Supporting Information

Construction of Spirotetrahydroquinolines fused with Medium-sized Rings via TBHP/Base-promoted Spirocyclization Reactions

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Table of Contents

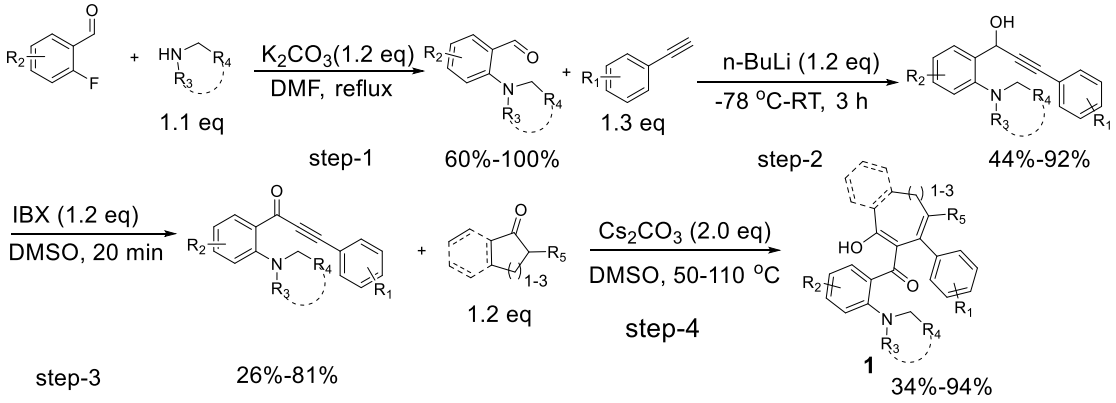
1. General methods

All reactions were performed in flame-dried glassware under an atmosphere of dry nitrogen, unless otherwise noted. Column chromatographic purification of products was carried out using silica gel (200~300 mesh). ^{1}H NMR spectra were recorded at 500 MHz or 600 MHz; ^{13}C NMR spectra were recorded at 125 MHz or 150 MHz, and in $CDCl_3$ (containing 0.03% TMS) solutions. ^{1}H NMR spectra were recorded with tetramethylsilane (δ = 0.00 ppm) as the internal reference; ^{13}C NMR spectra were recorded with $CDCl_3$ (δ = 77.00 ppm) as the internal reference. High-resolution mass spectra were recorded on a mass spectrometer with a TOF (for EI or ESI) or FT-ICR (for MALDI) analyzer. Single crystal X-raydiffraction data was collected in Bruker SMARTAPEX diffractiometers with molybdenum cathodes.

The crystal preparation and measurement methods of **2a** and **2a'** as follows: Place 60.0 mg of **2a** or **2a'** in a 50 ml round bottom flask, dissolve **2a** or **2a'** with 4 mL of dichloromethane, then add 20 mL of petroleum ether and shake well, seal the flask with a sealing film, pierce a few holes, and let it stand still at room temperature until crystals precipitate out. The crystal was carefully picked out from the solvent with a spatula, and observed under a microscope to confirm that it was transparent for single crystal X-ray diffraction.

2. Synthesis of 1

The medium-sized rings were prepared according to the reference [1,2].

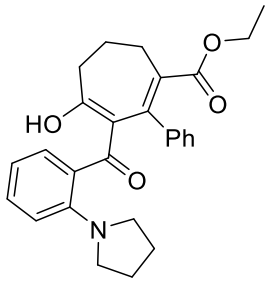


Step-1 Potassium carbonate (1.658g, 12.0 mmol, 1.2 equiv.) and secondary amine (12.0 mmol, 1.2 equiv.) were added to 2-fluorobenzaldehyde (10.0 mmol, 1.0 equiv.) in DMF (10 mL), and the solution was heated to reflux for 2-4 h. Then the reaction was cooled down to room temperature and quenched with a saturated aqueous solution of NH_4Cl (20 mL). The water phase was extracted with DCM (3×20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by column chromatography with petroleum ether/ethyl acetate as the eluent (petroleum ether:ethyl acetate = 20:1–5:1) to afforded the 2-aminobenzaldehyde as an orange oil (60%-100%).

Step-2 To a solution of alkyne (13.0 mmol, 1.3 equiv.) in anhydrous THF (10 mL), n-BuLi (2.5M, 12.0 mmol, 1.2 equiv.) was added at -78 °C. The resulting mixture was stirred at -78 °C for 1.0 h, then the 2-aminobenzaldehyde (10.0 mmol, 1.0 equiv.) was added and the reaction temperature was raised to room temperature until 2-aminobenzaldehyde disappeared by TLC analysis. The resulting mixture was quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by column chromatography with petroleum ether/ethyl acetate (10:1-5:1) as the eluent to afforded the alkynol (44%-92%).

Step-3 To a solution of alkynol (10.0 mmol, 1.0 equiv.) in DMSO (10 mL) in round-bottom flask, IBX (12 mmol, 1.2 equiv.) was added at room temperature. The reaction was stirred in air until the full conversion of alkynol monitored by TLC. After disappearance of starting material, the resulting mixture was quenched with water and filtered. Then the filtrate was extracted with ethyl acetate. The organic layer was combined, washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was subjected to column chromatography for purification, using petroleum ether/ethyl acetate as the eluent (30:1-20:1) to furnish the ynones (26%-81%).

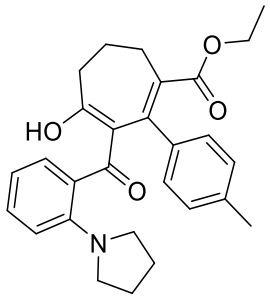
Step-4 In a round-bottom flask the ynone (2.0 mmol, 1.0 equiv), Cs_2CO_3 (4.0 mmol, 2.0 equiv.), DMSO (10.0 mL) and **t**he 1,3-dicarbonyl compound (2.4 mmol, 1.2 equiv.) was stirred at 60 °C. The progress of reaction was monitored by TLC. After disappearance of the ynone, the reaction mixture was then quenched by water, and the water layers were extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether:ethyl acetate = 30:1–20:1) afforded desired medium-sized rings **1**.



1a

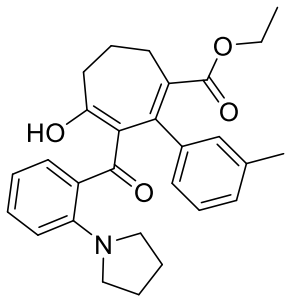
Ethyl 4-hydroxy-2-phenyl-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-diene-1-carboxylate (**1a**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 20:1); (6 mmol scale: 2.43 g, yield: 94%); m.p. 163-165 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 17.22 (s, 1H), 7.11-7.08 (m, 1H), 6.99-6.90 (m, 4H), 6.65 (d, *J* = 7.2 Hz, 2H), 6.54 (s, 1H), 6.39 (d, *J* = 8.3 Hz, 1H), 3.84 (q, *J* = 7.0 Hz, 2H), 3.98-2.30 (m, 10H), 1.82-1.56 (m, 4H), 0.78 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.5, 192.6, 169.4, 146.6, 145.9, 140.6, 131.1, 130.9, 130.0, 128.6, 126.5, 126.3, 114.7, 113.6, 60.2, 50.1, 34.7, 31.5, 28.4, 25.4, 13.4. HRMS

(ESI) calcd for $C_{27}H_{30}NO_4$ $[M+H]^+$: 432.2169, found: 432.2169.



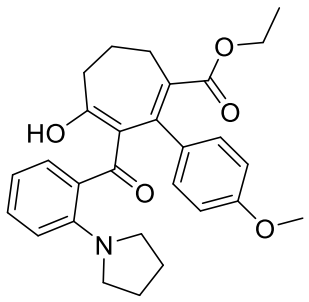
1b

Ethyl 4-hydroxy-3-(2-(pyrrolidin-1-yl)benzoyl)-2-(p-tolyl)cyclohepta-1,3-diene-1-carboxylate (**1b**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 20:1); (1 mmol scale: 417 mg, yield: 94%); m.p. 174-176 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 17.15 (s, 1H), 7.12-7.09 (m, 1H), 6.98 (s, 1H), 6.73 (d, *J* = 7.7 Hz, 2H), 6.52 (d, *J* = 7.8 Hz, 3H), 6.41-6.39 (m, 1H), 3.88 (q, *J* = 7.0 Hz, 2H), 2.98-2.56 (m, 7H), 2.44-2.29 (m, 3H), 2.17 (s, 3H), 1.83 (s, 2H), 1.55 (s, 2H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.7, 192.3, 169.4, 145.9, 137.7, 136.0, 131.1, 130.4, 129.9, 128.5, 127.2, 114.7, 113.8, 113.6, 60.2, 50.2, 34.6, 31.6, 28.4, 25.5, 21.0, 13.5. HRMS (ESI) calcd for $C_{28}H_{32}NO_4$ $[M+H]^+$: 446.2326, found: 446.2323.



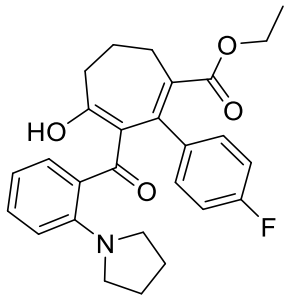
1c

Ethyl 4-hydroxy-3-(2-(pyrrolidin-1-yl)benzoyl)-2-(m-tolyl)cyclohepta-1,3-diene-1-carboxylate (**1c**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 20:1); (1.4 mmol scale: 506 mg, yield: 81%); m.p. 114-116 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 17.19 (s, 1H), 7.10 (s, 1H), 6.98 (s, 1H), 6.82-6.77 (m, 2H), 6.55 (s, 1H), 6.46-6.39 (m, 3H), 3.87-3.85 (m, 2H), 2.99-2.85 (m, 4H), 2.65-2.29 (m, 6H), 2.06 (s, 3H), 1.83 (s, 2H), 1.56 (s, 2H), 0.79 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 193.7, 192.5, 169.4, 145.8, 140.5, 136.0, 131.0, 130.6, 130.0, 129.4, 127.0, 126.4, 125.8, 114.6, 113.7, 113.5, 60.2, 50.1, 34.7, 31.5, 28.4, 25.5, 20.9, 13.4. HRMS (ESI) calcd for $C_{28}H_{32}NO_4$ $[M+H]^+$: 446.2326, found: 446.2326.



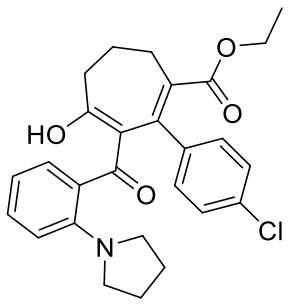
1d

Ethyl 4-hydroxy-2-(4-methoxyphenyl)-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-diene-1-carboxylate (**1d**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); (1.4 mmol scale: 634.7 mg, yield: 98%); m.p. 114-116 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 17.19 (s, 1H), 7.11-6.98 (m, 2H), 6.59-6.54 (m, 3H), 6.47 (d, *J* = 8.4 Hz, 2H), 6.41 (d, *J* = 8.4 Hz, 1H), 3.89 (q, *J* = 7.1 Hz, 2H), 3.67 (s, 3H), 3.02-2.29 (m, 10H), 1.85 (s, 2H), 1.59 (s, 2H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.8, 192.6, 169.5, 158.3, 145.9, 133.2, 131.1, 130.3, 129.9, 114.8, 113.8, 113.6, 112.1, 60.2, 55.1, 50.2, 34.6, 31.7, 28.5, 25.5, 13.6. HRMS (ESI) calcd for $C_{28}H_{32}NO_5$ $[M+H]^+$: 462.2275, found: 462.2281.



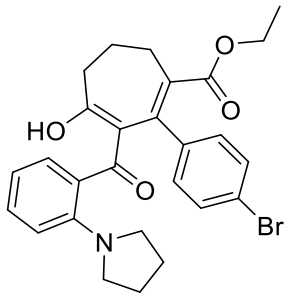
1e

Ethyl 2-(4-fluorophenyl)-4-hydroxy-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-diene-1-carboxylate (**1e**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (1.4 mmol scale: 593.8 mg, yield: 94%); m.p. 185-187 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 17.23 (s, 1H), 7.11-6.96 (m, 2H), 6.63 (d, *J* = 7.0 Hz, 4H), 6.54 (s, 1H), 6.43 (d, *J* = 8.2 Hz, 1H), 3.88 (q, *J* = 6.7, 6.1 Hz, 2H), 3.04-2.29 (m, 10H), 1.86 (s, 2H), 1.60 (s, 2H), 0.86 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 193.5, 192.7, 169.1, 161.5 (J_F = 244.3 Hz), 145.7 (d, *J* = 73.7 Hz), 136.7 (d, *J* = 3.2 Hz), 131.3 (J_F = 6.7 Hz), 130.3, 129.9, 114.8, 113.8, 113.6, 113.5, 113.4, 60.3, 50.2, 34.7, 31.6, 28.4, 25.5, 13.5. HRMS (ESI) calcd for $C_{27}H_{29}FNO_4$ $[M+H]^+$: 450.2075, found: 450.2078.



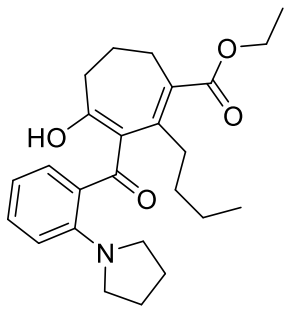
1f

Ethyl 2-(4-chlorophenyl)-4-hydroxy-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-diene-1-carboxylate (**1f**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (1.6 mmol scale: 531.6 mg, yield: 71%); m.p. 186-188 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 17.18 (s, 1H), 7.13-7.11 (m, 1H), 6.90 (d, *J* = 8.2 Hz, 3H), 6.57 (d, *J* = 7.9 Hz, 3H), 6.43-6.42 (m, 1H), 3.88 (q, *J* = 7.1, 2.5 Hz, 2H), 3.03-2.30 (m, 10H), 1.86 (s, 2H), 1.61 (s, 2H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.6, 193.0, 168.9, 145.8, 139.2, 132.3, 132.3, 131.34, 129.92, 129.86, 126.7, 114.7, 113.9, 113.7, 60.4, 50.2, 34.8, 31.5, 28.4, 25.5, 13.5. HRMS (ESI) calcd for $C_{27}H_{29}ClNO_4$ $[M+H]^+$: 466.1780, found: 466.1780.



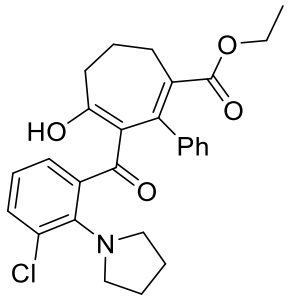
1g

Ethyl 2-(4-bromophenyl)-4-hydroxy-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-diene-1-carboxylate (**1g**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (1.4 mmol scale: 583.6 mg, yield: 82%); m.p. 157-159 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 17.15 (s, 1H), 7.26-7.05 (m, 3H), 6.92 (s, 1H), 6.54-6.49 (m, 3H), 6.43 (d, *J* = 8.4 Hz, 1H), 3.89 (q, *J* = 6.6, 6.0 Hz, 2H), 3.03 (s, 2H), 2.84-2.80 (m, 2H), 2.65-2.56 (m, 3H), 2.46-2.30 (m, 3H), 1.86 (s, 2H), 1.61 (s, 2H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.6, 192.8, 168.8, 145.9, 139.7, 131.3, 130.2, 130.0, 129.8, 129.7, 120.4, 114.8, 113.9, 113.7, 60.4, 50.2, 34.8, 31.5, 28.4, 25.5, 13.5. HRMS (ESI) calcd for $C_{27}H_{29}BrNO_4$ $[M+H]^+$: 510.1274, found: 510.1275.



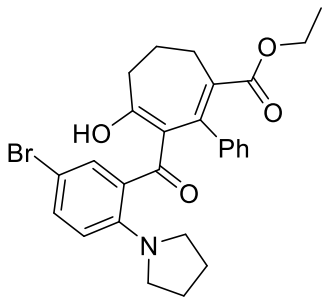
1h

Ethyl 2-butyl-4-hydroxy-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-diene-1-carboxylate (**1h**). Yellow oil, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (2 mmol scale: 747.3 mg, yield: 91%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 17.61 (s, 1H), 7.27-7.24 (m, 1H), 7.04 (d, *J* = 8.8 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 1H), 6.62-6.59 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.42 (q, *J* = 9.6 Hz, 2H), 3.12-3.09 (m, 2H), 2.82 (s, 1H), 2.72 (dd, *J* = 13.2, 5.7 Hz, 1H), 2.59 (q, *J* = 11.9 Hz, 1H), 2.39 (td, *J* = 13.5, 7.0 Hz, 1H), 2.31– 2.17 (m, 3H), 2.04 (s, 2H), 1.87-1.79 (m, 3H), 1.40-1.34 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.25-1.18 (m, 2H), 1.12-1.06 (m, 1H), 0.78 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 195.0, 189.6, 168.5, 150.2, 146.4, 131.5, 129.5, 128.2, 121.5, 115.3, 114.0, 112.2, 60.2, 50.4, 35.0, 34.1, 32.0, 30.6, 27.7, 25.7, 23.1, 14.2, 13.9. HRMS (ESI) calcd for $C_{25}H_{34}NO_4$ $[M+H]^+$: 412.2482, found: 412.2482.



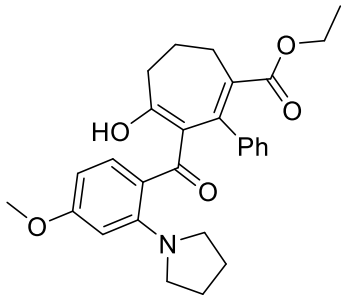
1i

Ethyl 3-(3-chloro-2-(pyrrolidin-1-yl)benzoyl)-4-hydroxy-2-phenylcyclohepta-1,3-diene-1-carboxylate (**1i**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (5.6 mmol scale: 909.8 mg, yield: 35%); m.p. 94-96 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 17.10 (s, 1H), 7.26-6.93 (m, 5H), 6.67-6.66 (m, 3H), 3.84 (s, 2H), 2.85-2.26 (m, 10H), 1.85 (s, 4H), 0.77 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.7, 131.5, 128.3, 127.2, 126.8, 60.4, 51.1, 34.9, 31.3, 28.6, 25.9, 13.4. HRMS (ESI) calcd for $C_{27}H_{29}ClNO_4$ $[M+H]^+$: 466.1780, found: 466.1780.



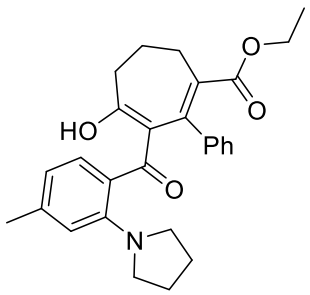
1j

Ethyl 3-(5-bromo-2-(pyrrolidin-1-yl)benzoyl)-4-hydroxy-2-phenylcyclohepta-1,3-diene-1-carboxylate (**1j**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (8.5 mmol scale: 3.07 g, yield: 71%); m.p. 164-166 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 17.12 (s, 1H), 7.13-6.94 (m, 5H), 6.68 (d, *J* = 7.0 Hz, 2H), 6.26 (d, *J* = 6.9 Hz, 1H), 3.90-3.86 (m, 2H), 2.96-2.31 (m, 10H), 1.85-1.59 (m, 4H), 0.82 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (125 MHz, $CDCl_3$): δ 193.4, 192.1, 169.1, 144.6, 140.3, 133.3, 131.9, 131.4, 128.9, 128.6, 126.7, 126.6, 115.4, 113.7, 60.3, 50.3, 34.7, 31.6, 28.4, 25.4, 13.4. HRMS (ESI) calcd for $C_{27}H_{29}BrNO_4$ $[M+H]^+$: 510.1274, found: 510.1275.



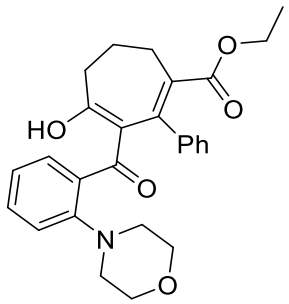
1k

Ethyl 4-hydroxy-3-(4-methoxy-2-(pyrrolidin-1-yl)benzoyl)-2-phenylcyclohepta-1,3-diene-1-carboxylate (**1k**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); (12.7 mmol scale: 926 mg, yield: 16%); m.p. 102-104 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 16.98 (s, 1H), 7.02-6.88 (m, 3H), 6.83-6.36 (m, 5H), 3.94-3.52 (m, 5H), 3.15-2.19 (m, 12H), 1.83 (s, 2H), 0.80 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 193.6, 170.8, 141.4, 140.5, 131.0, 128.4, 126.7, 126.5, 119.9, 116.1, 114.0, 60.3, 55.6, 50.6, 34.5, 31.6, 28.3, 25.3, 13.4. HRMS (ESI) calcd for $C_{28}H_{32}NO_5$ $[M+H]^+$: 462.2275, found: 462.2276.



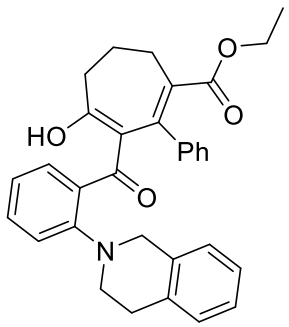
1l

Ethyl 4-hydroxy-3-(4-methyl-2-(pyrrolidin-1-yl)benzoyl)-2-phenylcyclohepta-1,3-diene-1-carboxylate (**1l**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (1.0 mmol scale: 249.3 mg, yield: 56%); m.p. 114-116 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 17.24 (s, 1H), 7.03-6.83 (m, 4H), 6.67 (d, *J* = 7.8 Hz, 2H), 6.37 (s, 1H), 6.21 (s, 1H), 3.92-3.80 (m, 5H), 3.15-2.19 (m, 10H), 2.22 (s, 3H), 1.82 (s, 2H), 1.55 (s, 2H), 0.79 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.3, 192.6, 169.5, 146.2, 141.5, 140.7, 130.7, 130.2, 128.7, 126.5, 126.4, 116.1, 113.9, 113.4, 60.2, 50.2, 34.7, 31.5, 28.5, 25.5, 21.8, 13.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{28}H_{32}NO_4$ 446.2326, found 446.2326.



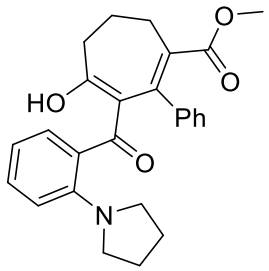
1m

Ethyl 4-hydroxy-3-(2-morpholinobenzoyl)-2-phenylcyclohepta-1,3-diene-1-carboxylate (**1m**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); (9.8 mmol scale: 3.50 g, yield: 80%); m.p. 133-135 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 17.11 (s, 1H), 7.11 (s, 1H), 6.96-6.79 (m, 5H), 6.58-6.56 (m, 3H), 3.84-3.71 (m, 6H), 2.84-2.76 (m, 6H), 2.48-2.25 (m, 4H), 0.78 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 195.6, 192.5, 169.8, 150.0, 140.4, 131.2, 130.5, 128.9, 127.8, 126.9, 126.5, 122.7, 118.7, 113.9, 66.8, 60.3, 53.0, 35.1, 31.2, 29.2, 13.4. HRMS (ESI) calcd for $C_{27}H_{30}NO_5$ $[M+H]^+$: 448.2118, found: 448.2119.



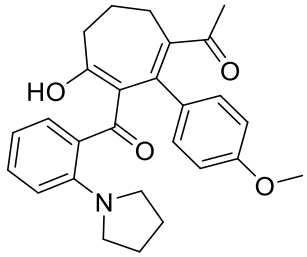
1n

Ethyl 3-(2-(3,4-dihydroisoquinolin-2(1H)-yl)benzoyl)-4-hydroxy-2-phenylcyclohepta-1,3-diene-1-carboxylate (**1n**). White solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (8.8 mmol scale: 2.28 g, yield: 53%); m.p. 121-123 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 17.00 (s, 1H), 7.14-7.06 (m, 5H), 6.94-6.87 (m, 4H), 6.61-6.48 (m, 4H), 4.26 (s, 1H), 4.03 (d, *J* = 11.7 Hz, 1H), 3.85-3.81 (m, 2H), 3.19-2.72 (m, 5H), 2.36-2.06 (m, 5H), 0.79 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 194.2, 193.9, 170.4, 149.7, 140.6, 134.9, 134.3, 131.4, 130.1, 128.6, 127.6, 127.0, 126.5, 126.2, 126.1, 125.7, 122.5, 118.8, 114.1, 60.2, 54.5, 51.3, 34.7, 31.3, 28.6, 28.2, 13.4. HRMS (ESI) calcd for $C_{32}H_{32}NO_4$ $[M+H]^+$:492.2169, found: 492.2170.



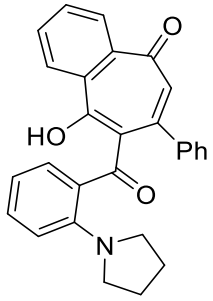
1o

Methyl 4-hydroxy-2-phenyl-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-diene-1-carboxylate (**1o**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); (0.8 mmol scale: 294.1 mg yield: 88%); m.p. 158-160 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 14.62 (s, 1H), 7.13 (s, 1H), 7.06-7.01 (m, 4H), 6.82 (d, *J* = 5.3 Hz, 2H), 6.72 (s, 1H), 6.62 (d, *J* = 6.0 Hz, 1H), 4.40 (s, 3H), 4.11-4.00 (m, 4H), 3.87-3.82 m, 3H), 3.72-3.59 (m, 3H), 3.25 (s, 2H), 3.12-3.06 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 193.6, 192.8, 169.8, 145.9, 140.4, 131.2, 130.5, 130.0, 128.5, 126.6, 126.5, 114.7, 113.6, 113.5, 51.3, 50.2, 34.7, 31.5, 28.5, 25.4. HRMS (ESI) calcd for $C_{26}H_{28}NO_4$ $[M+H]^+$: 418.2013, found: 418.2014.



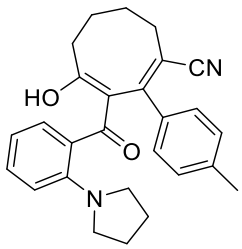
1p

1-(4-hydroxy-2-(4-methoxyphenyl)-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-dien-1-yl)ethan-1-one (**1p**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); (1.4 mmol scale: 352.1 mg, yield: 58%); m.p. 151-153 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 17.32 (s, 1H), 7.06 (s, 1H), 6.92 (s, 1H), 6.64 (d, *J* = 7.9 Hz, 2H), 6.52-6.49 (m, 3H), 6.41(d, *J* = 8.4 Hz, 1H), 3.69 (s, 3H), 3.07-2.77 (m, 6H), 2.49- 2.35 (m, 3H), 2.15 (s, 1H), 1.89 (s, 2H), 1.67 (m, 3H), 1.66-1.62 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 205.3, 193.7, 159.3, 145.9, 140.2, 132.8, 131.2, 130.6, 130.0, 113.8, 113.7, 112.8, 55.2, 50.3, 34.9, 31.5, 30.9, 28.9, 25.5. HRMS (ESI) calcd for $C_{27}H_{29}NNaO_4$ $[M+Na]^+$: 454.1989, found: 454.1989.



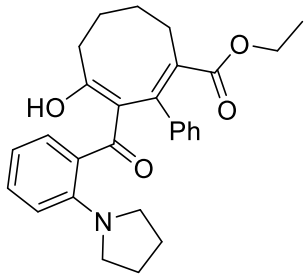
1q

9-hydroxy-7-phenyl-8-(2-(pyrrolidin-1-yl)benzoyl)-5H-benzo[7]annulen-5-one (**1q**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (0.7 mmol scale: 106 mg, yield: 34%); m.p. 211-213 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 16.74 (s, 1H), 8.49 (d, *J* = 7.5 Hz, 1H), 7.93 (d, *J* = 6.9 Hz, 1H), 7.78-7.73(m, 2H), 7.03-6.97 (m, 5H), 6.90 (d, *J* = 7.1 Hz, 2H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.39-6.36 (m, 2H), 2.99 (s, 4H), 1.76 (s, 4H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.0, 192.8, 172.9, 147.0, 146.5, 142.7, 142.4, 132.8, 132.1, 131.8, 131.8, 131.4, 130.0, 129.9, 128.3, 127.7, 127.4, 127.2, 125.8, 116.4, 114.9, 114.0, 51.1, 25.6. HRMS (ESI) calcd for $C_{28}H_{24}NO_3$ $[M+H]^+$: 422.1751, found: 422.1746.



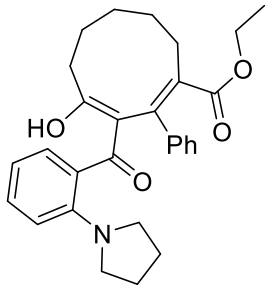
1r

(1E,3Z)-4-hydroxy-2-(4-methoxyphenyl)-3-(2-(pyrrolidin-1-yl)benzoyl)cycloocta-1,3-diene-1-carbonitrile (**1r**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 30:1); (1.0 mmol scale: 314.1 mg yield: 76%); m.p. 181-183 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ 17.09 (s, 1H), 7.13-7.00 (m, 1H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 8.1 Hz, 3H), 6.52-6.44 (m, 2H), 3.00-2.98 (m, 2H), 2.80-2.62 (m, 4H), 2.48-2.40 (m, 2H), 2.22 (s, 3H), 2.12-2.01 (m, 2H), 1.83 (s, 2H), 1.67-1.56 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.7, 187.0, 153.2, 145.8, 138.5, 135.5, 131.1, 128.8, 128.3, 128.2, 120.2, 114.9, 113.8, 112.1, 111.8, 50.4, 34.7, 32.2, 25.5, 24.2, 23.8, 21.1. HRMS (ESI) calcd for $C_{27}H_{29}N_2O_2$ $[M+H]^+$: 413.2224, found: 413.2226.



1s

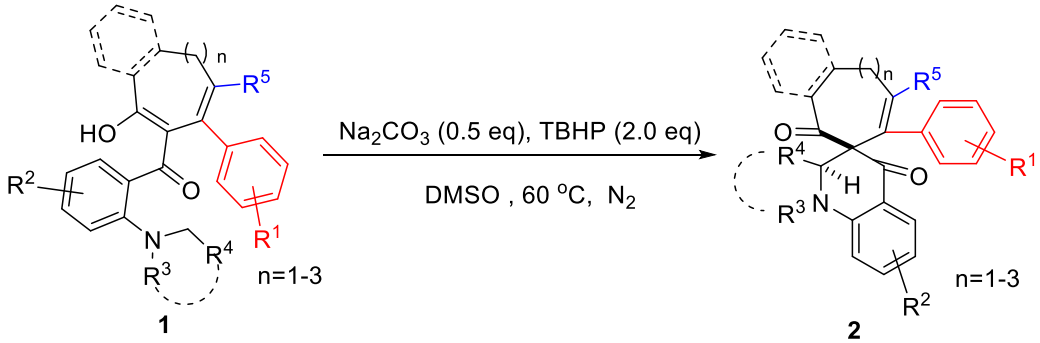
Ethyl (1E,3Z)-4-hydroxy-2-phenyl-3-(2-(pyrrolidin-1-yl)benzoyl)cycloocta-1,3-diene-1-carboxylate (**1s**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); (0.8 mmol scale: 343.1mg, yield: 96%); m.p. 127-129 ºC. ^{1}H NMR (600 MHz, $CDCl_3$): δ 14.52 (s, 1H), 7.15-7.14 (m, 1H), 7.07-7.01 (m, 4H), 6.78-6.74 (m, 3H), 6.64 (d, *J* = 5.7 Hz, 1H), 4.74-4.86 (m, 2H), 4.19-4.17 (m, 1H), 4.08 (s, 2H), 3.91 (t, *J* = 8.7 Hz, 1H), 3.84-3.81 (m, 2H), 3.64 (t, *J* = 9.4 Hz, 1H), 3.44-3.41 (m, 1H), 3.34-3.32 (m, 1H), 3.22 (s, 2H), 3.13-3.08 (m, 2H), 3.02 (s, 2H), 2.92-2.85 (m, 1H), 2.43 (t, *J* = 5.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 196.9, 187.7, 170.4, 145.8, 140.9, 134.0, 130.8, 129.2, 128.0, 126.9, 126.6, 114.6, 113.6, 113.5, 60.3, 50.2, 34.8, 31.2, 25.5, 24.4, 24.3, 13.4. HRMS (ESI) calcd for $C_{28}H_{32}N_2O_4$ $[M+H]^+$: 446.2326, found: 446.2326.



1t

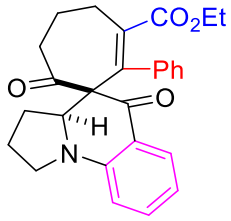
Ethyl (1E,3Z)-4-hydroxy-2-phenyl-3-(2-(pyrrolidin-1-yl)benzoyl)cyclonona-1,3-diene-1-cararboxylate (**1t**). Yellow solid, obtained in 3 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); (0.8 mmol scale: 305.5 mg yield: 83%); m.p. 104-106 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 14.49 (s, 1H), 7.15-7.14 (m, 1H), 7.09-7.03 (m, 4H), 6.78-6.75 (m, 3H), 6.63 (d, J = 6.2 Hz, 1H), 4.77-4.70 (m, 2H), 4.14 (d, J = 8.7 Hz, 1H), 4.05-4.01 (m, 3H), 3.87-3.79 (m, 4H), 3.30-3.23 (m, 3H), 3.18-3.16 (m, 4H), 3.03-3.00 (m, 3H), 2.46 (t, J = 5.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 195.2, 189.6, 170.0, 145.6, 142.3, 140.8, 137.2, 130.6, 128.7, 127.9, 127.1, 126.7, 122.2, 114.7, 113.5, 60.2, 49.9, 35.9, 33.4, 29.4, 25.6, 25.4, 24.9, 13.4. HRMS (ESI) calcd for $C_{29}H_{34}N_2O_4$ $[M+H]^+$: 460.2482, found: 460.2487.

3. Synthesis of 2



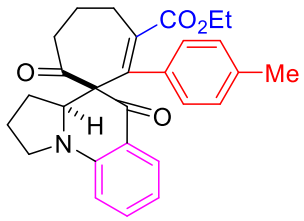
In a schlenk tube, **1** (0.2 mmol, 1.0 equiv.), DMSO (2.0 mL), Na_2CO_3 (0.1 mmol, 10.6 mg, 0.5 equiv) and TBHP (0.4 mmol, 38 μL, 2.0 equiv) were stirred at 60 °C under N_2. The progress of reaction was monitored by TLC. After disappearance of the **1**, the reaction mixture was then quenched with aqueous NH_4Cl (10 mL), and the water layers were extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under

reduced pressure. Purification by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1-10:1) afforded **2**.



2a

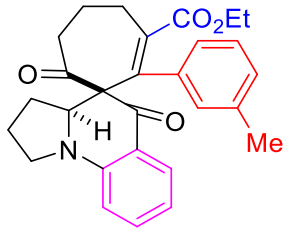
Ethyl (1S*,3a'S*)-5',7-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2a**). Yellow solid, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (66.7 mg, 78%); dr = 14:1. Major isomer: m.p. 206-208 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.36-7.32 (m, 1H), 7.27-7.23 (m, 3H), 7.17-7.16 (m, 2H), 6.70-6.67 (m, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 3.80 (q, *J* = 7.1 Hz, 2H), 3.74-3.71 (m, 1H), 3.42-3.37 (m, 1H), 3.26-3.23 (m, 1H), 3.04 (q, *J* = 9.4 Hz, 1H), 2.71-2.57 (m, 2H), 2.48-2.43 (m, 1H), 2.16-1.90 (m, 5H), 1.68-1.61 (m, 1H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 207.7, 188.8, 170.2, 149.2, 140.0, 138.5, 137.3, 135.5, 129.02, 129.00, 127.7, 127.5, 119.0, 116.1, 112.8, 71.7, 63.0, 60.4, 46.5, 40.6, 27.6, 27.5, 25.4, 23.0, 13.4. HRMS (ESI) calcd for $C_{27}H_{28}NO_4$ $[M+H]^+$:430.2013; found:430.2013. Another isomer: m.p. 157-159 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.04 -7.00 (m, 1H), 6.86 (s, 5H), 6.40-6.37 (m, 1H), 6.07 (d, *J* = 8.4 Hz, 1H), 4.50 (dd, *J* = 10.7, 5.1 Hz, 1H), 3.87-3.81 (m, 1H), 3.74 (q, *J* = 7.1 Hz, 2H), 3.35-3.31 (m, 1H), 3.26-3.20 (m, 1H), 2.78-2.73 (m, 1H), 2.51-2.35 (m, 3H), 2.25-1.97 (m, 5H), 0.70 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.3, 192.1, 169.6, 148.4, 140.2, 137.5, 135.4, 135.1, 130.2, 128.4, 127.1, 126.3, 119.0, 115.5, 112.3, 68.6, 61.9, 60.6, 45.8, 40.9, 27.8, 27.0, 24.4, 22.8, 13.3. HRMS (ESI) calcd for $C_{27}H_{27}NNaO_4$ $[M+Na]^+$: 452.1832, found: 452.1828.



2b

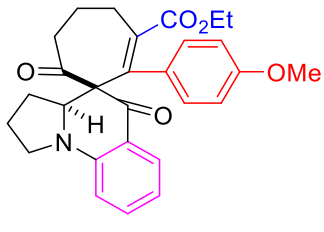
Ethyl (1S*,3a'S*)-5',7-dioxo-2-(p-tolyl)-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2b**). Yellow

solid, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (73.0 mg, 82%); dr = 5:1; m.p. 202-204 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 (d, *J* = 7.1 Hz, 1H), 7.35-7.32 (m, 1H), 7.04 (s, 4H), 6.69-6.66 (m, 1H), 6.51 (d, *J* = 8.3 Hz, 1H), 3.84-3.81 (m, 2H), 3.75 (dd, *J* = 9.1, 6.3 Hz, 1H), 3.42-3.38 (m, 1H), 3.26-3.23 (m, 1H), 3.05-3.00 (m, 1H), 2.69-2.58 (m, 2H), 2.47-2.42 (m, 1H), 2.29 (s, 3H), 2.14-1.93 (m, 5H), 1.68-1.63 (m, 1H), 0.80 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.8, 188.8, 170.2, 149.2, 140.1, 137.2, 137.1, 135.5, 135.4, 129.0, 128.9, 128.3, 119.0, 116.0, 112.8, 71.7, 63.0, 60.3, 46.5, 40.6, 27.6, 27.4, 25.4, 23.0, 21.1, 13.4. HRMS (ESI) calcd for $C_{28}H_{30}NO_4$ $[M+H]^+$: 444.2169, found: 444.2169.



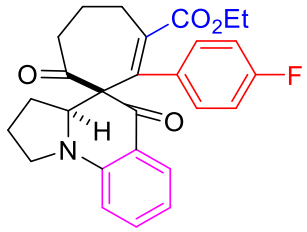
2c

Ethyl (1S*,3a'S*)-5',7-dioxo-2-(m-tolyl)-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2c**). Yellow solid, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (63.0 mg, 71%); dr = 5:1; m.p. 209-211 °C. Major ismmer: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.8 Hz, 1H), 7.36-7.39 (m, 1H), 7.13-7.11 (m, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 2H), 6.70-6.68 (m, 1H), 6.52 (d, *J* = 8.3 Hz, 1H), 3.84-3.74 (m, 3H), 3.42-3.38 (m, 1H), 3.27-3.23 (m, 1H), 3.09-3.04 (m, 1H), 2.70-2.64 (m, 1H), 2.58-2.55 (m, 1H), 2.46-2.42 (m, 1H), 2.28 (s, 3H), 2.18-1.91 (m, 5H), 1.68-1.62 (m, 1H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.9, 188.8, 170.3, 149.2, 140.1, 138.4, 137.3, 137.1, 135.5, 129.5, 129.1, 128.2, 127.6, 126.2, 119.1, 116.1, 112.8, 71.6, 63.1, 60.3, 46.5, 40.7, 27.7, 27.5, 25.6, 23.0, 21.3, 13.4. HRMS (ESI) calcd for $C_{28}H_{30}NO_4$ $[M+H]^+$: 444.2169, found: 444.2169.



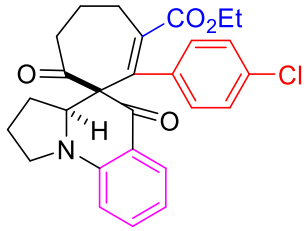
2d

Ethyl (1S*,3a'S*)-2-(4-methoxyphenyl)-5',7-dioxo-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2d**). Yellow solid, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1); yield: (67.1 mg, 73%); m.p. 164-166 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 (d, *J* = 7.8 Hz, 1H), 7.36-7.34 (m, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 8.5 Hz, 2H), 6.70-6.67 (m, 1H), 6.53 (d, *J* = 8.4 Hz, 1H), 3.87-3.84 (m, 2H), 3.77 (s, 3H), 3.76 -3.74 (m, 1H), 3.44-3.40 (m, 1H), 3.29-3.26 (m, 1H), 3.02-2.97 (m, 1H), 2.69-2.61 (m, 2H), 2.47-2.43 (m, 1H), 2.16 -1.94 (m, 5H), 1.72-1.65 (m, 1H), 0.86 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.7, 188.9, 170.3, 158.9, 149.2, 139.6, 137.5, 135.5, 130.6, 130.3, 129.0, 118.9, 116.0, 113.0, 112.8, 71.8, 63.0, 60.3, 55.1, 46.5, 40.5, 27.5, 27.4, 25.3, 23.0, 13.6. HRMS (ESI) calcd for $C_{28}H_{30}NO_5$ $[M+H]^+$: 460.2118, found: 460.2118.



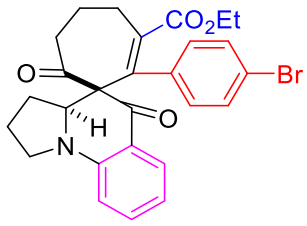
2e

Ethyl (1S*,3a'S*)-2-(4-fluorophenyl)-5',7-dioxo-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2e**). Yellow solid, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (51.5 mg, 57%); m.p. 215-217 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.91 (d, *J* = 7.9 Hz, 1H), 7.36-7.34 (m, 1H), 7.17 (dd, *J* = 7.8, 5.6 Hz, 2H), 6.96-6.93 (m, 2H), 6.69-6.67 (m, 1H), 6.53 (d, *J* = 8.4 Hz, 1H), 3.84 (q, *J* = 7.0 Hz, 2H), 3.71-3.68 (m, 1H), 3.44-3.40 (m, 1H), 3.30-3.27 (m, 1H), 2.98-2.93 (m, 1H), 2.67-2.62 (m, 2H), 2.48-2.44 (m, 1H), 2.15-1.92 (m, 5H), 1.73-1.65 (m, 1H), 0.85 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.2, 188.7, 169.9, 162.1 (J_F = 245.7 Hz), 149.1, 138.9, 138.1, 135.7, 134.3 (J_F = 3.3 Hz), 130.9 (J_F = 7.8 Hz), 129.0, 118.7, 116.2, 114.7 (J_F = 21.6 Hz), 112.9, 71.8, 62.9, 60.5, 46.5, 40.4, 27.55, 27.47, 25.2, 23.1, 13.5. HRMS (ESI) calcd for $C_{27}H_{27}FNO_4$ $[M+H]^+$: 448.1919, found: 448.1919.



2f

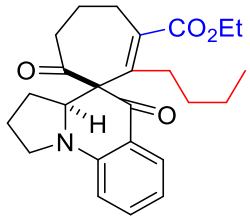
Ethyl (1S*,3a'S*)-2-(4-chlorophenyl)-5',7-dioxo-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2f**). Yellow solid, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (77.7 mg, 84%); m.p. 232-234 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.90 (d, *J* = 7.8 Hz, 1H), 7.36-7.34 (m, 1H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 6.69-6.67 (m, 1H), 6.53 (d, *J* = 8.4 Hz, 1H), 3.85 (q, *J* = 7.1 Hz, 2H), 3.70-3.67 (m, 1H), 3.44-3.40 (m, 1H), 3.30-3.26 (m, 1H), 2.98-2.93 (m, 1H), 2.67-2.62 (m, 2H), 2.49-2.45 (m, 1H), 2.14-1.90 (m, 5H), 1.74-1.66 (m, 1H), 0.85 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.1, 188.6, 169.8, 149.1, 139.0, 138.0, 137.0, 135.7, 133.6, 130.5, 129.0, 127.9, 118.7, 116.2, 112.9, 71.7, 62.9, 60.6, 46.5, 40.4, 27.55, 27.49, 25.2, 23.1, 13.5. HRMS (ESI) calcd for $C_{27}H_{26}ClNaNO_4$ $[M+Na]^+$: 486.1443, found: 486.1443.



2g

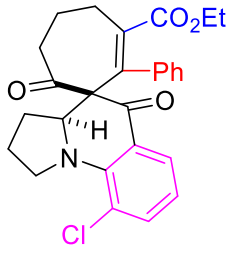
Ethyl (1S*,3a'S*)-2-(4-bromophenyl)-5',7-dioxo-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2g**). Yellow solid, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (82.6 mg, 81%); m.p. 204-206 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.37 (dd, *J* = 20.1, 8.4 Hz, 3H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.70-6.67 (m, 1H), 6.53 (d, *J* = 8.4 Hz, 1H), 3.85 (q, *J* = 7.1 Hz, 2H), 3.69 (dd, *J* = 9.2, 6.6 Hz, 1H), 3.45-3.40 (m, 1H), 3.31-3.26 (m, 1H), 2.98-2.92 (m, 1H), 2.67-2.61 (m, 2H), 2.49-2.44 (m, 1H), 2.16-1.89 (m, 5H), 1.75-1.66 (m, 1H), 0.85 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 207.1, 188.6, 169.8, 149.2, 139.0, 138.0, 137.5, 135.8, 130.91, 130.87, 129.1, 121.8, 118.7, 116.3, 112.9, 71.8, 62.9, 60.6, 46.5, 40.4, 27.6, 27.5, 25.2, 23.1, 13.5. HRMS (ESI) calcd for $C_{27}H_{27}BrNNaO_4$ $[M+Na]^+$:

530.0937, found: 530.0938.



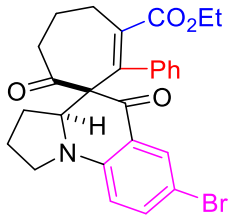
2h

Ethyl (1S*,3a'S*)-2-butyl-5',7-dioxo-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2h**). Yellow oil, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (33.9 mg, 41%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.78 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.35-7.27 (m, 1H), 6.60-6.54 (m, 2H), 4.29-4.22 (m, 2H), 4.07 (dd, *J* = 10.3, 6.2 Hz, 1H), 3.56-3.51 (m, 2H), 3.10-3.06 (m, 1H), 2.47-2.25 (m, 6H), 2.21-2.16 (m, 1H), 2.13-2.09 (m, 1H), 2.01-1.88 (m, 3H), 1.59-1.53 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.31-1.25 (m, 3H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.4, 189.0, 170.0, 148.9, 144.3, 136.2, 132.6, 129.3, 116.2, 115.5, 112.8, 74.4, 60.7, 60.6, 46.5, 37.2, 33.6, 33.0, 27.4, 27.1, 25.5, 23.42, 23.36, 14.1, 13.7. HRMS (ESI) calcd for $C_{25}H_{32}NO_4$ $[M+H]^+$: 410.2326, found: 410.2326.



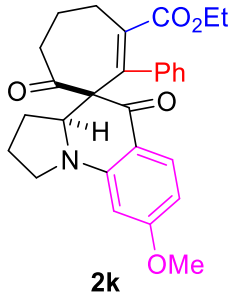
2i

Ethyl (1S*,3a'S*)-9'-chloro-5',7-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2i**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (77.2 mg, 83%); dr = 6:1; m.p. 204-206 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.94 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 18.5 Hz, 3H), 7.09 (s, 2H), 6.71-6.68 (m, 1H), 4.10-4.03 (m, 2H), 3.83-3.72 (m, 3H), 3.29-3.24 (m, 1H), 2.70-2.65 (m, 1H), 2.57-2.45 (m, 2H), 2.29-2.15 (m, 3H), 1.86-1.73 (m, 3H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 210.1, 189.3, 169.9, 146.9, 140.2, 138.2, 137.6, 137.3, 128.9, 128.1, 127.9, 127.5, 124.0, 120.7, 118.1, 71.1, 65.5, 60.4, 51.8, 40.9, 28.1, 27.4, 26.0, 24.8, 13.4. HRMS (ESI) calcd for $C_{27}H_{27}ClNO_4$ $[M+H]^+$: 464.1623, found: 464.1625.



2j

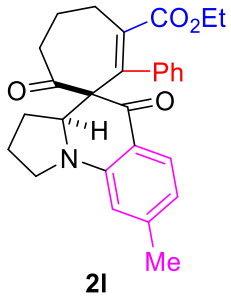
Ethyl (1S*,3a'S*)-7'-bromo-5',7-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2j**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (71.2 mg, 70%); m.p. 197-199 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, *J* = 1.9 Hz, 1H), 7.38 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.26 (d, *J* = 15.8 Hz, 3H), 7.14 (s, 2H), 6.42 (d, *J* = 8.9 Hz, 1H), 3.81 (q, *J* = 7.1 Hz, 2H), 3.71 (dd, *J* = 8.8, 6.5 Hz, 1H), 3.38-3.34 (m, 1H), 3.26-3.22 (m, 1H), 3.07-3.02 (m, 1H), 2.66-2.58 (m, 2H), 2.48-2.44 (m, 1H), 2.19-1.92 (m, 5H), 1.69-1.64 (m, 1H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.6, 187.7, 170.0, 147.9, 139.6, 138.2, 137.9, 137.5, 131.1, 128.9, 127.8, 127.6, 120.1, 114.8, 108.5, 71.4, 63.0, 60.4, 46.6, 40.6, 27.6, 27.5, 25.5, 23.0, 13.4. HRMS (ESI) calcd for $C_{27}H_{27}BrNO_4$ $[M+H]^+$: 508.1118, found: 508.1120.



2k

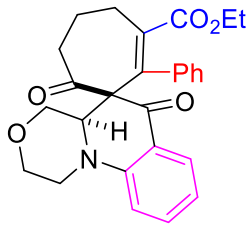
Ethyl (1S*,3a'S*)-8'-methoxy-5',7-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2k**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1); yield: (48.9 mg, 53%); m.p. 123-125 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.44 (d, *J* = 3.6 Hz, 1H), 7.26-7.21 (m, 3H), 7.18-7.13 (m, 2H), 7.07-7.01 (m, 1H), 6.51 (d, *J* = 9.0 Hz, 1 H), 3.84-3.76 (m, 5H), 3.69-3.63 (m, 1H), 3.45-3.37 (m, 1H), 3.21-3.02 (m, 2H), 2.76-2.65 (m, 1H), 2.59-2.53 (m, 1H), 2.48-2.42 (m, 1H), 2.24-2.11 (m, 2H), 2.08-2.00 (m, 1H), 1.98-1.86 (m, 2H), 1.67-1.55 (m, 1H), 0.77 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 208.1, 188.7, 170.2, 150.9, 145.2, 140.1, 138.5, 137.3, 129.0, 127.7, 127.5, 125.8, 118.9, 114.6, 109.3, 71.9, 63.7, 60.4, 55.6, 46.7, 40.7, 27.6, 27.5, 25.7, 22.9, 13.4. HRMS (ESI) calcd for $C_{28}H_{30}NO_5$ $[M+H]^+$: 460.2118,

found: 460.2118.



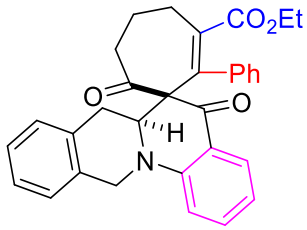
2l

Ethyl (1S*,3a'S*)-8'-methyl-5',7-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2l**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1); yield: (55.3 mg, 62%); m.p. 139-141 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.1 Hz, 1H), 7.23-7.16 (m, 5H), 6.51 (d, *J* = 8.1 Hz, 1H), 6.32 (s, 1H), 3.79 (q, *J* = 7.1 Hz, 2H), 3.73-3.70 (m, 1H), 3.41-3.37 (m, 1H), 3.26-3.22 (m, 1H), 3.04-3.00 (m, 1H), 2.71-2.60 (m, 2H), 2.47-2.43 (m, 1H), 2.29 (s, 3H), 2.15-1.90 (m, 5H), 1.68-1.58 (m, 1H), 0.76 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.6, 188.2, 170.2, 149.2, 146.7, 140.2, 138.6, 137.2, 129.0, 127.6, 127.4, 117.8, 116.9, 112.8, 71.7, 63.0, 60.3, 46.2, 40.5, 27.6, 27.5, 25.4, 23.0, 22.2, 13.4. HRMS (ESI) calcd for $C_{28}H_{30}NO_4$ $[M+H]^+$: 444.2169, found: 444.2169.



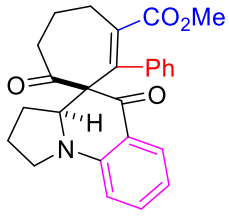
2m

Ethyl (1S*,4a'R*)-6',7-dioxo-2-phenyl-1',2',4',4a'-tetrahydro-6'H-spiro[cycloheptane-1,5'-[1,4]oxazino[4,3-a]quinolin]-2-ene-3-carboxylate (**2m**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1); yield: (43.9 mg, 49%); m.p. 160-162 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.02-8.01 (m, 1H), 7.45-7.42 (m, 1H), 7.25-74 (m, 3H), 7.16-7.15 (m, 2H), 6.88-6.84 (m, 2H), 4.15-4.13 (m, 1H), 3.93-3.91 (m, 1H), 3.80 (q, *J* = 7.1 Hz, 2H), 3.74-3.65 (m, 4H), 2.95-2.68 (m, 4H), 2.44-2.39 (m, 1H), 2.23-2.11 (m, 2H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.5, 187.6, 170.1, 151.6, 139.1, 138.4, 137.6, 135.8, 129.3, 129.0, 127.9, 127.8, 120.9, 118.9, 113.6, 71.0, 66.6, 66.2, 60.6, 60.5, 46.4, 40.3, 27.4, 25.6, 13.4. HRMS (ESI) calcd for $C_{27}H_{28}NO_5$ $[M+H]^+$: 446.1962, found: 446.1963.



2n

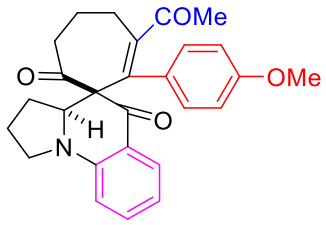
Ethyl (1S*,6a'S*)-5',7-dioxo-2-phenyl-6a',7'-dihydro-5'H,12'H-spiro[cycloheptane-1,6'-isoquinolino[2,3-a]quinolin]-2-ene-3-carboxylate (**2n**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1); yield: (33.9 mg, 34%); m.p. 120-122 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.27-7.26 (m, 3H), 7.22-7.19 (m, 2H), 7.01-6.90 (m, 3H), 6.81 (s, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.47 (t, *J* = 7.4 Hz, 1H), 5.89 (s, 1H), 3.93-3.91 (m, 1H), 3.82-3.78 (m, 1H), 3.76-3.70 (m, 2H), 3.49-3.42 (m, 1H), 3.30-3.26 (m, 1H), 2.96 (d, *J* = 15.2 Hz, 1H), 2.65 (dd, *J* = 11.3, 7.0 Hz, 1H), 1.98-1.90 (m, 1H), 1.79-1.72 (m, 1H), 1.63-1.60 (m, 1H), 0.92-0.85 (m, 1H), 0.72 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.6, 195.0, 169.7, 151.7, 139.7, 138.1, 137.3, 136.9, 135.1, 133.6, 131.0, 128.8, 128.4, 128.3, 127.9, 127.1, 126.6, 126.4, 120.0, 117.0, 112.2, 73.5, 64.3, 60.4, 42.8, 42.4, 30.2, 25.5, 24.9, 13.4. HRMS (ESI) calcd for $C_{32}H_{30}NO_4$ $[M+H]^+$: 492.2169, found: 492.2170.



2o

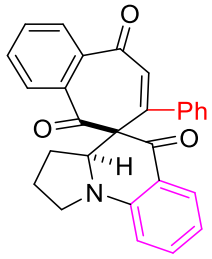
Methyl (1S*,3a'S*)-5',7-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2o**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (65.8 mg, 79%); dr = 7:1; m.p. 201-203 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96-7.88 (m, 1H), 7.38-7.32 (m, 1H), 7.28-7.22 (m, 3H), 7.20-7.13 (m, 2H), 6.69 (t, J = 7.8 Hz, 1H), 6.52 (d, *J* = 8.4 Hz, 1H), 3.77-3.71 (m, 1H), 3.45-3.37 (m, 1H), 3.32 (s, 3H), 3.29-3.22 (m, 1H), 3.07-2.99 (m, 1H), 2.70-2.65 (m, 1H), 2.63-2.57 (m, 1H), 2.49-2.42 (m, 1H), 2.21-1.88 (m, 5H), 1.70-1.60 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.6, 188.7, 170.5, 149.2, 140.6, 138.4, 137.2, 135.6, 129.1, 128.9, 127.8, 127.6, 119.0, 116.2, 112.9, 71.7, 63.1, 51.4, 46.5, 40.7, 27.7, 27.5, 25.4, 23.1. HRMS (ESI) calcd for $C_{26}H_{25}NNaO_4$ $[M+Na]^+$: 438.1676, found:

438.1676.



2p

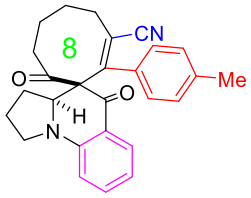
(1S*,3a'S*)-3-acetyl-2-(4-methoxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-5',7-dione (**2p**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1); yield: (67.7 mg, 79%); m.p. 155-157 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.9 Hz, 1H), 7.38-7.35 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 6.72-6.70 (m, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 3.78 (s, 3H), 3.76-3.75 (m, 1H), 3.43-3.39 (m, 1H), 3.28-3.25 (m, 1H), 3.04-2.99 (m, 1H), 2.58-2.53 (m, 2H), 2.29-2.25 (m, 1H), 2.12 (s, 2H), 2.06-1.95 (m, 2H), 1.82- 1.81 (m, 1H), 1.72 (s, 3H), 1.67-1.60 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 208.0, 207.8, 189.6, 159.4, 149.3, 146.0, 136.1, 135.6, 131.2, 129.7, 128.9, 119.2, 116.1, 113.6, 112.9, 71.1, 63.4, 55.1, 46.5, 40.8, 30.0, 27.4, 27.4, 25.6, 23.0. HRMS (ESI) calcd for $C_{27}H_{27}NNaO_4$ $[M+Na]^+$: 452.1832, found: 452.1832.



2q

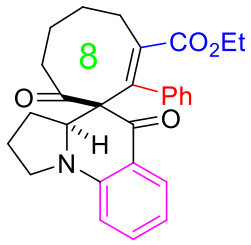
(3a'S*,6S*)-7-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[benzo[7]annulene-6,4'-pyrrolo[1,2-a]quinoline]-5,5',9-trione (**2q**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1); yield: (42.2 mg, 50%); m.p. 237-239 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09-8.08 (m, 1H), 7.51-7.44 (m, 2H), 7.36-7.32 (m, 5H), 7.26-7.22 (m, 2H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.76 (s, 1H), 6.58 (d, *J* = 8.5 Hz, 1H), 6.51-6.49 (m, 1H), 4.12-4.09 (m, 1H), 3.61-3.56 (m, 1H), 3.45-3.41 (m, 1H), 2.66-2.60 (m, 1H), 2.29-2.25 (m, 1H), 1.78-1.70 (m, 1H), 1.28-1.19 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 195.0, 188.4, 186.1, 148.1, 145.1, 139.8, 138.6, 136.7, 136.3, 132.6, 132.5, 131.4, 129.6, 128.7, 128.4, 128.3, 127.9, 127.7, 117.9, 115.6, 112.8, 69.0, 62.1, 46.8, 28.0, 23.4. HRMS (ESI) calcd for $C_{28}H_{22}NO_3$ $[M+H]^+$:

420.1594, found: 420.1595.



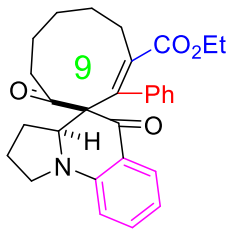
2r

(1S*,3a'S*)-5',8-dioxo-2-(p-tolyl)-1',2',3',3a'-tetrahydro-5'H-spiro[cyclooctane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carbonitrile (**2r**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (65.6 mg, 80%); dr = 5:1; m.p. 213-215 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.37-7.10 (m, 4H), 6.90-6.76 (m, 2H), 6.56 (d, *J* = 8.1 Hz, 1H), 3.73-2.98 (m, 4H), 2.34 (s, 3H), 2.57-2.27 (m, 3H), 2.01-1.68 (m, 8H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 208.5, 187.9, 151.3, 149.4, 138.7, 135.5, 134.6, 129.1, 129.0, 127.7, 121.5, 119.4, 116.9, 113.2, 71.8, 63.9, 46.7, 42.4, 30.4, 28.2, 27.7, 24.4, 23.0, 21.2. HRMS (ESI) calcd for $C_{27}H_{26}N_2NaO_2$ $[M+Na]^+$: 433.1886, found: 433.1887.



2s

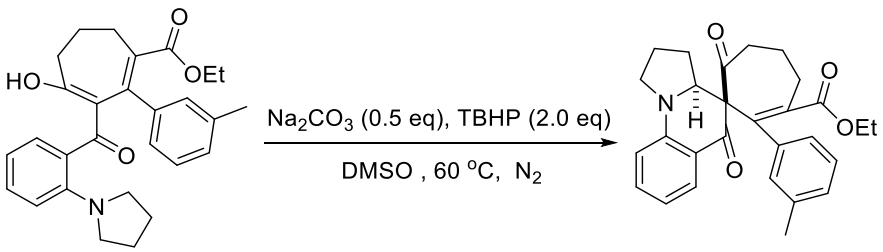
Ethyl (1S*,3a'S*)-5',8-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cyclooctane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2s**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (67.2 mg, 76%); dr = 4:1; m.p. 236-238 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.40-7.12 (m, 5H), 7.00 (s, 1H), 6.76 (s, 1H), 6.55 (s, 1H), 3.87-3.71 (m, 2H), 3.63 (m, 1H), 3.45 (s, 1H), 3.24-2.98 (m, 2H), 2.50-1.76(m, 11H), 0.75 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 211.0, 189.5, 170.4, 149.6, 138.6, 135.0, 129.9, 129.0, 127.5, 119.7, 117.0, 113.0, 71.0, 64.1, 60.3, 46.8, 42.4, 29.3, 28.6, 27.7, 24.7, 23.1, 13.4. HRMS (ESI) calcd for $C_{28}H_{30}NO_4$ $[M+H]^+$: 444.2169, found: 444.2176.



2t

Ethyl (1S*,3a'S*)-5',9-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cyclononane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate (**2t**). Yellow soild, obtained in 10 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: (61.5 mg, 67%); dr = 3:1; m.p. 230-232 °C. Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 (d, *J* = 7.7 Hz, 1H), 7.43-7.16 (m, 5H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.82-6.80 (m 1H), 6.57 (d, *J* = 8.2 Hz, 1H), 3.90-3.76 (m, 2H), 3.62-3.60 (m, 1H), 3.46-3.42 (m, 1H), 3.04-3.01 (m, 2H), 2.52-2.27 (m, 3H), 2.10-1.96 (m, 2H), 1.84-1.76 (m, 4H), 1.67-1.61 (m, 2H), 1.52-1.41 (m, 2H), 0.81 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 211.6, 189.94, 169.2, 149.6, 142.4, 138.2, 134.7, 130.9, 129.2, 128.9, 127.4, 127.3, 121.2, 117.4, 113.1, 71.8, 64.9, 60.3, 47.0, 45.7, 29.4, 28.1, 27.9, 26.7, 25.0, 23.1, 13.6. HRMS (ESI) calcd for $C_{29}H_{31}NNaO_4$ $[M+Na]^+$: 480.2145, found: 480.2145.

4. 1mmol-scale Reaction of 2c

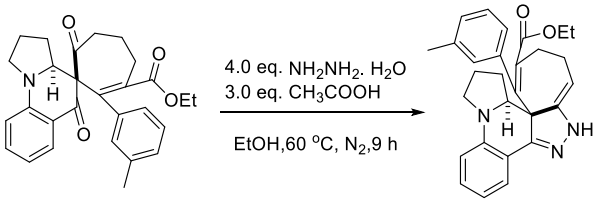


1c **2c**, 61%, dr = 6:1

In a schlenk tube, ethyl 4-hydroxy-2-phenyl-3-(2-(pyrrolidin-1-yl)benzoyl)cyclohepta-1,3-diene-1-carboxylate **1c** (1.0 mmol, 445.2 mg, 1.0 equiv), DMSO (10.0 mL), Na_2CO_3 (0.5 mmol, 53.0 mg, 0.5 equiv) and TBHP (2.0 mmol, 192 μL, 2.0 equiv) were stirred at 60 °C under N_2 for 16 h. Then, the reaction mixture was then quenched with aqueous NH_4Cl (20 mL), and the water layers were extracted with ethyl acetate (30 mL × 3). The combined organic layers were washed with brine, dried over anhydrous

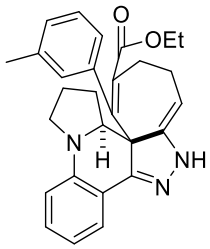
Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded **2c** (yellow solid, 270.2 mg, 61%, dr = 6:1).

5. Synthetic transformation of 2.



2c **3a**, 63%

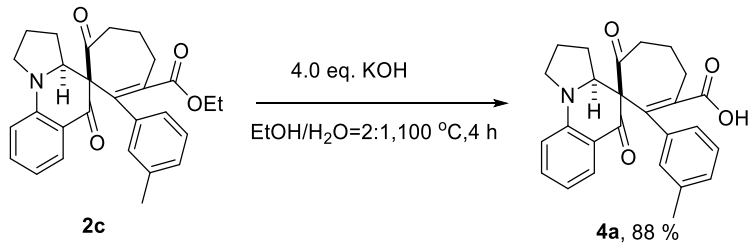
In a 10 mL dry high-pressure sealed reaction tube, **2c** (0.1 mmol, 44.3 mg), 50% $NH_2NH_2.H_2O$ (0.4 mmol, 39 μL, 4.0 equiv), AcOH (0.3 mmol, 17 μL, 3.0 equiv) were stirred at 60 °C under N_2 for 9 h. After the reaction was completed as monitored by thin-layer chromatography, the reaction mixture was then quenched by saturated sodium bicarbonate, and the water layers were extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded desired compound **3a** as a white oil. (27.5 mg, 63%).



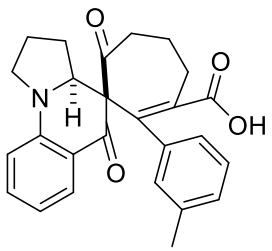
3a, 76 %

Ethyl (11as*,11bS*)-11-(m-tolyl)-8,9,11b,12,13,14-hexahydro-6H-cyclohepta[4,5]pyrazolo[4,3-c]pyrrolo[1,2-a]quinoline-10-carboxylate **(3a).** White oil, purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1); yield: 63%, 27.5 mg. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.09-6.93 (m, 5H), 6.66-6.55 (m, 2H), 6.31-6.29 (m, 1H), 5.19-5.08 (m, 1H), 4.10-4.00 (m, 2H), 3.59-3.50 (m, 1H), 3.45-3.35 (m, 1H), 2.94-2.84 (m, 1H), 2.80-2.71 (m, 2H), 2.69-2.59 (m, 2H), 2.49-2.39 (m, 1H), 2.29-2.15 (m, 6H), 1.00-0.93 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$)

δ 171.3, 154.2, 141.6, 141.6, 139.7, 137.3, 135.8, 131.6, 129.6, 128.9, 128.5, 127.8, 126.6, 126.1, 118.2, 115.3, 115.1, 112.8, 72.6, 60.5, 46.1, 32.5, 30.04, 30.02, 24.1, 21.3, 21.2, 13.7. HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{29}N_3O_2Na$ 462.2152, found 462.2150.

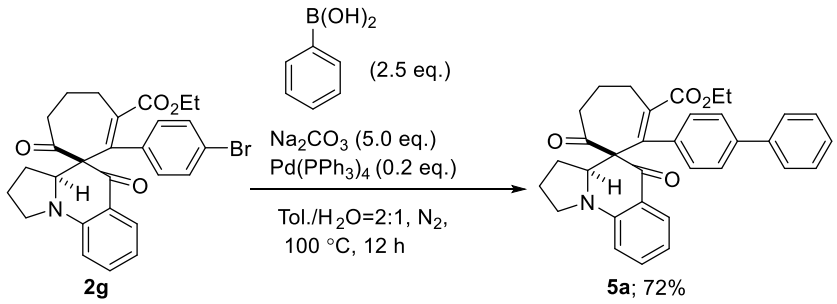


In a 10 mL dry high-pressure sealed reaction tube, **2a** (0.1 mmol, 44.3 mg) and KOH (22.4 mg, 0.4 mmol) were dissolved in EtOH/H_2O (1.0 mL:0.5 mL), and heated to reflux for 4 h. Then, the solvent was removed under reduced pressure, the resultant residue was dissolved in H_2O, acidified to pH = 1 with 2M HCl, and filtered to afford **4a** as a yellow solid (36.7 mg, 88%).

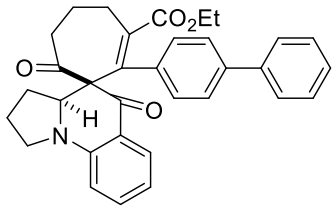


4a

(1S*,3a'S*)-5',7-dioxo-2-(m-tolyl)-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylic acid **(4a).** Yellow solid, yield: 88%, 36.7 mg, m.p. 134-136 °C. ^{1}H NMR (500 MHz, d^6-DMSO) δ 7.63 (d, *J* = 7.5 Hz, 1H), 7.37-7.28 (m, 1H), 7.18-7.10 (m, 1H), 7.03-6.93 (m, 3H), 6.67-6.52 (m, 2H), 4.92-4.77 (m, 1H), 3.19-3.11 (m, 2H), 2.25 (s, 3H), 2.13-1.86 (m, 7H), 1.82-1.72 (m, 1H), 1.57-1.38 (m, 2H). ^{13}C NMR (150 MHz, d^6-DMSO) 193.2, 175.5, 173.5, 149.2, 144.6, 139.5, 136.8, 135.3, 131.6, 129.8, 127.7, 127.5, 127.4, 126.4, 118.3, 115.5, 113.1, 60.2, 57.2, 46.4, 40.0, 34.1, 30.7, 24.1, 22.2, 21.3. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{26}NO_4$ 416.1856, found 416.1850.



In a schlenk tube, **2g** (0.1 mmol, 50.7 mg), benzoboric acid (0.25 mmol, 30.5 mg), $Pd(PPh_3)_4$ (0.02 mmol, 23.1 mg), Na_2CO_3 (0.5 mmol, 3.0 equiv, 53.0 mg) and Toluene/H_2O (1.0 mL:0.5 mL) were added under N_2 and stirred at 100 ℃ in an oil bath for 12 h. After the completion of the reaction monitored by TLC, the reaction mixture was quenched with aqueous sat. NH_4Cl solution (2 mL). Then the filtrate was extracted with ethyl acetate (3 mL × 3). The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. Purification by column chromatography with petroleum ether/ethyl acetate = 6:1 as the eluent to afford **5a** (Yellow oil, 36.3 mg, 72%).

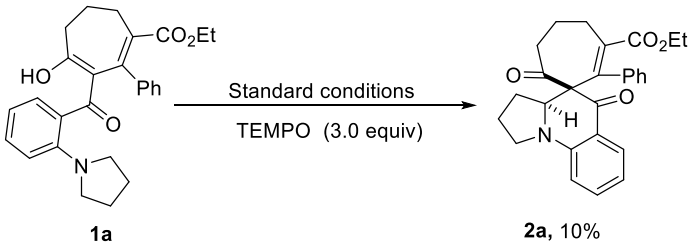


5a

***Ethyl (1S*,3a'S*)-2-([1,1'-biphenyl]-4-yl)-5',7-dioxo-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate* (5a).** Yellow oil, yield: 72%, 36.3 mg. ^1H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.45-7.39 (m, 2H), 7.38-7.30 (m, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.69 (t, *J* = 7.5 Hz, 1H), 6.53 (d, *J* = 8.5 Hz, 1H), 3.89-3.75 (m, 3H), 3.46-3.37 (m, 1H), 3.31-3.23 (m, 1H), 3.09-2.97 (m, 1H), 2.73-2.58 (m, 2H), 2.53-2.42 (m, 1H), 2.22-2.07 (m, 3H), 2.05-1.94 (m, 2H), 1.73-1.63 (m, 1H), 0.77 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.6, 188.8, 170.3, 149.2, 140.4, 140.3, 139.8, 137.6, 137.6, 135.6, 129.6, 129.1, 128.8, 127.4, 126.9, 126.3, 118.9, 116.2, 112.9, 71.8,

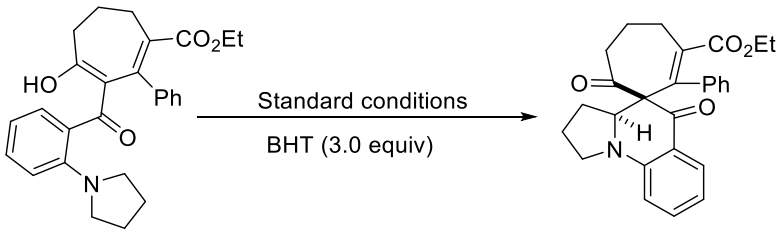
63.1, 60.5, 46.5, 40.6, 27.7, 27.6, 25.4, 23.1, 13.4. HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{33}H_{31}NNaO_4$ 528.2145, found 528.2157.

6. Radical inhibition experiment



1a **2a**, 10%

In a 25 mL dry high-pressure sealed reaction tube, **1a** (0.2 mmol, 86.3 mg), DMSO (2.0 mL), Na_2CO_3 (0.1 mmol, 10.6 mg, 0.5 equiv), TEMPO (0.6 mmol, 93.8 mg, 3.0 equiv) and TBHP (0.4 mmol, 38 μL, 2.0 equiv) were stirred at 60 °C under N_2 for 6 h. Then, the reaction mixture was then quenched with aqueous NH_4Cl (10 mL), and the water layers were extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded **2a** (yellow solid, 8.6 mg, 10%).



1a **2a**, 8%

In a 25 mL dry high-pressure sealed reaction tube, **1a** (0.2 mmol, 86.3 mg), DMSO (2.0 mL), Na_2CO_3 (0.1 mmol, 10.6 mg, 0.5 equiv), BHT (0.6 mmol, 132.2 mg, 3.0 equiv) and TBHP (0.4 mmol, 38 μL, 2.0 equiv) were stirred at 60 °C under N_2 for 6 h. Then, the reaction mixture was then quenched with aqueous NH_4Cl (10 mL), and the water layers were extracted with ethyl acetate (10 mL × 3). The combined organic layers were

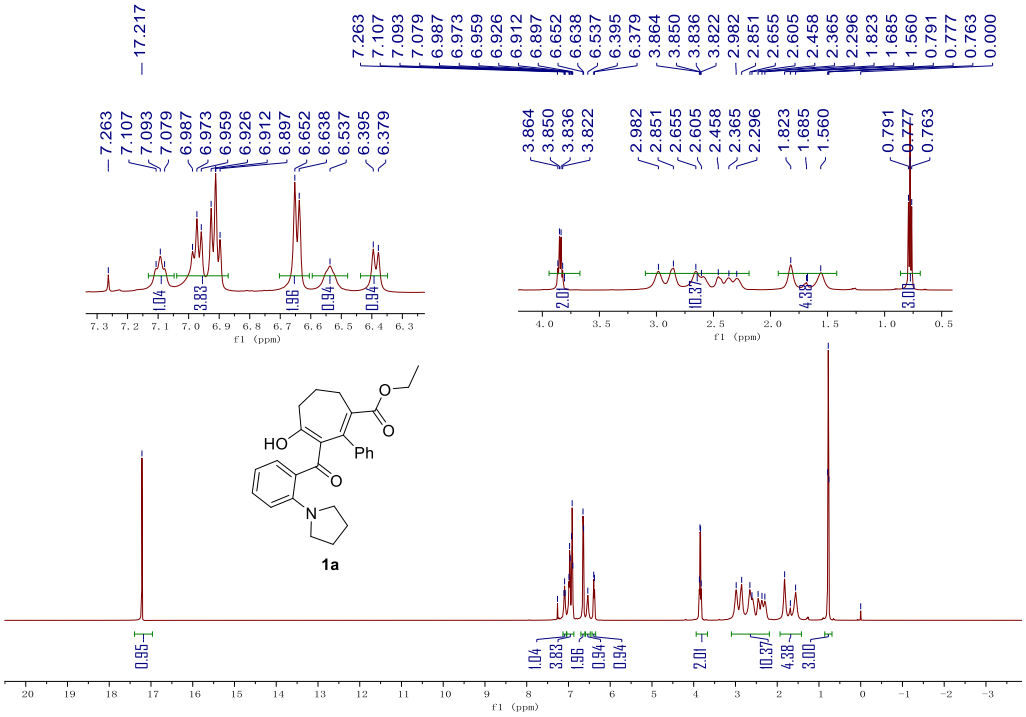
washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded **2a** (yellow solid, 6.9 mg, 8%).

7. References

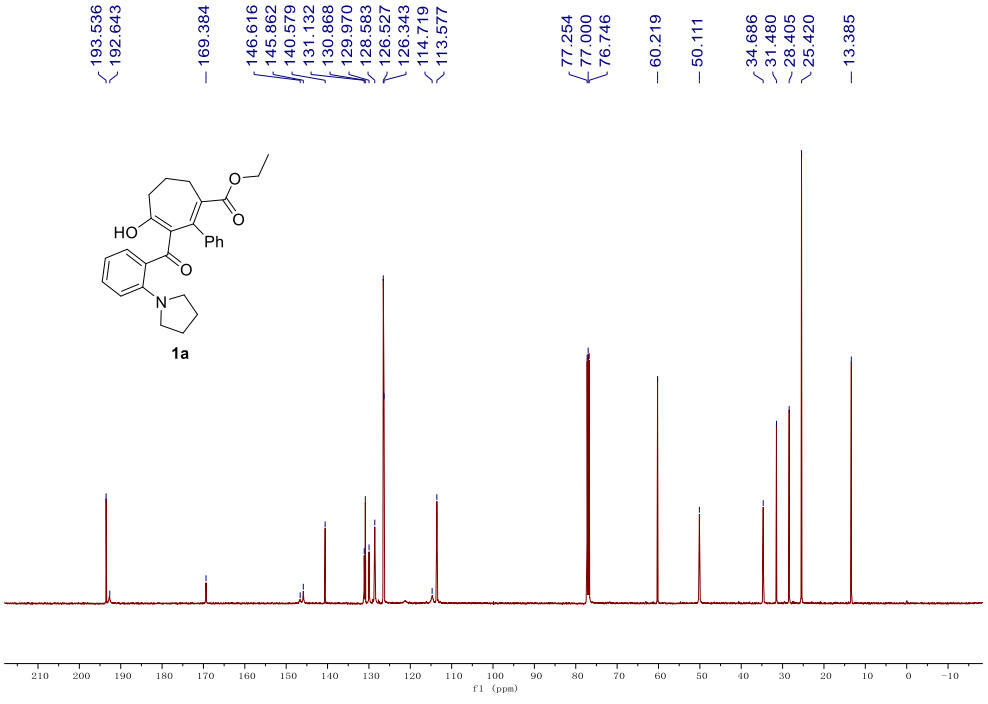
(1) (a) Zhou, Y.; Tao, X.; Yao, Q.; Zhao, Y.; Li, Y. *Chem. Eur. J,* **2016,** *22*, 17936. (b) Wang, M.; Kong, L.; Wang, Y.; Song, B.; Sun, Y.; Tang, R.; Li, Y. *Org. Lett*, **2018**, *20*, 6130. (c) He, P.; Wang, Z.; Kang, Q.; Fei, N.; Wang, C.; Li, Y., Synthesis of oxindole fused 1,3-oxazepanes via hydride transfer initiated ring expansion of pyrrolidine. *Organic Chemistry Frontiers* **2024**, 11, 3173-3178.

8. Copies of spectra of products

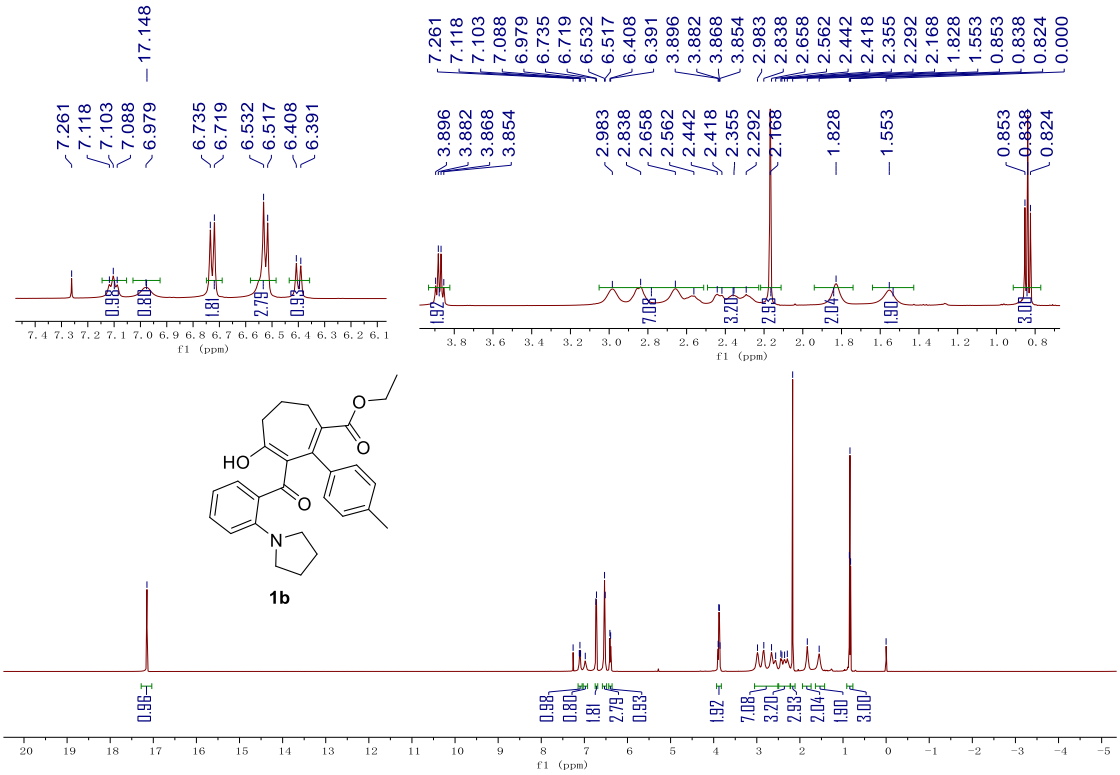
^{1}H NMR (500 MHz, $CDCl_3$)



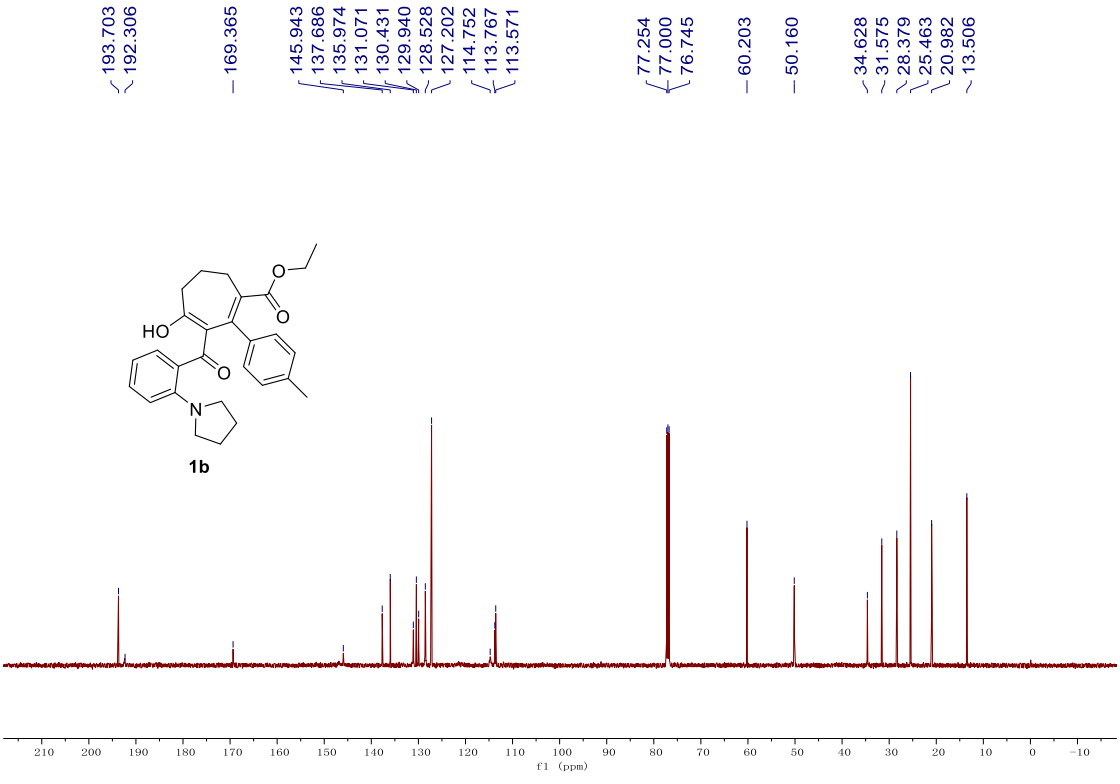
^{13}C NMR (125 MHz, $CDCl_3$)



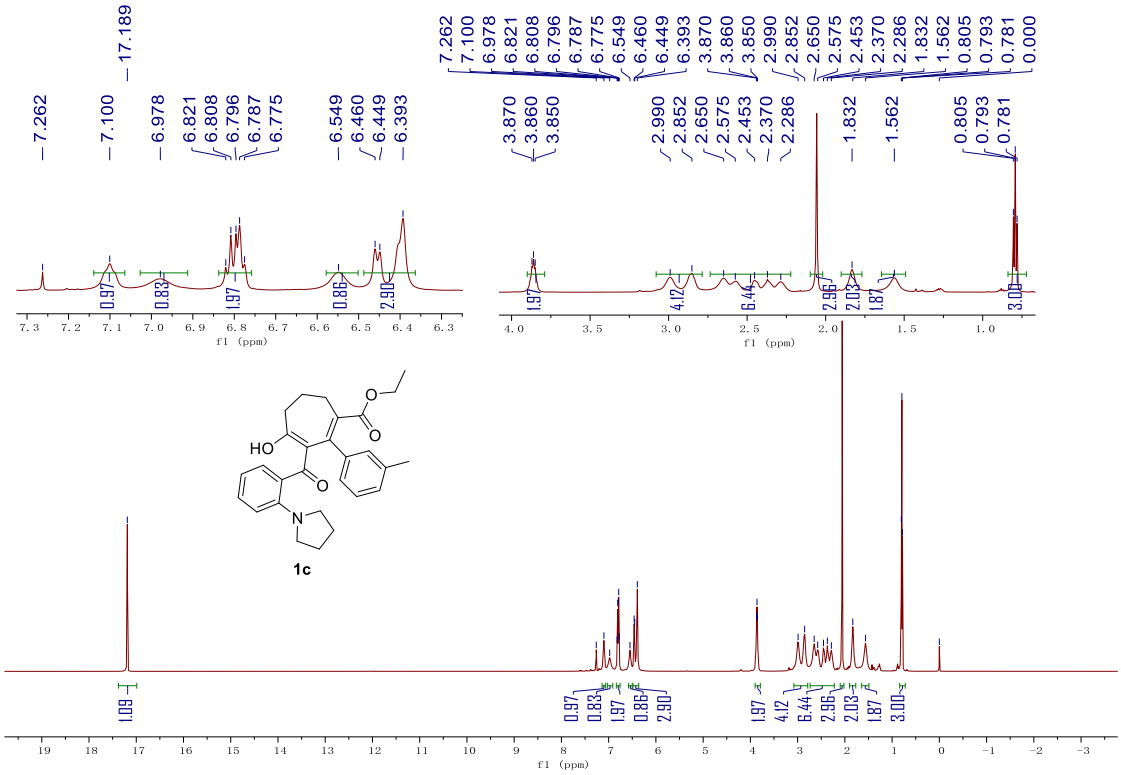
^{1}H NMR (500 MHz, $CDCl_3$)



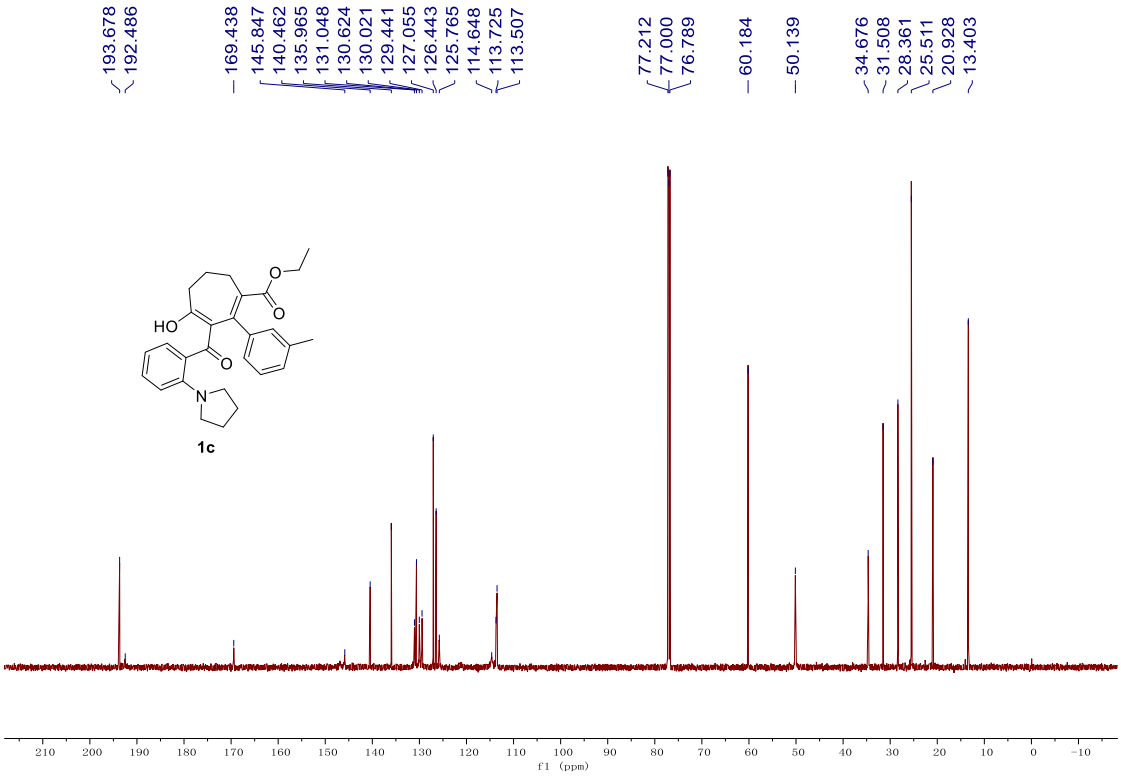
^{13}C NMR (125 MHz, $CDCl_3$)



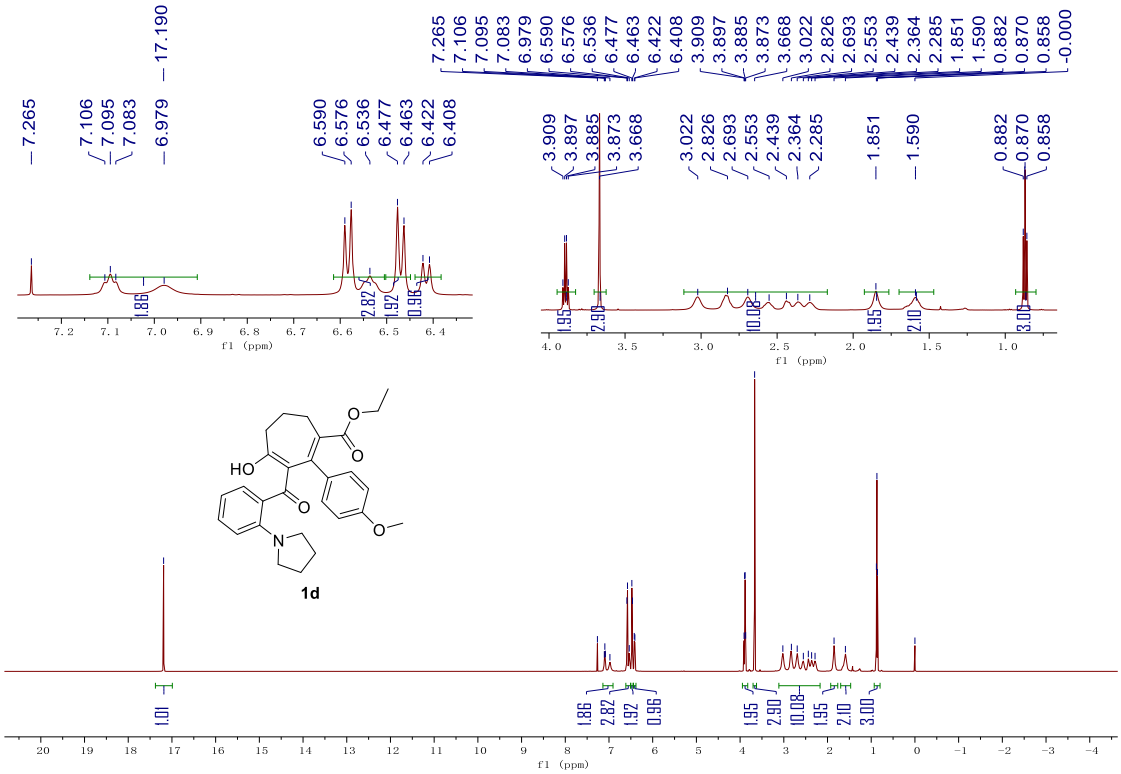
^{1}H NMR (600 MHz, $CDCl_3$)



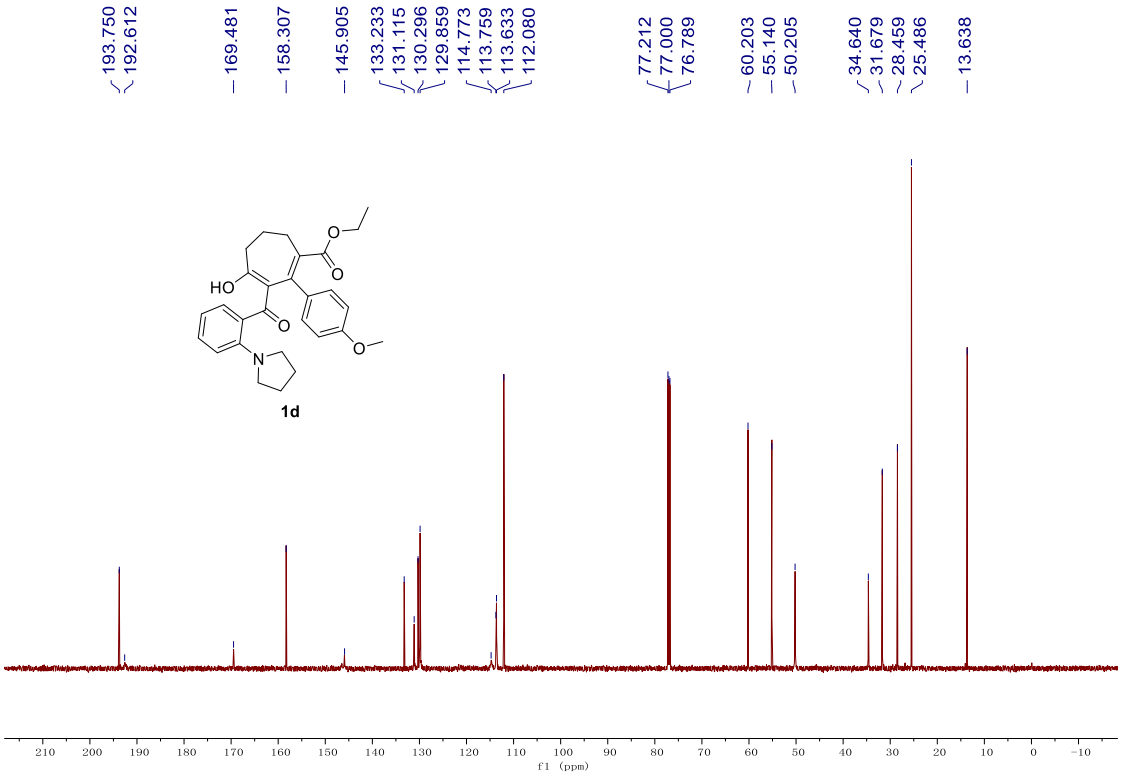
^{13}C NMR (150 MHz, $CDCl_3$)



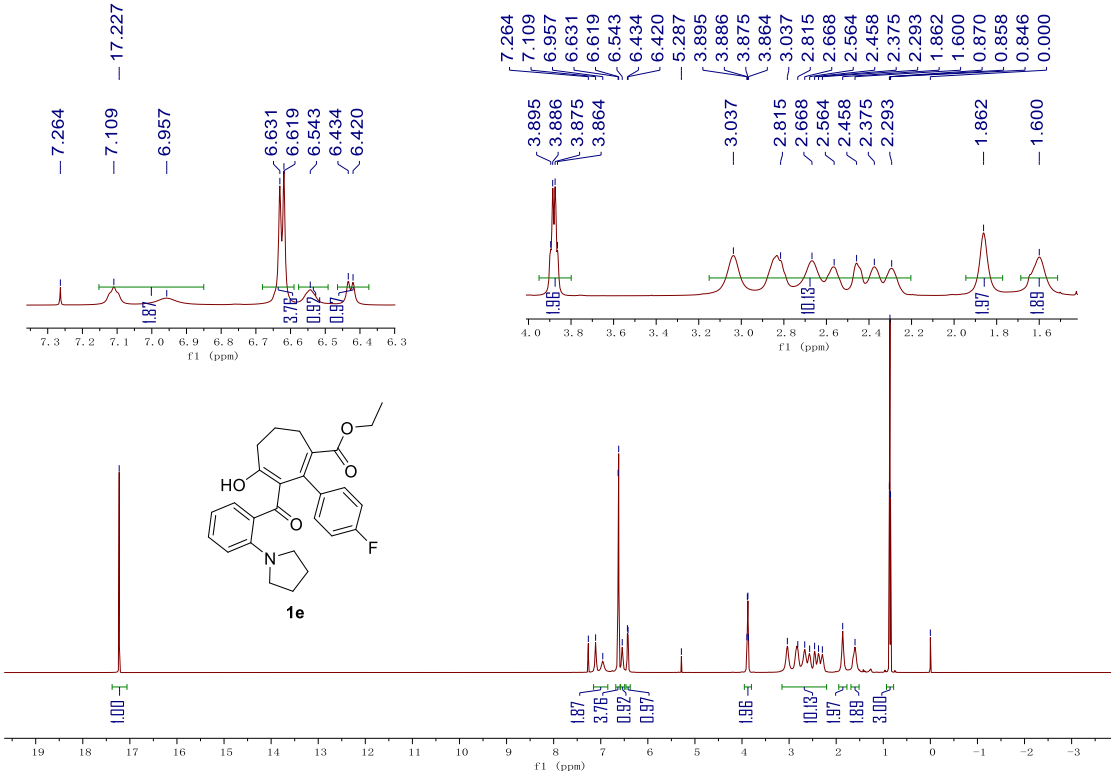
^{1}H NMR (600 MHz, $CDCl_3$)



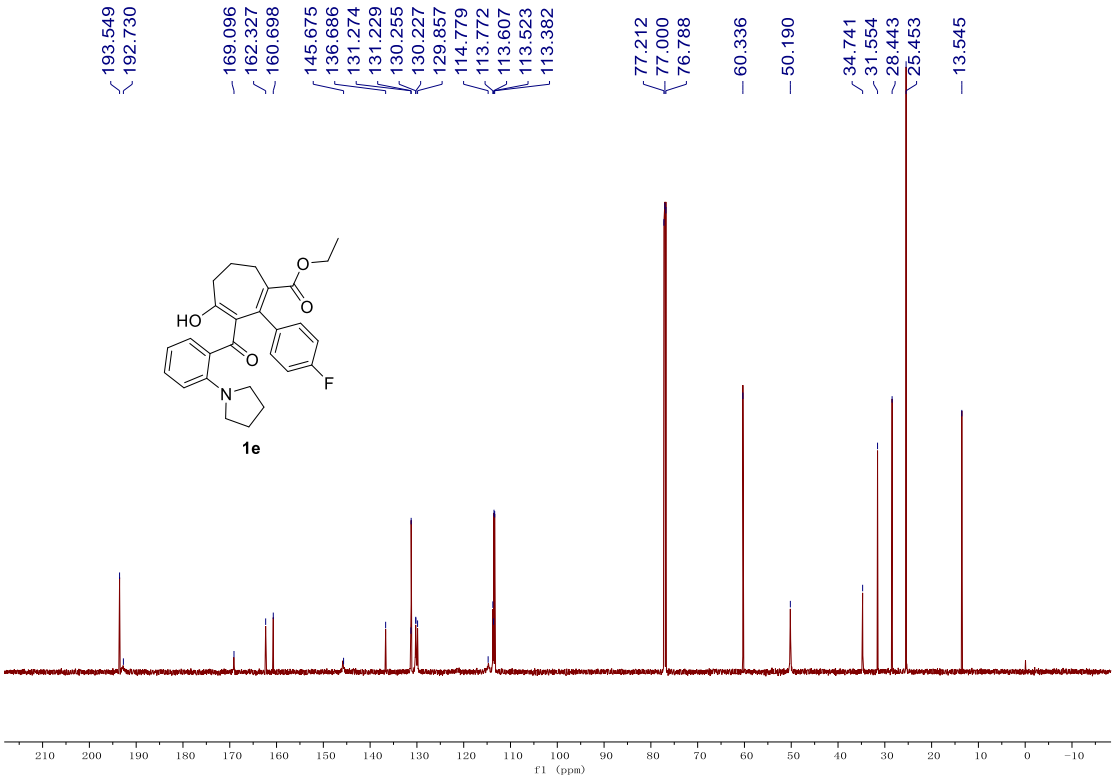
^{13}C NMR (150 MHz, $CDCl_3$)



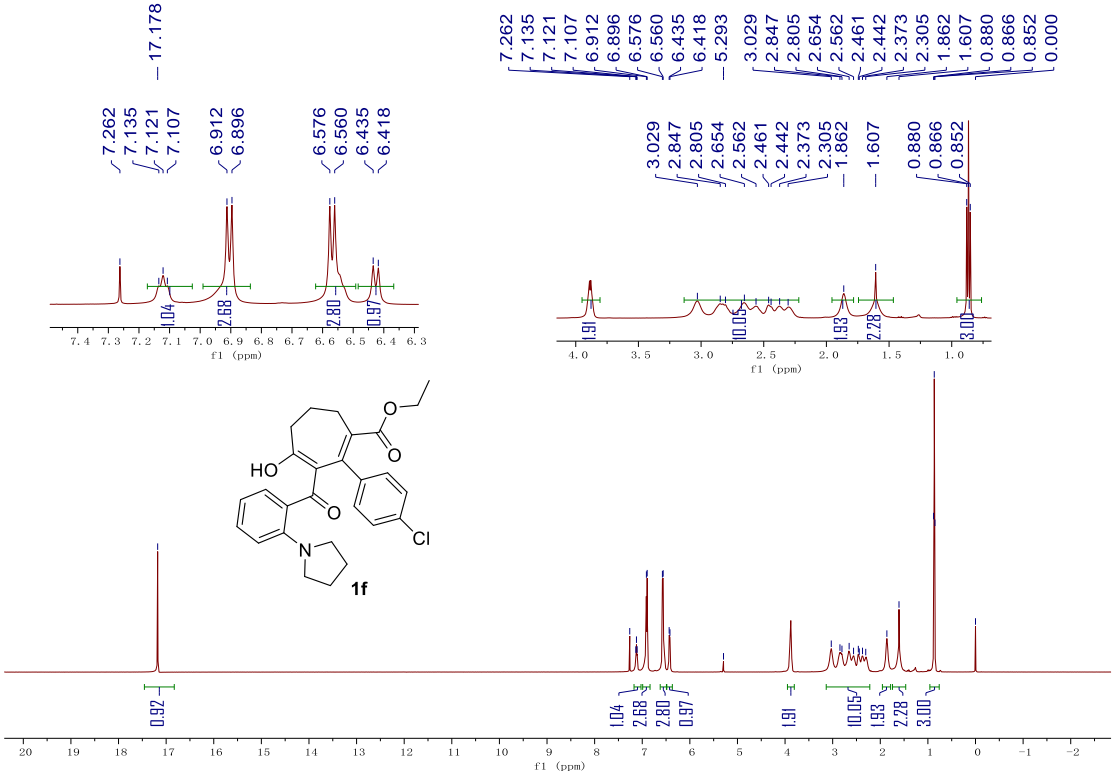
^{1}H NMR (600 MHz, $CDCl_3$)



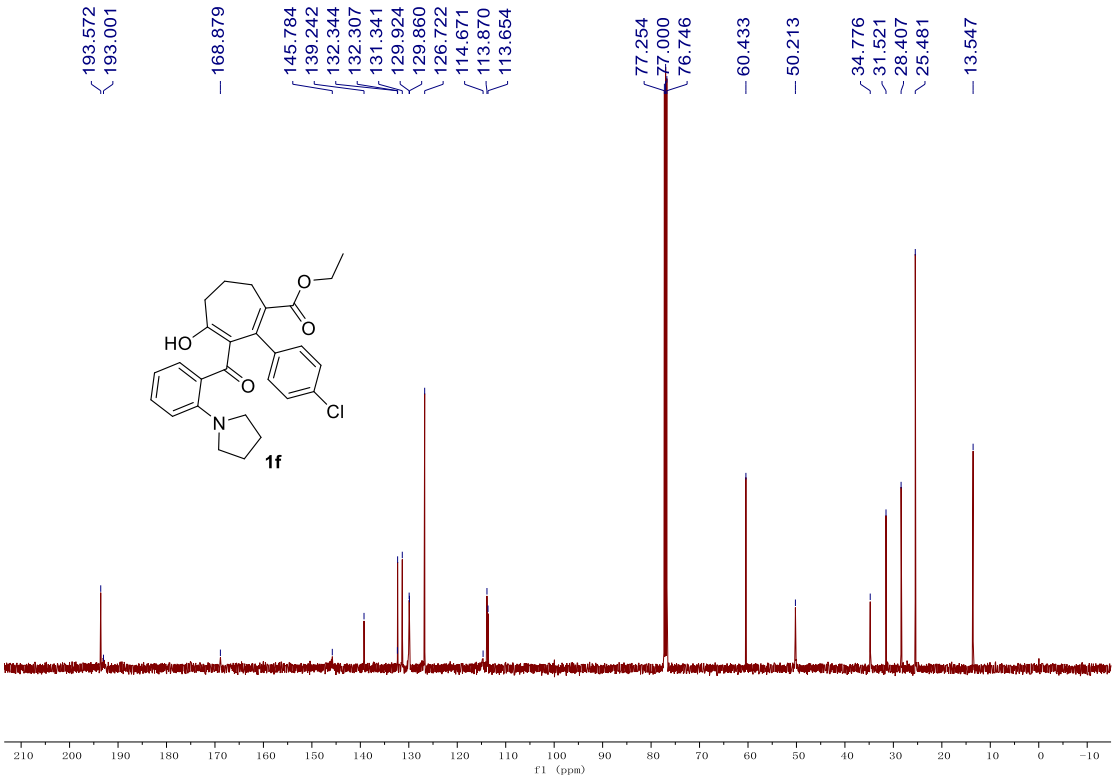
^{13}C NMR (150 MHz, $CDCl_3$)



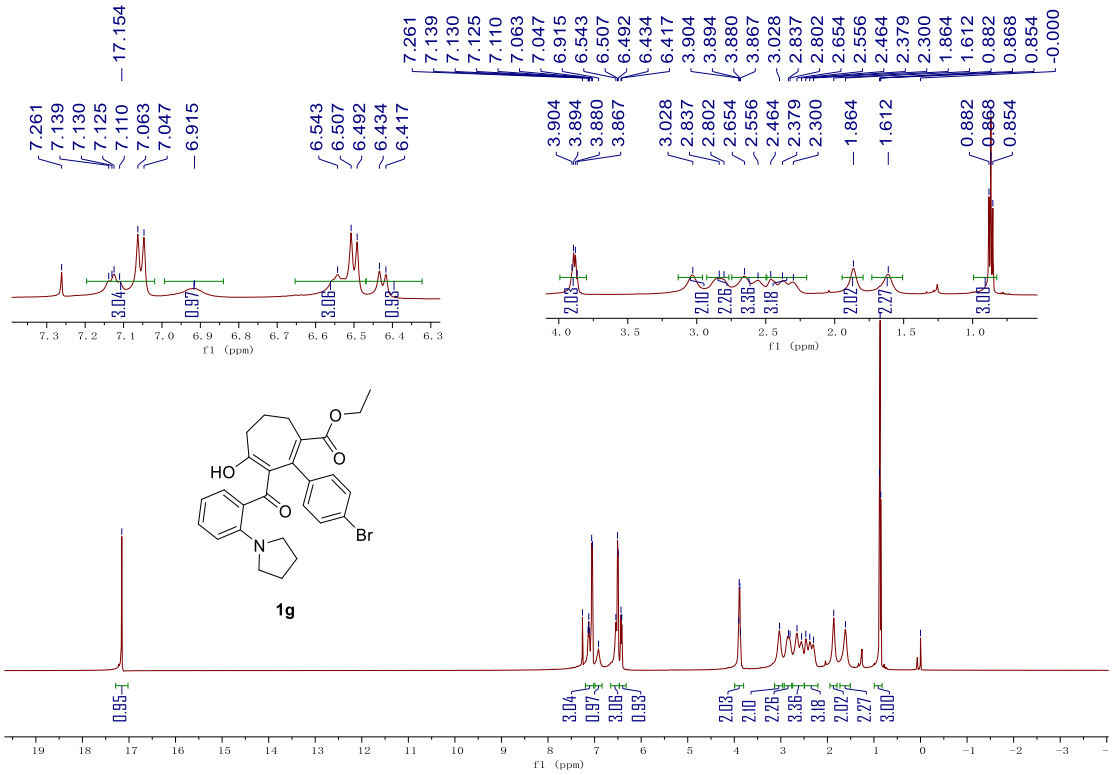
^{1}H NMR (500 MHz, $CDCl_3$)



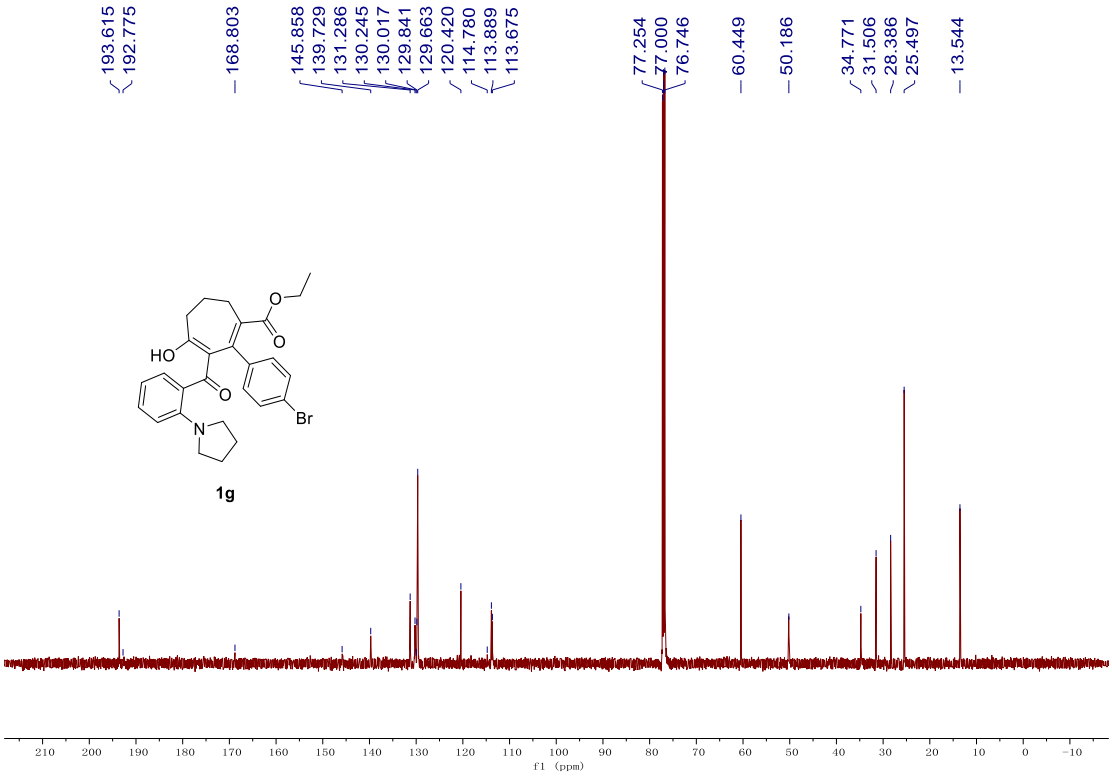
^{13}C NMR (125 MHz, $CDCl_3$)



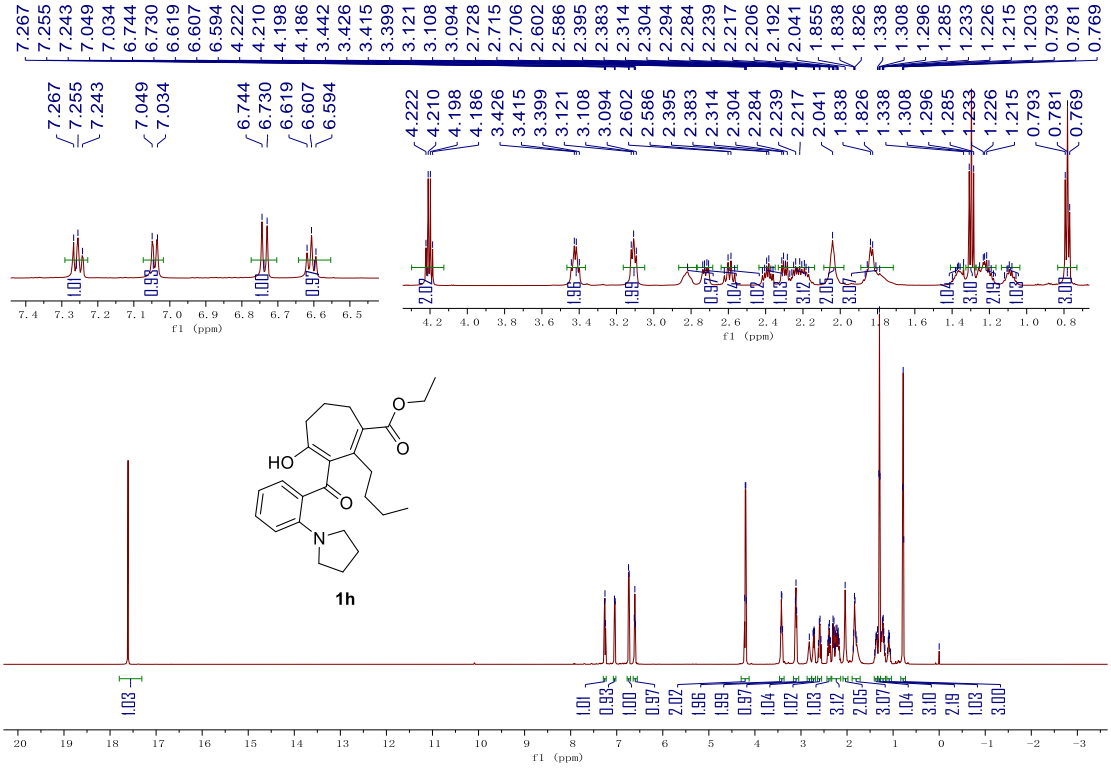
^{1}H NMR (500 MHz, $CDCl_3$)



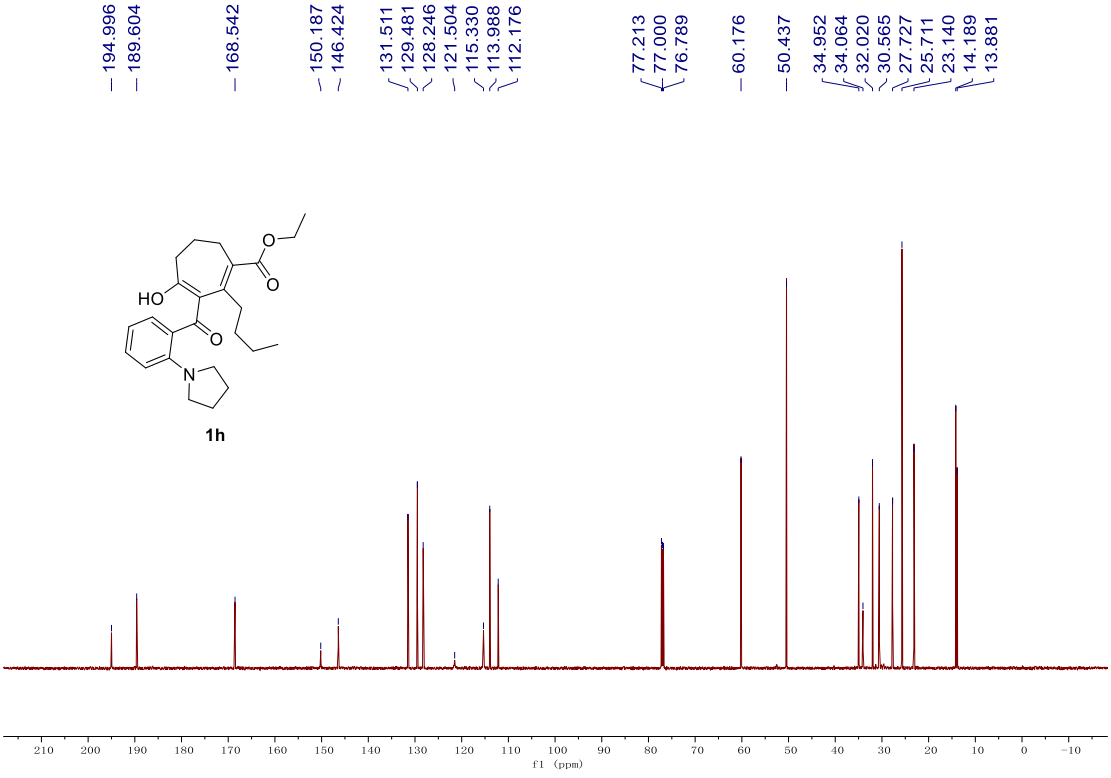
^{13}C NMR (125 MHz, $CDCl_3$)



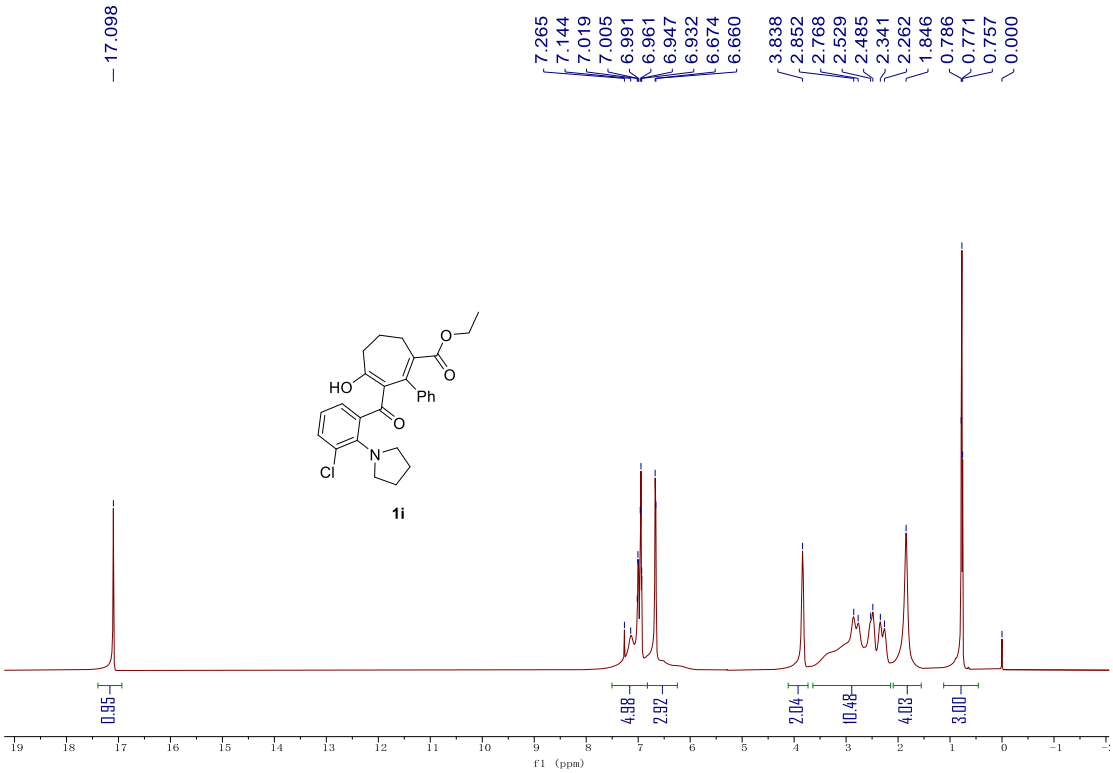
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



^{1}H NMR (500 MHz, $CDCl_3$)



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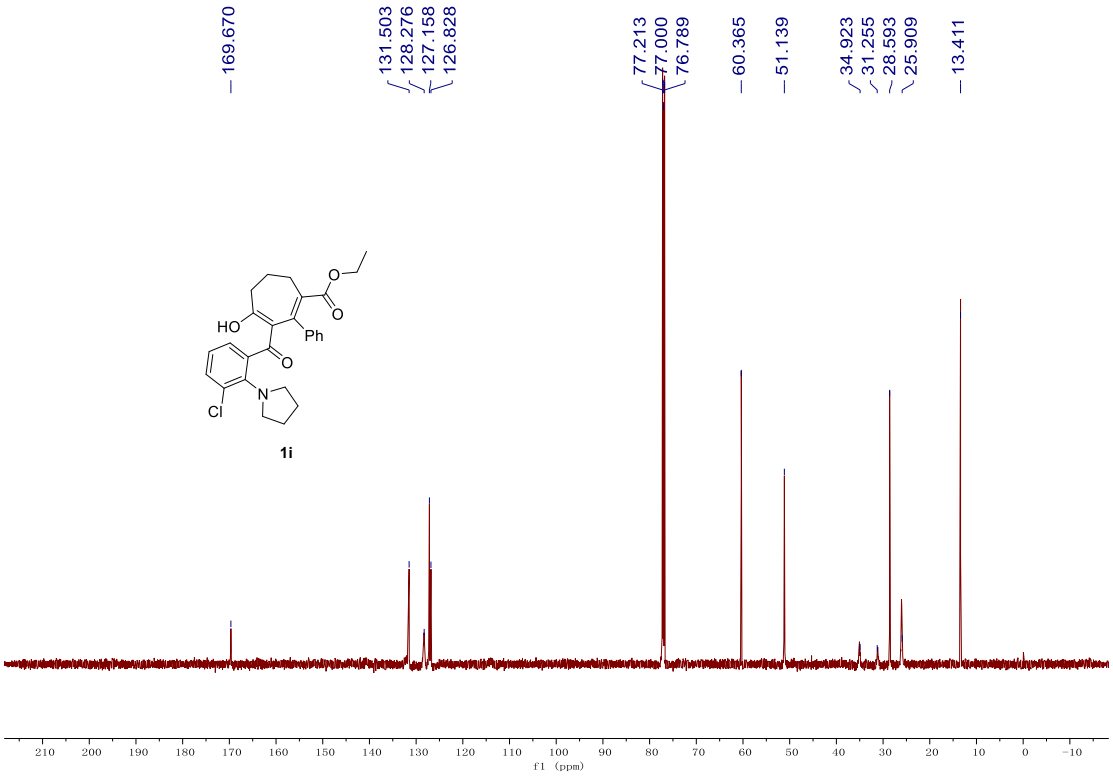

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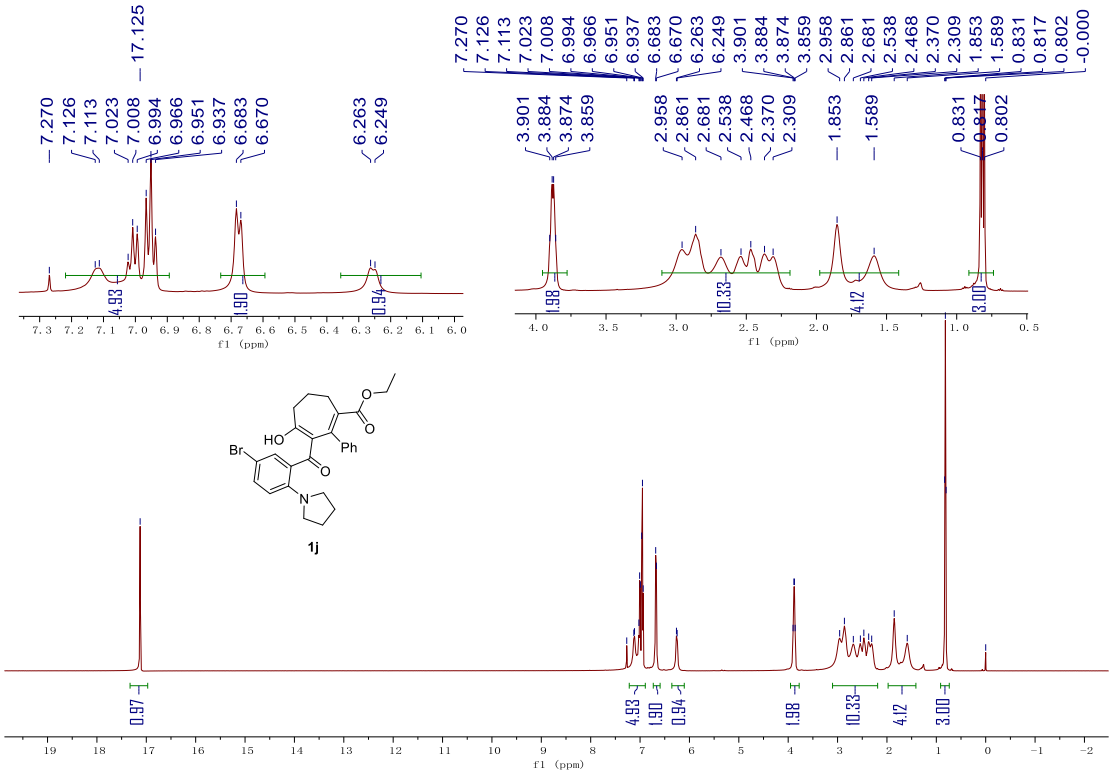
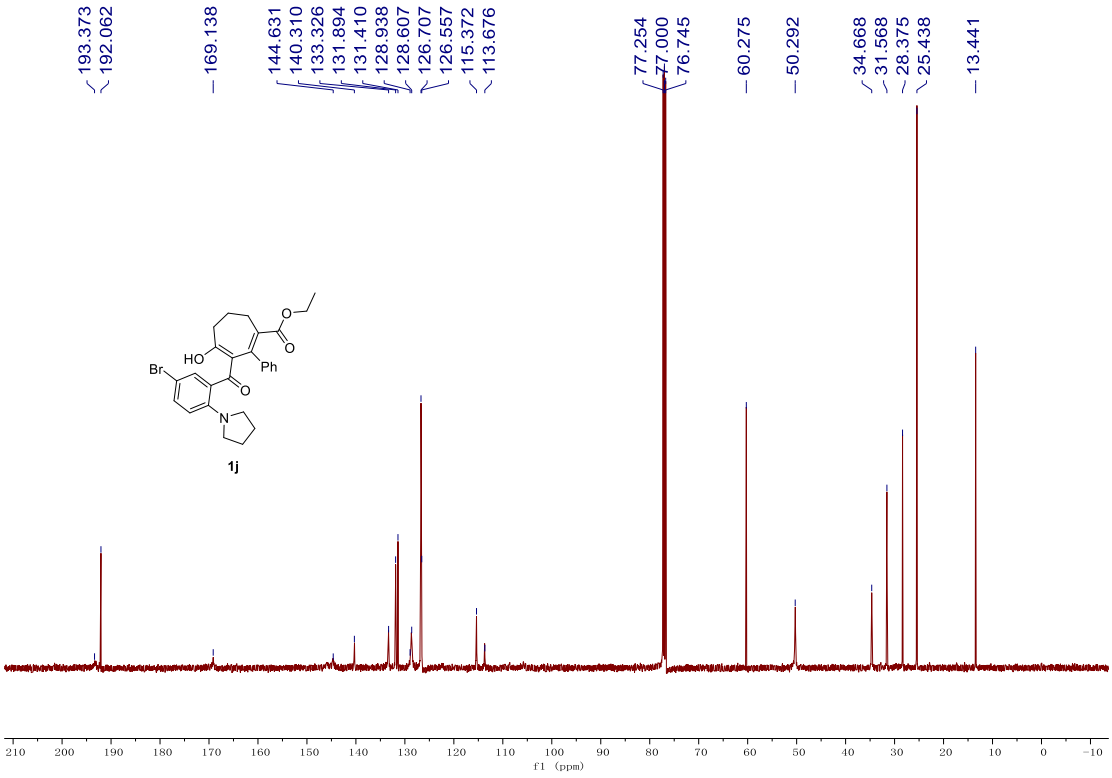
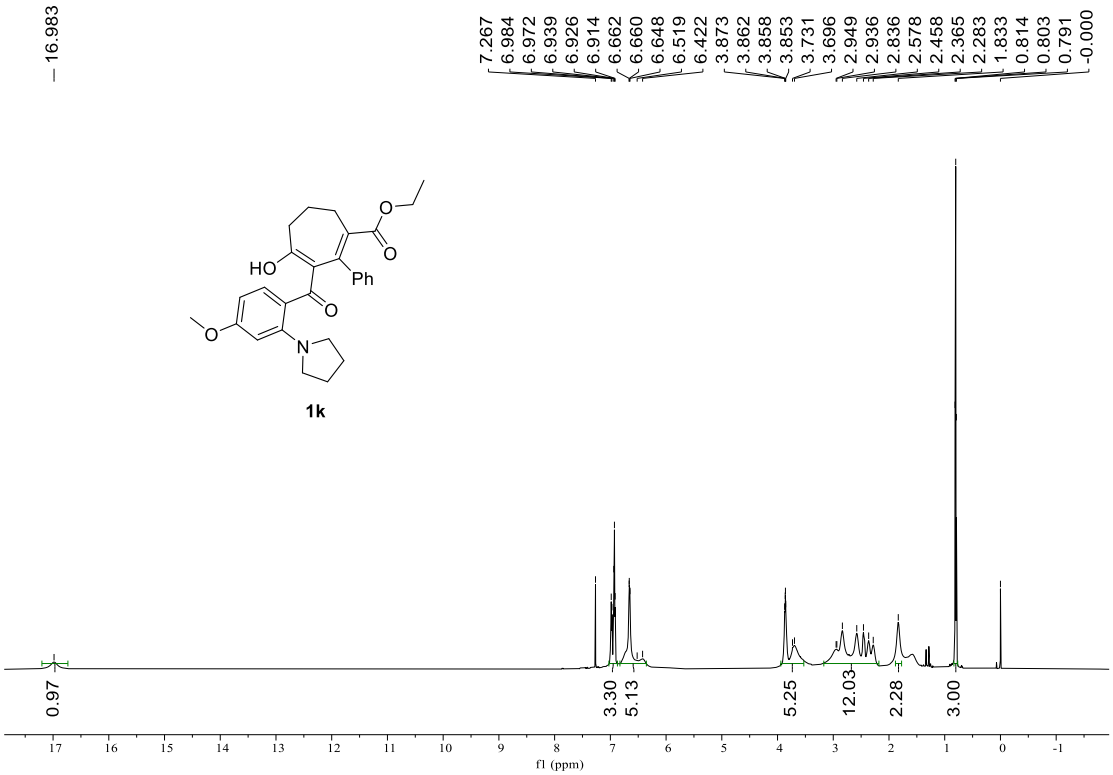


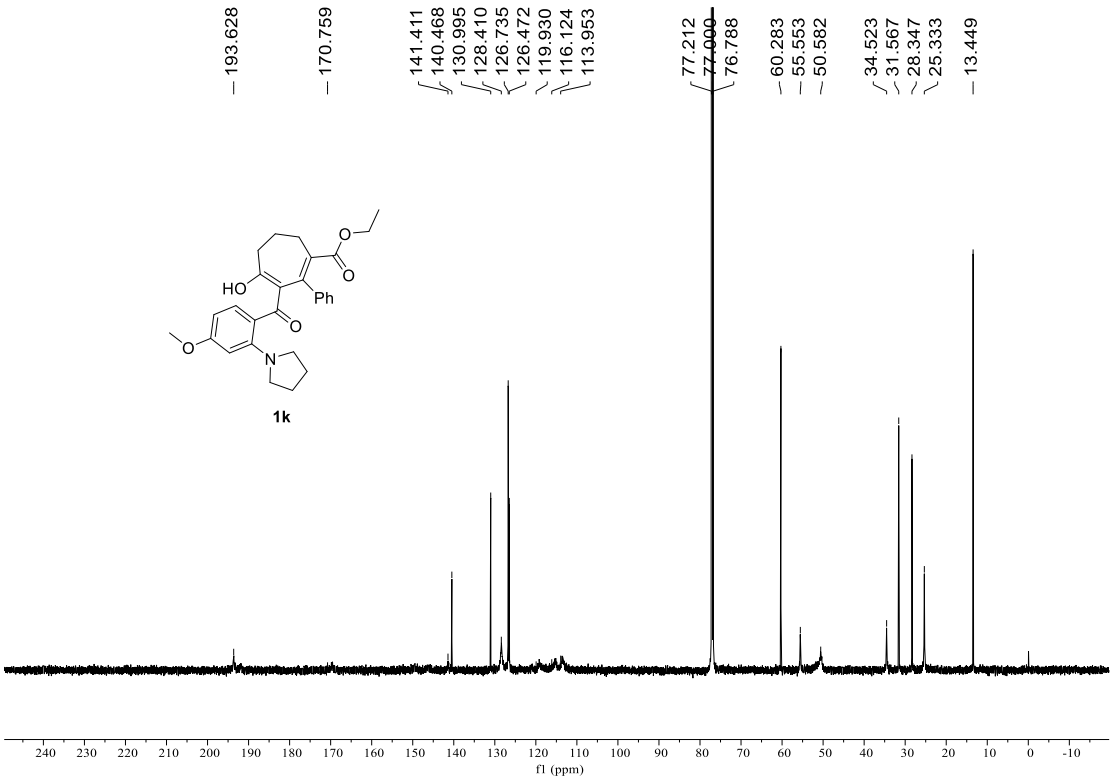
^{13}C NMR (125 MHz, $CDCl_3$)



^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



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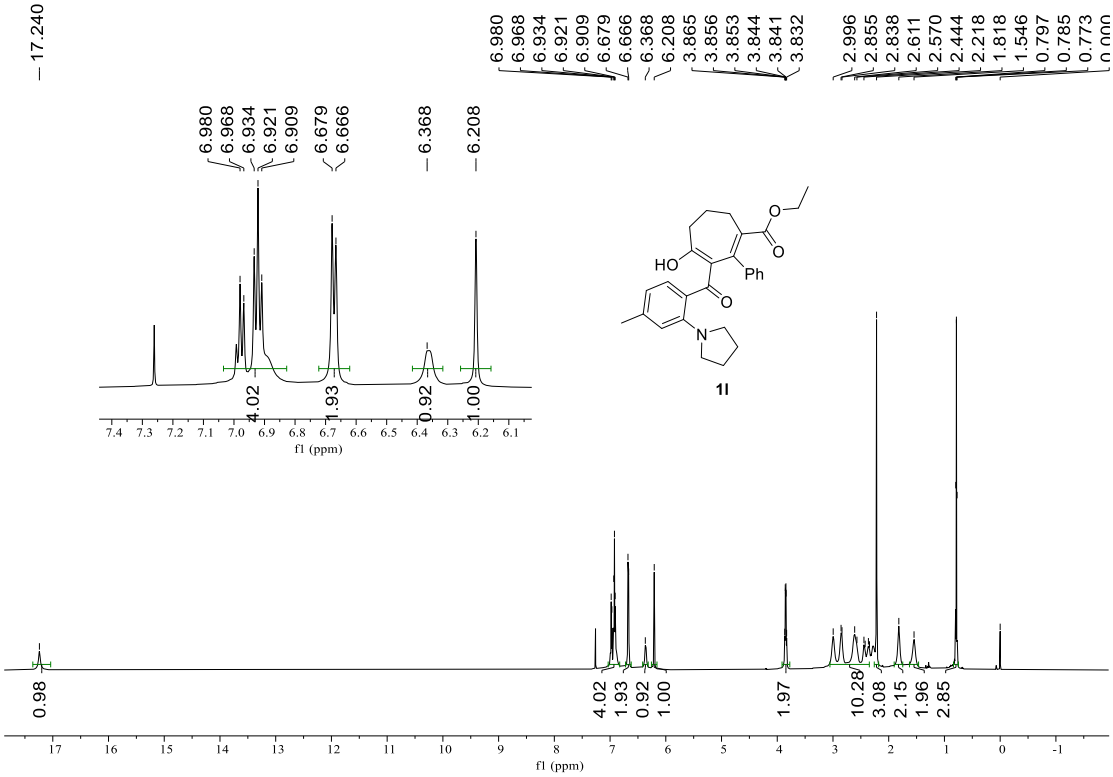
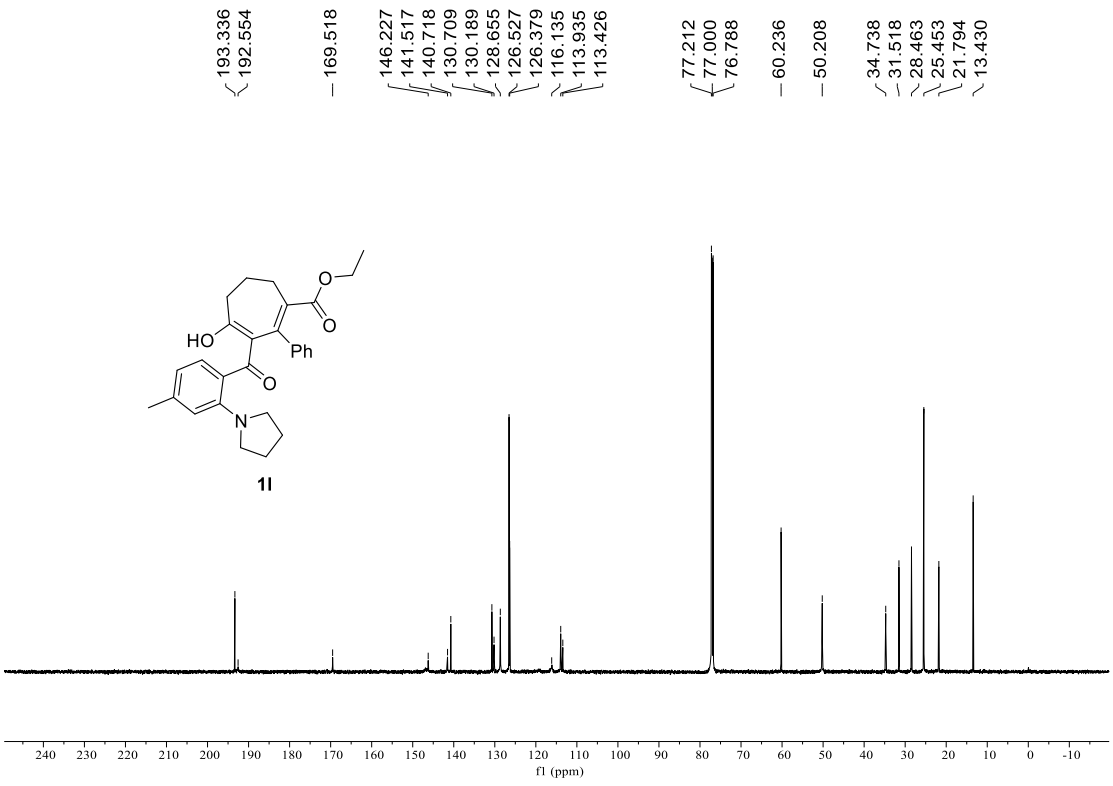


^{13}C NMR (150 MHz, $CDCl_3$)



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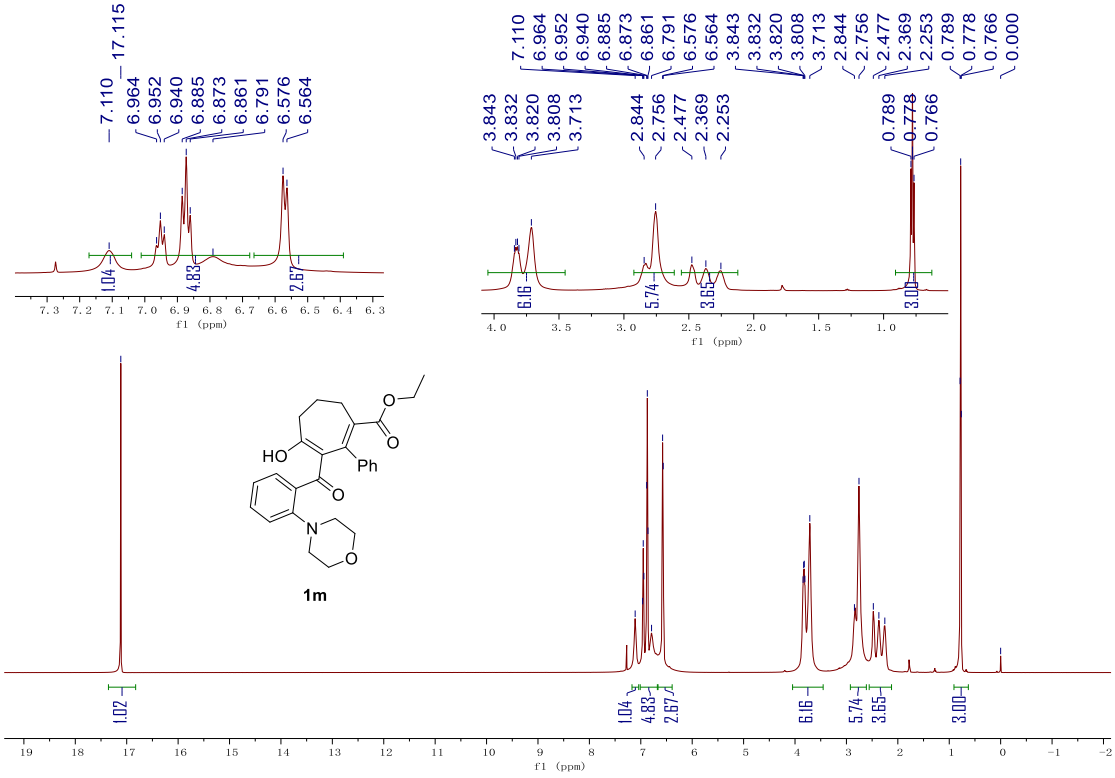

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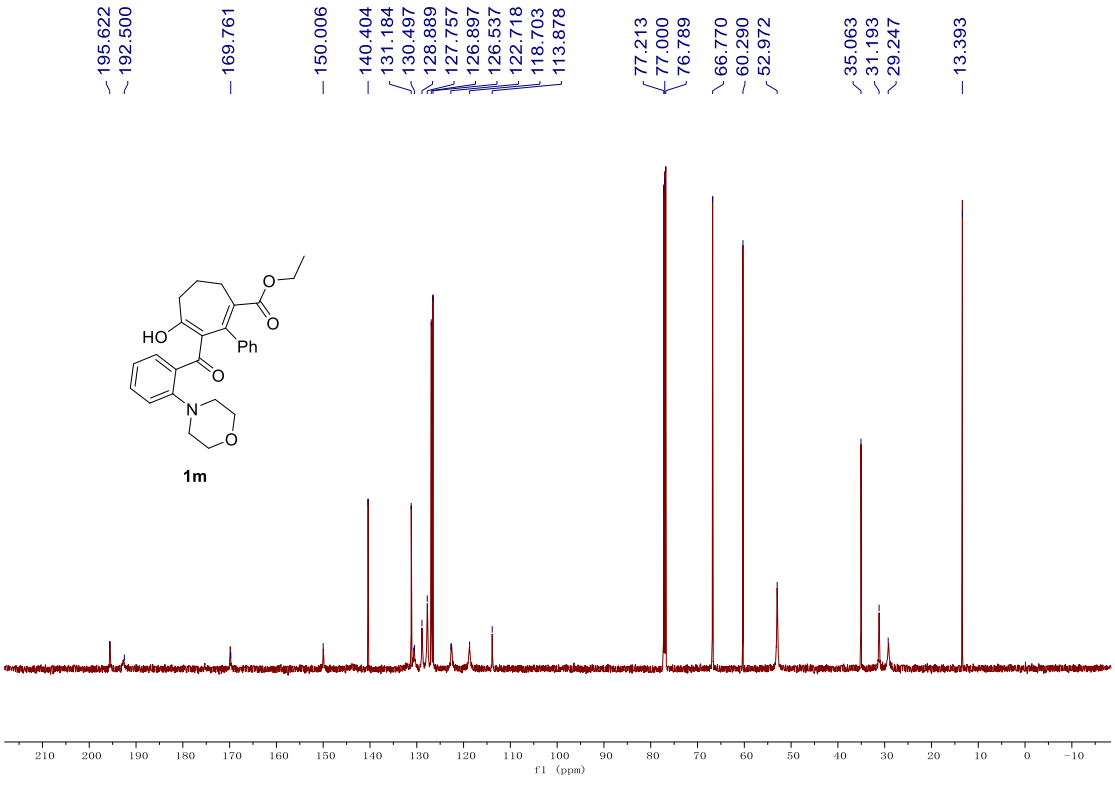

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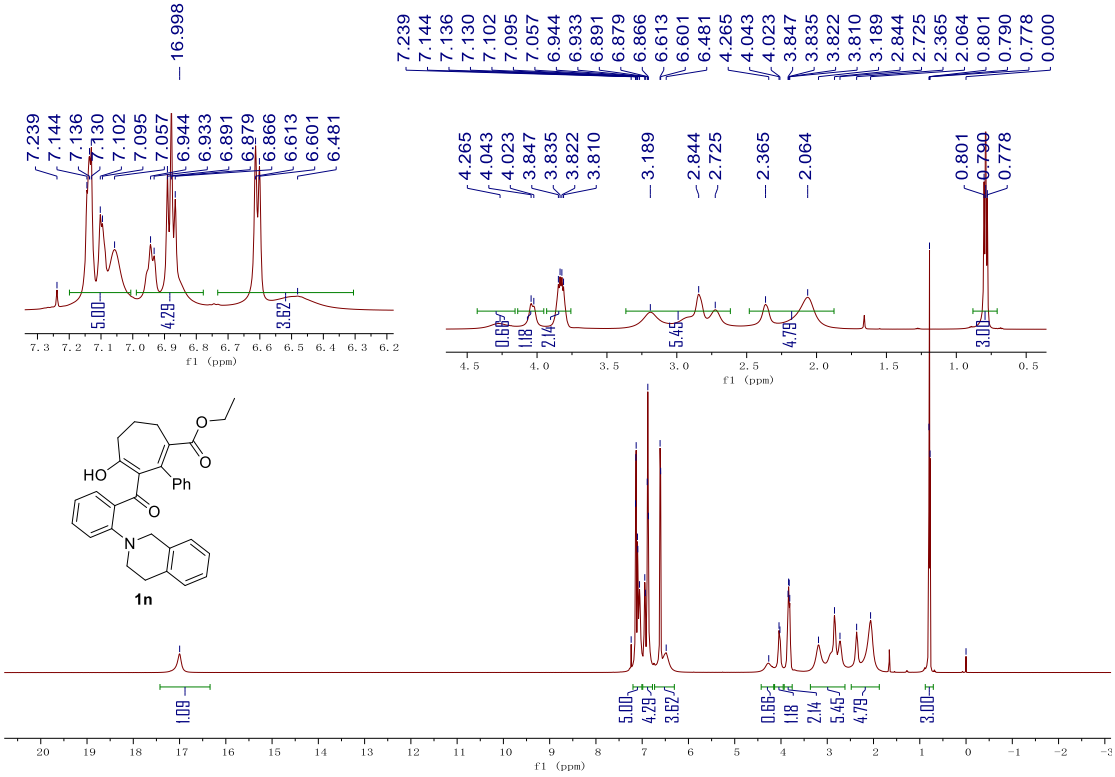

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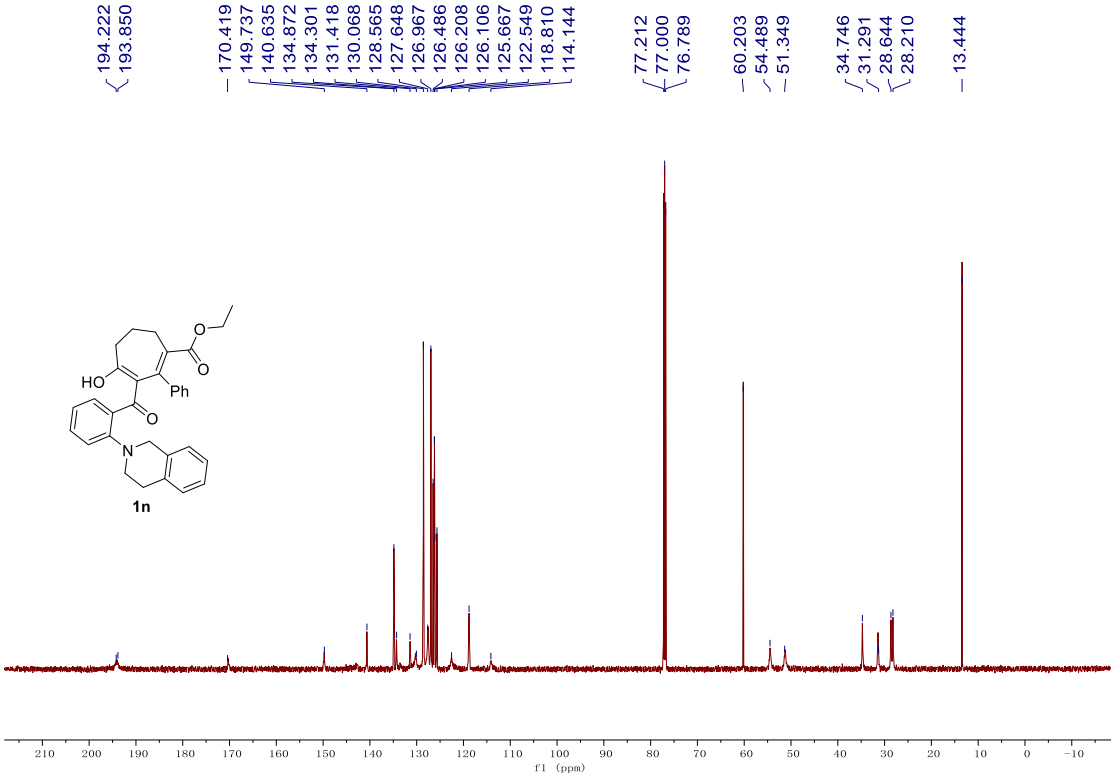

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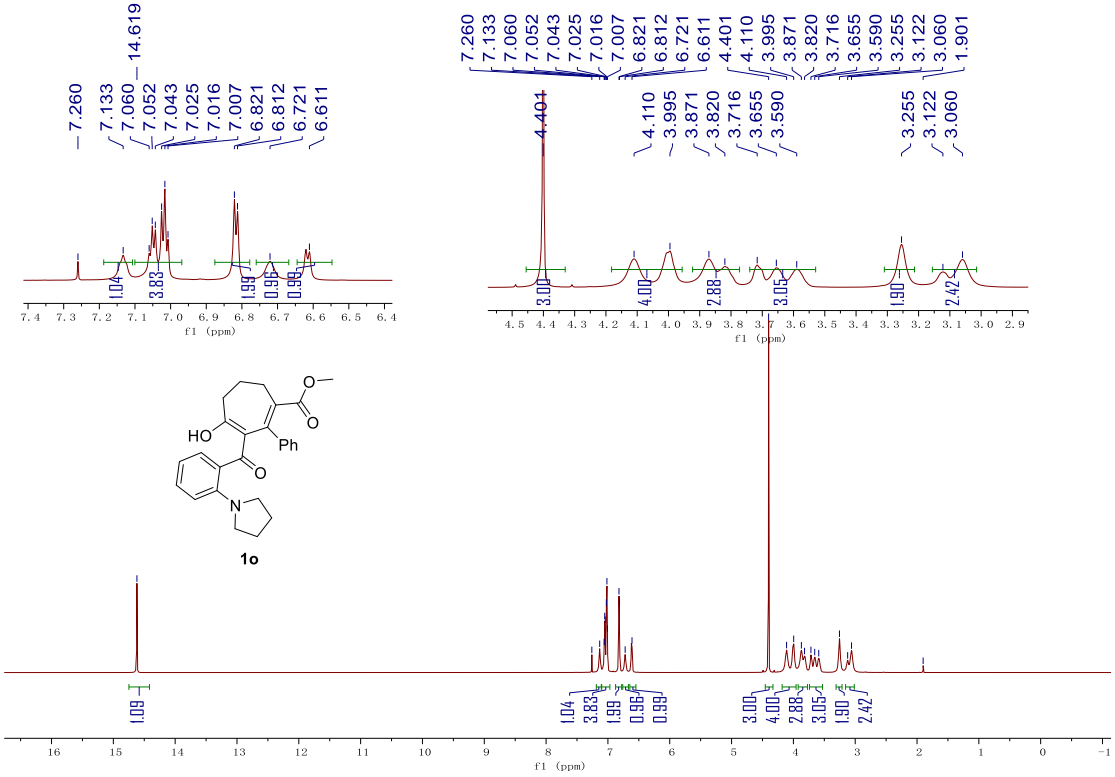

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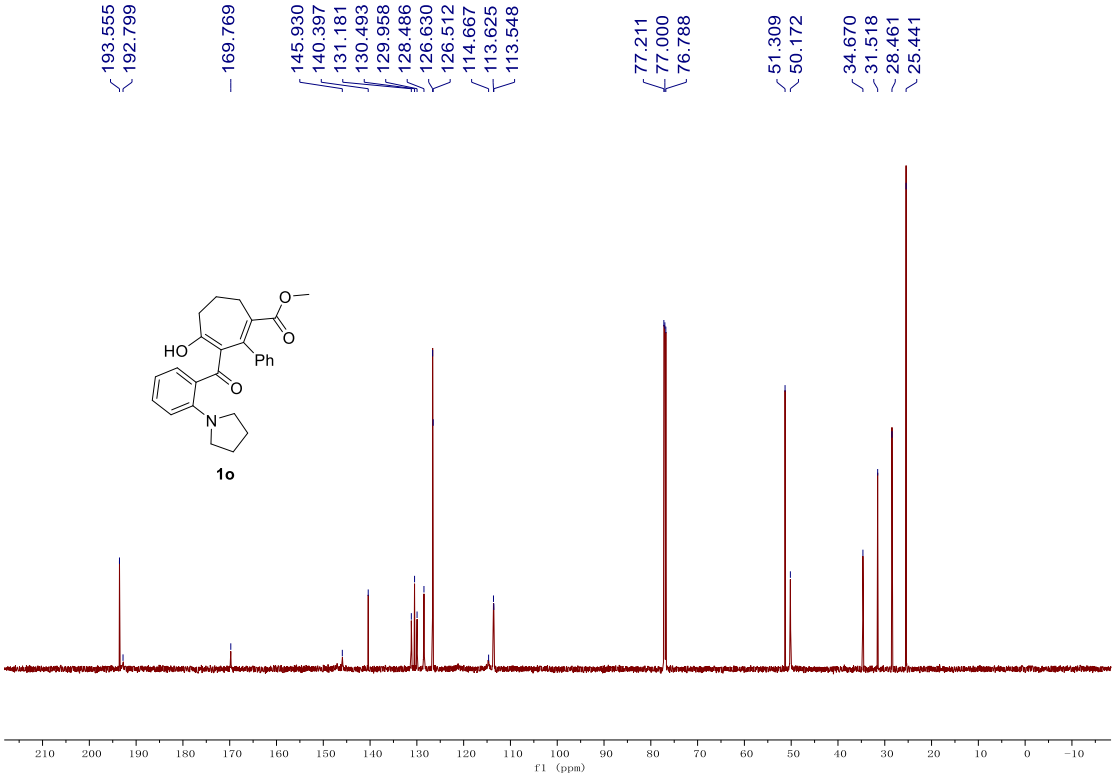

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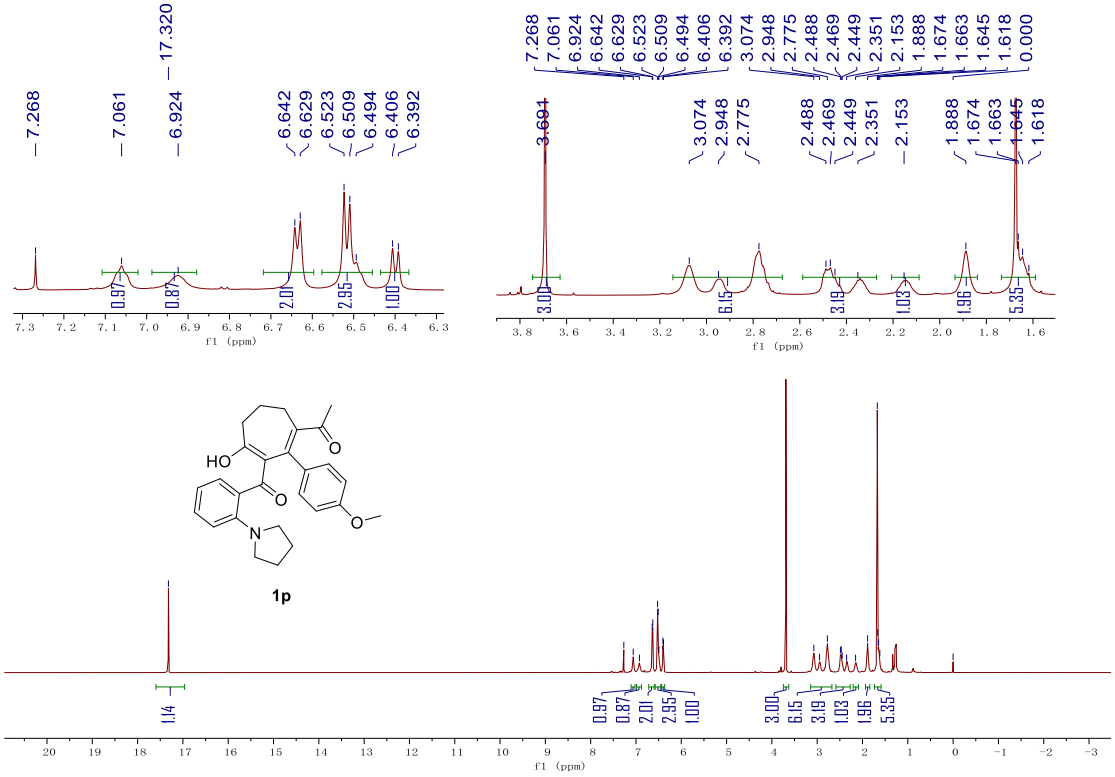

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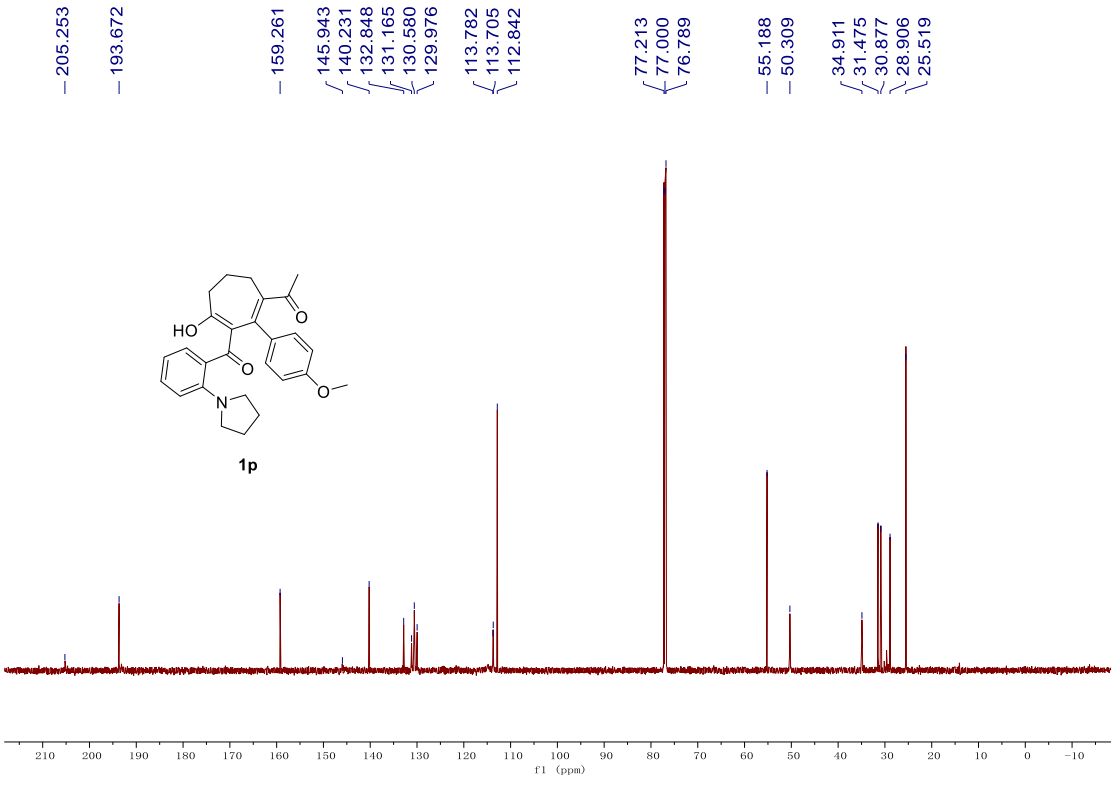

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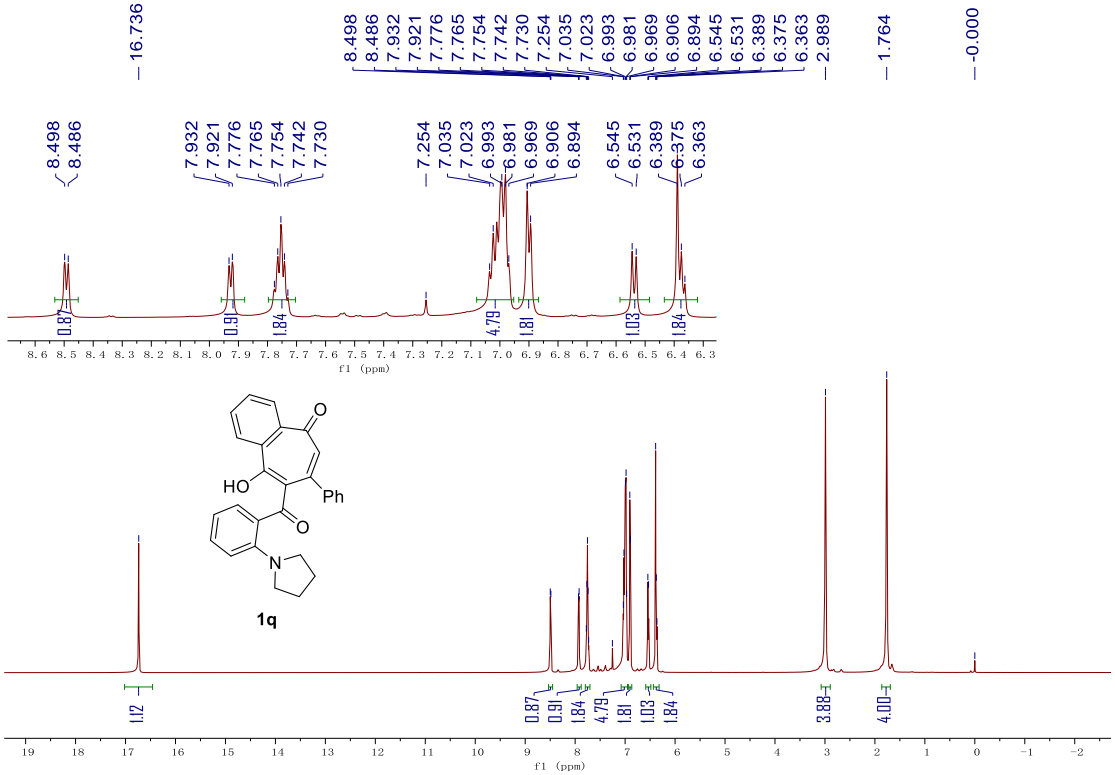

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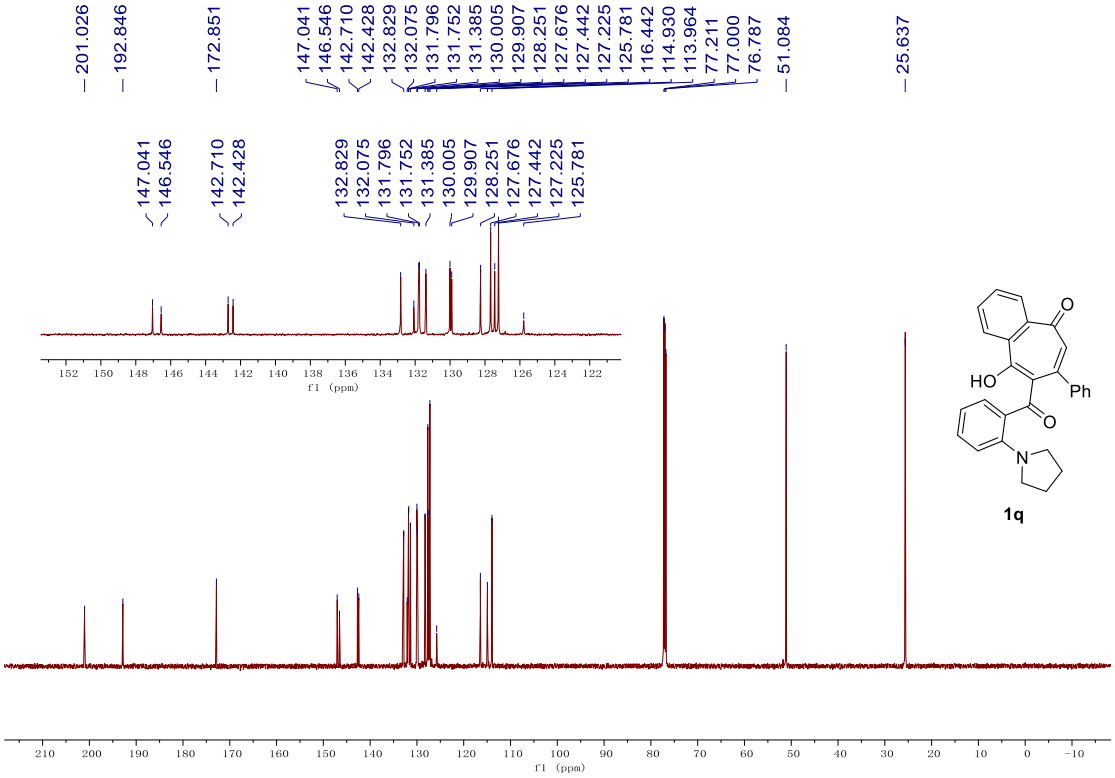
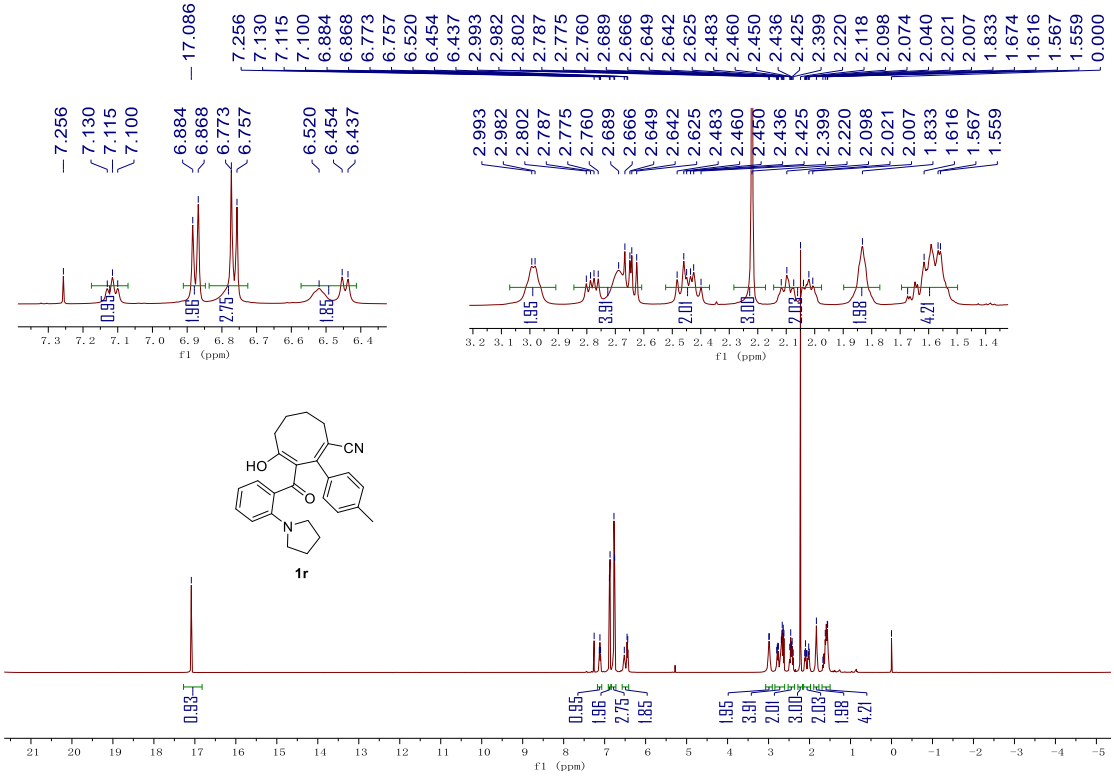
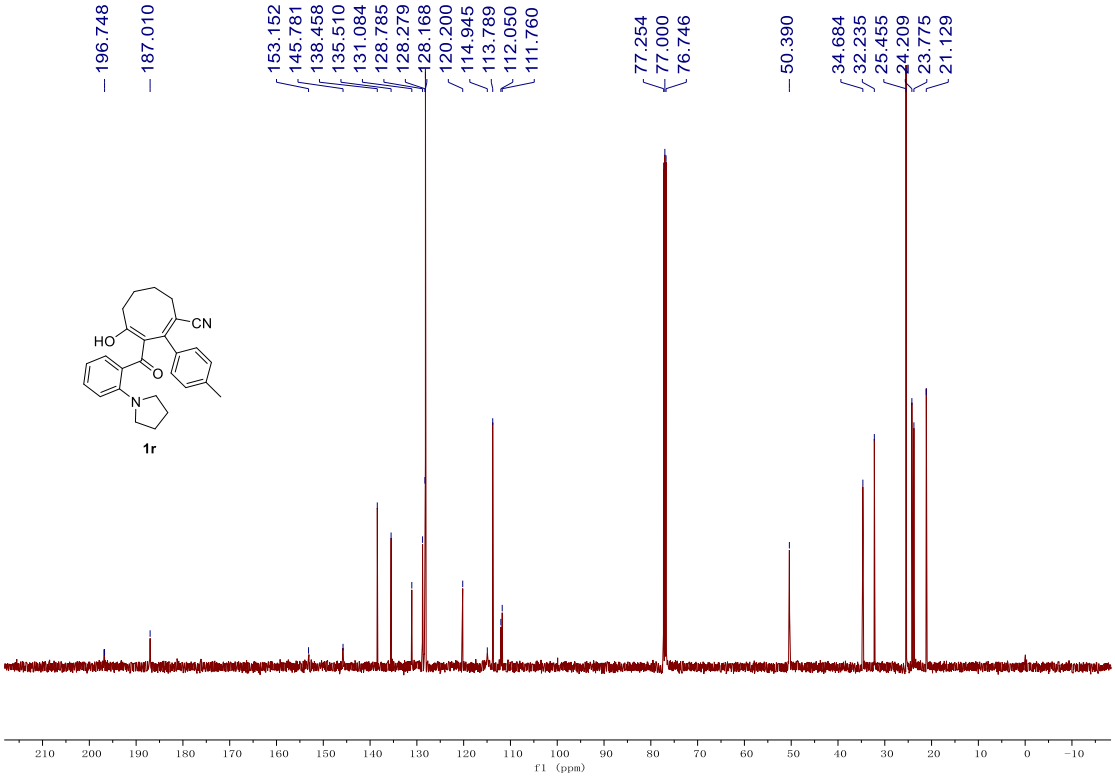


^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)



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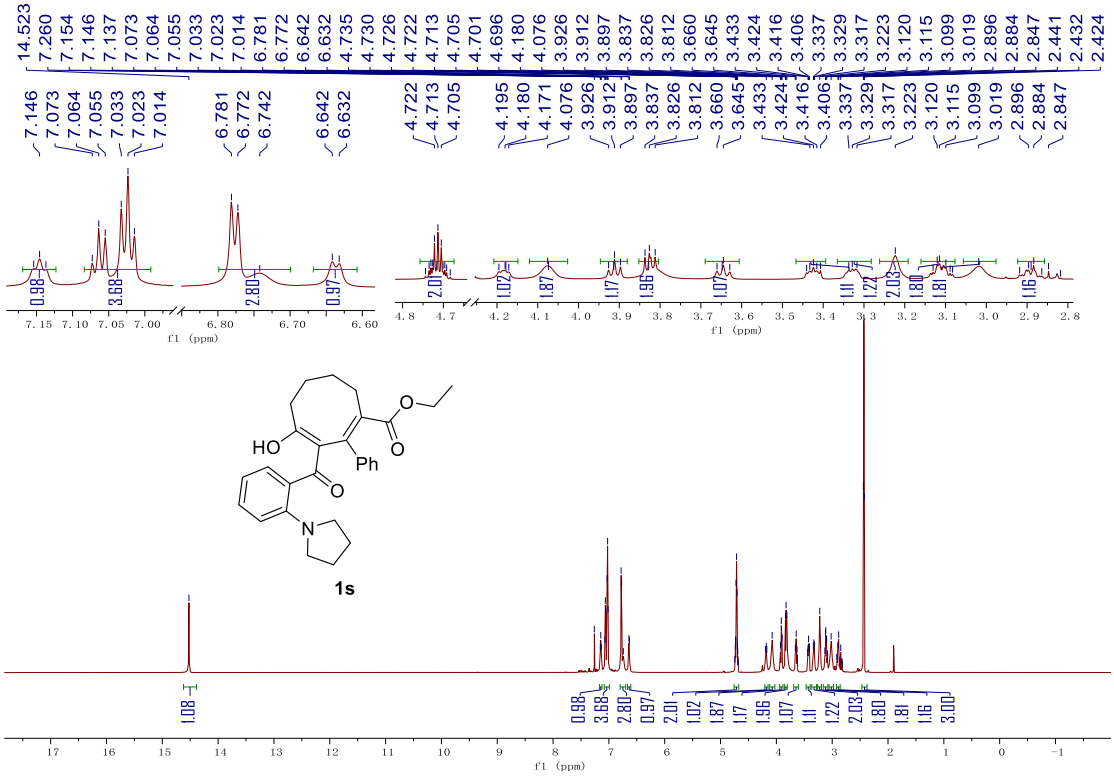

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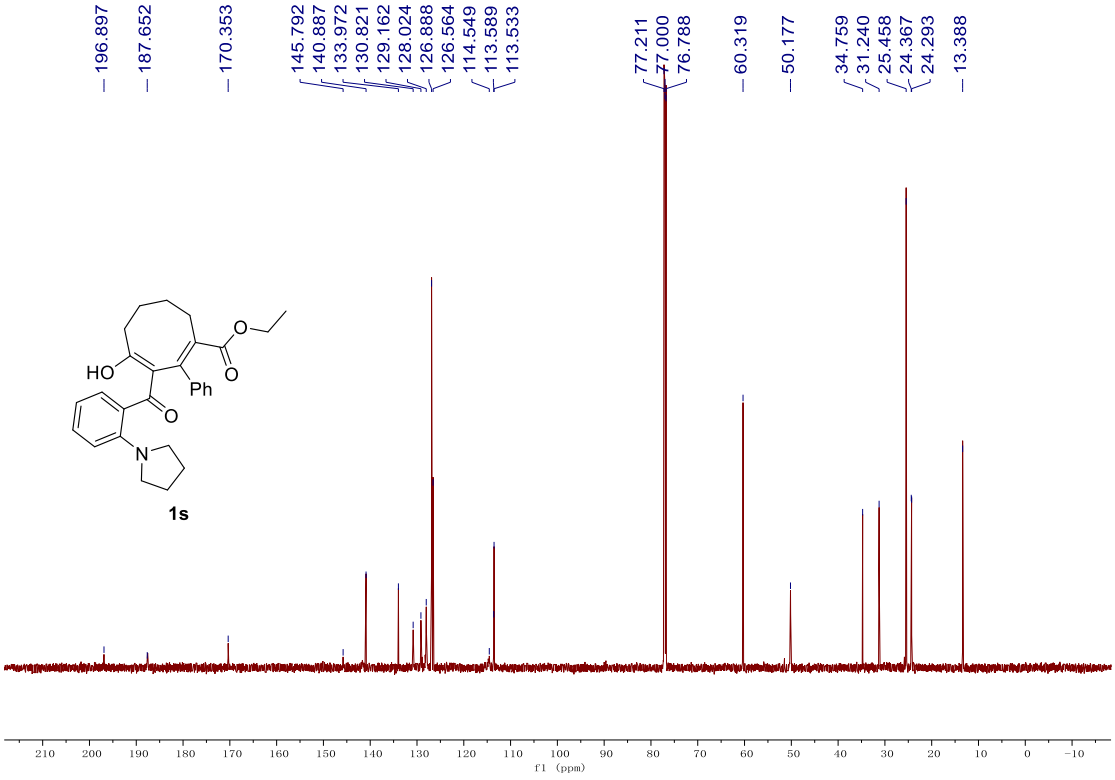

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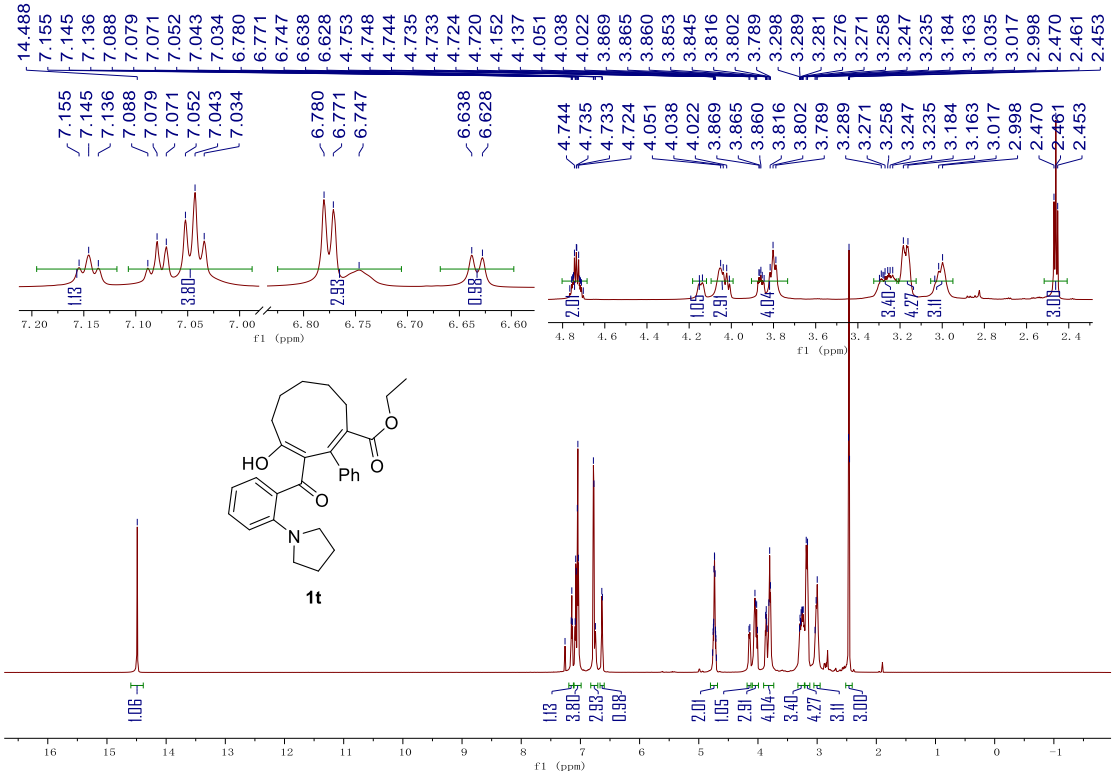
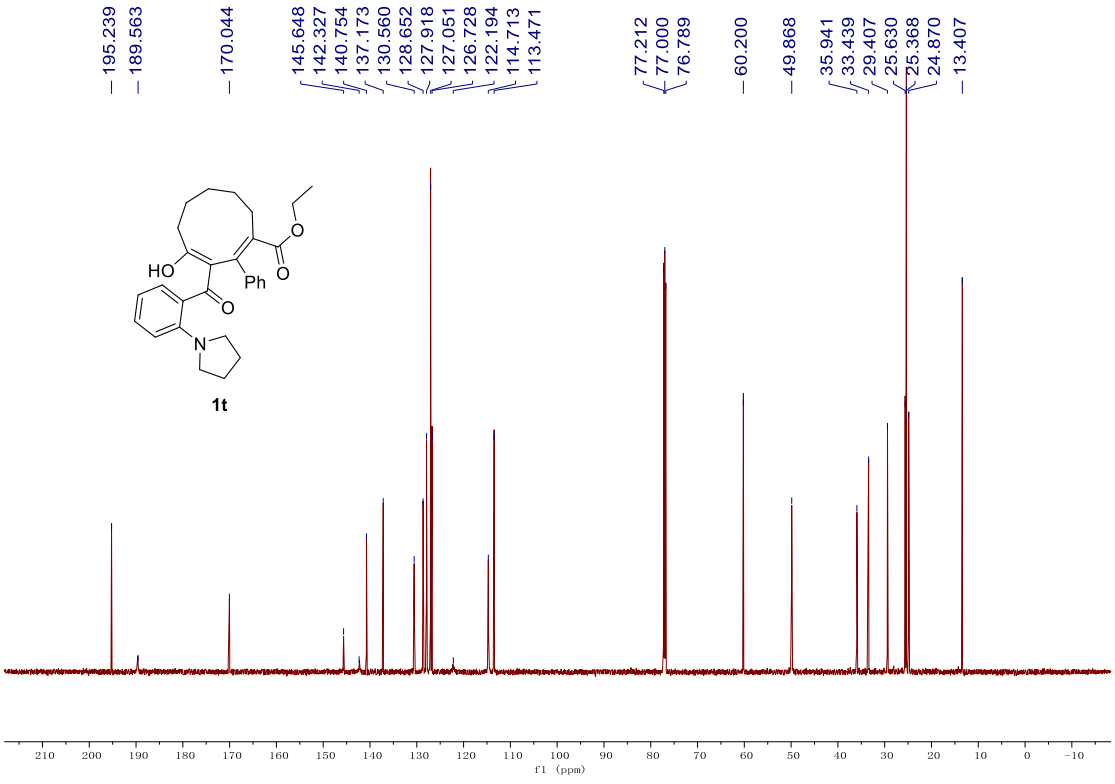


^{13}C NMR (150 MHz, $CDCl_3$)



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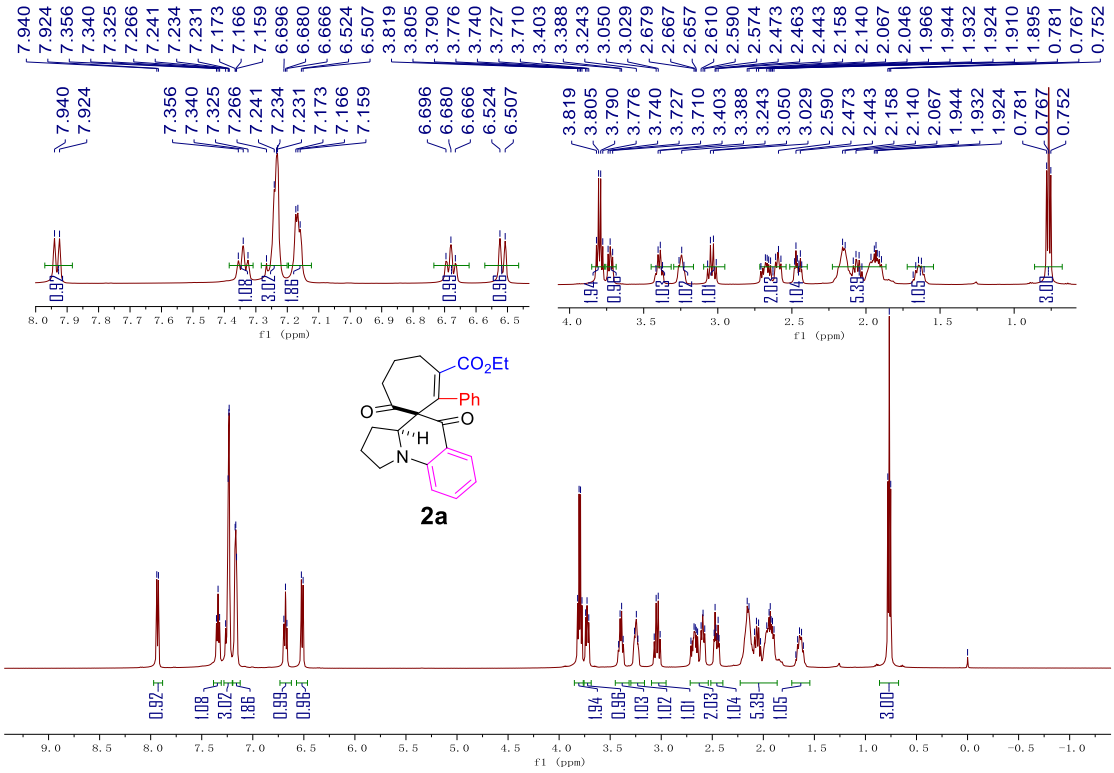
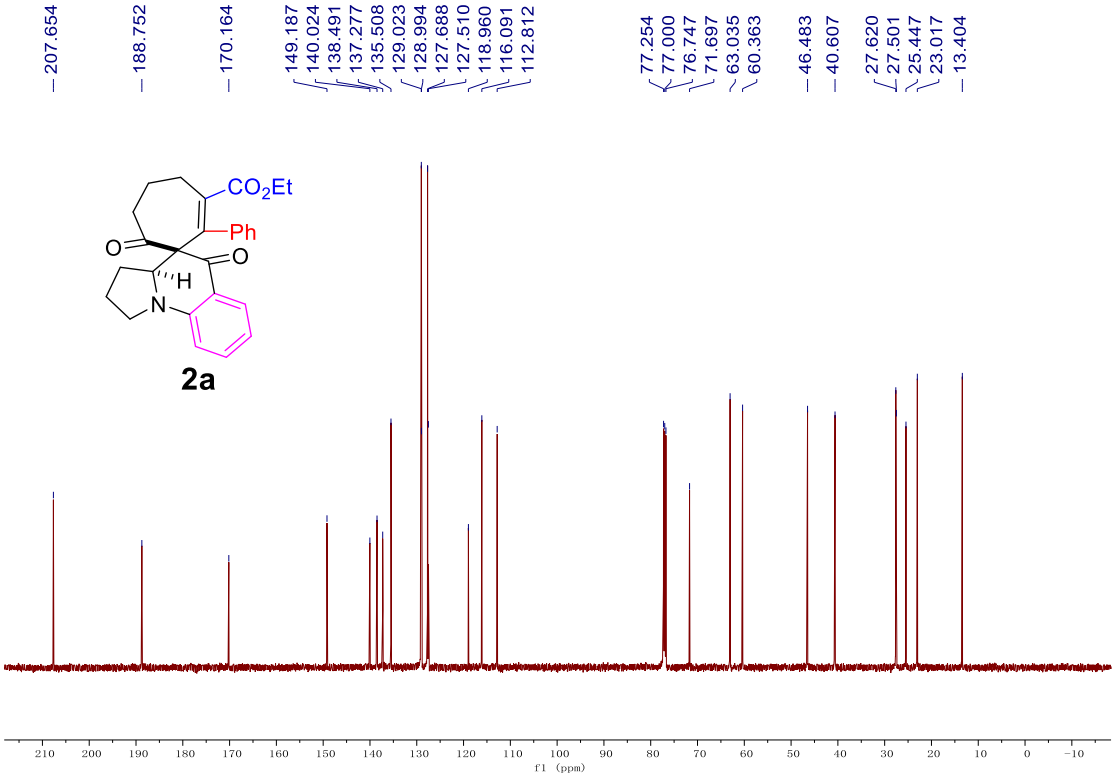


^{13}C NMR (125 MHz, $CDCl_3$)



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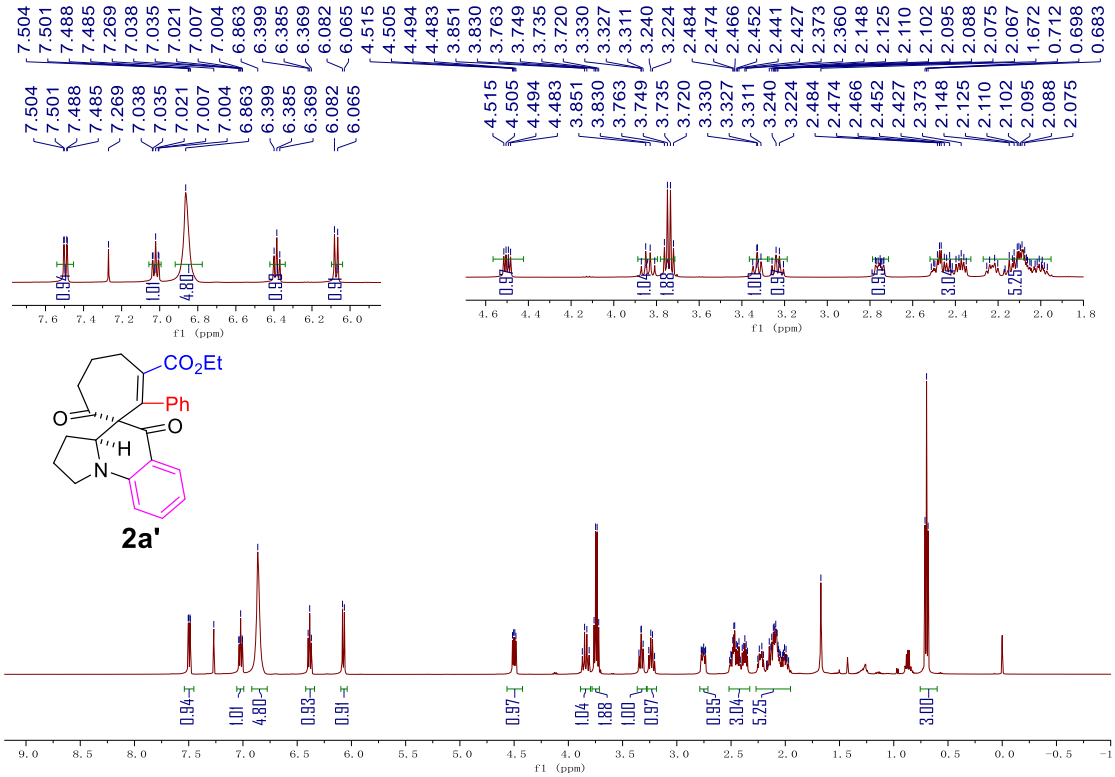

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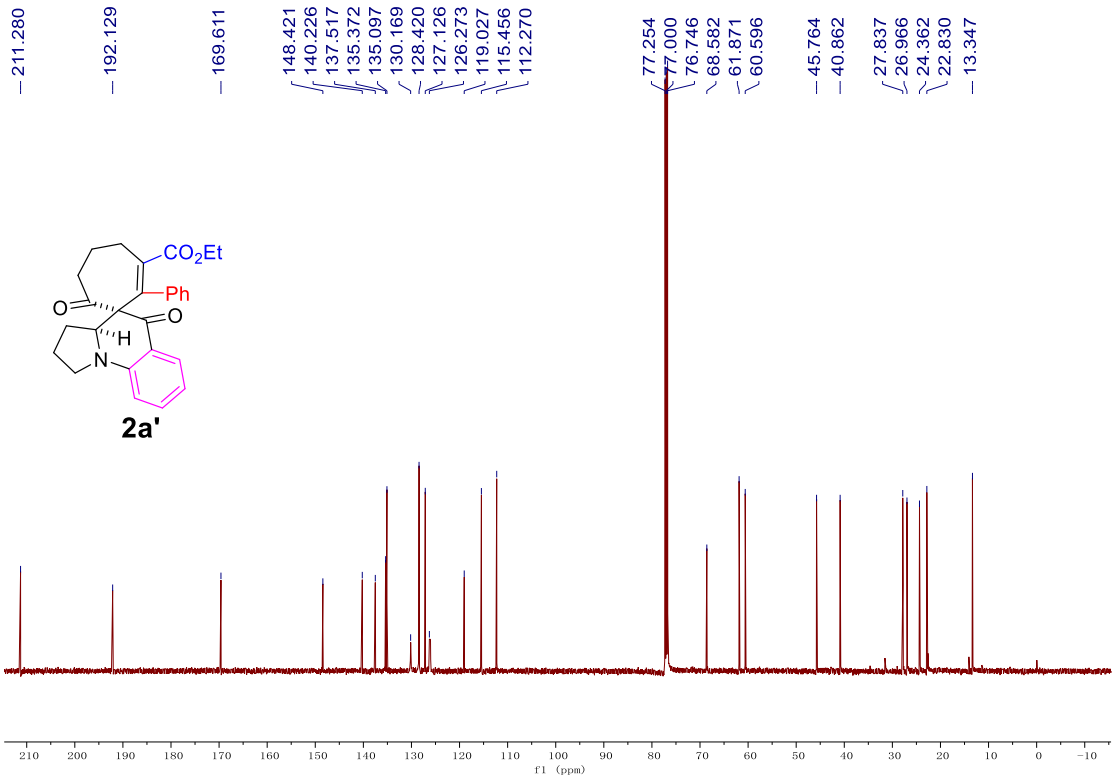

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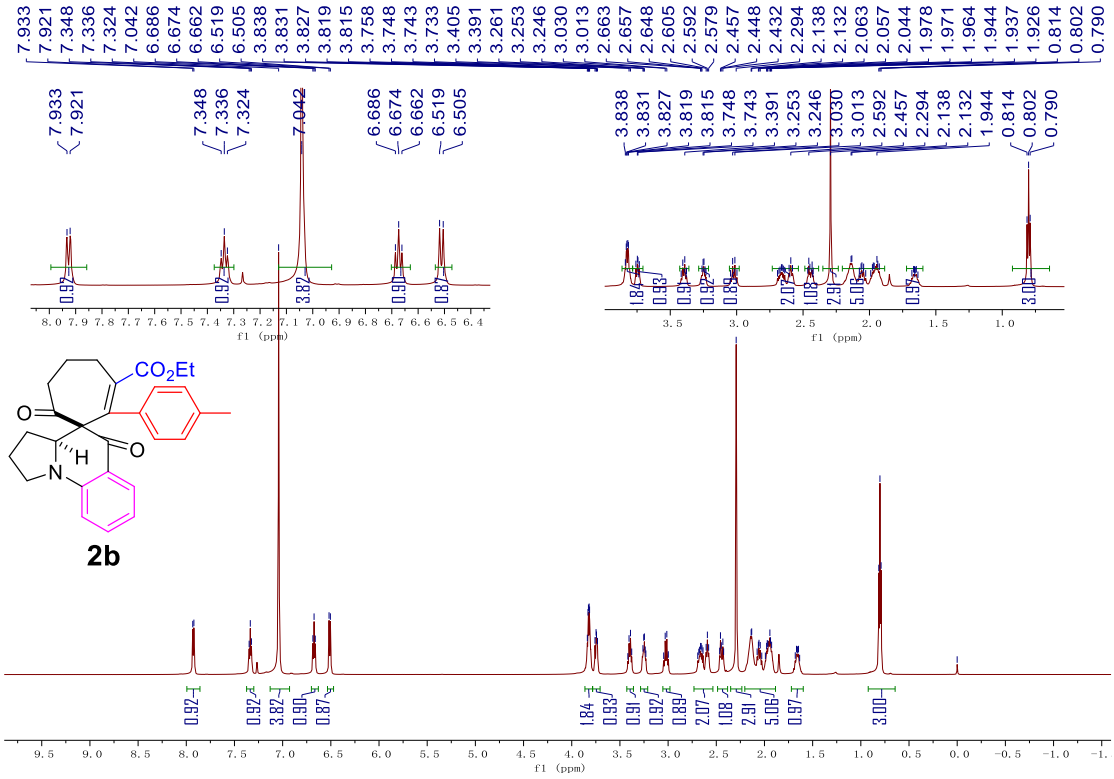

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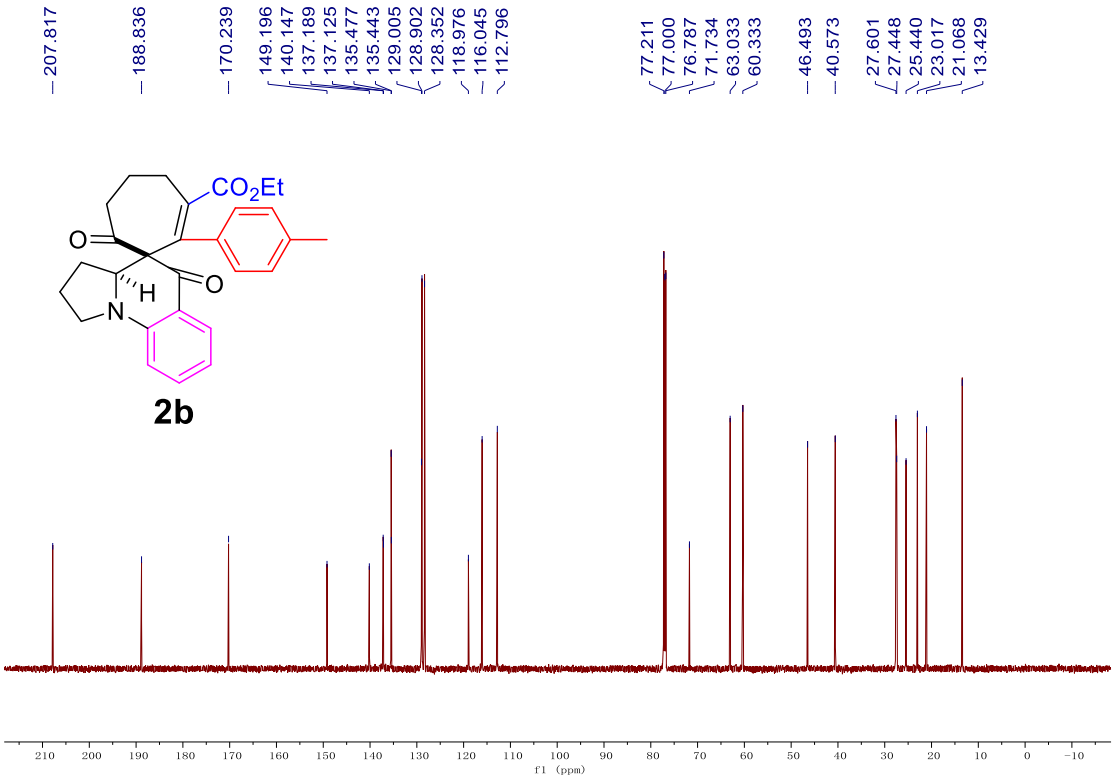

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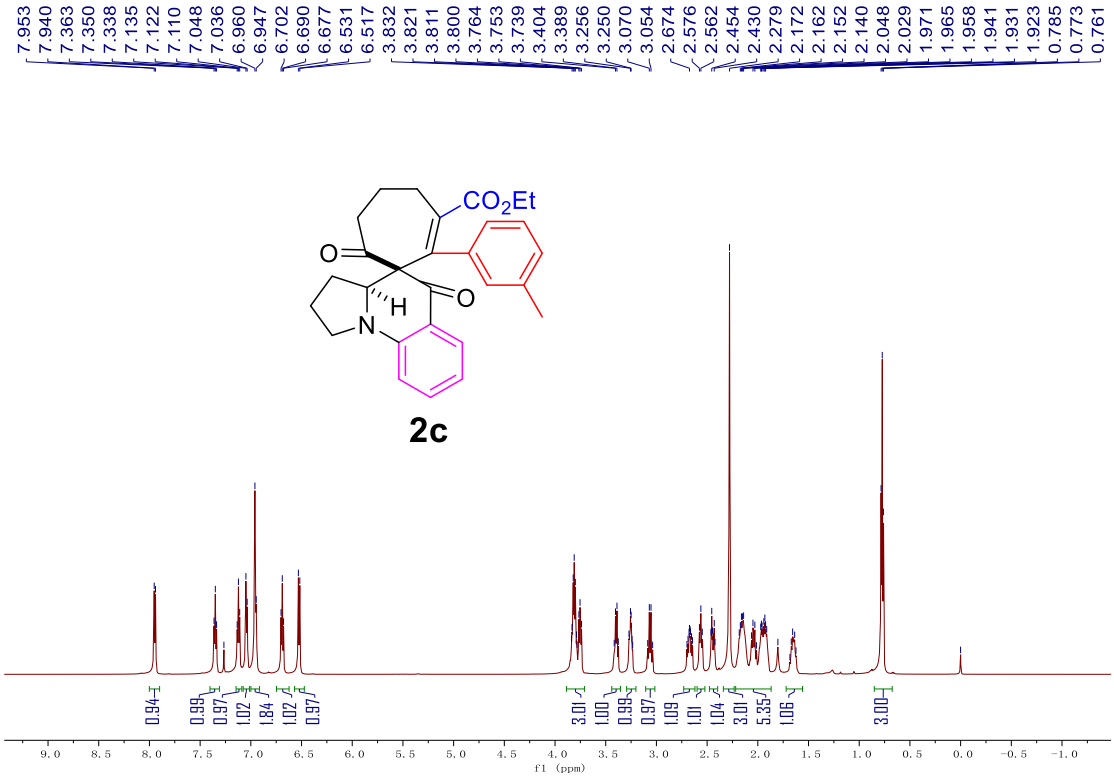

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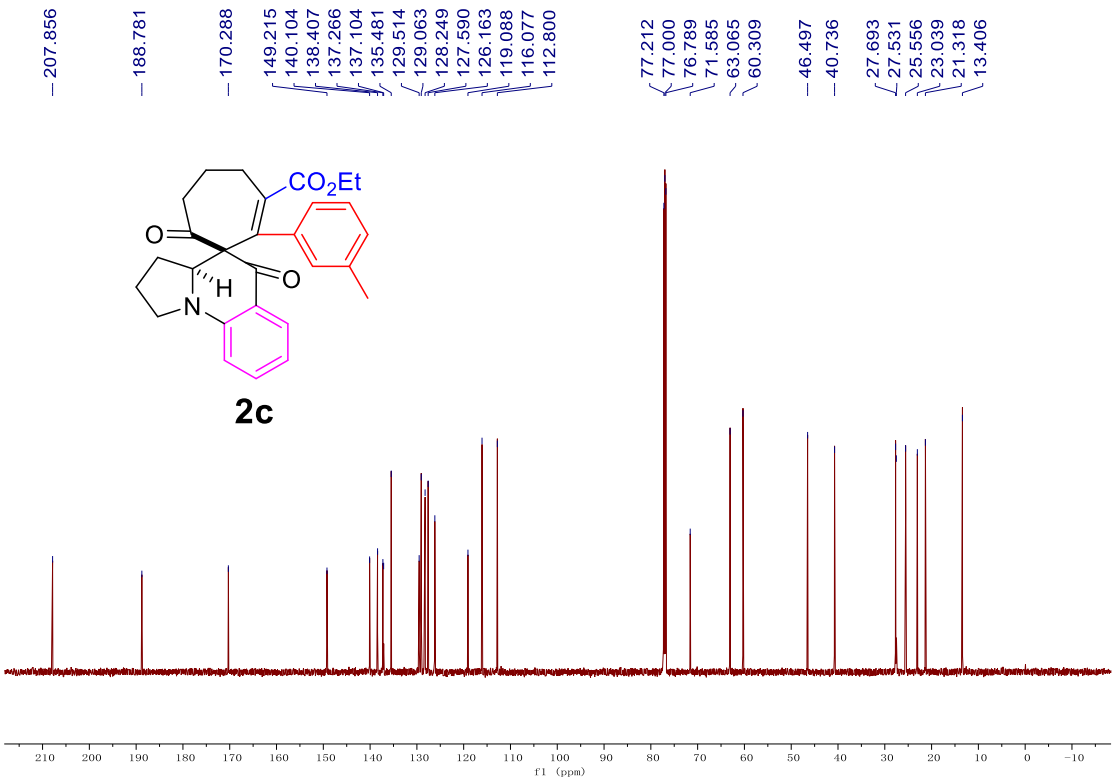

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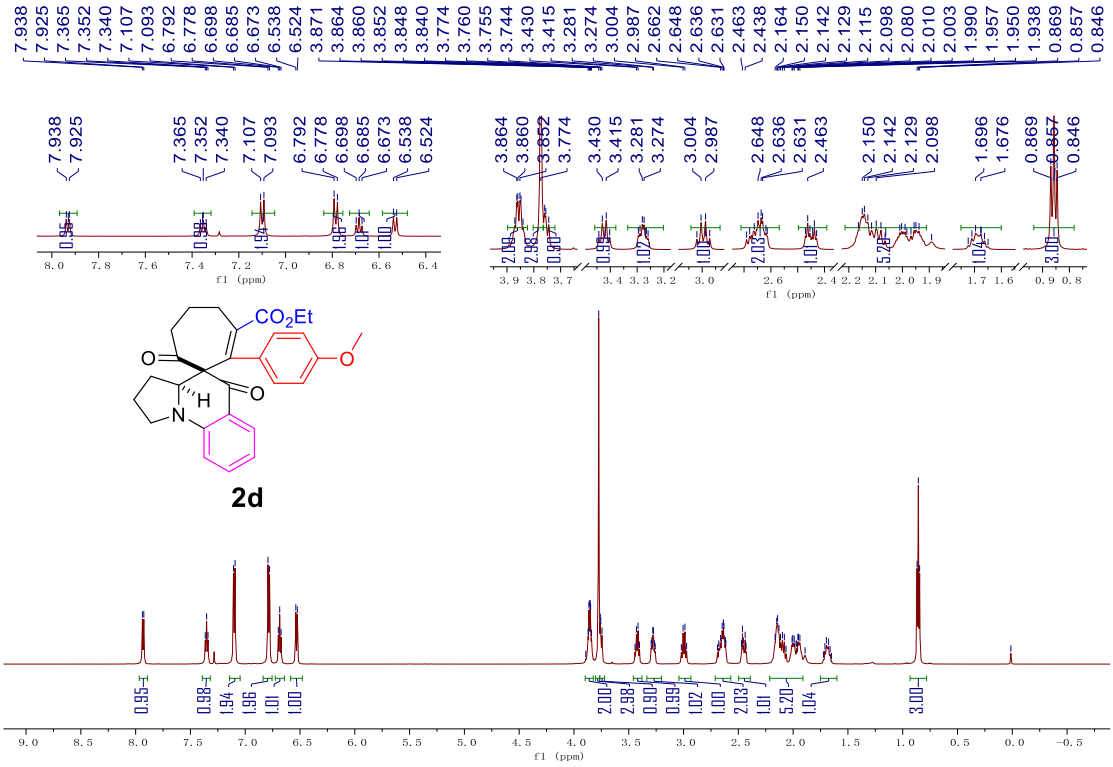

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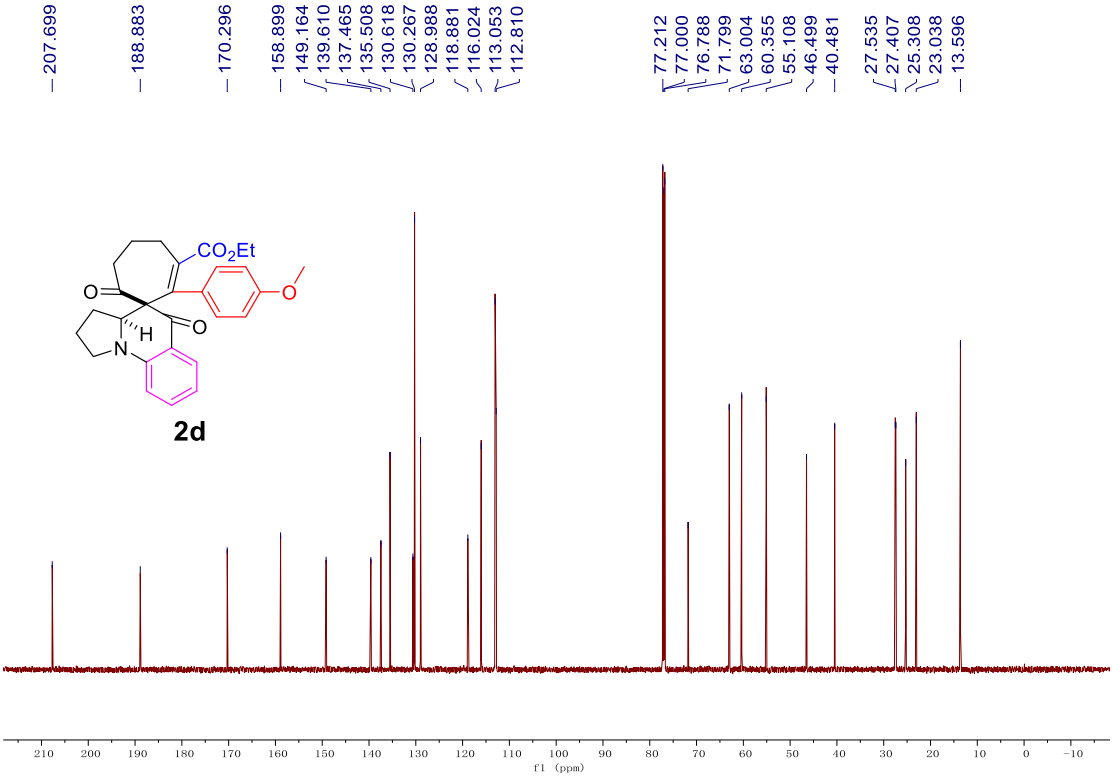

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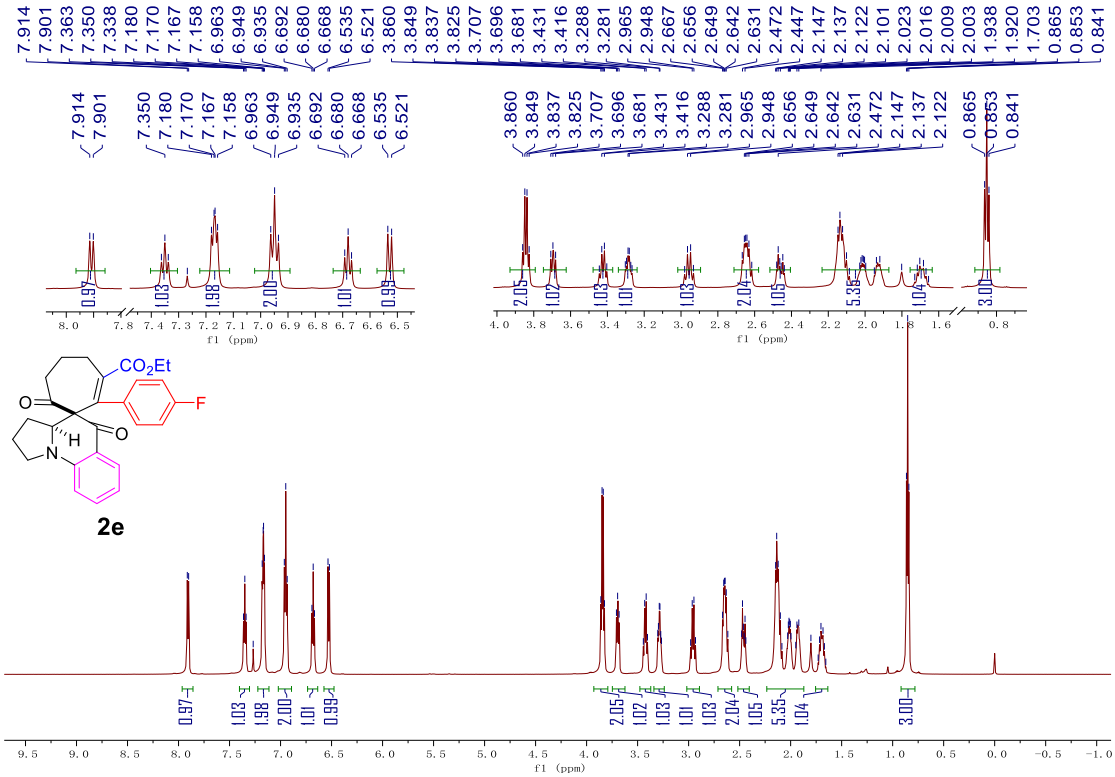

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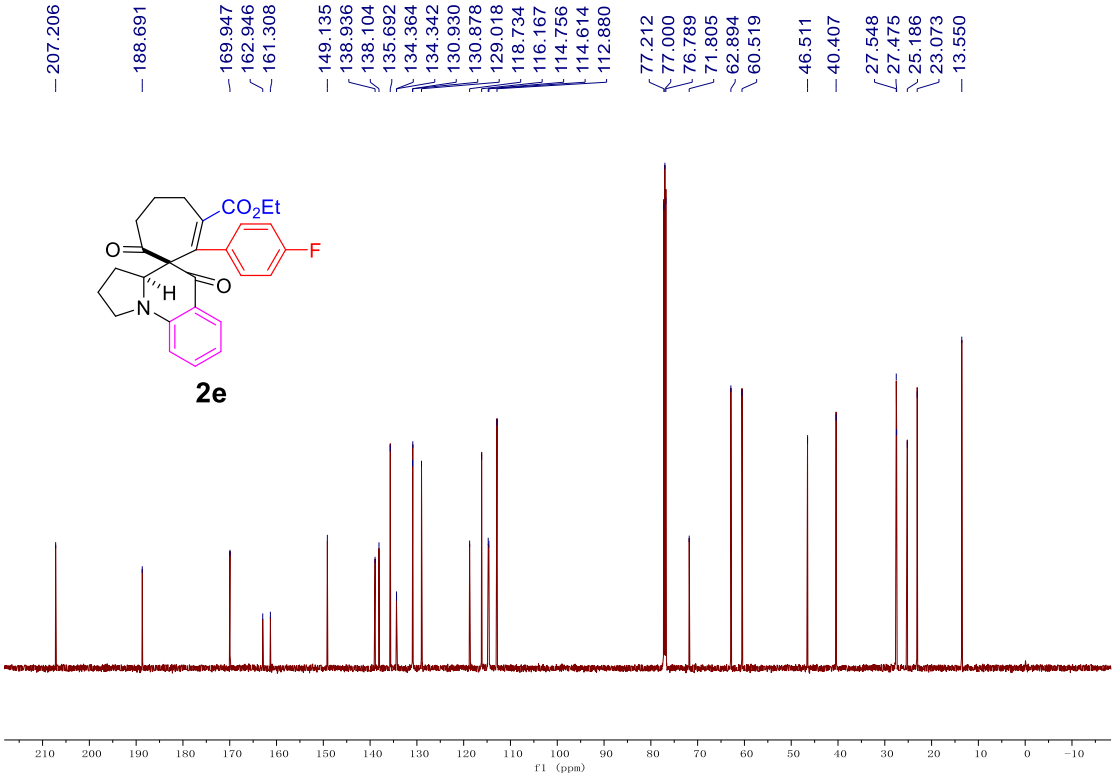

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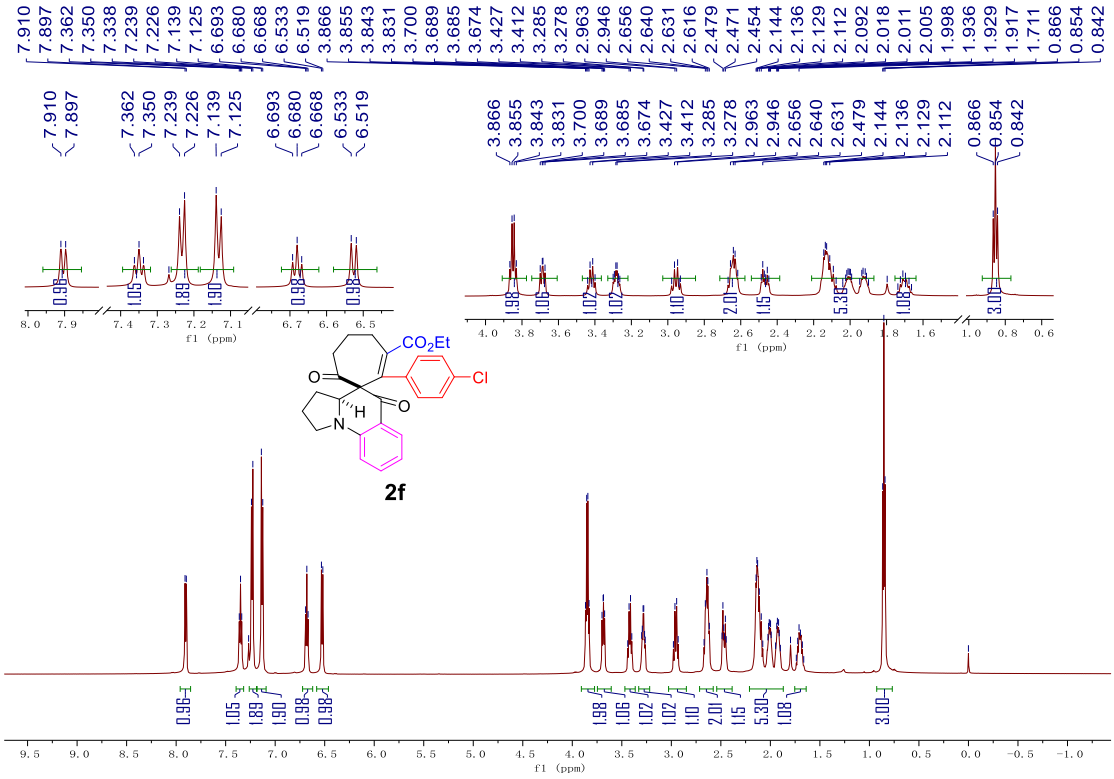

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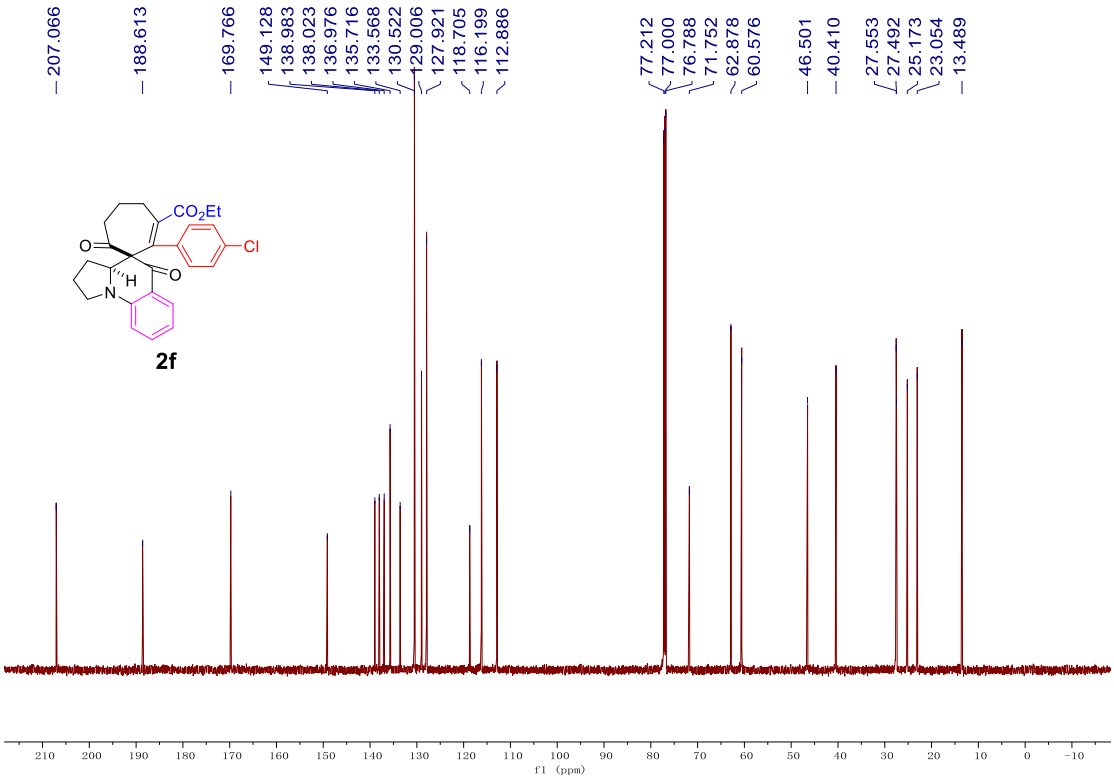

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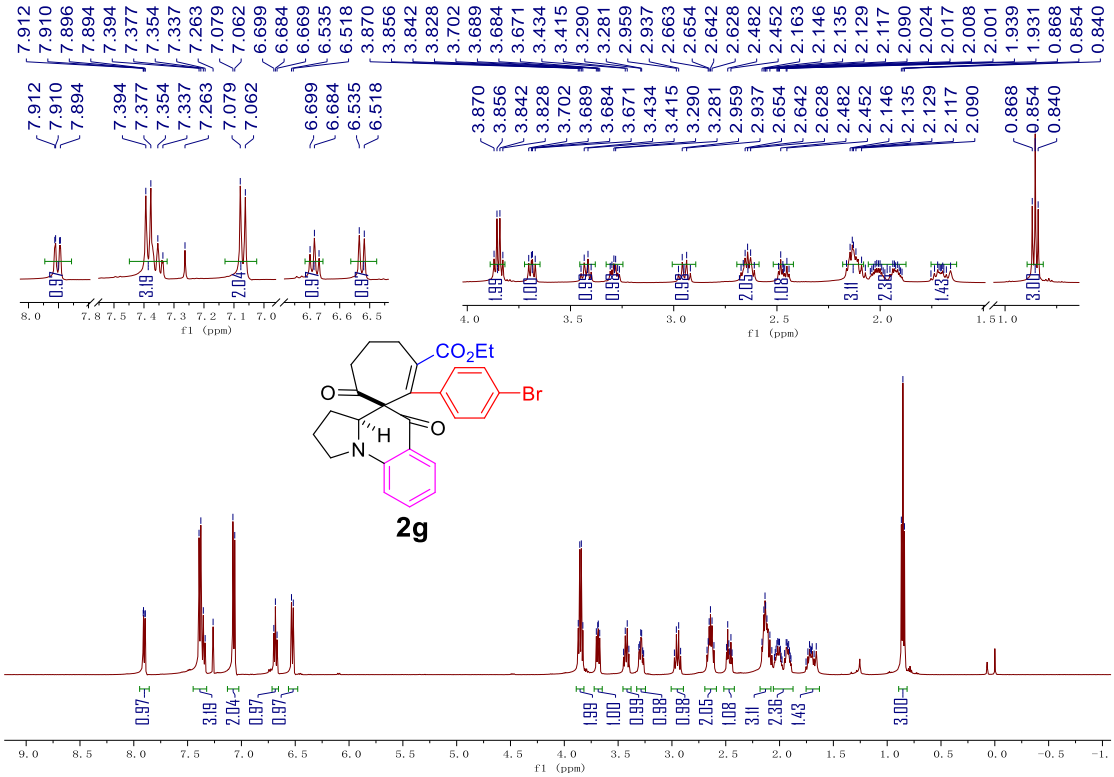
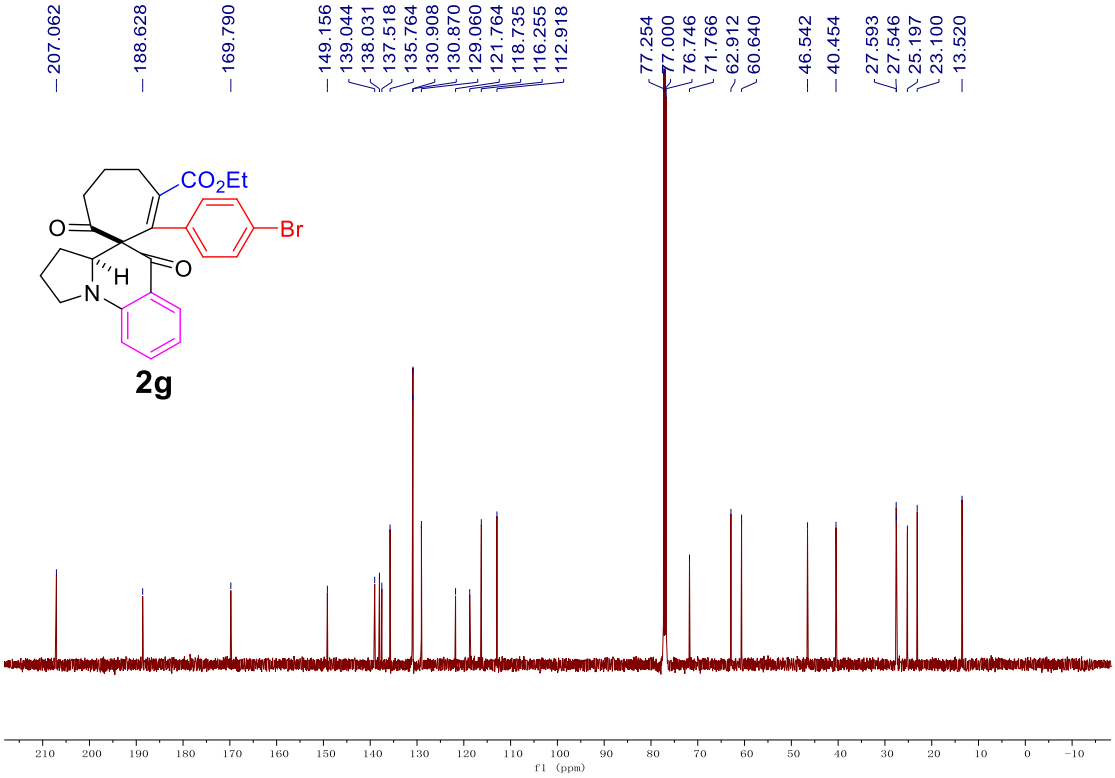


^{13}C NMR (125 MHz, $CDCl_3$)



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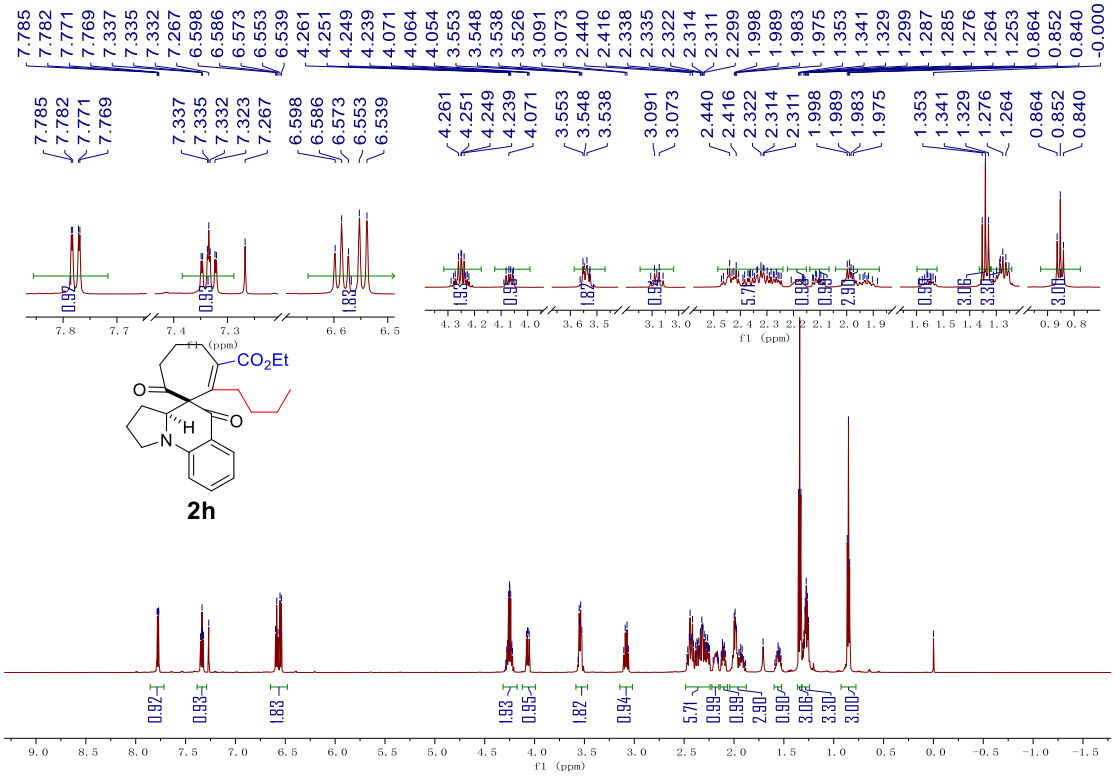

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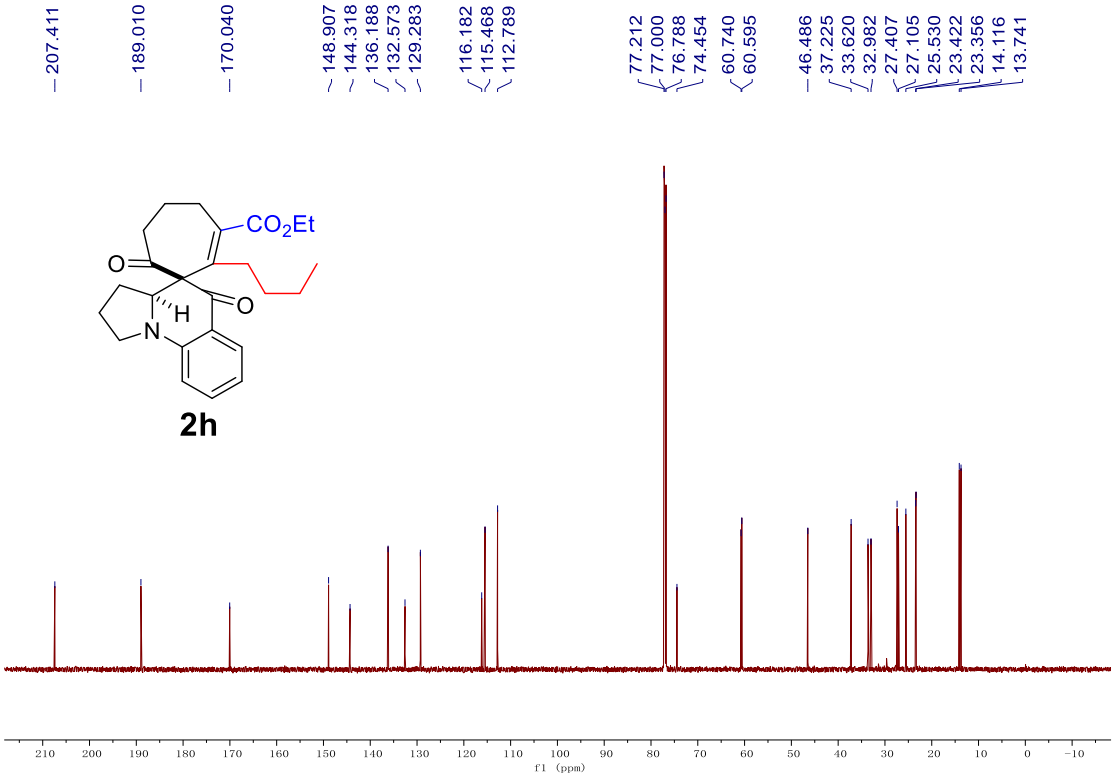

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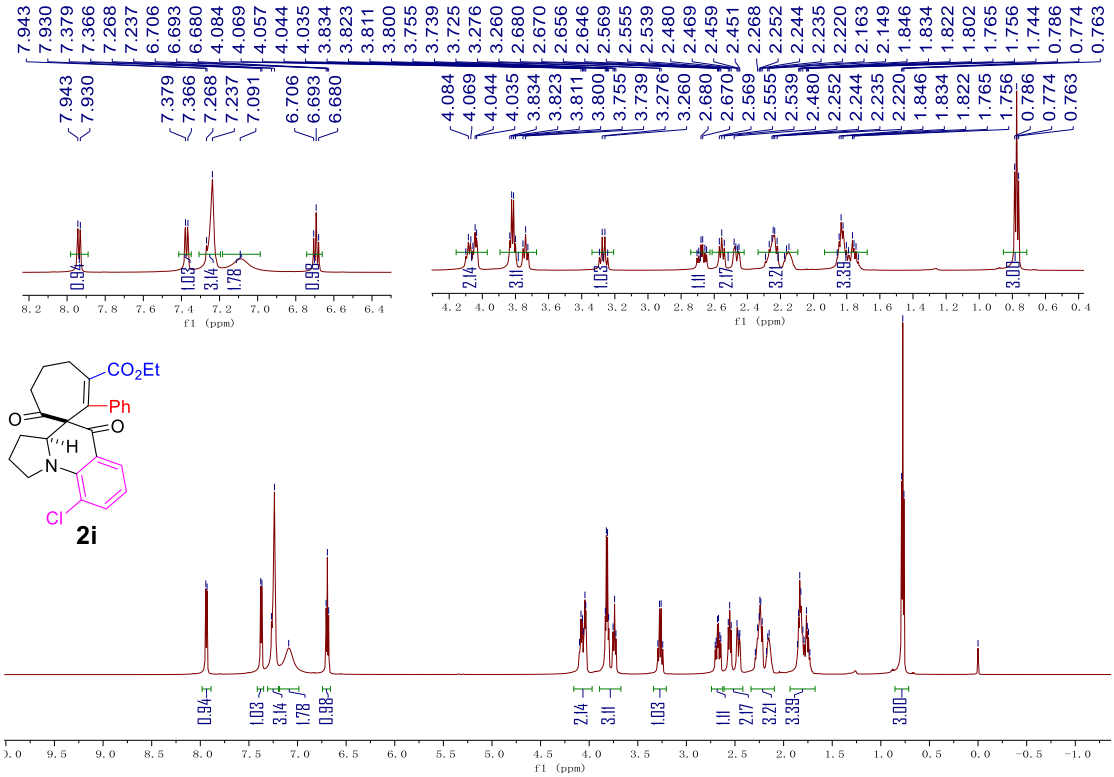

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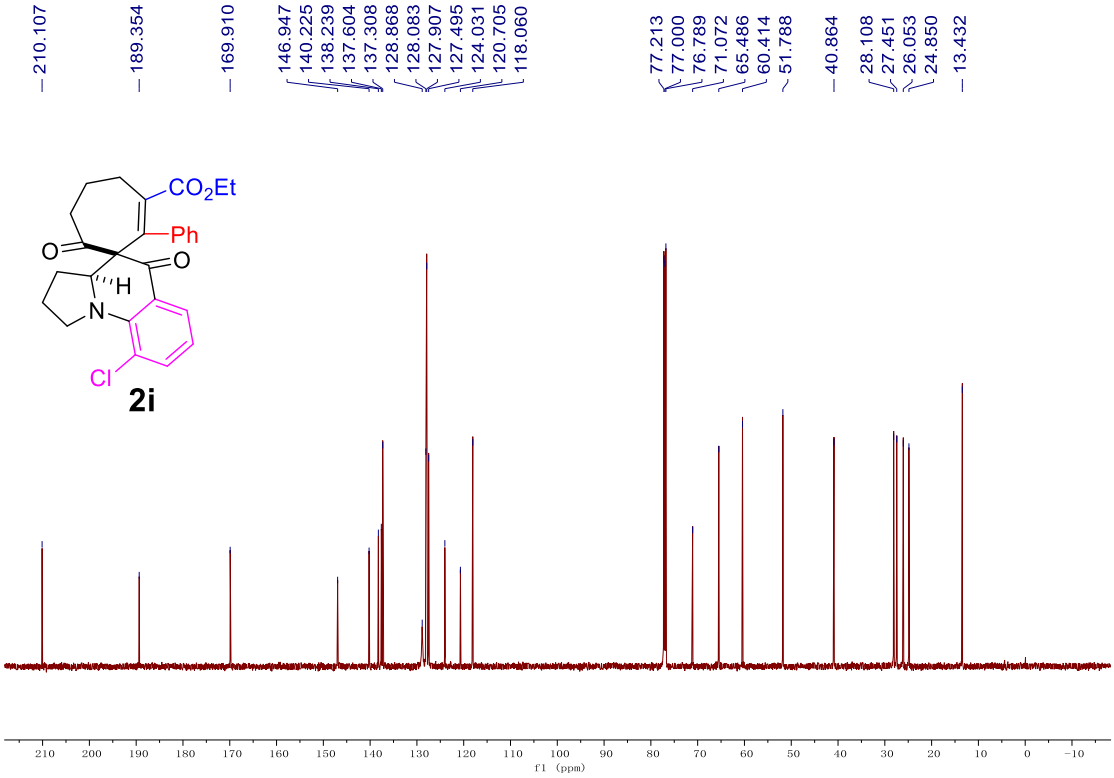
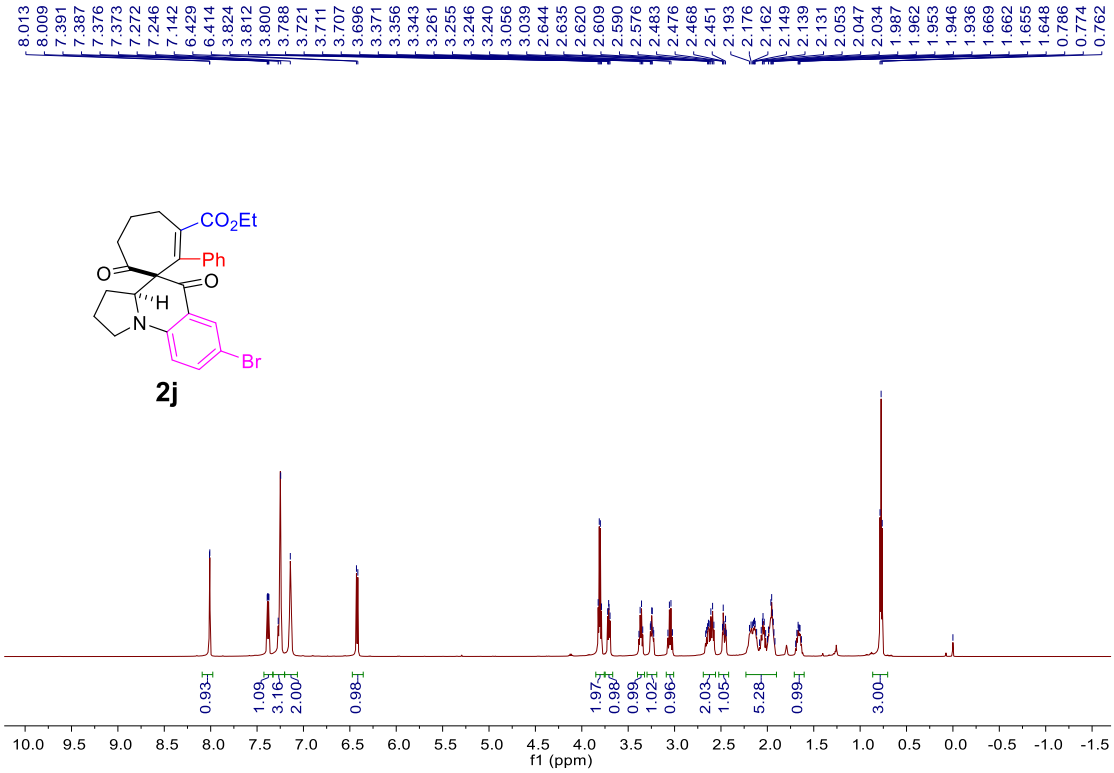
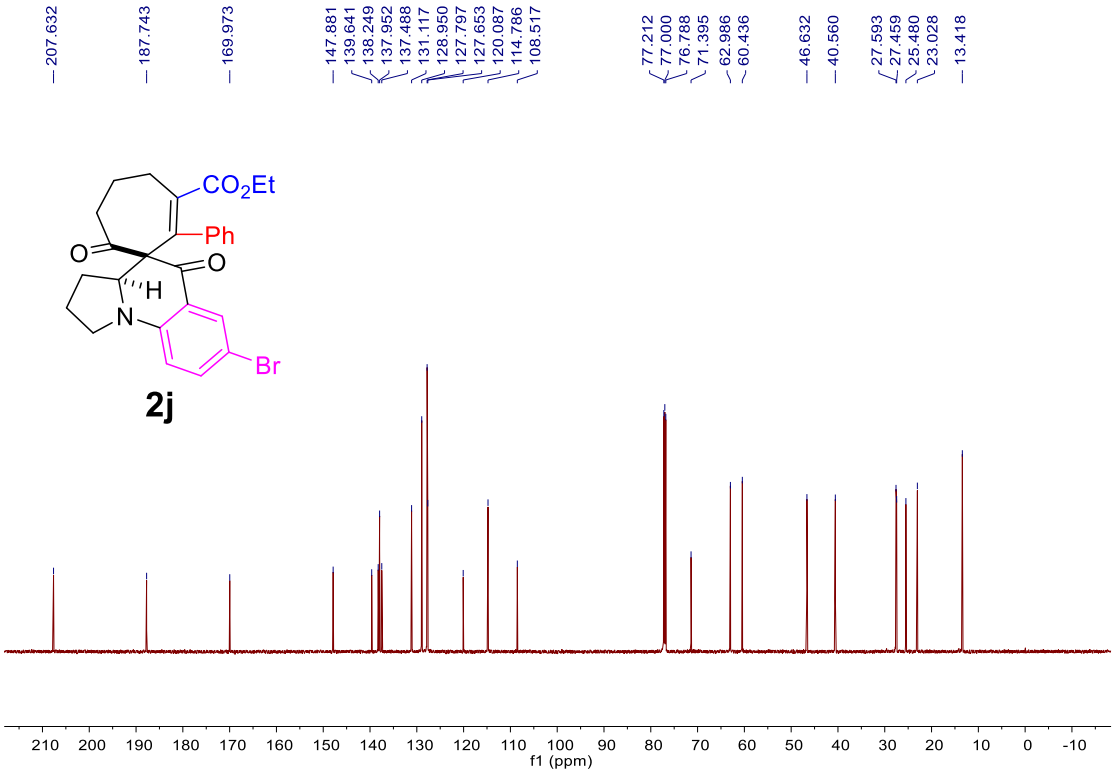


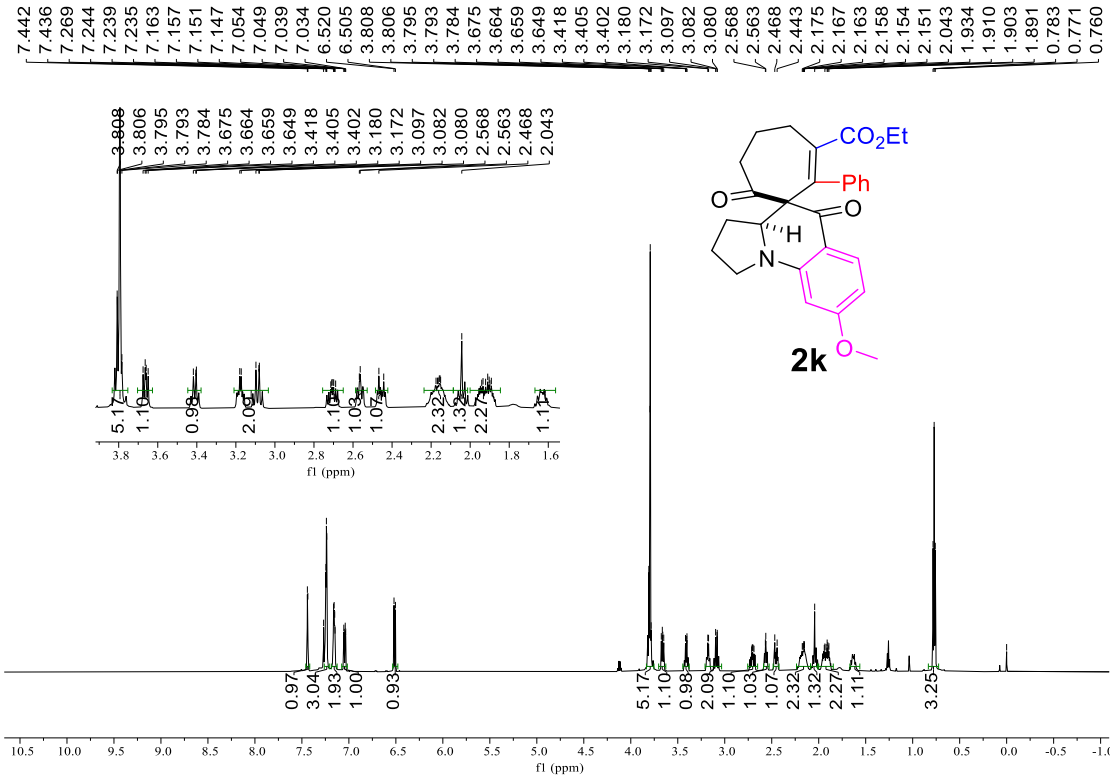
^{1}H NMR (600 MHz, $CDCl_3$)



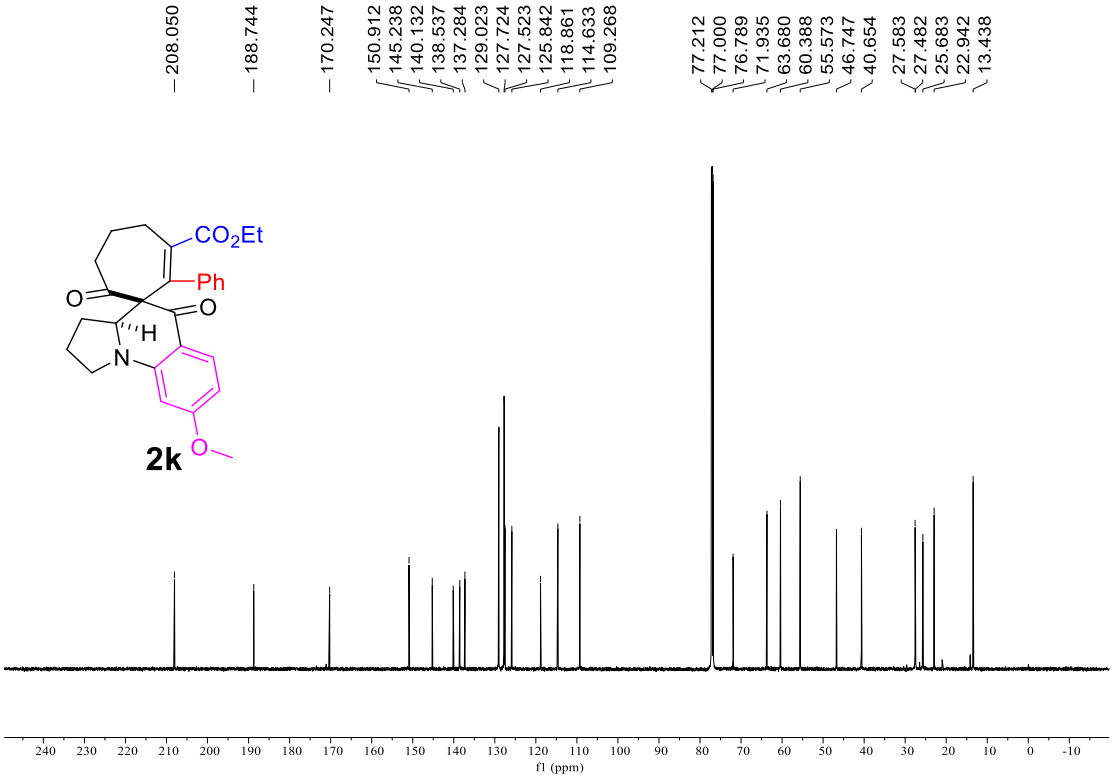
^{13}C NMR (150 MHz, $CDCl_3$)



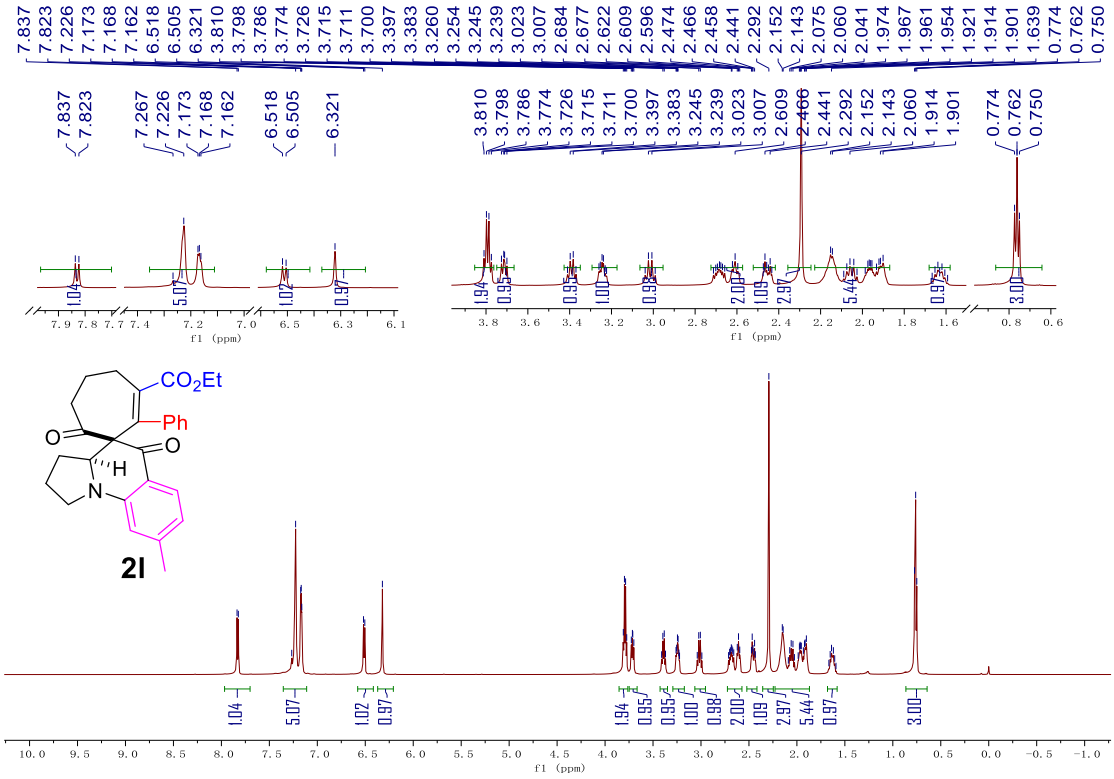
^{1}H NMR (600 MHz, $CDCl_3$)



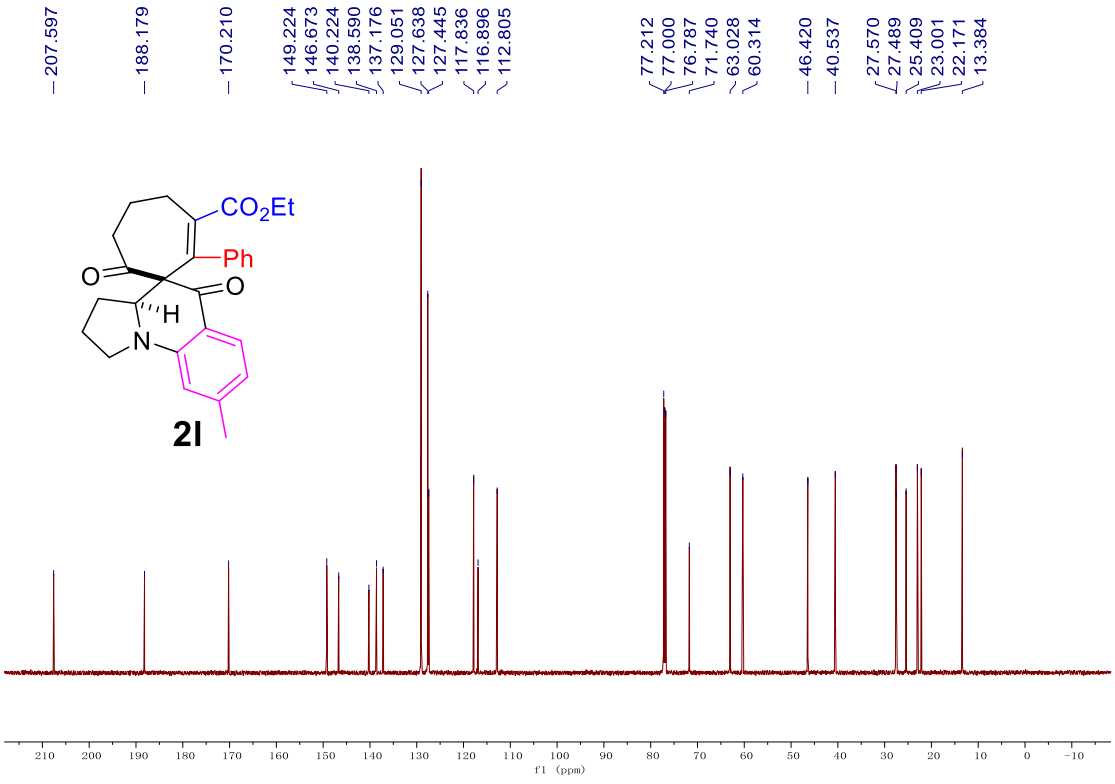
^{13}C NMR (150 MHz, $CDCl_3$)



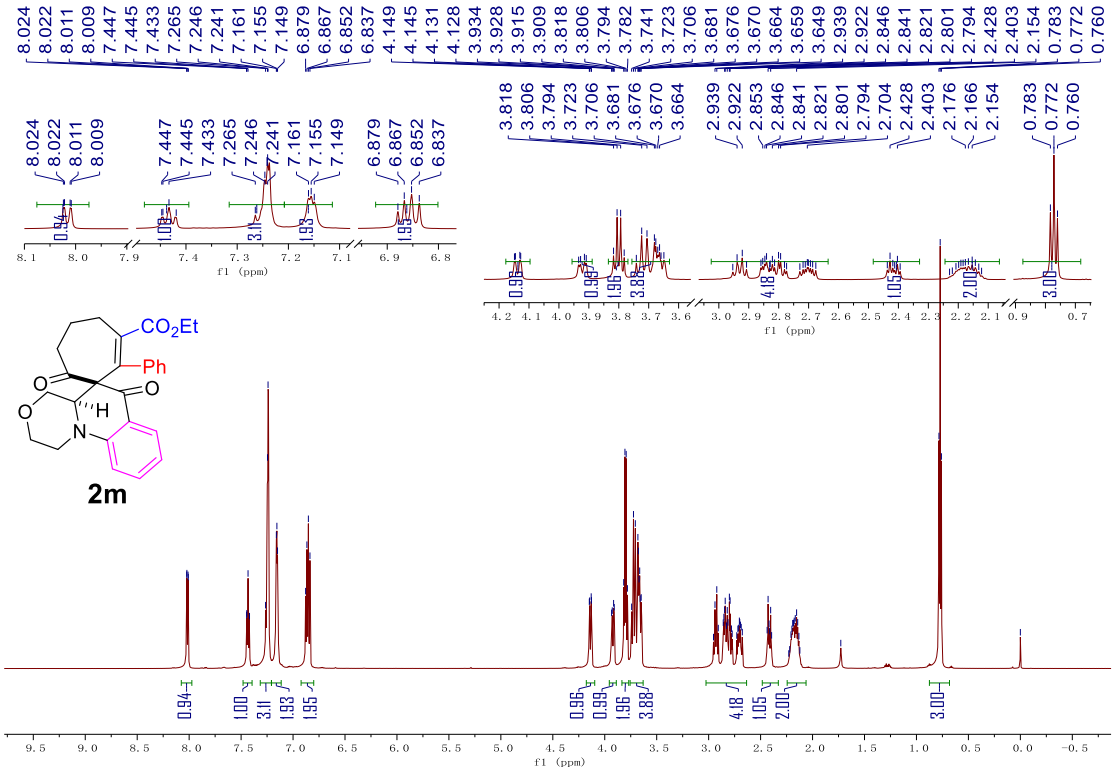
^{1}H NMR (600 MHz, $CDCl_3$)



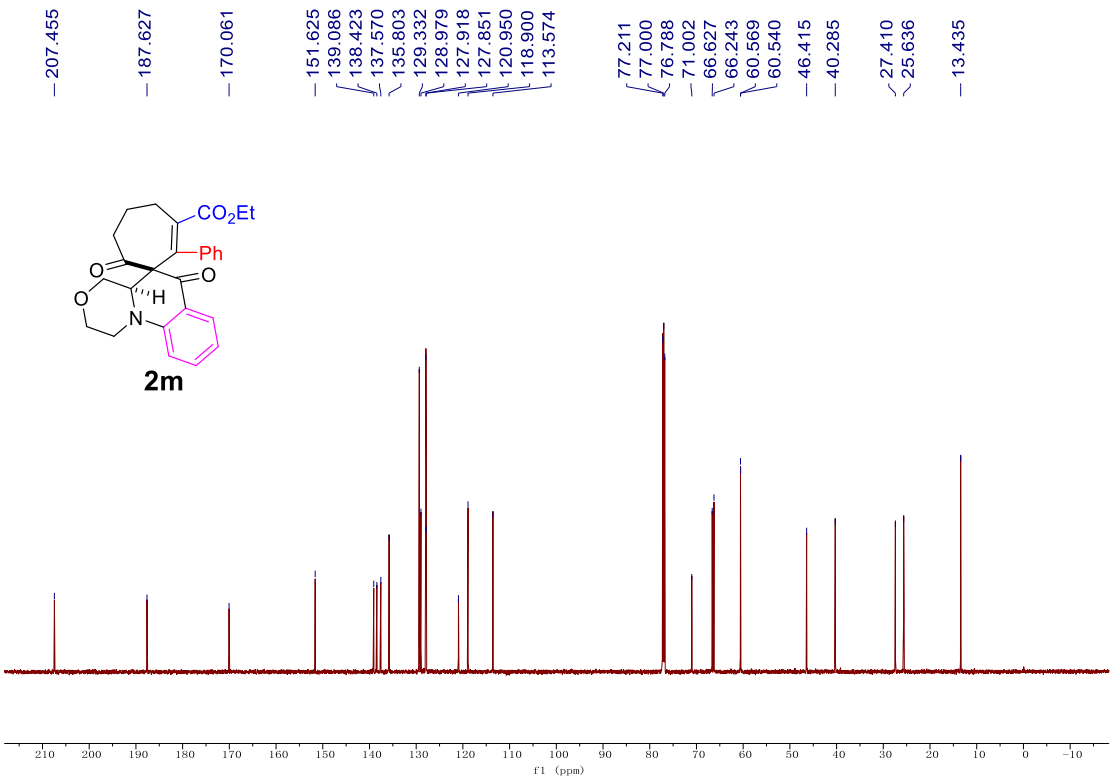
^{13}C NMR (150 MHz, $CDCl_3$)



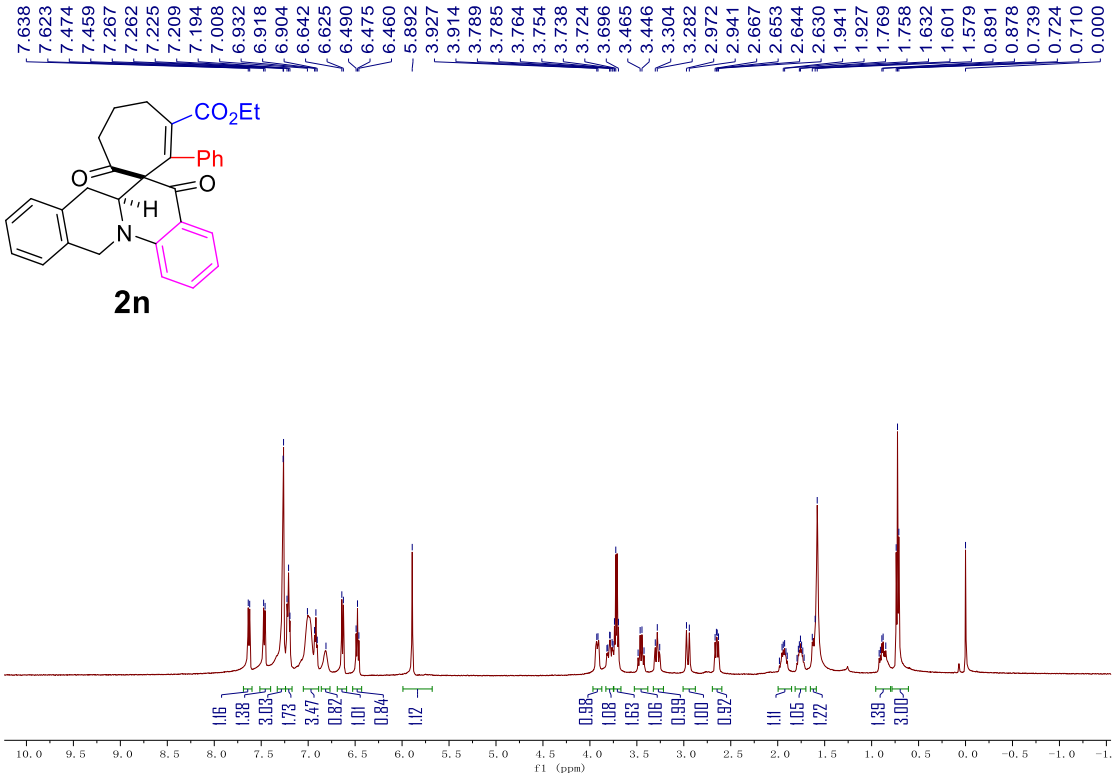
^{1}H NMR (600 MHz, $CDCl_3$)



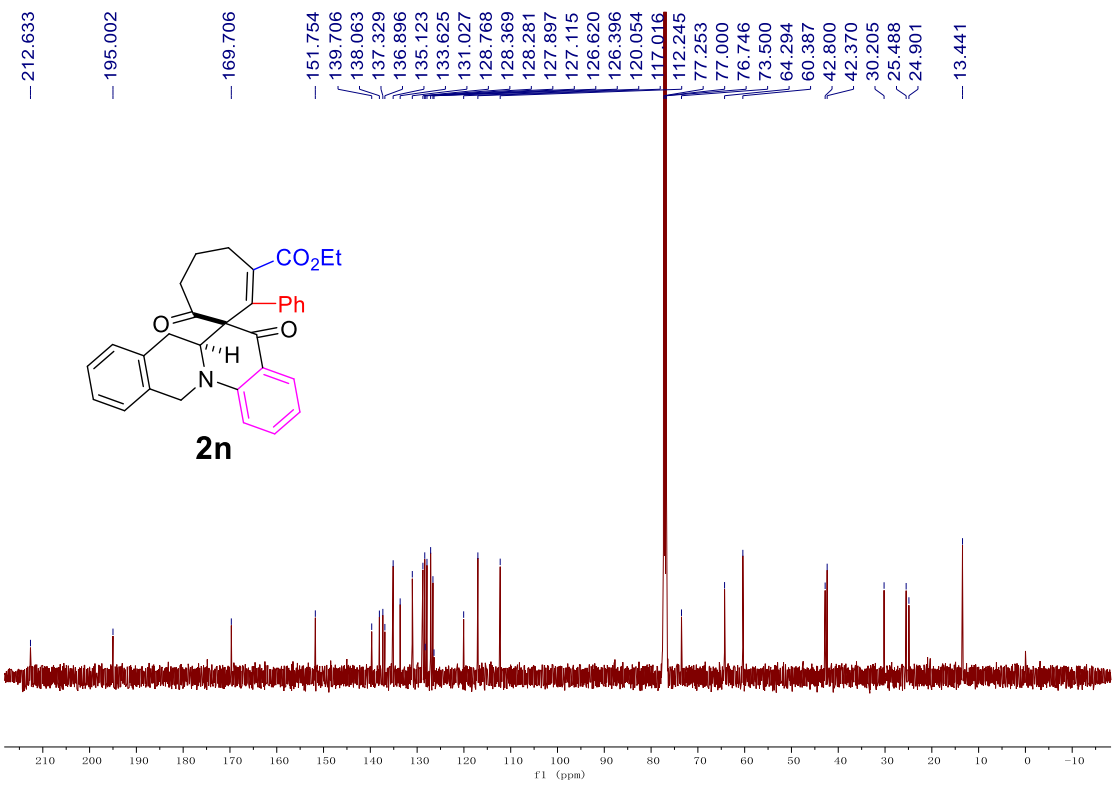
^{13}C NMR (150 MHz, $CDCl_3$)



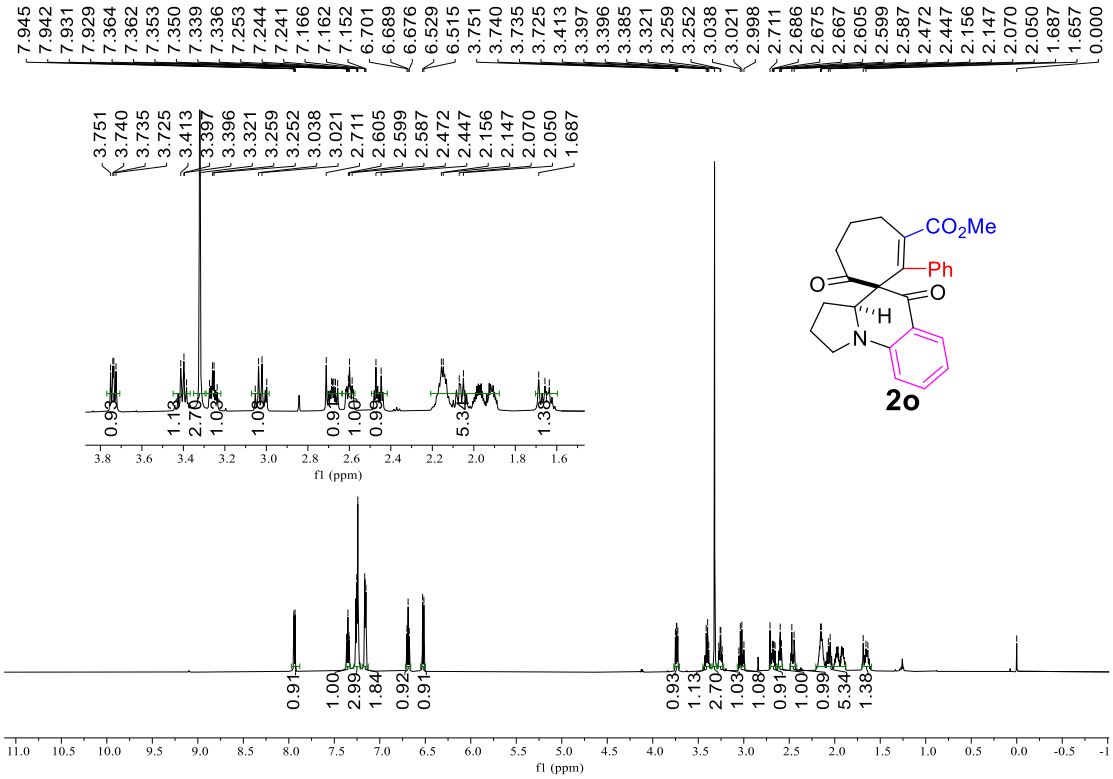
^{1}H NMR (500 MHz, $CDCl_3$)



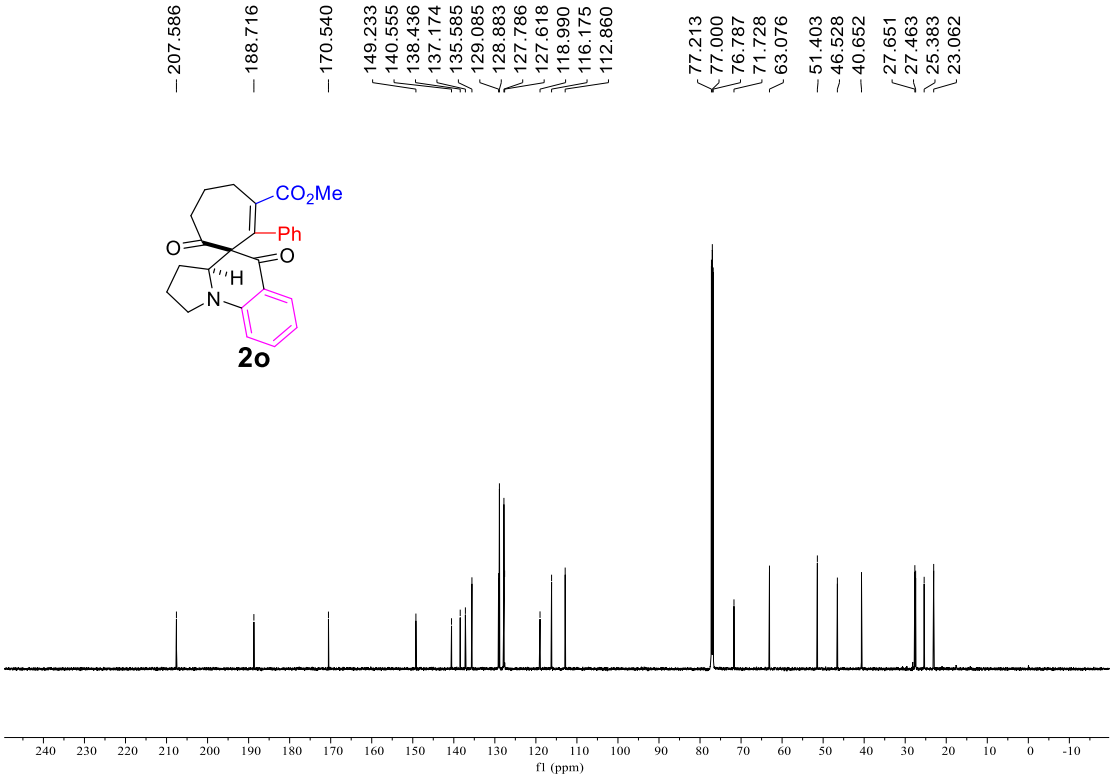
^{13}C NMR (125 MHz, $CDCl_3$)



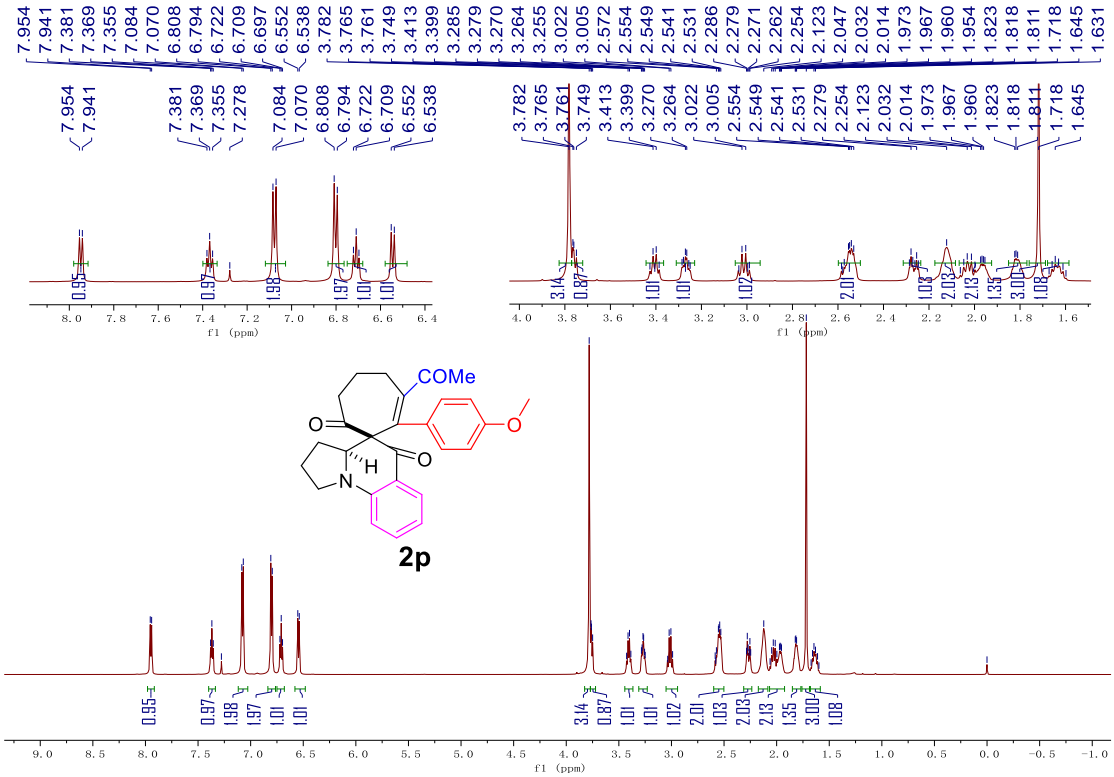
^{1}H NMR (600 MHz, $CDCl_3$)



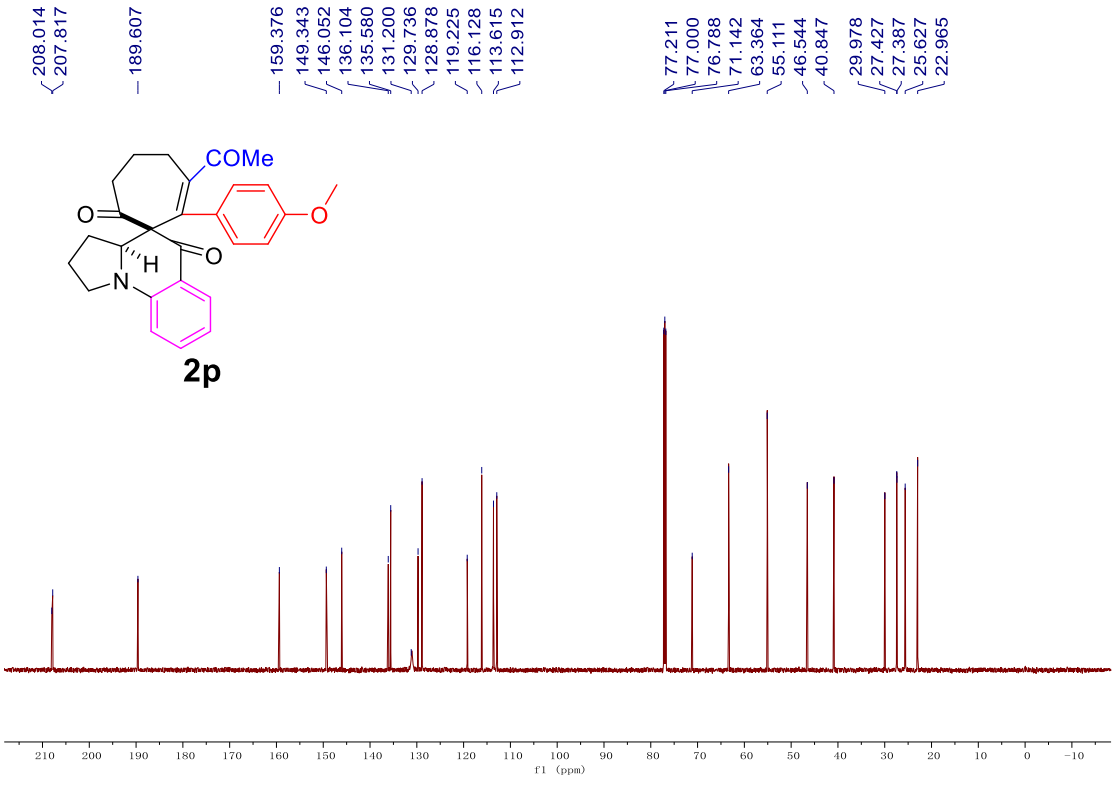
^{13}C NMR (150 MHz, $CDCl_3$)



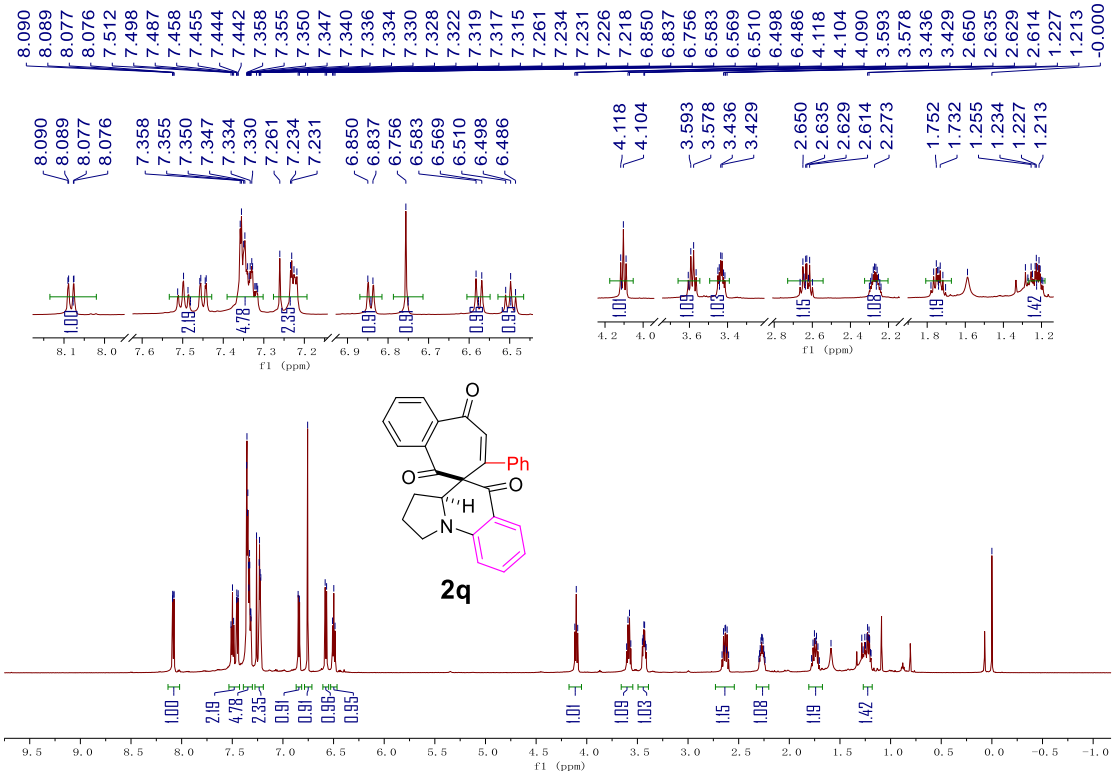
^{1}H NMR (600 MHz, $CDCl_3$)



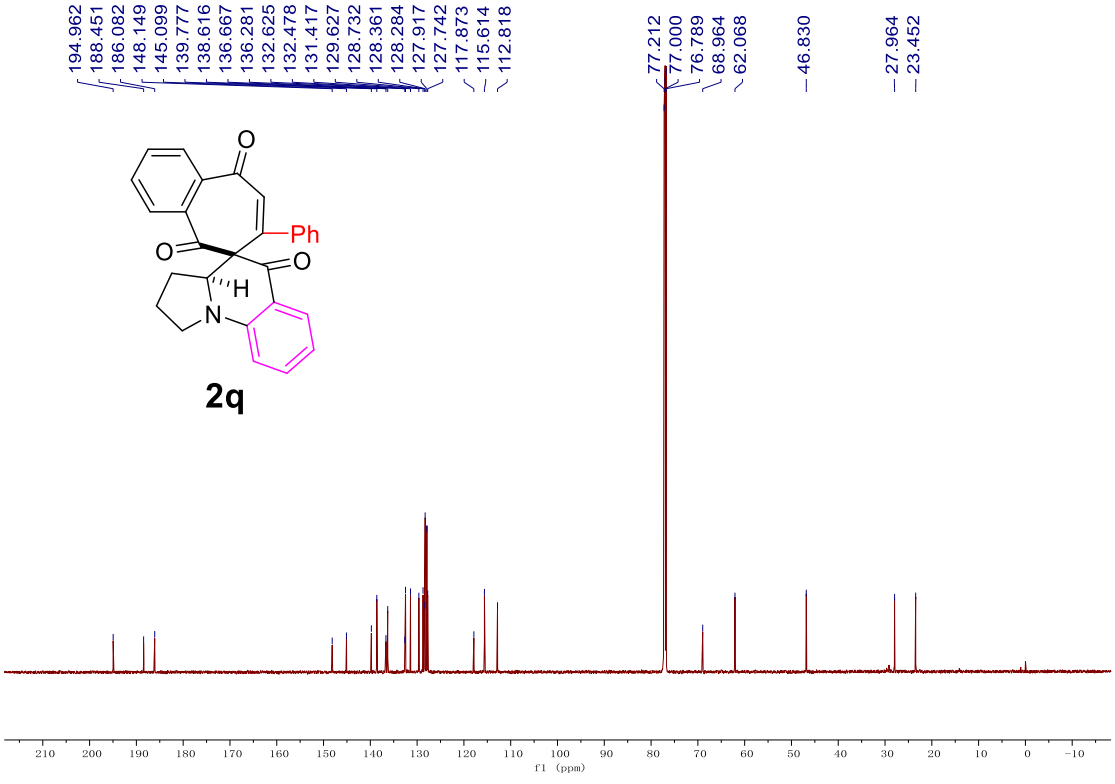
^{13}C NMR (150 MHz, $CDCl_3$)



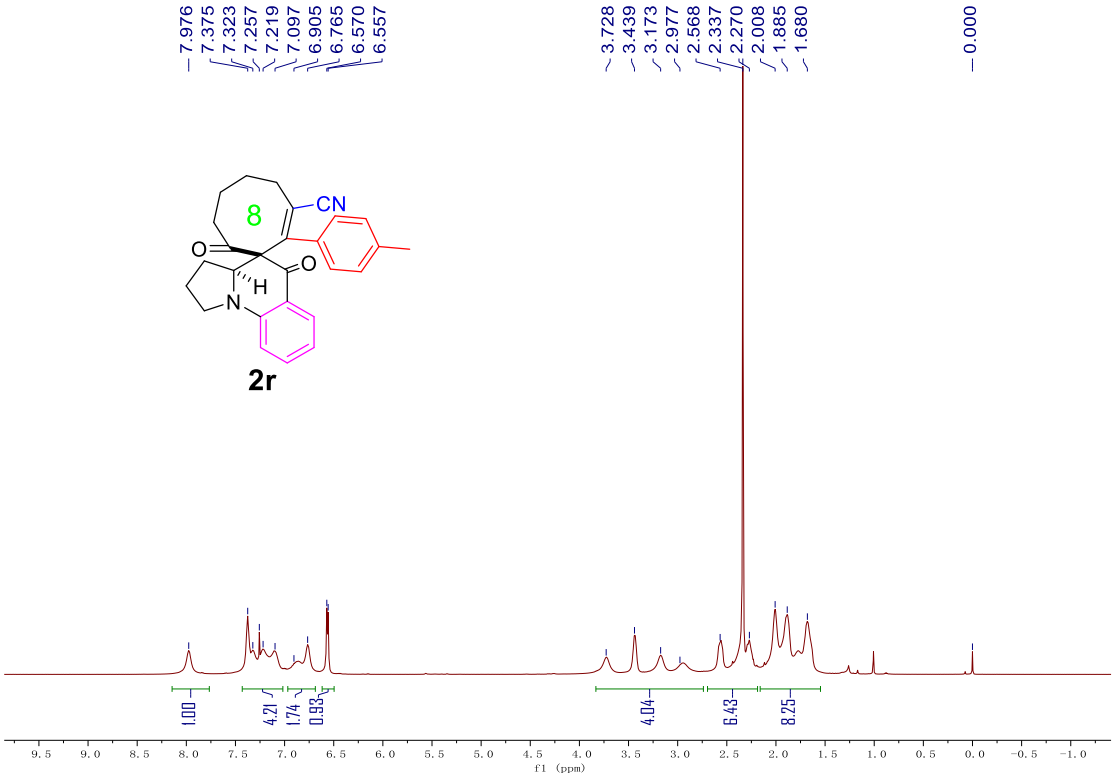
^{1}H NMR (600 MHz, $CDCl_3$)



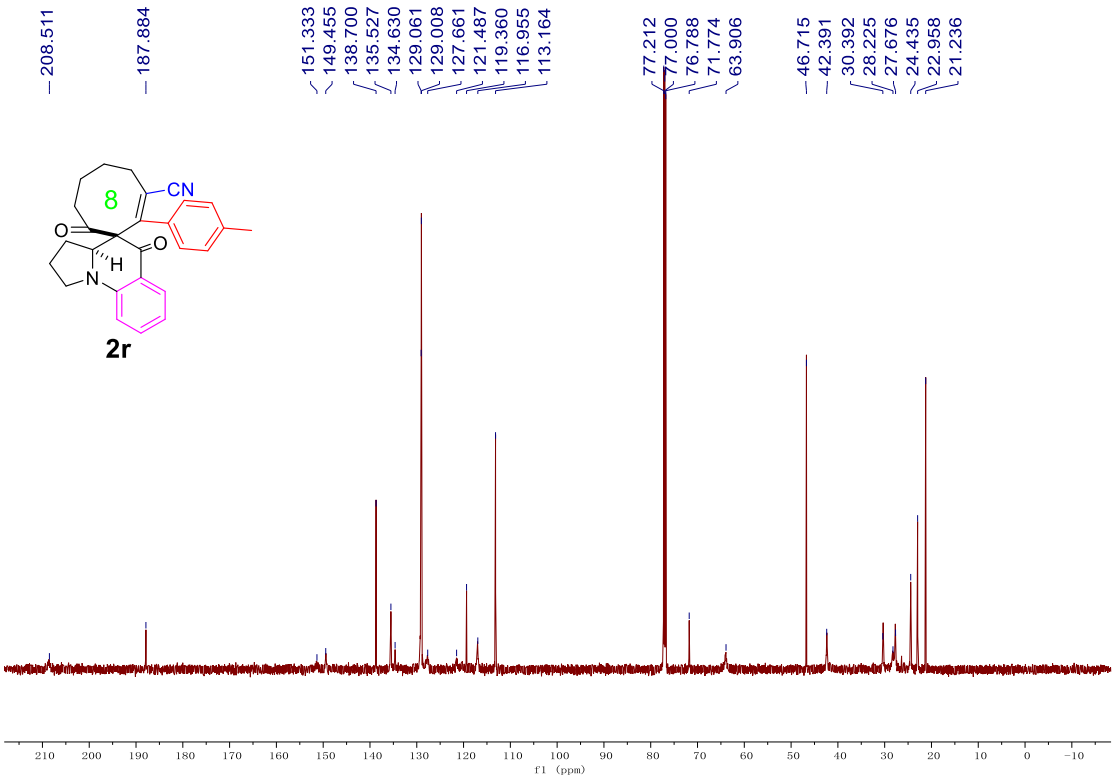
^{13}C NMR (150 MHz, $CDCl_3$)



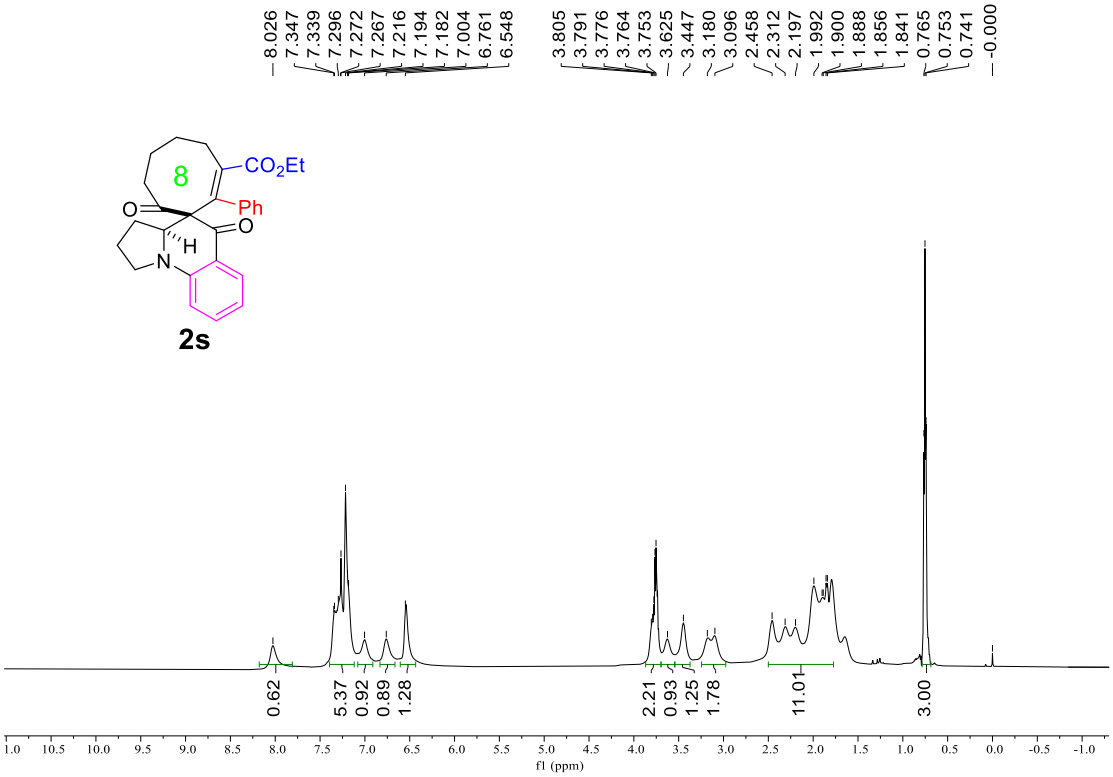
^{1}H NMR (600 MHz, $CDCl_3$)



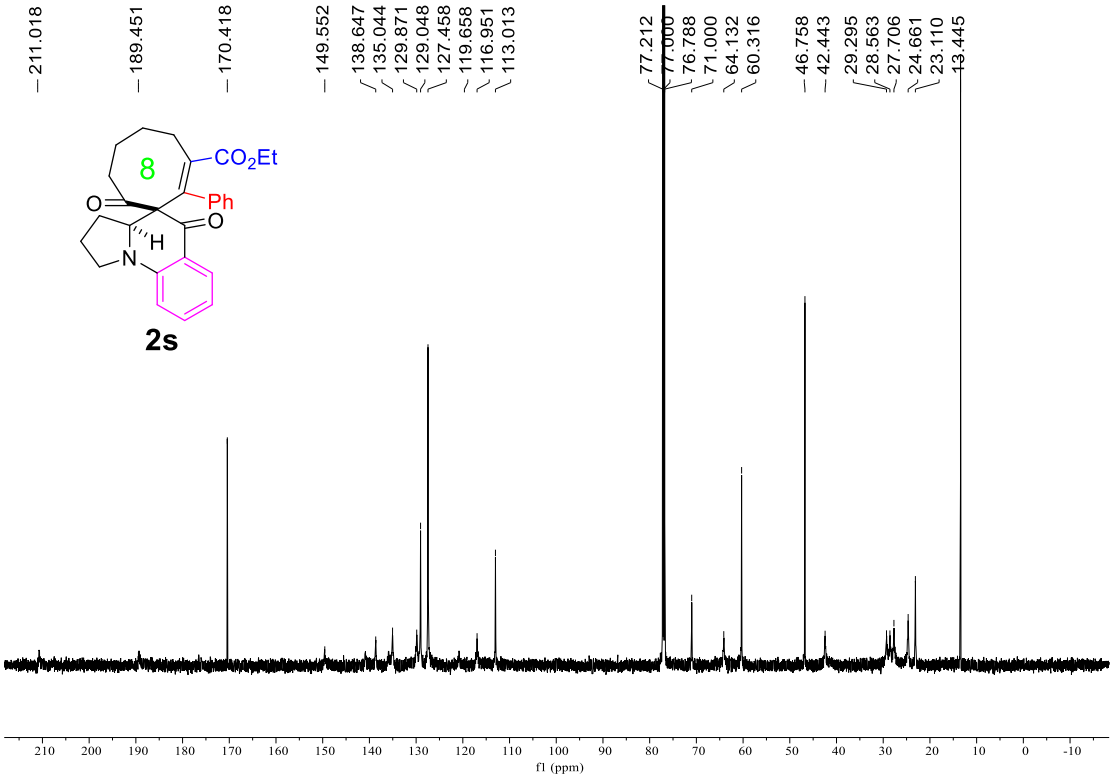
^{13}C NMR (150 MHz, $CDCl_3$)



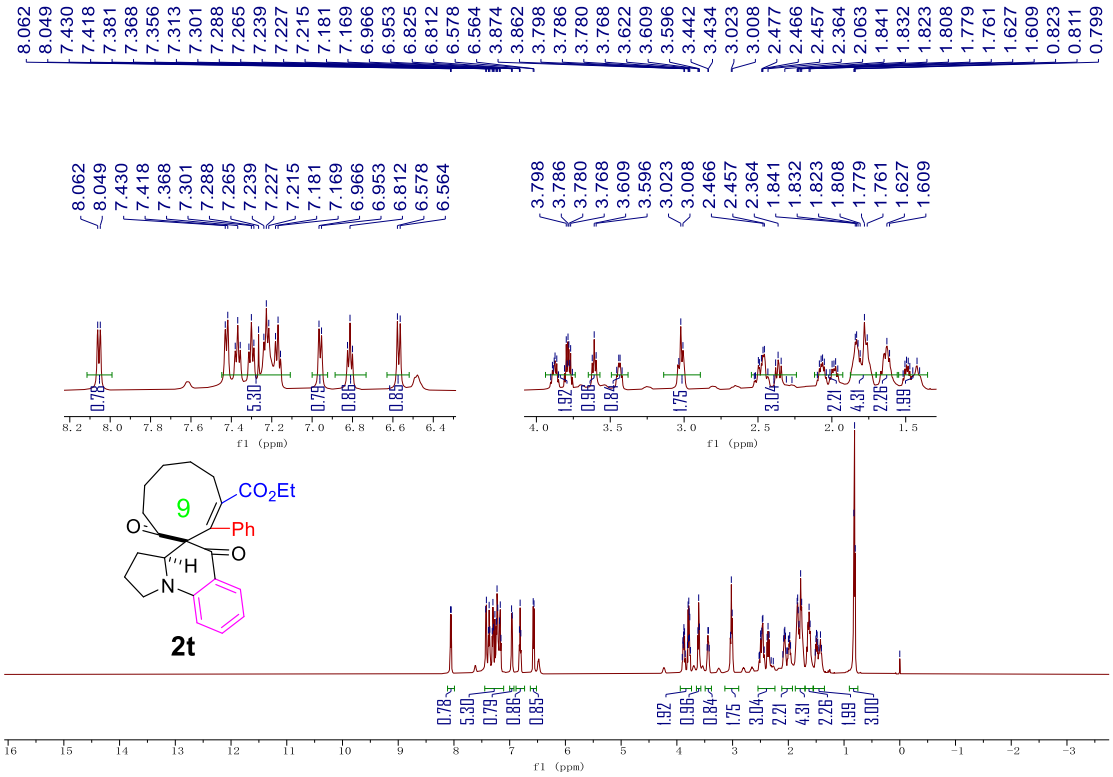
^{1}H NMR (600 MHz, $CDCl_3$)



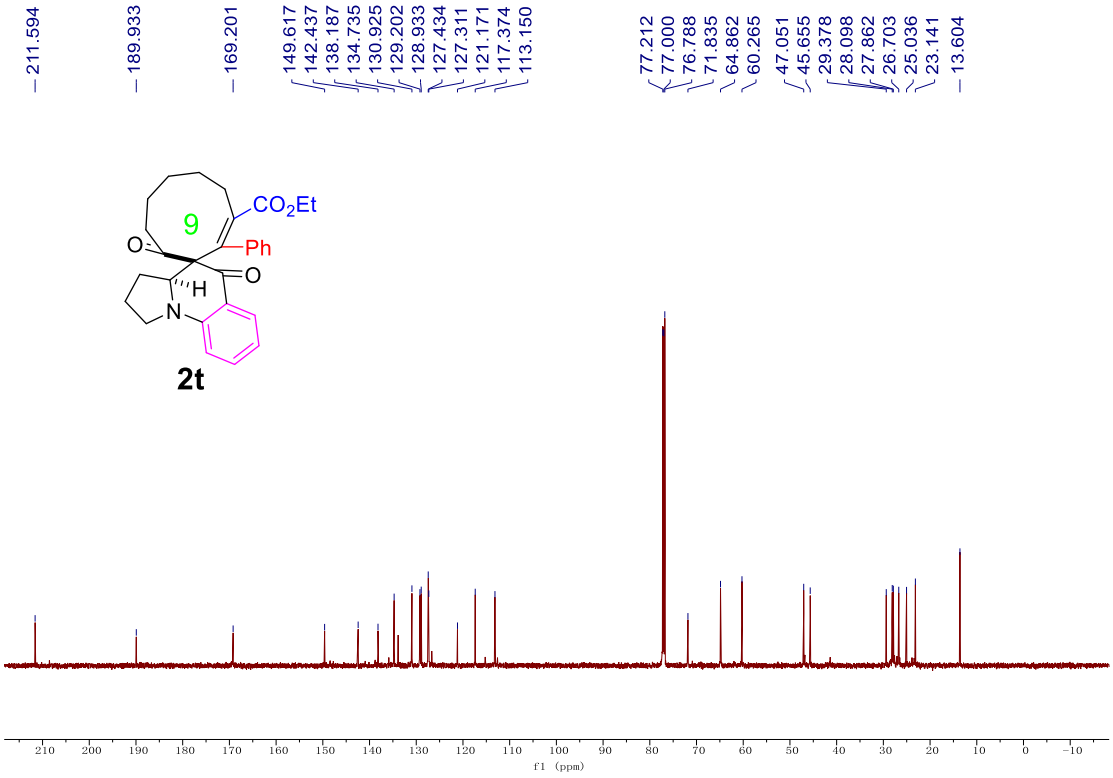
^{13}C NMR (150 MHz, $CDCl_3$)



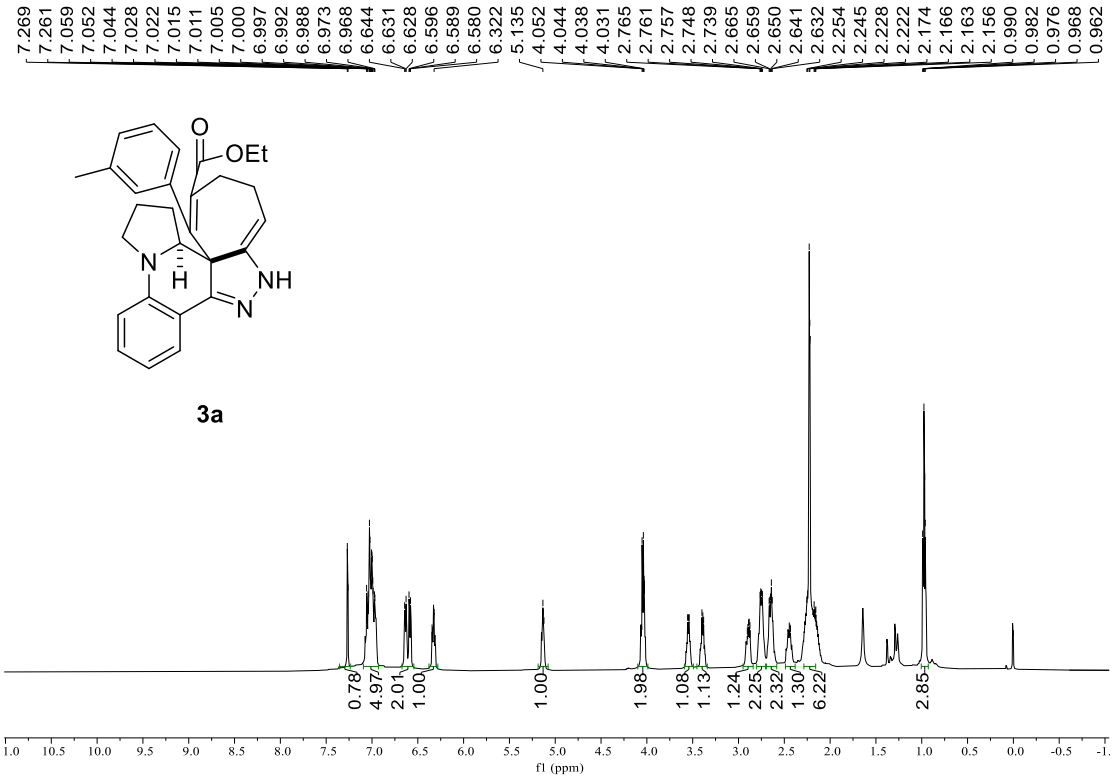
^{1}H NMR (600 MHz, $CDCl_3$)



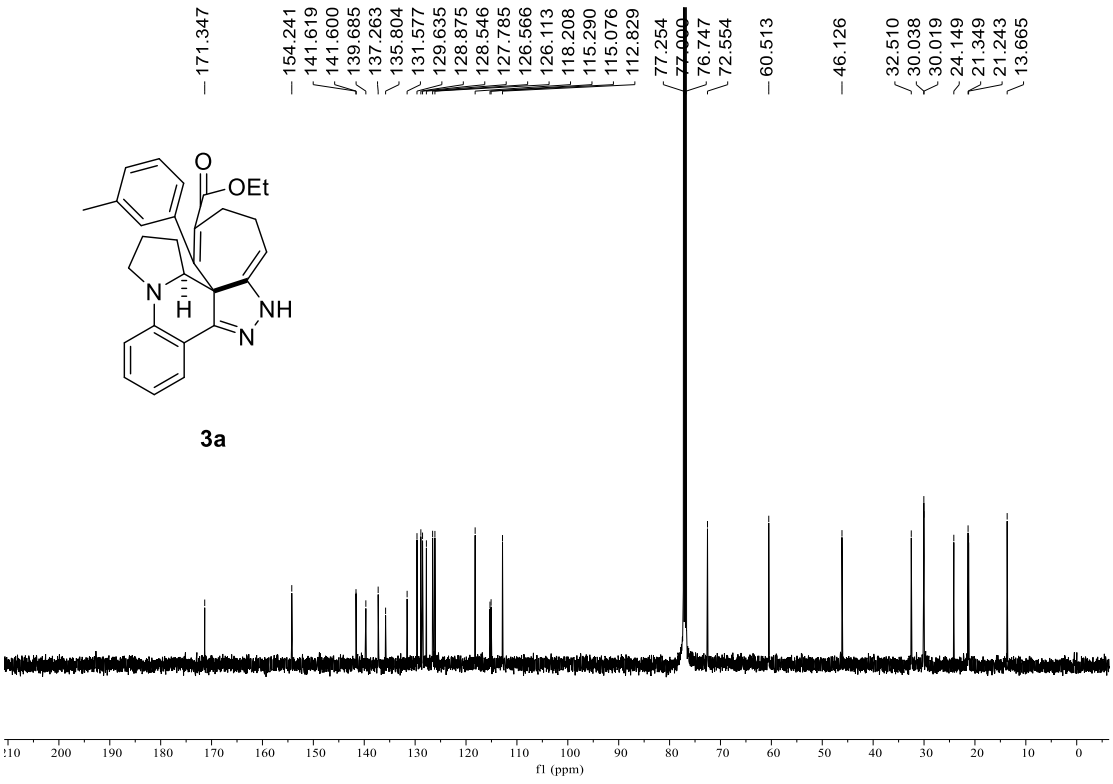
^{13}C NMR (150 MHz, $CDCl_3$)



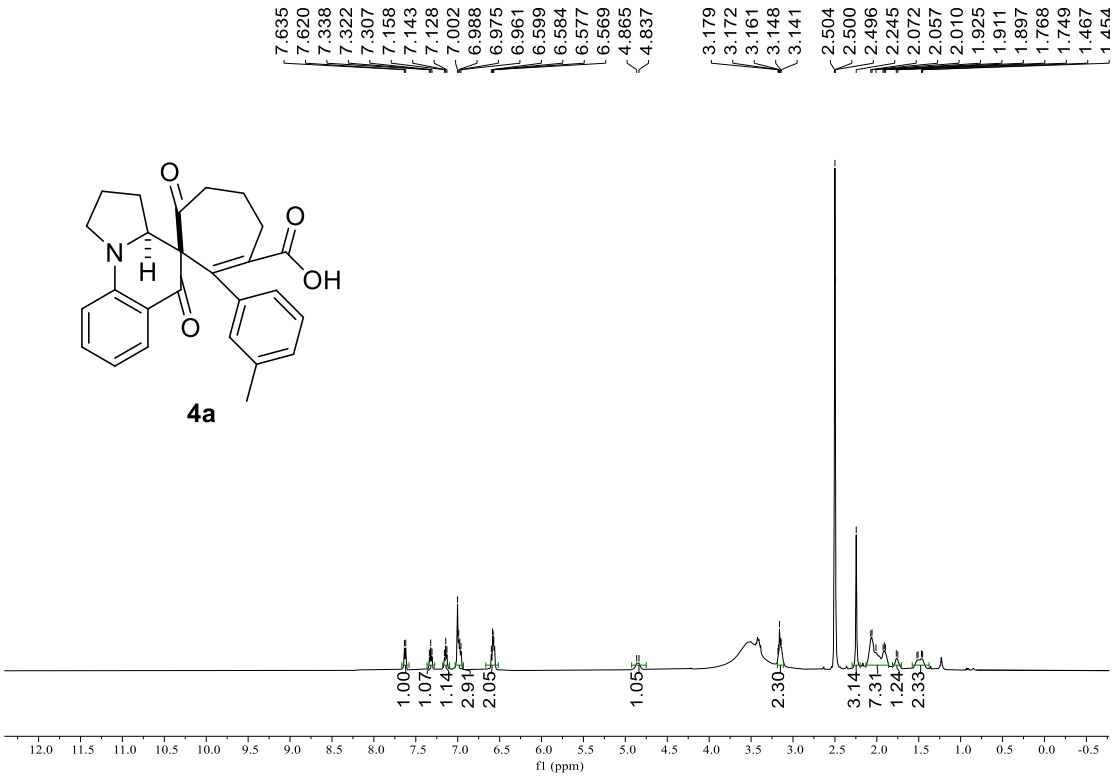
^{1}H NMR (500 MHz, $CDCl_3$)



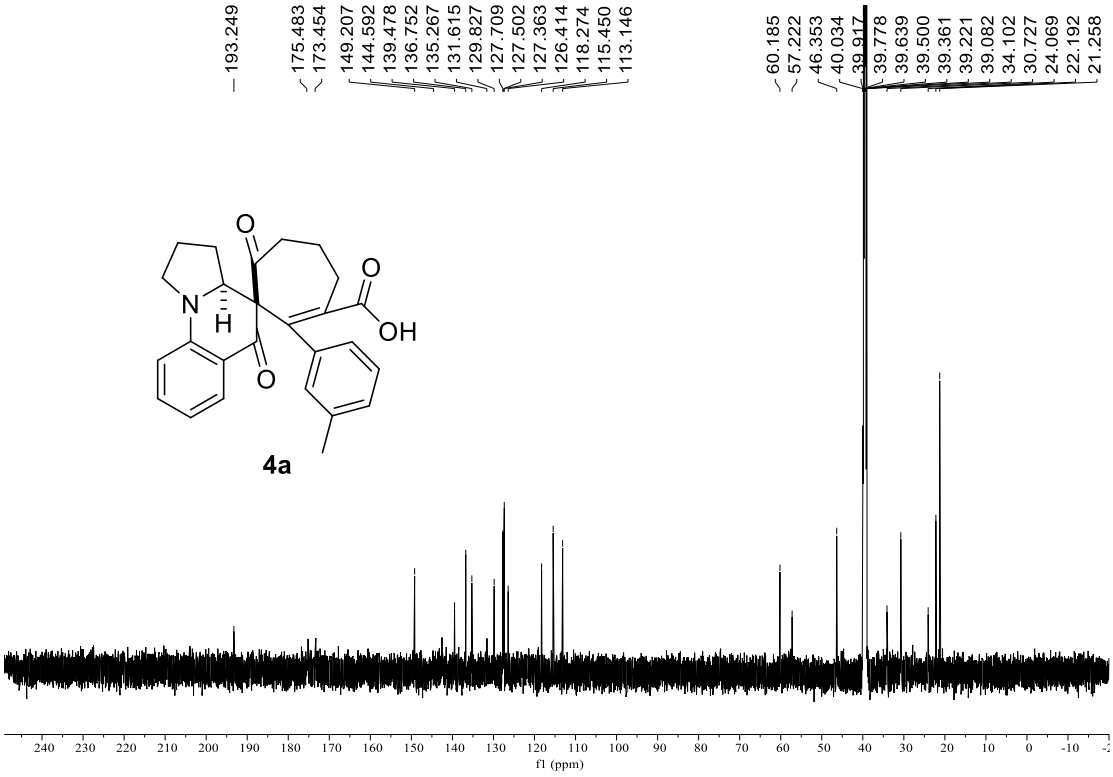
^{13}C NMR (125 MHz, $CDCl_3$)



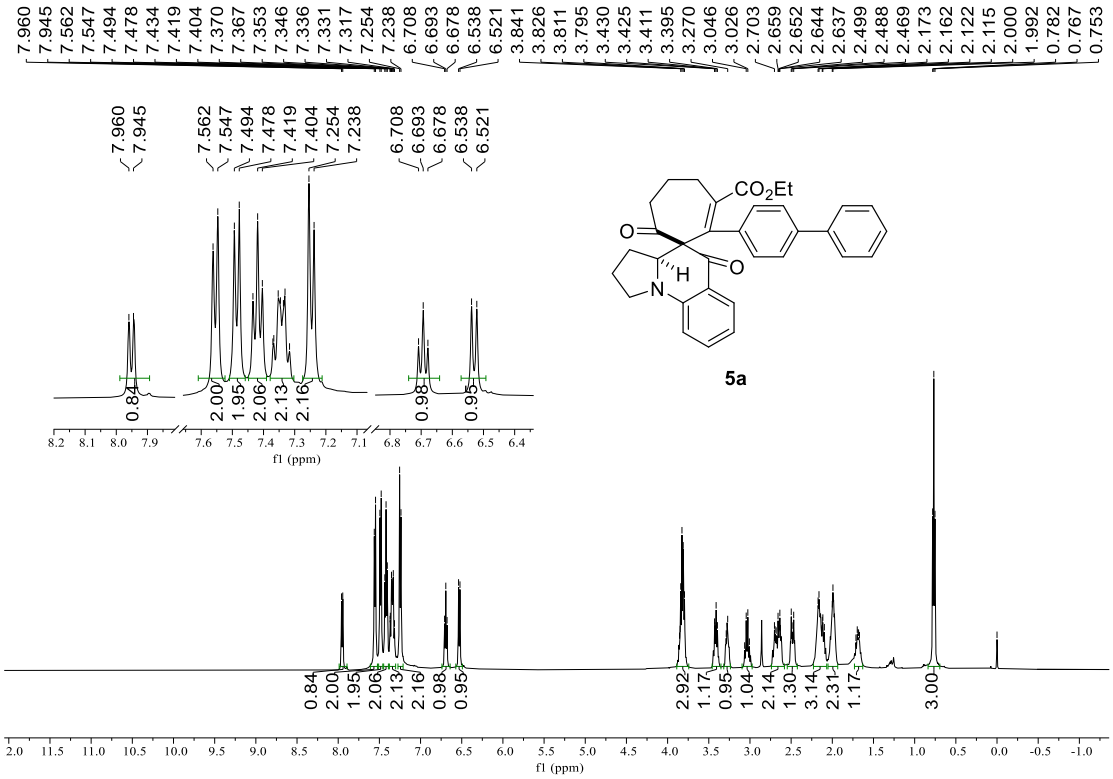
^{1}H NMR (500 MHz, $CDCl_3$)



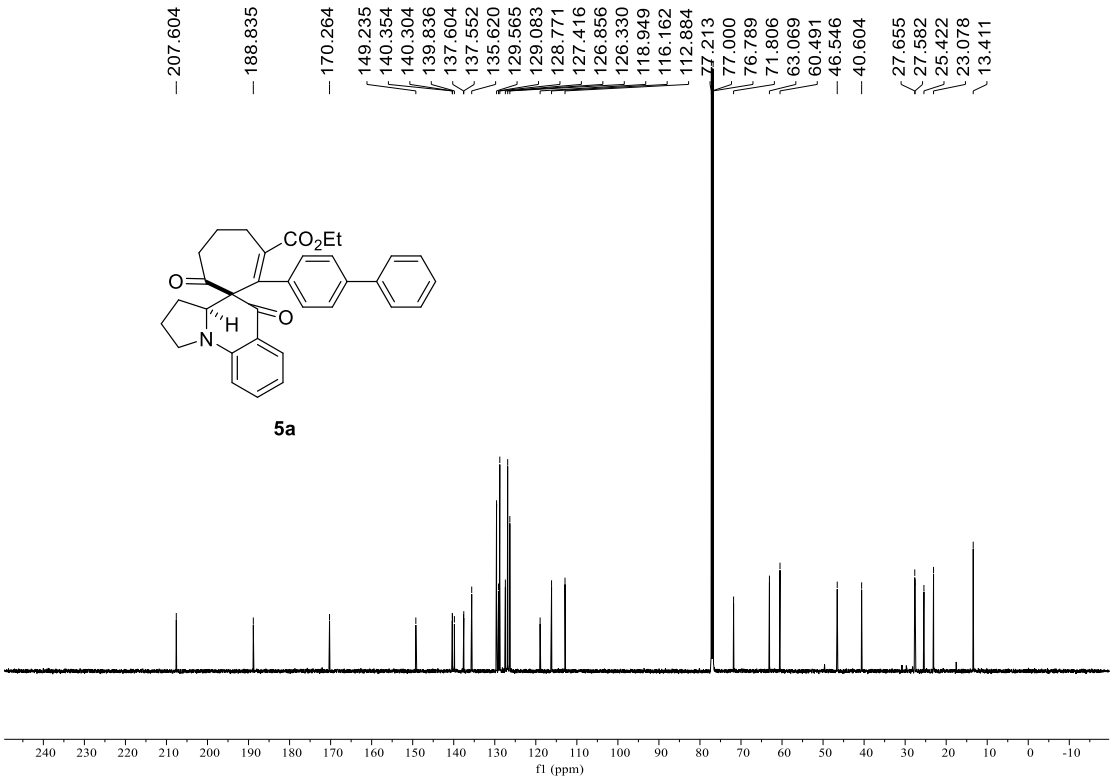
^{13}C NMR (150 MHz, $CDCl_3$)



^{1}H NMR (500 MHz, $CDCl_3$)



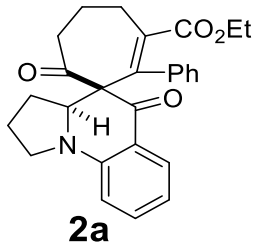
^{13}C NMR (150 MHz, $CDCl_3$)



9. X-ray crystallography of compound 2a.

Ethyl 5',7-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate **(2a, 2408683)**

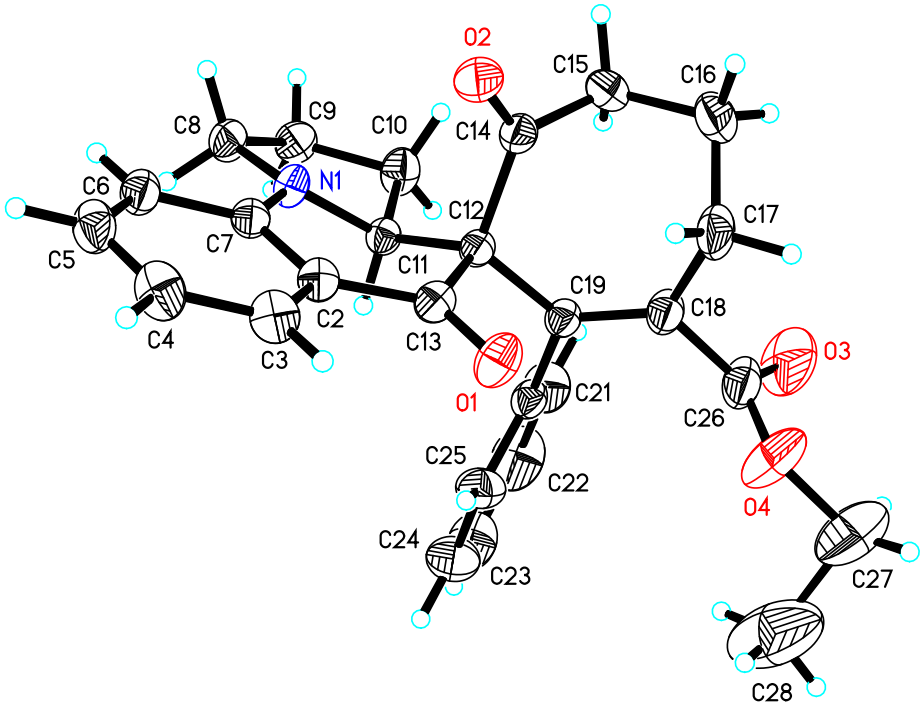
(Ortep ellipsoids are depicted at the 50% level)

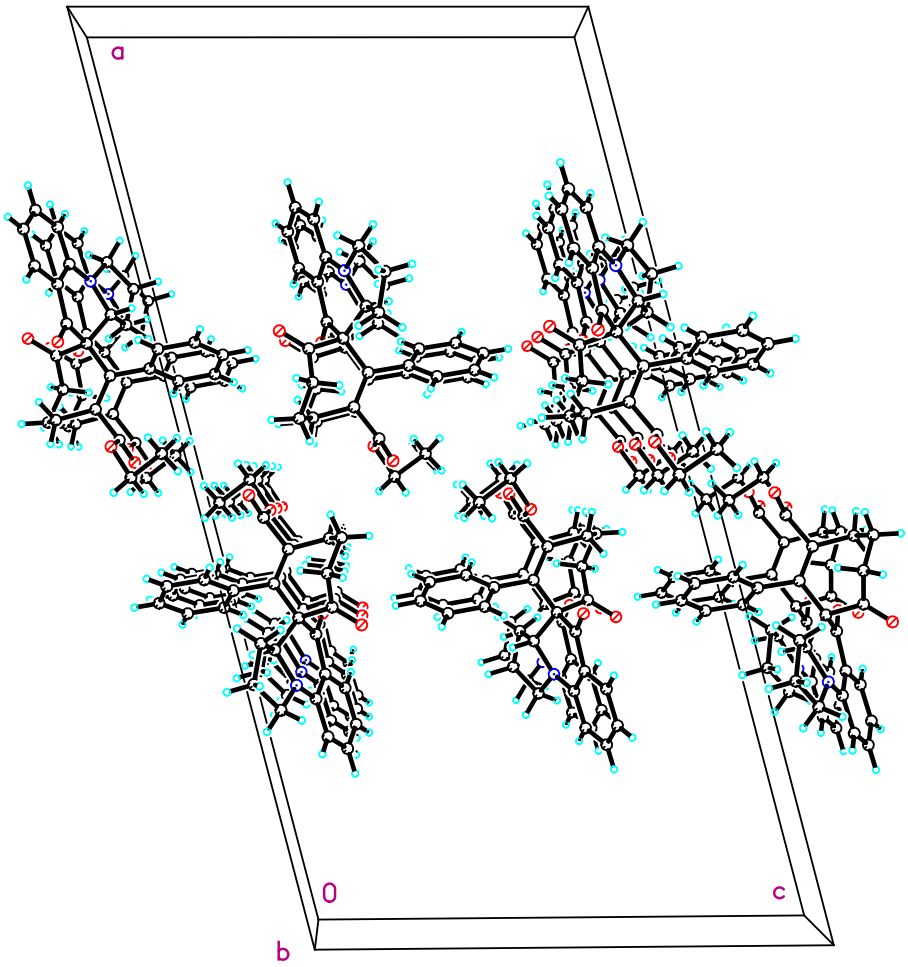


2a

Table S1. Crystal data and structure refinement for 2a.

Identification code	**2a**
Empirical formula	$C_{27}H_{27}NO_4$
Formula weight	429.49
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C 2/c
Unit cell dimensions	a = 34.8856(10) Å, α= 90° . b = 7.2721(2) Å, β= 104.4480(10)°. c = 18.6842(5) Å, γ = 90°.
Volume	4590.1(2) $Å^3$
Z	8
Density (calculated)	1.243 Mg/m^3
Absorption coefficient	0.083 mm^{-1}
F(000)	1824
Crystal size	0.20 x 0.14 x 0.12 mm^3
Theta range for data collection	2.412 to 26.000°.
Index ranges	-42<=h<=42, -7<=k<=8, -20<=l<=23
Reflections collected	22543
Independent reflections	4475 [R(int) = 0.0383]
Completeness to theta = 26.000°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6559
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4475 / 42 / 319
Goodness-of-fit on F^2	1.021
Final R indices [I>2sigma(I)]	R1 = 0.0473, wR2 = 0.1143
R indices (all data)	R1 = 0.0637, wR2 = 0.1274
Extinction coefficient	0.0156(11)
Largest diff. peak and hole	0.235 and -0.229 e.$Å^{-3}$

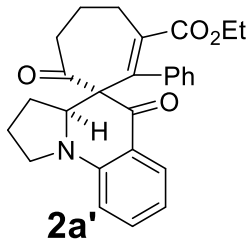

O2
C15
C16
C8
C9
C10
C14
N1
C6
C12
C17
C7
C5
C11
C19
C18
C2
C4
C3
C13
O3
O1
C21
C26
C25
C22
O4
C24
C23
C27
C28


a
0
c
b

10. X-ray crystallography of compound 2a'.

***Ethyl 5',7-dioxo-2-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[cycloheptane-1,4'-pyrrolo[1,2-a]quinolin]-2-ene-3-carboxylate* (2a', 2408693)**

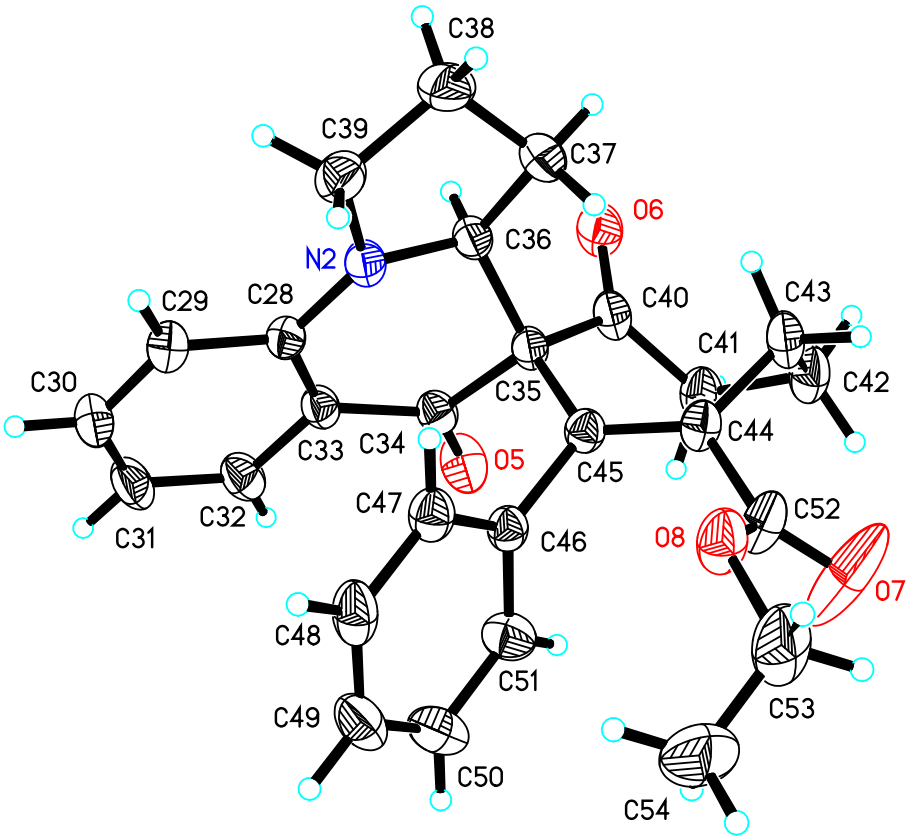
(Ortep ellipsoids are depicted at the 50% level)

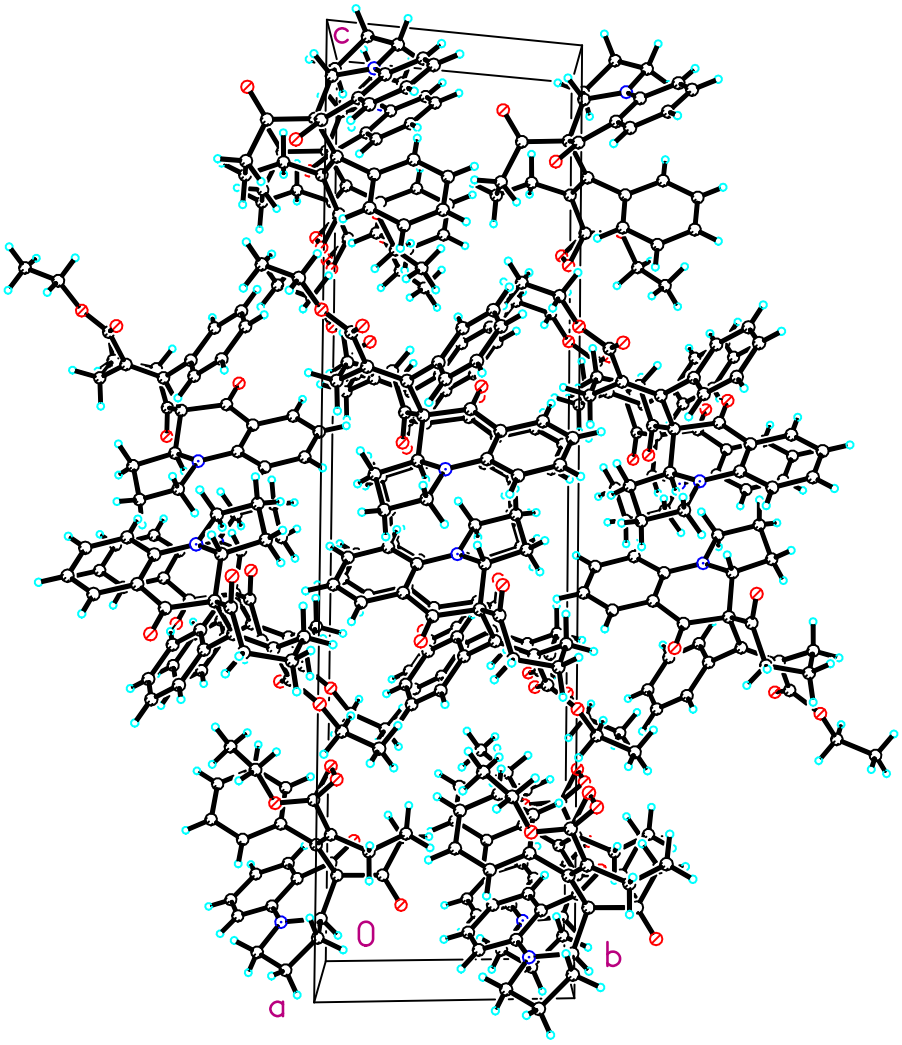


2a'

Table S1. Crystal data and structure refinement for 2a'.

Identification code	**2a'**
Empirical formula	$C_{27}H_{27}NO_4$
Formula weight	429.49
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a = 8.5471(5) Å, α= 90.700(2)° . b = 8.7952(4) Å, β= 93.038(2)°. c = 31.1174(17) Å, γ = 109.550(2)°.
Volume	2200.1(2) $Å^3$
Z	4
Density (calculated)	1.297 Mg/m^3
Absorption coefficient	0.087 mm^{-1}
F(000)	912
Crystal size	0.200 x 0.150 x 0.100 mm^3
Theta range for data collection	1.967 to 26.000°.
Index ranges	-10<=h<=10, -10<=k<=10, -38<=l<=38
Reflections collected	33637
Independent reflections	8642 [R(int) = 0.0383]
Completeness to theta = 26.000°	99. 7%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.5126
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8642 / 6 / 589
Goodness-of-fit on F^2	1.025
Final R indices [I>2sigma(I)]	R1 = 0.0512, wR2 = 0.1213
R indices (all data)	R1 = 0.0741, wR2 = 0.1389
Extinction coefficient	0.039(3)
Largest diff. peak and hole	0.329 and -0.277 $e.Å^{-3}$


C38
C39
C37
O6
N2
C36
C29
C28
C40
C43
C41
C30
C35
C42
C33
C34
O5
C44
C45
C47
C52
C32
C31
C46
O8
O7
C48
C51
C53
C49
C50
C54


c
0
b
a