A Tandem Oxidative Annulation Strategy for the Synthesis of Tetracyclic 3-Spirooxindole Benzofuranones

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Supporting Information

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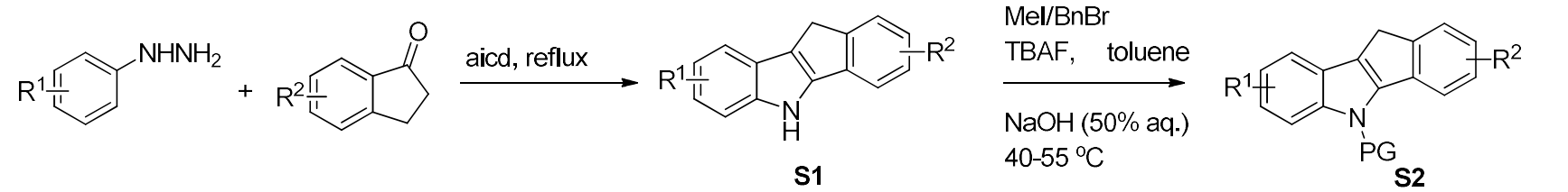
1. General information:

All reagents were obtained from commercial suppliers and used without further purification. The benzoic acid starting materials were prepared according to the know procedure.[1,2] Yields for all compounds were determined by the column chromatography which was generally performed on silica gel (200-300 mesh) using petroleum ether 40-60 (PE)/EtOAc as eluent, and reactions were monitored by thin layer chromatography (TLC) on a glass pate coated with silica gel with fluorescent indicator (GF254) using UV light. The ^{1}H reree and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker ADNANCE III 500 MHz using $CDCl_3$ as solvent with TMS as internal standard. Chemical shifts are given in ppm (δ) referenced to $CDCl_3$ with 7.28 for ^{1}H and 77.03 for ^{13}C, and to DMSO-d_6 with 2.50 for ^{1}H and 39.52 for ^{13}C. Signals are abbreviated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, and coupling constants are expressed in hertz. Melting points were measured on a SGW® X-4B apparatus and uncorrected. HRMS were recorded on Agilent 6210TOF LC/MS mass spectrometer.

2. General procedures for synthesizing raw materials:



S1

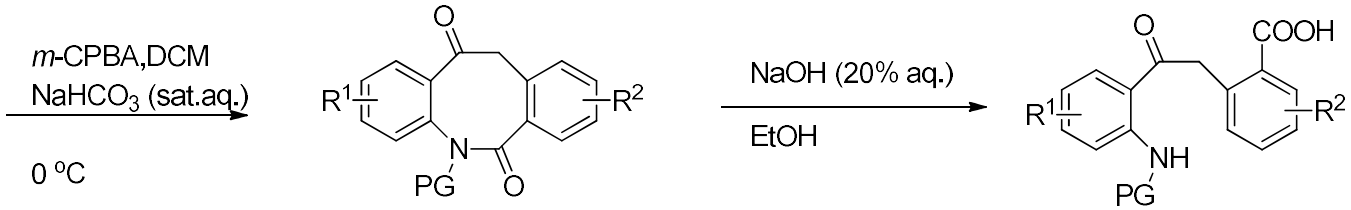
S2

R^1 = H, Me, OMe, F, Cl, CF_3.

R^2 = H, Me, OMe, Br, Cl, F.

R^1 = H, Me, OMe, F, Cl, CF_3.
R^2 = H, Me, OMe, Br, Cl, F.

R^1 = H, Me, OMe, F, Cl, CF_3.
R^2 = H, Me, OMe, Br, Cl, F.
PG = Me, Bn.



S3

13 / 15

R^1 = H, Me, OMe, F, Cl, CF_3.
R^2 = H, Me, OMe, Br, Cl, F.
PG = Me, Bn.

R^1 = H, Me, OMe, F, Cl, CF_3.
R^2 = H, Me, OMe, Br, Cl, F.
PG = Me, Bn.

General procedure A:

The benzoic acid starting materials were prepared according to the know procedure[1] and the preparation of **13a** was used here as an example.

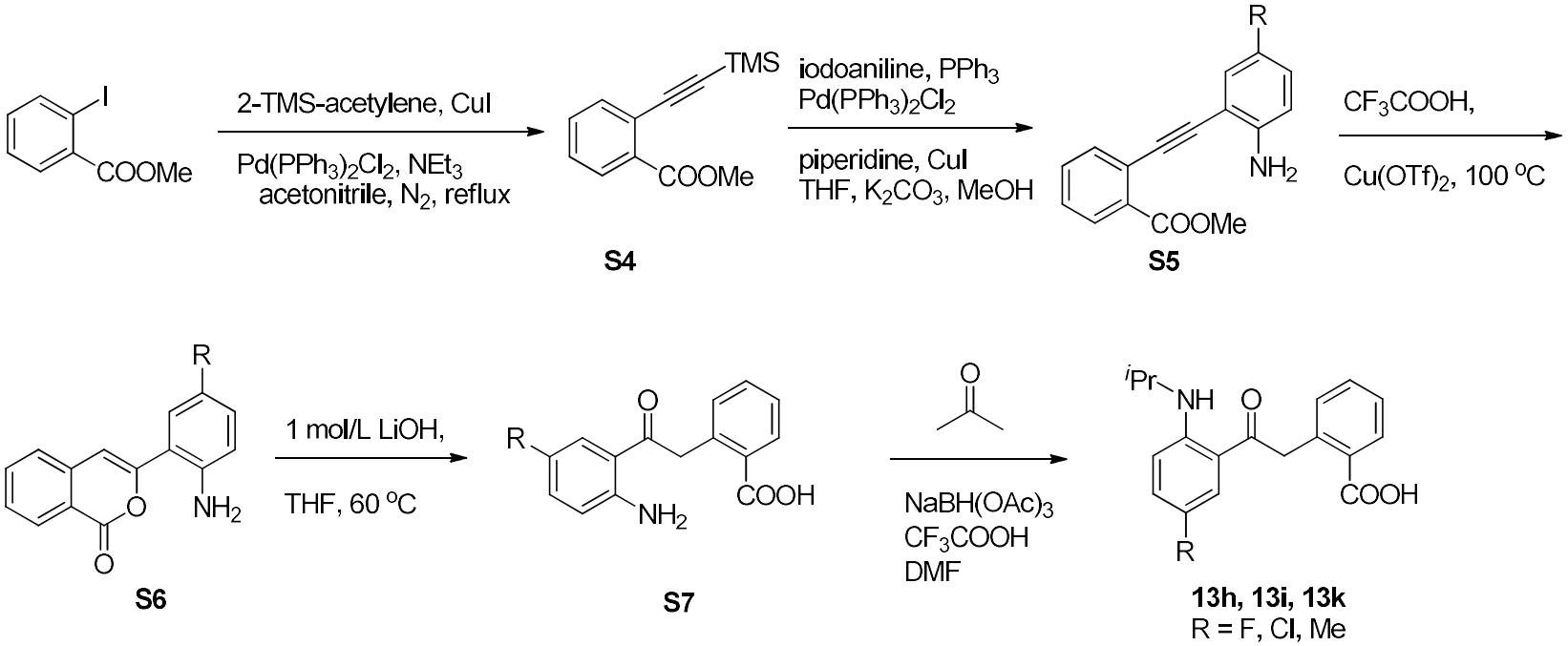
To a solution of phenyl hydrazine (1.1 g, 10 mmol) and 1-indanone (1.3 g, 10 mmol) in ethanol (7 mL) was added glacial acetic acid (50 μL). The resulting mixture was stirred at reflux for 15 minutes before it was cooled to room temperature. Upon cooling, long and white crystals precipitated out of

solution, which were collected via vacuum filtration and combined with isopropanol (34 mL). Sulfuric acid (36 N, 1.2 mL) was added via syringe and the resulting solution was stirred at reflux (90 °C) for 16 hours. Upon cooling to room temperature, the solution was basified to pH 10 with aqueous sodium hydroxide (2% NaOH by mass) resulting in the formation of precipitate. The solid was collected by vacuum filtration to yield **S1a** in 50% yield (1.0 g, 5 mmol).

To a solution of **S1a** (1.0 g, 5 mmol) in toluene (6.7 mL) was added aqueous sodium hydroxide (50% NaOH by mass, 2.7 mL), TBAF (130 mg, 1.34 mmol), and iodomethane (2.0 mL, 32 mmol). The reaction mixture was stirred vigorously at 40 °C for 17 hours and then at 55 °C for an additional 1.5 hours. Upon cooling to room temperature, the mixture was diluted with toluene (5 mL) and H_2O (5 mL), and the aqueous layer was extracted ethyl acetate (2 x 5 mL). Organic layers were combined, dried over anhydrous magnesium sulfate and concentrated *in vacuo*. Crude product was purified by flash column chromatography (PE/EtOAc = 50:1) to give **S2a** (0.9 g, 85%) as pale brown solid.

To a solution of **S2a** (0.9 mg, 4.2 mmol) in dichloromethane (108 mL) and saturated aqueous $NaHCO_3$ (13 mL) at 0 °C was added *m*-CPBA (77%, 2.3 g, 13.3 mmol) portionwise over 5 minutes. The reaction mixture was stirred at 0 °C for 30 minutes and then warmed to room temperature over 40 minutes. The reaction was subsequently quenched via addition of NaOH (1N, 38 mL) and the resulting aqueous layer was extracted dichloromethane (2 X 100 mL) and ethyl acetate (100 mL). Organic layers were combined and washed brine (100 mL), dried over anhydrous magnesium sulfate and concentrated *in vacuo* . The residue was purified by column chromatography (PE/EtOAc = 4:1) on silica gel to provide the **S3a** (0.8 g, 87%) as pale brown solid.

To a solution of azocine **S3a** (0.8 g, 3.7 mmol) in ethanol (8.8 mL) was added sodium hydroxide (20% aq., 2.2 mL), and the solution was stirred at room temperature for 0.5 h before neutralising with hydrochloric acid (3 M) and extracting with diethyl ether (3 X 10 mL). The combined organic phase were washed with water (3 X 10 mL) and saturated brine (10 mL), dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography (DCM/MeOH = 50:1) on silica gel to provide the **13a** (0.8 g, 90%) as a yellow solid.



General procedure B:

The benzoic acid starting materials with ^{i}Pr protecting group on nitrogen were prepared according to the know procedure[2] and the preparation of **13h** was used here as an example.

To a solution of methyl 2-iodobenzoate (4.7 mL, 28.7 mmol) in THF (103 mL) were added 2-TMS-acetylene (3.1 g, 31.3 mmol), PPh_3 (191.5 mg, 0.7 mmol), $Pd(PPh_3)_2Cl_2$ (1.0 g, 1.5 mmol), and Et_3N (24.0 mL, 172.4 mmol). The reaction mixture was degassed and stirred under an atmosphere of nitrogen for 20 min before the addition of CuI (116.3 mg, 0.6 mmol). The reaction was then stirred at rt for 12 h, after which time additional $Pd(PPh_3)_2Cl_2$ (205.0 mg, 0.29 mmol) and CuI (27.4 mg, 0.14 mmol) were added and stirring continued for 6 h. The reaction mixture was diluted with diethyl ether (140 mL) and then washed with HCl solution (0.1 M, 2 X 140 mL), H_2O (140 mL), and brine (140 mL). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. The

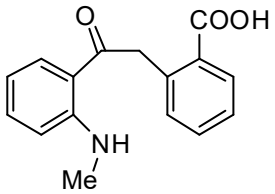
residue was purified by column chromatography (PE/EtOAc = 25:1) on silica gel to provide the **S4a** (5.9 g, 89%) as a pale yellow oil.

To a solution of compound **S4a** (1.7 g, 7.5 mmol) in THF (97 mL) were added 4-fluoro-2-iodoaniline (2.0 g, 8.3 mmol), PPh_3 (0.4 g, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (0.5 g, 0.8 mmol), and piperidine (10.8 mL, 109 mmol). The reaction mixture was degassed and stirred under an atmosphere of nitrogen for 20 min before the addition of CuI (0.3 g, 1.5 mmol) and K_2CO_3 (1.2 g, 10.0 mmol). The reaction mixture was stirred at reflux, MeOH (9.7 mL) was added dropwise, and heating was continued for 12 h. Additional $Pd(PPh_3)_2Cl_2$ (52.2 mg, 0.1 mmol) and CuI (30 mg, 0.2 mmol) were then added, and stirring was continued for 6 h at reflux. The reaction mixture was cooled to rt, diluted with ethyl acetate (500 mL), and then washed with HCl solution (0.1 M, 2 X 100 mL), H_2O (100 mL), and brine (100 mL). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo.* The residue was purified by column chromatography (PE/EtOAc = 6:1) on silica gel to provide **S5a** (1.4 g, 70%) as a yellow solid.

To a solution of alkyne **S5a** (1.4 g, 5.2 mmol) in trifluoroacetic acid (26 mL) was added $Cu(OTf)_2$ (37.6 mg, 0.1 mol). The solution was stirred at reflux for 5 h before it was cooled to room temperature.. Trifluoroacetic acid was evaporated under reduced pressure. The residue was partitioned between CH_2Cl_2 (260 mL) and water (260 mL). The organic layer was further washed with brine (2 x 260 mL), dried (Na_2SO_4), and concentrated *in vacuo***.** The residue was purified by column chromatography (PE/EtOAc = 5:1) on silica gel to provide the **S6a** (1.1 g, 81%) as a yellow solid.

To a solution of **S4a** (164.1 mg, 0.6 mmol), 2-propanone (27.2 mg, 0.9 mmol) and CF_3COOH (228 mg, 2 mmol) in DMF (2 mL). The solution was stirred at room temperature for 2 h. The reaction was added STAB (212 mg, 0.10 mmol) and stirred at 50 ^oC for 12 h. The reaction mixture was then cooled to rt and diluted with water (5 mL) before it was extracted with EtOAc (3 X 10 mL). The combined organic phase were washed with saturated brine (10 mL), dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography (DCM/MeOH = 50:1) on silica gel to provide the **13h** (44.4 mg, 24%) as a yellow solid.

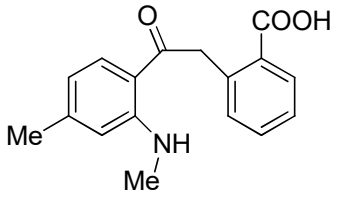
3. **Synthesis and characterization of raw materials:**



13a

2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13a):

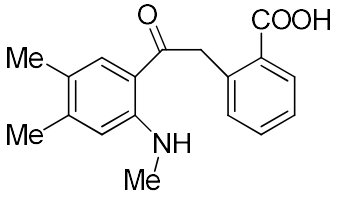
Following the general procedure A, **13a** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.8 g, 90% yield); Mp = 179-180 °C; R_f = 0.20 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1 H), 8.11 (d, *J* = 7.7 Hz, 1 H), 7.94 (d, *J* = 7.7 Hz, 1 H), 7.53 (t, *J* = 7.2 Hz, 1 H), 7.41 (dt, *J* = 14.7, 7.4 Hz, 2 H), 7.24 (d, *J* = 7.5 Hz, 1 H), 6.71 (d, *J* = 8.6 Hz, 1 H), 6.65 (t, *J* = 7.5 Hz, 1 H), 4.75 (s, 2 H), 2.85 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.6, 171.6, 151.8, 138.0, 135.1, 133.0, 132.5, 131.7, 131.7, 129.3, 127.2, 117.3, 114.4, 111.8, 44.9, 29.5 ppm.



13b

2-(2-(4-methyl-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13b):

Following the general procedure A, **13b** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.8 g, 87% yield); Mp = 161-162 °C; R_f = 0.23 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.70 (s, 1 H), 8.54 (q, *J* = 4.8 Hz, 1 H), 7.95–7.89 (m, 2 H), 7.51 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.38 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.31–7.28 (m, 1 H), 6.54 (s, 1 H), 6.47 (dd, *J* = 8.2, 1.2 Hz, 1 H), 4.72 (s, 2 H), 2.80 (d, *J* = 5.0 Hz, 3 H), 2.31 (s, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.0, 168.8, 151.9, 145.7, 138.2, 133.1, 132.3, 132.1, 131.5, 130.7, 127.1, 115.7, 115.3, 111.6, 45.0, 29.4, 22.3 ppm.

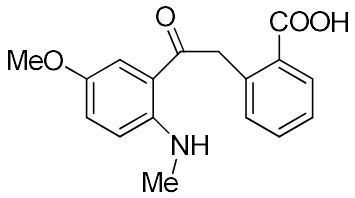


13c

2-(2-(4,5-dimethyl-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13c):

Following the general procedure A, **13c** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.5 g, 64% yield); Mp = 161-162 °C; R_f =

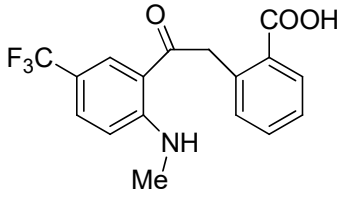
0.21 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.69 (s, 1 H), 8.35 (d, J = 5.0 Hz, 1 H), 7.92 (dd, J = 7.8, 1.3 Hz, 1 H), 7.78 (s, 1 H), 7.50 (td, J = 7.5, 1.4 Hz, 1 H), 7.37 (td, J = 7.6, 1.2 Hz, 1 H), 7.29 (d, J = 6.9 Hz, 1 H), 6.56 (s, 1 H), 4.73 (s, 2 H), 2.79 (d, J = 4.8 Hz, 3 H), 2.24 (s, 3 H), 2.18 (s, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.0, 168.7, 144.8, 138.0, 133.1, 132.4, 132.2, 131.4, 130.7, 127.1, 45.2, 30.6, 20.7, 18.9 ppm.



13d

2-(2-(5-methoxy-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13d):

Following the general procedure A, **13d** was purified by DCM/MeOH (25:1) and obtained as a yellow solid (0.9 g, 84% yield); Mp = 160-161 °C; R_f = 0.15 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.18 (s, 1 H), 7.95 (dd, J = 7.8, 1.3 Hz, 1 H), 7.59 – 7.46 (m, 2 H), 7.38 (td, J = 7.6, 1.2 Hz, 1 H), 7.34–7.27 (m, 1 H), 7.16 (dd, J = 9.1, 2.9 Hz, 1 H), 6.71 (d, J = 9.2 Hz, 1 H), 4.77 (s, 2 H), 3.76 (s, 3 H), 2.78 (s, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 198.9, 168.3, 148.3, 146.6, 137.6, 132.6, 131.7, 131.0, 130.3, 126.7, 123.4, 116.5, 114.8, 112.5, 55.8, 44.9, 29.3 ppm.

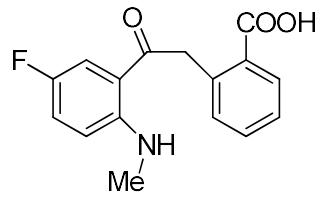


13e

2-(2-(2-(methylamino)-5-(trifluoromethyl)phenyl)-2-oxoethyl)benzoic acid (13e):

Following the general procedure A, **13e** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (1.0 g, 89% yield); Mp = 203-204 °C; R_f = 0.23 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.74 (s, 1 H), 8.89 (q, J = 4.7 Hz, 1 H), 8.29 (d, J = 1.2 Hz, 1 H), 7.96 (dd, J = 7.8, 1.3 Hz, 1

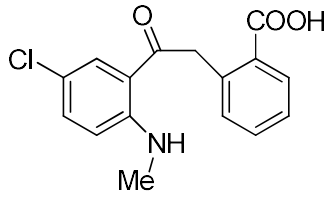
H), 7.70 (dd, *J* = 9.0, 1.9 Hz, 1 H), 7.54 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.40 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.36–7.30 (m, 1 H), 6.90 (d, *J* = 9.0 Hz, 1 H), 4.81 (s, 2 H), 2.87 (d, *J* = 5.0 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ 199.6 (s), 168.6 (s), 153.6 (s), 137.8 (s), 133.3 (s), 132.3 (s), 131.2 (s), 130.9 (d, *J* = 16.6 Hz), 129.4 (s), 127.3 (s), 126.4 (s), 124.3 (s), 116.5 (s), 114.1 (d, *J* = 32.7 Hz), 112.6 (s), 45.2 (s), 29.6 (s) ppm.



13f

2-(2-(5-fluoro-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13f):

Following the general procedure A, **13f** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.9 g, 92% yield); Mp = 191-192 °C; R_f = 0.22 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.71 (s, 1 H), 8.35 (d, *J* = 4.9 Hz, 1 H), 7.95 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.88 (dd, *J* = 10.4, 3.0 Hz, 1 H), 7.53 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.46–7.25 (m, 3 H), 6.74 (dd, *J* = 9.4, 4.6 Hz, 1 H), 4.74 (s, 2 H), 2.80 (d, *J* = 4.8 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ 199.2 (d, *J* = 2.8 Hz), 168.7 (s), 152.3 (d, *J* = 230.4 Hz), 148.7 (s), 137.9 (s), 133.2 (s), 132.3 (s), 131.2 (s), 130.8 (s), 127.3 (s), 123.0 (d, *J* = 22.9 Hz), 117.0 (d, *J* = 22.1 Hz), 116.7 (d, *J* = 5.5 Hz), 113.1 (d, *J* = 7.1 Hz), 45.4 (s), 29.8 (s) ppm.

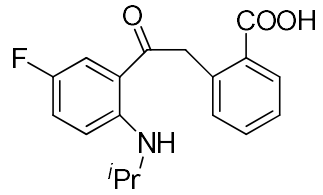


13g

2-(2-(5-chloro-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13g):

Following the general procedure A, **13g** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.8 g, 82% yield); Mp = 191-192 °C; R_f = 0.22 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.72 (s, 1 H), 8.50 (d, *J* = 4.2 Hz, 1 H), 8.04 (d, *J* = 2.5 Hz, 1 H), 7.95 (dd, *J* = 7.8, 1.3 Hz, 1

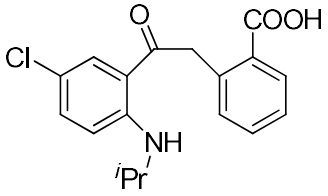
H), 7.53 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.45 (dd, *J* = 9.1, 2.5 Hz, 1 H), 7.39 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.36–7.28 (m, 1 H), 6.77 (d, *J* = 9.2 Hz, 1 H), 4.75 (s, 2 H), 2.80 (d, *J* = 3.7 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.1, 168.6, 150.4, 137.9, 134.9, 133.2, 132.3, 131.2, 131.0, 130.8, 127.3, 118.1, 117.6, 113.8, 45.3, 29.6 ppm.



13h

2-(2-(5-fluoro-2-(isopropylamino)phenyl)-2-oxoethyl)benzoic acid (13h):

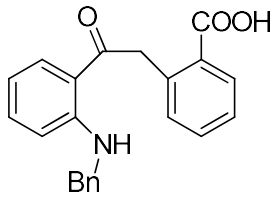
Following the general procedure B, **13h** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (44.4 mg, 24% yield); Mp = 150-151 ^{o}C; R_f = 0.21 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.71 (s, 1 H), 8.42 (d, *J* = 7.1 Hz, 1 H), 7.94 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.87 (dd, *J* = 10.4, 3.0 Hz, 1 H), 7.52 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.39 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.32 (ddd, *J* = 14.3, 10.6, 5.4 Hz, 2 H), 6.82 (dd, *J* = 9.5, 4.6 Hz, 1 H), 4.72 (s, 2 H), 3.71 (dd, *J* = 12.5, 6.3 Hz, 1 H), 1.14 (d, *J* = 6.3 Hz, 6 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ 199.0 (s), 168.2 (s), 151.6 (d, *J* = 230.4 Hz), 146.7 (s), 137.4 (s), 132.8 (s), 131.8 (s), 130.7 (s), 130.4 (s), 126.8 (s), 122.7 (d, *J* = 23.0 Hz), 116.8 (d, *J* = 21.9 Hz), 115.8 (d, *J* = 5.4 Hz), 113.6 (d, *J* = 6.9 Hz), 44.9 (s), 42.7 (s), 22.4 (s) ppm.



13i

2-(2-(5-chloro-2-(isopropylamino)phenyl)-2-oxoethyl)benzoic acid (13i):

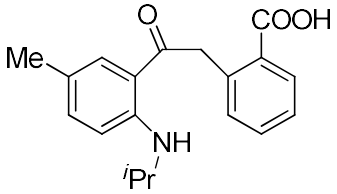
Following the general procedure B, **13i** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (50.4 mg, 25% yield); Mp = 158.7-159.7 °C; R_f = 0.22 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.72 (s, 1 H), 8.59 (d, *J* = 7.5 Hz, 1 H), 8.05 (d, *J* = 2.5 Hz, 1 H), 7.94 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.52 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.46–7.34 (m, 2 H), 7.30 (d, *J* = 7.5 Hz, 1 H), 6.84 (t, *J* = 10.4 Hz, 1 H), 4.74 (s, 2 H), 3.72 (dp, *J* = 12.8, 6.4 Hz, 1 H), 1.15 (t, *J* = 5.4 Hz, 6 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.0, 168.2, 148.3, 137.4, 134.5, 132.9, 131.9, 130.9, 130.6, 130.4, 126.8, 117.2, 117.0, 114.2, 44.8, 42.7, 22.4 ppm.



13j

2-(2-(2-(benzylamino)phenyl)-2-oxoethyl)benzoic acid (13j):

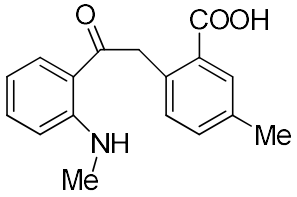
Following the general procedure A, **13j** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.6 g, 78% yield); Mp = 200-201 °C; R_f = 0.22 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.99 (dd, *J* = 8.1, 1.3 Hz, 1 H), 7.56 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.44–7.38 (m, 1 H), 7.37–7.33 (m, 1 H), 7.32–7.21 (m, 7 H), 6.71 (dd, *J* = 16.2, 8.1 Hz, 2 H), 4.77 (s, 2 H), 4.41 (s, 2 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 200.1, 168.7, 150.7, 139.5, 138.0, 135.2, 133.2, 132.4, 132.2, 131.3, 130.8, 129.0, 127.6, 127.4, 127.2, 117.6, 114.8, 112.5, 46.3, 45.3 ppm.



13k

2-(2-(2-(isopropylamino)-5-methylphenyl)-2-oxoethyl)benzoic acid (13k):

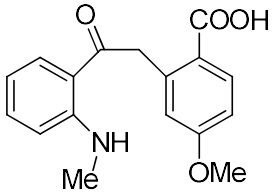
Following the general procedure B, **13k** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (80.1 mg, 43% yield); Mp = 171.8-172.8 °C; R_f = 0.19 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.69 (s, 1 H), 8.43 (d, *J* = 7.5 Hz, 1 H), 7.93 (dd, *J* = 7.8, 1.1 Hz, 1 H), 7.84 (s, 1 H), 7.51 (td, *J* = 7.5, 1.3 Hz, 1 H), 7.37 (dd, *J* = 10.9, 4.3 Hz, 1 H), 7.29 (d, *J* = 7.3 Hz, 1 H), 7.24 (dd, *J* = 8.6, 1.6 Hz, 1 H), 6.72 (d, *J* = 8.7 Hz, 1 H), 4.75 (s, 2 H), 3.69 (dd, *J* = 13.0, 6.5 Hz, 1 H), 2.24 (s, 3 H), 1.13 (d, *J* = 6.3 Hz, 6 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.3, 168.7, 147.8, 137.7, 136.0, 132.8, 131.7, 131.6, 130.9, 130.3, 126.7, 121.9, 116.3, 112.2, 44.8, 42.4, 22.6, 19.9 ppm.



15a

5-methyl-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15a):

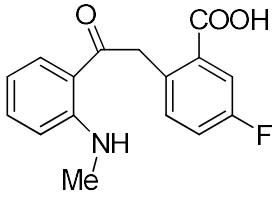
Following the general procedure A, **15a** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.7 g, 79% yield); Mp = 173.5-174.5 °C; R_f = 0.24 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.65 (s, 1 H), 8.53 (s, 1 H), 8.03 (d, *J* = 7.7 Hz, 1 H), 7.76 (s, 1 H), 7.43 (t, *J* = 7.4 Hz, 1 H), 7.32 (d, *J* = 7.3 Hz, 1 H), 7.18 (d, *J* = 7.4 Hz, 1 H), 6.73 (d, *J* = 8.4 Hz, 1 H), 6.64 (t, *J* = 7.2 Hz, 1 H), 4.70 (s, 2 H), 2.80 (d, *J* = 3.6 Hz, 3 H), 2.35 (s, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.9, 168.8, 151.7, 136.3, 135.3, 135.1, 133.1, 132.8, 132.2, 131.3, 131.1, 117.4, 114.3, 111.7, 44.8, 29.5, 20.9 ppm.



15b

4-methoxy-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15b):

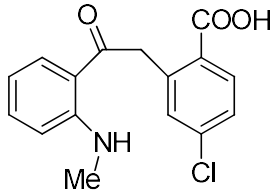
Following the general procedure A, **15b** was purified by DCM/MeOH (25:1) and obtained as a yellow solid (0.8 g, 78% yield); Mp = 194.5-195.5 °C; R_f = 0.14 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.41 (s, 1 H), 8.52 (d, J = 5.0 Hz, 1 H), 8.02 (dd, J = 8.1, 1.4 Hz, 1 H), 7.94 (d, J = 8.7 Hz, 1 H), 7.45–7.37 (m, 1 H), 6.92 (dd, J = 8.7, 2.7 Hz, 1 H), 6.89 (d, J = 2.6 Hz, 1 H), 6.73 (d, J = 8.1 Hz, 1 H), 6.68–6.60 (m, 1 H), 4.75 (s, 2 H), 3.81 (s, 3 H), 2.80 (d, J = 5.0 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.7, 168.2, 162.2, 151.7, 140.9, 135.2, 133.2, 132.2, 123.3, 118.7, 117.4, 114.2, 112.1, 111.6, 55.8, 45.5, 29.4 ppm.



15c

5-fluoro-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15c):

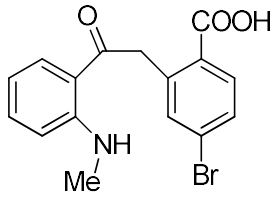
Following the general procedure A, **15c** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.9 g, 89% yield); Mp = 182-183 °C; R_f = 0.22 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.02 (s, 1 H), 8.51 (d, J = 4.9 Hz, 1 H), 8.03 (dd, J = 8.1, 1.4 Hz, 1 H), 7.67 (dd, J = 9.7, 2.7 Hz, 1 H), 7.53–7.18 (m, 3 H), 6.74 (d, J = 7.9 Hz, 1 H), 6.69–6.61 (m, 1 H), 4.76 (s, 2 H), 2.80 (d, J = 4.8 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ 199.0 (s), 167.1 (d, J = 2.5 Hz), 160.6 (d, J = 243.2 Hz), 151.3 (s), 134.9 (s), 134.7 (d, J = 7.6 Hz), 133.8 (d, J = 3.1 Hz), 132.9 (d, J = 6.9 Hz), 131.7 (s), 118.5 (d, J = 20.7 Hz), 116.8 (s), 116.6 (d, J = 22.9 Hz), 113.8 (s), 111.2 (s), 43.9 (s), 29.0 (s) ppm.



15d

4-chloro-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15d):

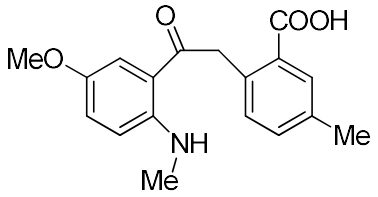
Following the general procedure A, **15d** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.8 g, 85% yield); Mp = 192-193 °C; R_f = 0.23 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.92 (s, 1 H), 8.55–8.45 (m, 1 H), 8.01 (dd, J = 8.1, 1.4 Hz, 1 H), 7.97–7.92 (m, 1 H), 7.49–7.41 (m, 3 H), 6.74 (d, J = 8.1 Hz, 1 H), 6.69-6.62 (m, 1 H), 4.78 (s, 2 H), 2.81 (d, J = 4.9 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 198.7, 167.4, 151.3, 140.3, 136.3, 135.0, 132.4, 132.2, 131.8, 129.9, 126.8, 116.8, 113.9, 111.3, 44.4, 29.0 ppm.



15e

4-bromo-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15e):

Following the general procedure A, **15e** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.8 g, 84% yield); Mp = 192-193 °C; R_f = 0.21 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.94 (s, 1 H), 8.49 (q, J = 4.7 Hz, 1 H), 8.01 (dd, J = 8.1, 1.4 Hz, 1 H), 7.89 – 7.78 (m, 1 H), 7.60 (td, J = 4.4, 2.1 Hz, 2 H), 7.54–7.39 (m, 1 H), 6.74 (d, J = 8.1 Hz, 1 H), 6.70 – 6.59 (m, 1 H), 4.77 (s, 2 H), 2.81 (d, J = 4.9 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 198.7, 167.5, 151.3, 140.3, 135.2, 134.9, 132.2, 131.7, 130.3, 129.7, 125.3, 116.7, 113.8, 111.2, 44.2, 29.0 ppm.

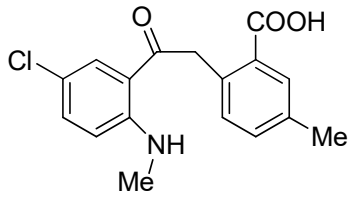


15f

2-(2-(5-methoxy-2-(methylamino)phenyl)-2-oxoethyl)-5-methylbenzoic acid (15f):

Following the general procedure A, **15f** was purified by DCM/MeOH (25:1) and obtained as a yellow solid (0.5 g, 60% yield); Mp = 162-163 °C; R_f =

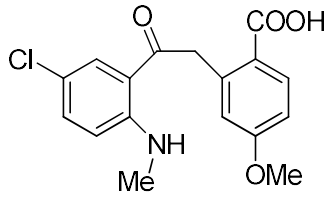
0.16 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.66 (s, 1 H), 8.17 (s, 1 H), 7.76 (d, J = 1.2 Hz, 1 H), 7.51 (d, J = 2.9 Hz, 1 H), 7.32 (dd, J = 7.7, 1.3 Hz, 1 H), 7.23–7.06 (m, 2 H), 6.71 (d, J = 9.2 Hz, 1 H), 4.70 (s, 2 H), 3.76 (s, 3 H), 2.78 (s, 3 H), 2.35 (s, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.5, 168.9, 148.8, 147.0, 136.3, 135.0, 132.9, 132.8, 131.3, 131.1, 123.8, 117.0, 115.2, 113.0, 56.2, 44.9, 29.8, 20.9 ppm.



15g

2-(2-(5-chloro-2-(methylamino)phenyl)-2-oxoethyl)-5-methylbenzoic acid (15g):

Following the general procedure A, **15g** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.6 g, 61% yield); Mp = 166-167 °C; R_f = 0.23 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (d, J = 5.1 Hz, 1 H), 8.03 (d, J = 2.5 Hz, 1 H), 7.75 (d, J = 1.4 Hz, 1 H), 7.43 (dd, J = 9.1, 2.5 Hz, 1 H), 7.29 (dd, J = 7.7, 1.4 Hz, 1 H), 7.15 (d, J = 7.7 Hz, 1 H), 6.76 (d, J = 9.2 Hz, 1 H), 4.68 (s, 2 H), 2.80 (d, J = 5.0 Hz, 3 H), 2.34 (s, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 199.1, 168.6, 150.0, 135.9, 134.4, 134.2, 132.5, 132.1, 131.2, 130.9, 130.7, 117.8, 117.2, 113.4, 44.5, 29.2, 20.5 ppm.

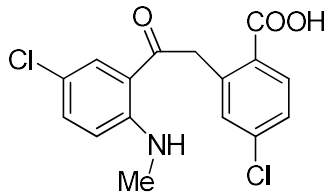


15h

2-(2-(5-chloro-2-(methylamino)phenyl)-2-oxoethyl)-4-methoxybenzoic acid (15h):

Following the general procedure A, **15h** was purified by DCM/MeOH (25:1) and obtained as a yellow solid (0.6 g, 63% yield); Mp = 182-183 °C; R_f = 0.16 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (d, J = 5.0 Hz, 1 H), 8.01 (s, 1 H), 7.95 (d, J = 8.6 Hz, 1 H), 7.43 (dd, J = 9.1, 2.2 Hz, 1 H), 6.89 (d, J = 7.9 Hz, 1 H), 6.83 (s, 1 H), 6.75 (d, J = 9.1 Hz, 1 H), 4.75 (s, 2 H), 3.80 (s, 3 H), 2.79 (d, J = 4.9 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ

= 199.4, 161.8, 150.3, 140.1, 134.8, 133.2, 131.1, 118.4, 118.3, 117.6, 113.8, 112.0, 55.7, 45.5, 29.6 ppm.

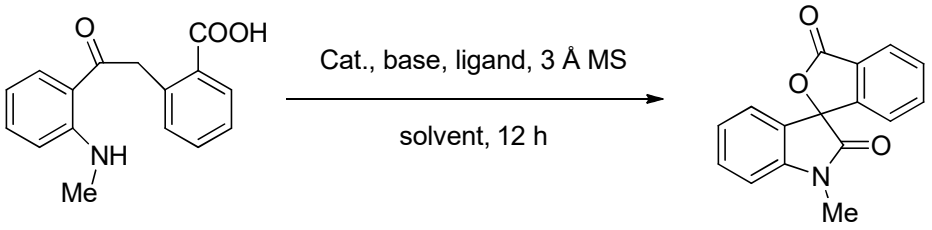


15i

4-chloro-2-(2-(5-chloro-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15i):

Following the general procedure A, **15i** was purified by DCM/MeOH (50:1) and obtained as a yellow solid (0.7 g, 67% yield); Mp = 171-172 °C; R_f = 0.21 (DCM/MeOH = 50:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.94 (s, 1 H), 8.48 (d, J = 5.0 Hz, 1 H), 8.01 (d, J = 2.5 Hz, 1 H), 7.95 (d, J = 8.3 Hz, 1 H), 7.47 (ddd, J = 5.9, 4.8, 2.4 Hz, 3 H), 6.78 (d, J = 9.2 Hz, 1 H), 4.77 (s, 2 H), 2.80 (d, J = 5.0 Hz, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ = 198.1, 167.3, 149.9, 140.0, 136.3, 134.6, 132.4, 132.2, 130.6, 129.6, 126.8, 117.5, 117.2, 113.5, 44.5, 29.2 ppm.

4. Conditions optimization of 3-spirooxindole benzofuranone:



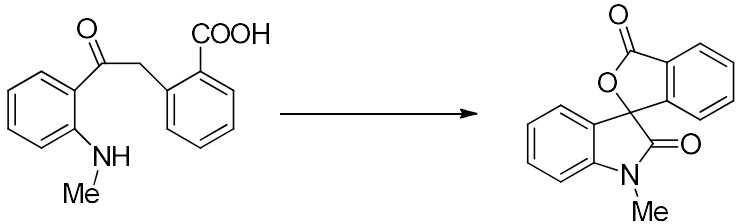
13a **14a**

entry[a]	Pd cat.	catalyst	ligand	base	solvent[b]	yields (%)[c]
1	$Pd(OAc)_2$	$Cu(OAc)_2/Ag_2CO_3$	Phen	Na_2CO_3	DMA	31
2	$Pd(OAc)_2$	$Cu(OAc)_2/Ag_2CO_3$	Phen	*t*-BuONa	DMA	12
3	$Pd(OAc)_2$	$Cu(OAc)_2/Ag_2CO_3$	Phen	K_3PO_4	DMA	50
4	$Pd(OAc)_2$	$Cu(OAc)_2/Ag_2CO_3$	Phen	Na_2SO_4	DMA	trace
5	$Pd(OAc)_2$	$Cu(OAc)_2/Ag_2CO_3$	Phen	K_3PO_4/ Na_2SO_4	DMA	44
6	$Pd(OAc)_2$	$Cu(OAc)_2/Ag_2CO_3$	Phen	*t*-BuOK	DMA	10
7	$Pd(OAc)_2$	CuO/Ag_2CO_3	Phen	K_3PO_4	DMA	65
8	--	CuO/Ag_2CO_3	Phen	K_3PO_4	DMA	64
9	--	CuO/Ag_2CO_3	Dipyridyl	K_3PO_4	DMA	62
10	--	CuO/Ag_2CO_3	PPh_3	K_3PO_4	DMA	46
11	--	CuO/Ag_2CO_3	BINAP	K_3PO_4	DMA	47
12	--	CuO/Ag_2CO_3	Brettphos	K_3PO_4	DMA	53
13	--	CuO/Ag_2CO_3	DPPE	K_3PO_4	DMA	50
14	--	$CuCl_2/Ag_2CO_3$	Phen	K_3PO_4	DMA	47
15	--	$CuBr_2/Ag_2CO_3$	Phen	K_3PO_4	DMA	65
16	--	$CuSO_4/Ag_2CO_3$	Phen	K_3PO_4	DMA	60
17	--	$CuBr_2/Ag_2CO_3$	Phen	K_3PO_4	DMA	54
18	--	$CuBr_2/Ag_2CO_3$	Phen	K_3PO_4	DMA	54
19	--	CuCl	Phen	K_3PO_4	DMA	44
20	--	CuBr	Phen	K_3PO_4	DMA	53
21	--	CuI	Phen	K_3PO_4	DMA	55

22	--	CuCN	Phen	K_3PO_4	DMA	47
23	--	$CuBr_2$	Phen	K_3PO_4	DMA	65
24[d]	--	$CuBr_2$	Phen	K_3PO_4	DMA	53
25[e]	--	$CuBr_2$	Phen	K_3PO_4	DMA	trace
26	--	$CuBr_2$	--	K_3PO_4	DMA	75
27	--	--	Phen	K_3PO_4	DMA	39
28	--	$CuBr_2$	--	KOH	DMA	trace
29	--	$CuBr_2$	--	Cs_2CO_3	DMA	36
30	--	$CuBr_2$	--	NaOMe	DMA	80
31	--	$CuBr_2$	--	NaOMe	DCE	40
32	--	$CuBr_2$	--	NaOMe	DMF	84

[a]Reaction condtions: benzoic acid **13a** (0.2 mmol), Pd catalyst (10 mol %), catalyst (20 mol %), ligand (20 mol %), base (2.0 equiv), 3 Å molecular sieves (0.4 g/mmol), solvent (1 mL), 12 h, 150 [o]C, O_2 atmosphere. [b]Anhydrous solvent. [c]Isolated yields. [d] Air atmosphere. [e] N_2 atmosphere.

5. General procedure for the oxidative annulation:



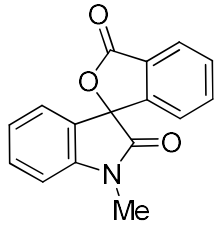
13a **14a**

In a 10 mL microwave tube was charged with substrate **13a** (53.6 mg, 0.2 mmol), sodium methoxide (21.6 mg, 0.4 mmol), $CuBr_2$ (9.0 mg, 0.04 mmol), 3 Å molecular sieves (150 mg) and anhydrous DMF 1 mL. The reaction mixture was evacuated and refilled with O_2 for 3 times before it was stirred at 150 ^oC for 12 h. The reaction mixture was then cooled to rt and diluted with water (5 mL) before it was extracted with

EtOAc (30 mL). The combined organic phase were washed with water (3 X 10 mL) and saturated brine (10 mL), dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography (PE/EtOAc = 3:1) on silica gel to provide the desired 3-spirooxindole benzofuranone **14a** (44.5 mg, 84%) as a white solid.

In a 50 mL microwave tube was charged with substrate **13a** (268.6 mg, 1.0 mmol), sodium methoxide (108 mg, 2.0 mmol), $CuBr_2$ (45 mg, 0.2 mmol), 3 Å molecular sieves (150 mg) and anhydrous DMF 5 mL. The reaction mixture was evacuated and refilled with O_2 for 3 times before it was stirred at 150 ^oC for 12 h. The reaction mixture was then cooled to rt and diluted with water (25 mL) before it was extracted with EtOAc (150 mL). The combined organic phase were washed with water (3 X 50 mL) and saturated brine (50 mL), dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography (PE/EtOAc = 3:1) on silica gel to provide the desired 3-spirooxindole benzofuranone **14a** (209.1 mg, 79%) as a white solid.

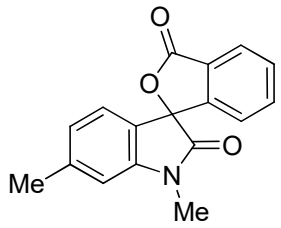
6. Synthesis and characterization of the 3-spirooxindole benzofuranone:



14a

1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14a):

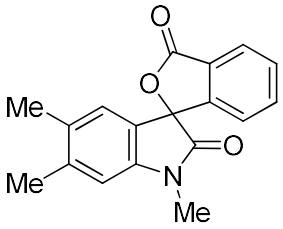
Following the general experiment procedure, **14a** was purified by PE/EtOAc (3:1) and obtained as a white solid (44.5 mg, 84% yield); Mp = 202.5-203.5 ^oC; R_f = 0.20 (PE/EtOAc = 3:1); ^1H NMR (500 MHz, DMSO-d_6) δ 8.04 (d, J = 7.4 Hz, 1 H), 7.78 (td, J = 7.4, 1.1 Hz, 1 H), 7.73 (td, J = 7.4, 0.9 Hz, 1 H), 7.54 (td, J = 7.8, 1.2 Hz, 1 H), 7.32 (d, J = 7.5 Hz, 1 H), 7.28 (d, J = 7.9 Hz, 1 H), 7.22–7.17 (m, 1 H), 7.11 (td, J = 7.5, 0.6 Hz, 1 H), 3.26 (s, 3 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ 170.6, 169.2, 146.5, 144.6, 135.5, 131.8, 130.7, 125.5, 125.0, 125.0, 124.1, 123.6, 122.3, 110.1, 84.2, 26.9 ppm; HRMS m/z (ESI) : calcd for $C_{16}H_{11}NO_3$ $[M + H]^+$ 266.0812, found 266.0812.



14b

1,6-dimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14b):

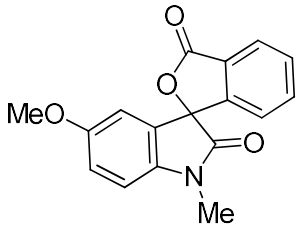
Following the general experiment procedure, **14b** was purified by PE/EtOAc (3:1) and obtained as a white solid (45.8 mg, 82% yield); Mp = 209.6-210.6 ^{o}C; R_f = 0.20 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 6.1, 2.1 Hz, 1 H), 7.64–7.60 (m, 2 H), 7.10 (dd, *J* = 5.9, 1.8 Hz, 1 H), 6.90 (s, 2 H), 6.82 (s, 1 H), 3.29 (s, 3 H), 2.44 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 169.6, 147.0, 144.7, 142.4, 134.7, 130.2, 126.1, 126.0, 125.0, 124.3, 121.9, 121.8, 110.0, 84.5, 26.9, 22.1 ppm; HRMS m/z (ESI) calcd for $C_{17}H_{14}NO_3$ $[M + H]^+$ 280.0971, found 280.0968.



14c

1,5,6-trimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14c):

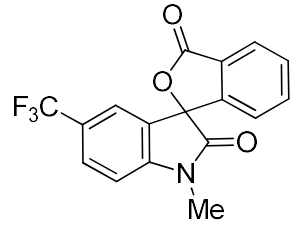
Following the general experiment procedure, **14c** was purified by PE/EtOAc (3:1) and obtained as a white solid (39.8 mg, 68% yield); Mp = 205.1-206.1 ^{o}C; R_f= 0.22 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04–7.99 (m, 1 H), 7.66–7.56 (m, 2 H), 7.10 (dd, *J* = 5.9, 1.8 Hz, 1 H), 6.79 (d, *J* = 2.1 Hz, 2 H), 3.28 (s, 3 H), 2.35 (s, 3 H), 2.17 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 169.7, 147.2, 142.6, 140.5, 134.7, 132.0, 130.2, 126.2, 126.1, 126.0, 121.9, 121.9, 110.6, 84.8, 27.0, 20.5, 19.3 ppm; HRMS m/z (ESI): calcd for $C_{18}H_{15}NO_3$ $[M + H]^+$ 294.1139, found 294.1125.



14d

5-methoxy-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14d):

Following the general experiment procedure, **14d** was purified by PE/EtOAc (2:1) and obtained as a white solid (48.4 mg, 82% yield); Mp = 161-162 ^{o}C; R_f = 0.21 (PE/EtOAc = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 6.2, 1.8 Hz, 1 H), 7.65–7.59 (m, 2 H), 7.11 (dd, *J* = 6.2, 1.5 Hz, 1 H), 6.97 (dd, *J* = 8.6, 2.5 Hz, 1 H), 6.91 (d, *J* = 8.6 Hz, 1 H), 6.61 (d, *J* = 2.5 Hz, 1 H), 3.71 (s, 3 H), 3.28 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 169.6, 156.8, 147.0, 137.9, 134.9, 130.4, 126.2, 126.0, 125.9, 121.9, 116.6, 111.8, 109.8, 84.8, 55.9, 27.1 ppm; HRMS m/z (ESI) calcd for $C_{17}H_{14}NO_4$ $[M + H]^+$ 296.0911, found 296.0917.

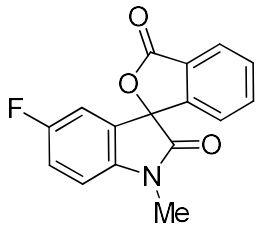


14e

1-methyl-5-(trifluoromethyl)-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14e):

Following the general experiment procedure, **14e** was purified by PE/EtOAc (3:1) and obtained as a white solid (44.0 mg, 66% yield). Mp = 200.1-200.8 ^{o}C; R_f = 0.25 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10–8.00 (m, 1 H), 7.75 (dd, *J* = 8.3, 0.9 Hz, 1 H), 7.71–7.62 (m, 2 H), 7.27 (d, *J* = 1.9 Hz, 1 H), 7.19–7.04 (m, 2 H), 3.35 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2 (s), 169.0 (s), 147.6 (s), 145.9 (s), 135.1 (s), 130.8 (s), 129.4 (q, *J* = 3.9 Hz),

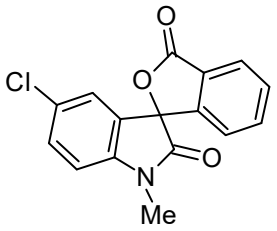
126.4 (s), 126.1 (s), 125.8 (s), 125.6 (s), 123.7 (d, J = 271.9 Hz), 122.4 (q, J = 3.7 Hz), 121.8 (s), 109.2 (s), 83.5 (s), 27.3 (s) ppm; HRMS m/z (ESI): calcd for $C_{17}H_{10}F_3NO_3$ $[M + H]^+$ 334.0690, found 334.0686.



14f

5-fluoro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14f):

Following the general experiment procedure, **14f** was purified by PE/EtOAc (3:1) and obtained as a white solid (48.1 mg, 85% yield); R_f = 0.24 (PE/EtOAc = 3:1); Mp = 193-194 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dd, J = 7.0, 2.3 Hz, 1 H), 7.48 (td, J = 7.8, 1.3 Hz, 1 H), 7.35 (td, J = 8.5, 2.4 Hz, 1 H), 7.13–7.10 (m, 1 H), 7.09 (t, J = 4.2 Hz, 1 H), 7.04 (dd, J = 7.5, 0.9 Hz, 1 H), 7.01 (d, J = 7.9 Hz, 1 H), 3.31 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0 (s), 169.2 (s), 160.5 (s), 158.6 (s), 146.3 (s), 140.5 (d, J = 2.2 Hz), 134.9 (s), 130.6 (s), 126.3 (d, J = 9.5 Hz), 125.7 (s), 121.8 (s), 118.1 (d, J = 23.6 Hz), 113.3 (d, J = 25.3 Hz), 101.0 (d, J = 7.9 Hz), 84.1 (s), 27.2 (s) ppm; HRMS m/z (ESI) calcd for $C_{16}H_{10}FNO_3$ $[M + H]^+$ 284.0720, found 284.0717.

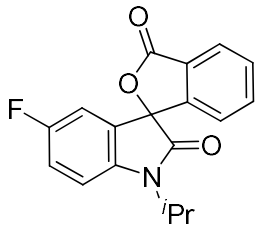


14g

5-chloro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14g):

Following the general experiment procedure, **14g** was purified by PE/EtOAc (3:1) and obtained as a white solid (47.8 mg, 80% yield); Mp = 177-178 °C;

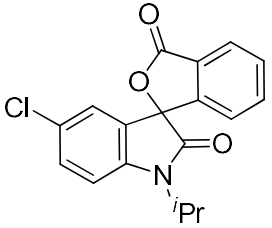
R_f = 0.23 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.05–8.02 (m, 1 H), 7.78 (td, J = 7.5, 1.3 Hz, 1 H), 7.74 (td, J = 7.4, 1.1 Hz, 1 H), 7.61 (dd, J = 8.4, 2.2 Hz, 1 H), 7.46 (d, J = 2.2 Hz, 1 H), 7.36 (dd, J = 4.6, 3.7 Hz, 1 H), 7.31 (d, J = 8.5 Hz, 1 H), 3.26 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 169.1, 146.2, 143.2, 135.0, 131.6, 130.7, 129.2, 126.4, 126.3, 125.7, 125.6, 121.8, 110.3, 83.9, 27.2 ppm; HRMS m/z (ESI) calcd for $C_{16}H_{10}ClNO_3$ $[M + H]^+$ 322.0246, found 322.0241.



14h

5-fluoro-1-isopropyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14h):

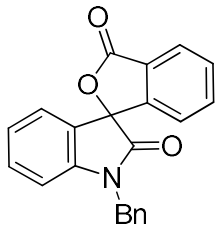
Following the general experiment procedure, **14h** was purified by PE/EtOAc (3:1) and obtained as a white solid (50.4 mg, 81% yield). Mp = 132-133 °C; R_f = 0.24 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 6.3, 1.7 Hz, 1 H), 7.64 (pd, J = 7.4, 1.3 Hz, 2 H), 7.13 (td, J = 8.7, 2.6 Hz, 1 H), 7.10–7.06 (m, 2 H), 6.78 (dd, J = 7.2, 2.6 Hz, 1 H), 4.59 (dt, J = 14.0, 7.0 Hz, 1 H), 1.57–1.53 (m, 6 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6 (s), 169.3 (s), 159.2 (d, J = 243.9 Hz), 146.6 (s), 139.3 (s), 134.9 (s), 130.5 (s), 127.0 (d, J = 7.8 Hz), 126.3 (s), 125.7 (s), 121.5 (s), 117.8 (d, J = 23.3 Hz), 113.5 (d, J = 25.0 Hz), 111.5 (d, J = 7.7 Hz), 84.0 (s), 45.2 (s), 19.5 (s), 19.1 (s) ppm; HRMS m/z (ESI) : calcd for $C_{18}H_{15}FNO_3$ $[M + H]^+$ 312.1043, found 312.103.



14i

5-chloro-1-isopropyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14i):

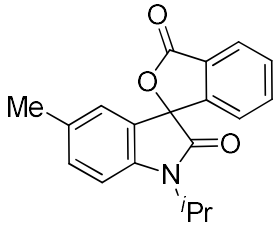
Following the general experiment procedure, **14i** was purified by PE/EtOAc (3:1) and obtained as a white solid (40.0 mg, 61% yield); Mp = 158.7-159.8 °C; R_f= 0.25 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05–8.02 (m, 1 H), 7.65 (pd, *J* = 7.4, 1.3 Hz, 2 H), 7.40 (dd, *J* = 8.5, 2.2 Hz, 1 H), 7.09 (dd, *J* = 10.1, 4.9 Hz, 2 H), 7.01 (d, *J* = 2.2 Hz, 1 H), 4.59 (dt, *J* = 14.0, 7.0 Hz, 1 H), 1.55 (t, *J* = 7.3 Hz, 6 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 169.2, 146.5, 141.9, 135.0, 131.3, 130.6, 128.8, 127.0, 126.3, 125.9, 125.7, 121.5, 111.7, 83.8, 45.3, 19.5, 19.1 ppm; HRMS m/z (ESI): calcd for $C_{18}H_{15}ClNO_3$ $[M + H]^+$ 328.0728, found 328.0735.



14j

1-benzyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14j):

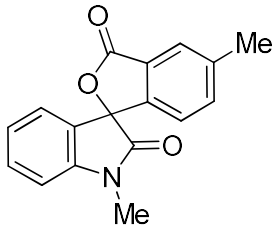
Following the general experiment procedure, **14j** was purified by PE/EtOAc (3:1) and obtained as a white solid (55.2 mg, 81% yield). Mp = 163.5-164.5 °C; R_f= 0.23 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.07 (d, *J* = 7.5 Hz, 1 H), δ 7.84–7.79 (m, 1 H), 7.76 (t, *J* = 7.4 Hz, 1 H), 7.46 (td, *J* = 7.9, 1.0 Hz, 1 H), 7.43–7.30 (m, 5 H), 7.29 (d, *J* = 7.5 Hz, 1 H), 7.24 (d, *J* = 7.3 Hz, 1 H), 7.21 (d, *J* = 7.9 Hz, 1 H), 7.09 (t, *J* = 7.5 Hz, 1 H), 5.02 (d, *J* = 3.3 Hz, 2 H) ppm; ^{13}C NMR (126 MHz, DMSO-d_6) δ 170.9, 169.1, 146.4, 143.5, 135.7, 135.6, 131.8, 130.8, 128.9, 127.7, 127.2, 125.7, 125.4, 125.0, 124.1, 123.8, 122.1, 110.7, 84.1, 43.5 ppm; HRMS m/z (ESI) : calcd for $C_{22}H_{15}NO_3$ $[M + H]^+$ 342.1128, found 342.1125.



14k

1-isopropyl-5-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14k):

Following the general experiment procedure, **14k** was purified by PE/EtOAc (3:1) and obtained as a white solid (52.8 mg, 86% yield); Mp = 171.8-172.7 ^{o}C; R_f = 0.21 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03–8.00 (m, 1 H), 7.62 (pd, *J* = 7.4, 1.3 Hz, 2 H), 7.25–7.18 (m, 1 H), 7.11–7.07 (m, 1 H), 7.03 (d, *J* = 8.1 Hz, 1 H), 6.87–6.81 (m, 1 H), 4.63–4.54 (m, 1 H), 2.26 (s, 3 H), 1.55 (dd, *J* = 8.7, 7.0 Hz, 6 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 169.7, 147.3, 140.9, 134.7, 133.0, 131.6, 130.2, 126.1, 126.0, 125.9, 125.3, 121.6, 110.5, 84.6, 45.0, 20.8, 19.6, 19.2 ppm; HRMS m/z (ESI): calcd for $C_{19}H_{18}NO_3$ $[M + H]^+$ 308.1283, found 308.1281.

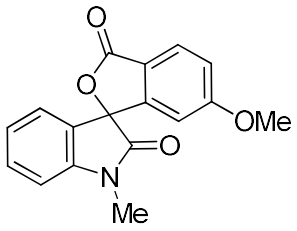


16a

1,5'-dimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16a):

Following the general experiment procedure, **16a** was purified by PE/EtOAc (3:1) and obtained as a white solid (34.6 mg, 62% yield); Mp =218.7-219.4 ^{o}C; R_f = 0.21 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.84 (s, 1 H), 7.58 (dd, *J* = 7.9, 0.7 Hz, 1 H), 7.53 (td, *J* = 7.8, 1.3 Hz, 1 H), 7.27 (d, *J* = 7.9 Hz, 1 H), 7.19 (d, *J* = 7.9 Hz, 1 H), 7.16 (dd, *J* = 7.4, 0.9 Hz, 1 H), 7.10 (td, *J* = 7.5, 0.7 Hz, 1 H), 3.25 (s, 3 H), 2.46 (s, 3 H) ppm; ^{13}C NMR (126 MHz,

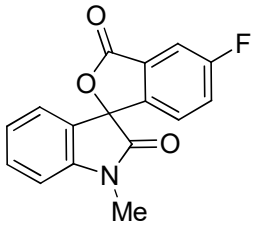
$CDCl_3$) δ 171.4, 169.7, 144.6, 144.2, 140.9, 135.9, 131.6, 126.2, 126.1, 125.2, 125.0, 123.7, 121.5, 109.1, 84.3, 27.0, 21.3 ppm; HRMS m/z (ESI): calcd for $C_{17}H_{14}NO_3$ $[M + H]^+$ 280.0966, found 280.0968.



16b

6'-methoxy-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16b):

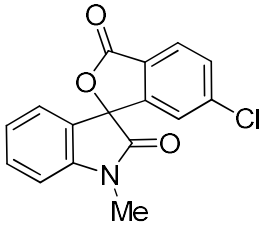
Following the general experiment procedure, **16b** was purified by PE/EtOAc (2:1) and obtained as a white solid (45.4 mg, 77% yield); Mp = 187.5-188.5 °C; R_f = 0.21 (PE/EtOAc = 2:1); ^1H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.5 Hz, 1 H), 7.46 (td, *J* = 7.8, 1.2 Hz, 1 H), 7.14–7.07 (m, 2 H), 7.04 (dd, *J* = 7.4, 0.8 Hz, 1 H), 7.00 (d, *J* = 7.9 Hz, 1 H), 6.47 (d, *J* = 2.0 Hz, 1 H), 3.80 (s, 3 H), 3.31 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 169.2, 165.26, 149.5, 144.6, 131.6, 127.5, 125.2, 125.0, 123.8, 118.2, 117.9, 109.1, 105.6, 83.8, 55.9, 27.0 ppm; HRMS m/z (ESI) : calcd for $C_{17}H_{13}NO_4$ $[M + H]^+$ 296.0920, found 296.0917.



16c

5'-fluoro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16c):

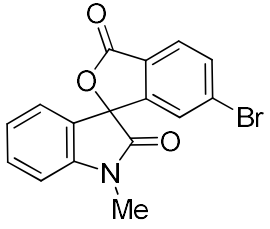
Following the general experiment procedure, **16c** was purified by PE/EtOAc (3:1) and obtained as a white solid (37.4 mg, 66% yield); Mp = 193-194 °C; R_f = 0.23 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89–7.87 (m, 1 H), 7.75 (dd, *J* = 8.2, 1.6 Hz, 1 H), 7.49 (td, *J* = 7.8, 1.3 Hz, 1 H), 7.26–7.26 (m, 1 H), 7.12 (td, *J* = 7.6, 0.9 Hz, 1 H), 7.05 (dd, *J* = 7.5, 0.8 Hz, 1 H), 7.02 (d, *J* = 7.9 Hz, 1 H), 3.32 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5 (d, *J* = 322.9 Hz), 163.8 (d, *J* = 251.5 Hz), 144.6 (s), 142.3 (d, *J* = 2.3 Hz), 131.9 (s), 128.3 (d, *J* = 9.3 Hz), 125.2 (s), 124.3 (s), 123.9 (s), 123.8 (d, *J* = 8.8 Hz), 122.8 (d, *J* = 24.3 Hz), 112.6 (s), 112.4 (s), 109.3 (s), 84.3 (s), 27.0 (s) ppm; HRMS m/z (ESI) calcd for $C_{16}H_{10}FNO_3$ $[M + H]^+$ 284.0720, found 284.0717.



16d

6'-chloro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16d):

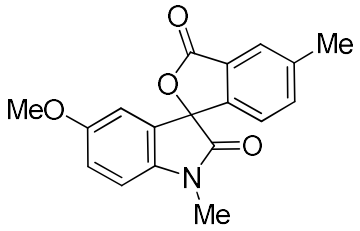
Following the general experiment procedure, **16d** was purified by PE/EtOAc (3:1) and obtained as a white solid (38.3 mg, 64% yield); Mp = 203.5-204.5 °C; R_f = 0.23 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.1 Hz, 1 H), 7.59 (dd, *J* = 8.2, 1.7 Hz, 1 H), 7.49 (td, *J* = 7.8, 1.3 Hz, 1 H), 7.12 (td, *J* = 7.6, 0.8 Hz, 1 H), 7.09 (d, *J* = 1.4 Hz, 1 H), 7.05 (dd, *J* = 7.4, 0.9 Hz, 1 H), 7.02 (d, *J* = 7.9 Hz, 1 H), 3.32 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 168.3, 148.3, 144.6, 141.5, 132.0, 131.1, 127.2, 125.2, 124.5, 124.1, 124.0, 122.3, 109.3, 83.9, 27.1 ppm; HRMS m/z (ESI) : calcd for $C_{16}H_{10}ClNO_3$ $[M + H]^+$ 300.0424, found 300.0422.



16e

6'-bromo-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16e):

Following the general experiment procedure, **16e** was purified by PE/EtOAc (3:1) and obtained as a white solid (45.3 mg, 66% yield); Mp = 224.8-225.8 ^{o}C; R_f = 0.21 (PE/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 7.0, 2.3 Hz, 1 H), 7.48 (td, *J* = 7.8, 1.3 Hz, 1 H), 7.35 (td, *J* = 8.5, 2.4 Hz, 1 H), 7.14–7.11 (m, 1 H), 7.09 (t, *J* = 4.2 Hz, 1 H), 7.04 (dd, *J* = 7.5, 0.9 Hz, 1 H), 7.01 (d, *J* = 7.9 Hz, 1 H), 3.31 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 168.5, 148.4, 144.6, 134.0, 132.0, 130.0, 127.3, 125.3, 125.3, 125.0, 124.1, 124.0, 109.3, 83.9, 27.1 ppm; HRMS m/z (ESI): calcd for $C_{16}H_{10}BrNO_3$ [M + H] $^{+}$ 343.9923, found 343.9917.

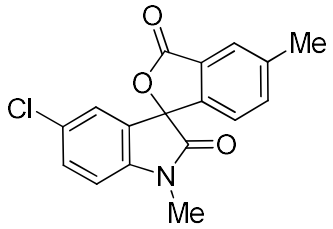


16f

5-methoxy-1,5'-dimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16f):

Following the general experiment procedure, **16f** was purified by PE/EtOAc (2:1) and obtained as a white solid (40.2 mg, 65% yield); Mp = 145.5-146.5 ^{o}C; R_f = 0.20 (PE/EtOAc = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (s, 1 H), 7.46–7.43 (m, 1 H), 7.00 (d, *J* = 7.9 Hz, 1 H), 6.97 (dd, *J* = 8.6, 2.5 Hz, 1 H), 6.90 (d, *J* = 8.6 Hz, 1 H), 6.61 (d, *J* = 2.5 Hz, 1 H), 3.72 (s, 3 H), 3.28 (s, 3 H), 2.49 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 169.7, 156.7, 144.3,

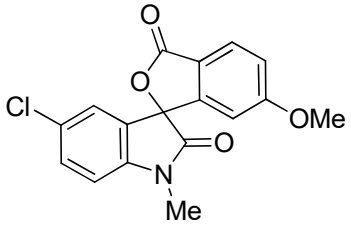
140.9, 137.8, 135.9, 126.1, 126.1, 121.5, 116.5, 111.7, 109.7, 84.6, 55.9, 27.0, 21.4 ppm; HRMS m/z (ESI): calcd for $C_{18}H_{16}NO_4$ $[M + H]^+$ 310.1081, found 310.1074.



16g

5-chloro-1,5'-dimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16g):

Following the general experiment procedure, **16g** was purified by PE/EtOAc (3:1) and obtained as a white solid (34.4 mg, 55% yield); Mp = 216.5-217.5 °C; R_f= 0.20 (PE/EtOAc = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84–7.80 (m, 1 H), 7.47 (dd, *J* = 7.9, 0.8 Hz, 1 H), 7.43 (dd, *J* = 8.4, 2.1 Hz, 1 H), 7.03–6.97 (m, 2 H), 6.93 (d, *J* = 8.4 Hz, 1 H), 3.30 (s, 3 H), 2.50 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 169.3, 143.6, 143.1, 141.2, 136.1, 131.5, 129.2, 126.6, 126.2, 126.0, 125.5, 121.5, 110.2, 83.8, 27.1, 21.3 ppm; HRMS m/z (ESI) calcd for $C_{17}H_{12}ClNO_3$ $[M + H]^+$ 314.0581, found 314.0578.

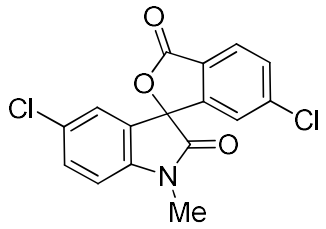


16h

5-chloro-6'-methoxy-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16h):

Following the general experiment procedure, **16h** was purified by PE/EtOAc (2:1) and obtained as a white solid (46.1 mg, 70% yield); Mp = 234-235 °C; R_f = 0.2 (PE/EtOAc = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.5 Hz, 1 H), 7.43 (dd, *J* = 8.3, 2.0 Hz, 1 H), 7.12 (dd, *J* = 8.6, 2.0 Hz, 1 H), 7.03 (d, *J* = 2.0 Hz, 1 H), 6.94 (d, *J* = 8.4 Hz, 1 H), 6.48 (d, *J* = 1.9 Hz, 1 H), 3.82 (s, 3 H), 3.30 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 168.8, 165.4, 148.9,

143.1, 131.5, 129.3, 127.8, 126.7, 125.7, 118.0, 118.0, 110.2, 105.7, 83.3, 56.0, 27.2 ppm; HRMS m/z (ESI): calcd for $C_{17}H_{12}ClNO_4$ [M + H] $^+$ 330.0529, found 330.0528.

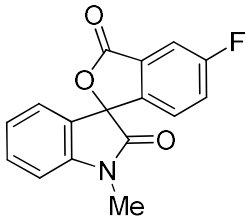


16i

5,6'-dichloro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16i):

Following the general experiment procedure, **16i** was purified by PE/EtOAc (3:1) and obtained as a white solid (41.4 mg, 62% yield); R_f = 0.21 (PE/EtOAc = 3:1); Mp = 238.9-239.9 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.2 Hz, 1 H), 7.61 (dd, *J* = 8.2, 1.7 Hz, 1 H), 7.46 (dd, *J* = 8.4, 2.1 Hz, 1 H), 7.10 (d, *J* = 1.3 Hz, 1 H), 7.04 (d, *J* = 2.1 Hz, 1 H), 6.96 (d, *J* = 8.4 Hz, 1 H), 3.31 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 167.9, 147.7, 143.1, 141.8, 131.9, 131.4, 129.5, 127.4, 125.7,125.7, 124.3, 122.3, 110.4, 83.3, 27.2 ppm; HRMS m/z (ESI): calcd for $C_{16}H_9Cl_2NO_3$ [M + H] $^+$ 334.0034, found 334.0032.

7. The data of crystal:



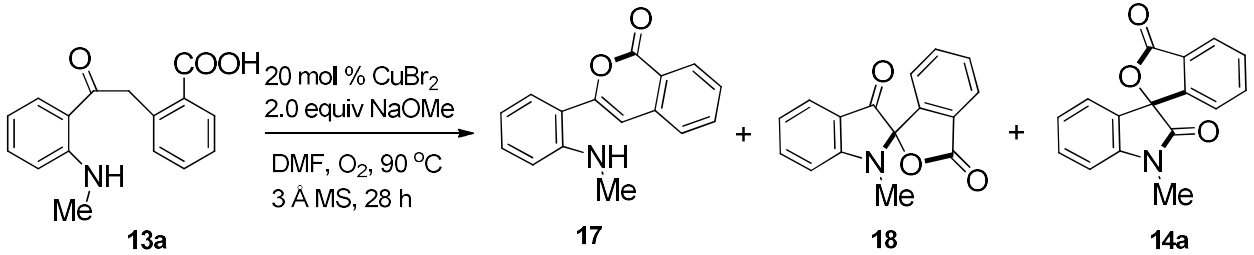
16c = 1

Compound	**16c = 1**
Formula	C16 H10 F N O3
Mr	283.25
Crystal system	monoclinic
Space group	*P2(1)/c*
a/Å	10.8437(15)
b/Å	16.386(2)
c/Å	7.5183(10)
α/°	90
β/°	100.479(15)

γ/°	90
V /Å^3	1313.6(3)
Z	4
D_{calcd} /g·cm^{-3}	1.432
μ /mm^{-1}	0.109
No. of data/parameter	2578/190
θ range/°	3.02-26.00
Obs reflns	1702
R_1 $[I>2\sigma(I)]$[a]	0.0491
wR_2 (all data)[b]	0.1226

[a] $R_1 = \sum||F_O| - |F_C||/\sum|F_O|$ [b] $wR_2 = \{\sum[w(F_O^2 - F_C^2)^2]/\sum[w(F_O^2)^2]\}^{1/2}$

8. Experiments about mechanistic studies:



In a 25 mL microwave tube was charged with substrate **13a** (132.5.0 mg, 0.5 mmol), sodium methoxide (54 mg, 1.0 mmol), $CuBr_2$ (22.5 mg, 0.1 mmol), 3 Å molecular sieves (150 mg) and anhydrous DMF 10 mL. The reaction mixture was evacuated and refilled with O_2 for 3 times before it was stirred at 90 °C for 28 h. The reaction mixture was then cooled to rt and diluted with water (5 mL) before it was extracted with EtOAc (30 mL). The combined organic phase were washed with and washed with water (3 X 10 mL) and saturated brine (10 mL), dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The

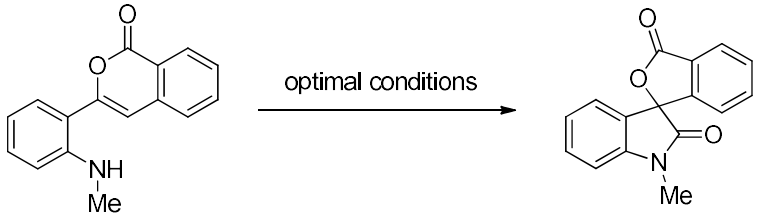
residue was purified by column chromatography (PE/EtOAc=3:1) on silica gel to provide the products **17** (12.6 mg, 10%), **18** (34.5 mg, 26%) and **14a** (39.8 mg, 30%). Substrate **13a** (35.2 g, 28%) was recovered.

3-(2-(methylamino)phenyl)-1H-isochromen-1-one (17)

The NMR data are consistent with those reported:[1] Mp = 155.8-156.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34–8.28 (m, 1 H), 7.77–7.70 (m, 1 H), 7.54–7.49 (m, 1 H), 7.48 (d, *J* = 7.9 Hz, 1 H), 7.43 (dd, *J* = 7.7, 1.6 Hz, 1 H), 7.39–7.32 (m, 1 H), 6.77 (tt, *J* = 4.0, 2.0 Hz, 1 H), 6.74 (t, *J* = 4.1 Hz, 2 H), 5.12 (s, 1 H), 2.91 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4, 155.4, 147.3, 137.8, 134.9, 131.5, 129.6, 129.5, 128.0, 125.8, 120.0, 117.6, 116.7, 111.0, 104.9, 30.6 ppm.

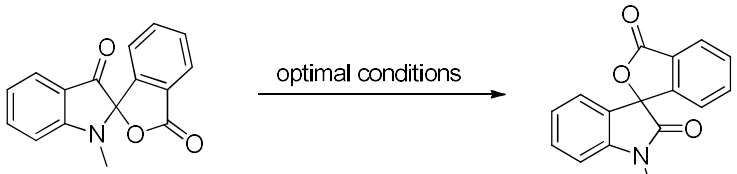
1-methyl-3'H-spiro[indoline-2,1'-isobenzofuran]-3,3'-dione (18)

The NMR data are consistent with those reported:[1] Mp = 212-213 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05–7.99 (m, 1 H), 7.66 (dtdd, *J* = 15.5, 9.5, 7.4, 1.3 Hz, 4 H), 7.34–7.29 (m, 1 H), 6.95–6.90 (m, 1 H), 6.88 (d, *J* = 8.2 Hz, 1 H), 2.76 (s, 3 H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.9, 168.2, 161.2, 142.3, 139.0, 134.8, 131.2, 128.6, 126.1, 126.0, 122.3, 119.6, 118.3, 109.0, 96.6, 27.8 ppm.



17 **14a**

In a 10 mL microwave tube was charged with substrate **17** (50.2 mg, 0.2 mmol), sodium methoxide (10.8 mg, 0.4 mmol), $CuBr_2$ (9.0 mg, 0.04 mmol), 3 Å molecular sieves (150 mg) and anhydrous DMF 1.0 mL. The reaction mixture was evacuated and refilled with O_2 for 3 times before it was stirred at 150 °C for 12 h. The reaction mixture was then cooled to rt and diluted with water (5 mL) before it was extracted with EtOAc (30 mL). The combined organic phase were washed with and washed with water (3 X 10 mL) and saturated brine (10 mL), dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography (PE/EtOAc=3:1) on silica gel to provide the products **14a** (40.3 mg, 76%).



18 **14a**

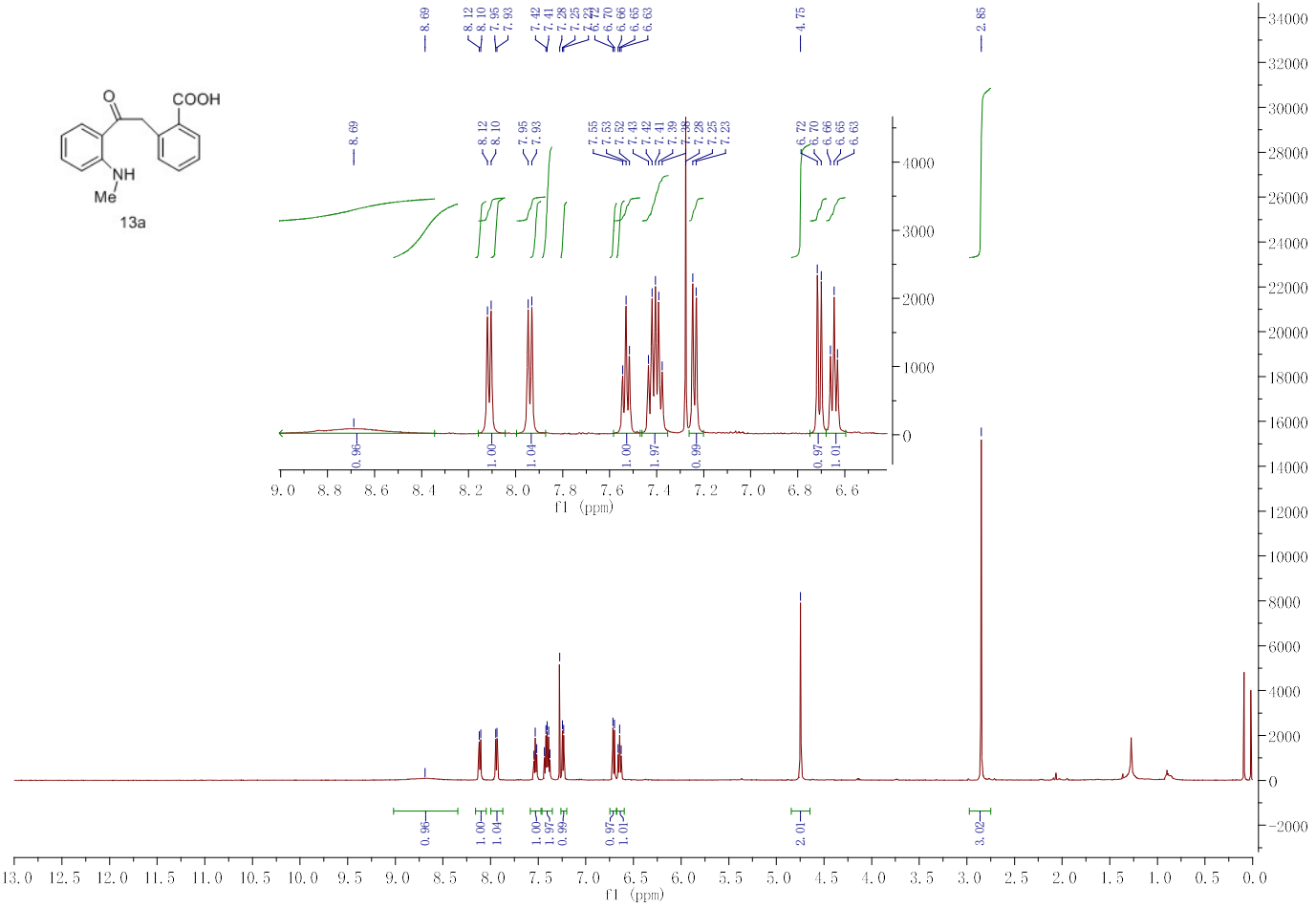
In a 10 mL microwave tube was charged with substrate **18** (55.8 mg, 0.2 mmol), sodium methoxide (10.8 mg, 0.4 mmol), $CuBr_2$ (9.0 mg, 0.04 mmol), 3 Å molecular sieves (150 mg) and anhydrous DMF 1.0 mL. The reaction mixture was evacuated and refilled with O_2 for 3 times before it was stirred at 150 °C for 12 h. The reaction mixture was then cooled to rt and diluted with water (5 mL) before it was extracted with EtOAc (30 mL). The combined organic phase were washed with and washed with water (3 X 10 mL) and saturated brine (10 mL), dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography (PE/EtOAc=3:1) on silica gel to provide the products **14a** (39.8 mg, 75%).

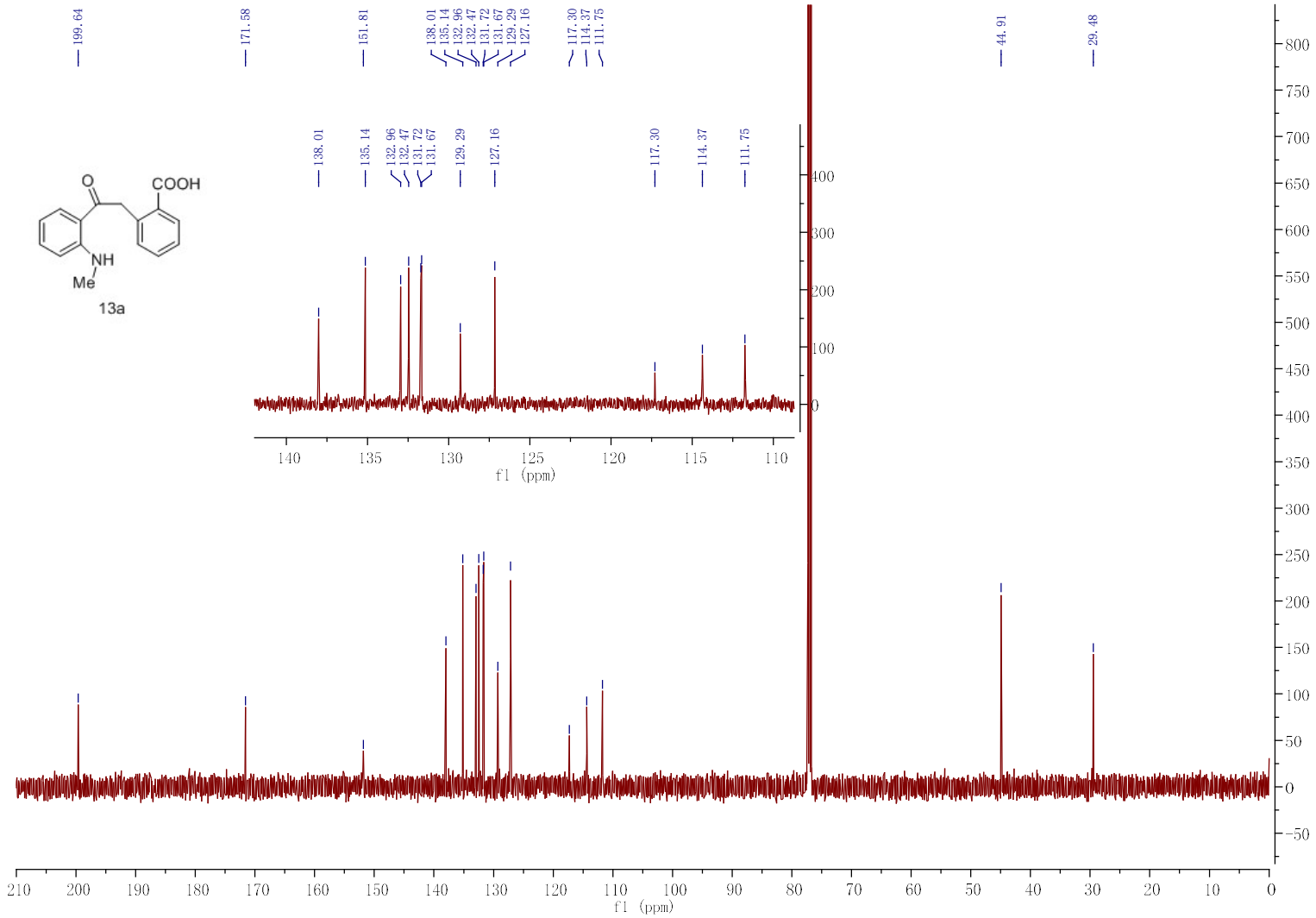
9. References:

1. R. M. Letcher, N.-C. Kwok, W.-H. Lo, K.-W. Ng, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 1715.
2. (a) D. A. Offermann, J. E. McKendrick, J. J. P. Sejberg, A. C. Spivey, *J. Org. Chem*. **2012**, *77*, 3197. (b) M. Hellal, J. -J. Bourguignon, F. J.-J. Bihel, *Tetrahedron Lett.*, **2008**, *49*, 62.

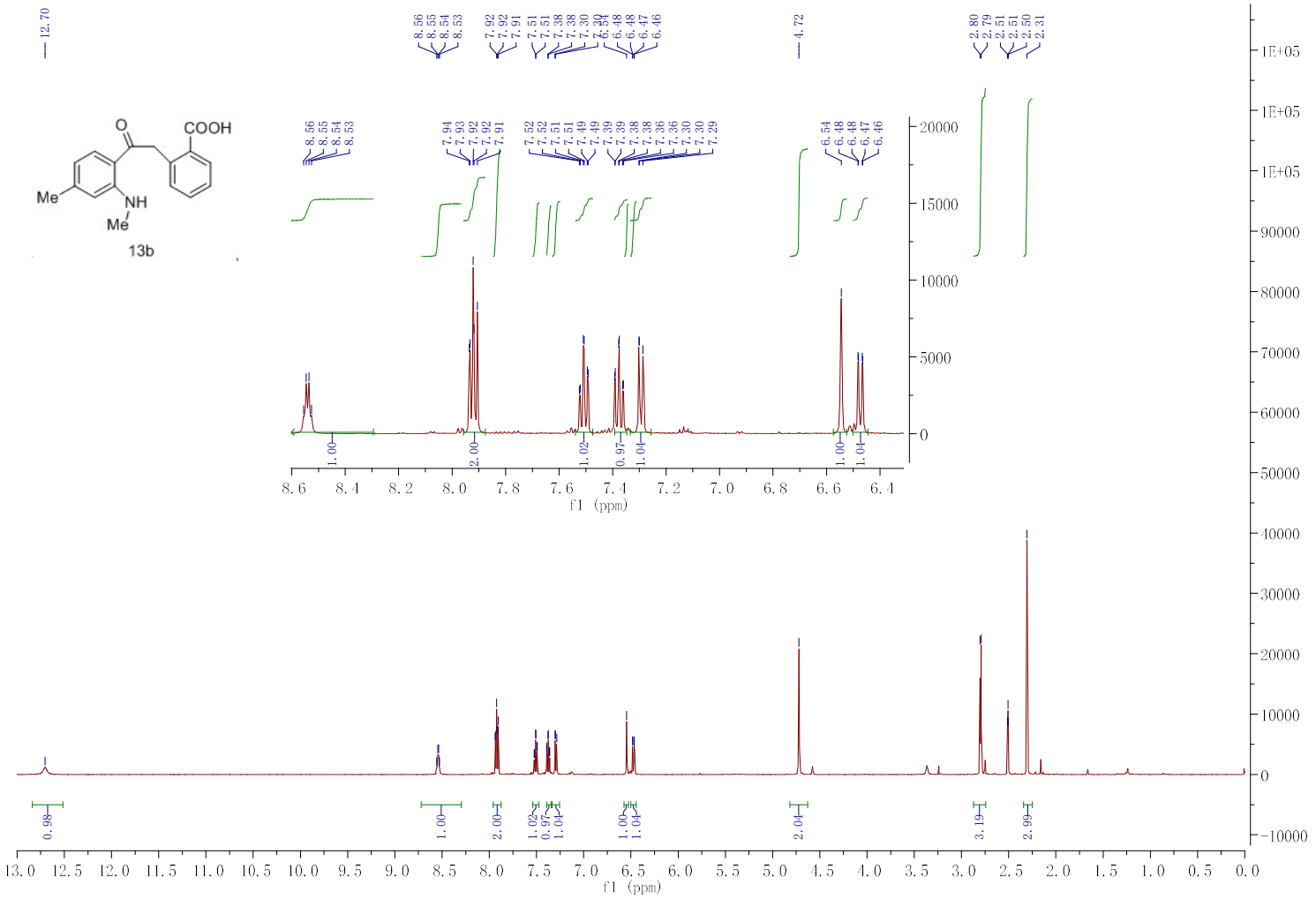
10. **NMR spectra of all new compounds:**

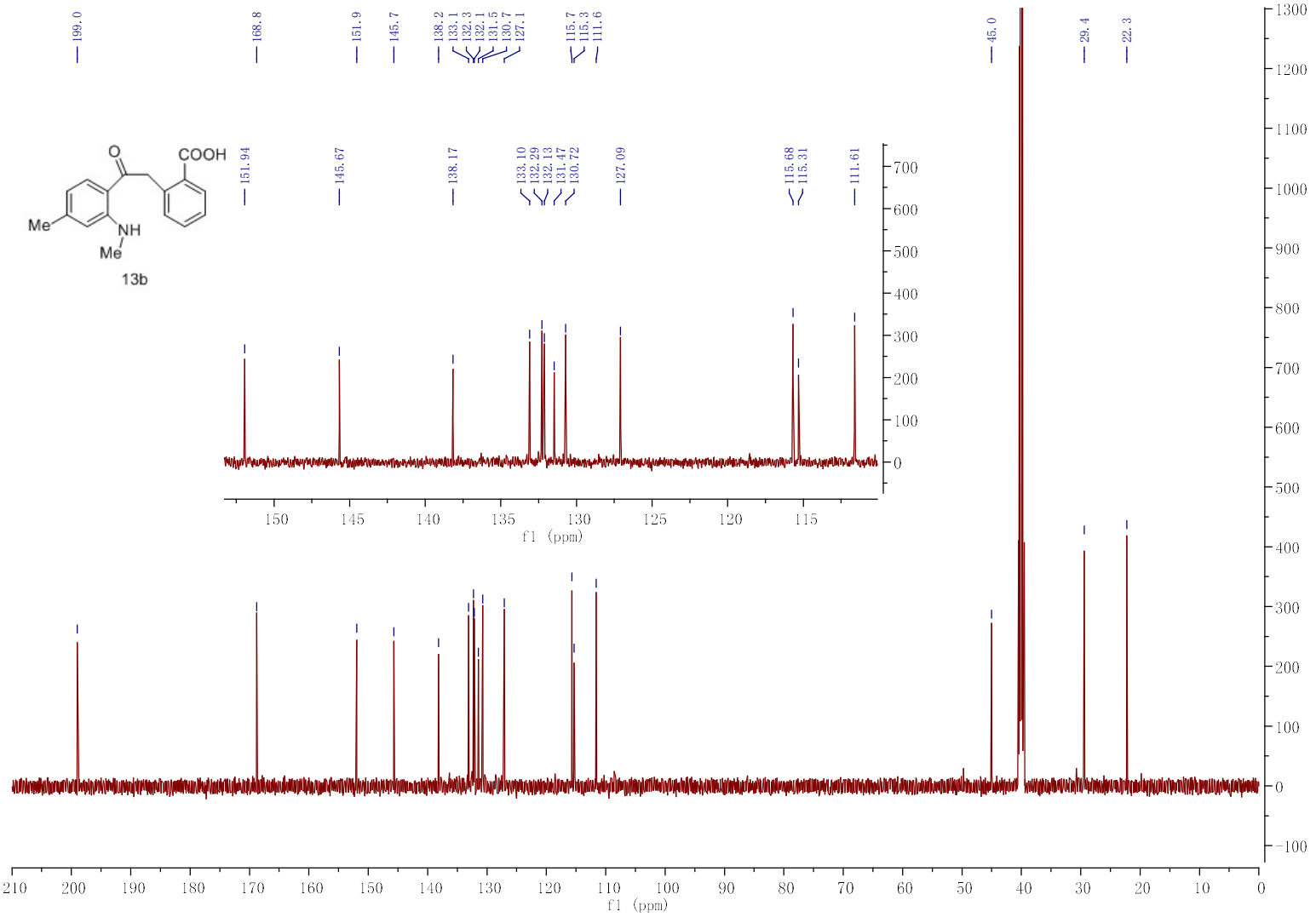
2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13a):



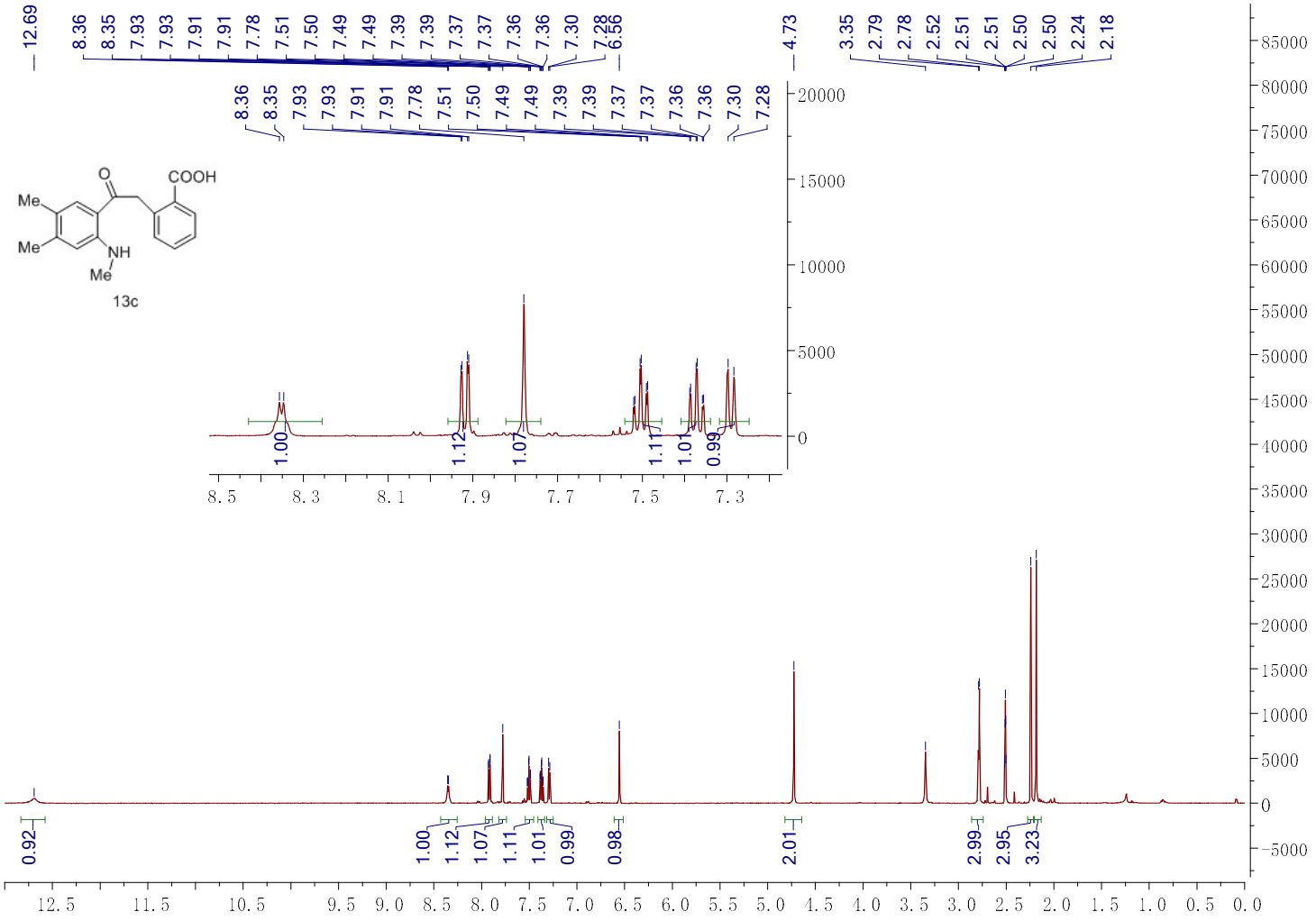

199.64
171.58
151.81
138.01
135.14
132.96
132.47
131.72
131.67
129.29
127.16
117.30
114.37
111.75
44.91
29.48
O
COOH
NH
Me
13a
f1 (ppm)

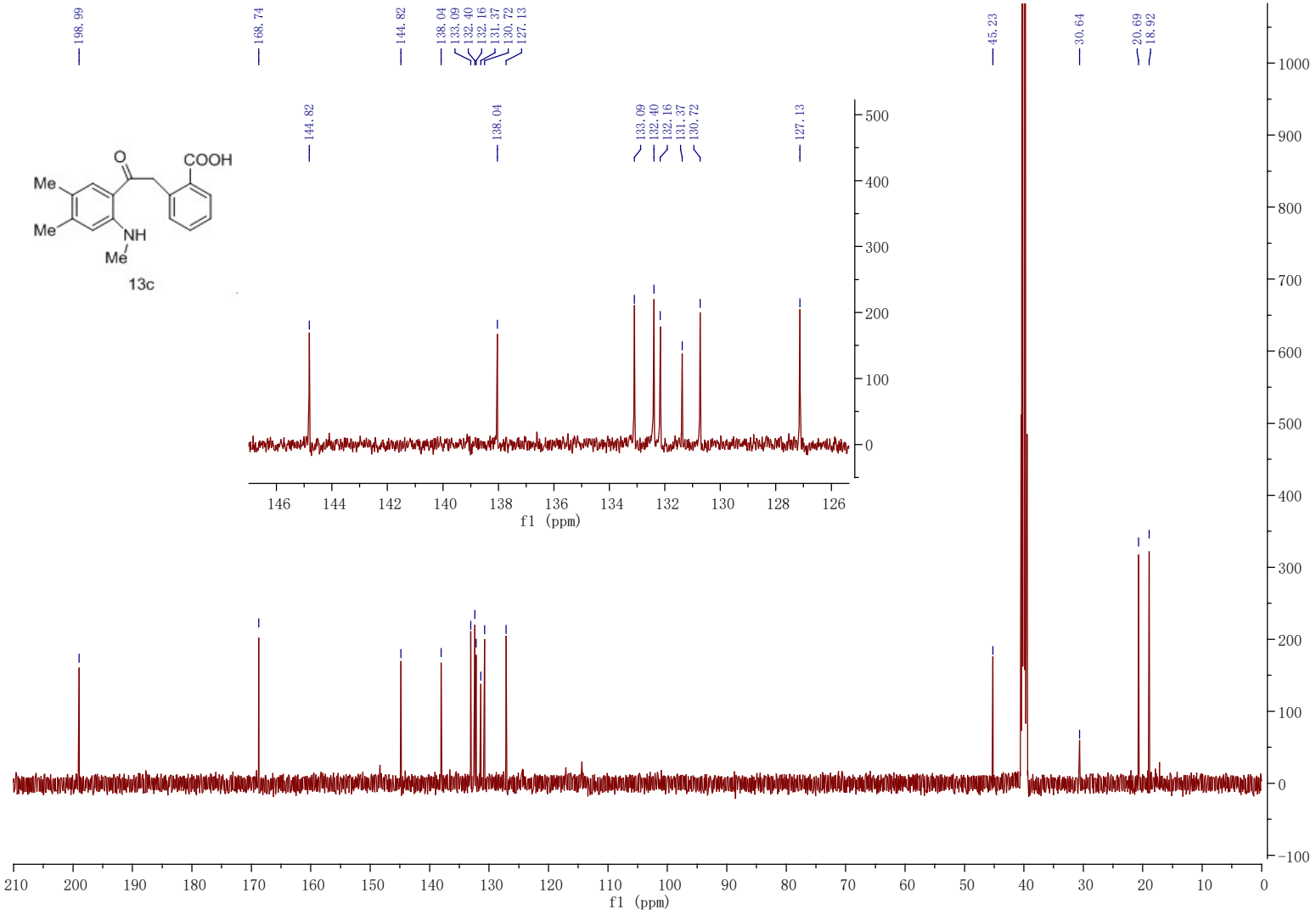
2-(2-(4-methyl-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13b):



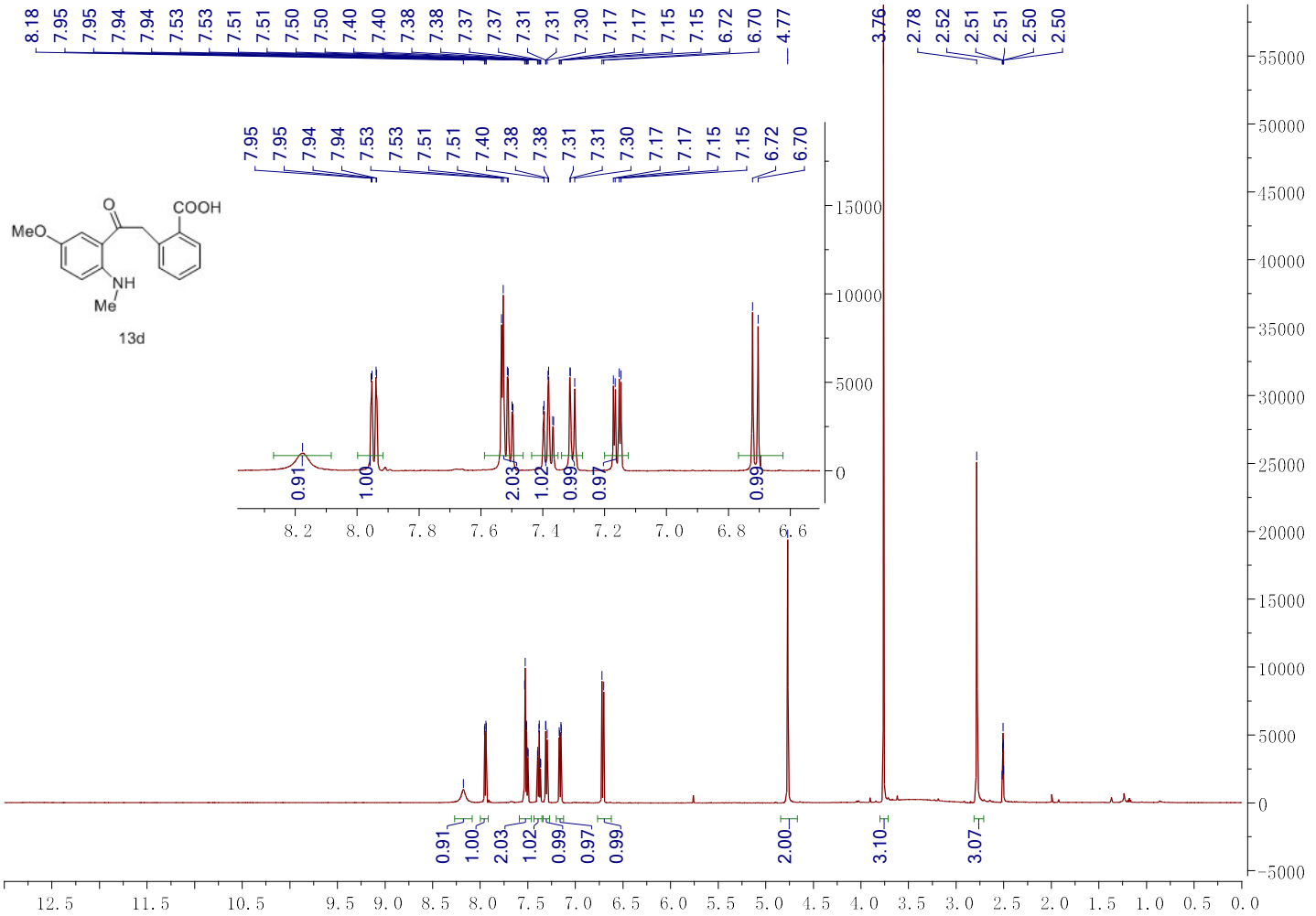

199.0
168.8
151.9
145.7
138.2
133.1
132.3
132.1
131.5
130.7
127.1
115.7
115.3
111.6
45.0
29.4
22.3
O
COOH
Me
NH
Me
13b
151.94
145.67
138.17
133.10
132.29
132.13
131.47
130.72
127.09
115.68
115.31
111.61
f1 (ppm)
f1 (ppm)

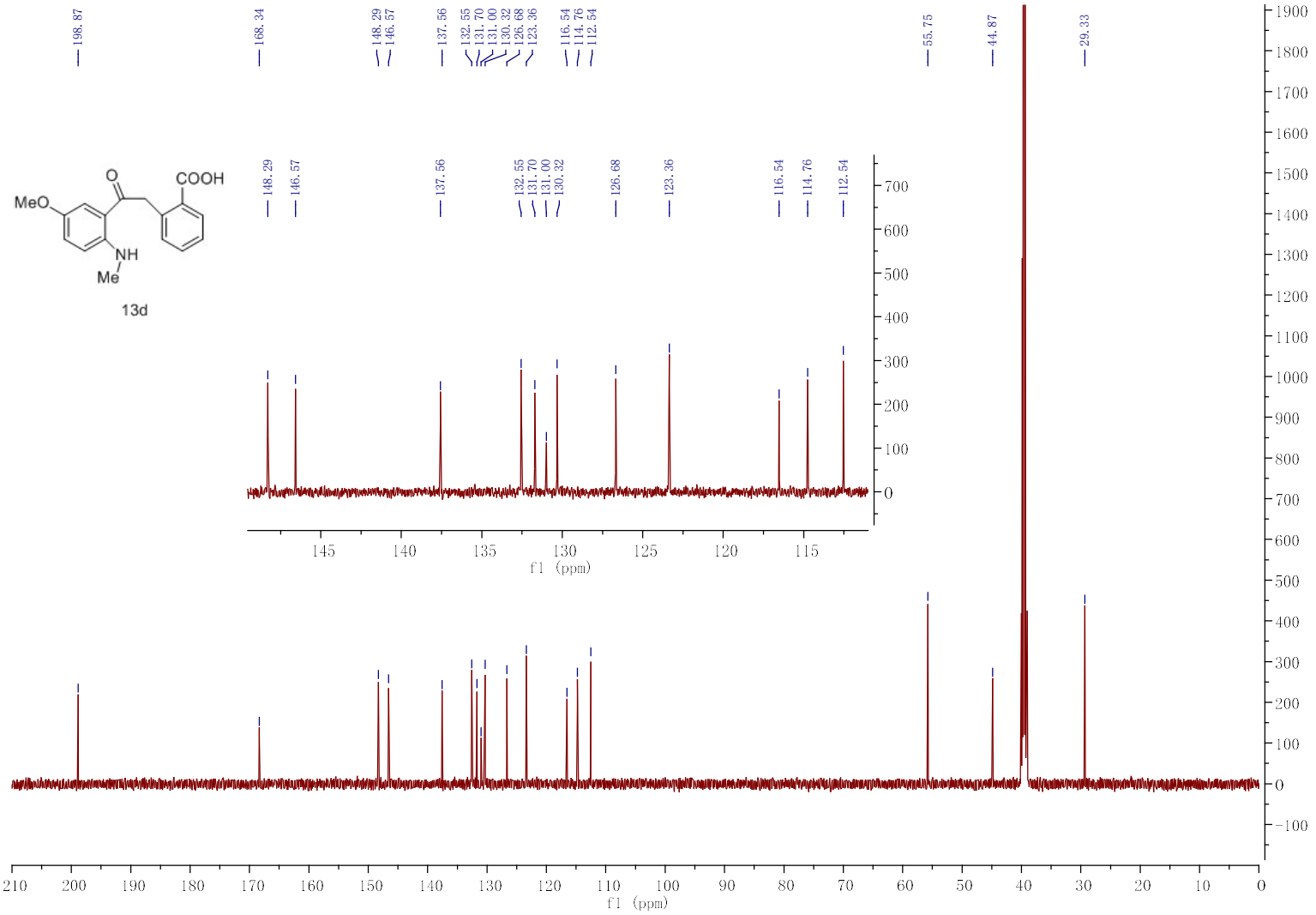
2-(2-(4,5-dimethyl-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13c):



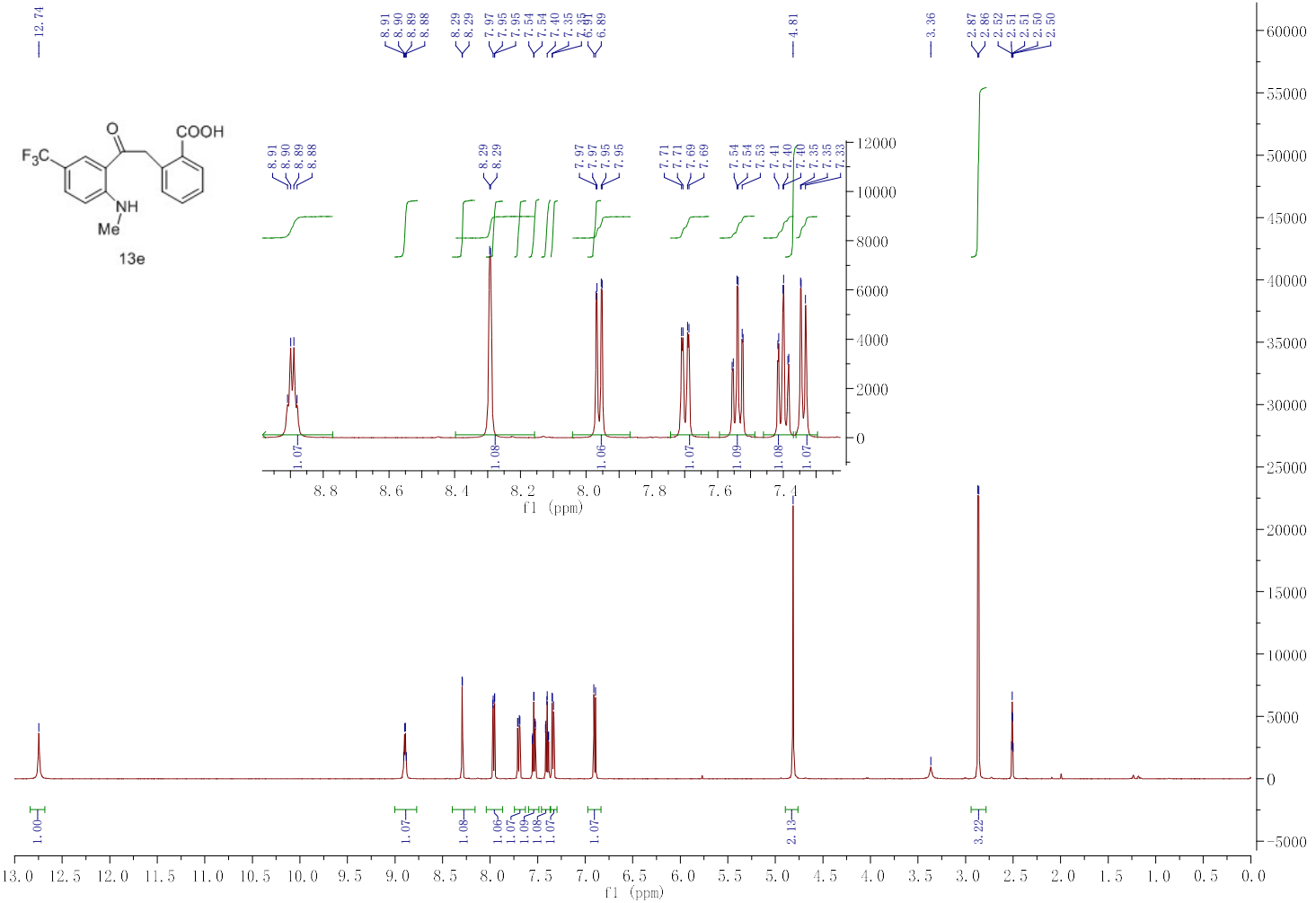

198.99
168.74
144.82
138.04
133.09
132.40
132.16
131.37
130.72
127.13
45.23
30.64
20.69
18.92
COOH
O
Me
Me
NH
Me
13c
f1 (ppm)
f1 (ppm)

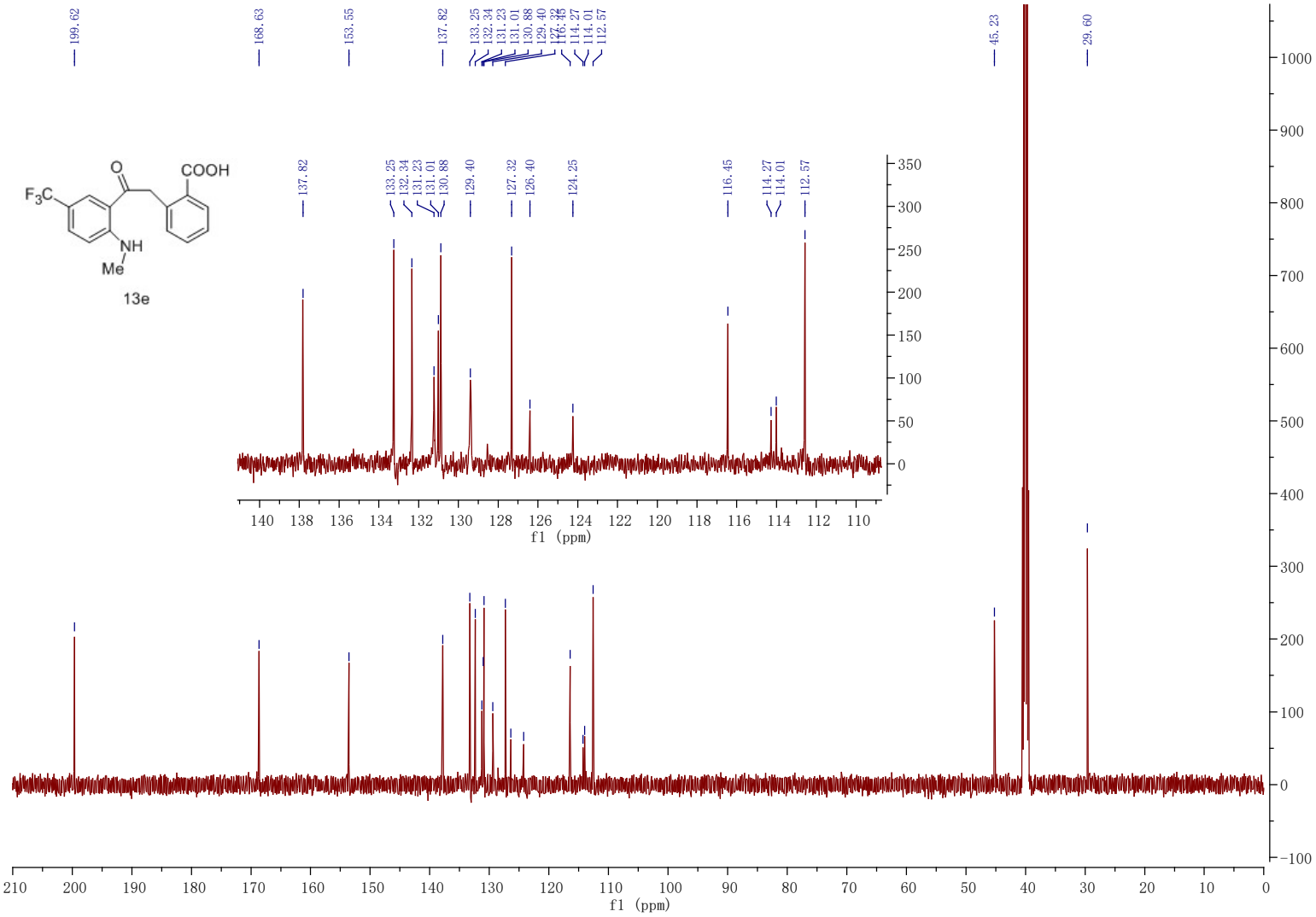
2-(2-(5-methoxy-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13d):



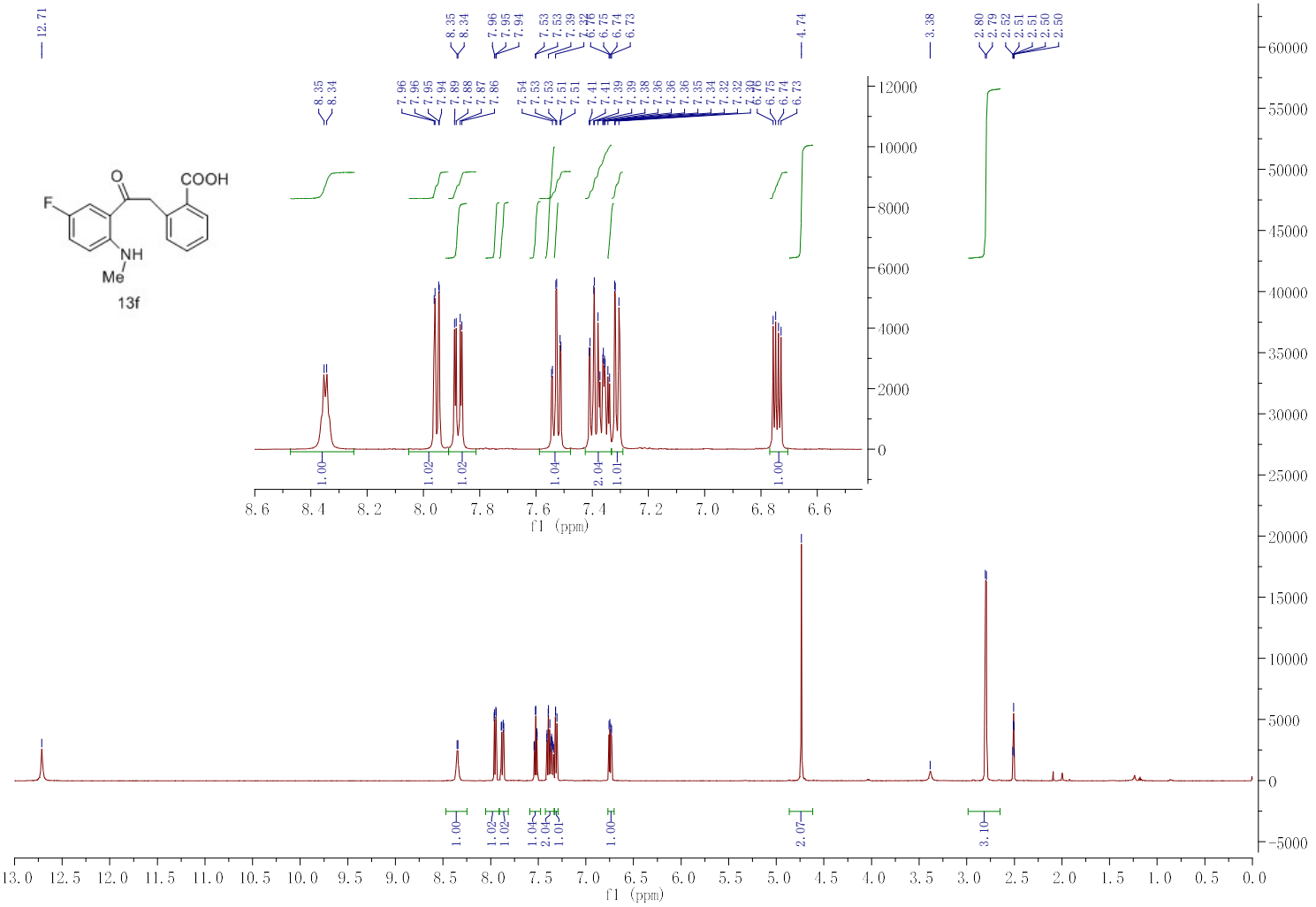

198.87
168.34
148.29
146.57
137.56
132.55
131.70
131.00
130.32
126.68
123.36
116.54
114.76
112.54
55.75
44.87
29.33
MeO
O
COOH
NH
Me
13d
f1 (ppm)

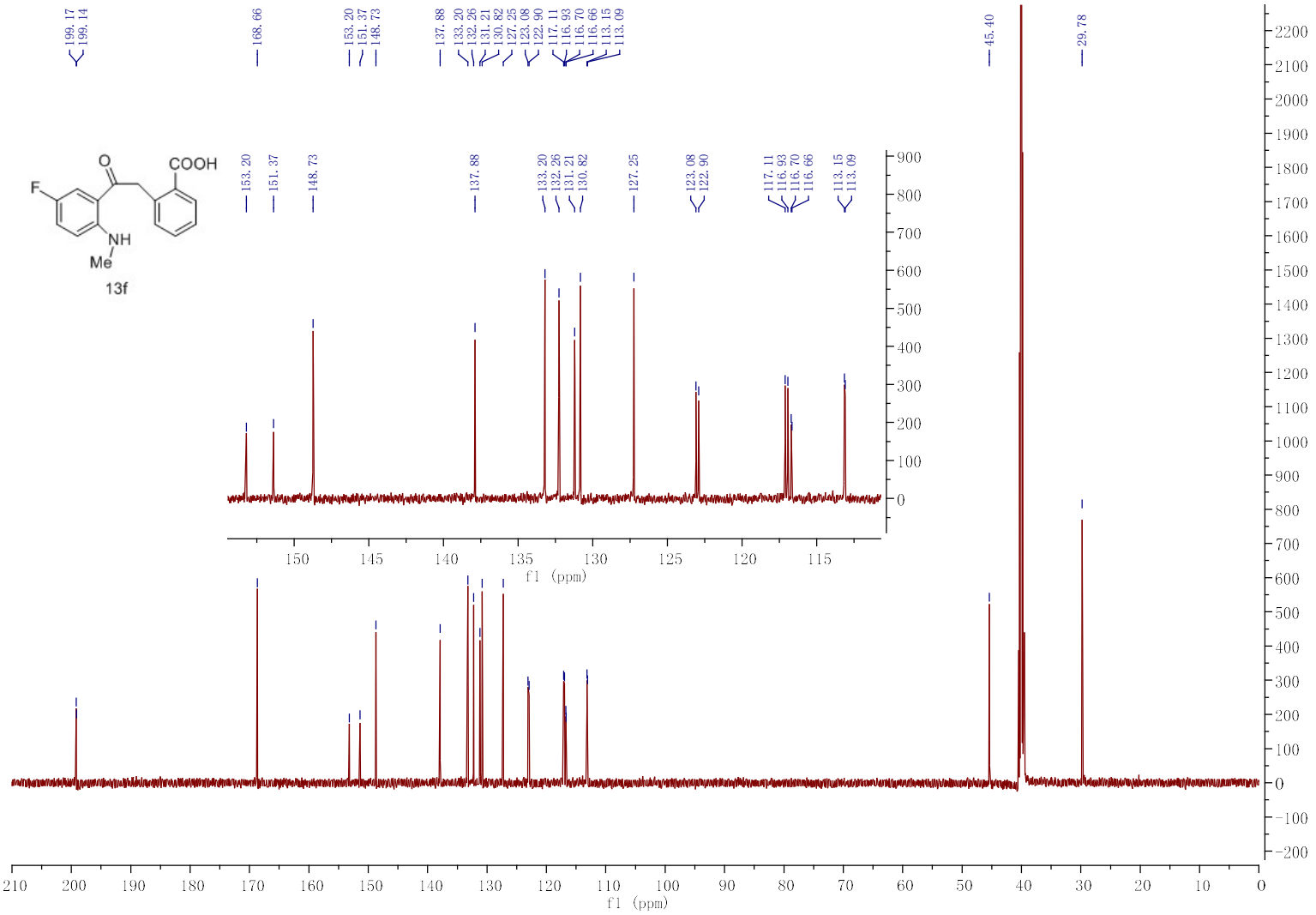
2-(2-(2-(methylamino)-5-(trifluoromethyl)phenyl)-2-oxoethyl)benzoic acid (13e):



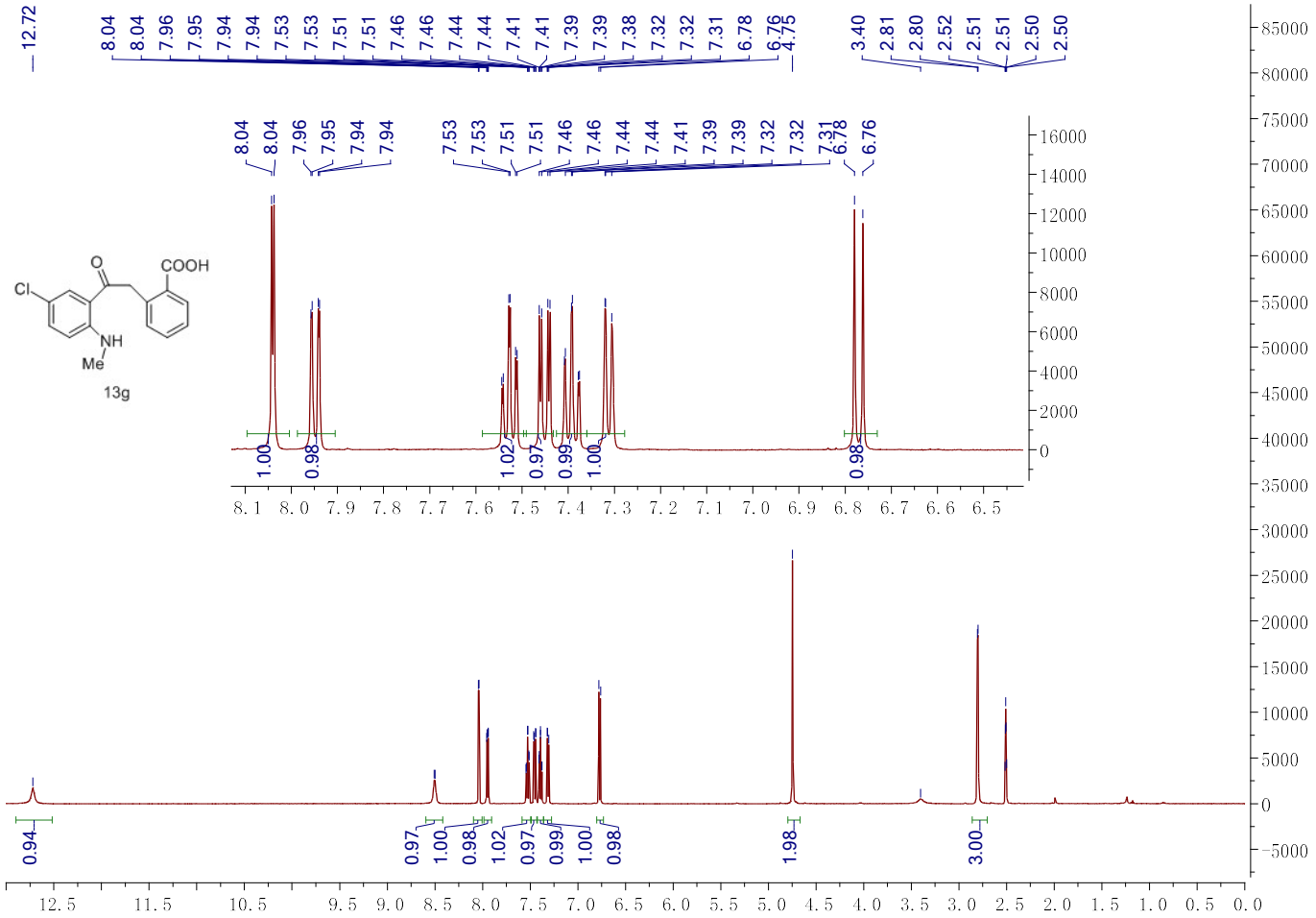

199.62
168.63
153.55
137.82
133.25
132.34
131.23
131.01
130.88
129.40
127.32
126.40
124.25
116.45
114.27
114.01
112.57
45.23
29.60
O
COOH
F3C
NH
Me
13e
f1 (ppm)

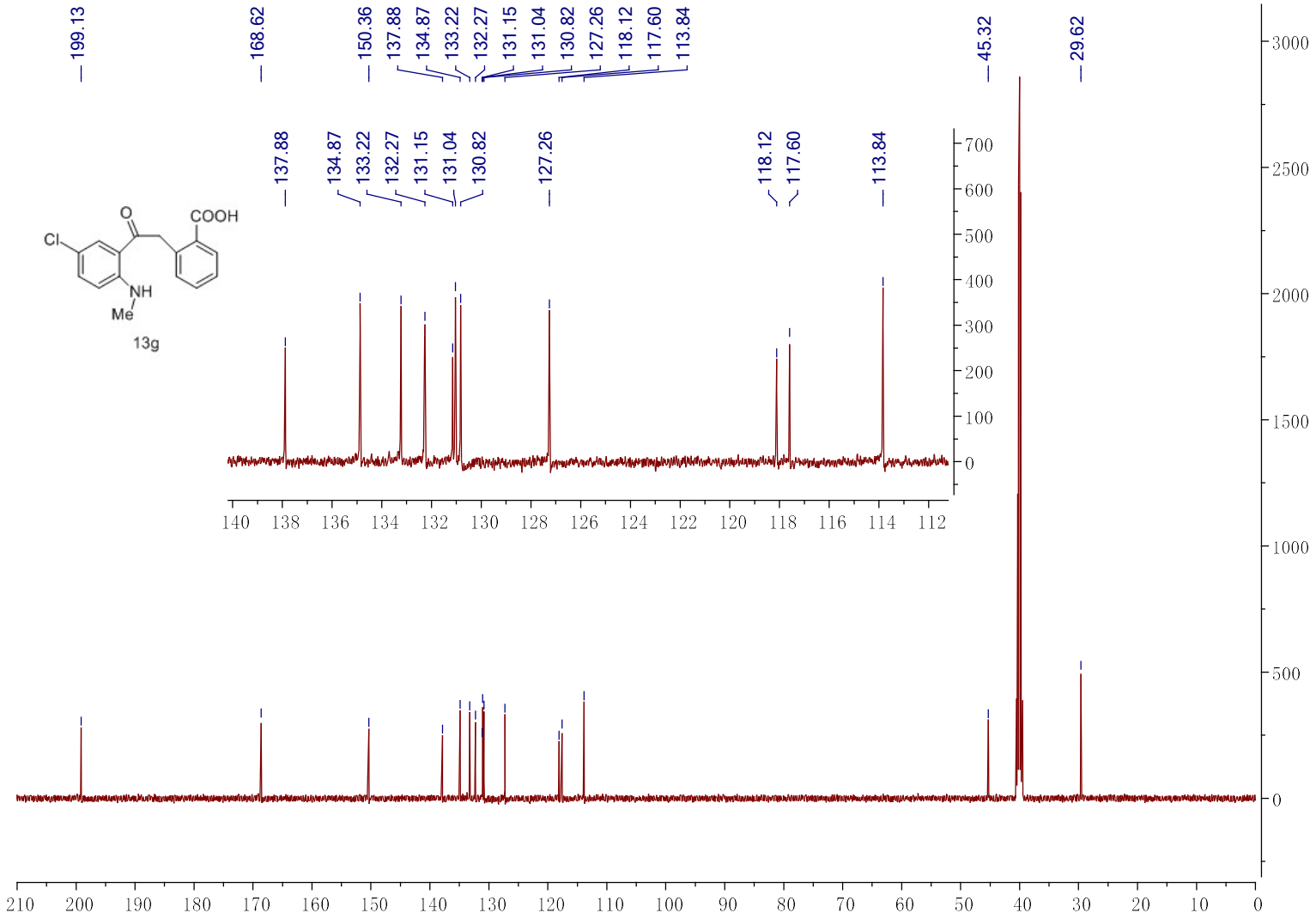
2-(2-(5-fluoro-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13f):



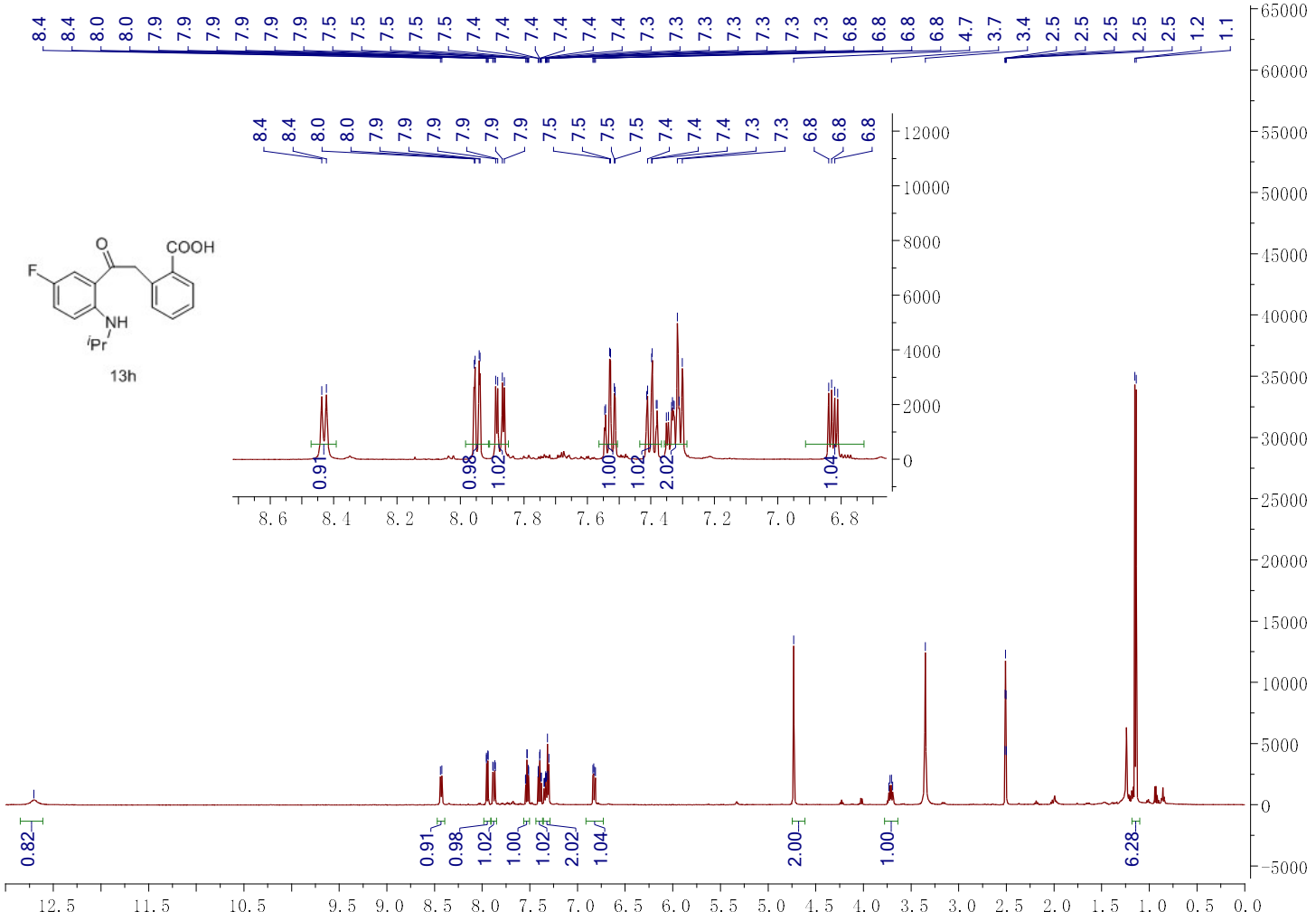

199.17
199.14
168.66
153.20
151.37
148.73
137.88
133.20
132.26
131.21
130.82
127.25
123.08
122.90
117.11
116.93
116.70
116.66
113.15
113.09
45.40
29.78
COOH
F
O
NH
Me
13f
f1 (ppm)

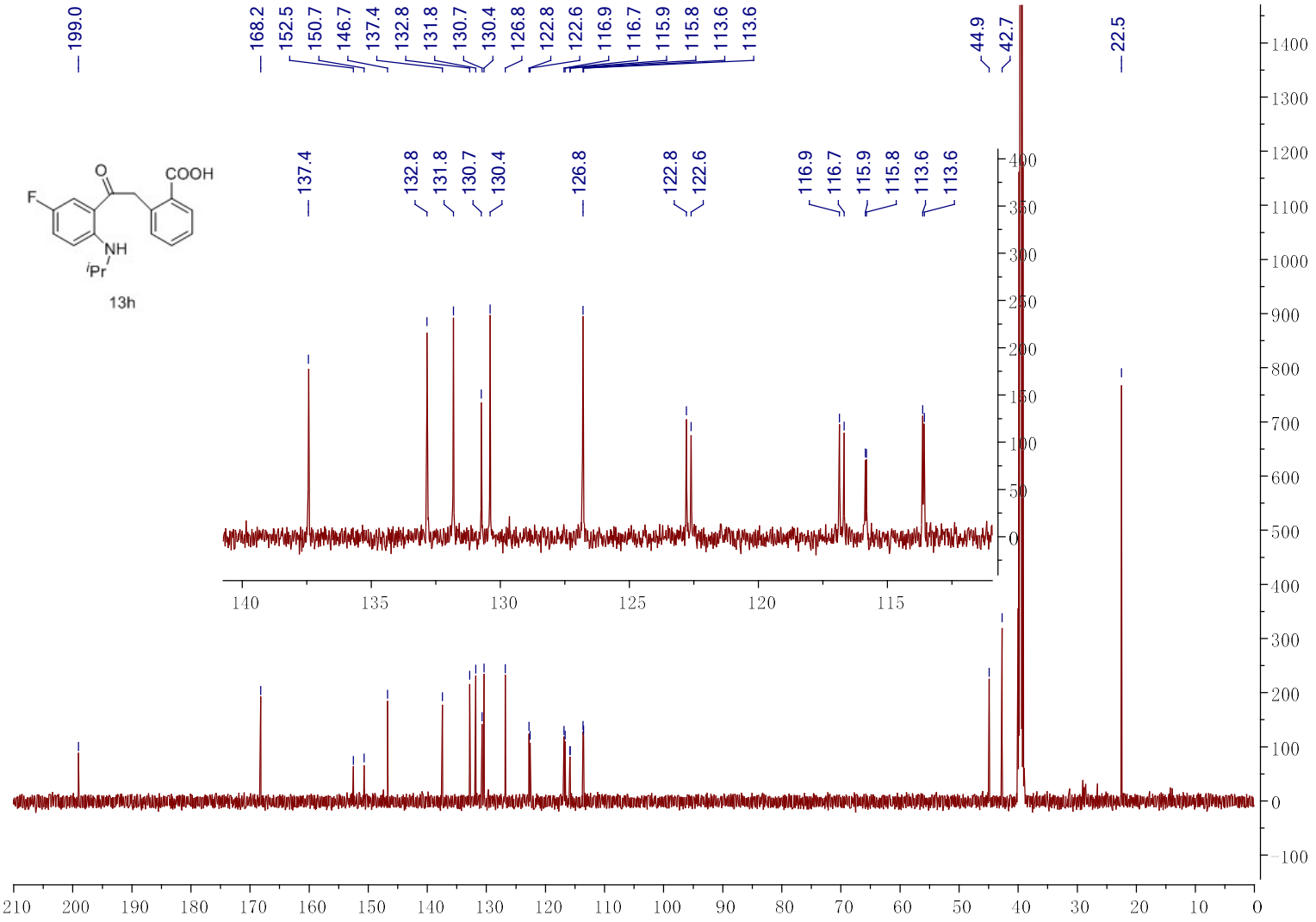
2-(2-(5-chloro-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (13g):




199.13
168.62
150.36
137.88
134.87
133.22
132.27
131.15
131.04
130.82
127.26
118.12
117.60
113.84
45.32
29.62
O
COOH
Cl
NH
Me
13g

2-(2-(5-fluoro-2-(isopropylamino)phenyl)-2-oxoethyl)benzoic acid (13h):




199.0
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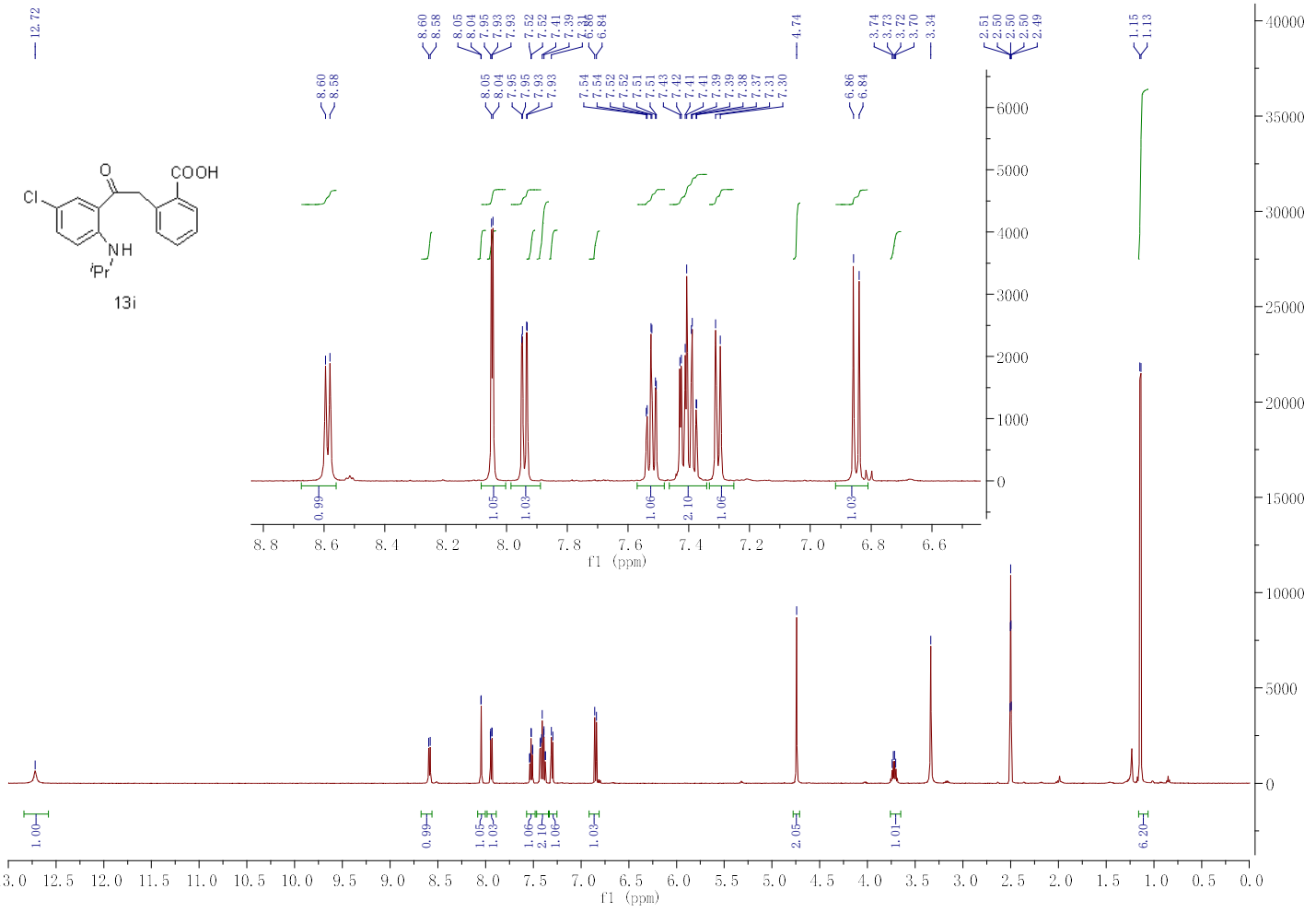
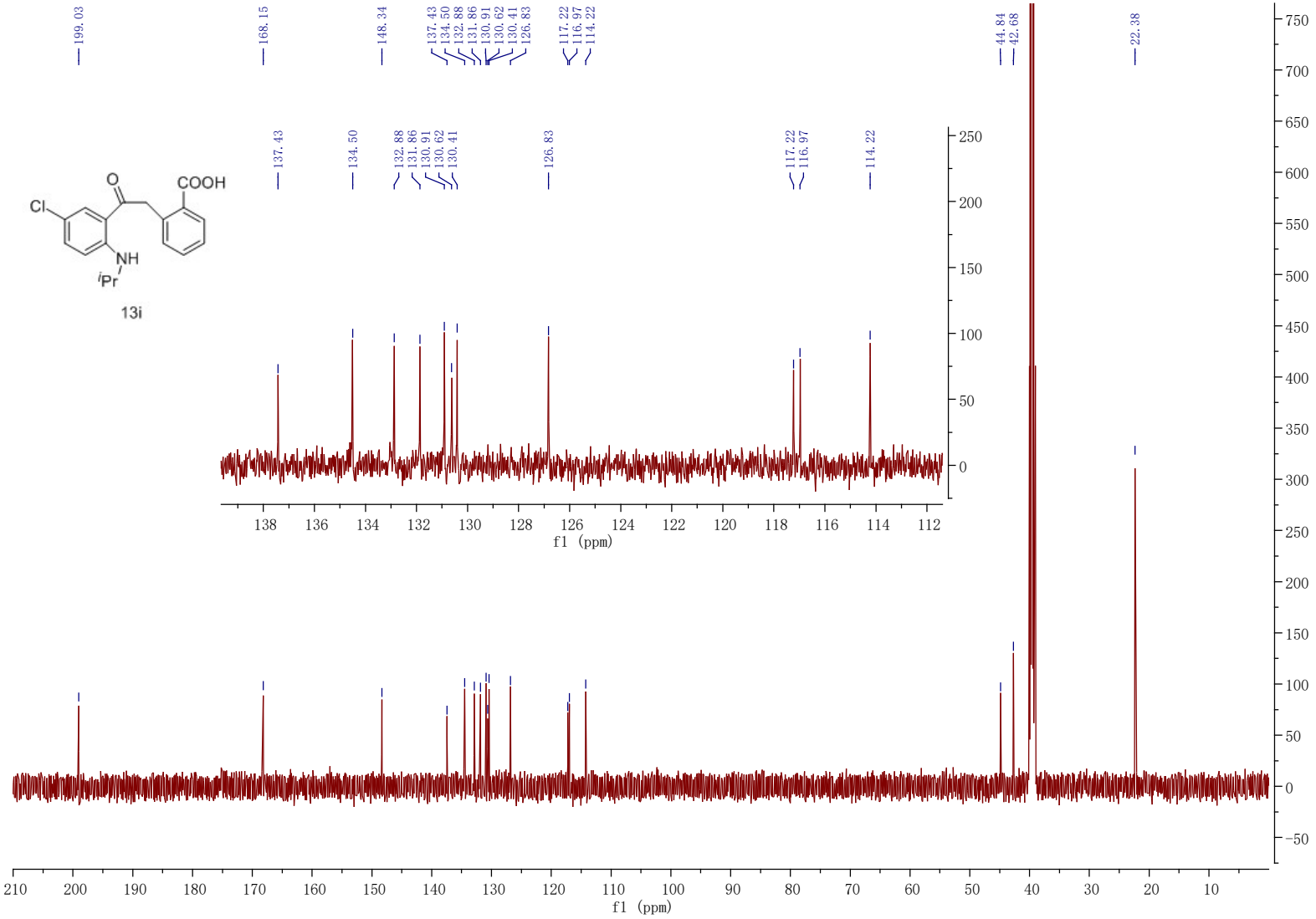
152.5
150.7
146.7
137.4
132.8
131.8
130.7
130.4
126.8
122.8
122.6
116.9
116.7
115.9
115.8
113.6
113.6
44.9
42.7
22.5
O
COOH
F
NH
iPr
13h
137.4
132.8
131.8
130.7
130.4
126.8
122.8
122.6
116.9
116.7
115.9
115.8
113.6
113.6

2-(2-(5-chloro-2-(isopropylamino)phenyl)-2-oxoethyl)benzoic acid (13i):




199.03
168.15
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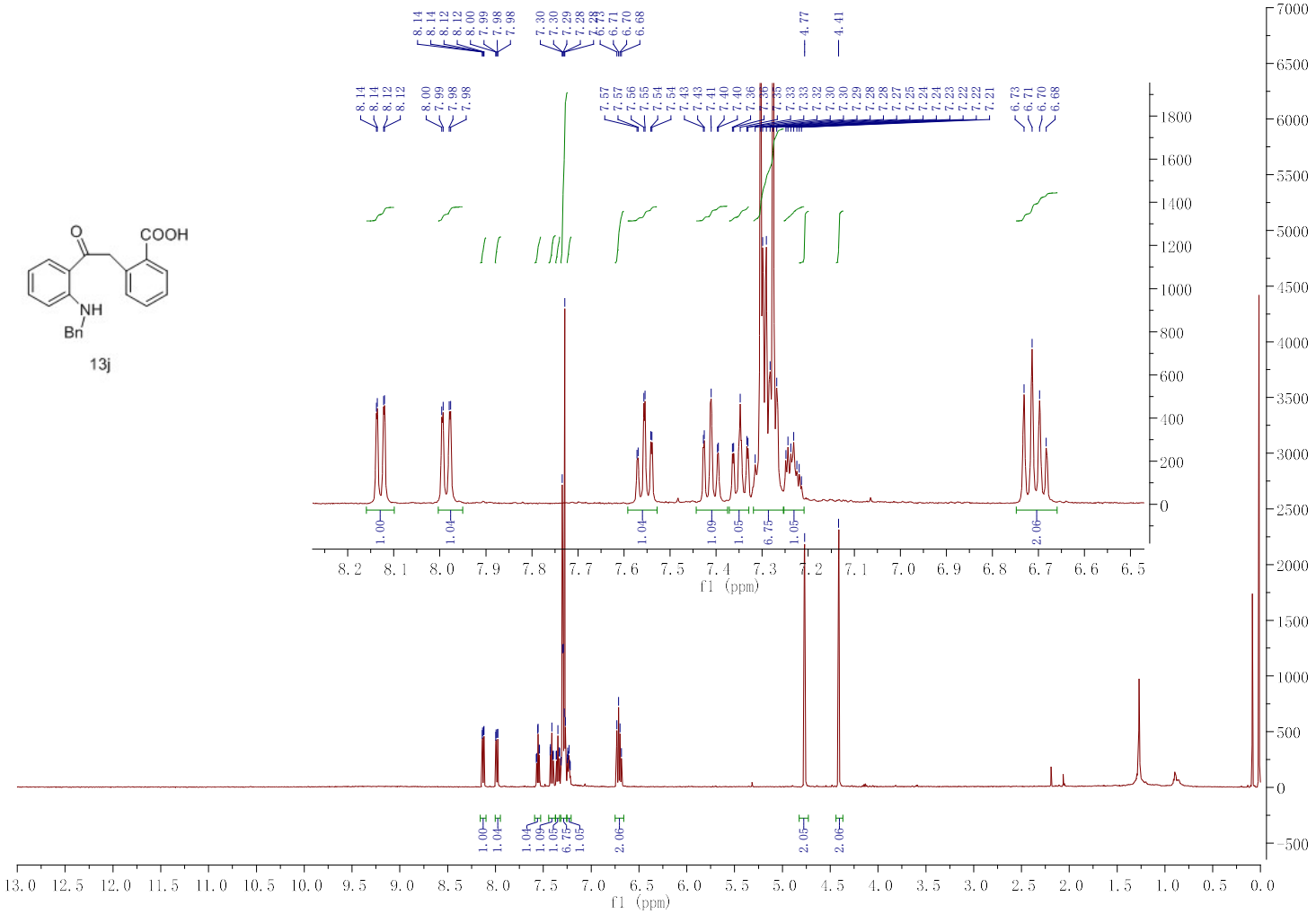
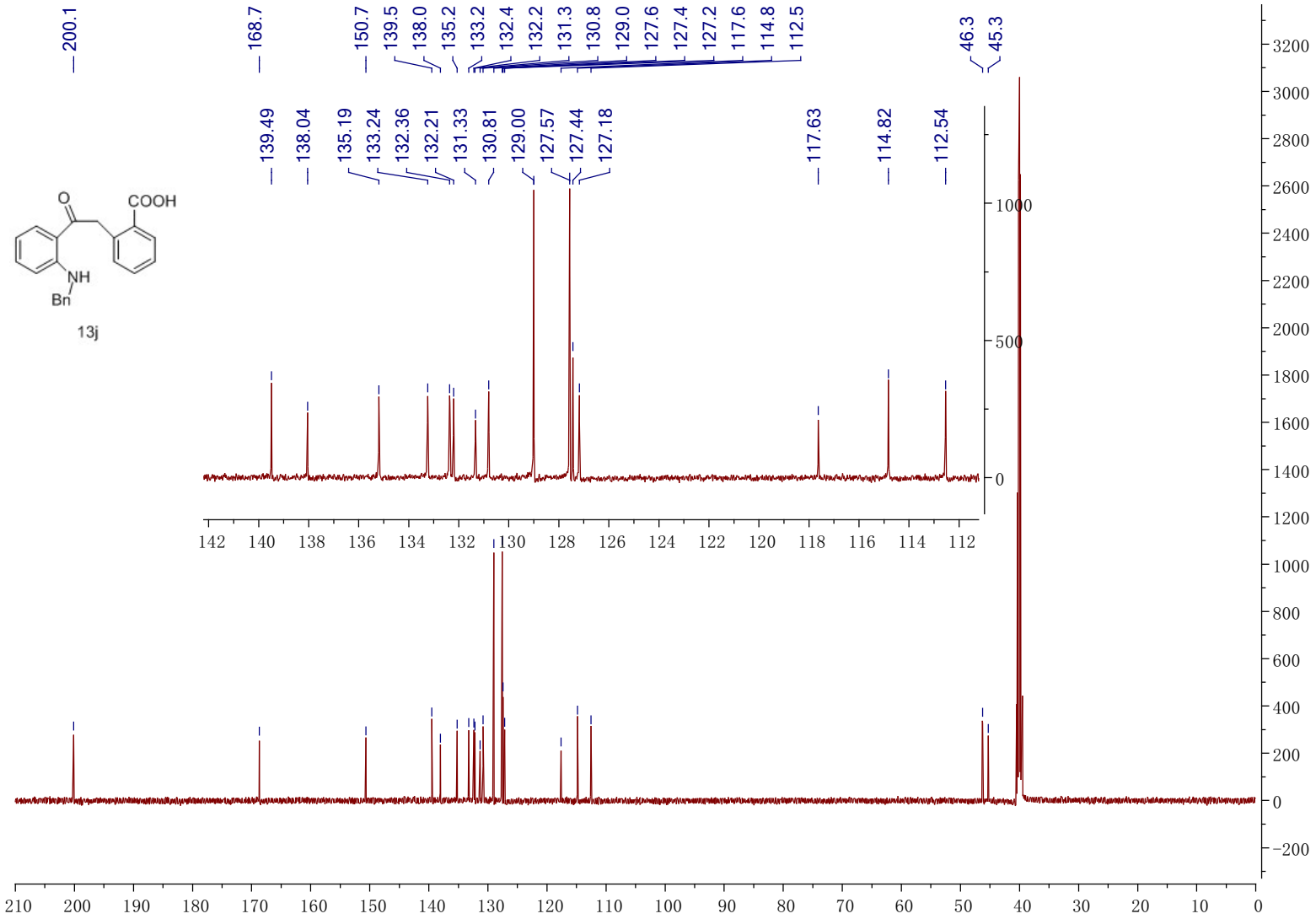
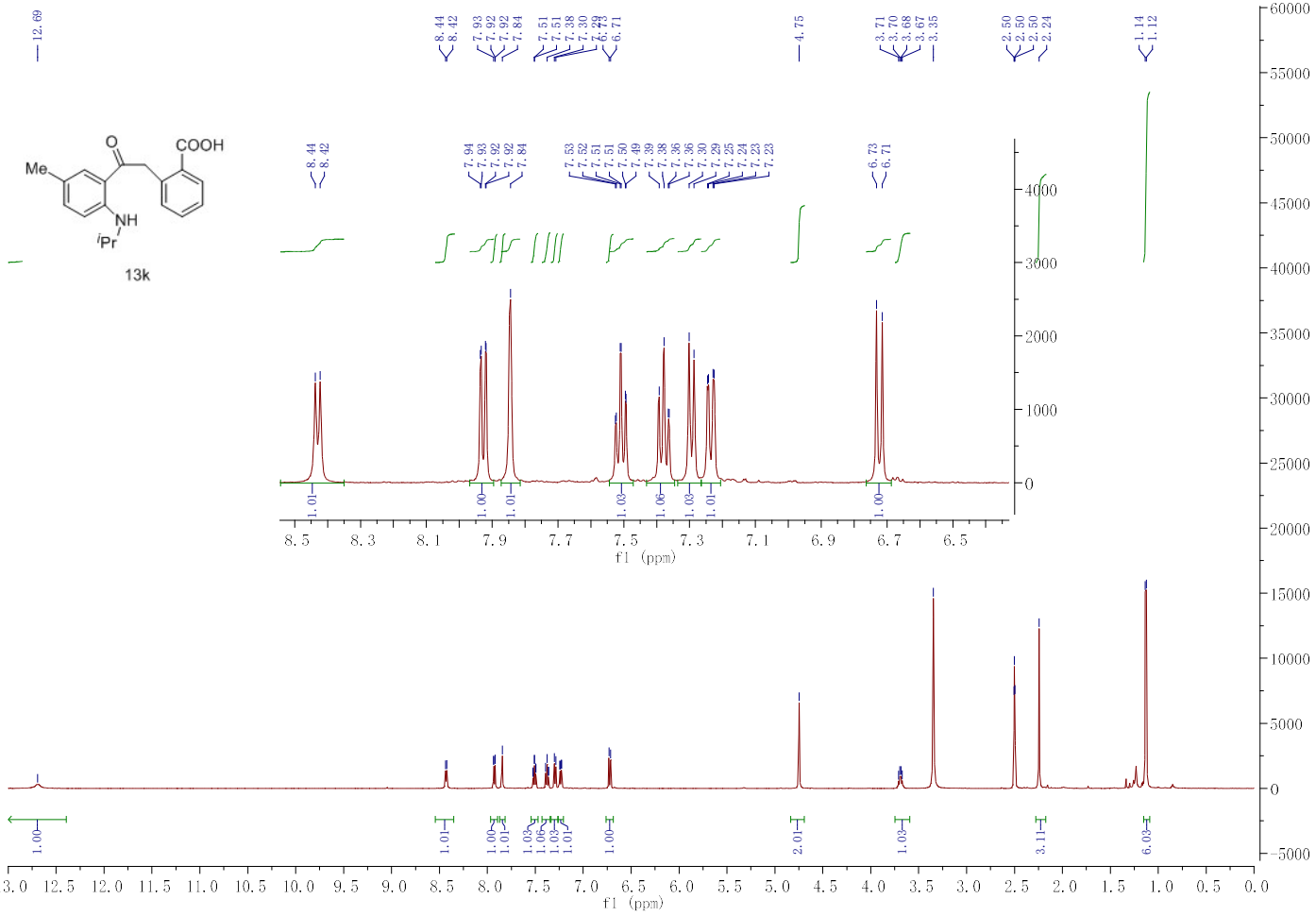
137.43
134.50
132.88
131.86
130.91
130.62
130.41
126.83
117.22
116.97
114.22
44.84
42.68
22.38
Cl
O
COOH
NH
iPr
13i
f1 (ppm)

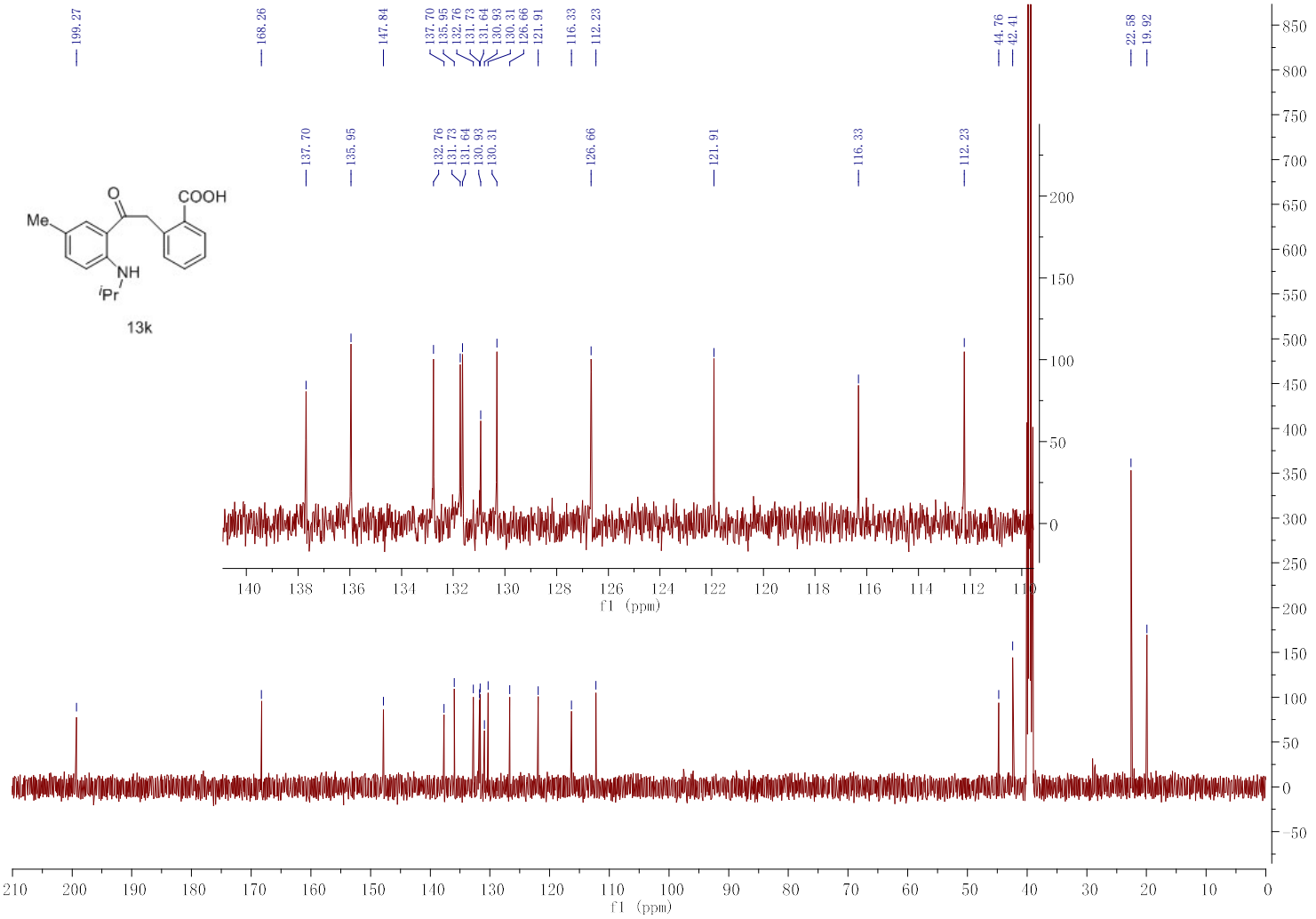
2-(2-(2-(benzylamino)phenyl)-2-oxoethyl)benzoic acid (13j):



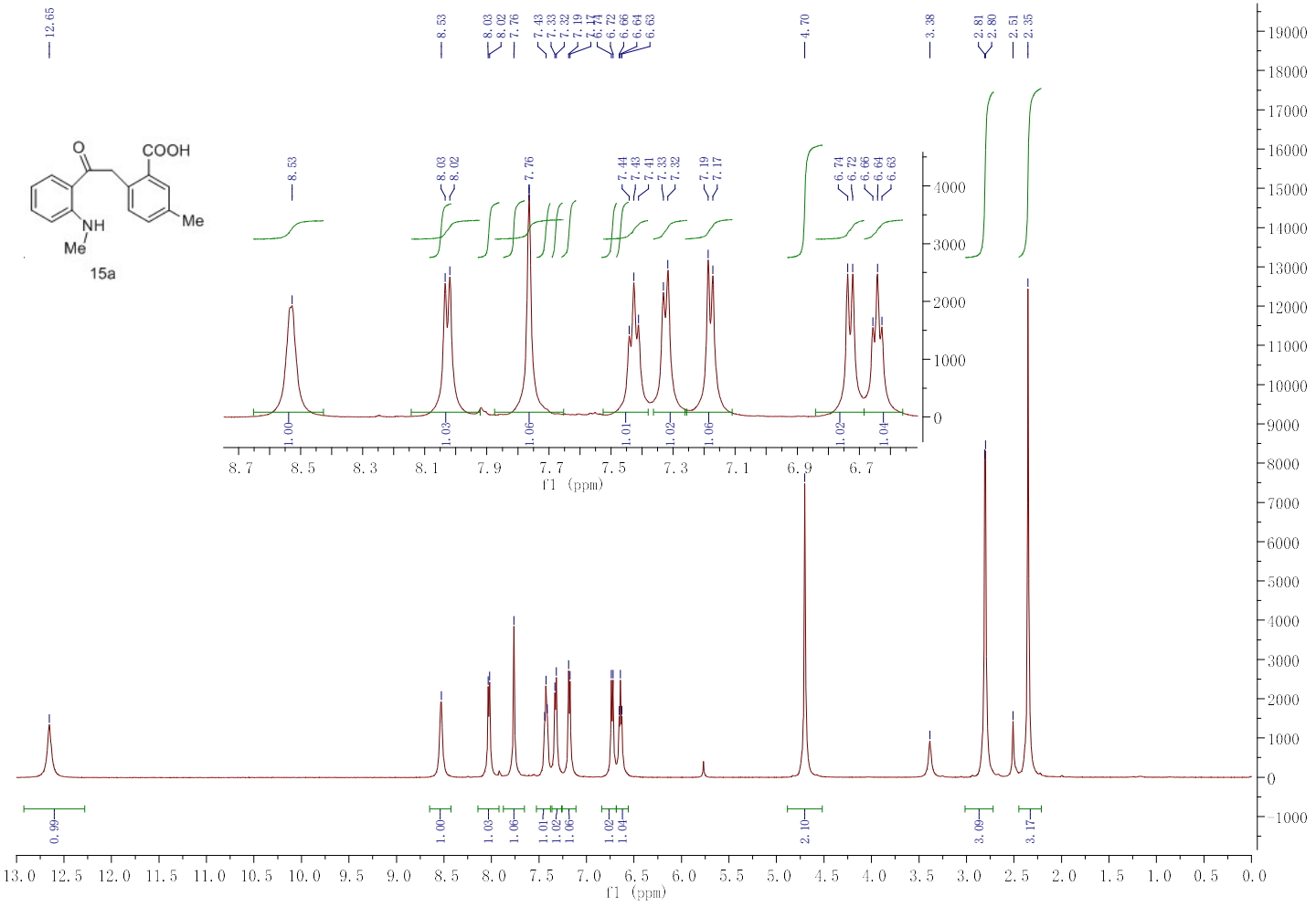

200.1
168.7
150.7
139.5
138.0
135.2
133.2
132.4
132.2
131.3
130.8
129.0
127.6
127.4
127.2
117.6
114.8
112.5
46.3
45.3
139.49
138.04
135.19
133.24
132.36
132.21
131.33
130.81
129.00
127.57
127.44
127.18
117.63
114.82
112.54
O
COOH
NH
Bn
13j

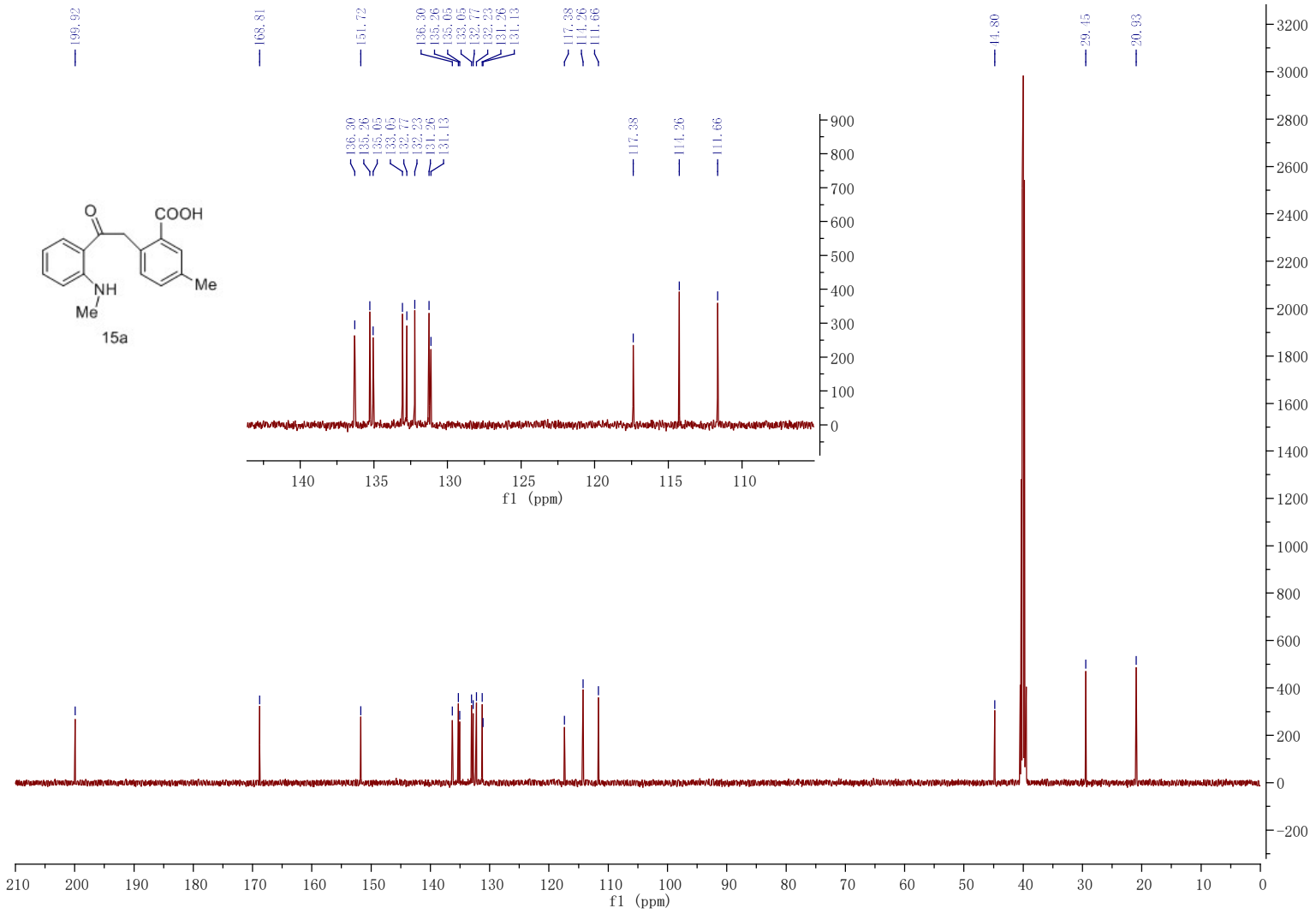
2-(2-(2-(isopropylamino)-5-methylphenyl)-2-oxoethyl)benzoic acid (13k):



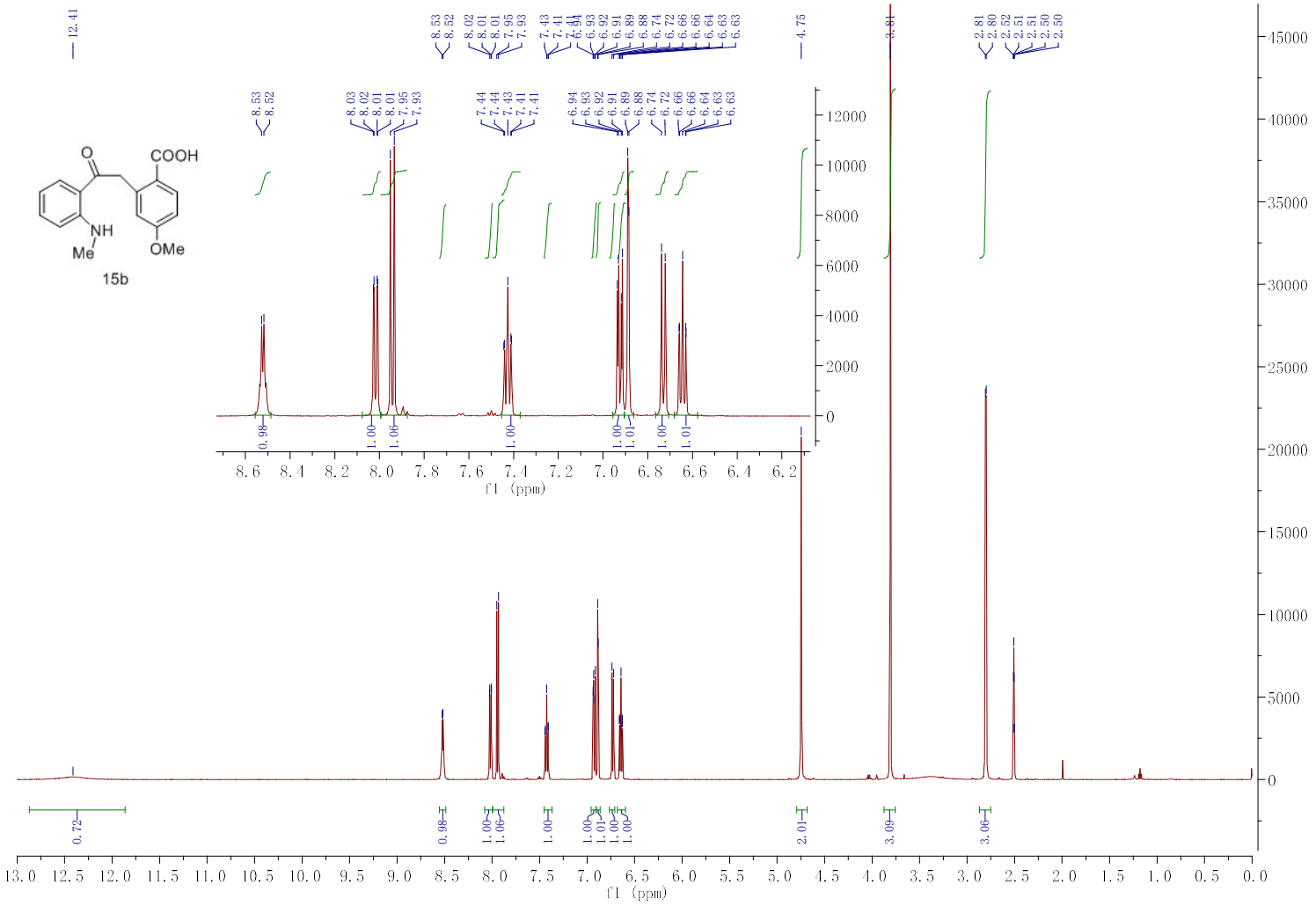

199.27
168.26
147.84
137.70
135.95
132.76
131.73
131.64
130.93
130.31
126.66
121.91
116.33
112.23
44.76
42.41
22.58
19.92
COOH
O
Me
NH
iPr
13k
f1 (ppm)

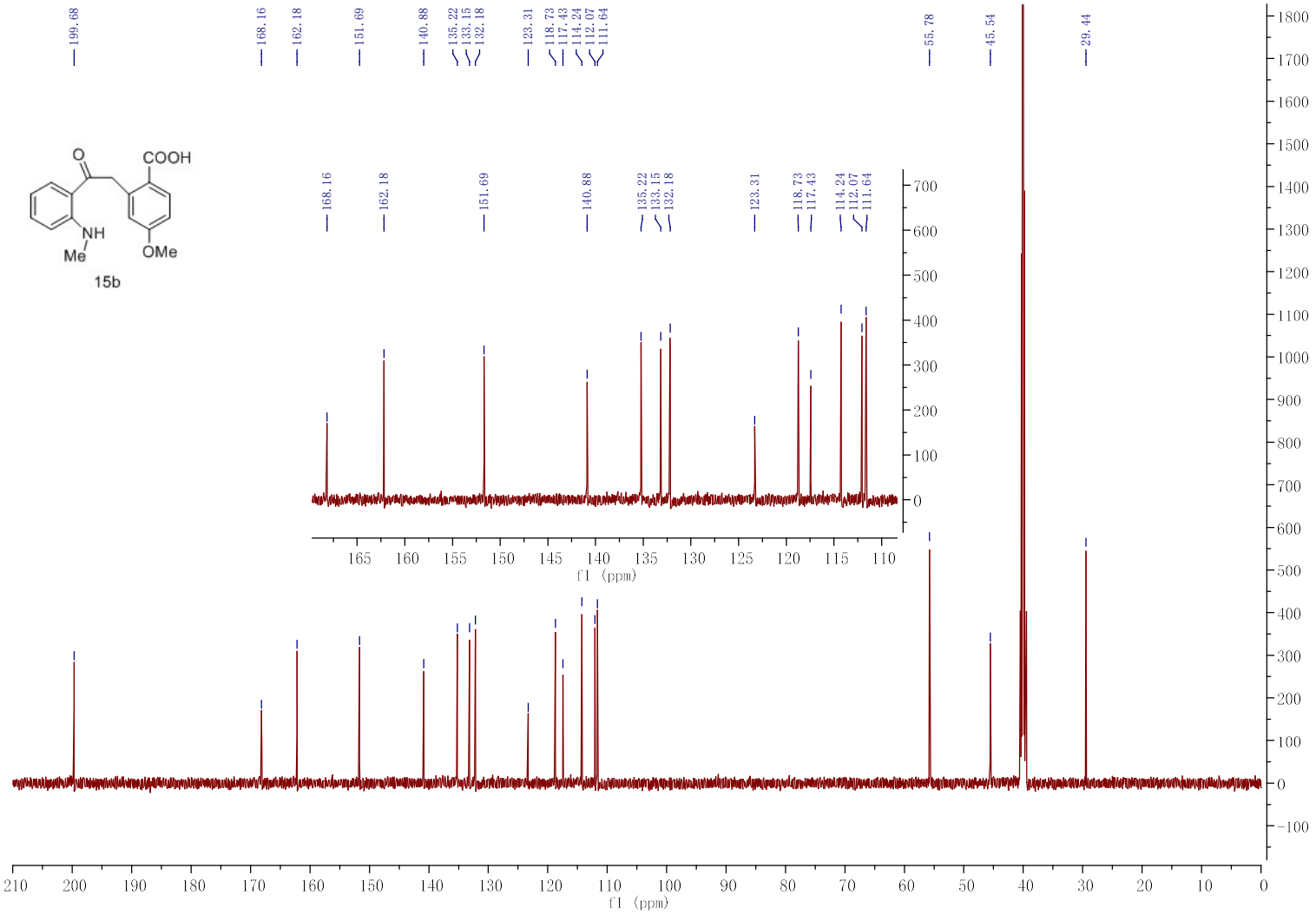
5-methyl-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15a):



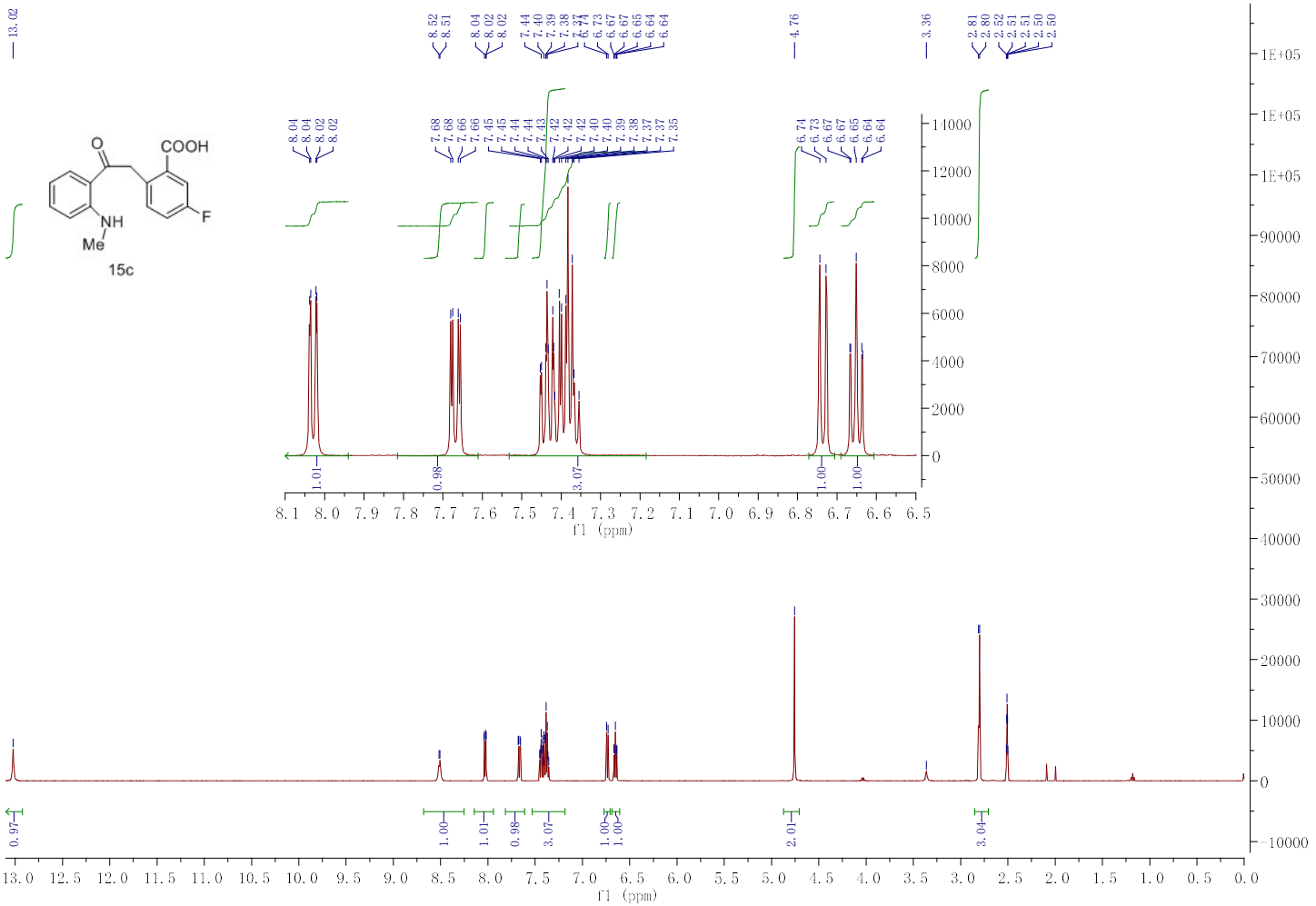

199.92
168.81
151.72
136.30
135.26
135.05
133.05
132.77
132.23
131.26
131.13
117.38
114.26
111.66
44.80
29.45
20.93
O
COOH
NH
Me
Me
15a
f1 (ppm)
f1 (ppm)

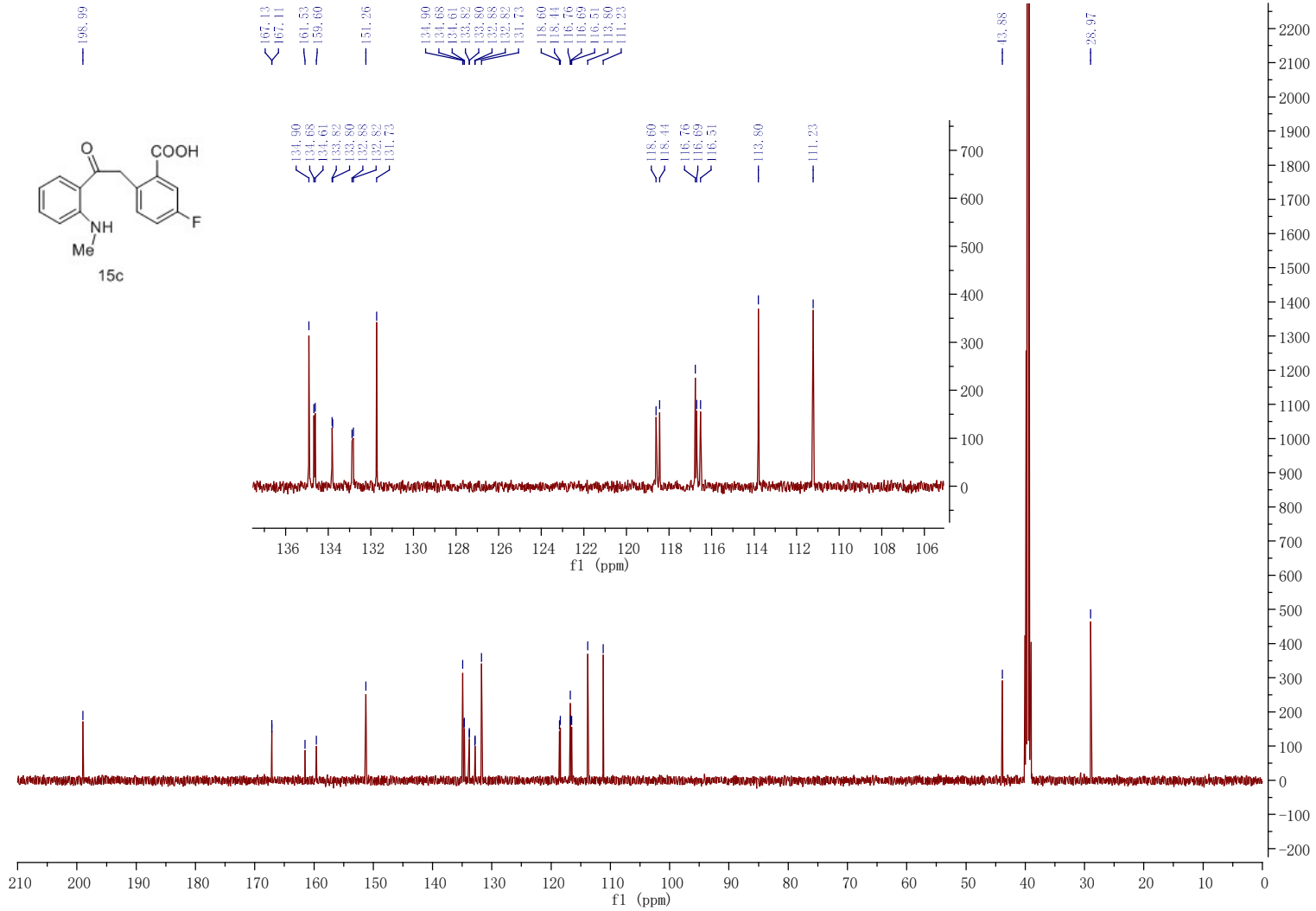
4-methoxy-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15b):



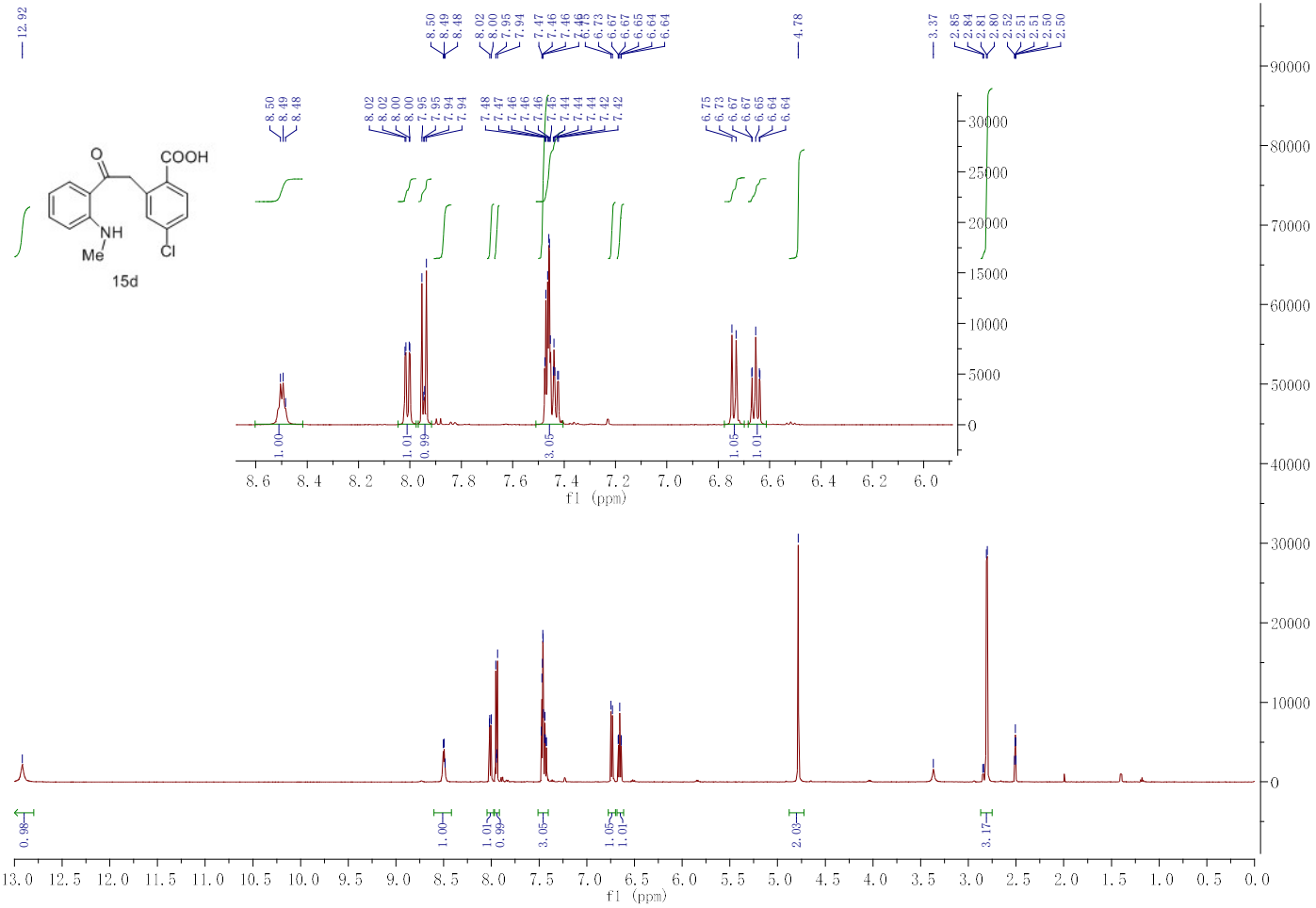

199.68
168.16
162.18
151.69
140.88
135.22
133.15
132.18
123.31
118.73
117.43
114.24
112.07
111.64
55.78
45.54
29.44
O
COOH
NH
Me
OMe
15b
f1 (ppm)

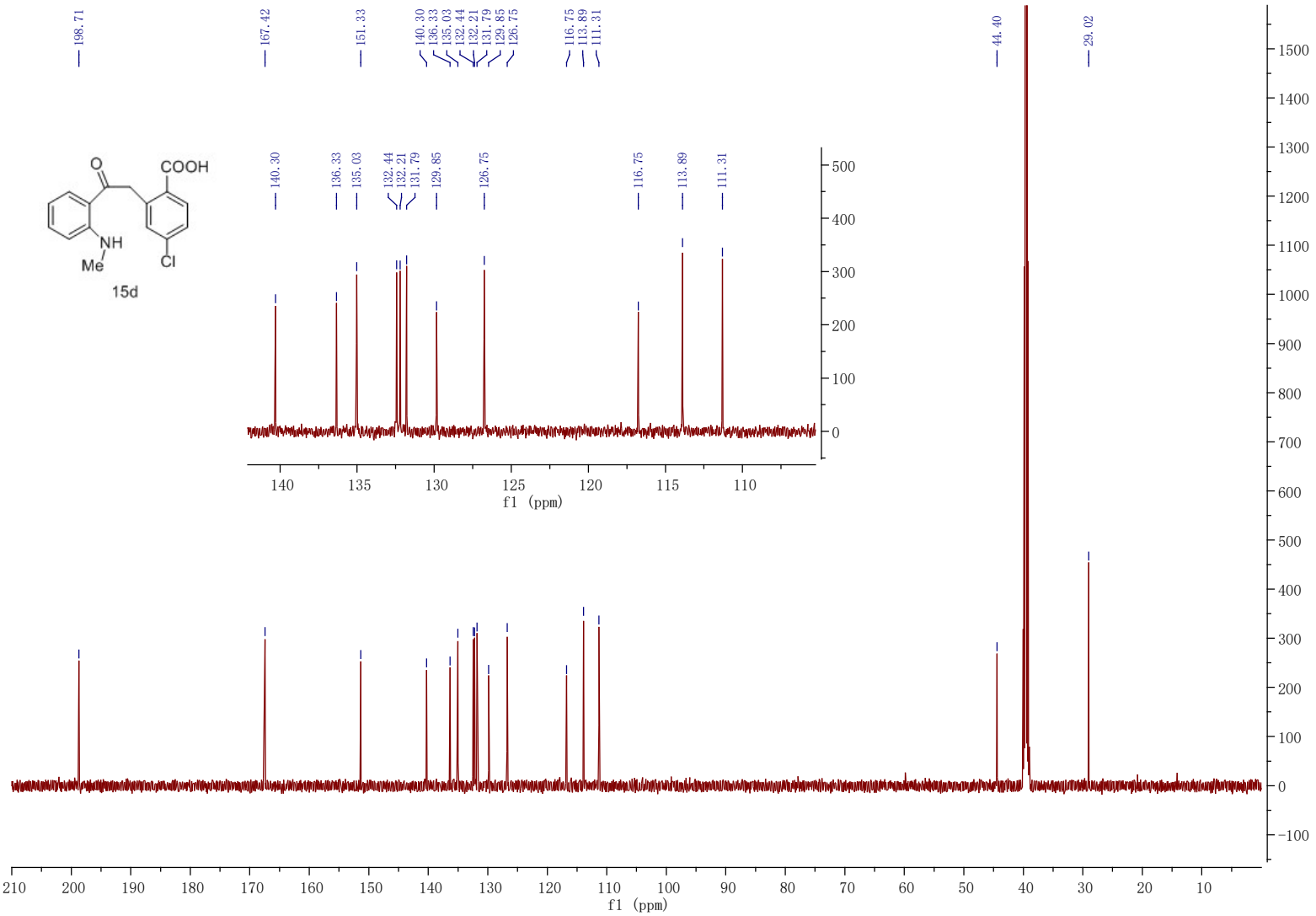
5-fluoro-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15c):



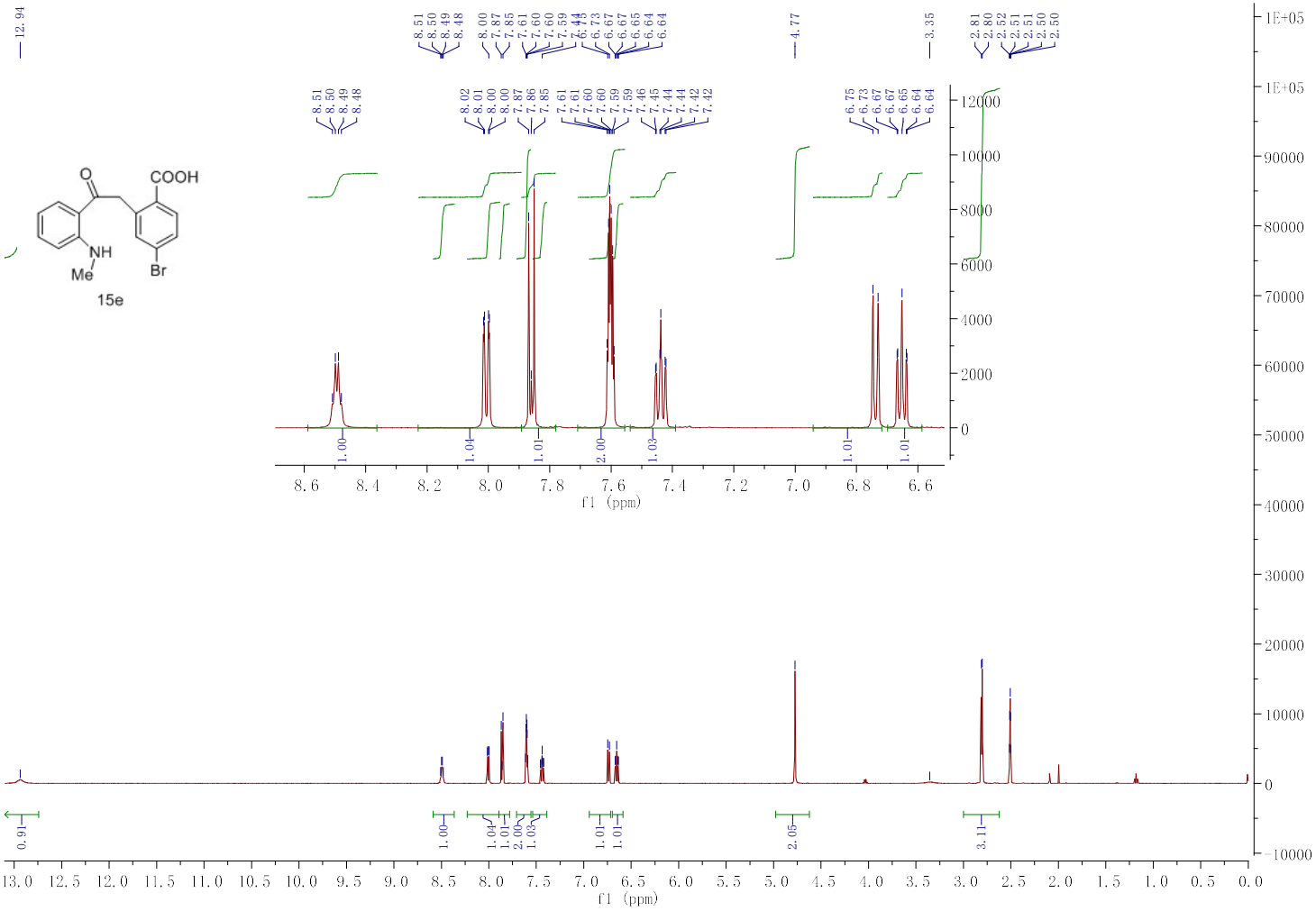

198.99
167.13
167.11
161.53
159.60
151.26
134.90
134.68
134.61
133.82
133.80
132.88
132.82
131.73
118.60
118.44
116.76
116.69
116.51
113.80
111.23
43.88
28.97
COOH
O
NH
Me
F
15c
f1 (ppm)

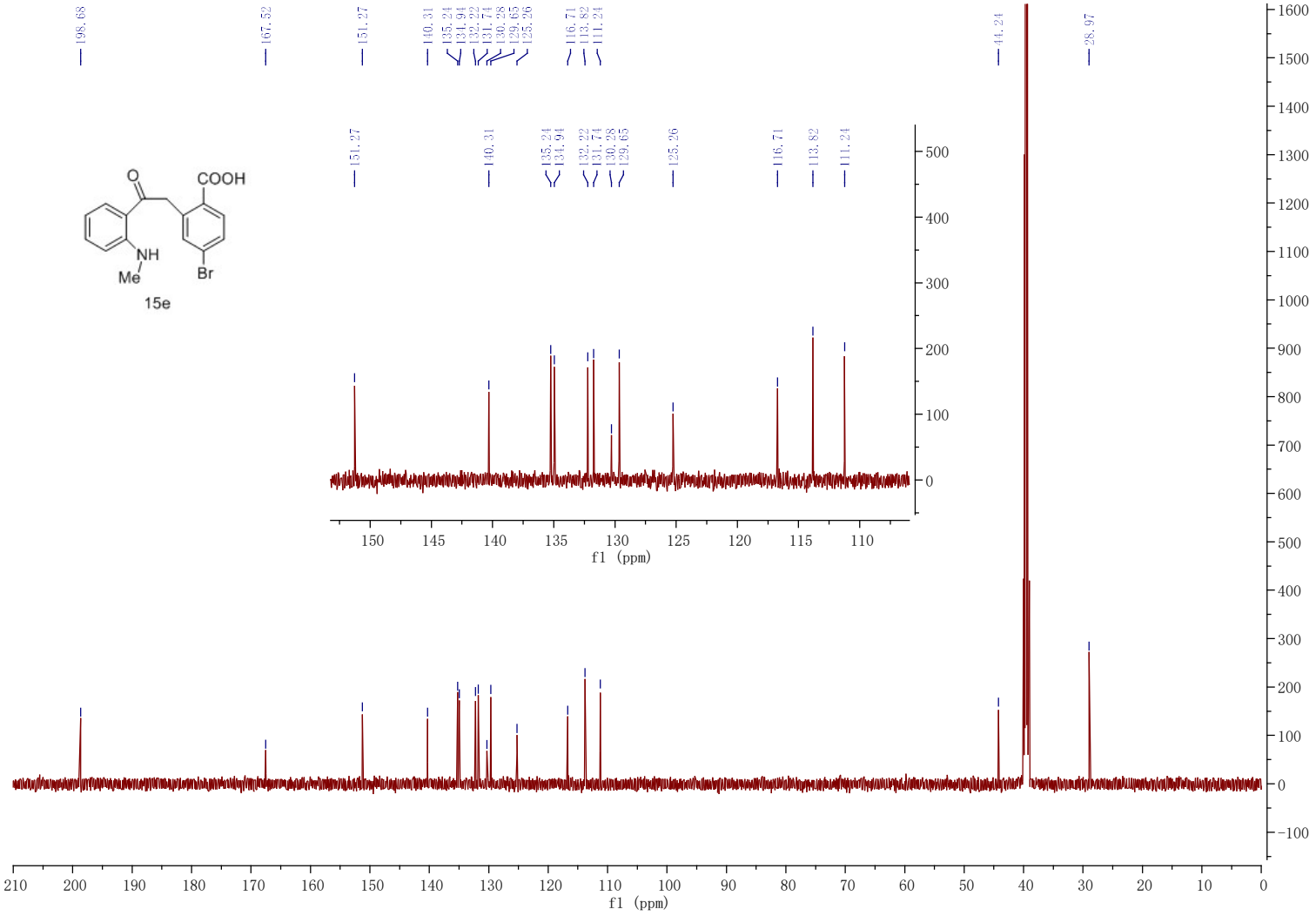
4-chloro-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15d):



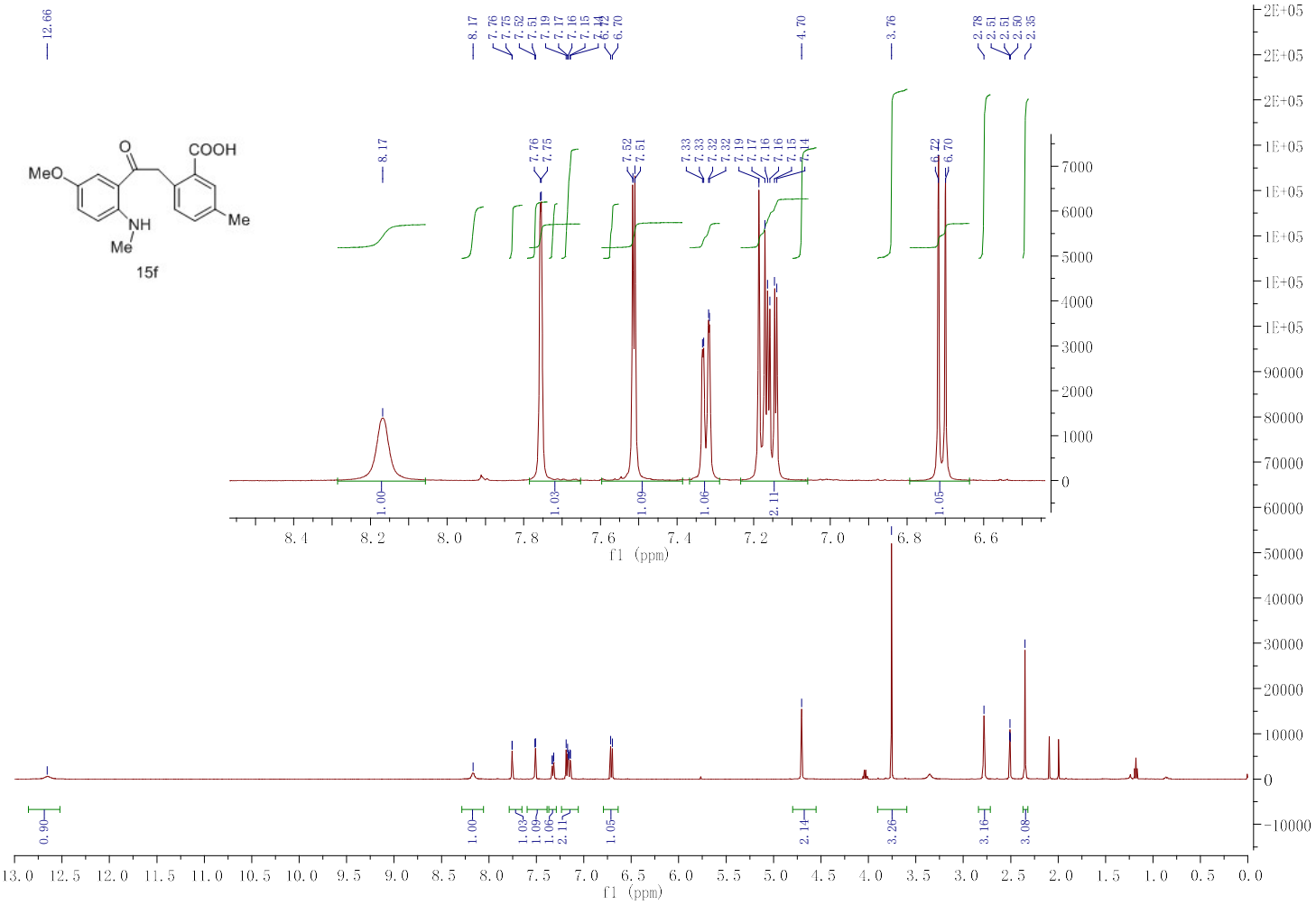

198.71
167.42
151.33
140.30
136.33
135.03
132.44
132.21
131.79
129.85
126.75
116.75
113.89
111.31
44.40
29.02
O
COOH
NH
Me
Cl
15d
f1 (ppm)
f1 (ppm)

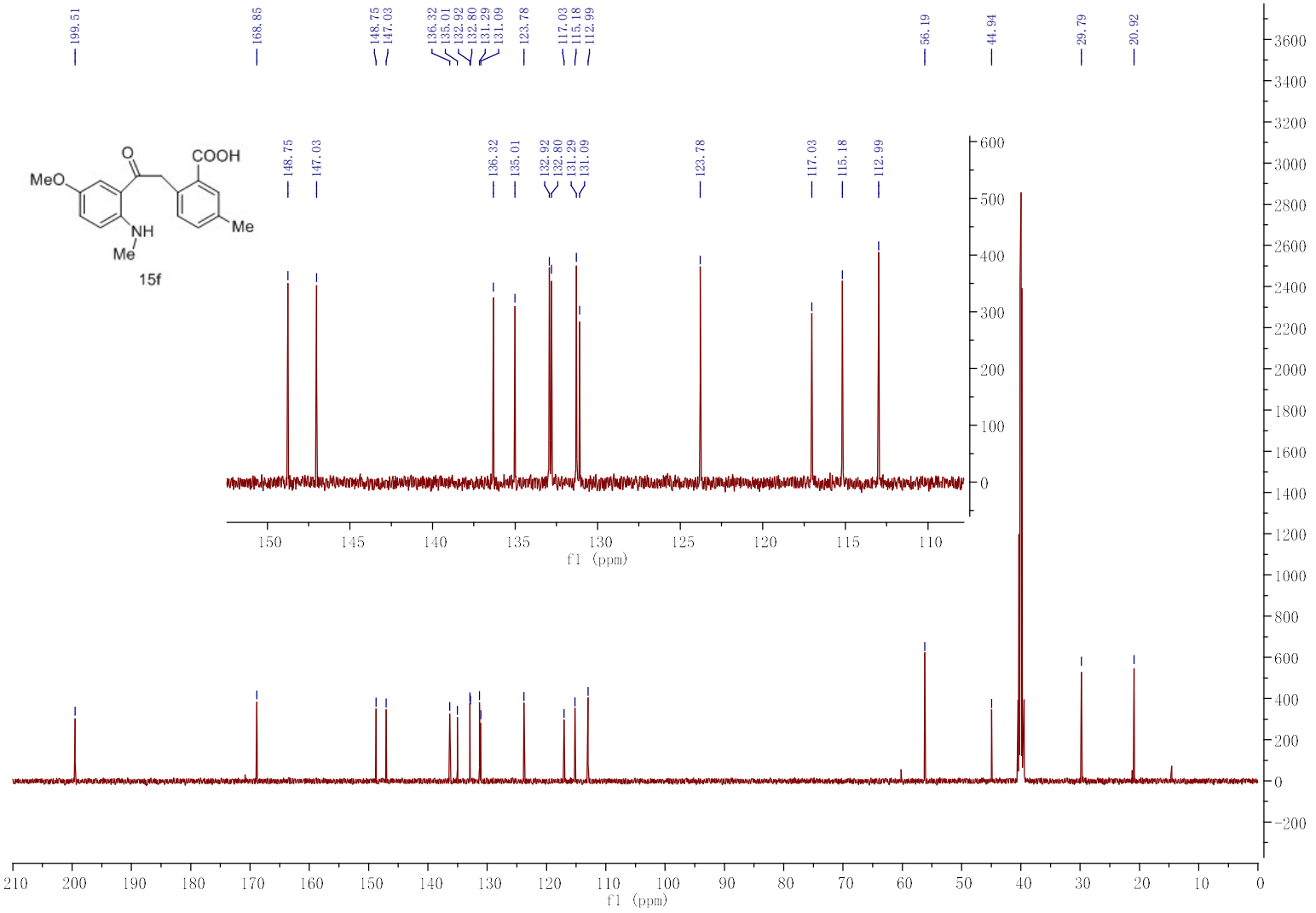
4-bromo-2-(2-(2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15e):



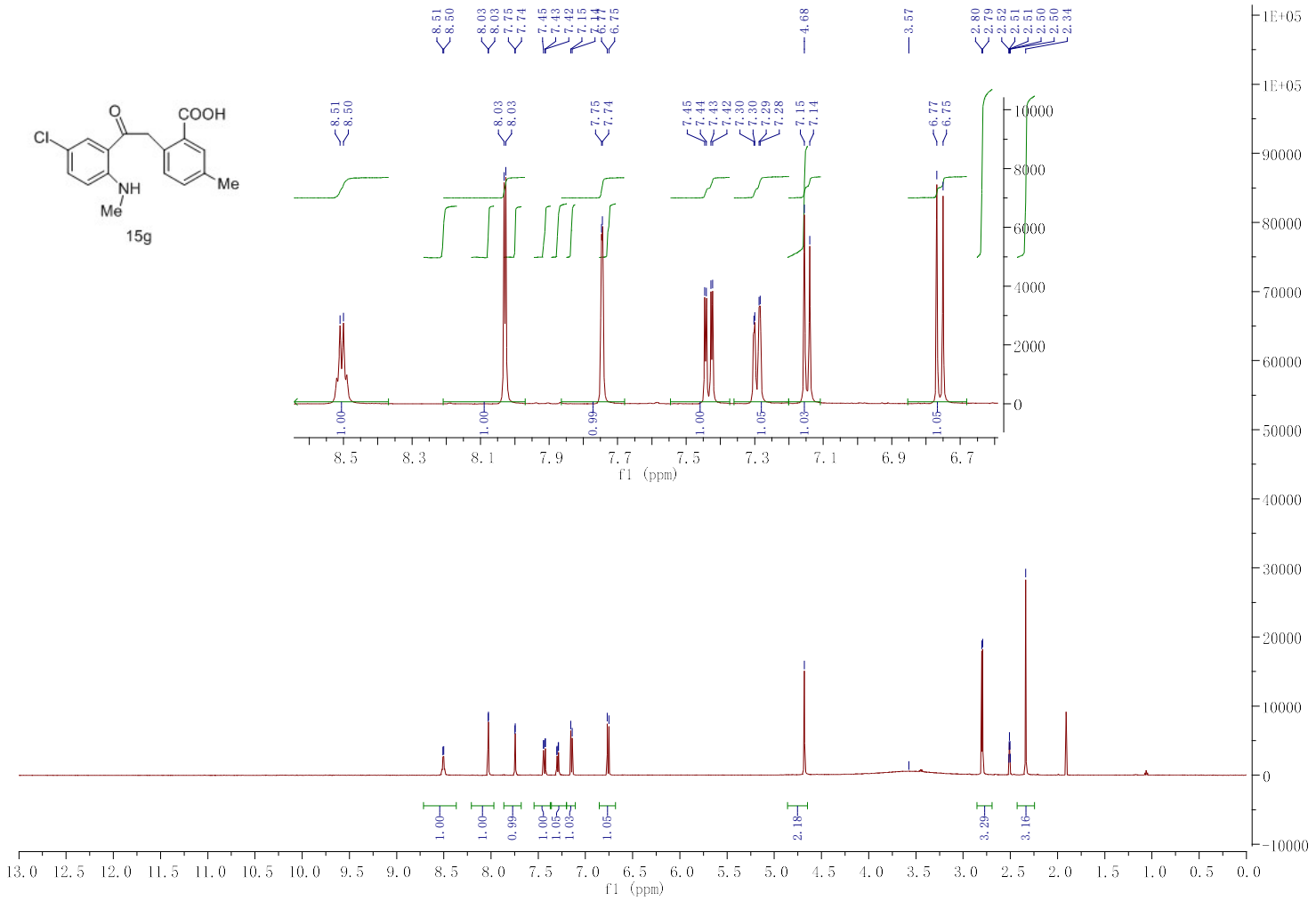

198.68
167.52
151.27
140.31
135.24
134.94
132.22
131.74
130.28
129.65
125.26
116.71
113.82
111.24
44.24
28.97
O
COOH
NH
Me
Br
15e
f1 (ppm)
f1 (ppm)

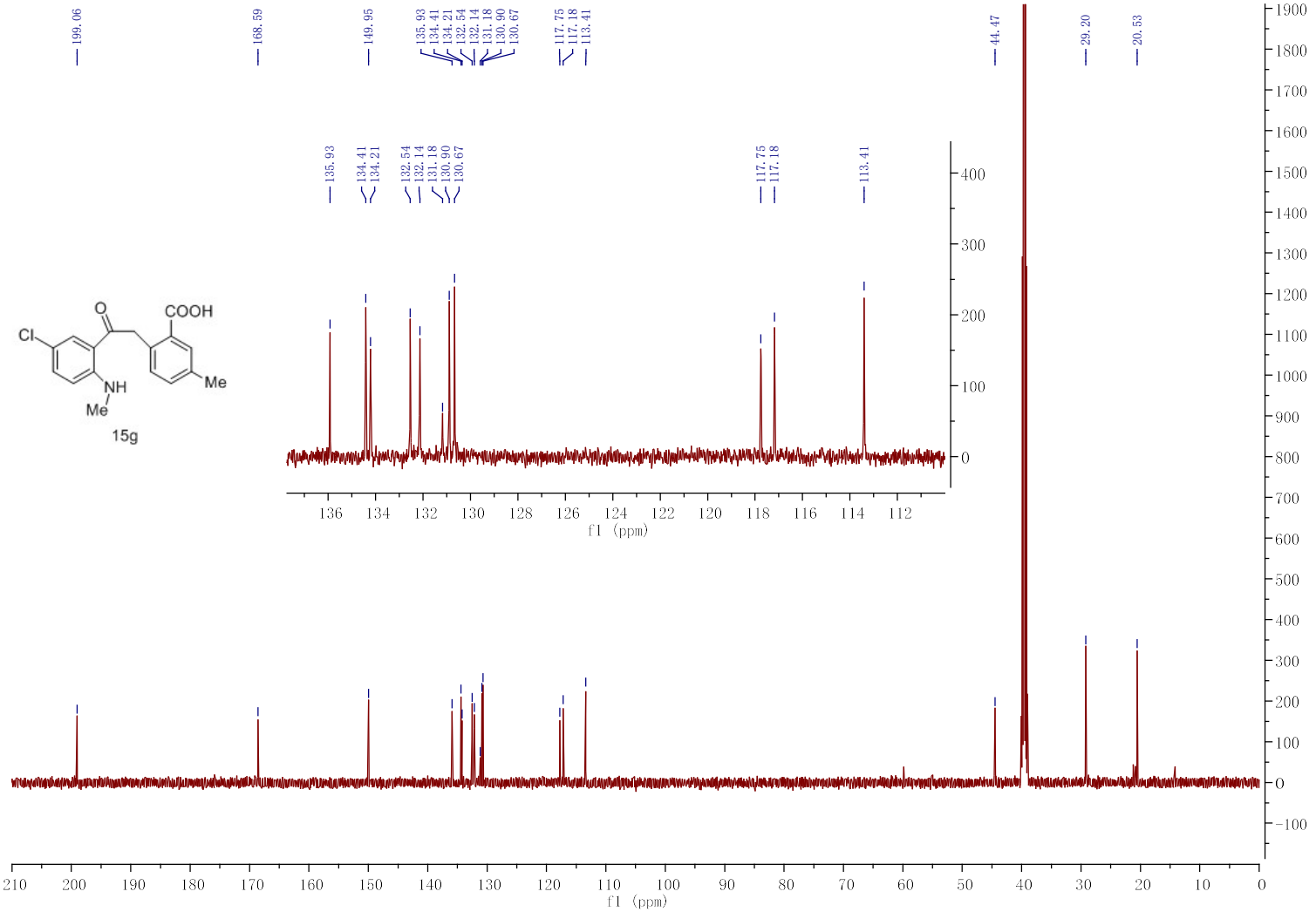
2-(2-(5-methoxy-2-(methylamino)phenyl)-2-oxoethyl)-5-methylbenzoic acid (15f):



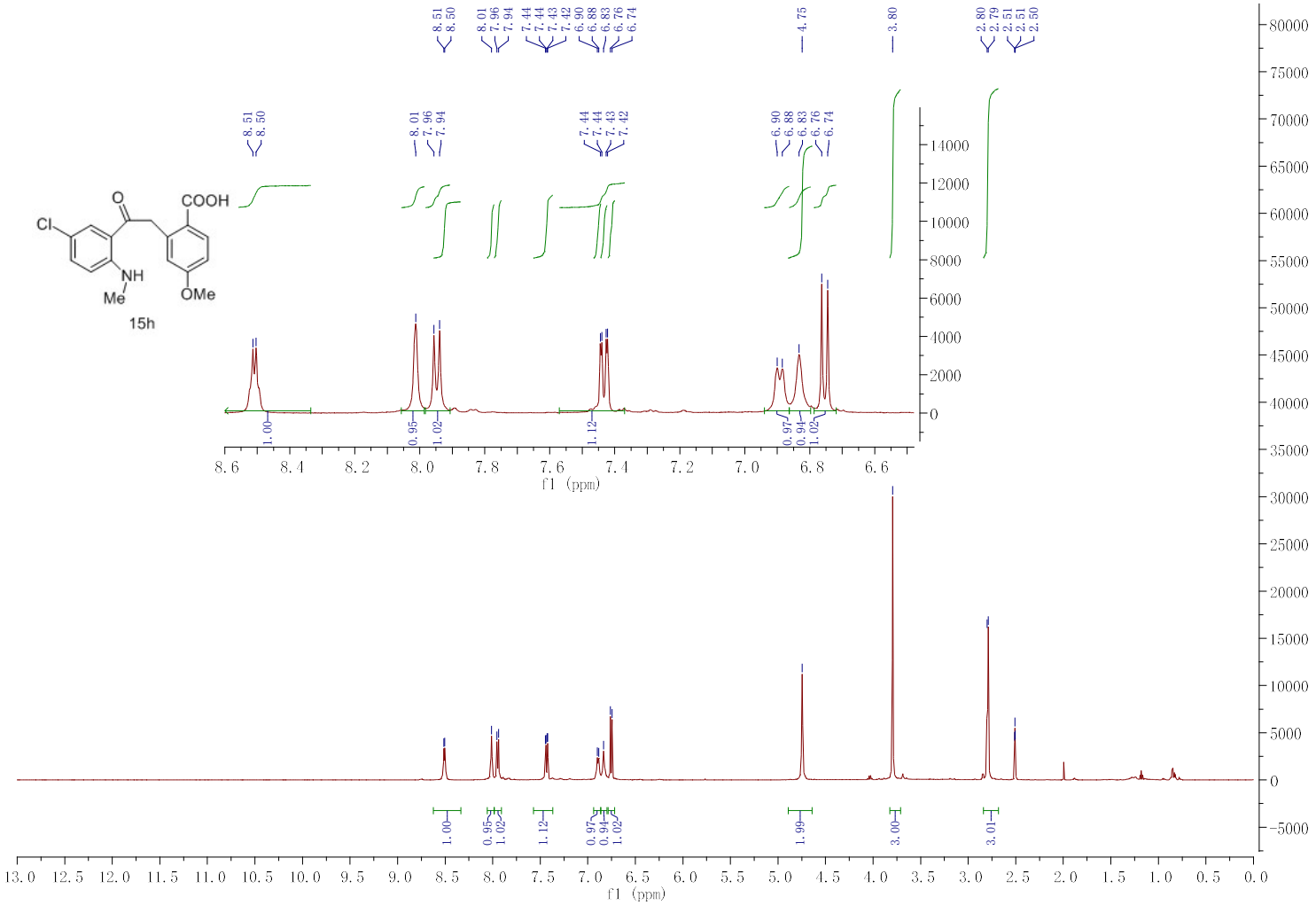

199.51
168.85
148.75
147.03
136.32
135.01
132.92
132.80
131.29
131.09
123.78
117.03
115.18
112.99
56.19
44.94
29.79
20.92
MeO
O
COOH
NH
Me
Me
15f
f1 (ppm)

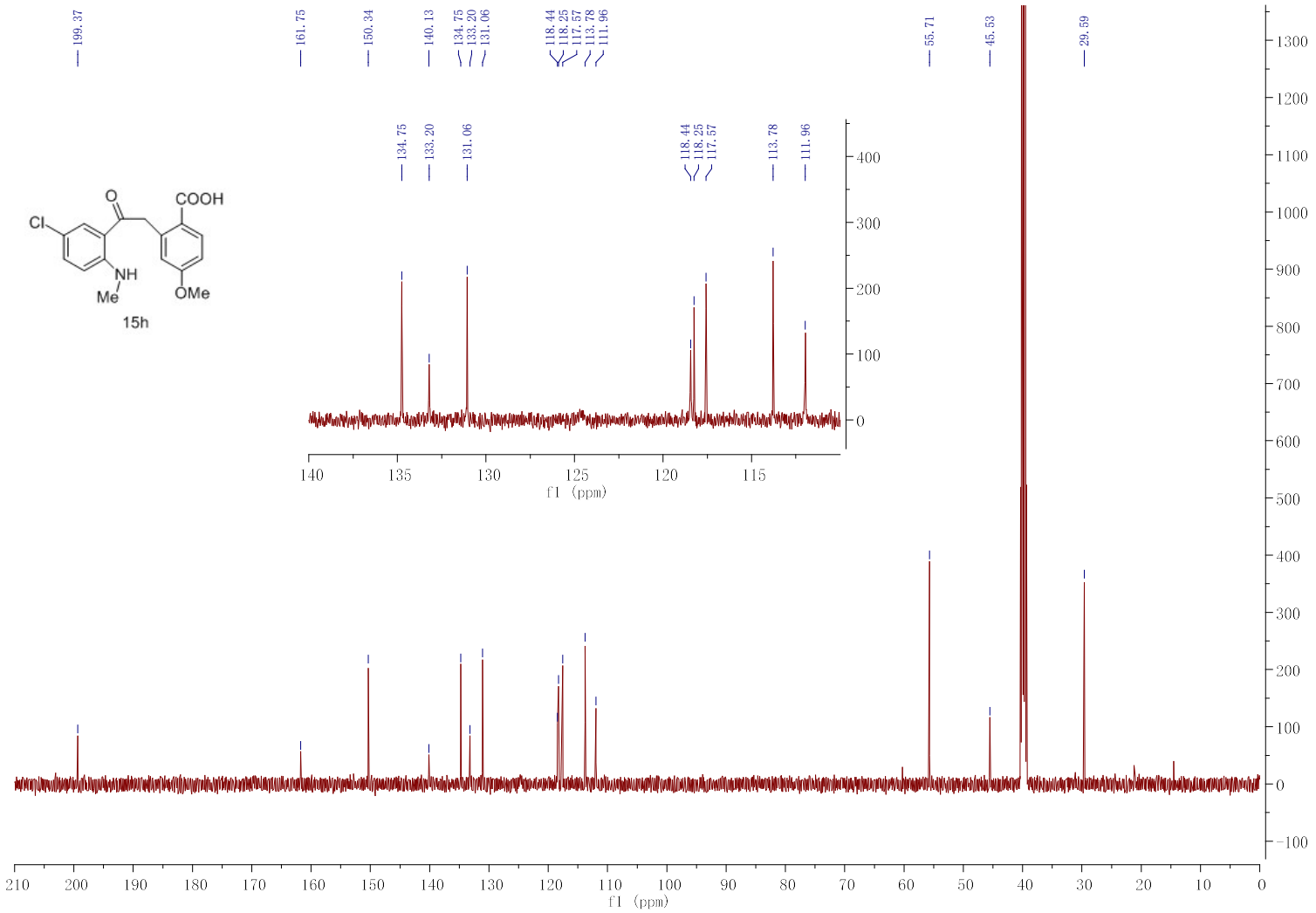
2-(2-(5-chloro-2-(methylamino)phenyl)-2-oxoethyl)-5-methylbenzoic acid (15g):



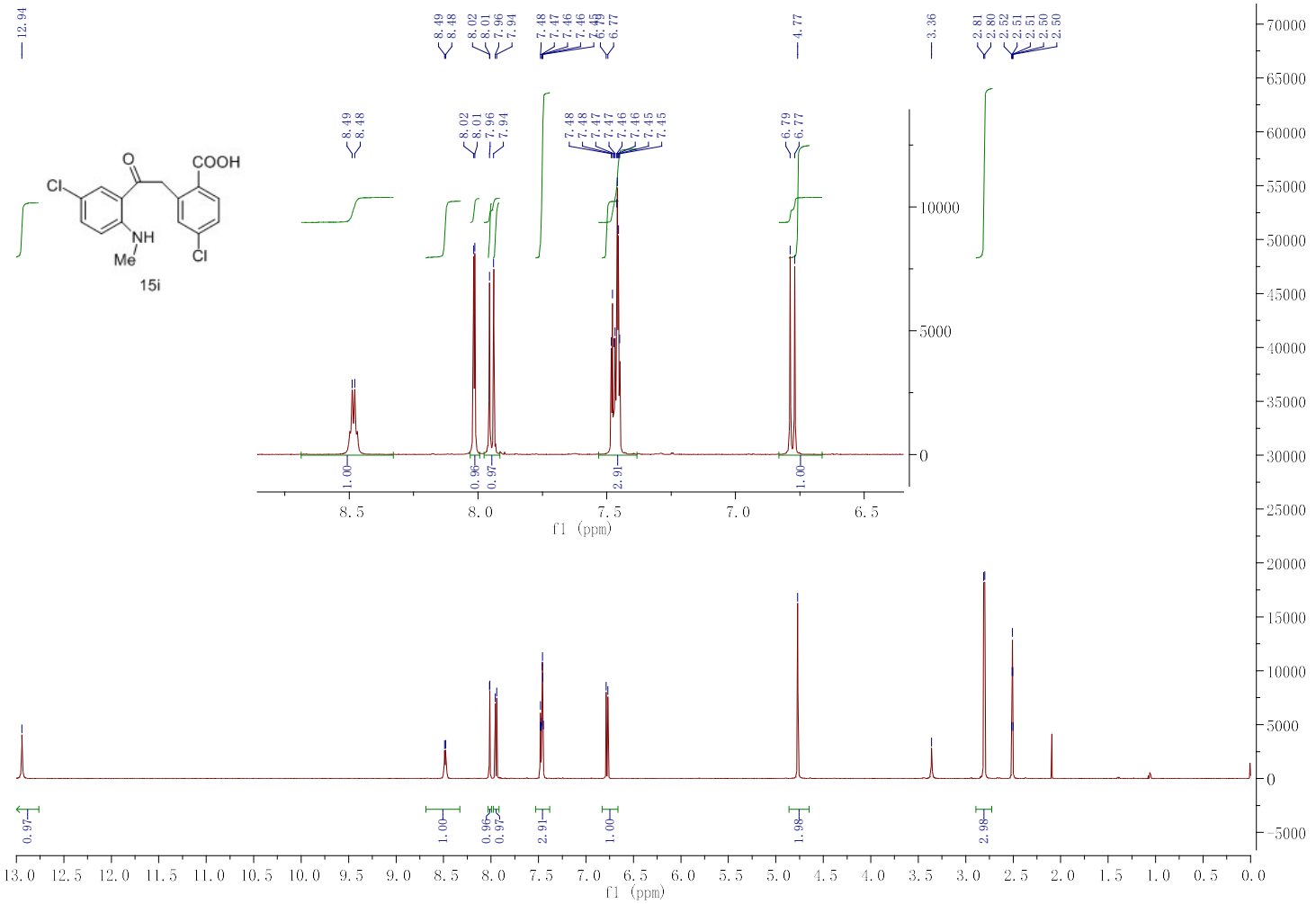

199.06
168.59
149.95
135.93
134.41
134.21
132.54
132.14
131.18
130.90
130.67
117.75
117.18
113.41
44.47
29.20
20.53
O
COOH
Cl
NH
Me
Me
15g
f1 (ppm)

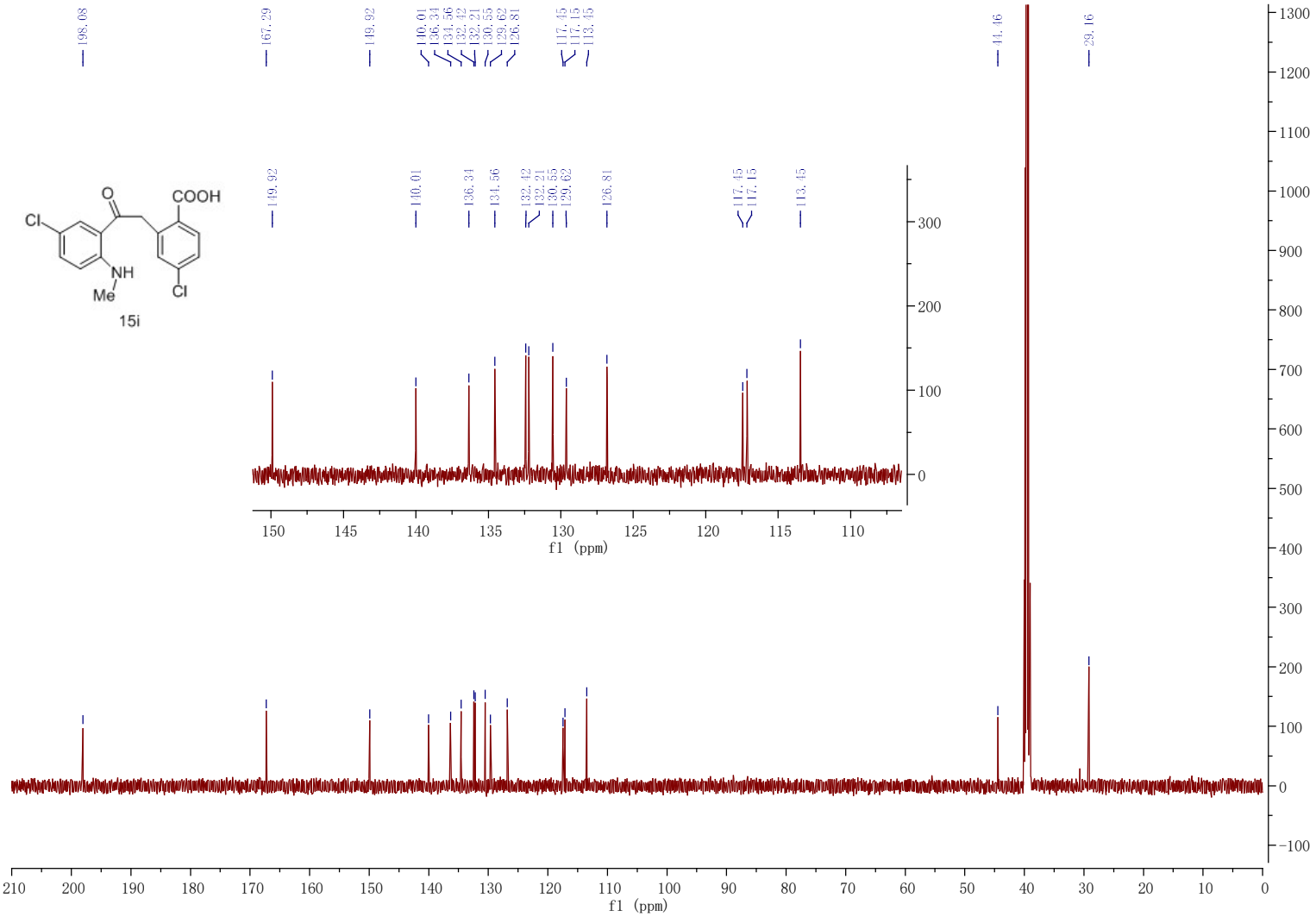
2-(2-(5-chloro-2-(methylamino)phenyl)-2-oxoethyl)-4-methoxybenzoic acid (15h):



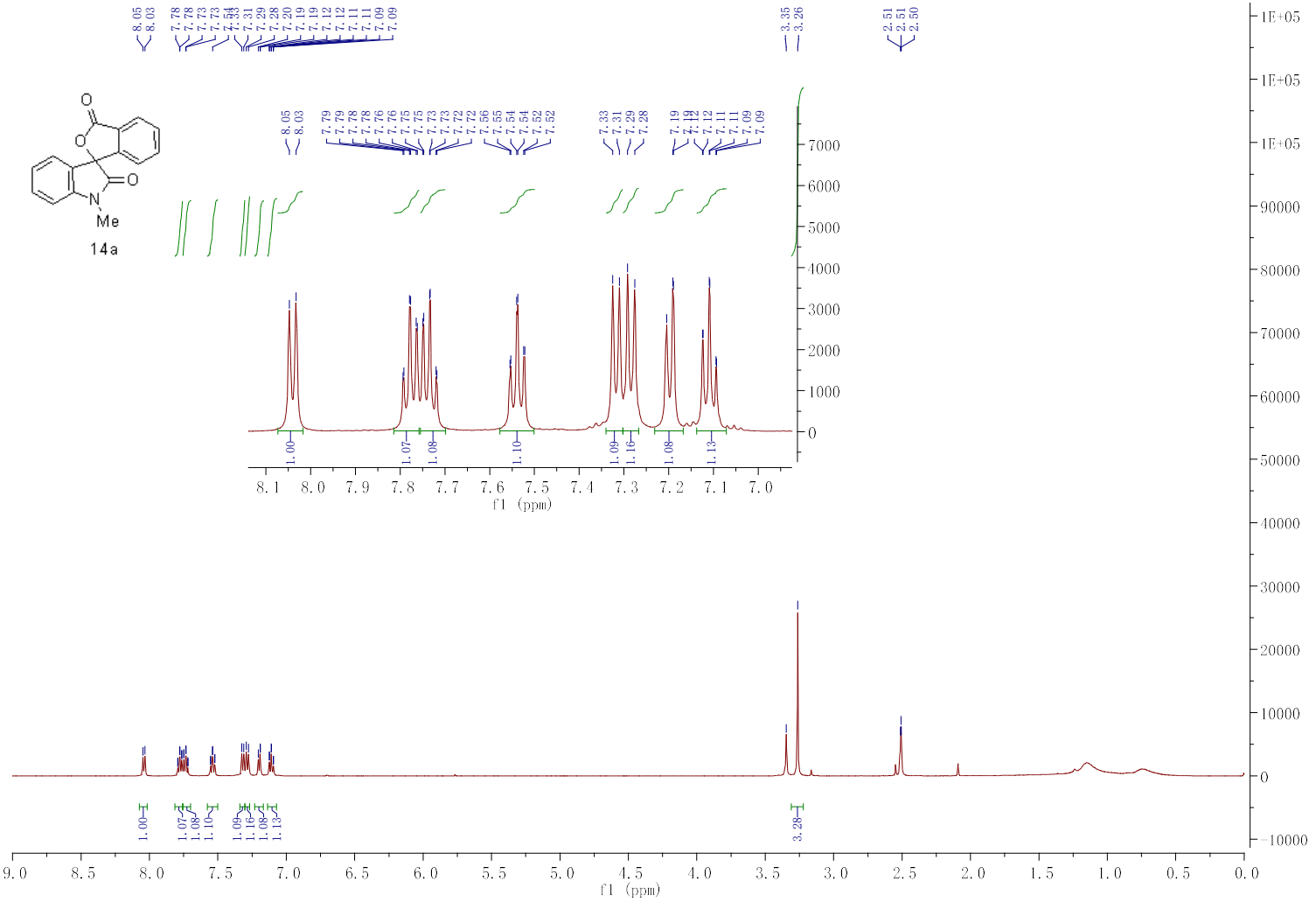

199.37
161.75
150.34
140.13
134.75
133.20
131.06
118.44
118.25
117.57
113.78
111.96
55.71
45.53
29.59
O
COOH
Cl
NH
Me
OMe
15h
f1 (ppm)
f1 (ppm)

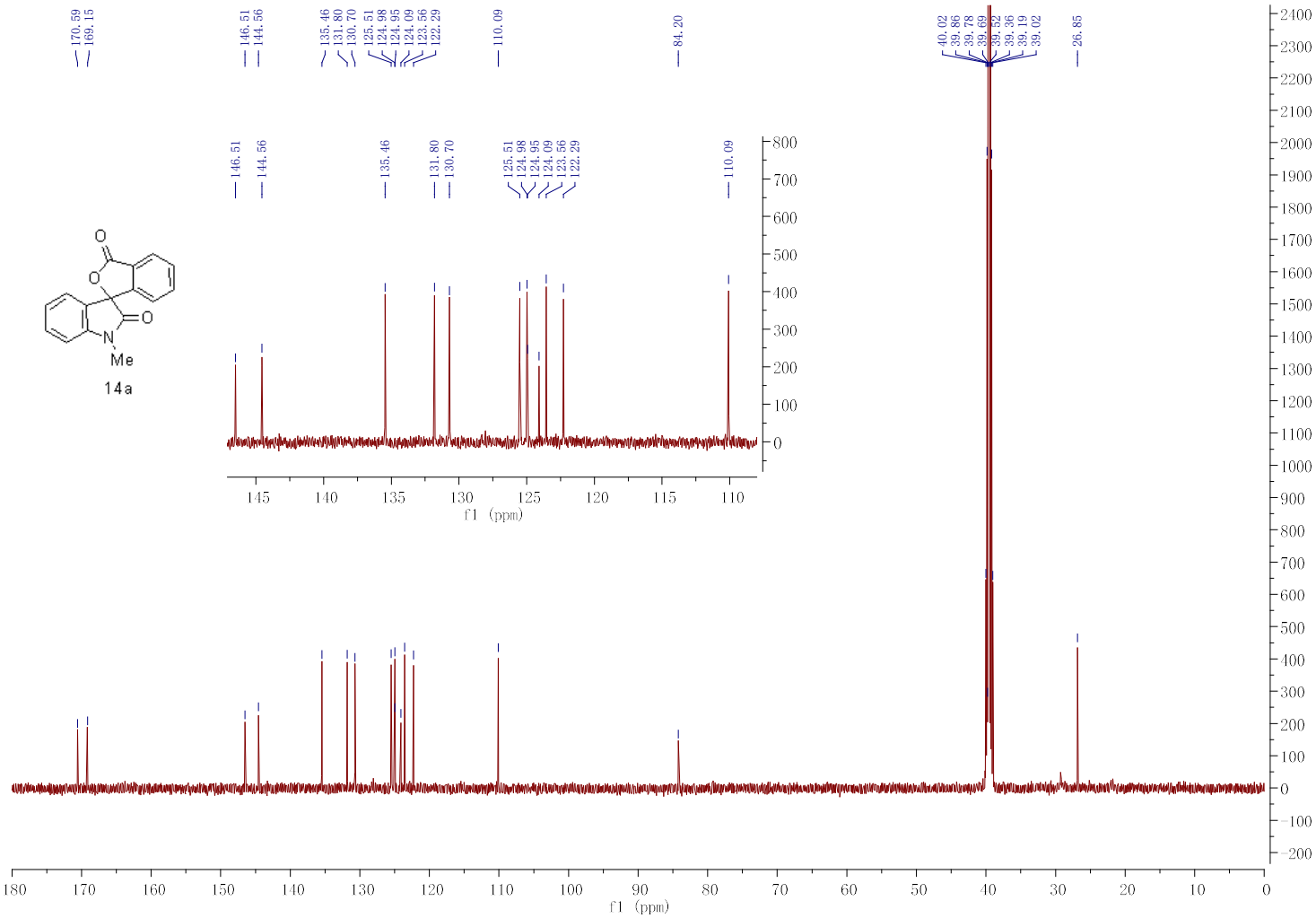
4-chloro-2-(2-(5-chloro-2-(methylamino)phenyl)-2-oxoethyl)benzoic acid (15i):



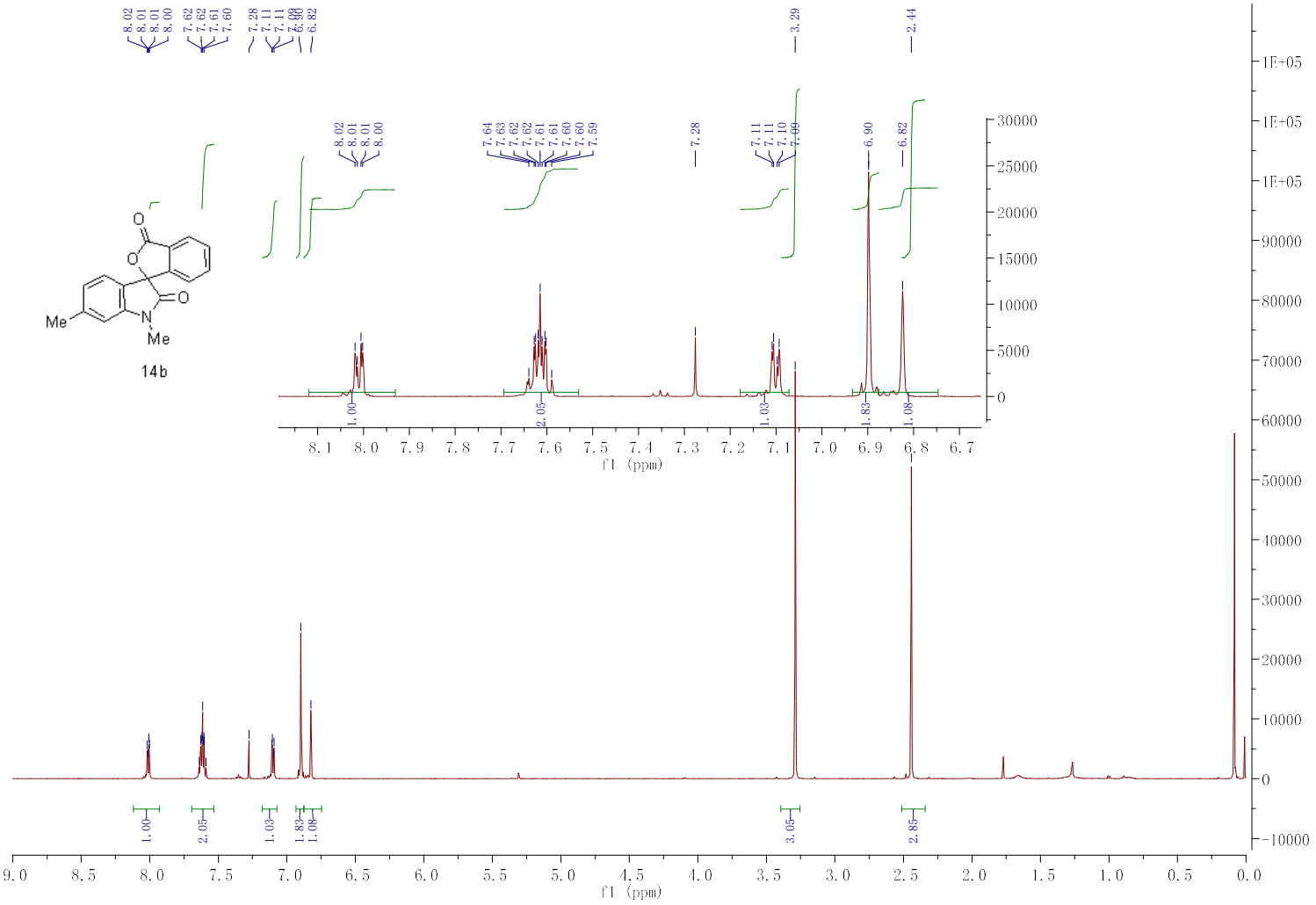

198.08
167.29
149.92
140.01
136.34
134.56
132.42
132.21
130.55
129.62
126.81
117.45
117.15
113.45
44.16
29.16
COOH
Cl
NH
Me
Cl
15i
f1 (ppm)
f1 (ppm)

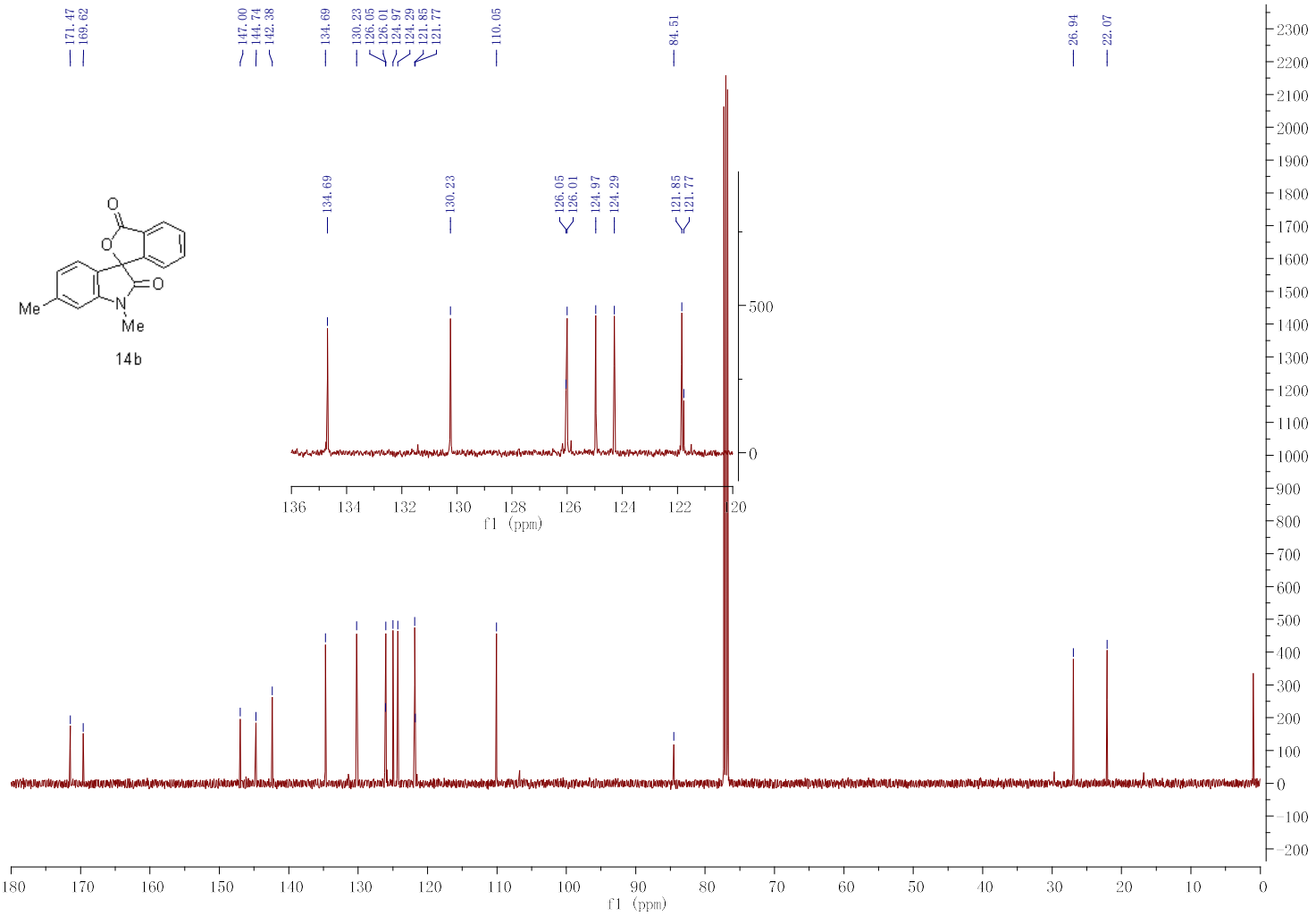
1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione(14a):



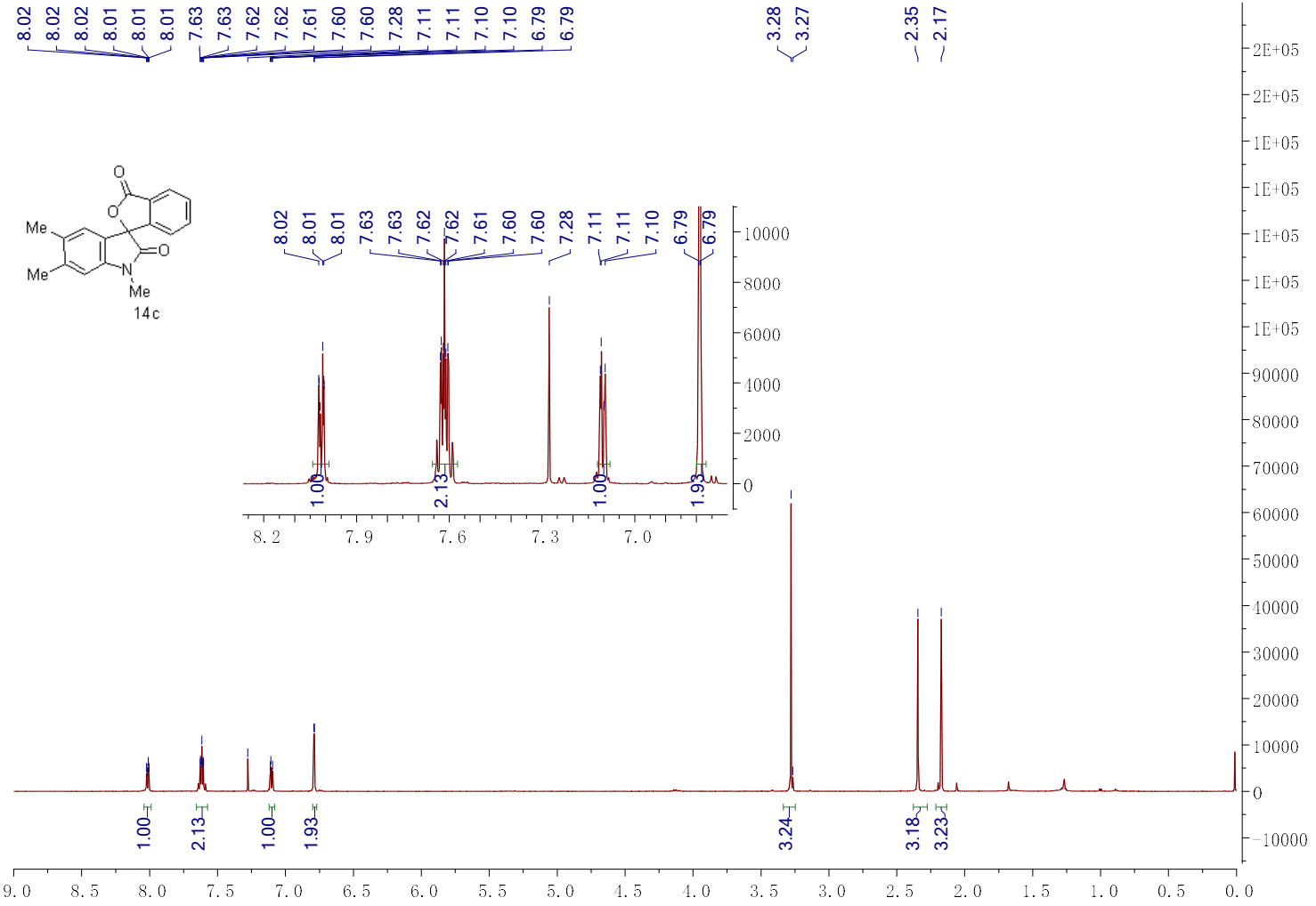

170.59
169.15
146.51
144.56
135.46
131.80
130.70
125.51
124.98
124.95
124.09
123.56
122.29
110.09
84.20
40.02
39.86
39.78
39.69
39.52
39.36
39.19
39.02
26.85
O
O
O
N
Me
14a
f1 (ppm)
f1 (ppm)

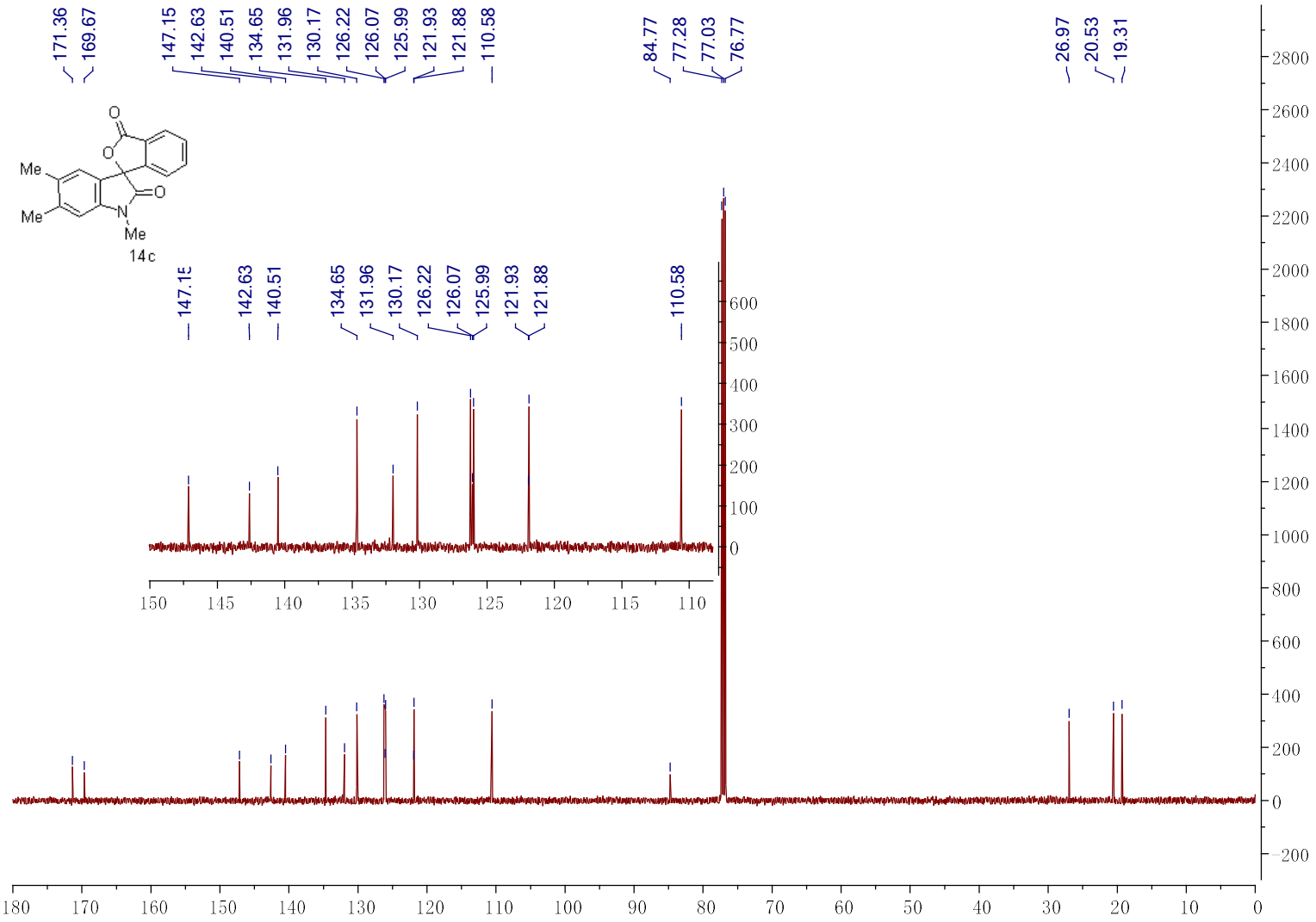
1,6-dimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14b):



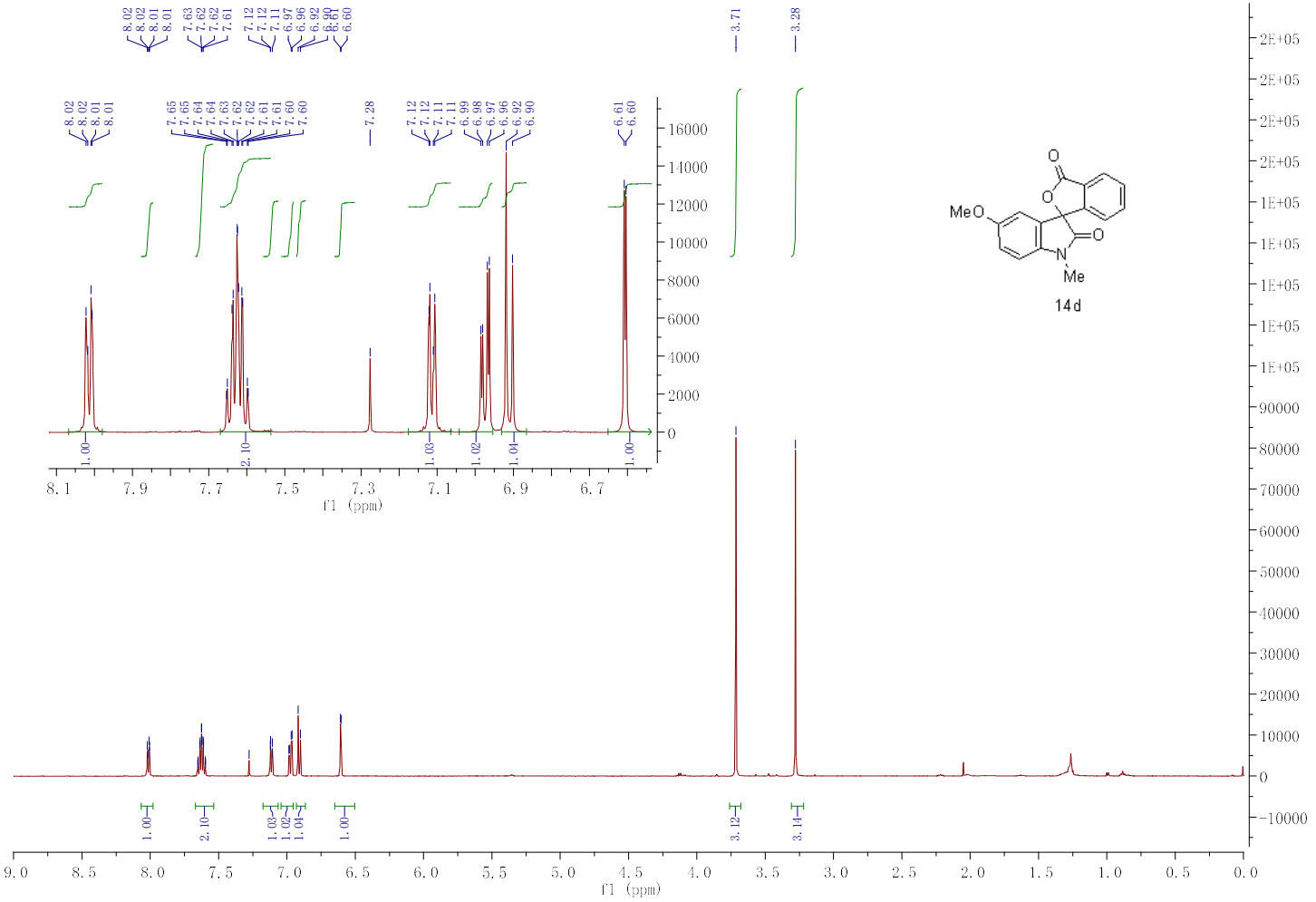

171.47
169.62
147.00
144.74
142.38
134.69
130.23
126.05
126.01
124.97
124.29
121.85
121.77
110.05
84.51
26.94
22.07
O
O
O
N
Me
Me
14b
f1 (ppm)
f1 (ppm)

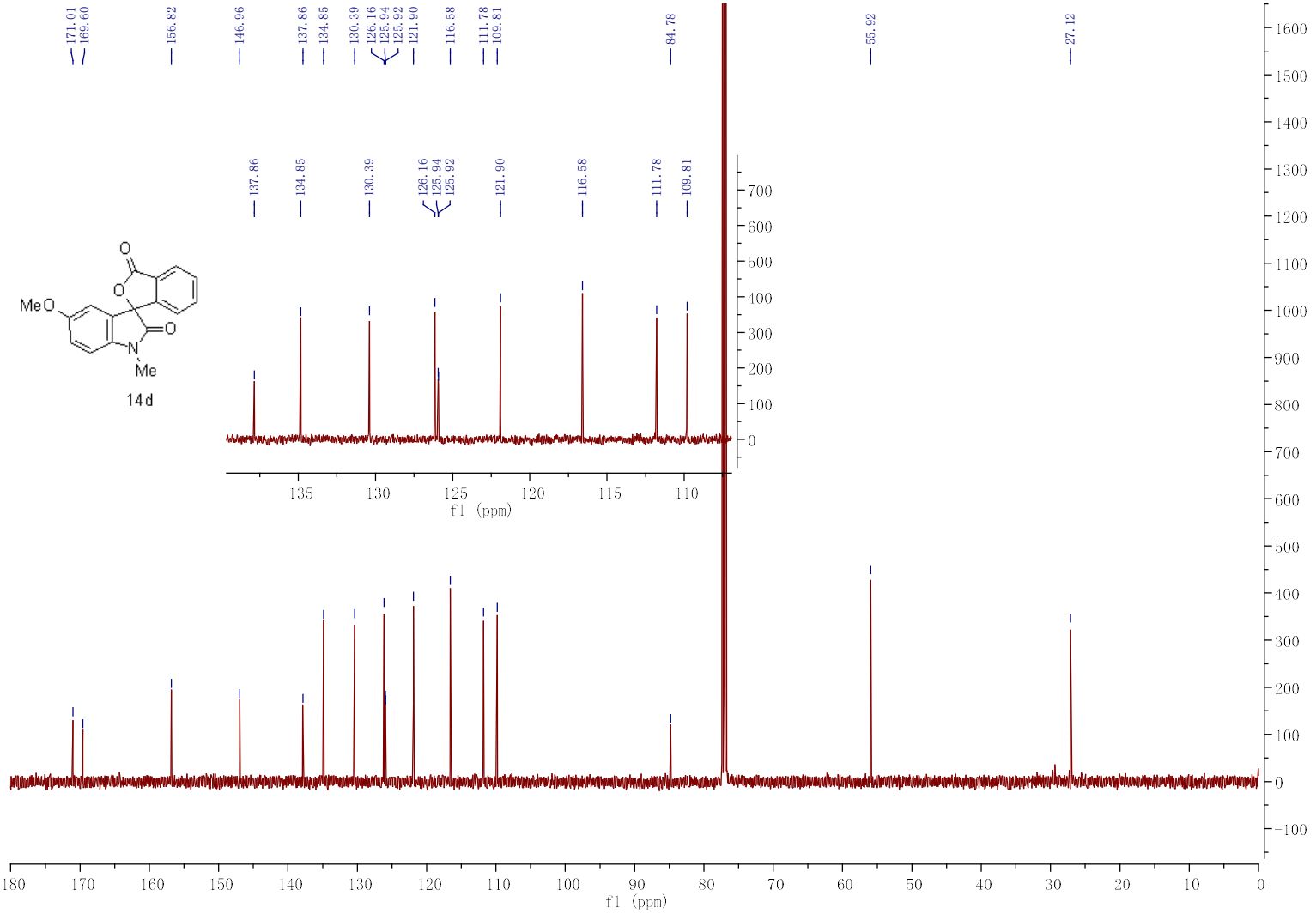
1,5,6-trimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14c):



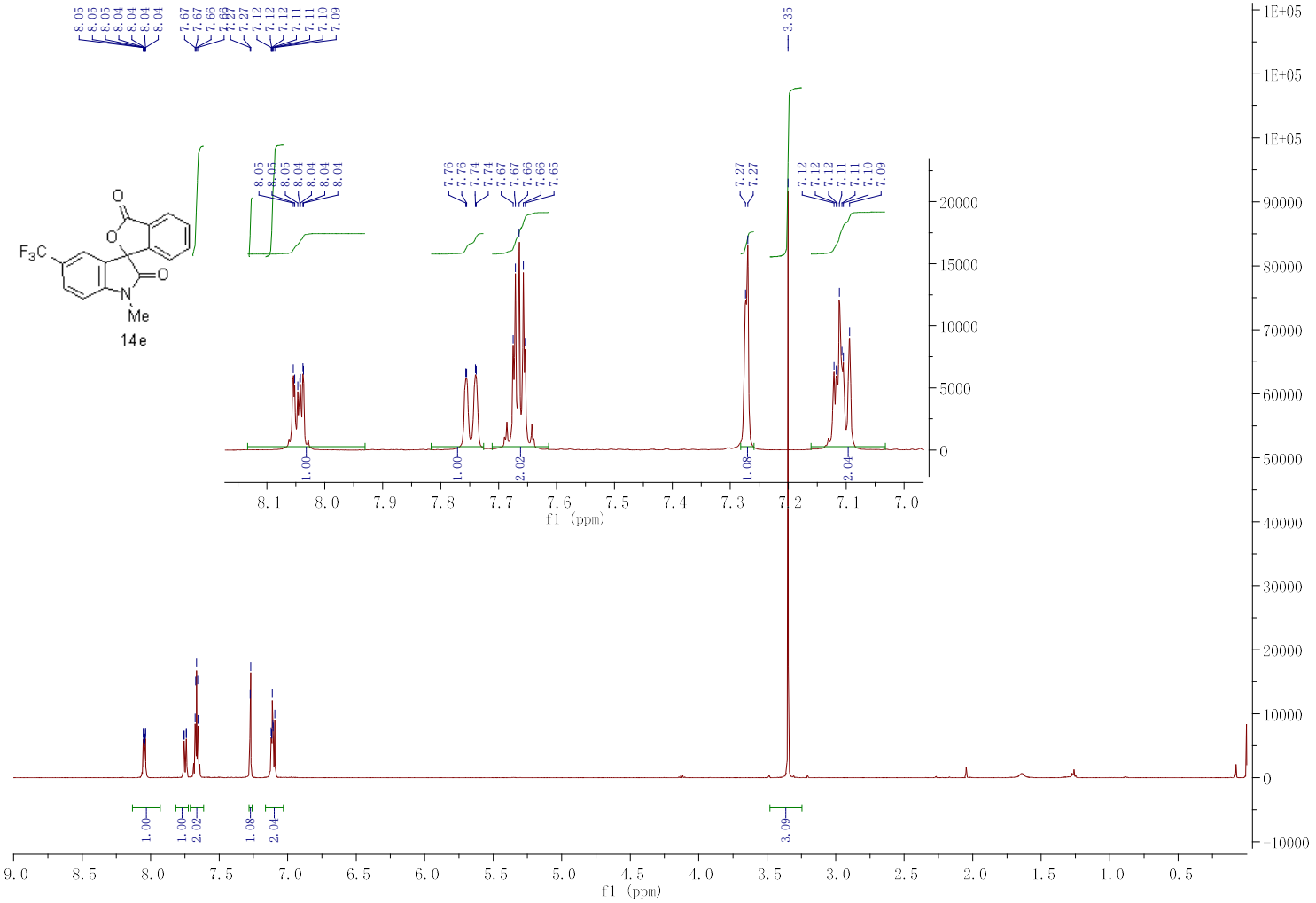

171.36
169.67
147.15
142.63
140.51
134.65
131.96
130.17
126.22
126.07
125.99
121.93
121.88
110.58
84.77
77.28
77.03
76.77
26.97
20.53
19.31
Me
Me
Me
14c

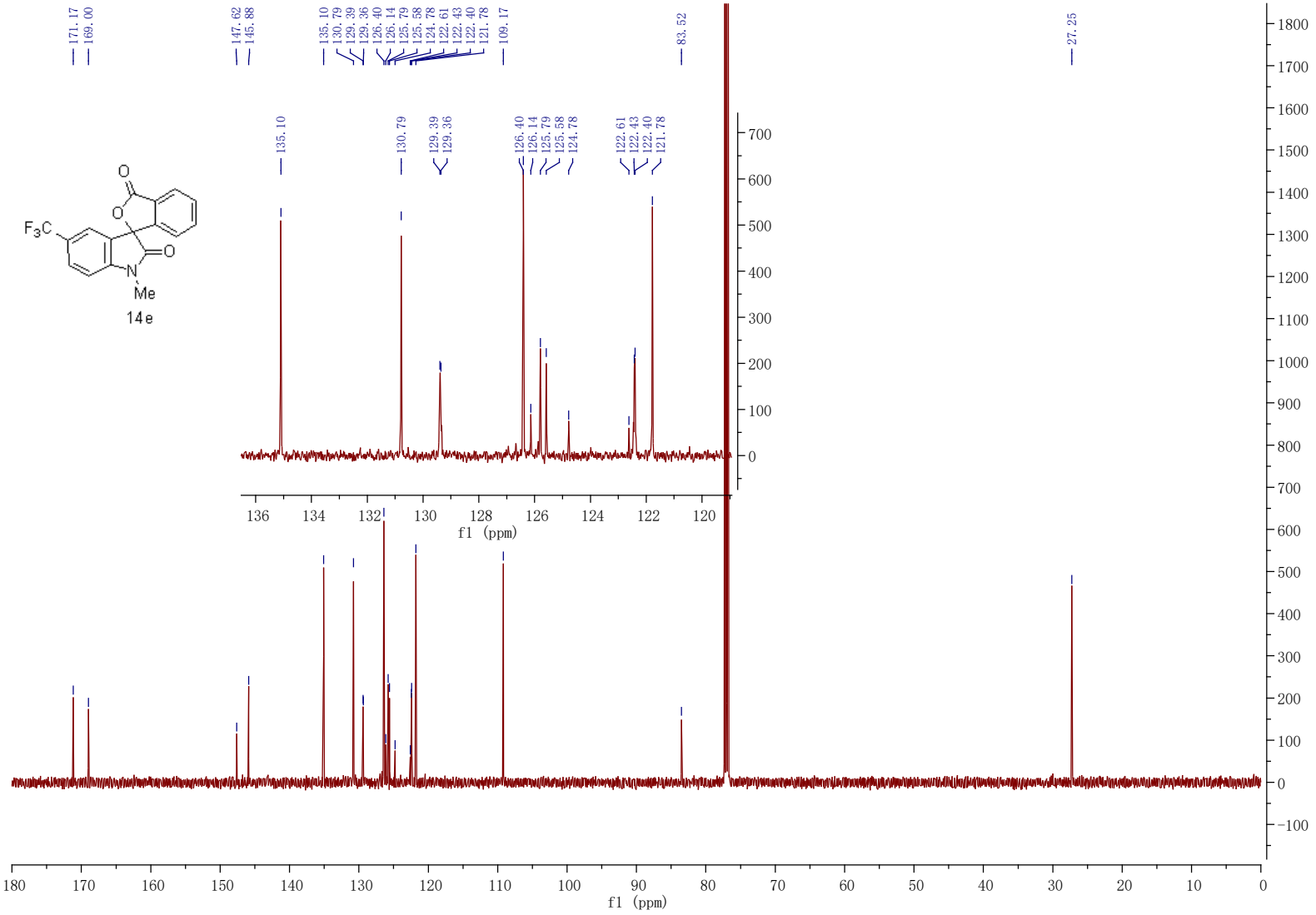
5-methoxy-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14d):



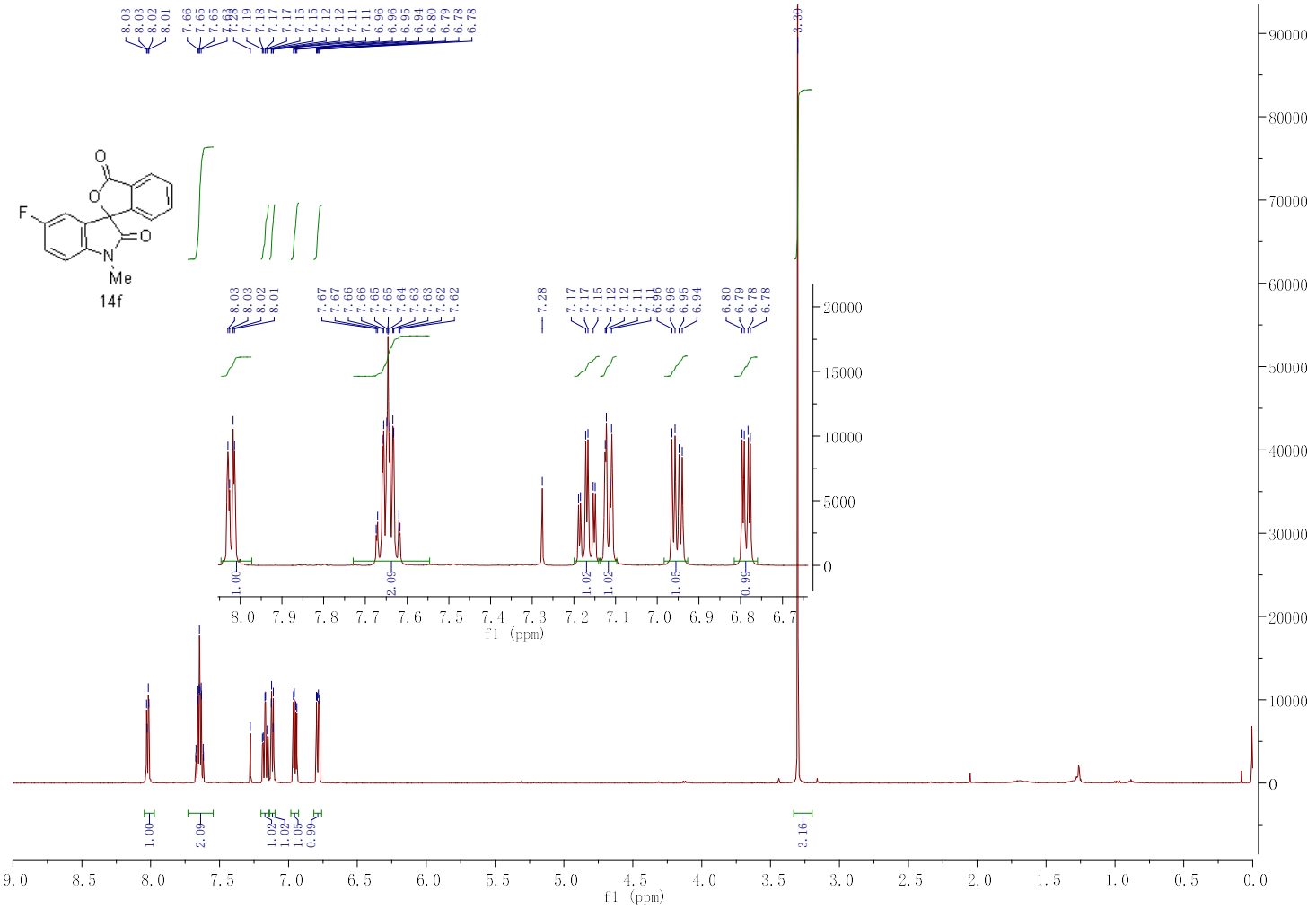

171.01
169.60
156.82
146.96
137.86
134.85
130.39
126.16
125.94
125.92
121.90
116.58
111.78
109.81
84.78
55.92
27.12
MeO
O
O
O
N
Me
14d
f1 (ppm)
f1 (ppm)

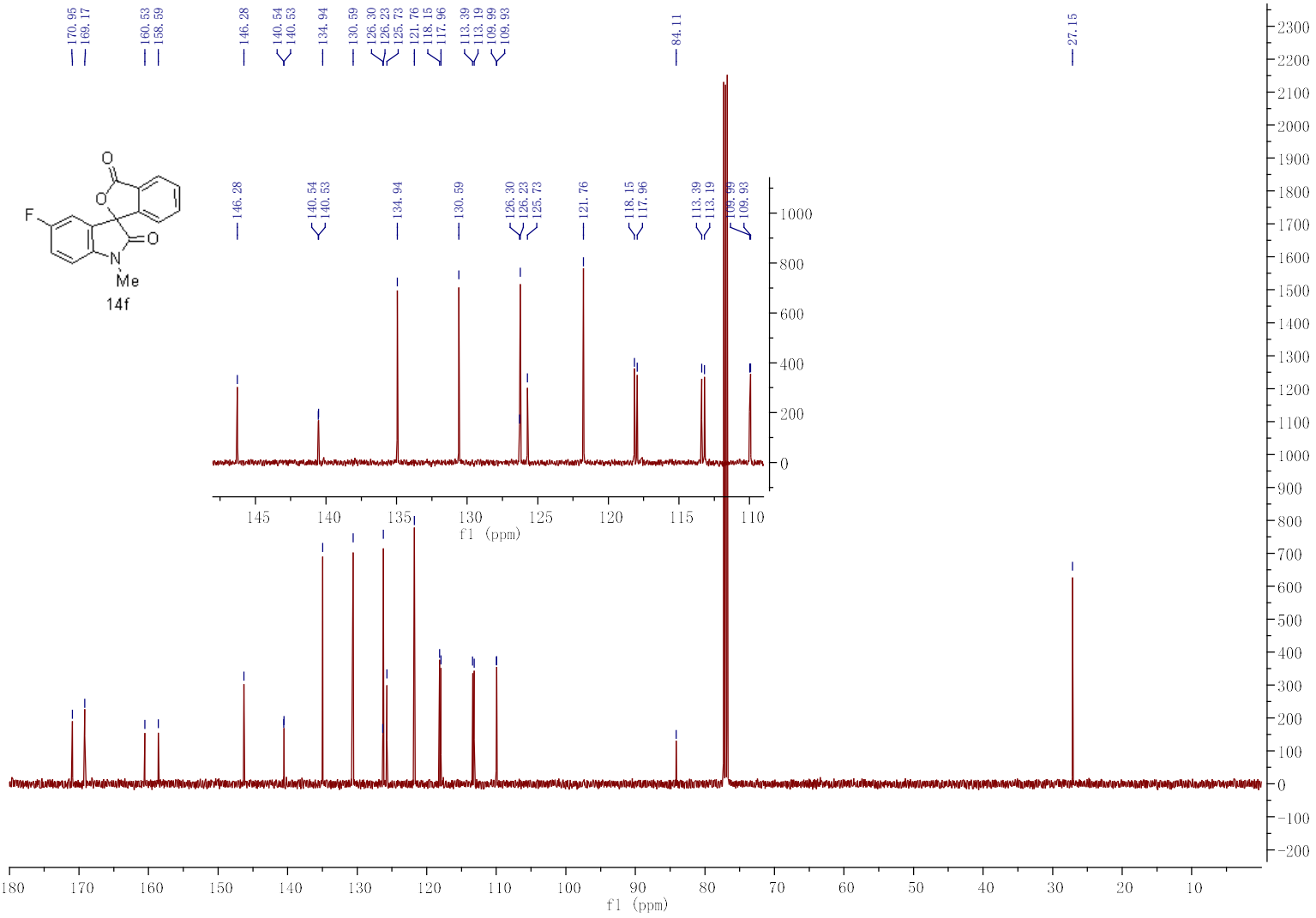
1-methyl-5-(trifluoromethyl)-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14e):



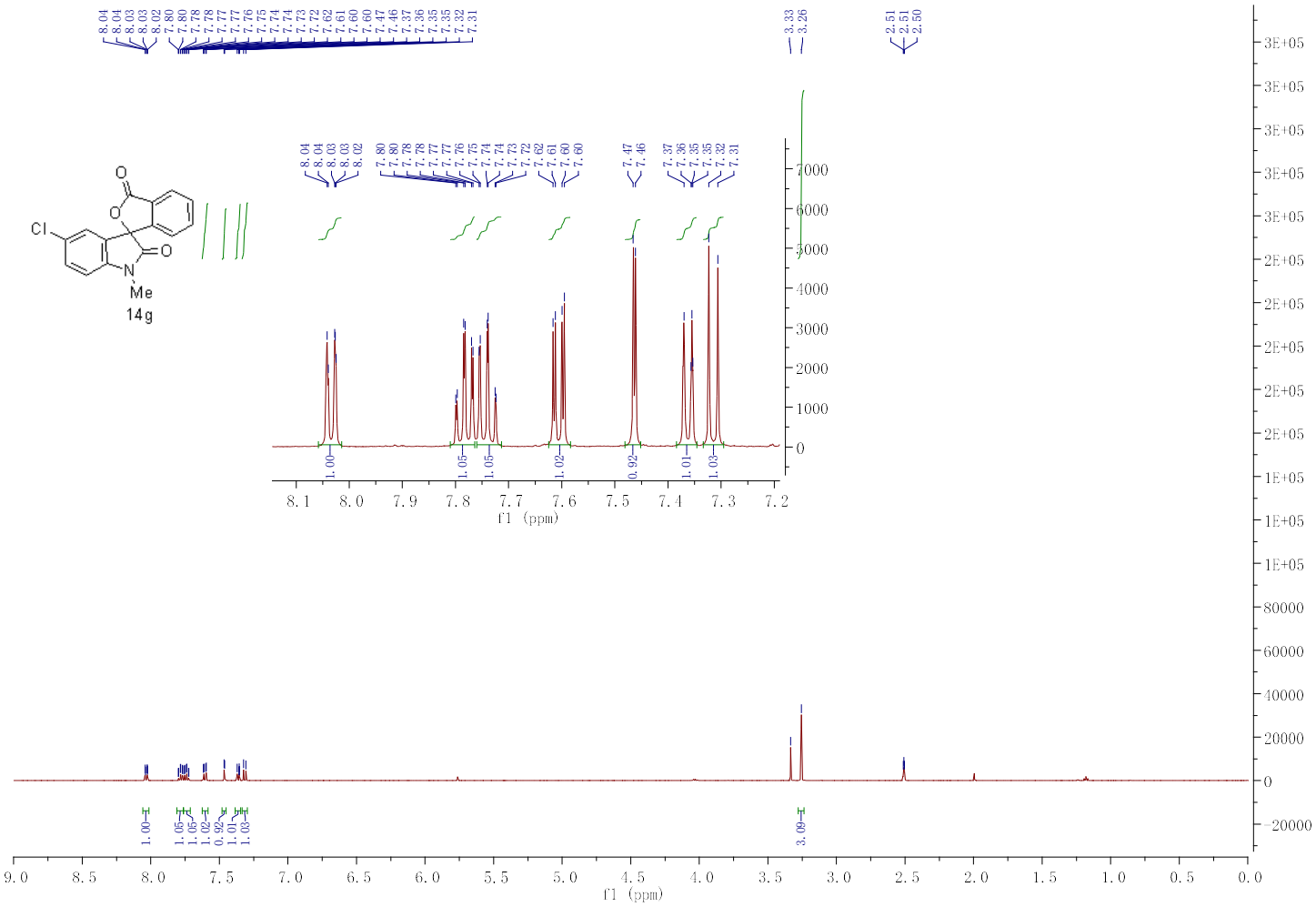

171.17
169.00
147.62
145.88
135.10
130.79
129.39
129.36
126.40
126.14
125.79
125.58
124.78
122.61
122.43
122.40
121.78
109.17
83.52
27.25
F3C
O
O
O
N
Me
14e
f1 (ppm)
f1 (ppm)

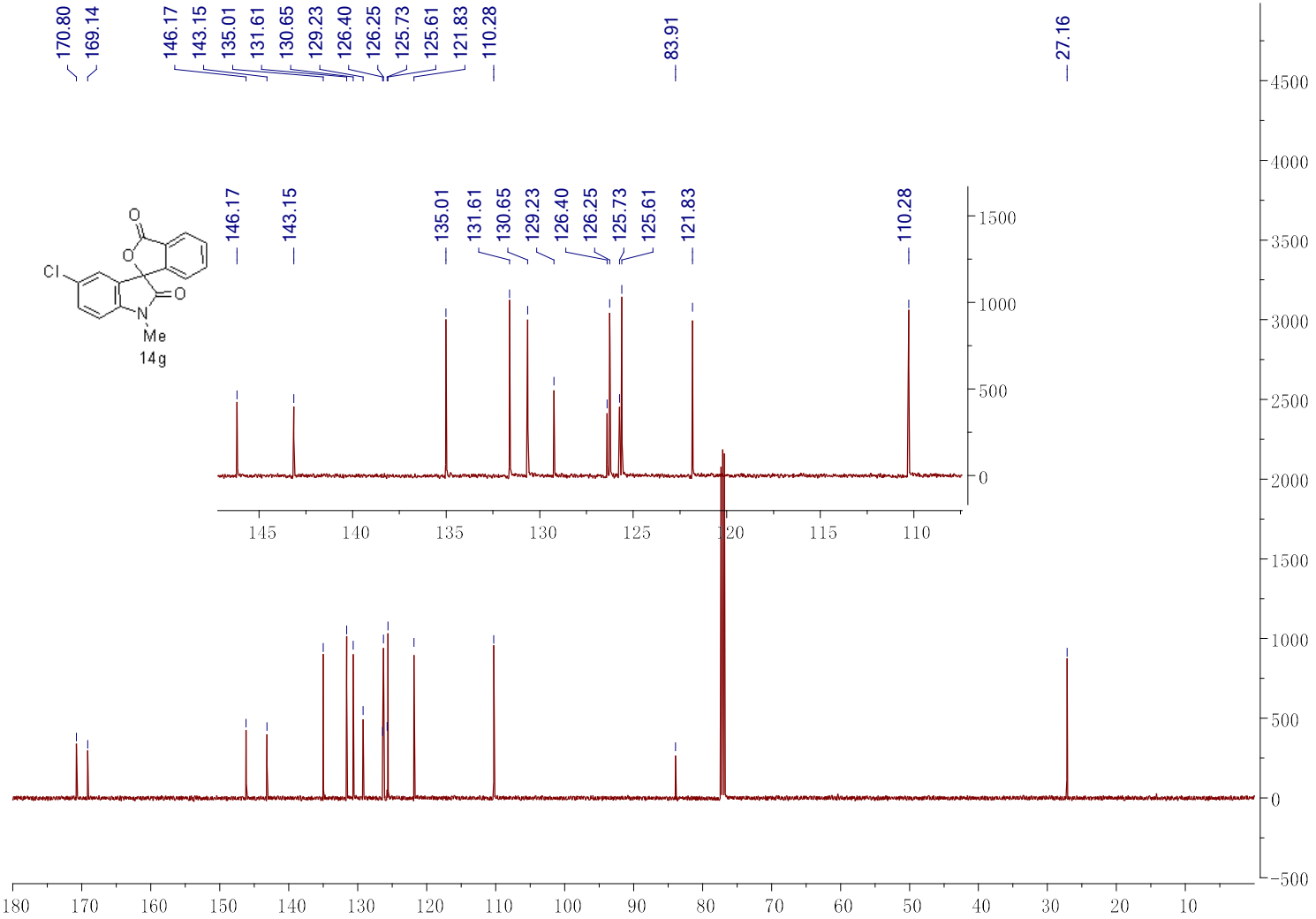
5-fluoro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14f):



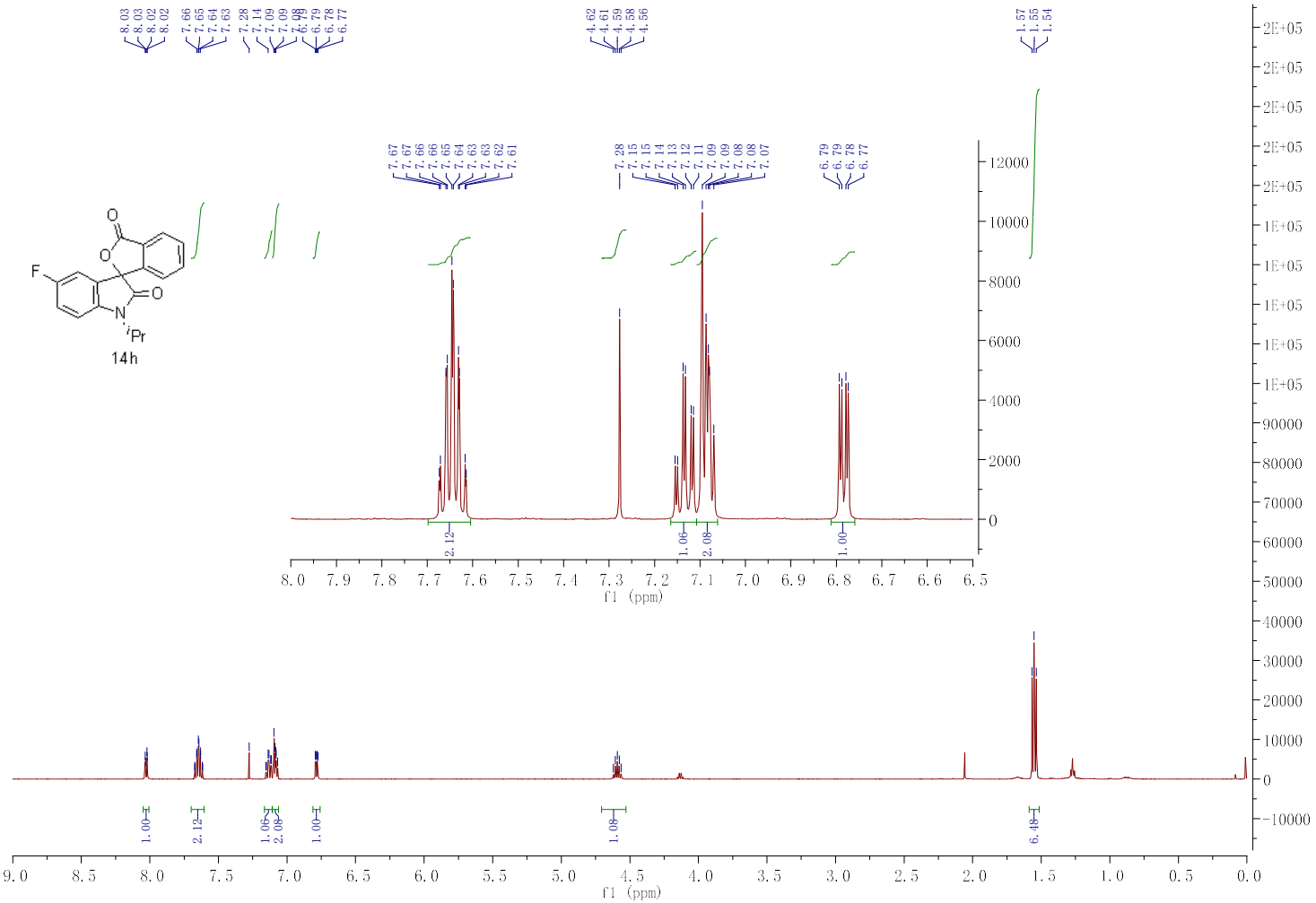

170.95
169.17
160.53
158.59
146.28
140.54
140.53
134.94
130.59
126.30
126.23
125.73
121.76
118.15
117.96
113.39
113.19
109.99
109.93
84.11
27.15
F
O
O
O
N
Me
14f
f1 (ppm)
f1 (ppm)

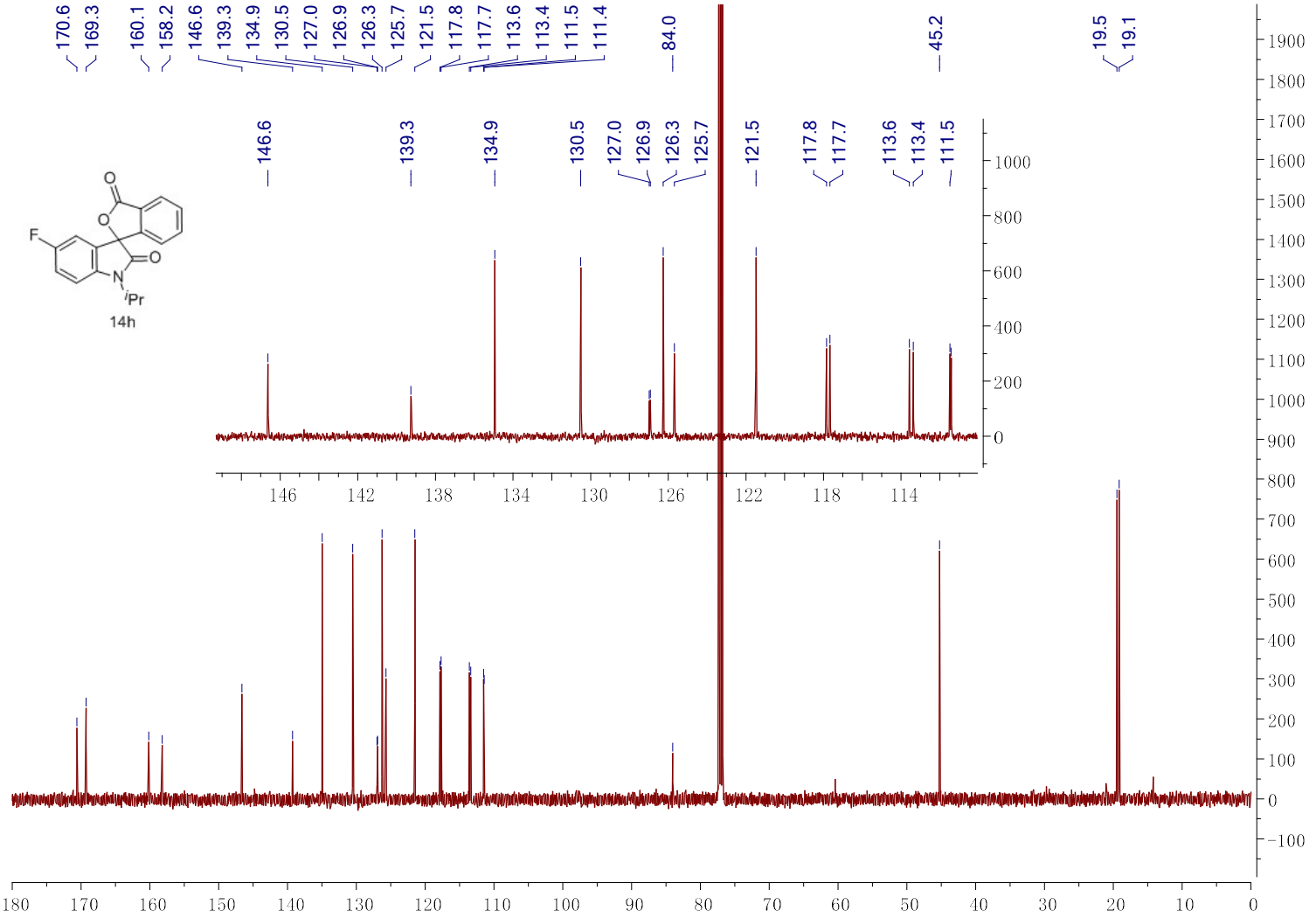
5-chloro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14g):



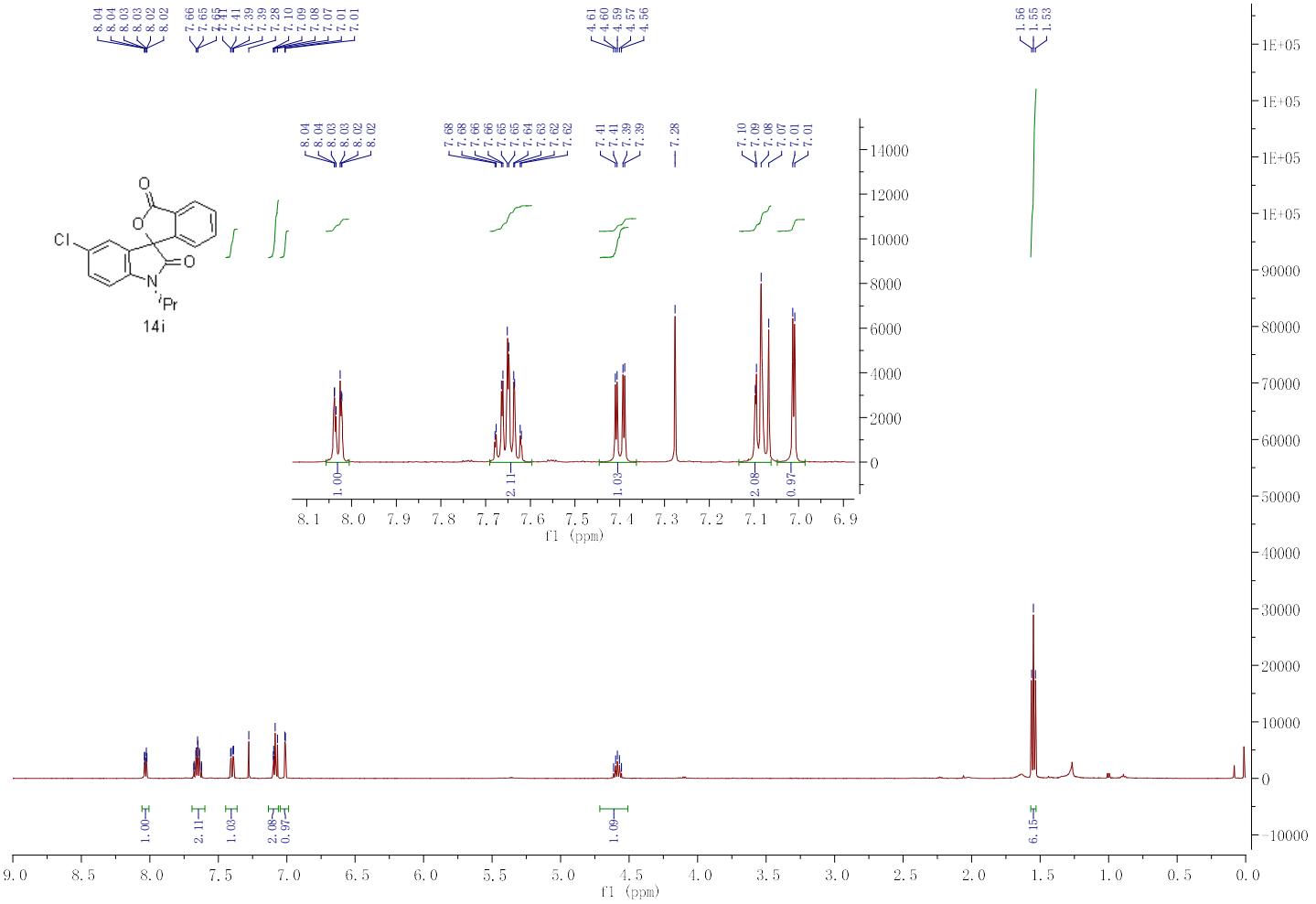

170.80
169.14
146.17
143.15
135.01
131.61
130.65
129.23
126.40
126.25
125.73
125.61
121.83
110.28
83.91
27.16
Cl
O
O
O
N
Me
14g

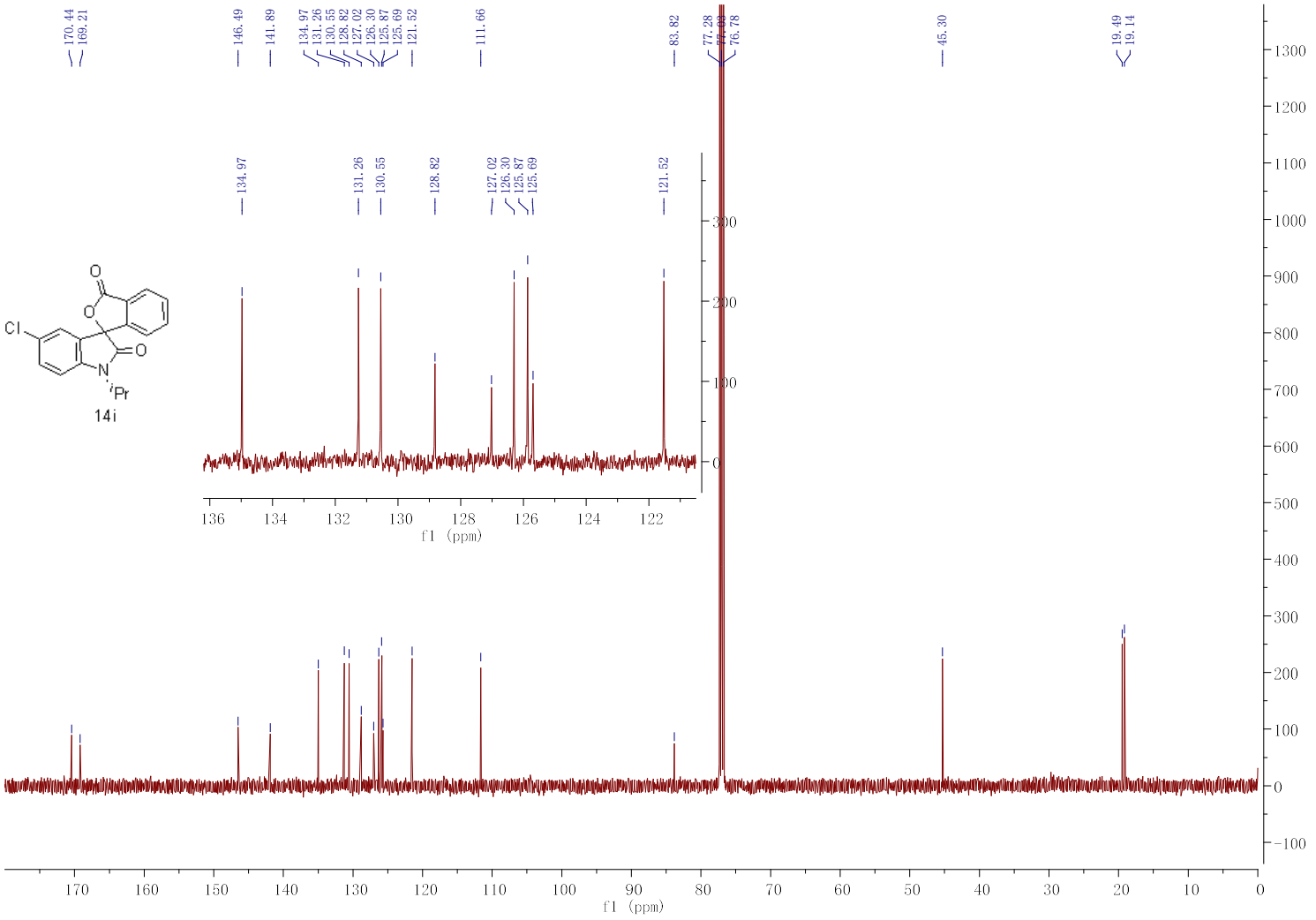
5-fluoro-1-isopropyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14h):



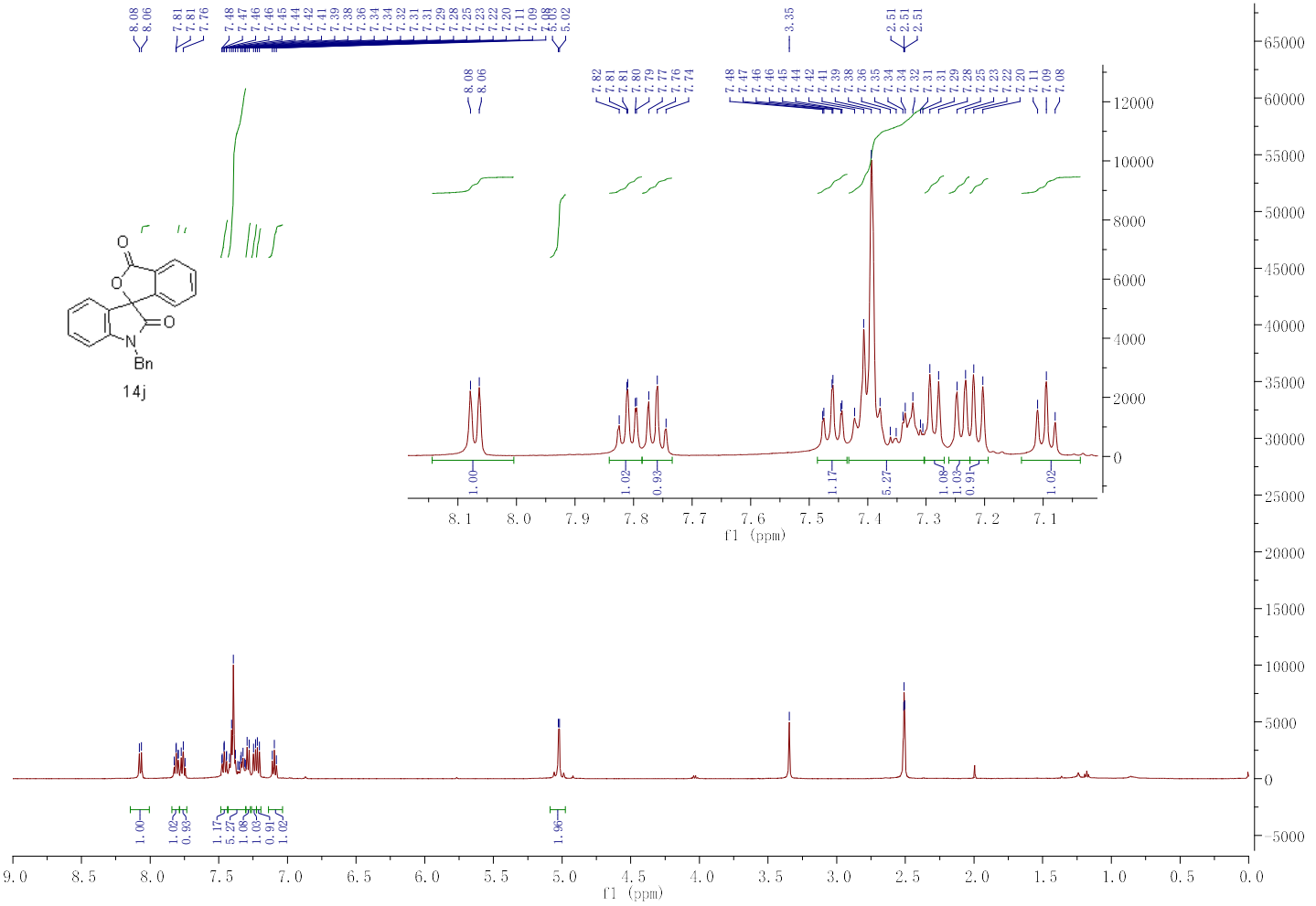

170.6
169.3
160.1
158.2
146.6
139.3
134.9
130.5
127.0
126.9
126.3
125.7
121.5
117.8
117.7
113.6
113.4
111.5
111.4
84.0
45.2
19.5
19.1
F
O
O
O
N
iPr
14h

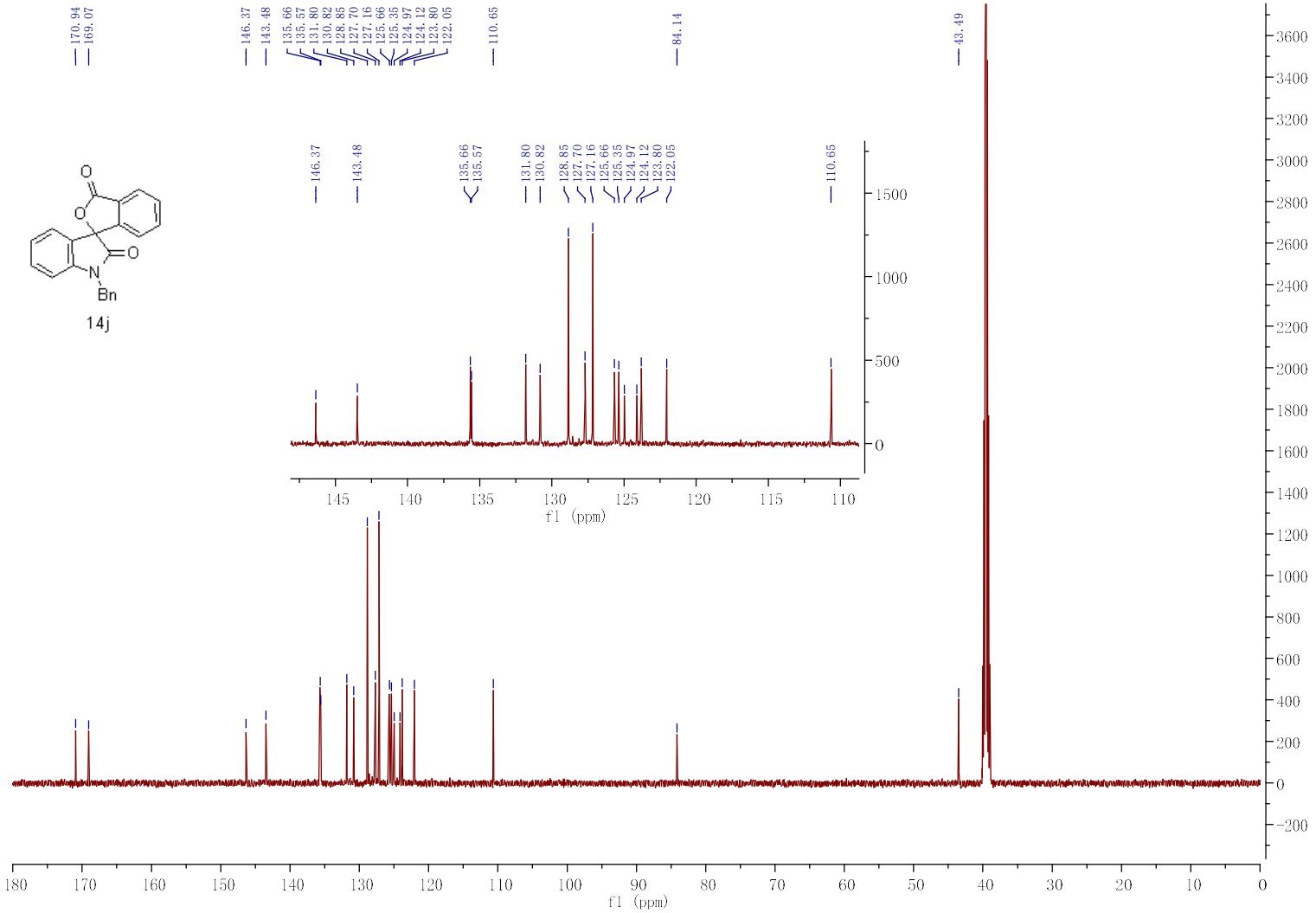
5-chloro-1-isopropyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14i):



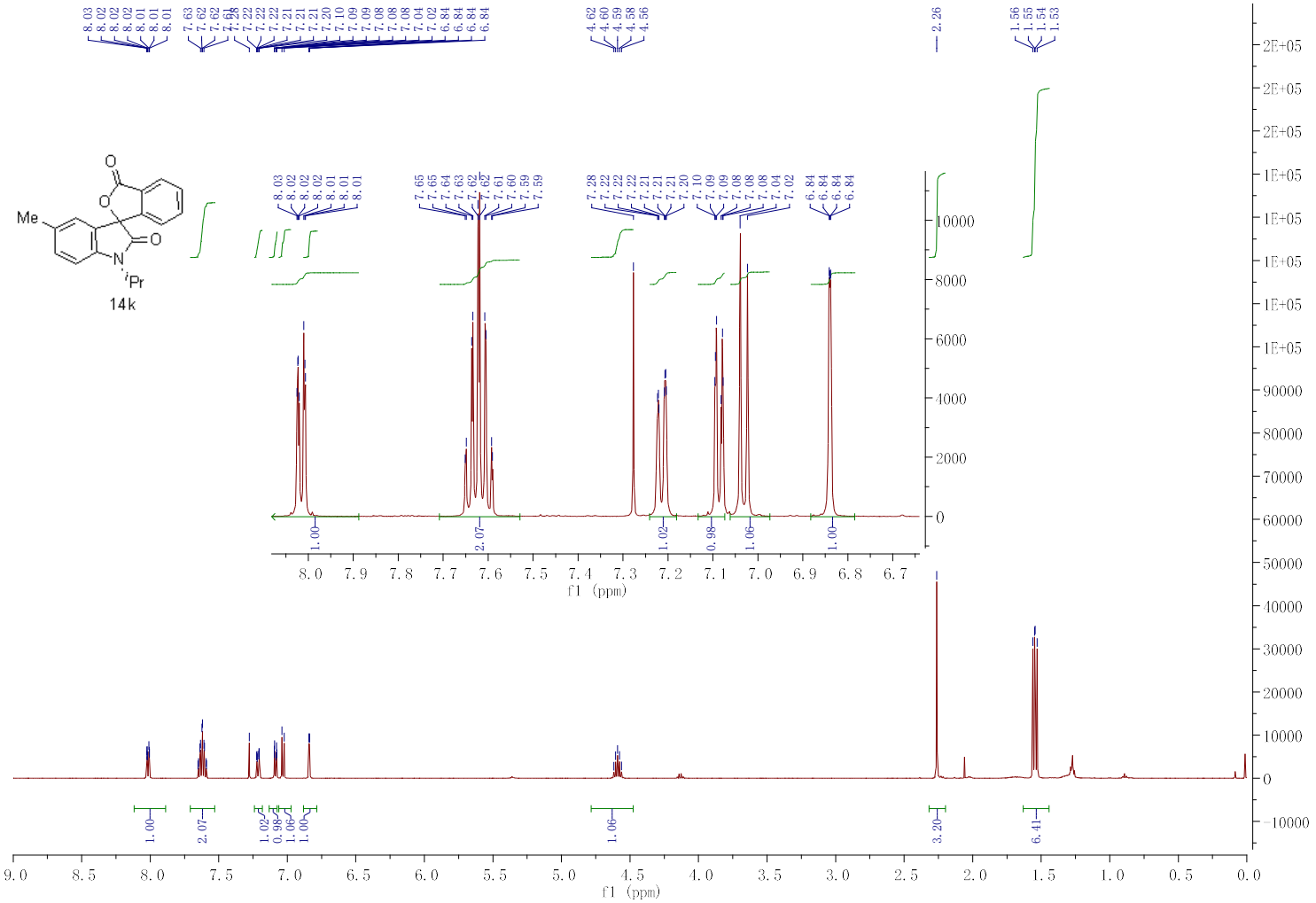

170.44
169.21
146.49
141.89
134.97
131.26
130.55
128.82
127.02
126.30
125.87
125.69
121.52
111.66
83.82
77.28
77.00
76.78
45.30
19.49
19.14
Cl
O
O
O
N
iPr
14i
f1 (ppm)
f1 (ppm)

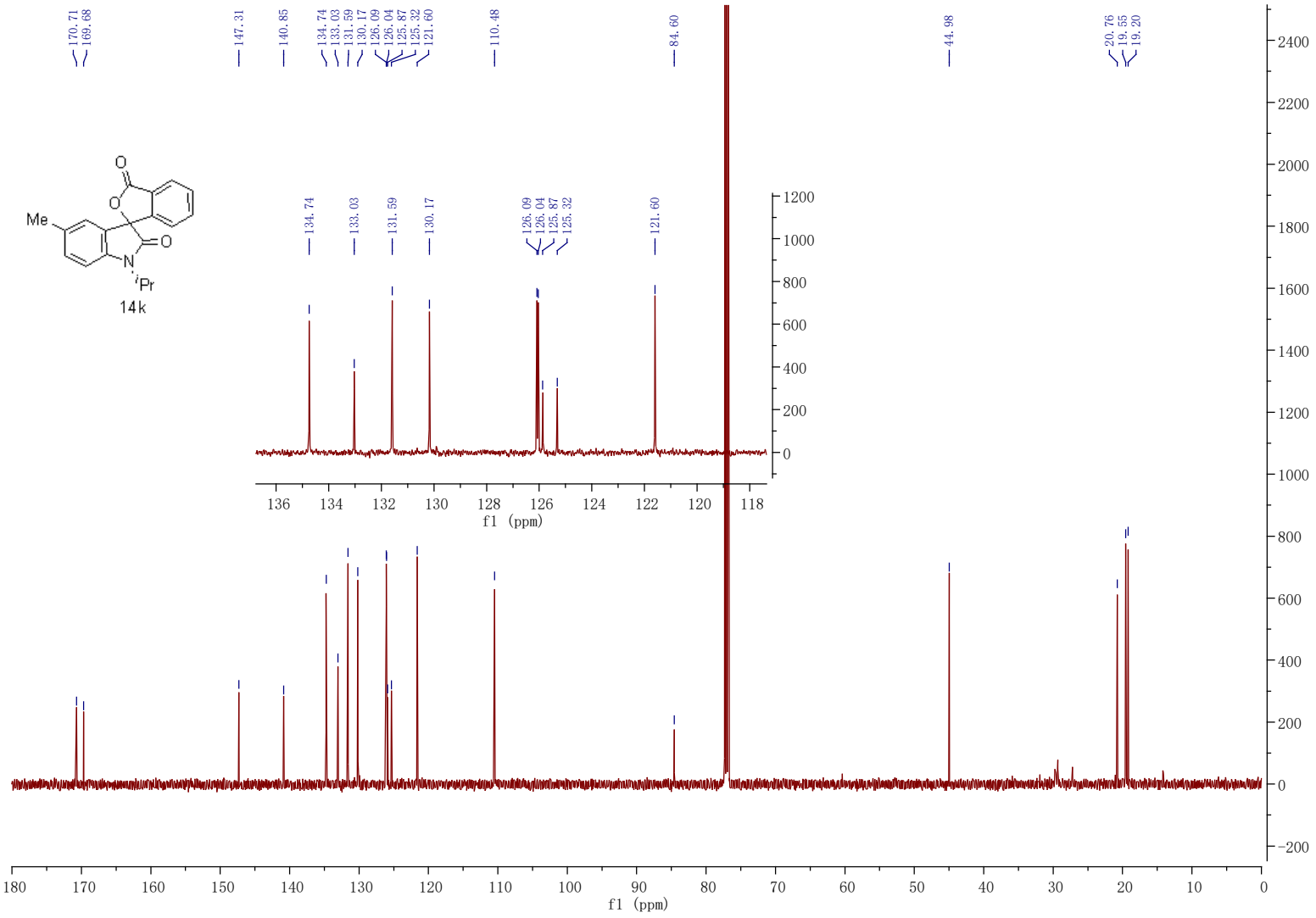
1-benzyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14j):



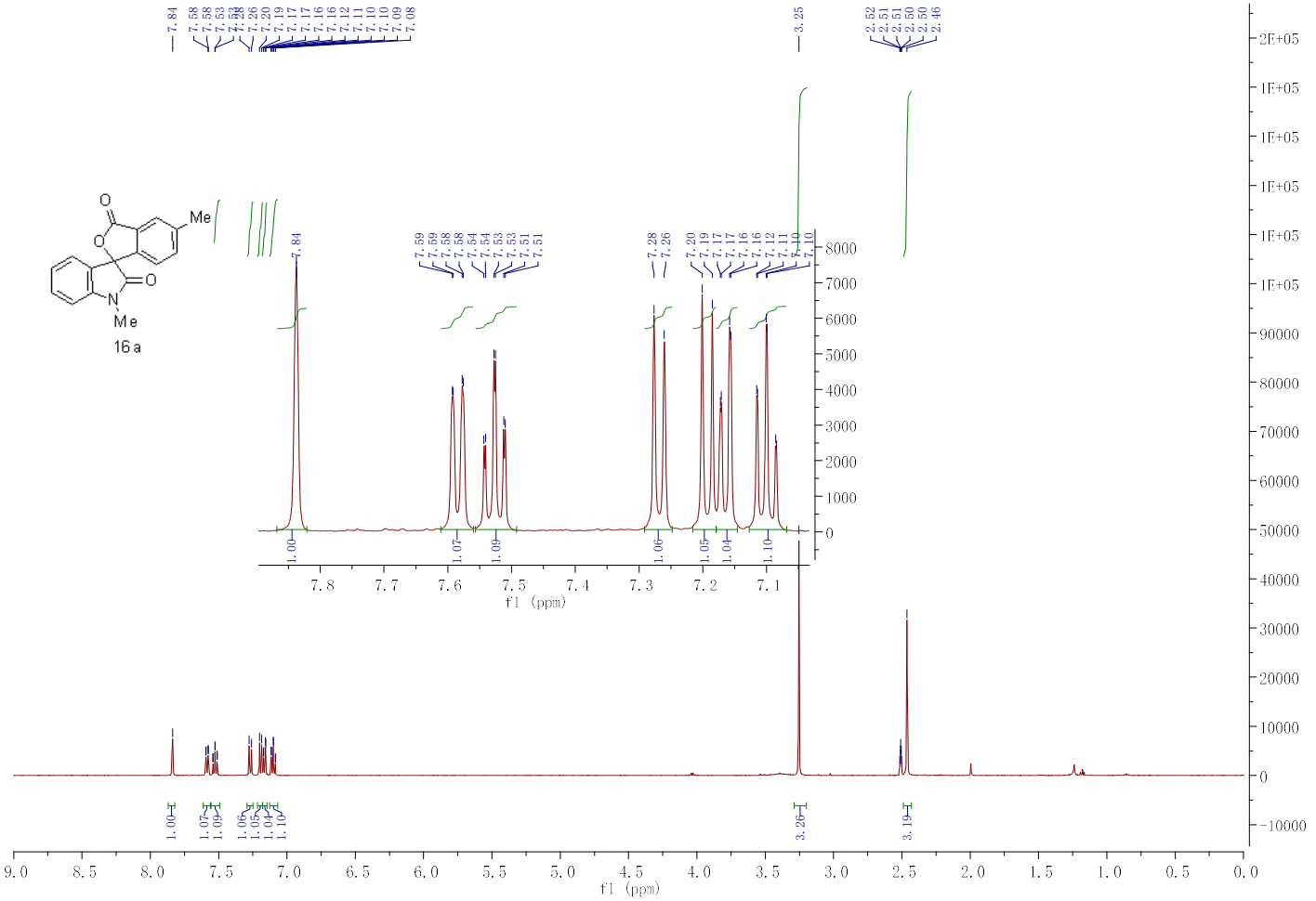

170.94
169.07
146.37
143.48
135.66
135.57
131.80
130.82
128.85
127.70
127.16
125.66
125.35
124.97
124.12
123.80
122.05
110.65
84.14
43.49
O
O
O
N
Bn
14j
f1 (ppm)
f1 (ppm)

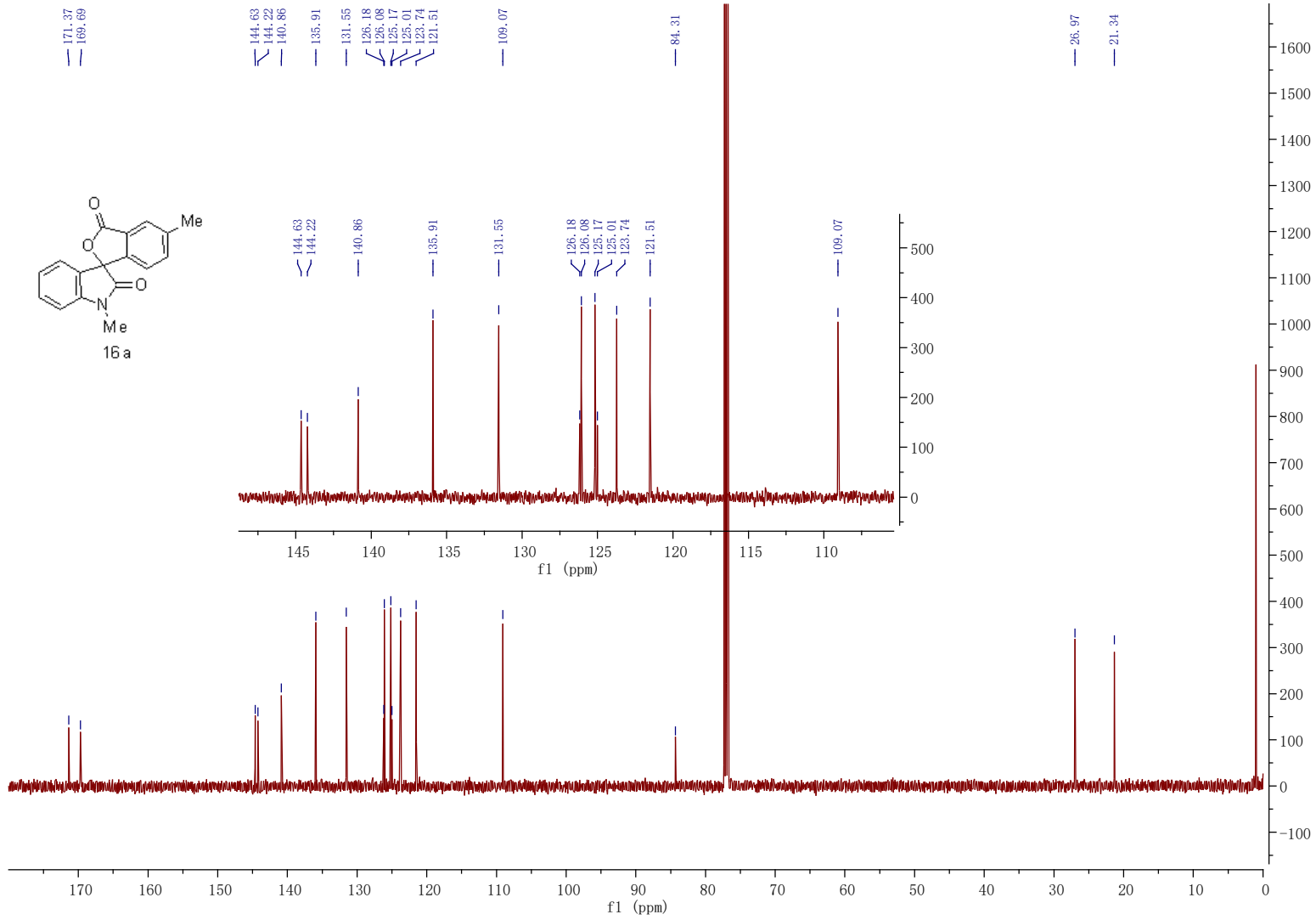
1-isopropyl-5-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (14k):



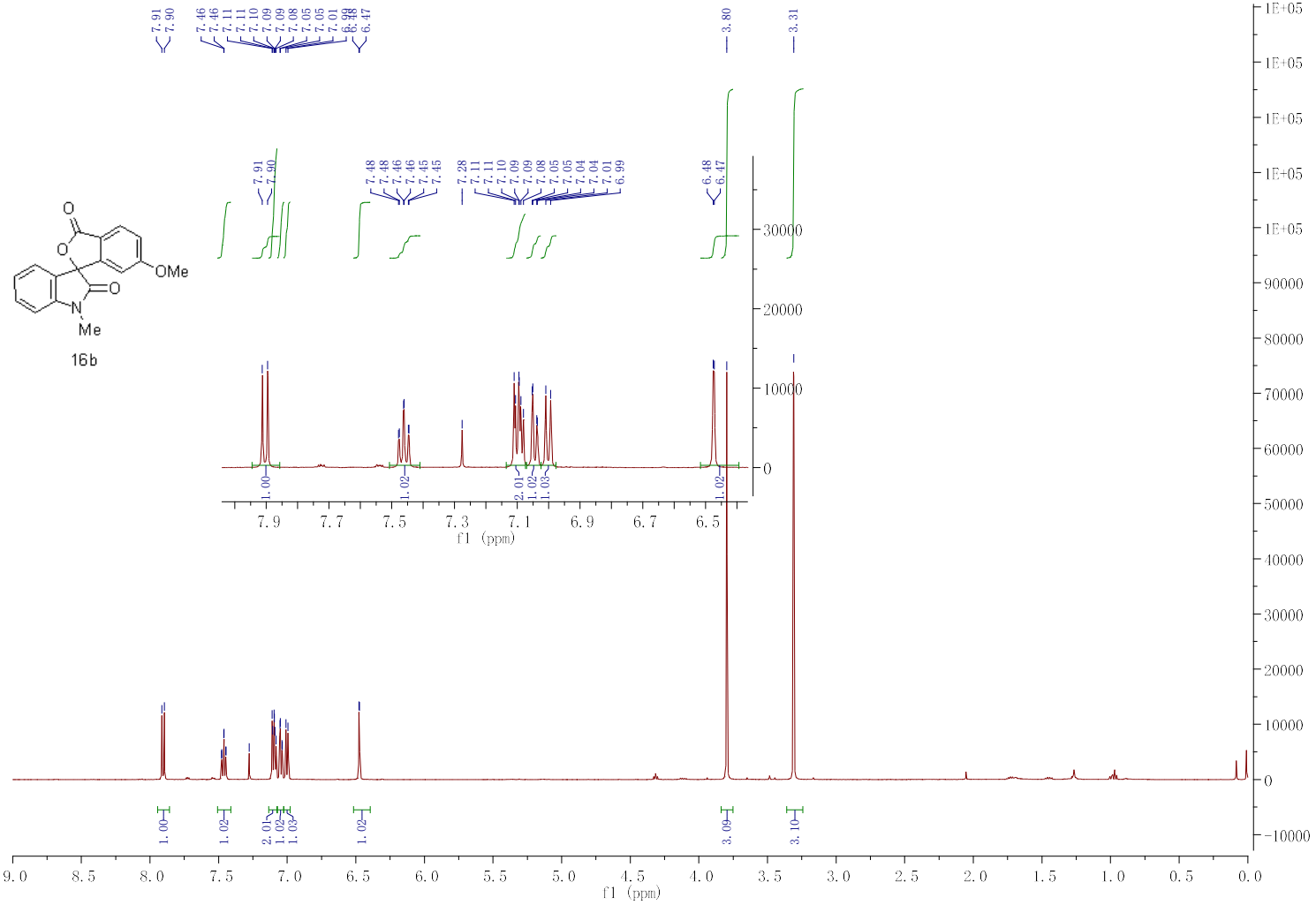

170.71
169.68
147.31
140.85
134.74
133.03
131.59
130.17
126.09
126.04
125.87
125.32
121.60
110.48
84.60
44.98
20.76
19.55
19.20
Me
O
O
O
N
iPr
14k
f1 (ppm)
f1 (ppm)

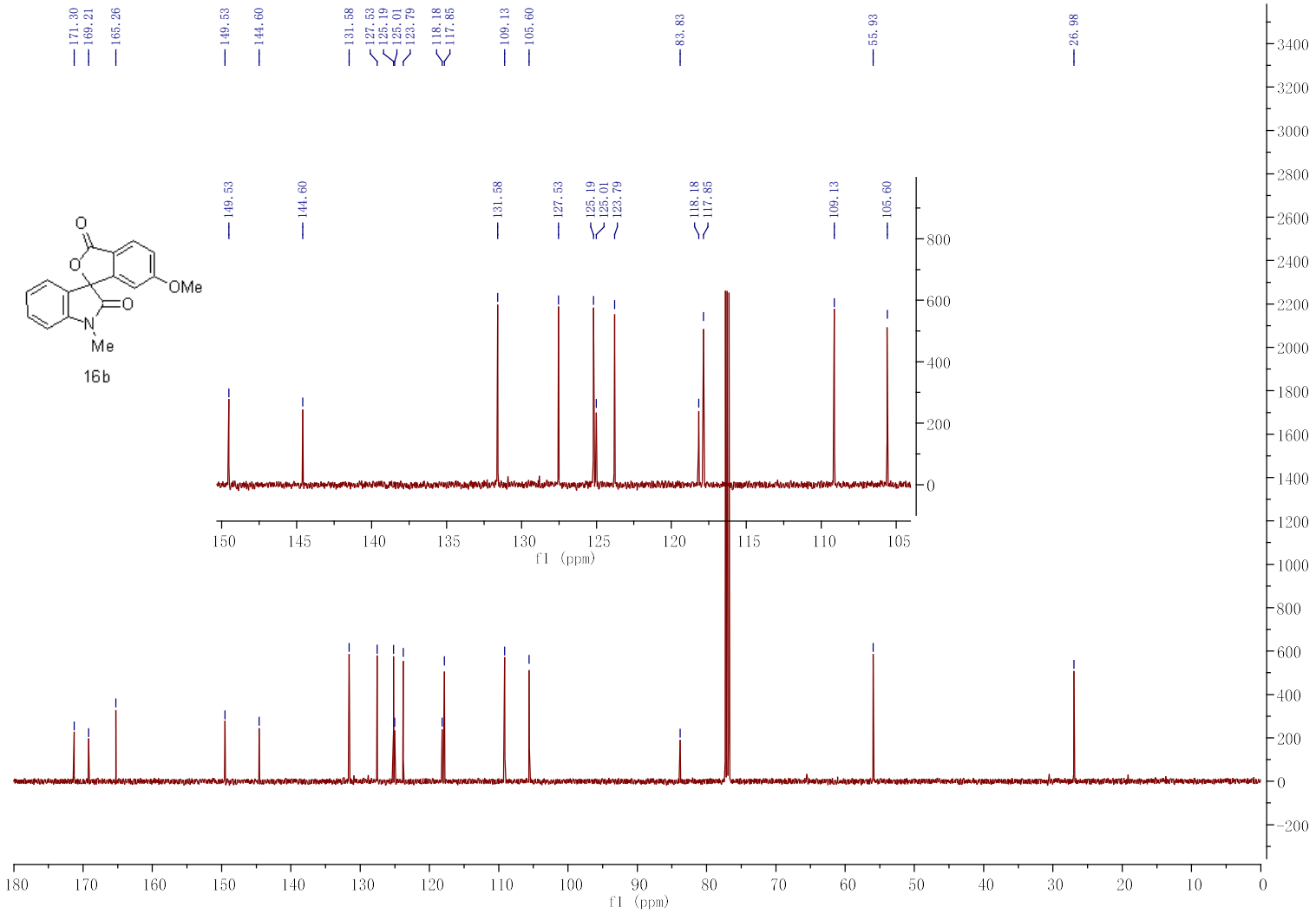
1,5'-dimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16a):



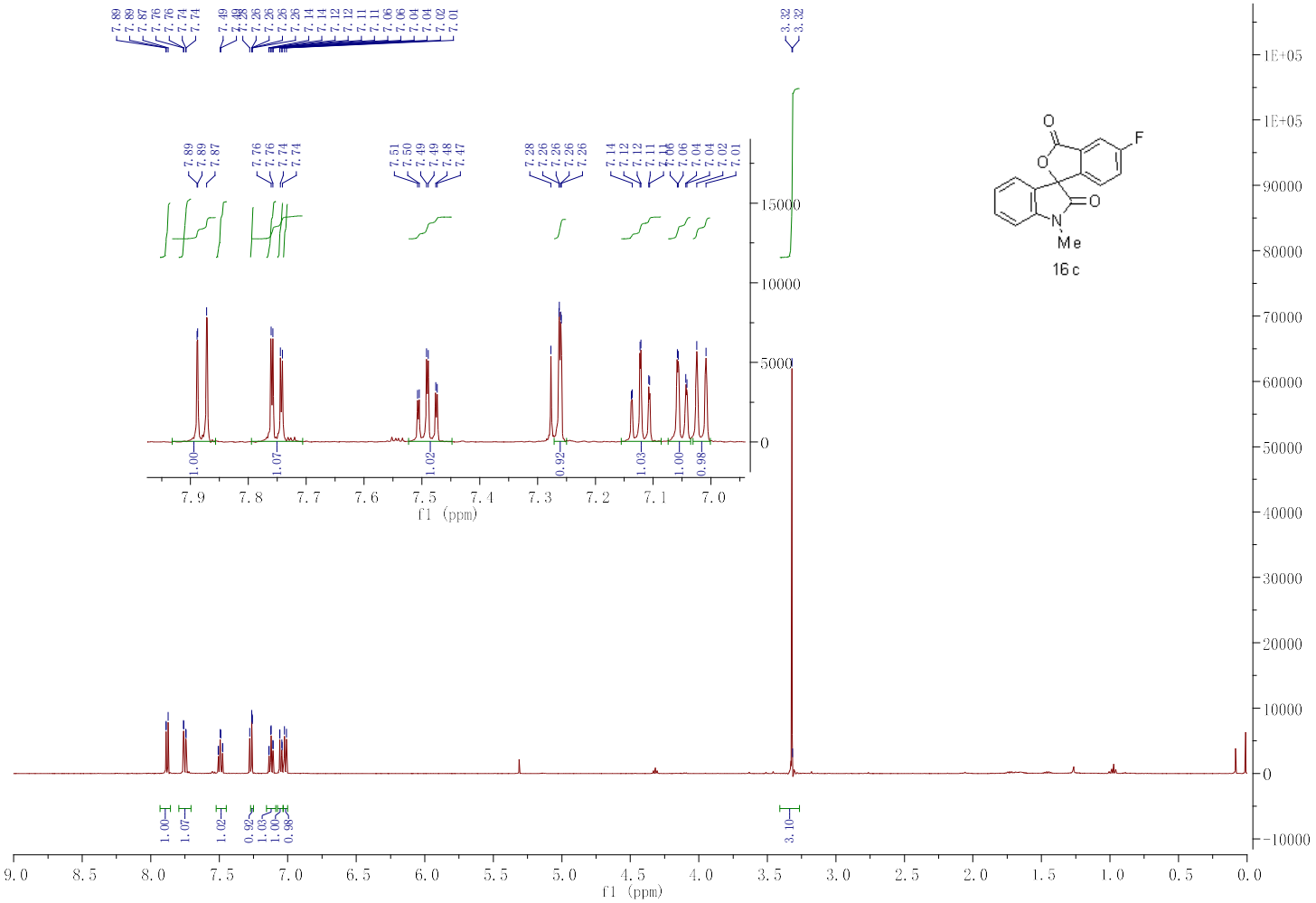

171.37
169.69
144.63
144.22
140.86
135.91
131.55
126.18
126.08
125.17
125.01
123.74
121.51
109.07
84.31
26.97
21.34
O
O
Me
O
N
Me
16a
f1 (ppm)
f1 (ppm)

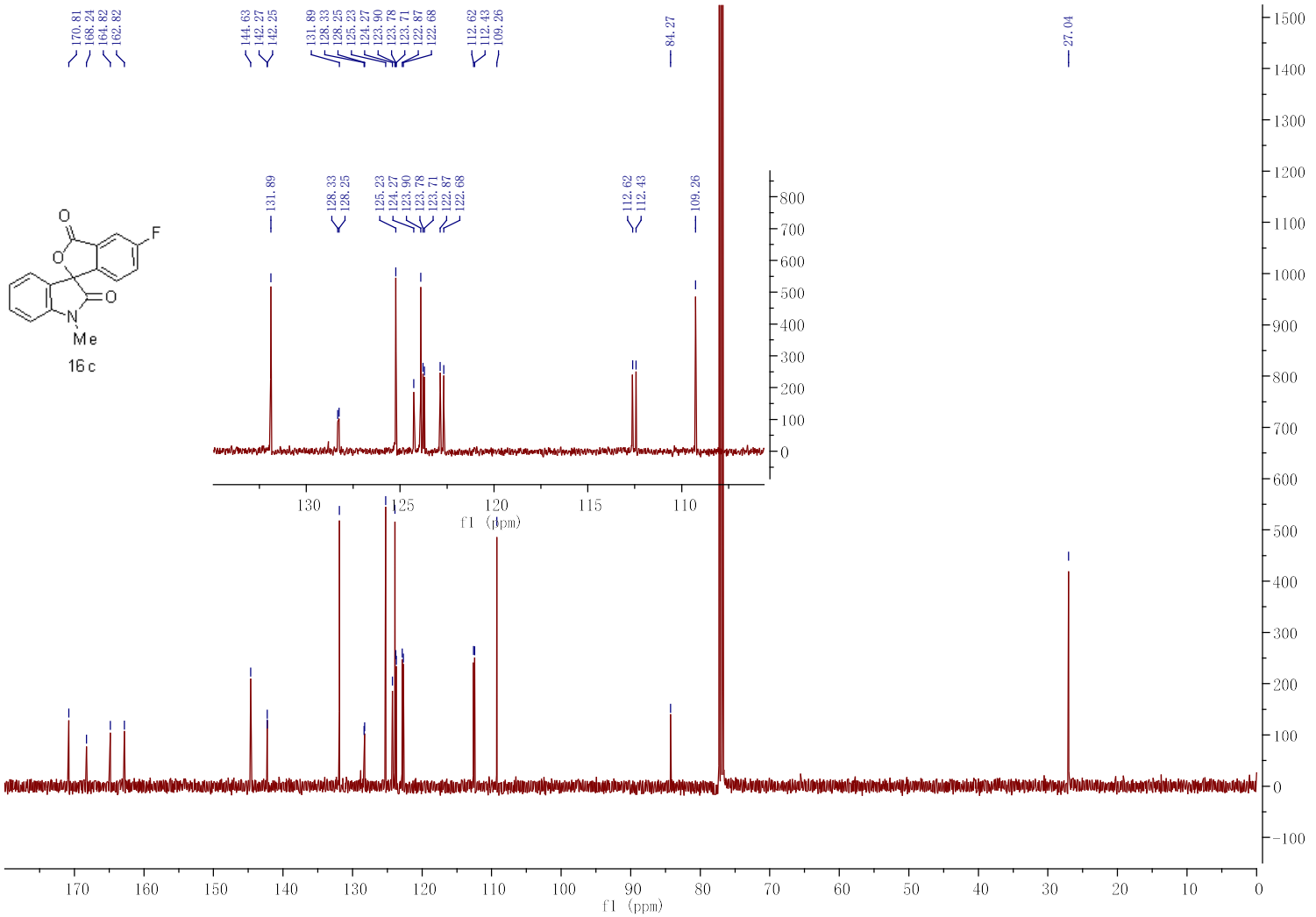
6'-methoxy-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16b):



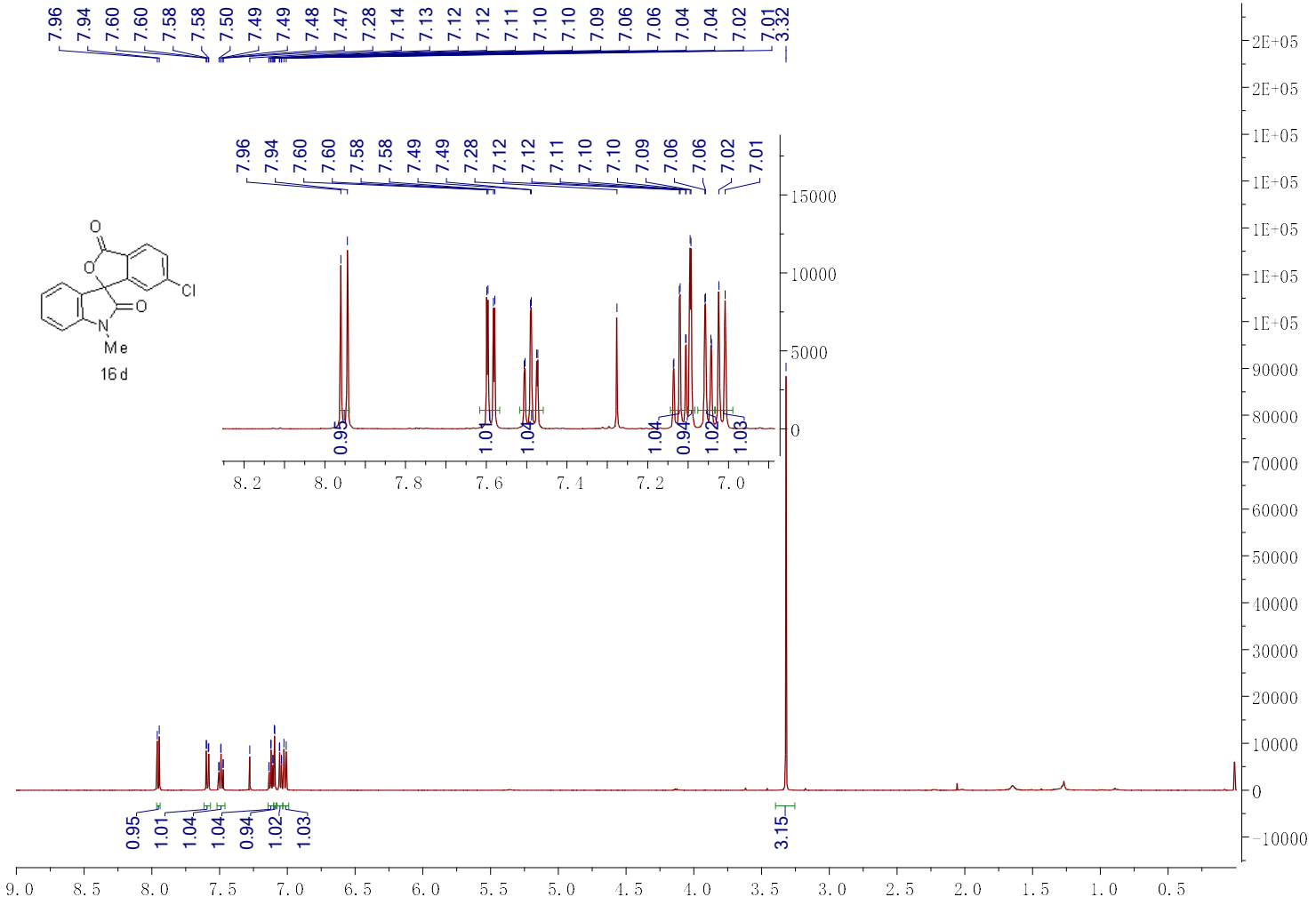

171.30
169.21
165.26
149.53
144.60
131.58
127.53
125.19
125.01
123.79
118.18
117.85
109.13
105.60
83.83
55.93
26.98
O
O
O
N
Me
OMe
16b
f1 (ppm)
f1 (ppm)

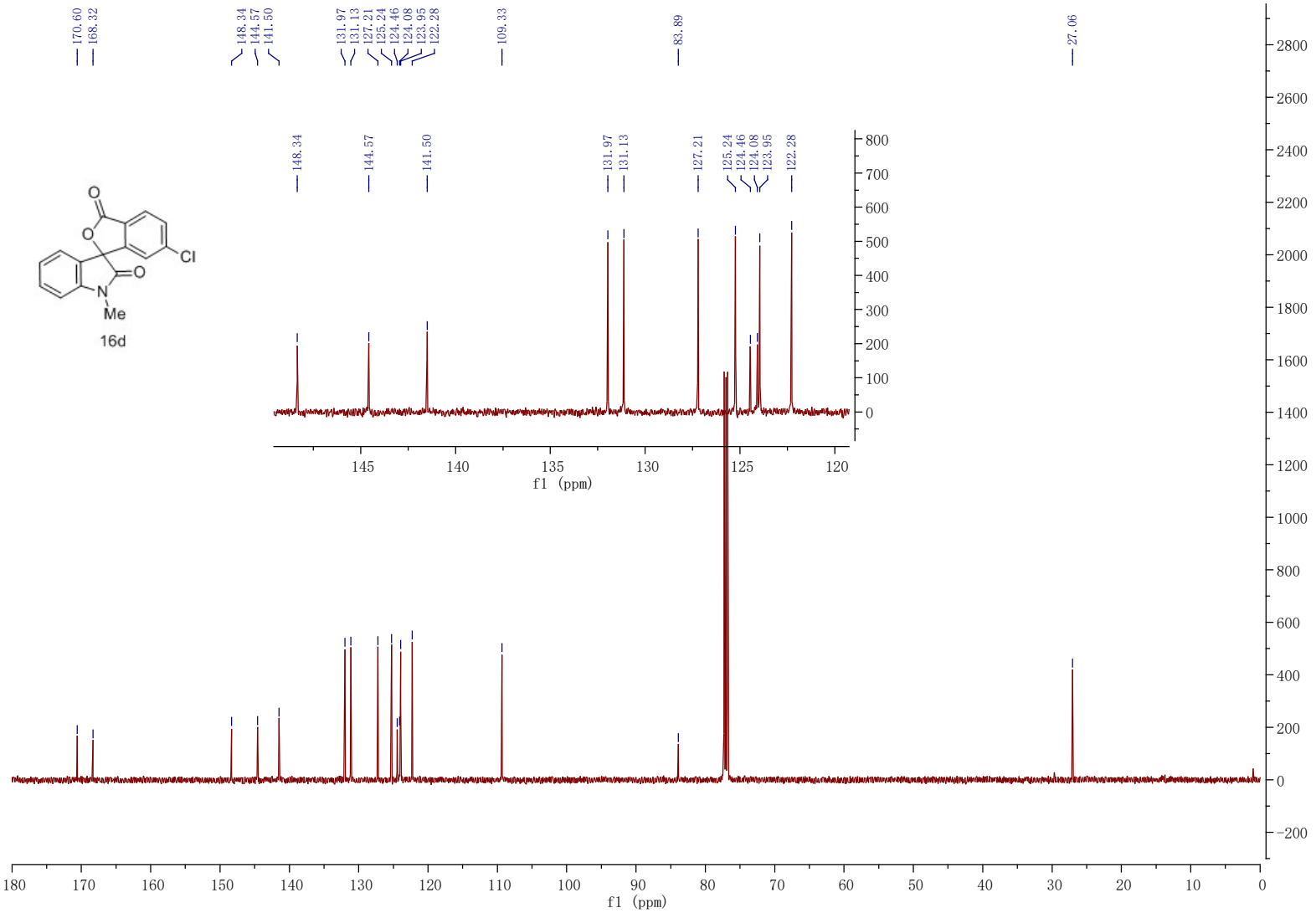
5'-fluoro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16c):



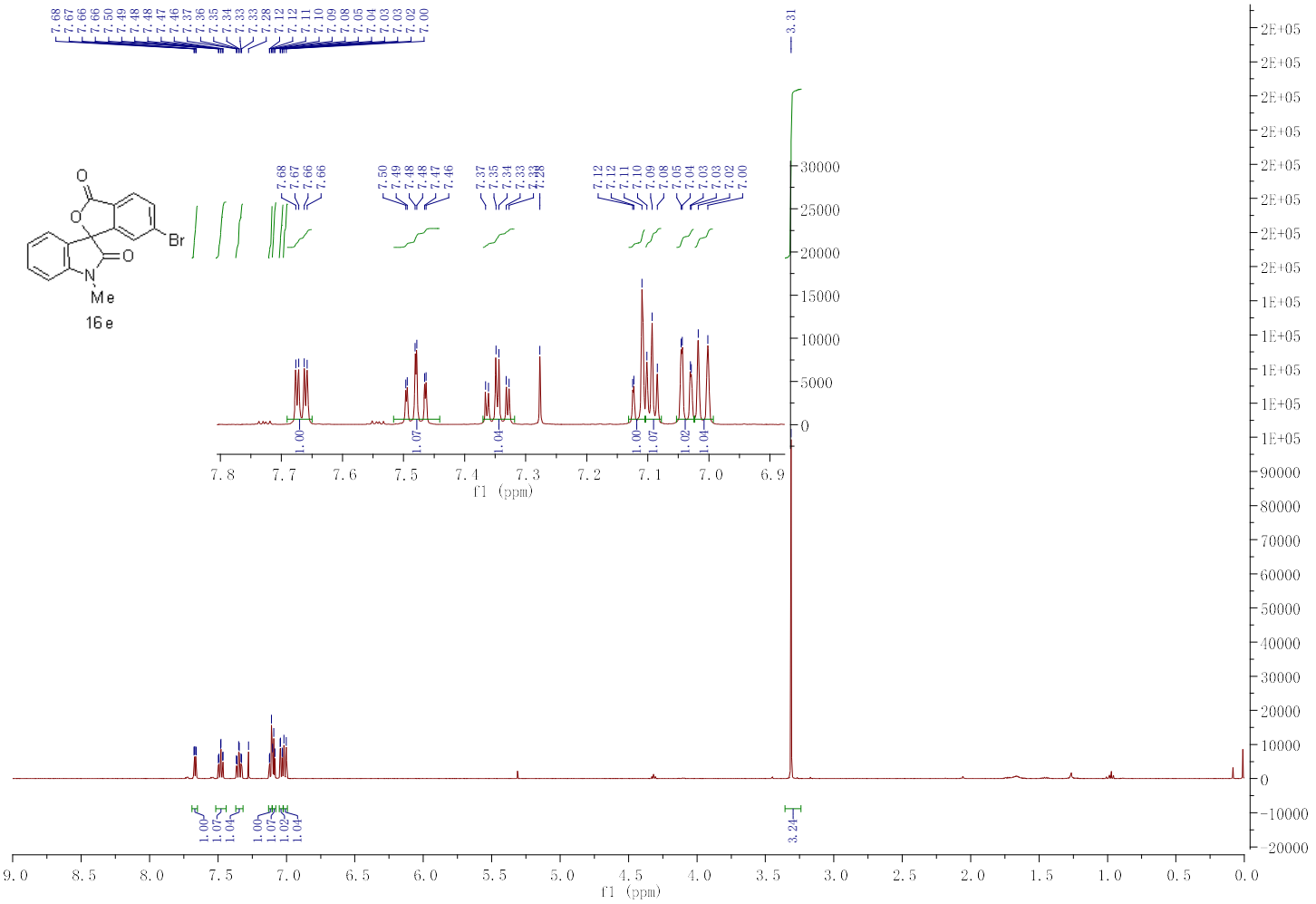

170.81
168.24
164.82
162.82
144.63
142.27
142.25
131.89
128.33
128.25
125.23
124.27
123.90
123.78
123.71
122.87
122.68
112.62
112.43
109.26
84.27
27.04
O
O
F
O
N
Me
16c
f1 (ppm)
f1 (ppm)

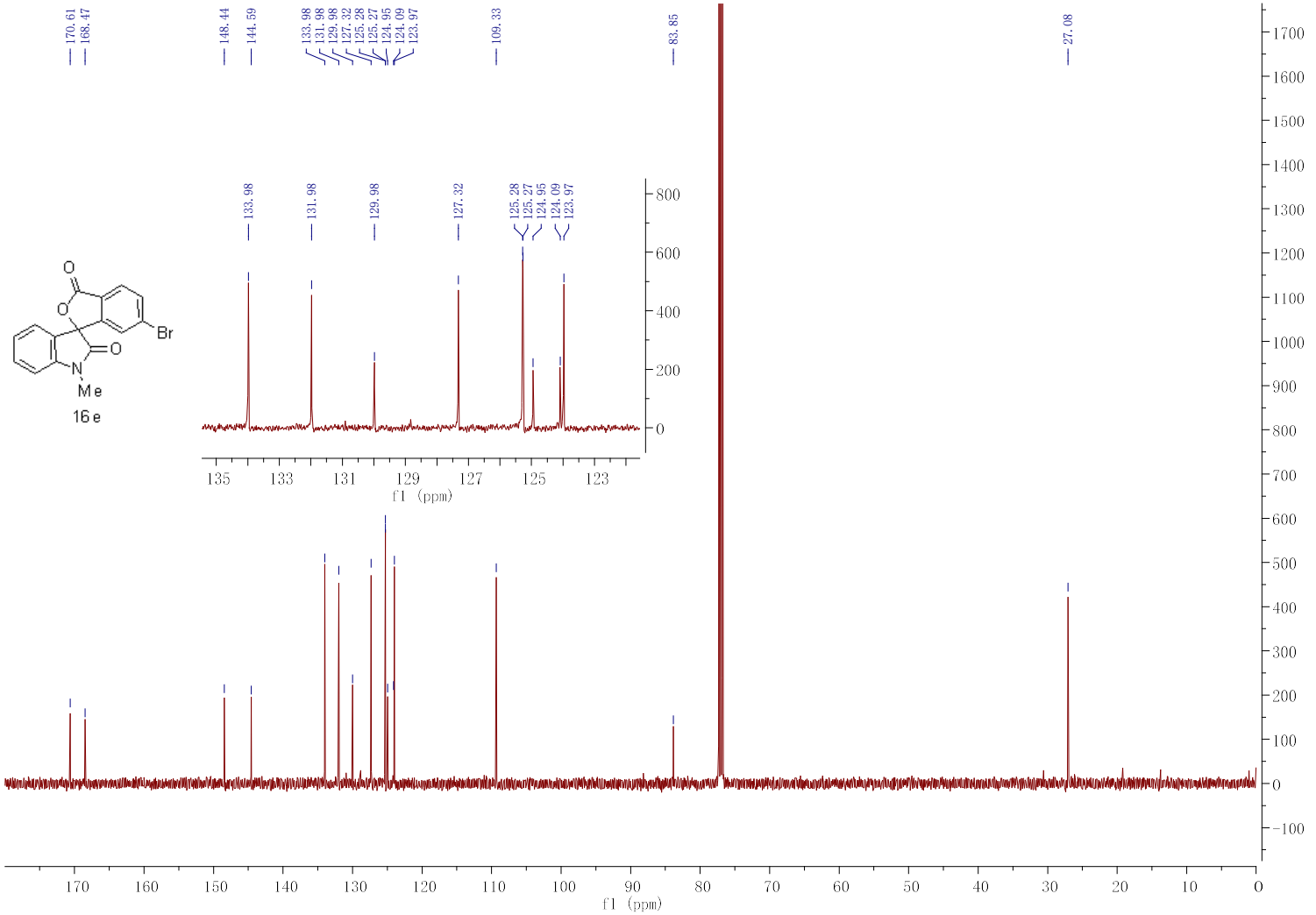
6'-chloro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16d):



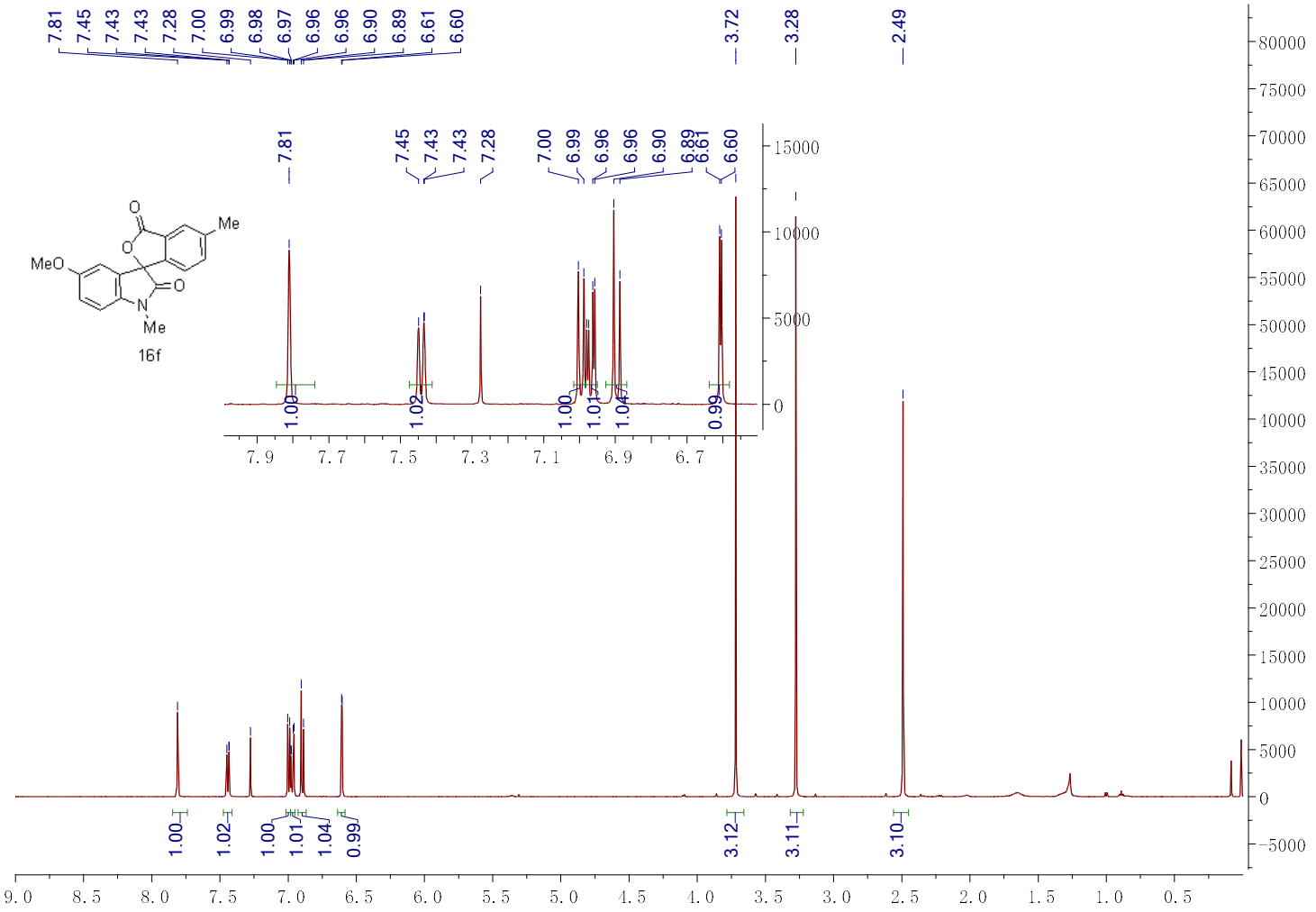

170.60
168.32
148.34
144.57
141.50
131.97
131.13
127.21
125.24
124.46
124.08
123.95
122.28
109.33
83.89
27.06
O
O
O
N
Me
Cl
16d
f1 (ppm)
f1 (ppm)

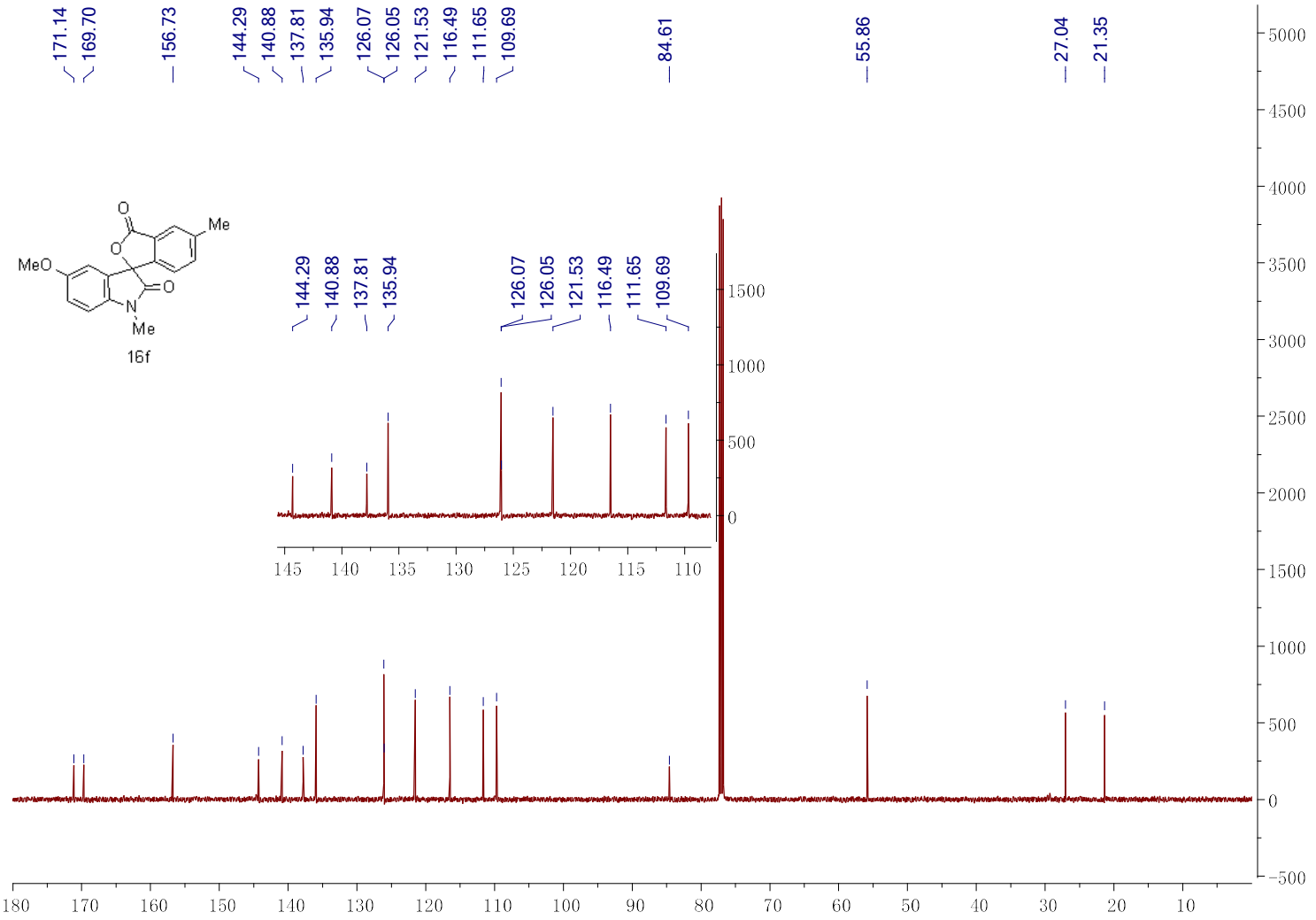
6'-bromo-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16e):



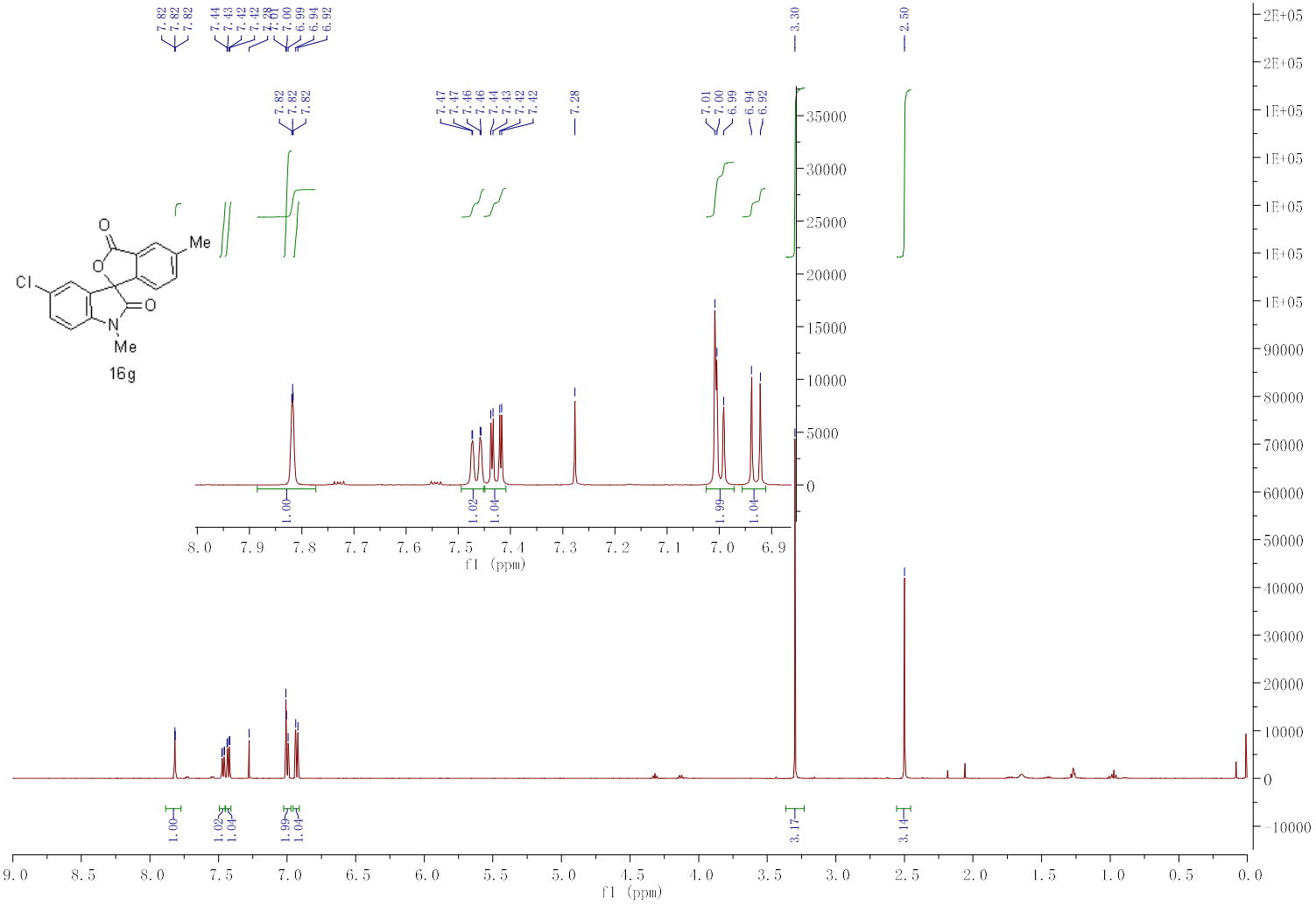

170.61
168.47
148.44
144.59
133.98
131.98
129.98
127.32
125.28
125.27
124.95
124.09
123.97
109.33
83.85
27.08
Br
O
O
O
N
Me
16e
f1 (ppm)
f1 (ppm)

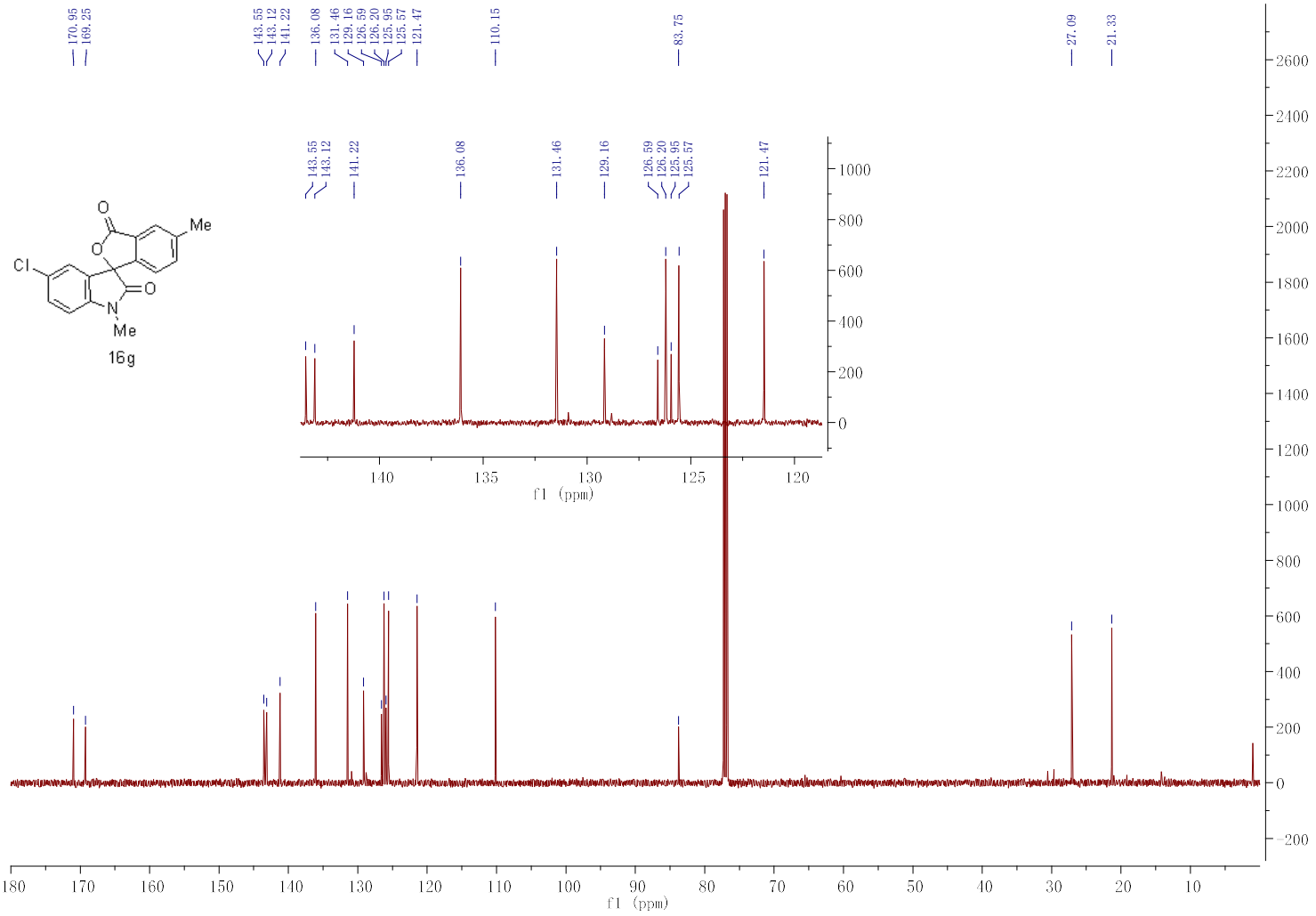
5-methoxy-1,5'-dimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16f):



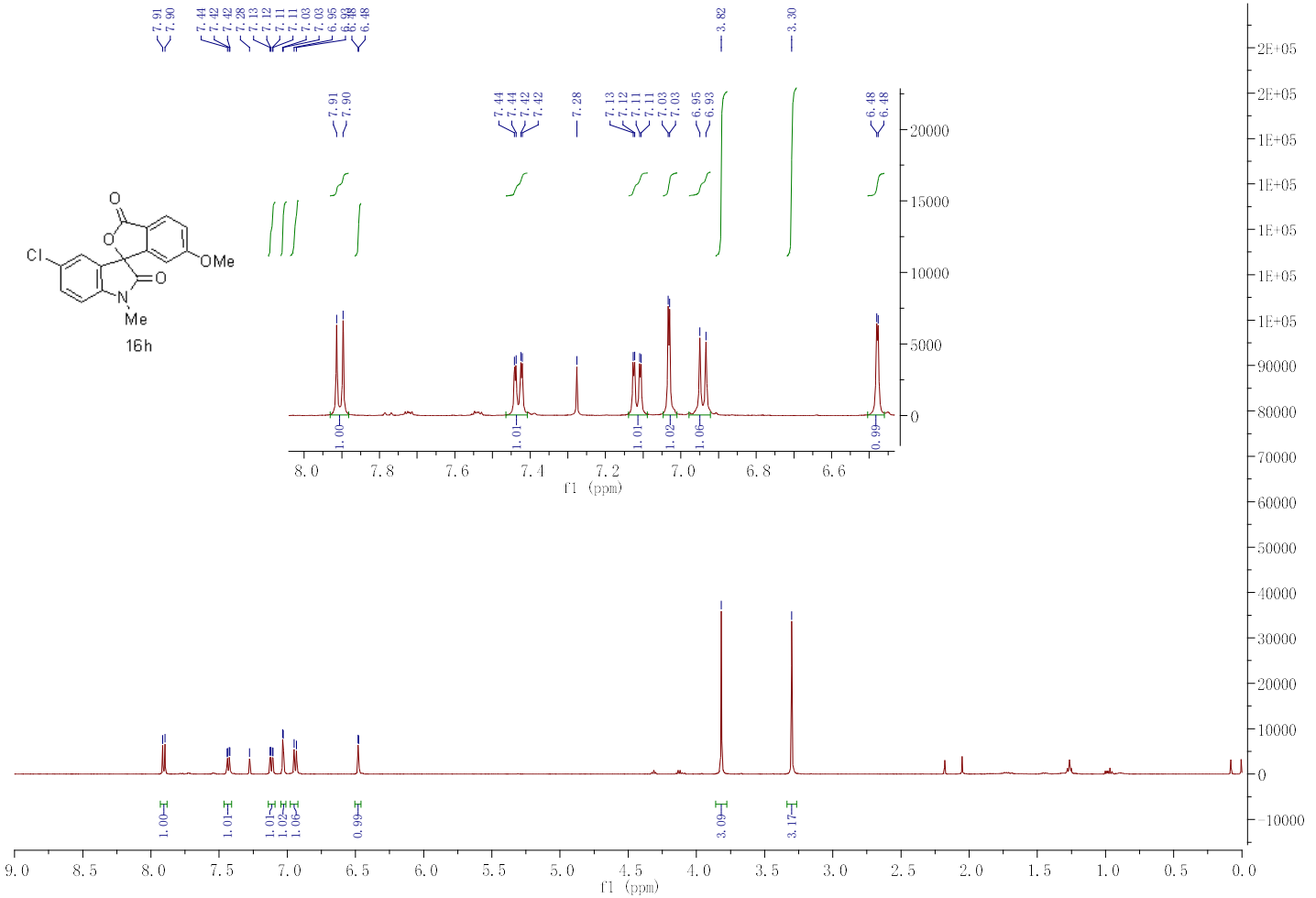

171.14
169.70
156.73
144.29
140.88
137.81
135.94
126.07
126.05
121.53
116.49
111.65
109.69
84.61
55.86
27.04
21.35
MeO
Me
O
O
O
N
Me
16f

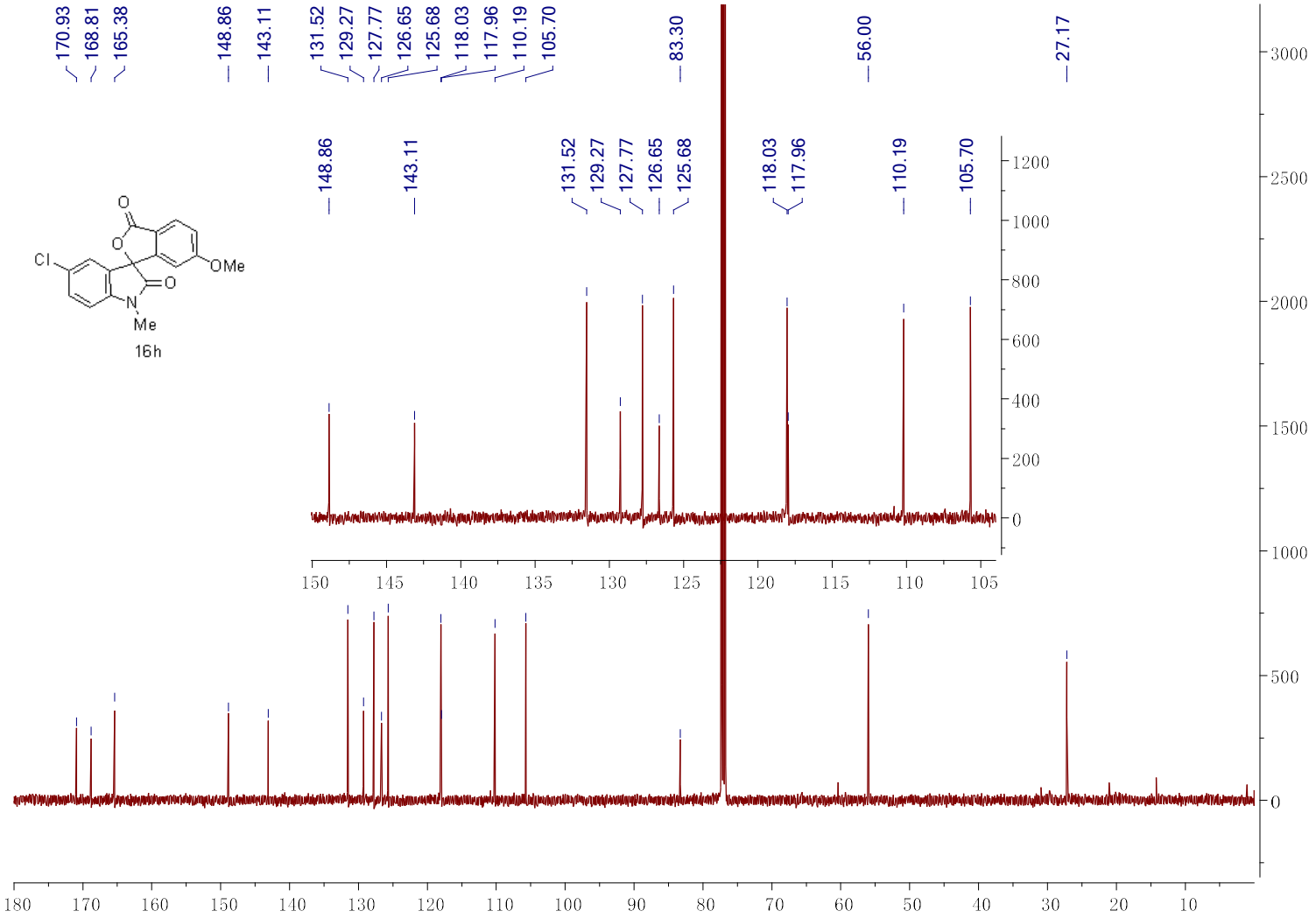
5-chloro-1,5'-dimethyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)]-2,3'-dione (16g):



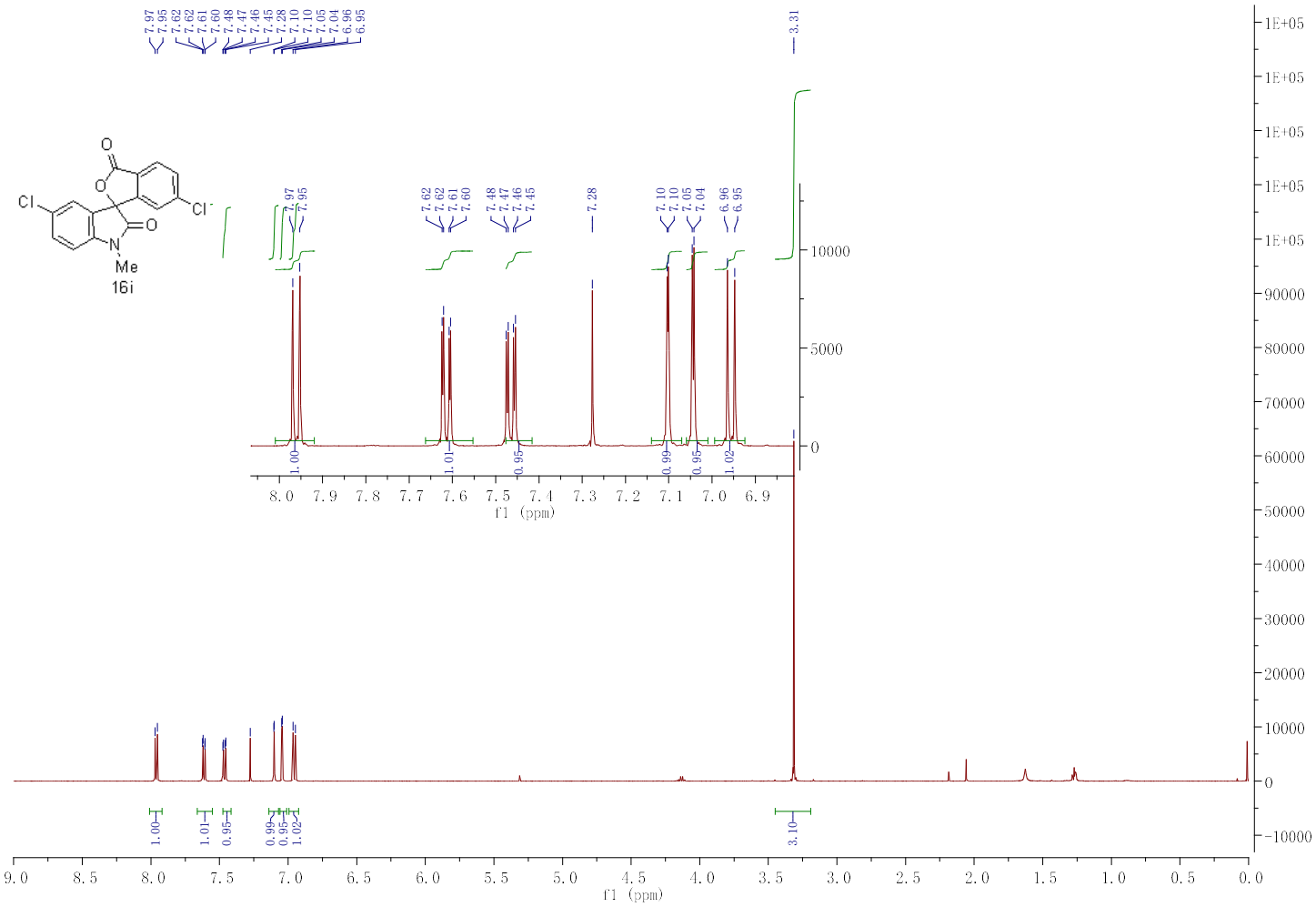

170.95
169.25
143.55
143.12
141.22
136.08
131.46
129.16
126.59
126.20
125.95
125.57
121.47
110.15
83.75
27.09
21.33
Me
Cl
O
O
O
N
Me
16g
f1 (ppm)
f1 (ppm)

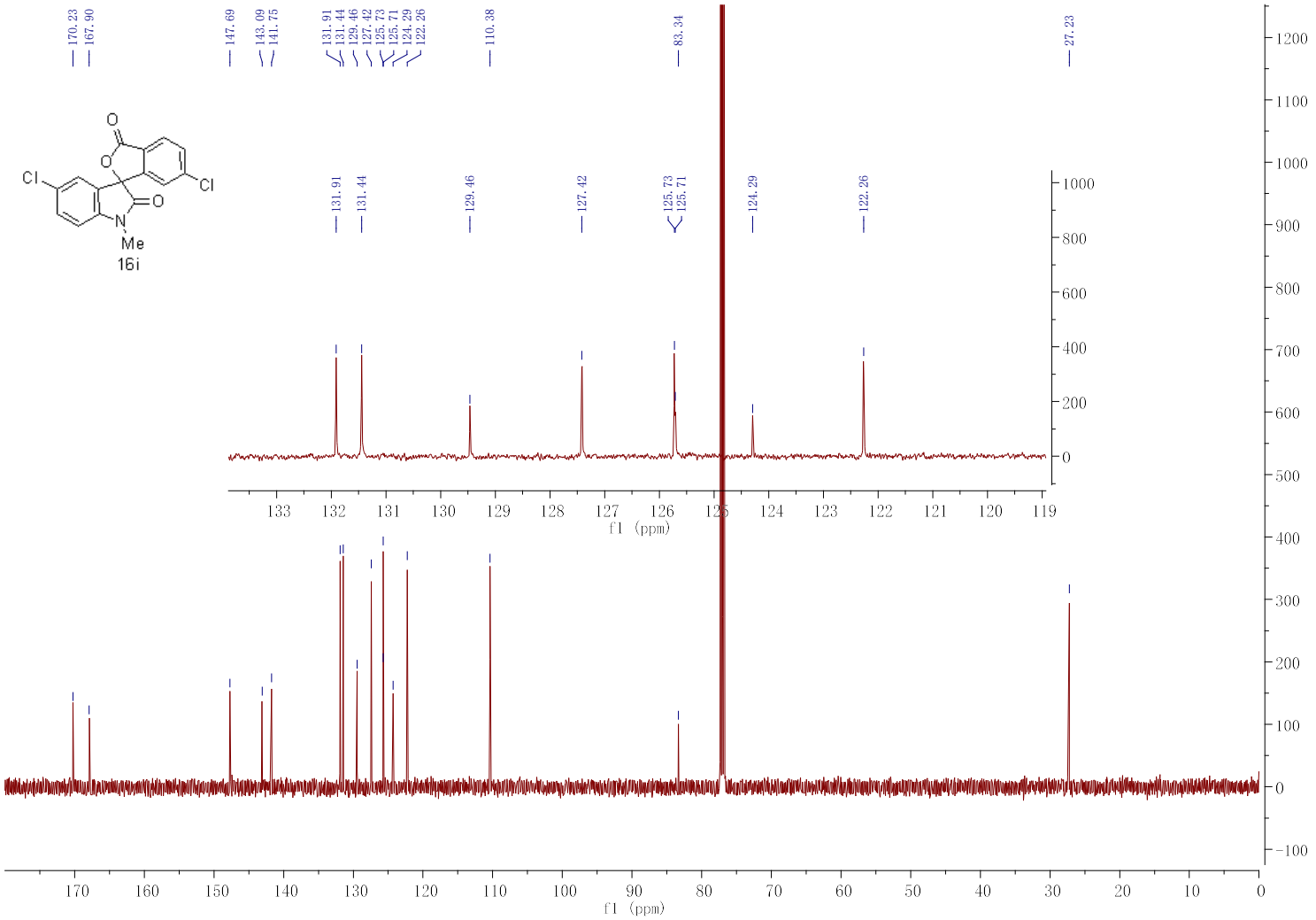
5-chloro-6'-methoxy-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16h):



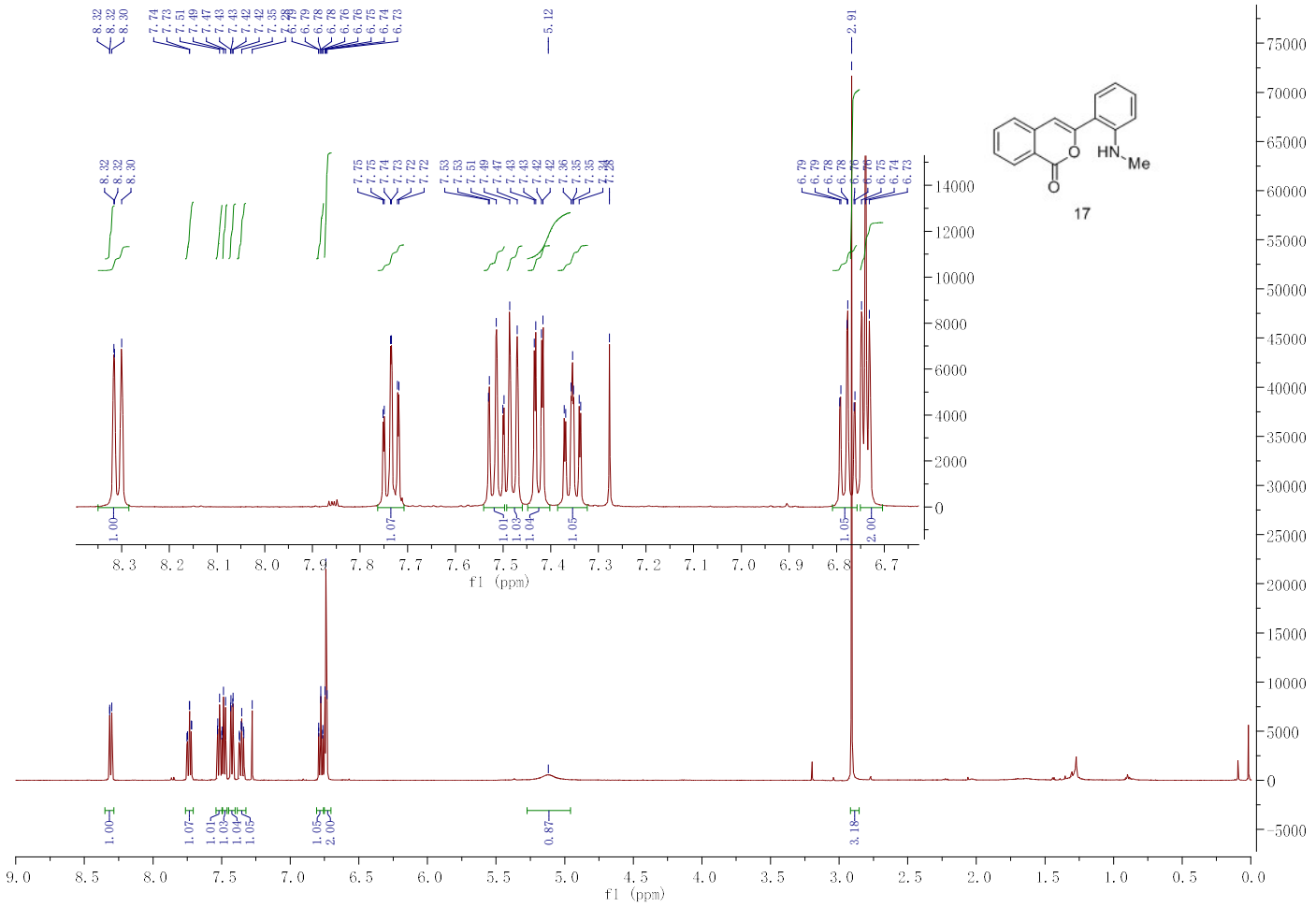

170.93
168.81
165.38
148.86
143.11
131.52
129.27
127.77
126.65
125.68
118.03
117.96
110.19
105.70
83.30
56.00
27.17
Cl
OMe
Me
16h

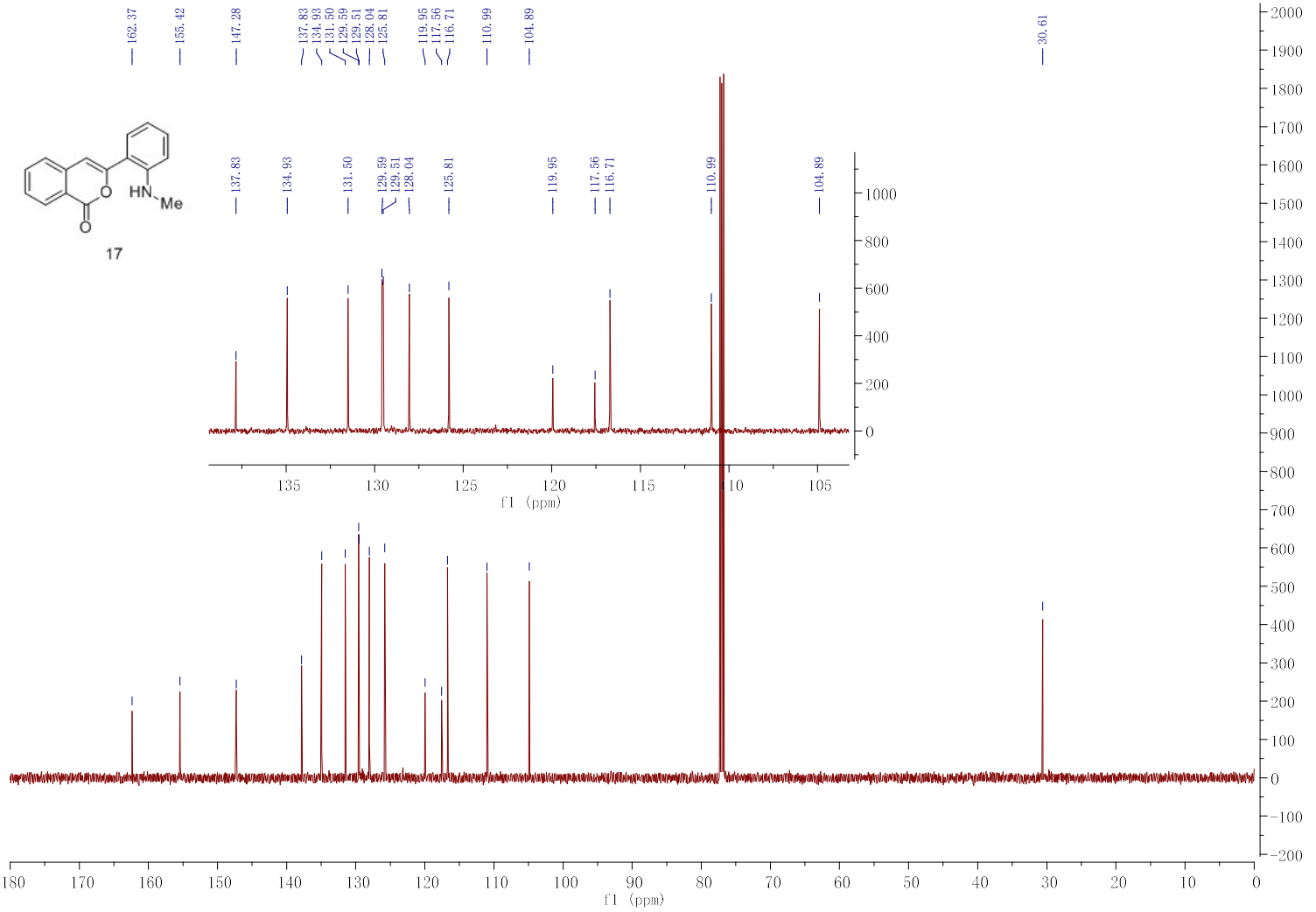
5,6'-dichloro-1-methyl-3'*H*-spiro(indoline-3,1'-isobenzofuran)-2,3'-dione (16i):



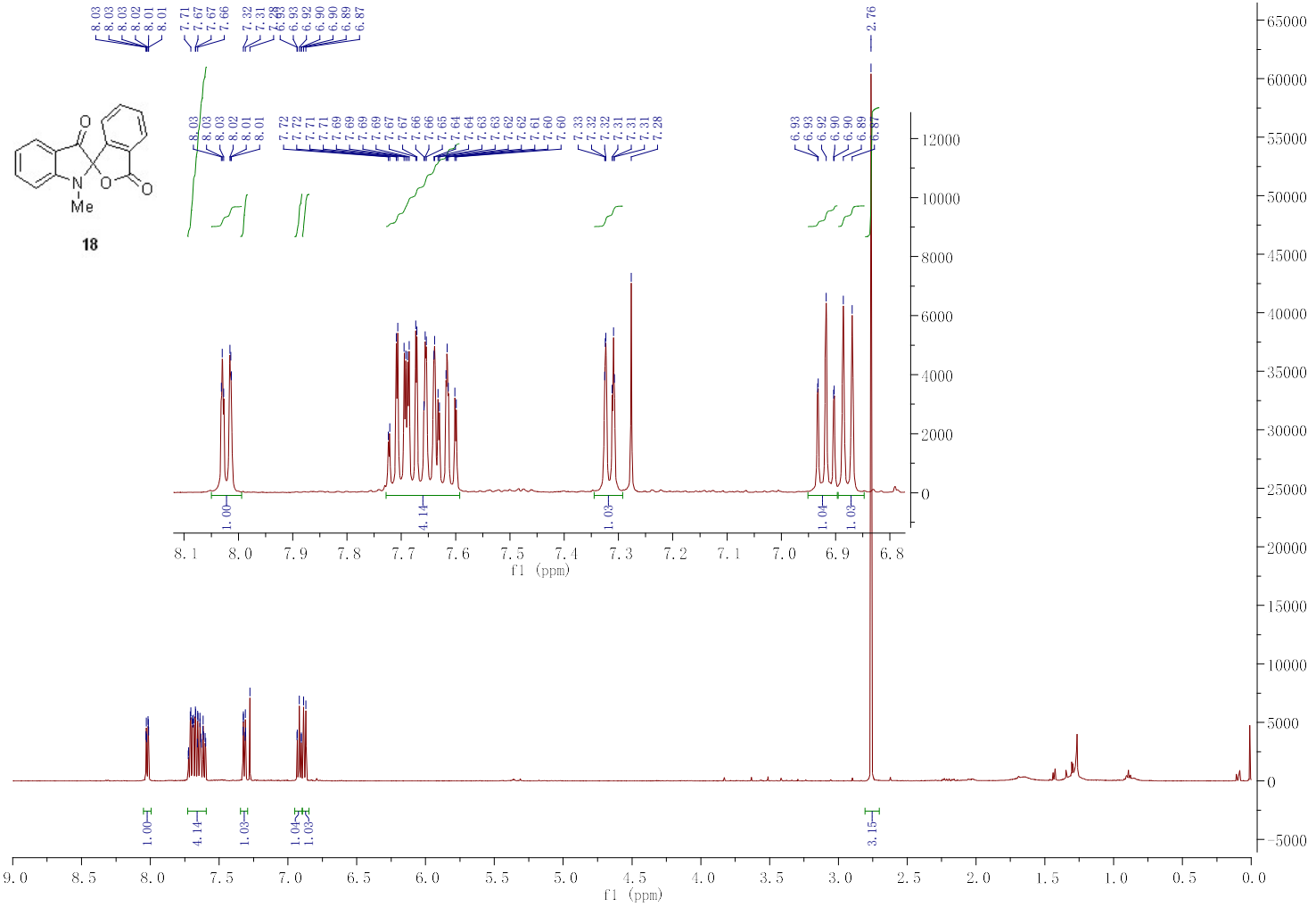

170.23
167.90
147.69
143.09
141.75
131.91
131.44
129.46
127.42
125.73
125.71
124.29
122.26
110.38
83.34
27.23
Cl
Cl
O
O
O
N
Me
16i
f1 (ppm)
f1 (ppm)

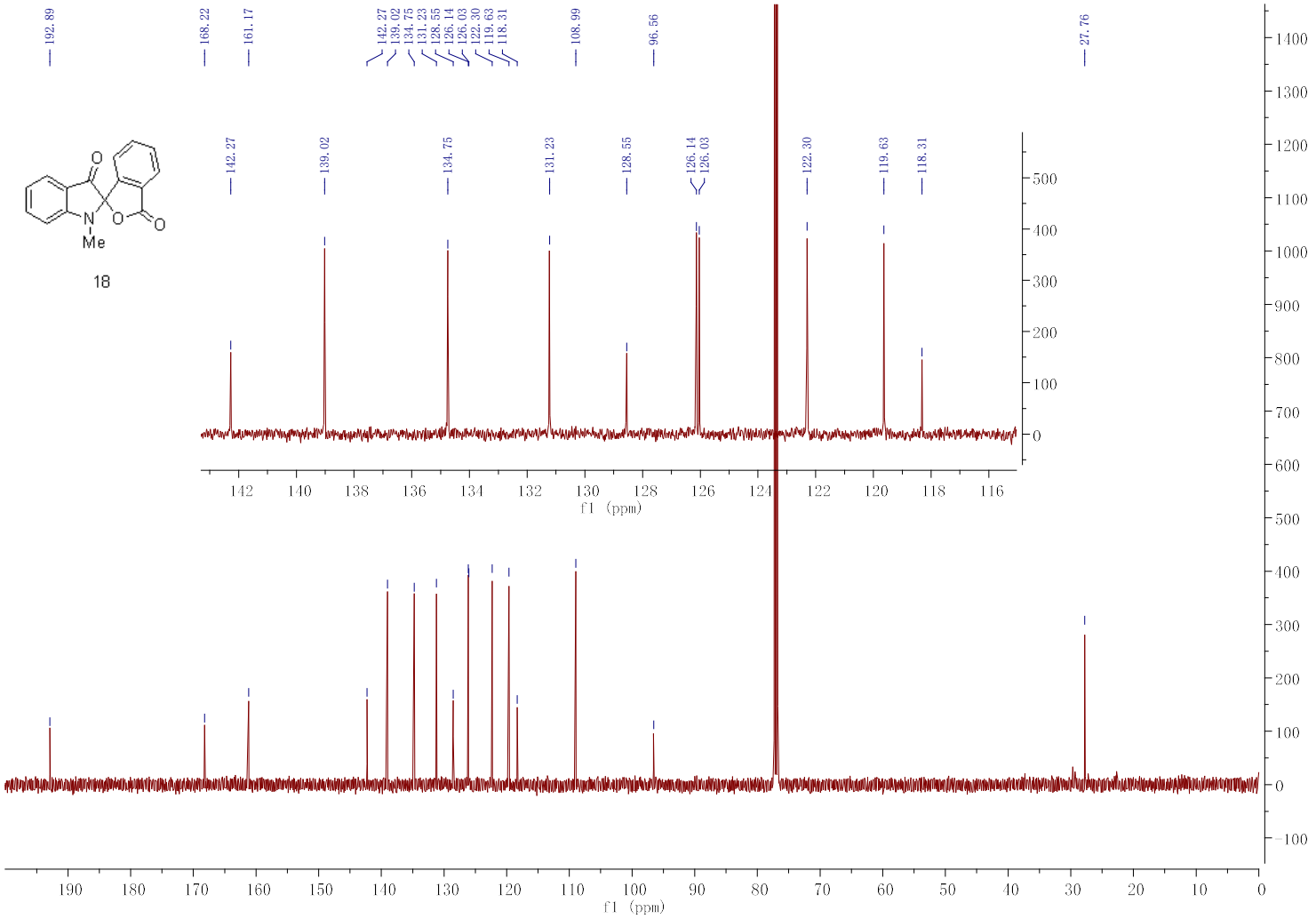
3-(2-(methylamino)phenyl)-1*H*-isochromen-1-one (17):




162.37
155.42
147.28
137.83
134.93
131.50
129.59
129.51
128.04
125.81
119.95
117.56
116.71
110.99
104.89
30.61
HN
Me
O
O
17
f1 (ppm)
f1 (ppm)

1-methyl-3'*H*-spiro[indoline-2,1'-isobenzofuran]-3,3'-dione (18):




192.89
168.22
161.17
142.27
139.02
134.75
131.23
128.55
126.14
126.03
122.30
119.63
118.31
108.99
96.56
27.76
O
N
Me
O
O
18
f1 (ppm)
f1 (ppm)