

Supporting Information

Synthesis of Oxazolines via Cascade Reaction between Azaoxyallyl Cations and 1, 2-Benzisoxazoles

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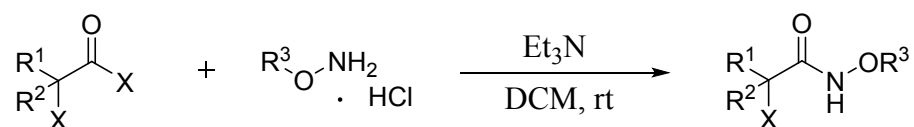
General Information

Reagents and Solvents: All solvents were purified and dried according to standard methods. PE refers to petroleum ether (b.p. 60 – 90 °C) and EA refers to ethyl acetate.

Chromatography: Flash column chromatography was carried out using commercially available 200-300 mesh under pressure and conducted by eluting with PE/EA, which are listed as volume/volume ratios.

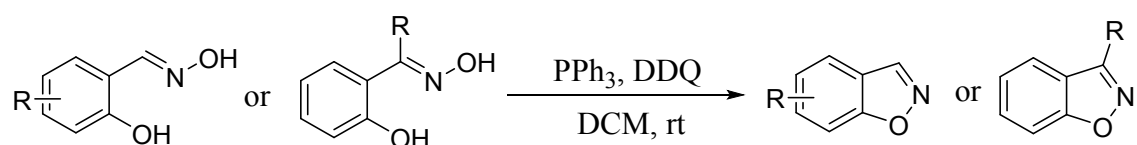
Data collection: Melting point (m.p.) was measured on a microscopic melting point apparatus. ^1H NMR and ^{13}C NMR spectra were collected on BRUKER AV-300 (300MHz) or BRUKER AV-400 (400MHz) spectrometer using CDCl_3 as solvent. Chemical shifts of ^1H NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane ($\delta=0.00$ ppm) with the solvent resonance as an internal standard (CDCl_3 , $\delta=7.26$ ppm). Data are reported as follows: chemical shift in ppm (δ), multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, brs = broad singlet, m= multiplet), coupling constant (Hz), and integration. Chemical shifts of ^{13}C NMR were reported in ppm with the solvent as the internal standard (CDCl_3 , $\delta=77.0$ ppm). High Resolution Mass measurement was performed on Agilent QTOF 6520 mass spectrometer electron spray ionization (ESI) as the ion source. Unless otherwise indicated, all other reagents and solvents were obtained from commercial suppliers and used without further purification. Absorption measurements were performed either using a Shimadzu UV-3600 Plus UV-Vis spectrophotometer. Emission measurements were performed using a Horiba, Ltd Fluoro Max-4 photoluminescence spectrometer.

General Procedures for the Preparation of α -Halohydroxamates¹



To a suspension of the *O*-alkoxyamine hydrochloride and triethylamine in DCM (0.25 M) was added dropwise the α -haloacid halide at 0 °C. The reaction mixture was stirred at this temperature until complete consumption of starting material (detected by TLC). The mixture was warmed to room temperature and quenched with water. The organic phase was washed with water ($\times 3$), then washed with brine ($\times 1$), dried over sodium sulfate, filtered and evaporated. Purification *via* a flash column chromatography (PE/EA=8/1) provided the α -halohydroxamates.

General Procedures for 1, 2-benzisoxazoles²

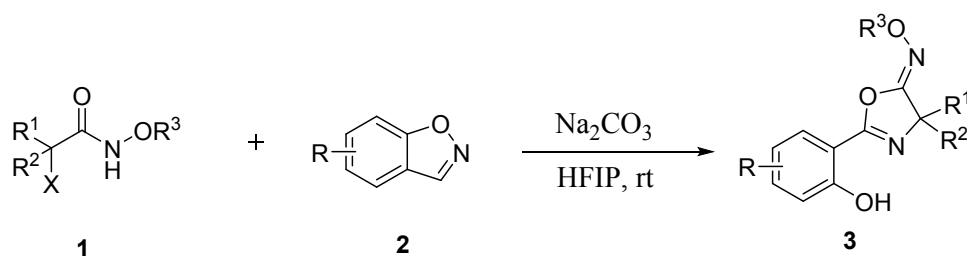


A mixture of Ph_3P (1.5 eq.) and DDQ (1.5 eq.) in dry DCM (5.0 mL) was stirred at room temperature for 1 min. Substituted salicylaldoximes (1.0 mmol) were then added. The green color of the reaction mixture changed to brown after 1 min. TLC monitoring showed completion of the reaction. The solvent was evaporated. Column chromatography of the crude mixture on silica gel using (PE/EA=3/1) as eluent gave the desired products.

1. C. S. Jeffrey, K. L. Barnes, J. A. Eickhoff and C. R. Carson, *J. Am. Chem. Soc.*, 2011, **133**, 7688-7691.

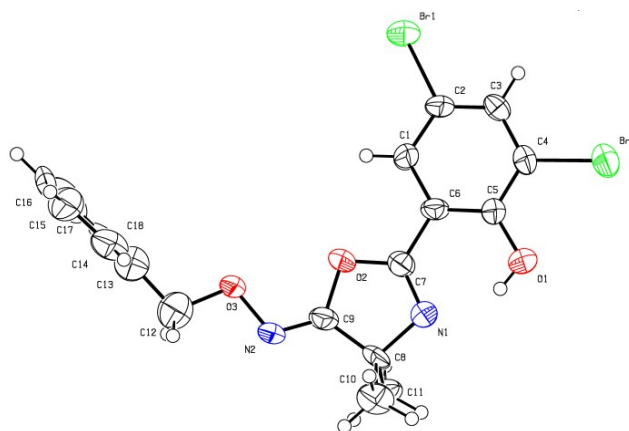
2. N. Iranpoor, H. Firouzabadi and N. Nowrouzi, *Tetrahedron Lett.*, 2006, **47**, 8247-8250.

Preparation of [3+2] Cyclization Reactions



To a 10 mL round-bottom flask was sequentially added α -halohydroxamate **1** (0.2 mmol, 1.0 eq.), Na_2CO_3 (0.40 mmol, 2.0 eq.), substituted 1, 2-benzisoxazoles **2** (0.3 mmol, 1.5 eq.) and HFIP (1.0 mL). The reaction mixture was stirred at room temperature for 3 hours. Upon completion of the reaction (monitored by TLC), the reaction mixture was diluted with EA. The crude material was then filtered through celite and washed with EA. The filtrate was concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/EA = 20/1) to afford the pure product.

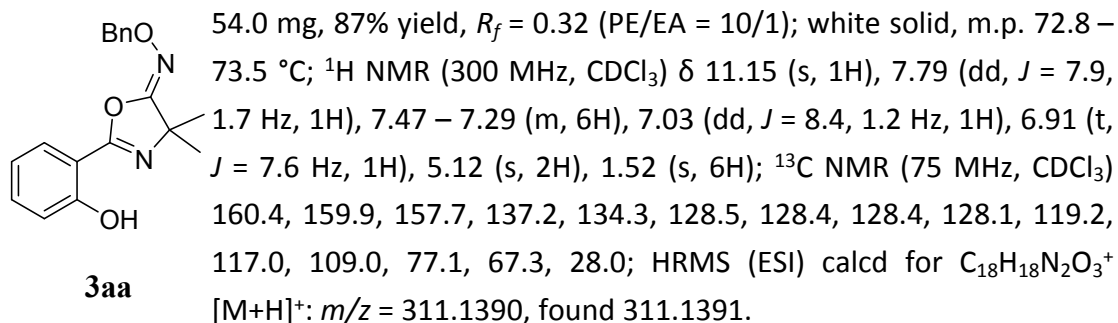
X-ray Crystallography Data of 3ao (CCDC 1900697)



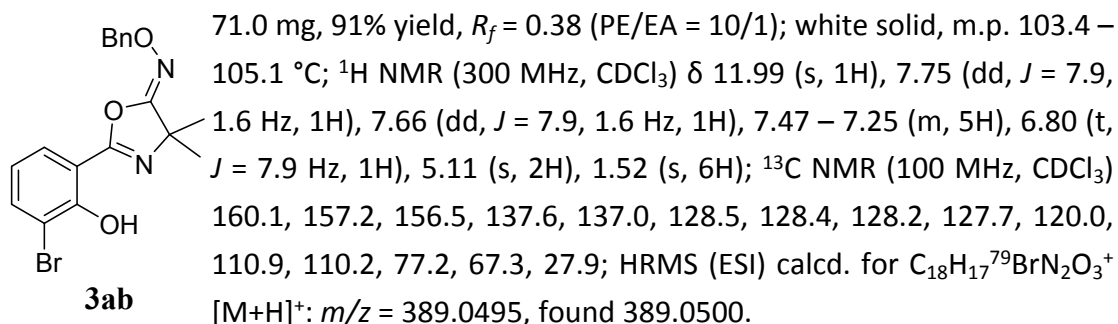
Empirical formula	$C_{18}H_{16}Br_2N_2O_3$
Formula weight	468.15
Temperature/K	293(2)
Crystal system	Triclinic
Space group	P-1
a/Å	5.5740(11)
b/Å	12.623(3)
c/Å	14.179(3)
$\alpha/^\circ$	110.91(3)
$\beta/^\circ$	95.03(3)
$\gamma/^\circ$	95.13(3)
Volume	920.5(4)
Z	2
$D_x, g/cm^3$	1.689
F(000)	464.0
Crystal size/mm ³	0.200 × 0.100 × 0.100
$\mu/m\text{m}^{-1}$	4.422
T_{\min}, T_{\max}	0.594, 0.643
Radiation	MoK α ($\lambda = 0.71073$)
Reflections collected	3762
h,k,l(max)	6,15,17
Data/restraints/parameters	3384/0/214
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.1018, wR_2 = 0.2194$
Final R indexes [all data]	$R_1 = 0.2092, wR_2 = 0.2571$
S	1.216
N_{par}	214

Copies of ¹H NMR and ¹³C NMR spectra of the Titled Compounds

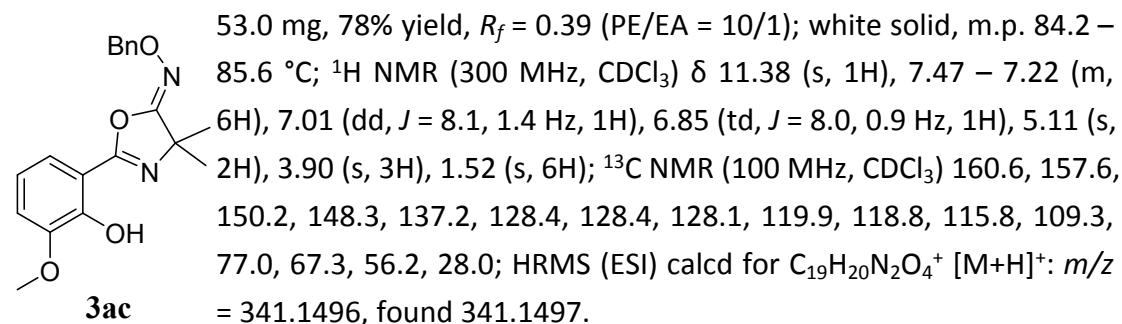
(Z)-2-(2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



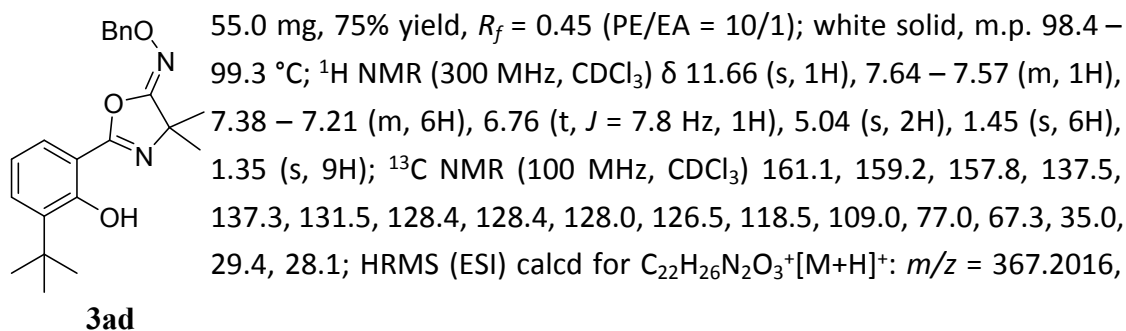
(Z)-2-(3-bromo-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



(Z)-2-(2-hydroxy-3-methoxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime

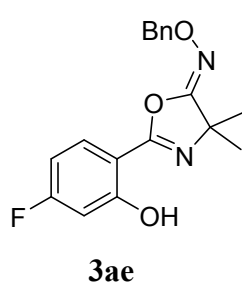


(Z)-2-(3-(tert-butyl)-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



found 367.2012.

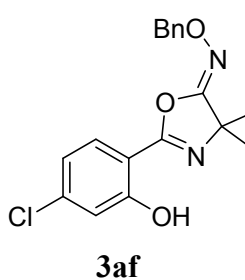
(Z)-2-(4-fluoro-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



3ae

56.0 mg, 85% yield, $R_f = 0.44$ (PE/EA = 10/1); white solid, m.p. 83.5 – 84.4 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ , ppm 11.43 (s, 1H), 7.76 (dd, $J = 8.8, 6.4$ Hz, 1H), 7.47 – 7.25 (m, 5H), 6.72 (dd, $J = 10.4, 2.5$ Hz, 1H), 6.63 (ddd, $J = 8.8, 8.1, 2.5$ Hz, 1H), 5.11 (s, 2H), 1.51 (s, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) 166.4 (d, $J = 252.0$ Hz), 162.0 (d, $J = 13.0$ Hz), 159.9, 157.4, 137.1, 130.3 (d, $J = 11.0$ Hz), 128.5, 128.4, 128.1, 107.2 (d, $J = 23.0$ Hz), 105.8 (d, $J = 3.0$ Hz), 104.3 (d, $J = 24.0$ Hz), 77.1, 67.2, 28.0; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{17}\text{FN}_2\text{O}_3^+$ $[\text{M}+\text{H}]^+$: $m/z = 329.1296$, found 329.1291.

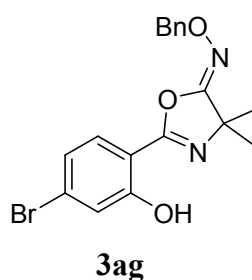
(Z)-2-(4-chloro-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



3af

57.0 mg, 83% yield, $R_f = 0.50$ (PE/EA = 10/1); white solid, m.p. 101.6 – 102.3 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 11.30 (s, 1H), 7.69 (d, $J = 8.5$ Hz, 1H), 7.47 – 7.25 (m, 5H), 7.04 (d, $J = 2.0$ Hz, 1H), 6.89 (dd, $J = 8.5, 2.0$ Hz, 1H), 5.11 (s, 2H), 1.51 (s, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) 160.5, 159.9, 157.2, 140.2, 137.0, 129.4, 128.5, 128.4, 128.1, 119.8, 117.4, 107.7, 77.2, 67.3, 28.0; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{17}\text{ClN}_2\text{O}_3^+$ $[\text{M}+\text{H}]^+$: $m/z = 345.1000$, found 345.1003.

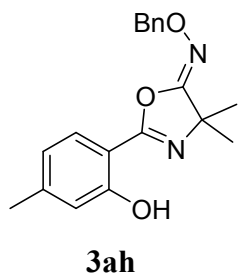
(Z)-2-(4-bromo-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



3ag

70.0 mg, 90% yield, $R_f = 0.50$ (PE/EA = 10/1); white solid, m.p. 99.8 – 100.7 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 11.20 (s, 1H), 7.53 (d, $J = 8.4$ Hz, 1H), 7.39 – 7.18 (m, 5H), 7.13 (d, $J = 1.8$ Hz, 1H), 6.96 (dd, $J = 8.5, 1.8$ Hz, 1H), 5.02 (s, 2H), 1.43 (s, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) 160.4, 160.0, 157.2, 137.0, 129.4, 128.5, 128.5, 128.4, 128.1, 122.7, 120.4, 108.1, 77.2, 67.3, 28.0; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{17}\text{BrN}_2\text{O}_3^+$ $[\text{M}+\text{H}]^+$: $m/z = 389.0495$, found 389.0491.

(Z)-2-(2-hydroxy-4-methylphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime

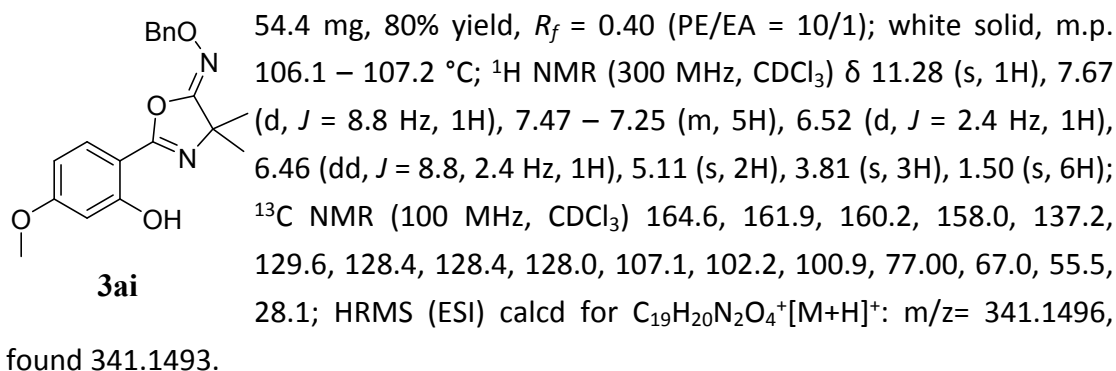


3ah

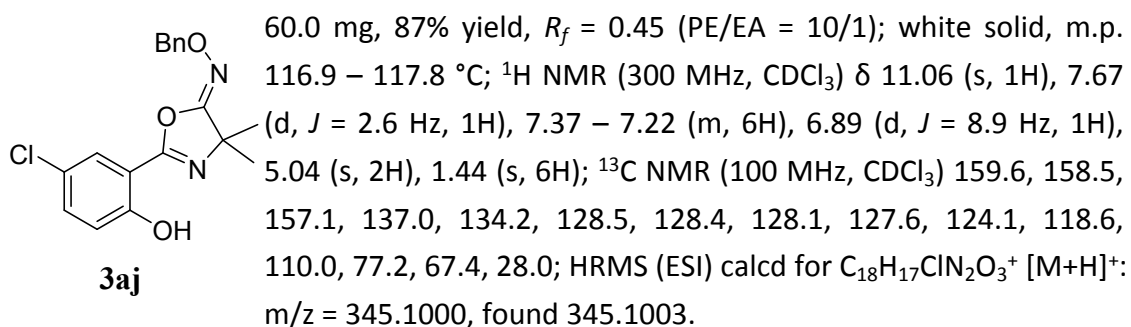
52.5 mg, 81% yield, $R_f = 0.42$ (PE/EA = 10/1); white solid, m.p. 70.3 – 71.2 °C; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 11.05 (s, 1H), 7.65 (d, $J = 8.0$ Hz, 1H), 7.47 – 7.19 (m, 5H), 6.83 (s, 1H), 6.71 (dd, $J = 8.0, 1.5$ Hz, 1H), 5.11 (s, 2H), 2.33 (s, 3H), 1.50 (s, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) 160.4, 159.9, 157.9, 145.5, 137.2, 128.5, 128.4, 128.2, 128.1, 120.4, 117.3, 106.5, 77.0, 67.18, 28.1, 22.0; HRMS (ESI)

calcd for $C_{19}H_{20}N_2O_3^+$ $[M+H]^+$: $m/z = 325.1547$, found 325.1545.

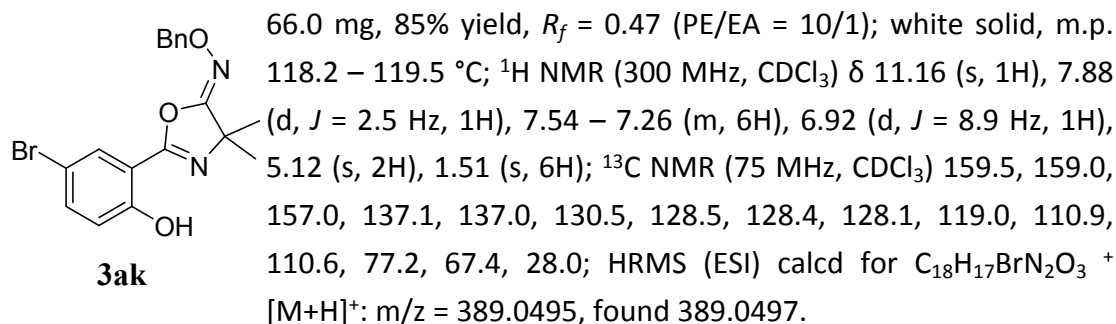
(Z)-2-(2-hydroxy-4-methoxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



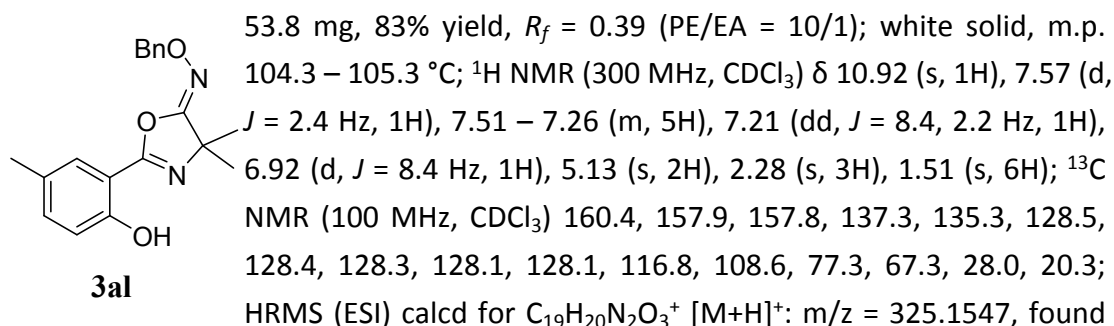
(Z)-2-(5-chloro-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



(Z)-2-(5-bromo-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime

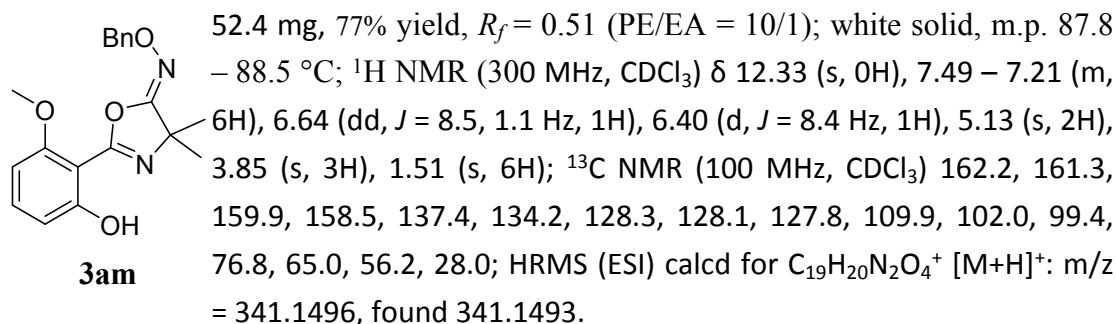


(Z)-2-(2-hydroxy-5-methylphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime

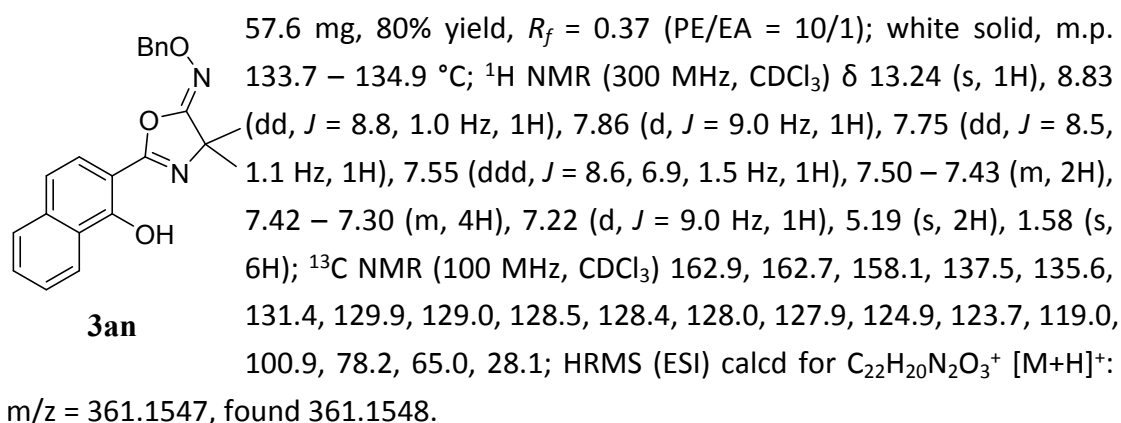


325.1542.

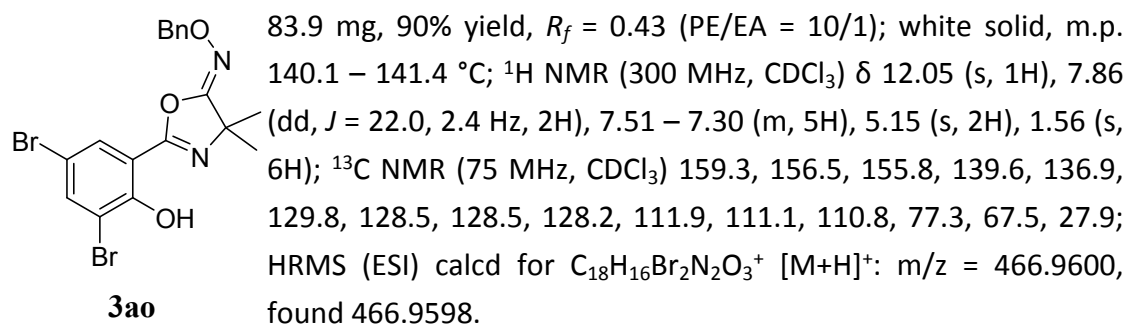
(Z)-2-(2-hydroxy-6-methoxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



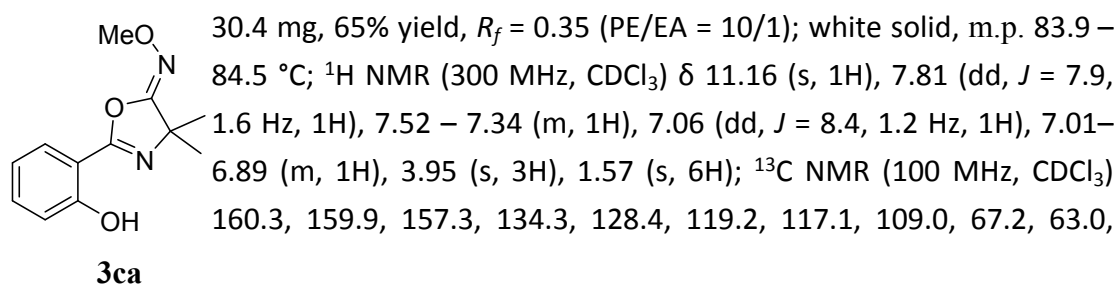
(Z)-2-(1-hydroxynaphthalen-2-yl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime



(Z)-2-(3,5-dibromo-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime

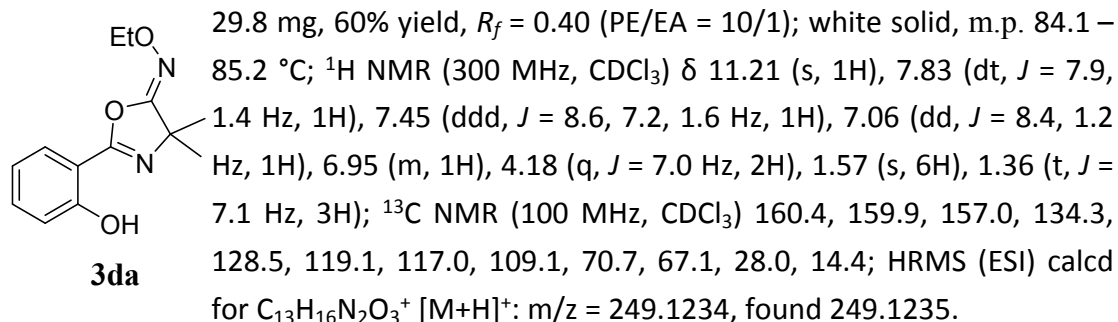


(Z)-2-(2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-methyl oxime

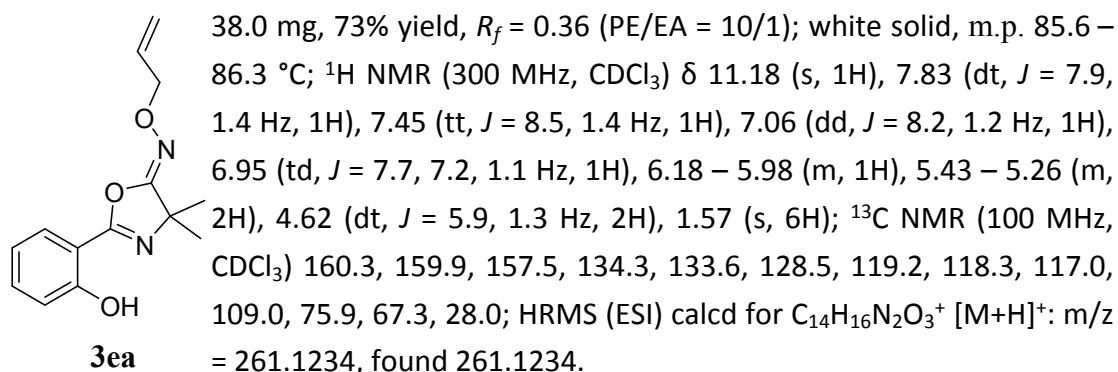


28.0; HRMS (ESI) calcd for $C_{12}H_{14}N_2O_3^+ [M+H]^+$: $m/z = 235.1077$, found 235.1077.

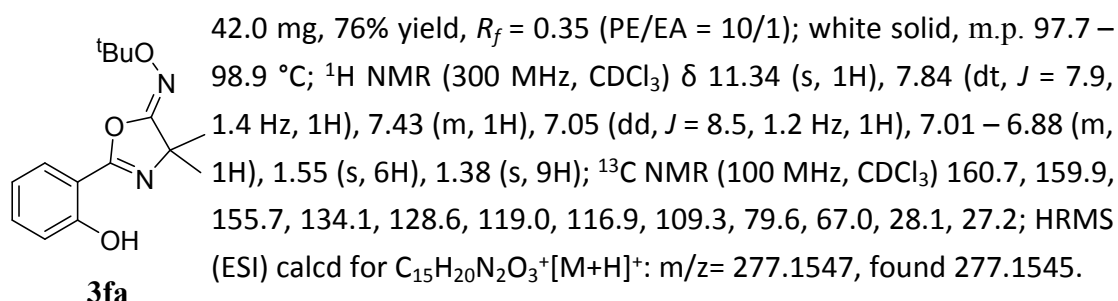
(Z)-2-(2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-ethyl oxime



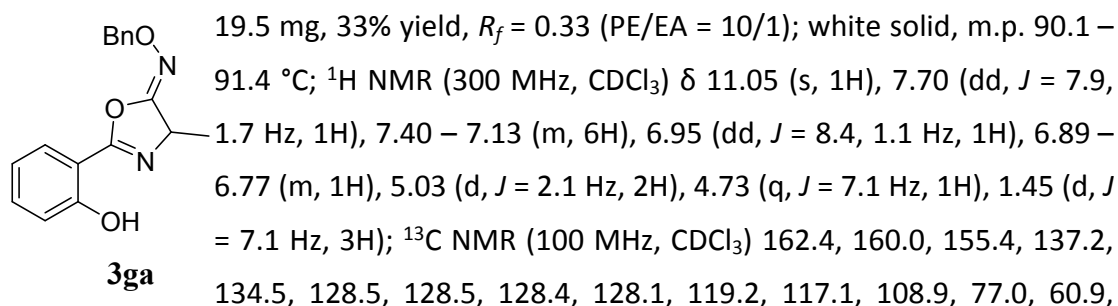
(Z)-2-(2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-allyl oxime



(Z)-2-(2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-(tert-butyl) oxime



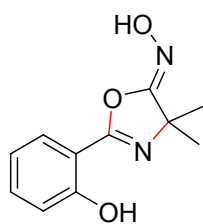
(Z)-2-(2-hydroxyphenyl)-4-methyloxazol-5(4H)-one O-benzyl oxime



20.4; HRMS (ESI) calcd for $C_{15}H_{20}N_2O_3^+ [M+H]^+$: $m/z = 297.1234$, found 297.1236.

(Z)-2-(2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one oxime

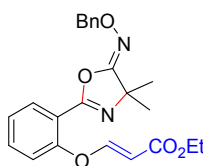
To an 10 mL round-bottom flask equipped with a magnetic stir bar, Pd/C (0.0075



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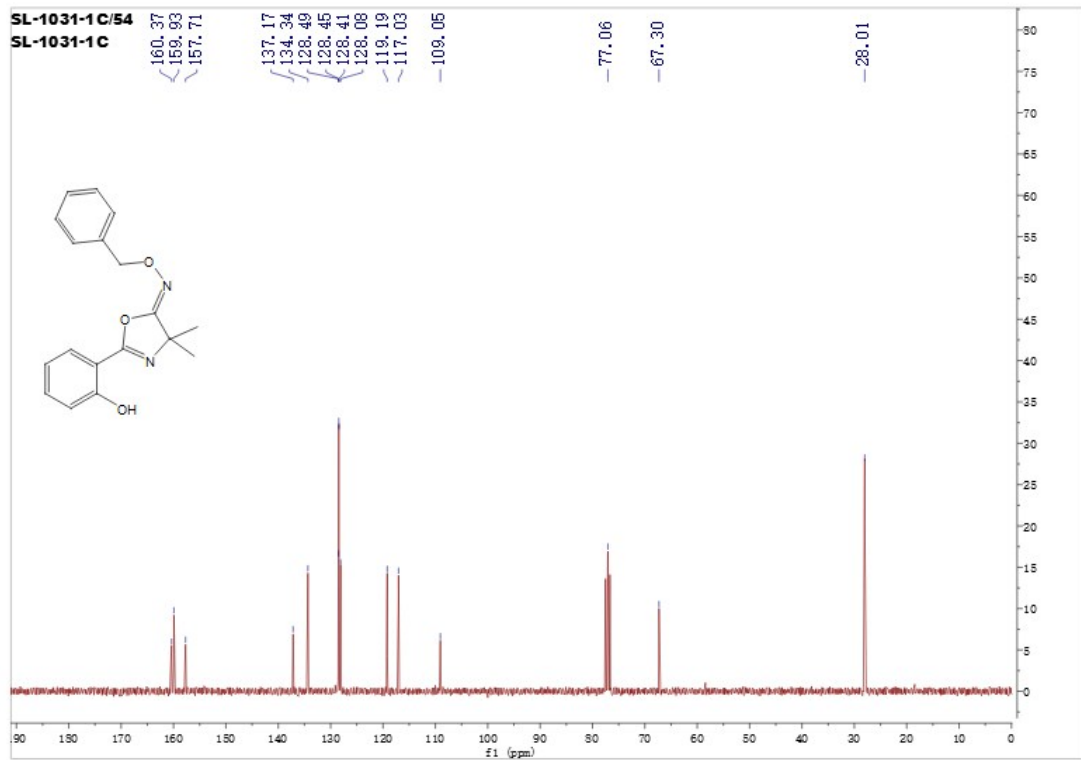
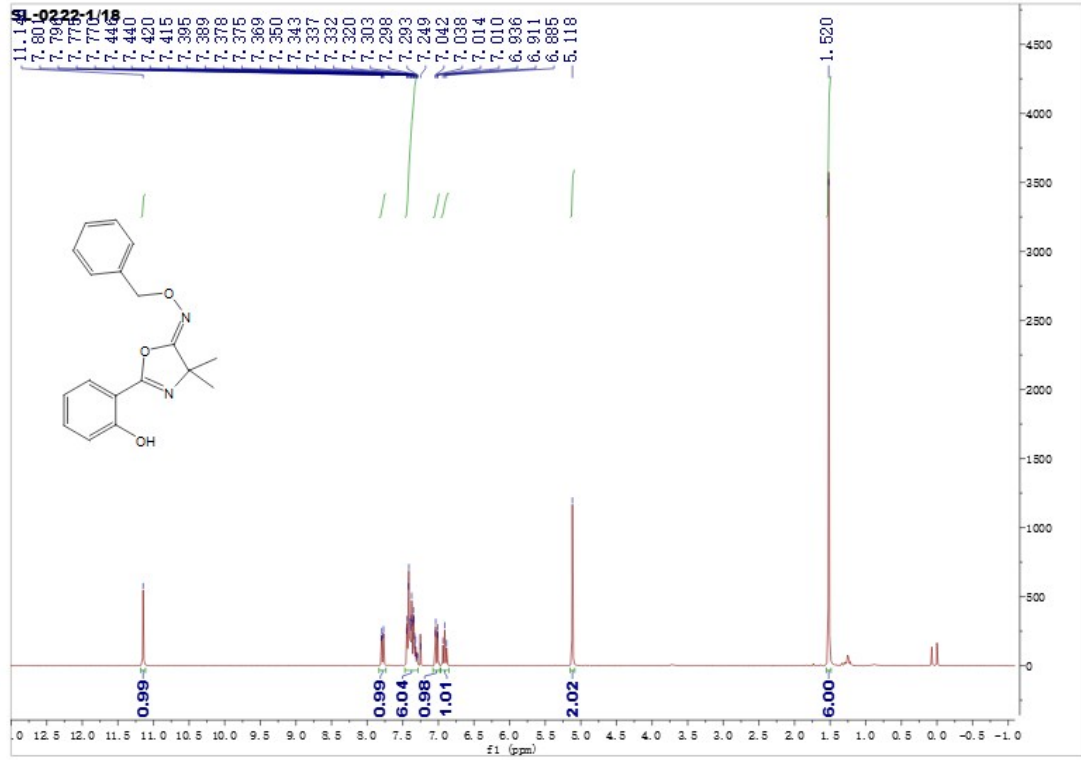
mmol, 0.1 eq.), and (Z)-2-(2-(benzyloxy)phenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime(3aa) (30.0 mg, 0.075 mmol, 1.0 eq.) were added. The tube was sealed with rubber stopper, evacuated and backfilled with H₂ (this process was repeated for 3 times), then MeOH (1.5 mL) via syringe was added at room temperature. The mixture was stirred at room temperature for 24 h. Upon completion, the reaction mixture was then purified by preparative thin layer chromatography using petroleum ether/ethyl acetate system (petroleum ether / ethyl acetate = 15/1) to give product 5 as a thick colorless oil in 97% yield(12.9 mg). ¹H NMR (400 MHz, CDCl₃) δ 11.12 (s, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.31 (s, 1H), 7.05 (d, *J* = 8.3 Hz, 1H), 6.95 (t, *J* = 8.1 Hz, 1H), 1.56 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 160.25, 159.94, 159.14, 134.44, 128.39, 119.28, 117.09, 108.98, 67.26, 27.88; HRMS (ESI) calcd for C₁₁H₁₂N₂O₃⁺ [M+H]⁺: *m/z* = 221.0881, found 221.0922.

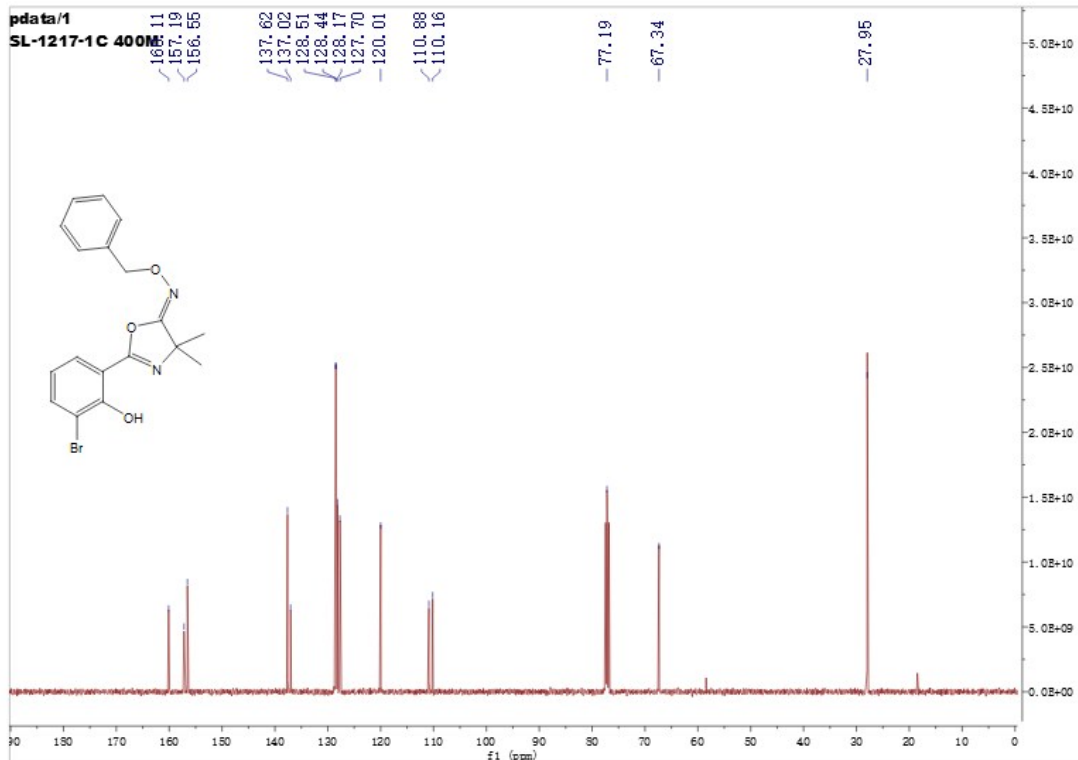
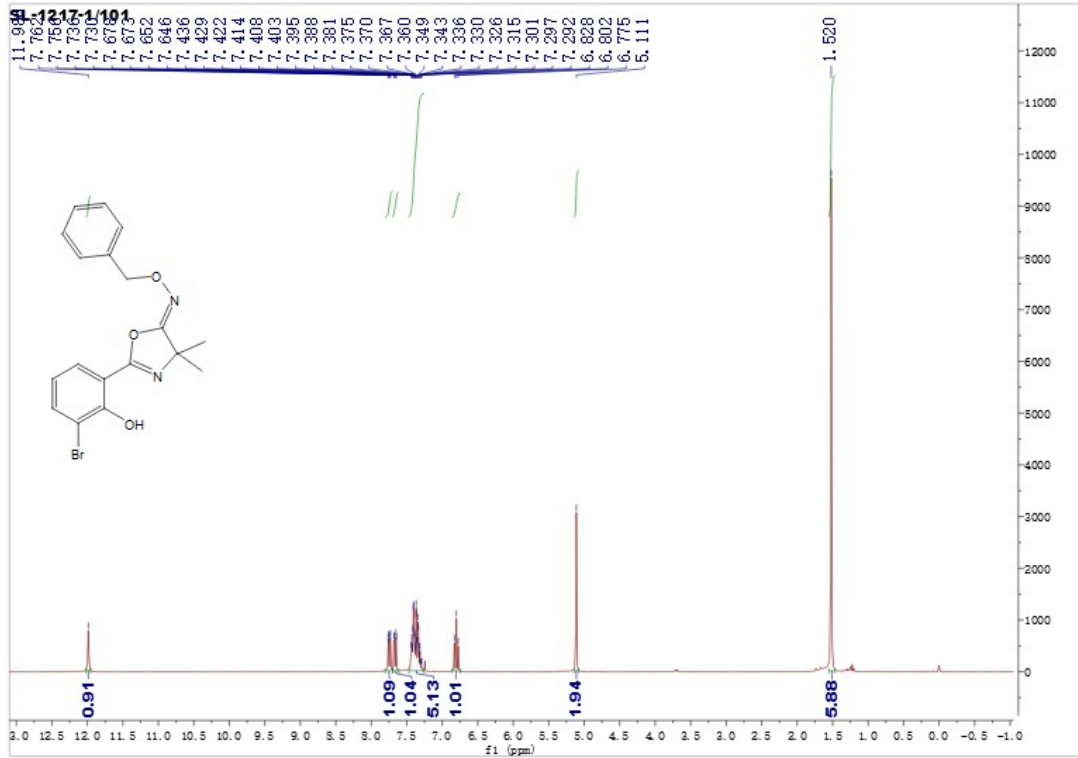
Ethyl (E)-3-(2-((Z)-5-((benzyloxy)imino)-4,4-dimethyl-4,5-dihydrooxazol-2-yl)phenoxy)acrylate

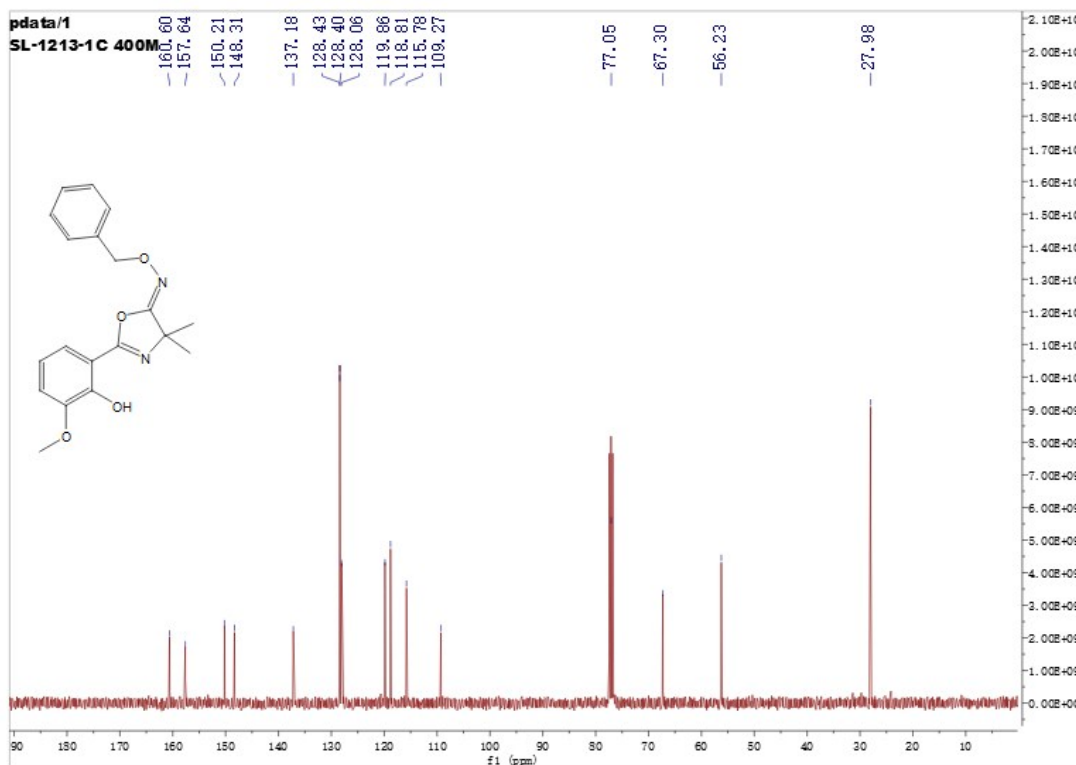
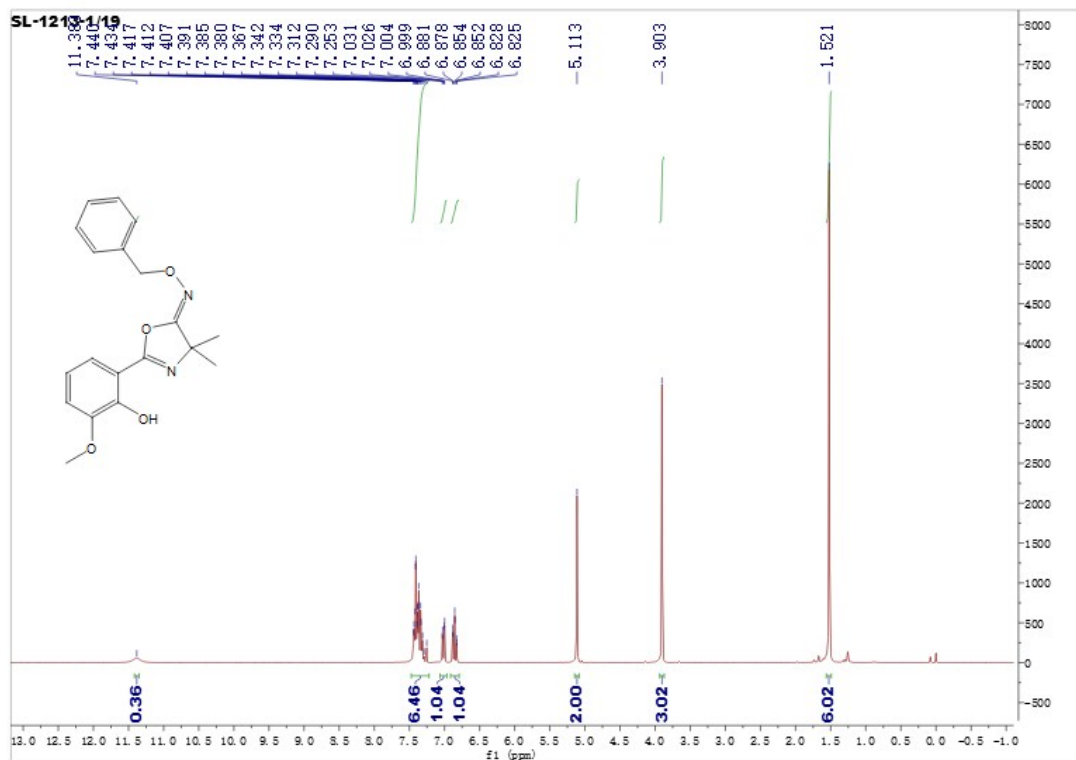


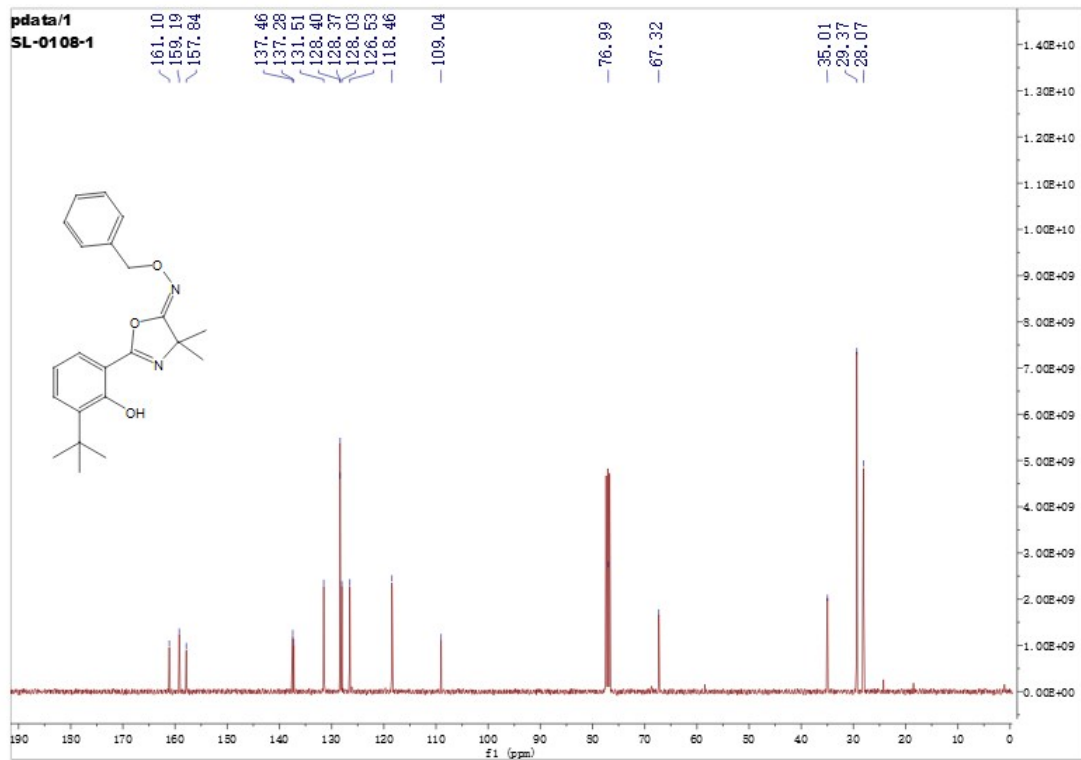
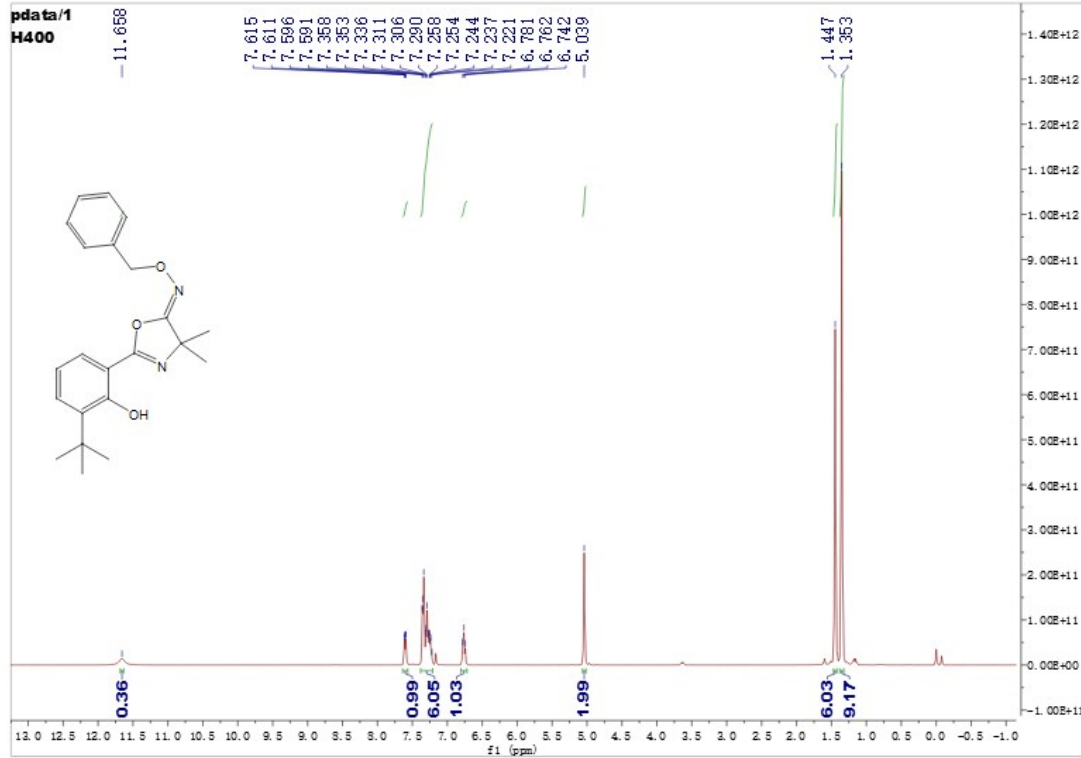
6

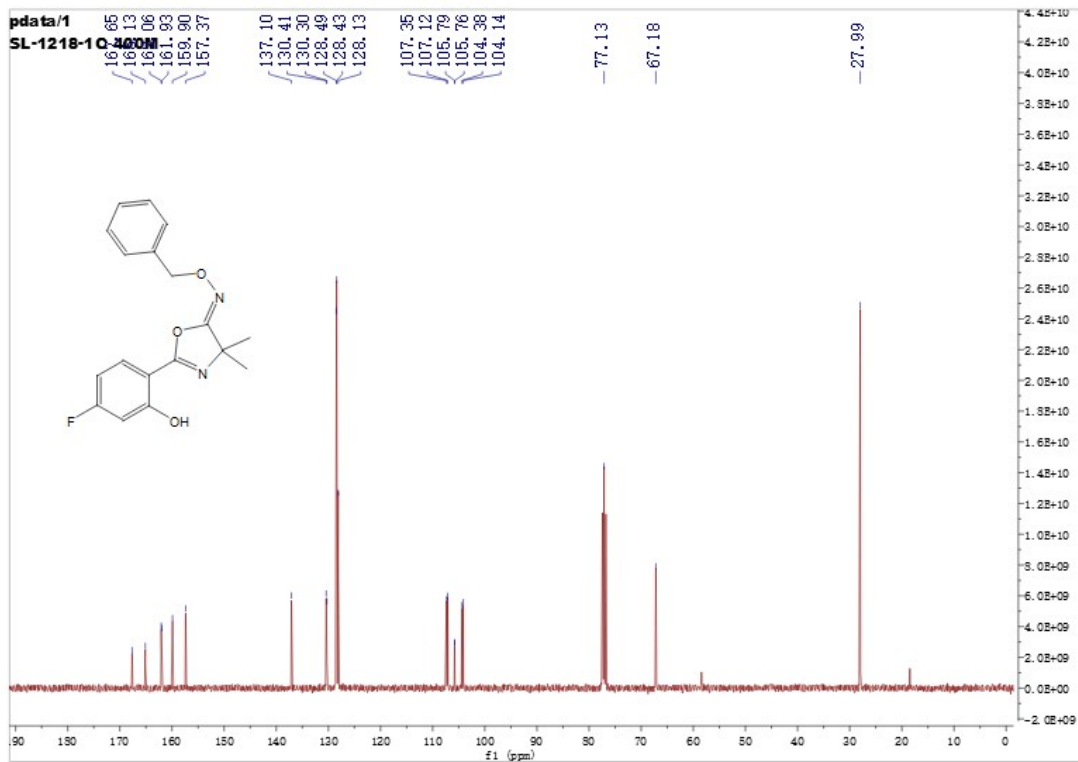
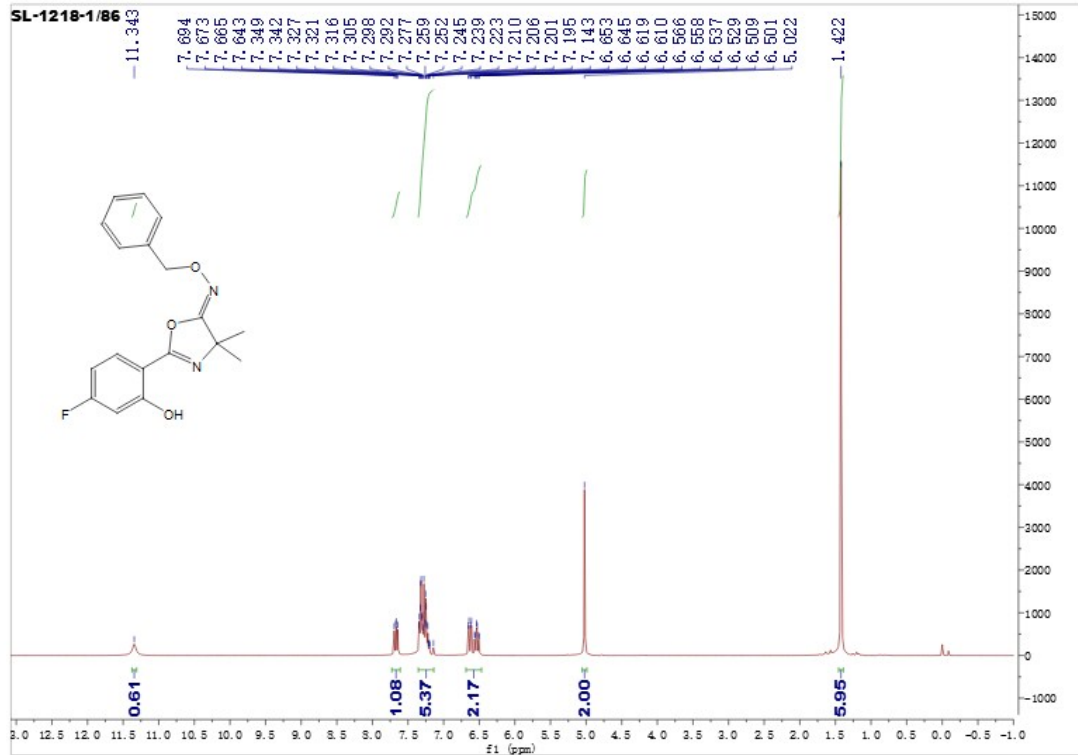
To an 10 mL round-bottom flask equipped with a magnetic stir bar, Dabco (0.0075 mmol, 0.1 eq.), ethyl propiolate (0.0825 mmol, 1.1 eq.) and (Z)-2-(2-(benzyloxy)phenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime(3aa) (30.0 mg, 0.075 mmol, 1.0 eq.) were added. The tube was sealed with rubber stopper, evacuated and backfilled with N₂ (this process was repeated for 3 times), then DCM (1.5mL) via syringe was added at room temperature. The mixture was stirred at room temperature for 24 h. Upon completion, the reaction mixture was then purified by preparative thin layer chromatography using petroleum ether/ethyl acetate system (petroleum ether / ethyl acetate = 10/1) to give product 6 as a thick colorless oil in 78% yield(29.0mg). ¹H NMR (400 MHz, CDCl₃) δ 7.95 (dd, *J* = 7.7, 2.2 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.57 – 7.51 (m, 1H), 7.43 – 7.32 (m, 3H), 7.29 – 7.25 (m, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 5.43 (dt, *J* = 12.4, 1.8 Hz, 1H), 5.10 (d, *J* = 2.8 Hz, 2H), 4.20 – 4.13 (m, 2H), 1.51 – 1.47 (m, 6H), 1.26 (td, *J* = 6.5, 3.6 Hz, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 166.96, 159.59, 155.78, 154.24, 144.77, 137.39, 133.54, 131.47, 128.34, 128.26, 127.89, 125.46, 120.42, 118.22, 102.21, 76.80, 68.25, 60.10, 27.64, 14.32; HRMS (ESI) calcd for C₂₃H₂₄N₂O₅⁺ [M+H]⁺: *m/z* = 409.1719, found 409.1759.

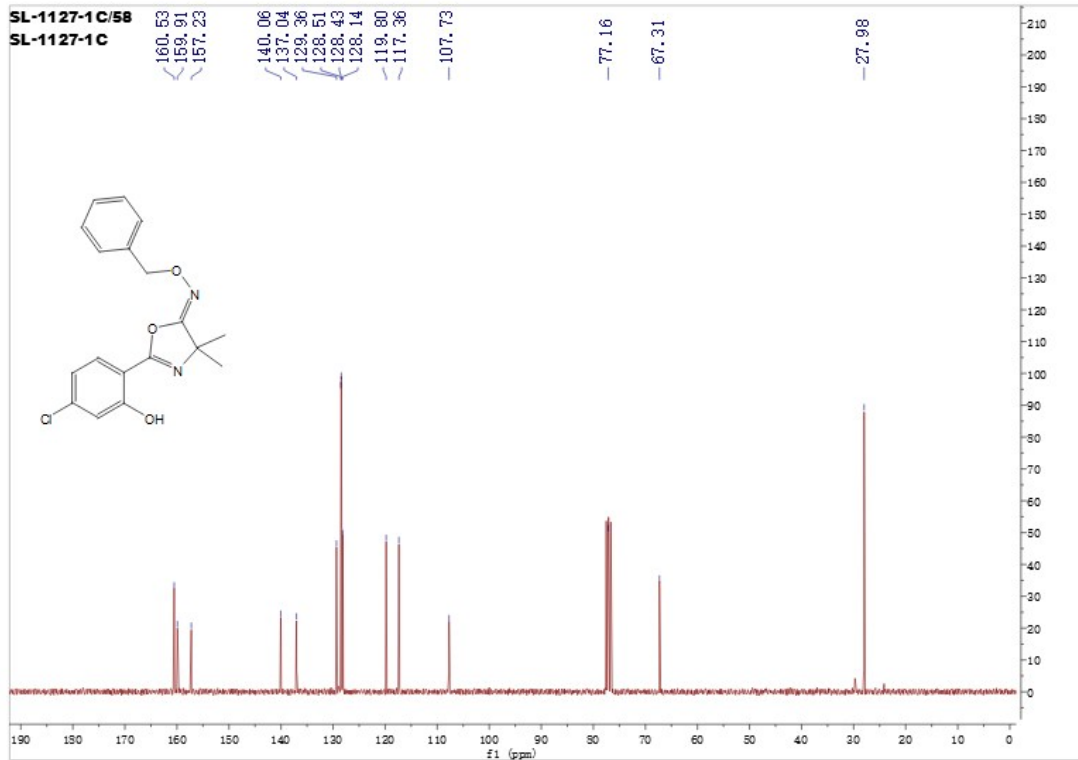
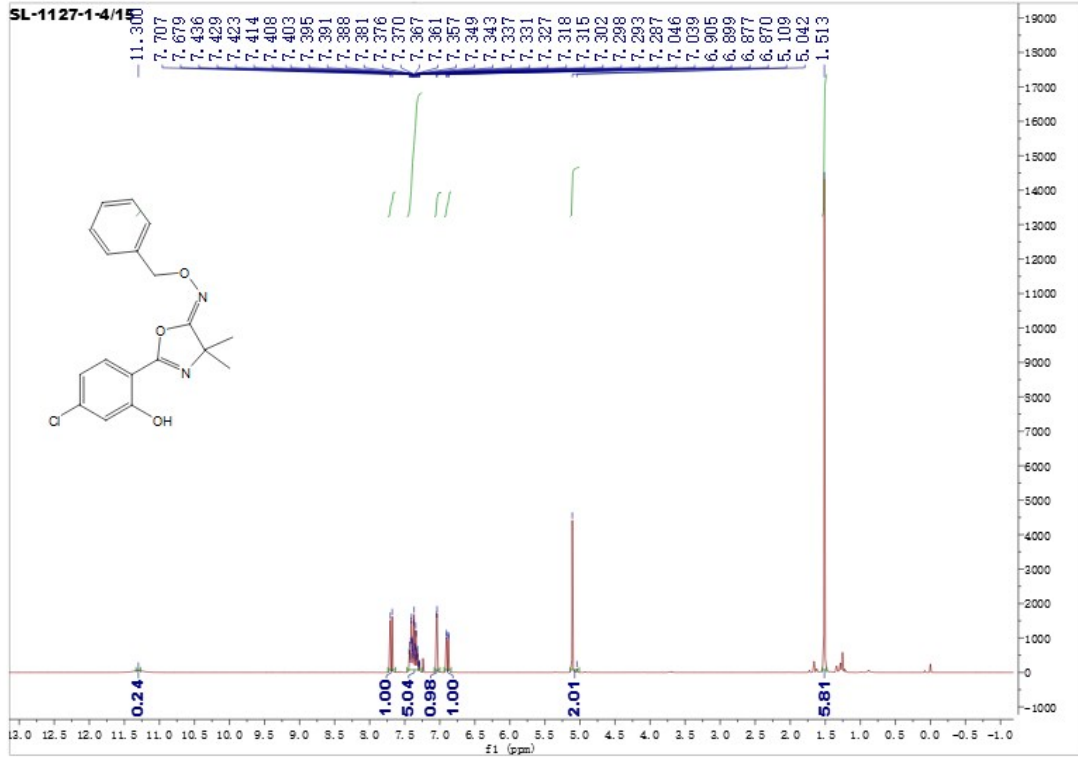


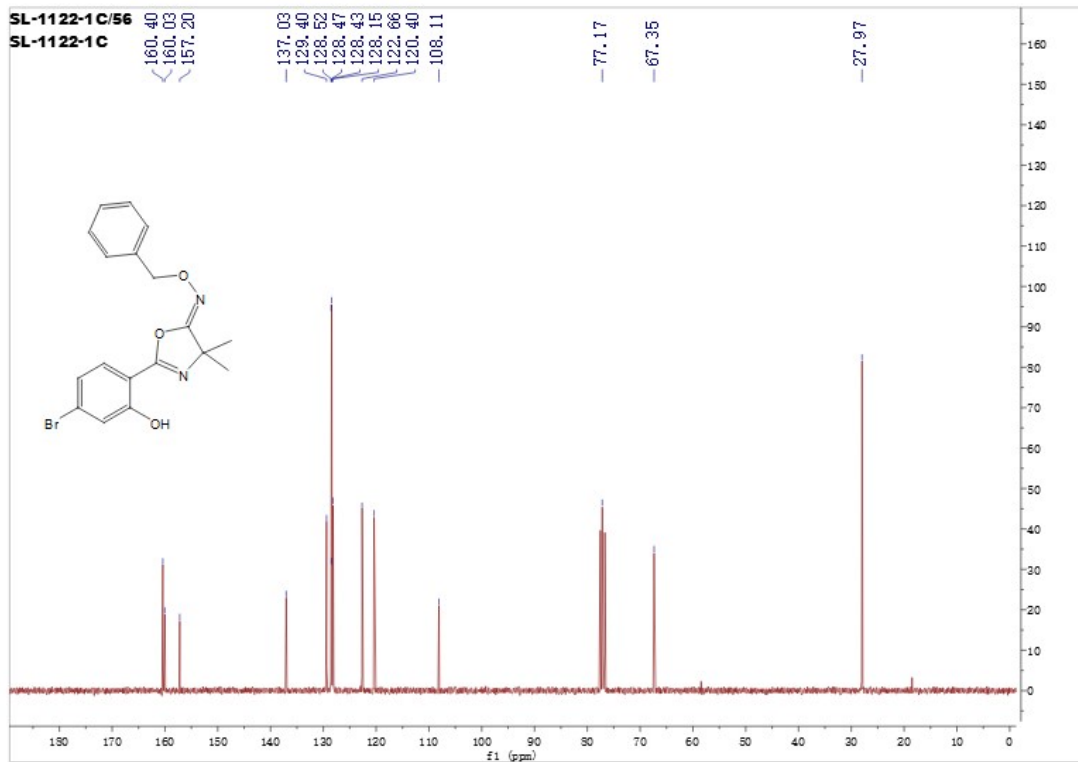
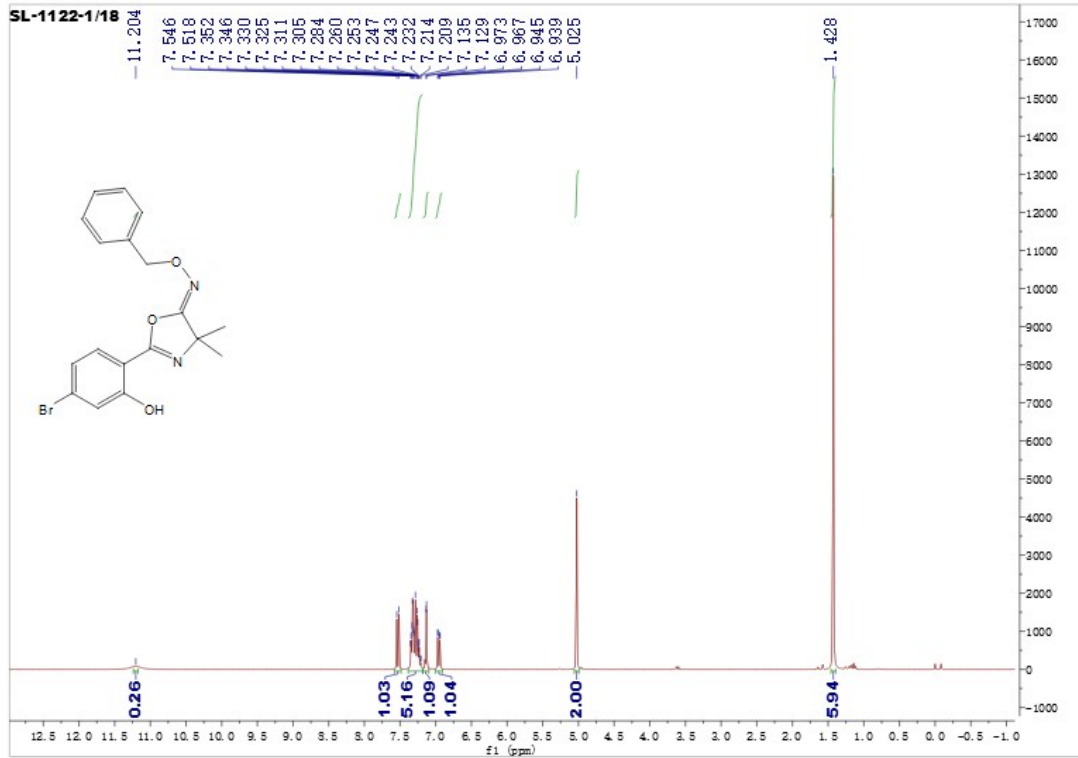


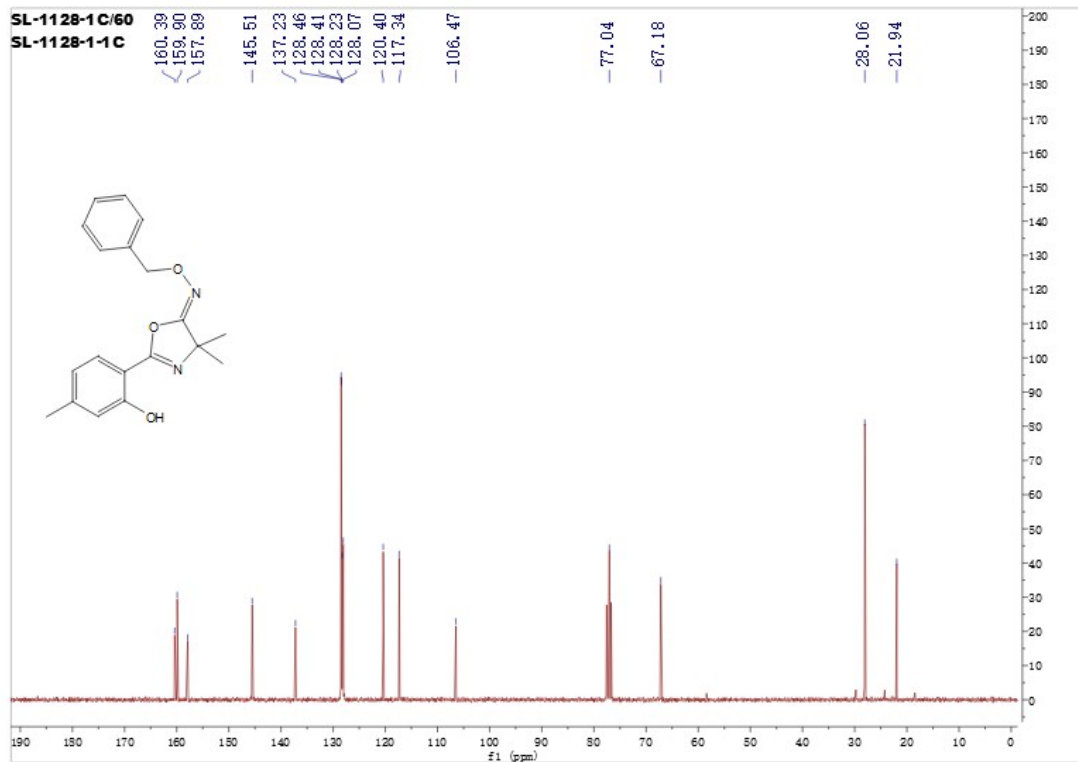
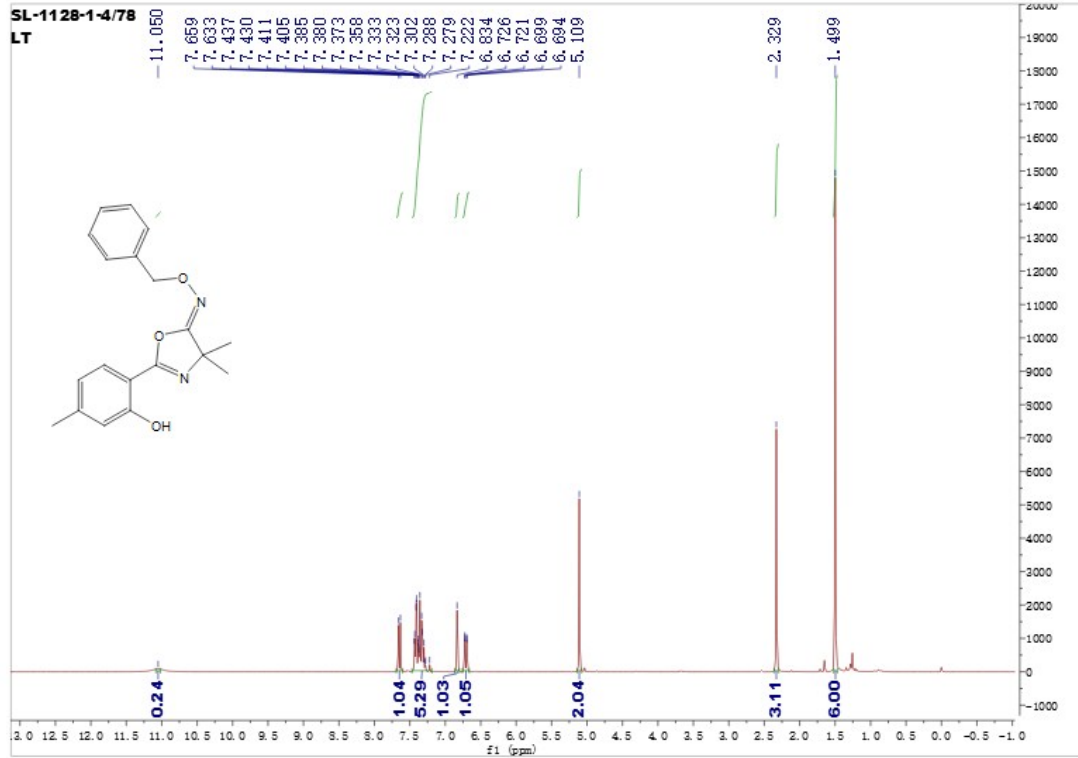


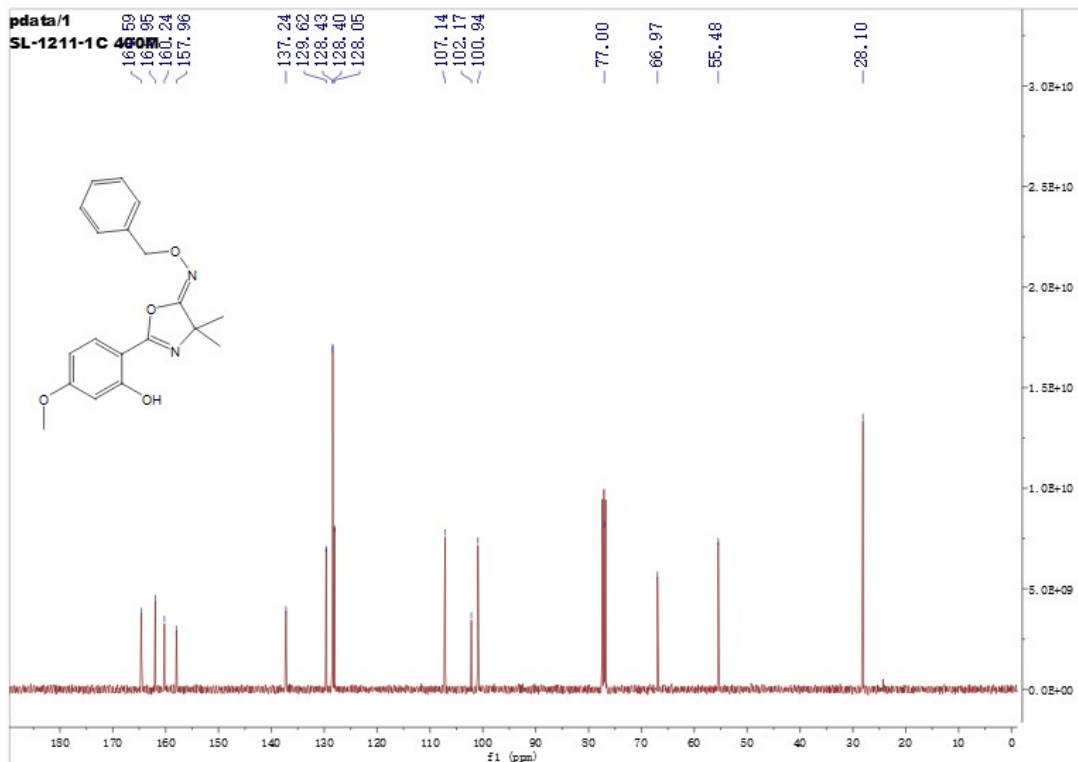
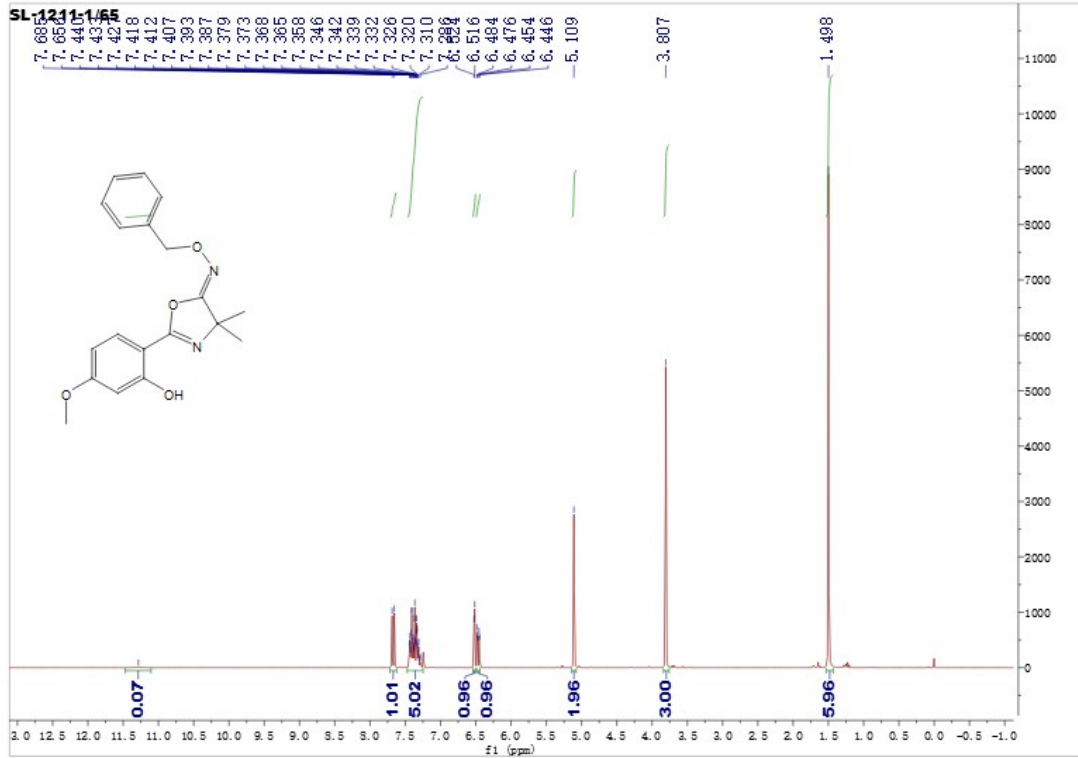


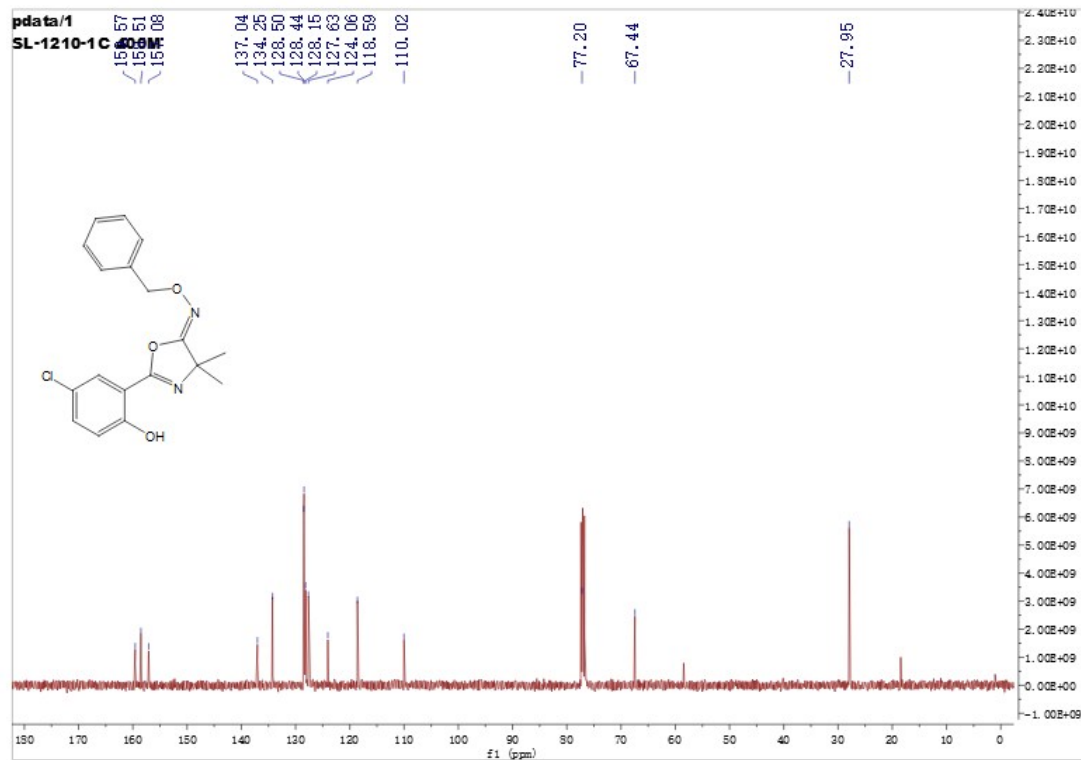
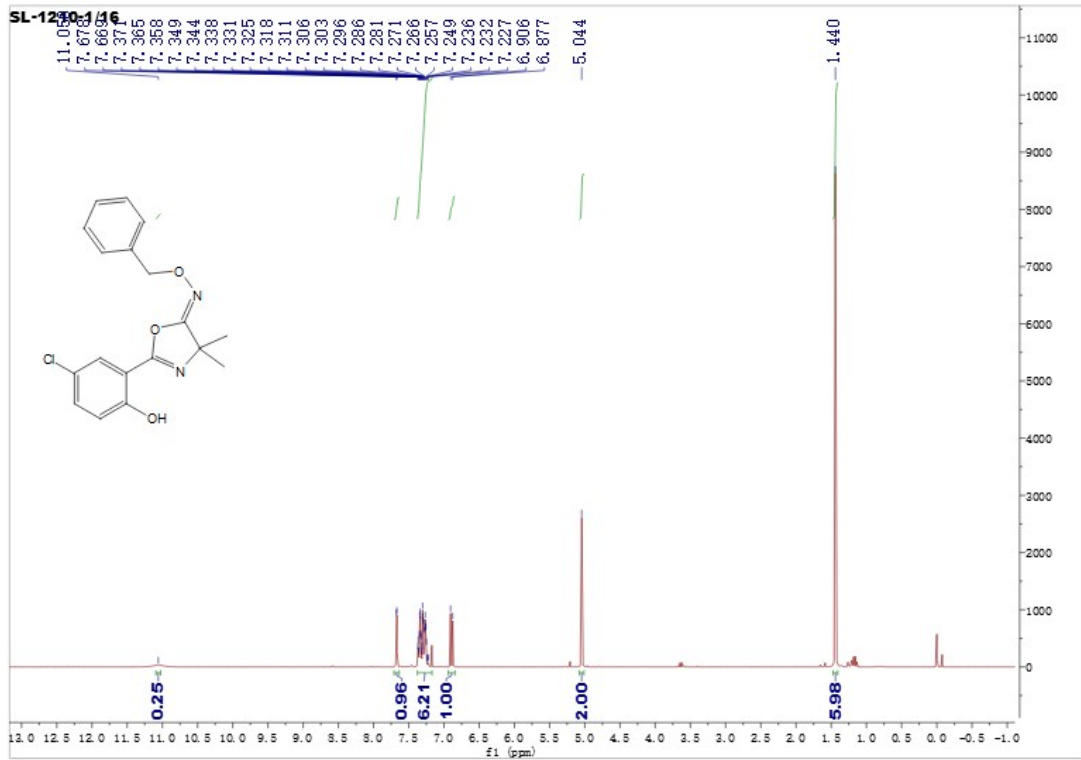


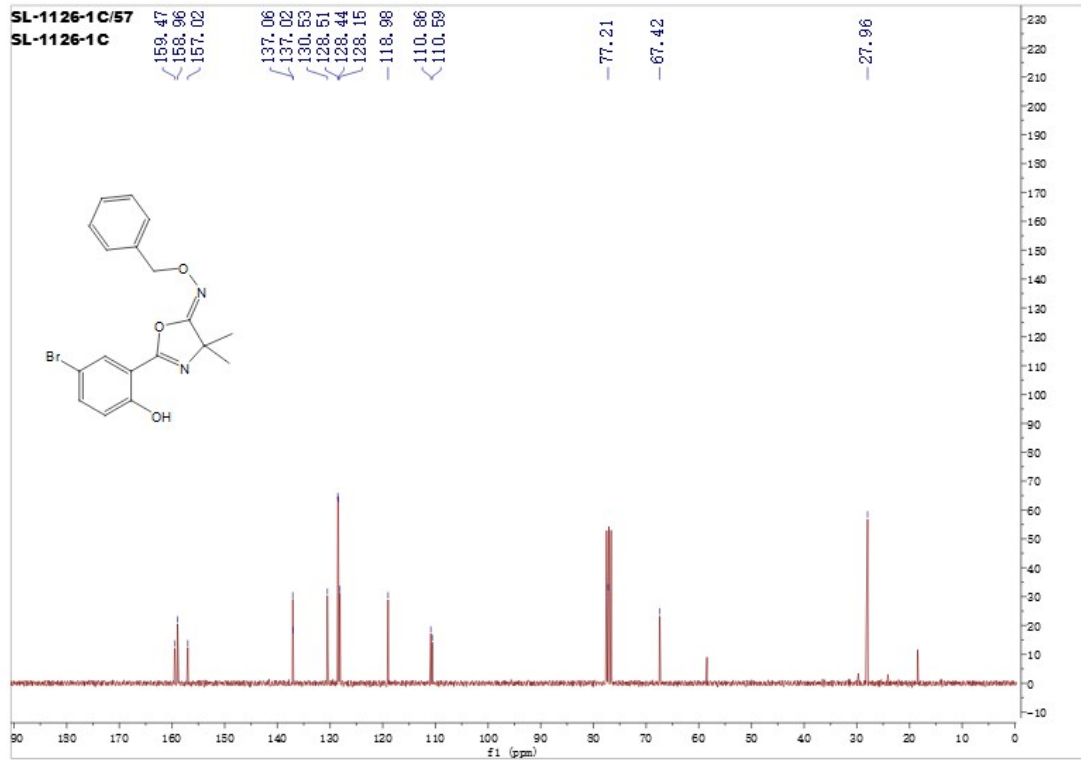
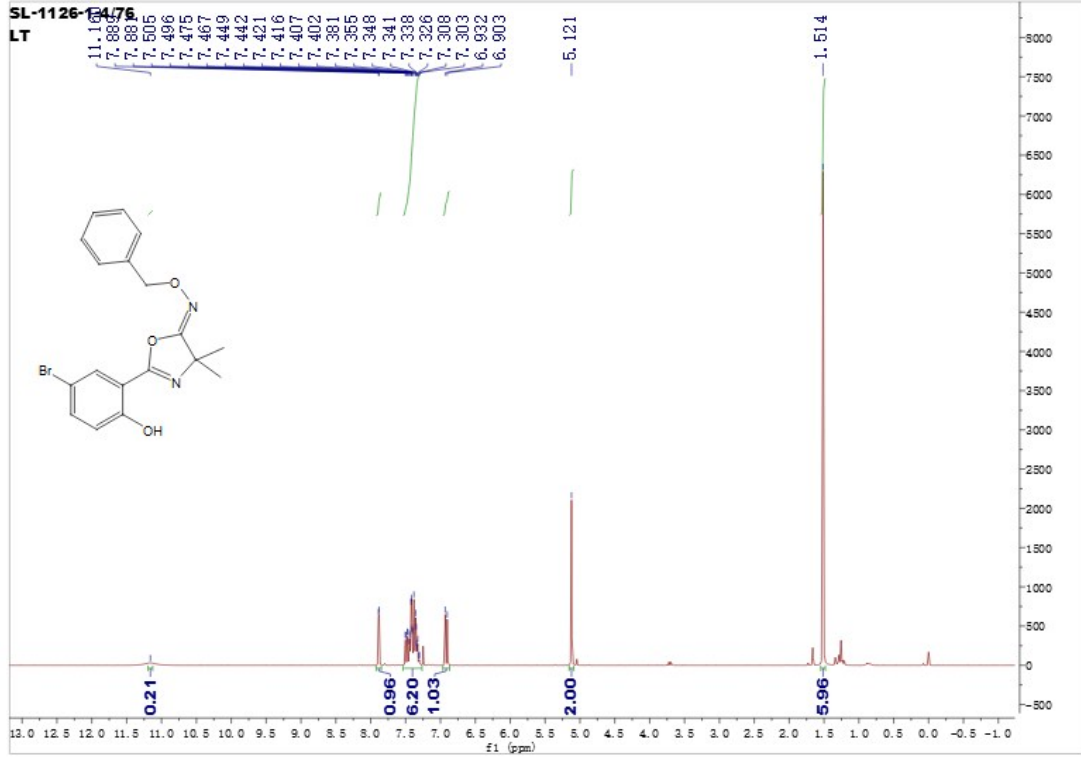


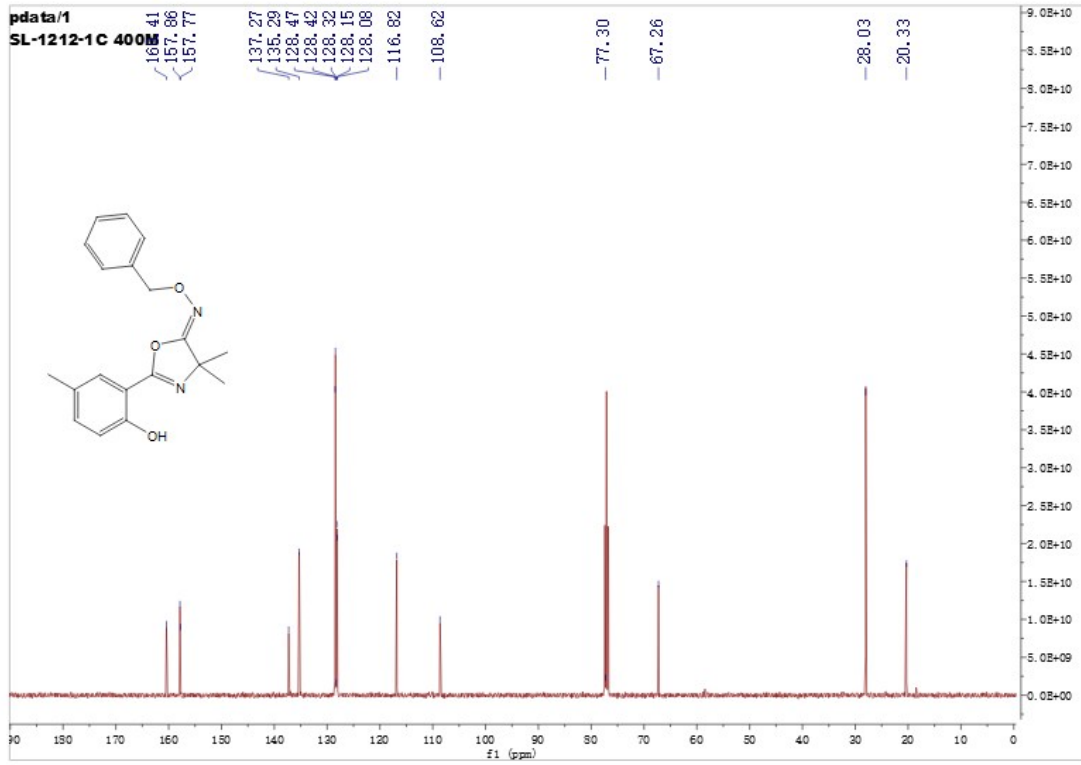
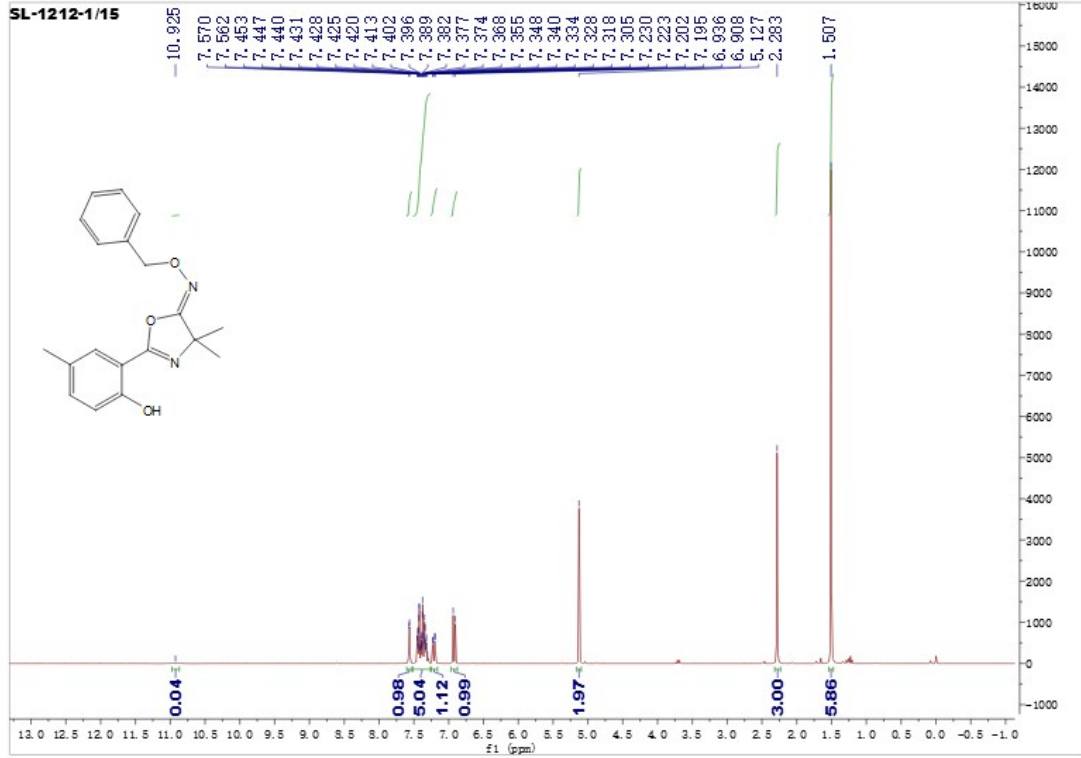


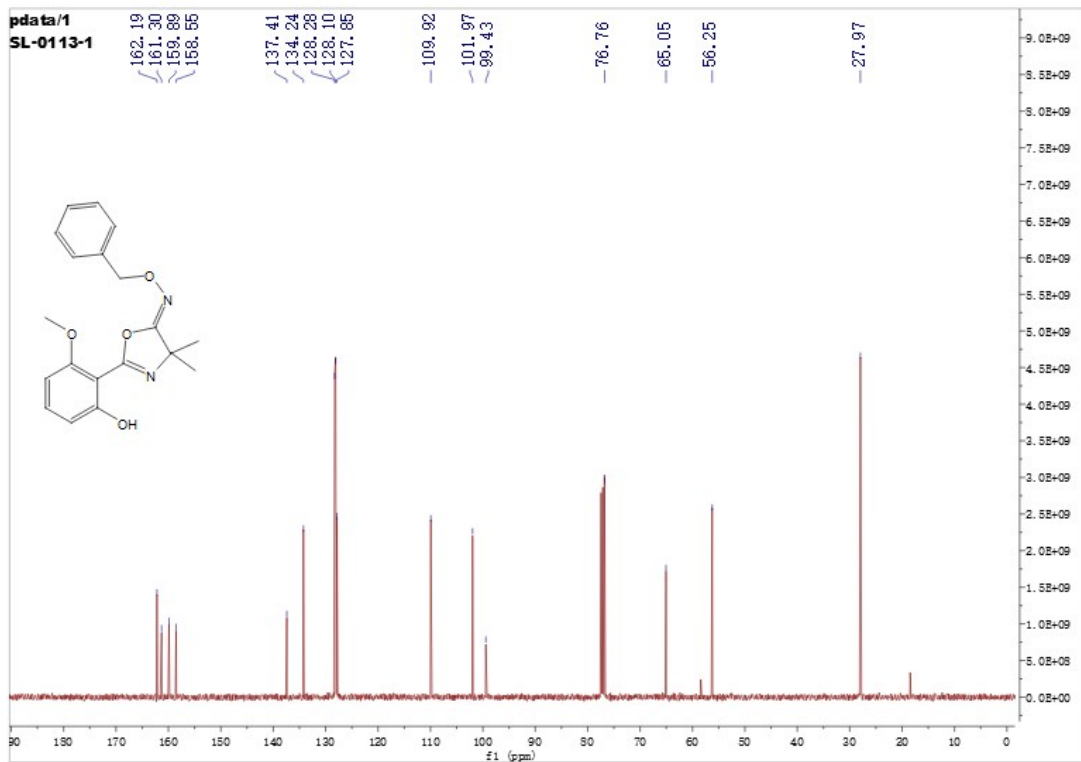
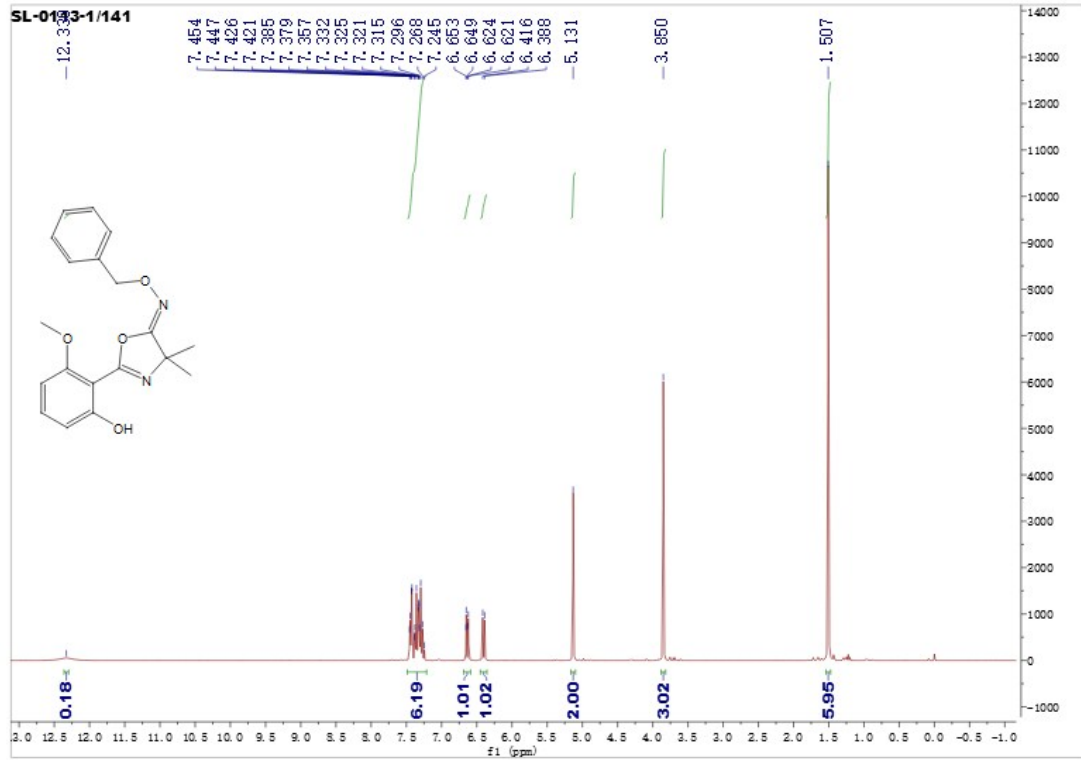


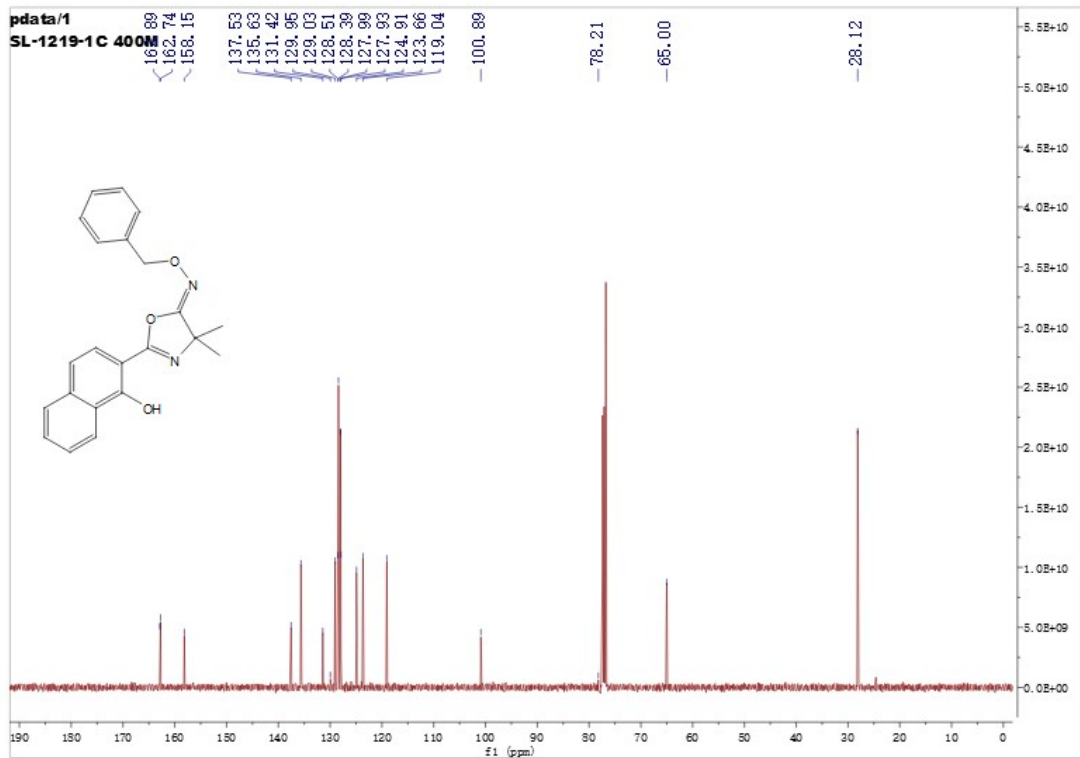
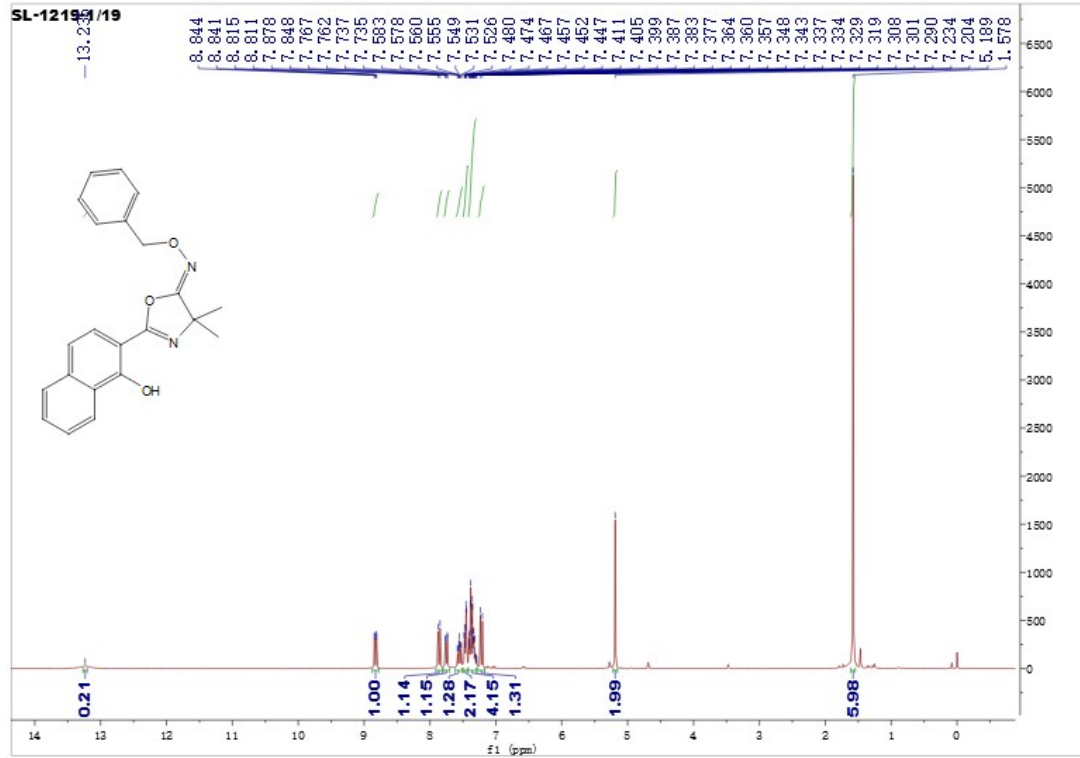


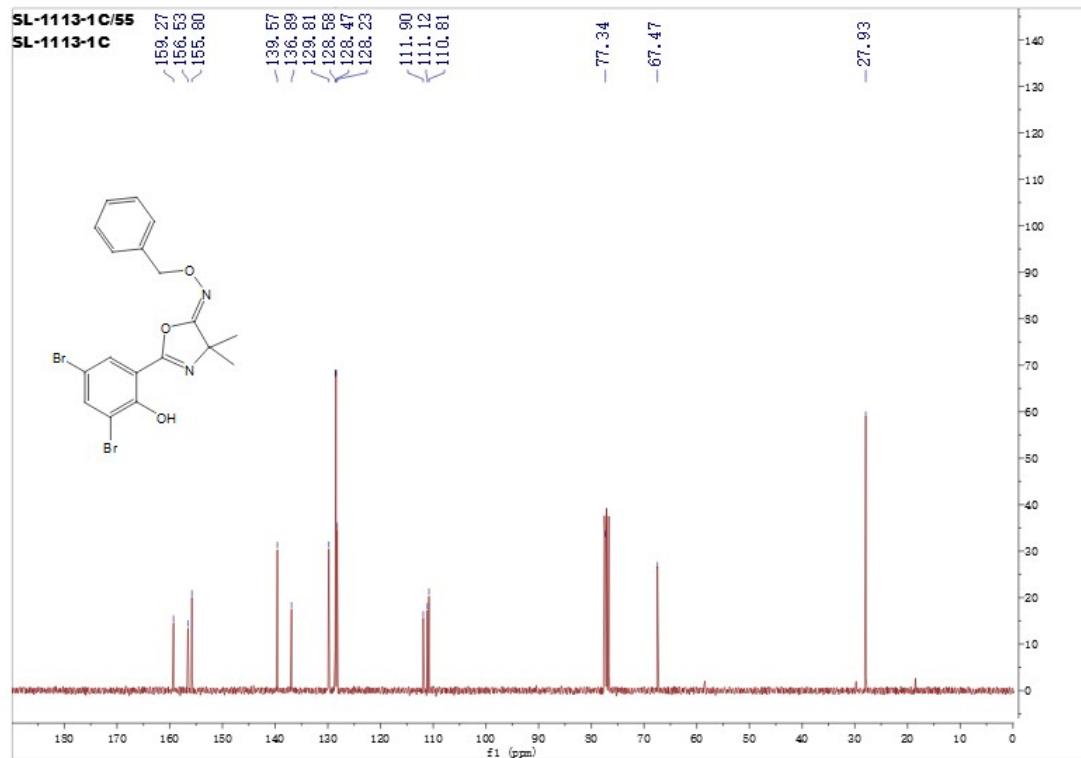
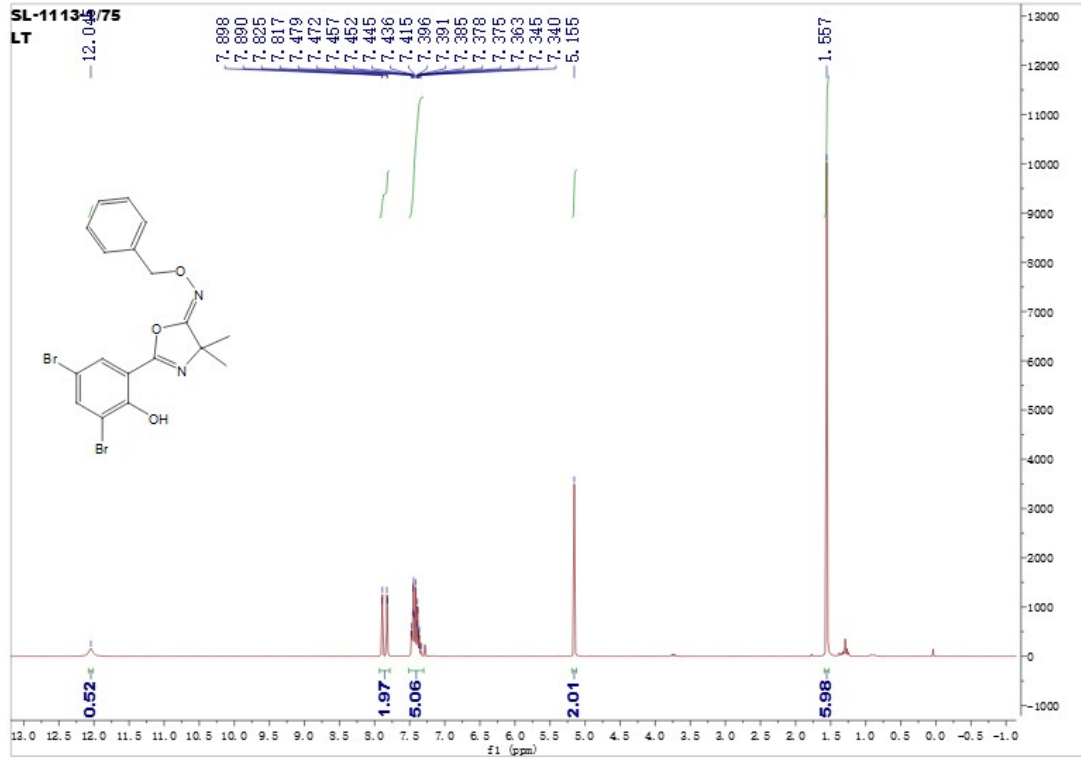


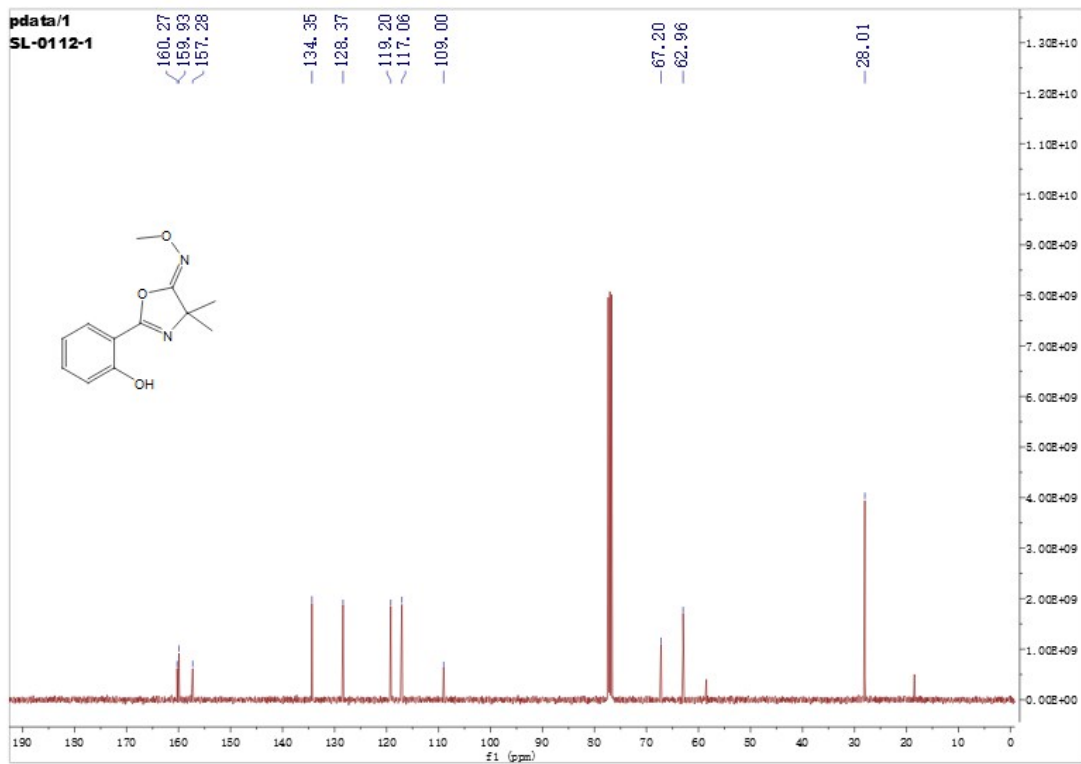
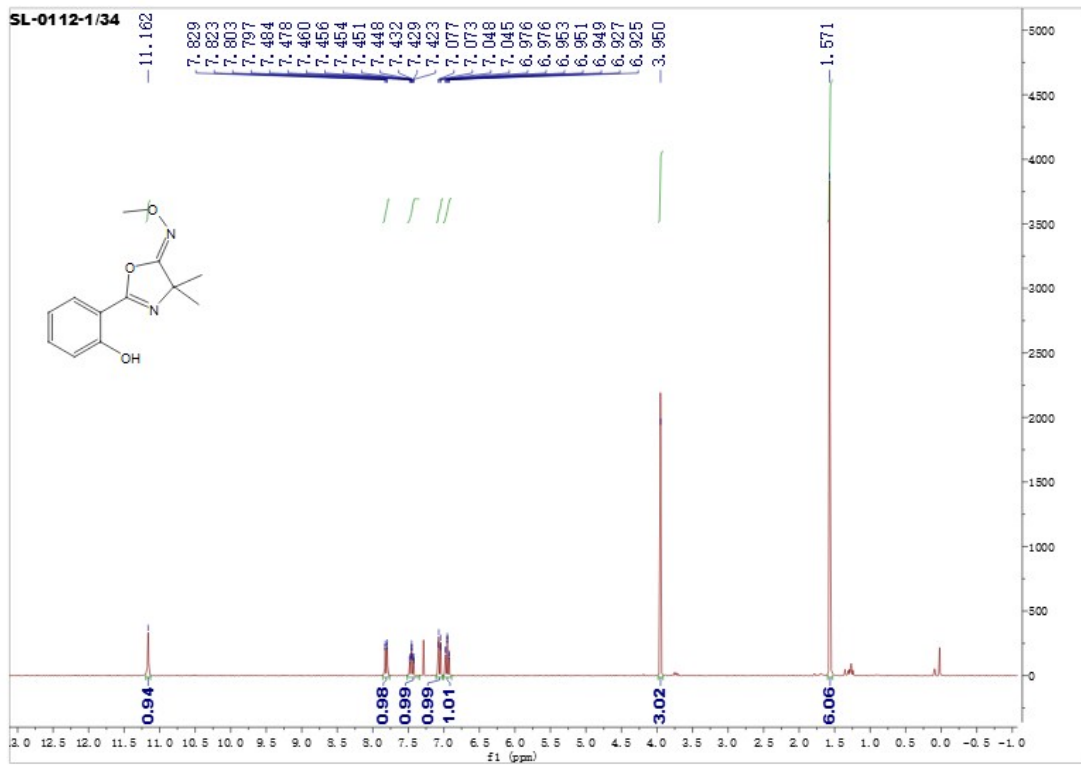


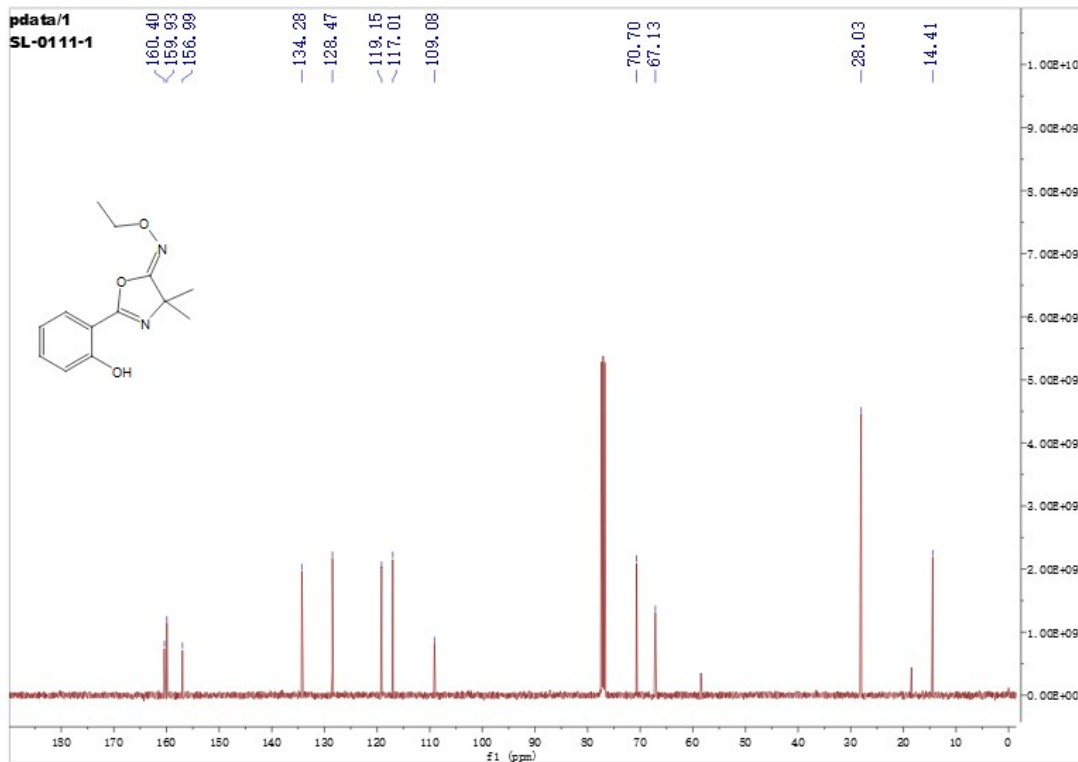
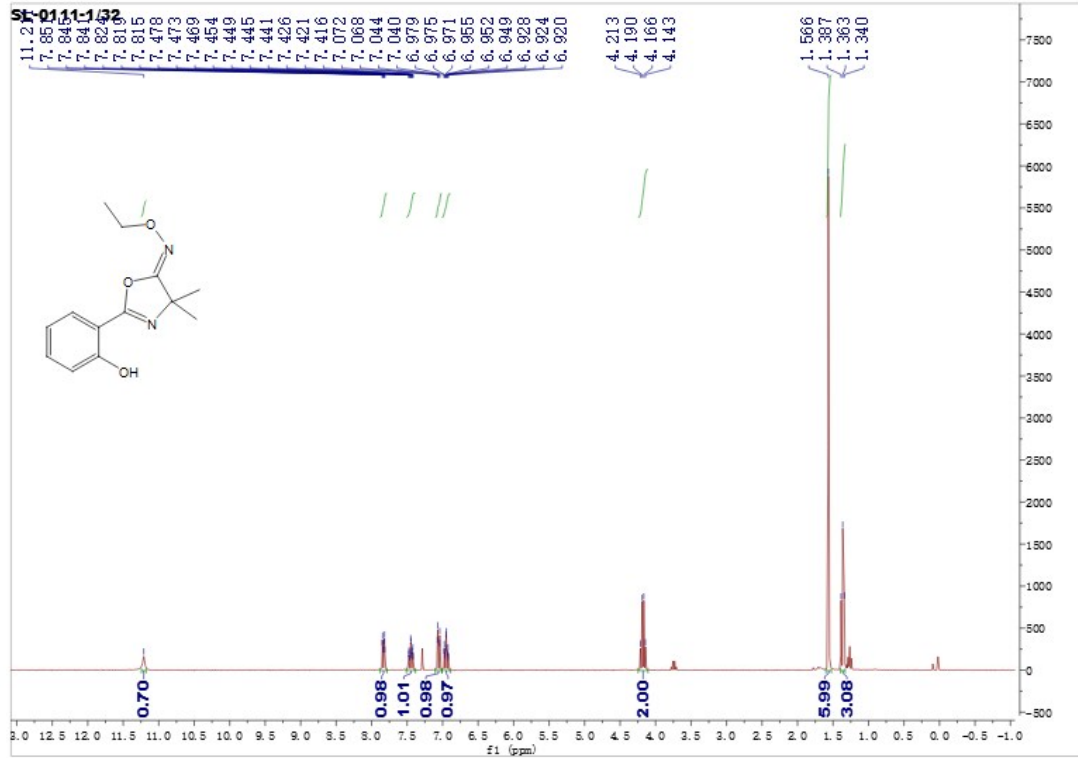


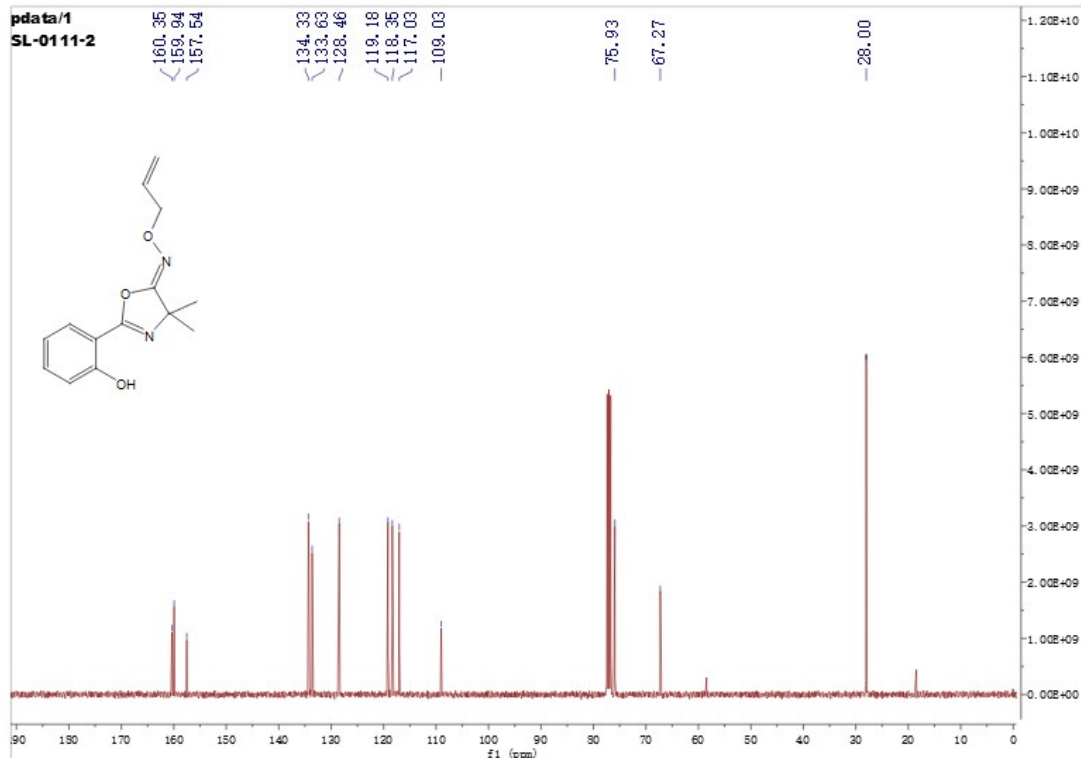
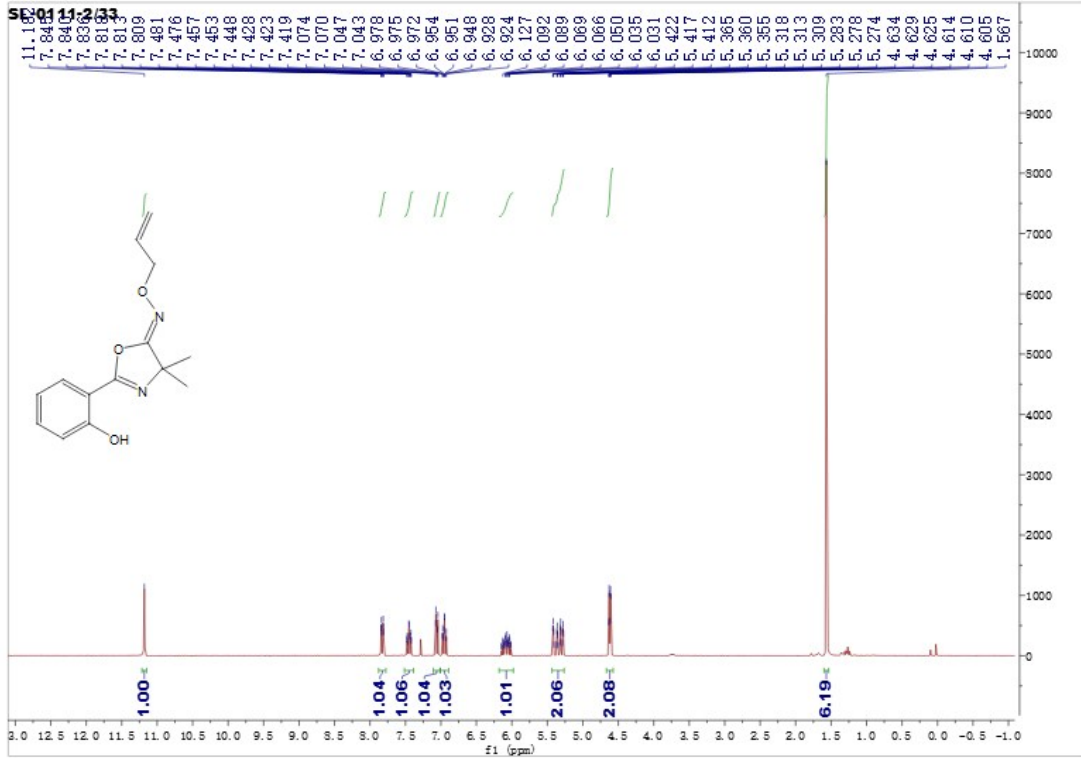


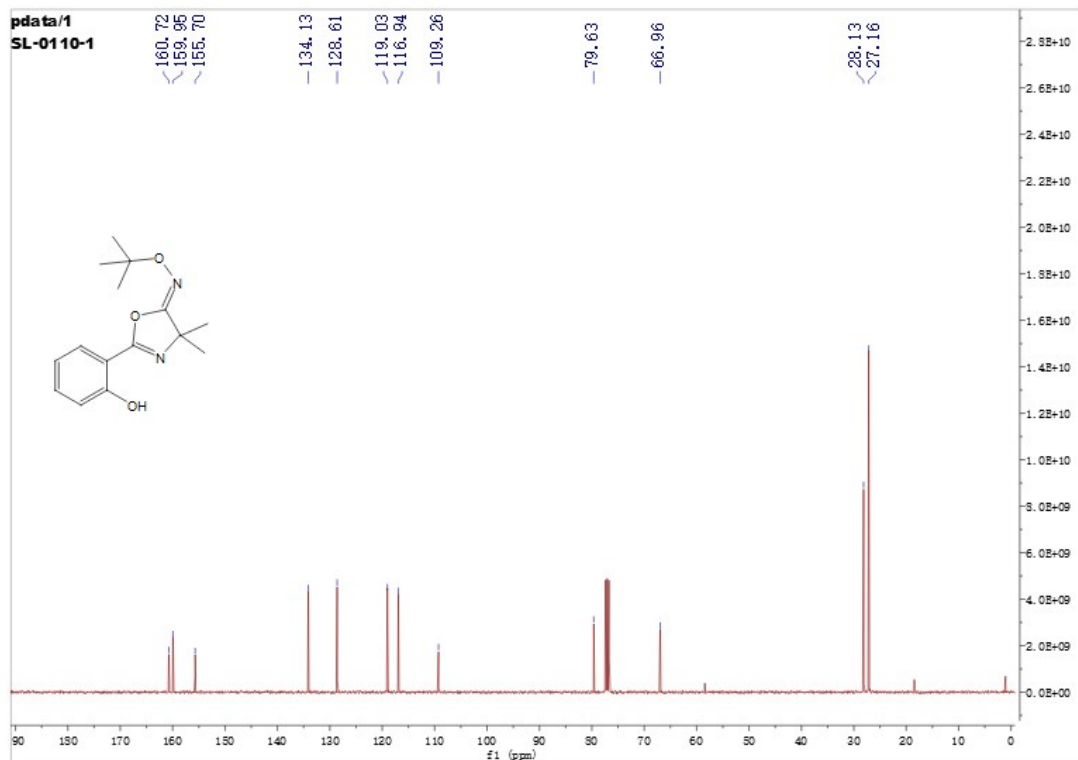
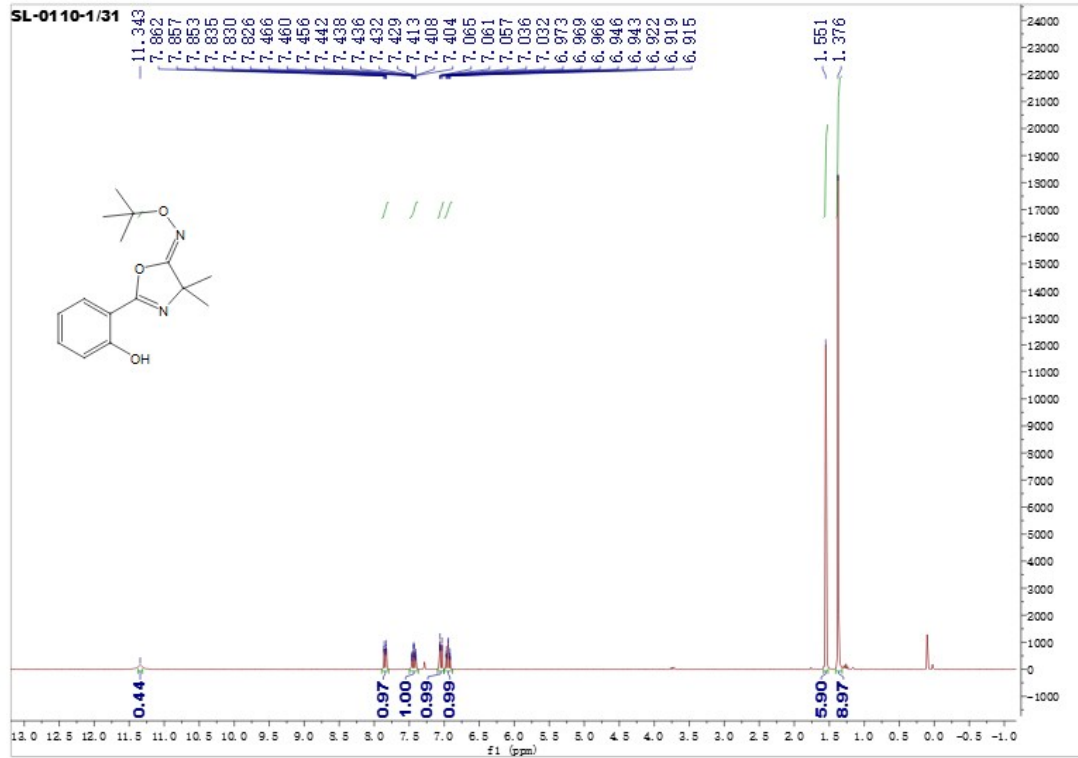


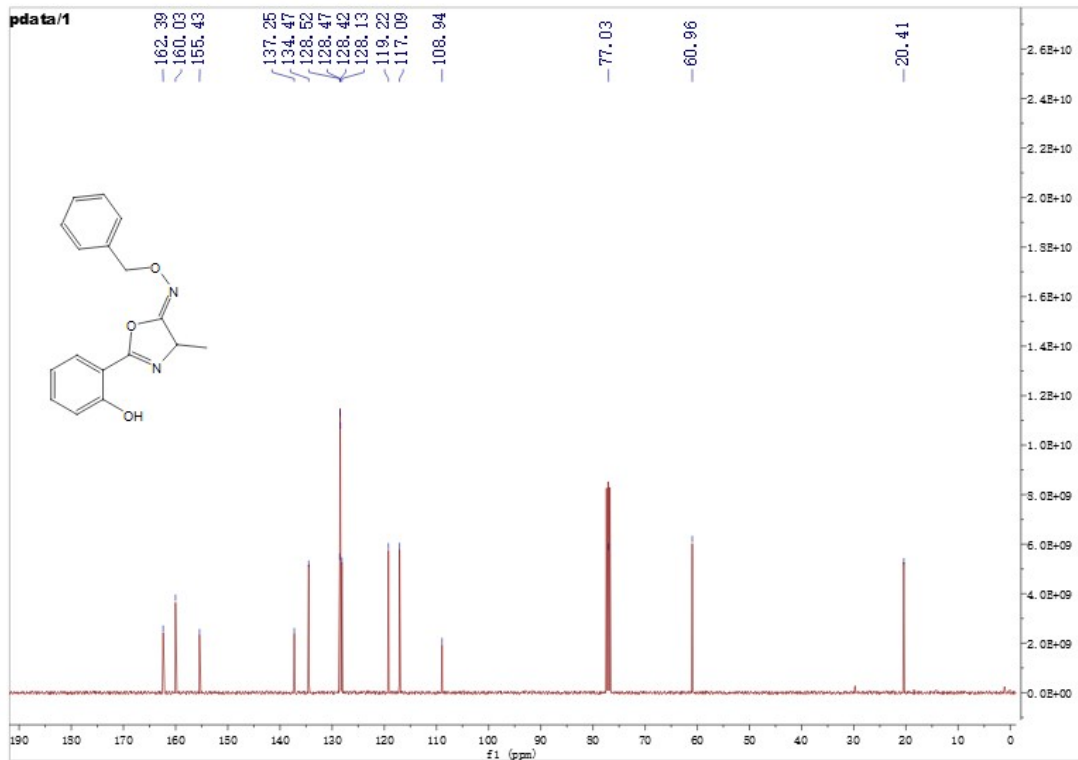
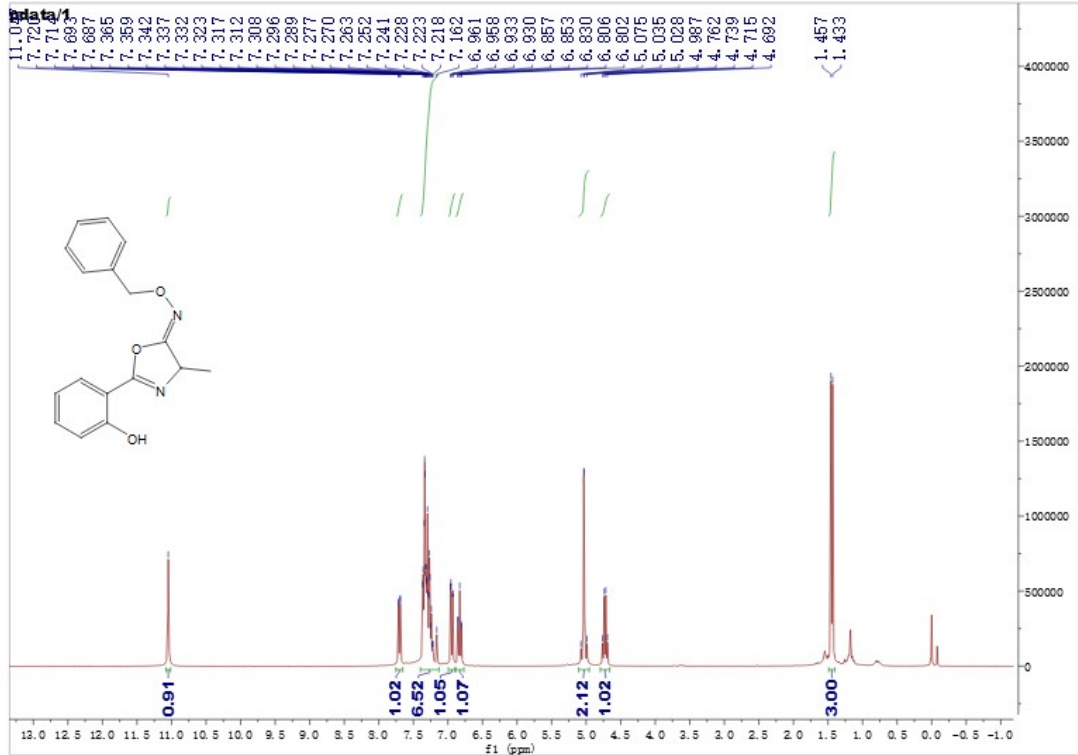


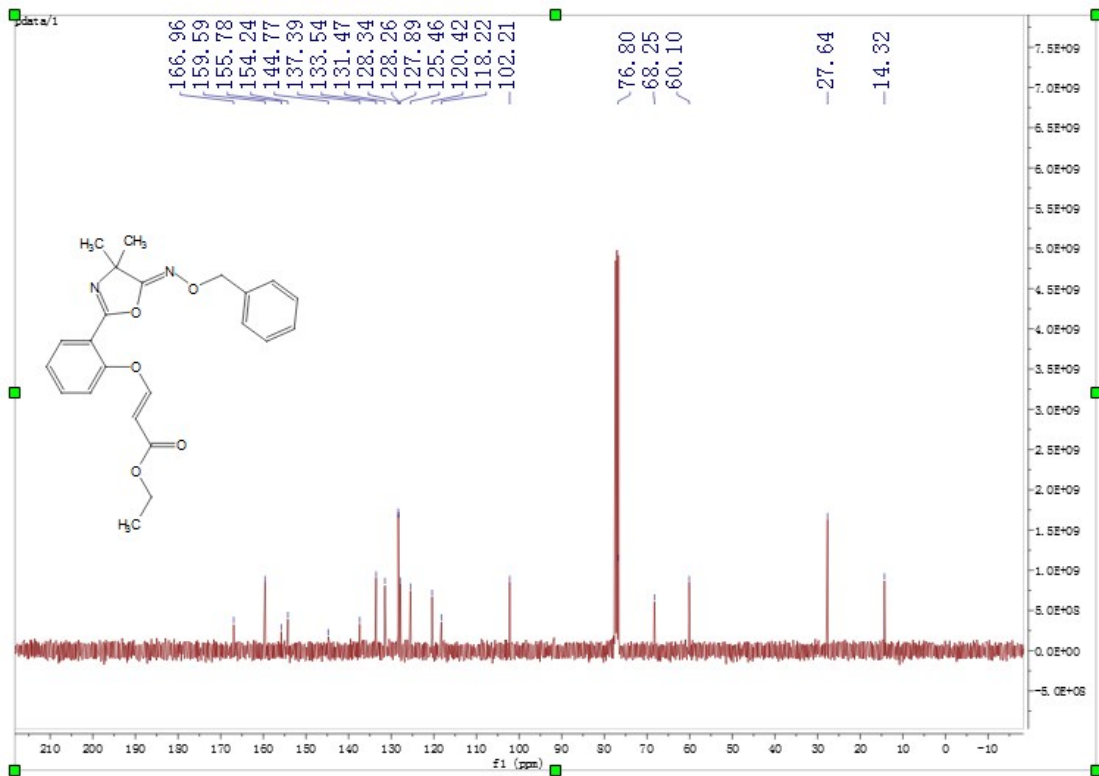
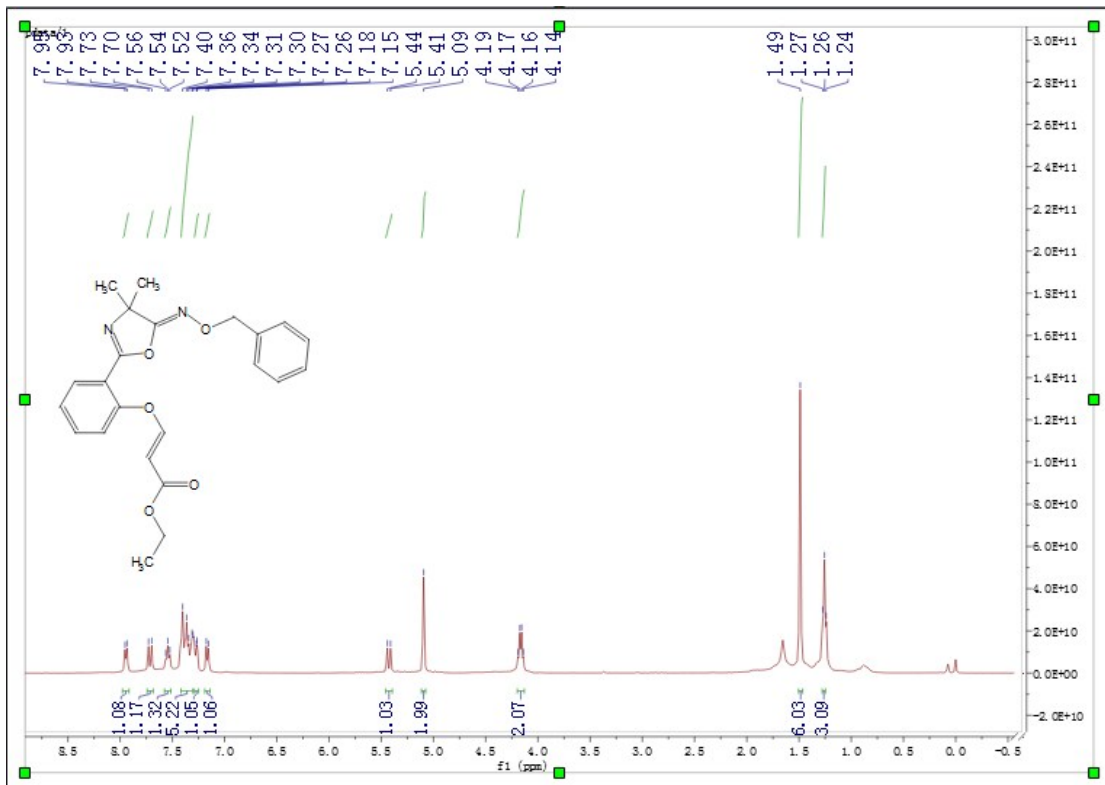


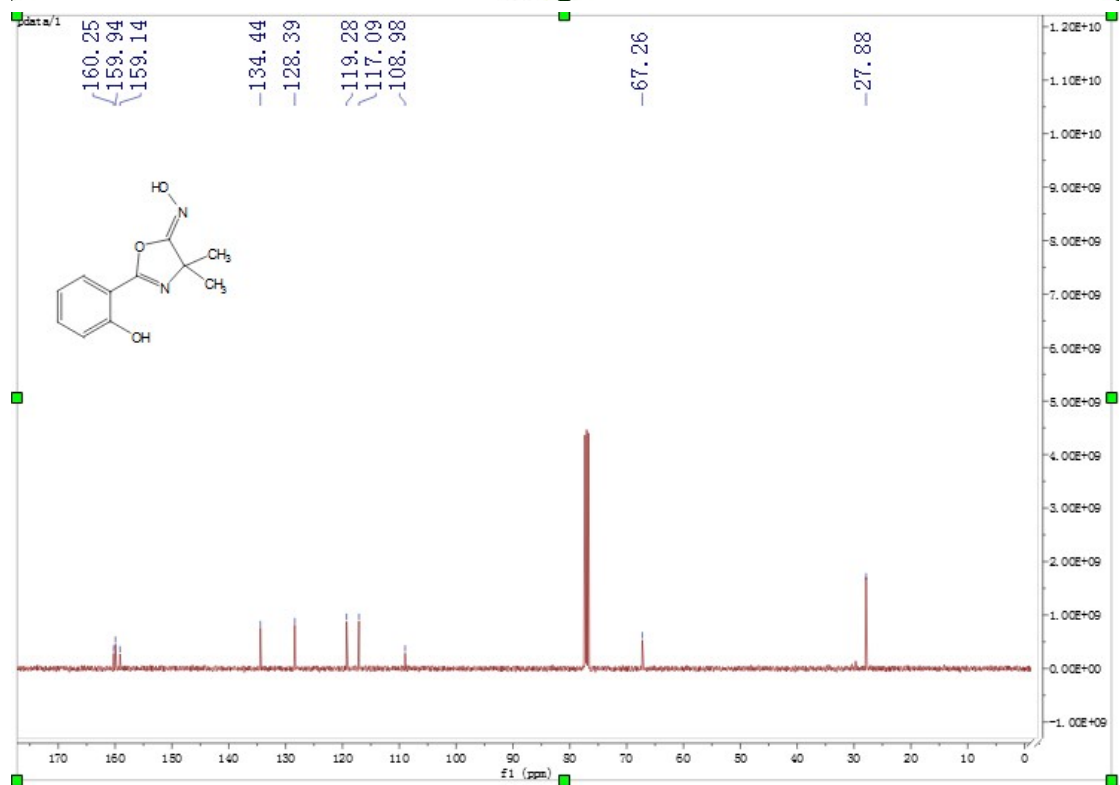
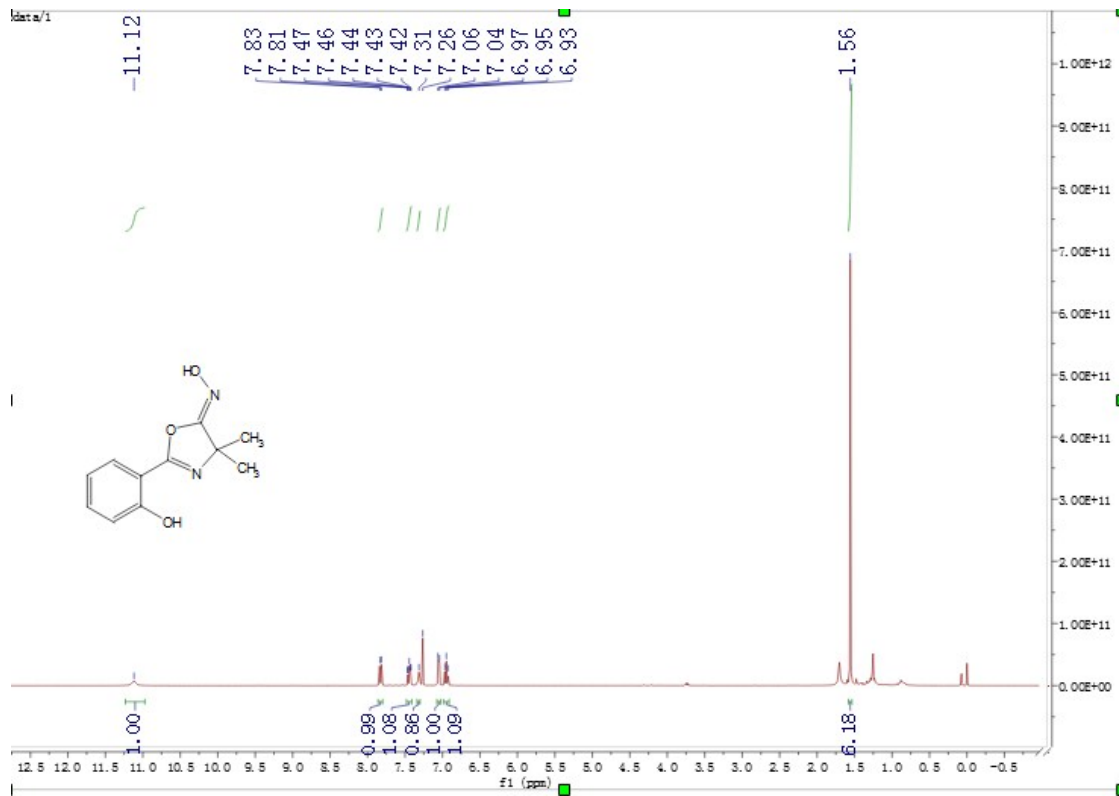












Optical Properties

(Z)-2-(2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime(3aa)

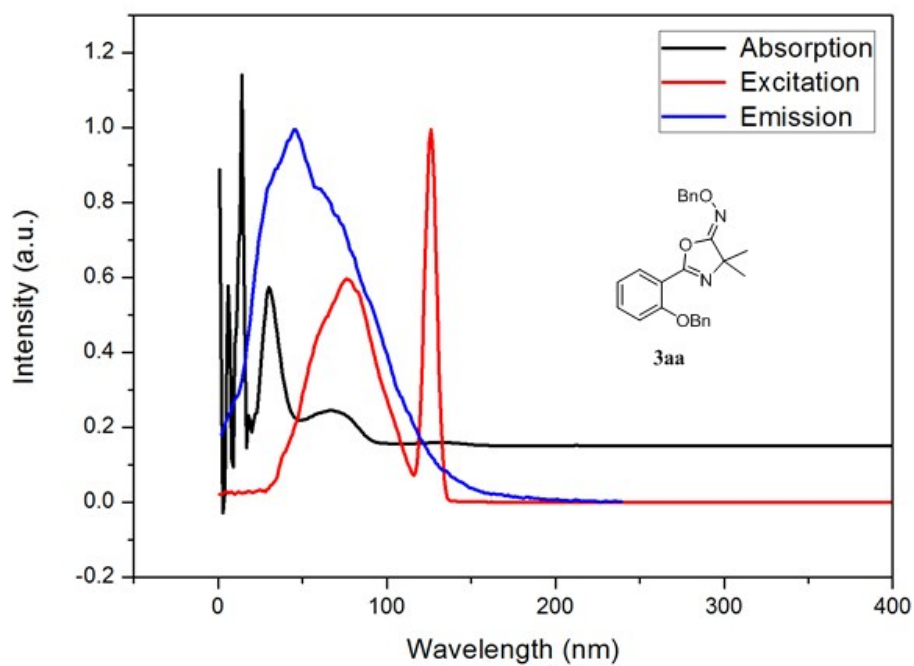


Figure S1: Normalized absorption (black line), excitation (red line, Detection: 267 nm) and emission (blue line, Ex.: 316 nm) spectra of **3aa**. The concentration of dichloromethane solution is $5 \times 10^{-5} \text{ mol L}^{-1}$.

(Z)-2-(2-hydroxy-4-methoxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime(3ai)

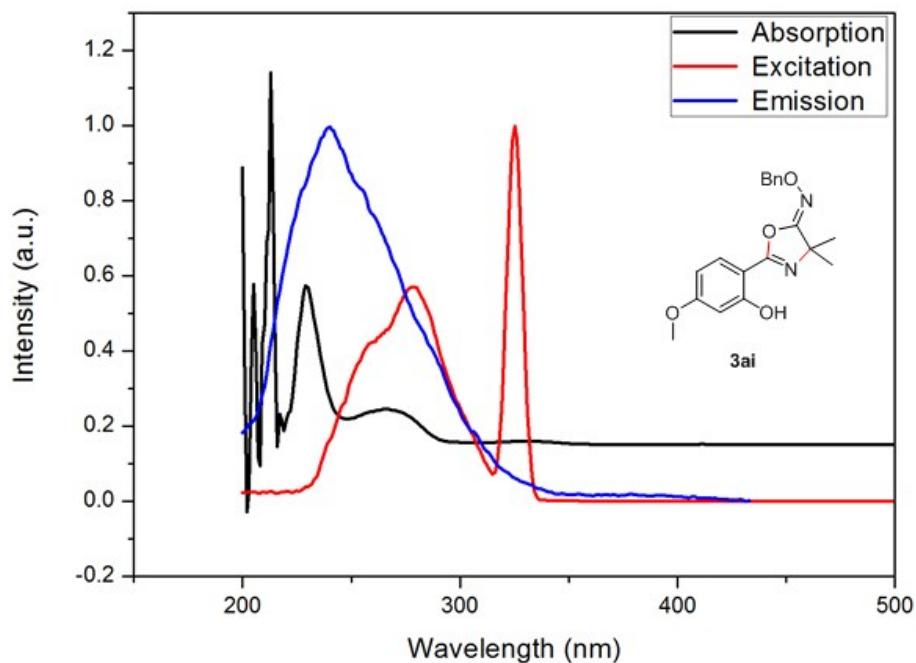


Figure S2: Normalized absorption (black line), excitation (red line, Detection: 267 nm) and emission (blue line, Ex.: 323 nm) spectra of **3ai**. The concentration of dichloromethane solution is $5 \times 10^{-5} \text{ mol L}^{-1}$.

(Z)-2-(3,5-dibromo-2-hydroxyphenyl)-4,4-dimethyloxazol-5(4H)-one O-benzyl oxime(3ao)

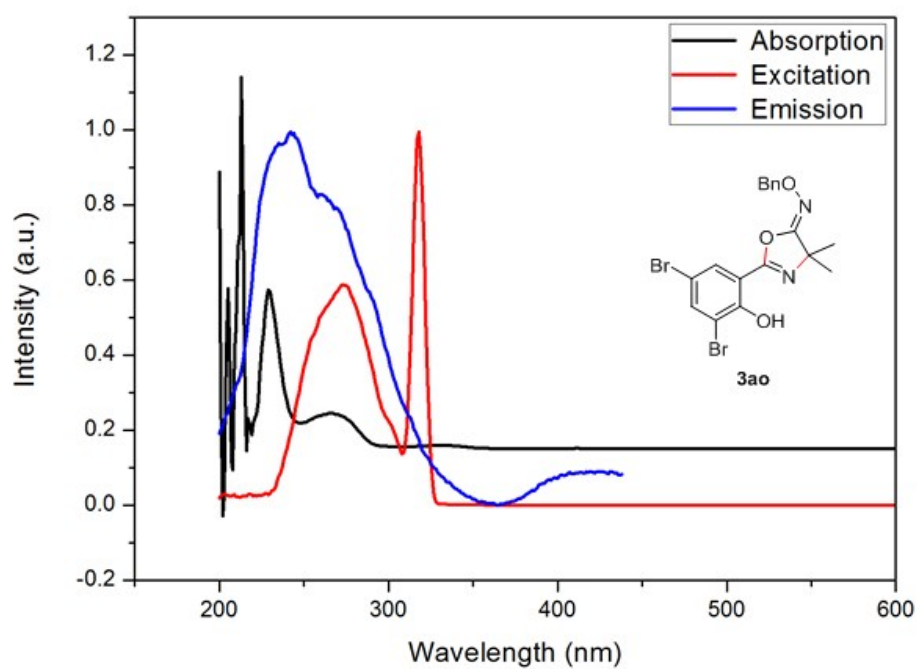


Figure S3: Normalized absorption (black line), excitation (red line, Detection: 266 nm) and

emission (blue line, Ex.: 316 nm) spectra of **3a**. The concentration of dichloromethane solution is $5 \times 10^{-5} \text{ mol L}^{-1}$.