Supporting Information for

Diversity-Oriented Synthesis of Spiro-Oxindole-based 2,5-Dihydropyrroles via Three-Component Cycloadditions and Evaluation on Their Cytotoxicity

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General

NMR spectra were measured respectively at 400 and 100 MHz on a Brucker-400 MHz spectrometer. The solvent used for NMR spectroscopy was $CDCl_3$, using tetramethylsilane as the internal reference. HRMS (Bio TOF Q) spectra were recorded with an ESI resource on P-SIMS-Gly of Bruker Daltonics Inc. Infrared spectra were recorded on a Nicolet MX-1E FT-IR spectromter.

Analytical grade solvents for the column chromatography and commercially available reagents were used as received. All starting materials commercially available were used directly. Substrates **1a, 1c-1r** and **1y** were synthesized according to the literature methods.[1]

General procedure for the synthesis of spiro-oxindole-based 2,5-dihydropyrroles 4

The solution of isatins **1** (0.12 mmol), 2-aminomalonate **2a** (0.1 mmol), trifluoroacetic acid (0.02 mmol), and 3Å molecular sieves (100 mg) in 1,2-dichloroethane (0.5 mL) was stirred at rt for 20 min. Then, this resultant mixture was added with but-2-ynedioate **3** (1.2 mmol) and another 0.5 mL of 1,2-dichloroethane. The reaction mixture was stirred at 60 ^{o}C for 36 hrs. Then the reaction mixture was filtered to remove molecular sieves, and the solid powder was washed with ethyl acetate. The resultant solution was evaporated under the reduced pressure, and the residue was purified through flash column chromatography on silica gel to yield pure products **4**.

5',5'-Diethyl 3',4'-dimethyl 2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4baa): (Flash column chromatography eluent, petroleum ether/ acetone = 3/1); Reaction time = 36 h; Yield: 99%; Yellow solid; m.p. 145-147 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.43 (s, 1H), 7.39 (d, J = 7.4 Hz, 1H), 7.26 – 7.20 (m, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 4.34 (dd, J = 14.1, 7.0 Hz, 4H), 3.84 (s, 3H), 3.75 (s, 1H), 3.55 (s, 3H), 1.34 (dt, J = 14.4, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 176.5, 168.6, 168.0, 162.6, 161.3, 141.2, 140.0, 139.7, 130.3, 128.9, 125.0, 123.2, 110.3, 80.0, 75.5, 63.1, 62.8, 52.5, 13.92, 13.89; IR (KBr): γ 3334, 2981, 2940, 1742,

1674, 1610, 1479, 1439, 1297, 1252, 1113, 1031, 871, 814, 709 cm^{-1}; ESI FTMS exact mass calcd for $(C_{21}H_{22}N_2O_9+H)^+$ requires m/z 447.1404, found m/z 447.1376.

5',5'-Diethyl 3',4'-dimethyl 1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4caa): (Flash column chromatography eluent, petroleum ether/ acetone = 6/1); Reaction time = 36 h; Yield: 90%; Light yellow solid; m.p. 132-134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.41 (dd, *J* = 7.4, 0.8 Hz, 1H), 7.31 (td, *J* = 7.8, 1.3 Hz, 1H), 7.06 (td, *J* = 7.6, 0.9 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 4.42 – 4.27 (m, 4H), 3.83 (s, 3H), 3.73 (s, 1H), 3.52 (s, 3H), 3.21 (s, 3H), 1.35 (t, *J* = 6.2 Hz, 3H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 174.3, 168.7, 168.0, 162.6, 161.1, 142.6, 140.2, 139.7, 129.9, 128.9, 125.0, 122.8, 109.7, 79.9, 75.1, 63.0, 53.0, 52.2, 27.3, 25.1, 13.9, 13.8; IR (KBr): γ 3444, 3349, 2984, 2939, 2859, 1742, 1660, 1607, 1469, 1429, 1297, 1239, 1183, 1031, 871, 804, 749, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{24}N_2O_9+Na)^+$ requires m/z 483.1374, found m/z 483.1353.

5',5'-Diethyl 3',4'-dimethyl 1-isopropyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4daa): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 4/1); Reaction time = 36 h; Yield: 76%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.43 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.27 (td, *J* = 7.8, 1.3 Hz, 1H), 7.02 (td, *J* = 7.6, 0.8 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 4.62 – 4.49 (m, 1H), 4.42 – 4.29 (m, 4H), 3.82 (s, 3H), 3.77 (s, 1H), 3.51 (s, 3H), 1.49 (d, *J* = 5.8 Hz, 3H), 1.47 (d, *J* = 5.7 Hz, 3H), 1.38 – 1.33 (m, 3H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) :174.0, 168.7, 168.0, 162.6, 161.2, 142.7, 140.1, 139.7, 130.0, 129.0, 125.0, 122.7, 109.9, 79.9, 75.1, 63.0, 62.8, 52.4, 52.3, 44.5, 19.1, 13.9, 13.8; IR (KBr): γ 3458, 3339, 2964, 2926, 2852, 1729, 1660, 1607, 1453, 1443, 1289, 1252, 1117, 1035, 871, 772 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{28}N_2O_9+Na)^+$ requires m/z 511.1687, found m/z 511.1662.

5',5'-Diethyl 3',4'-dimethyl 1-cyclopentyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4eaa): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 4/1); Reaction time = 36 h; Yield: 87%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.43 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.27 (td, *J* = 7.8, 1.3 Hz, 1H), 7.03 (td, *J* = 7.6, 0.8 Hz, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 4.69 (t, *J* = 8.7 Hz, 1H), 4.40 – 4.29 (m, 4H), 3.82 (s, 3H), 3.76 (s, 1H), 3.50 (s, 3H), 2.08 (dt, *J* = 15.0, 7.4 Hz, 2H), 1.92 (d, *J* = 2.9 Hz, 4H), 1.69 (s, 2H), 1.35 (t, *J* = 7.0 Hz, 3H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ (ppm) : 174.3, 168.7, 168.0, 162.6, 161.1, 142.6, 140.2, 139.7, 129.9, 128.9, 125.0, 122.8, 109.7, 79.9, 75.1, 63.0, 62.8, 53.0, 52.4, 52.2, 27.6, 27.3, 25.1, 25.1, 13.9, 13.8; IR (KBr): γ 3334, 2998, 2954, 2859, 1742, 1673, 1607, 1443, 1307, 1239, 1157, 1127, 1035, 874, 735, 700 cm^{-1}; ESI FTMS exact mass calcd for $(C_{26}H_{30}N_2O_9+Na)^+$ requires m/z 537.1844, found m/z 537.1833.

5',5'-Diethyl 3',4'-dimethyl 2-oxo-1-phenylspiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4faa): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 4/1); Reaction time = 36 h; Yield: 79%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.54 – 7.48 (m, 3H), 7.46 – 7.37 (m, 3H), 7.24 (td, *J* = 7.8, 1.6 Hz, 1H), 7.10 (td, *J* = 7.6, 0.9 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 4.46 – 4.28 (m, 4H), 3.88 (s, 1H), 3.85 (s, 3H), 3.59 (s, 3H), 1.65 (s, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 174.0, 168.6, 167.9, 162.6, 161.3, 144.0, 139.9, 139.9, 134.3, 130.2, 129.6, 128.2, 126.3, 125.0, 123.7, 109.6, 80.1, 75.4, 63.1, 62.9, 52.5, 29.7, 13.9, 13.8; IR (KBr): γ 3342, 2988, 2954, 2869, 1742, 1660, 1620, 1446, 1307, 1252, 1183, 1117, 1035, 939, 857, 789, 749, 693 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{26}N_2O_9+Na)^+$ requires m/z 545.1531, found m/z 545.1519.

5',5'-Diethyl 3',4'-dimethyl 1-benzyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4aaa): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 4/1); Reaction time = 36 h; Yield: 73%; Light yellow solid; m.p. 149-151 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.45 – 7.36 (m, 3H), 7.36 – 7.23 (m, 3H), 7.20 (td, *J* = 7.8, 1.2 Hz, 1H), 7.02 (td, *J* = 7.6, 0.8 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 5.12 (d, *J* = 15.6 Hz, 1H), 4.66 (d, *J* = 15.6 Hz, 1H), 4.41 – 4.31 (m, 4H), 3.85 (s, 3H), 3.80 (s, 1H), 3.40 (s, 3H), 1.36 (t, *J* = 5.2 Hz, 3H), 1.33 (t, *J* = 5.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 174.7, 168.6, 168.0, 162.6, 161.2, 143.2, 140.5, 139.6, 135.5, 130.2, 128.7, 128.6, 127.7, 124.7, 123.3, 109.3, 79.9, 75.0, 63.1, 62.9, 52.5, 52.3, 44.5, 13.9, 13.9; IR (KBr): γ 3349, 2984, 2954, 2859, 1729, 1660, 1613, 1498, 1429, 1262, 1035, 926, 854, 809, 690, 598 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{28}N_2O_9+H)^+$ requires m/z 537.1873, found m/z 537.1843.

5',5'-Diethyl 3',4'-dimethyl 1-(naphthalen-1-ylmethyl)-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4gaa): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 4/1); Reaction time = 36 h; Yield: 64%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 8.15 (d, *J* = 8.4 Hz, 1H),

7.89 (d, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.59 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.56 – 7.37 (m, 4H), 7.15 (td, *J* = 7.8, 1.2 Hz, 1H), 7.03 (td, *J* = 7.6, 0.7 Hz, 1H), 6.67 (d, *J* = 7.8 Hz, 1H), 5.57 (d, *J* = 16.3 Hz, 1H), 5.22 (d, *J* = 16.3 Hz, 1H), 4.38 (qd, *J* = 7.1, 1.7 Hz, 4H), 3.87 (s, 4H), 3.40 (s, 3H), 1.38 (t, *J* = 5.6 Hz, 3H), 1.34 (t, *J* = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 174.9, 168.6, 167.9, 162.7, 161.2, 143.6, 140.7, 139.4, 133.8, 131.0, 130.3, 130.2, 128.8, 128.7, 128.3, 126.6, 125.9, 125.3, 125.0, 124.7, 123.4, 123.0, 109.8, 80.0, 75.1, 63.2, 62.9, 52.6, 52.4, 42.7, 13.9, 13.8; IR (KBr): γ 3461, 3334, 2994, 2923, 2854, 1729, 1660, 1620, 1501, 1469, 1361, 1294, 1249, 1183, 1117, 1031, 854, 817, 690 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{30}N_2O_9+Na)^+$ requires m/z 609.1844, found m/z 609.1836.

5',5'-Diethyl 3',4'-dimethyl 4-chloro-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4haa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 62%; Light yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) ： 7.27 (t, *J* = 8.0 Hz, 1H), 6.98 (dd, *J* = 8.2, 0.6 Hz, 1H), 6.72 (d, *J* = 7.4 Hz, 1H), 4.40 – 4.28 (m, 4H), 3.89 (s, 1H), 3.85 (s, 3H), 3.58 (s, 3H), 3.19 (s, 3H), 1.37 – 1.33 (m, 3H), 1.33 – 1.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 173.7, 168.2, 167.6, 162.6, 161.5, 146.3, 141.6, 138.0, 131.8, 131.6, 124.0, 123.4, 106.8, 80.0, 75.2, 63.1, 62.8, 52.5, 26.8, 13.8; IR (KBr): γ 3334, 2981, 2926, 2859, 1742, 1657, 1617, 1484, 1439, 1371, 1252, 1130, 1034, 871, 749, 693 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{28}N_2O_9+H)^+$ requires m/z 495.1170, found m/z 495.1146.

5',5'-Diethyl 3',4'-dimethyl 1,5-dimethyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4iaa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 92%; Light yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.22 (s, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 4.40 – 4.30 (m, 4H), 3.83 (s, 3H), 3.73 (s, 1H), 3.53 (s, 3H), 3.19 (s, 3H), 2.30 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 174.5, 168.7, 168.0, 162.7, 161.2, 141.6, 139.8, 139.8, 132.9, 130.6, 128.4, 125.4, 108.0, 80.0, 75.3, 63.1, 62.8, 52.5, 52.4, 26.6, 21.0, 13.9, 13.8; IR (KBr): γ 3334, 2981, 2939, 2864, 1742, 1633, 1511, 1456, 1426, 1262, 1143, 1031, 871, 772, 693 cm^{-1}; ESI FTMS exact mass calcd for $(C_{23}H_{26}N_2O_9+H)^+$ requires m/z 475.1717, found m/z 475.1689.

5',5'-Diethyl 3',4'-dimethyl 5-methoxy-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4jaa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 87%; Light yellow solid; m.p. 127-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.07 (d, *J* = 2.6 Hz, 1H), 6.83 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 4.39 – 4.31 (m, 4H), 3.83 (s, 3H), 3.77 (s, 3H), 3.75 (s, 1H), 3.54 (s, 3H), 3.19 (s, 3H), 1.38 – 1.33 (m, 3H), 1.31 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 174.3, 168.6, 167.9, 162.6, 161.2, 156.5, 139.8, 139.7, 137.4, 129.8, 114.9, 111.7, 108.7, 80.0, 75.5, 63.0, 62.9, 55.8, 52.5, 52.4, 26.7, 13.9, 13.8; IR (KBr): γ 3344, 2981, 2926, 2872, 1742, 1660, 1607, 1456, 1361, 1294, 1239, 1183, 1117, 1035, 871, 745, 693 cm^{-1}; ESI FTMS exact mass calcd for $(C_{23}H_{26}N_2O_{10}+Na)^+$ requires m/z 513.1479, found m/z 513.1476.

5',5'-Diethyl 3',4'-dimethyl 5-bromo-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4kaa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 85%; Light yellow solid; m.p. 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.56 (d, *J* = 1.9 Hz, 1H), 7.44 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.69 (d, *J* = 8.3 Hz, 1H), 4.41 – 4.30 (m, 4H), 3.84 (s, 3H), 3.76 (s, 1H), 3.57 (s, 3H), 3.20 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.0, 168.3, 167.6, 162.5, 160.9, 143.0, 140.5, 138.6, 133.1, 130.9, 128.0, 115.9, 109.7, 80.1, 75.0, 63.2, 63.0, 52.6, 52.5, 26.7, 13.9, 13.8; IR (KBr): γ 3352, 2994, 2954, 2859, 1742, 1647, 1603, 1469, 1429, 1252, 1133, 1035, 939, 857, 749, 680 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{23}BrN_2O_9+Na)^+$ requires m/z 563.0462, found m/z 563.0476.

5',5'-Diethyl 3',4'-dimethyl 5-chloro-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4laa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 86%; Light yellow solid; m.p. 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.43 (d, *J* = 2.1 Hz, 1H), 7.29 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.74 (d, *J* = 8.3 Hz, 1H), 4.36 (m, 4H), 3.84 (s, 3H), 3.77 (s, 1H), 3.56 (s, 3H), 3.20 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.1, 168.4, 167.6, 162.5, 160.9, 142.5, 140.5, 138.7, 130.5, 130.1, 128.6, 125.3, 109.3, 80.1, 75.0, 63.2, 63.0, 52.6, 52.5, 26.8, 13.9, 13.8; IR (KBr): γ 3334, 2954, 2844, 1729, 1660, 1620, 1456, 1294, 1252, 1180, 1113, 1088, 1048, 867, 806, 749, 693 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{23}ClN_2O_9+H)^+$ requires m/z 495.1170, found m/z 495.1186.

5',5'-Diethyl 3',4'-dimethyl 5-fluoro-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4maa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 81%; Light yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.22 (dd, *J* = 7.5, 2.6 Hz, 1H), 7.01 (td, *J* = 8.8, 2.6 Hz, 1H), 6.74 (dd, *J* = 8.5, 4.0 Hz, 1H), 4.39 – 4.31 (m, 4H), 3.83 (s, 3H), 3.77 (s, 1H), 3.55 (s, 3H), 3.21 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.3, 168.5, 167.7, 162.5, 161.0, 160.7, 158.3, 140.3, 139.9, 139.0, 130.4, 116.6, 116.3, 113.1, 112.9, 108.9, 108.8, 80.1, 75.3, 75.3, 63.1, 63.0, 52.5, 26.8, 13.9, 13.8; IR (KBr): γ 3334, 2959, 2913, 2854, 1739, 1660, 1634, 1494, 1443, 1294, 1249, 1035, 864, 809, 693 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{23}FN_2O_9+H)^+$ requires m/z 479.1466, found m/z 479.1463.

5',5'-Diethyl 3',4'-dimethyl 1-benzyl-5-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4naa): (Flash column chromatography eluent, petroleum ether/ acetone = 6/1); Reaction time = 36 h; Yield: 61%; Light yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.38 (d, *J* = 7.0 Hz, 2H), 7.34 – 7.28 (m, 2H), 7.28 – 7.21 (m, 2H), 6.99 (dd, *J* = 7.9, 0.9 Hz, 1H), 6.59 (d, *J* = 7.9 Hz, 1H), 5.10 (d, *J* = 15.6 Hz, 1H), 4.63 (d, *J* = 15.6 Hz, 1H), 4.37 (m, 4H), 3.85 (s, 3H), 3.80 (s, 1H), 3.41 (s, 3H), 2.27 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.6, 168.6, 168.0, 162.7, 161.2, 140.8, 140.3, 139.7, 135.6, 133.0, 130.5, 128.7, 128.5, 127.7, 127.6, 125.4, 109.1, 79.9, 75.2, 63.1, 62.9, 52.5, 52.3, 44.5, 21.0, 13.9, 13.8; IR (KBr): γ 3334, 2978, 2936, 2872, 1732, 1647, 1620, 1469, 1443, 1389, 1255, 1117, 1035, 933, 857, 745, 690 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{30}N_2O_9+H)^+$ requires m/z 551.2030, found m/z 551.2040.

5',5'-Diethyl 3',4'-dimethyl 1-benzyl-5-methoxy-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4oaa): (Flash column chromatography eluent, petroleum ether/ acetone = 6/1); Reaction time = 36 h; Yield: 62%; Light yellow solid; m.p. 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.41 – 7.35 (m, 2H), 7.35 – 7.27 (m, 3H), 7.07 (d, *J* = 2.6 Hz, 1H), 6.72 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.60 (d, *J* = 8.5 Hz, 1H), 5.09 (d, *J* = 15.5 Hz, 1H), 4.63 (d, *J* = 15.6 Hz, 1H), 4.37 (m, 4H), 3.84 (s, 3H), 3.82 (s, 1H), 3.74 (s, 3H), 3.42 (s, 3H), 1.36 (t, *J* = 6.0 Hz, 3H), 1.33 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.5, 168.6, 167.9, 162.6, 161.1, 156.5, 140.4, 139.6, 136.4, 135.6, 129.9, 128.7, 127.7, 114.9, 111.6, 109.9, 79.9, 75.4, 63.1, 62.9, 55.7, 52.5, 52.3, 44.6, 13.9, 13.9; IR (KBr): γ 3444, 3334, 2984,

2923, 2859, 1729, 1610, 1498, 1469, 1371, 1296, 1252, 1170, 1120, 1018, 857, 745 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{30}N_2O_{10}+H)^+$ requires m/z 567.1979, found m/z 567.1973.

5',5'-Diethyl 3',4'-dimethyl 1-benzyl-5-bromo-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4paa): (Flash column chromatography eluent, petroleum ether/ acetone = 6/1); Reaction time = 36 h; Yield: 67%; Light yellow solid; m.p. 118-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.56 (d, *J* = 2.0 Hz, 1H), 7.39 – 7.26 (m, 6H), 6.57 (d, *J* = 8.3 Hz, 1H), 5.09 (d, *J* = 15.6 Hz, 1H), 4.66 (d, *J* = 15.6 Hz, 1H), 4.37 (m, 4H), 3.86 (s, 3H), 3.83 (s, 1H), 3.46 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.2, 168.3, 167.6, 162.5, 160.8, 142.2, 141.1, 138.5, 135.0, 133.0, 131.0, 128.8, 128.0, 127.6, 116.0, 110.8, 80.1, 74.9, 63.3, 63.1, 62.8, 52.6, 44.6, 13.9, 13.8; IR (KBr): γ 3458, 3346, 2988, 2923, 2862, 1739, 1657, 1607, 1484, 1364, 1297, 1235, 1103, 1028, 867, 817, 680 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{27}BrN_2O_9+Na)^+$ requires m/z 639.0776, found m/z 639.0770.

5',5'-Diethyl 3',4'-dimethyl 1-benzyl-6-bromo-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4qaa): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 6/1); Reaction time = 36 h; Yield: 63%; Light yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.29 (dd, *J* = 7.1, 3.8 Hz, 3H), 7.26 – 7.17 (m, 3H), 7.08 (dd, *J* = 7.9, 1.6 Hz, 1H), 6.77 (d, *J* = 1.6 Hz, 1H), 5.01 (d, *J* = 15.6 Hz, 1H), 4.54 (d, *J* = 15.6 Hz, 1H), 4.34 – 4.22 (m, 4H), 3.76 (s, 3H), 3.68 (s, 1H), 3.35 (s, 3H), 1.26 (dd, *J* = 15.3, 7.2 Hz, 6H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.6, 168.5, 167.8, 162.5, 161.0, 144.5, 140.9, 138.8, 134.9, 128.9, 127.9, 127.7, 127.6, 126.3, 126.1, 123.9, 112.7, 79.9, 74.6, 63.2, 63.0, 52.6, 52.5, 44.6, 13.9, 13.8; IR (KBr): γ 3334, 2981, 2954, 2859, 1742, 1660, 1617, 1484, 1429, 1294, 1252, 1113, 1035, 857, 817, 693 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{27}BrN_2O_9+Na)^+$ requires m/z 639.0776, found m/z 639.0786.

5',5'-Diethyl 3',4'-dimethyl 1-benzyl-7-bromo-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4raa): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 6/1); Reaction time = 36 h; Yield: 79%; Light yellow solid; m.p. 134-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.43-7.38 (m, 2H), 7.36 – 7.27 (m, 4H), 7.24 (s, 1H), 6.93 (dd, *J* = 8.1, 7.4 Hz, 1H), 5.47 – 5.25 (m, 2H), 4.40-4.31 (m, 4H), 3.84 (s, 3H), 3.80 (s, 1H), 3.51 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ (ppm): 175.6, 168.5, 167.7, 162.5, 161.0, 141.0, 140.8, 138.9, 137.2, 136.1, 132.14, 128.4, 127.1, 126.8, 124.7, 124.1, 102.5, 79.9, 74.3, 63.2, 63.0, 52.6, 52.5, 45.2, 13.9, 13.8; IR (KBr): γ 3334, 2968, 2872, 1729, 1660, 1607, 1474, 1443, 1307, 1239, 1173, 1031, 871, 749 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{27}BrN_2O_9+Na)^+$ requires m/z 639.0776, found m/z 639.0779.

5',5'-Diethyl 3',4'-dimethyl 5-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4saa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 99%; Yellow solid; m.p. 157-159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 8.28 (s, 1H), 7.20 (s, 1H), 7.08 – 7.00 (m, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 4.36 (m, 4H), 3.85 (s, 3H), 3.75 (s, 1H), 3.57 (s, 3H), 2.29 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 176.5, 168.6, 168.0, 162.6, 161.3, 139.9, 139.8, 138.7, 132.8, 130.6, 128.9, 125.6, 110.0, 80.0, 75.6, 63.1, 62.8, 52.5, 52.5, 21.0, 13.9, 13.8; IR (KBr): γ 3339, 2992, 2943, 2923, 2846, 1736, 1610, 1493, 1474, 1448, 1299, 1254, 1127, 1037, 864, 751 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{24}N_2O_9+Na)^+$ requires m/z 483.1374, found m/z 483.1364.

5',5'-Diethyl 3',4'-dimethyl 5-methoxy-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4taa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 99%; Light yellow solid; m.p. 140-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 8.21 (s, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.84 – 6.68 (m, 2H), 4.43 – 4.27 (m, 4H), 3.84 (s, 3H), 3.76 (s, 4H), 3.57 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.32 (t, *J* = 7.2 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 176.3, 168.6, 167.9, 162.6, 161.2, 156.3, 140.0, 139.6, 134.3, 130.2, 115.4, 111.6, 110.7, 80.0, 75.9, 63.1, 62.9, 55.7, 52.5, 52.5, 13.9, 13.8; IR (KBr): γ 3321, 2984, 2929, 2859, 1742, 1660, 1607, 1469, 1443, 1371, 1294, 1239, 1183, 1143, 1103, 1035, 857, 779, 735 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{24}N_2O_{10}+H)^+$ requires m/z 477.1509, found m/z 477.1517.

5',5'-Diethyl 3',4'-dimethyl 5-fluoro-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4uaa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 99%; Light yellow solid; m.p. 165-167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 8.42 (s, 1H), 7.18 (dd, *J* = 7.6, 2.6 Hz, 1H), 6.95 (td, *J* = 8.8, 2.6 Hz, 1H), 6.80 (dd, *J* = 8.5, 4.1 Hz, 1H), 4.35 (m, 4H), 3.85 (s, 3H), 3.80 (s, 1H), 3.58 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ (ppm): 176.5, 168.4, 167.7, 162.4, 161.1, 160.5, 158.1, 140.4, 139.0, 137.1, 130.8, 116.8, 116.6, 113.2, 112.9, 111.1, 111.0, 80.0, 75.8, 63.2, 63.0, 52.6, 13.9, 13.8; IR (KBr): γ 3468, 3349, 2971, 2939, 2862, 1742, 1670, 1607, 1484, 1443, 1347, 1294, 1249, 1183, 1130, 1035, 857, 755, 709 cm^{-1}; ESI FTMS exact mass calcd for $(C_{21}H_{21}FN_2O_9+H)^+$ requires m/z 465.1309, found m/z 465.1301.

5',5'-Diethyl 3',4'-dimethyl 7-bromo-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4vaa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 76%; Light yellow solid; m.p. 95-96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.70 (s, 1H), 7.37 (dd, *J* = 12.4, 4.1 Hz, 2H), 6.94 (t, *J* = 7.8 Hz, 1H), 4.41 – 4.30 (m, 4H), 3.85 (s, 3H), 3.78 (s, 1H), 3.58 (s, 3H), 1.35 (t, *J* = 6.7 Hz, 3H), 1.30 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.8, 168.4, 167.6, 162.5, 160.9, 140.6, 140.4, 138.7, 132.8, 130.5, 124.5, 124.04, 103.0, 80.1, 76.5, 63.2, 63.0, 52.6, 13.9, 13.8; IR (KBr): γ 3334, 2981, 2923, 2859, 1732, 1607, 1479, 1456, 1374, 1294, 1254, 1117, 1035, 857 cm^{-1}; ESI FTMS exact mass calcd for $(C_{21}H_{21}BrN_2O_9+Na)^+$ requires m/z 549.0305, found m/z 549.0320.

5',5'-Diethyl 3',4'-dimethyl 2-oxo-7-(trifluoromethyl)spiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4waa): (Flash column chromatography eluent, petroleum ether/ acetone = 6/1); Reaction time = 36 h; Yield: 58%; Light yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.87 (s, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 7.8 Hz, 1H), 4.36 (dd, *J* = 7.0, 5.0 Hz, 4H), 3.85 (s, 3H), 3.80 (s, 1H), 3.56 (s, 3H), 1.34 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 175.3, 168.4, 167.6, 162.4, 160.7, 141.1, 138.5, 138.3, 131.0, 128.7, 126.9, 126.8, 125.0, 123.1, 122.3, 112.5, 112.2, 80.1, 74.2, 63.2, 63.0, 52.6, 52.5, 13.9, 13.8; IR (KBr): γ 3349, 2981, 2949, 2859, 1739, 1660, 1607, 1498, 1446, 1299, 1235, 1130, 1031, 871, 814, 680 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{21}F_3N_2O_9+H)^+$ requires m/z 515.1277, found m/z 515.1286.

5',5'-Diethyl 3',4'-dimethyl 5,6-difluoro-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4xaa): (Flash column chromatography eluent, petroleum ether/ acetone = 5/1); Reaction time = 36 h; Yield: 52%; Light yellow solid; m.p. 175-177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 8.50 (s, 1H), 7.35 – 7.27 (m, 1H), 6.73 (dd, *J* = 9.7, 6.3 Hz, 1H), 4.35 (dt, *J* = 12.1, 7.1 Hz, 4H), 3.85 (s, 3H), 3.78 (s, 1H), 3.61 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 176.5,

168.4, 167.7, 162.4, 161.0, 140.6, 138.5, 137.4, 124.7, 115.0, 114.7, 100.7, 100.5, 80.0, 75.3, 63.3, 63.1, 52.7, 52.6, 13.9, 13.8; IR (KBr): γ 3344, 2954, 2841, 1729, 1660, 1607, 1484, 1443, 1265, 1209, 1143, 1601, 1031, 871, 807, 693, 598 cm^{-1}; ESI FTMS exact mass calcd for $(C_{21}H_{20}F_2N_2O_9+Na)^+$ requires m/z 505.1029, found m/z505.1020.

Tetraethyl 2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4bab): (Flash column chromatography eluent, petroleum ether/ acetone = 4/1); Reaction time = 36 h; Yield: 99%; Yellow sticky oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) : 8.28 (s, 1H), 7.41 (d, *J* = 7.4 Hz, 1H), 7.23 (dd, *J* = 7.7, 1.2 Hz, 2H), 7.03 (td, *J* = 7.6, 0.9 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 4.49 – 4.17 (m, 6H), 4.11 – 3.83 (m, 2H), 3.76 (s, 1H), 1.37-1.30 (m, 9H), 0.98 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 176.5, 168.7, 168.1, 162.1, 160.8, 141.2, 139.9, 139.8, 130.2, 129.2, 125.1, 123.2, 110.1, 80.0, 75.5, 63.0, 62.8, 61.8, 61.6, 13.9, 13.9, 13.4; IR (KBr): γ 3362, 3444, 2964, 2876, 1739, 1670, 1610, 1469, 1389, 1374, 1294, 1239, 1180, 1130, 1103, 1035, 857, 749 cm^{-1}; ESI FTMS exact mass calcd for $(C_{23}H_{26}N_2O_9+Na)^+$ requires m/z 497.1531, found m/z 497.1531.

Tetraethyl 1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4cab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 4/1); Reaction time = 36 h; Yield: 94%; Yellow sticky oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.43 (d, *J* = 7.3 Hz, 1H), 7.31 (td, *J* = 7.7, 1.1 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 4.41 – 4.15 (m, 6H), 4.00-3.88 (m, 2H), 3.74 (s, 1H), 3.20 (s, 3H), 1.37-1.29 (m, 9H), 0.95 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.7, 168.7, 168.1, 162.1, 160.7, 144.0, 139.9, 139.8, 130.2, 128.7, 124.7, 123.3, 108.1, 79.9, 75.1, 63.0, 62.8, 61.7, 61.3, 29.6, 26.5, 13.9, 13.8, 13.5; IR (KBr): γ 3334, 2994, 2954, 2859, 1739, 1660, 1484, 1429, 1262, 1035, 857, 804, 680, 598 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{28}N_2O_9+Na)^+$ requires m/z 511.1687, found m/z 511.1687.

Tetraethyl 1-cyclopentyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4eab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 6/1); Reaction time = 36 h; Yield: 87%; Yellow sticky oil; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.45 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.27 (td, *J* = 7.8, 1.3 Hz, 1H), 7.03 (td, *J* = 7.6, 0.7 Hz, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 4.73-4.64 (m, 1H), 4.39 – 4.25 (m, 6H), 4.06 – 3.87 (m, 2H), 3.77 (s, 1H), 2.14 – 1.88 (m, 6H), 1.71 – 1.62 (m, 2H), 1.37 – 1.29 (m, 9H), 0.93 (t, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.4, 168.8, 168.2, 162.1, 160.7, 142.7, 140.3, 139.6, 129.8, 129.2, 125.1, 122.8, 109.6, 79.9, 75.1, 62.9, 62.8, 61.7, 61.3, 53.0, 27.7, 27.3, 25.2, 25.1, 13.9, 13.9, 13.8, 13.6; IR (KBr): γ 3484, 3344, 2981, 2939, 2859, 1739,

1663, 1607, 1456, 1439, 1294, 1249, 1130, 1038, 867, 749 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{34}N_2O_9+Na)^+$ requires m/z 565.2157, found m/z 565.2131.

Tetraethyl 2-oxo-1-phenylspiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4fab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 6/1); Reaction time = 36 h; Yield: 84%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.56 – 7.34 (m, 6H), 7.23 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.10 (td, *J* = 7.6, 0.7 Hz, 1H), 6.81 (d, *J* = 7.9 Hz, 1H), 4.43 – 4.21 (m, 6H), 4.12 – 3.94 (m, 2H), 3.88 (s, 1H), 1.42 – 1.27 (m, 9H), 0.98 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.1, 168.8, 168.0, 162.1, 160.8, 144.0, 140.0, 139.8, 134.3, 130.1, 129.5, 128.4, 128.1, 126.2, 125.1, 123.7, 109.5, 80.1, 75.4, 63.0, 62.8, 61.8, 61.6, 13.9, 13.9, 13.9, 13.7; IR (KBr): γ 3458, 3336, 2981, 2951, 2861, 1739, 1663, 1608, 1484, 1439, 1307, 1257, 1183, 1133, 1048, 861, 821, 740, 710, 640 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{30}N_2O_9+H)^+$ requires m/z 551.2030, found m/z 551.2030.

Tetraethyl 1-benzyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4aab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 6/1); Reaction time = 36 h; Yield: 85%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.24 (m, 6H),7.19 (td, *J* = 7.8, 1.2 Hz, 1H) 7.02 (td, *J* = 7.6, 0.8 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 5.02 (d, *J* = 15.6 Hz, 1H), 4.74 (d, *J* = 15.6 Hz, 1H), 4.39 – 4.24 (m, 6H),4.01-3.95 (m, 1H), 3.82 – 3.77 (m, 2H), 1.38-1.28 (m, 9H), 0.81 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.8, 168.7, 168.1, 162.1, 160.7, 143.3, 140.2, 139.8, 135.5, 130.1, 128.8, 128.7, 127.7, 124.8, 123.3, 109.2, 79.9, 75.1, 63.0, 62.8, 61.8, 61.4, 44.5, 13.9, 13.9, 13.4; IR (KBr): γ 3349, 2939, 2859, 1729, 1660, 1607, 1484, 1443, 1294, 1249, 1130, 1035, 857, 804, 680 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{32}N_2O_9+Na)^+$ requires m/z 587.2000, found m/z 587.2009.

Tetraethyl 1,5-dimethyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4iab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 3/1); Reaction time = 36 h; Yield: 86%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.25 (m, 1H), 7.09 (m, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 4.38 – 4.26 (m, 6H), 4.01 – 3.89 (m, 2H), 3.74 (s, 1H), 3.18 (s, 3H), 2.30 (s, 3H), 1.38 – 1.29 (m, 9H), 0.96 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 174.6, 168.8, 168.1, 162.1, 160.7, 141.6, 140.0, 139.7, 132.9, 130.4, 128.6, 125.5, 107.9, 79.9, 75.3, 63.0, 62.8, 61.7, 61.3, 26.6, 21.0, 13.9, 13.8, 13.5; IR (KBr): γ 3461, 3352, 2981, 2923, 2859, 1739, 1667, 1607, 1501,

1456, 1361, 1294, 1252, 1130, 1035, 939, 844, 762, 693 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{30}N_2O_9+Na)^+$ requires m/z 525.1844, found m/z 525.1840.

Tetraethyl 5-methoxy-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4jab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 3/1); Reaction time = 36 h; Yield: 71%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.09 (d, *J* = 2.6 Hz, 1H), 6.83 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.70 (d, *J* = 8.5 Hz, 1H), 4.38-4.26 (m, 6H), 4.02 – 3.90 (m, 2H), 3.77 (s,*3*H), 3.76 (s, 1H),3.17 (s, 3H), 1.37 – 1.29 (m, 9H), 0.97 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.4, 168.7, 168.0, 162.1, 160.6, 156.5, 139.9, 139.8, 137.4, 130.0, 114.9, 111.7, 108.6, 79.9, 75.5, 62.9, 62.8, 61.7, 61.4, 55.8, 26.6, 13.9, 13.9, 13.8, 13.5; IR (KBr): γ 3334, 2991, 2926, 1742, 1660, 1607, 1456, 1374, 1252, 1198, 1127, 1035, 857, 762, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{30}N_2O_{10}+Na)^+$ requires m/z 541.1793, found m/z 541.1780.

Tetraethyl 5-bromo-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4kab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 3/1); Reaction time = 36 h; Yield: 79%; Light yellow solid; m.p. 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.58 (d, *J* = 2.0 Hz, 1H), 7.43 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.68 (d, *J* = 8.3 Hz, 1H), 4.40 – 4.26 (m, 6H), 4.04 – 3.92 (m, 2H), 3.77 (s, 1H), 3.19 (s, 3H), 1.40 – 1.30 (m, 9H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.2, 168.4, 167.8, 161.9, 160.4, 143.0, 140.5, 138.8, 132.9, 131.12, 128.0, 115.8, 109.6, 80.1, 75.0, 63.1, 63.0, 61.9, 61.6, 26.7, 13.9, 13.8, 13.5; IR (KBr): γ 3349, 2994, 2958, 2872, 1742, 1660, 1633, 1488, 1443, 1265, 1035, 923, 814, 732, 690 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{27}BrN_2O_9+Na)^+$ requires m/z 589.0792, found m/z 589.0781.

Tetraethyl 5-chloro-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4lab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 3/1); Reaction time = 36 h; Yield: 85%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.45 (d, *J* = 2.1 Hz, 1H), 7.28 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 4.40 – 4.24 (m, 6H), 4.04 – 3.92 (m, 2H), 3.78 (s, 1H), 3.19 (s, 3H), 1.40 – 1.30 (m, 9H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.3, 168.4, 167.8, 161.9, 160.4, 142.5, 140.5, 138.8, 130.7, 130.0, 128.6, 125.3, 109.1, 80.1, 75.0, 63.1, 63.0, 61.9, 61.6, 29.6, 26.7, 13.9, 13.8, 13.5; IR (KBr): γ 3459, 3334, 2981, 2929, 2862, 1725, 1660, 1607, 1501, 1473, 1361, 1284, 1252, 1120, 1031, 861, 819 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{27}ClN_2O_9+Na)^+$ requires m/z 545.1297, found m/z 545.1296.

Tetraethyl 6-bromo-1-methyl-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4yab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 5/1); Reaction time = 36 h; Yield: 73%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.31 (d, *J* = 7.9 Hz, 1H), 7.19 (dd, *J* = 7.9, 1.6 Hz, 1H), 6.95 (d, *J* = 1.6 Hz, 1H), 4.38 – 4.26 (m, 6H), 4.03 – 3.92 (m, 2H), 3.72 (s, 1H), 3.18 (s, 3H), 1.36 – 1.29 (m, 9H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.5, 168.6, 167.9, 162.0, 160.5, 145.3, 140.4, 138.9, 127.8, 126.1, 123.9, 111.7, 80.0, 74.7, 63.1, 62.9, 61.8, 61.5, 29.6, 26.7, 13.9, 13.8, 13.6; IR (KBr): γ 3349, 2981, 2926, 2872, 1745, 1660, 1617, 1498, 1456, 1357, 1289, 1249, 1031, 953, 871, 817, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{27}BrN_2O_9+Na)^+$ requires m/z 589.0792, found m/z 589.0799.

Tetraethyl 2-oxo-7-(trifluoromethyl)spiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4wab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 4/1); Reaction time = 36 h; Yield: 73%; Yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.78 (s, 1H), 7.64 (d, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 7.7 Hz, 1H), 4.38 – 4.26 (m, 6H), 4.05 – 3.95 (m, 2H), 3.81 (s, 1H), 1.61 (s, 1H), 1.37 – 1.29 (m, 9H), 0.98 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 175.4, 168.5, 167.7, 161.9, 160.2, 141.3, 138.5, 138.3, 131.2, 128.8, 126.8, 125.0, 123.1, 122.3, 112.4, 112.0, 80.0, 74.2, 63.1, 63.0, 62.7, 62.0, 61.7, 13.9, 13.8, 13.3; IR (KBr): γ 3331, 2926, 2852, 1732, 1663, 1617, 1469, 1449, 1361, 1294, 1252, 1184, 1130, 1031, 857, 789, 762 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{25}F_3N_2O_9+Na)^+$ requires m/z 565.1404, found m/z 565.1420.

Tetraethyl 7-bromo-2-oxospiro[indoline-3,2'-pyrrole]-3',4',5',5'(1'H)-tetracarboxylate (4vab): (Flash column chromatography eluent, petroleum ether/ ethyl acetate = 3/1); Reaction time = 36 h; Yield: 65%; Light yellow solid; m.p. 191-193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 7.58 (s, 1H), 7.39 – 7.37 (m, 2H), 6.95 (dd, *J* = 8.2, 7.5 Hz, 1H), 4.37 – 4.28 (m, 6H), 4.13 – 3.93 (m, 2H), 3.79 (s, 1H), 1.37 – 1.30 (m, 9H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 174.9, 168.5, 167.8, 161.9, 160.3, 140.6, 140.4, 138.8, 132.7, 130.8, 124.5, 124.1, 102.9, 80.1, 76.5, 63.1, 62.9, 61.9, 61.7, 13.9, 13.9, 13.8, 13.4; IR (KBr): γ 3349, 2968, 2913, 2859, 1739, 1647, 1610, 1494, 1443, 1297, 1249, 1130, 1035, 857, 804, 690 cm^{-1}; ESI FTMS exact mass calcd for $(C_{23}H_{25}BrN_2O_9+Na)^+$ requires m/z 575.0636, found m/z 575.0639.

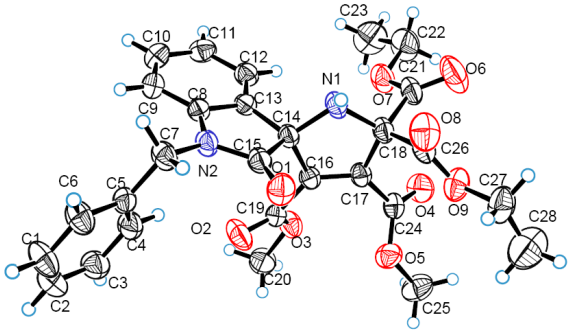
Cytotoxic evaluation of compounds 4 to mammary carcinoma cell line MCF7:

The cytotoxicity of the tested compounds to MCF7 cells was assayed using the CCK8 (Cell Counting Kit-8) method. MCF7 cells were seeded in 96-well plates at the density of 10^4 cells per well with 200 μl of complete culture medium. After adhesion for 24 hours, the medium was change to 1640 supplemented without FBS and the compounds was added to the medium to final concentrations ranging from 1 μg/ml to 100 μg/ml. The cells were then cultured for another 24 h. Cells that did not exposed to compounds were used as controls and the wells to which only culture medium was added served as blanks. At the end of compounds stimulation, the supernatant was removed, and 100 μl of 1640 medium containing 10 μl of CCK8 was added to each well for another 3 h at 37°C. The culture plates were then shaken for 10 min and the optical density (OD) values were read at 450 nm. The inhibition rate was calculated according to the following formula: Inhibition rate = $(OD_{450\ control} - OD_{450\ sample}) / OD_{450\ control} \times 100\%$, where OD stands for optical density at 450 nm.

References:

1. (a) B. M. Trost, Y. Zhang, *J. Am. Chem. Soc*. **2007**, *129*, 14548; (b) C. Marti, E. M. Carreira, *J. Am. Chem. Soc*. **2005**, *127*, 11505; (c) Z. Liu, P. Gu, M. Shi, P. McDowell, G. Li, *Org. Lett.* **2011**, *13*, 2314; (d) M. G. Bursavich, A. M. Gilbert, S. Lombardi, K. E. Georgiadis, E. Reifenberg, C. R. Flannery, E. A. Morris, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5630; (e) F. Da Settimo, G. Primofiore, A. Da Settimo, C. La Motta, F. Simorini, E. Novellino, G. Greco, A. Lavecchia, E. Boldrini, *J. Med. Chem.* **2003**, *46*, 1419; (f) K. Aikawa, S. Mimura, Y. Numata, K. Mikami, *Eur. J. Org. Chem.* **2011**, 62; (g) S.-H. Cao, X.-C. Zhang, Y. Wei, M. Shi, *Eur. J. Org. Chem.* **2011**, 2668; (h) F. Shi, Z.-L. Tao, S.-W. Luo, S.-J. Tu, L.-Z. Gong, *Chem. Eur. J.* **2012**, *18*, 6885.

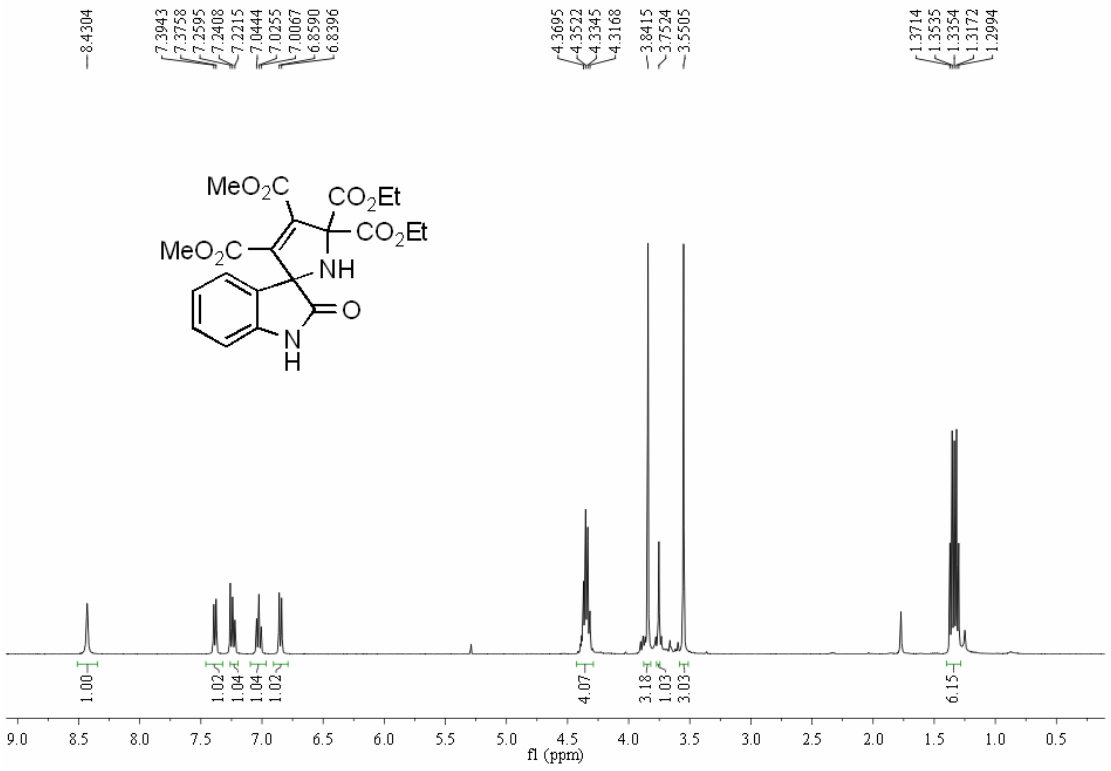
X-ray single crystal data for 4aaa:

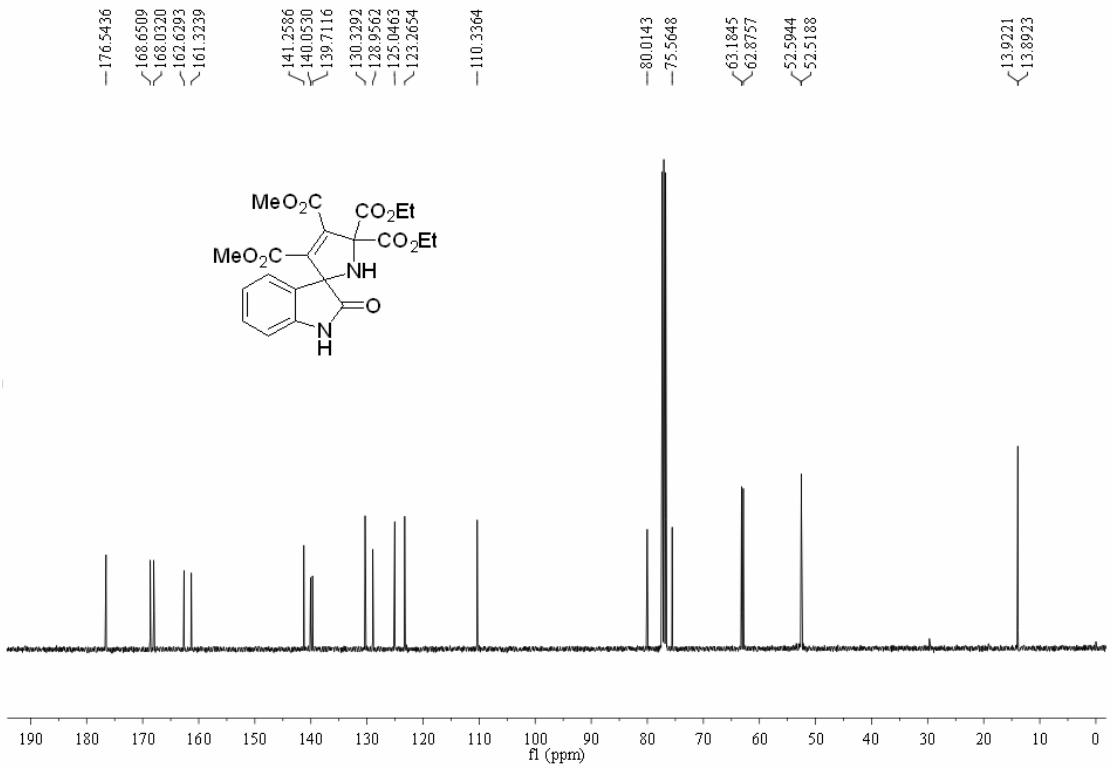


Empirical formula	$C_{28}H_{28}O_9N_2$
Formula weight	536.52
Temperature	295(2) K
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 18.8356(3) Å α =90.00°
	b = 9.57410(10) Å β = 103.7800(10)°
	c = 15.4158(2) Å γ = 90.00°
Volume	2699.98(6) Å^3
Z	4
Density (calculated)	1.320 mg/mm^3
F(000)	1128
Crystal size	0.40 × 0.32 × 0.30
Theta range for data collection	4.83 to 62.72°
Index ranges	-21 ≤ h ≤ 21, -11 ≤ k ≤ 10, -14 ≤ l ≤ 17
Reflections collected	11727
Independent reflections	4286[R(int) = 0.0228]
Data / restraints / parameters	4286/15/361
Goodness-of-fit on F^2	1.061
Final R indices [I>2σ(I)]	R_1 = 0.0436, wR_2 = 0.1179
R indices (all data)	R_1 = 0.0501, wR_2 = 0.1253
Largest diff. peak and hole	0.444/-0.379

^{1}H and ^{13}C NMR spectra of products 4

4baa:





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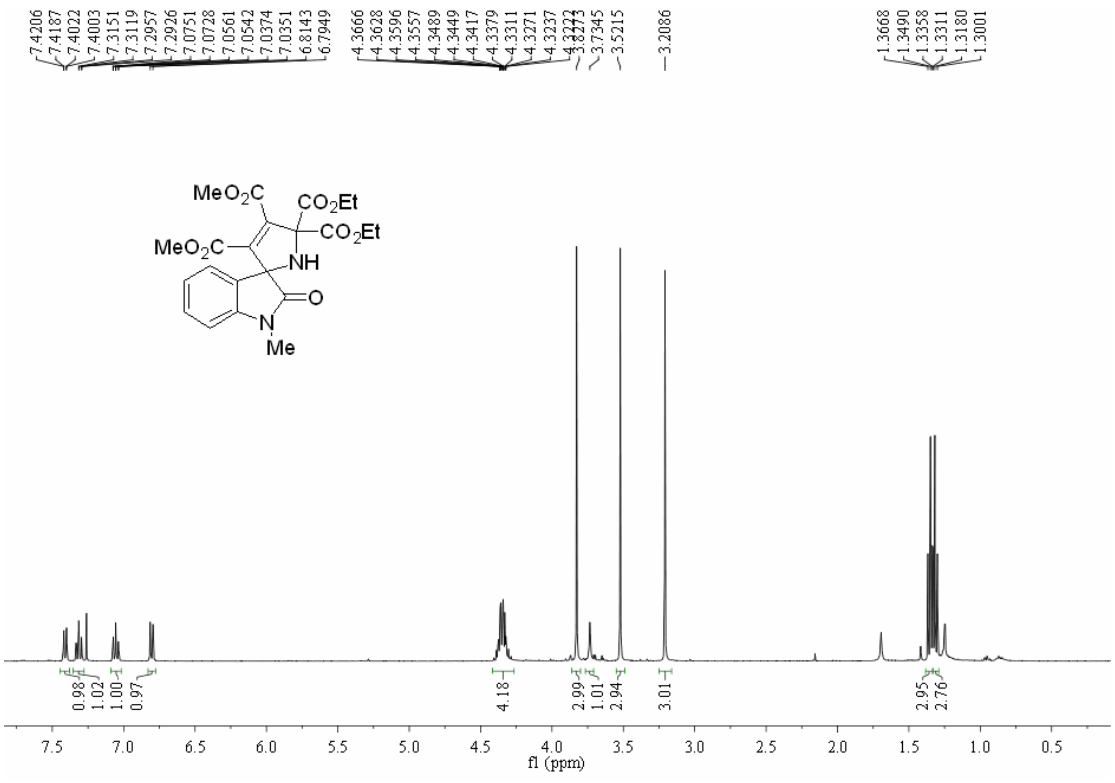
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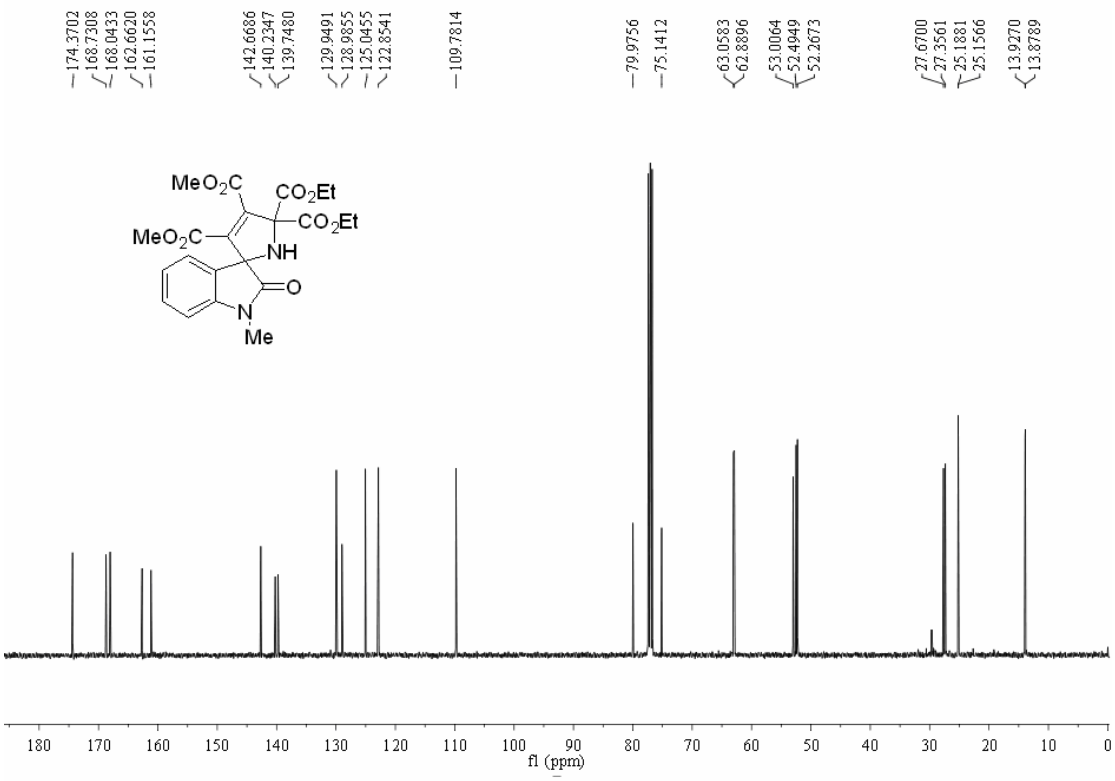
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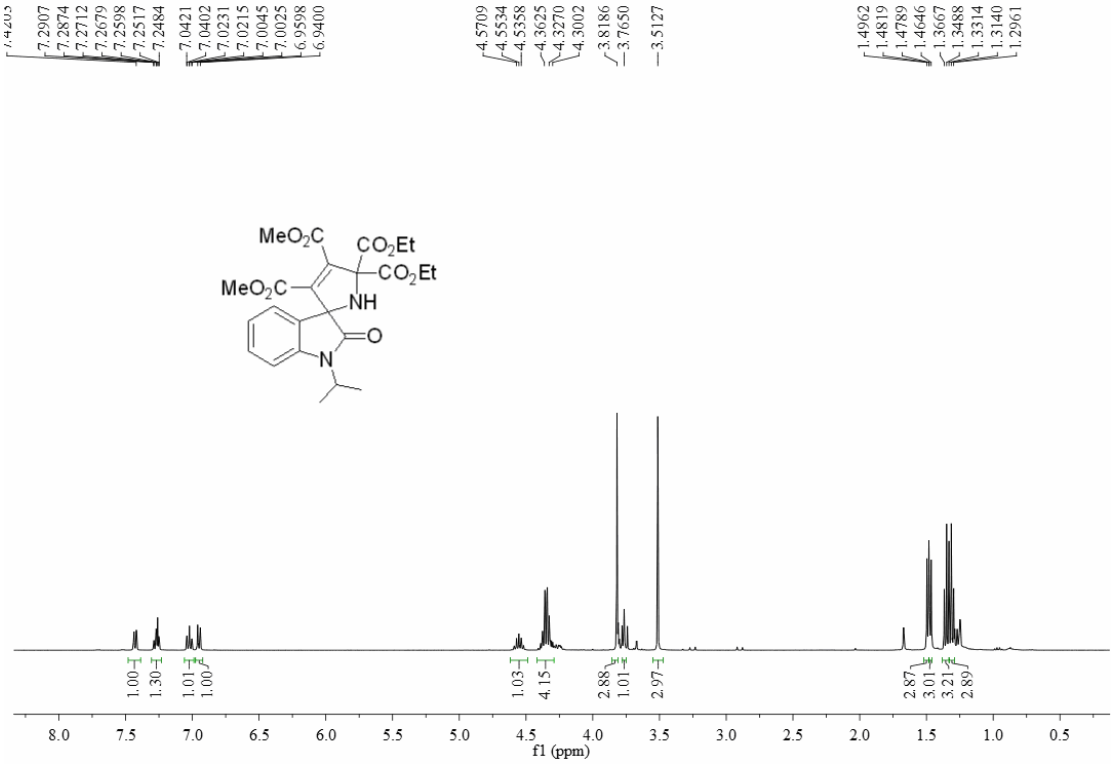
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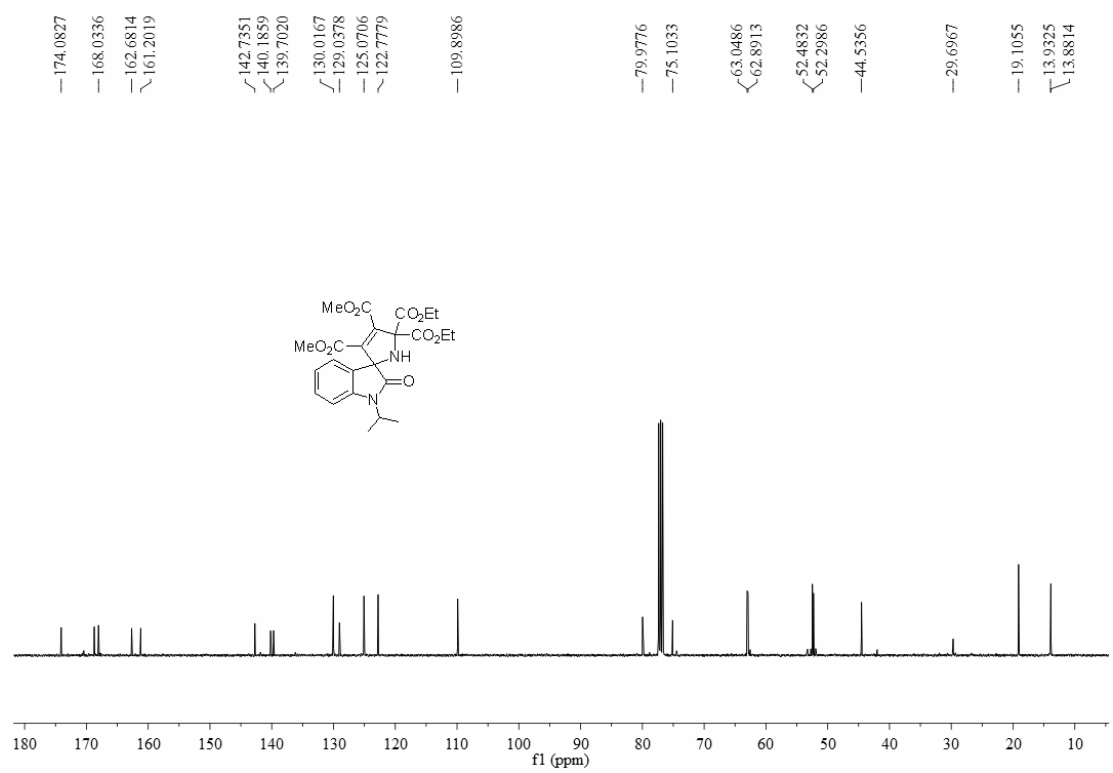
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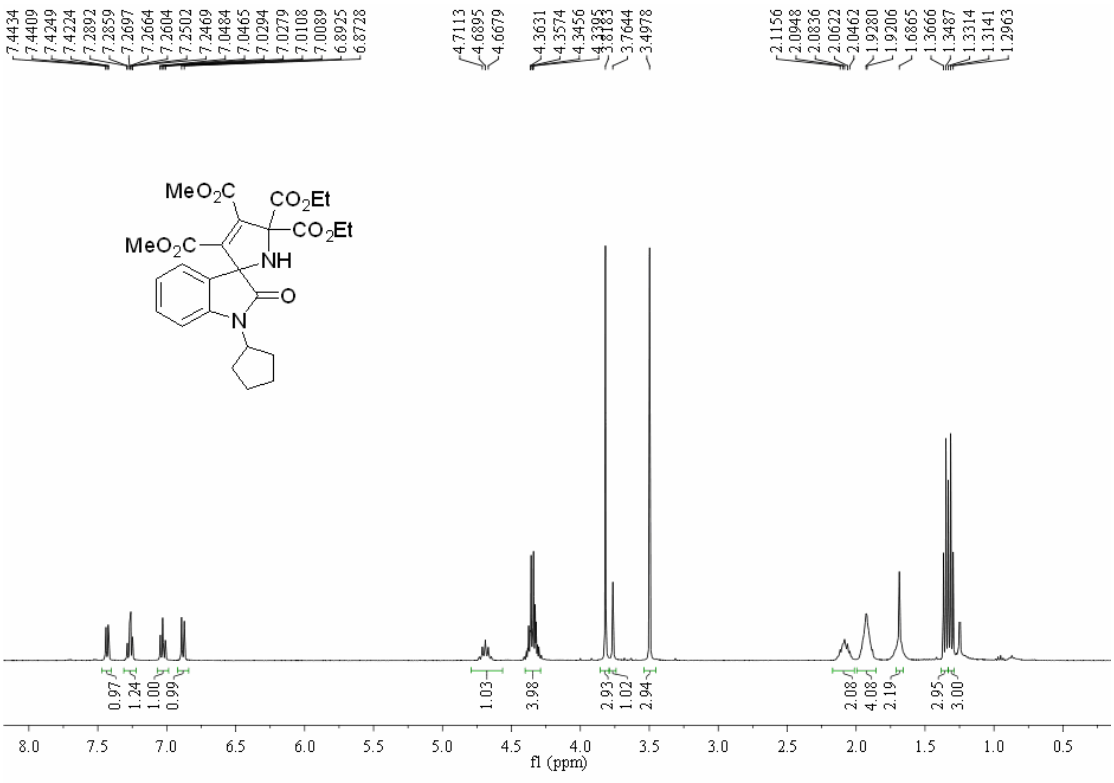
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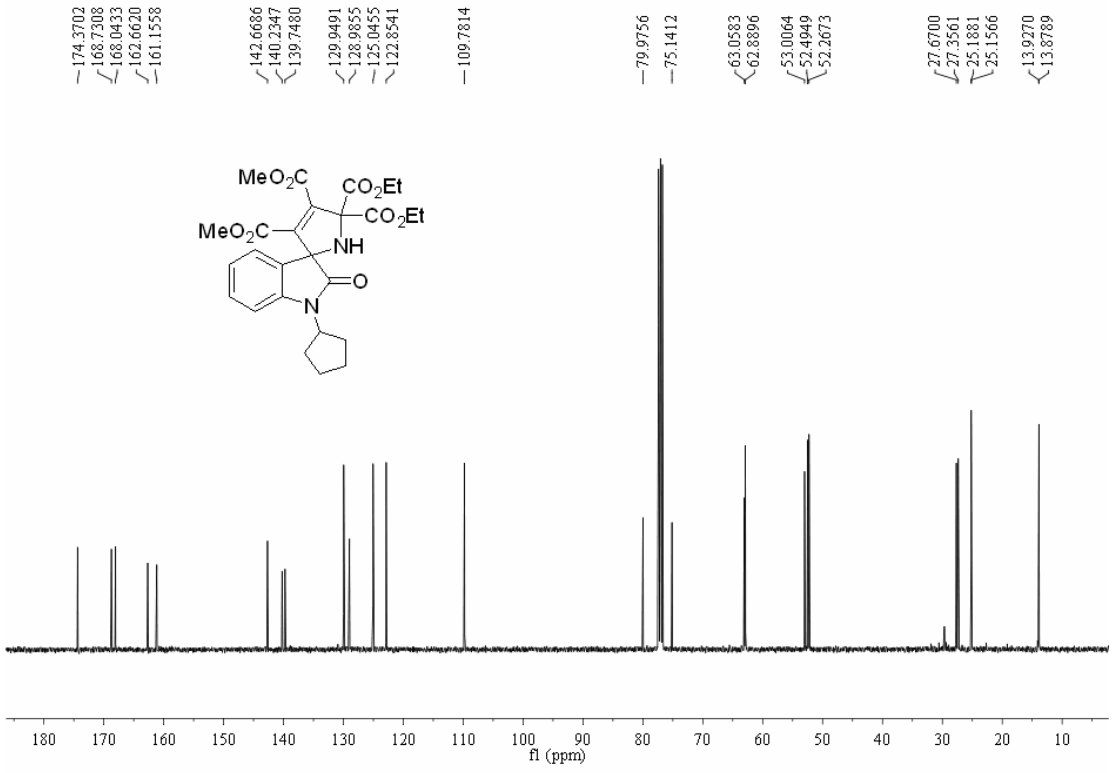
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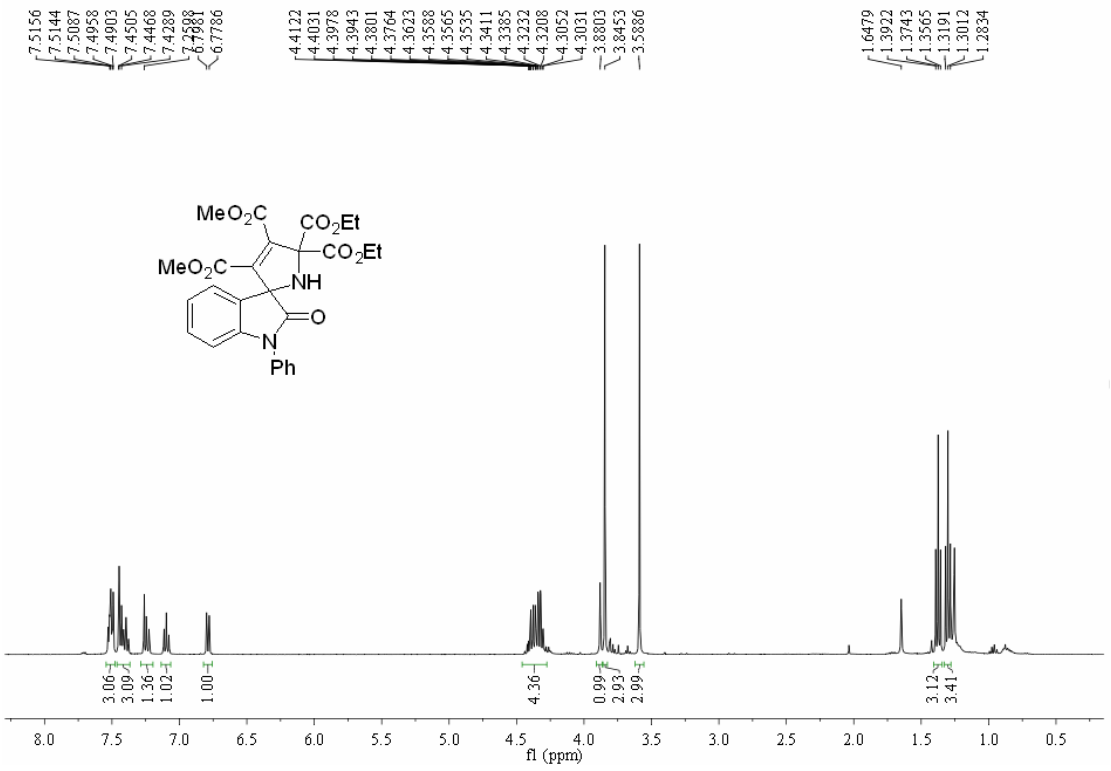
f1 (ppm)

4faa: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7.4468
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7.2588
6.7981
6.7786
4.4122
4.4031
4.3978
4.3943
4.3801
4.3764
4.3623
4.3588
4.3565
4.3535
4.3411
4.3385
4.3232
4.3208
4.3052
4.3031
3.8803
3.8453
3.5886
1.6479
1.3922
1.3743
1.3565
1.3191
1.3012
1.2834
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
Ph
3.06
3.09
1.36
1.02
1.00
4.36
0.99
2.93
2.99
3.12
3.41
8.0
7.5
7.0
6.5
6.0
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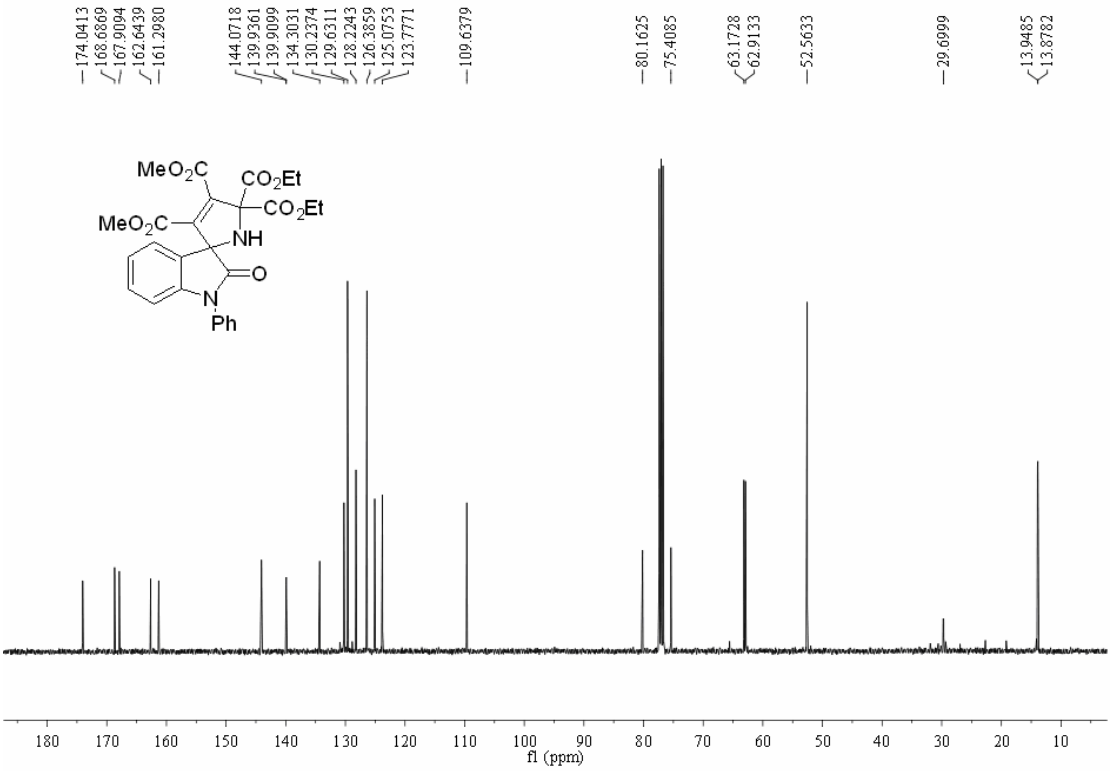
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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139.9361
139.9099
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130.2374
129.6311
128.2243
126.3859
125.0753
123.7771
109.6379
80.1625
75.4085
63.1728
62.9133
52.5633
29.6999
13.9485
13.8782
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
Ph
180
170
160
150
140
130
120
110
100
90
80
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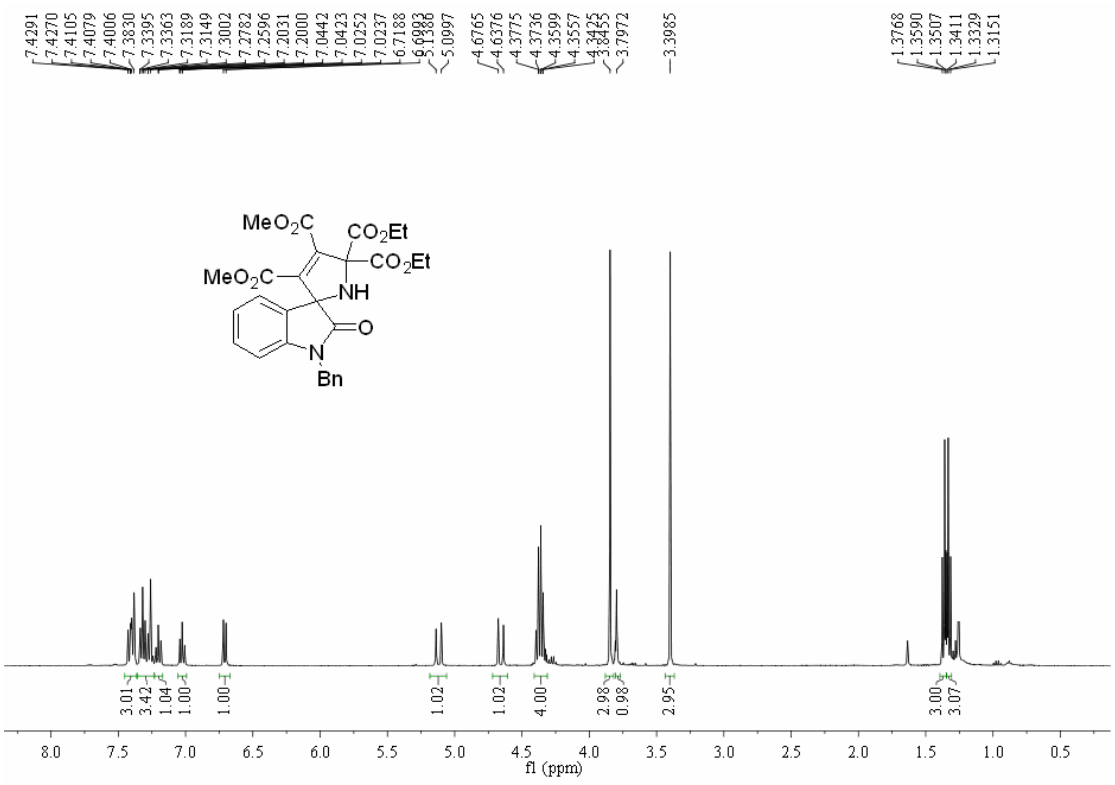
60
50
40
30
20
10
f1 (ppm)

4aaa: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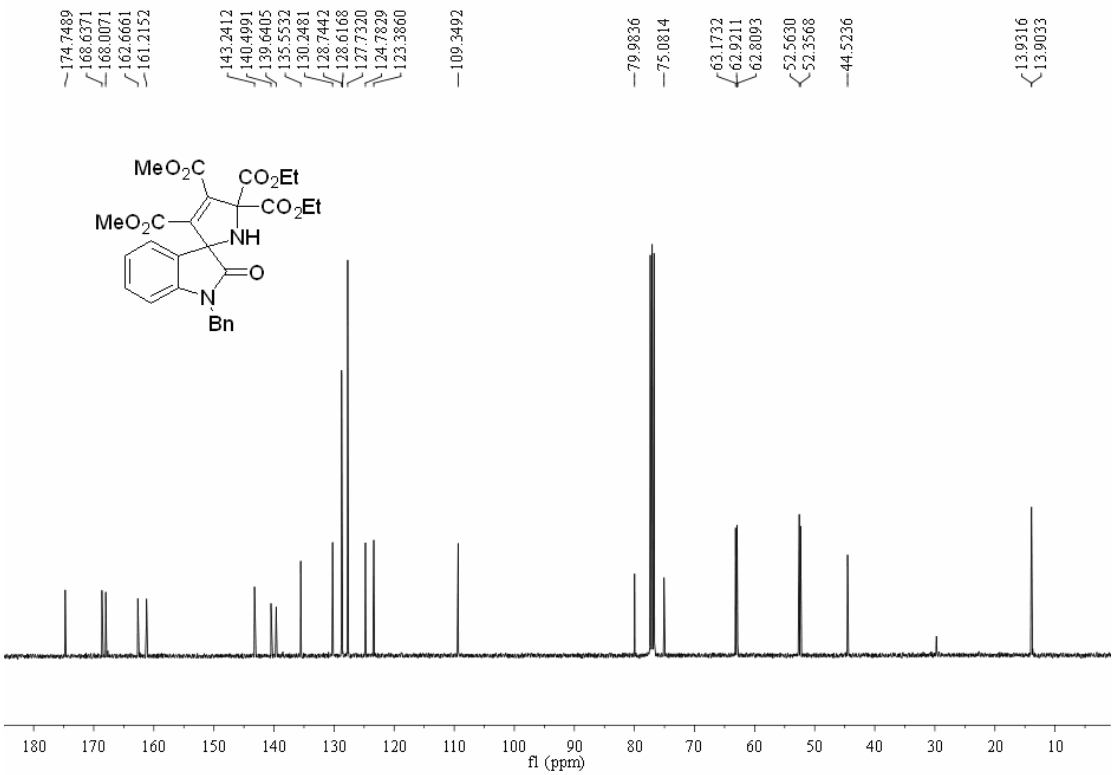
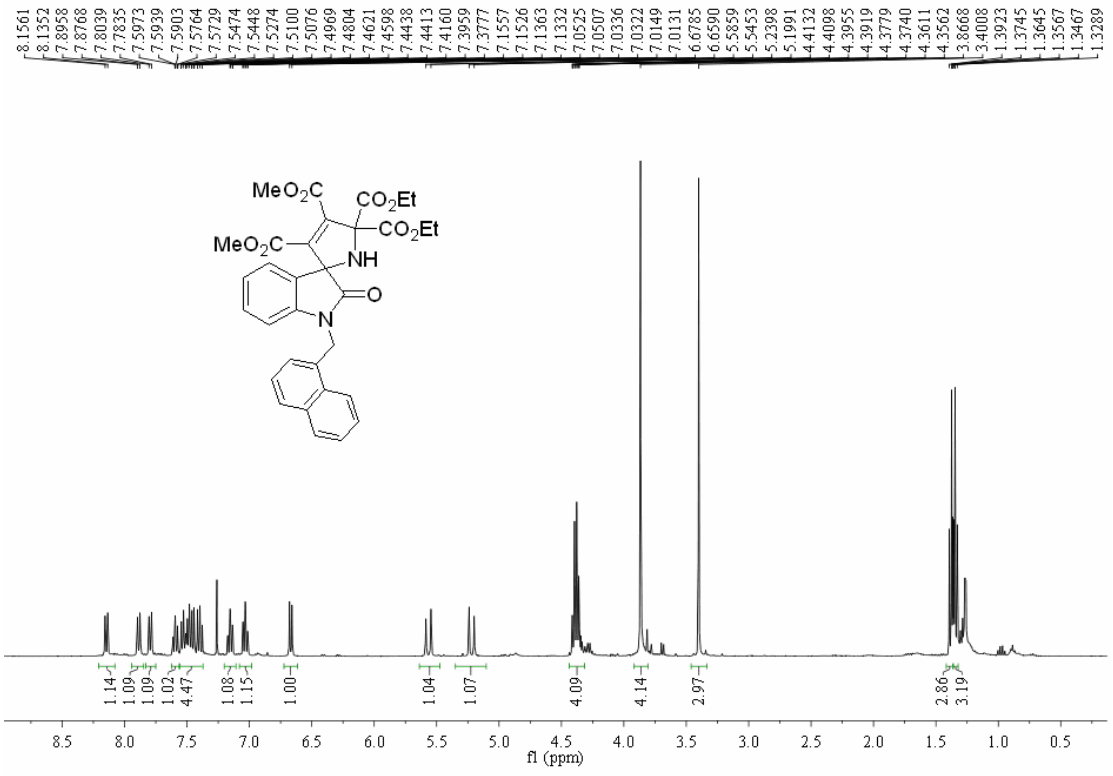
CO2Et
CO2Et
MeO2C
NH
O
N
Bn
fl (ppm)


MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
Bn
fl (ppm)

4gaa: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7.8958
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7.8039
7.7835
7.5973
7.5939
7.5903
7.5764
7.5729
7.5474
7.5448
7.5274
7.5100
7.5076
7.4969
7.4804
7.4621
7.4598
7.4438
7.4413
7.4160
7.3959
7.3777
7.1557
7.1526
7.1363
7.1332
7.0525
7.0507
7.0336
7.0322
7.0149
7.0131
6.6785
6.6590
5.5859
5.5453
5.2398
5.1991
4.4132
4.4098
4.3955
4.3919
4.3779
4.3740
4.3611
4.3562
3.8668
3.4008
1.3923
1.3745
1.3645
1.3567
1.3467
1.3289
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
1.14
1.09
1.09
1.02
4.47
1.08
1.15
1.00
1.04
1.07
4.09
4.14
2.97
2.86
3.19
8.5
8.0
7.5
7.0
6.5
6.0
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5.0
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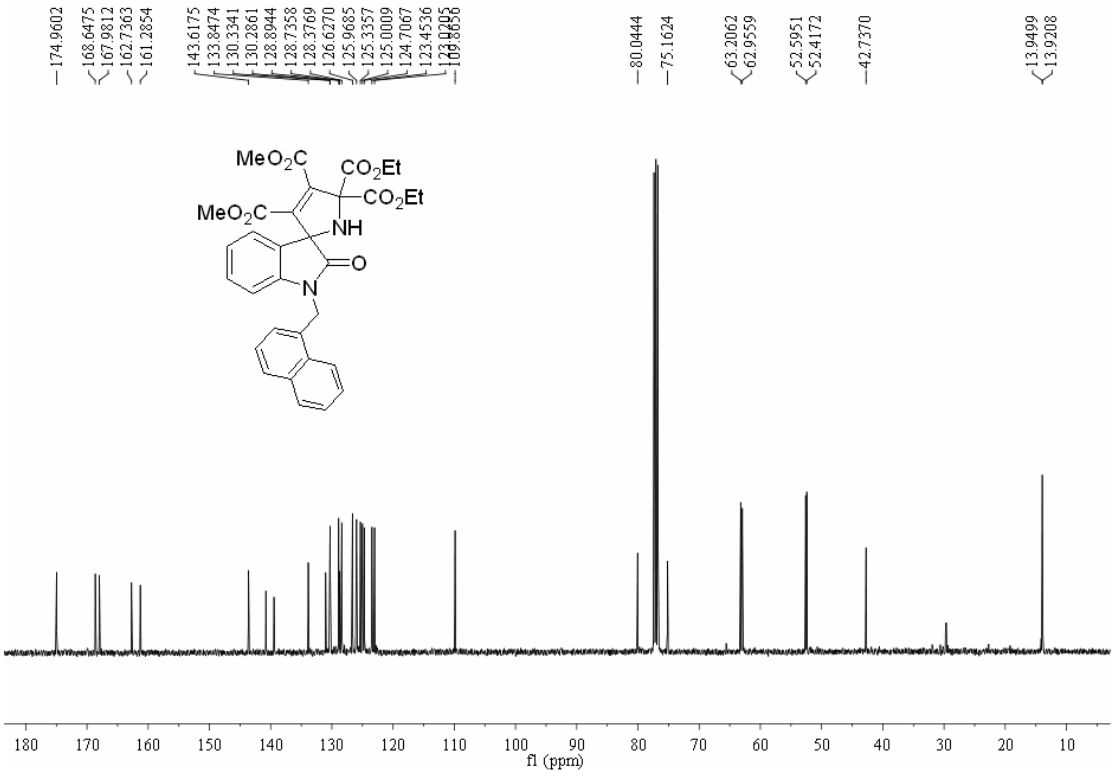
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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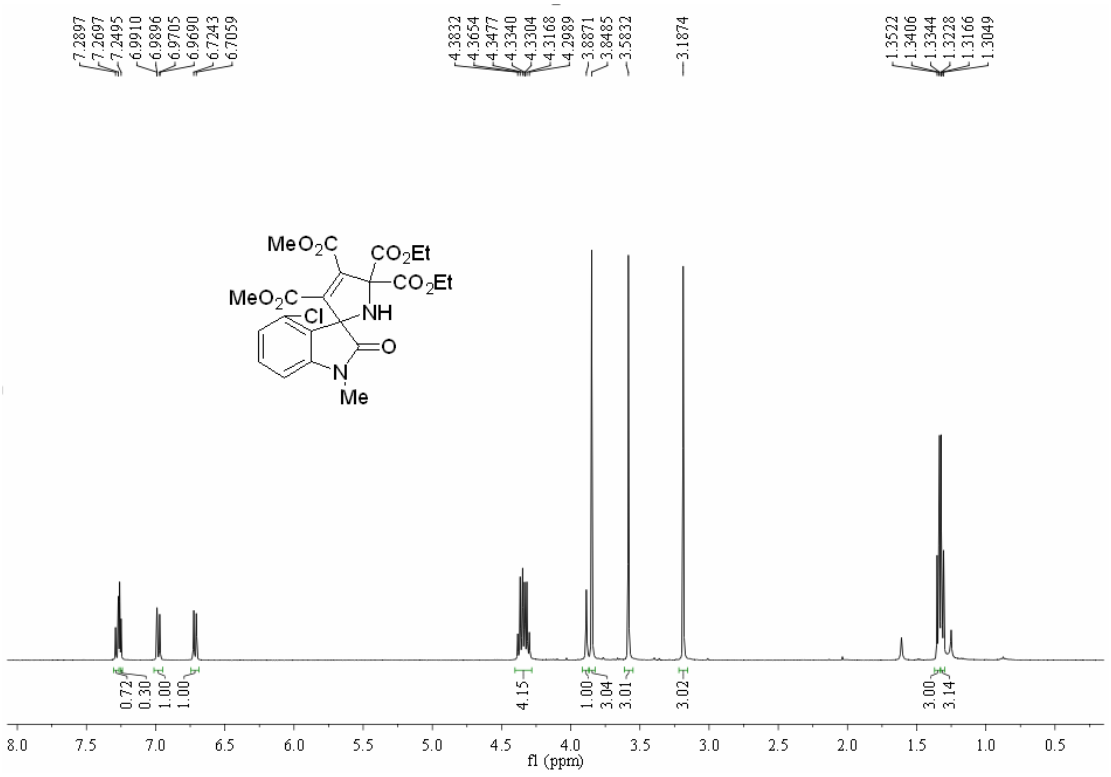
128.7358
128.3769
126.6270
125.9685
125.3357
125.0009
124.7067
123.4536
80.0444
75.1624
63.2062
62.9559
52.5951
52.4172
42.7370
13.9499
13.9208
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

4haa: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7.2697
7.2495
6.9910
6.9896
6.9705
6.9690
6.7243
6.7059
4.3832
4.3654
4.3477
4.3340
4.3304
4.3168
4.2989
3.8871
3.8485
3.5832
3.1874
1.3522
1.3406
1.3344
1.3228
1.3166
1.3049
MeO2C
CO2Et
CO2Et
MeO2C
Cl
NH
O
N
Me
0.72
0.30
1.00
1.00
4.15
1.00
3.04
3.01
3.02
3.00
3.14
8.0
7.5
7.0
6.5
6.0
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5.0
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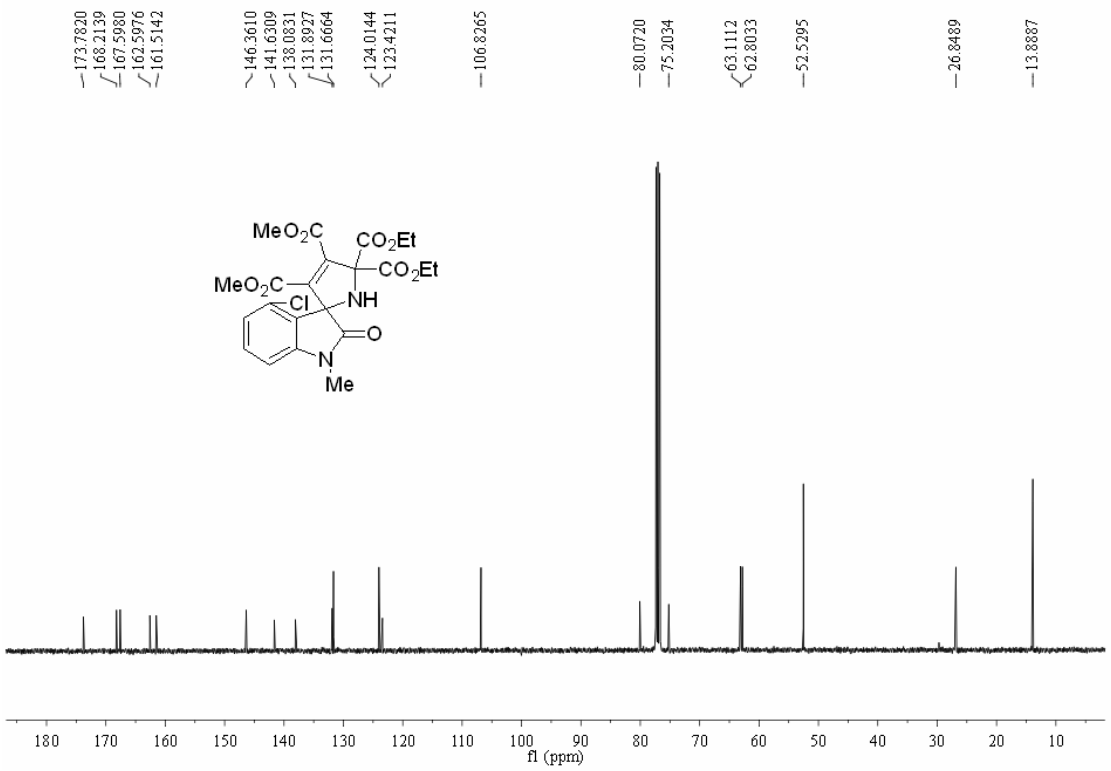
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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167.5980
162.5976
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146.3610
141.6309
138.0831
131.8927
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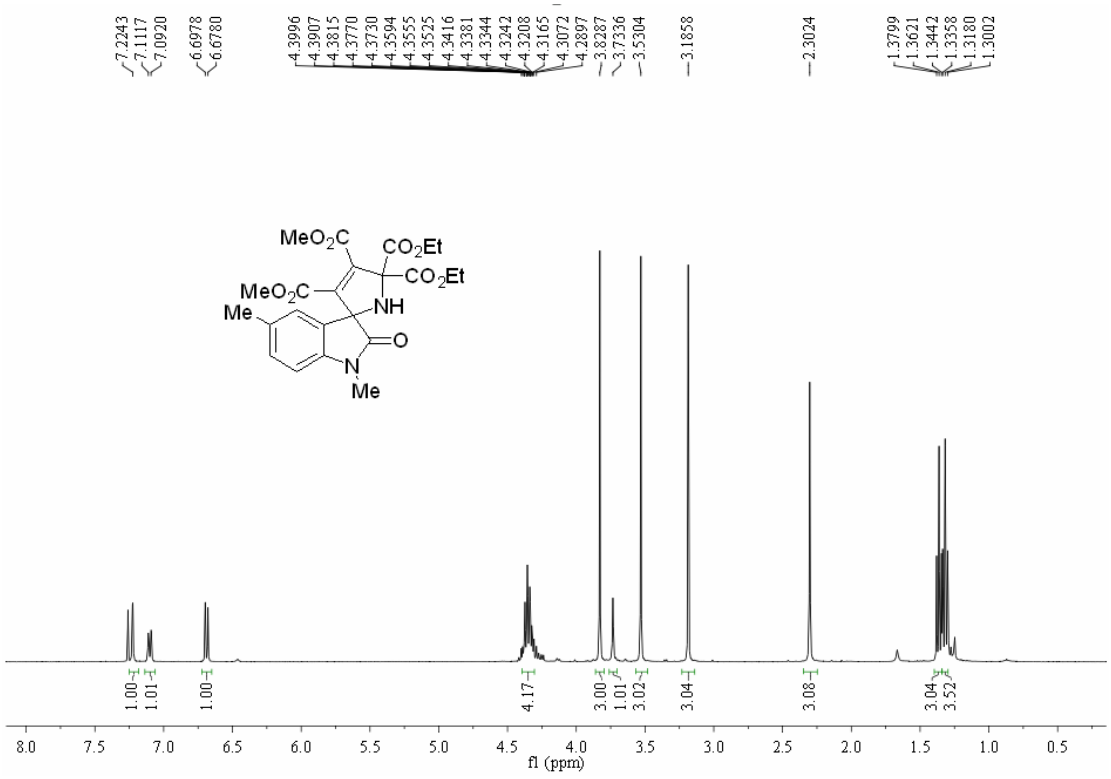
124.0144
123.4211
106.8265
80.0720
75.2034
63.1112
62.8033
52.5295
26.8489
13.8887
MeO2C
CO2Et
CO2Et
MeO2C
Cl
NH
O
N
Me
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

4iaa: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6.6780
4.3996
4.3907
4.3815
4.3770
4.3730
4.3594
4.3555
4.3525
4.3416
4.3381
4.3344
4.3242
4.3208
4.3165
4.3072
4.2897
3.8287
3.7336
3.5304
3.1858
2.3024
1.3799
1.3621
1.3442
1.3358
1.3180
1.3002
MeO2C
CO2Et
CO2Et
MeO2C
NH
Me
O
N
Me
1.00
1.01
1.00
4.17
3.00
1.01
3.02
3.04
3.08
3.04
3.52
8.0
7.5
7.0
6.5
6.0
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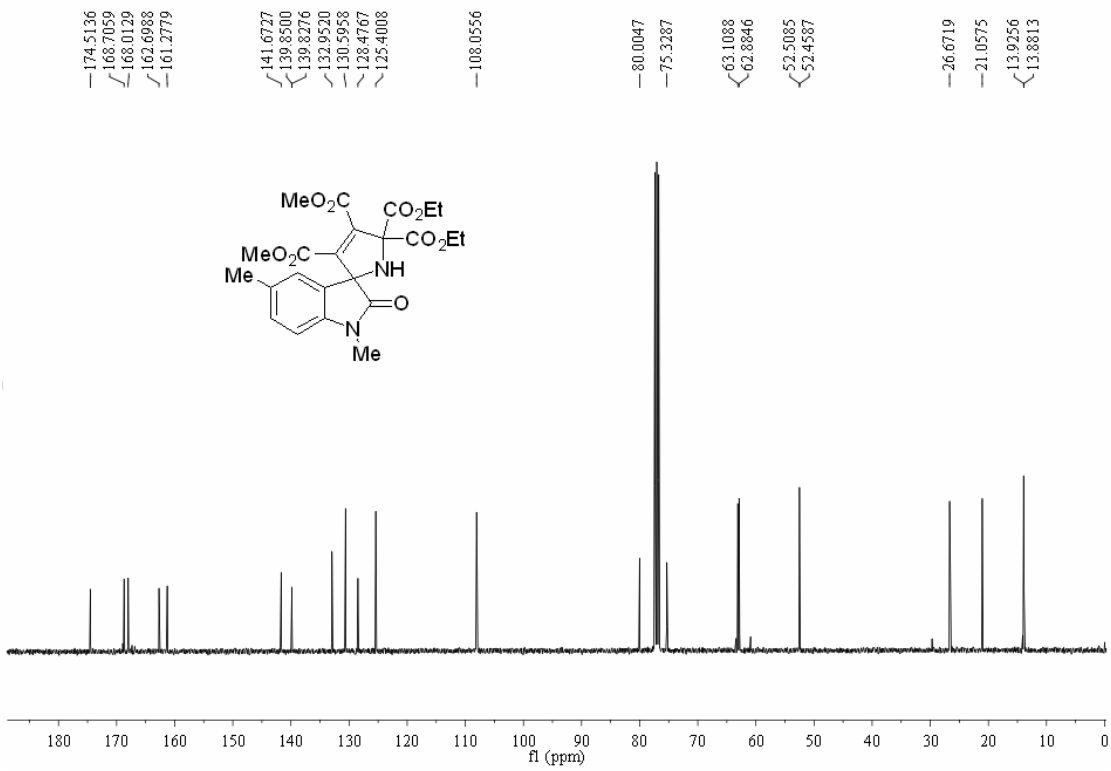
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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139.8500
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132.9520
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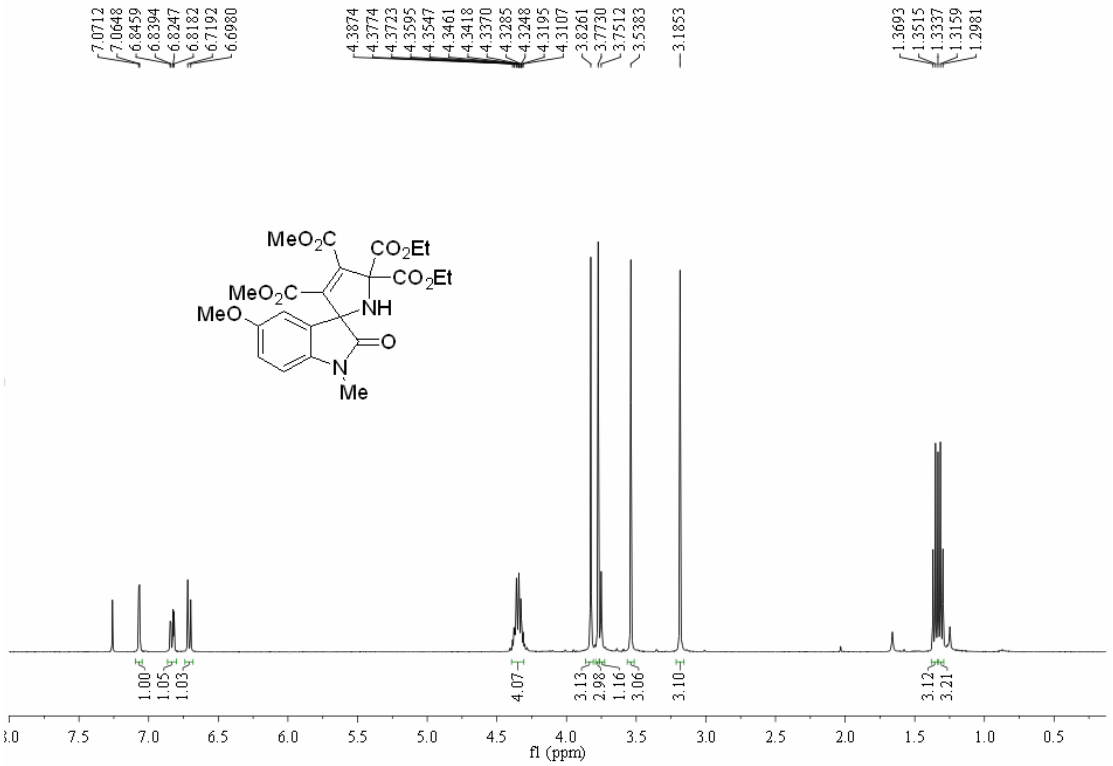
128.4767
125.4008
108.0556
80.0047
75.3287
63.1088
62.8846
52.5085
52.4587
26.6719
21.0575
13.9256
13.8813
MeO2C
CO2Et
CO2Et
MeO2C
NH
Me
O
N
Me
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

4jaa: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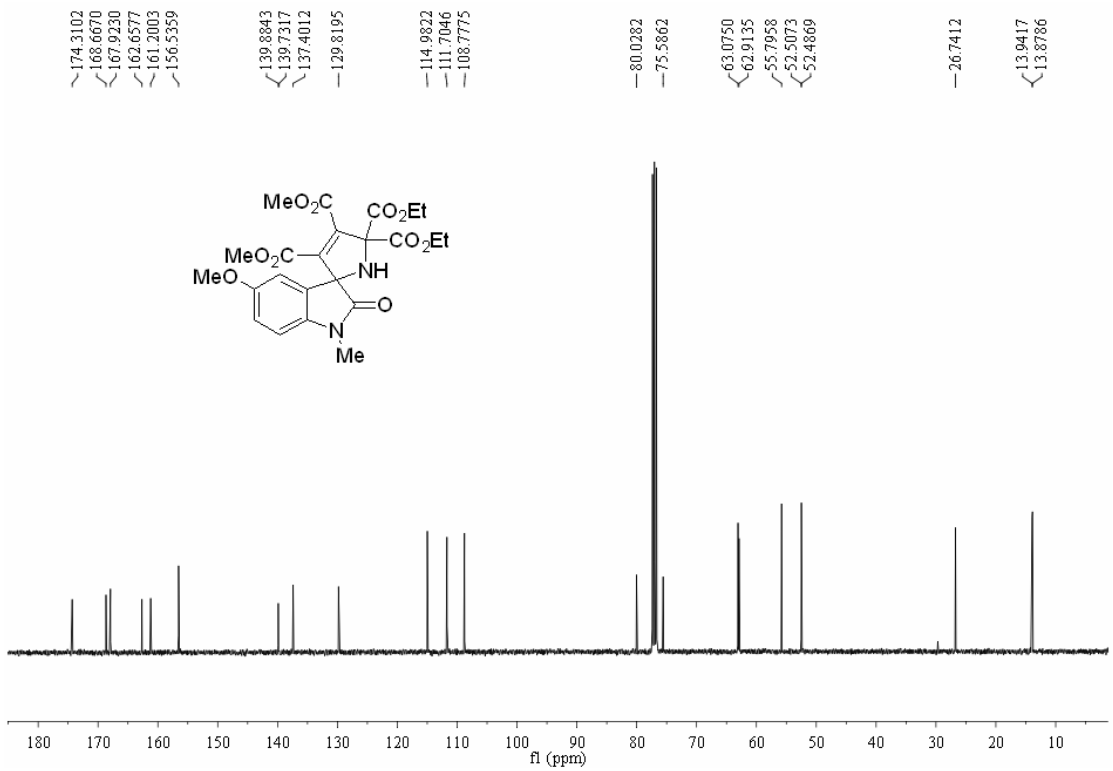
6.8394
6.8247
6.8182
6.7192
6.6980
4.3874
4.3774
4.3723
4.3595
4.3547
4.3461
4.3418
4.3370
4.3285
4.3248
4.3195
4.3107
3.8261
3.7730
3.7512
3.5383
3.1853
1.3693
1.3515
1.3337
1.3159
1.2981
MeO2C
CO2Et
CO2Et
MeO2C
NH
MeO
O
N
Me
1.00
1.05
1.03
4.07
3.13
2.98
1.16
3.06
3.10
3.12
3.21
fl (ppm)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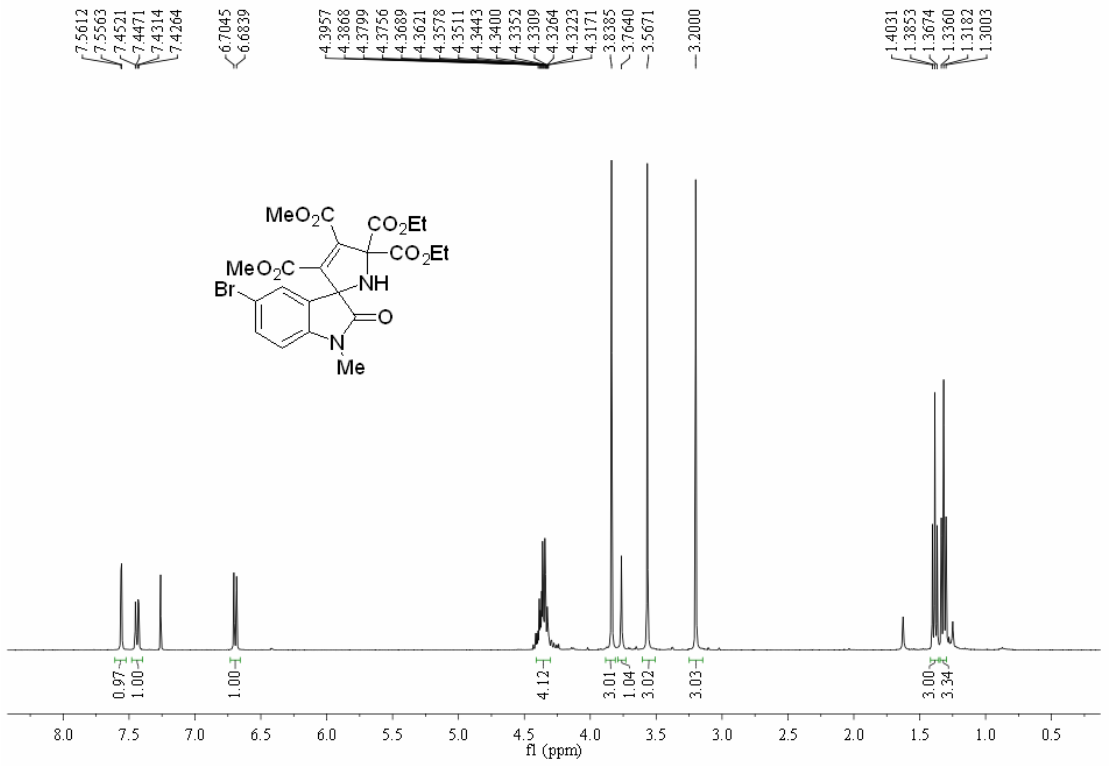
114.9822
111.7046
108.7775
80.0282
75.5862
63.0750
62.9135
55.7958
52.5073
52.4869
26.7412
13.9417
13.8786
MeO2C
CO2Et
CO2Et
MeO2C
NH
MeO
O
N
Me
fl (ppm)

4kaa: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6.7045
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4.3868
4.3799
4.3756
4.3689
4.3621
4.3578
4.3511
4.3443
4.3400
4.3352
4.3309
4.3264
4.3223
4.3171
3.8385
3.7640
3.5671
3.2000
1.4031
1.3853
1.3674
1.3360
1.3182
1.3003
MeO2C
CO2Et
CO2Et
MeO2C
NH
Br
O
N
Me
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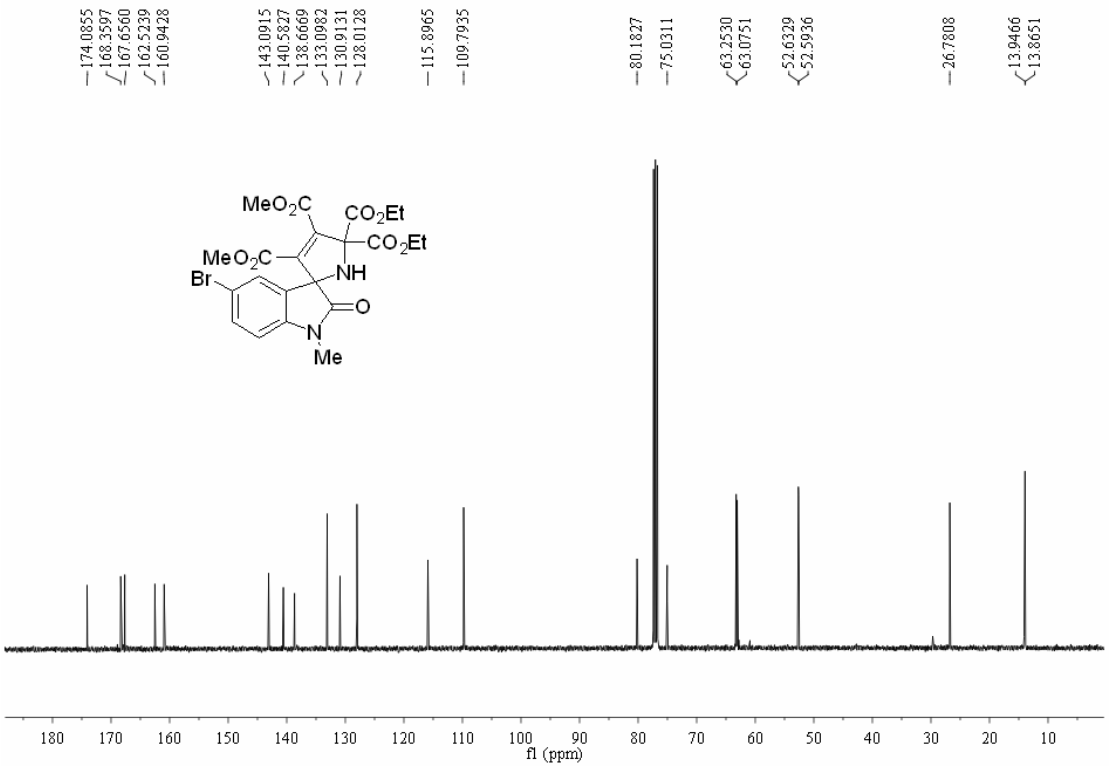
1.00
4.12
3.01
1.04
3.02
3.03
3.00
3.34
fl (ppm)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140.5827
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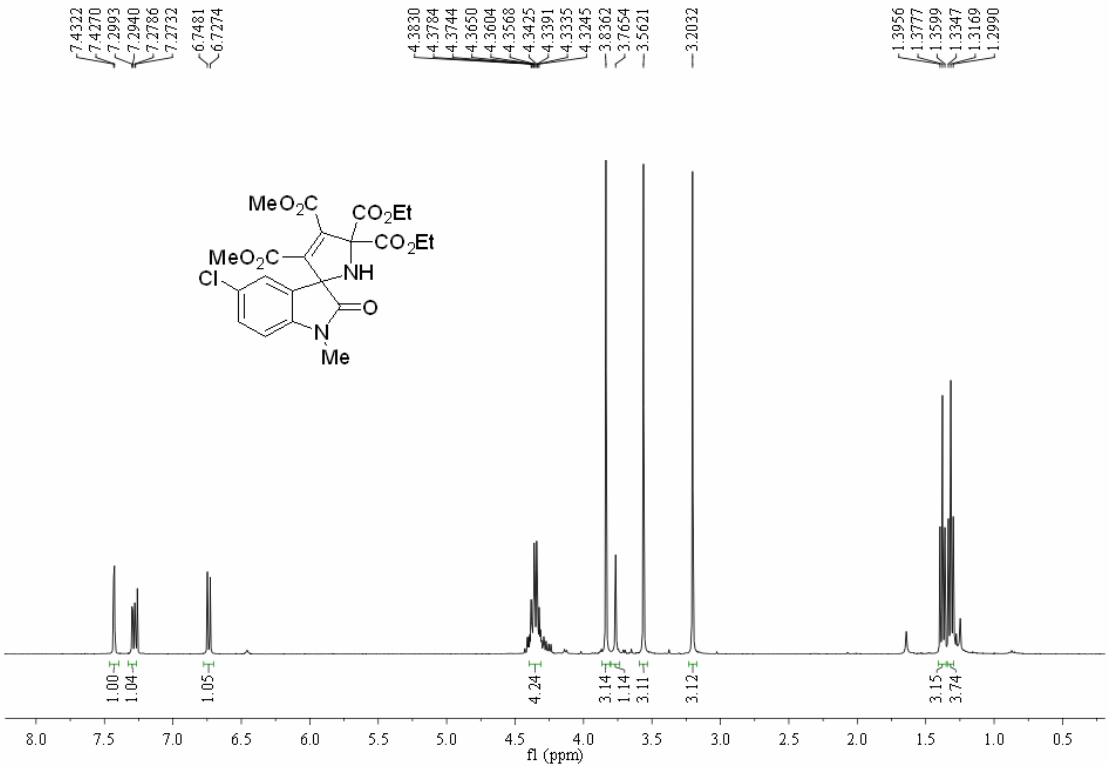
133.0982
130.9131
128.0128
115.8965
109.7935
80.1827
75.0311
63.2530
63.0751
52.6329
52.5936
26.7808
13.9466
13.8651
MeO2C
CO2Et
CO2Et
MeO2C
NH
Br
O
N
Me
fl (ppm)

4laa: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7.2732
6.7481
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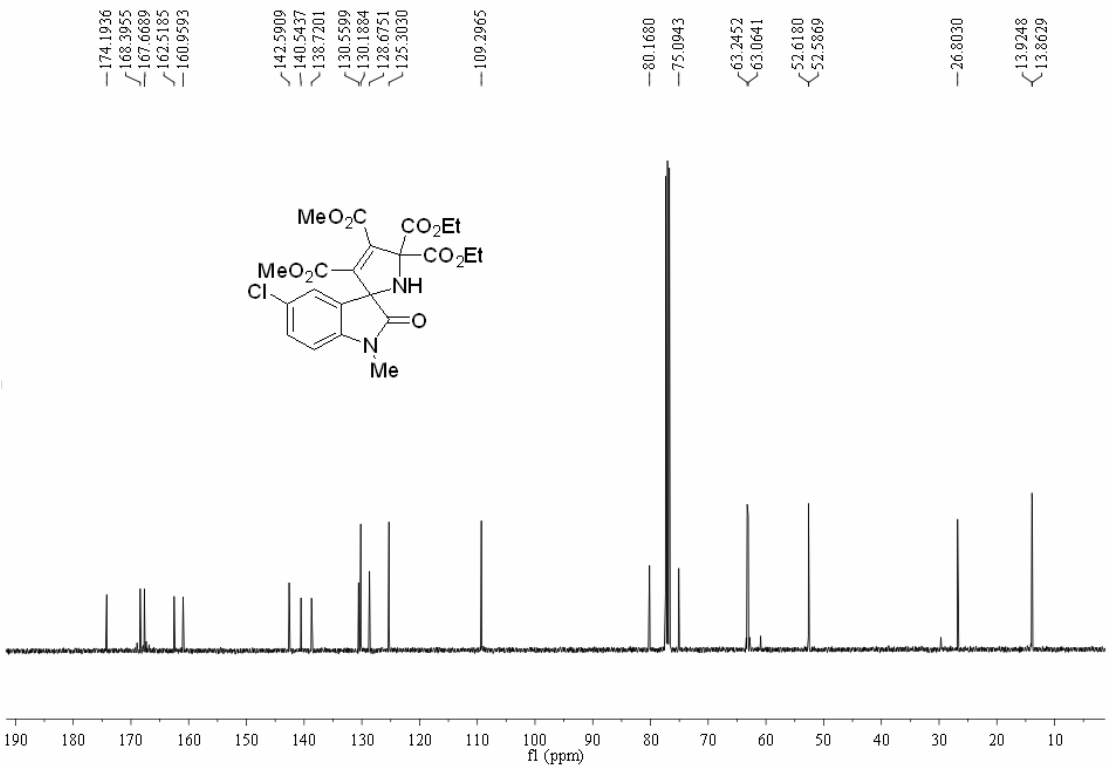
4.3650
4.3604
4.3568
4.3425
4.3391
4.3335
4.3245
3.8362
3.7654
3.5621
3.2032
1.3956
1.3777
1.3599
1.3347
1.3169
1.2990
MeO2C
CO2Et
CO2Et
MeO2C
NH
Cl
O
N
Me
1.00
1.04
1.05
4.24
3.14
1.14
3.11
3.12
3.15
3.74
fl (ppm)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130.1884
128.6751
125.3030
109.2965
80.1680
75.0943
63.2452
63.0641
52.6180
52.5869
26.8030
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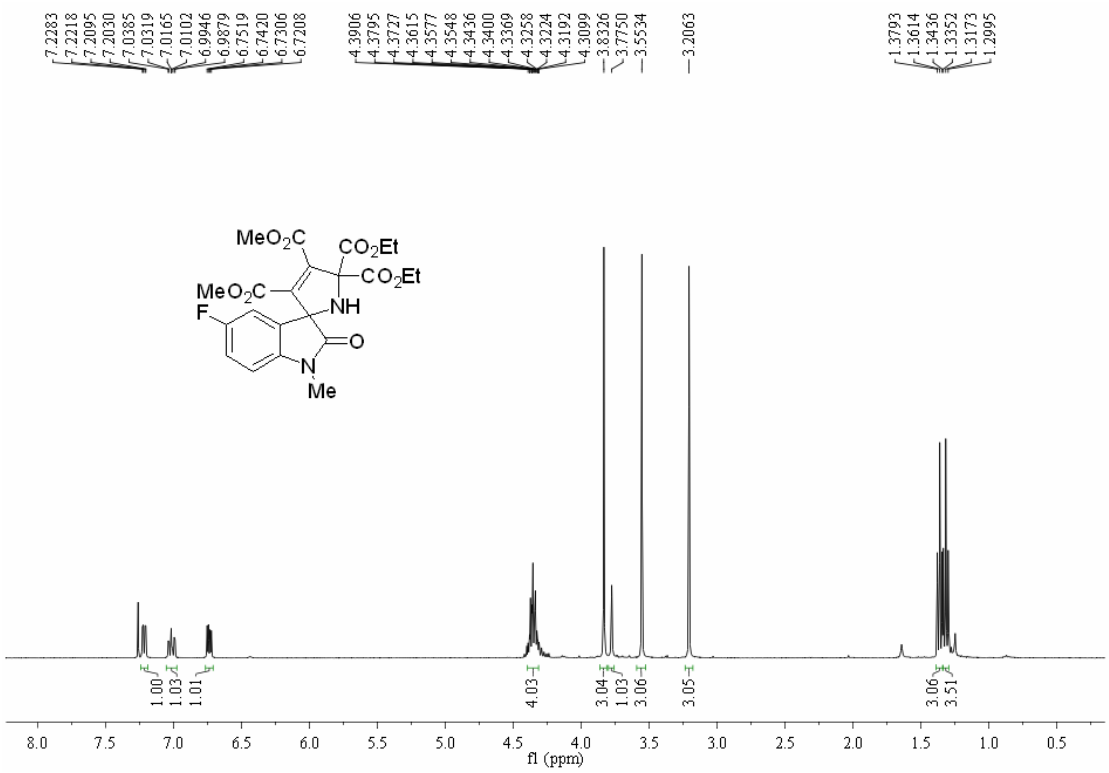
13.8629
MeO2C
CO2Et
CO2Et
MeO2C
NH
Cl
O
N
Me
fl (ppm)

4maa: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7.0165
7.0102
6.9946
6.9879
6.7519
6.7420
6.7306
6.7208
4.3906
4.3795
4.3727
4.3615
4.3577
4.3548
4.3436
4.3400
4.3369
4.3258
4.3224
4.3192
4.3099
3.8326
3.7750
3.5534
3.2063
1.3793
1.3614
1.3436
1.3352
1.3173
1.2995
MeO2C
CO2Et
CO2Et
MeO2C
NH
F
O
N
Me
1.00
1.03
1.01
4.03
3.04
1.03
3.06
3.05
3.06
3.51
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7.0
6.5
6.0
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4.0
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3.0
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1.5
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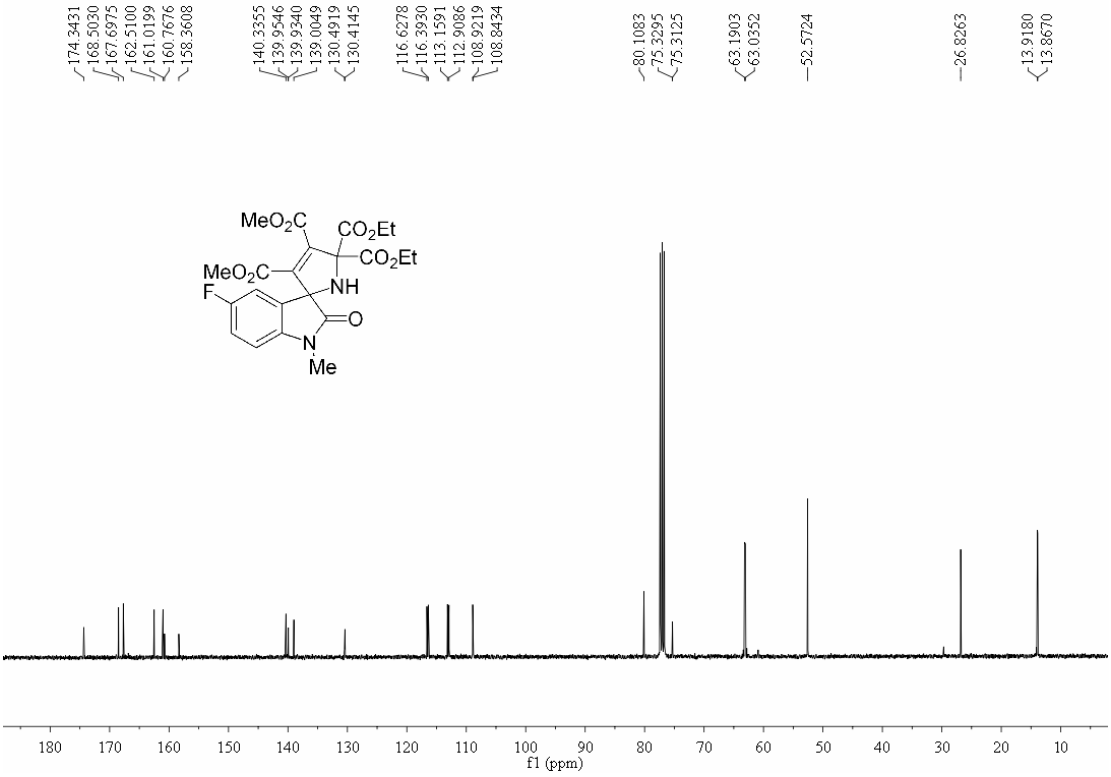
0.5
f1 (ppm)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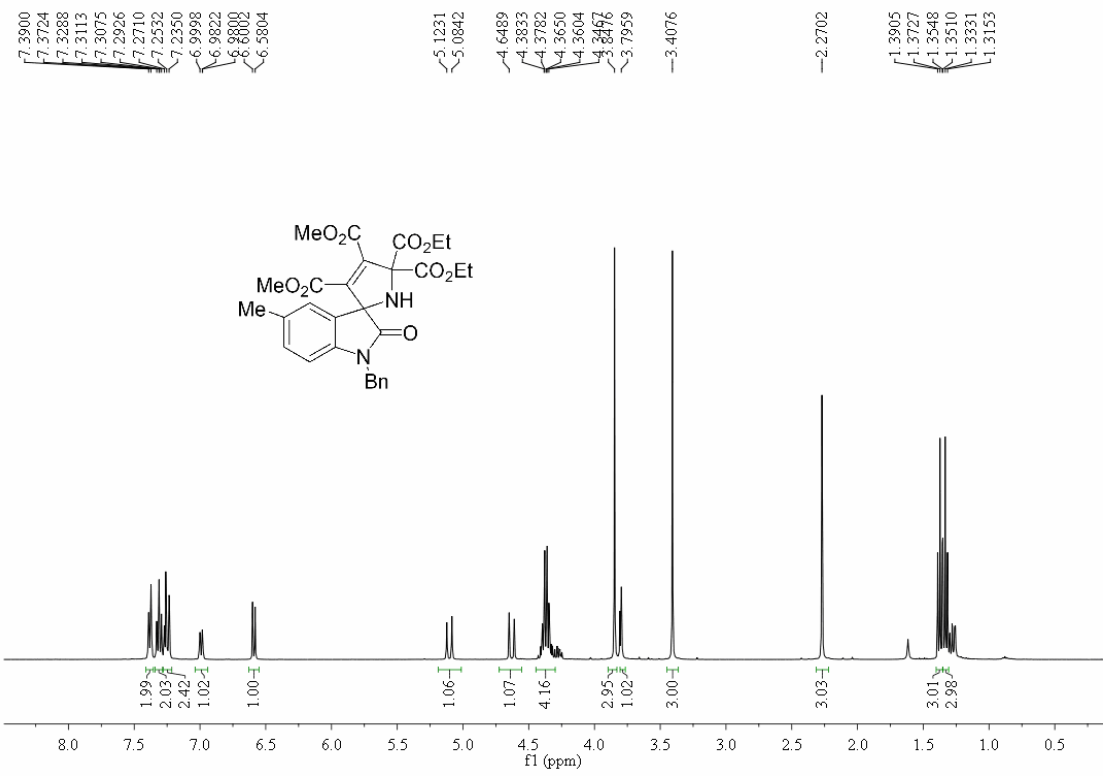
139.9340
139.0049
130.4919
130.4145
116.6278
116.3930
113.1591
112.9086
108.9219
108.8434
80.1083
75.3295
75.3125
63.1903
63.0352
52.5724
26.8263
13.9180
13.8670
MeO2C
CO2Et
CO2Et
MeO2C
NH
F
O
N
Me
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

4naa: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6.9822
6.6882
6.6802
6.5804
5.1231
5.0842
4.6489
4.3833
4.3782
4.3650
4.3604
4.3467
4.3426
3.7959
3.4076
2.2702
1.3905
1.3727
1.3548
1.3510
1.3331
1.3153
MeO2C
CO2Et
CO2Et
MeO2C
NH
Me
O
N
Bn
1.99
2.03
2.42
1.02
1.00
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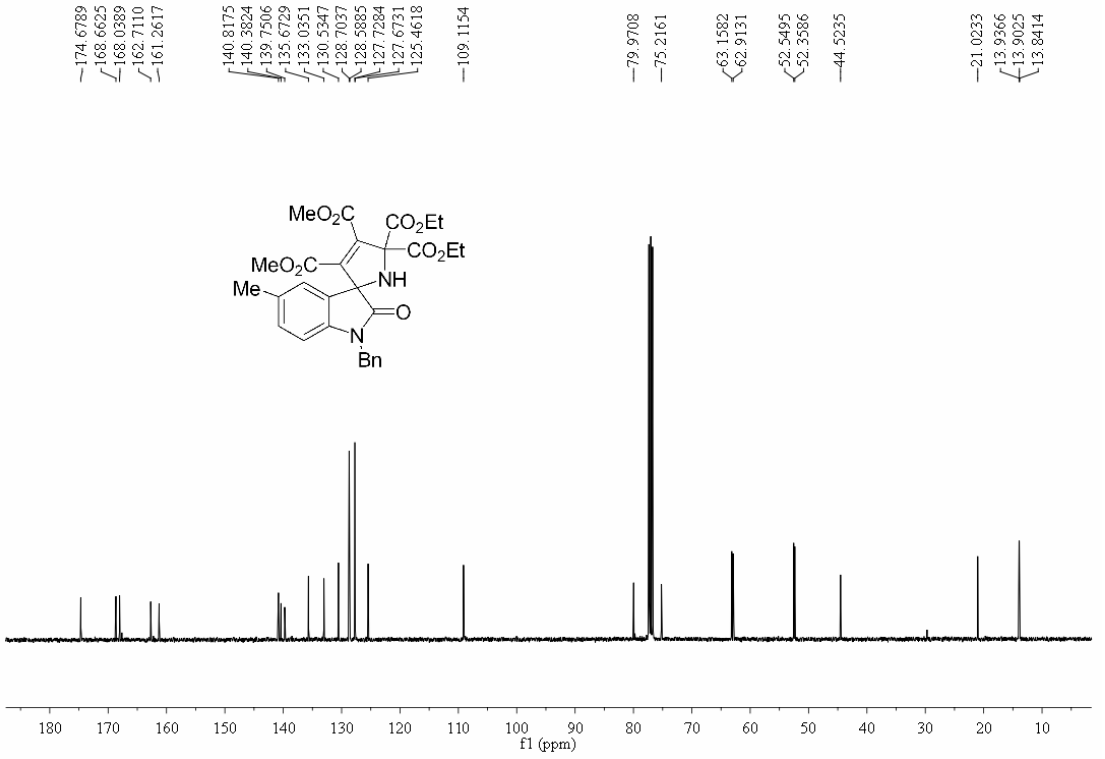
1.07
4.16
2.95
1.02
3.00
3.03
3.01
2.98
f1 (ppm)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140.3824
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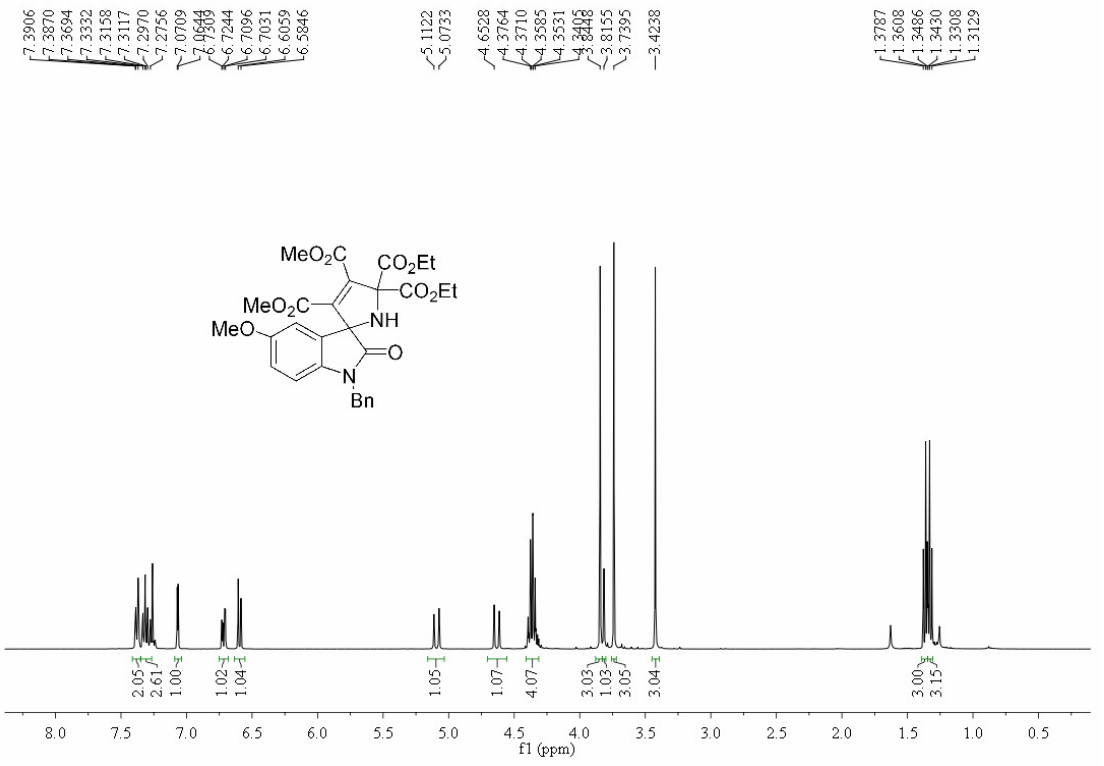
130.5347
128.7037
128.5885
127.7284
127.6731
125.4618
109.1154
79.9708
75.2161
63.1582
62.9131
52.5495
52.3586
44.5235
21.0233
13.9366
13.9025
13.8414
MeO2C
CO2Et
CO2Et
MeO2C
NH
Me
O
N
Bn
f1 (ppm)

4oaa: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CO2Et
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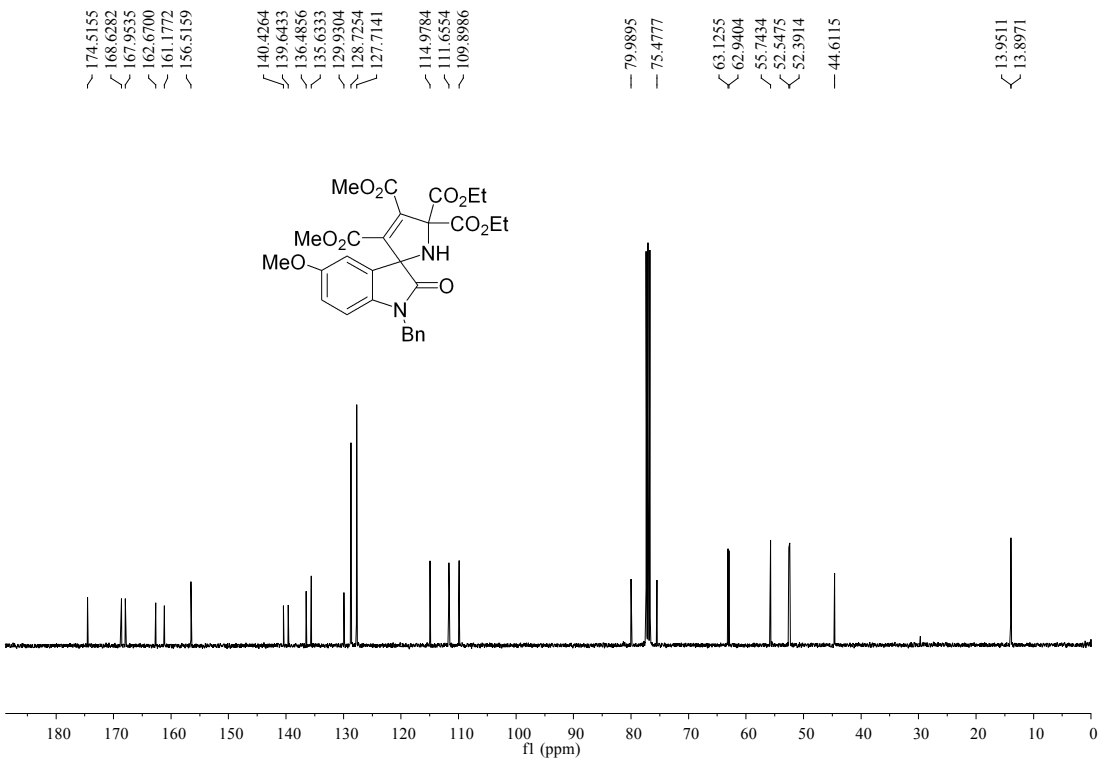
N
Bn
f1 (ppm)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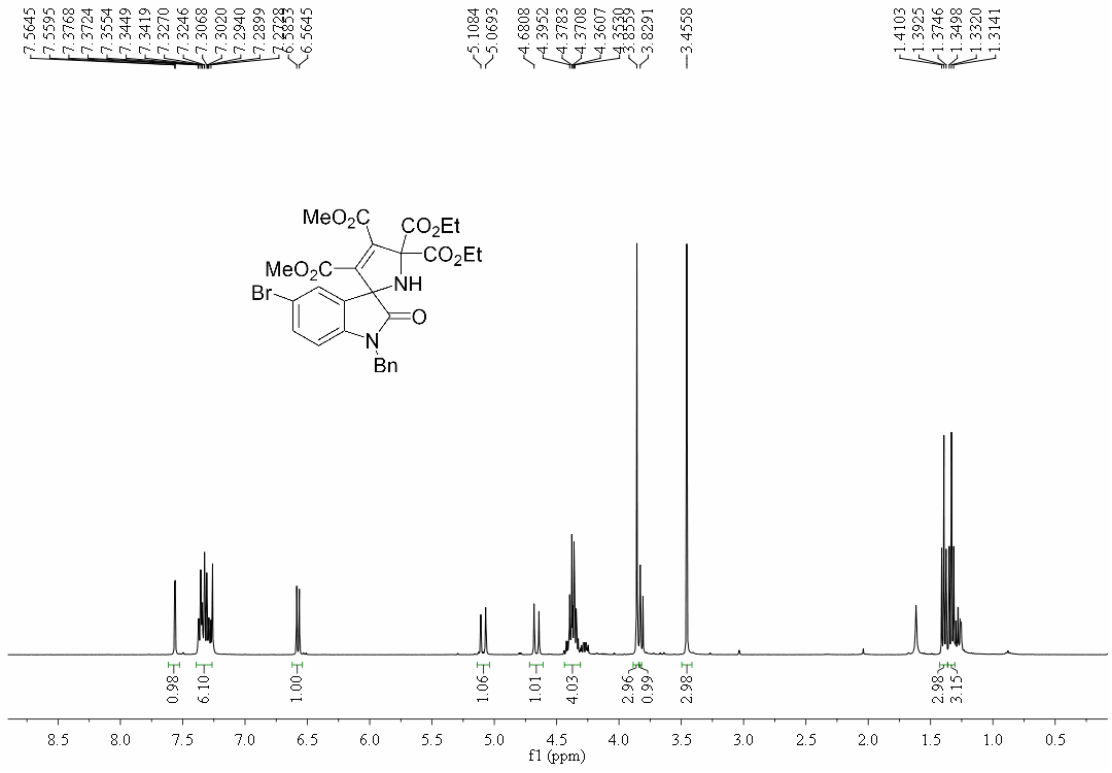
CO2Et
CO2Et
MeO2C
NH
MeO
O
N
Bn
f1 (ppm)

4paa: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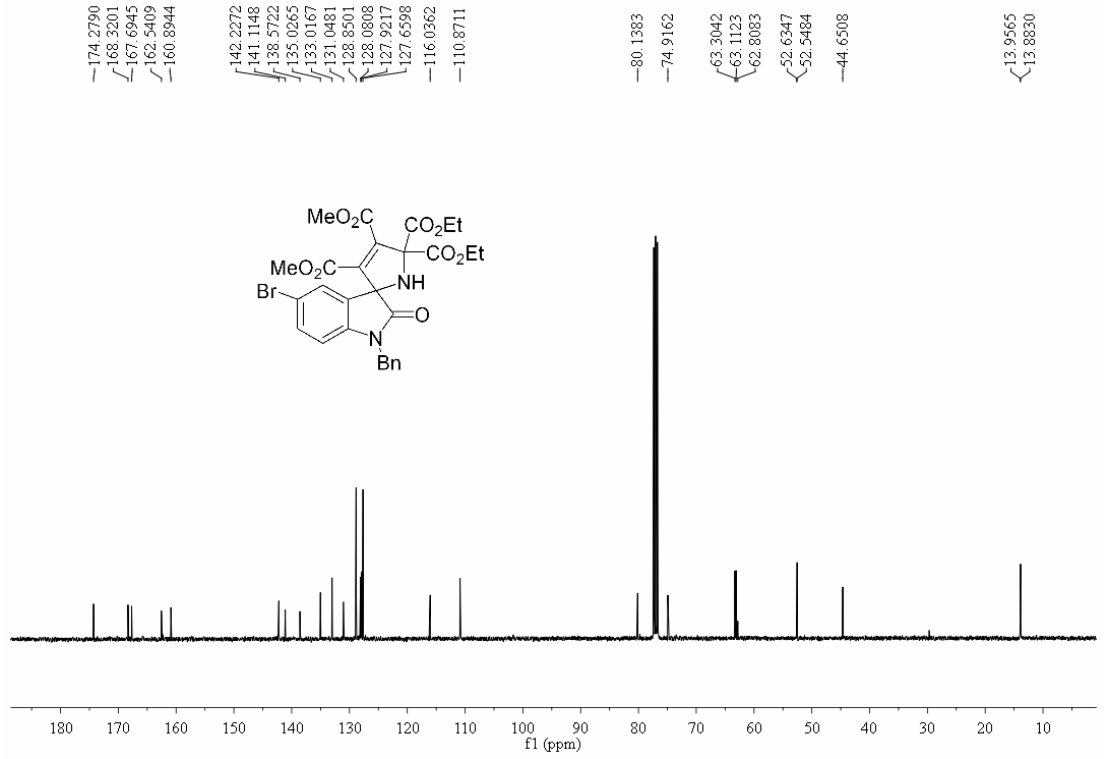
7.3020
7.2940
7.2899
7.2728
6.5553
6.5645
5.1084
5.0693
4.6808
4.3952
4.3783
4.3708
4.3607
4.3530
4.3539
3.8291
3.4558
1.4103
1.3925
1.3746
1.3498
1.3320
1.3141
MeO2C
CO2Et
CO2Et
MeO2C
NH
Br
O
N
Bn
0.98
6.10
1.00
1.06
1.01
4.03
2.96
0.99
2.98
2.98
3.15
f1 (ppm)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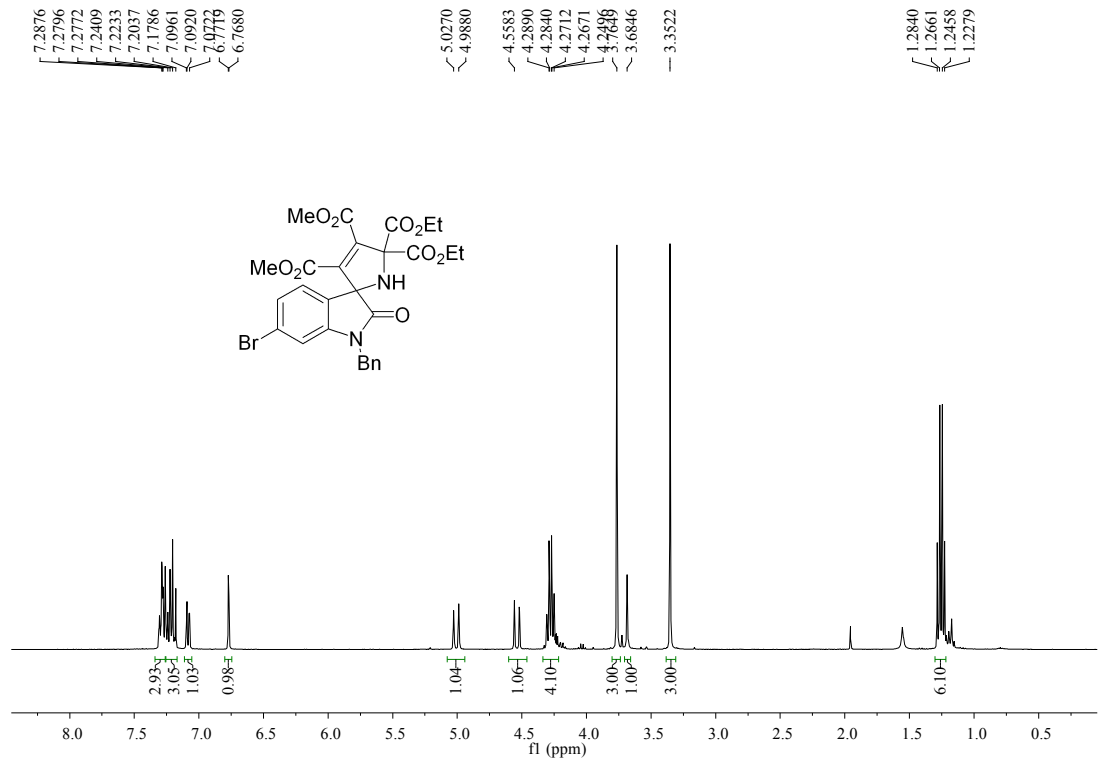
131.0481
128.8501
128.0808
127.9217
127.6598
116.0362
110.8711
80.1383
74.9162
63.3042
63.1123
62.8083
52.6347
52.5484
44.6508
13.9565
13.8830
MeO2C
CO2Et
CO2Et
MeO2C
NH
Br
O
N
Bn
f1 (ppm)

4qaa: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7.1786
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7.0920
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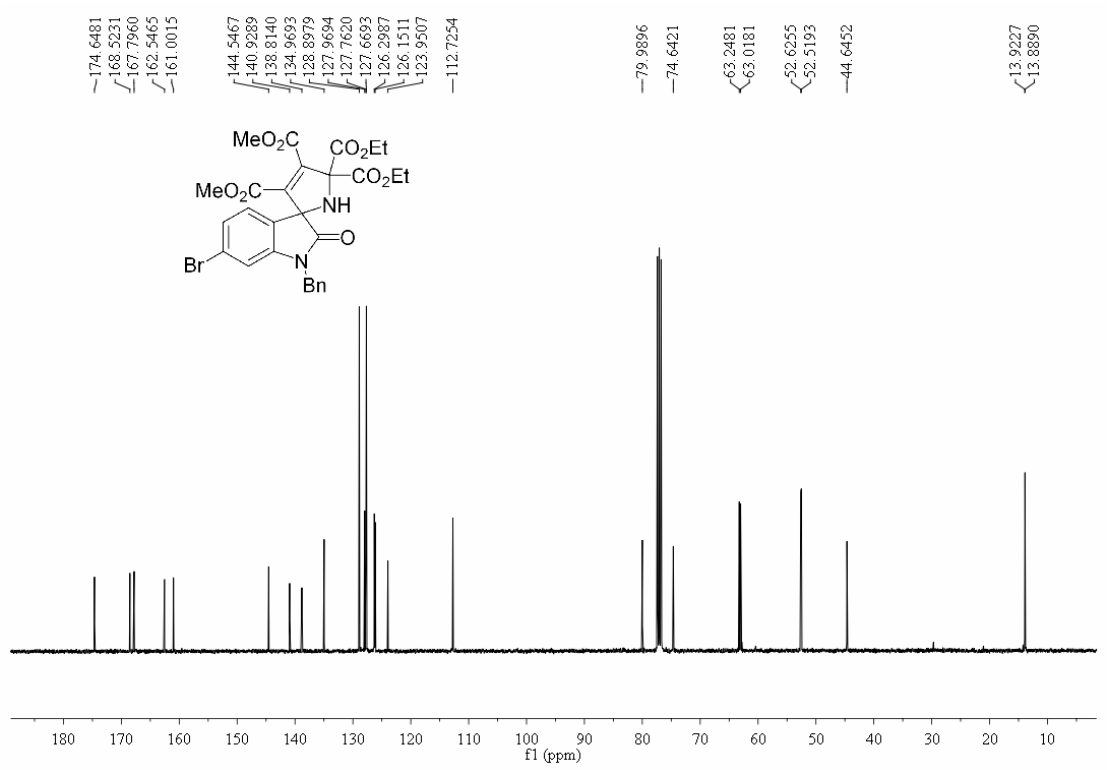
6.7770
6.7680
5.0270
4.9880
4.5583
4.2890
4.2840
4.2712
4.2671
4.2496
4.2447
3.7048
3.6846
3.3522
1.2840
1.2661
1.2458
1.2279
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
Br
N
Bn
2.93
3.05
1.03
0.98
1.04
1.06
4.10
3.00
1.00
3.00
6.10
f1 (ppm)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140.9289
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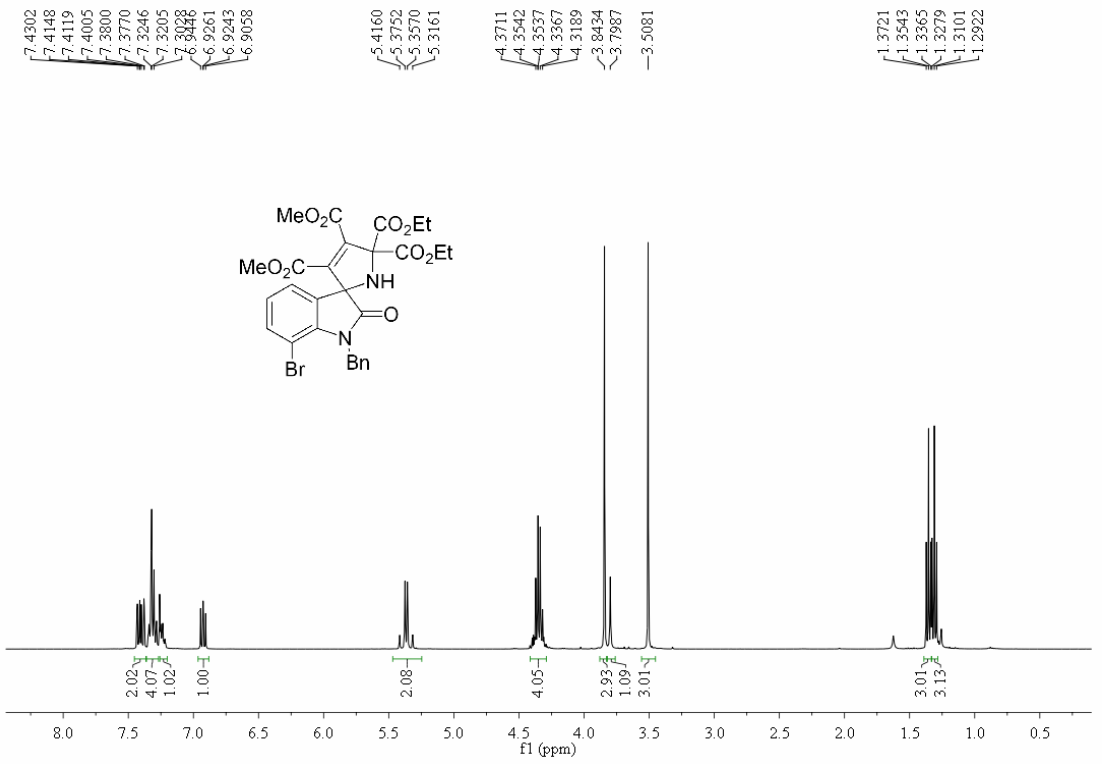
127.9694
127.7620
127.6693
126.2987
126.1511
123.9507
112.7254
79.9896
74.6421
63.2481
63.0181
52.6255
52.5193
44.6452
13.9227
13.8890
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
Br
N
Bn
f1 (ppm)

4raa: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7.3246
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7.3028
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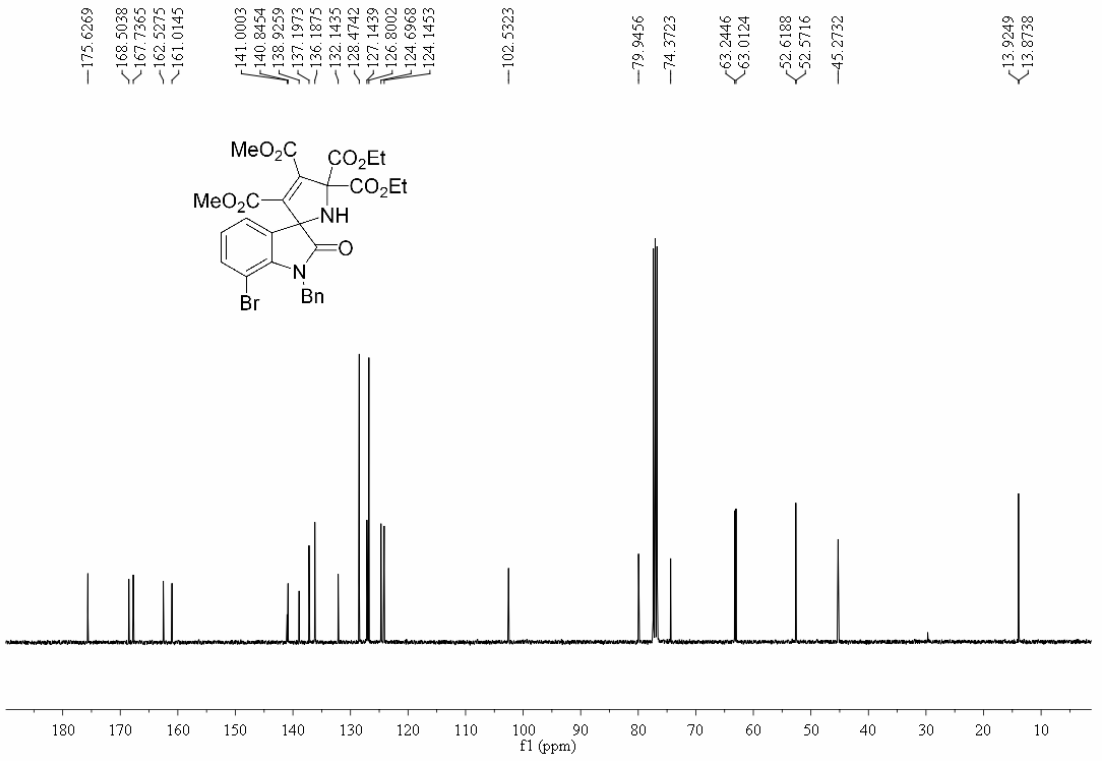
6.9261
6.9243
6.9058
5.4160
5.3752
5.3570
5.3161
4.3711
4.3542
4.3537
4.3367
4.3189
3.8434
3.7987
3.5081
1.3721
1.3543
1.3365
1.3279
1.3101
1.2922
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
Bn
Br
2.02
4.07
1.02
1.00
2.08
4.05
2.93
1.09
3.01
3.01
3.13
f1 (ppm)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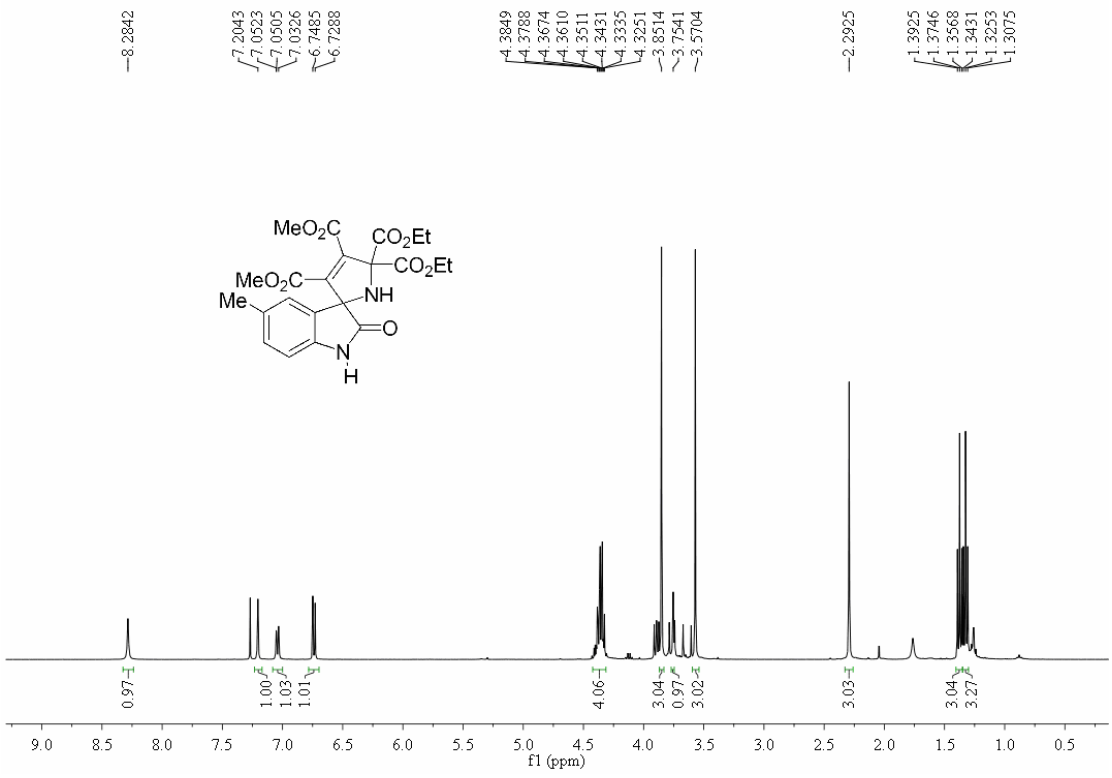
132.1435
128.4742
127.1439
126.8002
124.6968
124.1453
102.5323
79.9456
74.3723
63.2446
63.0124
52.6188
52.5716
45.2732
13.9249
13.8738
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
Bn
Br
f1 (ppm)

4saa: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7.0505
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6.7485
6.7288
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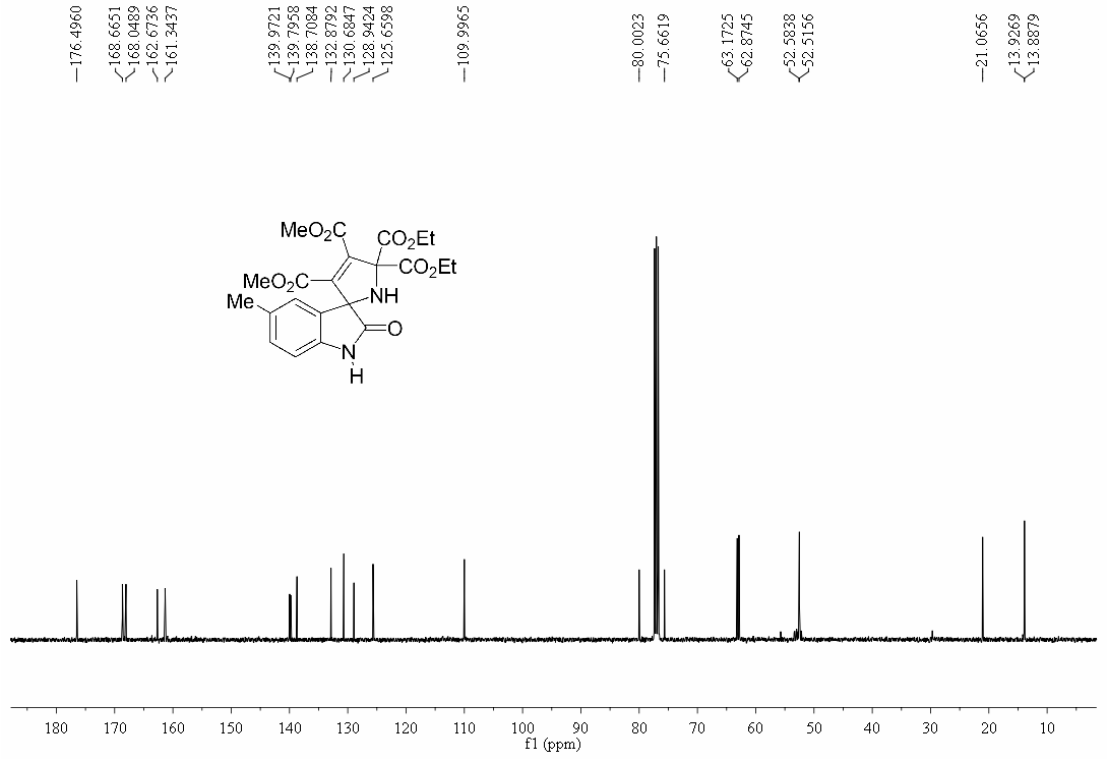
4.3788
4.3674
4.3610
4.3511
4.3431
4.3335
4.3251
3.8514
3.7541
3.5704
2.2925
1.3925
1.3746
1.3568
1.3431
1.3253
1.3075
MeO2C
CO2Et
CO2Et
MeO2C
Me
NH
O
N
H
0.97
1.00
1.03
1.01
4.06
3.04
0.97
3.02
3.03
3.04
3.27
f1 (ppm)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168.0489
162.6736
161.3437
139.9721
139.7958
138.7084
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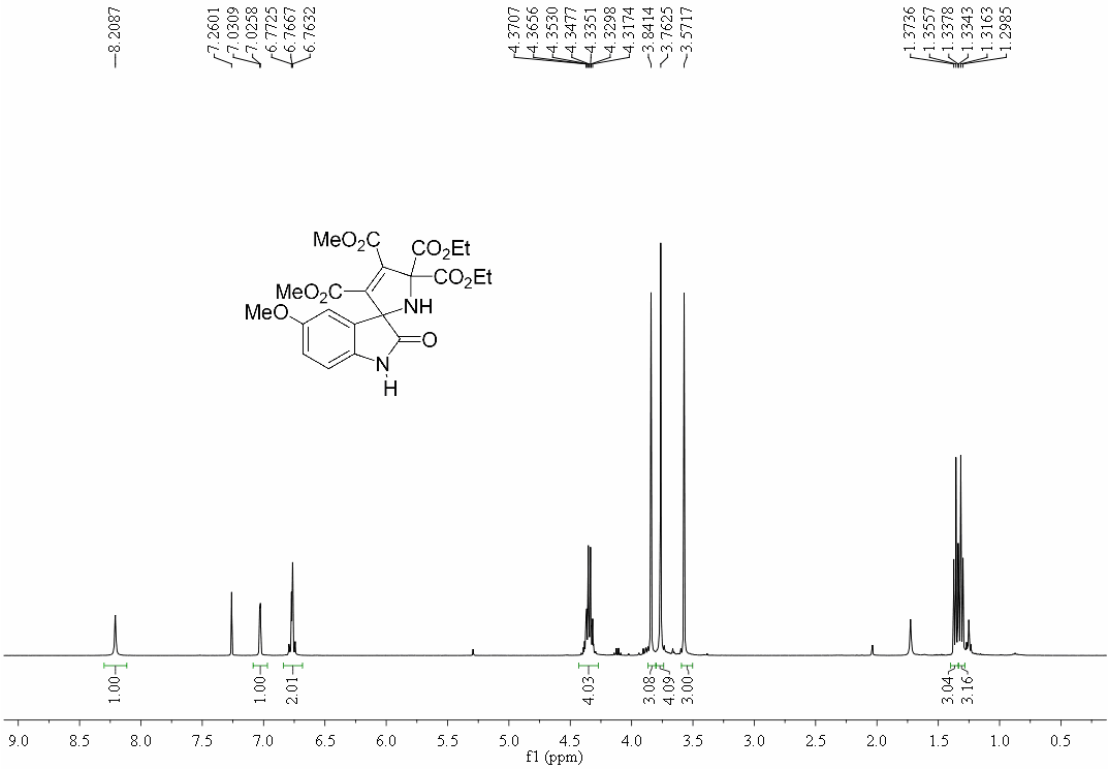
130.6847
128.9424
125.6598
109.9965
80.0023
75.6619
63.1725
62.8745
52.5838
52.5156
21.0656
13.9269
13.8879
MeO2C
CO2Et
CO2Et
MeO2C
Me
NH
O
N
H
f1 (ppm)

4taa: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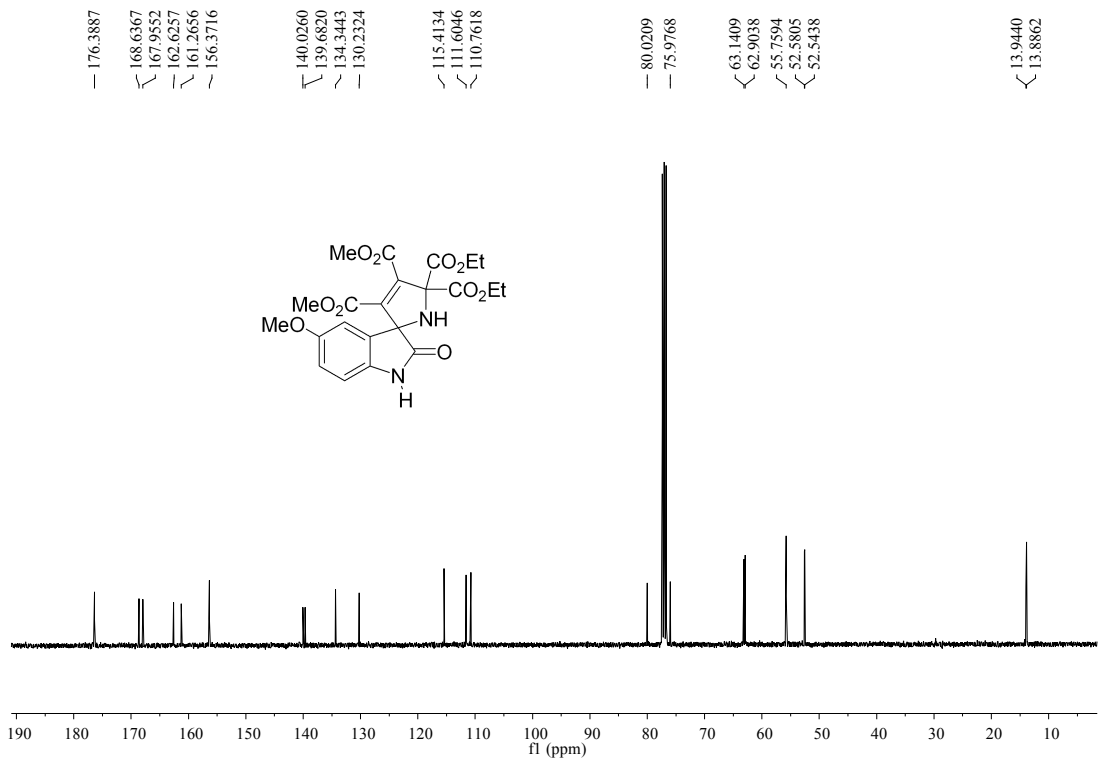
7.0258
6.7725
6.7667
6.7632
4.3707
4.3656
4.3530
4.3477
4.3351
4.3298
4.3174
3.8414
3.7625
3.5717
1.3736
1.3557
1.3378
1.3343
1.3163
1.2985
MeO2C
CO2Et
CO2Et
MeO2C
NH
MeO
O
N
H
1.00
1.00
2.01
4.03
3.08
4.09
3.00
3.04
3.16
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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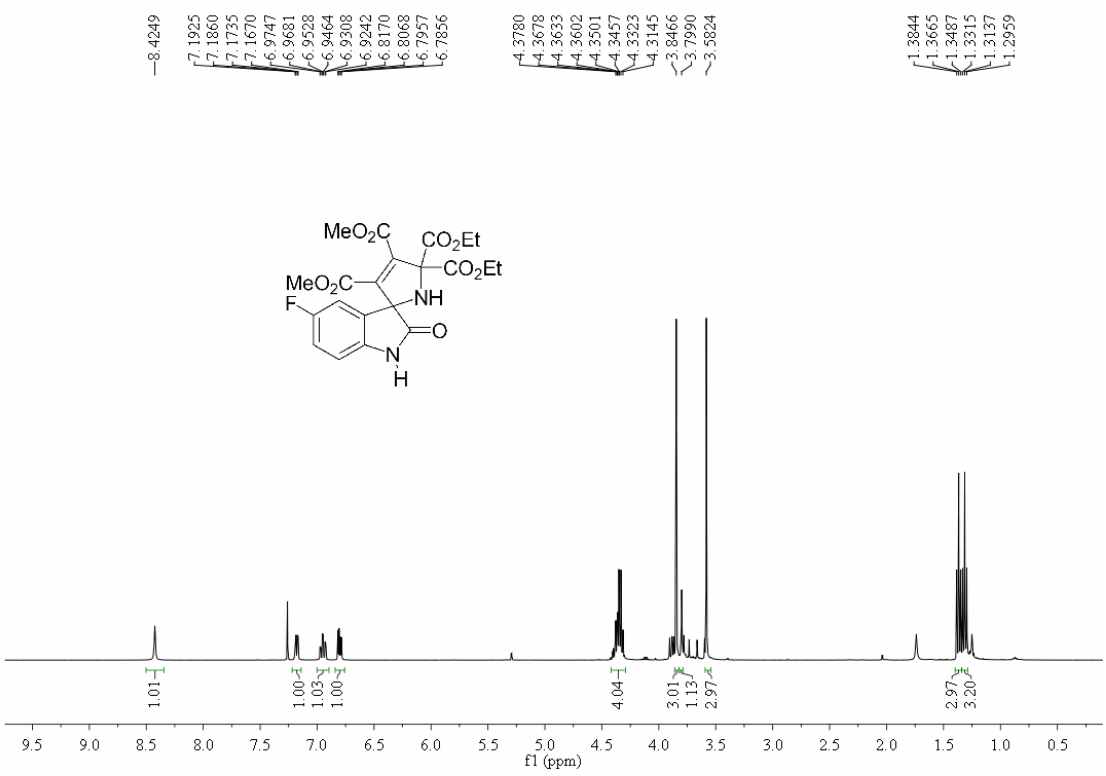
162.6257
161.2656
156.3716
140.0260
139.6820
134.3443
130.2324
115.4134
111.6046
110.7618
80.0209
75.9768
63.1409
62.9038
55.7594
52.5805
52.5438
13.9440
13.8862
MeO2C
CO2Et
CO2Et
MeO2C
NH
MeO
O
N
H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

4uaa: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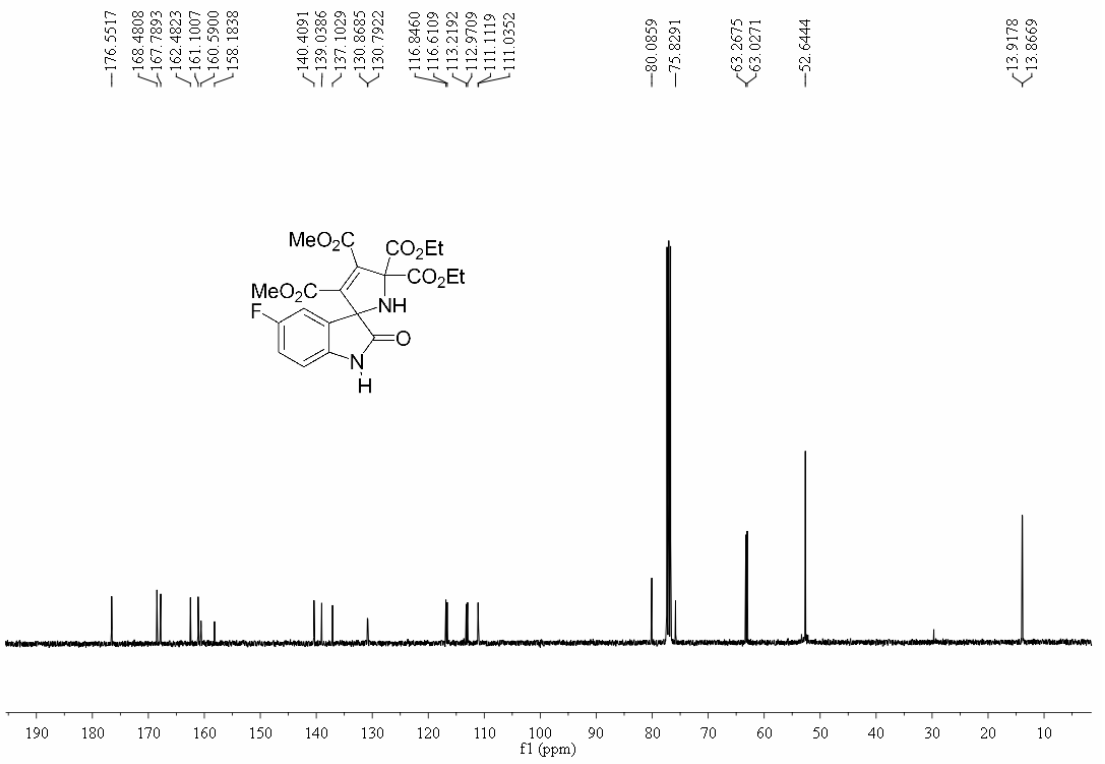
7.1860
7.1735
7.1670
6.9747
6.9681
6.9528
6.9464
6.9308
6.9242
6.8170
6.8068
6.7957
6.7856
4.3780
4.3678
4.3653
4.3602
4.3501
4.3457
4.3323
4.3145
3.8466
3.7990
3.5824
1.3844
1.3665
1.3487
1.3315
1.3137
1.2959
MeO2C
CO2Et
CO2Et
MeO2C
NH
F
O
N
H
1.01
1.00
1.03
1.00
4.04
3.01
1.13
2.97
2.97
3.20
f1 (ppm)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158.1838
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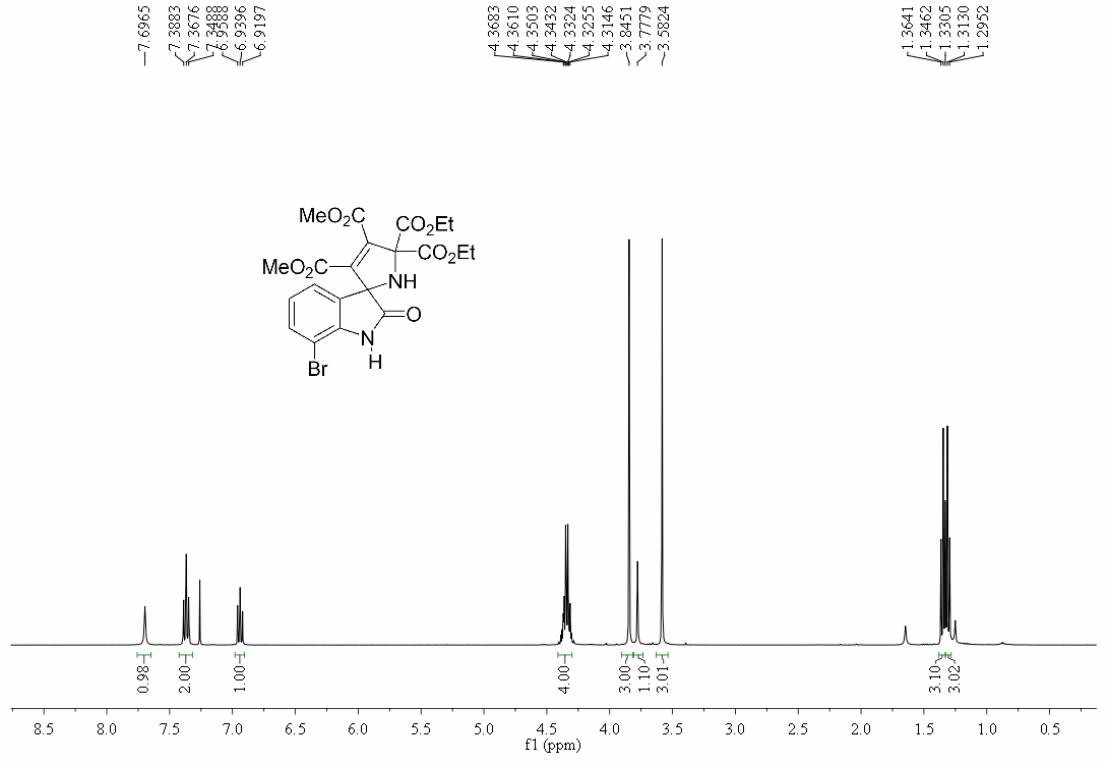
139.0386
137.1029
130.8685
130.7922
116.8460
116.6109
113.2192
112.9709
111.1119
111.0352
80.0859
75.8291
63.2675
63.0271
52.6444
13.9178
13.8669
MeO2C
CO2Et
CO2Et
MeO2C
NH
F
O
N
H
f1 (ppm)

4vaa: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6.9388
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6.9197
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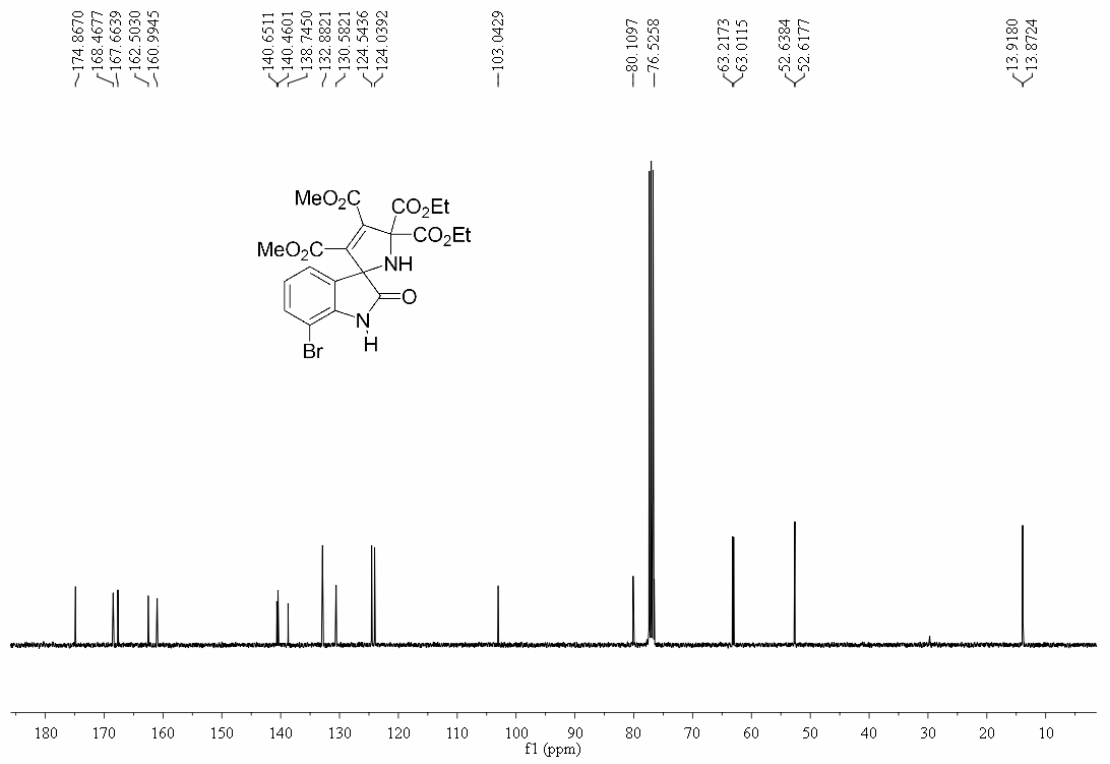
4.3610
4.3503
4.3432
4.3324
4.3255
4.3146
3.8451
3.7779
3.5824
1.3641
1.3462
1.3305
1.3130
1.2952
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
H
Br
0.98
2.00
1.00
4.00
3.00
1.10
3.01
3.10
3.02
f1 (ppm)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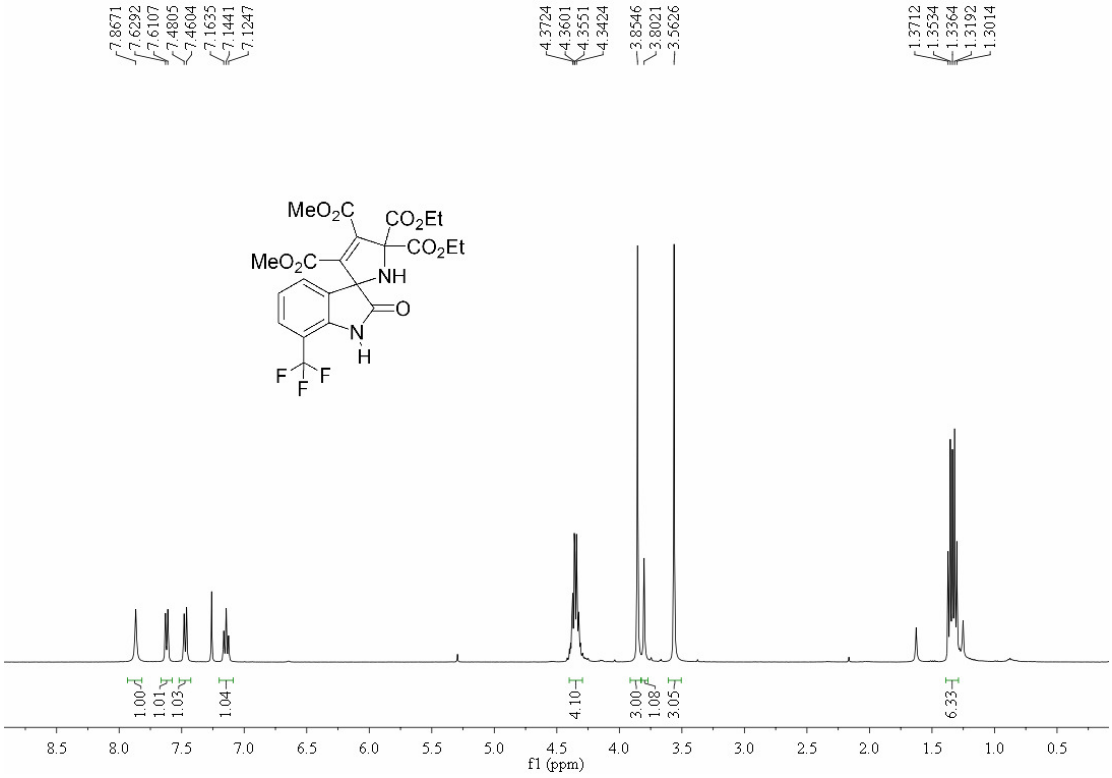
140.4601
138.7450
132.8821
130.5821
124.5436
124.0392
103.0429
80.1097
76.5258
63.2173
63.0115
52.6384
52.6177
13.9180
13.8724
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
H
Br
f1 (ppm)

4waa: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7.1441
7.1247
4.3724
4.3601
4.3551
4.3424
3.8546
3.8021
3.5626
1.3712
1.3534
1.3364
1.3192
1.3014
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
H
F
F
F
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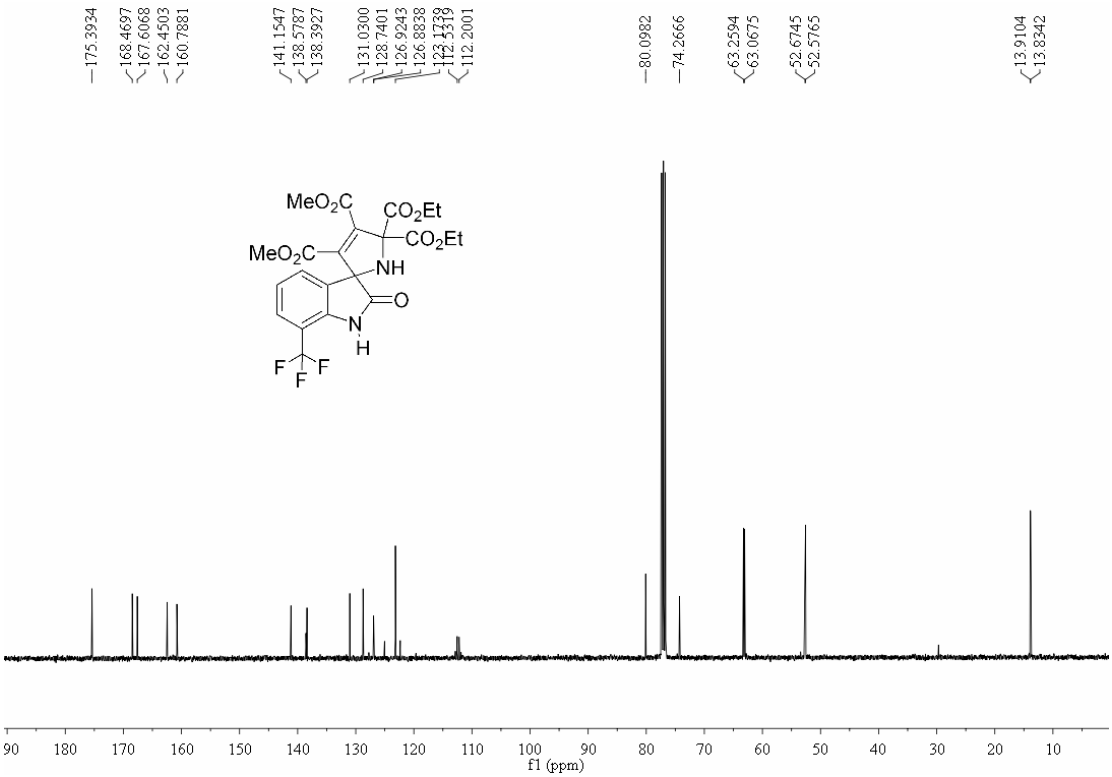
1.01
1.03
1.04
4.10
3.00
1.08
3.05
6.33
f1 (ppm)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138.5787
138.3927
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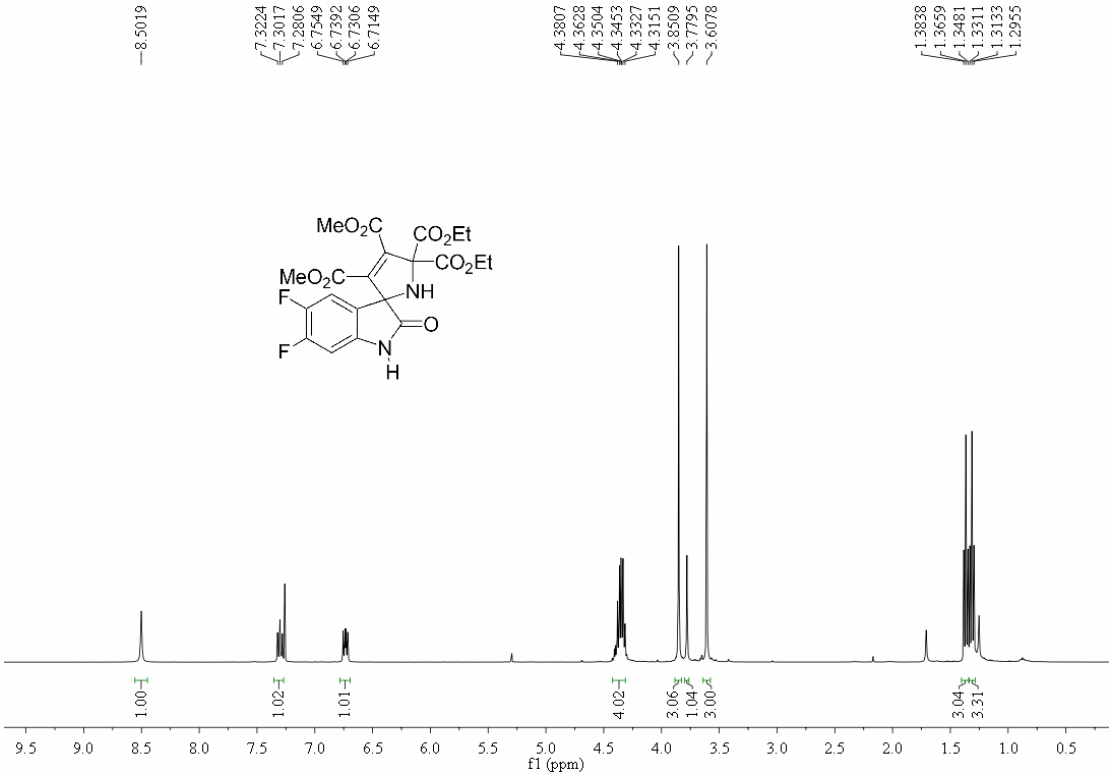
126.8838
122.2319
112.2001
80.0982
74.2666
63.2594
63.0675
52.6745
52.5765
13.9104
13.8342
MeO2C
CO2Et
CO2Et
MeO2C
NH
O
N
H
F
F
F
f1 (ppm)

4xaa: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6.7306
6.7149
4.3807
4.3628
4.3504
4.3453
4.3327
4.3151
3.8509
3.7795
3.6078
1.3838
1.3659
1.3481
1.3311
1.3133
1.2955
MeO2C
CO2Et
CO2Et
MeO2C
NH
F
O
F
N
H
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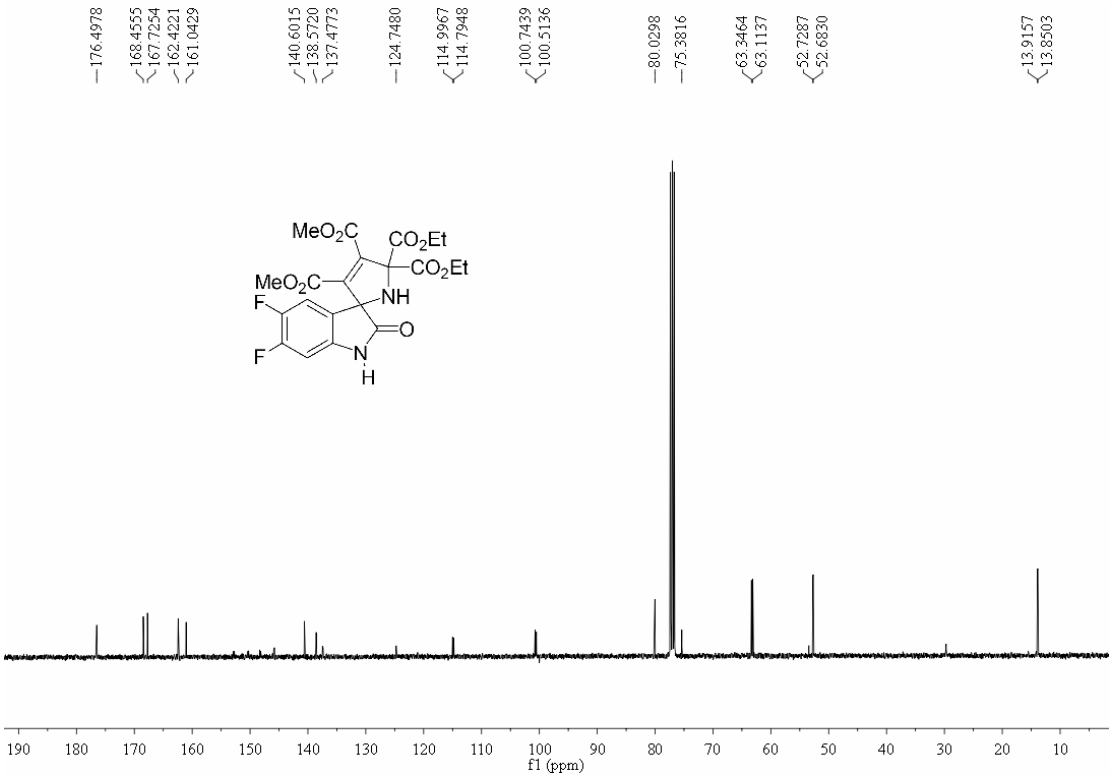
1.02
1.01
4.02
3.06
1.04
3.00
3.04
3.31
f1 (ppm)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140.6015
138.5720
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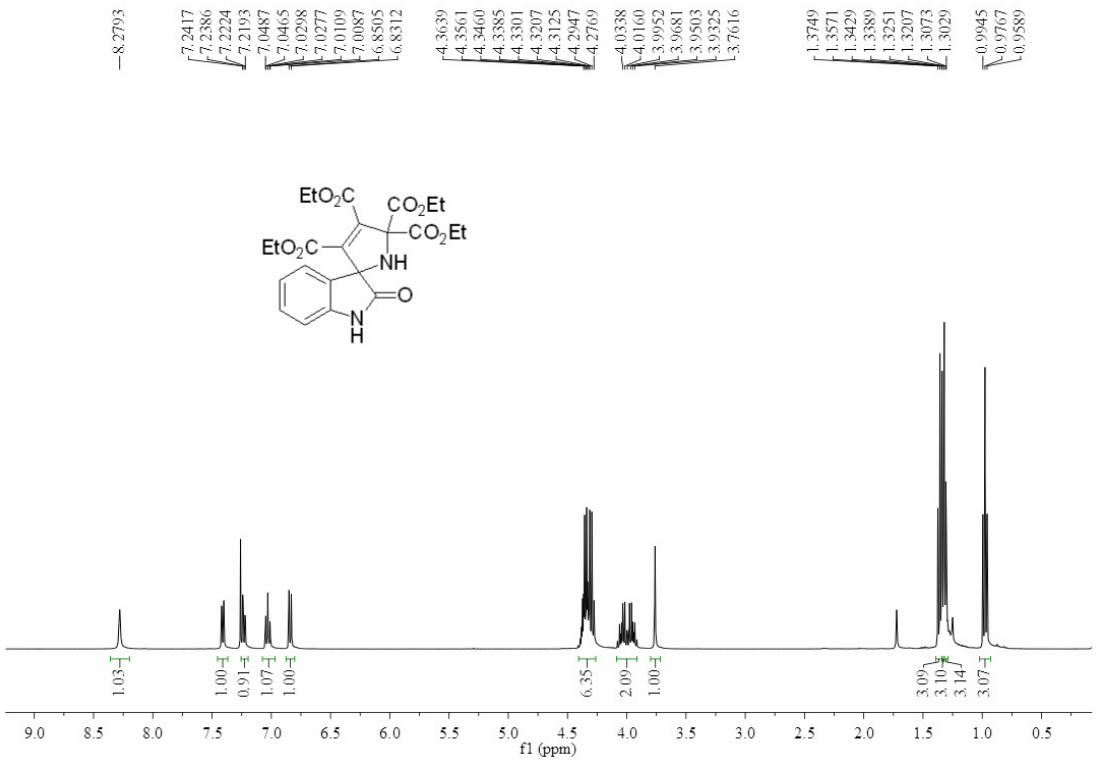
124.7480
114.9967
114.7948
100.7439
100.5136
80.0298
75.3816
63.3464
63.1137
52.7287
52.6830
13.9157
13.8503
MeO2C
CO2Et
CO2Et
MeO2C
NH
F
O
F
N
H
f1 (ppm)

4bab: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7.0277
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7.0087
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6.8312
4.3639
4.3561
4.3460
4.3385
4.3301
4.3207
4.3125
4.2947
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4.0338
4.0160
3.9952
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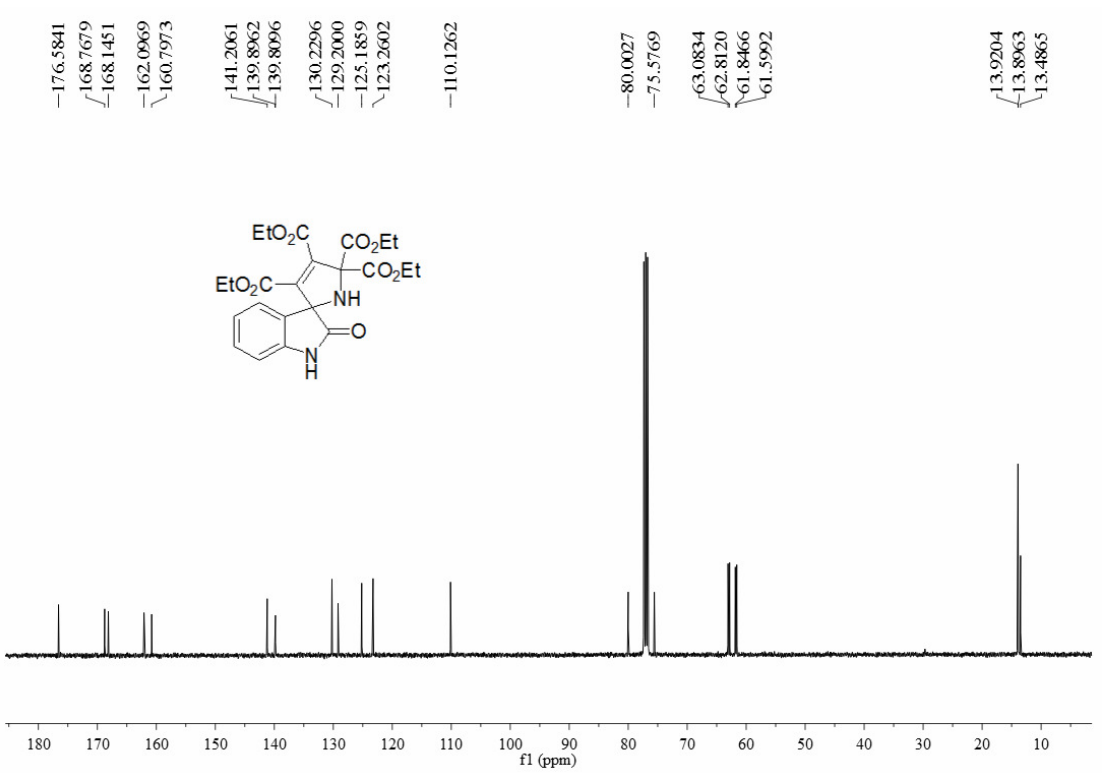
1.3571
1.3429
1.3389
1.3251
1.3207
1.3073
1.3029
0.9945
0.9767
0.9589
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
H
1.03
1.00
0.91
1.07
1.00
6.35
2.09
1.00
3.09
3.10
3.14
3.07
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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168.1451
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160.7973
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139.8962
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130.2296
129.2000
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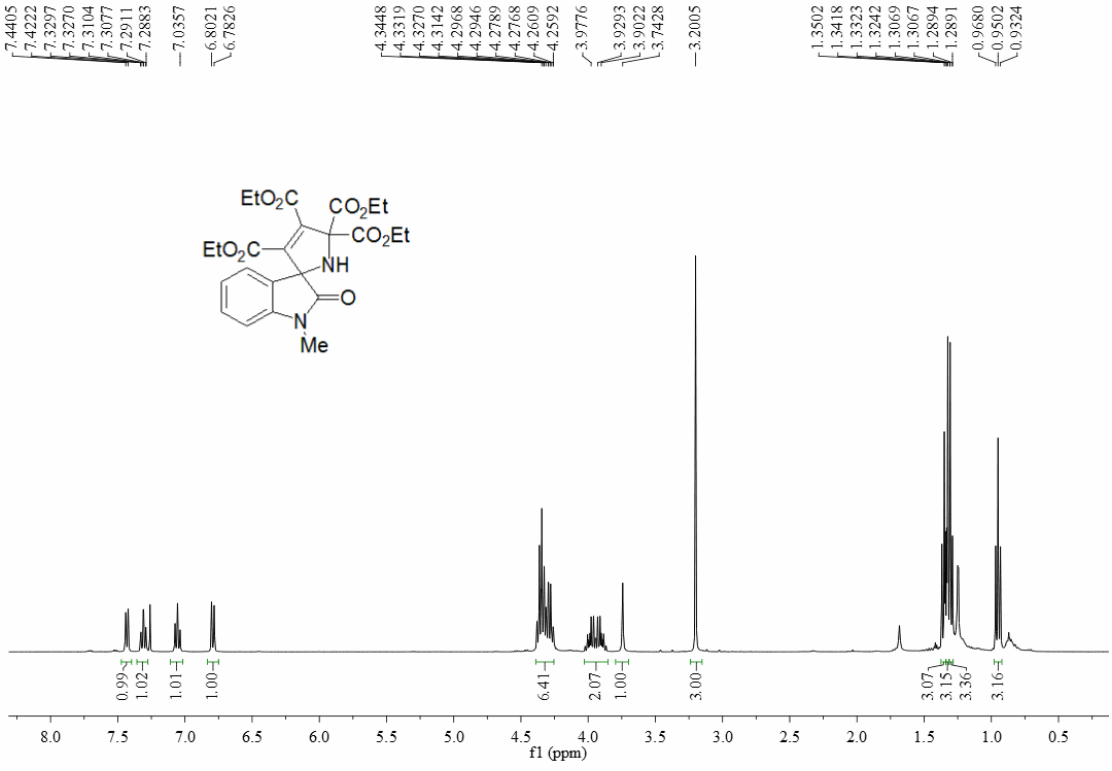
80.0027
75.5769
63.0834
62.8120
61.8466
61.5992
13.9204
13.8963
13.4865
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
H
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

4cab: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7.3104
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7.0357
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6.7826
4.3448
4.3319
4.3270
4.3142
4.2968
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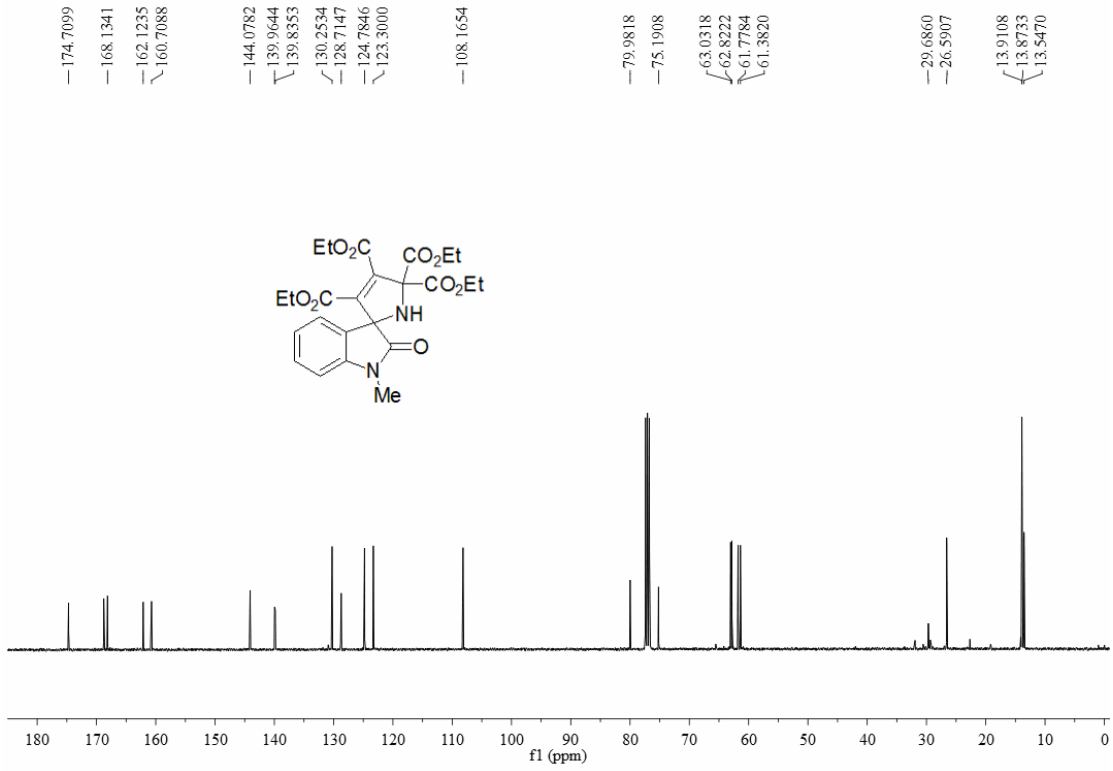
4.2789
4.2768
4.2609
4.2592
3.9776
3.9293
3.9022
3.7428
3.2005
1.3502
1.3418
1.3323
1.3242
1.3069
1.3067
1.2894
1.2891
0.9680
0.9502
0.9324
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
Me
0.99
1.02
1.01
1.00
6.41
2.07
1.00
3.00
3.07
3.15
3.36
3.16
f1 (ppm)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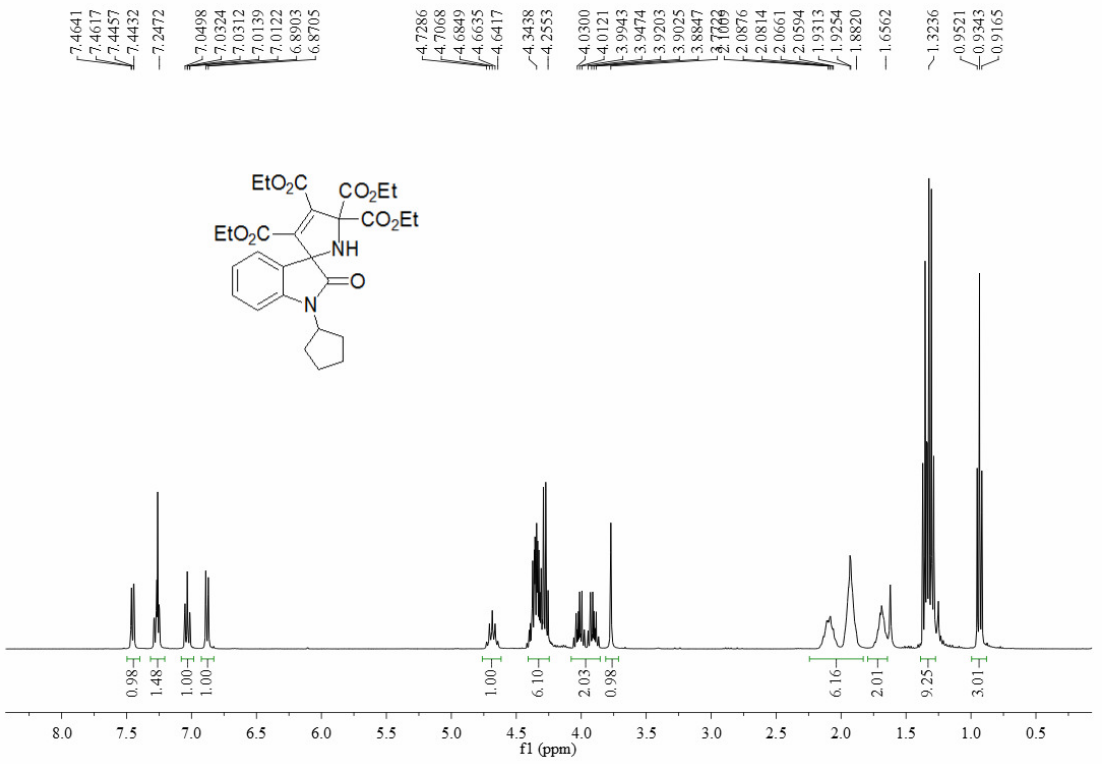
123.3000
108.1654
79.9818
75.1908
63.0318
62.8222
61.7784
61.3820
29.6860
26.5907
13.9108
13.8733
13.5470
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
Me
f1 (ppm)

4eab: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7.0324
7.0312
7.0139
7.0122
6.8903
6.8705
4.7286
4.7068
4.6849
4.6635
4.6417
4.3438
4.2553
4.0300
4.0121
3.9943
3.9474
3.9203
3.9025
3.8847
2.1069
2.0876
2.0814
2.0661
2.0594
1.9313
1.9254
1.8820
1.6562
1.3236
0.9521
0.9343
0.9165
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
0.98
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1.00
1.00
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2.03
0.98
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2.01
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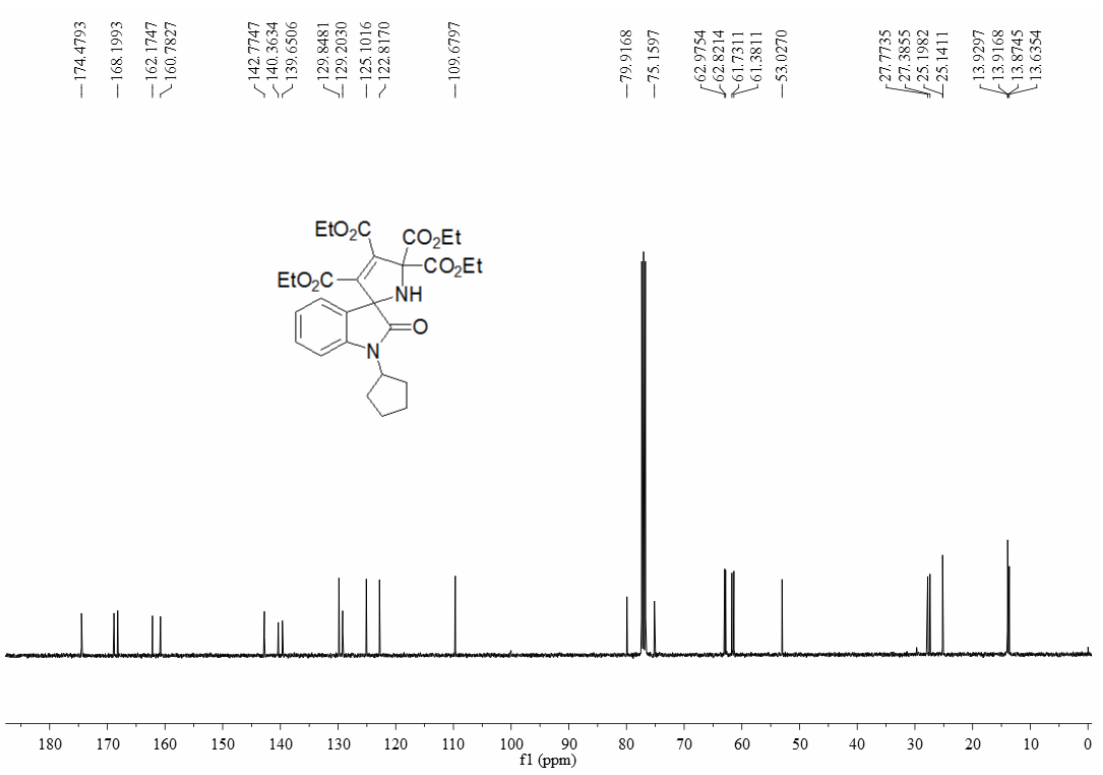
3.01
f1 (ppm)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139.6506
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125.1016
122.8170
109.6797
79.9168
75.1597
62.9754
62.8214
61.7311
61.3811
53.0270
27.7735
27.3855
25.1982
25.1411
13.9297
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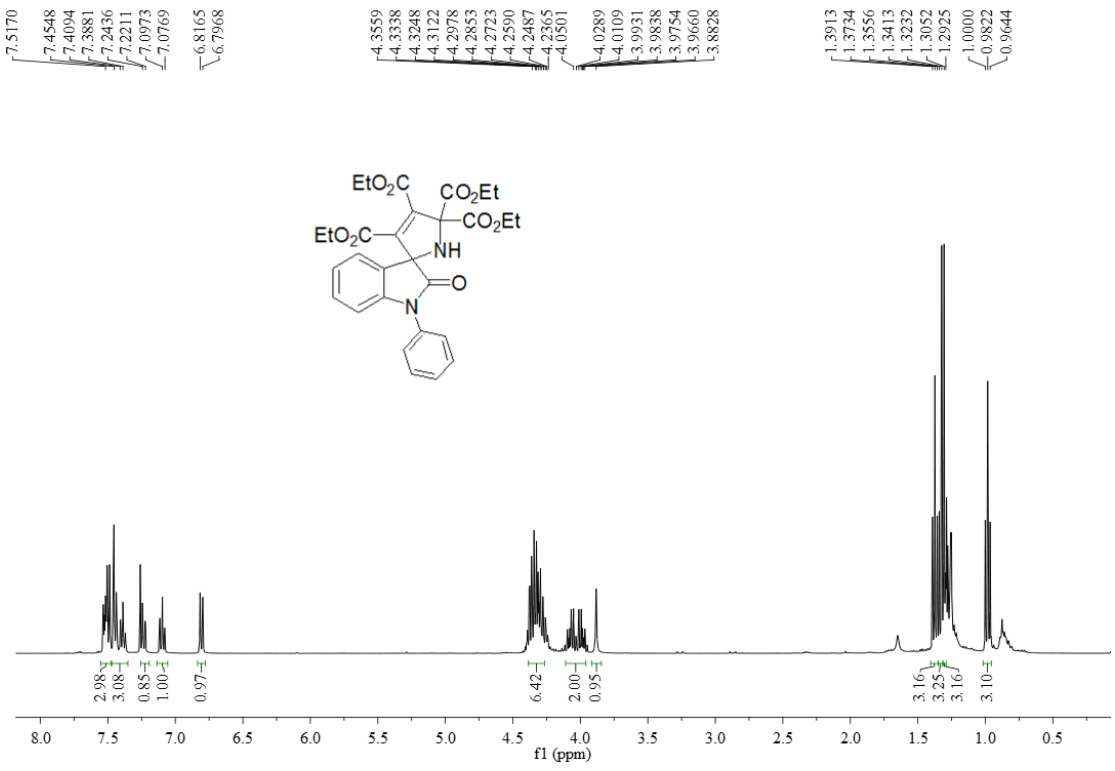
13.6354
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
f1 (ppm)

4fab: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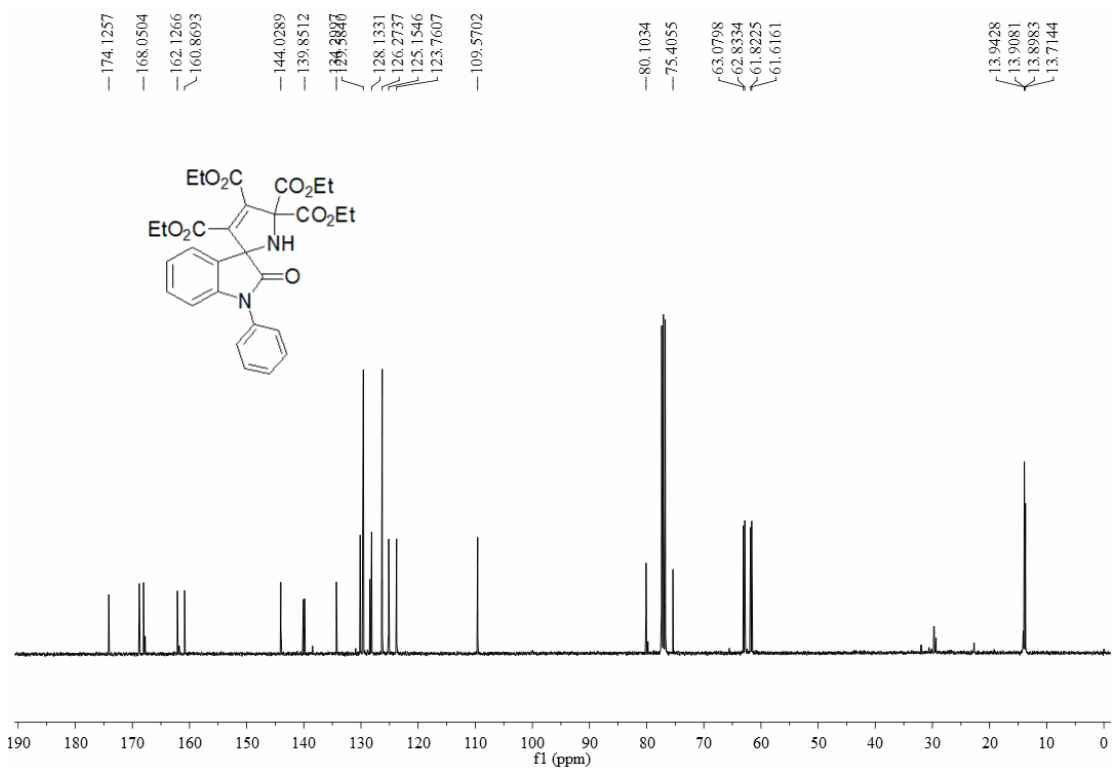
6.8165
6.7968
4.3559
4.3338
4.3248
4.3122
4.2978
4.2853
4.2723
4.2590
4.2487
4.2365
4.0501
4.0289
4.0109
3.9931
3.9838
3.9754
3.9660
3.8828
1.3913
1.3734
1.3556
1.3413
1.3232
1.3052
1.2925
1.0000
0.9822
0.9644
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
2.98
3.08
0.85
1.00
0.97
6.42
2.00
0.95
3.16
3.25
3.16
3.10
f1 (ppm)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144.0289
139.8512
128.1331
126.2737
125.1546
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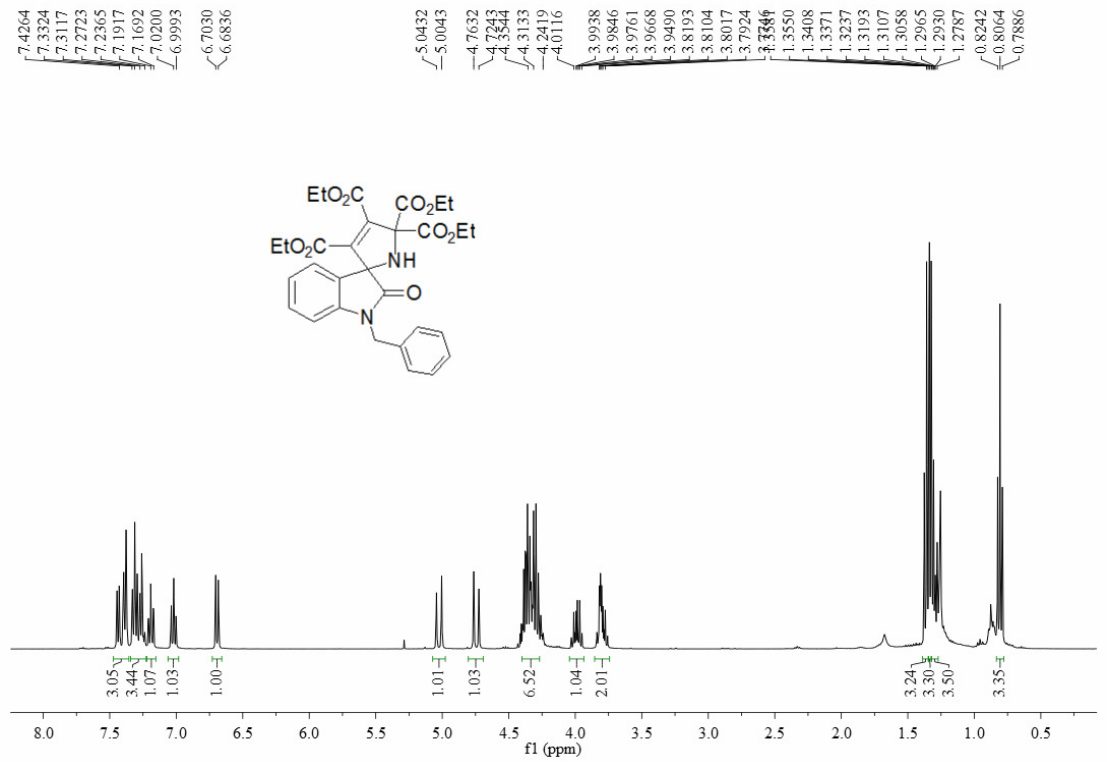
80.1034
75.4055
63.0798
62.8334
61.8225
61.6161
13.9428
13.9081
13.8983
13.7144
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
f1 (ppm)

4aab: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7.2365
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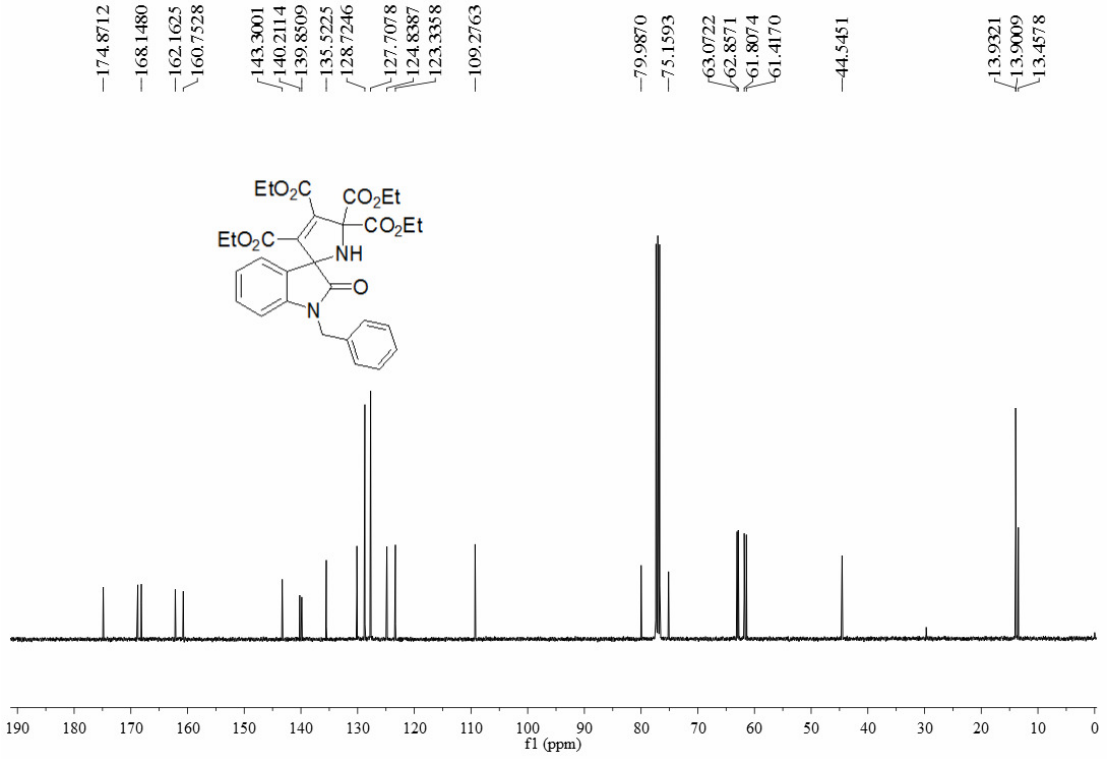
7.1692
7.0200
6.9993
6.7030
6.6836
5.0432
5.0043
4.7632
4.7243
4.3544
4.3133
4.2419
4.0116
3.9938
3.9846
3.9761
3.9668
3.9490
3.8193
3.8104
3.8017
3.7924
1.3550
1.3408
1.3371
1.3237
1.3193
1.3107
1.3058
1.2965
1.2930
1.2787
0.8242
0.8064
0.7886
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
3.05
3.44
1.07
1.03
1.00
1.01
1.03
6.52
1.04
2.01
3.24
3.30
3.50
3.35
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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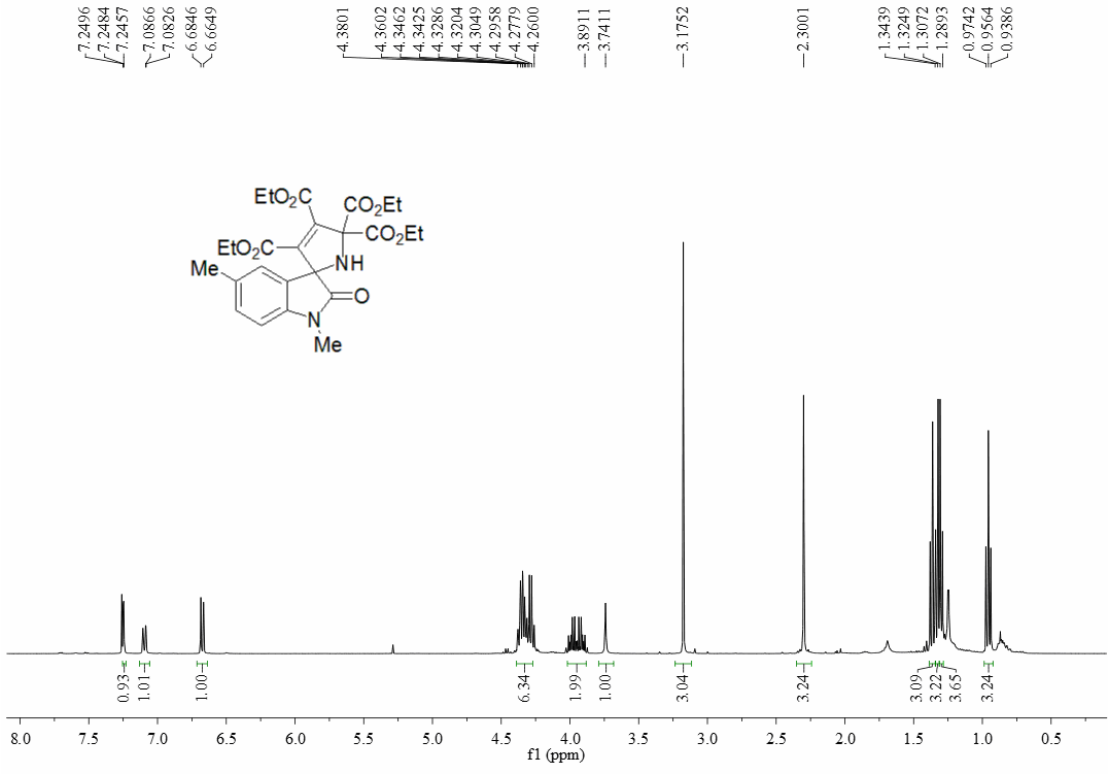
143.3001
140.2114
139.8509
135.5225
128.7246
127.7078
124.8387
123.3358
109.2763
79.9870
75.1593
63.0722
62.8571
61.8074
61.4170
44.5451
13.9321
13.9009
13.4578
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

4iab: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7.2457
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7.0826
6.6846
6.6649
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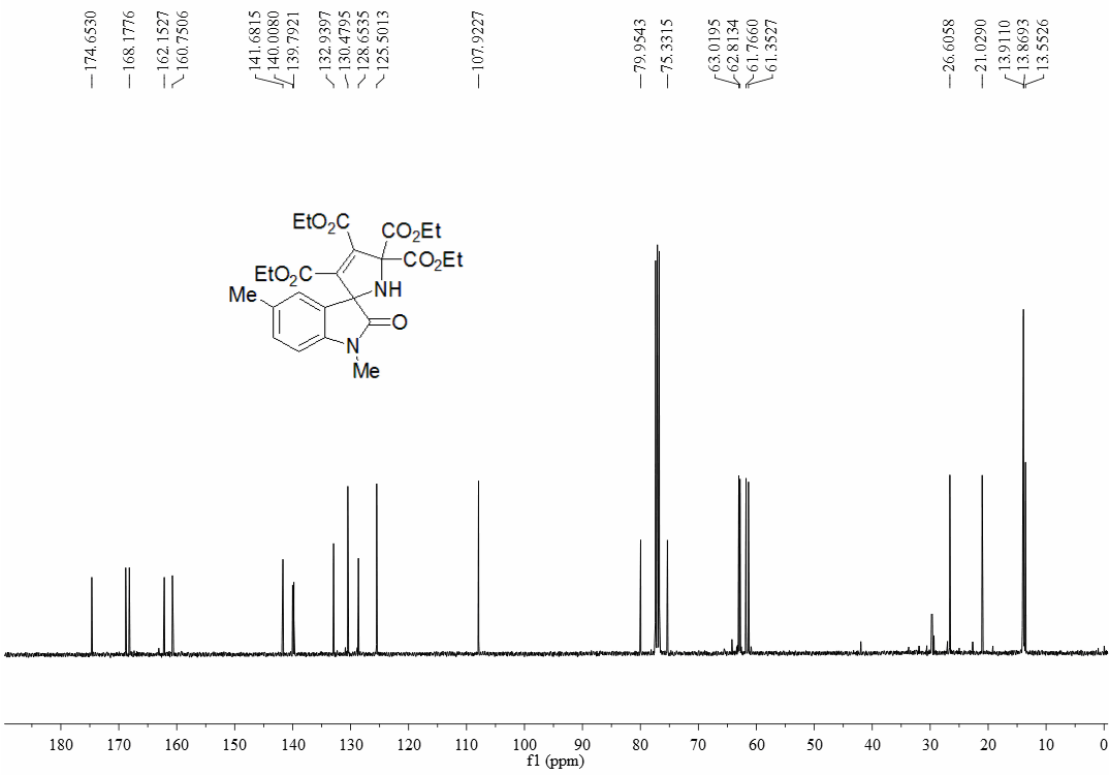
4.3602
4.3462
4.3425
4.3286
4.3204
4.3049
4.2958
4.2779
4.2600
3.8911
3.7411
3.1752
2.3001
1.3439
1.3249
1.3072
1.2893
0.9742
0.9564
0.9386
EtO2C
CO2Et
CO2Et
EtO2C
NH
Me
O
N
Me
0.93
1.01
1.00
6.34
1.99
1.00
3.04
3.24
3.09
3.22
3.65
3.24
f1 (ppm)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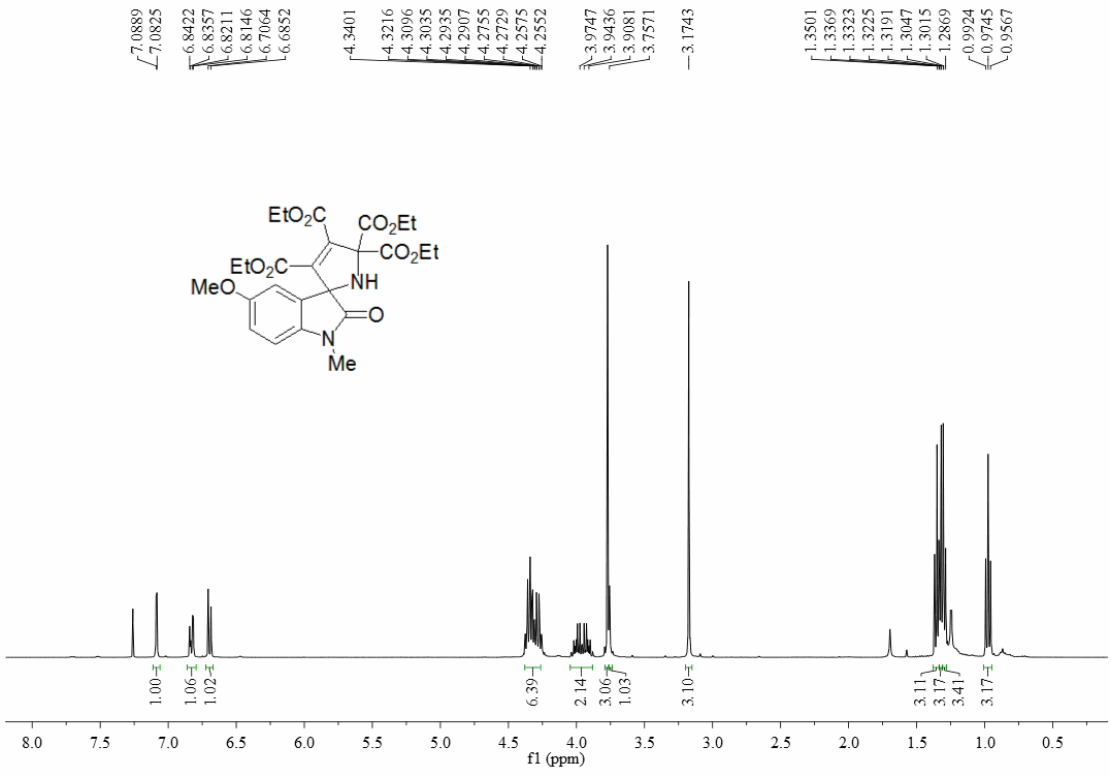
141.6815
140.0080
139.7921
132.9397
130.4795
128.6535
125.5013
107.9227
79.9543
75.3315
63.0195
62.8134
61.7660
61.3527
26.6058
21.0290
13.9110
13.8693
13.5526
EtO2C
CO2Et
CO2Et
EtO2C
NH
Me
O
N
Me
f1 (ppm)

4jab: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6.7064
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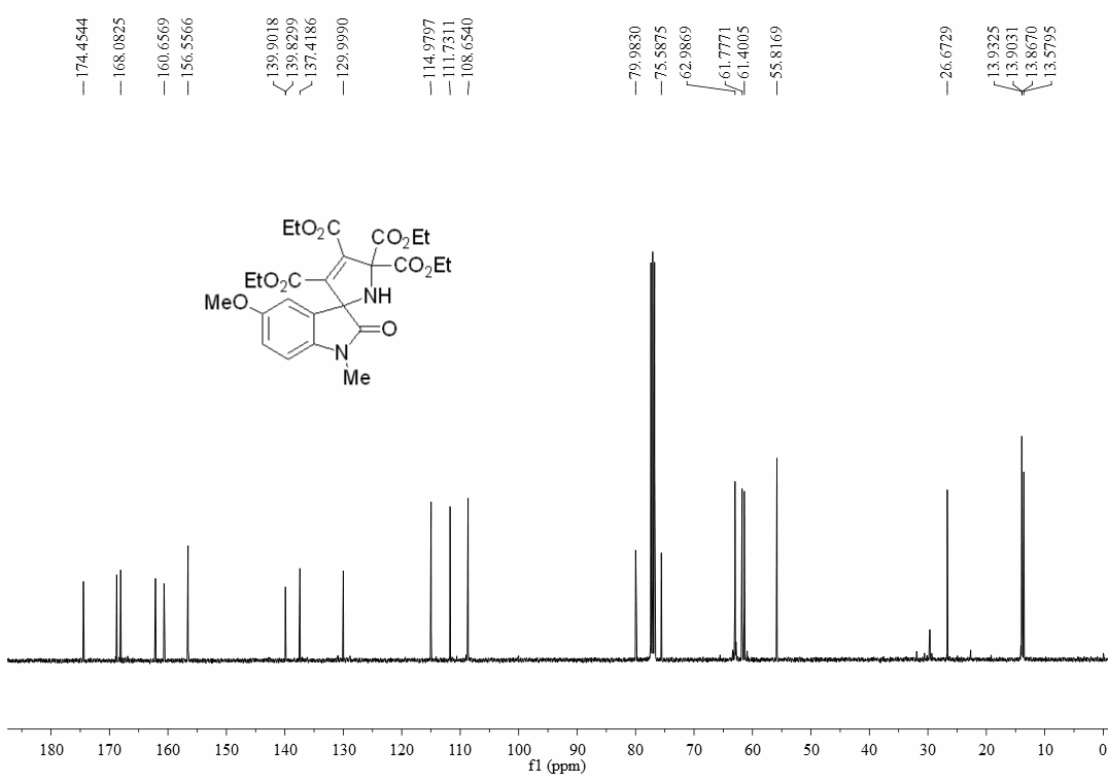
4.3401
4.3216
4.3096
4.3035
4.2935
4.2907
4.2755
4.2729
4.2575
4.2552
3.9747
3.9436
3.9081
3.7571
3.1743
1.3501
1.3369
1.3323
1.3225
1.3191
1.3047
1.3015
1.2869
0.9924
0.9745
0.9567
EtO2C
CO2Et
CO2Et
EtO2C
NH
MeO
O
N
Me
1.00
1.06
1.02
6.39
2.14
3.06
1.03
3.10
3.11
3.17
3.41
3.17
f1 (ppm)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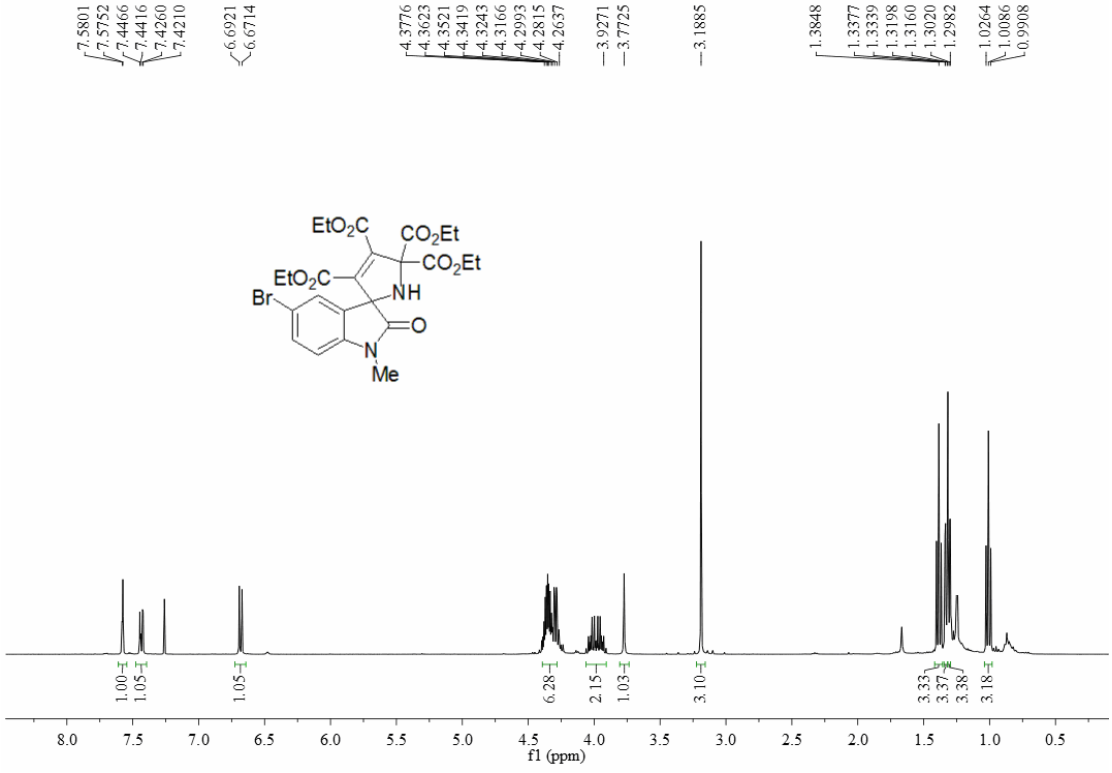
139.8299
137.4186
129.9990
114.9797
111.7311
108.6540
79.9830
75.5875
62.9869
61.7771
61.4005
55.8169
26.6729
13.9325
13.9031
13.8670
13.5795
EtO2C
CO2Et
CO2Et
EtO2C
NH
MeO
O
N
Me
f1 (ppm)

4kab: :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7.4260
7.4210
6.6921
6.6714
4.3776
4.3623
4.3521
4.3419
4.3243
4.3166
4.2993
4.2815
4.2637
3.9271
3.7725
3.1885
1.3848
1.3377
1.3339
1.3198
1.3160
1.3020
1.2982
1.0264
1.0086
0.9908
EtO2C
CO2Et
CO2Et
EtO2C
Br
NH
O
N
Me
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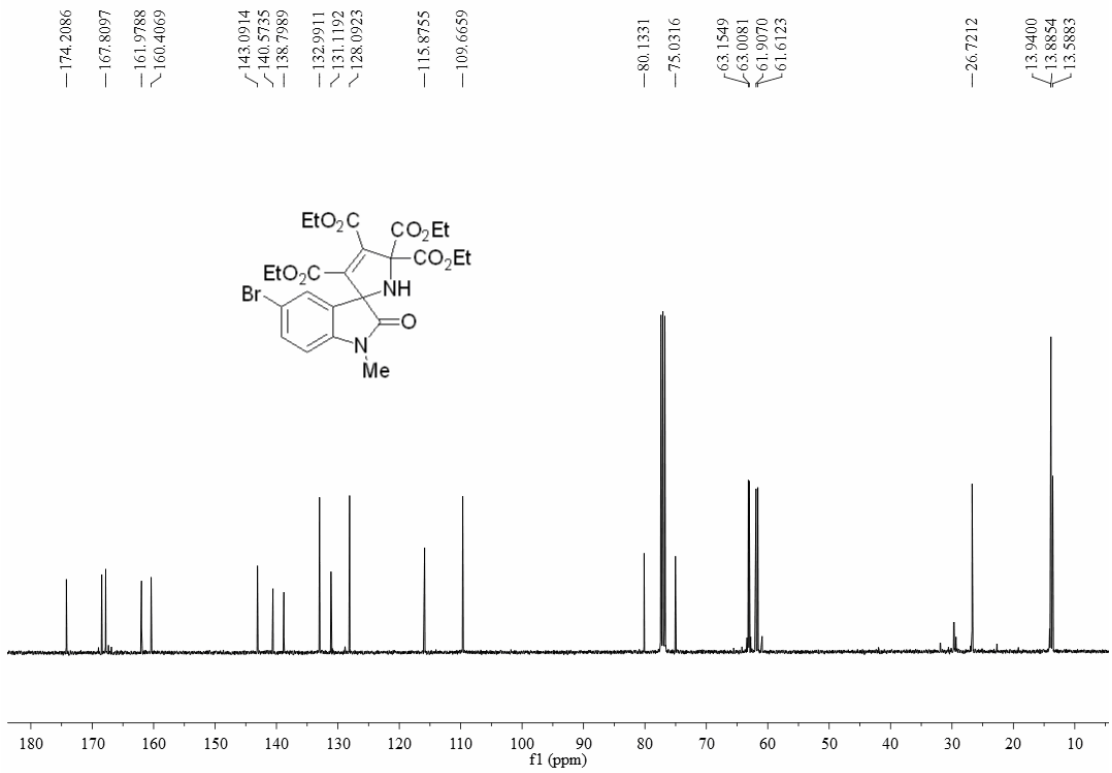
1.05
1.05
6.28
2.15
1.03
3.10
3.33
3.37
3.38
3.18
f1 (ppm)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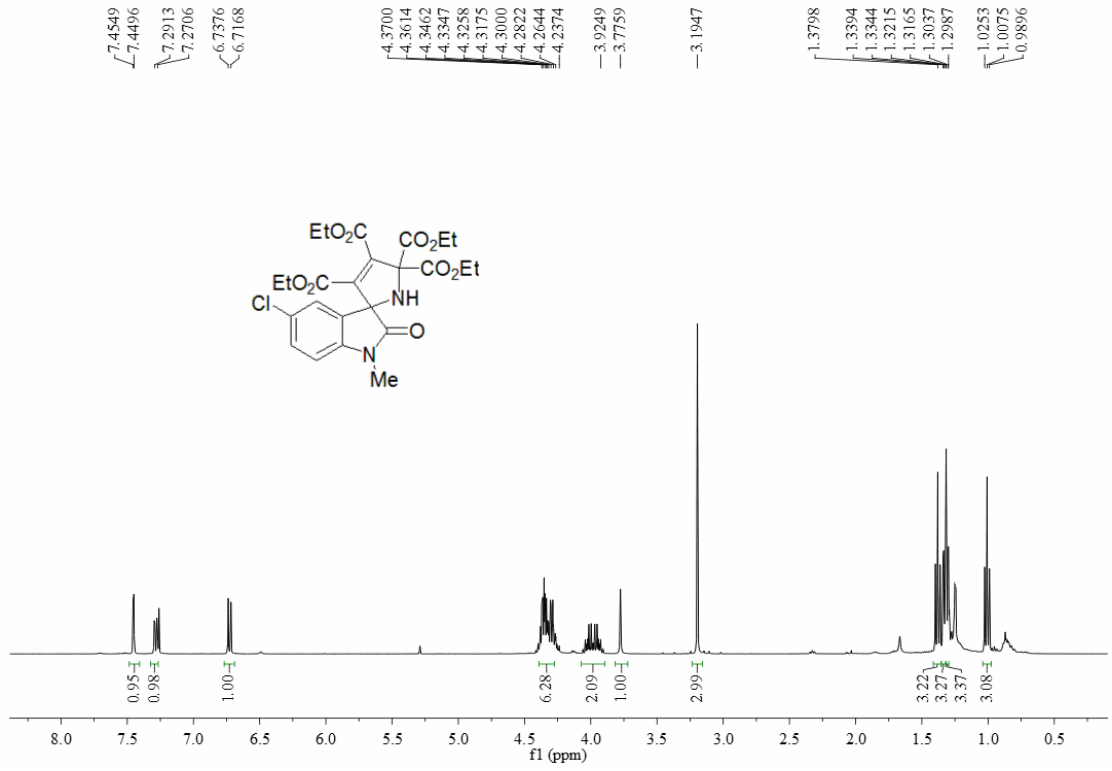
160.4069
143.0914
140.5735
138.7989
132.9911
131.1192
128.0923
115.8755
109.6659
80.1331
75.0316
63.1549
63.0081
61.9070
61.6123
26.7212
13.9400
13.8854
13.5883
EtO2C
CO2Et
CO2Et
EtO2C
Br
NH
O
N
Me
f1 (ppm)

4lab: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4.3462
4.3347
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4.3175
4.3000
4.2822
4.2644
4.2374
3.9249
3.7759
3.1947
1.3798
1.3394
1.3344
1.3215
1.3165
1.3037
1.2987
1.0253
1.0075
0.9896
EtO2C
CO2Et
CO2Et
EtO2C
Cl
NH
O
N
Me
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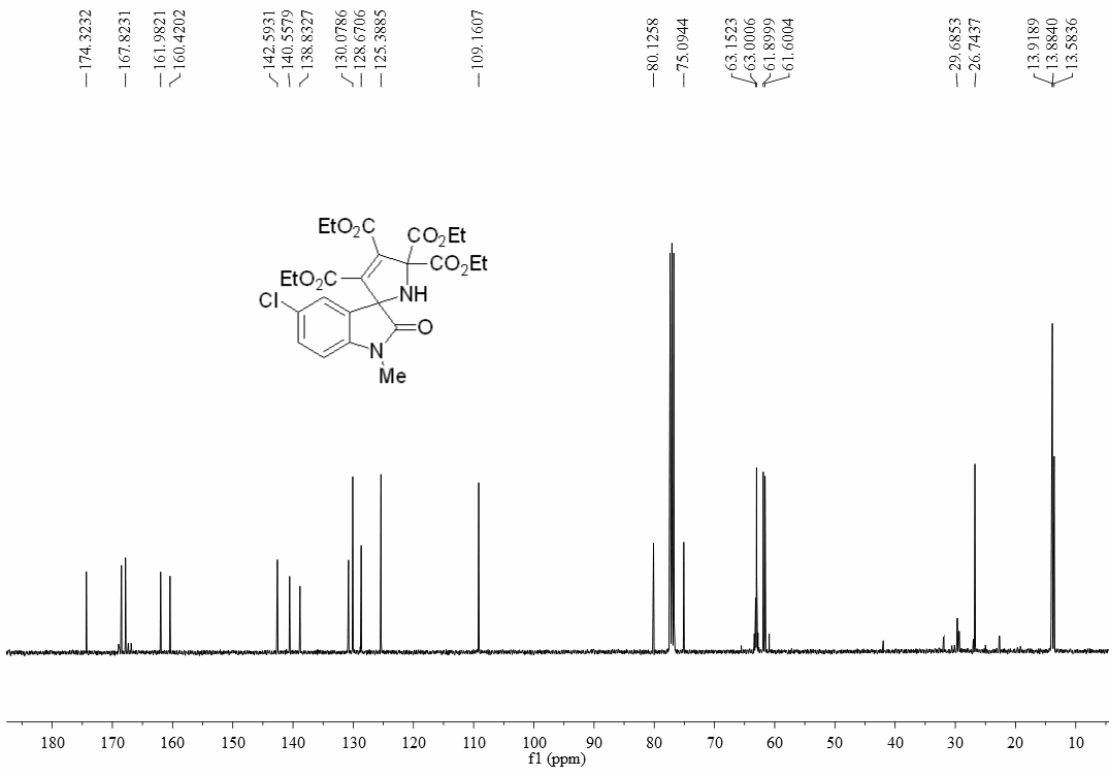
6.28
2.09
1.00
2.99
3.22
3.27
3.37
3.08
f1 (ppm)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161.9821
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142.5931
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138.8327
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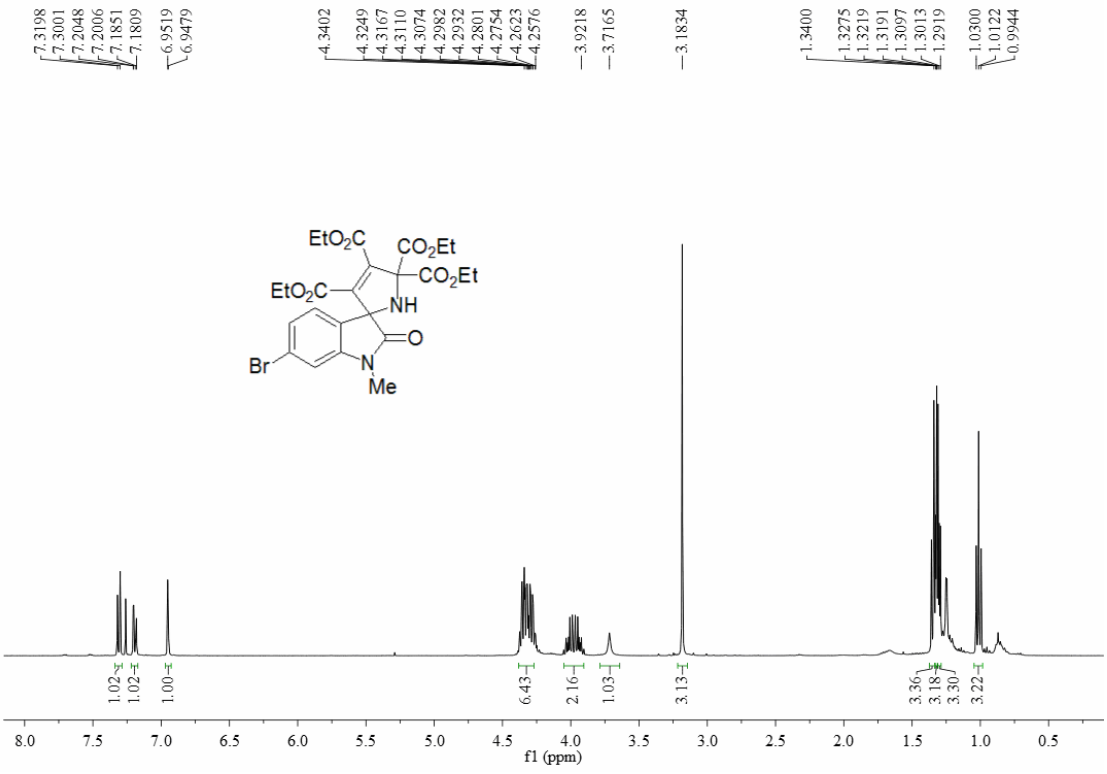
128.6706
125.3885
109.1607
80.1258
75.0944
63.1523
63.0006
61.8999
61.6004
29.6853
26.7437
13.9189
13.8840
13.5836
EtO2C
CO2Et
CO2Et
EtO2C
Cl
NH
O
N
Me
f1 (ppm)

4yab: :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7.1851
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6.9519
6.9479
4.3402
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4.3110
4.3074
4.2982
4.2932
4.2801
4.2754
4.2623
4.2576
3.9218
3.7165
3.1834
1.3400
1.3275
1.3219
1.3191
1.3097
1.3013
1.2919
1.0300
1.0122
0.9944
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
Br
N
Me
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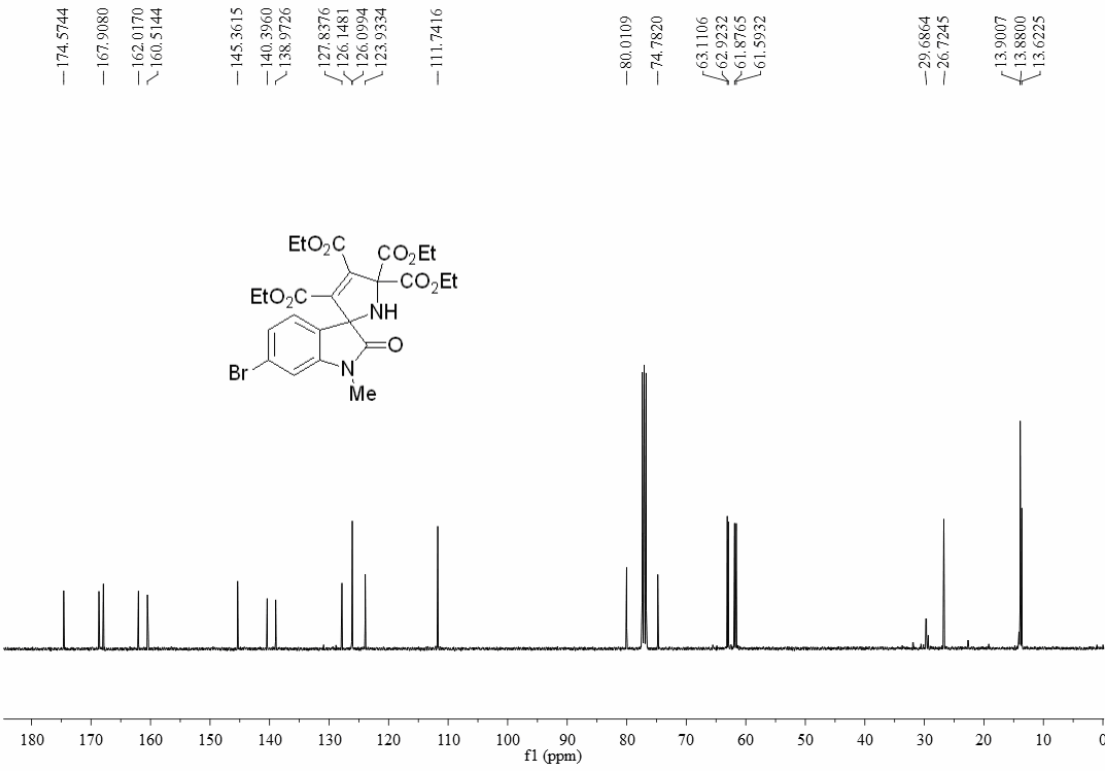
1.02
1.00
6.43
2.16
1.03
3.13
3.36
3.18
3.30
3.22
f1 (ppm)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140.3960
138.9726
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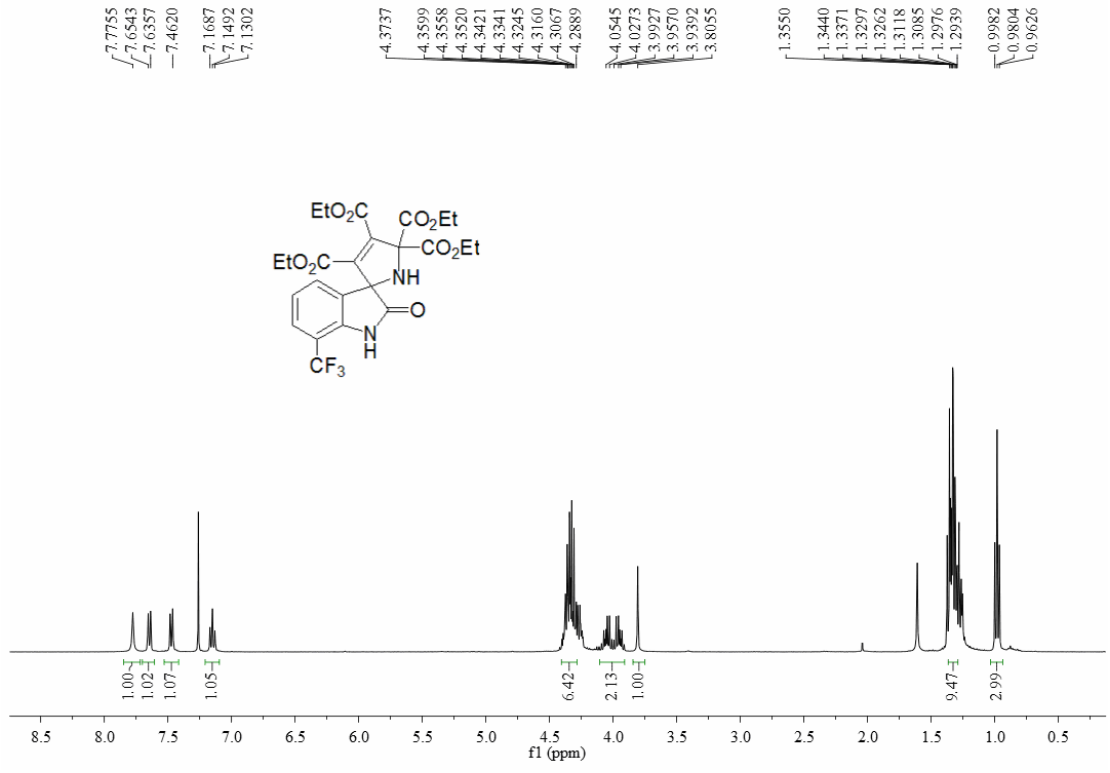
126.0994
123.9334
111.7416
80.0109
74.7820
63.1106
62.9232
61.8765
61.5932
29.6864
26.7245
13.9007
13.8800
13.6225
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
Br
N
Me
f1 (ppm)

4wab: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7.1492
7.1302
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4.3599
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4.3520
4.3421
4.3341
4.3245
4.3160
4.3067
4.2889
4.0545
4.0273
3.9927
3.9570
3.9392
3.8055
1.3550
1.3440
1.3371
1.3297
1.3262
1.3118
1.3085
1.2976
1.2939
0.9982
0.9804
0.9626
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
H
CF3
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1.02
1.07
1.05
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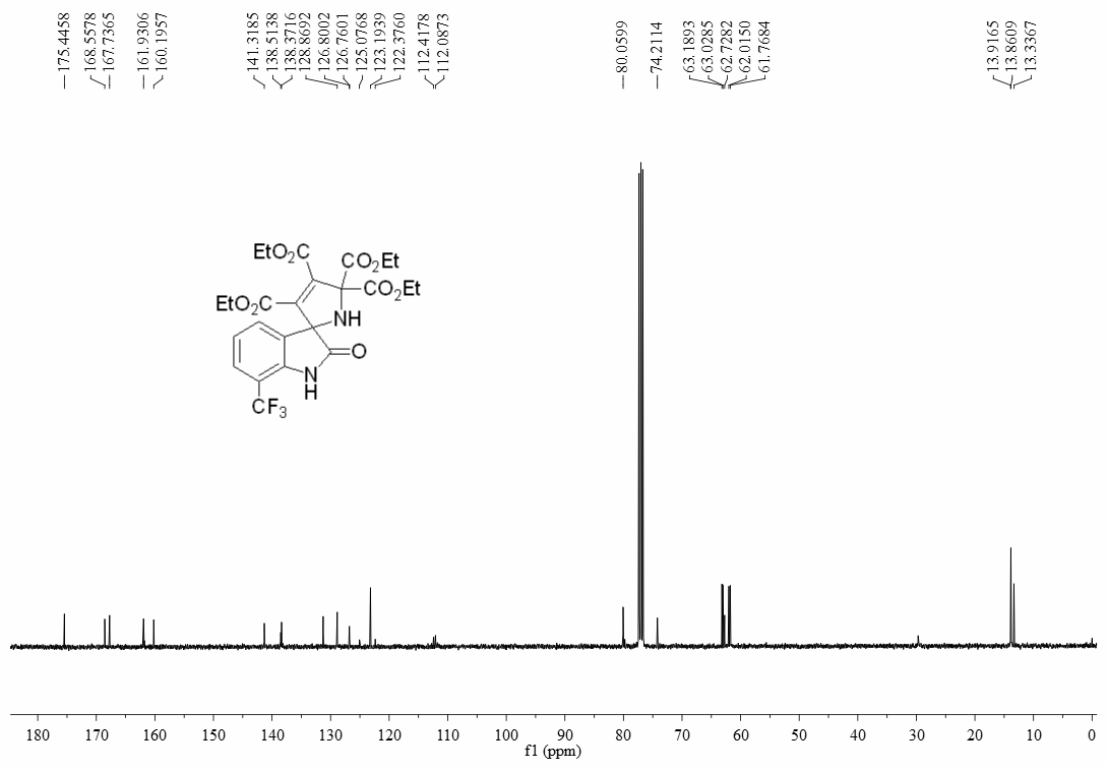
1.00
9.47
2.99
f1 (ppm)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126.7601
125.0768
123.1939
122.3760
112.4178
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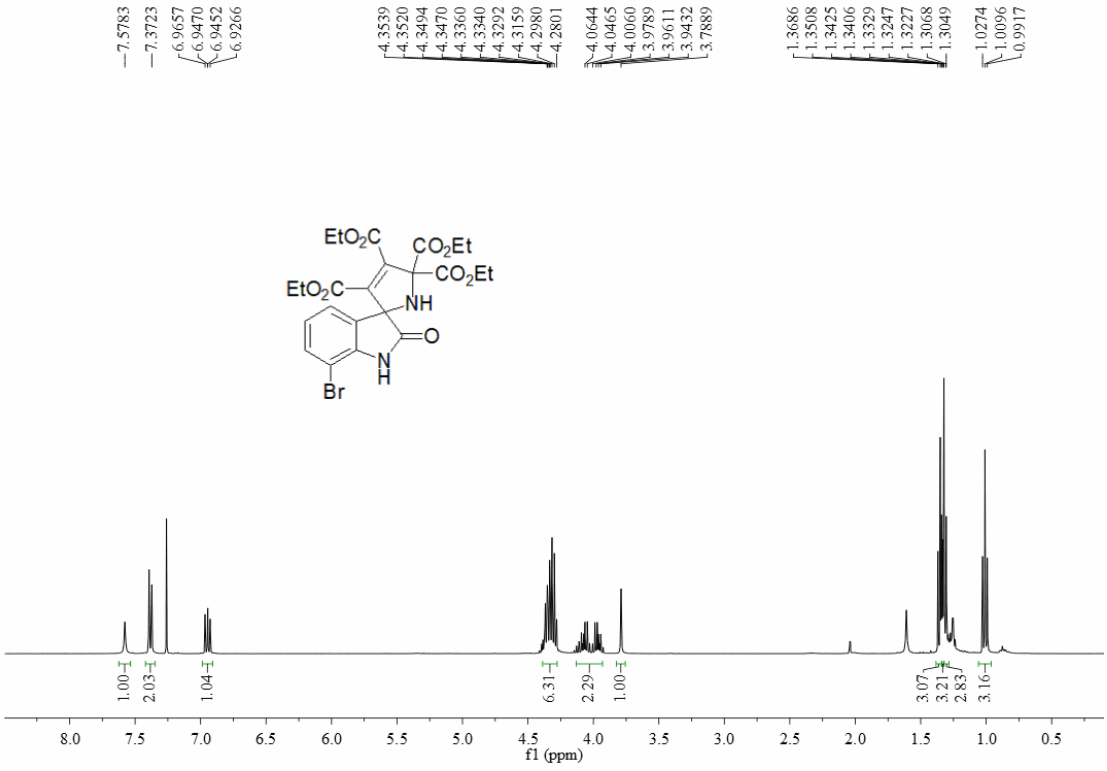
80.0599
74.2114
63.1893
63.0285
62.7282
62.0150
61.7684
13.9165
13.8609
13.3367
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
H
CF3
f1 (ppm)

4vab: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4.3360
4.3340
4.3292
4.3159
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4.2801
4.0644
4.0465
4.0060
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3.9611
3.9432
3.7889
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1.3508
1.3425
1.3406
1.3329
1.3247
1.3227
1.3068
1.3049
1.0274
1.0096
0.9917
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
H
Br
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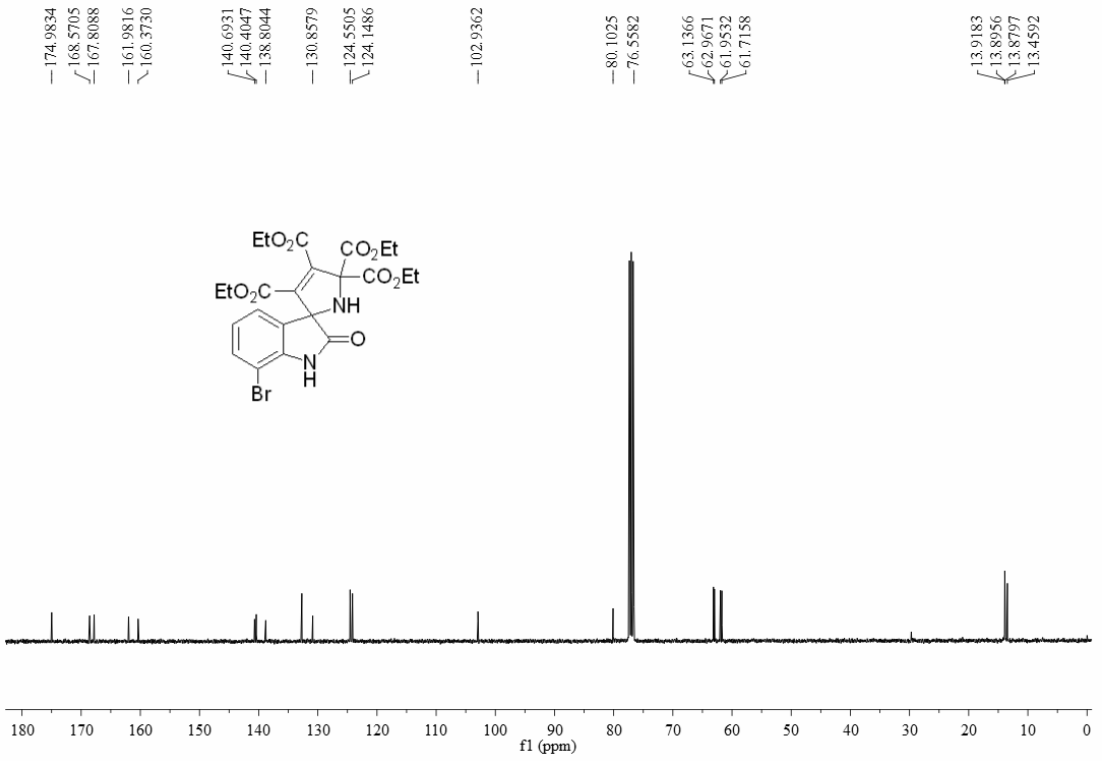
1.04
6.31
2.29
1.00
3.07
3.21
2.83
3.16
f1 (ppm)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160.3730
140.6931
140.4047
138.8044
130.8579
124.5505
124.1486
102.9362
80.1025
76.5582
63.1366
62.9671
61.9532
61.7158
13.9183
13.8956
13.8797
13.4592
EtO2C
CO2Et
CO2Et
EtO2C
NH
O
N
H
Br
f1 (ppm)