

Visible-Light-Induced Cascade Reaction of Etherification/C-C Coupling Cyclization: Efficient Synthesis of Dibenzo[b,d]oxepin-7(6H)-ones

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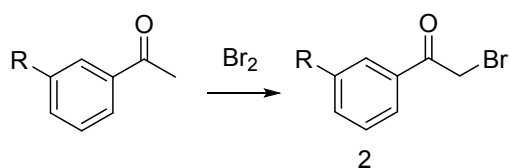
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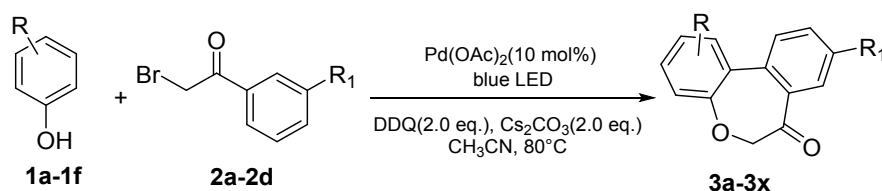
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1. Preparation of α -Bromoacetophenones (Compound 2). (General Procedure A)



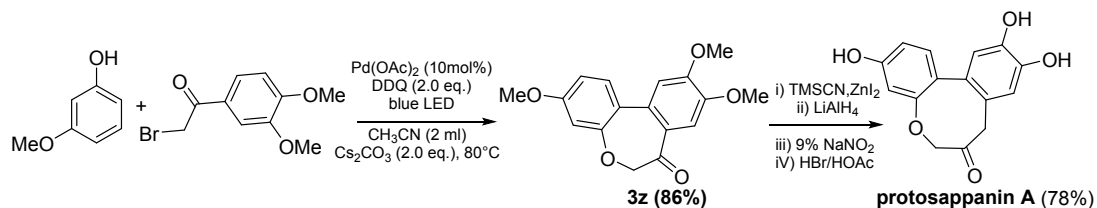
General Procedure A: To a solution of the appropriate acetophenone and acetic acid (4 equiv) were added to the flask with stirring under ice-cooling. Then anhydrous AlCl₃ (0.02 equiv) was added. Liquid bromine (1 equiv) in the acetic acid (3 equiv) was added in the flask during 1h. The mixture was stirred for 3 h, and then cooled down to room temperature, the K₂CO₃ saturated solution was added to the mixture, which was extracted with ethyl acetate three times. The organic phase was dried over Na₂SO₄. After filtration, the solvent was evaporated under reduced pressure. The residue was purified by chromatography on silica gel using a mixture of petroleum ether /dichloromethane (4:1, v/v) to give bromination product 2.

2. Preparation of Dibenzo[b,d]oxepin-7(6H)-ones (Compound 3). (General Procedure B)



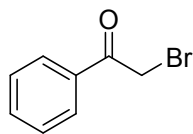
General Procedure B: To a mixture of the suitable phenol (0.45 mmol), α -bromoacetophenone (0.47 mmol), Pd(OAc)₂ (10 mol%), DDQ (2.0 equiv) and Cs₂CO₃(2.0 equiv) was added in CH₃CN 2ml. The mixture was stirred for 10h at 80°C under 25W blue LED. After completion of the reaction, the reaction mixture was cooled down to room temperature and water was added to the mixture, which was extracted with ethyl acetate three times. The organic phase was dried over Na₂SO₄. After filtration, the solvent was evaporated under reduced pressure. The residue was purified by flash silica gel column chromatography eluting with petroleum ether/ethyl acetate gradient (6:1, v/v).

3. Preparation of Protosappanin A. (General Procedure C)



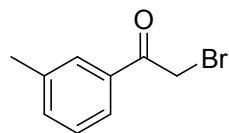
General Procedure C: Prepared compound **3z** by General Procedure B. (i) **3z** (1 mmol) was dissolved in DCM, and Et₃N (0.4 equiv) and TMSCN (1.1 equiv) were added. The mixture was stirred for 12 h at 30 °C and then was treated with a few of 6% aqueous NaHCO₃. Then the mixture was extracted with DCM three times. The organic phase was dried over Na₂SO₄. After filtration, the solvent was evaporated under reduced pressure. The crude was used directly in the next step without further purification. (ii) Anhydrous ether (0.2 M for substrate) and LiAlH₄ were added. The mixture was stirred for 12 h at 0 °C under nitrogen atmosphere. Ice water was carefully added to the above reaction solution to quench the reaction. Extraction by DCM, dried over Na₂SO₄. After filtration, the solvent was evaporated under reduced pressure. The residue was purified by the recrystallization method using ether. (iii) Obtained product was dissolved in anhydrous ether (0.2 M for substrate), then 9% NaNO₂ solution (5 equiv) was slowly added at 0 °C. The mixture was stirred for 1.5 h, added ice water. After filtration, Protosappanin A derivative was obtained. (iv) Protosappanin A derivative (1 mmol), 40% HBr (3.5 equiv) and HOAc (10 equiv) were added in the flask. The mixture was stirred for 12 h at 110 °C under nitrogen atmosphere, then cooled down to room temperature. The mixture was poured into ice water, and adjusted pH to about 5-6, which was extracted three times with ethyl acetate at room temperature. The organic phase was dried over Na₂SO₄. After filtration, the solvent was evaporated under reduced pressure to give white solid. Finally, Protosappanin A was purified by silica gel column chromatography eluting with petroleum ether/ethyl acetate gradient (20:1, v/v).

4. Spectra Data



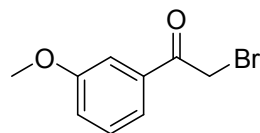
2a

Following the general procedure A. White solid. m.p. 48.2 – 49.7 °C.



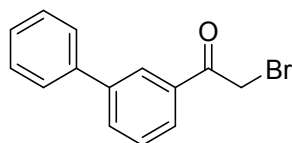
2b

Prepared according General Procedure A. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 7.81 (d, J = 9.7 Hz, 2H), 7.50 (d, J = 7.5 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 4.92 (s, 2H), 2.39 (s, 3H). Yellow liquid.



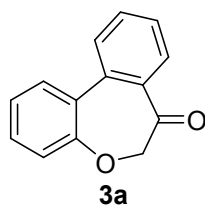
2c

Prepared according General Procedure A. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 7.55 (d, J = 7.7 Hz, 1H), 7.52 – 7.49 (m, 1H), 7.40 (t, J = 7.9 Hz, 1H), 7.17 – 7.13 (m, 1H), 4.44 (s, 2H), 3.86 (s, 3H).



2d

Prepared according General Procedure A. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ = 8.29 (t, J = 1.6 Hz, 1H), 7.99 (dd, J = 17.3, 7.8 Hz, 2H), 7.76 (d, J = 7.4 Hz, 2H), 7.65 (t, J = 7.8 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 7.43 (t, J = 7.3 Hz, 1H), 5.07 (s, 2H). Brown liquid.



3a

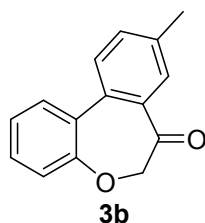
Prepared according General Procedure B. White solid (80%). m.p. 77.3 – 80.0 °C.

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ = 7.78 (dd, J = 12.0, 4.5 Hz, 2H), 7.72 – 7.65 (m, 2H), 7.57 (td, J = 7.6, 1.1 Hz, 1H), 7.47 (td, J = 7.7, 1.7 Hz, 1H), 7.38 (td, J = 7.6, 1.3 Hz, 1H), 7.27 (dd, J = 7.9, 1.2 Hz, 1H), 4.91 (s, 2H).

^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ = 204.0, 156.8, 136.6, 136.4, 134.3, 133.0, 131.0, 130.7, 129.9, 129.4, 128.7, 126.6, 121.9, 83.1.

HRMS (EI) calcd for $\text{C}_{14}\text{H}_{10}\text{O}_2$ $[\text{M}+\text{H}]^+$: 211.0759. Found: 211.0763. Anal. calcd for $\text{C}_{14}\text{H}_{10}\text{O}_2$: C, 79.98; H, 4.79. Found: C, 79.99; H, 4.78.

FT-IR (KBr disc): ν = 2919, 1688, 1599, 1494, 1239, 1062 cm^{-1} .



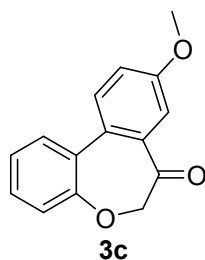
Prepared according General Procedure B. White solid (82%). m.p. 55.9 – 56.7 °C.

^1H NMR (400 MHz, CDCl_3): δ = 7.72 (s, 1H), 7.56 (dd, J = 7.7, 1.7 Hz, 1H), 7.49 (dd, J = 8.0, 1.5 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.37 (dt, J = 7.6, 1.7 Hz, 1H), 7.29 (dt, J = 7.5, 1.4 Hz, 1H), 7.21 (dd, J = 7.9, 1.3 Hz, 1H), 4.82 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ = 204.0, 156.8, 138.1, 135.8, 134.5, 134.3, 133.2, 130.1, 129.9, 129.8, 129.4, 125.9, 121.3, 82.7, 20.9.

HRMS (EI) calcd for $\text{C}_{15}\text{H}_{12}\text{O}_2$ $[\text{M}+\text{H}]^+$: 225.0915. Found: 225.0923. Anal. calcd for $\text{C}_{15}\text{H}_{12}\text{O}_2$: C, 80.34; H, 5.39. Found: C, 80.32; H, 5.41.

FT-IR (KBr disc): ν = 2915, 1682, 1600, 1510, 1297, 1061 cm^{-1} .



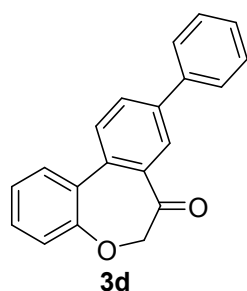
Prepared according General Procedure B. White solid (84%). m.p. 53.4 – 55.6 °C.

^1H NMR (400 MHz, CDCl_3) δ = 7.53 (d, J = 7.4 Hz, 1H), 7.48 (d, J = 8.6 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.34 (t, J = 6.9 Hz, 1H), 7.29 (d, J = 7.1 Hz, 1H), 7.24 – 7.16 (m, 2H), 4.81 (s, 2H), 3.89 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ = 203.5 , 159.3 , 156.6 , 136.9 , 132.9 , 131.0 , 130.0 , 129.8 , 129.6 , 125.9 , 121.2 , 121.0 , 112.8 , 82.5 , 55.6 .

HRMS (EI) calcd for $\text{C}_{15}\text{H}_{12}\text{O}_3$ $[\text{M}+\text{H}]^+$: 241.0865. Found: 241.0873. Anal.calcd for $\text{C}_{15}\text{H}_{12}\text{O}_3$: C, 74.99; H, 5.03. Found: C, 75.02; H, 5.05.

FT-IR (KBr disc): ν = 2917, 1685, 1603, 1508, 1298, 1062 cm^{-1} .



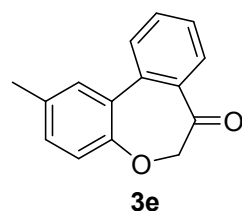
Prepared according General Procedure B. White solid (79%). m.p. 121.0 – 122.8 $^{\circ}\text{C}$.

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ = 8.13 – 8.02 (m, 2H), 7.82 – 7.71 (m, 4H), 7.57 – 7.37 (m, 5H), 7.29 (dd, J = 7.9, 1.3 Hz, 1H), 4.96 (s, 2H).

^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ = 203.3, 156.4, 139.7, 138.4, 136.4, 135.1, 132.1, 131.7, 130.5, 130.2, 130.1, 129.2, 128.2, 126.8, 126.7, 126.1, 121.5, 82.5.

HRMS (EI) calcd for $\text{C}_{20}\text{H}_{14}\text{O}_2$ $[\text{M}+\text{H}]^+$: 287.1072. Found: 287.1066. Anal.calcd for $\text{C}_{20}\text{H}_{14}\text{O}_2$: C, 83.90; H, 4.93. Found: C, 83.87; H, 4.96.

FT-IR (KBr disc): ν = 2920, 1685, 1592, 1499, 1351, 1269, 1078 cm^{-1} .



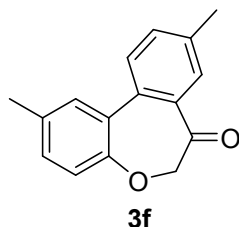
Prepared according General Procedure B. White solid (83%). m.p. 106.6 – 109.3 $^{\circ}\text{C}$.

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ = 7.76 (dd, J = 11.8, 4.5 Hz, 2H), 7.69 – 7.63 (m, 1H), 7.55 (td, J = 7.6, 1.2 Hz, 1H), 7.48 (d, J = 1.7 Hz, 1H), 7.25 (dd, J = 8.1, 1.6 Hz, 1H), 7.14 (d, J = 8.1 Hz, 1H), 4.86 (s, 2H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ = 204.2, 154.7, 136.7, 136.5, 135.7, 134.2, 132.6, 131.3, 131.0, 129.8, 129.4, 128.5, 121.5, 83.1, 20.9.

HRMS (EI) calcd for $\text{C}_{15}\text{H}_{12}\text{O}_2$ $[\text{M}+\text{H}]^+$: 225.0915. Found: 225.0922. Anal. calcd for $\text{C}_{15}\text{H}_{12}\text{O}_2$: C, 80.34; H, 5.39. Found: C, 80.36; H, 5.37.

FT-IR (KBr disc): ν = 2910, 1678, 1599, 1502, 1282, 1054 cm^{-1} .



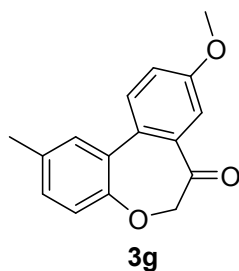
Prepared according General Procedure B. White solid (85%). m.p. 83.7 – 85.1 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3) δ = 7.70 (s, 1H), 7.45 (s, 1H), 7.34 (d, J = 1.7 Hz, 1H), 7.16 (dd, J = 8.2, 1.8 Hz, 1H), 7.09 (d, J = 8.1 Hz, 1H), 4.78 (s, 1H), 2.44 (s, 1H), 2.39 (s, 2H).

^{13}C NMR (100 MHz, CDCl_3) δ = 203.7, 154.9, 144.3, 137.2, 135.4, 133.7, 133.0, 130.8, 130.7, 130.0, 129.7, 128.8, 121.1, 82.7, 21.8, 21.0.

HRMS (EI) calcd for $\text{C}_{16}\text{H}_{14}\text{O}_2$ $[\text{M}+\text{H}]^+$: 239.1072. Found: 239.1069. Anal. calcd for $\text{C}_{16}\text{H}_{14}\text{O}_2$: C, 80.65; H, 5.92. Found: C, 80.62; H, 5.95.

FT-IR (KBr disc): ν = 2928, 1688, 1494, 1239, 1045 cm^{-1} .



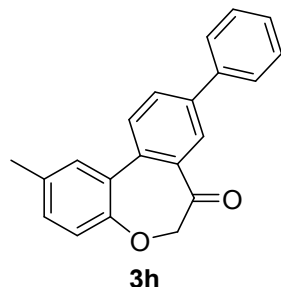
Prepared according General Procedure B. Light yellow solid (88%). m.p. 80.6– 81.4 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3) δ = 7.48 (d, J = 8.6 Hz, 1H), 7.40 (d, J = 2.8 Hz, 1H), 7.31 (s, 1H), 7.21 (dd, J = 8.6, 2.9 Hz, 1H), 7.16 – 7.06 (m, 2H), 4.78 (s, 2H), 3.89 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ = 203.8, 159.2, 154.4, 137.0, 135.4, 132.5, 130.90, 130.3, 130.1, 123.0, 120.9, 120.9, 112.7, 82.6, 55.6, 21.0.

HRMS (EI) calcd for C₁₅H₁₂O₃ [M+H]⁺: 255.1022. Found: 255.1029. Anal.calcd for C₁₅H₁₂O₃: C, 74.99; H, 5.03. Found: C, 74.96; H, 5.05.

FT-IR (KBr disc): ν = 2926, 1685, 1486, 1240, 1043 cm⁻¹.



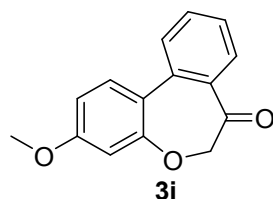
Prepared according General Procedure C. White solid (80%). m.p. 82.4 – 84.7 °C.

¹H NMR (400 MHz, CDCl₃) δ = 8.14 (d, J = 2.1 Hz, 1H), 7.90 (dd, J = 8.1, 2.1 Hz, 1H), 7.68 (dd, J = 5.2, 3.3 Hz, 2H), 7.63 (d, J = 8.1 Hz, 1H), 7.48 (dd, J = 10.2, 4.8 Hz, 2H), 7.42 – 7.37 (m, 2H), 7.19 (dd, J = 8.1, 2.0 Hz, 1H), 7.13 (d, J = 8.1 Hz, 1H), 4.84 (s, 2H), 2.42 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ = 204.3, 154.8, 140.9, 139.5, 136.6, 136.1, 135.7, 132.6, 132.0, 131.0, 130.7, 130.1, 129.1, 128.1, 127.2, 121.2, 82.9, 21.1.

HRMS (EI) calcd for C₂₁H₁₆O₂ [M+H]⁺: 301.1228. Found: 301.1231. Anal.calcd for C₂₁H₁₆O₂: C, 83.98; H, 5.37. Found: C, 83.95; H, 5.40.

FT-IR (KBr disc): ν = 2902, 1681, 1484, 1230, 1007 cm⁻¹.



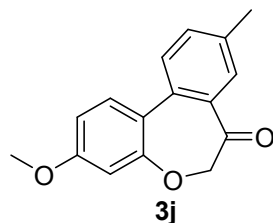
Prepared according General Procedure B. White solid (85%). m.p. 113.4 – 115.7 °C.

¹H NMR (400 MHz, DMSO-*d*₆) δ = 7.78 (dd, J = 7.8, 1.3 Hz, 1H), 7.74 (td, J = 7.7, 1.4 Hz, 1H), 7.62 (d, J = 8.7 Hz, 1H), 7.59 (d, J = 7.8 Hz, 1H), 7.50 (td, J = 7.6, 1.1 Hz, 1H), 6.96 (dd, J = 8.7, 2.6 Hz, 1H), 6.84 (d, J = 2.6 Hz, 1H), 4.90 (s, 2H), 3.82 (s, 3H).

¹³C NMR (100 MHz, DMSO-*d*₆) δ = 203.8, 161.4, 158.0, 136.8, 135.8, 134.3, 131.5, 129.5, 129.5, 127.9, 125.1, 112.7, 107.5, 82.8, 56.0.

HRMS (EI) calcd for C₁₅H₁₂O₃ [M+H]⁺: 241.0864. Found: 241.0859. Anal.calcd for C₁₅H₁₂O₃: C, 74.99; H, 5.03. Found: C, 74.96; H, 5.06.

FT-IR (KBr disc): ν = 2917, 1680, 1608, 1256, 1168, 1036 cm⁻¹.



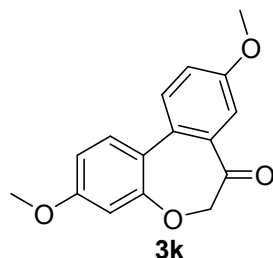
Prepared according General Procedure B. White solid (87%). m.p. 137.9 – 139.4 °C.

¹H NMR (400 MHz, CDCl₃) δ = 7.72 (d, *J* = 0.7 Hz, 1H), 7.45 (dd, *J* = 13.4, 5.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 1H), 6.85 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.75 (d, *J* = 2.6 Hz, 1H), 4.80 (s, 2H), 3.84 (s, 3H), 2.42 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ = 204.0, 161.1, 157.9, 137.4, 135.3, 134.7, 134.5, 130.8, 130.0, 129.2, 125.4, 112.3, 106.4, 82.6, 55.7, 21.0.

HRMS (EI) calcd for C₁₆H₁₄O₃ [M+H]⁺: 255.1021. Found: 255.1018. Anal.calcd for C₁₆H₁₄O₃: C, 75.58; H, 5.55. Found: C, 75.60; H, 5.52.

FT-IR (KBr disc): ν = 2919, 1680, 1608, 1256, 1168, 1036 cm⁻¹.



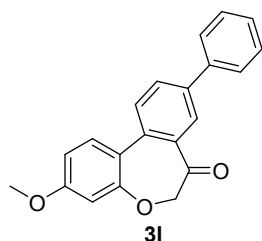
Prepared according General Procedure B. White solid (89%). m.p. 133.7 – 135.1 °C.

¹H NMR (400 MHz, CDCl₃) δ = 7.47 – 7.39 (m, 3H), 7.23 – 7.17 (m, 1H), 6.85 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.75 (s, 1H), 4.80 (s, 2H), 3.89 (s, 3H), 3.84 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ = 203.3, 160.7, 158.8, 157.6, 136.2, 130.6, 130.6, 130.1, 125.1, 121.2, 112.7, 112.2, 106.2, 82.3, 55.6, 55.6.

HRMS (EI) calcd for C₁₆H₁₄O₄ [M+H]⁺: 271.0976. Found: 271.0982. Anal.calcd for C₁₆H₁₄O₄: C, 71.10; H, 5.22. Found: C, 71.12; H, 5.21.

FT-IR (KBr disc): ν = 2916, 1683, 1610, 1258, 1167, 1036 cm⁻¹.



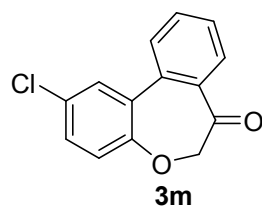
Prepared according General Procedure B. White solid (80%). m.p. 140.7 – 143.4 °C.

¹H NMR (400 MHz, CDCl₃) δ = 8.16 (d, *J* = 2.0 Hz, 1H), 7.87 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.69 – 7.65 (m, 2H), 7.55 (dd, *J* = 9.7, 8.6 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 6.89 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.79 (d, *J* = 2.6 Hz, 1H), 4.86 (s, 2H), 3.86 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ = 203.6, 161.4, 158.1, 140.2, 139.5, 136.1, 136.0, 132.1, 131.0, 129.8, 129.1, 128.2, 128.0, 127.1, 125.1, 112.4, 106.5, 82.6, 55.7.

HRMS (EI) calcd for C₂₁H₁₆O₃ [M+H]⁺: 317.1177. Found: 317.1169. Anal. calcd for C₂₁H₁₆O₃: C, 79.73; H, 5.10. Found: C, 79.76; H, 5.07.

FT-IR (KBr disc): ν = 2914, 1693, 1459, 1237, 1035 cm⁻¹.



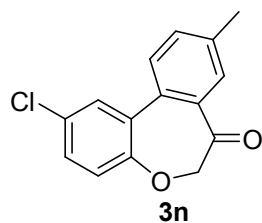
Prepared according General Procedure B. White solid (78%). m.p. 143.6 – 145.1 °C.

¹H NMR (400 MHz, CDCl₃) δ = 7.92 (d, *J* = 8.7 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.57 – 7.49 (m, 3H), 7.37 – 7.31 (m, 1H), 7.17 (d, *J* = 8.5 Hz, 1H), 4.82 (s, 2H).

¹³C NMR (100 MHz, CDCl₃) δ = 203.2, 155.3, 136.1, 135.6, 134.8, 133.8, 131.2, 130.0, 130.0, 129.7, 129.3, 128.6, 122.9, 82.8.

HRMS (EI) calcd for C₁₄H₉ClO₂ [M+H]⁺: 245.0371. Found: 245.0362. Anal. calcd for C₁₄H₉ClO₂: C, 68.73; H, 3.71; Cl, 14.49. Found: C, 68.75; H, 3.73; Cl, 14.51.

FT-IR (KBr disc): ν = 2926, 1682, 1594, 1484, 1280, 1022 cm⁻¹.



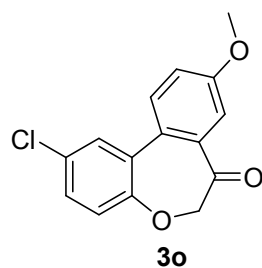
Prepared according General Procedure B. White solid (81%). m.p. 152.0 – 154.0 °C.

¹H NMR (400 MHz, CDCl₃) δ = 7.73 (s, 1H), 7.56 – 7.47 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.31 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 1H), 4.80 (s, 2H), 2.45 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ = 203.3, 155.3, 138.8, 135.8, 134.8, 134.6, 132.92, 131.1, 130.0, 129.8, 129.7, 129.3, 122.8, 82.7, 21.0.

HRMS (EI) calcd for C₁₅H₁₁ClO₂ [M+H]⁺: 259.0528. Found: 259.0537. Anal. calcd for C₁₅H₁₁ClO₂: C, 69.64; H, 4.29; Cl, 13.70. Found: C, 69.67; H, 4.32; Cl, 13.73.

FT-IR(KBr disc): ν = 2978, 1686, 1562, 1486, 1288, 1040 cm⁻¹.



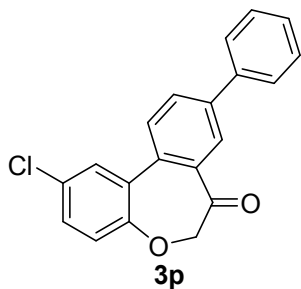
Prepared according General Procedure B. White solid (83%). m.p. 164.9 – 166.4 °C.

¹H NMR (400 MHz, CDCl₃) δ = 7.51 (d, *J* = 2.5 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.29 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.23 (dd, *J* = 8.6, 2.9 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 4.80 (s, 2H), 3.91 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ = 202.8, 159.7, 155.1, 137.0, 134.6, 131.1, 131.0, 129.6, 129.3, 128.4, 122.7, 121.0, 113.0, 82.5, 55.7.

HRMS (EI) calcd for C₁₅H₁₁ClO₃ [M+H]⁺: 275.0475. Found: 275.0483. Anal. calcd for C₁₅H₁₁ClO₃: C, 65.59; H, 4.04; Cl, 12.90. Found: C, 65.62; H, 4.05; Cl, 12.93.

FT-IR(KBr disc): ν = 2924, 1682, 1608, 1484, 1288, 1034 cm⁻¹.



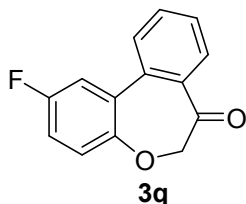
Prepared according General Procedure B. White solid (76%). m.p. 145.6 – 147.3 °C.

¹H NMR (400 MHz, CDCl₃) δ = 8.15 (s, 1H), 7.89 (d, *J* = 6.1 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.60 – 7.54 (m, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H), 7.33 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.17 (d, *J* = 8.5 Hz, 1H), 4.83 (s, 2H).

¹³C NMR (100 MHz, CDCl₃) δ = 203.0 , 155.4 , 141.5 , 139.1 , 136.4 , 134.5 , 134.4 , 132.1 , 131.2 , 130.0 , 123.0 , 129.8 , 129.0 , 128.2 , 128.2 , 127.1 , 122.9 , 82.7 .

HRMS (EI) calcd for C₂₀H₁₃ClO₂ [M+H]⁺: 321.0682. Found: 321.0675. Anal.calcd for C₂₀H₁₃ClO₂: C, 74.89; H, 4.09; Cl, 11.05. Found: C, 74.91; H, 4.12; Cl, 11.08.

FT-IR(KBr disc): ν = 2926, 1680, 1612, 1485, 1286, 1036 cm⁻¹.



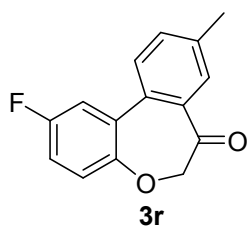
Prepared according General Procedure B. White solid (76%). m.p. 131.6 – 132.2 °C.

¹H NMR (400 MHz, CDCl₃) δ = 7.92 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.69 (td, *J* = 7.7, 1.5 Hz, 1H), 7.51 (dd, *J* = 11.0, 4.4 Hz, 2H), 7.30 – 7.26 (m, 1H), 7.20 (dd, *J* = 8.8, 5.0 Hz, 1H), 7.07 (ddd, *J* = 8.8, 7.7, 3.0 Hz, 1H), 4.82 (s, 2H).

¹³C NMR (100 MHz, DMSO-*d*₆) δ = 203.8, 160.1 (d, *J* = 240 Hz), 153.1, 136.5, 135.5 (d, *J* = 10 Hz), 134.8, 134.3, 130.1, 129.5, 129.3, 123.8 (d, *J* = 10 Hz), 117.4 (d, *J* = 30Hz), 116.9 (d, *J* = 20 Hz), 83.2.

HRMS (EI) calcd for C₁₄H₉FO₂ [M+H]⁺: 229.0665. Found: 229.0659. Anal.calcd for C₁₄H₉FO₂: C, 73.68; H, 3.98; F, 8.32. Found: C, 73.65; H, 3.95; F, 8.34.

FT-IR (KBr disc): ν = 2928, 1688, 1484, 1282, 1168 cm⁻¹.



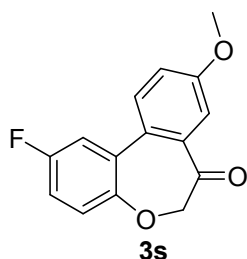
Prepared according General Procedure B. White solid (79%). m.p. 121.7 – 123.3 °C.

¹H NMR (400 MHz, DMSO-*d*₆) δ = 7.61 (d, *J* = 3.8 Hz, 3H), 7.53 (dd, *J* = 9.8, 2.7 Hz, 1H), 7.37 – 7.21 (m, 2H), 4.88 (s, 2H), 2.42 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ = 174.7, 158.2 (d, *J* = 240 Hz), 150.7, 137.8, 133.9, 133.4 (d, *J* = 10 Hz), 129.3, 129.2, 118.0, 117.7, 115.1 (d, *J* = 10 Hz), 114.5, 114.3, 66.3, 21.4.

HRMS (EI) calcd for C₁₅H₁₁FO₂ [M+H]⁺: 243.0821. Found: 243.0817. Anal. calcd for C₁₅H₁₁FO₂: C, 74.37; H, 4.58; F, 7.84. Found: C, 74.35; H, 4.61; F, 7.86.

FT-IR (KBr disc): ν = 2919, 1722, 1494, 1274, 1185, 1054 cm⁻¹.



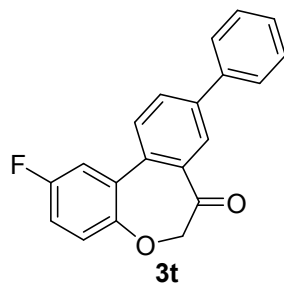
Prepared according General Procedure B. White solid (81%). m.p. 115.7 – 116.5 °C.

¹H NMR (400 MHz, CDCl₃) δ = 7.47 – 7.40 (m, 2H), 7.25 – 7.20 (m, 2H), 7.17 (dd, *J* = 8.8, 5.0 Hz, 1H), 7.01 (td, *J* = 8.7, 8.3, 3.0 Hz, 1H), 4.79 (s, 2H), 3.90 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ = 203.1, 160.2 (s, *J* = 240 Hz), 159.7, 159.0, 152.5, 137.0, 134.5 (d, *J* = 9.0 Hz), 130.9, 128.6, 122.6, 122.5, 120.9, 116.1 (d, *J* = 21 Hz), 115.8 (d, *J* = 23 Hz), 113.0, 82.6, 55.6.

HRMS (EI) calcd for C₁₅H₁₁FO₃ [M+H]⁺: 259.0776. Found: 259.0782. Anal. calcd for C₁₅H₁₁FO₃: C, 69.76; H, 4.29; F, 7.36. Found: C, 69.78; H, 4.31; F, 7.39.

FT-IR (KBr disc): ν = 2918, 1725, 1497, 1275, 1186, 1052 cm⁻¹.



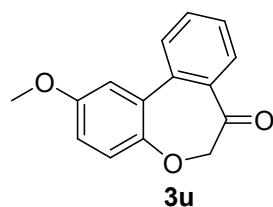
Prepared according General Procedure B. White solid (75%). m.p. 142.1 – 144.7 °C.

¹H NMR (400 MHz, CDCl₃) δ = 8.16 (d, *J* = 2.0 Hz, 1H), 7.92 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.31 (dd, *J* = 9.2, 3.0 Hz, 1H), 7.21 (dd, *J* = 8.8, 5.0 Hz, 1H), 7.11 – 7.05 (m, 1H), 4.85 (s, 2H).

¹³C NMR (100 MHz, CDCl₃) δ = 203.5, 160.4 (d, *J* = 240 Hz), 153.0, 141.6, 139.3, 136.6, 134.8, 134.6 (d, *J* = 10 Hz), 132.2, 130.1, 129.1, 128.3, 127.2, 123.0 (d, *J* = 10 Hz), 116.9, 116.7 (d, *J* = 10 Hz), 116.4, 83.0.

HRMS (EI) calcd for C₂₀H₁₃FO₂ [M+H]⁺: 305.0978. Found: 305.0969. Anal. calcd for C₂₀H₁₃FO₂: C, 78.94; H, 4.31; F, 6.24. Found: C, 78.92; H, 4.43; F, 6.37.

FT-IR (KBr disc): ν = 2910, 1678, 1476, 1239, 1168, 1032 cm⁻¹.



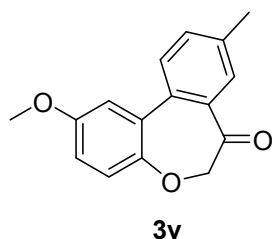
Prepared according General Procedure B. White solid (83%). m.p. 92.5-94.1 °C.

¹H NMR (400 MHz, DMSO-*d*₆) δ = 7.60 (d, *J* = 8.6 Hz, 1H), 7.43 (s, 1H), 7.34 (d, *J* = 8.5 Hz, 1H), 7.27 (s, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 4.84 (s, 2H), 3.87 (s, 3H), 2.35 (s, 3H).

¹³C NMR (100 MHz, DMSO-*d*₆) δ = 203.3, 158.7, 153.9, 136.4, 134.9, 132.0, 130.4, 129.8, 129.6, 129.5, 120.4, 120.3, 112.2, 82.1, 55.1, 20.5.

HRMS (EI) calcd for C₁₅H₁₂O₃ [M+H]⁺: 241.0866. Found: 241.0875. Anal. calcd for C₁₅H₁₂O₃: C, 74.99; H, 5.03. Found: C, 74.98; H, 5.05.

FT-IR (KBr disc): ν = 2918, 1682, 1608, 1258, 1167, 1035 cm⁻¹.



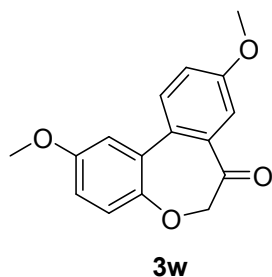
Prepared according General Procedure B. White solid (86%). m.p. 116.5 – 118.8 °C.

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ = 7.60 (d, J = 8.6 Hz, 1H), 7.43 (s, 1H), 7.34 (d, J = 8.5 Hz, 1H), 7.27 (s, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 4.84 (s, 2H), 3.87 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ = 203.3 , 158.7 , 153.9 , 136.4 , 134.9 , 132.0 , 130.4 , 129.8 , 129.6 , 129.5 , 120.4 , 120.3 , 112.2 , 82.1 , 55.1 , 20.5 .

HRMS (EI) calcd for $\text{C}_{16}\text{H}_{14}\text{O}_3$ $[\text{M}+\text{H}]^+$: 255.1023. Found: 255.1031. Anal.calcd for $\text{C}_{16}\text{H}_{14}\text{O}_3$: C, 75.58; H, 5.55. Found: C, 75.55; H, 5.57.

FT-IR (KBr disc): ν = 2916, 1680, 1608, 1257, 1168, 1033 cm^{-1} .



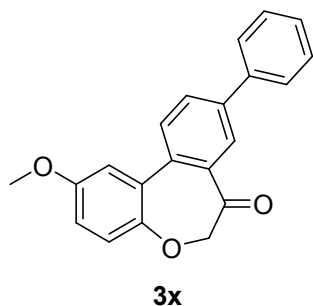
Prepared according General Procedure B. White solid (88%). m.p. 112.3 – 114.9 °C.

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ = 7.58 – 7.52 (m, 2H), 7.32 (d, J = 8.5 Hz, 1H), 7.30 – 7.26 (m, 1H), 6.93 (d, J = 8.5 Hz, 1H), 6.82 (s, 1H), 4.87 (s, 2H), 3.85 (s, 3H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ = 202.9 , 160.4 , 158.4 , 157.2 , 135.9 , 130.3 , 130.2 , 129.7 , 124.7 , 120.8 , 112.3 , 111.8 , 105.9 , 81.9 , 55.2 .

HRMS (EI) calcd for $\text{C}_{16}\text{H}_{14}\text{O}_4$ $[\text{M}+\text{H}]^+$: 271.0972. Found: 271.0978. Anal.calcd for $\text{C}_{16}\text{H}_{14}\text{O}_4$: C, 71.10; H, 5.22. Found: C, 71.13; H, 5.19.

FT-IR (KBr disc): ν = 2914, 1683, 1610, 1259, 1166, 1032 cm^{-1} .



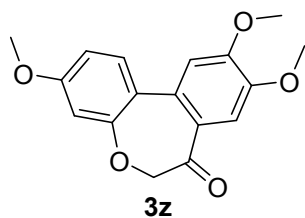
Prepared according General Procedure B. White solid (81%). m.p. 120.8 – 122.7 °C.

¹H NMR (400 MHz, DMSO-*d*₆) δ = 7.70 (d, *J* = 7.2 Hz, 2H), 7.66 (d, *J* = 7.4 Hz, 1H), 7.60 (s, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.38 (dd, *J* = 22.5, 8.0 Hz, 3H), 7.01 (s, 1H), 6.94 (d, *J* = 7.3 Hz, 1H), 3.84 (s, 3H), 3.62 (s, 2H).

¹³C NMR (100 MHz, DMSO-*d*₆) δ = 203.5 , 161.3 , 158.0 , 140.1 , 136.0 , 135.8 , 132.0 , 130.8 , 129.7 , 128.9 , 128.1 , 127.9 , 127.0 , 125.0 , 112.3 , 111.8 , 106.4 , 82.5 , 55.6 .

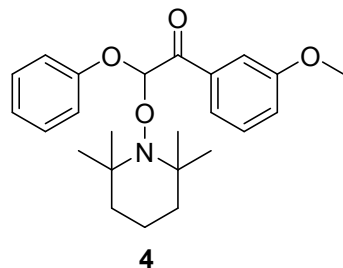
HRMS (EI) calcd for C₂₁H₁₆O₃ [M+H]⁺: 317.1179. Found: 316.1187. Anal. calcd for C₂₁H₁₆O₃: C, 79.73; H, 5.10. Found: C, 79.75; H, 5.07.

FT-IR (KBr disc): ν = 2915, 1685, 1612, 1260, 1165, 1035 cm⁻¹.



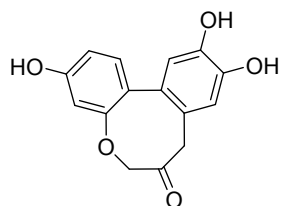
Prepared according General Procedure B. White solid. m.p. 206.5 – 207.2 °C.

¹H NMR (400 MHz, CDCl₃) δ = 7.49 (s, 1H), 7.47 (d, *J* = 8.8 Hz, 1H), 6.93 (s, 1H), 6.86 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.76 (d, *J* = 2.4 Hz, 1H), 4.77 (s, 2H), 4.00 (s, 3H), 3.97 (s, 3H), 3.86 (s, 3H).



^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ = 8.07 (d, J = 5.6 Hz, 2H), 7.68 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.4 Hz, 2H), 7.32 – 7.24 (m, 3H), 6.99 (dd, J = 7.6, 1.9 Hz, 2H), 6.96 – 6.90 (m, 1H), 3.74 (s, 3H), 1.72 – 1.54 (m, 5H), 1.42 – 1.33 (m, 1H), 1.23 (s, 6H), 1.01 (s, 6H).

^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ = 194.3 , 160.0 , 158.0 , 135.9 , 129.8 , 129.6 , 124.5 , 121.7 , 120.6 , 120.4 , 114.8 , 112.4 , 59.5 , 55.5 , 34.9 , 27.0 , 17.7 .



Protosappanin A.

White solid (78%), White solid. m.p. 253.7–254.9 °C.

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ = 9.68 (s, 1H), 8.93 (s, 1H), 8.91 (s, 1H), 7.07 (d, J = 8.2 Hz, 1H), 6.68 (dd, J = 8.2, 2.3 Hz, 1H), 6.67 – 6.61 (m, 3H), 4.47 (s, 2H), 3.32 (s, 2H).

6. ^1H and ^{13}C NMR spectra for compounds

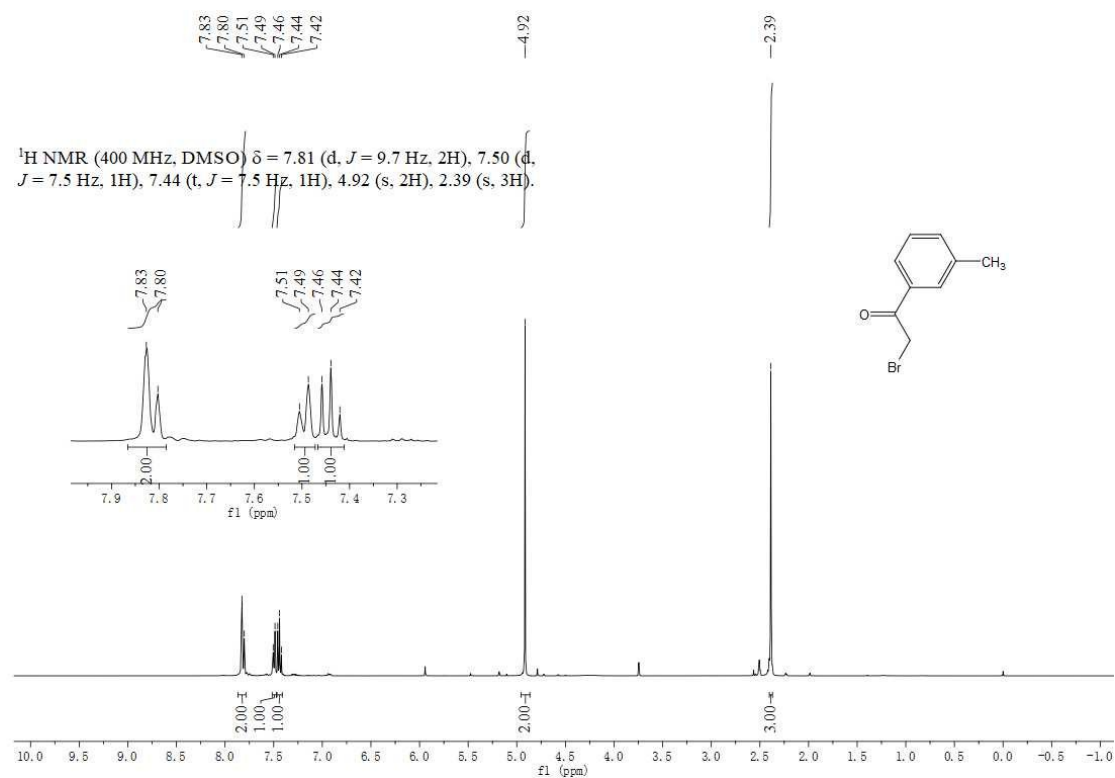


Fig. S1 NMR spectra of **2b**

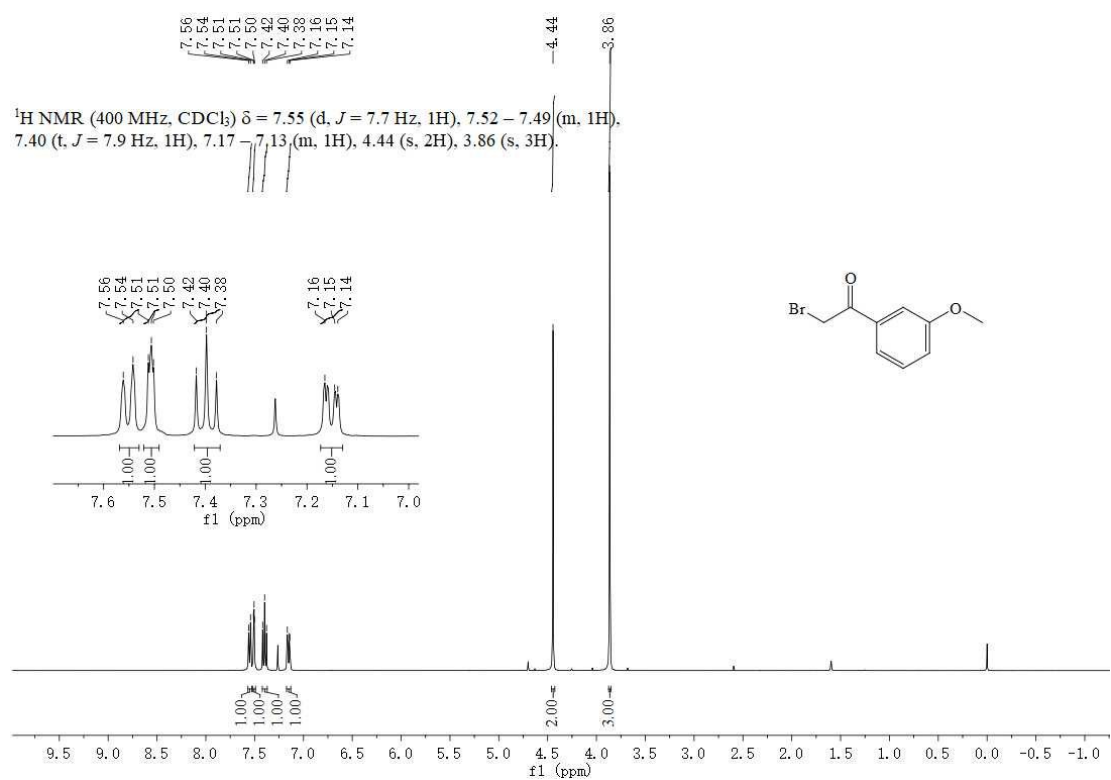


Fig. S2 NMR spectra of **2c**

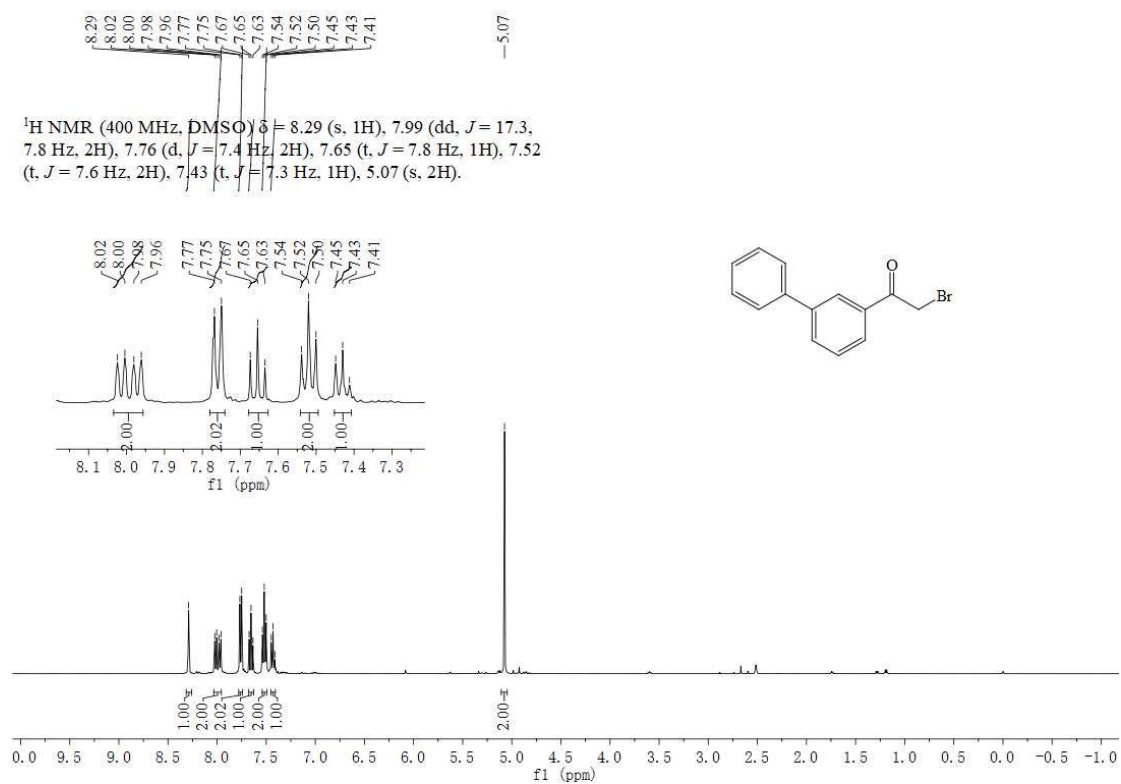


Fig. S3 NMR spectra of **2d**

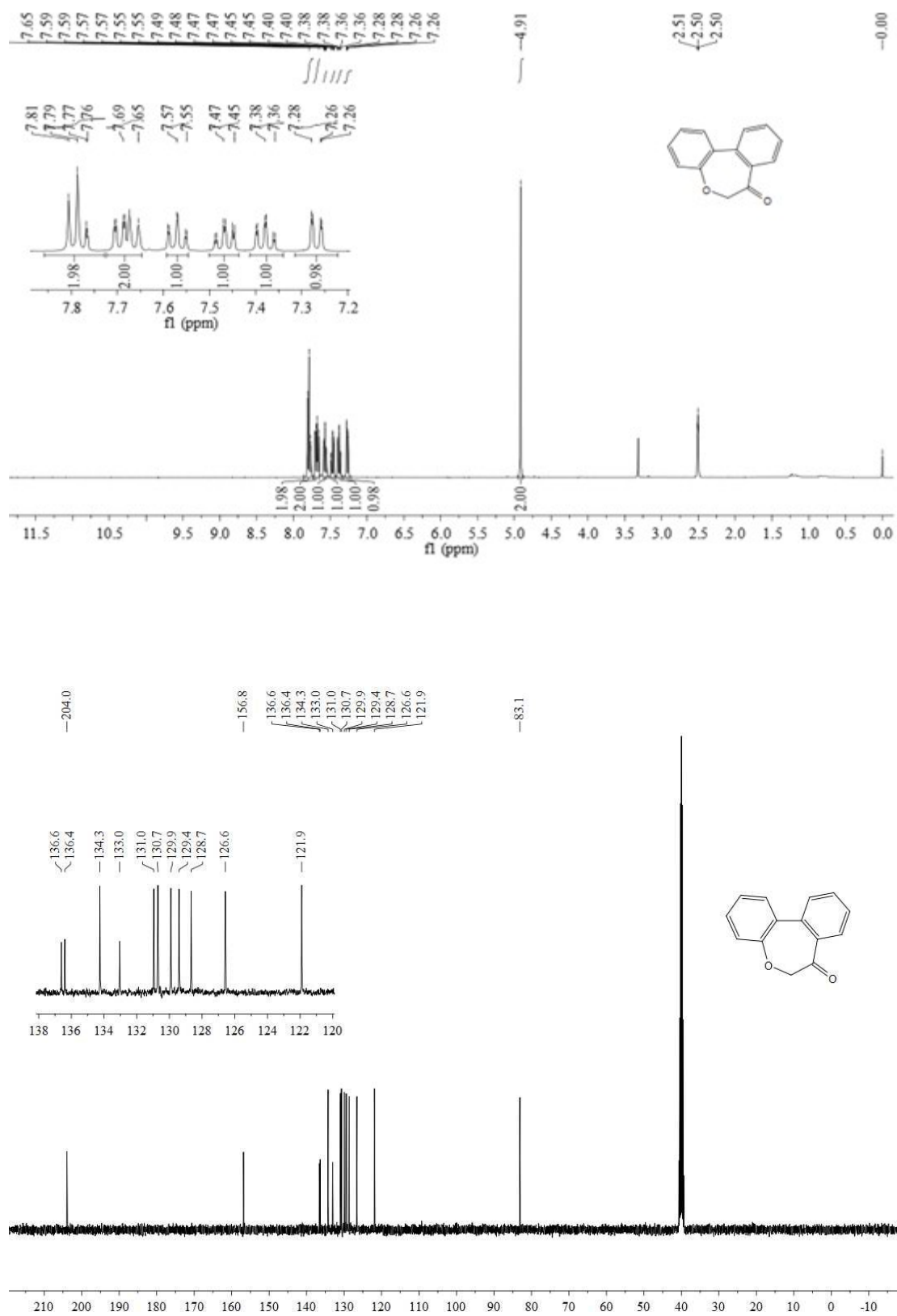


Fig. S4 NMR spectra of **3a**

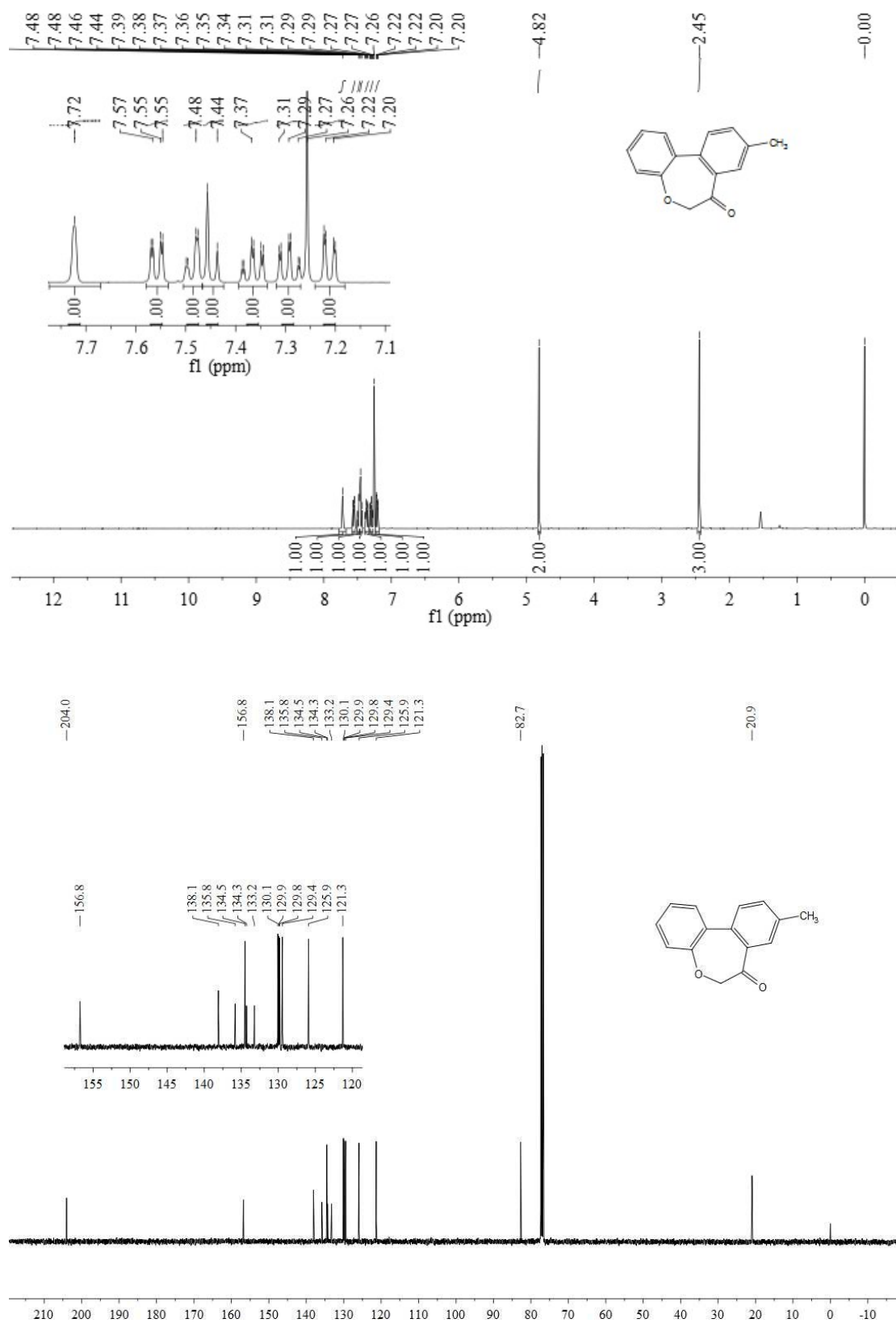


Fig. S5 NMR spectra of **3b**

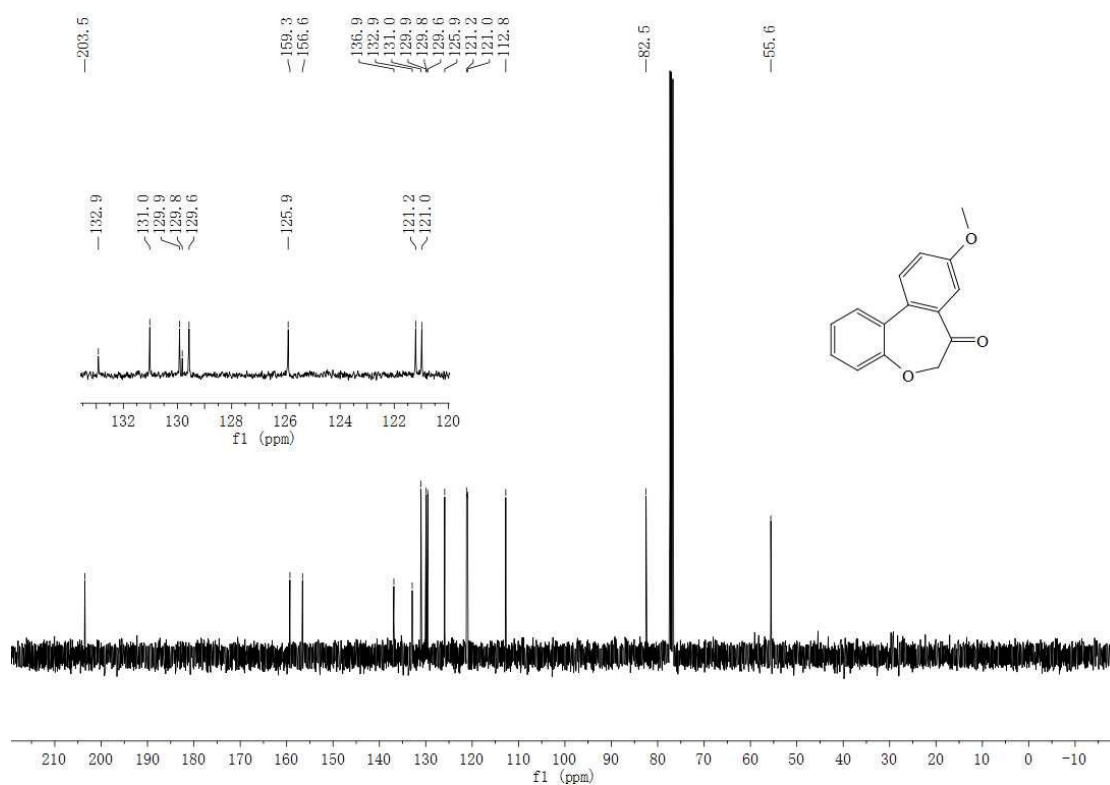
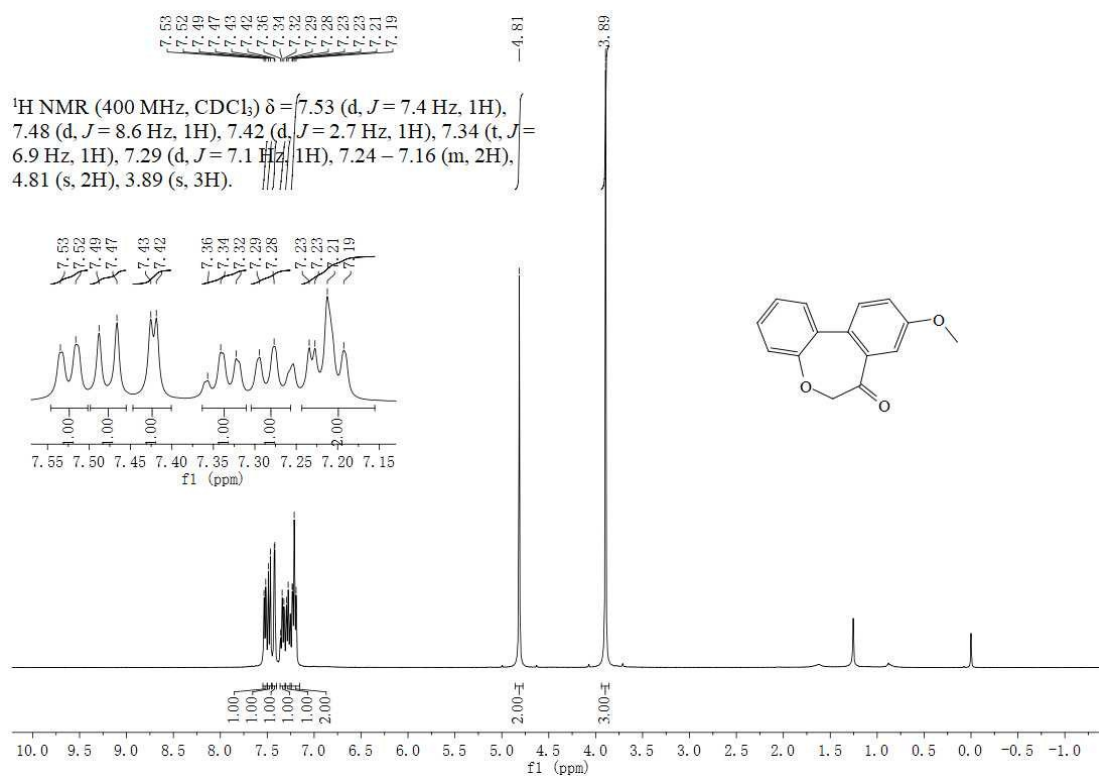


Fig. S6 NMR spectra of **3c**

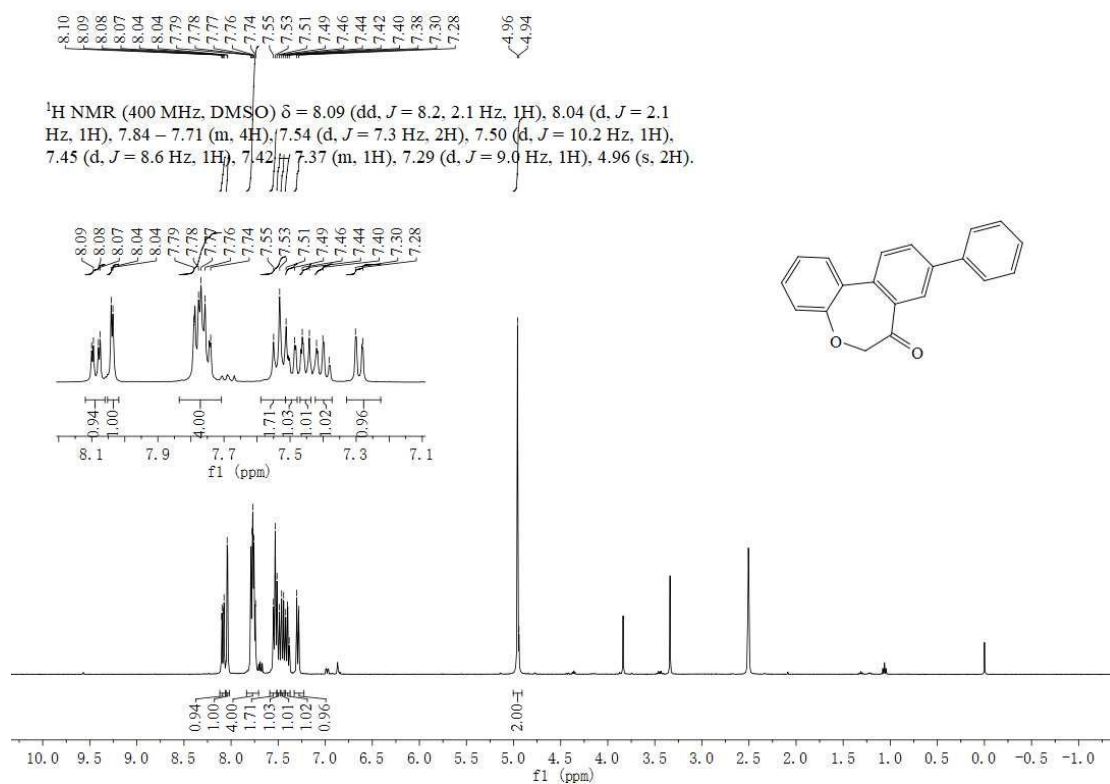


Fig. S7 NMR spectra of **3d**

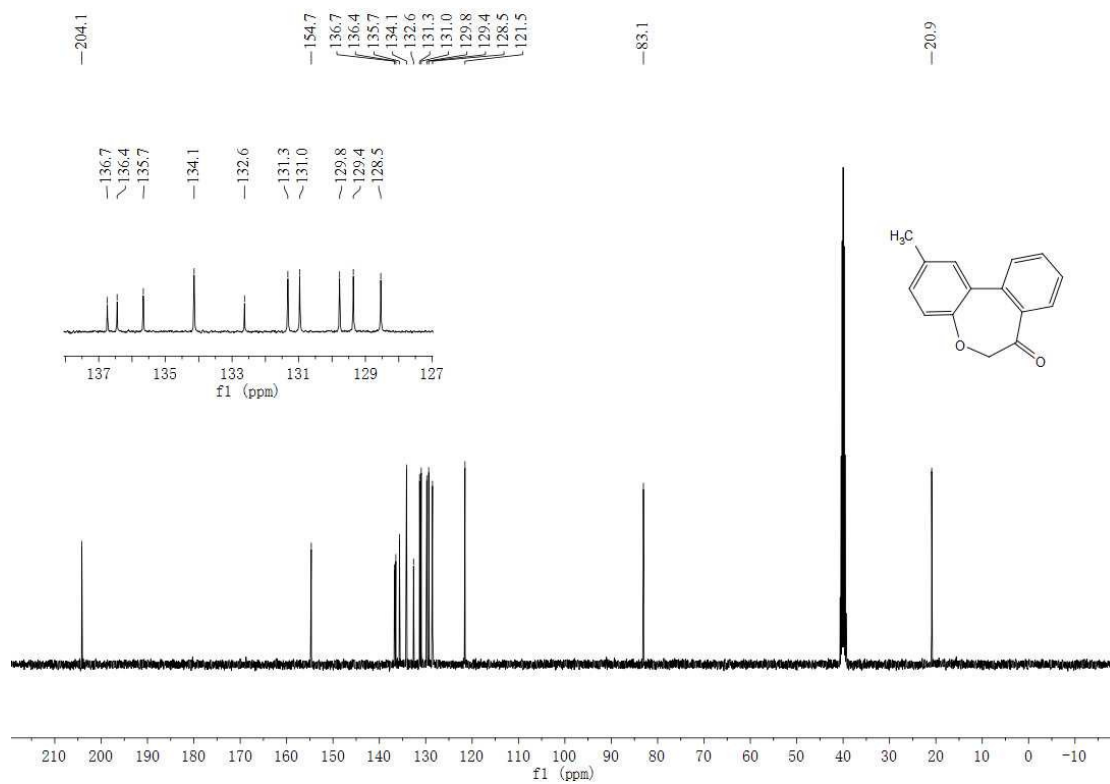
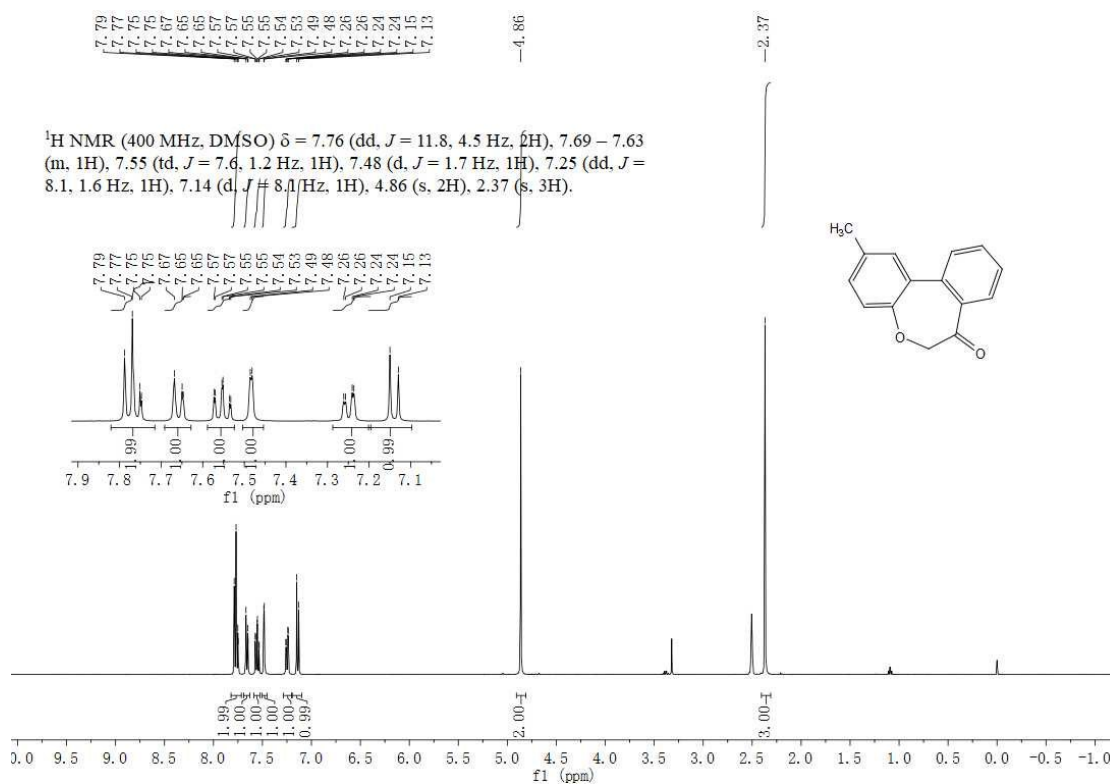


Fig. S8 NMR spectra of **3e**

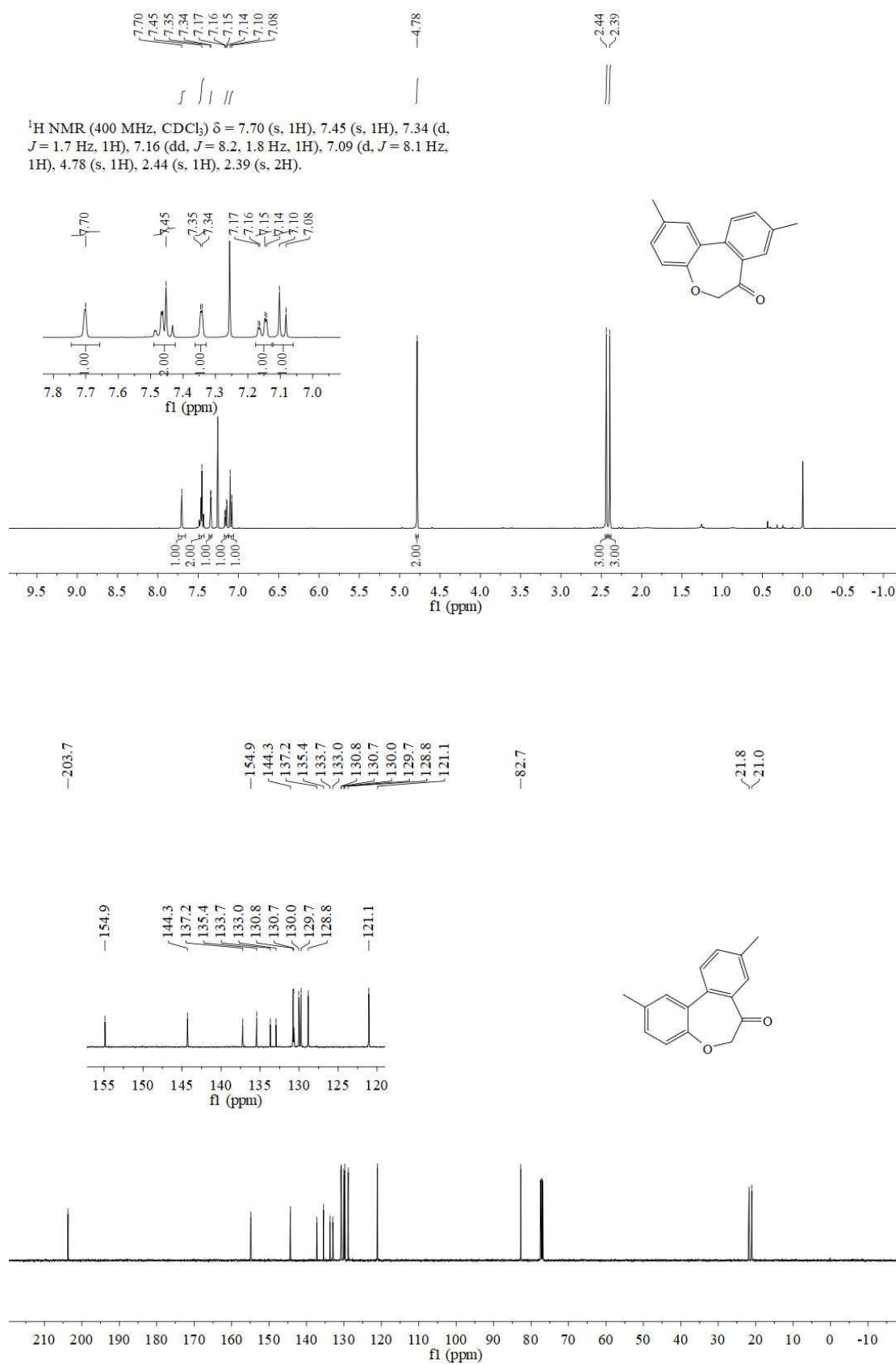


Fig. S9 NMR spectra of **3f**

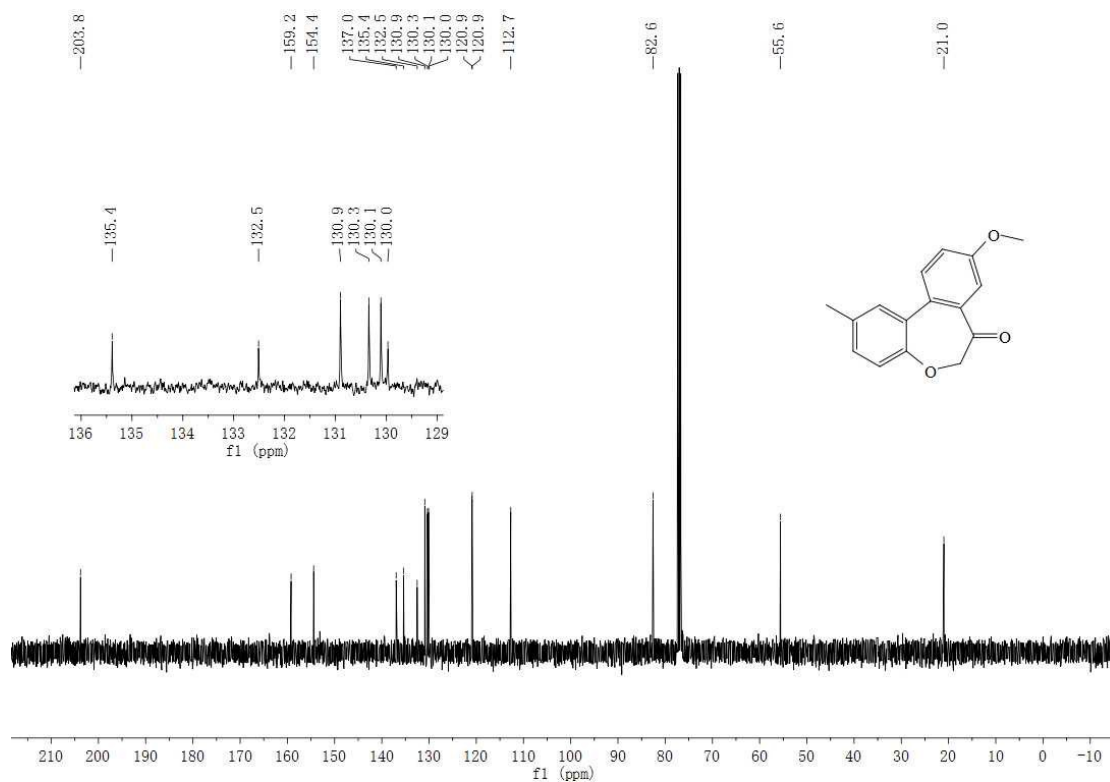
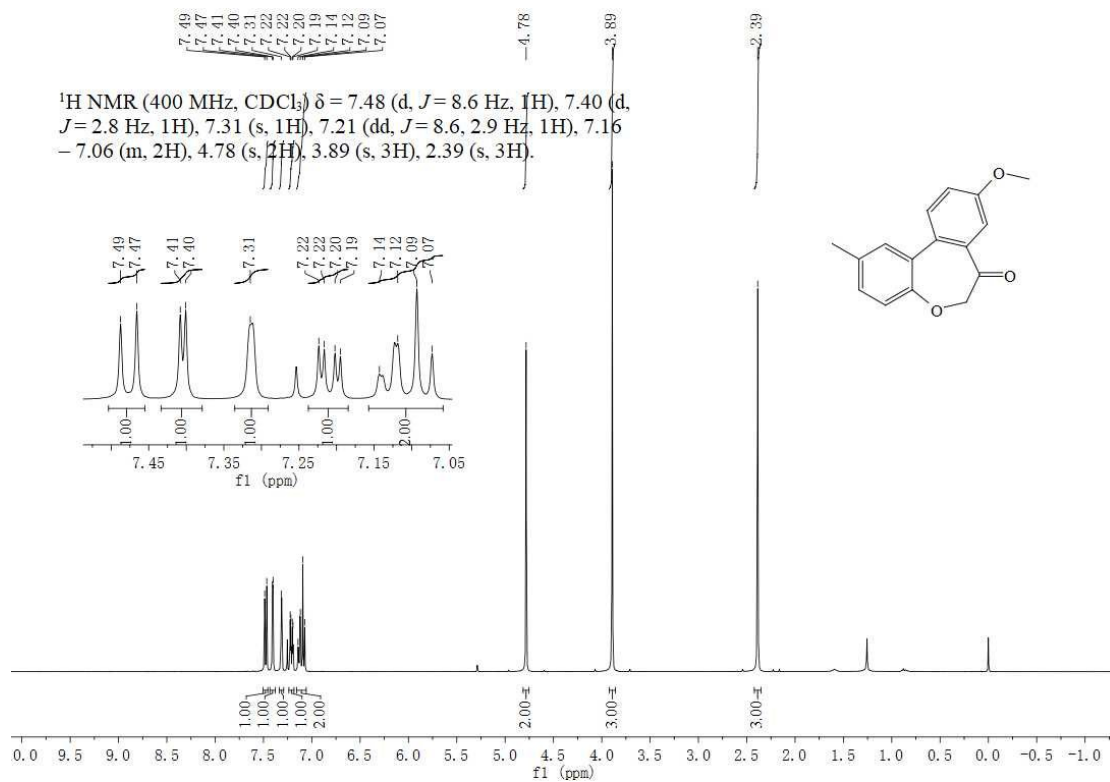


Fig. S10 NMR spectra of **3g**

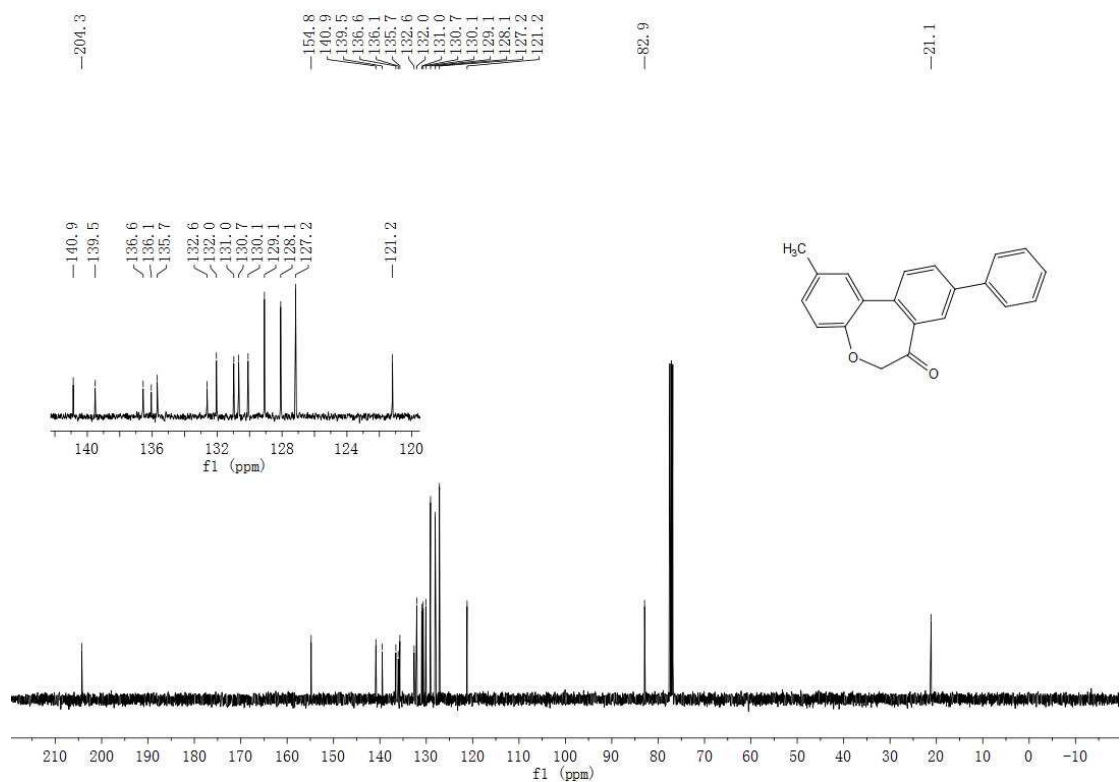
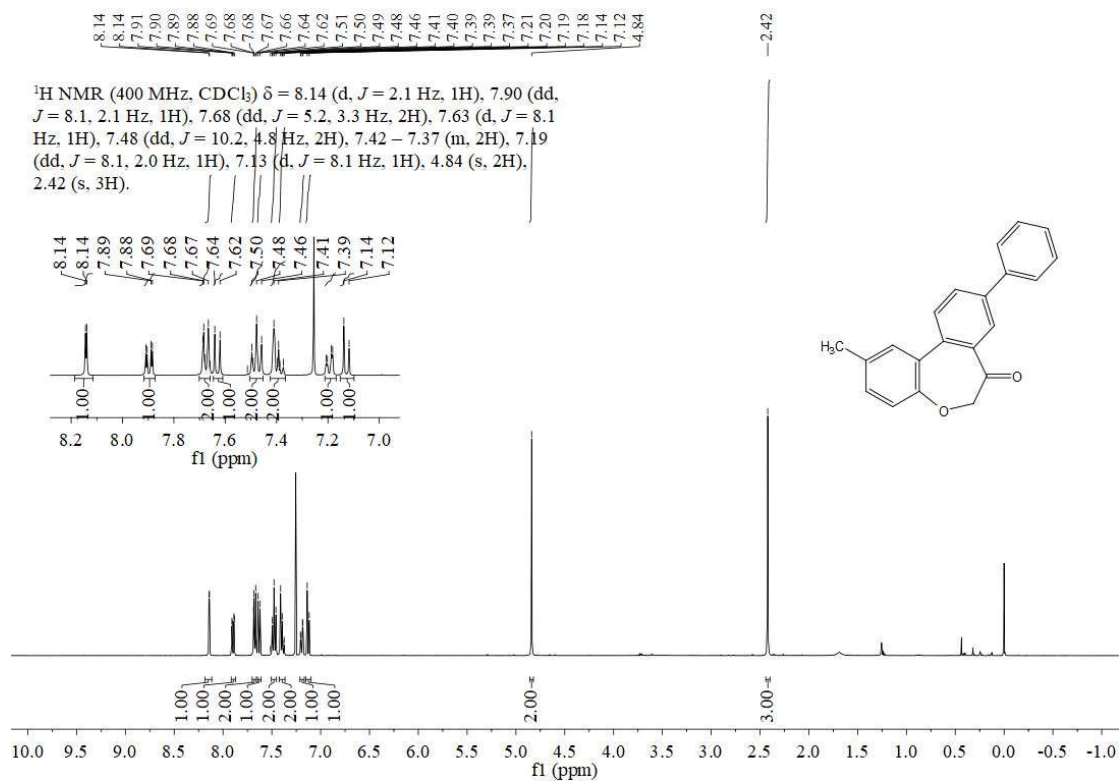


Fig. S11 NMR spectra of **3h**

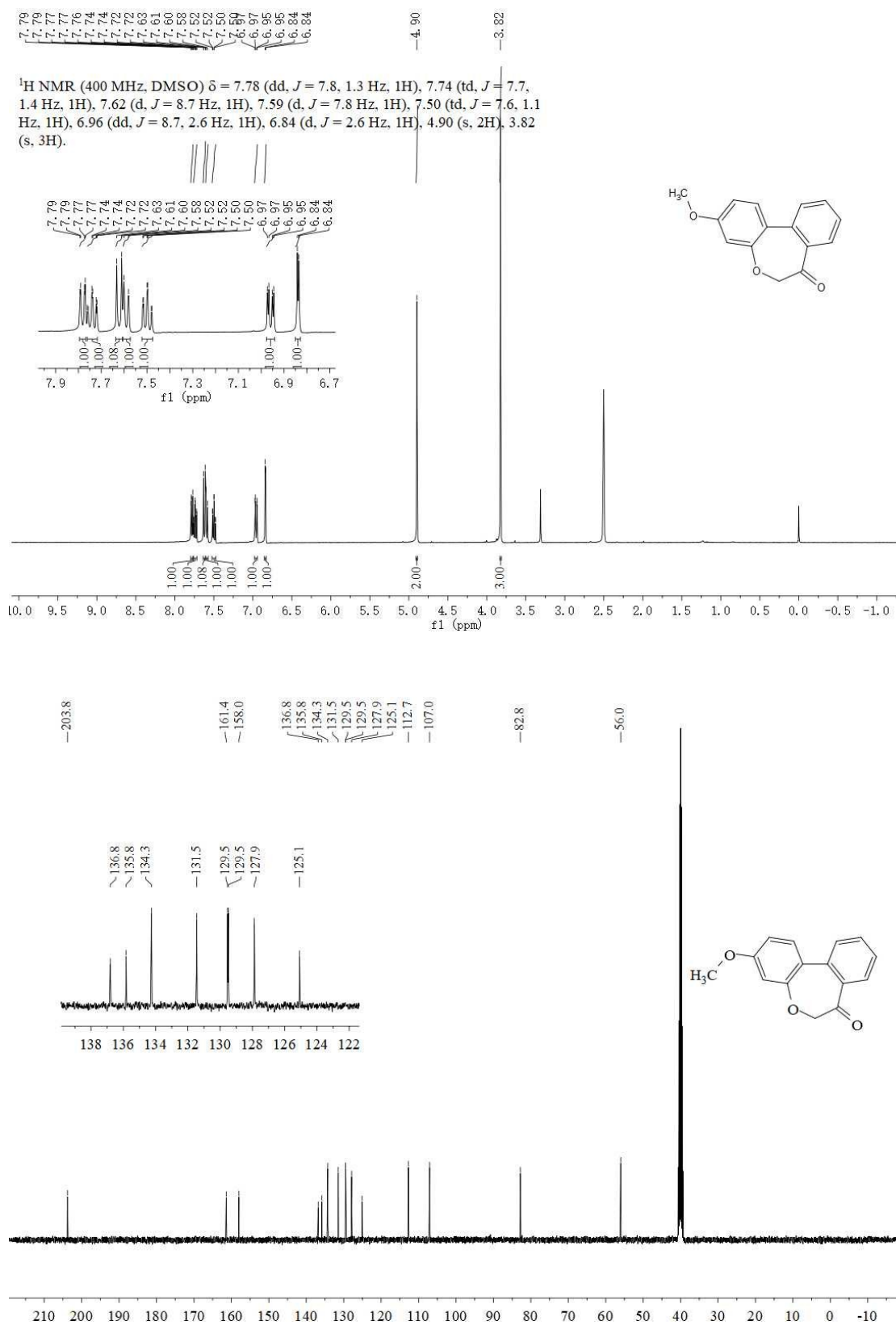


Fig. S12 NMR spectra of **3i**

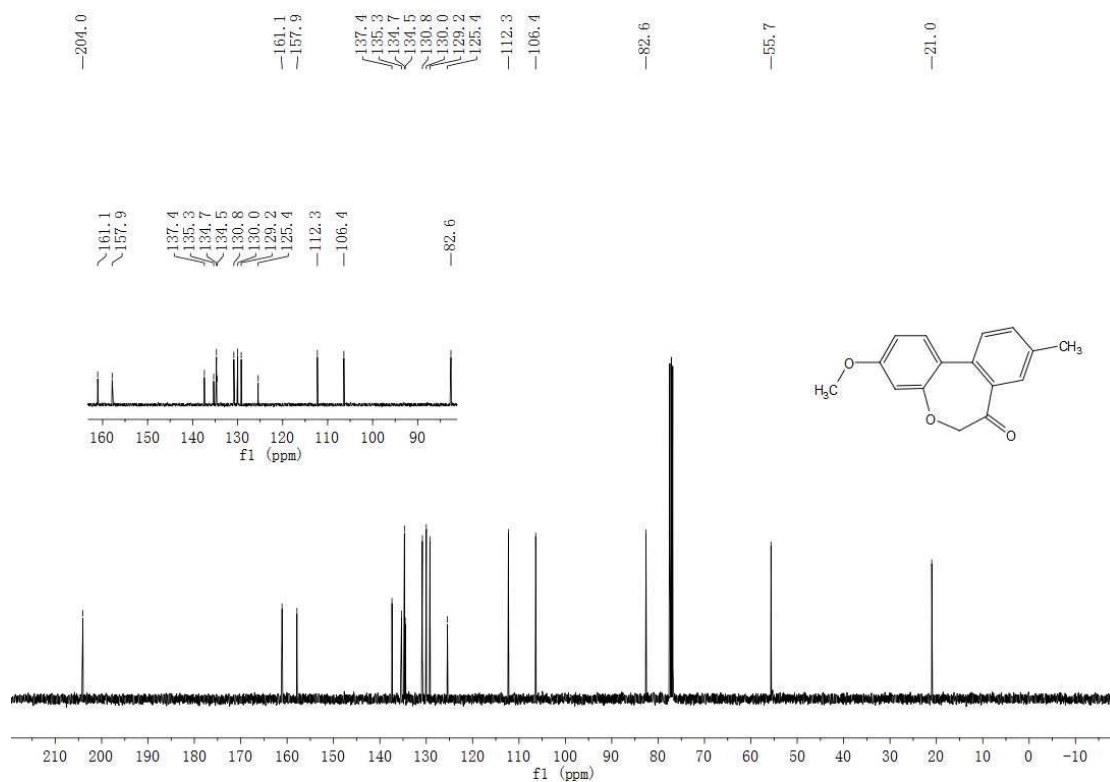
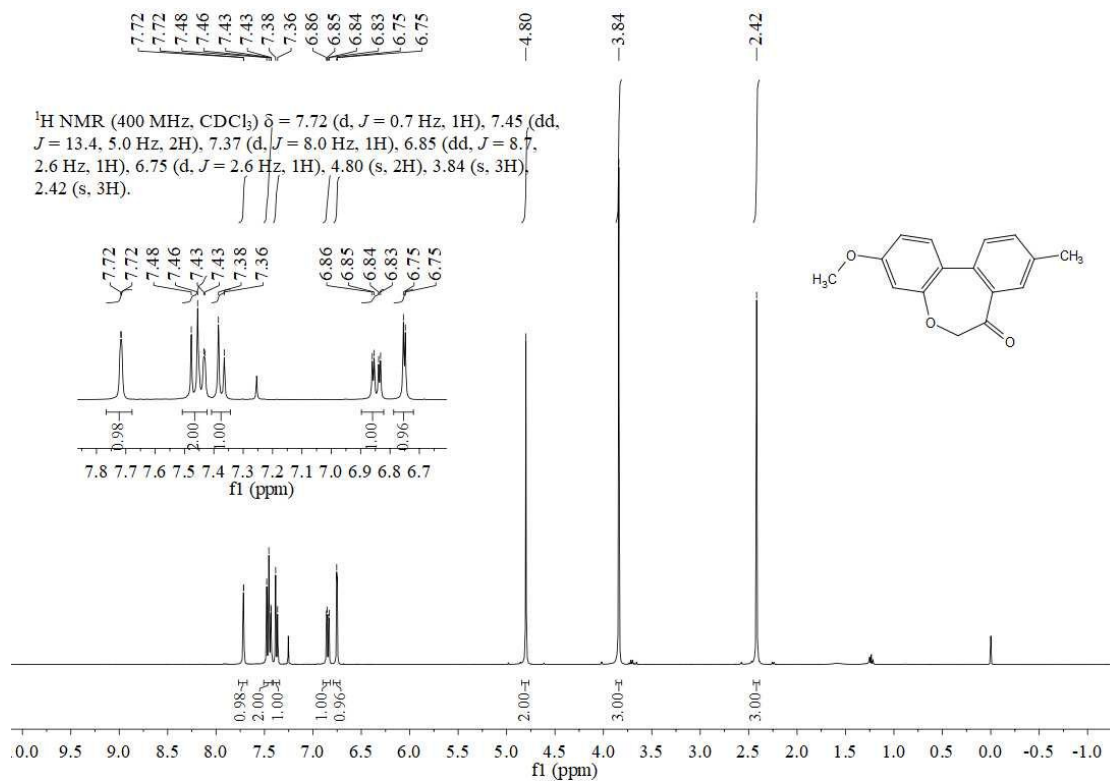


Fig. S13 NMR spectra of **3j**

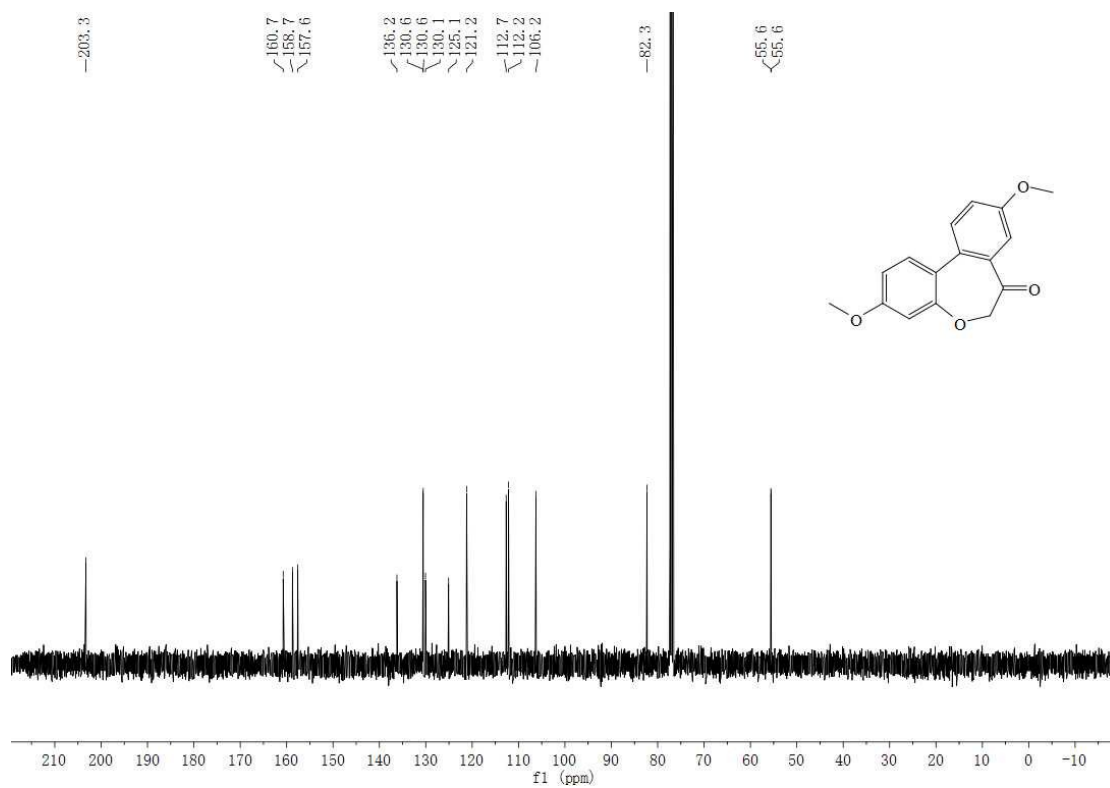
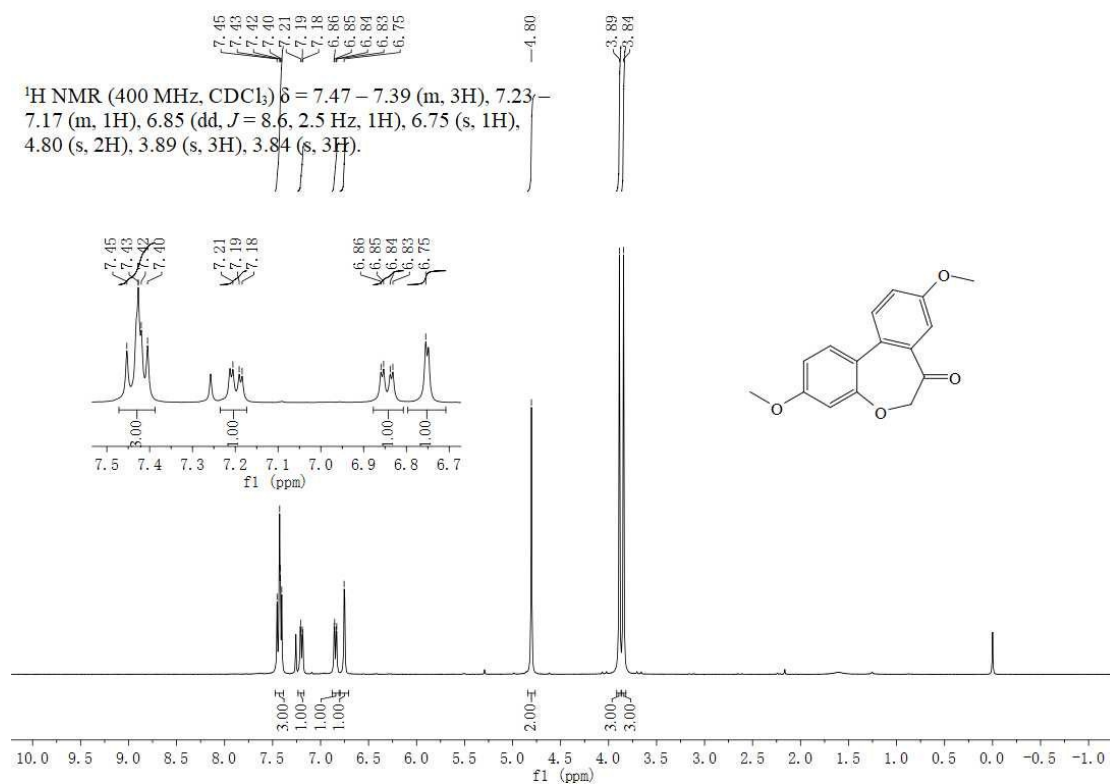


Fig. S14 NMR spectra of **3k**

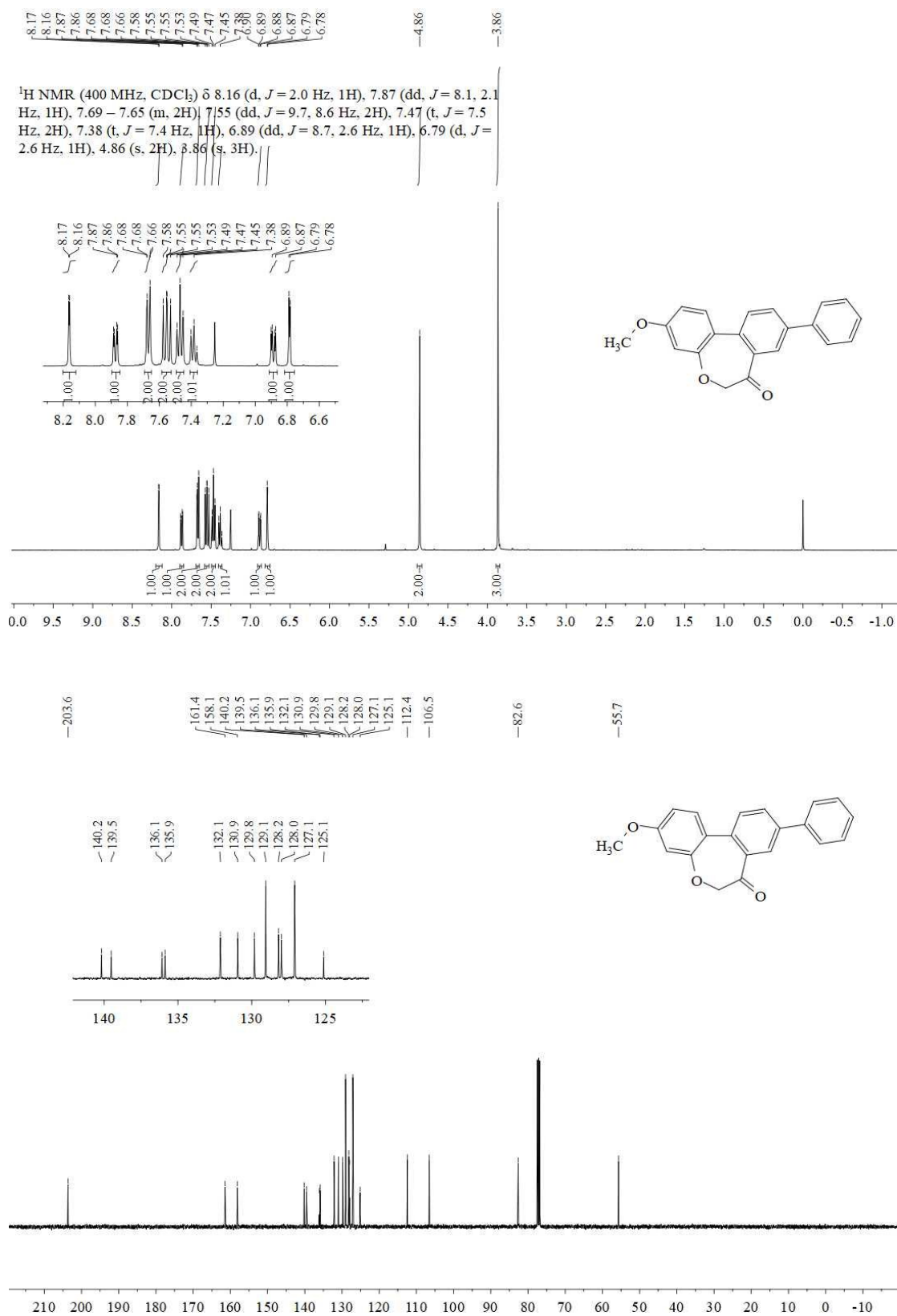


Fig. S15 NMR spectra of **31**

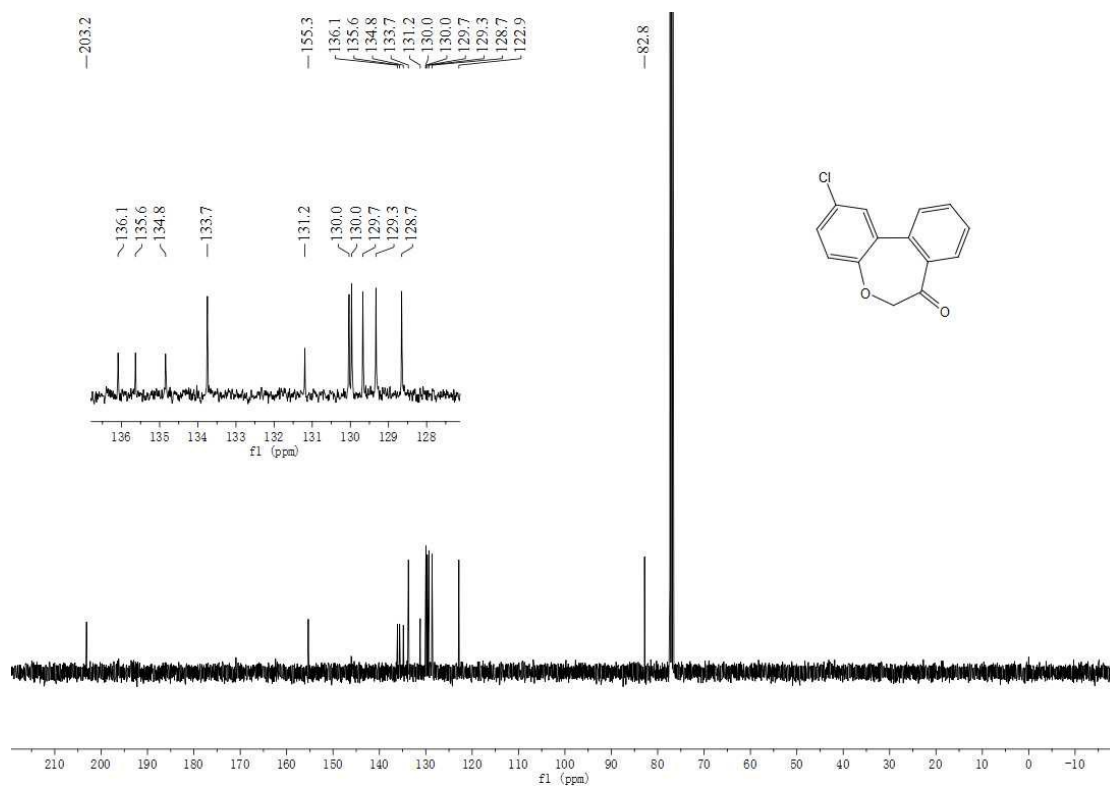
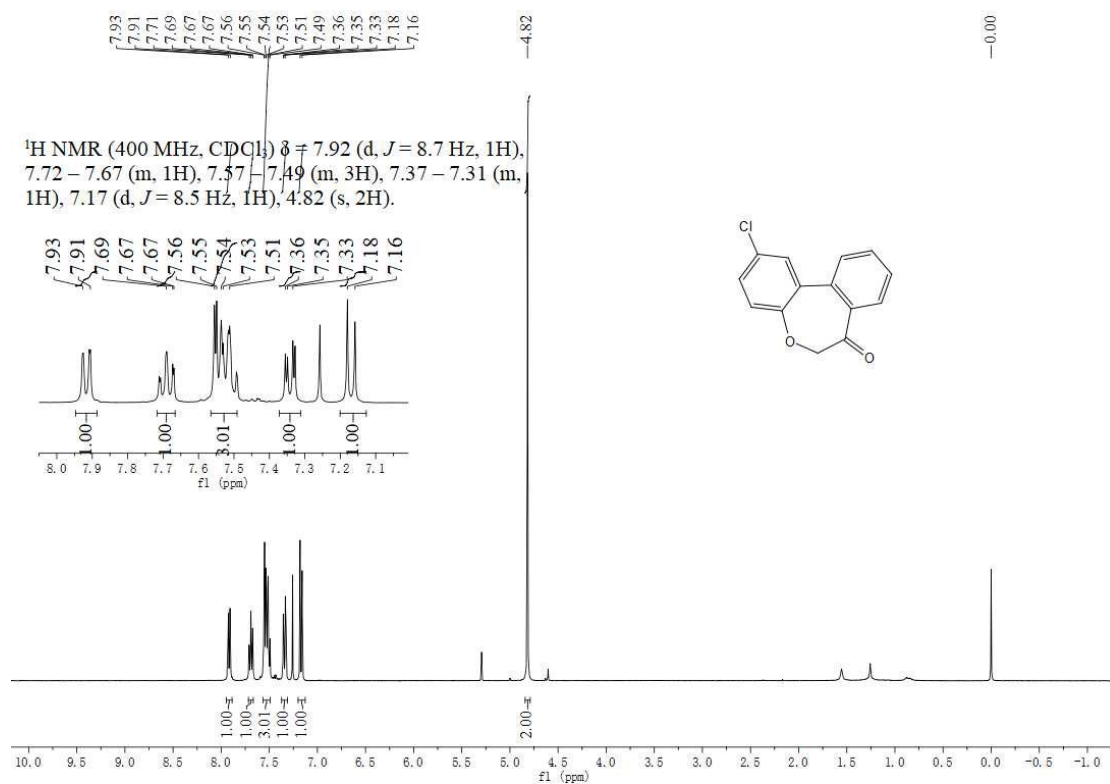


Fig. S16 NMR spectra of **3m**

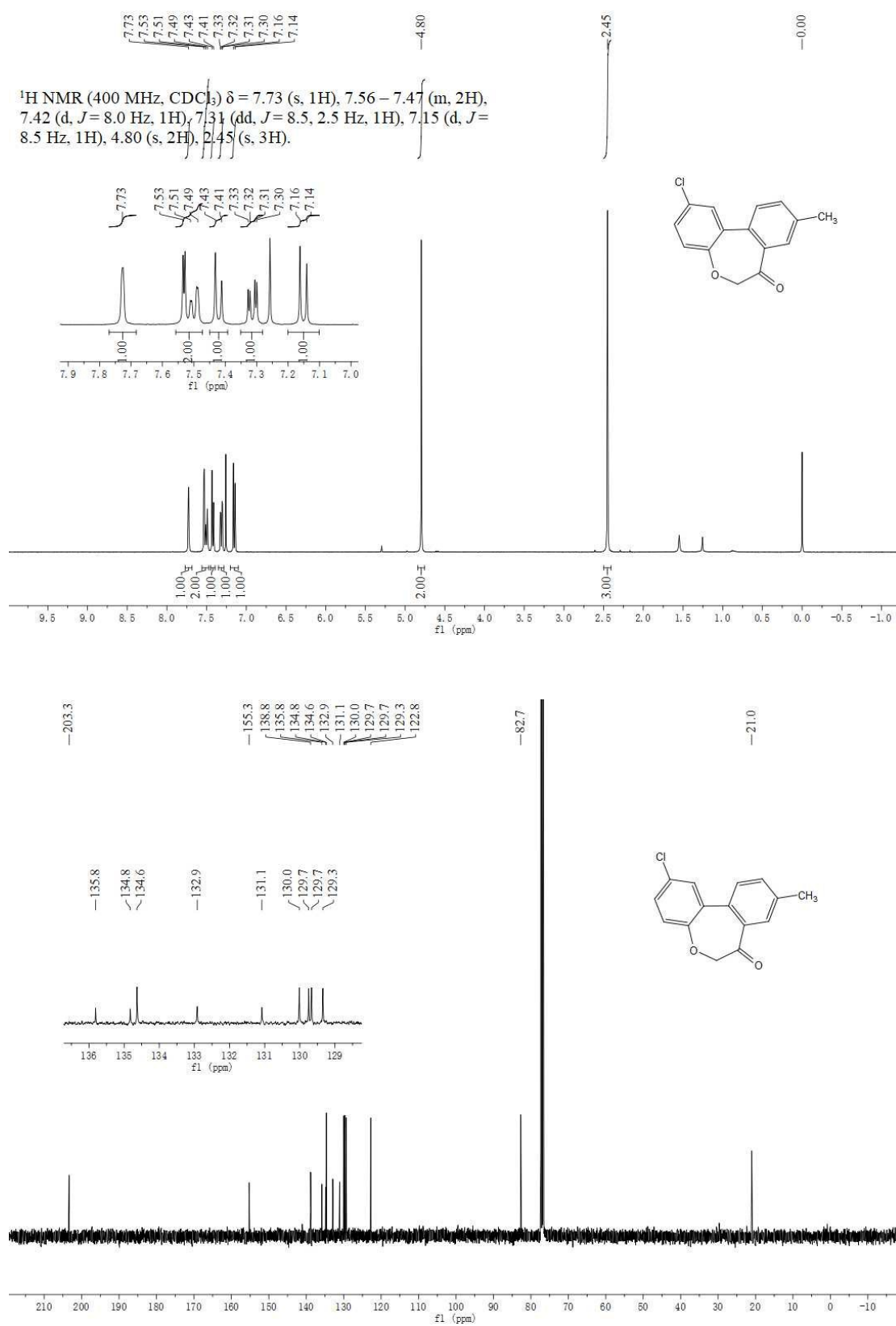


Fig. S17 NMR spectra of **3n**

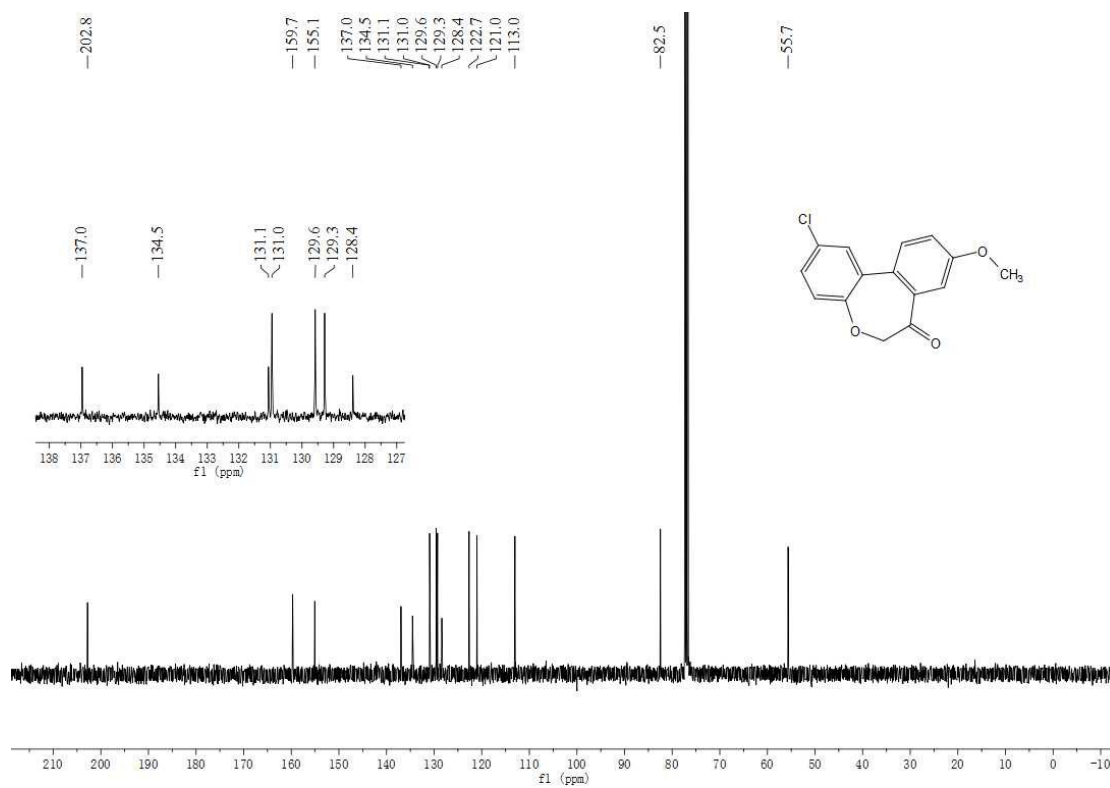
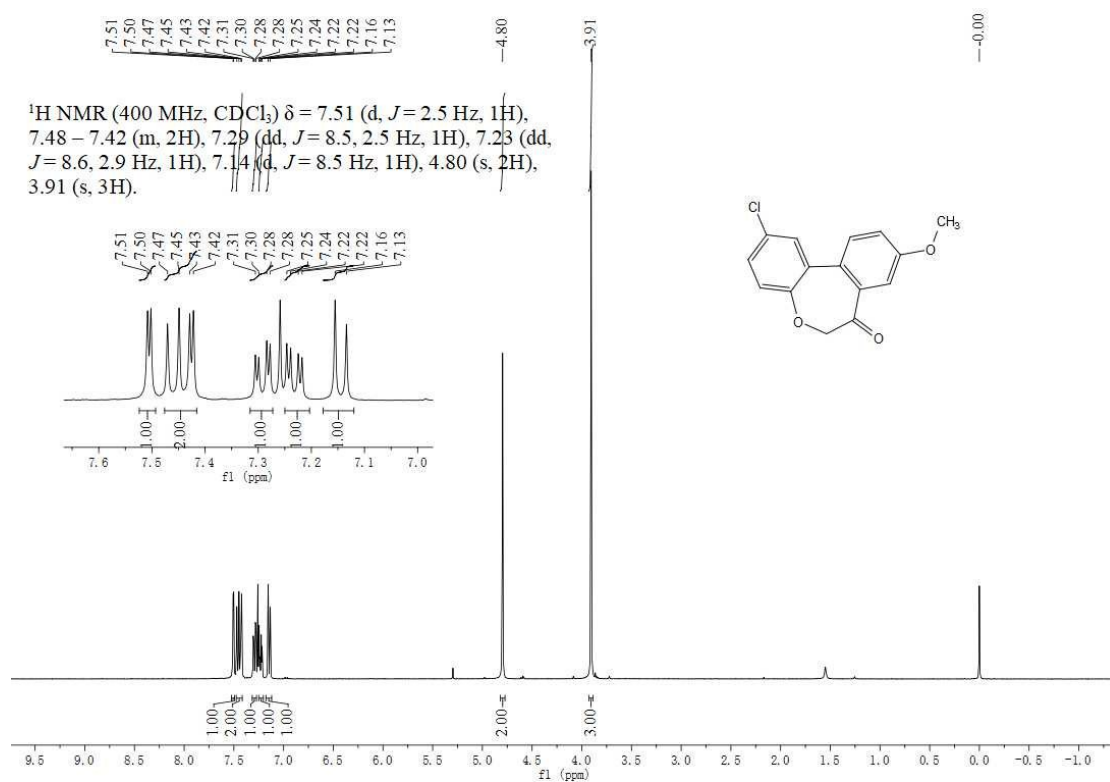


Fig. S18 NMR spectra of **3o**

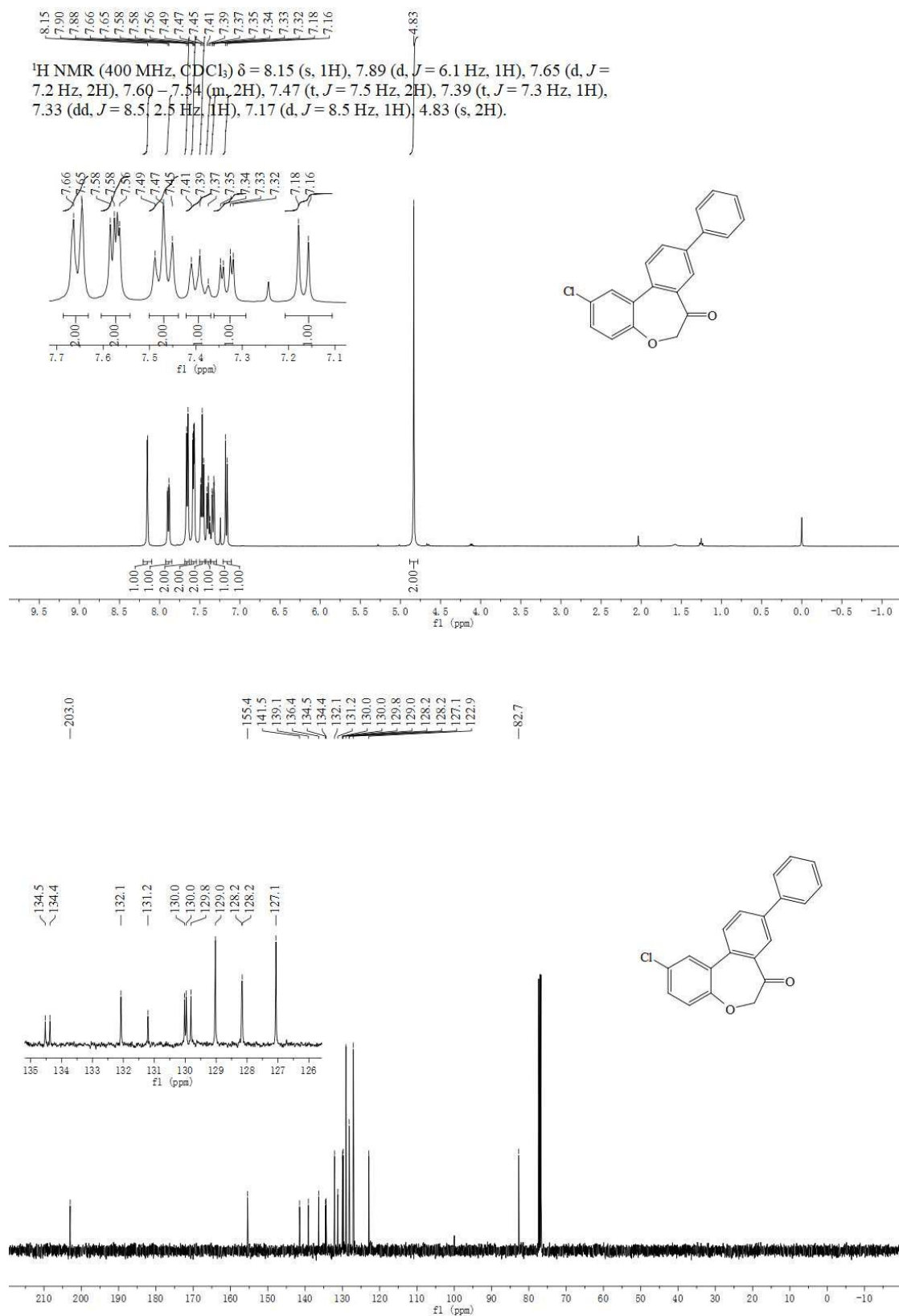


Fig. S19 NMR spectra of **3p**

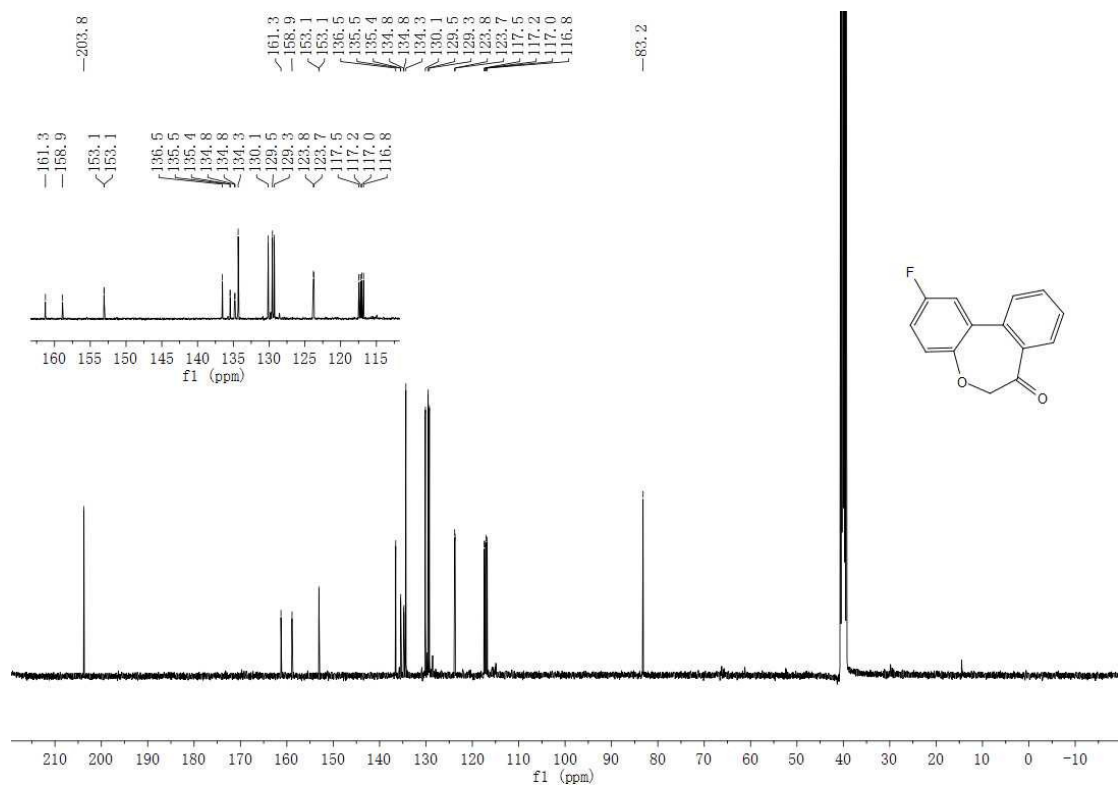
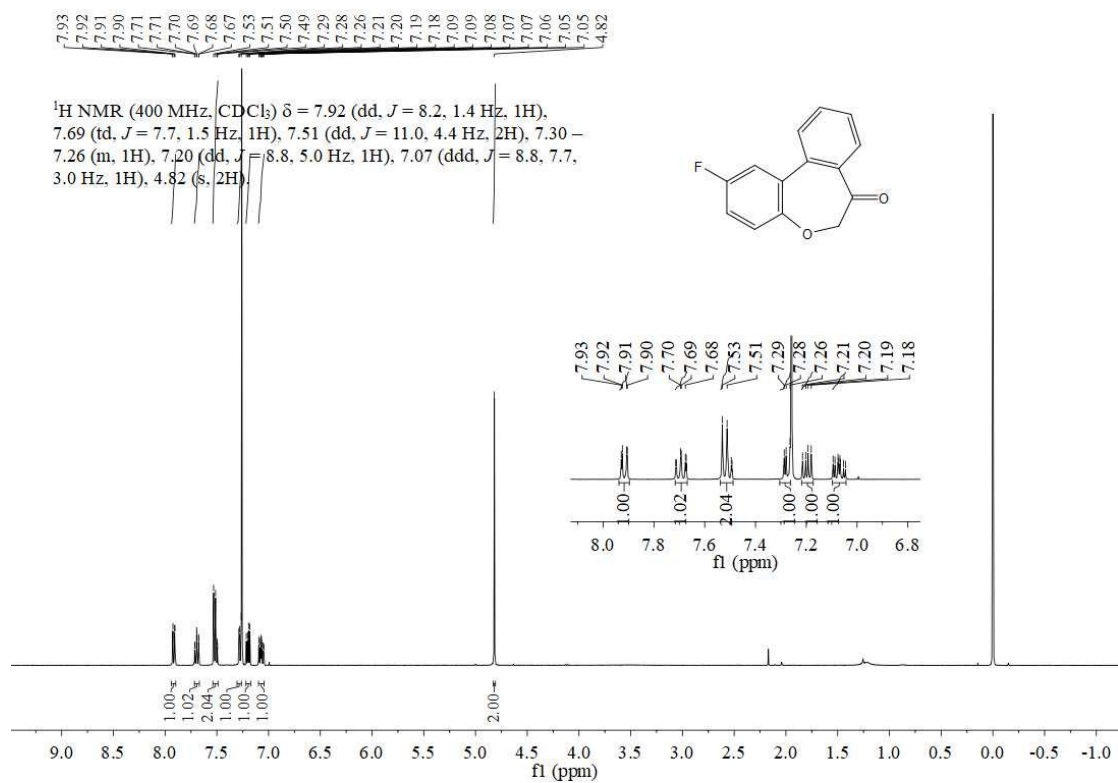


Fig. S20 NMR spectra of **3q**

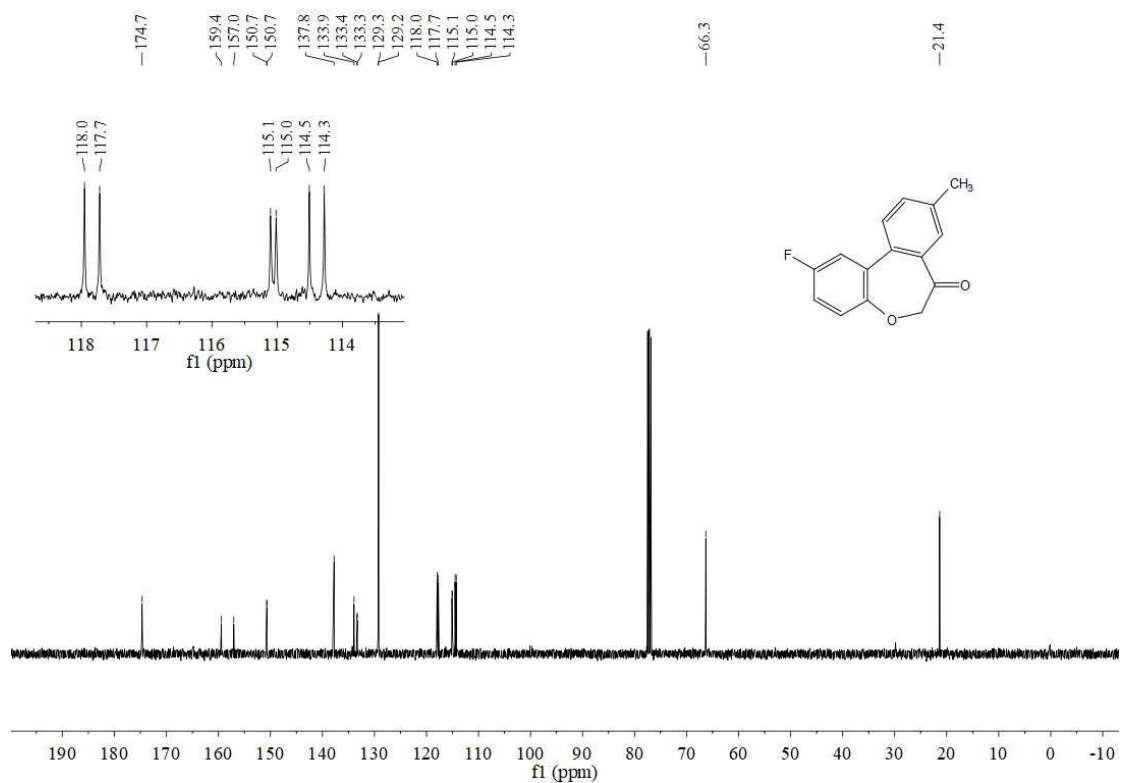
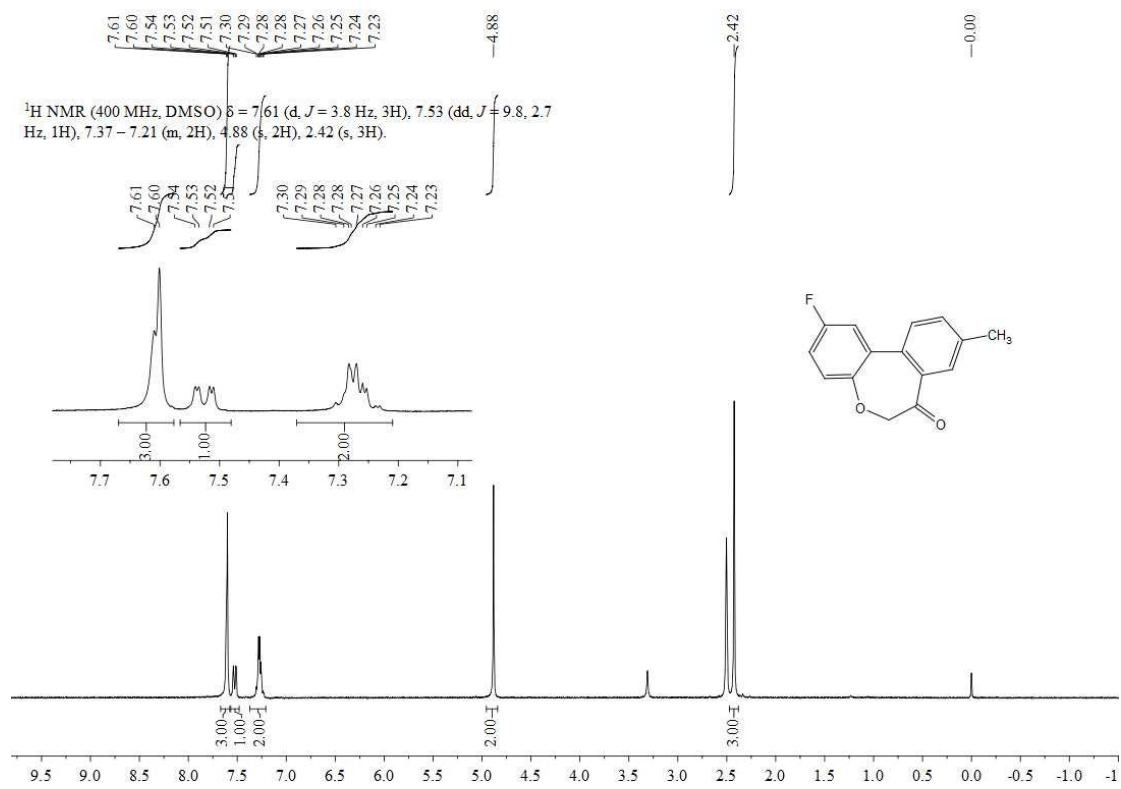


Fig. S21 NMR spectra of **3r**

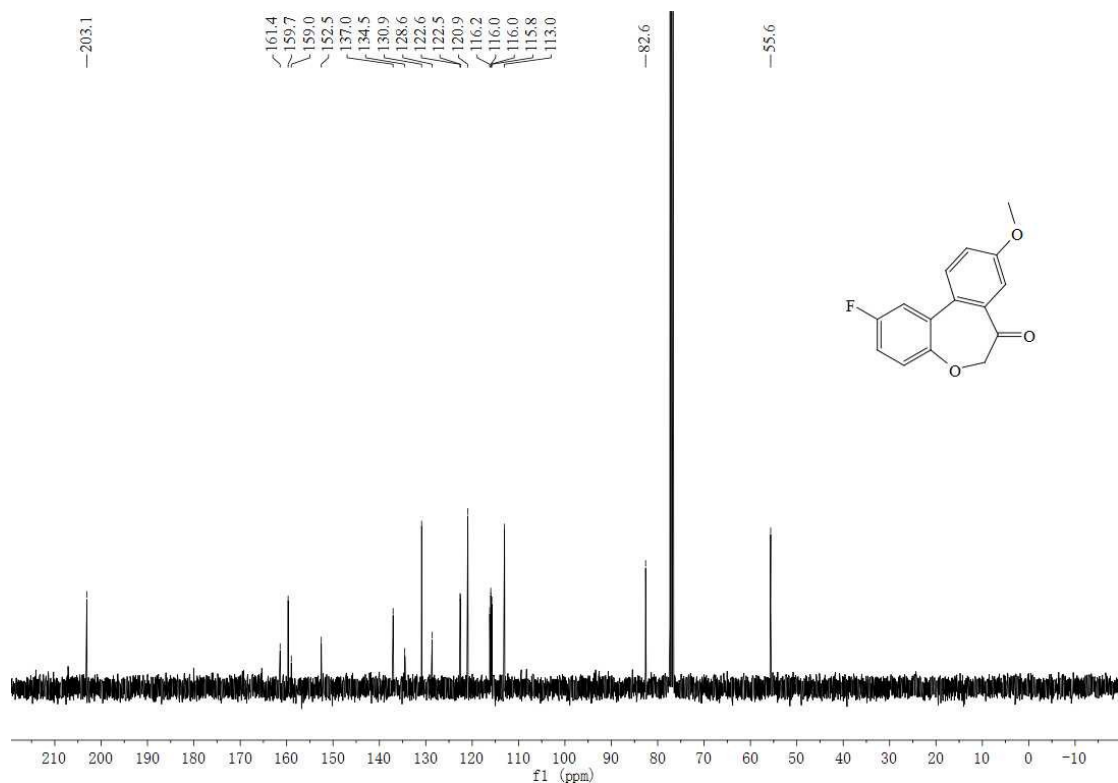
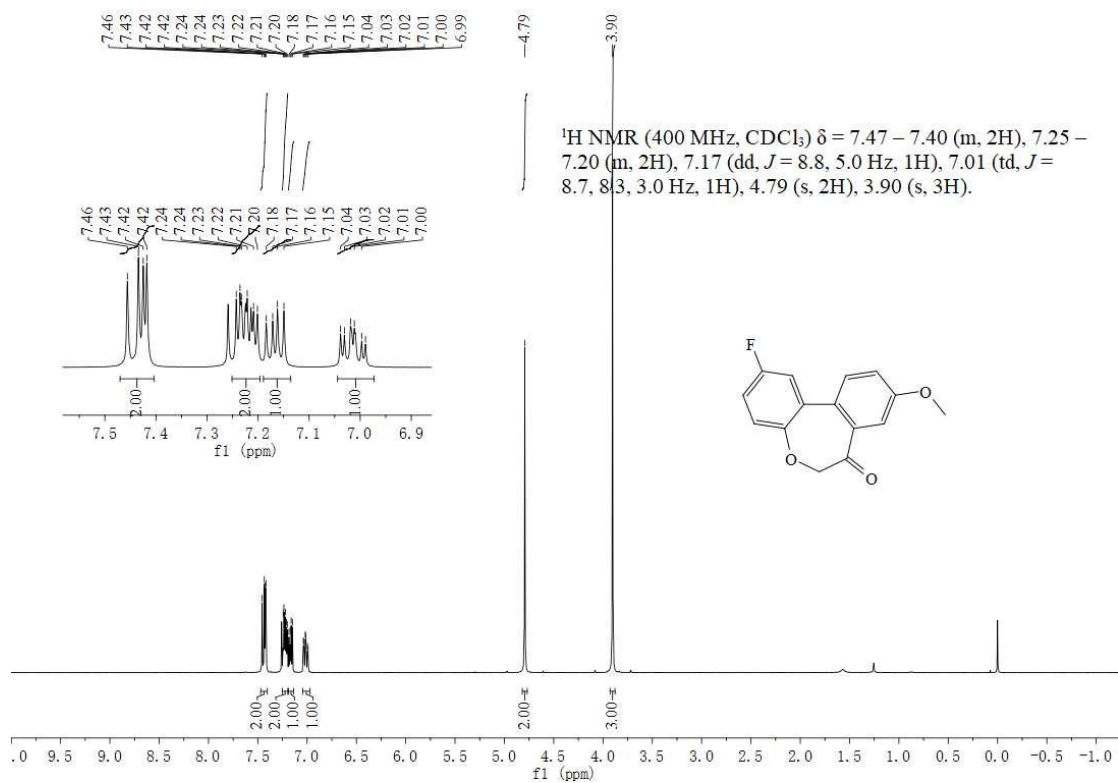


Fig. S22 NMR spectra of **3s**

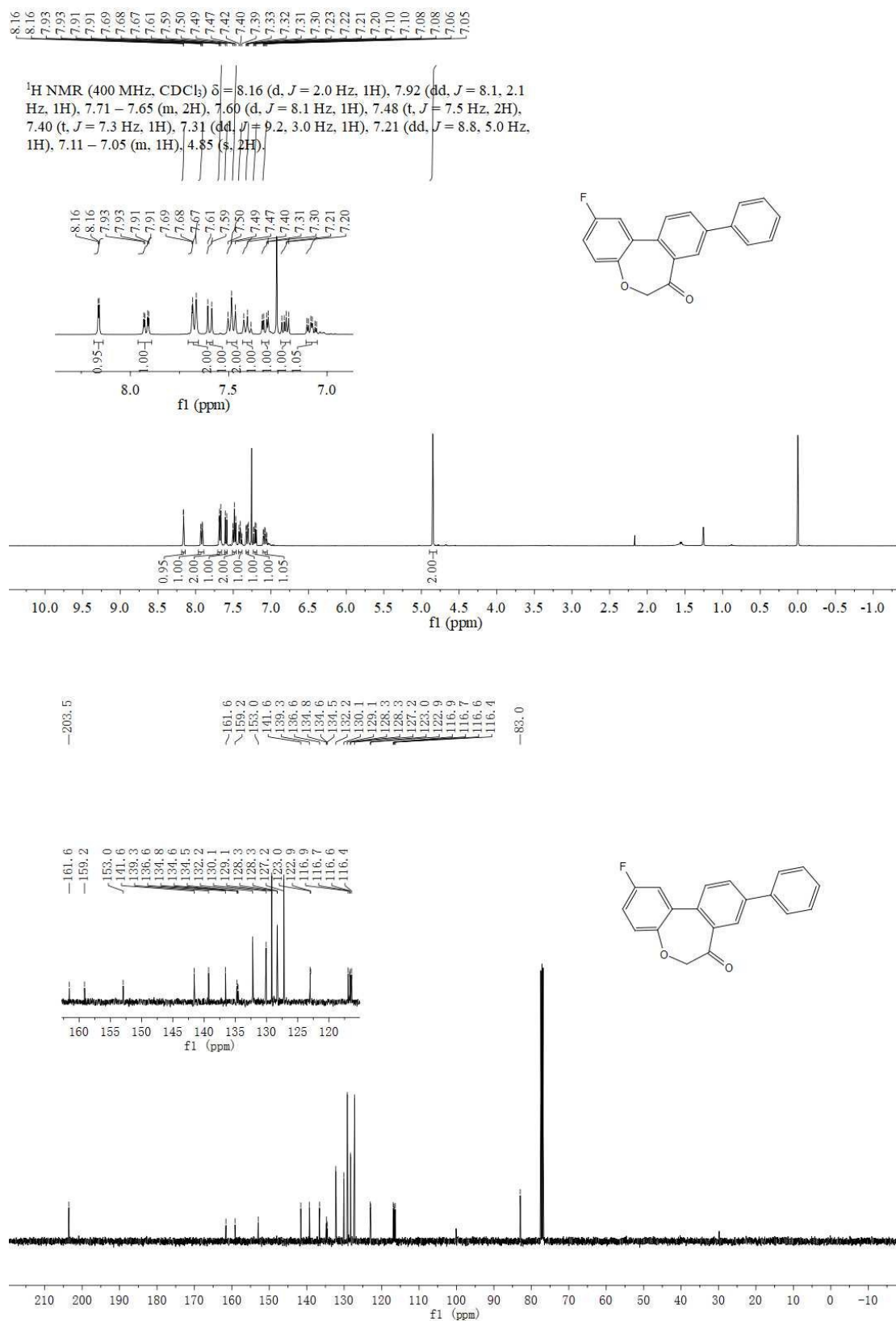


Fig. S23 NMR spectra of **3t**

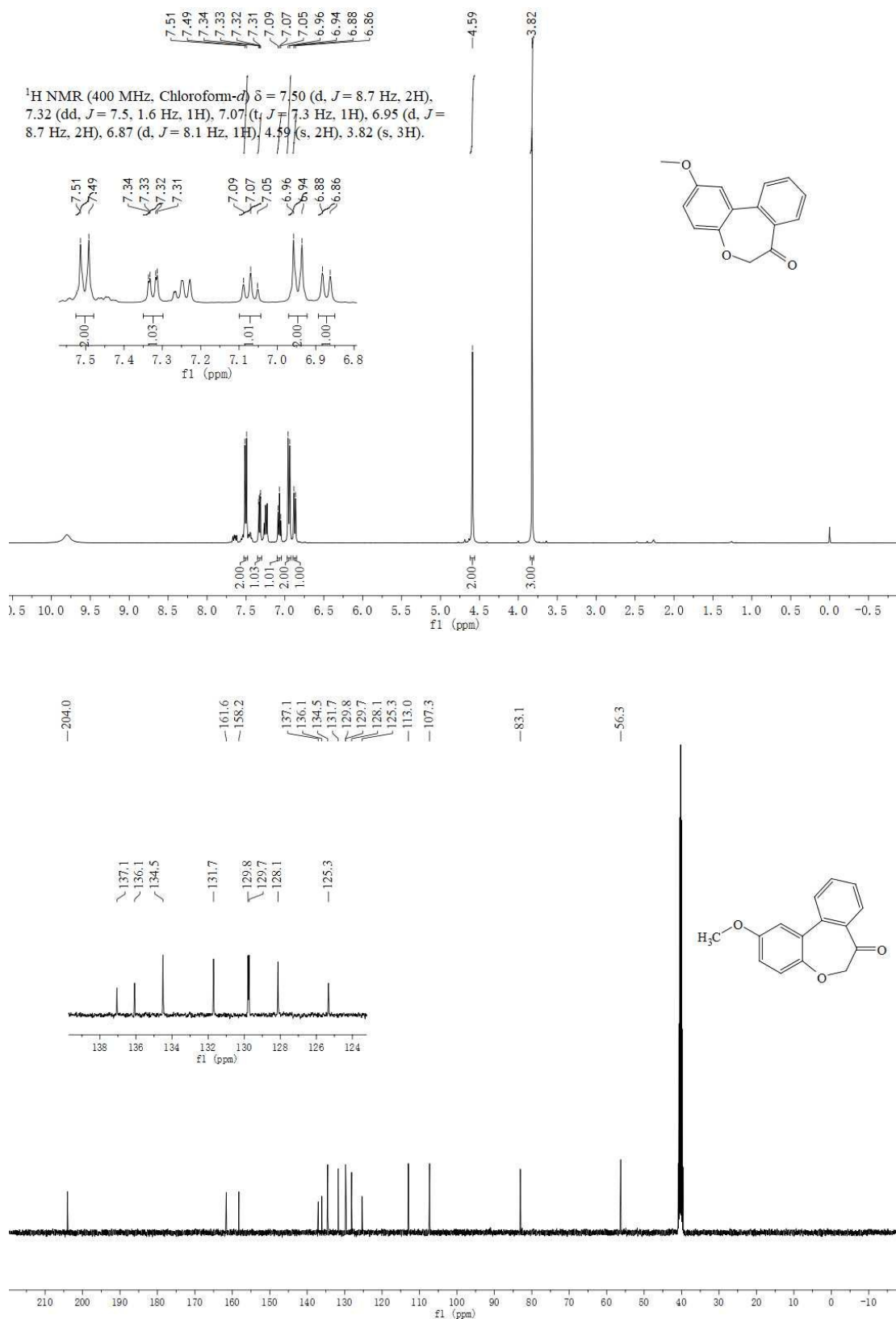


Fig. S24 NMR spectra of **3u**

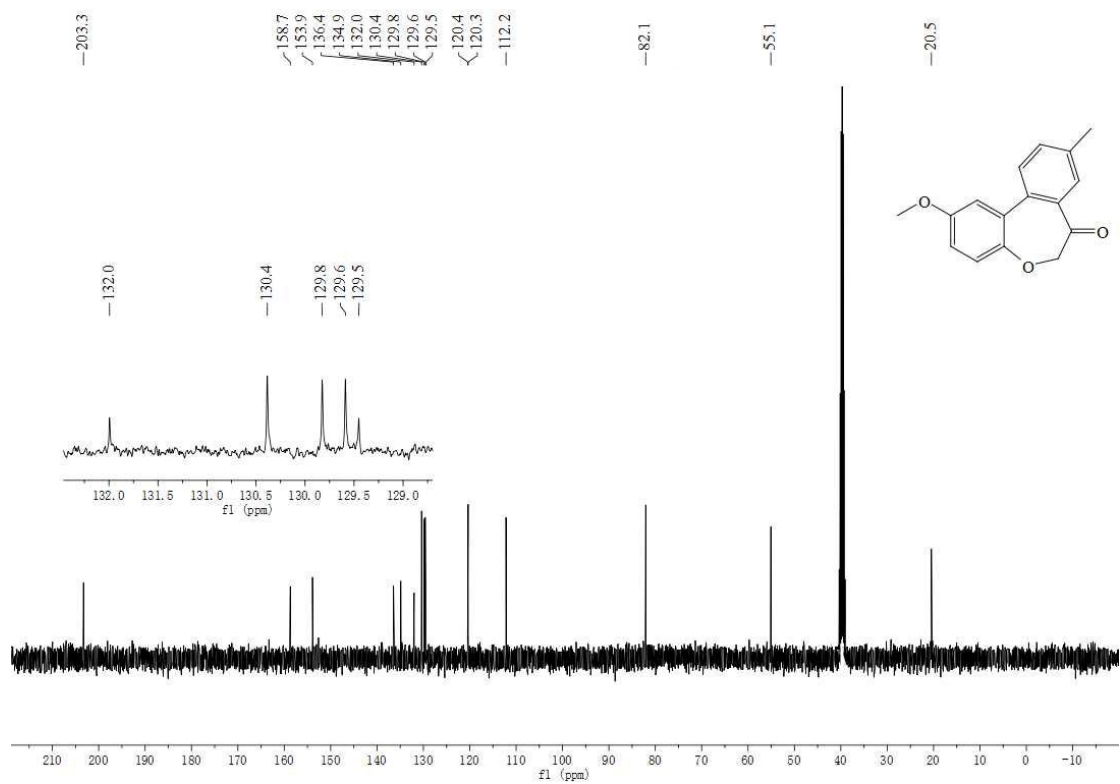
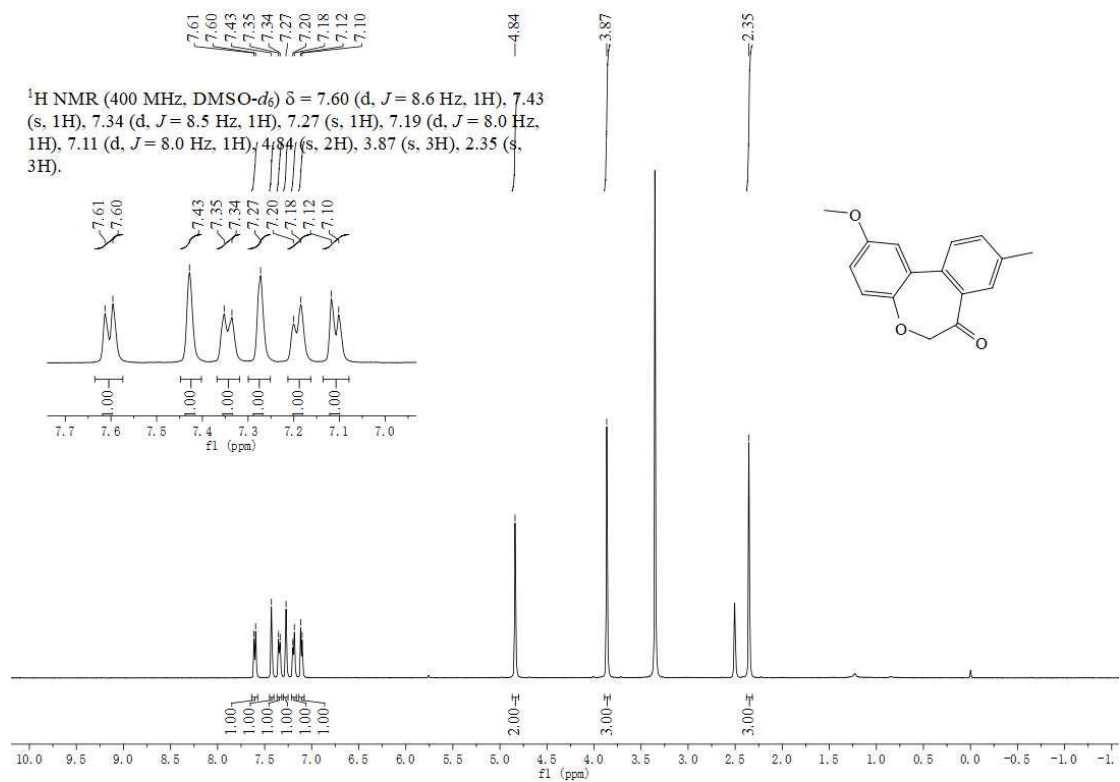


Fig. S25 NMR spectra of **3v**

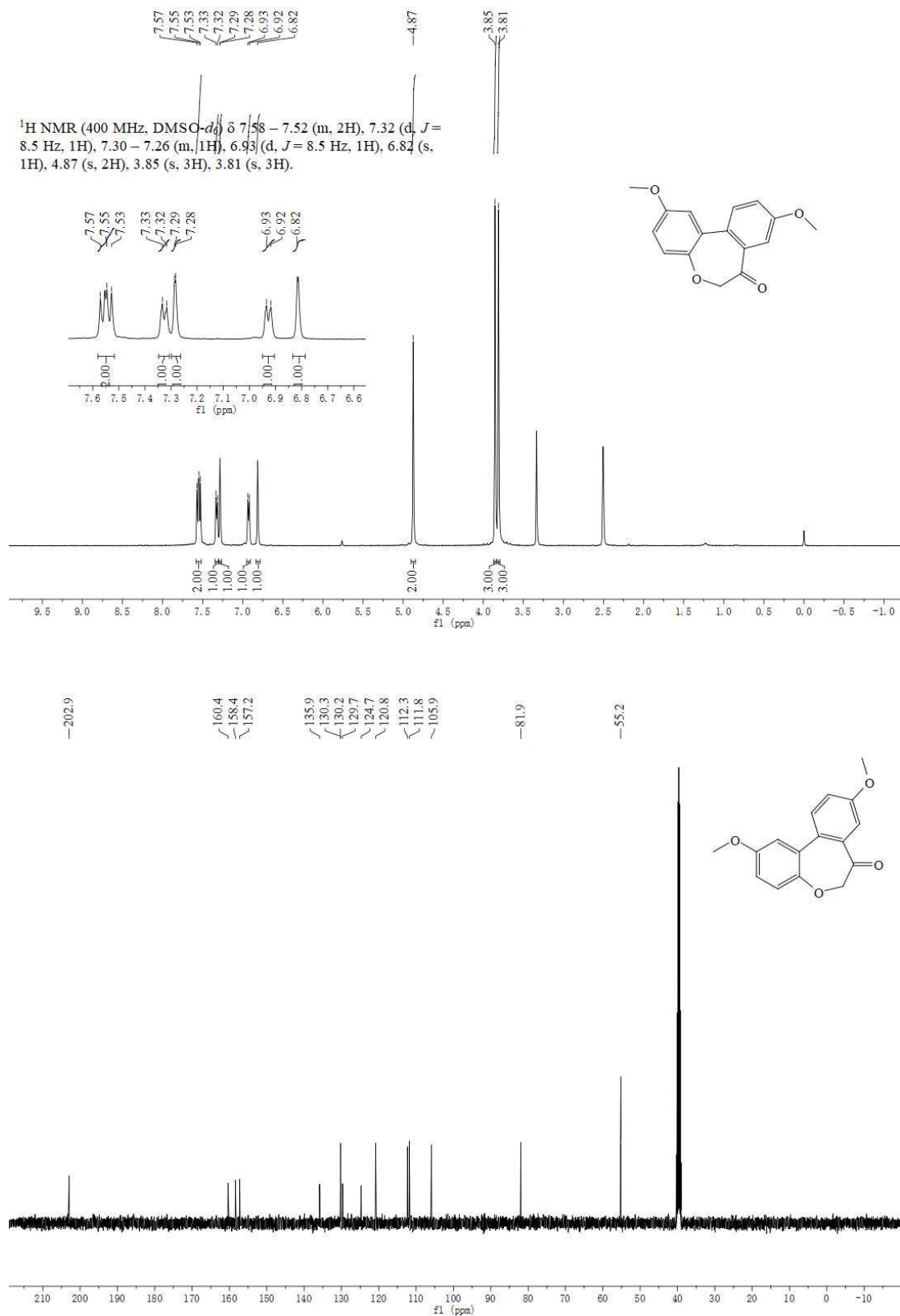


Fig. S26 NMR spectra of **3w**

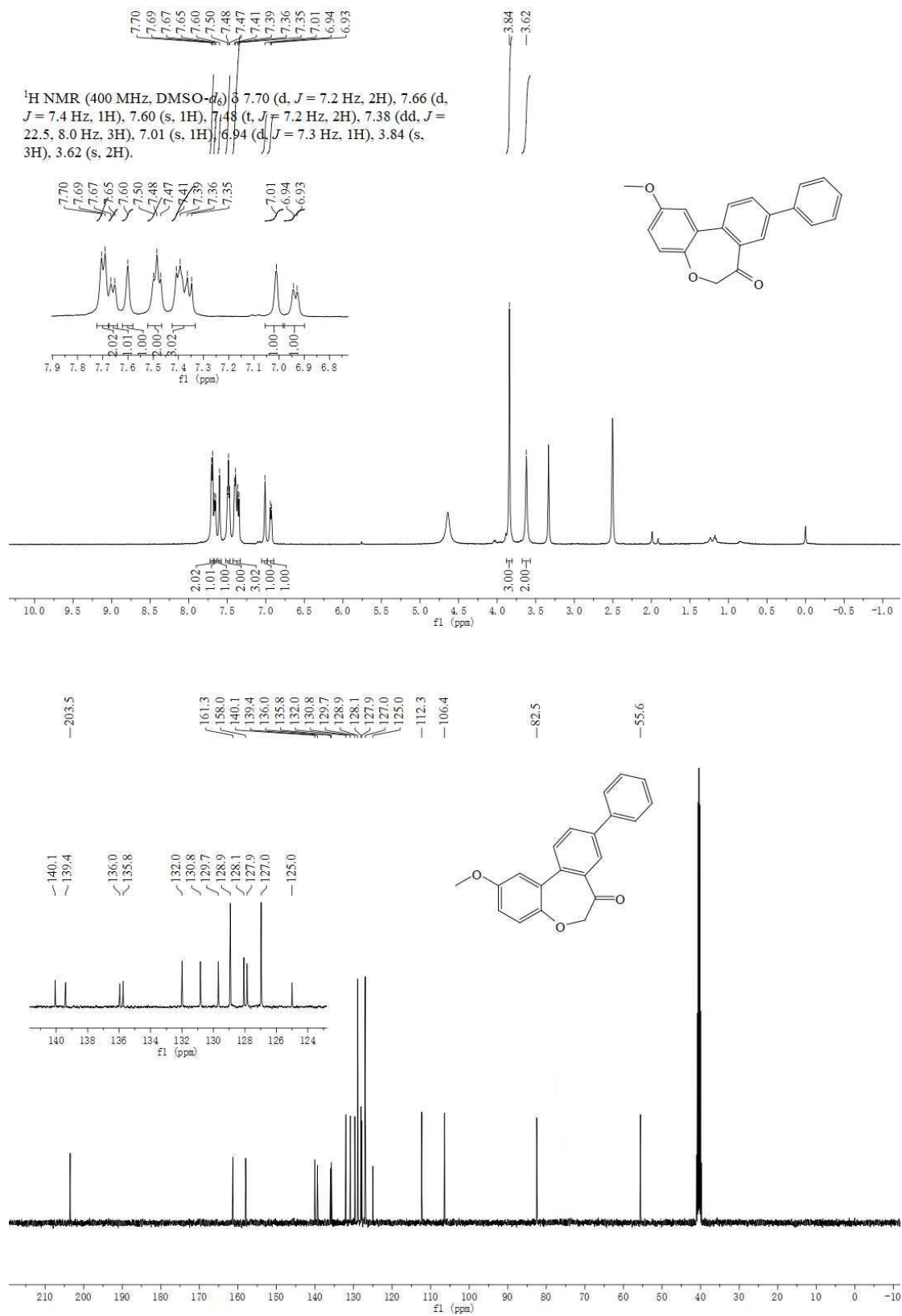


Fig. S27 NMR spectra of **3x**

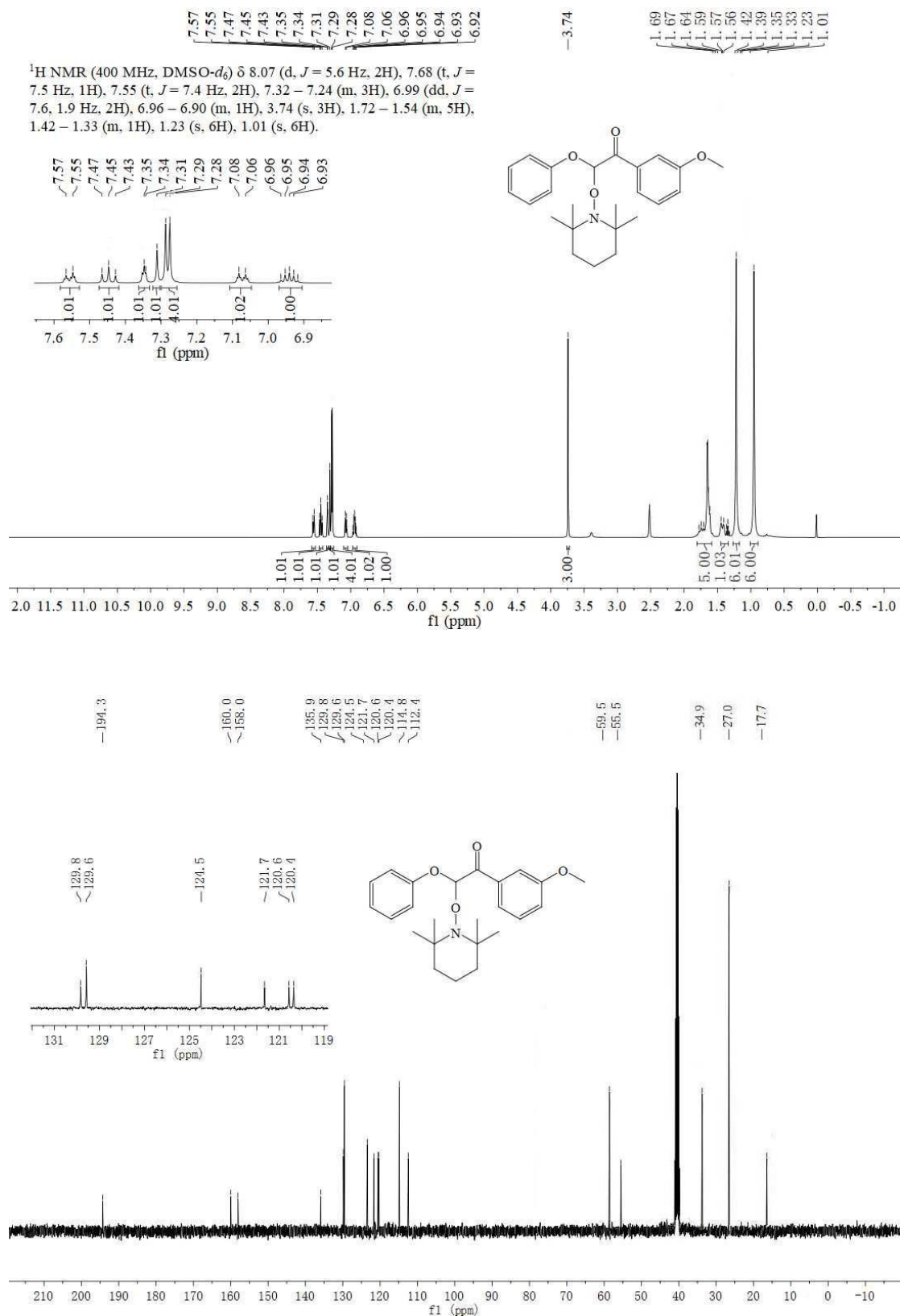


Fig. S28 NMR spectra of 4

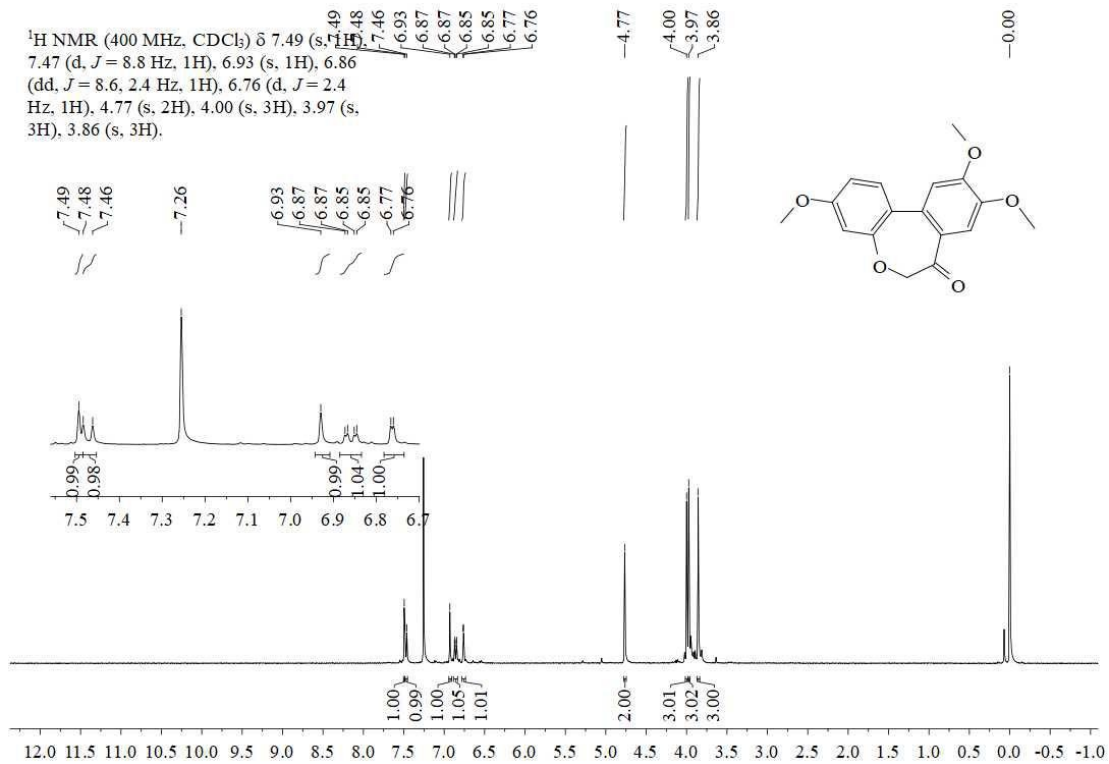


Fig. S29 NMR spectra of **3z**

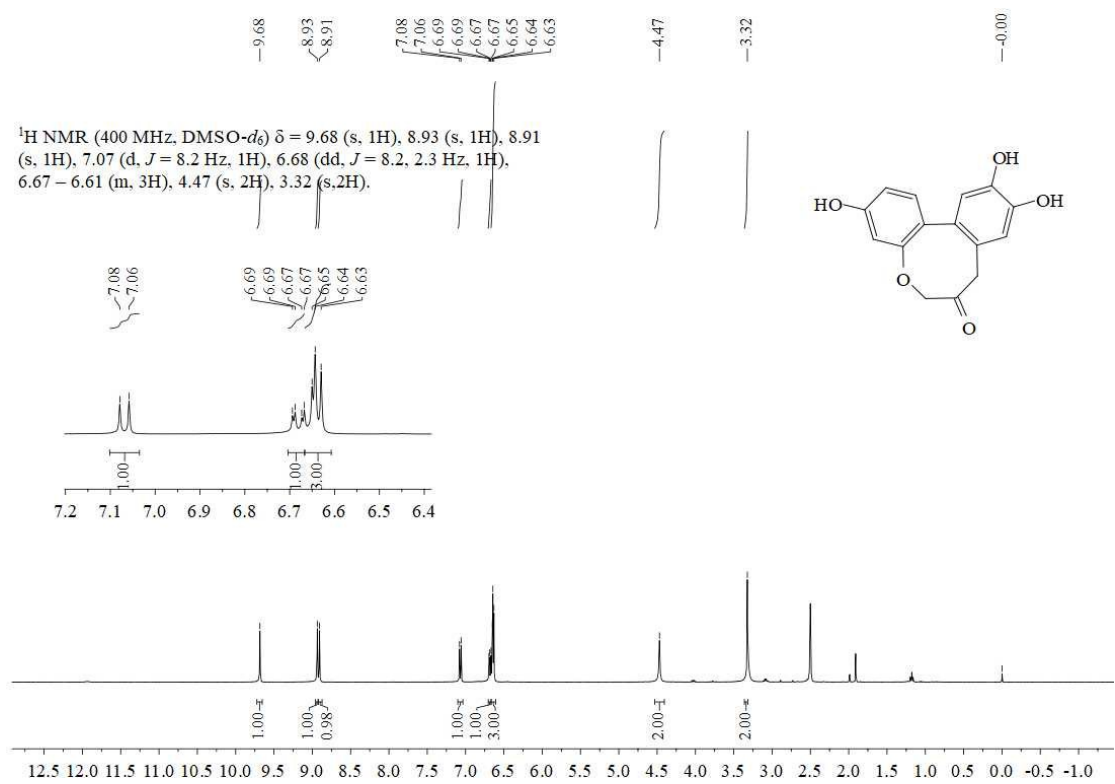


Fig. S30 NMR spectra of **Protosappanin A**