Supporting Information

Electrochemical enabled cascaded cyclization of enaminones with thiocyanate and alcohols access to 2-alkoxythiazoles

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Contents

1. General information

All glassware was oven dried at 110 ˚C for hours and cooled down under vacuum. The instrument for electrolysis was dual display potentiostat (DJS-292B) (made in China). Cyclic voltammograms were obtained on a CHI 605E potentiostat. All undivided cells were purchased from Jiehengda® limited liability company (https://www.whjiehengda.com). All the electrode clamps were purchased from Gaoss Uinon® (https://gaossunion.cn.made-in-china.com). The anodic electrode was graphite rod (ϕ 6 mm) and cathodic electrode was platinum plate (15 mm×15 mm×0.2 mm). Enamines were synthesized according to literature procedures.[1,2] Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 silica gel or neutral alumina in petroleum (bp. 60-90 ºC). ^{1}H and ^{13}C NMR data were recorded with Bruker Advance III (400 MHz) spectrometers with tetramethylsilane as an internal standard. All chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. All chemical shifts are reported relative to tetramethylsilane and d-solvent peaks (0 ppm for ^{1}H, 77.00 ppm for ^{13}C) or DMSO-d6 (2.50 ppm for ^{1}H, 39.6 ppm for ^{13}C), respectively. High-resolution mass spectra (HRMS) were measured with ESI in positive mode.

2. Experimental procedure

General procedure for the synthesis of 2-alkoxythiazoles via three-component cascade reaction in one pot: In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, enaminones (0.3 mmol), potassium thiocyanate (87.5 mg, 0.9 mmol), $LiClO_4$ (127.7 mg, 1.2 mmol) and DCE/CH_3OH (10 mL, v/v = 9.5/0.5) were combined and added. The flask was equipped with graphite rod (ϕ 6 mm) as anode and Pt plate electrodes (15 mm×15 mm×0.2 mm) as cathode. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under N_2 atmosphere at room temperature for 6 h. When the reaction was finished, the solvent was removed with a rotary evaporator. The pure product was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

General procedure for cyclic voltammetry (CV): Cyclic voltammetry was performed in a three electrode cell connected to a schlenk line under nitrogen at room temperature. The working electrode was a glassy carbon electrode, the counter electrode a platinum wire. The reference was an Ag/AgCl electrode submerged in saturated aqueous KCl solution, **1a** (2.5 mM), and KSCN (7.5 mM), DCE/CH_3OH (10 mL, v/v = 9.5/0.5) containing 0.01 M $LiClO_4$ were poured into the electrochemical cell in all experiments. The scan rate is 0.05 V/s, ranging from 0 V to 2.5 V. The peak potentials vs. Ag/AgCl for used. An obvious oxidation peak of **1a** was observed at 1.76 V. The oxidation peak of KSCN could also be observed at 1.15 V.

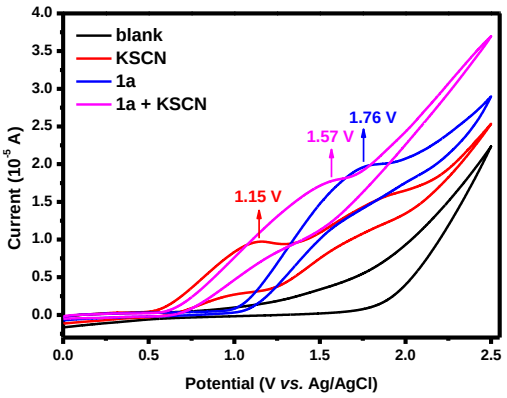
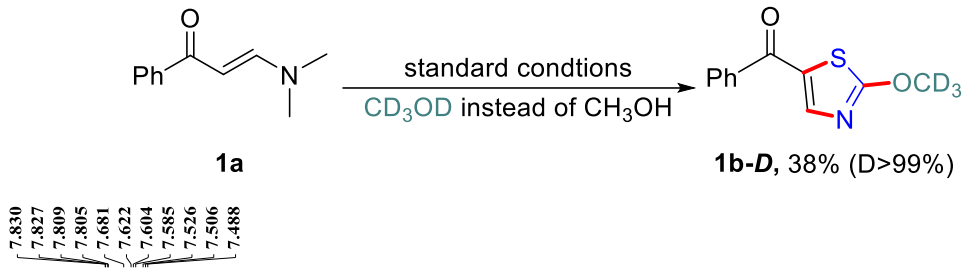


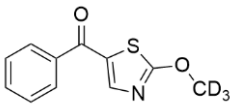
Figure S1. Cyclic voltammetry experiments

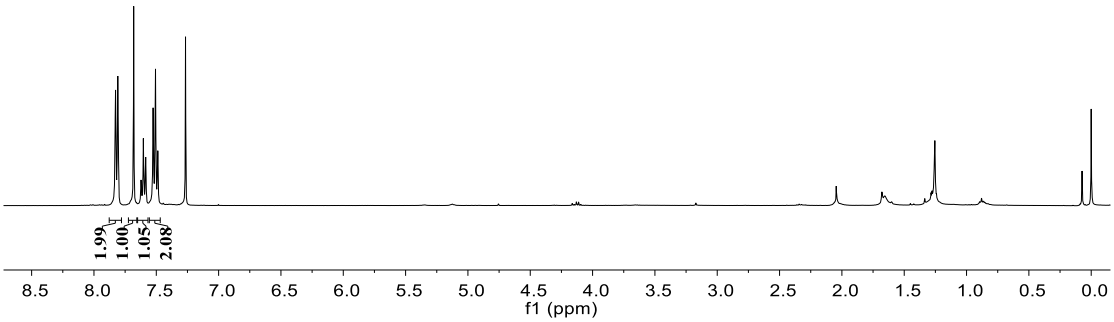
Preliminary mechanistic studies.

(1) Deuteration experiments



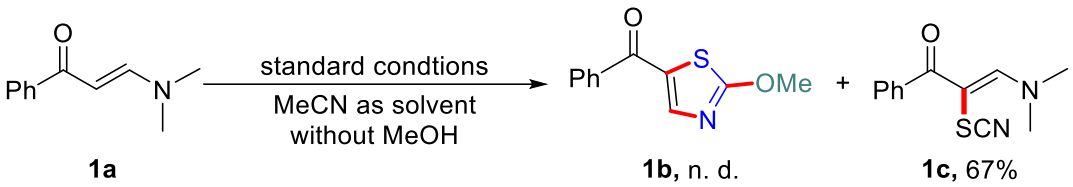
1a **1b-*D*,** 38% (D>99%)





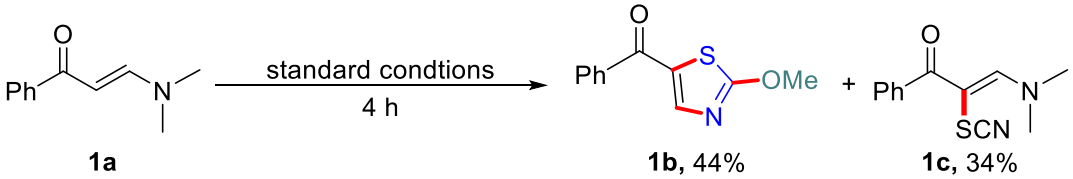
In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, enaminones (52.6 mg, 0.3 mmol), potassium thiocyanate (87.5 mg, 0.9 mmol), $LiClO_4$ (127.7 mg, 1.2 mmol) and DCE/CD_3OD (10 mL, v/v = 9.5/0.5) were combined and added. The flask was equipped with graphite rod (ϕ= 6 mm) as anode and Pt plate electrodes (15 mm×15 mm×0.2 mm) as cathode. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under N_2 atmosphere at room temperature for 6 h. When the reaction was finished, the solvent was removed with a rotary evaporator. The product **1b-*D*** was isolated in 38% yield by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

(2) Intermediate verification experiments



1a **1b**, n. d. **1c**, 67%

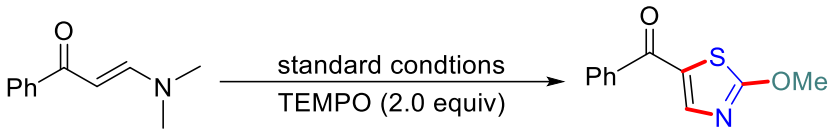
In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, enaminones (52.6 mg, 0.3 mmol), potassium thiocyanate (87.5 mg, 0.9 mmol), $LiClO_4$ (127.7 mg, 1.2 mmol) and MeCN (10 mL) were combined and added. The flask was equipped with graphite rod (ϕ 6 mm) as anode and Pt plate electrodes (15 mm×15 mm×0.2 mm) as cathode. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under N_2 atmosphere at room temperature for 6 h. When the reaction was finished, the solvent was removed with a rotary evaporator. The product **1c** was isolated in 67% yield by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.



1a **1b**, 44% **1c**, 34%

In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, enaminones (52.6 mg, 0.3 mmol), potassium thiocyanate (87.5 mg, 0.9 mmol), $LiClO_4$ (127.7 mg, 1.2 mmol) and DCE/ CH_3OH (10 mL, v/v = 9.5/0.5) were combined and added. The flask was equipped with graphite rod (ϕ 6 mm) as anode and Pt plate electrodes (15 mm×15 mm×0.2 mm) as cathode. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under N_2 atmosphere at room temperature for 4 h. When the reaction was finished, the solvent was removed with a rotary evaporator. The product **1b** was isolated in 44% yield and the product **1c** was isolated in 34% yield by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

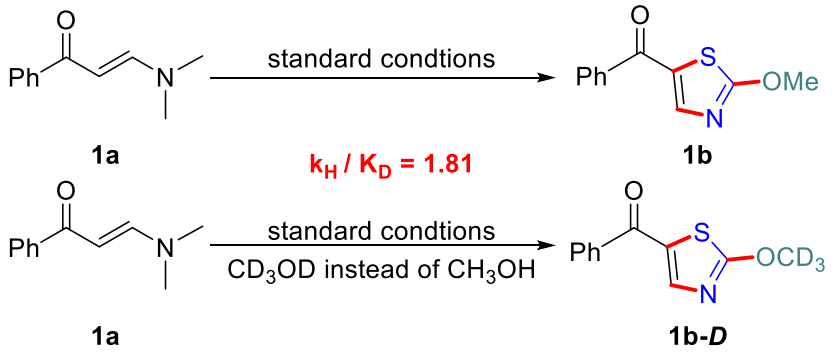
(3) The reaction of **1a** and **KSCN** with TEMPO under the standard conditions.



1a **1b**, n. d.

In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, enaminones (52.6 mg, 0.3 mmol), potassium thiocyanate (87.5 mg, 0.9 mmol), $LiClO_4$ (127.7 mg, 1.2 mmol), TEMPO (93.8 mg, 0.6 mmol), and DCE/CH_3OH (10 mL, v/v = 9.5/0.5) were combined and added. The flask was equipped with graphite rod (ϕ 6 mm) as anode and Pt plate electrodes (15 mm×15 mm×0.2 mm) as cathode. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under N_2 atmosphere at room temperature for 6 h. When the reaction was finished, the **1b** was not detected.

(4) Parallel KIE Experiment



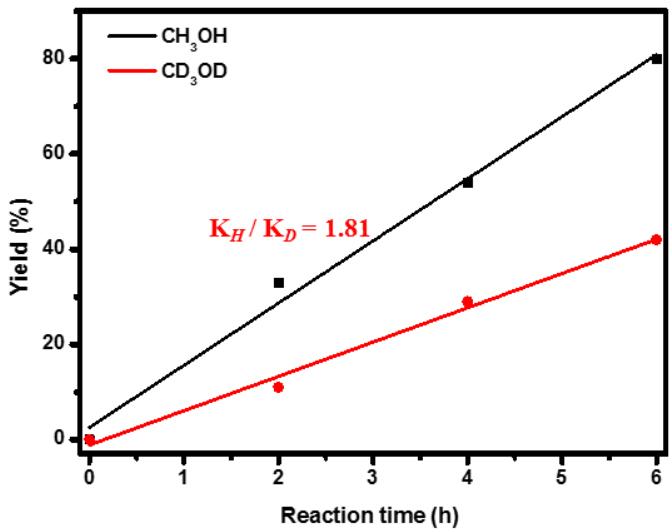
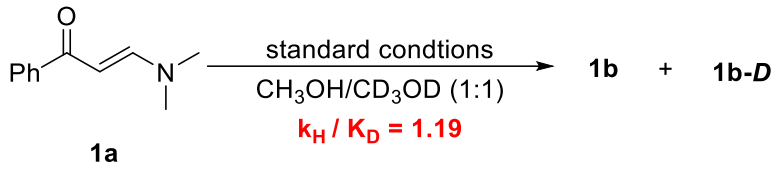
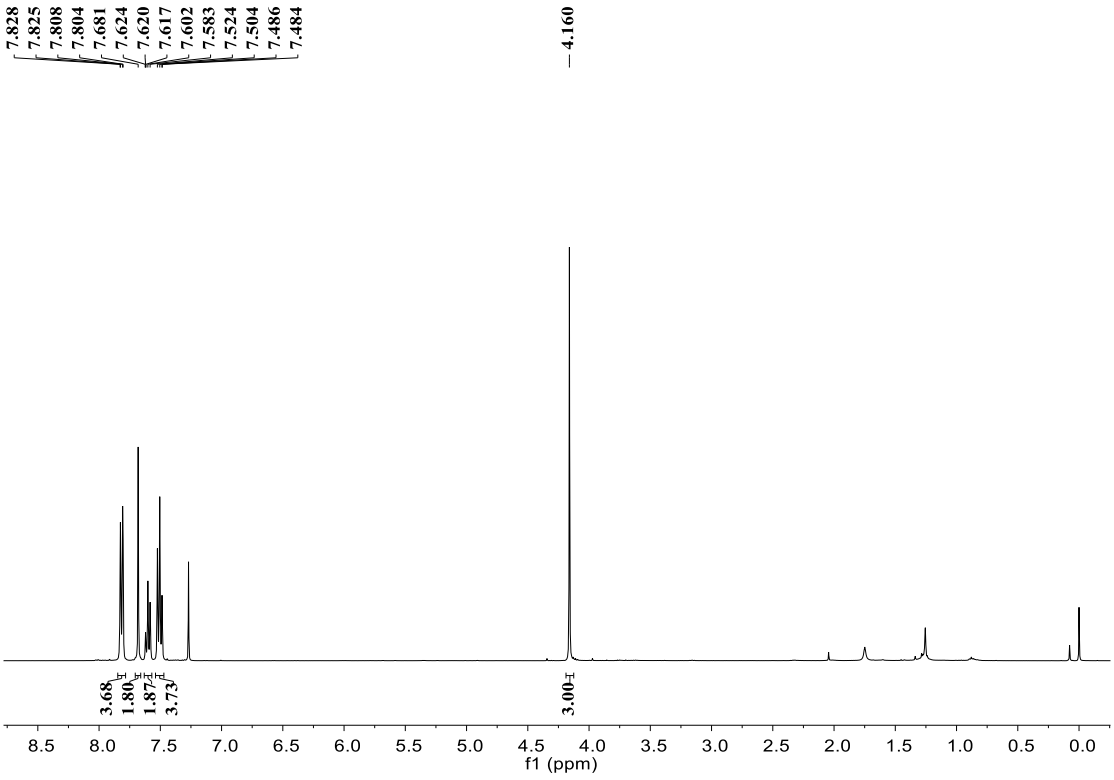


Figure S2. Kinetic isotopic effect experiments.

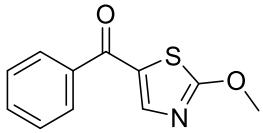
(5) Intermolecular Competition KIE Experiment



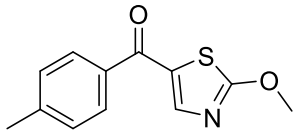
In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, enaminones (52.6 mg, 0.3 mmol), potassium thiocyanate (87.5 mg, 0.9 mmol), $LiClO_4$ (127.7 mg, 1.2 mmol) and DCE/CH_3OH/CD_3OD (10 mL, v/v/v = 9.5/0.25/0.25) were combined and added. The flask was equipped with graphite rod (ϕ 6 mm) as anode and Pt plate electrodes (15 mm×15 mm×0.2 mm) as cathode. The reaction mixture was stirred and electrolyzed at a constant current of 5 mA under N_2 atmosphere at room temperature for 6 h. When the reaction was finished, the solvent was removed with a rotary evaporator. The product **1b** and **1b-*D*** was isolated by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent. The value of K_H/K_D was confirmed through ^1H NMR.



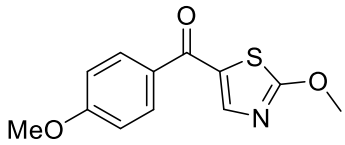
3. Detail descriptions for products



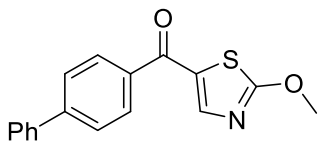
(2-Methoxythiazol-5-yl)(phenyl)methanone (1b): Yield 81% (53.1 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.68 (s, 1H), 7.64 – 7.56 (m, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 4.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.59, 180.10, 146.13, 137.73, 133.01, 132.64, 128.97, 128.79, 59.17. HRMS (ESI) calculated for $C_{11}H_{10}NO_2S$ $[M+H]^+$: 220.0427; found: 220.0430.



(2-Methoxythiazol-5-yl)(p-tolyl)methanone (2b): Yield 84% (58.6 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.68 (s, 1H), 7.30 (d, *J* = 7.9 Hz, 2H), 4.15 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.96, 179.64, 145.42, 143.23, 134.83, 132.91, 129.24, 128.92, 58.87, 21.54. HRMS (ESI) calculated for $C_{12}H_{12}NO_2S$ $[M+H]^+$: 234.0583; found: 234.0584.

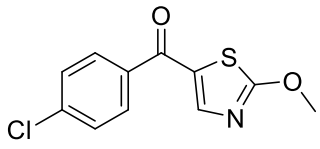


(4-Methoxyphenyl)(2-methoxythiazol-5-yl)methanone (3b): Yield 77% (57.5 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.7 Hz, 2H), 7.59 (s, 1H), 6.90 (d, *J* = 8.7 Hz, 2H), 4.07 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.84, 179.38, 163.18, 144.83, 132.88, 131.07, 130.03, 113.83, 58.84, 55.43. HRMS (ESI) calculated for $C_{12}H_{12}NO_3S$ $[M+H]^+$: 250.0532; found: 250.0535.

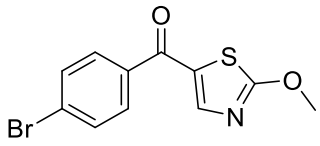


[1,1'-Biphenyl]-4-yl(2-methoxythiazol-5-yl)methanone (4b): Yield 64% (56.9 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.64 (s, 1H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.54 (dd, *J* = 7.3, 1.8 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.30 (t, *J* =

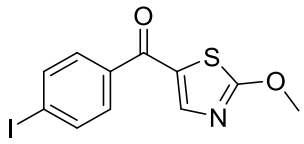
7.2 Hz, 1H), 4.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.74, 179.78, 145.66, 145.27, 139.71, 136.14, 132.85, 129.38, 128.90, 128.16, 127.20, 127.18, 58.93. HRMS (ESI) calculated for $C_{17}H_{14}NO_2S$ $[M+H]^+$: 296.0740; found: 296.0742.



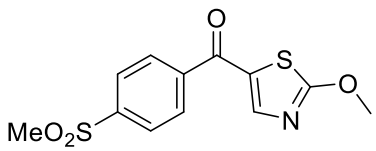
(4-chlorophenyl)(2-methoxythiazol-5-yl)methanone (5b): Yield 66% (50.6 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.5 Hz, 2H), 7.66 (s, 1H), 7.49 (d, J = 8.5 Hz, 2H), 4.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.00, 180.07, 145.90, 138.91, 135.80, 132.49, 130.16, 128.96, 59.06. HRMS (ESI) calculated for $C_{11}H_8NClNaO_2S$ $[M+Na]^+$: 275.9856; found: 275.9857.



(4-Bromophenyl)(2-methoxythiazol-5-yl)methanone (6b): Yield 65% (58.3 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.5 Hz, 2H), 7.61 – 7.53 (m, 3H), 4.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.12, 180.09, 145.93, 136.24, 132.45, 131.93, 130.27, 127.44, 59.07. HRMS (ESI) calculated for $C_{11}H_8NBrNaO_2S$ $[M+Na]^+$: 319.9351; found: 319.9353.

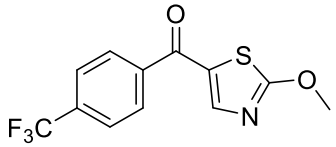


(4-Iodophenyl)(2-methoxythiazol-5-yl)methanone (7b): Yield 75% (77.2 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, J = 8.4, 2.2 Hz, 2H), 7.57 (d, J = 2.2 Hz, 1H), 7.45 (dd, J = 8.5, 2.1 Hz, 2H), 4.08 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.27, 180.01, 145.89, 137.84, 136.73, 132.39, 130.14, 99.91, 59.04. HRMS (ESI) calculated for $C_{11}H_8NINaO_2S$ $[M+Na]^+$: 367.9213; found: 367.9213.

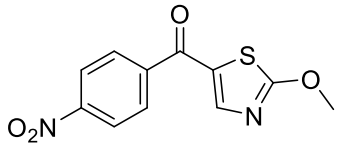


(2-Methoxythiazol-5-yl)(4-(methylsulfonyl)phenyl)methanone (8b): Yield 52%

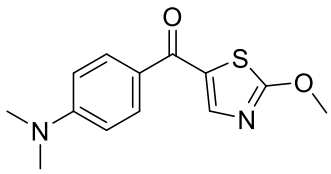
(48.5 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 2H), 7.90 (d, J = 8.4 Hz, 2H), 7.58 (s, 1H), 4.12 (s, 3H), 3.05 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.78, 180.67, 146.91, 143.66, 142.09, 132.17, 129.50, 127.80, 59.28, 44.35. HRMS (ESI) calculated for $C_{12}H_{11}NNaO_4S_2$ $[M+Na]^+$: 320.0022; found: 320.0021.



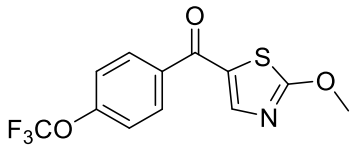
(2-Methoxythiazol-5-yl)(4-(trifluoromethyl)phenyl)methanone (9b): Yield 50% (40.7 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.1 Hz, 2H), 7.78 (d, J = 8.1 Hz, 2H), 7.66 (s, 1H), 4.18 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 186.16, 180.44, 146.57, 140.59, 133.91 (q, J = 32.7 Hz), 132.37, 129.02, 125.69 (q, J = 3.7 Hz), 123.56 (q, J = 272.7 Hz), 59.17. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.05. HRMS (ESI) calculated for $C_{12}H_9F_3NNaO_2S$ $[M+H]^+$: 288.0301; found: 288.0305.



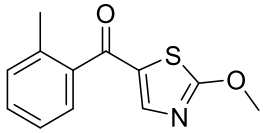
(2-Methoxythiazol-5-yl)(4-nitrophenyl)methanone (10b): Yield 57% (45.3 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.7 Hz, 2H), 7.96 (d, J = 8.7 Hz, 2H), 7.66 (s, 1H), 4.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.42, 180.75, 149.93, 146.93, 142.65, 132.14, 129.64, 123.89, 59.32. HRMS (ESI) calculated for $C_{11}H_8NNaO_4S$ $[M+Na]^+$: 287.0097; found: 287.0099.



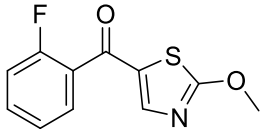
(4-(Dimethylamino)phenyl)(2-methoxythiazol-5-yl)methanone (11b): Yield 57% (57.5 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 9.0 Hz, 2H), 7.68 (s, 1H), 6.71 (d, J = 9.0 Hz, 2H), 4.14 (s, 3H), 3.08 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.13, 178.82, 153.39, 143.50, 133.41, 131.38, 124.75, 110.86, 58.72, 40.05. HRMS (ESI) calculated for $C_{13}H_{14}N_2NaO_2S$ $[M+Na]^+$: 285.0668; found: 285.0671.



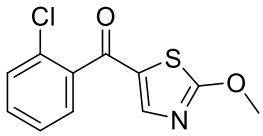
(2-Methoxythiazol-5-yl)(4-(trifluoromethoxy)phenyl)methanone (12b): Yield 63% (57.7 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.7 Hz, 2H), 7.68 (s, 1H), 7.35 (d, J = 7.3 Hz, 2H), 4.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.69, 180.14, 152.16, 146.04, 135.81, 132.42, 130.68, 124.15, 120.29 (q, J = 258.9 Hz), 59.07. ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.66. HRMS (ESI) calculated for $C_{12}H_8N_2F_3NaO_3S$ $[M+Na]^+$: 326.0069; found: 326.0071.



(2-Methoxythiazol-5-yl)(o-tolyl)methanone (13b): Yield 41% (28.7 mg), white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53 (s, 1H), 7.54 – 7.41 (m, 2H), 7.40 – 7.25 (m, 2H), 4.12 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 188.99, 179.58, 147.27, 137.15, 135.87, 133.23, 131.18, 130.79, 128.07, 125.68, 59.84, 19.22. HRMS (ESI) calculated for $C_{12}H_{12}NO_2S$ $[M+H]^+$: 234.0583; found: 234.0585.

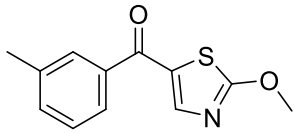


(2-Fluorophenyl)(2-methoxythiazol-5-yl)methanone (14b): Yield 60% (42.6 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.48 (m, 3H), 7.27 (td, J = 7.5, 1.0 Hz, 1H), 7.23 – 7.16 (m, 1H), 4.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.00, 180.49, 159.50 (d, J = 252.6 Hz), 146.97 (d, J = 3.7 Hz), 133.11 (d, J = 8.2 Hz), 133.03, 130.09 (d, J = 2.7 Hz), 126.27 (d, J = 15.0 Hz), 124.31 (d, J = 3.7 Hz), 116.52 (d, J = 21.7 Hz), 59.09. ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.34 – -114.76 (m). HRMS (ESI) calculated for $C_{11}H_9FNO_2S$ $[M+H]^+$: 238.0333; found: 238.0337.

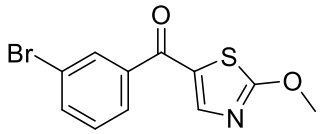


(2-Chlorophenyl)(2-methoxythiazol-5-yl)methanone (15b): Yield 41% (31.3 mg),

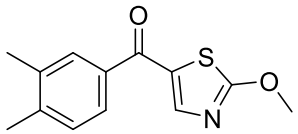
white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.32 (m, 5H), 4.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.34, 180.79, 147.66, 137.41, 132.72, 131.46, 131.24, 130.40, 128.87, 126.63, 59.18. HRMS (ESI) calculated for $C_{11}H_8NClNaO_2S$ $[M+Na]^+$: 275.9856; found: 275.9859.



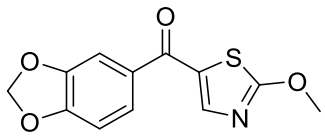
(2-Methoxythiazol-5-yl)(m-tolyl)methanone (16b): Yield 77% (53.4 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.57 – 7.48 (m, 2H), 7.36 – 7.25 (m, 2H), 4.08 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.57, 179.82, 145.86, 138.52, 137.55, 133.21, 132.89, 129.29, 128.41, 125.98, 58.94, 21.32. HRMS (ESI) calculated for $C_{12}H_{11}NNaO_2S$ $[M+Na]^+$: 256.0403; found: 256.0405.



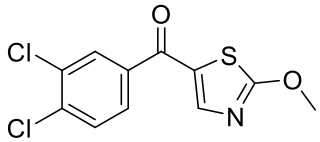
(3-Bromophenyl)(2-methoxythiazol-5-yl)methanone (17b): Yield 68% (60.6 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (t, J = 1.8 Hz, 1H), 7.69 – 7.61 (m, 2H), 7.60 (s, 1H), 7.30 (t, J = 7.9 Hz, 1H), 4.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.62, 180.19, 146.30, 139.25, 135.28, 132.25, 131.65, 130.14, 127.22, 122.79, 59.08. HRMS (ESI) calculated for $C_{11}H_8NBrNaO_2S$ $[M+Na]^+$: 319.9351; found: 319.9352.



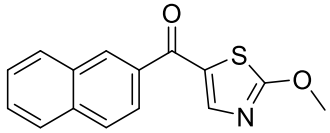
(3,4-Dimethylphenyl)(2-methoxythiazol-5-yl)methanone (18b): Yield 56% (41.6 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.51 (s, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.16 (d, J = 7.7 Hz, 1H), 4.06 (s, 3H), 2.25 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.09, 179.52, 145.35, 141.92, 137.03, 135.16, 132.93, 129.89, 129.65, 126.48, 58.80, 19.86, 19.65. HRMS (ESI) calculated for $C_{13}H_{13}NNaO_2S$ $[M+Na]^+$: 270.0559; found: 270.0561.



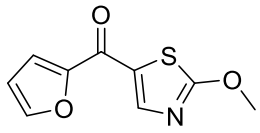
Benzo[d][1,3]dioxol-5-yl(2-methoxythiazol-5-yl)methanone (19b): Yield 56% (44.3 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.37 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.24 (d, *J* = 1.8 Hz, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.00 (s, 2H), 4.08 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.45, 179.53, 151.51, 148.11, 145.00, 132.68, 131.77, 124.90, 108.93, 107.99, 101.87, 58.90. HRMS (ESI) calculated for $C_{12}H_9NNaO_4S$ $[M+Na]^+$: 286.0144; found: 368. 286.0147.



(3,4-Dichlorophenyl)(2-methoxythiazol-5-yl)methanone (20b): Yield 55% (47.9 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 1.9 Hz, 1H), 7.68 (s, 1H), 7.65 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 1H), 4.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.64, 180.32, 146.23, 137.04, 137.01, 133.28, 132.03, 130.74, 130.67, 127.77, 59.15. HRMS (ESI) calculated for $C_{11}H_7NNaO_2S$ $[M+Na]^+$: 309.9467; found: 309.9468.

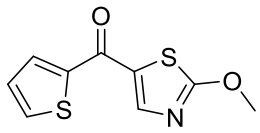


(2-Methoxythiazol-5-yl)(naphthalen-2-yl)methanone (21b): Yield 32% (25.9 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 1.8 Hz, 1H), 7.99 – 7.86 (m, 4H), 7.77 (s, 1H), 7.65 – 7.55 (m, 2H), 4.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.31, 179.93, 145.94, 135.27, 134.82, 132.99, 132.38, 130.14, 129.26, 128.70, 128.32, 127.86, 127.01, 124.90, 59.01. HRMS (ESI) calculated for $C_{15}H_{11}NNaO_2S$ $[M+Na]^+$: 292.0403; found: 292.0403.

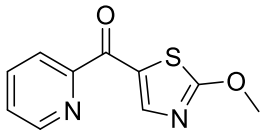


Furan-2-yl(2-methoxythiazol-5-yl)methanone (22b): Yield 71% (44.8 mg), white

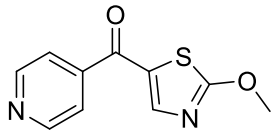
solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.59 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.27 (d, *J* = 3.5 Hz, 1H), 6.53 (dd, *J* = 3.6, 1.7 Hz, 1H), 4.08 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.74, 172.53, 152.15, 146.21, 145.18, 131.37, 118.15, 112.44, 58.88. HRMS (ESI) calculated for $C_9H_7NNaO_3S$ $[M+Na]^+$: 232.0039; found: 232.0042.



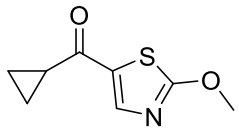
(2-Methoxythiazol-5-yl)(thiophen-2-yl)methanone (23b): Yield 83% (56.1 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.75 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.62 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.11 (dd, *J* = 4.9, 3.8 Hz, 1H), 4.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.46, 177.72, 143.99, 142.11, 133.32, 132.39, 132.11, 128.00, 58.95. HRMS (ESI) calculated for $C_9H_7NNaO_2S_2$ $[M+Na]^+$: 247.9810; found: 247.9811.



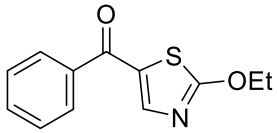
(2-Methoxythiazol-5-yl)(pyridin-2-yl)methanone(24b): Yield 55% (37.0 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 5.4 Hz, 1H), 8.52 (s, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.90 (td, *J* = 7.7, 1.7 Hz, 1H), 7.60 – 7.44 (m, 1H), 4.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.83, 182.32, 152.94, 148.22, 148.17, 137.18, 127.17, 127.00, 123.25, 58.68. HRMS (ESI) calculated for $C_{10}H_8N_2NaO_2S$ $[M+Na]^+$: 243.0199; found: 243.0202.



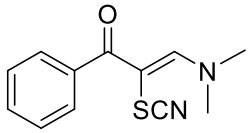
(2-Methoxythiazol-5-yl)(pyridin-4-yl)methanone (25b): Yield 72% (47.5 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.9 Hz, 2H), 7.61 (s, 1H), 7.58 – 7.45 (m, 2H), 4.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.85, 180.79, 150.58, 147.07, 144.16, 131.94, 130.88, 122.01, 59.30. HRMS (ESI) calculated for $C_{10}H_8N_2NaO_2S$ $[M+Na]^+$: 243.0199; found: 243.0200.



Cyclopropyl(2-methoxythiazol-5-yl)methanone (26b): Yield 42% (23.1 mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 4.14 (s, 3H), 2.47 – 2.33 (m, 1H), 1.25 – 1.20 (m, 2H), 1.07 – 0.99 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.27, 179.65, 142.62, 134.00, 58.83, 29.66, 17.64, 11.10. HRMS (ESI) calculated for $C_8H_9NNaO_2S$ $[M+Na]^+$: 206.0246; found: 206.0248.



(2-Ethoxythiazol-5-yl)(phenyl)methanone (27b): Yield 36% (25.5mg), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.79 (m, 2H), 7.68 (s, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 3H), 4.55 (q, *J* = 7.1 Hz, 2H), 1.48 (t, *J* = 7.1 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.42, 179.51, 146.19, 137.68, 132.41, 128.80, 128.61, 68.69, 14.38. HRMS (ESI) calculated for $C_{12}H_{11}NNaO_2S$ $[M+Na]^+$: 256.0403; found: 256.0405.



(Z)-3-(dimethylamino)-1-phenyl-2-thiocyanatoprop-2-en-1-one (1c): Yield 36% (25.5mg), pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.53 – 7.38 (m, 5H), 3.37 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.67, 158.37, 139.74, 130.30, 128.18, 127.93, 113.21, 87.34. HRMS (ESI) calculated for $C_{12}H_{12}N_2NaOS$ $[M+Na]^+$: 255.0563; found: 255.0566.

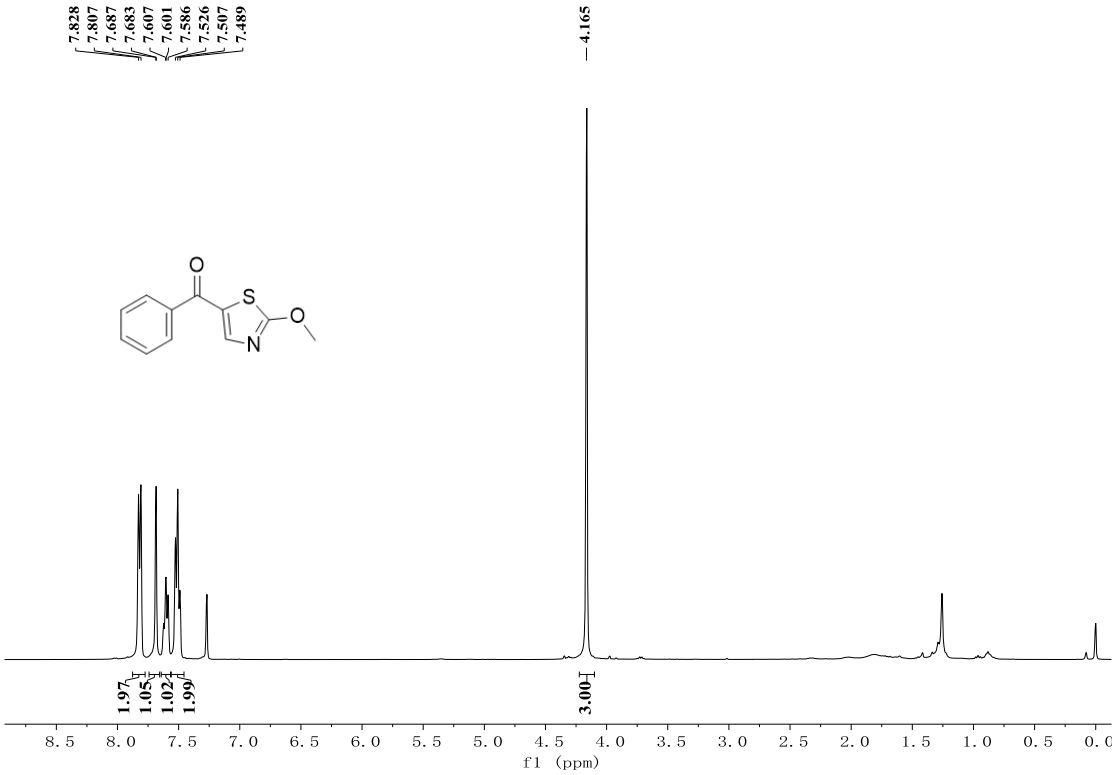
4. References

1. F. Wang, R. Fu, J. Chen, J. Rong, E. Wang, J. Zhang, Z. and Zhang, Y. Jiang, *Chem. Commun.*, 2022, **58**, 3477-3480.
2. Y. Gao, Y. Liu, ,L.Wei, and J. Wan*, Res. Chem. Intermed.,* 2017, **43**, 5547–5555.

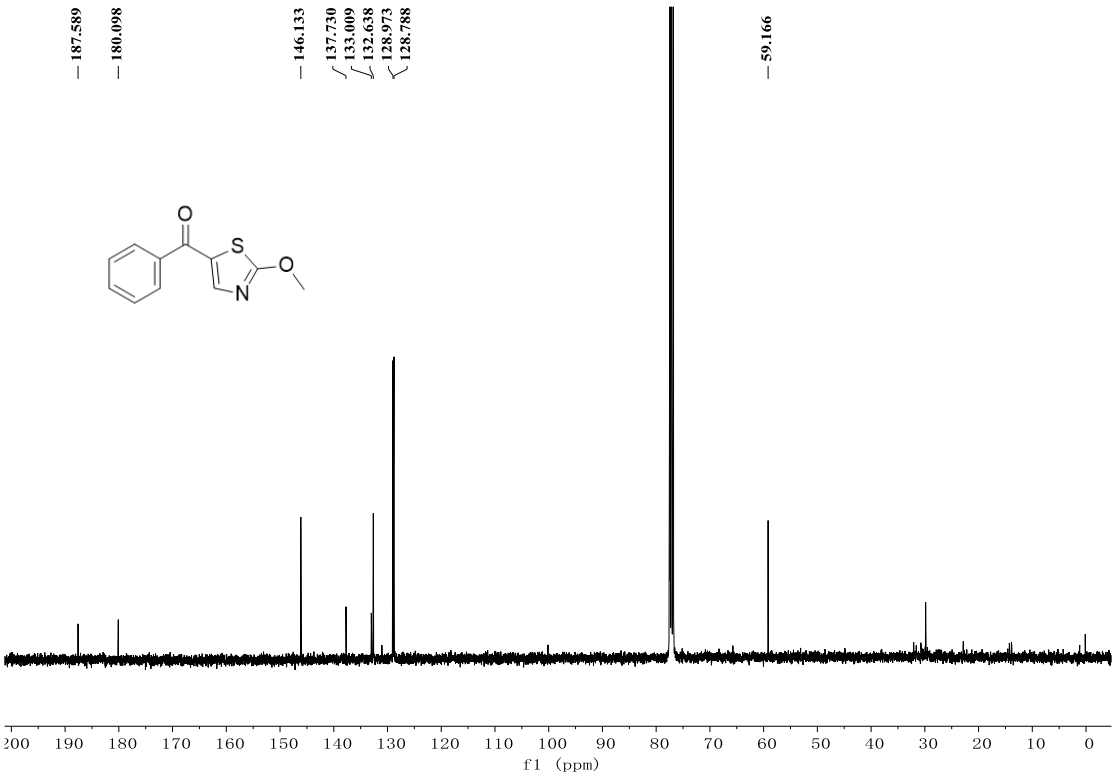
5. Copies of product NMR Spectra

1b

^{1}H NMR

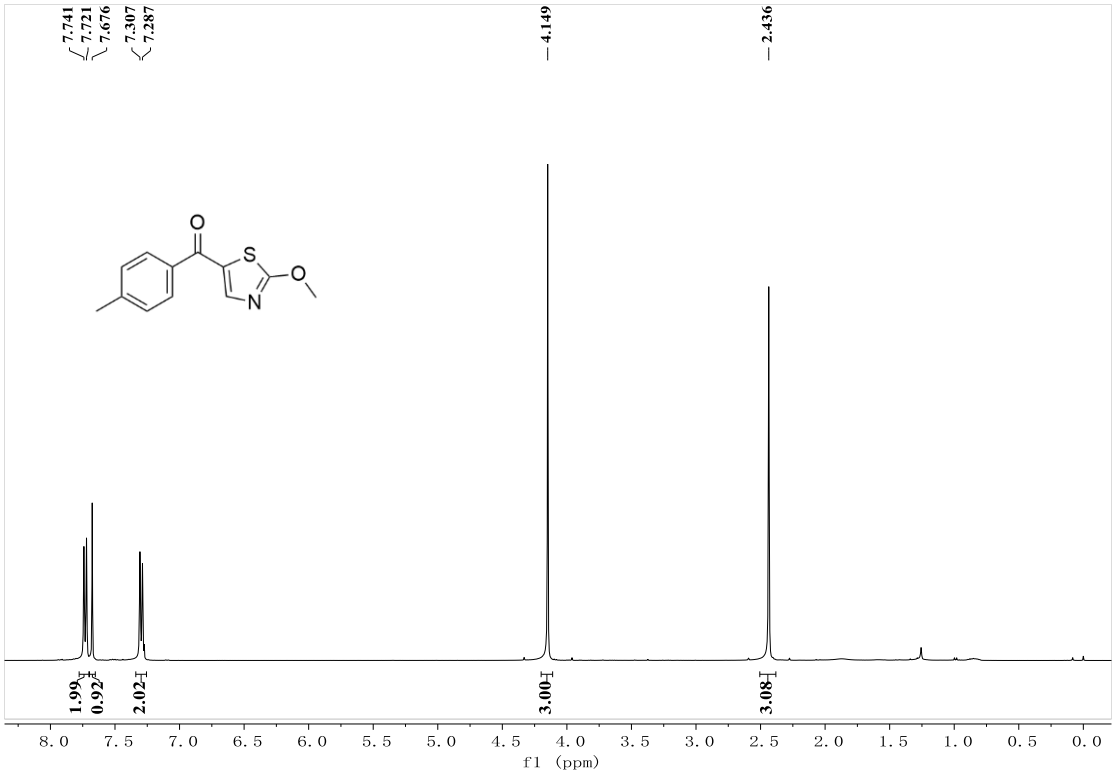


^{13}C NMR

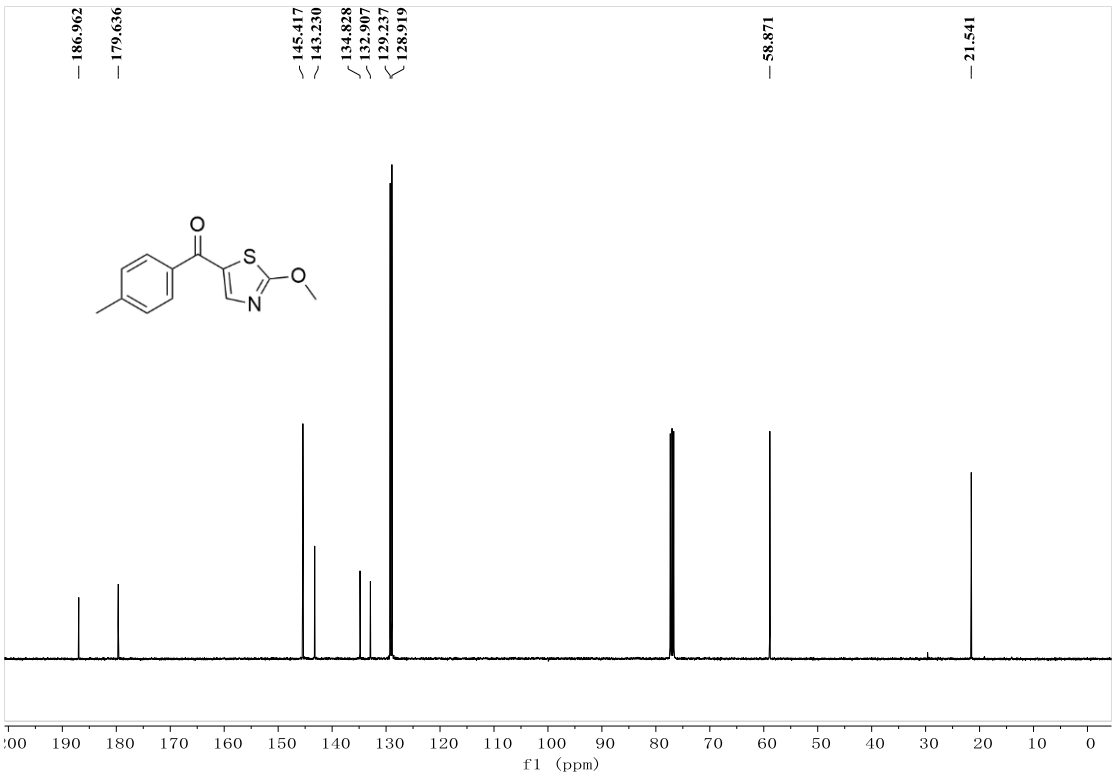


2b

^{1}H NMR

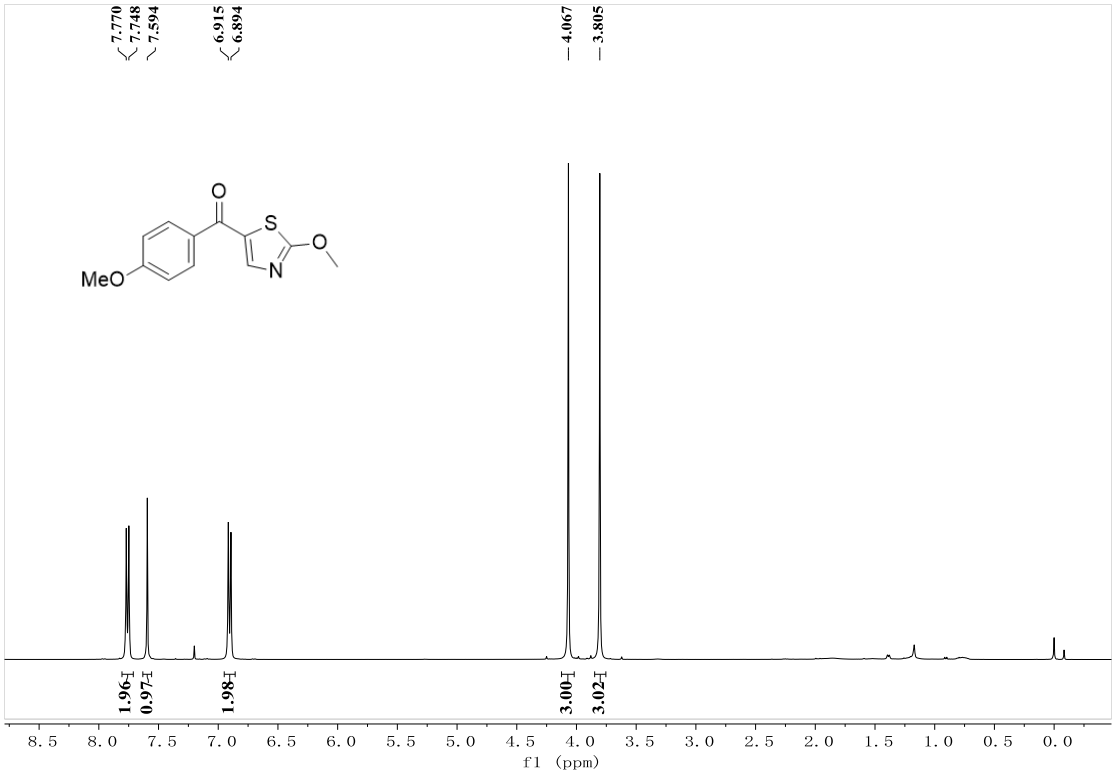


^{13}C NMR

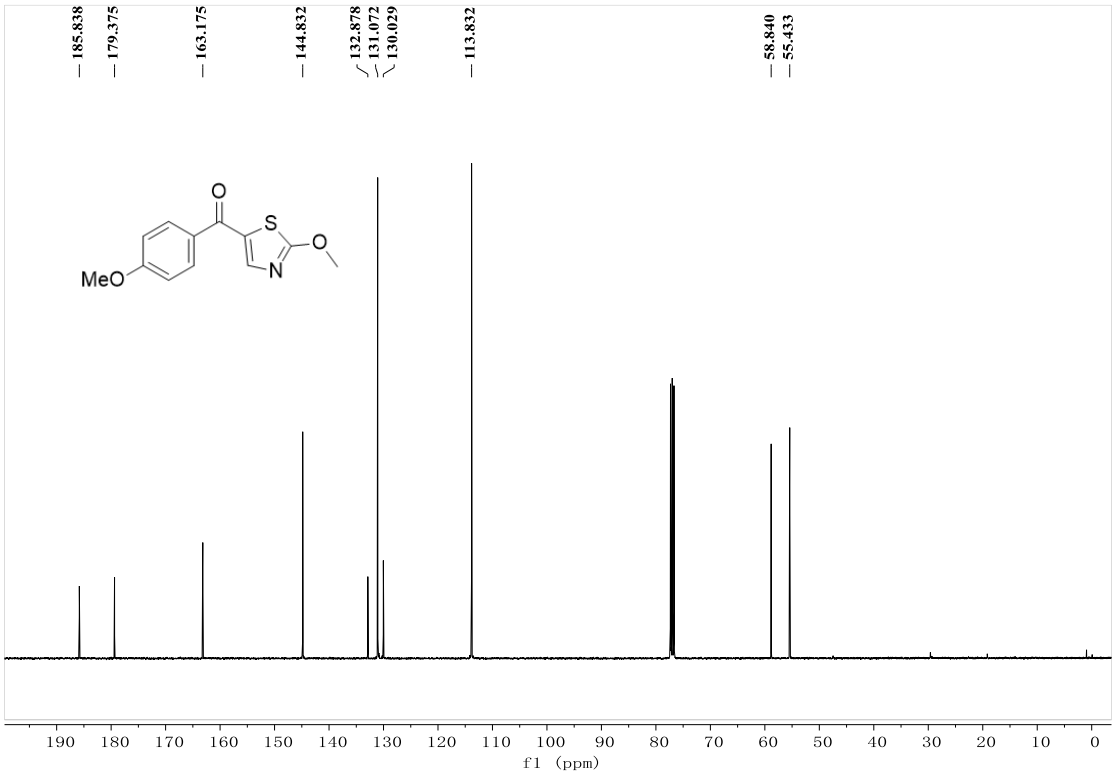


3b

^{1}H NMR

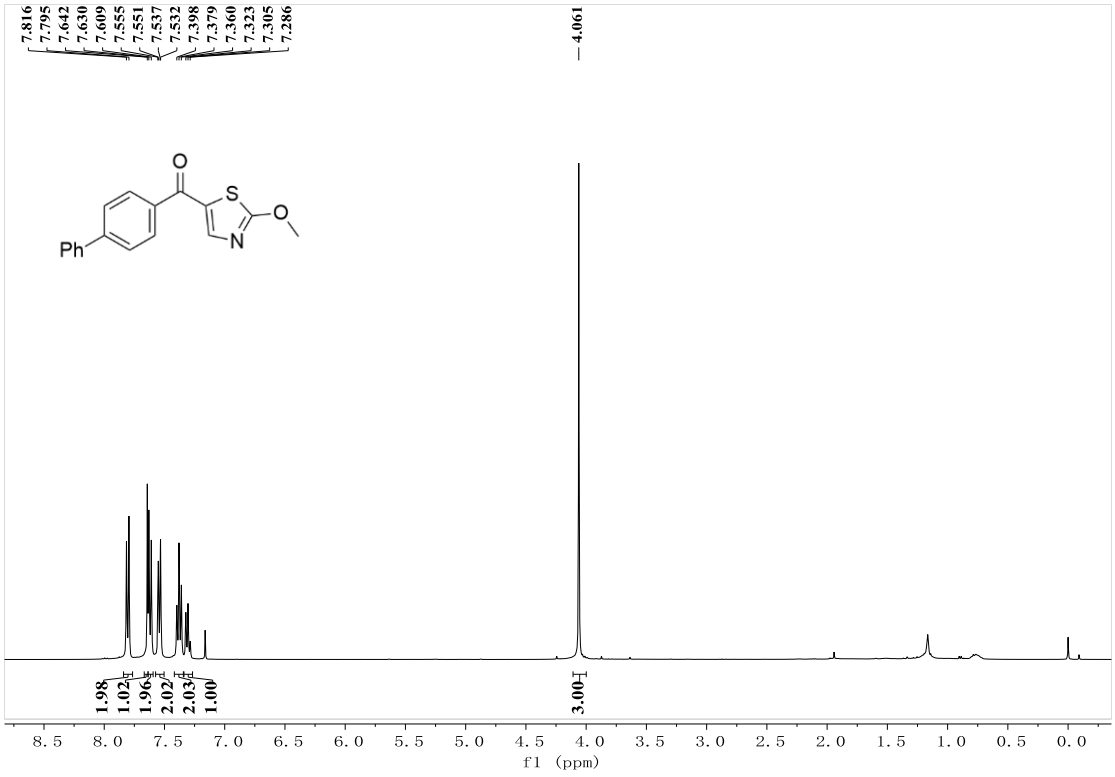


^{13}C NMR

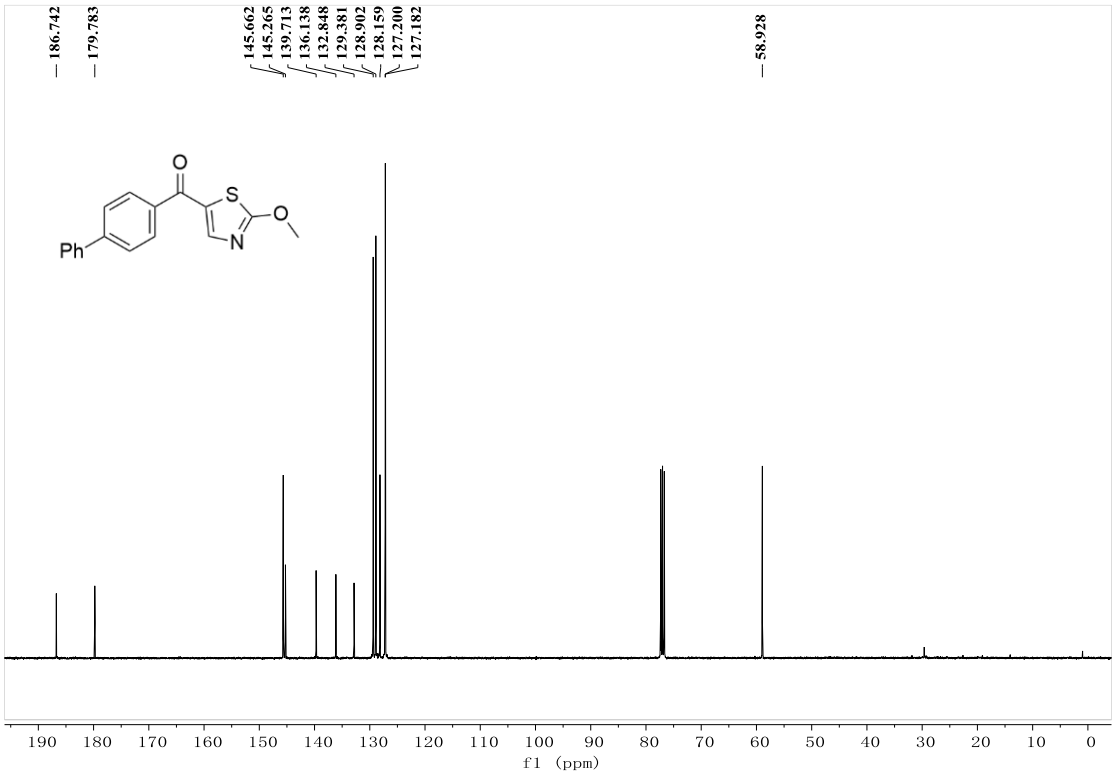


4b

^{1}H NMR

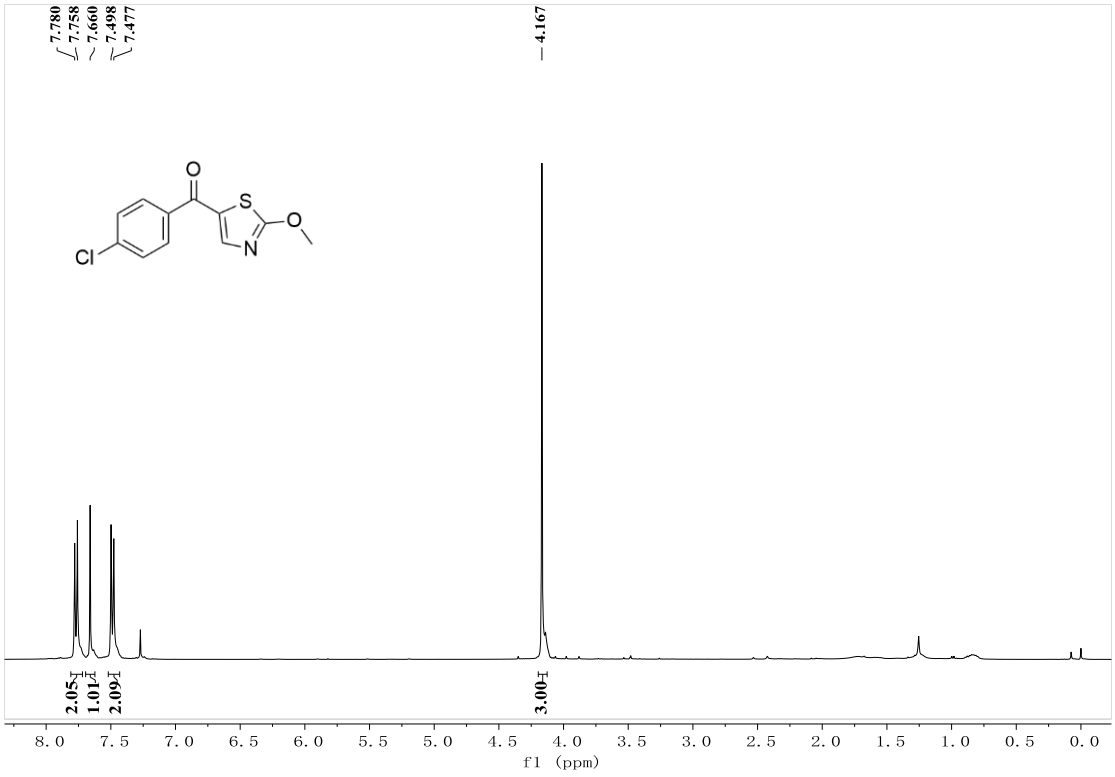


^{13}C NMR

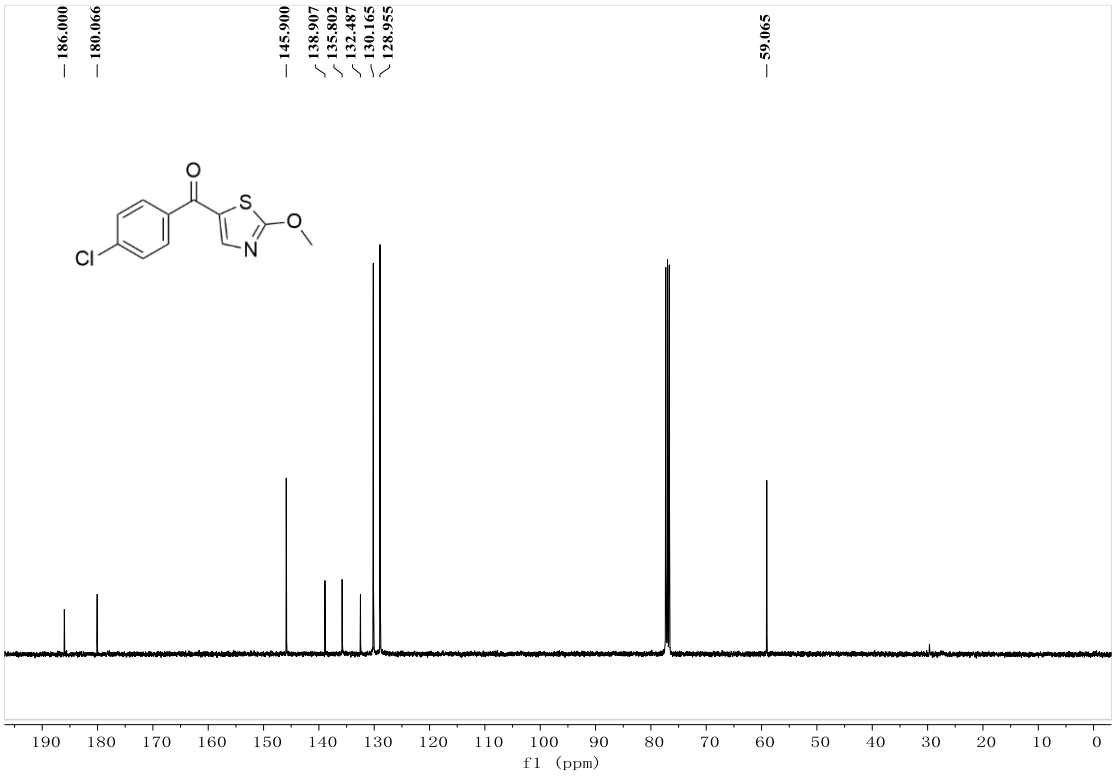


5b

^{1}H NMR

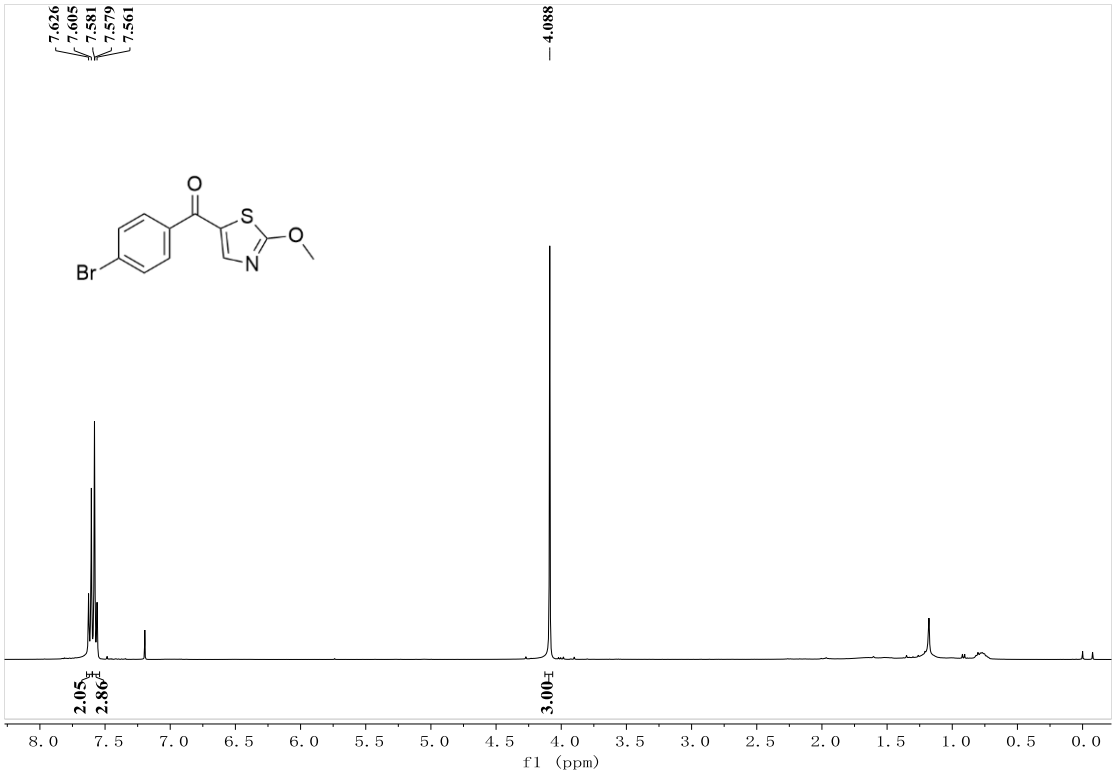


^{13}C NMR

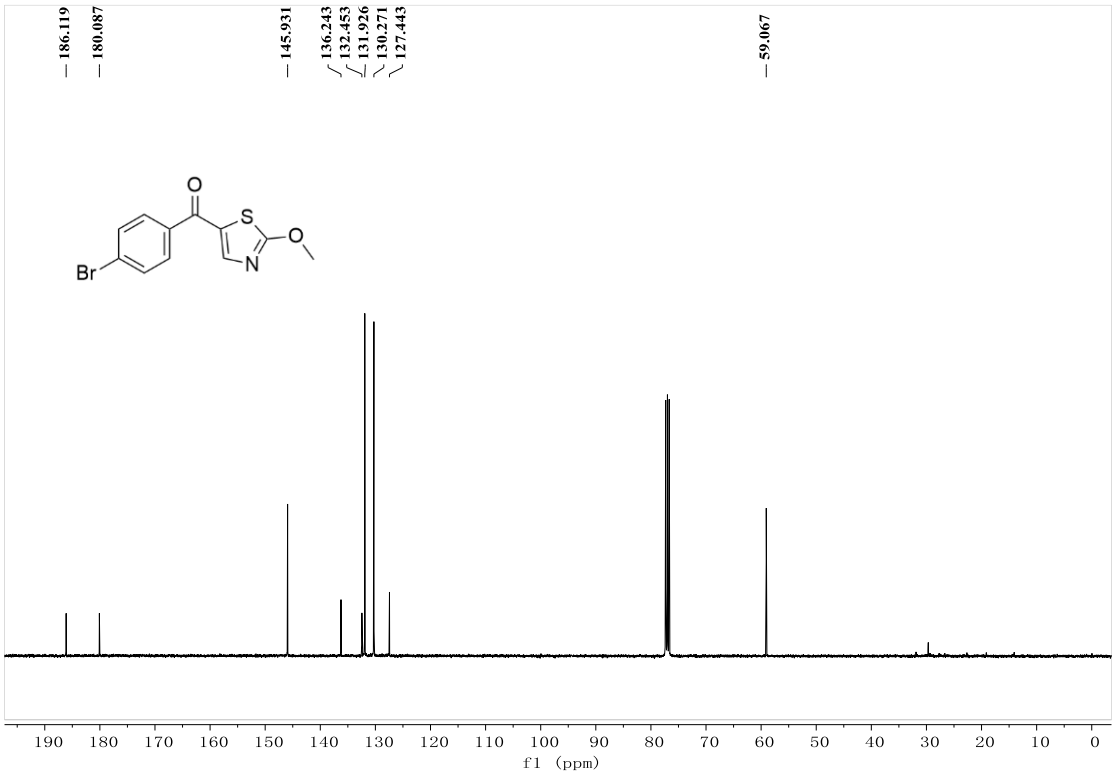


6b

^{1}H NMR

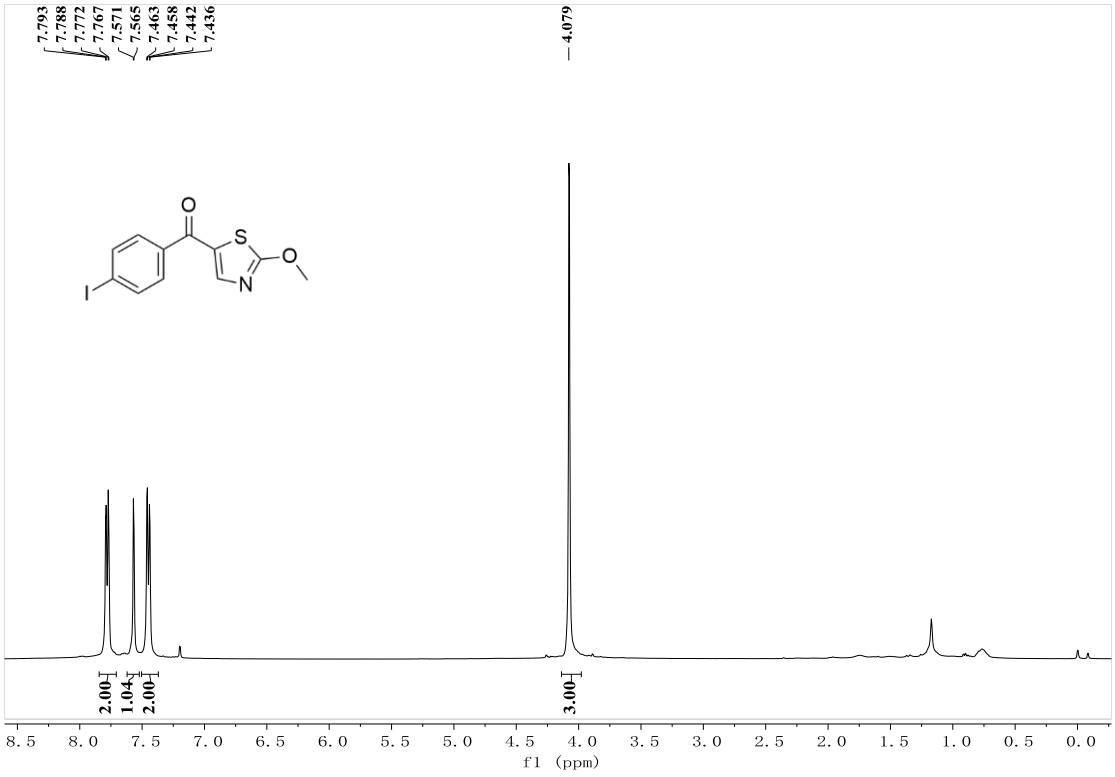


^{13}C NMR

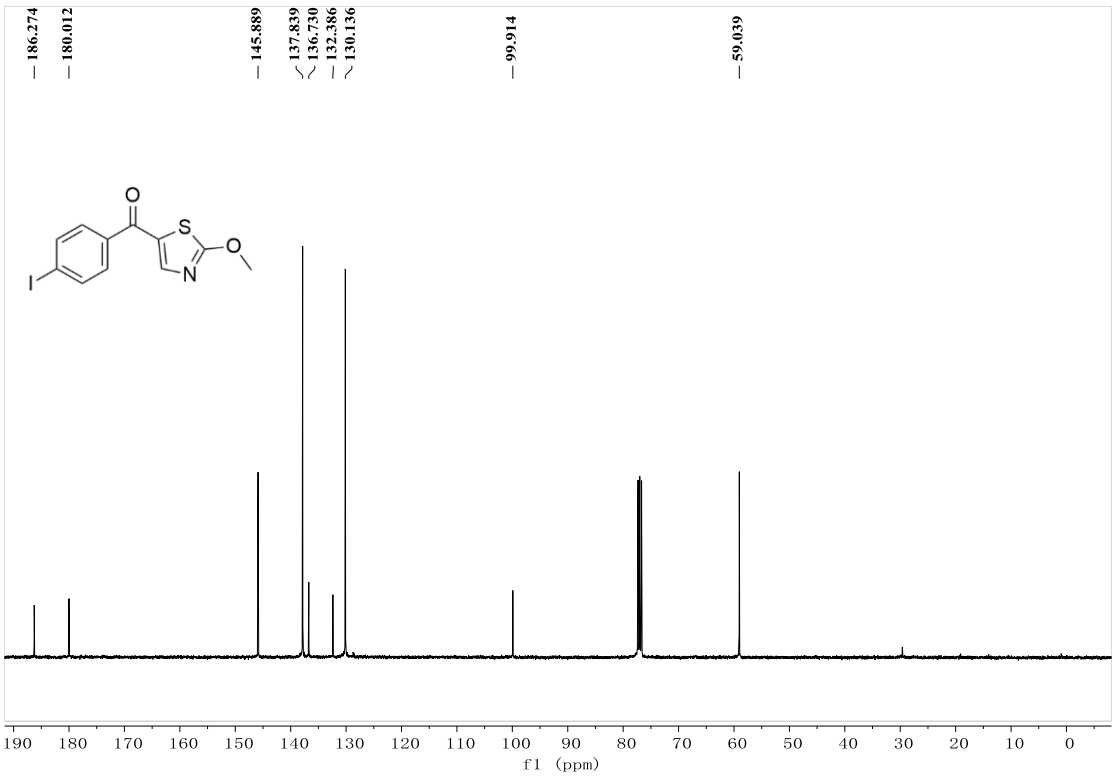


7b

^{1}H NMR

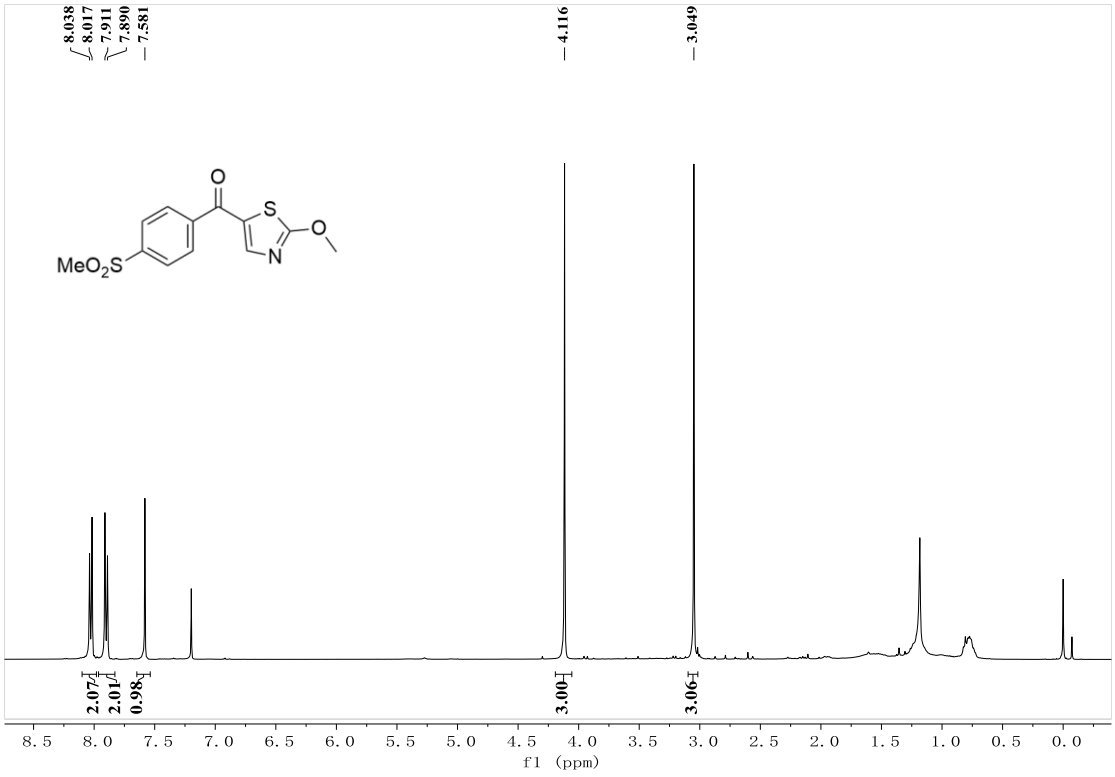


^{13}C NMR

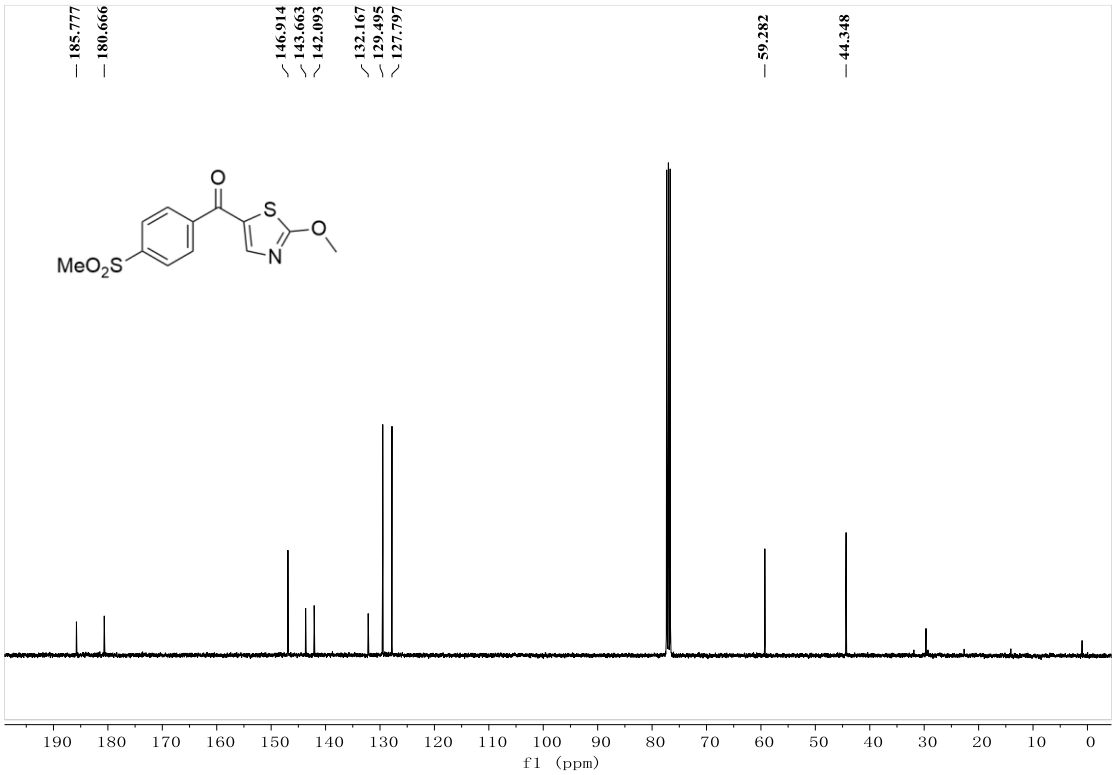


8b

^{1}H NMR

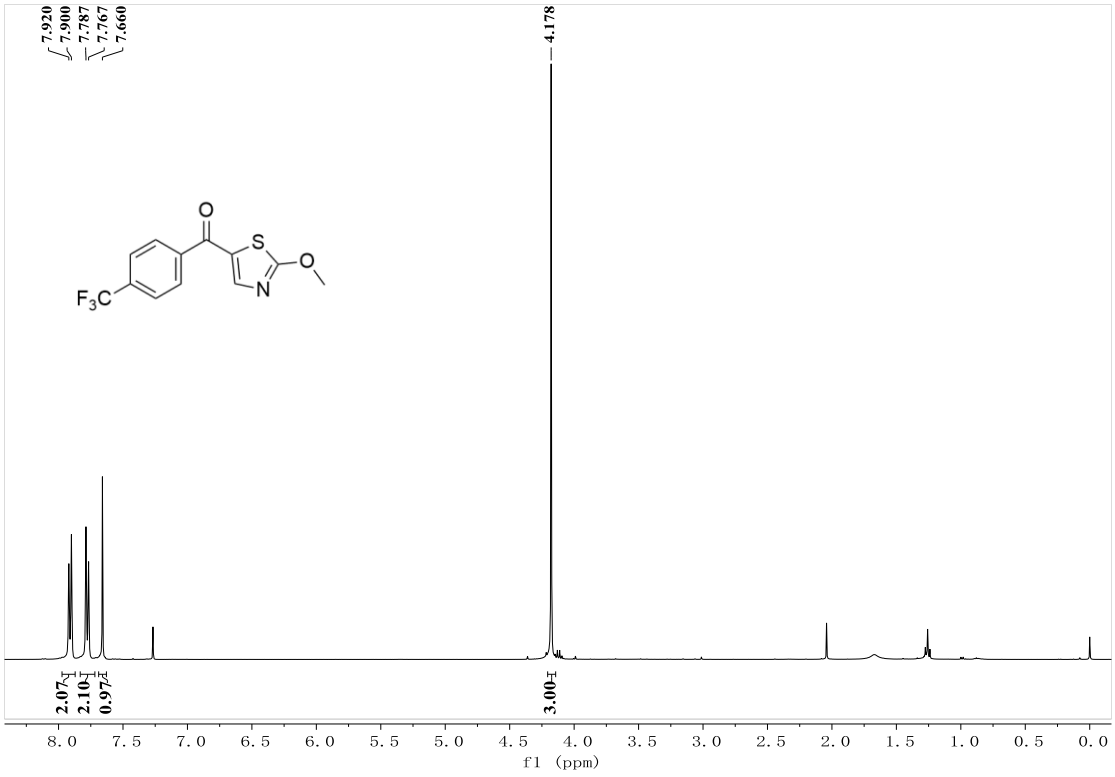


^{13}C NMR

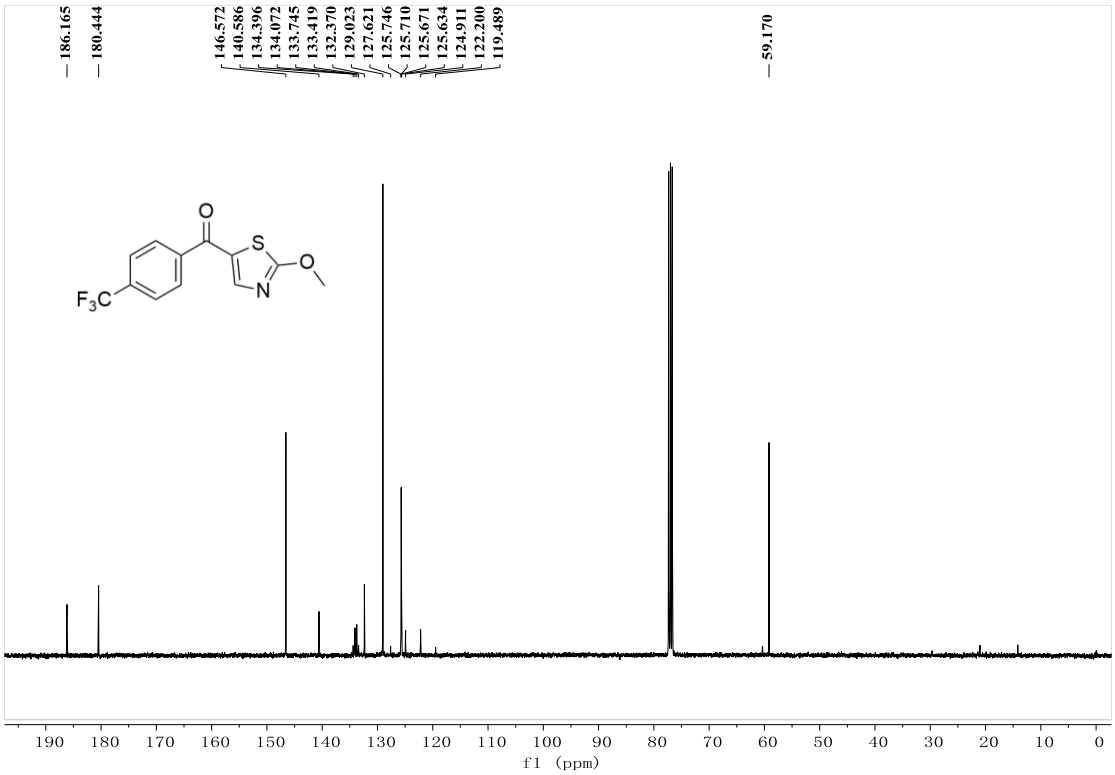


9b

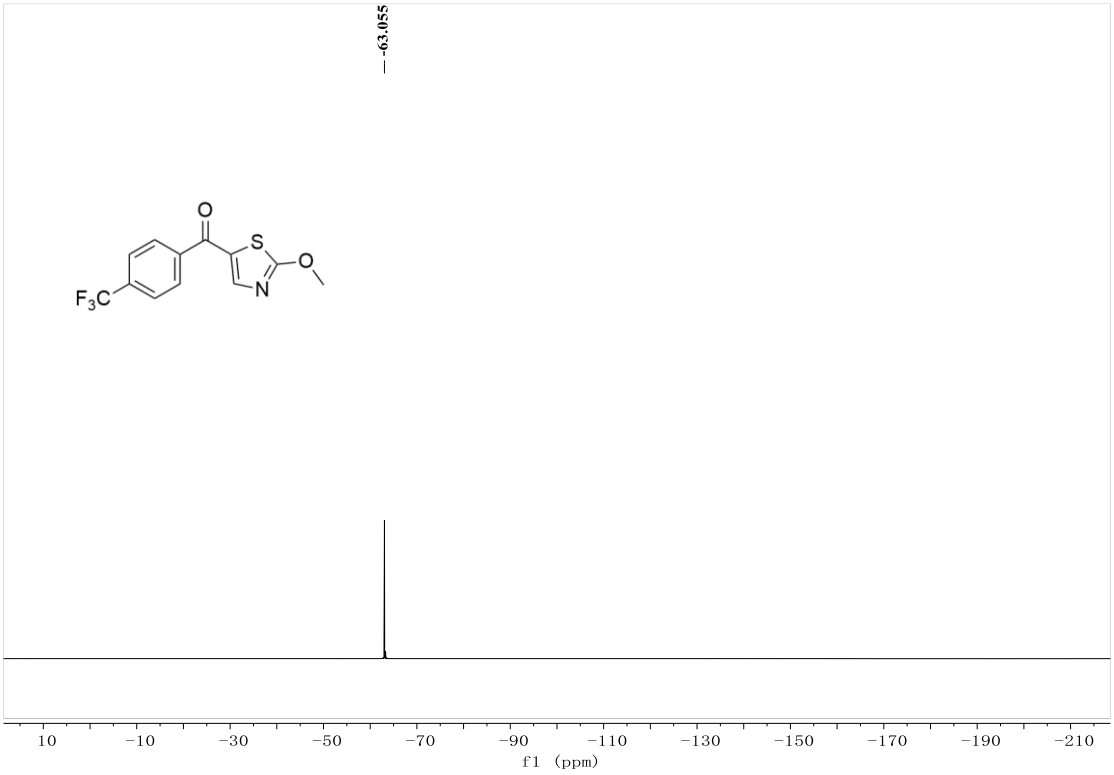
^{1}H NMR



^{13}C NMR

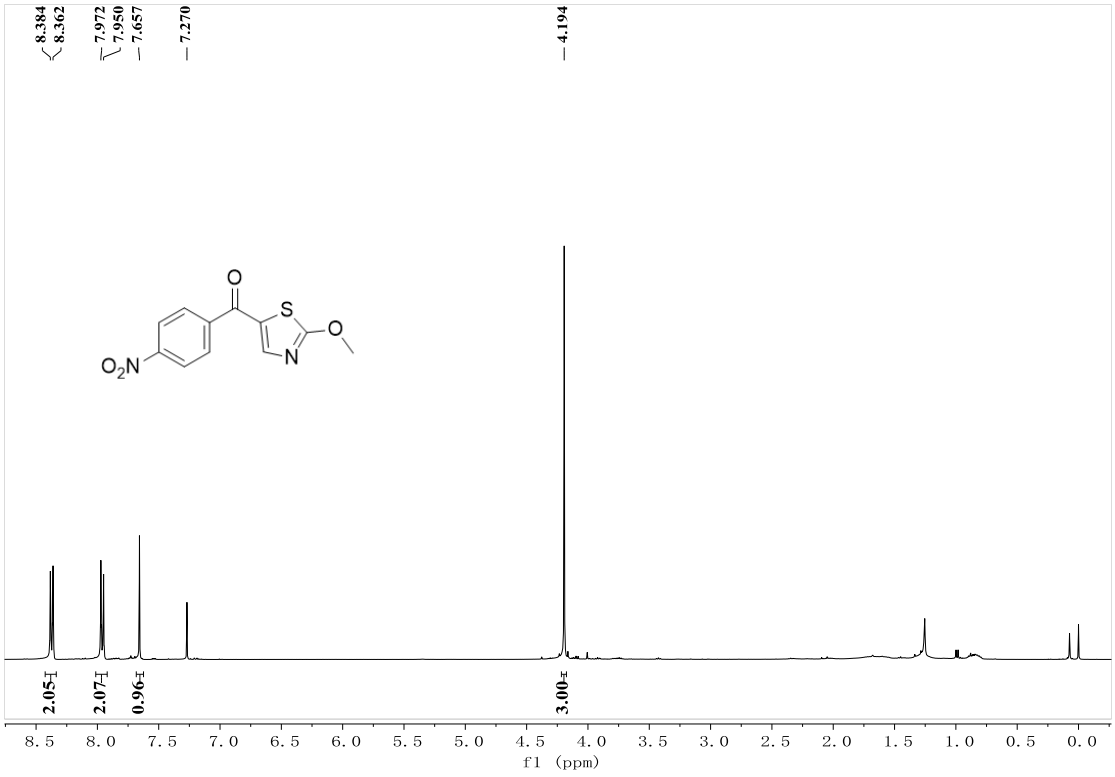


^{19}F NMR

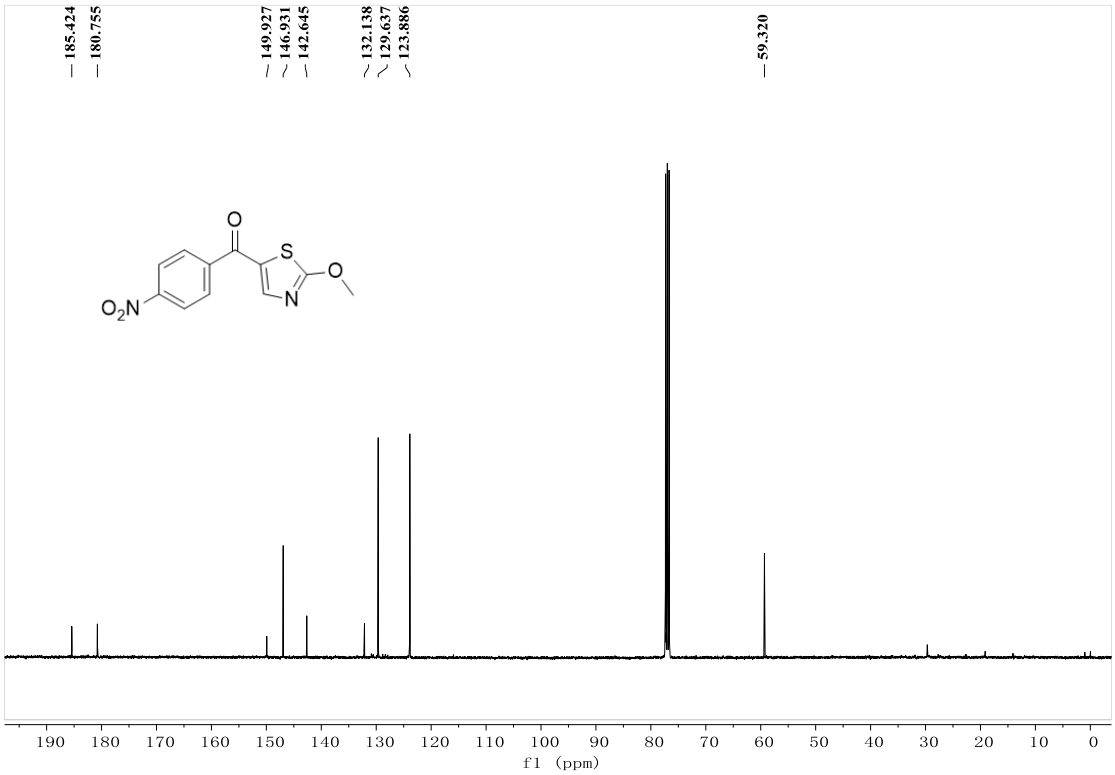


10b

^{1}H NMR

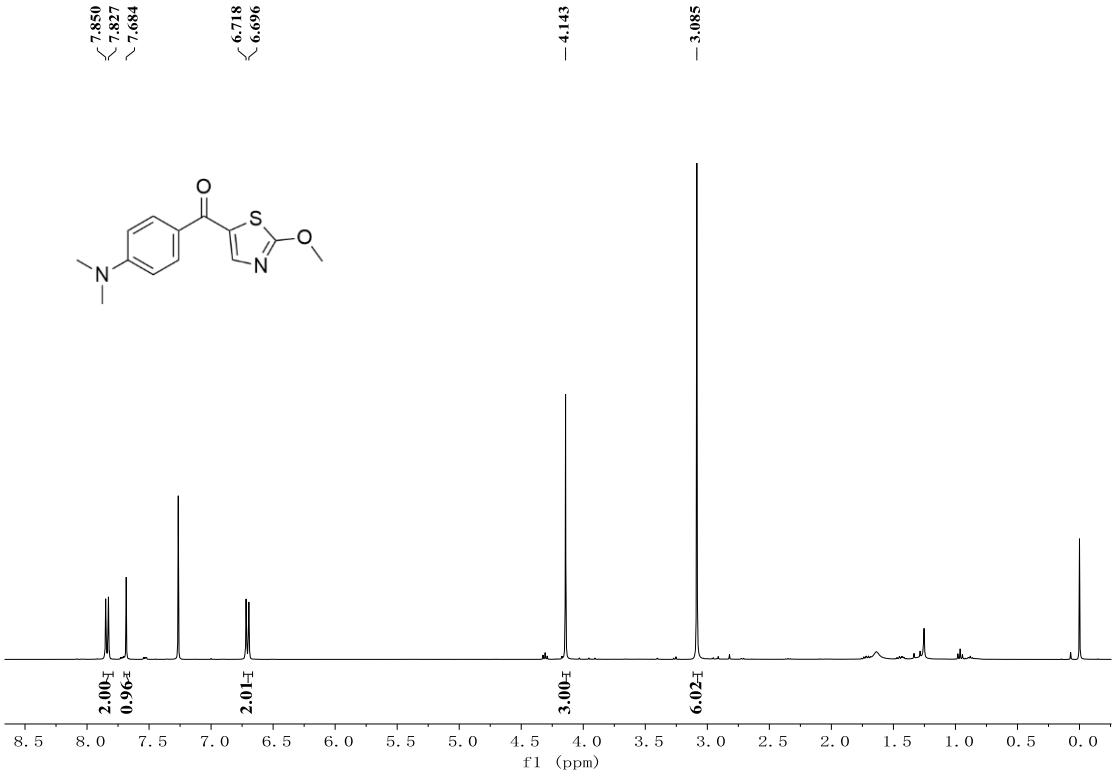


^{13}C NMR

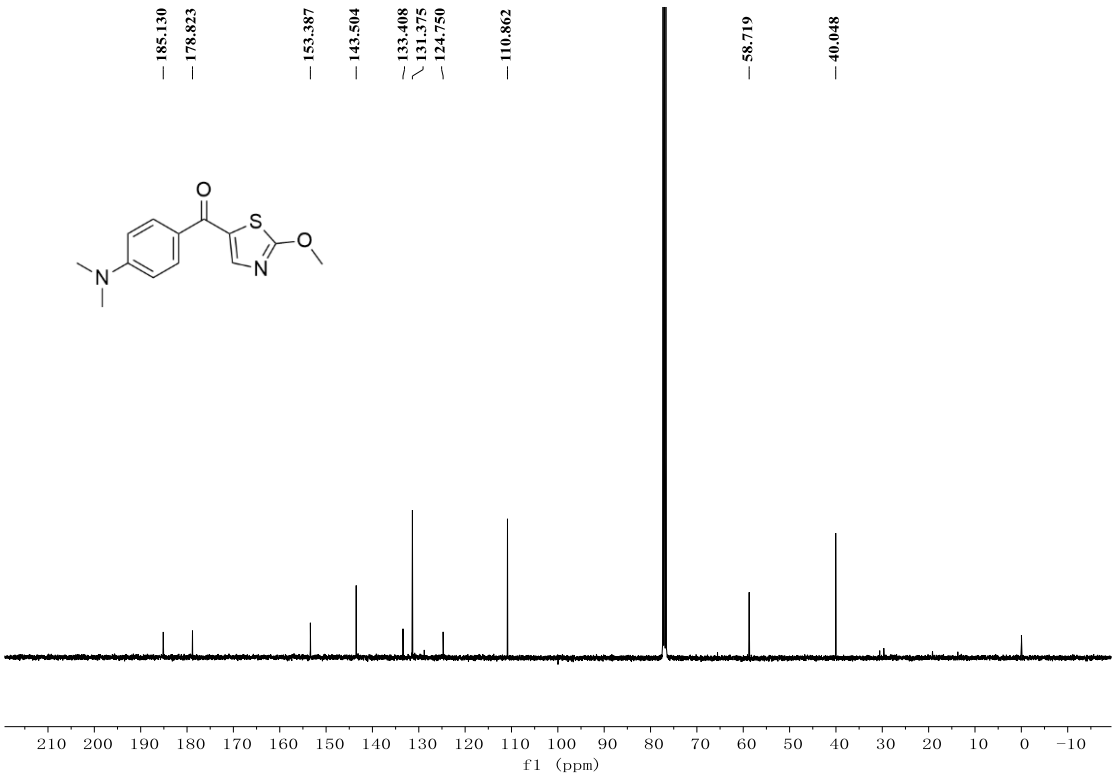


11b

^{1}H NMR

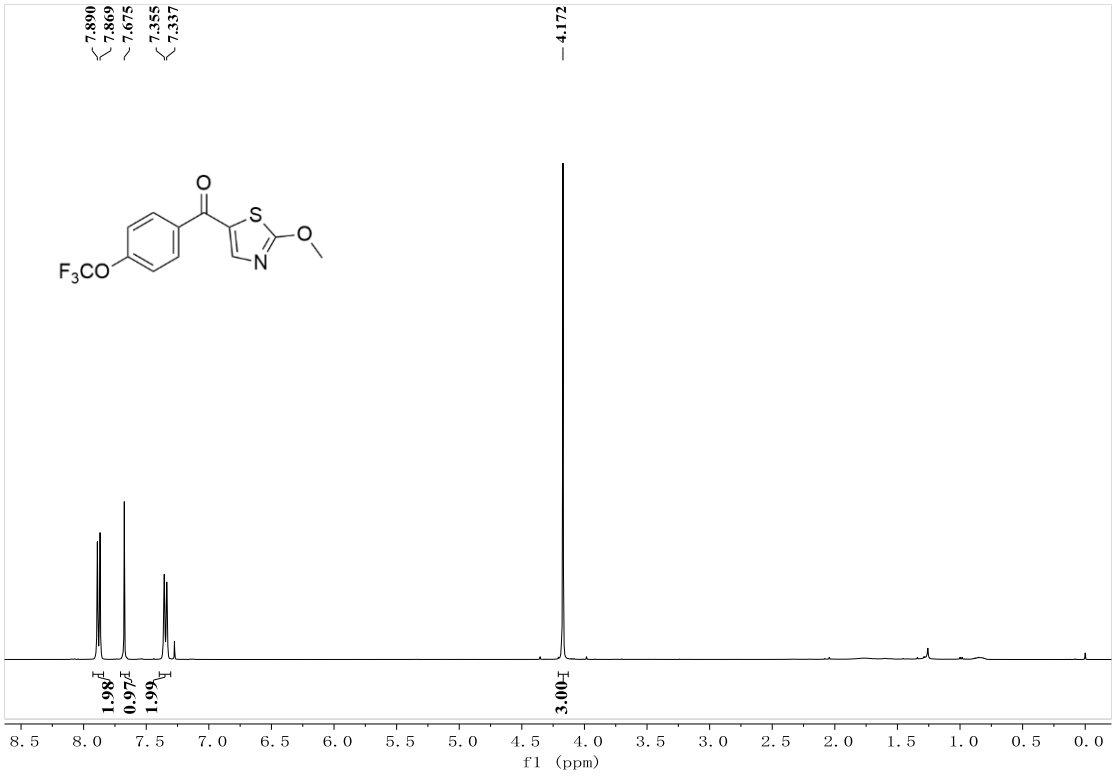


^{13}C NMR

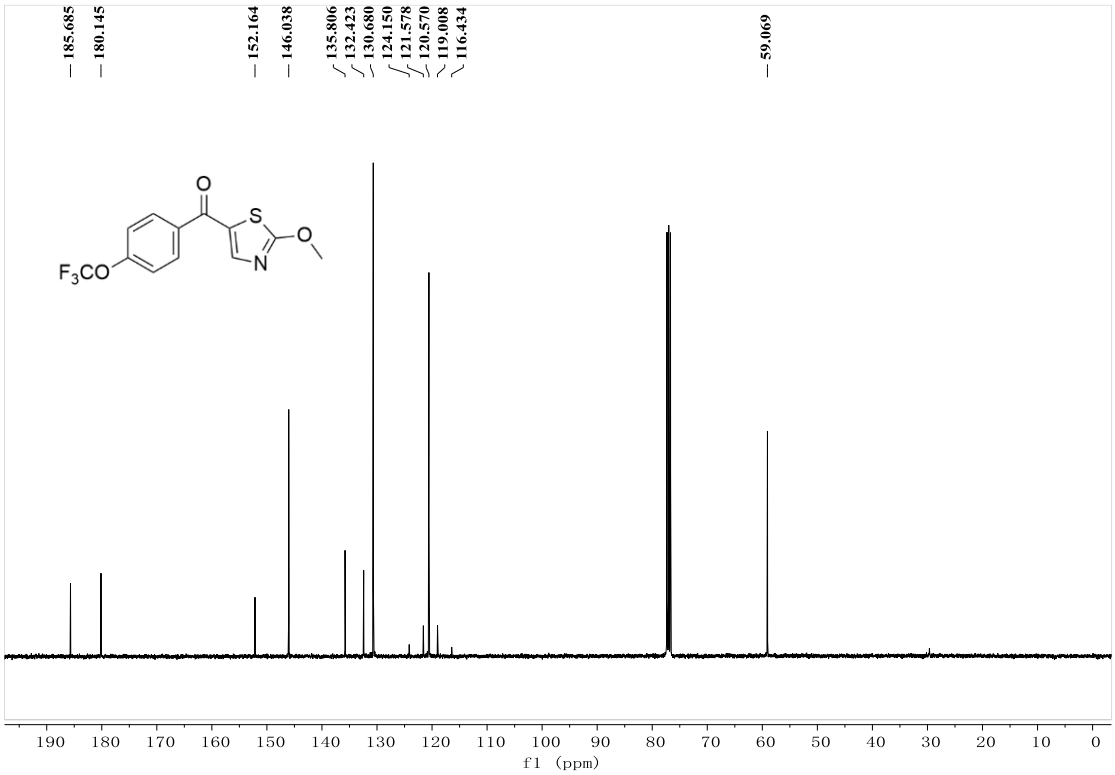


12b

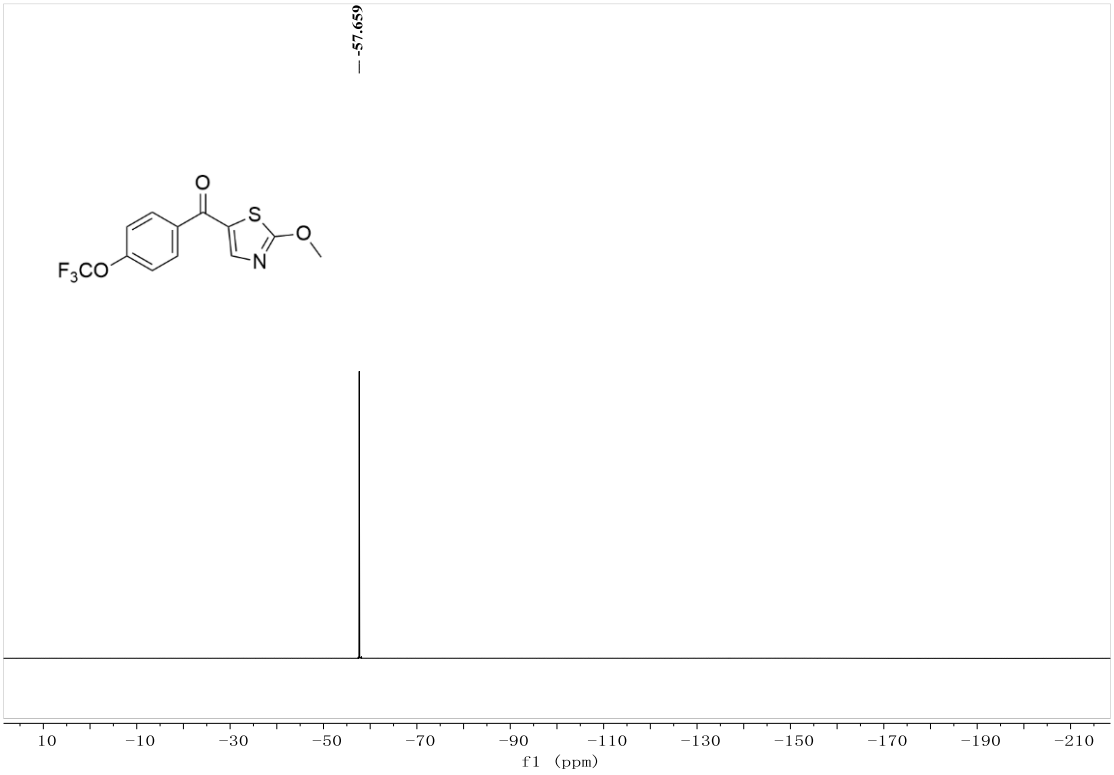
^{1}H NMR



^{13}C NMR

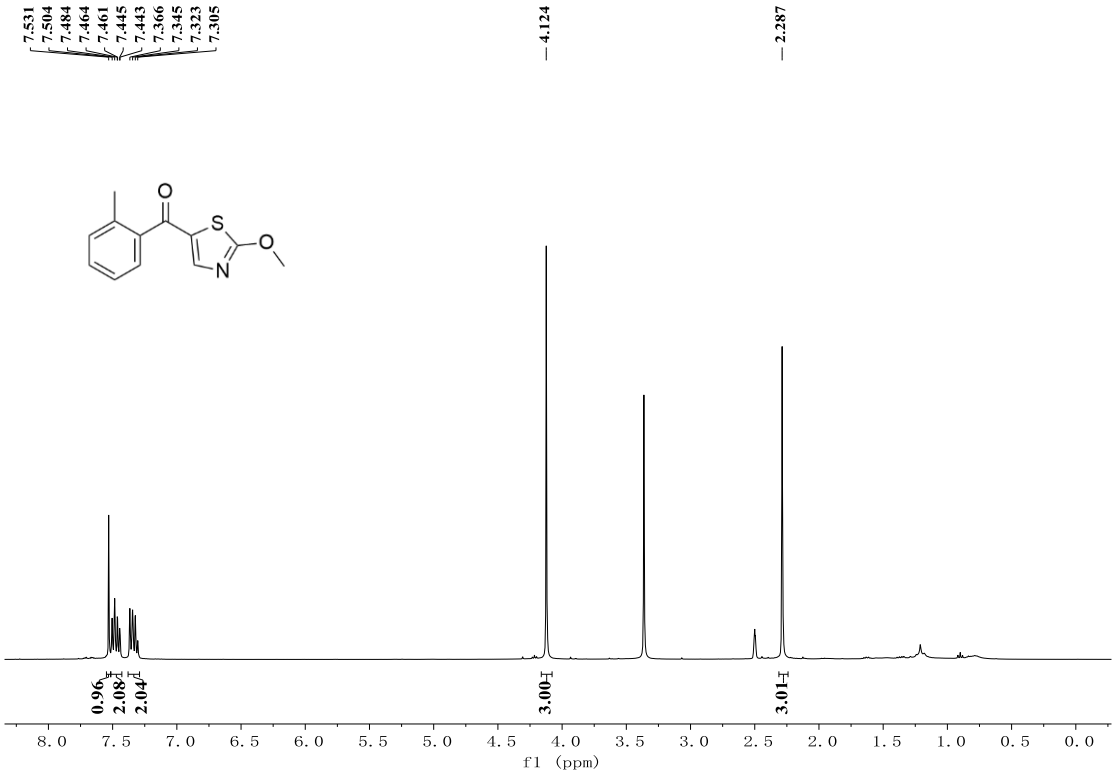


^{19}F NMR

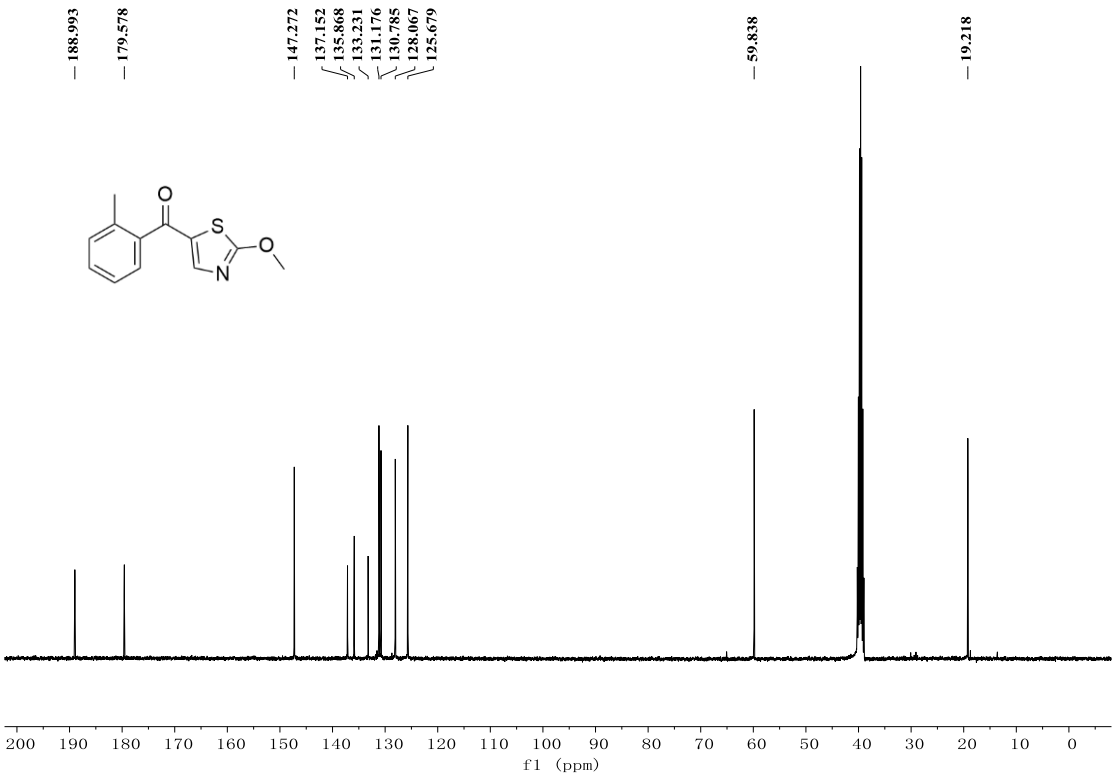


13b

^{1}H NMR

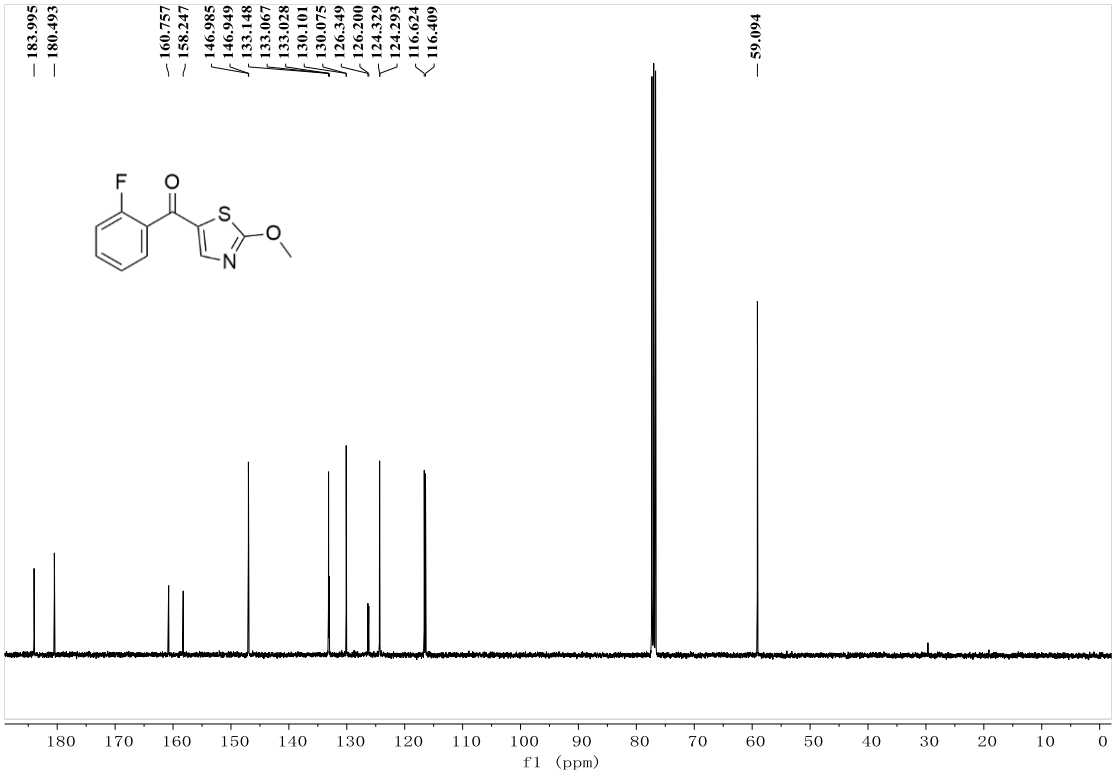


^{13}C NMR

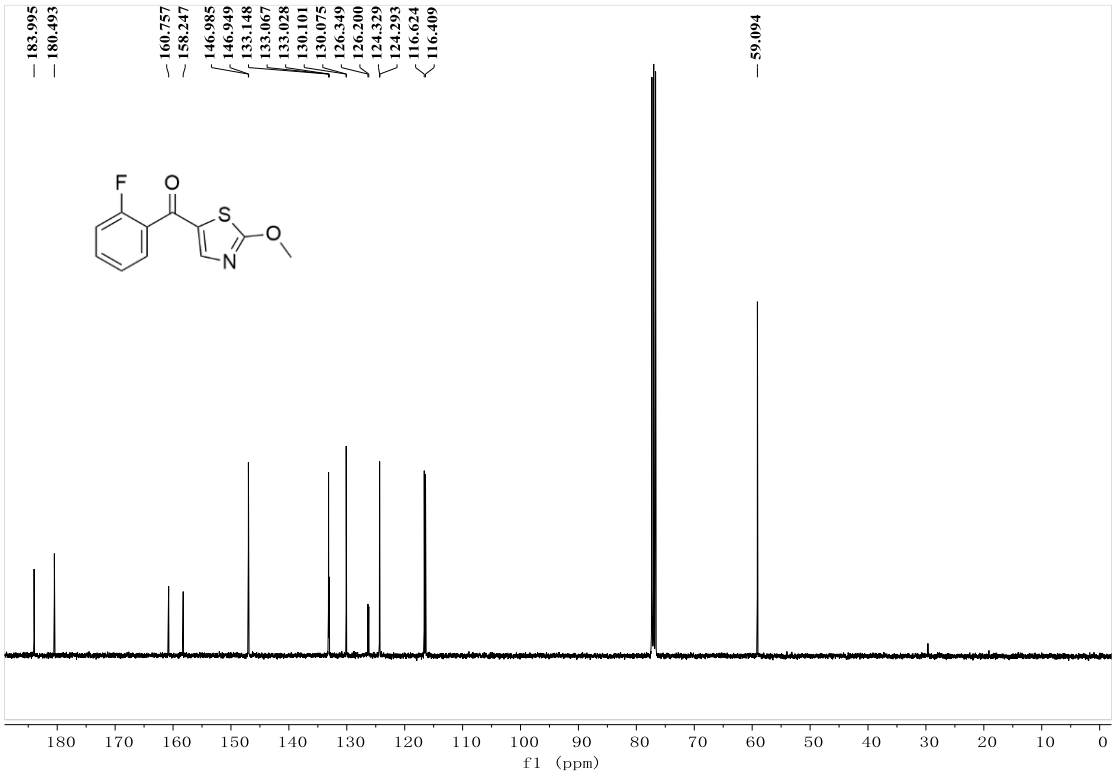


14b

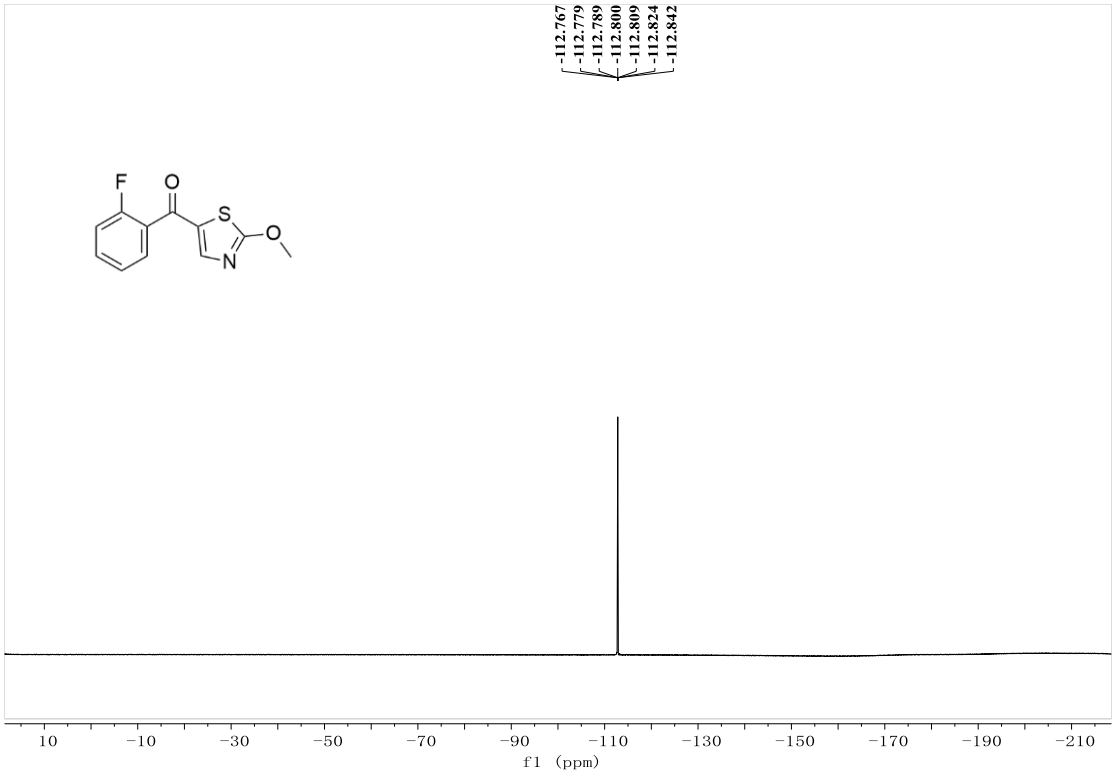
^{1}H NMR



^{13}C NMR

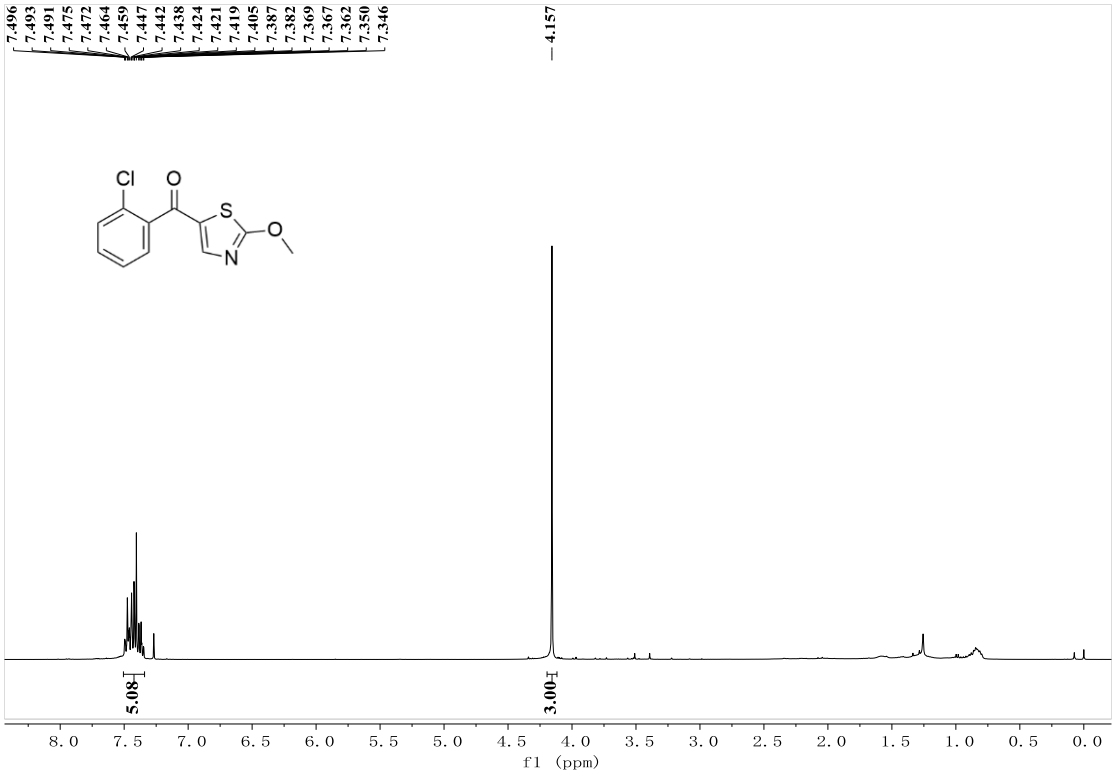


^{19}F NMR

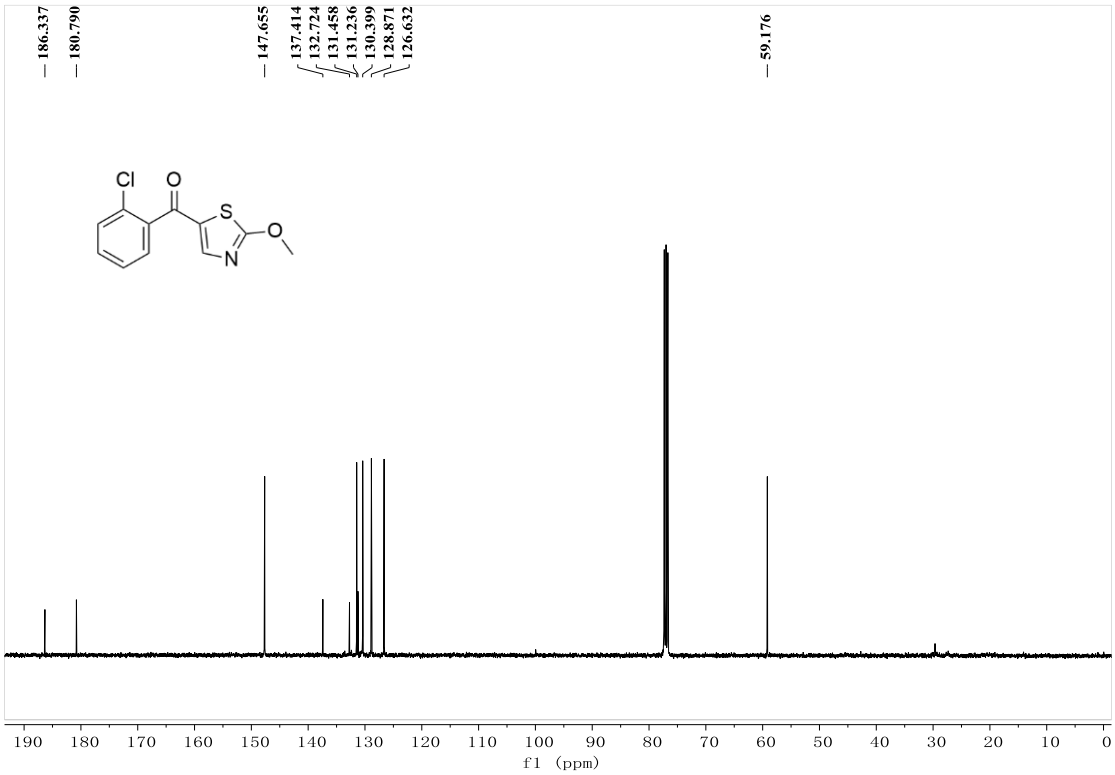

-112.767
-112.779
-112.789
-112.800
-112.809
-112.824
-112.842
F
O
S
O
N
10
−10
−30
−50
−70
−90
−110
−130
−150
−170
−190
−210
f1 (ppm)

15b

^{1}H NMR

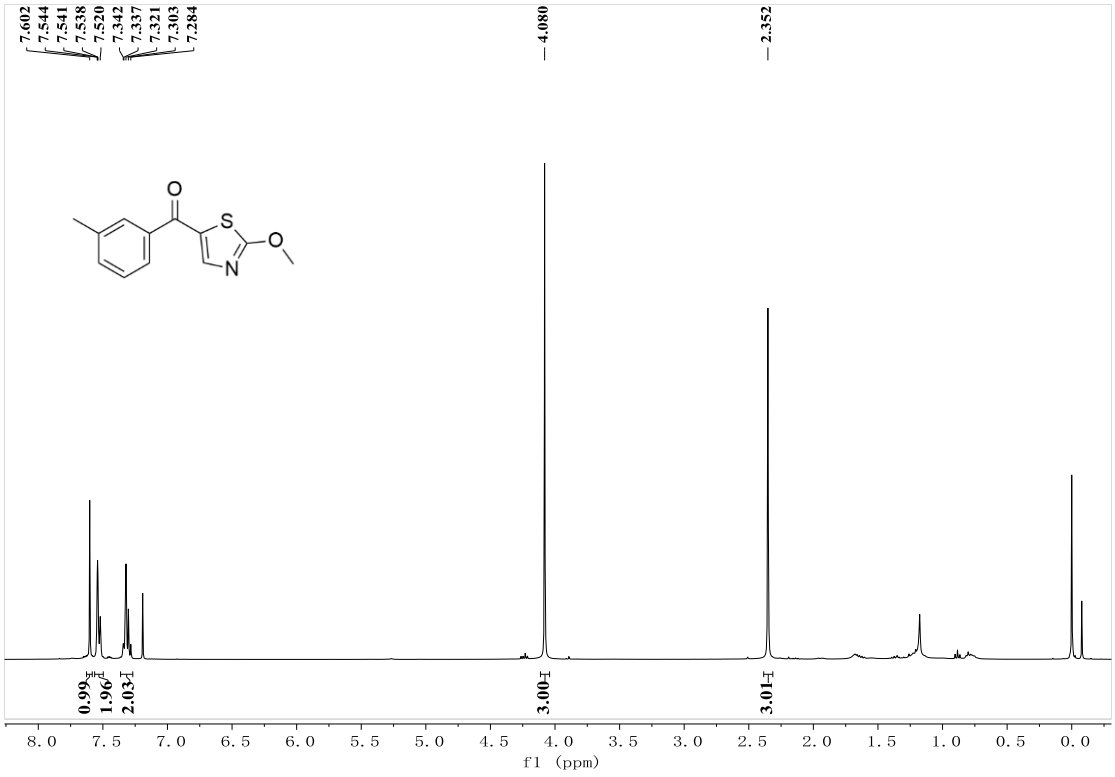


^{13}C NMR

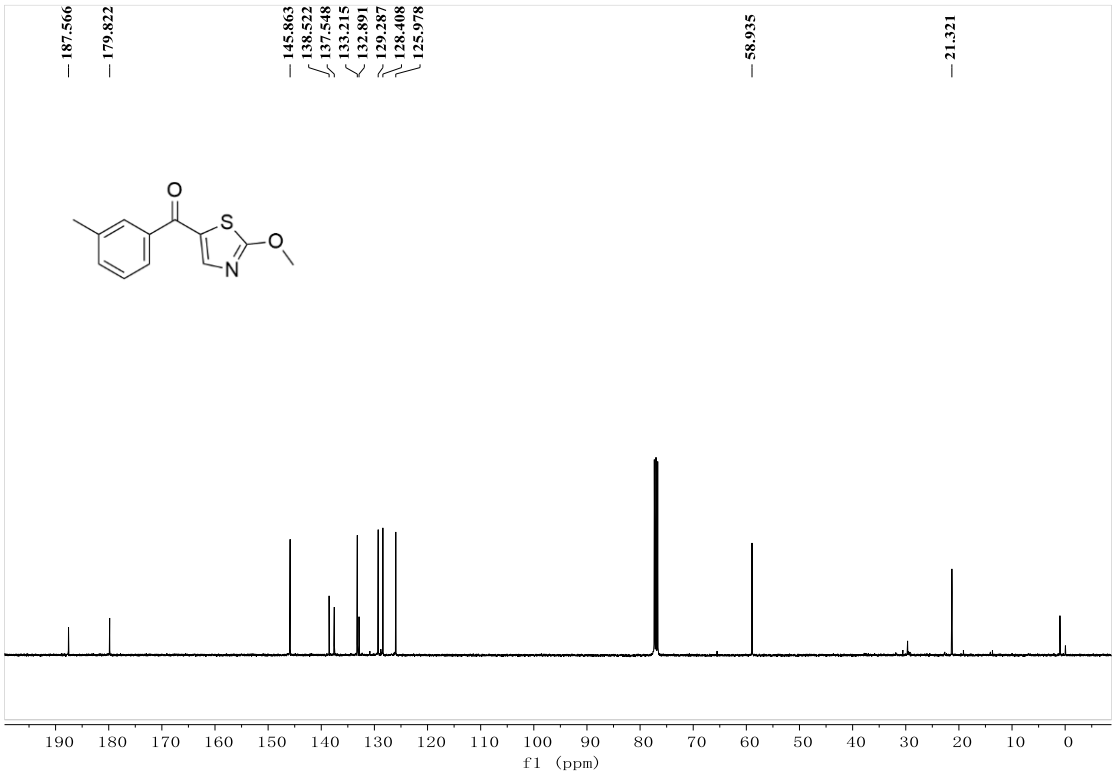


16b

^{1}H NMR

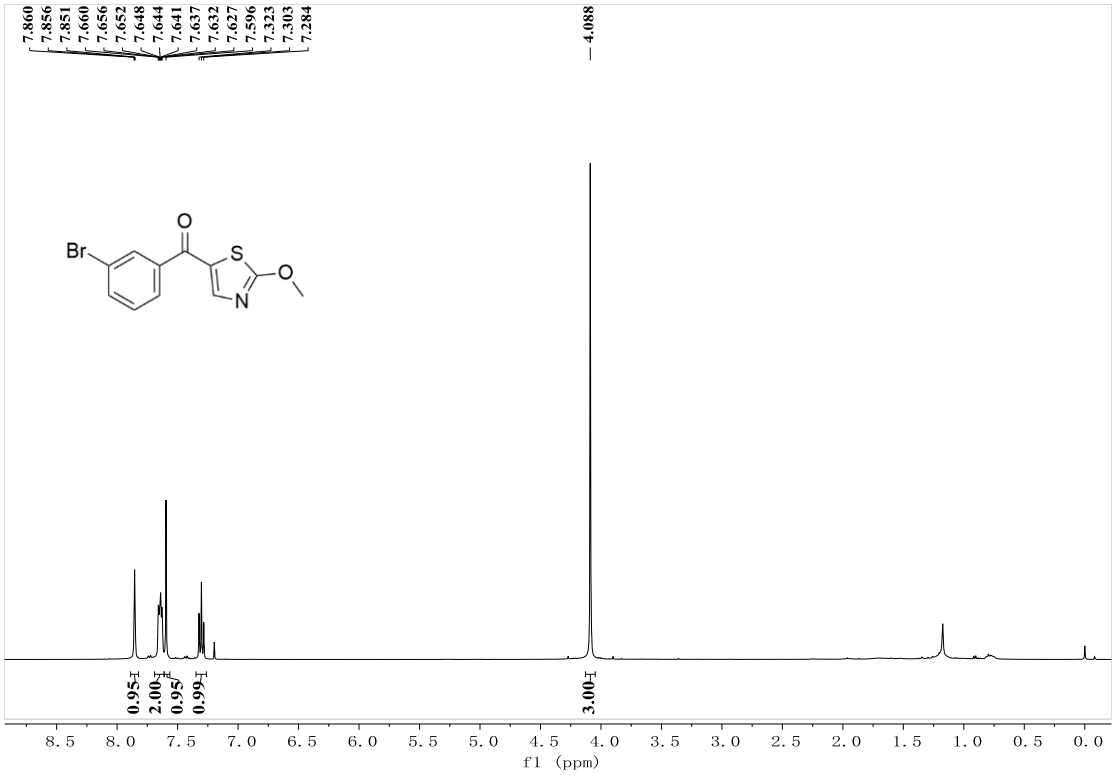


^{13}C NMR

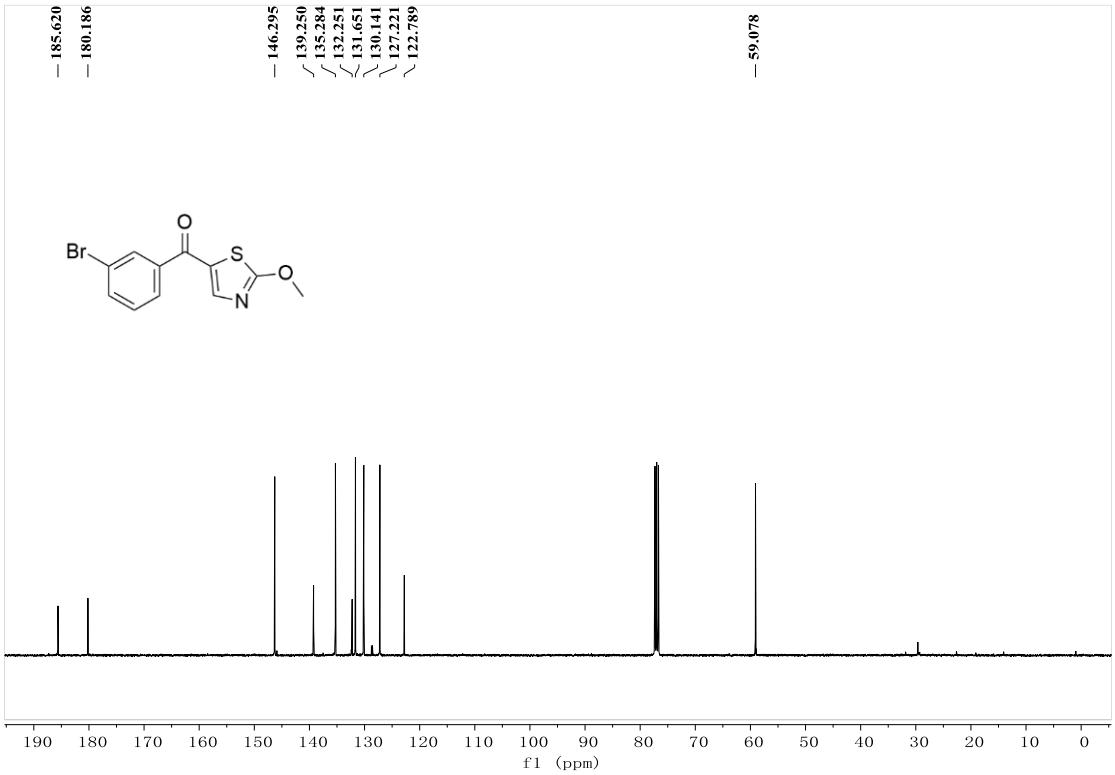


17b

^{1}H NMR

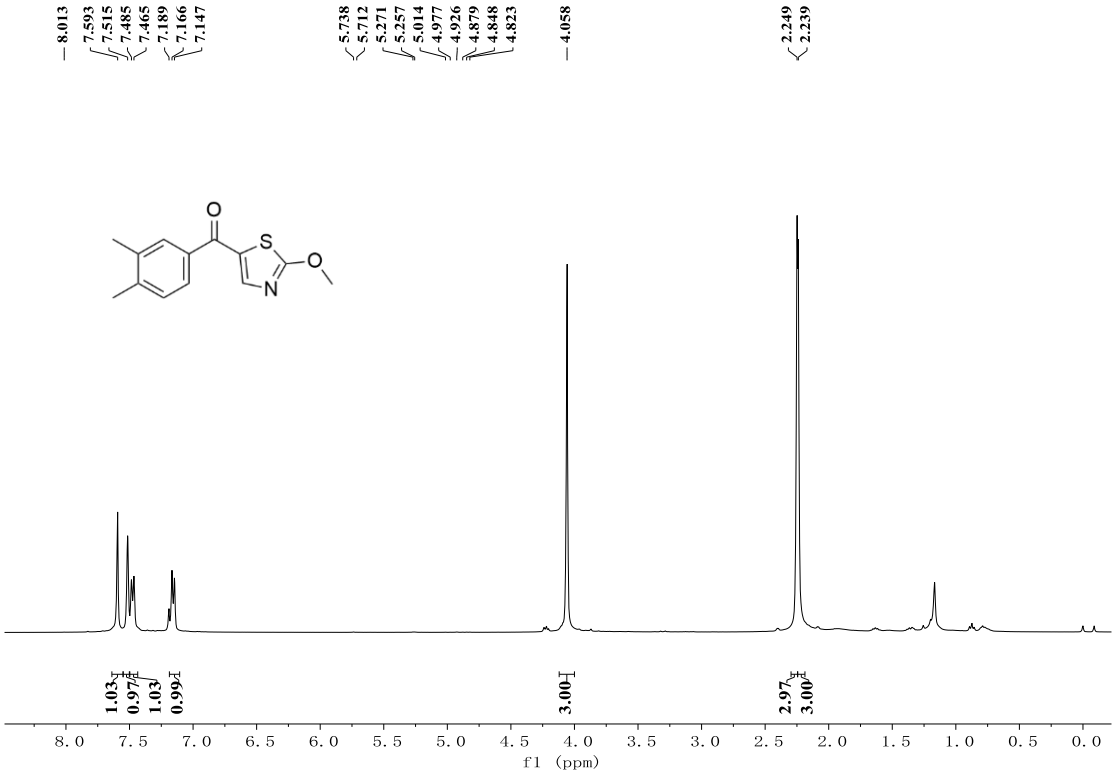


^{13}C NMR

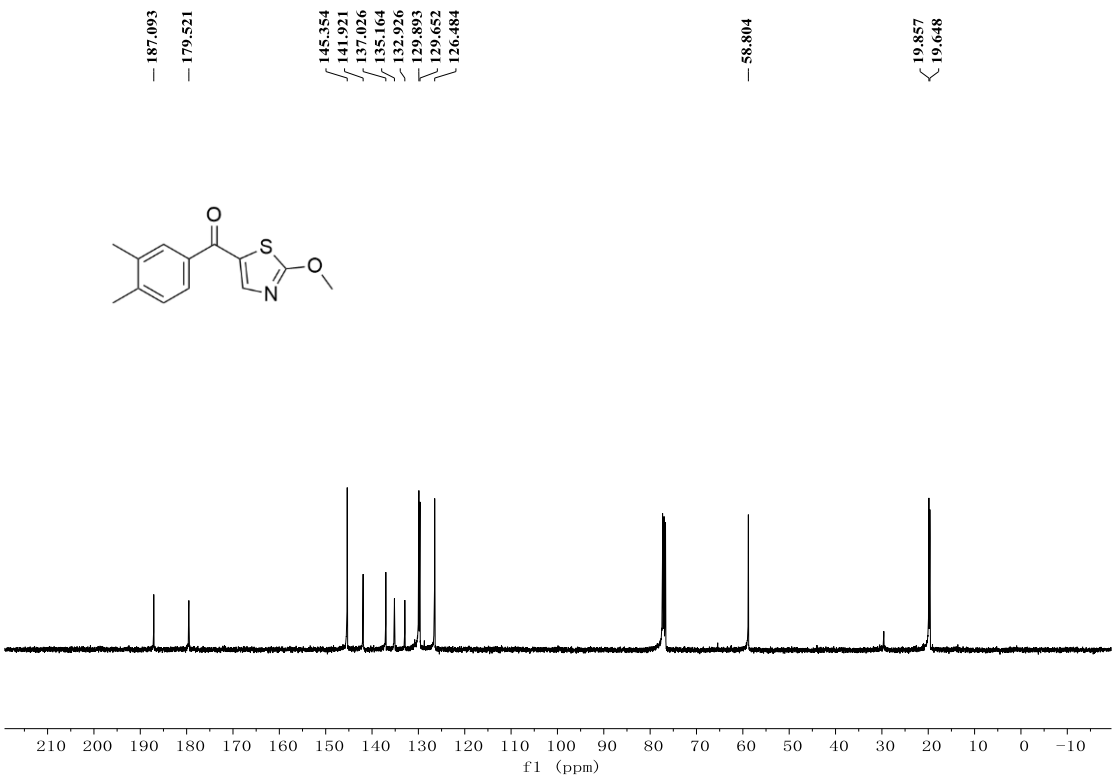


18b

^{1}H NMR

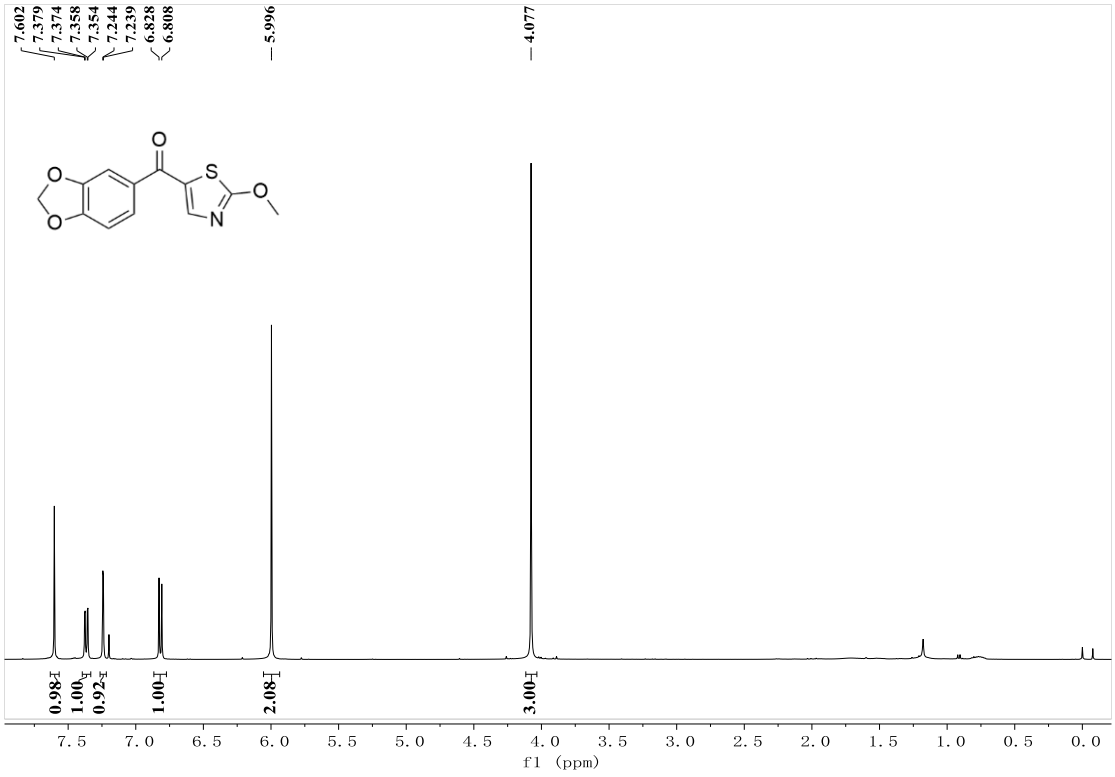


^{13}C NMR

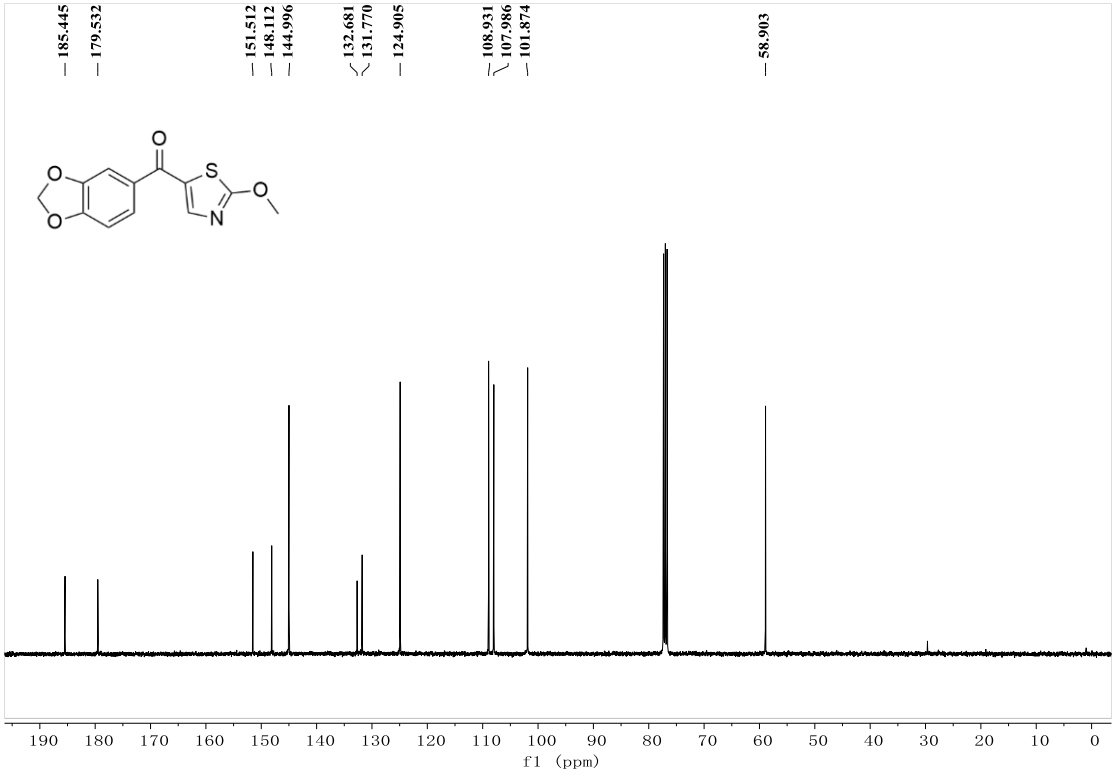


19b

^{1}H NMR

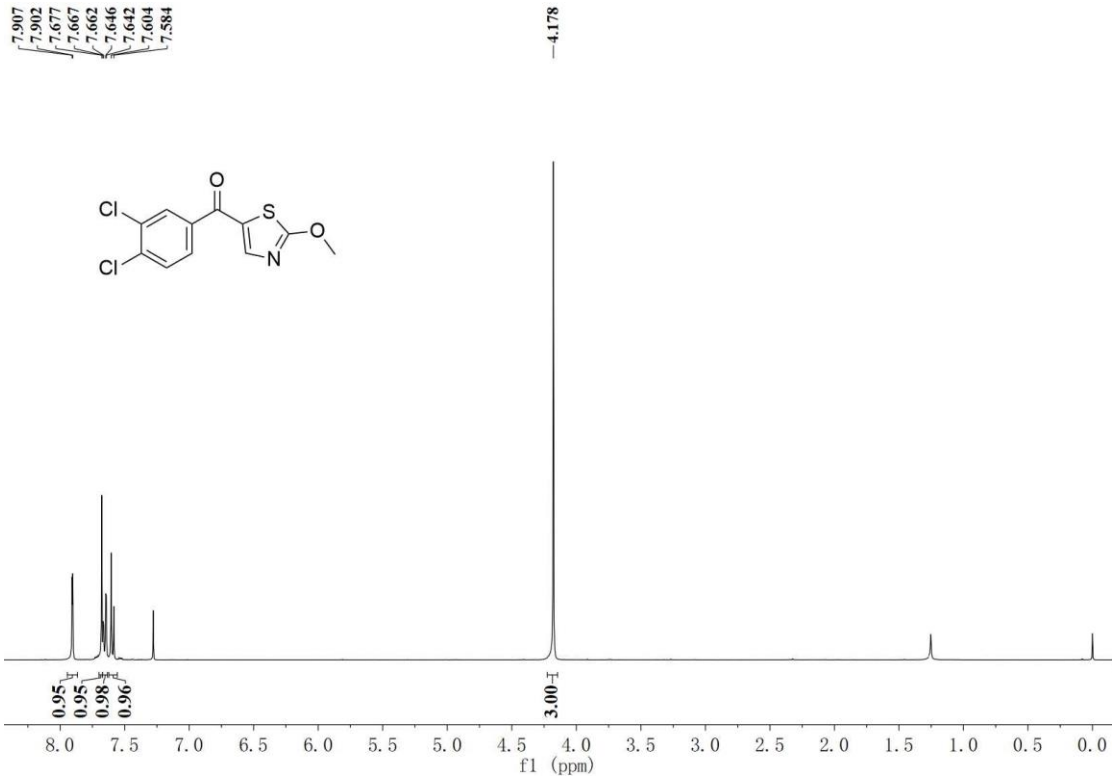


^{13}C NMR

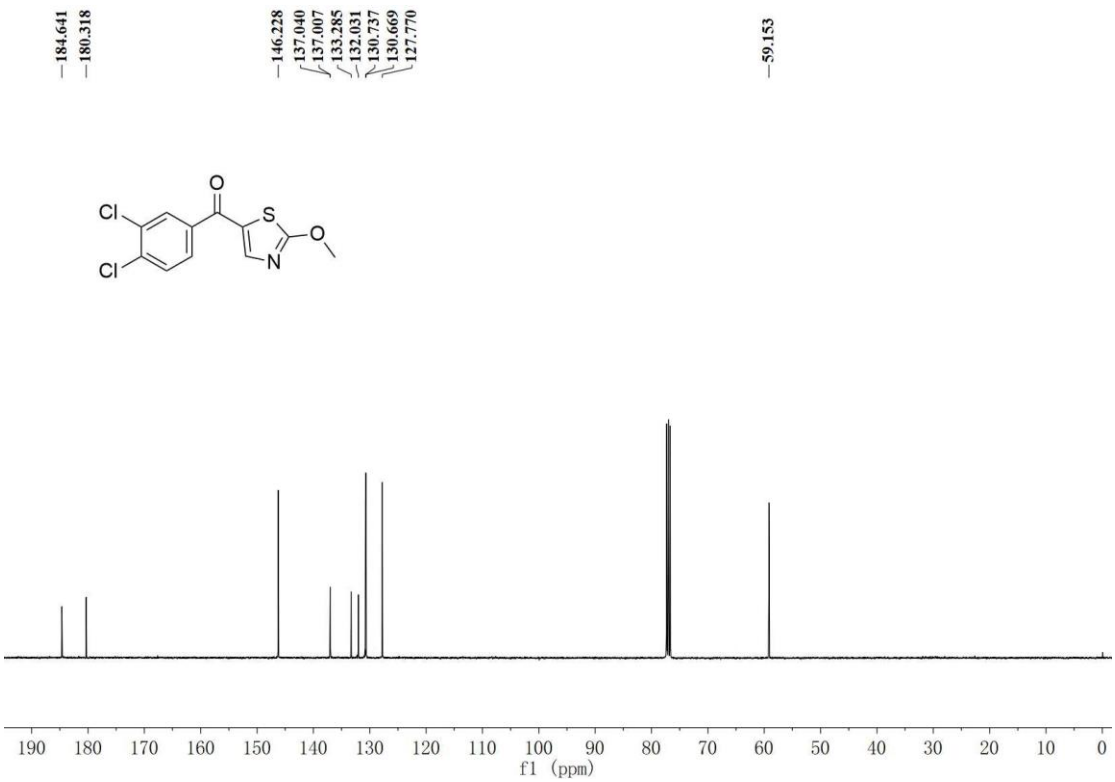


20b

^{1}H NMR

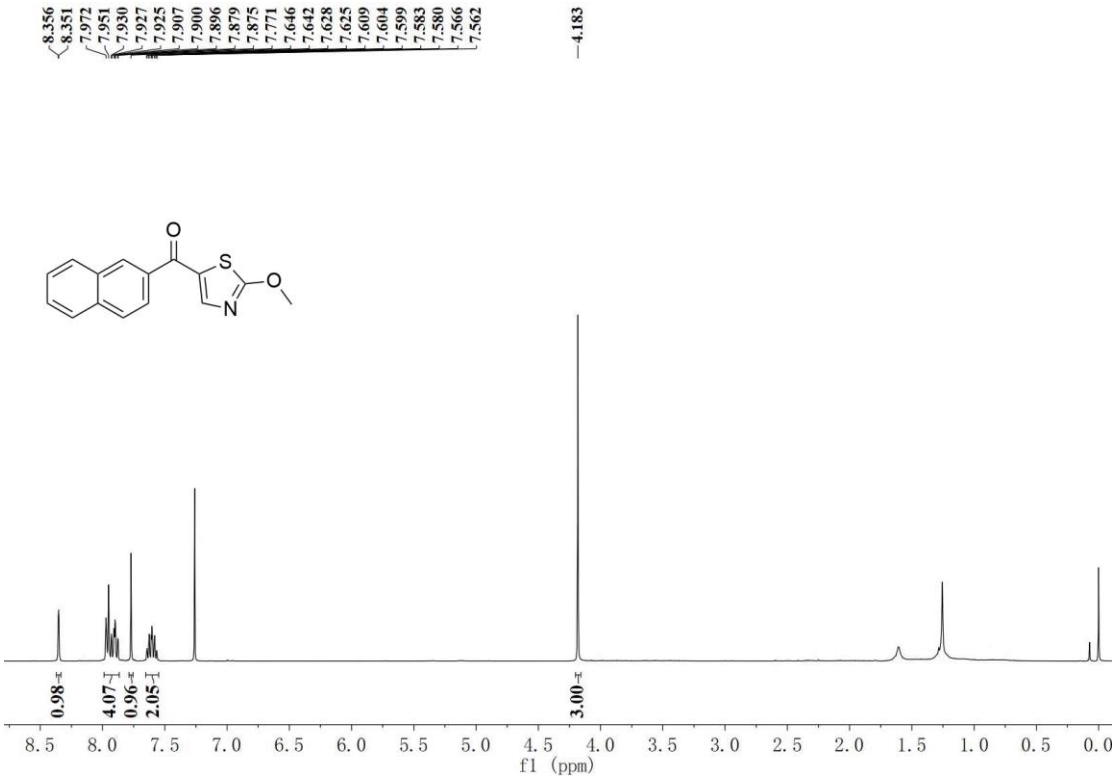


^{13}C NMR

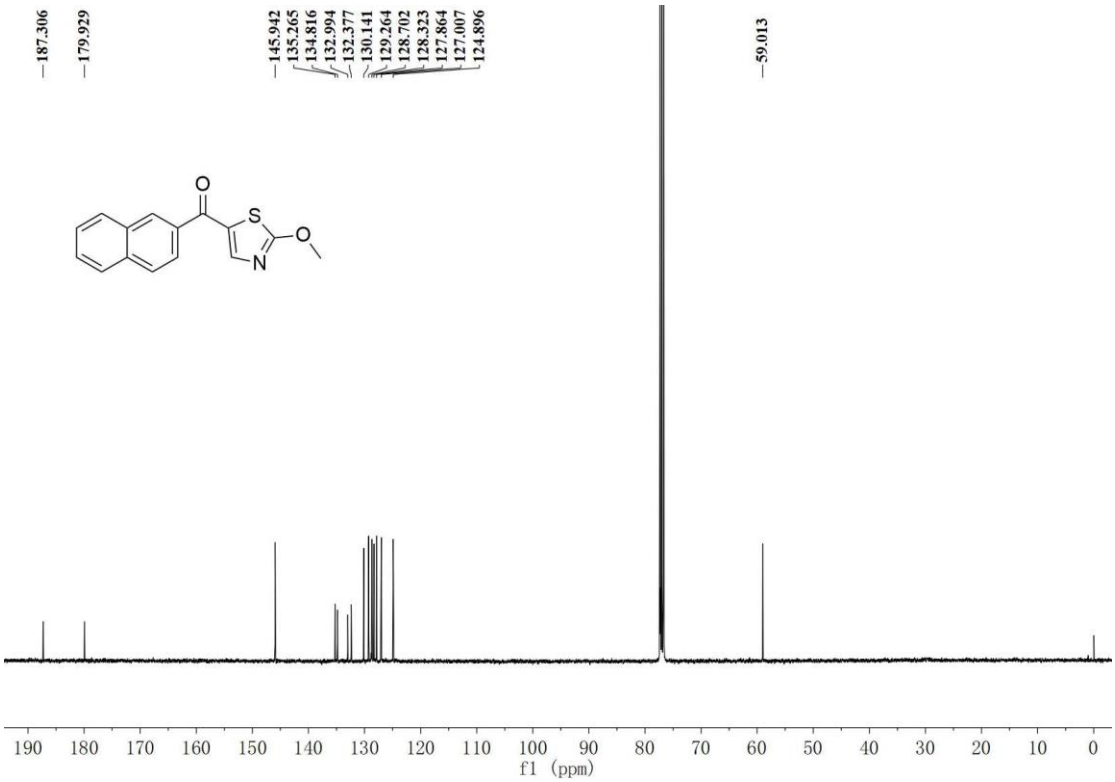


21b

^{1}H NMR

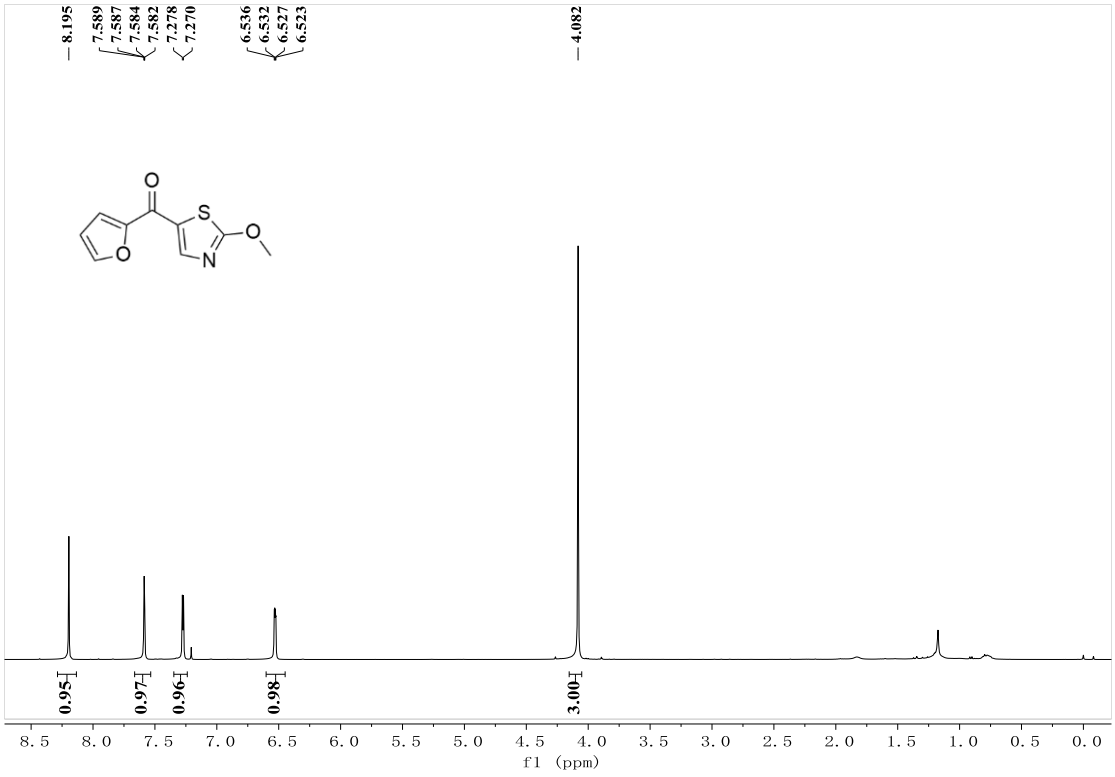


^{13}C NMR

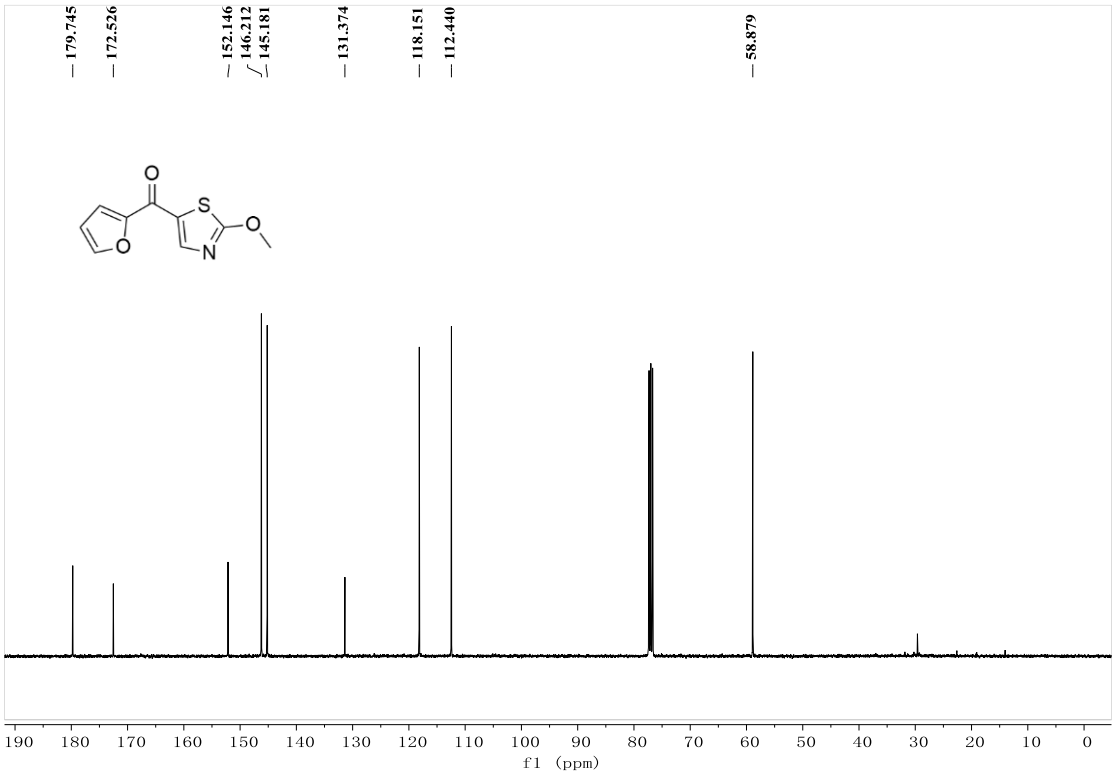


22b

^{1}H NMR

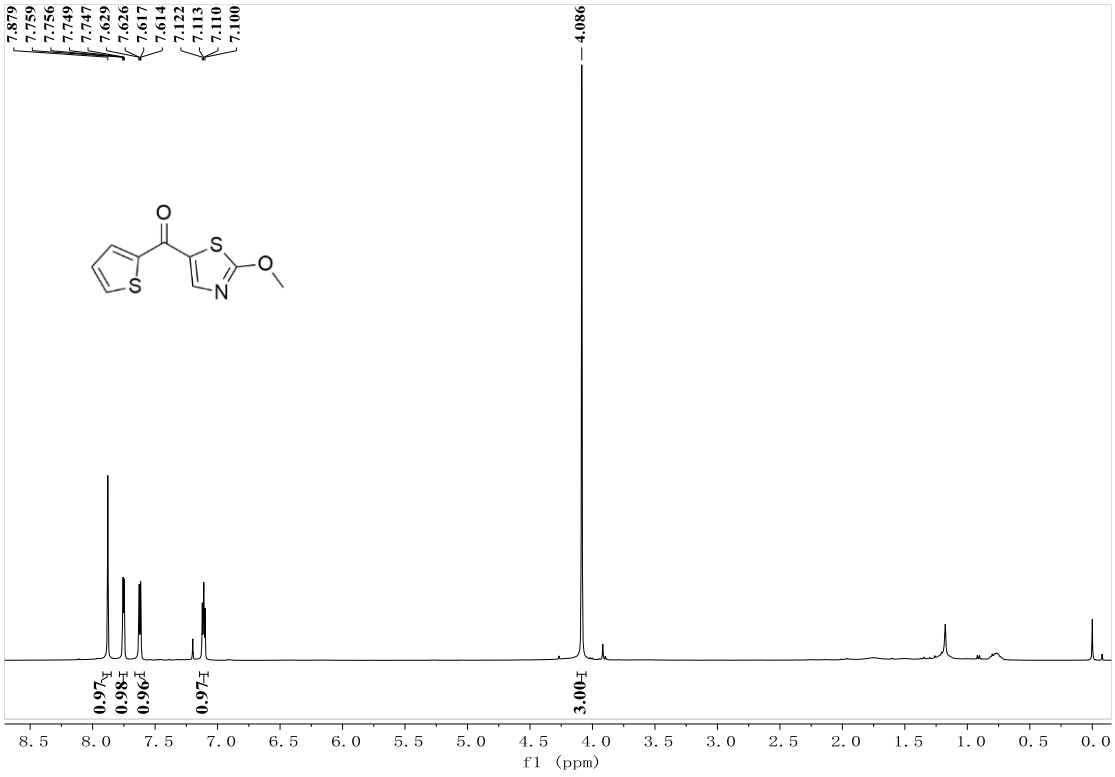


^{13}C NMR

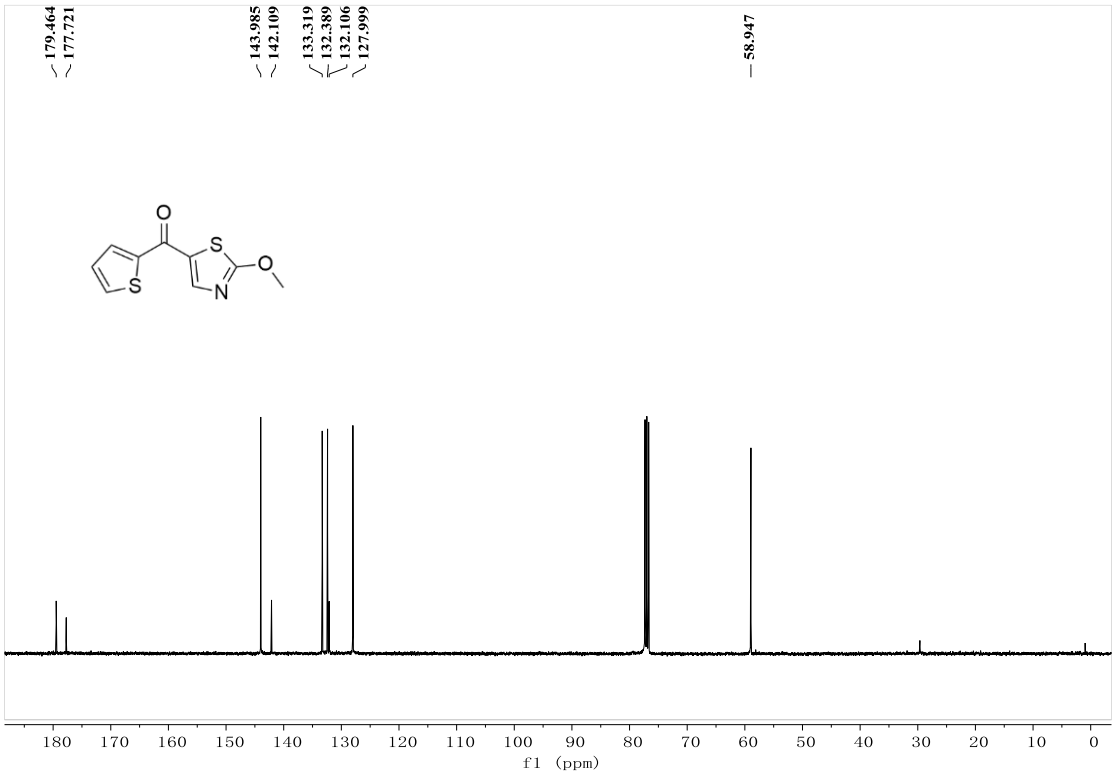


23b

^{1}H NMR

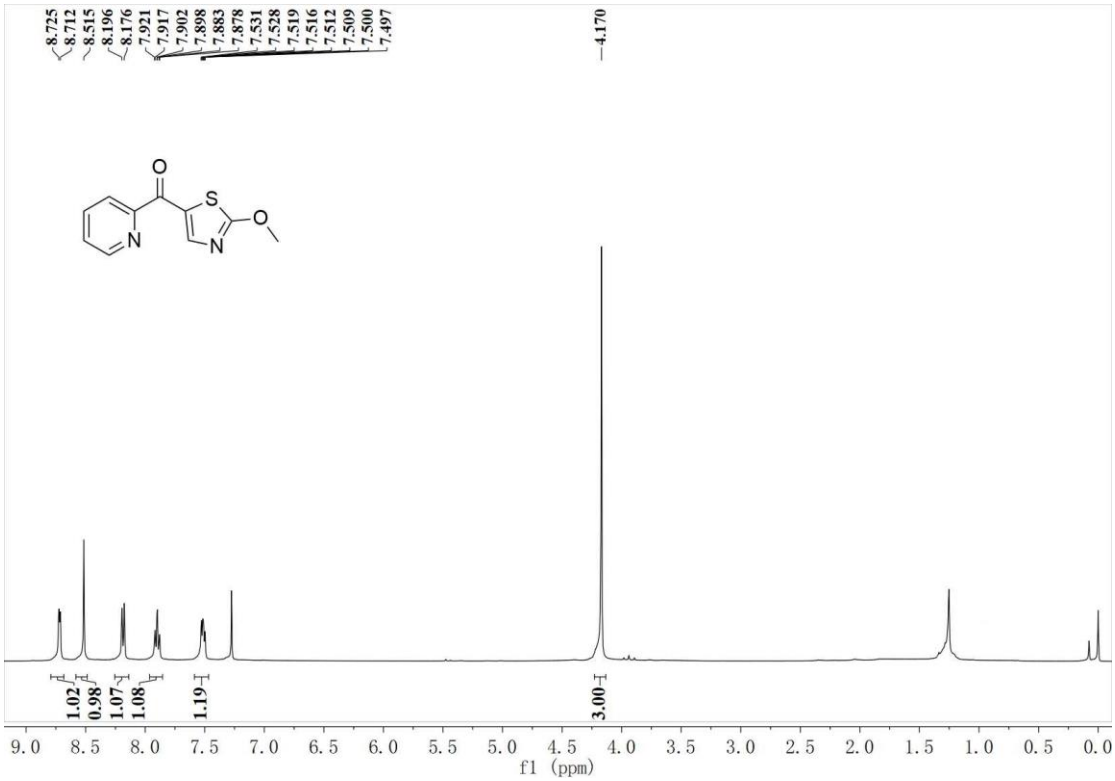


^{13}C NMR

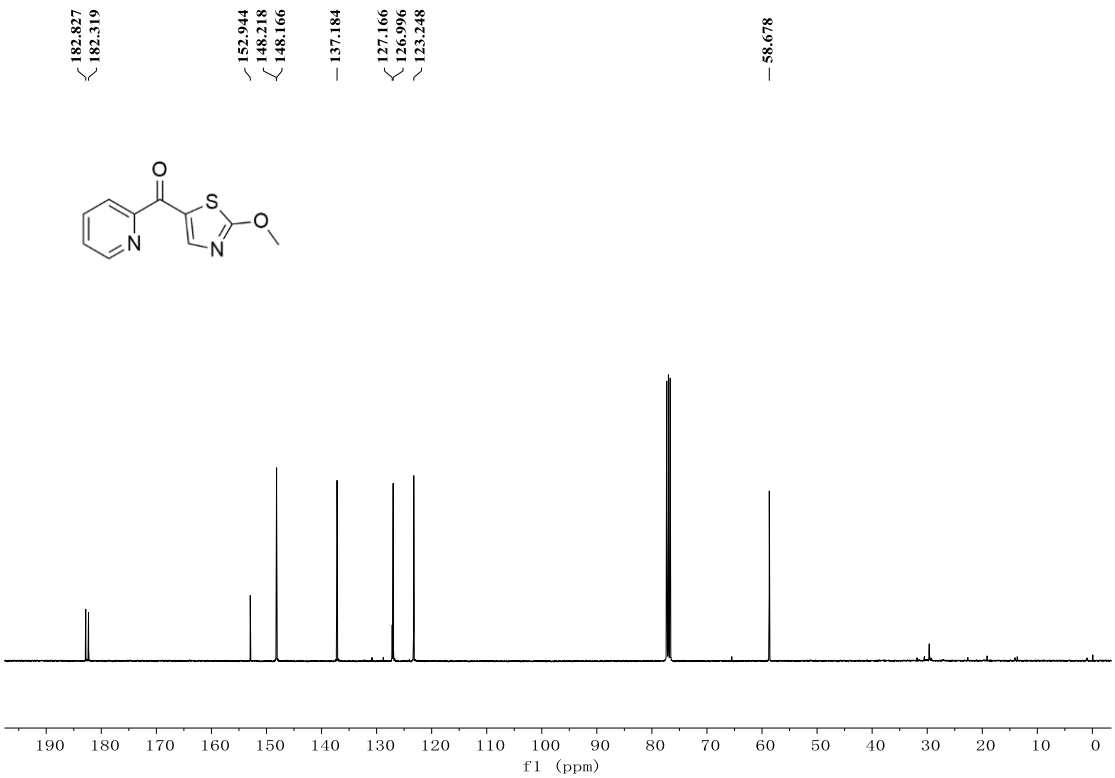


24b

^{1}H NMR

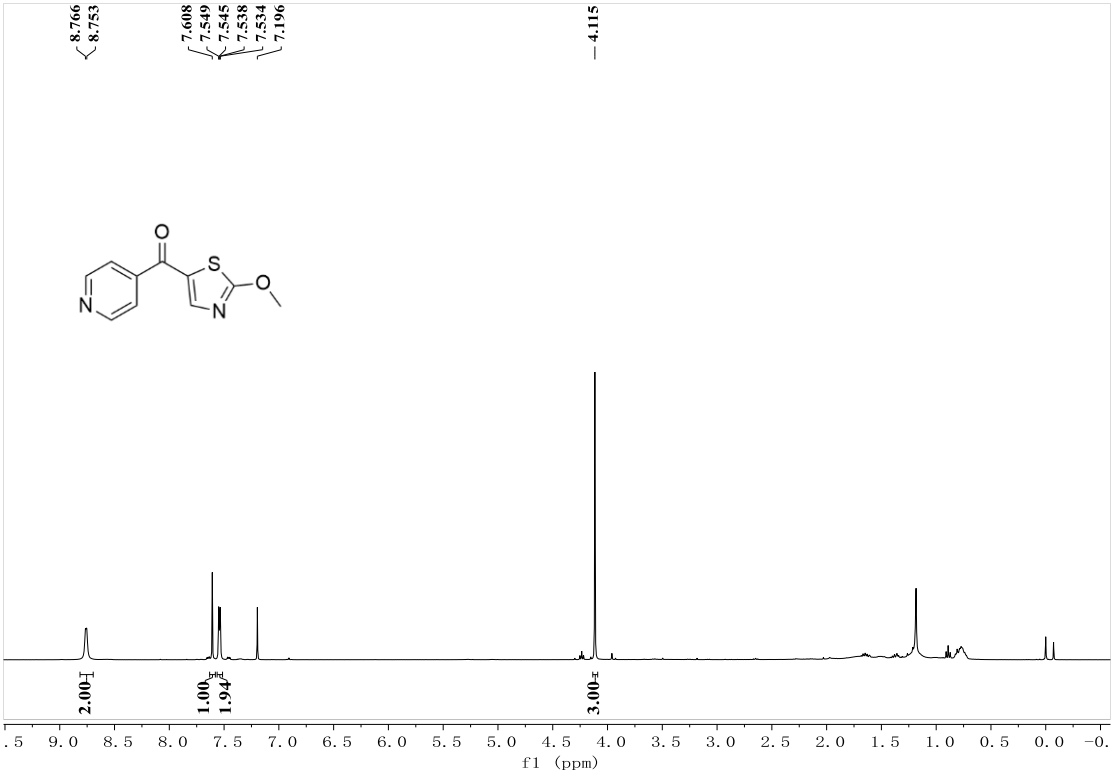


^{13}C NMR

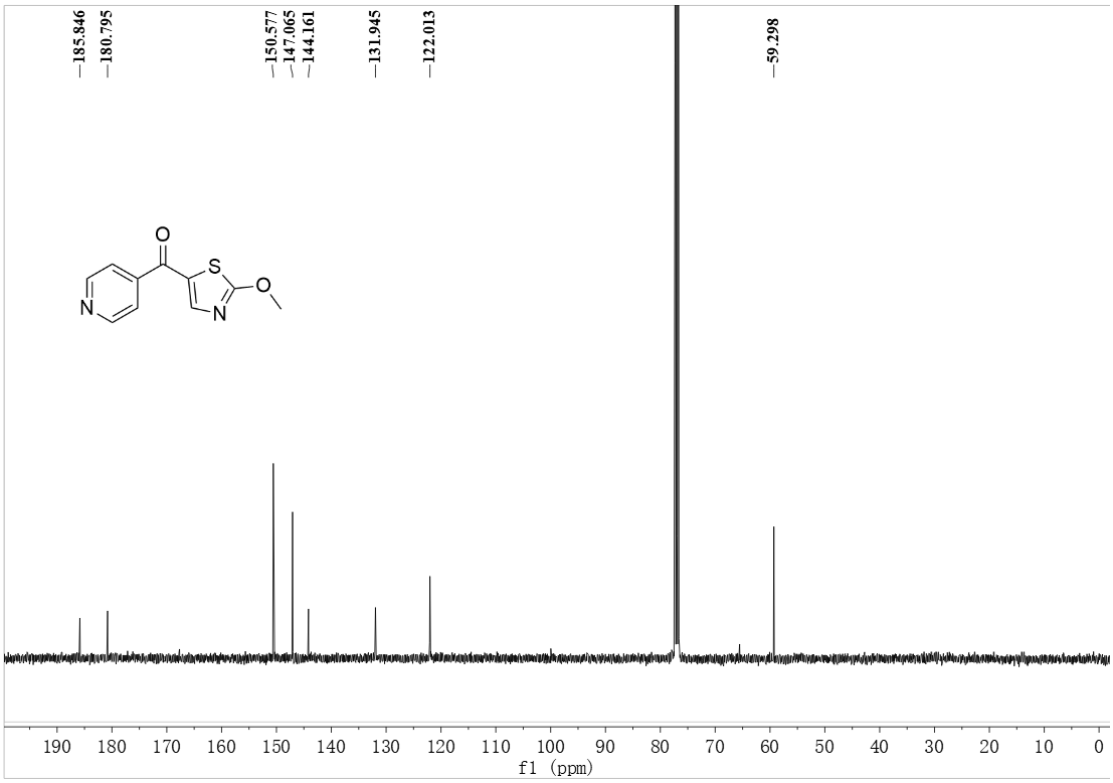


25b

^{1}H NMR

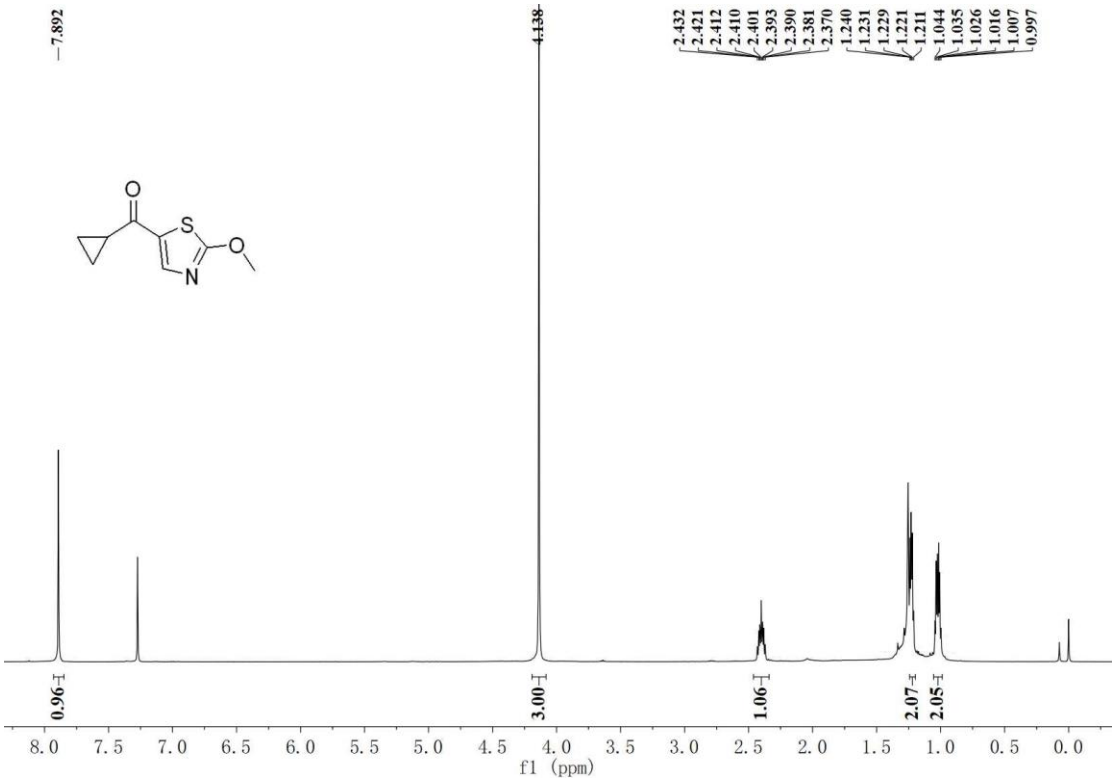


^{13}C NMR

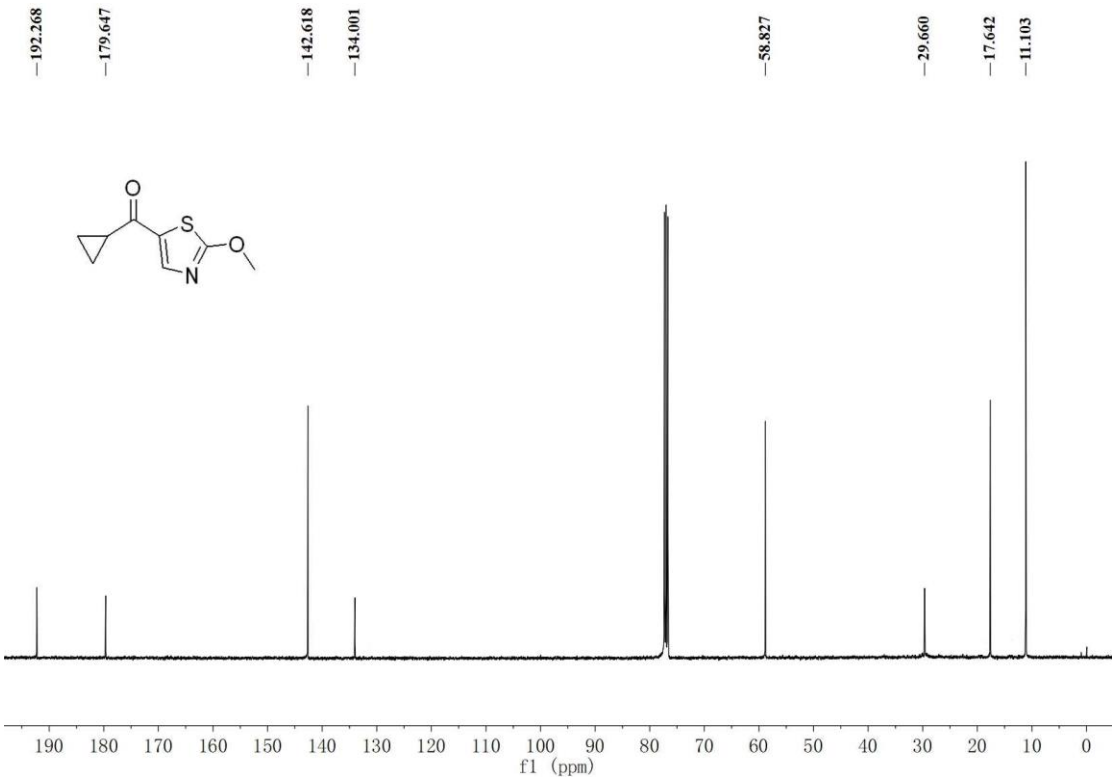


26b

^{1}H NMR

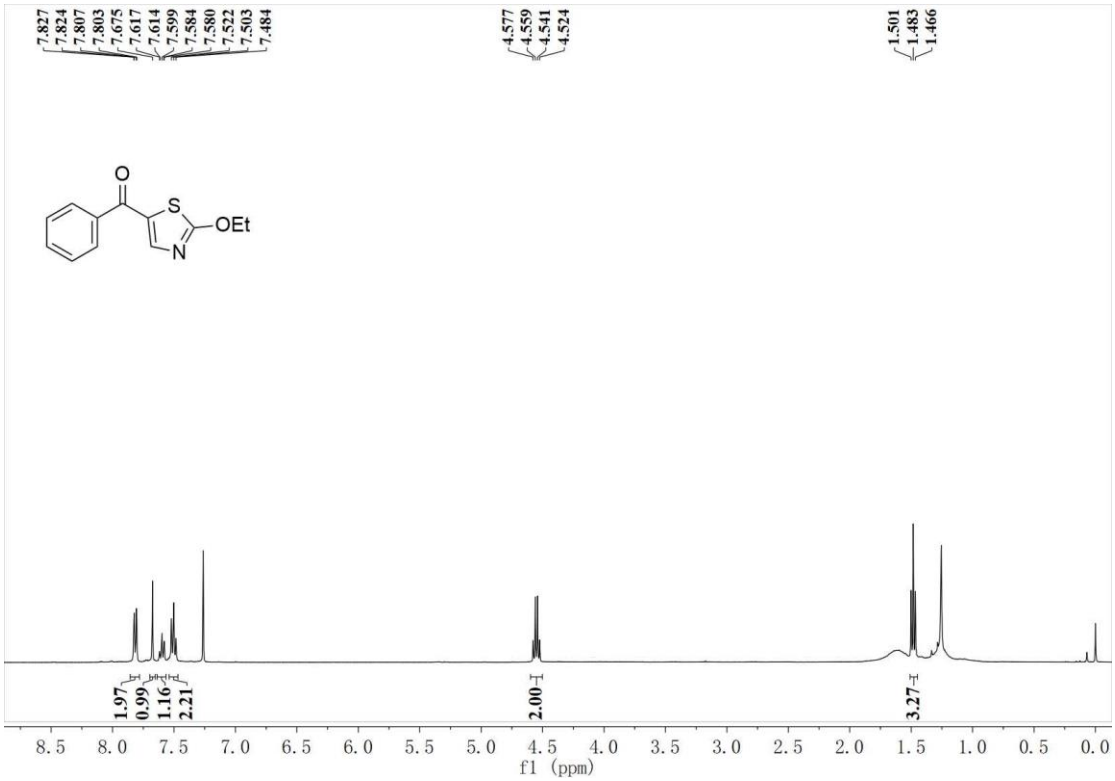


^{13}C NMR

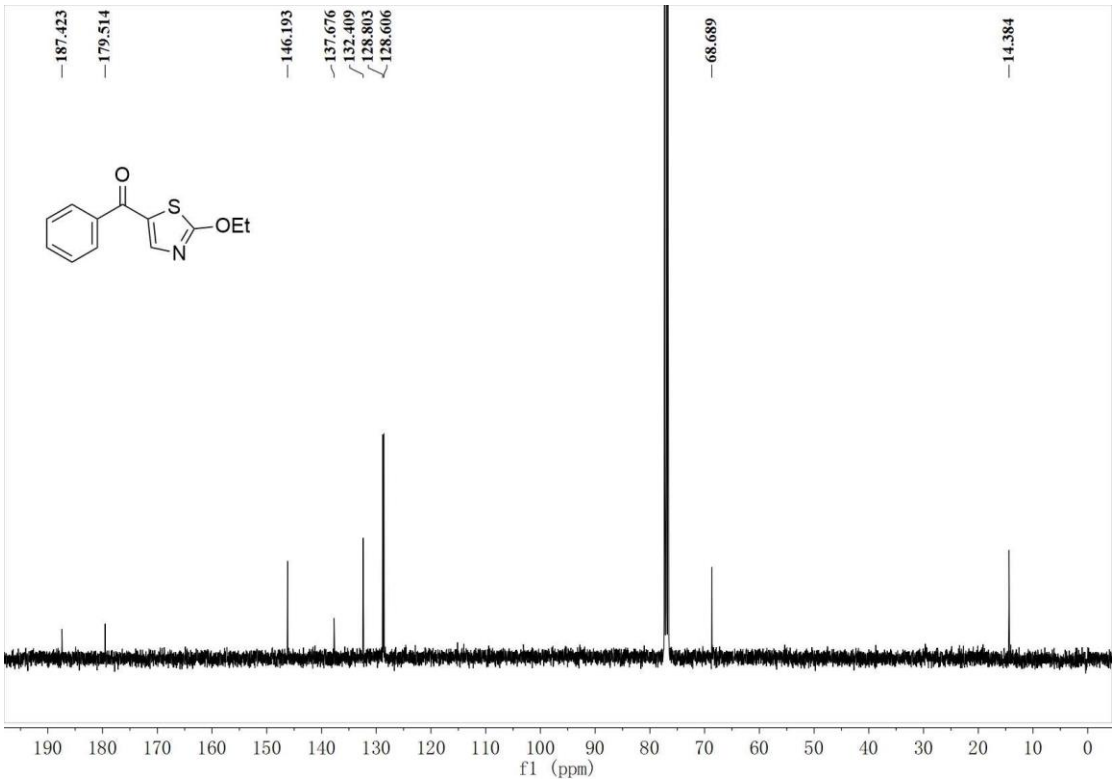


27b

^{1}H NMR

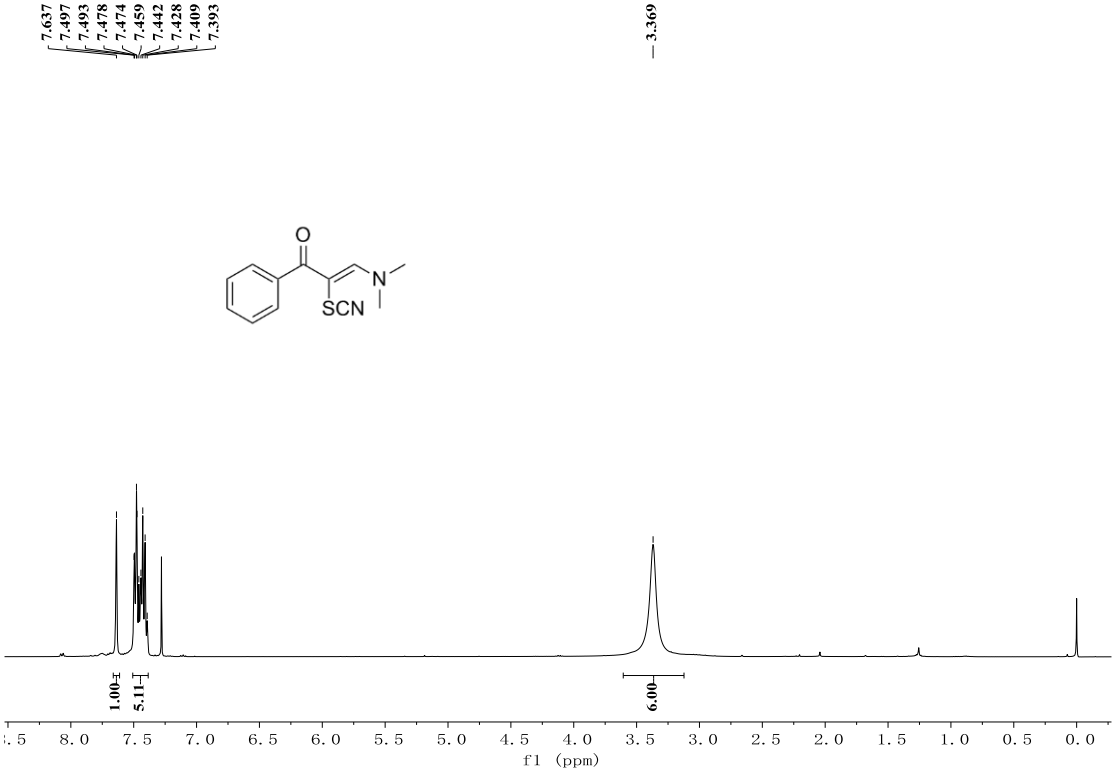


^{13}C NMR

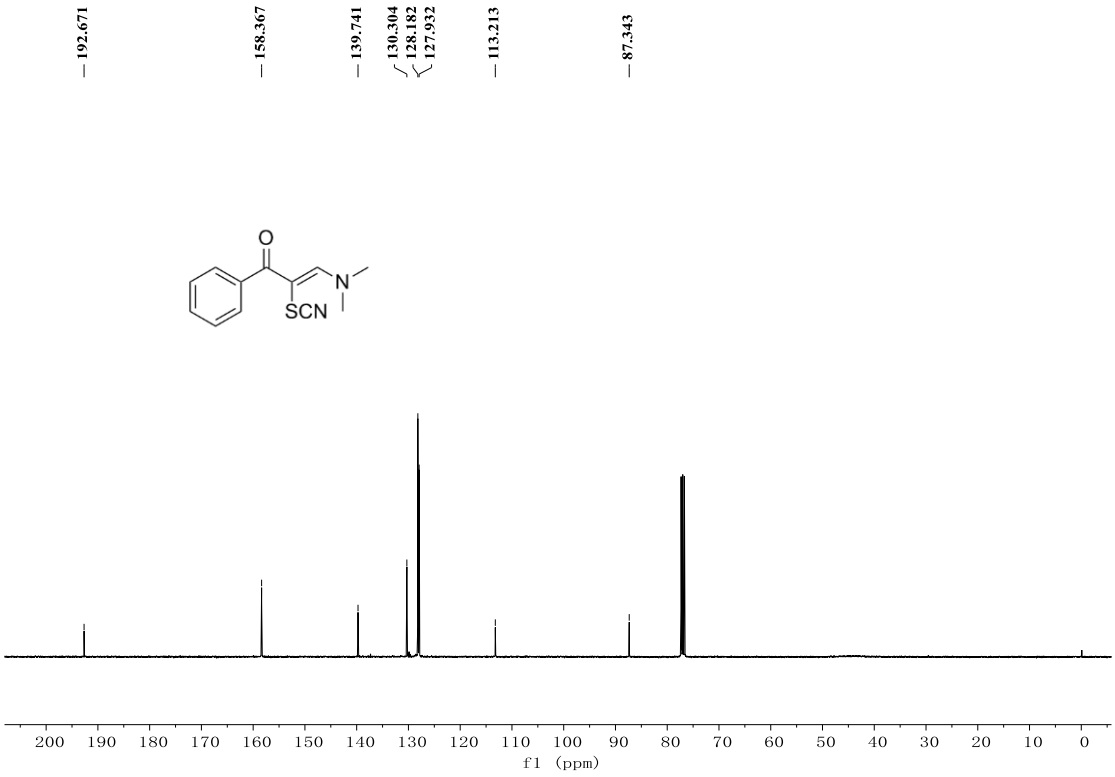


1c

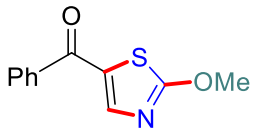
^{1}H NMR



^{13}C NMR



6. Crystallography Data



1b

Crystallography Data of **1b**：CCDC 2245830 contain the supplementary crystallographic data for **1b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.CCDC

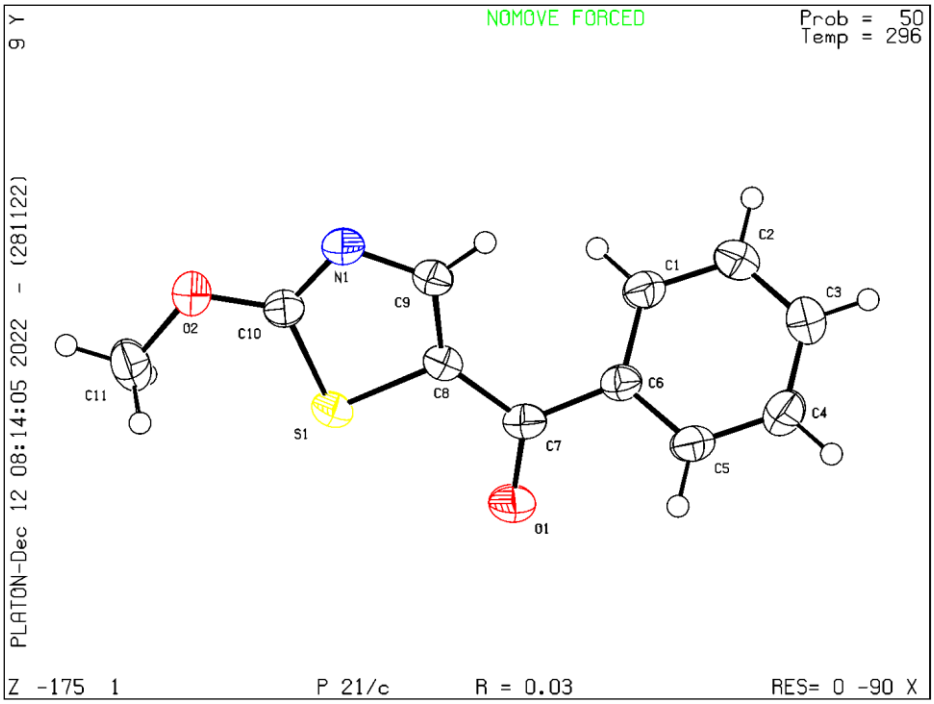


Table 1 Crystal data and structure refinement for 1b.

Identification code	1
Empirical formula	$C_{11}H_9NO_2S$
Formula weight	219.25
Temperature/K	296(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.545(5)
b/Å	3.9268(16)

c/Å	21.018(9)
α/°	90
β/°	106.758(6)
γ/°	90
Volume/Å^3	991.5(7)
Z	4
ρ_{calc}g/cm^3	1.469
μ/mm^{-1}	0.302
F(000)	456.0
Crystal size/mm^3	0.260 × 0.250 × 0.220
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.984 to 49.994
Index ranges	-10 ≤ h ≤ 14, -4 ≤ k ≤ 4, -24 ≤ l ≤ 24
Reflections collected	4629
Independent reflections	1748 [R_{int} = 0.0157, R_{sigma} = 0.0177]
Data/restraints/parameters	1748/0/137
Goodness-of-fit on F^2	1.010
Final R indexes [I>=2σ (I)]	R_1 = 0.0305, wR_2 = 0.0943
Final R indexes [all data]	R_1 = 0.0349, wR_2 = 0.0979
Largest diff. peak/hole / e Å^{-3}	0.18/-0.26

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 1b. U_{eq} s defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
S1	4865.0(3)	4800.1(10)	3262.7(2)	33.55(18)
O2	6981.6(10)	5921(4)	3985.5(6)	44.4(3)

O1	2474.3(11)	5010(4)	2716.8(6)	51.5(4)
N1	5595.9(11)	7639(4)	4411.5(6)	37.3(3)
C6	1882.5(13)	6758(4)	3631.2(7)	31.3(4)
C7	2737.9(14)	5918(4)	3298.2(7)	33.2(4)
C8	3914.6(13)	6211(4)	3657.5(7)	29.3(4)
C5	893.2(14)	8188(5)	3247.8(8)	37.8(4)
C9	4465.9(13)	7641(4)	4248.1(7)	33.1(4)
C1	2001.8(14)	6024(5)	4293.5(8)	37.9(4)
C4	49.7(15)	8896(5)	3522.1(10)	44.8(4)
C10	5909.2(13)	6210(4)	3939.0(8)	32.6(4)
C3	179.2(15)	8178(5)	4181.9(9)	46.8(5)
C2	1144.7(15)	6740(5)	4562.2(9)	45.9(5)
C11	7261.1(17)	4262(5)	3447.7(10)	49.2(5)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 1b. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\cdots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	38.1(3)	37.3(3)	26.3(3)	-4.97(16)	10.94(18)	-0.03(16)
O2	32.6(7)	60.2(8)	41.3(7)	-1.6(6)	12.1(5)	4.1(6)
O1	43.0(7)	79.0(10)	29.9(7)	-16.1(6)	6.5(6)	-5.0(6)
N1	35.9(8)	45.7(8)	28.3(7)	-5.3(6)	6.1(6)	-0.5(6)
C6	32.5(8)	31.8(8)	27.6(8)	-1.4(6)	5.7(6)	-2.9(7)
C7	36.7(9)	34.7(8)	25.9(8)	-0.8(7)	5.4(6)	-2.4(7)
C8	33.9(8)	29.4(8)	25.6(7)	-0.3(6)	9.9(6)	0.2(6)
C5	37.8(9)	44.4(10)	27.5(8)	1.7(7)	3.5(7)	0.2(8)
C9	35.4(9)	37.2(9)	26.8(8)	-3.0(7)	8.9(7)	0.8(7)
C1	34.4(9)	45.9(10)	31.0(8)	5.5(8)	5.7(7)	0.5(8)
C4	33.7(9)	51.3(11)	45.6(10)	1.3(9)	5.4(7)	5.9(8)

C10	33.7(8)	34.1(8)	29.4(8)	4.3(7)	8.1(6)	2.0(7)
C3	37.9(10)	59.6(12)	46.7(10)	-2.4(9)	18.0(8)	2.2(8)
C2	45.3(10)	61.5(12)	32.6(9)	3.6(8)	13.9(8)	-1.0(9)
C11	45.9(11)	54.1(11)	55.2(12)	0.2(9)	26.8(9)	7.0(9)

Table 4 Bond Lengths for 1b.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	C10	1.7232(17)	C6	C5	1.389(2)
S1	C8	1.7285(16)	C6	C7	1.478(2)
O2	C10	1.325(2)	C7	C8	1.456(2)
O2	C11	1.433(2)	C8	C9	1.356(2)
O1	C7	1.223(2)	C5	C4	1.372(3)
N1	C10	1.297(2)	C1	C2	1.380(2)
N1	C9	1.359(2)	C4	C3	1.378(3)
C6	C1	1.387(2)	C3	C2	1.366(3)

Table 5 Bond Angles for 1b.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	S1	C8	88.08(8)	C7	C8	S1	117.54(12)
C10	O2	C11	117.05(14)	C4	C5	C6	120.46(16)
C10	N1	C9	109.34(14)	N1	C9	C8	116.78(14)
C1	C6	C5	119.09(15)	C2	C1	C6	119.82(16)
C1	C6	C7	123.11(14)	C5	C4	C3	120.00(17)
C5	C6	C7	117.71(14)	N1	C10	O2	120.40(15)
O1	C7	C8	118.87(15)	N1	C10	S1	116.41(13)
O1	C7	C6	120.93(15)	O2	C10	S1	123.19(12)
C8	C7	C6	120.19(14)	C2	C3	C4	120.05(16)

C9	C8	C7	132.89(15)	C3	C2	C1	120.58(17)
C9	C8	S1	109.38(12)				

Table 6 Torsion Angles for 1b.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C1	C6	C7	O1	143.99(18)	S1	C8	C9	N1	-1.01(19)
C5	C6	C7	O1	-32.6(2)	C5	C6	C1	C2	-0.4(3)
C1	C6	C7	C8	-36.9(2)	C7	C6	C1	C2	-176.96(17)
C5	C6	C7	C8	146.50(16)	C6	C5	C4	C3	-0.2(3)
O1	C7	C8	C9	167.31(18)	C9	N1	C10	O2	179.77(15)
C6	C7	C8	C9	-11.8(3)	C9	N1	C10	S1	0.49(19)
O1	C7	C8	S1	-6.9(2)	C11	O2	C10	N1	179.03(16)
C6	C7	C8	S1	173.93(12)	C11	O2	C10	S1	-1.8(2)
C10	S1	C8	C9	1.00(13)	C8	S1	C10	N1	-0.90(14)
C10	S1	C8	C7	176.54(14)	C8	S1	C10	O2	179.85(15)
C1	C6	C5	C4	0.6(3)	C5	C4	C3	C2	-0.4(3)
C7	C6	C5	C4	177.36(16)	C4	C3	C2	C1	0.6(3)
C10	N1	C9	C8	0.4(2)	C6	C1	C2	C3	-0.2(3)
C7	C8	C9	N1	-175.60(17)					

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2 ×10^3) for 1b.

Atom	*x*	*y*	*z*	U(eq)
H5	802	8669	2802	45
H9	4089	8578	4528	40
H1	2658	5053	4556	45
H4	-610	9861	3263	54

H3	-391	8673	4368	56
H2	1225	6240	5006	55
H11A	6966	5546	3047	74
H11B	6949	2011	3391	74
H11C	8056	4116	3545	74