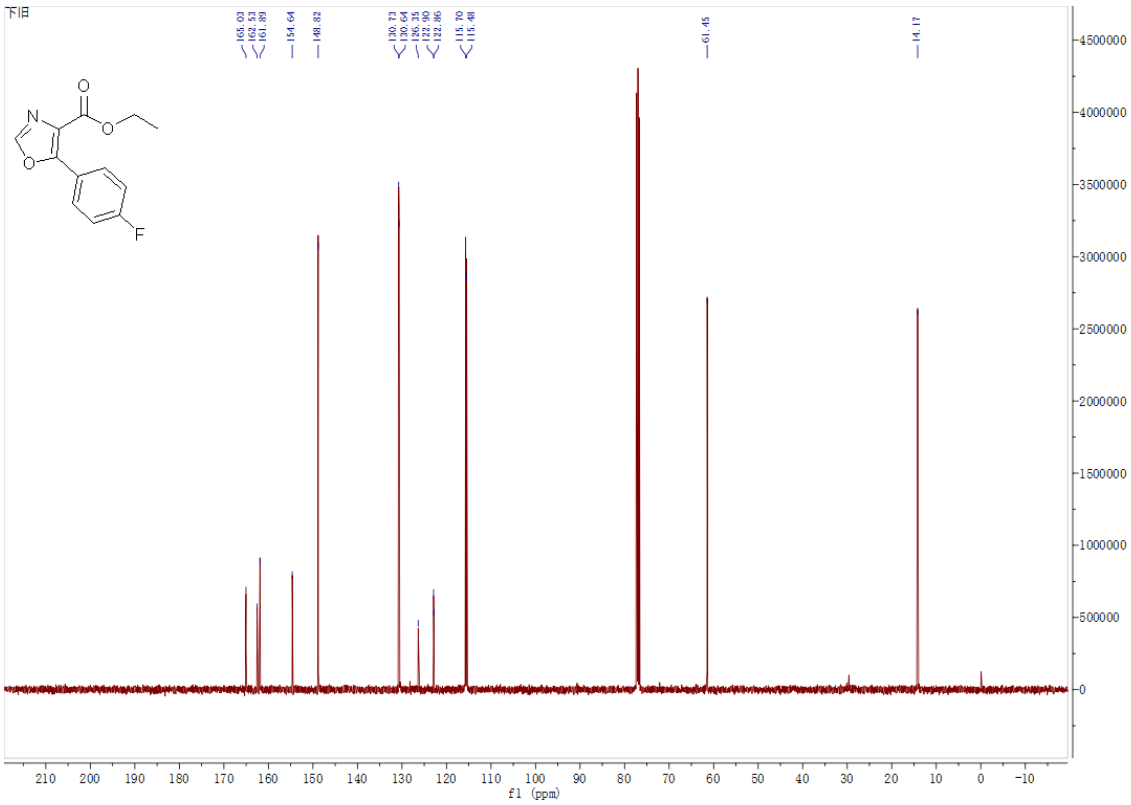
Ethyl 5-(2,4-dichlorophenyl)oxazole-4-carboxylate (3i)

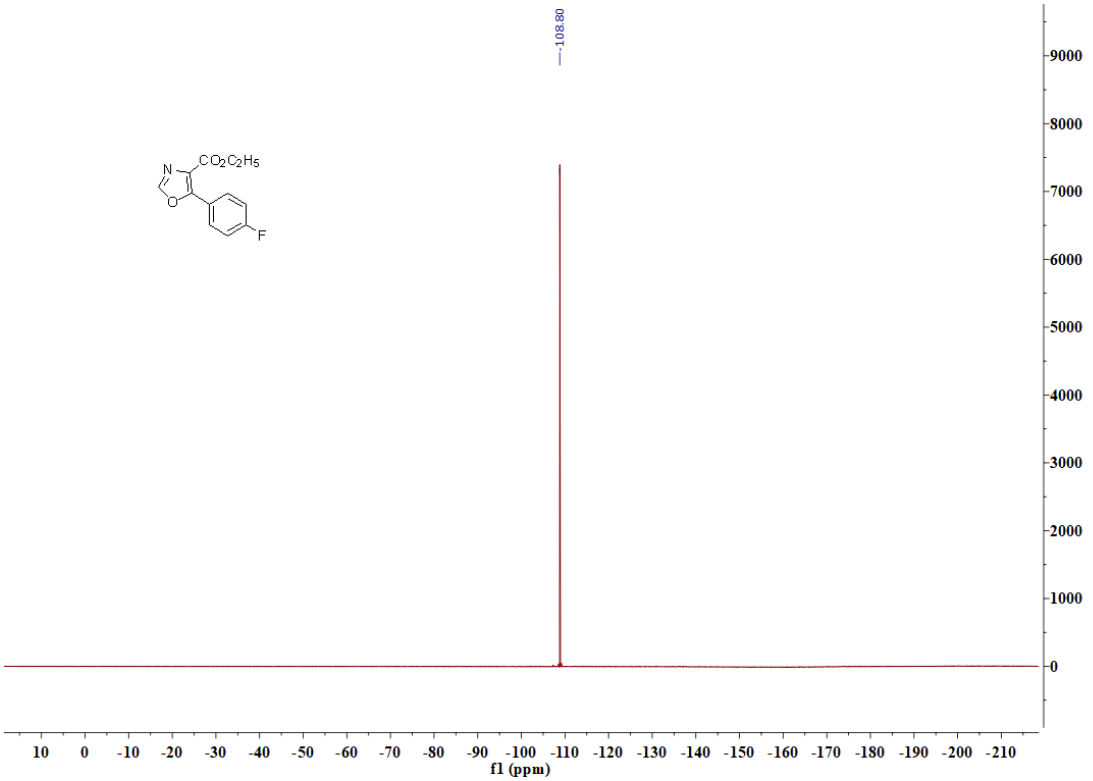


Supplementary Figure 9. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3i in $CDCl_3$

Ethyl 5-(4-fluorophenyl)oxazole-4-carboxylate (3j)

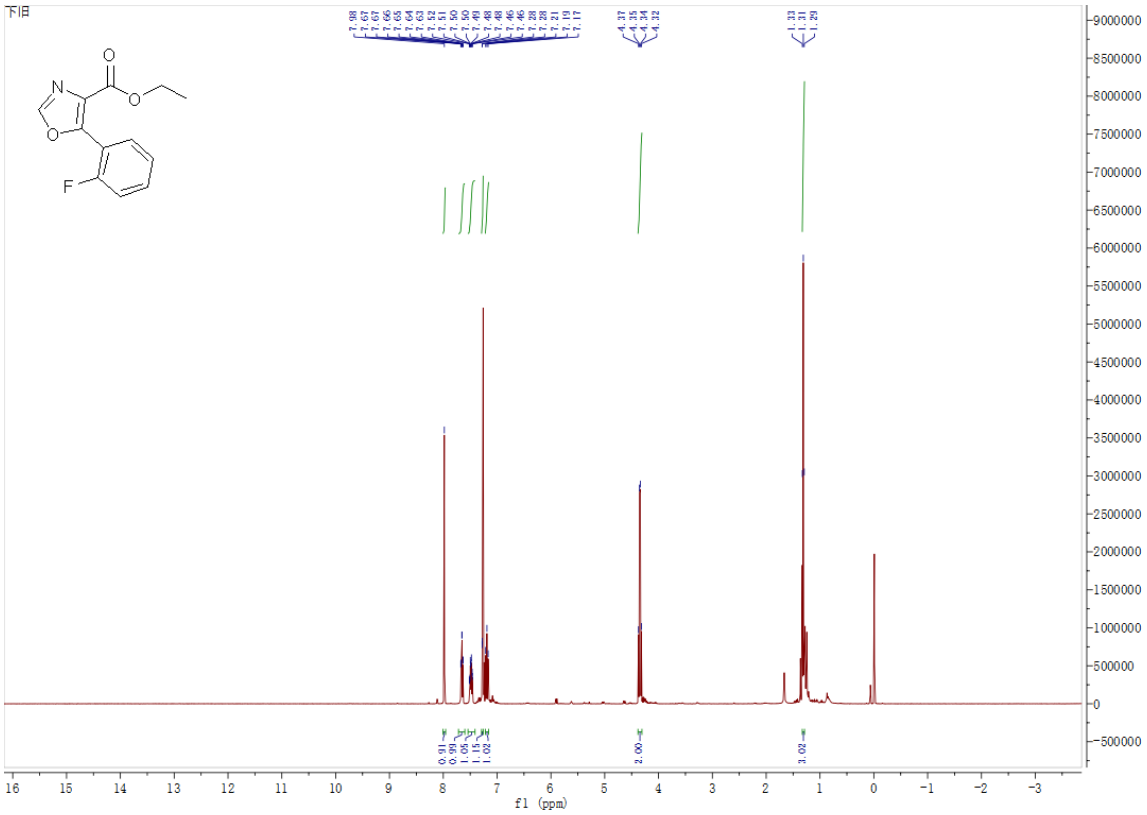


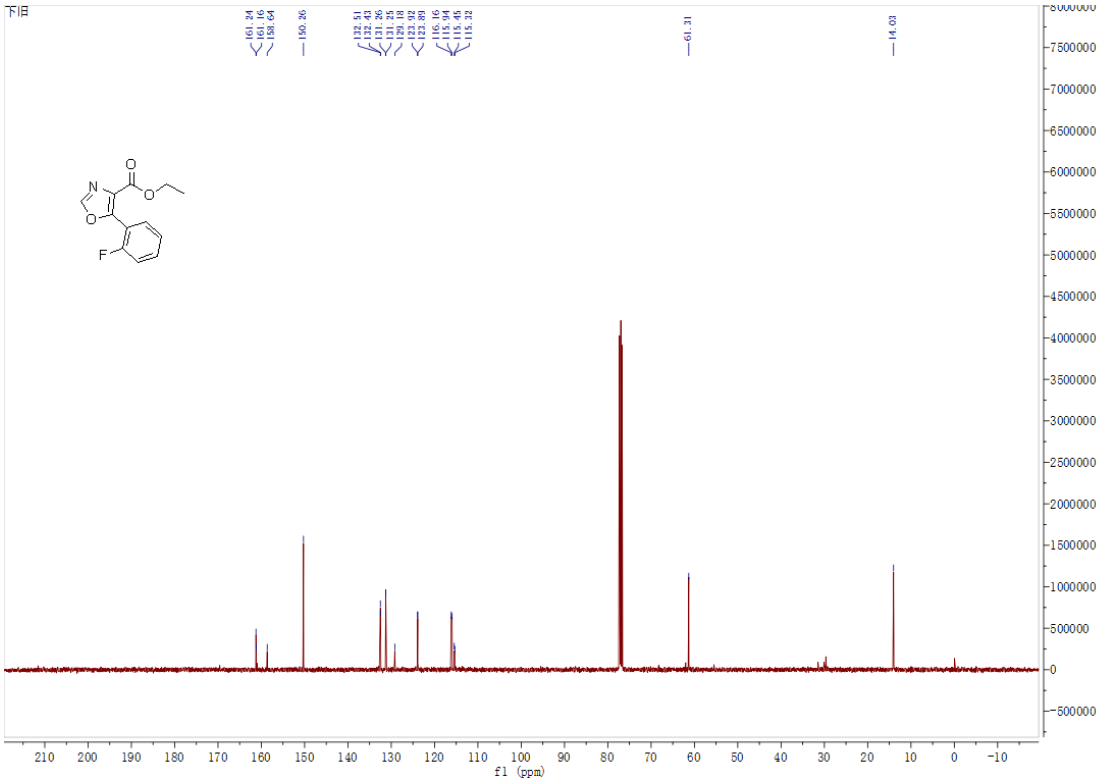


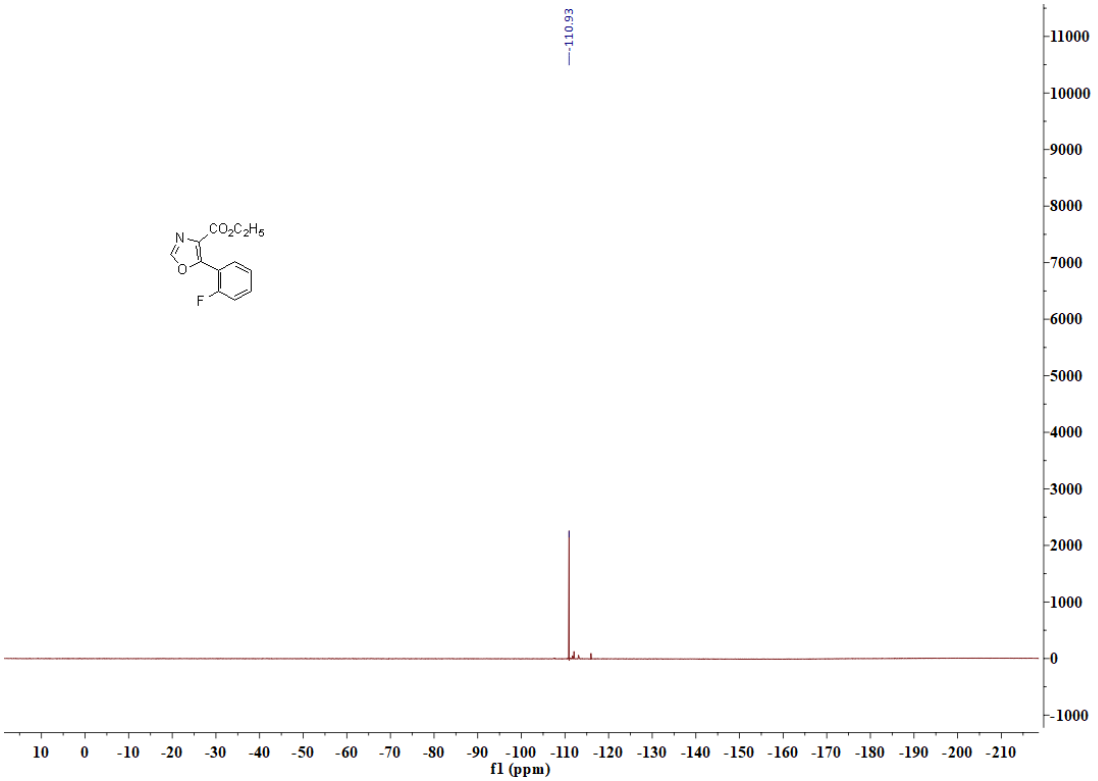


Supplementary Figure 10. ^{1}H (400 MHz) ^{13}C {1H} (101 MHz) and ^{19}F {1H} (376 MHz) NMR Spectrum of 3j in $CDCl_3$

Ethyl 5-(2-fluorophenyl)oxazole-4-carboxylate (3k)

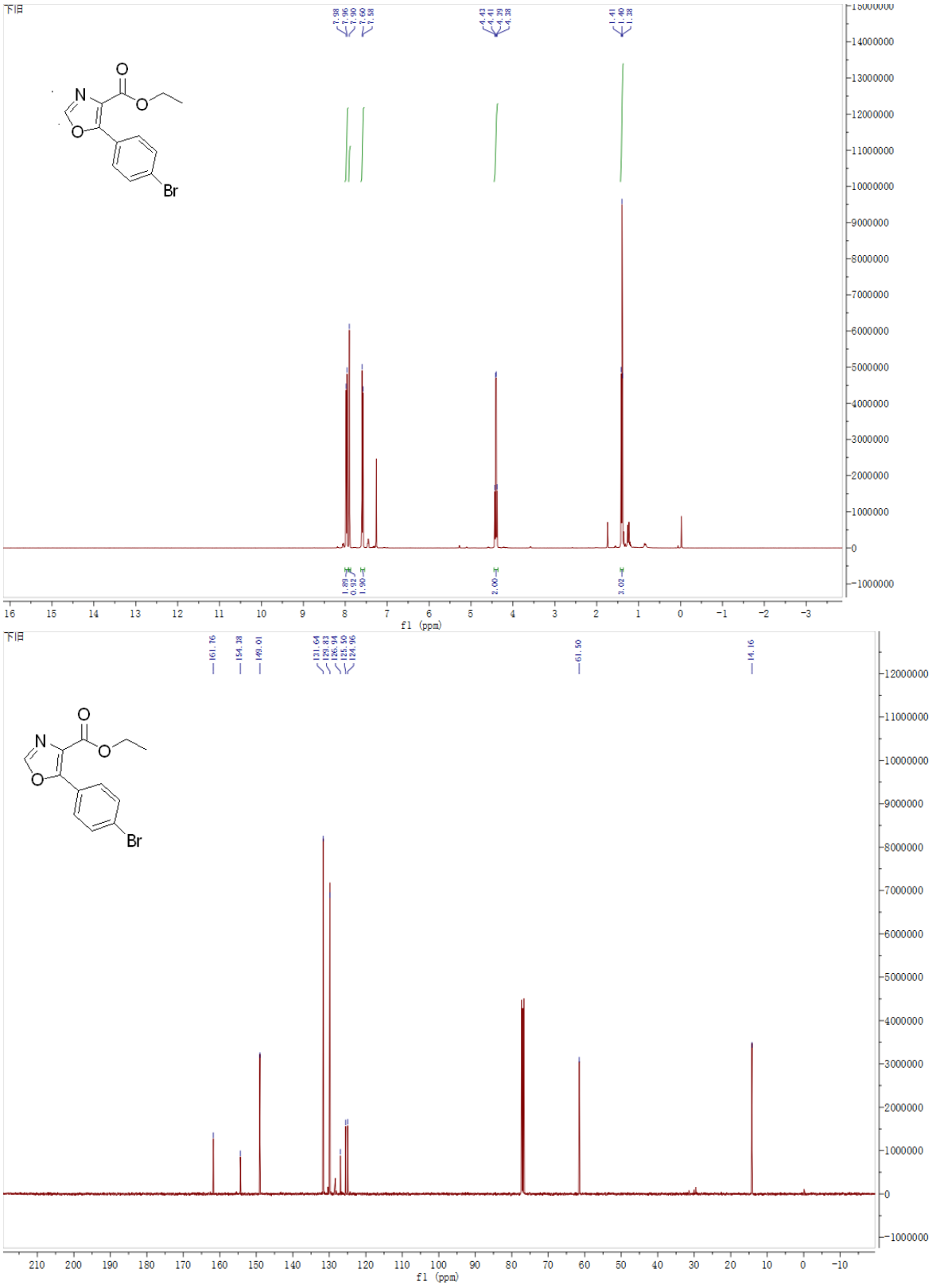






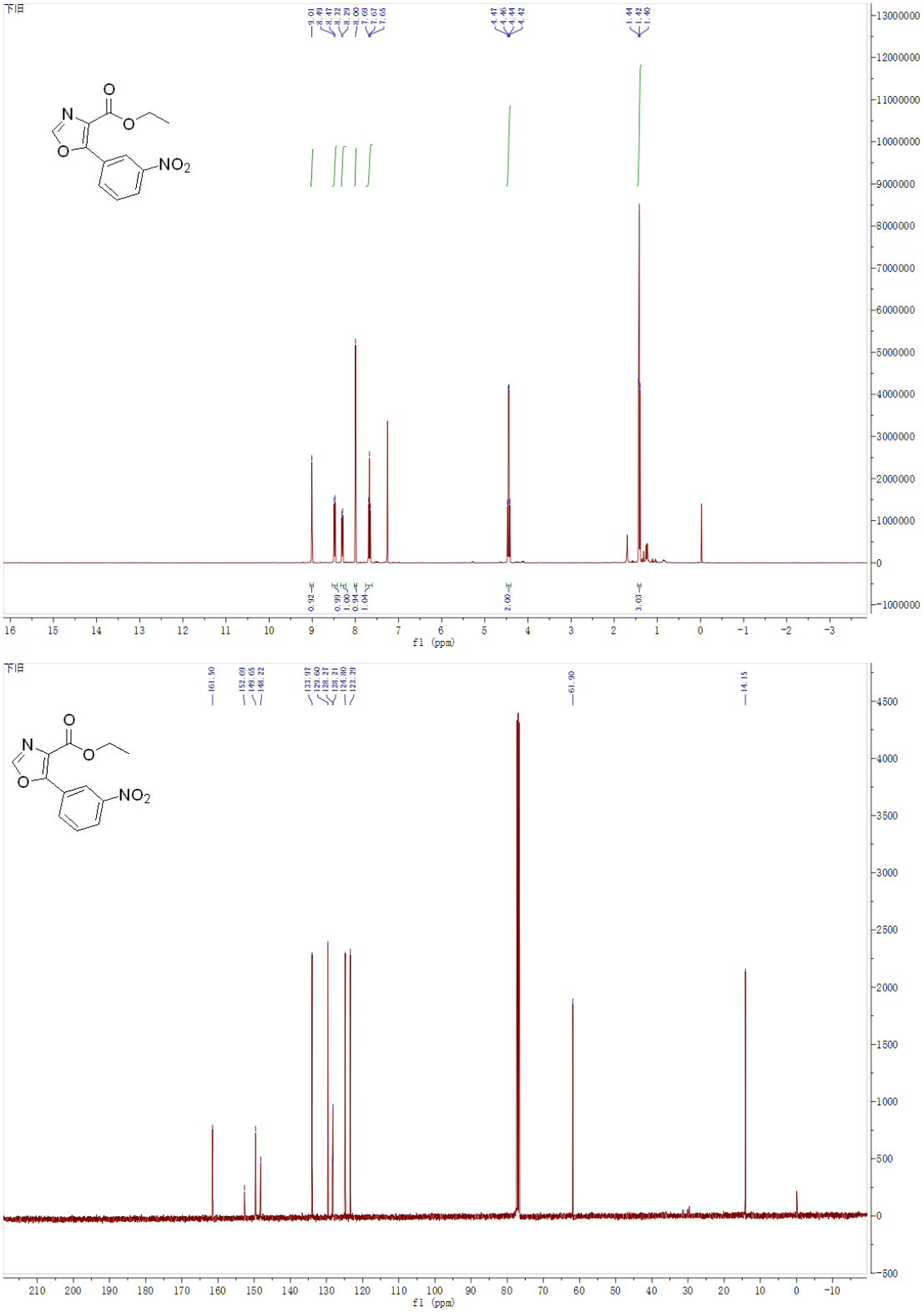
Supplementary Figure 11. ^{1}H (400 MHz) ^{13}C {1H} (101 MHz) and ^{19}F {1H} (376 MHz) NMR Spectrum of 3k in $CDCl_3$

Ethyl 5-(4-bromophenyl)oxazole-4-carboxylate (3l)



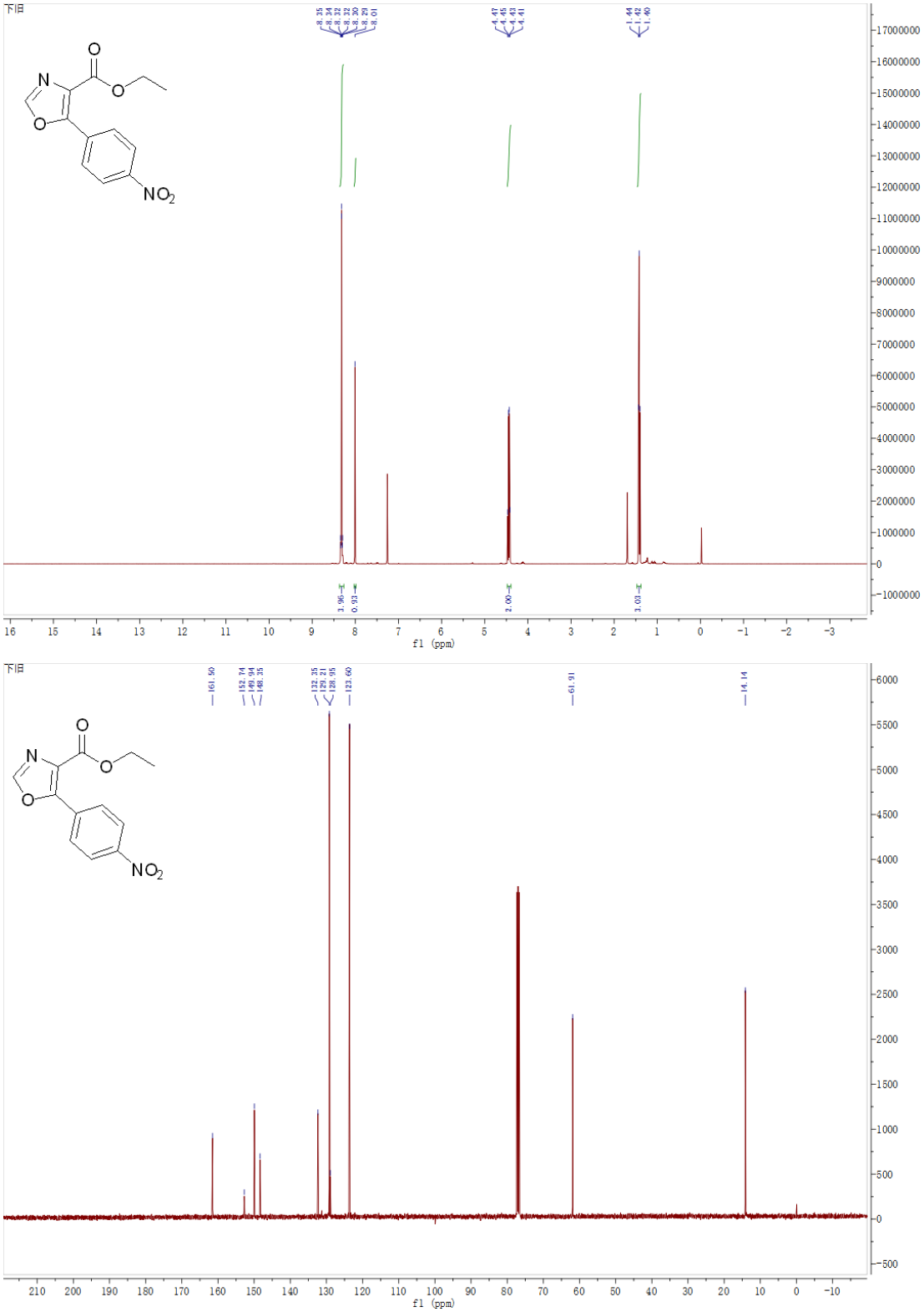
Supplementary Figure 12. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3l in $CDCl_3$

Ethyl 5-(3-nitrophenyl)oxazole-4-carboxylate (3m)



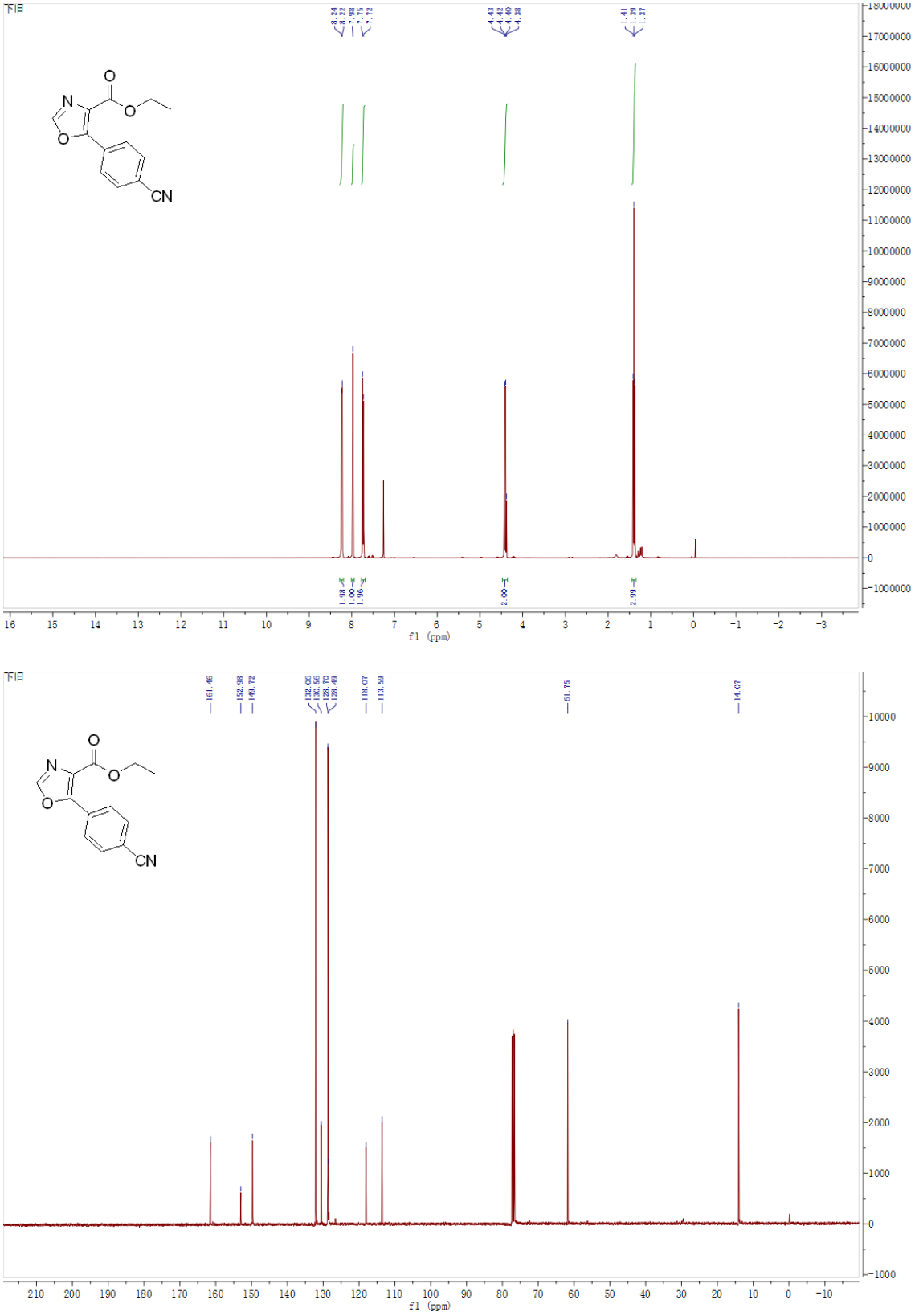
Supplementary Figure 13. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3m in $CDCl_3$

Ethyl 5-(4-nitrophenyl)oxazole-4-carboxylate (3n)



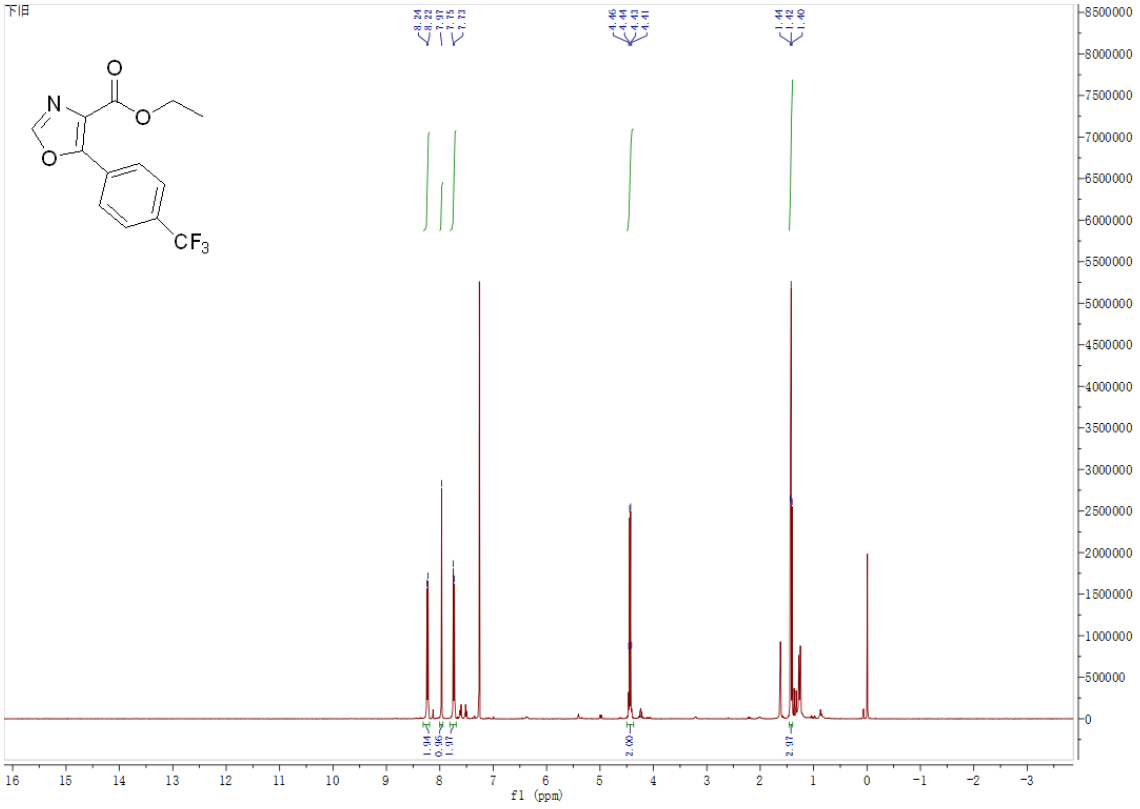
Supplementary Figure 14. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3n in $CDCl_3$

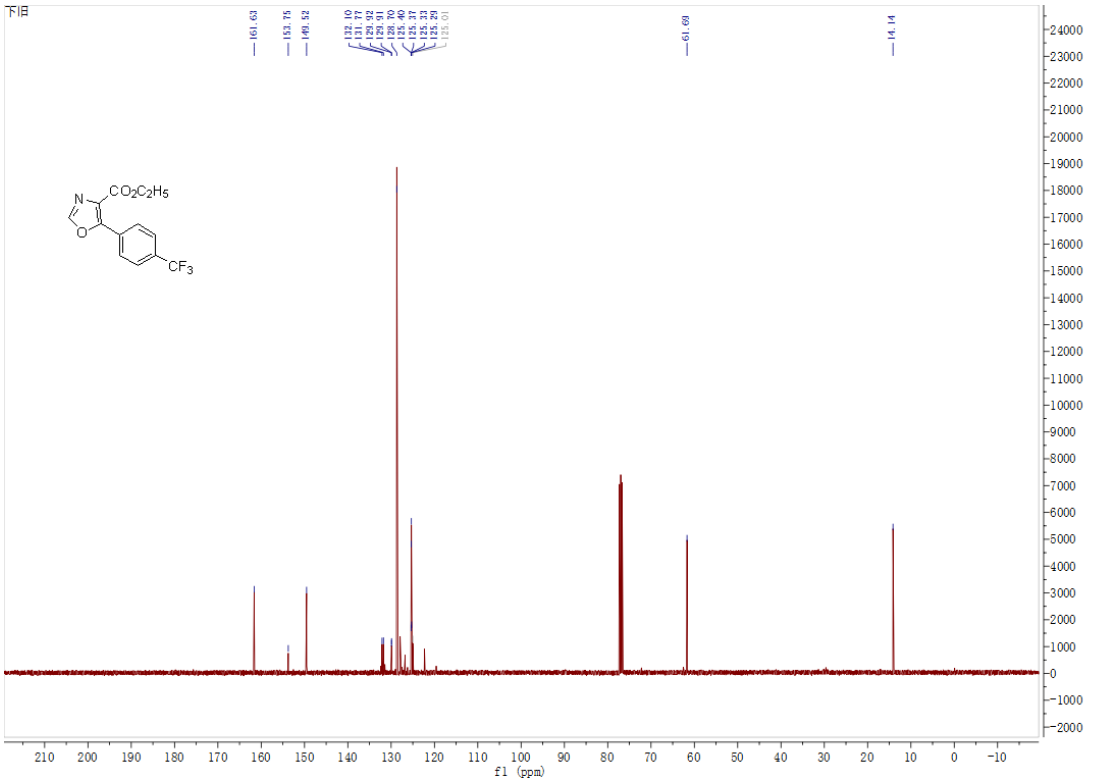
Ethyl 5-(4-cyanophenyl)oxazole-4-carboxylate (3o)

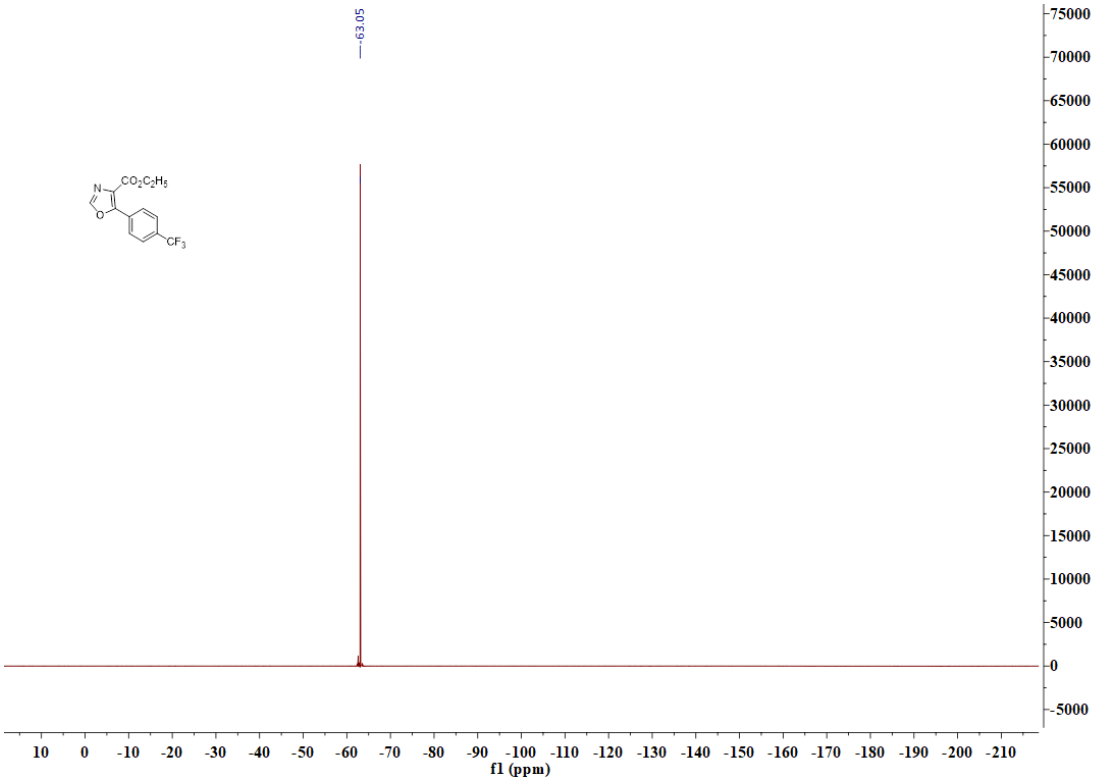


Supplementary Figure 15. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3o in $CDCl_3$

Ethyl 5-(4-(trifluoromethyl)phenyl)oxazole-4-carboxylate (3p)

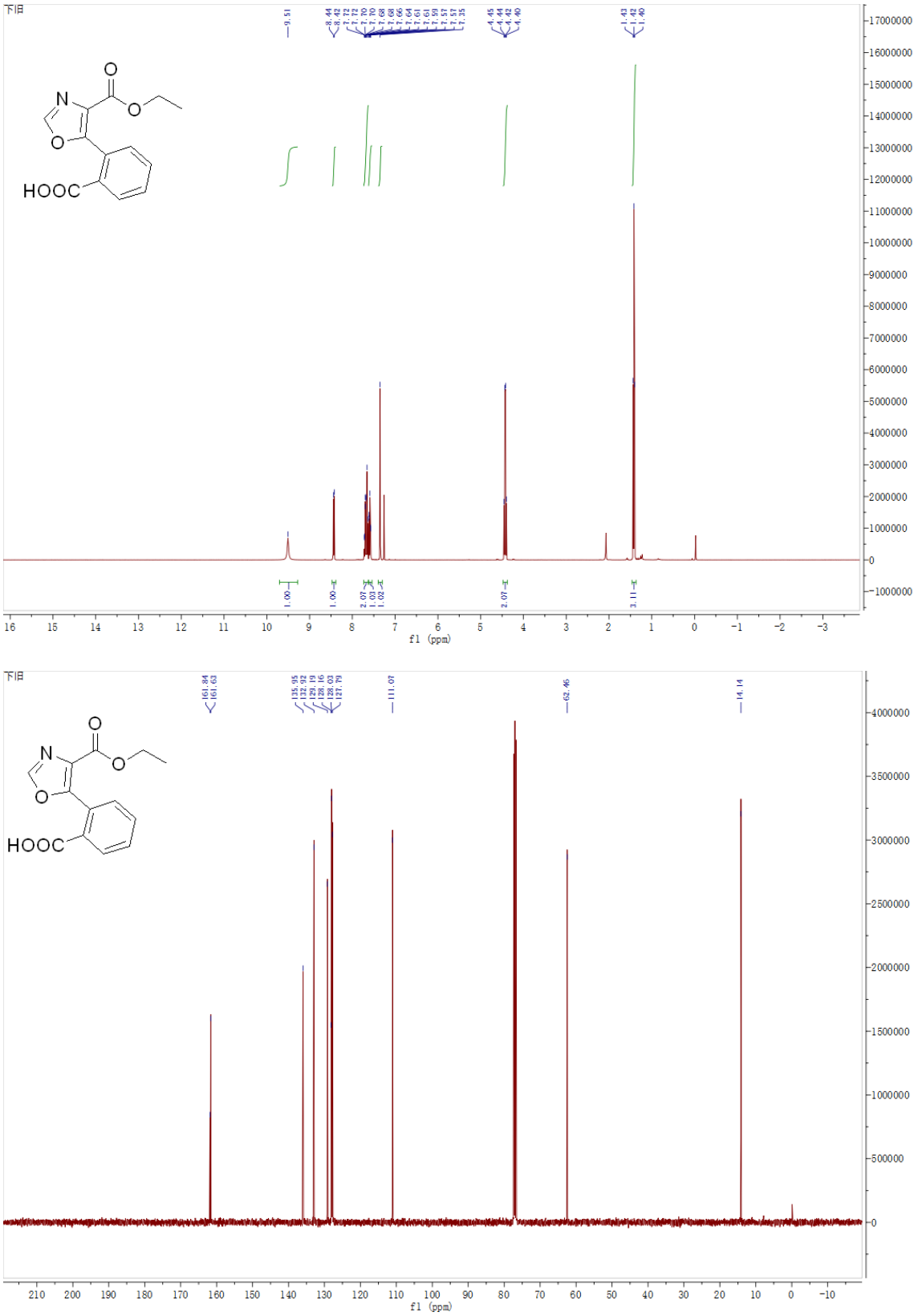






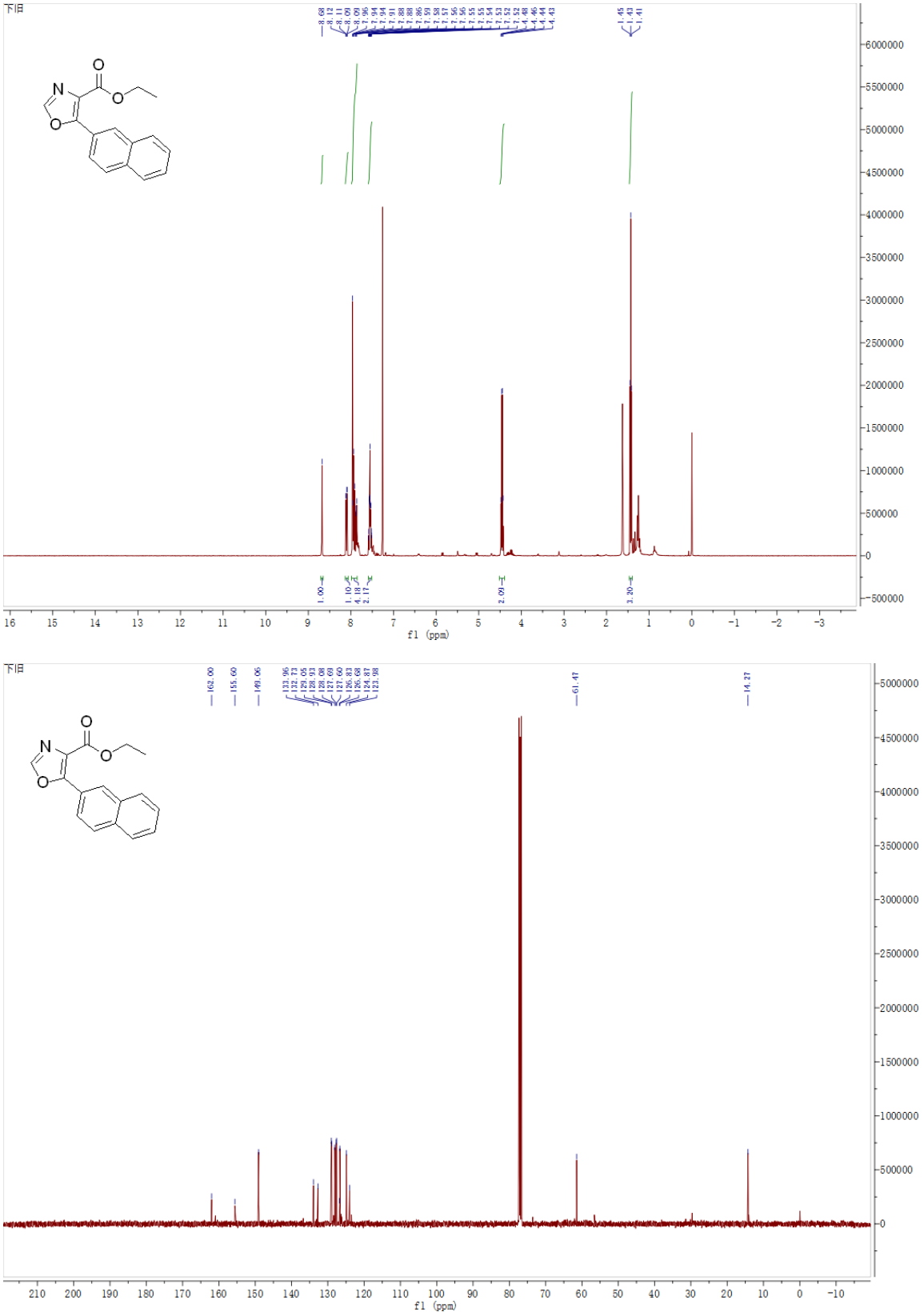
Supplementary Figure 16. ^{1}H (400 MHz) ^{13}C {1H} (101 MHz) and ^{19}F {1H} (376 MHz) NMR Spectrum of 3p in $CDCl_3$

2-(4-(Ethoxycarbonyl)oxazol-5-yl)benzoic acid (3q)



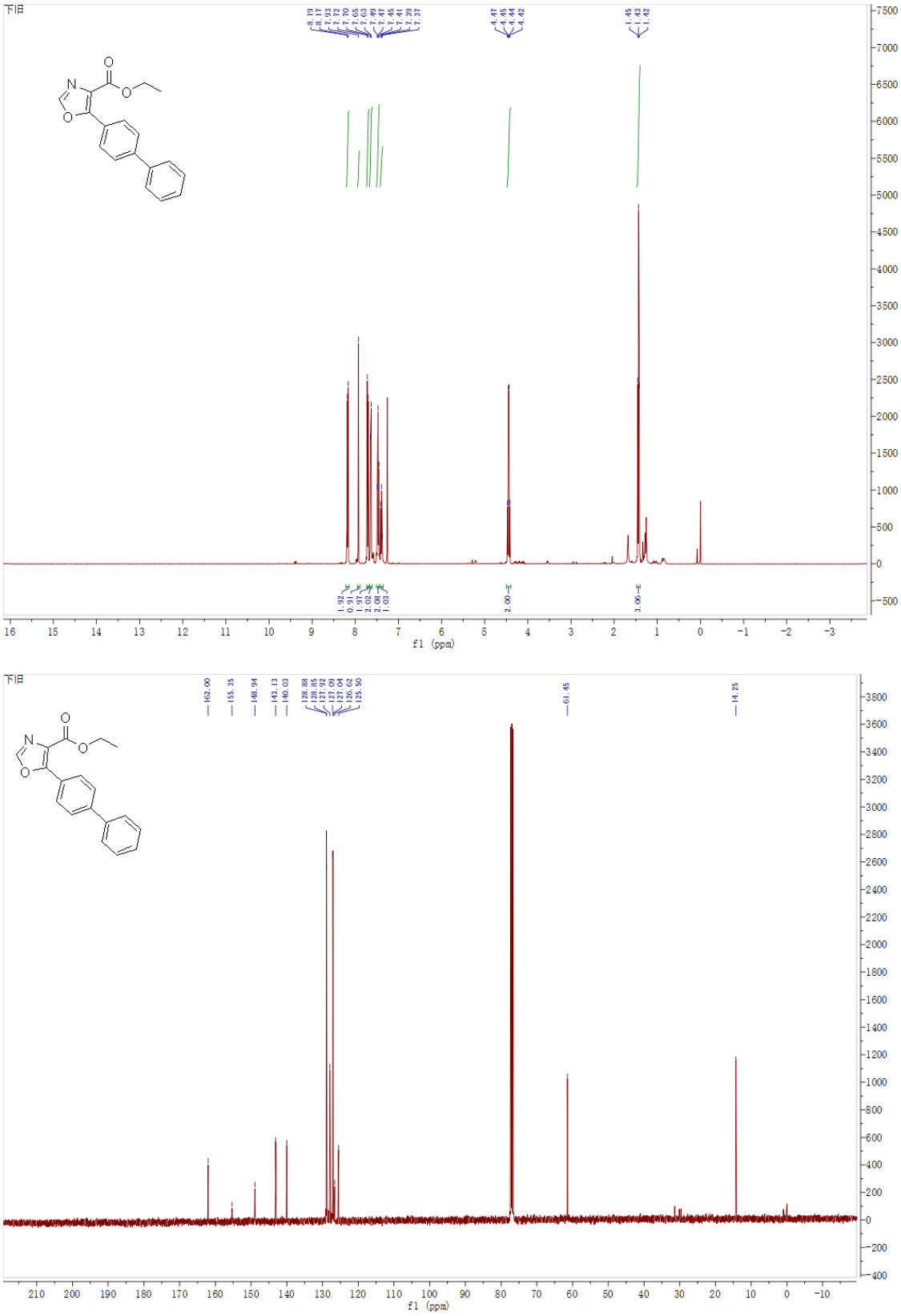
Supplementary Figure 17. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3q in $CDCl_3$

Ethyl 5-(naphthalen-2-yl)oxazole-4-carboxylate (3r)



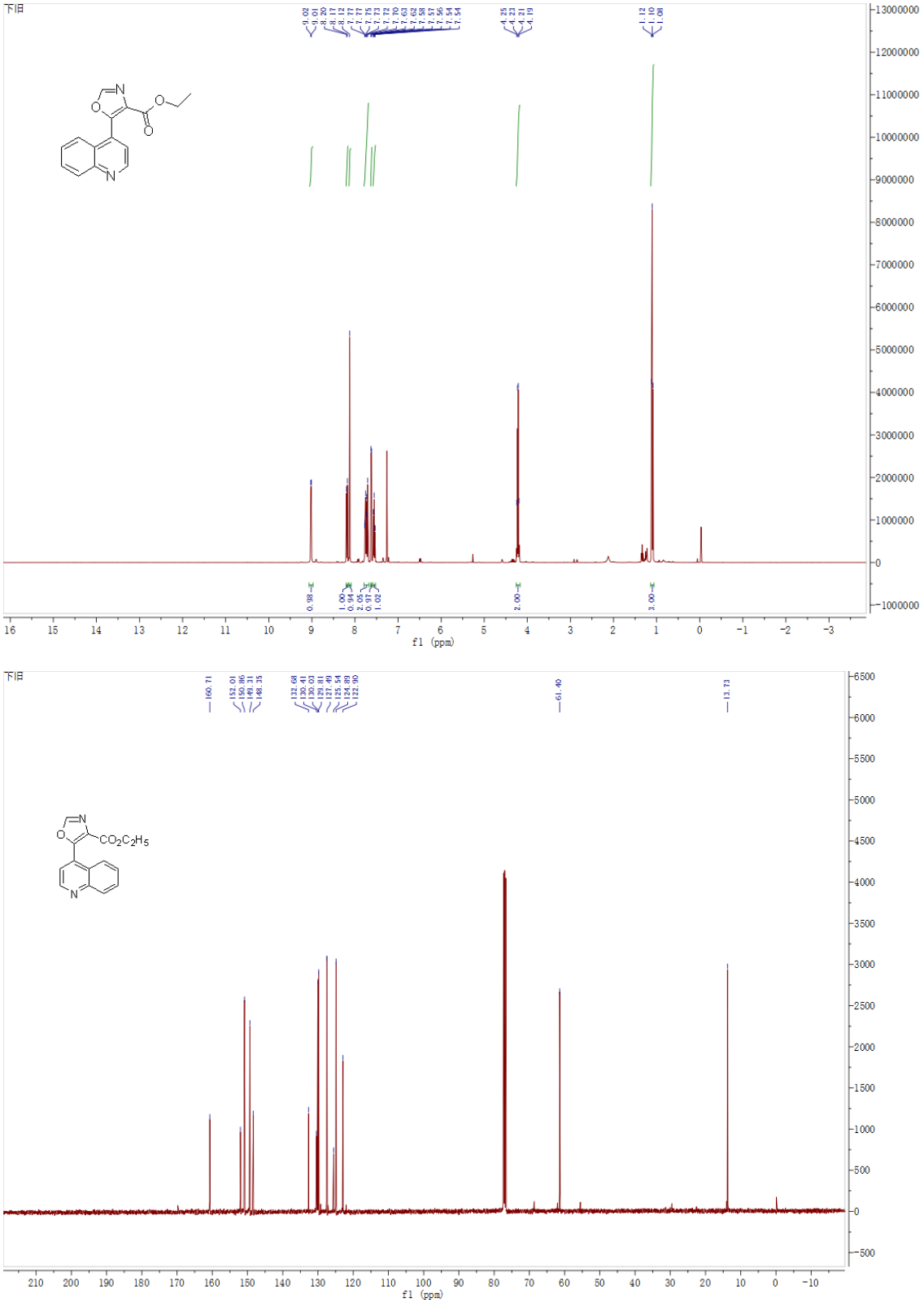
Supplementary Figure 18. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3r in $CDCl_3$

Ethyl 5-([1,1'-biphenyl]-4-yl)oxazole-4-carboxylate (3s)



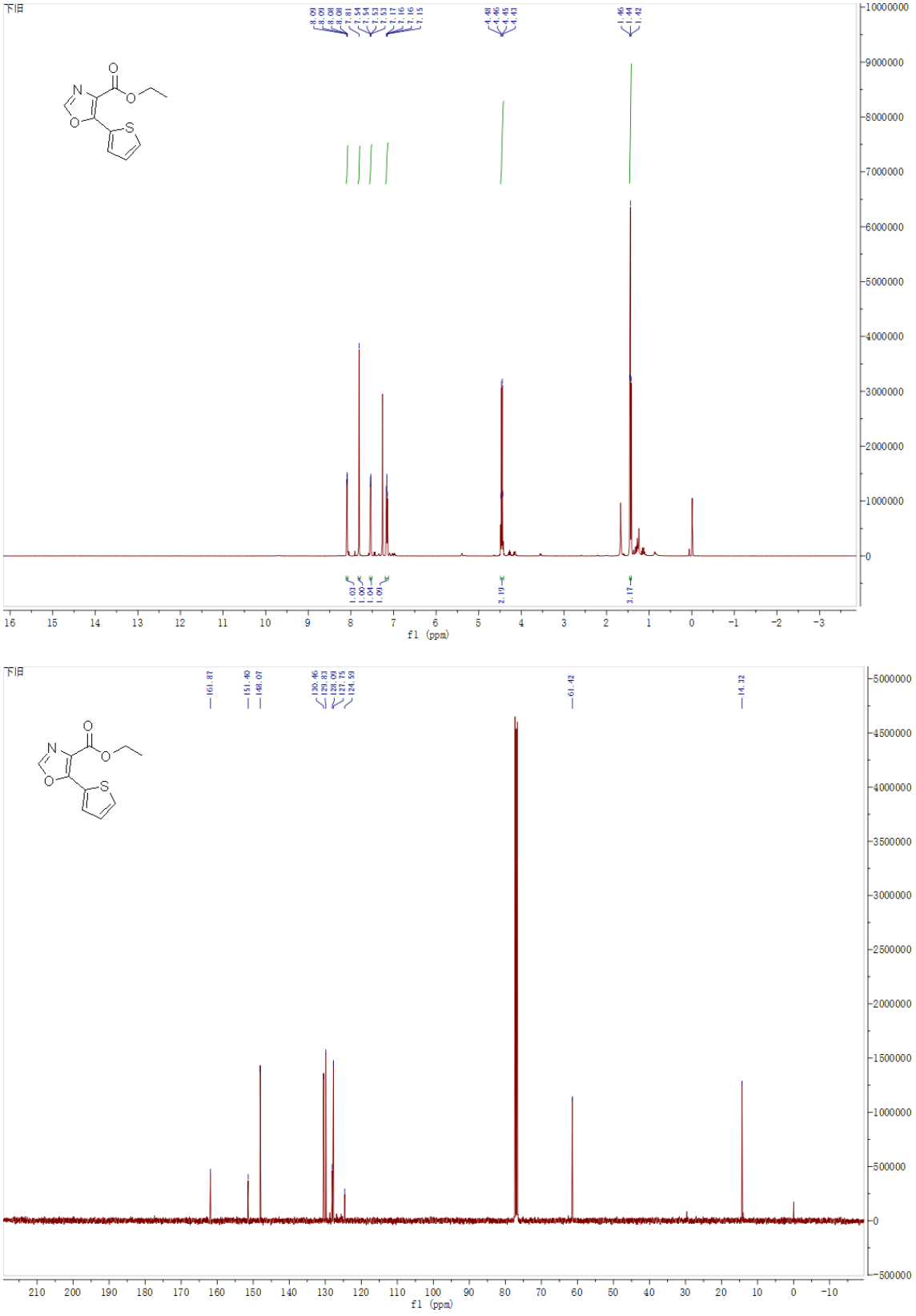
Supplementary Figure 19. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3s in $CDCl_3$

Ethyl 5-(quinolin-4-yl)oxazole-4-carboxylate (3t)



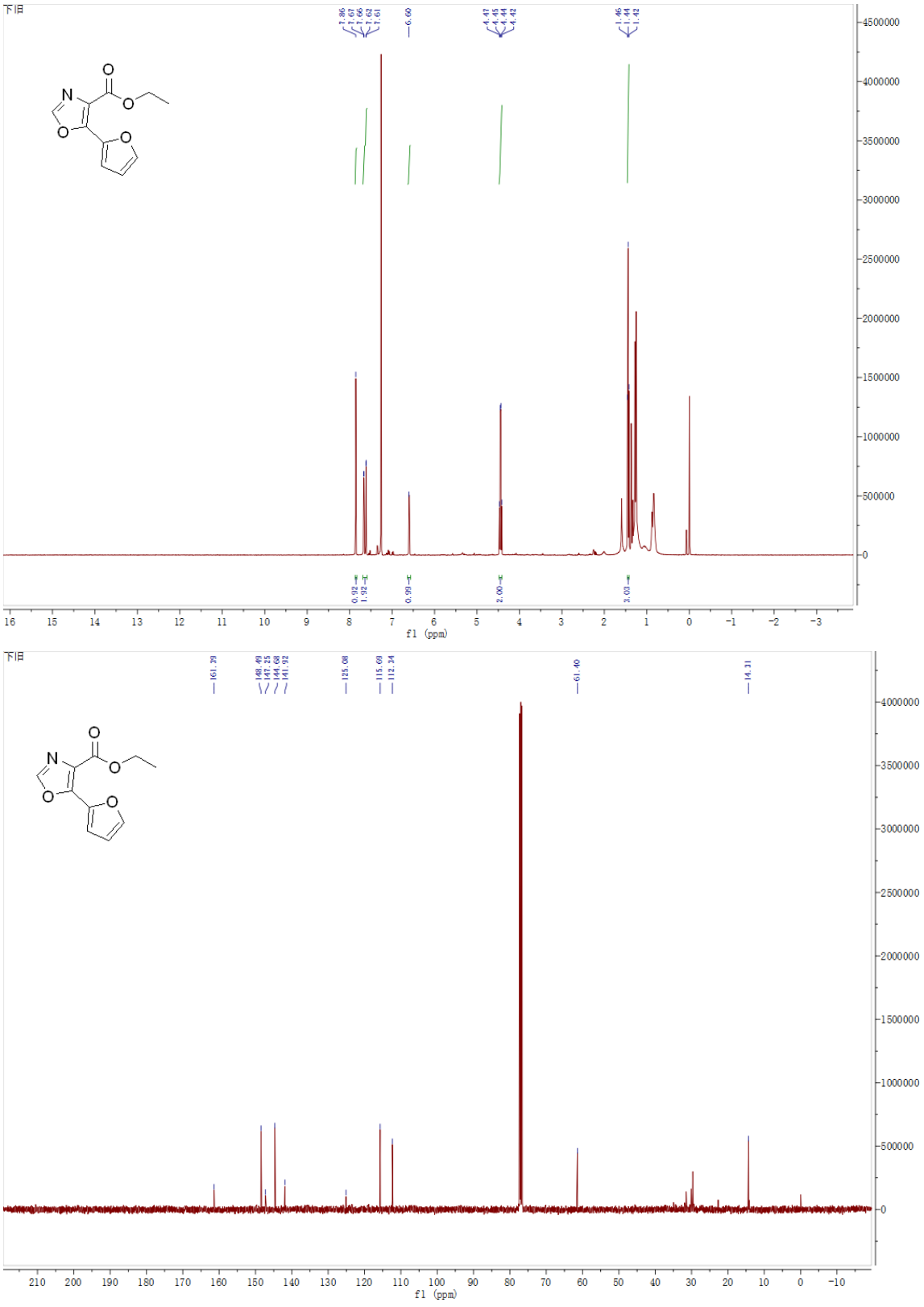
Supplementary Figure 20. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3t in $CDCl_3$

Ethyl 5-(thiophen-2-yl)oxazole-4-carboxylate (3u)



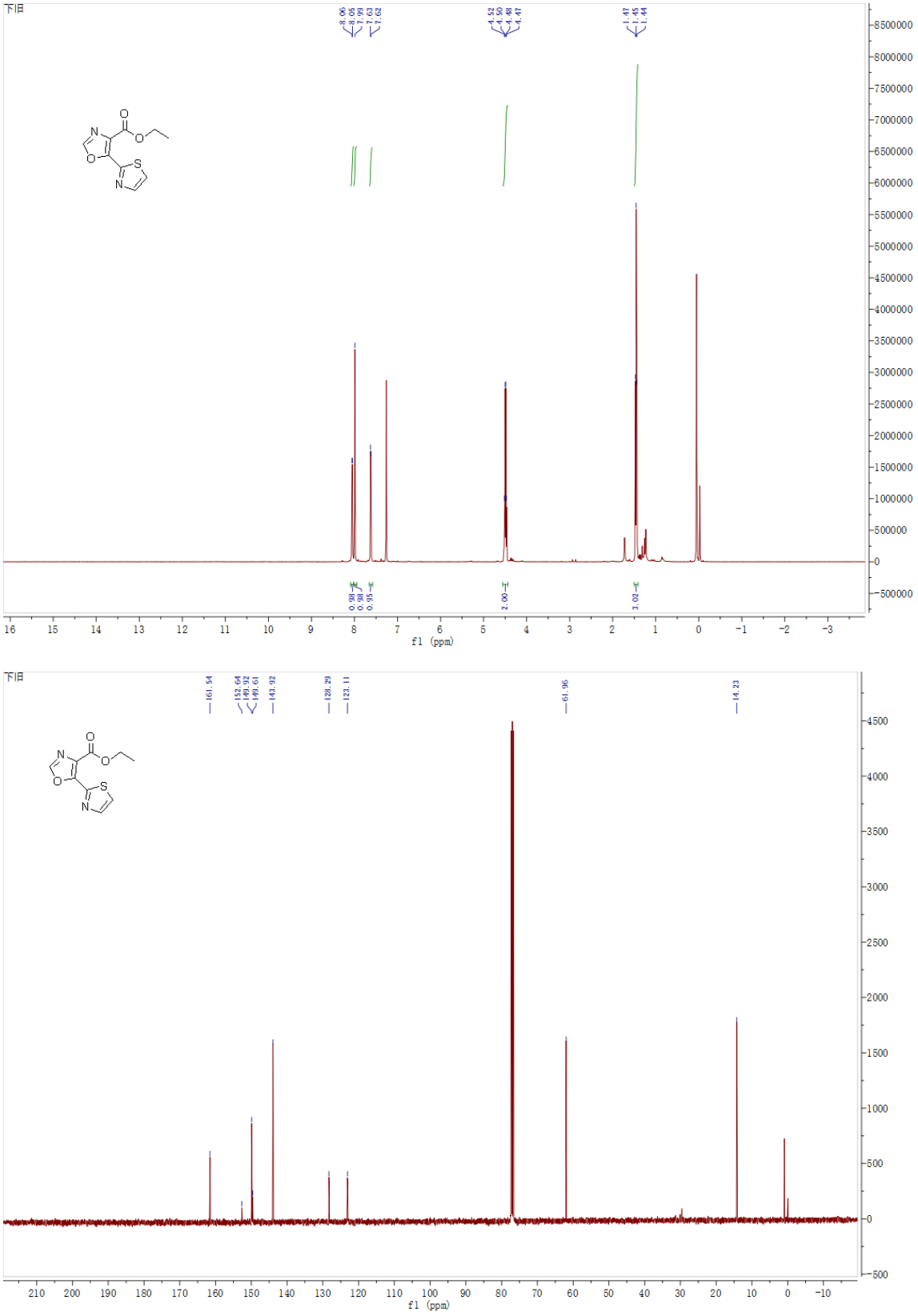
Supplementary Figure 21. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3u in $CDCl_3$

Ethyl 5-(furan-2-yl)oxazole-4-carboxylate (3v)



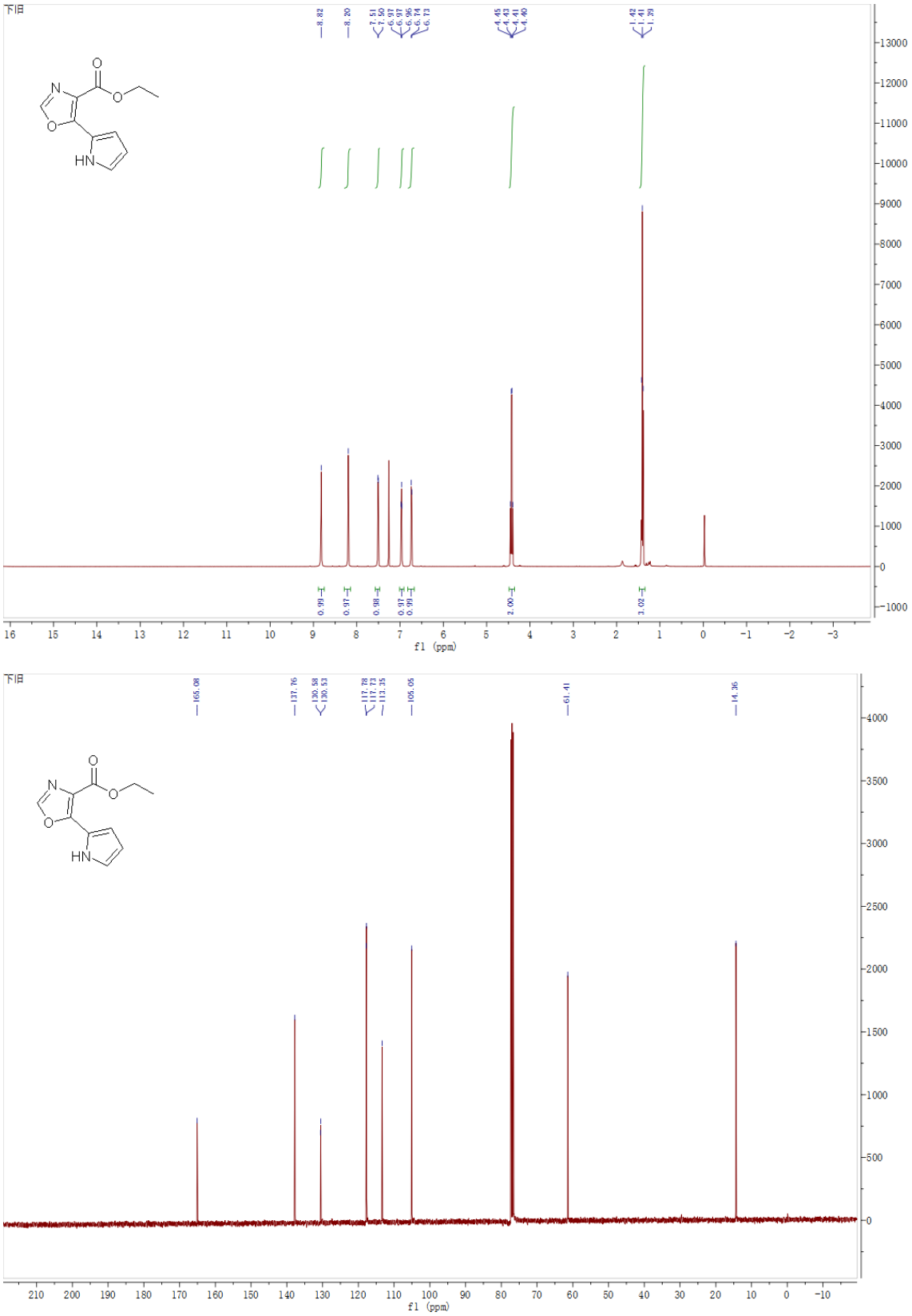
Supplementary Figure 22. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3v in $CDCl_3$

Ethyl 5-(thiazol-2-yl)oxazole-4-carboxylate (3w)



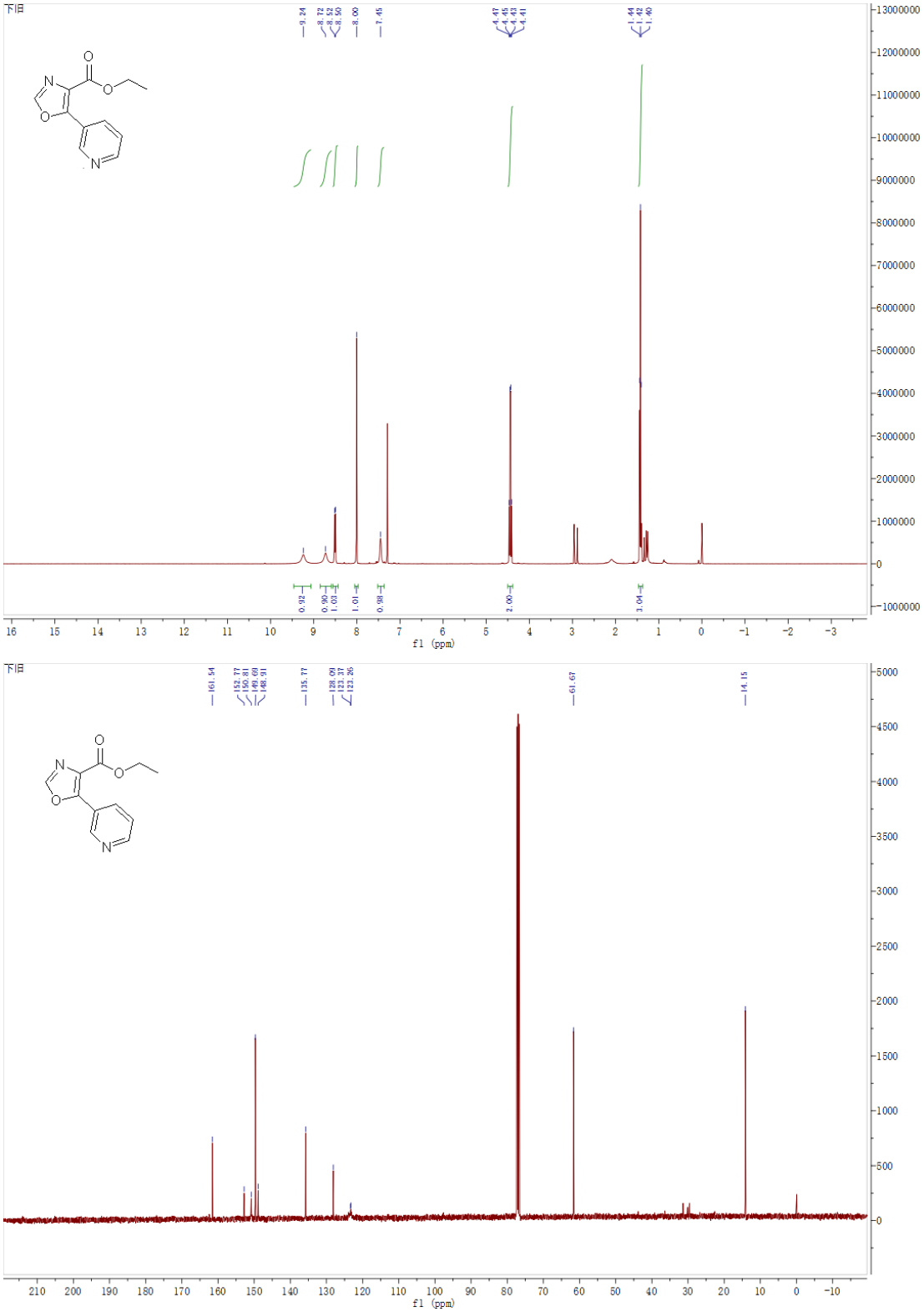
Supplementary Figure 23. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3w in $CDCl_3$

Ethyl 5-(1H-pyrrol-2-yl)oxazole-4-carboxylate (3x)



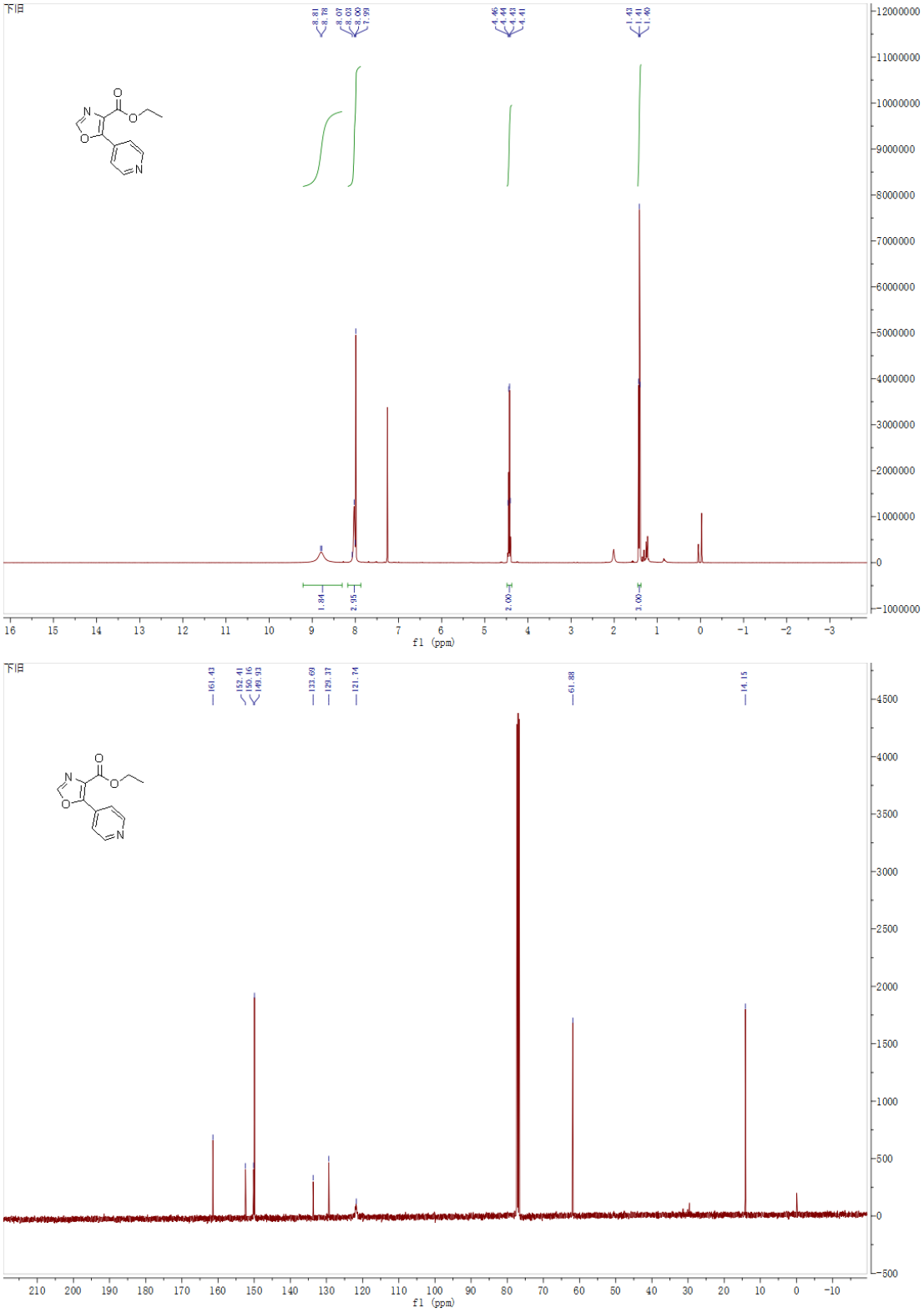
Supplementary Figure 24. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3x in $CDCl_3$

Ethyl 5-(pyridin-3-yl)oxazole-4-carboxylate (3y)



Supplementary Figure 25. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3y in $CDCl_3$

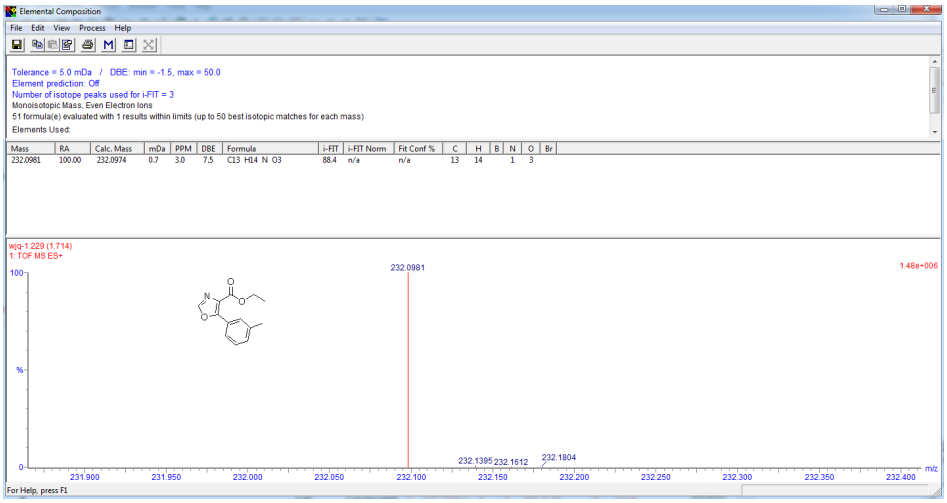
Ethyl 5-(pyridin-4-yl)oxazole-4-carboxylate (3z)



Supplementary Figure 26. ^{1}H (400 MHz) and ^{13}C {1H} (101 MHz) NMR Spectrum of 3z in $CDCl_3$

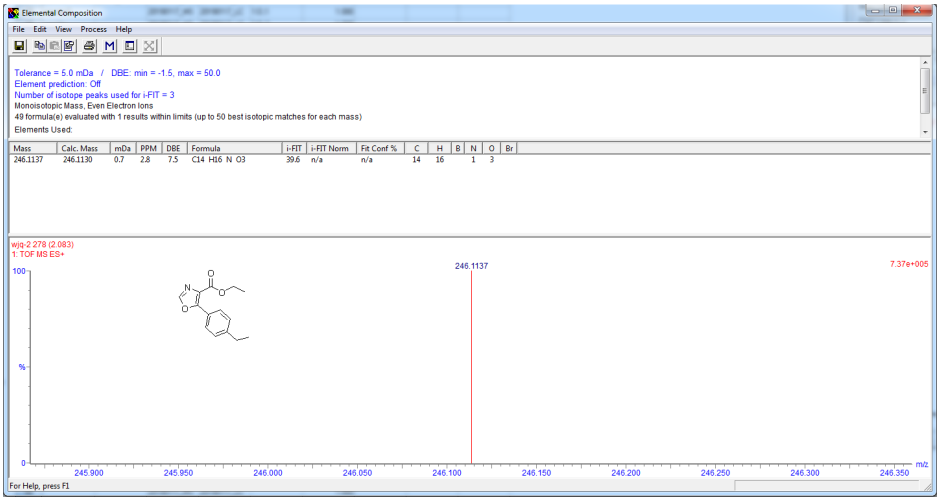
5. HRMS spectra

Ethyl 5-(m-tolyl)oxazole-4-carboxylate (3c)



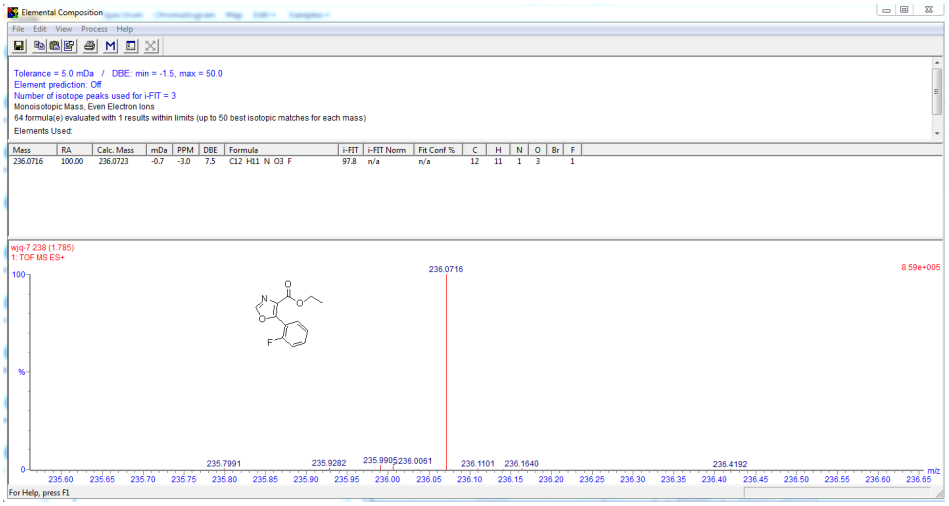
Supplementary Figure 27. HRMS Spectrum of 3c in MeOH

Ethyl 5-(4-ethylphenyl)oxazole-4-carboxylate (3e)



Supplementary Figure 28. HRMS Spectrum of 3e in MeOH

Ethyl 5-(2-fluorophenyl)oxazole-4-carboxylate (3k)

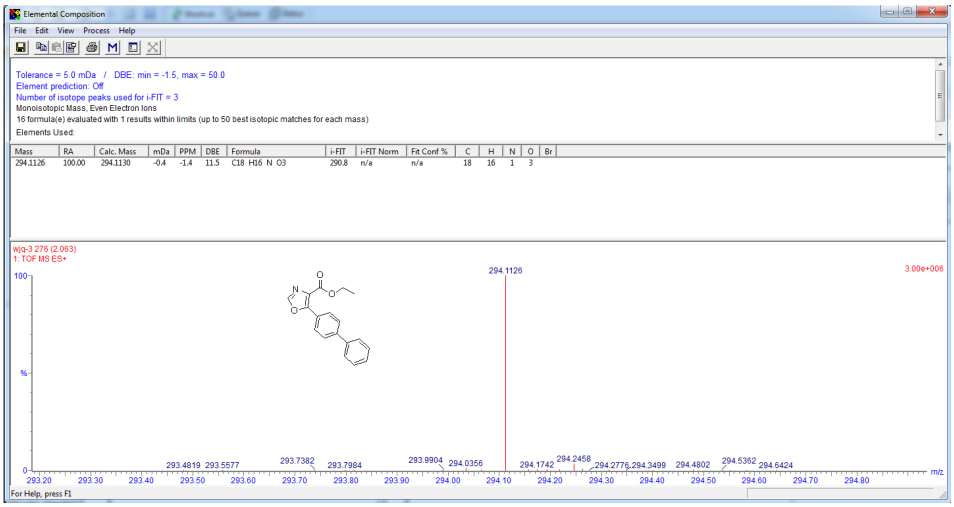


Supplementary Figure 29. HRMS Spectrum of 3k in MeOH

2-(4-(Ethoxycarbonyl)oxazol-5-yl)benzoic acid (3q)

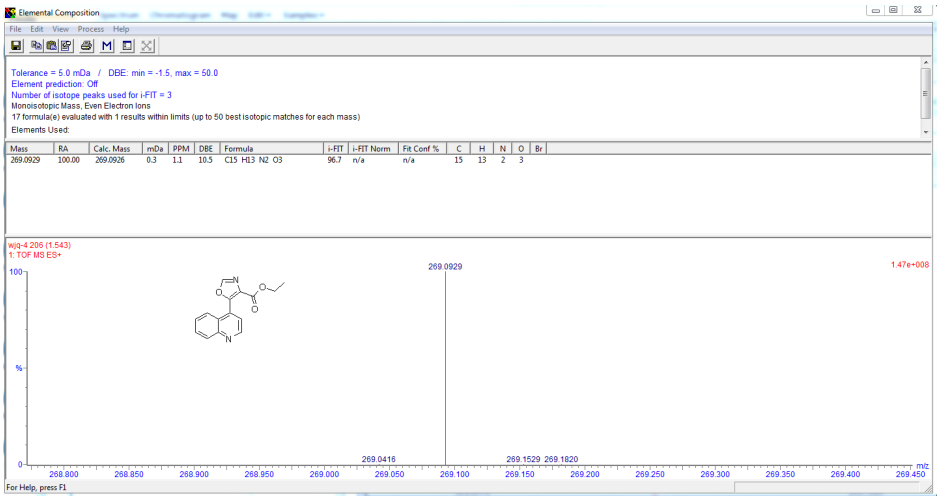
Supplementary Figure 30. HRMS Spectrum of 3q in MeOH

Ethyl 5-([1,1'-biphenyl]-4-yl)oxazole-4-carboxylate (3s)



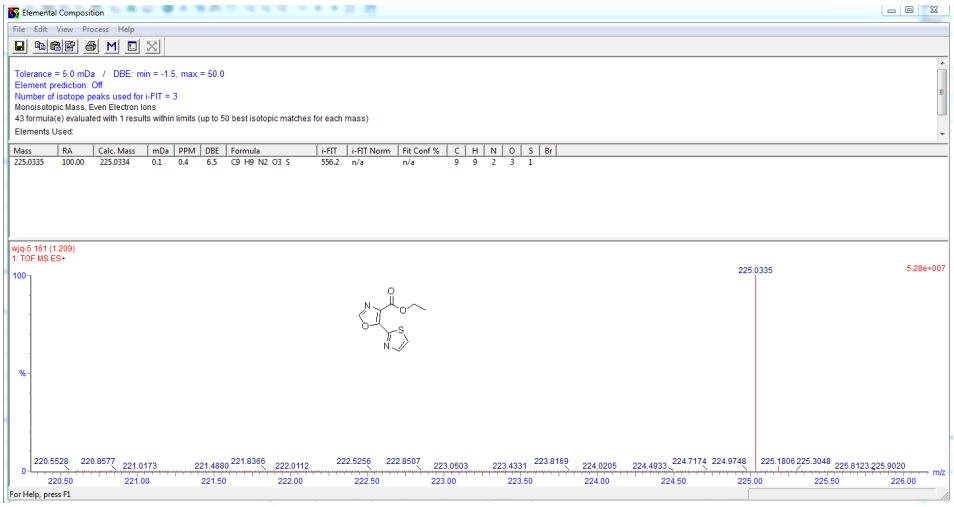
Supplementary Figure 31. HRMS Spectrum of 3s in MeOH

Ethyl 5-(quinolin-4-yl)oxazole-4-carboxylate (3t)



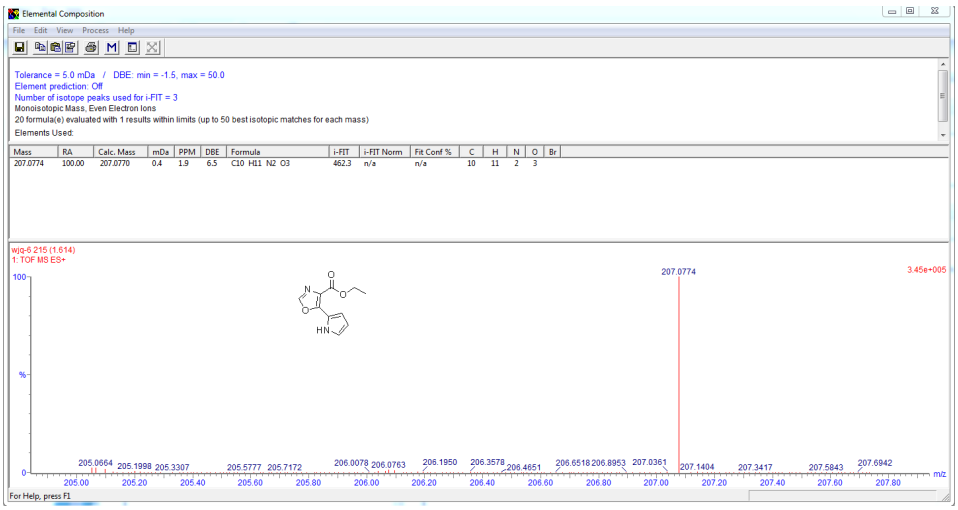
Supplementary Figure 32. HRMS Spectrum of 3t in MeOH

Ethyl 5-(thiazol-2-yl)oxazole-4-carboxylate (3w)



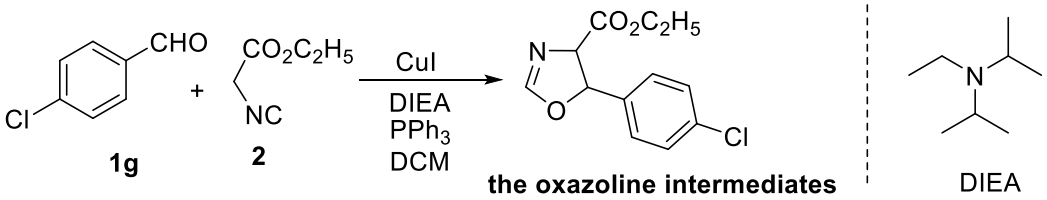
Supplementary Figure 33. HRMS Spectrum of 3w in MeOH

Ethyl 5-(1H-pyrrol-2-yl)oxazole-4-carboxylate (3x)



Supplementary Figure 34. HRMS Spectrum of 3x in MeOH

6. Synthesis of oxazoline intermediate[6]



Into a 10 mL Schlenk tube with rubber stopper was added triphenylphosphine (26.2 mg, 0.1 mmol, 0.1 equiv), CuI (9.5 mg, 0.05 mmol, 0.05 equiv) and *p*-chlorobenzaldehyde (140.6 mg, 1 mmol, 1 equiv). A vacuum pump fitted with a hose and a needle was pierced through the rubber stopper and the Schlenk tube subjected to vacuum and refilled with a balloon of N_2 fitted onto a hose and secured to a needle. This process was repeated three more times to remove as much air as possible. Then, DCM (2.0 mL), ethyl isocyanoacetate (113.1 mg, 1 mmol, 1 equiv) and DIEA (12.9 mg, 0.1 mmol, 0.1 equiv) were injected into the tube by a hypodermic syringe. The mixture was stirred at room temperature for 6 h. Then the Schlenk tube opened to air and the solvent was removed by rotary evaporator, the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (10 mL×3). The combined organic layer was dried with anhydrous Na_2SO_4 and then filtered. And the solvent was removed by rotary evaporator. The crude product was purified by silica gel column chromatography (eluant: EA:PE=1:4) to afford the desired product with 55% yield (139.5 mg).

7. References.

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