Electronic Supporting Information

Chemodivergent mechanosynthesis of cyclopentenyl and pyrrolinyl spirobarbiturates from unsaturated barbiturates and enamino esters

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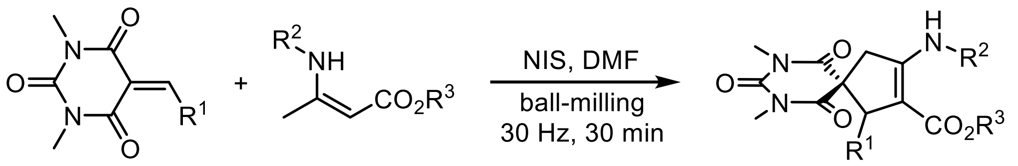
1. General information

All reagents were obtained from commercial sources and used without further purification. NMR spectra were recorded on a 500 MHz NMR spectrometer (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR). ^{1}H NMR chemical shifts were determined relative to internal TMS at δ 0.0 ppm. ^{13}C NMR chemical shifts were determined relative to $CDCl_3$ at δ 77.16 ppm. Data for ^{1}H NMR and ^{13}C NMR are reported as follows: chemical shift (δ, ppm) and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and bs = broad singlet). All melting points were determined on a XT-4 binocular microscope melting point apparatus. High-resolution mass spectra (HRMS) were measured with ESI-TOF in the positive mode. Unsaturated barbiturates **1**[1] and enamino esters **2**[2] were prepared according to the reported protocols.

2. Synthetic procedures for the synthesis of 3, 4 and 6aa

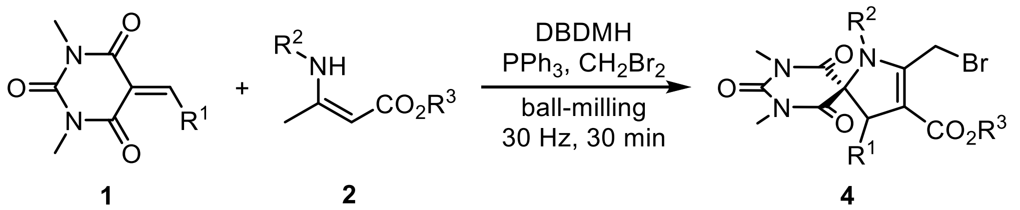
2.1 General procedure for the synthesis of cyclopentenyl spirobarbiturates 3



1 **2** **3**

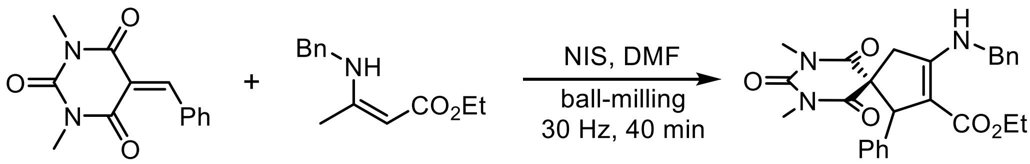
A mixture of unsaturated barbiturates **1** (0.2 mmol), enamino esters **2** (0.24 mmol), NIS (0.24 mmol) and DMF (30 μL) together with four stainless balls (6 mm in diameter) was introduced into a stainless steel jar (5 mL). The reaction vessel along with another identical empty vessel was closed and fixed on the vibration arms of a Retsch MM400 mixer mill, and was vibrated vigorously at a rate of 1800 rounds per minute (30 Hz) at room temperature for 30 min. After completion of the reaction, the resulting mixture was extracted with ethyl acetate, and the combined solution was evaporated to remove the solvent in vacuo. Then, the residue was separated by flash column chromatography on silica gel with ethyl acetate/petroleum ether as the eluent to afford cyclopentenyl spirobarbiturates **3**.

2.2 General procedure for the synthesis of pyrrolinly spirobarbiturates 4



A mixture of unsaturated barbiturates **1** (0.2 mmol), enamino esters **2** (0.24 mmol), DBDMH (0.2 mmol), PPh_3 (0.2 mmol) and CH_2Br_2 (30 μL) together with four stainless balls (6 mm in diameter) was introduced into a stainless steel jar (5 mL). The reaction vessel along with another identical empty vessel was closed and fixed on the vibration arms of a Retsch MM400 mixer mill, and was vibrated vigorously at a rate of 1800 rounds per minute (30 Hz) at room temperature for 30 min. After completion of the reaction, the resulting mixture was extracted with ethyl acetate, and the combined solution was evaporated to remove the solvent in vacuo. Then, the residue was separated by flash column chromatography on silica gel with ethyl acetate/petroleum ether as the eluent to afford pyrrolinly spirobarbiturates **4**.

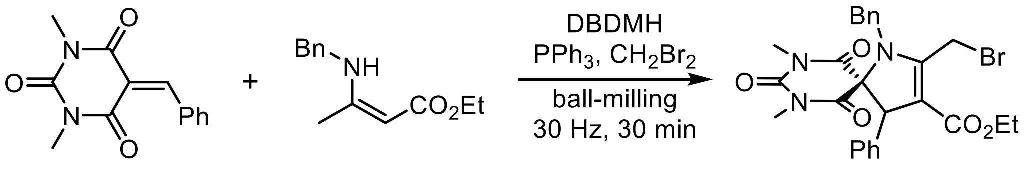
2.3 Procedure for the gram-scale synthesis of 3aa



1a (4.0 mmol) **2a** (4.8 mmol) **3aa** (1.617 g, 88%)

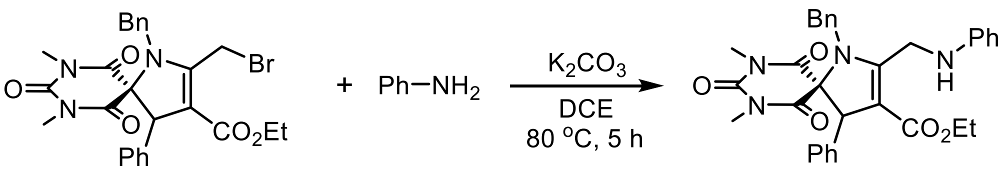
A mixture of unsaturated barbiturate **1a** (0.976 g, 4.0 mmol), enamino ester **2a** (1.051 g, 4.8 mmol), NIS (1.080 g, 4.8 mmol) and DMF (0.6 mL) together with a stainless ball (12 mm in diameter) was introduced into a stainless steel jar (25 mL). The reaction vessel along with another identical empty vessel was closed and fixed on the vibration arms of a Retsch MM400 mixer mill, and was vibrated vigorously at a rate of 1800 rounds per minute (30 Hz) at room temperature for 40 min. After completion of the reaction, the resulting mixture was extracted with ethyl acetate, and the combined solution was evaporated to remove the solvent in vacuo. Then, the residue was separated by flash column chromatography on silica gel with ethyl acetate/petroleum ether (1/4, v/v) as the eluent to afford **3aa** in 88% yield (1.617 g).

2.4 Procedure for the gram-scale synthesis of 4aa



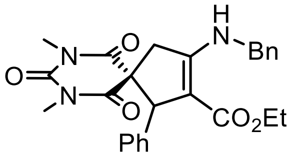
A mixture of unsaturated barbiturate **1a** (0.976 g, 4.0 mmol), enamino ester **2a** (1.051 g, 4.8 mmol), DBDMH (1.144 g, 4.0 mmol), PPh_3 (1.048 g, 4.0 mmol), and CH_2Br_2 (0.6 mL) together with a stainless ball (12 mm in diameter) was introduced into a stainless steel jar (25 mL). The reaction vessel along with another identical empty vessel was closed and fixed on the vibration arms of a Retsch MM400 mixer mill, and was vibrated vigorously at a rate of 1800 rounds per minute (30 Hz) at room temperature for 40 min. After completion of the reaction, the resulting mixture was extracted with ethyl acetate, and the combined solution was evaporated to remove the solvent in vacuo. Then, the residue was separated by flash column chromatography on silica gel with ethyl acetate/petroleum ether (1/6, v/v) as the eluent to afford **4aa** in 67% yield (1.451 g).

2.5 Procedure for the synthesis of 6aa

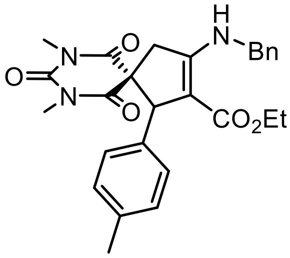


In a 25 mL of glass tube, a mixture of **4aa** (108.1 mg, 0.2 mmol), aniline (37.2 mg, 0.4 mmol), K_2CO_3 (27.6 mg, 0.2 mmol), and DCE (2 mL) was stirred and heated in an oil bath at 80 °C for 5 h. After cooling, the reaction mixture was filtered under reduced pressure, and then, the solution was concentrated in vacuo. The residue was separated by column chromatography on silica gel with ethyl acetate/petroleum ether (1:4) as the eluent to afford substitution product **6aa** (95.2 mg, 86% yield).

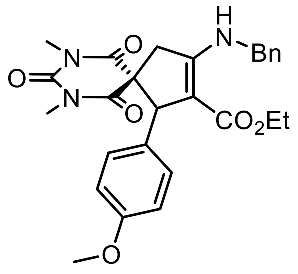
3. Characterization data for 3, 4 and 6aa



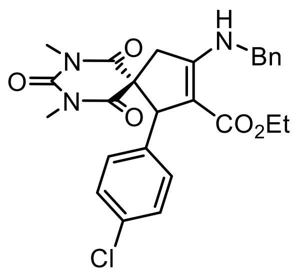
Ethyl 3-(benzylamino)-7,9-dimethyl-6,8,10-trioxo-1-phenyl-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3aa). White solid, 91% yield (84.3 mg), mp 157–159 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (bs, 1H), 7.44–7.37 (m, 4H), 7.34–7.29 (m, 1H), 7.26–7.19 (m, 3H), 7.01 (bs, 2H), 4.56 (d, J = 6.3 Hz, 2H), 4.47 (s, 1H), 3.93–3.86 (m, 1H), 3.82–3.74 (m, 1H), 3.49 (d, J = 16.8 Hz, 1H), 3.39 (d, J = 16.8 Hz, 1H), 3.37 (s, 3H), 2.56 (s, 3H), 0.79 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 168.7, 167.1, 163.0, 151.2, 139.6, 138.3, 129.0 (2C), 128.1 (2C), 128.0 (2C), 127.9, 127.8, 127.1 (2C), 91.5, 63.1, 60.6, 58.7, 48.6, 35.4, 29.4, 28.4, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{28}N_3O_5$ $[M + H]^+$ 462.2029, found 462.2036.



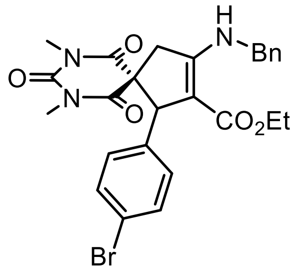
Ethyl 3-(benzylamino)-7,9-dimethyl-6,8,10-trioxo-1-(*p*-tolyl)-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ba). White solid, 89% yield (84.8 mg), mp 139–141 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (bs, 1H), 7.43–7.36 (m, 4H), 7.33–7.28 (m, 1H), 7.03 (d, J = 7.9 Hz, 2H), 6.88 (d, J = 6.5 Hz, 2H), 4.55 (d, J = 6.3 Hz, 2H), 4.43 (s, 1H), 3.93–3.77 (m, 2H), 3.48 (d, J = 16.8 Hz, 1H), 3.36(s, 3H), 3.35 (d, J = 16.8 Hz, 1H), 2.58 (s, 3H), 2.29 (s, 3H), 0.82 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 168.8, 167.1, 162.9, 151.2, 138.4, 137.5, 136.4, 129.0 (2C), 128.7 (2C), 127.8 (2C), 127.7, 127.1 (2C), 91.6, 62.8, 60.6, 58.7, 48.6, 35.2, 29.3, 28.4, 21.2, 14.1; HRMS (ESI-TOF) calcd for $C_{27}H_{30}N_3O_5$ $[M + H]^+$ 476.2185, found 476.2182.



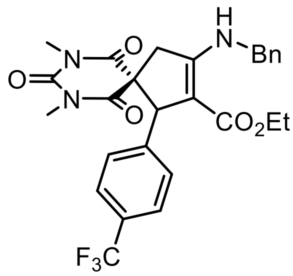
Ethyl 3-(benzylamino)-1-(4-methoxyphenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ca). White solid, 84% yield (82.2 mg), mp 141–143 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.00 (bs, 1H), 7.43–7.36 (m, 4H), 7.34–7.28 (m, 1H), 6.92 (d, J = 7.2 Hz, 2H), 6.77 (d, J = 8.7 Hz, 2H), 4.55 (d, J = 6.3 Hz, 2H), 4.42 (s, 1H), 3.94–3.86 (m, 1H), 3.85–3.78 (m, 1H), 3.78–3.75 (m, 3H), 3.49 (d, J = 16.8 Hz, 1H), 3.35 (d, J = 16.8 Hz, 1H), 3.37 (s, 3H), 2.63 (s, 3H), 0.84 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.3, 168.8, 167.1, 162.8, 159.3, 151.3, 138.4, 131.6, 129.1 (2C), 129.0 (2C), 127.8, 127.1 (2C), 113.5 (2C), 91.8, 62.6, 60.6, 58.7, 55.4, 48.6, 35.2, 29.3, 28.6, 14.2; HRMS (ESI-TOF) calcd for $C_{27}H_{30}N_3O_6$ $[M + H]^+$ 492.2135, found 492.2139.



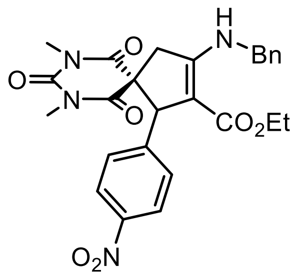
Ethyl 3-(benzylamino)-1-(4-chlorophenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3da). White solid, 92% yield (91.1 mg), mp 156–158 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.02 (bs, 1H), 7.42–7.36 (m, 4H), 7.34–7.29 (m, 1H), 7.22 (d, J = 8.7 Hz, 2H), 6.96 (d, J = 7.4 Hz, 2H), 4.55 (d, J = 6.3 Hz, 2H), 4.43 (s, 1H), 3.93–3.86 (m, 1H), 3.84–3.77 (m, 1H), 3.49 (d, J = 16.8 Hz, 1H), 3.374 (d, J = 16.8 Hz, 1H), 3.372 (s, 3H), 2.64 (s, 3H), 0.83 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.1, 168.6, 166.9, 163.1, 151.1, 138.3, 138.2, 133.7, 129.4 (2C), 129.1 (2C), 128.3 (2C), 127.9, 127.1 (2C), 91.3, 62.3, 60.3, 58.8, 48.6, 35.5, 29.4, 28.6, 14.2; HRMS (ESI-TOF) calcd for $C_{26}H_{27}ClN_3O_5$ $[M + H]^+$ 496.1639, found 496.1643.



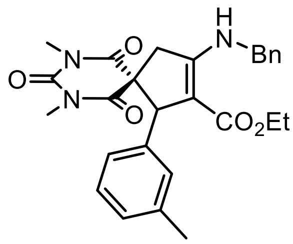
Ethyl 3-(benzylamino)-1-(4-bromophenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ea). White solid, 91% yield (97.9 mg), mp 151–153 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.02 (bs, 1H), 7.43–7.34 (m, 6H), 7.33–7.28 (m, 1H), 6.90 (d, J = 7.4 Hz, 2H), 4.55 (d, J = 6.3 Hz, 2H), 4.41 (s, 1H), 3.93–3.86 (m, 1H), 3.85–3.77 (m, 1H), 3.49 (d, J = 16.8 Hz, 1H), 3.370 (d, J = 16.8 Hz, 1H), 3.368 (s, 3H), 2.63 (s, 3H), 0.84 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.0, 168.5, 166.8, 163.2, 151.0, 138.8, 138.2, 131.2 (2C), 129.7 (2C), 129.0 (2C), 127.8, 127.1 (2C), 121.8, 91.2, 62.3, 60.2, 58.8, 48.6, 35.5, 29.4, 28.5, 14.2; HRMS (ESI-TOF) calcd for $C_{26}H_{27}BrN_3O_5$ [M + H]$^+$ 540.1134, found 540.1143.



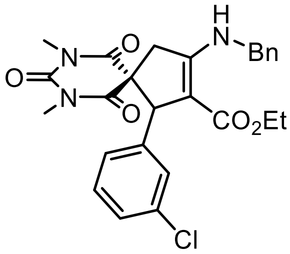
Ethyl 3-(benzylamino)-7,9-dimethyl-6,8,10-trioxo-1-(4-(trifluoromethyl)phenyl)-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3fa). White solid, 83% yield (88.0 mg), mp 149–151 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.05 (bs, 1H), 7.51 (d, J = 8.1 Hz, 2H), 7.44–7.36 (m, 4H), 7.34–7.29 (m, 1H), 7.15 (d, J = 7.1 Hz, 2H), 4.56 (d, J = 6.3 Hz, 2H), 4.51 (s, 1H), 3.93–3.85 (m, 1H), 3.82–3.75 (m, 1H), 3.51 (d, J = 16.8 Hz, 1H), 3.41 (d, J = 16.8 Hz, 1H), 3.38 (s, 3H), 2.55 (s, 3H), 0.79 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.9, 168.4, 166.7, 163.3, 150.9, 144.0, 138.1, 130.2 (q, J = 32.5 Hz), 129.0 (2C), 128.5 (2C), 127.9, 127.1 (2C), 125.0 (q, J = 2.8 Hz, 2C), 124.1 (q, J = 272.1 Hz), 91.0, 62.4, 60.2, 58.8, 48.6, 35.7, 29.4, 28.4, 14.0; HRMS (ESI-TOF) calcd for $C_{27}H_{27}F_3N_3O_5$ [M + H]$^+$ 530.1903, found 530.1914.



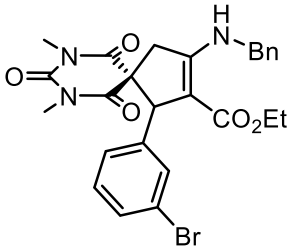
Ethyl 3-(benzylamino)-7,9-dimethyl-1-(4-nitrophenyl)-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ga). White solid, 76% yield (77.4 mg), mp 159–161 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (t, J = 8.7 Hz, 2H), 8.07 (bs, 1H), 7.46–7.36 (m, 4H), 7.35–7.30 (m, 1H), 7.22 (d, J = 7.5 Hz, 2H), 4.57 (d, J = 6.3 Hz, 2H), 4.54 (s, 1H), 3.92–3.77 (m, 2H), 3.53 (d, J = 16.9 Hz, 1H), 3.41 (d, J = 16.9 Hz, 1H), 3.39 (s, 3H), 2.62 (s, 3H), 0.81 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 168.2, 166.5, 163.5, 150.8, 147.5 (2C), 138.0, 129.08 (2C), 129.07 (2C), 127.9, 127.1 (2C), 123.3 (2C), 90.9, 61.9, 60.1, 58.9, 48.7, 35.8, 29.5, 28.5, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{27}N_4O_7$ $[M + H]^+$ 507.1880, found 507.1871.



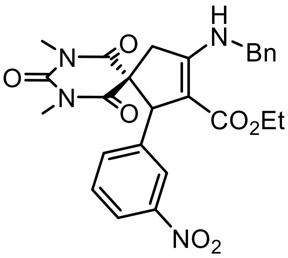
Ethyl 3-(benzylamino)-7,9-dimethyl-6,8,10-trioxo-1-(*m*-tolyl)-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ha). White solid, 91% yield (86.5 mg), mp 141–143 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (bs, 1H), 7.43–7.37 (m, 4H), 7.34–7.28 (m, 1H), 7.11 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 7.5 Hz, 1H), 6.79 (bs, 2H), 4.56 (d, J = 6.3 Hz, 2H), 4.43 (s, 1H), 3.96–3.88 (m, 1H), 3.83–3.74 (m, 1H), 3.47 (d, J = 16.7 Hz, 1H), 3.38 (d, J = 16.7 Hz, 1H), 3.37 (s, 3H), 2.57 (s, 3H), 2.29 (s, 3H), 0.82 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 168.7, 167.1, 163.0, 151.2, 139.4, 138.4, 137.7, 129.0 (2C), 128.6 (2C), 128.0, 127.8, 127.1 (2C), 125.1, 91.4, 63.1, 60.7, 58.6, 48.6, 35.3, 29.3, 28.4, 21.4, 14.2; HRMS (ESI-TOF) calcd for $C_{27}H_{30}N_3O_5$ $[M + H]^+$ 476.2186, found 476.2191.



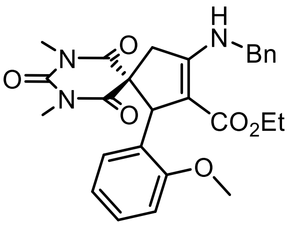
Ethyl 3-(benzylamino)-1-(3-chlorophenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ia). White solid, 88% yield (87.7 mg), mp 146–148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (bs, 1H), 7.44–7.36 (m, 4H), 7.34–7.29 (m, 1H), 7.23–7.15 (m, 2H), 7.02 (s, 1H), 6.90 (bs, 1H), 4.55 (d, J = 6.3 Hz, 2H), 4.42 (s, 1H), 3.97–3.89 (m, 1H), 3.84–3.76 (m, 1H), 3.48 (d, J = 16.8 Hz, 1H), 3.37 (s, 3H), 3.36 (d, J = 16.8 Hz, 1H), 2.66 (s, 3H), 0.84 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 168.4, 166.8, 163.4, 151.0, 141.8, 138.1, 134.2, 129.3, 129.0 (2C), 128.1 (2C), 127.8, 127.1 (2C), 126.2, 90.9, 62.3, 60.4, 58.8, 48.6, 35.4, 29.4, 28.5, 14.2; HRMS (ESI-TOF) calcd for $C_{26}H_{27}ClN_3O_5$ $[M + H]^+$ 496.1639, found 496.1644.



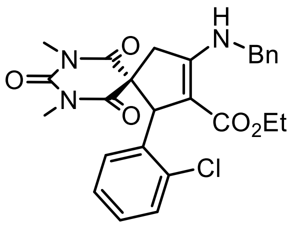
Ethyl 3-(benzylamino)-1-(3-bromophenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ja). White solid, 85% yield (91.8 mg), mp 136–138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (bs, 1H), 7.43–7.35 (m, 5H), 7.34–7.29 (m, 1H), 7.17 (s, 1H), 7.12 (t, J = 7.8 Hz, 1H), 6.95 (bs, 1H), 4.55 (d, J = 6.3 Hz, 2H), 4.41 (s, 1H), 3.98–3.90 (m, 1H), 3.84–3.76 (m, 1H), 3.47 (d, J = 16.8 Hz, 1H), 3.37 (s, 3H), 3.36 (d, J = 16.8 Hz, 1H), 2.66 (s, 3H), 0.84 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 168.4, 166.8, 163.4, 151.0, 142.1, 138.1, 131.0 (2C), 129.6, 129.0 (2C), 127.8, 127.1 (2C), 126.7, 122.3, 90.8, 62.3, 60.4, 58.8, 48.6, 35.4, 29.4, 28.6, 14.2; HRMS (ESI-TOF) calcd for $C_{26}H_{27}BrN_3O_5$ $[M + H]^+$ 540.1134, found 540.1138.



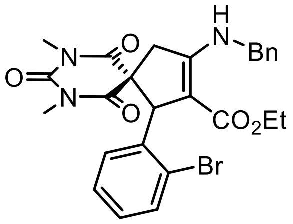
Ethyl 3-(benzylamino)-7,9-dimethyl-1-(3-nitrophenyl)-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ka). White solid, 73% yield (73.7 mg), mp 156–158 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.15–8.08 (m, 1H), 8.08 (bs, 1H), 7.91 (s, 1H), 7.48–7.35 (m, 6H), 7.35–7.30 (m, 1H), 4.58 (d, J = 6.3 Hz, 2H), 4.55 (s, 1H), 3.94–3.77 (m, 2H), 3.52 (d, J = 16.8 Hz, 1H), 3.39 (s, 3H), 3.38 (d, J = 16.8 Hz, 1H), 2.62 (s, 3H), 0.82 (t, J = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.7, 168.2, 166.5, 163.7, 150.8, 148.1, 142.2, 138.0, 134.1, 129.1 (2C), 129.0, 127.9, 127.0 (2C), 123.0 (2C), 90.6, 61.9, 60.1, 58.9, 48.7, 35.6, 29.5, 28.6, 14.2; HRMS (ESI-TOF) calcd for $C_{26}H_{27}N_4O_7$ [M + H]$^+$ 507.1880, found 507.1883.



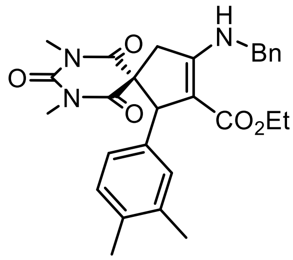
Ethyl 3-(benzylamino)-1-(2-methoxyphenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3la). White solid, 82% yield (80.8 mg), mp 203–205 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.97 (bs, 1H), 7.42–7.36 (m, 4H), 7.33–7.28 (m, 1H), 7.16 (td, J = 7.8, 1.6 Hz, 1H), 7.04 (dd, J = 7.6, 1.4 Hz, 1H), 6.85 (t, J = 7.5 Hz, 1H), 6.78 (d, J = 8.2 Hz, 1H), 5.14 (s, 1H), 4.54 (d, J = 6.3 Hz, 2H), 3.96–3.89 (m, 1H), 3.81–3.74 (m, 1H), 3.74–3.71 (m, 3H), 3.54 (d, J = 16.9 Hz, 1H), 3.36 (s, 3H), 3.33 (d, J = 16.9 Hz, 1H), 2.60 (s, 3H), 0.80 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.7, 169.1, 167.0, 162.7, 156.6, 151.5, 138.5, 129.5, 129.0 (2C), 128.6, 127.9, 127.7, 127.1 (2C), 120.5, 109.4, 91.5, 59.3, 58.6, 55.8, 53.8, 48.6, 36.2, 29.2, 28.3, 14.1; HRMS (ESI-TOF) calcd for $C_{27}H_{30}N_3O_6$ [M + H]$^+$ 492.2135, found 492.2133.



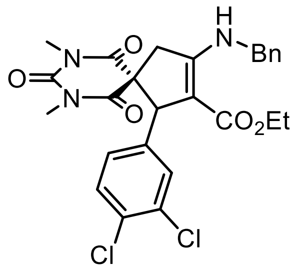
Ethyl 3-(benzylamino)-1-(2-chlorophenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ma). White solid, 87% yield (86.0 mg), mp 173–175 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (bs, 1H), 7.43–7.37 (m, 4H), 7.34–7.28 (m, 2H), 7.19–7.11 (m, 3H), 5.18 (s, 1H), 4.55 (d, J = 6.3 Hz, 2H), 3.90–3.83 (m, 1H), 3.82–3.75 (m, 1H), 3.55 (d, J = 16.8 Hz, 1H), 3.36 (d, J = 16.8 Hz, 1H), 3.34 (s, 3H), 2.66 (s, 3H), 0.80 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 168.8, 166.8, 163.0, 151.1, 138.3, 137.3, 133.7, 130.4, 129.02 (2C), 128.96, 128.8, 127.8, 127.1 (2C), 126.7, 92.0, 59.4, 58.7, 57.0, 48.6, 36.2, 29.4, 28.5, 14.0; HRMS (ESI-TOF) calcd for $C_{26}H_{27}ClN_3O_5$ $[M + H]^+$ 496.1639, found 496.1648.



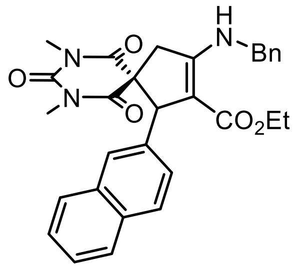
Ethyl 3-(benzylamino)-1-(2-bromophenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3na). White solid, 86% yield (92.9 mg), mp 167–169 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (bs, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.43–7.36 (m, 4H), 7.34–7.29 (m, 1H), 7.20 (t, J = 7.4 Hz, 1H), 7.11 (dd, J = 7.8, 1.5 Hz, 1H), 7.06 (td, J = 7.6, 1.6 Hz, 1H), 5.17 (s, 1H), 4.55 (dd, J = 6.3, 2.1 Hz, 2H), 3.89–3.76 (m, 2H), 3.57 (d, J = 16.8 Hz, 1H), 3.35 (s, 3H), 3.34 (d, J = 16.8 Hz, 1H), 2.66 (s, 3H), 0.81 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 168.8, 166.7, 162.9, 151.1, 139.0, 138.3, 132.3, 130.6, 129.1, 129.0 (2C), 127.8, 127.2, 127.1 (2C), 124.6, 92.6, 59.8, 59.4, 58.7, 48.6, 36.2, 29.4, 28.5, 14.0; HRMS (ESI-TOF) calcd for $C_{26}H_{27}BrN_3O_5$ $[M + H]^+$ 540.1134, found 540.1131.



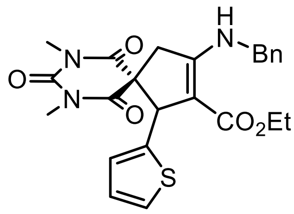
Ethyl 3-(benzylamino)-1-(3,4-dimethylphenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3oa). White solid, 90% yield (88.1 mg), mp 131–133 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (bs, 1H), 7.43–7.37 (m, 4H), 7.34–7.28 (m, 1H), 6.98 (d, J = 7.7 Hz, 1H), 6.78–6.66 (m, 2H), 4.55 (d, J = 6.3 Hz, 2H), 4.41 (s, 1H), 3.95–3.87 (m, 1H), 3.86–3.79 (m, 1H), 3.47 (d, J = 16.8 Hz, 1H), 3.37 (s, 3H), 3.34 (d, J = 16.8 Hz, 1H), 2.58 (s, 3H), 2.20 (s, 3H), 2.19 (s, 3H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 168.8, 167.2, 162.9, 151.3, 138.4, 136.7, 136.2, 136.1, 129.3, 129.0 (3C), 127.7, 127.1 (2C), 125.4, 91.6, 62.8, 60.8, 58.7, 48.6, 35.2, 29.3, 28.5, 19.8, 19.5, 14.2; HRMS (ESI-TOF) calcd for $C_{28}H_{32}N_3O_5$ $[M + H]^+$ 490.2342, found 490.2345.



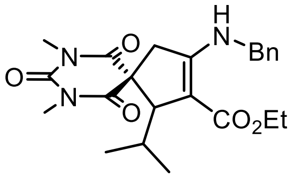
Ethyl 3-(benzylamino)-1-(3,4-dichlorophenyl)-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3pa). White solid, 88% yield (93.7 mg), mp 167–169 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (bs, 1H), 7.44–7.35 (m, 4H), 7.35–7.29 (m, 2H), 7.12 (s, 1H), 6.87 (d, J = 5.9 Hz, 1H), 4.55 (d, J = 6.3 Hz, 2H), 4.39 (s, 1H), 3.96–3.89 (m, 1H), 3.87–3.79 (m, 1H), 3.48 (d, J = 16.9 Hz, 1H), 3.37 (s, 3H), 3.34 (d, J = 16.9 Hz, 1H), 2.71 (s, 3H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 168.3, 166.7, 163.4, 150.9, 140.2, 138.0, 132.4, 131.8, 130.0, 129.9, 129.0 (2C), 127.9, 127.4, 127.1 (2C), 90.7, 61.6, 60.2, 58.9, 48.6, 35.4, 29.4, 28.6, 14.2; HRMS (ESI-TOF) calcd for $C_{26}H_{26}Cl_2N_3O_5$ $[M + H]^+$ 530.1250, found 530.1258.



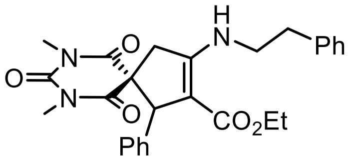
Ethyl 3-(benzylamino)-7,9-dimethyl-1-(naphthalen-2-yl)-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3qa). White solid, 83% yield (85.2 mg), mp 170–172 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (bs, 1H), 7.80–7.74 (m, 2H), 7.72 (d, J = 8.5 Hz, 1H), 7.51–7.38 (m, 7H), 7.35–7.29 (m, 1H), 7.14 (bs, 1H), 4.64 (s, 1H), 4.59 (d, J = 6.3 Hz, 2H), 3.86–3.74 (m, 2H), 3.56 (d, J = 16.8 Hz, 1H), 3.41 (d, J = 16.8 Hz, 1H), 3.40 (s, 3H), 2.36 (s, 3H), 0.71 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 168.6, 167.1, 163.2, 151.1, 138.3, 137.1, 133.1, 133.0, 129.0 (2C), 127.9, 127.8, 127.68, 127.65, 127.1 (2C), 127.0, 126.2, 126.0 (2C), 91.5, 63.0, 60.6, 58.7, 48.6, 35.4, 29.4, 28.4, 14.1; HRMS (ESI-TOF) calcd for $C_{30}H_{30}N_3O_5$ $[M + H]^+$ 512.2186, found 512.2181.



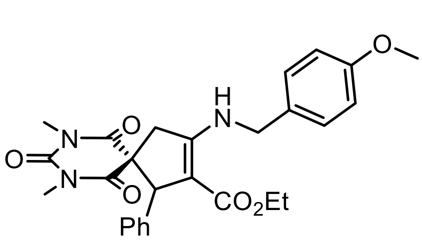
Ethyl 3-(benzylamino)-7,9-dimethyl-6,8,10-trioxo-1-(thiophen-2-yl)-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ra). White solid, 51% yield (47.3 mg), mp e–148 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (bs, 1H), 7.42–7.36 (m, 4H), 7.33–7.28 (m, 1H), 7.16 (d, J = 5.0 Hz, 1H), 6.92–6.88 (m, 1H), 6.73 (d, J = 3.0 Hz, 1H), 4.73 (s, 1H), 4.55 (d, J = 6.3 Hz, 2H), 4.01–3.94 (m, 1H), 3.89–3.81 (m, 1H), 3.54 (d, J = 16.8 Hz, 1H), 3.37 (s, 3H), 3.29 (d, J = 16.8 Hz, 1H), 2.83 (s, 3H), 0.90 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 168.3, 166.9, 162.9, 151.2, 144.2, 138.2, 129.0 (2C), 127.7, 127.0 (2C), 126.7, 125.5, 125.0, 92.1, 60.7, 58.8, 56.9, 48.5, 34.8, 29.4, 28.8, 14.2; HRMS (ESI-TOF) calcd for $C_{24}H_{26}N_3O_5S$ $[M + H]^+$ 468.1593, found 468.1594.



Ethyl 3-(benzylamino)-1-isopropyl-7,9-dimethyl-6,8,10-trioxo-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3sa). White solid, 46% yield (39.5 mg), mp 80–82 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.12 (bs, 1H), 7.39–7.32 (m, 4H), 7.30–7.24 (m, 1H), 4.52 (dd, J = 15.6, 6.6 Hz, 1H), 4.47 (dd, J = 15.6, 6.3 Hz, 1H), 4.18–4.11 (m, 1H), 4.04–3.97 (m, 1H), 3.47 (d, J = 16.7 Hz, 1H), 3.30 (s, 3H), 3.29 (s, 3H), 3.23 (t, J = 5.9 Hz, 1H), 2.90 (d, J = 16.7 Hz, 1H), 1.74–1.66 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H), 0.94 (d, J = 7.0 Hz, 3H), 0.82 (d, J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.2, 169.4, 167.9, 163.8, 151.6, 138.5, 128.8 (2C), 127.6, 126.9 (2C), 89.8, 60.73, 60.69, 58.8, 48.5, 34.9, 32.9, 29.4, 29.2, 22.7, 18.3, 14.5; HRMS (ESI-TOF) calcd for $C_{23}H_{30}N_3O_5$ [M + H]$^+$ 428.2185, found 428.2188.

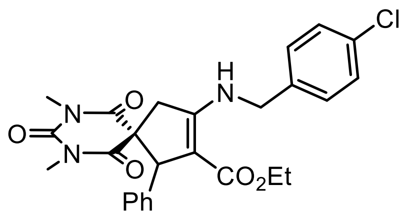


Ethyl 7,9-dimethyl-6,8,10-trioxo-3-(phenethylamino)-1-phenyl-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ab). White solid, 89% yield (84.4 mg), mp 97–99 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.71 (bs, 1H), 7.35 (t, J = 7.4 Hz, 2H), 7.29–7.18 (m, 6H), 7.00–6.93 (m, 2H), 4.42 (s, 1H), 3.92–3.85 (m, 1H), 3.81–3.73 (m, 1H), 3.61–3.55 (m, 2H), 3.40 (d, J = 16.7 Hz, 1H), 3.37 (s, 3H), 3.31 (d, J = 16.7 Hz, 1H), 3.02–2.92 (m, 2H), 2.57 (s, 3H), 0.78 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.2, 168.7, 166.9, 162.8, 151.2, 139.6, 138.4, 128.9 (2C), 128.8 (2C), 128.1 (2C), 128.0 (2C), 127.9, 126.8, 91.0, 63.0, 60.5, 58.6, 46.4, 37.6, 35.1, 29.3, 28.4, 14.1; HRMS (ESI-TOF) calcd for $C_{27}H_{30}N_3O_5$ [M + H]$^+$ 476.2186, found 476.2192.

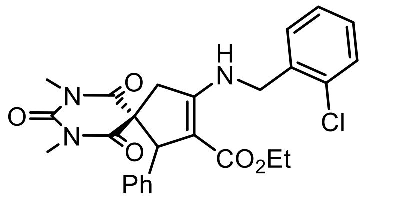


Ethyl 3-((4-methoxybenzyl)amino)-7,9-dimethyl-6,8,10-trioxo-1-phenyl-7,9-

diazaspiro[4.5]dec-2-ene-2-carboxylate (3ac). White solid, 90% yield (88.2 mg), mp 128–130 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.95 (bs, 1H), 7.31 (d, J = 8.6 Hz, 2H), 7.25–7.19 (m, 3H), 7.01 (bs, 2H), 6.92 (d, J = 8.6 Hz, 2H), 4.48 (d, J = 6.2 Hz, 2H), 4.46 (s, 1H), 3.92–3.85 (m, 1H), 3.80 (d, J = 6.4 Hz, 3H), 3.80–3.73 (m, 1H), 3.49 (d, J = 16.8 Hz, 1H), 3.40 (d, J = 16.8 Hz, 1H), 3.37 (s, 3H), 2.56 (s, 3H), 0.78 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.2, 168.7, 167.0, 163.0, 159.2, 151.1, 139.6, 130.3, 128.4 (2C), 128.1 (2C), 127.94 (2C), 127.87, 114.3 (2C), 91.2, 63.0, 60.6, 58.6, 55.4, 48.0, 35.4, 29.3, 28.4, 14.0; HRMS (ESI-TOF) calcd for $C_{27}H_{30}N_3O_6$ $[M + H]^+$ 492.2135, found 492.2129.

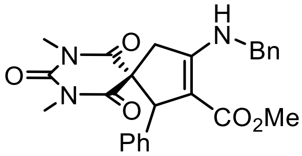


Ethyl 3-((4-chlorobenzyl)amino)-7,9-dimethyl-6,8,10-trioxo-1-phenyl-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ad). White solid, 87% yield (86.5 mg), mp 130–132 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.02 (bs, 1H), 7.38 (d, J = 8.5 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 7.26–7.20 (m, 3H), 7.08–6.93 (m, 2H), 4.52 (d, J = 6.4 Hz, 2H), 4.46 (s, 1H), 3.94–3.86 (m, 1H), 3.82–3.74 (m, 1H), 3.46 (d, J = 16.7 Hz, 1H), 3.37 (s, 3H), 3.36 (d, J = 16.7 Hz, 1H), 2.56 (s, 3H), 0.79 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.2, 168.7, 167.1, 162.9, 151.1, 139.4, 137.0, 133.6, 129.2 (2C), 128.4 (2C), 128.2 (2C), 128.0 (3C), 91.9, 63.1, 60.6, 58.8, 47.9, 35.4, 29.4, 28.5, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{27}ClN_3O_5$ $[M + H]^+$ 496.1639, found 496.1647.

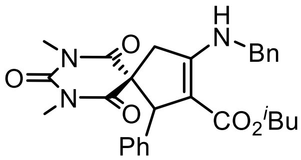


Ethyl 3-((2-chlorobenzyl)amino)-7,9-dimethyl-6,8,10-trioxo-1-phenyl-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ae). White solid, 81% yield (80.4 mg), mp 146–148 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.08 (bs, 1H), 7.51 (d, J = 7.5 Hz, 1H), 7.40 (d, J = 7.9 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.28 (d, J = 7.2 Hz, 1H), 7.26–7.19

(m, 3H), 7.01 (bs, 2H), 4.63 (d, J = 6.7 Hz, 2H), 4.47 (s, 1H), 3.95–3.87 (m, 1H), 3.83–3.76 (m, 1H), 3.49 (d, J = 16.8 Hz, 1H), 3.38 (d, J = 16.8 Hz, 1H), 3.37 (s, 3H), 2.55 (s, 3H), 0.80 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 168.6, 167.1, 162.9, 151.1, 139.4, 136.0, 132.9, 129.7, 129.0, 128.6, 128.1 (2C), 127.9 (3C), 127.5, 91.9, 63.1, 60.5, 58.7, 46.3, 35.2, 29.3, 28.4, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{27}ClN_3O_5$ $[M + H]^+$ 496.1639, found 496.1643.

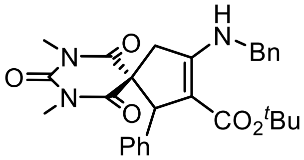


Methyl 3-(benzylamino)-7,9-dimethyl-6,8,10-trioxo-1-phenyl-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3af). White solid, 92% yield (82.3 mg), mp 190–192 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (bs, 1H), 7.44–7.36 (m, 4H), 7.34–7.28 (m, 1H), 7.27–7.20 (m, 3H), 7.01 (bs, 2H), 4.56 (d, J = 6.3 Hz, 2H), 4.47 (s, 1H), 3.50 (d, J = 16.8 Hz, 1H), 3.38 (s, 3H), 3.37 (s, 3H), 3.34 (d, J = 16.8 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 168.6, 167.5, 163.4, 151.1, 139.3, 138.3, 129.0 (2C), 128.2 (2C), 128.0, 127.9 (2C), 127.8, 127.1 (2C), 91.1, 62.8, 60.6, 50.3, 48.6, 35.3, 29.3, 28.5; HRMS (ESI-TOF) calcd for $C_{25}H_{26}N_3O_5$ $[M + H]^+$ 448.1873, found 448.1879.

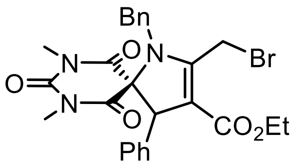


Isobutyl 3-(benzylamino)-7,9-dimethyl-6,8,10-trioxo-1-phenyl-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ag). White solid, 86% yield (84.1 mg), mp 160–162 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (bs, 1H), 7.45–7.35 (m, 4H), 7.33–7.28 (m, 1H), 7.27–7.17 (m, 3H), 7.02 (bs, 2H), 4.55 (d, J = 6.3 Hz, 2H), 4.47 (s, 1H), 3.72 (dd, J = 10.5, 6.4 Hz, 1H), 3.49 (d, J = 17.1 Hz, 1H), 3.50–3.44 (m, 1H), 3.39 (d, J = 17.1 Hz, 1H), 3.37 (s, 3H), 2.55 (s, 3H), 1.48–1.38 (m, 1H), 0.43 (d, J = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 168.7, 167.2, 163.2, 151.1, 139.5, 138.3, 129.0 (2C), 128.2 (2C), 128.0 (3C), 127.7, 127.1 (2C), 91.3, 69.0, 63.1, 60.5, 48.5, 35.4, 29.3, 28.4, 27.6, 18.68, 18.66; HRMS (ESI-TOF) calcd for $C_{28}H_{32}N_3O_5$ $[M + H]^+$

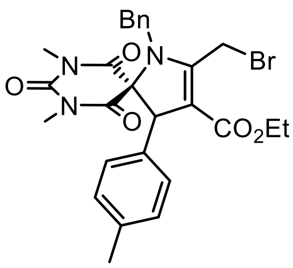
490.2342, found 490.2338.



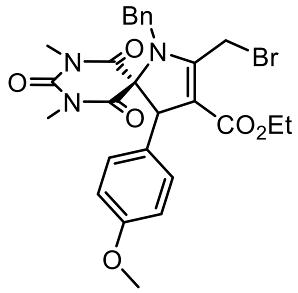
***tert*-Butyl 3-(benzylamino)-7,9-dimethyl-6,8,10-trioxo-1-phenyl-7,9-diazaspiro[4.5]dec-2-ene-2-carboxylate (3ah).** White solid, 85% yield (83.0 mg), mp 143–145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (bs, 1H), 7.43–7.36 (m, 4H), 7.33–7.28 (m, 1H), 7.26–7.19 (m, 3H), 7.01 (bs, 2H), 4.53 (d, J = 6.4 Hz, 2H), 4.42 (s, 1H), 3.45 (d, J = 17.7 Hz, 1H), 3.41 (d, J = 17.7 Hz, 1H), 3.37 (s, 3H), 2.53 (s, 3H), 1.03 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 168.9, 166.9, 162.3, 151.1, 140.0, 138.5, 128.9 (2C), 128.0 (4C), 127.8, 127.7, 127.2 (2C), 92.7, 78.8, 63.6, 60.4, 48.5, 35.5, 29.3, 28.3, 28.1 (3C); HRMS (ESI-TOF) calcd for $C_{28}H_{32}N_3O_5$ $[M + H]^+$ 490.2342, found 490.2347.



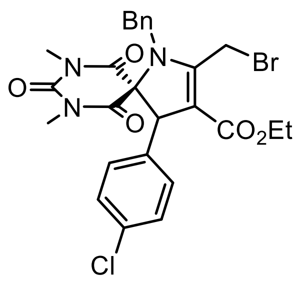
Ethyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-6,8,10-trioxo-4-phenyl-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4aa). White solid, 78% yield (84.5 mg), mp 133–135 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 7.2 Hz, 2H), 7.34–7.22 (m, 6H), 7.15 (bs, 1H), 6.91 (bs, 1H), 4.66 (d, J = 9.4 Hz, 1H), 4.61 (s, 1H), 4.58 (d, J = 14.5 Hz, 1H), 4.53 (d, J = 9.4 Hz, 1H), 4.48 (d, J = 14.5 Hz, 1H), 4.02–3.94 (m, 1H), 3.89–3.81 (m, 1H), 3.23 (s, 3H), 2.56 (s, 3H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 165.2, 164.4, 159.5, 150.0, 136.7, 134.8, 129.7 (2C), 128.6 (3C), 128.53 (2C), 128.50 (2C), 128.4, 100.7, 79.7, 61.1, 59.4, 50.7, 29.3, 28.4, 19.9, 14.0; HRMS (ESI-TOF) calcd for $C_{26}H_{27}BrN_3O_5$ $[M + H]^+$ 540.1134, found 540.1130.



Ethyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-6,8,10-trioxo-4-(p-tolyl)-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ba). White solid, 69% yield (76.9 mg), mp 66–68 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 (d, J = 6.9 Hz, 2H), 7.34–7.25 (m, 3H), 7.06 (bs, 3H), 6.80 (bs, 1H),4.67 (d, J = 9.0 Hz, 1H), 4.58–4.45 (m, 4H), 4.01–3.94 (m, 1H), 3.92–3.84 (m, 1H), 3.23 (s, 3H), 2.59 (s, 3H), 2.29 (s, 3H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.5, 165.3, 164.4, 159.2, 150.1, 138.1, 135.0, 133.6, 129.6 (2C), 129.0 (2C), 128.6 (2C), 128.5, 128.3 (2C), 101.0, 79.8, 60.8, 59.4, 50.7, 29.3, 28.4, 21.2, 20.0, 14.0; HRMS (ESI-TOF) calcd for $C_{27}H_{29}BrN_3O_5$ [M + H]$^+$ 554.1291, found 554.1285.

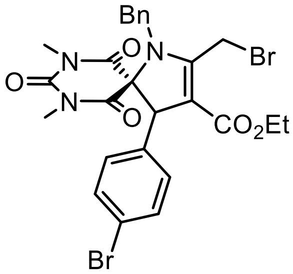


Ethyl 1-benzyl-2-(bromomethyl)-4-(4-methoxyphenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ca). White solid, 62% yield (70.6 mg), mp 66–68 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (d, J = 7.2 Hz, 2H), 7.33–7.25 (m, 3H), 7.06 (bs, 1H), 6.80 (bs, 3H), 4.67 (d, J = 9.6 Hz, 1H), 4.58–4.46 (m, 2H), 4.02–3.94 (m, 1H), 3.91–3.84 (m, 1H), 3.77 (s, 3H), 3.22 (s, 3H), 2.63 (s, 3H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.5, 165.4, 164.4, 159.6, 159.2, 150.1, 134.9, 129.7 (4C), 128.7, 128.6 (2C), 128.5, 113.7 (2C), 101.1, 79.7, 60.5, 59.4, 55.4, 50.7, 29.3, 28.5, 20.0, 14.1; HRMS (ESI-TOF) calcd for $C_{27}H_{29}BrN_3O_6$ [M + H]$^+$ 570.1240, found 570.1233.

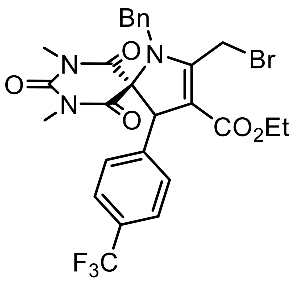


Ethyl 1-benzyl-2-(bromomethyl)-4-(4-chlorophenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4da). White solid, 73% yield (84.5

mg), mp 132–134 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 6.8 Hz, 2H), 7.33–7.20 (m, 5H), 7.12 (bs, 1H), 6.86 (bs, 1H), 4.69 (d, J = 9.5 Hz, 1H), 4.57–4.48 (m, 4H), 4.02–3.94 (m, 1H), 3.92–3.84 (m, 1H), 3.21 (s, 3H), 2.64 (s, 3H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 165.1, 164.2, 159.7, 149.9, 135.4, 134.4, 134.3, 129.8 (4C), 128.6 (5C), 100.4, 79.1, 60.1, 59.6, 50.6, 29.3, 28.5, 19.7, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{26}BrClN_3O_5$ $[M + H]^+$ 574.0744, found 574.0751.

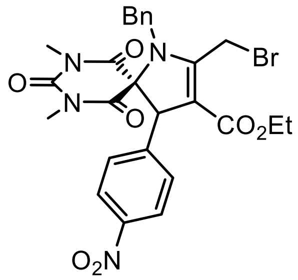


Ethyl 1-benzyl-2-(bromomethyl)-4-(4-bromophenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ea). White solid, 76% yield (94.3 mg), mp 73–75 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.34 (m, 4H), 7.33–7.25 (m, 3H), 7.03 (bs, 1H), 6.81 (bs, 1H), 4.69 (d, J = 10.1 Hz, 1H), 4.57–4.48 (m, 4H), 4.02–3.94 (m, 1H), 3.92–3.85 (m, 1H), 3.21 (s, 3H), 2.64 (s, 3H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 165.0, 164.1, 159.7, 149.9, 135.9, 134.4, 131.5 (2C), 130.2 (2C), 129.8 (2C), 128.7, 128.6 (2C), 122.5, 100.3, 79.0, 60.2, 59.6, 50.6, 29.3, 28.5, 19.7, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{26}Br_2N_3O_5$ $[M + H]^+$ 620.0219, found 620.0215.

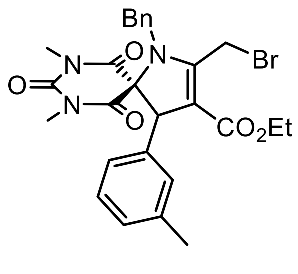


Ethyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-6,8,10-trioxo-4-(4-(trifluoromethyl)phenyl)-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4fa). White solid, 61% yield (74.1 mg), mp 66–68 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (bs, 2H), 7.42 (d, J = 6.5 Hz, 2H), 7.34–7.24 (m, 4H), 7.07 (bs, 1H), 4.70 (s, 1H), 4.63 (s, 1H), 4.60–4.48 (m, 3H), 4.02–3.94 (m, 1H), 3.92–3.84 (m, 1H), 3.22 (s, 3H), 2.57

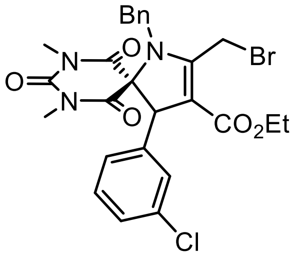
(s, 3H), 0.89 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.2, 164.9, 164.1, 160.0, 149.8, 141.0, 134.2, 130.6 (q, *J* = 26.0 Hz), 130.0 (2C), 129.1 (2C), 128.8, 128.7 (2C), 125.3 (2C), 123.9 (q, *J* = 218.0 Hz), 100.1, 78.9, 60.3, 59.6, 50.6, 29.4, 28.4, 19.7, 14.0; HRMS (ESI-TOF) calcd for $C_{27}H_{26}BrF_3N_3O_5$ [M + H]$^+$ 608.1008, found 608.1018.



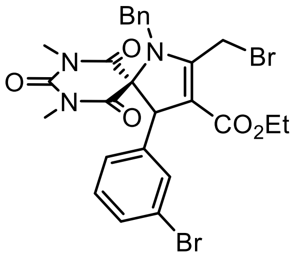
Ethyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-4-(4-nitrophenyl)-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ga). White solid, 58% yield (67.6 mg), mp 86–88 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.14 (bs, 2H), 7.50–7.28 (m, 6H), 7.14 (bs, 1H), 4.73 (d, *J* = 10.1 Hz, 1H), 4.65 (s, 1H), 4.60–4.50 (m, 3H), 4.01–3.94 (m, 1H), 3.93–3.85 (m, 1H), 3.22 (s, 3H), 2.62 (s, 3H), 0.92 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 167.9, 164.7, 163.9, 160.2, 149.6, 147.7, 144.4, 133.9, 130.1 (2C), 129.6 (2C), 128.9, 128.7 (2C), 123.5 (2C), 99.9, 78.4, 59.8, 59.7, 50.5, 29.4, 28.5, 19.5, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{26}BrN_4O_7$ [M + H]$^+$ 585.0985, found 585.0991.



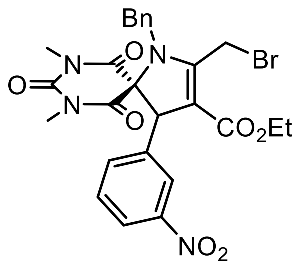
Ethyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-6,8,10-trioxo-4-(m-tolyl)-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ha). White solid, 77% yield (85.7 mg), mp 61–64 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (d, *J* = 7.0 Hz, 2H),7.33–7.25 (m, 3H), 7.15 (bs, 1H), 7.05 (d, *J* = 7.3 Hz, 1H), 6.94 (bs, 1H), 6.70 (bs, 1H), 4.65 (d, *J* = 9.8 Hz, 1H), 4.58 (d, *J* = 14.6 Hz, 1H), 4.57 (s, 1H), 4.52 (d, *J* = 9.8 Hz, 1H), 4.47 (d, *J* = 14.6 Hz, 1H), 4.04–3.96 (m, 1H), 3.91–3.83 (m, 1H), 3.22 (s, 3H), 2.57 (s, 3H), 2.29 (s, 3H), 0.89 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.6, 165.2, 164.4, 159.4, 150.1, 138.0, 136.5, 134.9, 129.7 (2C), 129.1 (2C), 128.6 (2C), 128.5, 128.1, 125.6, 100.8, 79.9, 61.1, 59.4, 50.7, 29.2, 28.4, 21.4, 19.9, 14.0; HRMS (ESI-TOF) calcd for $C_{27}H_{29}BrN_3O_5$ [M + H]$^+$ 554.1291, found 554.1293.



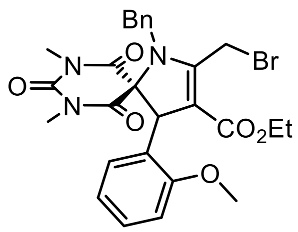
Ethyl 1-benzyl-2-(bromomethyl)-4-(3-chlorophenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ia). White solid, 79% yield (90.8 mg), mp 64–66 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 6.8 Hz, 2H), 7.34–7.04 (m, 6H), 6.98–6.70 (m, 1H), 4.72 (bs, 1H), 4.60–4.44 (m, 4H), 4.06–3.96 (m, 1H), 3.92–3.84 (m, 1H), 3.21 (s, 3H), 2.65 (s, 3H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 164.9, 164.1, 159.9, 149.8, 138.8, 134.4 (2C), 129.8 (2C), 129.4, 128.6 (5C), 126.7, 100.1, 79.2, 60.2, 59.6, 50.6, 29.3, 28.5, 19.7, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{26}BrClN_3O_5$ [M + H]$^+$ 574.0744, found 574.0739.



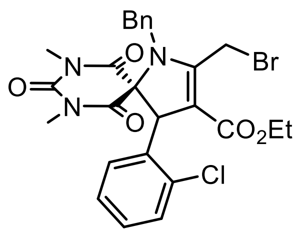
Ethyl 1-benzyl-2-(bromomethyl)-4-(3-bromophenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ja). White solid, 76% yield (93.6 mg), mp 65–67 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 7.0 Hz, 2H), 7.40 (d, J = 7.8 Hz, 1H), 7.34–7.24 (m, 4H), 7.20–6.78 (m, 2H), 4.72 (bs, 1H), 4.62–4.42 (m, 4H), 4.06–3.96 (m, 1H), 3.91–3.83 (m, 1H), 3.21 (s, 3H), 2.65 (s, 3H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz,$CDCl_3$) δ 168.1, 164.9, 164.1, 159.9, 149.8, 139.1, 134.4, 131.4 (2C), 129.8 (3C), 128.6 (3C), 127.1, 123.0, 100.0, 79.1, 60.2, 59.5, 50.5, 29.3, 28.5, 19.6, 14.0; HRMS (ESI-TOF) calcd for $C_{26}H_{26}Br_2N_3O_5$ [M + H]$^+$ 620.0219, found 620.0223.



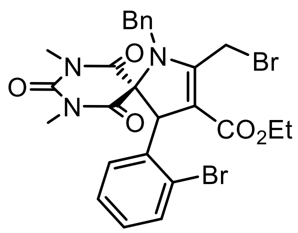
Ethyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-4-(3-nitrophenyl)-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ka). White solid, 61% yield (71.1 mg), mp 140–142 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, J = 9.2, 2.2 Hz, 1H), 7.93 (bs, 1H), 7.48 (bs, 1H), 7.42 (d, J = 7.0 Hz, 2H), 7.35–7.25 (m, 4H), 5.00–4.25 (m, 5H), 4.03–3.95 (m, 1H), 3.93–3.85 (m, 1H), 3.23 (s, 3H), 2.62 (s, 3H), 0.93 (t, J = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 164.8, 163.8, 160.3, 149.6, 148.2, 139.2, 134.5 (2C), 134.0, 129.9 (2C), 129.3, 128.8, 128.7 (2C), 123.4 (2C), 99.9, 78.5, 59.7, 50.4, 29.4, 28.5, 19.5, 14.1; HRMS (ESI-TOF) calcd for $C_{26}H_{26}BrN_4O_7$ $[M + H]^+$ 585.0985, found 585.0988.



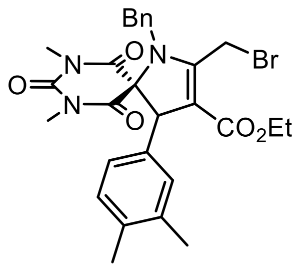
Ethyl 1-benzyl-2-(bromomethyl)-4-(2-methoxyphenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4la). White solid, 67% yield (76.6 mg), mp 64–66 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 6.7 Hz, 2H), 7.31–7.23 (m, 3H), 7.19 (td, J = 7.8, 1.4 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.90 (t, J = 7.5 Hz, 1H), 6.75 (d, J = 8.3 Hz, 1H), 5.16 (s, 1H), 4.78 (d, J = 9.7 Hz, 1H), 4.56 (d, J = 14.3 Hz, 1H), 4.53 (d, J = 9.7 Hz, 1H), 4.48 (d, J = 14.3 Hz, 1H), 4.05–3.98 (m, 1H), 3.90–3.83 (m, 1H), 3.65 (s, 3H), 3.16 (s, 3H), 2.57 (s, 3H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 165.5, 164.5, 159.1, 156.4, 150.4, 134.4, 130.4, 130.0 (2C), 129.1, 128.49, 128.48 (2C), 125.3, 120.8, 109.4, 100.1, 77.9, 59.3, 55.7, 52.6, 50.4, 29.0, 28.1, 20.0, 14.0; HRMS (ESI-TOF) calcd for $C_{27}H_{29}BrN_3O_6$ $[M + H]^+$ 570.1240, found 570.1247.



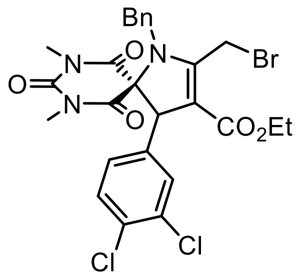
Ethyl 1-benzyl-2-(bromomethyl)-4-(2-chlorophenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ma). White solid, 75% yield (86.3 mg), mp 63–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 6.5 Hz, 2H), 7.32–7.26 (m, 4H), 7.24–7.21 (m, 2H), 7.20–7.16 (m, 1H), 5.23 (s, 1H), 4.74 (d, J = 9.6 Hz, 1H), 4.58 (d, J = 9.6 Hz, 1H), 4.56 (d, J = 14.3 Hz, 1H), 4.51 (d, J = 14.3 Hz, 1H), 3.99–3.91 (m, 1H), 3.88–3.81 (m, 1H), 3.16 (s, 3H), 2.64 (s, 3H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 165.2, 164.1, 159.6, 149.9, 134.8, 134.1, 133.5, 131.4, 130.1 (2C), 129.4, 128.8, 128.7, 128.6 (2C), 127.0, 100.6, 77.8, 59.4, 55.5, 50.4, 29.1, 28.3, 19.7, 13.9; HRMS (ESI-TOF) calcd for $C_{26}H_{26}BrClN_3O_5$ $[M + H]^+$ 574.0744, found 574.0748.



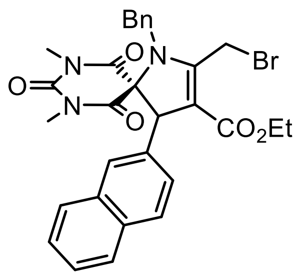
Ethyl 1-benzyl-2-(bromomethyl)-4-(2-bromophenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4na). White solid, 80% yield (98.6 mg), mp 118–120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 7.9 Hz, 1H), 7.41 (d, J = 6.8 Hz, 2H), 7.32–7.26 (m, 4H), 7.23 (dd, J =7.7, 1.5 Hz, 1H), 7.10 (td, J = 7.6, 1.5 Hz, 1H), 5.22 (s, 1H), 4.75 (d, J = 9.9 Hz, 1H), 4.59–4.50 (m, 3H), 3.97–3.90 (m, 1H), 3.88–3.81 (m, 1H), 3.17 (s, 3H), 2.65 (s, 3H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 165.2, 164.1, 159.5, 150.0, 136.6, 134.2, 132.2, 131.7, 130.1 (2C), 129.7, 128.7, 128.6 (2C), 127.6, 124.3, 101.2, 77.8, 59.5, 58.2, 50.4, 29.1, 28.4, 19.7, 13.9; HRMS (ESI-TOF) calcd for $C_{26}H_{26}Br_2N_3O_5$ $[M + H]^+$ 620.0219, found 620.0225.



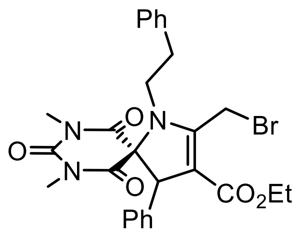
Ethyl 1-benzyl-2-(bromomethyl)-4-(3,4-dimethylphenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4oa). White solid, 72% yield (81.7 mg), mp 152–154 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J =7.1 Hz, 2H), 7.33–7.24 (m, 3H), 7.01 (bs, 1H), 6.86 (bs, 1H), 6.65 (bs, 1H), 4.67 (d, J = 7.9 Hz, 1H), 4.58–4.42 (m, 4H), 4.01–3.95 (m, 1H), 3.94–3.86 (m, 1H), 3.23 (s, 3H), 2.58 (s, 3H), 2.20 (s, 6H), 0.93 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 165.3, 164.5, 159.1, 150.1, 136.7, 135.1, 133.8, 129.5 (5C), 128.6 (2C), 128.4, 125.8, 101.0, 80.0, 60.8, 59.5, 50.7, 29.2, 28.4, 20.0, 19.8, 19.6, 14.1; HRMS (ESI-TOF) calcd for $C_{28}H_{31}BrN_3O_5$ [M + H]$^+$ 568.1447, found 568.1452.



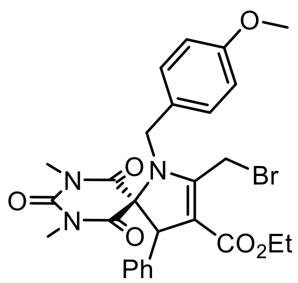
Ethyl 1-benzyl-2-(bromomethyl)-4-(3,4-dichlorophenyl)-7,9-dimethyl-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4pa). White solid, 73% yield (89.1 mg), mp 130–132ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J = 6.4 Hz, 2H), 7.39–7.27 (m, 4H), 7.24–6.66 (m, 2H), 4.75 (bs, 1H), 4.56–4.44 (m, 4H), 4.05–3.97 (m, 1H), 3.95–3.88 (m, 1H), 3.21 (s, 3H), 2.70 (s, 3H), 0.97 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 164.9, 164.0, 160.0, 149.8, 137.1, 134.2, 132.5, 130.6 (3C), 129.9 (2C), 128.8, 128.7 (2C), 127.9, 100.0, 78.7, 59.7, 59.5, 50.5, 29.4, 28.6, 19.6, 14.2; HRMS (ESI-TOF) calcd for $C_{26}H_{25}BrCl_2N_3O_5$ [M + H]$^+$ 608.0355, found 608.0351.



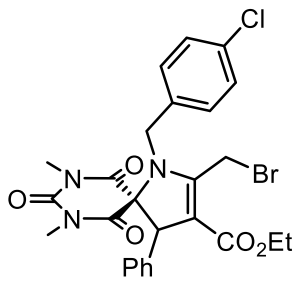
Ethyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-4-(naphthalen-2-yl)-6,8,10-trioxo-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4qa). White solid, 68% yield (79.9 mg), mp 85–87 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86–7.68 (m, 3H), 7.64–7.36 (s, 5H), 7.34–7.26 (m, 3H), 7.23–6.86 (m, 1H), 4.82–4.71 (m, 2H), 4.65–4.46 (m, 3H), 3.96–3.81 (m, 2H), 3.26 (s, 3H), 2.37 (s, 3H), 0.81 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 165.2, 164.4, 159.6, 150.0, 134.8, 133.1, 133.0, 129.8 (2C), 128.63 (2C), 128.56, 128.1 (2C), 127.7 (2C), 126.5, 126.4, 126.3, 125.9, 100.8, 79.7, 61.1, 59.5, 50.7, 29.3, 28.4, 19.9, 14.0; HRMS (ESI-TOF) calcd for $C_{30}H_{29}BrN_3O_5$ [M + H]$^+$ 590.1291, found 590.1282.



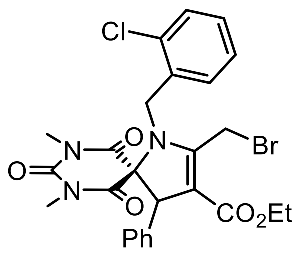
Ethyl 2-(bromomethyl)-7,9-dimethyl-6,8,10-trioxo-1-phenethyl-4-phenyl-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ab). White solid, 71% yield (78.9 mg), mp 60–62 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.24 (m, 5H), 7.23–7.18 (s, 3H), 7.11 (bs, 1H), 6.94 (bs, 1H), 4.57 (d, J = 10.3 Hz, 1H), 4.50 (s, 1H), 4.48 (d, J = 10.3 Hz, 1H), 4.00–3.92 (m, 1H), 3.88–3.81 (m, 1H), 3.64–3.51 (m, 2H), 3.37 (s, 3H), 3.05–2.93 (m, 2H), 2.58 (s, 3H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 165.2, 164.3, 159.9, 150.2, 138.5, 136.9, 129.0 (2C), 128.7 (2C), 128.5, 128.4 (4C), 126.9, 99.4, 80.8, 61.3, 59.3, 48.0, 36.0, 29.6, 28.6, 19.3, 14.0; HRMS (ESI-TOF) calcd for $C_{27}H_{29}BrN_3O_5$ [M + H]$^+$ 554.1291, found 554.1298.



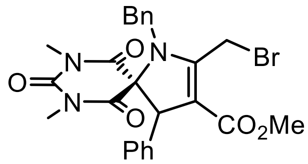
Ethyl 2-(bromomethyl)-1-(4-methoxybenzyl)-7,9-dimethyl-6,8,10-trioxo-4-phenyl-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ac). White solid, 75% yield (85.8 mg), mp 63–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J = 8.3Hz, 2H), 7.28–7.04 (m, 4H), 6.87 (bs, 1H), 6.81 (d, J = 8.3 Hz, 2H), 4.70 (d, J = 9.0 Hz, 1H), 4.63–4.57 (m, 2H), 4.55 (d, J = 14.0 Hz, 1H), 4.43 (d, J = 14.0 Hz, 1H), 4.01–3.93 (m, 1H), 3.89–3.81 (m, 1H), 3.77 (s, 3H), 3.21 (s, 3H), 2.55 (s, 3H), 0.86 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 165.2, 164.4, 159.8, 159.5, 150.0, 136.8, 131.5 (2C), 128.6 (4C), 128.4, 126.1, 113.8 (2C), 100.4, 79.2, 61.0, 59.4, 55.4, 49.9, 29.2, 28.3, 20.0, 14.0; HRMS (ESI-TOF) calcd for $C_{27}H_{29}BrN_3O_6$ $[M + H]^+$ 570.1240, found 570.1243.



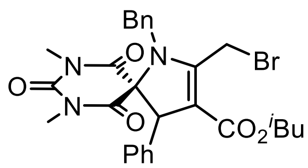
Ethyl 2-(bromomethyl)-1-(4-chlorobenzyl)-7,9-dimethyl-6,8,10-trioxo-4-phenyl-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ad). White solid, 70% yield (80.9 mg), mp 172–174 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.30–7.24 (m, 3H), 7.12 (bs, 1H), 6.96 (bs, 1H), 4.62–4.54 (m, 2H), 4.52–4.41 (m, 3H), 4.01–3.93 (m, 1H), 3.89–3.81 (m, 1H), 3.30 (s, 3H), 2.59 (s, 3H), 0.87 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 165.3, 164.2, 159.2, 150.0, 136.6, 134.3, 134.1, 130.4 (2C), 128.9 (2C), 128.5, 128.4 (4C), 101.3, 80.5, 60.9, 59.5, 50.3, 29.4, 28.5, 19.8, 14.0; HRMS (ESI-TOF) calcd for $C_{26}H_{26}BrClN_3O_5$ $[M + H]^+$ 574.0744, found 574.0752.



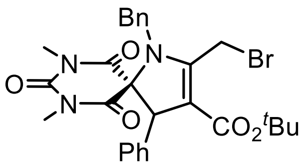
Ethyl 2-(bromomethyl)-1-(2-chlorobenzyl)-7,9-dimethyl-6,8,10-trioxo-4-phenyl-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ae). White solid, 64% yield (73.8 mg), mp 158–159 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61–7.56 (m, 1H), 7.36–7.33 (m, 1H), 7.30–6.85 (m, 7H), 4.74 (d, J = 10.3 Hz, 1H), 4.66 (d, J = 16.3 Hz, 1H), 4.64–4.57 (m, 3H), 4.03–3.95 (m, 1H), 3.90–3.83 (m, 1H), 3.22 (s, 3H), 2.57 (s, 3H), 0.88 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 165.0, 164.2, 159.3, 150.1, 136.6, 134.3, 133.2, 130.5, 129.8, 129.6, 128.47 (2C), 128.45 (4C), 126.9, 100.7, 61.3, 59.5, 48.1, 29.3, 28.4, 19.4, 14.0; HRMS (ESI-TOF) calcd for $C_{26}H_{26}BrClN_3O_5$ $[M + H]^+$ 574.0744, found 574.0748.



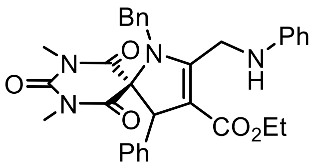
Methyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-6,8,10-trioxo-4-phenyl-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4af). White solid, 75% yield (78.8 mg), mp 77–79 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, J = 6.9 Hz, 2H), 7.35–7.22 (m, 6H), 7.14 (bs, 1H), 6.91 (bs, 1H), 4.68 (d, J = 9.7 Hz, 1H), 4.60 (s, 1H), 4.56 (d, J = 14.6 Hz, 1H), 4.52 (d, J = 9.7 Hz, 1H), 4.50 (d, J = 14.6 Hz, 1H), 3.45 (s, 3H), 3.22 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 165.2, 164.9, 159.8, 150.0, 136.6, 134.7, 129.7 (2C), 128.63 (2C), 128.57, 128.52, 128.47 (4C), 100.3, 79.7, 60.9, 50.9, 50.7, 29.3, 28.4, 19.9; HRMS (ESI-TOF) calcd for $C_{25}H_{25}BrN_3O_5$ $[M + H]^+$ 526.0978, found 526.0975.



Isobutyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-6,8,10-trioxo-4-phenyl-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ag). White solid, 76% yield (86.3 mg), mp 105–107 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45 (d, J =7.0 Hz, 2H), 7.35–7.12 (m, 7H), 6.90 (bs, 1H), 4.68 (d, J = 8.7 Hz, 1H), 4.63–4.53 (m, 3H), 4.48 (d, J = 14.5 Hz, 1H), 3.77 (dd, J = 10.7, 6.4 Hz, 1H), 3.56 (dd, J = 10.7, 6.0 Hz, 1H), 3.22 (s, 3H), 2.55 (s, 3H), 1.56–1.46 (m, 1H), 0.50 (dd, J = 6.8, 1.2 Hz , 6H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.6, 165.2, 164.5, 159.8, 150.0, 136.8, 134.7, 129.8 (2C), 128.6 (2C), 128.53 (5C), 128.48, 100.4, 79.6, 69.8, 61.1, 50.7, 29.3, 28.3, 27.6, 19.9, 18.8 (2C); HRMS (ESI-TOF) calcd for $C_{28}H_{31}BrN_3O_5$ $[M + H]^+$ 568.1447, found 568.1444.



***tert*-Butyl 1-benzyl-2-(bromomethyl)-7,9-dimethyl-6,8,10-trioxo-4-phenyl-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (4ah).** White solid, 72% yield (81.5 mg), mp 104–106 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (d, J = 7.1 Hz, 2H), 7.34–7.14 (m, 7H), 6.88 (bs, 1H), 4.64–4.52 (m, 4H), 4.46 (d, J = 14.5 Hz, 1H), 3.23 (s, 3H), 2.55 (s, 3H), 1.11 (s, 9H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.8, 165.3, 163.7, 158.6, 150.1, 137.1, 135.0, 129.7 (2C), 128.6 (5C), 128.5, 128.3 (2C), 102.2, 79.9, 79.6, 61.6, 50.8, 29.3, 28.3, 28.0 (3C), 20.1; HRMS (ESI-TOF) calcd for $C_{28}H_{31}BrN_3O_5$ $[M + H]^+$ 568.1447, found 568.1453.



Ethyl 1-benzyl-7,9-dimethyl-6,8,10-trioxo-4-phenyl-2-((phenylamino)methyl)-1,7,9-triazaspiro[4.5]dec-2-ene-3-carboxylate (6aa). White solid, mp 107–109 ºC; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38 (d, J = 6.3 Hz, 2H), 7.31–7.22 (m, 6H), 7.19 (t, J = 7.6 Hz, 2H), 7.11–6.94 (m, 2H), 6.76 (t, J = 7.0 Hz, 1H), 6.64 (d, J = 8.1 Hz, 2H), 4.62 (s, 1H), 4.53 (d, J = 14.7 Hz, 1H), 4.44 (d, J = 14.7 Hz, 1H), 4.41 (d, J = 12.4 Hz, 1H), 4.34 (d, J = 12.4 Hz, 1H), 4.16 (bs, 1H), 3.98–3.90 (m, 1H), 3.86–3.79 (m, 1H), 3.23

(s, 3H), 2.58 (s, 3H), 0.82 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 165.4, 164.9, 162.4, 150.1, 147.9, 136.8, 135.4, 129.6 (2C), 129.3 (2C), 128.6 (2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 118.4, 113.9 (2C), 100.7, 80.5, 61.3, 59.3, 51.0, 39.5, 29.3, 28.4, 14.0; HRMS (ESI-TOF) calcd for $C_{28}H_{31}BrN_3O_5$ $[M + H]^+$ 553.2451, found 553.2454.

4. Single-crystal X-ray crystallography of 3ma and 4oa

Single crystal of **3ma** were obtained by slow evaporation from a mixture of acetone/*n*-hexane at 5 ºC. Single-crystal X-ray diffraction data were collected on a diffractometer (Bruker D8 Venture) equipped with a CCD area detector using graphite-monochromated MoKα radiation (λ = 0.71073 Å) in the scan range 5.086 < 2θ < 49.996°. Crystallographic data have been deposited in the Cambridge Crystallographic Data Centre as deposition number CCDC 2305863.

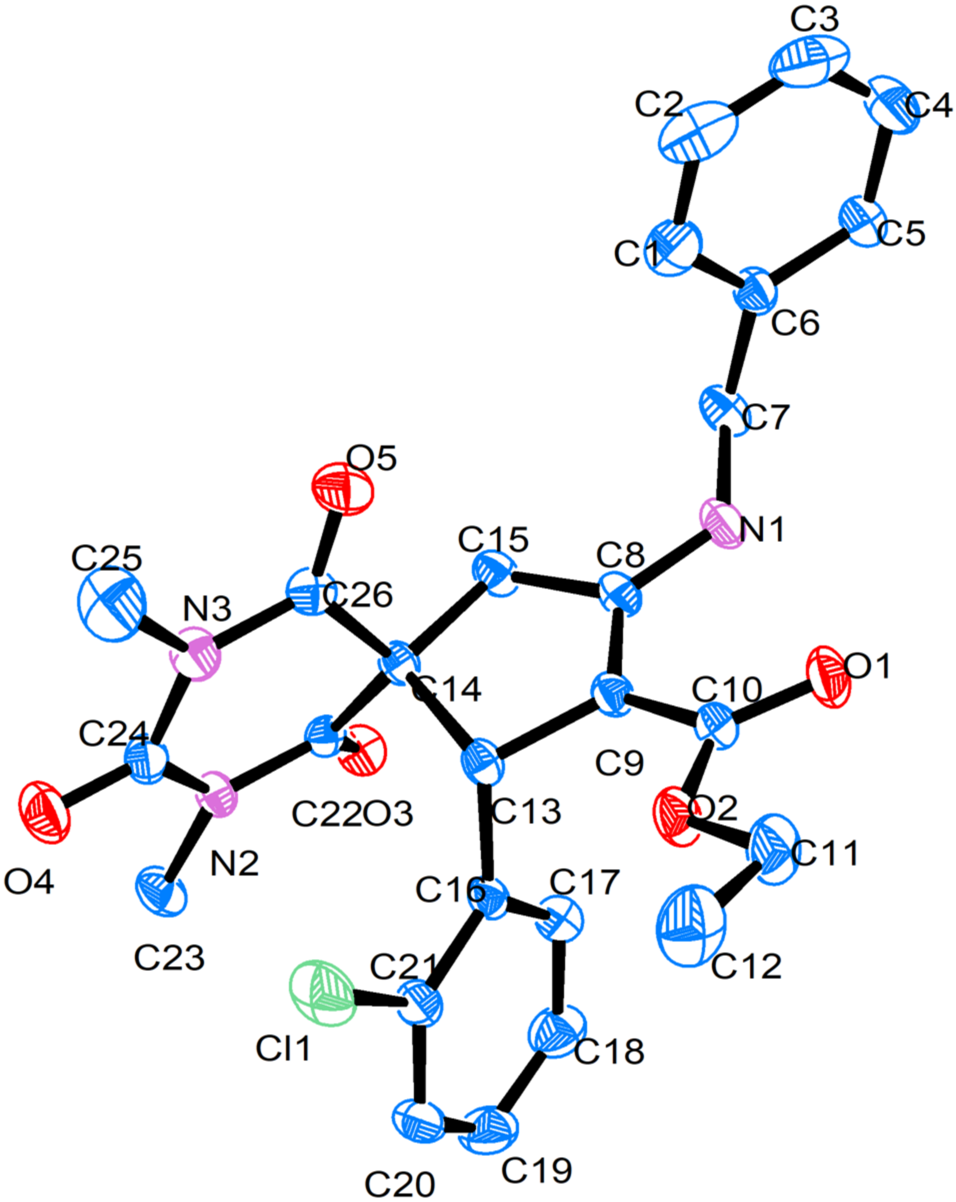


Figure S1. ORTEP Diagrams of 3ma with 30% thermal ellipsoids

Table S1. Crystal data and structure refinement for 3ma

Identification code	CCDC 2305863
Empirical formula	$C_{26}H_{26}ClN_3O_5$
Formula weight	495.95
Temperature/K	296.15
Crystal system	triclinic
Space group	P-1
a/Å	8.2719(11)
b/Å	10.9748(14)
c/Å	14.3779(18)
α/°	91.073(2)
β/°	98.225(2)
γ/°	110.945(2)
Volume/Å^3	1203.0(3)
Z	2
ρ_{calc}g/cm^3	1.369
μ/mm^{-1}	0.202
F(000)	520.0
Crystal size/mm^3	0.26 × 0.24 × 0.21
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	5.086 to 49.996
Index ranges	$-7 \le h \le 9$, $-13 \le k \le 12$, $-17 \le l \le 14$
Reflections collected	6128
Independent reflections	4196 [R_{int} = 0.0147, R_{sigma} = 0.0323]
Data/restraints/parameters	4196/1/319
Goodness-of-fit on F^2	1.057
Final R indexes [I>=2σ (I)]	R_1 = 0.0474, wR_2 = 0.1220
Final R indexes [all data]	R_1 = 0.0686, wR_2 = 0.1297
Largest diff. peak/hole [e Å^{-3}]	0.53/-0.41

Single crystal of **4oa** were obtained by slow evaporation from a mixture of acetone/*n*-hexane at 5 ºC. Single-crystal X-ray diffraction data were collected on a diffractometer (Bruker D8 Venture) equipped with a CCD area detector using graphite-monochromated MoKα radiation (λ = 0.71073 Å) in the scan range 4.48 < 2θ < 50.00°. Crystallographic data have been deposited in the Cambridge Crystallographic Data Centre as deposition number CCDC 2305868.

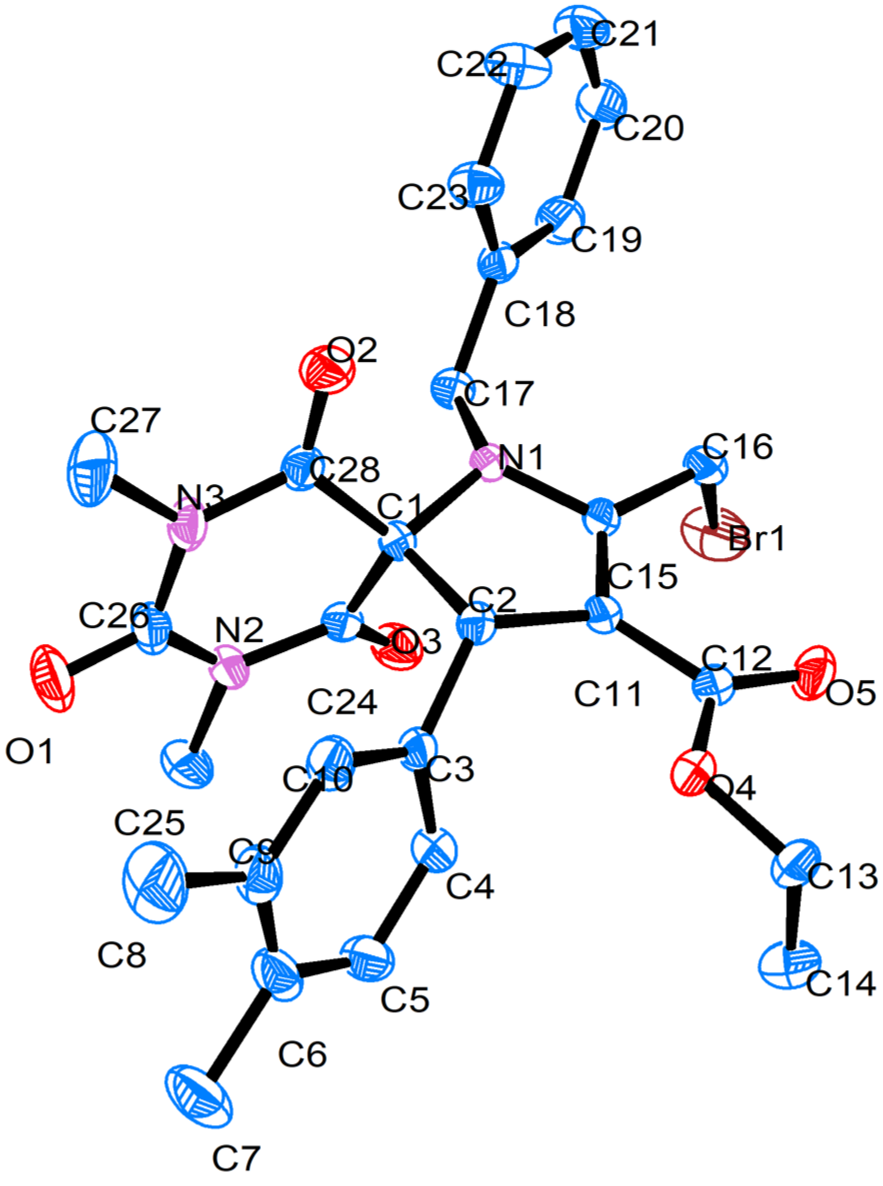


Figure S2. ORTEP Diagrams of 4oa with 30% thermal ellipsoids

Table S2. Crystal data and structure refinement for 4oa

Identification code	CCDC 2305868
Empirical formula	$C_{28.01}H_{30.01}BrN_3O_5$
Formula weight	568.65
Temperature/K	298.0
Crystal system	triclinic
Space group (number)	P-1 (2)
a/Å	11.0881(8)
b/Å	11.9277(9)
c/Å	12.1514(9)
α/°	115.124(2)
β/°	105.133(3)
γ/°	100.196(3)
Volume/Å^3	1326.22(17)
Z	2
ρ_{calc}g/cm^3	1.424
μ/mm^{-1}	1.593
F(000)	588
Crystal size/mm^3	0.26×0.25×0.22
Crystal colour	colourless
Crystal shape	block
Radiation	MoK_α (λ=0.71073 Å)
2θ range for data collection/°	4.48 to 50.00 (0.84 Å)
Index ranges	$-13 \le h \le 13, -14 \le k \le 14, -14 \le l \le 14$
Reflections collected	37795
Independent reflections	4666 [R_{int} = 0.1052, R_{sigma} = 0.0570]
Data/Restraints/Parameters	4666/0/347
Goodness-of-fit on F^2	1.051
Final R indexes [I>=2σ (I)]	R_1 = 0.0415, wR_2 = 0.1067
Final R indexes [all data]	R_1 = 0.0609, wR_2 = 0.1144
Largest peak/hole [eÅ^{-3}]	0.29/-0.45

5. References

[1] R. Gu, K. Flidrova and J.-M. Lehn, *J. Am. Chem. Soc.*, 2018, **140**, 5560–5568.

[2] J.-Y. Liu, G.-E. Cao, W. Xu, J. Cao and W.-L. Wang, *Appl. Organometal. Chem.*, 2010, **24**, 685–691.

6. Copies of NMR spectra for 3, 4 and 6aa

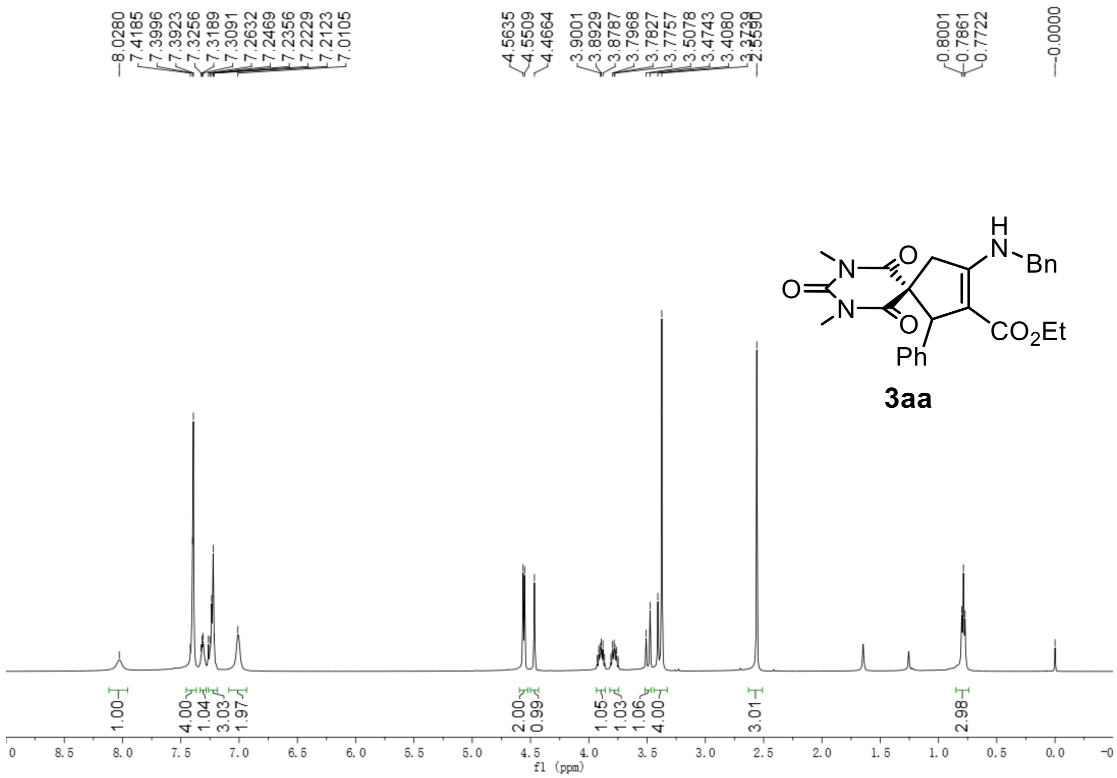


Figure S3. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3aa

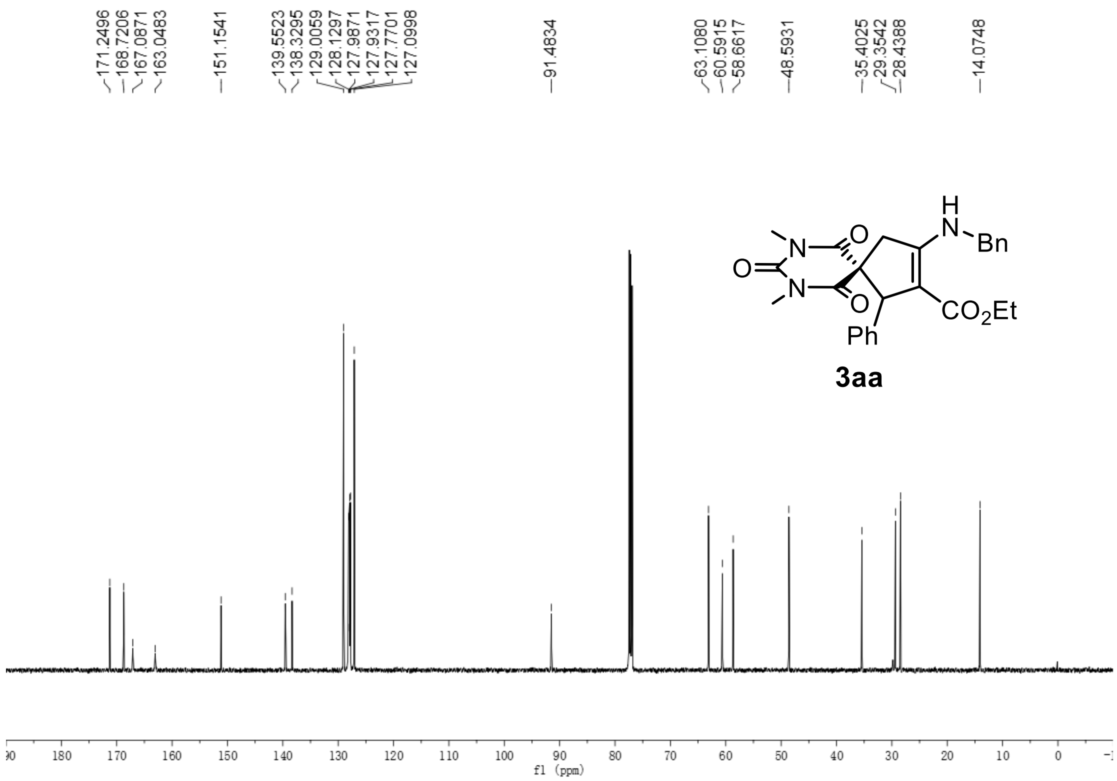


Figure S4. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3aa

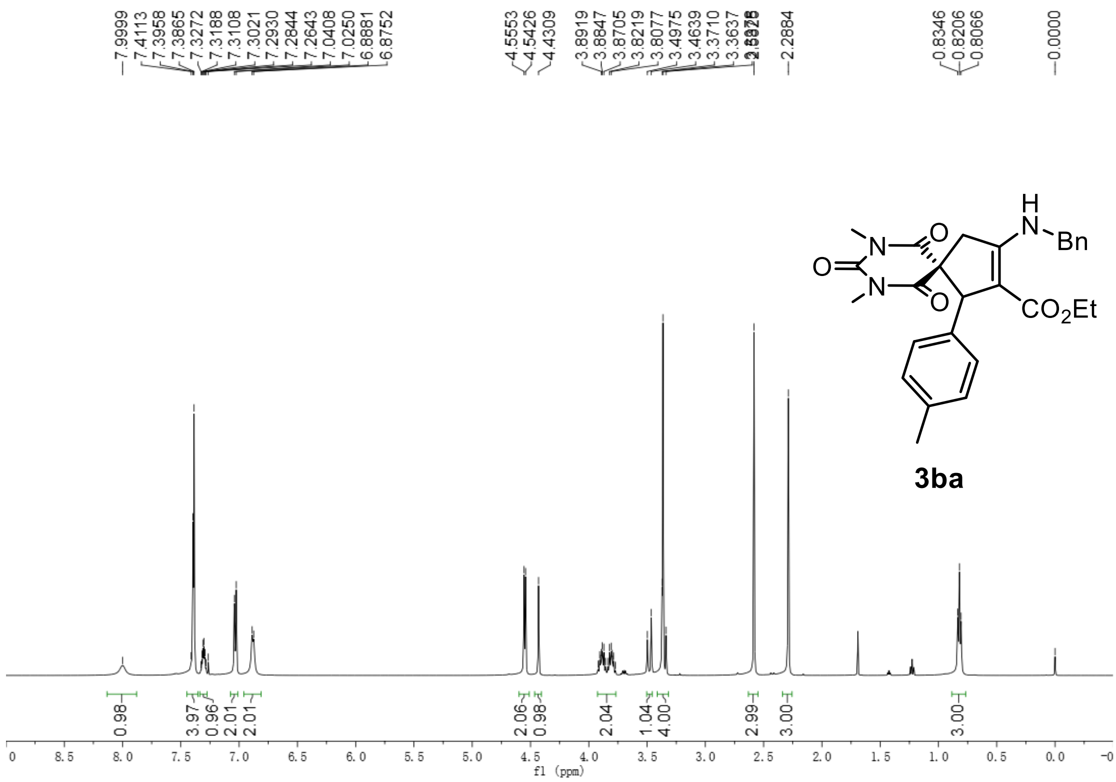


Figure S5. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ba

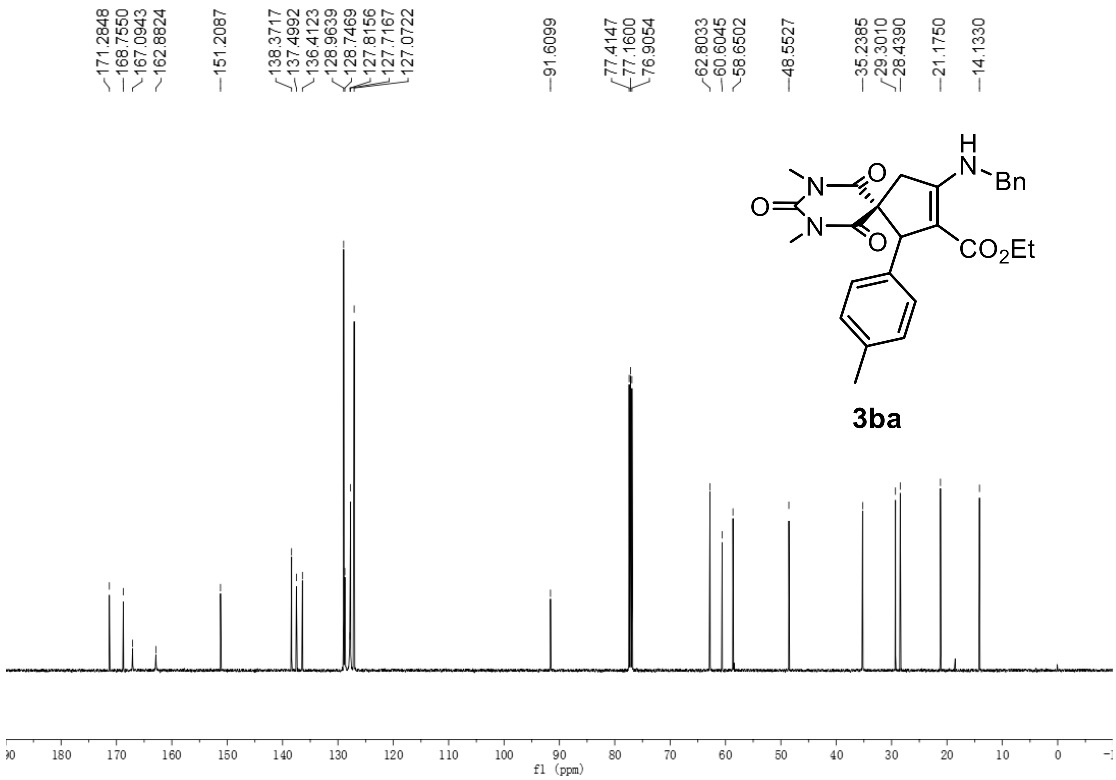


Figure S6. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ba

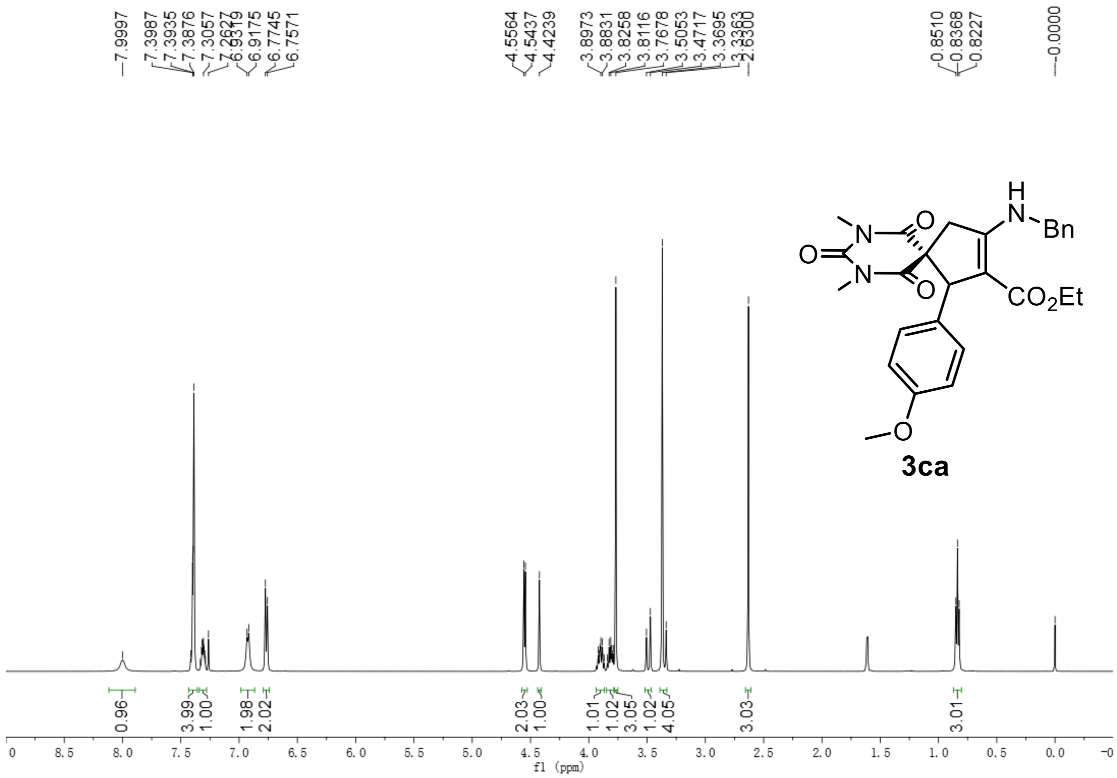


Figure S7. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3ca

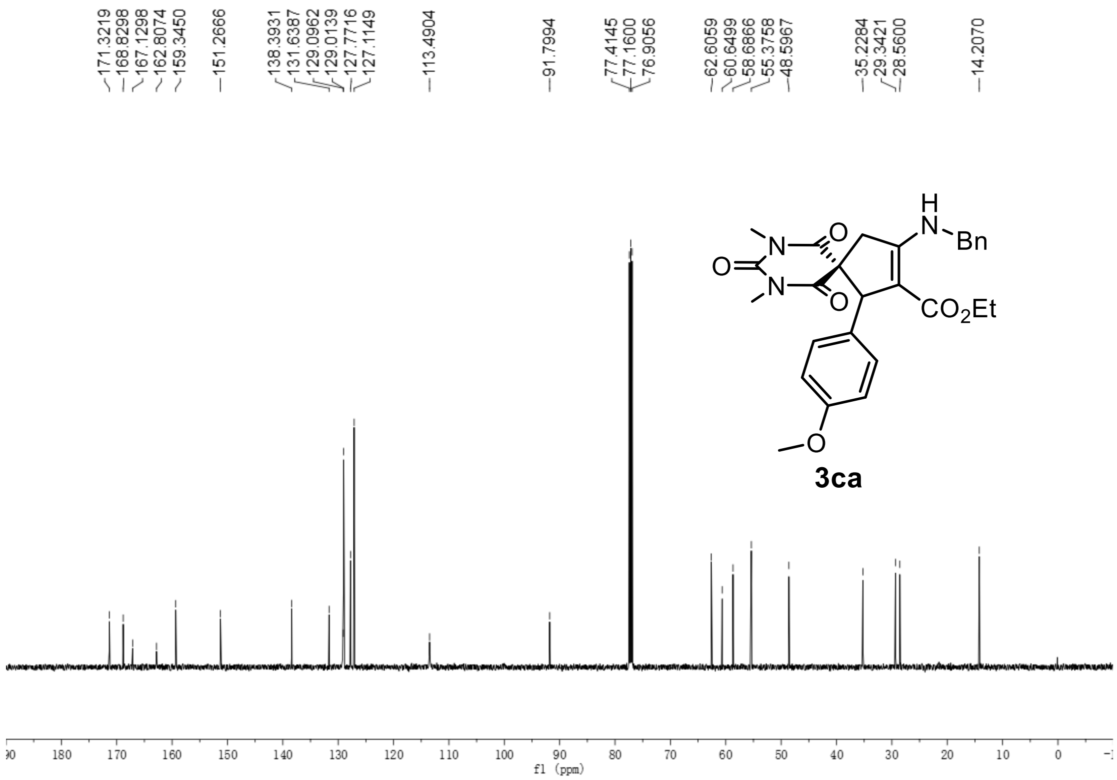


Figure S8. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3ca

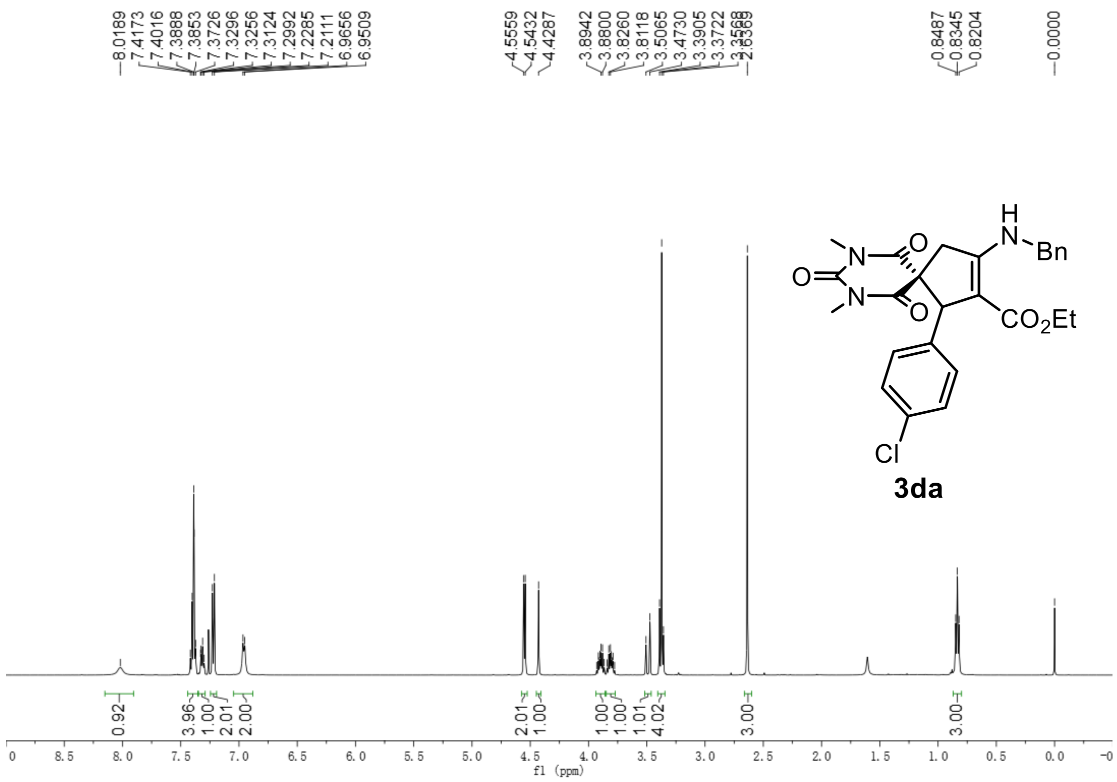


Figure S9. ^{1}H NMR (500 MHz, CDCl₃) of compound 3da

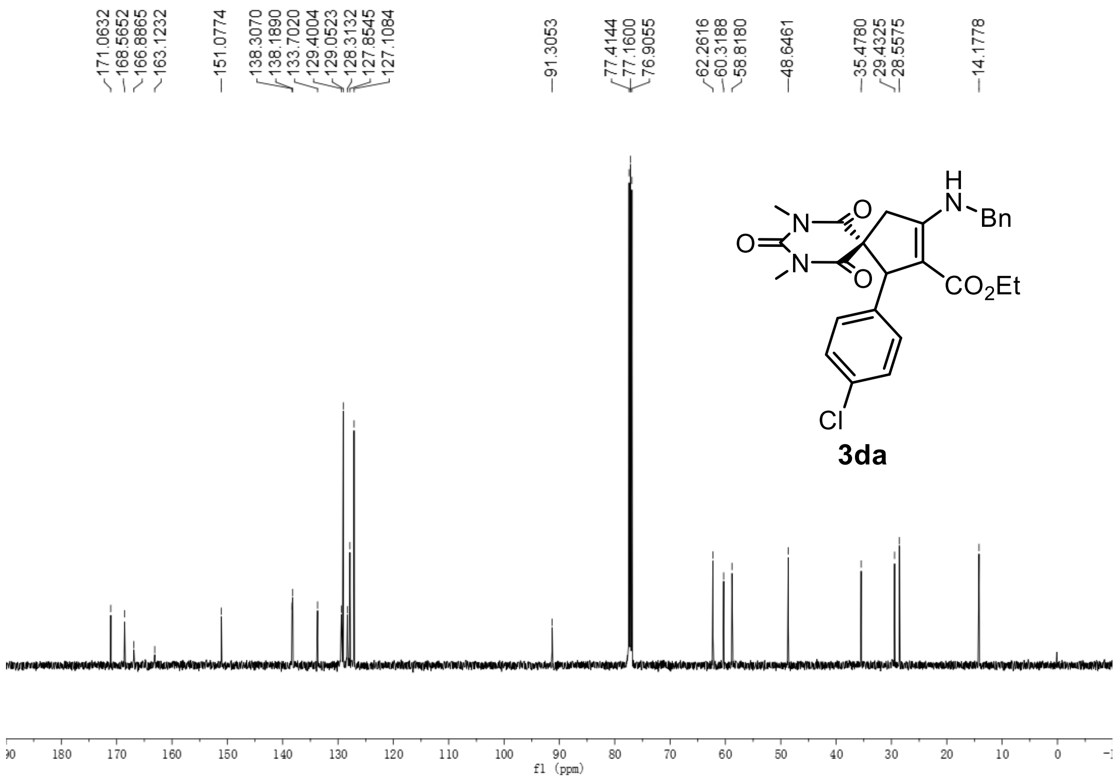


Figure S10. ^{13}C NMR (125 MHz, CDCl₃) of compound 3da

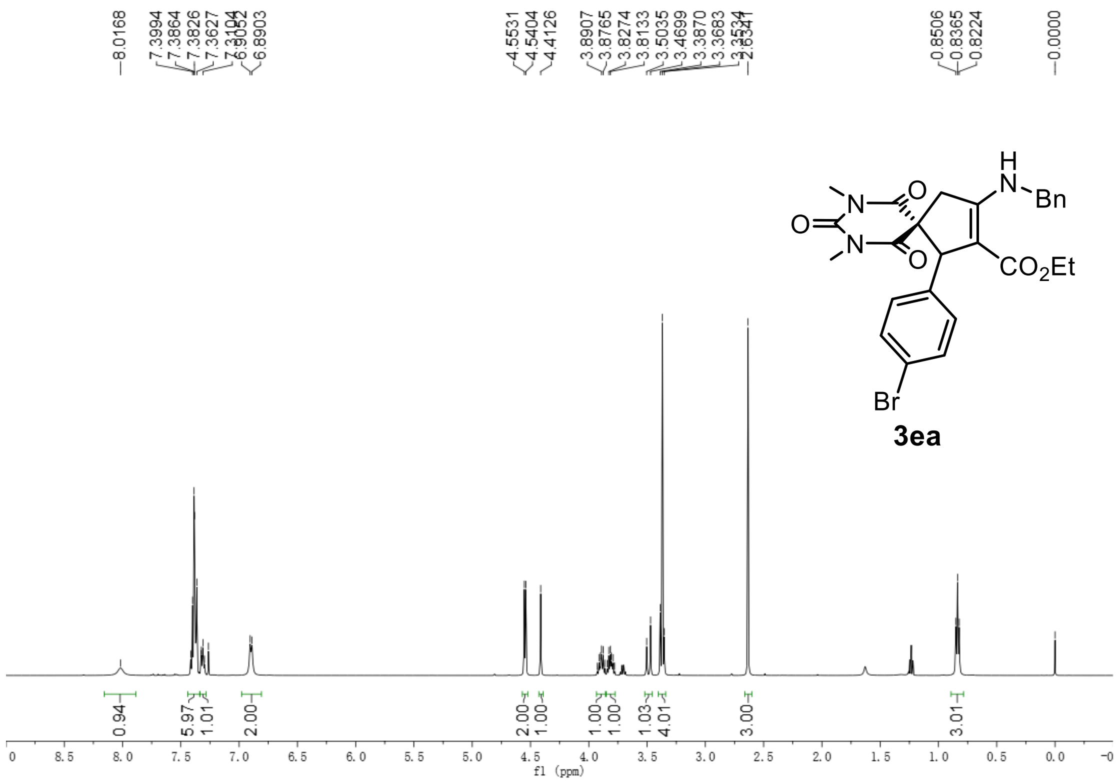


Figure S11. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ea

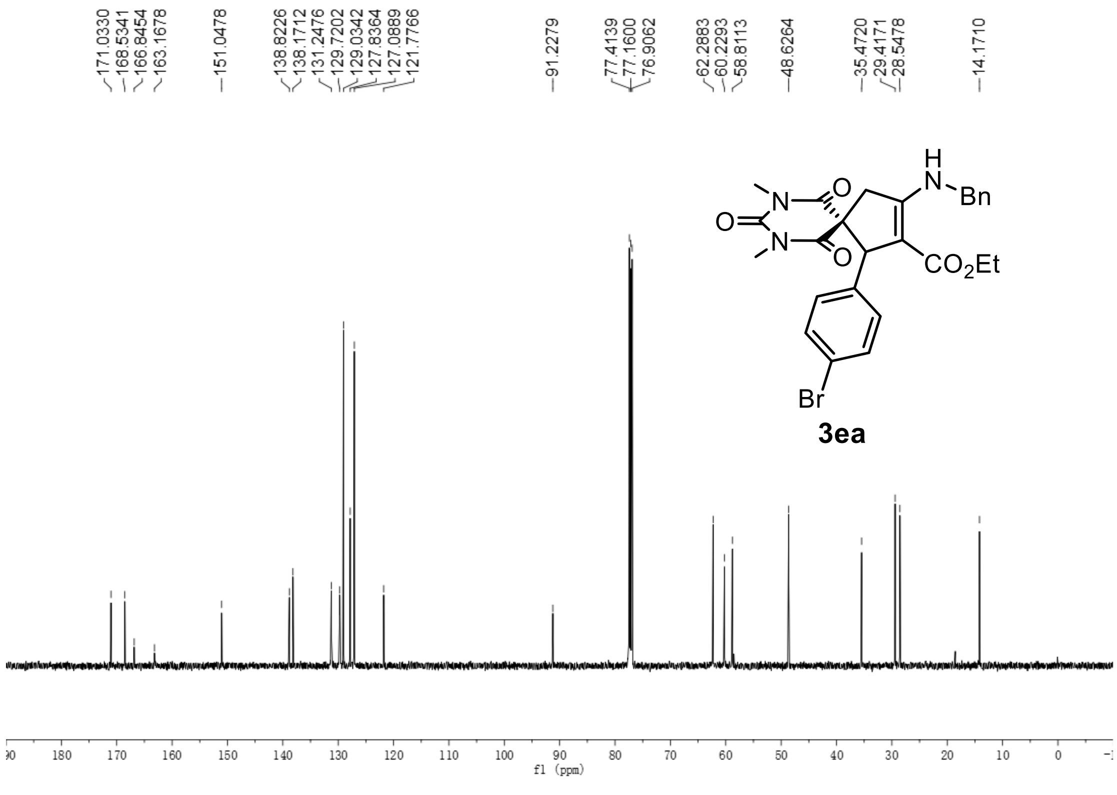


Figure S12. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ea

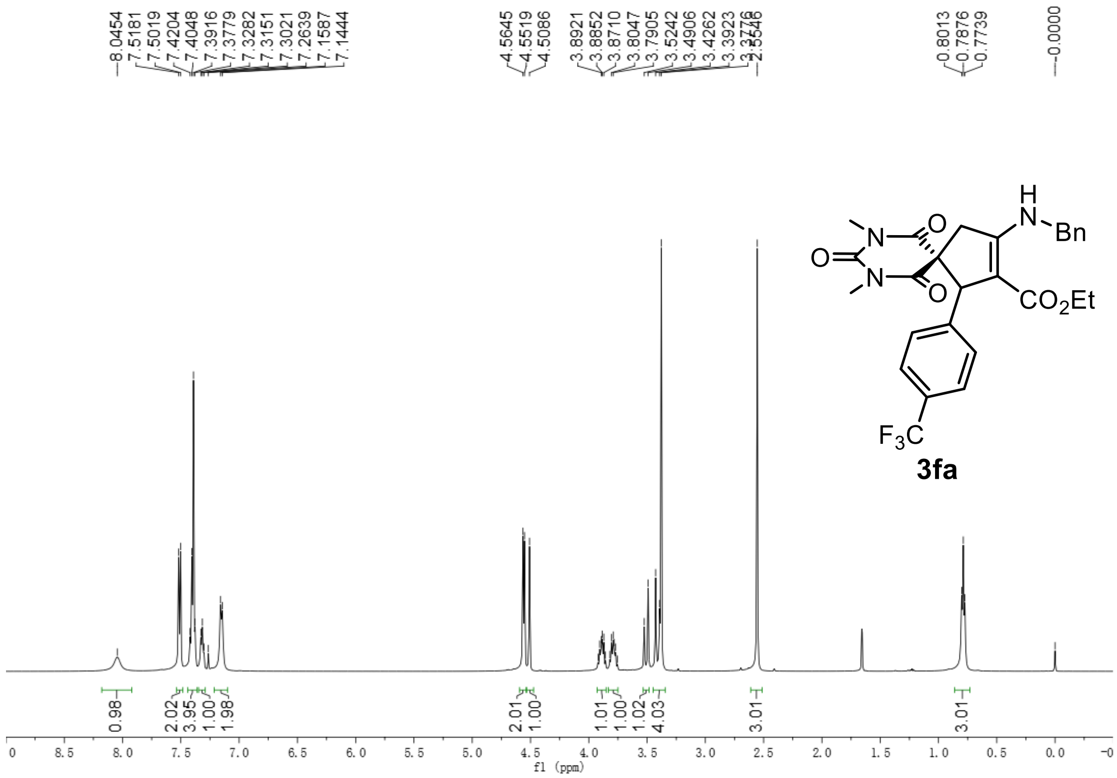


Figure S13. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3fa

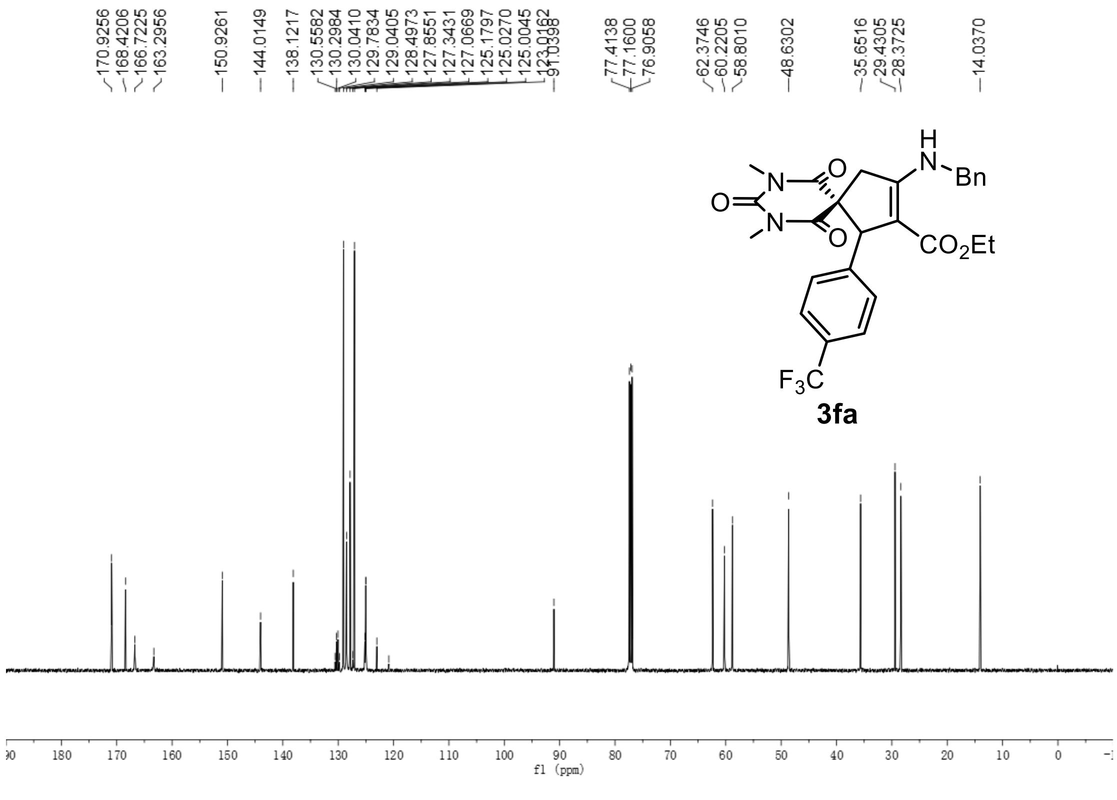


Figure S14. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3fa

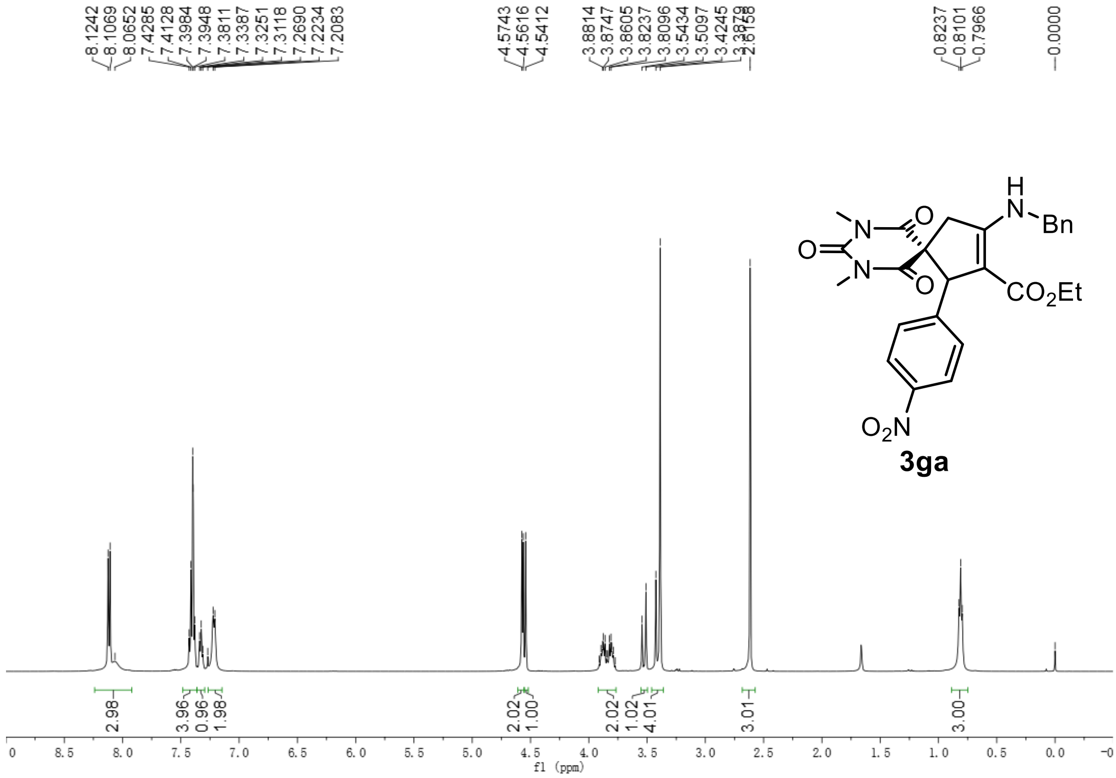


Figure S15. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ga

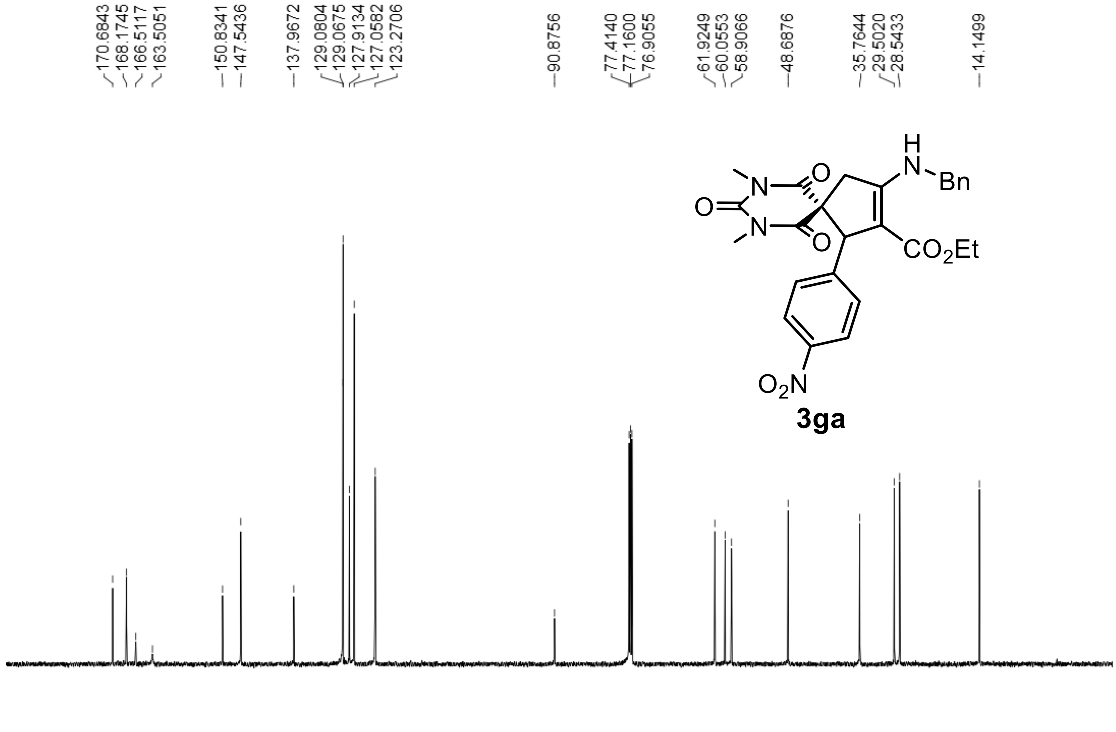


Figure S16. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ga

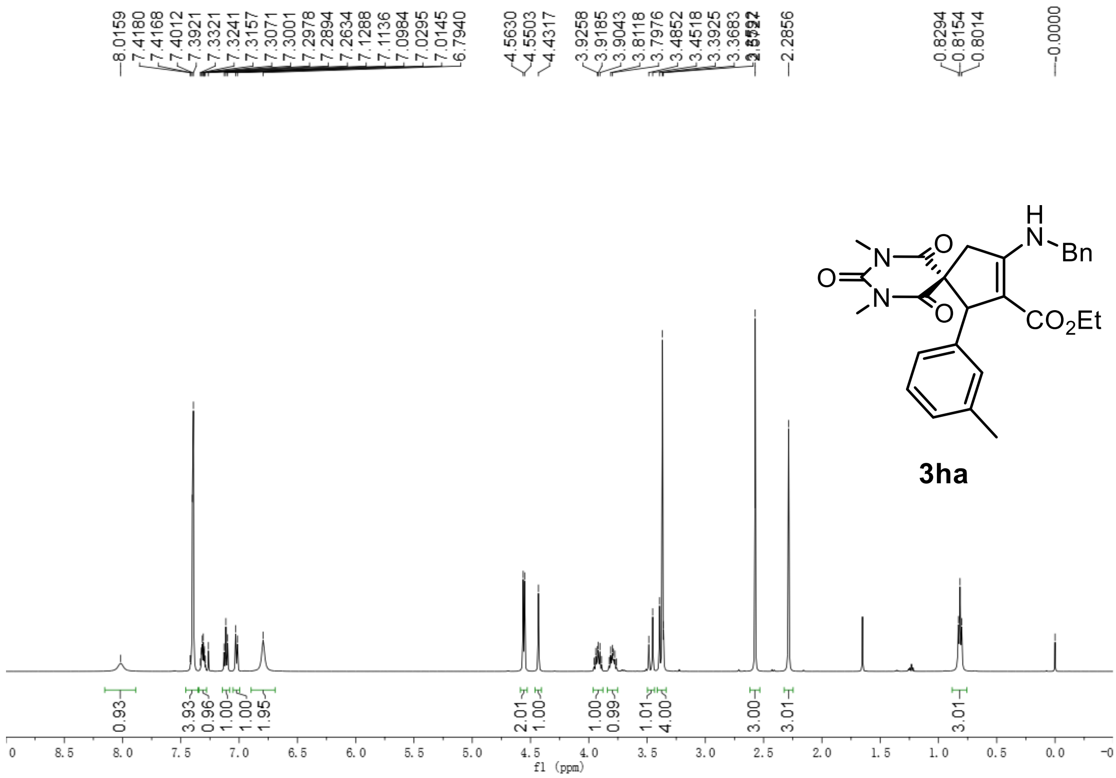


Figure S17. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ha

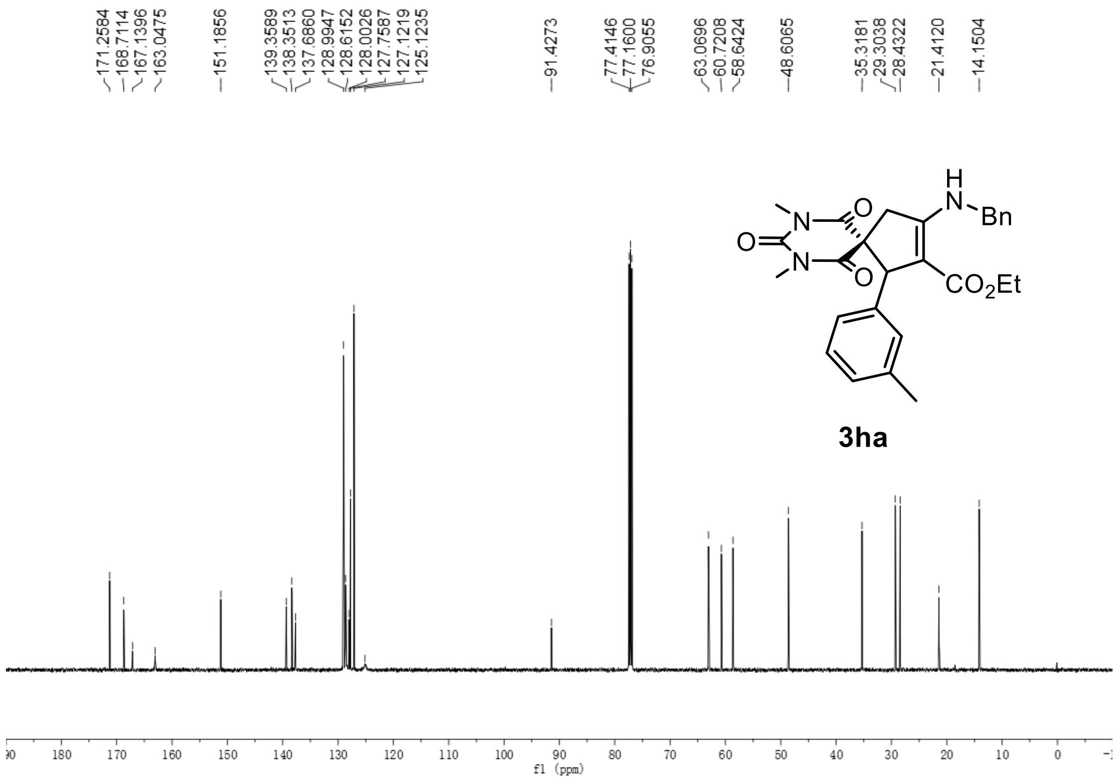


Figure S18. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ha

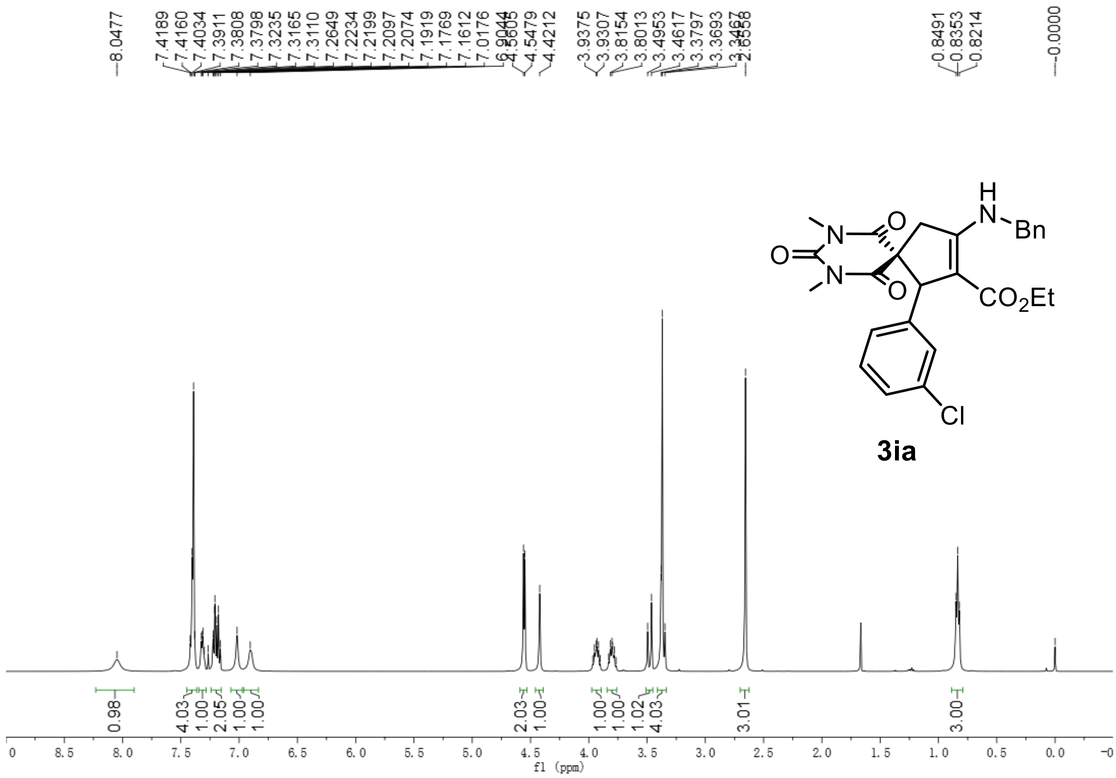


Figure S19. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ia

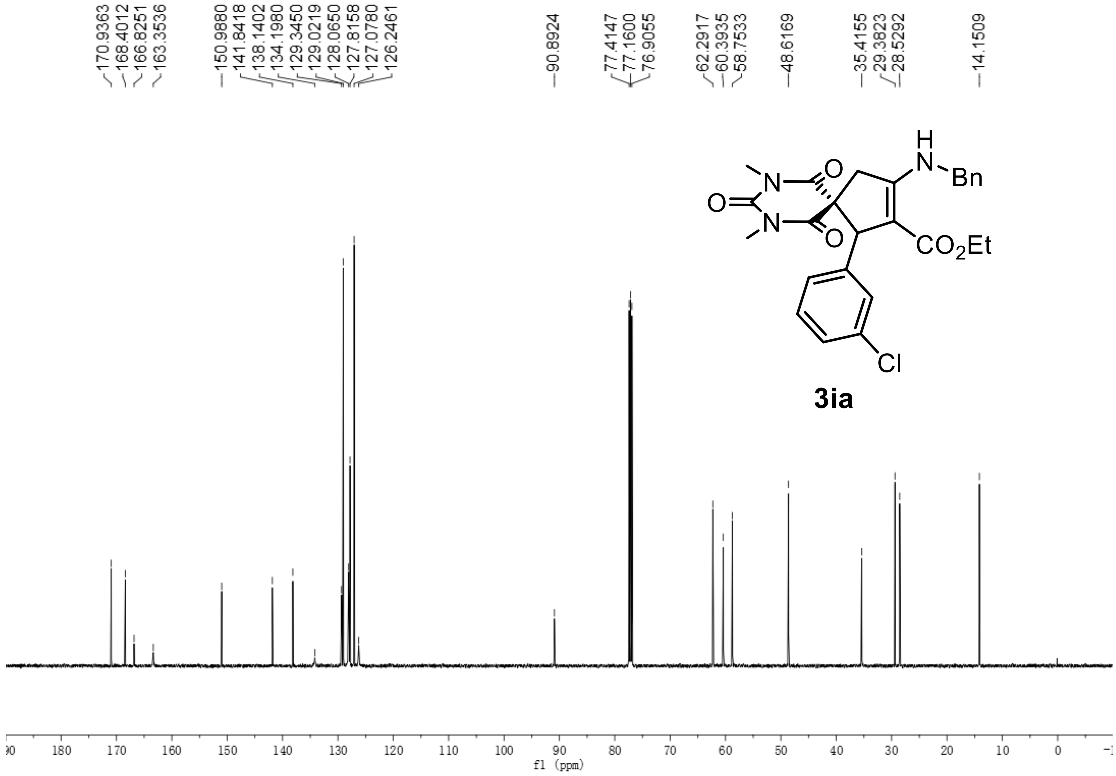


Figure S20. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ia

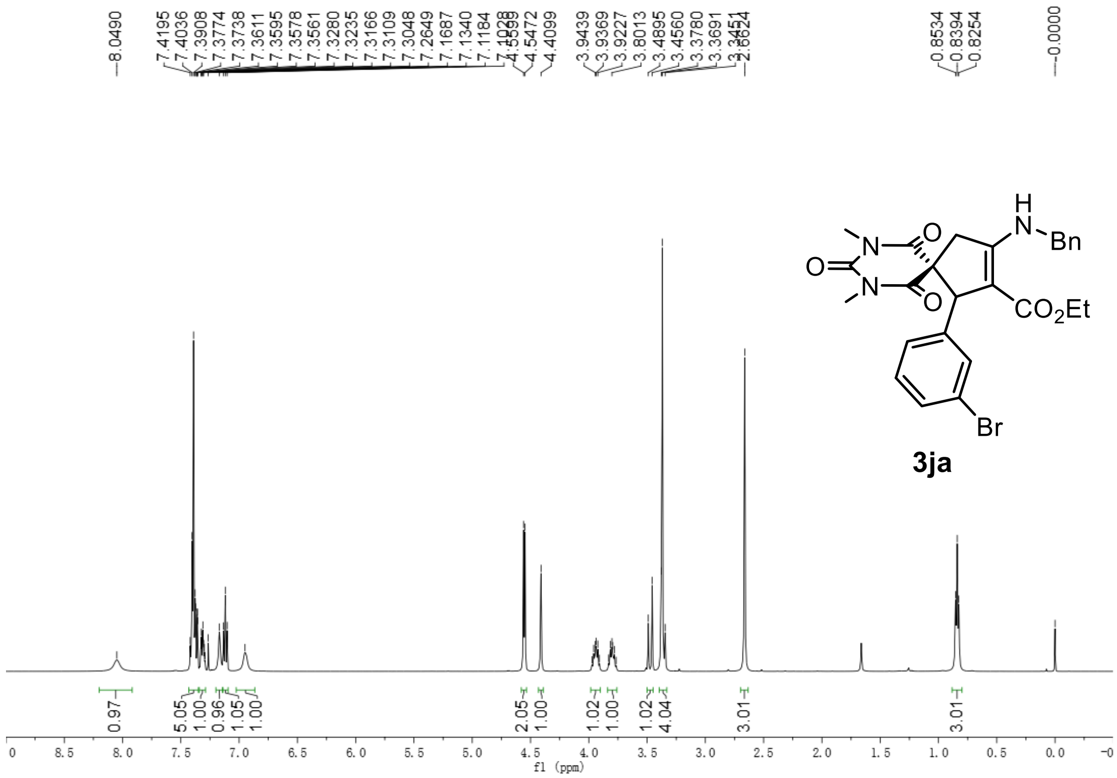


Figure S21. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ja

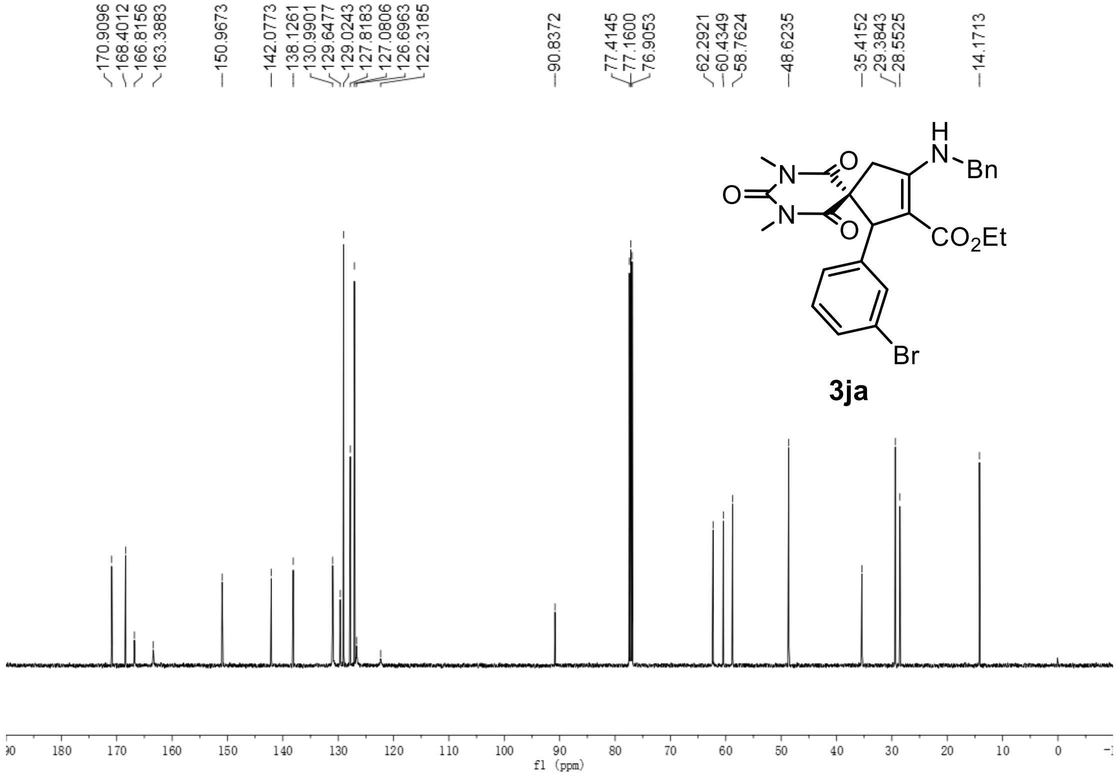


Figure S22. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ja

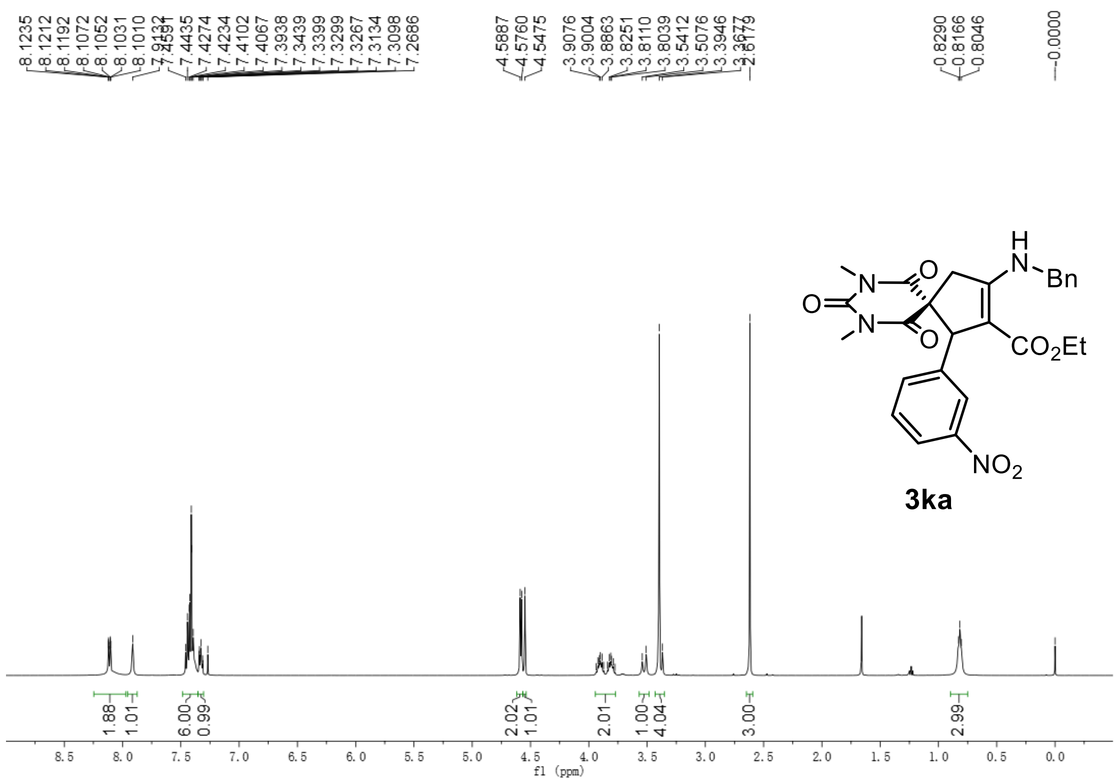


Figure S23. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3ka

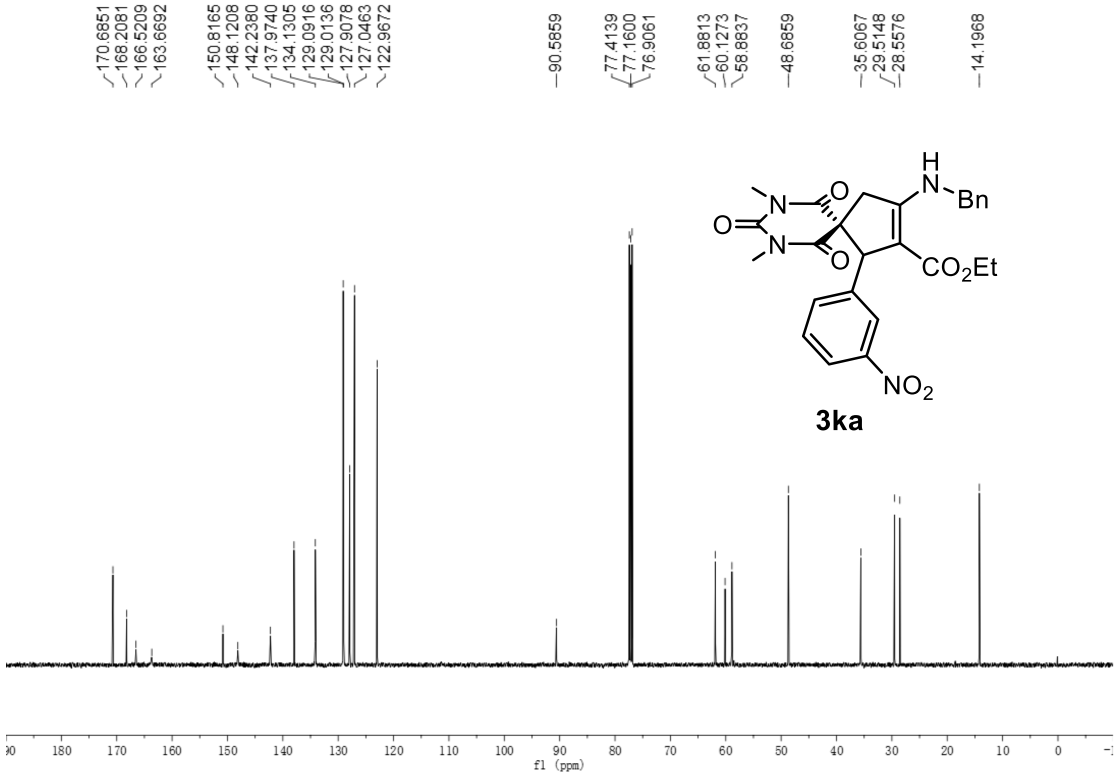


Figure S24. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3ka

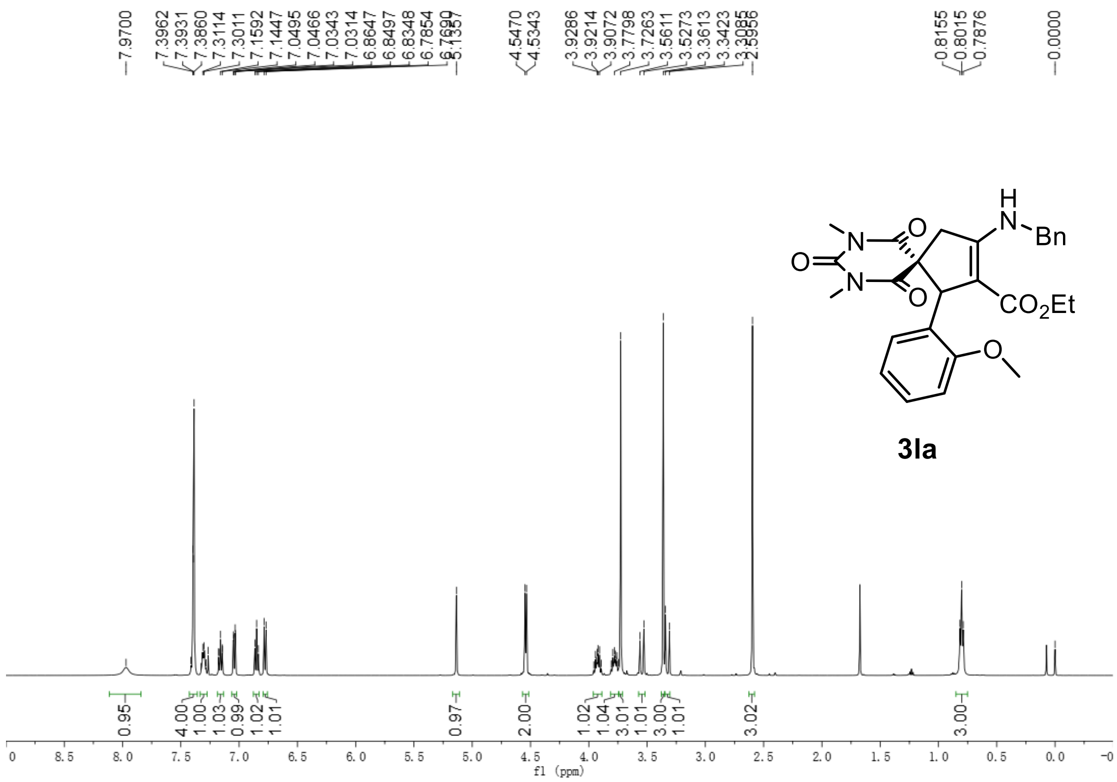


Figure S25. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3la

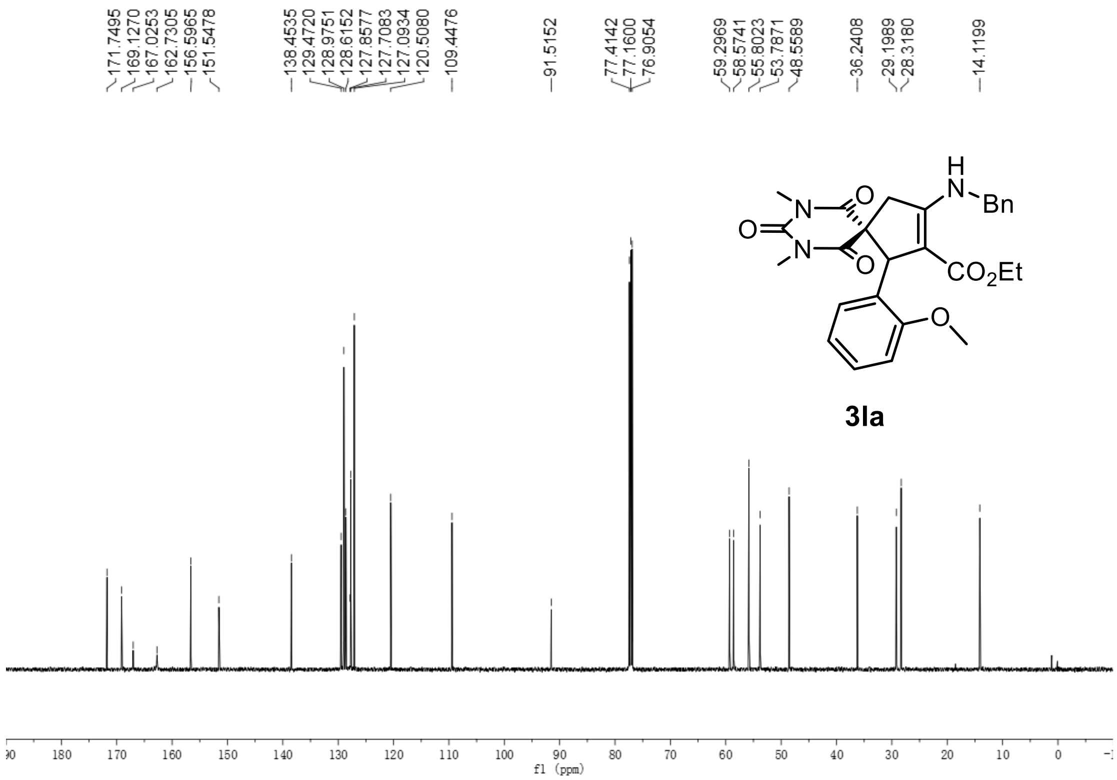
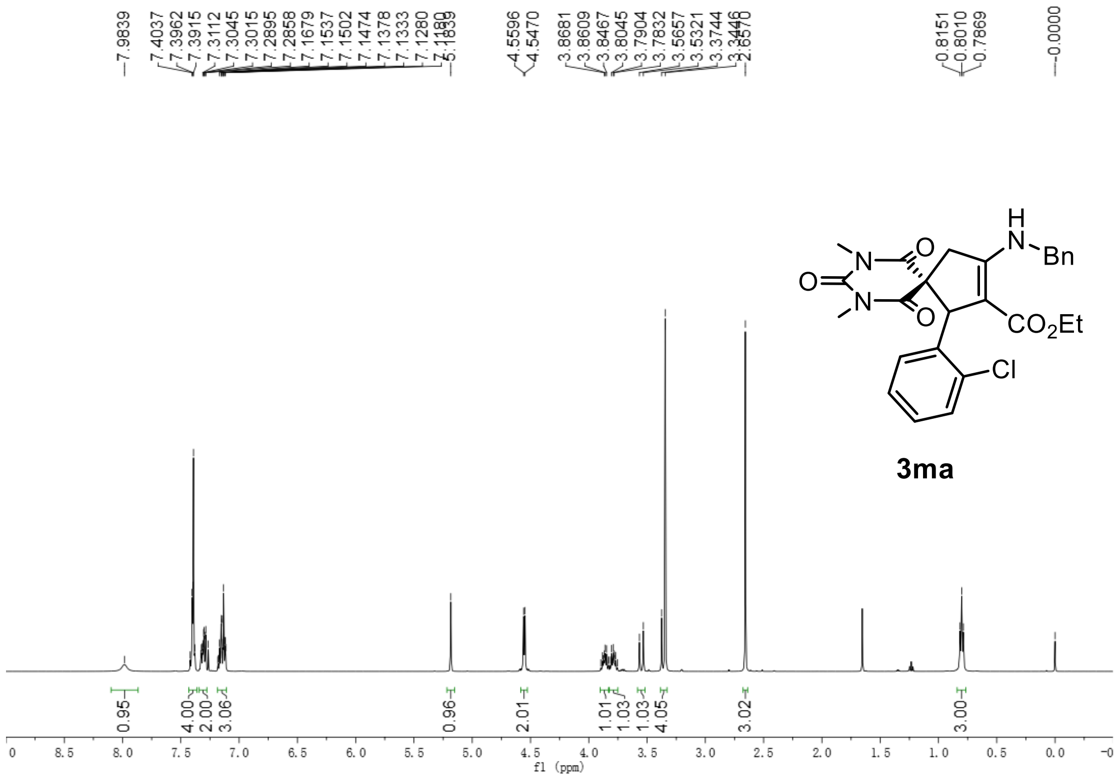
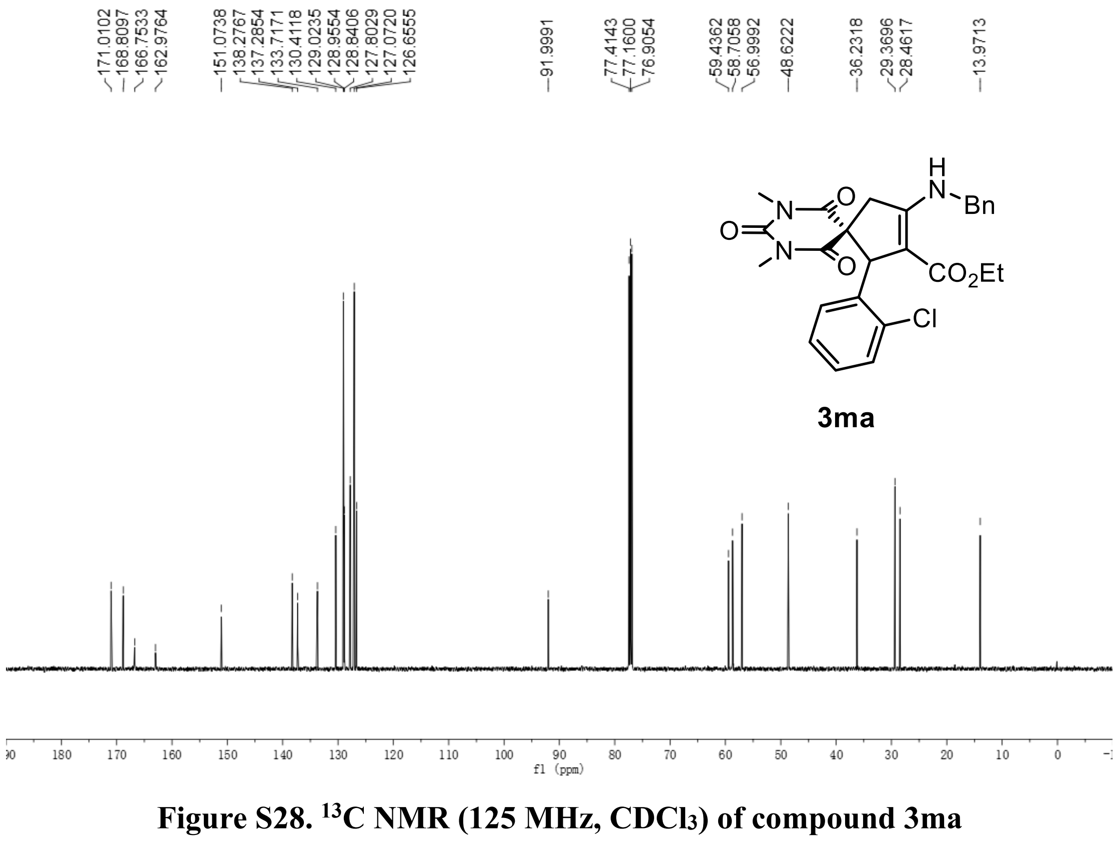


Figure S26. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3la



3ma

Figure S27. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3ma



3ma

Figure S28. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3ma

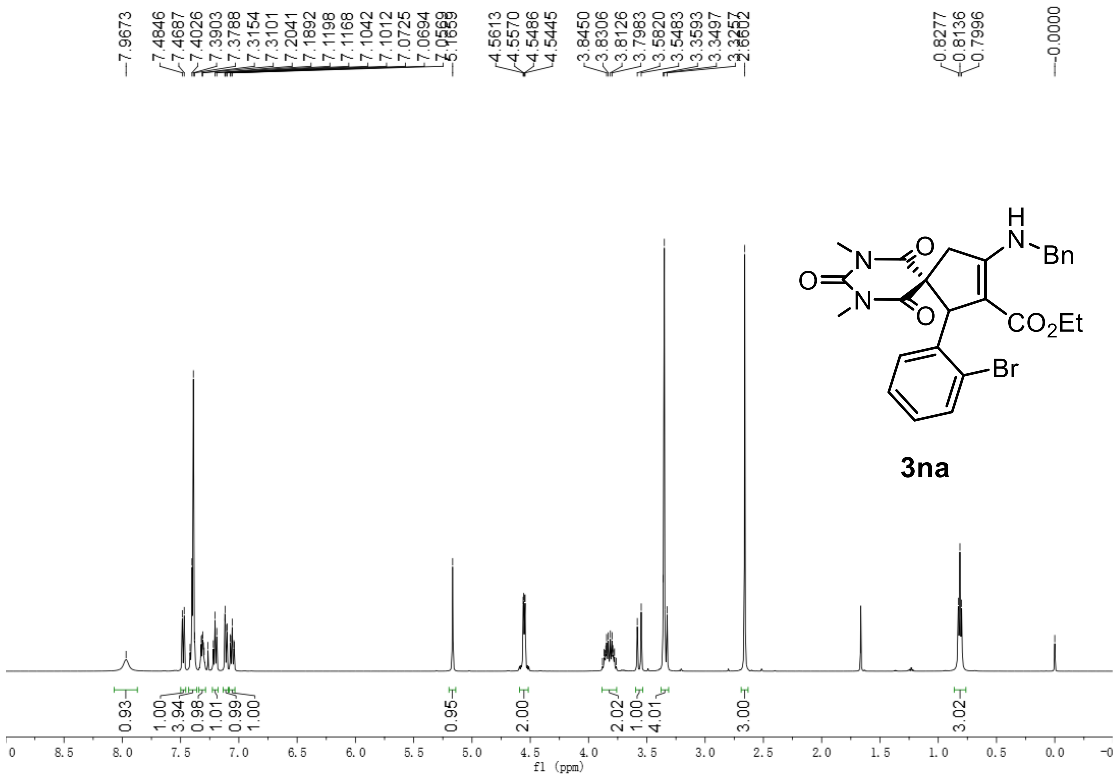


Figure S29. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3na

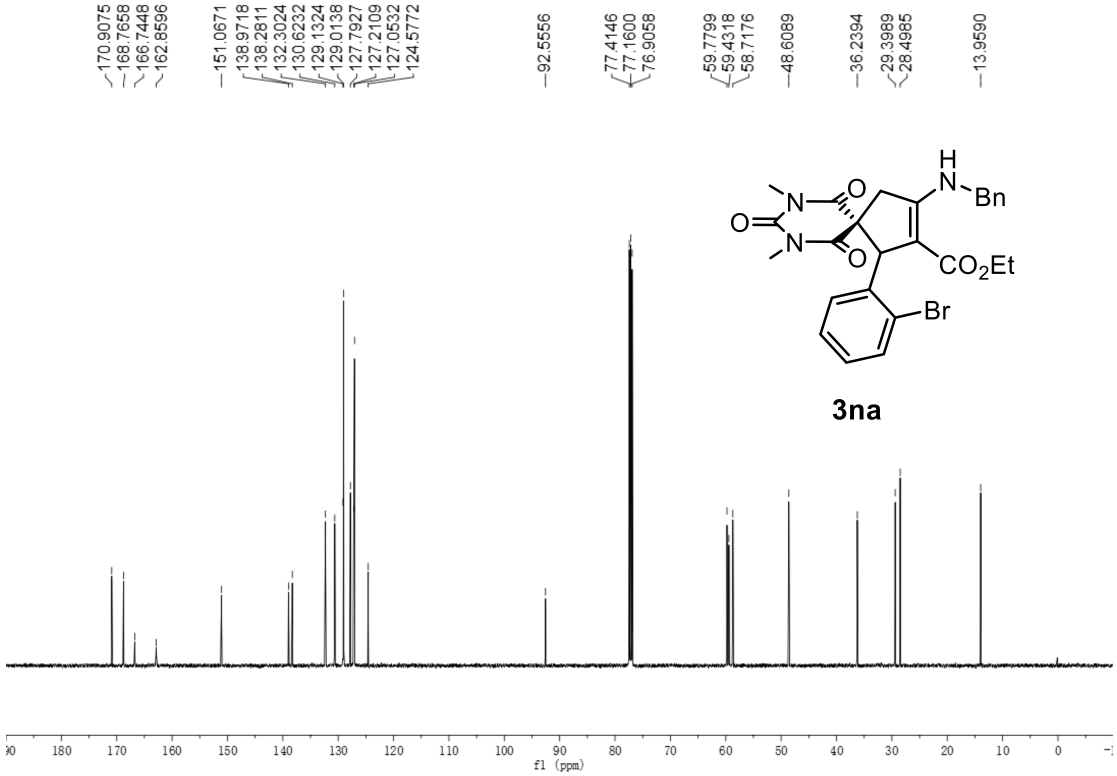


Figure S30. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3na

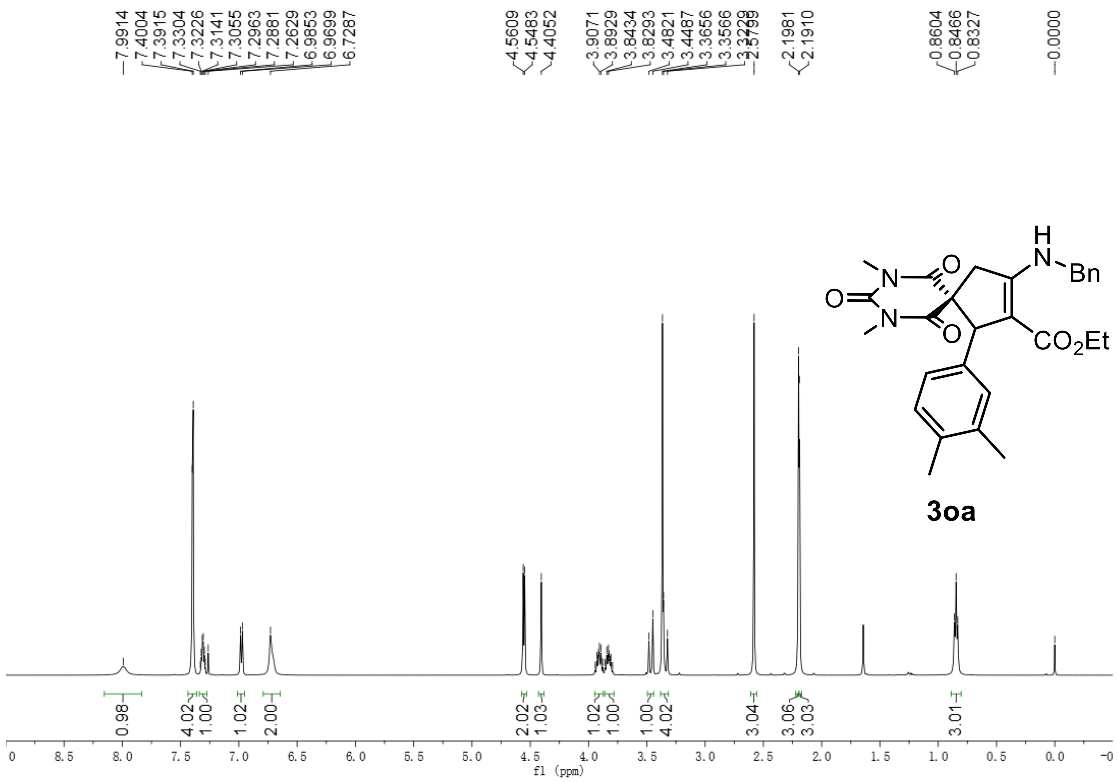


Figure S31. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3oa

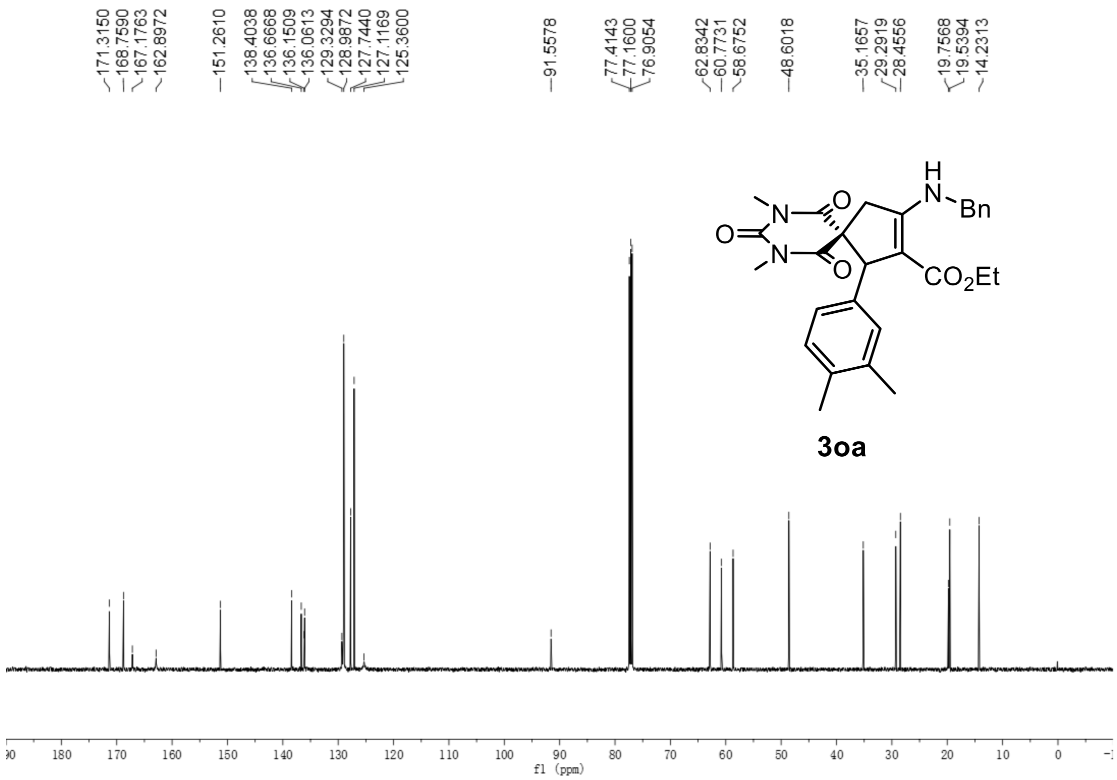


Figure S32. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3oa

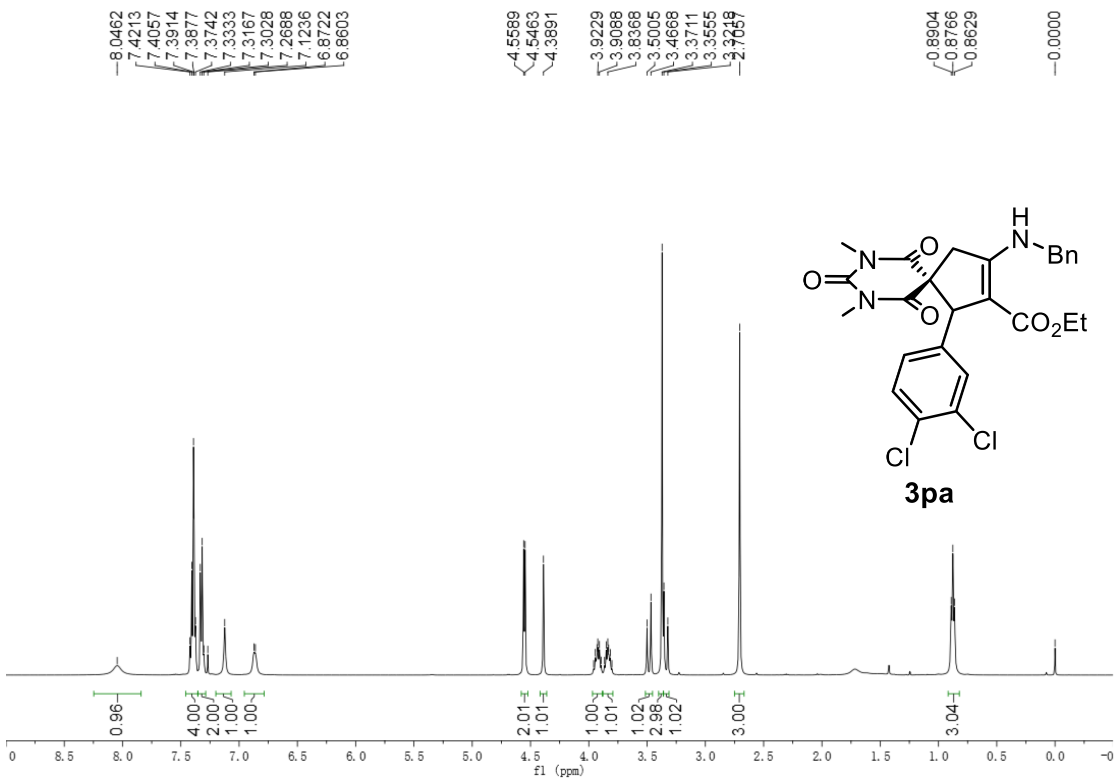


Figure S33. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3pa

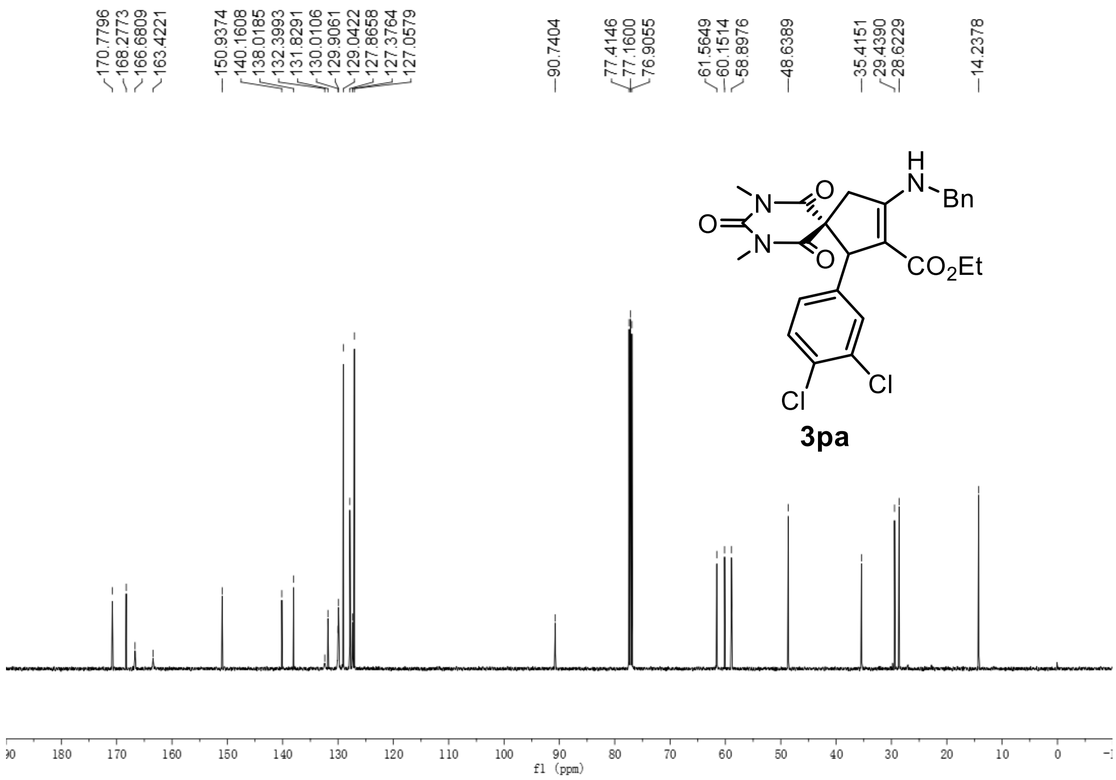


Figure S34. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3pa

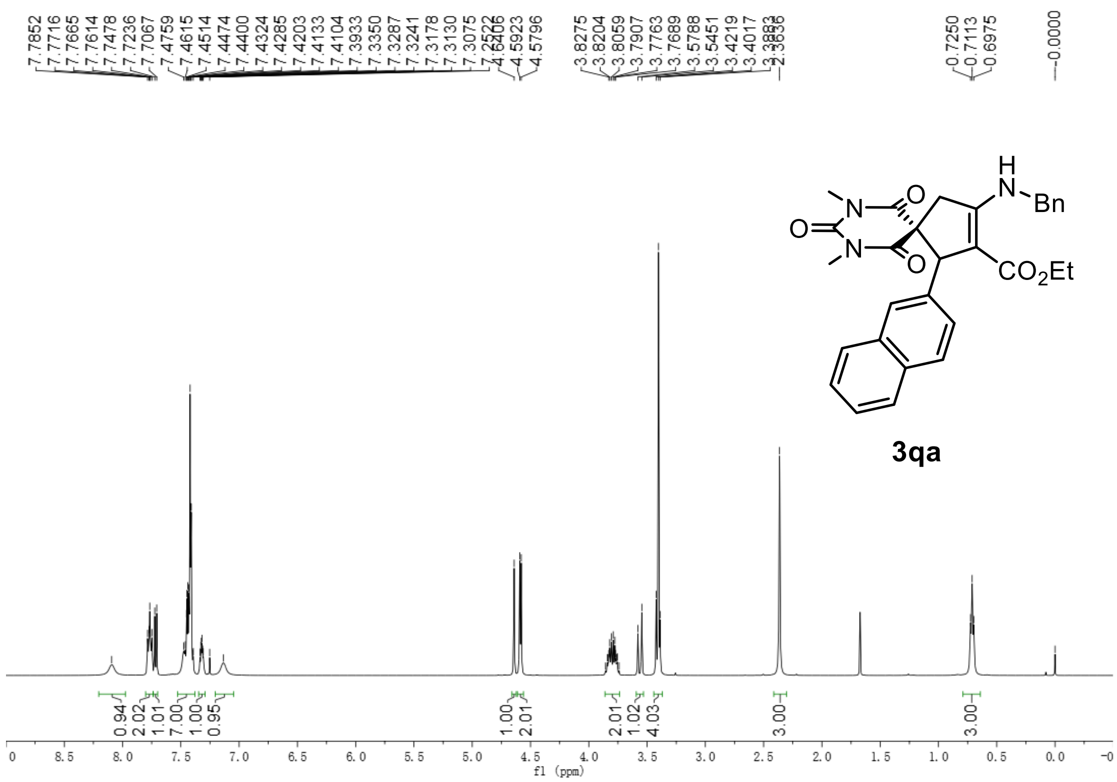


Figure S35. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3qa

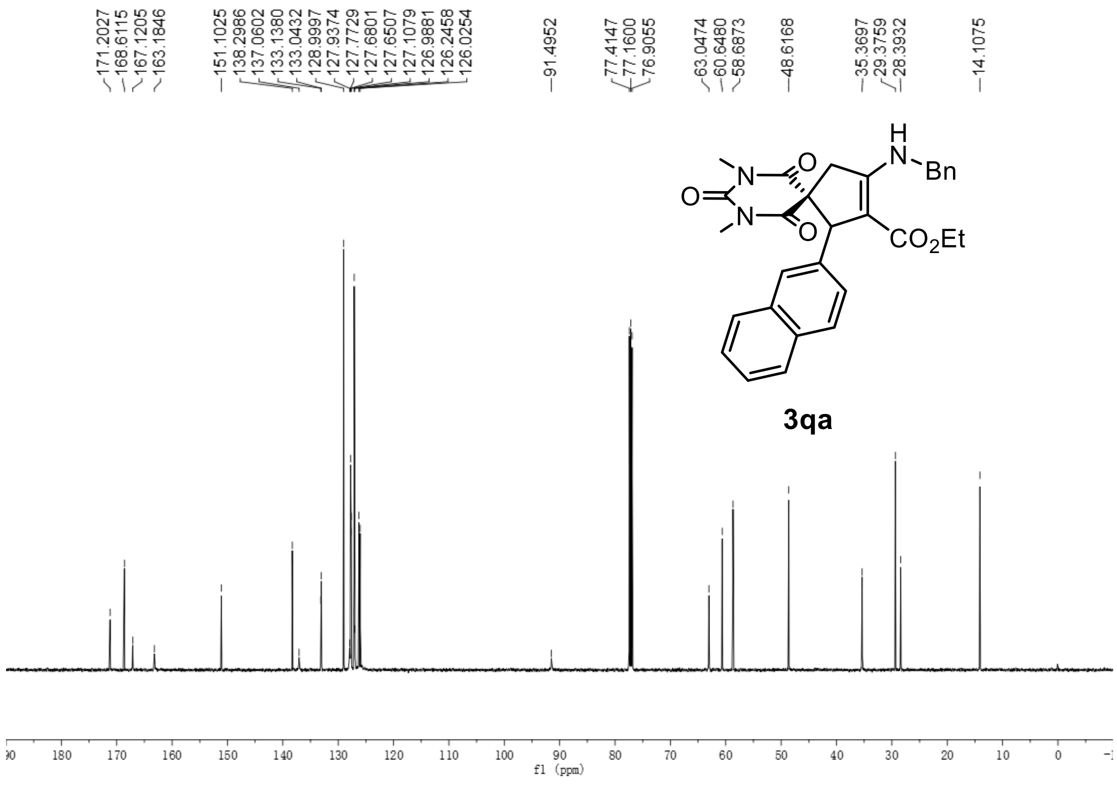


Figure S36. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3qa

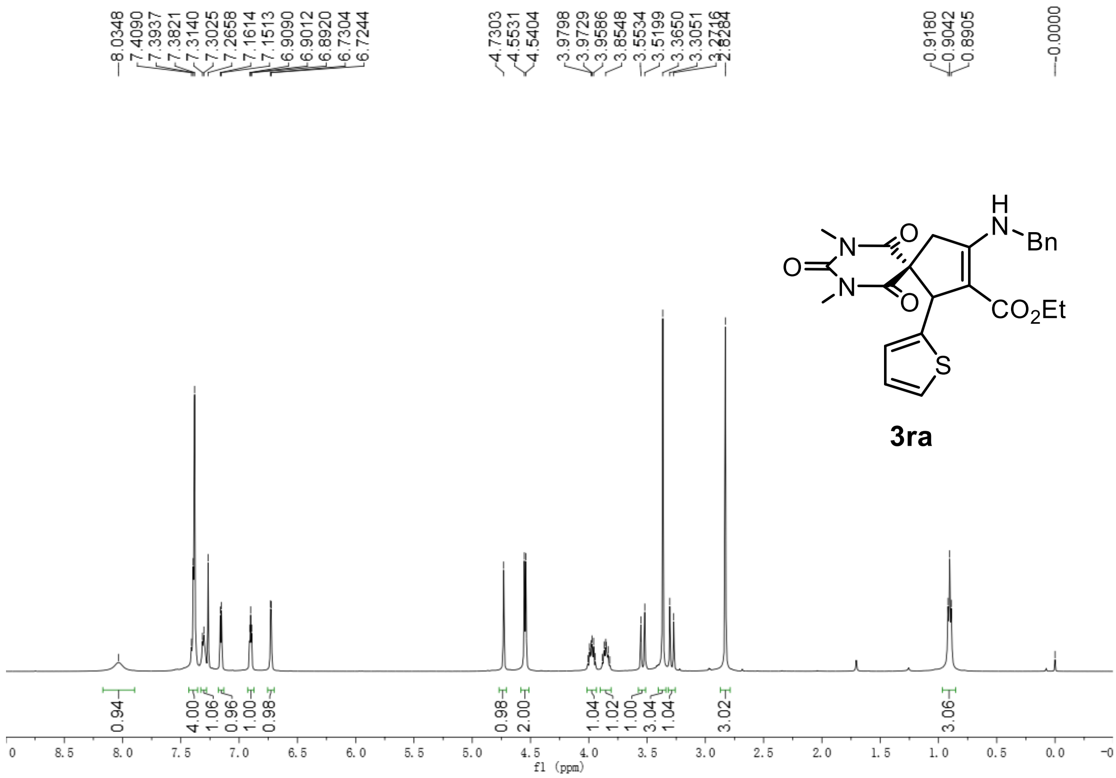


Figure S37. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3ra

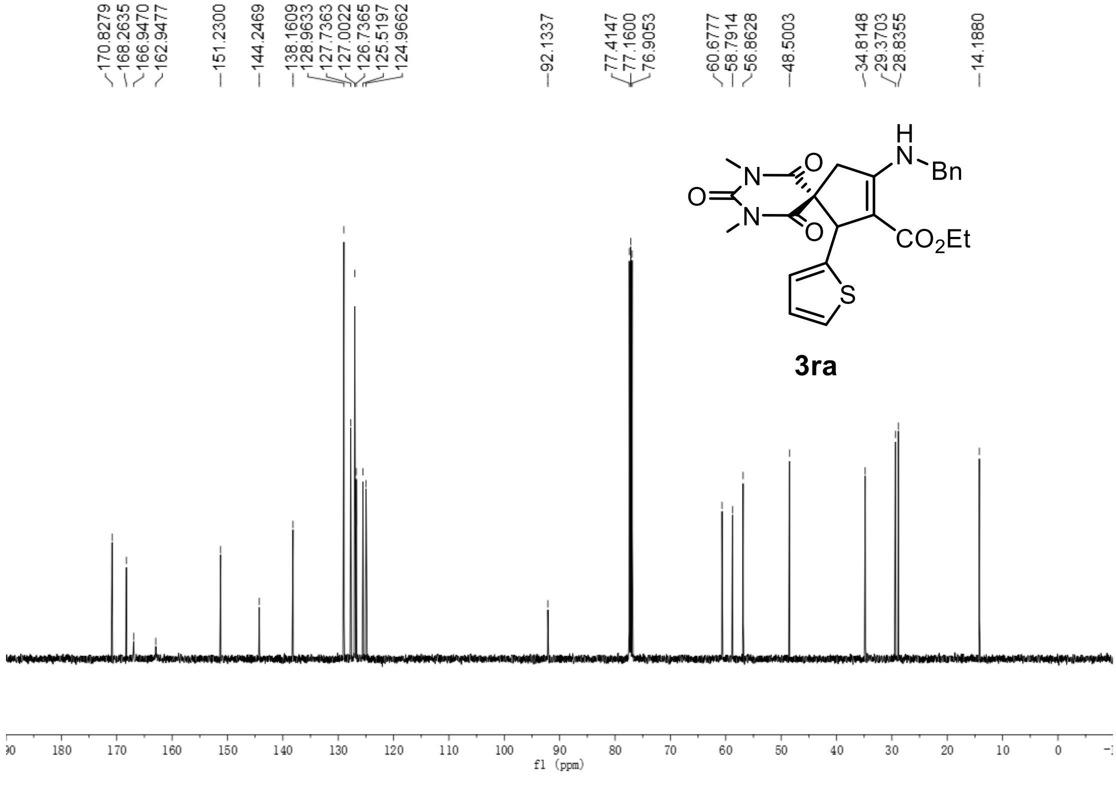


Figure S38. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3ra

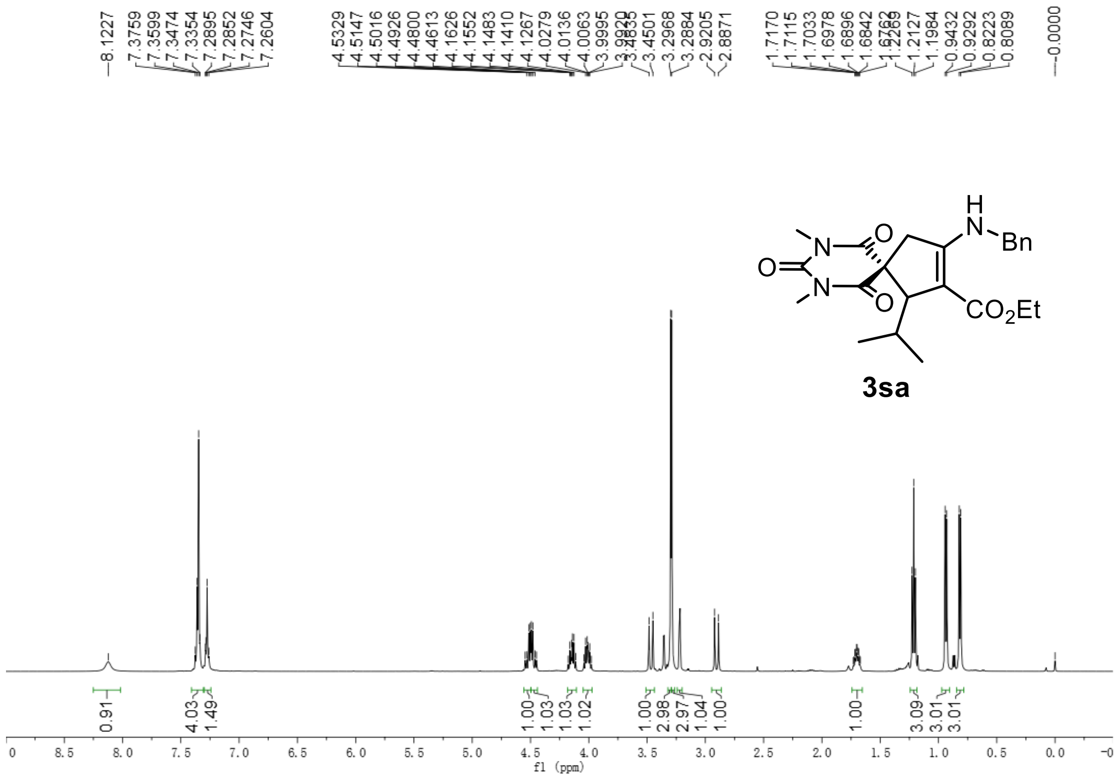


Figure S39. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3sa

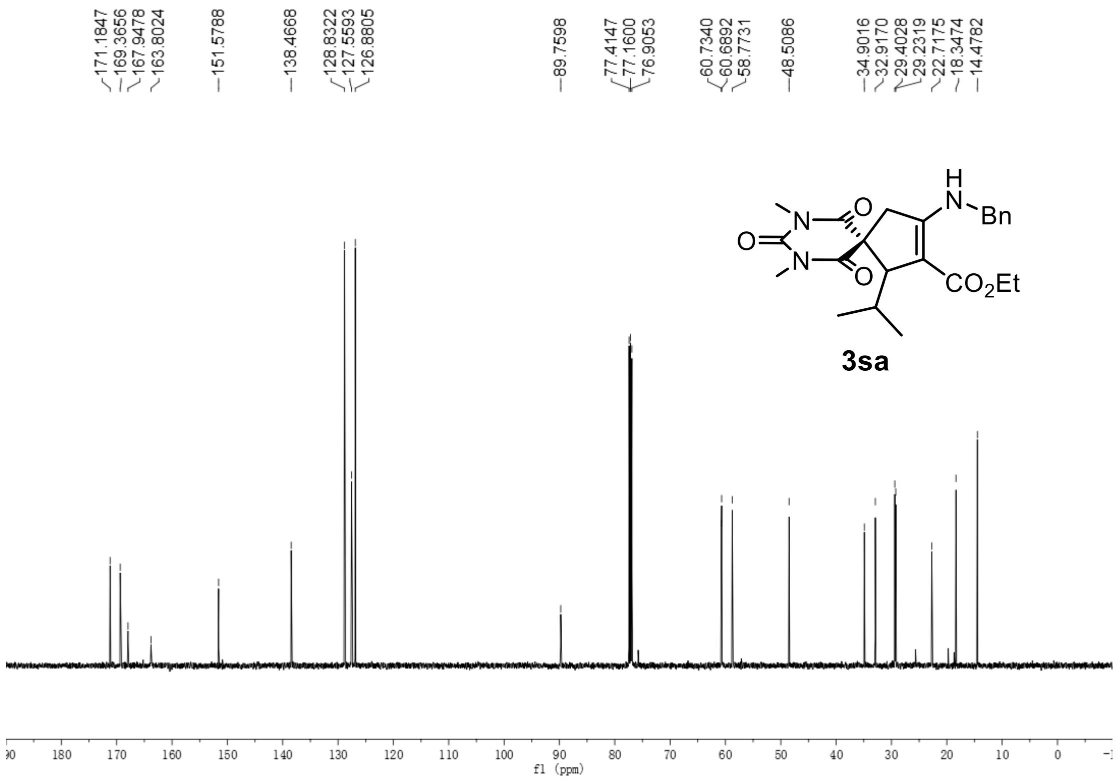


Figure S40. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3sa

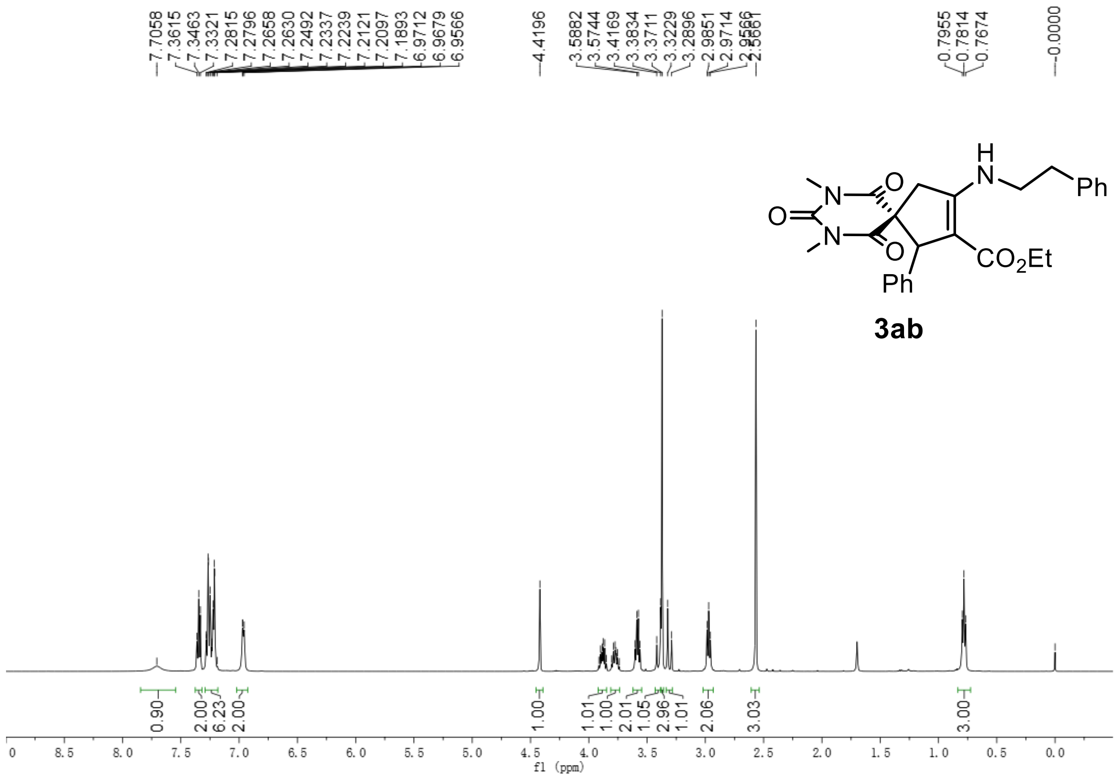


Figure S41. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ab

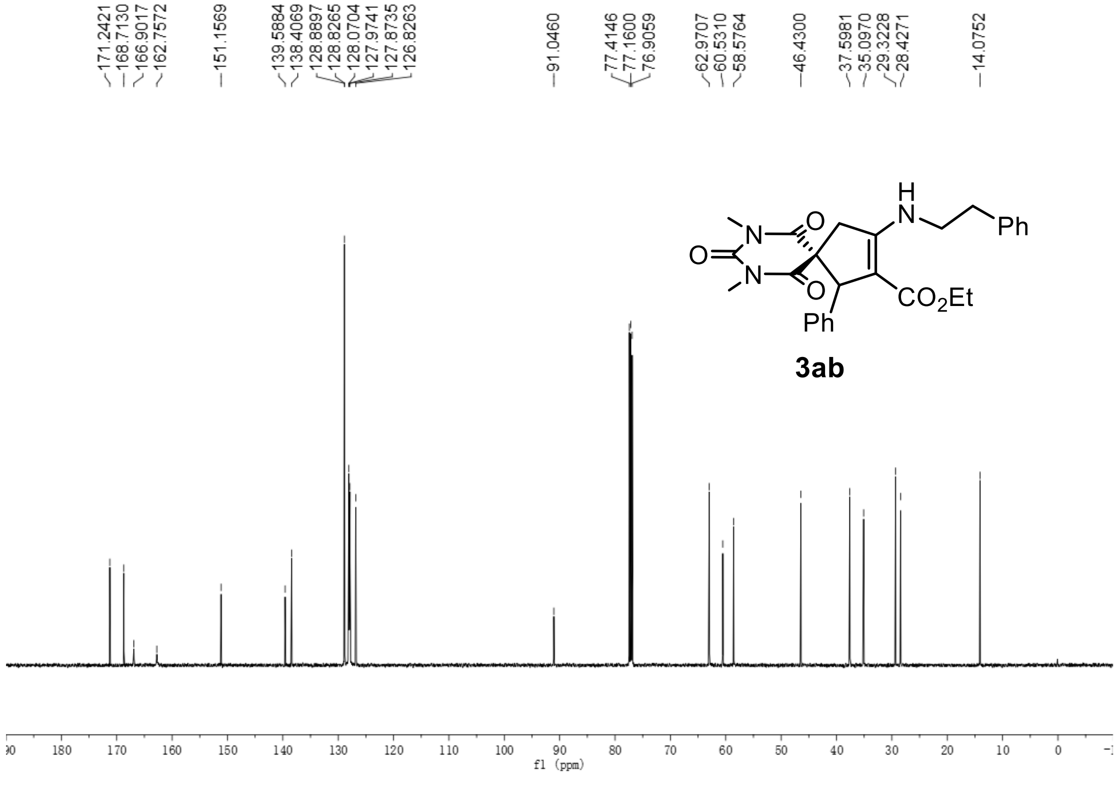


Figure S42. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ab

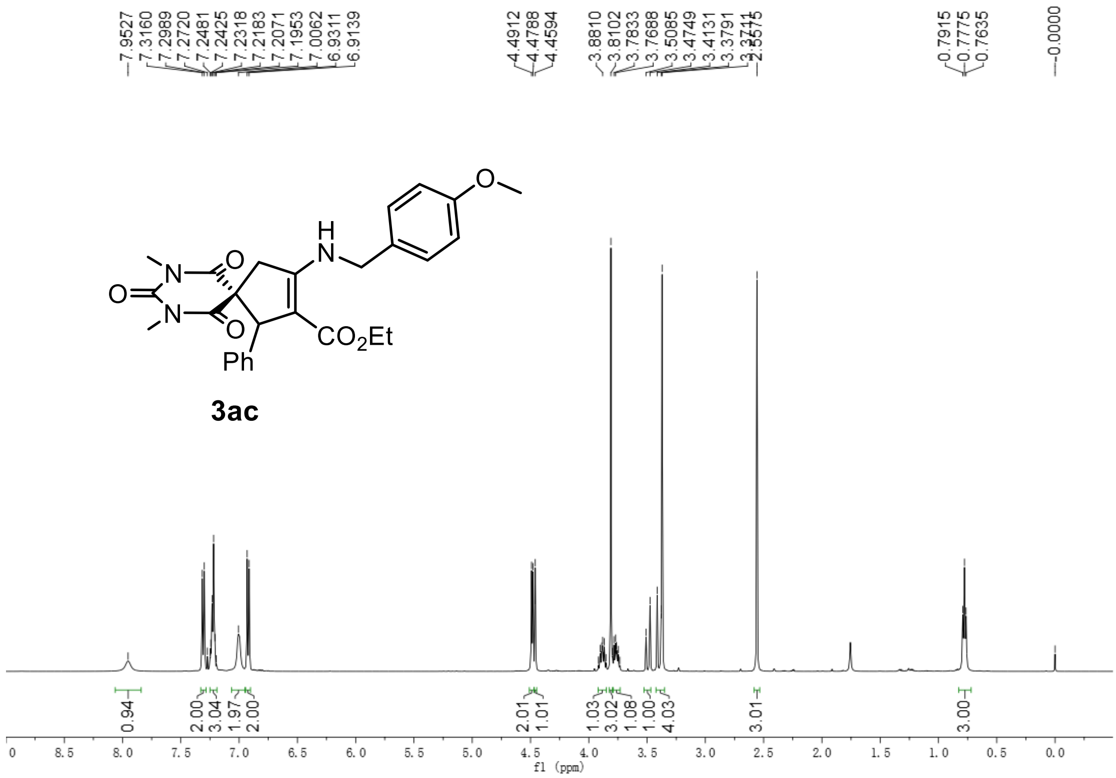


Figure S43. ¹H NMR (500 MHz, CDCl₃) of compound 3ac

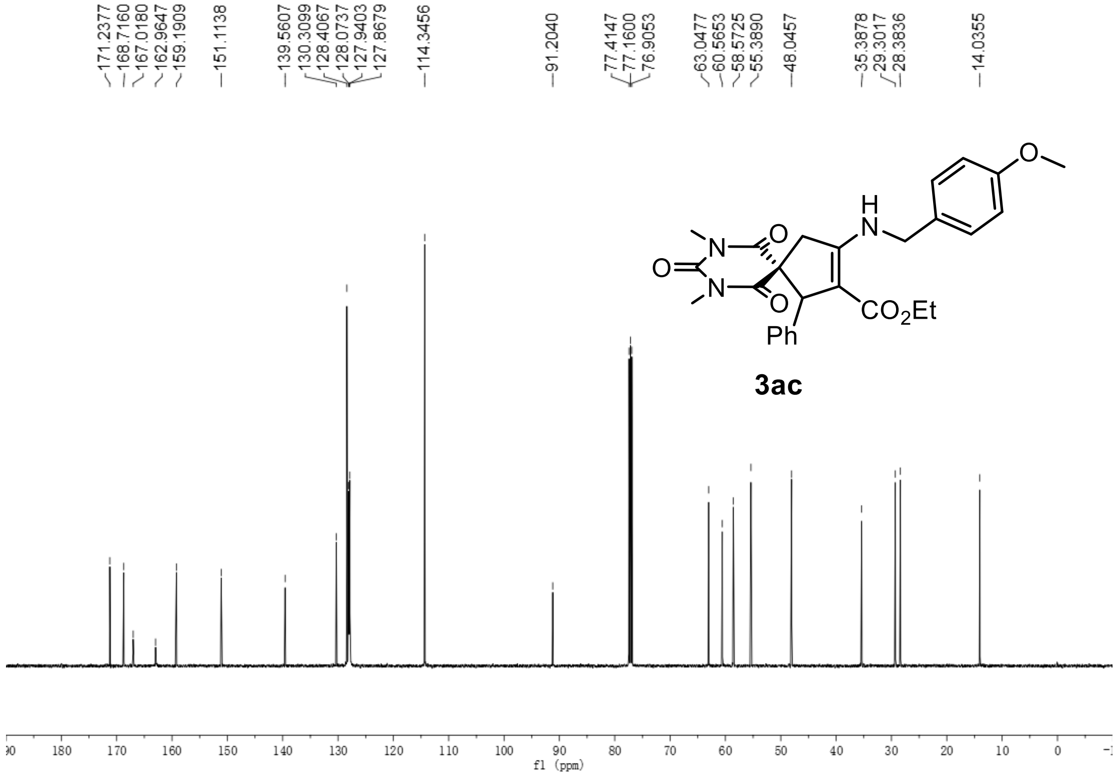


Figure S44. ¹³C NMR (125 MHz, CDCl₃) of compound 3ac

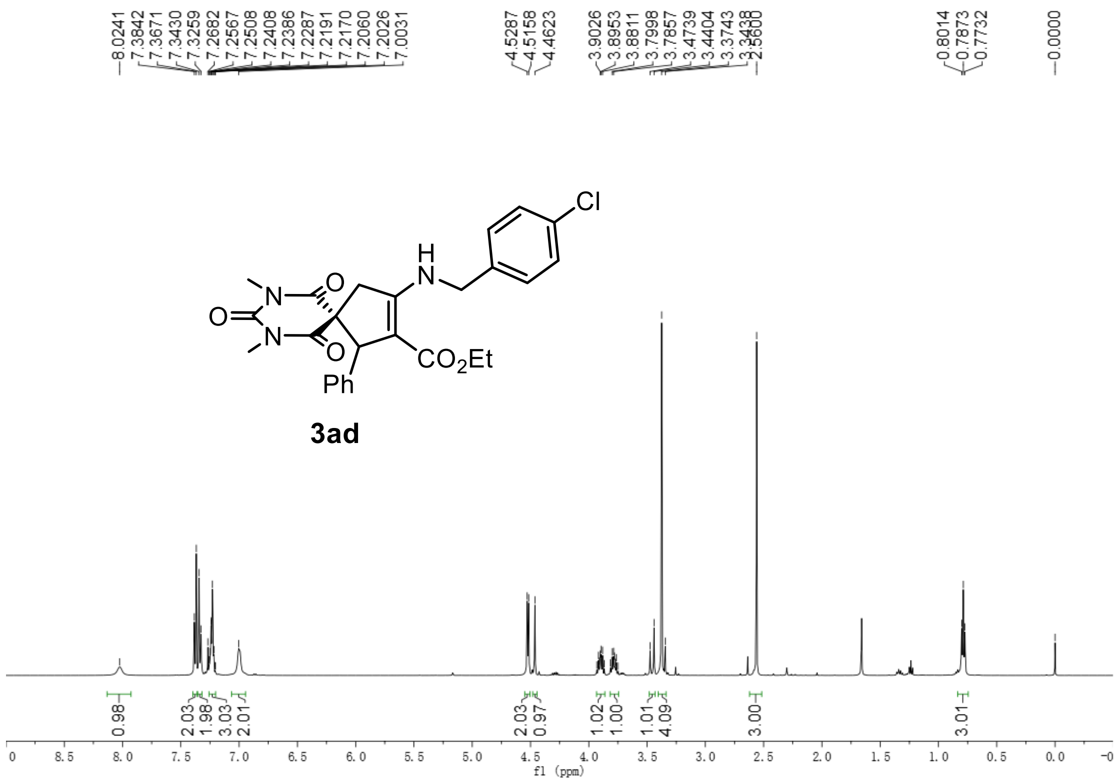


Figure S45. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ad

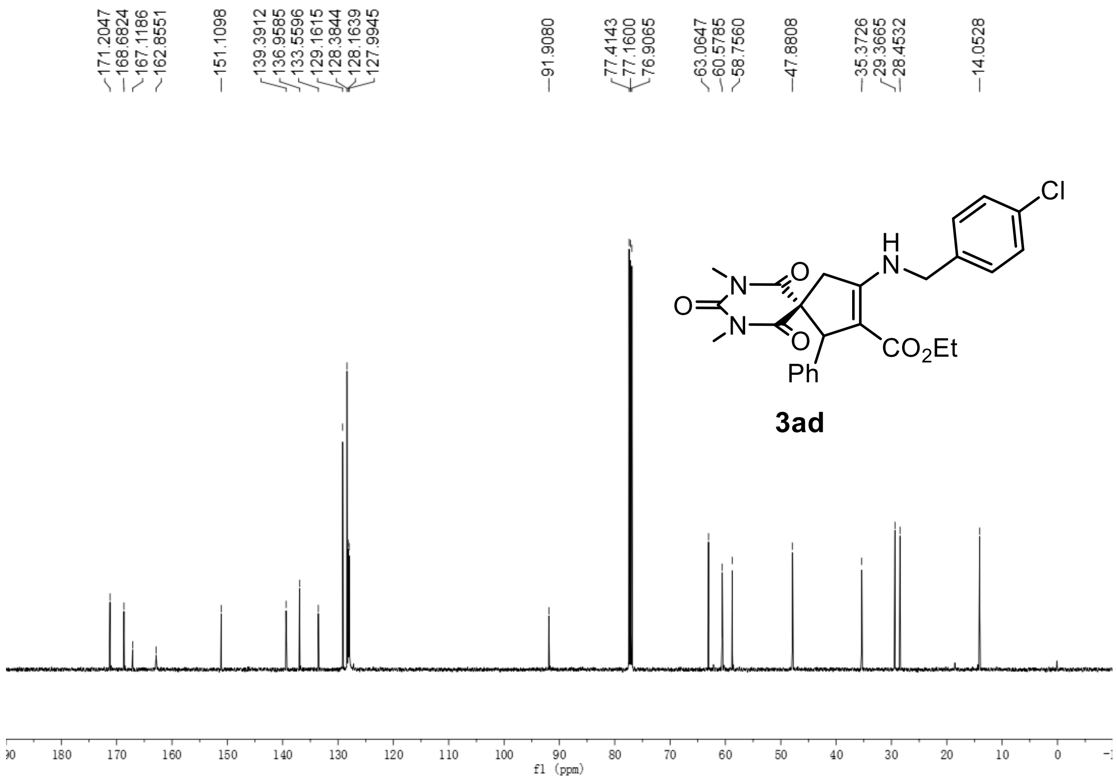


Figure S46. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ad

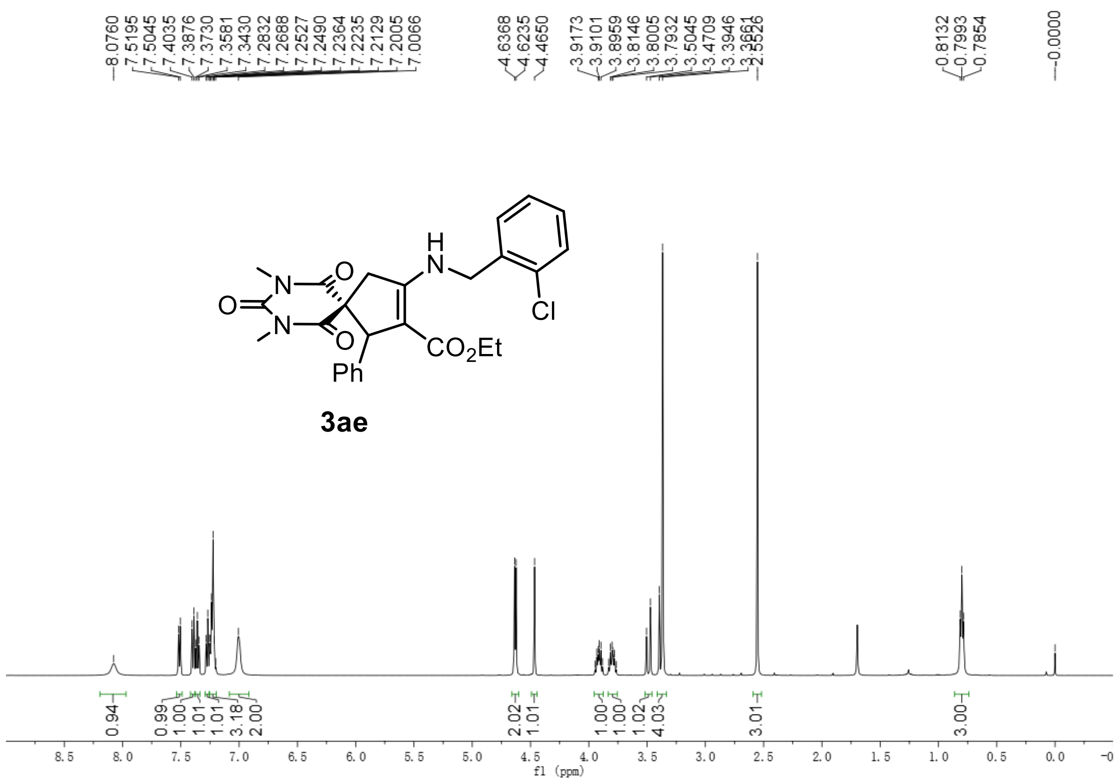


Figure S47. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3ae

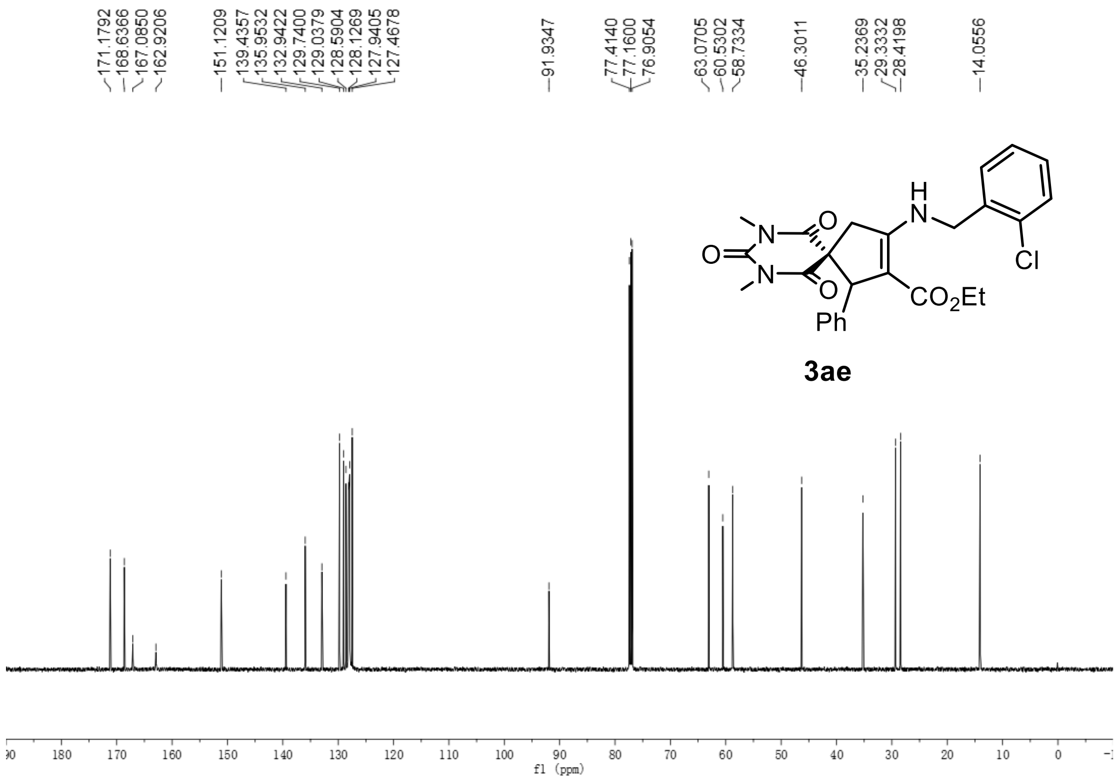


Figure S48. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3ae

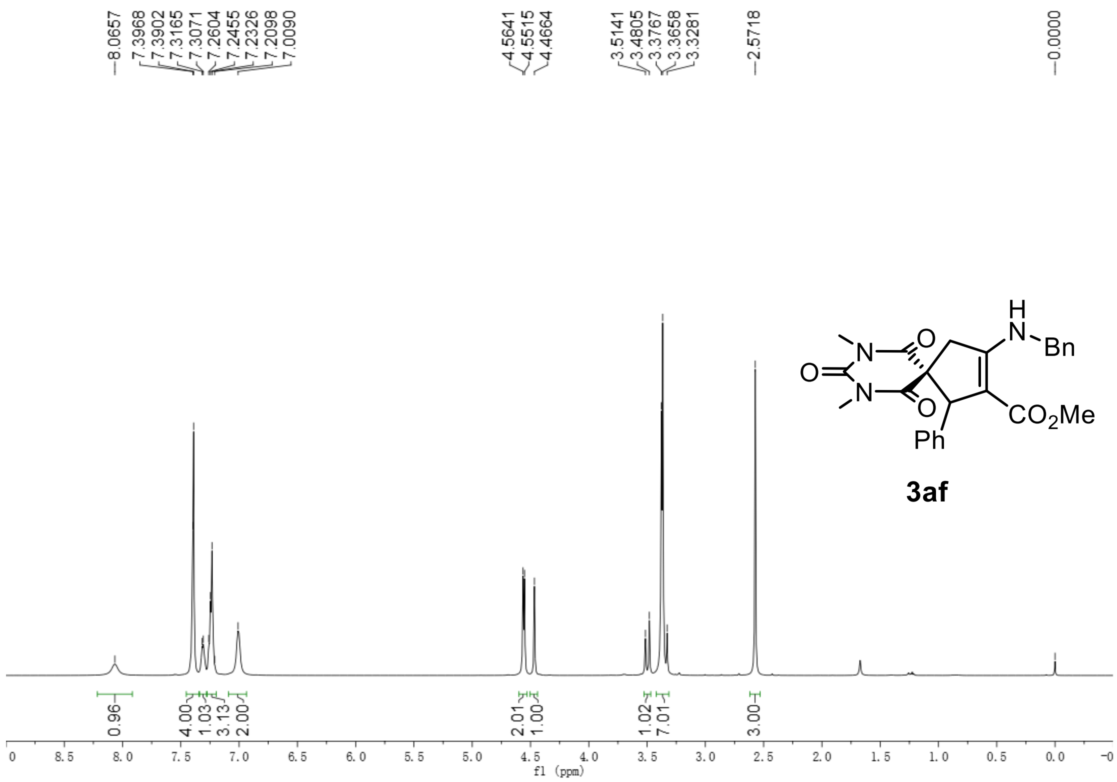


Figure S49. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 3af

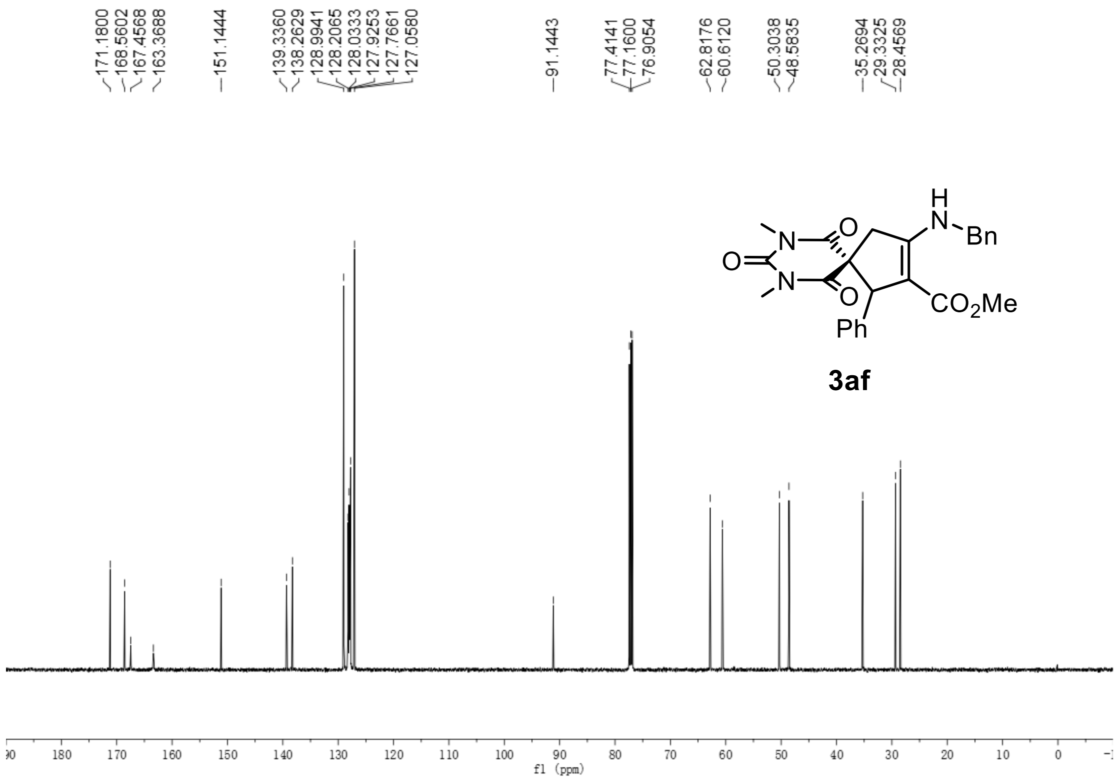


Figure S50. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 3af

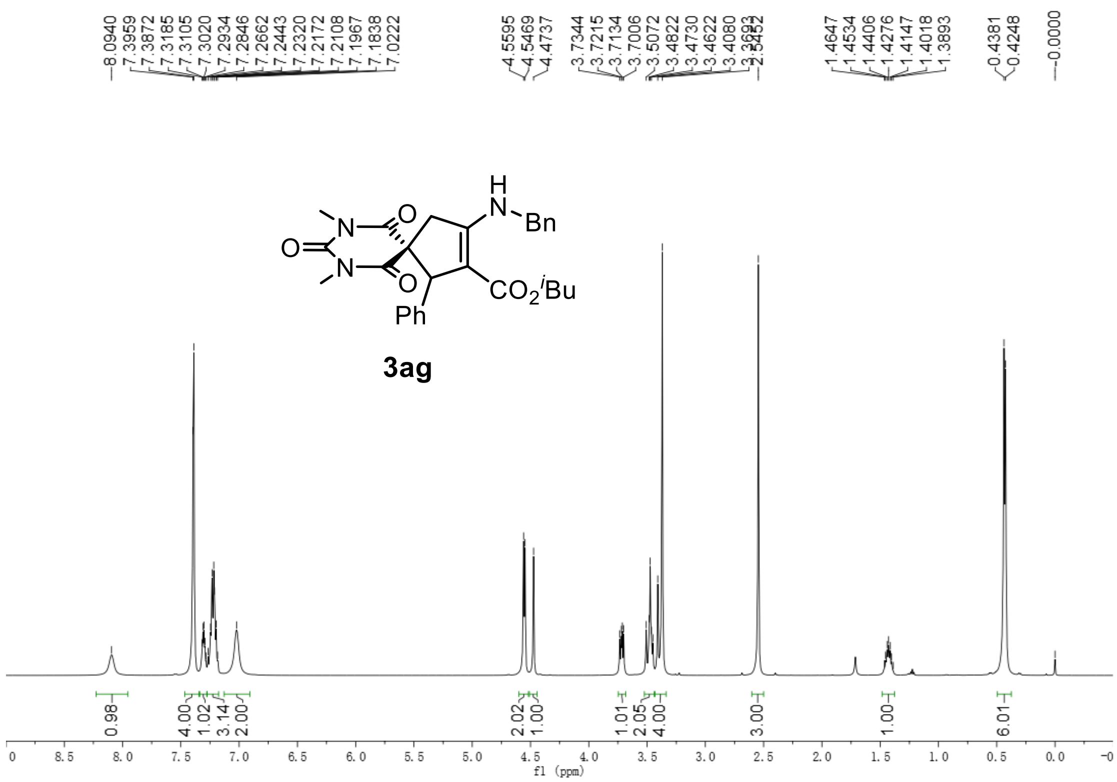


Figure S51. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ag

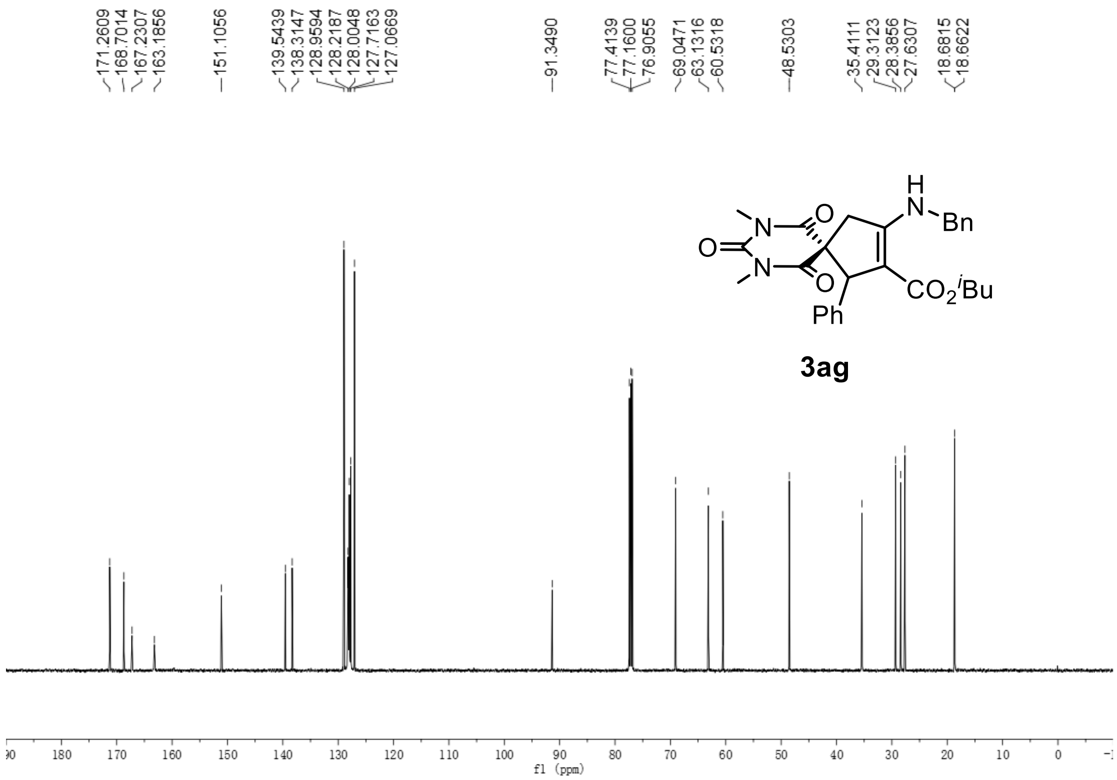


Figure S52. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ag

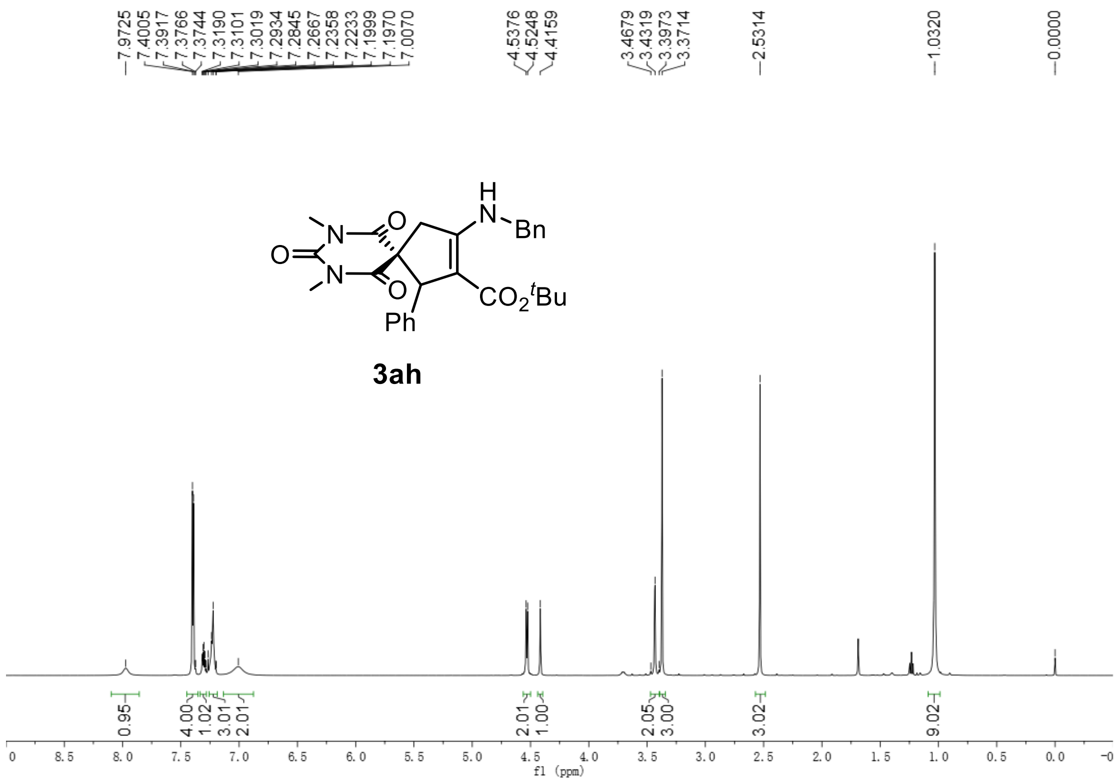


Figure S53. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 3ah

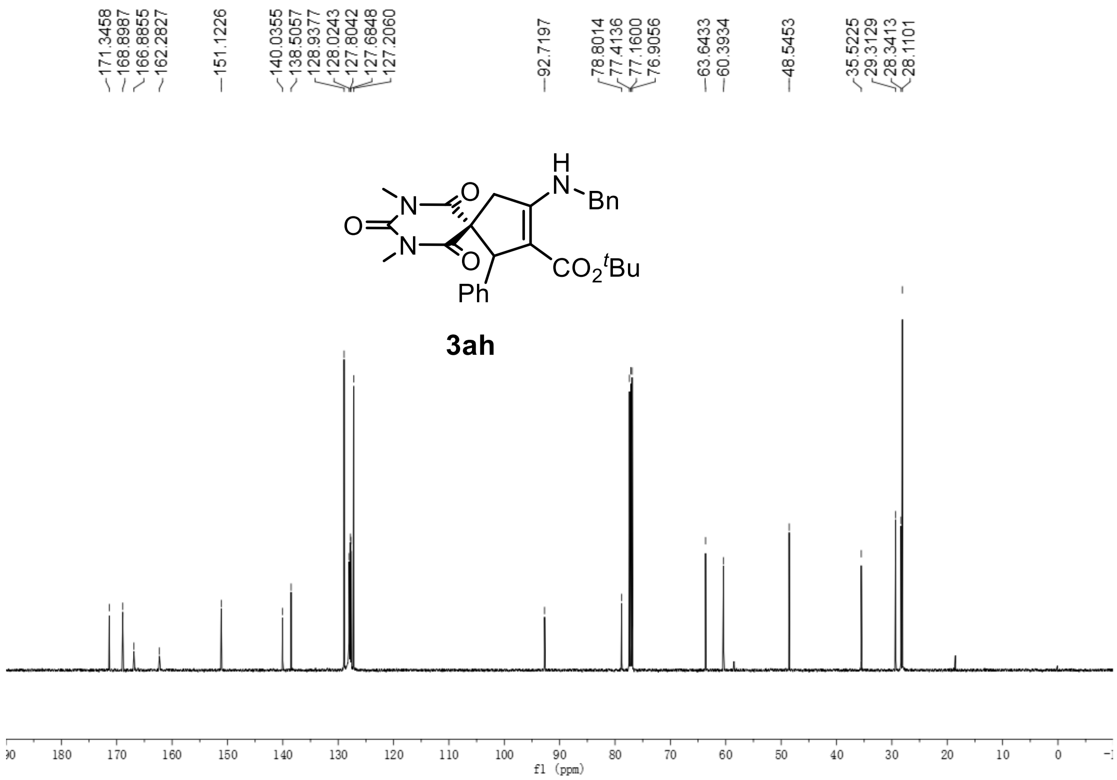


Figure S54. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 3ah

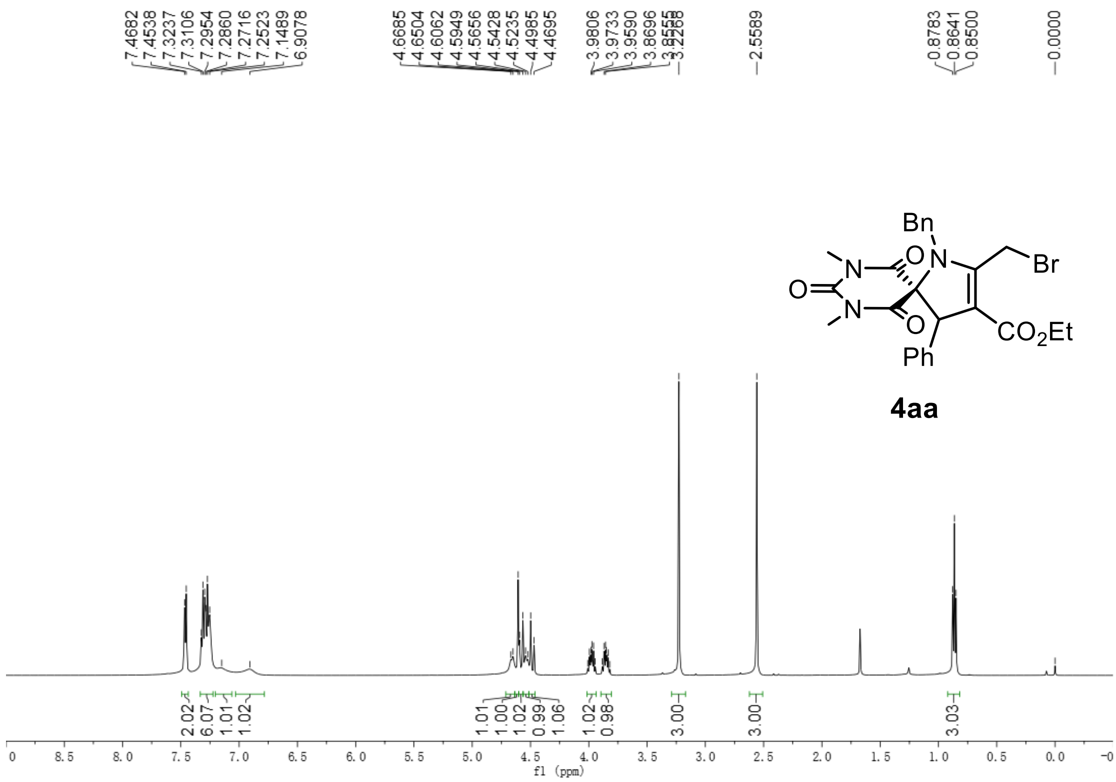


Figure S55. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4aa

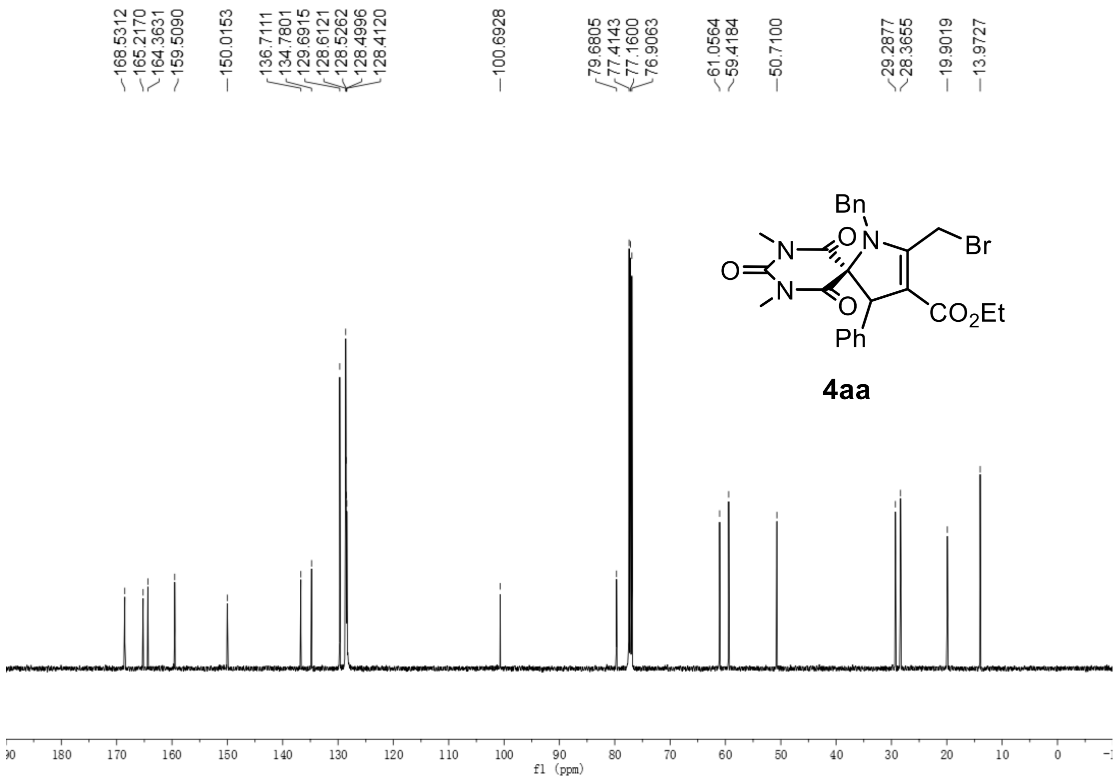


Figure S56. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4aa

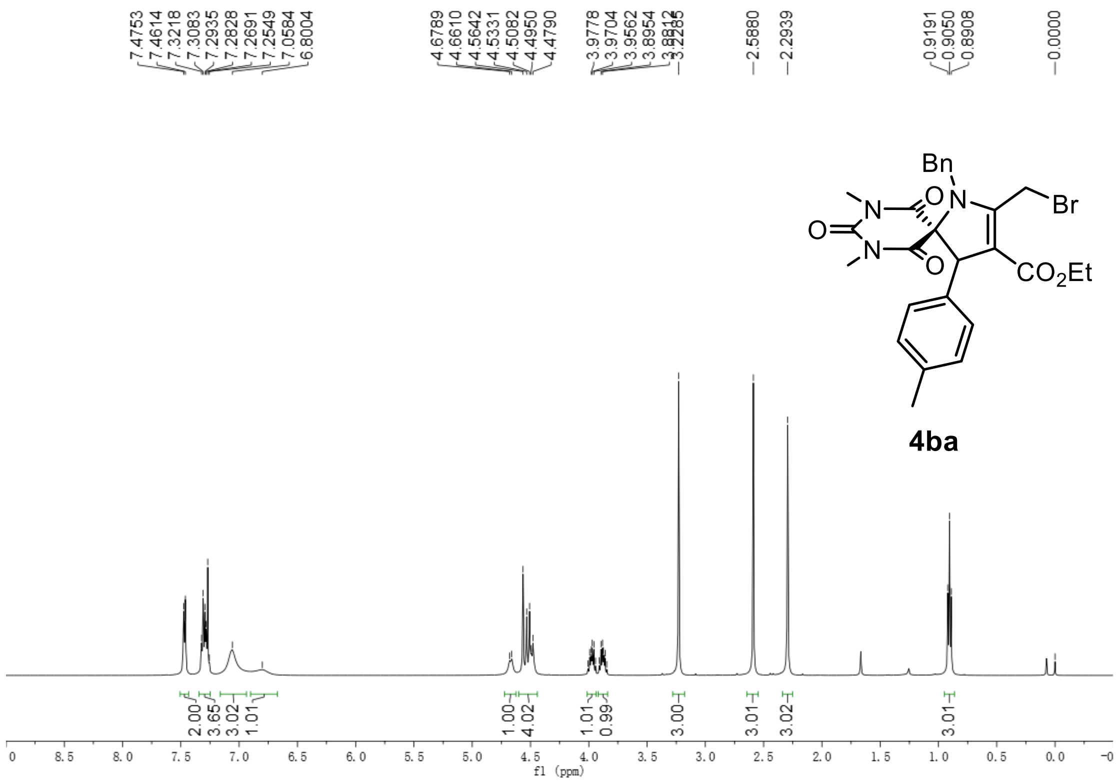


Figure S57. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ba

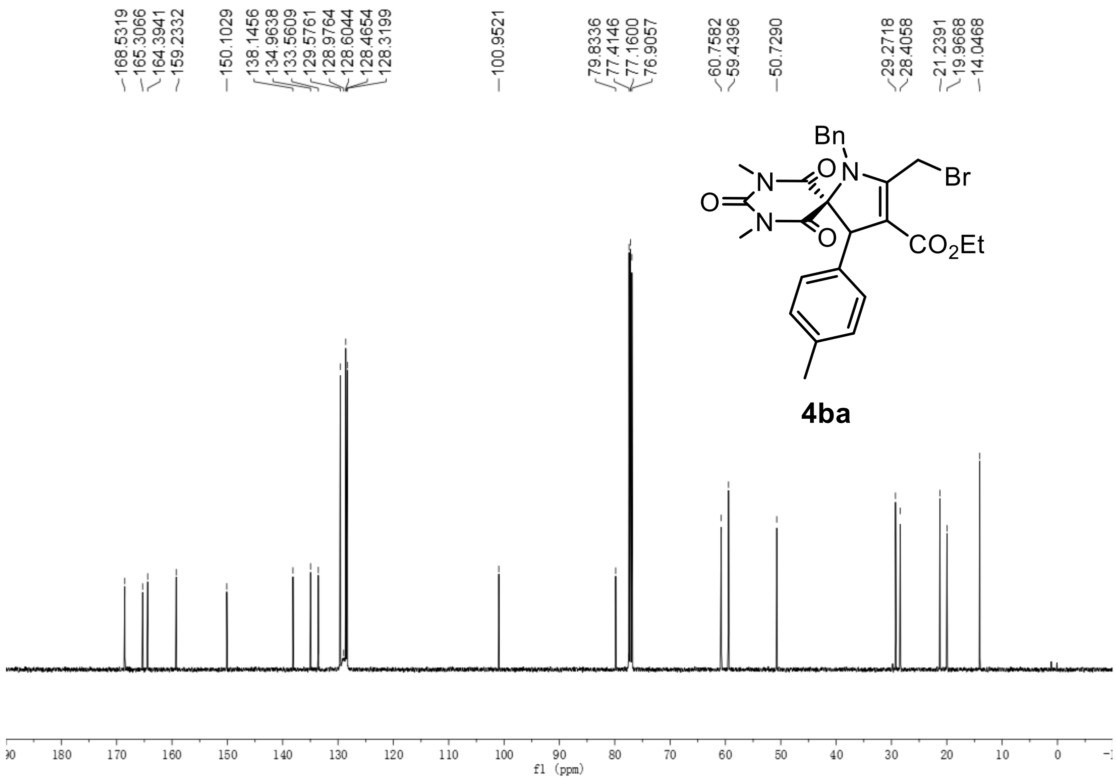


Figure S58. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ba

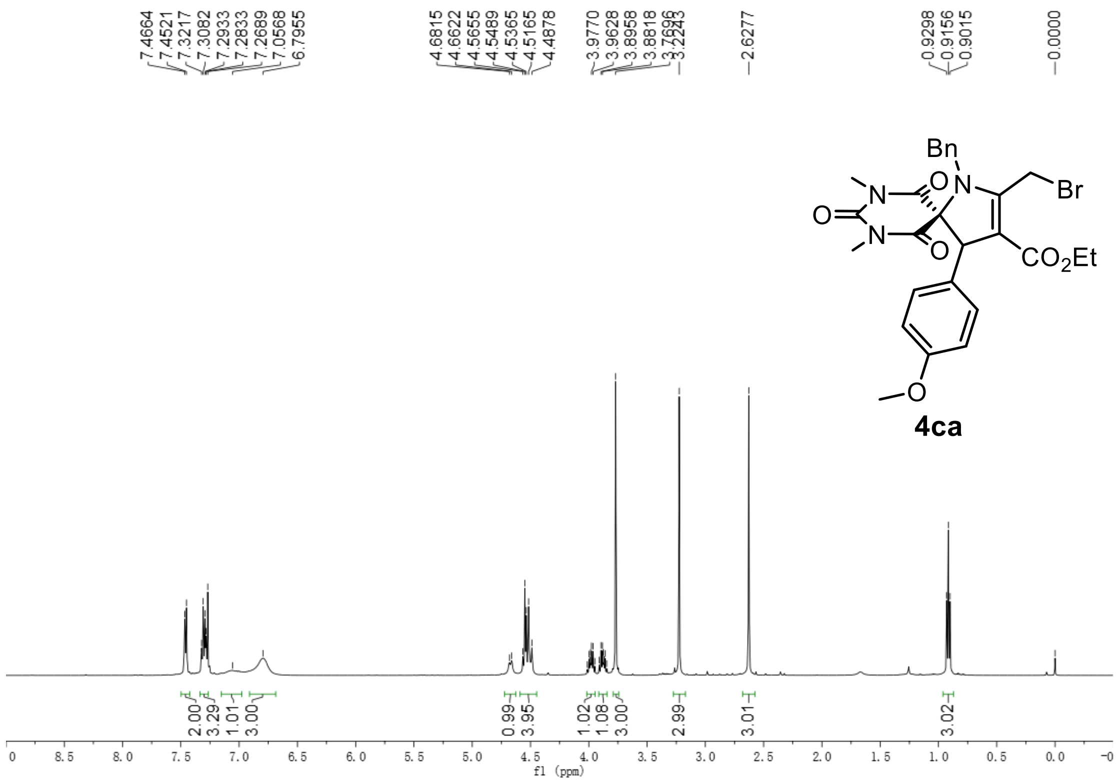


Figure S59. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4ca

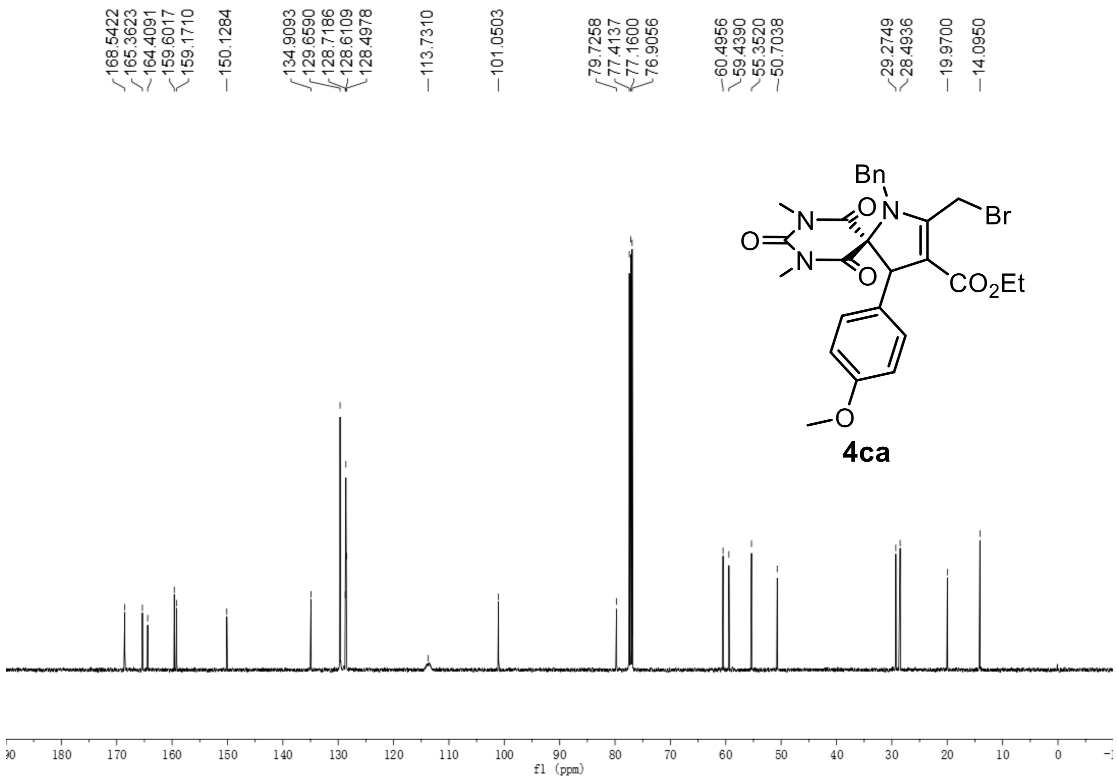


Figure S60. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4ca

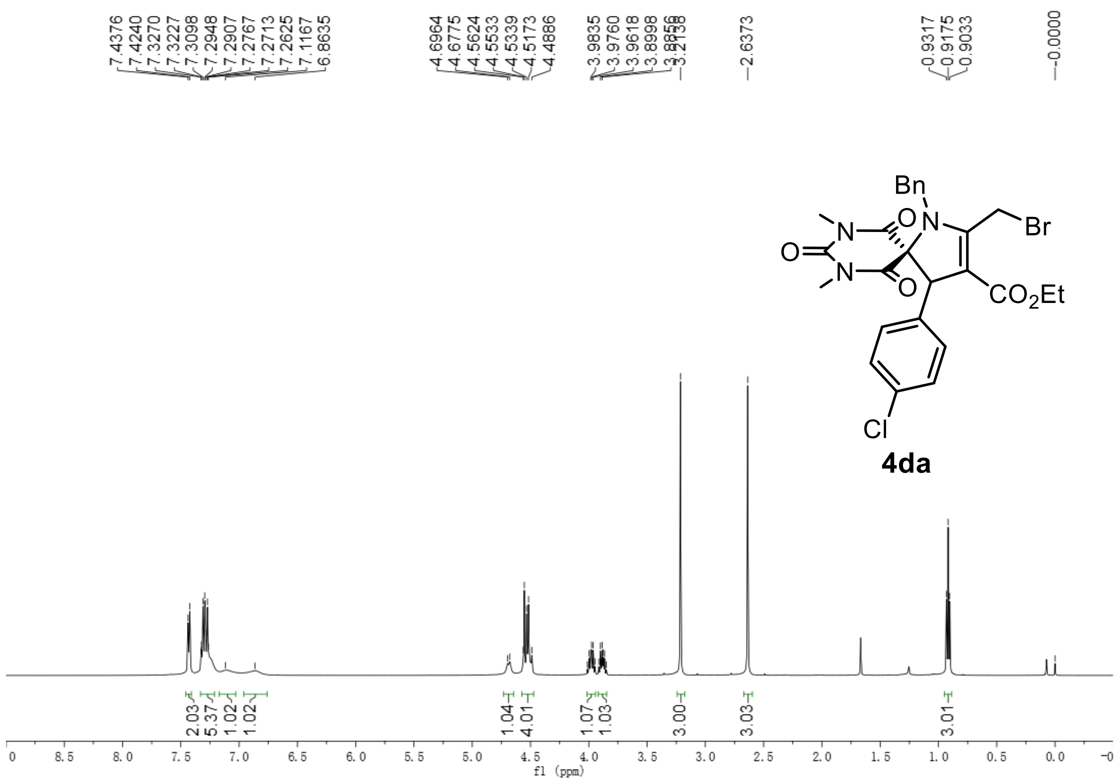


Figure S61. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4da

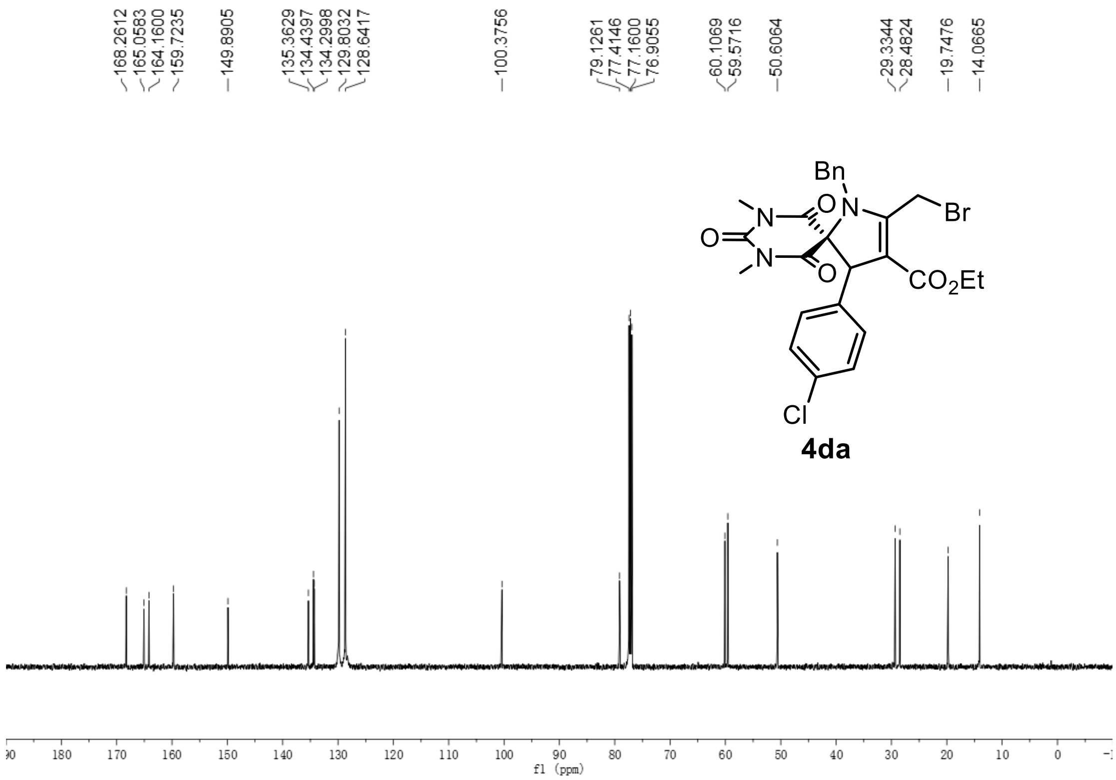


Figure S62. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4da

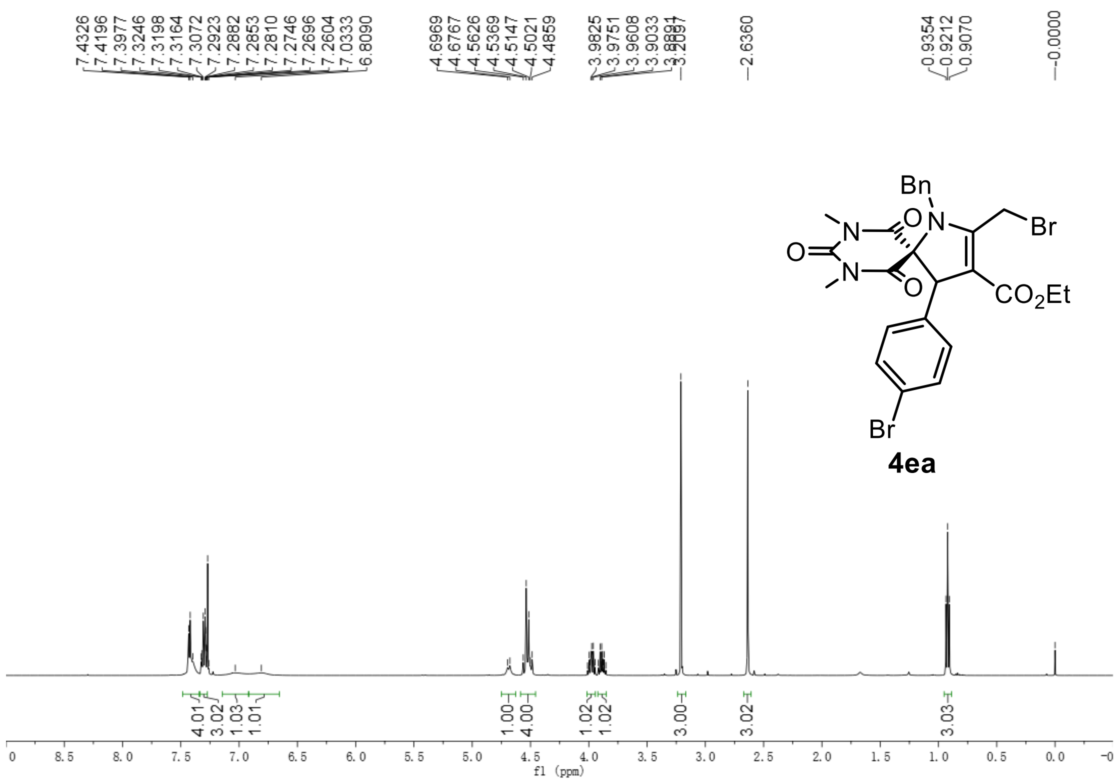


Figure S63. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ea

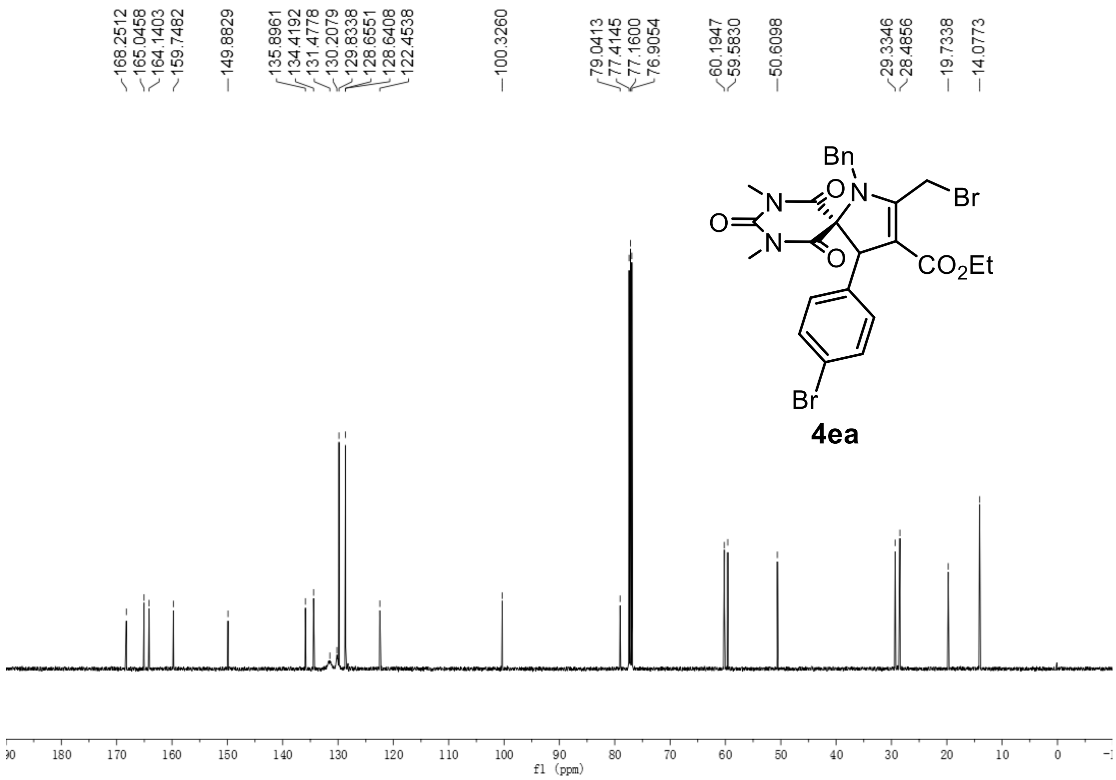


Figure S64. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ea

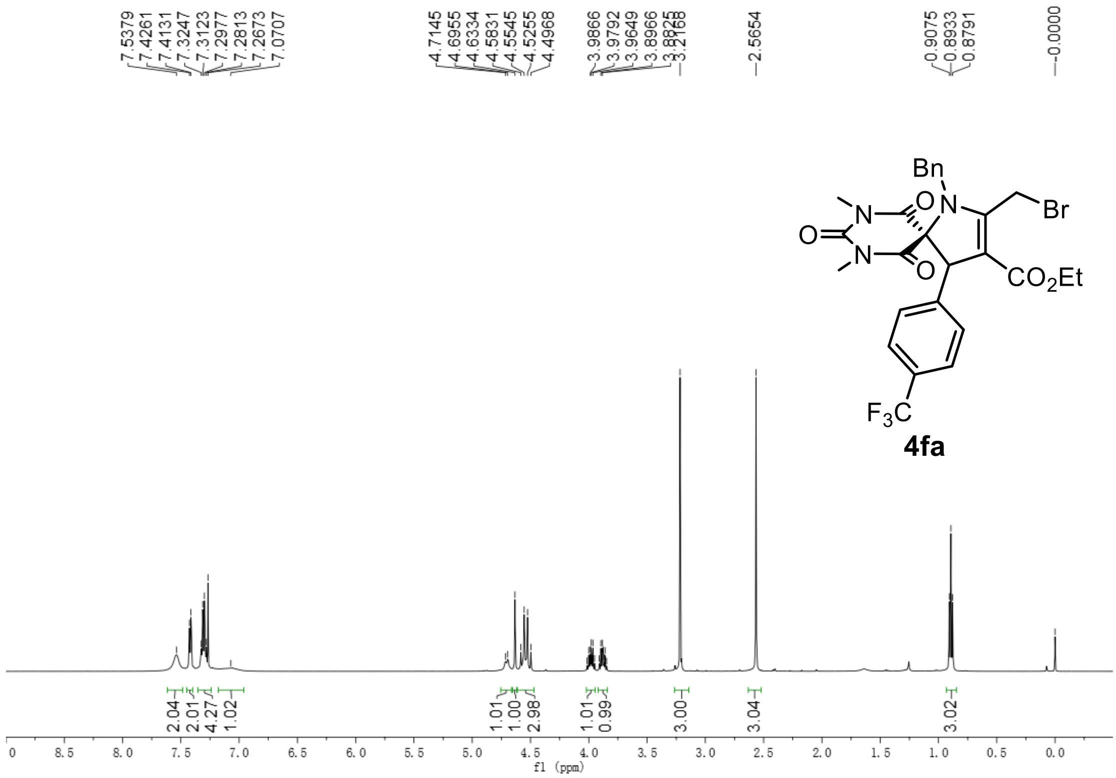


Figure S65. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4fa

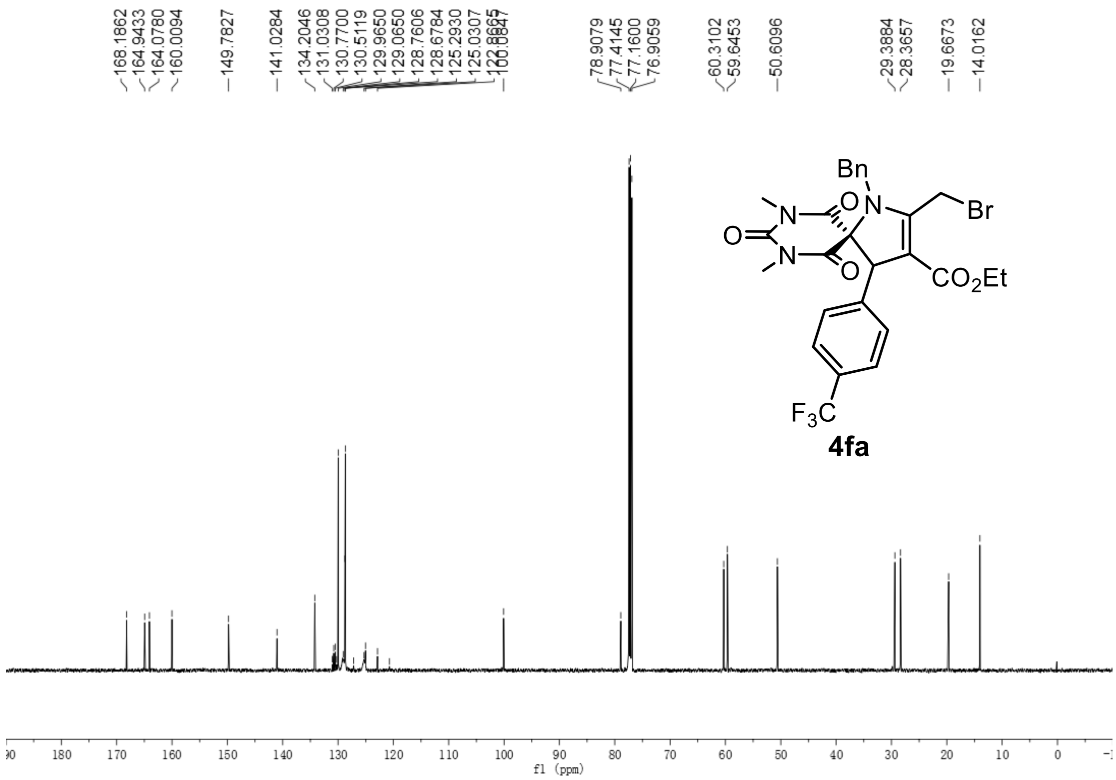


Figure S66. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4fa

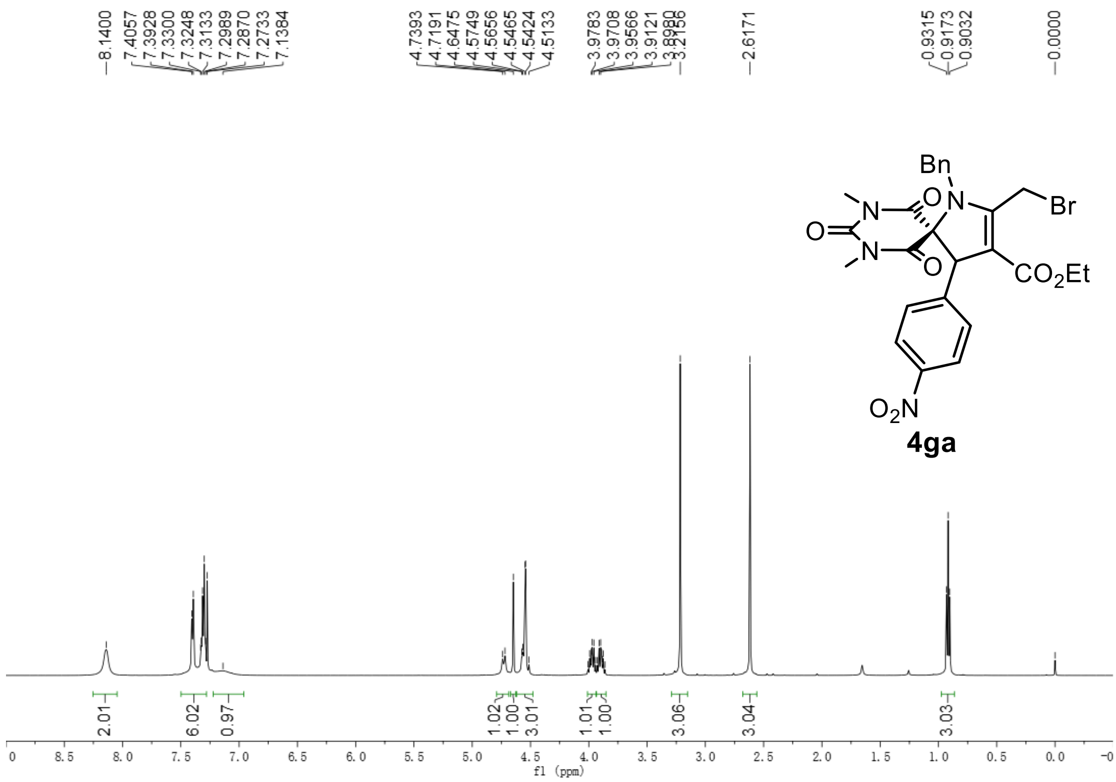


Figure S67. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ga

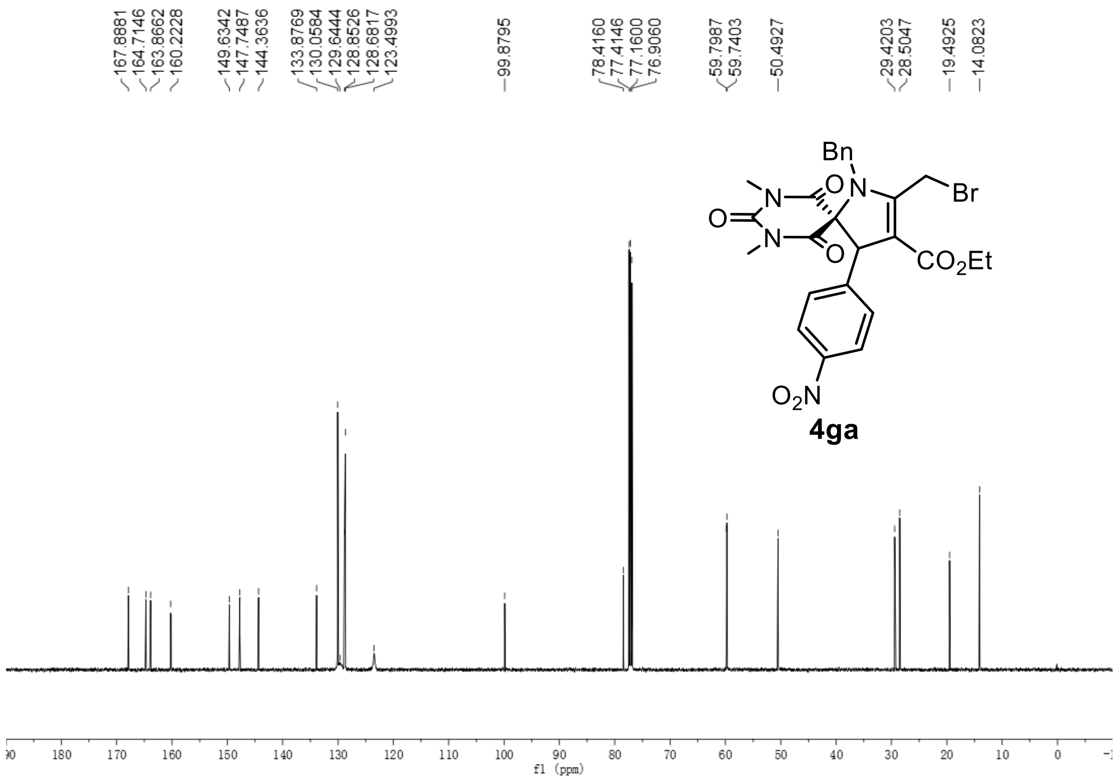


Figure S68. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ga

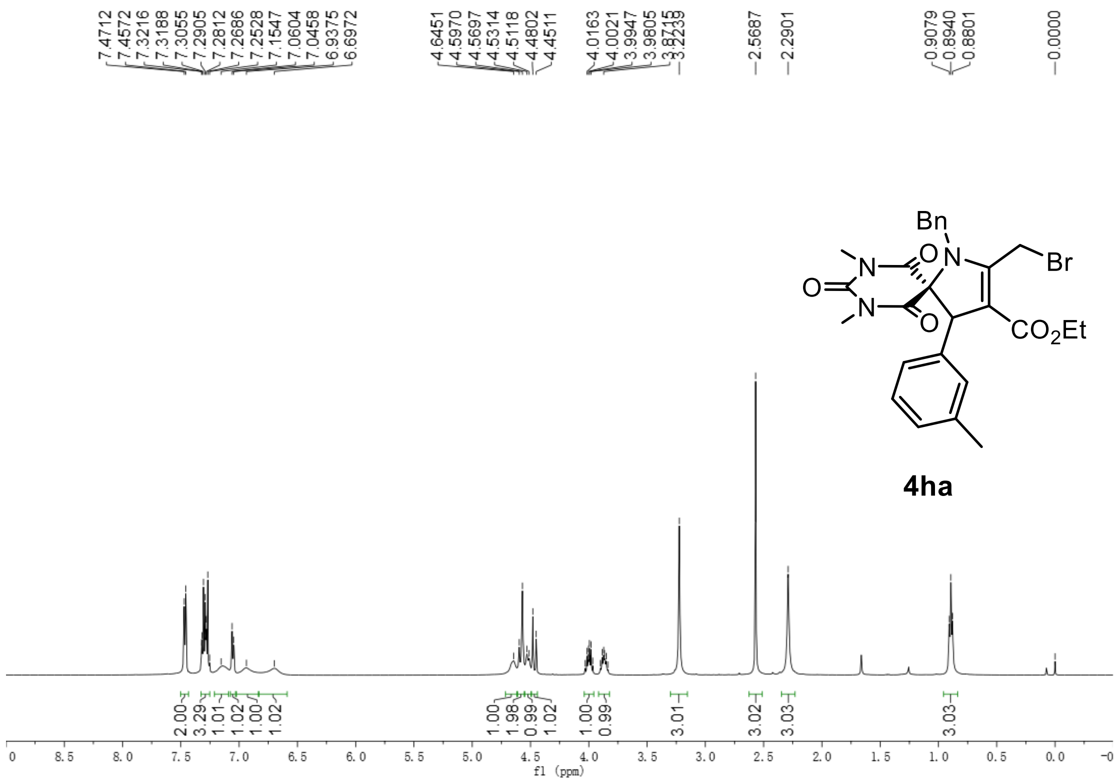


Figure S69. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ha

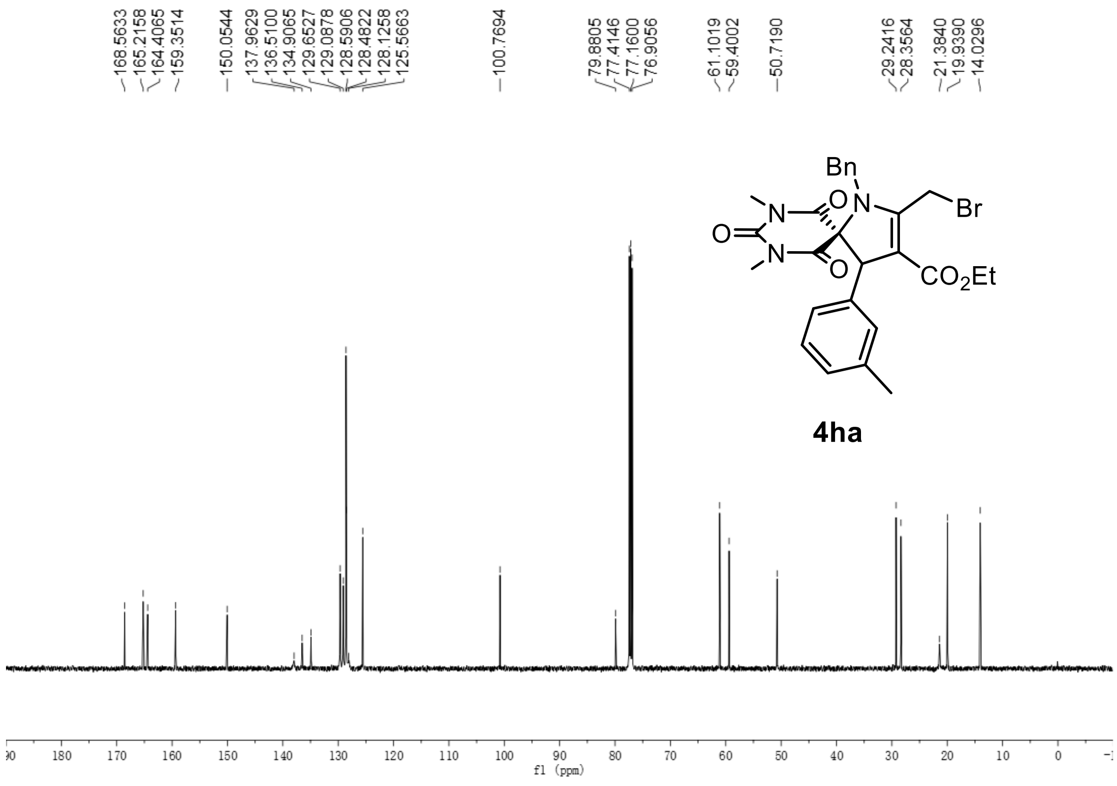


Figure S70. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ha

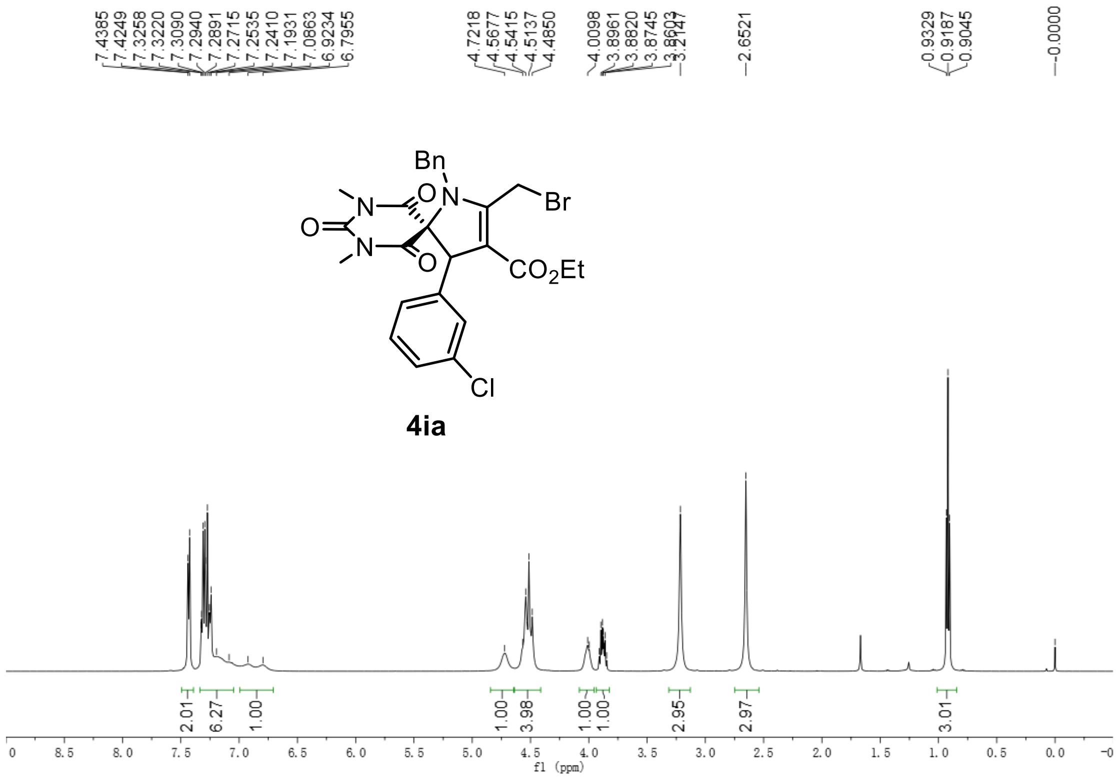


Figure S71. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ia

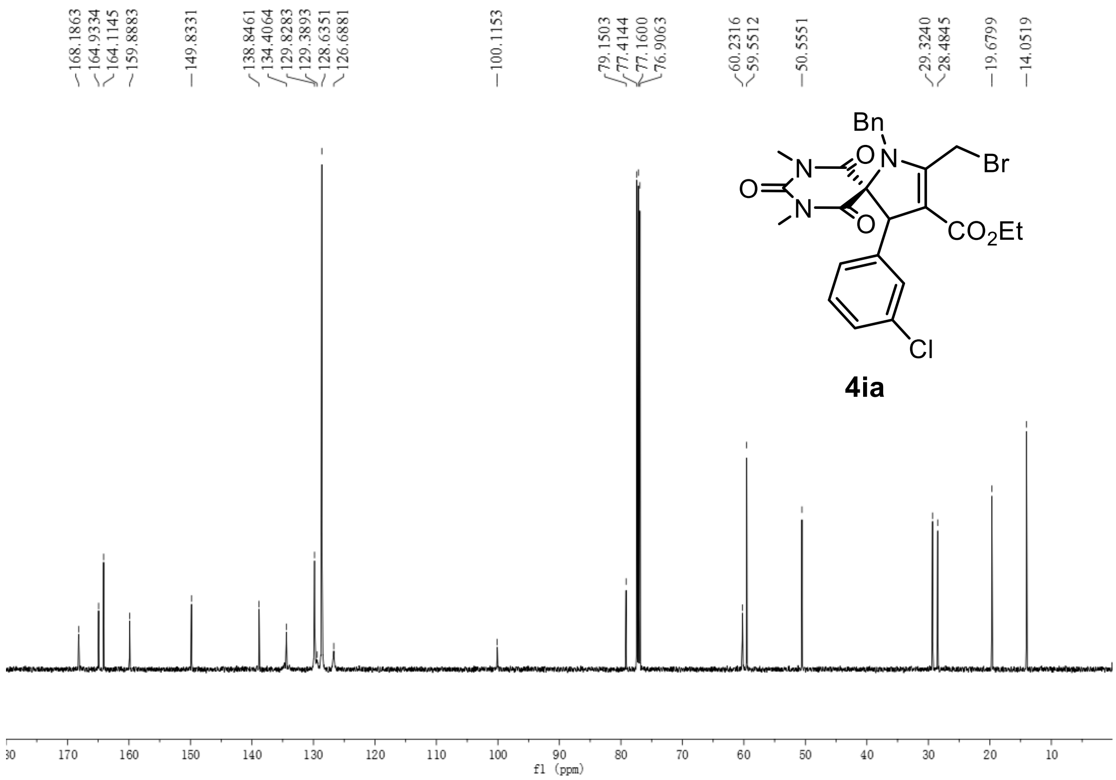


Figure S72. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ia

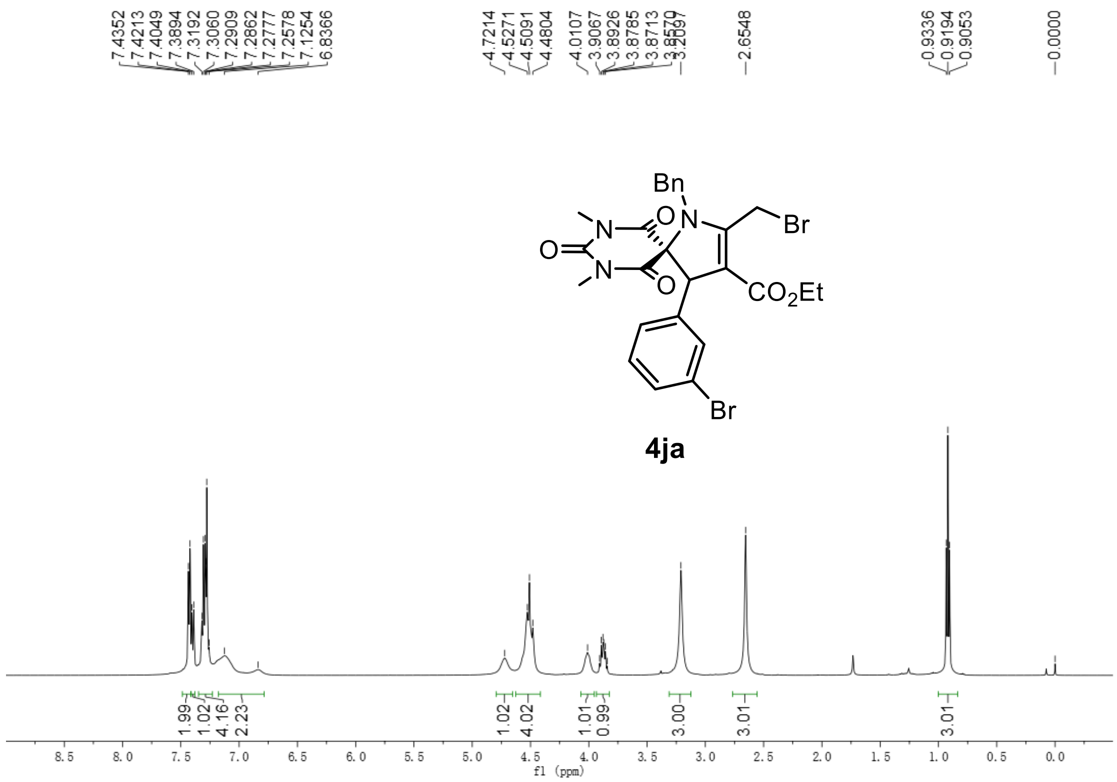


Figure S73. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ja

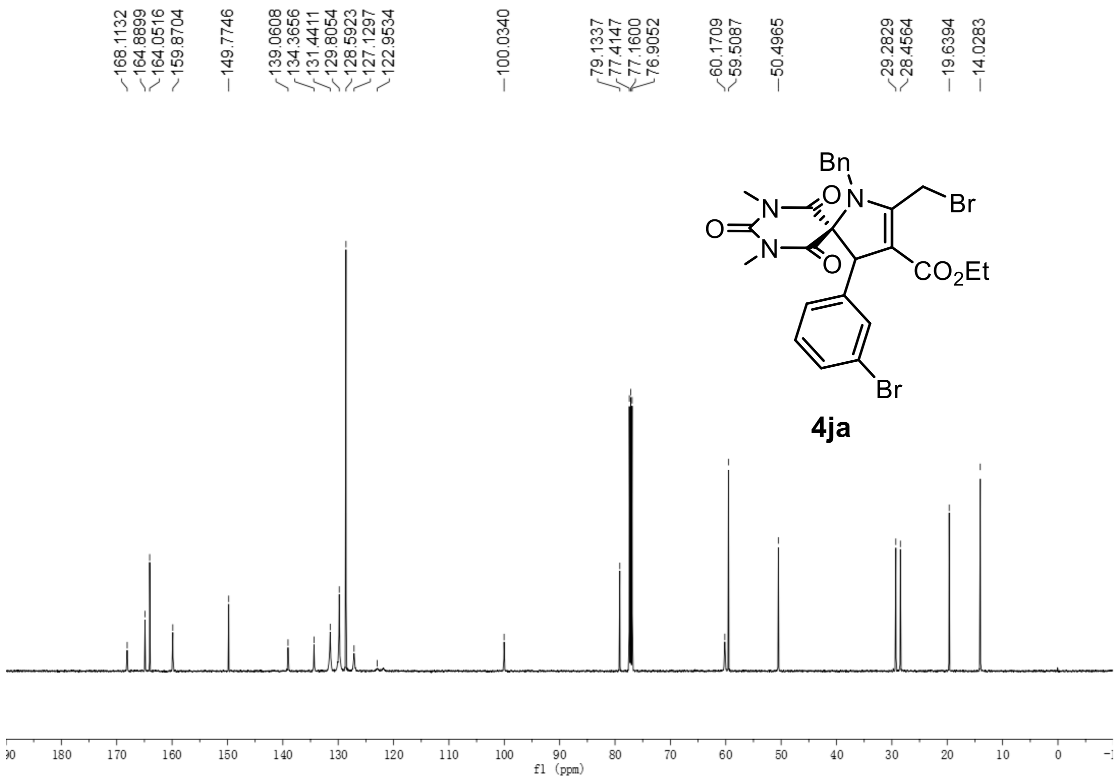


Figure S74. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ja

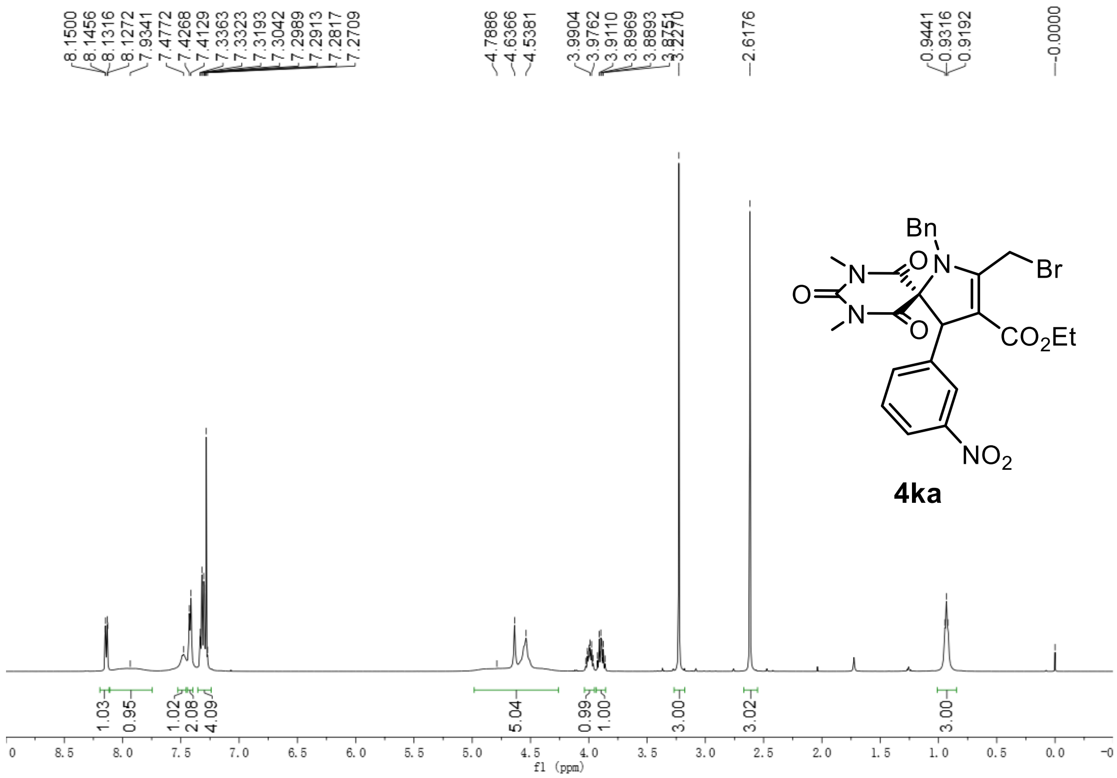


Figure S75. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4ka

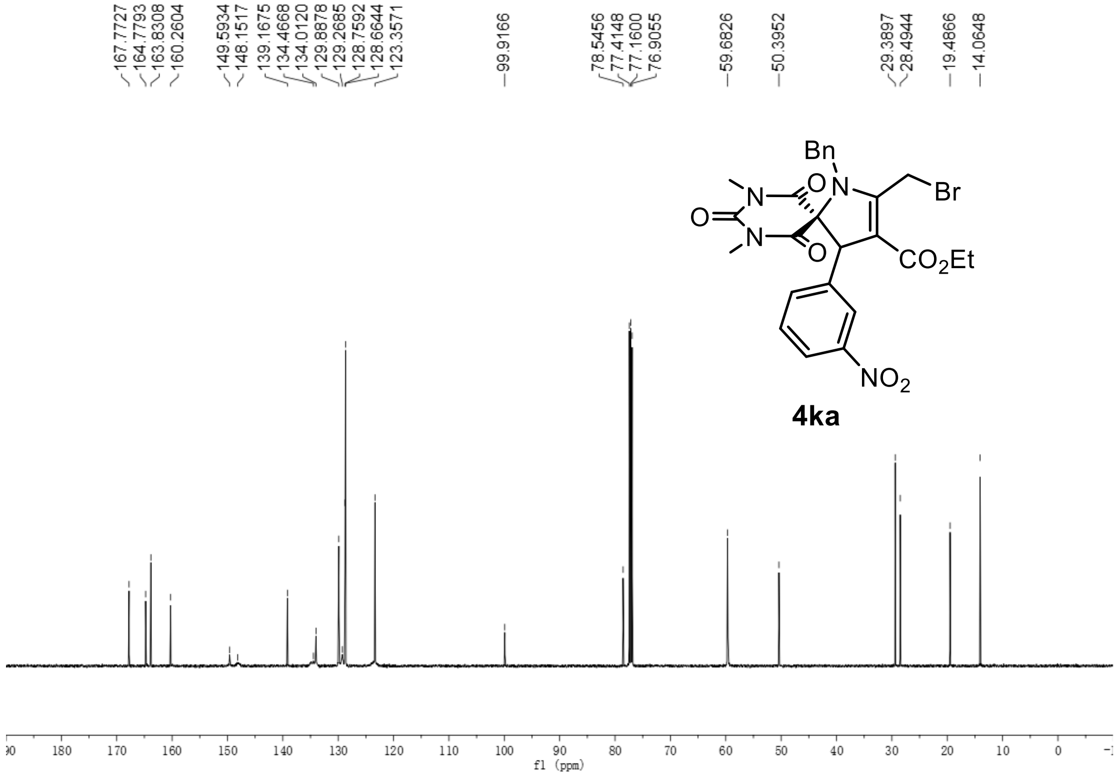


Figure S76. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4ka

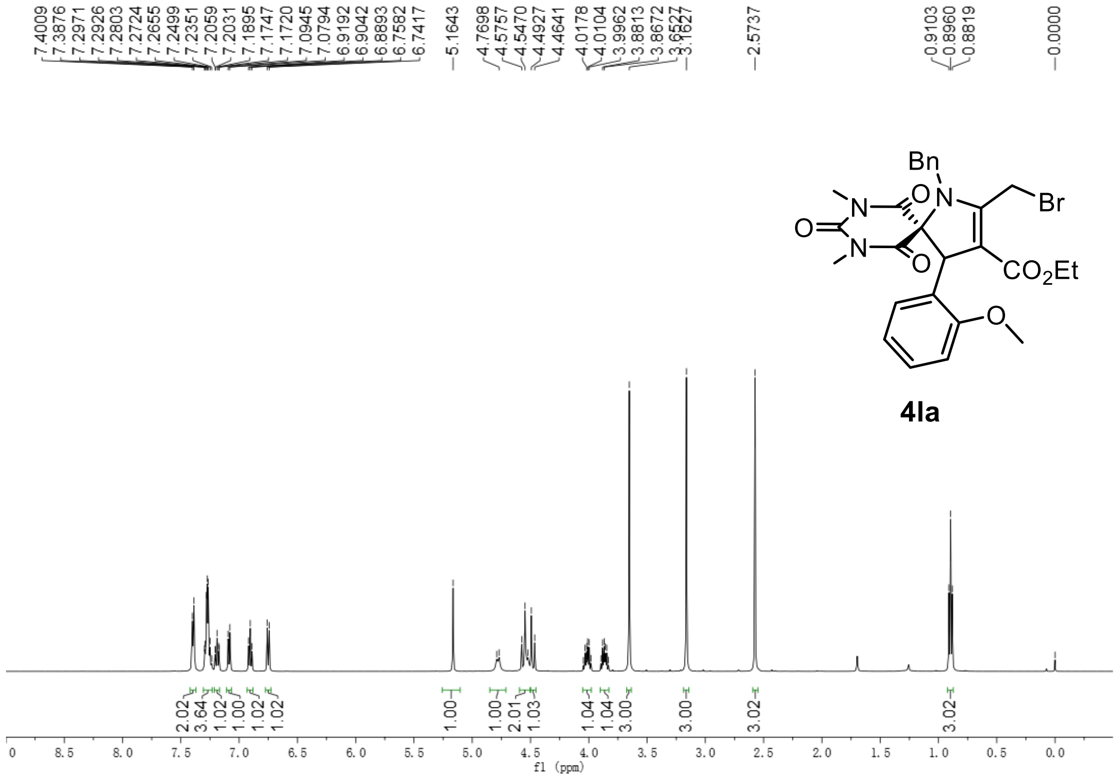


Figure S77. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4la

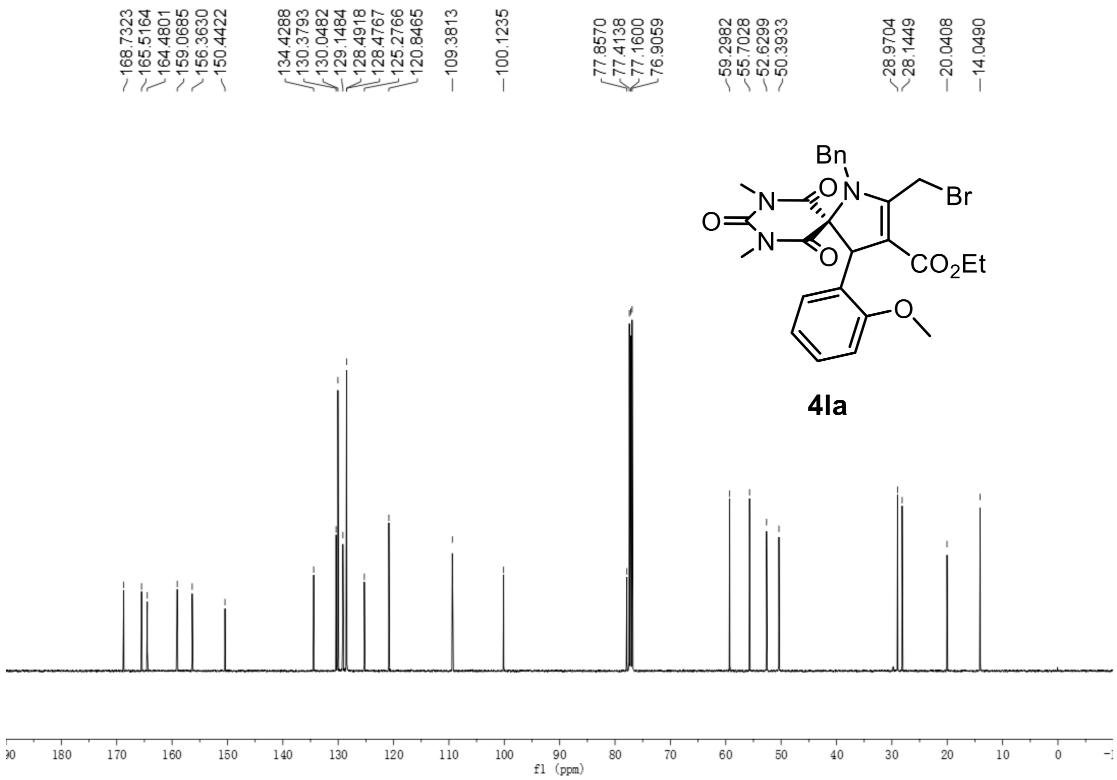


Figure S78. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4la

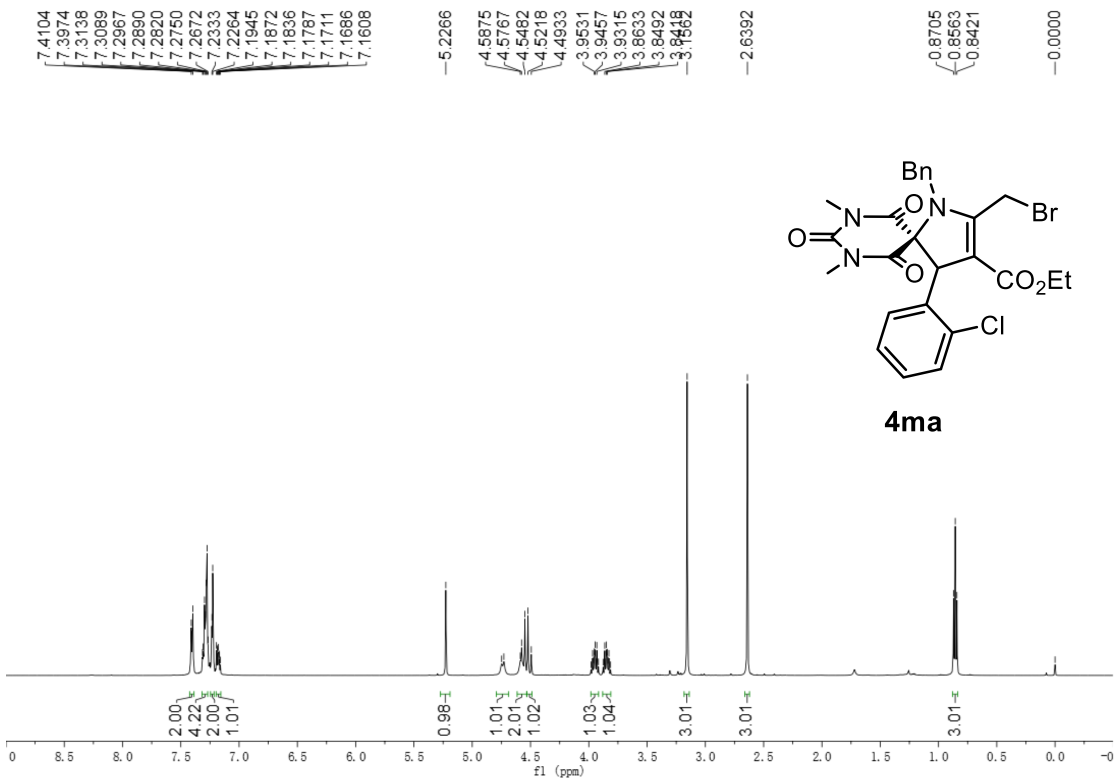


Figure S79. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4ma

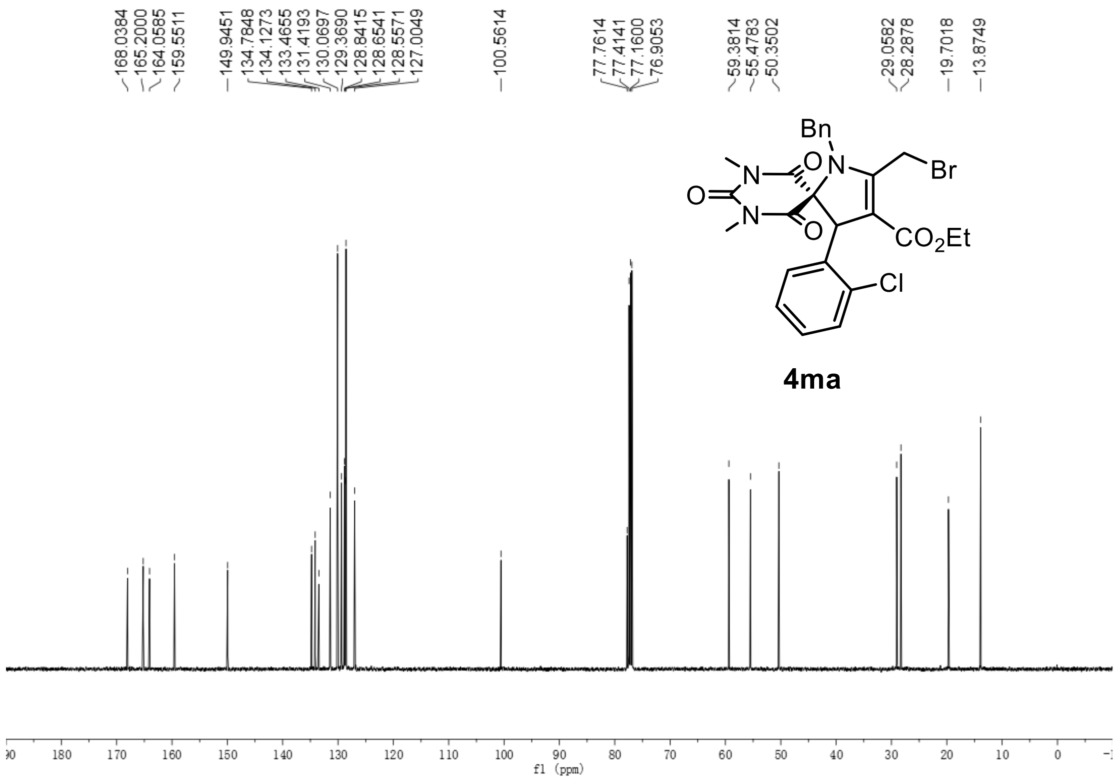


Figure S80. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4ma

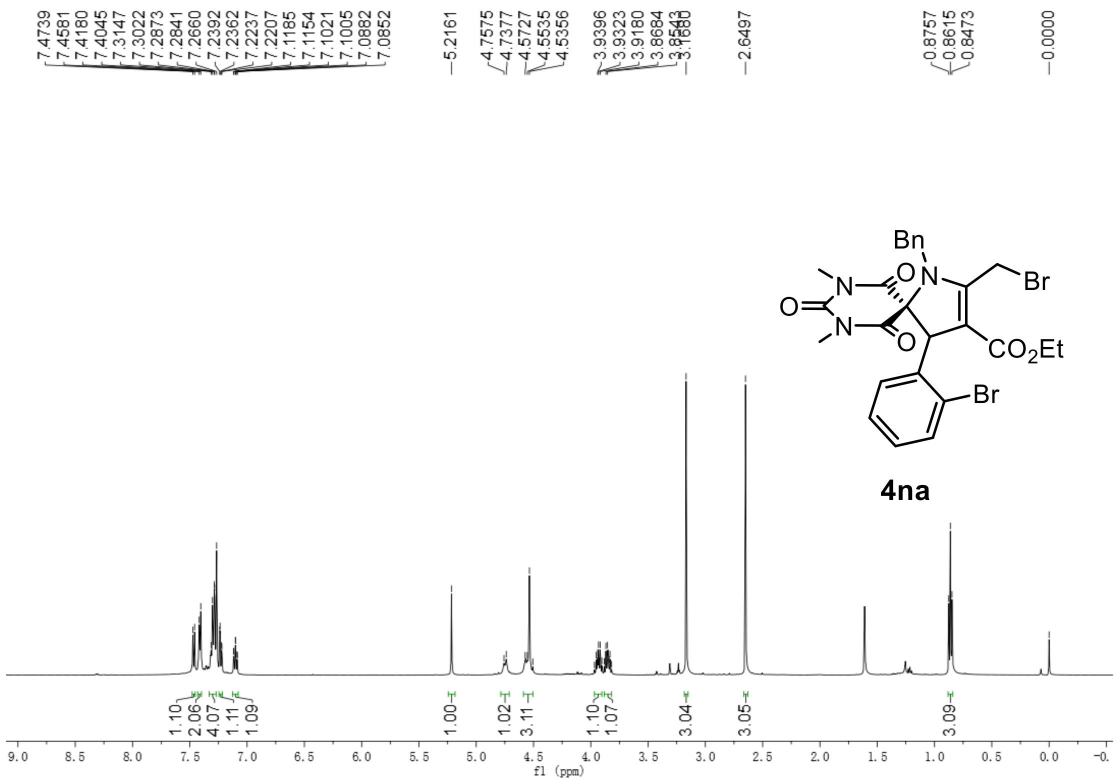


Figure S81. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4na

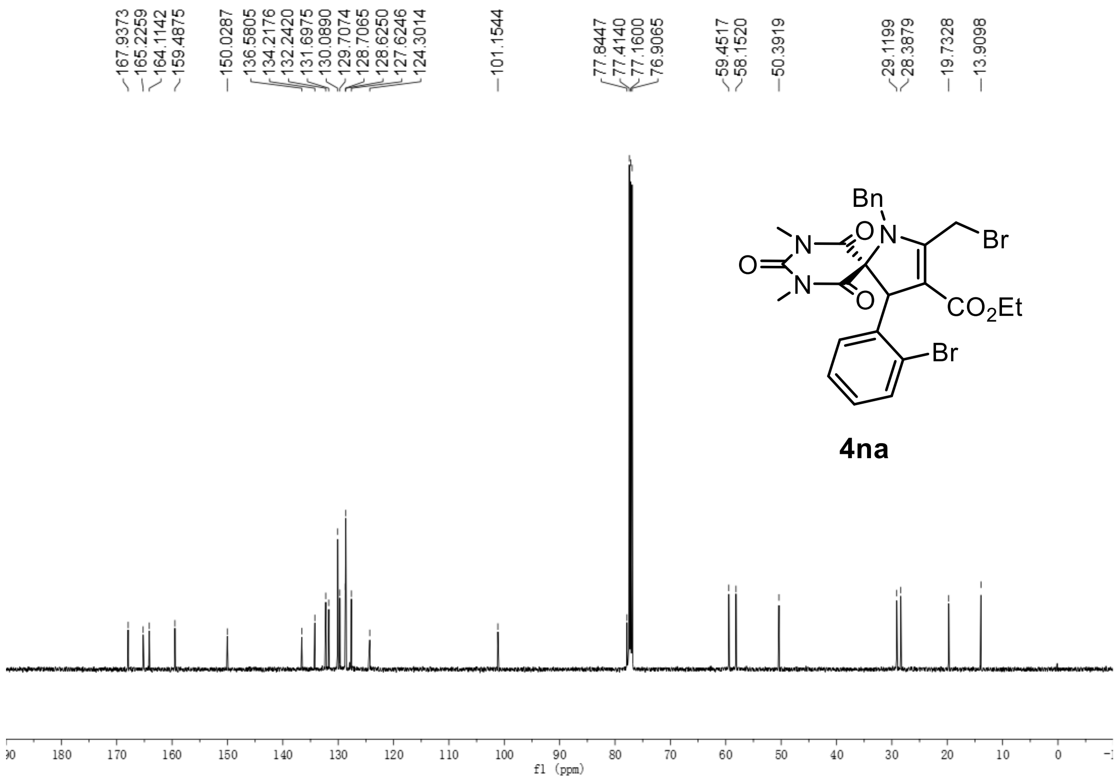


Figure S82. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4na

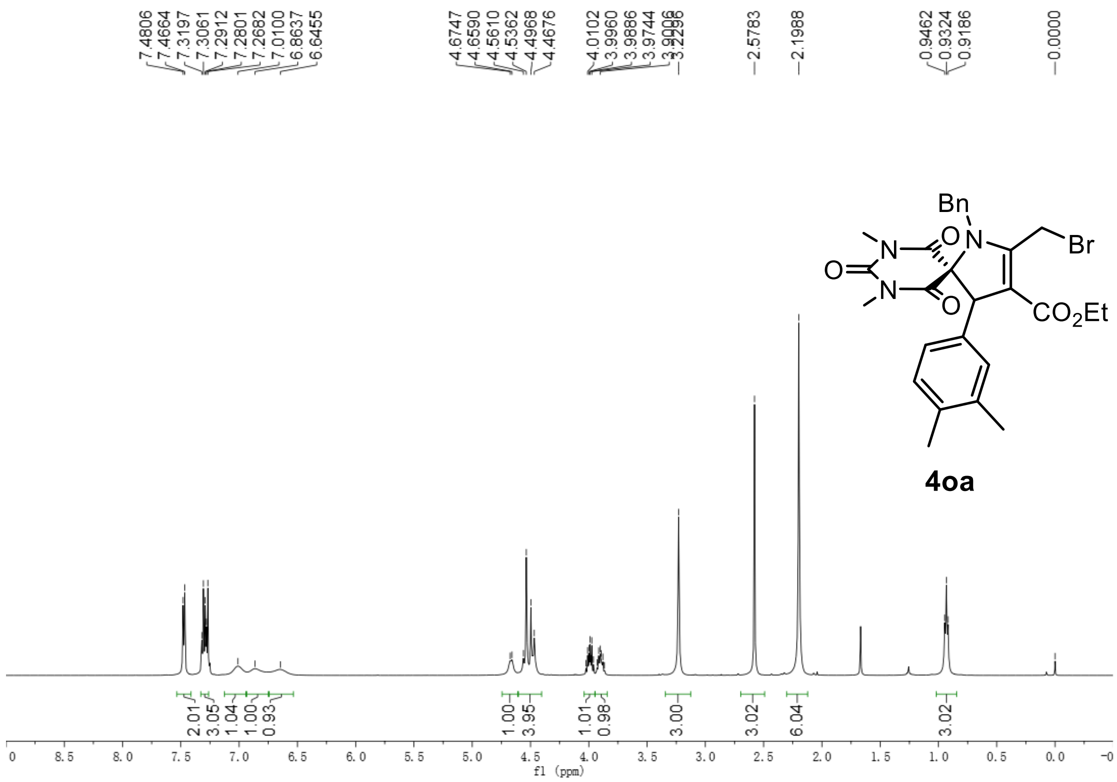


Figure S83. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4oa

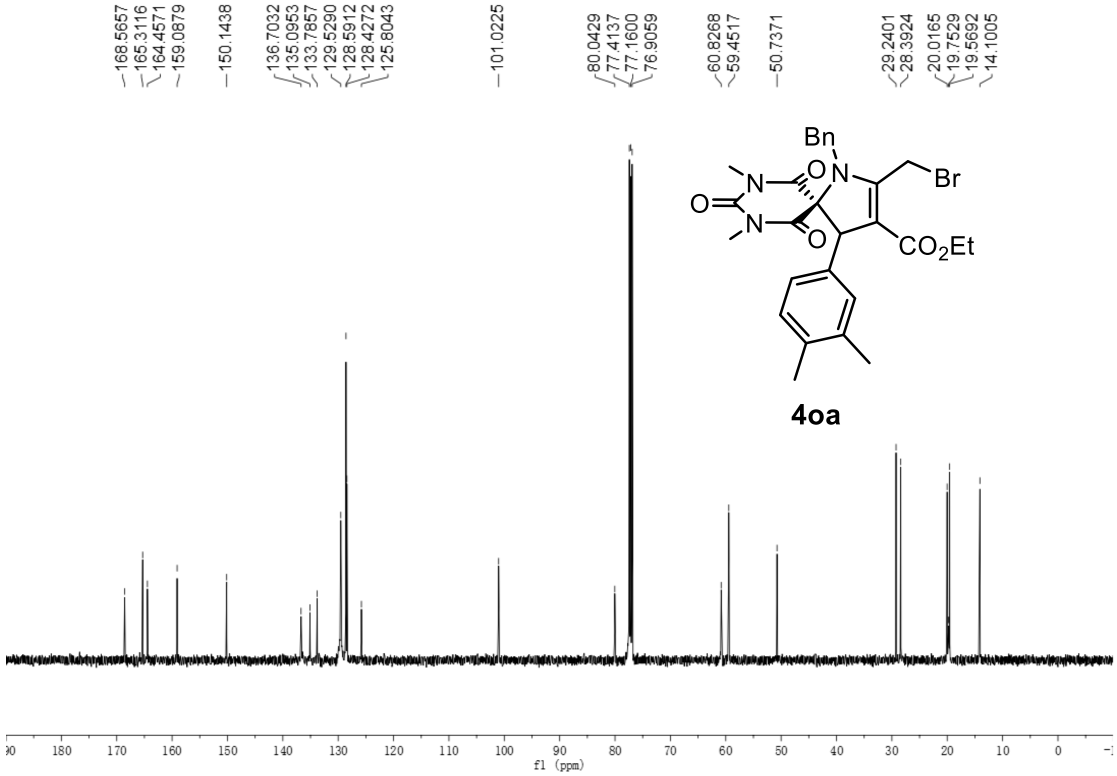


Figure S84. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4oa

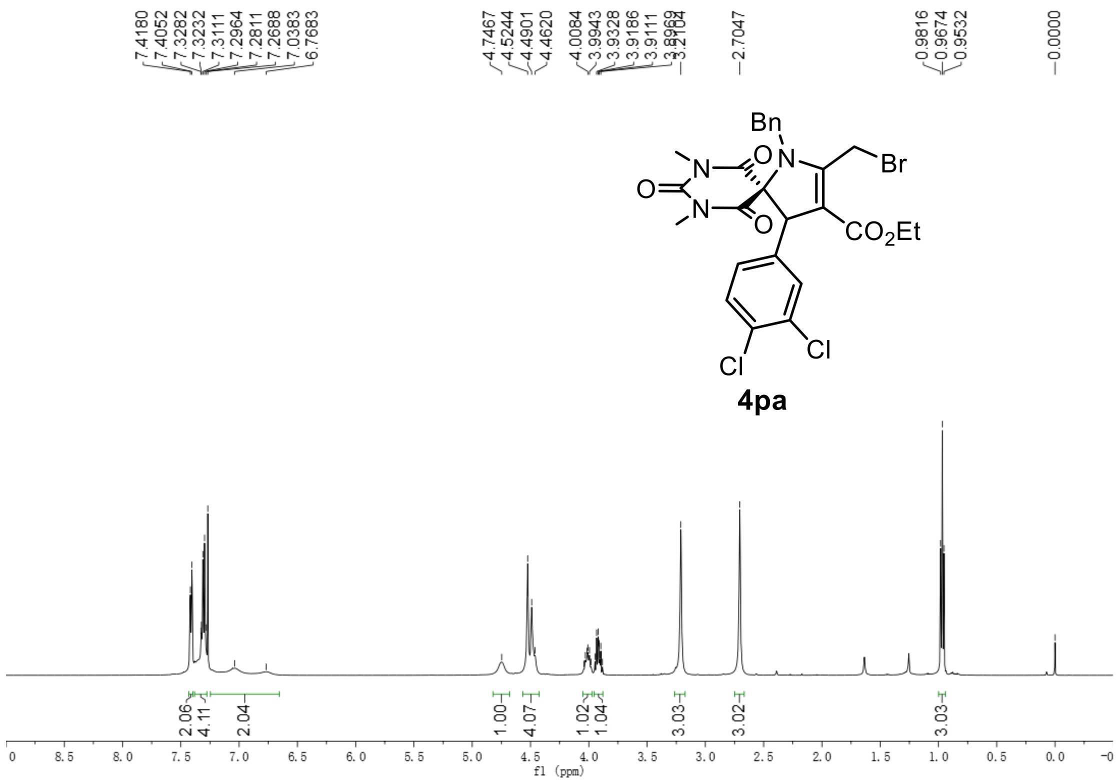


Figure S85. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4pa

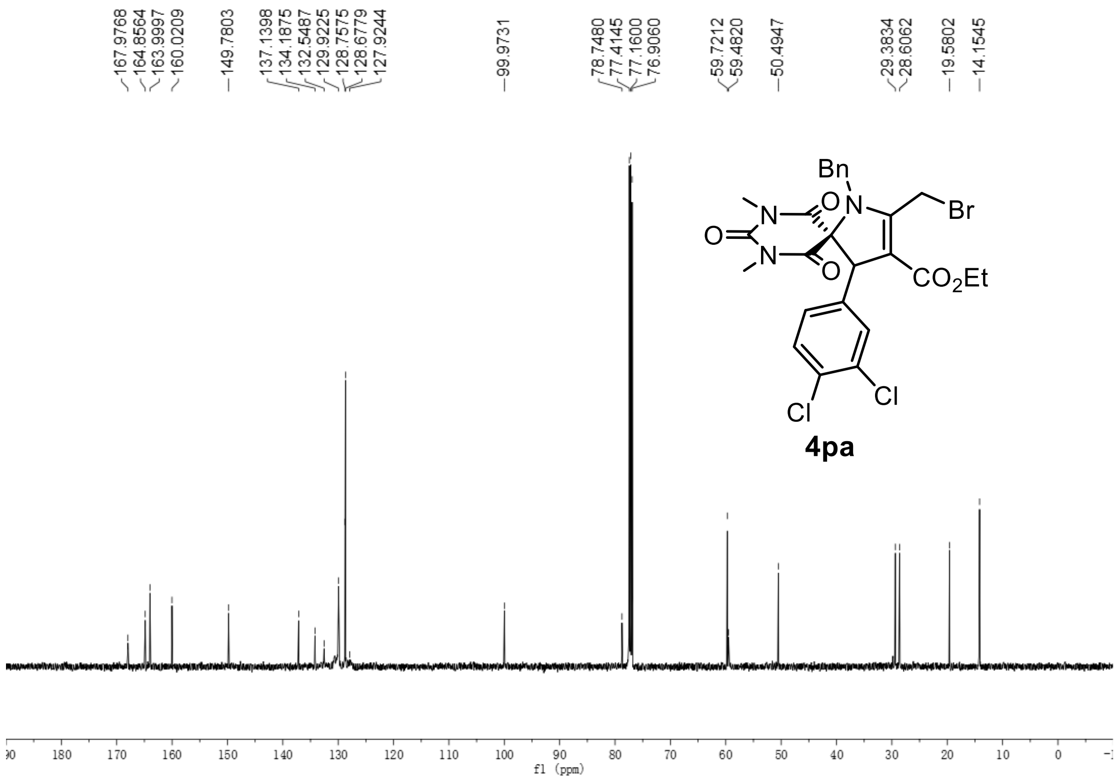


Figure S86. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4pa

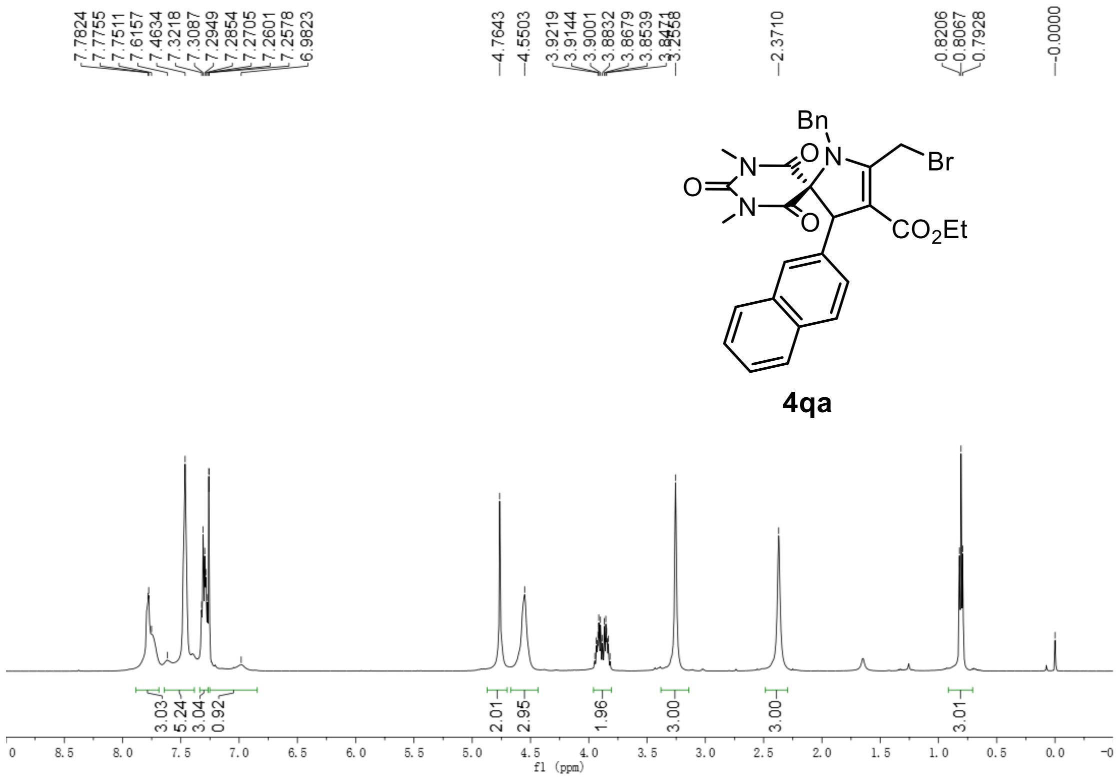


Figure S87. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4qa

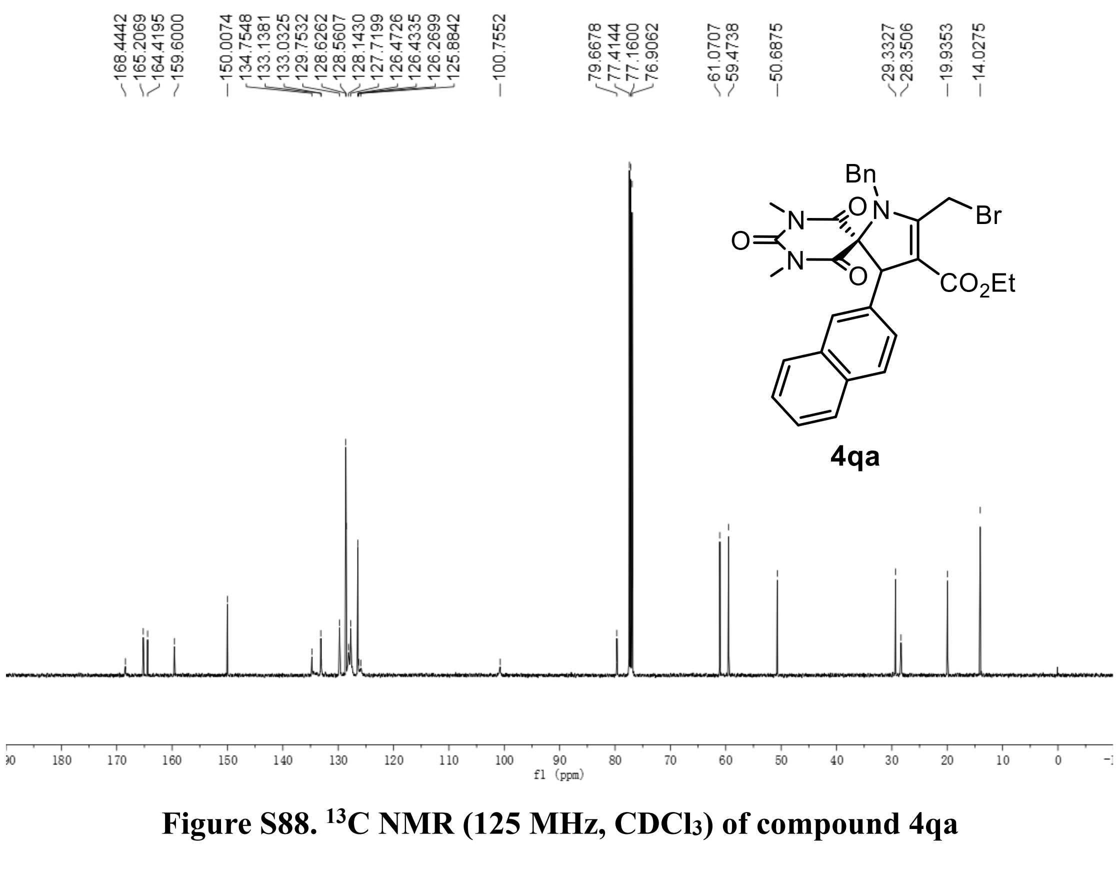


Figure S88. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4qa

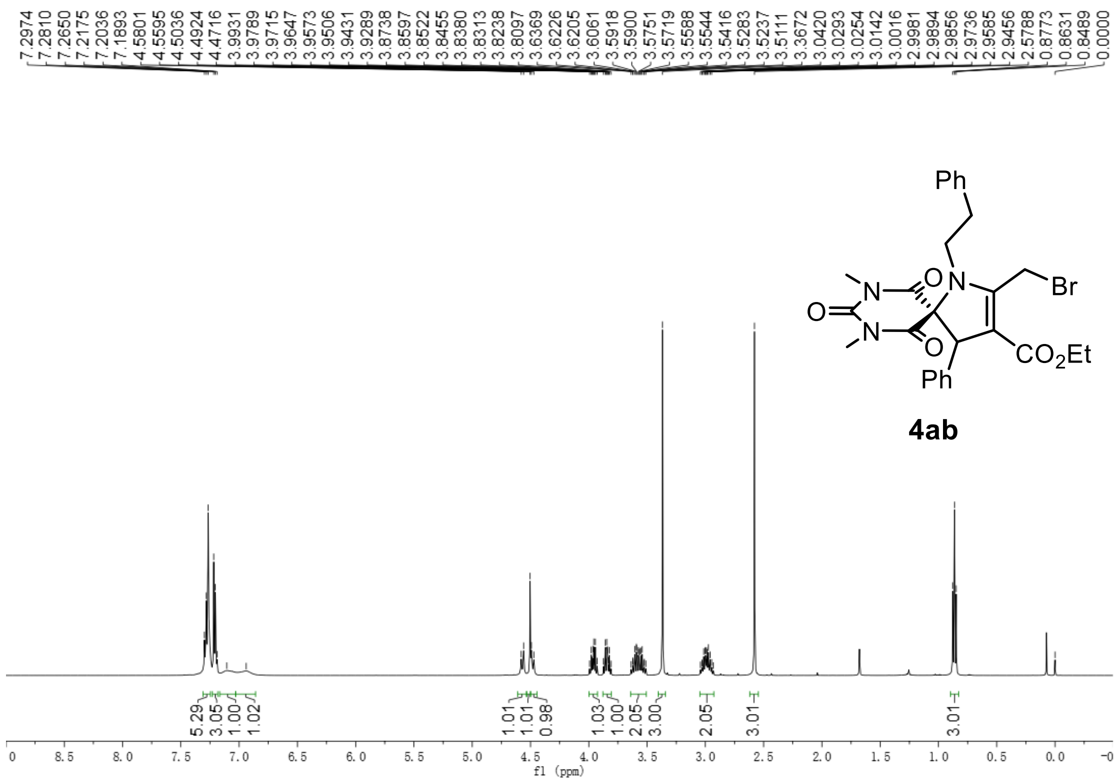


Figure S89. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ab

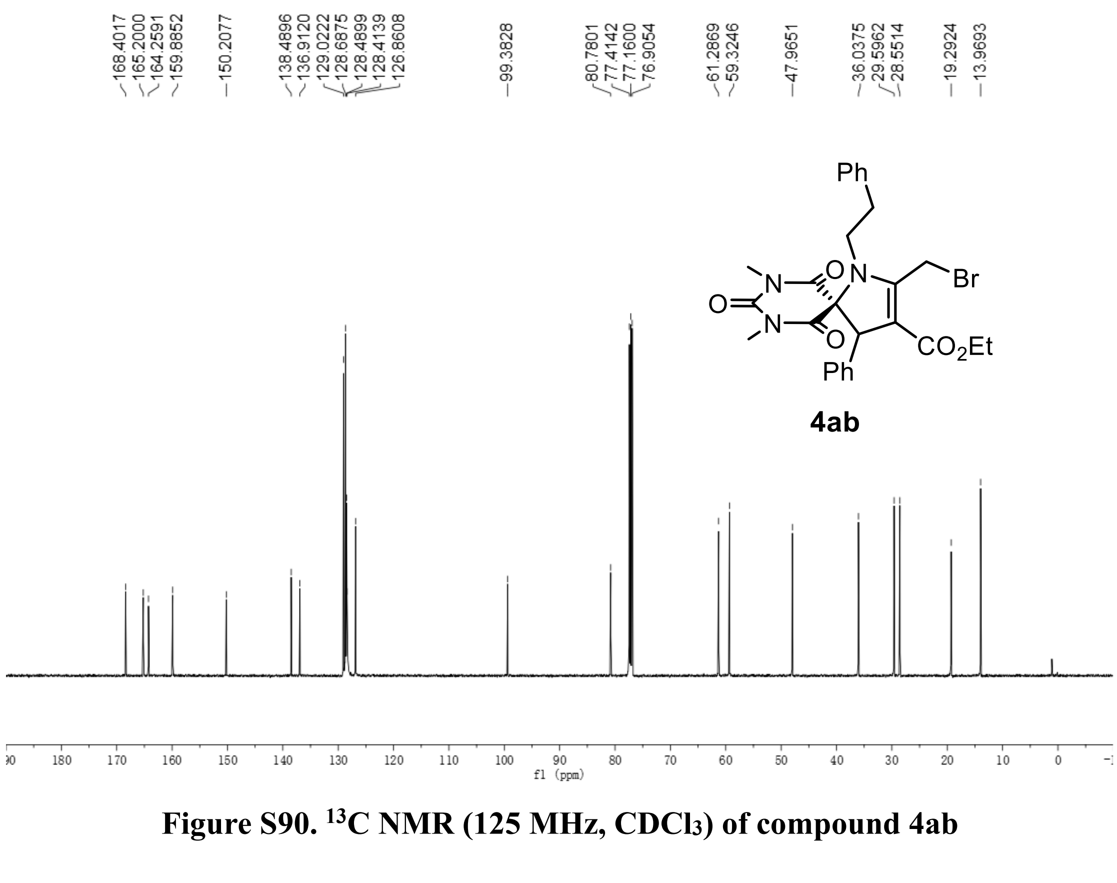


Figure S90. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ab

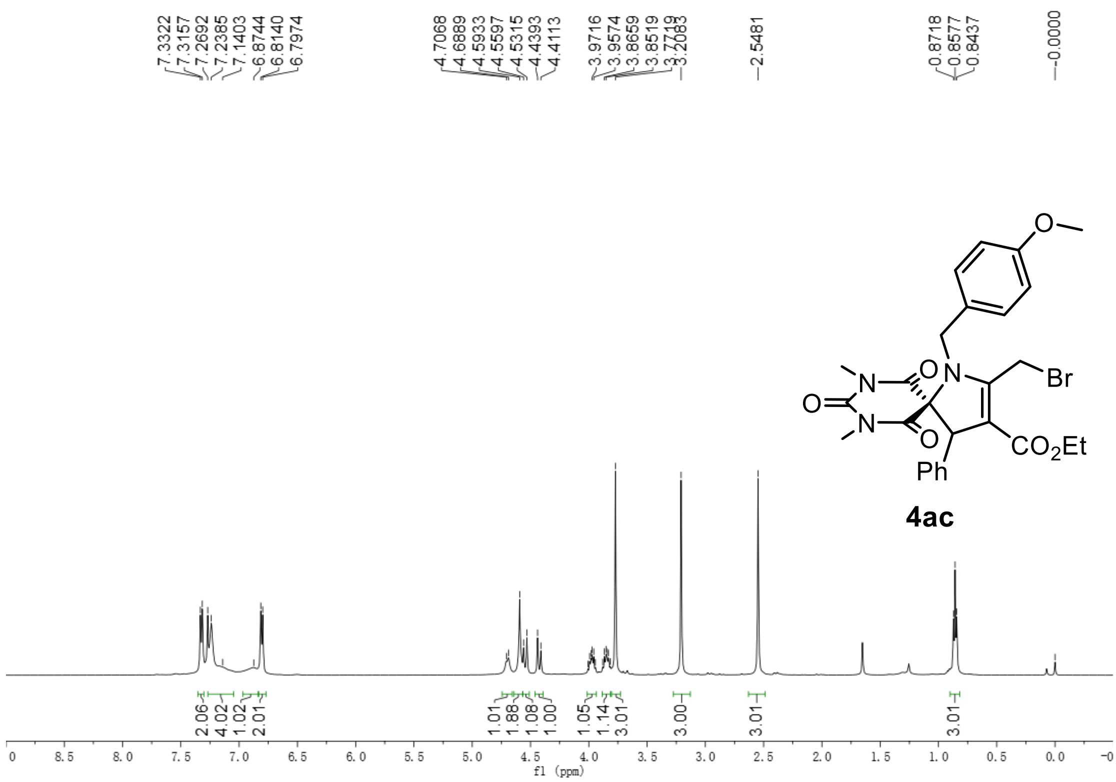


Figure S91. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4ac

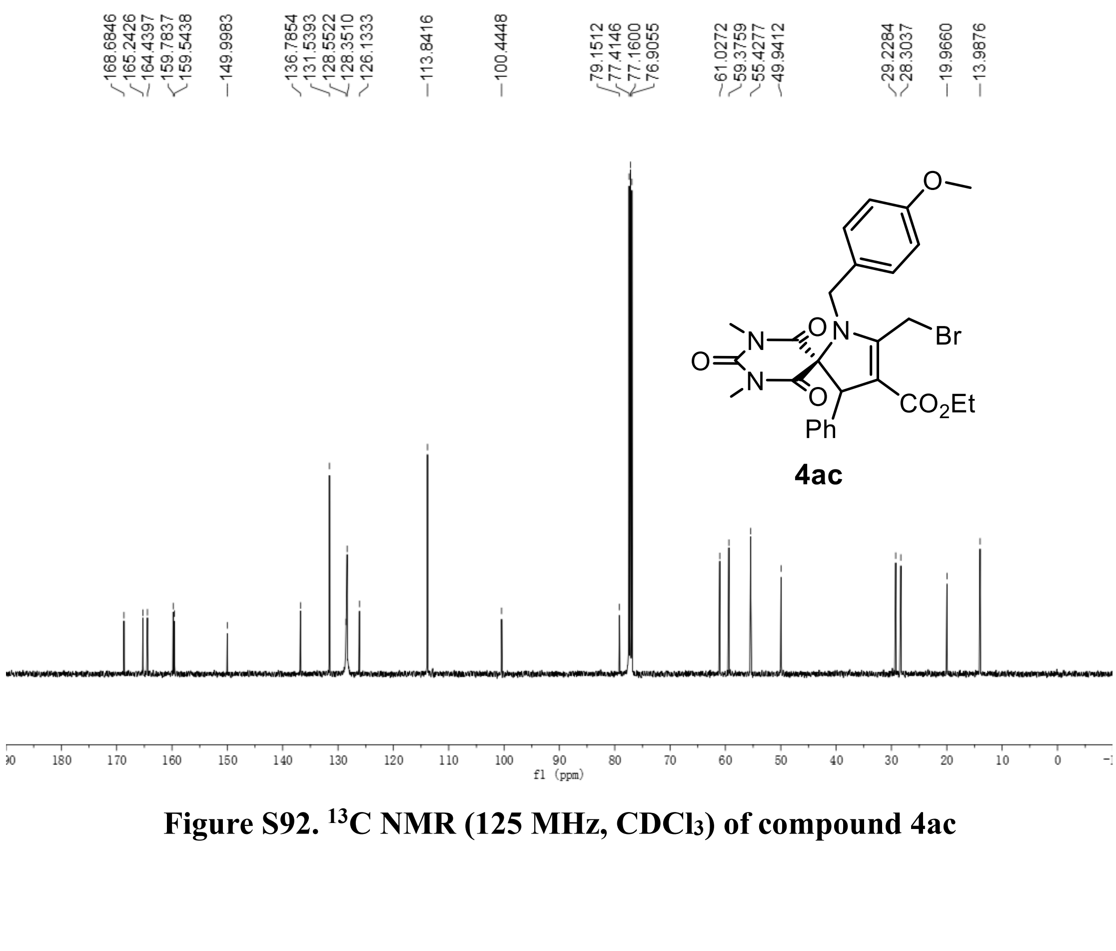


Figure S92. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4ac

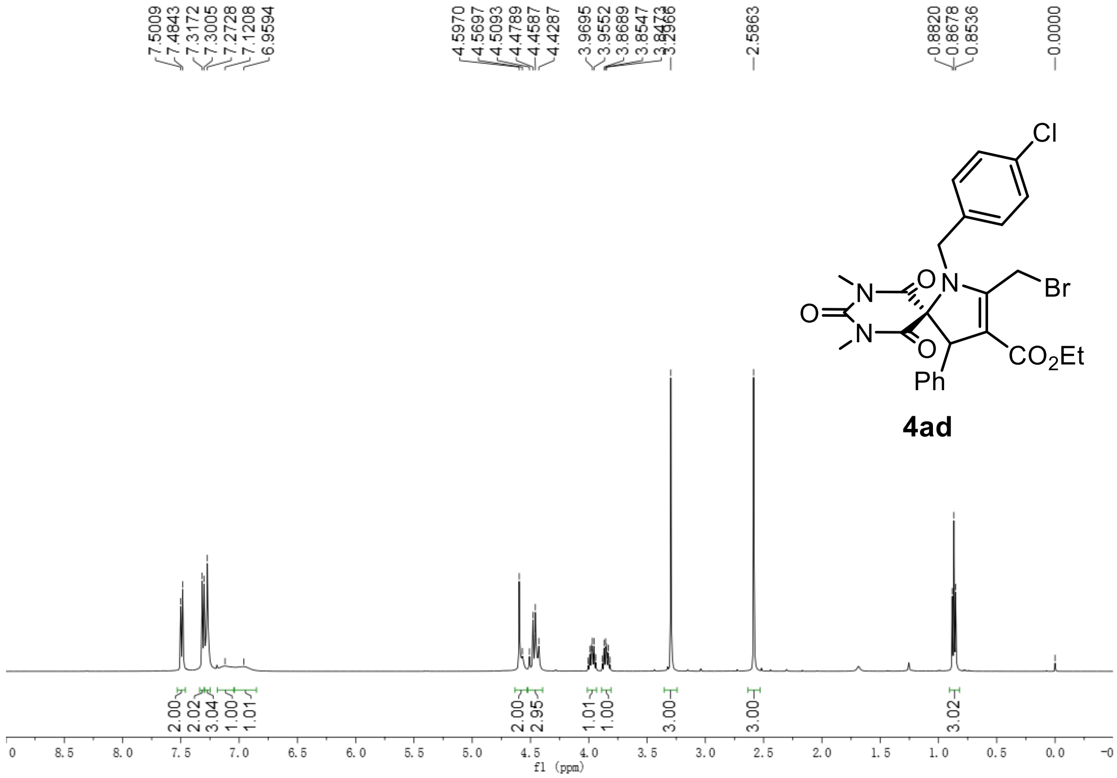


Figure S93. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ad

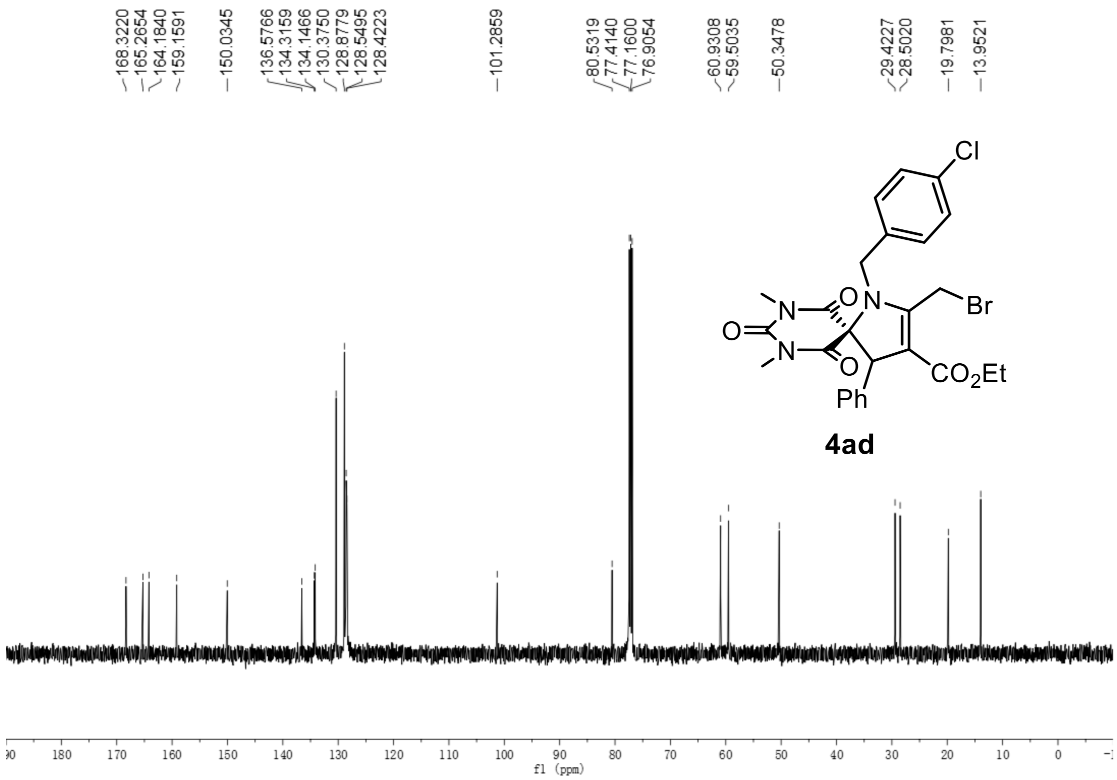


Figure S94. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ad

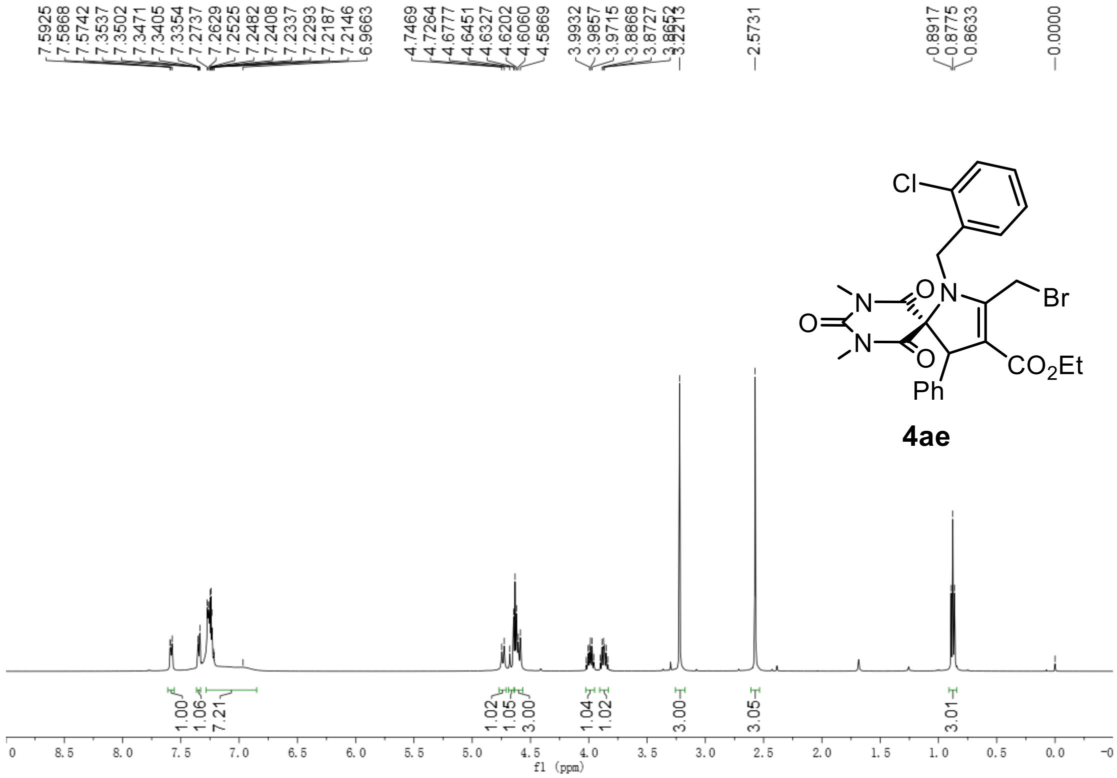


Figure S95. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ae

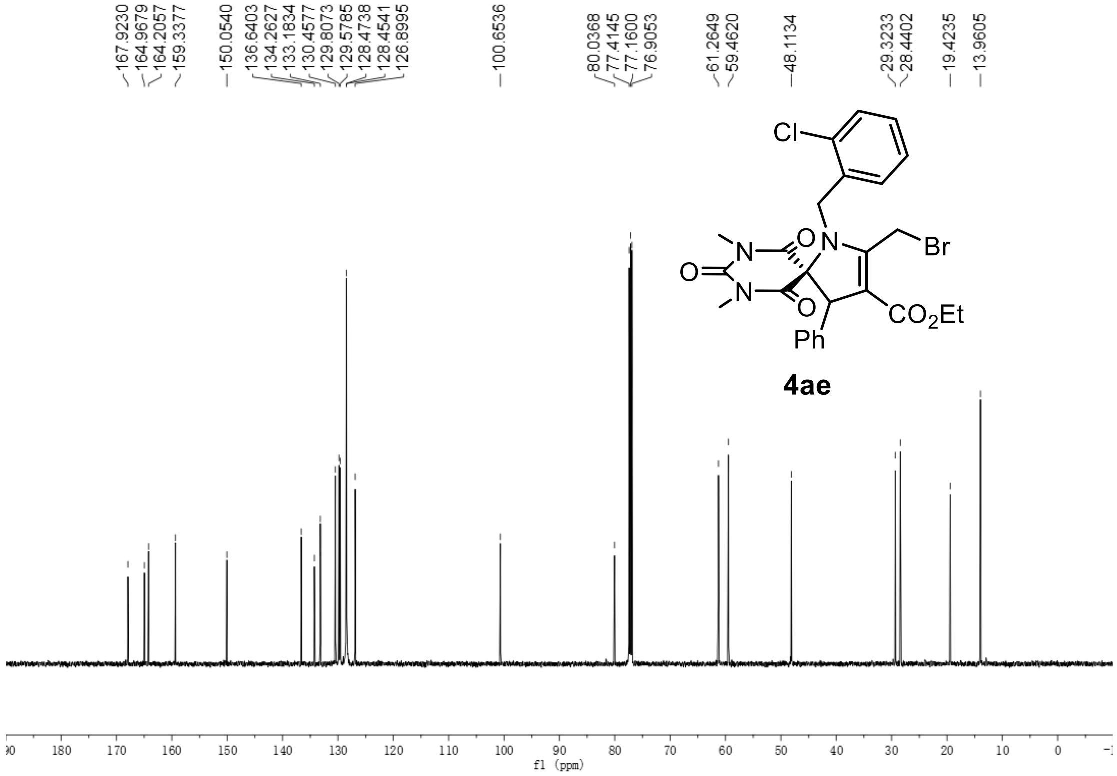


Figure S96. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ae

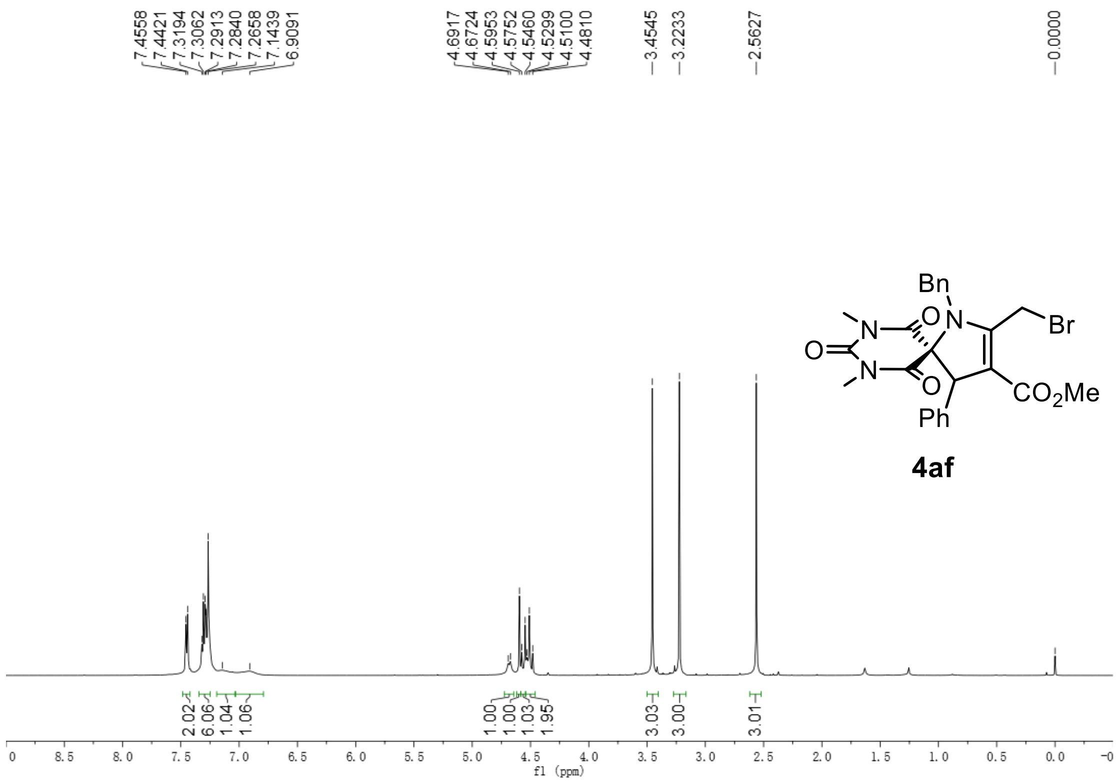


Figure S97. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4af

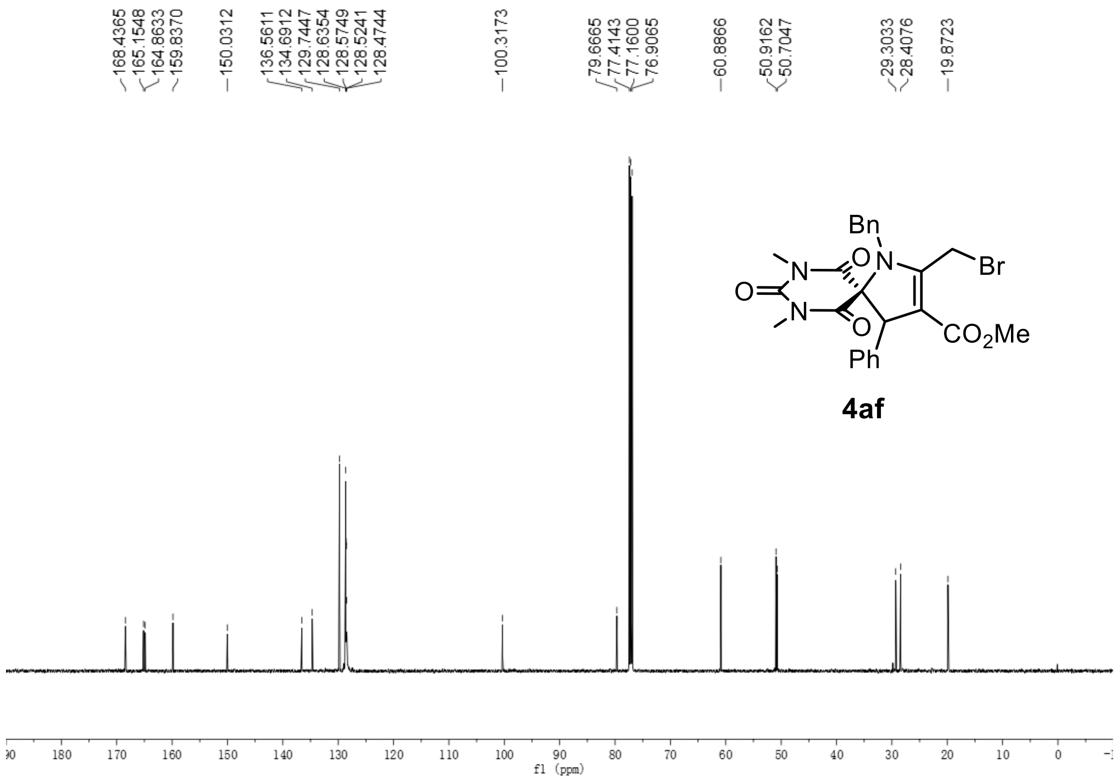


Figure S98. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4af

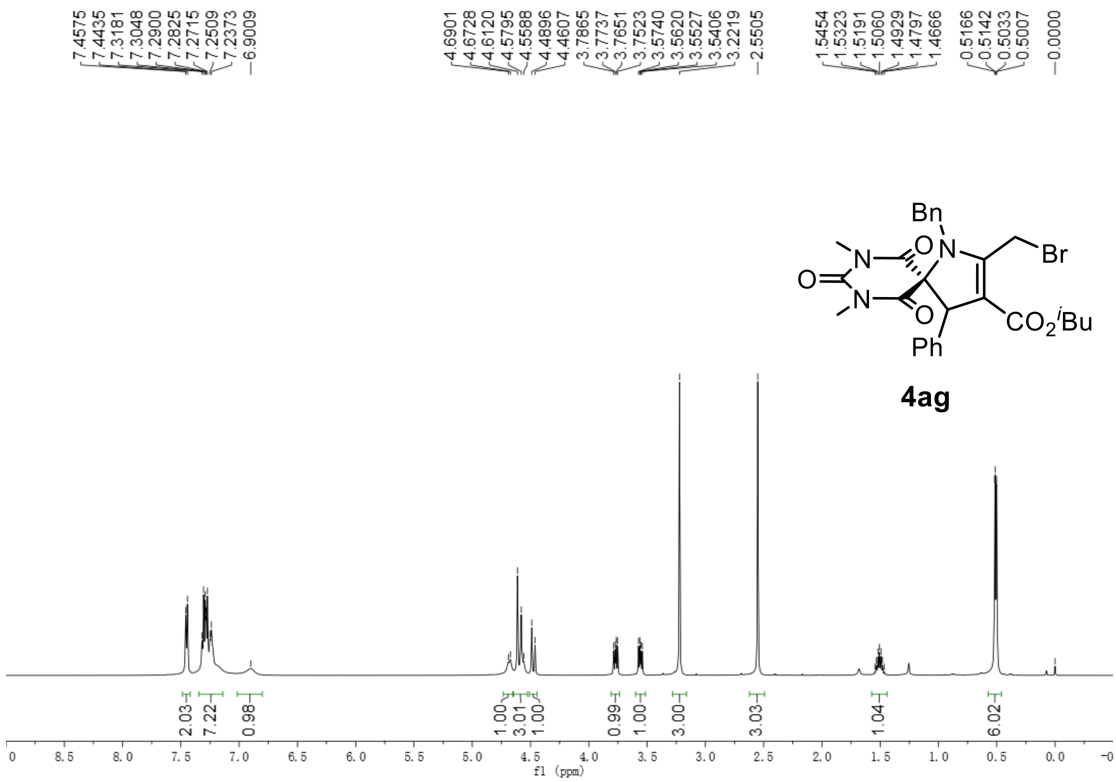


Figure S99. ^{1}H NMR (500 MHz, CDCl$_3$) of compound 4ag

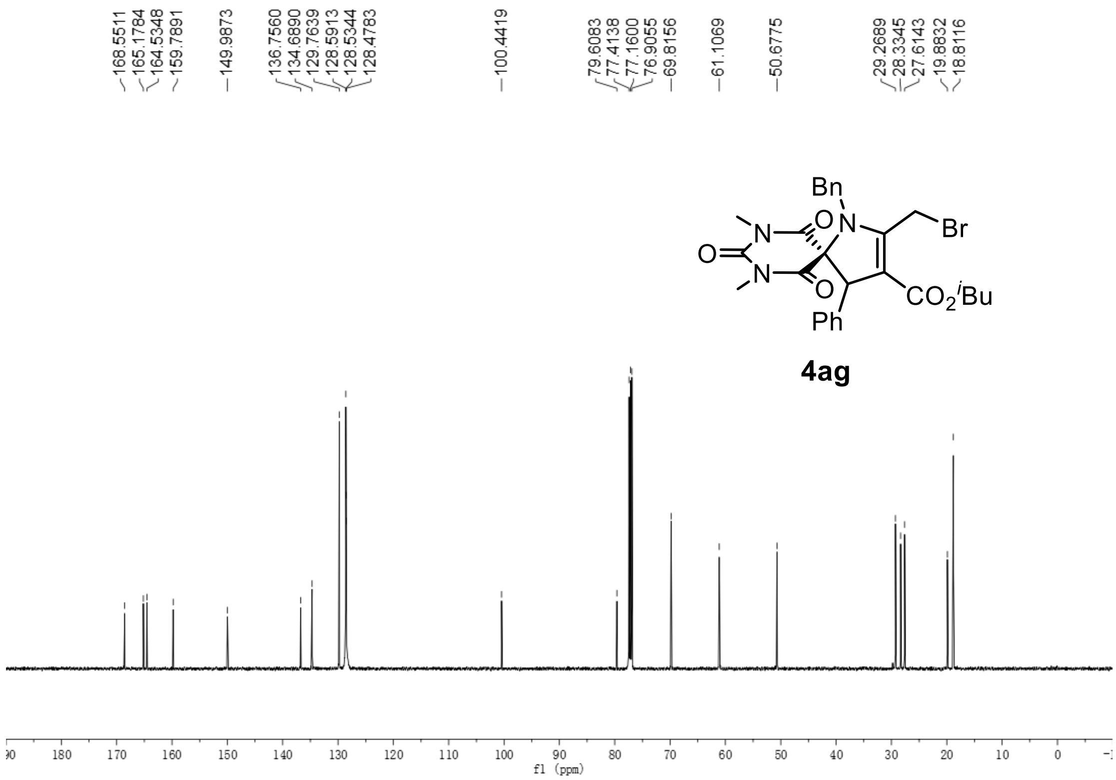


Figure S100. ^{13}C NMR (125 MHz, CDCl$_3$) of compound 4ag

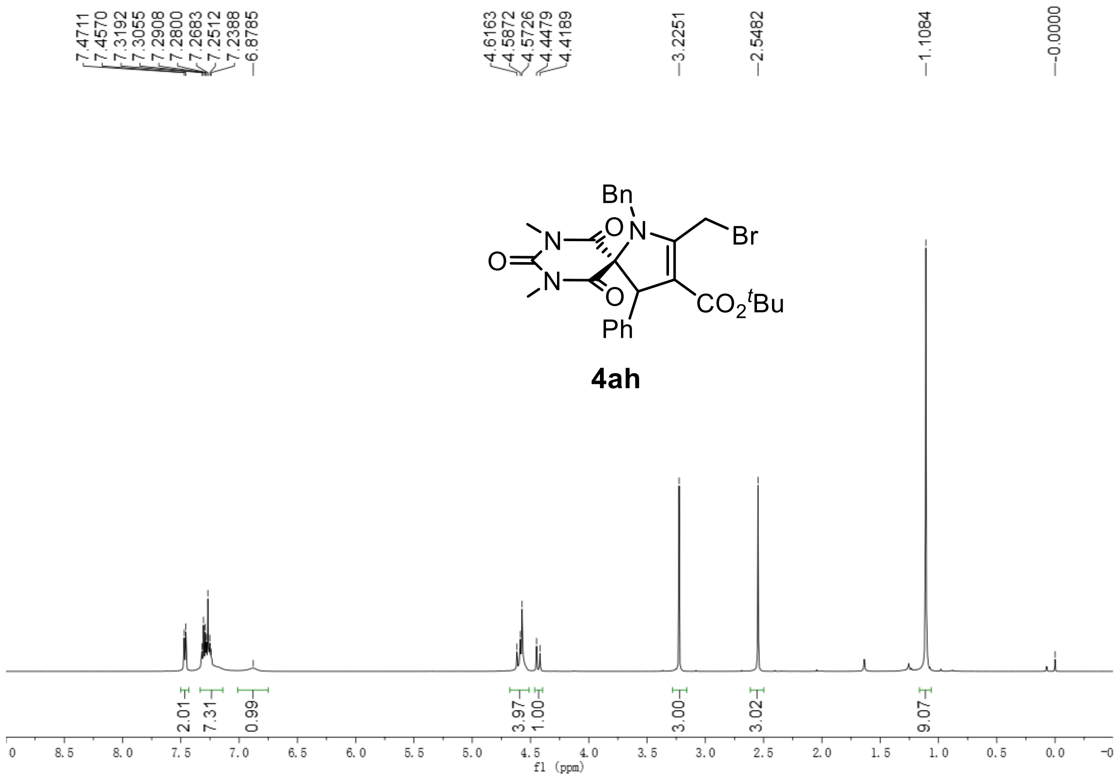


Figure S101. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 4ah

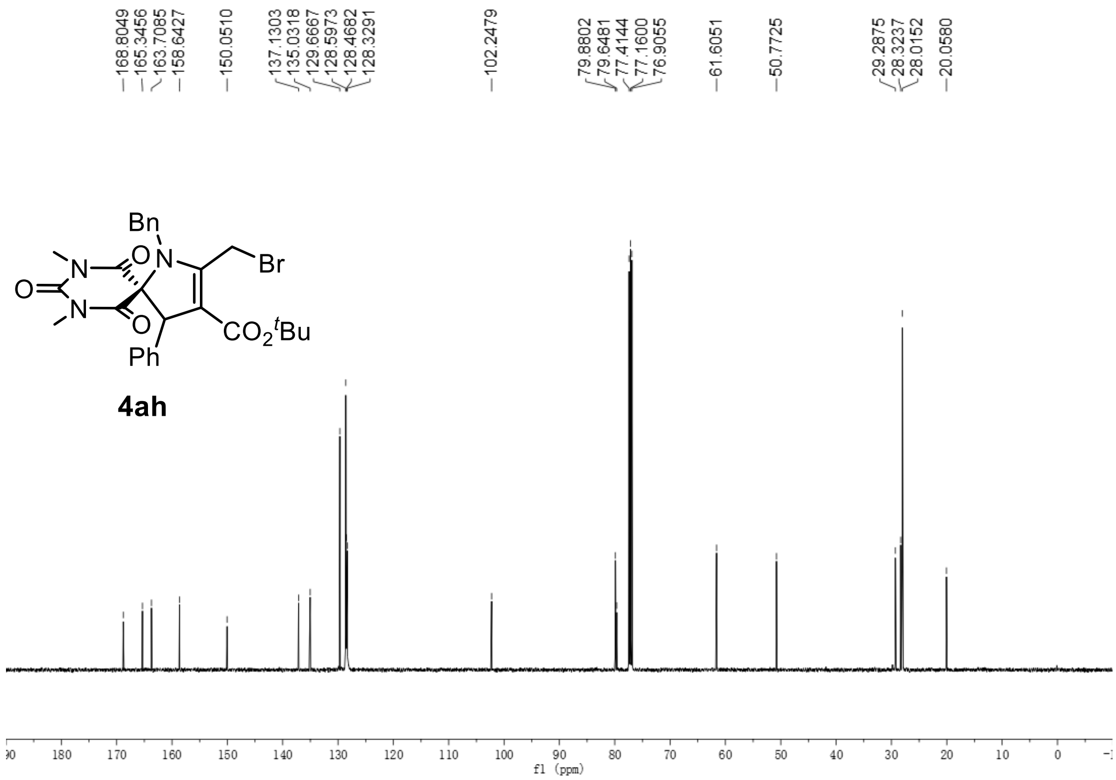


Figure S102. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 4ah

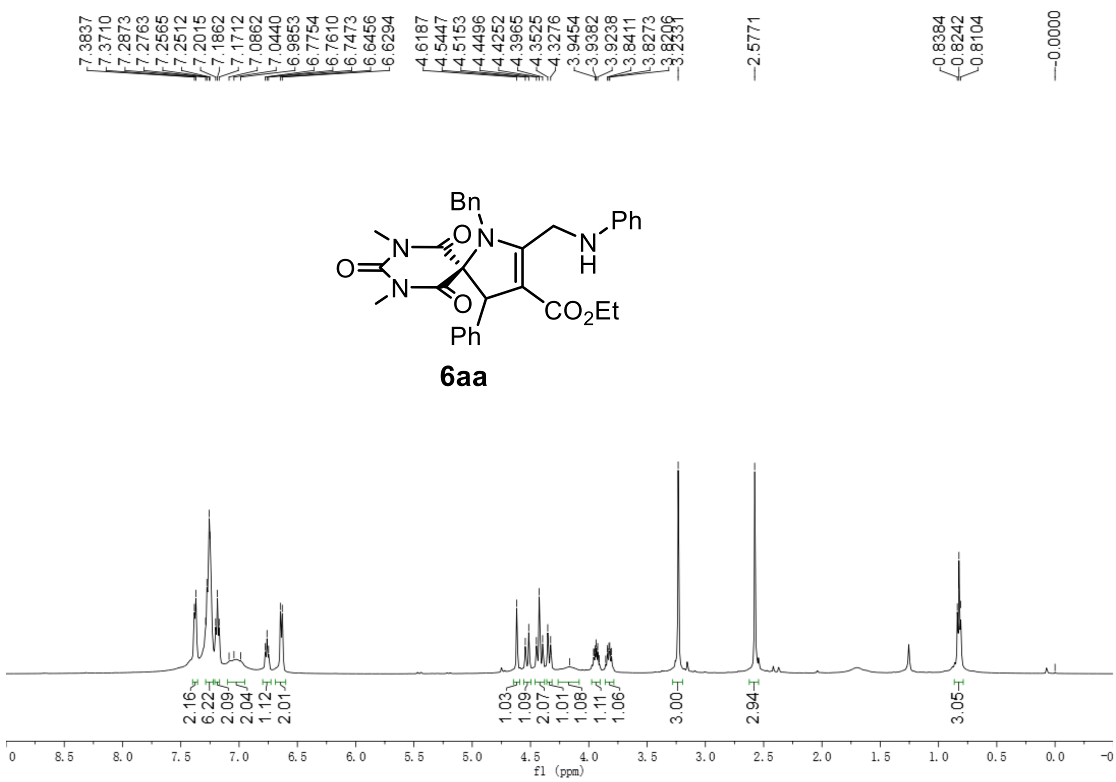


Figure S103. ^{1}H NMR (500 MHz, $CDCl_3$) of compound 6aa

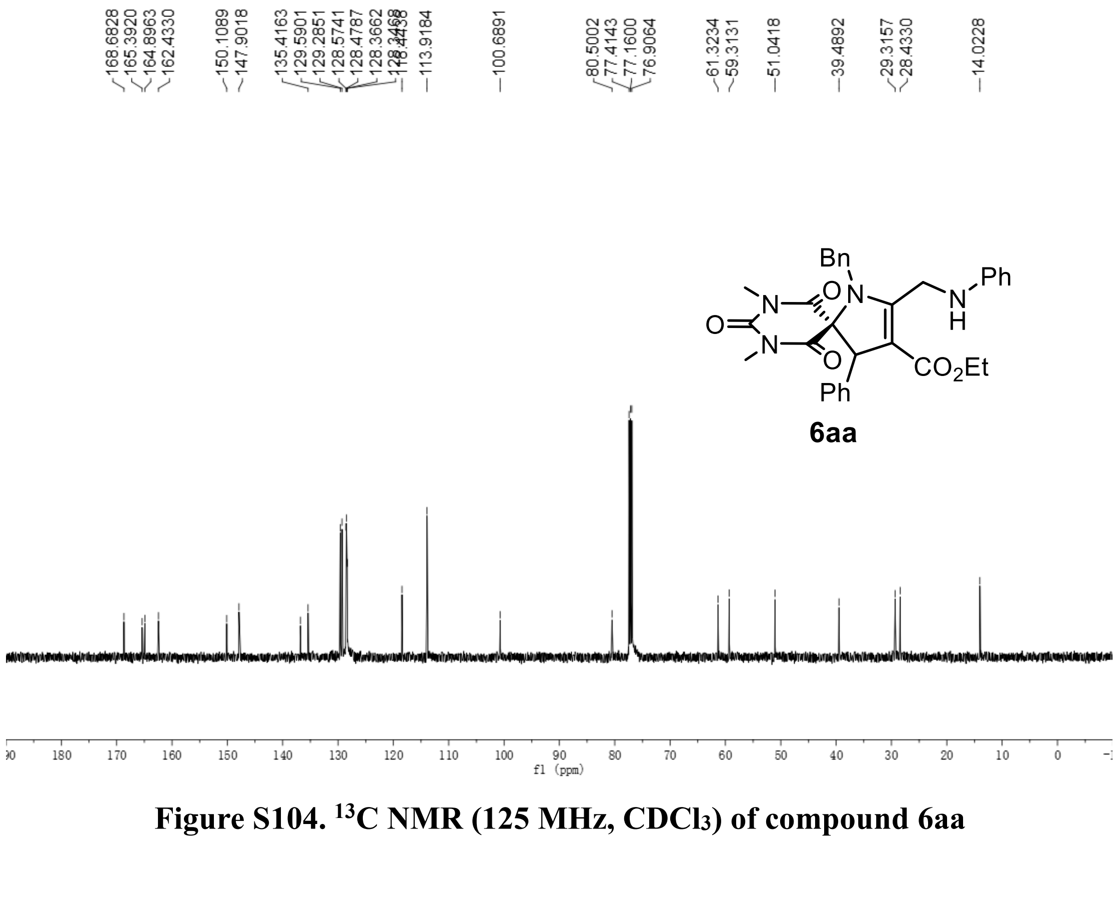


Figure S104. ^{13}C NMR (125 MHz, $CDCl_3$) of compound 6aa