

Electronic supplementary information

Synthesis of Cyclopenta[*b*]benzofurans *via* Biomimetic Oxidative

Phenol-Enamine [3+2] Cycloaddition

Muhammad Adnan Bashir,^{‡a} Xuanjie Chen,^{‡a} Tie Wang,^a Hui Guo,^b and Hongbin Zhai^{*a,c,d}

^aThe State Key Laboratory of Chemical Oncogenomics, Guangdong Provincial Key Laboratory of Nano-Micro Materials Research, School of Chemical Biology and Biotechnology, Shenzhen Graduate School of Peking University, Shenzhen 518055, China; Institute of Marine Biomedicine, Shenzhen Polytechnic, Shenzhen 518055, China.

^bTsinghua-Berkeley Shenzhen Institute and The Institute of Biopharmaceutical and Health Engineering Tsinghua Shenzhen International Graduate School, Tsinghua University, Shenzhen 518055, People's Republic of China.

^cShenzhen Bay Laboratory, Shenzhen 518055, China

^dInstitute of Marine Biomedicine, Shenzhen Polytechnic, Shenzhen 518055, China

*Email: zhaih@pku.edu.cn

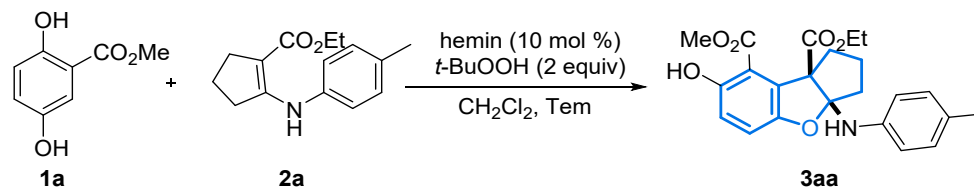
1. General Information

All reactions involving air or moisture sensitive reagents or intermediates were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Solvent purification was conducted according to Purification of Laboratory Chemicals (Perrin, D. D. Armarego, W. L. and Perrins, D. R., Pergamon Press: Oxford, 1980). Yields refer to isolated compounds, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Tsingdao silica gel plates (60F-254) using Tsingdao silica gel (60, particle size 0.040–0.063 mm). And the silica gel from the same company was also used for flash column chromatography. NMR spectra were recorded on a Brüker AVANCE 400 (1H: 400 MHz, 13C: 101 MHz) or a Brüker AVANCE 500 (1H: 500 MHz, 13C: 126MHz) instrument. Chemical shifts were reported in parts per million (ppm) with respect to the residual solvent signal CDCl₃ (1H NMR: δ = 7.26; 13C NMR: δ = 77.00). Peak multiplicities were reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, m = multiplet, br = broad signal. High resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight) spectrometer.

All the substrates were prepared according to the reported literature methods.¹⁻⁶

2. Optimization of Reaction Conditions

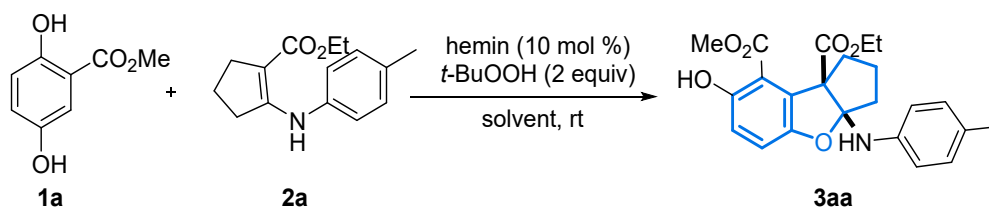
Table S1. The reaction of **1a** with **2a** under different temperatures



Entry ^a	Temperature (°C)	Yield ^b (%)
1	70	35
2	40	68
3	rt	91
4	0	27
5	-10	20

^aReactions were performed with **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst and *t*-BuOOH (0.4 mmol) in DCM (5.0 mL) at different temperatures. ^bIsolated yield.

Table S2. The reaction of **1a** with **2a** in different solvents



Entry ^a	Solvent	Yield ^b (%)
1	CHCl ₃	43
2	DCE	61
3	CCl ₄	38
4	DCM	91
5	Methanol	10
6	Toluene	76
7	Et ₂ O	traces
8	THF	traces
9	Acetone	traces

^aReactions were performed with **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst and *t*-BuOOH (0.4 mmol) in solvent (5.0 mL). ^bIsolated yield.

3. General Procedure

To a Schlenk flask equipped with magnetic stirrer bar, methyl 2,5-dihydroxybenzoate **1a** (0.2 mmol, 1.0 equiv), ethyl 2-(*p*-tolylamino)cyclopent-1-ene-1-carboxylate **2a** (0.3 mmol, 1.5 equiv), hemin (0.01 mmol, 13.5 mg) and DCM toluene (5.0 mL) were added. After stirring for a while, TBHP (73 μ L, 2.0 equiv.) was added *via* a microsyringe and the resulted mixture was stirred at room temperature for 24 h. Upon the completion of reaction (monitored by TLC), the mixture was directly subjected to chromatography and purified by flash chromatography on silica gel with petroleum ether/ethyl acetate as an eluent (20:1 to 10:1) to afford the desired product **3aa**.

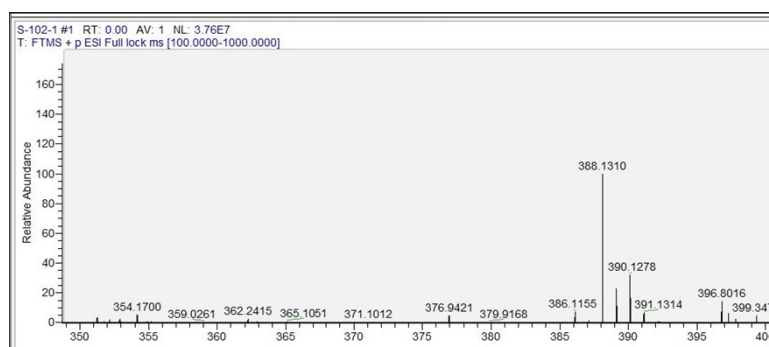


Figure S1. HRMS of **3ca**

4. UV-Vis Study

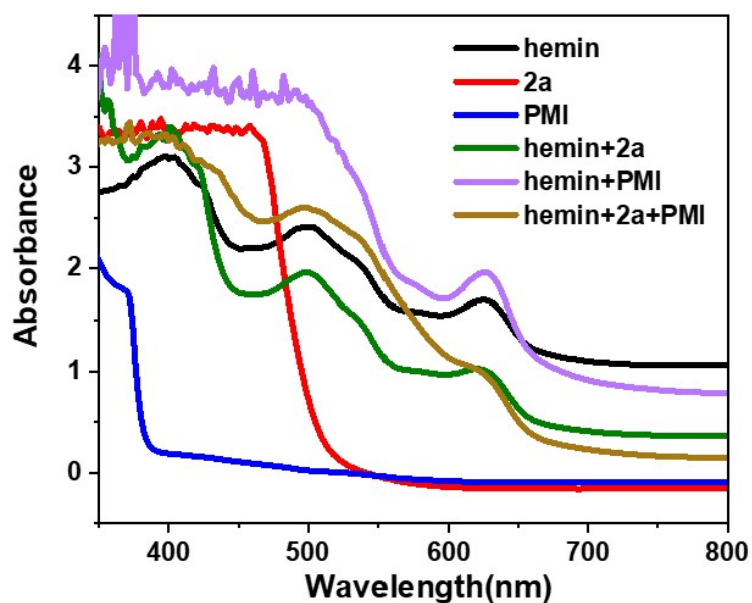
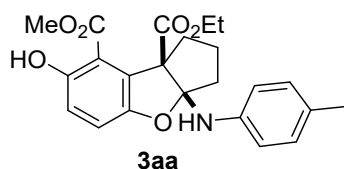


Figure S2. UV-Vis spectrum

5. Analytical Data of Products

8b-ethyl 8-methyl 7-hydroxy-3a-(*p*-tolylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[*b*]benzofuran-8,8b-dicarboxylate 3aa



A brown solid, 75 mg, 91% yield.

m.p.: 109-110 °C.

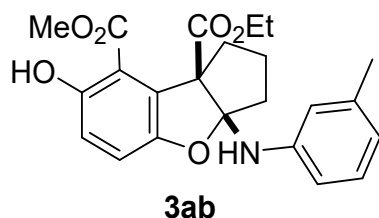
TLC: $R_f = 0.45$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.54 (s, 1H), 7.06 – 7.00 (d, 2H), 6.98 – 6.95 (d, 1H), 6.94 – 6.86 (m, 3H), 4.64 (s, 1H), 4.25 – 4.08 (m, 2H), 3.85 (s, 3H), 3.12 – 2.98 (m, 1H), 2.49 – 2.42 (m, 1H), 2.28 (s, 3H), 2.23 – 2.14 (m, 1H), 2.01 – 1.94 (m, 1H), 1.92 – 1.85 (m, 1H), 1.72 – 1.63 (m, 1H), 1.22 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 171.9, 169.6, 156.7, 152.3, 140.8, 131.8, 129.3, 129.1, 122.0, 118.3, 117.9, 111.4, 108.4, 68.9, 61.3, 51.4, 39.1, 38.3, 23.9, 20.6, 14.2.

HRMS (ESI): $\text{C}_{23}\text{H}_{26}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 412.1755; found: 412.1755.

8b-ethyl 8-methyl 7-hydroxy-3a-(*m*-tolylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[*b*]benzofuran-8,8b-dicarboxylate 3ab



A yellow oil, 68 mg, 83% yield.

TLC: $R_f = 0.54$ (Hexane/EtOAc = 10:1) [UV, PMA].

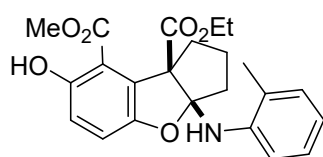
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.55 (s, 1H), 7.16 – 7.07 (s, 1H), 6.98 (d, $J = 8.8$ Hz, 1H), 6.89 (d, $J = 8.8$ Hz, 1H), 6.85 – 6.72 (m, 3H), 4.26 – 4.05 (m, 2H), 3.86 (s, 3H), 3.04 (m, $J = 13.4$,

11.0, 6.9 Hz, 1H), 2.63 – 2.50 (m, 1H), 2.30 (s, 3H), 2.22 (ddd, $J = 13.1, 11.3, 6.5$ Hz, 1H), 2.04 – 1.96 (m, 1H), 1.95 – 1.87 (m, 1H), 1.78 – 1.64 (m, 1H), 1.22 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.9, 169.6, 156.8, 152.3, 143.4, 138.6, 129.1, 128.7, 122.7, 121.7, 118.4, 118.0, 117.9, 111.0, 108.4, 69.1, 61.4, 51.5, 39.3, 38.3, 24.0, 21.5, 14.3.

HRMS (ESI): $\text{C}_{23}\text{H}_{26}\text{NO}_6^+$ [(M+H) $^+$]: calcd.:412.1755; found: 412.1760

8b-ethyl 8-methyl 7-hydroxy-3a-(*o*-tolylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[*b*]benzofuran-8,8b-dicarboxylate 3ac



3ac

A yellow oil, 66 mg, 80% yield.

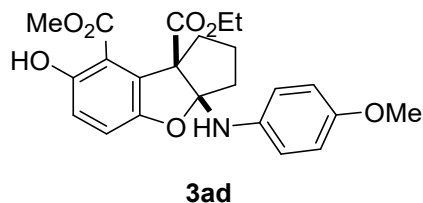
TLC: $R_f = 0.54$ (Hexane/EtOAc = 10:1) [UV, PMA].

^1H NMR (500 MHz, CDCl_3) 10.54 (s, 1H), 7.32 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.18 – 7.09 (m, 2H), 6.97 (d, $J = 8.9$ Hz, 1H), 6.93 – 6.88 (m, 2H), 4.29 (dd, $J = 10.9, 7.1$ Hz, 1H), 4.11 (dd, $J = 10.9, 7.2$ Hz, 1H), 3.87 (s, 3H), 3.05 (ddd, $J = 13.0, 10.3, 6.7$ Hz, 1H), 2.67 – 2.58 (m, 1H), 2.20 (ddd, $J = 13.1, 10.6, 6.5$ Hz, 1H), 2.12 (s, 3H), 2.01 – 1.90 (m, 2H), 1.80 – 1.69 (m, 1H), 1.23 (t, $J = 7.2$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 172.1, 169.6, 156.8, 152.3, 141.7, 130.3, 129.1, 128.9, 126.5, 121.9, 120.4, 118.4, 118.1, 111.0, 108.3, 69.7, 61.6, 51.5, 38.8, 38.1, 24.2, 18.1, 14.2.

HRMS (ESI): $\text{C}_{23}\text{H}_{26}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 412.1755; found: 412.1760.

8b-ethyl 8-methyl 7-hydroxy-3a-((4-methoxyphenyl)amino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[*b*]benzofuran-8,8b-dicarboxylate 3ad



A yellow solid, 79 mg, 92% yield.

m.p.: 75-76 °C.

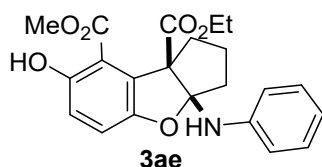
TLC: $R_f = 0.55$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.54 (s, 1H), 7.03 (dd, $J = 8.8$ Hz, 2H), 6.99 (d, $J = 8.8$ Hz, 1H), 6.89 (d, $J = 8.8$ Hz, 1H), 6.80 (dd, $J = 8.8$ Hz, 2H), 4.27 – 4.11 (m, 2H), 3.85 (s, 3H), 3.78 (s, 3H), 3.28 – 2.84 (m, 1H), 2.38 – 2.23 (m, 1H), 2.21 – 2.06 (m, 1H), 2.03 – 1.91 (m, 1H), 1.91 – 1.79 (m, 1H), 1.71 – 1.57 (m, 1H), 1.23 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 171.9, 169.6, 156.7, 156.1, 152.2, 136.4, 129.3, 125.3, 118.3, 117.8, 114.0, 112.1, 108.4, 68.6, 61.3, 55.5, 51.5, 38.7, 38.3, 23.8, 14.3.

HRMS (ESI): $\text{C}_{23}\text{H}_{26}\text{NO}_7^+$ [(M+H) $^+$]: calcd.: 428.1704; found: 428.1703

8b-ethyl 8-methyl 7-hydroxy-3a-(phenylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3ae



A yellow oil, 69 mg, 87% yield.

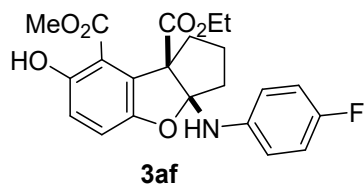
TLC: $R_f = 0.45$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.47 (s, 1H), 7.17 – 7.08 (m, 2H), 6.89 (m, $J = 8.7, 6.2$ Hz, 4H), 6.81 (d, $J = 8.9$ Hz, 1H), 4.73 (s, 1H), 4.13 – 3.97 (m, 2H), 3.77 (s, 3H), 3.02 – 2.90 (m, 1H), 2.52 – 2.41 (m, 1H), 2.19 – 2.07 (m, 1H), 1.96 – 1.78 (m, 2H), 1.70 – 1.55 (m, 1H), 1.12 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.9, 168.6, 155.8, 151.3, 142.4, 128.0, 127.8, 120.8, 119.8, 117.4, 116.9, 109.9, 107.4, 68.1, 60.4, 50.5, 38.4, 37.3, 22.9, 13.2.

HRMS (ESI): $\text{C}_{22}\text{H}_{24}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 398.1598; found: 398.1599.

8b-ethyl 8-methyl 3a-((4-fluorophenyl)amino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3af



A dark brown oil, 61 mg, 73% yield.

TLC: $R_f = 0.33$ (Hexane/EtOAc = 10:1) [UV, PMA].

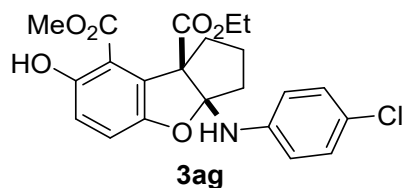
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.46 (s, 1H), 6.93 – 6.87 (m, 3H), 6.87 – 6.79 (m, 3H), 4.17 – 3.98 (m, 2H), 3.76 (s, 3H), 3.02 – 2.89 (m, 1H), 2.33 – 2.21 (m, 1H), 2.10 – 1.97 (m, 1H), 1.95 – 1.86 (m, 1H), 1.85 – 1.72 (m, 1H), 1.67 – 1.49 (m, 1H), 1.13 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.8, 159.2, 156.8, 128.0, 123.1, 123.0, 117.4, 116.8, 114.4, 114.2, 110.4, 107.4, 67.8, 60.4, 50.5, 38.0, 37.3, 22.7, 13.3.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -121.14.

HRMS (ESI): $\text{C}_{22}\text{H}_{23}\text{FNO}_6^+$ [(M+H) $^+$]: calcd.: 416.1504; found: 416.1505.

8b-ethyl 8-methyl 3a-((4-chlorophenyl)amino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3ag



A dark brown oil, 69 mg, 80% yield.

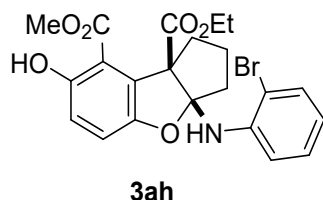
TLC: $R_f = 0.34$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.55 (s, 1H), 7.16 (d, $J = 8.8$ Hz, 2H), 6.97 (d, $J = 8.9$ Hz, 1H), 6.92 – 6.85 (m, 3H), 4.22 – 4.04 (m, 2H), 3.85 (s, 3H), 3.04 (ddd, $J = 13.4, 11.1, 6.9$ Hz, 1H), 2.54 – 2.46 (m, 1H), 2.20 – 2.11 (m, 1H), 2.03 – 1.96 (m, 1H), 1.94 – 1.87 (m, 1H), 1.74 – 1.63 (m, 1H), 1.19 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.8, 168.5, 155.9, 151.1, 141.0, 127.9, 127.7, 125.8, 120.9, 117.5, 116.8, 109.6, 107.4, 68.0, 60.4, 50.5, 38.5, 37.4, 22.8, 13.2.

HRMS (ESI): $C_{22}H_{23}ClNO_6^+$ [(M+H)⁺]: calcd.: 432.1208; found: 432.1210.

8b-ethyl 8-methyl 3a-((2-bromophenyl)amino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3ah



A yellow oil, 77 mg, 81% yield.

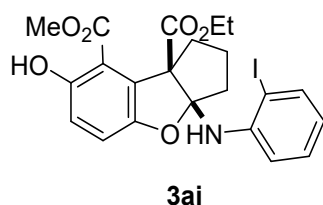
TLC: $R_f = 0.35$ (Hexane/EtOAc = 10:1) [UV, PMA].

¹H NMR (500 MHz, CDCl₃) δ 10.57 (s, 1H), 7.73 (dd, $J = 7.9, 1.5$ Hz, 1H), 7.30 (dd, $J = 8.2, 1.6$ Hz, 1H), 7.26 – 7.19 (m, 1H), 6.98 (d, $J = 8.9$ Hz, 1H), 6.90 (d, $J = 8.9$ Hz, 1H), 6.66 (dd, $J = 7.4, 1.6$ Hz, 1H), 5.18 (s, 1H), 4.35 – 4.25 (m, 1H), 4.25 – 4.10 (m, 1H), 3.87 (s, 3H), 3.12 – 3.02 (m, 1H), 2.67 – 2.58 (m, 1H), 2.24 (ddd, $J = 13.0, 10.5, 6.5$ Hz, 1H), 2.04 – 1.97 (m, 1H), 1.94 (ddt, $J = 13.3, 6.8, 3.0$ Hz, 1H), 1.72 (m, $J = 12.6, 10.4, 6.3, 3.9$ Hz, 1H), 1.20 (t, $J = 7.2$ Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 171.7, 169.6, 157.0, 152.2, 144.0, 139.2, 129.0, 128.8, 122.8, 119.7, 118.5, 118.1, 110.6, 108.3, 91.6, 76.8, 69.5, 62.1, 51.6, 39.5, 38.3, 24.0, 14.1.

HRMS (ESI): $C_{22}H_{23}BrNO_6^+$ [(M+H)⁺]: calcd.: 476.0703; found: 476.0705.

8b-ethyl 8-methyl 7-hydroxy-3a-((2-iodophenyl)amino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3ai



A dark brown oil, 86 mg, 82% yield.

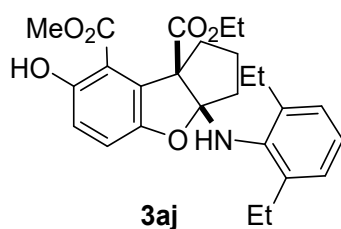
TLC: $R_f = 0.35$ (Hexane/EtOAc = 10:1) [UV, PMA].

¹H NMR (500 MHz, CDCl₃) δ 10.57 (s, 1H), 7.73 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.30 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.24 (dd, *J* = 7.1, 1.4 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 1H), 6.90 (d, *J* = 8.9 Hz, 1H), 5.18 (s, 1H), 4.30 (dd, *J* = 10.9, 7.1 Hz, 1H), 4.16 (dd, *J* = 10.9, 7.1 Hz, 1H), 3.87 (s, 3H), 3.12 – 3.02 (m, 1H), 2.67 – 2.58 (m, 1H), 2.24 (ddd, *J* = 13.0, 10.5, 6.5 Hz, 1H), 2.04 – 1.98 (m, 1H), 1.94 (ddd, *J* = 13.3, 6.6, 3.5 Hz, 1H), 1.79 – 1.66 (m, 1H), 1.20 (t, *J* = 7.2 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 171.7, 169.6, 157.0, 152.2, 144.0, 139.2, 129.0, 128.8, 122.8, 119.7, 118.5, 118.1, 110.6, 108.3, 91.6, 76.8, 69.5, 62.1, 51.6, 39.5, 38.3, 24.0, 14.1.

HRMS (ESI): C₂₂H₂₃INO₆⁺ [(M+H)⁺]: calcd.: 524.0565; found: 524.0569.

8b-ethyl 8-methyl 3a-((2,6-diethylphenyl)amino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3aj



A yellow oil, 79 mg, 87% yield.

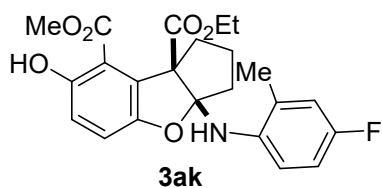
TLC: *R_f* = 0.51 (Hexane/EtOAc = 10:1) [UV, PMA].

¹H NMR (500 MHz, CDCl₃) δ 10.57 (s, 1H), 7.22 – 7.05 (m, 3H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 4.28 – 4.15 (m, 2H), 3.87 (s, 3H), 3.08 (td, *J* = 13.0, 6.7 Hz, 1H), 2.93 (dt, *J* = 14.8, 7.4 Hz, 2H), 2.68 (dt, *J* = 14.3, 7.4 Hz, 2H), 2.05 – 1.95 (m, 2H), 1.82 – 1.67 (m, 2H), 1.53 (dd, *J* = 12.5, 6.3 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.18 (t, *J* = 7.5 Hz, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 171.0, 168.7, 155.7, 151.0, 142.5, 137.2, 128.5, 125.6, 125.4, 117.1, 116.3, 113.3, 107.5, 67.6, 60.2, 50.4, 37.3, 35.8, 23.9, 22.5, 14.6, 13.3.

HRMS (ESI): C₂₆H₃₂NO₆⁺ [(M+H)⁺]: calcd.: 454.2224; found: 454.2225.

8b-ethyl 8-methyl 3a-((4-fluoro-2-methylphenyl)amino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3ak



A yellow oil, 68 mg, 79% yield.

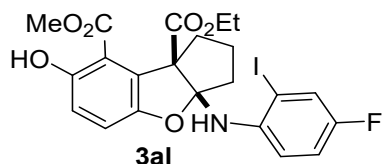
TLC: $R_f = 0.51$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.46 (s, 1H), 7.26 – 7.19 (m, 1H), 6.88 (d, $J = 8.9$ Hz, 1H), 6.80 (d, $J = 8.8$ Hz, 1H), 6.78 – 6.70 (m, 2H), 4.33 – 4.21 (m, 1H), 4.17 (dt, $J = 10.9, 7.1$ Hz, 1H), 4.04 (dd, $J = 10.8, 7.1$ Hz, 1H), 3.77 (s, 3H), 2.96 (ddd, $J = 13.4, 10.9, 6.9$ Hz, 1H), 2.38 – 2.28 (m, 1H), 2.05 (s, 3H), 2.01 – 1.93 (m, 1H), 1.93 – 1.85 (m, 1H), 1.85 – 1.75 (m, 1H), 1.68 – 1.51 (m, 1H), 1.14 (t, $J = 7.2$ Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 171.0, 168.6, 159.0, 156.6, 155.8, 151.2, 136.6, 136.5, 132.2, 132.1, 128.0, 122.9, 122.9, 117.4, 116.9, 115.9, 115.6, 111.7, 111.5, 110.6, 107.3, 68.3, 60.5, 50.5, 37.5, 37.2, 23.0, 17.2, 17.2, 13.2.

HRMS (ESI): $\text{C}_{23}\text{H}_{25}\text{FNO}_6^+$ [(M+H) $^+$]: calcd.: 430.1660; found: 430.1666.

8b-ethyl 8-methyl 3a-((4-fluoro-2-iodophenyl)amino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3al



A yellow oil, 86 mg, 79% yield.

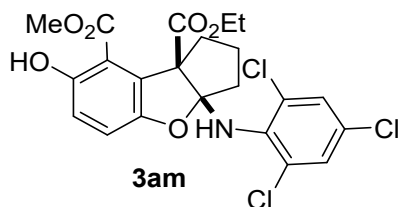
TLC: $R_f = 0.50$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.56 (s, 1H), 7.47 (dd, $J = 7.8, 2.9$ Hz, 1H), 7.34 – 7.27 (m, 1H), 6.97 (d, $J = 8.8$ Hz, 2H), 6.89 (d, $J = 9.0$ Hz, 1H), 4.93 (s, 1H), 4.32 – 4.13 (m, 2H), 3.86 (s, 3H), 3.11 – 3.02 (m, 1H), 2.53 – 2.44 (m, 1H), 2.20 – 2.11 (m, 1H), 2.04 – 1.96 (m, 1H), 1.92 (dq, $J = 9.8, 3.3$ Hz, 1H), 1.74 – 1.65 (m, 1H), 1.21 (t, $J = 7.2$ Hz, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 171.6, 169.5, 157.0, 152.1, 129.0, 125.7, 125.5, 121.3, 121.3, 118.5, 118.0, 115.6, 115.4, 111.0, 108.3, 69.2, 62.0, 51.6, 39.1, 38.2, 23.9, 14.2.

HRMS (ESI): C₂₂H₂₂FINO₆⁺ [(M+H)⁺]: calcd.: 542.0470; found: 542.0472.

8b-ethyl 8-methyl 7-hydroxy-3a-((2,4,6-trichlorophenyl)amino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3am



A white solid, 85 mg, 85% yield.

m.p.: 100-101 °C.

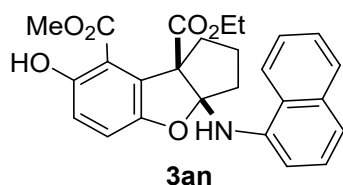
TLC: R_f = 0.53 (Hexane/EtOAc = 10:1) [UV, PMA].

¹H NMR (500 MHz, CDCl₃) δ 10.53 (s, 1H), 7.37 (s, 2H), 6.95 (d, *J* = 8.9 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 4.60 (s, 1H), 4.23 (dd, *J* = 7.1, 3.1 Hz, 2H), 3.86 (s, 3H), 3.10 (td, *J* = 13.0, 7.1 Hz, 1H), 2.53 (td, *J* = 12.9, 6.2 Hz, 1H), 2.05 – 1.94 (m, 2H), 1.91 – 1.82 (m, 1H), 1.59 (t, *J* = 2.9 Hz, 1H), 1.28 – 1.21 (m, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 171.5, 169.6, 156.9, 152.0, 137.1, 135.2, 131.5, 129.6, 128.7, 118.3, 118.1, 113.3, 108.5, 76.8, 68.4, 61.5, 51.5, 38.1, 36.7, 29.7, 23.7, 14.3.

HRMS (ESI): C₂₂H₂₁Cl₃NO₆⁺ [(M+H)⁺]: calcd.: 500.0429; found: 500.0430.

8b-ethyl 8-methyl 7-hydroxy-3a-(naphthalen-1-ylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3an



A dark brown oil, 71 mg, 79% yield.

TLC: R_f = 0.45 (Hexane/EtOAc = 10:1) [UV, PMA].

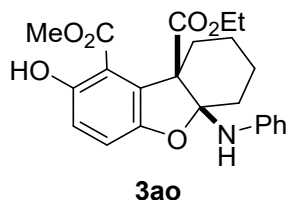
¹H NMR (500 MHz, CDCl₃) δ 10.58 (s, 1H), 7.97 (dd, *J* = 6.3, 3.4 Hz, 1H), 7.83 (dd, *J* = 6.3, 3.3 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.48 (dt, *J* = 6.4, 3.4 Hz, 2H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 5.02 (s, 1H), 4.44 –

4.34 (m, 1H), 4.33 – 4.23 (m, 1H), 3.91 (s, 3H), 3.12 (ddd, $J = 13.2, 10.6, 6.8$ Hz, 1H), 2.58 – 2.45 (m, 1H), 2.19 (ddd, $J = 13.1, 10.9, 6.5$ Hz, 1H), 2.08 – 1.99 (m, 1H), 1.91 (dq, $J = 9.8, 3.5$ Hz, 1H), 1.78 – 1.65 (m, 1H), 1.29 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 171.2, 168.6, 155.8, 151.3, 137.8, 133.3, 128.6, 128.1, 127.3, 124.8, 124.7, 122.6, 121.1, 118.1, 117.4, 117.0, 110.6, 107.4, 68.5, 60.7, 50.5, 37.3, 37.2, 23.1, 13.3.

HRMS (ESI): $\text{C}_{26}\text{H}_{26}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 448.1755; found: 448.1756.

9a-ethyl 1-methyl 2-hydroxy-5a-(phenylamino)-6,7,8,9-tetrahydrodibenzo[*b,d*]furan-1,9a(5a*H*)-dicarboxylate 3ao



A yellow oil, 73 mg, 89% yield.

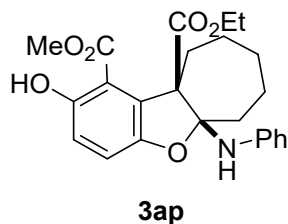
TLC: $R_f = 0.60$ (Hexane/EtOAc = 10:1) [UV, PMA].

^1H NMR (500 MHz, CDCl_3) δ 10.30 (s, 1H), 7.21 (d, $J = 7.8$ Hz, 2H), 7.04 (s, 1H), 7.03 – 6.95 (m, 3H), 6.90 (d, $J = 9.0$ Hz, 1H), 4.33 – 4.18 (m, 2H), 3.88 (s, 3H), 2.78 (dd, $J = 14.5, 4.1$ Hz, 1H), 2.70 (dd, $J = 14.5, 4.1$ Hz, 1H), 2.68 (dd, $J = 14.7, 3.8$ Hz, 2H), 1.80 – 1.71 (m, 1H), 1.61 – 1.48 (m, 2H), 1.46 – 1.36 (m, 1H), 1.29 (t, $J = 7.2$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 172.0, 169.7, 156.1, 149.8, 142.2, 132.9, 128.6, 123.8, 122.9, 119.2, 117.8, 109.7, 100.3, 61.2, 60.5, 51.6, 33.9, 29.9, 20.8, 20.4, 14.2.

HRMS (ESI): $\text{C}_{23}\text{H}_{26}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 412.1755; found: 412.1757.

10a-ethyl 1-methyl 2-hydroxy-5a-(phenylamino)-5a,6,7,8,9,10-hexahydro-10a*H*-cyclohepta[*b*]benzofuran-1,10a-dicarboxylate 3ap



A yellow oil, 73 mg, 86% yield.

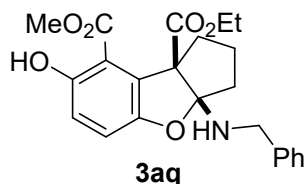
TLC: $R_f = 0.60$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.65 (d, $J = 1.3$ Hz, 1H), 7.26 – 7.16 (m, 2H), 7.05 (dd, $J = 8.8, 1.3$ Hz, 1H), 7.00 – 6.87 (m, 4H), 3.87 (d, $J = 1.3$ Hz, 3H), 3.77 (d, $J = 1.3$ Hz, 3H), 2.67 (dd, $J = 15.6, 6.3$ Hz, 1H), 2.53 (dd, $J = 15.3, 10.8$ Hz, 1H), 2.44 – 2.33 (m, 1H), 2.14 – 2.00 (m, 1H), 1.92 (m, $J = 13.0, 4.5$ Hz, 1H), 1.81 – 1.69 (m, 2H), 1.51 (ddd, $J = 13.8, 9.3, 4.4$ Hz, 1H), 1.41 (ddd, $J = 13.1, 10.3, 5.7$ Hz, 1H), 0.90 (dd, $J = 14.5, 11.0$ Hz, 1H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 172.7, 169.8, 157.3, 150.7, 142.8, 128.6, 128.3, 122.2, 121.8, 119.1, 118.8, 109.3, 102.7, 67.0, 52.2, 51.7, 34.5, 30.8, 30.5, 23.3, 22.7.

HRMS (ESI): $\text{C}_{24}\text{H}_{28}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 426.1911; found: 426.1919.

8b-ethyl 8-methyl 3a-(benzylamino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[*b*]benzofuran-8,8b-dicarboxylate 3aq



A yellow oil, 63 mg, 77% yield.

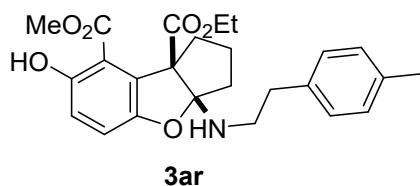
TLC: $R_f = 0.57$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.53 (s, 1H), 7.35 – 7.29 (m, 3H), 7.28 (d, $J = 2.1$ Hz, 1H), 7.24 (d, $J = 6.7$ Hz, 1H), 6.96 (d, $J = 8.8$ Hz, 1H), 6.87 (d, $J = 8.9$ Hz, 1H), 4.14 – 4.05 (m, 3H), 3.99 (d, $J = 13.2$ Hz, 1H), 3.83 (s, 3H), 3.05 (td, $J = 13.0, 6.9$ Hz, 1H), 2.42 – 2.34 (m, 1H), 2.07 – 1.94 (m, 2H), 1.92 – 1.83 (m, 1H), 1.71 – 1.57 (m, 1H), 1.07 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 171.8, 169.7, 156.6, 152.4, 140.2, 129.4, 128.3, 127.7, 127.0, 118.1, 117.5, 113.5, 108.5, 68.0, 61.1, 51.4, 47.4, 38.4, 37.9, 29.7, 23.6, 14.2.

HRMS (ESI): $\text{C}_{23}\text{H}_{26}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 412.1755; found: 412.1760.

8b-ethyl 8-methyl 7-hydroxy-3a-((4-methylphenethyl)amino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3ar



A white solid, 78 mg, 89% yield.

m.p.: 90-92 °C.

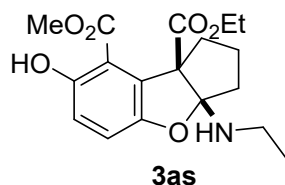
TLC: $R_f = 0.58$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.53 (s, 1H), 7.08 (s, 4H), 6.91 (s, 1H), 6.86 (s, 1H), 4.14 – 3.97 (m, 2H), 3.81 (s, 3H), 3.26 – 3.18 (m, 1H), 3.04 – 2.93 (m, 2H), 2.83 – 2.74 (m, 1H), 2.73 – 2.63 (m, 1H), 2.39 – 2.32 (m, 1H), 2.31 (s, 3H), 2.00 – 1.90 (m, 2H), 1.88 – 1.79 (m, 1H), 1.64 – 1.51 (m, 1H), 1.10 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 171.8, 169.7, 156.5, 152.4, 136.4, 135.7, 129.3, 129.1, 128.6, 118.0, 117.5, 113.6, 108.4, 67.9, 61.1, 51.4, 44.6, 38.3, 38.0, 36.4, 23.5, 21.0, 14.2.

HRMS (ESI): $\text{C}_{25}\text{H}_{30}\text{NO}_6^+$ [(M+H) $^+$]: calcd.:440.2068; found: 440.2070.

8b-ethyl 8-methyl 3a-(ethylamino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3as



A dark brown oil, 57 mg, 81% yield.

TLC: $R_f = 0.55$ (Hexane/EtOAc = 10:1) [UV, PMA].

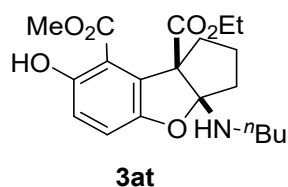
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.44 (s, 1H), 6.83 (d, $J = 8.9$ Hz, 1H), 6.80 – 6.72 (m, 1H), 4.18 – 3.95 (m, 2H), 3.73 (s, 3H), 2.90 (ddd, $J = 14.4, 12.9, 7.1$ Hz, 2H), 2.65 (dd, $J = 11.0, 7.2$ Hz, 1H), 2.31 – 2.19 (m, 1H), 1.94 – 1.79 (m, 2H), 1.78 – 1.68 (m, 1H), 1.50 (dd, $J = 12.7, 6.3$ Hz, 1H), 1.11 (t, 3H), 0.98 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.9, 168.7, 155.5, 151.4, 128.3, 117.0, 116.4, 112.7, 107.4,

76.3, 66.8, 60.0, 50.4, 37.3, 36.8, 36.7, 22.5, 14.6, 13.3.

HRMS (ESI): C₁₈H₂₄NO₆⁺ [(M+H)⁺]: calcd.: 350.1598; found: 350.1590.

8b-ethyl 8-methyl 3a-(butylamino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3at



A yellow oil, 60 mg, 79% yield.

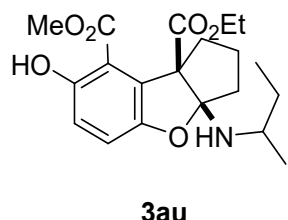
TLC: R_f = 0.55 (Hexane/EtOAc = 10:1) [UV, PMA].

¹H NMR (400 MHz, CDCl₃) δ 10.44 (s, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 4.15 – 3.96 (m, 2H), 3.73 (s, 3H), 2.95 – 2.80 (m, 2H), 2.60 (dd, *J* = 11.1, 7.5 Hz, 1H), 2.27 – 2.17 (m, 1H), 1.89 – 1.80 (m, 2H), 1.79 – 1.69 (m, 1H), 1.55 – 1.45 (m, 1H), 1.38 – 1.21 (m, 4H), 1.11 (t, *J* = 7.1 Hz, 3H), 0.81 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 170.9, 168.7, 155.5, 151.4, 128.3, 117.0, 116.5, 112.8, 107.4, 66.9, 60.0, 50.4, 41.9, 37.2, 36.8, 31.6, 28.7, 22.5, 19.3, 13.3, 12.9.

HRMS (ESI): C₂₀H₂₈NO₆⁺ [(M+H)⁺]: calcd.: 378.1911; found: 378.1919.

8b-ethyl 8-methyl 3a-(sec-butylamino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3au (dr 1.3:1)



A yellow oil, 61 mg, 81% yield.

TLC: R_f = 0.55 (Hexane/EtOAc = 10:1) [UV, PMA].

¹H NMR (400 MHz, CDCl₃) δ 10.48 (s, 0.39H), δ 10.47 (s, 0.52H), 6.91– 6.82 (m, 2H), 4.17– 4.09 (m, 2H), 3.80 (s, 3H), 3.01 – 2.94 (m, 2H), 2.33 – 2.28 (m, 1H), 1.99 – 1.81 (m, 3H), 1.66– 1.54 (m, 2H), 1.41 – 1.23 (m, 2H), 1.22 – 1.18 (m, 3H), 1.14 (d, *J* = 6.3 Hz, 1.32H), 1.00 (d, *J*

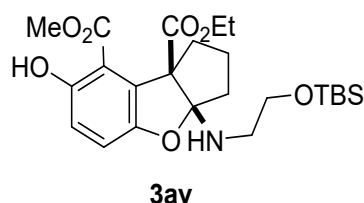
= 6.5 Hz, 1.60H), 0.88– 0.82 (m, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 170.9, 170.9, 168.7, 168.7, 155.2, 155.2, 151.4, 151.3, 128.6, 128.5, 116.8, 116.8, 116.4, 116.4, 113.3, 113.0, 107.5, 107.4, 67.4, 67.3, 59.9, 59.8, 50.3, 49.9, 49.1, 37.1, 37.0, 36.6, 36.6, 30.8, 30.0, 22.7, 22.7, 22.4, 21.0, 13.3, 13.2, 9.68, 8.73.

HRMS (ESI): $\text{C}_{20}\text{H}_{28}\text{NO}_6^+$ [(M+H) $^+$]: calcd.:378.1911; found: 378.1918.

Compound **3au** was synthesized using racemic ethyl 2-(*sec*-butylamino)cyclopentane-1-carboxylate following the *general procedure*. The *dr* was 1.3:1, which was determined from ^1H NMR analysis of product. The two diastereoisomers were not separated by column chromatography.

8b-ethyl 8-methyl 3a-((2-((*tert*-butyldimethylsilyl)oxy)ethyl)amino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3av



A dark brown oil, 77 mg, 80% yield.

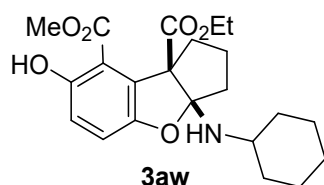
TLC: R_f = 0.56 (Hexane/EtOAc = 10:1) [UV, PMA].

^1H NMR (500 MHz, CDCl_3) δ 10.53 (s, 1H), 6.90 (d, J = 8.9 Hz, 1H), 6.83 (d, J = 8.8 Hz, 1H), 3.81 (s, 3H), 3.74 – 3.66 (m, 2H), 3.64 (s, 3H), 3.10 – 2.94 (m, 2H), 2.77 (dt, J = 12.0, 4.3 Hz, 1H), 2.32 – 2.24 (m, 1H), 1.98 – 1.88 (m, 2H), 1.88 – 1.78 (m, 1H), 1.64 – 1.50 (m, 1H), 0.82 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 171.5, 168.7, 155.5, 151.5, 128.1, 117.0, 116.5, 112.5, 107.3, 67.0, 61.6, 51.2, 50.4, 44.4, 37.4, 37.1, 24.8, 22.5, 17.1, -6.3, -6.4.

HRMS (ESI): $\text{C}_{24}\text{H}_{38}\text{NO}_7\text{Si}^+$ [(M+H) $^+$]: calcd.:480.2412; found: 480.2414.

8b-ethyl 8-methyl 3a-(cyclohexylamino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3aw



A yellow oil, 65 mg, 81% yield.

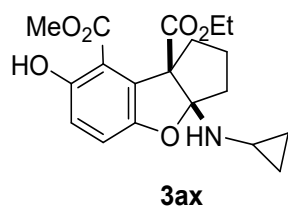
TLC: $R_f = 0.65$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.49 (s, 1H), 6.90 (d, $J = 8.8$ Hz, 1H), 6.84 (d, $J = 8.8$ Hz, 1H), 4.24 – 4.04 (m, 2H), 3.81 (s, 3H), 3.05 – 2.91 (m, 1H), 2.87 – 2.77 (m, 1H), 2.32 (ddt, $J = 12.7$, 6.0, 1.8 Hz, 1H), 2.10 – 2.04 (m, 1H), 1.99 (td, $J = 12.8$, 6.3 Hz, 1H), 1.90 (ddt, $J = 13.4$, 6.9, 1.7 Hz, 1H), 1.86 – 1.79 (m, 2H), 1.72 – 1.64 (m, 3H), 1.62 – 1.52 (m, 2H), 1.33 – 1.25 (m, 1H), 1.21 (t, $J = 7.1$ Hz, 3H), 1.16 – 0.98 (m, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 172.0, 169.8, 156.3, 152.4, 129.5, 117.9, 117.5, 114.0, 108.5, 68.4, 61.0, 52.5, 51.3, 38.1, 37.7, 36.1, 35.5, 25.8, 25.3, 25.2, 23.7, 14.4.

HRMS (ESI): $\text{C}_{19}\text{H}_{22}\text{NO}_6^+$ [(M+H) $^+$]: calcd.:404.2068; found: 404.2070.

8b-ethyl 8-methyl 3a-(cyclopropylamino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3ax



A brown oil, 64 mg, 89% yield.

TLC: $R_f = 0.65$ (Hexane/EtOAc = 10:1) [UV, PMA].

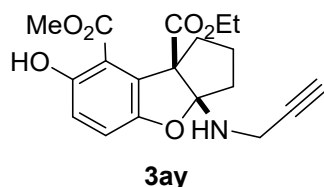
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.51 (s, 1H), 6.94 (d, $J = 8.8$ Hz, 1H), 6.85 (d, $J = 8.8$ Hz, 1H), 4.19 – 4.02 (m, 2H), 3.80 (s, 3H), 2.95 (td, $J = 13.0$, 6.9 Hz, 1H), 2.50 – 2.39 (m, 2H), 2.14 – 2.04 (m, 1H), 1.94 – 1.88 (m, 1H), 1.86 – 1.77 (m, 1H), 1.66 – 1.53 (m, 1H), 1.16 (t, $J = 7.1$ Hz, 3H), 0.56 – 0.50 (m, 1H), 0.47 (dd, $J = 7.1$, 4.2 Hz, 1H), 0.41 (dd, $J = 9.6$, 5.9 Hz, 1H), 0.33 – 0.25 (m, 1H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 171.7, 169.7, 156.5, 152.3, 129.5, 118.0, 117.5, 114.3, 108.5,

77.3, 51.3, 38.2, 37.6, 25.2, 23.6, 14.2, 8.5, 4.7.

HRMS (ESI): C₁₉H₂₃NO₆⁺ [(M+H)⁺]: calcd.: 362.1598; found: 362.1590.

8b-ethyl 8-methyl 7-hydroxy-3a-(prop-2-yn-1-ylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3ay



A yellow oil, 56 mg, 78% yield.

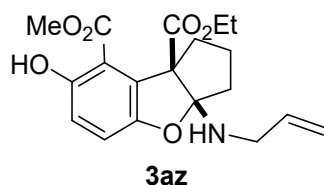
TLC: $R_f = 0.56$ (Hexane/EtOAc = 10:1) [UV, PMA].

¹H NMR ¹H NMR (500 MHz, CDCl₃) δ 6.95 (s, 1H), 6.86 (d, $J = 8.8$ Hz, 1H), 4.26 – 4.09 (m, 2H), 3.82 (s, 3H), 3.68 (dd, $J = 16.2, 2.5$ Hz, 1H), 3.53 (dd, $J = 16.2, 2.5$ Hz, 1H), 3.07 – 2.94 (m, 1H), 2.33 – 2.24 (m, 1H), 2.18 (s, 1H), 2.02 – 1.92 (m, 2H), 1.90 – 1.82 (m, 1H), 1.68 – 1.56 (m, 1H), 1.21 (t, $J = 7.1$ Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 171.5, 169.6, 169.5, 156.7, 156.5, 152.2, 152.2, 129.3, 129.2, 118.2, 118.1, 117.5, 117.5, 112.6, 108.4, 108.4, 81.8, 76.8, 71.0, 68.0, 61.3, 51.4, 38.3, 37.6, 32.8, 23.4, 14.2.

HRMS (ESI): C₁₉H₂₂NO₆⁺ [(M+H)⁺]: calcd.: 360.1442; found: 360.1448.

8b-ethyl 8-methyl 3a-(allylamino)-7-hydroxy-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8,8b-dicarboxylate 3az



A colorless oil, 55 mg, 76% yield.

TLC: $R_f = 0.54$ (Hexane/EtOAc = 10:1) [UV, PMA].

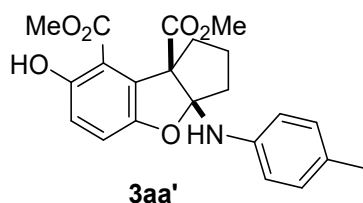
¹H NMR (400 MHz, CDCl₃) δ 10.52 (s, 1H), 6.93 (d, $J = 8.8$ Hz, 1H), 6.85 (d, $J = 8.8$ Hz, 1H), 5.96 – 5.82 (m, 1H), 5.15 (dq, $J = 17.1, 1.7$ Hz, 1H), 5.04 (dq, $J = 10.3, 1.5$ Hz, 1H), 4.14 (q, J

= 7.2 Hz, 2H), 3.82 (s, 3H), 3.58 – 3.47 (m, 1H), 3.44 – 3.34 (m, 1H), 3.00 (td, $J = 13.1, 6.8$ Hz, 1H), 2.36 – 2.26 (m, 1H), 2.01 – 1.92 (m, 2H), 1.89 – 1.77 (m, 1H), 1.70 – 1.46 (m, 3H), 1.19 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 170.8, 168.7, 155.5, 151.4, 135.7, 128.3, 117.0, 116.5, 114.4, 112.4, 107.4, 75.7, 67.0, 60.1, 57.5, 50.4, 45.0, 37.3, 36.9, 22.5, 17.4, 13.3.

HRMS (ESI): $\text{C}_{19}\text{H}_{24}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 362.1598; found: 362.1598

Dimethyl 7-hydroxy-3a-(*p*-tolylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[*b*]benzofuran-8,8b-dicarboxylate 3aa'



A yellow oil, 71 mg, 89% yield.

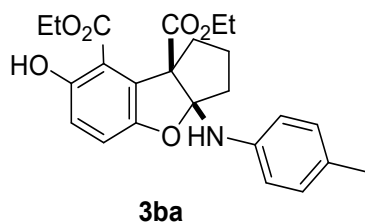
TLC: $R_f = 0.55$ (Hexane/EtOAc = 10:1) [UV, PMA].

^1H NMR (400 MHz, CDCl_3) δ 10.47 (s, 1H), 6.96 (d, $J = 8.1$ Hz, 2H), 6.89 (d, $J = 8.9$ Hz, 1H), 6.87 – 6.83 (m, 2H), 6.81 (d, $J = 8.8$ Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 2.96 (ddd, $J = 13.4, 11.4, 6.9$ Hz, 1H), 2.42 – 2.30 (m, 1H), 2.20 (s, 3H), 2.15 – 2.05 (m, 1H), 1.93 – 1.86 (m, 1H), 1.85 – 1.77 (m, 1H), 1.64 – 1.52 (m, 1H).

^{13}C NMR (101 MHz, CDCl_3) δ 171.4, 168.6, 155.8, 151.2, 139.7, 131.1, 128.3, 127.9, 121.4, 117.4, 116.9, 110.6, 107.3, 68.0, 51.4, 50.5, 38.1, 37.4, 22.8, 19.7.

HRMS (ESI): $\text{C}_{22}\text{H}_{24}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 398.1598; found: 398.1599.

diethyl 7-hydroxy-3a-(*p*-tolylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[*b*]benzofuran-8,8b-dicarboxylate 3ba



A dark brown oil, 69 mg, 81% yield.

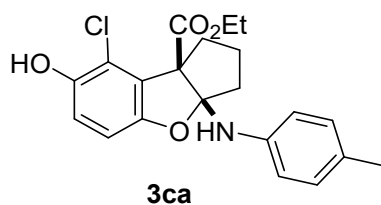
TLC: $R_f = 0.55$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 10.69 (s, 1H), 7.04 (d, $J = 8.1$ Hz, 2H), 6.97 (d, $J = 8.8$ Hz, 1H), 6.93 – 6.87 (m, 3H), 4.60 – 4.45 (m, 1H), 4.27 – 4.06 (m, 3H), 3.11 – 2.98 (m, 1H), 2.55 – 2.40 (m, 1H), 2.29 (s, 3H), 2.17 (td, $J = 12.2, 6.5$ Hz, 1H), 2.10 – 2.01 (m, 1H), 1.94 – 1.86 (m, 1H), 1.74 – 1.63 (m, 1H), 1.39 (t, $J = 7.2$ Hz, 3H), 1.20 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 172.0, 169.5, 156.8, 152.2, 140.8, 131.9, 129.3, 129.0, 122.0, 118.3, 117.7, 111.6, 108.9, 68.8, 61.6, 61.3, 39.0, 38.6, 23.9, 20.7, 14.2, 14.0.

HRMS (ESI): $\text{C}_{24}\text{H}_{28}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 426.1911; found: 426.1915.

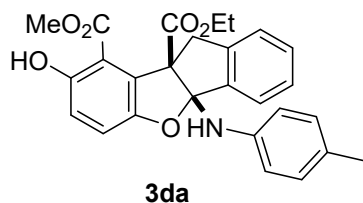
ethyl(3aS,8bR)-8-chloro-7-hydroxy-3a-(p-tolylamino)-1,2,3,3a-tetrahydro-8bH-cyclopenta[b]benzofuran-8b-carboxylate 3ca



Trace amount of product confirmed by HRMS.

HRMS (ESI): $\text{C}_{21}\text{H}_{23}\text{ClNO}_4^+$ [(M+H) $^+$]: calcd.: 388.1310; found: 388.1310.

9b-ethyl 9-methyl 8-hydroxy-4b-(p-tolylamino)-4b,10-dihydro-9bH-indeno[1,2-b]benzofuran-9,9b-dicarboxylate 3da



A brown oil, 82 mg, 89% yield.

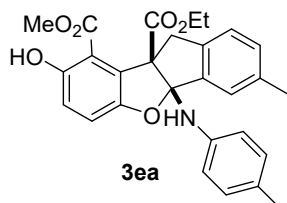
TLC: $R_f = 0.55$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.53 (s, 1H), 7.38 (d, $J = 7.7$ Hz, 1H), 7.28 (d, $J = 7.4$ Hz, 1H), 7.24 – 7.14 (m, 2H), 6.95 (d, $J = 9.0$ Hz, 1H), 6.79 (dd, $J = 16.7, 8.4$ Hz, 3H), 6.46 (d, $J = 7.9$ Hz, 2H), 4.44 (s, 1H), 4.35 (d, $J = 17.4$ Hz, 1H), 3.82 (s, 3H), 3.75 (d, $J = 7.9$ Hz, 1H), 3.45 – 3.32 (m, 1H), 3.24 (d, $J = 17.4$ Hz, 1H), 2.11 (s, 3H), 0.85 (t, $J = 7.2$ Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.2, 168.4, 156.5, 149.5, 145.3, 142.6, 139.2, 138.8, 132.9, 130.0, 128.8, 128.7, 128.4, 128.4, 128.1, 127.0, 126.2, 125.4, 123.6, 118.0, 117.5, 117.4, 110.4, 107.4, 75.7, 66.6, 61.7, 60.4, 58.2, 50.8, 43.1, 19.5, 13.1, 12.8.

HRMS (ESI): $\text{C}_{27}\text{H}_{26}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 460.1755; found: 460.1760

9b-ethyl 9-methyl 8-hydroxy-3-methyl-4b-(p-tolylamino)-4b,10-dihydro-9bH-indeno-[1,2-b]benzofuran-9,9b-dicarboxylate 3ea



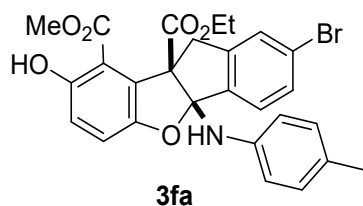
A brown oil, 81 mg, 86% yield.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.62 (s, 1H), 7.29 (s, 1H), 7.19 (d, $J = 1.7$ Hz, 1H), 7.13 (d, $J = 7.8$ Hz, 1H), 7.03 (d, $J = 8.9$ Hz, 1H), 6.89 (d, $J = 8.9$ Hz, 1H), 6.85 (d, $J = 8.3$ Hz, 2H), 6.54 (d, 2H), 4.52 (s, 1H), 4.37 (d, $J = 17.2$ Hz, 1H), 3.89 (s, 3H), 3.84 – 3.72 (m, 1H), 3.47 – 3.34 (m, 1H), 3.27 (d, $J = 17.2$ Hz, 1H), 2.34 (s, 3H), 2.19 (s, 3H), 0.91 (t, $J = 7.2$ Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 170.6, 168.6, 156.3, 149.5, 140.2, 139.6, 137.3, 136.6, 130.7, 129.0, 123.7, 123.6, 117.6, 117.3, 116.5, 111.0, 107.4, 66.4, 60.2, 50.7, 43.6, 20.2, 19.4, 12.7.

HRMS (ESI): $\text{C}_{27}\text{H}_{26}\text{NO}_6^+$ [(M+H) $^+$]: calcd.: 474.1911; found: 474.1920.

9b-ethyl 9-methyl 2-bromo-8-hydroxy-4b-(p-tolylamino)-4b,10-dihydro-9bH-indeno[1,2-b]benzofuran-9,9b-dicarboxylate 3fa



A dark brown oil, 90 mg, 84% yield.

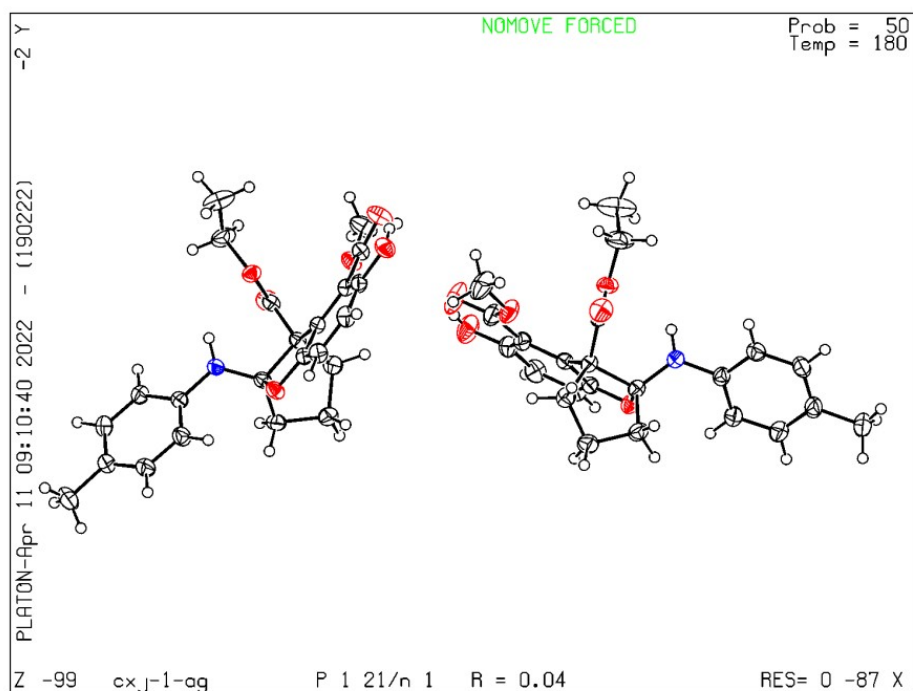
TLC: $R_f = 0.55$ (Hexane/EtOAc = 10:1) [UV, PMA].

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.50 (s, 1H), 7.31 (d, 2H), 7.18 (d, 1H), 6.94 (d, $J = 8.9$ Hz, 1H), 6.80 (dd, $J = 12.7, 8.5$ Hz, 3H), 6.51 – 6.42 (m, 2H), 4.39 – 4.29 (m, 2H), 3.81 (s, 3H), 3.82 – 3.69 (m, 1H), 3.50 – 3.37 (m, 1H), 3.20 (d, $J = 17.6$ Hz, 1H), 2.12 (s, 3H), 0.86 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 171.1, 169.3, 157.5, 150.5, 143.6, 140.2, 139.8, 130.9, 129.8, 129.3, 129.1, 128.0, 126.4, 124.5, 118.9, 118.6, 118.3, 111.4, 108.4, 67.6, 61.4, 51.6, 44.0, 29.6, 20.4, 13.7.

HRMS (ESI): $\text{C}_{27}\text{H}_{24}\text{BrNO}_6^+$ [(M+H) $^+$]: calcd.: 538.0860; found: 538.0866

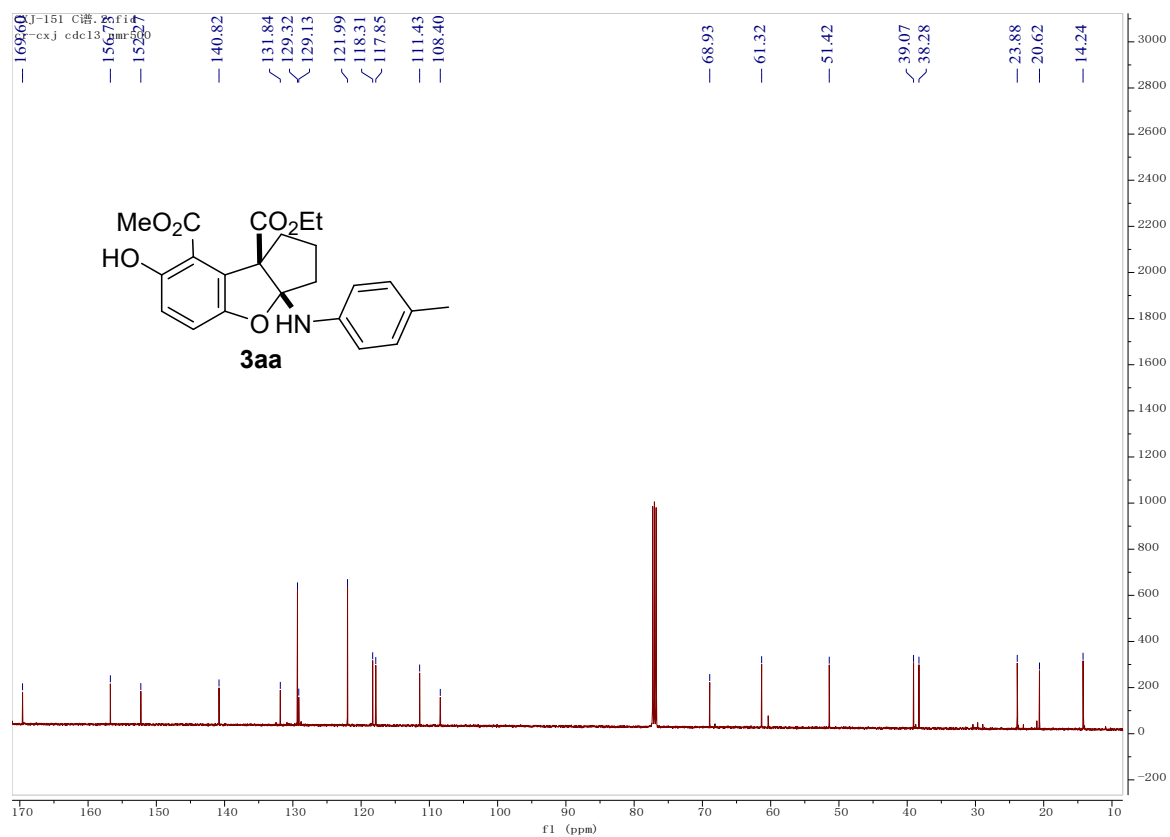
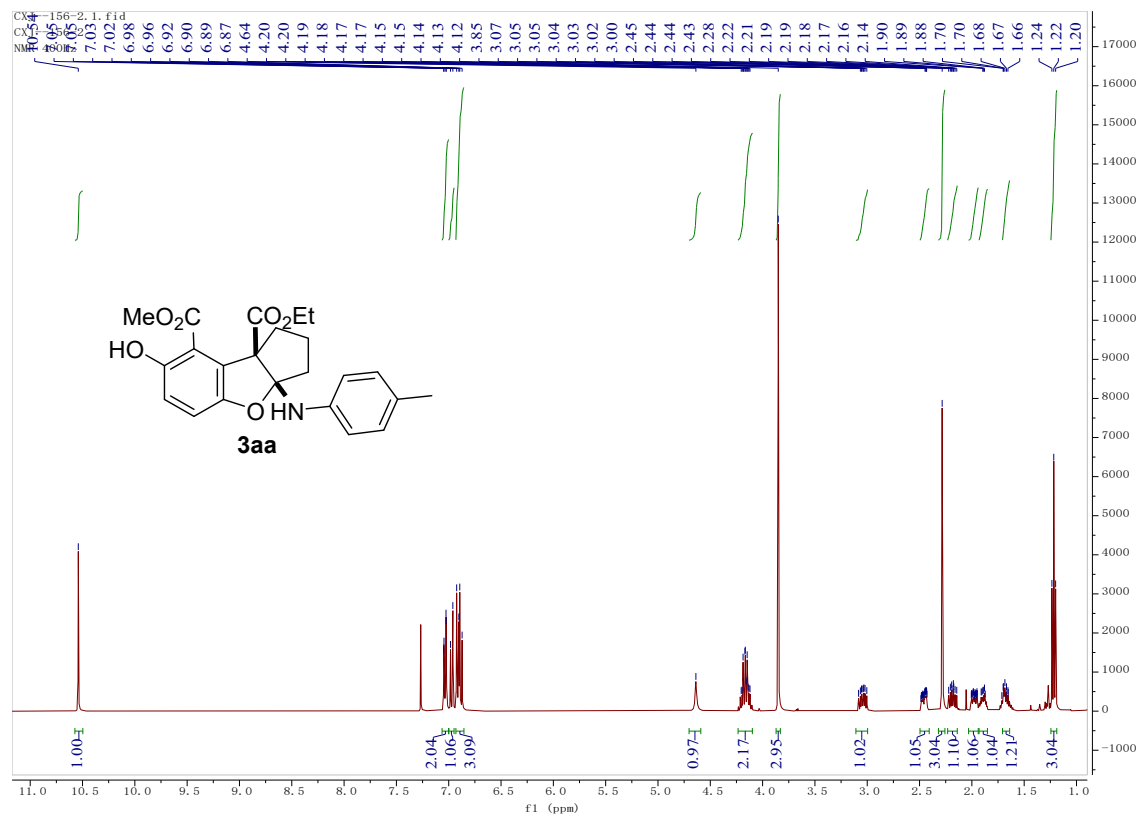
6. X-ray Crystallographic Analysis of 3aa

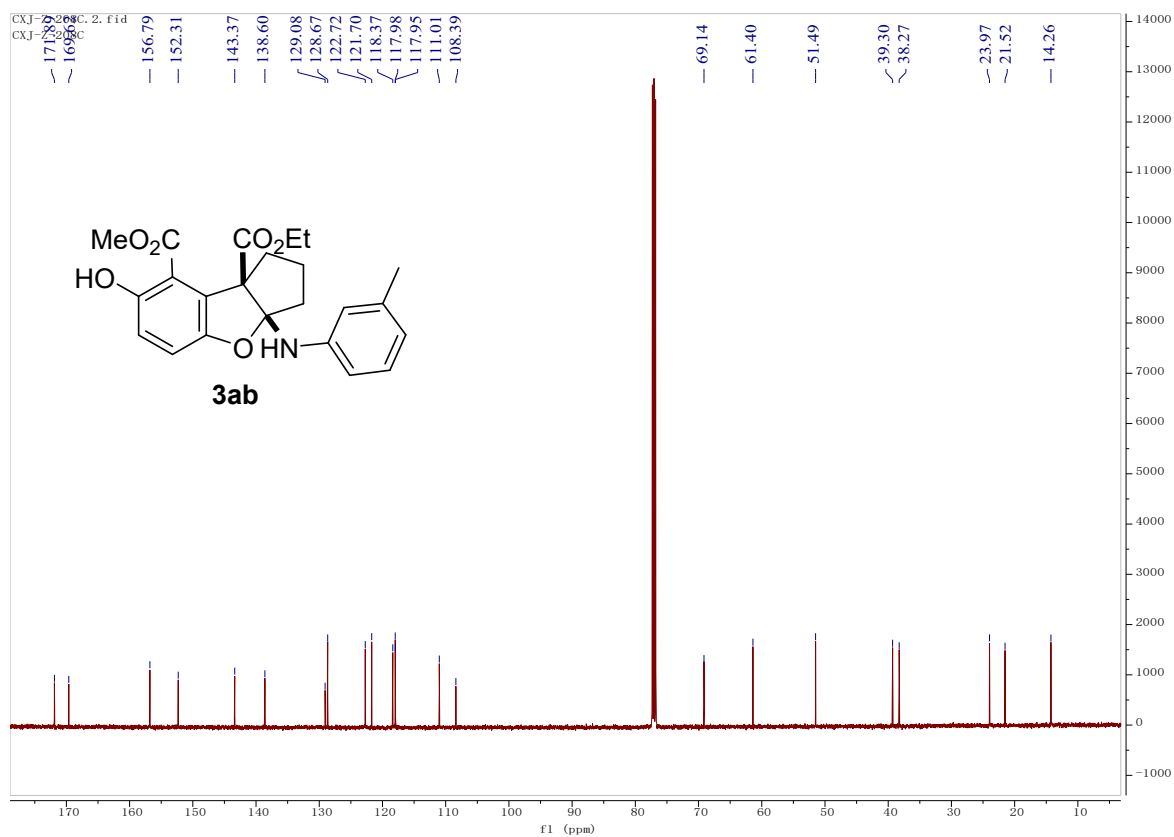
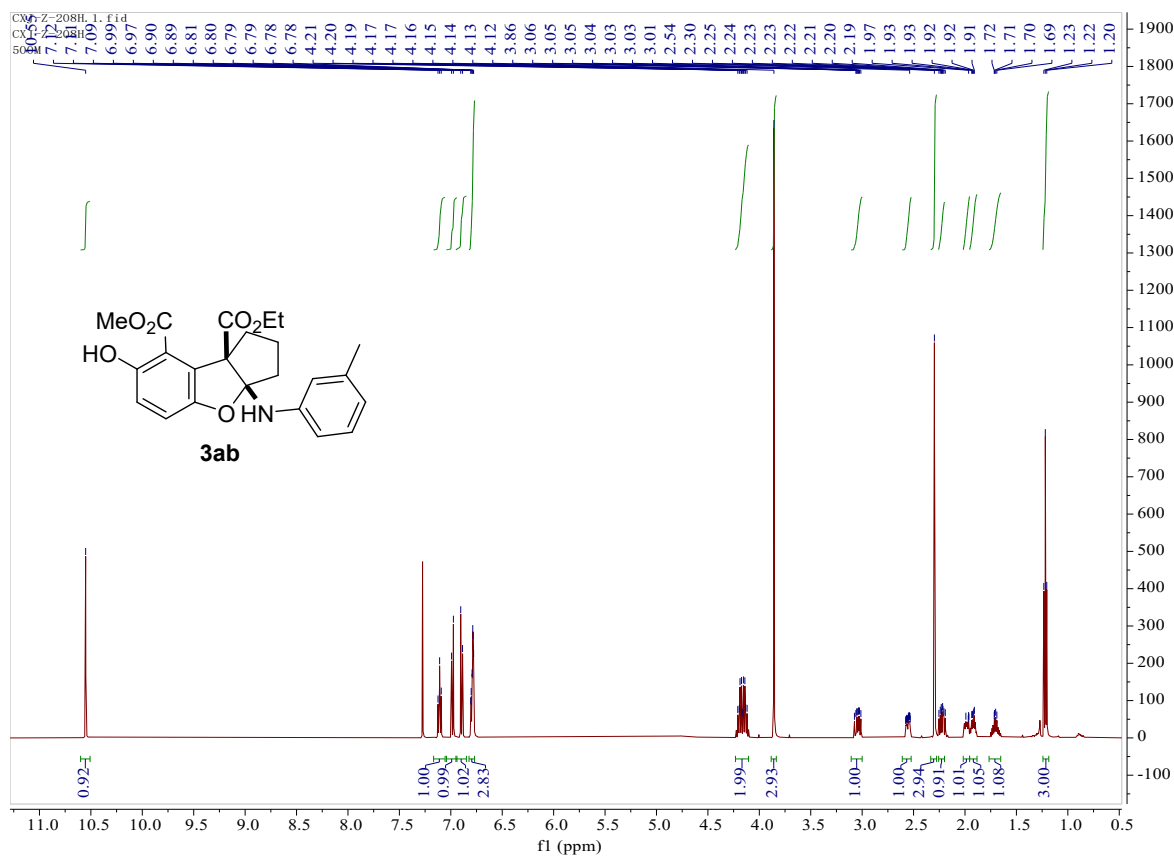


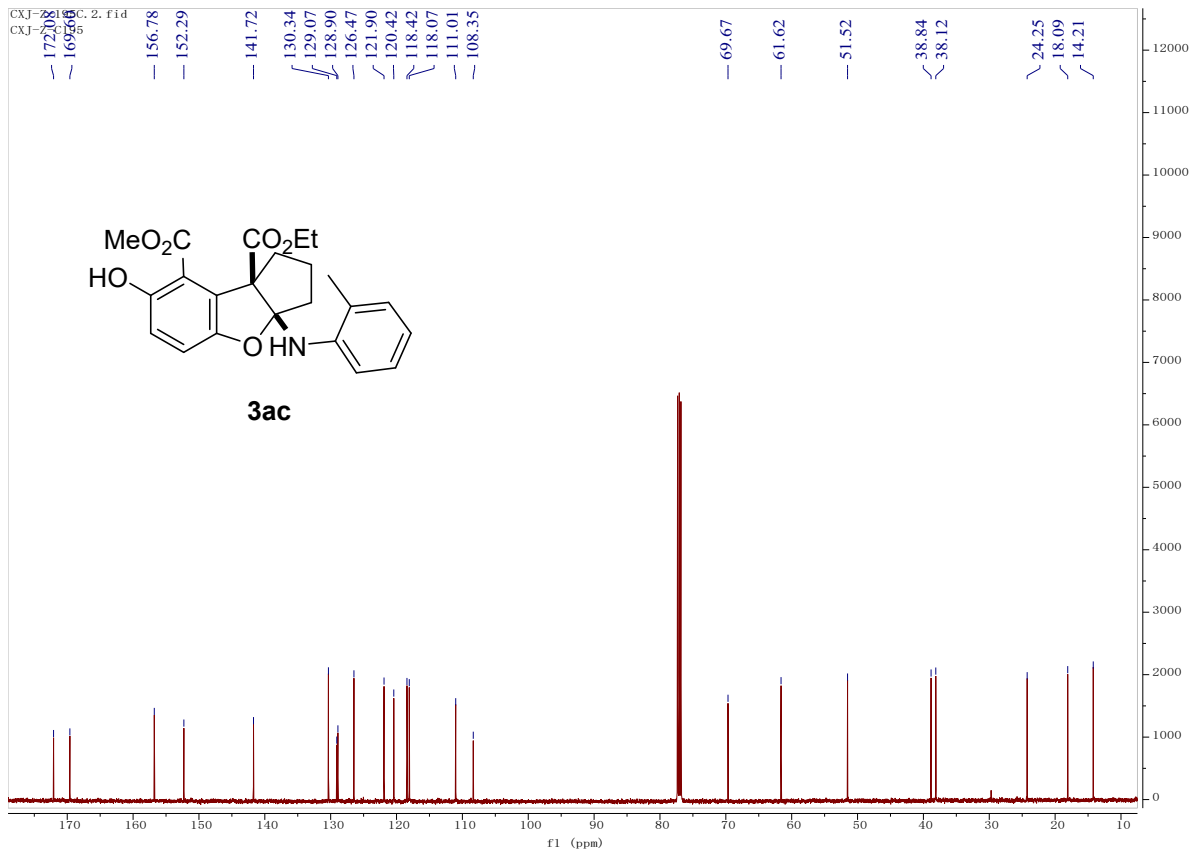
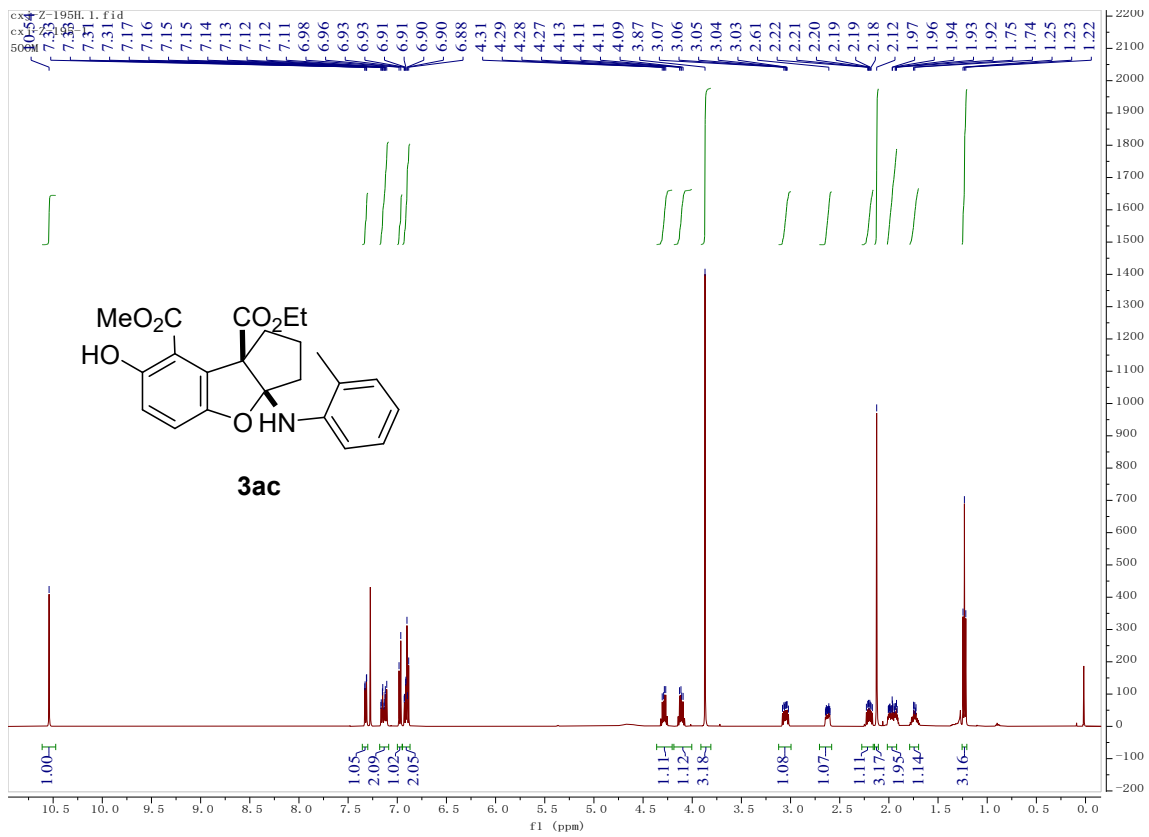
Bond precision	C-C = 0.0019 Å	Wavelength=1.54184	
Cell	a=20.52336(13) alpha=90	b=8.40993(5) beta=98.5520(6)	c=25.93692(17) gamma=90
Temperature	180 K		
Volume	Calculated 4426.94(5)	Reported 4426.94(5)	
Space group	P 21/n	P 1 21/n 1	
Hall group	-P 2yn	-P 2yn	
Moiety formula	C ₂₃ H ₂₅ NO ₆ ⁺ [solvent]	2(C ₂₃ H ₂₅ NO ₆)	
Sum formula	C ₄₂ H ₄₈ N ₂ O ₆ S	C ₄₂ H ₄₈ N ₂ O ₆ S	
Mr	411.44	822.88	
Dx, g cm ⁻³	1.235	1.235	
Z	8	4	
Mu (mm ⁻¹)	0.737	0.737	
F000	1744.0	1744.0	
F000'	1749.71		
h,k,lmax	25,10,32	25,10,32	
Nref	9282	9077	
Tmin,Tmax	0.876,0.929		
Tmin'	0.863		
Correction method=	Not given		

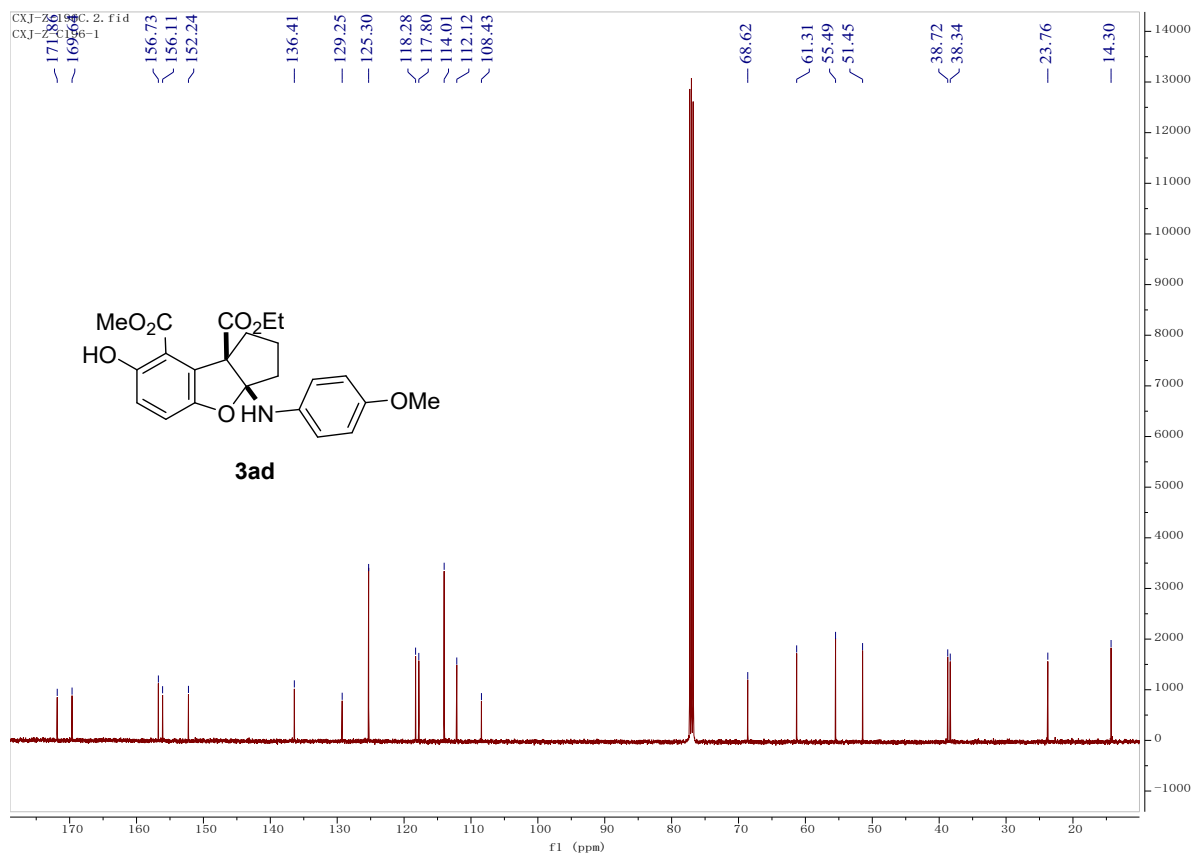
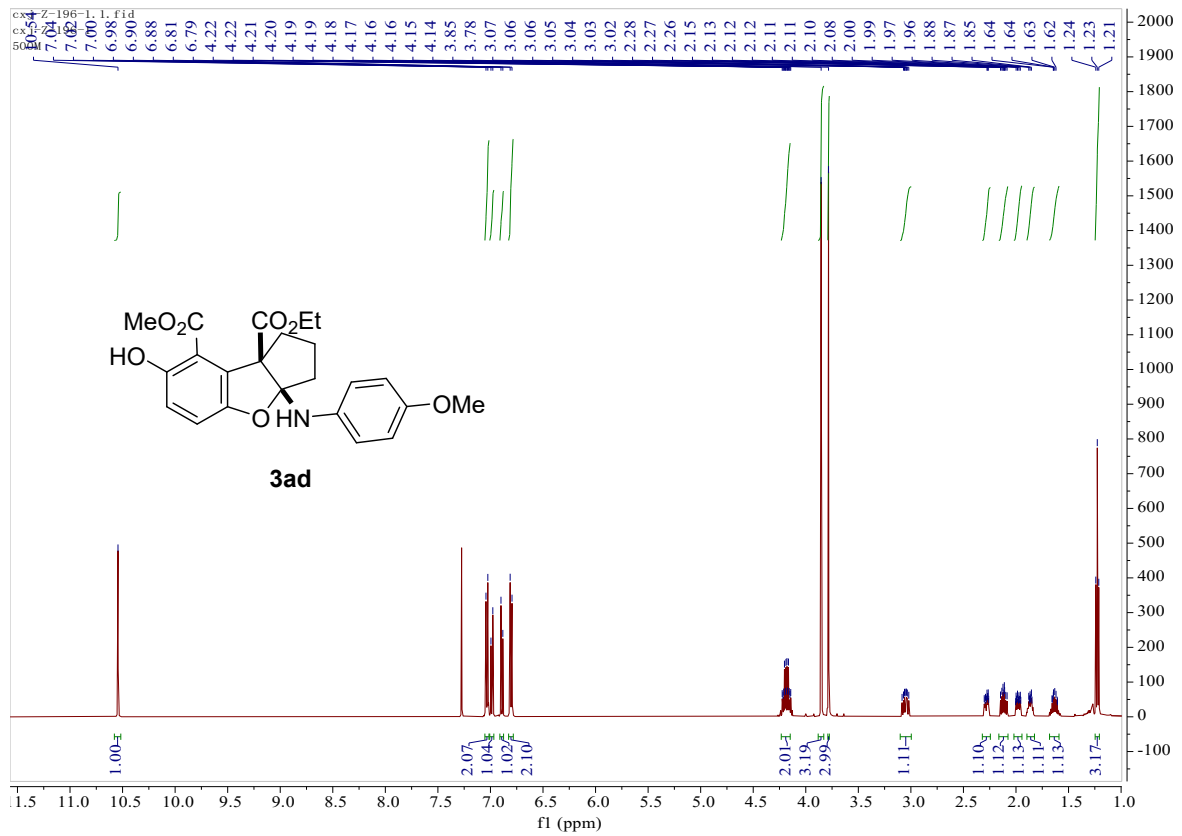
Data completeness= 0.978	Theta(max)= 76.327
R(reflections)= 0.0448(8426)	wR2(reflections)= 0.1270 (7236)
S = 1.032	Npar= 549

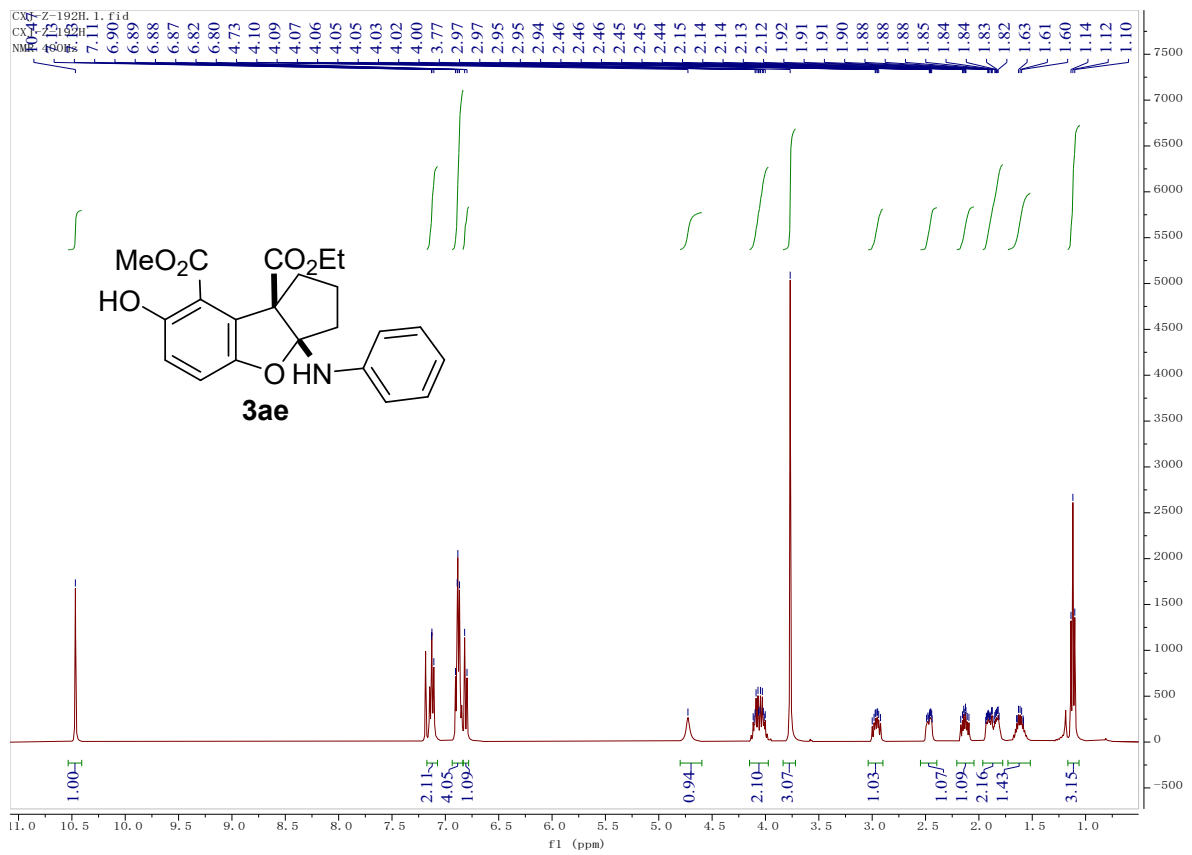
7. Copies of ^1H , ^{13}C and ^{19}F NMR Spectra of Products

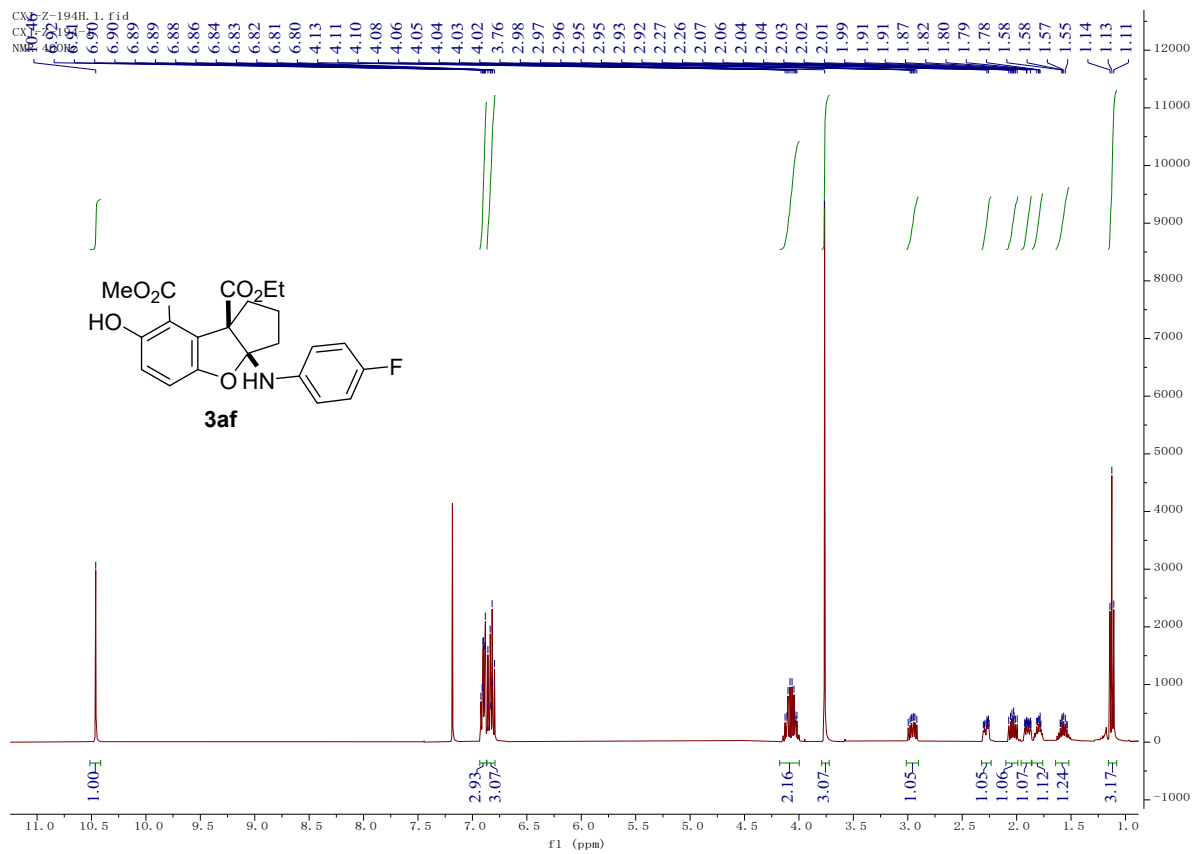
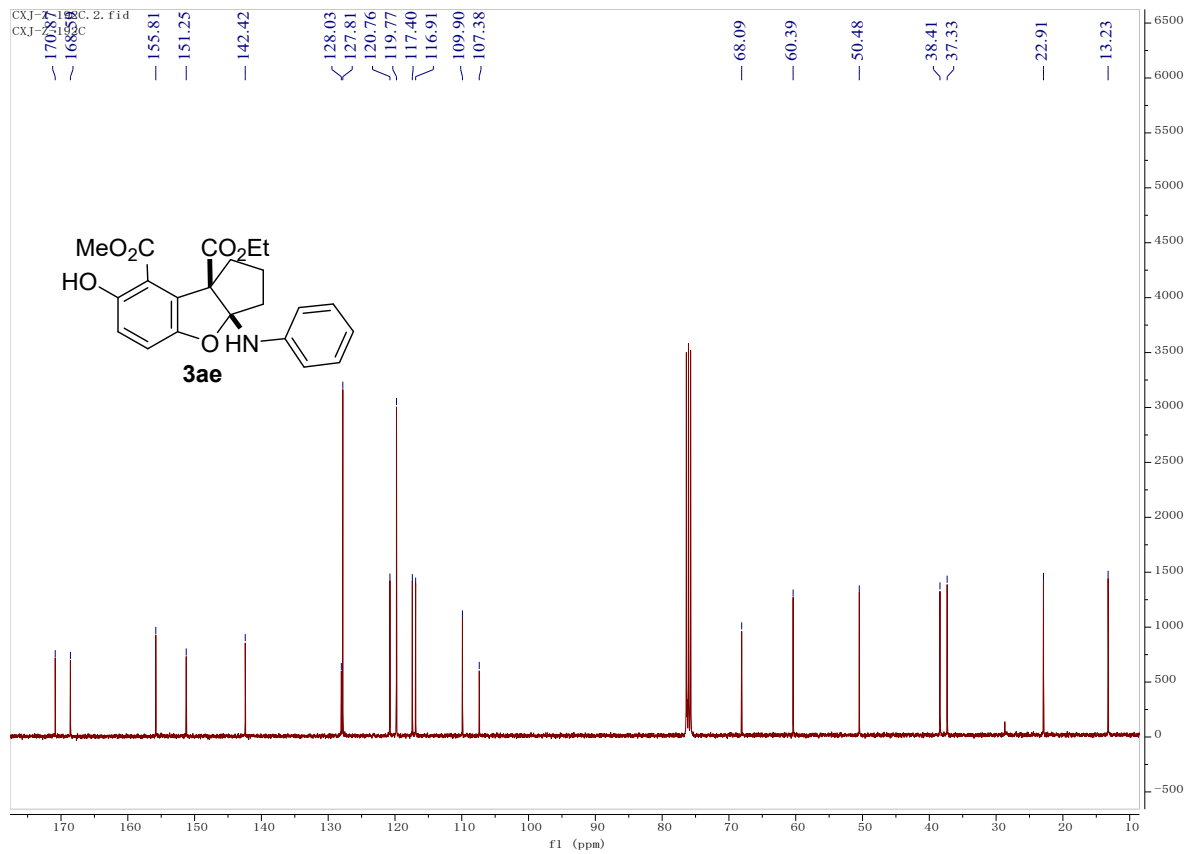


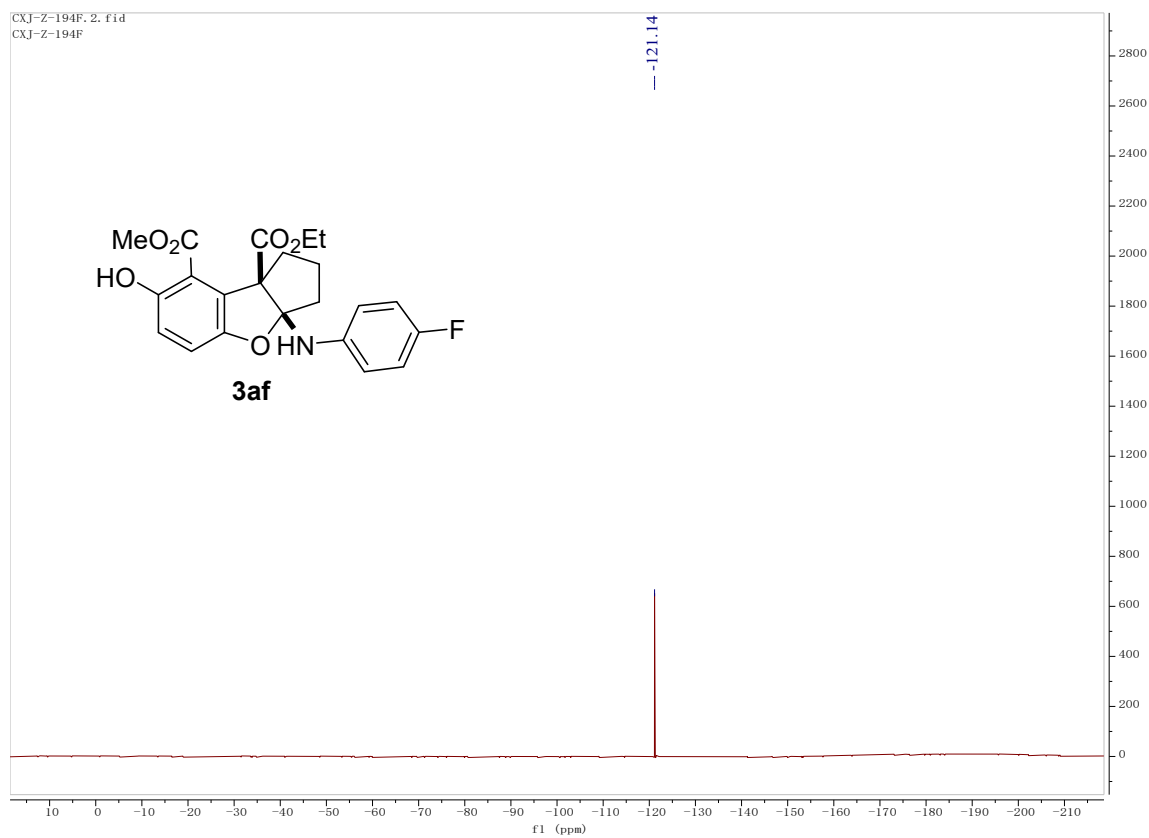
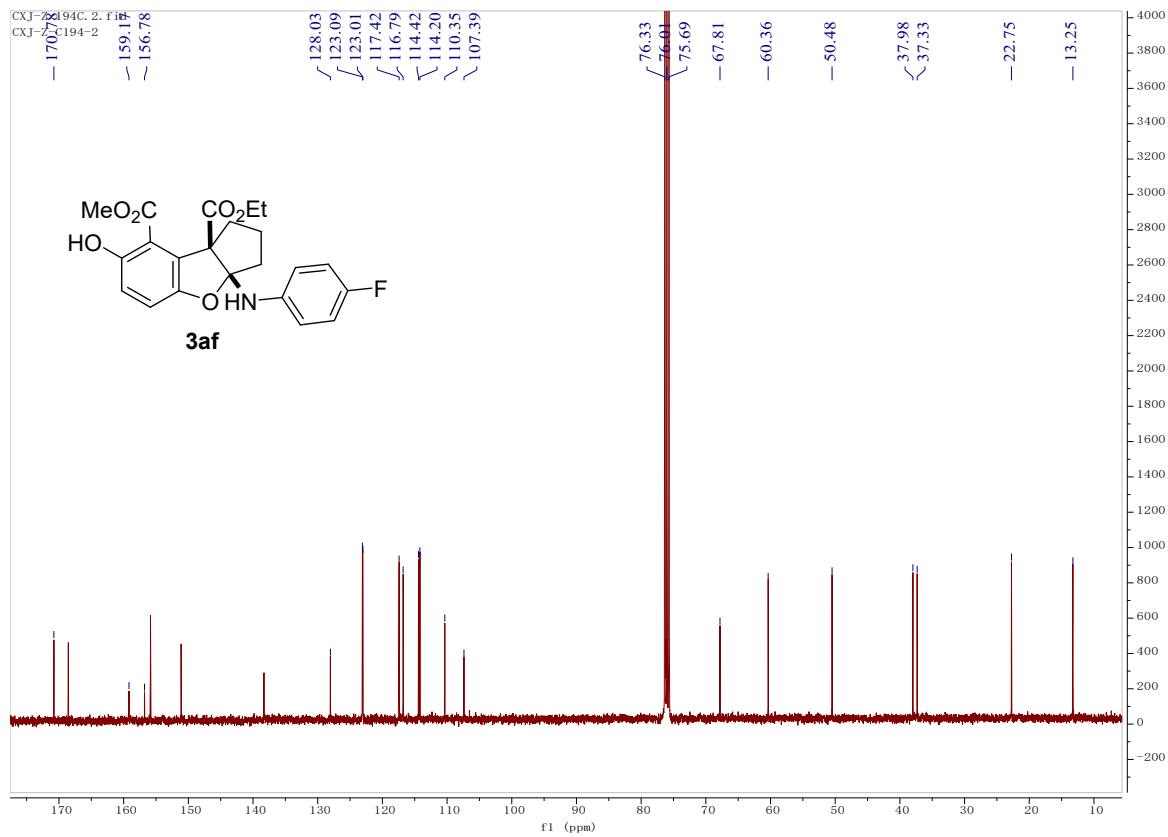


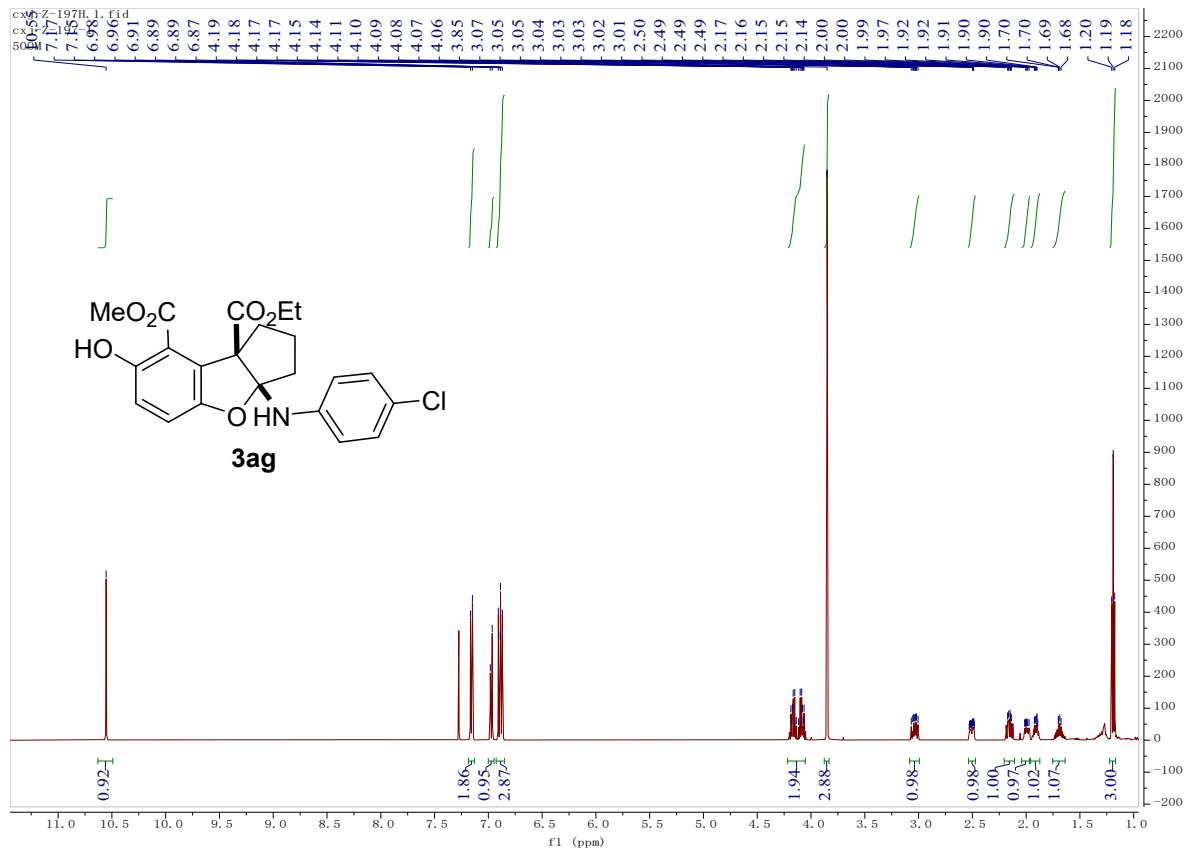


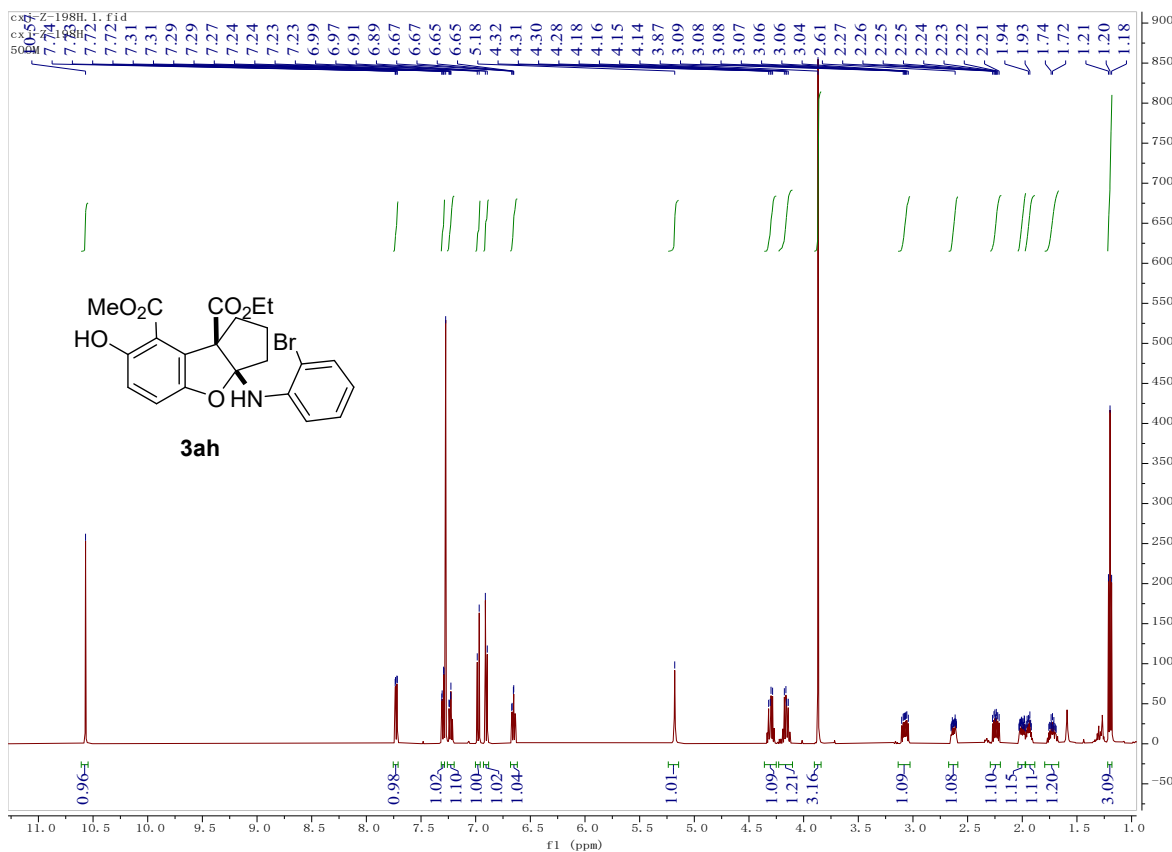
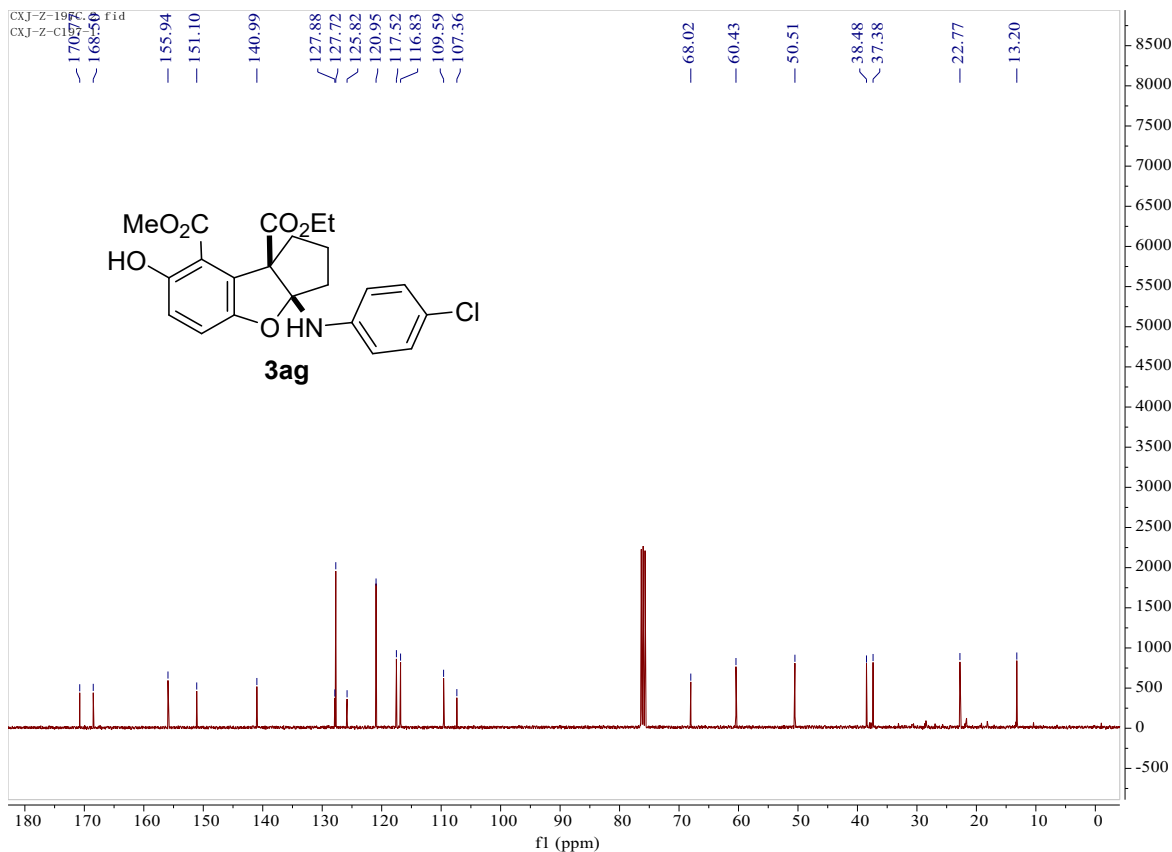


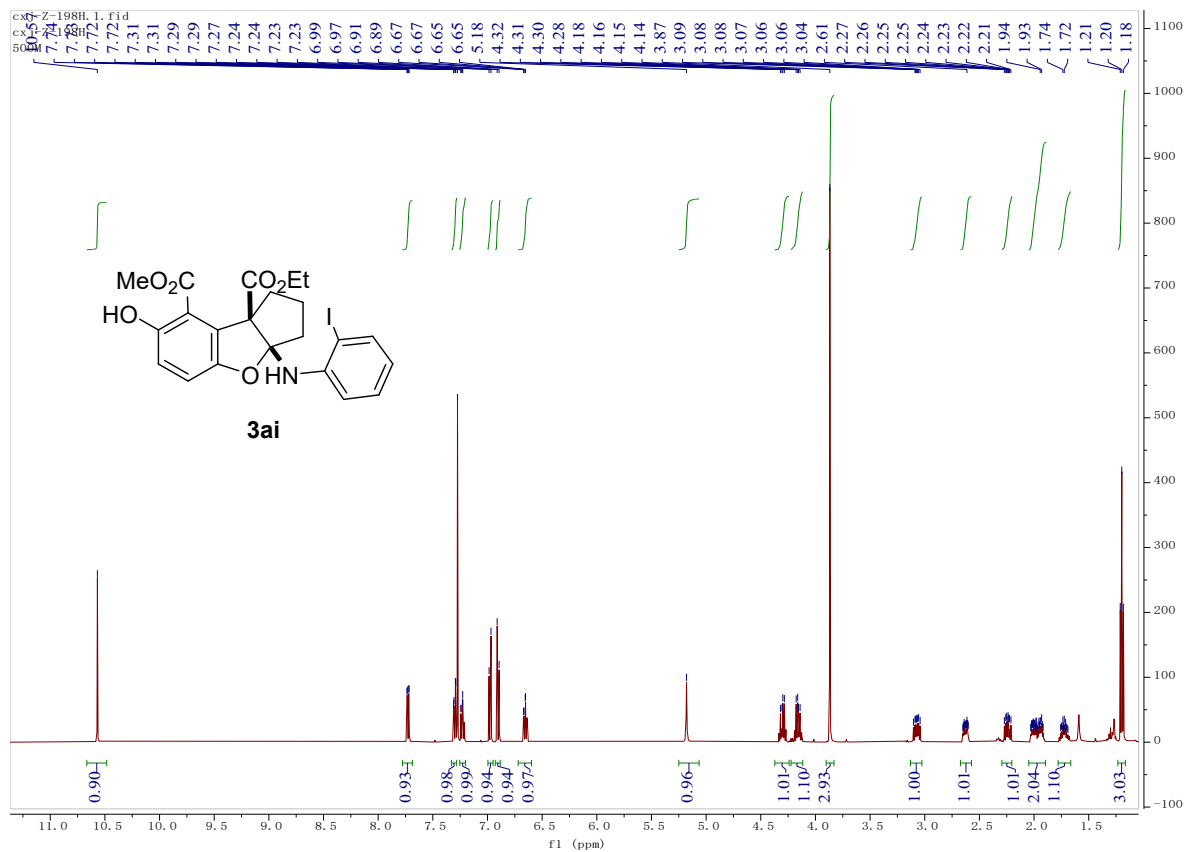
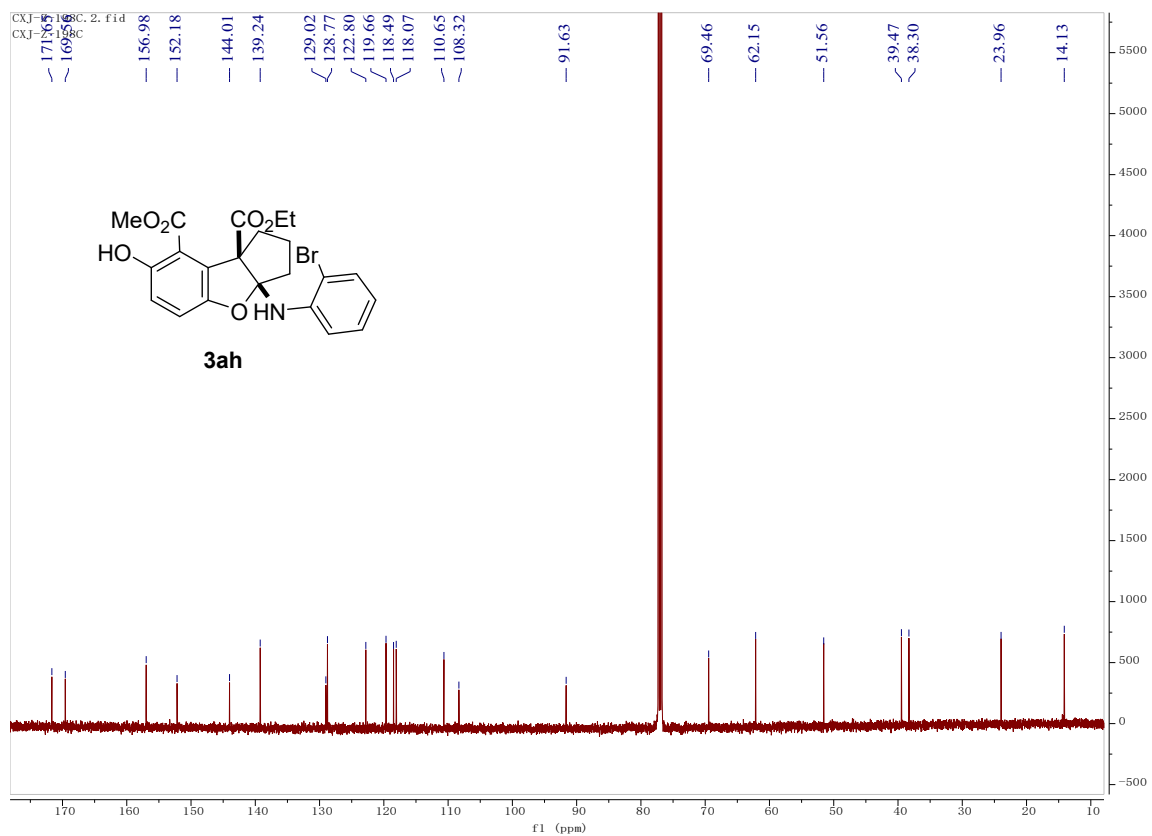


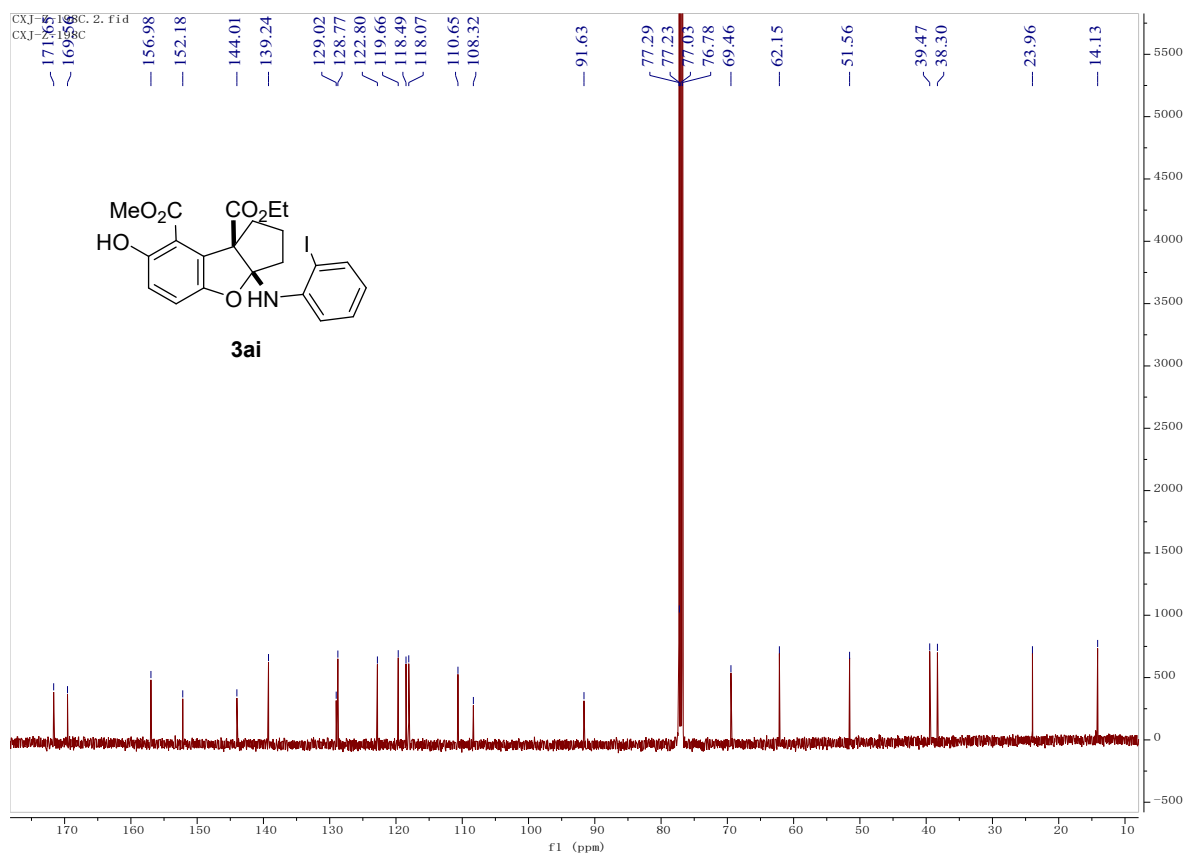


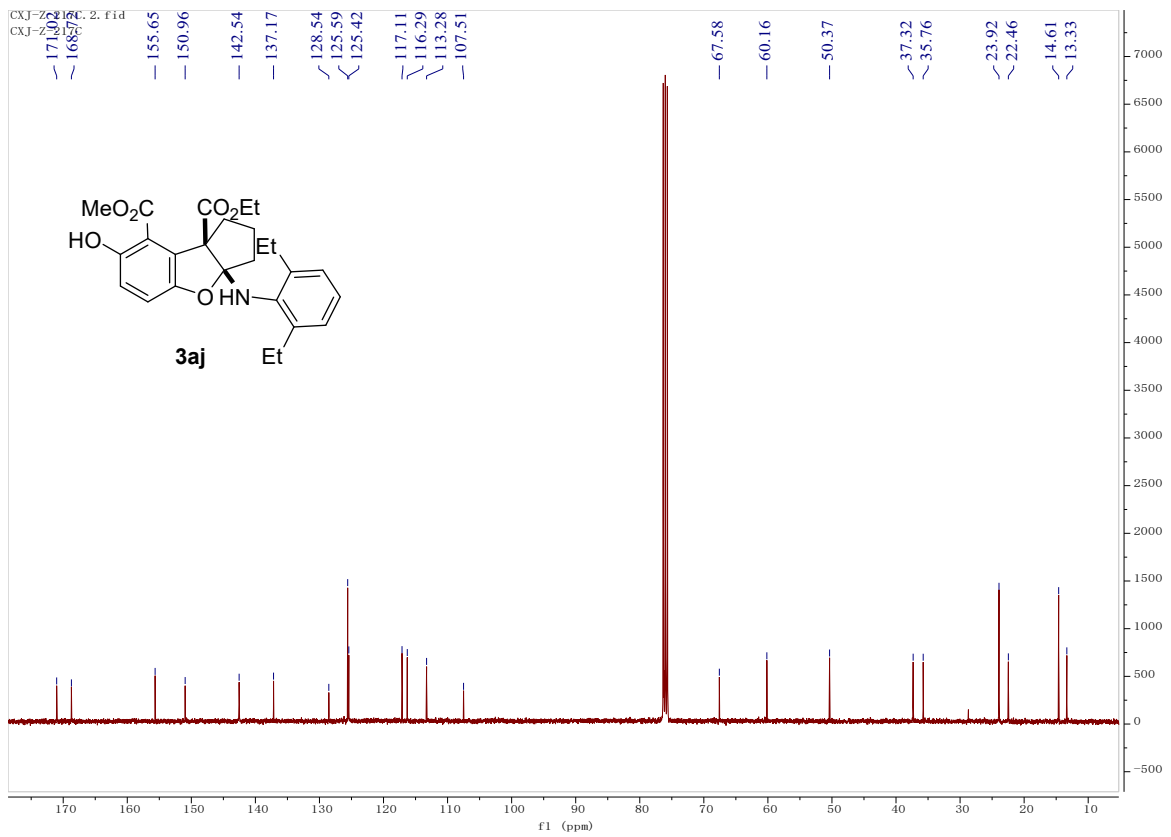
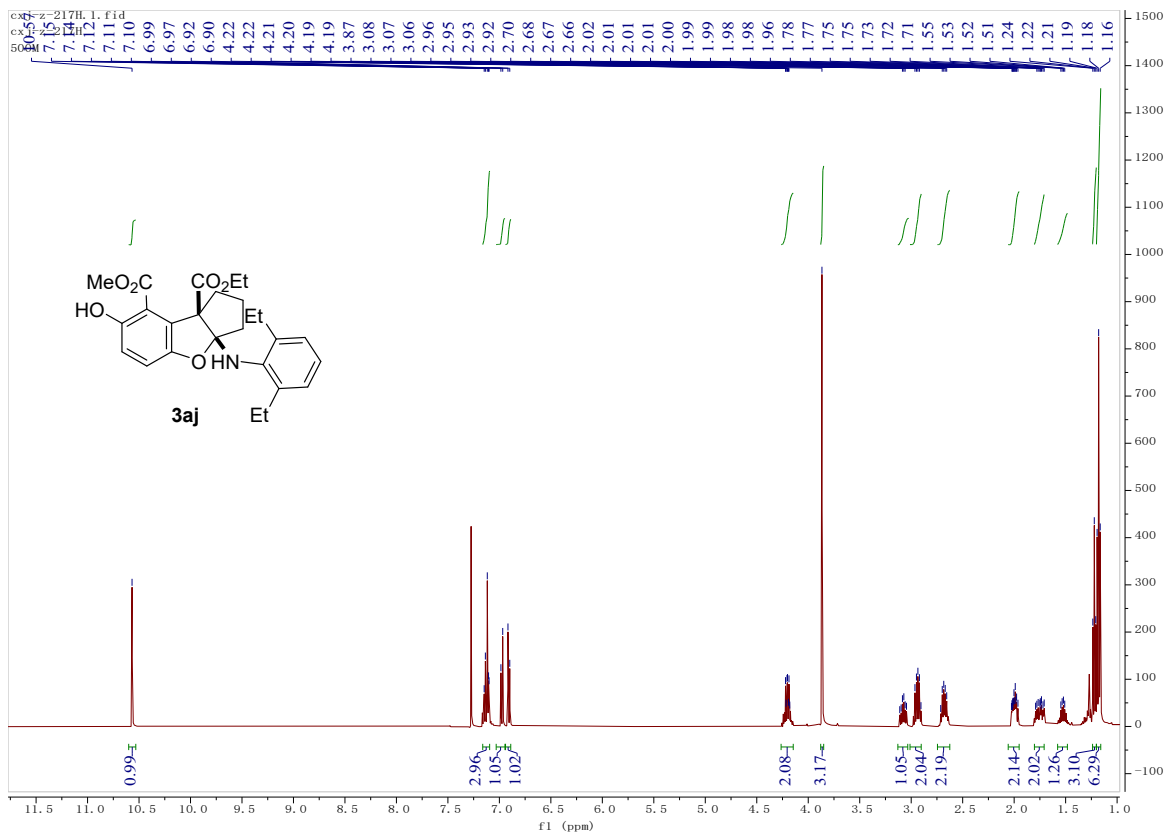


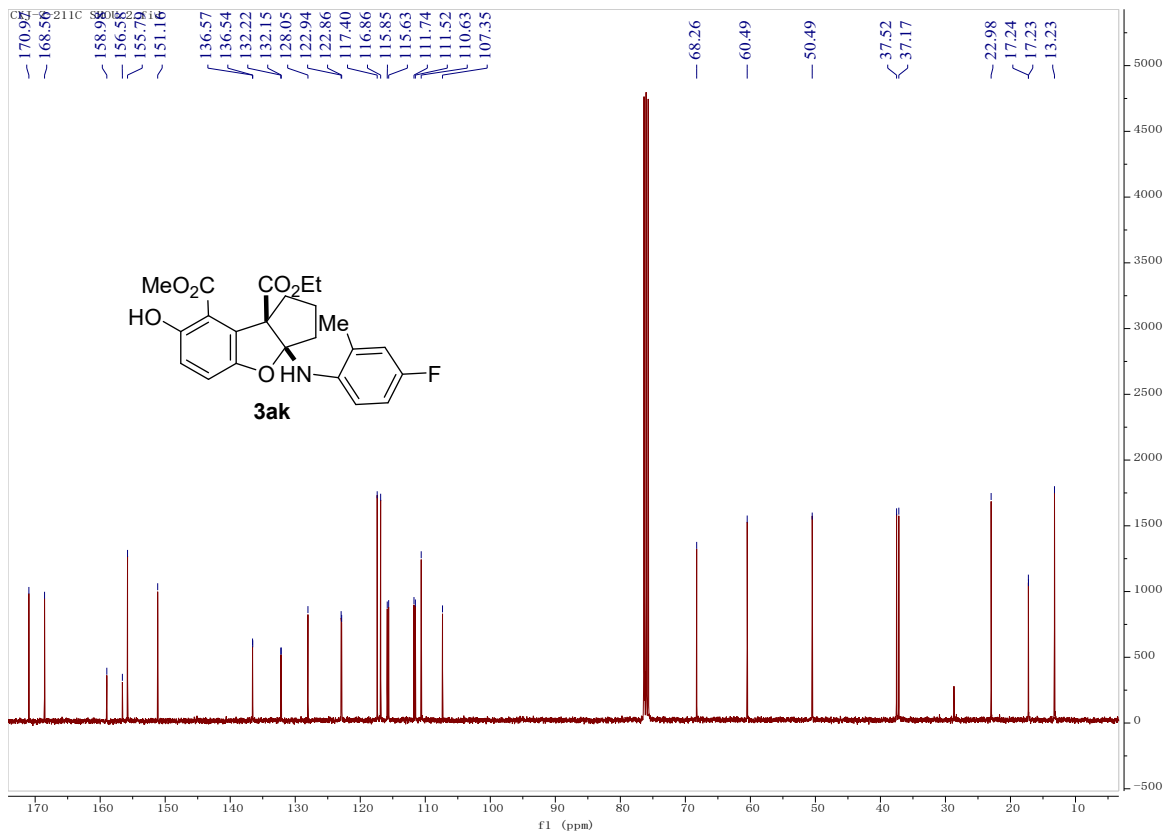
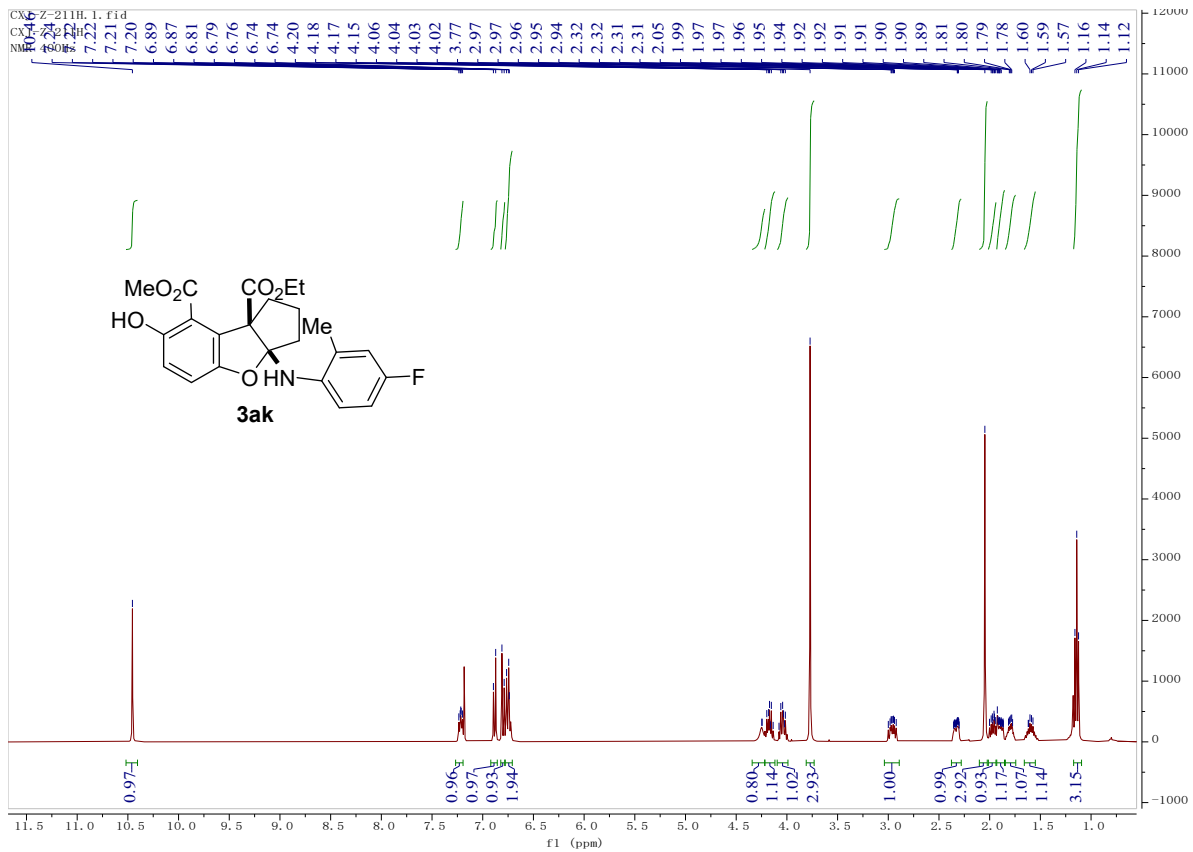


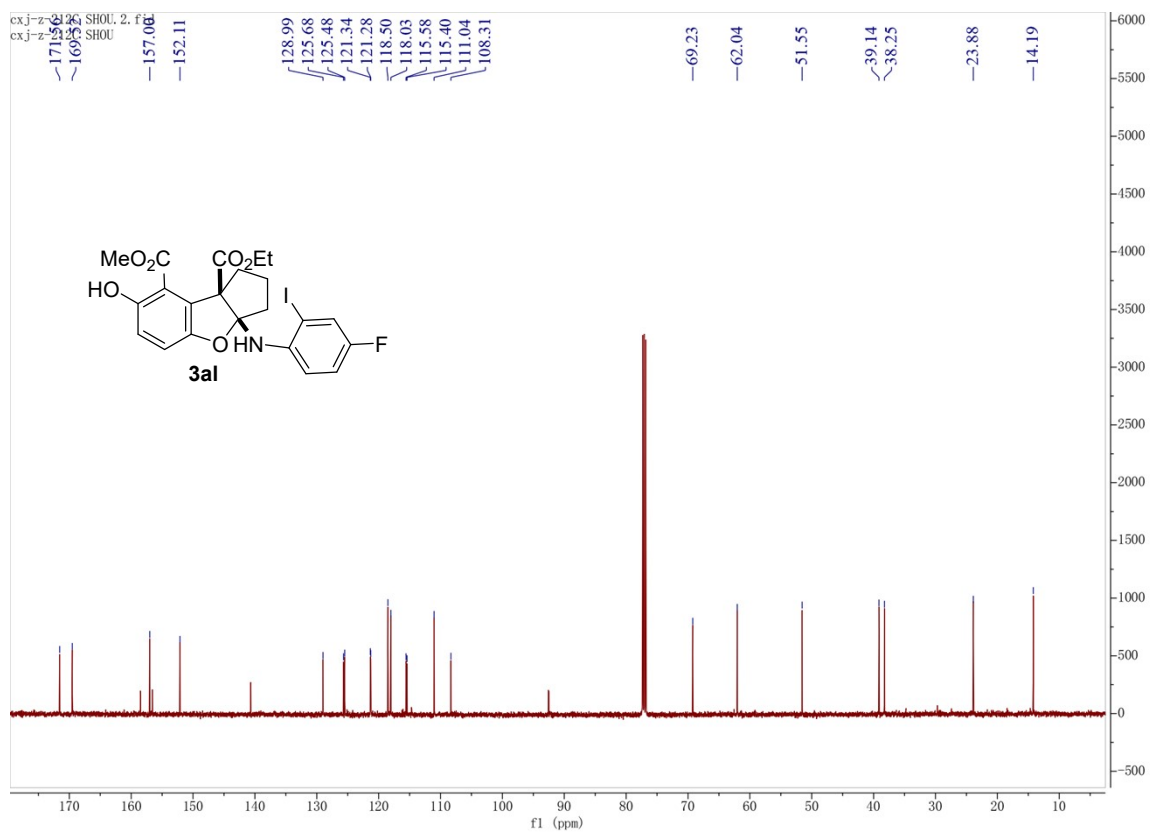
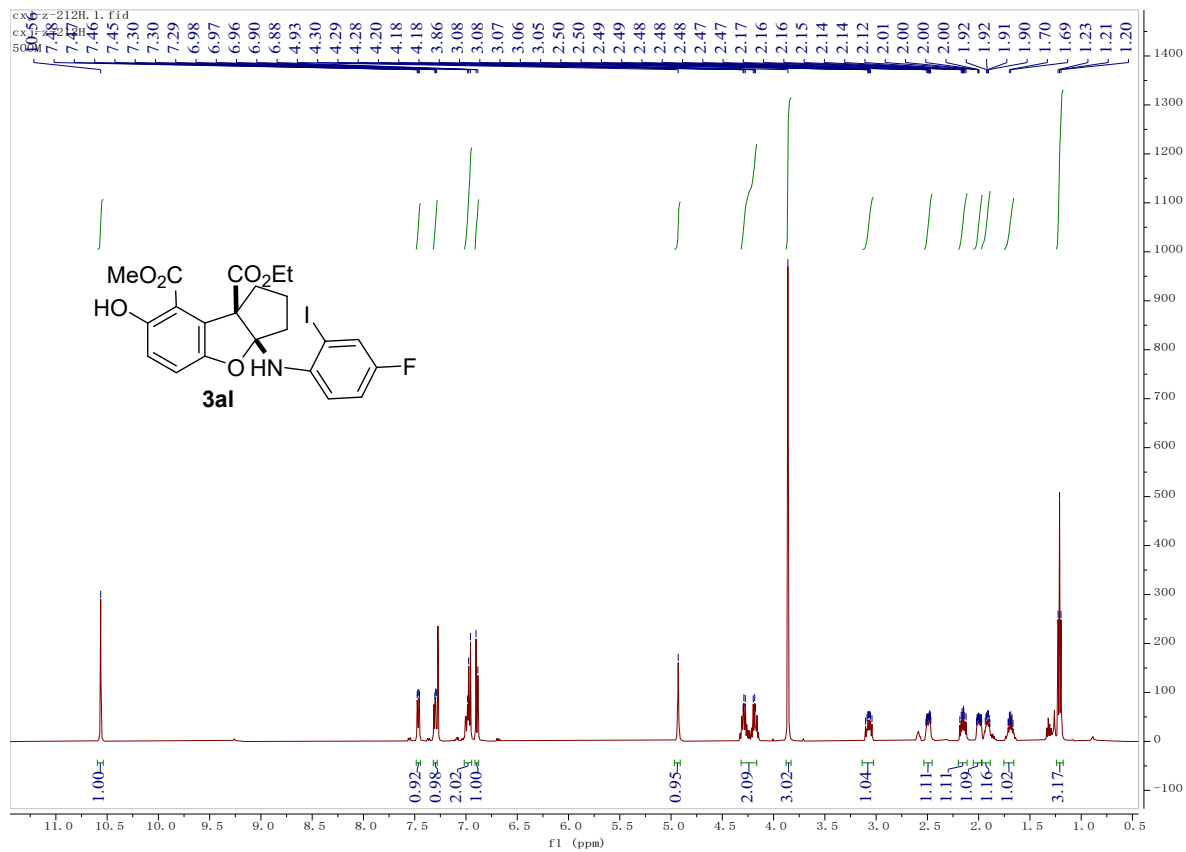


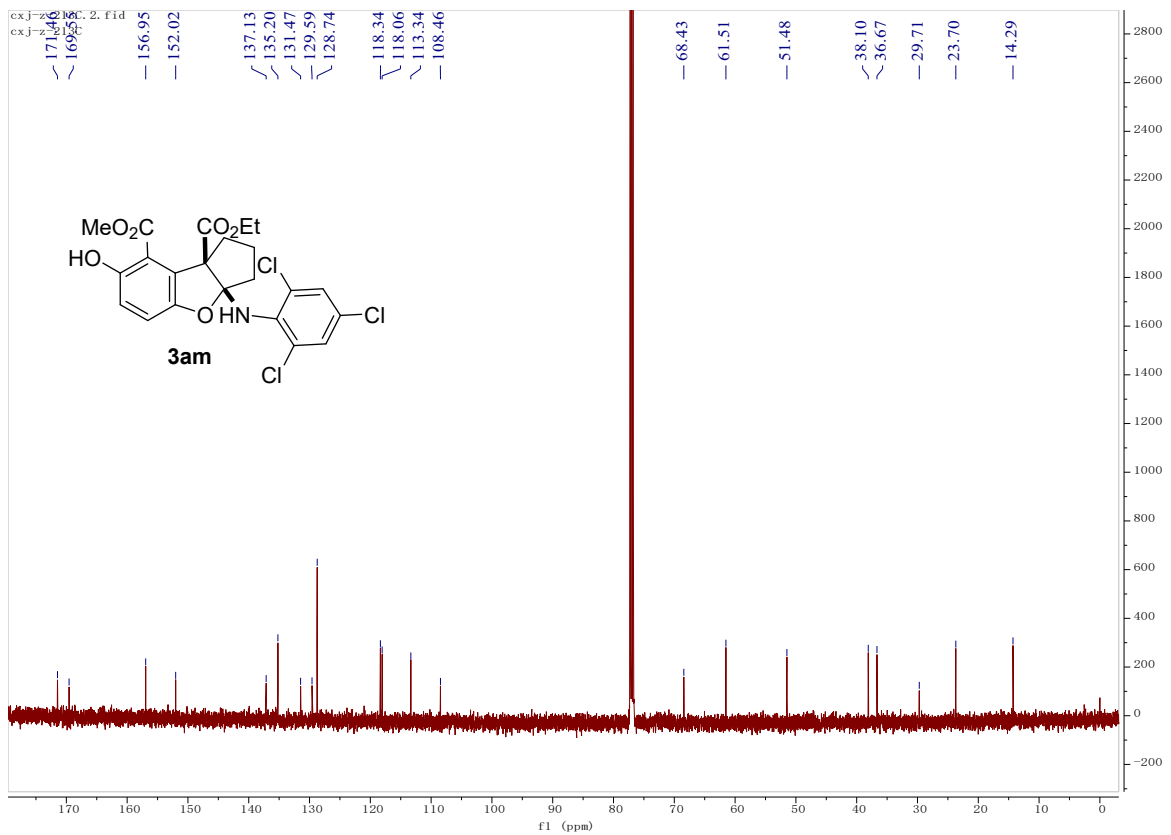
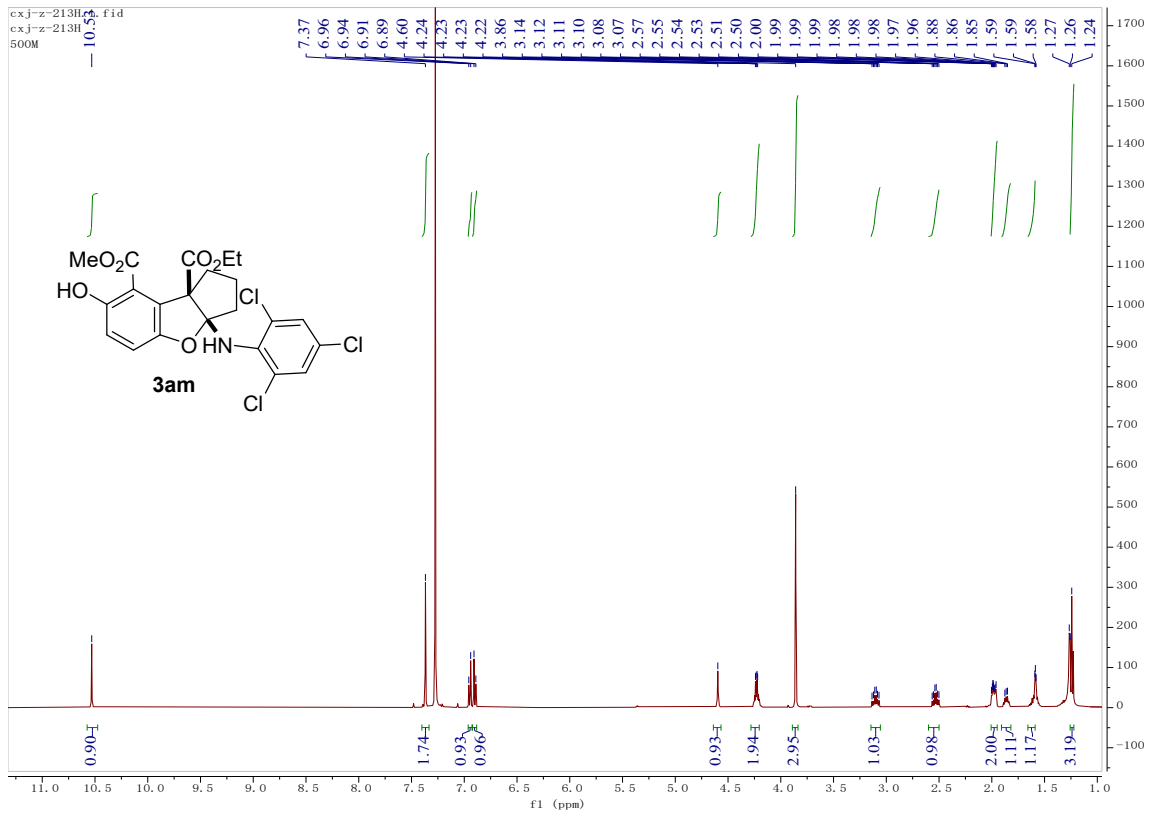


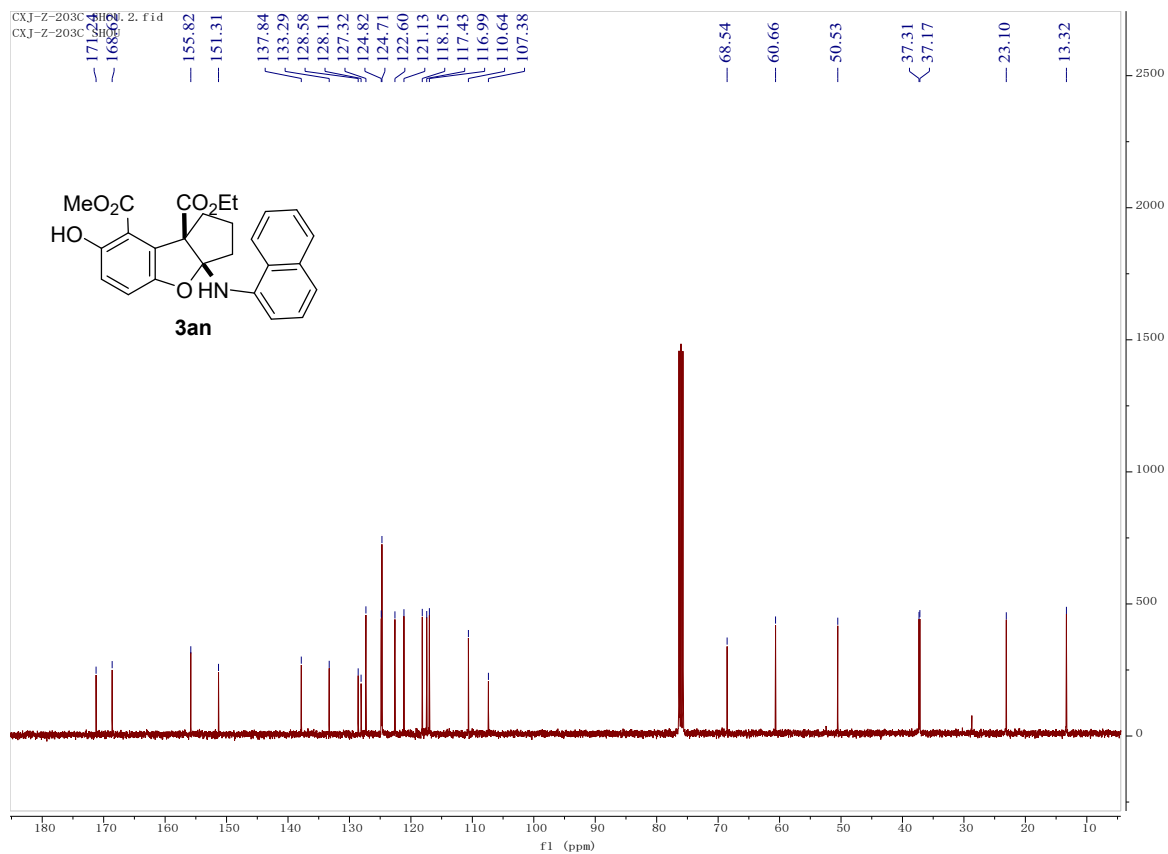
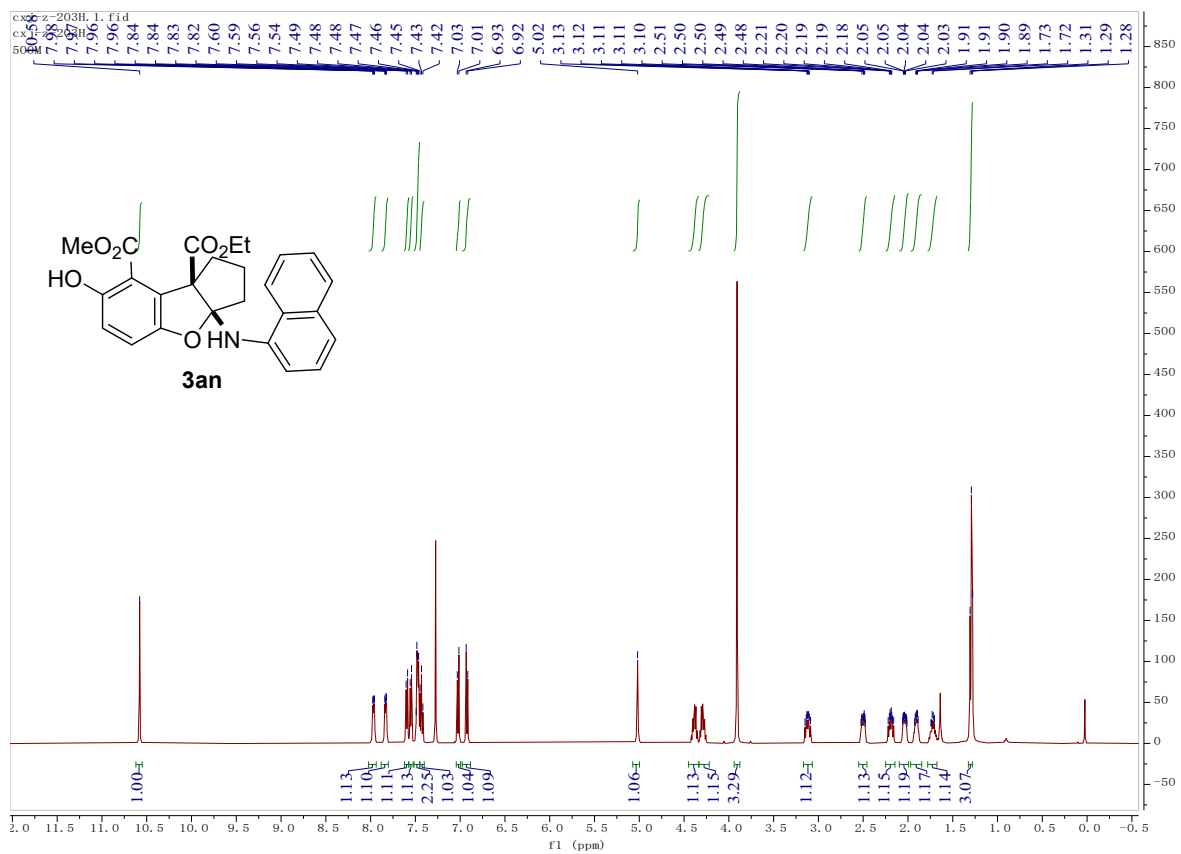


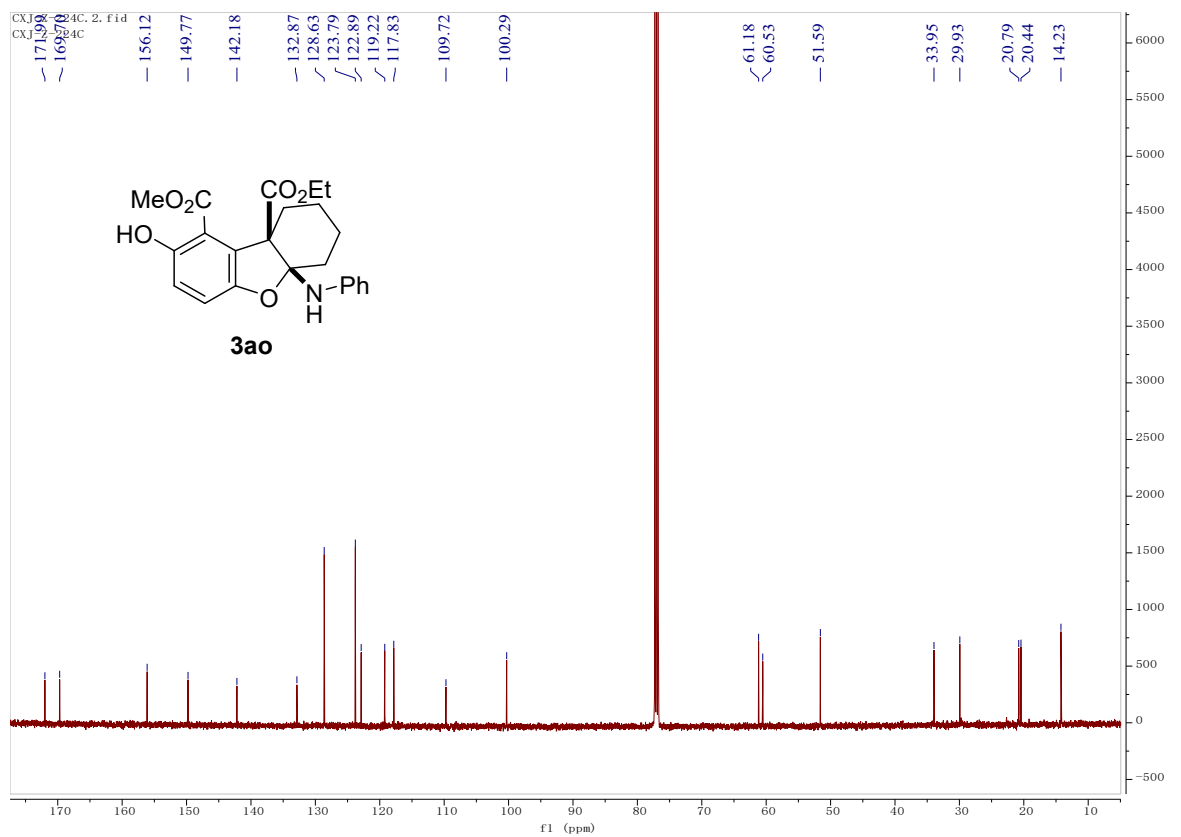
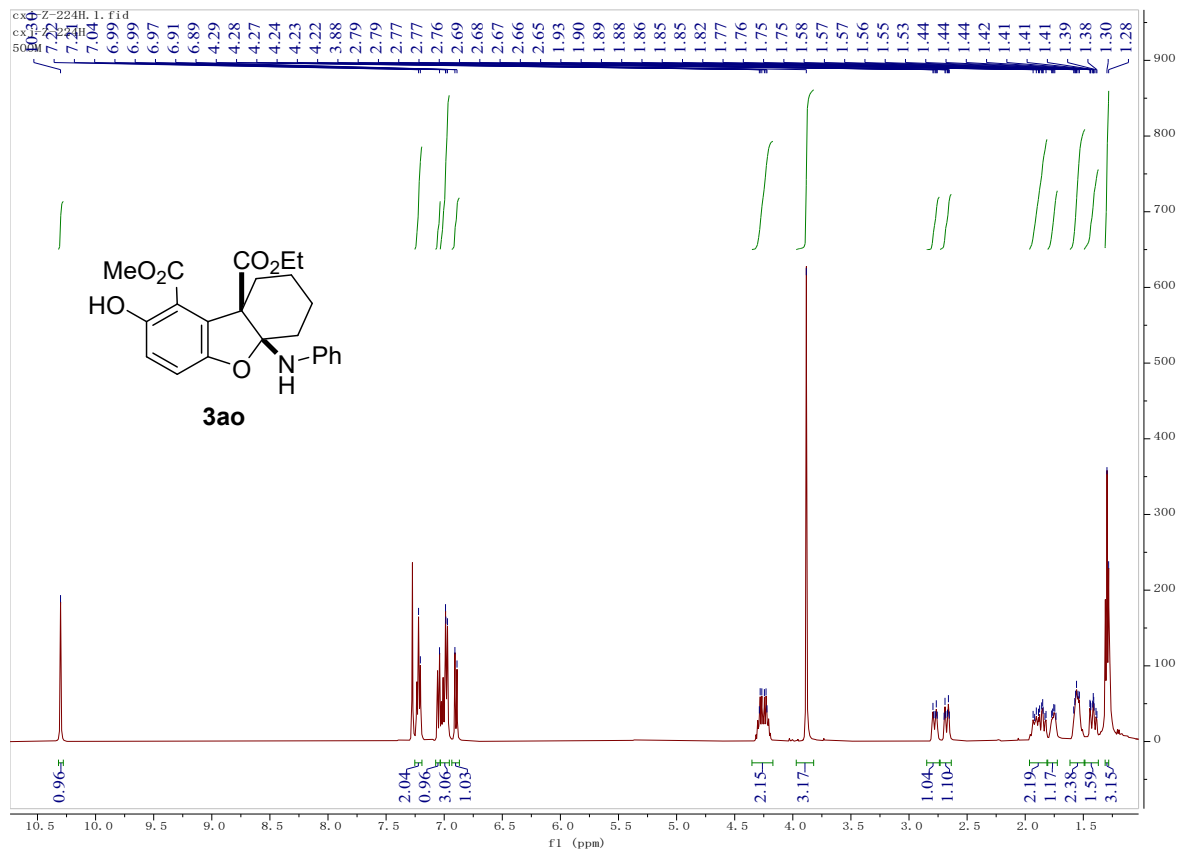


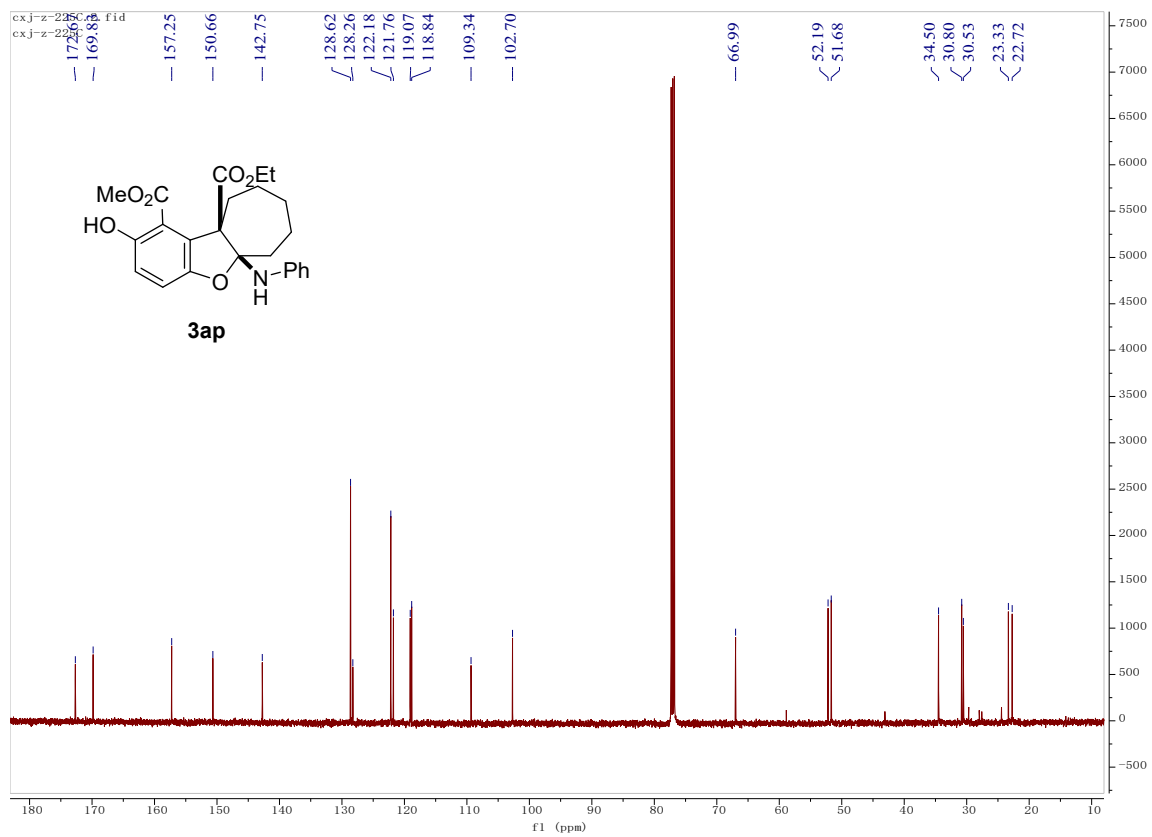
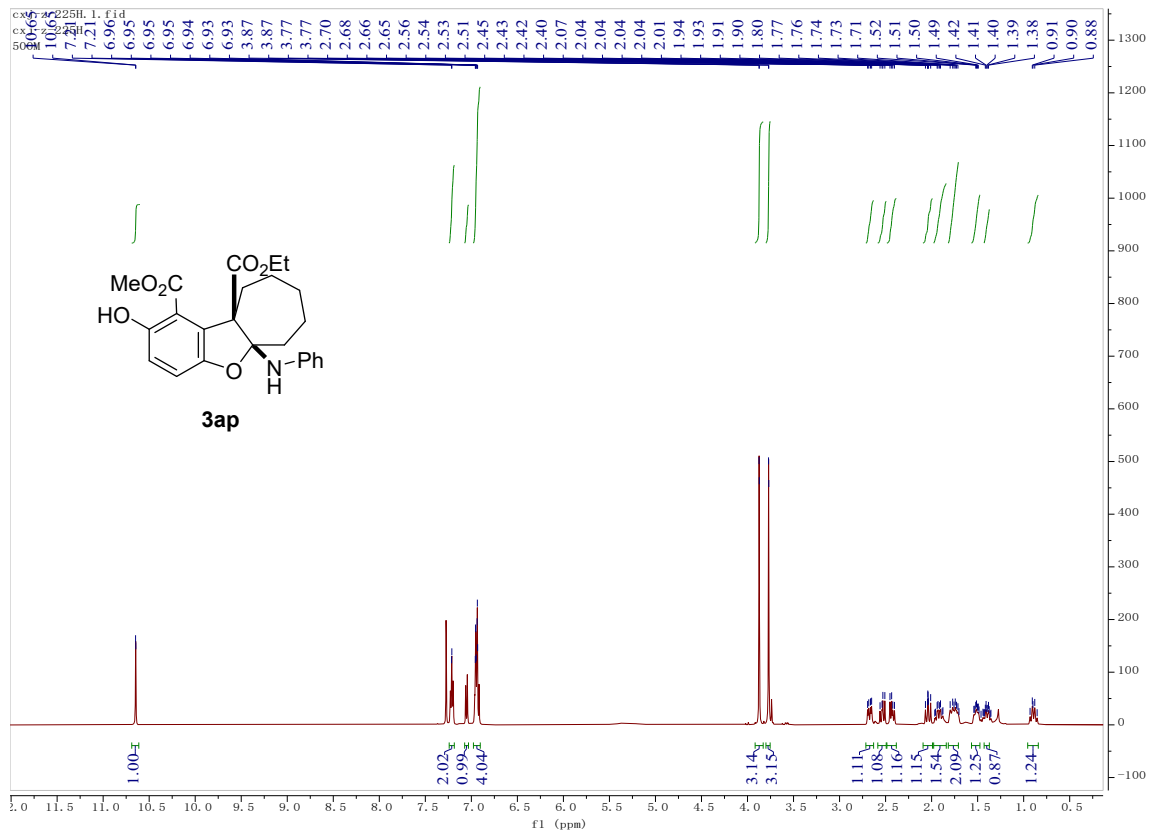


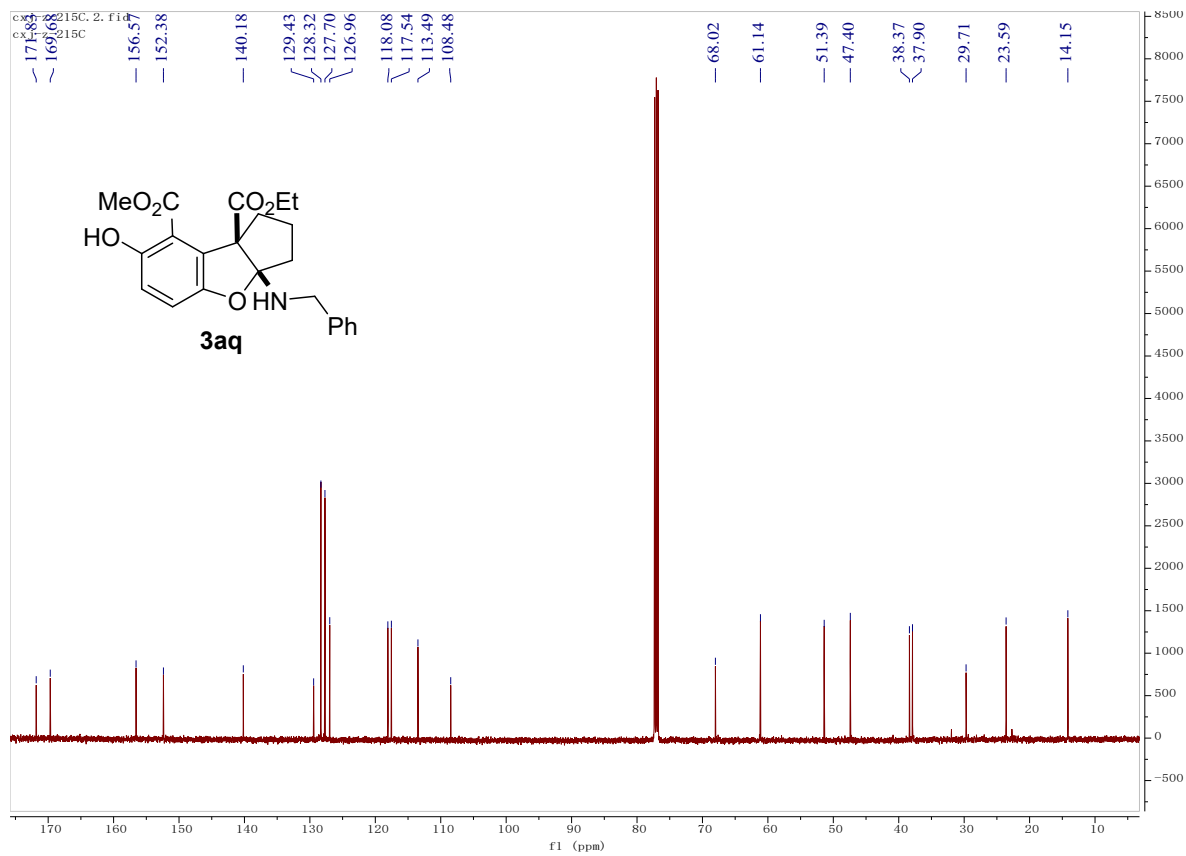
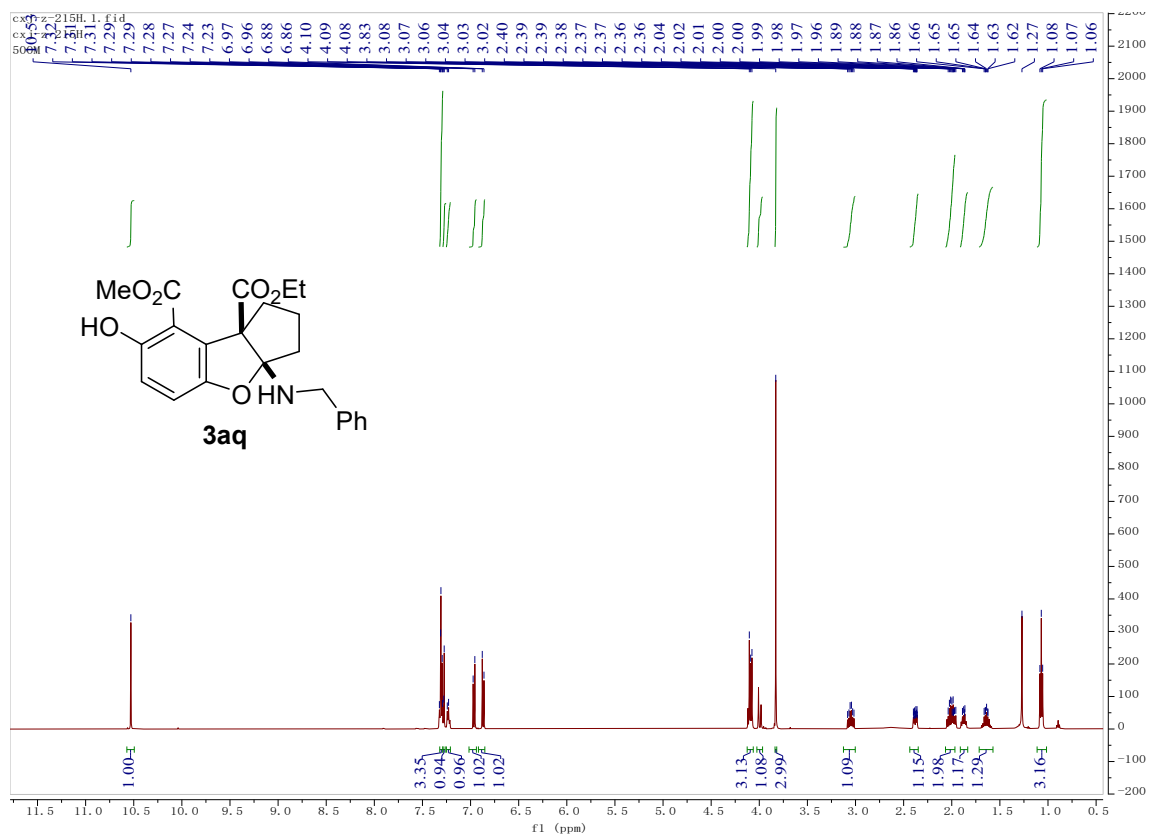


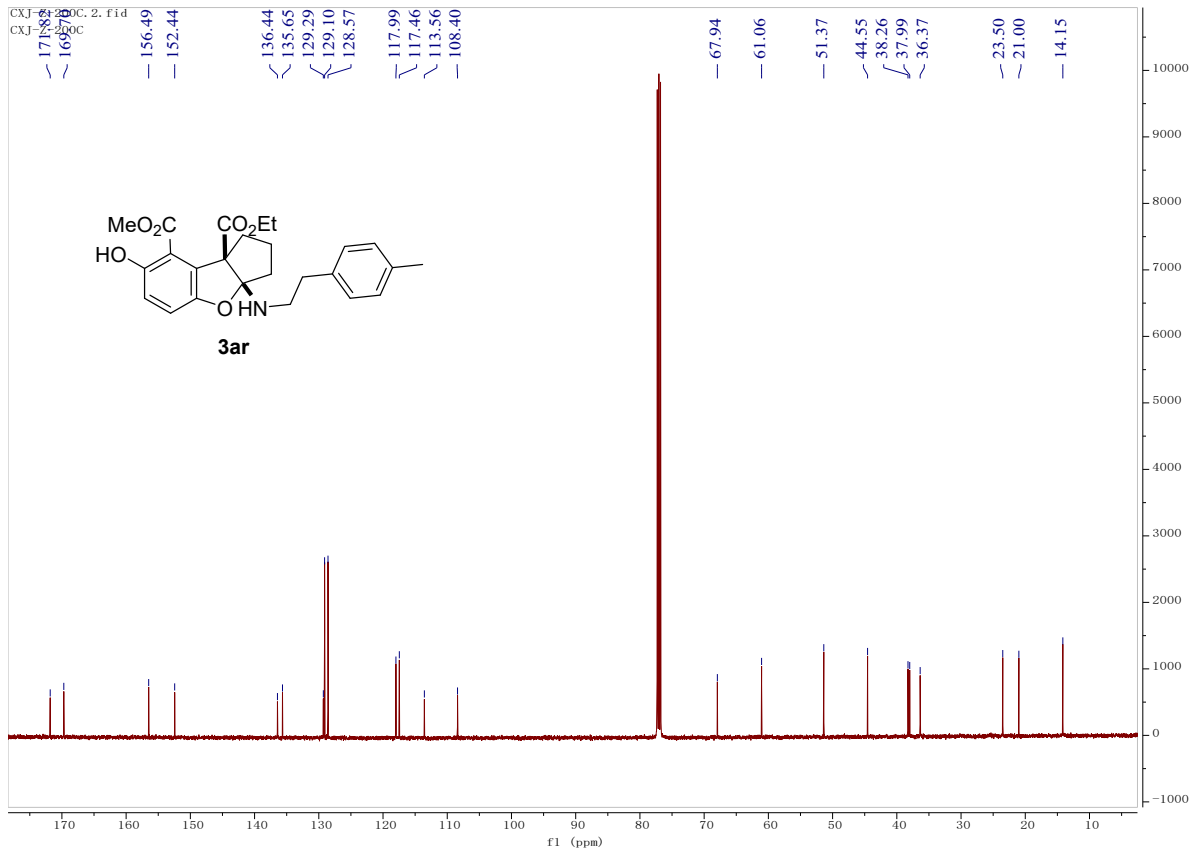
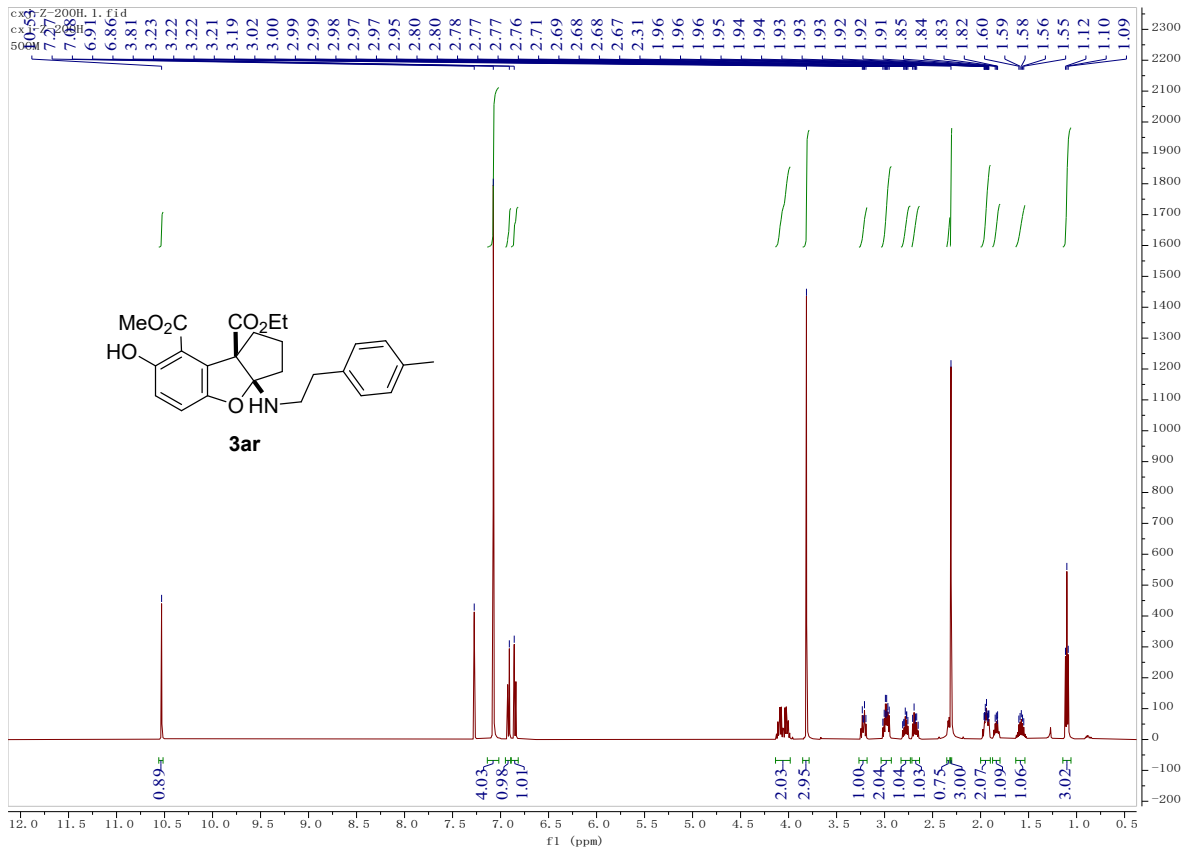


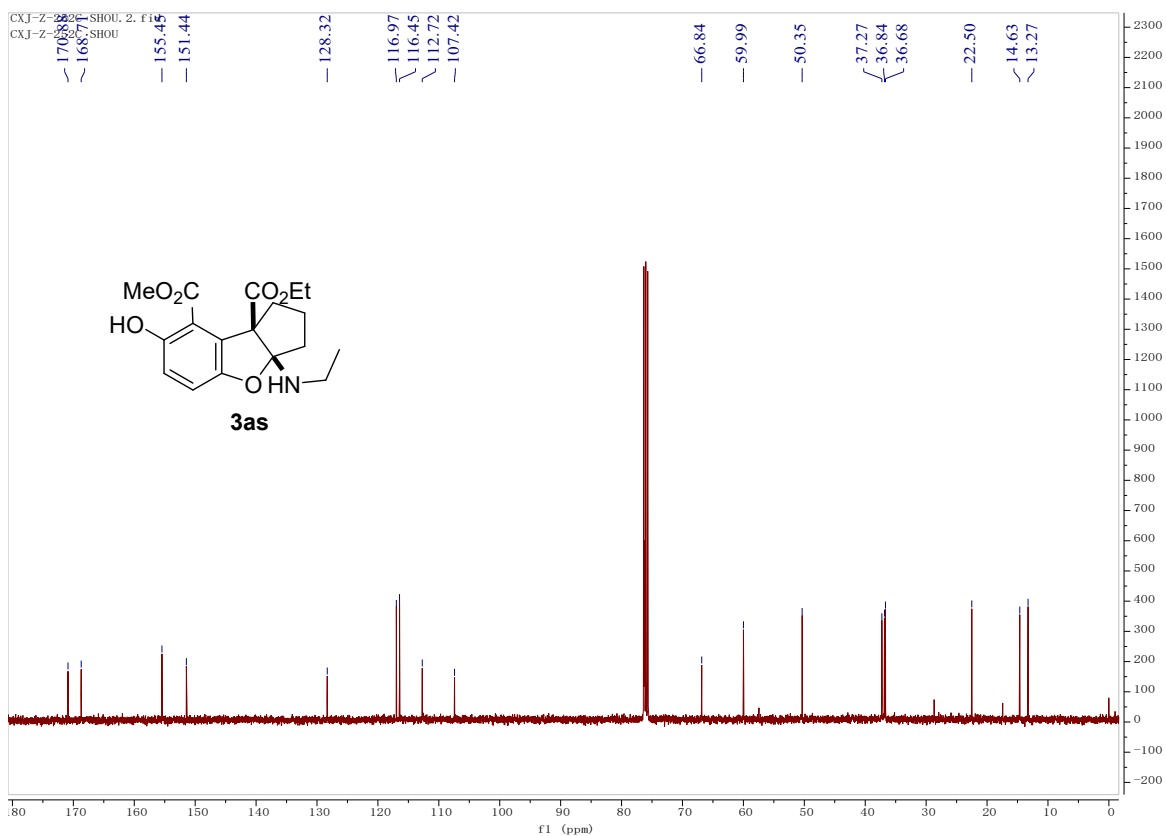
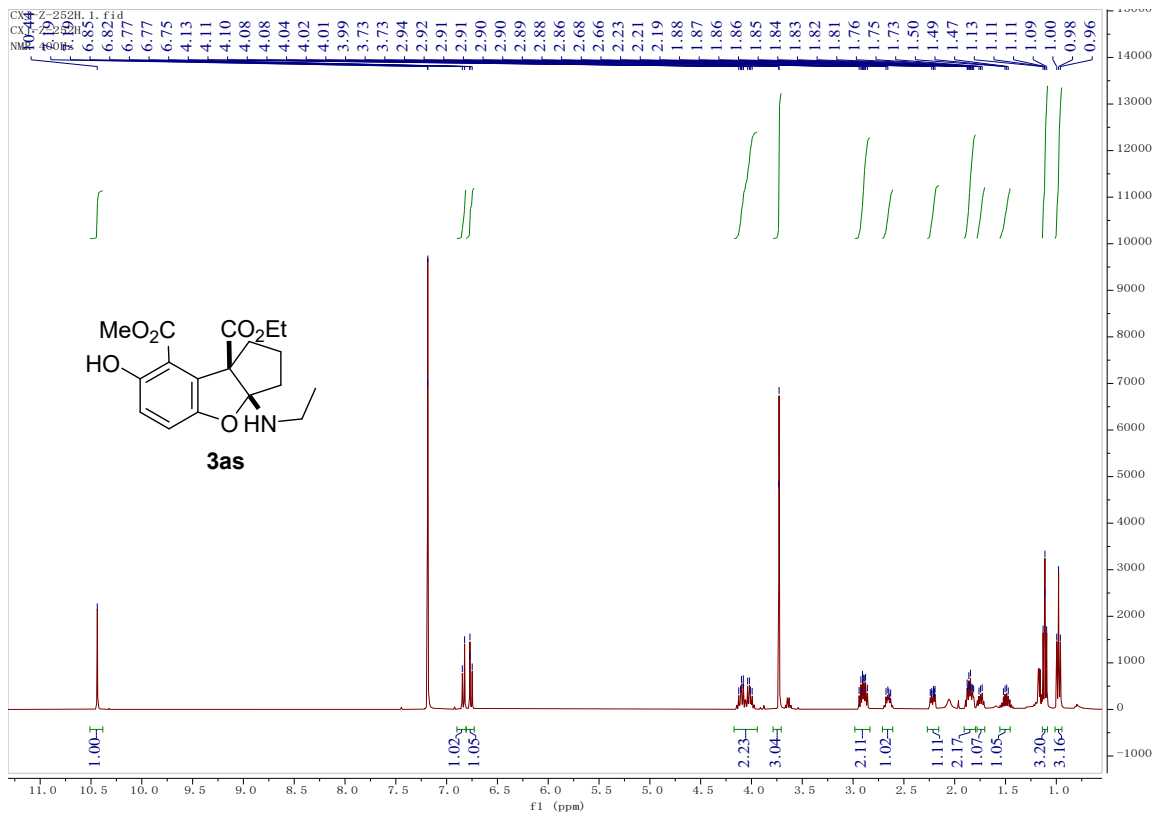


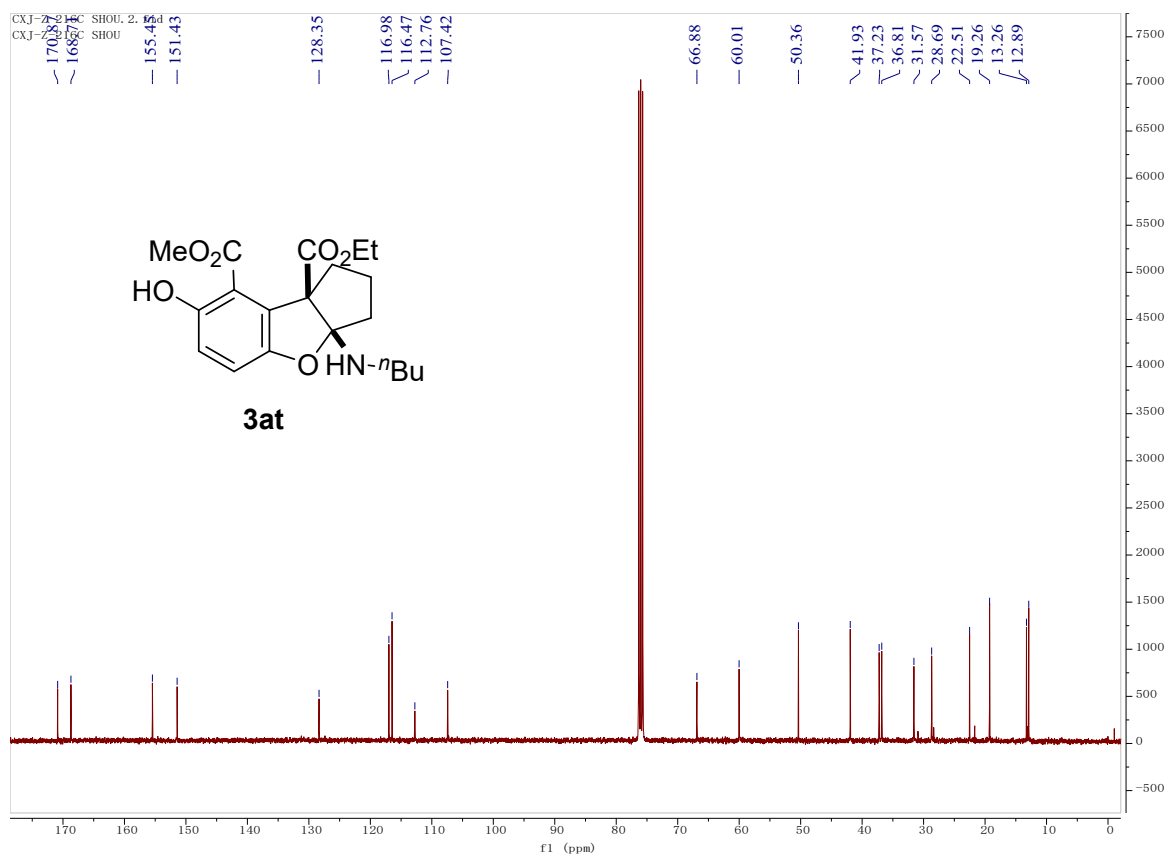
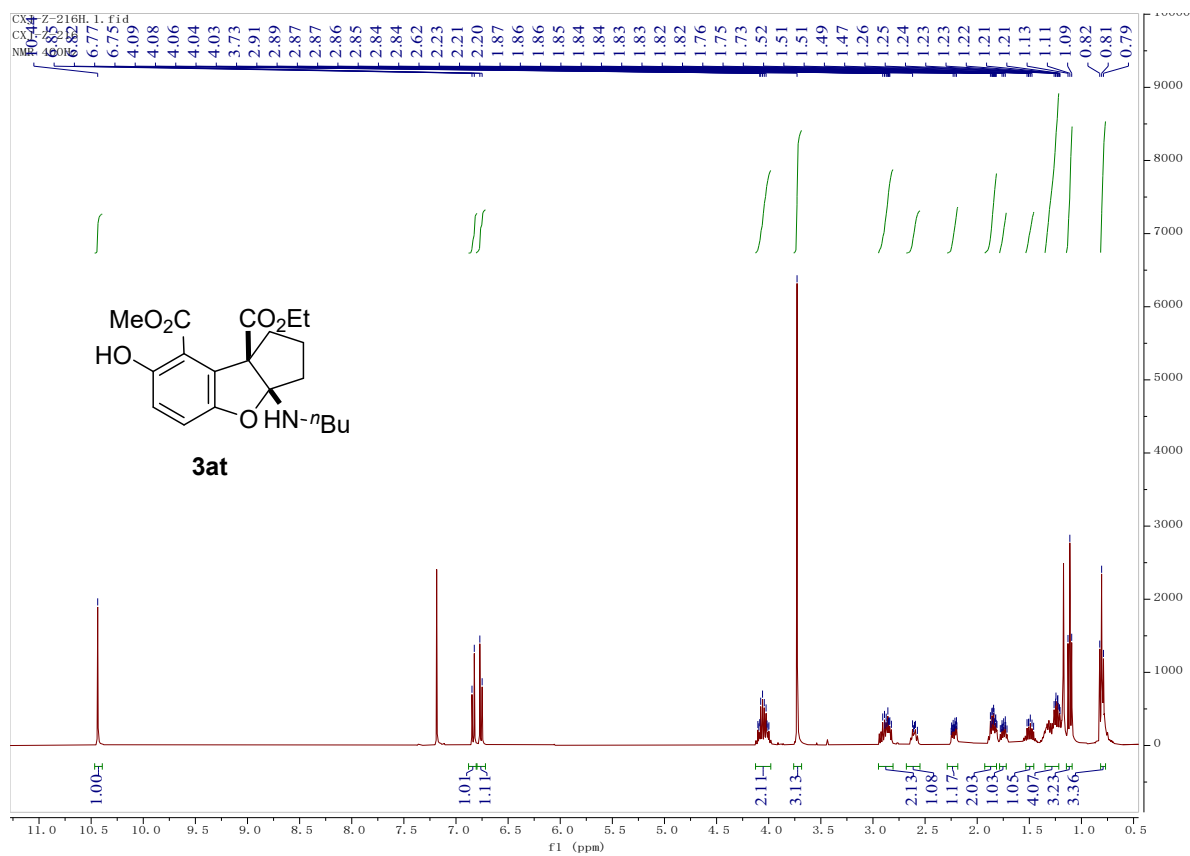


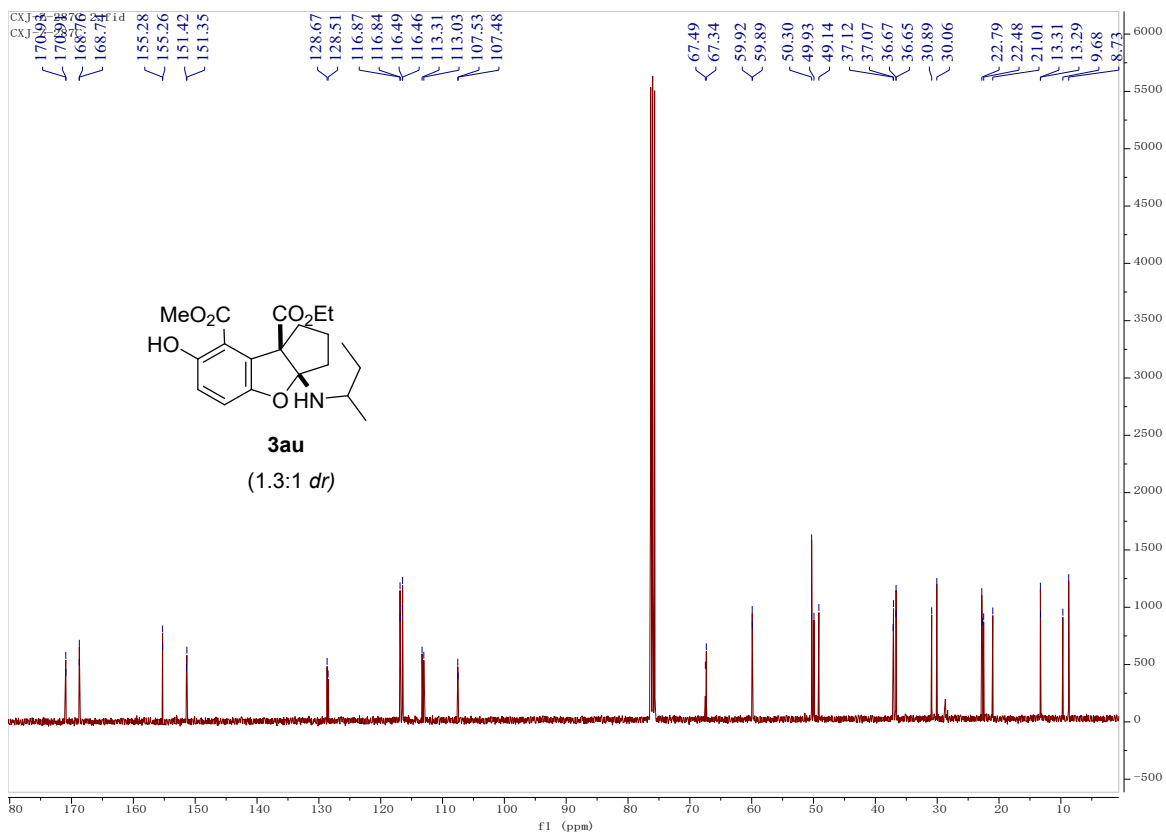
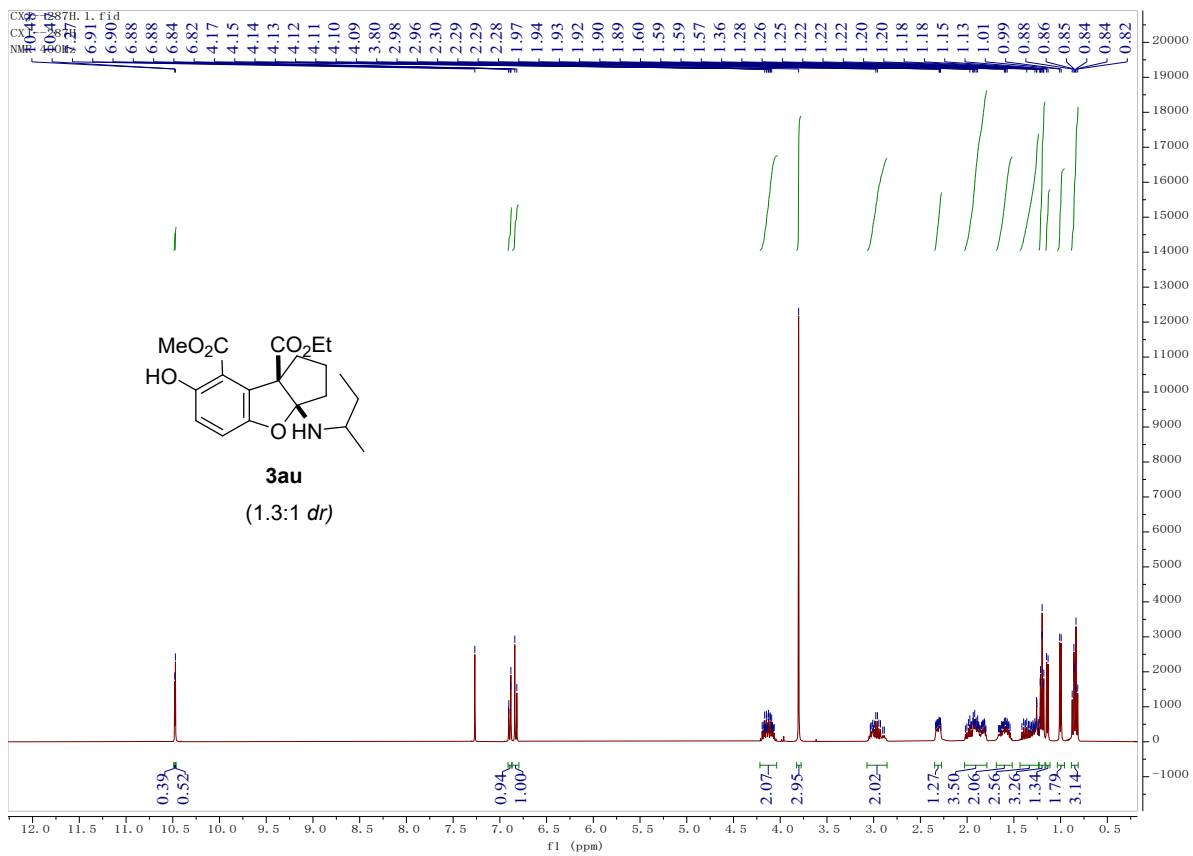


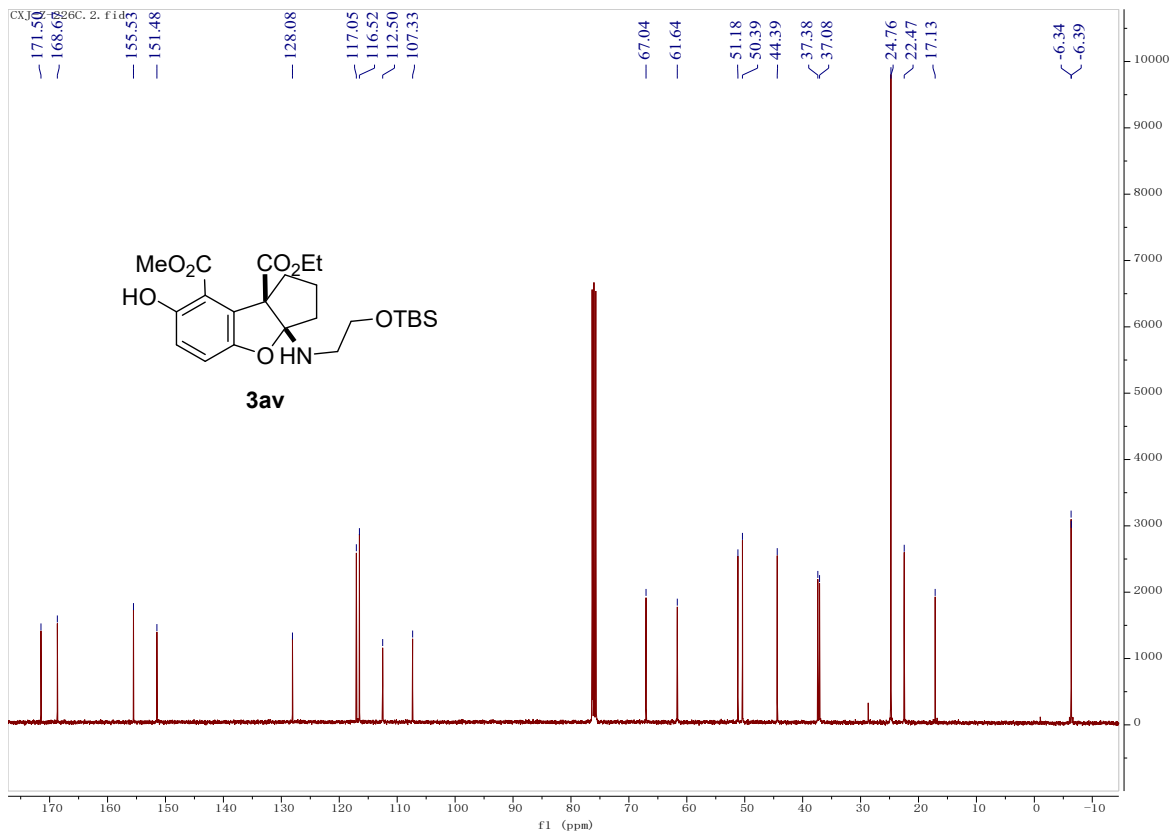
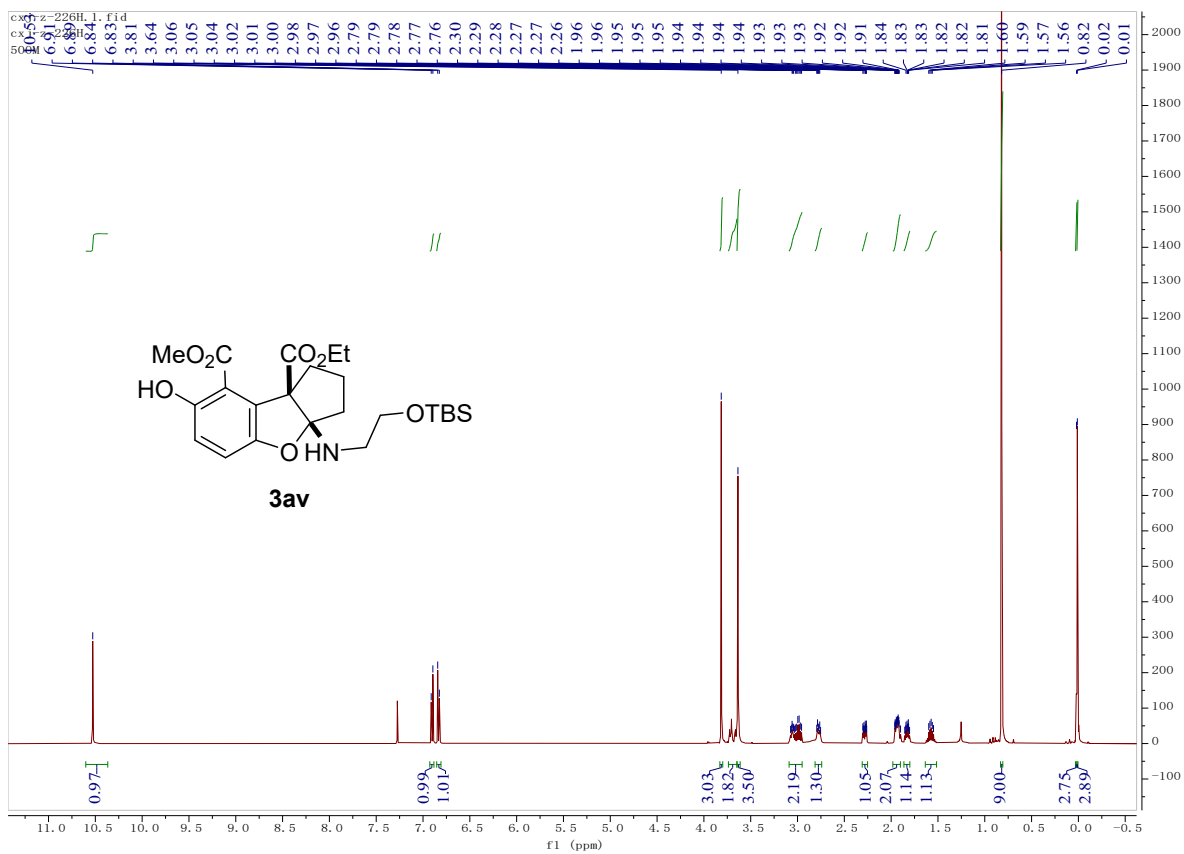


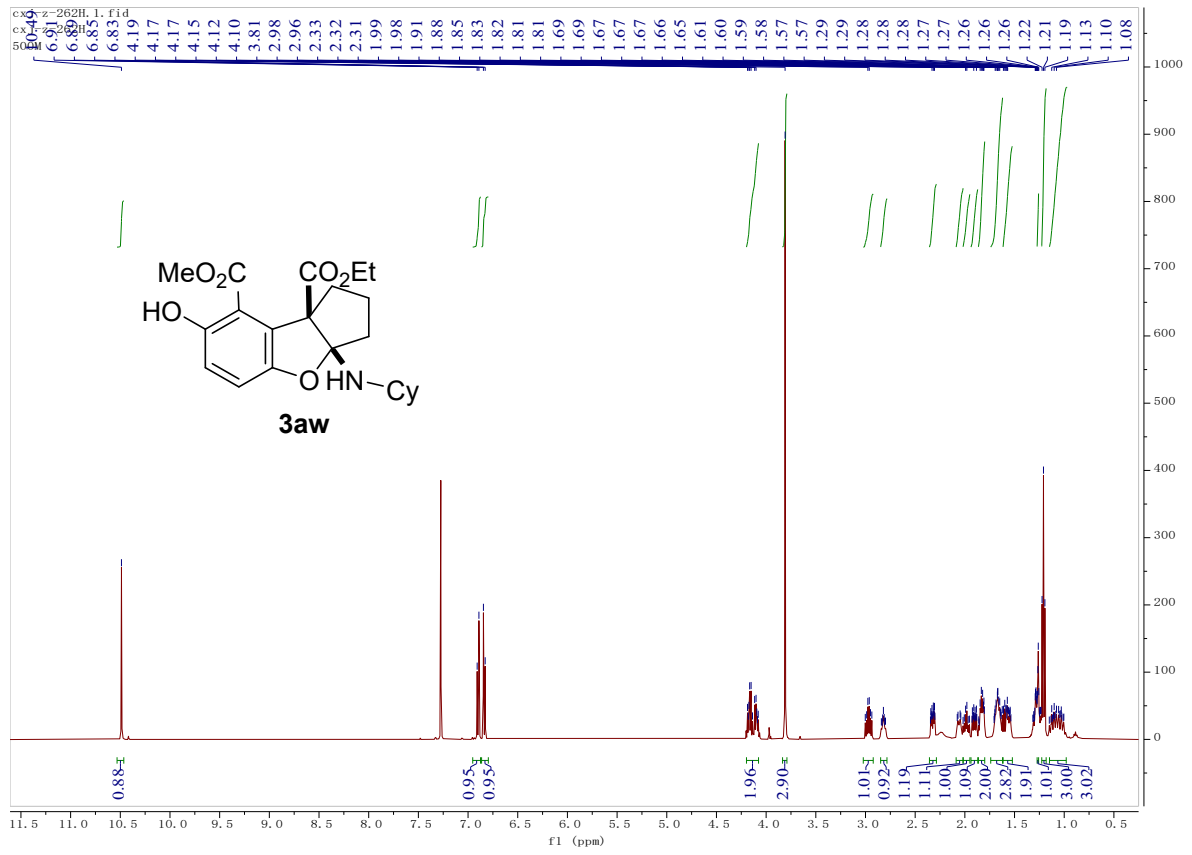


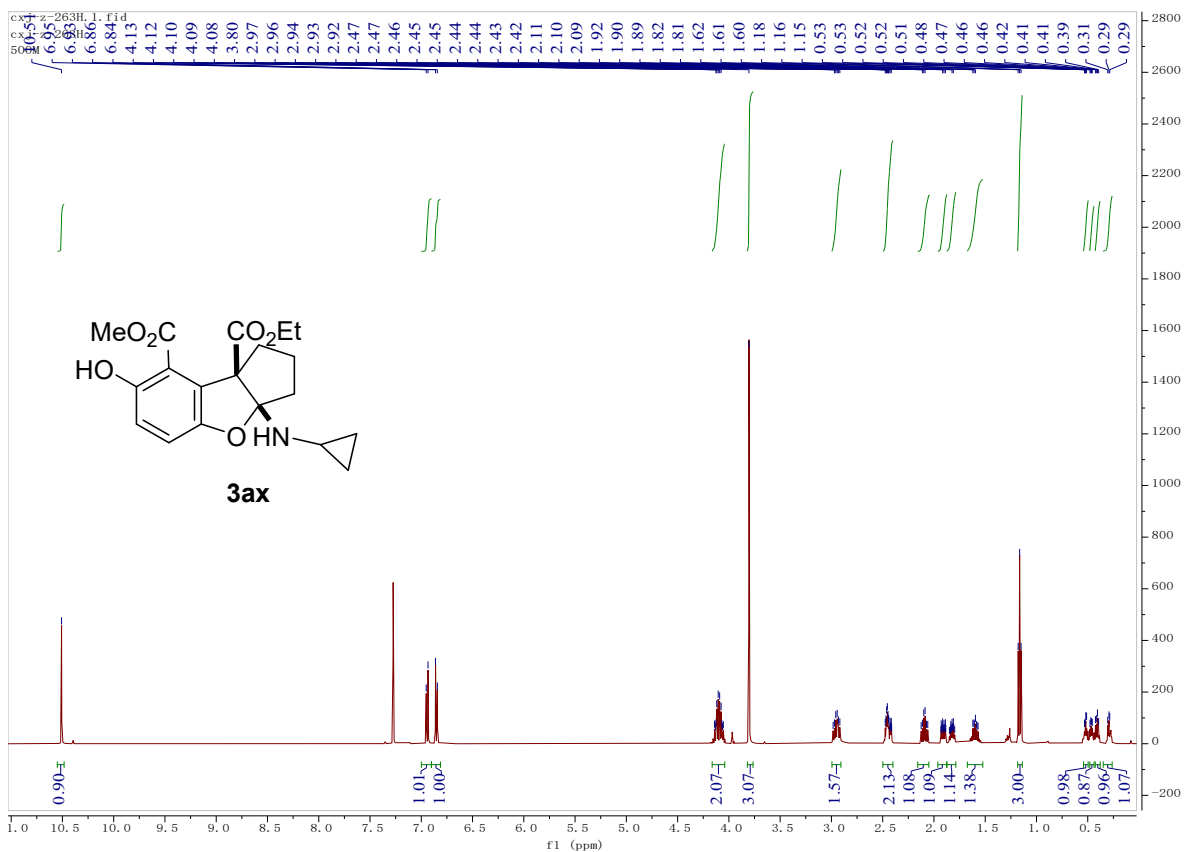
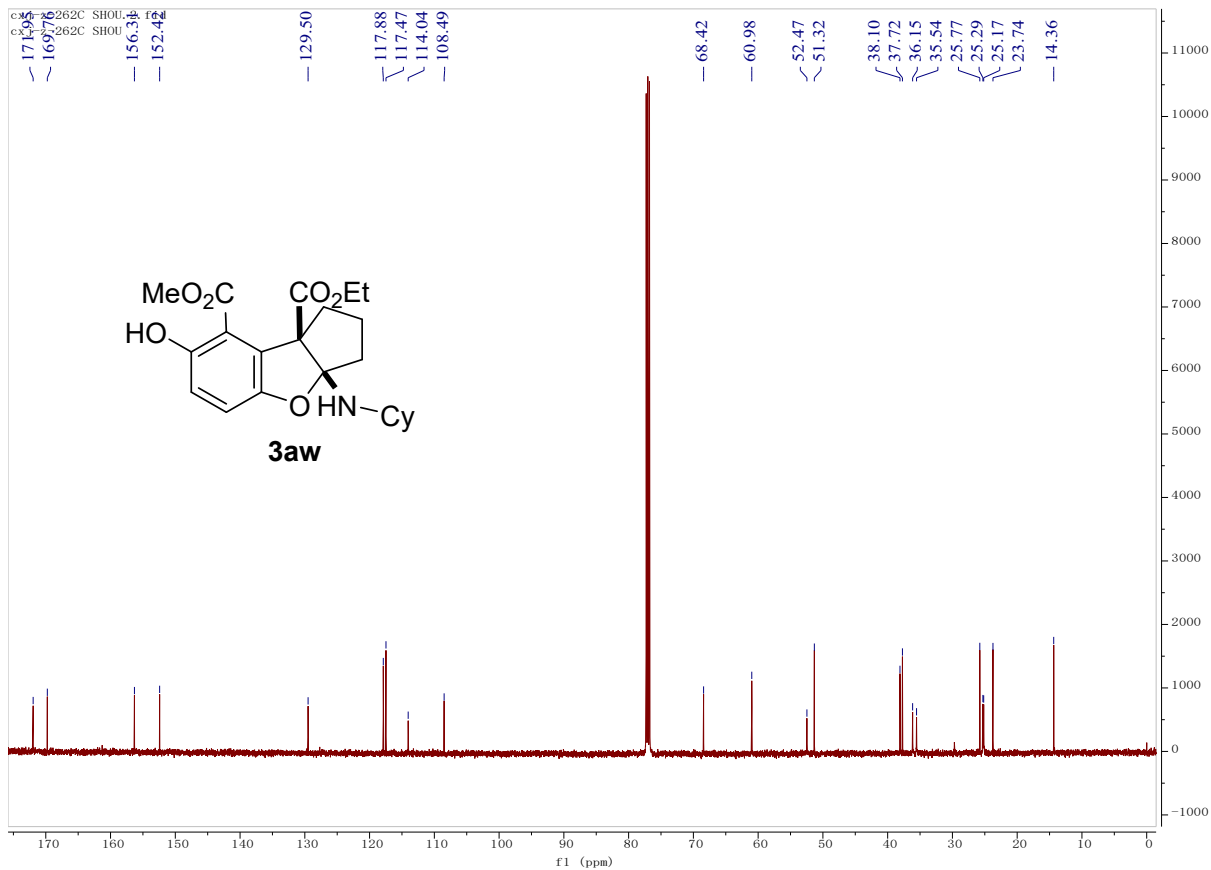


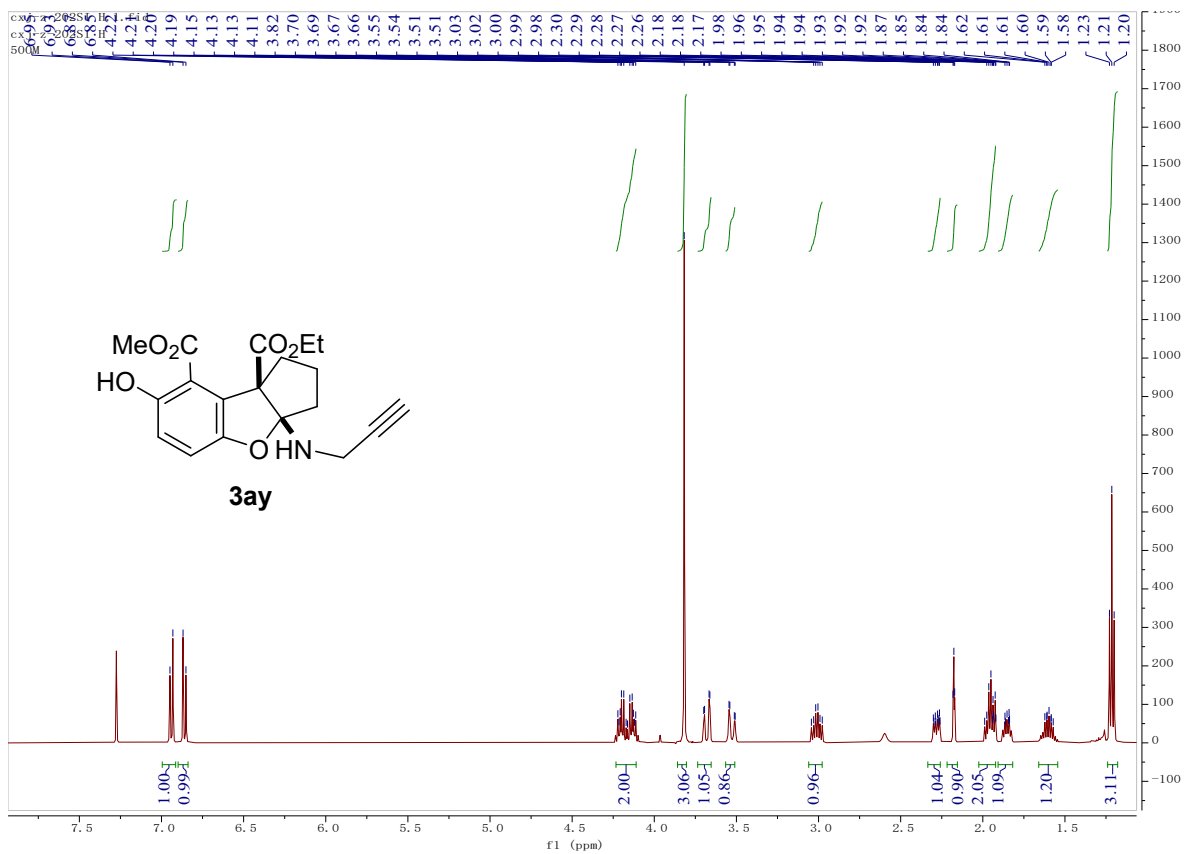
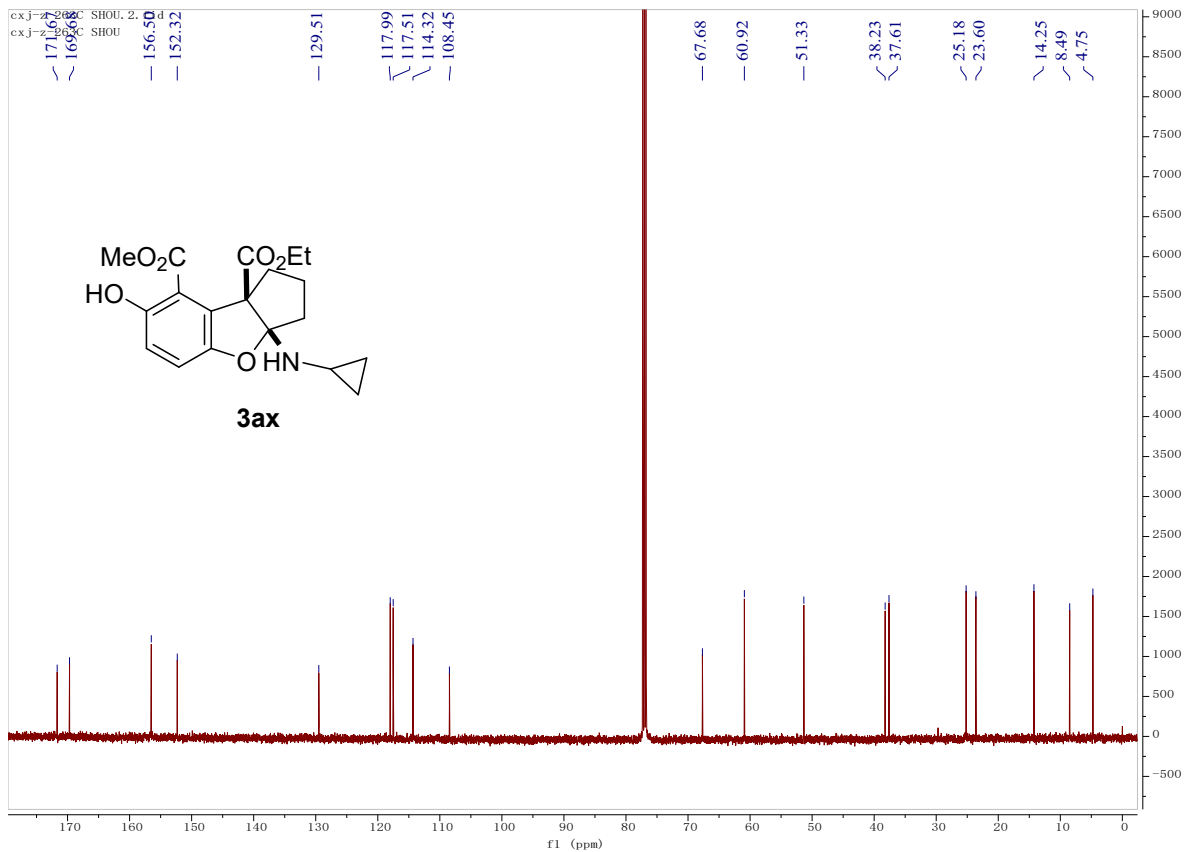


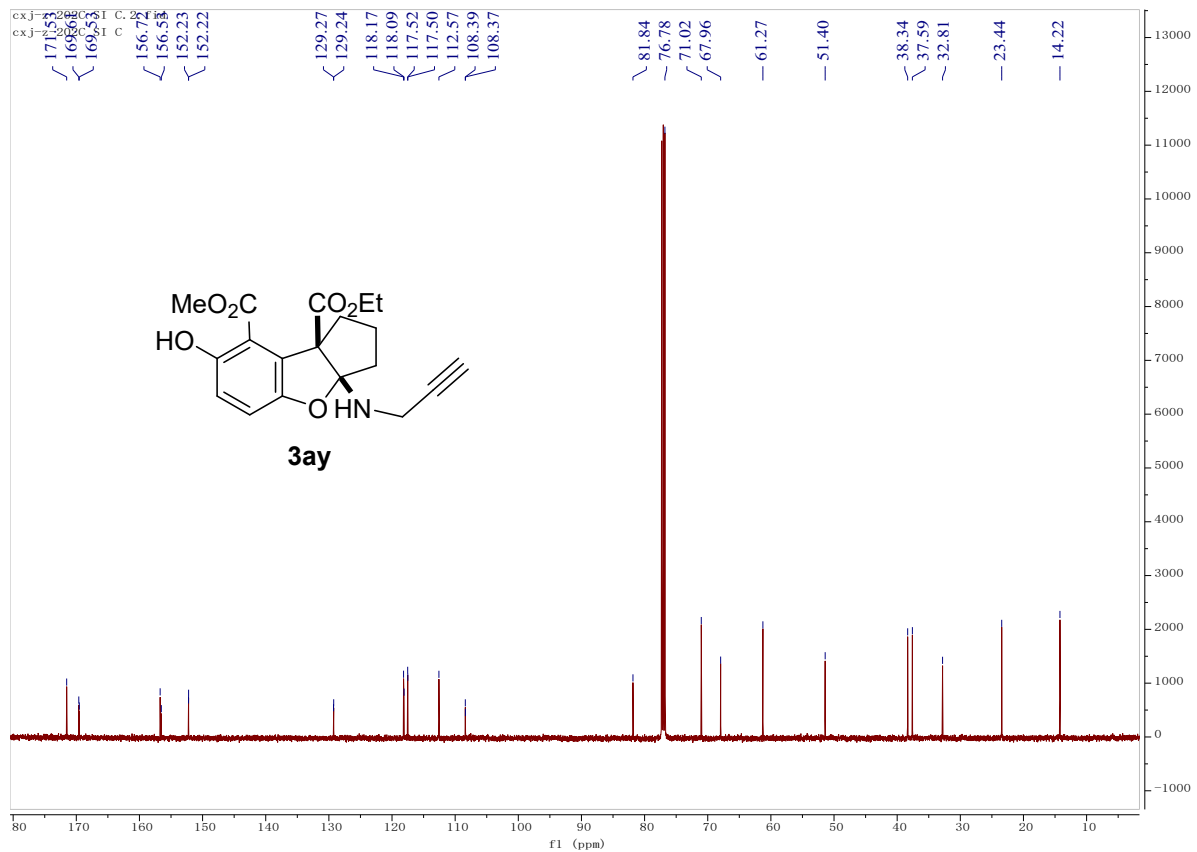


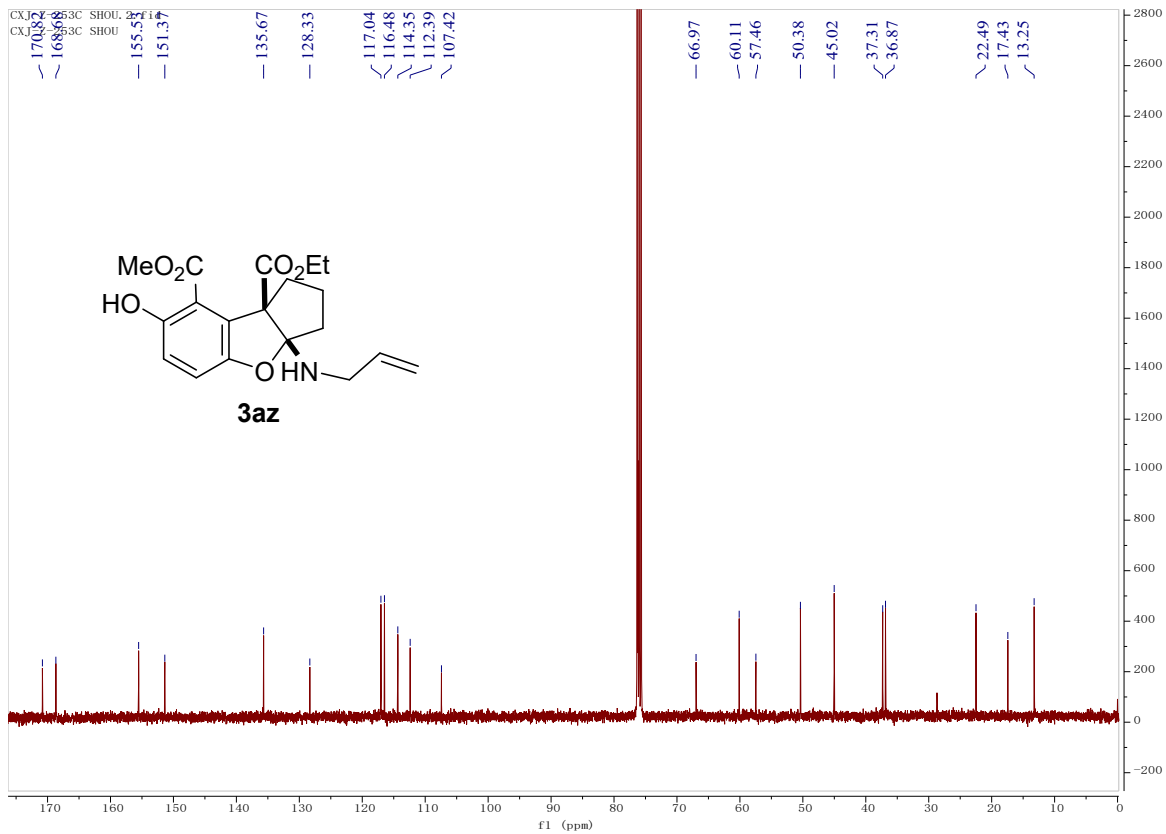
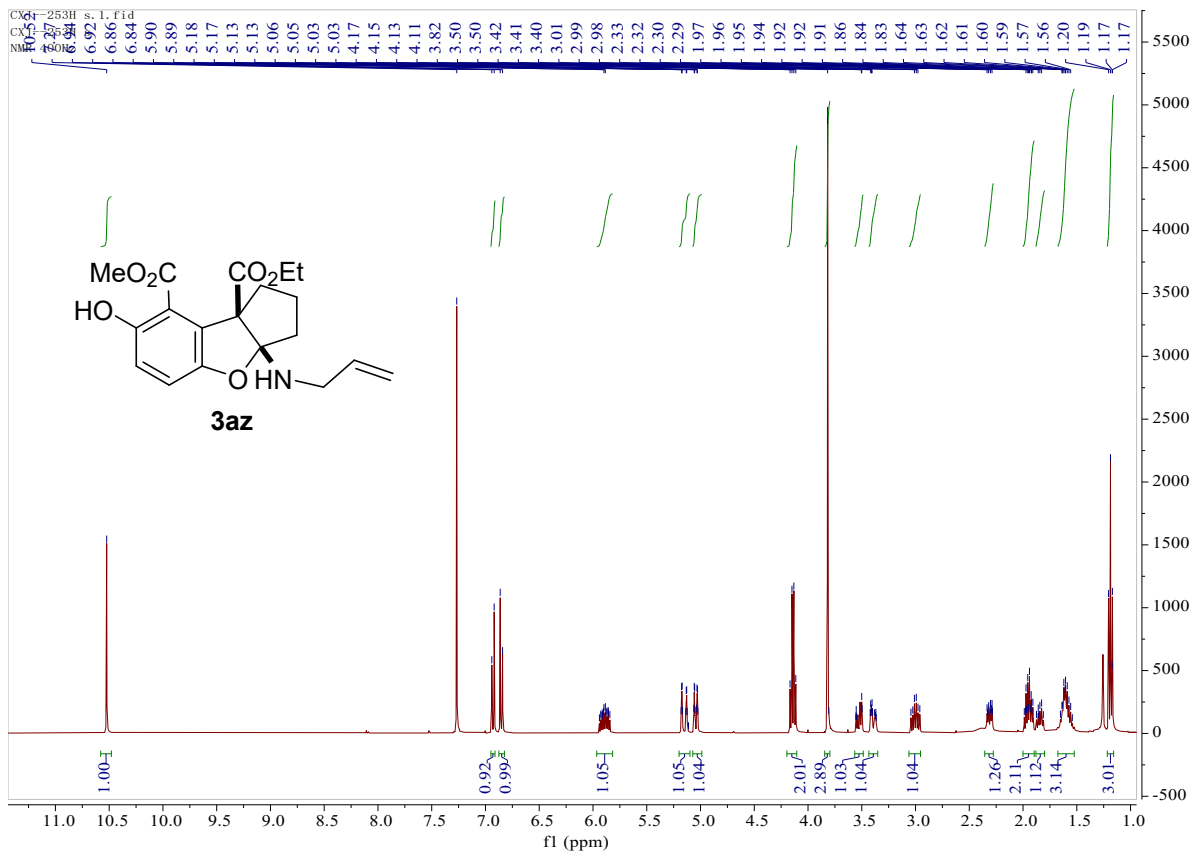


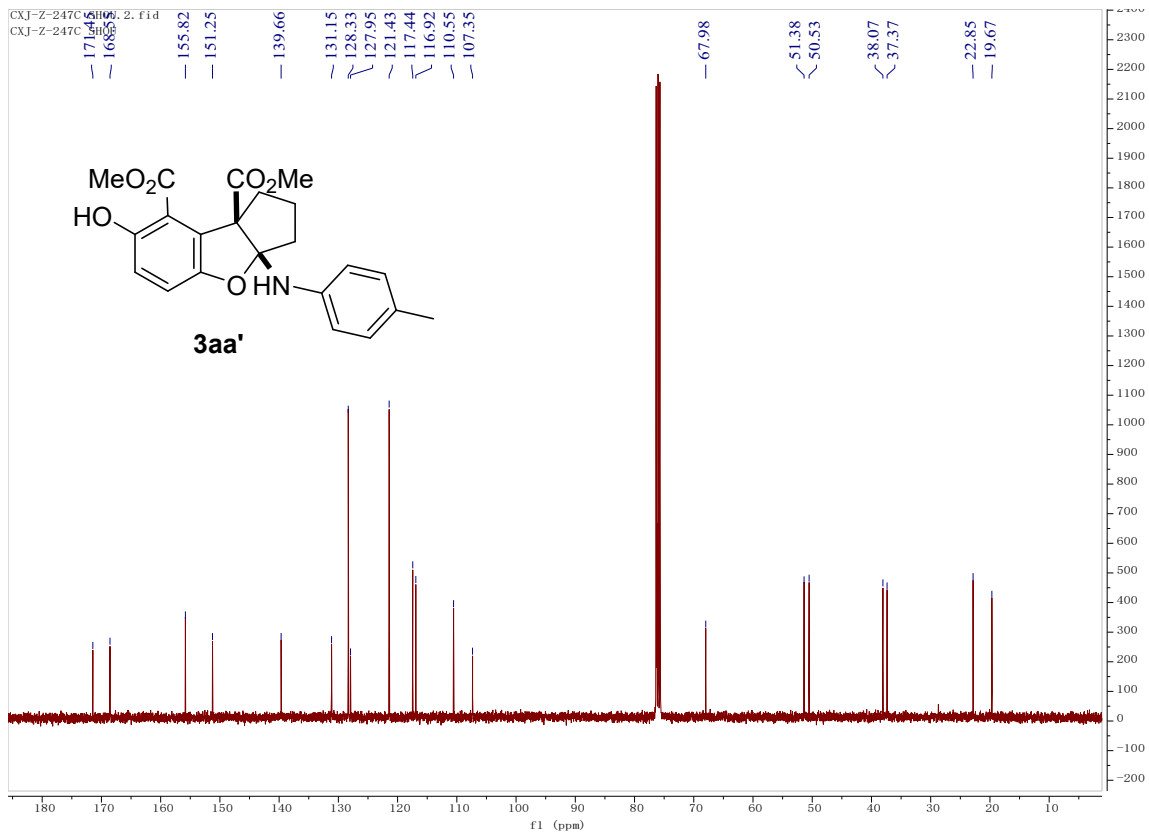
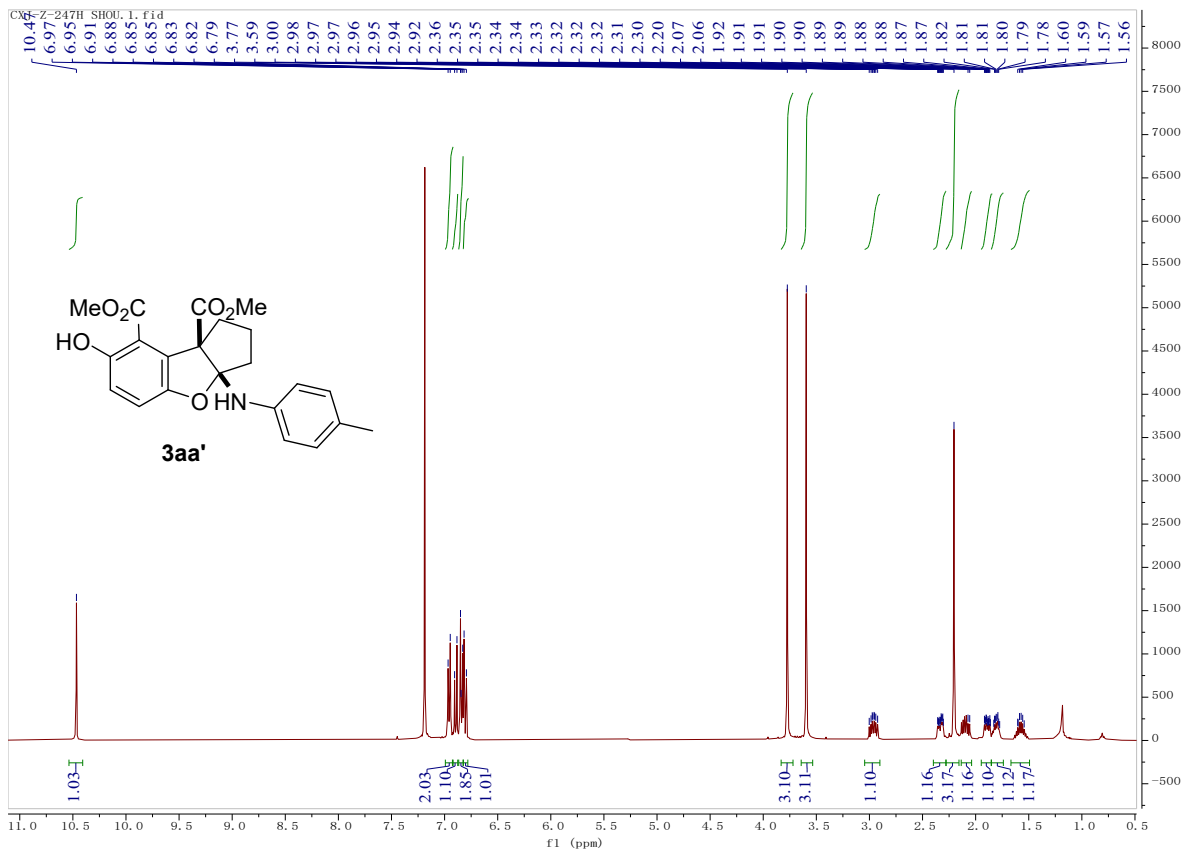


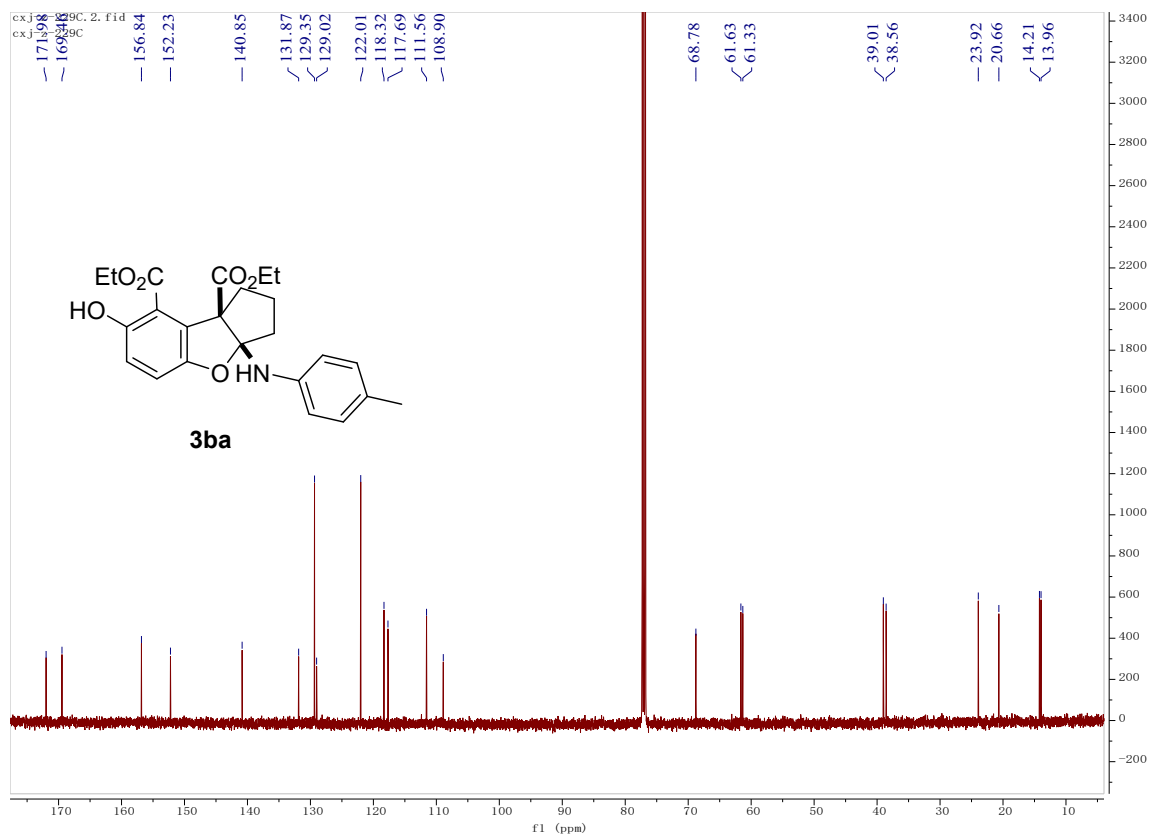
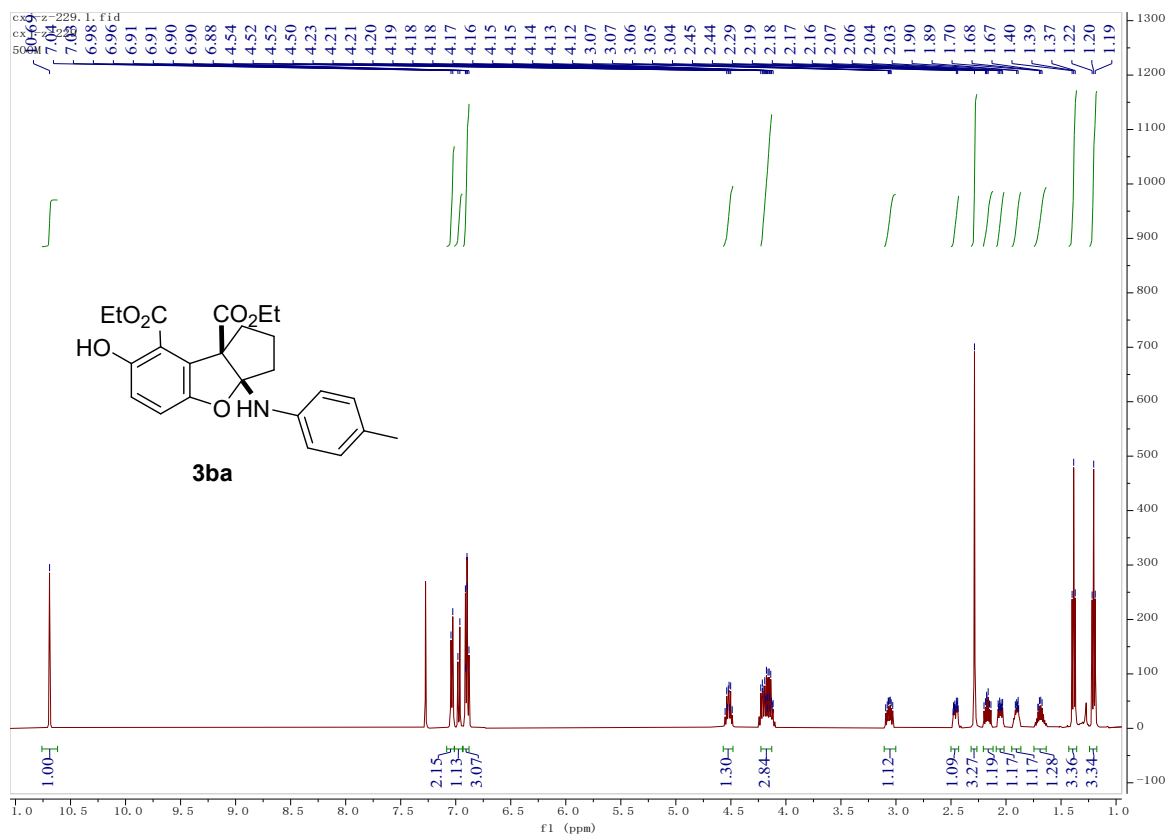


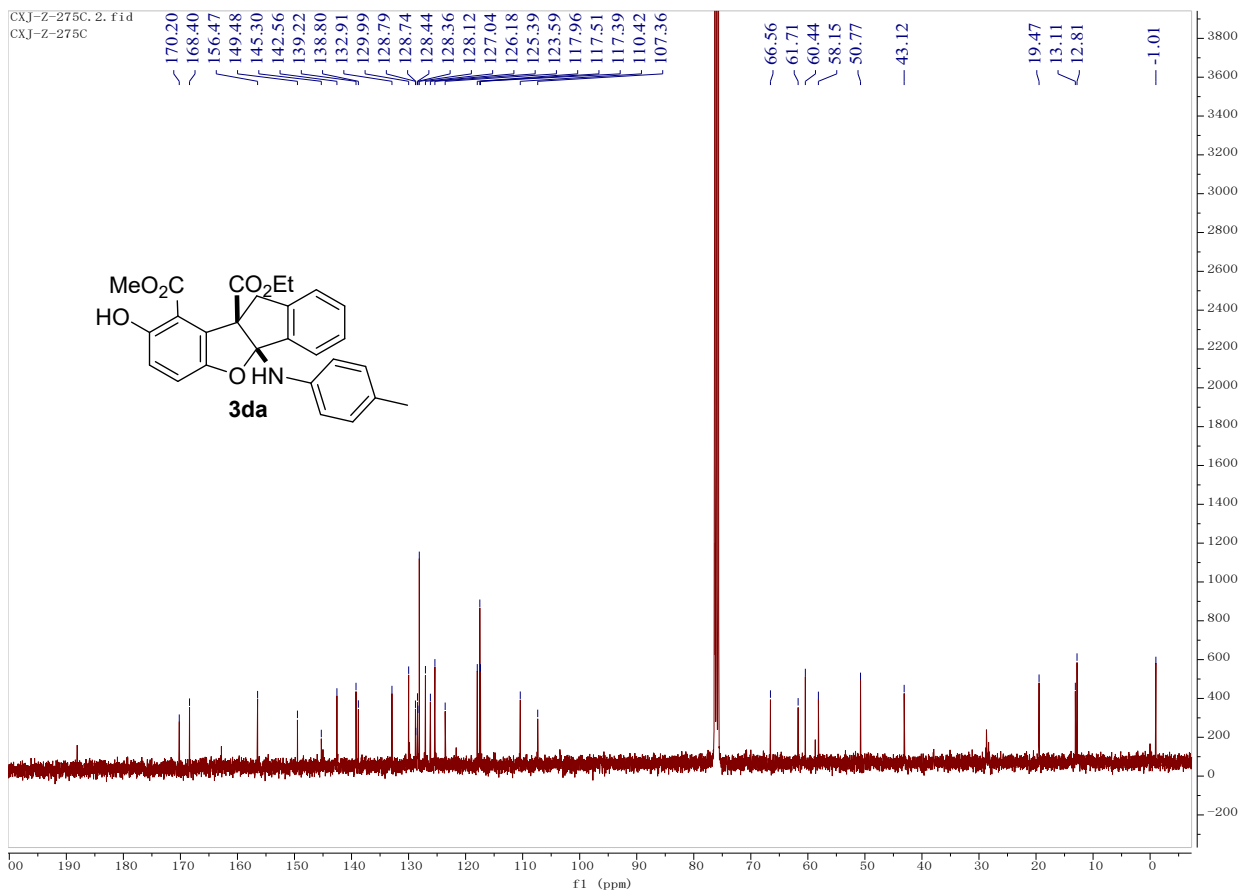
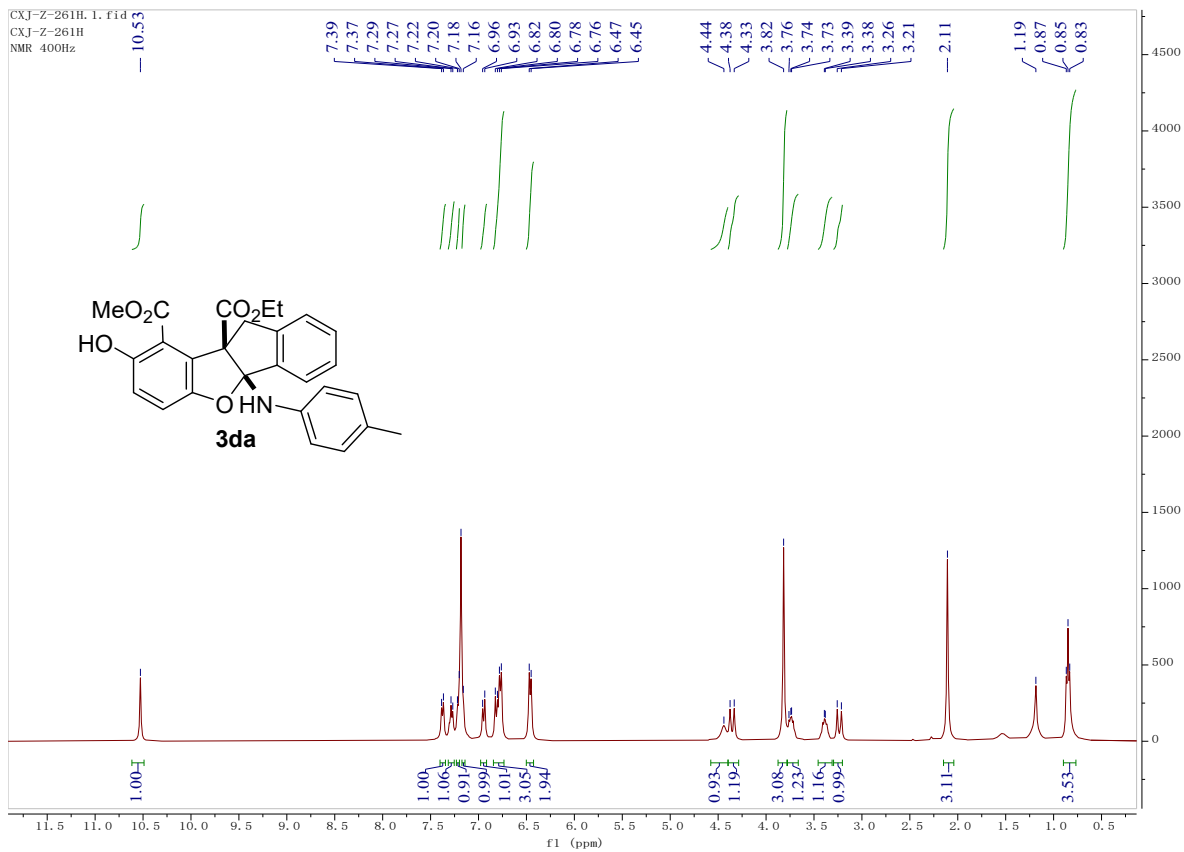




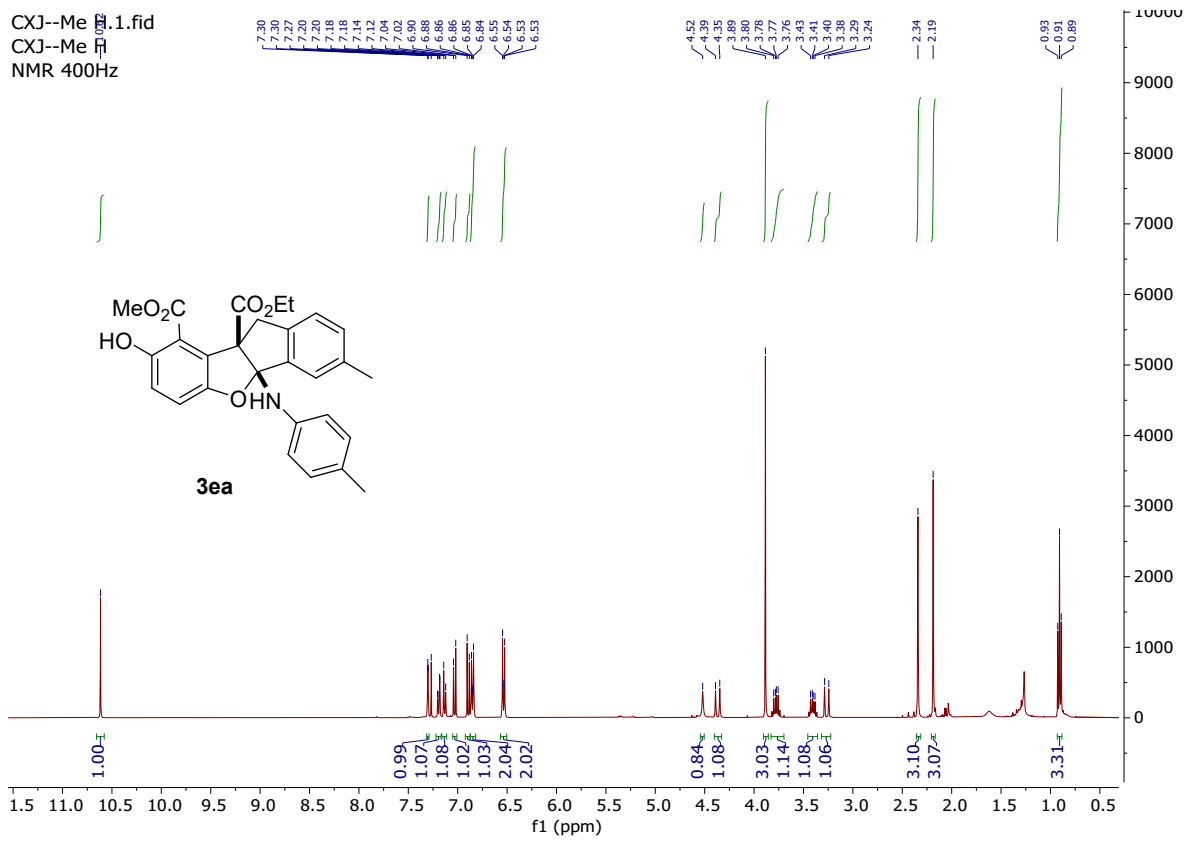




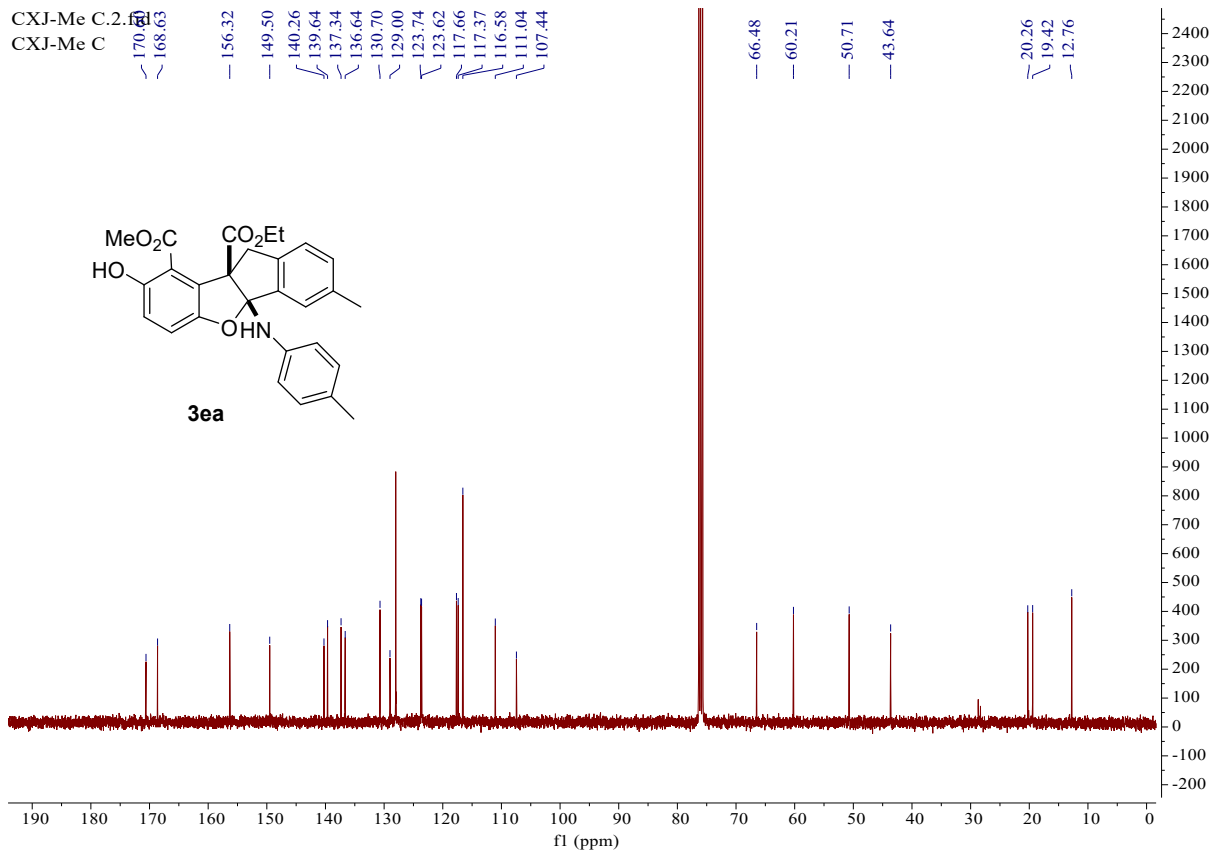




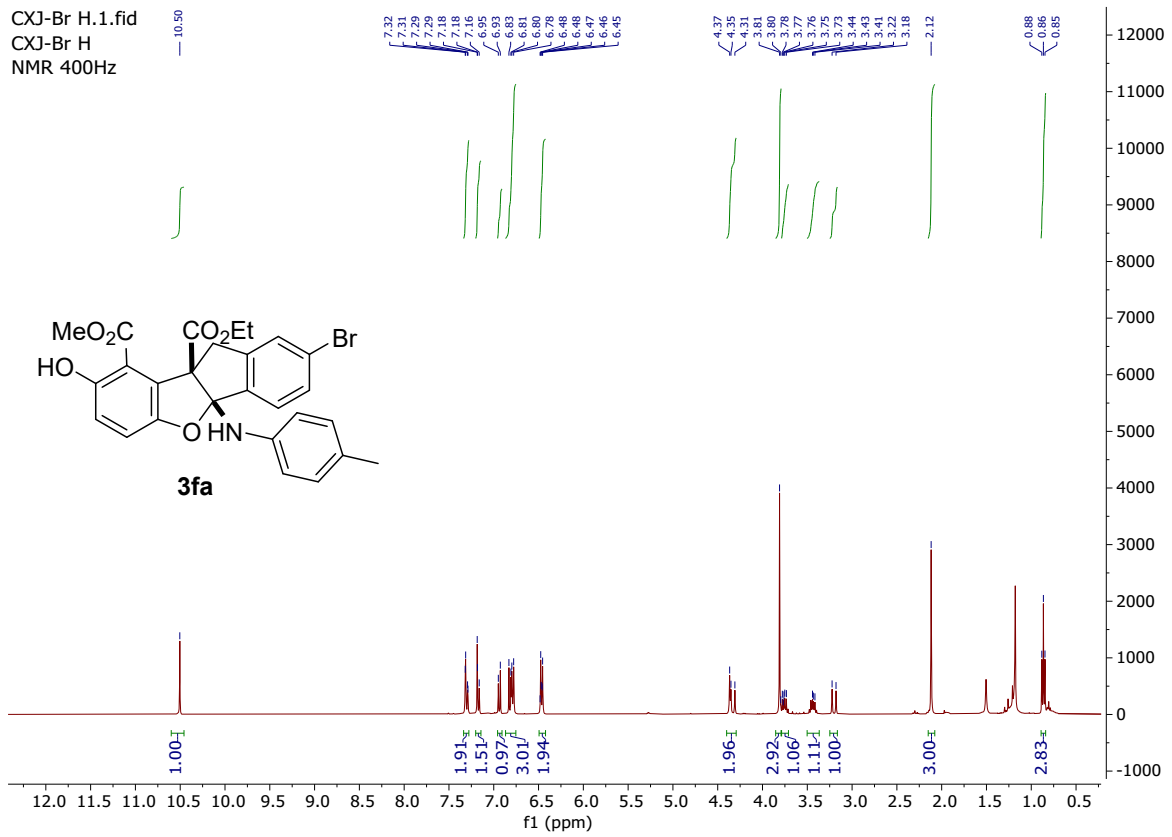
CXJ--Me 1.fid
 CXJ--Me f1
 NMR 400Hz

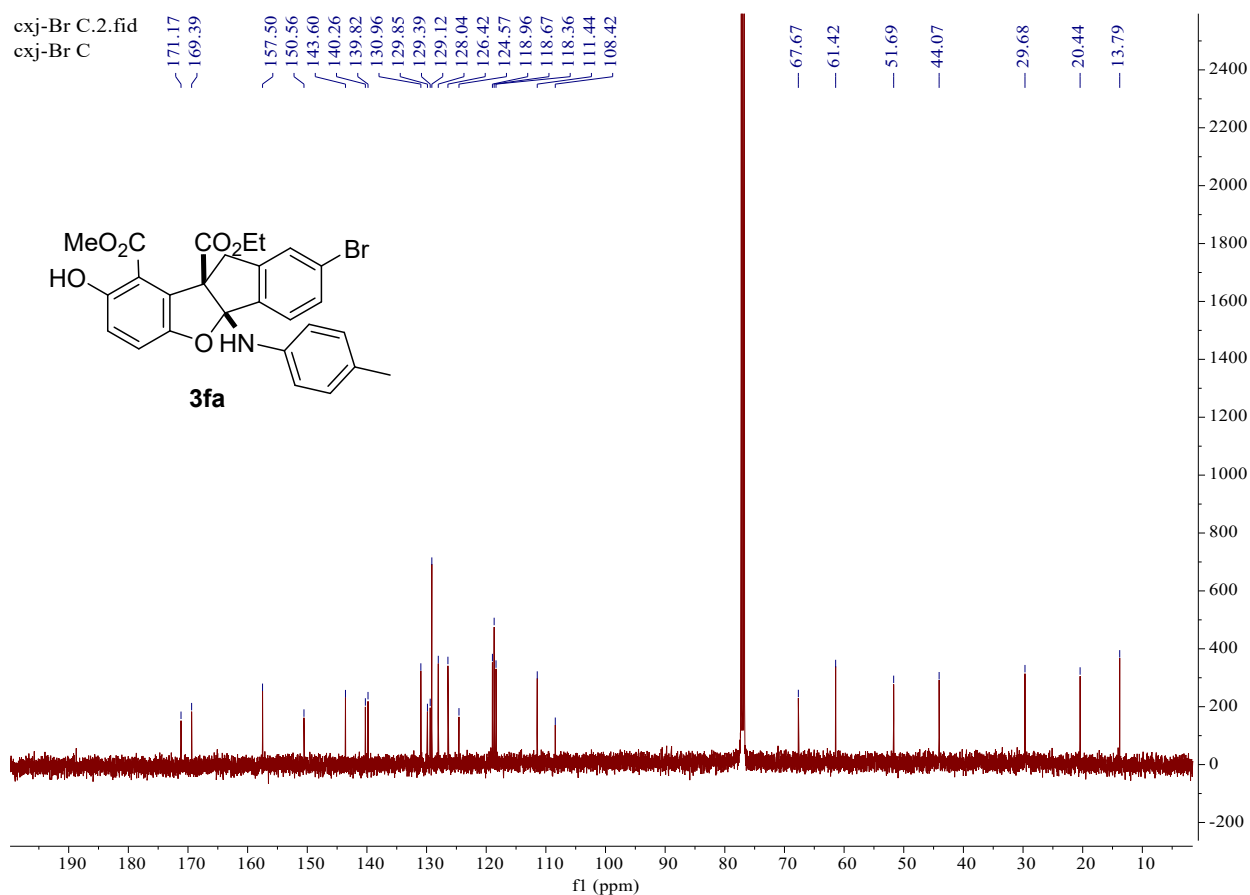


CXJ--Me C.2.fid
 CXJ--Me C



CXJ-Br H.1.fid
CXJ-Br H
NMR 400Hz





8. References

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