Supporting Information

Synthesis of Spiropyrans and Arylquinones via Ru(II)-Catalyzed Conditions-Controlled Coupling of 3-Aryl-2H-benzoxazinones with Benzoquinones

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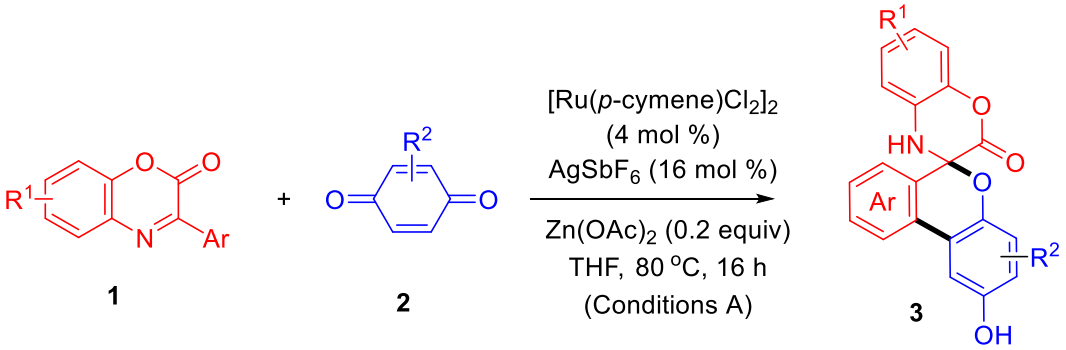
Contents

1. General Information

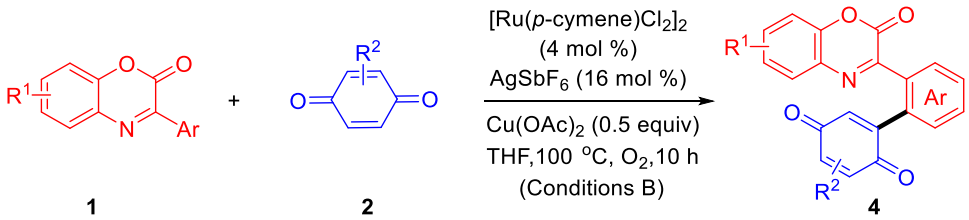
Unless otherwise noted, all the reactions were carried out in an argon-filled glove box. Anhydrous solvents were purified and dried by standard procedures. All chemicals were obtained from commercial sources and were used as received unless otherwise noted. Benzoxazines,[1] benzoquinones[2] were prepared by following literature reports. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 400 spectrometer (400 MHz for ^{1}H, 101 MHz for ^{13}C). All coupling constants were reported in Hz. The residual solvent signals were used as references for ^{1}H and ^{13}C NMR spectra and the chemical shifts were converted to the TMS scale ($CDCl_3$: δ ^{1}H = 7.26 ppm, δ ^{13}C = 77.16 ppm). HRMS data were obtained using a TOF mode. Column chromatography was performed on silica gel (200-300 mesh) using ethyl acetate (EA)/petroleum ether (PE).

1.1 General Procedure for Synthesis of 3.



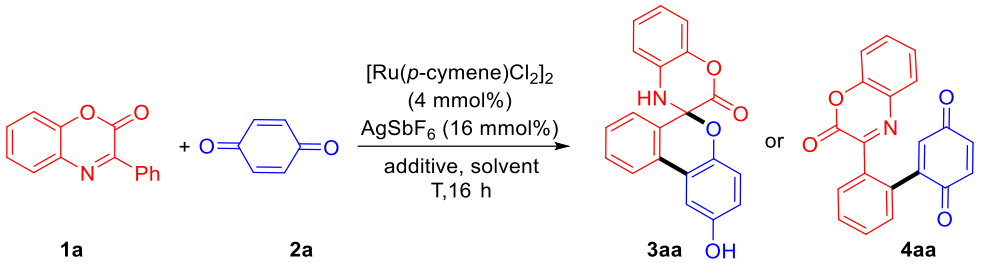
Benzoxazines (0.20 mmol), benzoquinones (0.30 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4 mol %), $AgSbF_6$ (16 mol %), $Zn(OAc)_2$ (0.04 mmol), and THF (3.0 mL) were charged into a pressure tube. The reaction mixture was stirred at 80 °C for 16 hours under the nitrogen atmosphere. After the solvent was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA (**9**:1) to afford compound **3**.

1.2 General Procedure for Synthesis of 4.



Benzoxazines (0.20 mmol), benzoquinones (0.44 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4 mol %), $AgSbF_6$ (16 mol %), $Cu(OAc)_2$ (0.1 mmol), and THF (3.0 mL) were charged into a pressure tube. The reaction mixture was stirred at 100 °C for 10 hours under the oxygen atmosphere. After the solvent was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA (12:1) to afford compound **4**.

1.3 Optimization of Reaction Conditions.[a,b] (Table S1)

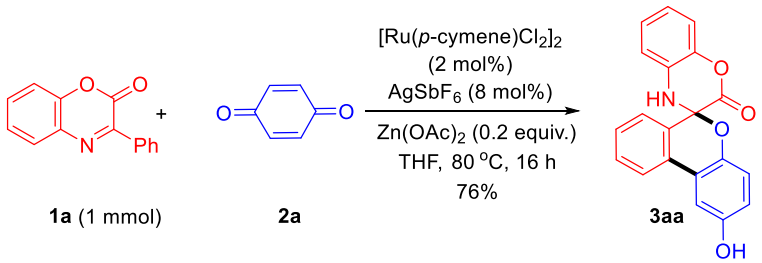


entry	additive (equiv)	solvent	T(°C)	yield (%)[a,b]
				3aa/4aa
1	K_2CO_3 (2.0)	DCE	30	20/8
2	K_2CO_3 (2.0)	MeCN	30	ND
3	K_2CO_3 (2.0)	DCM	30	13/7
4	K_2CO_3 (2.0)	MeOH	30	ND
5	K_2CO_3 (2.0)	THF	30	30/13
6	LiOAc (2.0)	THF	30	ND
7	NaOAc (2.0)	THF	30	10/7
8	MesCOOH (2.0)	THF	30	30/13
9	HOAc (2.0)	THF	30	10/10
10	$Zn(OAc)_2$ (0.2)	THF	30	35/4
11	$Zn(OAc)_2$ (0.2)	THF	60	50/4
12	**$Zn(OAc)_2$ (0.2)**	**THF**	**80**	**85/trace**
13	$Cu(OAc)_2$ (0.2)	THF	80	67/20
14	$Zn(OAc)_2$ (0.5)	THF	80	60/trace
15	Ag_2O (2.0)	THF	80	ND
16	$Cu(OAc)_2$ (2.0)	THF	80	52/10
17	Ag_2CO_3 (2.0)	THF	80	trace/15
18[c]	$Cu(OAc)_2$ (2.0)	THF	80	trace/23
19[c,d]	$Cu(OAc)_2$ (2.0)	THF	80	trace/52
20[c,d]	**$Cu(OAc)_2$ (2.0)**	**THF**	**100**	**trace/55**
21[c,d]	**$Cu(OAc)_2$ (0.5)**	**THF**	**100**	**trace/55**

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4 mol %), $AgSbF_6$ (16 mol %), additive, solvent (3.0 mL) under N_2 for 16 hours. [b]Isolated yield after column chromatography. [c] under O_2. [d]**2a** (0.44 mmol) was used.

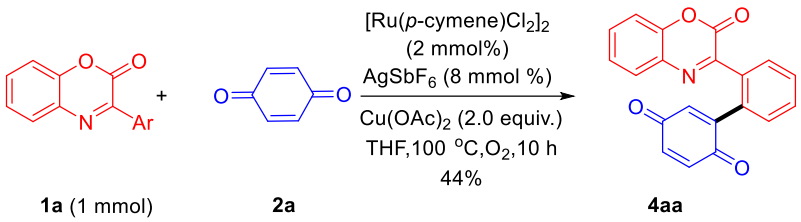
2. Scale-up Synthesis and derivatization of the product

2.1 Scale-up Synthesis



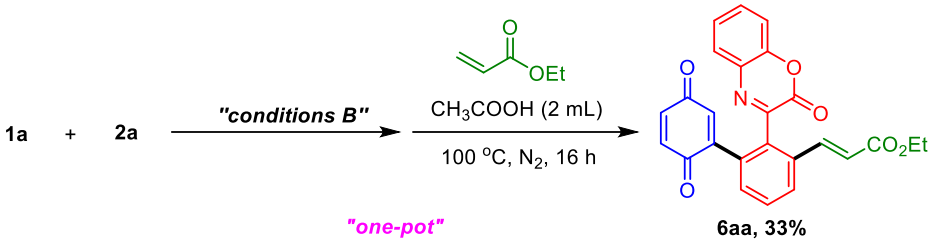
Benzoxazinones (1.0 mmol), benzoquinone (3.0 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.02 mmol, 2 mol %), $AgSbF_6$ (0.08 mmol, 8 mol %), $Zn(OAc)_2$ (0.2 mmol), and THF (10 mL) were charged into a pressure tube. The reaction mixture was stirred at 80 °C for 16 hours under the nitrogen atmosphere. After the

solvent was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA (9:1) to afford compound **3aa** in 76% yield (0.2516 g).

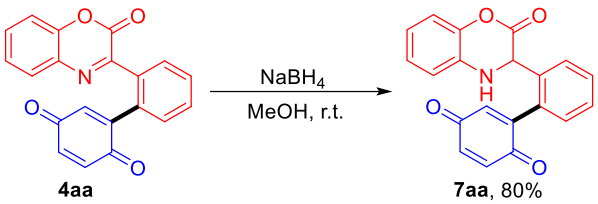


Benzoxazines (1.0 mmol), benzoquinone (2.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.02 mmol, 2 mol %), $AgSbF_6$ (0.08 mmol, 8 mol %), $Cu(OAc)_2$ (2.0 mmol), and THF (10 mL) were charged into a pressure tube. The reaction mixture was stirred at 100 °C for 10 hours under the oxygen atmosphere. After the solvent was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA (12:1) to afford compound **4aa** in 44% yield (0.1448 g).

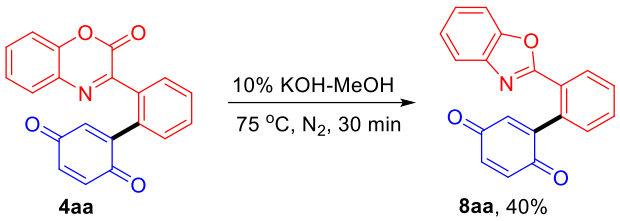
2.2 **derivatization of the 4aa**



Benzoxazinones (0.20 mmol), benzoquinones (0.44 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4 mol%), $AgSbF_6$ (16 mol %), $Cu(OAc)_2$ (0.4 mmol), and THF (3.0 mL) were charged into a pressure tube. The reaction mixture was stirred at 100 °C for 10 hours under the oxygen atmosphere.[3] After the reaction vessel was cooled to room temperature, the solvent was removed by decompression concentration, then Ethyl acrylate (2.0 equiv) and CH_3COOH (2 mL) were charged into the pressure tube, and the reaction mixture was stirred at 100 °C for 16 h under the nitrogen atmosphere. And then quenched with water, the mixture was diluted with DCM. The organic phase was separated and washed with brine and then dried over anhydrous $MgSO_4$. The organic phase was removed under reduced pressure and the residue was purified by silica gel chromatography with PE/EA (5:1) to afford the desired product **6aa** in 33% yield (28.2 mg).



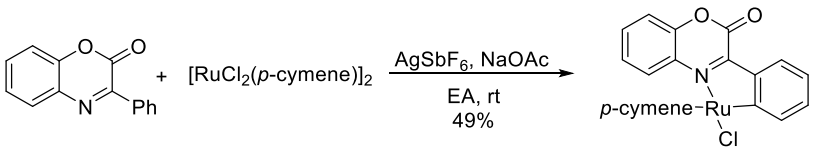
4aa (65.8 mg, 0.2 mmol, 1.0 equiv.), $NaBH_4$ (15.1 mg, 0.4 mmol, 2.0 equiv.) and MeOH (4.0 mL) were charged into a pressure tube. The reaction mixture was stirred at room temperature for 16 h, and then quenched with water. After a half of solvent was evaporated *in vacuo*, the mixture was diluted with EtOAc (15 mL), 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 (10:1) as eluent to afford the desired product **7aa** in 80 % yield (52.9 mg).



In a glovebox, **4aa** (65.8 mg, 0.2 mmol) were refluxed in 10% KOH-MeOH solution (2.0 mL) for 30 min.[4] After the reaction was cooled to the room temperature, the solvent was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA (3:1) to afford the desired product **8aa** in 40% yield (24 mg).

3. Mechanistic Studies

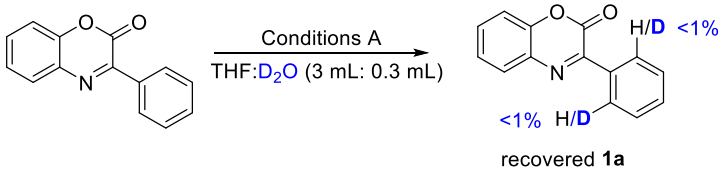
3.1 Synthesis of ruthenium complexes 11.

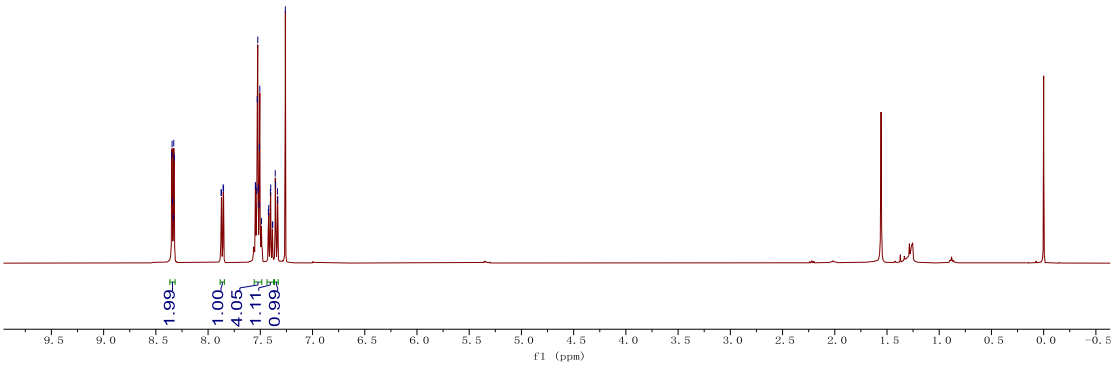


Benzoxazines **1a** (0.11 mmol, 2.2 equiv), $[RuCl_2(p\text{-cymene})]_2$ (0.05 mmol, 1.0 equiv), $AgSbF_6$ (0.2 mmol, 4.0 equiv), NaOAc (0.44 mmol, 4.4 equiv), and EtOAc (1.0 mL) were charged into a pressure tube. The reaction mixture was stirred at room temperature for 24 h in the nitrogen atmosphere. After the solvent was removed under reduced pressure, the residue was dissolved with dichloromethane and recrystallized to get the pure product **11a** in 49 % yield (24.4 mg).

3.2 H/D exchange under conditions A

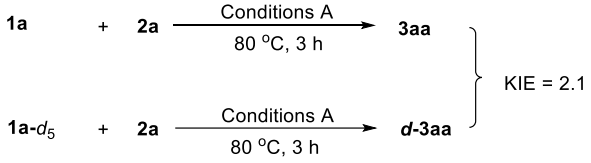
1a (0.20 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4 mol %), $AgSbF_6$ (16 mol %), 0.04 mmol $Zn(OAc)_2$, 0.2 mL D_2O, and THF (3 mL) were charged into a pressure tube, and the mixture was heated at 80 °C for 16 h, no H/D exchange was observed on the basis of ^1H NMR analysis, indicating that the C-H activation was largely irreversible in the catalytic system.

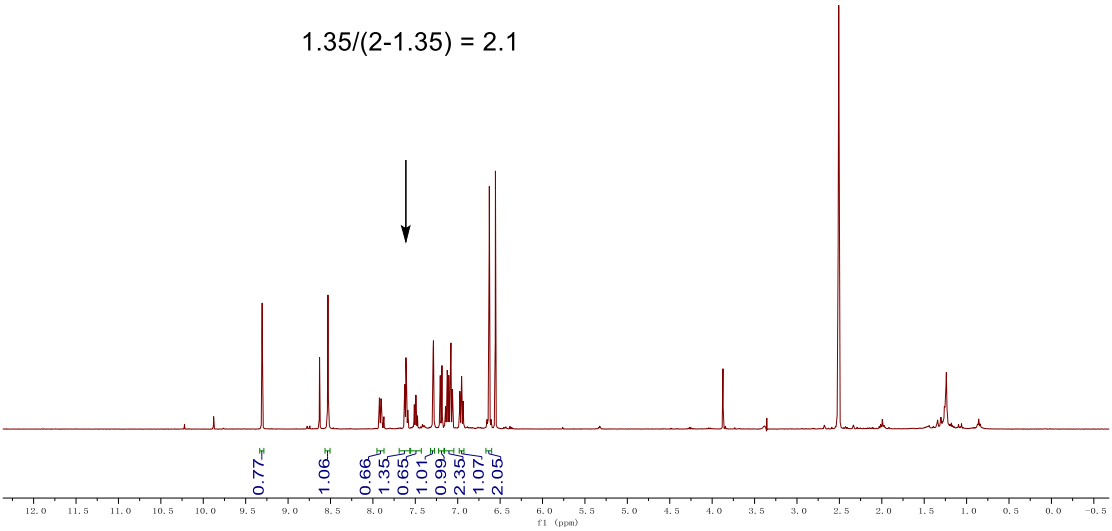




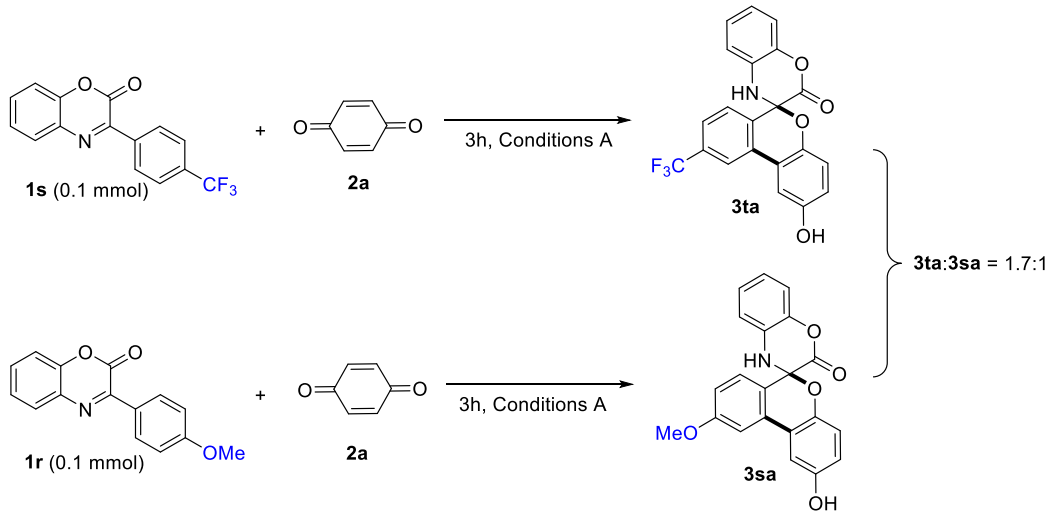
3.3 KIE Experiments

Two independent reactions with **1a** or deuterated substrate **1a**-d_5 under the standard conditions were performed. **1a** (0.1 mmol) or **1a**-d_5 (0.1 mmol), **2a** (0.15 mmol), $AgSbF_6$ (16 mol %), $Zn(OAc)_2$ (0.02 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4 mol %), and THF (3.0 mL) were stirred side-by-side at 80 °C for 3 h under nitrogen. Both reactions were quenched and these two mixtures were rapidly combined, and the volatiles were removed under reduced pressure. The residue was purified by silica gel chromatography with 25 mg of **3aa** and *d*-**3aa** were recovered. KIE value (k_H/k_D = 2.1:1) was determined on the basis of ^{1}H NMR analysis. suggesting the C-H activation is probably involved in the rate-determining step.

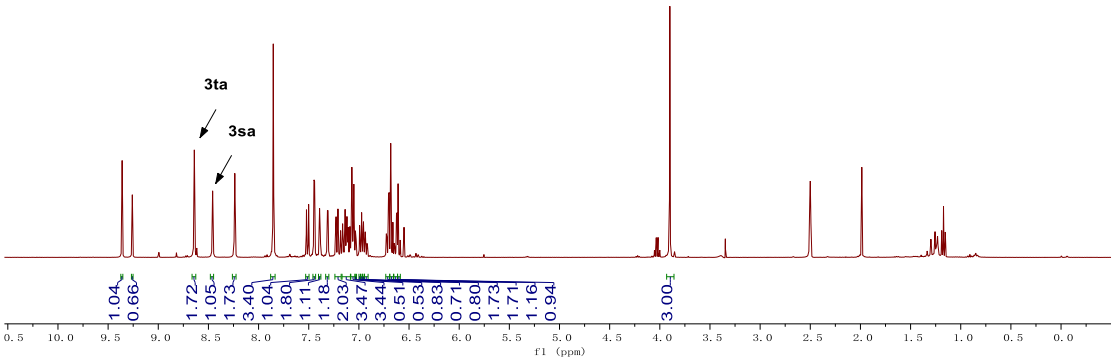




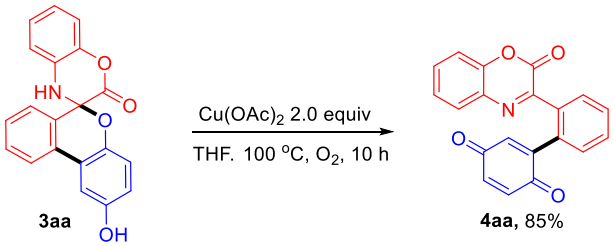
3.4 Intermolecular competition experiment



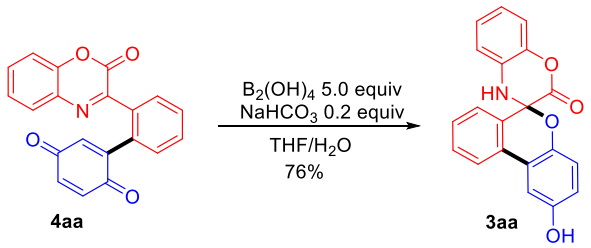
Two independent reactions with **1s** or **1t** under the standard conditions were performed. **1s** (0.1 mmol) or **1t** (0.1 mmol), **2a** (0.15 mmol), $AgSbF_6$ (16 mol %), $Zn(OAc)_2$ (0.02 mmol), $[RuCl_2(p\text{-cymene})]_2$ (4 mol %), and THF (3.0 mL) were stirred side-by-side at 80 °C for 3 hours under nitrogen. Both reactions were quenched and these two mixtures were rapidly combined, and the volatiles were removed under reduced pressure. The residue was purified by silica gel chromatography with 35 mg of **3sa** and **3ta** were recovered. KIE value (k_{tsa}/k_{3sa} = 1.7:1) was determined on the basis of ^{1}H NMR analysis.



3.5 Interconvertible experiment

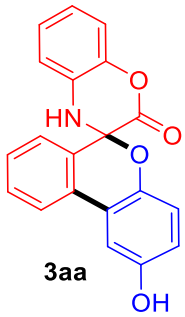


3aa (66.2 mg,0.2 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (4 mol%), $AgSbF_6$ (16 mol%), $Cu(OAc)_2$ (0.4 mmol), and THF (3.0 mL) were charged into a pressure tube. The reaction mixture was stirred at 100 °C for 10 hours under the oxygen atmosphere. After the solvent was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA (12:1) to afford compound **4aa** (85%, 55.6 mg).

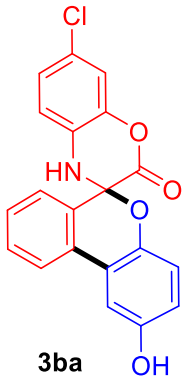


4aa (65.8 mg, 0.2 mmol, 1.0 equiv.), $B_2(OH)_4$ (89.6 mg, 1 mmol, 5.0 equiv), $NaHCO_3$ (3.4 mg, 0.04 mmol, 0.2 equiv), H_2O (0.3 mL) and THF (0.6 mL) were charged into a pressure tube. The reaction mixture was stirred at 60 °C for 6 hours.[5] Then extracted with EtOAc and H_2O, the organic phase was removed under reduced pressure, the residue was purified by silica gel chromatography using PE/EA (3:1) to afford the desired product **3aa** in 76% yield. (50.3 mg).

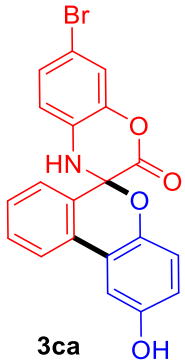
4. Characterization Data



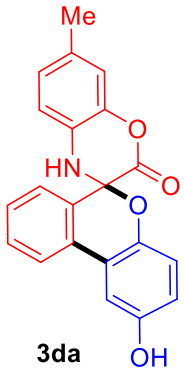
3aa White solid, 56.3 mg, 85 % yield, mp: 206 – 207 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.29 (s, 1H), 8.52 (s, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 7.0 Hz, 2H), 7.53 – 7.45 (m, 1H), 7.28 (s, 1H), 7.19 (dd, J = 8.1, 1.3 Hz, 1H), 7.14 – 7.05 (m, 2H), 6.99 – 6.91 (m, 1H), 6.64 – 6.61 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.5, 152.9, 142.5, 140.2 130.7, 130.3, 130.2, 129.2, 128.3, 126.5, 125.1, 122.3, 121.8, 120.2, 117.9, 116.6, 115.9, 115.8, 109.4, 84.8. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{14}NO_4^+$ = 332.0917, found: 332.0914.



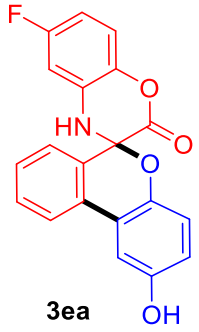
3ba White solid, 57.1 mg, 78 % yield, mp: 206 – 209 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.32 (s, 1H), 8.69 (s, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.63 – 7.59 (m, 2H), 7.53 – 7.45 (m, 1H), 7.38 (d, J = 2.3 Hz, 1H), 7.29 (d, J = 2.1 Hz, 1H), 7.19 (dd, J = 8.5, 2.3 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 6.67 – 6.62 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.0, 153.1, 142.3, 140.5, 130.7, 130.4, 129.4, 128.8, 128.4, 126.5, 125.0, 123.5, 122.3, 121.8, 118.0, 117.0, 116.7, 116.0, 109.5, 84.4. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}ClNO_4^+$ = 366.0528, found: 366.0541.



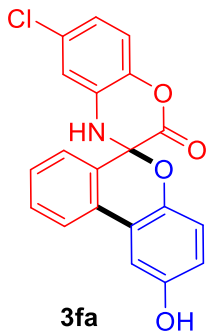
3ca White solid, 65.6 mg, 80 % yield, mp: 197 – 200 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.33 (s, 1H), 8.71 (s, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.53 – 7.45 (m, 2H), 7.32 – 7.29 (m, 2H), 7.03 (d, J = 8.4 Hz, 1H), 6.68 – 6.66 (m, 2H).**^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.0, 153.1, 142.4, 140.8, 130.7, 130.5, 129.8, 128.8, 128.4, 127.8, 126.5, 122.4, 121.8, 118.7, 118.0, 117.5, 116.8, 110.7, 109.5, 84.5. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}BrNO_4^+$ = 410.0022, found: 410.0035.



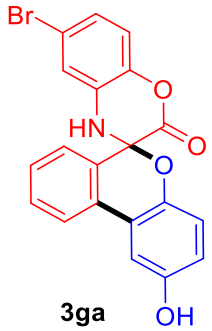
3da White solid, 50.37 mg, 73% yield, mp: 195 – 196 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.31 (s, 1H), 8.38 (s, 1H), 7.91 – 7.89 (m, 1H), 7.61 – 7.58 (m, 2H), 7.50 – 7.46 (m, 1H), 7.28 (s, 1H), 7.02 – 6.91 (m, 3H), 6.67– 6.65 (m, 2H), 2.28 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.7, 152.9, 142.6, 140.1, 130.8, 130.2, 129.5, 129.4, 128.3, 127.6, 126.4, 125.6, 122.2, 121.9, 117.9, 116.6, 116.1, 115.7, 109.4, 84.9, 20.2. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{16}NO_4^+$ = 346.1074, found: 346.1061.



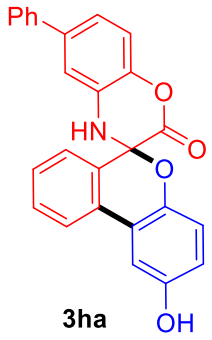
3ea White solid, 53.2 mg, 76 % yield, mp: 238 – 240 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.34 (s, 1H), 8.76 (s, 1H), 7.92 (s, 1H), 7.61 – 7.59 (m, 2H), 7.51 – 7.49 (m, 1H), 7.29 – 7.20 (m, 2H), 6.84 – 6.78 (m, 2H), 6.65 – 6.63 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.2, 159.0 (d, J = 239.4 Hz), 153.0 (d, J = 14.3 Hz), 142.3, 136.6, 131.5 (d, J = 8.5 Hz), 130.6, 130.4, 128.8 (d, J = 4.7 Hz), 128.3, 126.4, 122.3, 121.7, 117.9, 117.2 (d, J = 10.1 Hz), 116.7 (d, J = 9.1 Hz), 109.4 (d, J = 7.7 Hz), 106.4 (d, J = 24.1 Hz), 102.4 (d, J = 28.0 Hz), 84.1 (d, J = 7.4 Hz). **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}FNO_4^+$ = 350.0823, found: 350.0831.



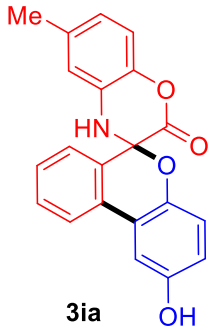
3fa White solid, 57.1 mg, 78 % yield, mp: 222 – 224 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.33 (s, 1H), 8.74 (s, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.52 – 7.48 (m, 1H), 7.29 – 7.28 (m, 1H), 7.25 (d, J = 8.6 Hz, 1H), 7.06 (d, J = 2.4 Hz, 1H), 6.99 (dd, J = 8.6, 2.5 Hz, 1H), 6.65 – 6.64 (m, 2H).**^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.0, 153.1, 142.2, 139.1, 131.6, 131.5, 130.6, 130.5, 128.8, 128.4, 126.5, 122.3, 121.7, 119.8, 118.0, 117.5, 116.7, 115.2, 109.4, 84.2. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}ClNO_4^+$ = 366.0528, found: 366.0537.



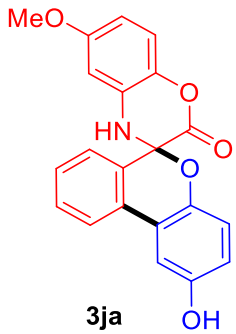
3ga White solid, 69.7 mg, 85 % yield, mp: 222 – 223 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.33 (s, 1H), 8.73 (s, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.63 – 7.48 (m, 2H), 7.52 – 7.48 (m, 1H), 7.29 (s, 1H), 7.21 – 7.18 (m, 2H), 7.13 – 7.10 (m, 1H), 6.66 – 6.66 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.0, 153.1, 142.2, 139.5, 131.9, 130.6, 130.5, 128.8, 128.4, 126.5, 122.7, 122.4, 121.7, 118.0, 118.0, 117.9, 116.7, 116.7, 109.5, 84.2. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}BrNO_4^+$ = 410.0022 found: 410.0032.



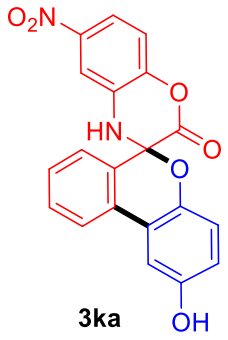
3ha White solid, 62.8 mg, 77 % yield, mp: 228 – 230 °C.**^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.31 (s, 1H), 8.65 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.66 – 7.58 (m, 4H), 7.55 – 7.43 (m, 3H), 7.39-– 7.35 (d, J = 7.3 Hz, 1H), 7.32 – 7.28 (m, 3H), 7.24 (dd, J = 2.1 Hz, 1H), 6.70 – 6.60 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.4, 142.5, 139.8, 139.6, 137.4, 130.8, 130.5, 130.4, 130.4, 129.0, 128.4, 127.5, 126.5, 122.3, 121.8, 118.7, 117.9, 116.6, 116.5, 116.4, 113.9, 113.8, 109.4, 84.8. **HRMS** $[M+H]^+$ calculated for $C_{26}H_{18}NO_4^+$ = 408.1230, found: 408.1236.



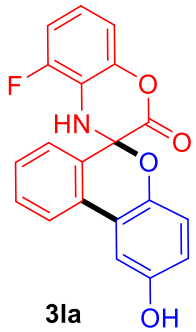
3ia White solid, 47.7 mg, 69 % yield, mp: 234 – 235 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.30 (s, 1H), 8.44 (s, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.61 – 7.58 (m, 2H), 7.50 – 7.47 (m, 1H), 7.29 (d, J = 2.3 Hz, 1H), 7.07 (d, J = 8.1 Hz, 1H), 6.86 (d, J = 2.0 Hz, 1H), 6.75 (dd, J = 8.3, 2.0 Hz, 1H), 6.65-6.61 (m, 2H), 2.27 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.6, 152.9, 142.6, 138.2, 134.4, 130.8, 130.3, 129.8, 129.4, 128.3, 126.5, 122.3, 121.8, 120.7, 117.9, 116.6, 116.1, 115.6, 109.4, 84.9, 20.7. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{16}NO_4^+$ = 346.1074, found: 346.1084.



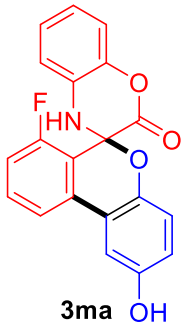
3ja White solid, 52.1 mg, 72 % yield, mp: 249 – 250 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.30 (s, 1H), 8.49 (s, 1H), 7.91 (dd, J = 7.8, 1.9 Hz, 1H), 7.60 (t, J = 7.4 Hz, 2H), 7.52 – 7.44 (m, 1H), 7.28 (d, J = 1.9 Hz, 1H), 7.12 (dd, J = 8.9, 1.9 Hz, 1H), 6.71 – 6.48 (m, 4H), 3.73 (d, J = 1.9 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.6, 156.6, 152.9, 142.5, 134.4, 130.9, 130.8, 130.3, 129.3, 128.3, 126.4, 122.3, 121.8, 117.9, 116.6, 116.4, 109.4, 105.2, 101.2, 84.7, 55.3. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{16}NO_5^+$ = 362.1023, found: 362.1023.



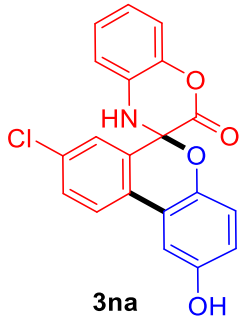
3ka White solid, 62.6 mg, 83 % yield, mp: 245 – 247 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.32 (s, 1H), 8.74 (s, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.65 – 7.56 (m, 2H), 7.49 (t, J = 7.5 Hz, 1H), 7.29 (s, 1H), 7.27 – 7.22 (m, 1H), 6.83 (dd, J = 9.5, 3.0 Hz, 1H), 6.77 (td, J = 8.7, 2.9 Hz, 1H), 6.64 (d, J = 1.5 Hz, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.2, 153.1, 142.3, 136.6, 131.6, 130.7, 130.4, 128.9, 128.4, 126.4, 122.3, 121.7, 118.0, 116.7, 109.5, 106.5, 106.3, 102.6, 102.3, 84.2. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}N_2O_6^+$ = 377.0768, found: 377.0846.



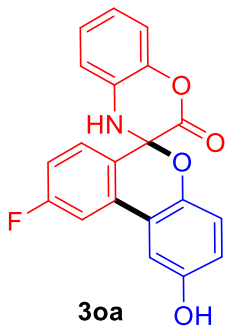
3la White solid, 56.0 mg, 80 % yield, mp: 246 – 248 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.33 (s, 1H), 8.75 (s, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.74 – 7.56 (m, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.30 (s, 1H), 7.28 – 7.20 (m, 1H), 6.87 – 6.81 (m, 1H), 6.81 – 6.73 (m, 1H), 6.65 (s, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.2, 159.3 (d, J = 239.3 Hz), 153.0, 142.3, 136.6 (d, J = 2.1 Hz), 131.5 (d, J = 11.8 Hz), 130.6, 130.4, 128.9, 128.4, 126.4, 122.3, 121.7, 117.9, 117.2 (d, J = 10.2 Hz), 116.7, 109.4, 106.4 (d, J = 24.0 Hz), 102.5 (d, J = 27.6 Hz), 84.2. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}FNO_4^+$ = 350.0823, found: 350.0826.



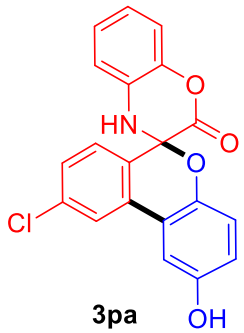
3ma White solid, 27.9 mg, 40 % yield, mp:175 – 177 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.36 (s, 1H), 8.48 (s, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.66 – 7.54 (m, 1H), 7.39 – 7.26 (m, 2H), 7.22 (d, J = 8.1 Hz, 1H), 7.11 – 7.03 (m, 1H), 6.93 (t, J = 7.8 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.73 (d, J = 8.8 Hz, 1H), 6.65 (d, J = 8.6 Hz, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.5, 158.7 (d, J = 248.1 Hz), 152.9, 141.3, 140.0, 131.9 (d, J = 9.2 Hz), 131.5, 131.5, 128.7, 125.5, 119.4, 119.4 (d, J = 140.1 Hz), 118.0, 117.8, 116.9 (d, J = 13.1 Hz), 116.2, 115.4, 115.1, 109.7, 82.3 (d, J = 2.5 Hz). **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}O_4NF^+$ = 350.0823, found: 350.0835.



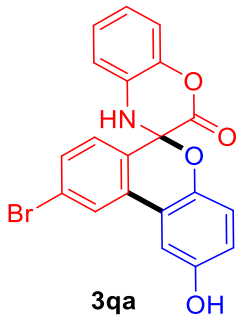
3na White solid, 35.1 mg, 48 % yield, mp: 217 – 219 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.36 (s, 1H), 8.60 (s, 1H), 7.99 – 7.92 (m, 1H), 7.69 – 7.63 (m, 2H), 7.28 (d, J = 2.2 Hz, 1H), 7.20 (dd, J = 8.1, 1.3 Hz, 1H), 7.15 – 7.11 (m, 1H), 7.06 (dd, J = 7.9, 1.7 Hz, 1H) 6.98 – 6.94 (m, 1H), 6.68 – 6.61 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.0, 153.1, 142.4, 140.1, 132.7, 131.0, 130.3, 129.9, 129.8, 126.4, 125.2, 124.5, 121.0, 120.3, 118.1, 117.1, 115.9, 115.9, 109.5, 84.4. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}ClNO_4^+$ = 366.0528, found: 366.0531.



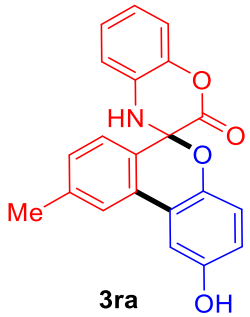
3oa White solid, 44.8 mg, 64 % yield, mp: 237 – 238 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.35 (s, 1H), 8.56 (s, 1H), 7.79 (dd, J = 10.2, 2.6 Hz, 1H), 7.70 – 7.62 (m, 1H), 7.39 – 7.27 (m, 2H), 7.20 (d, J = 8.0 Hz, 1H), 7.16 – 7.03 (m, 2H), 6.99 – 6.91 (m, 1H), 6.70 – 6.60 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 163.5 (d, J = 245.8 Hz), 159.4, 153.0, 142.8, 140.2, 133.6 (d, J = 8.8 Hz), 130.0, 129.2 (d, J = 8.9 Hz), 125.5 (d, J = 2.9 Hz), 125.2, 121.1, 121.1, 120.3, 118.0, 117.5, 115.9, 115.1 (d, J = 22.1 Hz), 110.0, 109.2 (d, J = 23.4 Hz), 84.7. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}FNO_4^+$ = 350.0823, found: 350.0829.



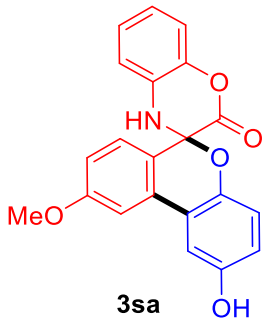
3pa White solid, 52.7 mg, 72 % yield, mp: 238 – 240 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.34 (s, 1H), 8.58 (s, 1H), 7.99 (d, J = 2.1 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.54 (dd, J = 8.4, 2.1 Hz, 1H), 7.33 (d, J = 2.6 Hz, 1H), 7.20 (dd, J = 8.1, 1.3 Hz, 1H), 7.14 – 7.10 (m , 1H), 7.06 (dd, J = 7.9, 1.7 Hz, 1H), 6.98 – 6.93 (m, 1H), 6.70 – 6.61 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.3, 153.1, 142.7, 140.1, 135.4, 133.0, 129.9, 128.7, 128.0, 128.0, 125.2, 122.1, 120.7, 120.3, 118.1, 117.5, 115.9, 115.9, 109.9, 84.6. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}ClNO_4^+$ = 366.0528, found: 366.0536.



3qa White solid, 58.2 mg, 71 % yield, mp: 233 – 234 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.33 (s, 1H), 8.57 (s, 1H), 8.11 (d, J = 2.0 Hz, 1H), 7.69 – 7.67 (m, 1H), 7.56 – 7.54 (m, 1H), 7.33 (d, J = 2.7 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.14 – 7.11 (m, 1H), 7.06 (dd, J = 7.9, 1.6 Hz, 1H), 6.98 – 6.93 (m, 1H), 6.72 – 6.60 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.2, 153.1, 142.7, 140.1, 133.2, 131.0, 129.9, 128.9, 128.3, 125.2, 125.0, 124.1, 120.6, 120.3, 118.1, 117.5, 115.9, 115.9, 109.8, 84.6. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{13}BrNO_4^+$ = 410.0022, found: 410.0025.

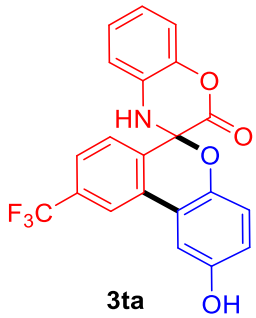


3ra White solid, 51.2 mg, 74 % yield, mp: 226 – 228 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.25 (s, 1H), 8.47 (s, 1H), 7.72 (s, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.32 – 7.21 (m, 2H), 7.18 (d, J = 8.1 Hz, 1H), 7.15 – 7.03 (m, 2H), 6.95 – 6.92 (m, 1H), 6.64 – 6.59 (s, 2H), 2.44(s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.6, 152.9, 142.7, 140.2, 139.8, 130.6, 130.2, 128.9, 126.5, 126.4, 125.1, 122.6, 121.9, 120.1, 117.8, 116.5, 115.9, 115.8, 109.4, 84.8, 21.0. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{16}NO_4^+$ = 346.1074, found: 346.1071.



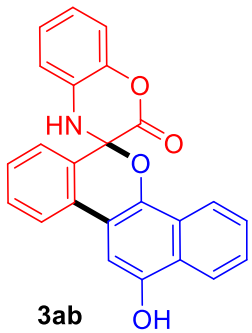
3sa

White solid, 42.7 mg, 59 % yield, mp: 220 – 222 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.28 (s, 1H), 8.46 (s, 1H), 7.51 (d, J = 8.6 Hz, 1H), 7.39 (d, J = 2.6 Hz, 1H), 7.31 (d, J = 2.6 Hz, 1H), 7.17 (dd, J = 8.0, 1.3 Hz, 1H), 7.13 – 7.02 (m, 3H), 6.96 – 6.91 (m, 1H), 6.67 – 6.57 (m, 2H), 3.89 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 160.7, 159.8, 152.9, 142.9, 140.2, 132.4, 130.2, 128.0, 125.1, 121.8, 121.7, 120.1, 117.8, 116.8, 115.9, 115.8, 114.2, 109.7, 107.1, 84.8, 55.5. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{16}NO_5^+$ = 362.1023, found: 362.1028.



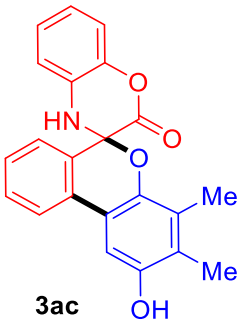
3ta

White solid, 49.5 mg, 62% yield, mp: 156 – 157 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.37 (s, 1H), 8.65 (s, 1H), 8.24 (s, 1H), 7.88 – 7.84 (m, 2H), 7.45 (d, J = 2.6 Hz, 1H), 7.22 (dd, J = 8.2, 1.3 Hz, 1H), 7.16 – 7.12 (m, 1H), 7.06 (dd, J = 7.9, 1.6 Hz, 1H), 6.99 – 6.95 (m, 1H), 6.75 – 6.64 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.1, 153.2, 141.4 (d, J = 248.0 Hz), 133.0, 132.1, 131.0 (d, J = 32.1 Hz), 129.7, 128.0, 125.3, 125.3, 124.8, 122.6, 120.6, 120.4, 119.2, 119.1, 118.2, 117.8, 116.0 (d, J = 6.9 Hz), 110.0, 84.6. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{13}F_3NO_4^+$ = 400.0791, found: 400.0800.



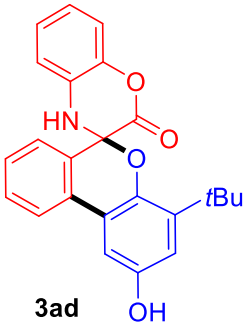
3ab

White solid, 40.5 mg, 53 % yield, mp: 210 – 212 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.07 (s, 1H), 8.68 (s, 1H), 8.08 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 7.9 Hz, 1H), , 7.71 – 7.63 (m, 2H), 7.57 – 7.49 (m, 1H), 7.46 – 7.39 (m, 2H), 7.38 – 7.33 (m, 1H), 7.31 (s, 1H), 7.26 (d, J = 7.9 Hz, 1H), 7.17 – 7.07 (m, 2H), 7.38 – 7.33 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.7, 148.6, 140.5, 137.3, 131.0, 130.5, 130.2, 128.9, 128.2, 126.7, 126.6, 125.8, 125.6, 125.5, 125.2, 122.4, 122.2, 120.6, 120.4, 116.2, 116.1, 115.7, 101.9, 85.1. **HRMS** $[M-H]^-$ = calculated for $C_{24}H_{14}NO_4^-$ = 380.0928, found: 380.0926.



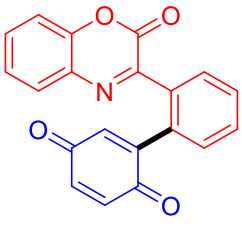
3ac

White solid, 52.6 mg, 73 % yield, mp: 217 – 218 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.46 (s, 1H), 7.80 – 7.73 (m, 1H), 7.64 – 7.55 (m, 2H), 7.48 – 7.44 (m, 1H), 7.20 (dd, J = 8.0, 1.3 Hz, 1H), 7.16 – 7.04 (m, 3H), 6.99 – 6.94 (m, 1H), 2.01 (s, 3H), 1.68 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 160.0, 150.5, 140.6, 140.1, 131.4, 130.5, 130.2, 129.1, 127.7, 126.2, 126.2, 125.0, 125.0, 121.9, 120.4, 118.9, 116.1, 115.5, 106.2, 84.4, 12.1, 11.0. **HRMS** $[M+H]^+$ calculated for $C_{22}H_{18}NO_4^+$ = 360.1230, found: 360.1225.



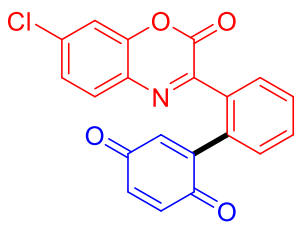
3ad

White solid, 32.5 mg, 42% yield, mp: 217 – 220 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 9.13 (s, 1H), 8.52 (s, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.63 – 7.54 (m, 2H), 7.49 – 7.45 (m, 1H), 7.15 – 7.06 (m, 4H), 6.96 – 6.62 (m, 1H), 6.66 (d, J = 2.8 Hz, 1H), 0.98 (s, 9H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 159.6, 151.9, 141.2, 140.2, 139.3, 131.2, 130.6, 130.2, 128.8, 128.1, 126.1, 125.2, 122.6, 121.9, 120.2, 115.9, 115.9, 114.8, 107.2, 84.5, 34.0, 29.4. **HRMS** $[M+H]^+$ calculated for $C_{24}H_{22}NO_4^+$ = 388.1543, found: 388.1550.



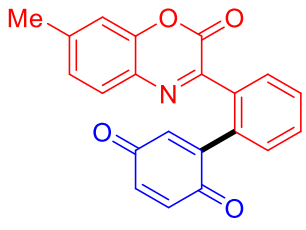
4aa

Yellow solid, 36.3 mg, 55 % yield, mp: 156 – 157 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 – 8.05 (m, 1H), 7.66 – 7.56 (m, 3H), 7.53 – 7.49 (m, 1H), 7.45 – 7.40 (m, 1H), 7.35 – 7.30 (m, 2H), 6.84 (d, J = 2.5 Hz, 1H), 6.77 (dd, J = 10.1, 2.5 Hz, 1H), 6.67 (d, J = 10.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.5, 186.2, 152. 7, 152.3, 148.8, 146.6, 136.7, 136.6, 133.9, 133.3, 132.9, 131.7, 131.2, 131.0, 130.8, 130.8, 129.8, 129.1, 125.8, 116.6. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{12}NO_4^+$ = 330.0761, found: 330.0758.



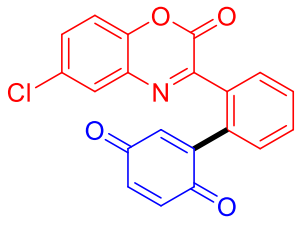
4ba

Yellow solid, 34.2 mg, 47 % yield, mp: 180 – 183 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 8.02 (m, 1H), 7.67 – 7.57 (m, 2H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.47 – 7.39 (m, 1H), 7.35 – 7.26 (m, 2H), 6.84 (d, *J* = 2.6 Hz, 1H), 6.78 (dd, *J* = 10.1, 2.6 Hz, 1H), 6.66 (d, *J* = 10.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.5, 186.2, 152.6, 151.5, 148.5, 146.9, 137.5, 136.6, 133.7, 133.2, 133.1, 131.2, 130.8, 130.8, 129.8, 129.8, 126.4, 116.9 (two signals was missing due to overlap). **HRMS** $[M+H]^+$ calculated for $C_{20}H_{11}ClNO_4^+$ = 364.0371, found: 364.0367.



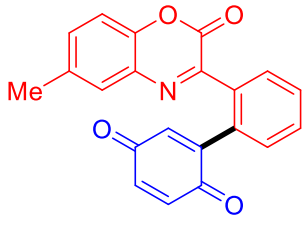
4da

Yellow solid, 39.9 mg, 58 % yield, mp: 156 – 157 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.05 (m, 1H), 7.62 – 7.54 (m, 2H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.41 – 7.39 (m, 1H), 7.16 – 7.10 (m, 1H), 7.09 (s, 1H), 6.80 (d, *J* = 2.6 Hz, 1H), 6.75 (dd, *J* = 10.1, 2.5 Hz, 1H),, 6.65 (d, *J* = 10.1 Hz, 1H), 2.46 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.5, 186.1, 152.4, 151.3, 148.8, 146.4, 143.2, 136.7, 136.5, 134.0, 133.2, 132.8, 130.7, 130.7, 129.7, 129.2, 128.6, 126.9, 116.6, 21.9. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{14}NO_4^+$ = 344.0917, found: 344.0920.



4fa

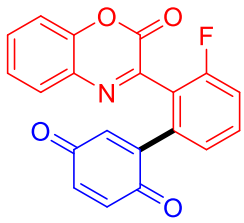
Yellow solid, 34.9 mg, 48 % yield, mp: 118 – 120 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 – 8.02 (m, 1H), 7.63 – 7.61 (m, 2H), 7.57 (d, *J* = 2.5 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.26 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 2.6 Hz, 1H), 6.80 (dd, *J* = 10.1, 2.6 Hz, 1H), 6.67 (d, *J* = 10.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.5, 186.2, 153.9, 151.7, 148.4, 145.2, 136.7, 136.6, 133.6, 133.2, 133.2, 131.7, 131.6, 131.3, 130.9, 130.9, 130.9, 129.8, 128.4, 117.8. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{11}ClNO_4^+$ = 364.0371, found: 364.0380.



4ia

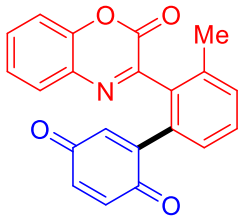
Yellow solid, 29.6 mg, 43 % yield, mp: 120 – 121 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 8.03 (m, 1H), 7.63 – 7.56 (m, 2H), 7.45 – 7.39 (m, 1H), 7.37 (s, 1H), 7.34 – 7.27 (m,

1H), 7.19 (d, *J* = 8.4 Hz, 1H), 6.83 (d, *J* = 2.5 Hz, 1H), 6.77 (dd, *J* = 10.1, 2.5 Hz, 1H), 6.67 (d, *J* = 9.9 Hz, 1H), 2.41 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.6 186.1, 152.6, 152.5, 148.7, 144.5, 136.7, 136.5, 135.8, 134.1, 133.2, 132.9, 132.7, 131.0, 130.8, 130.8, 130.7, 129.8, 128.9, 116.2, 20.9. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{14}NO_4^+$ = 344.0917, found: 344.0919.



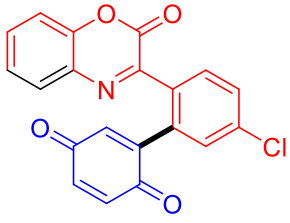
4ma

Yellow solid, 34.1 mg, 49 % yield, mp: 147 – 148 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 – 7.52 (m, 3H), 7.38 – 7.29 (m, 3H), 7.29 – 7.21 (m, 1H), 6.94 – 6.90 (m, 1H), 6.75 – 6.71 (m, 1H), 6.59 (dd, *J* = 10.1, 2.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.1, 185.9, 161.0 (d, *J* = 251.8 Hz), 151.5, 151.1, 146.8, 146.0 (d, *J* = 2.5 Hz), 136.5, 135.1, 134.9 (d, *J* = 3.3 Hz), 132.2, 132.2, 132.1, 130.9, 129.3, 126.2 (d, *J* = 3.2 Hz), 125.7, 122.8 (d, *J* = 16.3 Hz), 117.8 (d, *J* = 22.0 Hz), 116.8. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{11}FNO_4^+$ = 348.0667, found: 348.0670.



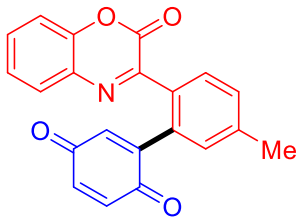
4ua

Yellow solid, 44.1 mg, 64 % yield, mp: 156 – 157 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.51 – 7.45 (m, 2H), 7.37 – 7.32 (m, 2H), 7.24 (dd, *J* = 7.5, 1.4 Hz, 1H), 6.81 (d, *J* = 2.5 Hz, 1H), 6.67 (dd, *J* = 10.1, 2.6 Hz, 1H), 6.57 (d, *J* = 10.1 Hz, 1H), 2.38 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.6, 186.0, 161.6, 152.4, 151.4, 149.6, 146.4, 136.9, 136.6, 135.5, 133.0, 132.2, 131.2, 131.2, 128.8, 126.2, 125.7, 116.9, 116.5, 114.6, 55.8. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{14}NO_4^+$ = 344.0917, found: 344.0920.



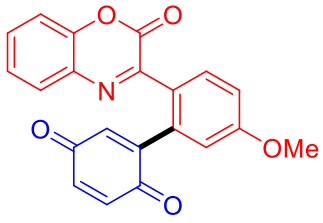
4oa

Yellow solid, 38.6 mg, 53 % yield, mp: 176 – 178 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.60 – 7.50 (m, 3H), 7.41 (d, *J* = 2.2 Hz, 1H), 7.37 – 7.29 (m, 2H), 6.84 – 6.78 (m, 2H), 6.69 (d, *J* = 9.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.2, 185.7, 152.1, 151.4, 147.8, 146.6, 137.2, 136.7, 136.7, 135.1, 133.0, 132.3, 132.2, 132.0, 131.1, 130.7, 129.8, 129.1, 125.9, 116.7. **HRMS** $[M+H]^+$ calculated for $C_{20}H_{11}ClNO_4^+$ = 364.0371, found: 364.0365.



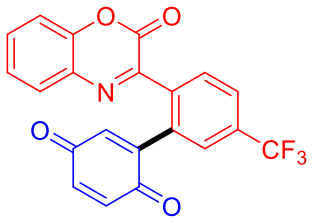
4qa

Yellow solid, 33.7 mg, 49 % yield, mp: 172 – 174 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.1 Hz, 1H), 7.56 (dd, J = 7.9, 1.6 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.41 (dd, J = 8.1, 1.8 Hz, 1H), 7.36 – 7.27 (m, 2H), 7.22 (d, J = 1.8 Hz, 1H), 6.83 – 6.74 (m, 2H), 6.67 (d, J = 9.9 Hz, 1H), 2.47 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.6, 186.3, 152.3, 152.3, 149.2, 146.5, 141.6, 136.8, 136.6, 133.4, 132.5, 131.5, 131.2, 131.1, 130.9, 130.5, 129.0, 125.7, 116.5, 21.6. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{14}NO_4^+$ = 344.0917, found: 344.0915.



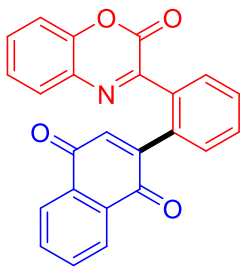
4sa

Yellow solid, 34.6 mg, 48 % yield, mp: 156 – 157 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.8 Hz, 1H), 7.52 (dd, J = 7.9, 1.6 Hz, 1H), 7.50 – 7.45 (m, 1H), 7.56 – 7.43 (m, 2H), 7.35 – 7.25 (m, 2H), 7.10 (dd, J = 8.8, 2.7 Hz, 1H), 6.91 (d, J = 2.6 Hz, 1H), 6.81 – 6.76 (m, 2H), 6.74 – 6.67 (m, 1H), 3.91 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.3, 186.4, 155.1, 152.1, 147.5, 146.8, 138.1, 136.5, 136.4, 135.0, 133.5, 133.3, 132.5, 131.8, 130.8, 130.1, 129.3, 128.1, 125.8, 116.8, 20.5. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{14}NO_5^+$ = 360.0866, found: 360.0873.



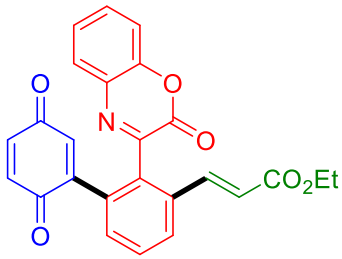
4ta

Yellow solid, 34.1 mg, 43 % yield, mp: 156 – 157 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.2 Hz, 1H), 7.86 (dd, J = 8.4, 1.8 Hz, 1H), 7.68 (d, J = 1.8 Hz, 1H), 7.61 (dd, J = 7.9, 1.6 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.41 – 7.31 (m, 2H), 6.88 (d, J = 2.5 Hz, 1H), 6.80 (dd, J = 10.1, 2.5 Hz, 1H), 6.69 (d, J = 10.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.1, 185.6, 152.0, 151.5, 147.4, 146.7, 137.1 (d, J = 1.5 Hz), 136.8, 136.6, 134.0, 133.5, 132.8 (q, J = 33.2 Hz), 132.4, 131.4, 131.1, 129.4, 127.6 (d, J = 3.9 Hz), 126.5 (d, J = 3.7 Hz), 126.1, 123.5 (q, J = 272.8 Hz), 116.8. **HRMS** $[M+H]^+$ calculated for $C_{21}H_{11}F_3NO_4^+$ = 398.0635, found: 398.0623.



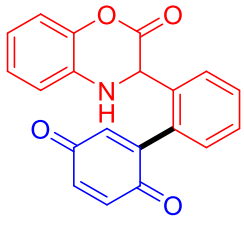
4ab

Yellow solid, 31.8 mg, 42 % yield, mp:108–111 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.08 – 8.03 (m, 1H), 8.00 (d, J = 7.7 Hz, 1H), 7.89 – 7.79 (m, 1H), 7.76 – 7.73 (m, 2H), 7.70 – 7.65 (m, 2H), 7.63 – 7.59 (m, 1H), 7.54 – 7.47 (m, 1H), 7.42 – 7.40 (m, 1H), 7.26 – 7.15 (m, 2H), 7.11 (s, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 184.4, 184.1, 153.1, 152.0, 149.8, 146.1, 135.1, 134.3, 134.2, 133.7, 133.6, 131.6, 131.4, 131.3, 130.6, 130.5, 130.4, 128.9, 128.1, 126.2, 125.6, 125.4, 116.1. **HRMS** $[M+Na]^+$ calculated for $C_{24}H_{13}O_4NNa^+$ = 402.0737, found: 402.0747.



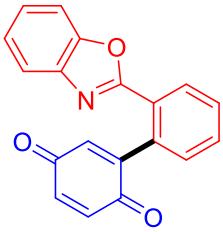
6aa

Yellow solid, 28.2 mg, 33 % yield, mp: 123 – 126 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.9, 1H), 7.71 – 7.64 (m, 2H), 7.64 – 7.58 (m, 1H), 7.57 – 7.53 (m, 1H), 7.42 (d, J = 7.6 Hz, 1H), 7.40 – 7.32 (m, 2H), 6.78 (d, J = 2.5 Hz, 1H), 6.69 (dd, J = 10.1, 2.5 Hz, 1H), 6.60 (d, J = 10.1 Hz, 1H), 6.41 (d, J = 15.7 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 187.0, 186.0, 166.3, 153.3, 152.2, 146.8, 146.8, 141.6, 136.5, 136.4, 135.5, 135.0, 134.1, 133.5, 132.3, 131.7, 130.9, 130.4, 129.5, 128.6, 126.0, 122.1, 116.9, 60.8, 14.3. **HRMS** $[M+Na]^+$ calculated for $C_{25}H_{17}O_6NNa^+$ = 450.0948, found: 450.0941.



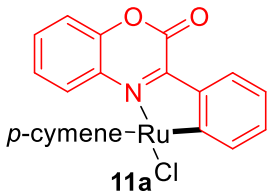
7aa

Yellow solid, 52.9 mg, 80 % yield, mp: 175 – 177 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.45 (s, 1H), 9.38 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.64 – 7.57 (m, 1H), 7.47 – 7.44 (m, 2H), 7.39 (d, J = 2.3 Hz, 1H), 7.13 – 7.04 (m, 2H), 6.98 – 6.92 (m, 1H), 6.85 (d, J = 8.0 Hz, 1H), 6.72 – 6.67 (m, 2H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 152.2, 144.1, 139.9, 132.4, 131.7, 130.0, 129.2, 128.3, 127.6, 122.0, 121.8, 121.2, 119.5, 118.2, 116.9, 116.4, 114.9, 109.1, 87.0, 84.9. **HRMS** $[M+Na]^+$ calculated for $C_{20}H_{13}O_4NNa^+$ = 354.0737, found: 354.0739.



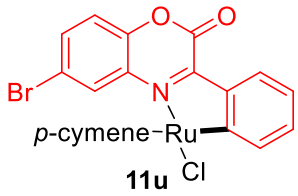
8aa

Red solid, 24 mg, 40 % yield, mp: 95 –97 ºC. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.96 (d, J = 7.5 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.18 – 7.14 (m, 1H), 7.06 – 7.00 (m, 3H), 6.99 – 6.92 (m, 3H), 6.90 (d, J = 7.7 Hz, 1H), 6.70 (d, J = 8.7 Hz, 1H). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 169.0, 151.9, 148.2, 147.0, 144.2, 137.7, 135.6, 133.3, 131.9, 127.6, 127.1, 126.9, 125.1, 125.1, 123.5, 121.8, 120.8, 118.5, 117.3. **HRMS** $[M+H]^+$ calculated for $C_{19}H_{12}O_3N^+$ = 302.0812, found: 302.0810.



11a

Red solid, 49 % yield, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.92 (dd, J = 8.2, 1.6 Hz, 1H), 8.85 (dd, J = 8.0, 1.5 Hz, 1H), 8.26 (dd, J = 7.6, 1.2 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.50 – 7.46 (m, 1H), 7.36 (dd, J = 8.0, 1.6 Hz, 1H), 7.23 (dd, J = 7.5, 1.5 Hz, 1H), 7.17 – 7.12 (m, 1H), 5.76 (dd, J = 6.2, 1.4 Hz, 1H), 5.70 (dd, J = 6.1, 1.4 Hz, 1H), 5.30 – 5.26 (m, 2H), 2.29 – 2.22 (m, 1H), 2.13 (s, 1H), 0.94 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.5 (C_q), 158.4 (C_q), 150.2 (C_q), 144.2 (C_q), 142.7 (C_q), 139.3 (CH), 133.9 (C_q), 133.8 (CH), 131.0 (CH), 130.6 (CH), 128.7 (CH), 125.2 (CH), 123.5 (CH), 116.5 (CH), 103.9 (C_q), 102.8 (C_q), 95.6 (CH), 92.4 (CH), 85.3 (CH), 85.2 (CH), 31.1 (CH), 22.7 (CH_3), 21.7 (CH_3), 18.9 (CH_3). **HRMS** $[M+Na]^+$ calculated for $C_{24}H_{22}ClNNaO_2Ru^+$ = 516.0275, found: 516.0281.



11u

Rufous solid, 19 % yield, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.85 (d, J = 8.0 Hz, 1H), 8.28 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 8.7 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.15 (t, J = 7.6 Hz, 1H), 5.83 (d, J = 6.1 Hz, 1H), 5.77 (d, J = 6.1 Hz, 1H), 5.21 (d, J = 6.2 Hz, 1H), 5.11 (d, J = 6.1 Hz, 1H), 2.36 – 2.20 (m, 1H), 2.19 (s, 3H), 1.63 (s, 3H), 1.01 (d, J = 6.8 Hz, 3H), 0.76 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.0 (C_q), 158.7 (C_q), 149.6 (C_q), 143.2 (C_q), 142.5 (C_q), 139.5 (CH), 134.7 (C_q), 134.1 (CH), 133.0 (CH), 131.4 (CH), 131.3 (CH), 123.6 (CH), 117.9 (CH), 117.6 (C_q), 105.3 (C_q), 104.7 (C_q), 97.1 (CH), 92.6 (CH), 85.1 (CH), 82.2 (CH), 31.2 (CH), 23.3 (CH_3), 21.1 (CH_3), 18.9 (CH_3). **HRMS** $[M+K]^+$ calculated for $C_{24}H_{21}BrClKNO_4Ru+$ = 609.9119, found: 609.9178.

5. References

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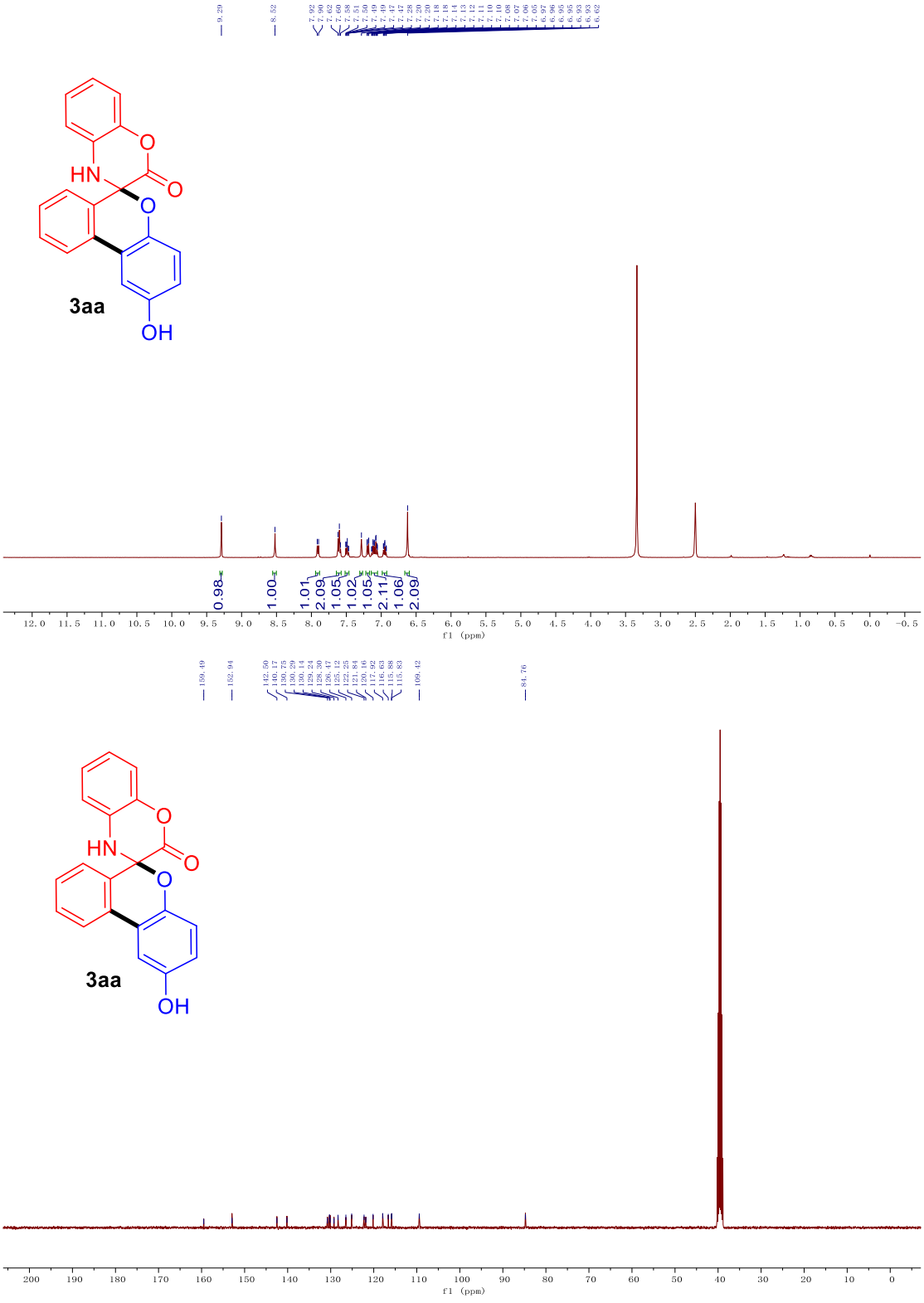
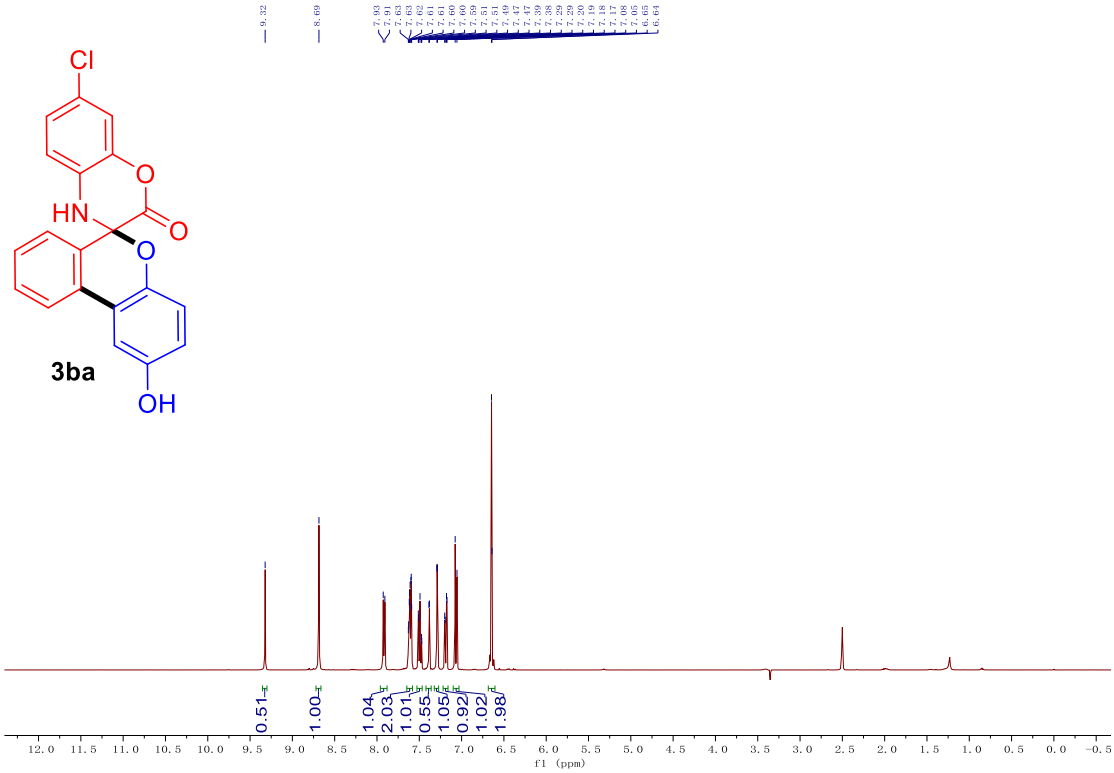
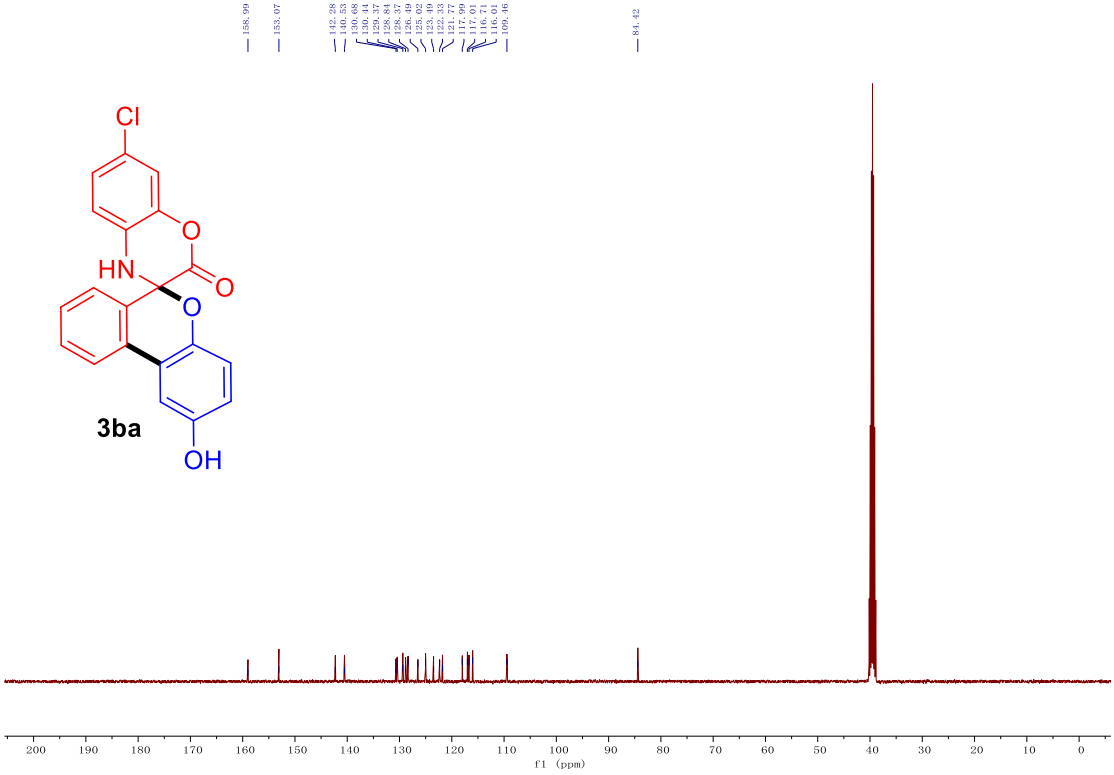
6. NMR Spectra

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

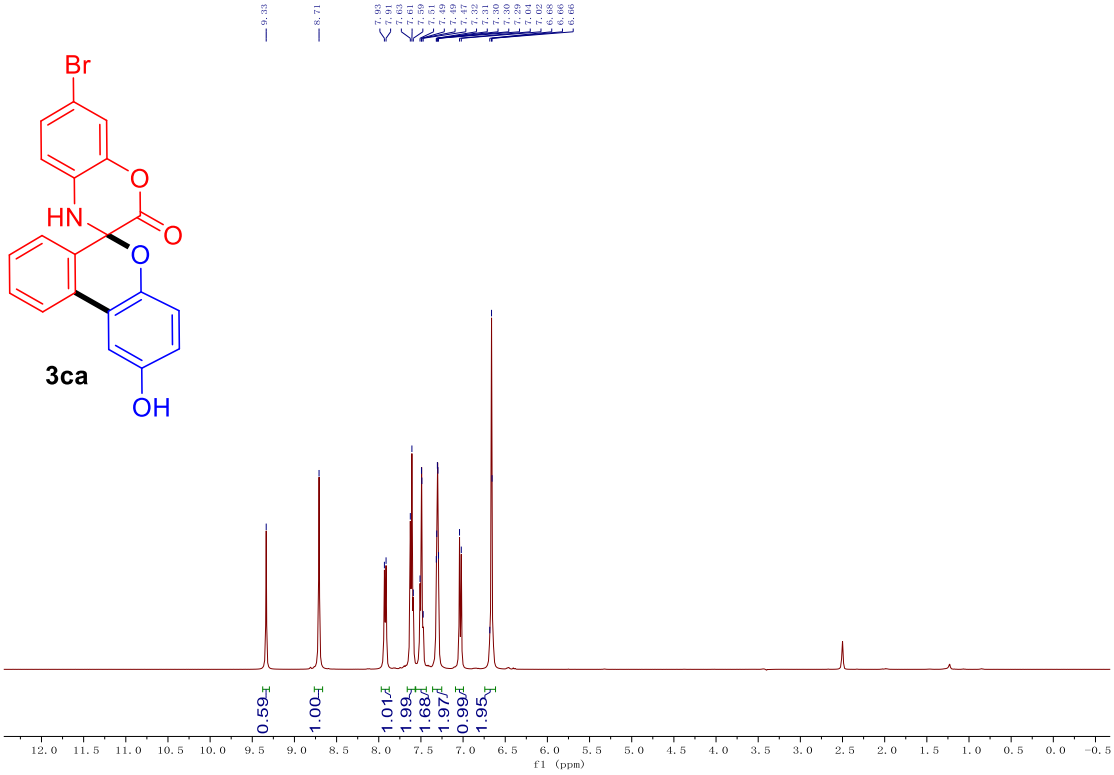


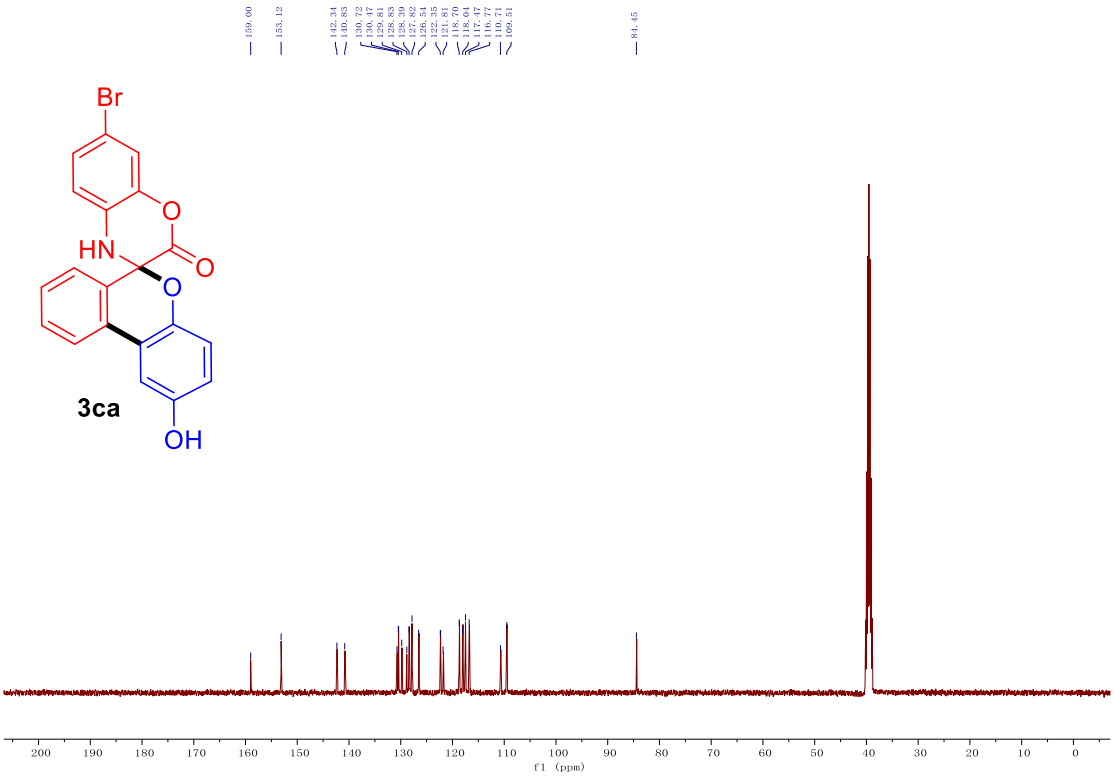
^{1}H and ^{13}C NMR Spectra of compound **3ba**



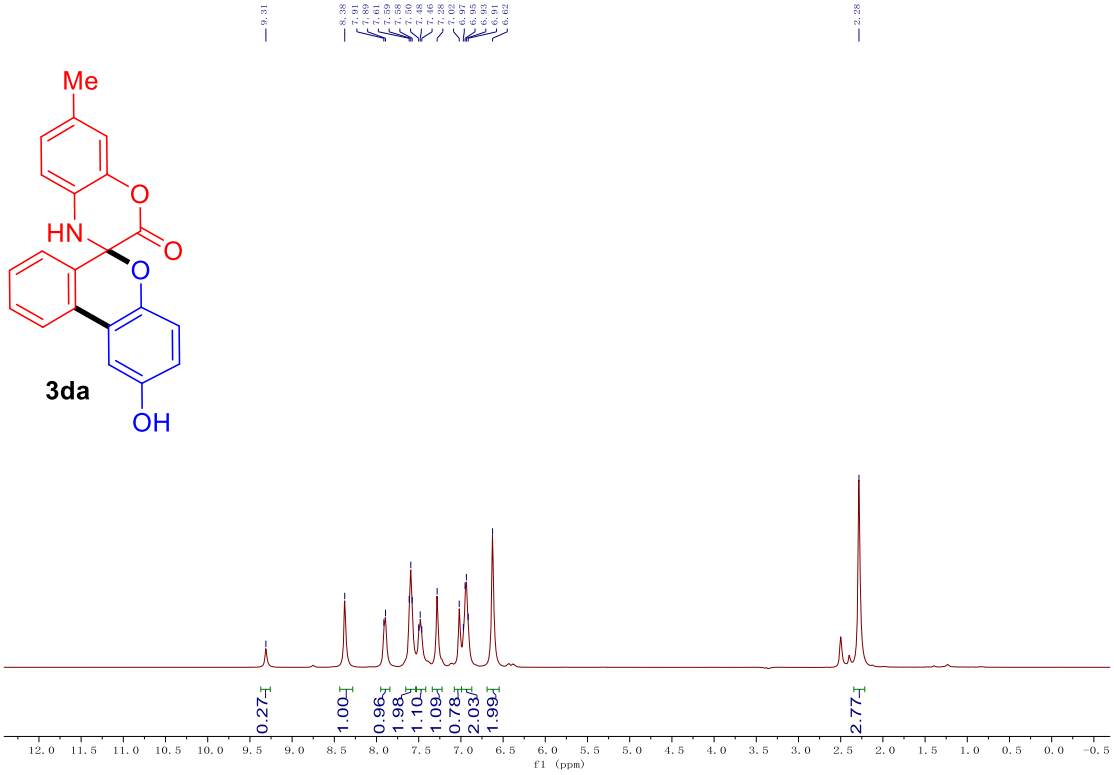


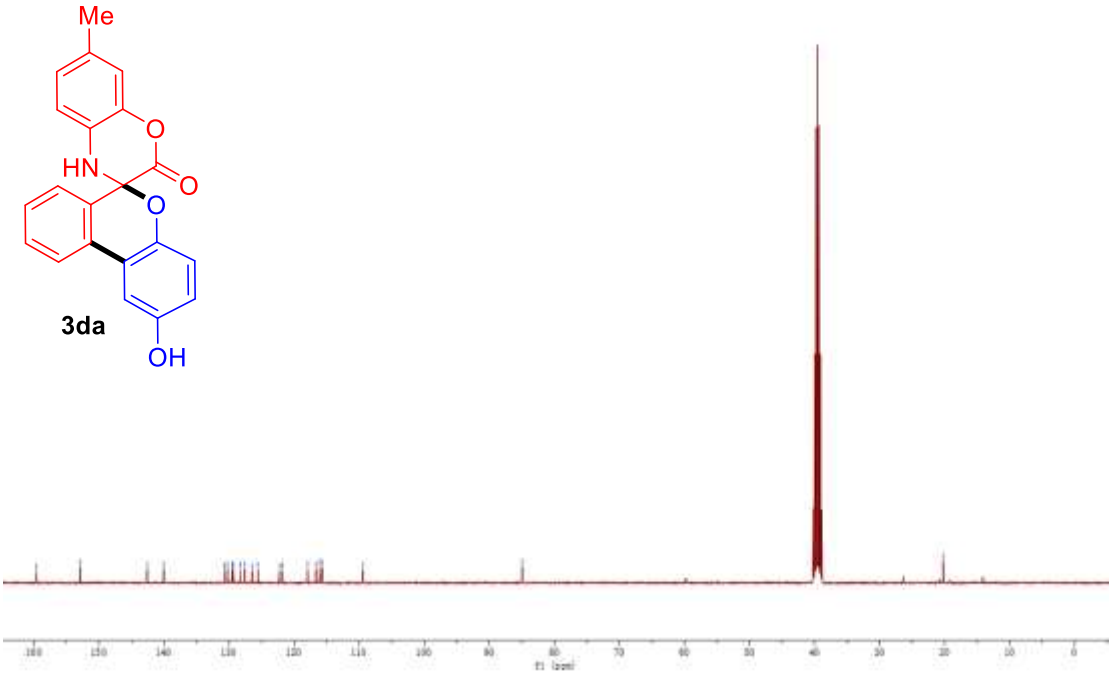
^{1}H and ^{13}C NMR Spectra of compound **3ca**



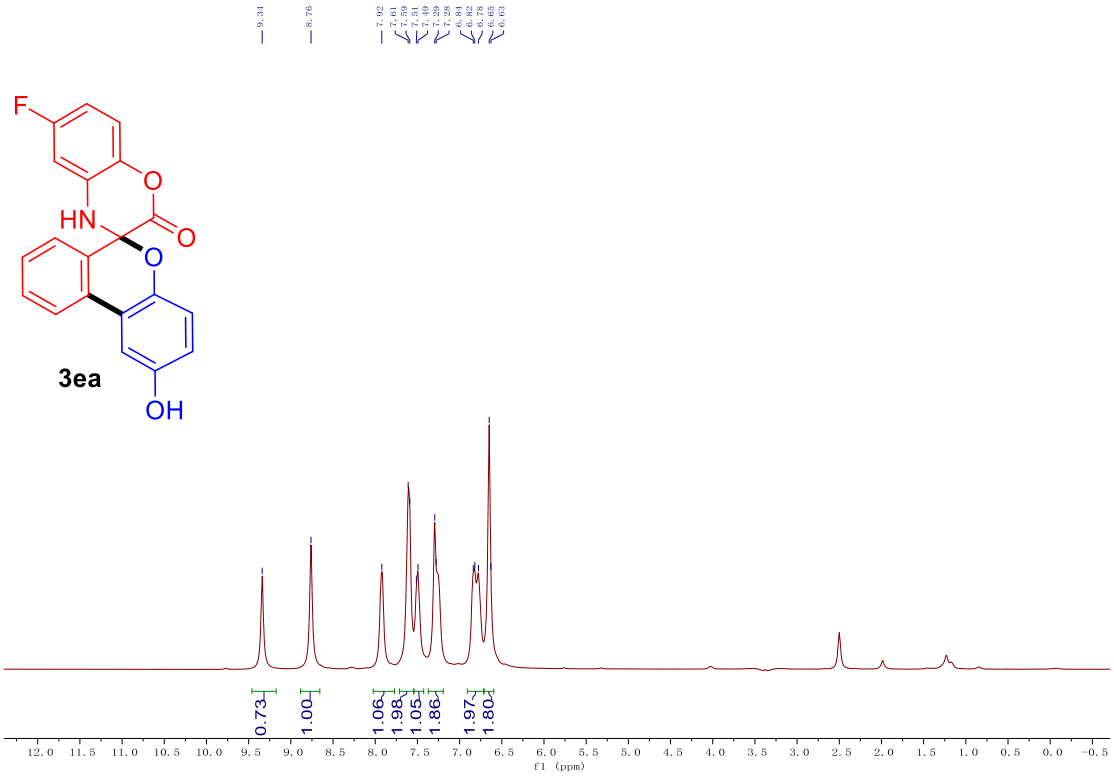


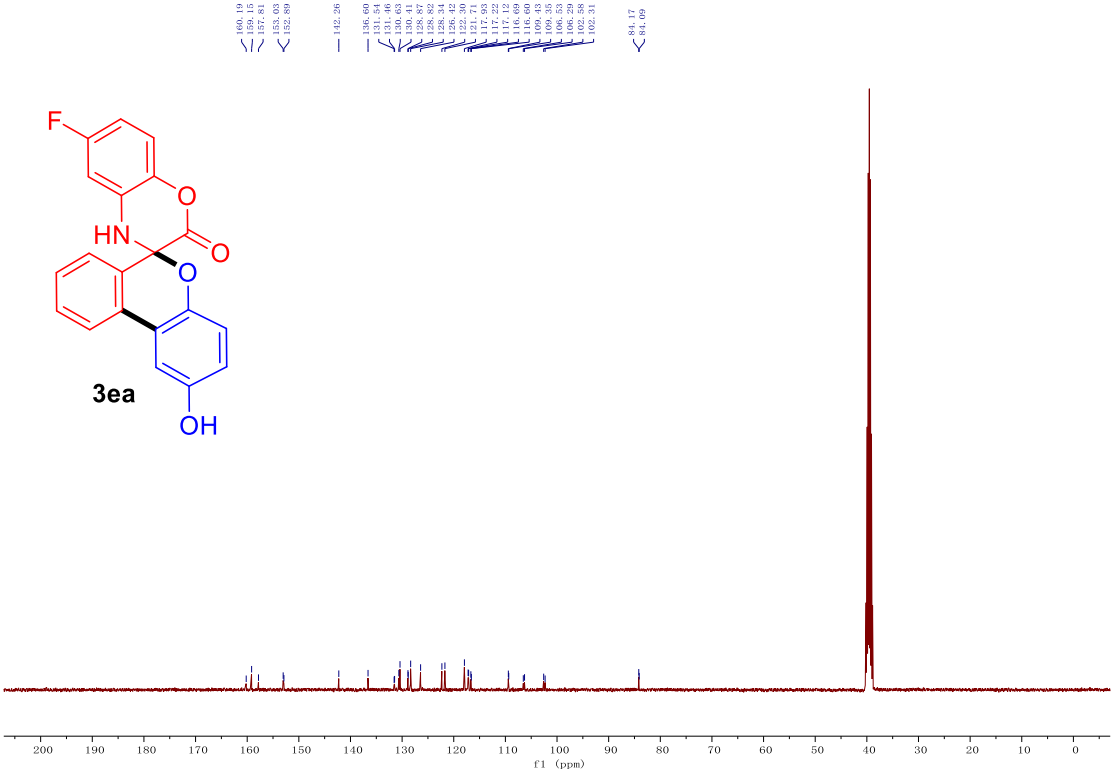
^{1}H and ^{13}C NMR Spectra of compound **3da**



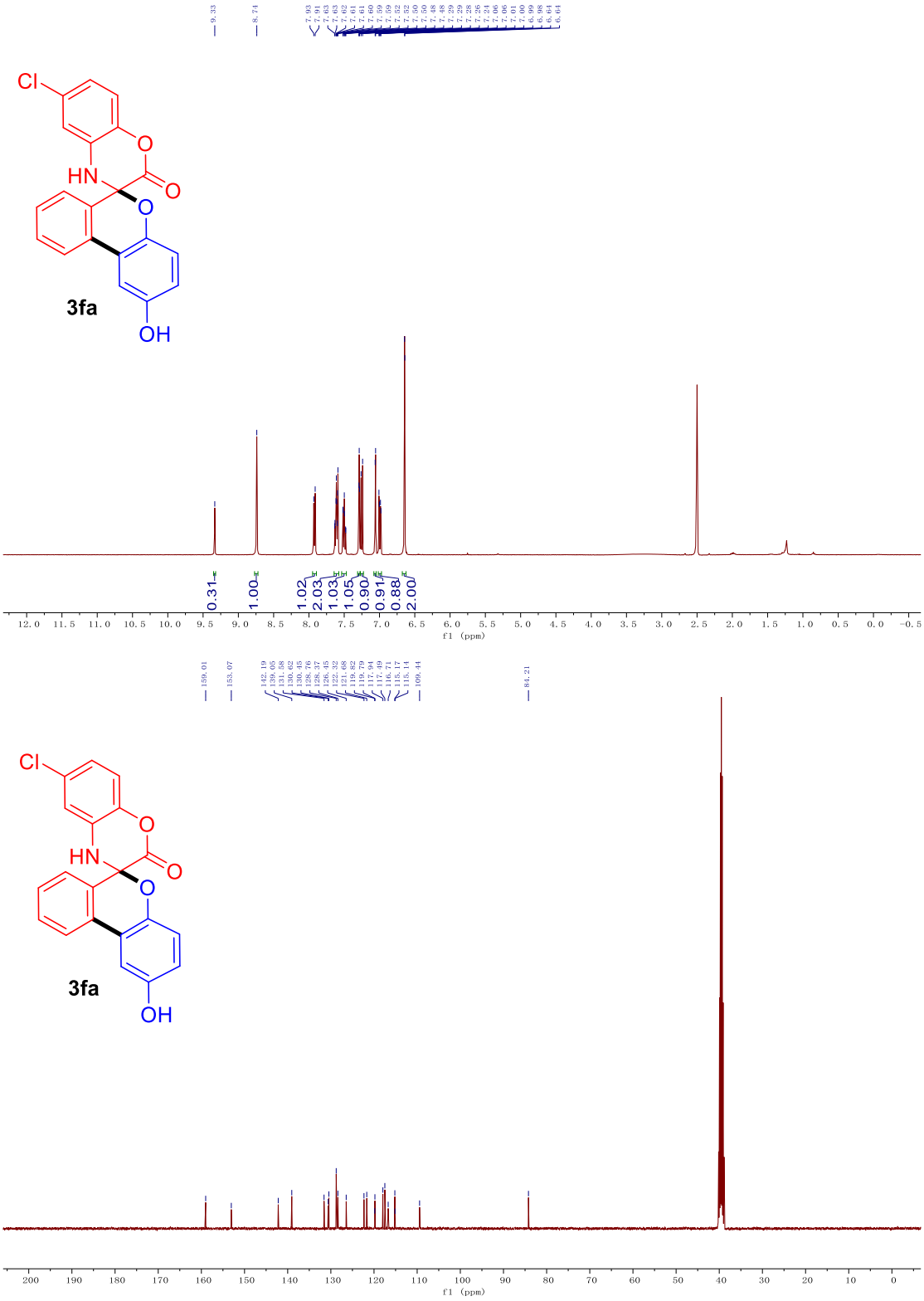


^{1}H and ^{13}C NMR Spectra of compound **3ea**

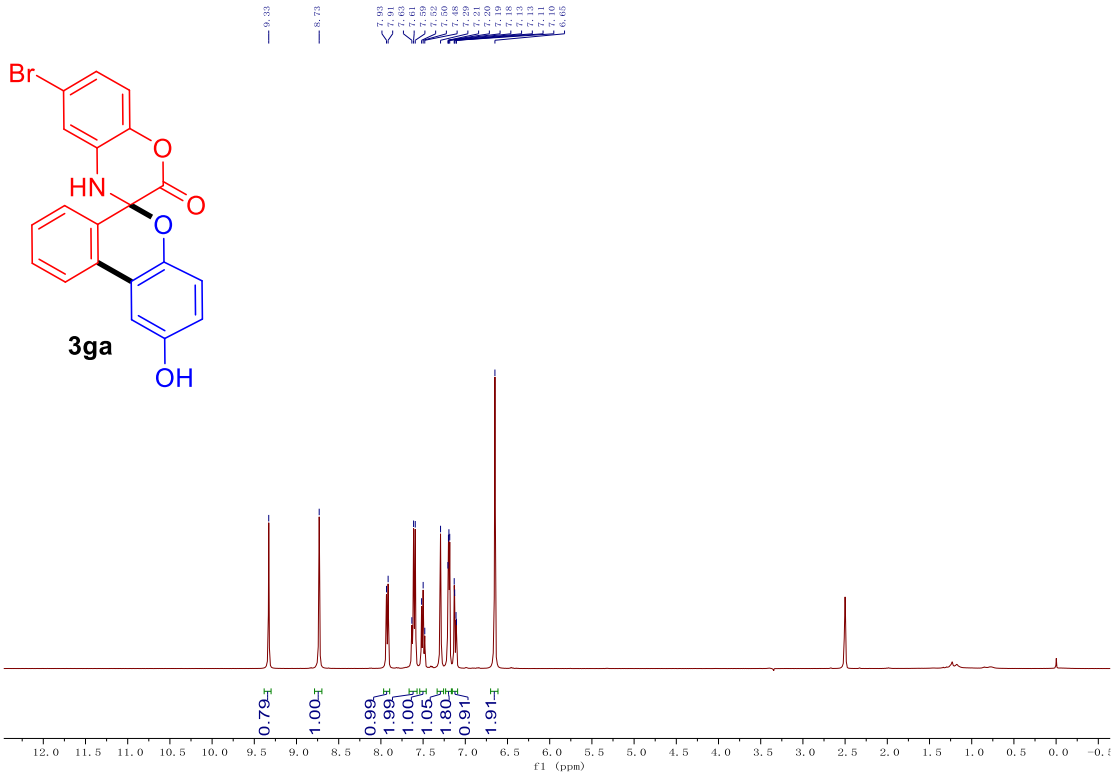


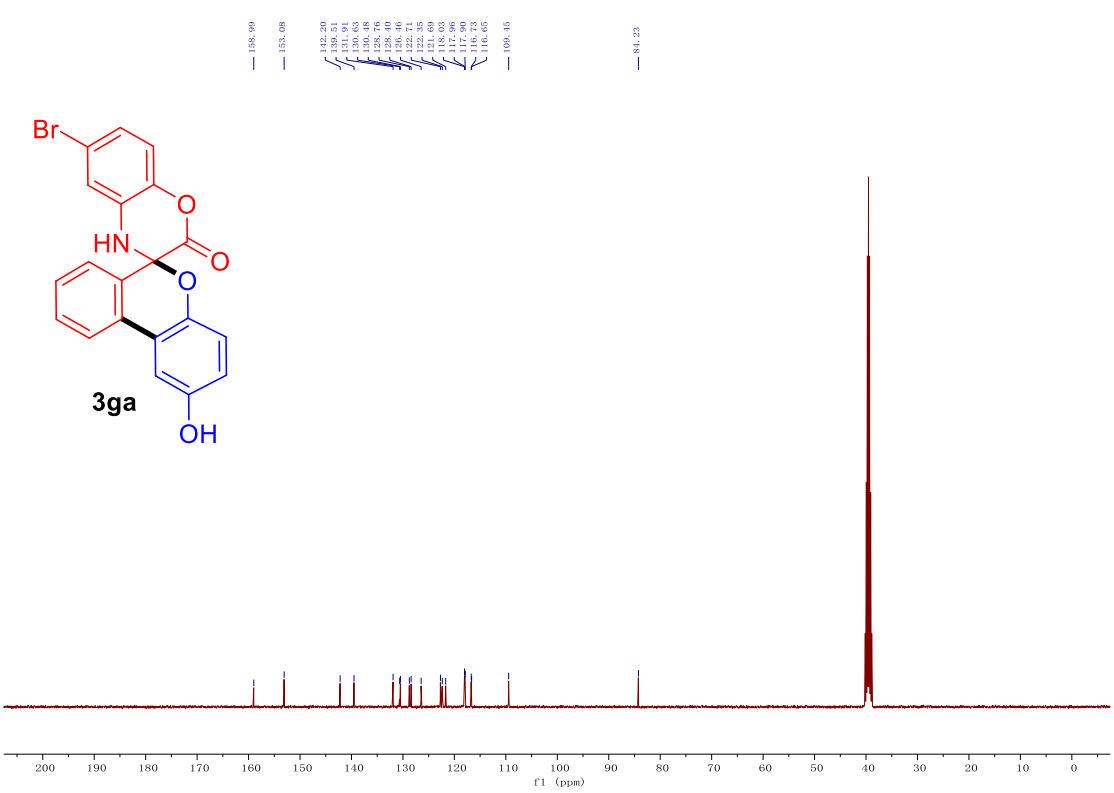


^{1}H and ^{13}C NMR Spectra of compound **3fa**

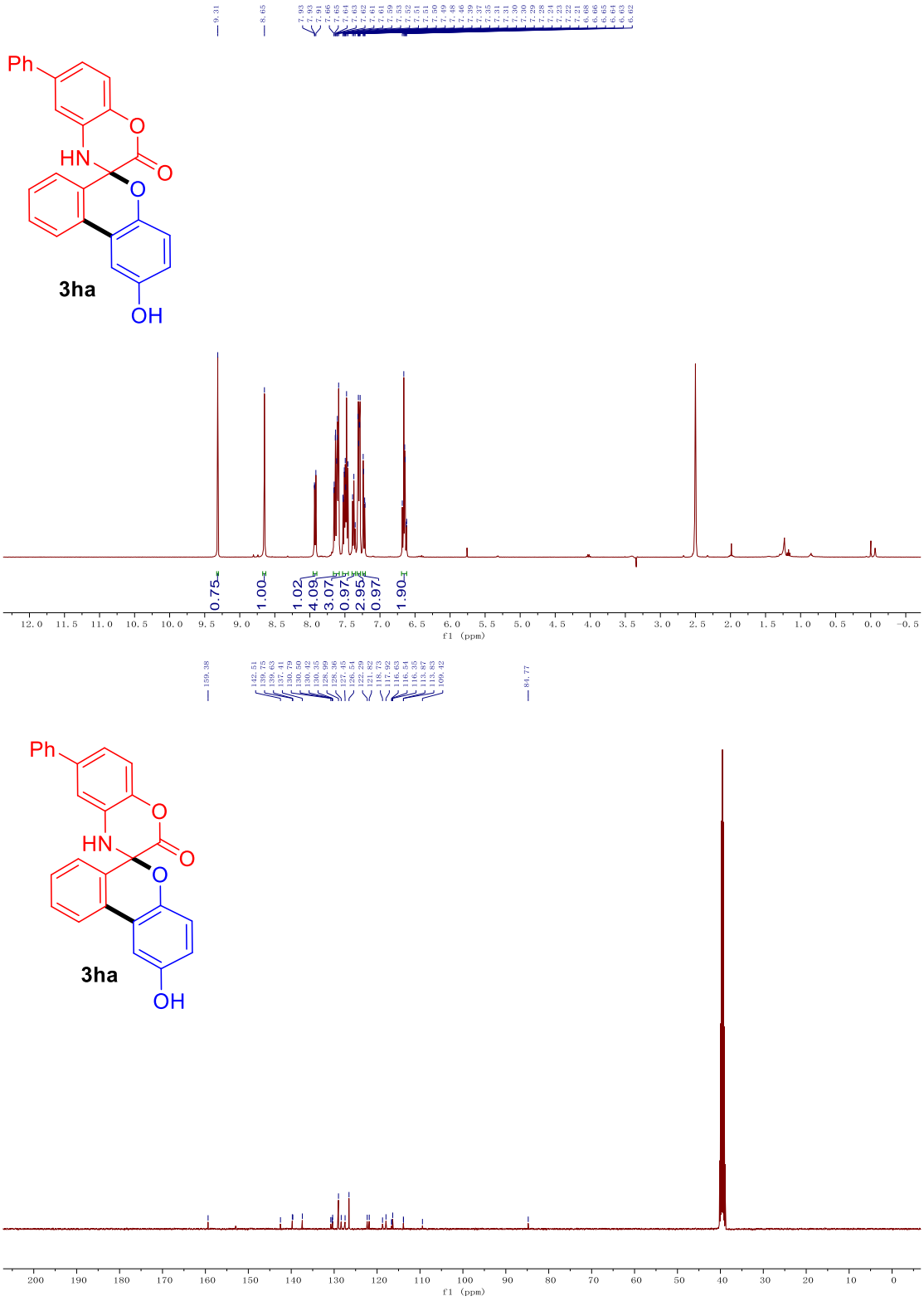


^{1}H and ^{13}C NMR Spectra of compound **3ga**

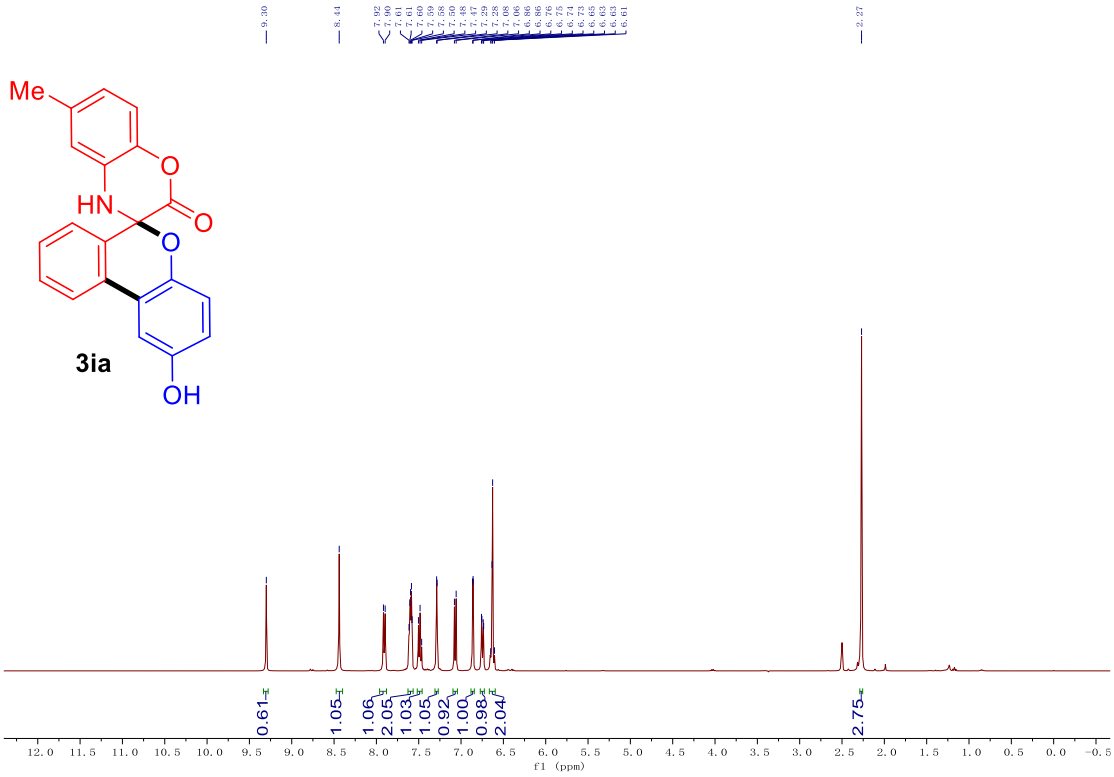


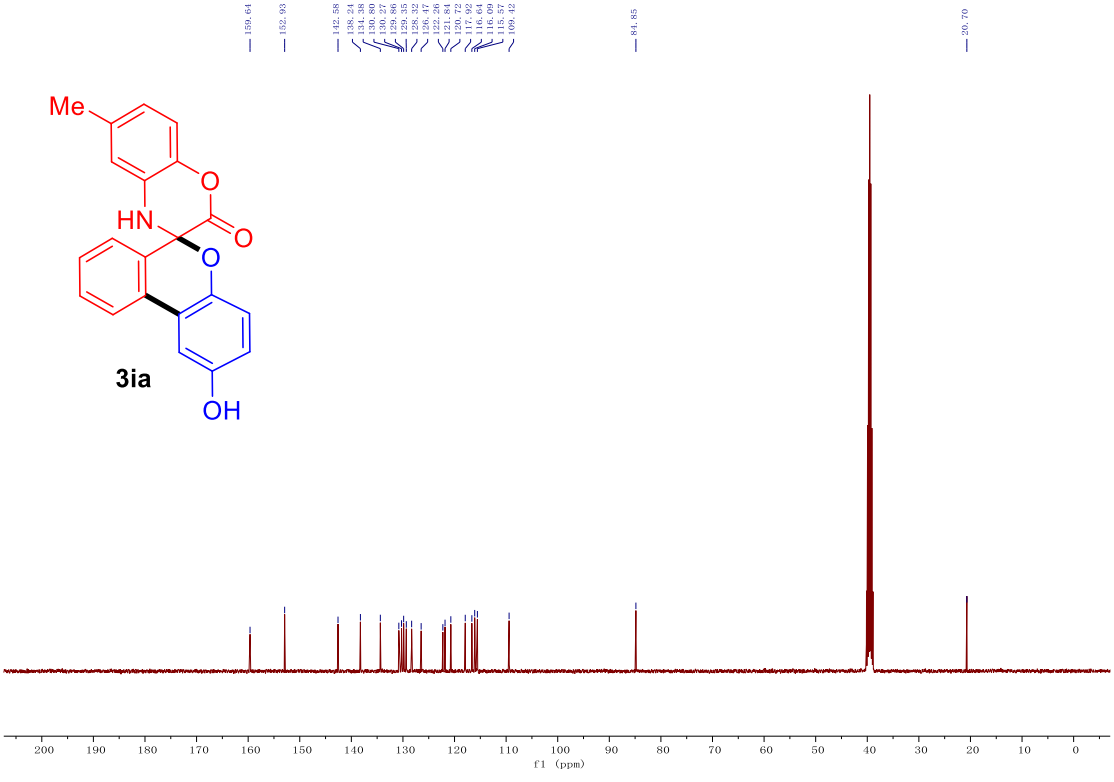


^{1}H and ^{13}C NMR Spectra of compound **3ha**

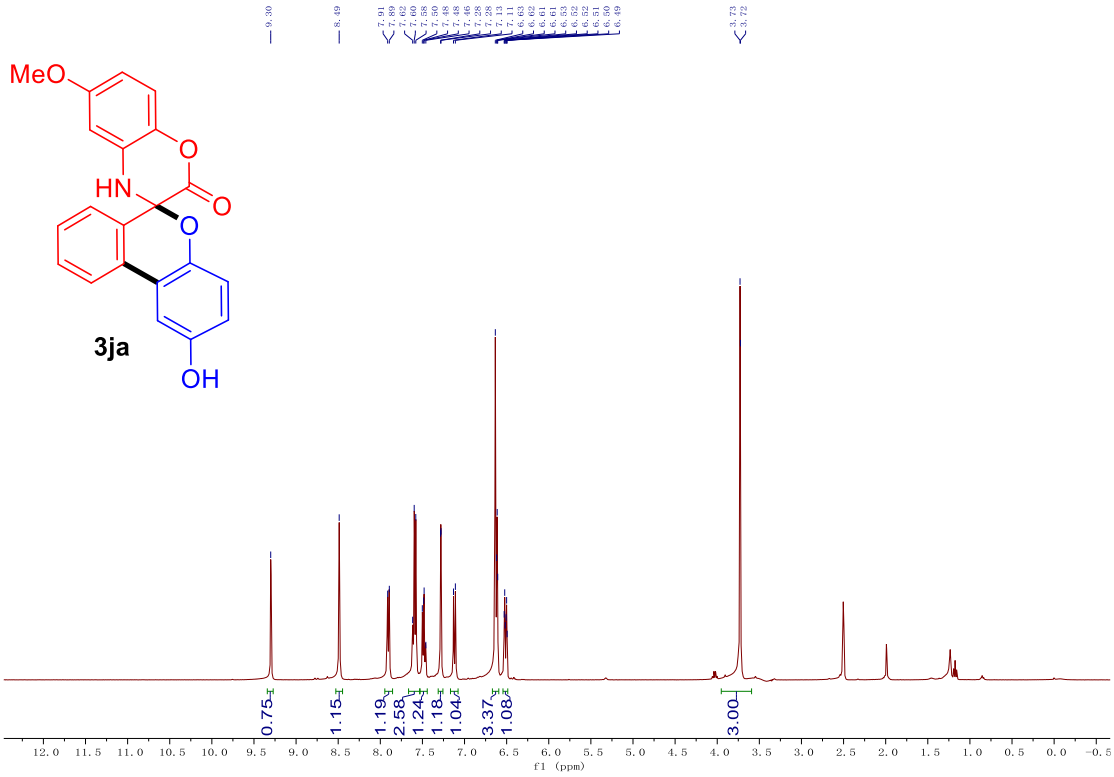


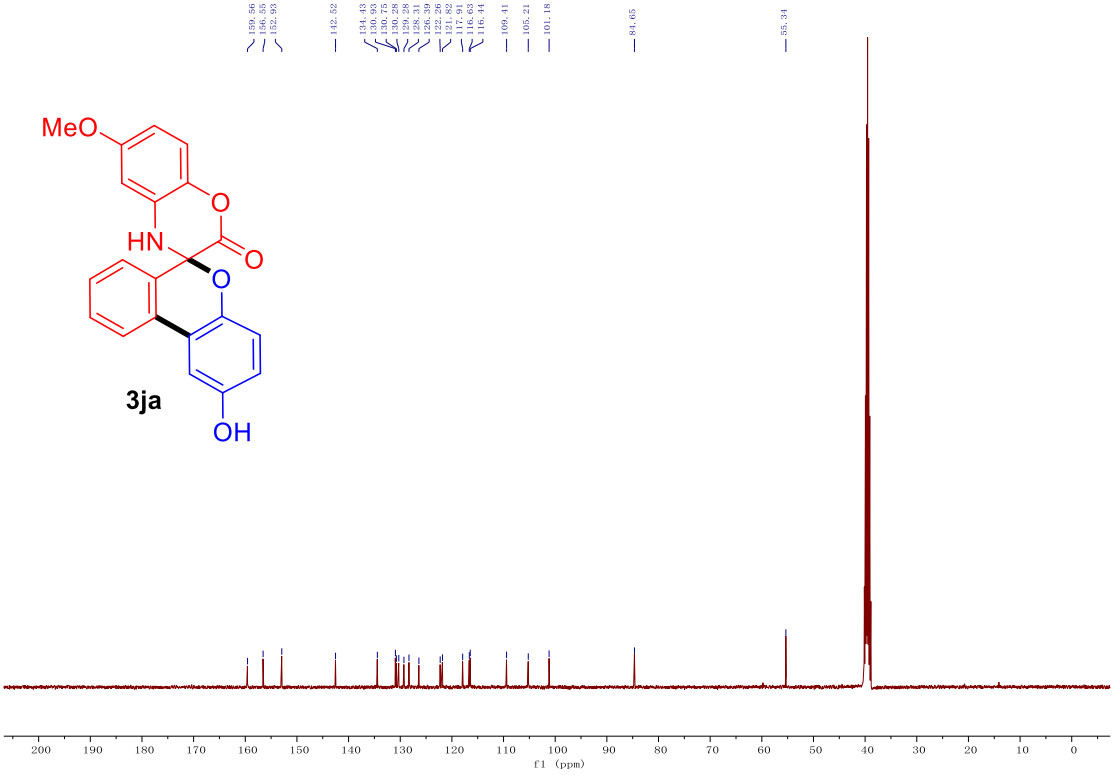
^{1}H and ^{13}C NMR Spectra of compound **3ia**



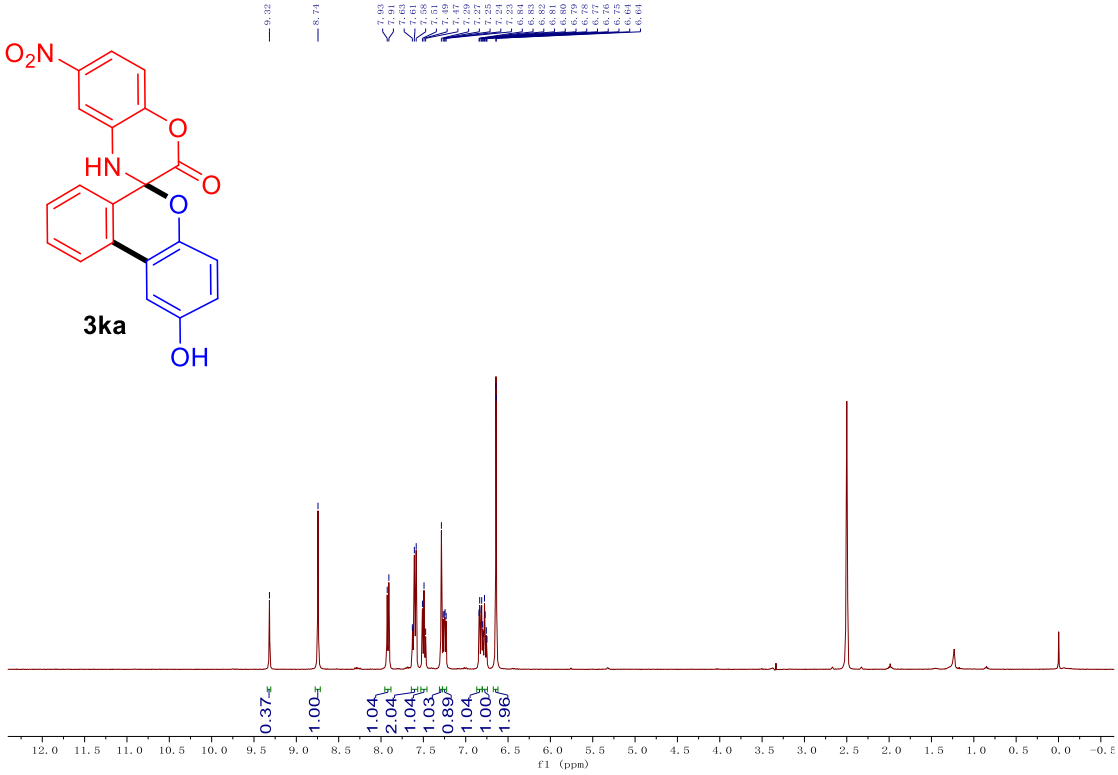


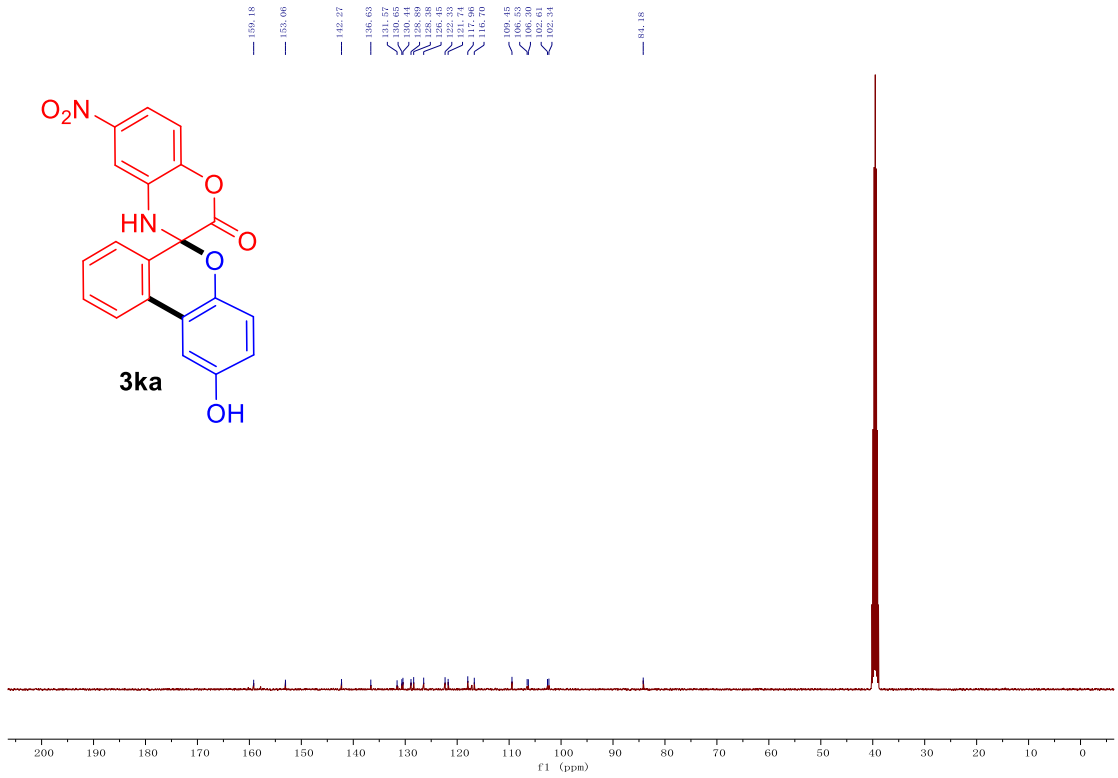
^{1}H and ^{13}C NMR Spectra of compound **3ja**



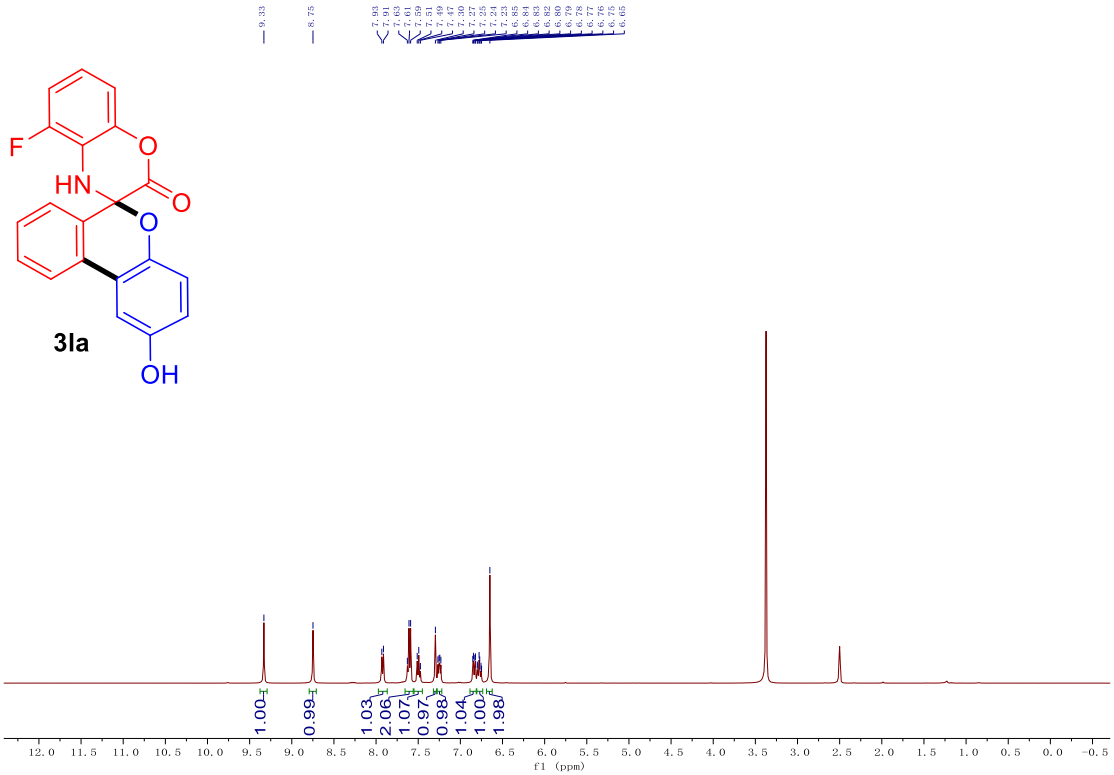


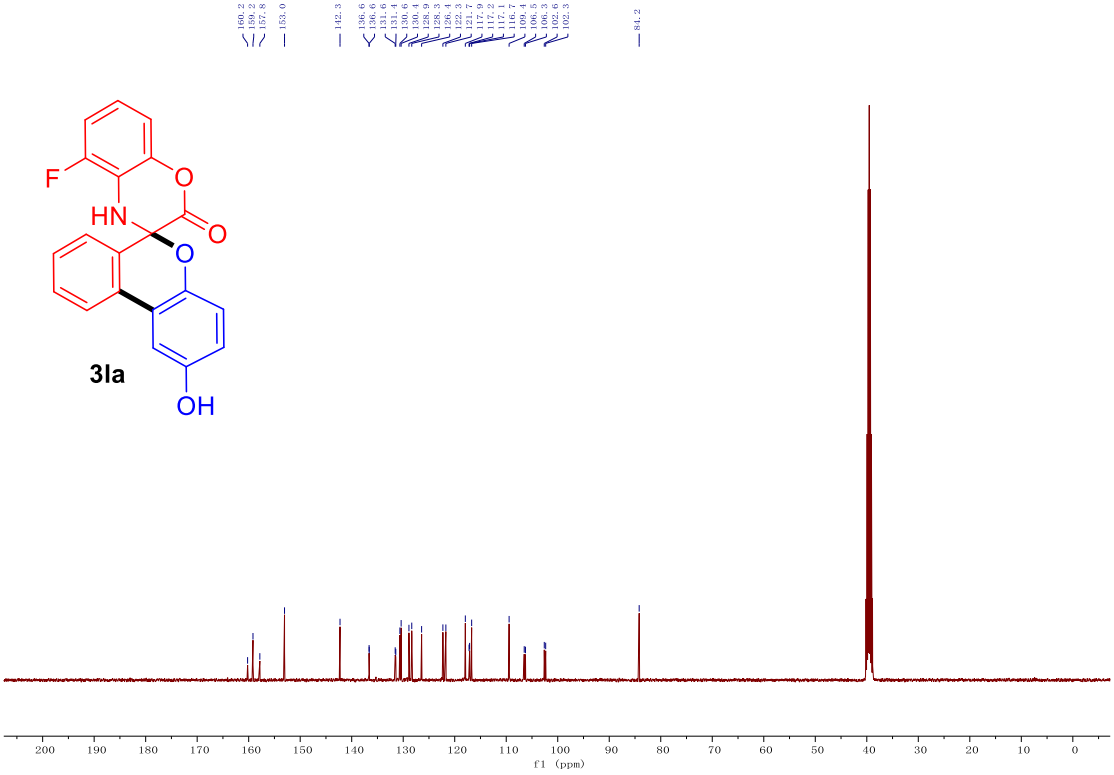
^{1}H and ^{13}C NMR Spectra of compound **3ka**



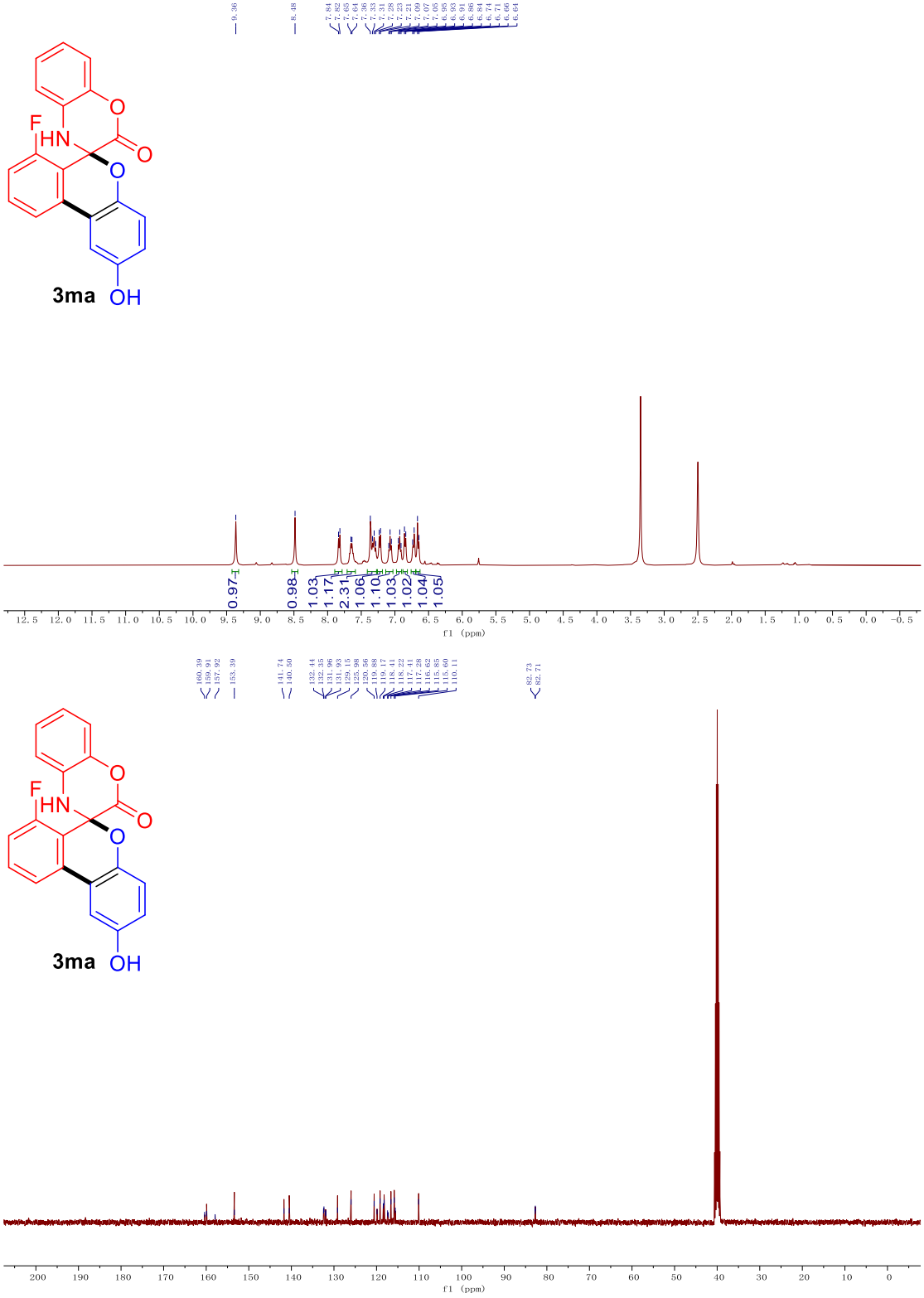


^{1}H and ^{13}C NMR Spectra of compound **3la**

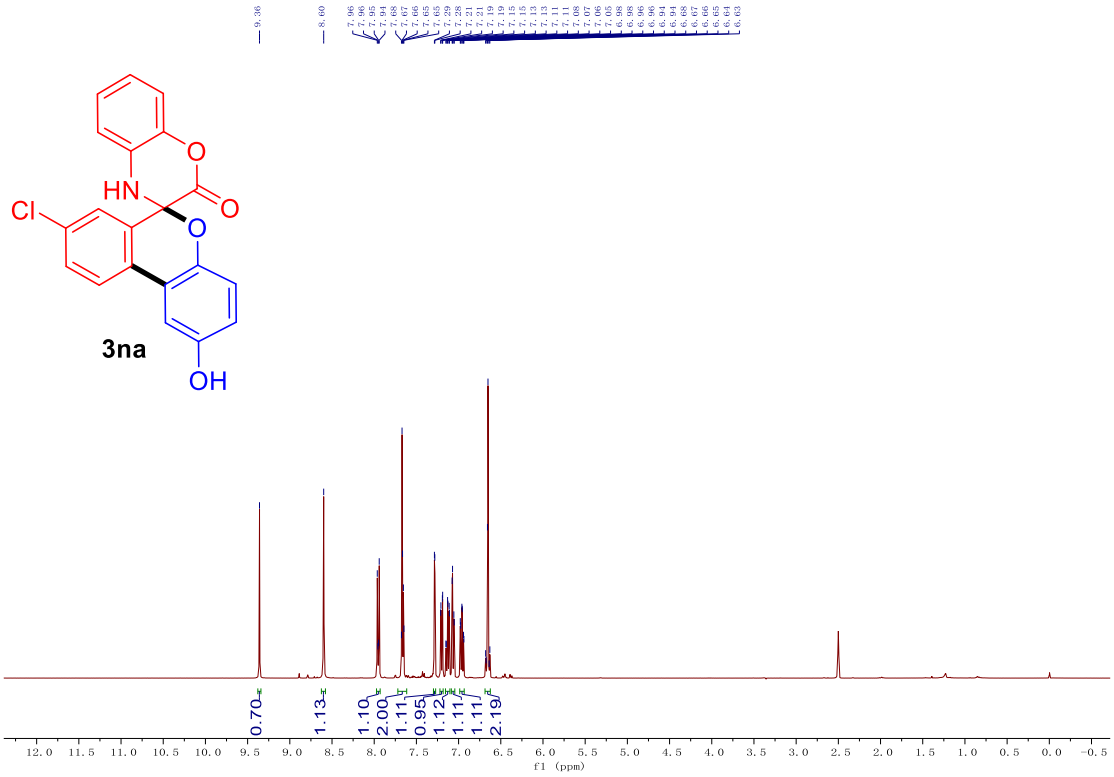


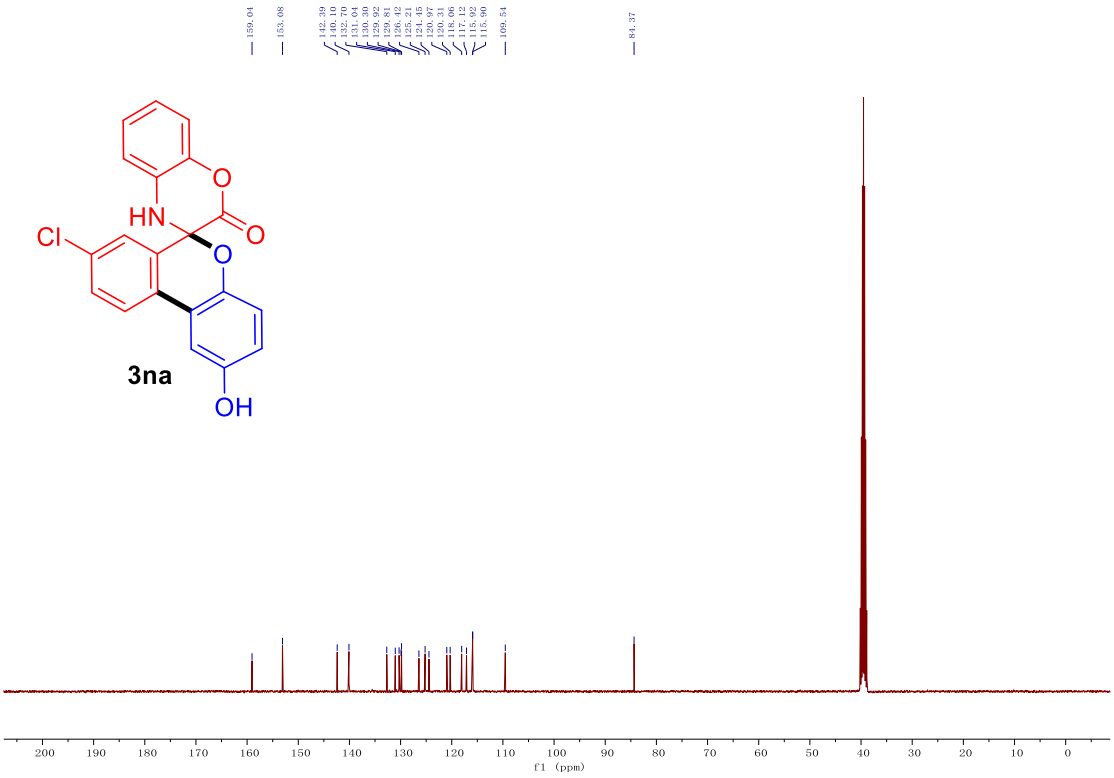


^{1}H and ^{13}C NMR Spectra of compound **3ma**

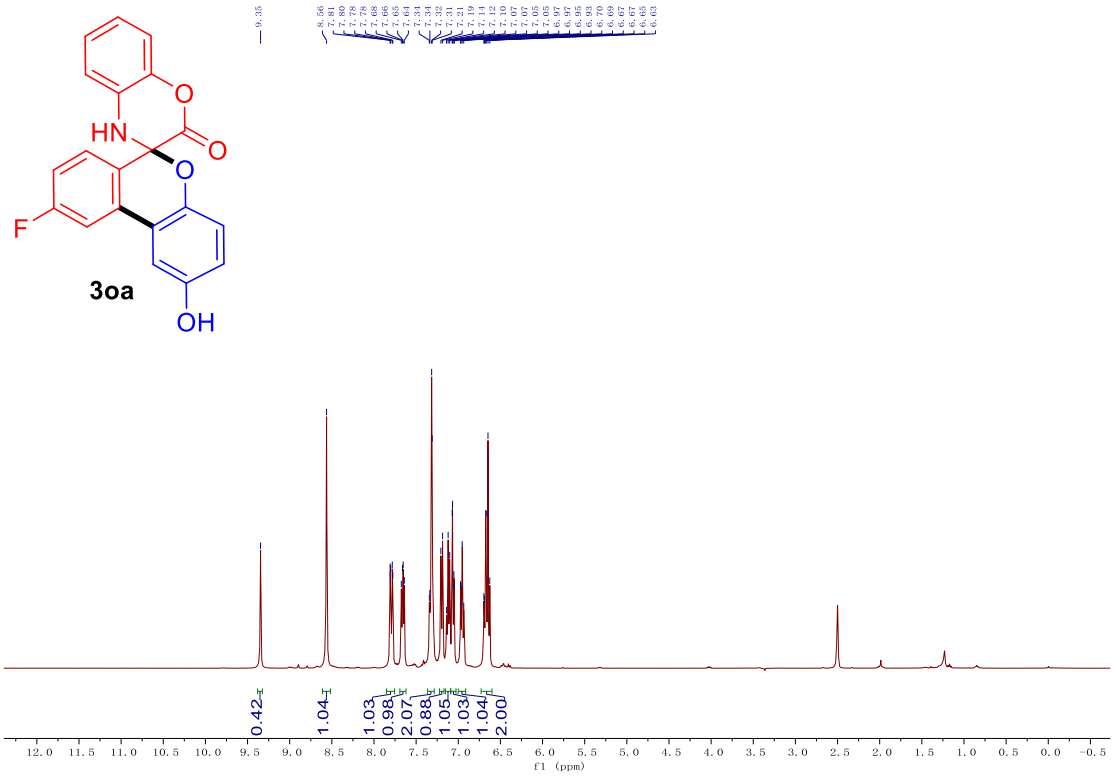


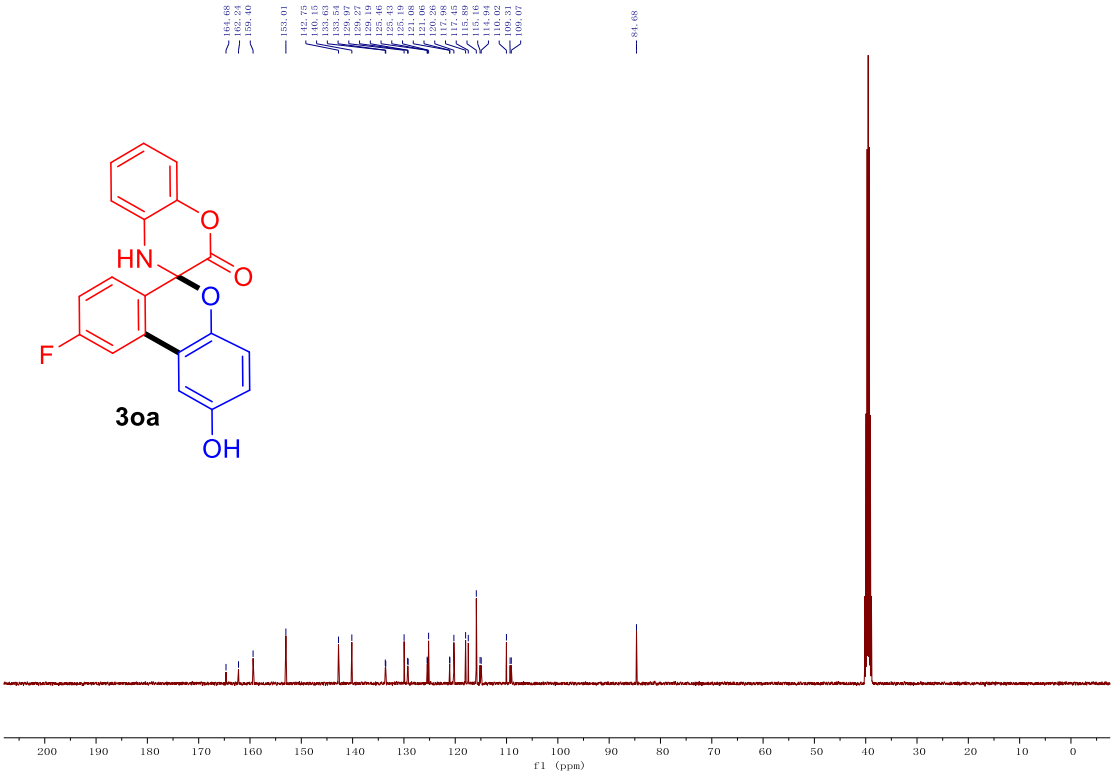
^{1}H and ^{13}C NMR Spectra of compound **3na**



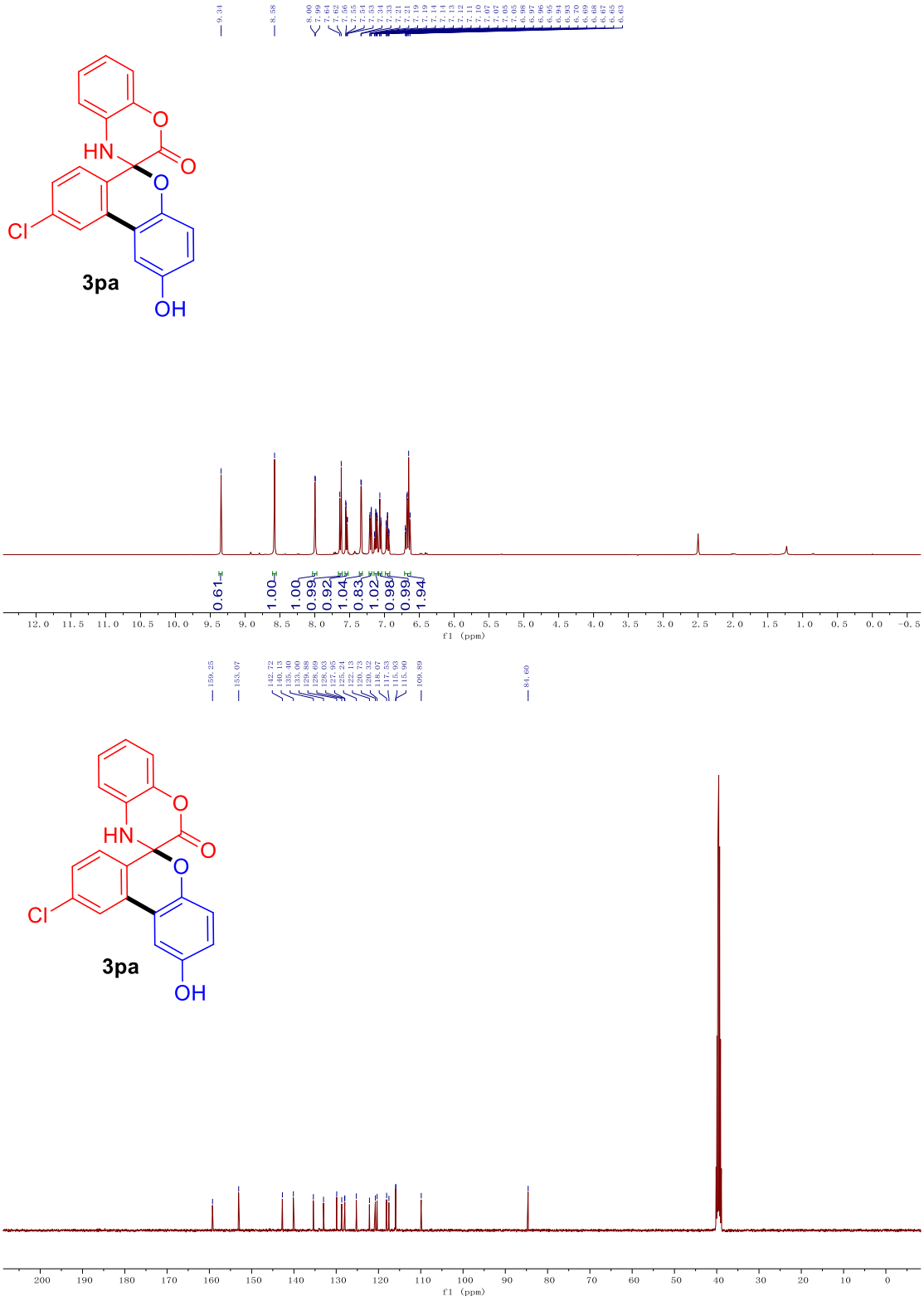


^{1}H and ^{13}C NMR Spectra of compound **3oa**

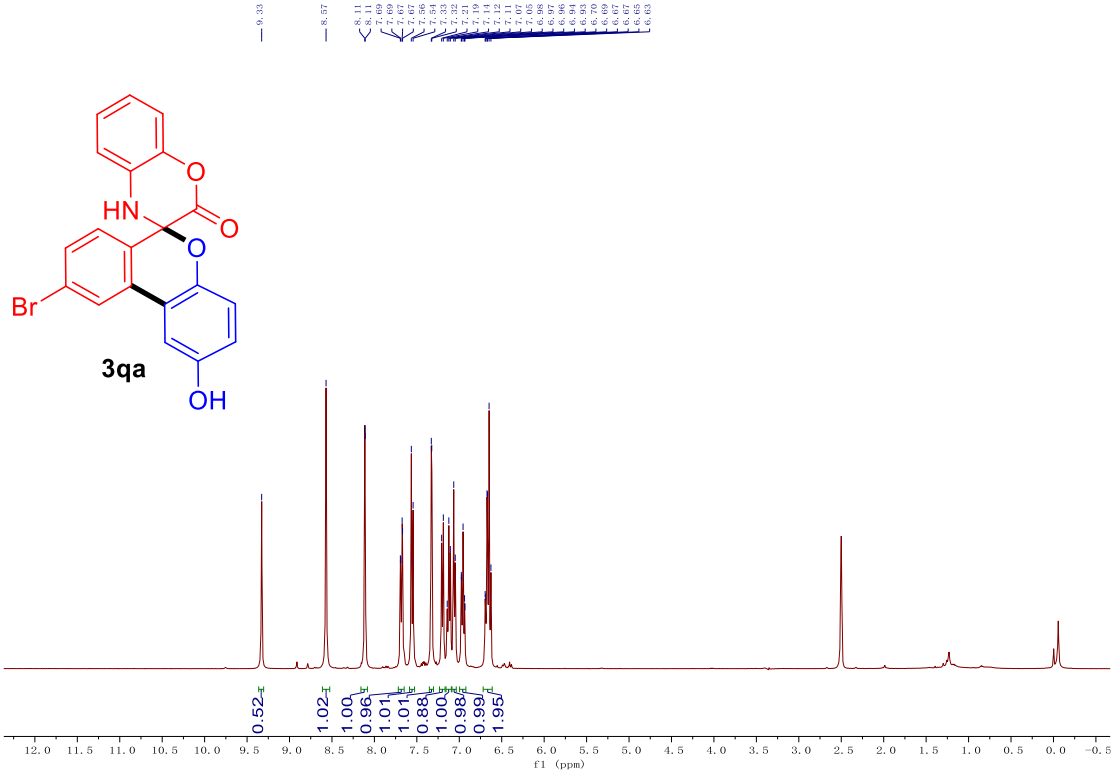


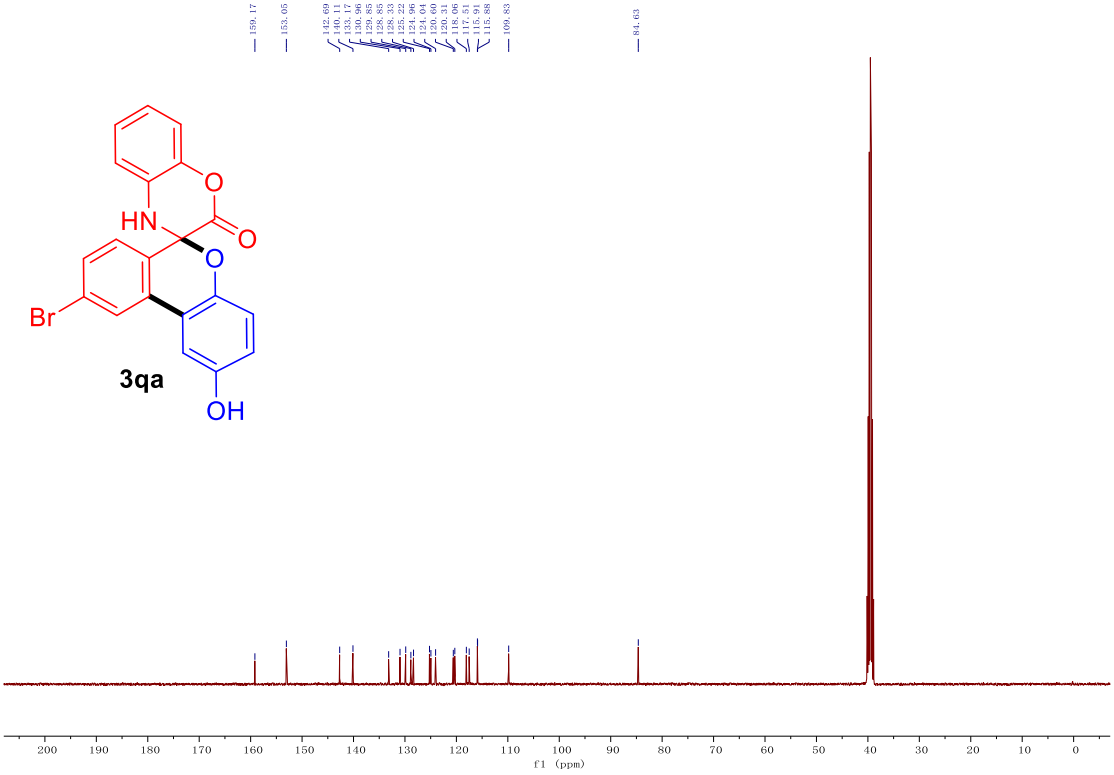


^{1}H and ^{13}C NMR Spectra of compound **3pa**

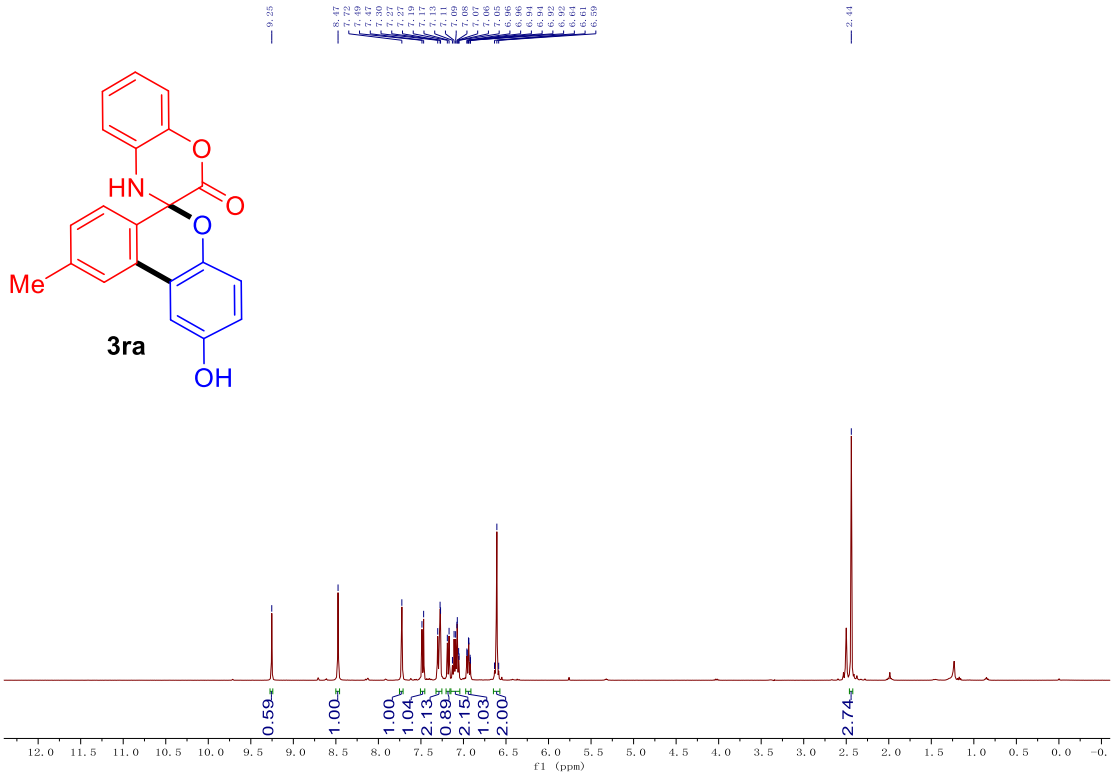


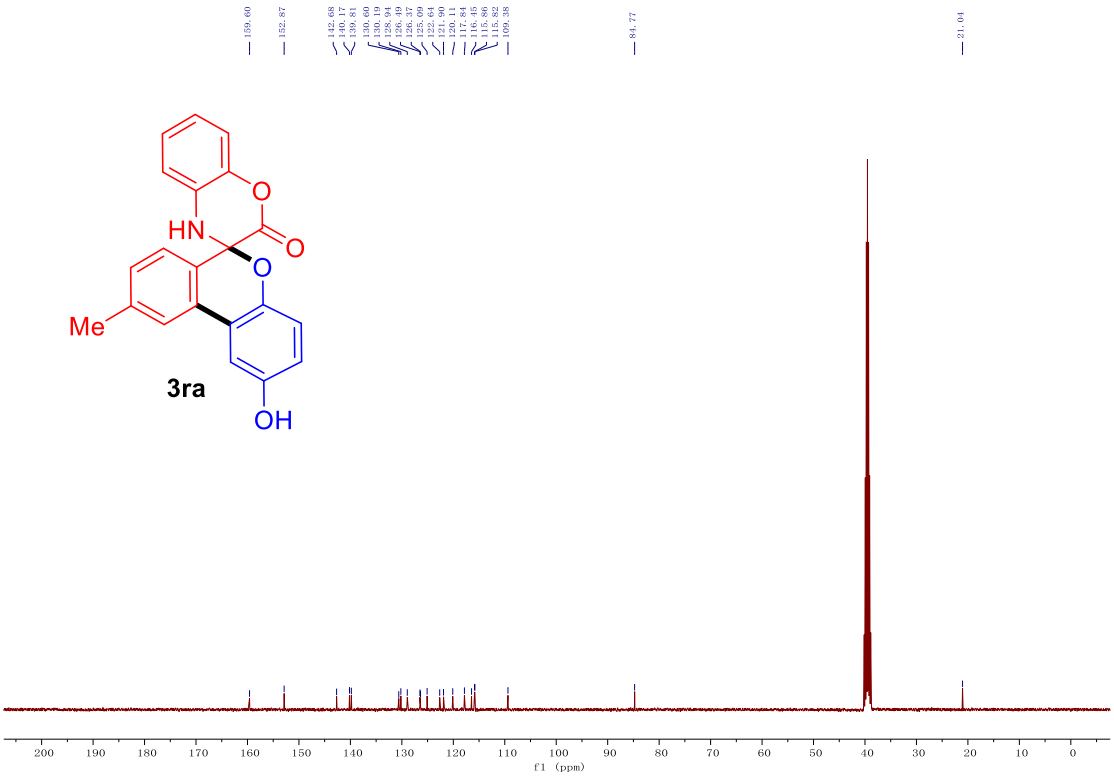
^{1}H and ^{13}C NMR Spectra of compound **3qa**



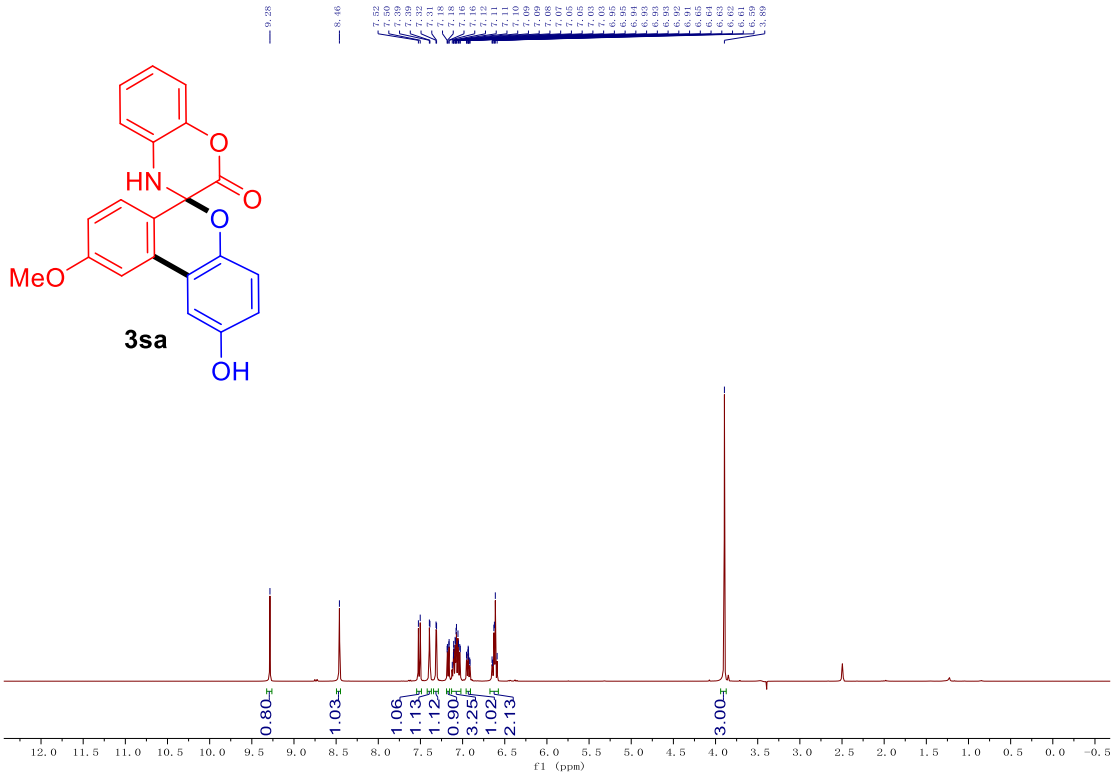


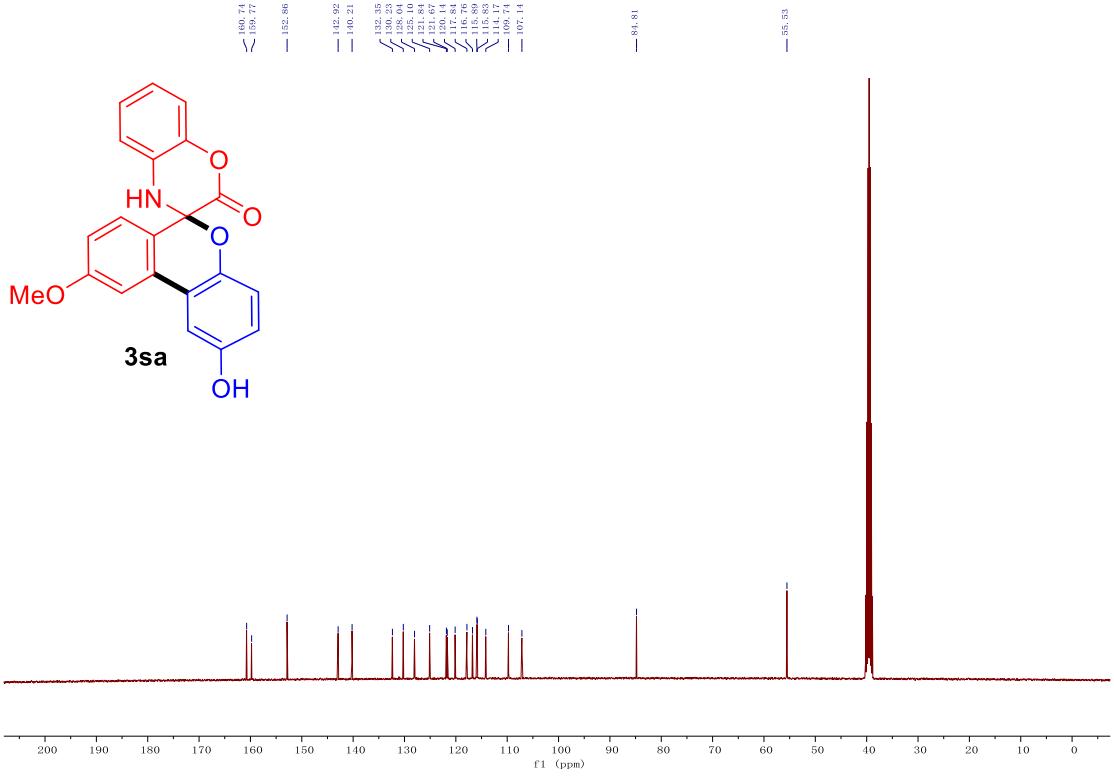
^{1}H and ^{13}C NMR Spectra of compound **3ra**



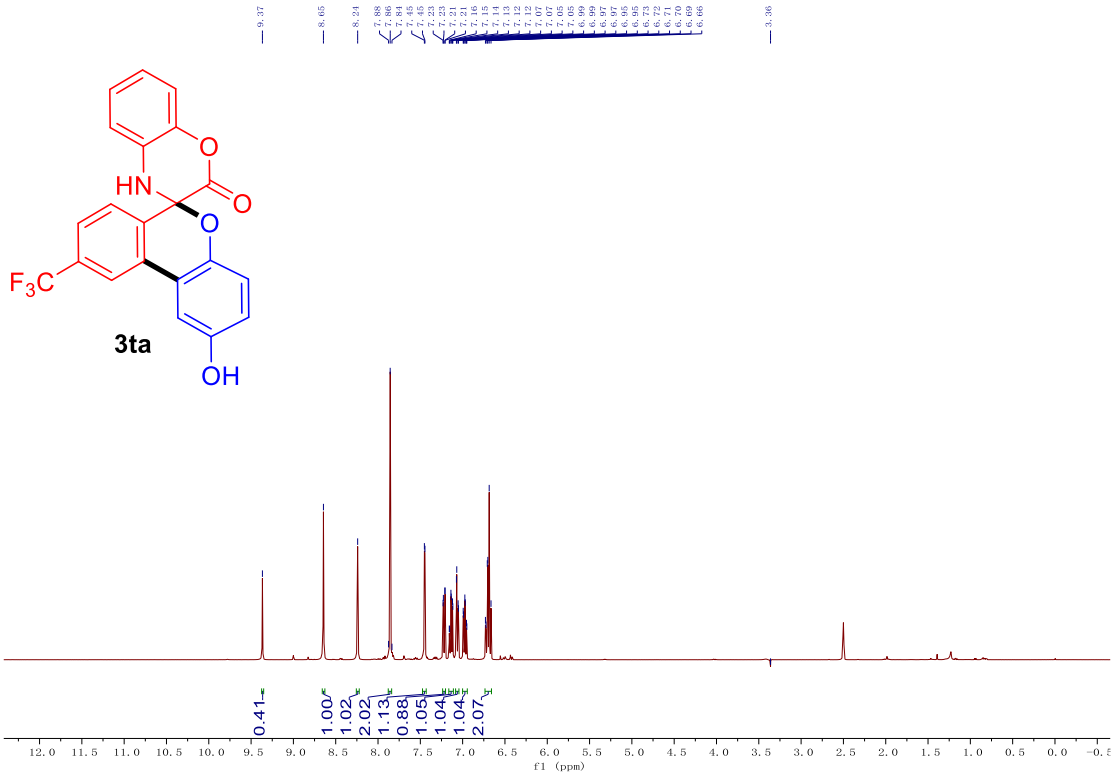


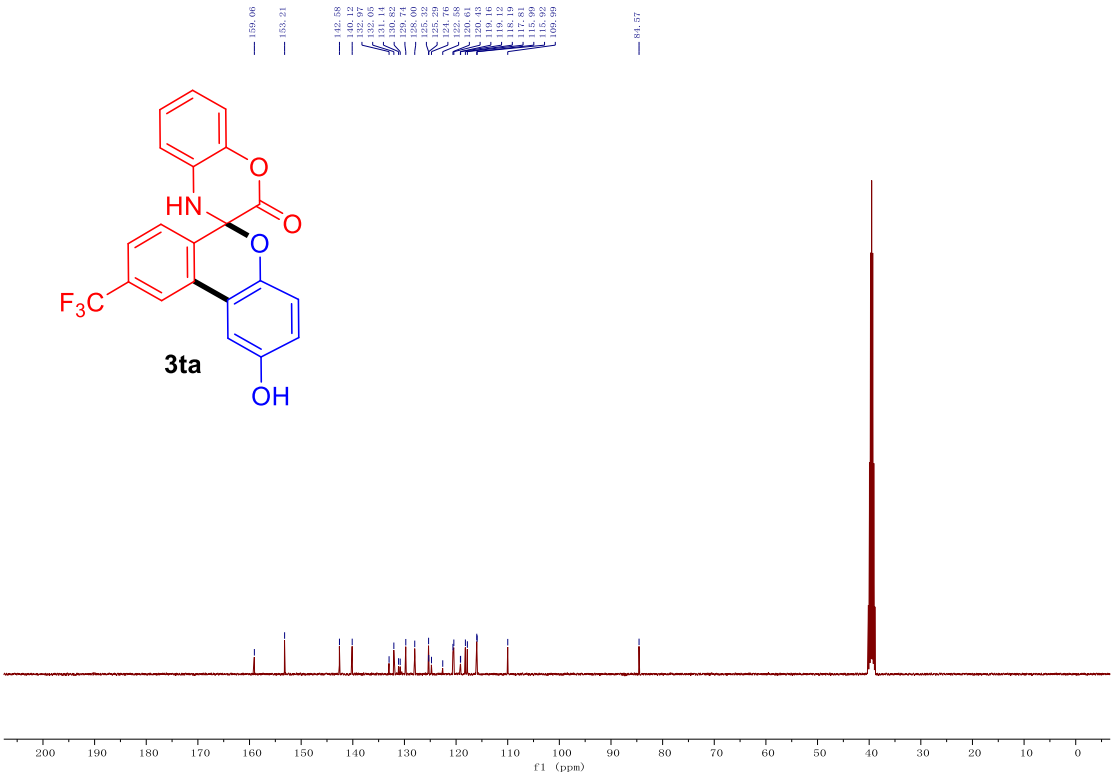
^{1}H and ^{13}C NMR Spectra of compound **3sa**



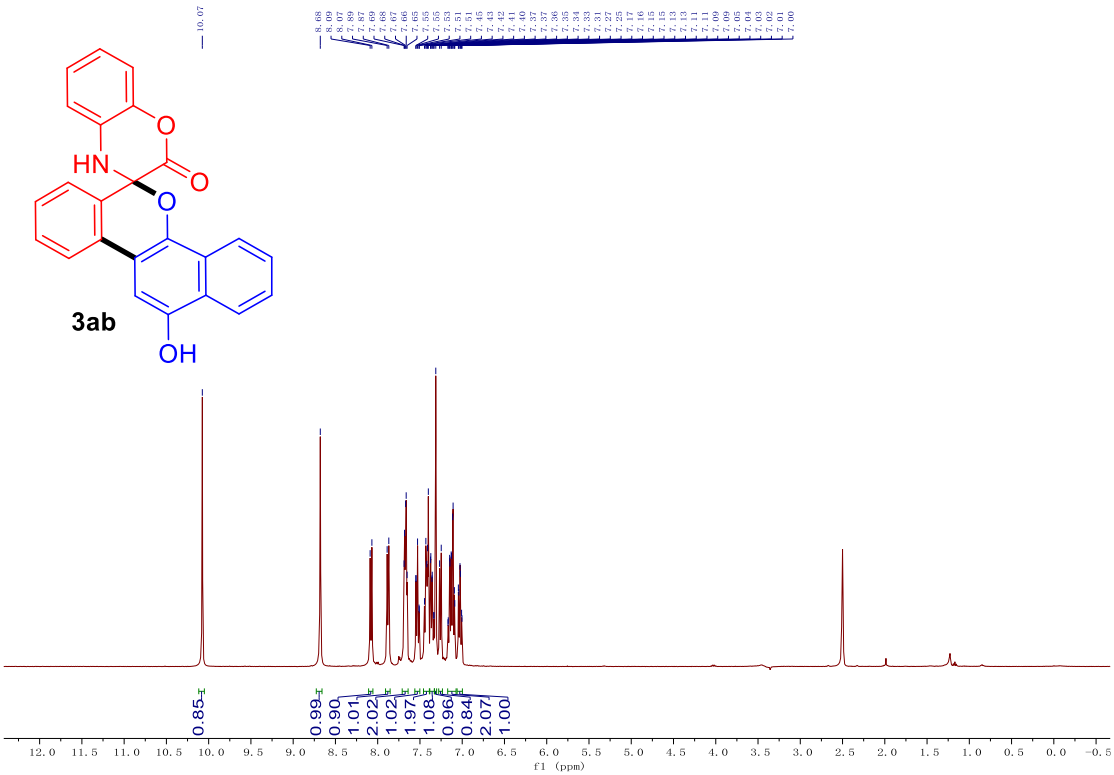


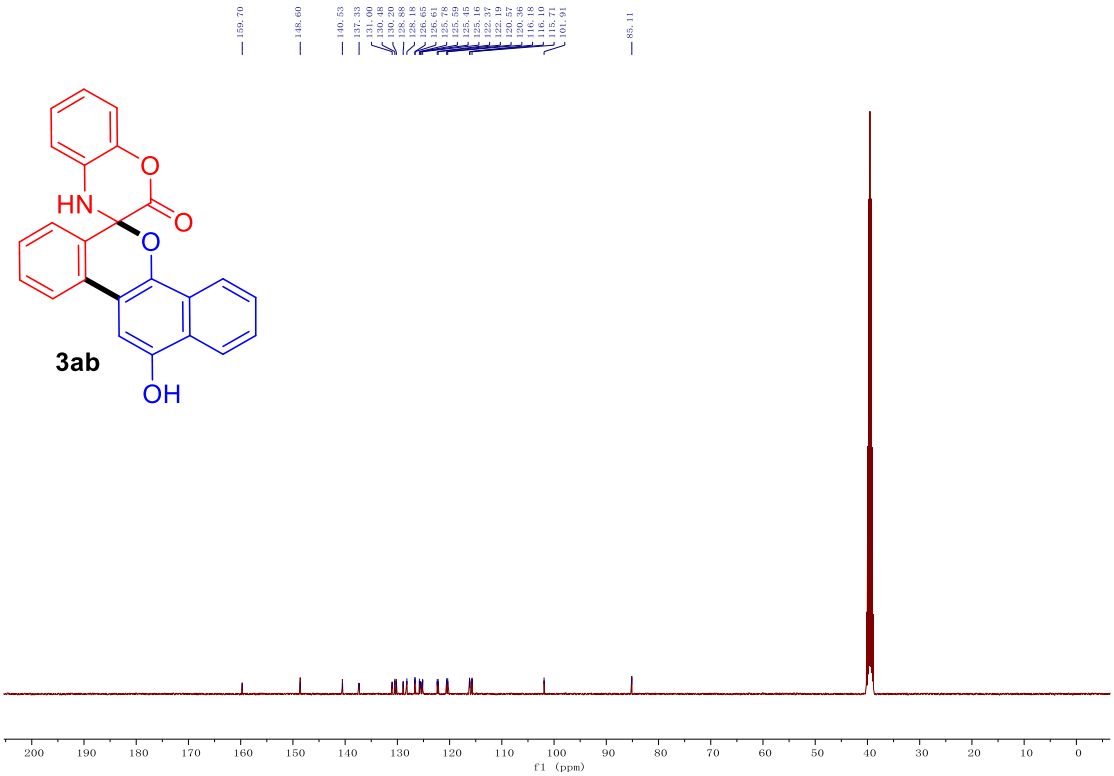
^{1}H and ^{13}C NMR Spectra of compound **3ta**



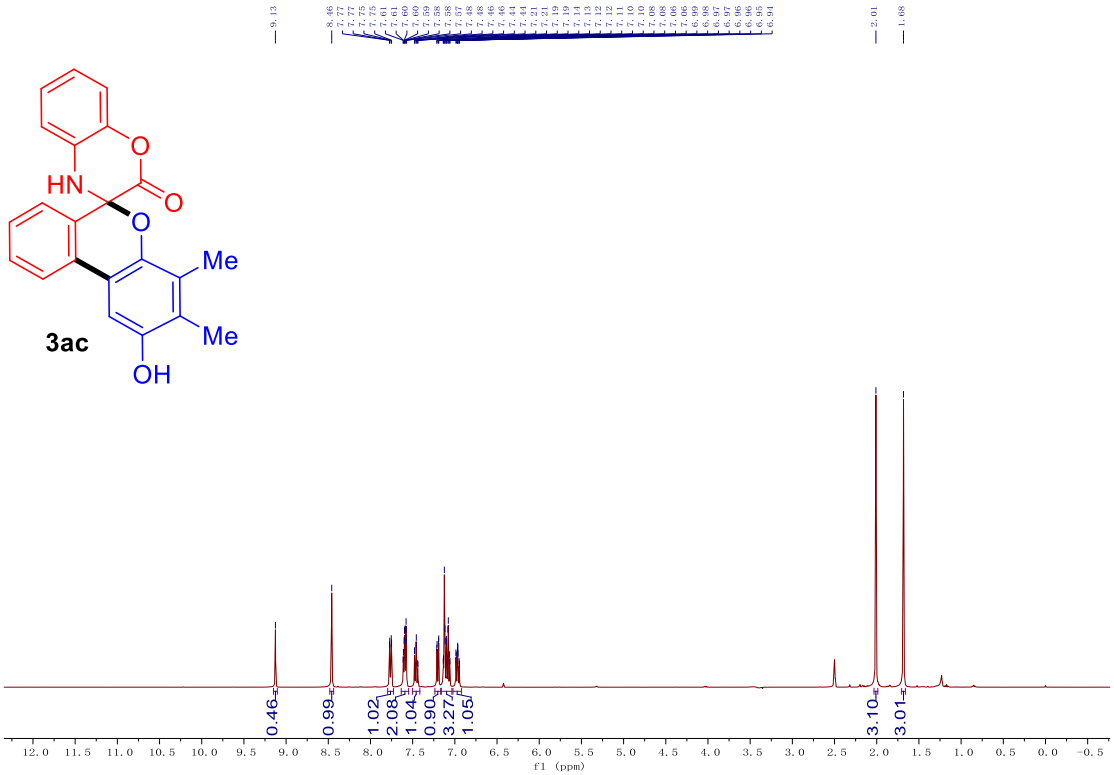


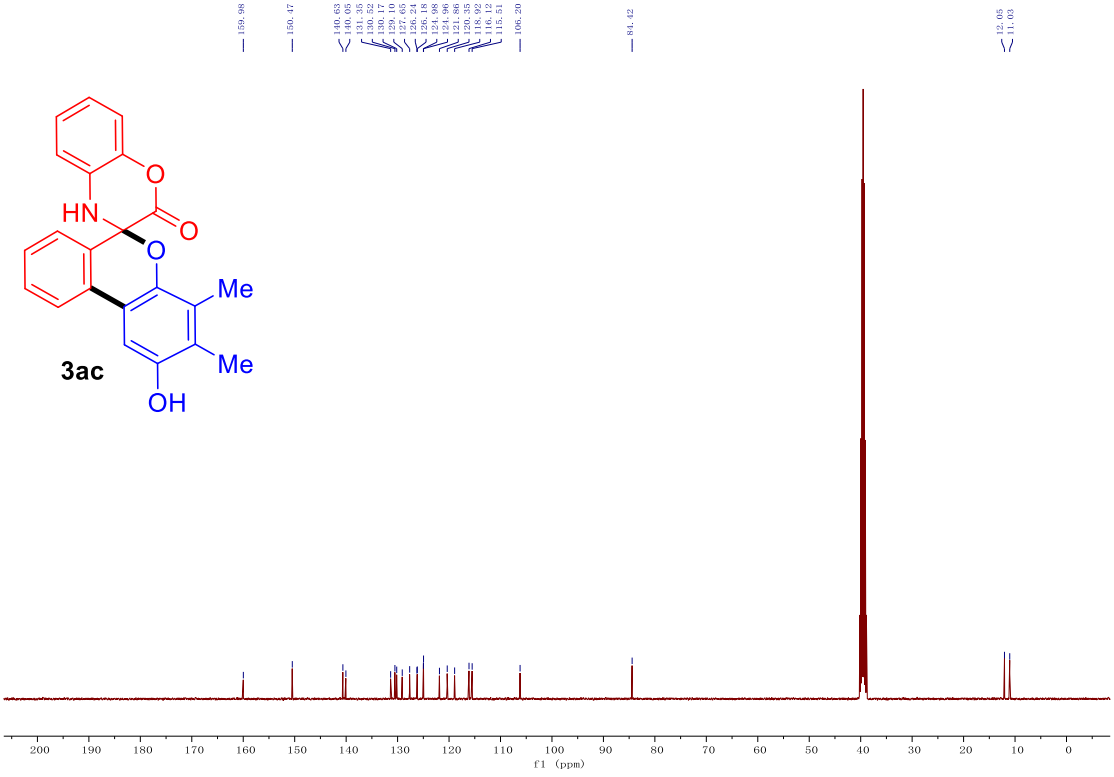
^{1}H and ^{13}C NMR Spectra of compound **3ab**



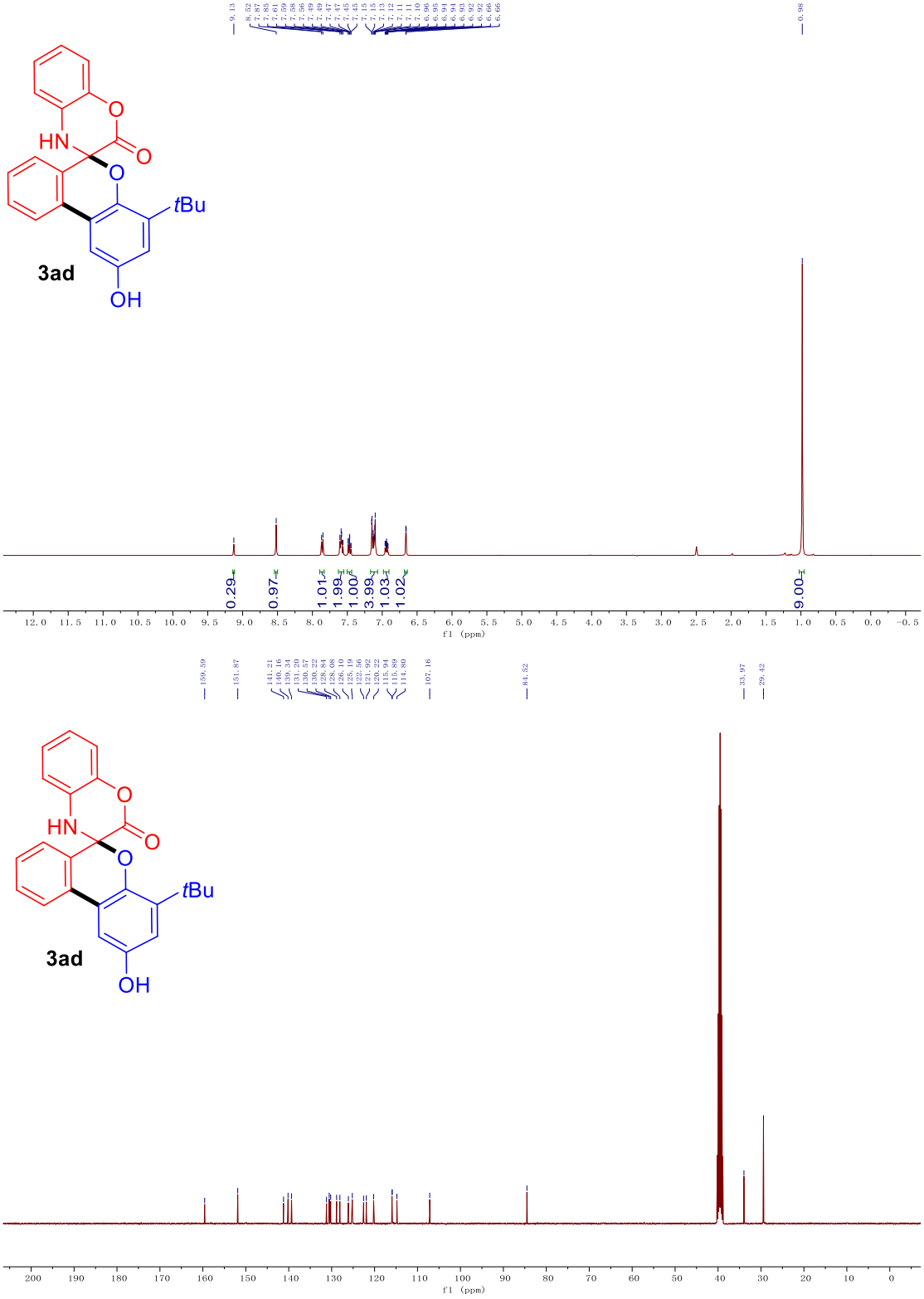


^{1}H and ^{13}C NMR Spectra of compound **3ac**

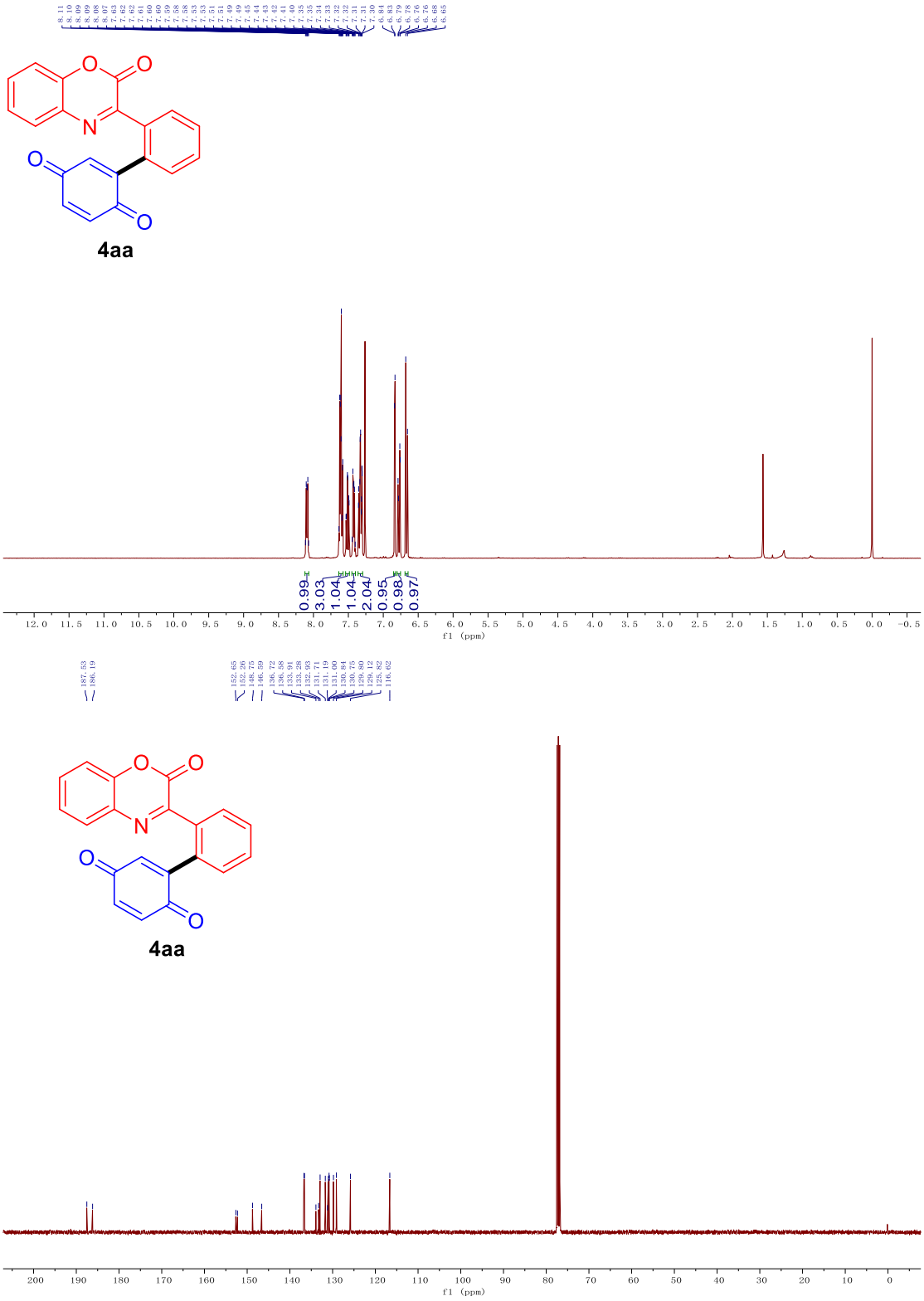




^{1}H and ^{13}C NMR Spectra of compound **3ae**



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



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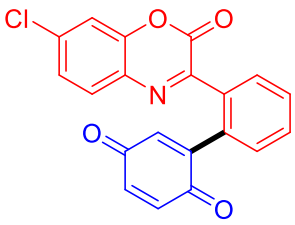
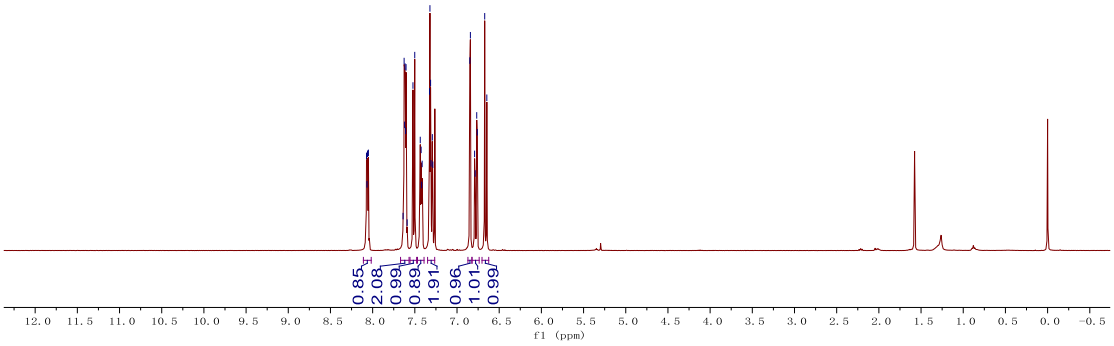
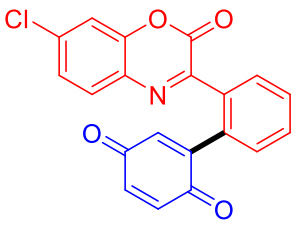


4ba





4ba

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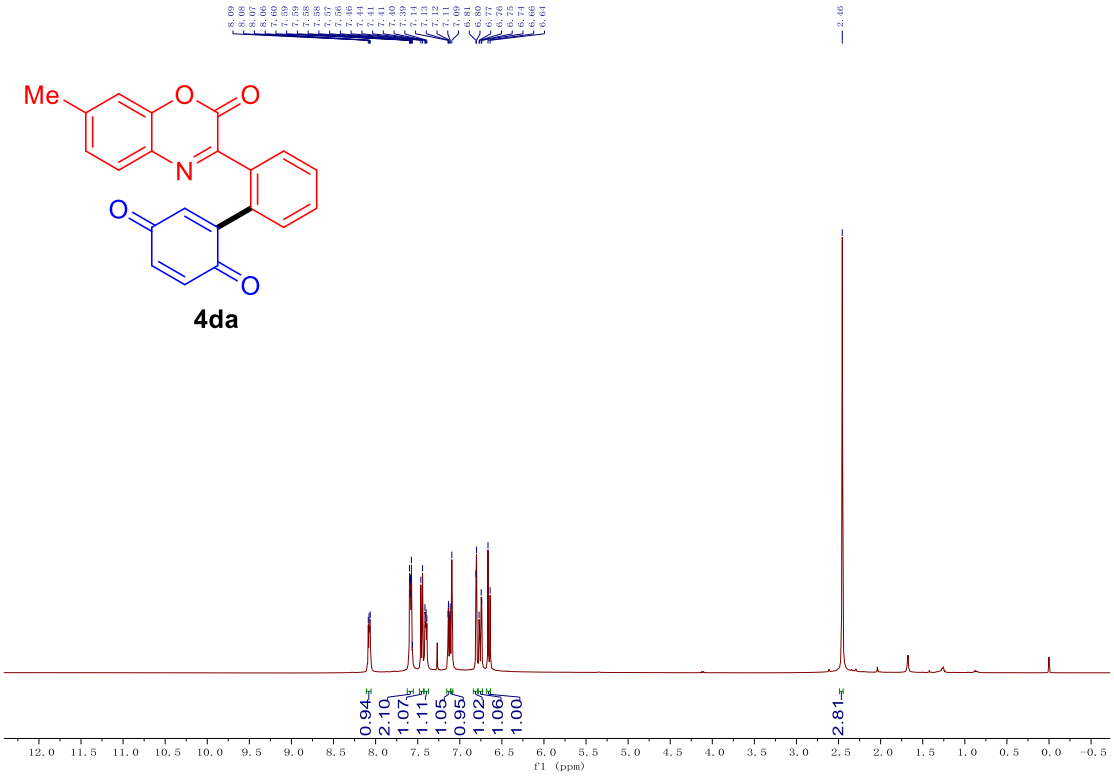

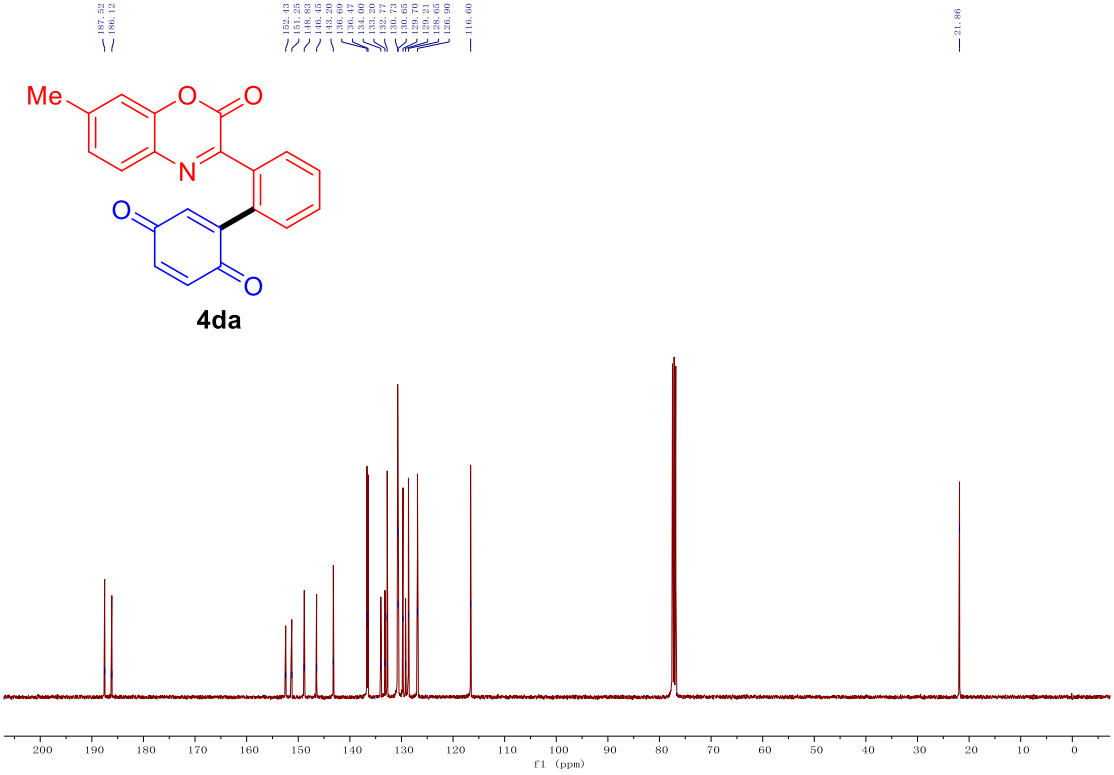

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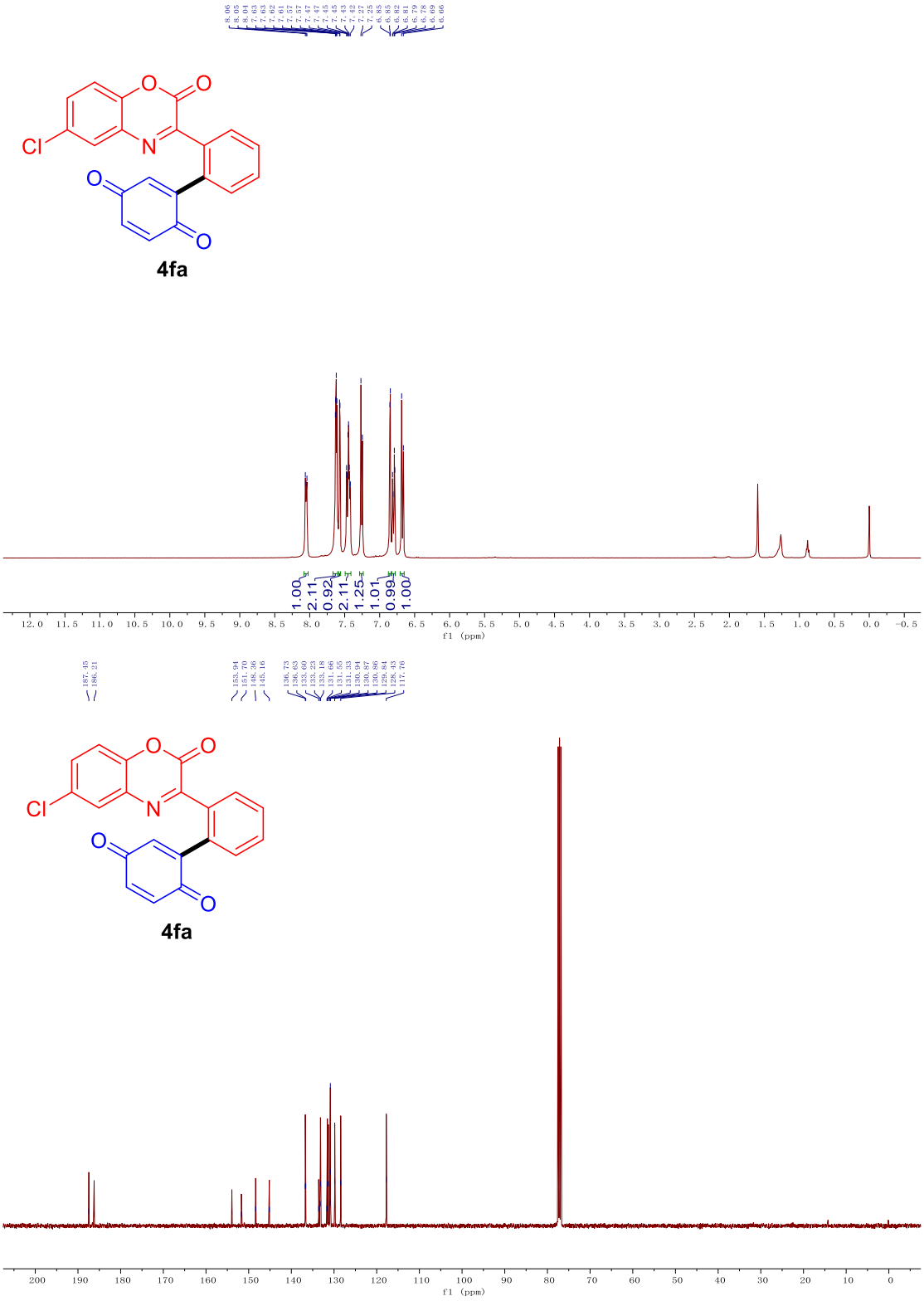

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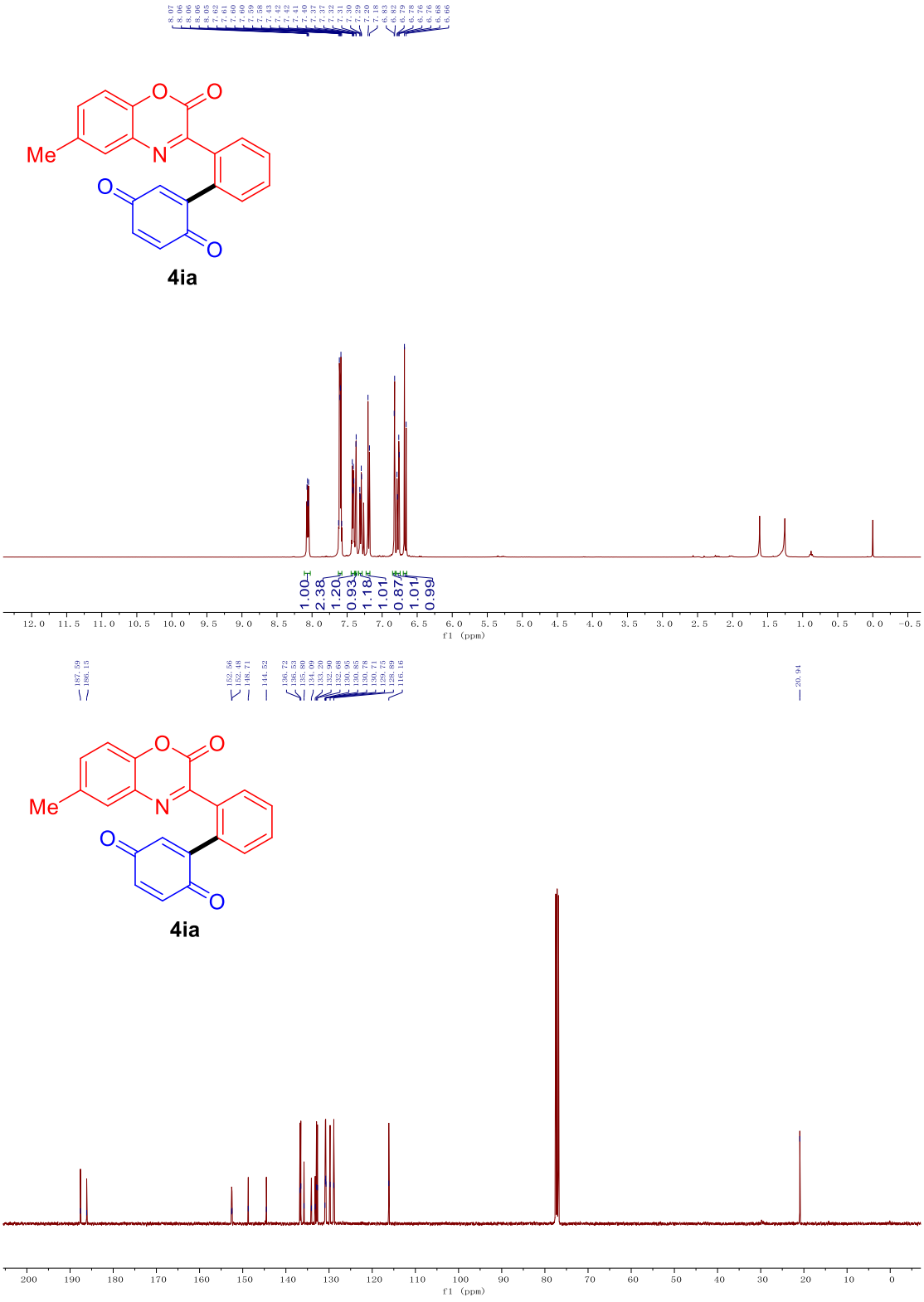
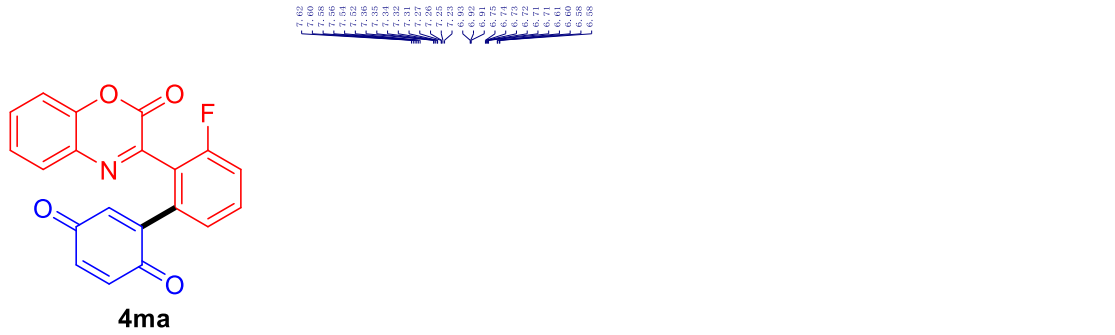


^{1}H and ^{13}C NMR Spectra of compound **4ma**



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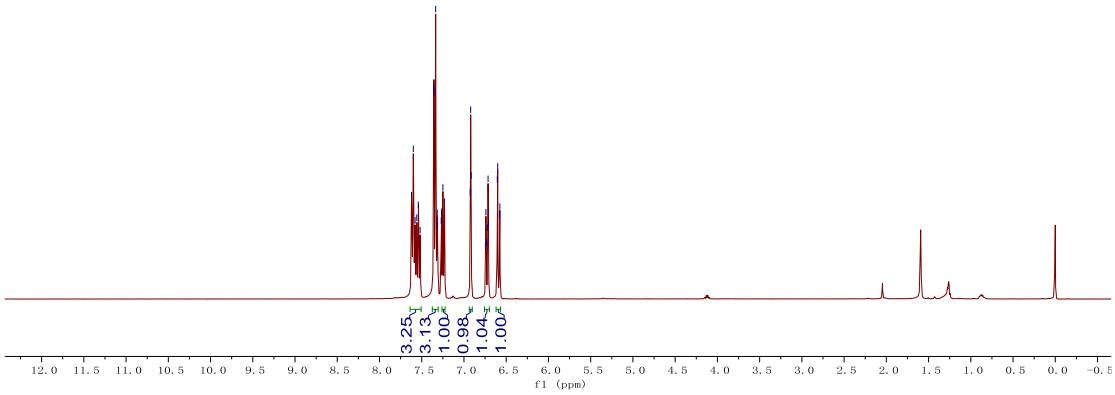
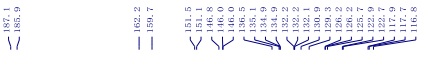
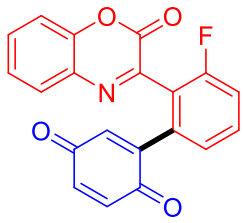
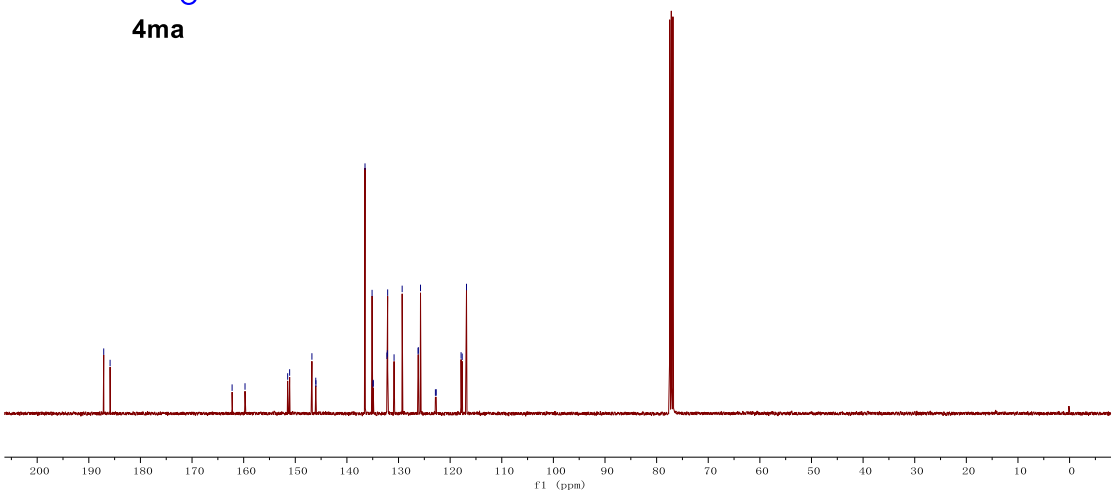


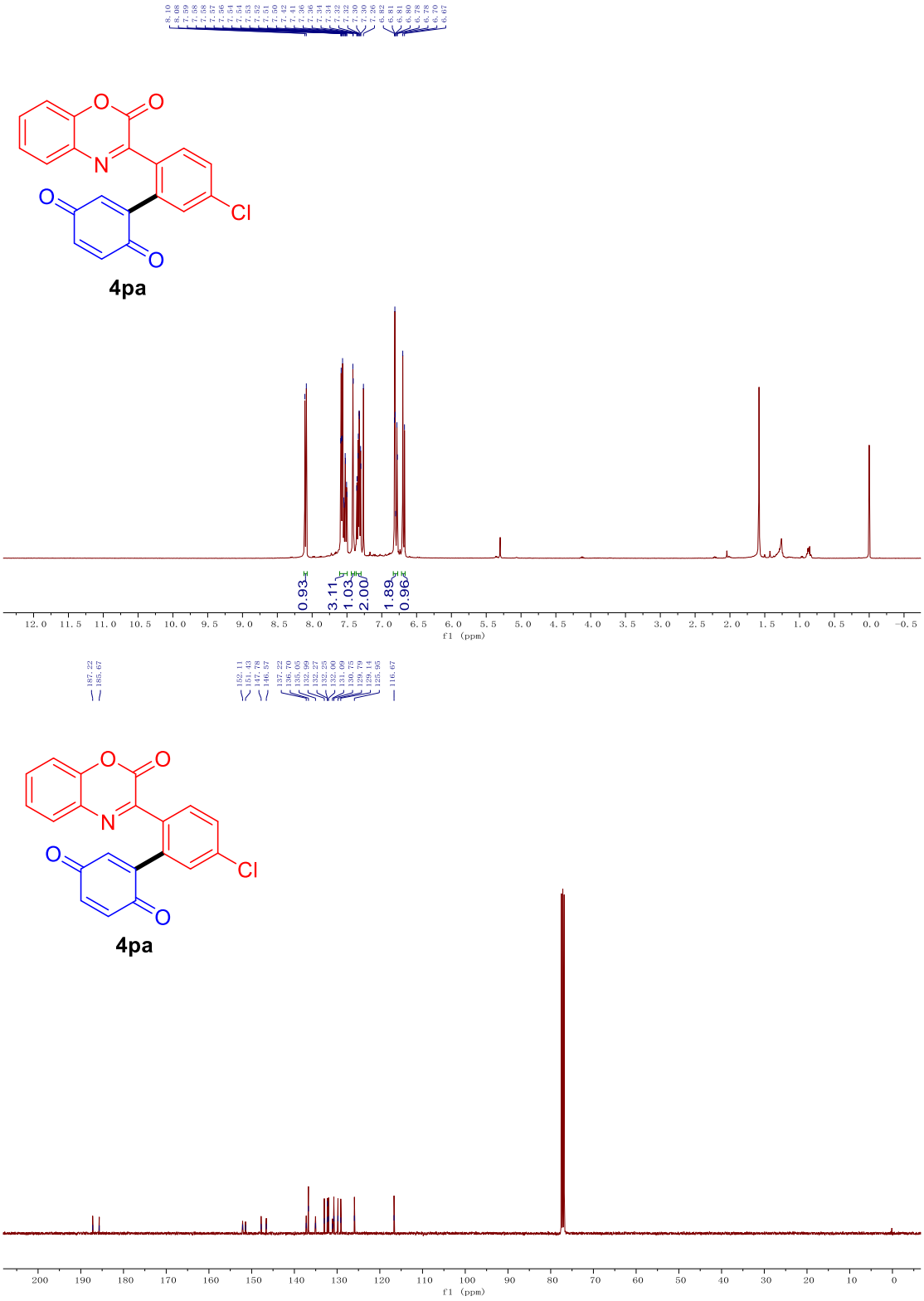




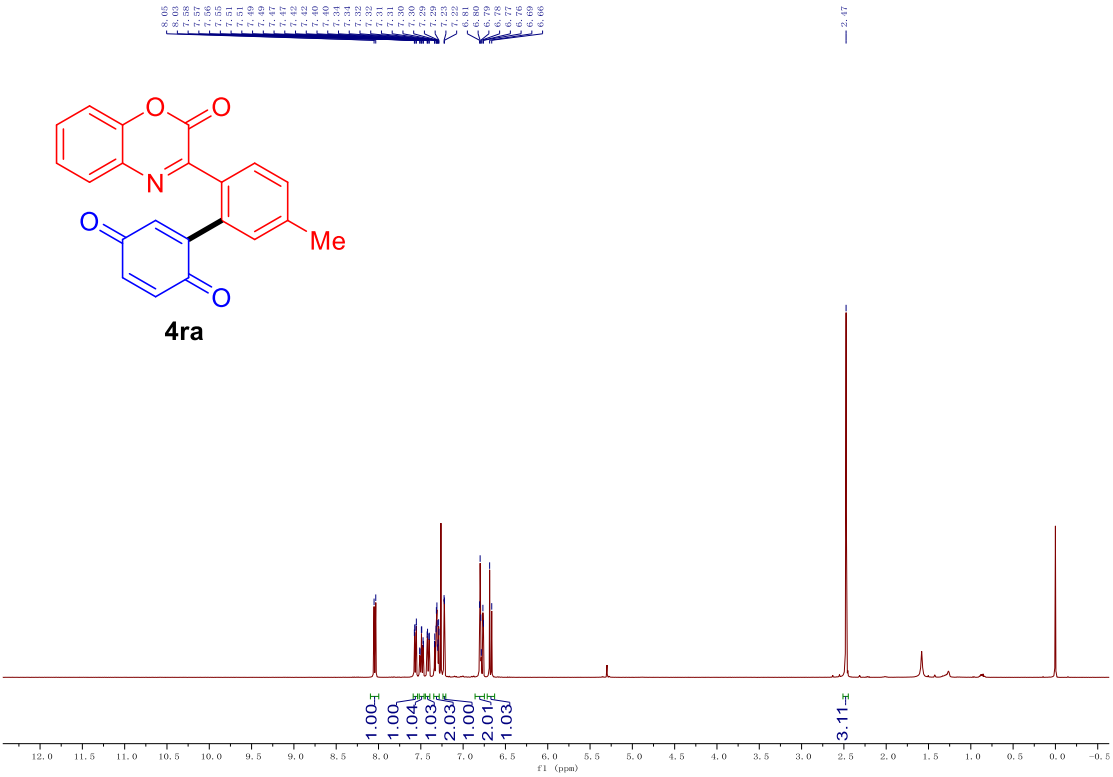
4ma

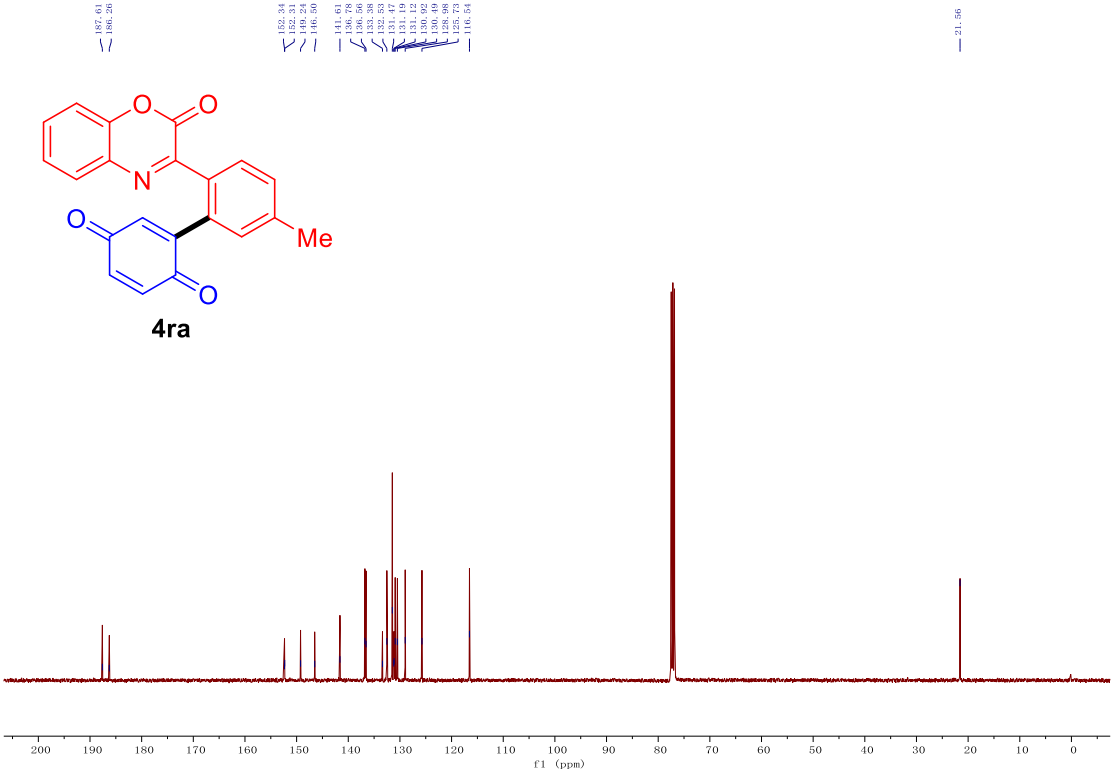


^{1}H and ^{13}C NMR Spectra of compound **4pa**

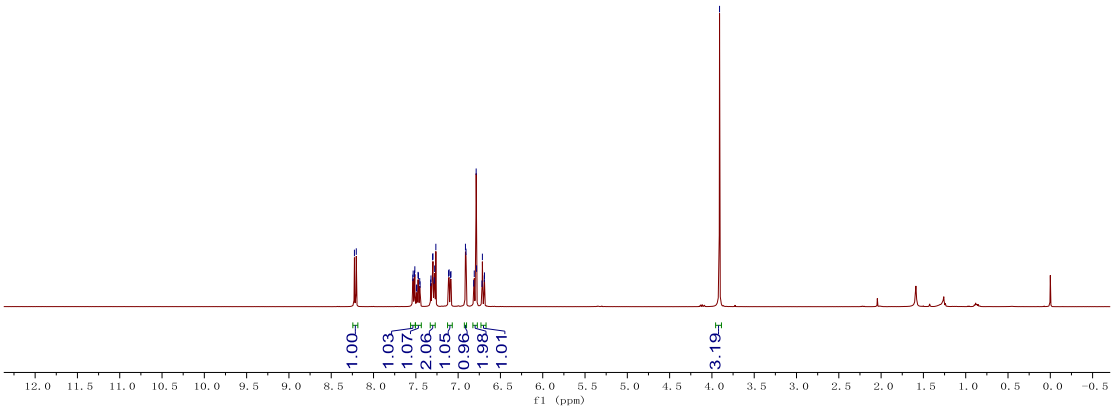


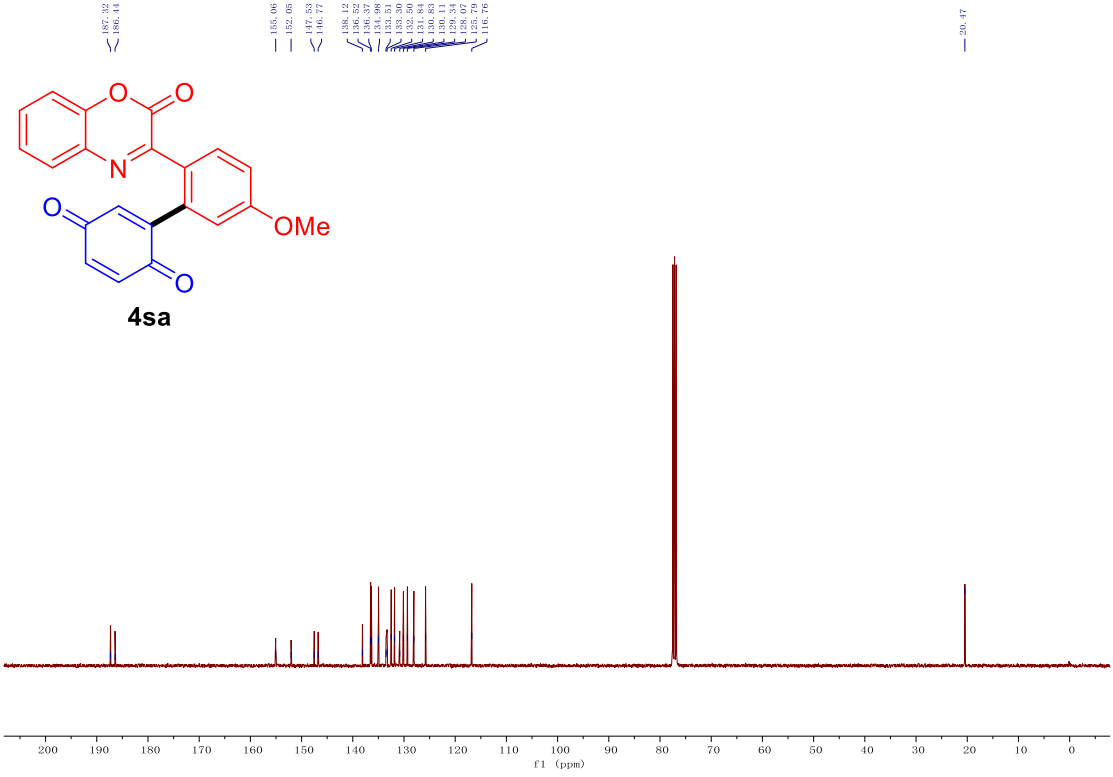
^{1}H and ^{13}C NMR Spectra of compound **4ra**



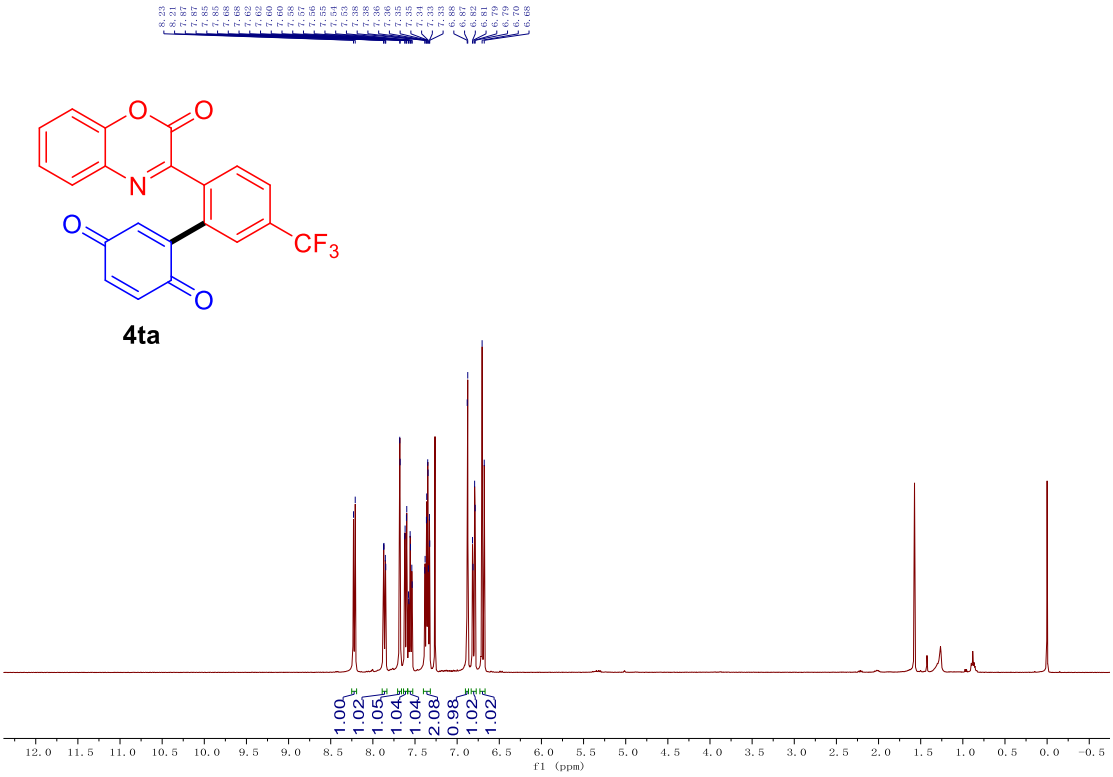


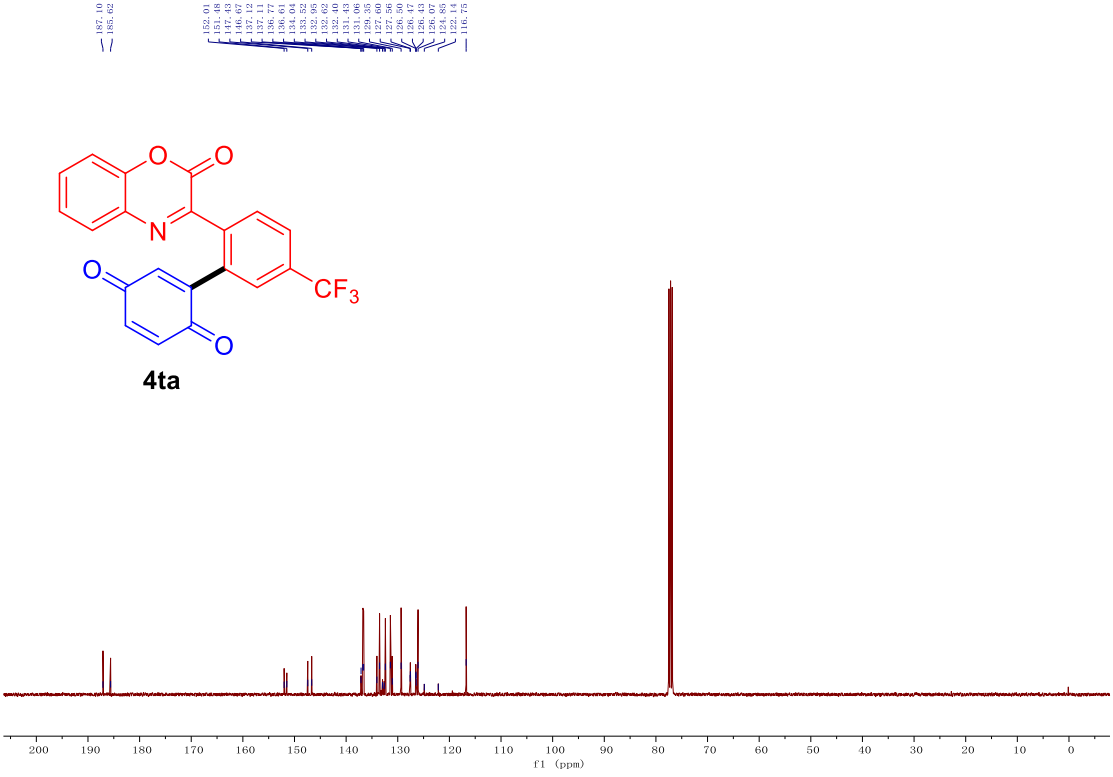
^{1}H and ^{13}C NMR Spectra of compound **4sa**



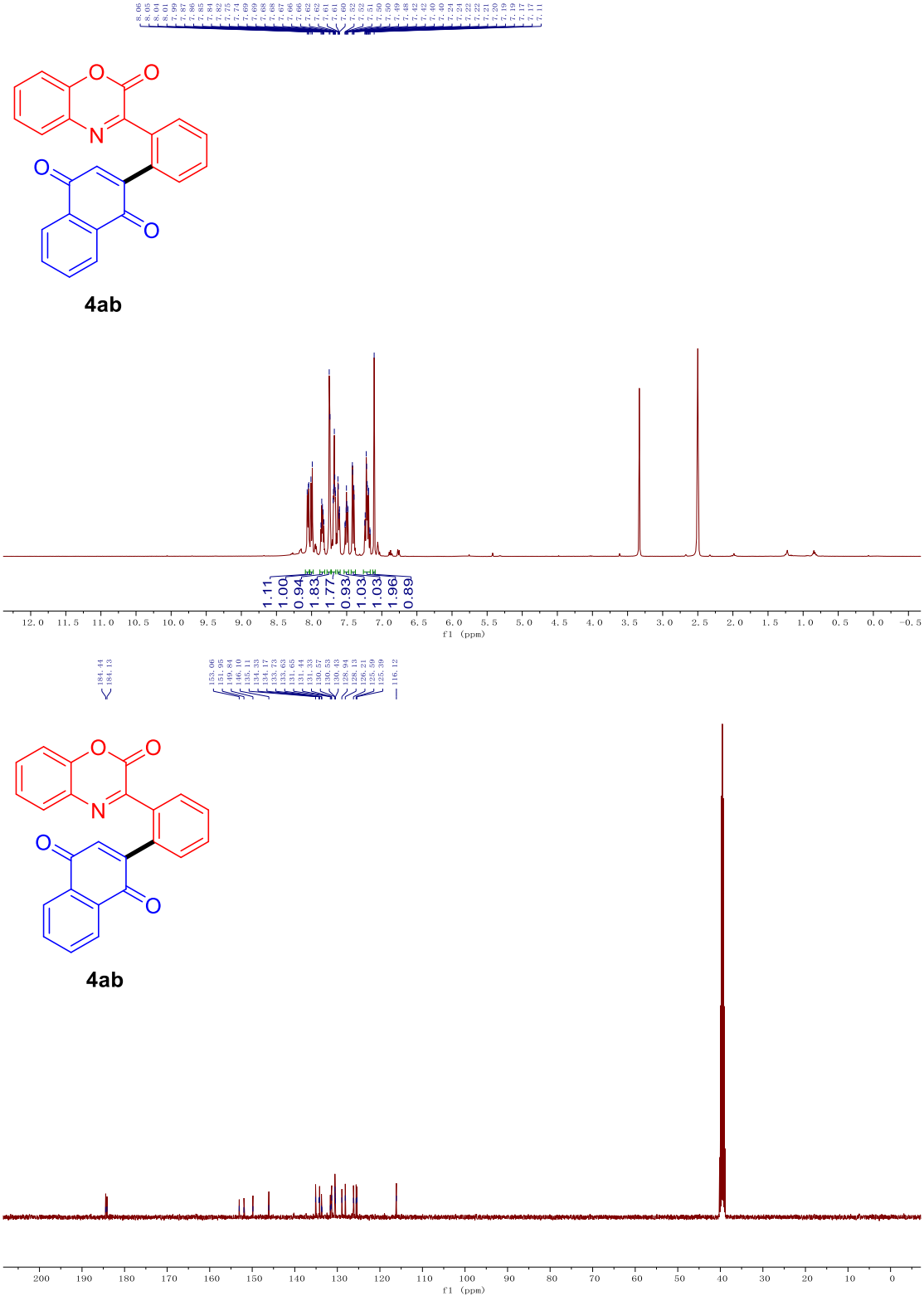


^{1}H and ^{13}C NMR Spectra of compound **4ta**

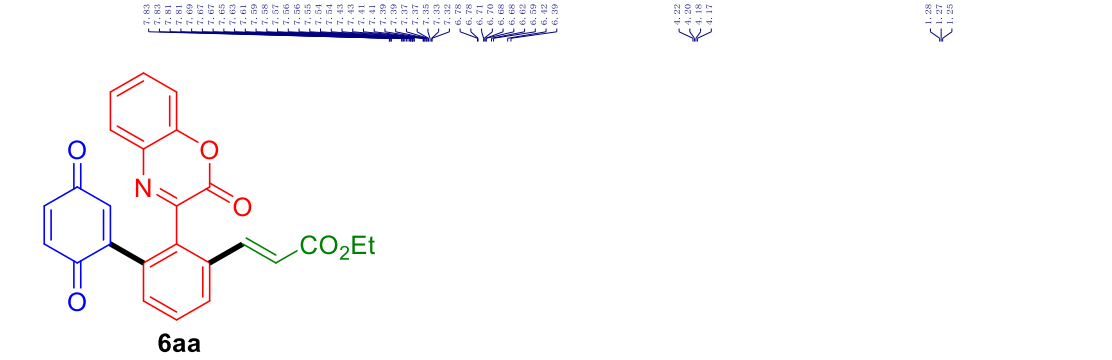


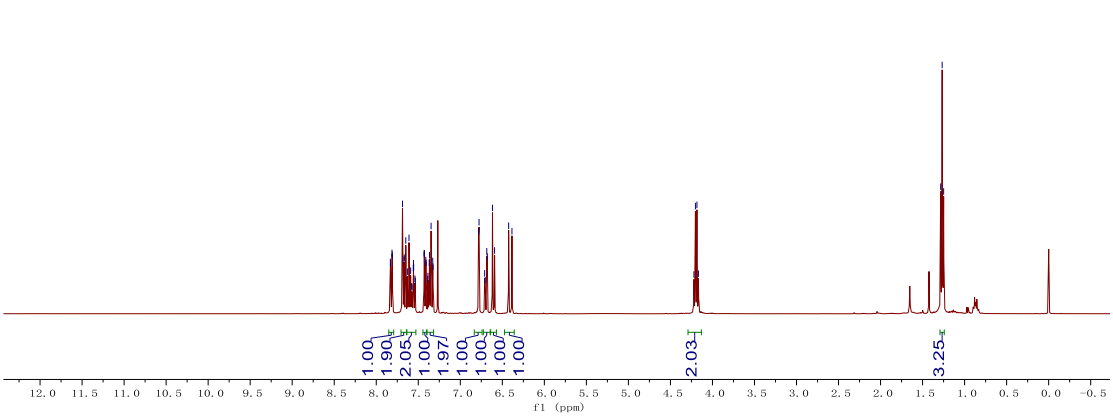


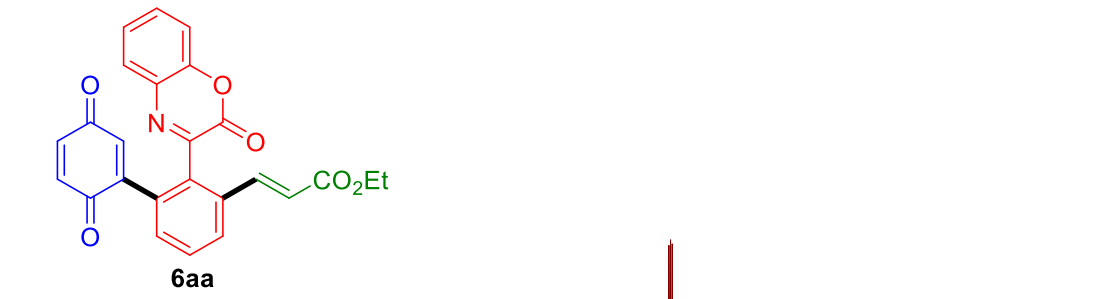
^{1}H and ^{13}C NMR Spectra of compound **4ab**

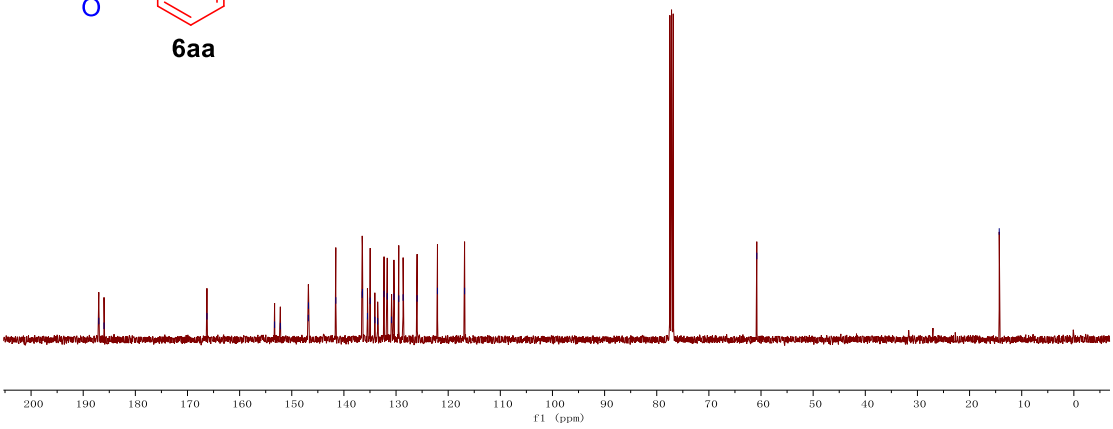


^{1}H and ^{13}C NMR Spectra of compound **6aa**

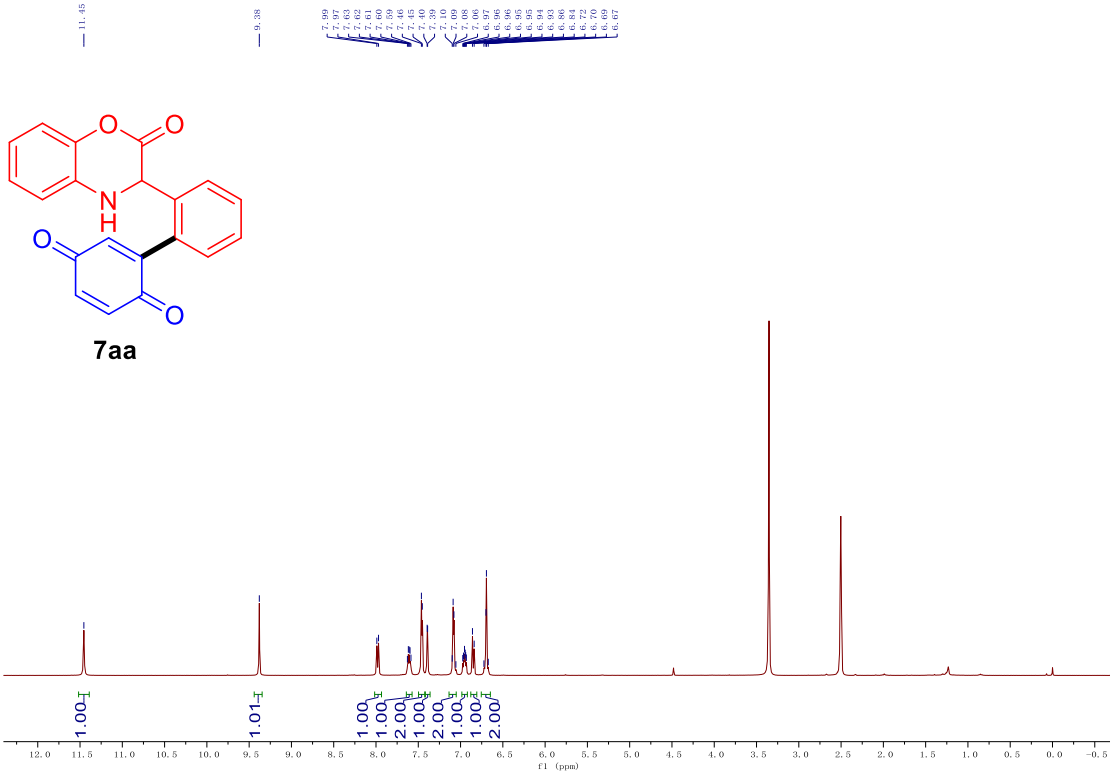


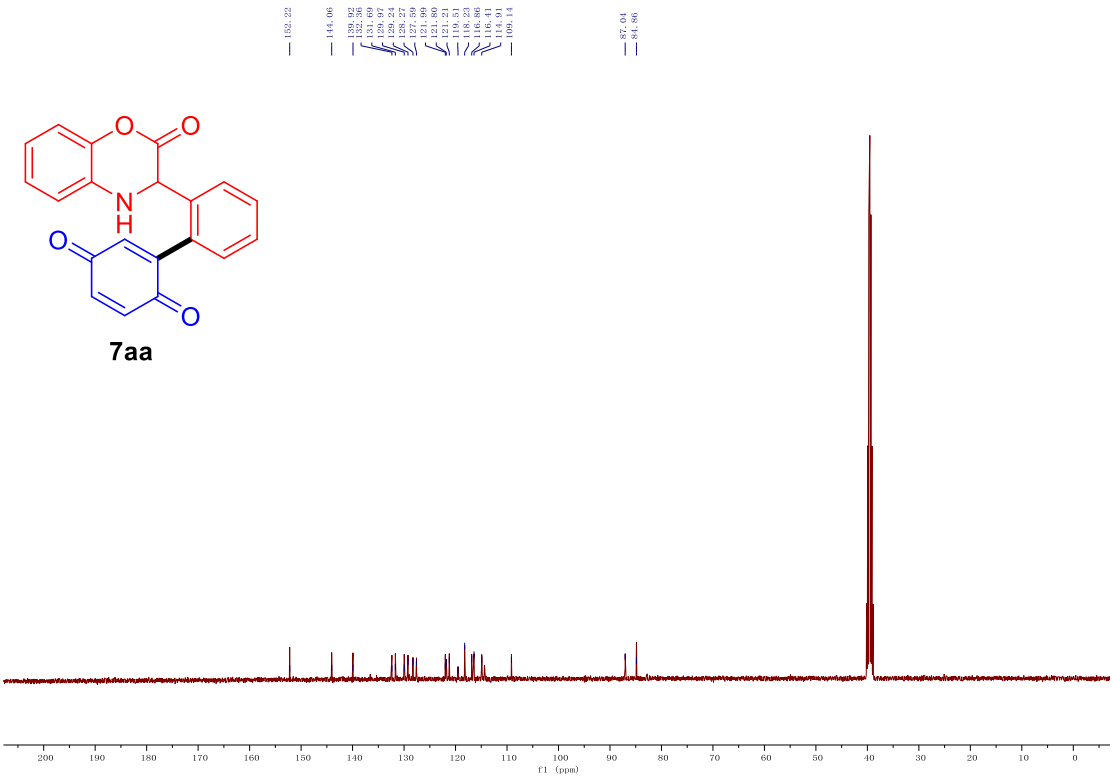




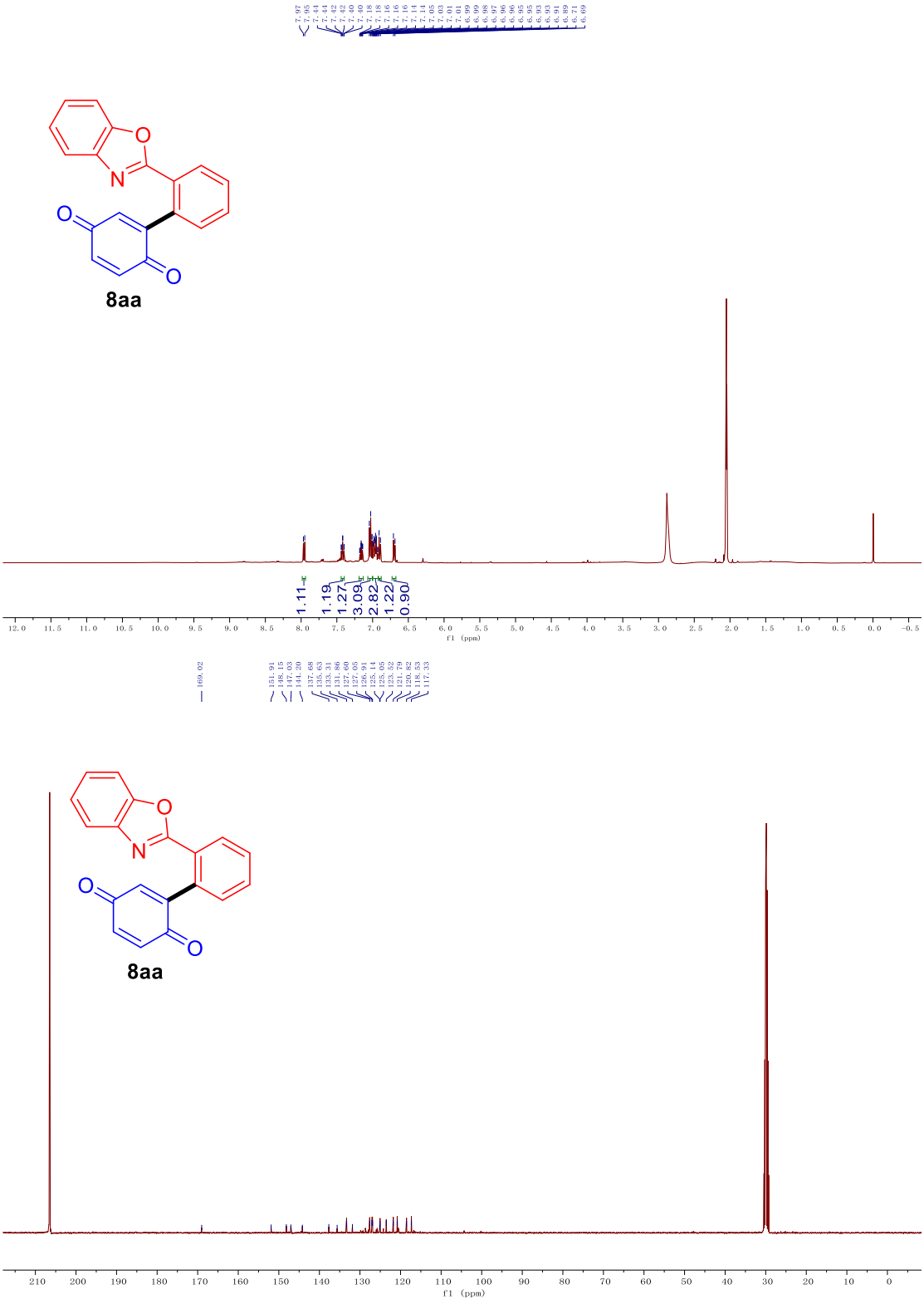


^{1}H and ^{13}C NMR Spectra of compound **7aa**

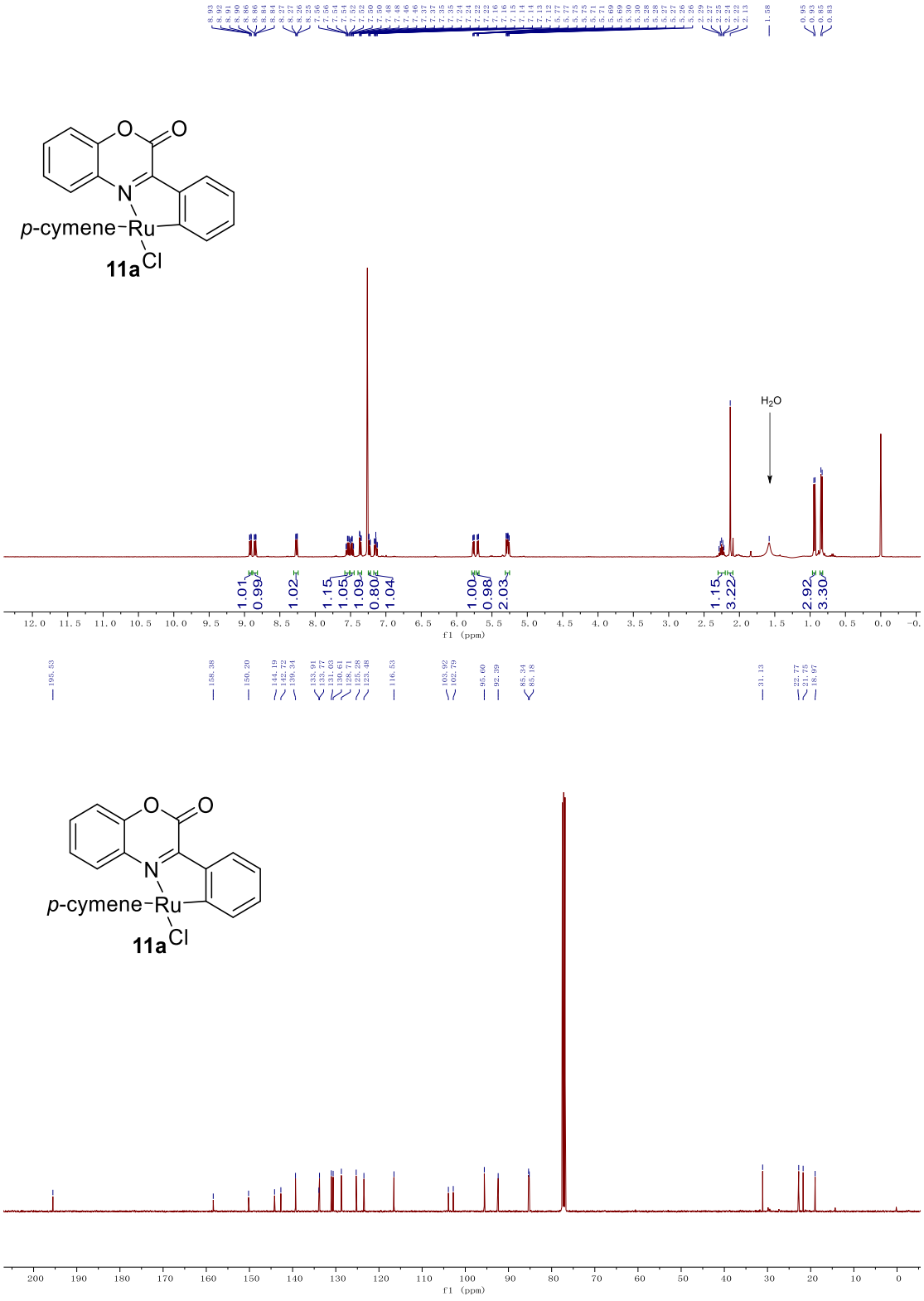




^{1}H and ^{13}C NMR Spectra of compound **8aa**



^{1}H and ^{13}C NMR Spectra of compound **11a**



^{1}H and ^{13}C NMR Spectra of compound **11u**