Electronic Supplementary Material (ESI) for ChemComm.

Supporting information section for:

Pd-Catalyzed Direct C-H Functionalization of Imidazolones with Halides.

Mickaël Muselli, Christine Baudequin, Christophe Hoarau* and Laurent Bischoff*

IRCOF-INSA Rouen, Université de Rouen, Place Emile Blondel,
76130 Mont Saint Aignan Cedex, France

Table of contents

.

1. General comments

1.1 Solvents and reagents

All commercially available reagents were purchased from Sigma/Aldrich or Alfa Aesar and used without further purification. Solvents were dried from molecular sieves and kept under argon. Cuprous iodide was purified following reported procedure[1]. Triphenylphosphine was recrystallized from ethanol.

1.2 Chromatography

All reactions were monitored by thin-layer chromatography using Merck silica gel 60 F254 pre-coated aluminum plates (0.25 mm) under UV light (254 nm) and/or by the use of ethanolic vanillin or aqueous potassium permanganate. Flash chromatography was performed with indicated solvents using silica gel (particle size 30–63 µm) purchased from Merck.

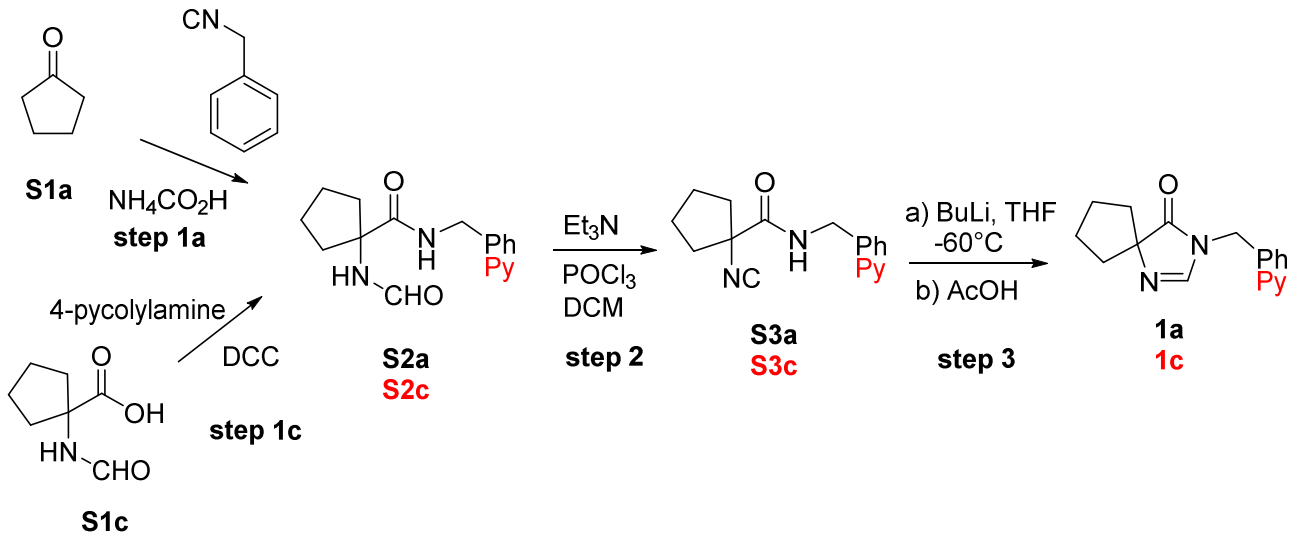
1.3 Instruments

^{1}H,^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Advance at 300 MHz for ^{1}H, 75 MHz for ^{13}C using the solvent signal as an internal standard. Chemical shifts are reported in parts per million (ppm). Coupling constants (J) are given in Hertz and reported as d (doublet), t (triplet), q (quartet) and m (multiplet). HR-MS analyses were performed with a Waters LCT U Premier XE (ESI).

[1] Dieter, *J Am Chem SOC,* 1985, **107,** 4679.

2. Synthesis of 2-H Imidazolones 1a and 1c

3-benzyl-1,3-diazaspiro[4.4]non-1-en-4-one **(1a)** and 3-(pyridin-4-ylmethyl)-1,3-diazaspiro[4.4]non-1-en-4-one **(1c)** were prepared according to the previously reported procedure[2].



Step 1a : A saturated solution of ammonium formate (6.31 g, 0.1 mol) in water was added to a solution of cyclopentanone (5.05g, 0.06 mol) and benzyl isocyanide (5.86g, 0.05 mol) in ethanol (80 ml). The resulting mixture was heated at reflux until completion and then cooled and filtered to give **S2a** (9.11 g, 74%).

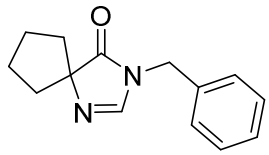
Step 1c : To a stirred solution of **S1c** (3.175g, 20.2 mmol) in CH_2Cl_2 (40 ml) was added 4-pycolylamine (2.05 ml, 20.2 mmol) followed by DCC (6.24g, 30.3 mmol). After 2 hours stirring at room temperature, the mixture was filtred through a celite pad, concentrated under reduced pressure and the crude product purified by flash column chromatography on silica gel using a mixture of CH_2Cl_2 /EtOH 98:2 to obtain product **S2c** (3.4 g, 68%) as a yellow oily liquid.

Step 2: A cold solution of $POCl_3$ (3.68 g, 0.024 mmol) in CH_2Cl_2 *(5* ml) was added dropwise into a well-stirred suspension of **S2c** (4.95 g, 0.02 mol) and triethylamine (8.09 g, 0.08 mol) in CH_2Cl_2 (70 ml), maintaining the temperature at - *5* °C. The cooling bath was removed and the reaction mixture stirred at room temperature for 1.5 h and then cooled and filtered. The filtrate was transferred to a beaker and stirred for 20 min with a saturated solution of sodium carbonate (6.89 g, 0.065 mol) in water. The resulting sludge was washed with two 40-ml portions of water. The organic layer was dried with $MgSO_4$ and then evaporated to dryness to give the pure product **S3c** (2.48 g, 54%) as a brown oily liquid.

Step 3: A solution of butyllithium (4.2 mmol) in hexane was slowly dropped into a well stirred solution of **S3c** (4 mmol) in THF (50 ml), maintaining the temperature at -60°C. The reaction mixture was stirred until the temperature rose to 0°C, and then neutralized with 20% aqueous acetic acid. The resulting mixture was evaporated to dryness and the residue was washed with water and then purified by flash column chromatography on silica gel using a mixture of Petroleum Ether/EtOAc 1:1 to obtain product **1c** (77%) as a yellow oily liquid.

[2] S.Marcaccini *et al, Liebigs Ann. Chem*. 1991, 843 – 849.

3-benzyl-1,3-diazaspiro[4.4]non-1-en-4-one (1a)

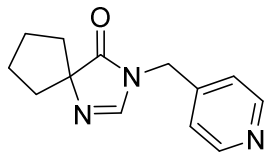


1a

MW : 228.29 g.mol^{-1}
FB : $C_{14}H_{16}N_2O$
Aspect : yellow pale oily liquid
Isolated Yield : 74%

For **step 1a**, filtered and washed with ether to give pure product **S2a** (74%); for ***step 2***, recrystallized from diisopropyl ether (50%); for ***step 3***, eluted by petroleum ether: ethyl acetate = 2:8 to give pure product 1a (74%) as yellow pale oily liquid : **^{1}H NMR** (300 MHz, DMSO) δ 7.99 (s, 1H), 7.43 – 7.16 (m, 5H), 4.63 (s, 2H), 1.88 – 1.57 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 184.58, 152.05, 135.44, 129.05, 128.21, 127.55, 77.51, 44.62, 37.18, 25.72. **HRMS** (CI): calculated for $C_{14}H_{17}N_2O$ $[M+H]^+$: 229.1341 found 229.1335. **IR** (ATR, cm^{-1}) : 3033, 2956, 2872, 1717, 1604, 1345, 722.

3-(pyridin-4-ylmethyl)-1,3-diazaspiro[4.4]non-1-en-4-one (1c)



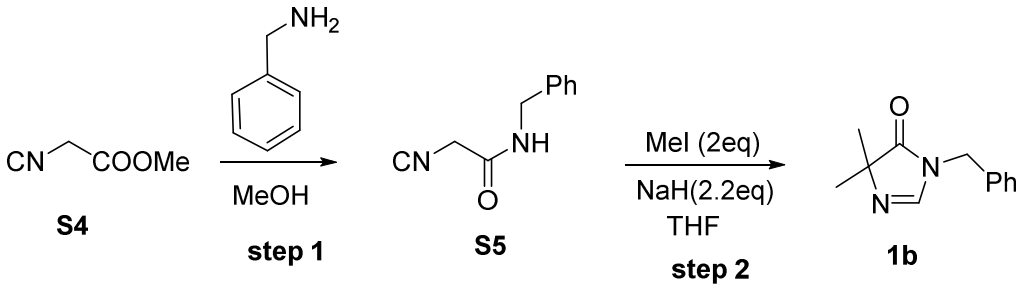
1c

MW : 229.28 g.mol^{-1}
FB : $C_{13}H_{15}N_3O$
Aspect : yellow oily liquid
Isolated Yield : 77%

For **step 1c**, purified by column chromatography through silica gel using a mixture of CH_2Cl_2 /EtOH 98:2 to give the pure product **S2c** (70%) : **^{1}H NMR** (300 MHz, DMSO) δ 8.45 (d, *J* = 6.0 Hz, 2H), 8.38 (s, 1H), 8.33 (t, *J* = 6.0 Hz, 1H), 7.97 (d, *J* = 1.3 Hz, 1H), 7.24 (d, *J* = 6.0 Hz, 2H), 4.27 (d, *J* = 6.0 Hz, 2H), 2.09 – 1.85 (m, 4H), 1.65 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.61, 162.23, 149.30, 148.52, 122.06, 66.76, 42.26, 36.55, 23.89. **HRMS** (CI): calculated for $C_{13}H_{18}N_3O_2$ $[M+H]^+$: 248.1399 found 248.1391. **IR** (ATR, cm^{-1}) : 3672, 3264, 2970, 1650, 1602, 1519, 1383, 1066, 605 ; for ***step 2***, the organic layer was washed with water, dried with $MgSO_4$ and then evaporated to dryness, to give pure **S3c** (54%): **^{1}H NMR** (300 MHz, DMSO) δ 8.98 (t, *J* = 5.8 Hz, 1H), 8.50 (d, J = 6Hz, 2H), 7.23 (d, *J* = 6 Hz, 2H), 4.34 (d, *J* = 5.8 Hz, 2H), 2.23 – 2.01 (m, 4H), 1.89 – 1.71 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.20, 150.12, 122.17, 45.76, 42.83, 40.39, 24.30, 8.65, 1.05. **HRMS** (CI): calculated for $C_{13}H_{16}N_3O$ $[M+H]^+$: 230.1293 found 230.1287. **IR** (ATR, cm^{-1}) : 3663, 3254, 2970, 2127, 1666, 1602, 1522, 1067, 800; for ***step 3***, eluted by petroleum ether : ethyl acetate = 1:1 to give product **1c** (77%) as a yellow oily liquid : **^{1}H NMR** (300 MHz, DMSO) δ 8.54 (d, *J* = 6.0 Hz, 2H), 8.02 (s, 1H), 7.19 (d, *J* = 6.0 Hz, 2H), 4.70 (s, 2H), 1.86 – 1.66 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 185.20, 173.23, 150.44, 149.75, 122.04, 77.86, 43.47, 37.40, 25.90. **HRMS** (CI): calculated for $C_{13}H_{15}N_3O$ $[M+H]^+$: 230.1293 found 230.1289. **IR** (ATR, cm^{-1}) : 3671, 3200, 2971, 2902, 1720, 1658, 1522, 1382, 1067, 451.

3. Synthesis of 2-H imidazolone 1b

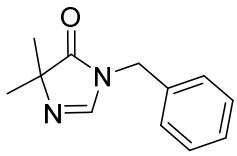
3-benzyl-5,5-dimethyl-3,5-dihydro-4H-imidazol-4-one (**1b**) was prepared according to the previously reported procedure[3].



Step 1 : A mixture of methyl isocyanoacetate **S4** (2.97 g, 0.03 mol) and benzylamine (7.5 g, 0.07 mol) in methanol (20 ml) was stirred for 16 hours at room temperature, then the reaction mixture was concentrated under reduced pressure, and the residue taken up with ethyl acetate (100 ml). The solution was washed with water, dried with anhydrous sodium sulfate, and evaporated *in vacuo*. The residual crystals were washed with ether and then collected by filtration to give the amide **S5** (4 g, 77%) as white needles (m.p = 121°C).

Step 2 : A mixture of **S5** (174 mg, 1mmol), iodomethane (125 uL, 2 mmol) and tetrahydrofuran (2ml) was added dropwise to a stirred suspension of sodium hydride (95%, 53mg, 2.2 mmol) and tetrahydrofuran (3ml) at 25°C, during this time internal temperature rose up to 40°C. After one hour stirring at room temperature, the mixture was cooled and neutralized with 10% acetic acid and then concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel using a mixture of Petroleum Ether/EtOAc 1:1 to obtain product **1b** (148 mg, 73%) as a yellow oily liquid.

3-benzyl-5,5-dimethyl-3,5-dihydro-4H-imidazol-4-one (1b)



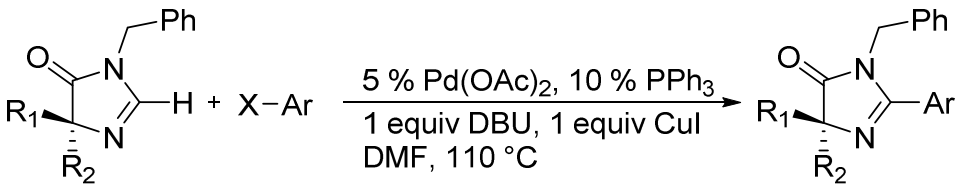
MW : 202.26 g.mol^{-1}
FB : $C_{12}H_{14}N_2O$
Aspect : yellow pale oily liquid
Isolated Yield : 73%

.

For **step 1**, filtered and washed with ether to give pure product (4 g, 77%) : **^{1}H NMR** (300 MHz, DMSO) δ 8.67 (s, 1H), 7.40 – 7.16 (m, 5H), 4.41 (s, 2H), 4.30 (d, *J* = 5.9 Hz, 2H); for **step 2**, purified by flash column chromatography on silica gel using a mixture of Petroleum Ether/EtOAc 1:1 to obtain product **1b** (148 mg, 73%) as a yellow oily liquid : **^{1}H NMR** (300 MHz, DMSO) δ : 8.01 (s, 1H), 7.41 – 7.17 (m, 5H), 4.62 (s, 2H), 1.19 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 184.90, 151.27, 135.53, 128.89, 128.01, 127.32, 77.16, 68.13, 44.22, 23.48. **HRMS** (CI): calculated for $C_{12}H_{15}N_2O$ $[M+H]^+$: 203.1184 found 203.1175. **IR** (ATR, cm^{-1}) : 3064, 2930, 1717, 1607, 1344, 711.

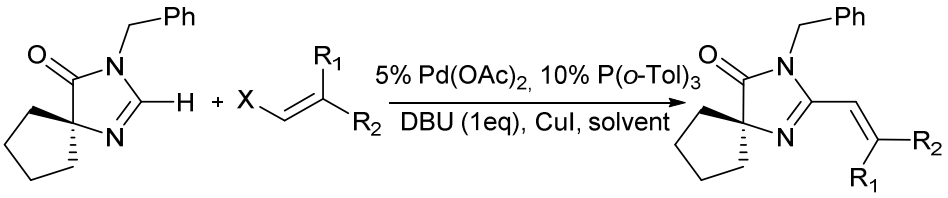
[3] K.Matsumoto *et al, Synthesis,* 1975, 249-250.

4. Representative experimental procedure for Arylation



General Procedure – Palladium-Copper-catalysed direct intermolecular arylation of C-H bond : 3-benzyl-1,3-diazaspiro[4.4]non-1-en-4-one or 3-benzyl-5,5-dimethyl-3,5-dihydro-4H-imidazol-4-one (0.45 mmol) was placed in an over-dried screw-caped sealed tube (10 mL) containing a magnetic stir bar with $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%), CuI (1 equiv.) and DBU (1 equiv.). A solution of halide (1 equiv.) in DMF (1.3 mL) was added. The resulting mixture was purged with nitrogen and stirred at 110°C overnight. After dilution with diethyl ether, filtration on cotton, washing with 10% aqueous ammonia (2*25 mL), brine (2*25 mL), dried over Na_2SO_4 anhydrous and concentrated *in vacuo*, the crude product was purified by flash column chromatography through silica gel using a mixture of appropriate solvents as eluent to give pure arylated product.

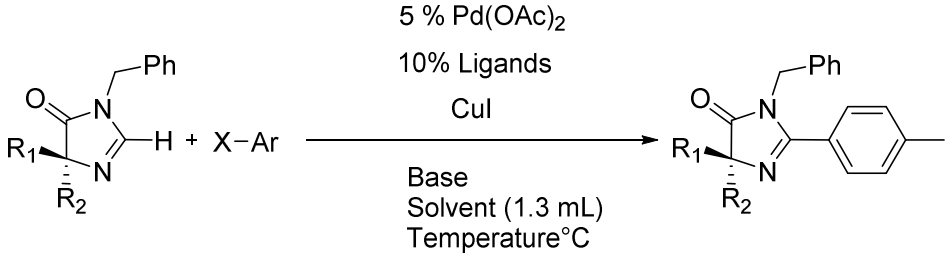
5. Representative experimental procedure for vinylation



General Procedure – Palladium-Copper-catalyzed direct intermolecular vinyllation of C-H bond : 3-benzyl-1,3-diazaspiro[4.4]non-1-en-4-one (0.45 mmol) was placed in an over-dried screw-caped sealed tube (10 mL) containing a magnetic stir bar with $Pd(OAc)_2$ (5 mol%), tri-(*o*-tolyl)Phosphine (10 mol%), CuI (1 equiv.) and DBU (1 equiv.). A solution of halide (1 equiv.) in appropriate solvent (1.3 mL) was added. The resulting mixture was purged with nitrogen and stirred at 110°C overnight. After dilution with dichloromethane, filtration through cotton, washing with 10% aqueous ammonia (2*25 mL), brine (2*25 mL), dried over Na_2SO_4 anhydrous and concentrated *in vacuo*, the crude product was purified by flash column chromatography on silica gel using a mixture of appropriate solvents as eluent to give pure vinylated product.

6. Optimization of reaction conditions

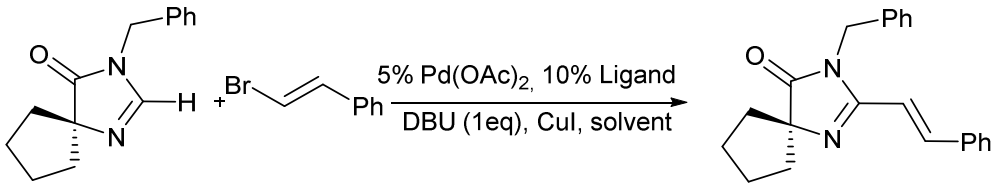
1. Optimization of arylation of C-H bond



Entry	Base (eq)	Ligand	Solvent (T°C)	CuI (equiv	Yields[b] [%]
1	DBU (2eq)	PPh_3	DMF (130°C)	1	92
2	K_3PO_4 (2eq)	PPh_3	DMF (130°C)	1	55
3	K_2CO_3 (2eq)	PPh_3	DMF (130°C)	1	73
4	KOAc (2eq)	PPh_3	DMF (130°C)	1	72
5	Cs2CO3 (2eq)	PPh_3	DMF (130°C)	1	81
6	DBU (2eq)	PCy_3	DMF (130°C)	1	44
7	DBU (2eq)	CyJohnPhos	DMF (130°C)	1	31
8	DBU (2eq)	TTBP	DMF (130°C)	1	0
9	CsF (1eq)	PPh3	DMF (130°)	1	68
10	DBU (2eq)	None	DMF (130°C)	1	65
11	Cs2CO3 (2eq)	None	DMF (130°C)	1	45
12	K2CO3 (2eq)	None	DMF (130°C)	1	63
13	DBU (2eq)	PPh_3	DMF (130°C)	0	0
14	KOAc (2eq)	PPh_3	DMF (130°C)	0	0
15	Cs2CO3 (2eq)	PPh_3	DMF (130°C)	0	55
16	DBU (2eq)	PPh_3	DMF (110°C)	1	92
17	DBU (2eq)	PPh_3	DMF (90°C)	1	60
18	DBU (2eq)	PPh_3	Dioxane (110°C)	1	23
19	DBU (2eq)	PPh_3	Dioxane (90°C)	1	0

20	DBU (2eq)	PPh_3	MeCN (110°C)	1	80
21	DBU (1eq)	PPh_3	DMF (110°C)	**1**	**92**

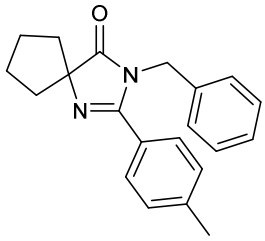
2. Optimization of vinylation of C-H bond



Entry	Base	Ligand	Solvent (T°C)	Yields[b] [%]
1	DBU	PPh_3	DMF (130°C)	12
2	DBU	PCy_3	DMF (130°C)	0
3	DBU	PPh_3	DMF (110°C)	21
4	DBU	PPh_3	DMF (90°C)	16
5	DBU	(4-F)PPh_3	DMF (110°C)	28
6	DBU	(o-Me)PPh_3	DMF (110°C)	41
7	DBU	(o-Me)PPh_3	MeCN(110°C)	54
8	KOAc	(o-Me)PPh_3	MeCN (110°C)	0
9	**DBU**	**(o-Me)PPh_3**	**Toluene (110°c)**	**73**

7. Analytical data of isolated products

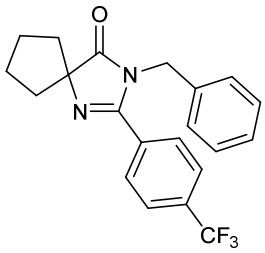
3-benzyl-2-(p-tolyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aA)



MW : 318.42 g.mol^{-1}
FB : $C_{21}H_{22}N_2O$
Aspect : white solid
Isolated Yield : 92%
Melting point : 77°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 132 mg (92% yield) of the title product obtained as a white solid.
^{1}H NMR (300 MHz, DMSO) : δ 7.40 (d, *J* = 7.9 Hz, 2H), 7.31 – 7.16 (m, 5H), 6.97 (d, *J* = 7.9 Hz, 2H), 4.74 (s, 2H), 2.31 (s, 3H), 1.98 – 1.79 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 187.29, 161.12, 141.12, 136.88, 129.36, 128.81, 128.21, 127.58, 127.04, 126.85, 77.19, 44.96, 37.81, 26.23, 21.56. **HRMS** (CI): calculated for $C_{21}H_{22}N_2O$ $[M+H]^+$: 318.1732 found 318.1729. **IR** (ATR, cm^{-1}) : 2955, 1720, 1620, 1332, 696.

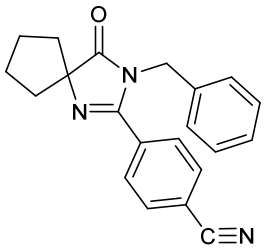
3-benzyl-2-(4-(trifluoromethyl)phenyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aB)



MW : 372.39 g.mol^{-1}
FB : $C_{21}H_{19}F_3N_2O$
Aspect : Yellow-orange liquid
Isolated yield : 88%

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 147 mg (88% yield) of the title product obtained as a yellow-orange oily liquid.
^{1}H NMR (300 MHz, DMSO) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.30 – 7.15 (m, 3H), 6.93 (d, *J* = 6.5 Hz, 2H), 4.76 (s, 2H), 1.96 – 1.83 (m, 8H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.35, 160.16, 136.48, 133.28, 130.76, 130.69, 128.50, 128.35, 127.45, 127.36, 127.30, 126.50, 124.83, 124.22, 77.87, 44.69, 37.83, 26.05.**^{19}F NMR** (282 MHz, DMSO) δ : -61.42 (s). **HRMS** (CI): calculated for $C_{21}H_{19}N_3O$ $[M+H]^+$: 330.1606 found 330.1603. **IR** (ATR, cm^{-1}) : 3666, 2960, 2871, 1722,1630, 1336, 1068.

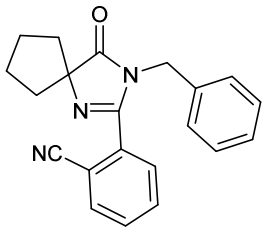
4-(3-benzyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-2-yl)benzonitrile (3aC)



MW : 329.40 g.mol^{-1}
FB : $C_{21}H_{19}N_3O$
Aspect : Yellow pale solid
Isolated yield : 86%
Melting point : 157°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 127 mg (86% yield) of the title product obtained as a yellow pale solid.
^{1}H NMR (300 MHz, DMSO) δ : 7.90 (d, *J* = 8.3 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.27 – 7.16 (m, 3H), 6.92 (d, *J* = 6.7 Hz, 2H), 4.75 (s, 2H), 1.96 – 1.82 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 186.60, 159.54, 136.13, 134.26, 132.36, 128.98, 128.94, 127.90, 126.65, 117.91, 114.53, 77.69, 44.90, 37.81, 26.12 **HRMS** (CI): calculated for $C_{21}H_{19}N_3O$ $[M+H]^+$: 330.1606 found 330.1603. **IR** (ATR, cm^{-1}) : 3664, 2971, 2910, 2228, 1729, 1600, 1385, 1071

2-(3-benzyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-2-yl)benzonitrile (3aD)

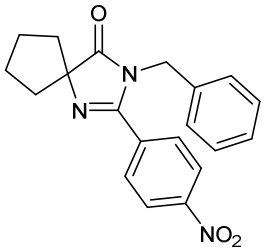


MW : 329.40 g.mol^{-1}
FB : $C_{21}H_{19}N_3O$
Aspect : White solid
Isolated yield : 74%
Melting point : 148°C

Flash chromatography using Petroleum Ether/EtOAc 70:30 as eluent resulted in 110 mg (74% yield) of the title product obtained as a white solid.

^{1}H NMR (300 MHz, DMSO) δ 7.85 (d, *J* = 7.7 Hz, 1H), 7.81 – 7.62 (m, 3H), 7.21 – 7.14 (m, 3H), 6.84 – 6.74 (m, 2H), 4.63 (s, 2H), 1.98 – 1.84 (m, 8H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 185.66 (s), 157.68 (s), 135.76 (s), 133.22 (s), 133.19 (s), 132.32 (s), 130.62 (s), 128.91 (s), 128.66 (s), 127.71 (s), 126.85 (s), 116.05 (s), 112.62 (s), 78.13 (s), 44.42 (s), 37.46 (s), 25.93 (s). **HRMS** (CI): calculated for $C_{21}H_{19}N_3O$ $[M+H]^+$: 330.1606 found 330.1609. **IR** (ATR, cm^{-1}) : 3409, 2967, 2230, 1730, 1631, 1379, 1342, 1023, 733.

3-benzyl-2-(4-nitrophenyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aE)

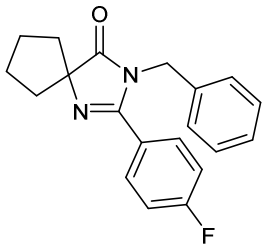


MW : 349.39 g.mol^{-1}
FB : $C_{20}H_{19}N_3O_3$
Aspect : Yellow solid
Isolated yield : 90%
Melting point : 128°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 142 mg (90% yield) of the title product obtained as a yellow solid.

^{1}H NMR (300 MHz, DMSO) δ 8.24 (d, j= 8.8 Hz, 2H), 7.79 (d, j = 8.8 Hz, 2H), 7.25 – 7.15 (m, 3H), 6.93 (d, *J* = 6.2 Hz, 2H), 4.78 (s, 2H), 1.98 – 1.83 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 186.58, 159.33, 149.06, 136.10, 135.97, 129.43, 129.01, 127.95, 126.64, 123.75, 77.77, 44.93, 37.83, 26.14.**HRMS** (CI): calculated for $C_{20}H_{19}N_3O_3$ $[M+H]^+$: 350.1505 found 350.1506.**IR** (ATR, cm^{-1}) : 2949, 1726, 1588, 1519, 1351, 1071, 855, 702.

3-benzyl-2-(4-fluorophenyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aF)

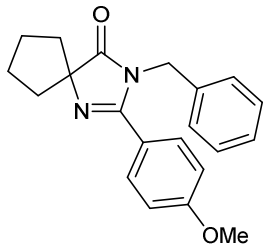


MW : 322.38 g.mol^{-1}
FB : $C_{20}H_{19}FN_2O$
Aspect : Yellow-orange solid
Isolated yield : 88%
Melting point : 76°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 116 mg (88% yield) of the title product obtained as a yellow-orange solid

^{1}H NMR (300 MHz, DMSO) δ 7.56 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.30 – 7.16 (m, 5H), 6.95 (d, *J* = 7.0 Hz, 2H), 4.75 (s, 2H), 1.98 – 1.79 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 187.06, 165.87, 162.53, 160.22, 130.55, 130.44, 128.93, 127.77, 126.80, 116.08, 115.79, 77.39, 44.97, 37.84, 26.21.. **^{19}F NMR** (282 MHz, DMSO) δ : -109.43 – -109.58 (m). **HRMS** (CI): calculated for $C_{20}H_{19}FN_2O$ $[M+H]^+$: 323.1560 found 323.1568. **IR** (ATR, cm^{-1}) : 2971, 2874, 1729, 1614, 1333, 956, 728, 592.

3-benzyl-2-(4-methoxyphenyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aG)

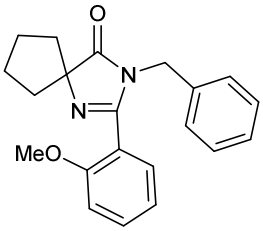


FW : 334.42 g.mol^{-1}
FB : $C_{21}H_{22}N_2O_2$
Aspect : Orange liquid
Isolated yield : 79%

Flash chromatography using Petroleum Ether/EtOAc 80:20 as eluent resulted in 119 mg (79% yield) of the title product obtained as a orange oily liquid.

^{1}H NMR (300 MHz, DMSO) δ : 7.46 (d, *J* = 8.8 Hz, 1H), 7.32 – 7.20 (m, 3H), 7.01 – 6.91 (m, 4H), 4.76 (s, 2H), 3.77 (s, 3H), 1.95 – 1.77 (m, 8H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 187.22, 161.50, 136.79, 129.80, 128.75, 127.51, 126.66, 122.08, 113.98, 76.99, 55.34, 44.90, 37.72, 26.13.**HRMS** (CI): calculated for $C_{21}H_{22}N_2O_2$ $[M+H]^+$: 335.1760 found 335.1760. **IR** (ATR, cm^{-1}) : 3064, 2935, 1722, 1608, 1339, 722.

3-benzyl-2-(2-methoxyphenyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aH)

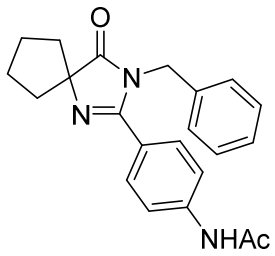


FW : 334.42 g.mol^{-1}
FB : $C_{21}H_{22}N_2O_2$
Aspect : Beige solid
Isolated yield : 74%
Melting point : 74°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 111 mg (74% yield) of the title product obtained as a beige solid.

^{1}H NMR (300 MHz, DMSO) δ 7.52 – 7.43 (m, 1H), 7.23 – 7.09 (m, 5H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.82 (dd, *J* = 7.5, 1.6 Hz, 2H), 4.46 (s, 2H), 3.68 (s, 3H), 1.93 – 1.76 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.24, 159.77, 157.07, 136.89, 132.07, 130.65, 128.35, 127.35, 127.28,120.85, 119.59, 110.78, 77.37, 55.36, 44.51, 37.65, 26.03. **HRMS** (CI): calculated for $C_{21}H_{22}N_2O_2$ $[M+H]^+$: 335.1760 found 335.1767. **IR** (ATR, cm^{-1}) : 2961, 1713, 1613, 1596, 1333, 757.

N-(4-(3-benzyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-2-yl)phenyl)acetamide (3al)

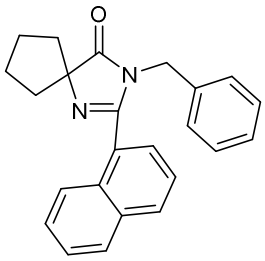


FW : 361.44 g.mol^{-1}
FB : $C_{22}H_{23}N_3O_2$
Aspect : Yellow solid
Isolated yield : 62%
Melting point : 172°C

Flash chromatography using Petroleum Ether/EtOAc 50:50 as eluent resulted in 101 mg (62% yield) of the title product obtained as a yellow solid.

^{1}H NMR (300 MHz, DMSO) δ 7.73 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.28 – 7.24 (m, 3H), 7.04 - 6.96 (m, 2H), 4.72 (s, 2H), 2.16 (s, 3H), 2.11 – 1.93 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 187.27, 168.71, 160.77, 140.54, 136.71, 132.27, 129.27, 128.94, 127.73, 126.80, 119.29, 77.64, 45.05, 37.88, 26.27, 24.83**.HRMS** (CI): calculated for $C_{22}H_{23}N_3O_2$ $[M+H]^+$: 362.1869 found 362.1859. **IR** (ATR, cm^{-1}) : 3244, 2959, 1722, 1645, 1342. **IR** (ATR, cm^{-1}) : 3272, 3033, 2925, 2854, 1737, 1610, 722.

3-benzyl-2-(naphthalen-1-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aJ)

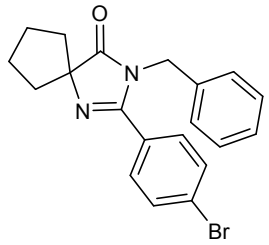


MW : 354.45 g.mol^{-1}
FB : $C_{24}H_{22}N_2O$
Aspect : Yellow pale solid
Isolated yield : 90%
Melting point : 76°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 143 mg (90% yield) of the title product obtained as a yellow pale solid.

^{1}H NMR (300 MHz, DMSO) δ : 8.07 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 7.4 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.59 – 7.44 (m, 4H), 7.09 – 7.03 (m, 3H), 6.70 – 6.63 (m, 2H), 4.43 (s, 2H), 2.06 – 1.95 (m, 8H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 185.85, 159.01, 135.40, 132.55, 131.98, 131.54, 127.99, 127.80, 126.88, 125.77, 124.76, 124.71, 124.66, 124.61, 124.48, 120.87, 76.65, 43.98, 36.87, 25.20. **HRMS** (CI): calculated for $C_{24}H_{22}N_2O$ $[M+H]^+$: 355.1810 found 355.1805. **IR** (ATR, cm^{-1}) : 2955, 1723, 1607, 1260, 1068.

3-benzyl-2-(4-bromophenyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aK)

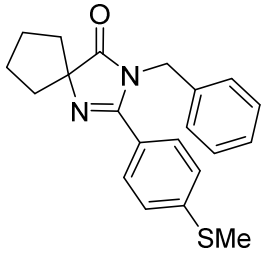


FW : 382.38 g.mol^{-1}
FB : $C_{20}H_{19}BrN_2O$
Aspect : yellow liquid
Isolated yield : 71%

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 122 mg (71% yield) of the title product obtained as a yellow oily liquid.

^{1}H NMR (300 MHz, DMSO) δ : 7.65 – 7.50 (m, 4H), 7.20 (m, 3H), 6.98 – 6.83 (m, 2H), 4.72 (s, 2H), 1.96 – 1.75 (m, 8H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.90, 160.24, 136.45, 131.89, 129.78, 128.88, 128.76, 127.73, 126.69, 125.43, 77.36, 44.89, 37.74, 26.13. **HRMS** (CI): calculated for $C_{20}H_{19}BrN_2O$ $[M+H]^+$: 383.0759 found 383.0771. **IR** (ATR, cm^{-1}) : 2959, 1725, 1616, 1328, 1070, 1008, 697.

3-benzyl-2-(4-(methylthio)phenyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aL)

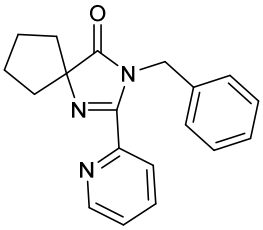


FW : 350.48 g.mol^{-1}
FB : $C_{21}H_{22}N_2OS$
Aspect : colorless liquid
Isolated yield : 52%

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 82 mg (52% yield) of the title product obtained as a colorless oily liquid.

^{1}H NMR (300 MHz, DMSO) δ 7.50 – 7.38 (m, 2H), 7.32 – 7.18 (m, 5H), 6.99 (d, *J* = 6.9 Hz, 2H), 4.76 (s, 2H), 2.48 (s, 3H), 2.01 – 1.74 (m, 8H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 187.19, 160.65, 142.68, 136.71, 128.84, 128.53, 127.61, 126.69, 125.99, 125.60, 77.36, 44.94, 37.78, 26.18, 15.10. **HRMS** (CI): calculated for $C_{21}H_{22}N_2OS$ $[M+H]^+$: 351.1531 found 351.1540. . **IR** (ATR, cm^{-1}) : 3062, 2951, 1723, 1610, 1336, 722.

3-benzyl-2-(pyridin-2-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aM)

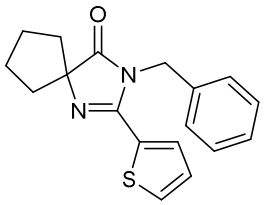


MW : 305.38 g.mol^{-1}
FB : $C_{19}H_{19}N_3O$
Aspect : White solid
Isolated yield : 91%
Melting point : 83°C

Flash chromatography using Petroleum Ether/EtOAc 70:30 as eluent resulted in 125 mg (91% yield) of the title product obtained as a white solid.

^{1}H NMR (300 MHz, DMSO) δ : 8.67 – 8.63 (m, 1H), 7.97 – 7.84 (m, 2H), 7.53 (ddd, *J* = 6.9, 4.8, 1.8 Hz, 1H), 7.24 – 7.12 (m, 3H), 7.04 – 6.99 (d, *J* = 6.7 Hz, 2H), 5.22 (s, 2H), 2.01 – 1.78 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 187.14, 158.39, 149.63, 148.60, 137.78, 136.99, 128.41, 127.43, 127.20, 125.32, 123.92, 77.41, 44.97, 37.73, 26.25. **HRMS** (CI): calculated for $C_{21}H_{19}N_3O$ $[M+H]^+$: 306.1606 found 306.1592. **IR** (ATR, cm^{-1}) : 2926, 1726, 1597, 1440, 1339, 1116, 959, 682.

3-benzyl-2-(thiophen-2-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aN)

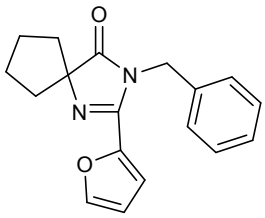


FW : 310.41 g.mol^{-1}
FB : $C_{18}H_{18}N_2OS$
Aspect : Yellow oil
Isolated yield : 49%

Flash chromatography using Petroleum Ether/EtOAc 65:35 as eluent resulted in 69 mg (49% yield) of the title product obtained as a yellow oily liquid.

^{1}H NMR (300 MHz, DMSO) δ : 7.76 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.40 (dd, *J* = 3.8, 1.0 Hz, 1H), 7.37 – 7.30 (m, 2H), 7.24 (dd, *J* = 8.5, 6.0 Hz, 1H), 7.14 – 7.07 (m, 3H), 5.01 (s, 2H), 1.97 – 1.81 (m, 8H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ : 187.07, 155.03, 136.53, 131.68, 129.53, 129.25, 129.03, 127.80, 127.67, 126.16, 77.13, 44.70, 37.89, 26.27. **HRMS** (CI): calculated for $C_{18}H_{18}N_2OS$ $[M+H]^+$: 311.1218 found 311.1217. **IR** (ATR, cm^{-1}) : 3035, 3017, 2974, 2873, 1729, 1609, 1439, 1335, 1257, 702.**IR** (ATR, cm^{-1}) : 2954, 1721, 1598, 1339, 714.

3-benzyl-2-(furan-2-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aO)

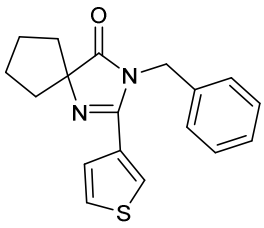


FW : 294.35 g.mol^{-1}
FB : $C_{18}H_{18}N_2O_2$
Aspect : Brown liquid
Isolated yield : 47%

Flash chromatography using Petroleum Ether/EtOAc 70:30 as eluent resulted in 62 mg (47% yield) of the title product obtained as a brown oily liquid.

^{1}H NMR (300 MHz, DMSO) δ 7.89 (d, *J* = 1.3 Hz, 1H), 7.35 – 7.22 (m, 3H), 7.12 (d, *J* = 7.0 Hz, 2H), 7.04 (d, *J* = 3.3 Hz, 1H), 6.62 (dd, *J* = 3.6, 1.8 Hz, 1H), 4.99 (s, 2H), 1.95 – 1.80 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) : δ 186.63, 151.36, 144.90, 143.67, 136.70, 128.84, 127.59, 126.40, 114.54, 111.89, 76.94, 44.69, 37.97, 26.21. **HRMS** (CI): calculated for $C_{18}H_{18}N_2O_2$ $[M+H]^+$: 295.1447 found 295.1457. **IR** (ATR, cm^{-1}) : 3663, 3138, 2959, 2872, 1726, 1336, 720.

3-benzyl-2-(thiophen-3-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aP)

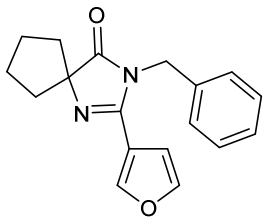


FW : 310.41 g.mol^{-1}
FB : $C_{18}H_{18}N_2OS$
Aspect : Orange liquid
Isolated yield : 75%

Flash chromatography using Petroleum Ether/EtOAc 70:30 as eluent resulted in 105 mg (75% yield) of the title product obtained as an orange oily liquid.

^{1}H NMR (300 MHz, DMSO) δ 7.91 (dd, *J* = 2.8, 1.3 Hz, 1H), 7.62 (dd, *J* = 5.1, 2.9 Hz, 1H), 7.35 – 7.22 (m, 4H), 7.04 (d, *J* = 7.0 Hz, 2H), 4.90 (s, 2H), 1.96 – 1.82 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 186.99, 156.45, 136.68, 130.72, 128.99, 127.84, 127.66, 127.38, 126.61, 126.30, 76.98, 44.65, 37.80, 26.18. **HRMS** (CI): calculated for $C_{18}H_{18}N_2OS$ $[M+H]^+$: 311.1218 found 311.1217. **IR** (ATR, cm^{-1}) : 3032, 3014, 2961, 2868, 1727, 1605, 1434, 1338, 1261, 696.

3-benzyl-2-(furan-3-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (3aQ)

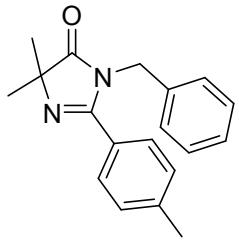


FW : 294.35 g.mol^{-1}
FB : $C_{18}H_{18}N_2O_2$
Aspect : Brown liquid
Isolated yield : 35%

Flash chromatography using Petroleum Ether/EtOAc 70:30 as eluent resulted in 46 mg (35% yield) of the title product obtained as a brown oily liquid.

^{1}H NMR (300 MHz, DMSO) : δ 8.09 (s, 1H), 7.75 (t, *J* = 1.6 Hz, 1H), 7.36 – 7.22 (m, 3H), 7.09 (d, *J* = 7.1 Hz, 2H), 6.76 (d, *J* = 1.3 Hz, 1H), 4.92 (s, 2H), 1.98 – 1.77 (m, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) : δ 186.94, 154.44, 143.73, 143.54, 136.48, 129.16, 127.79, 126.04, 116.44, 109.89, 76.93, 44.34, 37.86, 26.25. **HRMS** (CI): calculated for $C_{18}H_{18}N_2O_2$ $[M+H]^+$: 295.1447 found 295.1449. **IR** (ATR, cm^{-1}) : 3130, 2957, 2871, 1724, 1403, 1161, 873, 696.

3-benzyl-5,5-dimethyl-2-(p-tolyl)-3,5-dihydro-4H-imidazol-4-one (3bA)

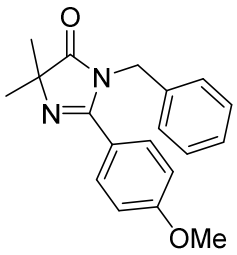


FW : 292.38 g.mol^{-1}
FB : $C_{19}H_{20}N_2O$
Aspect : yellow pale solid
Isolated yield : 91%
Melting point : 79°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 120 mg (91% yield) of the title product obtained as a yellow pale solid.

^{1}H NMR (300 MHz, DMSO) δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.31 – 7.19 (m, 5H), 6.97 (d, *J* = 6.8 Hz, 2H), 4.72 (s, 2H), 2.32 (s, 3H), 1.33 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.90, 161.06, 141.09, 136.62, 129.20, 128.67, 127.99, 127.48, 126.81, 126.65, 67.36, 44.76, 24.10, 21.38. **IR** (ATR, cm^{-1}) : 2973, 2928, 1727, 1622, 699.

3-benzyl-2-(4-methoxyphenyl)-5,5-dimethyl-3,5-dihydro-4H-imidazol-4-one (3bB)



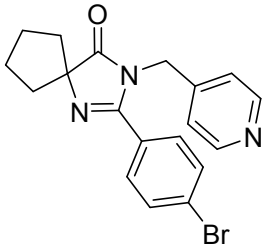
FW : 308.38 g.mol^{-1}
FB : $C_{19}H_{20}N_2O_2$
Aspect : yellow oily liquid
Isolated yield : 71%

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 99 mg (71% yield) of the title product obtained as a yellow oily liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ : 7.36 (d, *J* = 8.7 Hz, 2H), 7.28 – 7.18 (m, 3H), 7.04 – 6.92 (m, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 4.70 (s, 2H), 3.77 (s, 3H), 1.43 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 187.11, 161.65, 160.84, 136.74, 129.81, 128.83, 127.62, 126.68, 122.05, 114.04, 67.40, 55.40, 44.93, 24.24.

HRMS (CI): calculated for $C_{19}H_{20}N_2O_2$ $[M+H]^+$: 309.1603 found 309.1607. **IR** (ATR, cm^{-1}) : 3033, 2972, 2930, 1724, 1608, 1512, 1252, 694.

2-(4-bromophenyl)-3-(pyridin-4-ylmethyl)-1,3-diazaspiro[4.4]non-1-en-4-one (3cK)

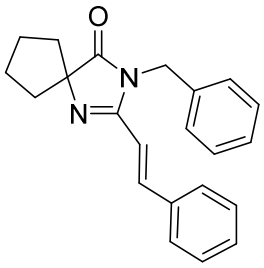


FW : 384.27 g.mol^{-1}
FB : $C_{19}H_{18}BrN_3O$
Aspect : Yellow oily liquid
Isolated yield : 62%

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 173 mg (62% yield) of the title product obtained as a yellow oily liquid.

^{1}H NMR (300 MHz, DMSO) δ 8.46 (d, *J* = 5.9 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 5.9 Hz, 2H), 4.77 (s, 2H), 2.00 – 1.84 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.91, 159.53, 150.48, 145.50, 138.18, 132.26, 129.64, 125.88, 121.55, 77.53, 44.09, 37.92, 26.23. **HRMS** (CI): calculated for $C_{19}H_{19}BrN_3O$ $[M+H]^+$: 384.0711 found 384.0713 **IR** (ATR, cm^{-1}) : 3664, 2969, 1725, 1601, 1336, 1068, 721.

(E)-3-benzyl-2-styryl-1,3-diazaspiro[4.4]non-1-en-4-one (5aA)

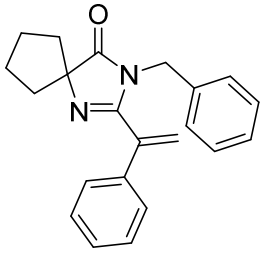


MW : 330.43 g.mol^{-1}
FB : $C_{22}H_{22}N_2O$
Aspect : brown solid
Isolated yield : 73%
Melting point : 111°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 108 mg (73% yield) of the title product obtained as a brown solid.

^{1}H NMR (300 MHz, DMSO) δ : 7.67 – 7.61 (m, 3H), 7.43 – 7.31 (m, 5H), 7.27 – 7.19 (m, 3H), 6.97 (d, *J* = 16.0 Hz, 1H), 4.91 (s, 2H), 1.95 – 1.72 (m, 8H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 186.44, 157.86, 139.35, 136.47, 135.01, 129.76, 129.05, 128.86, 127.89, 127.57, 126.74, 113.83, 77.03, 43.73, 37.80, 26.21. **HRMS** (CI): calculated for $C_{22}H_{22}N_2O$ $[M+H]^+$: 331.1810 found 331.1800. **IR** (ATR, cm^{-1}) : 3027, 2923, 2854, 1721, 1591, 1347, 692

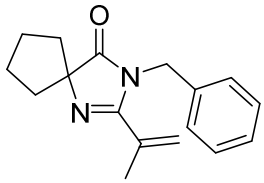
3-benzyl-2-(1-phenylvinyl)-1,3-diazaspiro[4.4]non-1-en-4-one (5aB)



FW : 330.43 g.mol^{-1}
FB : $C_{22}H_{22}N_2O$
Aspect : White solid
Isolated yield : 51%
Melting point : 100°C

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 76 mg (51% yield) of the title product obtained as a white solid.
^{1}H NMR (300 MHz, DMSO) δ 7.38 – 7.13 (m, 8H), 6.99 – 6.86 (m, 2H), 5.93 (s, 1H), 5.49 (s, 1H), 4.36 (s, 2H), 2.00 – 1.77 (m, 8H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.46, 160.66, 139.29, 136.53, 135.70, 129.03, 128.93, 128.47, 127.49, 127.10, 126.30, 120.74, 77.35, 44.30, 37.72, 26.11.**HRMS** (CI): calculated for $C_{22}H_{22}N_2O$ $[M+H]^+$: 331.1810 found 331.1820. **IR** (ATR, cm^{-1}) : 3061, 2940, 1723, 1609, 1340, 701.

3-benzyl-2-(prop-1-en-2-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (5aC)

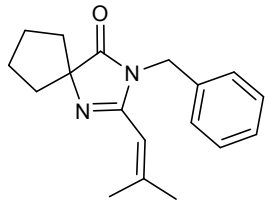


FW : 268.36 g.mol^{-1}
FB : $C_{17}H_{20}N_2O$
Aspect : Yellow liquid
Isolated yield : 49%

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 59 mg (49% yield) of the title product obtained as a yellow oily liquid.
^{1}H NMR (300 MHz, DMSO) δ : 7.37 – 7.25 (m, 3H), 7.06 (d, *J* = 7.2 Hz, 2H), 5.46 (s, 1H), 5.27 (s, 1H), 4.75 (s, 2H), 1.91—1.85 (m, 6H), 1.83 (s, 3H), 1.77 – 1.72 (m, 2H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 187.08, 161.39, 136.77, 135.13, 128.84, 127.58, 126.71, 120.80, 77.36, 44.70, 37.69, 26.16, 21.30.

HRMS (CI): calculated for $C_{22}H_{22}N_2O$ $[M+H]^+$: 269.1654 found 294.1651. **IR** (ATR, cm^{-1}) : 3672, 2969, 1723, 1580, 1337, 1076, 722.

3-benzyl-2-(2-methylprop-1-en-1-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (5aD)

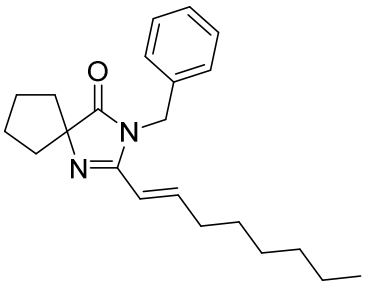


FW : 282.38 g.mol^{-1}
FB : $C_{18}H_{18}N_2O$
Aspect : Yellow liquid
Isolated yield : 51%

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 65 mg (51% yield) of the title product obtained as a yellow oily liquid.

^{1}H NMR (300 MHz, DMSO) δ : 7.38 – 7.24 (m, 3H), 7.14 (d, *J* = 7.0 Hz, 2H), 5.88 – 5.84 (m, 1H), 4.68 (s, 2H), 2.03 (d, *J* = 1.0 Hz, 3H), 1.87 (m, 6H), 1.82 (d, *J* = 1.1 Hz, 3H), 1.71 (m, 2H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 186.19, 157.39, 150.22, 136.74, 128.78, 127.59, 126.85, 112.21, 77.09, 43.70, 37.73, 26.82, 26.03, 20.50. **HRMS** (CI): calculated for $C_{18}H_{18}N_2O$ $[M+H]^+$: 283.1810 found 283.1813. **IR** (ATR, cm^{-1}) : 3665, 2967, 1719, 1600, 1345, 697.

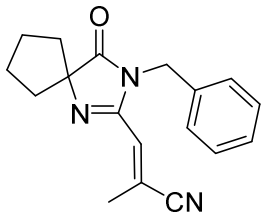
(E)-3-benzyl-2-(oct-1-en-1-yl)-1,3-diazaspiro[4.4]non-1-en-4-one (5aE)



FW : 338.49 g.mol^{-1}
FB : $C_{22}H_{30}N_2O$
Aspect : Yellow oily liquid
Isolated yield : 50%

Flash chromatography using Petroleum Ether/EtOAc 75:25 as eluent resulted in 76 mg (50% yield) of the title product obtained as a yellow oily liquid.
^{1}H NMR (300 MHz, DMSO) δ : 7.36 – 7.23 (m, 3H), 7.15 (d, *J* = 6.9 Hz, 2H), 6.77 (dt, *J* = 15.3, 7.1 Hz, 1H), 6.15 (d, *J* = 15.6 Hz, 1H), 4.75 (s, 2H), 2.11 (dt, *J* = 13.9, 7.1 Hz, 2H), 1.86 – 1.69 (m, 8H), 1.36 – 1.11 (m, 8H), 0.83 (t, *J* = 6.7 Hz, 3H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ : 186.28, 158.27, 144.17, 136.42, 129.11, 128.07, 126.83, 116.73, 77.36, 65.94, 43.69, 37.70, 31.66, 28.92, 26.21, 25.56, 22.58, 15.36.**HRMS** (CI): calculated for $C_{22}H_{30}N_2O$ $[M+H]^+$: 339.2436 found 339.2442.**IR** (ATR, cm^{-1}) : 3065, 2929, 2855, 1713, 1625, 1343, 697.

(E)-3-(3-benzyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-2-yl)-2-methylacrylonitrile (5aF)

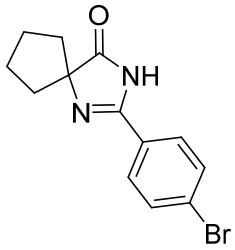


FW : 293.37 g.mol^{-1}
FB : $C_{18}H_{19}N_3O$
Aspect : Yellow pale solid
Isolated yield : 30%
Melting point : 107°C

Flash chromatography using Petroleum Ether/EtOAc 65:35 as eluent resulted in 41 mg (30% yield) of the title product obtained as a yellow pale solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ : 7.41 – 7.28 (m, 3H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.49 (q, *J* = 1.6 Hz, 1H), 4.69 (s, 2H), 2.29 (d, *J* = 1.6 Hz, 3H), 2.02 (m, 6H), 1.90 – 1.79 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ : 185.45, 154.96, 135.74, 129.34, 128.59, 128.35, 126.82, 122.19, 119.32, 77.36, 43.82, 38.02, 26.17, 18.21. **HRMS** (CI): calculated for $C_{18}H_{19}N_3O$ $[M+H]^+$: 294.1606 found 294.1607 **IR** (ATR, cm^{-1}) : 3067, 2955, 2910, 2242, 1729, 1604, 1337.

2-(4-bromophenyl)-1,3-diazaspiro[4.4]non-1-en-4-one (7a)

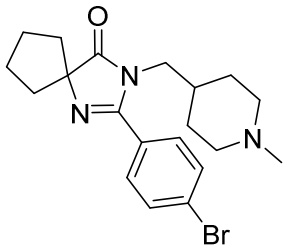


FW : 292.16 g.mol^{-1}
FB : $C_{13}H_{13}BrN_2O$
Aspect : White solid
Isolated yield : 95%

To a solution of **3cK** (0.4 mmol, 154 mg**)** in acetonitrile(2.2 ml), was added iodomethane (0.4 mmol, 25 ul) and the mixture was refluxed for 1,5 hours. The solvent was removed *in vacuo*, the residue was taken up in methanol (2 ml). PtO_2 (20 mg) was added and the resulting mixture was stirred under H_2 at atmospheric pressure at room temperature overnight. The mixture was filtered through a celite pad and concentrated *in vacuo*. The crude product was purified by Flash chromatography using Petroleum Ether/EtOAc 80:20 as eluent resulted in 111 mg (95% yield) of the title product obtained as a white solid.

^{1}H NMR (300 MHz, DMSO) δ 11.46 (s, 1H), 7.89 (d, *J* = 7.5 Hz, 2H), 7.73 (d, *J* = 7.5 Hz, 2H), 1.93 – 1.69 (m, 8H).**^{13}C NMR** (75 MHz, DMSO) δ 187.91, 156.86, 131.87, 128.78, 128.03, 125.24, 77.65, 37.06, 25.56. **HRMS** (CI): calculated for $C_{13}H_{14}BrN_2O$ $[M+H]^+$: 293.0289 found 293.0286. **IR** (ATR, cm^{-1}) : 3148, 3100, 2964, 2869, 1712, 1620, 1436, 1081, 664.

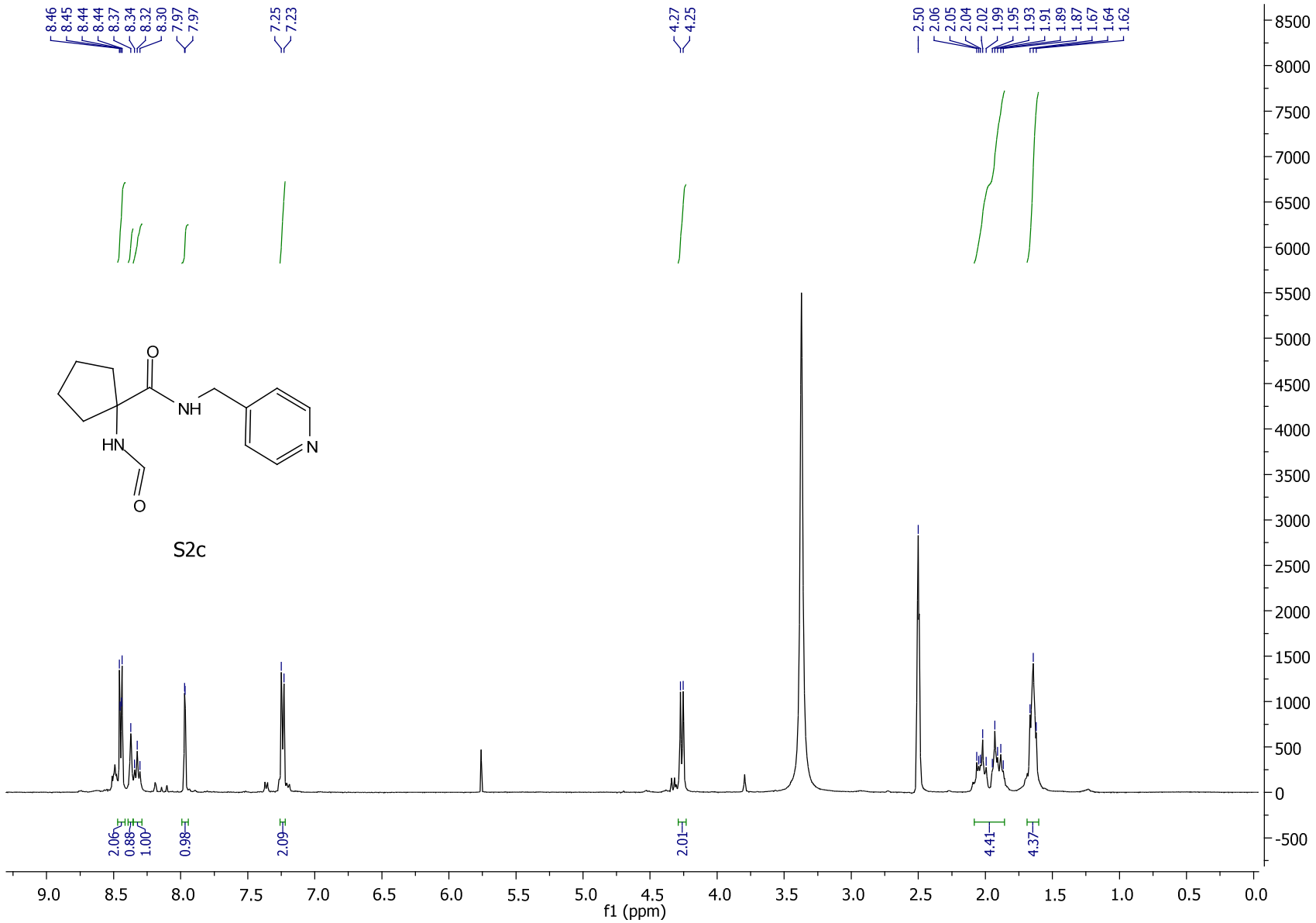
2-(4-bromophenyl)-3-((1-methylpiperidin-4-yl)methyl)-1,3-diazaspiro[4.4]non-1-en-4-one (7b)

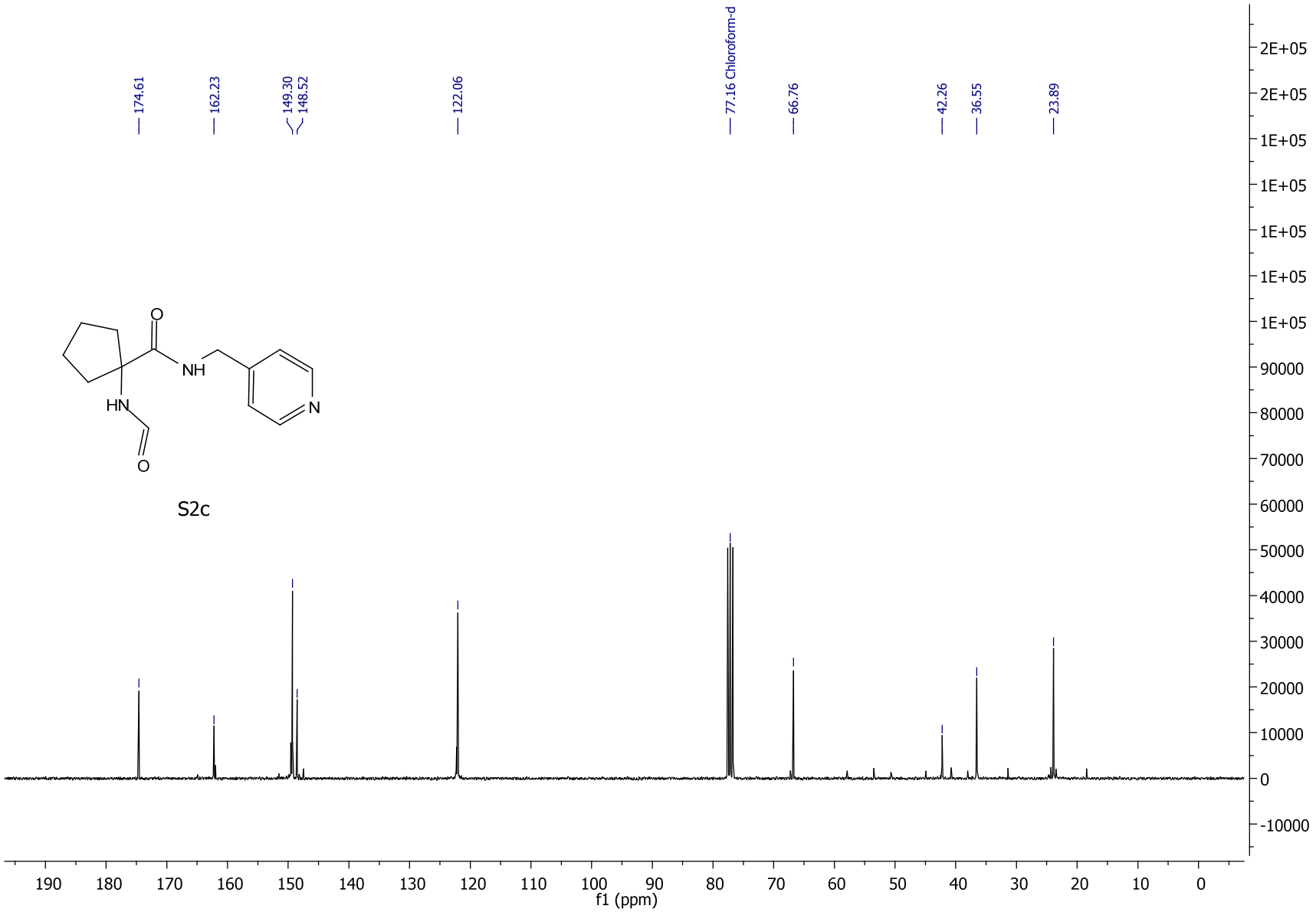


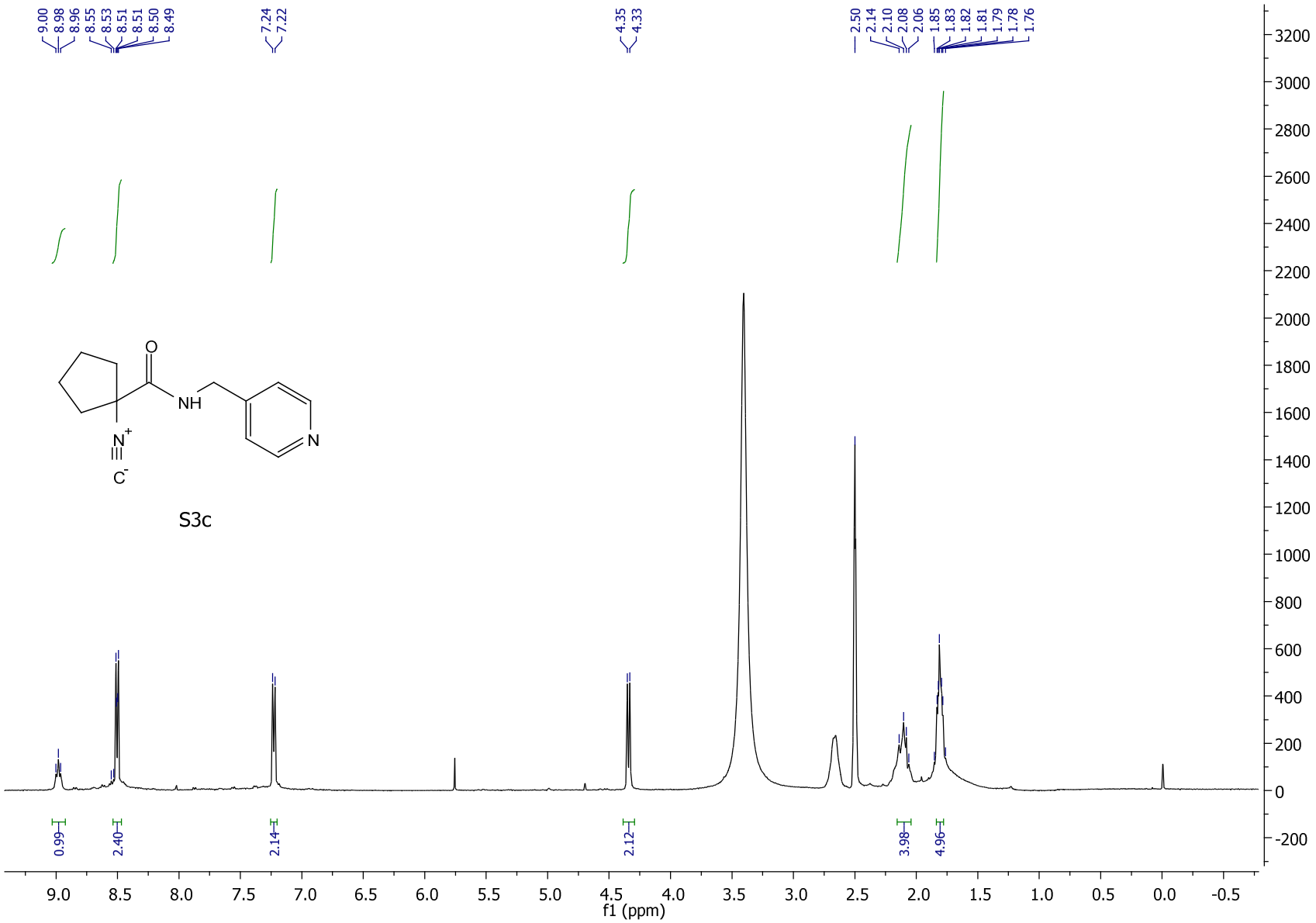
FW : 404.35 g.mol^{-1}
FB : $C_{20}H_{26}BrN_3O$
Aspect : yellow oily liquid
Isolated yield : 53%

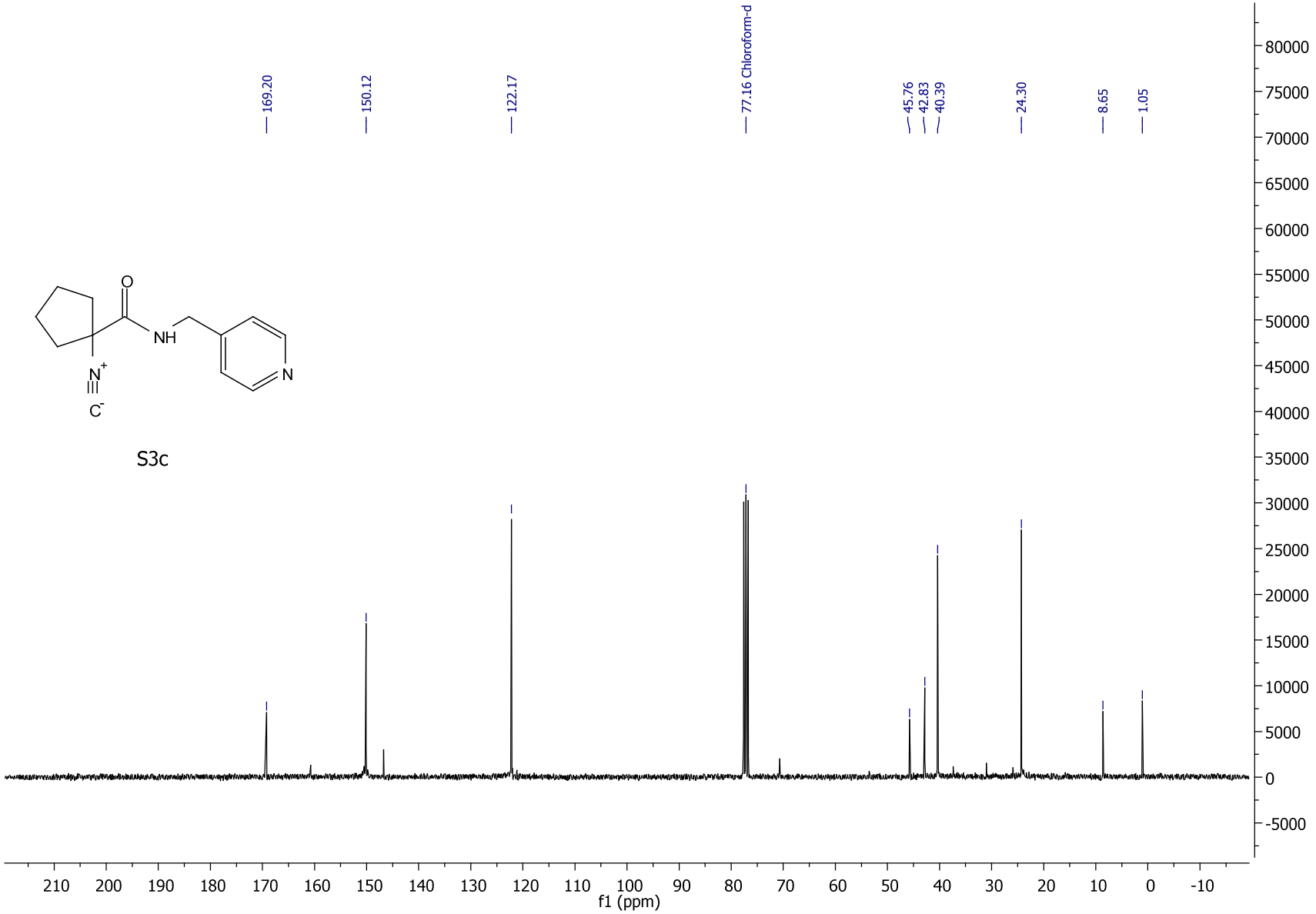
To a solution of **3cK** (0.4 mmol, 154 mg**)** in acetonitrile(2.2 ml), was added iodomethane (0.4 mmol,25 ul) and the mixture was refluxed for 1,5 hours. The solvent was removed *in vacuo* and was taken up in methanol (2 ml), $NaBH_4$ (1 mmol, 38 mg) was added and the reaction mixture was stirred for 4 hours. PtO_2 (20 mg) was added and the resulting mixture was stirred under H_2 at atmospheric pressure at room temperature overnight. The mixture was filtered through a celite pad and concentrated *in vacuo*. to give crude product, which was purified by Flash chromatography using Petroleum Ether/EtOAc 20:80 as eluent resulted in 86 mg (53% yield) of the title product obtained as a yellow oily liquid.

^{1}H NMR (300 MHz, $CDCl_3$) δ : 7.50 (m, 4H), 3.47 (d, *J* = 7.1 Hz, 2H), 2.70 (d, *J* = 11.6 Hz, 1H), 2.17 (s, 1H), 2.00 (dd, *J* = 15.6, 11.7 Hz, 4H), 1.75 (td, *J* = 11.7, 1.9 Hz, 1H), 1.40 (d, *J* = 11.7 Hz, 1H), 1.07 (td, *J* = 11.7, 3.0 Hz, 1H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 187.27, 161.32, 130.78, 130.37, 128.93, 128.17, 77.36, 55.12, 46.69, 46.31, 37.87, 34.36, 29.68, 26.21. **HRMS** (CI): calculated for $C_{20}H_{27}N_3O$ $[M+H]^+$: 404.1337 found 404.1343 **IR** (ATR, cm^{-1}) : 3426, 2929, 2784, 1723, 1620, 1447, 1337, 1070, 699.

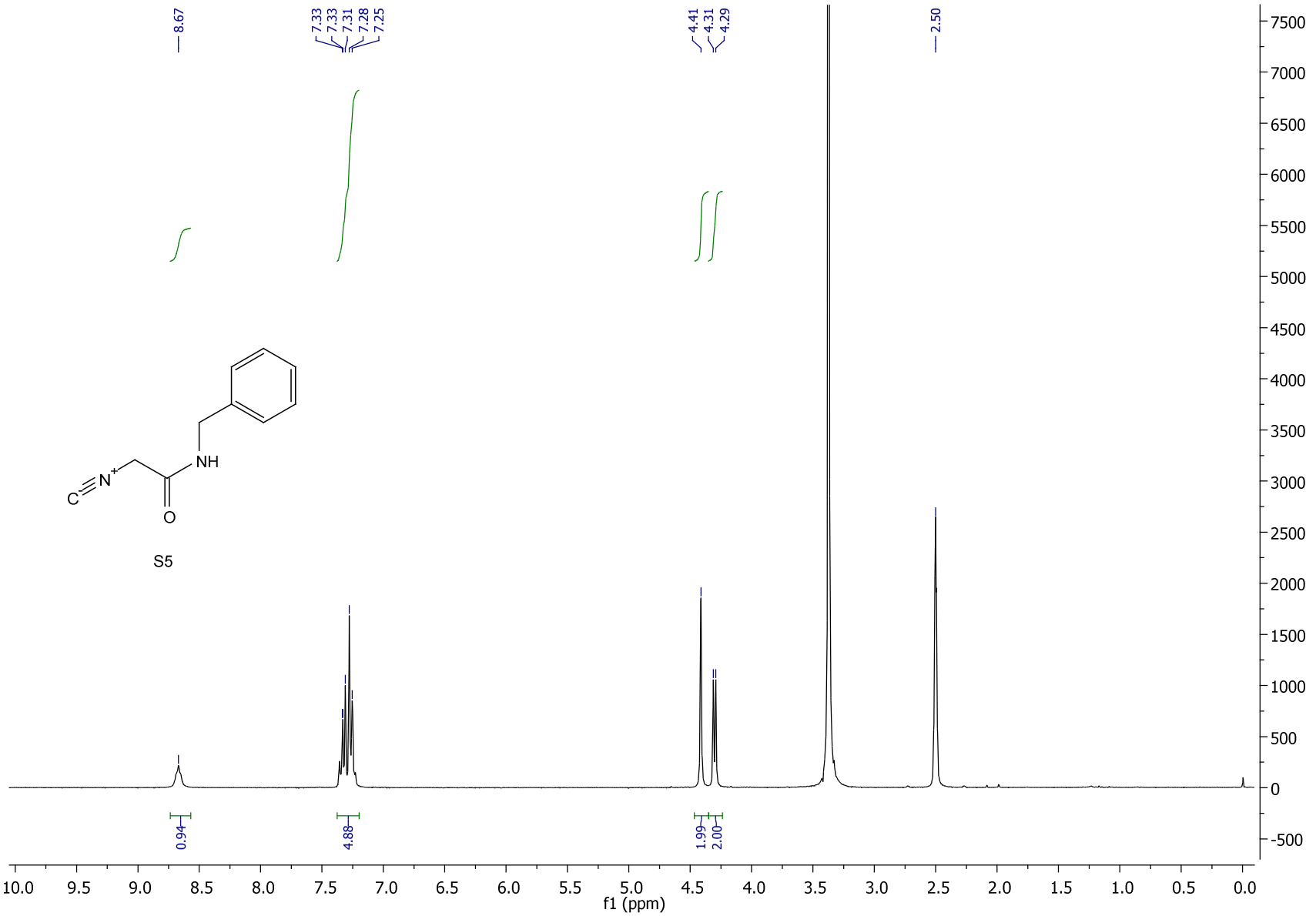

8.46
8.45
8.44
8.44
8.37
8.34
8.32
8.30
7.97
7.97
7.25
7.23
4.27
4.25
2.50
2.06
2.05
2.04
2.02
1.99
1.95
1.93
1.91
1.89
1.87
1.67
1.64
1.62
O
NH
HN
N
O
S2c
2.06
0.88
1.00
0.98
2.09
2.01
4.41
4.37
f1 (ppm)

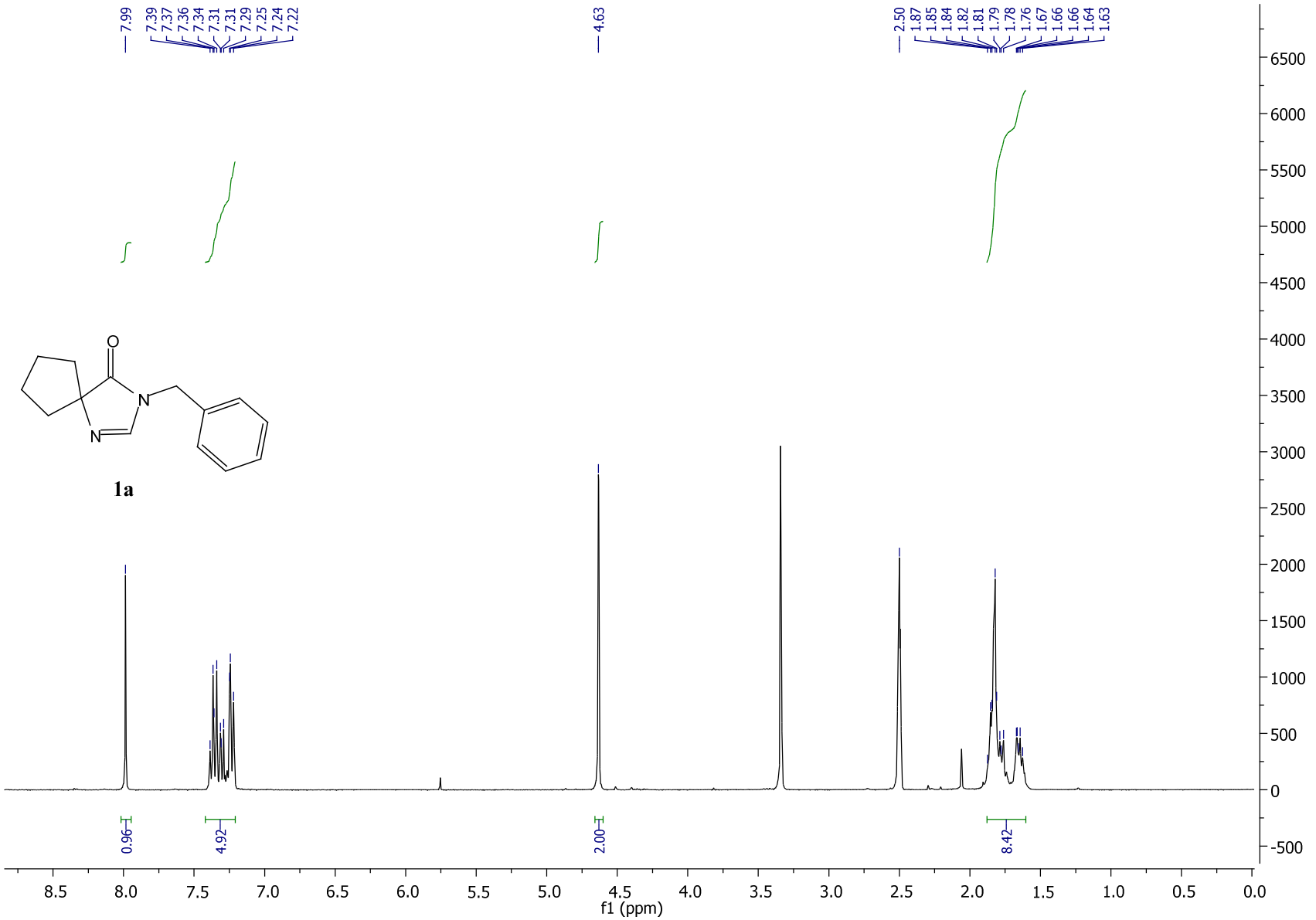

174.61
162.23
149.30
148.52
122.06
77.16 Chloroform-d
66.76
42.26
36.55
23.89
O
NH
HN
N
O
S2c
2E+05
2E+05
1E+05
1E+05
1E+05
1E+05
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

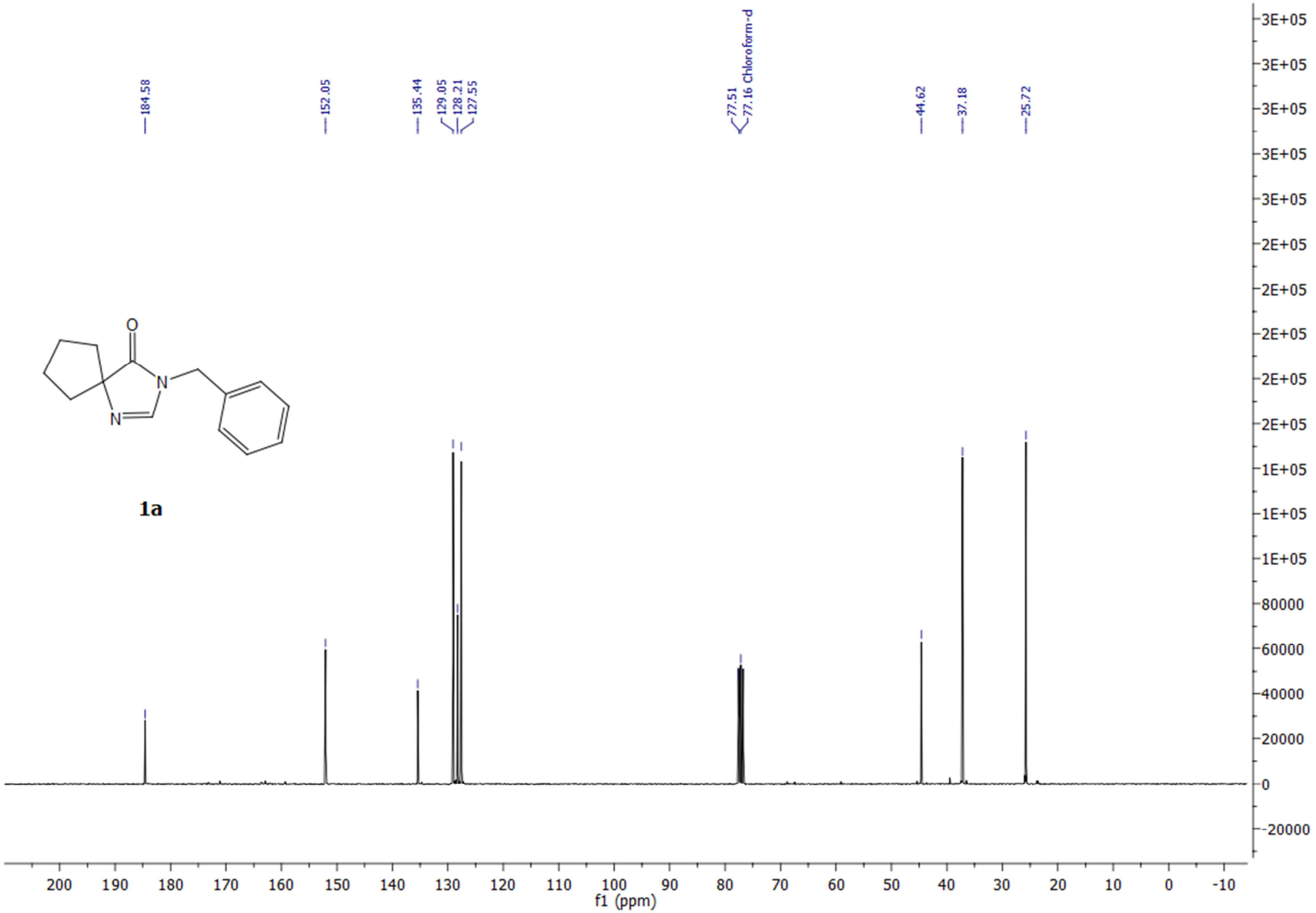

9.00
8.98
8.96
8.55
8.53
8.51
8.51
8.50
8.49
7.24
7.22
4.35
4.33
2.50
2.14
2.10
2.08
2.06
1.85
1.83
1.82
1.81
1.79
1.78
1.76
O
NH
N+
C-
N
S3c
0.99
2.40
2.14
2.12
3.98
4.96
f1 (ppm)

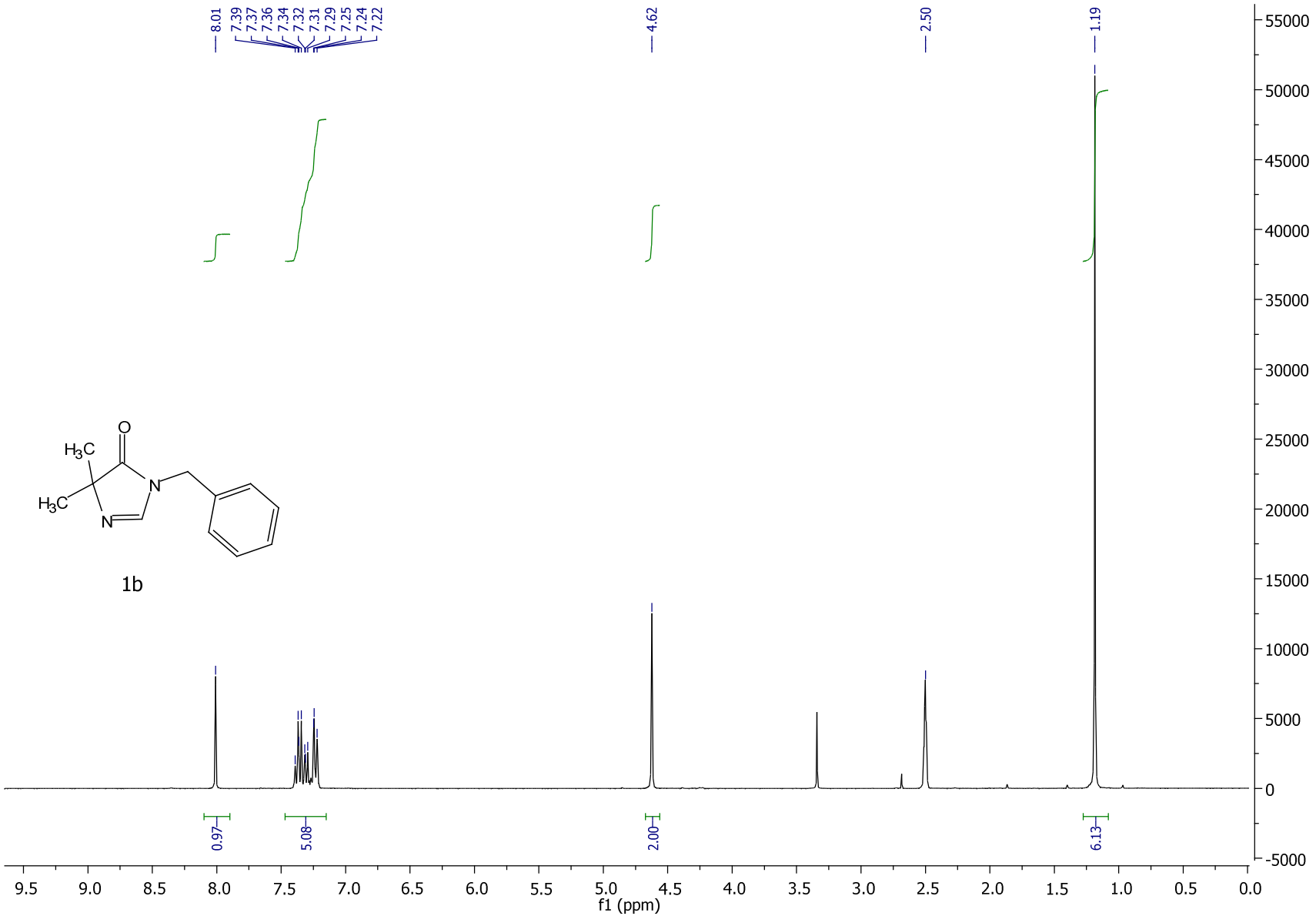

169.20
150.12
122.17
77.16 Chloroform-d
45.76
42.83
40.39
24.30
8.65
1.05
O
NH
N
N+
C-
f1 (ppm)

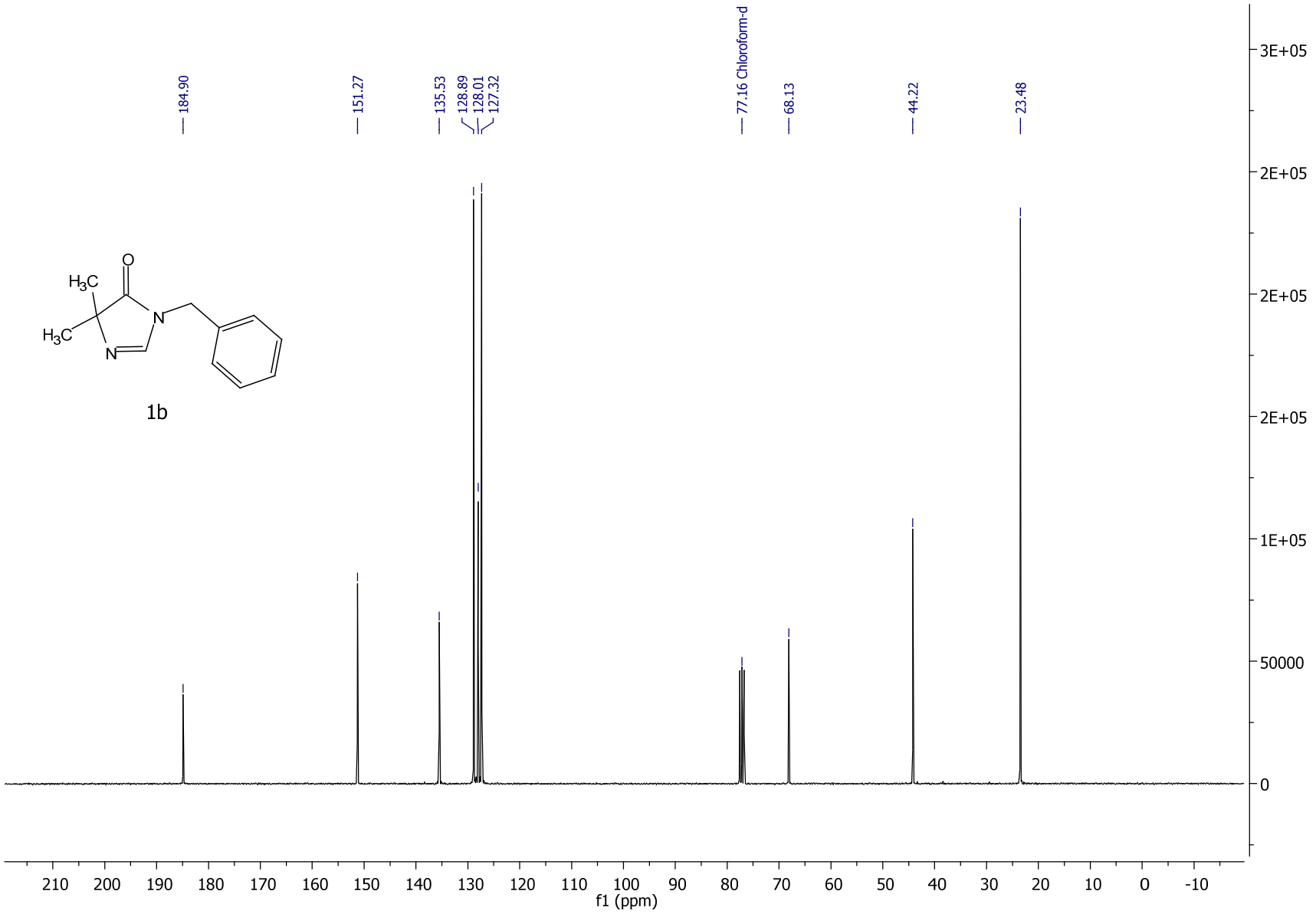
S3c


8.67
7.33
7.33
7.31
7.28
7.25
4.41
4.31
4.29
2.50
NH
O
S5
0.94
4.88
1.99
2.00
f1 (ppm)

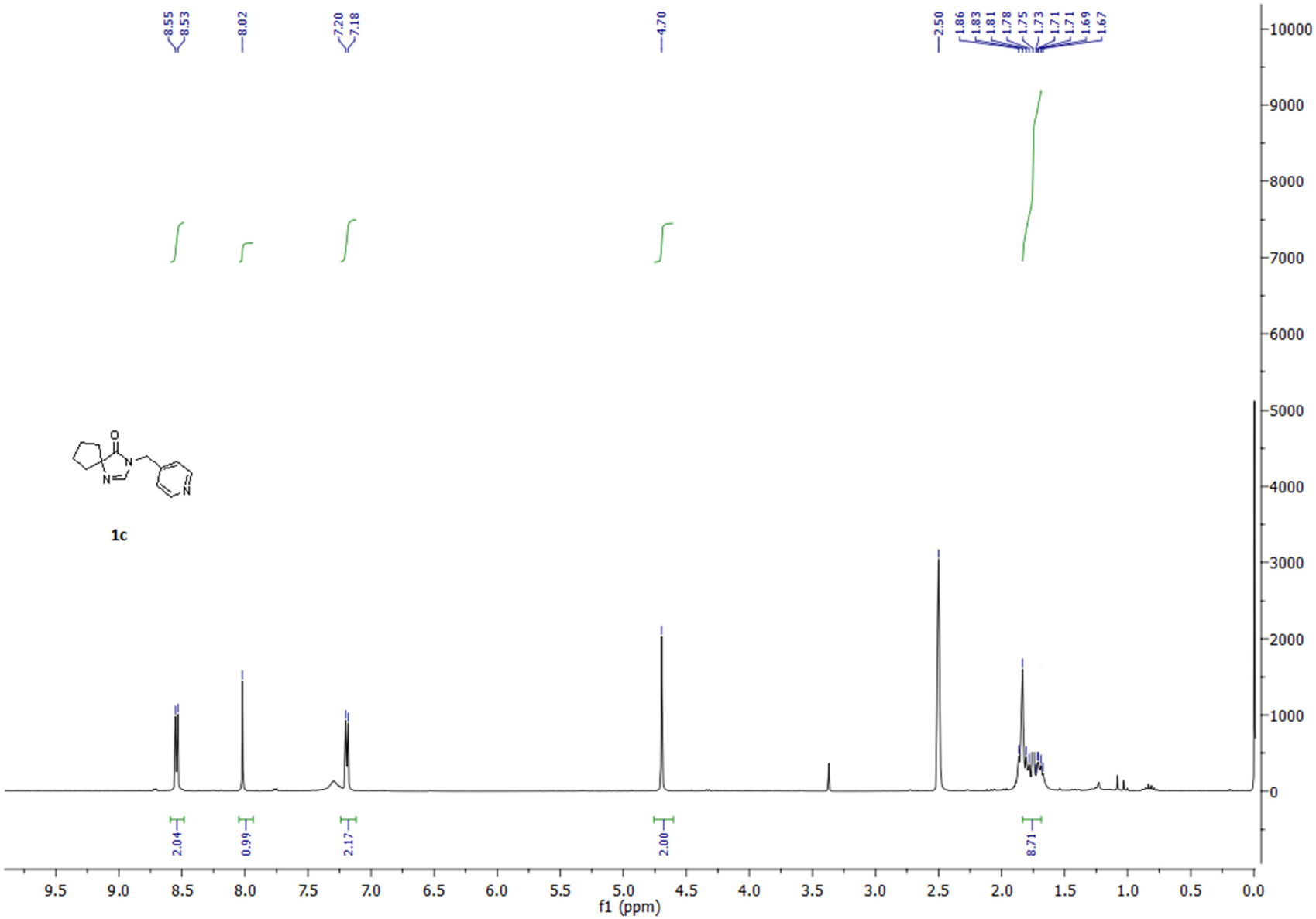

7.99
7.39
7.37
7.36
7.34
7.31
7.31
7.29
7.25
7.24
7.22
4.63
2.50
1.87
1.85
1.84
1.82
1.81
1.79
1.78
1.76
1.67
1.66
1.66
1.64
1.63
O
N
N
1a
0.96
4.92
2.00
8.42
f1 (ppm)


184.58
152.05
135.44
129.05
128.21
127.55
77.51
77.16 Chloroform-d
44.62
37.18
25.72
O
N
N
1a
3E+05
3E+05
3E+05
3E+05
3E+05
2E+05
2E+05
2E+05
2E+05
2E+05
2E+05
1E+05
1E+05
1E+05
80000
60000
40000
20000
0
-20000
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

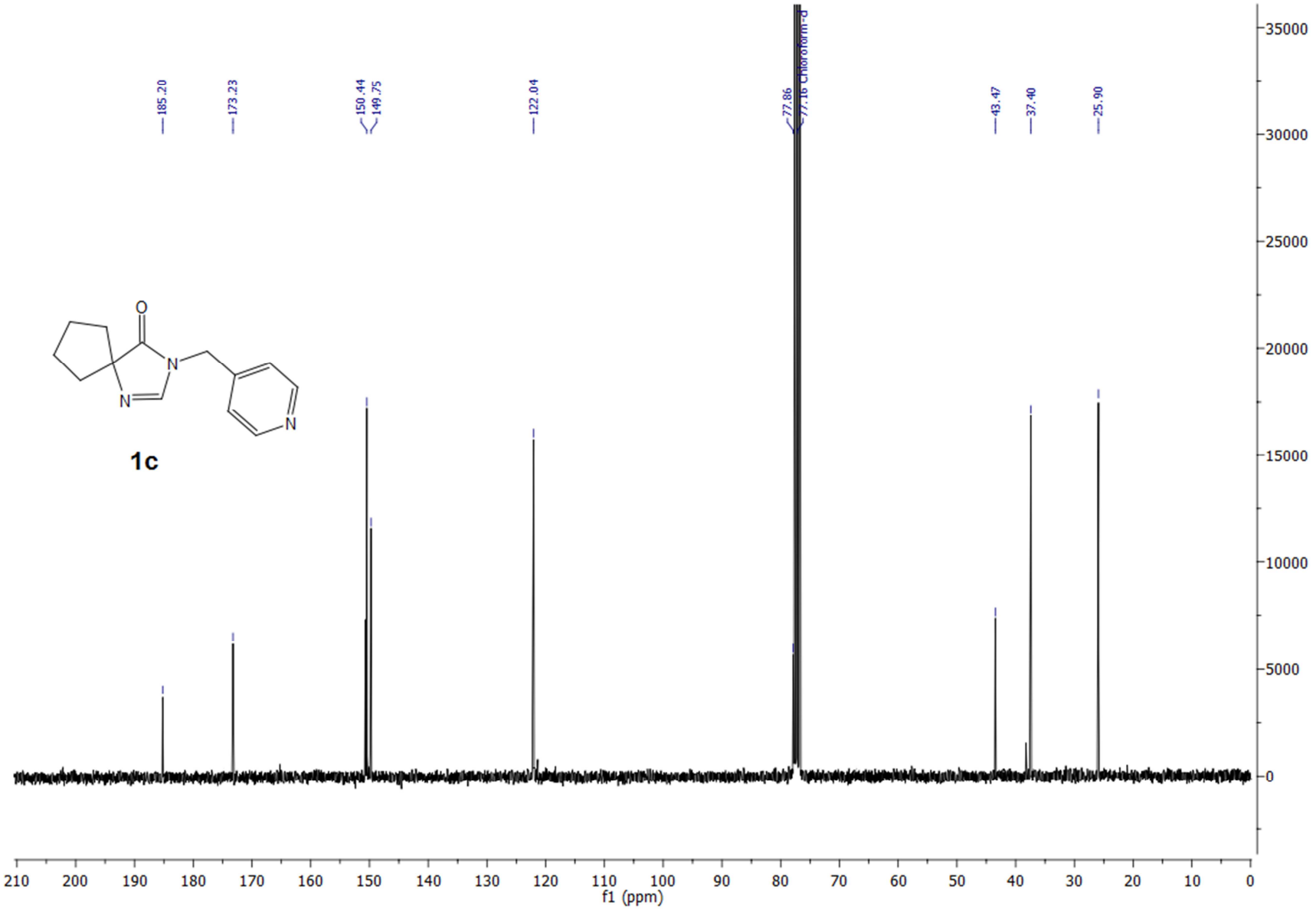

8.01
7.39
7.37
7.36
7.34
7.32
7.31
7.29
7.25
7.24
7.22
4.62
2.50
1.19
O
H3C
H3C
N
N
1b
0.97
5.08
2.00
6.13
f1 (ppm)

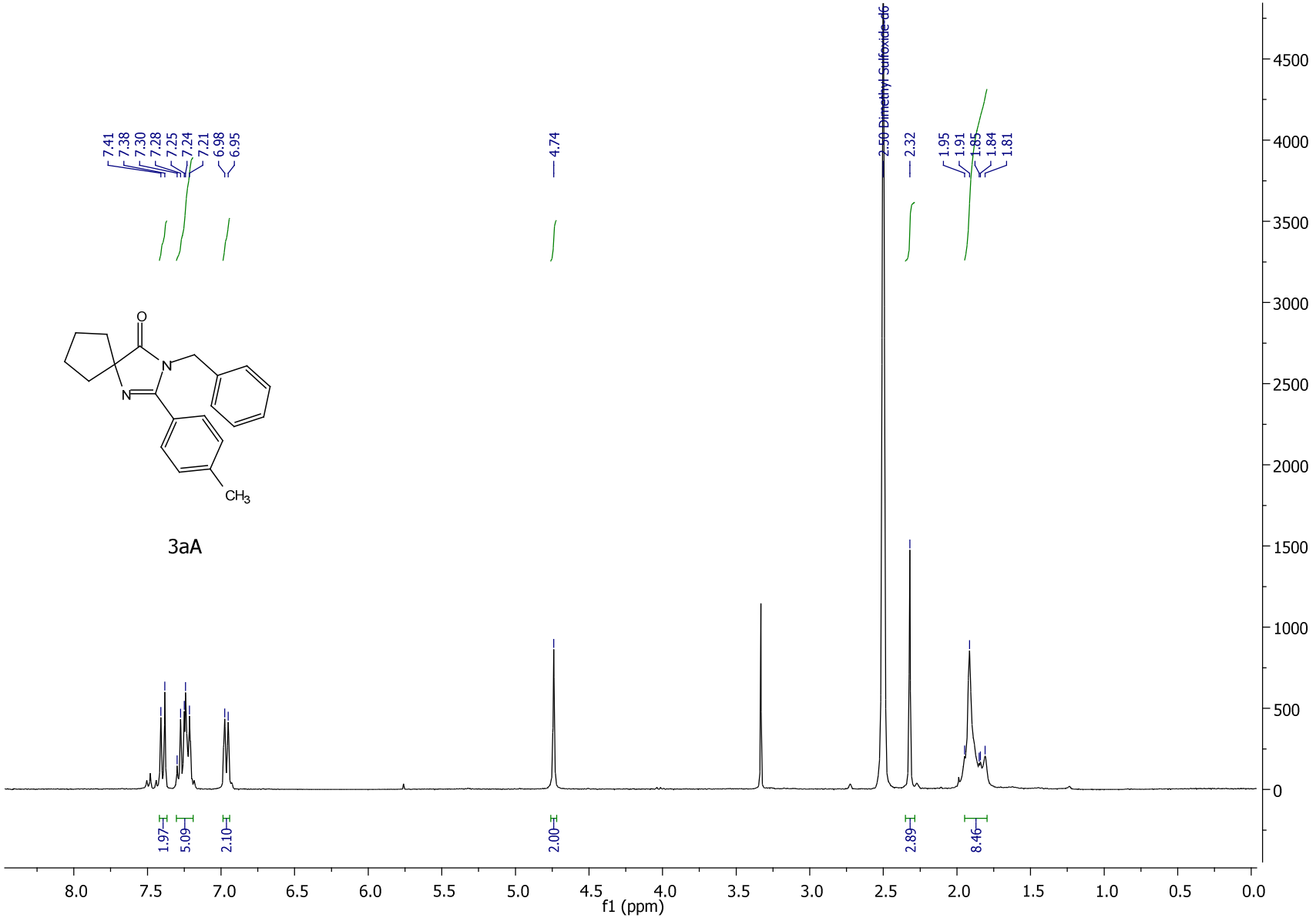

184.90
151.27
135.53
128.89
128.01
127.32
77.16 Chloroform-d
68.13
44.22
23.48
3E+05
2E+05
2E+05
2E+05
1E+05
50000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

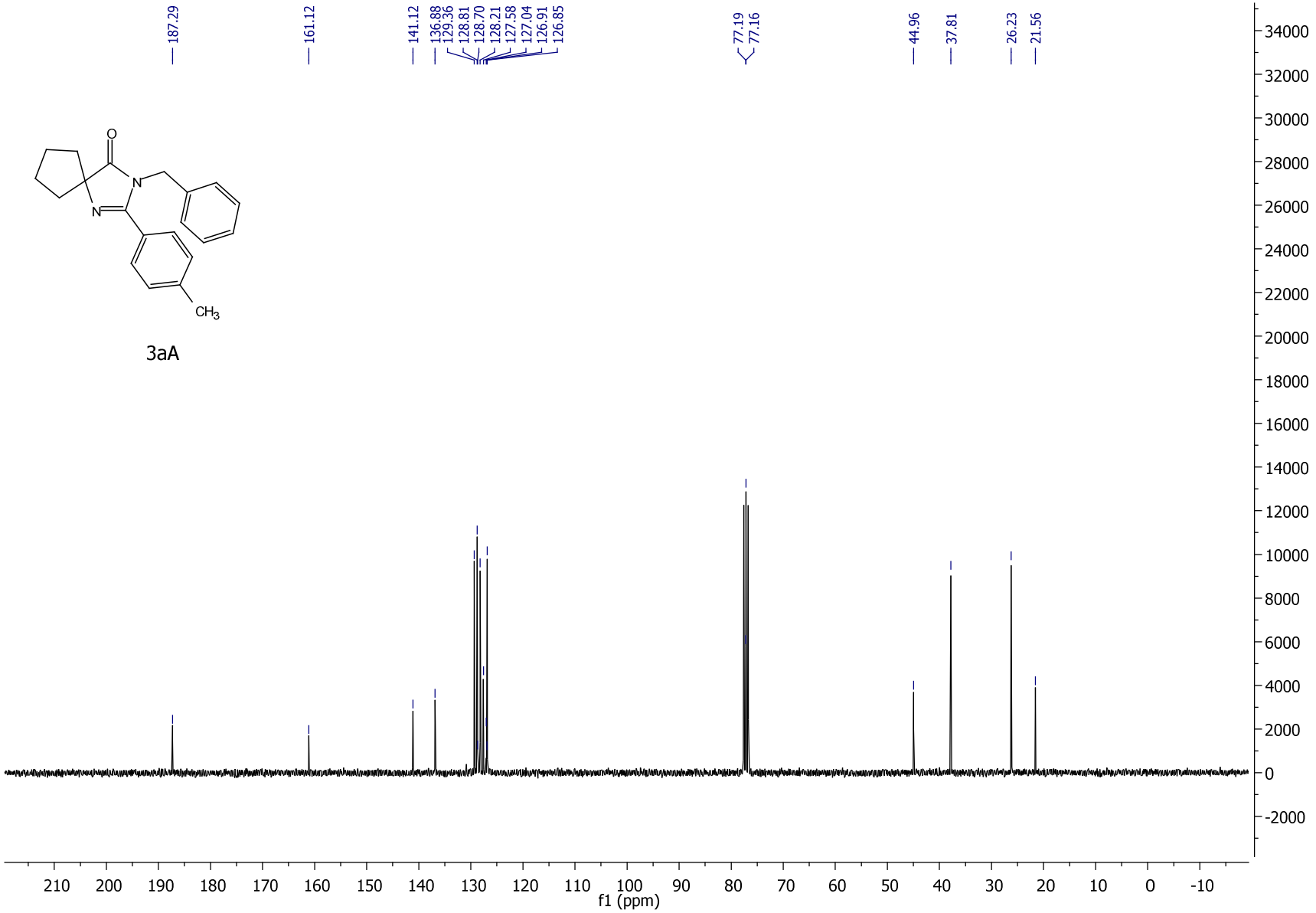
1b

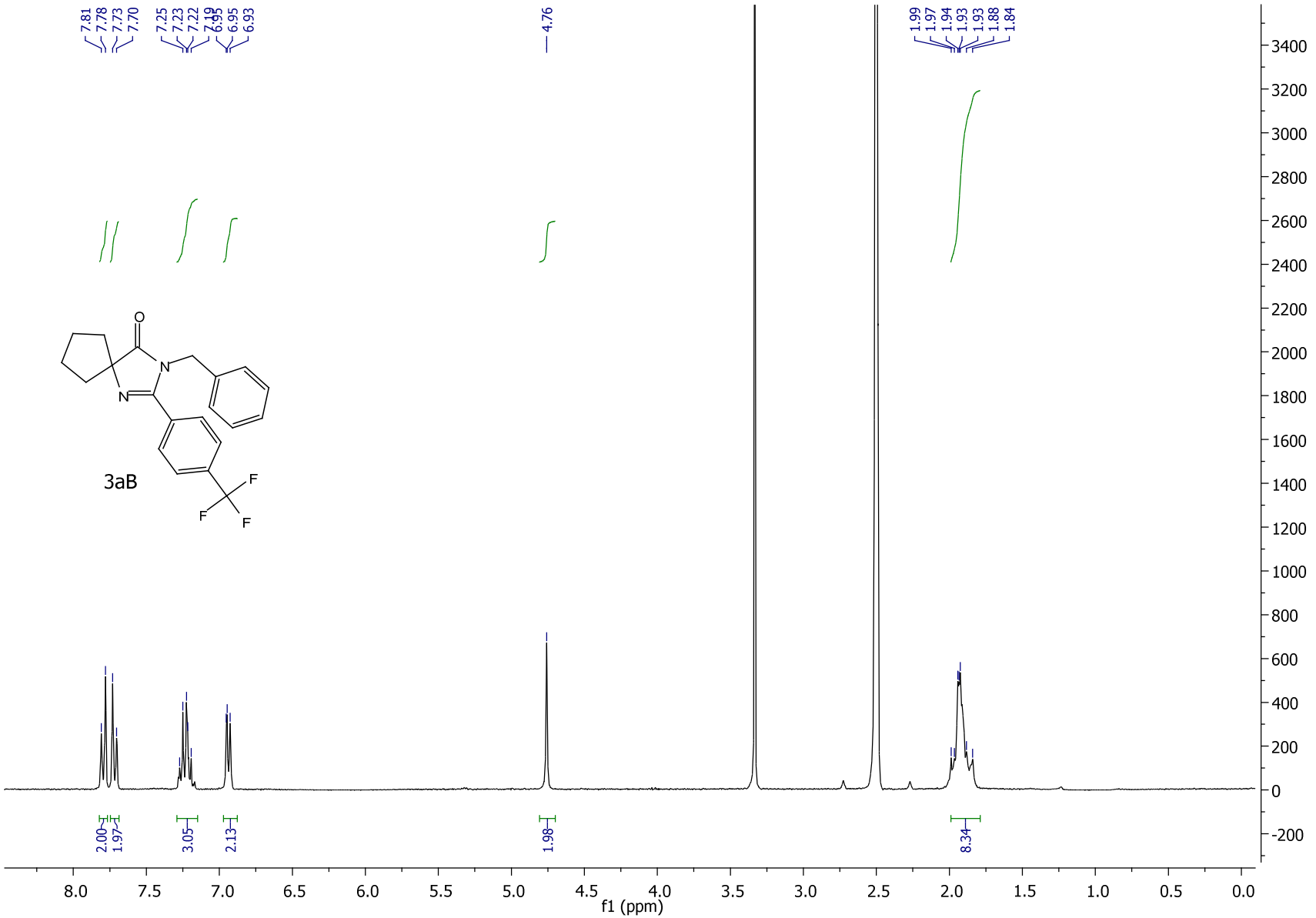

8.55
8.53
8.02
7.20
7.18
4.70
2.50
1.86
1.83
1.81
1.78
1.75
1.73
1.71
1.71
1.69
1.67
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
2.04
0.99
2.17
2.00
8.71
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

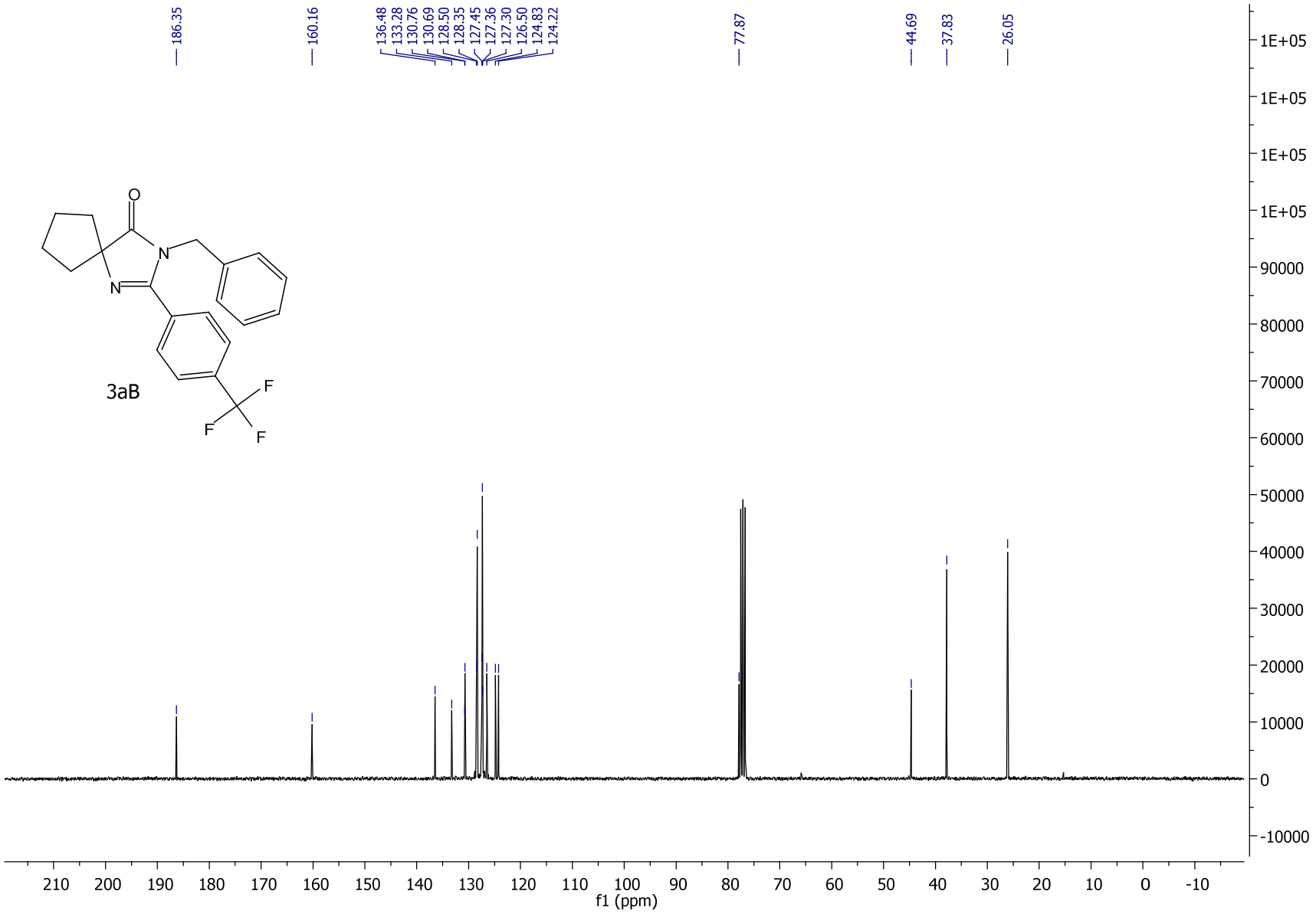
1c

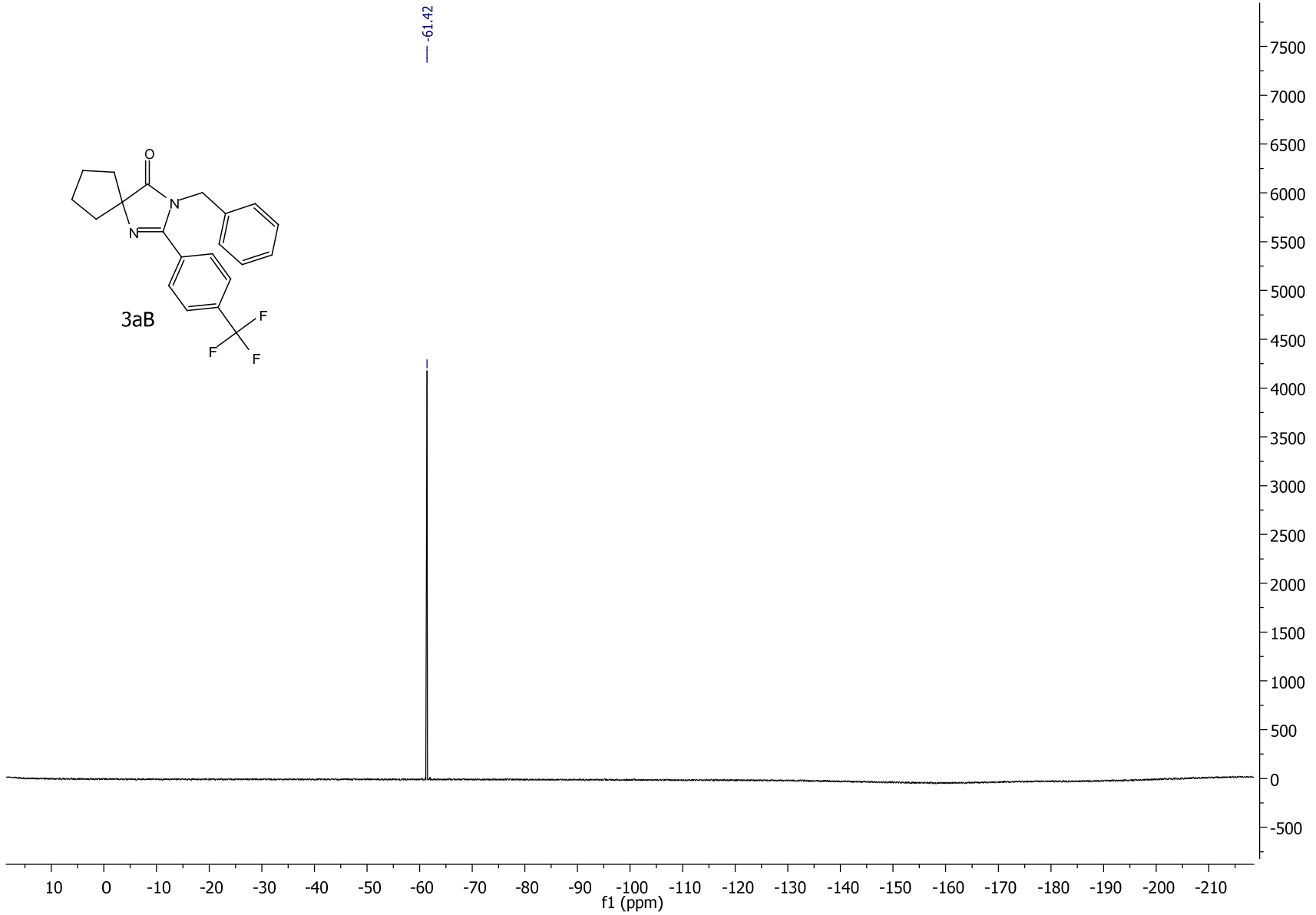

185.20
173.23
150.44
149.75
122.04
77.86
77.16 Chloroform-d
43.47
37.40
25.90
O
N
N
N
1c
35000
30000
25000
20000
15000
10000
5000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

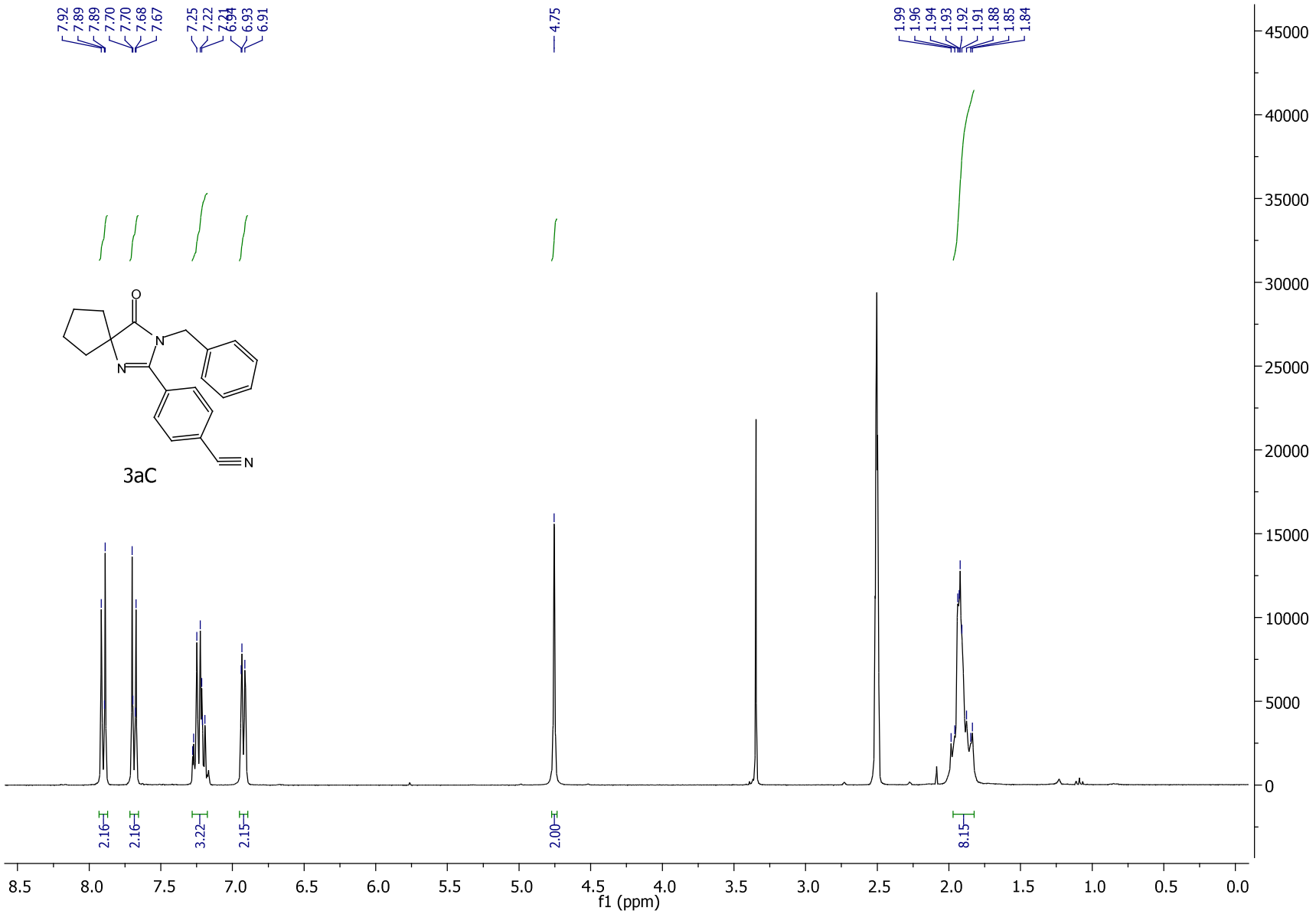

7.41
7.38
7.30
7.28
7.25
7.24
7.21
6.98
6.95
4.74
2.50 Dimethyl Sulfoxide-d6
2.32
1.95
1.91
1.85
1.84
1.81
O
N
N
CH3
3aA
1.97
5.09
2.10
2.00
2.89
8.46
f1 (ppm)

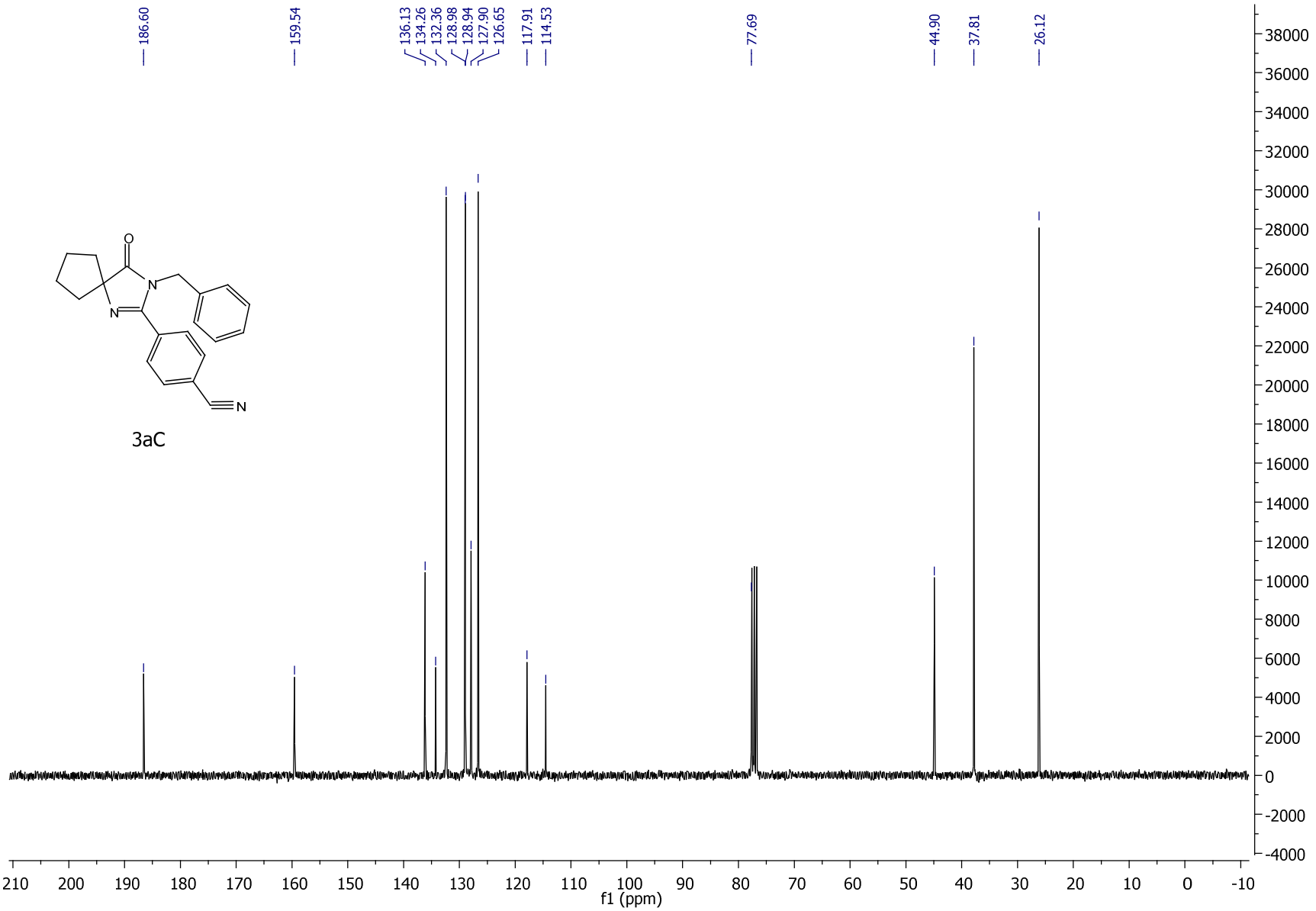

187.29
161.12
141.12
136.88
129.36
128.81
128.70
128.21
127.58
127.04
126.91
126.85
77.19
77.16
44.96
37.81
26.23
21.56
O
N
N
CH3
3aA
f1 (ppm)

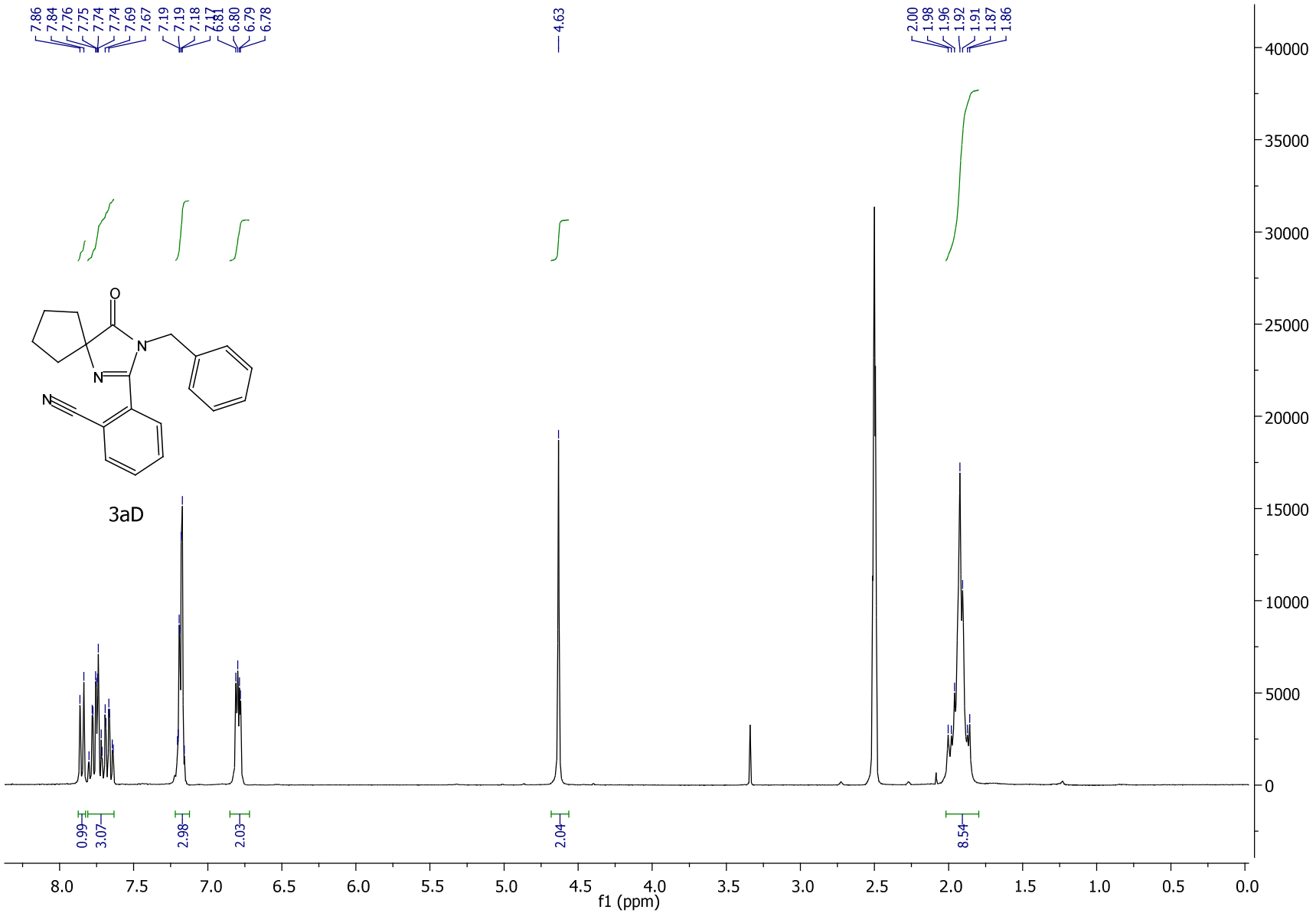

7.81
7.78
7.73
7.70
7.25
7.23
7.22
7.19
6.95
6.93
4.76
1.99
1.97
1.94
1.93
1.93
1.88
1.84
O
N
N
F
F
F
3aB
2.00
1.97
3.05
2.13
1.98
8.34
f1 (ppm)

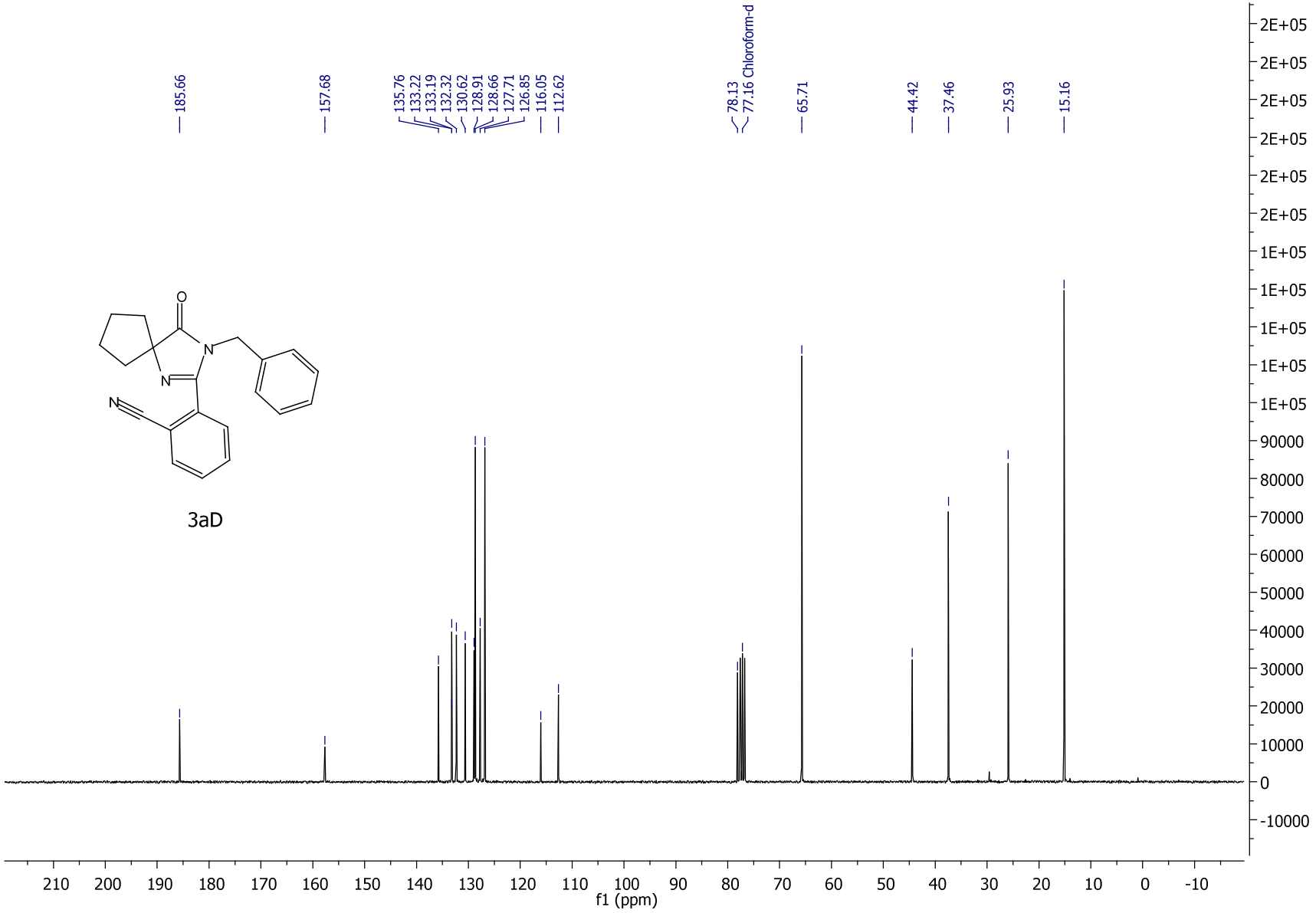

186.35
160.16
136.48
133.28
130.76
130.69
128.50
128.35
127.45
127.36
127.30
126.50
124.83
124.22
77.87
44.69
37.83
26.05
O
N
N
F
F
F
3aB
1E+05
1E+05
1E+05
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

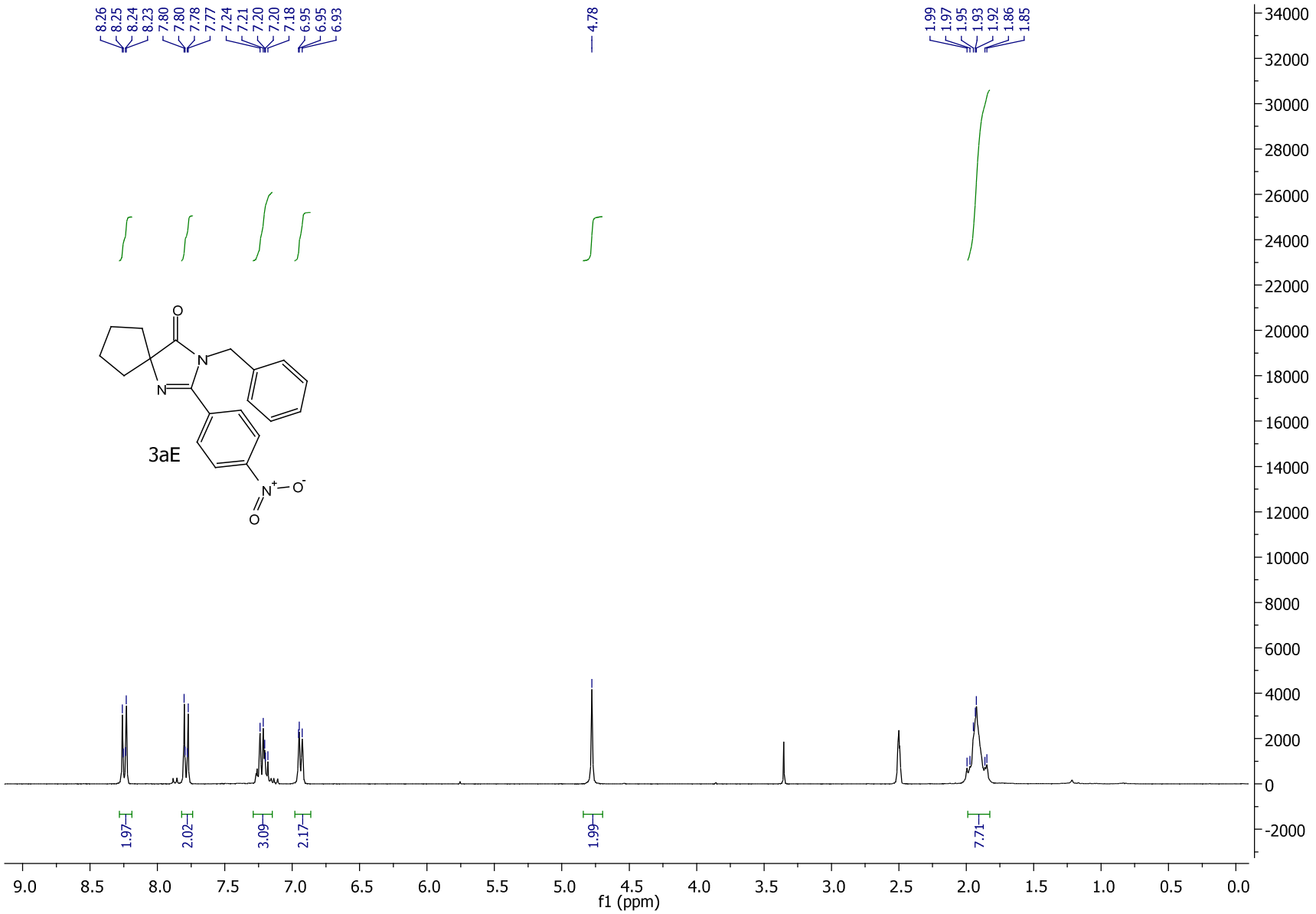

-61.42
O
N
N
F
F
F
3aB
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

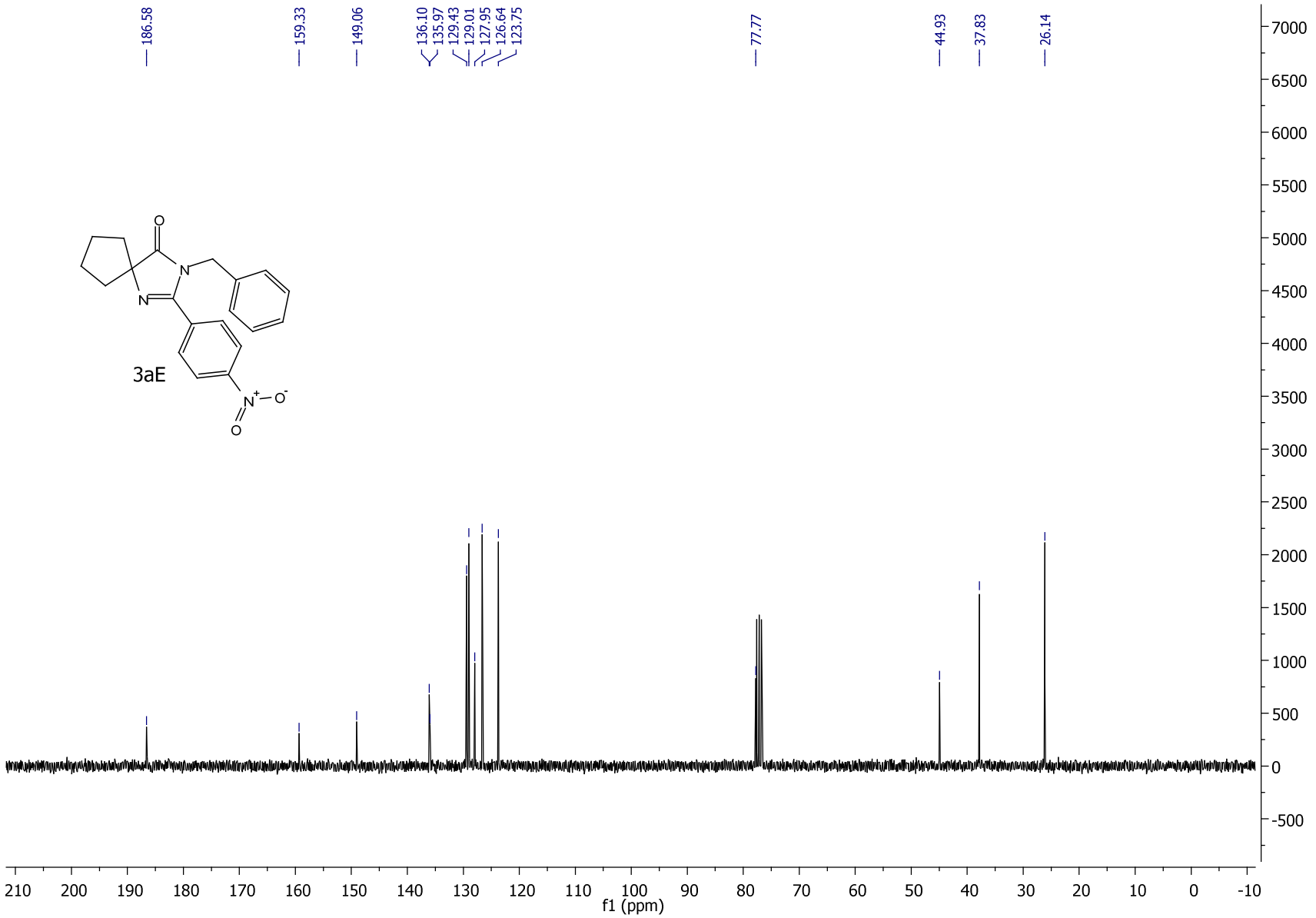

7.92
7.89
7.89
7.70
7.70
7.68
7.67
7.25
7.22
7.21
6.94
6.93
6.91
4.75
1.99
1.96
1.94
1.93
1.92
1.91
1.88
1.85
1.84
O
N
N
N
3aC
2.16
2.16
3.22
2.15
2.00
8.15
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

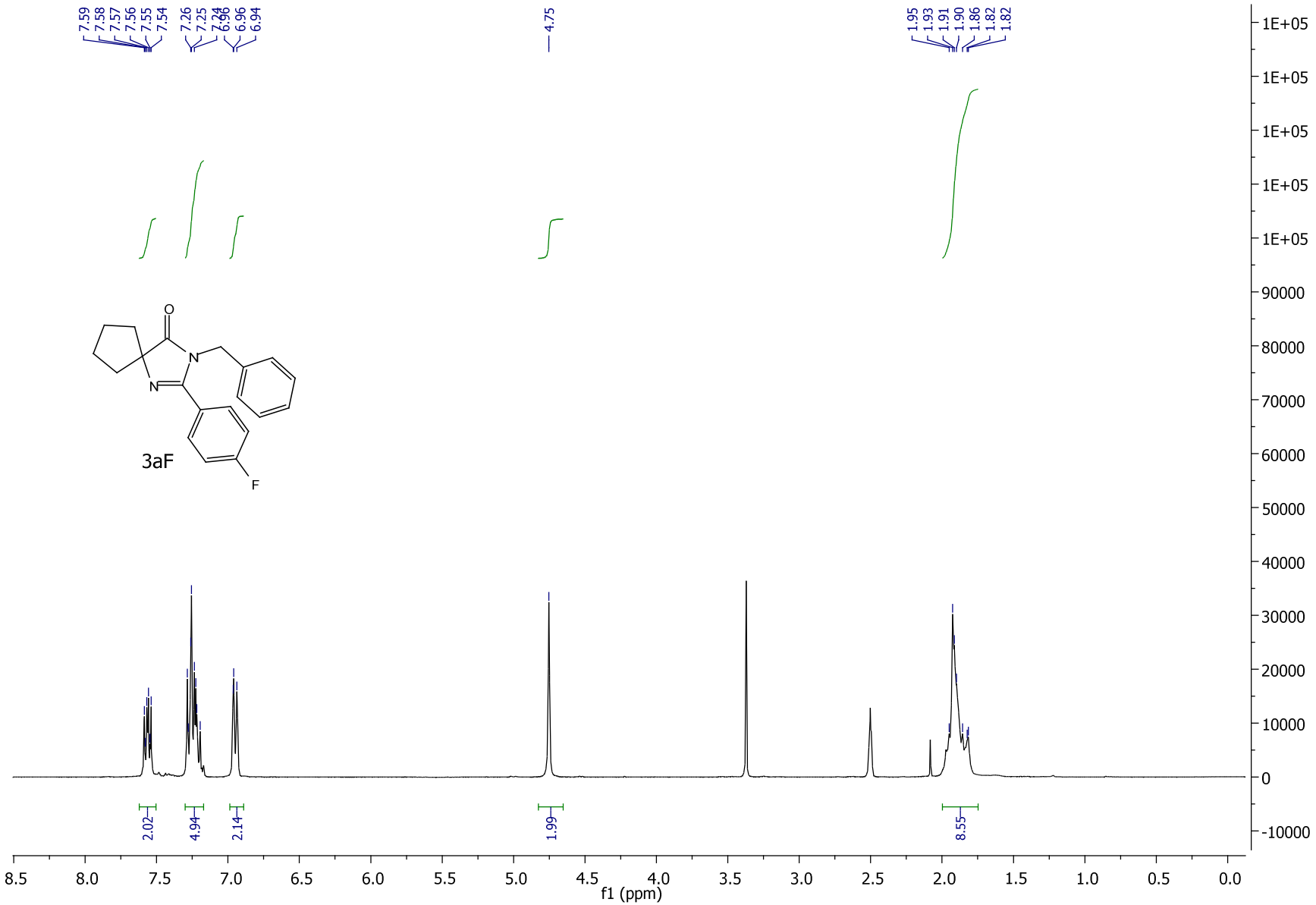

186.60
159.54
136.13
134.26
132.36
128.98
128.94
127.90
126.65
117.91
114.53
77.69
44.90
37.81
26.12
O
N
N
N
3aC
f1 (ppm)

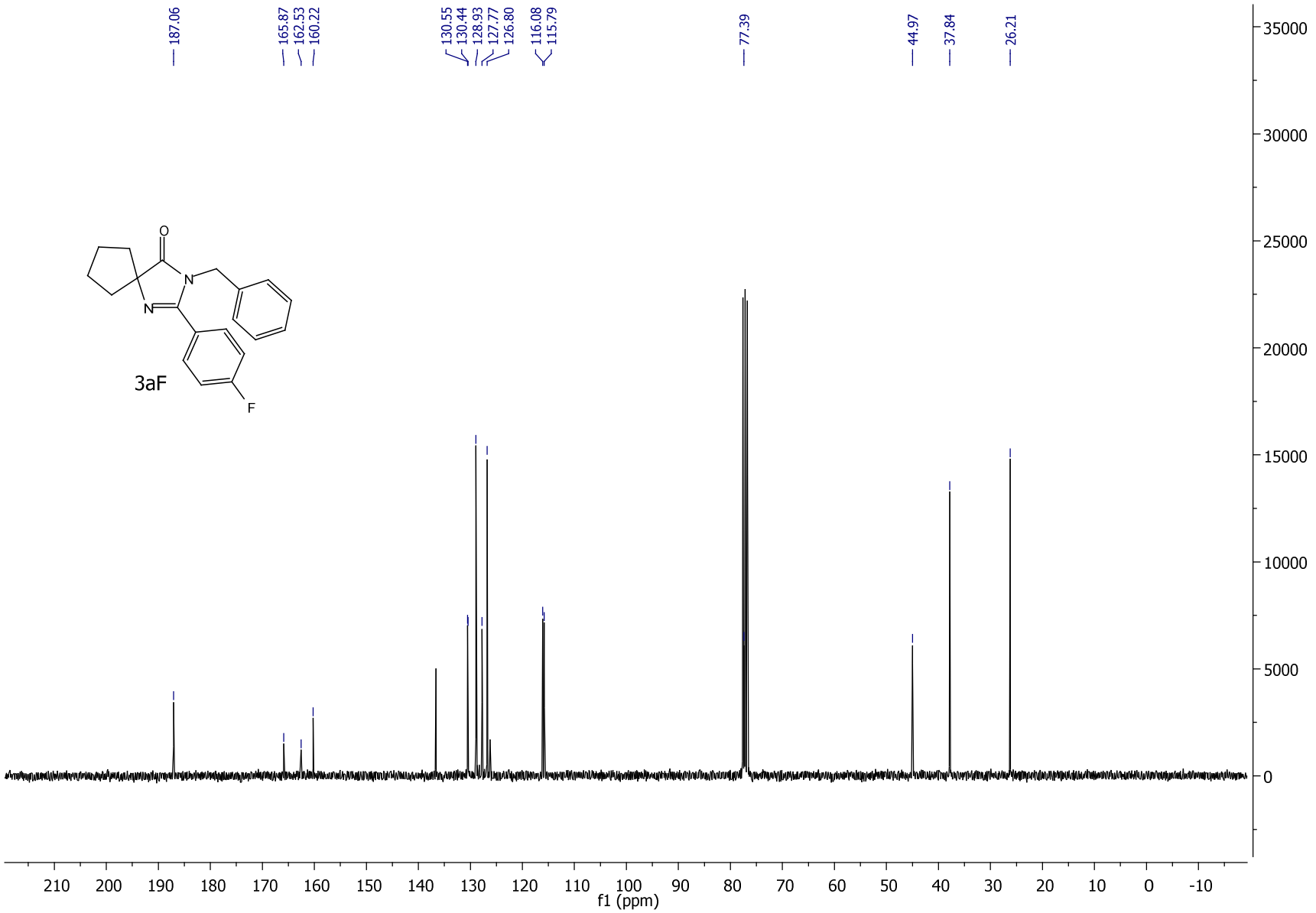

7.86
7.84
7.76
7.75
7.74
7.74
7.69
7.67
7.19
7.19
7.18
7.17
6.81
6.80
6.79
6.78
4.63
2.00
1.98
1.96
1.92
1.91
1.87
1.86
O
N
N
N
3aD
0.99
3.07
2.98
2.03
2.04
8.54
f1 (ppm)

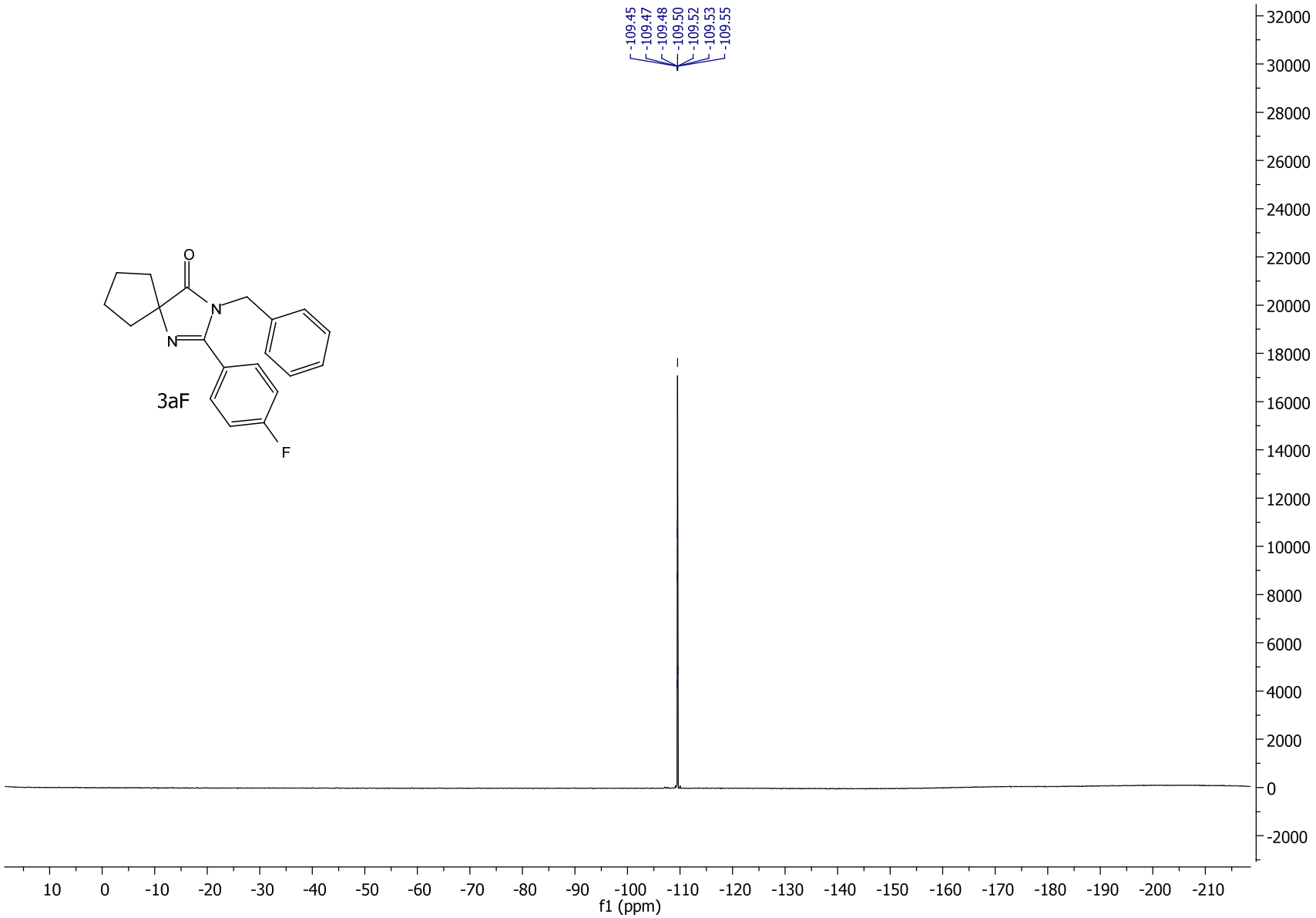

185.66
157.68
135.76
133.22
133.19
132.32
130.62
128.91
128.66
127.71
126.85
116.05
112.62
78.13
77.16 Chloroform-d
65.71
44.42
37.46
25.93
15.16
O
N
N
N
3aD
f1 (ppm)

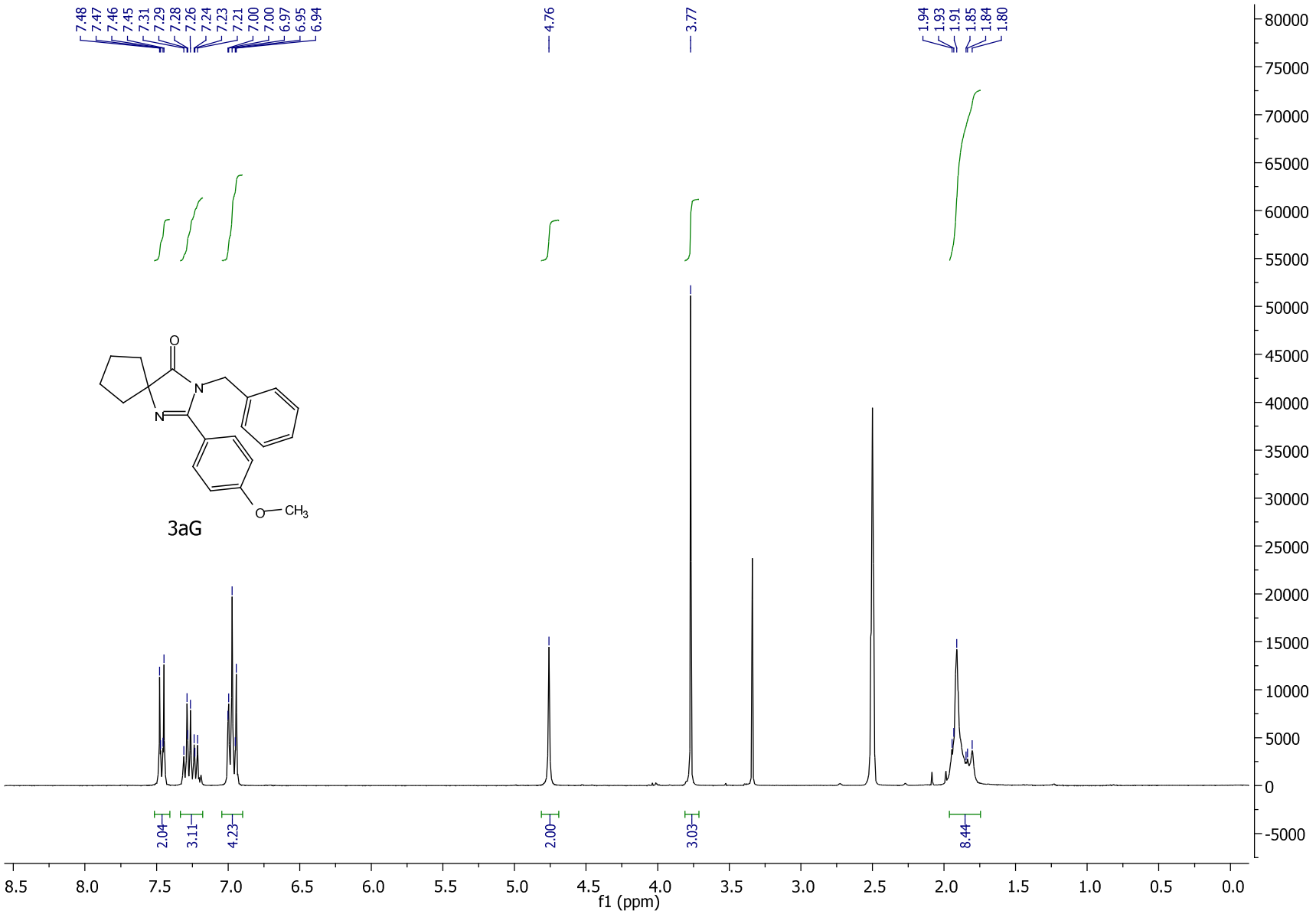

8.26
8.25
8.24
8.23
7.80
7.80
7.78
7.77
7.24
7.21
7.20
7.20
7.18
6.95
6.95
6.93
4.78
1.99
1.97
1.95
1.93
1.92
1.86
1.85
3aE
1.97
2.02
3.09
2.17
1.99
7.71
f1 (ppm)

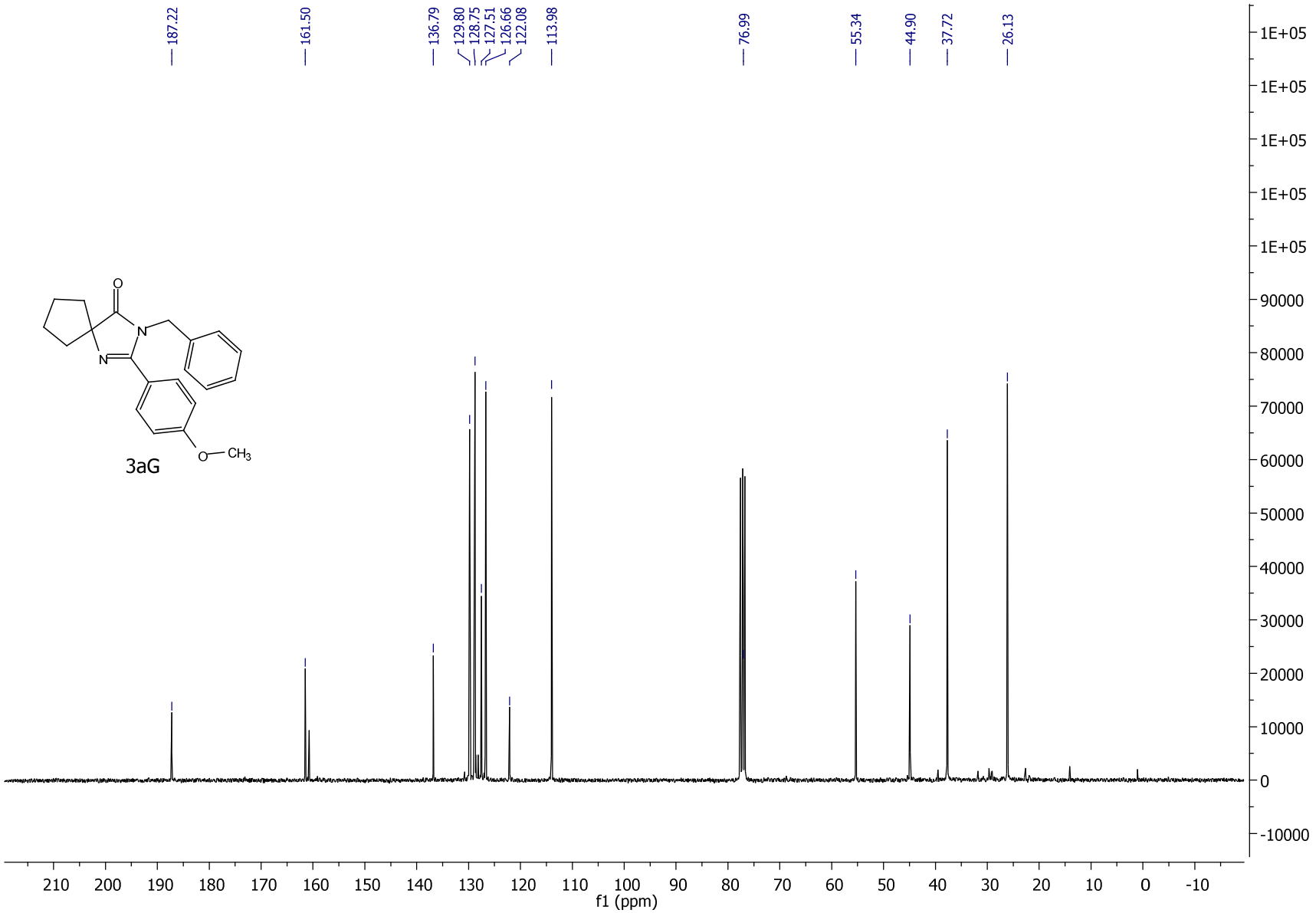

186.58
159.33
149.06
136.10
135.97
129.43
129.01
127.95
126.64
123.75
77.77
44.93
37.83
26.14
3aE
f1 (ppm)

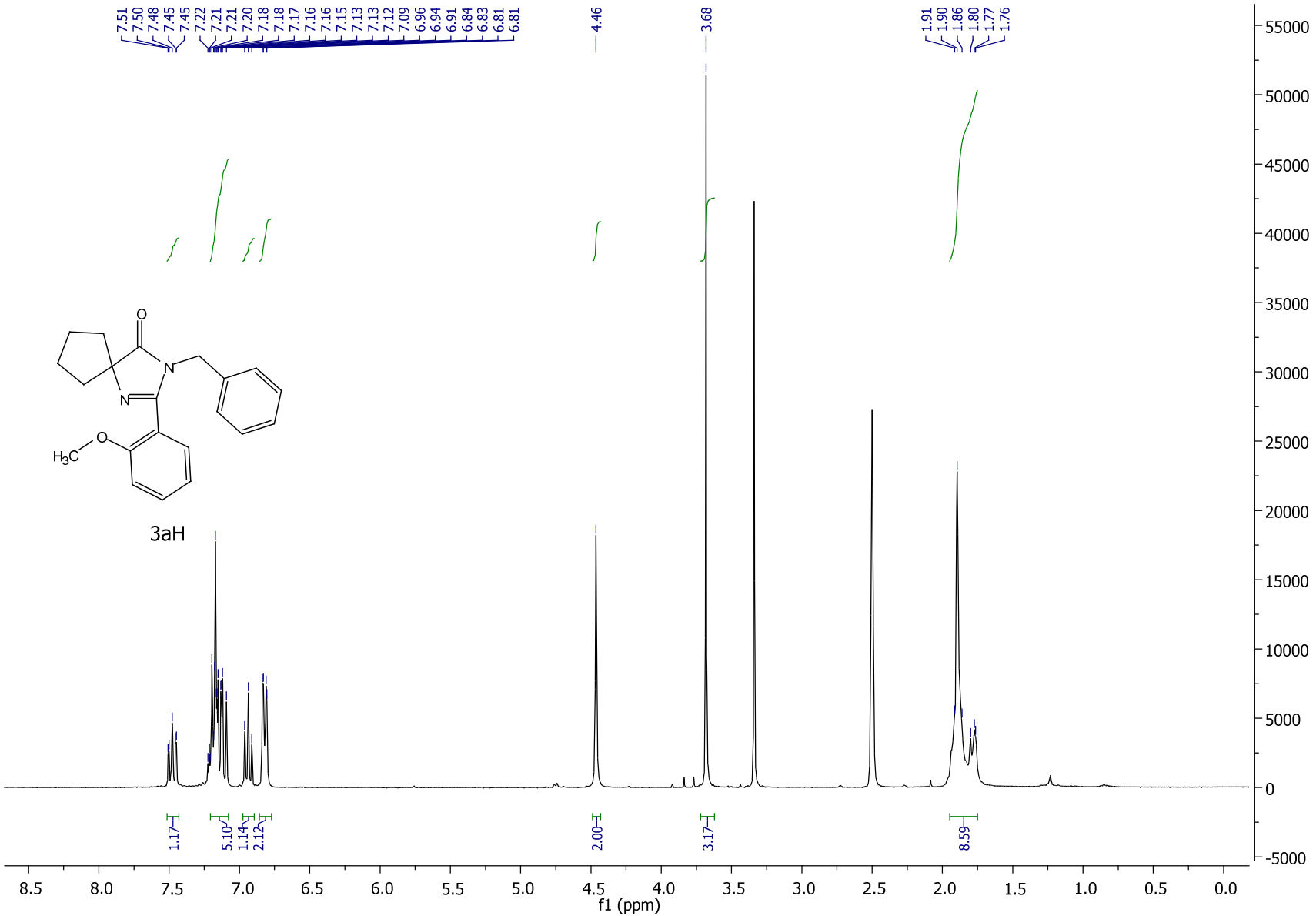

7.59
7.58
7.57
7.56
7.55
7.54
7.26
7.25
7.24
6.96
6.94
4.75
1.95
1.93
1.91
1.90
1.86
1.82
1.82
O
N
N
F
3aF
2.02
4.94
2.14
1.99
8.55
f1 (ppm)

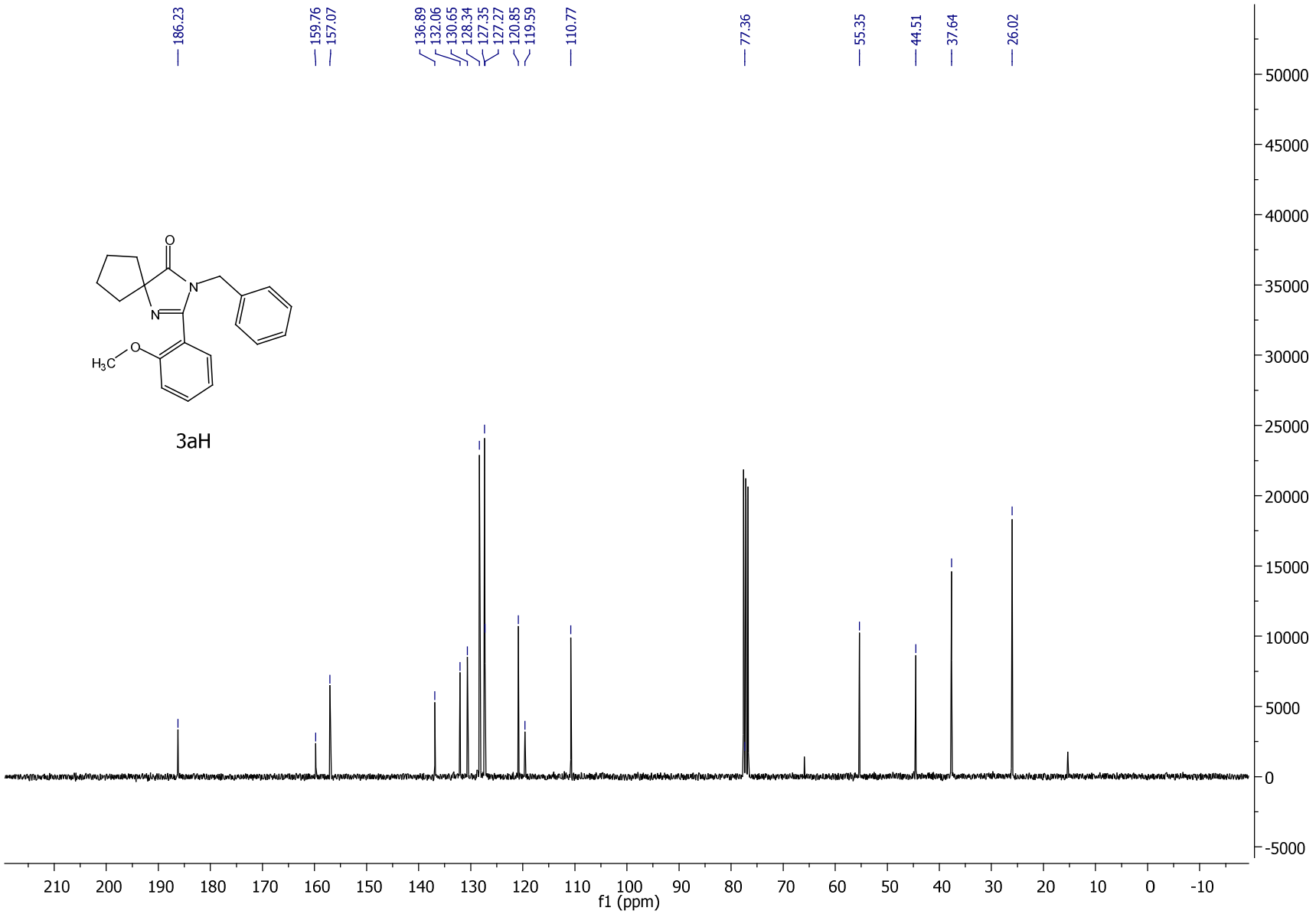

187.06
165.87
162.53
160.22
130.55
130.44
128.93
127.77
126.80
116.08
115.79
77.39
44.97
37.84
26.21
O
N
N
F
3aF
35000
30000
25000
20000
15000
10000
5000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

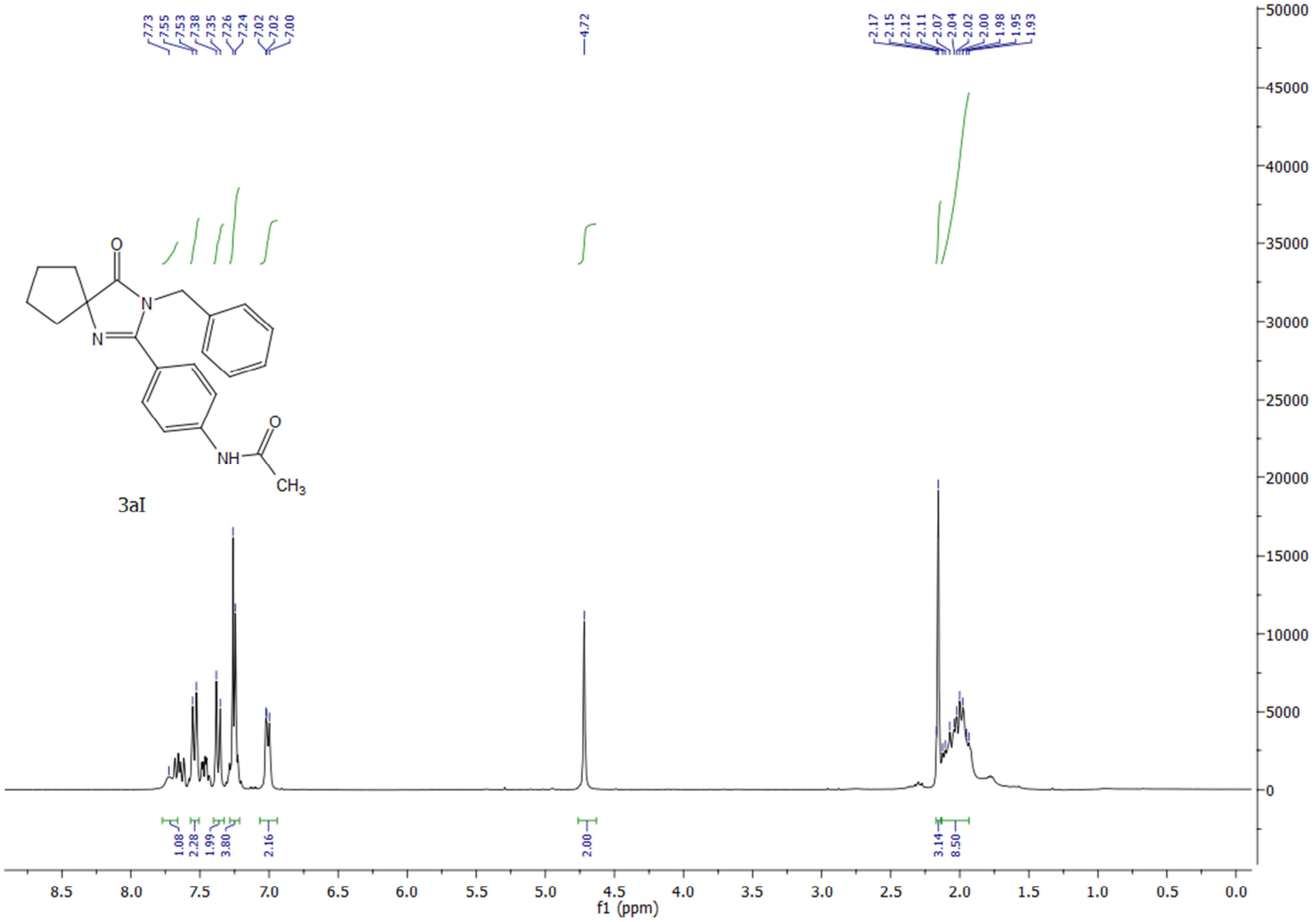

-109.45
-109.47
-109.48
-109.50
-109.52
-109.53
-109.55
O
N
N
F
3aF
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

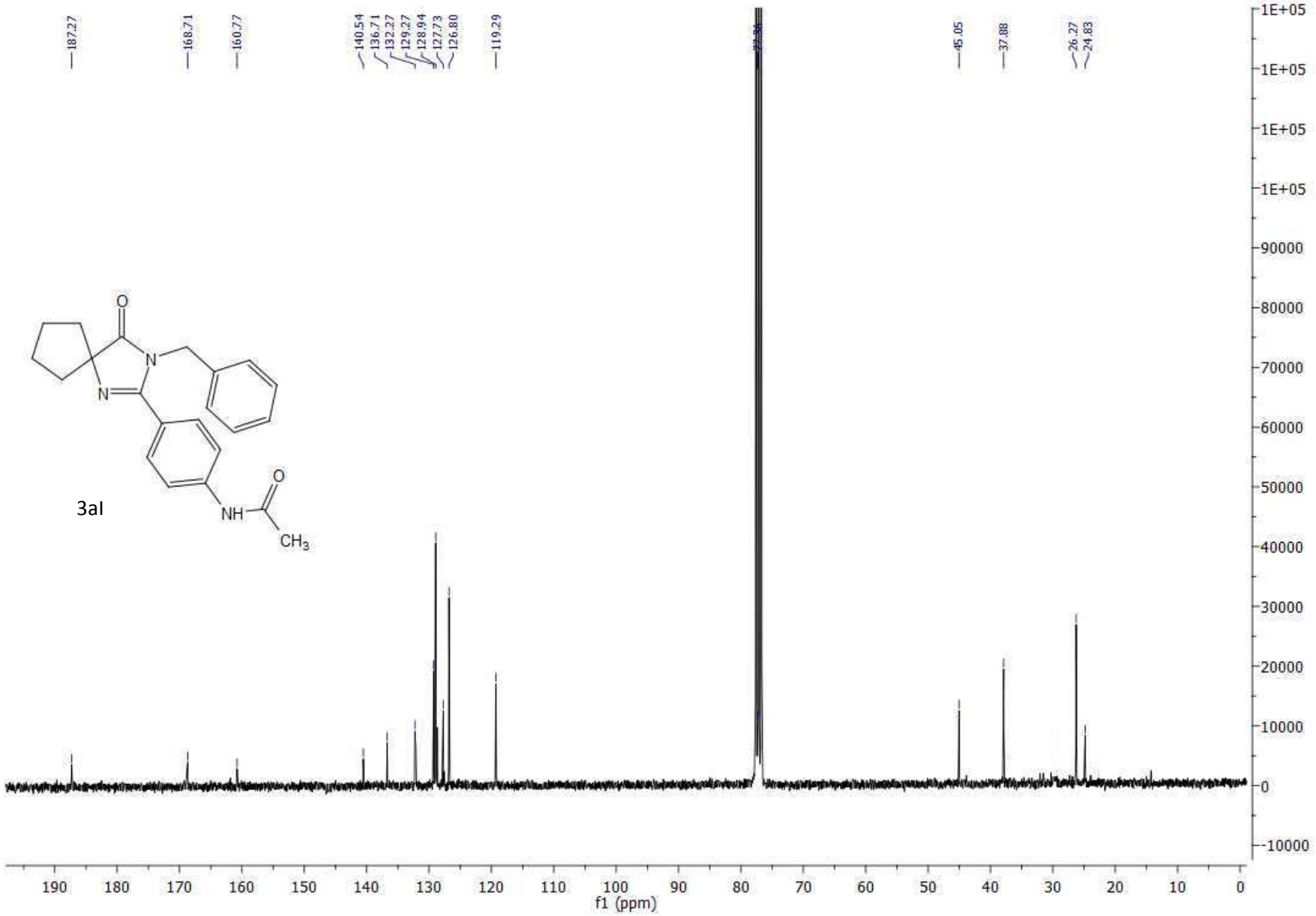

7.48
7.47
7.46
7.45
7.31
7.29
7.28
7.26
7.24
7.23
7.21
7.00
7.00
6.97
6.95
6.94
4.76
3.77
1.94
1.93
1.91
1.85
1.84
1.80
O
N
N
O
CH3
3aG
2.04
3.11
4.23
2.00
3.03
8.44
f1 (ppm)

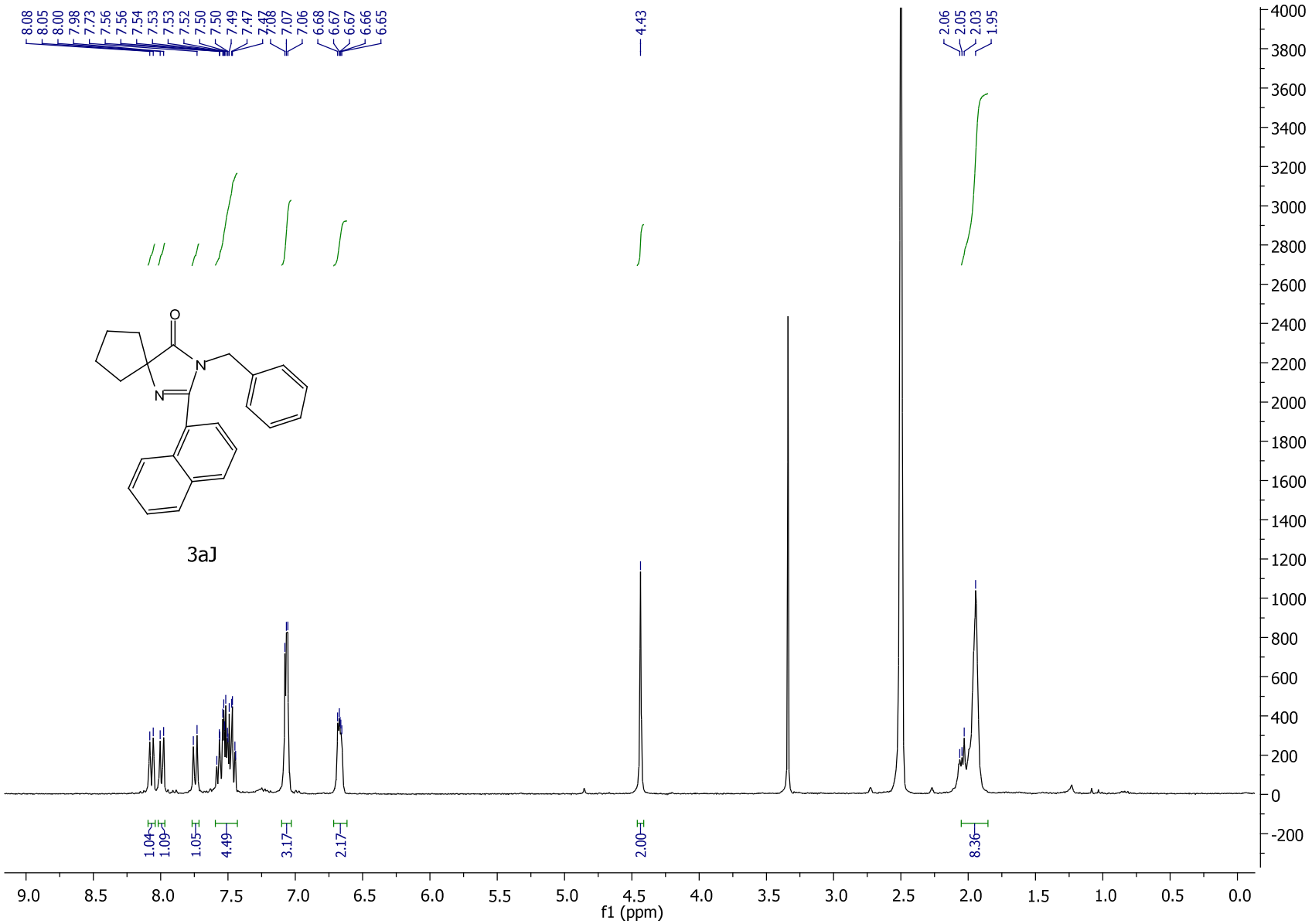

187.22
161.50
136.79
129.80
128.75
127.51
126.66
122.08
113.98
76.99
55.34
44.90
37.72
26.13
3aG
O
N
N
O
CH3
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

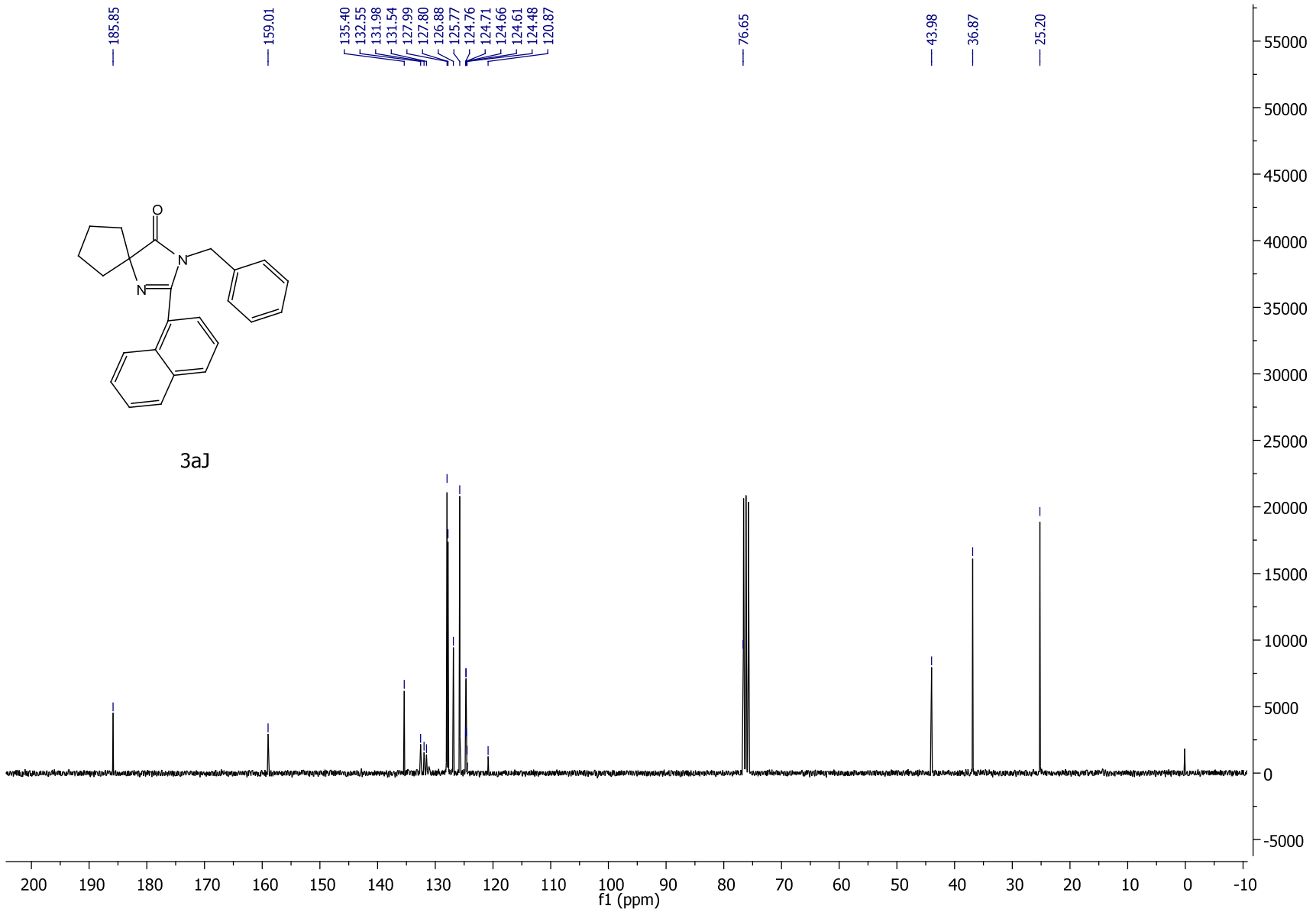

7.51
7.50
7.48
7.45
7.45
7.22
7.21
7.21
7.20
7.18
7.18
7.17
7.16
7.16
7.15
7.13
7.13
7.12
7.09
6.96
6.94
6.91
6.84
6.83
6.81
6.81
4.46
3.68
1.91
1.90
1.86
1.80
1.77
1.76
O
N
N
O
H3C
3aH
1.17
5.10
1.14
2.12
2.00
3.17
8.59
f1 (ppm)

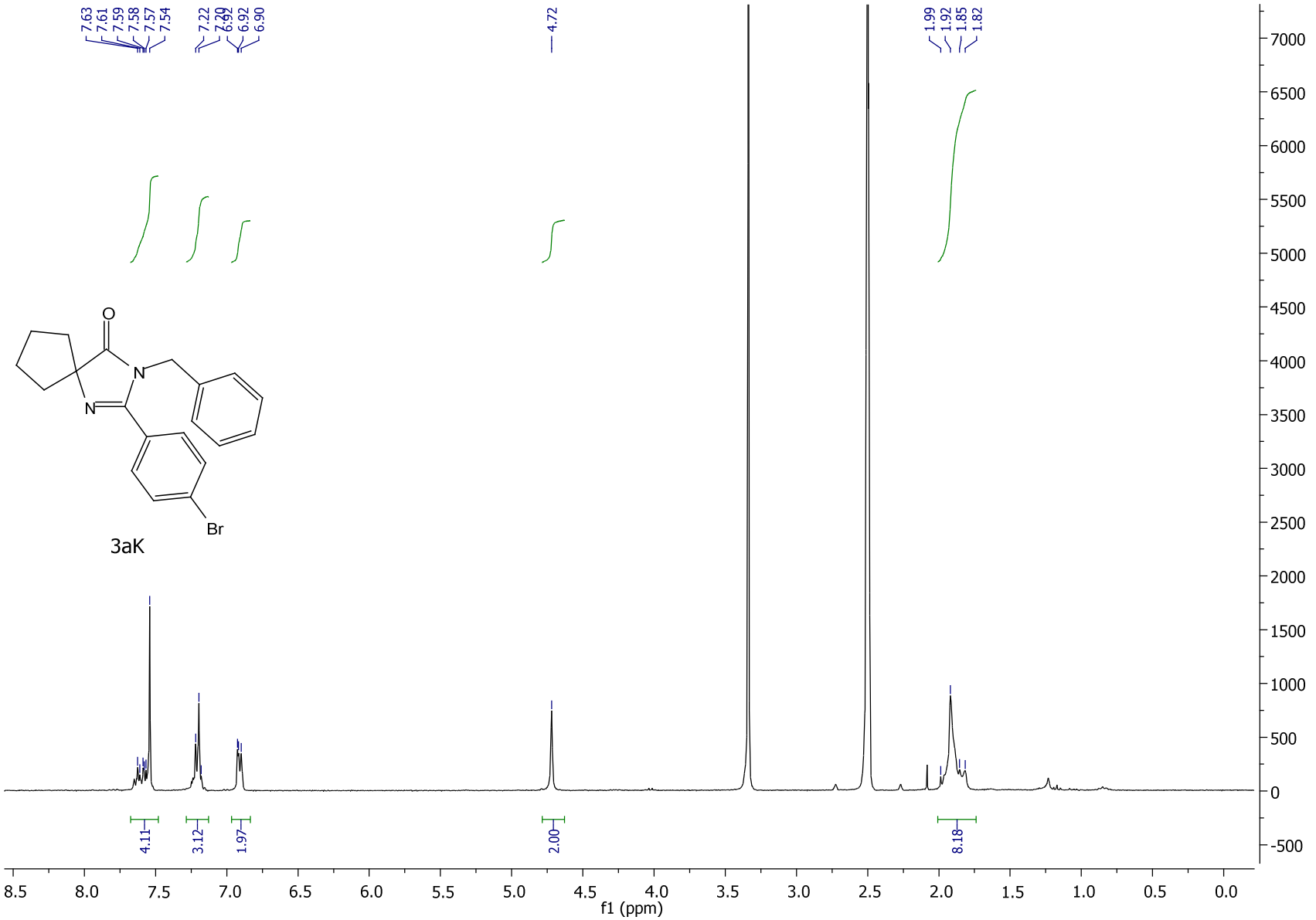

186.23
159.76
157.07
136.89
132.06
130.65
128.34
127.35
127.27
120.85
119.59
110.77
77.36
55.35
44.51
37.64
26.02
O
N
N
O
H3C
3aH
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

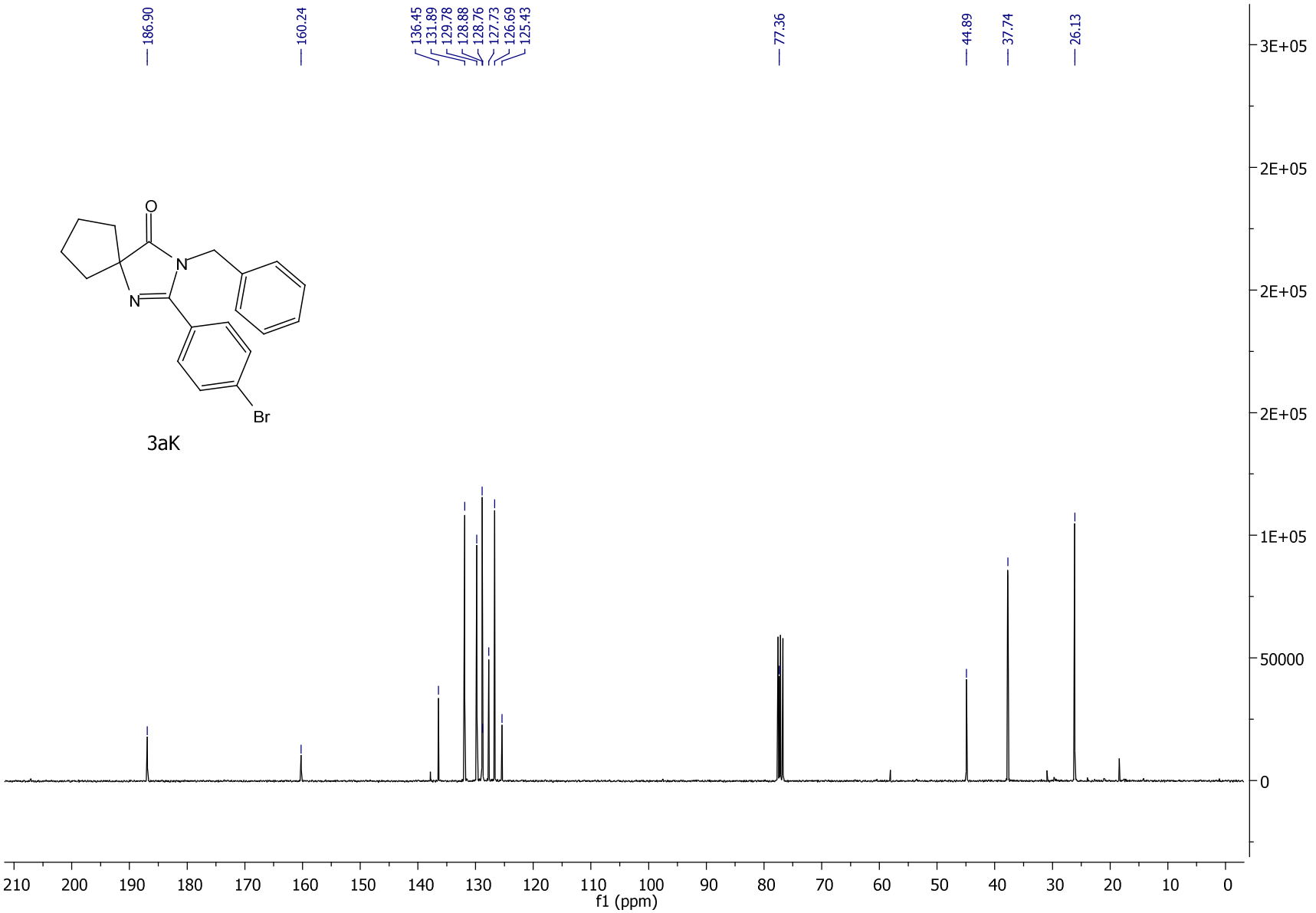

7.73
7.55
7.53
7.38
7.35
7.26
7.24
7.02
7.02
7.00
4.72
2.17
2.15
2.12
2.11
2.07
2.04
2.02
2.00
1.98
1.95
1.93
O
N
N
O
NH
CH3
3aI
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
1.08
2.28
1.99
3.80
2.16
2.00
3.14
8.50
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

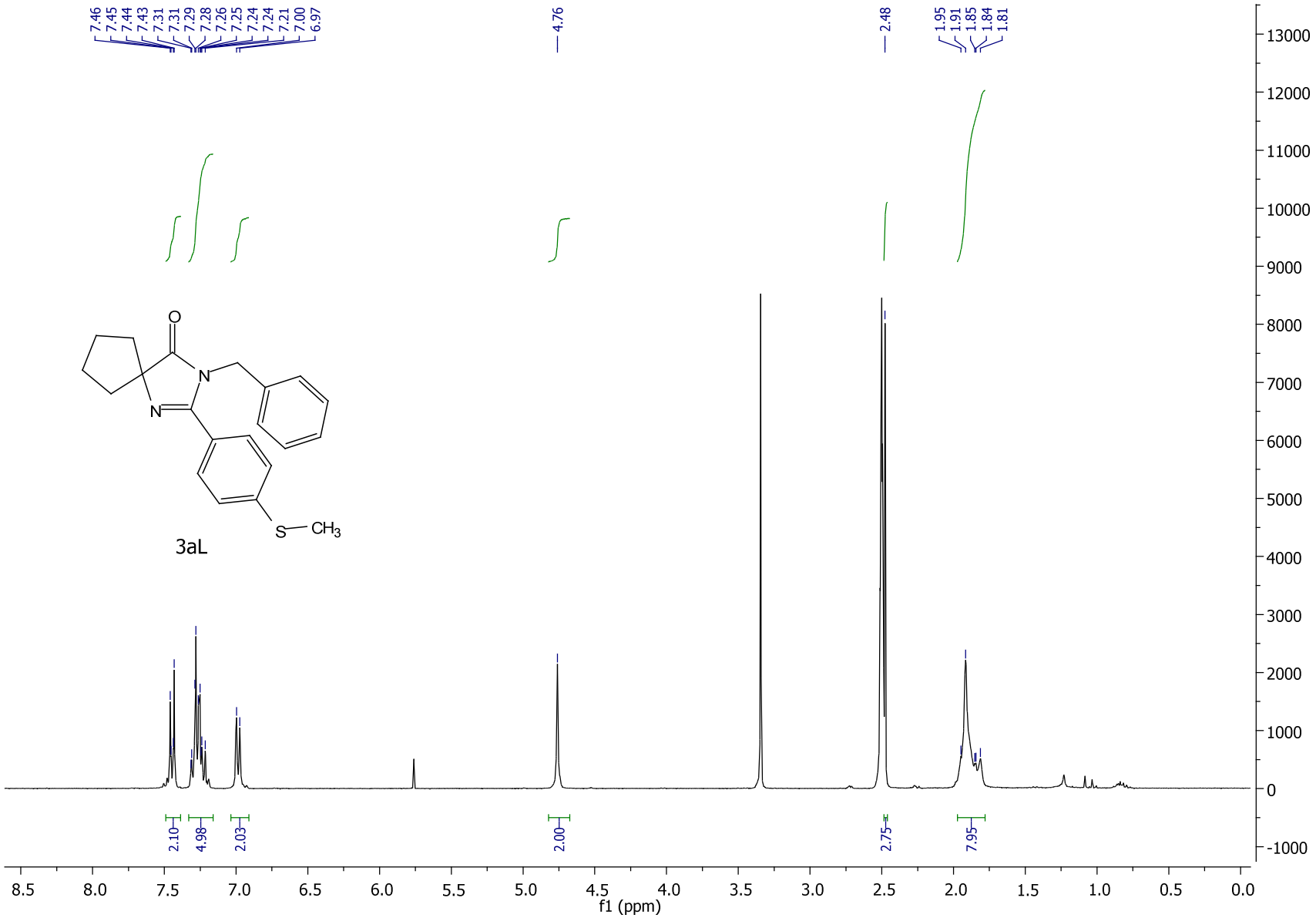

187.27
168.71
160.77
140.54
136.71
132.27
129.27
128.94
127.73
126.80
119.29
45.05
37.88
26.27
24.83
O
N
N
O
NH
CH3
3aI
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

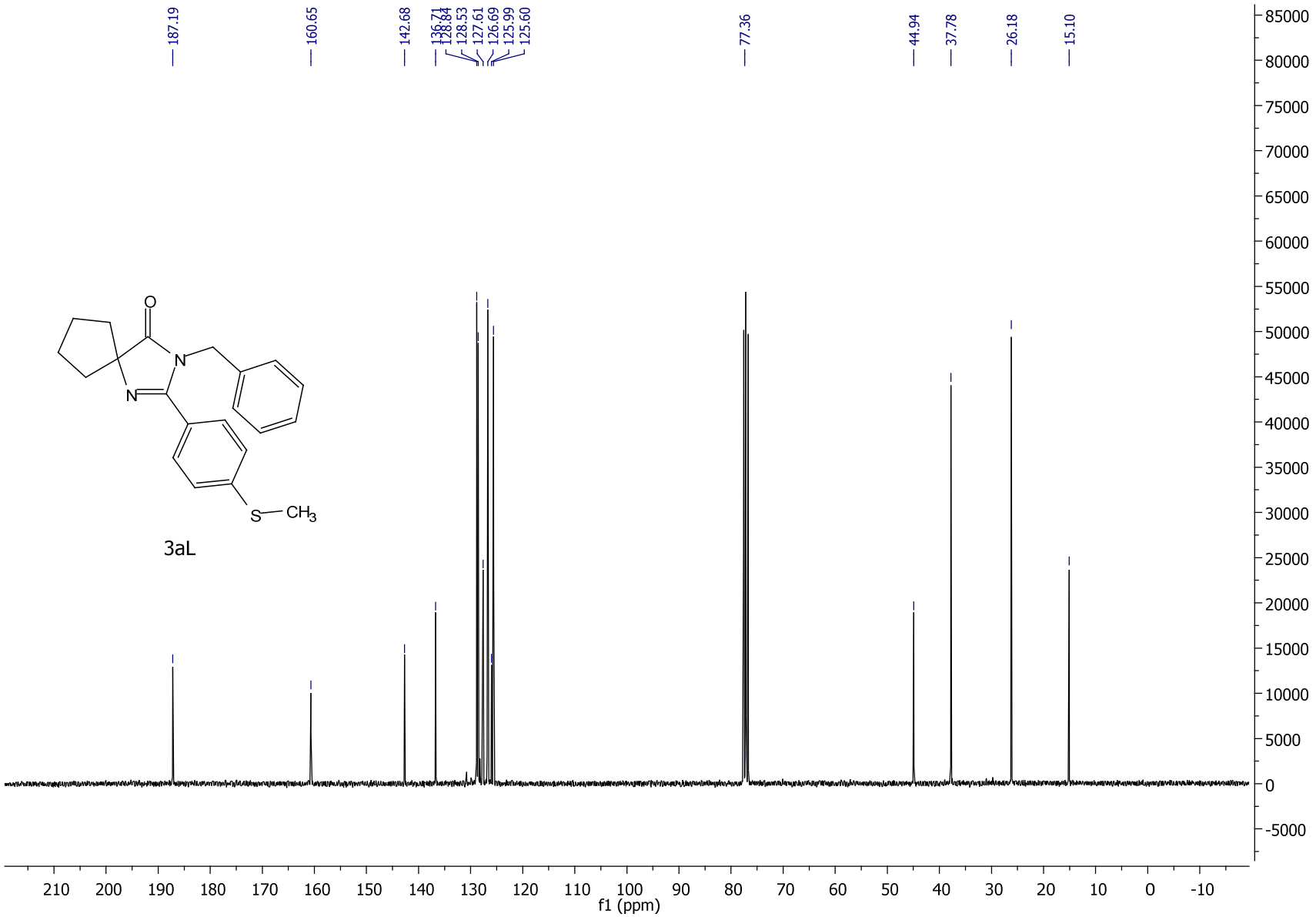

8.08
8.05
8.00
7.98
7.73
7.56
7.56
7.54
7.53
7.53
7.52
7.50
7.50
7.49
7.47
7.47
7.08
7.07
7.06
6.68
6.67
6.67
6.66
6.65
4.43
2.06
2.05
2.03
1.95
O
N
N
3aJ
1.04
1.09
1.05
4.49
3.17
2.17
2.00
8.36
f1 (ppm)

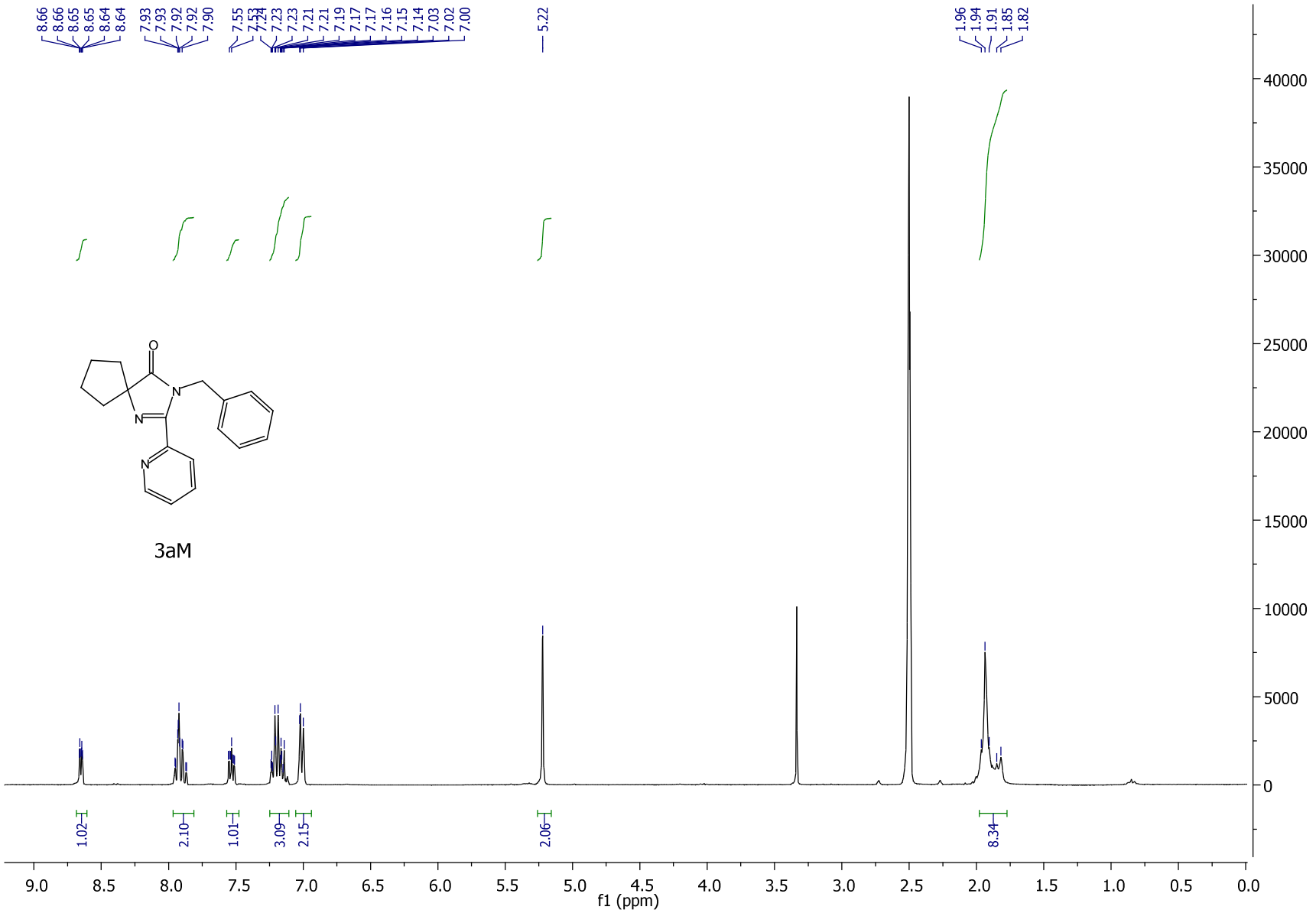

185.85
159.01
135.40
132.55
131.98
131.54
127.99
127.80
126.88
125.77
124.76
124.71
124.66
124.61
124.48
120.87
76.65
43.98
36.87
25.20
O
N
N
3aJ
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

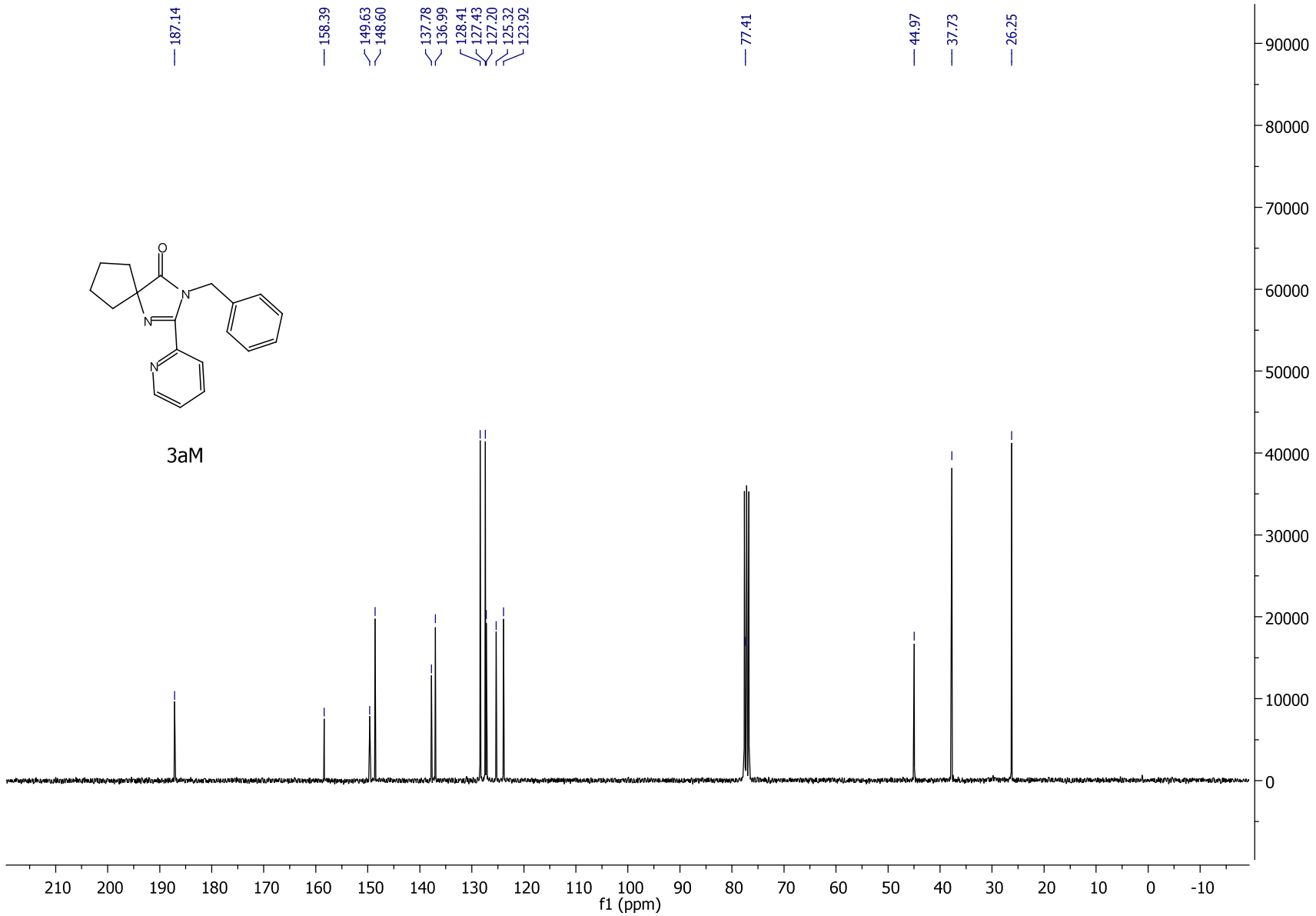

7.63
7.61
7.59
7.58
7.57
7.54
7.22
7.20
6.92
6.92
6.90
4.72
1.99
1.92
1.85
1.82
O
N
N
Br
3aK
4.11
3.12
1.97
2.00
8.18
f1 (ppm)

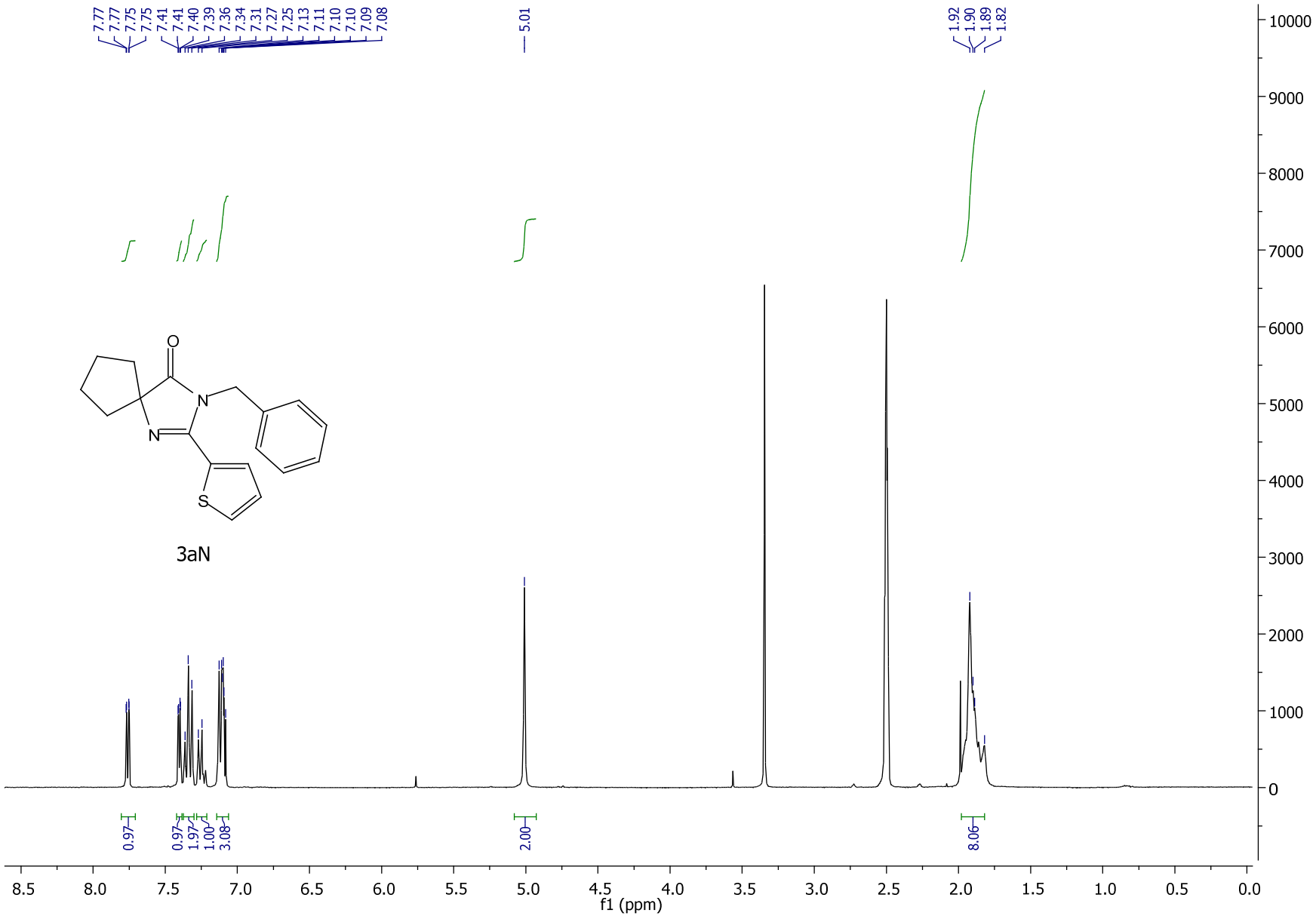

186.90
160.24
136.45
131.89
129.78
128.88
128.76
127.73
126.69
125.43
77.36
44.89
37.74
26.13
O
N
N
Br
3aK
3E+05
2E+05
2E+05
2E+05
1E+05
50000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

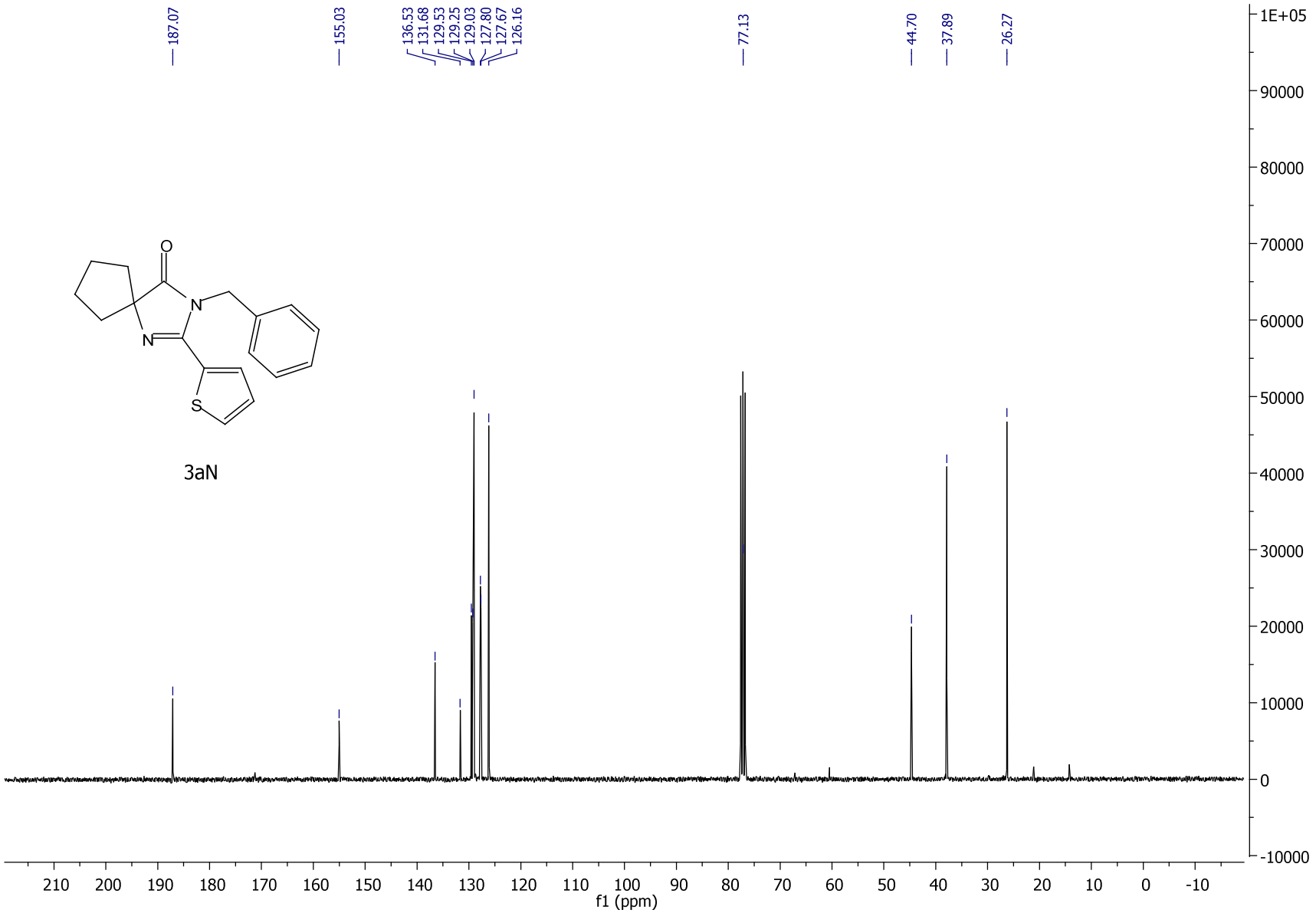

7.46
7.45
7.44
7.43
7.31
7.31
7.29
7.28
7.26
7.25
7.24
7.24
7.21
7.00
6.97
4.76
2.48
1.95
1.91
1.85
1.84
1.81
O
N
N
S
CH3
3aL
2.10
4.98
2.03
2.00
2.75
7.95
f1 (ppm)

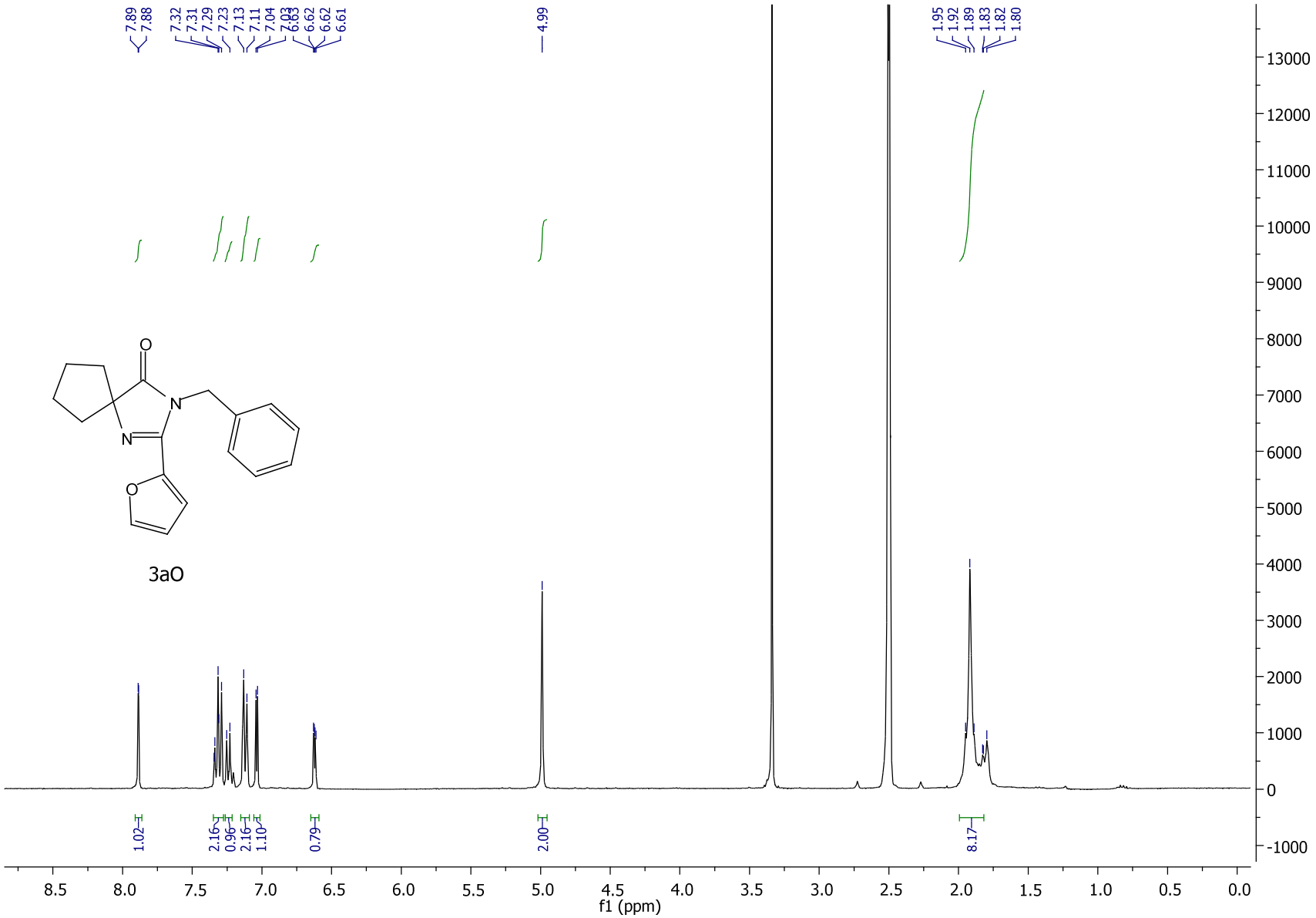

187.19
160.65
142.68
136.71
128.84
128.53
127.61
126.69
125.99
125.60
77.36
44.94
37.78
26.18
15.10
O
N
N
S
CH3
3aL
f1 (ppm)

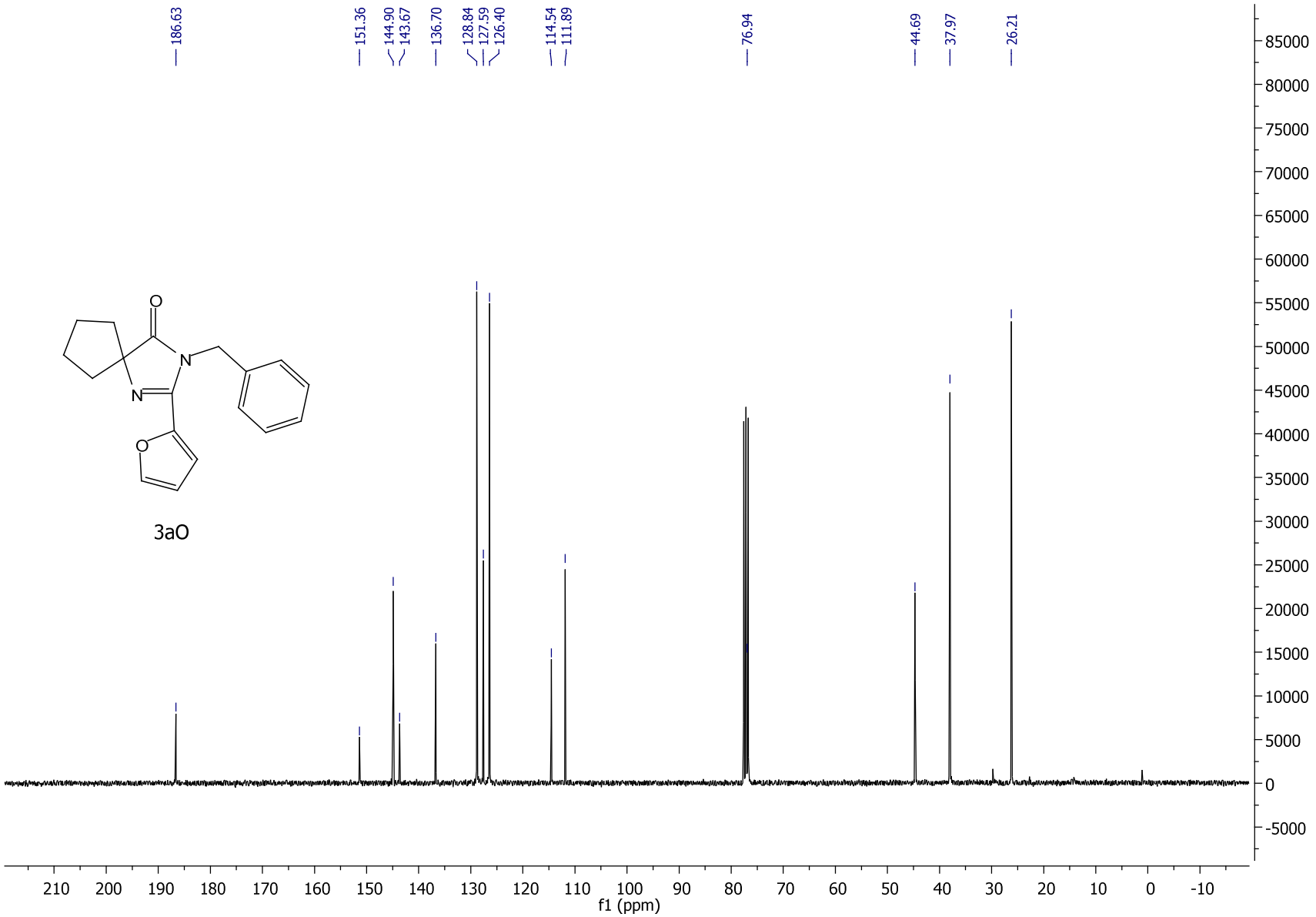

8.66
8.66
8.65
8.65
8.64
8.64
7.93
7.93
7.92
7.92
7.90
7.55
7.53
7.24
7.23
7.23
7.21
7.21
7.19
7.17
7.17
7.16
7.15
7.14
7.03
7.02
7.00
5.22
1.96
1.94
1.91
1.85
1.82
O
N
N
N
3aM
40000
35000
30000
25000
20000
15000
10000
5000
0
1.02
2.10
1.01
3.09
2.15
2.06
8.34
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

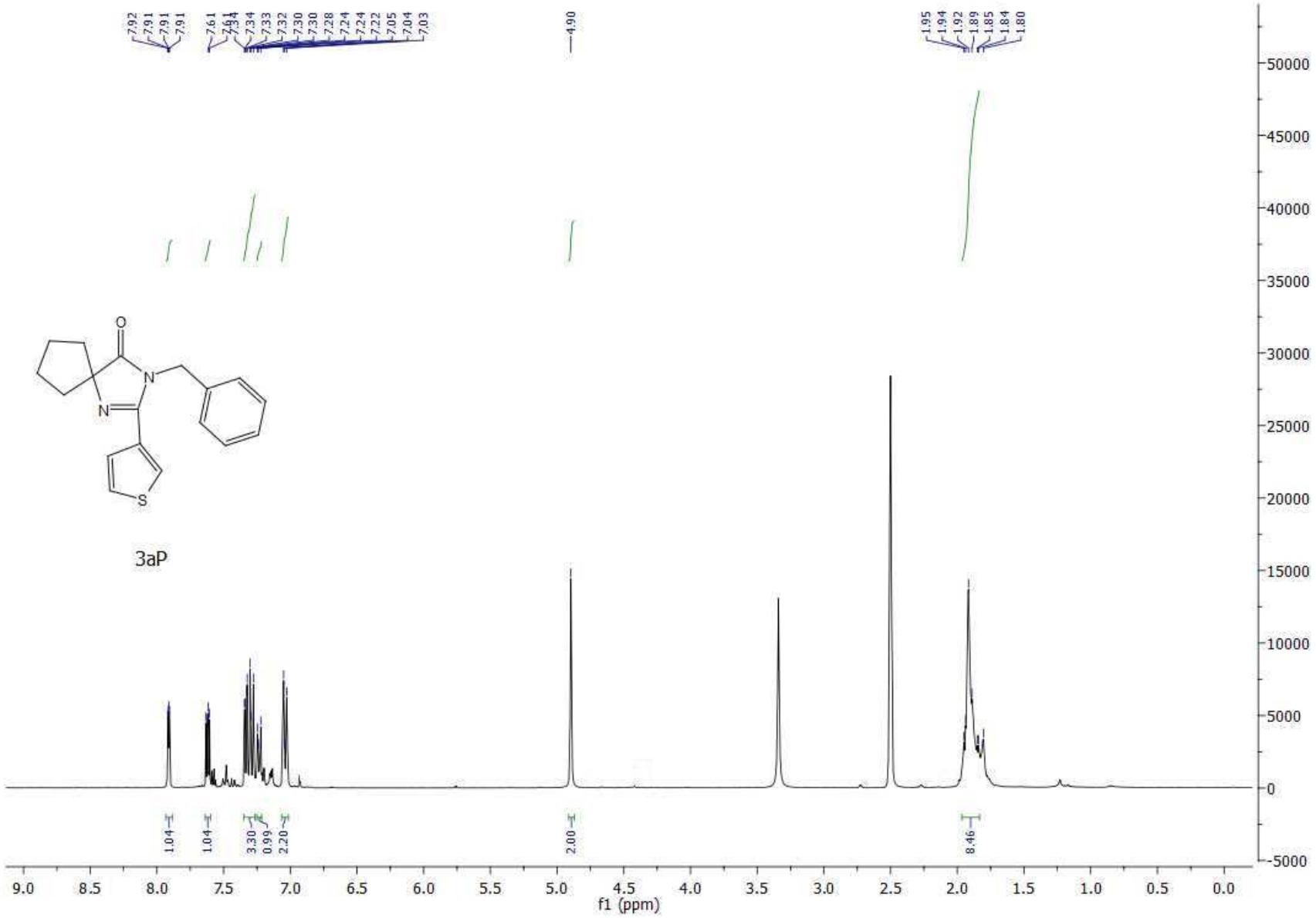

187.14
158.39
149.63
148.60
137.78
136.99
128.41
127.43
127.20
125.32
123.92
77.41
44.97
37.73
26.25
O
N
N
N
3aM
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

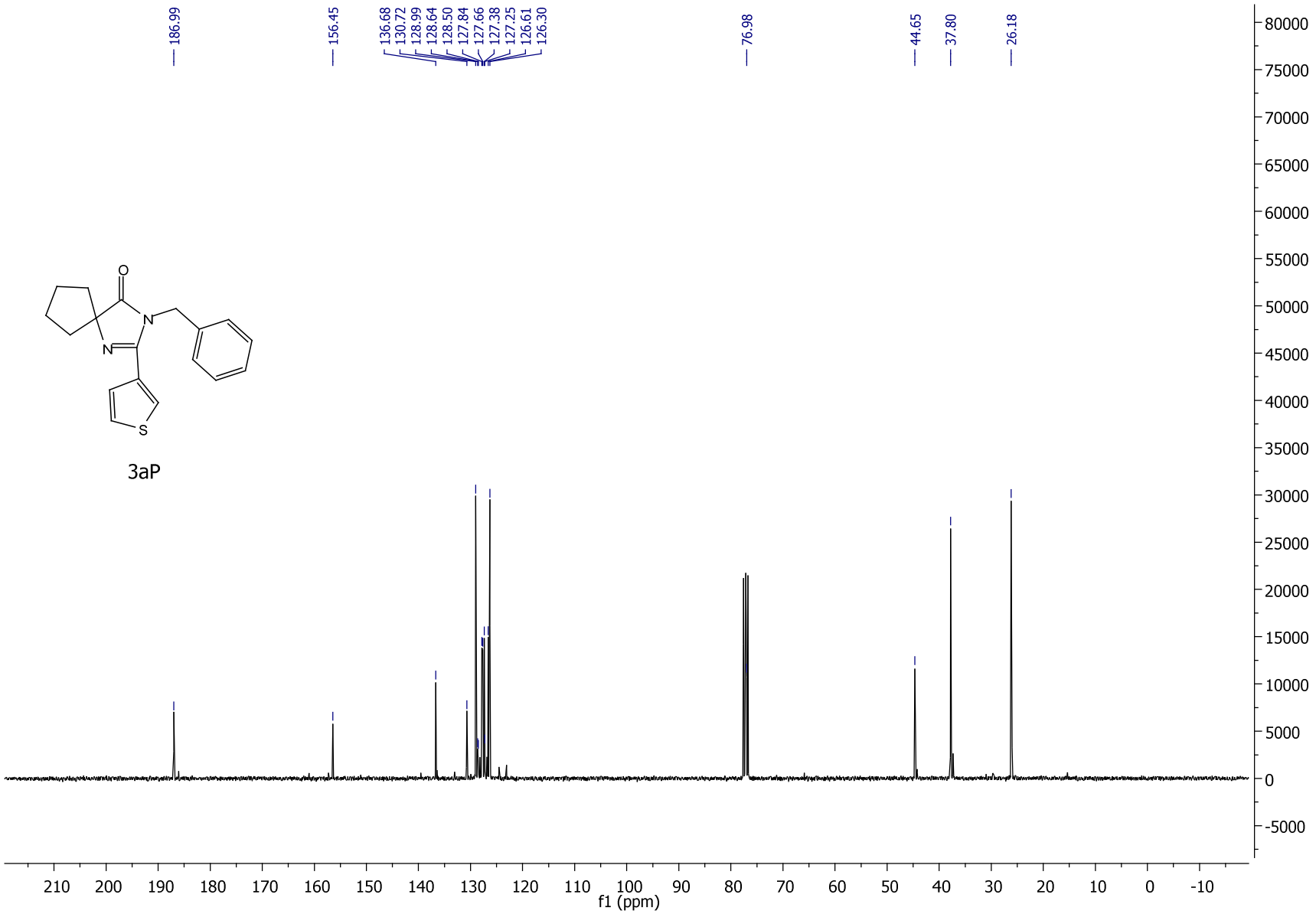

7.77
7.77
7.75
7.75
7.41
7.41
7.40
7.39
7.36
7.34
7.31
7.27
7.25
7.13
7.11
7.10
7.10
7.09
7.08
5.01
1.92
1.90
1.89
1.82
O
N
N
S
3aN
0.97
0.97
1.97
1.00
3.08
2.00
8.06
f1 (ppm)

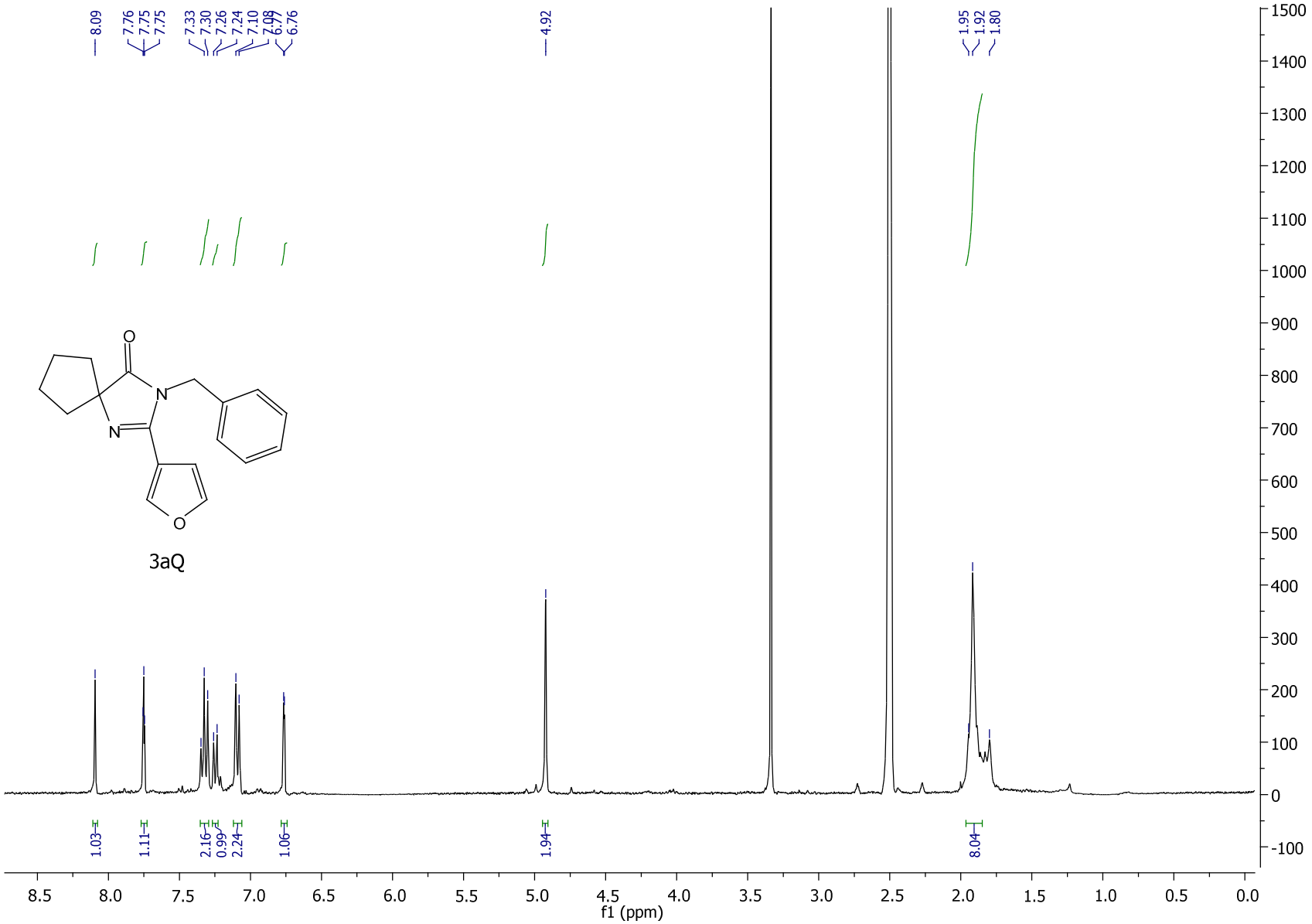

187.07
155.03
136.53
131.68
129.53
129.25
129.03
127.80
127.67
126.16
77.13
44.70
37.89
26.27
O
N
N
S
3aN
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

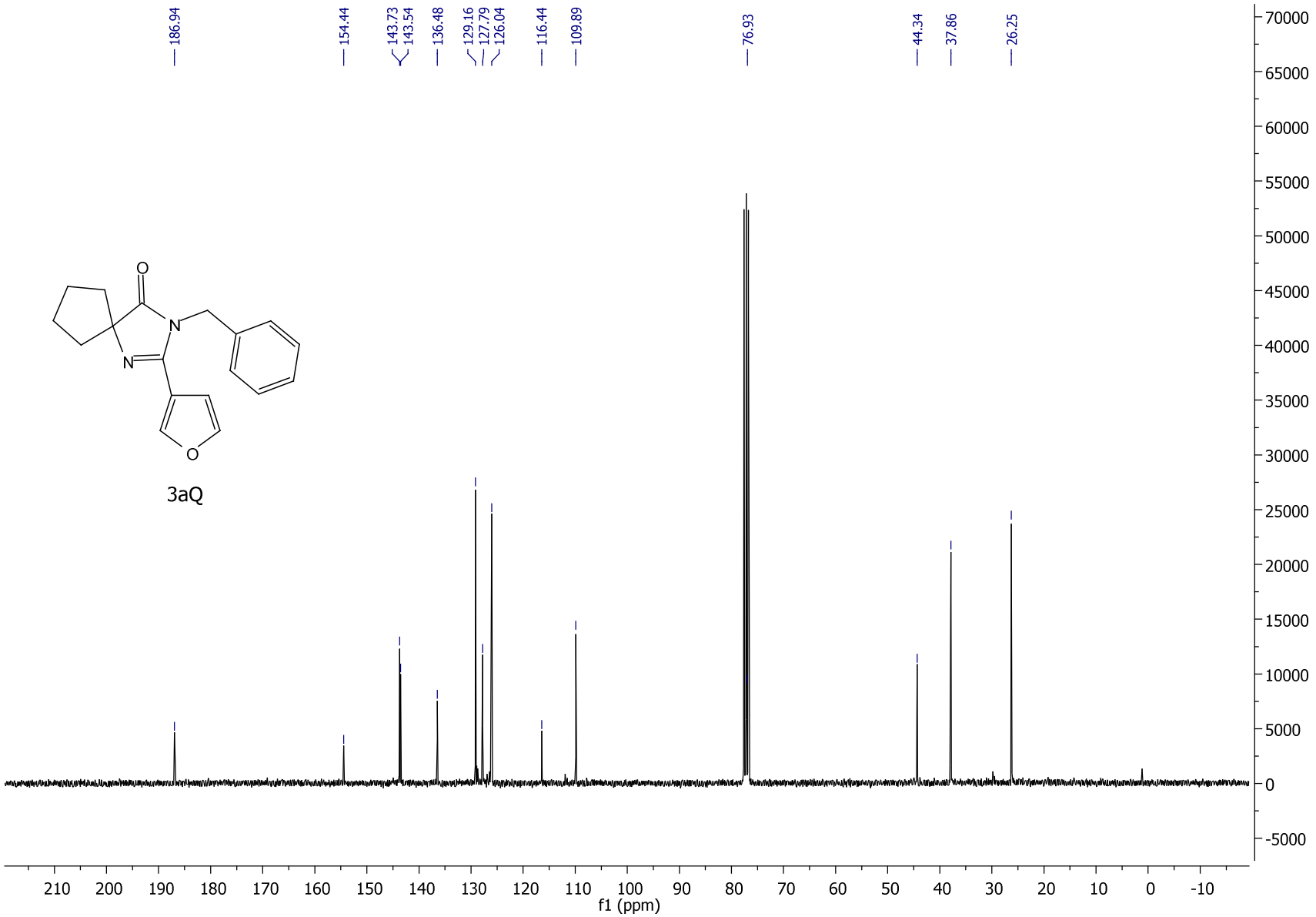

7.89
7.88
7.32
7.31
7.29
7.23
7.13
7.11
7.04
7.03
6.83
6.62
6.62
6.61
4.99
1.95
1.92
1.89
1.83
1.82
1.80
O
N
N
O
3aO
1.02
2.16
0.96
2.16
1.10
0.79
2.00
8.17
f1 (ppm)

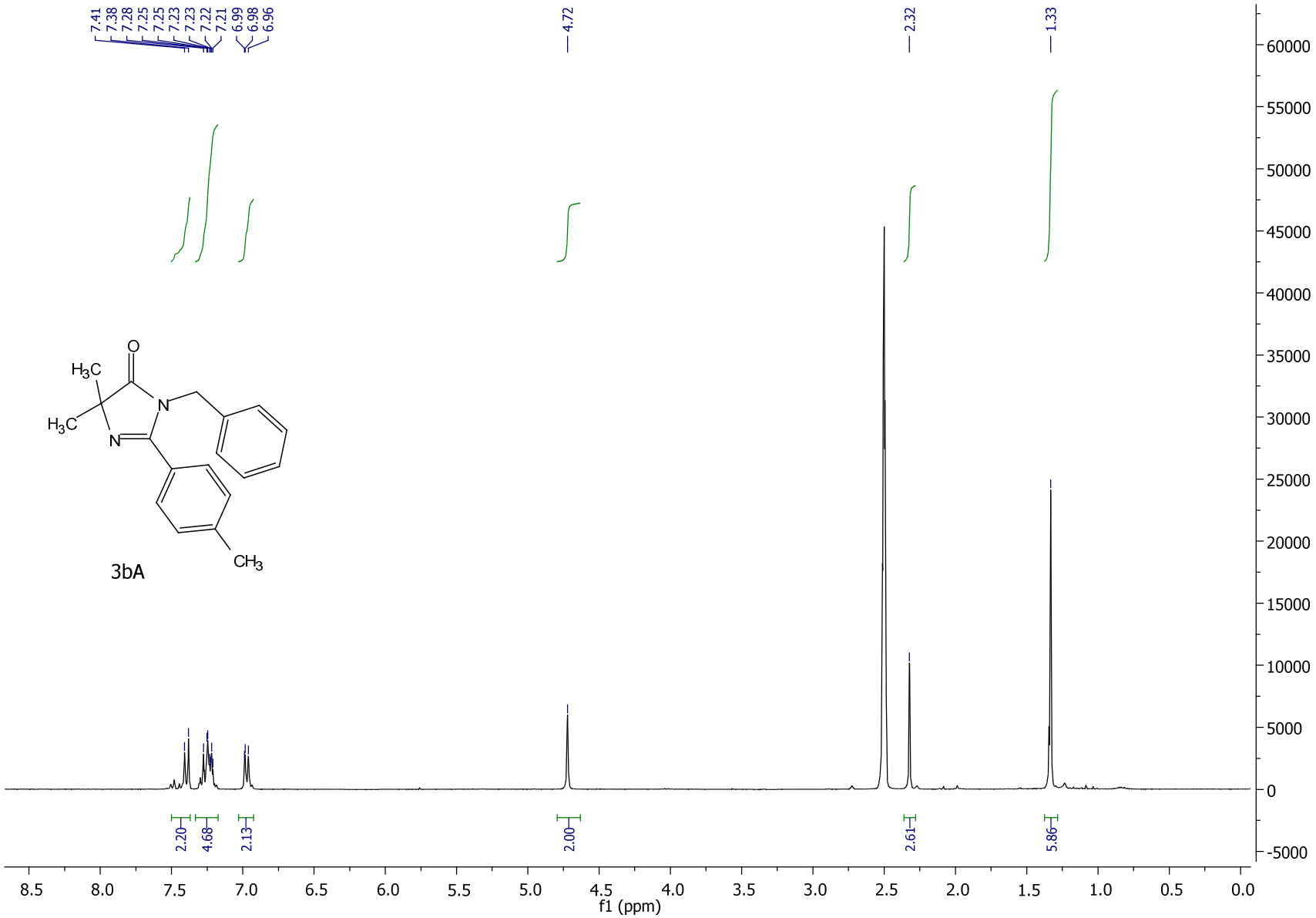

186.63
151.36
144.90
143.67
136.70
128.84
127.59
126.40
114.54
111.89
76.94
44.69
37.97
26.21
O
N
N
O
3aO
85000
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

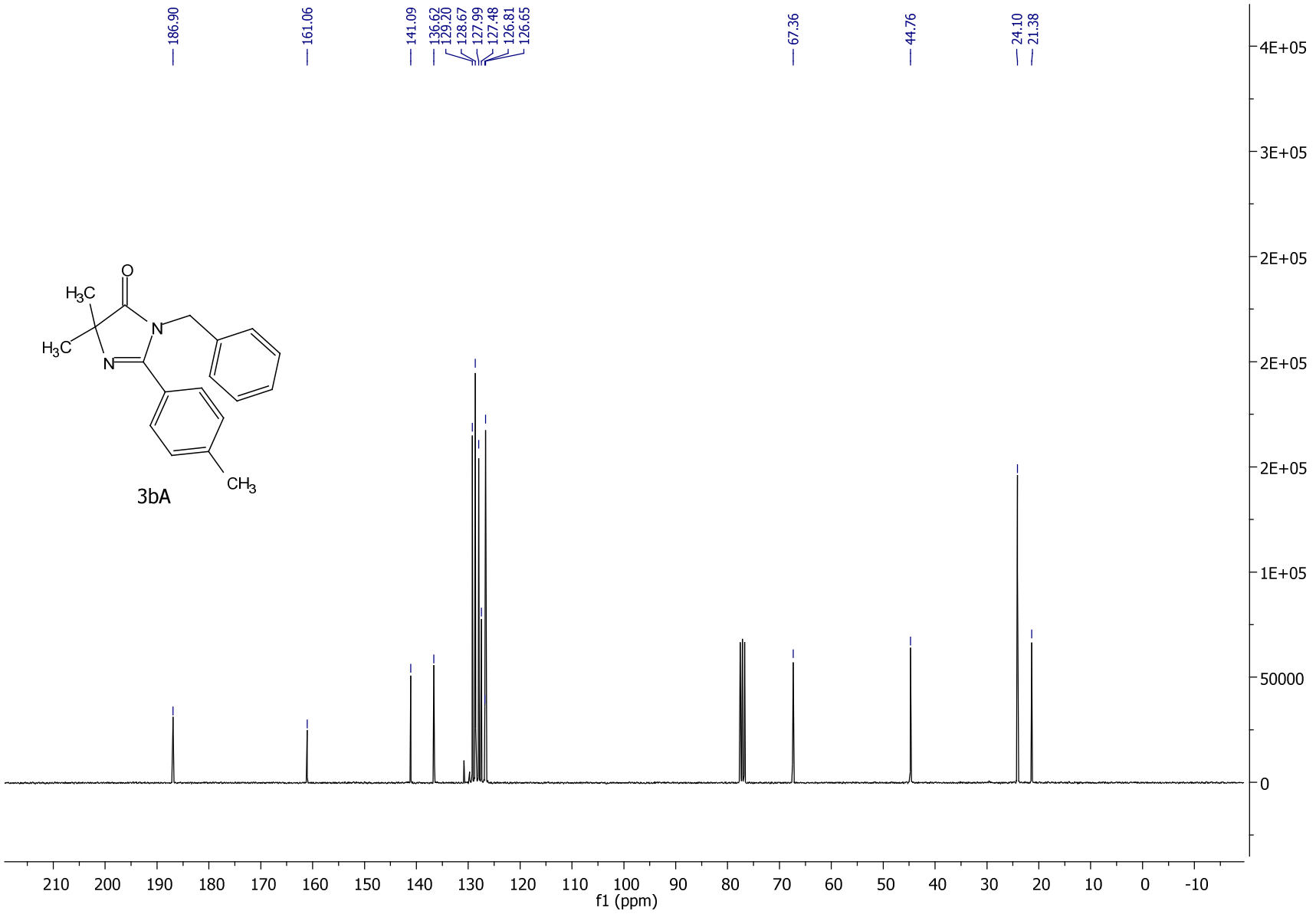

7.92
7.91
7.91
7.91
7.61
7.61
7.34
7.34
7.33
7.32
7.30
7.30
7.28
7.24
7.24
7.22
7.05
7.04
7.03
4.90
1.95
1.94
1.92
1.89
1.85
1.84
1.80
O
N
N
S
3aP
1.04
1.04
3.30
0.99
2.20
2.00
8.46
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

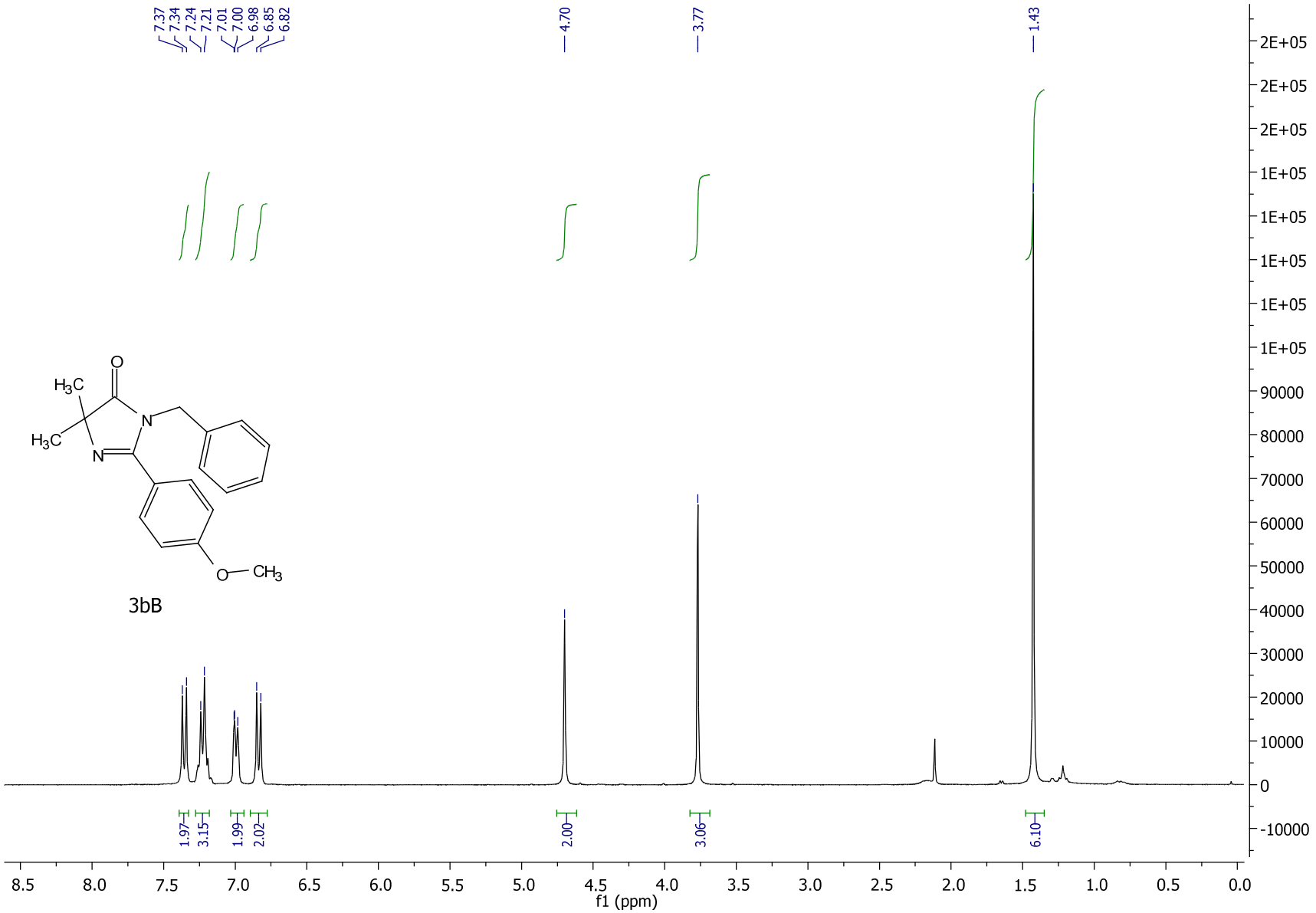

186.99
156.45
136.68
130.72
128.99
128.64
128.50
127.84
127.66
127.38
127.25
126.61
126.30
76.98
44.65
37.80
26.18
O
N
N
S
3aP
f1 (ppm)

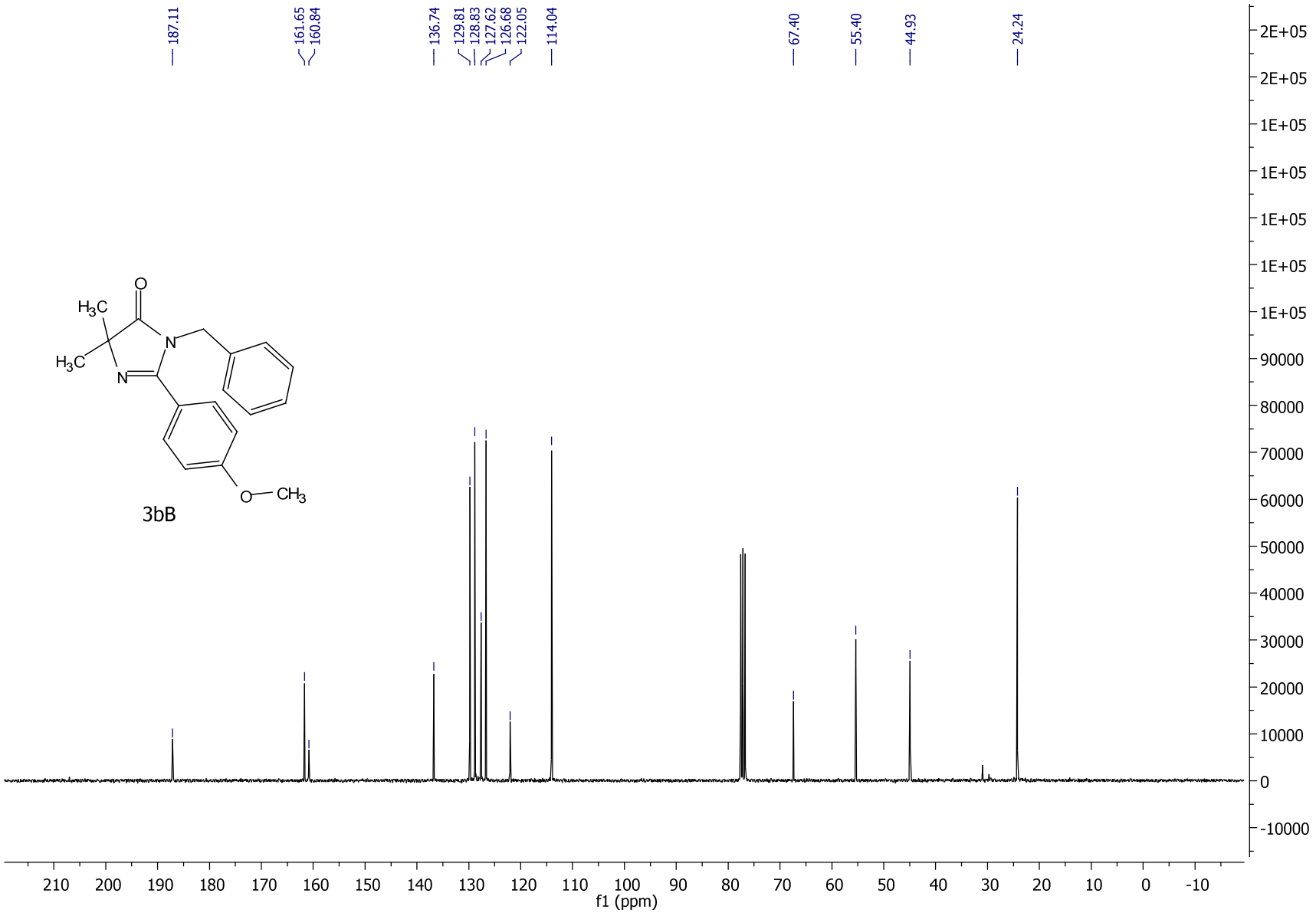

8.09
7.76
7.75
7.75
7.33
7.30
7.26
7.24
7.10
7.09
6.97
6.76
4.92
1.95
1.92
1.80
O
N
N
O
3aQ
1.03
1.11
2.16
0.99
2.24
1.06
1.94
8.04
f1 (ppm)

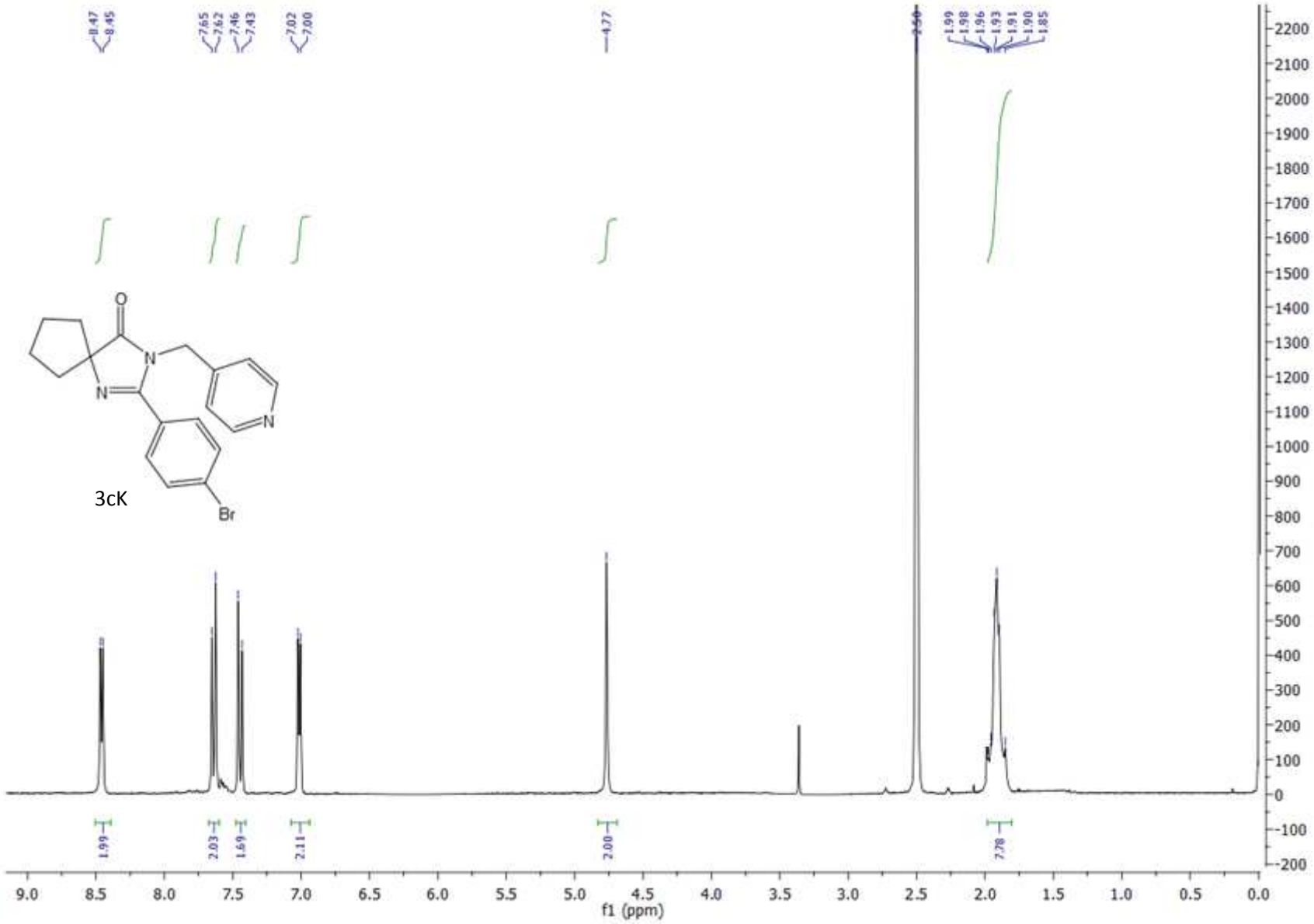

186.94
154.44
143.73
143.54
136.48
129.16
127.79
126.04
116.44
109.89
76.93
44.34
37.86
26.25
O
N
N
O
3aQ
f1 (ppm)

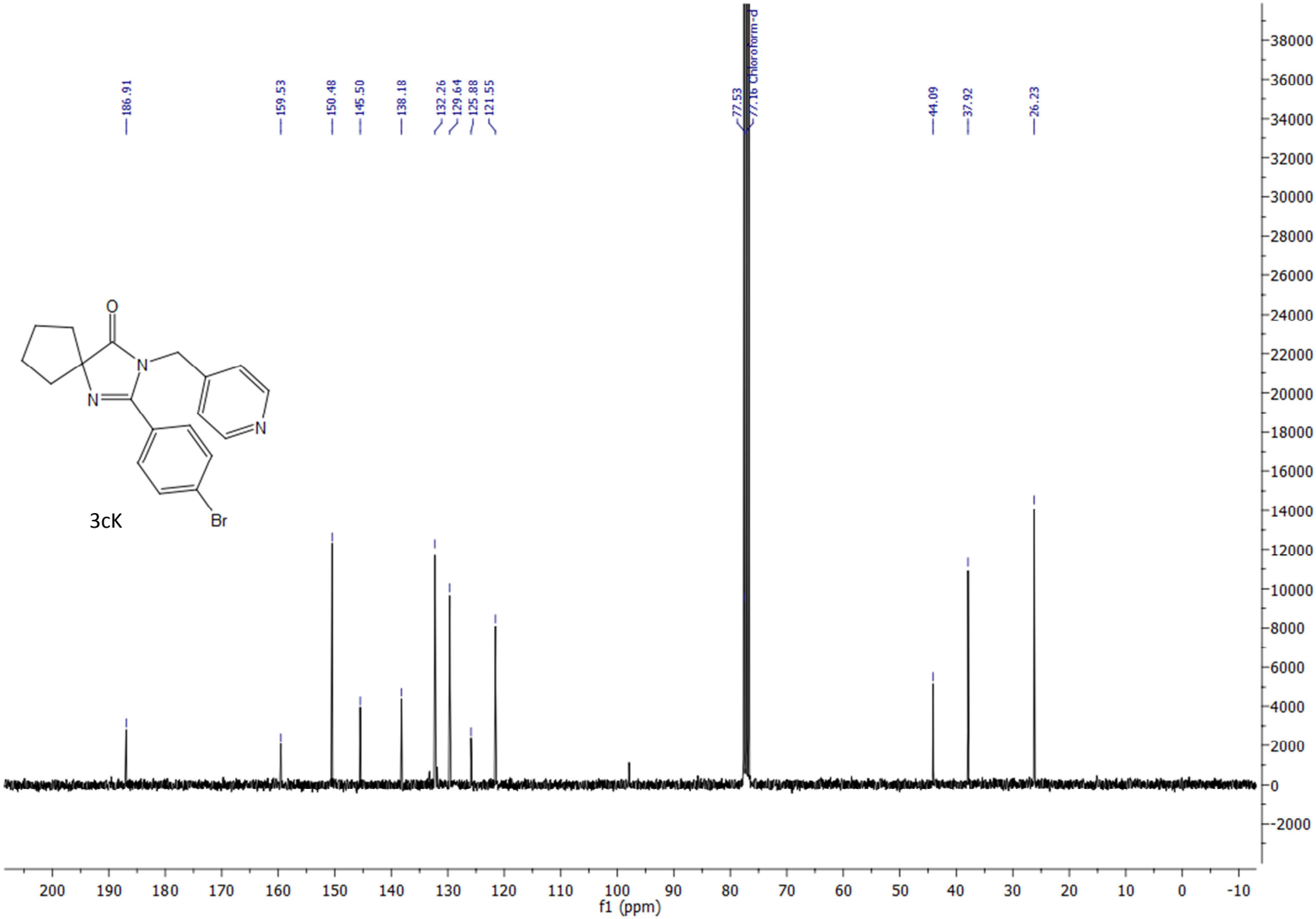

7.41
7.38
7.28
7.25
7.25
7.23
7.23
7.22
7.21
6.99
6.98
6.96
4.72
2.32
1.33
O
H3C
H3C
N
N
CH3
3bA
2.20
4.68
2.13
2.00
2.61
5.86
f1 (ppm)

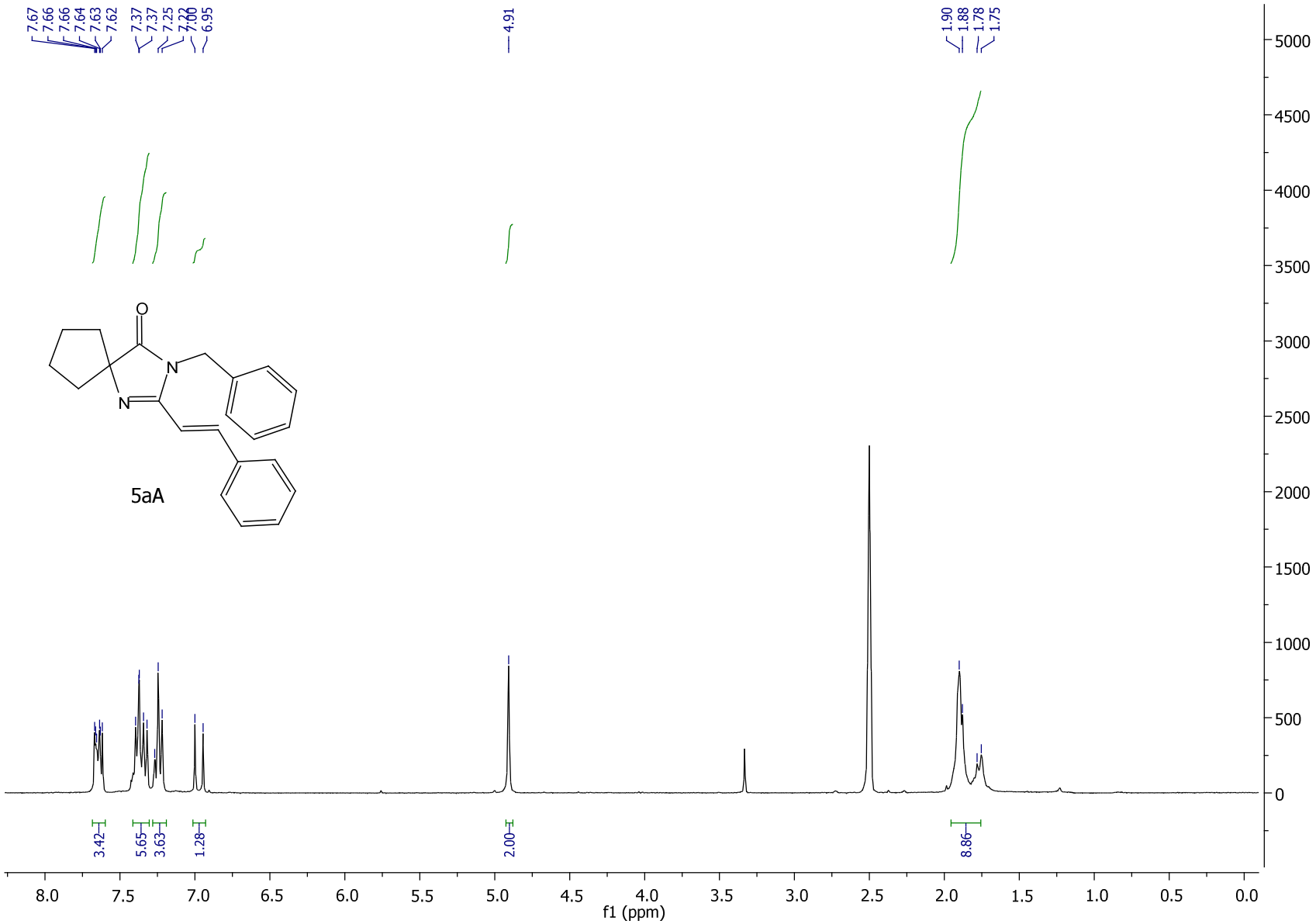

186.90
161.06
141.09
136.62
129.20
128.67
127.99
127.48
126.81
126.65
67.36
44.76
24.10
21.38
4E+05
3E+05
2E+05
2E+05
2E+05
1E+05
50000
0
O
H3C
H3C
N
N
CH3
3bA
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

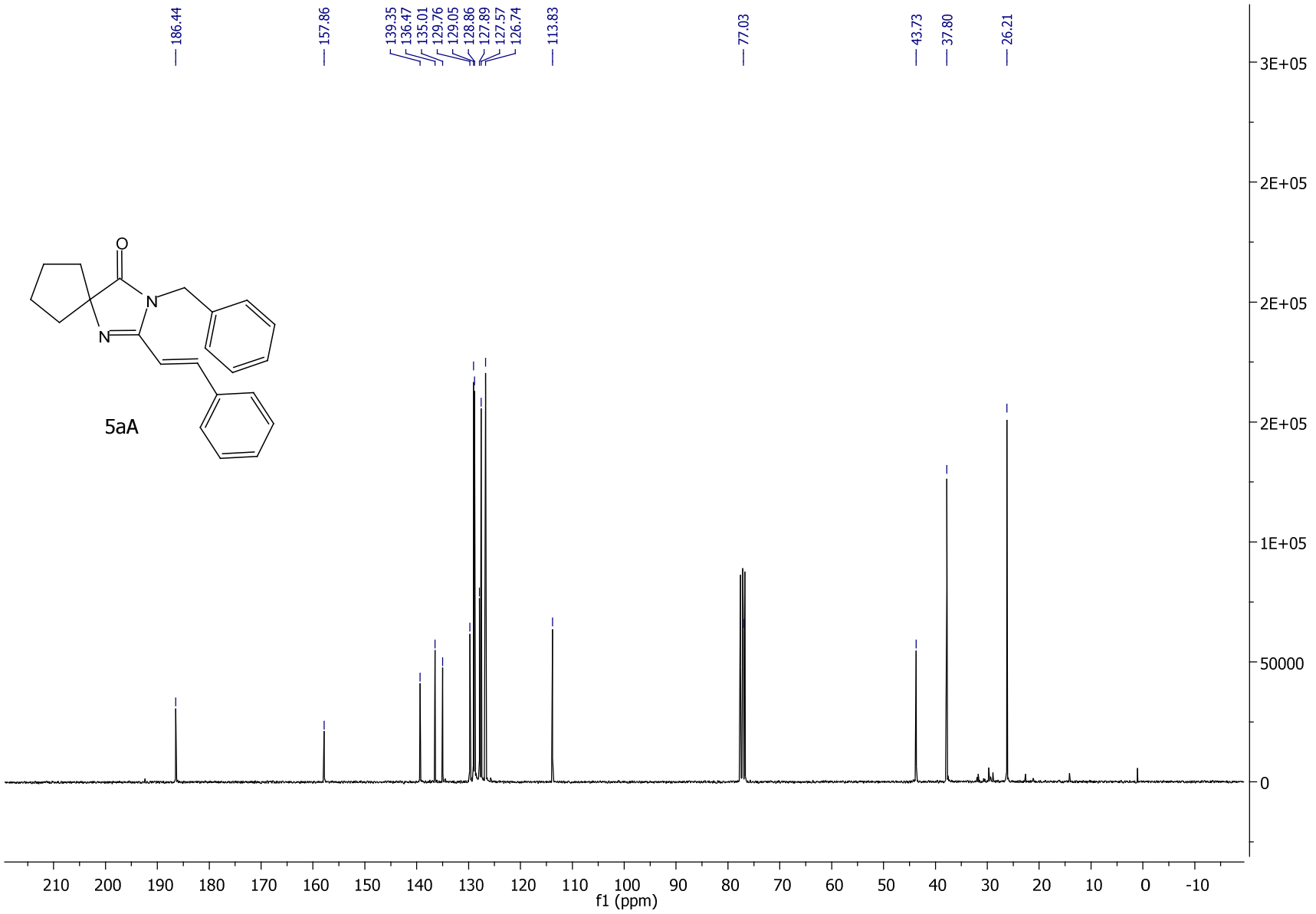

7.37
7.34
7.24
7.21
7.01
7.00
6.98
6.85
6.82
4.70
3.77
1.43
H3C
H3C
O
N
N
O
CH3
3bB
1.97
3.15
1.99
2.02
2.00
3.06
6.10
f1 (ppm)

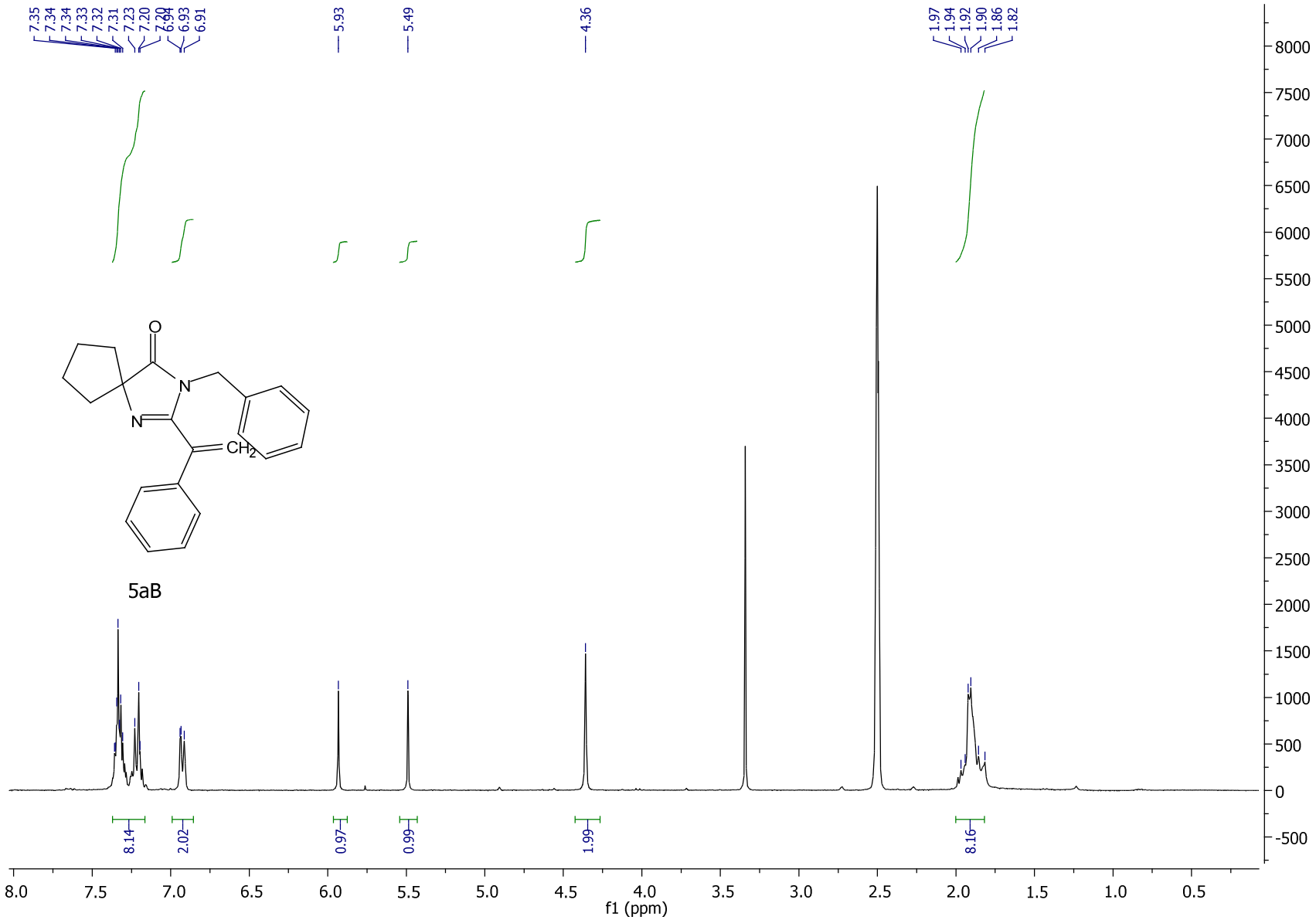

187.11
161.65
160.84
136.74
129.81
128.83
127.62
126.68
122.05
114.04
67.40
55.40
44.93
24.24
3bB
f1 (ppm)

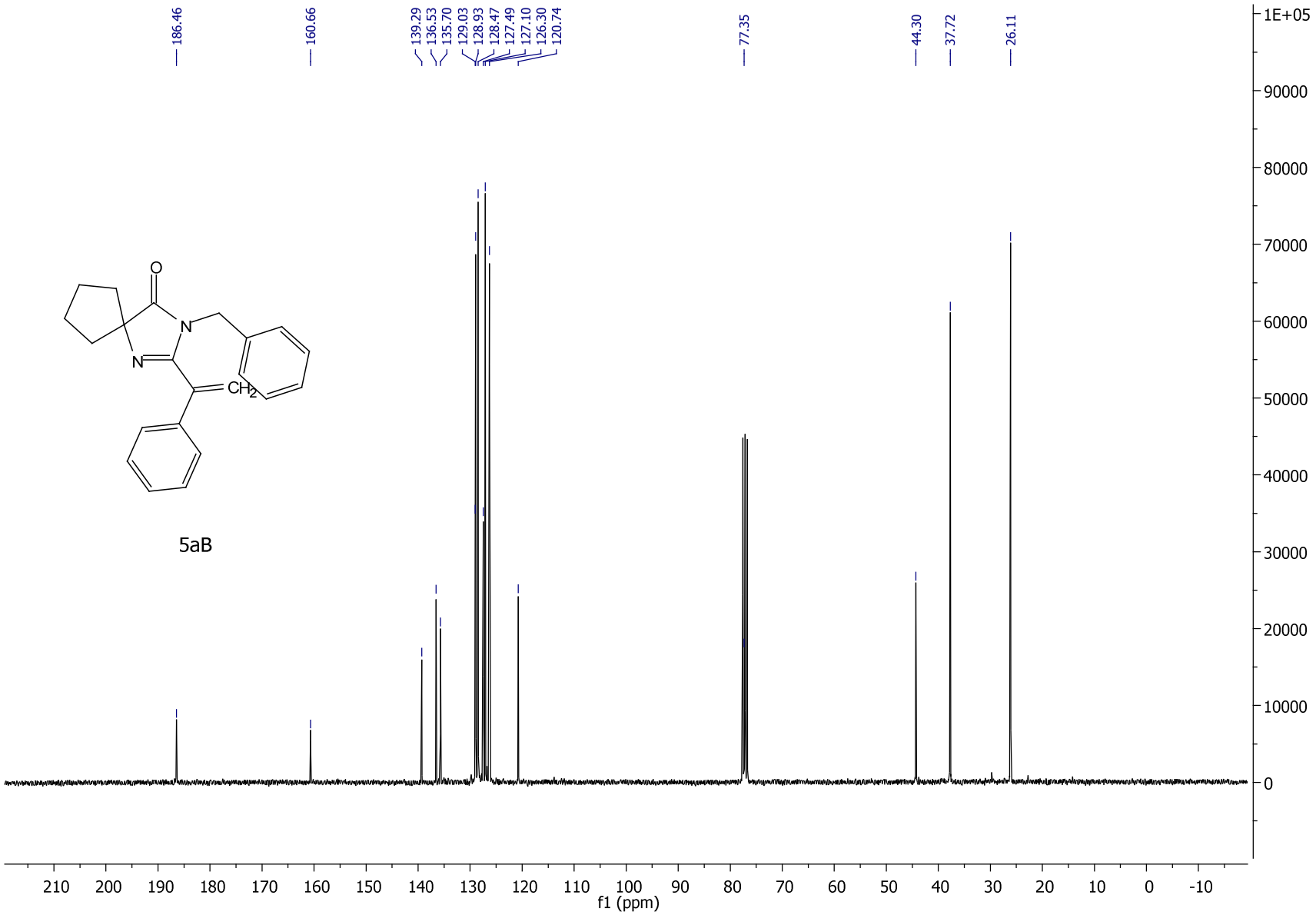

8.47
8.45
7.65
7.62
7.46
7.43
7.02
7.00
4.77
2.50
1.99
1.98
1.96
1.93
1.91
1.90
1.85
O
N
N
N
Br
3cK
1.99
2.03
1.69
2.11
2.00
7.78
f1 (ppm)

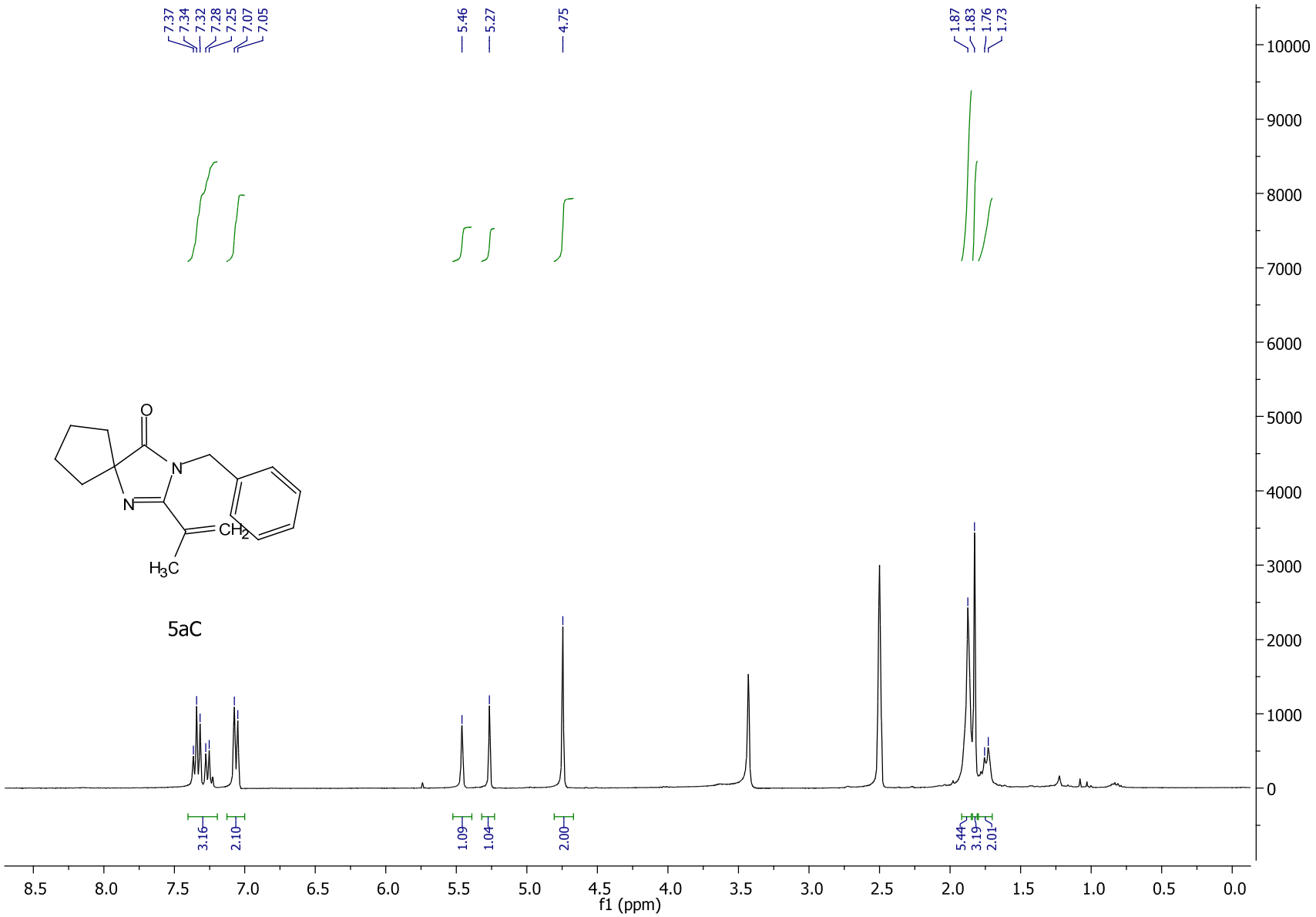

186.91
159.53
150.48
145.50
138.18
132.26
129.64
125.88
121.55
77.53
77.16 Chloroform-d
44.09
37.92
26.23
O
N
N
N
Br
3cK
f1 (ppm)

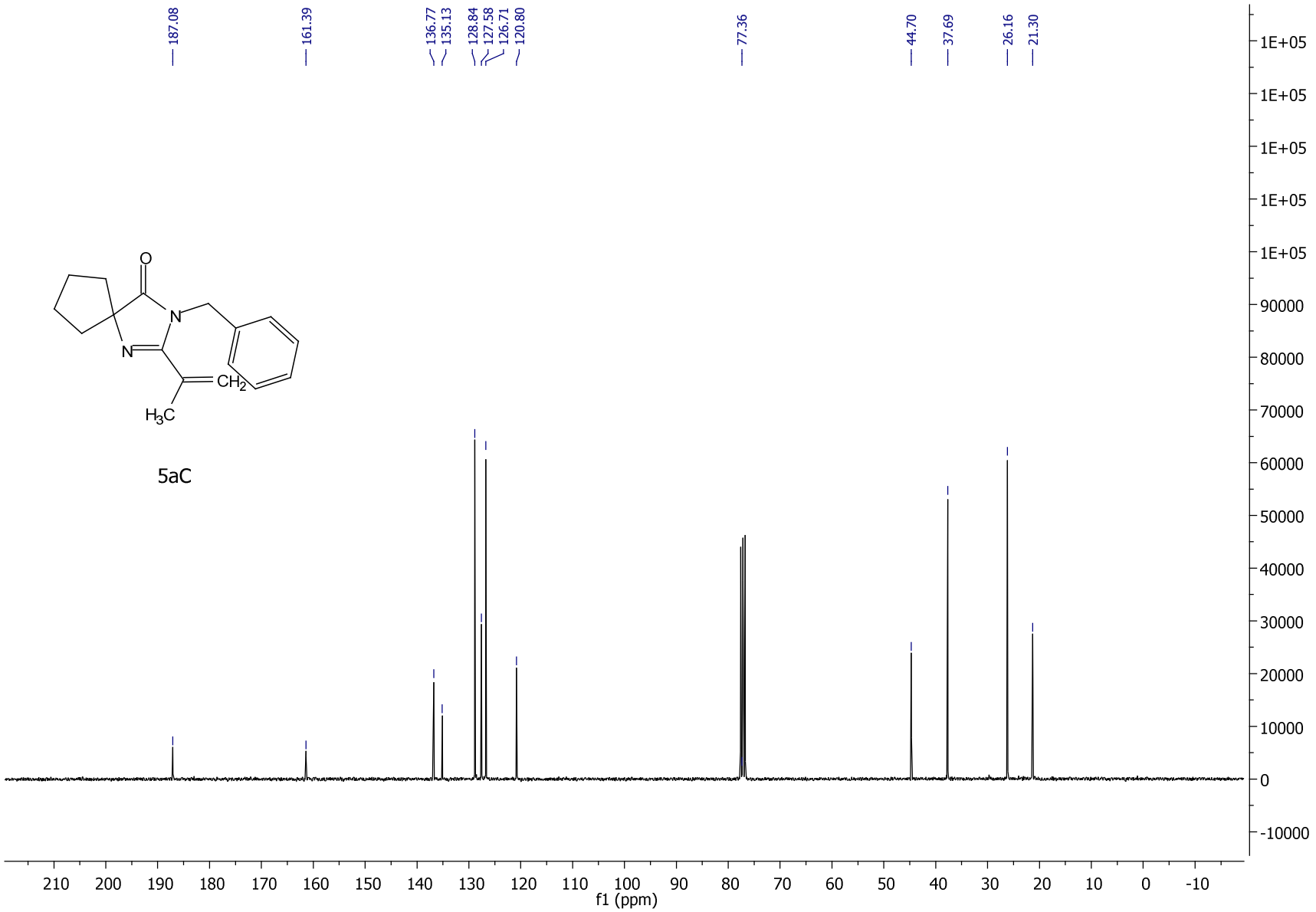

7.67
7.66
7.66
7.64
7.63
7.62
7.37
7.37
7.25
7.22
7.00
6.95
4.91
1.90
1.88
1.78
1.75
O
N
N
5aA
3.42
5.65
3.63
1.28
2.00
8.86
f1 (ppm)

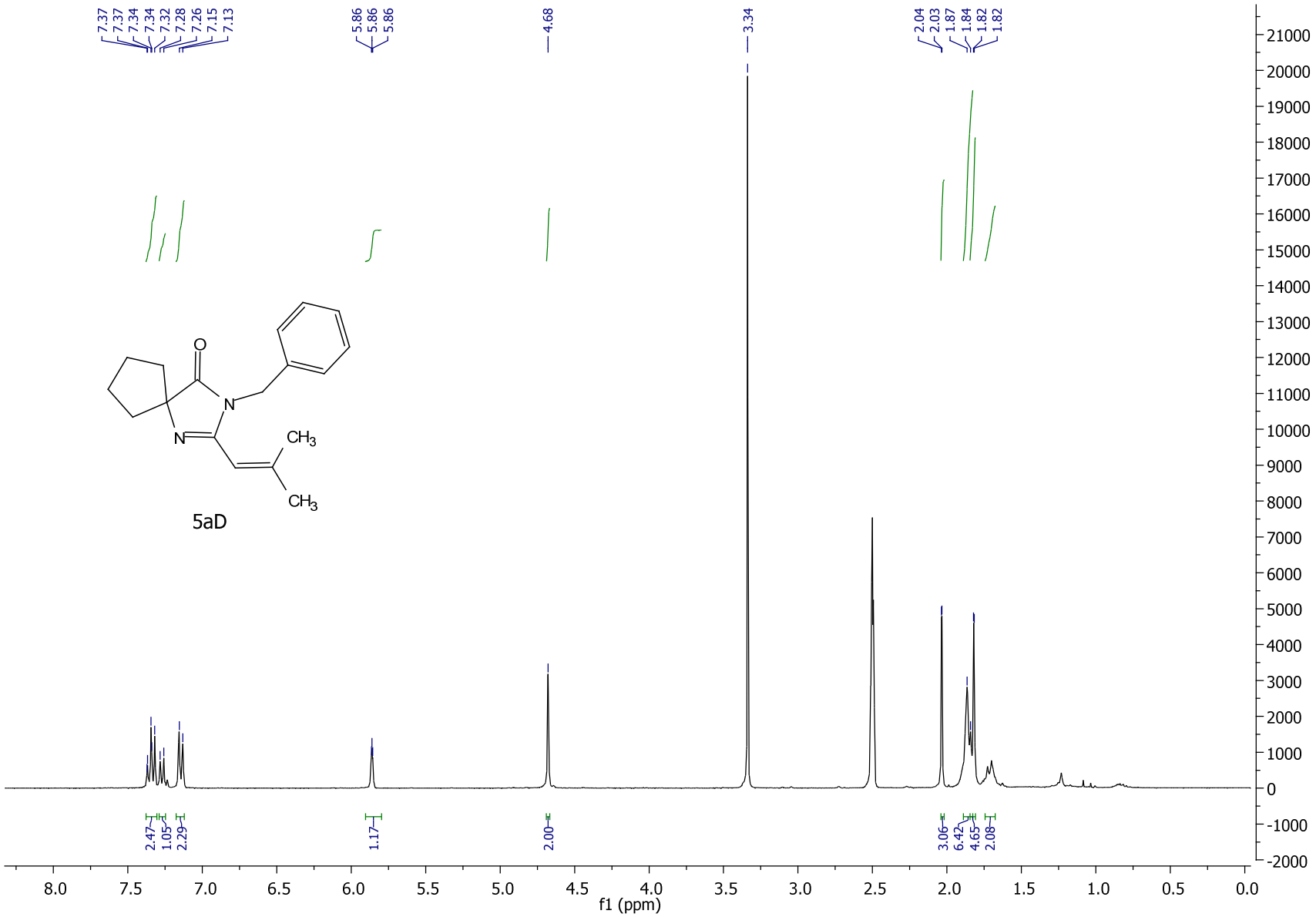

186.44
157.86
139.35
136.47
135.01
129.76
129.05
128.86
127.89
127.57
126.74
113.83
77.03
43.73
37.80
26.21
O
N
N
5aA
3E+05
2E+05
2E+05
2E+05
1E+05
50000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

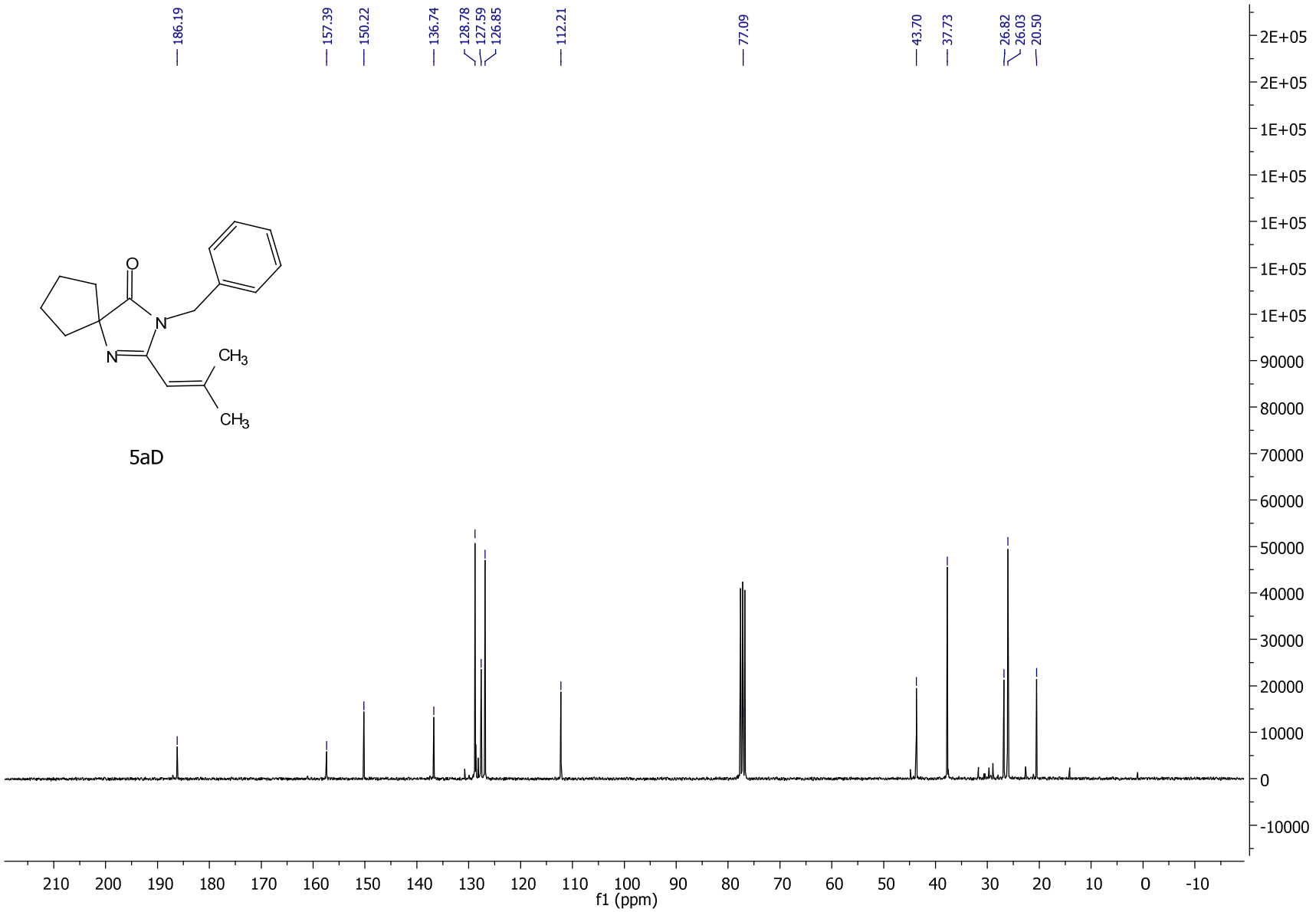

7.35
7.34
7.34
7.33
7.32
7.31
7.23
7.20
7.20
6.94
6.93
6.91
5.93
5.49
4.36
1.97
1.94
1.92
1.90
1.86
1.82
O
N
N
CH2
5aB
8.14
2.02
0.97
0.99
1.99
8.16
f1 (ppm)

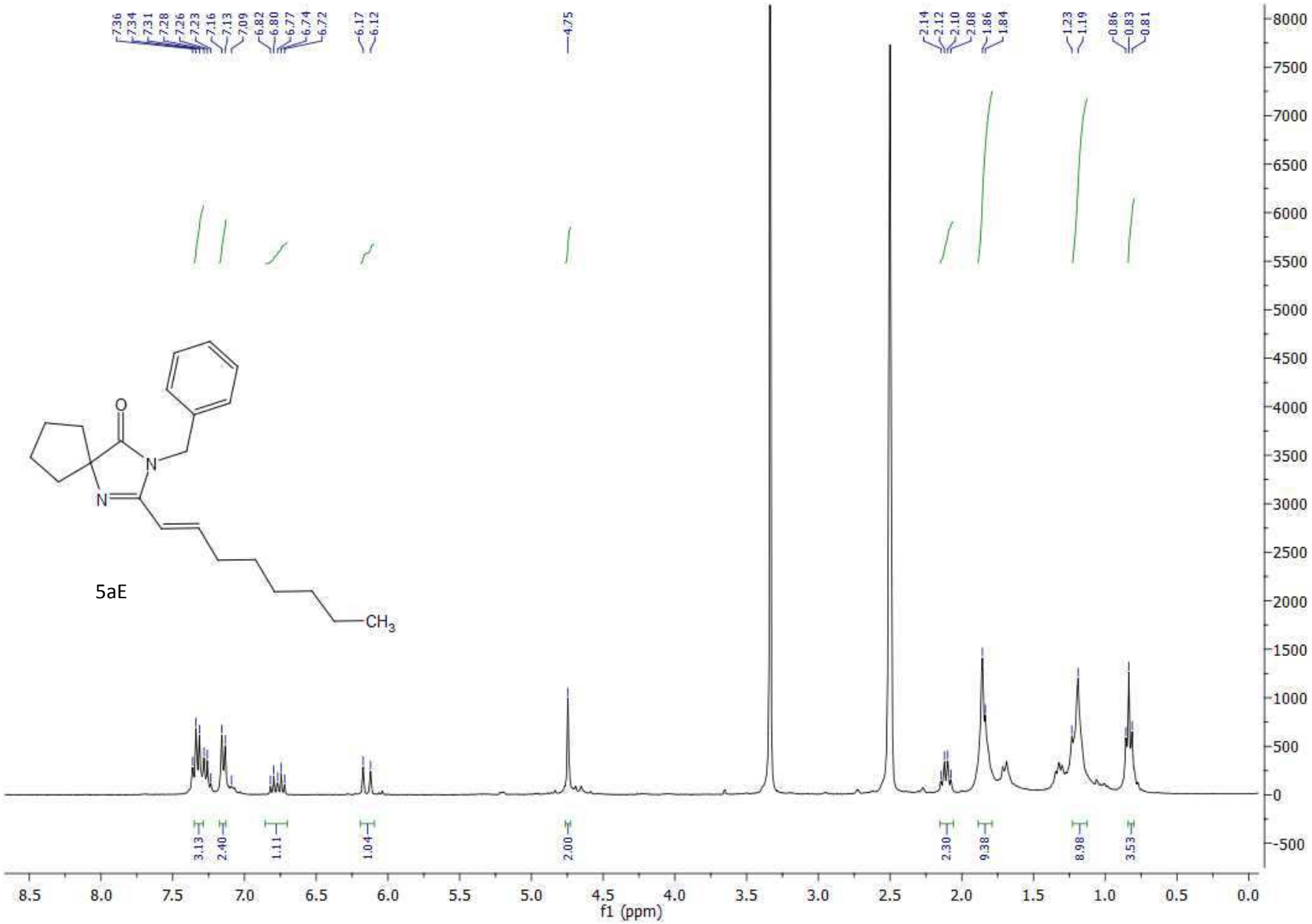

186.46
160.66
139.29
136.53
135.70
129.03
128.93
128.47
127.49
127.10
126.30
120.74
77.35
44.30
37.72
26.11
O
N
N
CH2
5aB
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

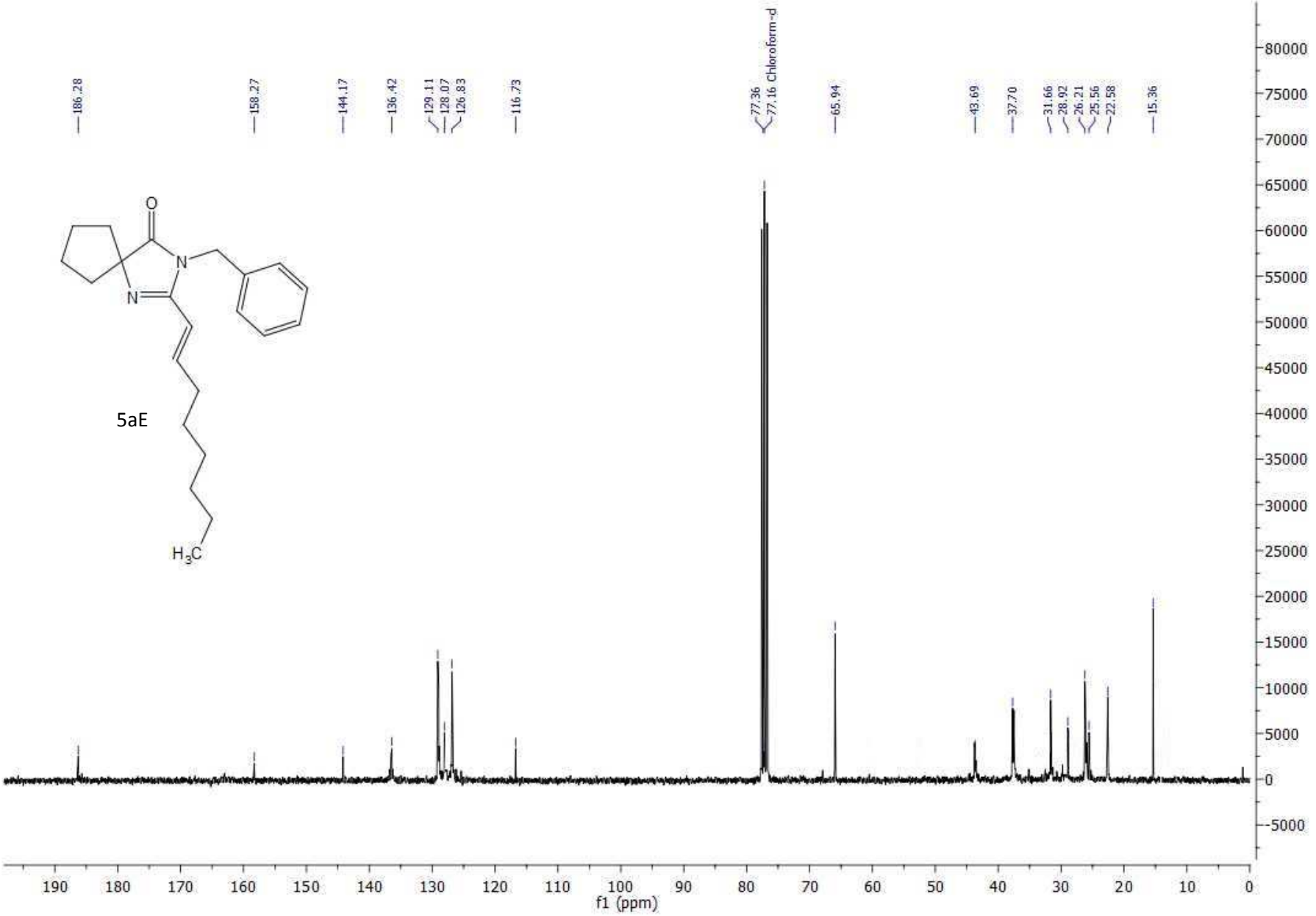

7.37
7.34
7.32
7.28
7.25
7.07
7.05
5.46
5.27
4.75
1.87
1.83
1.76
1.73
O
N
N
CH2
H3C
5aC
3.16
2.10
1.09
1.04
2.00
5.44
3.19
2.01
f1 (ppm)


187.08
161.39
136.77
135.13
128.84
127.58
126.71
120.80
77.36
44.70
37.69
26.16
21.30
O
N
N
CH2
H3C
5aC
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

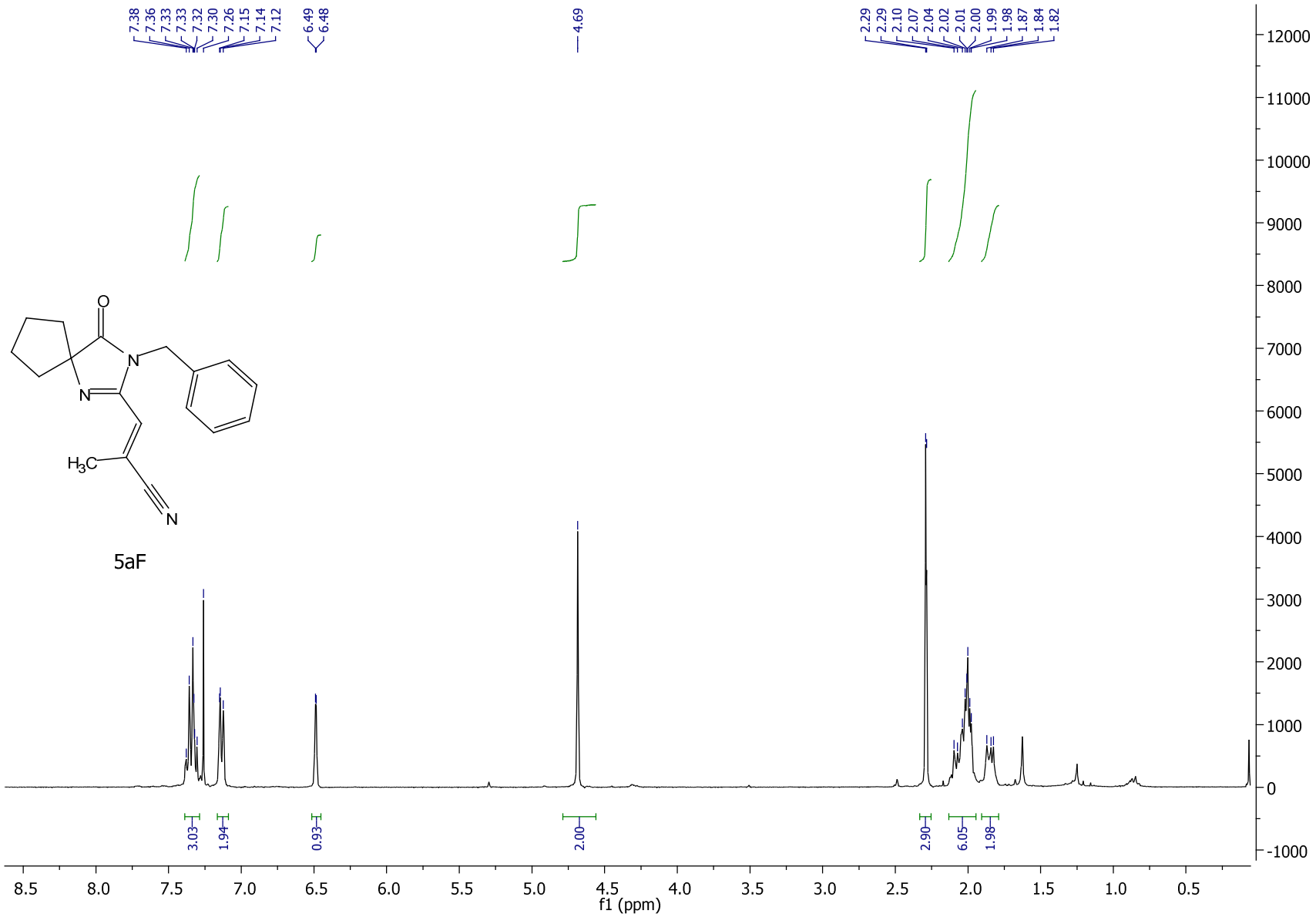

7.37
7.37
7.34
7.34
7.32
7.28
7.26
7.15
7.13
5.86
5.86
5.86
4.68
3.34
2.04
2.03
1.87
1.84
1.82
1.82
O
N
N
CH3
CH3
5aD
2.47
1.05
2.29
1.17
2.00
3.06
6.42
4.65
2.08
f1 (ppm)

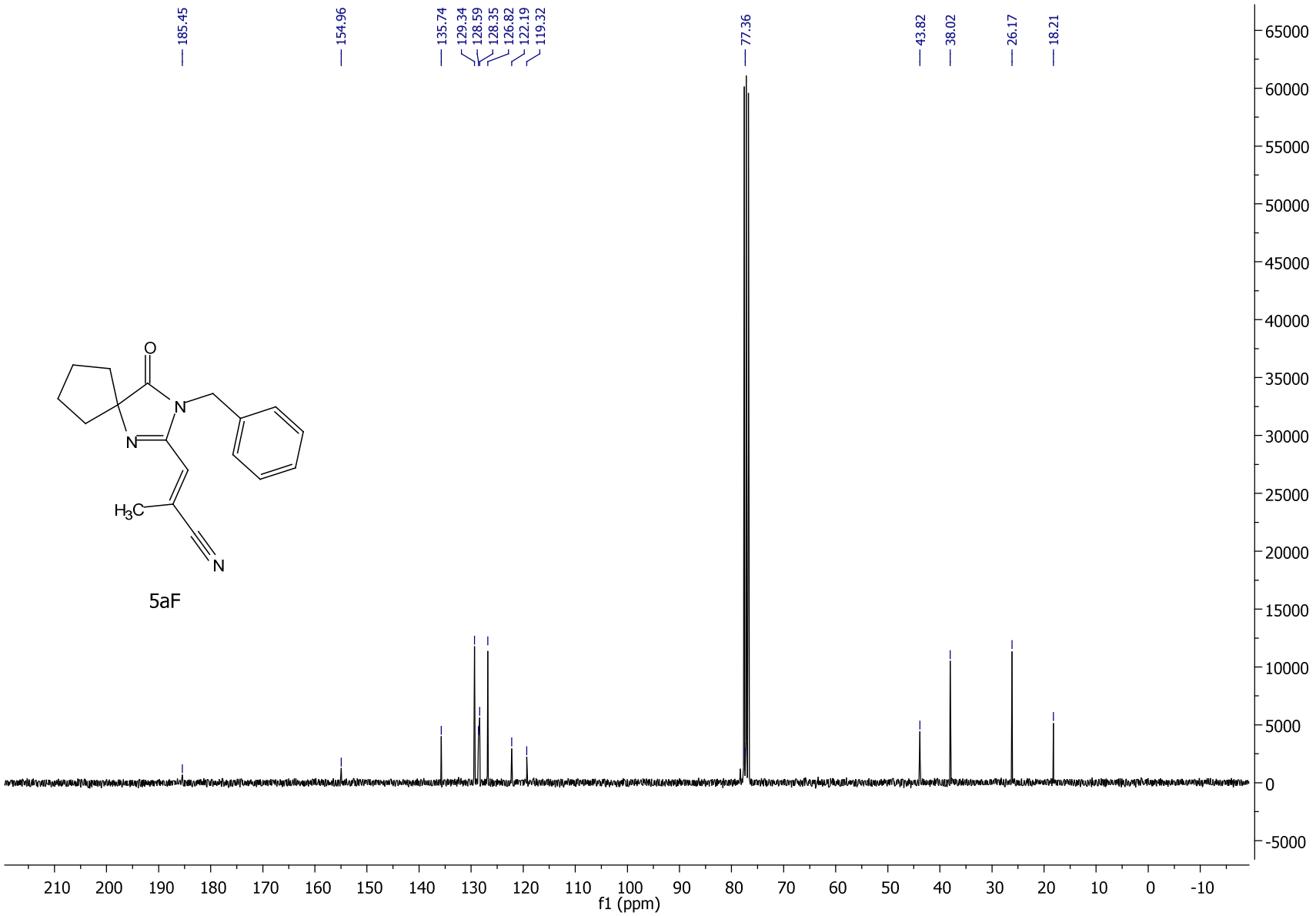

186.19
157.39
150.22
136.74
128.78
127.59
126.85
112.21
77.09
43.70
37.73
26.82
26.03
20.50
O
N
N
CH3
CH3
5aD
2E+05
2E+05
1E+05
1E+05
1E+05
1E+05
1E+05
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

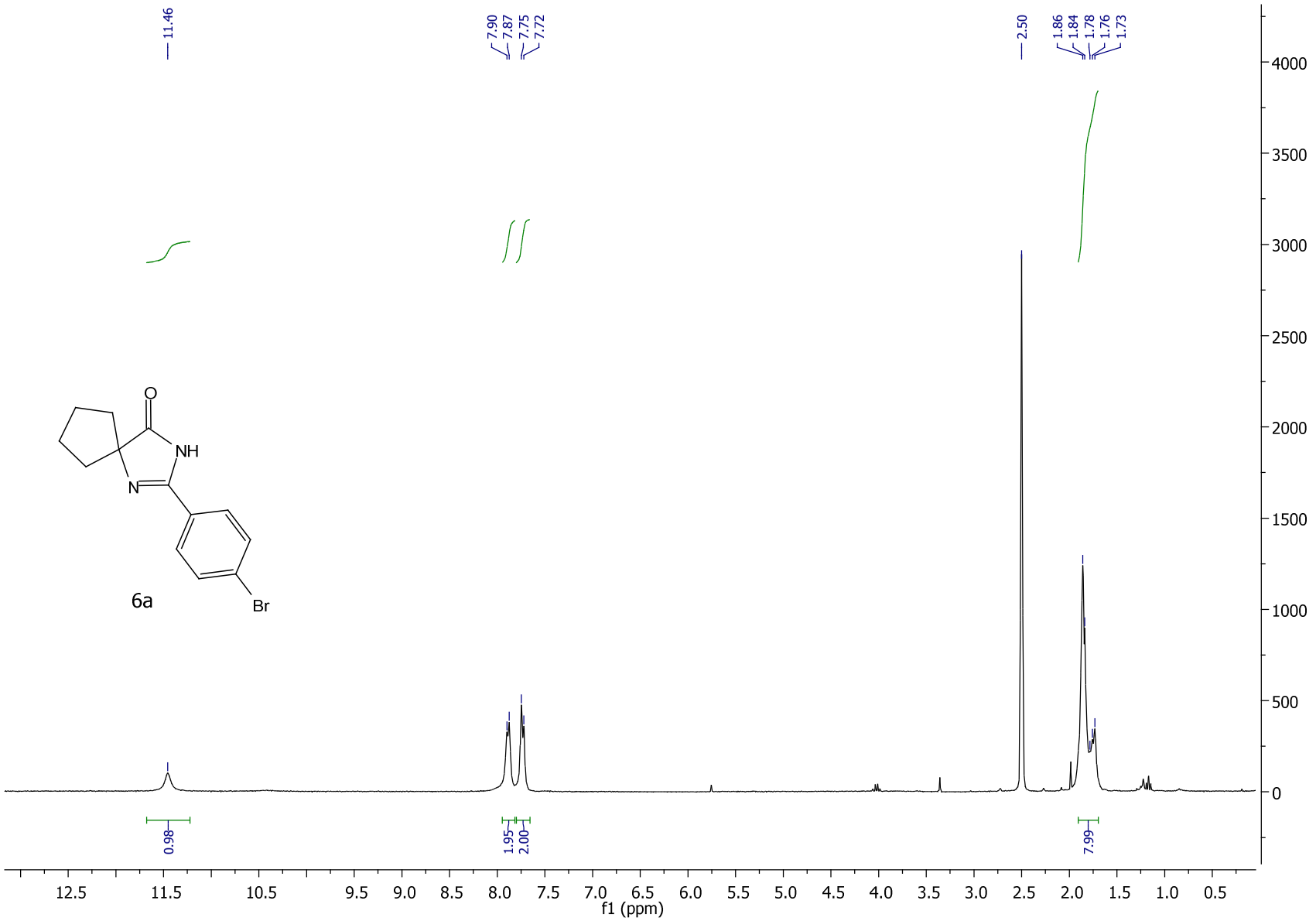

7.36
7.34
7.31
7.28
7.26
7.23
7.16
7.13
7.09
6.82
6.80
6.77
6.74
6.72
6.17
6.12
4.75
2.14
2.12
2.10
2.08
1.86
1.84
1.23
1.19
0.86
0.83
0.81
O
N
N
CH3
5aE
3.13
2.40
1.11
1.04
2.00
2.30
9.38
8.98
3.53
f1 (ppm)

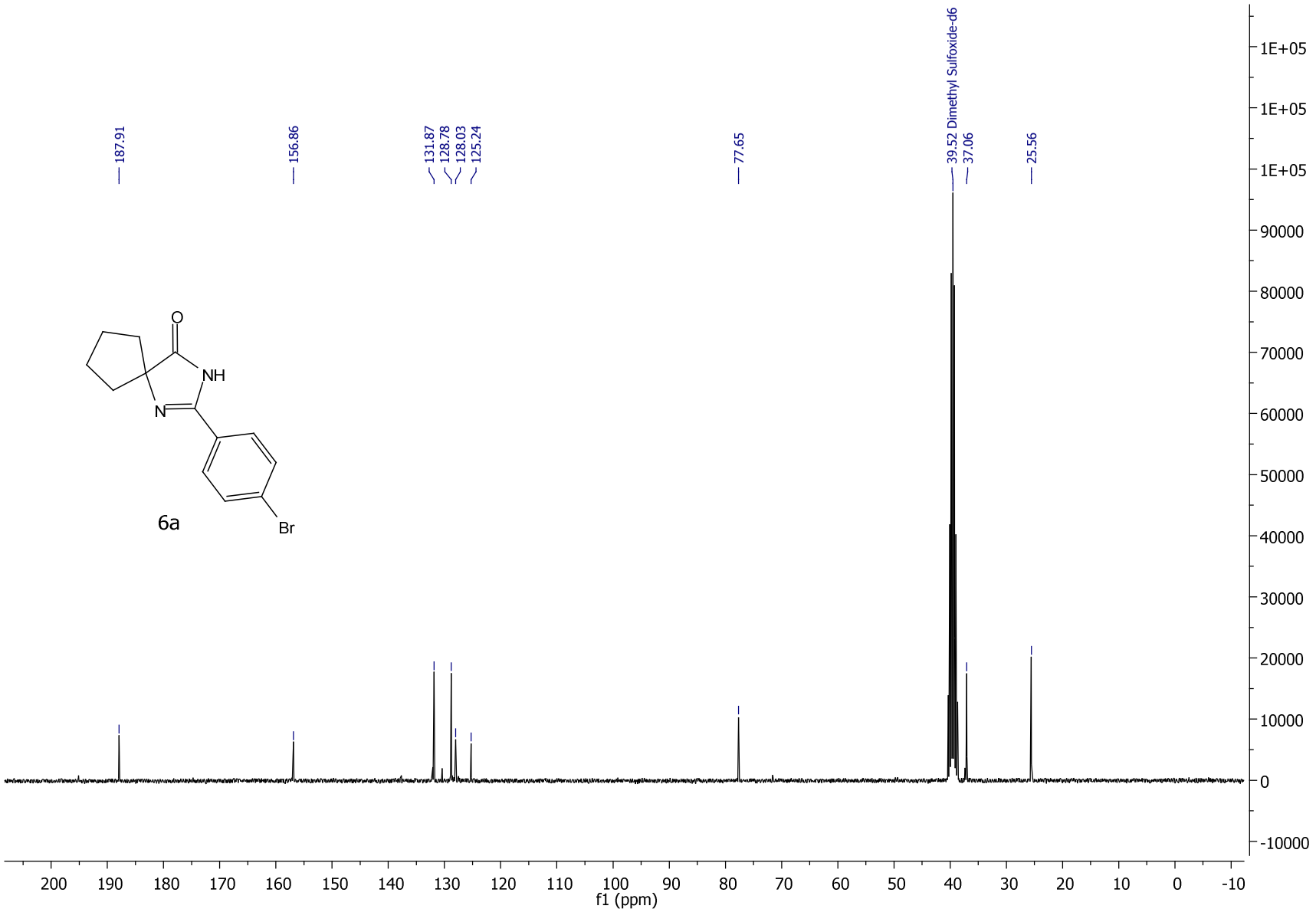

186.28
158.27
144.17
136.42
129.11
128.07
126.83
116.73
77.36
77.16 Chloroform-d
65.94
43.69
37.70
31.66
28.92
26.21
25.56
22.58
15.36
O
N
N
H_3C
f1 (ppm)

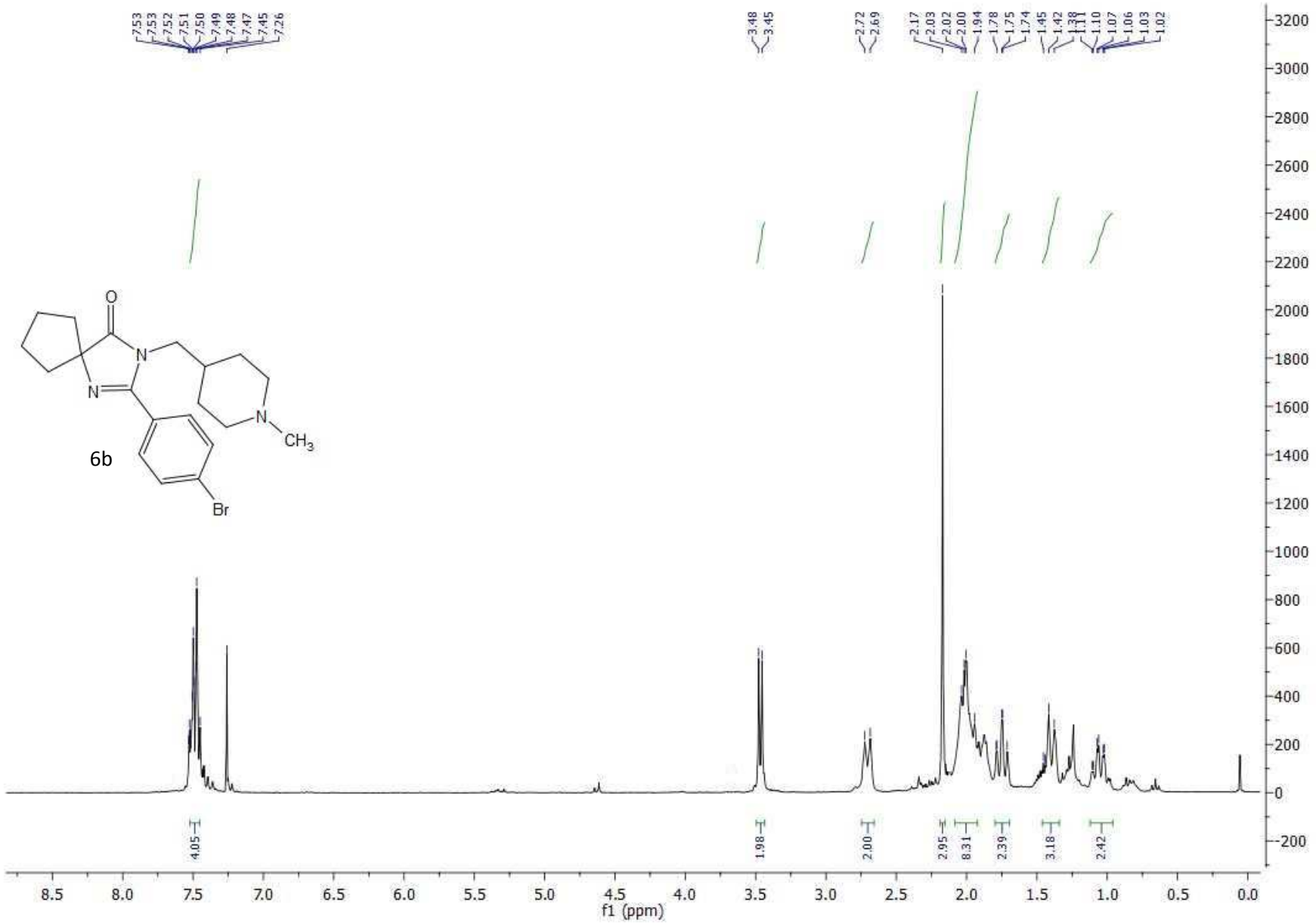
5aE

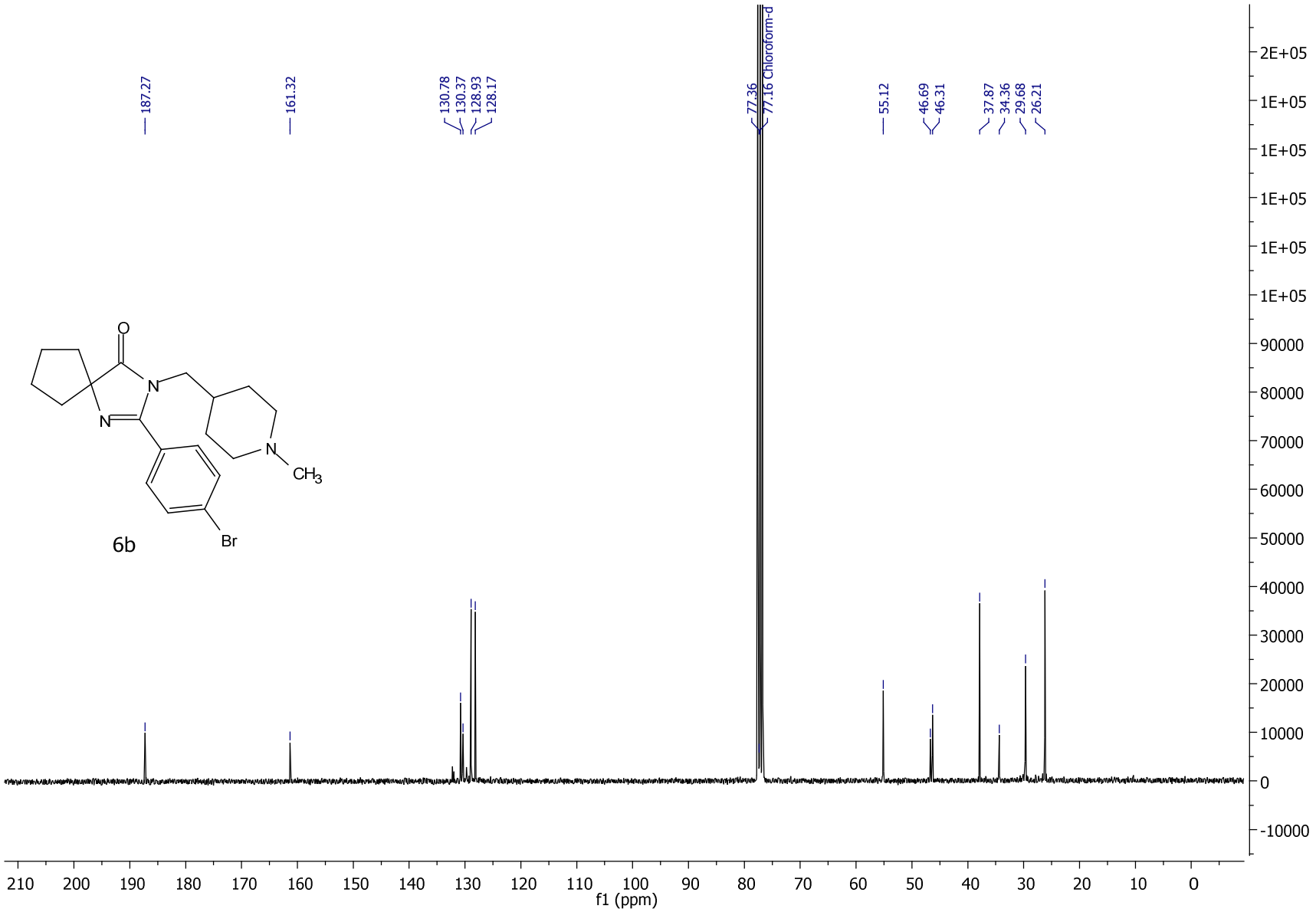

7.38
7.36
7.33
7.33
7.32
7.30
7.26
7.15
7.14
7.12
6.49
6.48
4.69
2.29
2.29
2.10
2.07
2.04
2.02
2.01
2.00
1.99
1.98
1.87
1.84
1.82
O
N
N
H3C
N
5aF
3.03
1.94
0.93
2.00
2.90
6.05
1.98
f1 (ppm)


185.45
154.96
135.74
129.34
128.59
128.35
126.82
122.19
119.32
77.36
43.82
38.02
26.17
18.21
O
N
N
H3C
N
5aF
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


11.46
7.90
7.87
7.75
7.72
2.50
1.86
1.84
1.78
1.76
1.73
O
NH
N
Br
6a
0.98
1.95
2.00
7.99
f1 (ppm)


187.91
156.86
131.87
128.78
128.03
125.24
77.65
39.52 Dimethyl Sulfoxide-d6
37.06
25.56
O
NH
N
Br
6a
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.53
7.53
7.52
7.51
7.50
7.49
7.48
7.47
7.45
7.26
3.48
3.45
2.72
2.69
2.17
2.03
2.02
2.00
1.94
1.78
1.75
1.74
1.45
1.42
1.38
1.11
1.10
1.07
1.06
1.03
1.02
O
N
N
N
CH3
Br
6b
4.05
1.98
2.00
2.95
8.31
2.39
3.18
2.42
f1 (ppm)


187.27
161.32
130.78
130.37
128.93
128.17
77.36
77.16 Chloroform-d
55.12
46.69
46.31
37.87
34.36
29.68
26.21
O
N
N
N
CH3
Br
6b
2E+05
1E+05
1E+05
1E+05
1E+05
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)