

Supplementary Information

Palladium-Catalyzed Difunctionalization/De aromatization of *N*-Benzylacrylamides with α -Carbonyl Alkyl Bromides: Facile Access to Azaspirocyclohexadienones

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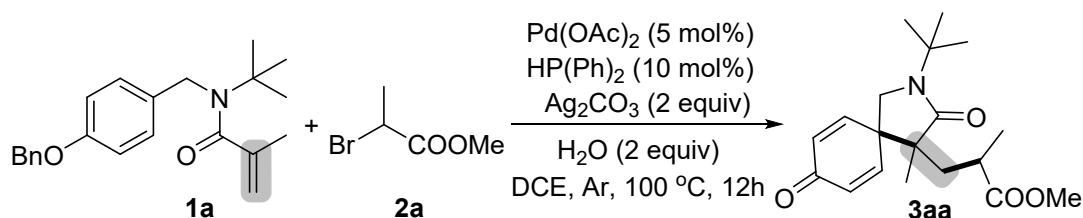
(A) General Information

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz advance spectrometer at room temperature in CDCl_3 with tetramethylsilane as internal standard. High-resolution mass spectra (HRMS) were recorded on an electrospray ionization (ESI) apparatus using time-of-flight (TOF) mass spectrometry. All products were identified by ^1H and ^{13}C NMR, products including **3aa**, **3db-3dl**, **3ja-3na**, **3oh-3ph** and **3ra** were identified by HRMS. Unless otherwise noted, all reactions were carried out using standard Schlenk techniques, and all starting materials and solvents were commercially available and were used without further purification. Reactions were monitored by thin-layer chromatography or GC-MS analysis. Column chromatography (petroleum ether/ethyl acetate) was performed on silica gel (200-300 mesh).

(B) Typical experimental procedure

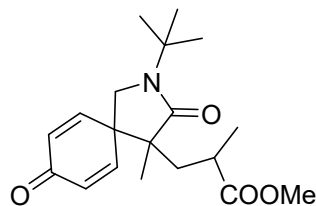
(a) Substrates **1** were prepared according to the literatures.^[1-2]

(b) Typical experimental procedure for the synthesis of compound **3aa**:



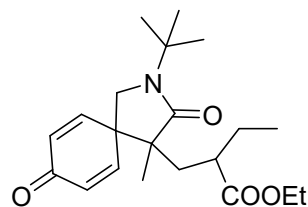
To a Schlenk tube were added **1a** (0.2 mmol), **2a** (0.3 mmol), $\text{Pd}(\text{OAc})_2$ (5 mol%; 0.01 mmol), $\text{HP}(\text{Ph})_2$ (10 mol%; 0.02 mmol), Ag_2CO_3 (2 equiv; 0.4 mmol), H_2O (2 equiv; 0.4 mmol) and DCE (2 mL). Then the tube was stirred at 100 °C (oil bath temperature) under Ar atmosphere for 12 h until complete consumption of starting material as monitored by TLC and/or GC-MS analysis. After the reaction was finished, the reaction mixture was filtered, organic layer was dried over Na_2SO_4 . Then removal of the solvent, the crude product was purified by column chromatography (petroleum ether/ethyl acetate, 2:1) to provide the desired product **3aa**.

(C) Analytical data



methyl 3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3aa) (d.r. = 1 : 1):

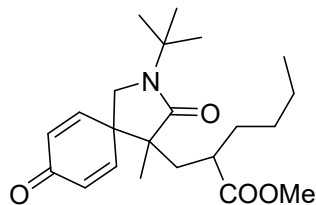
53.3 mg, 81% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 7.02-6.84 (m, 2H), 6.45-6.37 (m, 2H), 3.66 (s, 1.5H), 3.63 (s, 1.5H), 3.54 (d, $J = 10.4$ Hz, 0.5H), 3.42-3.37 (m, 1H), 3.30 (d, $J = 10.4$ Hz, 0.5H), 2.93-2.89 (m, 0.5H), 2.66-2.63 (m, 0.5H), 2.59-2.53 (m, 0.5H), 1.98-1.92 (m, 0.5H), 1.62-1.57 (m, 0.5H), 1.42 (s, 4.5H), 1.39 (s, 4.5H), 1.20-1.19 (m, 0.5H), 1.17 (d, $J = 7.2$ Hz, 1.5H), 1.13 (d, $J = 7.2$ Hz, 1.5H), 1.03 (s, 1.5H), 1.00 (s, 1.5H); ^{13}C NMR (100 MHz, CDCl_3) δ : 185.0, 184.9, 177.7, 177.0, 176.4, 175.3, 149.6, 148.4, 148.3, 148.2, 131.4, 131.1, 131.1, 130.3, 54.6, 54.4, 52.6, 52.6, 51.8, 51.8, 49.6, 49.6, 48.2, 48.1, 37.7, 37.2, 34.7, 34.6, 27.6, 27.6, 20.7, 20.4, 17.5, 16.7; HRMS m/z (ESI) calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_4$ ($[\text{M}+\text{H}]^+$) 334.2013, found 334.2016.



ethyl-2-((2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)butanoate (3db) (d.r. = 1 : 1):

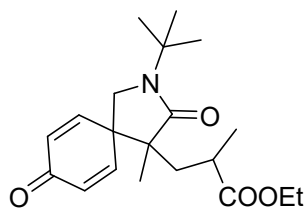
36.8 mg, 51% yield ; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 7.01 (dd, $J = 12.0$ Hz, $J = 3.2$ Hz, 0.5H), 6.97-6.90 (m, 1H), 7.01 (dd, $J = 12.0$ Hz, $J = 3.2$ Hz, 0.5H), 6.44-6.38 (m, 2H), 4.18-4.05 (m, 2H), 3.48 (d, $J = 10.4$ Hz, 0.5H), 3.43-3.34 (m, 1H), 3.32 (d, $J = 10.4$ Hz, 0.5H), 2.79-2.73 (m, 0.5H), 2.51-2.38 (m, 1H), 1.89 (dd, $J = 14.4$ Hz, $J = 8.4$ Hz, 1H), 1.66 (dd, $J = 14.0$ Hz, $J = 2.4$ Hz, 0.5H), 1.57-1.51 (m, 2H), 1.42 (s, 4.5H), 1.39 (s, 4.5H), 1.27-1.21 (m, 3H), 1.02 (s, 1.5H), 1.01 (s, 1.5H), 0.89-0.81 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 184.9, 184.9, 176.7, 176.3, 175.9, 175.5, 149.6, 148.5, 148.5, 148.2, 131.2, 131.2, 131.0, 130.4, 60.3, 60.2, 54.5, 54.4,

52.6, 52.5, 49.6, 49.5, 48.2, 48.1, 41.6, 41.6, 35.7, 35.4, 31.5, 28.2, 28.1, 27.6, 27.5, 22.6, 17.6, 16.7, 14.2, 14.1, 14.0, 11.5, 11.4; HRMS m/z (ESI) calcd for $C_{21}H_{32}NO_4$ ($[M+H]^+$) 362.2326, found 362.2307.



methyl 2-((2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)hexanoate (3dc) (d.r. = 1 : 1):

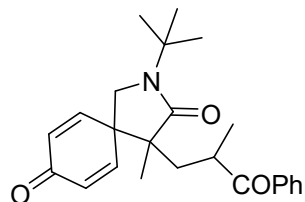
34.5 mg, 46% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.01 (dd, $J = 12.0$ Hz, $J = 3.2$ Hz, 0.5H), 6.97-6.90 (m, 1H), 6.85 (dd, $J = 12.0$ Hz, $J = 2.8$ Hz, 0.5H), 6.45-6.38 (m, 2H), 3.66 (s, 1.5H), 3.62 (s, 1.5H), 3.51 (d, $J = 10.4$ Hz, 0.5H), 3.43-3.31 (m, 1H), 3.32 (d, $J = 10.4$ Hz, 0.5H), 2.85-2.80 (m, 0.5H), 2.54-2.45 (m, 1H), 1.88 (dd, $J = 14.4$ Hz, $J = 8.4$ Hz, 0.5H), 1.68 (dd, $J = 14.4$ Hz, $J = 2.4$ Hz, 0.5H), 1.55-1.49 (m, 0.5H), 1.42 (s, 4.5H), 1.39 (s, 4.5H), 1.31-1.15 (m, 6H), 1.01 (s, 1.5H), 1.00 (s, 1.5H), 0.90-0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 184.9, 177.4, 176.6, 176.2, 175.4, 149.6, 148.5, 148.4, 148.2, 131.3, 131.1, 130.9, 130.3, 54.5, 54.4, 52.6, 52.5, 51.6, 51.6, 49.6, 48.2, 40.1, 40.1, 36.2, 35.9, 34.9, 34.8, 31.5, 29.3, 29.1, 27.6, 22.5, 22.4, 17.5, 16.6, 13.9, 13.8; HRMS m/z (ESI) calcd for $C_{22}H_{34}NO_4$ ($[M+H]^+$) 376.2482, found 376.2487.



ethyl 3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3dd) (d.r. = 1 : 1):

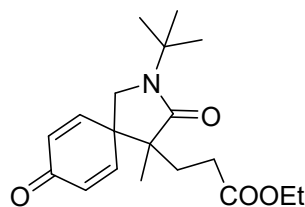
57.6 mg, 83% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.02-6.84 (m, 2H), 6.44-6.38 (m, 2H), 4.13-4.06 (m, 2H), 3.51 (d, $J = 10.4$ Hz, 0.5H), 3.42-3.36 (m, 1H), 3.31 (d, $J = 10.4$ Hz, 0.5H), 2.91-2.87 (m, 0.5H), 2.62-2.53 (m, 1H), 1.97 (dd, $J = 14.4$ Hz, $J = 7.2$ Hz, 0.5H), 1.58 (dd, $J = 14.4$ Hz, $J = 2.0$ Hz, 0.5H), 1.42 (s, 4.5H), 1.40 (s, 4.5H), 1.27-1.20 (m, 3.5H), 1.16 (d, $J = 6.0$ Hz, 1.5H), 1.12 (d, $J = 6.0$ Hz,

1.5H), 1.04 (s, 1.5H), 1.02 (s, 1.5H); ^{13}C NMR (100 MHz, CDCl_3) δ : 185.0, 184.9, 177.3, 176.6, 176.4, 175.4, 149.6, 148.5, 148.2, 131.3, 131.2, 131.1, 130.3, 60.5, 60.4, 54.5, 54.4, 52.7, 52.6, 49.6, 48.2, 48.2, 37.6, 37.1, 34.9, 34.8, 27.6, 20.8, 20.5, 17.6, 16.7, 14.2, 14.1; HRMS m/z (ESI) calcd for $\text{C}_{20}\text{H}_{30}\text{NO}_4$ ($[\text{M}+\text{H}]^+$) 348.2169, 348.2179.



2-(tert-butyl)-4-methyl-4-(2-methyl-3-oxo-3-phenylpropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3de) (d.r. = 1.2 : 1):

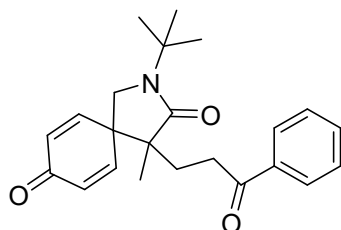
59.9 mg, 78% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 8.03 (d, $J = 6.8$ Hz, 0.9H), 7.94 (d, $J = 7.2$ Hz, 1.1H), 7.59-7.53 (m, 1H), 7.49-7.44 (m, 2H), 7.11 (dd, $J = 10.4$ Hz, $J = 3.2$ Hz, 0.55H), 7.01 (dd, $J = 10.4$ Hz, $J = 3.2$ Hz, 0.45H), 6.86-6.81 (m, 1H), 6.51-6.35 (m, 2H), 4.15-4.09 (m, 0.55H), 3.83-3.79 (m, 0.45H), 3.75 (d, $J = 10.4$ Hz, 0.55H), 3.49 (d, $J = 10.4$ Hz, 0.45H), 3.35 (d, $J = 10.4$ Hz, 0.45H), 3.22 (d, $J = 10.4$ Hz, 0.55H), 3.09-3.03 (m, 0.55H), 2.32 (dd, $J = 14.0$ Hz, $J = 8.0$ Hz, 0.45H), 2.06 (d, $J = 16.0$ Hz, 1H), 1.66-1.62 (m, 0.55H), 1.45 (s, 4H), 1.27 (s, 5H), 1.16-1.10 (m, 2.45H), 0.98 (s, 1.4H), 0.86 (s, 1.6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 204.3, 202.6, 185.1, 185.0, 176.8, 175.1, 150.2, 148.7, 148.2, 148.0, 136.2, 135.9, 133.2, 132.7, 132.0, 131.4, 130.9, 129.7, 128.8, 128.6, 128.6, 128.5, 54.6, 52.8, 52.6, 49.5, 48.7, 48.2, 36.4, 36.2, 35.9, 35.1, 27.6, 27.5, 21.3, 21.1, 18.2, 17.3; HRMS m/z (ESI) calcd for $\text{C}_{24}\text{H}_{30}\text{NO}_3$ ($[\text{M}+\text{H}]^+$) 380.2220, found 380.2226.



ethyl 3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoate (3df):

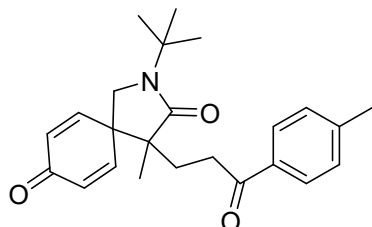
47.9 mg, 72% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 7.00 (dd, $J = 10.0$ Hz, $J = 3.2$ Hz, 1H), 6.89 (dd, $J = 10.0$ Hz, $J = 3.2$ Hz, 1H), 6.44-6.38 (m, 2H), 4.10 (q, $J = 7.2$ Hz, 2H), 3.46-3.35 (m, 2H), 2.50-2.42 (m, 1H), 2.31-2.23 (m, 1H), 2.10-

2.03 (m, 1H), 1.68-1.60 (m, 1H), 1.42 (s, 9H), 1.23 (t, $J = 7.2$ Hz, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 184.9, 175.9, 173.1, 148.9, 148.2, 131.3, 130.8, 60.6, 54.5, 52.0, 49.7, 47.9, 29.0, 28.8, 27.6, 16.8, 14.2; HRMS m/z (ESI) calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_4$ ($[\text{M}+\text{H}]^+$) 334.2013, found 334.2014.



2-(tert-butyl)-4-methyl-4-(3-oxo-3-phenylpropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dg):

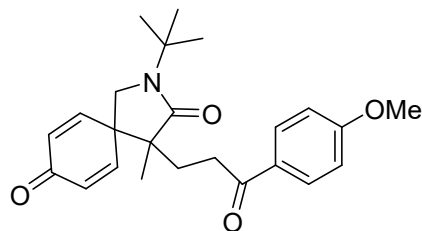
55.5 mg, 76% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 7.93 (d, $J = 7.6$ Hz, 2H), 7.55 (t, $J = 7.2$ Hz, 1H), 7.45 (t, $J = 7.2$ Hz, 2H), 7.06 (d, $J = 10.4$ Hz, 1H), 6.93 (d, $J = 10.0$ Hz, 1H), 6.46-6.39 (m, 2H), 3.56 (d, $J = 10.4$ Hz, 1H), 3.36 (d, $J = 10.4$ Hz, 1H), 3.27-3.19 (m, 1H), 3.04-2.96 (m, 1H), 2.27-2.20 (m, 1H), 1.76-1.69 (m, 1H), 1.42 (s, 9H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 199.4, 185.0, 176.0, 149.3, 148.1, 136.7, 133.1, 131.6, 130.5, 128.6, 128.0, 54.5, 52.3, 49.7, 48.2, 33.0, 28.0, 27.6, 17.0; HRMS m/z (ESI) calcd for $\text{C}_{23}\text{H}_{28}\text{NO}_3$ ($[\text{M}+\text{H}]^+$) 366.2064, found 336.2085.



2-(tert-butyl)-4-methyl-4-(3-oxo-3-(p-tolyl)propyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dh):

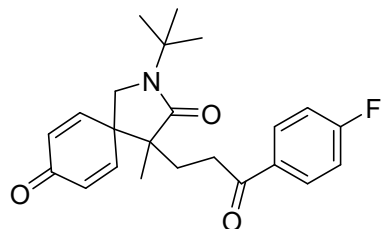
56.1 mg, 74% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 7.84 (d, $J = 8.0$ Hz, 2H), 7.24 (d, $J = 8.0$ Hz, 2H), 7.06 (dd, $J = 10.4$ Hz, $J = 3.2$ Hz, 1H), 6.92 (dd, $J = 10.4$ Hz, $J = 3.2$ Hz, 1H), 6.46-6.39 (m, 2H), 3.56 (d, $J = 10.4$ Hz, 1H), 3.35 (d, $J = 10.4$ Hz, 1H), 3.21-3.14 (m, 1H), 3.02-2.93 (m, 1H), 2.40 (s, 3H), 2.26-2.19 (m, 1H), 1.76-1.69 (m, 1H), 1.42 (s, 9H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 199.1, 185.0, 176.1, 149.3, 148.1, 143.9, 134.2, 131.6, 130.4, 129.3, 128.2, 54.5, 52.3, 49.7,

48.3, 32.9, 28.1, 27.6, 21.6, 16.9; HRMS m/z (ESI) calcd for $C_{24}H_{30}NO_3$ ($[M+H]^+$) 380.2220, found 380.2230.



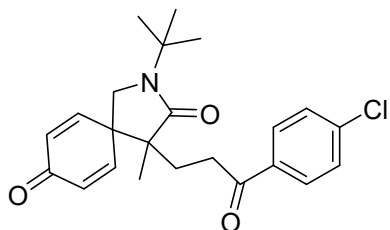
2-(tert-butyl)-4-(3-(4-methoxyphenyl)-3-oxopropyl)-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3di):

59.3 mg, 75% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.92 (d, $J = 8.4$ Hz, 2H), 7.06 (dd, $J = 10.4$ Hz, $J = 2.8$ Hz, 1H), 6.94-6.91 (m, 3H), 6.46-6.39 (m, 2H), 3.86 (s, 3H), 3.56 (d, $J = 10.4$ Hz, 1H), 3.35 (d, $J = 10.4$ Hz, 1H), 3.19-3.11 (m, 1H), 2.99-2.91 (m, 1H), 2.26-2.19 (m, 1H), 1.76-1.69 (m, 1H), 1.42 (s, 9H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 198.0, 185.0, 176.1, 163.5, 149.4, 148.1, 131.6, 130.4, 130.3, 129.8, 113.7, 55.5, 54.5, 52.4, 49.7, 48.3, 32.7, 28.2, 27.6, 16.9; HRMS m/z (ESI) calcd for $C_{22}H_{30}NO_4$ ($[M+H]^+$) 396.2169, found 396.2152.



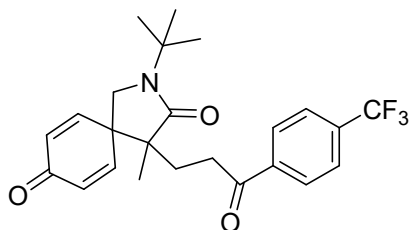
2-(tert-butyl)-4-(3-(4-fluorophenyl)-3-oxopropyl)-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dj):

53.6 mg, 70% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.95-7.92 (m, 3H), 7.18-7.14 (m, 3H), 6.59 (dd, $J = 10.4$ Hz, $J = 2.0$ Hz, 1H), 6.10-6.07 (m, 1H), 3.93-3.87 (m, 1H), 3.54 (dd, $J = 10.8$ Hz, $J = 1.6$ Hz, 1H), 3.43 (dd, $J = 10.8$ Hz, $J = 1.6$ Hz, 1H), 2.93-2.89 (m, 1H), 2.50-2.44 (m, 1H), 2.40-2.27 (m, 1H), 2.05-1.96 (m, 1H), 1.48 (s, 9H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 197.1, 196.4, 177.4, 166.0 (d, $J = 255.4$ Hz), 149.3, 133.0 (d, $J = 2.8$ Hz), 130.7, 130.6, 129.1, 116.2, 116.0, 56.2, 54.5, 49.3, 46.7, 39.4, 36.5, 27.6, 22.1; HRMS m/z (ESI) calcd for $C_{23}H_{27}NO_3$ ($[M+H]^+$) 384.1969, found 384.1979.



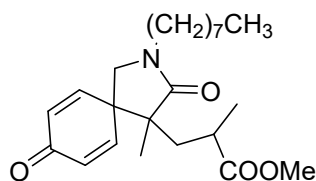
2-(tert-butyl)-4-(3-(4-chlorophenyl)-3-oxopropyl)-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dk):

54.3 mg, 68% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 7.88 (d, $J = 8.8$ Hz, 2H), 7.42 (d, $J = 8.8$ Hz, 2H), 7.05 (dd, $J = 10.4$ Hz, $J = 2.8$ Hz, 1H), 6.92 (dd, $J = 10.4$ Hz, $J = 2.8$ Hz, 1H), 6.46-6.39 (m, 2H), 3.56 (d, $J = 10.4$ Hz, 1H), 3.38 (d, $J = 10.4$ Hz, 1H), 3.27-3.19 (m, 1H), 3.00-2.92 (m, 1H), 2.27-2.19 (m, 1H), 1.73-1.66 (m, 1H), 1.42 (s, 9H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 198.1, 184.9, 176.0, 149.1, 148.0, 139.5, 135.0, 131.6, 130.6, 129.5, 128.9, 54.5, 52.2, 49.7, 48.2, 33.0, 27.8, 27.6, 17.0; HRMS m/z (ESI) calcd for $\text{C}_{23}\text{H}_{27}\text{ClNO}_3$ ($[\text{M}+\text{H}]^+$) 400.1674, found 400.1678.



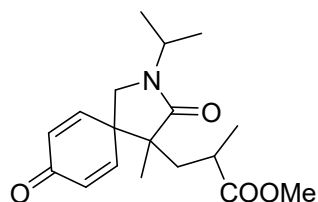
2-(tert-butyl)-4-methyl-4-(3-oxo-3-(4-(trifluoromethyl)phenyl)propyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dl):

53.7 mg, 62% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 8.01-7.93 (m, 3H), 7.77-7.70 (m, 3H), 6.76 (dd, $J = 10.4$ Hz, $J = 2.0$ Hz, 1H), 6.19 (d, $J = 10.4$ Hz, 1H), 3.61-3.50 (m, 1H), 3.34 (d, $J = 10.8$ Hz, 1H), 3.17-3.13 (m, 1H), 2.74 (dd, $J = 17.2$ Hz, $J = 6.0$ Hz, 1H), 2.46-2.31 (m, 1H), 2.01-1.98 (m, 1H), 1.43 (s, 9H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 198.3, 197.5, 177.7, 147.6, 138.9, 134.6 (q, $J = 32.5$ Hz), 131.2, 129.1, 128.8, 128.4, 125.7 (q, $J = 3.7$ Hz), 123.5 (d, $J = 271.1$ Hz), 57.8, 54.3, 48.9, 43.3, 39.5, 37.1, 27.5, 19.6; HRMS m/z (ESI) calcd for $\text{C}_{24}\text{H}_{27}\text{F}_3\text{NO}_3$ ($[\text{M}+\text{H}]^+$) 434.1938, found 434.1950.



Methyl 2-methyl-3-(4-methyl-2-octyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoate (3ja) (d.r. = 1 : 1):

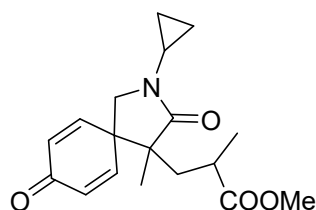
38.1 mg, 49% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 7.02-6.84 (m, 2H), 6.46-6.37 (m, 2H), 3.66 (s, 1.5H), 3.64 (s, 1.5H), 3.51 (d, $J = 10.4$ Hz, 0.5H), 3.38-3.29 (m, 2H), 3.23 (d, $J = 10.4$ Hz, 0.5H), 3.19-3.12 (m, 0.5H), 2.98-2.90 (m, 0.5H), 2.73-2.65 (m, 0.5), 2.59-2.53 (m, 0.5H), 1.99 (dd, $J = 14.4$ Hz, $J = 7.2$ Hz, 0.5H), 1.61 (dd, $J = 14.4$ Hz, $J = 3.2$ Hz, 0.5H), 1.53-1.46 (m, 2H), 1.30-1.27 (m, 11H), 1.17-1.13 (m, 3H), 1.08 (s, 1.5H), 1.03 (s, 1.5H), 0.88 (t, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ : 185.0, 184.9, 177.6, 177.0, 175.9, 175.1, 149.5, 148.2, 148.1, 147.9, 131.7, 131.1, 131.1, 130.2, 52.1, 52.0, 51.9, 51.8, 51.4, 51.3, 49.0, 42.9, 42.8, 37.6, 37.4, 34.9, 34.7, 31.8, 31.7, 29.2, 29.2, 29.1, 27.2, 27.0, 27.0, 26.8, 22.6, 20.6, 20.4, 17.5, 17.0, 14.1; HRMS m/z (ESI) calcd for $\text{C}_{23}\text{H}_{36}\text{NO}_4$ ($[\text{M}+\text{H}]^+$) 390.2639, found 390.2645.



methyl 3-(2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3ka) (d.r. = 1.5 : 1):

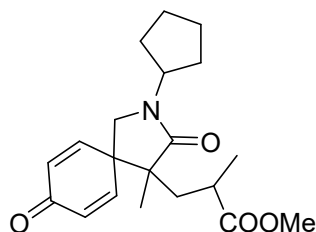
47.9 mg, 75% yield; Yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 7.01-6.83 (m, 2H), 6.46-6.36 (m, 2H), 4.45-4.27 (m, 1H), 3.66 (s, 1.8H), 3.63 (s, 1.2H), 3.48 (d, $J = 10.4$ Hz, 0.6H), 3.30-3.26 (m, 1H), 3.16 (d, $J = 10.4$ Hz, 0.4H), 2.96-2.91 (m, 0.4H), 2.74-2.66 (m, 0.6H), 2.60-2.54 (m, 0.6H), 1.97 (dd, $J = 14.4$ Hz, $J = 7.2$ Hz, 0.4H), 1.63-1.46 (m, 1H), 1.20-1.15 (m, 6H), 1.13-1.11 (m, 3H), 1.07 (s, 1.2H), 1.02 (s, 1.8H); ^{13}C NMR (100 MHz, CDCl_3) δ : 184.9, 184.8, 177.6, 176.9, 175.3, 174.3, 149.4, 148.1, 147.9, 147.8, 131.7, 131.2, 131.1, 130.2, 52.3, 52.2, 51.8, 51.7, 48.8, 48.7, 46.4, 46.4,

42.8, 37.6, 37.2, 34.8, 34.6, 20.6, 20.3, 19.6, 19.4, 19.2, 17.3, 16.7; HRMS m/z (ESI) calcd for $C_{18}H_{26}NO_4$ ($[M+H]^+$) 320.1856, found 320.1855.



methyl 3-(2-cyclopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3la) (d.r. = 2 : 1)

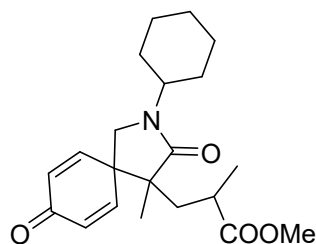
37.4 mg, 59% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 6.98-6.80 (m, 2H), 6.46-6.35 (m, 2H), 3.68 (s, 2H), 3.63 (s, 1H), 3.56 (d, J = 10.0 Hz, 0.65H), 3.30-3.25 (m, 0.65H), 3.11 (d, J = 10.4 Hz, 0.35H), 2.95-2.89 (m, 0.35H), 2.73-2.68 (m, 1H), 2.64-2.55 (m, 1H), 1.95 (dd, J = 14.4 Hz, J = 7.2 Hz, 0.35H), 1.61-1.46 (m, 0.65H), 1.16-1.12 (m, 3.65H), 1.09-1.06 (m, 0.65H), 1.06 (s, 1H), 0.98 (s, 2H), 0.84-0.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 184.9, 184.8, 177.6, 177.1, 177.0, 176.1, 149.6, 148.0, 147.8, 147.4, 132.0, 131.2, 130.0, 52.5, 52.4, 51.9, 51.8, 51.8, 51.7, 49.0, 48.8, 37.5, 37.3, 34.8, 34.6, 25.6, 20.6, 20.4, 17.3, 16.9, 5.3, 5.2, 5.1, 4.9; HRMS m/z (ESI) calcd for $C_{18}H_{24}NO_4$ ($[M+H]^+$) 318.1700, found 318.1709.



methyl 3-(2-cyclopentyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3ma) (d.r. = 1 : 1):

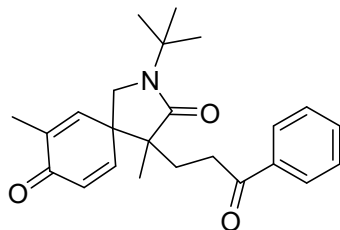
60.4 mg, 85% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.01-6.83 (m, 2H), 6.46-6.37 (m, 2H), 4.58-4.41 (m, 1H), 3.66 (s, 1.5H), 3.63 (s, 1.5H), 3.51 (d, J = 10.4 Hz, 0.5H), 3.33-3.27 (m, 0.5H), 3.16 (d, J = 10.4 Hz, 0.5H), 2.97-2.89 (m, 0.5H), 2.74-2.66 (m, 0.5H), 2.60-2.54 (m, 0.5H), 1.99-1.84 (m, 2H), 1.69-1.40 (m, 8H), 1.16-1.12 (m, 3H), 1.07 (s, 1.5H), 1.01 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 185.0, 184.9, 177.6, 176.9, 175.8, 174.8, 149.5, 148.2, 147.9, 147.8, 131.8, 131.2, 131.1, 130.2, 52.5, 52.3, 52.2, 51.9, 51.8, 49.0, 48.9, 47.5, 47.4, 37.6, 37.2, 34.9, 34.6, 28.8,

28.8, 28.6, 28.5, 24.3, 24.2, 24.2, 20.6, 20.3, 17.4, 16.8; HRMS m/z (ESI) calcd for $C_{20}H_{28}NO_4$ ($[M+H]^+$) 346.2013, found 346.2030.



methyl 3-(2-cyclohexyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3na) (d.r. = 1.5 : 1):

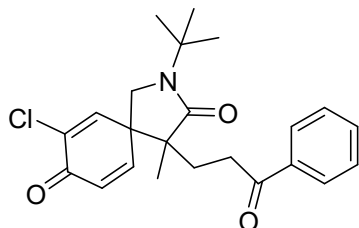
58.9 mg, 82% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.00-6.83 (m, 2H), 6.45-6.36 (m, 2H), 4.02-3.87 (m, 1H), 3.66 (s, 1.8H), 3.63 (s, 1.2H), 3.47 (d, $J = 10.4$ Hz, 0.6H), 3.33-3.28 (m, 0.6H), 3.20 (d, $J = 10.4$ Hz, 0.4H), 2.96-2.91 (m, 0.4H), 2.73-2.65 (m, 0.4H), 2.58-2.53 (m, 0.6H), 1.99-1.94 (m, 1H), 1.84-1.59 (m, 6H), 1.41-1.26 (m, 5H), 1.17-1.12 (m, 3H), 1.06 (s, 1.2H), 1.02 (s, 1.8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 184.9, 184.9, 177.6, 176.9, 175.4, 174.4, 149.5, 148.3, 148.0, 131.6, 131.1, 131.1, 130.2, 52.2, 52.2, 51.9, 51.7, 50.7, 49.0, 48.9, 47.4, 37.6, 37.2, 34.8, 34.6, 30.2, 30.0, 29.9, 29.8, 25.4, 25.4, 25.3, 25.2, 20.6, 20.4, 17.4, 16.8; HRMS m/z (ESI) calcd for $C_{21}H_{30}NO_4$ ($[M+H]^+$) 360.2169, found 360.2168.



2-(tert-butyl)-4,7-dimethyl-4-(3-oxo-3-phenylpropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3og) (d.r. > 20 : 1):

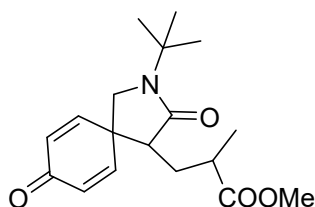
51.5 mg, 68% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 1H NMR (400 MHz, $CDCl_3$) δ : 7.93 (d, $J = 7.2$ Hz, 2H), 7.55 (t, $J = 7.2$ Hz, 1H), 7.44 (t, $J = 7.6$ Hz, 2H), 7.02 (dd, $J = 12.0$ Hz, $J = 2.8$ Hz, 1H), 6.68 (s, 1H), 6.43 (d, $J = 12.0$ Hz, 1H), 3.52 (d, $J = 10.4$ Hz, 1H), 3.35 (d, $J = 10.0$ Hz, 1H), 3.27-3.19 (m, 1H), 3.03-2.94 (m, 1H), 2.24-2.17 (m, 1H), 1.95 (s, 3H), 1.74-1.67 (m, 1H), 1.42 (s, 9H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 199.5, 185.6, 176.4, 147.9, 144.2, 137.1, 136.7, 133.1,

131.2, 128.6, 128.0, 54.4, 52.3, 49.9, 48.1, 33.1, 28.1, 27.6, 16.9, 16.1; HRMS m/z (ESI) calcd for $C_{24}H_{30}NO_3$ ($[M+H]^+$) 380.2220, found 380.2224.



2-(tert-butyl)-7-chloro-4-methyl-4-(3-oxo-3-phenylpropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3pg) (d.r. = 6 : 1):

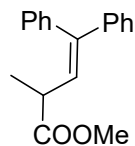
36.7 mg, 46% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.95-7.93 (m, 2.65H), 7.84 (d, $J = 7.2$ Hz, 0.35H), 7.58-7.44 (m, 2H), 7.10-7.08 (m, 1.85 H), 6.93 (s, 0.15H), 6.56-6.53 (m, 1 H), 3.62-3.52 (m, 1H), 3.43-3.36 (m, 1H), 3.29-3.23 (m, 0.85H), 3.04-2.97 (m, 0.85H), 2.86-2.82 (m, 0.15H), 2.70-2.66 (m, 0.15H), 2.28-2.21 (m, 1H), 1.75-1.68 (m, 1H), 1.43 (s, 9H), 1.1 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 199.2, 178.0, 175.6, 148.2, 145.1, 136.6, 134.3, 133.2, 130.6, 128.7, 128.6, 128.5, 128.0, 54.7, 52.9, 50.9, 49.4, 33.0, 28.0, 27.6, 17.1; HRMS m/z (ESI) calcd for $C_{23}H_{27}ClNO_3$ ($[M+H]^+$) 400.1674, found 400.1680.



methyl 3-(2-(tert-butyl)-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3ra) (d.r. = 1 : 1):

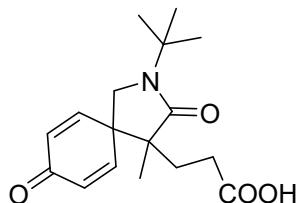
44.7 mg, 70% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 6.95-6.81 (m, 2H), 6.44-6.39 (m, 2H), 3.65 (s, 1.5H), 3.64 (s, 1.5H), 3.53 (dd, $J = 12.0$ Hz, $J = 7.0$ Hz, 1H), 3.28-3.24 (m, 1H), 2.98-2.94 (m, 0.5H), 2.76-2.68 (m, 1H), 2.61-2.54 (m, 0.5H), 2.13-2.06 (m, 0.5H), 1.52-1.49 (m, 0.5H), 1.42 (s, 4.5H), 1.41 (s, 4.5H), 1.36-1.34 (m, 0.5H), 1.20-1.17 (m, 0.5H), 1.14 (d, $J = 7.2$ Hz, 1.5H), 1.08 (d, $J = 6.8$ Hz, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 185.3, 185.2, 176.3, 176.0, 173.7, 173.0, 150.5, 149.8, 147.7, 147.4, 131.6, 131.2, 130.7, 130.6, 54.5, 54.5, 51.6, 51.5, 51.3, 51.2, 49.3, 49.2,

46.5, 46.1, 36.9, 36.4, 30.4, 29.9, 27.6, 27.6, 17.8, 17.2; HRMS m/z (ESI) calcd for $C_{18}H_{26}NO_4$ ($[M+H]^+$) 320.1856, found 320.1865.



methyl 2-methyl-4,4-diphenylbut-3-enoate (5aa)^[3]:

39.9 mg, 75% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.40-7.32 (m, 3H), 7.27-7.19 (m, 7H), 6.12 (d, $J = 10.4$ Hz, 1H), 3.68 (s, 3H), 3.33-3.26 (m, 1H), 1.27 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 175.4, 143.1, 141.9, 139.4, 129.7, 128.4, 128.1, 127.7, 127.4, 127.4, 51.9, 40.3, 18.5;



3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoic acid (6aa):

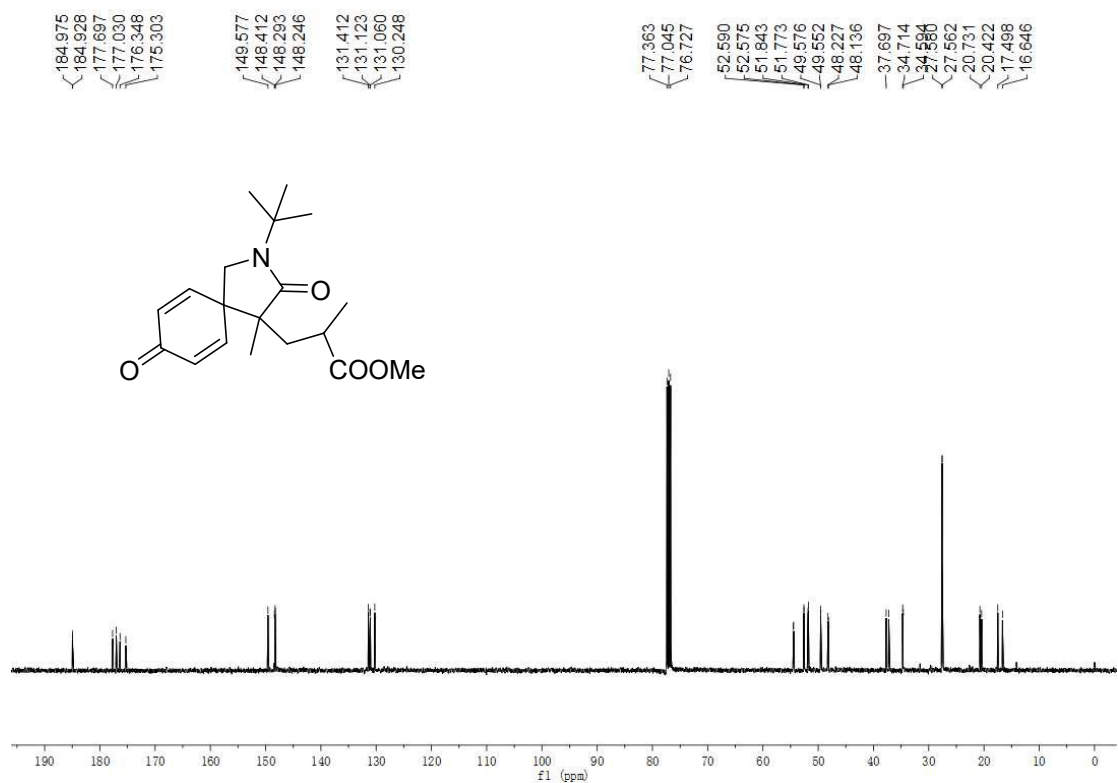
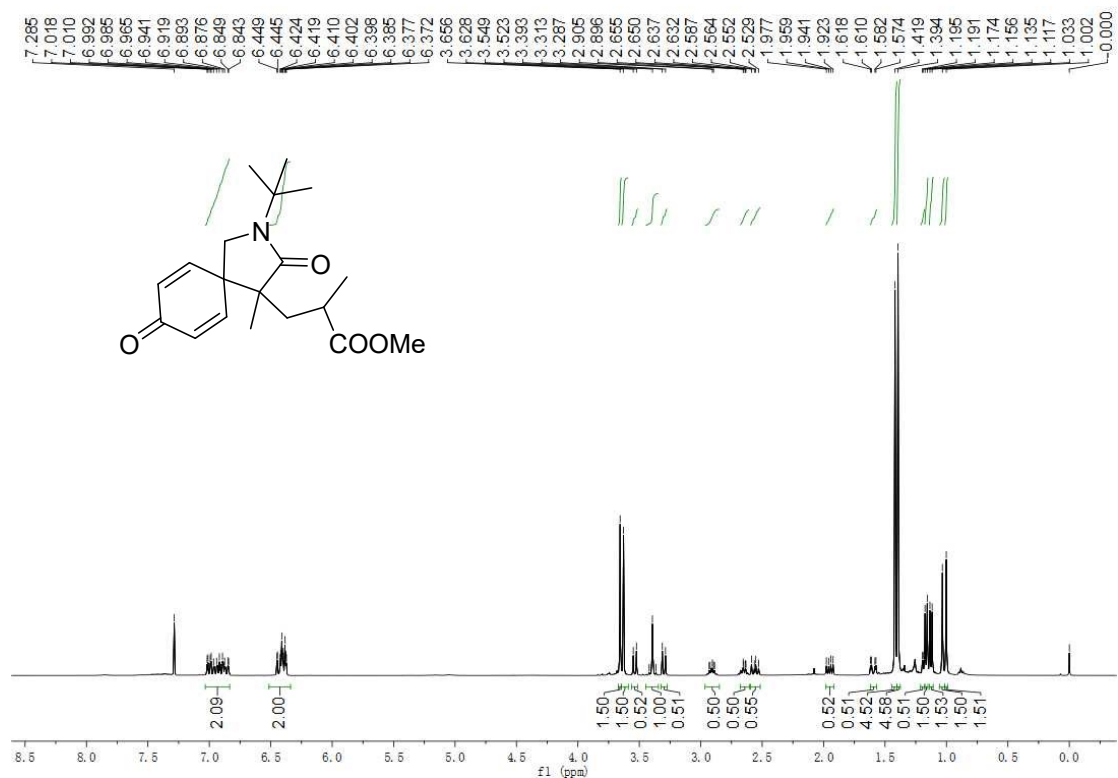
51.9 mg, 85% yield; Yellow oil; 1H NMR (400 MHz, $CDCl_3$) δ : 7.00 (dd, $J = 10.4$ Hz, $J = 2.8$ Hz, 1H), 6.89 (dd, $J = 10.4$ Hz, $J = 2.8$ Hz, 1H), 6.45-6.39 (m, 2H), 3.45 (d, $J = 10.4$ Hz, 1H), 3.38 (d, $J = 10.4$ Hz, 1H), 2.57-2.49 (m, 1H), 2.38-2.29 (m, 1H), 2.10-2.00 (m, 1H), 1.67-1.57 (m, 1H), 1.42 (s, 9H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 184.9, 177.4, 176.0, 148.8, 148.1, 131.3, 130.9, 54.6, 52.0, 49.8, 47.9, 28.8, 28.5, 27.6, 16.8;

(D) References

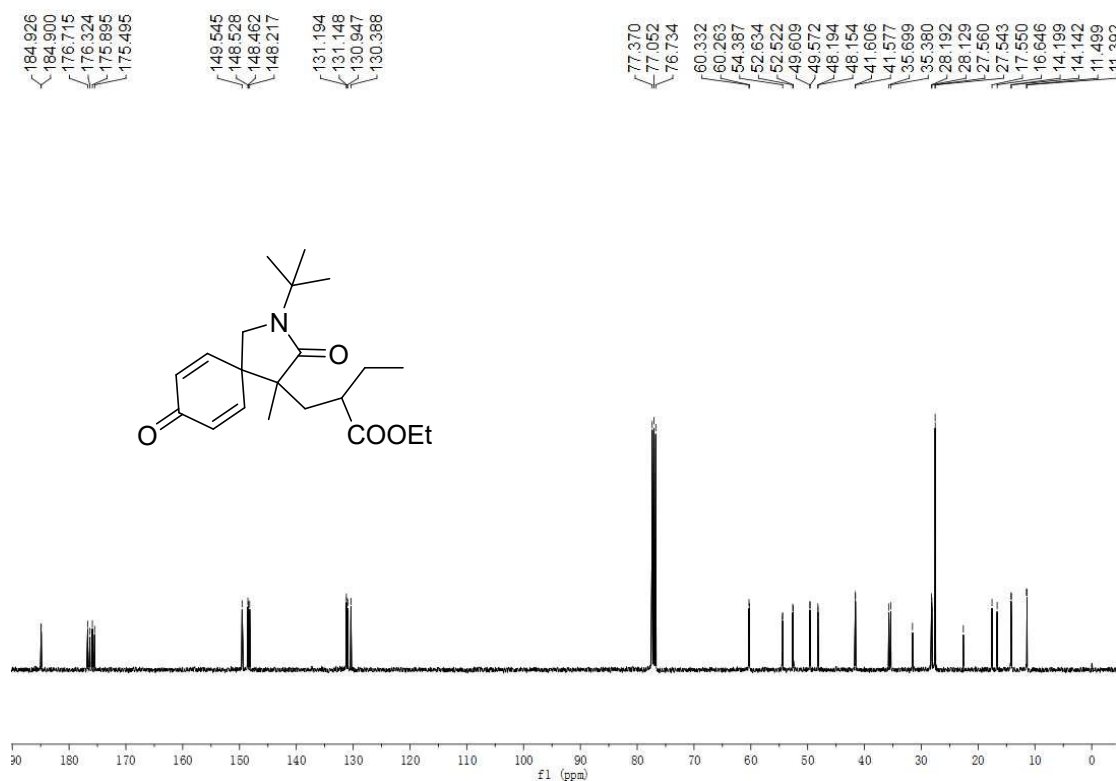
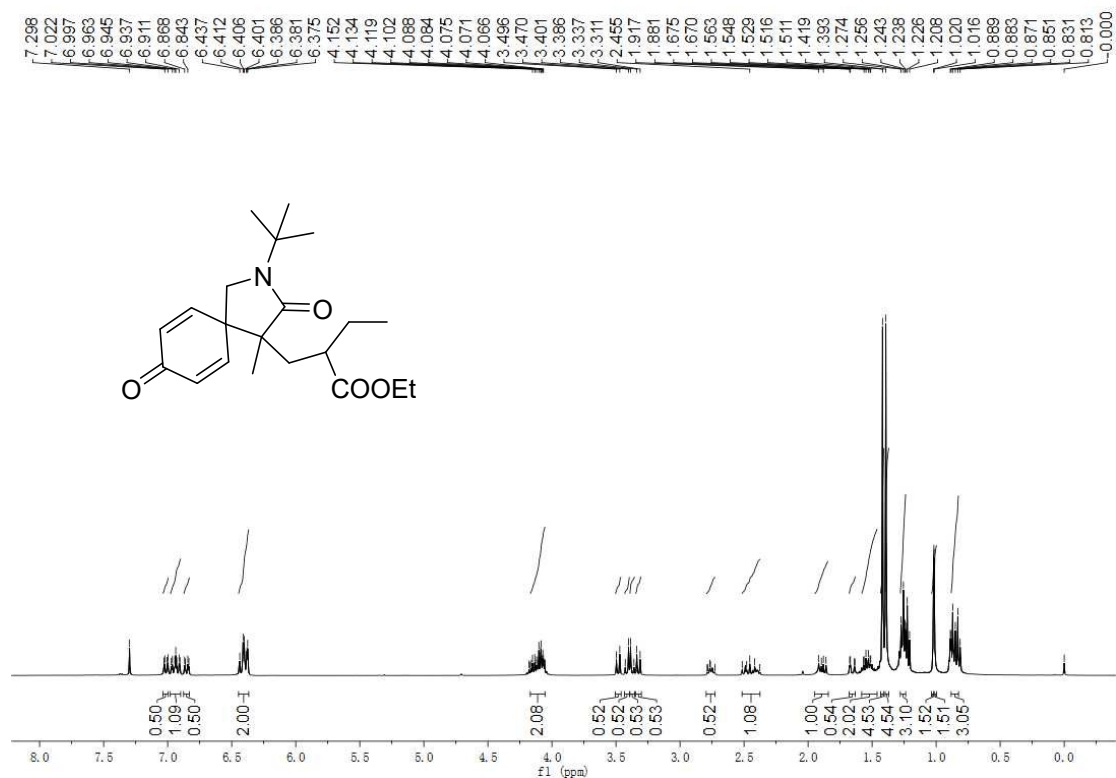
- [1] Z. Zhang, X.-J. Tang, W.R. Dolbier, Jr, *Org. Lett.*, **2016**, 18, 1048.
- [2] L. Yuan, S.-M. Jiang, Z.-Z. Li, Y. Zhu, J. Yu, L. Li, M.-Z. Li, S. Tang and R.-R. Sheng, *Org. Biomol. Chem.*, **2018**, 16, 2406.
- [3] J.-H. Fan, W.-T. Wei, M. -B. Zhou, R.-J. Song and J.-H. Li, *Angew. Chem. Int. Ed.*, **2014**, 53, 6650.

(E) Spectra

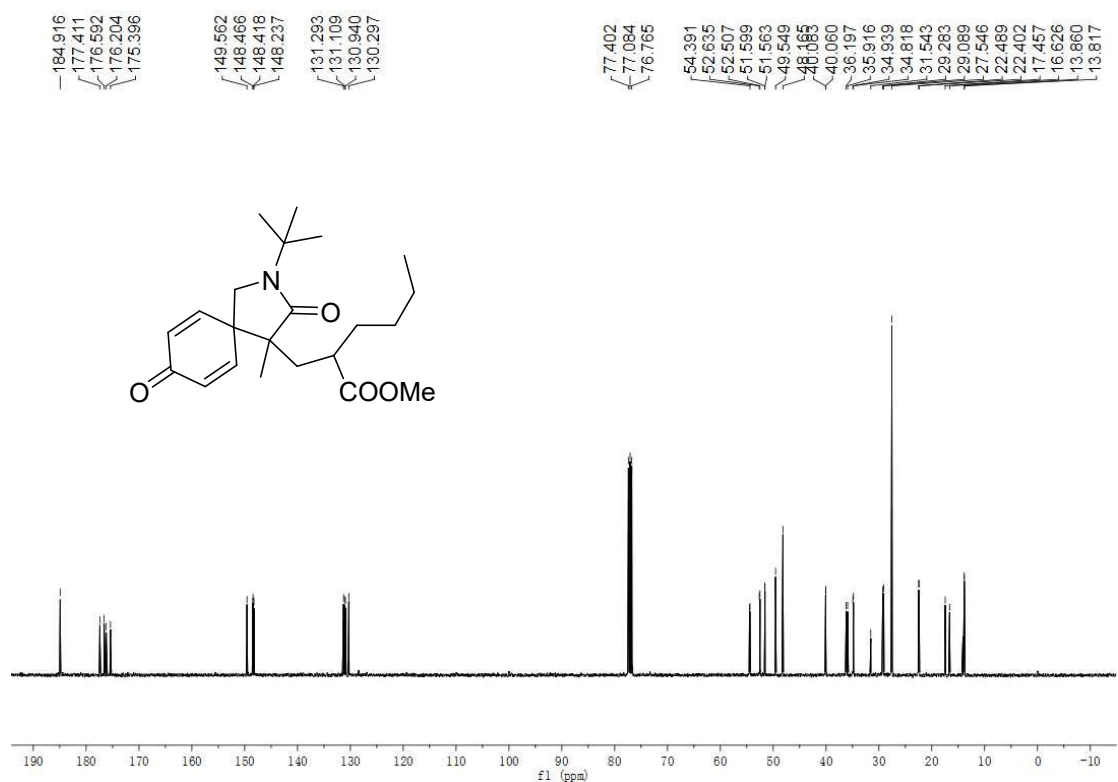
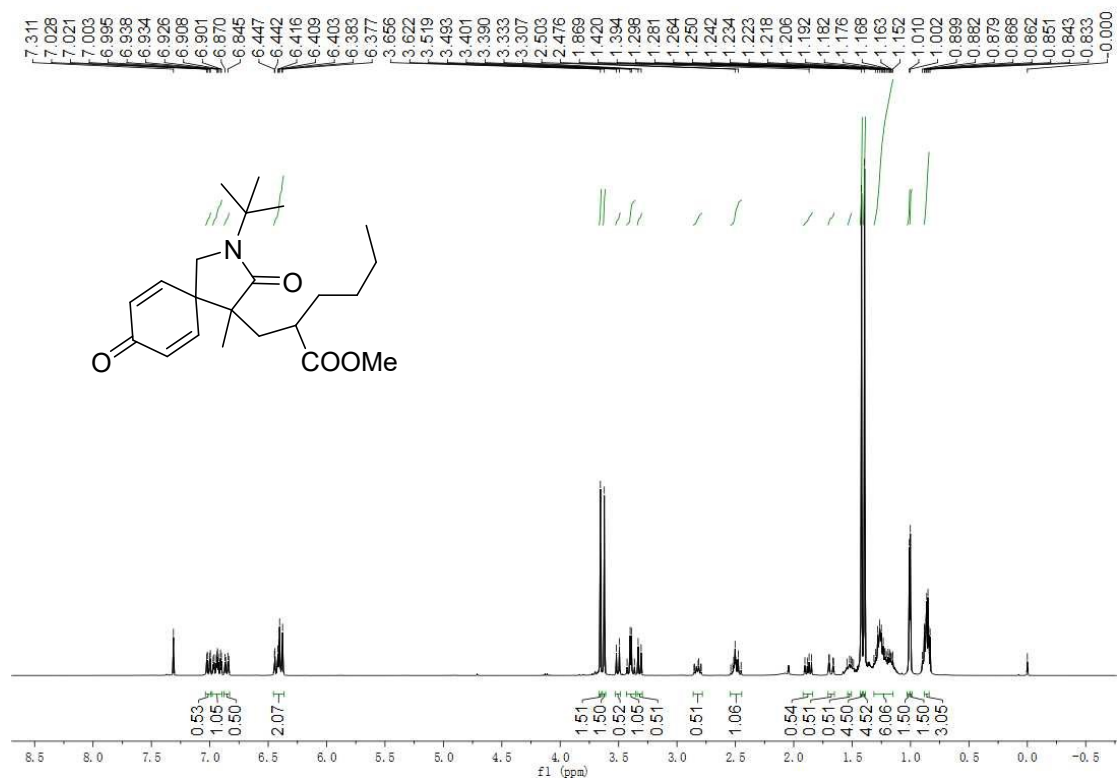
methyl 3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3aa):



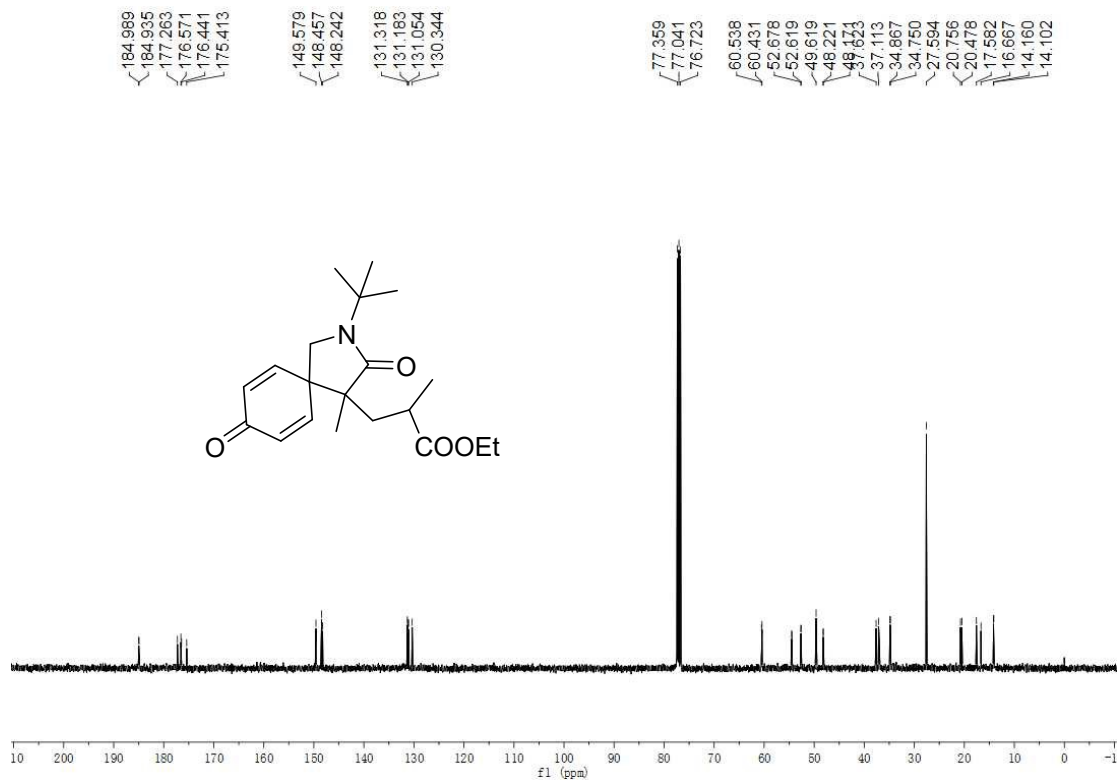
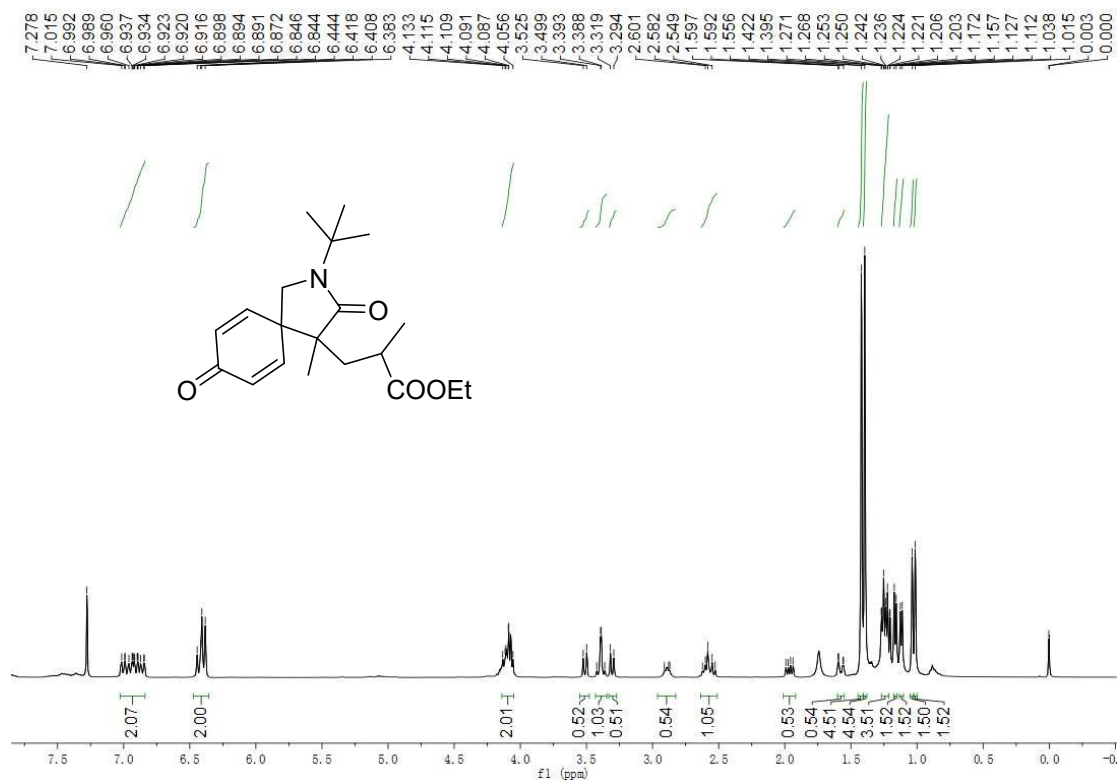
ethyl-2-((2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)butanoate (3db) :



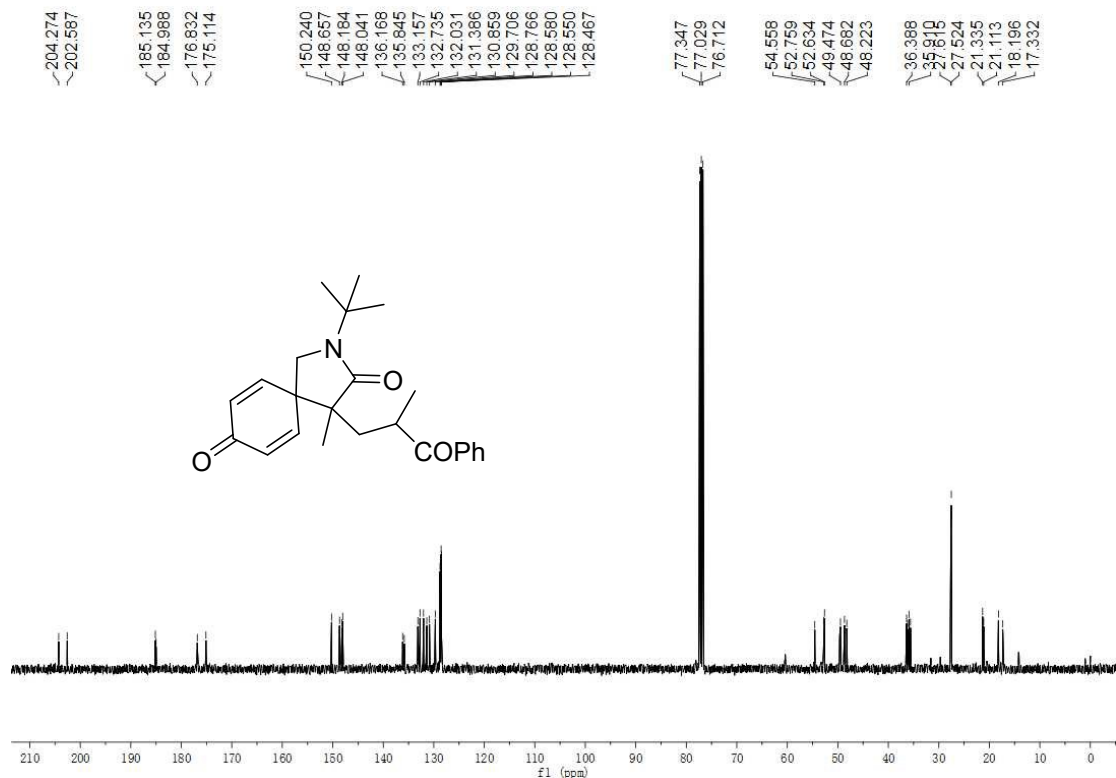
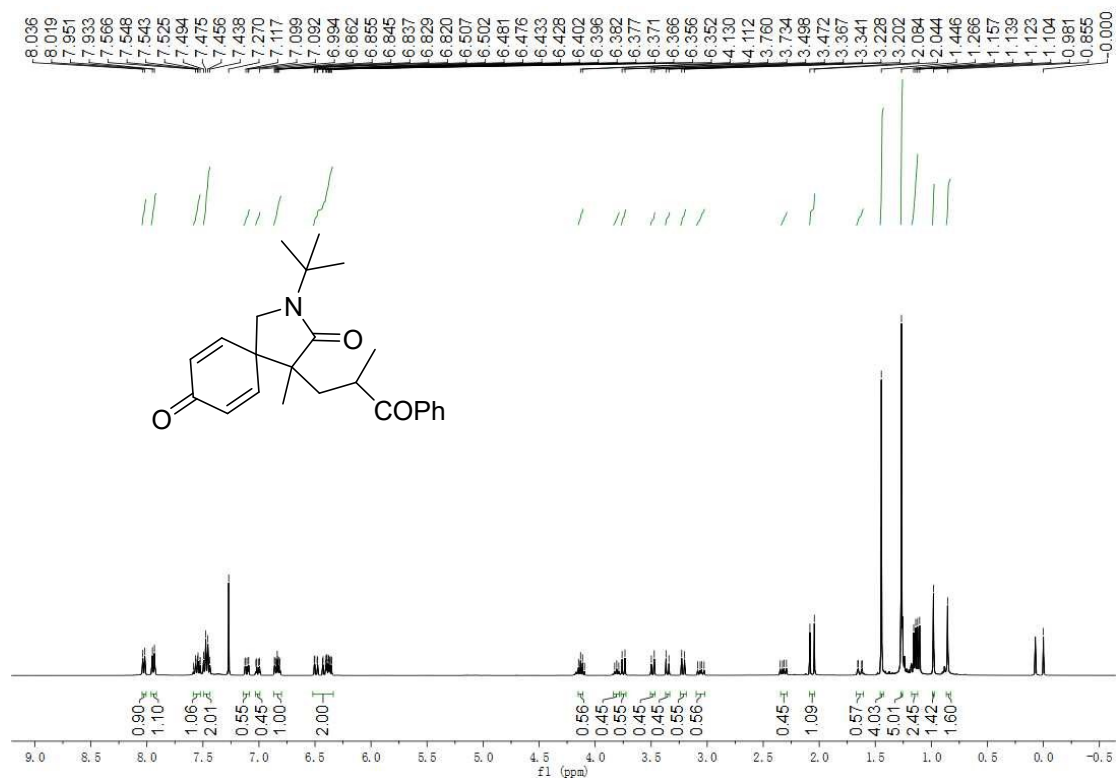
methyl 2-((2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)methyl)hexanoate (3dc):



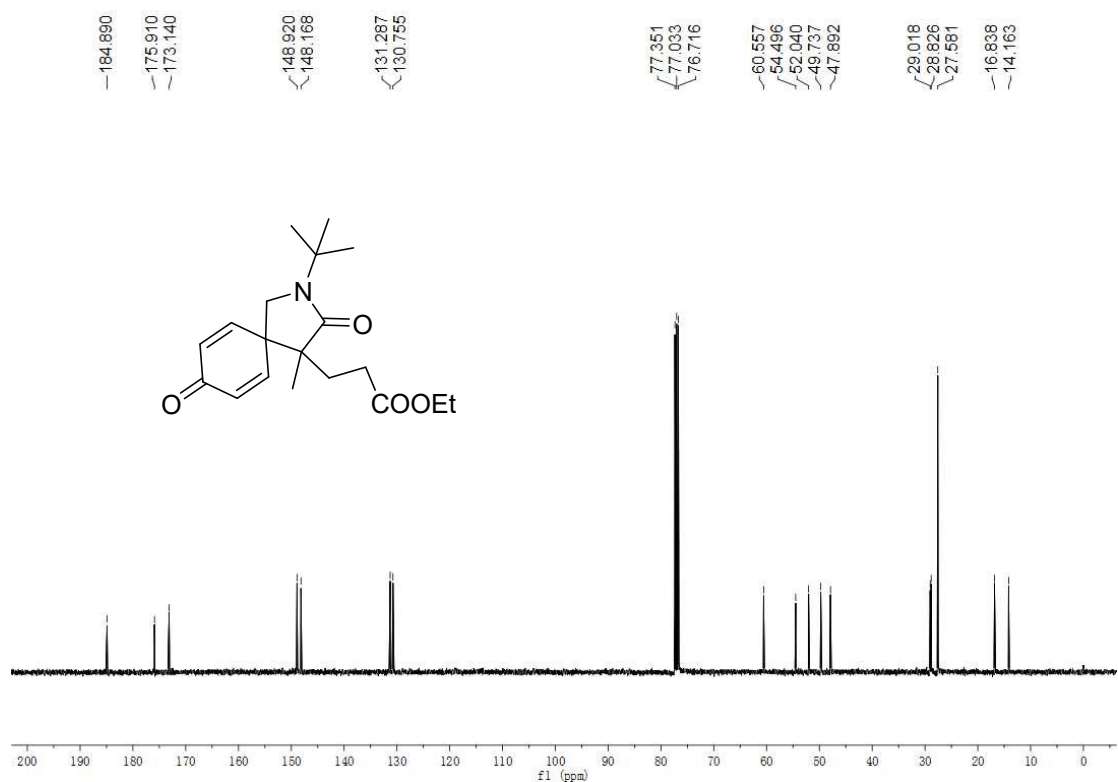
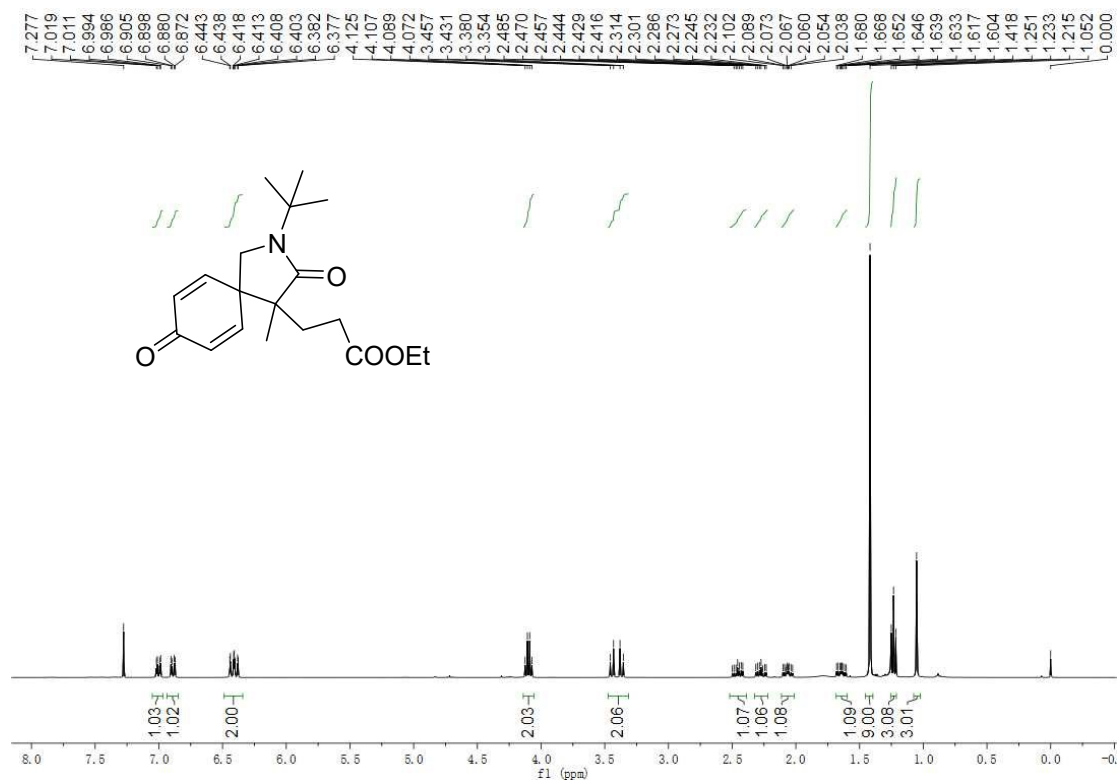
ethyl 3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3dd):



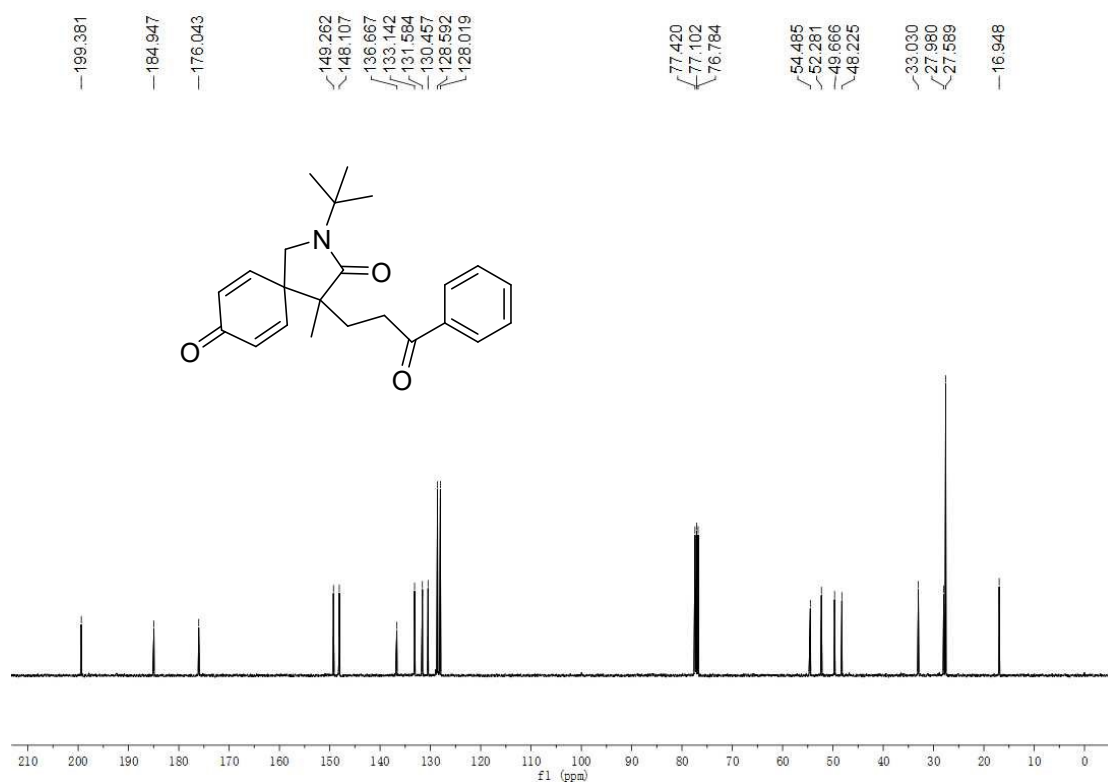
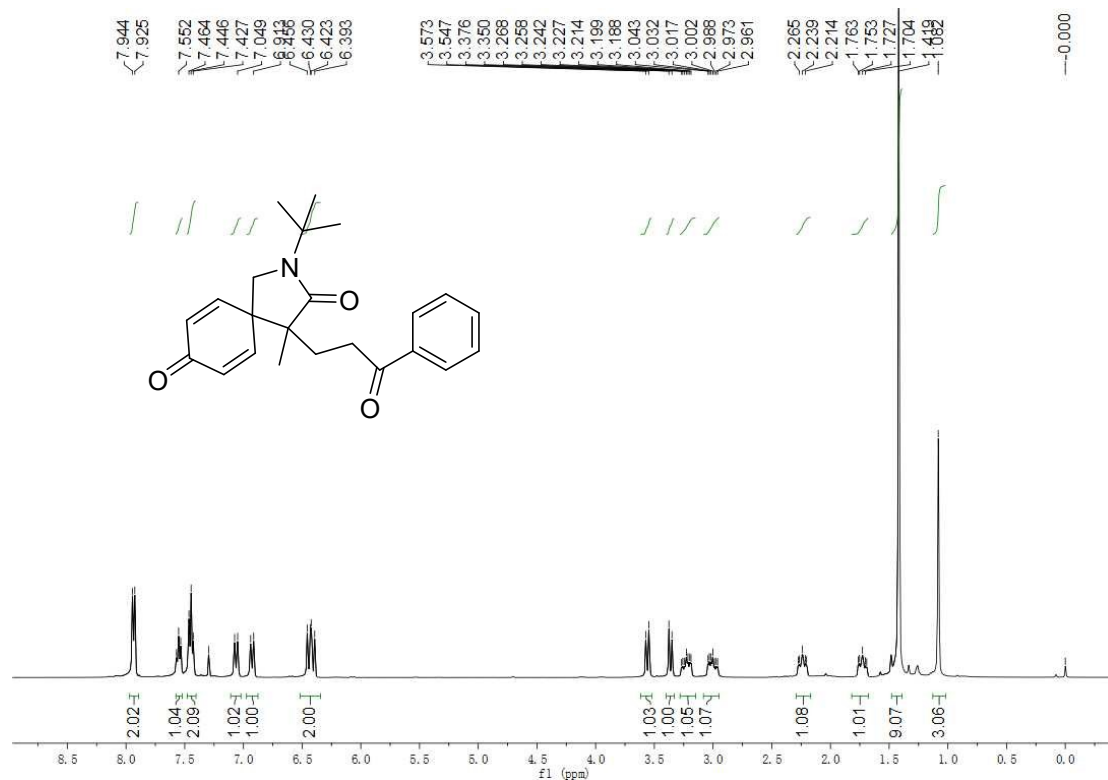
2-(tert-butyl)-4-methyl-4-(2-methyl-3-oxo-3-phenylpropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3de):



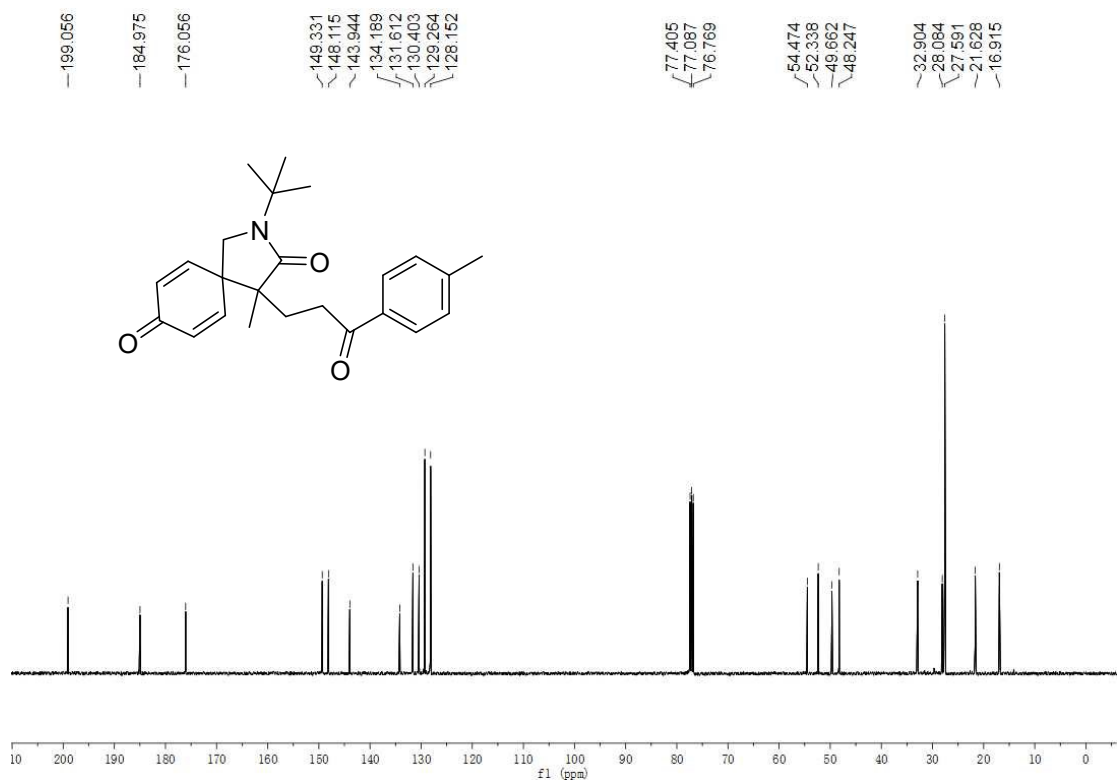
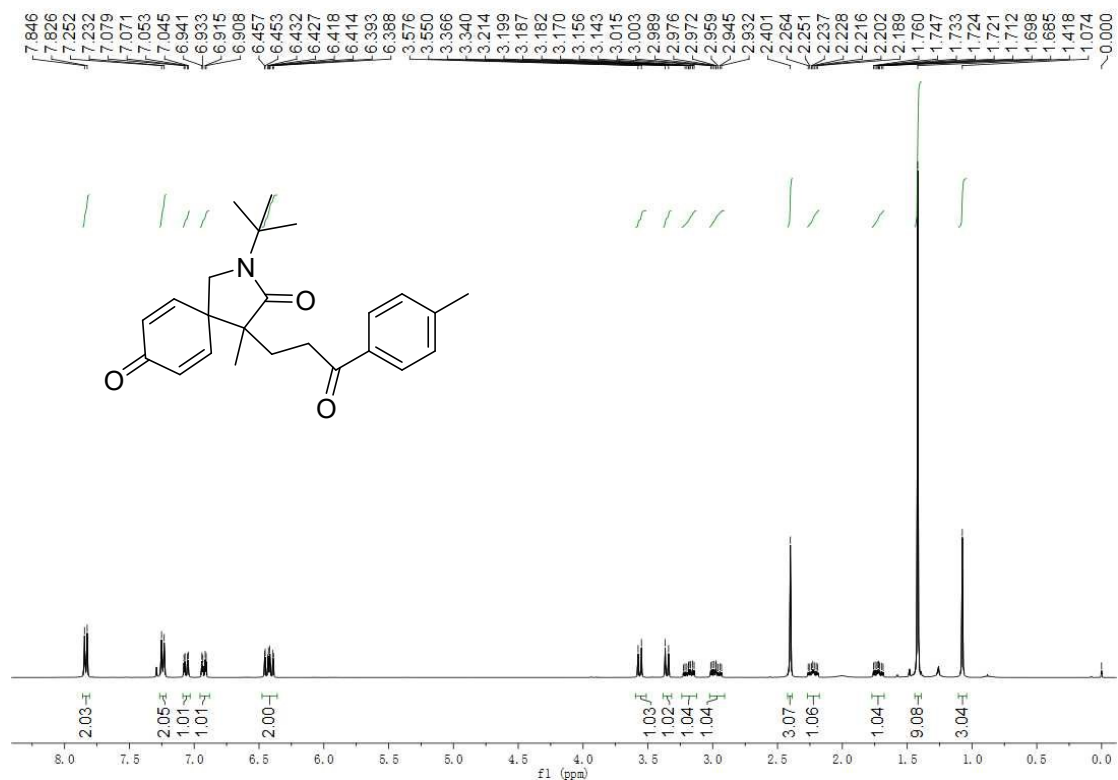
ethyl 3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)prop
anoate (3df):



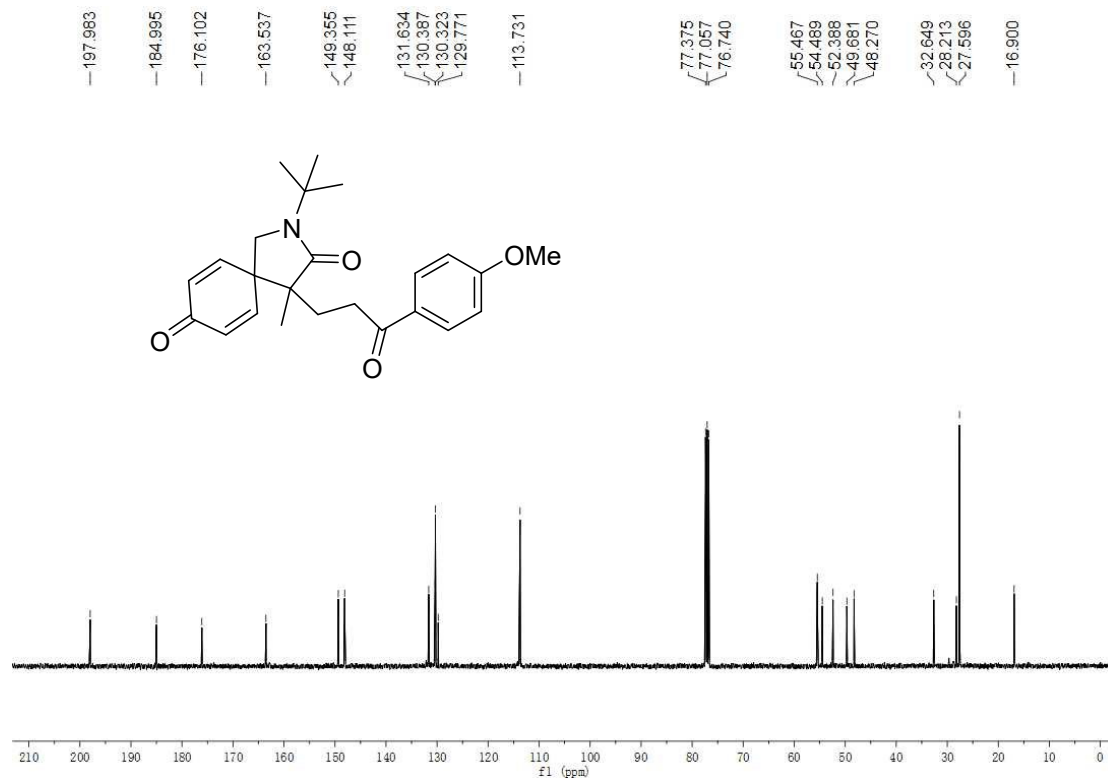
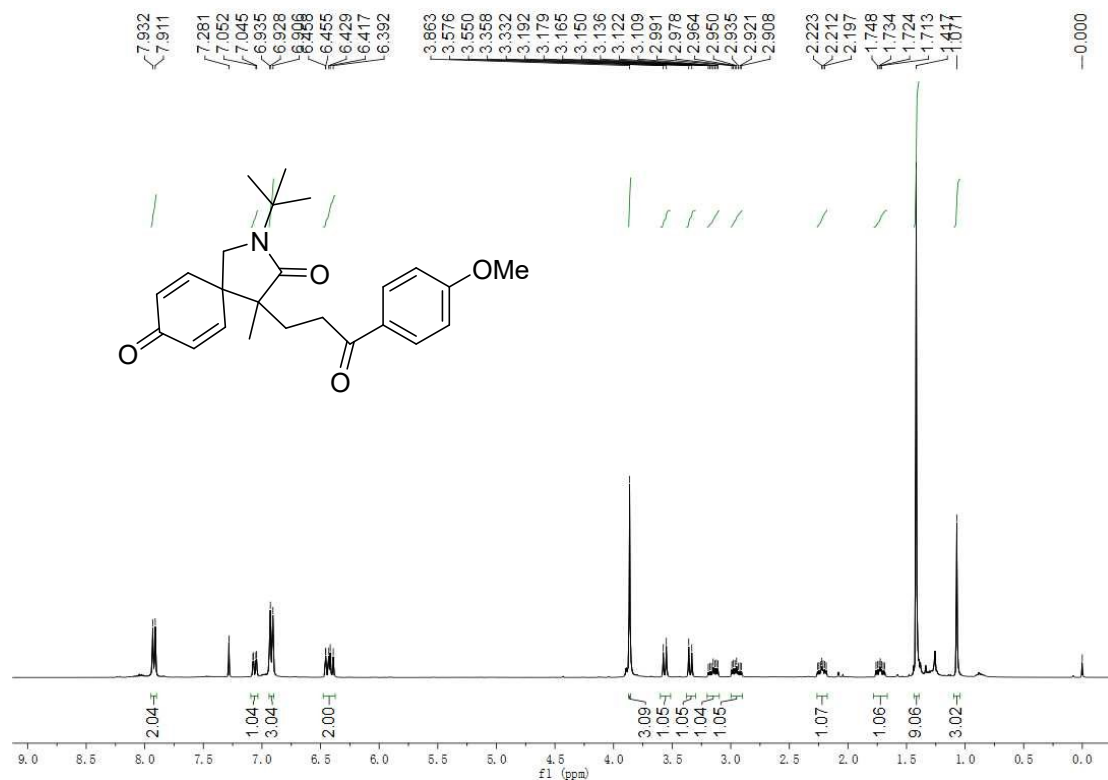
2-(tert-butyl)-4-methyl-4-(3-oxo-3-phenylpropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dg):



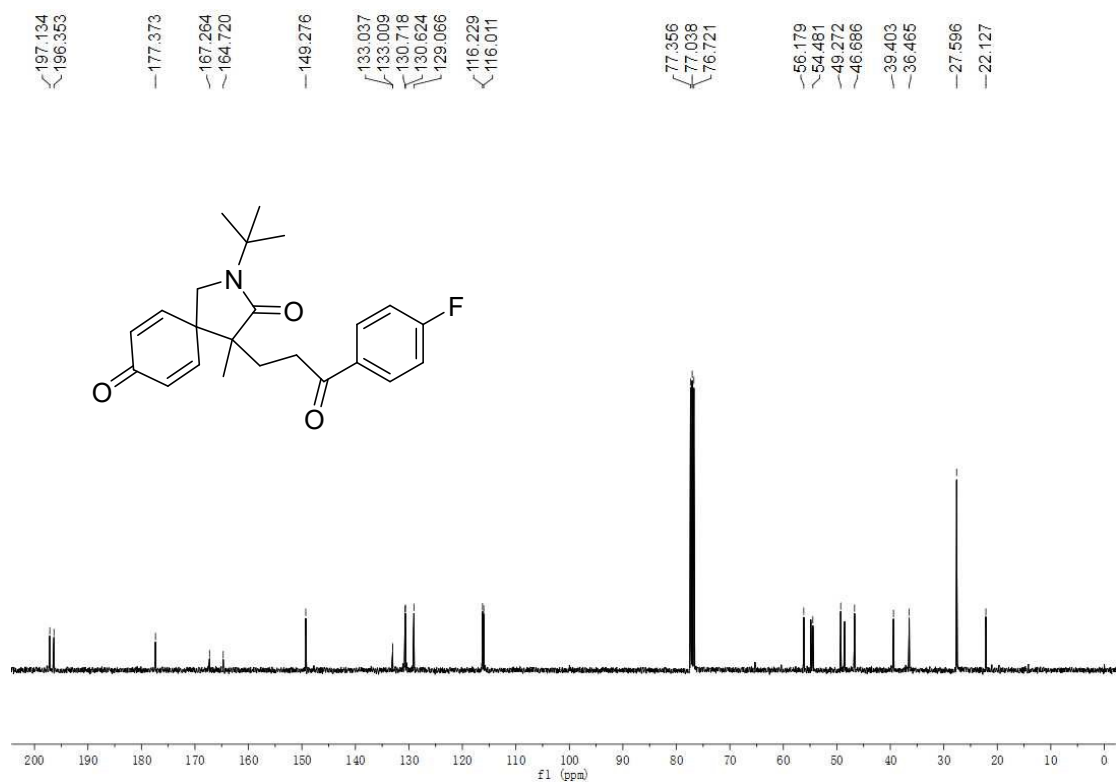
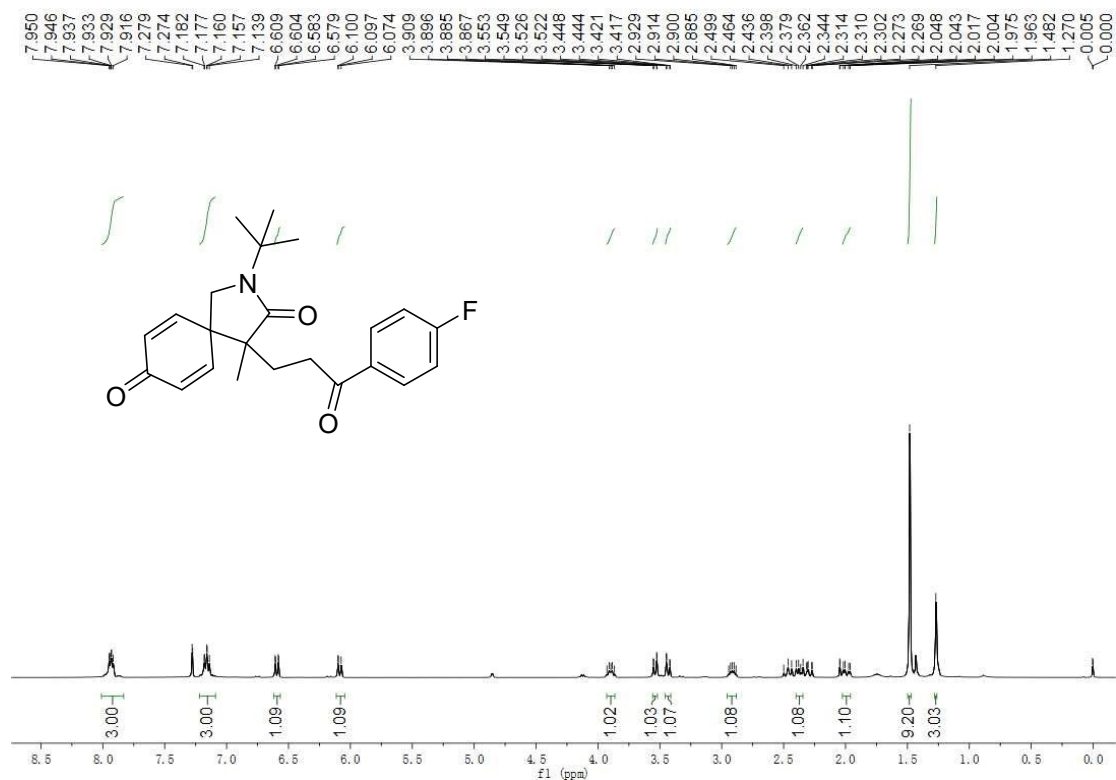
2-(tert-butyl)-4-methyl-4-(3-oxo-3-(p-tolyl)propyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dh):



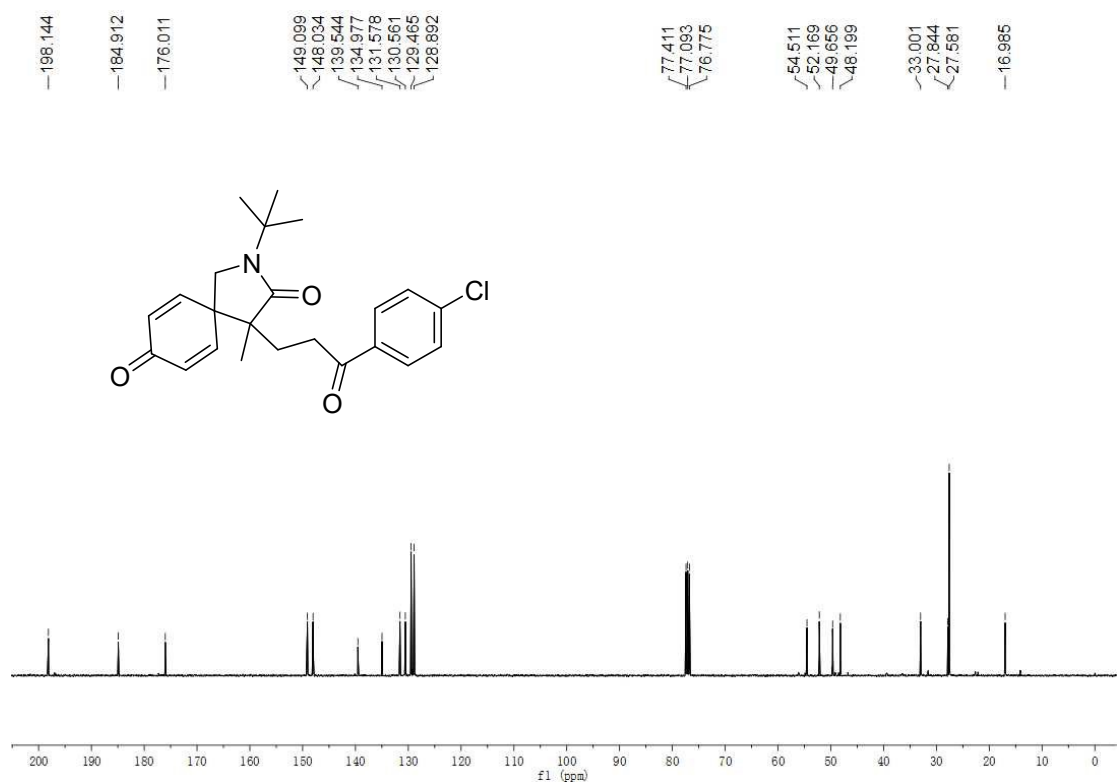
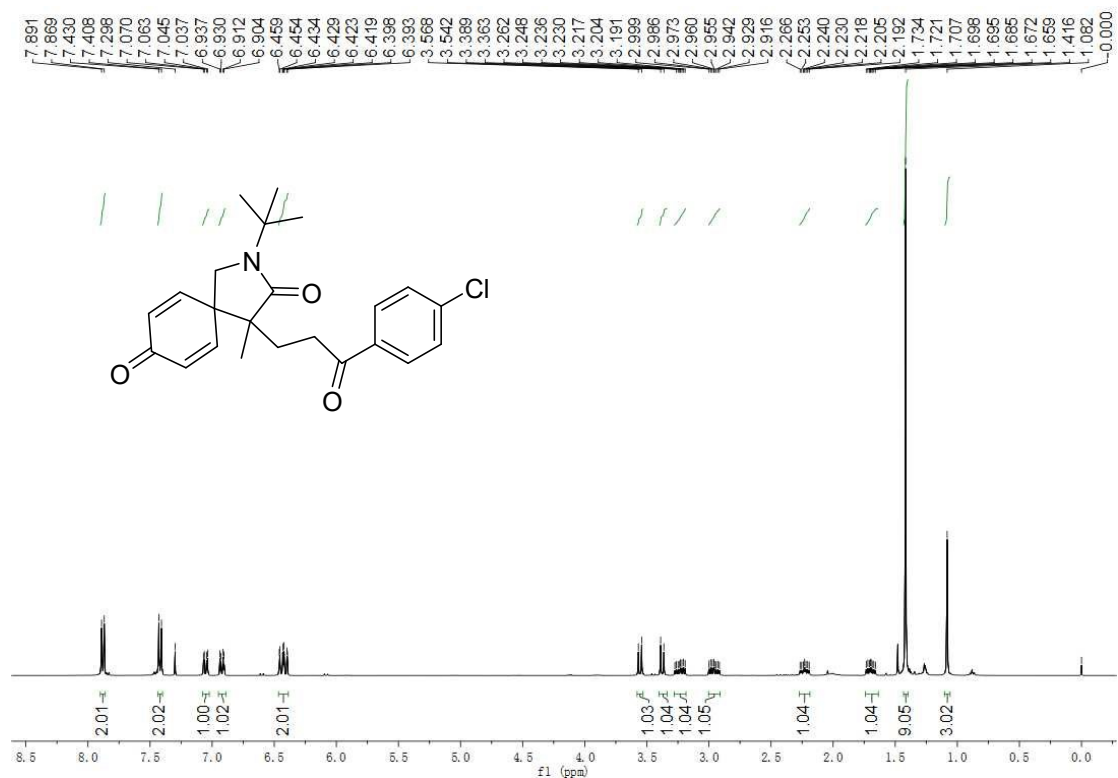
2-(tert-butyl)-4-(3-(4-methoxyphenyl)-3-oxopropyl)-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3di):



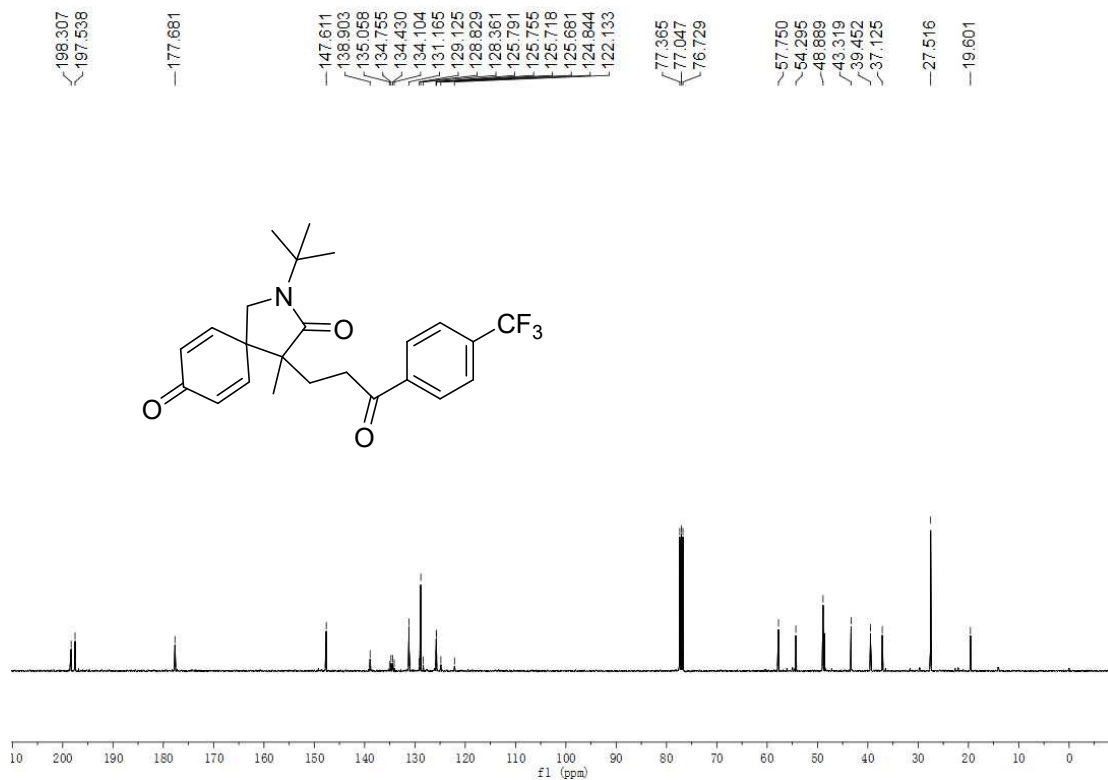
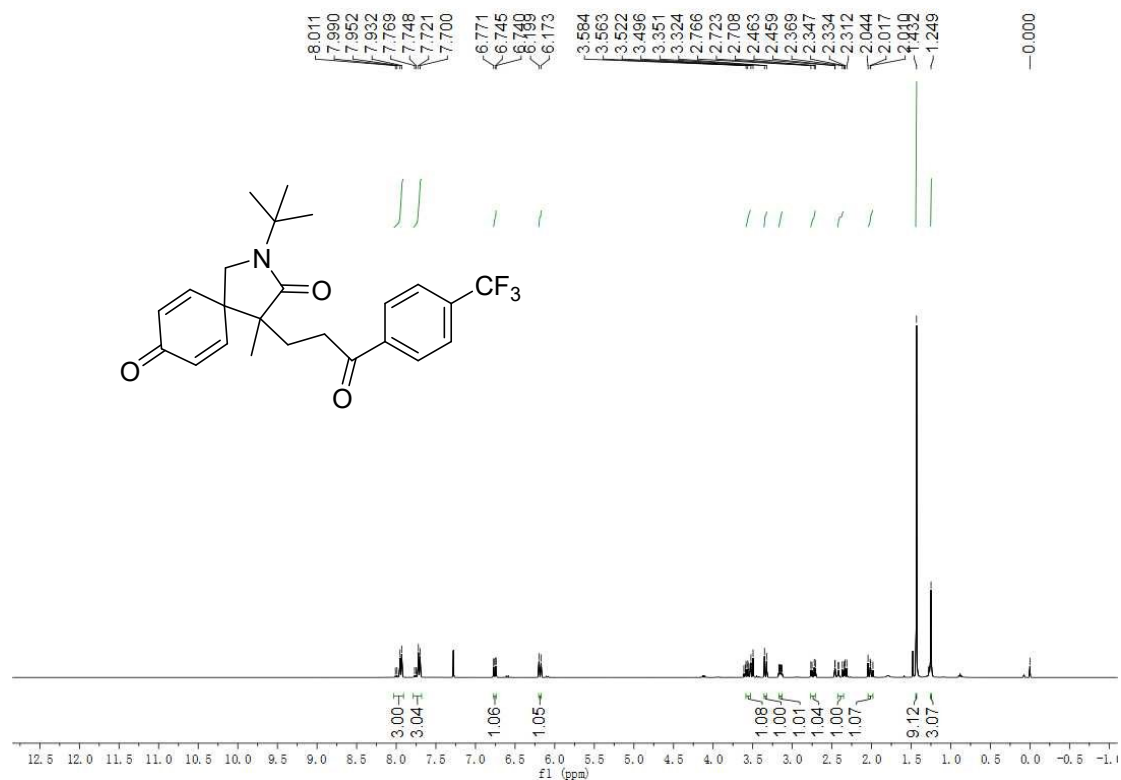
2-(tert-butyl)-4-(3-(4-fluorophenyl)-3-oxopropyl)-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dj):



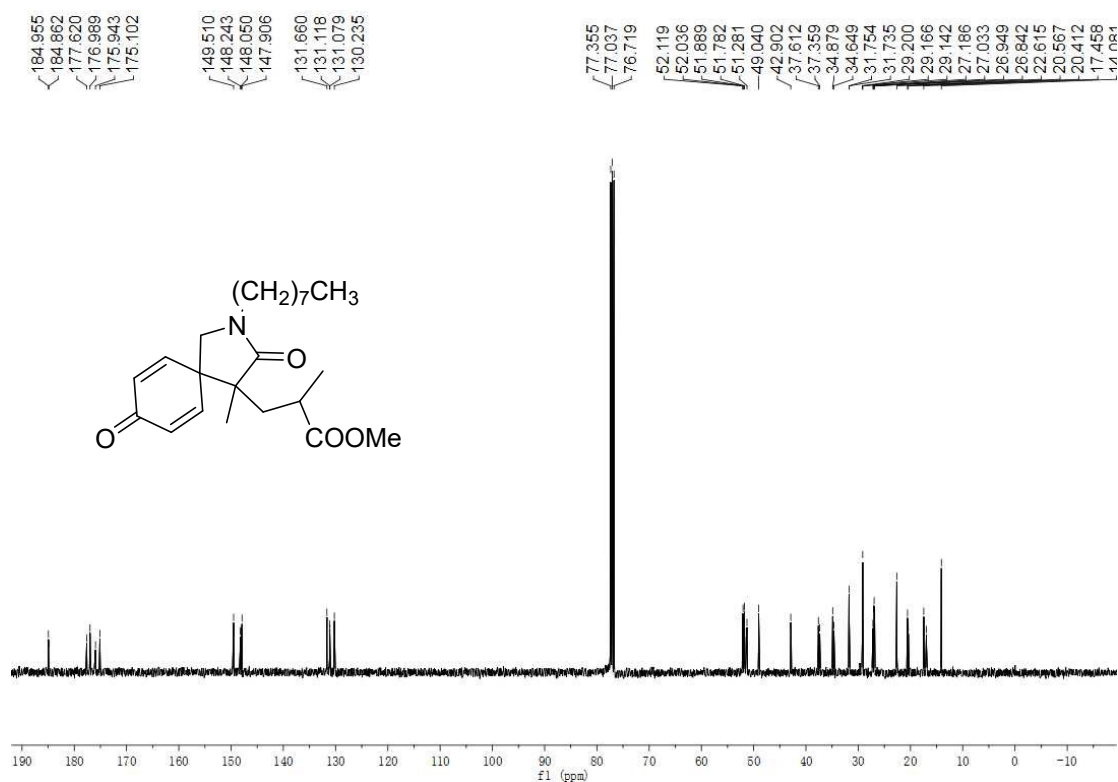
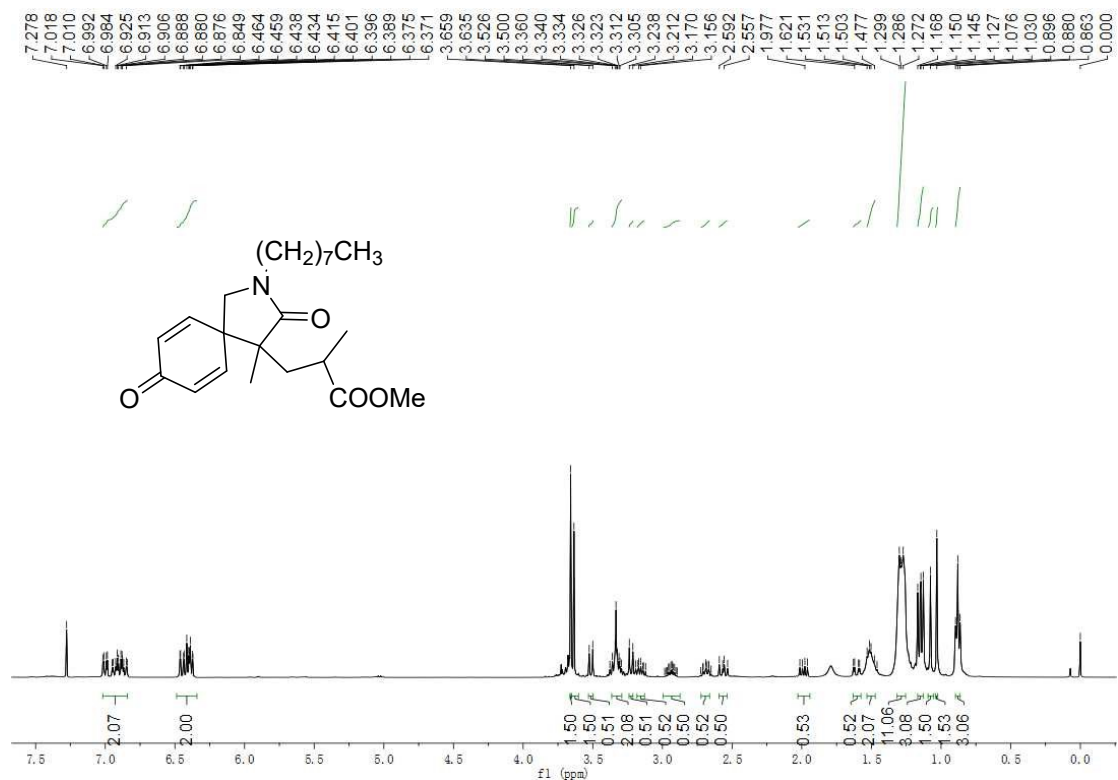
2-(tert-butyl)-4-(3-(4-chlorophenyl)-3-oxopropyl)-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dk):



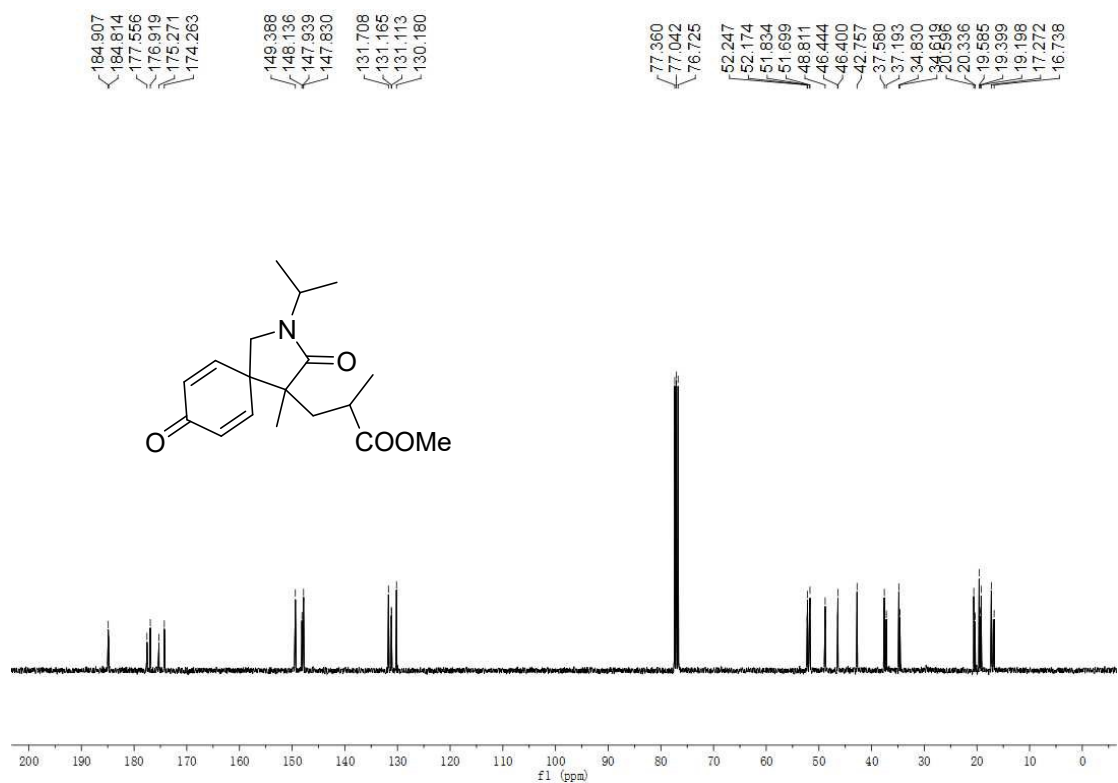
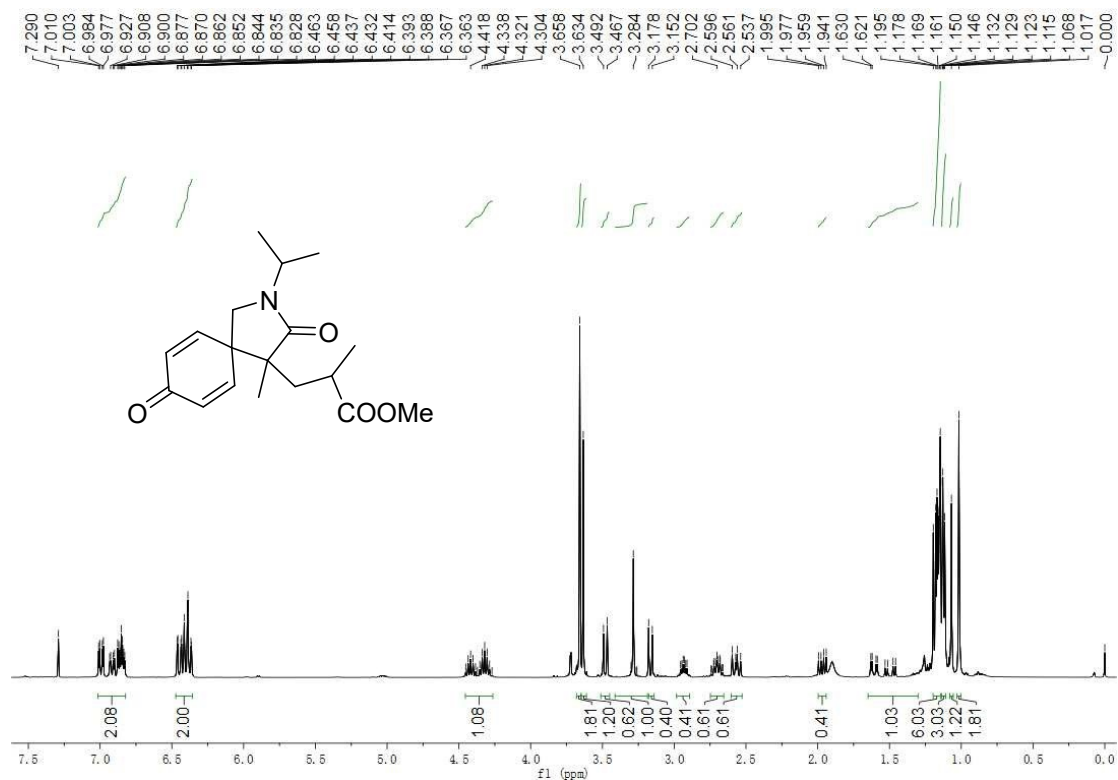
2-(tert-butyl)-4-methyl-4-(3-oxo-3-(4-(trifluoromethyl)phenyl)propyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3dl):



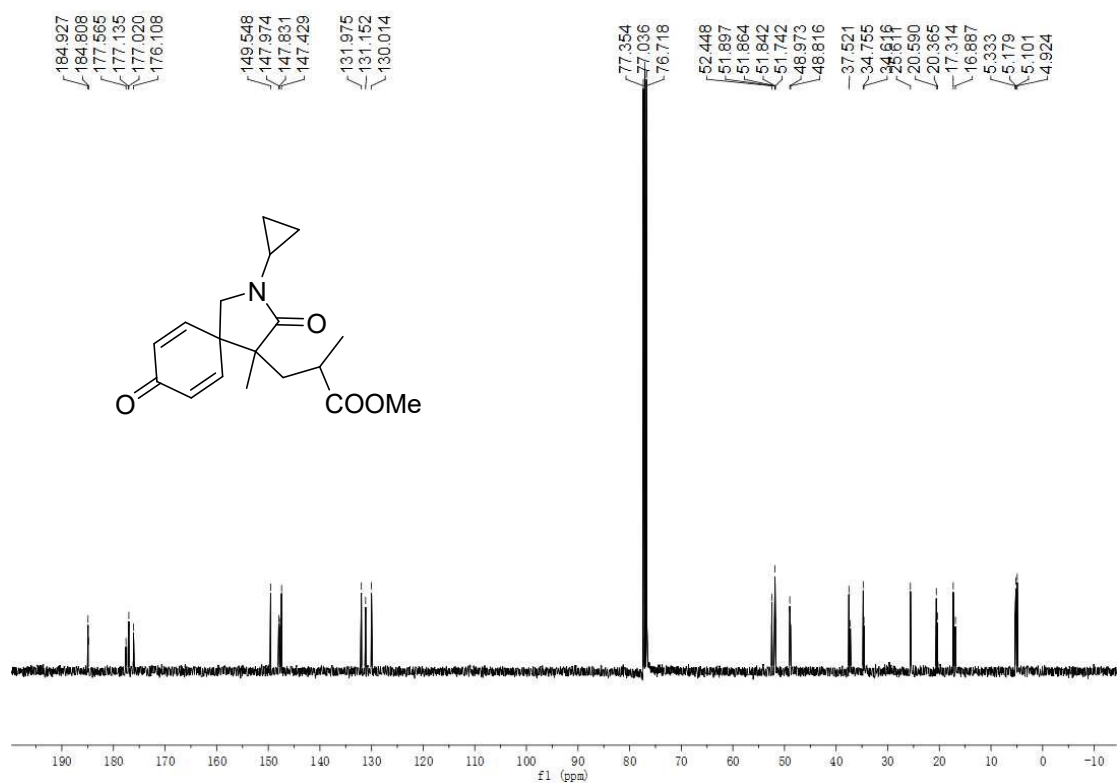
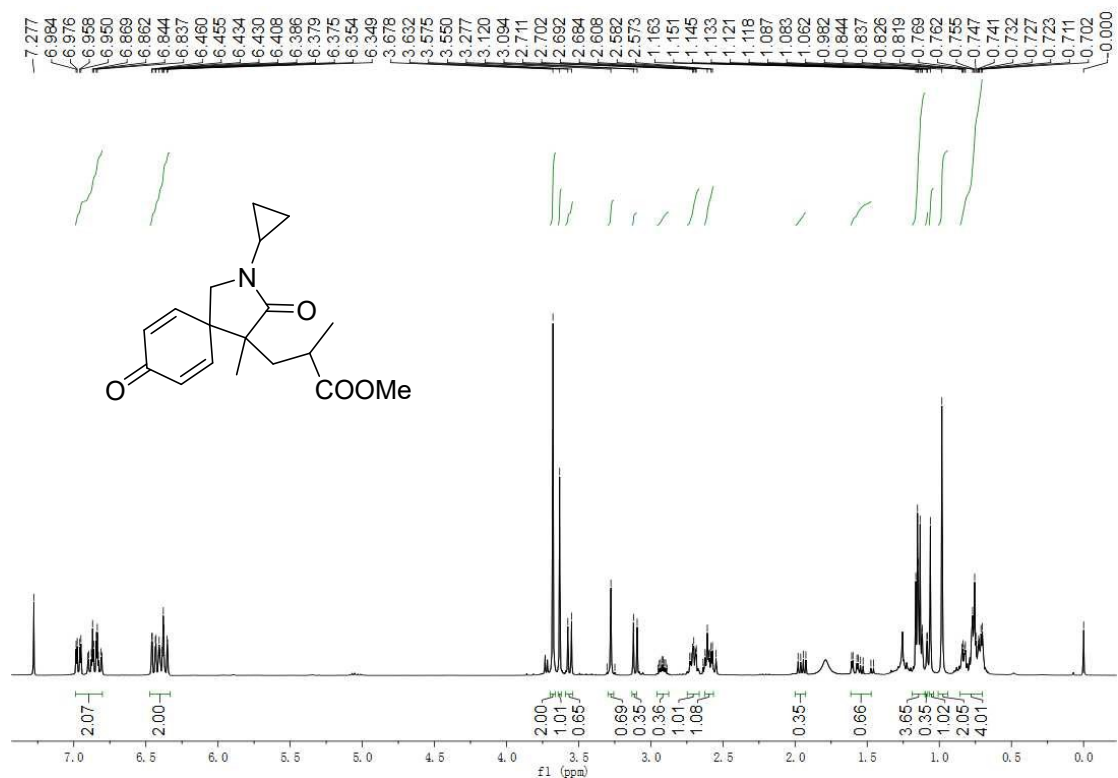
Methyl 2-methyl-3-(4-methyl-2-octyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoate (3ja):



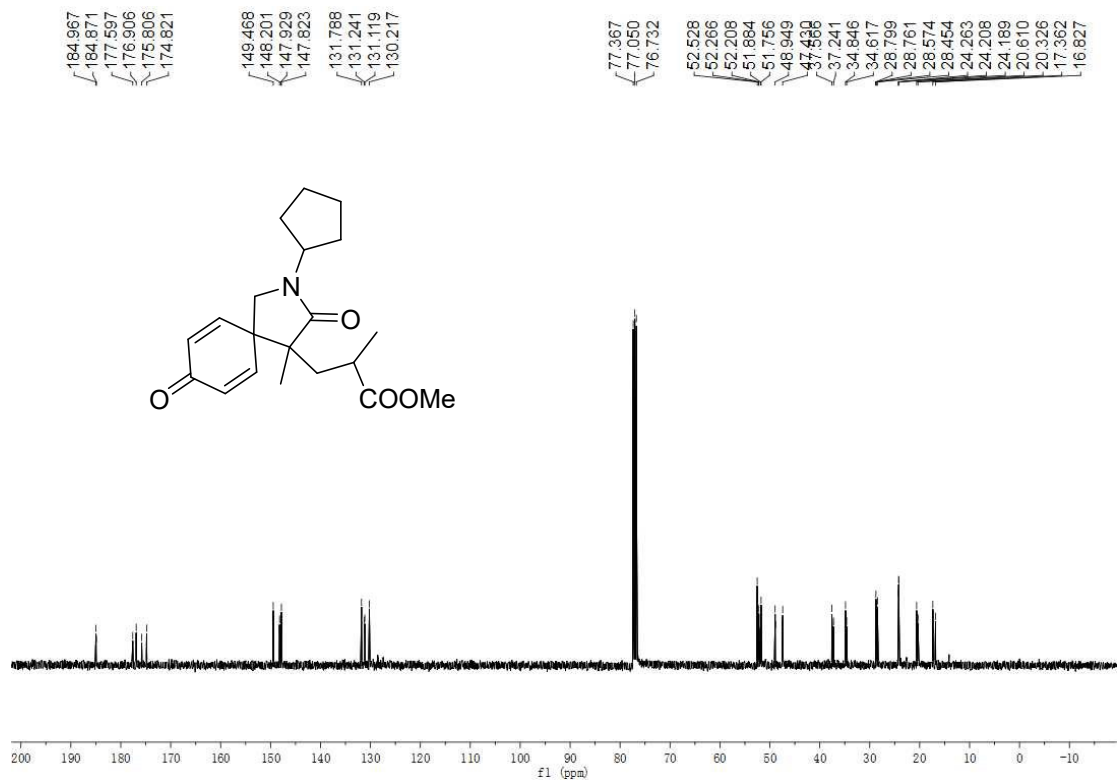
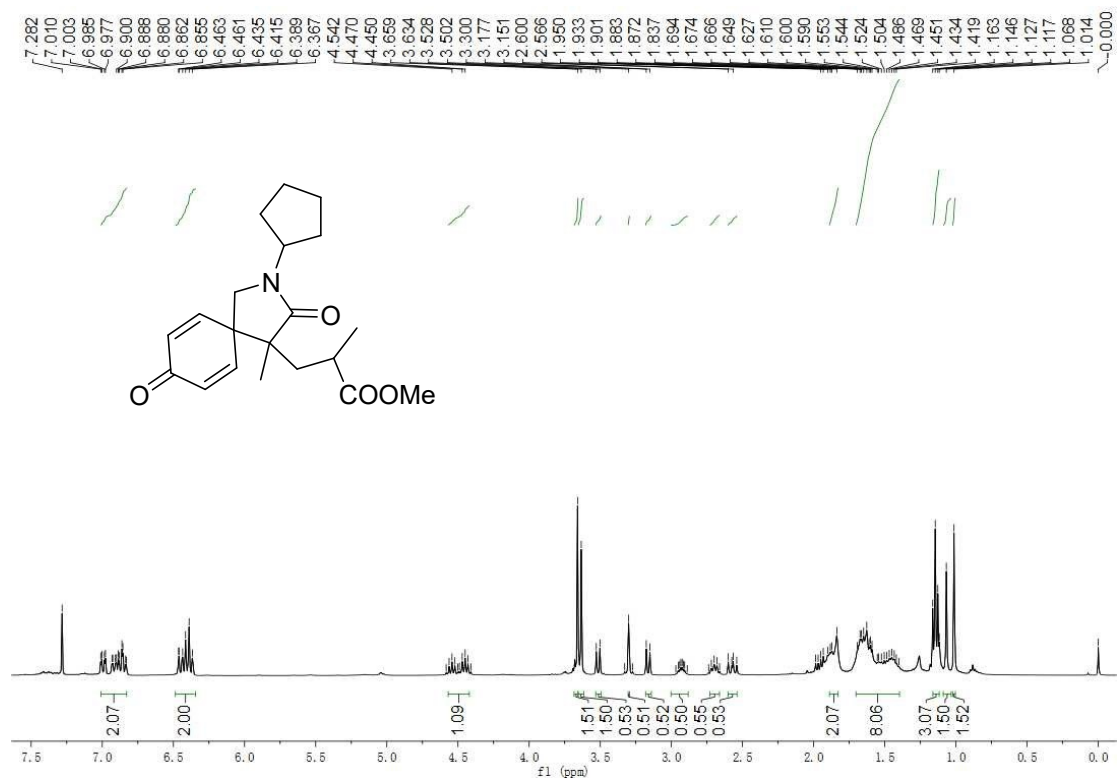
methyl 3-(2-isopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3ka):



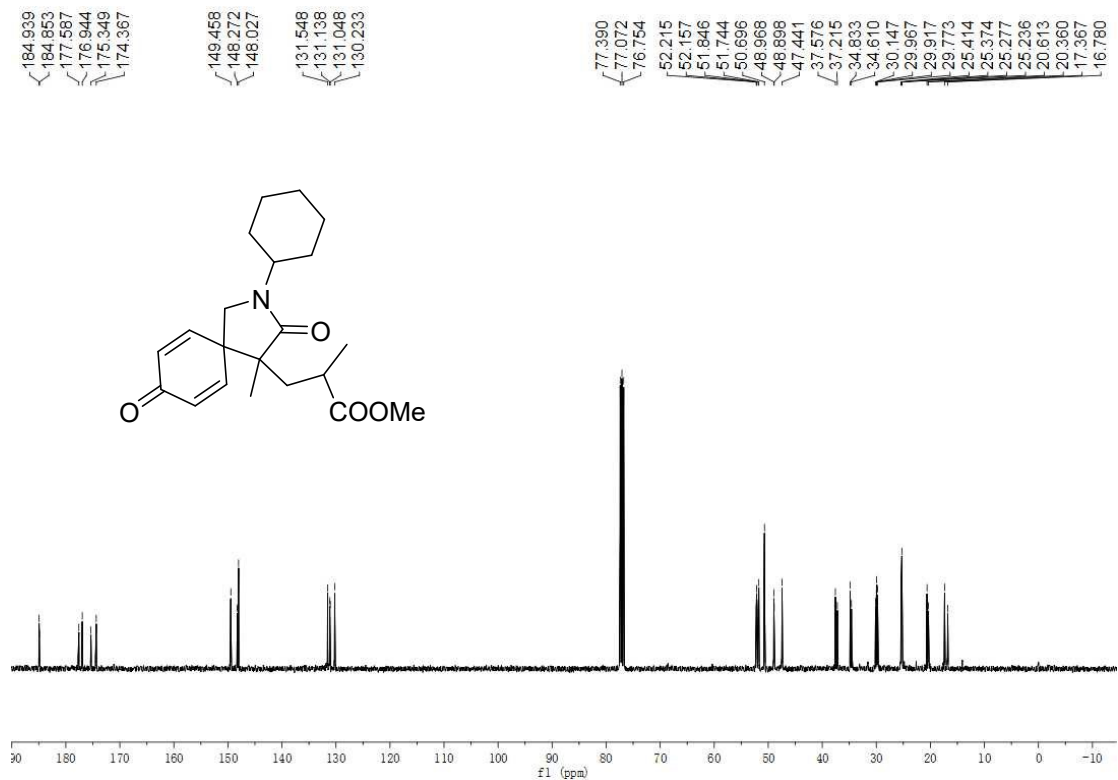
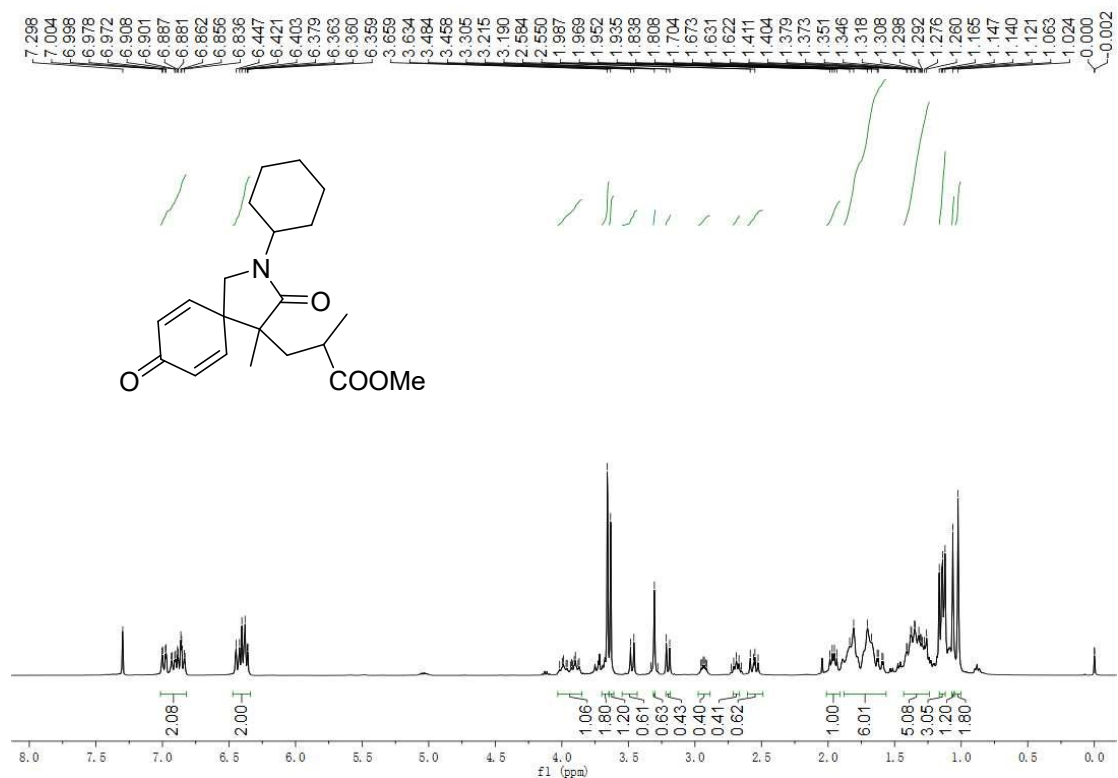
Methyl 3-(2-cyclopropyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3la):



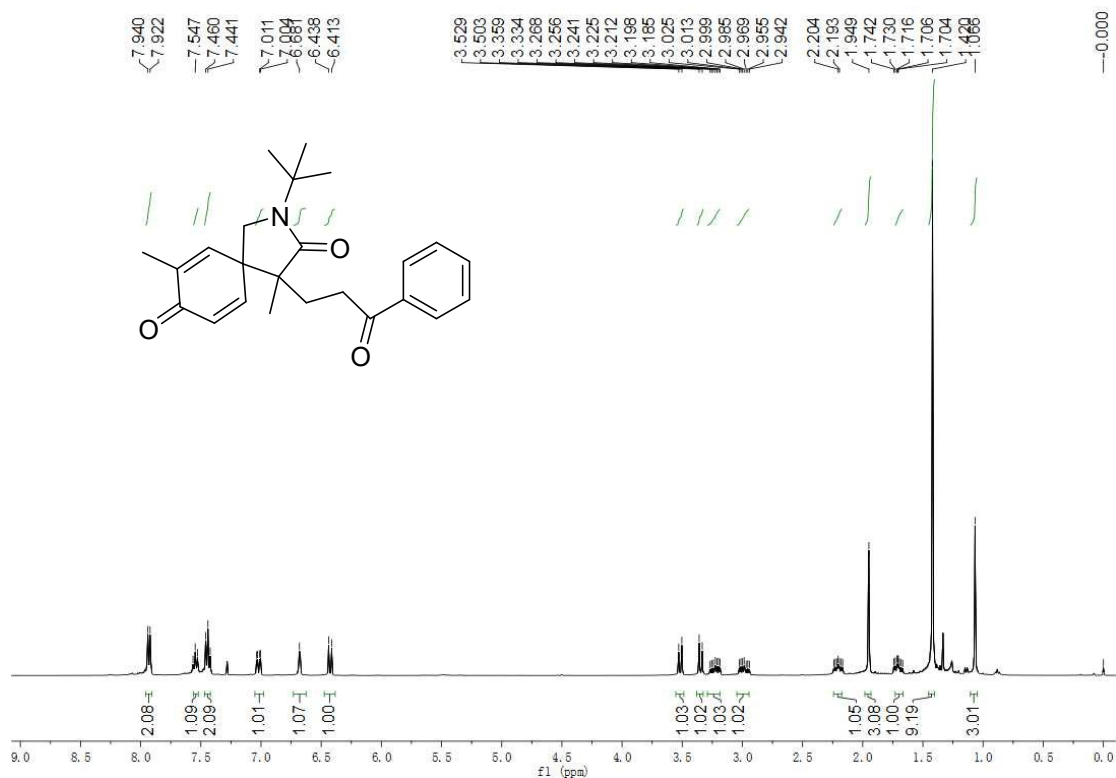
methyl 3-(2-cyclopentyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3ma):



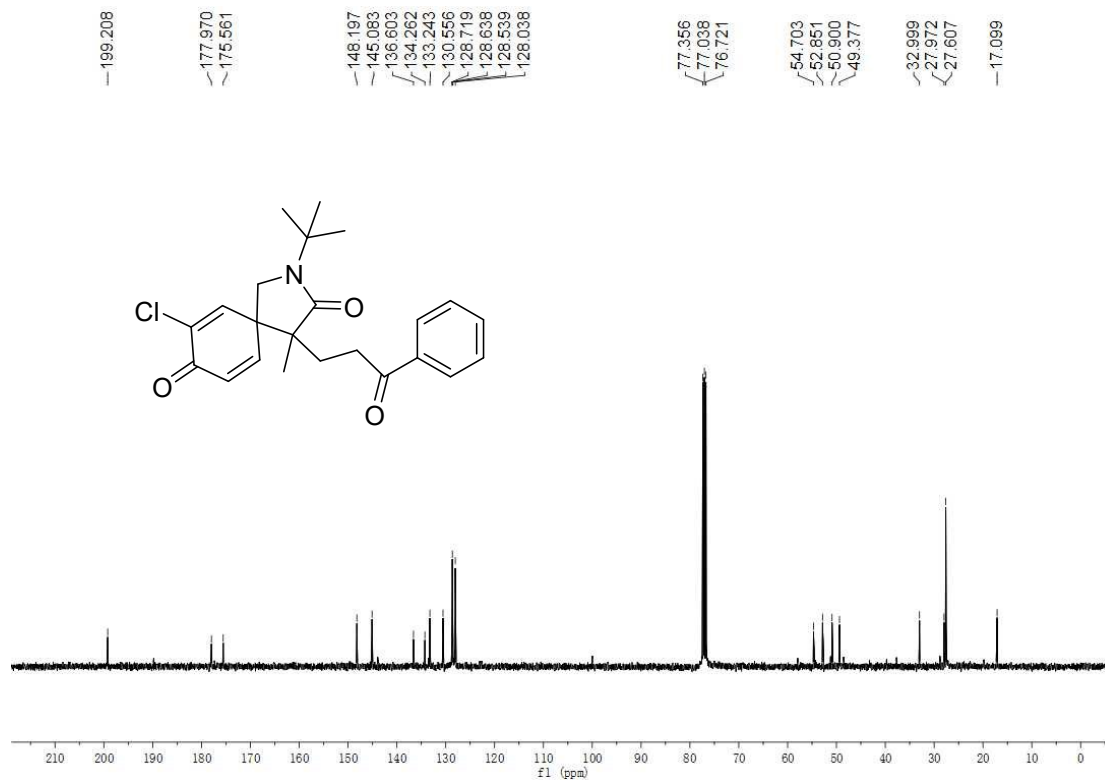
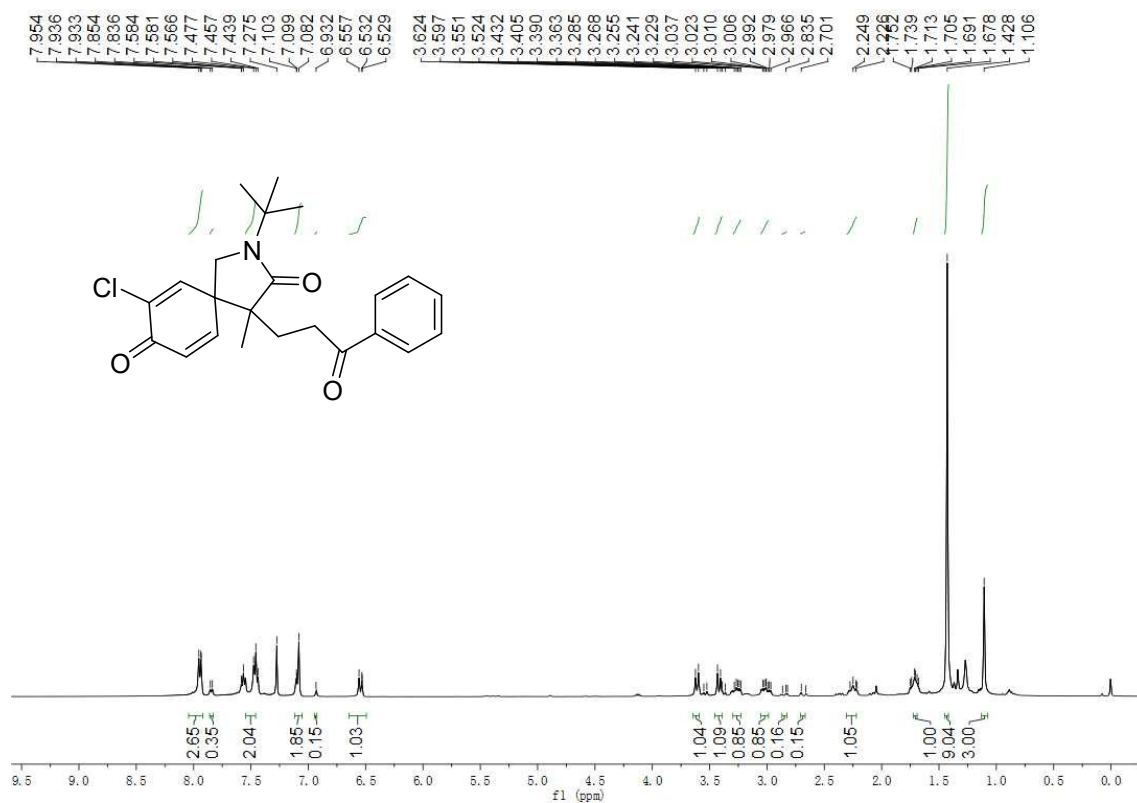
methyl 3-(2-cyclohexyl-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3na):



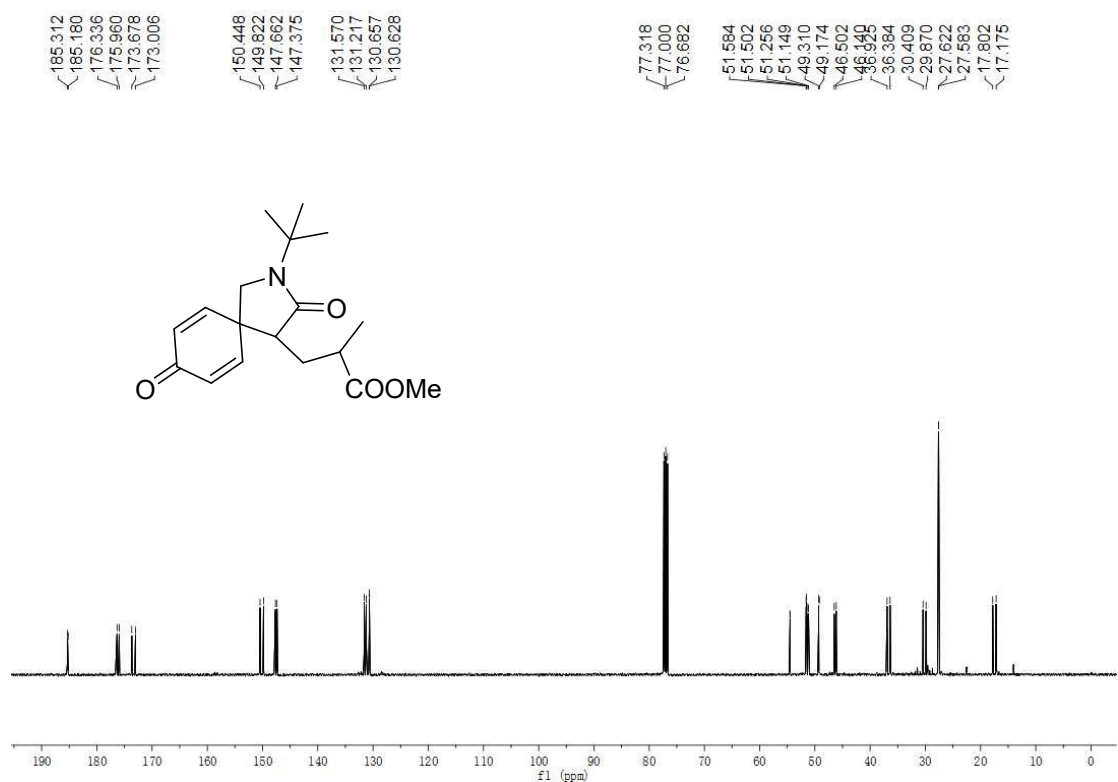
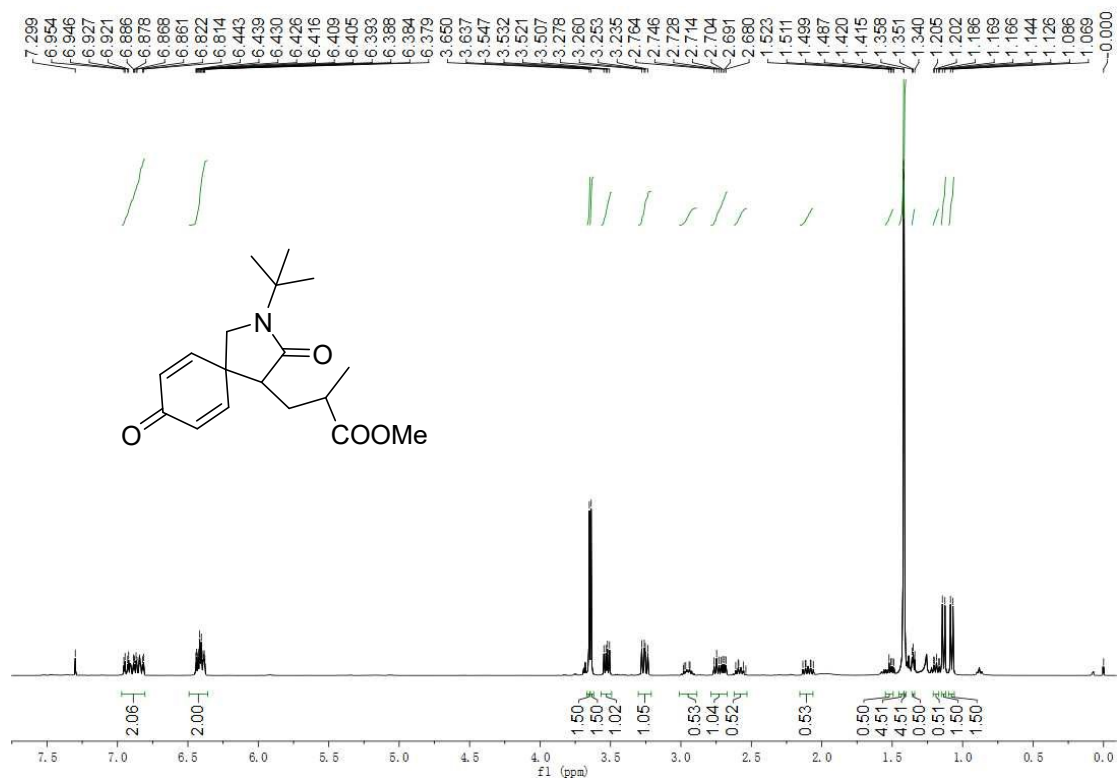
2-(tert-butyl)-4,7-dimethyl-4-(3-oxo-3-phenylpropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3og):



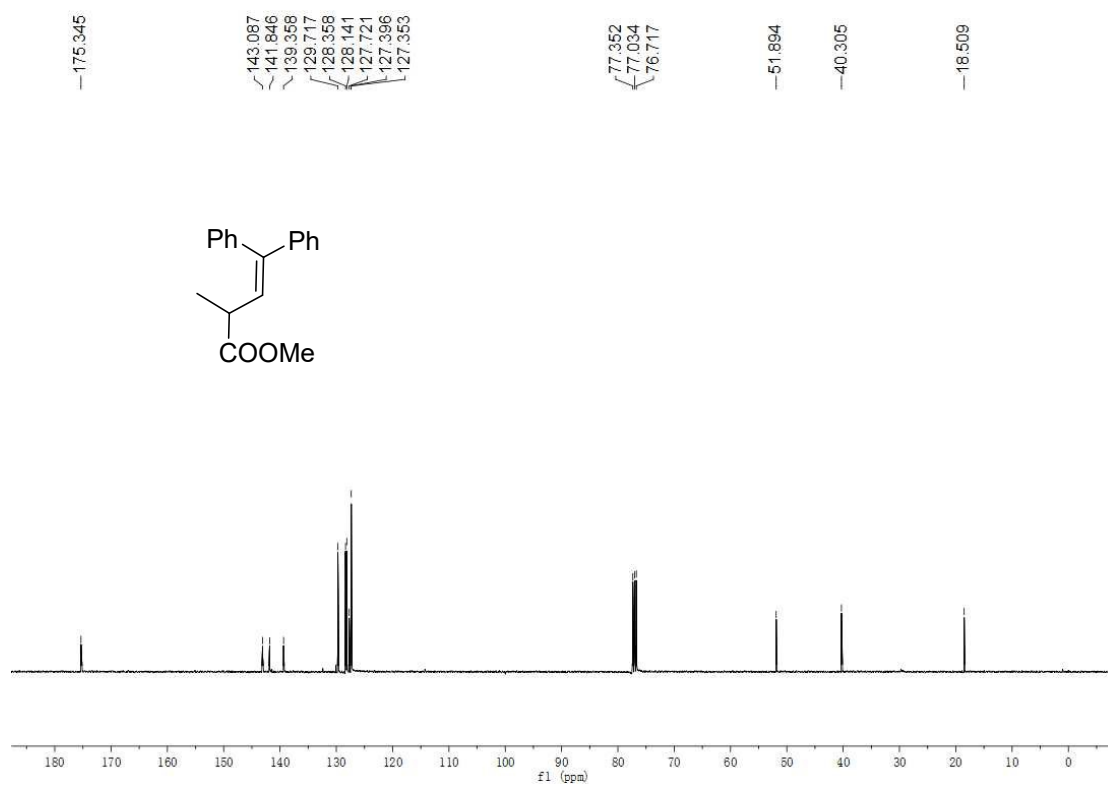
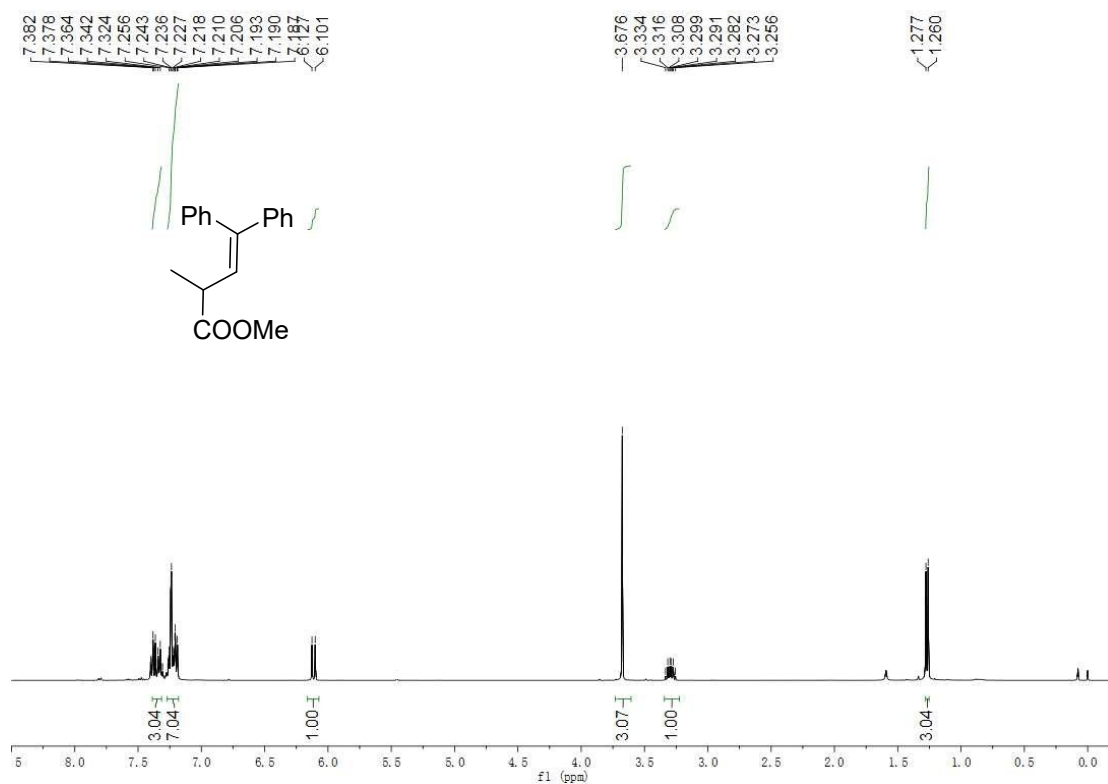
2-(tert-butyl)-7-chloro-4-methyl-4-(3-oxo-3-phenylpropyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (3pg) :



methyl 3-(2-(tert-butyl)-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)-2-methylpropanoate (3ra):



methyl 2-methyl-4,4-diphenylbut-3-enoate (5aa):



3-(2-(tert-butyl)-4-methyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-4-yl)propanoic acid (6aa):

