Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Rhodium(III)-catalyzed oxidative cross-coupling of benzoxazinones with styrenes via C–H activation

Xifa Yang,*[a] Song Li,[a] Yuhao He,[a] Danhua Dai,[a] Mengyao Bao,[a] Ziyang Luo,[a] Xiangyang Liu,[a] Yuehua Geng,[a] and Liangxin Fan*[b]

[a] Institute of Pesticide, College of Plant Protection, Henan Agricultural University, Zhengzhou, 450002, China

[b] College of Sciences, Henan Agricultural University, Zhengzhou, 450002, China

Email: fanlx@henau.edu.cn; yangxifachem@163.com

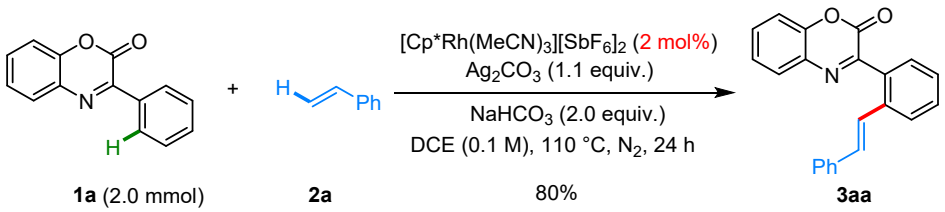
C. Scale-up reaction and synthetic utilization 2

D. Mechanistic studies: 5

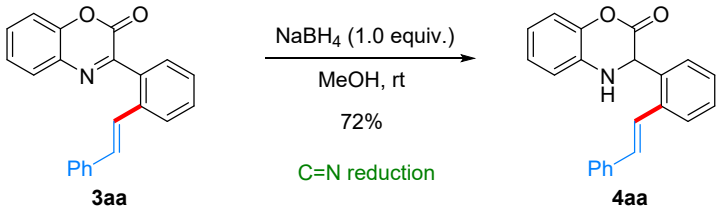
E. References: 10

F. NMR spectra: 11

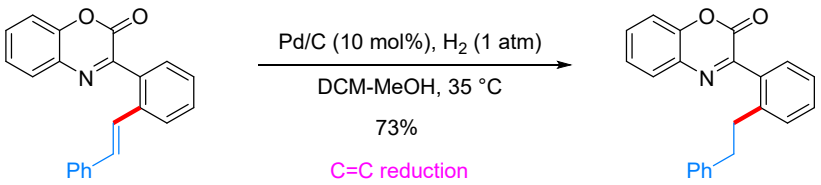
A. Scale-up reaction and synthetic utilization



3-phenyl-2*H*-benzo[*b*][1,4]oxazin-2-one **1a** (0.45 g, 2.0 mmol), styrene **2a** (0.25g, 2.4 mmol, 1.2 equiv.), $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ 33.3 mg, 0.04 mmol, 2 mol%), $NaHCO_3$ (0.34 g, 4.0 mmol, 2.0 equiv.), Ag_2CO_3 (0.66 g, 2.2 mmol, 1.1 equiv.) and DCE (10 mL) were charged into a pressure tube. The reaction mixture was stirred at 110 °C for 24 h. After completion of the reaction, the reaction mixture was filtered through a short pad of celite, the solvent was removed under reduced pressure and the crude reaction mixture was directly purified through column chromatography on silica gel using PE/EA/DCM (20:1:1) as eluent to afford the desired product **3aa** in 80 % yield (0.52 g).

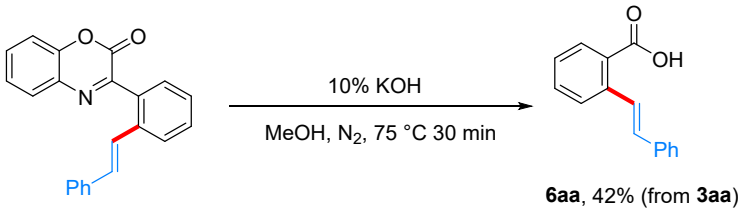


(*E*)-3-(2-styrylphenyl)-2*H*-benzo[*b*][1,4]oxazin-2-one **3aa** (65.1 mg, 0.2 mmol), $NaBH_4$ (7.6 mg, 0.2 mmol, 1.0 equiv.) and MeOH (4.0 mL) were charged into a pressure tube. The reaction mixture was stirred at room temperature for 16 h, and then quenched with water. After a half of solvent was evaporated *in vacuo*, the mixture was diluted with EtOAc, washed with brine, and then dried over anhydrous $MgSO_4$, and solvent was removed under reduced pressure, the obtained residue was purified by column chromatography using PE/EA/DCM (20:1:1) as eluent to afford the desired product **4aa** in 72 % yield (White solid, 47.1 mg, mp: 202-204 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.74 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 7.7 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.46 (d, J = 7.4 Hz, 3H), 7.42 – 7.28 (m, 4H), 7.28 – 7.22 (m, 3H), 7.16 – 7.02 (m, 3H), 6.07 (s, 1H), 3.41 (s, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.3, 142.8, 137.4, 137.0, 135.0, 132.7, 131.4, 130.4, 129.4, 128.8, 128.2, 128.0, 127.8, 127.3, 127.2, 126.9, 123.1, 117.3, 86.7, 29.8. **HRMS** $[M+H]^+$ calculated for $C_{22}H_{18}NO_2^+$ = 328.1332, found: 328.1340.



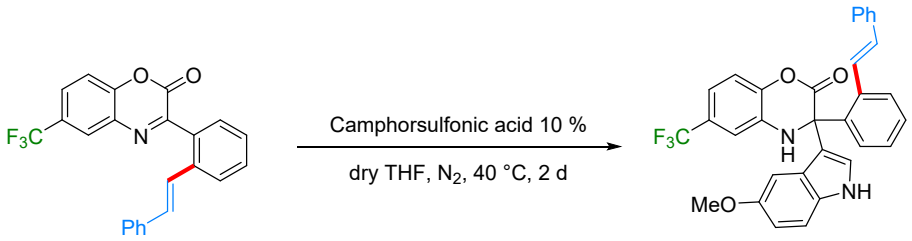
3aa **5aa**

Pd/C (21.3 mg, palladium on activated carbon, 10% Pd basis, 0.1 equiv.) was added to a solution of **3aa** (65.1 mg, 0.2 mmol) in DCM/MeOH (3.0 mL, 1:1). The reaction mixture was stirred under H_2 atmosphere (1 atm) at 35 °C for 16 h. After the reaction was complete (monitored by TLC), the crude reaction mixture was filtered with celite and washed with EtOAc. The solvent was removed under reduced pressure. Then the residue was purified by silica gel column chromatography (PE/EA/DCM = 20:1:1) to afford the desired product **5aa** in 73% yield (White solid, 47.8 mg, mp: 81-83 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (dd, J = 7.9, 1.6 Hz, 1H), 7.58 – 7.50 (m, 2H), 7.47 – 7.30 (m, 5H), 7.21 – 7.09 (m, 3H), 7.08 – 7.01 (m, 2H), 3.09 – 3.00 (m, 2H), 3.00 – 2.90 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 154.7, 152.7, 146.8, 141.6, 141.1, 133.8, 131.6, 131.5, 130.5, 130.4, 129.9, 129.6, 128.6, 128.5, 126.2, 126.1, 125.8, 116.6, 37.9, 35.4. **HRMS** $[M+H]^+$ calculated for $C_{22}H_{18}NO_2^+$ = 328.1332, found: 328.1343.

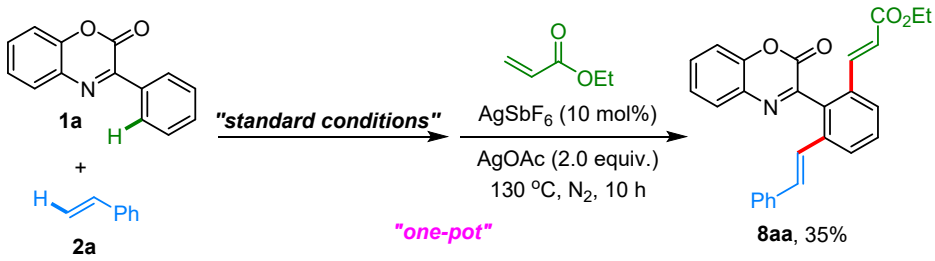


6aa, 42% (from **3aa**)

In a glovebox, **3aa** (0.15 mmol) were refluxed in 10% KOH-MeOH solution (2.0 mL) for 30 min. The mixture was left overnight and then acidulate with acetic acid (15 %). the crude reaction mixture was filtered with celite and washed with DCM. The solvent was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA/DCM (5:1:1) to afford the desired product **6aa** in 42% yield. White solid 42% (14.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.11 – 8.04 (m, 2H), 7.76 (dd, J = 8.0, 1.2 Hz, 1H), 7.58 (td, J = 7.6, 1.6 Hz, 3H), 7.37 (td, J = 7.6, 1.6 Hz, 3H), 7.31 – 7.27 (m, 1H), 7.04 (d, J = 16.2 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.9, 140.3, 137.5, 133.2, 132.0, 131.8, 128.9, 128.1, 127.7, 127.5, 127.4, 127.3, 127.1. **HRMS** $[M+H]^+$ calculated for $C_{15}H_{13}O_2^+$ = 225.0910, found: 225.0909. Analytical data are in accordance with the literature values[1].



In a glovebox, (*E*)-3-(2-styrylphenyl)-6-(trifluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one **3na** (0.20 mmol, 1.0 equiv.), Camphorsulfonic acid (10 mol%) and dry THF (2.0 mL) were charged into a pressure tube. The reaction mixture was stirred at 40 °C for 2 days. After the reaction vessel was cooled to room temperature, the crude reaction mixture was filtered with celite and washed with DCM. The solvent was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA/DCM (10:1:1) to afford the desired product in 45% yield (White solid 45%, 23.0 mg, mp: 120-122 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.19 (s, 1H), 7.56 (d, J = 7.7 Hz, 1H), 7.43 (d, J = 15.9 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.31 – 7.16 (m, 11H), 6.95 – 6.79 (m, 4H), 6.65 (d, J = 8.6 Hz, 1H), 5.12 (s, 1H), 3.68 (d, J = 1.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.2, 154.6, 140.7, 137.7, 137.0, 135.9, 135.0, 132.3, 132.1, 129.4, 129.4, 129.0, 128.5, 128.2, 127.5, 127.2, 126.8, 125.9, 125.9, 124.1 (q, J = 269.0 Hz), 122.3 (d, J = 33.5 Hz), δ 122.3 (dd, J = 7.7, 3.7 Hz), 114.6, 114.0 (dd, J = 7.6, 3.7 Hz), 113.5, 113.4, 112.4, 102.9, 65.2, 55.9. **HRMS** $[M+Na]^+$ calculated for $C_{32}H_{23}F_3NaN_2O_3^+$ = 563.1553, found: 563.1538.

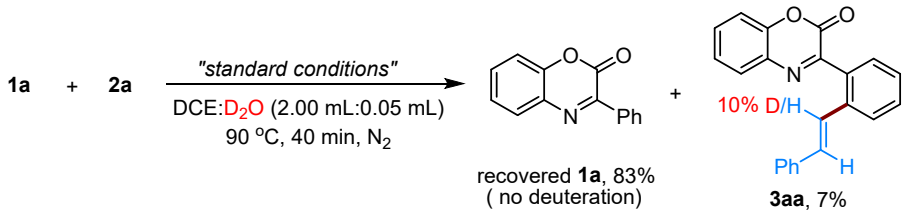


In a glovebox, Oxazinone **1a** (0.20 mmol, 1.0 equiv.), styrene **2a** (0.24 mmol, 1.2 equiv.), $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ (4 mol%), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2.0 equiv.), Ag_2CO_3 (60.6 mg, 0.2 mmol, 1.1 equiv.) and DCE (2.0 mL) were charged into a pressure tube. The reaction mixture was stirred at 110 °C for 12 h. After the reaction vessel was cooled to room temperature, Ethyl acrylate (1.2 equiv.) $AgSbF_6$ (10 mol%) and AgOAc (2.0 equiv.) were charged into the pressure tube, and the reaction mixture was stirred at 130 °C for 12 h. After the reaction vessel was cooled to room temperature, the crude reaction mixture was filtered with celite and washed with DCM. The solvent

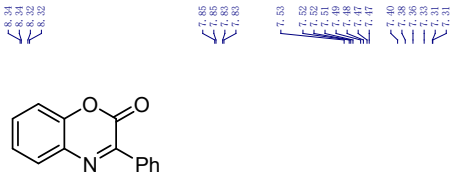
was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA/DCM (10:1:1) to afford the desired product. Yellow solid 35% (29.3 mg), mp: 115-117 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.69 – 7.50 (m, 4H), 7.43 (dd, *J* = 17.4, 8.5 Hz, 2H), 7.34 – 7.21 (m, 5H), 7.06 – 6.89 (m, 2H), 6.41 (dd, *J* = 15.8, 1.2 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 1.25 (td, *J* = 7.1, 1.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.5, 154.2, 152.4, 146.9, 141.4, 138.0, 136.9, 134.6, 133.2, 133.2, 132.3, 131.3, 130.2, 130.0, 128.8, 128.3, 128.1, 126.9, 126.2, 126.0, 125.3, 121.5, 116.9, 60.7, 14.3. **HRMS** $[M+H]^+$ calculated for $C_{27}H_{22}NO_4^+$ = 424.1543, found: 424.1534.

B. Mechanistic studies:

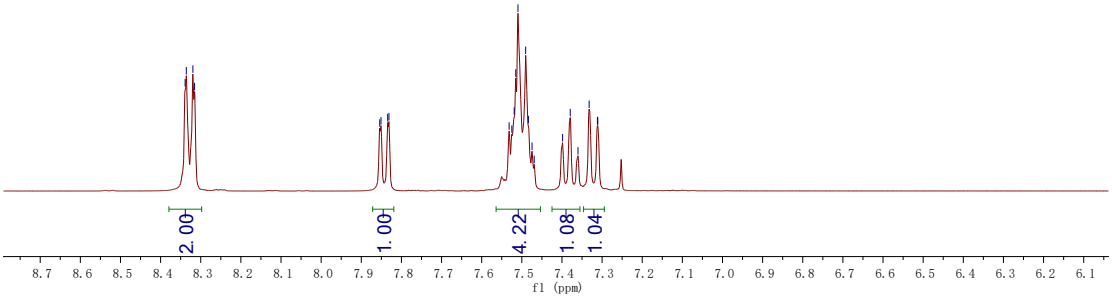
a) deuteration experiment

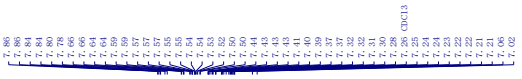


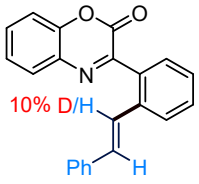
1a (44.6 mg, 0.20 mmol), **2a** (25.0 mg, 0.24 mmol, 1.2 equiv.), $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ (6.7 mg, 0.008 mmol, 4 mol%), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2.0 equiv.), Ag_2CO_3 (60.6 mg, 0.22 mmol, 1.1 equiv.), 0.05 mL D_2O and DCE (2.0 mL) were charged into a pressure tube, and the mixture was heated at 90 °C for 40 minutes. The reaction mixture was filtered through a short pad of celite, the solvent was removed under reduced pressure and the crude reaction mixture was directly purified through column chromatography on silica gel using petroleum ether/ethyl acetate (20:1) as eluent to recover the starting material **1a** in 83% yield and no H/D exchange in 1**aa** was observed, while 10% H/D exchange was observed at the alkenyl C-H site of product **3aa**.



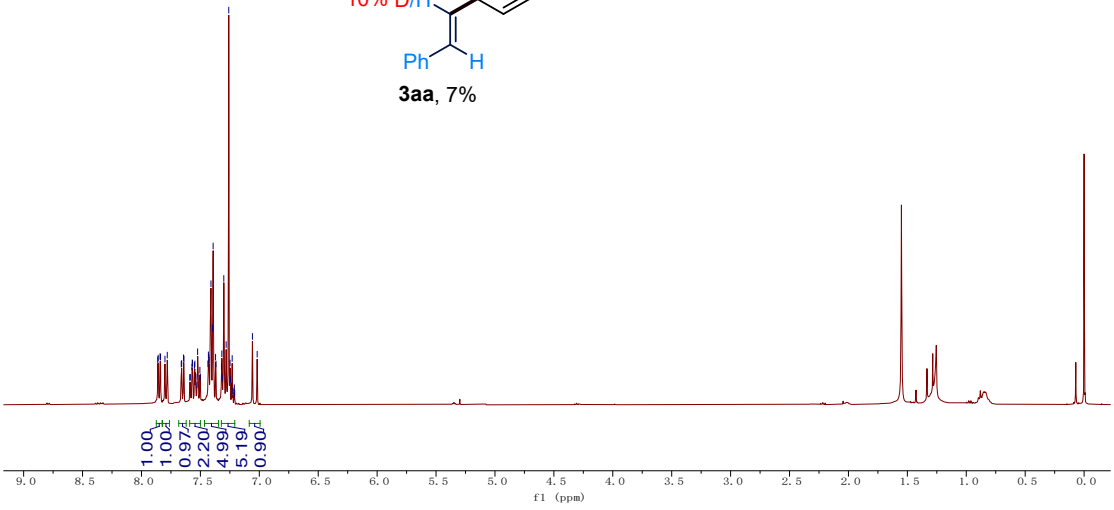
recovered **1a**



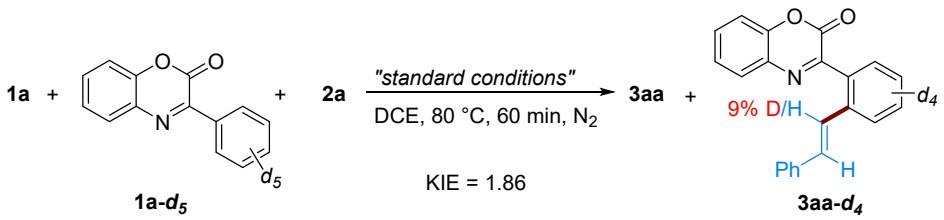




3aa, 7%

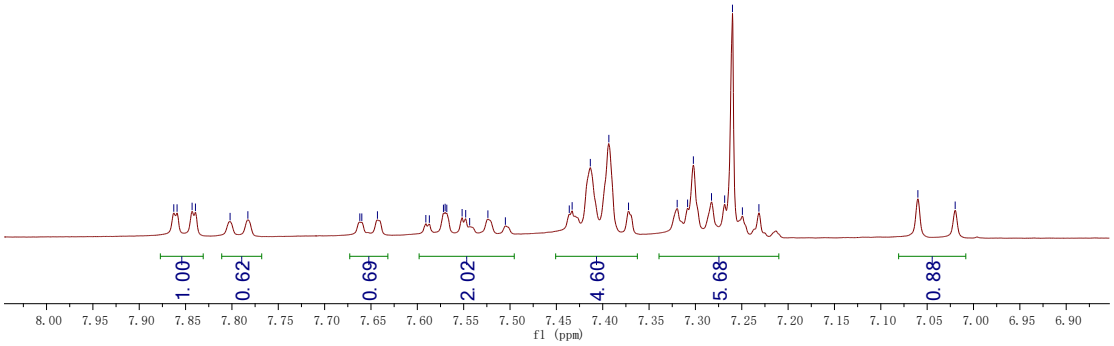


b) competitive KIE: aryl C-H activation

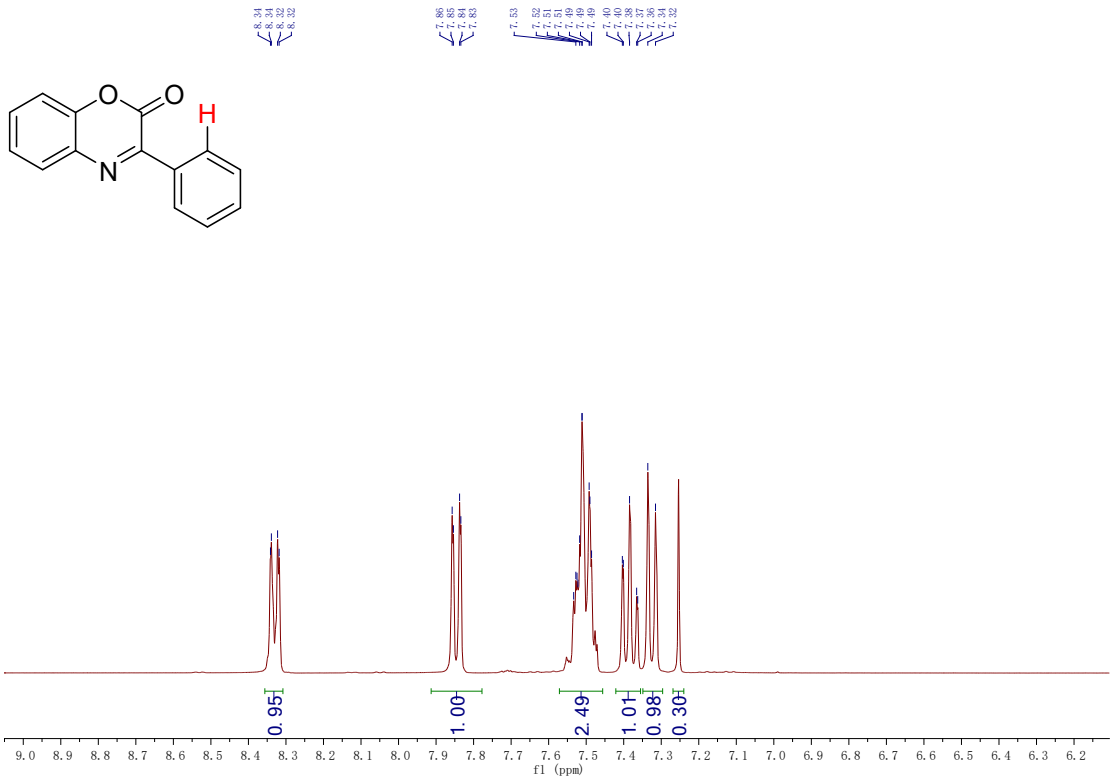


1a (44.6 mg, 0.2 mmol) and **1a**-d_5 (45.7 mg, 0.2 mmol, 1.0 equiv.), **2a** (26.9 mg, 0.24 mmol, 1.2 equiv.), $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ (6.7 mg, 0.008 mmol, 4 mol%), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2.0 equiv.), Ag_2CO_3 (60.6 mg, 0.22 mmol, 1.1 equiv.) and DCE (2.0 mL) were charged into a pressure tube, and the mixture was heated at 80 °C for 60 min under nitrogen. The reaction was quenched and the volatiles were removed under reduced pressure. The residue was purified by silica gel chromatography and gave 3.6 mg of **3aa** and **3aa-*d*$_4$** with 36.4 mg of **1a** and **1a-*d*$_4$** were recovered. KIE value determined on the basis of ^{1}H NMR analysis of **3aa** and **3aa-*d*$_4$** as well as the recovered **1a** were gave 1.6 and 1.5, respectively.

3aa : **3aa-*d*** = 0.62/(1-0.62) = 1.6

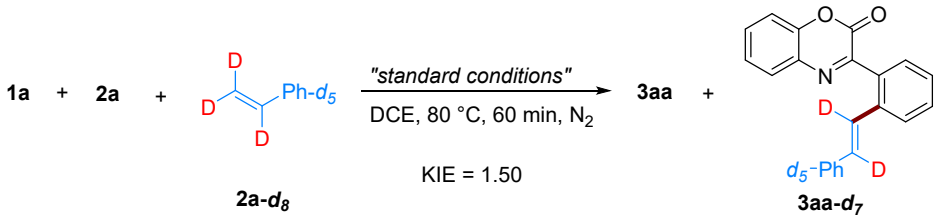


KIE value determined on the basis of ^{1}H NMR analysis of the recovered **1a**



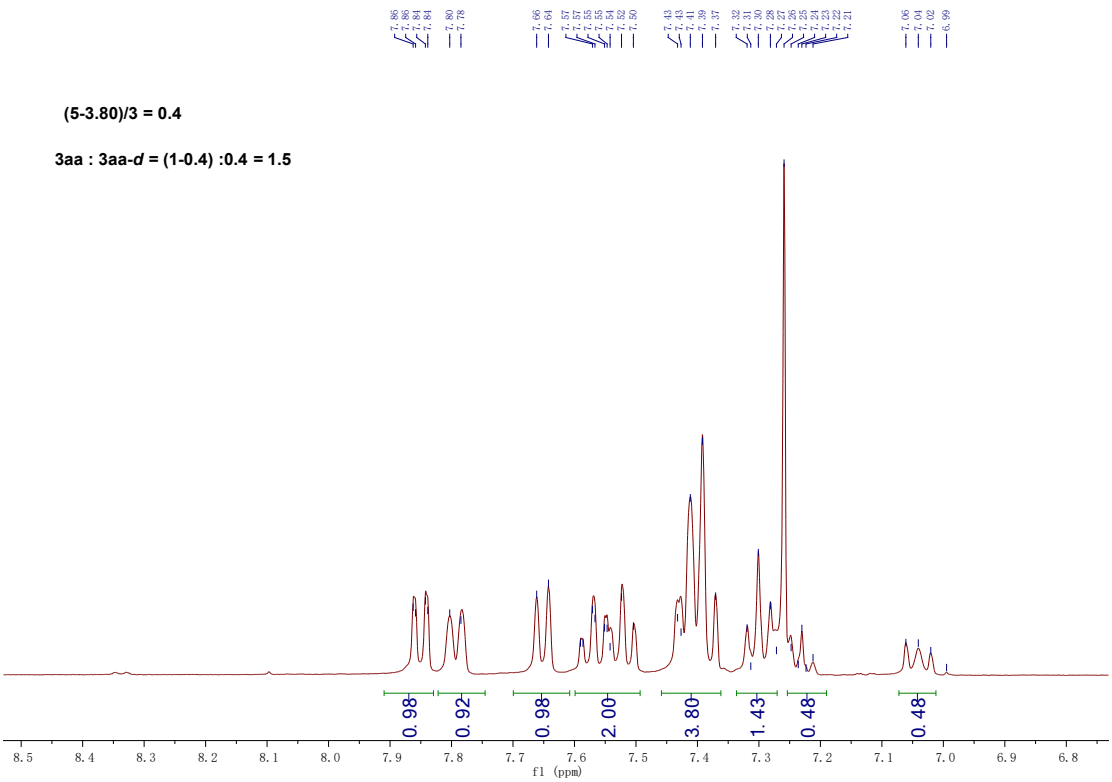
	C_{17}-H	C_{17}-D
t = 0	1	1
conversion	-kx	-x
t = 60 min	(1-kx)/(1-x) = (2-0.95)/0.95	
	(1-kx)228+223x = 364;	k = KIE = 1.5

c) competitive KIE: *β*-H elimination

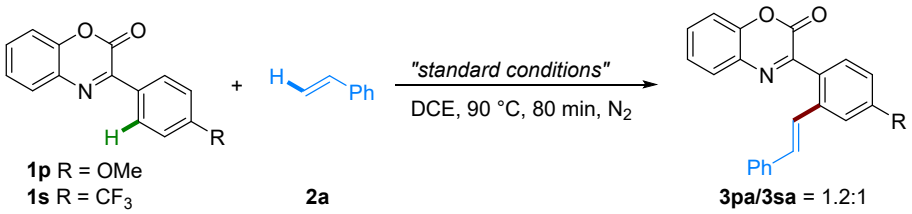


2a-*d*$_8$ **3aa-*d*$_7$**

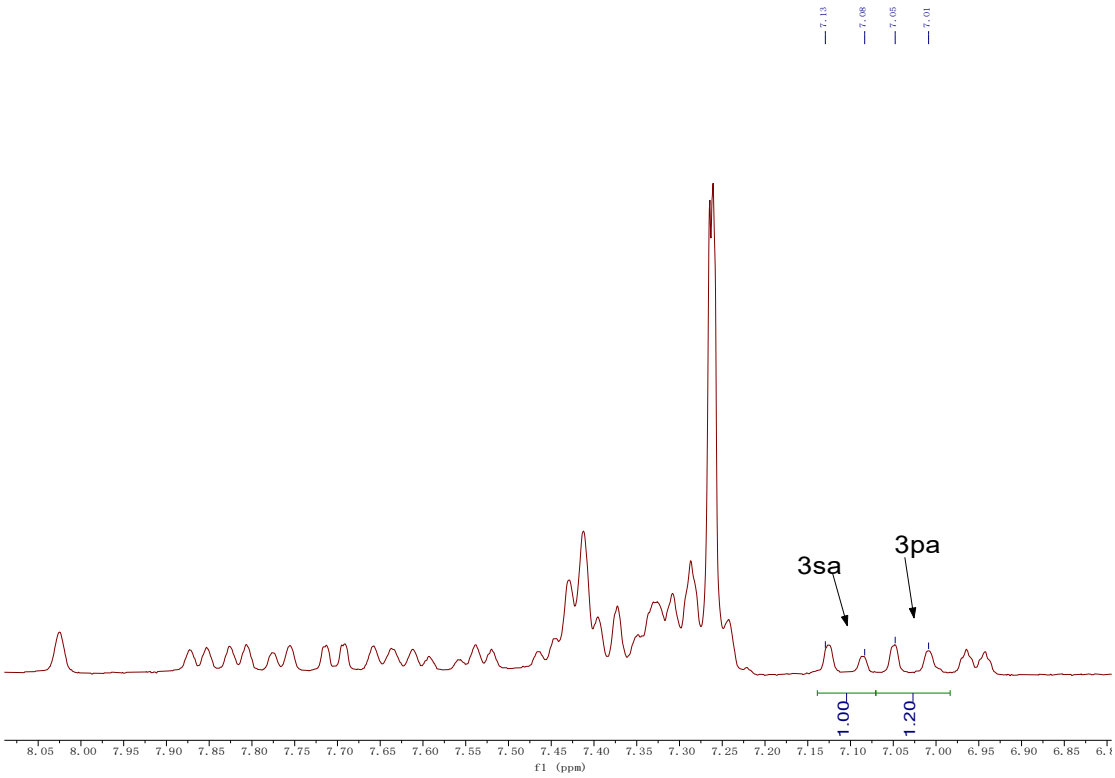
1a (44.6 mg, 0.20 mmol), **2a** (25.0 mg, 0.24 mmol, 1.2 equiv.), **2a-*d*$_8$** (26.9 mg, 0.24 mmol, 1.2 equiv.), $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ (6.7 mg, 0.008 mmol, 4 mol%), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2.0 equiv.), Ag_2CO_3 (60.6 mg, 0.22 mmol, 1.1 equiv.) and DCE (2.0 mL) were charged into a pressure tube, and the mixture was heated at 80 °C for 60 min under nitrogen. The reaction was quenched and the volatiles were removed under reduced pressure. The residue was purified by silica gel chromatography with 4.0 mg of **3aa** and **3aa-*d*$_7$** were recovered. KIE value (k_H/k_D = 1.5:1) was determined on the basis of ^{1}H NMR analysis of **3aa** and **3aa-*d*$_7$.**



d) intermolecular competition experiment



1p (50.7 mg, 0.20 mmol), **1s** (58.2 mg, 0.20 mmol, 1.0 equiv.), **2a** (25.0 mg, 0.24 mmol, 1.2 equiv.), $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ (6.7 mg, 0.008 mmol, 4 mol%), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2.0 equiv.), Ag_2CO_3 (60.6 mg, 0.22 mmol, 1.1 equiv.) and DCE (2.0 mL) were charged into a pressure tube, and the mixture was heated at 90 °C for 80 min under nitrogen. The reaction was quenched and the volatiles were removed under reduced pressure. The residue was purified by silica gel chromatography with 15.0 mg of **3pa** and **3sa** were recovered. The ratio of **3pa** and **3sa** (1.2:1) was determined on the basis of ^1H NMR analysis of **3pa** and **3sa.**

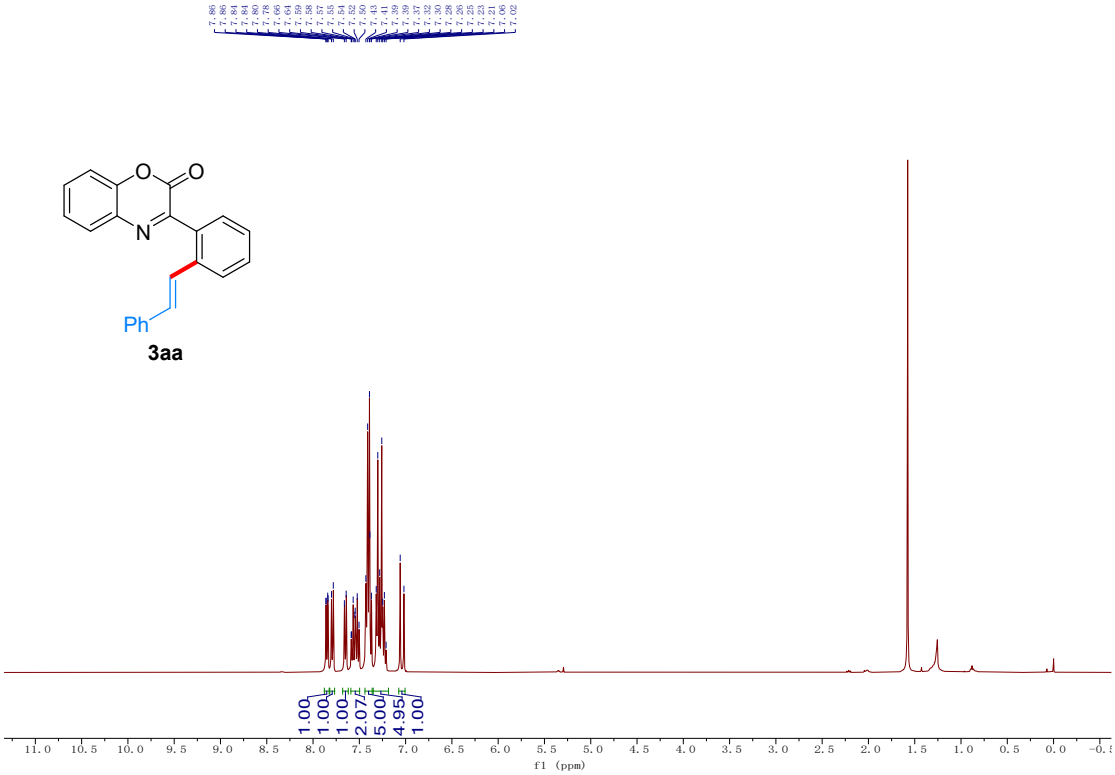


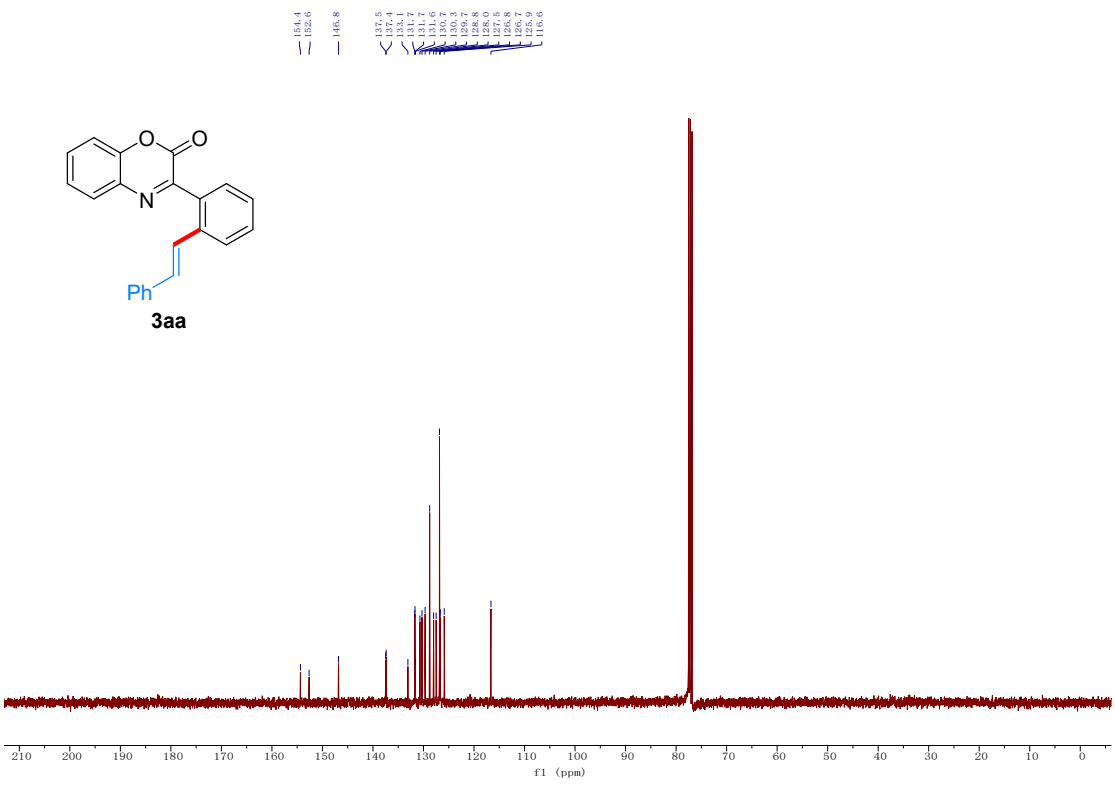
E. References:

1. A. A. Folgueiras-Amador, K. Philipps, S. Guilbaud, J. Poelakker and T. Wirth, *Angew. Chem. Int. Ed.,* 2017, **56**, 15446-15450.

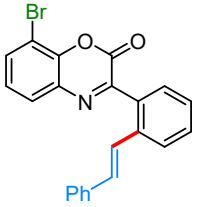
F. NMR spectra:

^{1}H and ^{13}C NMR Spectra of compound **3aa**

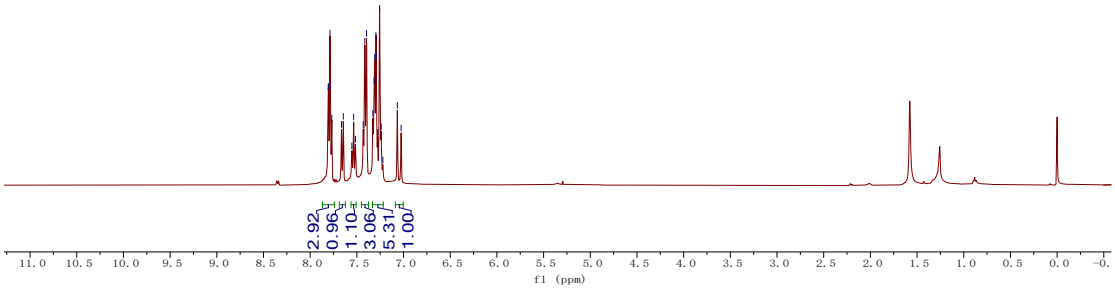


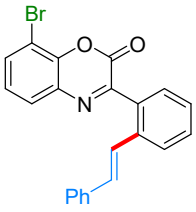


^{1}H and ^{13}C NMR Spectra of compound **3ba**



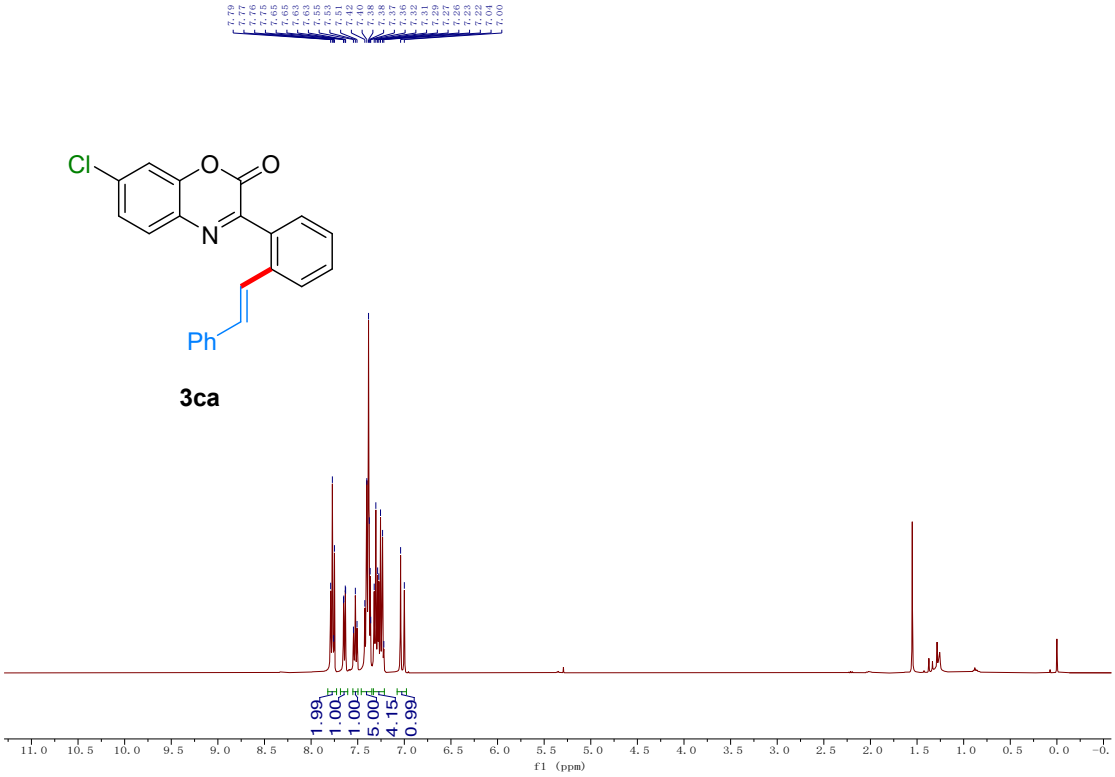
3ba

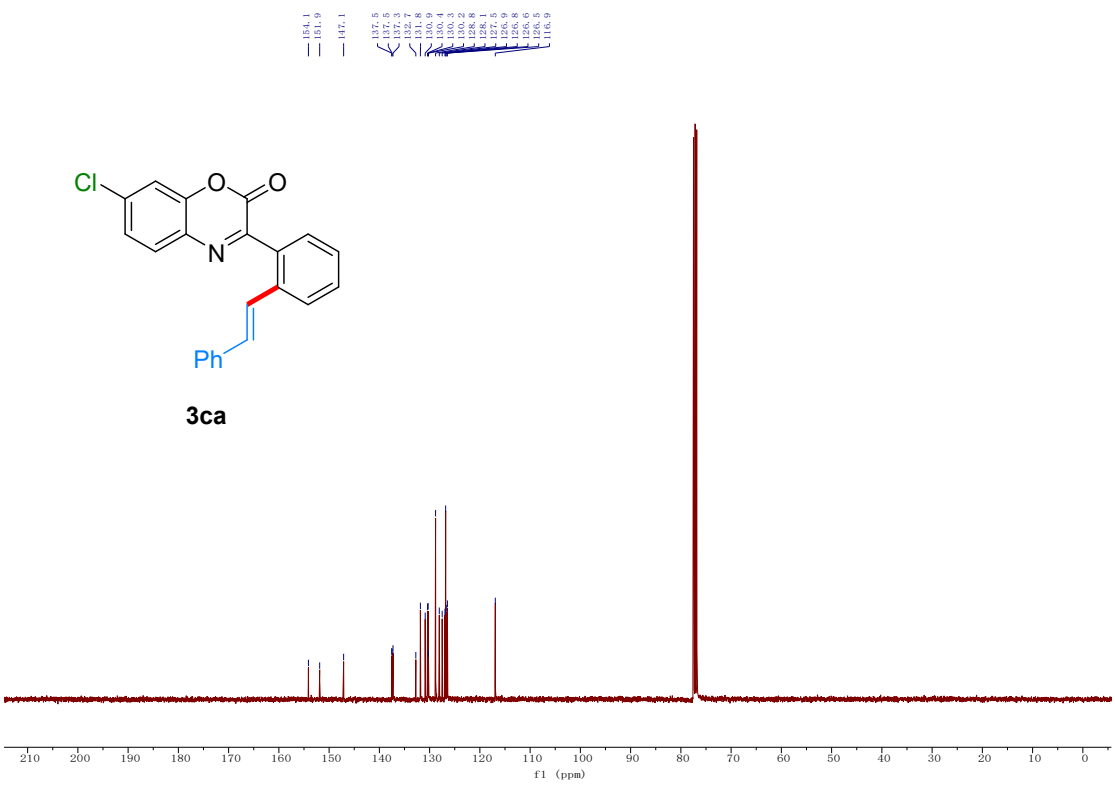




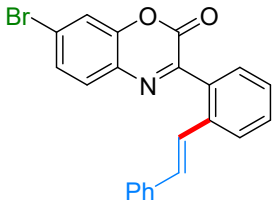
3ba

^{1}H and ^{13}C NMR Spectra of compound **3ca**

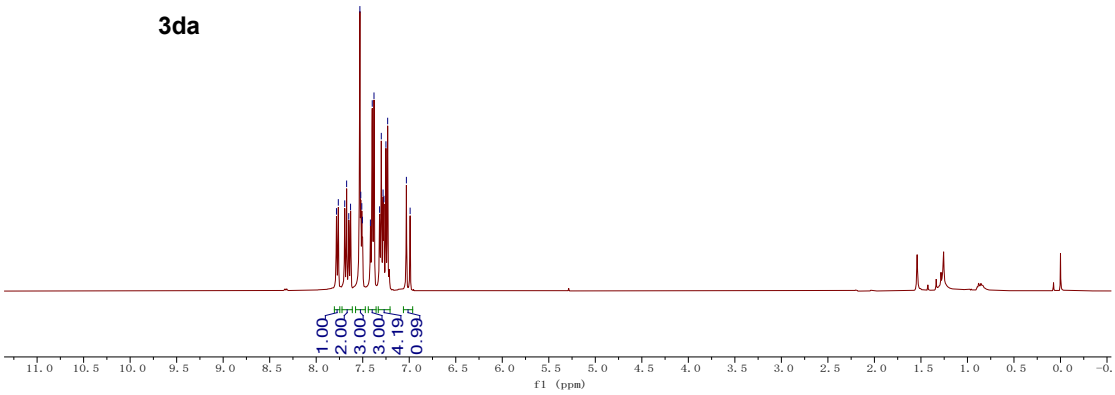


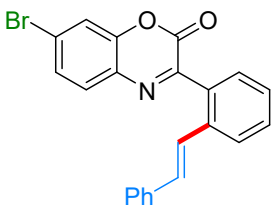


^{1}H and ^{13}C NMR Spectra of compound **3da**



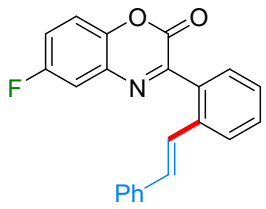
3da



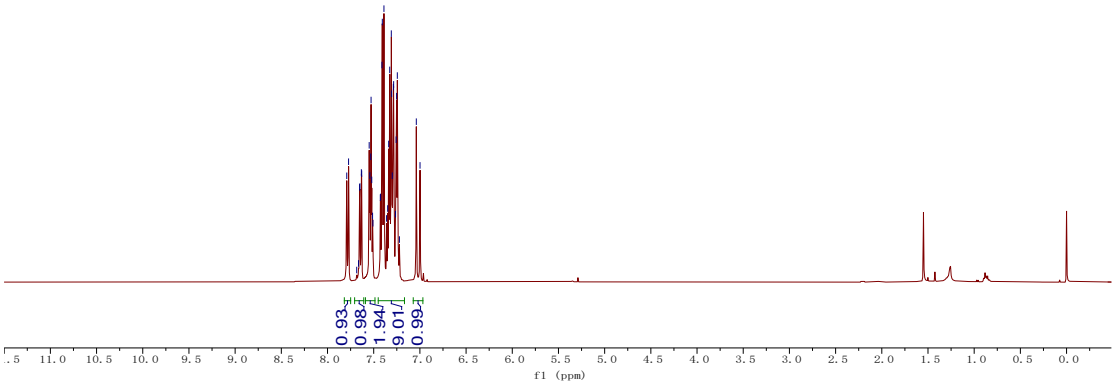


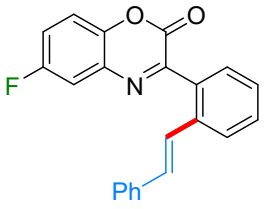
3da

^{1}H and ^{13}C NMR Spectra of compound **3ea**



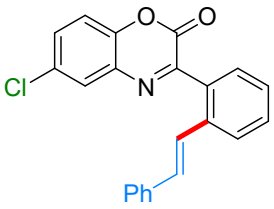
3ea



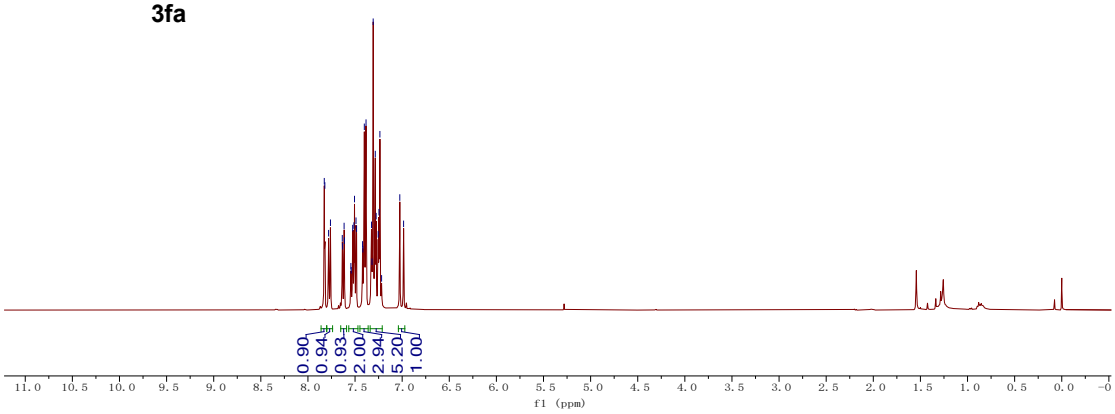


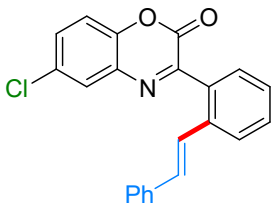
3ea

^{1}H and ^{13}C NMR Spectra of compound **3fa**

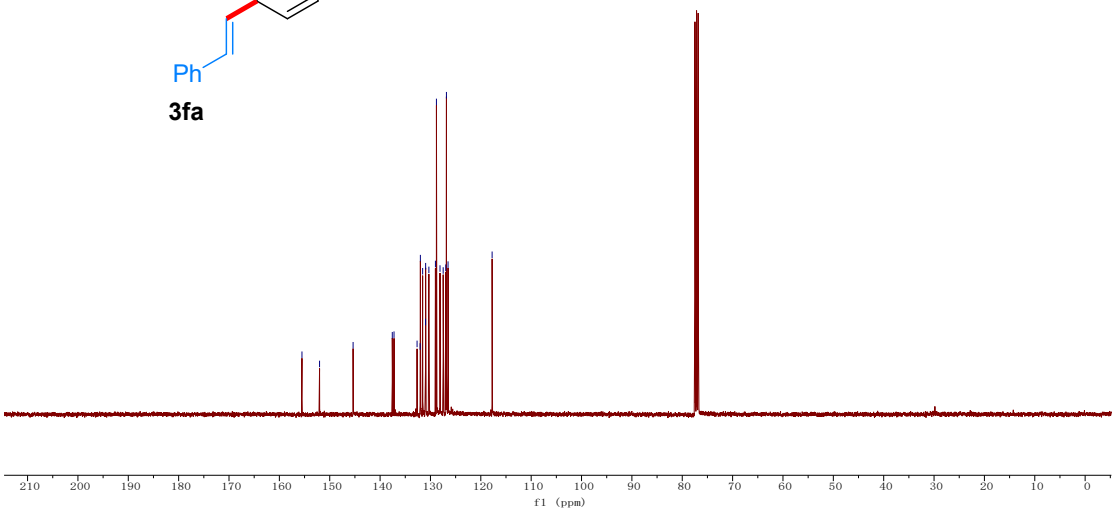


3fa

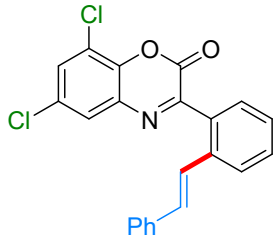




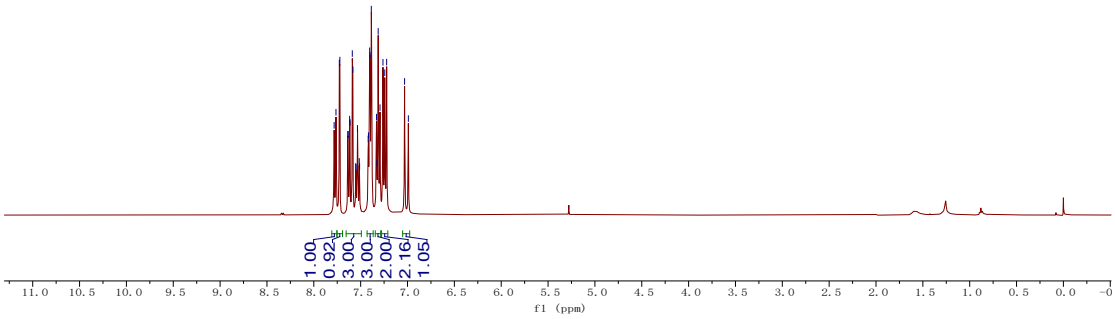
3fa

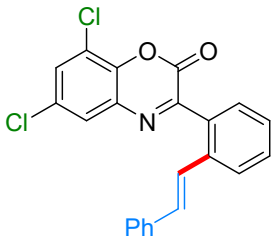


^{1}H and ^{13}C NMR Spectra of compound **3ga**

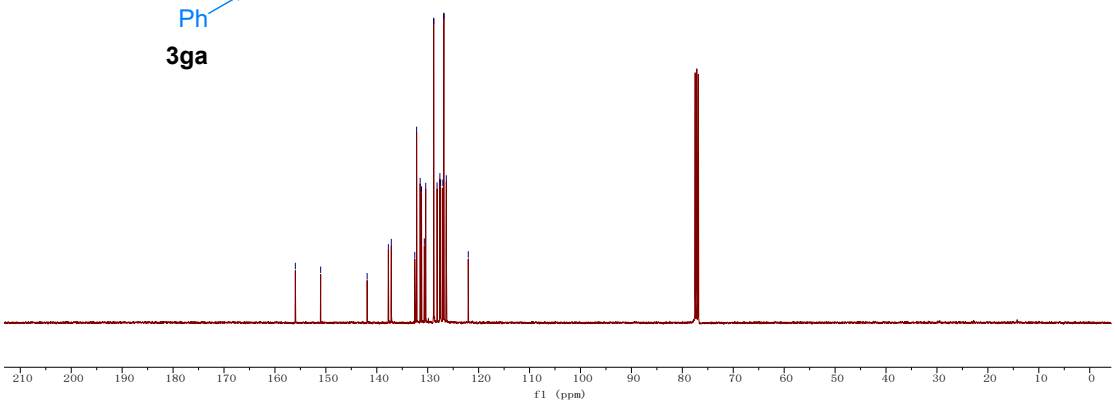


3ga

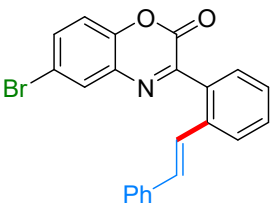




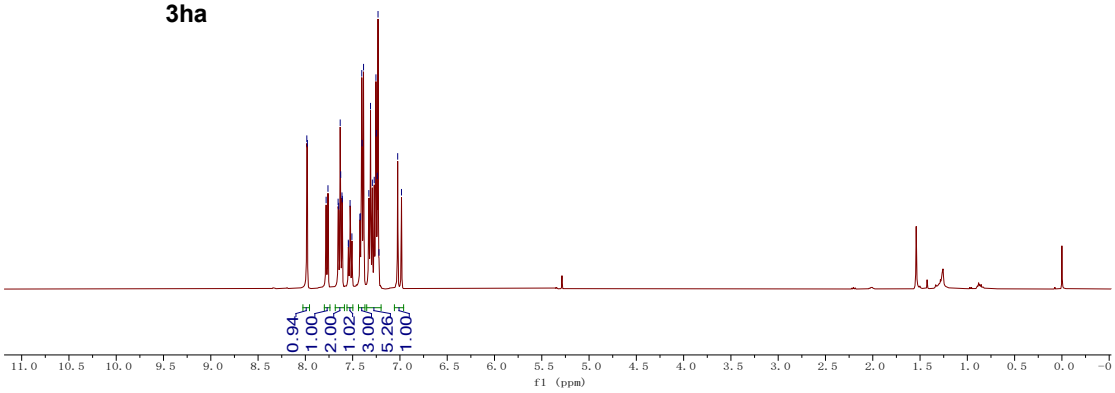
3ga

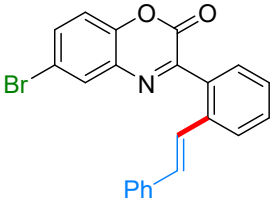


^{1}H and ^{13}C NMR Spectra of compound **3ha**



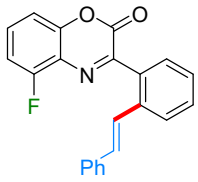
3ha



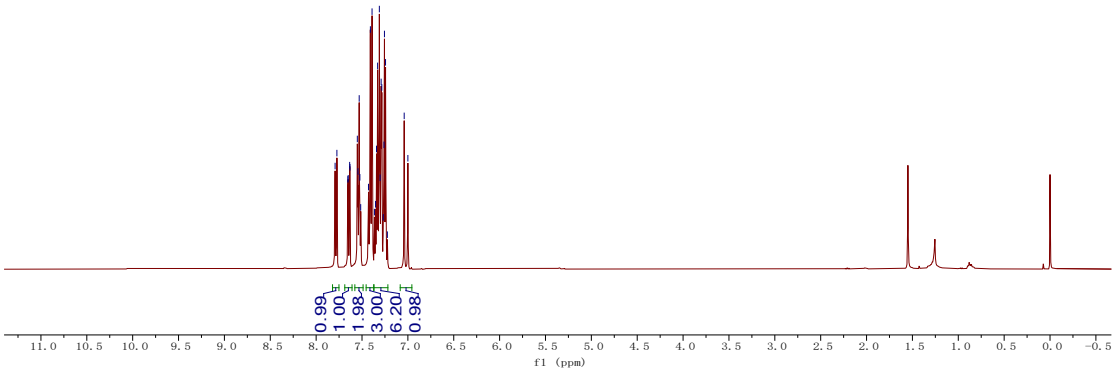


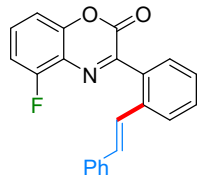
3ha

^{1}H and ^{13}C NMR Spectra of compound **3ia**



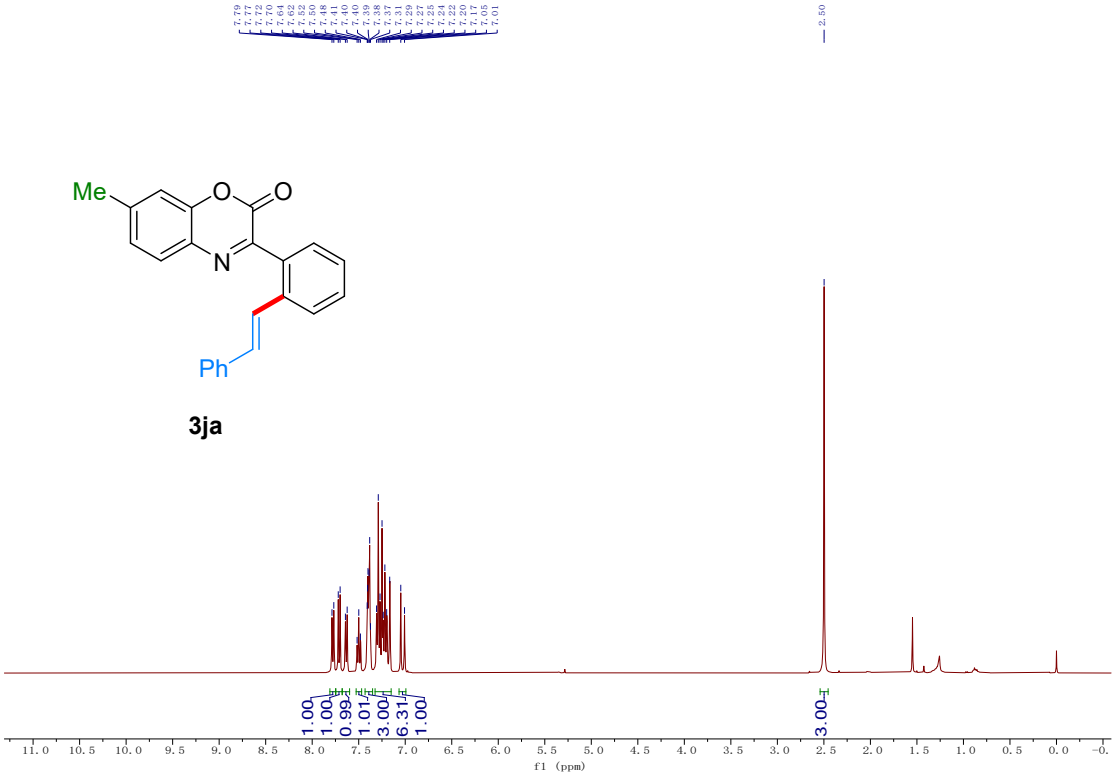
3la

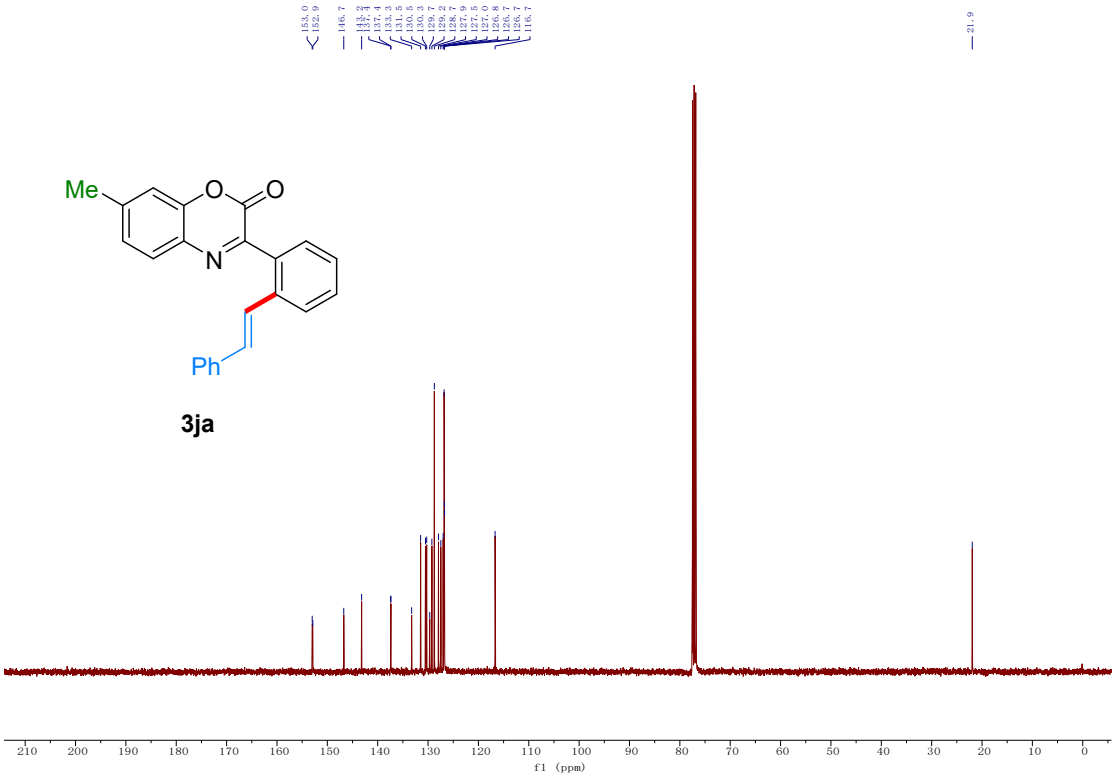




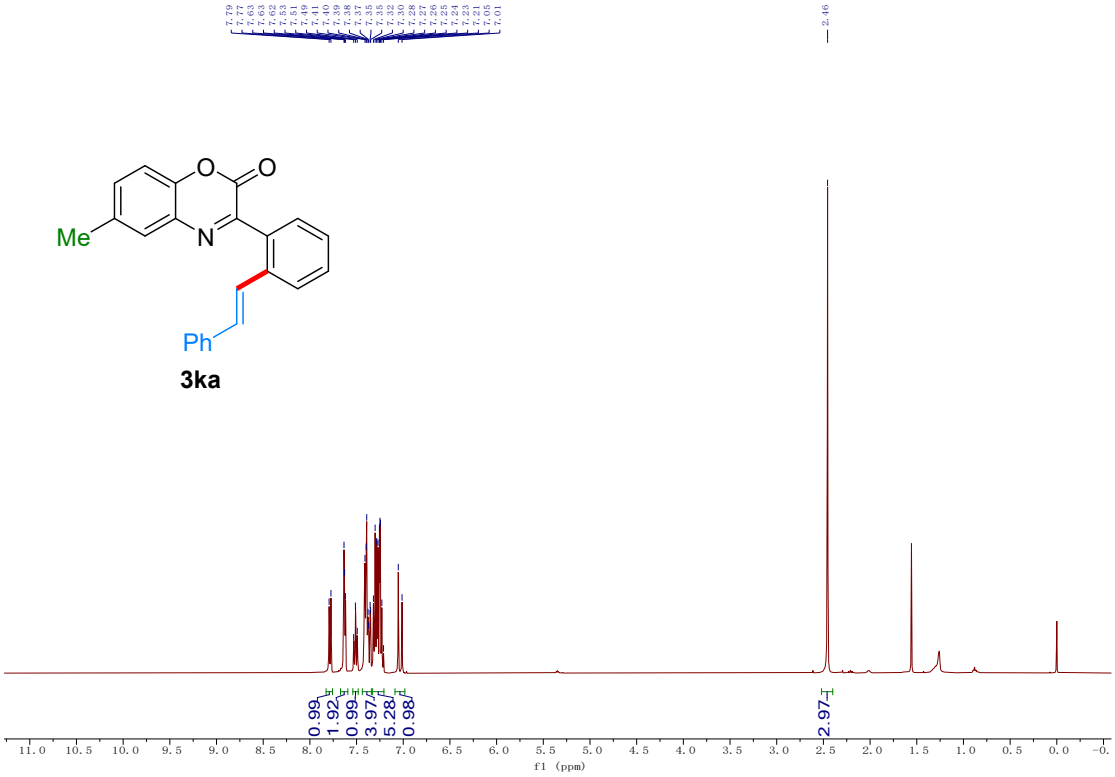
3la

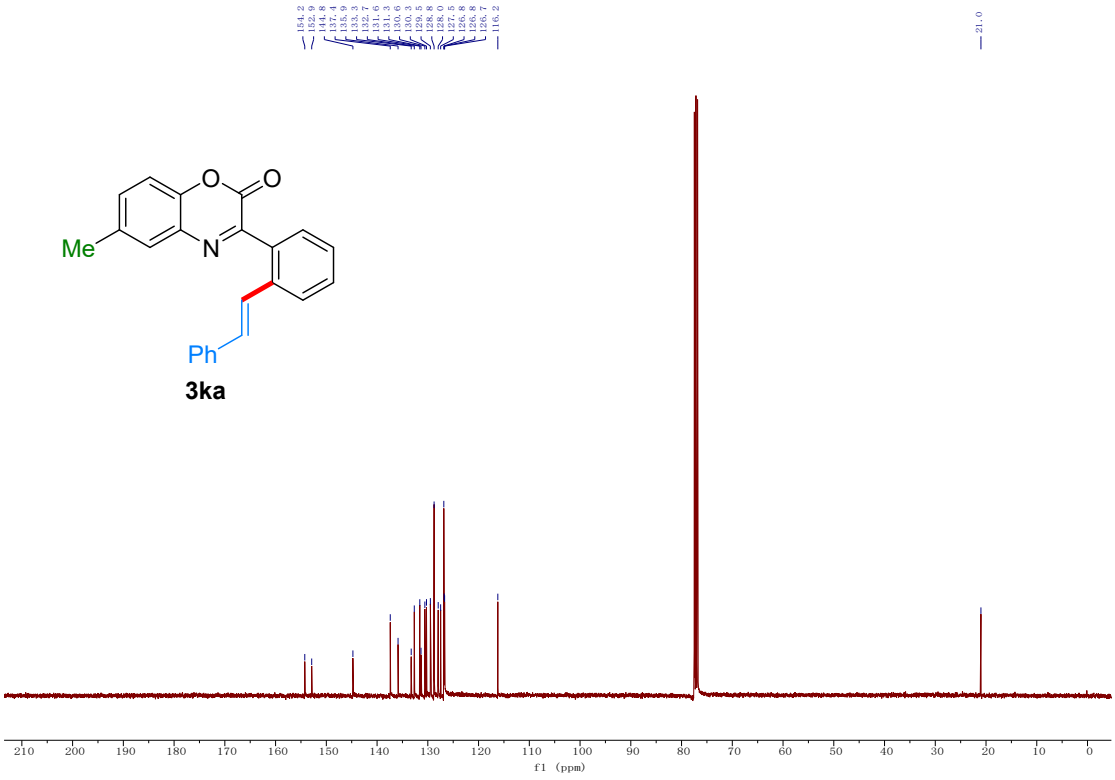
^{1}H and ^{13}C NMR Spectra of compound **3ja**



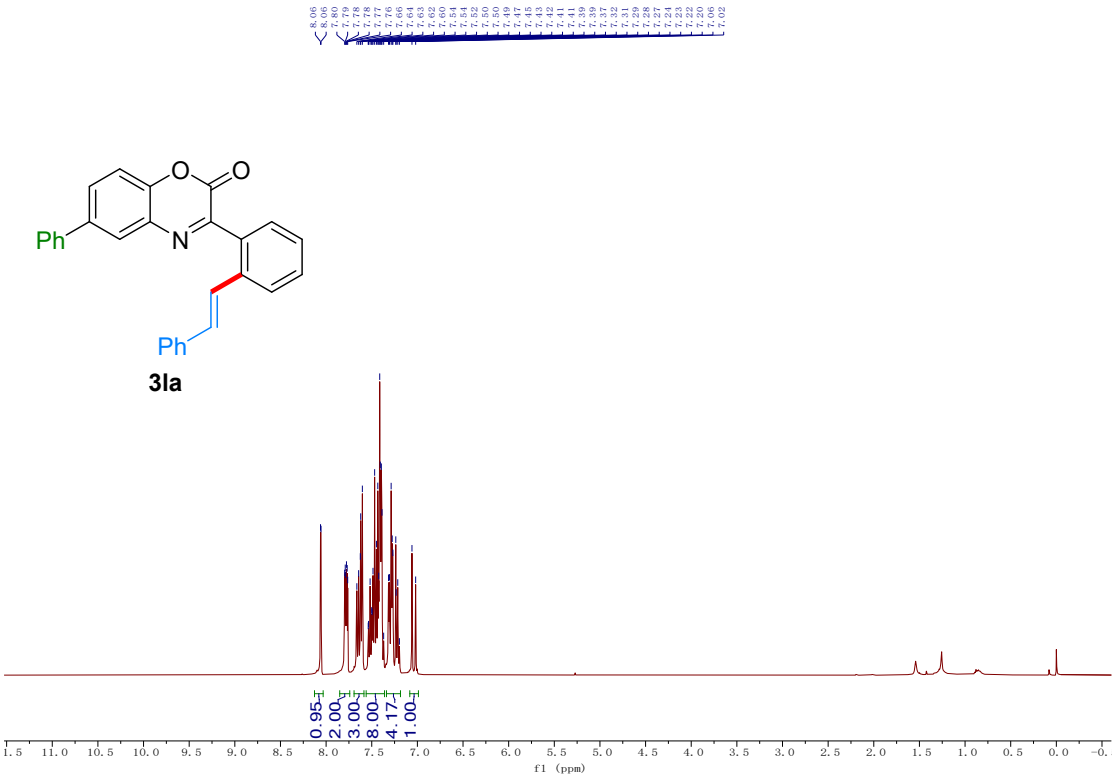


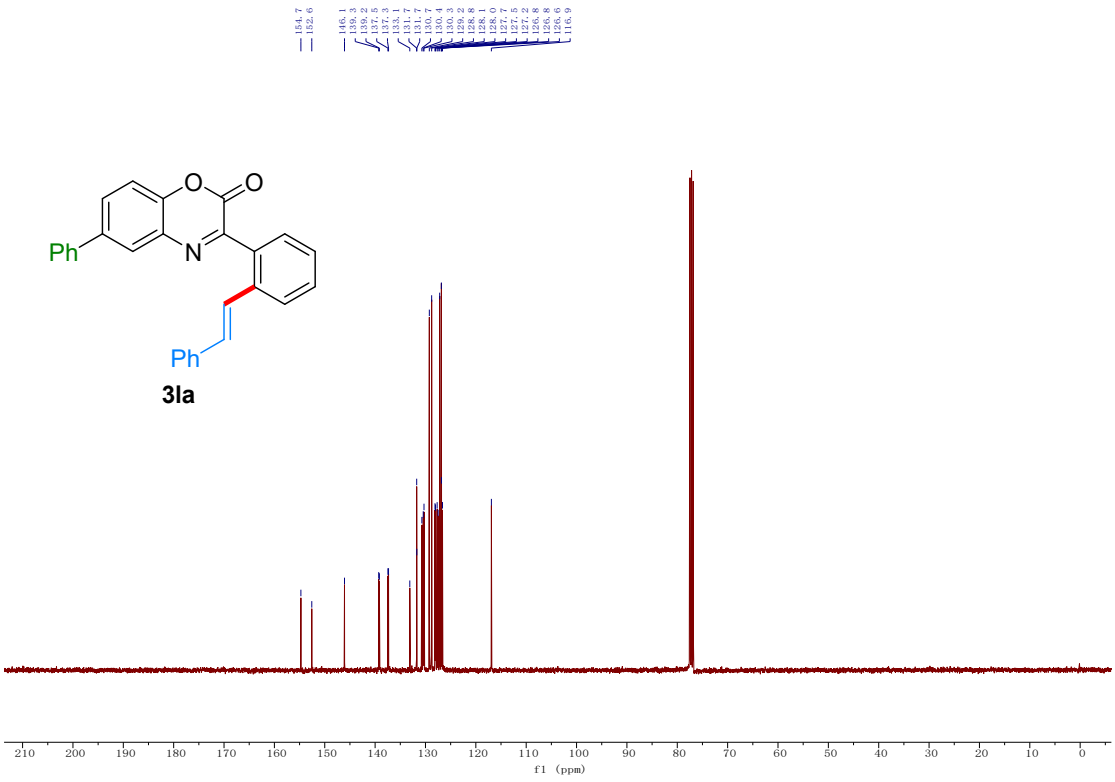
^{1}H and ^{13}C NMR Spectra of compound **3ka**



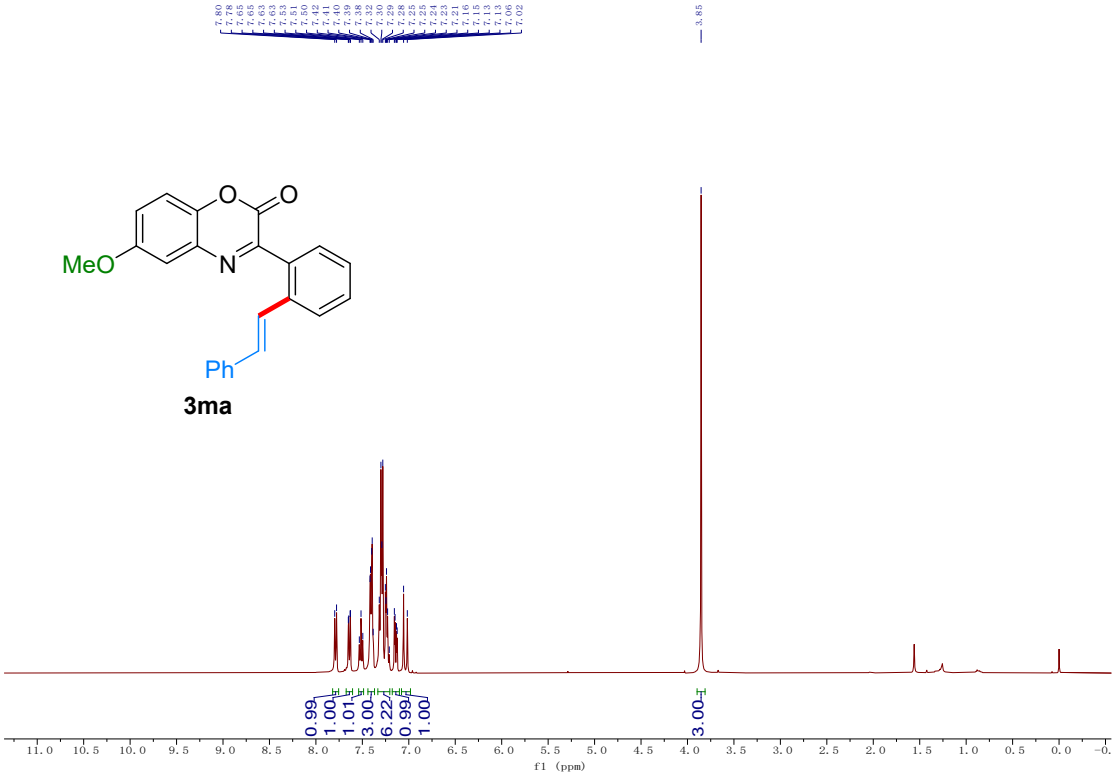


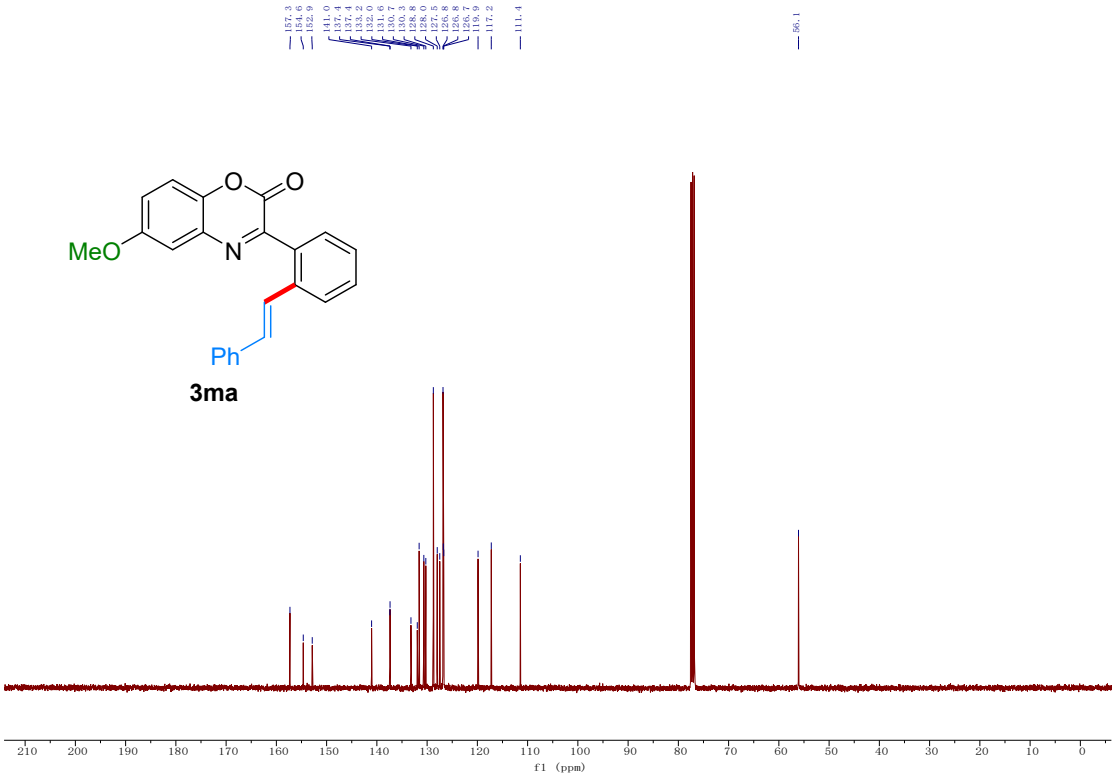
^{1}H and ^{13}C NMR Spectra of compound **3la**



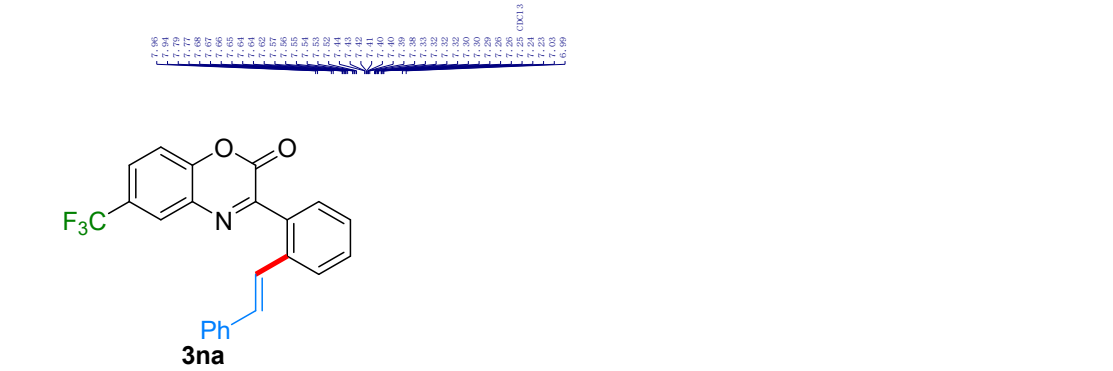


^{1}H and ^{13}C NMR Spectra of compound **3ma**

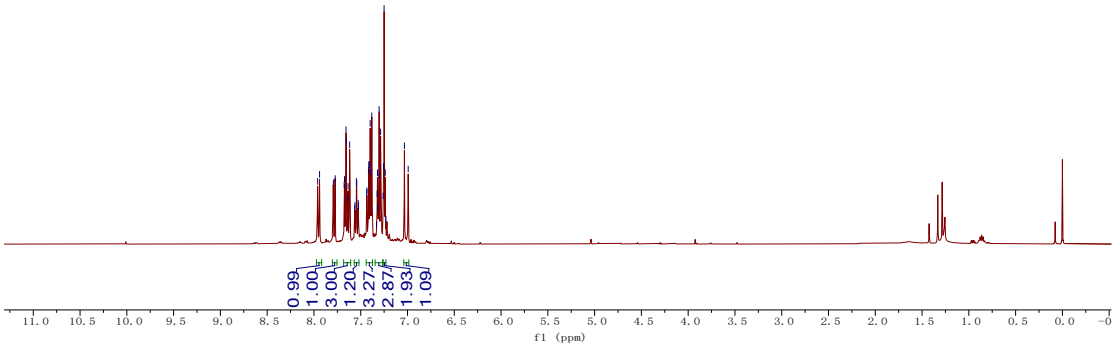


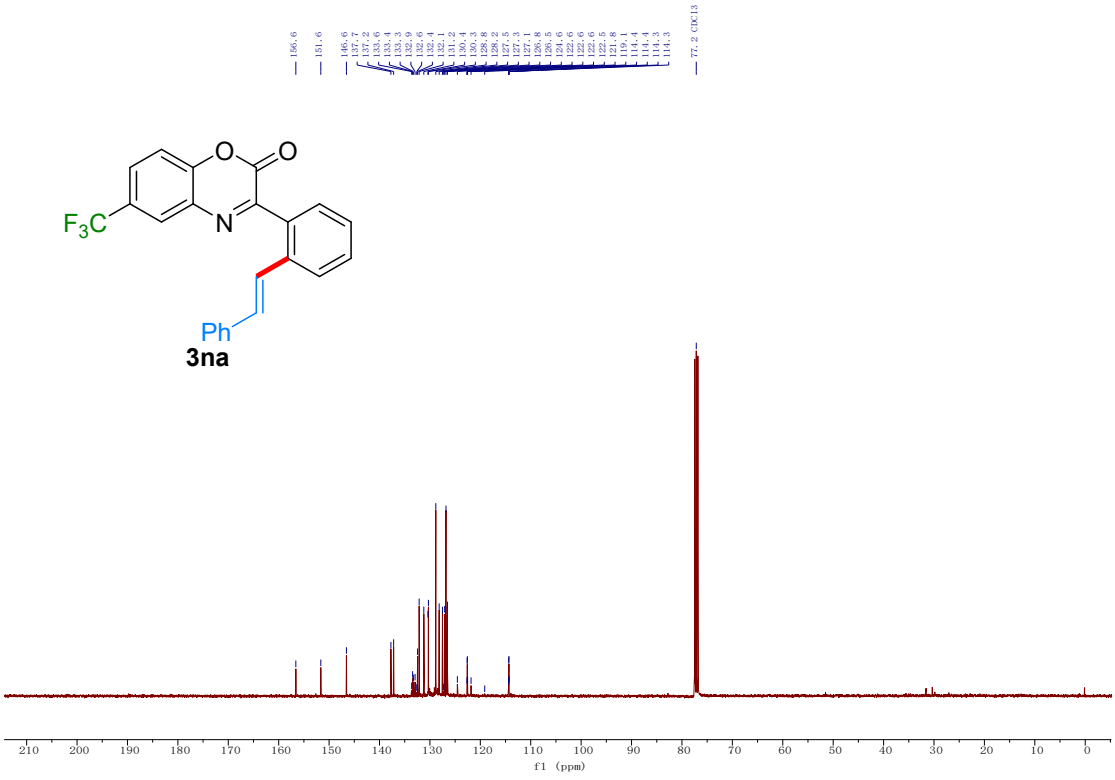


^{1}H and ^{13}C NMR Spectra of compound **3na**



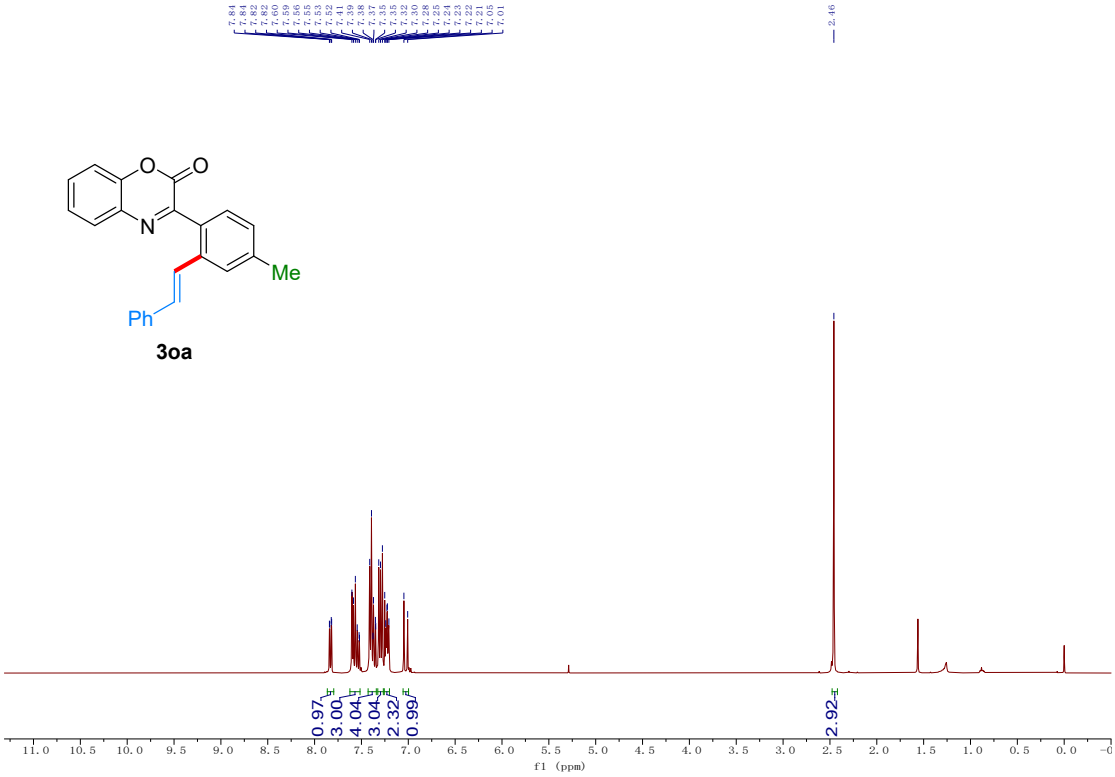
3na

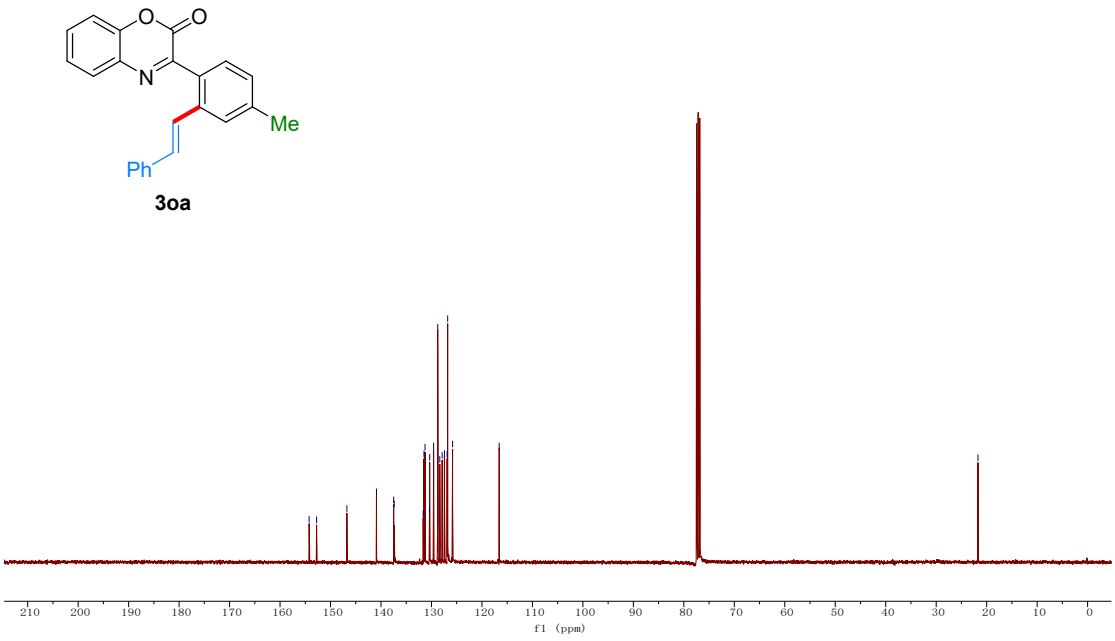




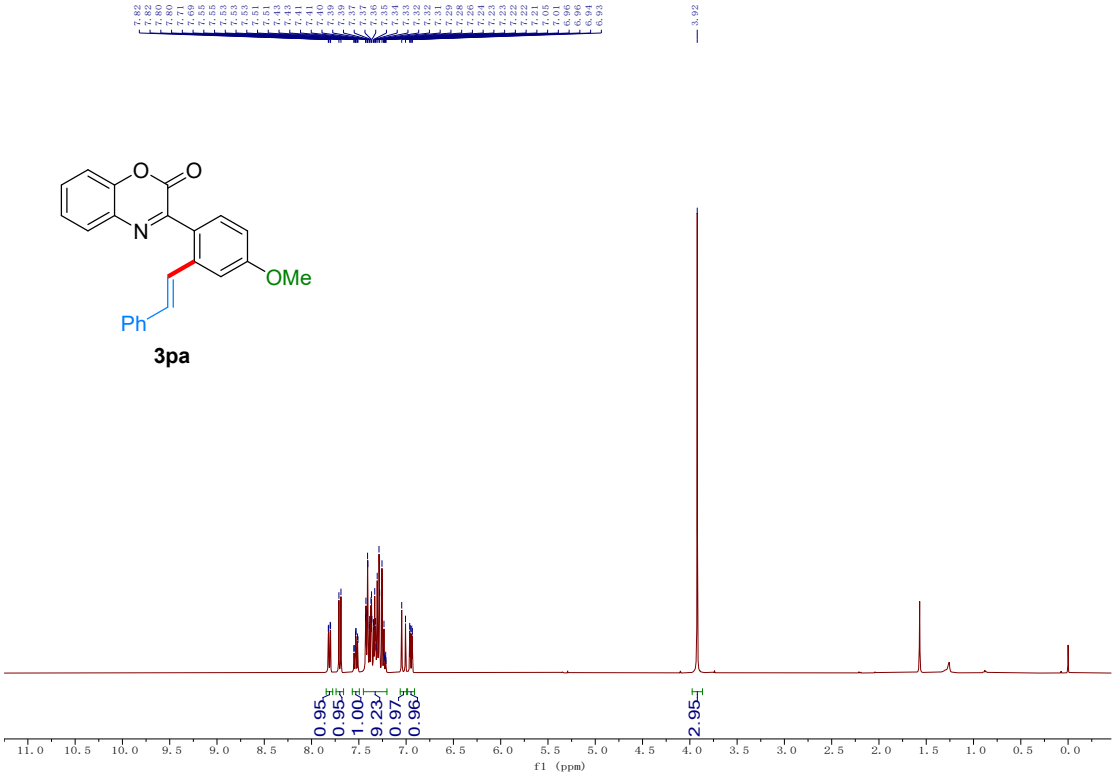
3na

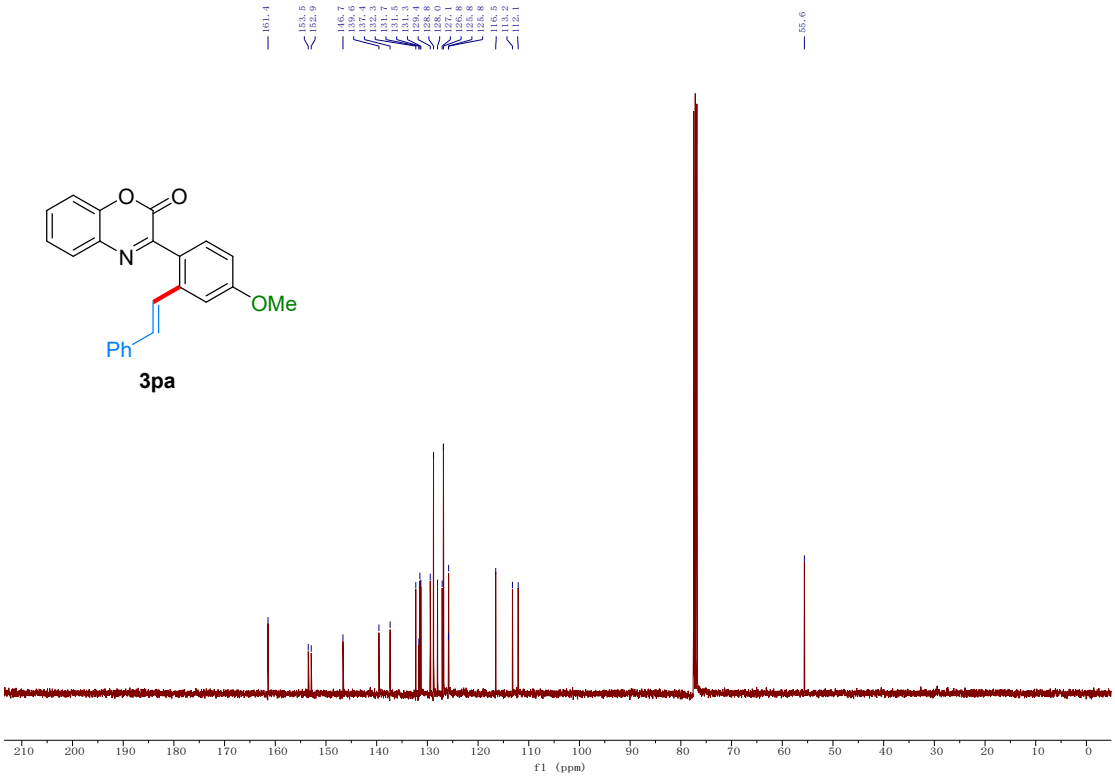
^{1}H and ^{13}C NMR Spectra of compound **3oa**



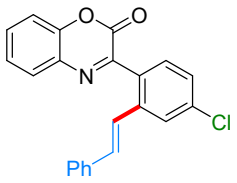


^{1}H and ^{13}C NMR Spectra of compound **3pa**

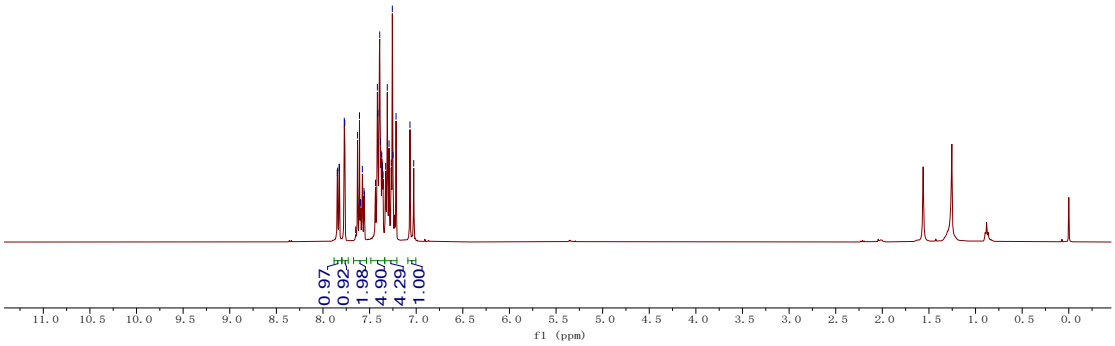


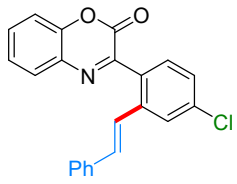


^{1}H and ^{13}C NMR Spectra of compound **3qa**



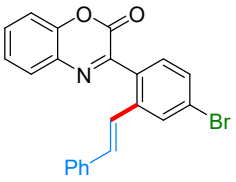
3qa



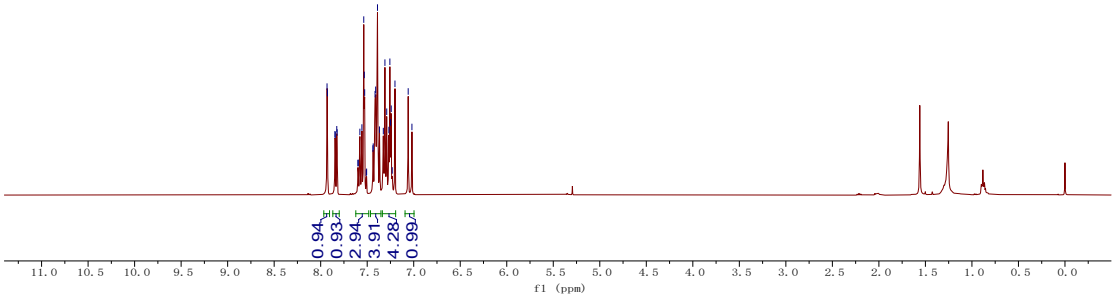


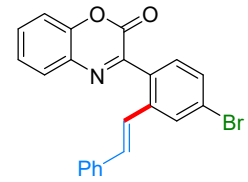
3qa

^{1}H and ^{13}C NMR Spectra of compound **3ra**



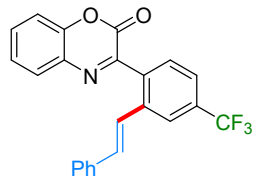
3ra



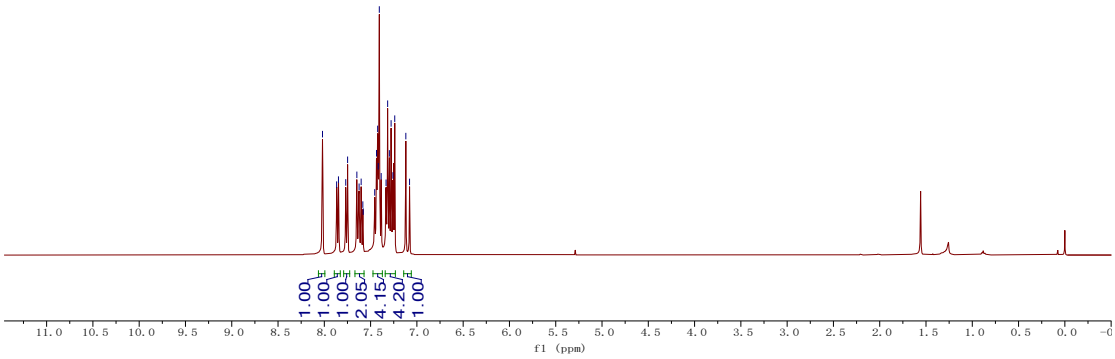


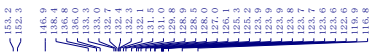
3ra

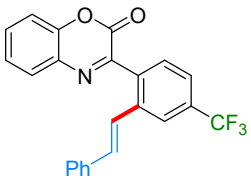
^{1}H and ^{13}C NMR Spectra of compound **3sa**



3sa

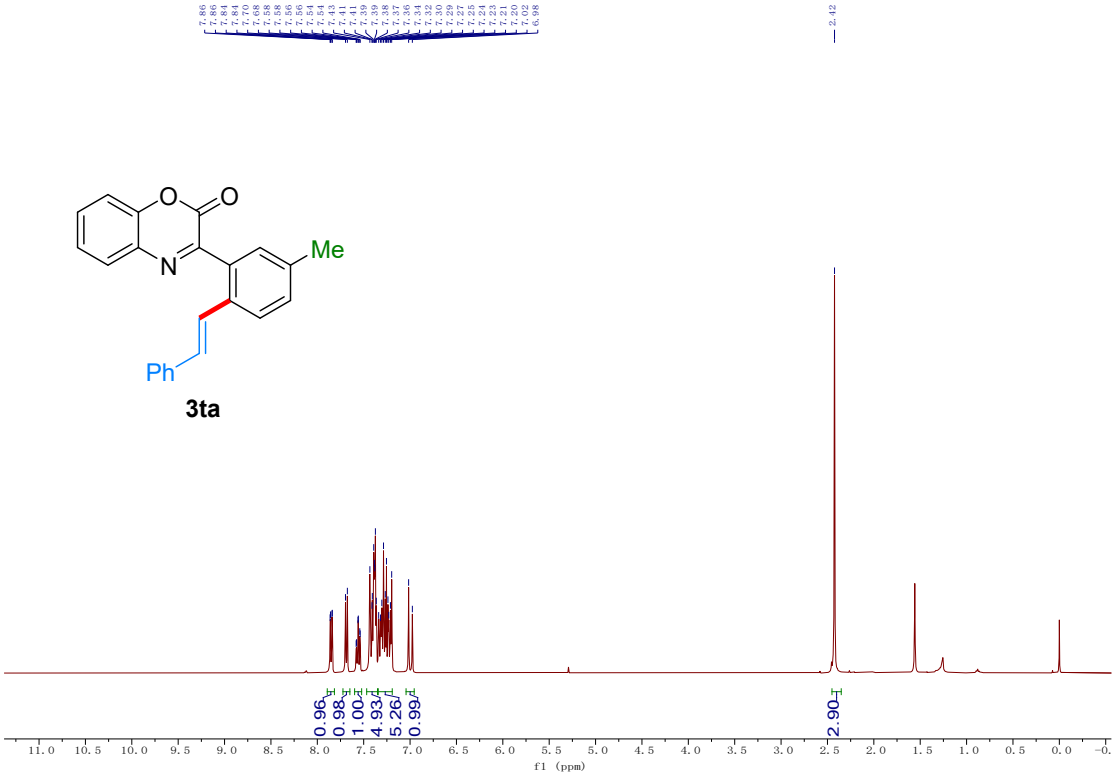


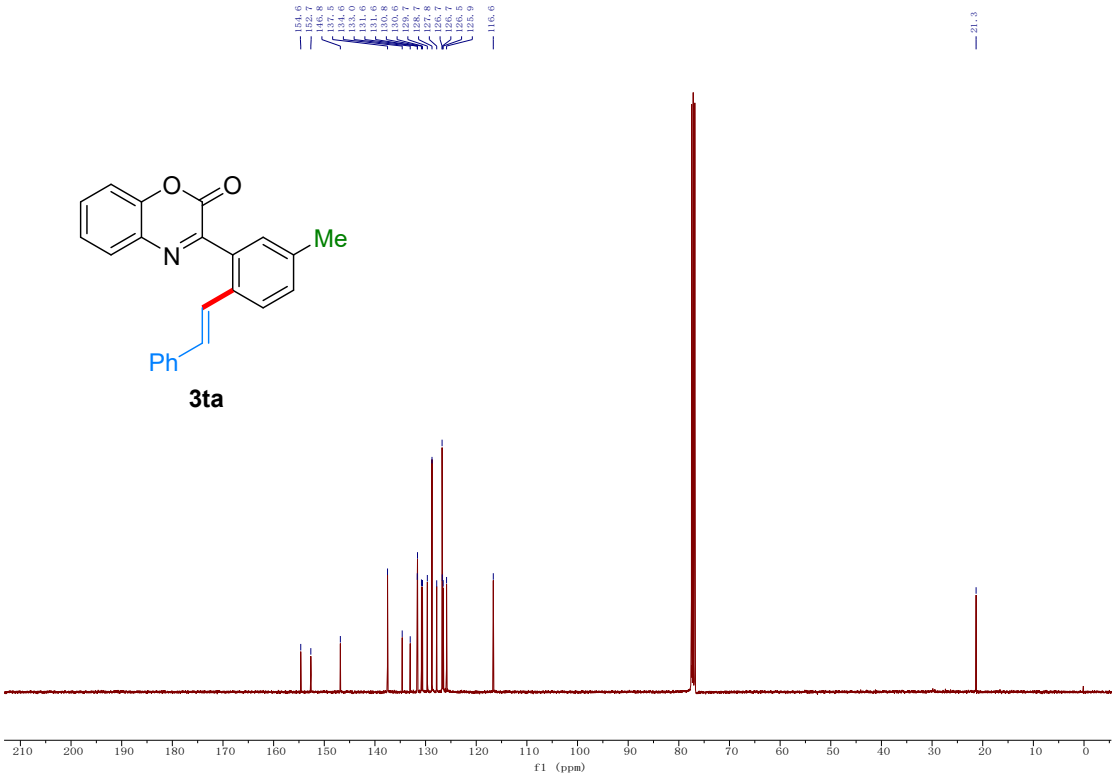




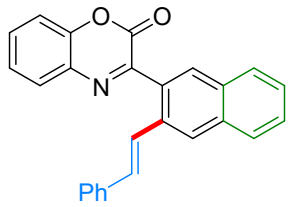
3sa

^{1}H and ^{13}C NMR Spectra of compound **3ta**

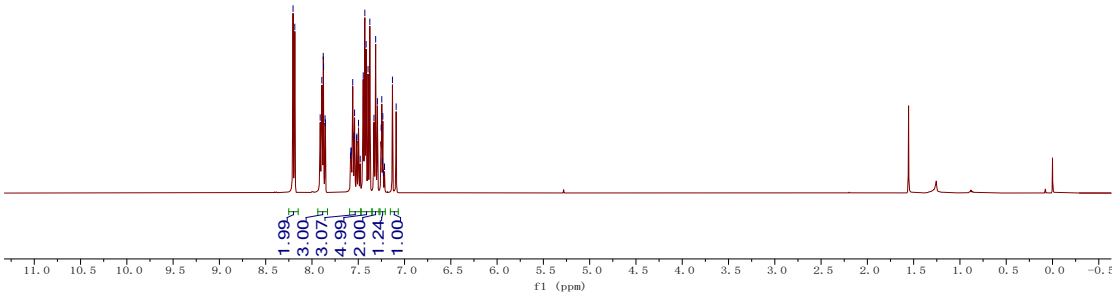


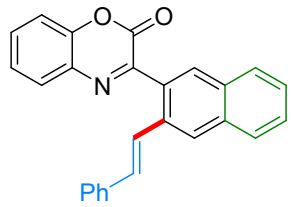


^{1}H and ^{13}C NMR Spectra of compound **3ua**

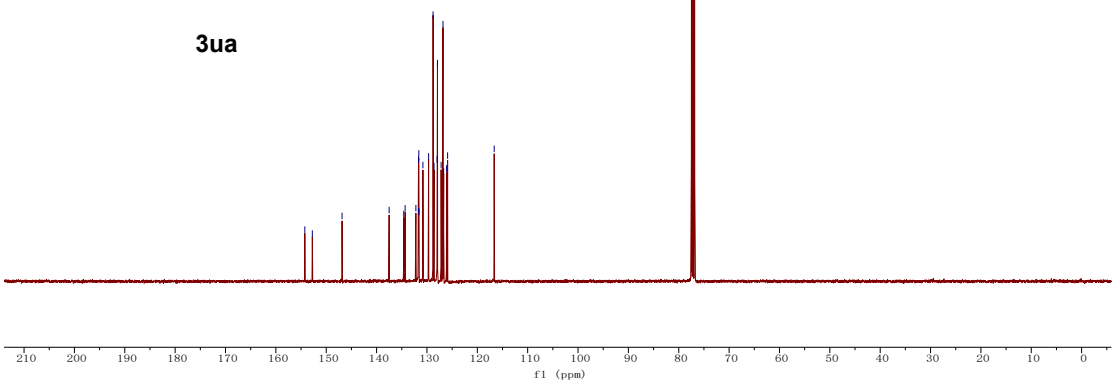


3ua

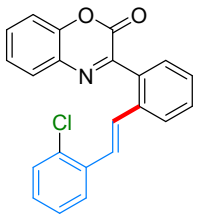




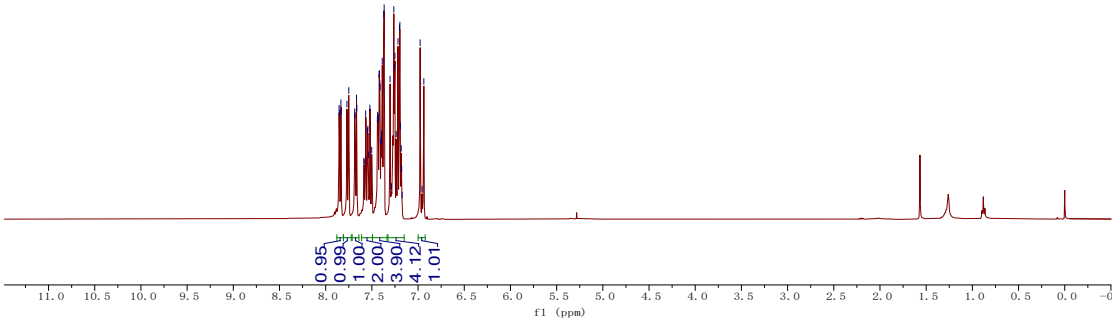
3ua

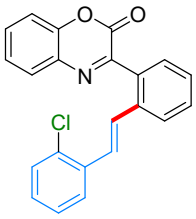


^{1}H and ^{13}C NMR Spectra of compound **3ab**



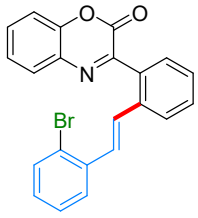
3ab



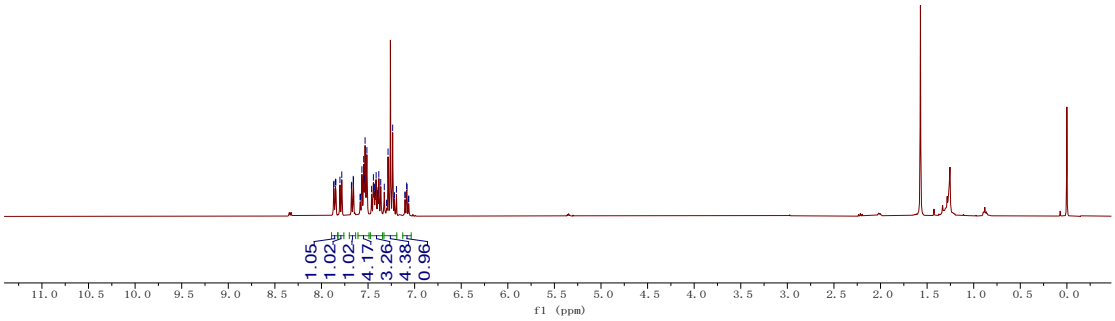


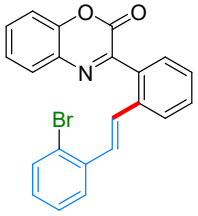
3ab

^{1}H and ^{13}C NMR Spectra of compound **3ac**



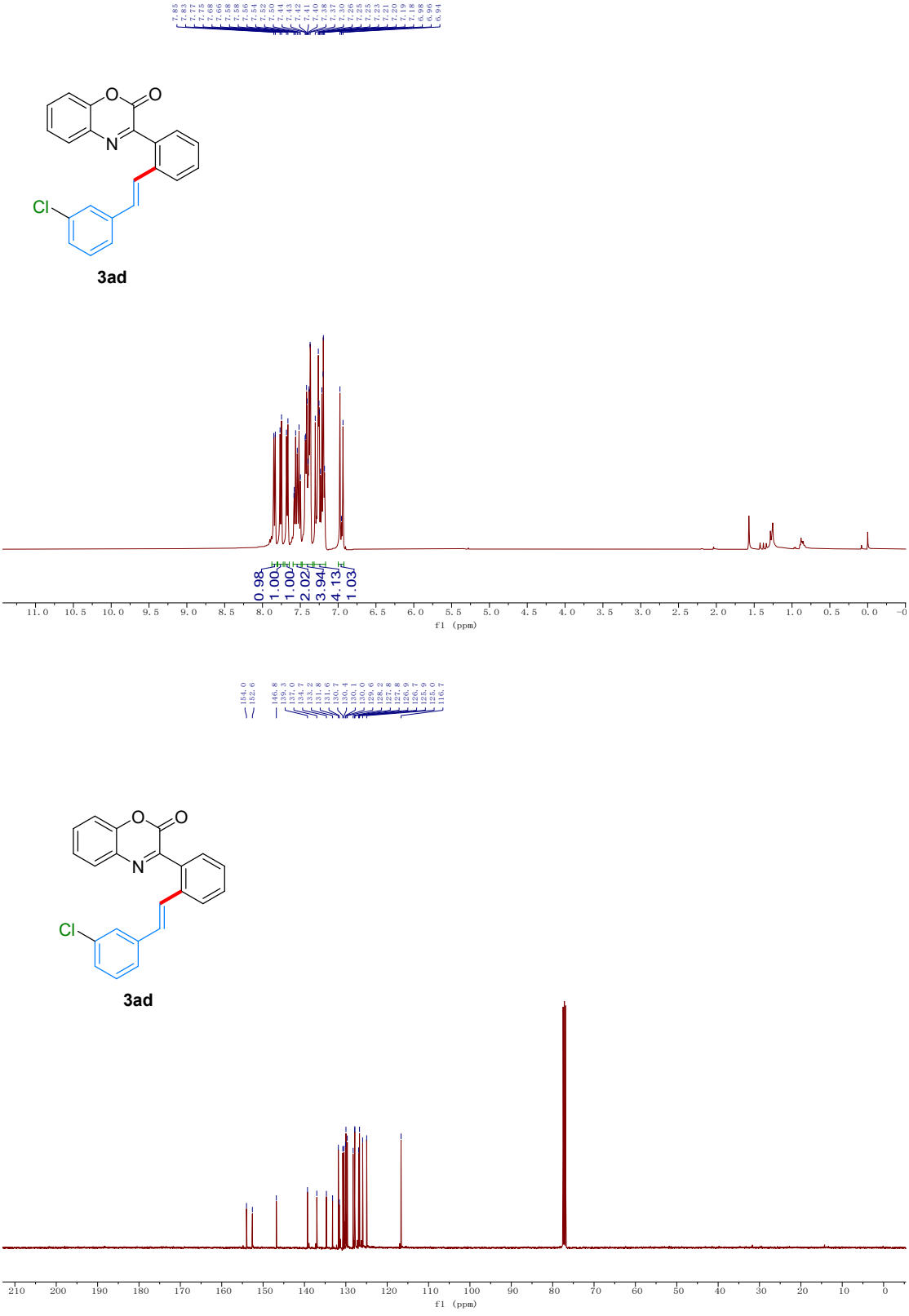
3ac



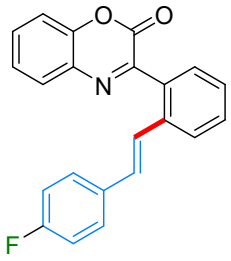


3ac

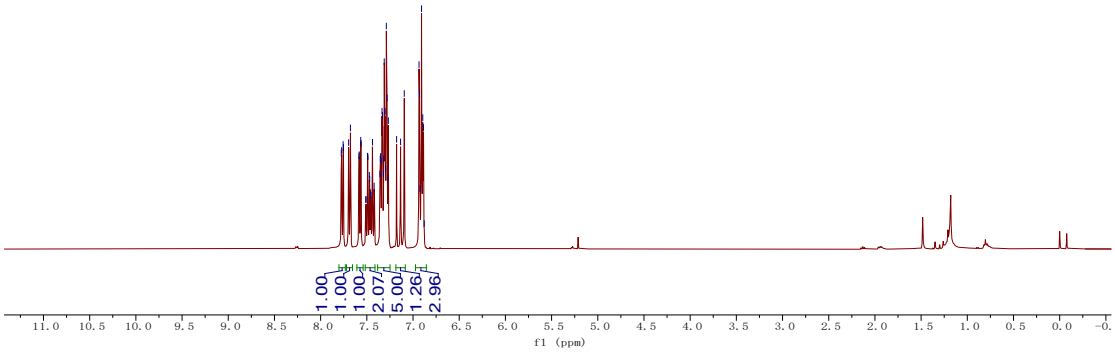
^{1}H and ^{13}C NMR Spectra of compound **3ad**

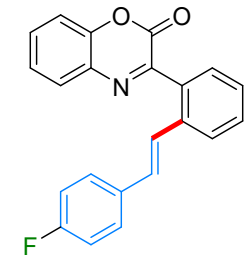


^{1}H and ^{13}C NMR Spectra of compound **3ae**



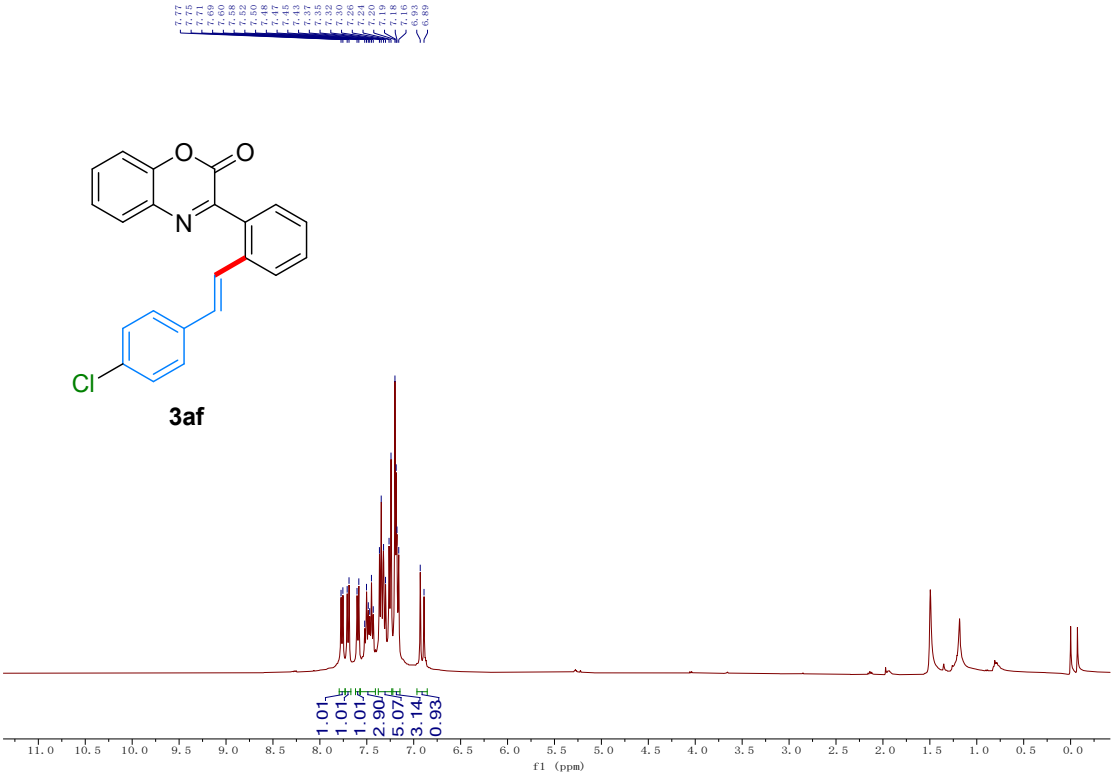
3ae

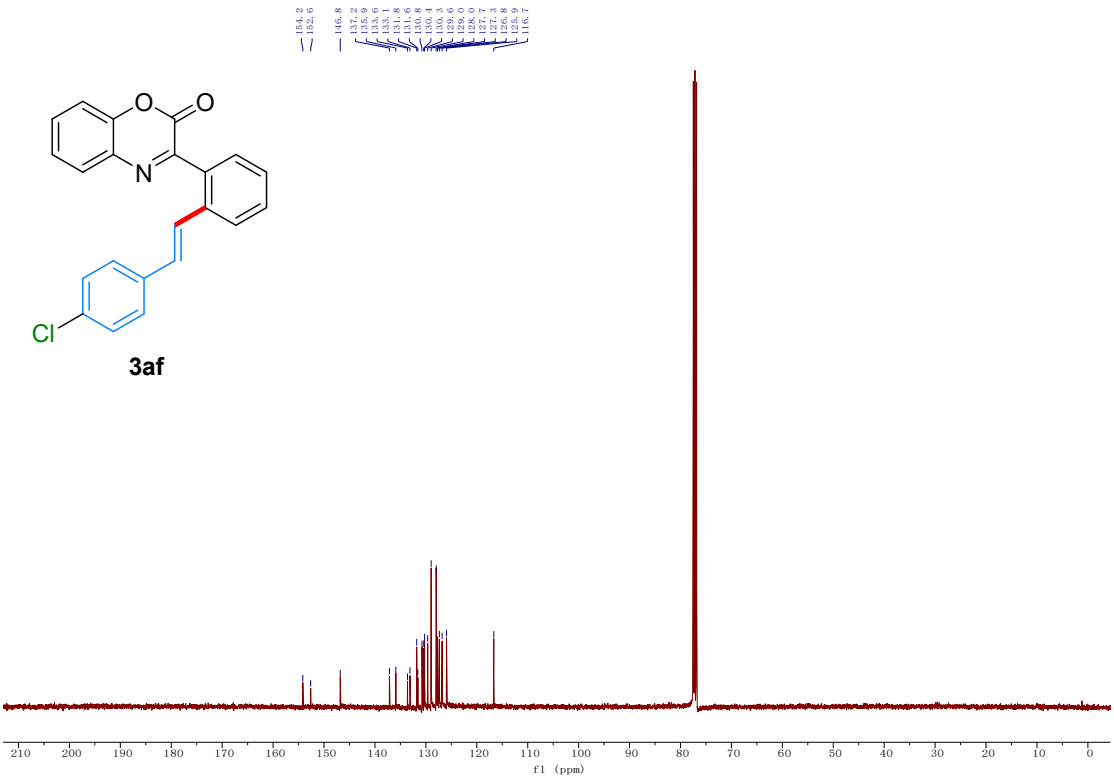




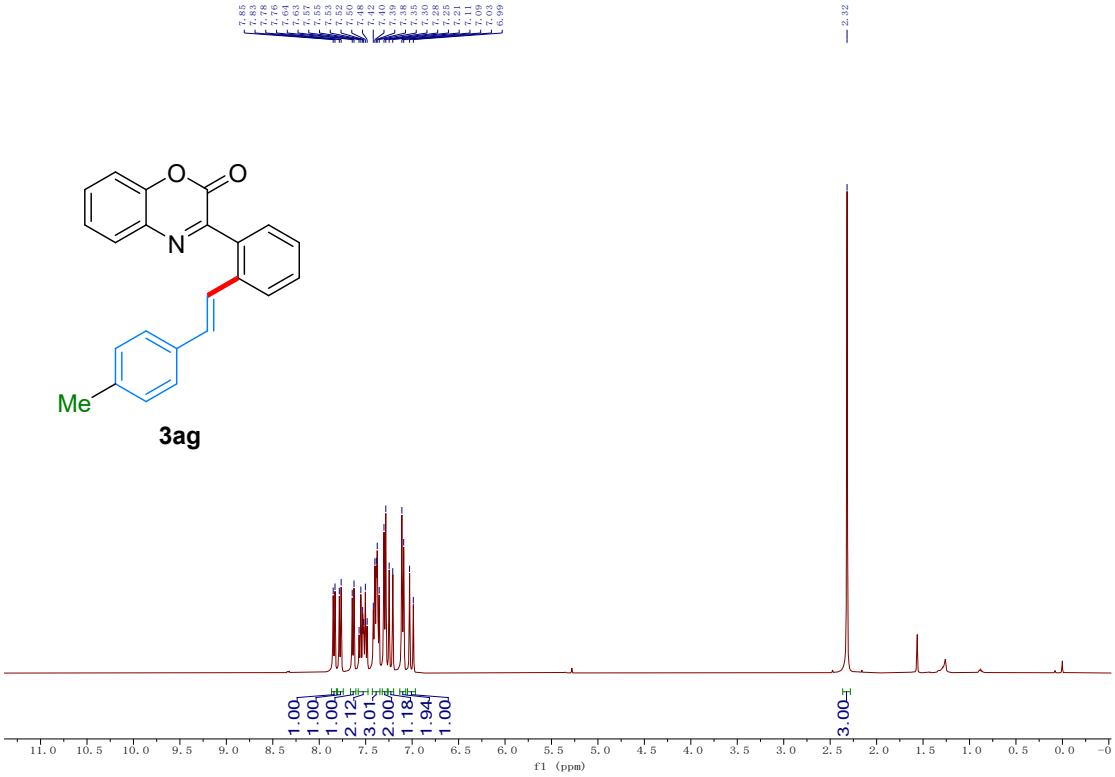
3ae

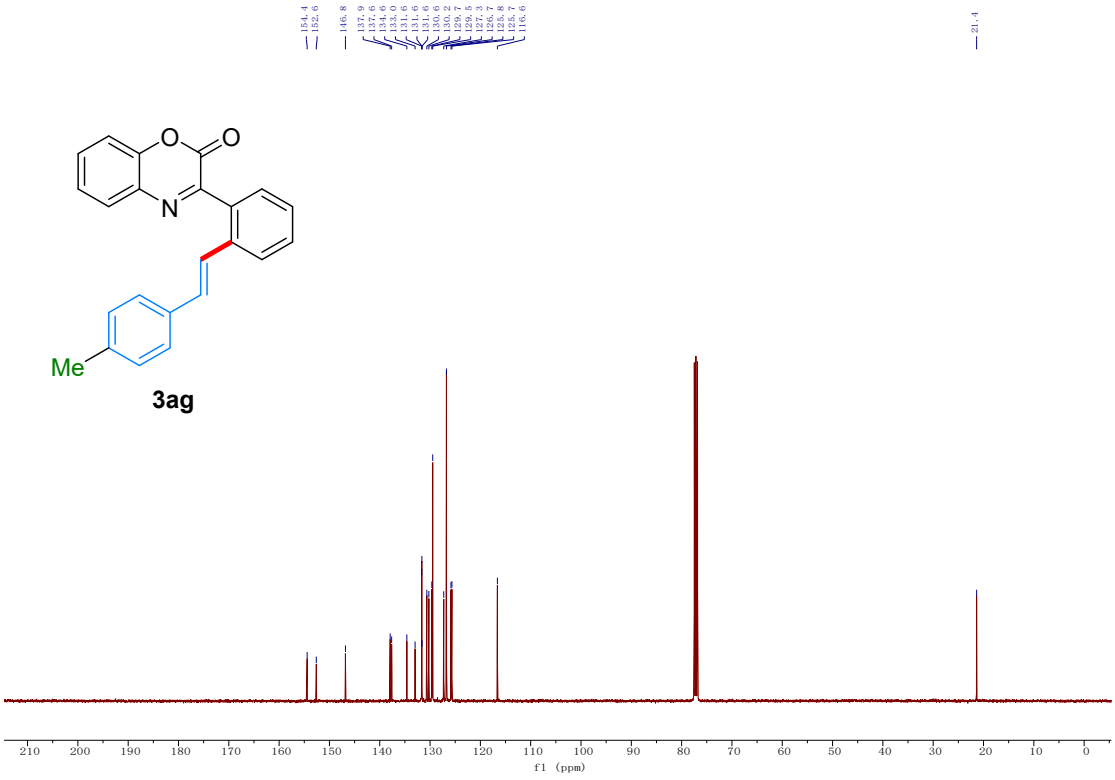
^{1}H and ^{13}C NMR Spectra of compound **3af**



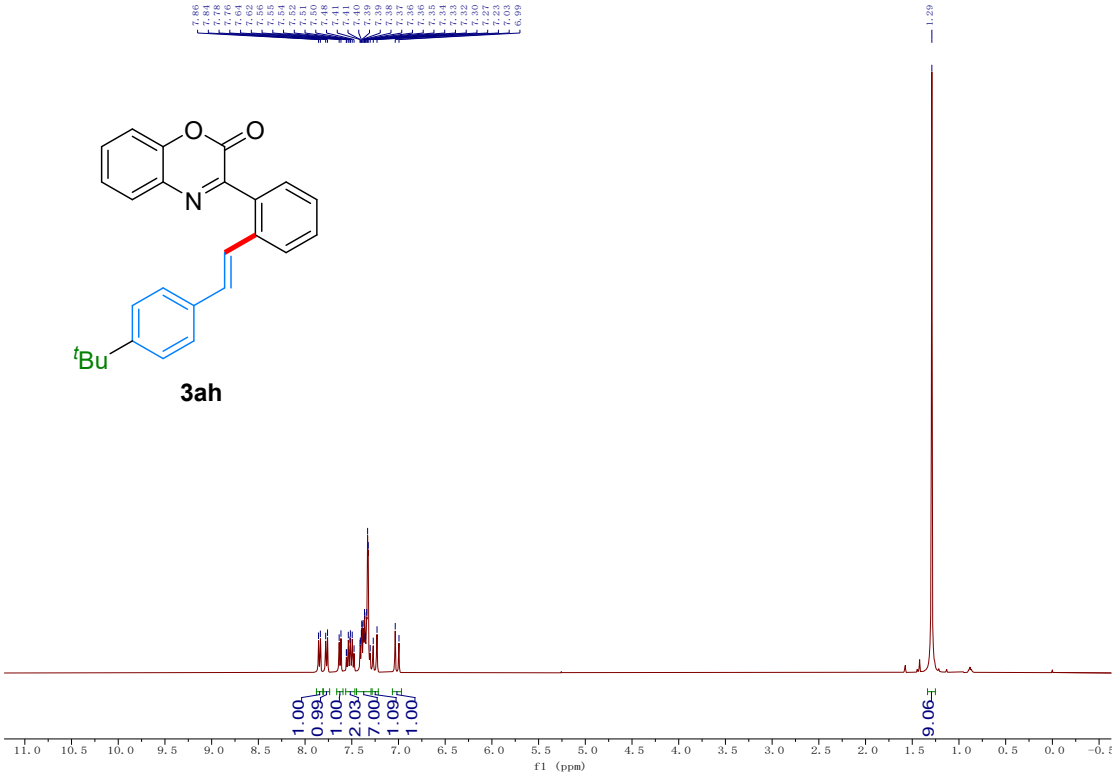


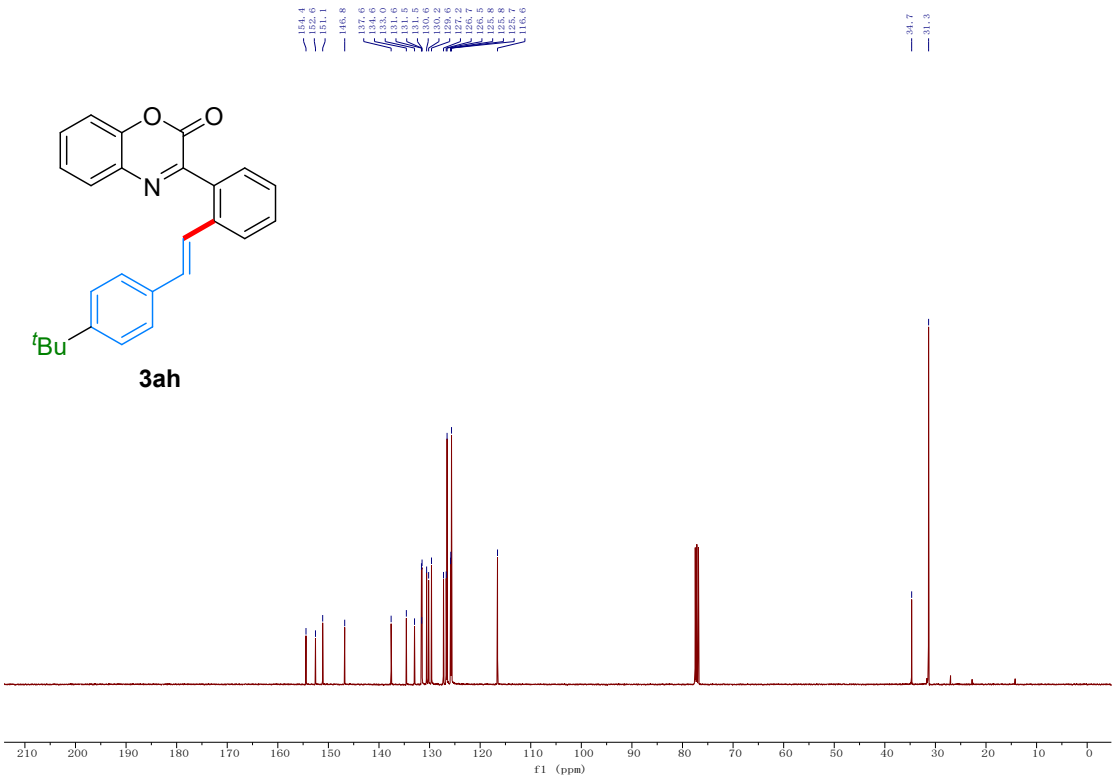
^{1}H and ^{13}C NMR Spectra of compound **3ag**



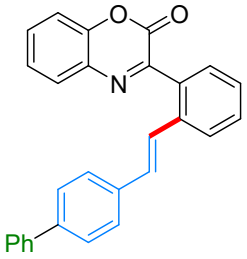


^{1}H and ^{13}C NMR Spectra of compound **3ah**

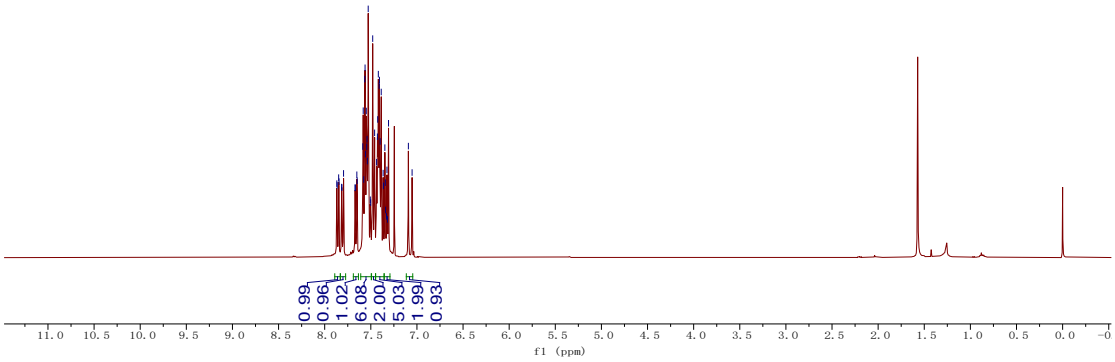


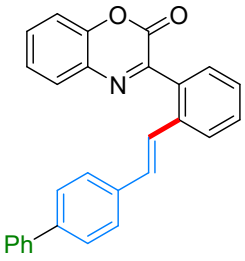


^{1}H and ^{13}C NMR Spectra of compound **3ai**

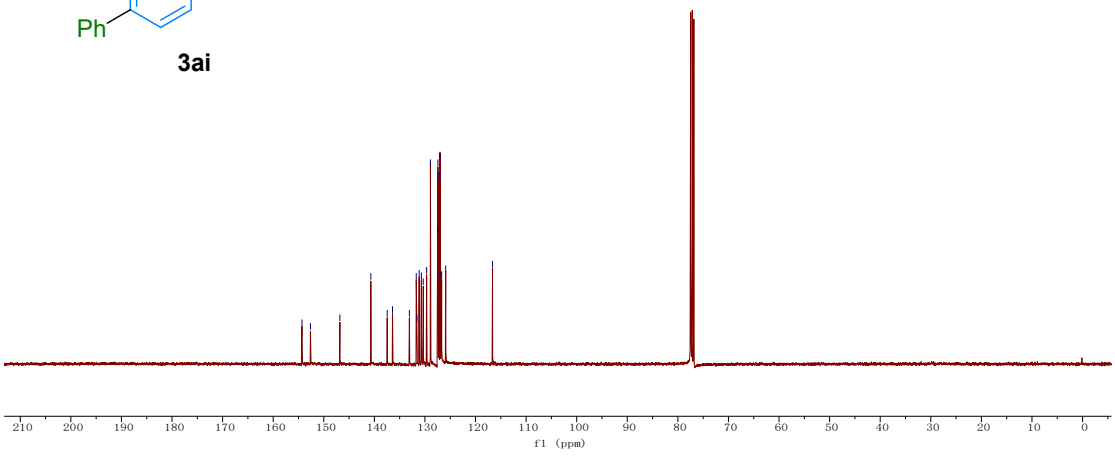


3ai

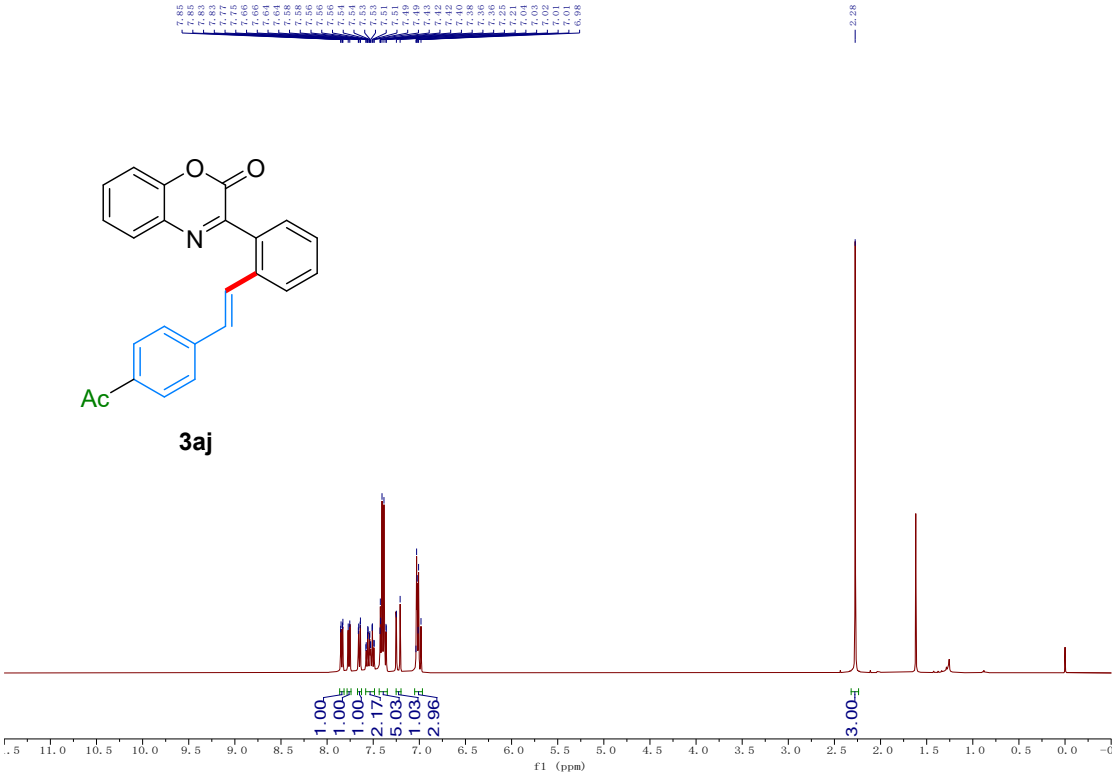


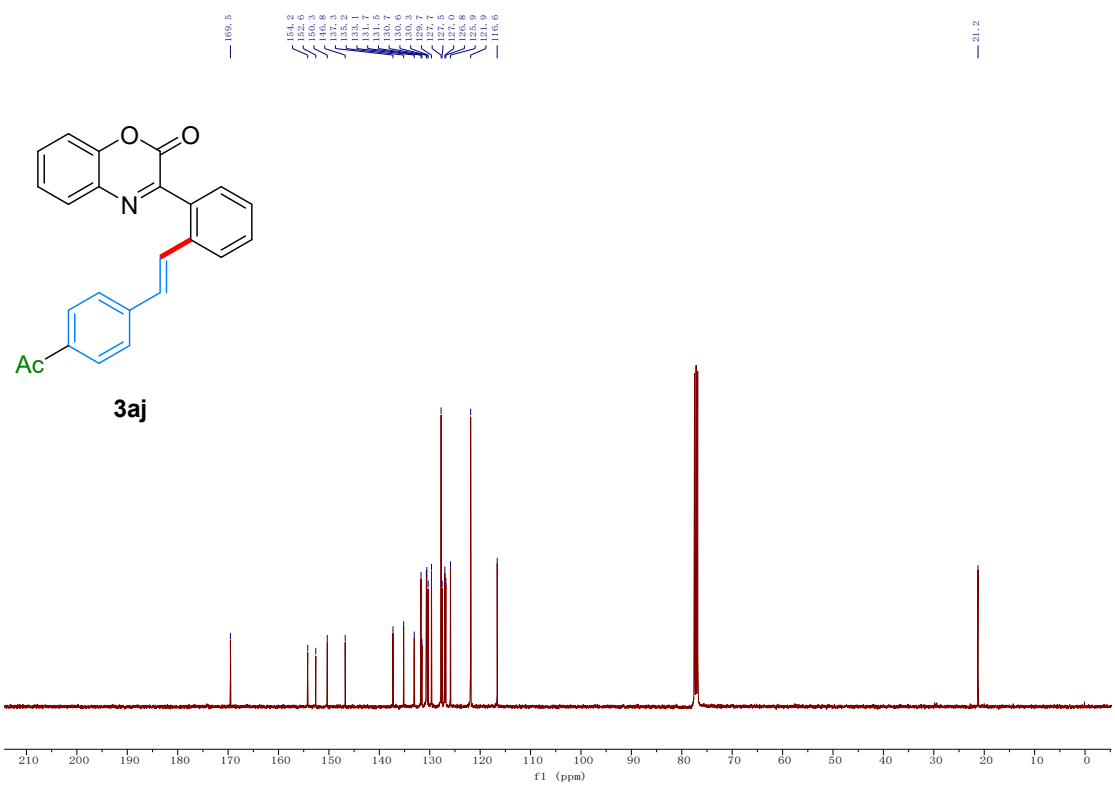


3ai

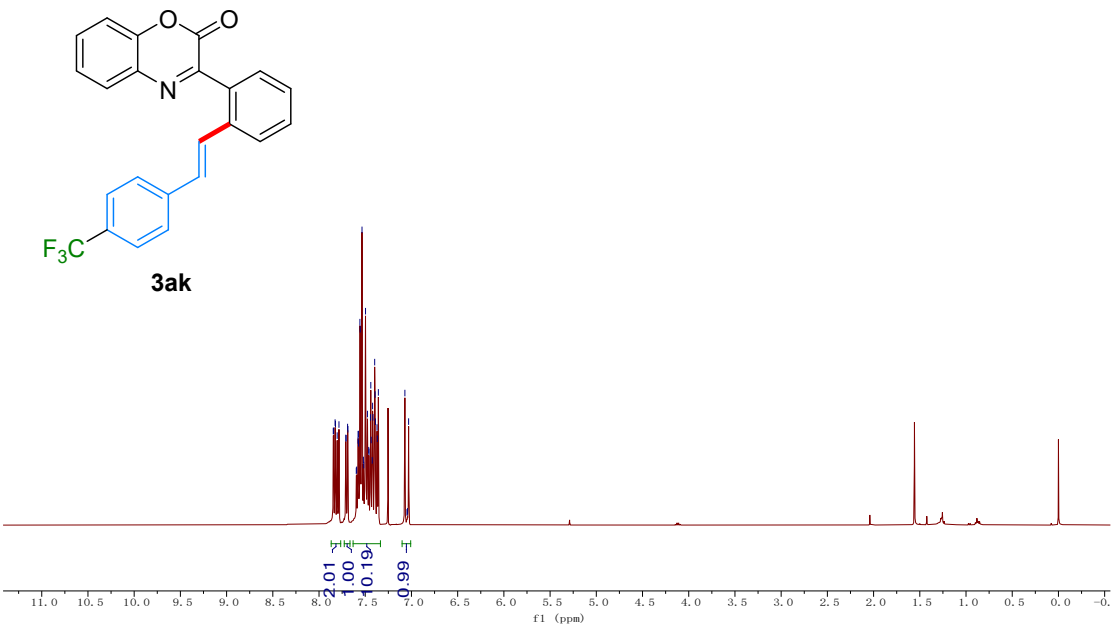


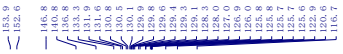
^{1}H and ^{13}C NMR Spectra of compound **3aj**

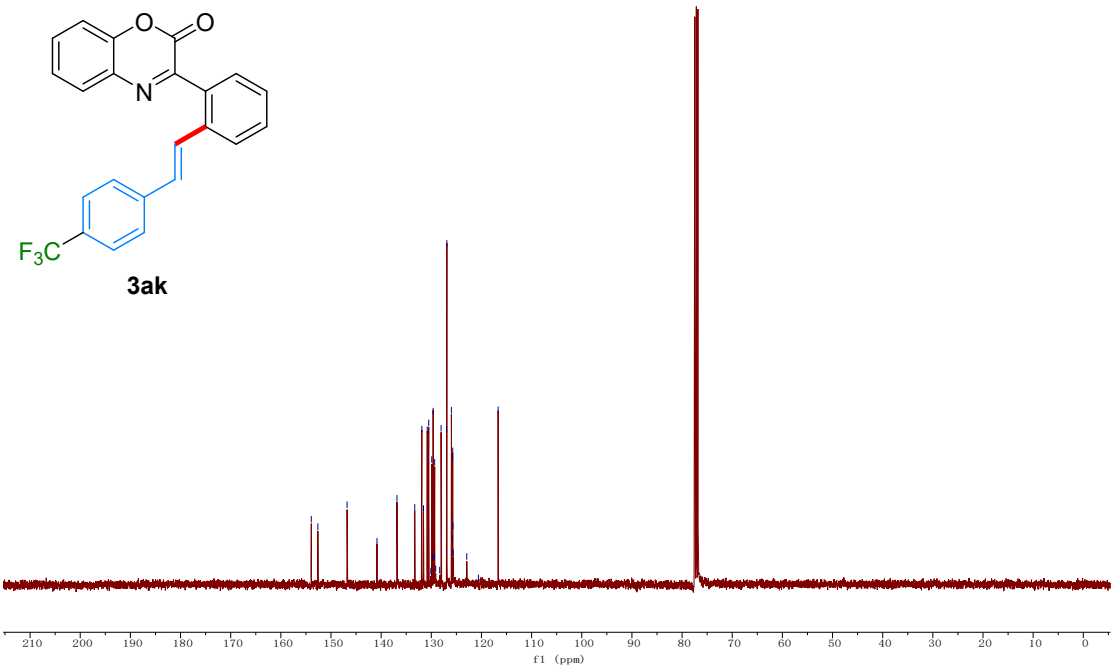




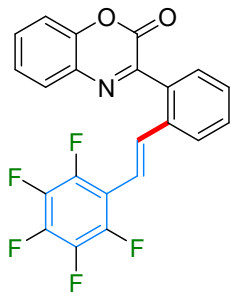
^{1}H and ^{13}C NMR Spectra of compound **3ak**



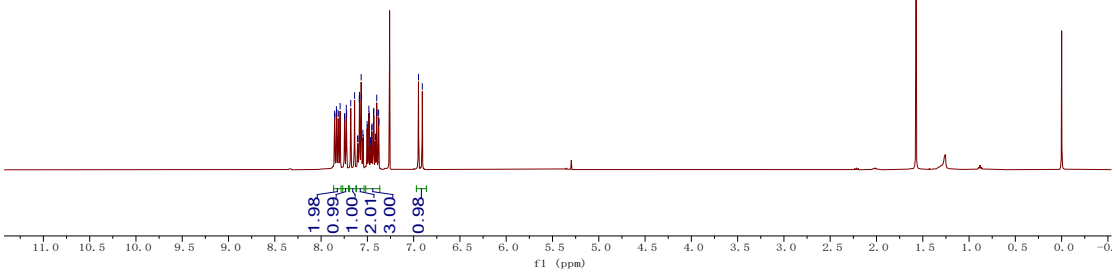


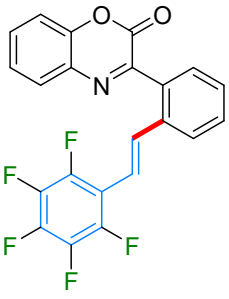


^{1}H and ^{13}C NMR Spectra of compound **3al**



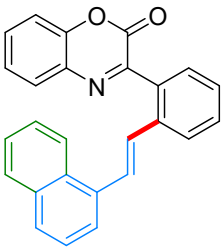
3al



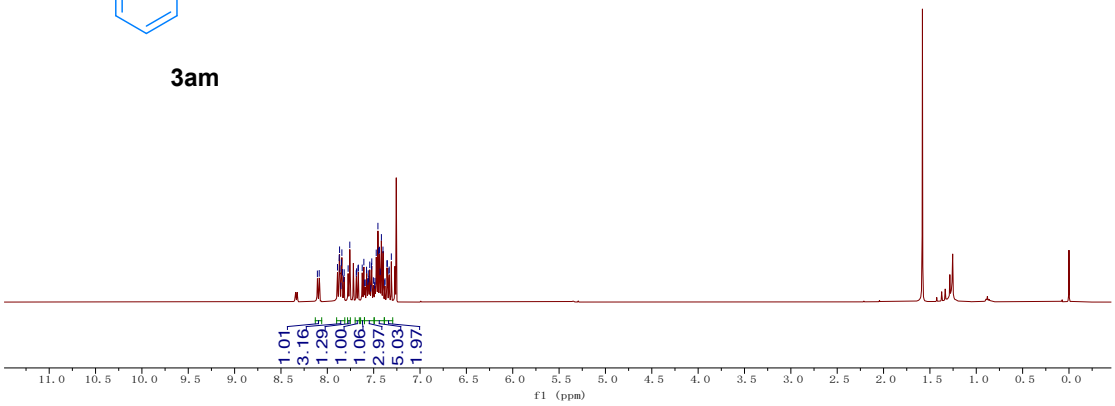


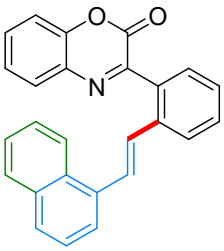
3al

^{1}H and ^{13}C NMR Spectra of compound **3am**



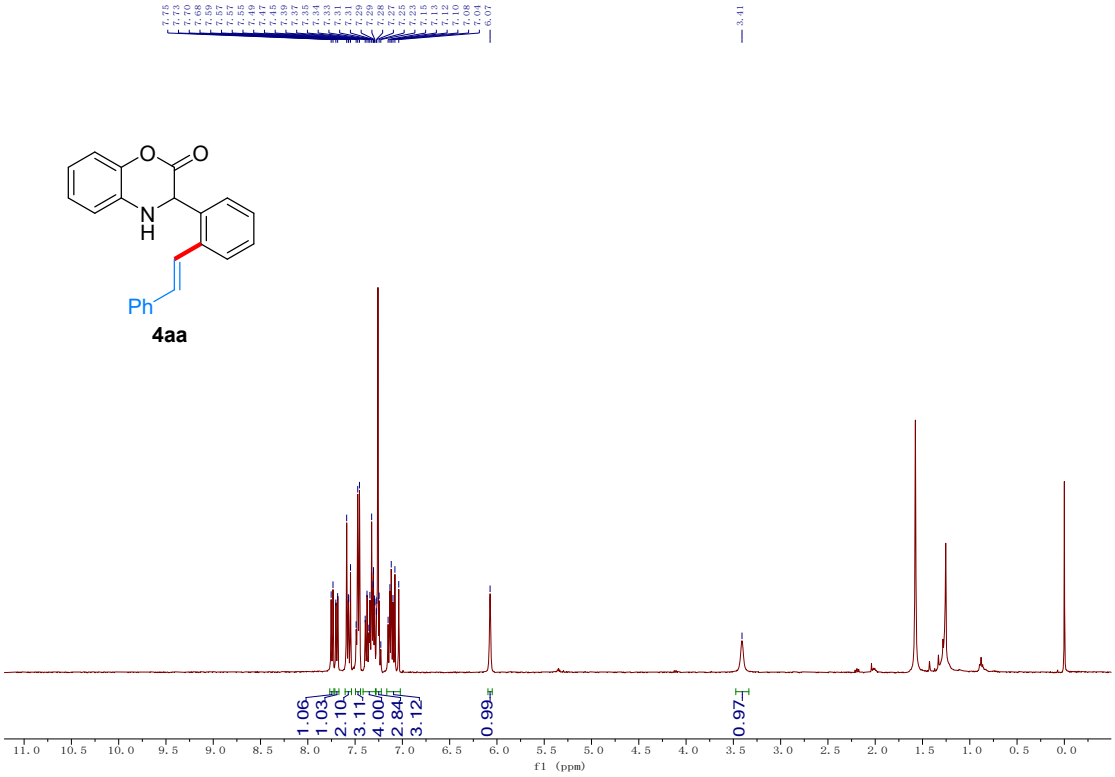
3am

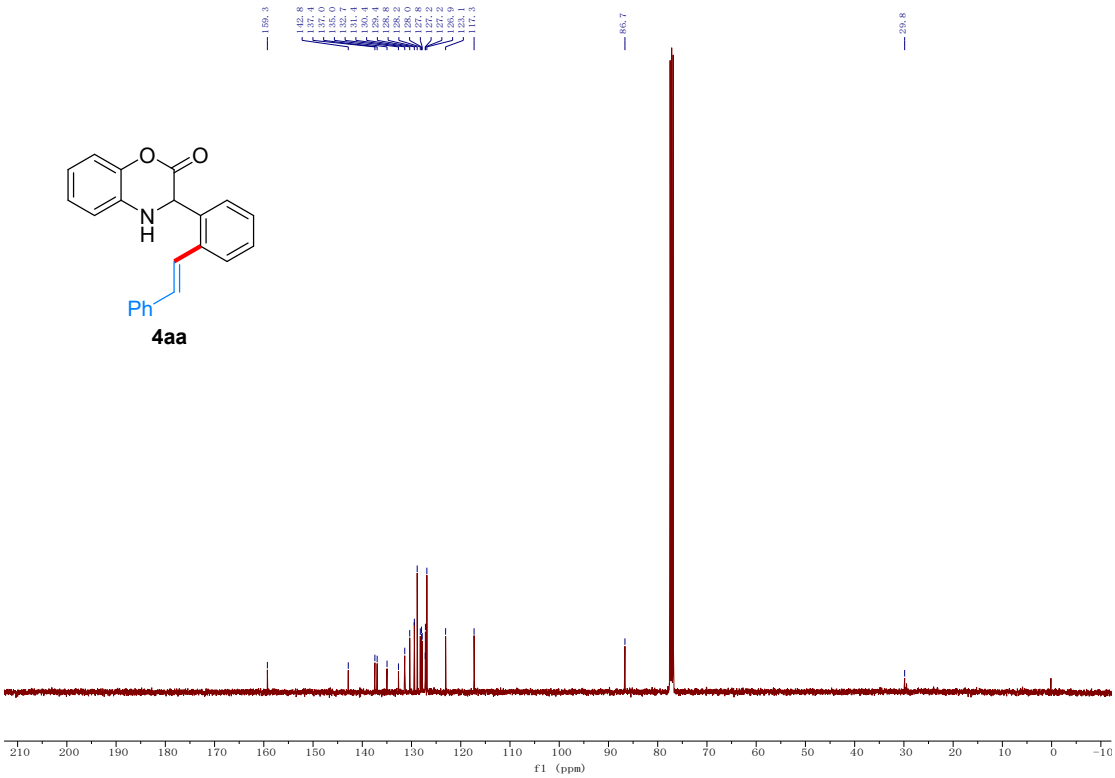




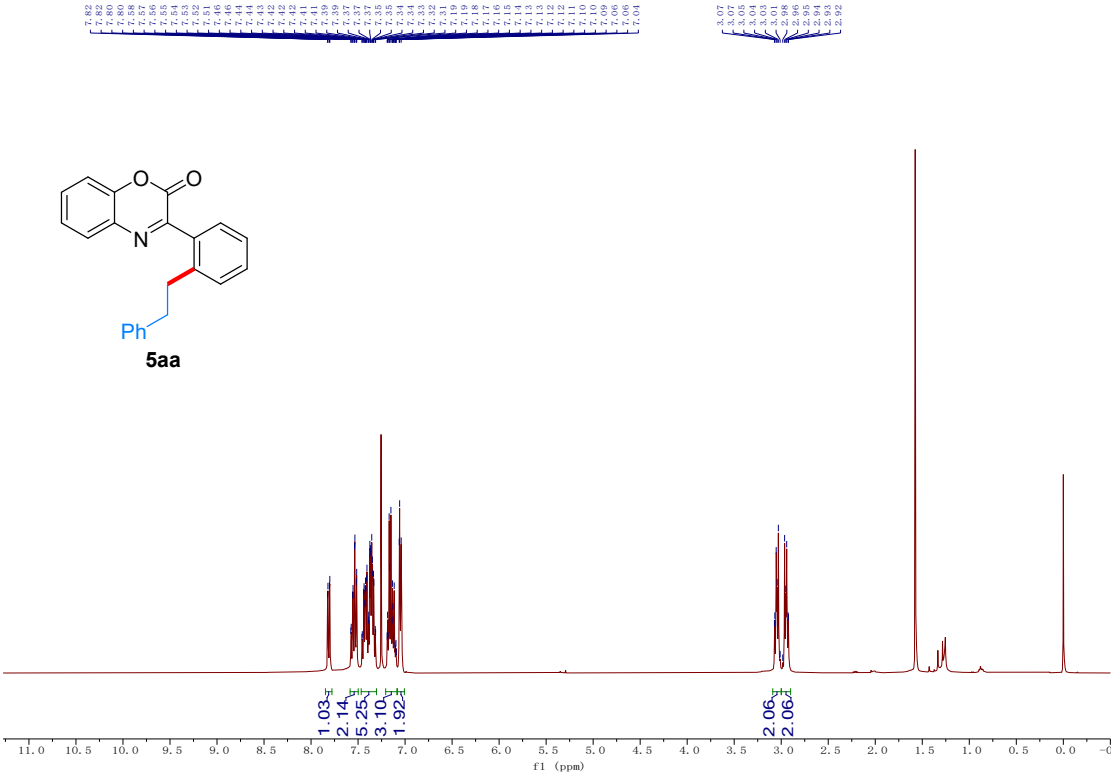
3am

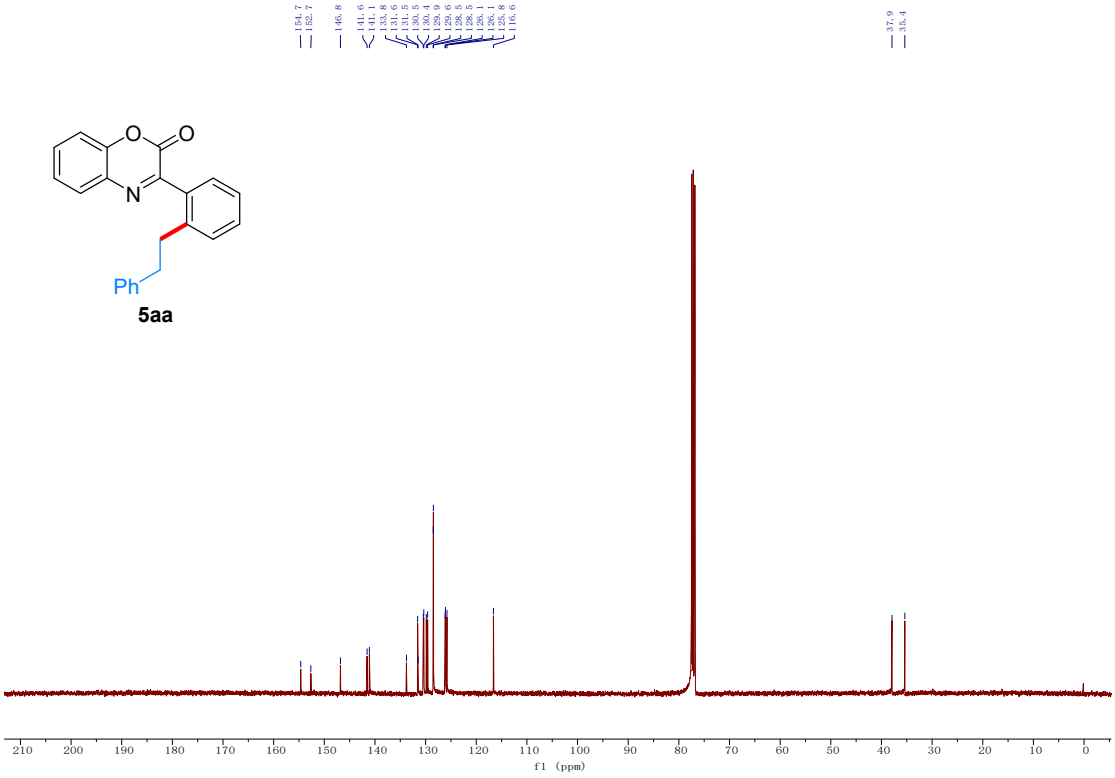
^{1}H and ^{13}C NMR Spectra of compound **4aa**



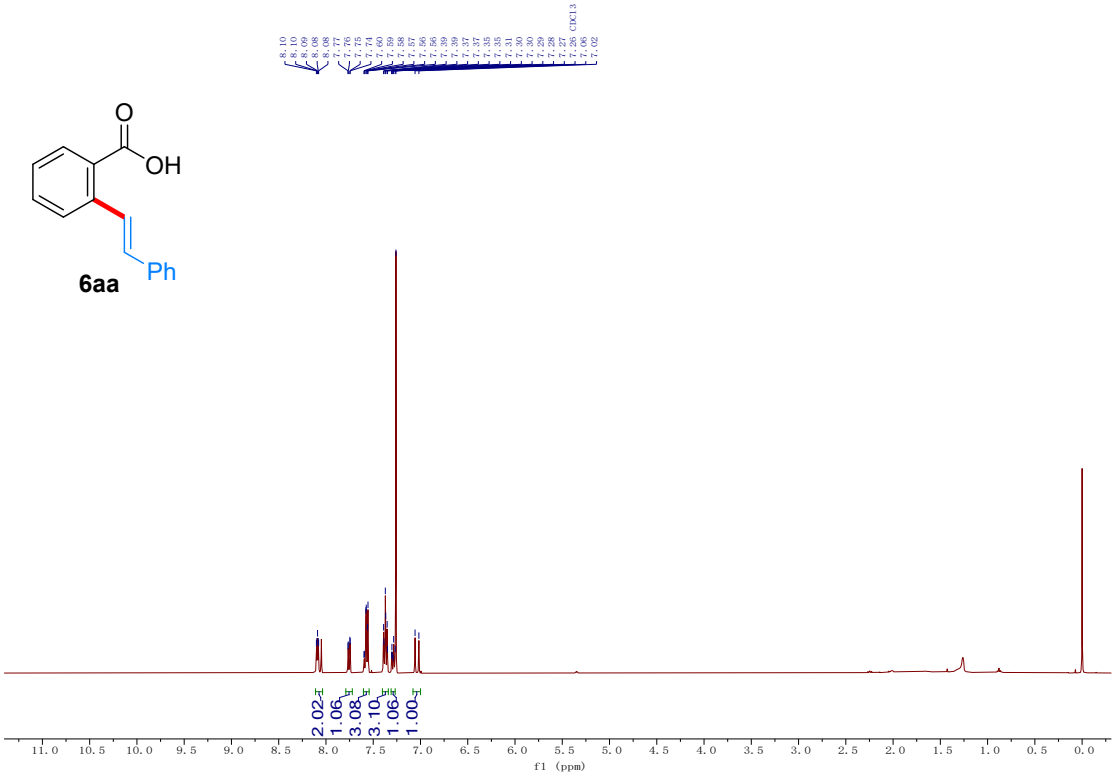


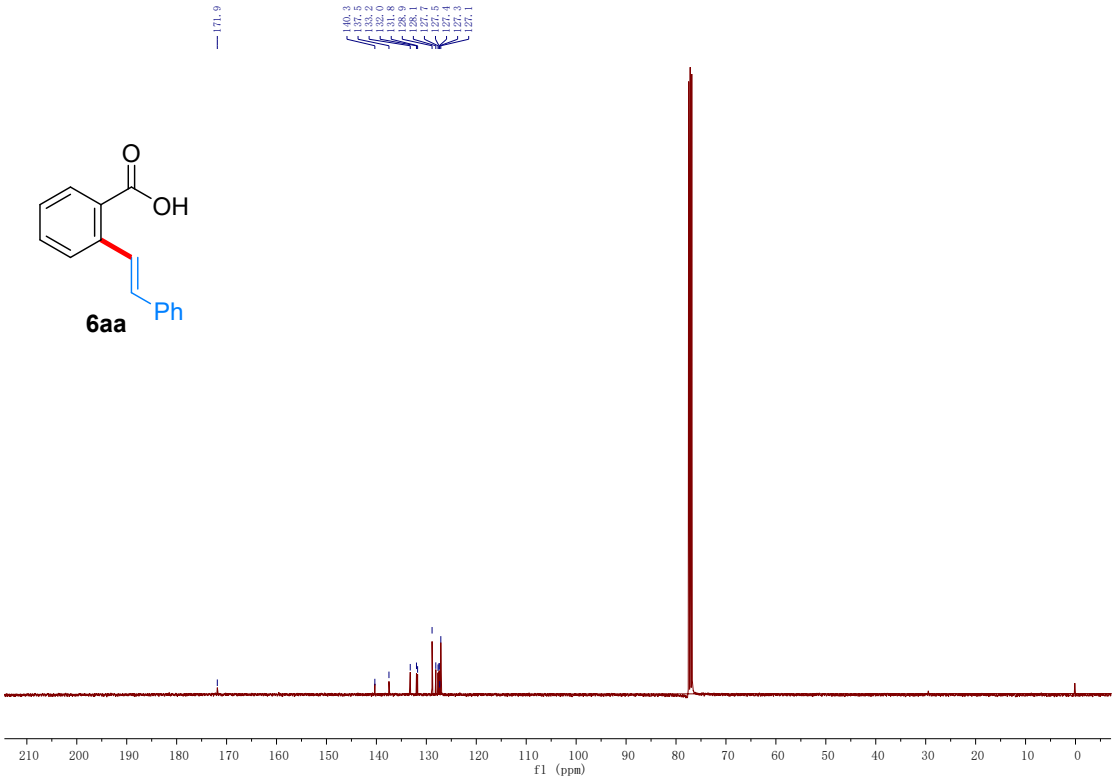
^{1}H and ^{13}C NMR Spectra of compound **5aa**



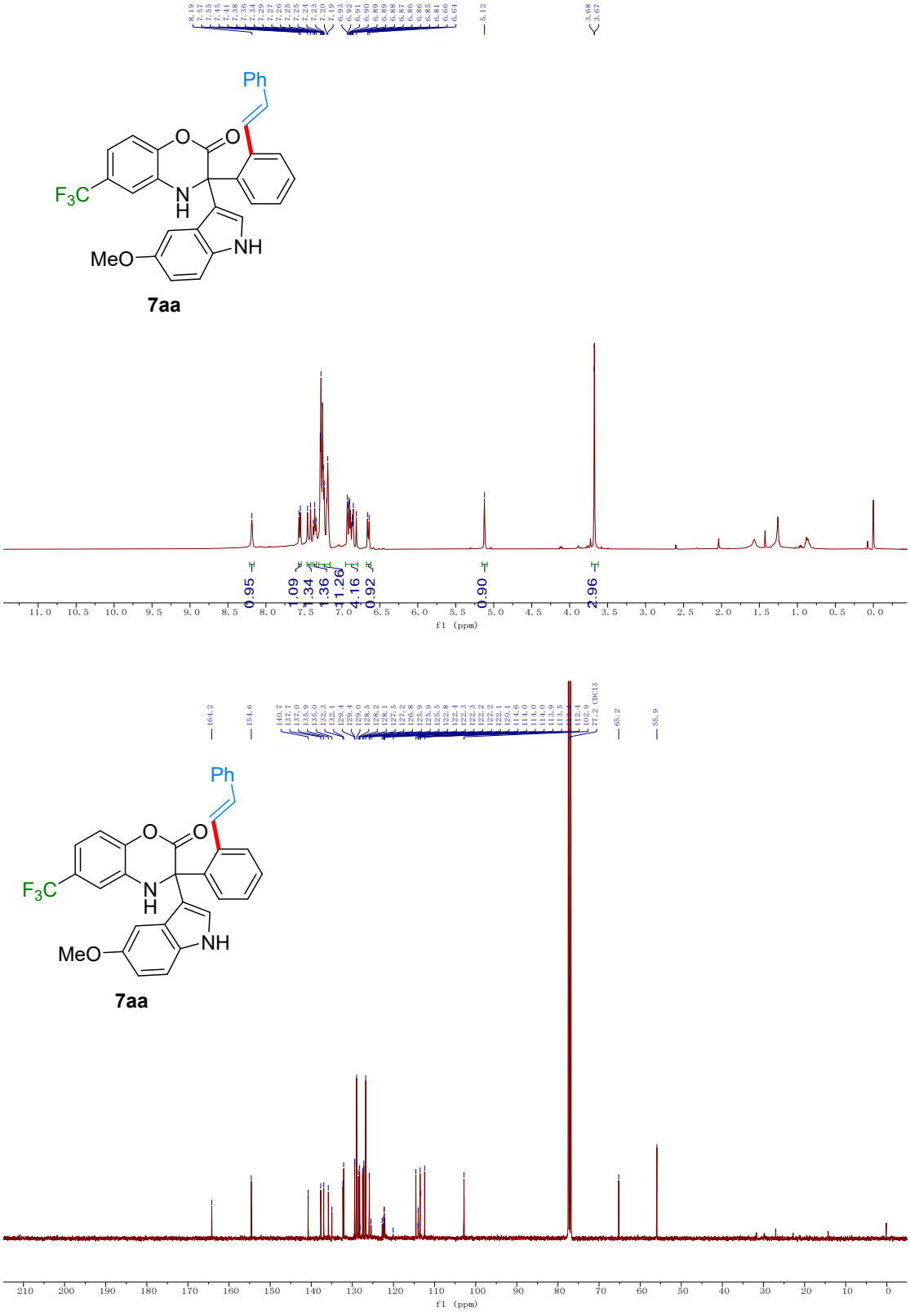


^{1}H and ^{13}C NMR Spectra of compound **6aa**





^{1}H and ^{13}C NMR Spectra of compound **7aa**



^{1}H and ^{13}C NMR Spectra of compound **8aa**