Supporting information

Cercosporin-photocatalyzed sp^3 (C-H) Activation for the Synthesis of Pyrrolo[3,4-*c*]quinolones

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1. General Methods.

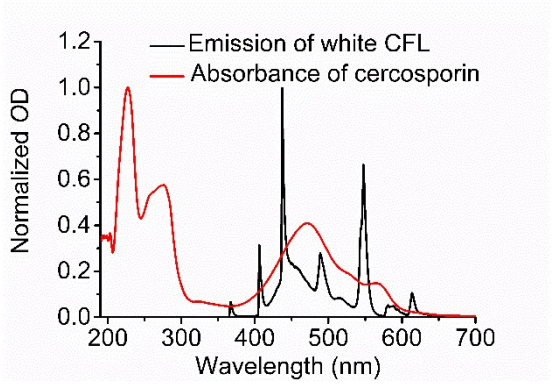
Cercosporin was biosynthesized by a cercosporin producing strain in our laboratory.[1] All other commercially available reagents and solvents were used without further purification. Thin-layer chromatography was performed using silica gel plates F254. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV400 (400 MHz) spectrometer in $CDCl_3$ solutions with internal solvent signals (for ^{1}H and ^{13}C) as reference (7.26 ppm and 77.2 ppm, respectively). ^{1}H NMR data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, m = multiplet), coupling constants (Hz), and numbers of protons. Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. UV-Vis and fluorescence measurements were performed with Shimadzu UV-3600plus spectrophotometer and F-2700 spectrofluorometer. High resolution mass spectra (HRMS) were recorded on Waters Xevo G2 Q-TOF instrument. All the reactions were carried out in 10 mL borosilicate Schlenk tubes with the irradiation of a PHILIPS 15 W white CFL (13.7 mW/cm^2)[1a] at room temperature.

2. General Procedures for the Synthesis of Products

A 10 mL schlenk tube was added tertiary aniline **1** (0.25 mmol, 67.5 mg, 1.0 equiv.), maleimide **2** (0.25 mmol, 43.25 mg, 1.0 equiv.), cercosporin (0.0025 mmol, 1.36 mg, 0.01 equiv.) and CH_3CN (2 mL). The solution was irradiated under stirring with a 15 W household fluorescent lamps (distance app. 4 cm) at room temperature. After the reaction was complete after 20 h, the solvent was removed under reduced pressure, and

the residual was treated with silica gel chromatography using hexane/EtOAc = 10:1 as eluent to give desired product(s). Compounds **3** could be further purified by recrystalization from CH_2Cl_2 and hexane.

3. Spectroscopic Investigation of the Mechanism



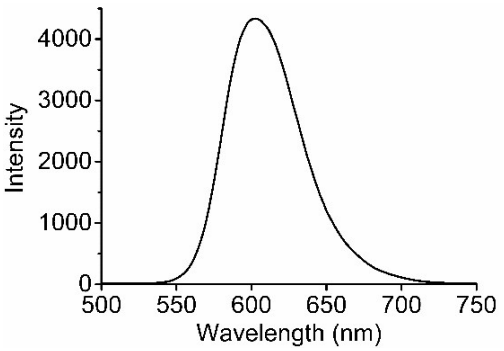


Figure S1. (Left) Normalized absorption of cercosporin and emission of white CFL; (Right) emission spectra of cercosporin at 298K in CH_3CN solution.

3.1 Procedures for quenching experiments. In a typical experiment, an appropriate amount of quencher was added to a solution of cercosporin in degassed CH_3CN in a quartz cuvette (The concentration of cercosporin was controlled at 1.565×10^{-5} M). After stirring and irradiation by 15 w CFL for 2 minutes, the emission and absorption spectra of the sample were collected. For the emission spectra, all cercosporin solutions were excited at 425 nm and the emission intensity at 597 nm was observed.

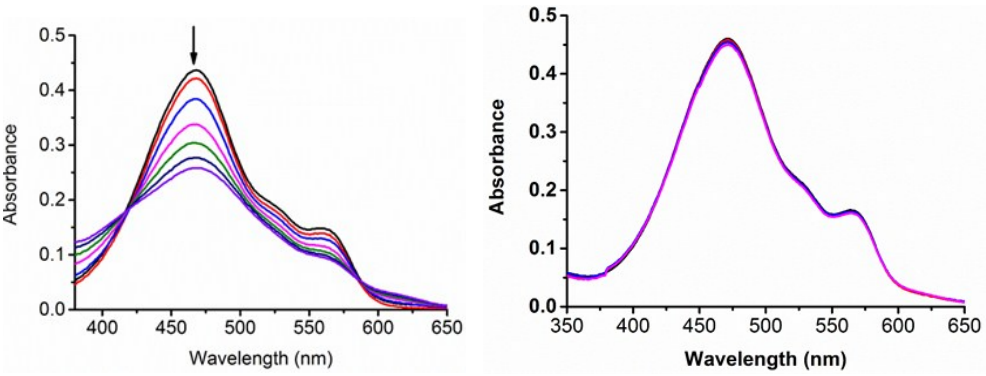


Figure S2. Titration of **1a** (Left) and **2a** (Right) to cercosporin in degassed CH_3CN with

excitation at 425 nm.

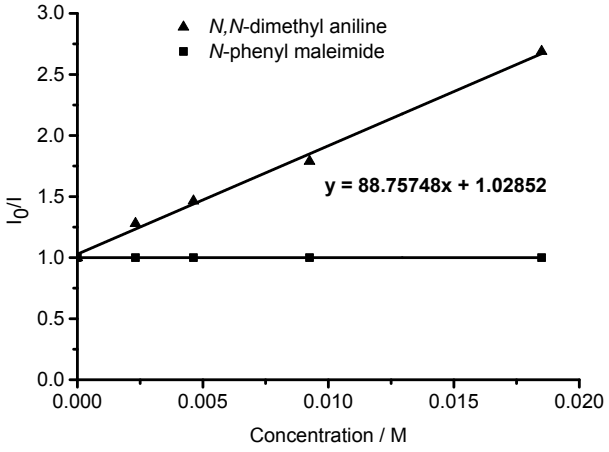


Figure S3. Stern-Volmer plots for the cercosporin emission quenching by *N*,*N*-dimethylaniline and *N*-phenylmaleimide.

4. Isotope Effects Experiments.

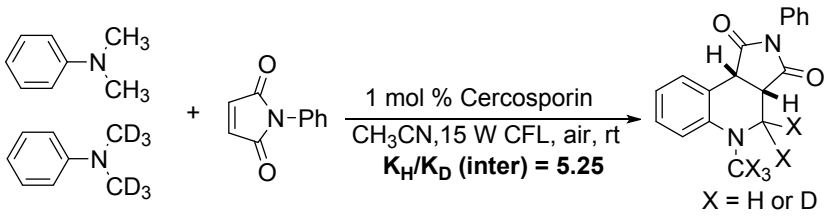
4.1 Procedure for the synthesis of isotope substracts. *N*,*N*-Di(trideuteriomethyl) aniline and *N*-methyl-*N*-trideuteriomethyl aniline were prepared using a modified procedure according to literature[2].

N-methyl-*N*-trideuteriomethyl aniline (**D_3-1a**). To a solution of benzene (4.2 mL), water (0.6 mL), *N*-methylaniline (322 mg, 3 mmol), tetra-*n*-butylammonium iodide (39 mg, 0.11 mmol) and potassium hydroxide (210 mg, 3.75 mmol) was added iodomethane-*d*3 (544 mg, 3.75 mmol) dropwise at room temperature. Then the reaction mixture was heated at 90 °C for 24 h before it was cooled to RT. The organic layer was extracted with diethyl ether and washed with water, saturated sodium carbonate, and dried over Na_2SO_4. The solution was filtrated, concentrated and eluted through a silica gel column (petroleum ether/ethyl acetate 20:1) to give compound **D_3-1a** in about 90%

yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.26 (t, J = 7.6 Hz, 2H), 6.70-6.75 (m, 3H), 2.94 (s, 3H) ppm.

N,*N*-di(trideuteriomethyl) aniline (**D_6-1a**). To a solution of benzene (4.2 mL), water (0.6 mL), aniline (279 mg, 3 mmol), *tetra*-*n*-butylammonium iodide (78 mg, 0.21 mmol) and potassium hydroxide (421 mg, 7.5 mmol), was added iodomethane-*d*3 (1088 mg, 7.5 mmol) dropwise at room temperature. Then the reaction mixture was heated at 90 °C for 24 h before it was cooled to RT. The organic layer was extracted with diethyl ether and washed with water, saturated sodium carbonate, and dried over Na_2SO_4. The solution was concentrated and eluted through a silica gel column (petroleum ether/ethyl acetate 20:1) to give compound **D_6-1a** in about 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.25 (m, 2H), 6.70-6.75 (m, 3H) ppm.

4.2 Intermolecular deuterium isotope effects. To a 10 mL round bottom flask was added 0.1 mmol of *N*,*N*-di(trideuteriomethyl) aniline, 0.1 mmol of *N*,*N*-dimethyl aniline, 0.1 mmol of *N*-phenyl maleimide, 1.0 mg (0.0018 mmol) of cercosporin and CH_3CN (1.0 mL). The solution was irradiated under stirring with 15 W household fluorescent lamps (distance app. 4 cm) at room temperature for 4 hours. k_H/k_D (inter) was determined to be 5.25 by the relative intensity of ^{1}H NMR signals of C(2)H_2 (δ3.62 and 3.13) with C(3)H and C(4)H (δ3.56 and 4.16 respectively).



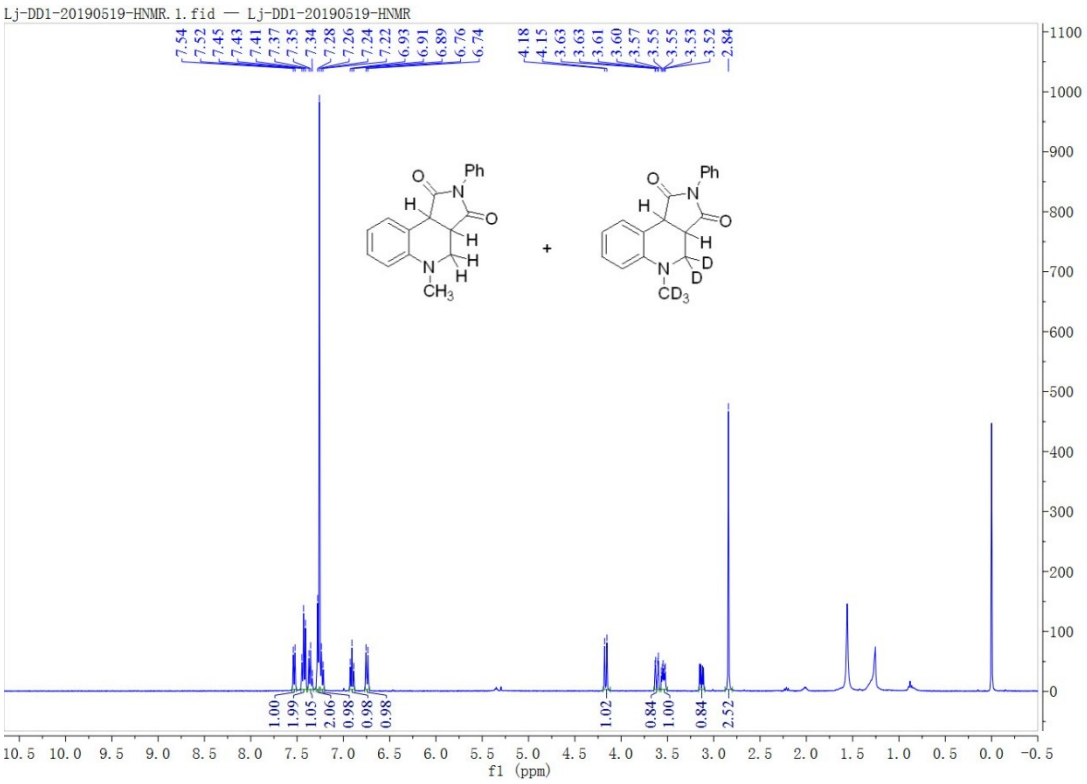
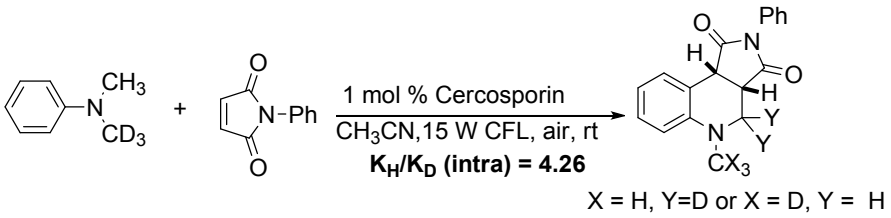


Figure S4. Intermolecular KIE.

4.3 Intramolecular deuterium isotope effects. The intramolecular deuterium isotope effect was measured by using *N*-methyl-*N*-trideuteriomethyl aniline as the substrate. k_H/k_D (intra) was determined to be 4.26 by the relative intensity of ^{1}H NMR signals of N-CH_3 (δ2.84) and N-CH_2 (δ3.62 and 3.14) ppm.



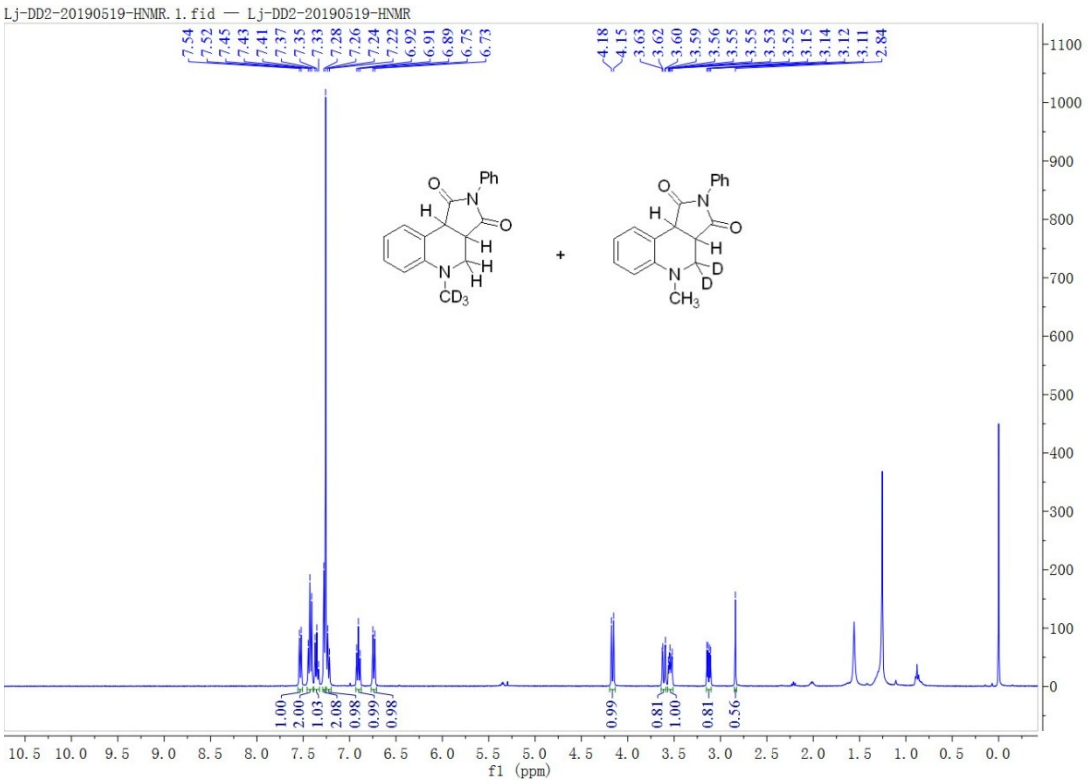
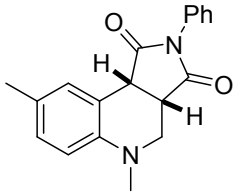


Figure S5. Intramolecular KIE.

5. Characterization Data for All Compounds

*5,8-Dimethyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3a**)*.[3-5,7-8]



3a

The product was obtained as white solid, mp. 193-195 °C, yield 68.8 mg, 90%, following the general procedure using *4,N,N*-trimethylaniline and *N*-phenylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 7.2 Hz, 2H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.65 (d, *J* = 8.3 Hz, 1H), 4.12 (d, *J* = 9.5 Hz, 1H), 3.58 (dd, *J* = 11.4, 2.6 Hz, 1H), 3.51 (ddd, *J* = 9.6, 4.2, 2.7 Hz, 1H), 3.05 (dd, *J* = 11.4, 4.4 Hz, 1H), 2.80 (s, 3H), 2.30 (s, 3H) ppm.

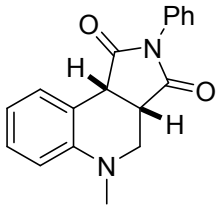
*5,7-Dimethyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3b**)* [2, 4, 7, 9-11] and *5,9-Dimethyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3c**)*[2,4,7,9,11]

3b + **3c** (1:1.85)

The products were obtained as white solid, yield 60 %, 45.9 mg, with the ratio **3b**: **3c**= 1:1.85; following the general procedure using *N,N,3*-Trimethylaniline and *N*-phenylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.49–7.40 (m, 3.83 H), 7.37–7.27 (m,

2.56 H), 7.12 (t, *J* = 8.0 Hz, 0.59 H), 6.83 (d, *J* = 8.0 Hz, 0.68 H), 6.72 (d, *J* = 8.0 Hz, 0.37H), 6.63 (d, *J* = 8.0 Hz, 0.59 H), 6.55 (s, 0.34 H), 4.50 (d, *J* = 8.0 Hz, 0.57 H), 4.12 (d, *J* = 12.0 Hz, 0.37 H), 3.55–3.52 (m, 2.0 H), 3.08 (dd, *J* = 11.5, 4.4 Hz, 0.39 H), 2.95 (dd, *J* = 11.3, 4.8 Hz, 0.64H), 2.82 (s, 1.18 H), 2.80 (d, *J* = 14.5 Hz, 3 H), 2.59 (s, 1.78 H), 2.32 (s, 1.17 H) ppm.

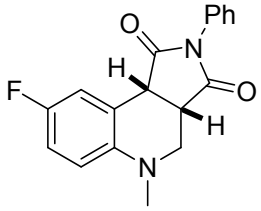
*5-Methyl-2-phenyl-3a, 4, 5, 9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline -1,3(2H)-dione (**3d**)*.[3-8]



3d

The product was obtained as white solid, mp. 194-196 °C, yield 91 %, 66.7 mg; following the general procedure using *N,N*-dimethylaniline and *N*-phenylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.27 – 7.21 (m, 3H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 4.15 (d, *J* = 9.5 Hz, 1H), 3.61 (dd, *J* = 11.5, 2.7 Hz, 1H), 3.53 (dt, *J* = 9.6, 3.8 Hz, 1H), 3.11 (dd, *J* = 11.4, 4.4 Hz, 1H), 2.83 (s, 3H) ppm.

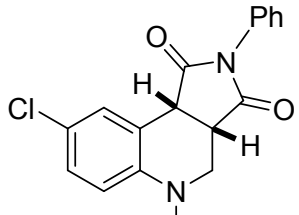
*8-Fluoro-5-methyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinolone-1,3(2H)-dione (**3e**)*[4,5,8]



3e

The product was obtained as white solid, mp. 172-174 °C, yield 44.9 mg, 58%, following the general procedure using 4-fluoro-*N,N*-dimethylaniline and *N*-phenylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (t, J = 8.3 Hz, 2H), 7.36 (t, J = 6.9 Hz, 1H), 7.25–7.29 (m, 3H), 6.93 (t, J = 8.7 Hz, 1H), 6.67 (dd, J = 9.2, 4.6 Hz, 1H), 4.11 (d, J = 9.5 Hz, 1H), 3.59 (d, J = 8.0 Hz, 1H), 3.53-3.51 (m, 1H), 3.07 (dd, J = 10.7, 4.5 Hz, 1H), 2.81 (s, 3H) ppm.

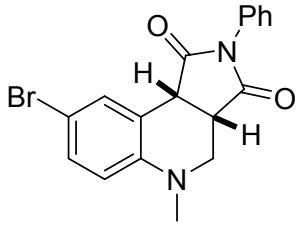
*8-Chloro-5-methyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3f**)*[4,5,8]



3f

The product was obtained as white solid, mp. 155-157 °C, yield 52.1 mg, 64%, following the general procedure using 4-chloro-*N,N*-dimethylaniline and *N*-phenylmaleimide. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.50 (d, J = 2.8 Hz, 1H), 7.44 (m, 1H), 7.35 (m, 1H),7.24 (m, 2H), 7.17 (J = 8.8, 2.4 Hz, 2H), 6.65 (d, J = 8.8 Hz, 1H), 4.08 (d, J = 9.6 Hz, 1H), 3.60 (dd, J = 11.6 Hz, 2.8 Hz, 1H), 3.50 (m, 1H), 3.08 (dd, J = 11.6 Hz, 4.4 Hz, 1H), 2.81 (s, 3H) ppm.

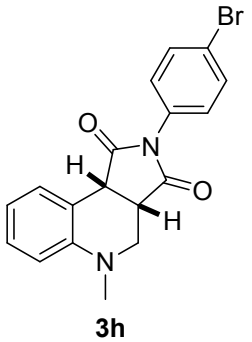
*8-Bromo-5-methyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3g**)*[4-6, 8]



3g

The product was obtained as white solid, mp. 157-159 °C, yield 84.4 mg, 91%, following the general procedure using 4-bromo-*N,N*-dimethylaniline and *N*-phenylmaleimide. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.64 (s, 1H), 7.45-7.42 (t, *J* = 7.6 Hz, 2H), 7.38-7.35 (t, *J* = 7.36 Hz 1H), 7.31 (d, *J* = 8.7 Hz, 1H), 7.27-7.25 (m, 2H), 6.60 (d, *J* = 8.7 Hz, 1H), 4.10 (d, *J* = 9.6 Hz, 1H), 3.60 (dd, *J* = 12 Hz, 2.8 Hz, 1H), 3.53 (m, 1H), 3.11 (dd, *J* = 11.5 Hz, 4.4 Hz, 1H), 2.82 (s, 3H) ppm.

*2-(4-Bromophenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3h**)*[12]

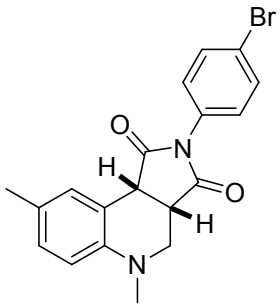


3h

The product was obtained as white solid, mp. 222-226 °C, yield 57.3 mg, 62%, following the general procedure using *N,N*-dimethylaniline and (4-bromophenyl)maleinimide. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.56-7.50 (m, 3H),

7.24-7.17 (m, 3H), 6.95-6.87 (t, *J* = 7.7 Hz, 1H), 6.74(d, *J* = 8.2 Hz, 1H), 4.16 (d, *J* = 9.6 Hz, 1H), 3.61(dd, *J* = 11.5, 2.6 Hz, 1H), 3.52 (m, 1H), 3.11 (dd, *J* = 11.5 Hz, 4.4 Hz, 1H), 2.83 (s, 3H) ppm.

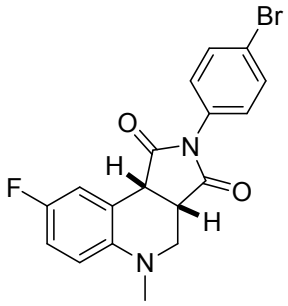
*2-(4-Bromophenyl)-5,8-dimethyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3i**)*[4]



3i

The product was obtained as white solid, mp. 183-185 °C, yield 85.4 mg, 89%, following the general procedure using *4,N,N*-trimethylaniline and (4-bromophenyl)maleinimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.6 Hz, 1H), 7.55 (d, *J* = 2.1 Hz, 2H), 7.33 (s, 1H), 7.19 (dd, *J* = 8.3 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 4.11 (d, *J* = 9.5 Hz, 1H), 3.59 (dd, *J* = 11.4, 4 Hz, 1H), 3.54 (d, *J* = 8.0 Hz, 1H), 3.04 (d, *J* = 7.3 Hz, 1H), 2.80 (s, 3H), 2.30 (s, 3H) ppm.

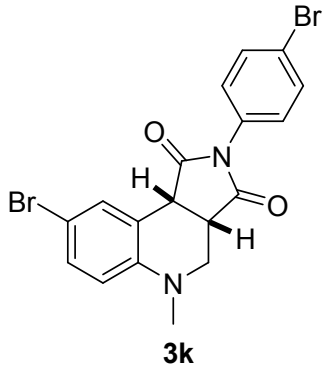
*2-(4-Bromophenyl)-5-methyl-8-fluoro-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3j**)*(new compound).



3j

The product was obtained as white solid, mp. 175-177 °C, 50.5 mg, yield 52%, following the general procedure using 4-fluoro-*N,N* dimethylaniline and (4-bromophenyl)maleinimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.27-7.24 (m, 1H), 7.18 (d, J = 8.6 Hz, 2H), 6.94 (td, J = 8.6 Hz, 3.0 Hz, 1H), 6.66 (dd, J = 9.0 Hz, 4.6 Hz, 1H), 4.11 (d, J = 9.6 Hz, 1H), 3.58 (dd, J = 11.5, 2.7 Hz, 1H), 3.52 (m, 1H), 3.06 (dd, J = 11.5, 4.4 Hz, 1H), 2.81 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 177.07, 174.84, 157.86 (d, $^{1}J_{C\text{-}F}$ = 237 Hz), 144.99, 144.97, 132.21, 130.87, 127.82, 122.42, 119.86 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 117.07 (d, $^{2}J_{C\text{-}F}$ = 23 Hz), 115.31 (d, $^{2}J_{C\text{-}F}$ = 21 Hz), 113.52 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 51.01, 43.49, 42.24, 39.75 ppm. HRMS (ESI-QTOF) exact mass calcd for $C_{18}H_{15}BrFN_2O_2$ $[M + H]^+$ 389.0301, found 389.0304.

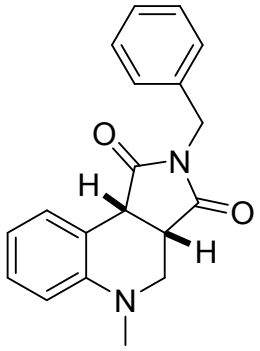
*2-(4-Bromophenyl)-5-methyl-8-bromo-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3k**)* (new compound).



3k

The product was obtained as white solid, mp. 180-185 °C, yield 93 mg, 83%, following the general procedure using 4-bromo-*N,N*-dimethylaniline and (4-bromophenyl)maleinimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.56 (d, J = 8.4 Hz, 2H), 7.33 (dd, J = 8.7, 2.3 Hz, 1H), 7.18 (d, J = 8.4 Hz, 2H), 6.61 (d, J = 8.7 Hz, 1H), 4.11 (d, J = 9.5 Hz, 1H), 3.60 (dd, J = 11.5, 2.6 Hz, 1H), 3.53 (m, 1H), 3.10 (dd, J = 11.6, 4.4 Hz, 1H), 2.81 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 176.86, 174.75, 147.46, 132.71, 132.21, 131.57, 130.82, 127.77, 122.44, 120.14, 114.28, 111.80, 50.34, 43.34, 41.79, 39.45 ppm. HRMS (ESI-QTOF) exact mass calcd for $C_{18}H_{15}Br_2N_2O_2$ $[M + H]^+$ 450.9480, found 450.9483.

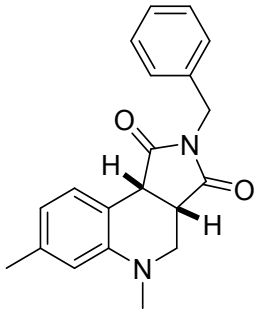
2-Benzyl-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione ***(3l)***[5,6,8]



3l

The product was obtained as white solid, mp. 106-110 °C, yield 46 mg, 60 %, following the general procedure using *N,N*-dimethylaniline and *N*-benzylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.5 Hz, 1H), 7.32-7.17 (m, 6H), 6.89 (t, J = 7.4 Hz, 1H), 6.71 (d, J = 8.2 Hz, 1H), 4.65 (q, J = 14.3 Hz, 2H), 3.99 (d, J = 9.4 Hz, 1H), 3.49 (dd, J = 11.5, 2.7 Hz, 1H), 3.36 (m, 1H), 3.05 (dd, J = 11.5, 4.5 Hz, 1H), 2.80 (s, 3H) ppm.

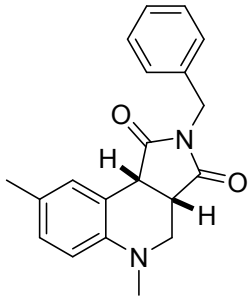
*2-Benzyl-5,7-dimethyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3m**)* (new compound).



3m

The product was obtained as white solid, mp. 120-122 °C, yield 54 mg, 67%, following the general procedure using *N,N,3*-trimethylaniline and *N*-benzylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.27 (m, 5H), 7.10 (t, J = 7.8 Hz, 1H), 6.79 (d, J = 7.5 Hz, 1H), 6.60 (d, J = 8.1 Hz, 1H), 4.67 (q, J = 14.3 Hz, 2H), 4.35 (d, J = 9.6 Hz, 1H), 3.49 (dd, J = 11.4, 1.5 Hz, 1H), 3.36 (dd, J = 9.5, 5.1 Hz, 1H), 2.88 (dd, J = 11.3, 4.8 Hz, 1H), 2.74 (s, 3H), 2.55 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 179.12, 176.25, 149.98, 138.38, 135.63, 128.55, 128.21, 127.93, 127.71, 122.65, 119.57, 110.52, 52.39, 44.90, 42.79, 39.64, 39.41, 20.30 ppm. HRMS (ESI-QTOF) exact mass calcd for $C_{20}H_{21}N_2O_2$ $[M + H]^+$ 321.1603, found 321.1624.

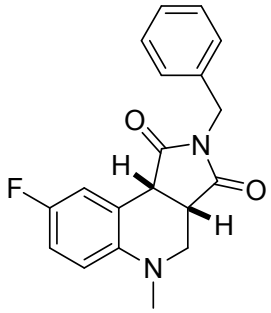
*2-Benzyl-5,8-dimethyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3n**)*[3-5,8]



3n

The product was obtained as white solid, mp. 117-119 °C, yield 58.4 mg, 73%, following the general procedure using *4,N,N*-trimethylaniline and *N*-benzylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.25 (m, 6H),7.01 (dd, J = 8.2, 2.5 Hz, 1H), 6.92 (d, J = 8.3 Hz, 1H), 4.63 (q, J = 14.3 Hz, 2H), 3.94 (d, J = 9.4 Hz, 1H), 3.46 (dd, J = 8, 2.4 Hz, 1H), 3.35 (m, 1H), 2.97 (dd, J = 11.4, 4.5 Hz, 1H), 2.76 (s, 3H), 2.29 (s, 3H) ppm.

*2-Benzyl-5-methyl-8-fluoro-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3o**)*[8]

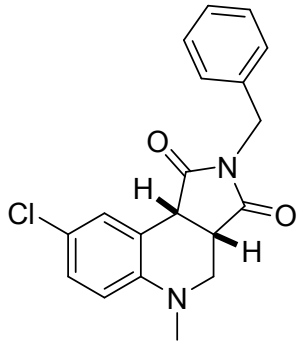


3o

The product was obtained as white solid, mp. 115-117 °C, yield 42.9 mg, 53%, following the general procedure using 4-fluoro-*N,N*-dimethylaniline and *N*-benzylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 5H), 7.22 (dd, J = 8.7 Hz, 3.0 Hz, 1H), 6.92 (td, J = 8.6, 3.0 Hz, 1H), 6.62 (dd, J = 9.0, 4.6 Hz, 1H), 4.66 (q, J = 11.6 Hz, 2H), 3.94 (d, J = 9.4 Hz, 1H), 3.47 (dd, J = 11.5, 2.8 Hz, 1H), 3.35 (m,

1H), 2.99 (dd, *J* = 11.5, 4.6 Hz, 1H), 2.77 (s, 3H) ppm.

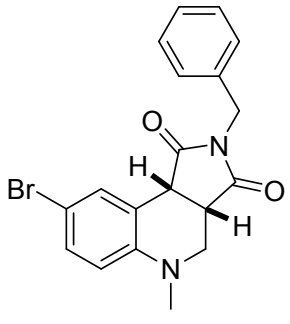
*2-Benzyl-5-methyl-8-chloro-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3p**)*[8]



3p

The product was obtained as white solid, mp. 134-136 °C, yield 68.8 mg, 81%, following the general procedure using 4-chloro-*N,N*-dimethylaniline and *N*-benzylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 2.4 Hz, 1H), 7.27 (m, 5H), 7.15 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.62 (d, *J* = 8.8 Hz, 1H), 4.65 (q, *J* = 14.4 Hz, 2H), 3.92 (d, *J* = 9.2 Hz, 1H), 3.47 (dd, *J* = 11.6, 2.8 Hz, 1H), 3.35 (m, 1H), 3.02 (dd, *J* = 11.6, 4.4 Hz, 1H), 2.78 (s, 3H) ppm.

*2-Benzyl-5-methyl-8-bromo-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3q**)*[5,8]

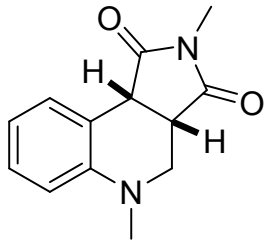


3q

The product was obtained as white solid, mp. 148-150°C, yield 64 mg, 66 %, following

the general procedure using 4-bromo-*N,N*-dimethylaniline and *N*-benzylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.31-7.27 (m, 6H), 6.57 (d, J = 8.7 Hz, 1H), 4.66 (q, J = 14.3 Hz, 2H), 3.93 (d, J = 9.4 Hz, 1H), 3.51 (dd, J = 11.5, 2.9 Hz, 1H), 3.48 (ddd, J = 9.5, 4.6, 2.9 Hz, 1H), 3.37 (m, 1H), 3.03 (dd, J = 11.5, 4.5 Hz, 1H), 2.78 (s, 3H) ppm.

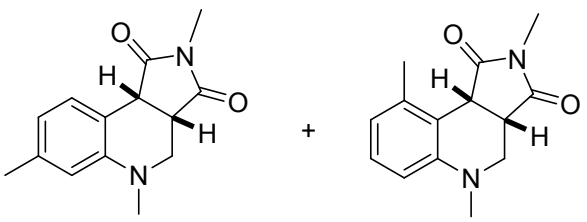
*2,5-Dimethyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3r**)*[5-8]



3r

The product was obtained as white solid, mp. 170-172 °C, yield 45.4 mg, 79%, following the general procedure using *N,N*-dimethylaniline and *N*-methylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.5 Hz, 1H), 7.21 (t, 1H), 6.89 (t, J = 7.6 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 4.00 (d, J = 9.2 Hz, 1H), 3.53 (dd, J =11.2, 2.4 Hz, 1H), 3.38 (m, 1H), 3.03 (d, J = 11.6, 4.4 Hz, 1H), 2.99 (s, 3H), 2.80 (s, 3H) ppm.

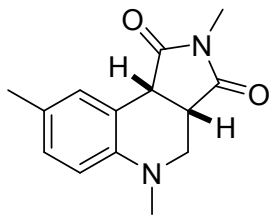
*2,5,7-Trimethyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3s**)* and *2,5,9-Trimethyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3t**)* (new compound).



3S + **3t** (1: 4.75)

The products were obtained as white solid, yield 87 %, 53 mg, the ratio of **3s** : **3t** = 1: 4.26, following the general procedure using *N,N,3*-trimethylaniline and *N*-methylmaleimide. ^{1}H NMR (400 MHz, CDCl3) δ 7.36 (d, J = 8 Hz, 0.24 H), 7.10 (t, J = 7.8 Hz, 1 H), 6.80 (d, J = 7.5 Hz, 0.96 H), 6.72 (d, J = 7.6 Hz, 0.19 H), 6.58 (d, J = 8.2 Hz, 0.99 H), 6.51 (s, 0.17 H), 4.35 (d, J = 9.6 Hz, 0.96 H), 3.5 (d, J =11.4 Hz, 1H), 3.36 (dd, J = 9.8, 4.9 Hz, 1.15H), 3.0 (s, 2.79 H), 2.98 (s, 0.56 H), 2.88 (dd, J = 11.4, 4.8 Hz, 1.09 H), 2.78 (s, 0.62 H), 2.74 (s, 2.89 H), 2.58 (s, 2.85 H), 2.31 (s, 0.56 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 177.45, 175.53, 169.05, 146.35, 134.31, 132.30, 132.14, 131.02, 130.78, 129.34, 129.11, 127.87, 127.35, 122.27, 121.61, 118.30, 112.60 ppm. HRMS (ESI-QTOF) exact mass calcd for $C_{14}H_{17}N_2O_2$ $[M + H]^+$ 245.1290, found 245.1299.

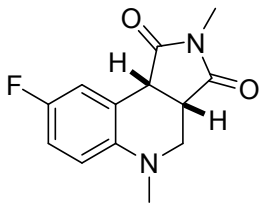
2,5,8-Trimethyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione ***(3u)***.[3,5,7,8]



3u

The product was obtained as white solid, mp. 173-176 °C, yield 50 mg, 82 %, following the general procedure using *N,N,4*-trimethylaniline and *N*-methylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (s, 1H), 7.01 (d, J = 8.2 Hz, 1H), 6.61 (d, J = 8.3 Hz, 1H), 3.96 (d, J = 9.4 Hz, 1H), 3.51 (dd, J =11.4, 2.4 Hz, 1H), 3.34 (ddd, J = 9.5, 4.4, 2.4 Hz, 1H), 2.99 (s, 3H), 2.96 (d, J =4.1 Hz, 1H), 2.76 (s, 3H), 2.30 (s, 3H) ppm.

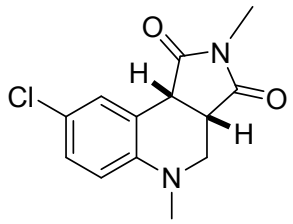
*2,5-Dimethyl-8-fluoro-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3v**)*[8]



3v

The product was obtained as white solid, mp. 142-145 °C, yield 39 mg, 63 %, following the general procedure using 4-fluoro-*N,N*-dimethylaniline and *N*-methylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (dd, J = 8 Hz, 4 Hz, 1H), 6.91 (td, J = 8.6, 3.0 Hz, 1H), 6.62 (dd, J = 9.0, 4.6 Hz, 1H), 3.96 (d, J = 9.4 Hz, 1H), 3.51 (dd, J =11.5, 2.5 Hz, 1H), 3.37 (ddd, J = 9.5, 4.5, 2.6 Hz 1H), 3.0 (s, 3H), 2.98 (d, J = 4 Hz, 1H), 2.77 (s, 3H) ppm.

*2,5-Dimethyl-8-chloro-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3w**)*[8]

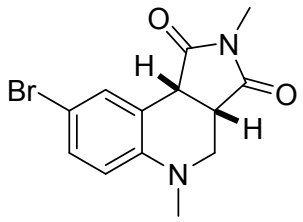


3w

The product was obtained as white solid, mp. 174-176 °C, yield 46.8 mg, 71 %, following the general procedure using 4-chloro-*N,N*-dimethylaniline and *N*-methylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 2 Hz, 1H), 7.16-7.13 (dd, J = 8.8, 2.4 Hz, 1H), 6.61 (d, J = 8.8 Hz, 1H), 3.95 (d, J = 8.8 Hz, 1H), 3.54-3.50 (dd,

J =7.6, 2.0 Hz, 1H), 3.36 (m, 1H), 3.02 (m, 1H), 2.99 (s, 3H), 2.78 (s, 3H) ppm.

*2,5-Dimethyl-8-bromo-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3x**)*[5-8]



3x

The product was obtained as white solid, mp. 187-190 °C, yield 52.5 mg, 68 %, following the general procedure using 4-bromo-*N,N*-dimethylaniline and N-methylmaleimide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.29 (dd, J = 8.8, 2.3 Hz, 1H), 6.56 (d, J = 8.7 Hz, 1H), 3.93 (d, J = 9.4 Hz, 1H), 3.53 (dd, J =11.5, 2.5 Hz, 1H), 3.36 (m, 1H), 3.04 (dd, J = 8, 4 Hz, 1H), 3.0 (s, 3H), 2.77 (s, 3H) ppm.

6. References

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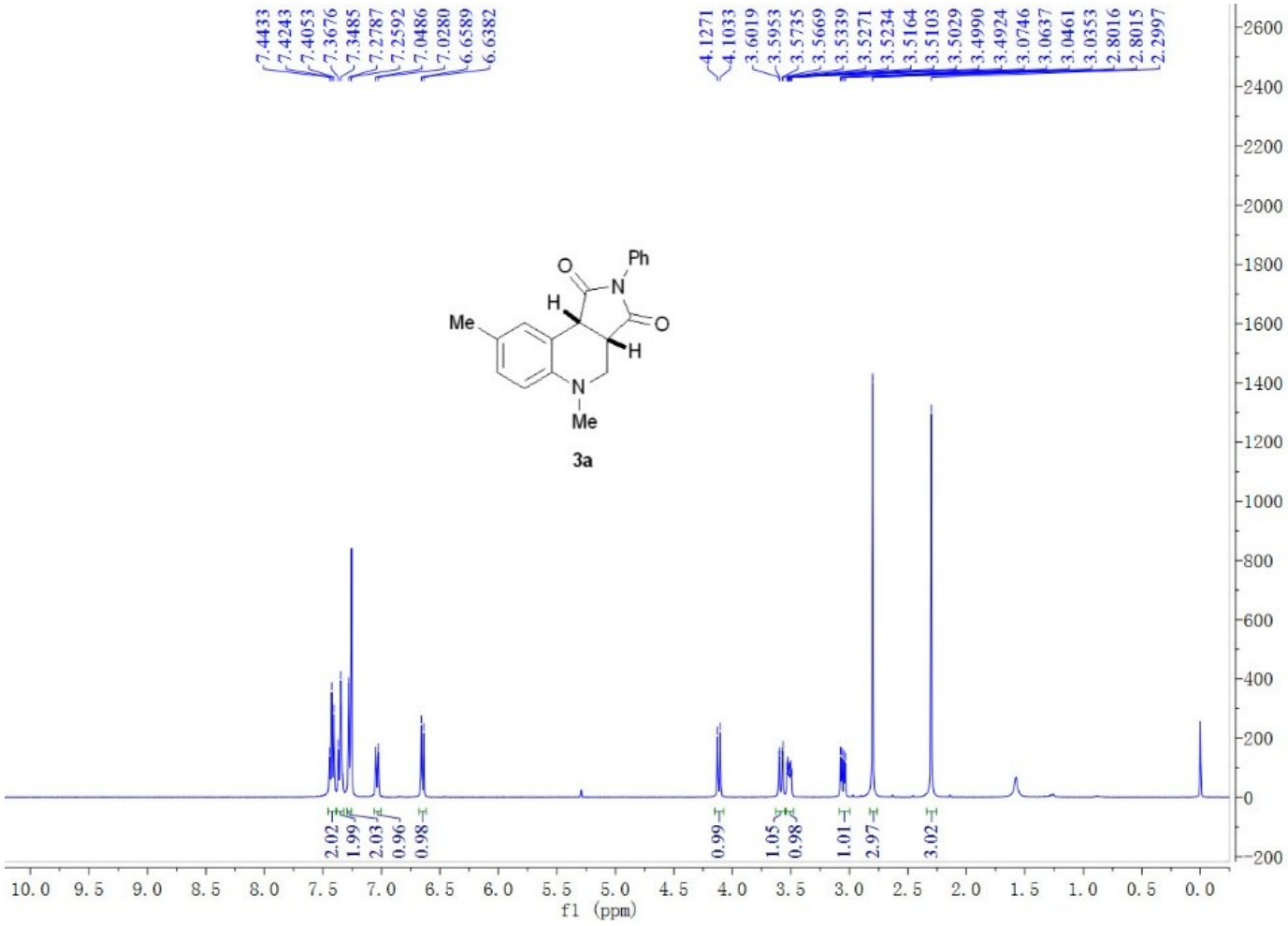
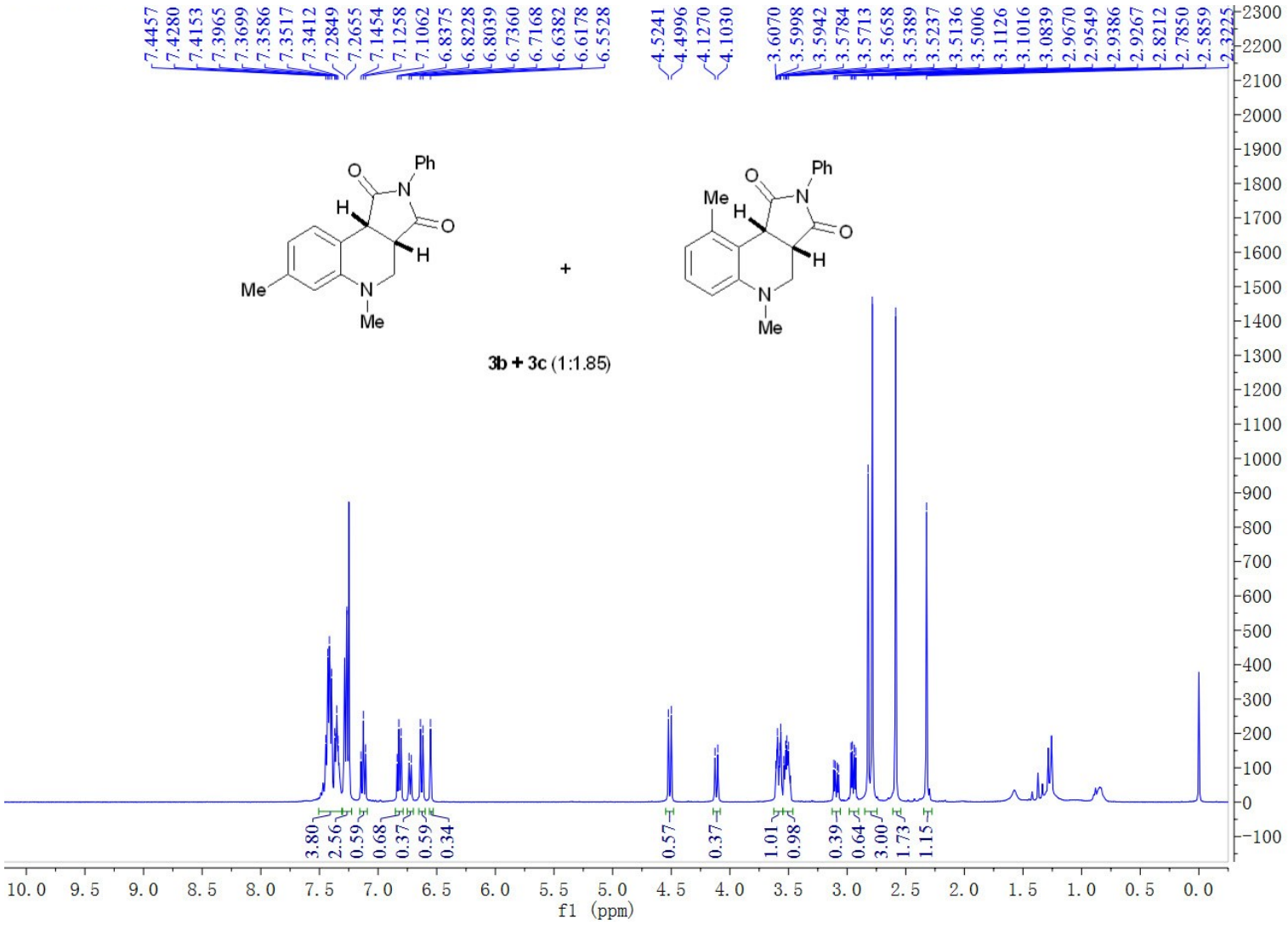
7. Copies of ^{1}H NMR, ^{13}C NMR and HRMS Spectra

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N
Me
+
Me
3b + 3c (1:1.85)
3.80
2.56
0.59
0.68
0.37
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0.34
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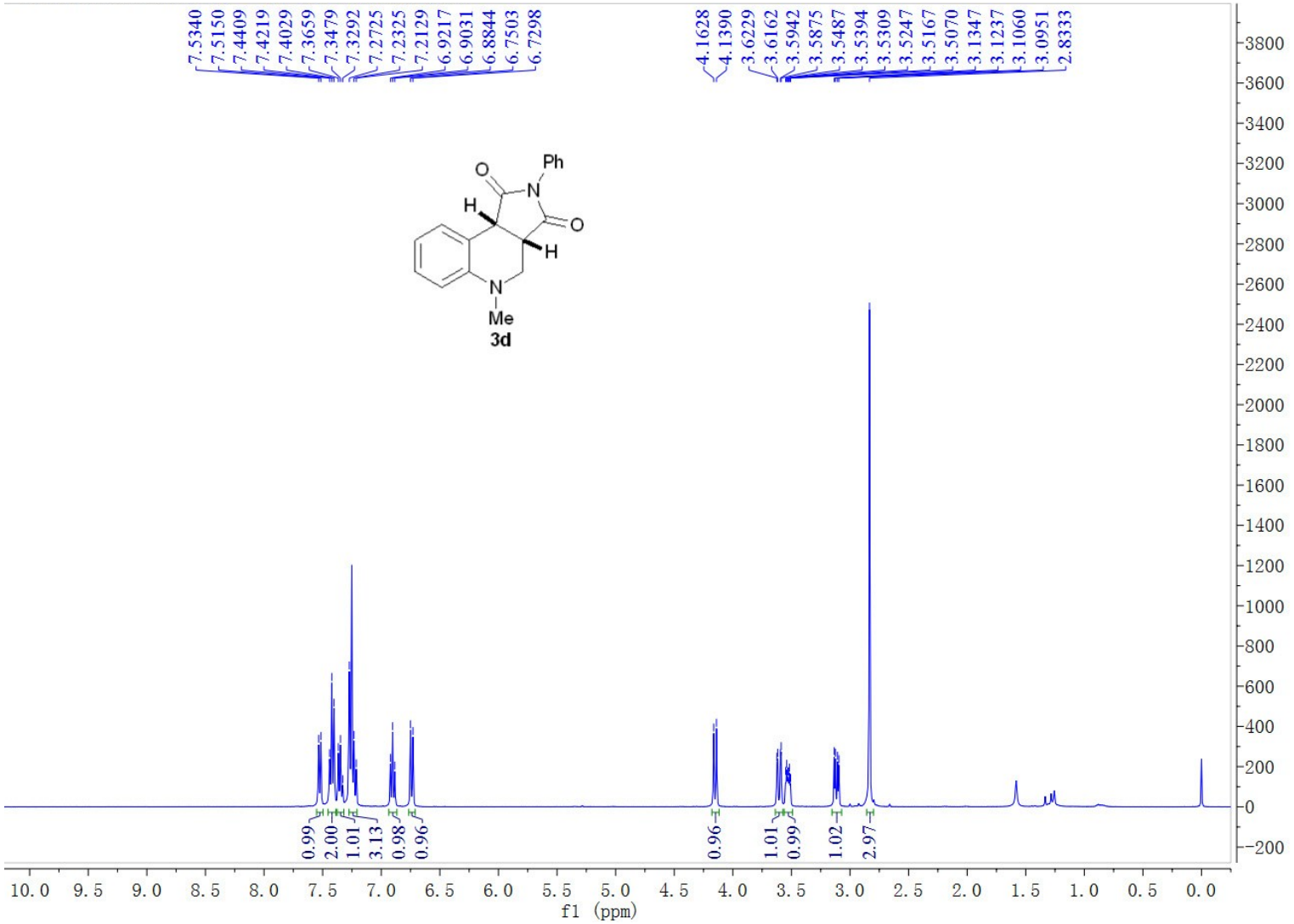
1.15
f1 (ppm)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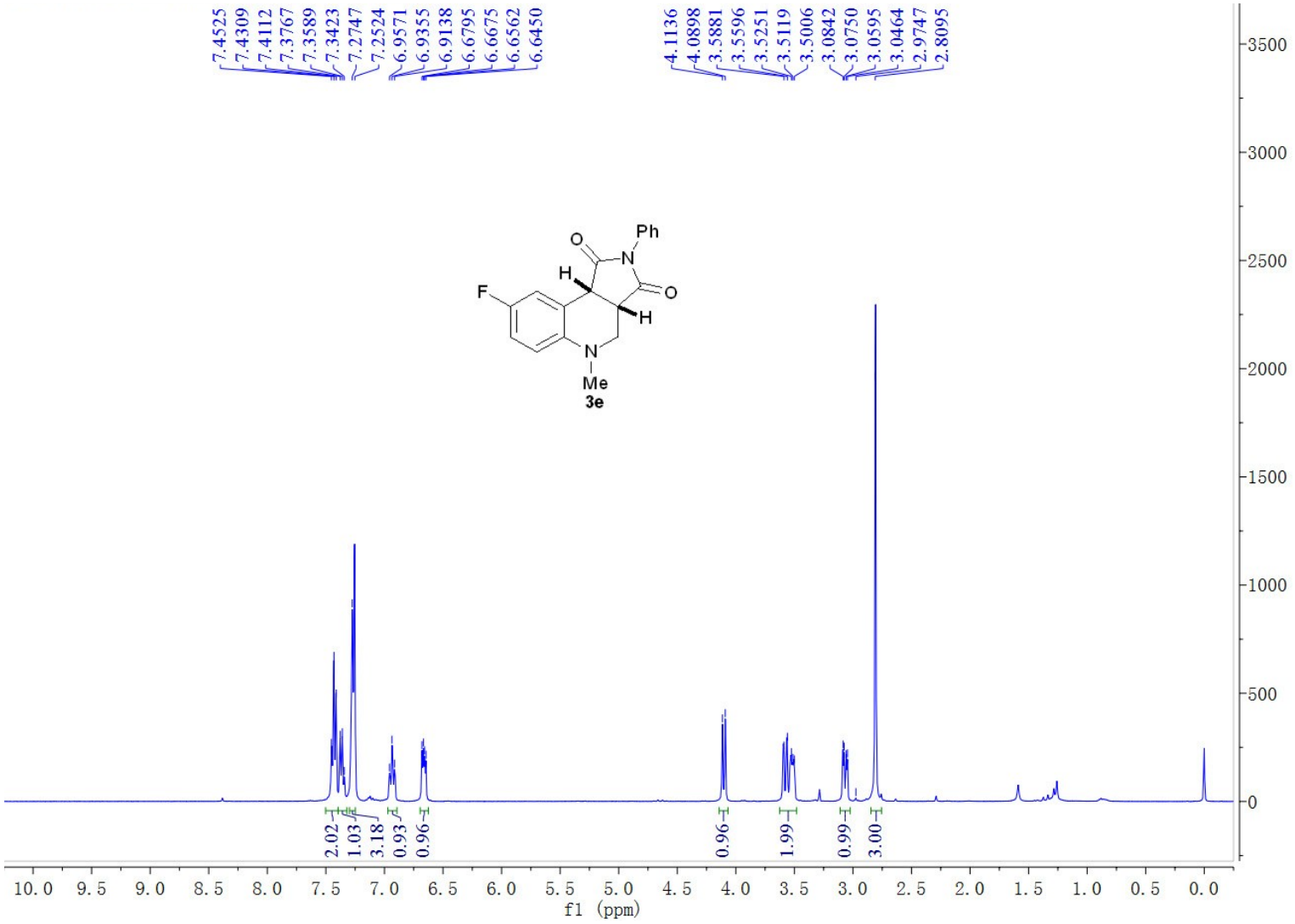
2.97
f1 (ppm)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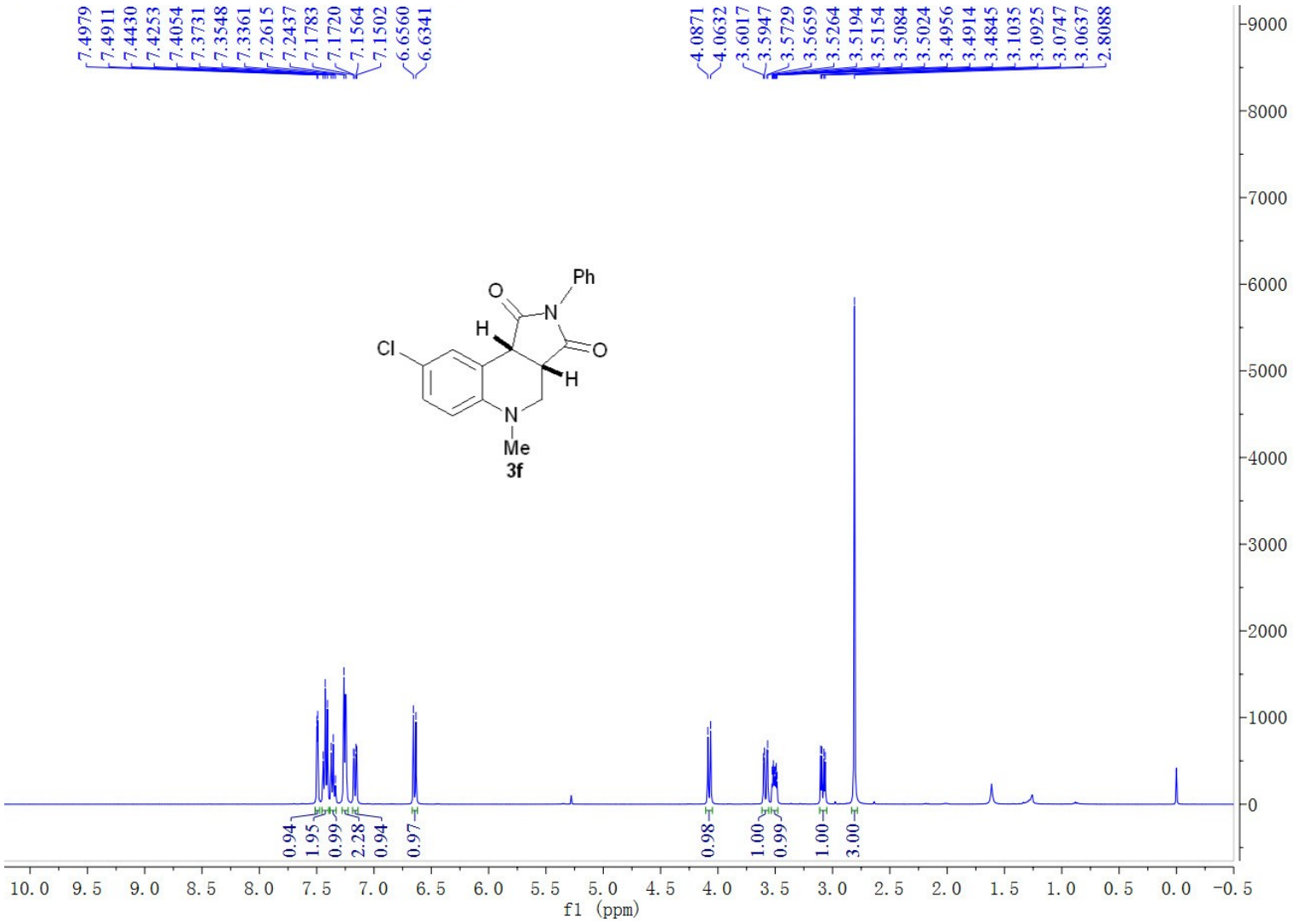
f1 (ppm)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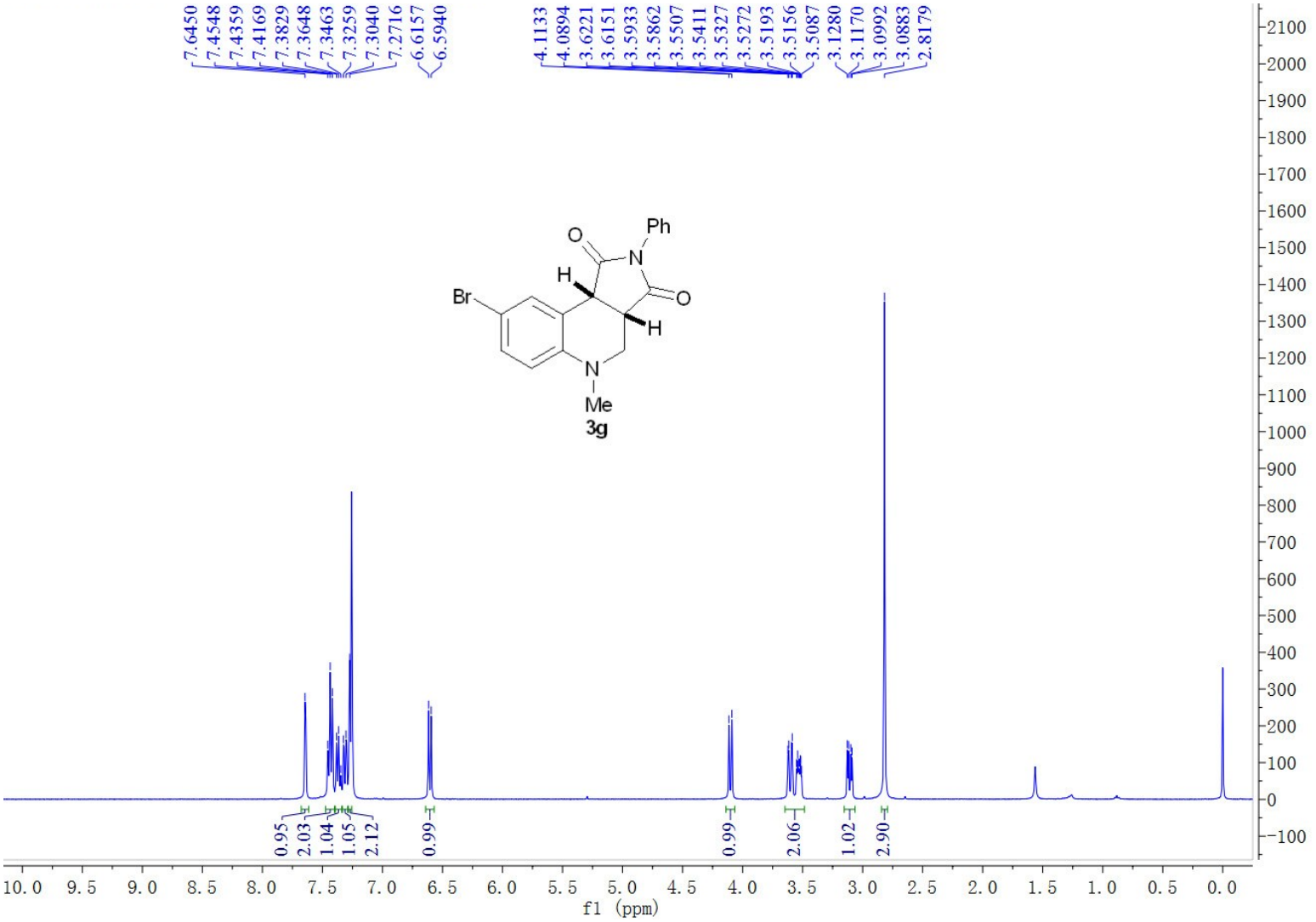
f1 (ppm)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N
Me
3g
0.95
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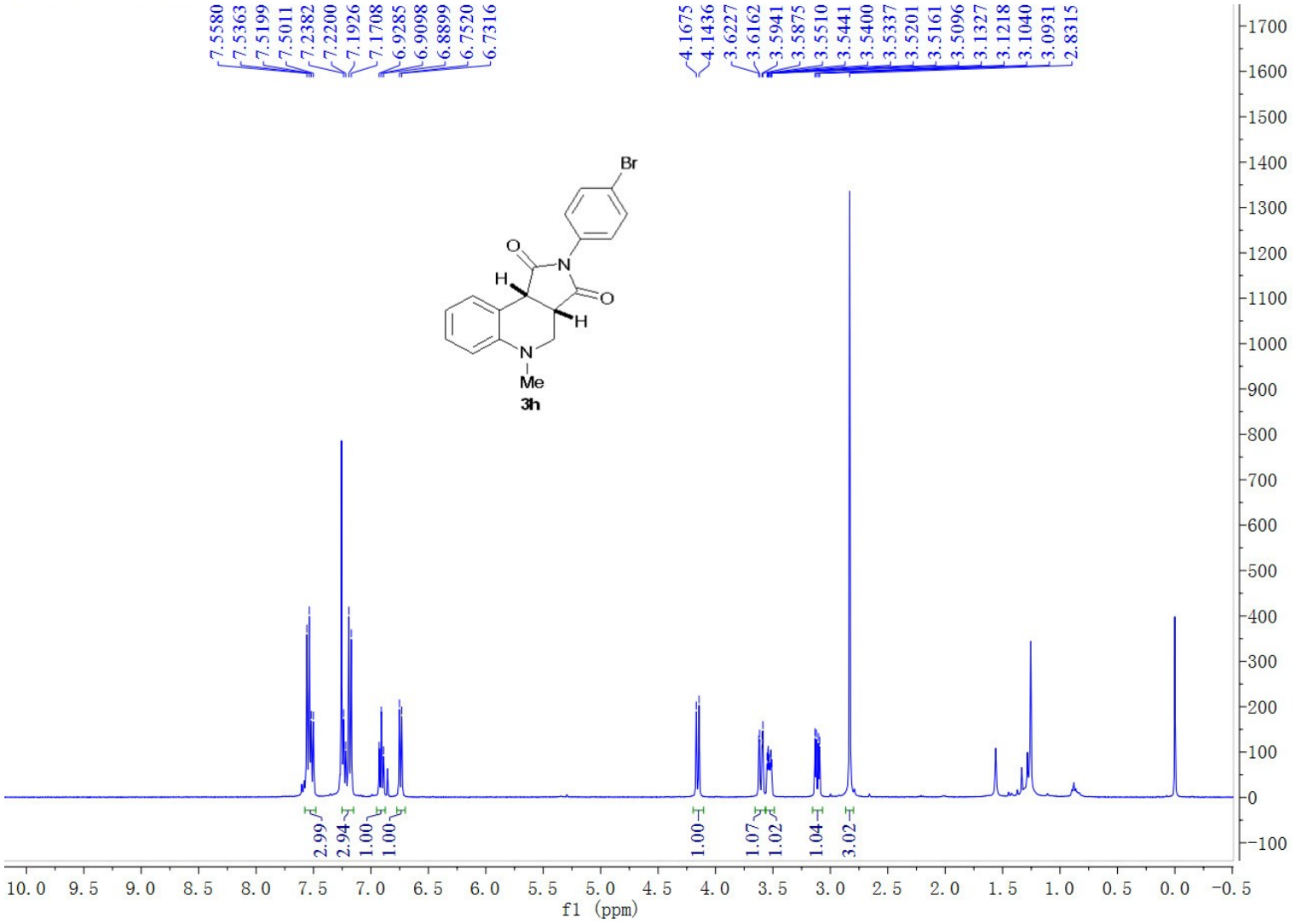
1.04
1.05
2.12
0.99
0.99
2.06
1.02
2.90
f1 (ppm)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7.5199
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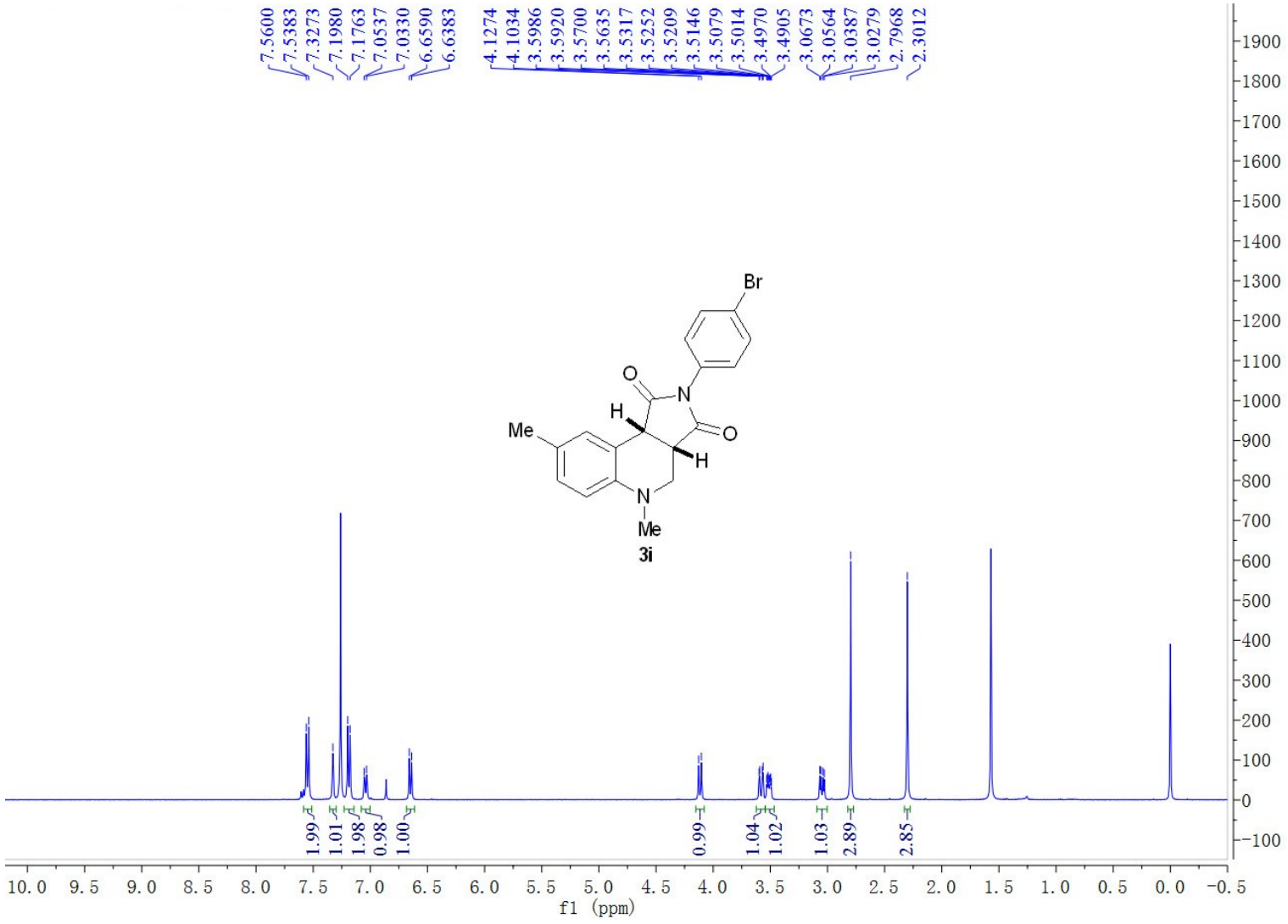
7.2382
7.2200
7.1926
7.1708
6.9285
6.9098
6.8899
6.7520
6.7316
4.1675
4.1436
3.6227
3.6162
3.5941
3.5875
3.5510
3.5441
3.5400
3.5337
3.5201
3.5161
3.5096
3.1327
3.1218
3.1040
3.0931
2.8315
Br
O
N
H
O
H
N
Me
3h
2.99
2.94
1.00
1.00
1.00
1.07
1.02
1.04
3.02
f1 (ppm)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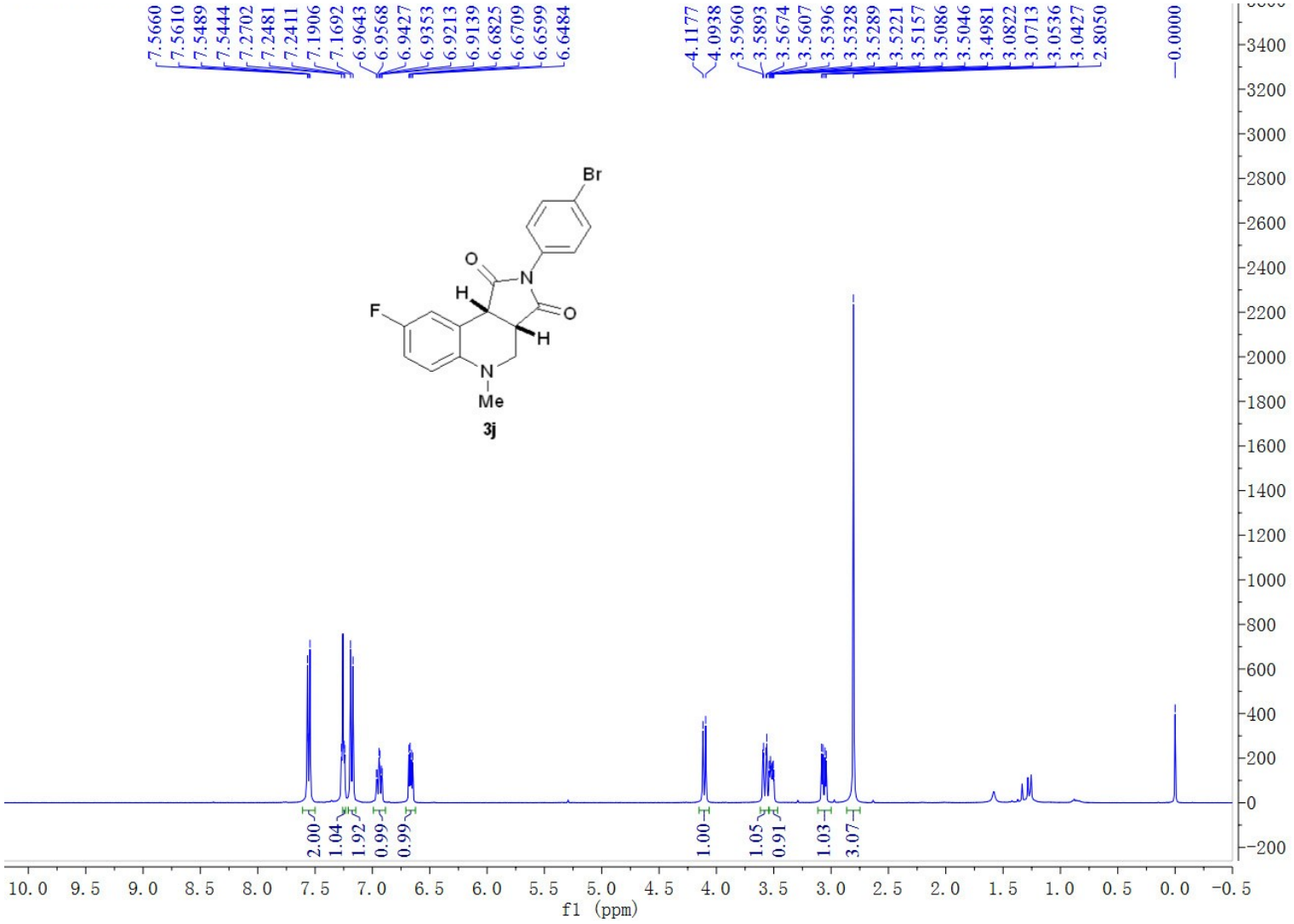
7.5383
7.3273
7.1980
7.1763
7.0537
7.0330
6.6590
6.6383
4.1274
4.1034
3.5986
3.5920
3.5700
3.5635
3.5317
3.5252
3.5209
3.5146
3.5079
3.5014
3.4970
3.4905
3.0673
3.0564
3.0387
3.0279
2.7968
2.3012
Br
O
N
H
Me
O
H
N
Me
3i
1.99
1.01
1.98
0.98
1.00
0.99
1.04
1.02
1.03
2.89
2.85
f1 (ppm)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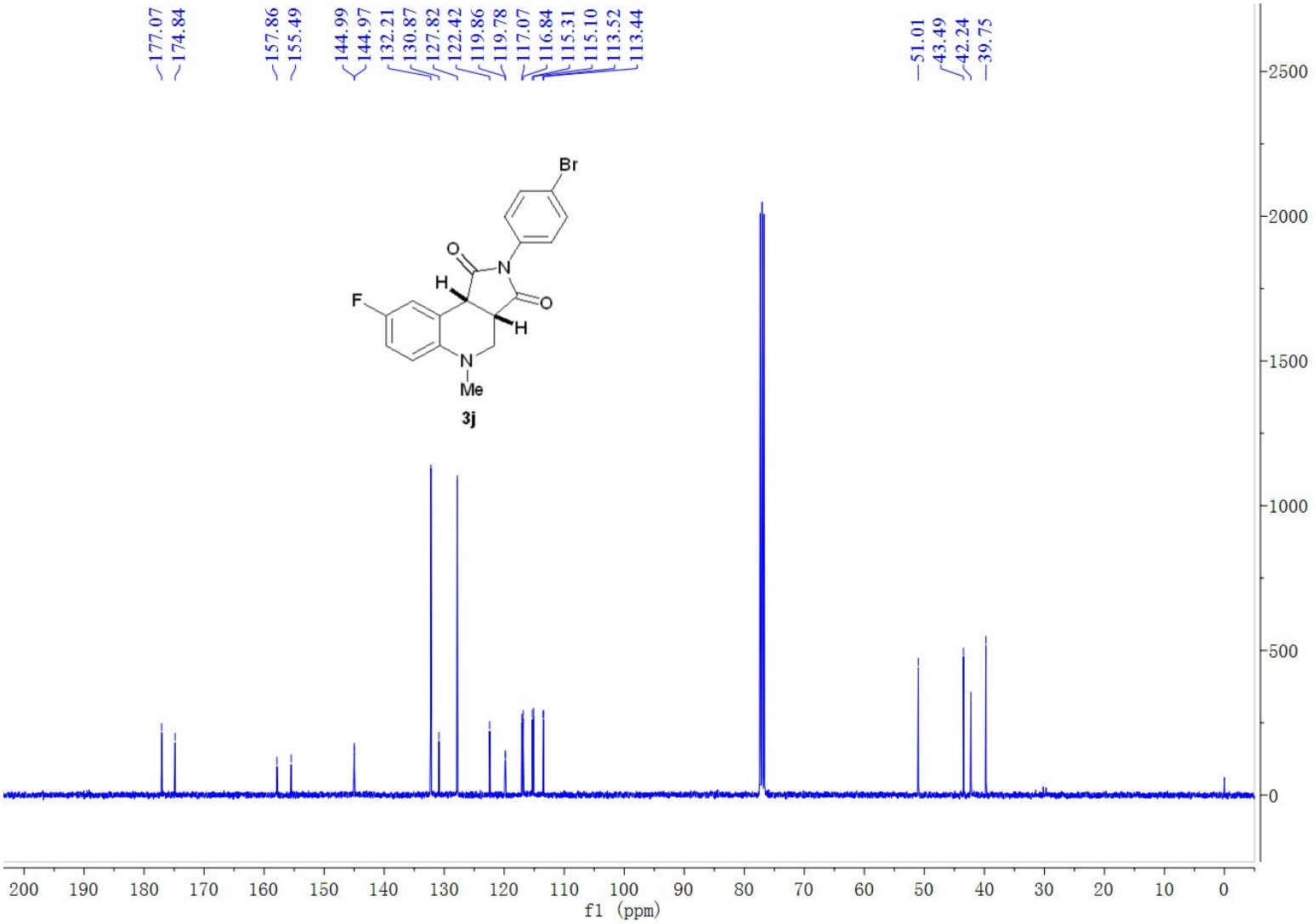
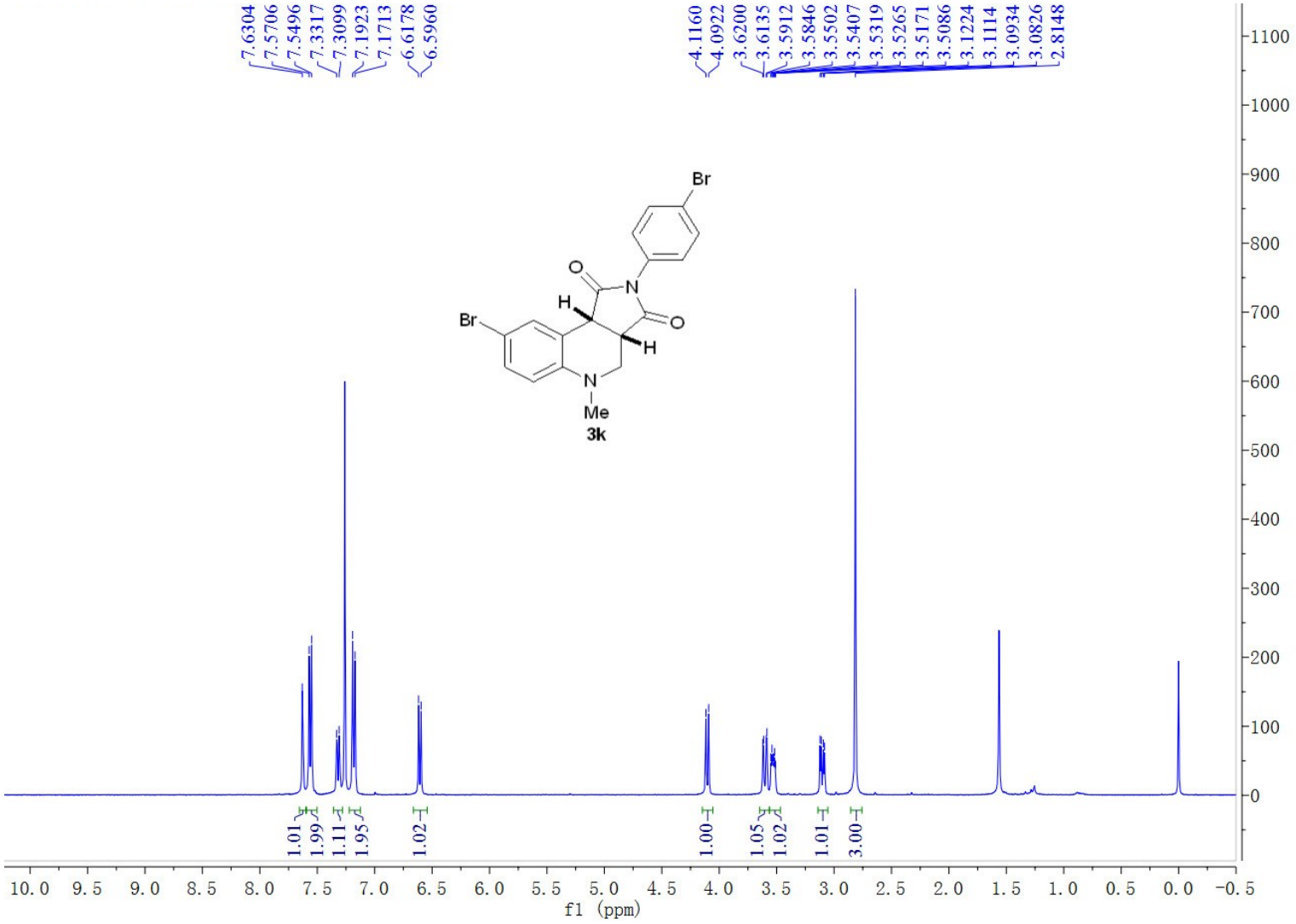
7.5489
7.5444
7.2702
7.2481
7.2411
7.1906
7.1692
6.9643
6.9568
6.9427
6.9353
6.9213
6.9139
6.6825
6.6709
6.6599
6.6484
4.1177
4.0938
3.5960
3.5893
3.5674
3.5607
3.5396
3.5328
3.5289
3.5221
3.5157
3.5086
3.5046
3.4981
3.0822
3.0713
3.0536
3.0427
2.8050
0.0000
Br
O
N
H
O
F
H
N
Me
3j
2.00
1.04
1.92
0.99
0.99
1.00
1.05
0.91
1.03
3.07
f1 (ppm)


177.07
174.84
157.86
155.49
144.99
144.97
132.21
130.87
127.82
122.42
119.86
119.78
117.07
116.84
115.31
115.10
113.52
113.44
51.01
43.49
42.24
39.75
Br
O
N
H
O
F
H
N
Me
3j
2500
2000
1500
1000
500
0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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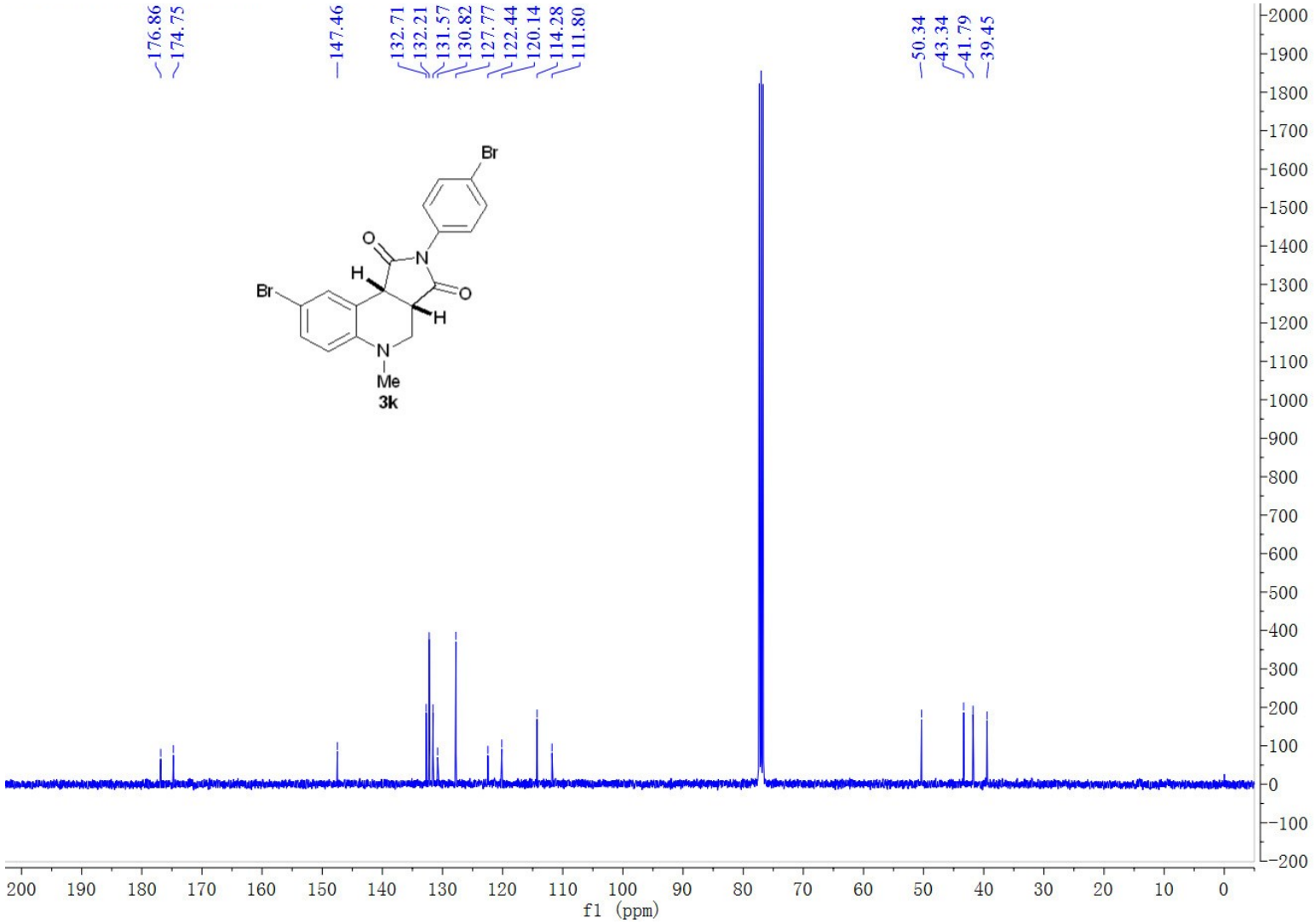
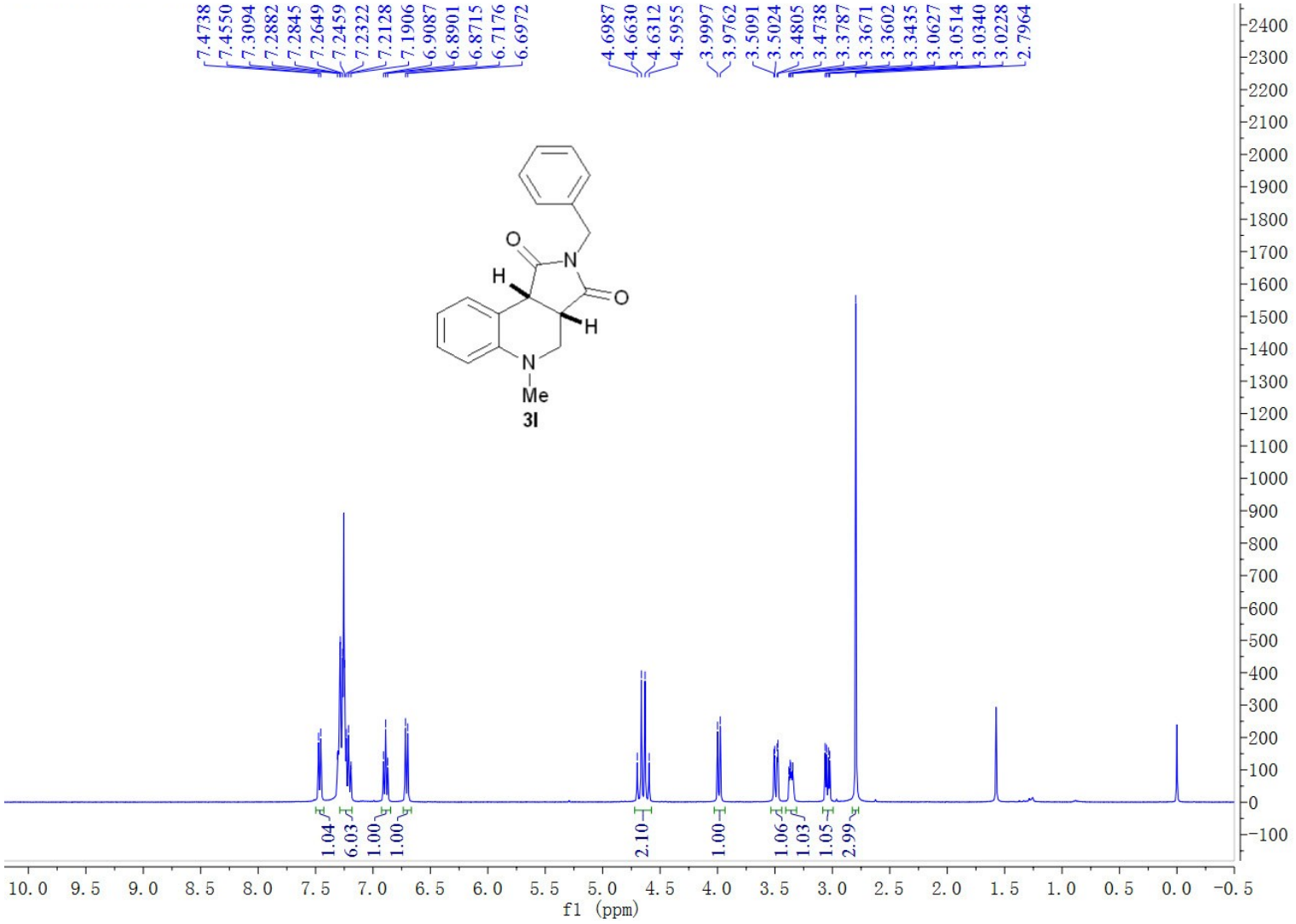
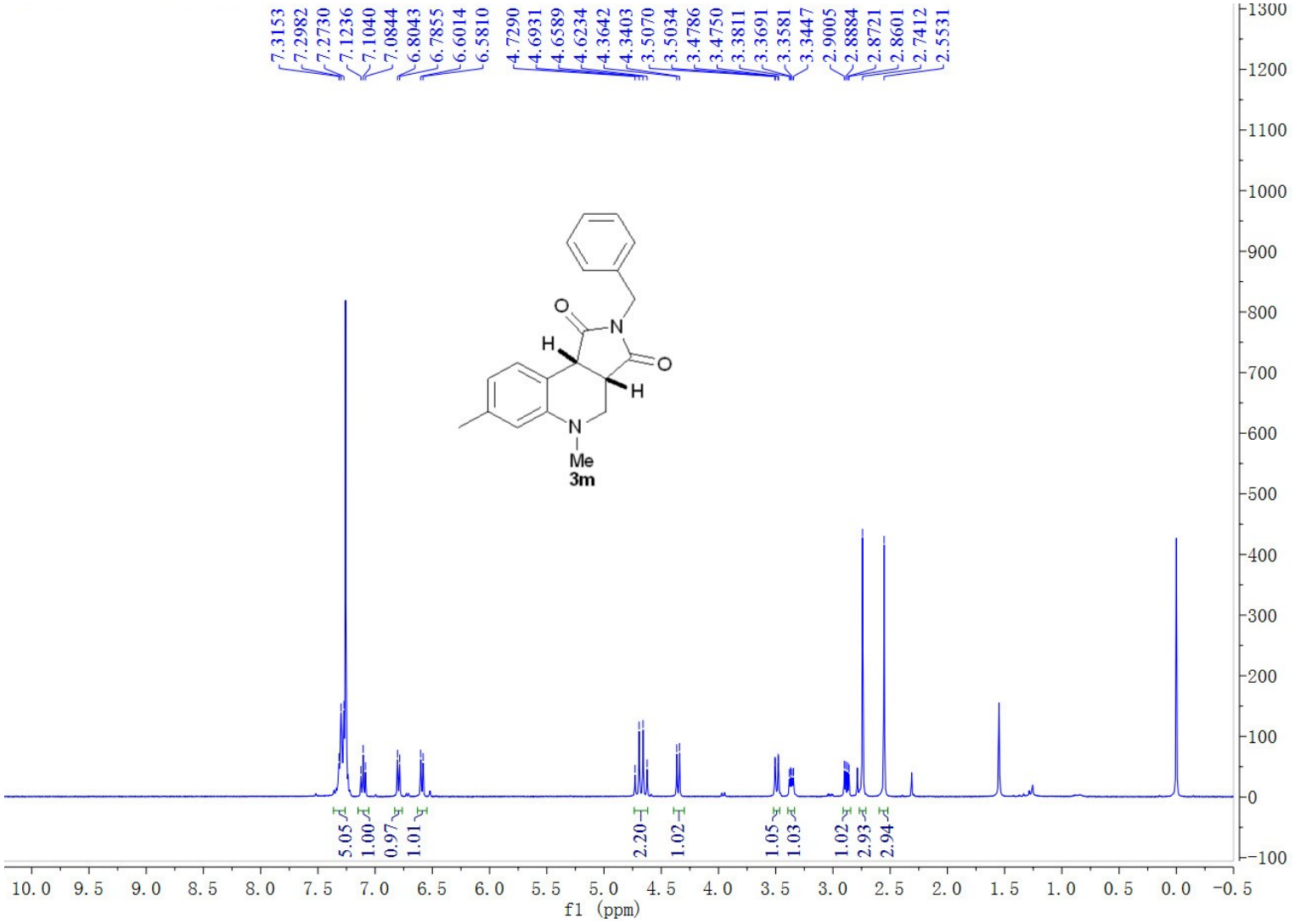
7.5706
7.5496
7.3317
7.3099
7.1923
7.1713
6.6178
6.5960
4.1160
4.0922
3.6200
3.6135
3.5912
3.5846
3.5502
3.5407
3.5319
3.5265
3.5171
3.5086
3.1224
3.1114
3.0934
3.0826
2.8148
Br
O
N
H
O
Br
H
N
Me
3k
1.01
1.99
1.11
1.95
1.02
1.00
1.05
1.02
1.01
3.00
f1 (ppm)


176.86
174.75
147.46
132.71
132.21
131.57
130.82
127.77
122.44
120.14
114.28
111.80
50.34
43.34
41.79
39.45
Br
O
N
H
O
Br
H
N
Me
3k
f1 (ppm)


7.4738
7.4550
7.3094
7.2882
7.2845
7.2649
7.2459
7.2322
7.2128
7.1906
6.9087
6.8901
6.8715
6.7176
6.6972
4.6987
4.6630
4.6312
4.5955
3.9997
3.9762
3.5091
3.5024
3.4805
3.4738
3.3787
3.3671
3.3602
3.3435
3.0627
3.0514
3.0340
3.0228
2.7964
O
N
H
O
H
N
Me
3l
1.04
6.03
1.00
1.00
2.10
1.00
1.06
1.03
1.05
2.99
f1 (ppm)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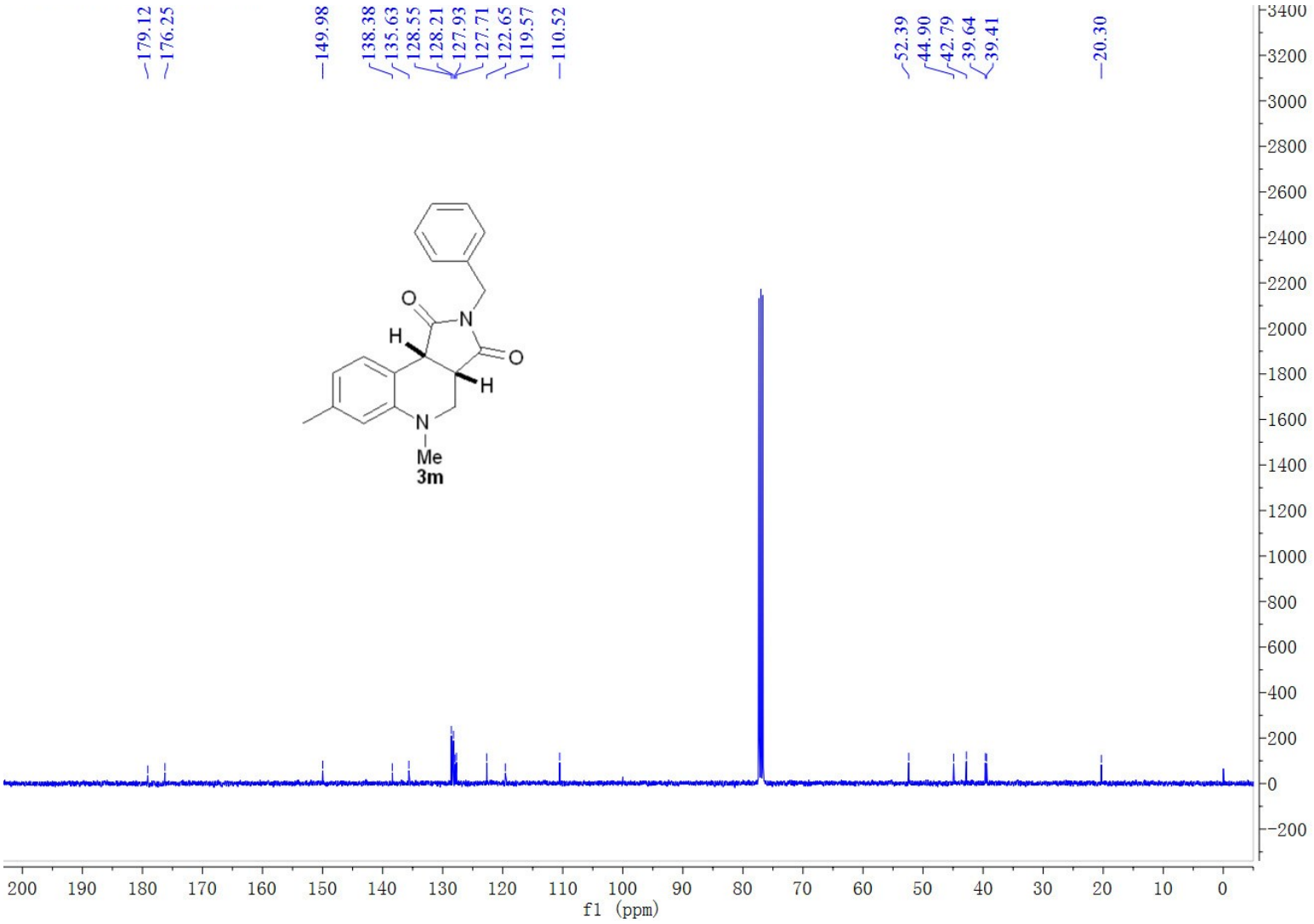
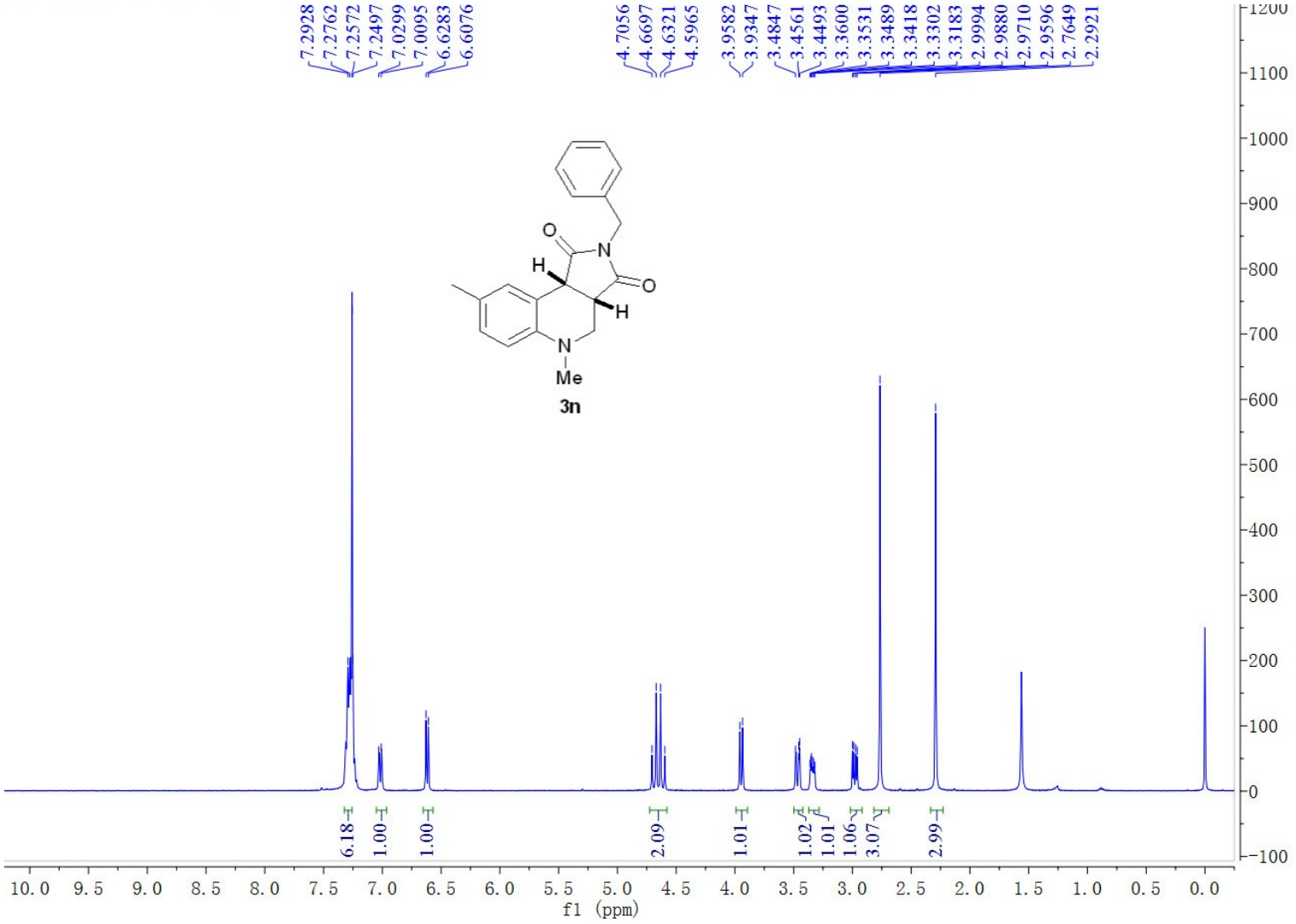
7.2982
7.2730
7.1236
7.1040
7.0844
6.8043
6.7855
6.6014
6.5810
4.7290
4.6931
4.6589
4.6234
4.3642
4.3403
3.5070
3.5034
3.4786
3.4750
3.3811
3.3691
3.3581
3.3447
2.9005
2.8884
2.8721
2.8601
2.7412
2.5531
O
N
H
O
H
N
Me
3m
5.05
1.00
0.97
1.01
2.20
1.02
1.05
1.03
1.02
2.93
2.94
f1 (ppm)


179.12
176.25
149.98
138.38
135.63
128.55
128.21
127.93
127.71
122.65
119.57
110.52
52.39
44.90
42.79
39.64
39.41
20.30
O
N
H
O
H
N
Me
3m
f1 (ppm)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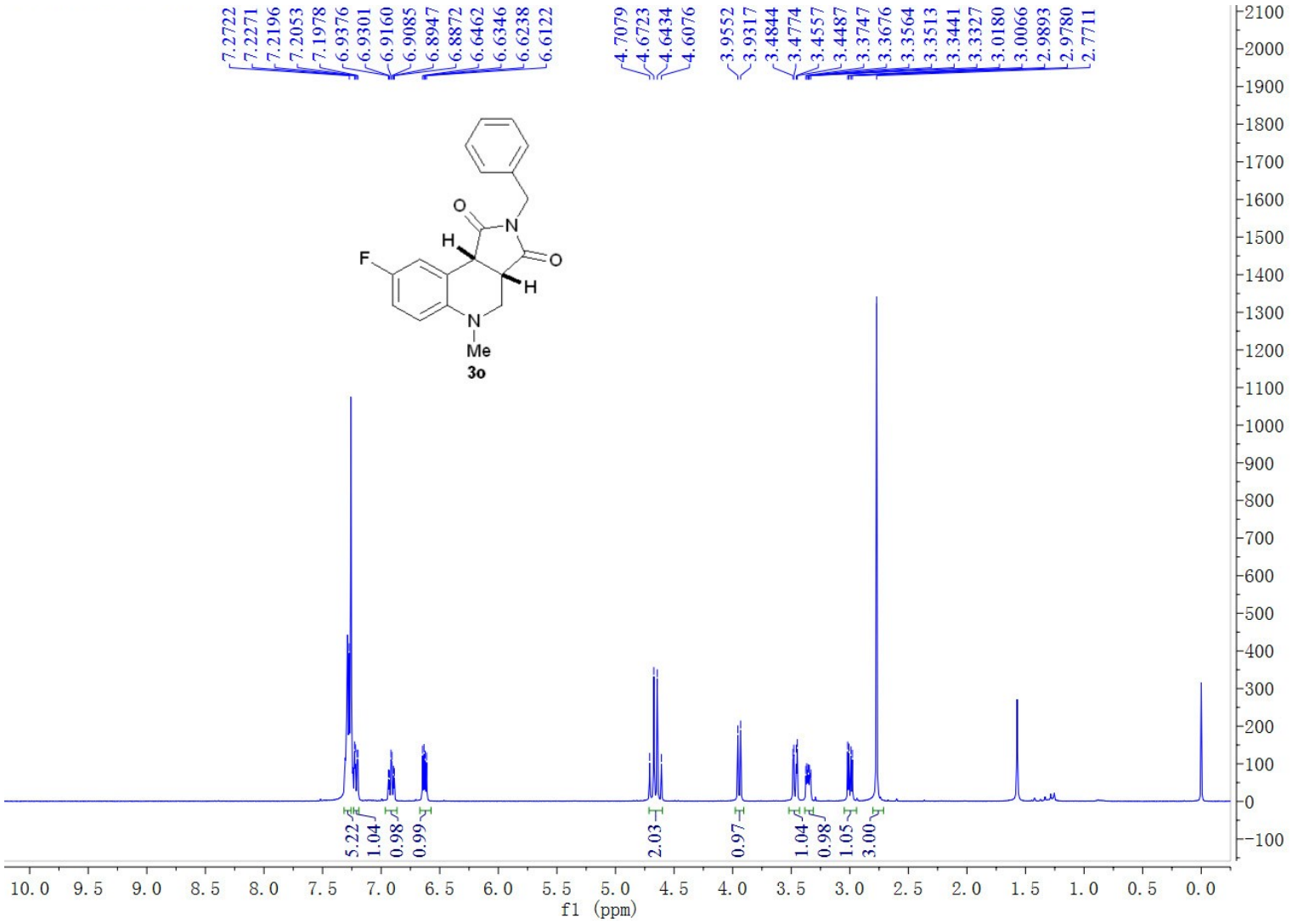
7.2762
7.2572
7.2497
7.0299
7.0095
6.6283
6.6076
4.7056
4.6697
4.6321
4.5965
3.9582
3.9347
3.4847
3.4561
3.4493
3.3600
3.3531
3.3489
3.3418
3.3302
3.3183
2.9994
2.9880
2.9710
2.9596
2.7649
2.2921
O
N
H
O
H
N
Me
3n
6.18
1.00
1.00
2.09
1.01
1.02
1.01
1.06
3.07
2.99
f1 (ppm)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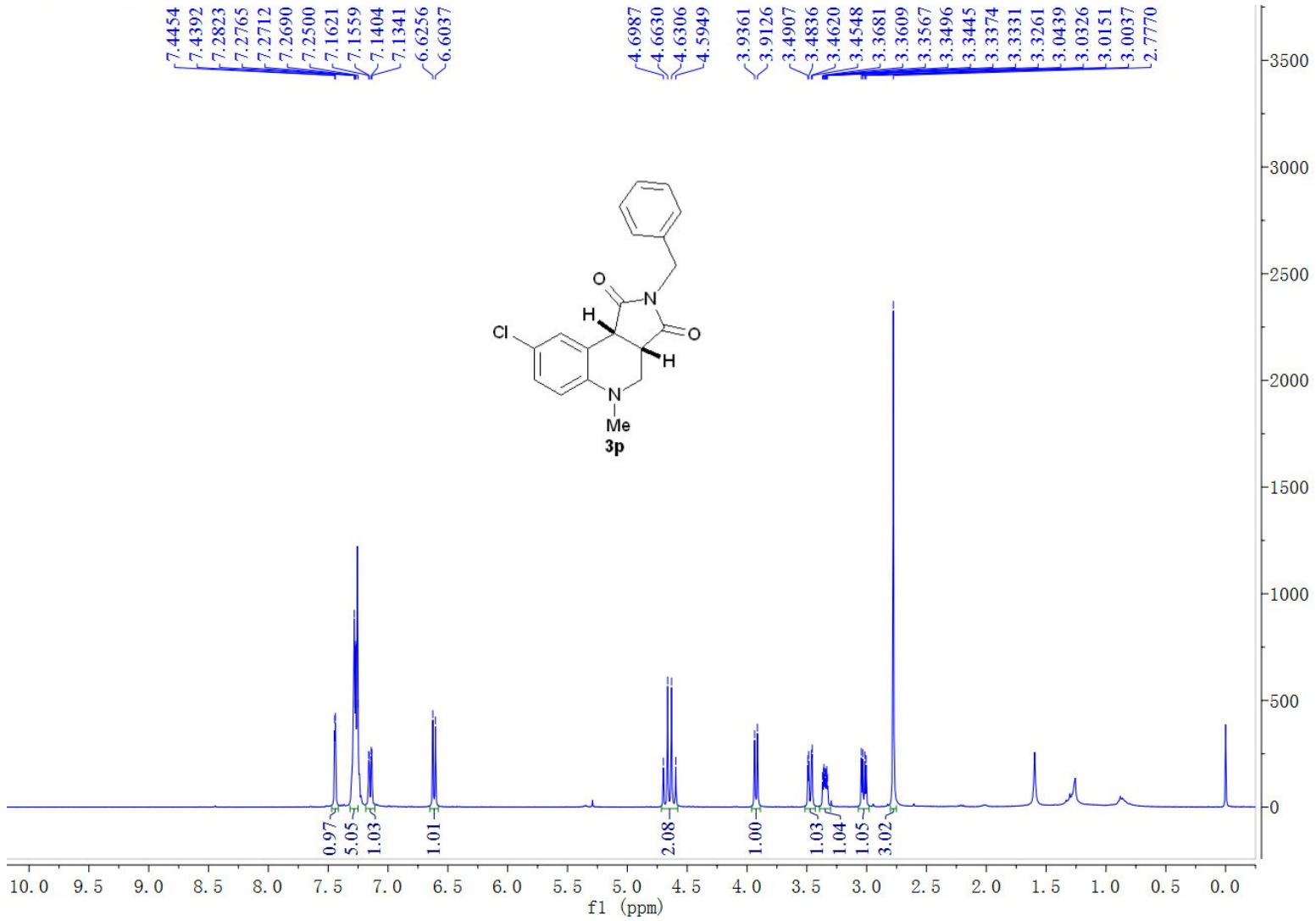
7.2196
7.2053
7.1978
6.9376
6.9301
6.9160
6.9085
6.8947
6.8872
6.6462
6.6346
6.6238
6.6122
4.7079
4.6723
4.6434
4.6076
3.9552
3.9317
3.4844
3.4774
3.4557
3.4487
3.3747
3.3676
3.3564
3.3513
3.3441
3.3327
3.0180
3.0066
2.9893
2.9780
2.7711
O
N
H
F
O
H
N
Me
3o
5.22
1.04
0.98
0.99
2.03
0.97
1.04
0.98
1.05
3.00
f1 (ppm)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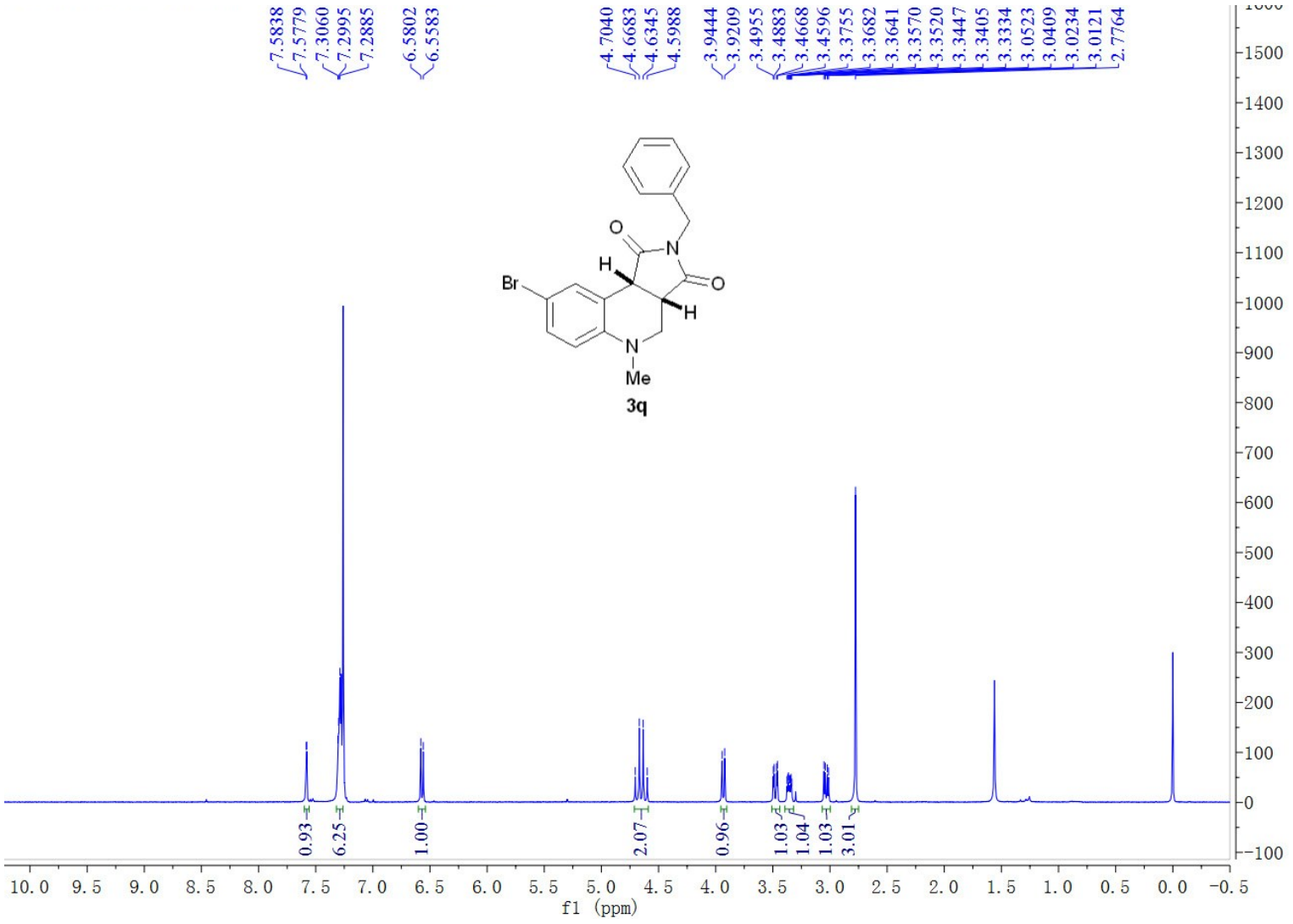
7.2823
7.2765
7.2712
7.2690
7.2500
7.1621
7.1559
7.1404
7.1341
6.6256
6.6037
4.6987
4.6630
4.6306
4.5949
3.9361
3.9126
3.4907
3.4836
3.4620
3.4548
3.3681
3.3609
3.3567
3.3496
3.3445
3.3374
3.3331
3.3261
3.0439
3.0326
3.0151
3.0037
2.7770
O
N
H
O
Cl
H
N
Me
3p
0.97
5.05
1.03
1.01
2.08
1.00
1.03
1.04
1.05
3.02
3500
3000
2500
2000
1500
1000
500
0
10.0 9.5 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 0.0
f1 (ppm)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6.5802
6.5583
4.7040
4.6683
4.6345
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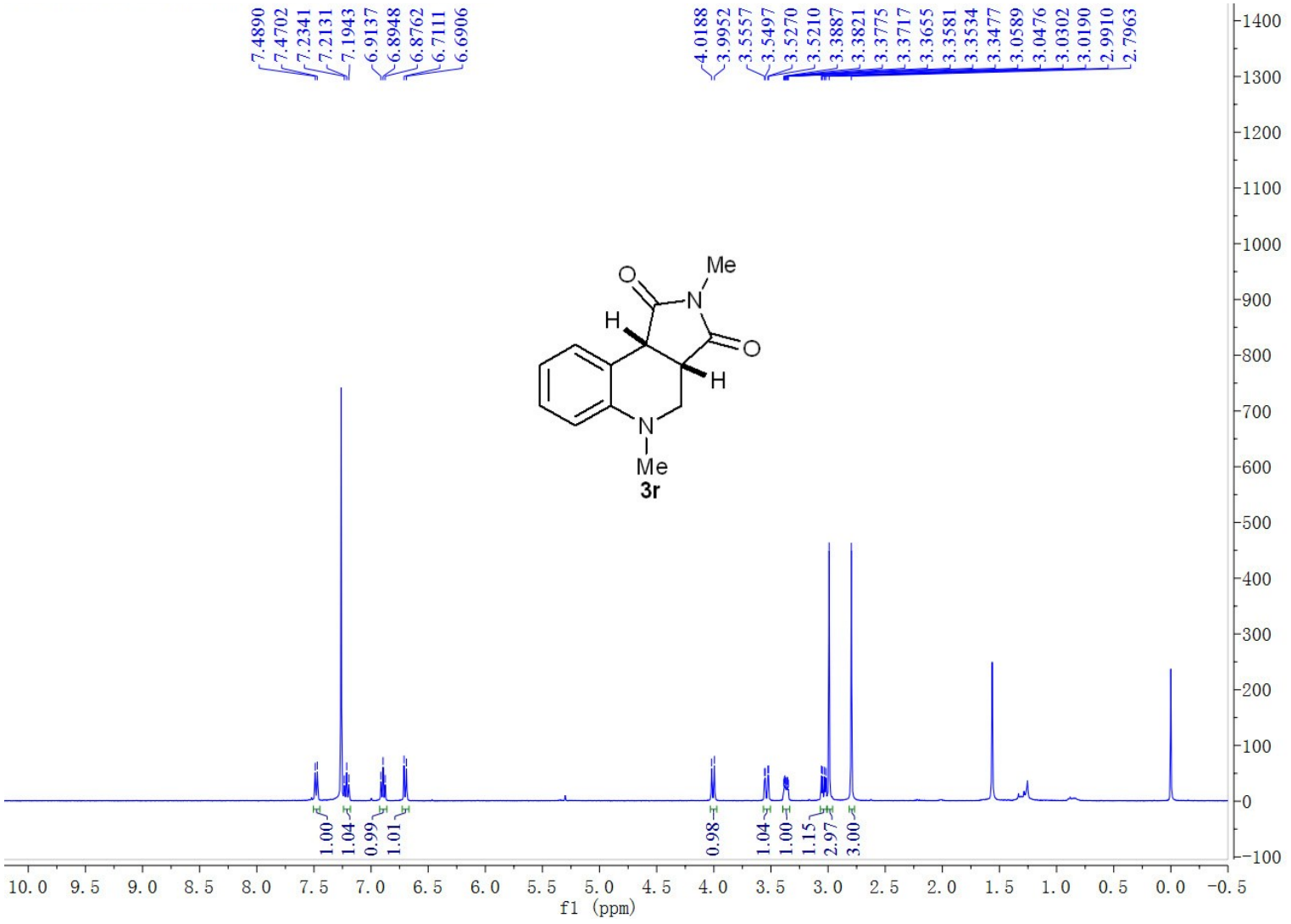
3.9444
3.9209
3.4955
3.4883
3.4668
3.4596
3.3755
3.3682
3.3641
3.3570
3.3520
3.3447
3.3405
3.3334
3.0523
3.0409
3.0234
3.0121
2.7764
Br
O
N
H
O
H
N
Me
3q
0.93
6.25
1.00
2.07
0.96
1.03
1.04
1.03
3.01
f1 (ppm)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7.1943
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6.8762
6.7111
6.6906
4.0188
3.9952
3.5557
3.5497
3.5270
3.5210
3.3887
3.3821
3.3775
3.3717
3.3655
3.3581
3.3534
3.3477
3.0589
3.0476
3.0302
3.0190
2.9910
2.7963
Me
O
N
H
O
H
N
Me
3r
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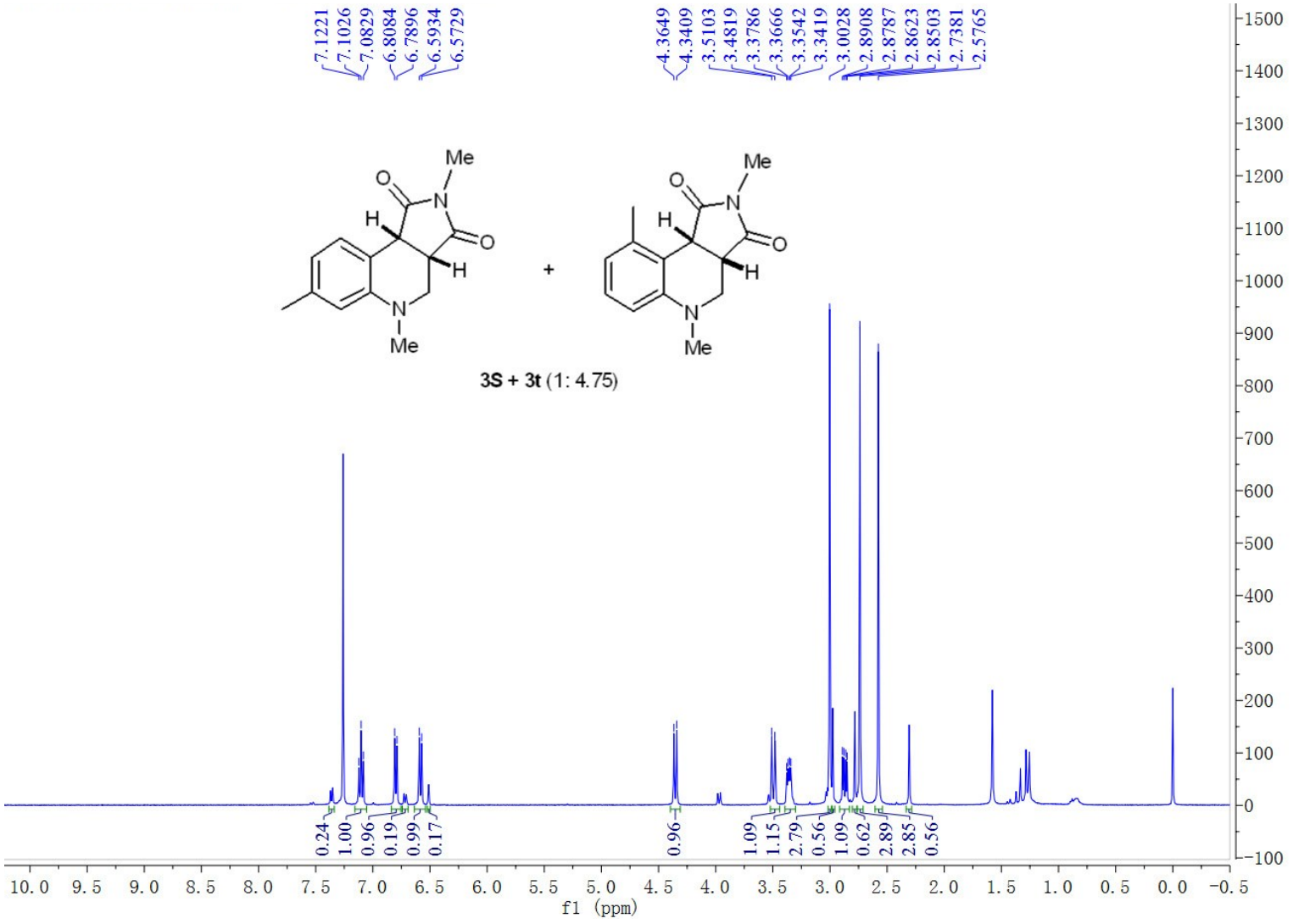
1.04
0.99
1.01
0.98
1.04
1.00
1.15
2.97
3.00
f1 (ppm)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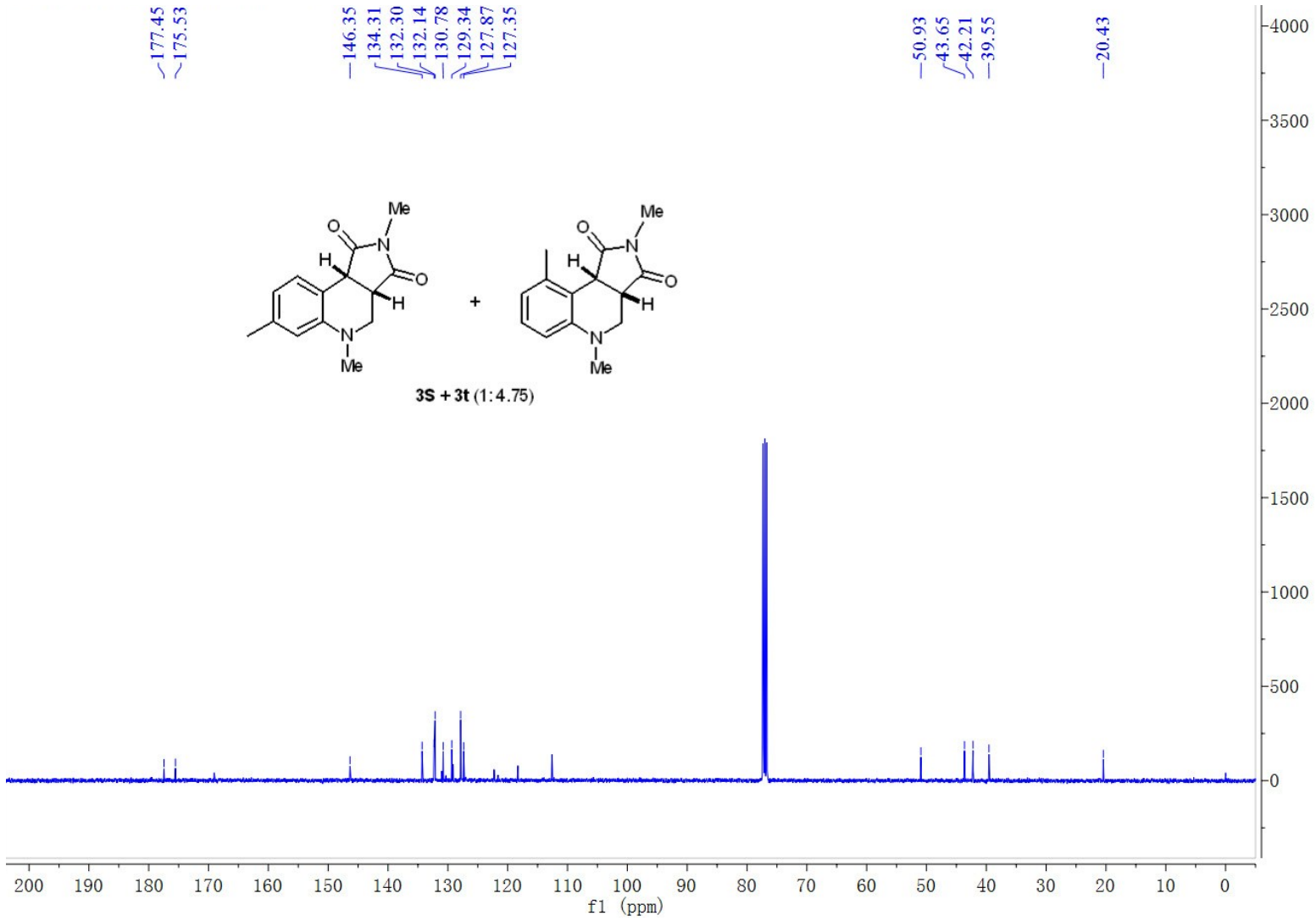
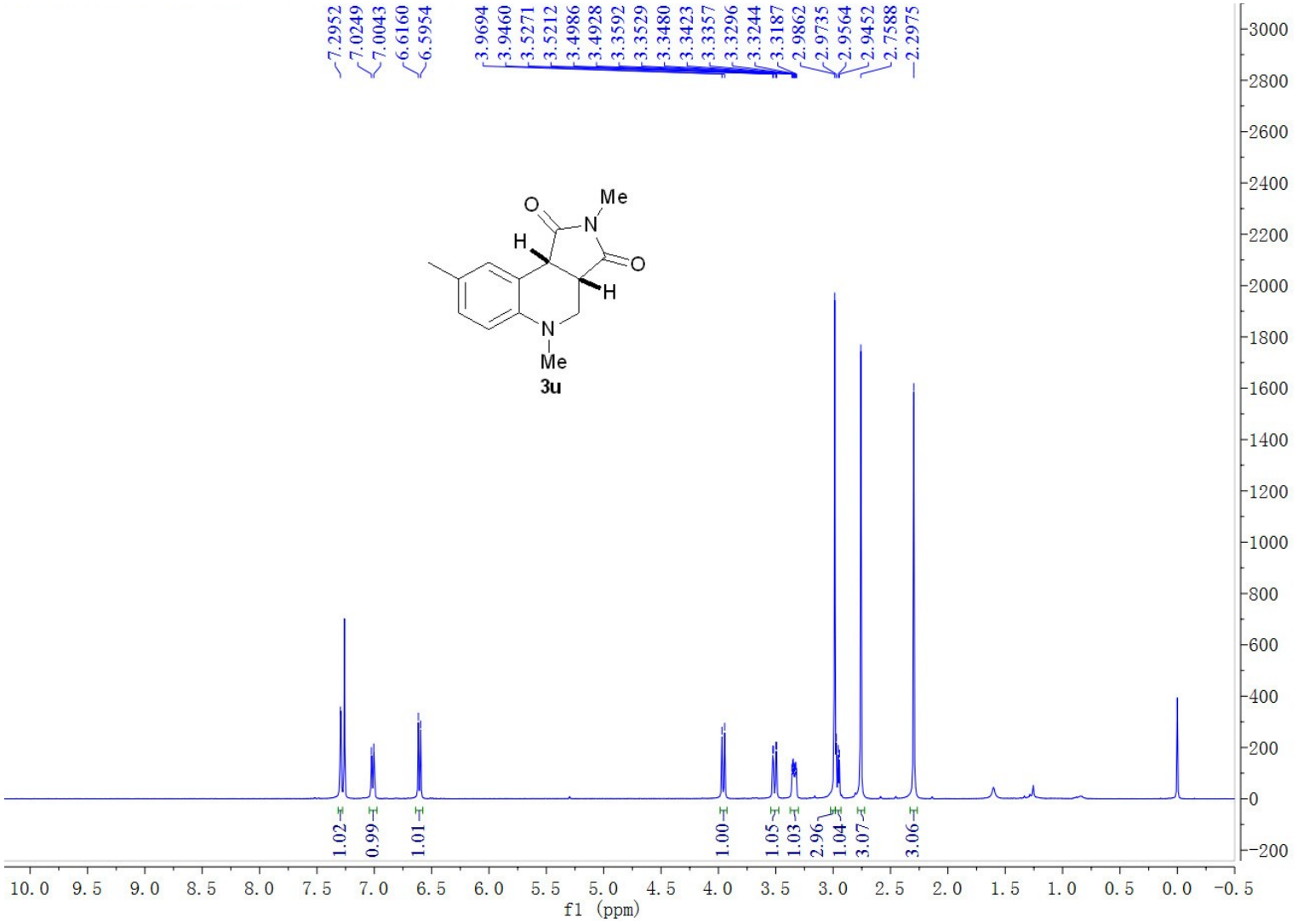
7.0829
6.8084
6.7896
6.5934
6.5729
4.3649
4.3409
3.5103
3.4819
3.3786
3.3666
3.3542
3.3419
3.0028
2.8908
2.8787
2.8623
2.8503
2.7381
2.5765
Me
O
N
H
O
H
N
Me
+
Me
O
N
H
O
H
N
Me
3S + 3t (1: 4.75)
0.24
1.00
0.96
0.19
0.99
0.17
0.96
1.09
1.15
2.79
0.56
1.09
0.62
2.89
2.85
0.56
f1 (ppm)


177.45
175.53
146.35
134.31
132.30
132.14
130.78
129.34
127.87
127.35
50.93
43.65
42.21
39.55
20.43
Me
O
N
H
O
H
N
Me
+
3S + 3t (1:4.75)
4000
3500
3000
2500
2000
1500
1000
500
0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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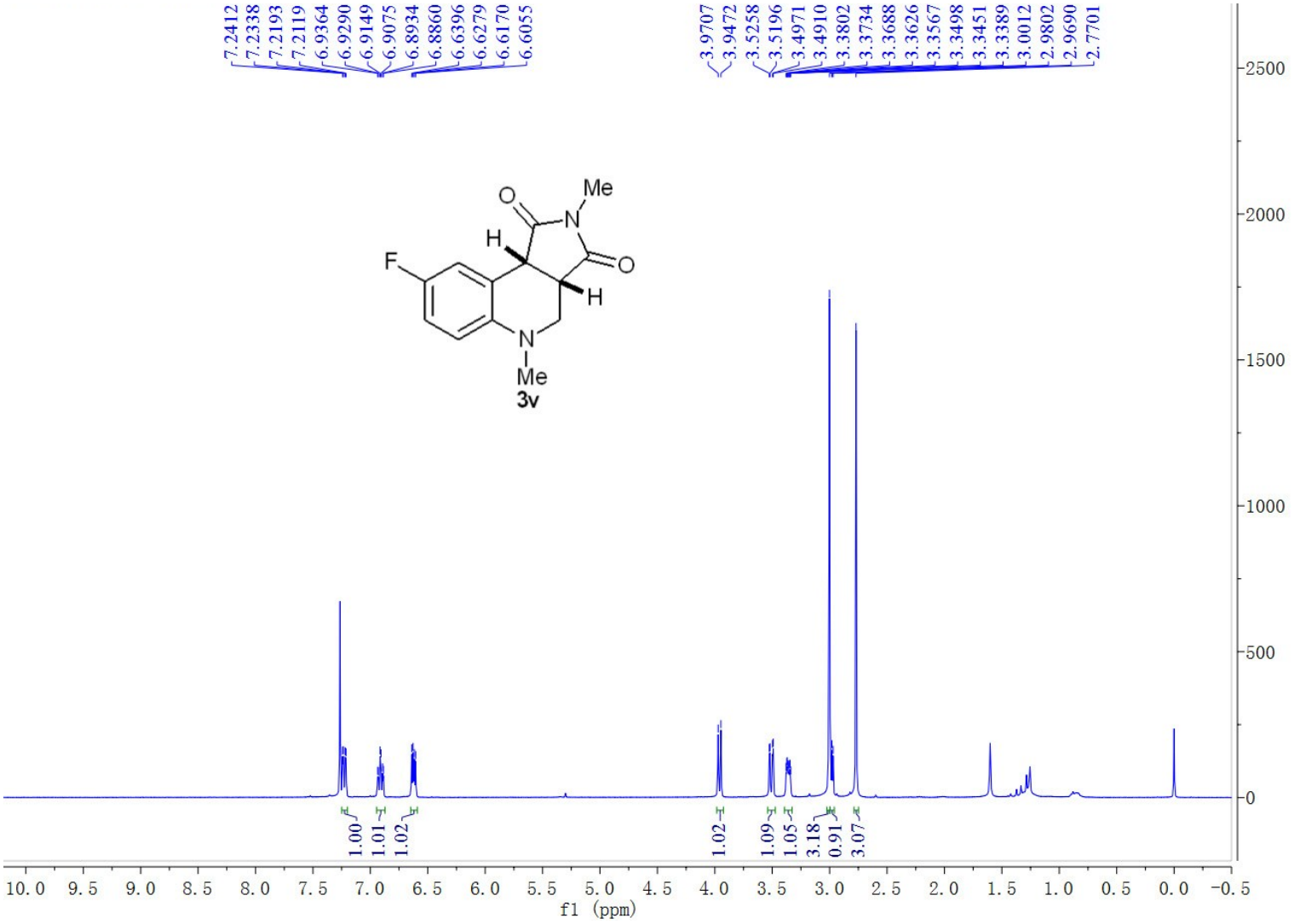
3.9460
3.5271
3.5212
3.4986
3.4928
3.3592
3.3529
3.3480
3.3423
3.3357
3.3296
3.3244
3.3187
2.9862
2.9735
2.9564
2.9452
2.7588
2.2975
O
N
Me
H
O
H
N
Me
3u
1.02
0.99
1.01
1.00
1.05
1.03
2.96
1.04
3.07
3.06
f1 (ppm)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6.9149
6.9075
6.8934
6.8860
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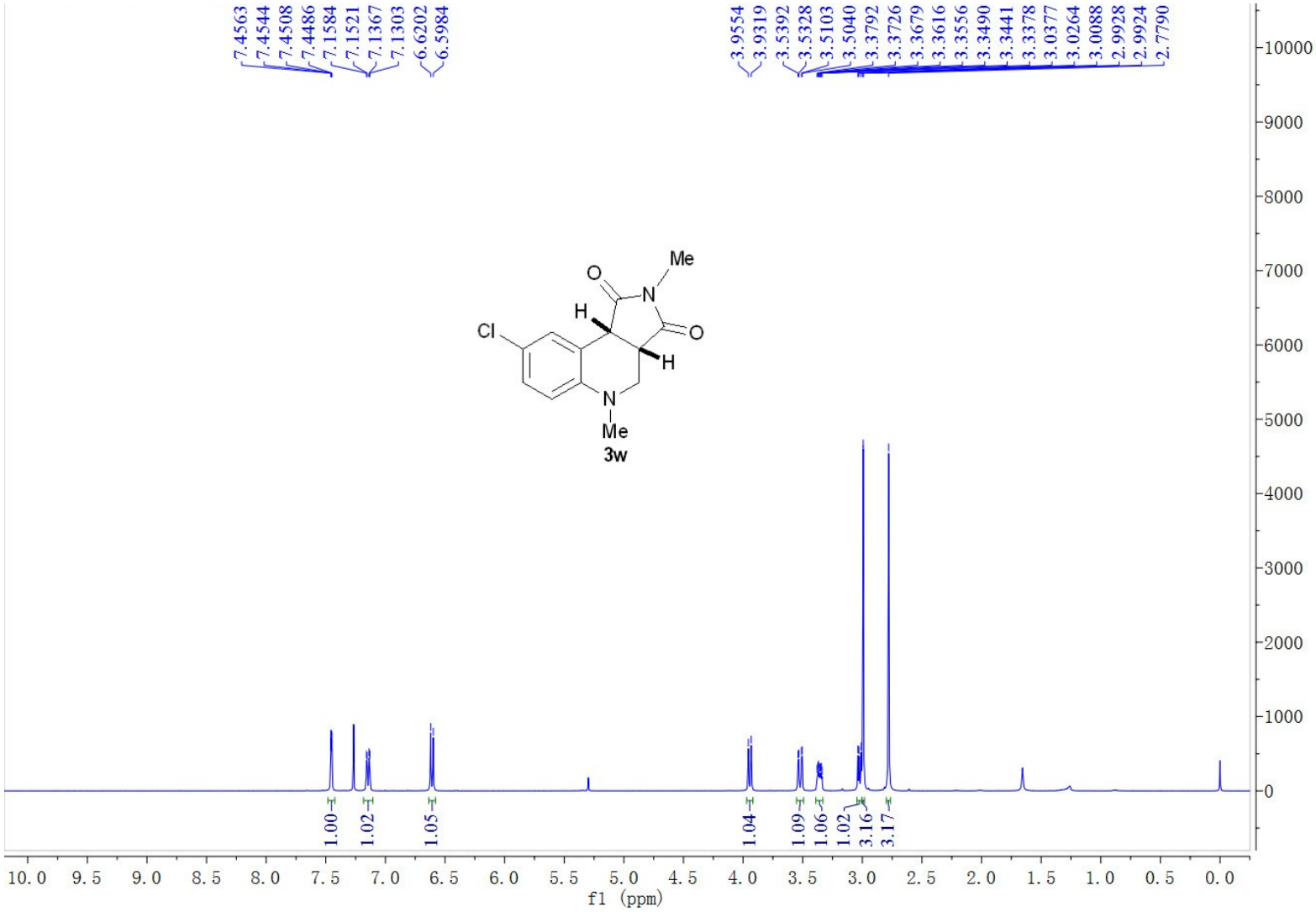
6.6279
6.6170
6.6055
3.9707
3.9472
3.5258
3.5196
3.4971
3.4910
3.3802
3.3734
3.3688
3.3626
3.3567
3.3498
3.3451
3.3389
3.0012
2.9802
2.9690
2.7701
O
N
Me
H
F
O
H
N
Me
3v
2500
2000
1500
1000
500
0
1.00
1.01
1.02
1.02
1.09
1.05
3.18
0.91
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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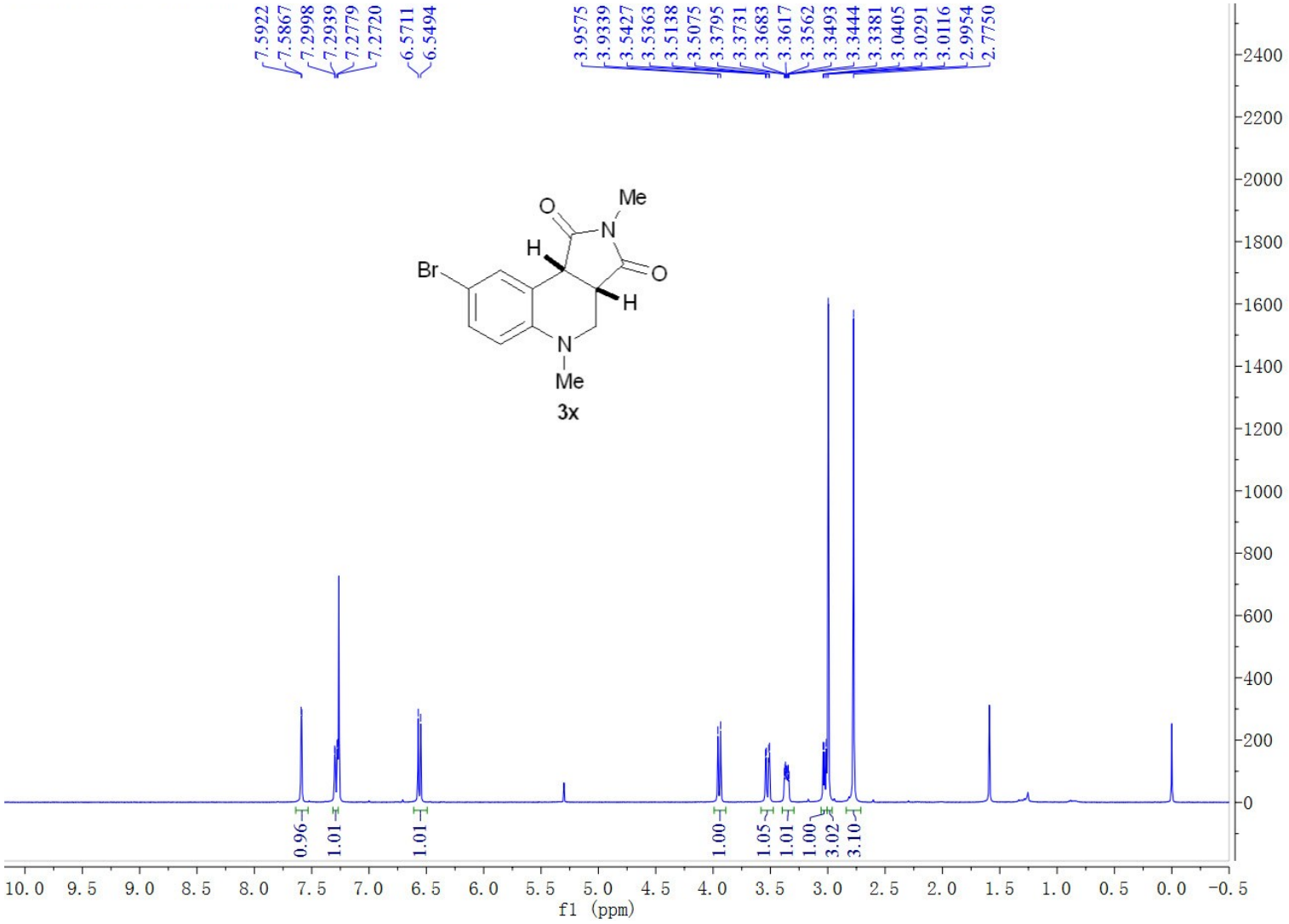
7.4544
7.4508
7.4486
7.1584
7.1521
7.1367
7.1303
6.6202
6.5984
3.9554
3.9319
3.5392
3.5328
3.5103
3.5040
3.3792
3.3726
3.3679
3.3616
3.3556
3.3490
3.3441
3.3378
3.0377
3.0264
3.0088
2.9928
2.9924
2.7790
Me
O
N
H
Cl
O
H
N
Me
3w
1.00
1.02
1.05
1.04
1.09
1.06
1.02
3.16
3.17
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10.0 9.5 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 0.0
f1 (ppm)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7.2998
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7.2779
7.2720
6.5711
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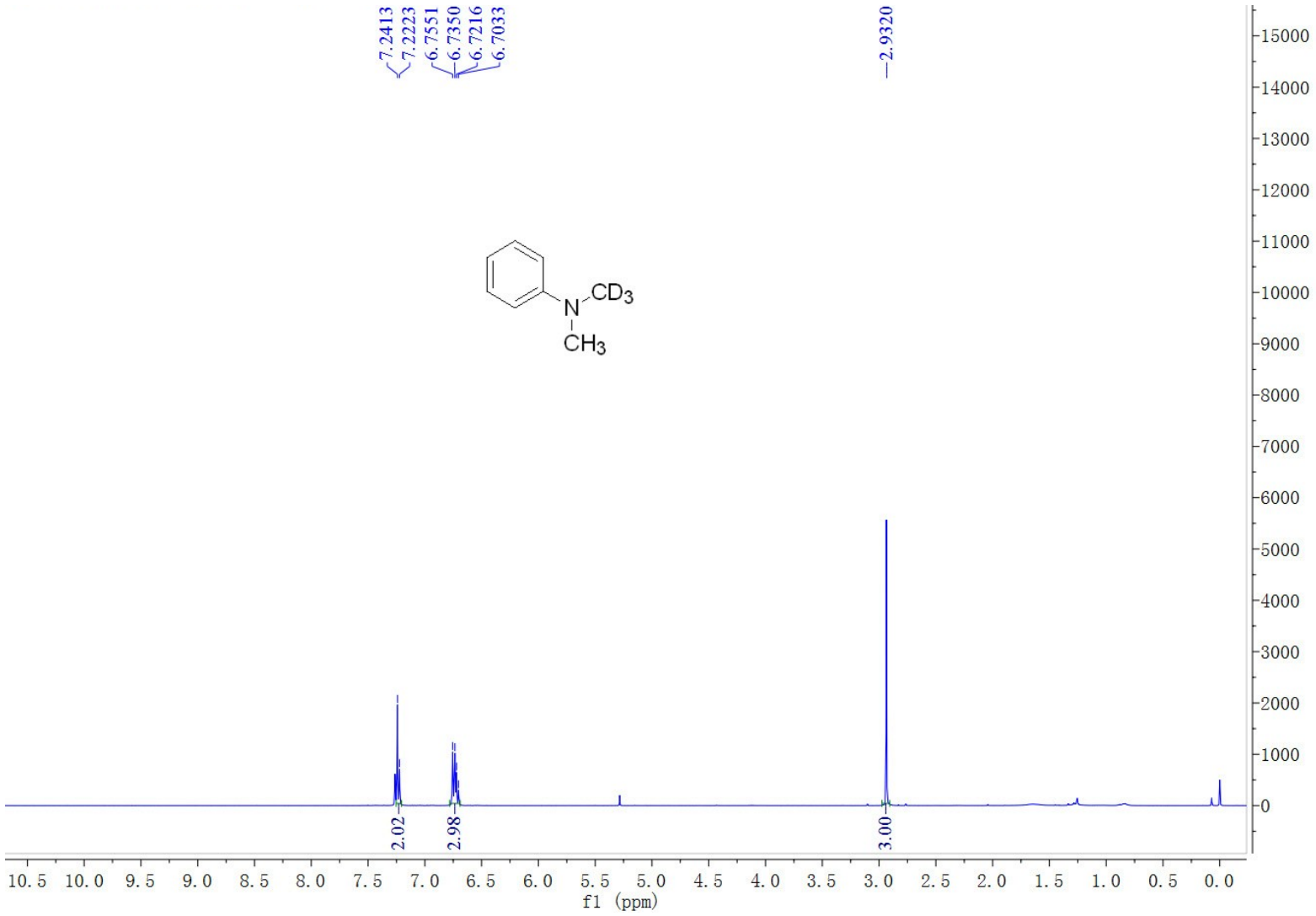
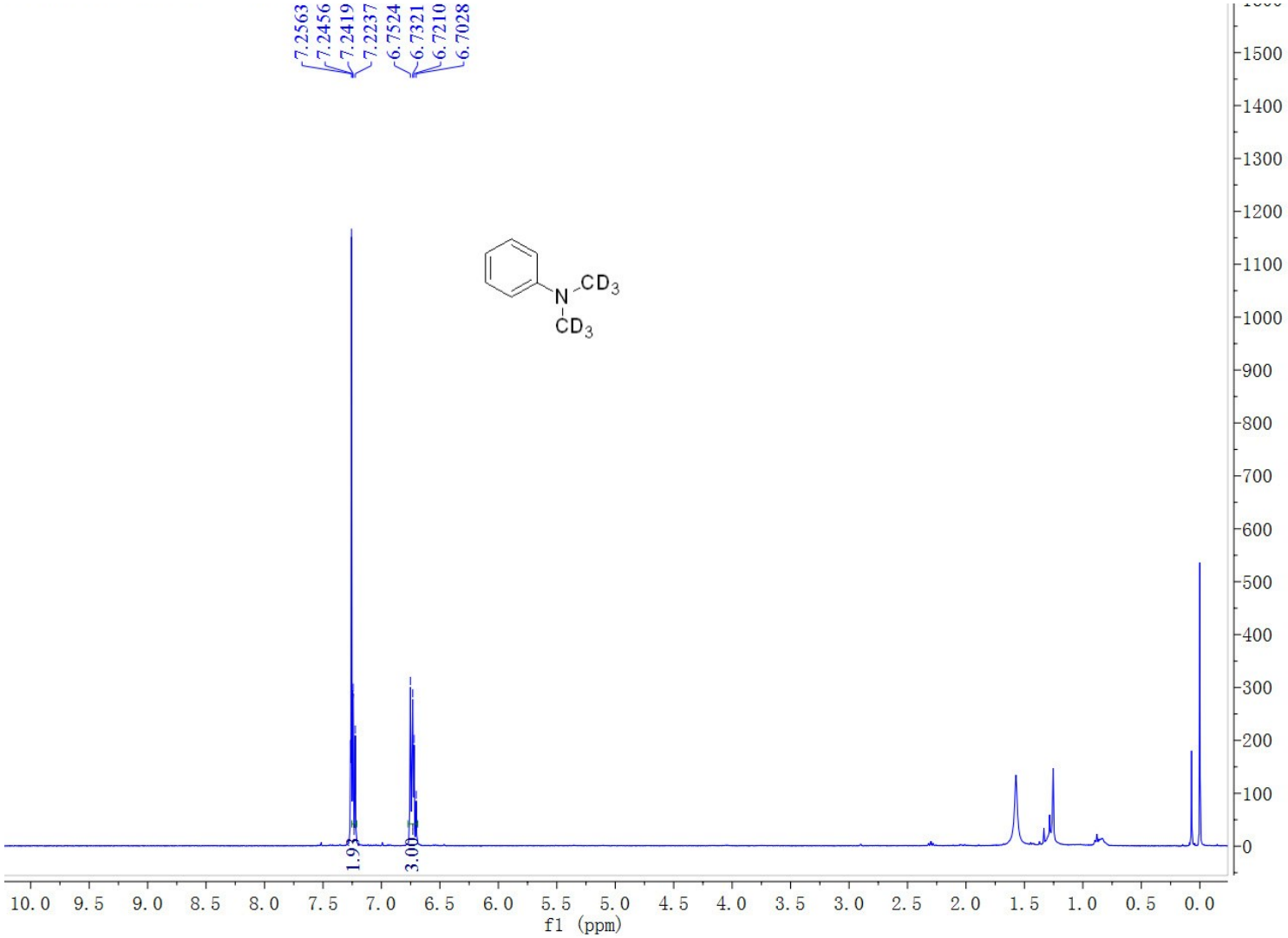
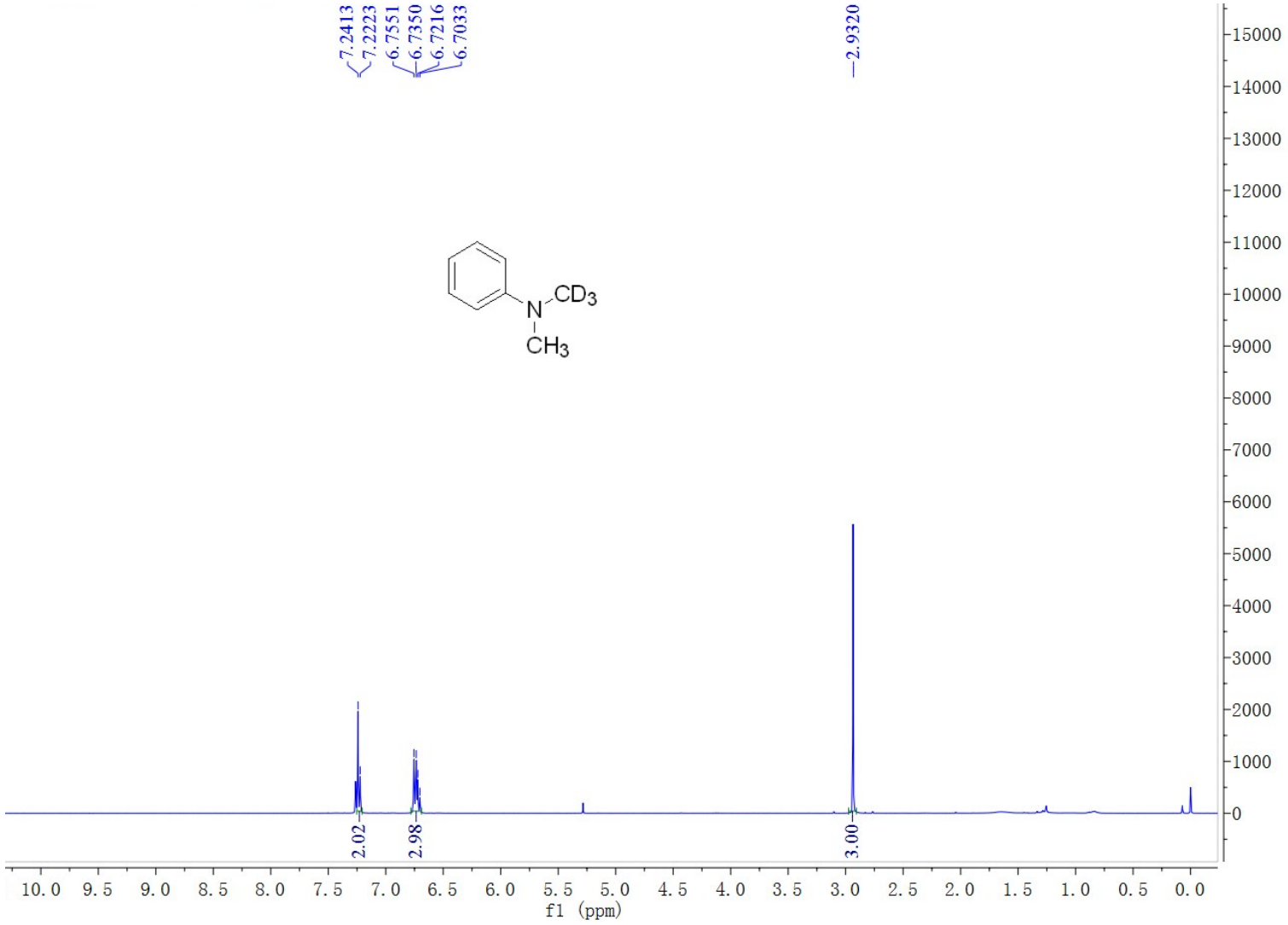
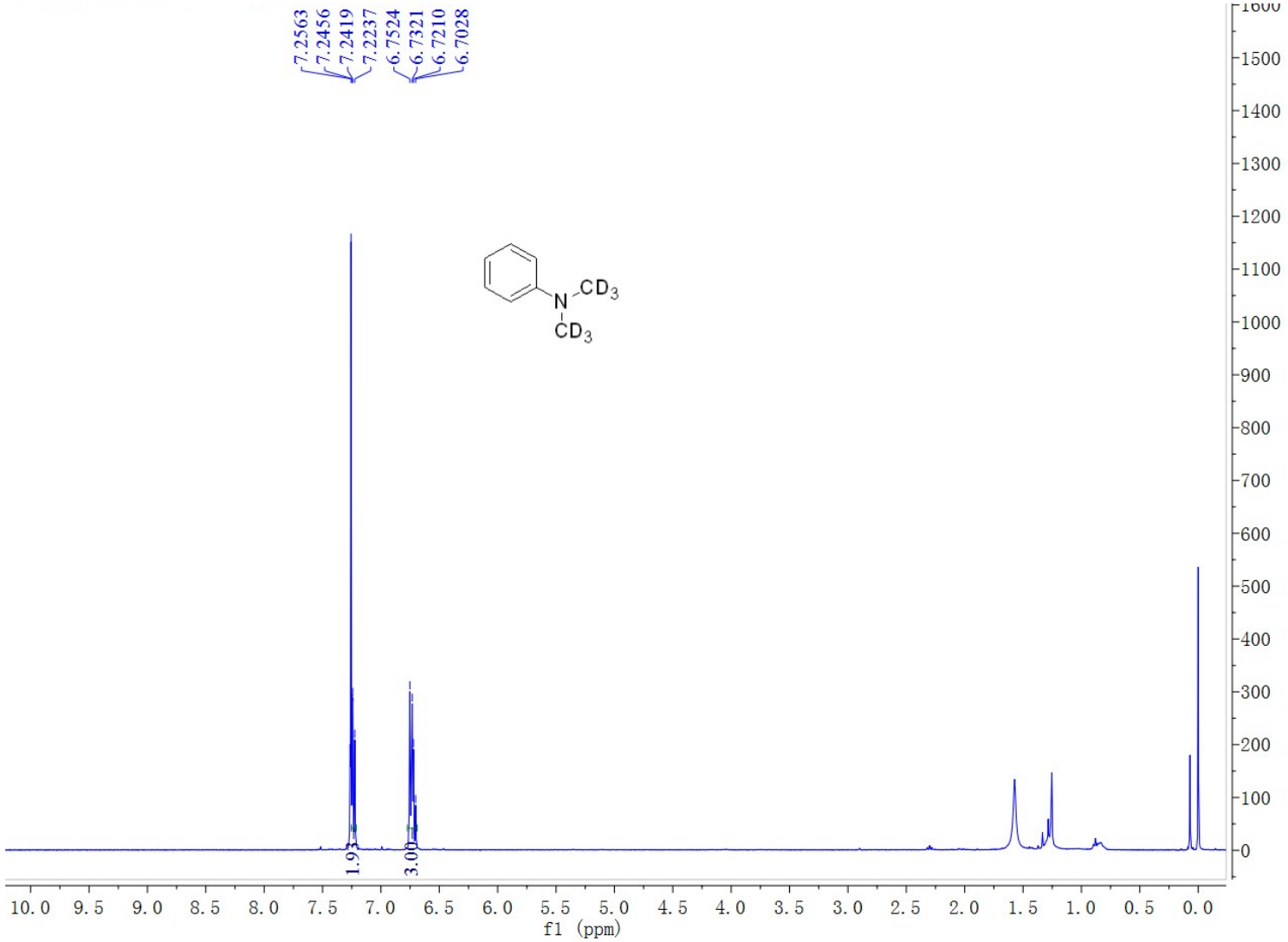
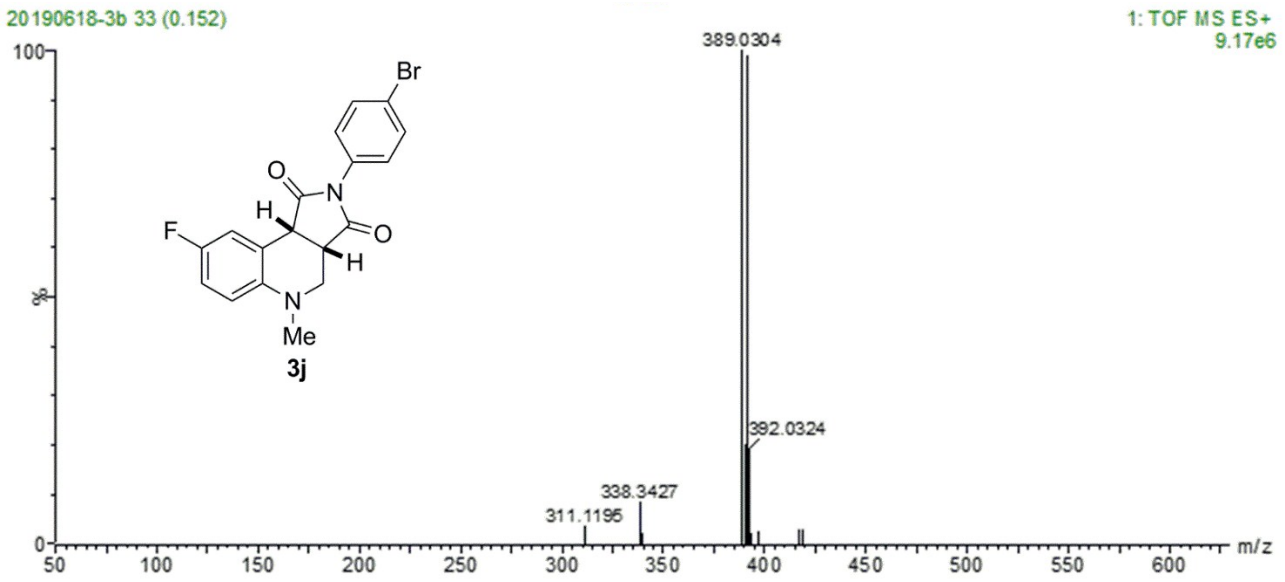
3.9339
3.5427
3.5363
3.5138
3.5075
3.3795
3.3731
3.3683
3.3617
3.3562
3.3493
3.3444
3.3381
3.0405
3.0291
3.0116
2.9954
2.7750
O
Me
N
H
Br
O
H
N
Me
3x
0.96
1.01
1.01
1.00
1.05
1.01
1.00
3.02
3.10
f1 (ppm)

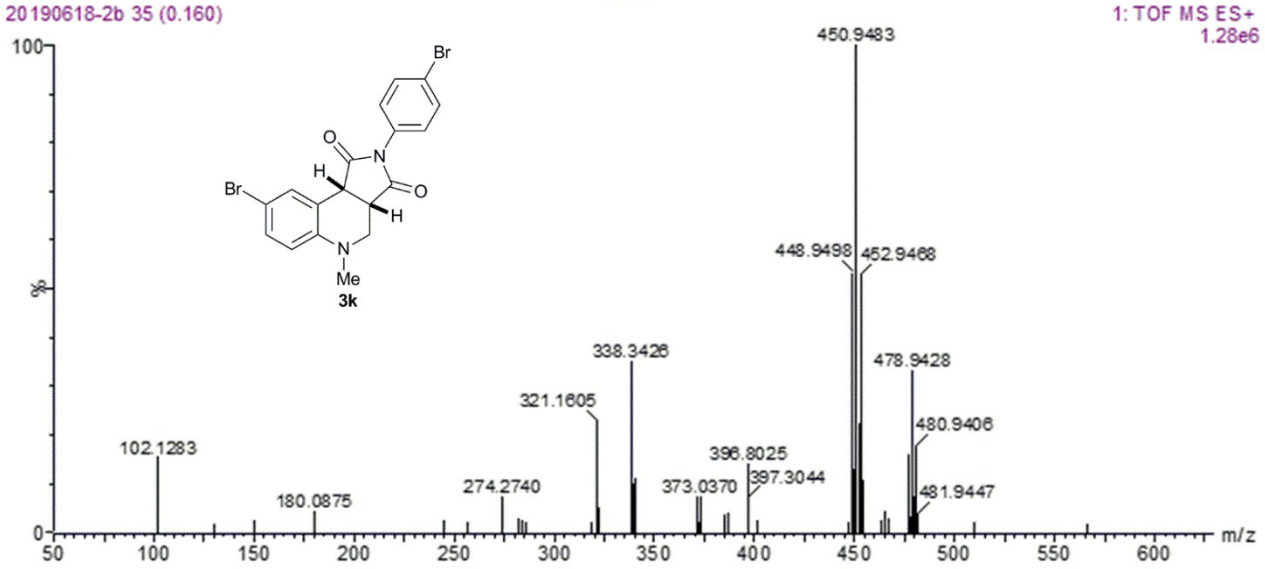

7.2413
7.2223
6.7551
6.7350
6.7216
6.7033
2.9320
N
CD3
CH3
2.02
2.98
3.00
f1 (ppm)

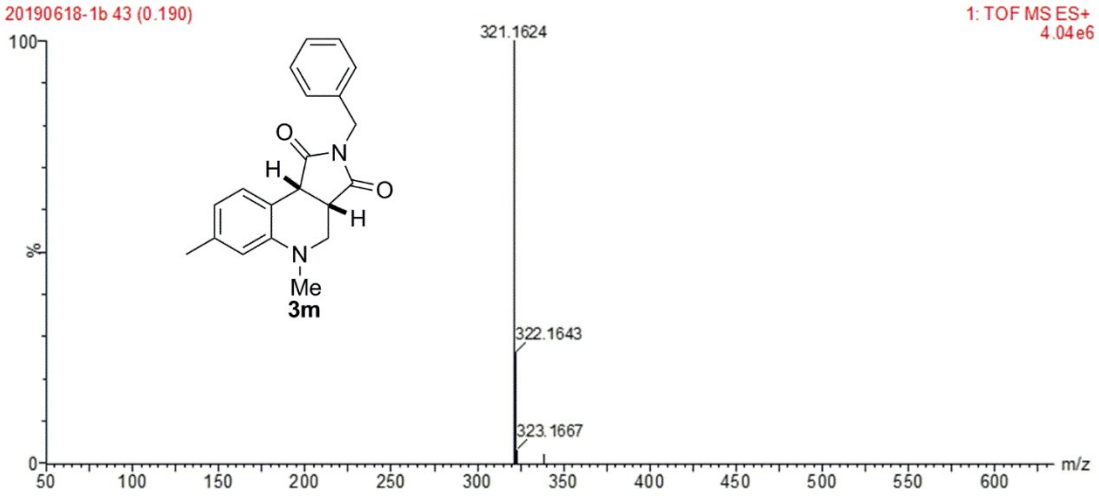

7.2563
7.2456
7.2419
7.2237
6.7524
6.7321
6.7210
6.7028
N
CD3
CD3
1.93
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0

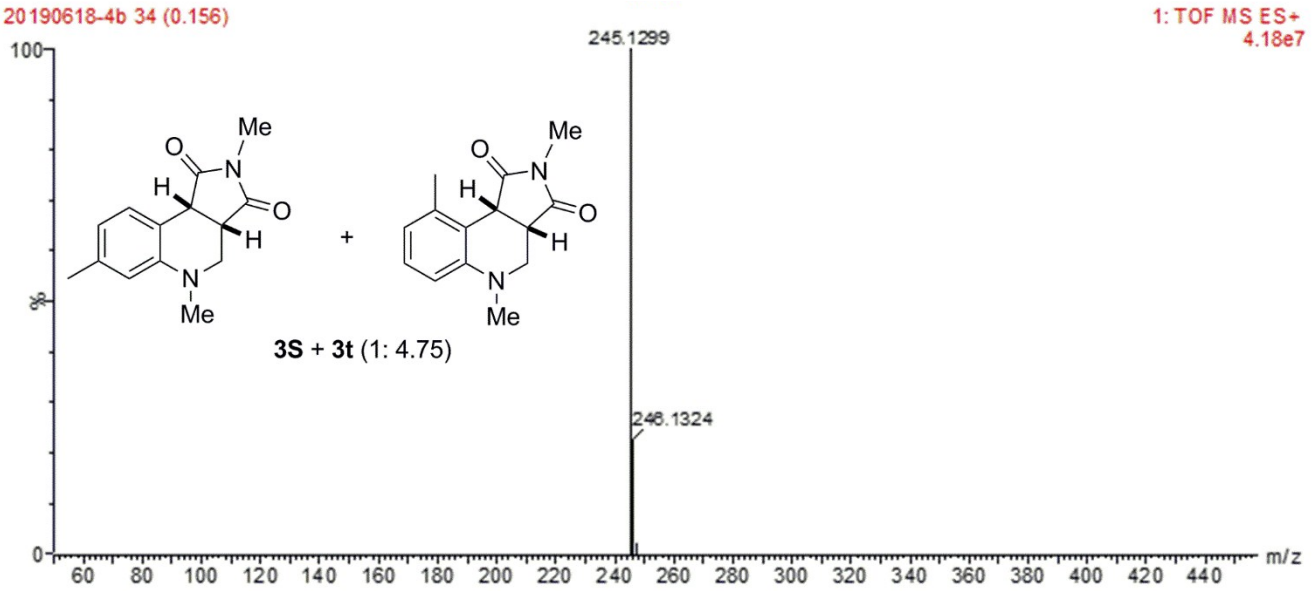

7.2413
7.2223
6.7551
6.7350
6.7216
6.7033
2.9320
N
CD3
CH3
2.02
2.98
3.00
f1 (ppm)


7.2563
7.2456
7.2419
7.2237
6.7524
6.7321
6.7210
6.7028
CD3
N
CD3
1.93
3.00
10.0 9.5 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 0.0
f1 (ppm)
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0


20190618-3b 33 (0.152)
1: TOF MS ES+
9.17e6
389.0304
392.0324
338.3427
311.1195
100
%
0
50
100
150
200
250
300
350
400
450
500
550
600
m/z
Br
O
N
H
F
O
H
N
Me
3j


20190618-2b 35 (0.160)
1: TOF MS ES+
1.28e6
100
%
0
Br
O
N
H
O
Br
H
N
Me
3k
450.9483
448.9498
452.9468
338.3426
478.9428
321.1605
480.9406
102.1283
396.8025
397.3044
274.2740
373.0370
481.9447
180.0875
m/z
50
100
150
200
250
300
350
400
450
500
550
600


20190618-1b 43 (0.190)
1: TOF MS ES+
4.04e6
321.1624
322.1643
323.1667
100
%
0
50
100
150
200
250
300
350
400
450
500
550
600
m/z
O
N
O
H
H
N
Me
3m


20190618-4b 34 (0.156)
1: TOF MS ES+
4.18e7
245.1299
246.1324
100
%
0
m/z
60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440
Me
O
N
O
H
H
N
Me
+
3S + 3t (1: 4.75)